Introduction to Organic Chemistry

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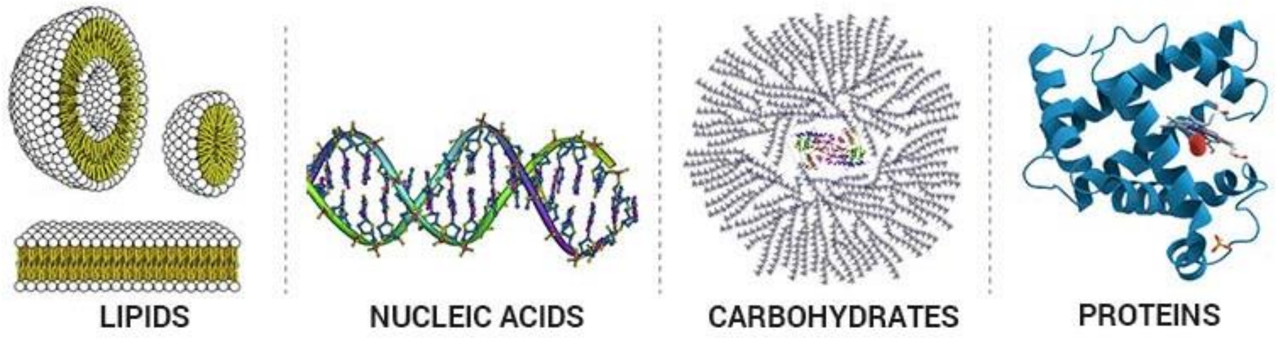
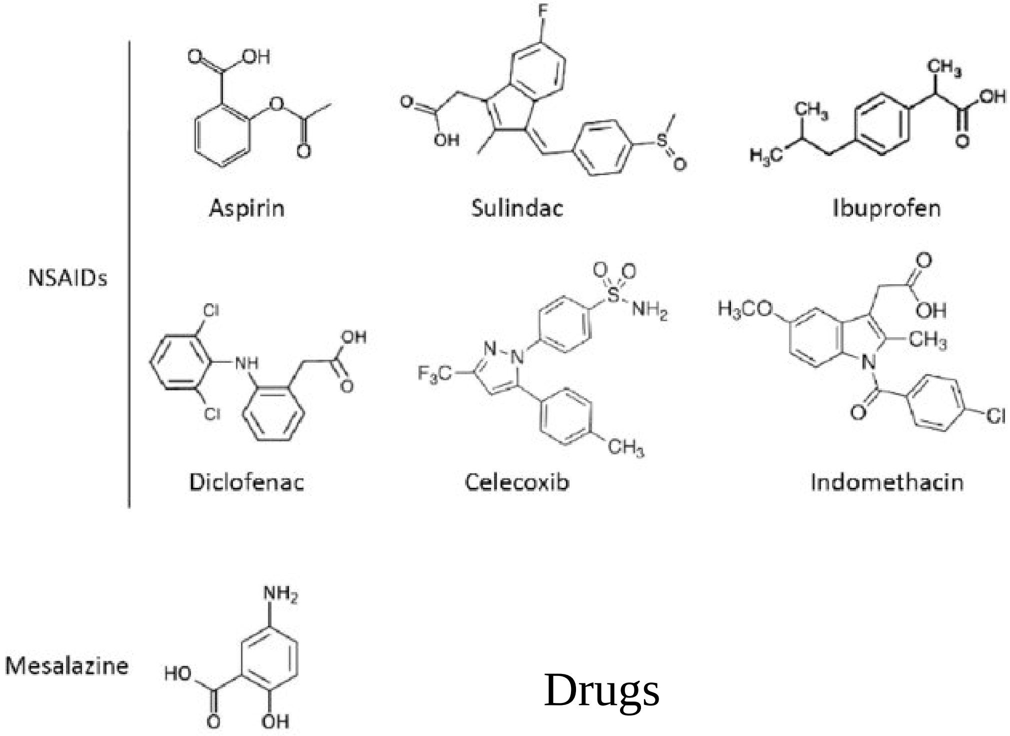
What is Organic Chemistry?

Organic chemistry is the study of the structure, properties, composition, reactions, and preparation of carbon-containing compounds. Most organic compounds contain carbon and hydrogen, but they may also include any number of other elements (e.g., nitrogen, oxygen, halogens, phosphorus, silicon, sulfur).



Biomolecules

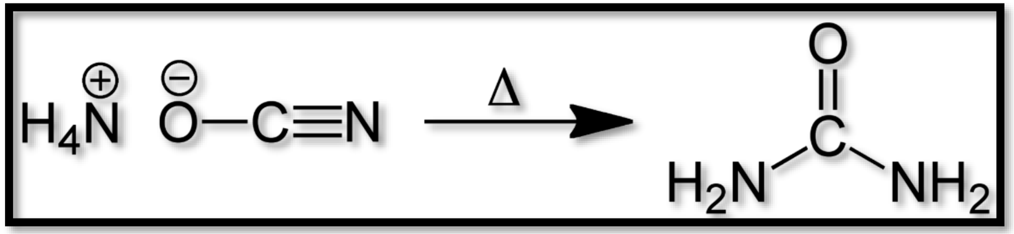


Drugs

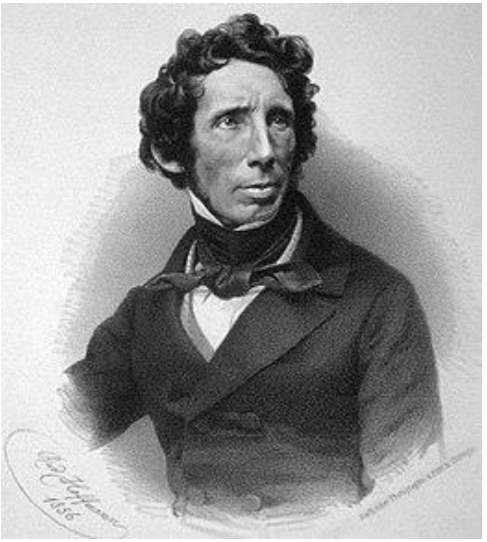
History

According to the Vital Force Hypothesis, which was developed by the scientist Berzelius in 1809, organic molecules can only be created in live cells and cannot be created in a laboratory.

Jöns Jacob Berzelius

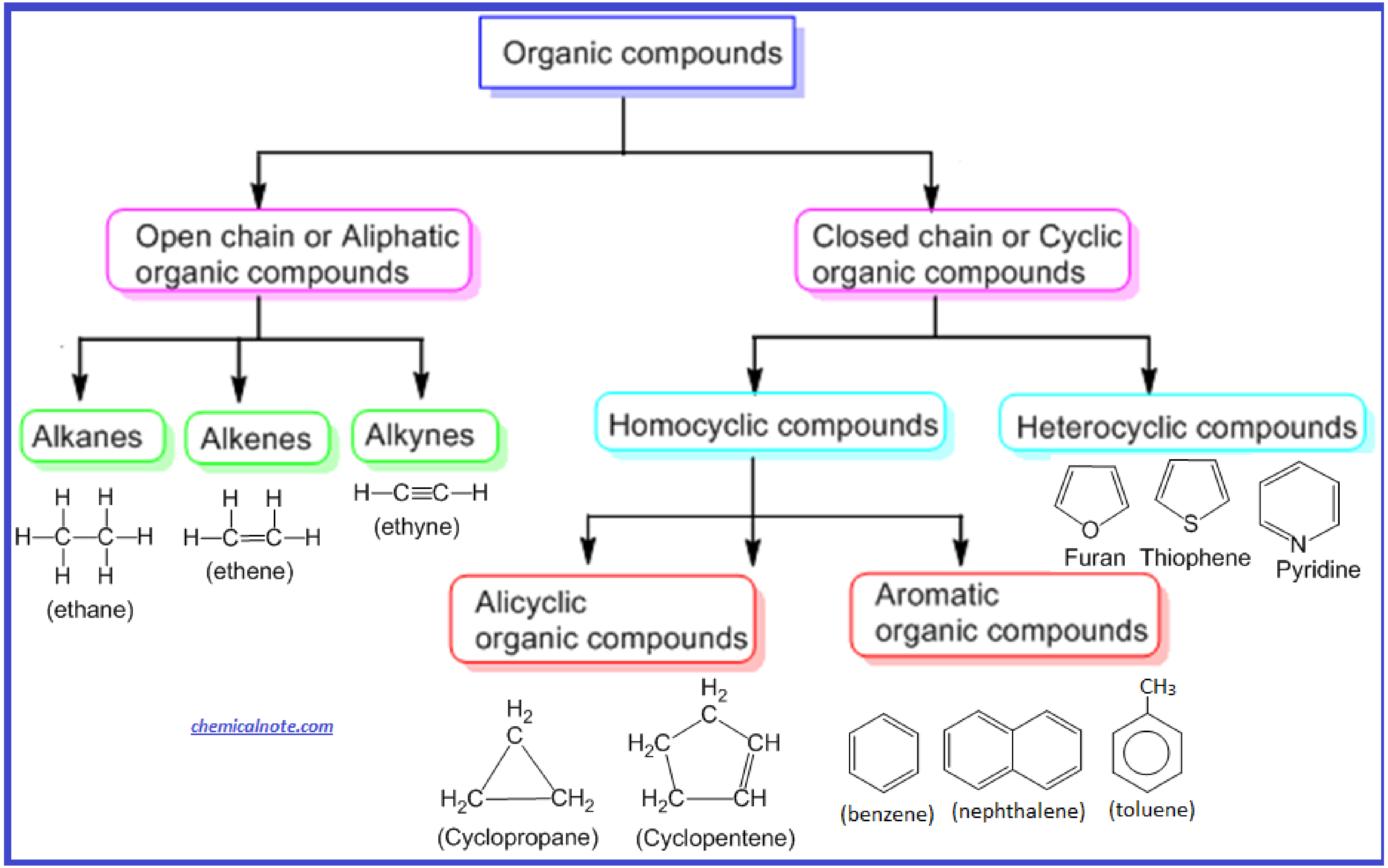


Wohler Synthesis of urea, 1828



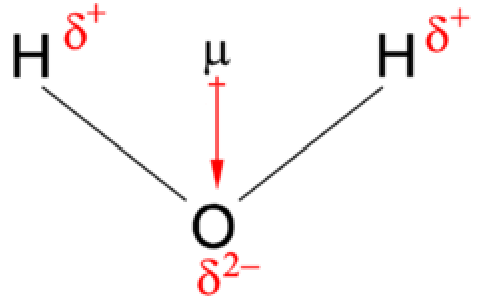
Friedrich Wöhler

Classification of Organic Compounds



Bonding and Structure

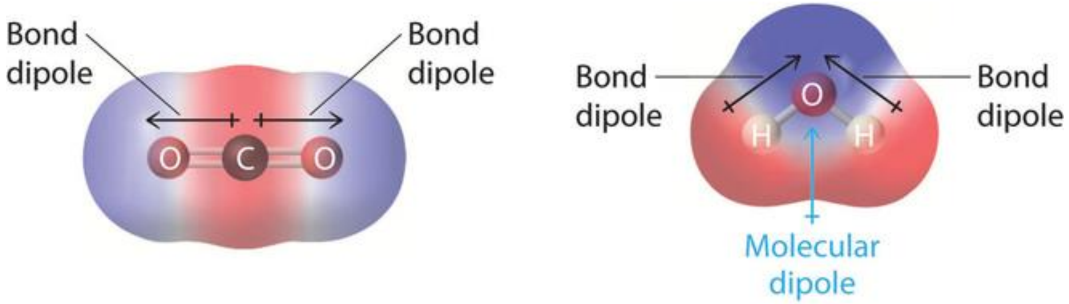
Dipole Moment: A charge separation results in dipole moments. Dipole moments are caused by changes in electronegativity and can appear in ionic bonds between two ions or covalent bonds between atoms. The dipole moment increases with increasing electronegativity disparity. Another element affecting the size of the dipole moment is the distance between the charge separations. A molecule's polarity can be determined by its dipole moment. The unit of dipole moment is Debye (D).



$$\mu = e \times d$$

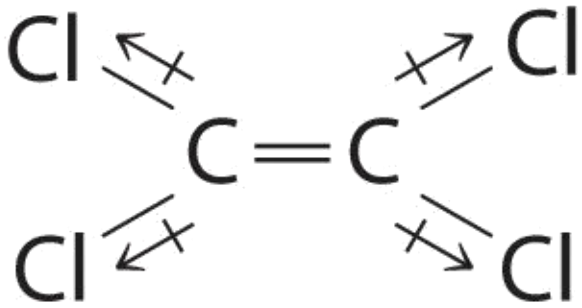
e= charge at the polar end

d= distance between the charges

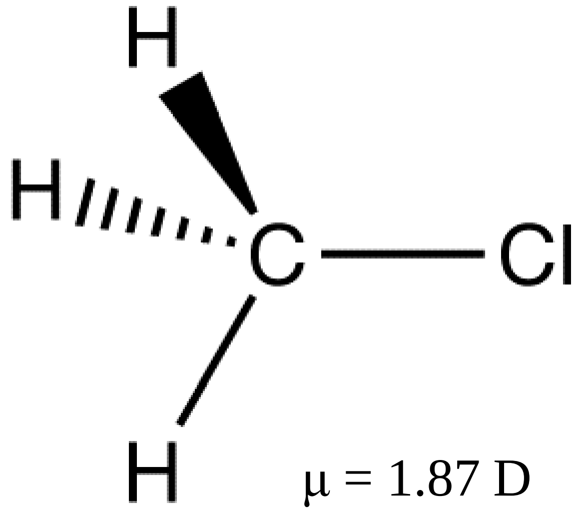


(a) No net dipole moment (b) Net dipole moment

Dipole Moment



μ = 0 D



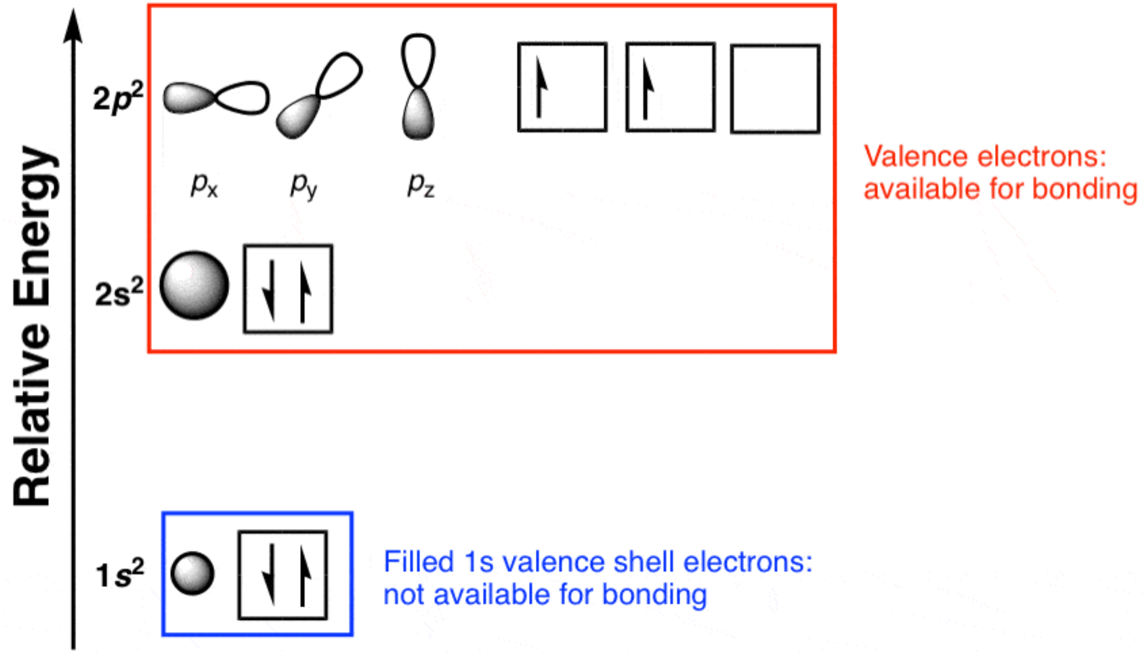
μ = 1.87 D

Bonding and Structure

How Do We Know Methane (CH_4) Is Tetrahedral?

