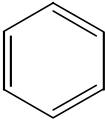


Chapter 1 Introduction to Organic Chemistry:

What is organic chemistry?

Functional Groups in Organic Chemistry:

R means

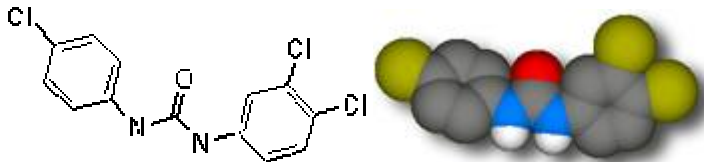
Group	Structure	Comments
Alkanes	R-H	
Alkenes	$R_2C=CR_2$	
Alkynes	$R-C\equiv C-R$	
Alkyl Halides	$R-X$ X = F, Cl, Br, I	
Aromatics		
Alcohol	R-OH	
Ether	R-O-R	
Amine	$RNH_2, R_2NH, \text{ etc}$	
Aldehyde	$R-\overset{\overset{O}{\parallel}}{C}-H$	
Ketone	$R-\overset{\overset{O}{\parallel}}{C}-R'$	
Carboxylic Acid	$R-\overset{\overset{O}{\parallel}}{C}-OH$	
Ester	$R-\overset{\overset{O}{\parallel}}{C}-O-R'$	
Amide	$R-\overset{\overset{O}{\parallel}}{C}-NR_2$	
Acyl Halide	$R-\overset{\overset{O}{\parallel}}{C}-X$	
Anhydride	$R-\overset{\overset{O}{\parallel}}{C}-O-\overset{\overset{O}{\parallel}}{C}-R$	
Nitrile	$R-C\equiv N$	

Why study organic chemistry?

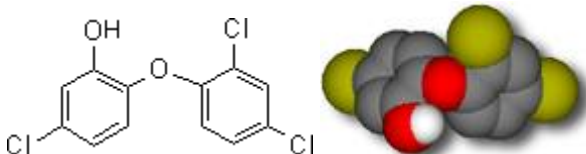
Case Studies from the internet:

Case 1. Antibacterials in Soap.

Triclocarban (also called TCC, Cutisan, Solubacter, and trichlorocarbanilide) is a trivial name for 3-(4-chlorophenyl)-1-(3,4-dichlorophenyl)urea:



Triclocarban. Click on the structures for a 3D [Chime](#) molecular model.



Triclosan. Click on the structures for a 3D [Chime](#) molecular model.

Triclosan (also known as CH 3635, Irgasan Ch 3635, Irgasan DP 300, and Ster-Zac) is shown at left; it has a similar structure.

Triclosan and triclocarban have been used as effective antiseptics in soap since the 1960's.

Triclosan has been incorporated into a wide range of consumer goods, including cosmetics, [toothpaste](#), and [plastics](#) for children's toys and kitchen and table utensils.

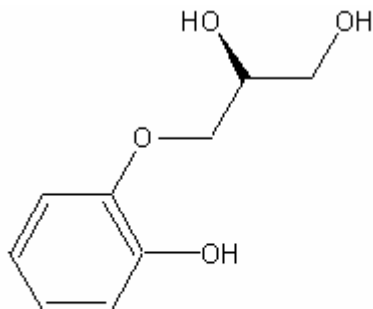
Neither substance is very soluble in water, but both are fat-soluble and easily cross cell membranes. Once inside the cell, triclosan poisons a specific enzyme that many bacteria and fungus need for survival. Triclosan blocks the active site of an enzyme called enoyl-acyl carrier-protein reductase (ENR for short), preventing the bacteria from manufacturing fatty acids it needs for building cell membranes and other vital functions. Humans don't have this enzyme, so triclosan is harmless to them. One molecule of triclosan permanently disables an ENR molecule, which explains why triclosan has powerful antibiotic action even at very low concentrations. Triclocarban's structural similarity suggests a similar mode of action.

The highly specific way that triclosan kills has researchers concerned about its role in fostering antibiotic-resistant strains of bacteria. Researchers have recently demonstrated that mutations in the bacterial gene that produces ENR can produce triclosan-resistant bacteria. Because triclosan is now so widespread in the environment, it's likely that new antibiotics targeting ENR would be ineffective.

From <http://antoine.frostburg.edu/chem/senese/101/consumer/faq/triclosan.shtml>

Case 2: Pharmaceuticals: Synthetic Drugs from natural products

Guaifenesin is a natural substance that was isolated around the early 1500's. Guaifenesin was purported to cure rheumatism. Though it has since been proven ineffective on rheumatism, it is at present, a widely used cough expectorant in nearly every cough, cold, flu, and allergy medication on the market.