1. The Electronic Configuration Of The Valence Electrons Of Carbon Is $2s^2 2p^2$

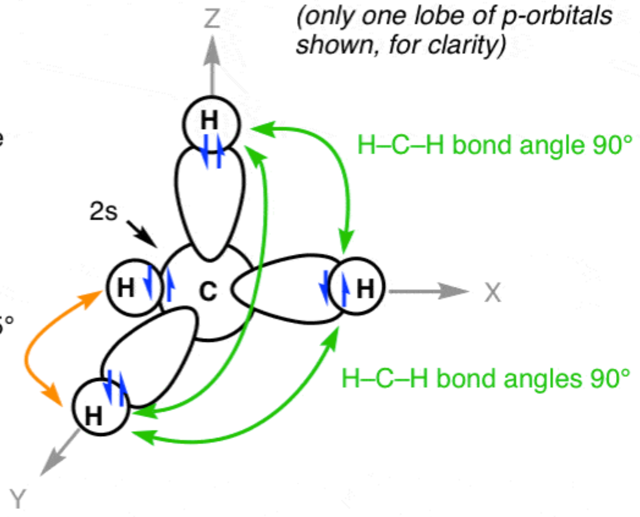
Electron configuration for carbon, shown as a potential energy diagram



A Reasonable (but wrong, as it turns out) Proposal:

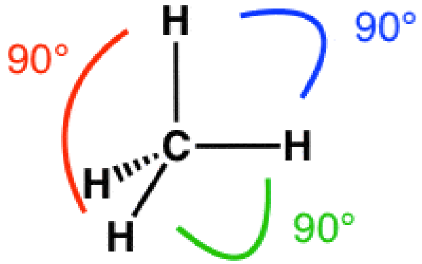
a) When combining with 4 hydrogens to make CH_4 , shouldn't we expect 3 of the C–H bonds to line up along the x, y, and z axes too? *(i.e. with the three p-orbitals?)*

b) And perhaps the other C-H bond to be as far away as possible from the bonding pairs?

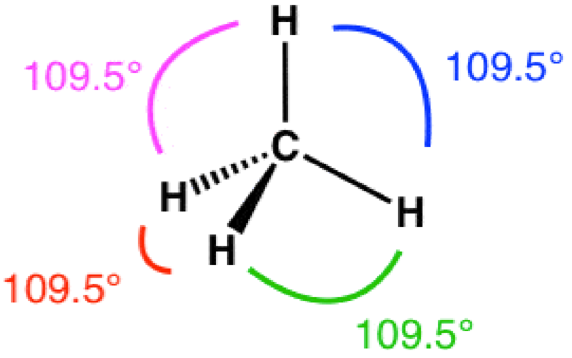


Bonding and Structure: Hybridization

A "reasonable" proposed structure for methane



Actual structure of methane



- 3 C-H bonds aligned along X, Y, Z axes (p-orbitals)
- one C–H bond at arbitrary angle (135° ?) (s-orbital)

- All H–C–H bond angles 109.5°
- C–H bonds all equal lengths (1.09 Å)

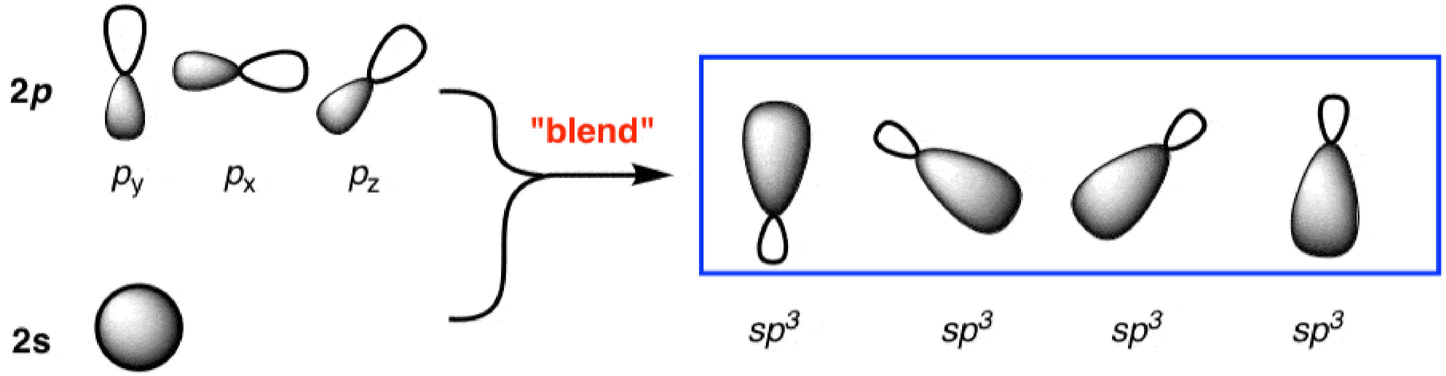
Big question: What orbitals are involved in the C–H bonds in methane?

Clearly not "pure" p-orbitals

Hybrid Orbitals

One answer to the question: **sp^3 "Hybrid" Orbitals**

Three 2p orbitals and a single 2s orbital "hybridize" (blend) to make four identical sp^3 "hybrid" orbitals



4 unhybridized orbitals (2s, $2p_x$, $2p_y$, $2p_z$)

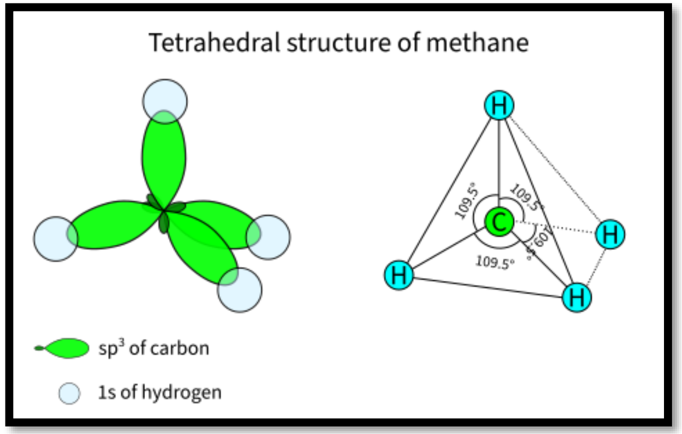
Three higher-energy *2p* orbitals and one lower-energy *2s* orbital

Linus Pauling "The Nature of The Chemical Bond" (1931)

4 hybridized *sp^3* orbitals

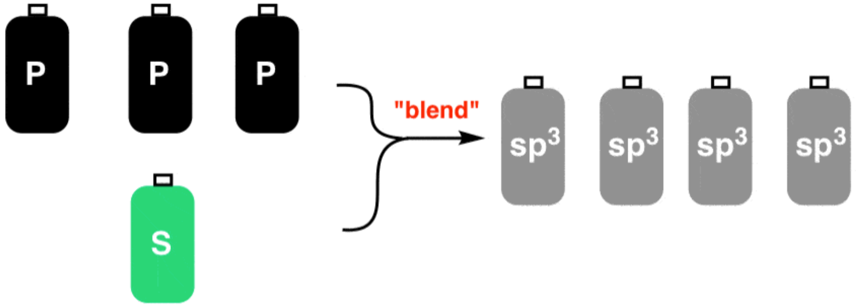
Four sp^3 hybrid orbitals of identical energy which each have 25% *s* character and 75% *p* character

Oriented at 109.5° relative to each other



Potentially helpful analogy?

Imagine the blending the contents of three bottles of Pepsi with a single bottle of Sprite



4 "unhybridized" bottles of pop
·Three Pepsi (P)
·One Sprite (S)

4 "hybridized" sp^3 bottles of pop

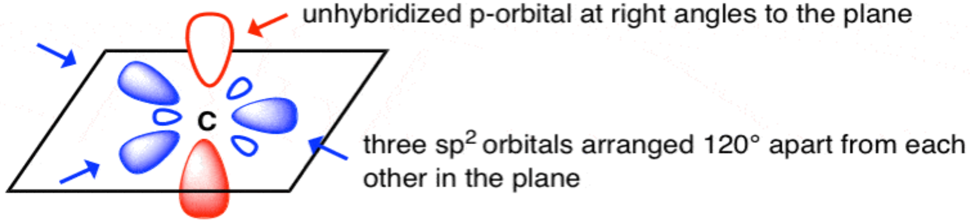
The contents of each bottle have 25% Sprite character and 75% Pepsi character

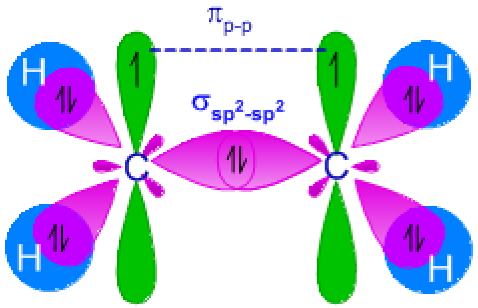
Best not to think of orbitals as rigid "containers"

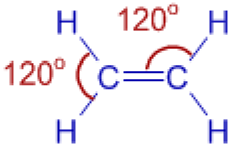
Orbitals are described by mathematical probability functions that can be mixed and added together

Hybrid Orbitals

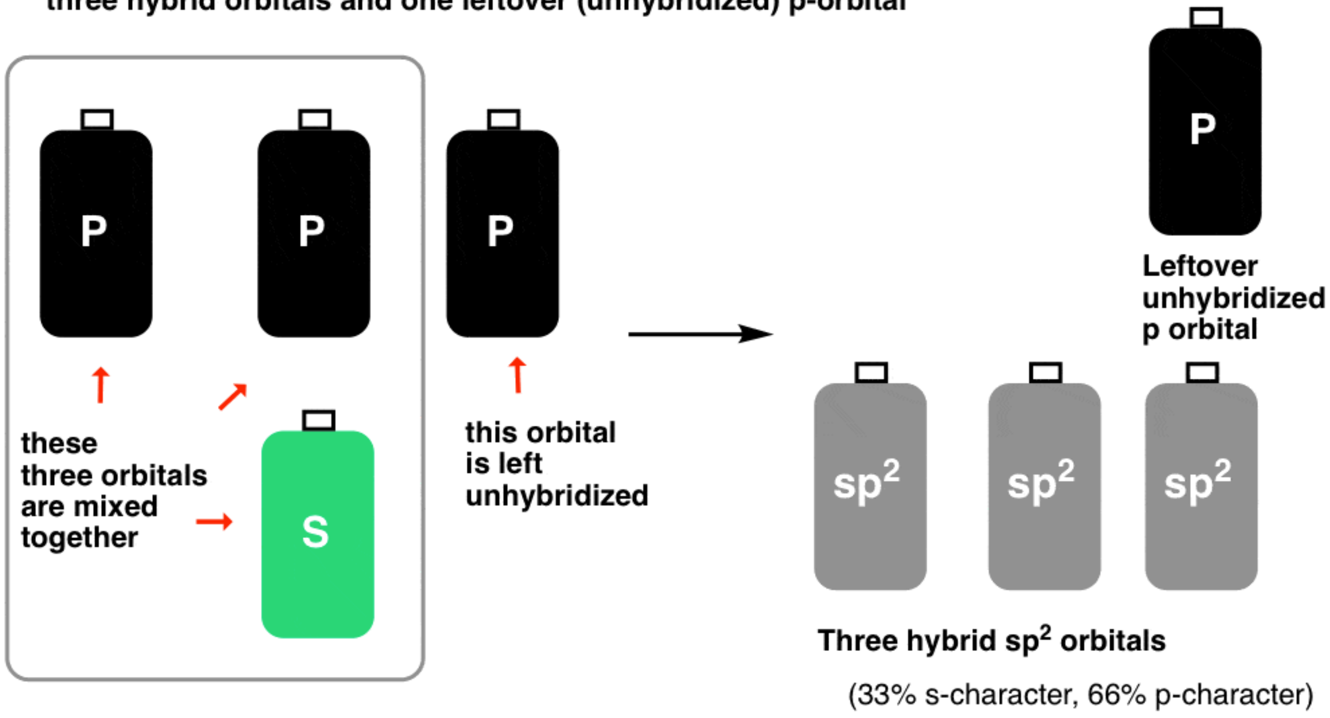
sp^2 orbital hybridization about a central atom (C)



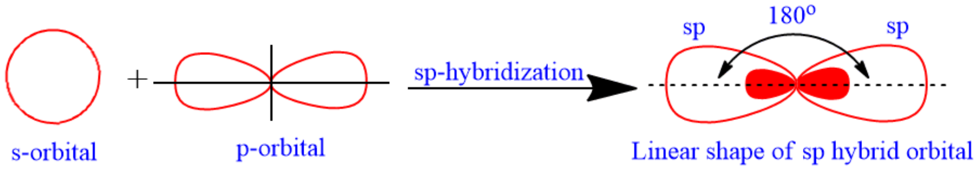


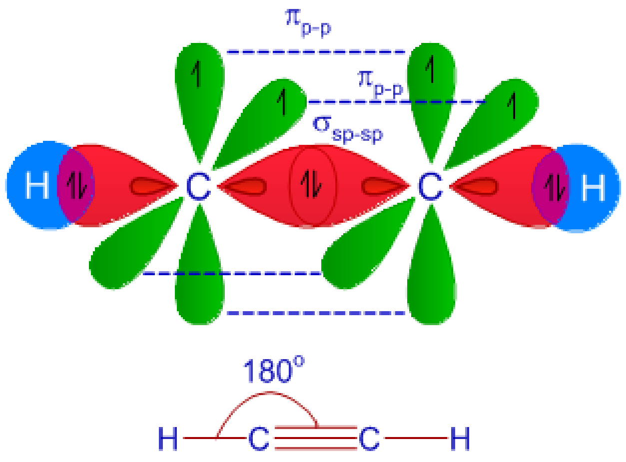


sp^2 hybridization: Only two p-orbitals are hybridized with the s-orbital, giving three hybrid orbitals and one leftover (unhybridized) p-orbital