(2S)-3-(2-hydroxyphenoxy)propane-1,2-diol

S(+)-Guaifenesin

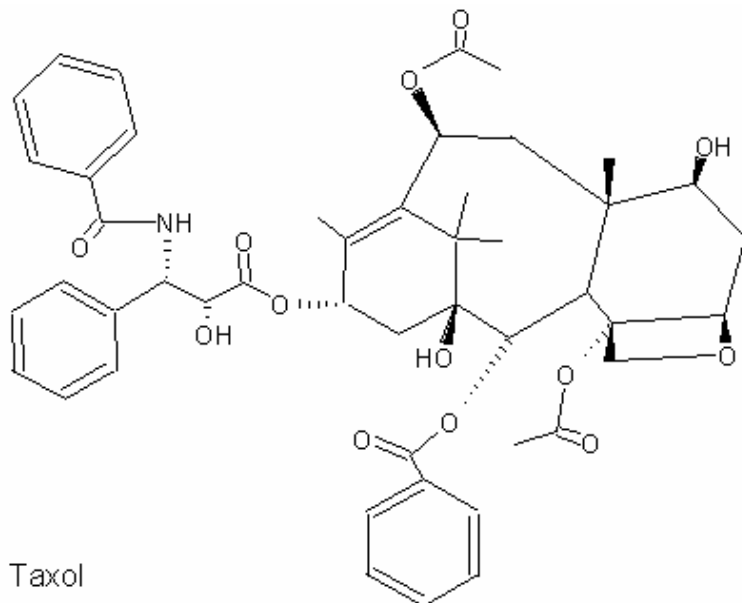
The extraction from the natural source involves a very simple steam distillation process followed by a series of acid-base extractions to remove the guaifenesin resin from the other substituents in the distillate.

As with most natural ingredients, the natural extraction processes are not efficient enough, or the compound simply isn't abundant enough from its natural sources for a large-scale distribution. Thus, synthetic processes must be designed to obtain the needed compound.

<http://facultystaff.vwc.edu/~jeaster/courseinfo/312/312Nature2003.html>

Taxol has been touted as the most promising anti-tumor agent of the twentieth century. It was approved for use as a chemosynthetic drug in the fight against ovarian cancer in 1994. Taxol was first discovered in nature in the Pacific Yew tree. The problem with using this source is that in order to harvest the taxanes from the bark the tree had to be killed. The Pacific Yew tree is the slowest growing tree in the world. To harvest enough taxanes to

make enough Taxol for one person with cancer would require the decimation of six two-hundred-year-old trees.



Taxol

5-beta, 20-epoxy-1,2-alpha,4,7-beta,10-beta,13-alpha-hexahydroxy-tax-11-en-9-one, 4,10-diacetate, 2-benzoate, 13-ester with (2R,3S)-N-benzoyl-3-phenyl-isoserine

Chemists have been working on a laboratory synthesis of Taxol since the early seventies. Three groups of chemists, as of 1996, have completely synthesized Taxol in the laboratory. Each of the groups used a slightly different method to synthesize Taxol many complicated rings. This synthesis however was very important, not just to the world of chemistry and medicine, but also to the cancer victims, who are now survivors. The complete synthesis of Taxol can be found in the three journal articles listed below.

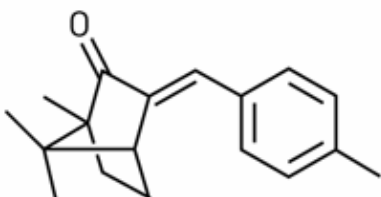
<http://facultystaff.vwc.edu/~jeaster/courseinfo/312/312Nature2003.html>

Nicolau, K.C., et al., Synthesis of Novel Taxoids, **1994**, *Journal of American Chemical Society*, **116**, pp. 1591-1592.

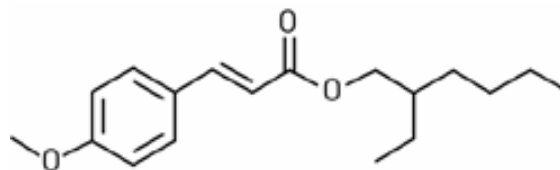
Holton, R.A., et al., First Total Synthesis of Taxol. 1. Functionalization of the B Ring, **1994**, *Journal of American Chemical Society*, **116**, pp. 1597-1598.

Danishefsky, S.J., et al., Total Synthesis of Baccatin III and Taxol, **1996**, *Journal of American Chemical Society*, **118** (12), pp. 2843-2859.

Case 3: Sunscreen chemicals:



4-Methylbenzylidene camphor



Octyl methoxycinnamate

THERE ARE TWO basic types of active ingredients: inorganic and organic. Both afford protection against UV-B rays in the 280- to 320-nm range, the primary culprits in sunburn. Some offer additional protection from UV-A rays in the 320- to 400-nm range, which can penetrate more deeply into the skin and do greater long-term damage.

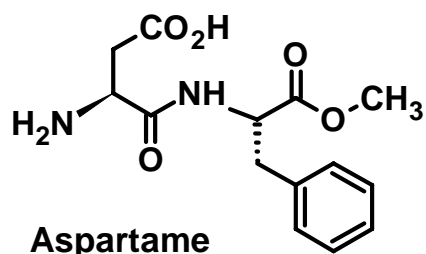
Inorganic sunscreens use titanium dioxide and zinc oxide. They work primarily by reflecting and scattering UV light. The organics include widely used ingredients such as octyl methoxycinnamate (OMC), 4-methylbenzylidene camphor (4-MBC), avobenzone, oxybenzone, and homosalate. They work primarily by absorbing UV light and dissipating it as heat.

Recent scientific work by environmental toxicologist Margaret Schlumpf and colleagues at the University of Zurich's Institute of Pharmacology & Toxicology suggests that OMC and 4-MBC—two widely used organic sunscreens—are potential endocrine disruptors. But industry research and government advisory committee reviews have disputed the work. The Food & Drug Administration still approves OMC for use in the U.S., though it never approved 4-MBC. The European Union's Scientific Committee for Cosmetic Products & Non-Food Products continues to approve OMC and 4-MBC.

From [MARC REISCH](#), June 24, 2002 Volume 80, Number 25, CENEAR 80 25 p. 38, ISSN 0009-2347 – web site: <http://pubs.acs.org/cen/whatstuff/stuff/8025sunscreens.html>

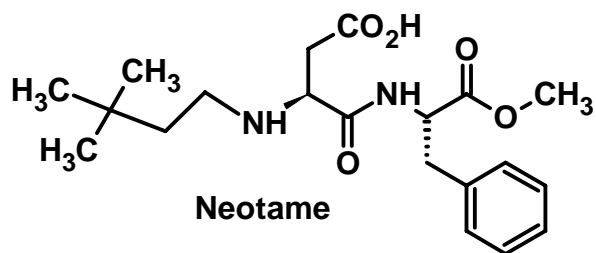
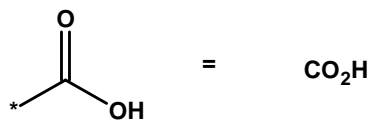
Case 4: Artificial Sweeteners

Aspartame is synthesized from aspartic acid and phenylalanine. The body breaks down aspartame into these amino acids along with a small amount of methanol. Methanol is metabolized to formaldehyde and formic acid. Formaldehyde is classified by the World Health Organization as a probable human carcinogen and is the major source of controversy over aspartame's safety.



Aspartame

However, Walters says, people with the rare genetic disorder phenylketonuria (PKU) lack an enzyme for properly metabolizing phenylalanine, so they need to regulate their aspartame intake. In the U.S., all products containing aspartame must, by law, carry a warning for PKU patients.

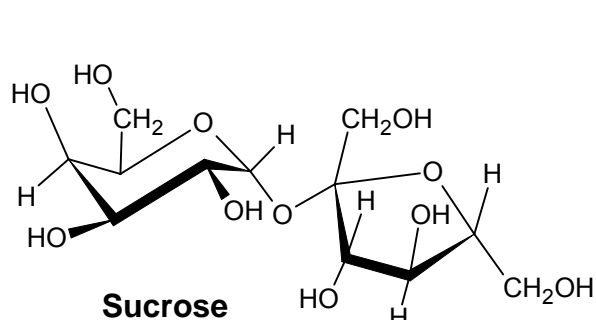


Neotame

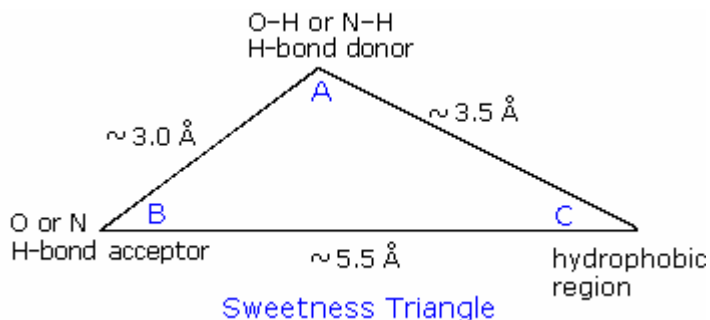
Neotame, a new FDA-approved sweetener derived from aspartame, has a structure that prevents the peptide bond between phenylalanine and aspartic acid from breaking, making it safer for PKU patients.

By [VICTORIA GILMAN](#), June 21, 2004, Volume 82, Number 25, p. 43, Chemical & Engineering News, ISSN 0009-2347 Copyright © 2004 – web