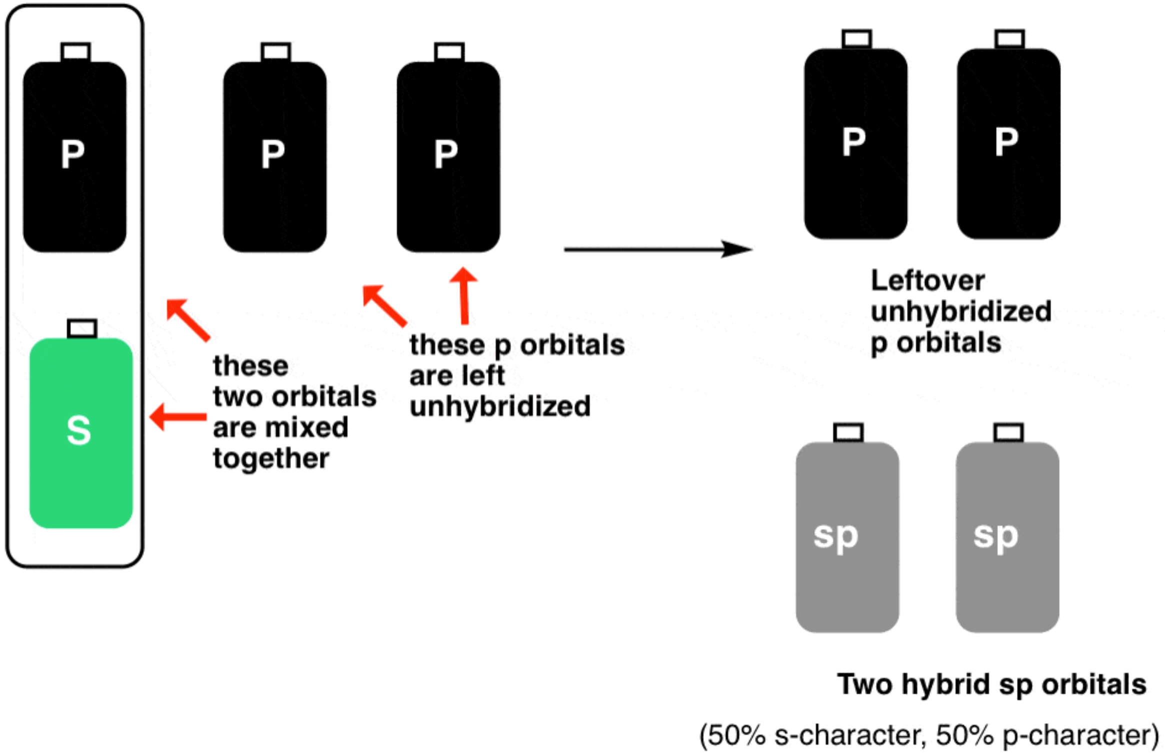


Hybrid Orbitals



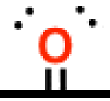


sp hybridization: Only one p-orbitals is hybridized with the s-orbital, giving two hybrid orbitals and two leftover (unhybridized) p-orbitals

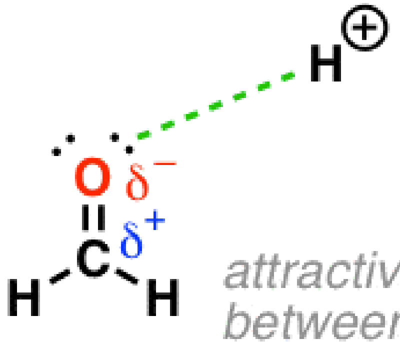


Resonance: Introduction

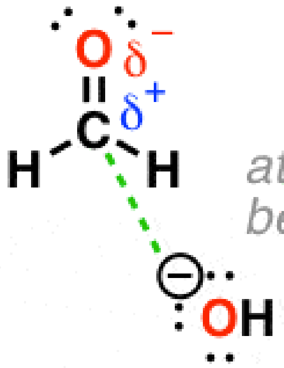
So what about applying this concept to these molecules?



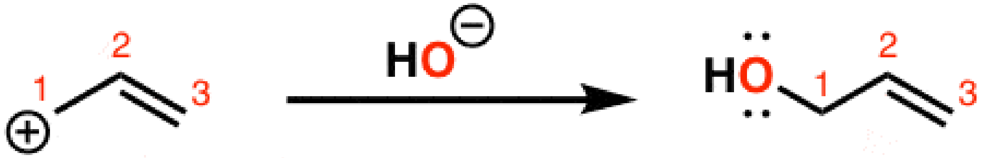
The Lewis structure of this molecule appears to tell us
that one oxygen is more negative than the other (bears



attractive interaction between H and O

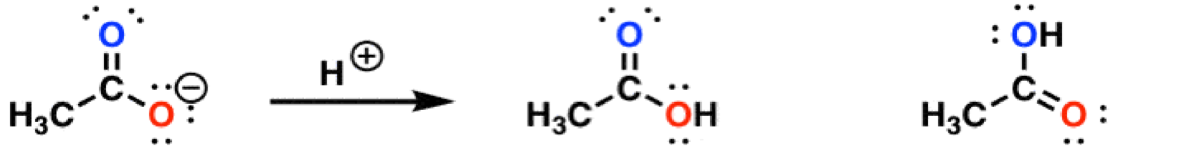


attractive interaction between C and O



Just one problem: This does not agree with experiment!

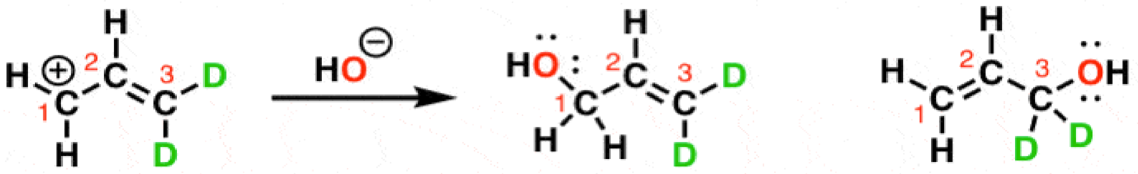
It is possible to "label" the atoms of these molecules (using isotopes) so that we can test this hypothesis. For example we can build an acetate ion where one of the oxygens is O^{16} and the other is O^{18}, add acid, and see where the hydrogen ends up.



Predicted yield: 100%	*Predicted yield: 0%*
Actual yield: 50%	*Actual yield: 50%*

In this experiment we actually obtain a 1:1 mixture of **two products**. *The hydrogen adds to either oxygen with equal probability.*

Similarly, we can perform the same type of experiment with the allyl cation, where we have labelled C_3 with deuterium (a heavy isotope of hydrogen that will not affect the reaction)



Allyl cation

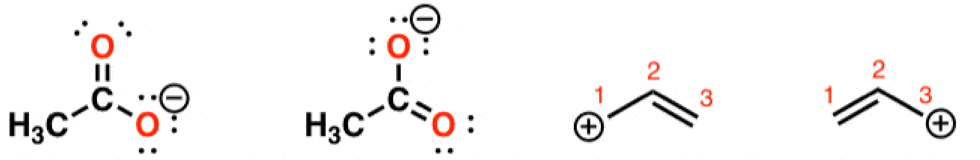
Predicted yield: 100%	*Predicted yield: 0%*
Actual yield: 50%	*Actual yield: 50%*

Again, the oxygen adds to C_1 and C_3 with equal probability (but does not react with C_2).

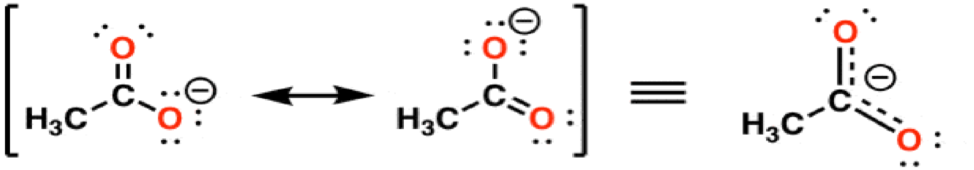
We could NOT have predicted this purely from analyzing electronegativities. Clearly there is another factor we have been ignoring!

So how *could* we have predicted this result?

If you look at the structures of these two molecules you can see that it is possible to draw them two different ways.

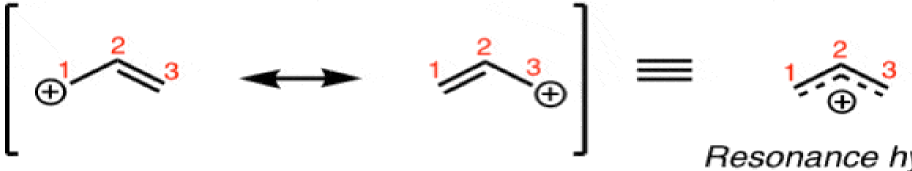


numbering is for placeholding, not IUPAC



Acetate ion resonance forms

Resonance hybrid



Allyl carbocation resonance forms

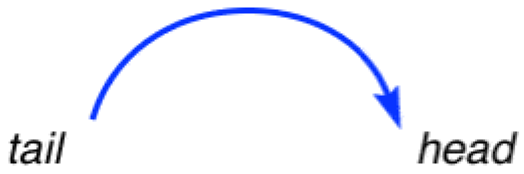
Resonance hybrid

*The "double-headed" arrow denotes that two molecules are resonance isomers (NOT in equilibrium)

Movements of electrons

Introducing Curved Arrows: A Way to show the "Movement" of electrons.

Electrons move ***from*** the tail ***to*** the head



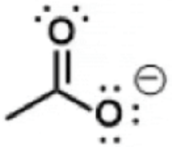
Take a pair of electrons from ***here*** *(bond / lone pair)*

and move them ***here*** *(bond / lone pair)*

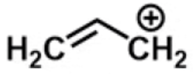
The curved arrow shows "movement" of a pair of electrons... it's an extremely useful accounting system that lets us keep track of changes in **bonding** and **charge**

The tail ***must*** be at a source of electrons, **either a lone pair or a bond.** The head ***must*** be able to accept a pair of electrons without breaking the octet rule

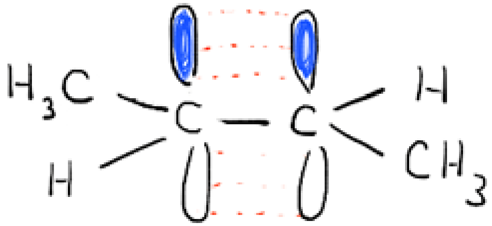
Acetate Ion Resonance



Allyl Cation Resonance

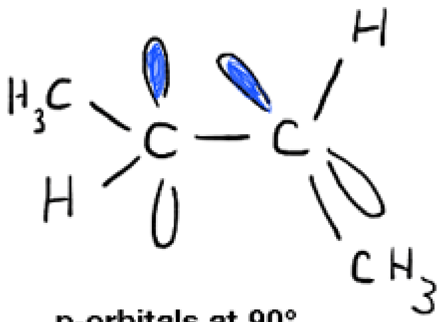


Conjugation and Delocalization



p-orbitals in same plane

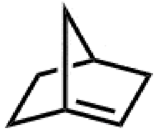
(overlap possible)



p-orbitals at 90°

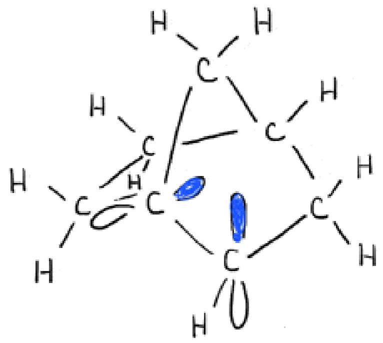
(no overlap possible)

"Bridgehead" alkenes - a case where orbital overlap cannot occur



Depiction of a
"bridgehead" alkene

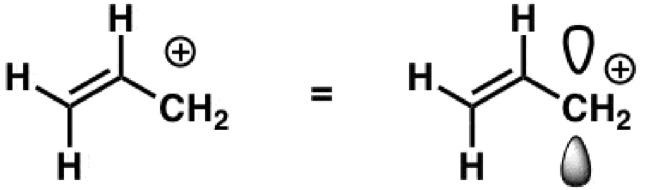
(too unstable to be isolated)



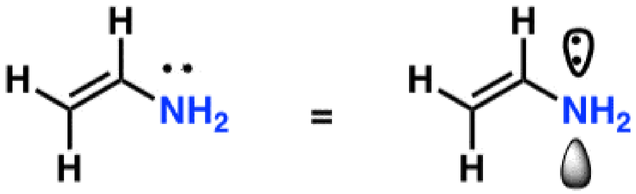
Note how p-orbitals are not aligned properly
in order for a pi bond to form - they are
at 90° to each other

Resembles a di-radical, not an alkene
(very unstable!)

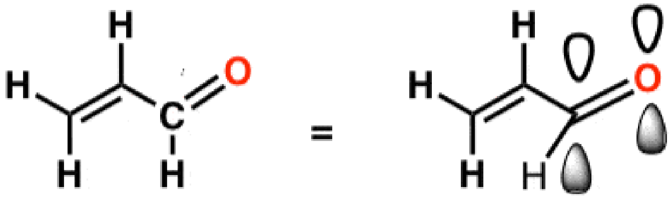
Examples of Conjugation



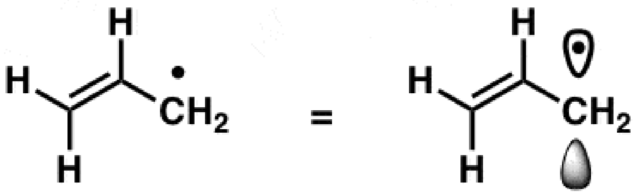
1. Conjugation with empty p-orbital (of carbocation)



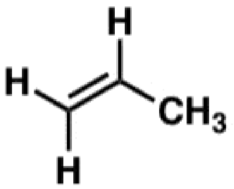
2. Conjugation with lone pair (on nitrogen)



3. Conjugation with another pi bond

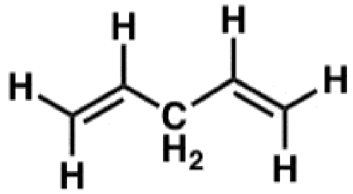


4. Conjugation with a radical



No conjugation

(CH_3 has no available orbitals to overlap with p orbitals of pi bond)



Also no conjugation

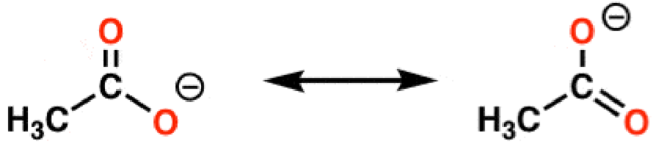
(CH_2 has no available orbitals to overlap with p orbitals of pi bond)

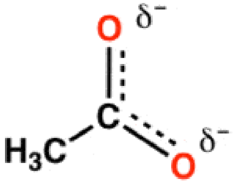
Consequence of conjugation: Bond Lengths

Equal resonance forms:

Actual structure
(from X-ray crystallography)

Acetate ion

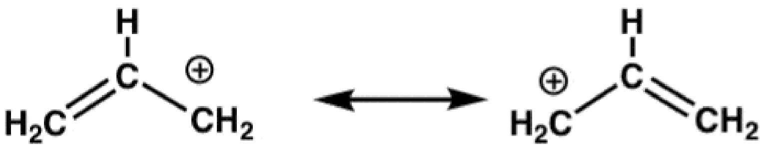


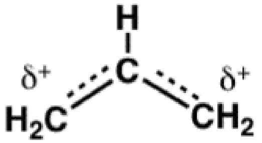


1.26 A

both bond
lengths equal

Allyl cation

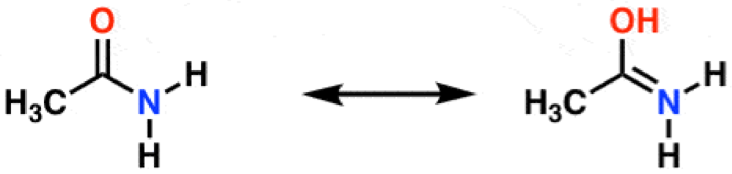


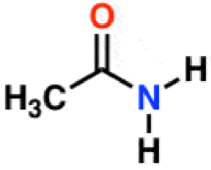


1.393 (calc)

both bond
lengths equal

Unequal resonance forms: minor contributor can still have influence on structure





shorter than
a normal C-N bond

longer than a
normal C=O bond

shorter than
a normal C-C bond

Unequal resonance forms

The minor resonance contributor can still have influence on structure

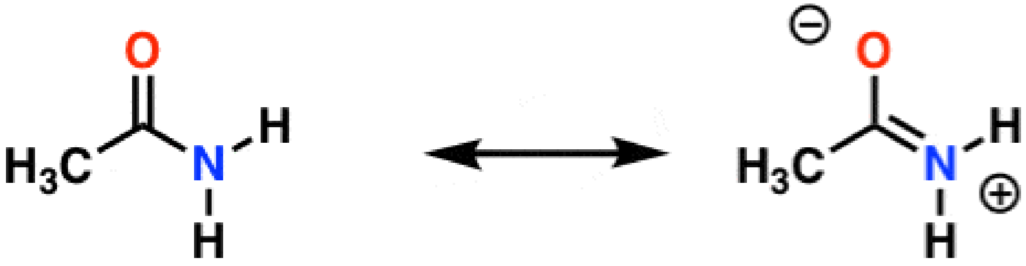
Butadiene

Major contributor ***Minor contributor***

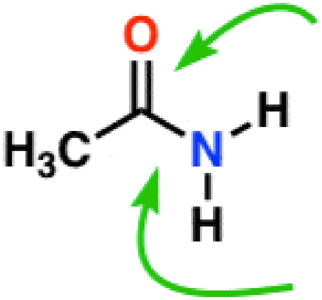
1.48 Å

shorter than
a normal C-C bond
(1.51 Å)

Acetamide



Major contributor ***Minor contributor***

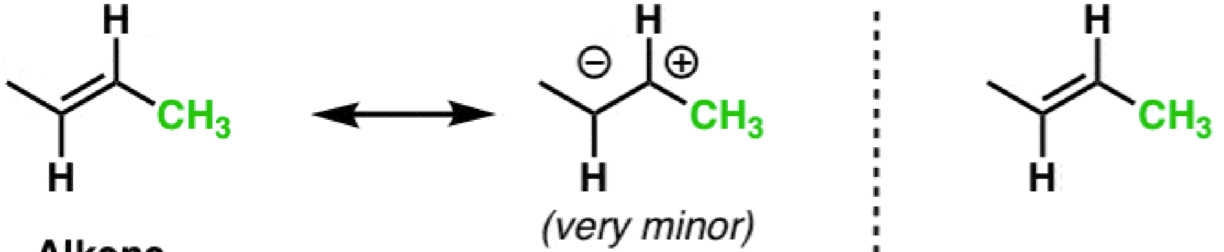


1.26 Å **longer than a**
normal C=O bond
(1.20 Å)

1.33 Å
shorter than
a normal C-N bond (1.47 Å)

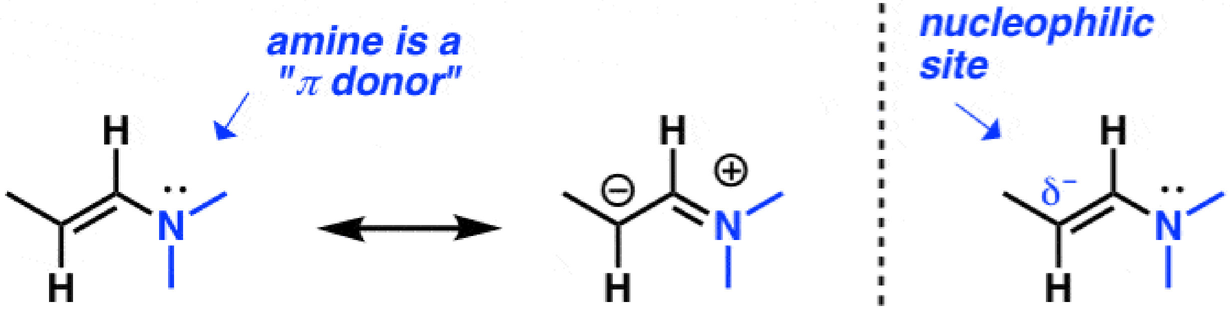
Consequences of Conjugation (2) - Effect on Reactivity

Major Contributor	*Minor contributor*	*Hybrid*	*Reactivity*



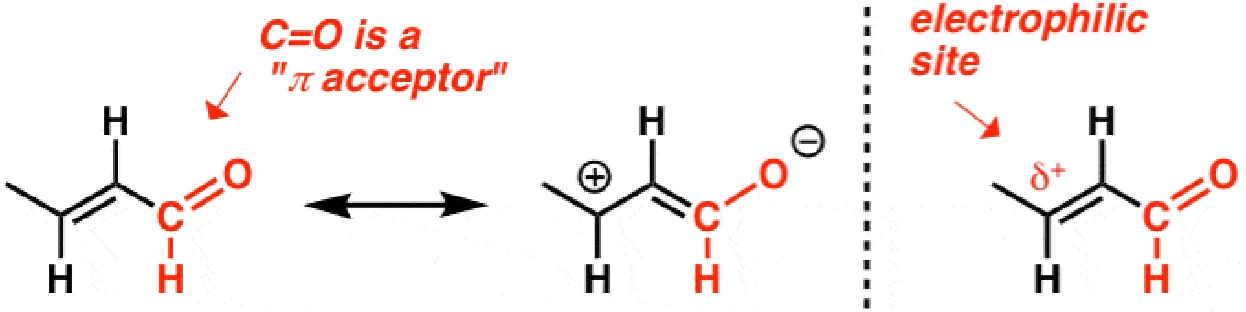
Alkene

• poorly reactive with mild electophiles (e.g. CH_3I) or nucleophiles (e.g. $CH_3S^{\ominus}$)



Enamine

• **reacts with CH_3I (Stork enamine rxn)**
• not reactive with mild nucleophiles



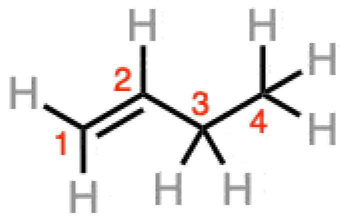
α,β unsaturated aldehyde

• not reactive with CH_3I
• **reacts with nucleophiles (e.g. $CH_3S^{\ominus}$)**

('conjugate addition')

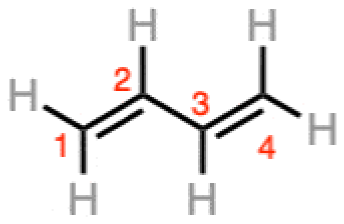
The effect of conjugation on stability: resonance energy

We might expect 1,3-butadiene to have an enthalpy of hydrogenation twice that of 1-butene, but in fact is is a **little bit less.**



But-1-ene

$\Delta H_{hyd} = –30.1$ kcal/mol



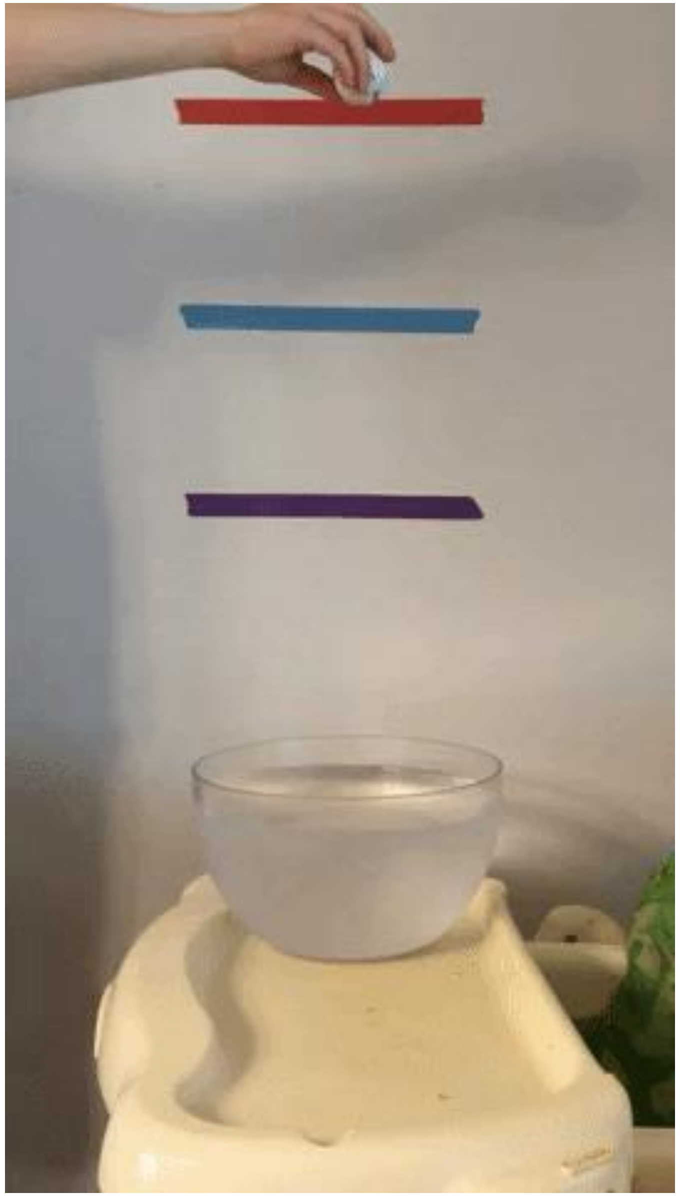
1,3-Butadiene

$\Delta H_{hyd} = –56.6$ kcal/mol

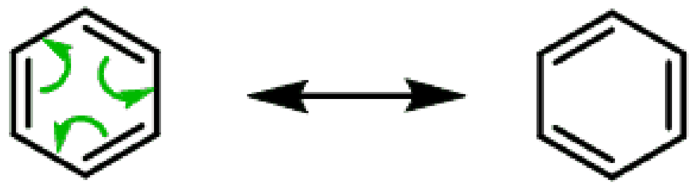
(not 60.2 kcal/mol)

More stable than expected
by 3.6 kcal/mol due to conjugation

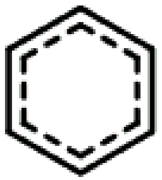
This “extra” stability is called, “**resonance energy**”



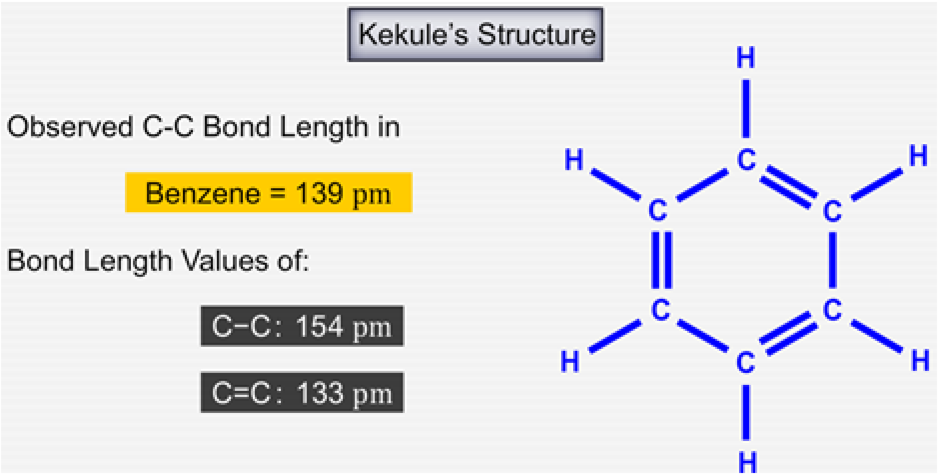
Benzene and Resonance



Resonance structures

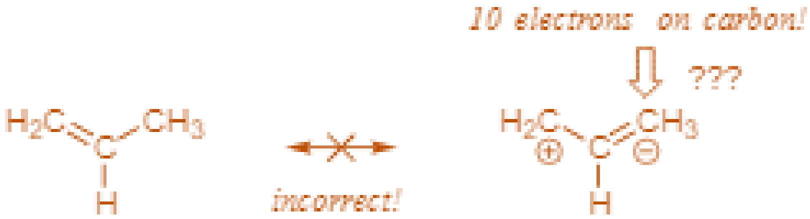


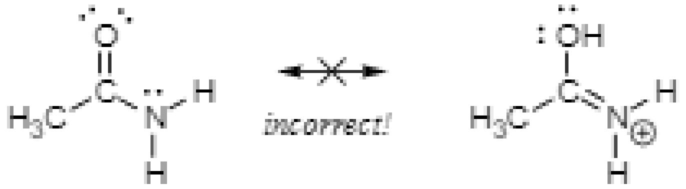
Hybrid



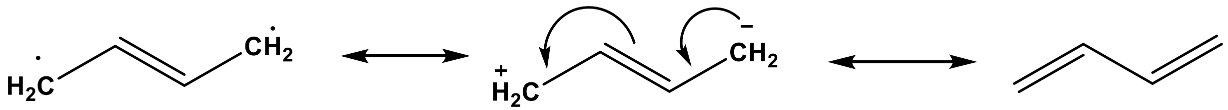
Rules of Resonance

- All canonical structures must follow Lewis structure

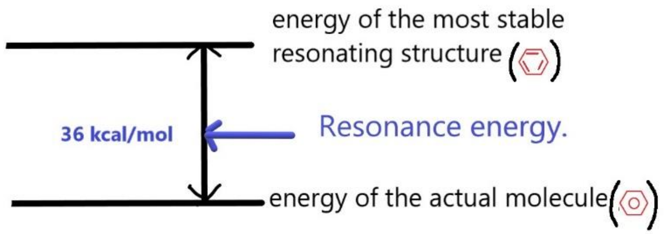




- The position of the nuclei must be same in all the structures.
- All atoms must lie on the same plane, where planarity is maximum.
- All the canonical forms must have same number of unpaired electrons

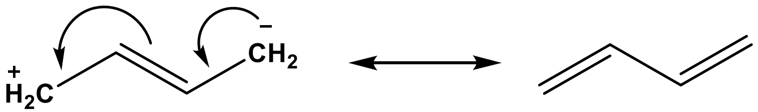


- The energy of the actual molecule is lower than the any form. The delocalization is a stabilizing phenomenon

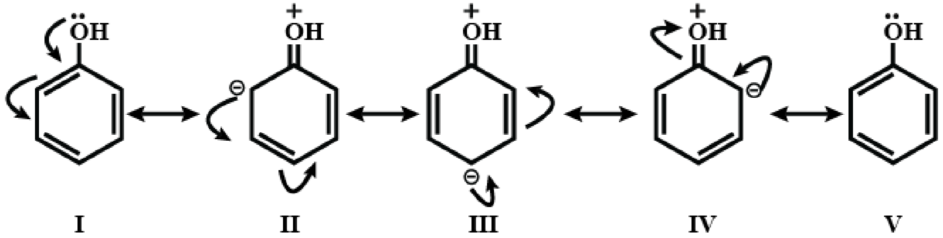


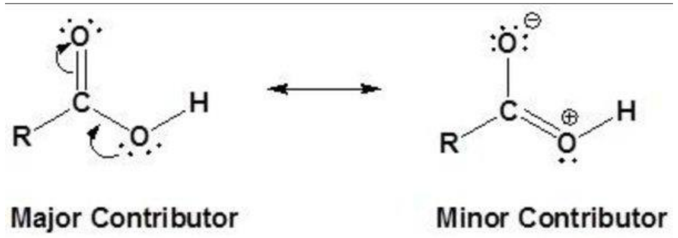
- All canonical forms do not contribute equally to true molecule. Few rules may guide us through the understanding the stability of the imaginary structures.