<http://pubs.acs.org/cen/whatstuff/stuff/8225sweeteners.html>

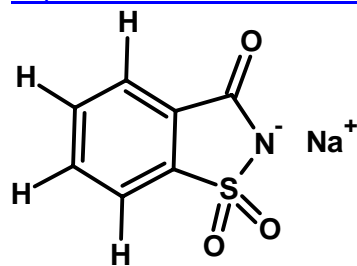


Sucrose

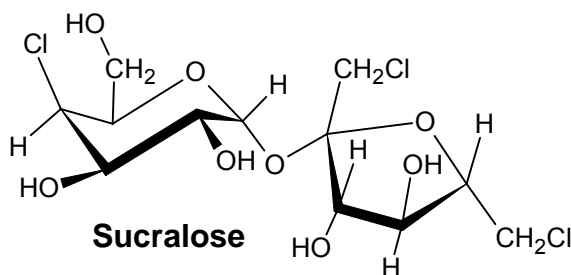


Sweetness Triangle

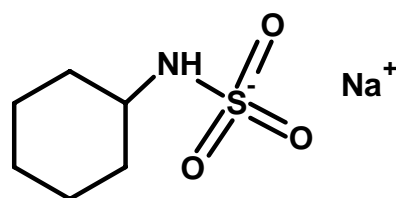
<http://www.cem.msu.edu/%7ereusch/VirtualText/carbhyd2.htm#swet>



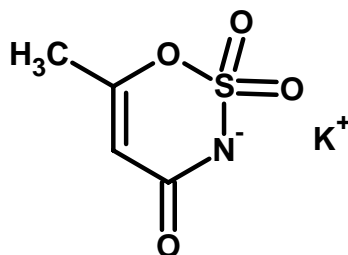
Saccharin



Sucralose



Cyclamate



acesulfame-K

Orbitals and Bonding. Review of atomic orbitals.:

Draw an s orbital:

Nu

For the s orbital: Where is an electron likely to be found?

Draw the 3 p orbitals:

Nu

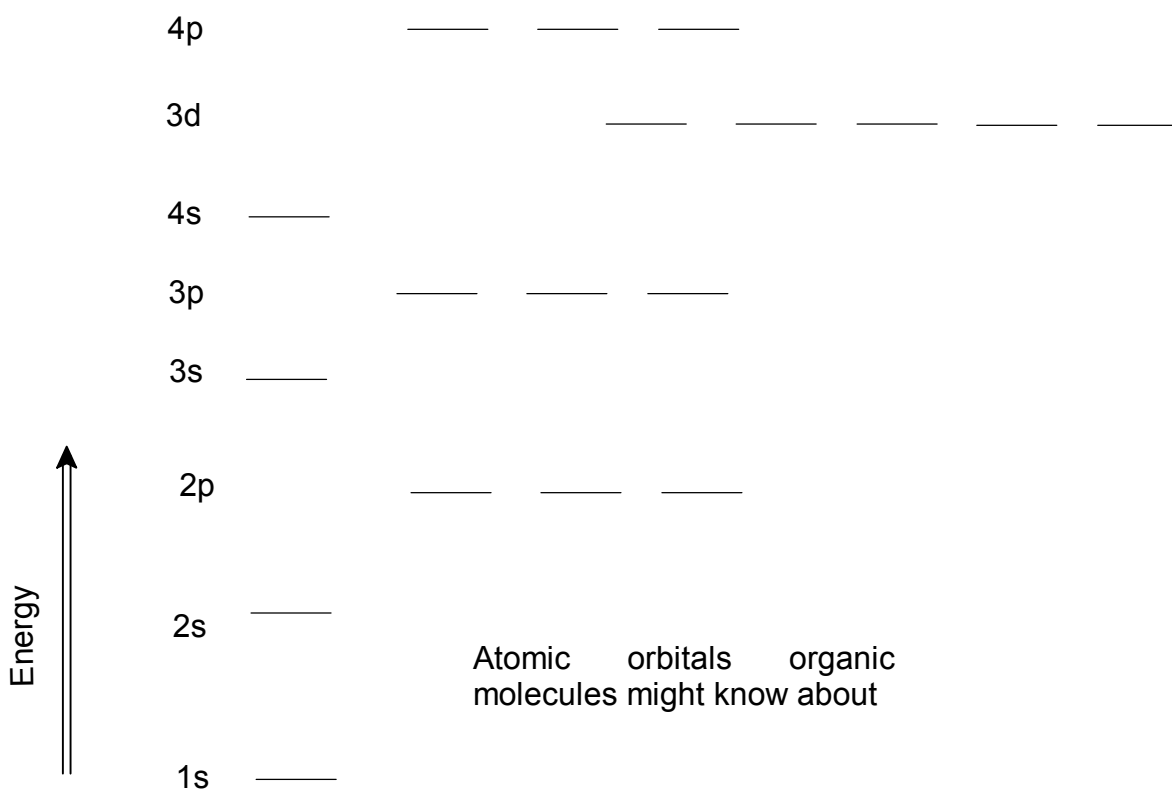
Nu

Nu

For p orbitals: Where is an electron likely be found? Where is an electron not likely be found?

Which orbital is more stable?

What is the meaning of expanded shells?



AUFBAU Principal:

Using s and p orbitals, we can describe most of the properties of the non-metallic atoms and some metals.