➢ Structures with more covalent bonds are more stable than with fewer ones.

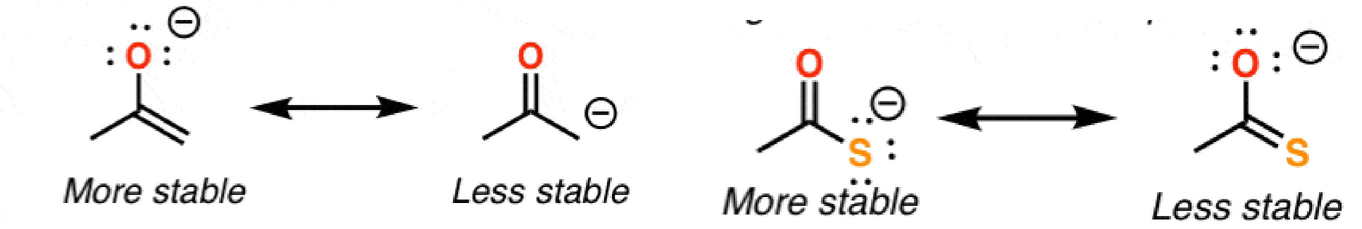


➢ Stability is decreased by increase in charge separation. Structures with formal charges are less stable than uncharged structures. Structure with more than two formal charges usually contributes very little.

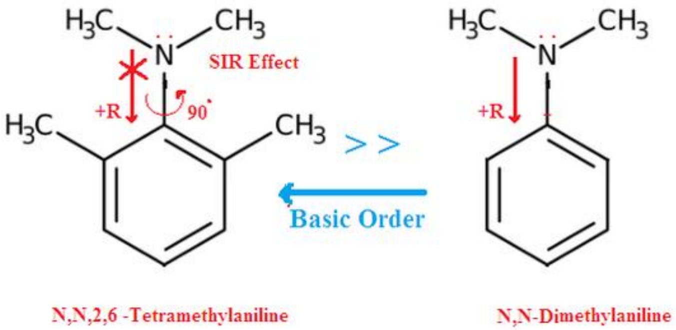


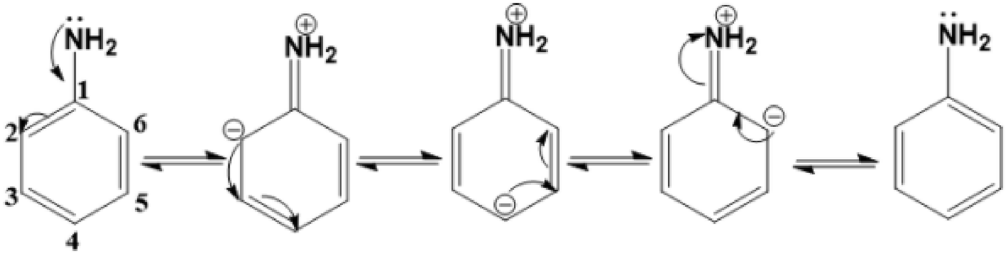


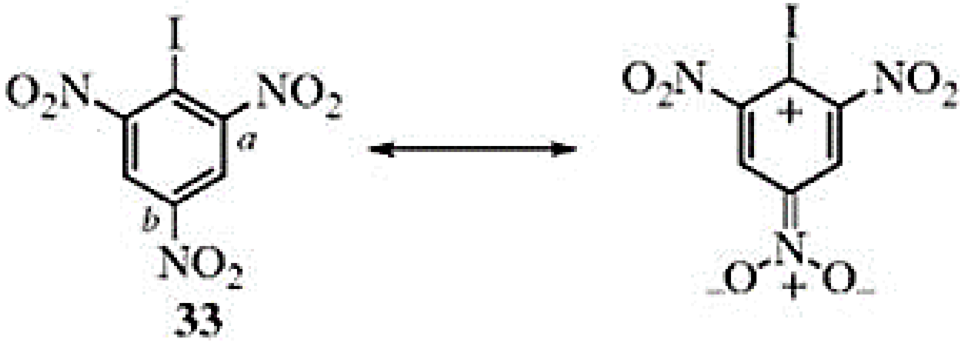
➢ The structure that carry negative charge on a more electronegative atom are more stable than those carry charge on less electronegative atom.



Steric Effect



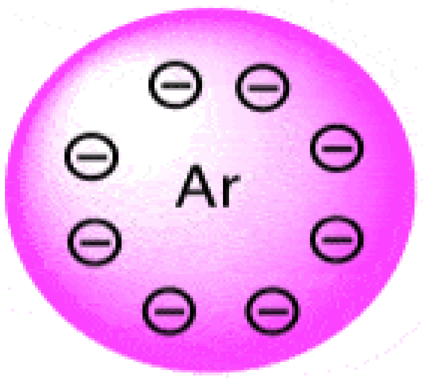




a= 1.45Å
b= 1.35Å

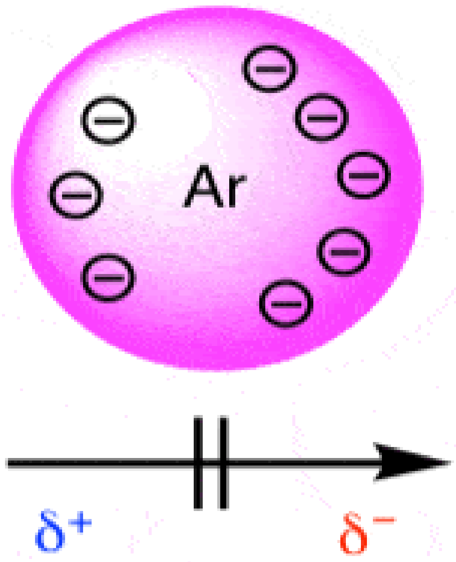
4. Van der Waals - Dispersion forces

if valence electrons are perfectly distributed, **Ar** *has no dipole*



This is "long term average"

but on an instantaneous basis, there can be an imbalance of charges.



This creates a "temporary dipole"

These temporary dipoles attract

This tendency to create "temporary dipoles" is called *polarizability*

Polarizability increases with atomic size

Surface Area and Boiling points

Dispersion forces are a "surface area" phenomenon

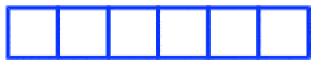
- Hydrocarbons bind together through dispersion forces
- Alkane boiling points increase with chain length. This is due to their increased surface area available for dispersion forces.

Boiling point increases with molecular weight

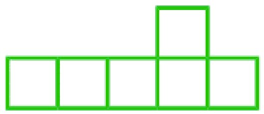
Methane	Ethane	Propane	Butane	Pentane	Hexane	Heptane	Octane
–164°C	–89°C	–42°C	–0.5°C	36°C	69°C	98°C	125°C

	melting point	boiling point
$CH_3CH_2CH_2CH_2CH_2CH_3$	–95°C	69°C
$CH_3CH(CH_3)CH_2CH_2CH_3$	–154°C	60°C
$CH_3CH(CH_3)CH(CH_3)CH_3$	–135°C	58°C
$CH_3C(CH_3)_2CH_2CH_3$	–98°C	50°C

within the branched series, increased symmetry leads to higher melting point, lower boiling point



easy



HARD

$CH_3CH_2CH_2CH_2CH_3$

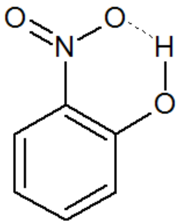
melting point: –95°C

$CH_3CH(CH_3)CH_2CH_3$

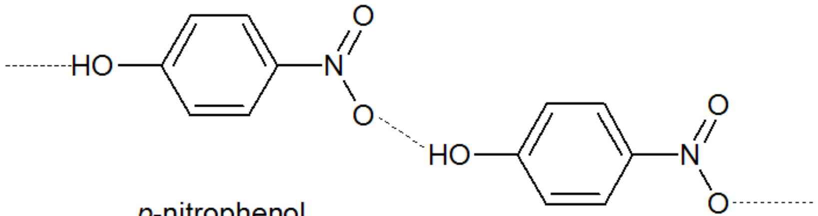
melting point: –154°C

Better stacking = higher melting point

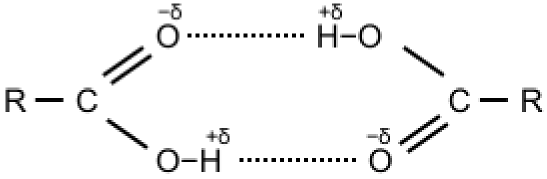
Few examples of H-Bonding

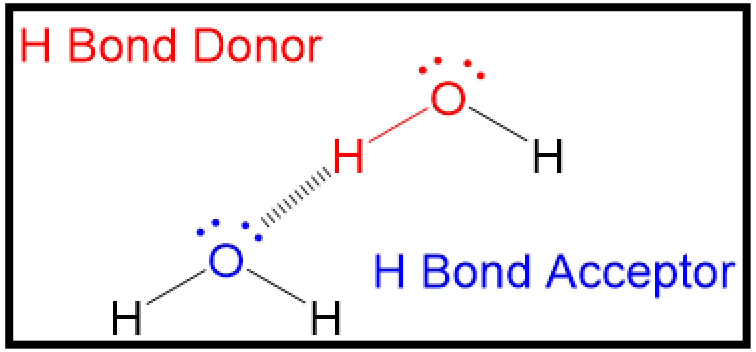


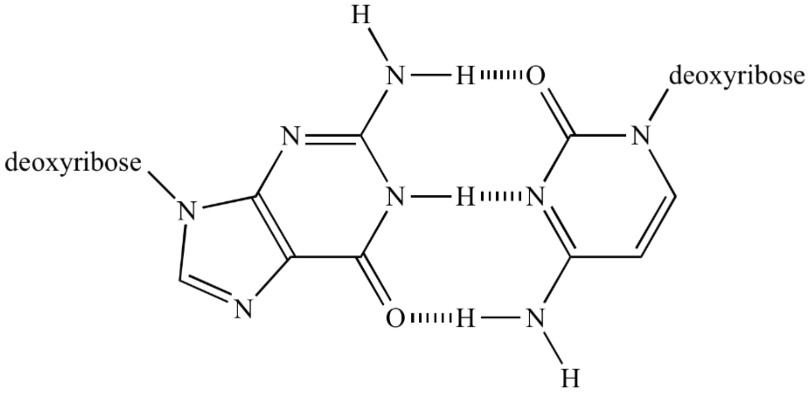
o-nitrophenol
(intramolecular
hydrogen bonding)

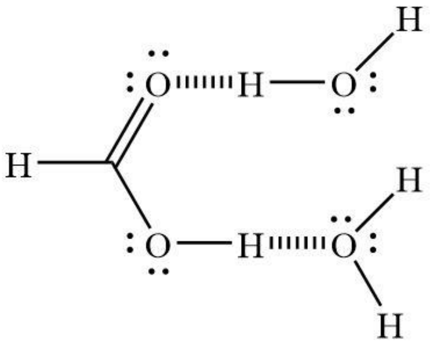


p-nitrophenol
(intermolecular hydrogen bonding)