Let's get reacquainted around the periodic table:

The top row: H

He

1s

1s

The main row: Li

Be

B

C

N

O

F

Ne

[1s²]

2s

2s

2p

2p

2p

2p

2p

2p

The next row:

Na

Mg

Al

Si

P

S

Cl

Ar

[1s² 2s² 2p⁶]

3s

3s

3p

3p

3p

3p

3p

3p

Next:

some metals: Cr, Mn, Ni, Cu, Zn

Br

[Ar]4s²3d¹⁰

4p

Next:

more metals: Pd, Ag, Sn

I

[Kr]5s²4d¹⁰

5p

Finally:

more metals: Os, Pt, Hg, Pb

VALENCE and the Octet Rule: The number of electrons (Group #) or the # of deficient electrons to the closed shell (octet) will give an approximation of how many other atoms can be attached to this atom.

Go through the top row.

The main row.

The 3rd row..

What are the main differences between the main row and the next row?

General Bonding Rules for neutral molecules.

Atom	H	B	C	N	O	F,Cl,Br,I
Bonds						
Examples						

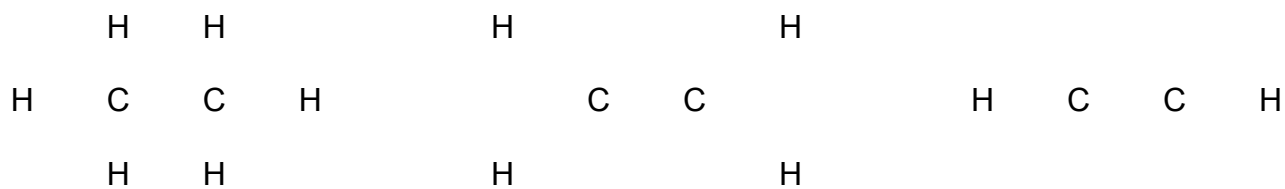
This is simplified, we will look at charged molecules after Lewis Structures.

Lewis Structures:

Basic Concepts for drawing molecules correctly:

1. Total # of electrons = Sum(# of electrons from each atom) Anion => add e^- ; Cation => subtract e^- .
2. Arrange atoms, unique atom almost always in the center.
3. Arrange electrons to make **octets around all "main row"** atoms. Row 3 can **expand octets**.
4. Match the electron count with total number of electrons and assign **formal charge**.
5. The least formal charge is the best structure. Other structures may be possible:
Resonance.

Electron counting. How many electrons? Then fill in the bonds and lone pairs.



Alternatively, think about connectivity.
C with 3H has how many bonds to C?

C with 2H has how many bonds to C?

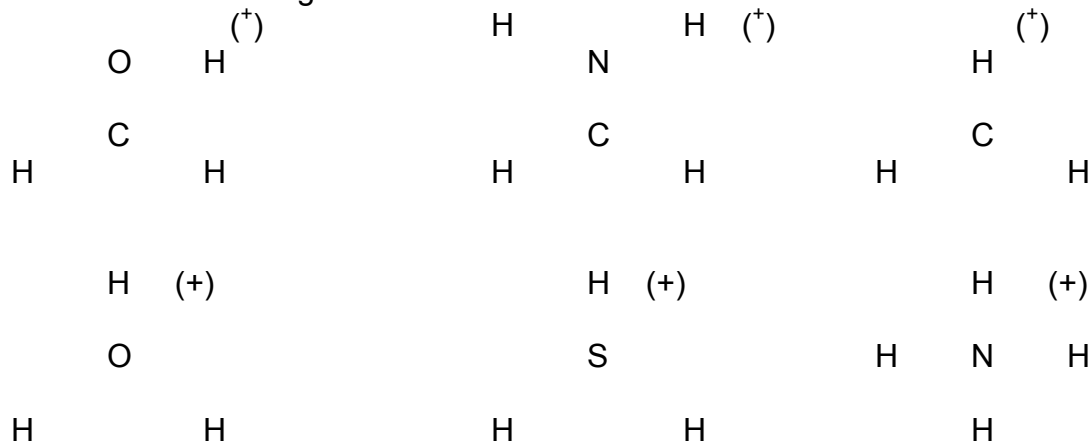
C with 1H has how many bonds to C?

Charged Molecules

General Bonding Rules for charged molecules.

Atom	H ⁺	H: ⁻	C ⁺	C ⁻	N ⁺	N ⁻	O ⁺	O ⁻	X ⁻
Bonds									
Examples									

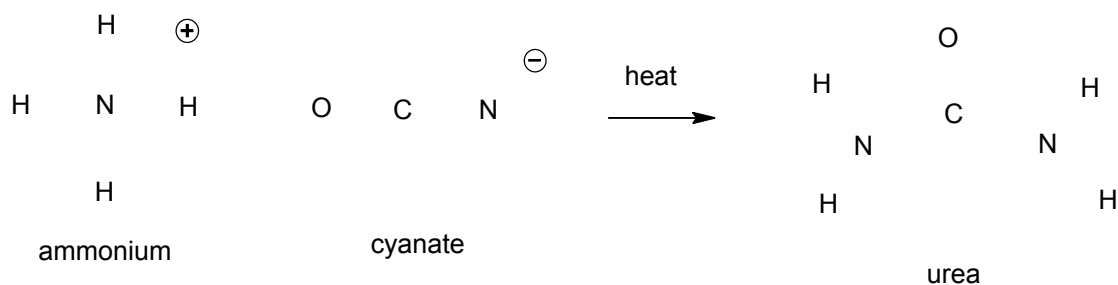
Consider these charged structures:



We will consider calculating individual atomic charges in the next chapter.