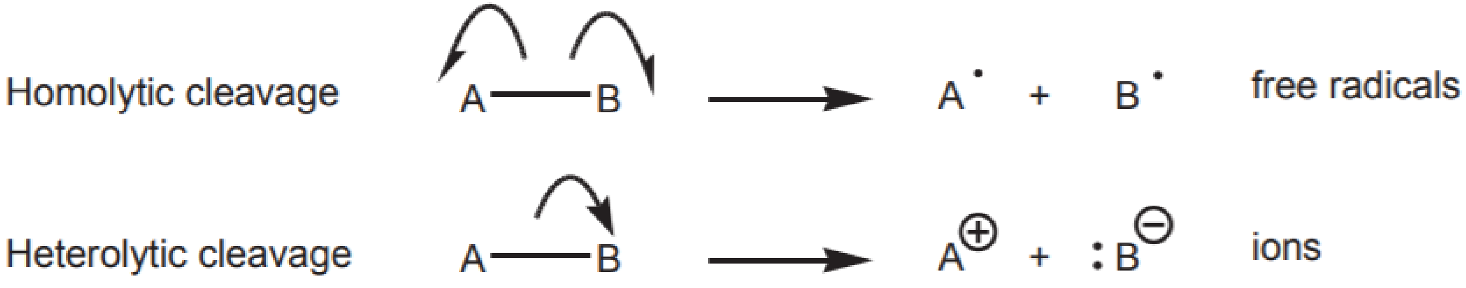


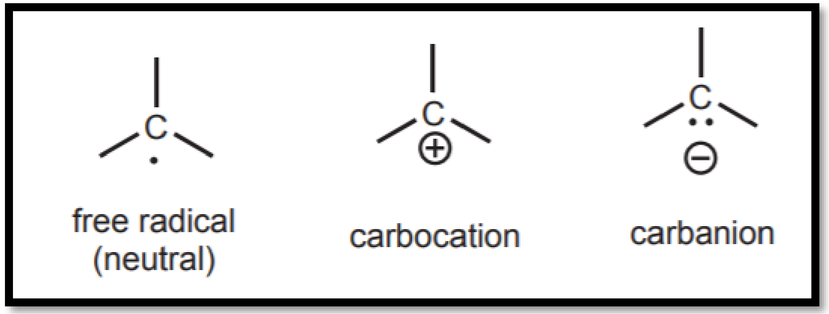


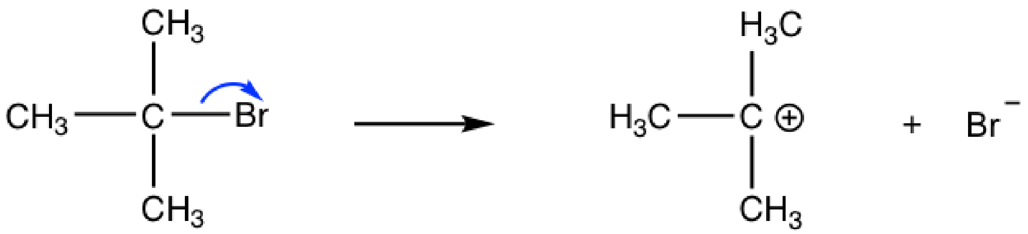


The H-Bonding energy ranges from 5- 50 kcal/mole

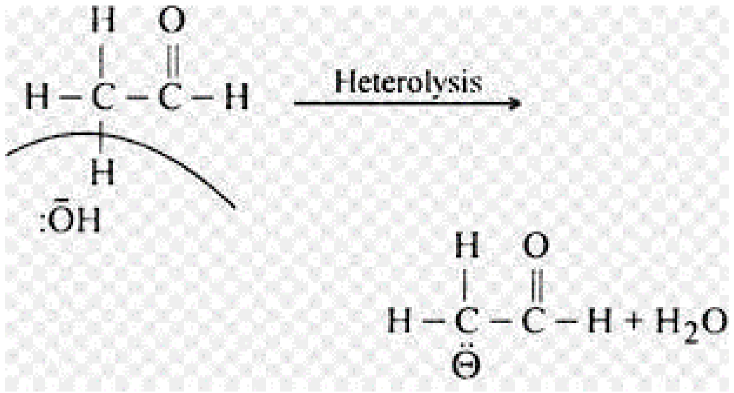
Breaking of Bonds

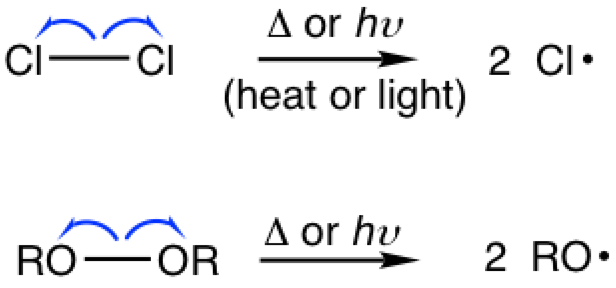


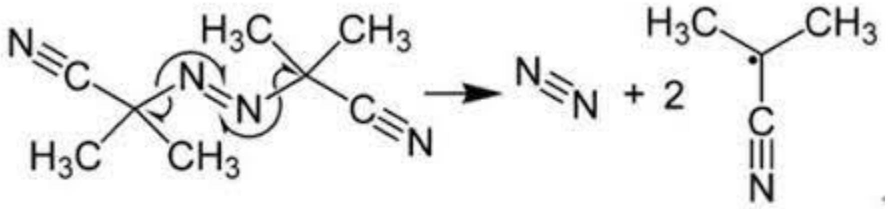




example of heterolytic bond cleavage





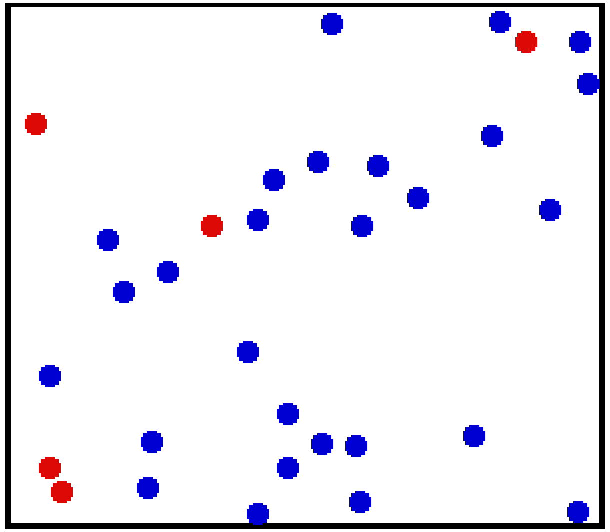


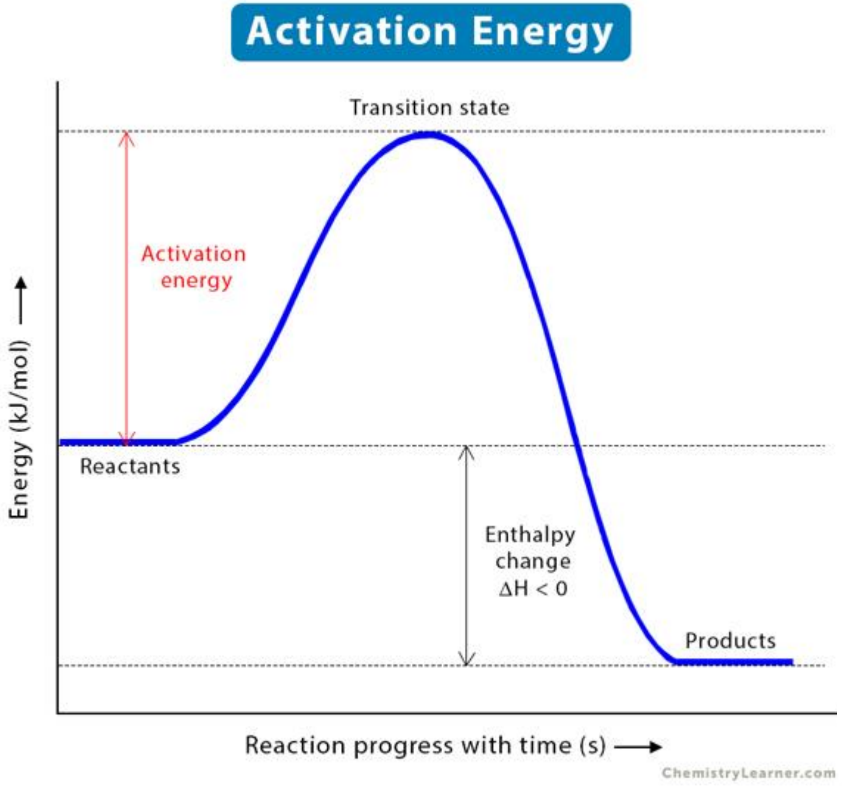
Azobisisobutyronitrile (AIBN)

Why and How does Chemicals React ?

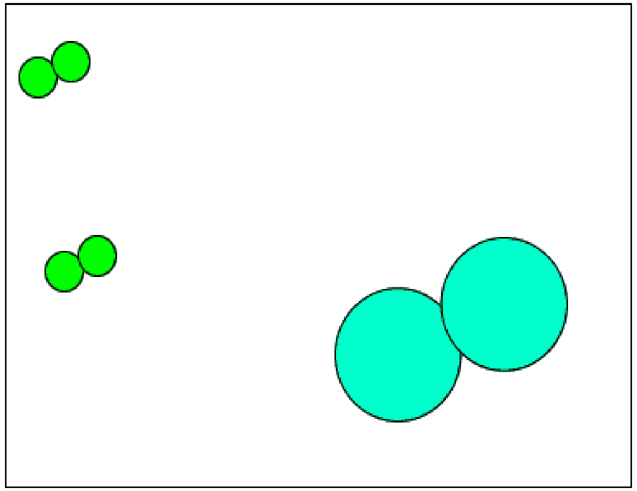
To understand the organic chemistry we should be fluent in two aspect

1. **STRUCTURE**
2. **REACTIVITY**





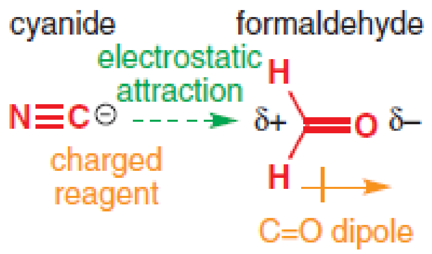
Under normal conditions hydrogen and oxygen molecules collide without reacting.

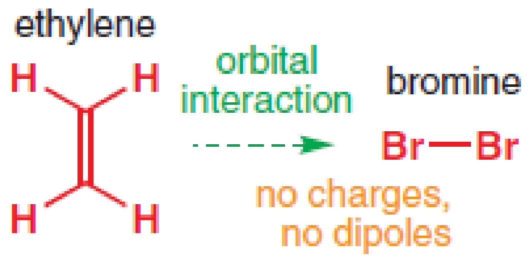


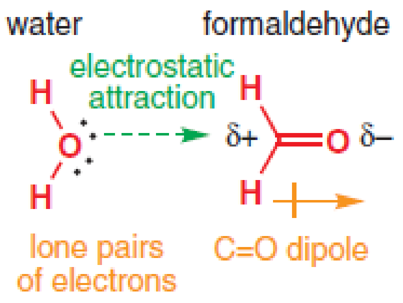
Why and How does Chemicals React ?

The reaction can happen when the molecules interacts through

1. Electrostatic Attraction : Dipole
2. Orbital Overlap







- In general, molecules repel each other, and need to overcome a barrier with a minimum amount of *activation energy* in order to react.
- Most organic reactions involve interactions between full and empty orbitals.
- Many, but not all, also involve charge interactions, which help overcome electronic repulsion.
- Some ionic reactions involve nothing but charge attraction.

Why and How does Chemicals React ?
Mechanism of Reaction

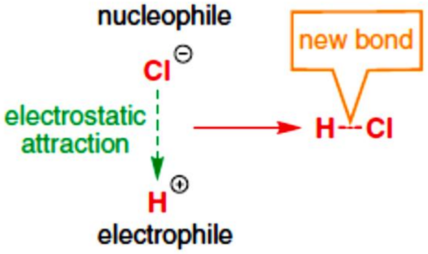
The flow of electrons from one molecule to another is known as Reaction Mechanism

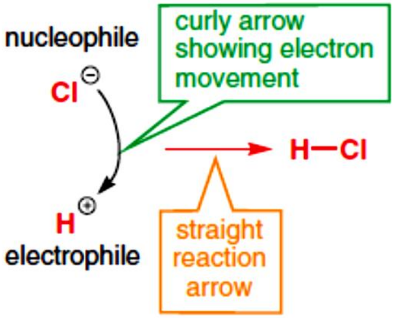
- **A bond forms when electrons move from a nucleophile to an electrophile:**

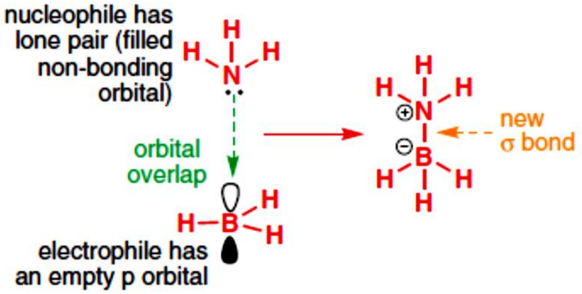
from nucleophile (Nu or Nu^-) $\xrightarrow{\text{electron movement}}$ to electrophile (E or E^+)

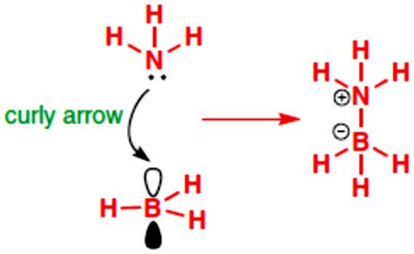
The nucleophile donates electrons.
The electrophile accepts electrons.

electrons flow from "electron rich" areas to "electron poor" areas









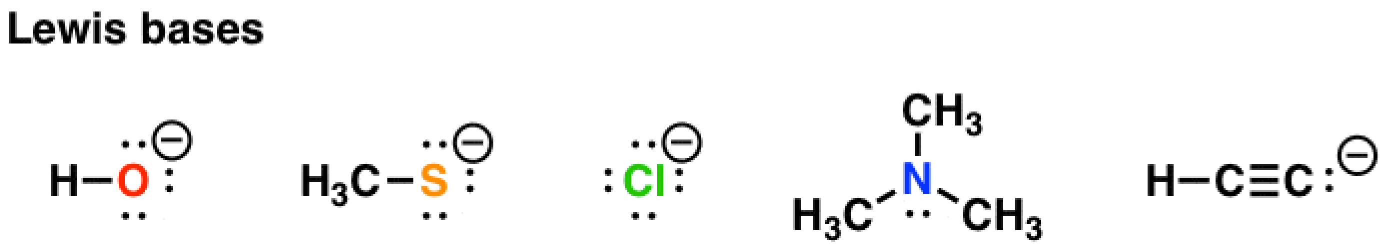
What are Nucleophiles and Electrophiles?

Let's start with "nucleophiles" (from "nucleus loving", or "positive-charge loving"). A nucleophile is a reactant that provides a pair of electrons to form a new covalent bond.

Sound familiar? It should! This is the exact definition of a Lewis base.

In other words, **nucleophiles are Lewis bases.**

When the nucleophile donates a pair of electrons to a proton (H+) it's called a Brønsted base, or simply, "base".

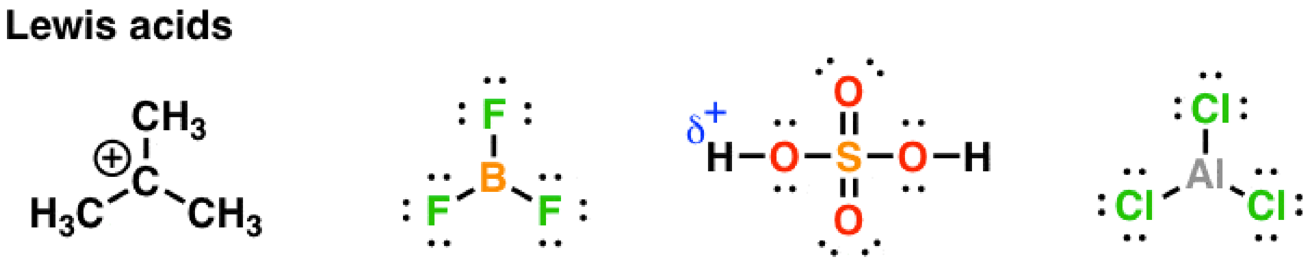


What are Nucleophiles and Electrophiles?

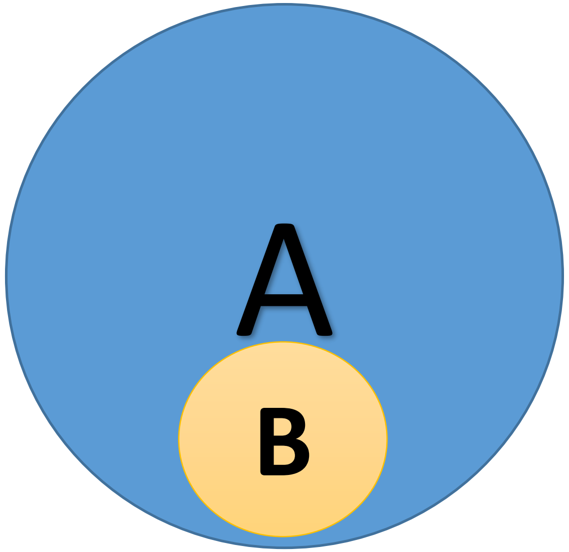
Now let's talk about electrophilicity (from "electron-loving", or "negative-charge loving"). An electrophile is a species that accepts a pair of electrons to form a new covalent bond.

Again, this should sound familiar: this is the definition of a **Lewis acid!**

An electrophile that accepts an electron pair at hydrogen is called a Brønsted acid, or just "acid".



Nucleophilicity vs Basicity



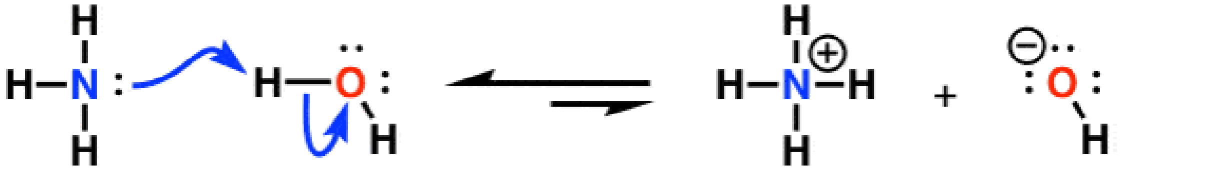
A= Nucleophilicity
B= Basicity

Basicity: nucleophile attacks hydrogen
Nucleophilicity: nucleophile attacks any atom other than hydrogen.

What's a base?

- A base donates a pair of electrons to a proton

Example



weaker base pKa = 14 pKa = 10 *stronger base*

How do we measure basicity?

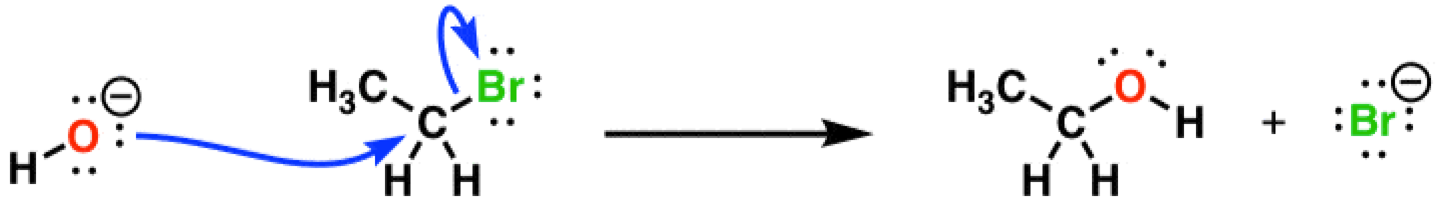
- Because most species can participate in reversible acid-base reactions, we can measure basicity by the position of an *equilibrium*.

- In other words, we're measuring *relative stability* of the species involved. "Stability" is a *thermodynamic* property.

Acid-base reactions reflect relative stabilities

Nucleophilicity vs Basicity

Example



irreversible reaction

How do we measure nucleophilicity?

- Reactions of nucleophiles with carbon are most often **irreversible** and are not in equilibrium.
- Therefore we have to measure nucleophilicity by the **rate** of the reaction.

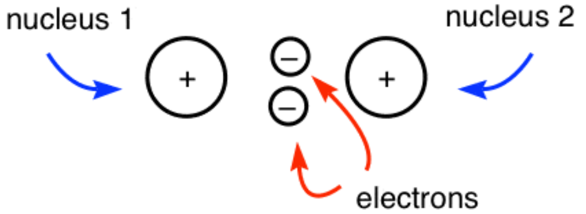
There’s one important thing to remember with reaction rates. They don’t always reflect overall stability. There are a few more variables at play here.

Steric hindrance: Reactions where nucleophiles attack carbon-based electrophiles are significantly more sensitive to steric effects, because empty orbitals on carbon are not as accessible.

Solvents: The medium (solvent) in which a reaction takes place can greatly affect the rate of a reaction. Specifically, the solvent can greatly attenuate (reduce) the nucleophilicity of some Lewis bases through hydrogen bonding.

Molecular Orbital Theory: Why do bond form ?

Forces in a chemical bond



- Electrons held between two nuclei
- Attractive forces outweigh repulsive forces
- Net *lowering* of energy (i.e. more stable), relative to the two atoms being apart
- We call this net lowering of energy the "bond dissociation energy"

e.g. H_2 = 104 kcal/mol

Electrostatic attraction (+ –) outweighs electrostatic repulsion (+ +) and (– –)

Molecular Orbital # 1: Constructive overlap between atomic p orbitals gives a "bonding" pi orbital

Note - no "node" between p orbitals - this is continuous overlap

Constructive overlap of atomic orbitals

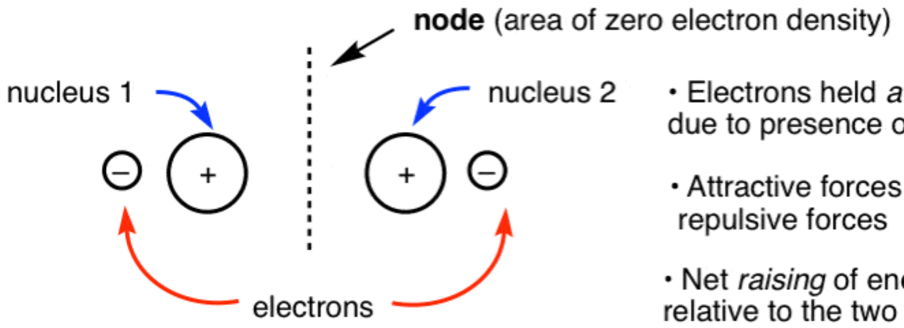
In this orbital two negatively charged electrons are held between two positively charged nuclei

Attractive terms in Coulomb's law will outweigh repulsive terms

Electrons in this orbital will be lower-energy (more stable) than in the atomic orbitals of the individual atoms

Hence, we call this a "bonding" orbital
Or just a π orbital

Forces in a chemical "antibond"



- Electrons held *away* from two nuclei due to presence of a **node**
- Attractive forces are outweighed by repulsive forces
- Net *raising* of energy (i.e. less stable), relative to the two atoms being apart

Electrostatic repulsion (+ +) and (– –) outweighs electrostatic attraction (+ –)

Molecular Orbital # 2: Destructive overlap between atomic p orbitals gives an "antibonding" pi orbital (π*)

Note the node is where the orbitals change sign

Destructive overlap of atomic orbitals (i.e. they don't overlap at all)

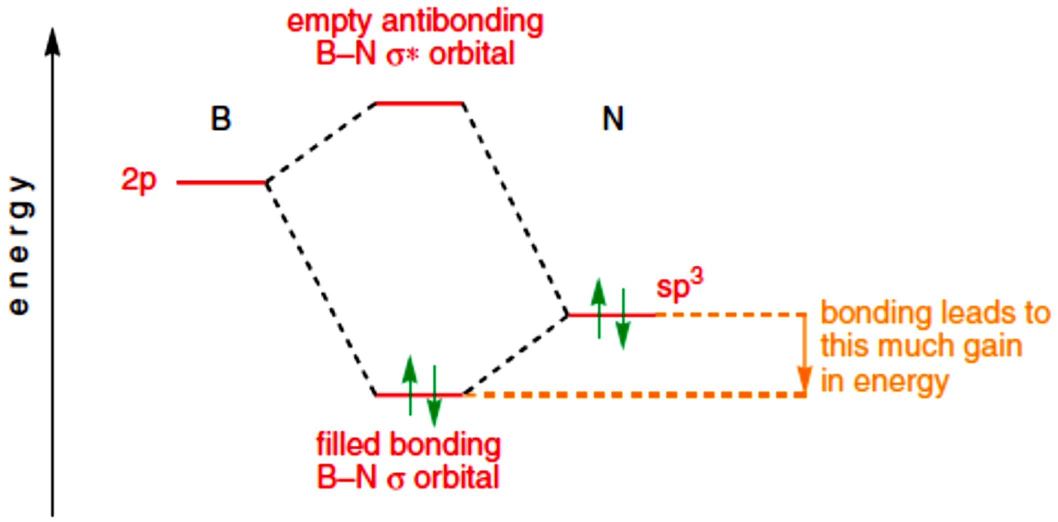
In this orbital two negatively charged electrons are held *away from* two positively charged nuclei

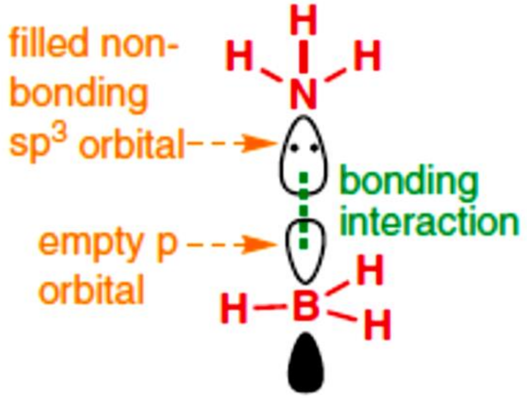
Attractive terms in Coulomb's law will be outweighed by repulsive terms

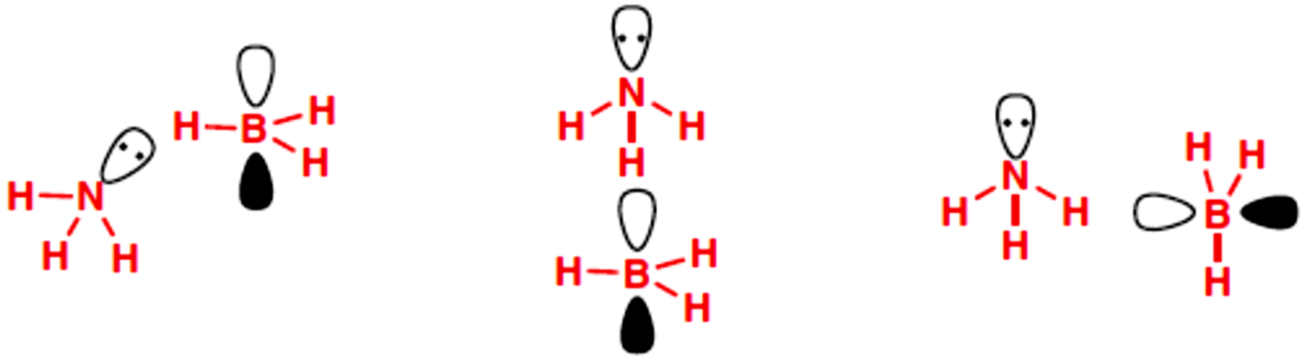
Electrons in this orbital will be higher-energy (less stable) than in the atomic orbitals of the individual atoms

Linear Combination of Atomic Orbitals

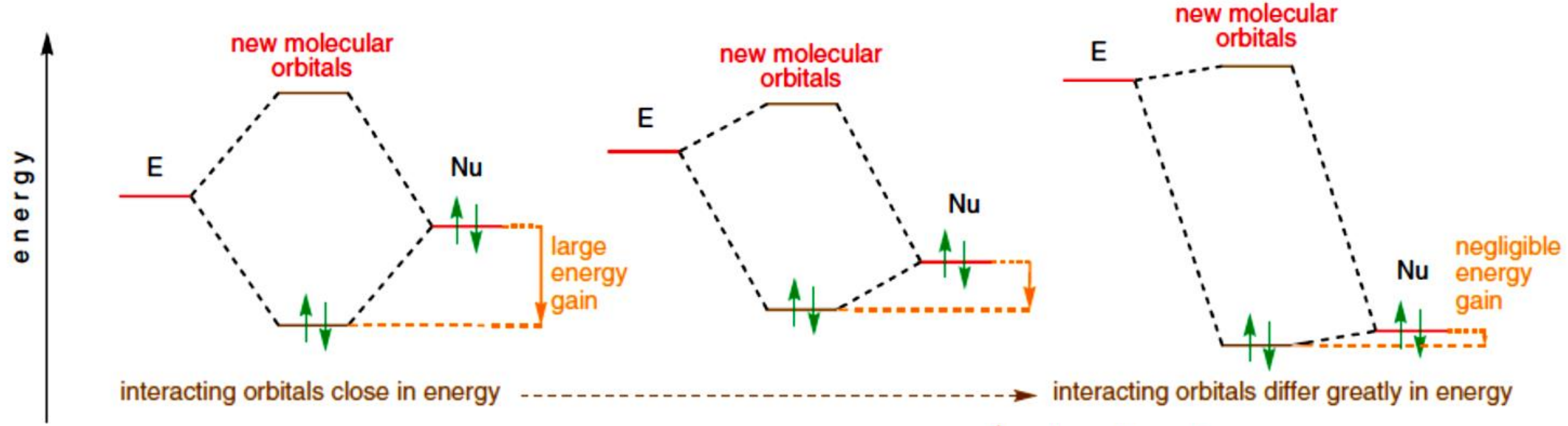
How does Chemicals React ?
MO Diagram

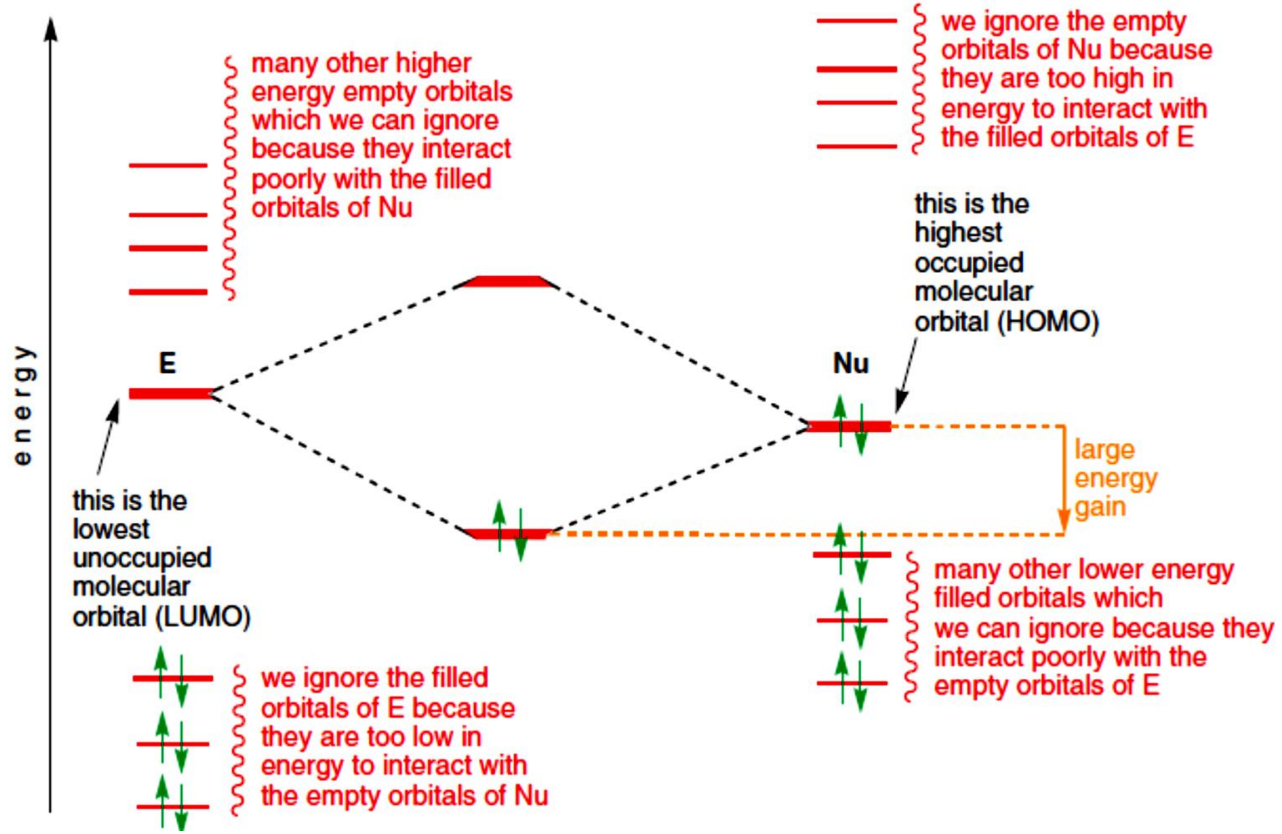






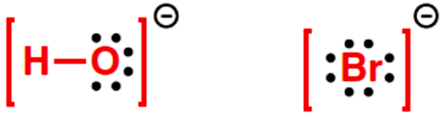
Possible approach of molecules which are not a feasible for interaction


new molecular orbitals
new molecular orbitals
new molecular orbitals
energy
E
Nu
large energy gain
E
Nu
E
Nu
negligible energy gain
interacting orbitals close in energy
interacting orbitals differ greatly in energy


energy
many other higher energy empty orbitals which we can ignore because they interact poorly with the filled orbitals of Nu
we ignore the empty orbitals of Nu because they are too high in energy to interact with the filled orbitals of E
this is the highest occupied molecular orbital (HOMO)
E
Nu
this is the lowest unoccupied molecular orbital (LUMO)
large energy gain
many other lower energy filled orbitals which we can ignore because they interact poorly with the empty orbitals of E
we ignore the filled orbitals of E because they are too low in energy to interact with the empty orbitals of Nu

- **The best nucleophiles have high-energy occupied molecular orbitals (HOMOs).**
- **The best electrophiles have low-energy unoccupied molecular orbitals (LUMOs).**