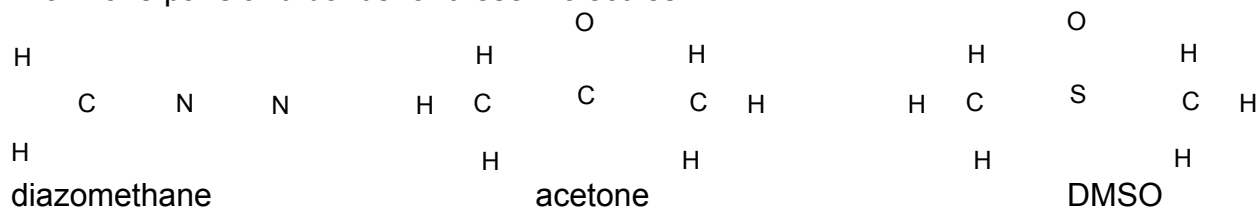
The first organic reaction. In the 1860's, a German chemist Friedrich Wöhler found that if he heated the salt, ammonium cyanate, he made something that smelled familiar. He verified it was what he thought it was.

Draw proper structures for the following reaction: $\text{NH}_4^+ \text{OCN}^- \rightarrow \text{H}_2\text{NCONH}_2$



Drawing Organic Molecules

Draw lone pairs and bonds for these molecules.

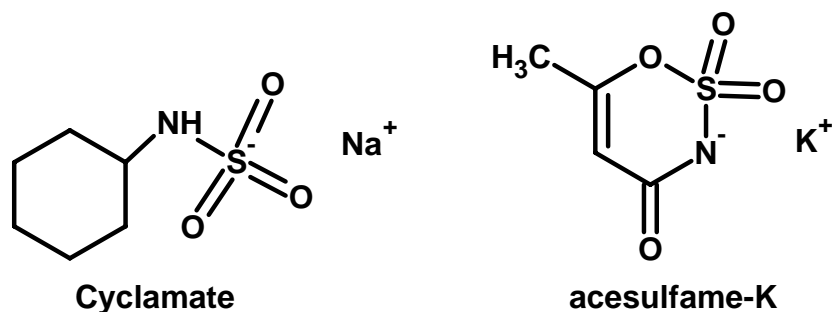


Fusing valence bond theory and Lewis structures.

The simple neutral hydrogen forms of the elements:

Element	Compound	Element	Compound
H		O	
Li		P	
Be		Al	
B		Si	
C		P (trivalent)	
N		P (pentavalent)	

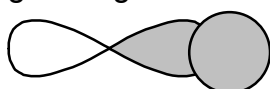
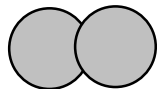
Counting C's, H's, N's and O's (and S)



Sigma and Pi bonds.

Sigma bonds form the framework of molecules.

Which of the following are sigma bonds?

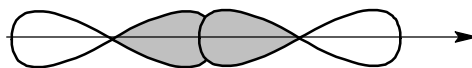
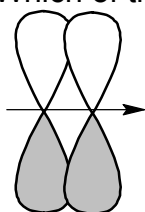


Identify the sigma bonds in the structures above.

What happens when you break a sigma bond?

Pi bonds are formed outside the main framework of the molecule.

Which of the following are pi bonds?

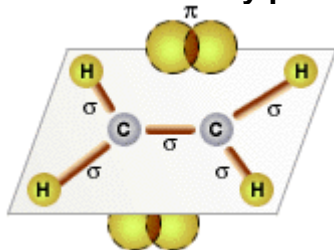


Identify the pi bonds in the structures above. What happens when you break a pi bond?

Where do the terms sigma and pi bonds come from?

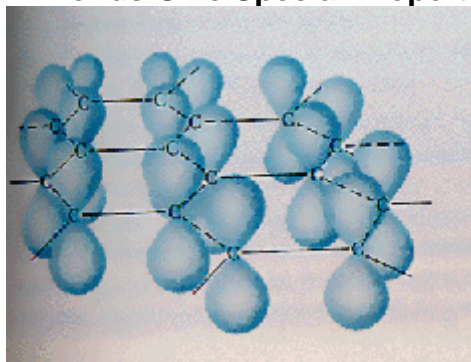
Using toothpicks and paper clips make some sigma and pi bonds.

Here is summary picture showing both sigma and pi bonds in ethylene.

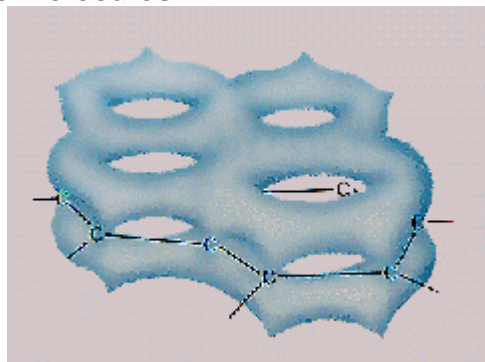


graphic from http://home.att.net/~cat6a/carb_bonds-I.htm

Pi Bonds Give Special Properties to Organic Molecules



atomic p orbitals

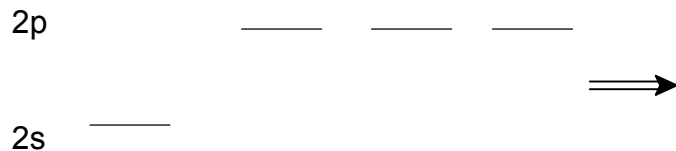


bonding pi orbitals

above graphics from: <http://invsee.asu.edu/nmodules/Carbonmod/pibond.html>

Hybridization: a simple labeling system that explains molecular shape and reactivity. To assign hybridization count the number of areas of electron density around an atom. Because of the limitation of the octet rule: we consider the case of 2, 3 and 4 areas. This leads to the possibility of 2, 3, or 4 bonds for C. Here are the energy levels of the 2nd row.

Atomic orbitals in 2nd row

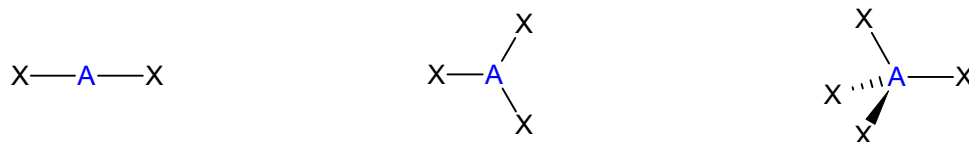


For 4 sigma bonds, we would need $s + p + p + p = sp^3$
Consequently, there would be the possibility of _____ pi bonds.

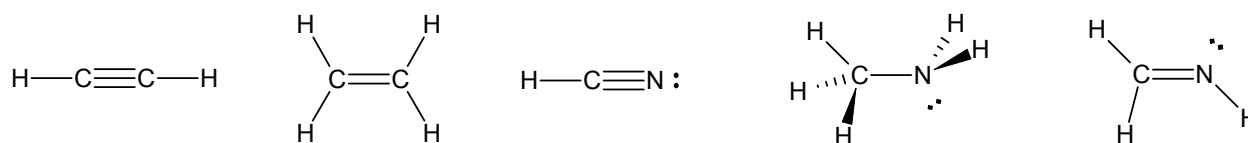
For 3 sigma bonds, we would need $s + p + p = sp^2$
Consequently, there would be the possibility of _____ pi bonds.

For 2 sigma bonds, we would need $s + p = sp$
Consequently, there would be the possibility of _____ pi bonds.

Shapes can be predicted by the same theory. Count the areas of electron density around the following atoms A. These are the basic shapes. **Linear 180°; trigonal planar 120°; tetrahedral 109.5°.**



Now for some real structures:



Note LP count as attachments (like sigma bonds)
Double/triple bonds don't count: only sigma bonds.

Figuring out hybridization is straight forward. For the 2nd row, we have one 2s orbital and 3 2p type orbitals. 2s is more stable than p, so it is always included in the new hybrid orbital. We use hybrids to describe bonding between 2 atoms, 3 atoms, and 4 atoms. Hybrid orbitals are just the mix of the s and the p orbitals.

For 4 attachments, $s+p+p+p$, called sp^3 . All possible s and p orbitals are used. This is called saturated. For sp^3 , we have 1 part s and 3 parts p.

The percentage of s = _____ The percentage of p = _____.

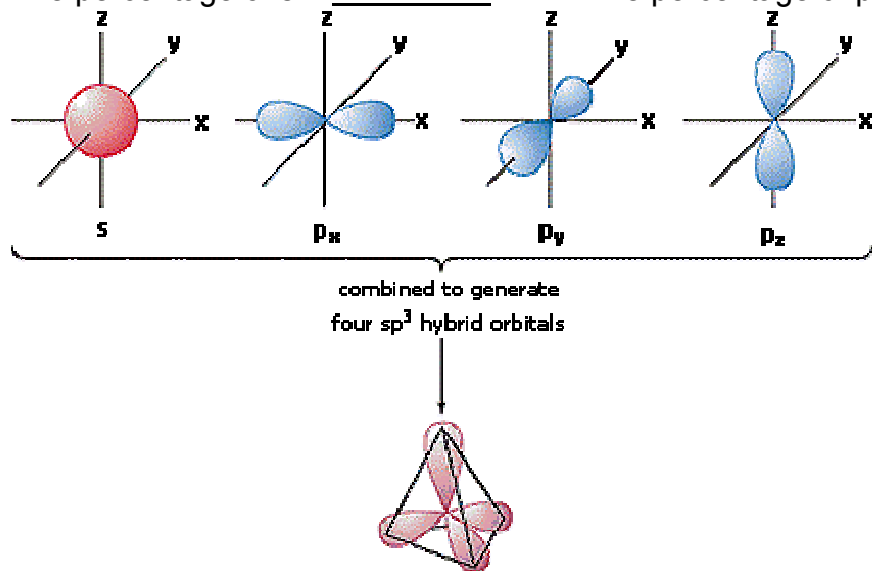


Figure used with permission: <http://www.cem.msu.edu/~reusch/VirtualText/intro3.htm#strc8>