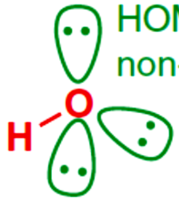
nucleophiles with a
negative charge



hydroxide bromide

usually drawn simply as:

$HO^{\ominus}$ $Br^{\ominus}$



HOMO =
non-bonding sp^3 orbital

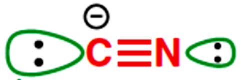
hydroxide

cyanide ion

usually drawn
simply as:

$^{\ominus}C\equiv N$

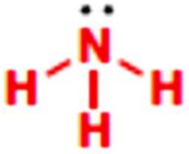
HOMO =



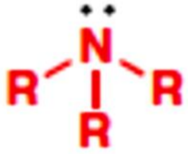
sp lone pair
on C

sp lone pair

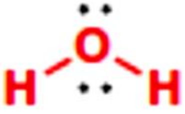
nucleophiles with a
lone pair



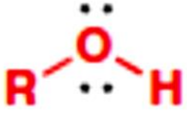
ammonia



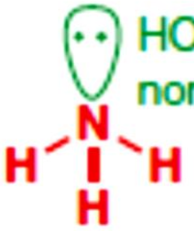
an amine



water



an alcohol



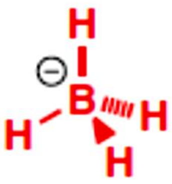
HOMO =
non-bonding sp^3 orbital

a nucleophile with a
C=C double bond

HOMO =
bonding
π orbital

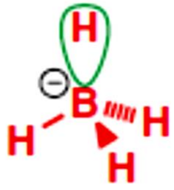
ethylene

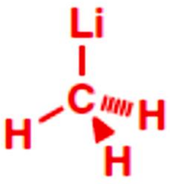
nucleophiles with a σ **bond**
between electropositive atoms



borohydride
anion

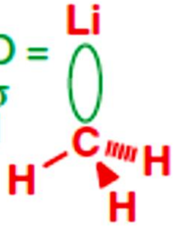
HOMO =
B–H σ orbital

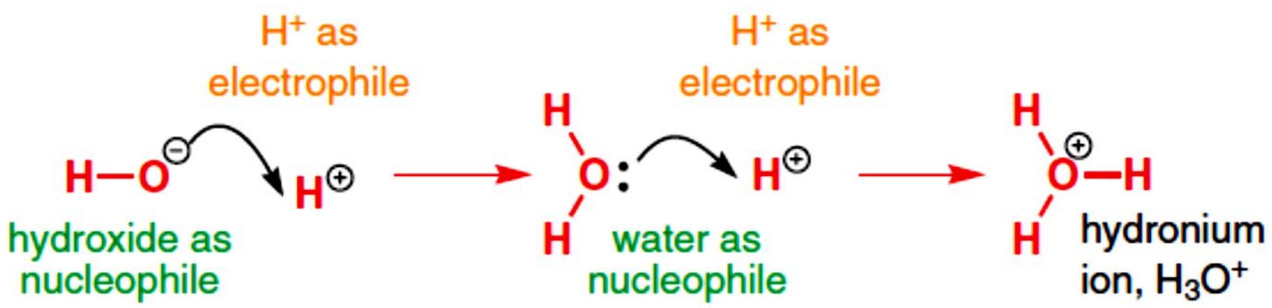


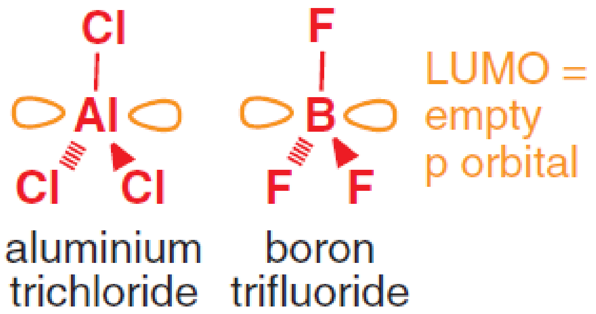


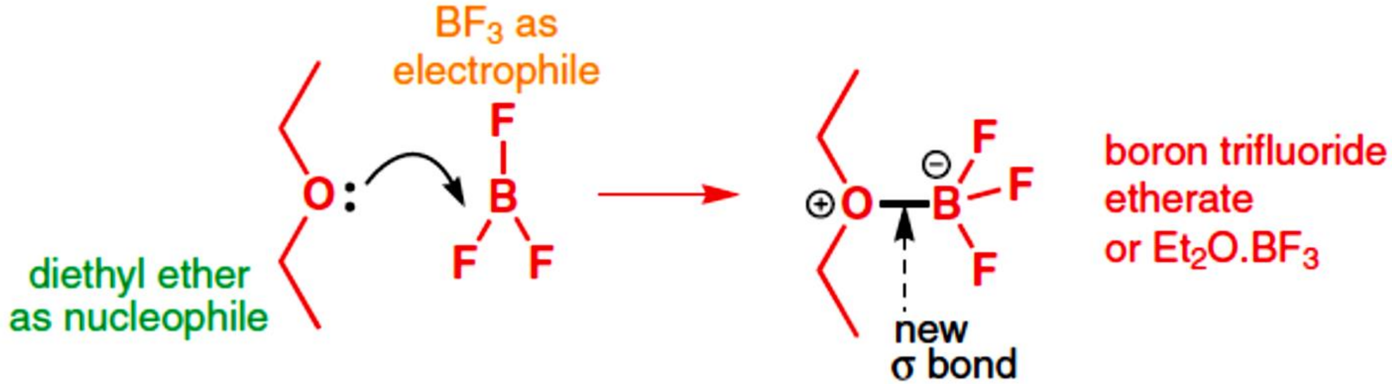
methyllithium

HOMO =
C–Li σ
orbital

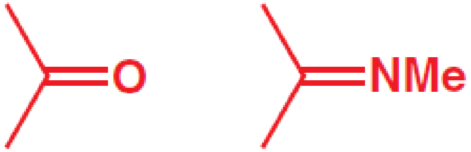


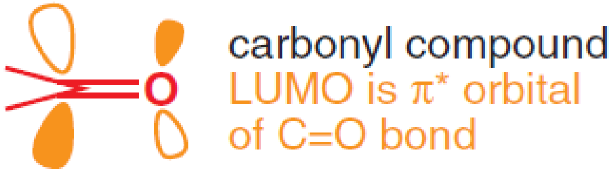


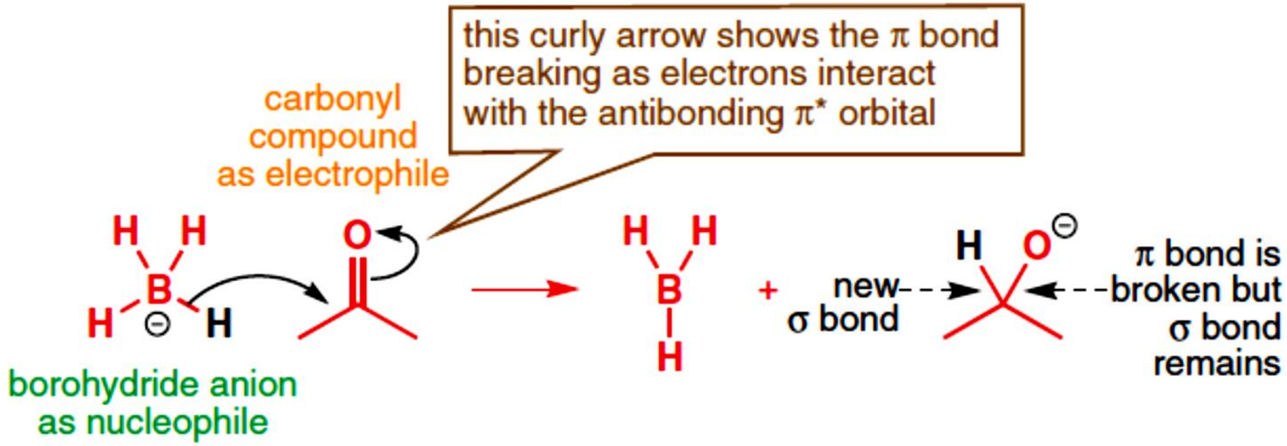


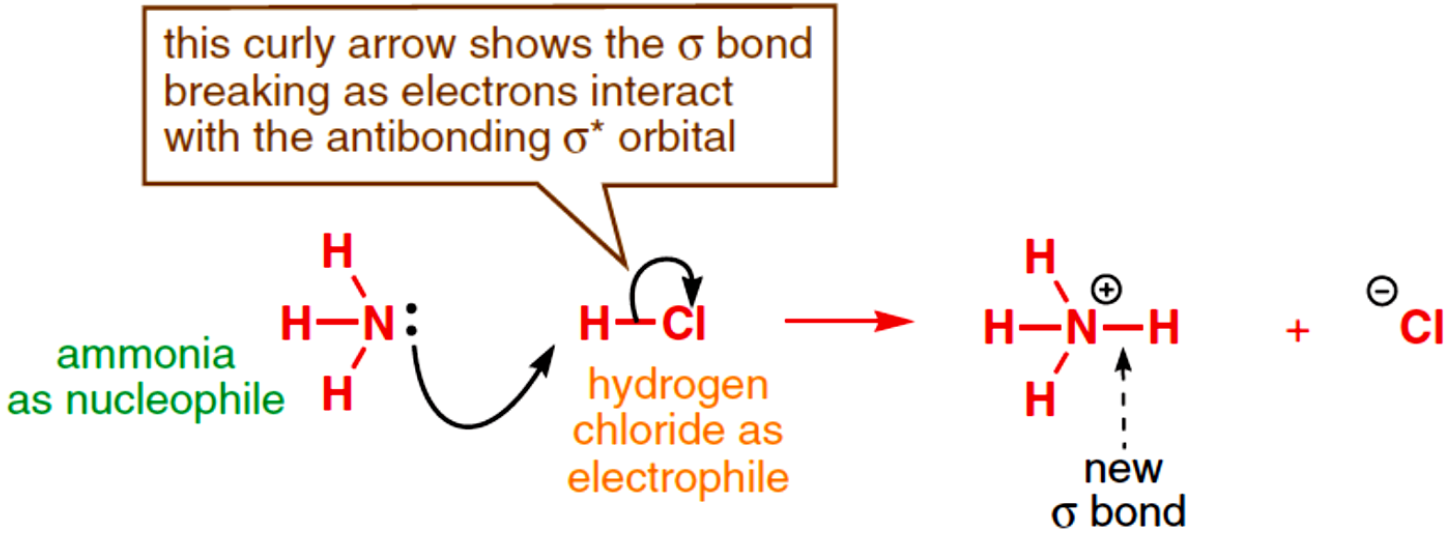


electrophiles with a **double-bonded electronegative atom**

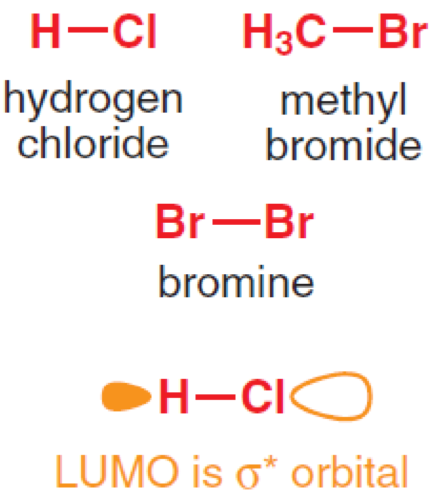


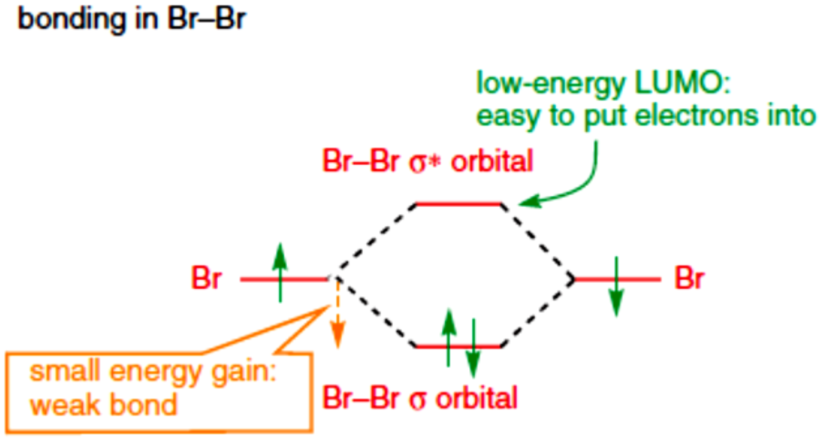


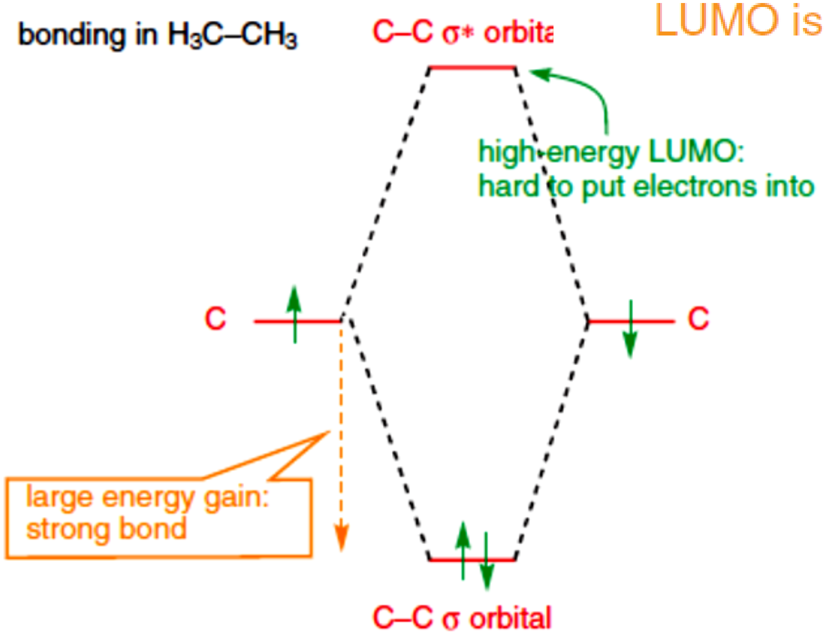


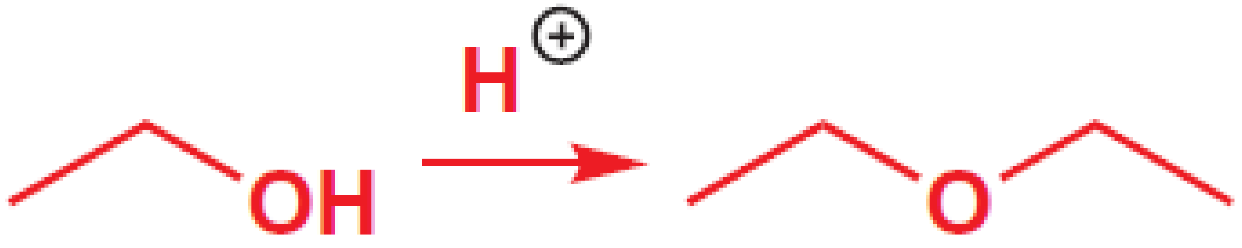


electrophiles with a **single bond to an electronegative atom**









ethanol

diethyl ether