Also see: <http://alumni.imsa.edu/~ishmael/bonding/hy/sp3.html>

Describe the shape and structure of CH_4 .

Describe the shape and structure of NH_3 .

Describe the shape and structure of H_2O .

For 3 attachments, $s+p+p =$.

2 parts p and 1 part s. The percentage of s = _____ The percentage of p = _____.

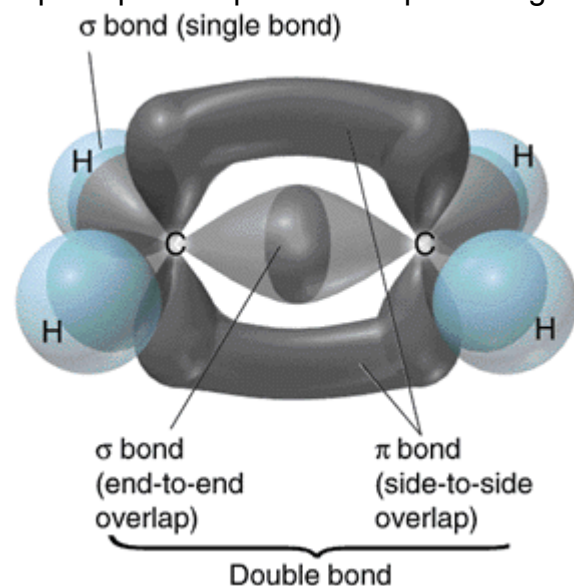


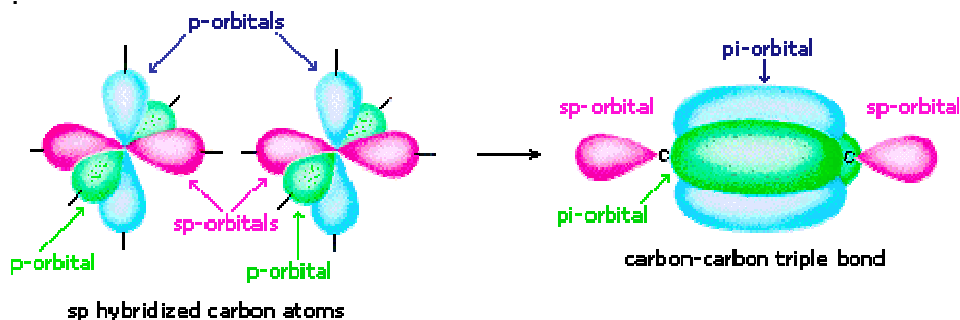
Figure used without permission:

http://chem.ufl.edu/~chm2040/Notes/Chapter_12/multiple.html

See also: <http://alumni.imsa.edu/~ishmael/bonding/hy/sp2.html>

Describe the bonding in $\text{CH}_2=\text{CH}_2$.Draw and describe the bonding in BH_3 .**For 2 attachments, $s + p =$**

2 parts p and 1 part s. The percentage of s = _____ The percentage of p = _____.

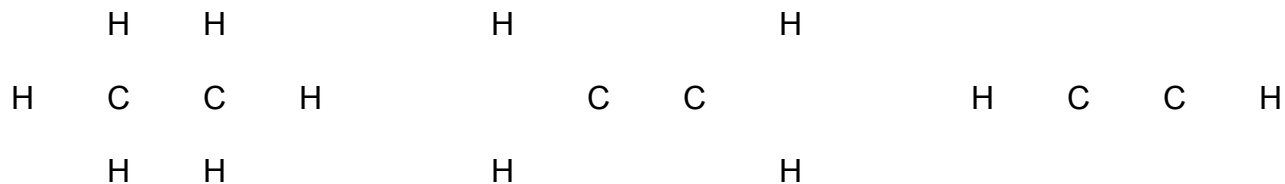
Figure used with permission: <http://www.cem.msu.edu/~reusch/VirtualText/intro3.htm#strc8>See also: <http://alumni.imsa.edu/~ishmael/bonding/hy/sp2.html>Describe the bonding in $\text{H}-\text{C}\equiv\text{C}-\text{H}$ Describe the bonding in $\text{H}-\text{C}\equiv\text{N}:$ Describe the bonding in $:\text{C}\equiv\text{O}:$

The systematic consequences of hybridization.

Comparison of bond types. You need to know relative values.

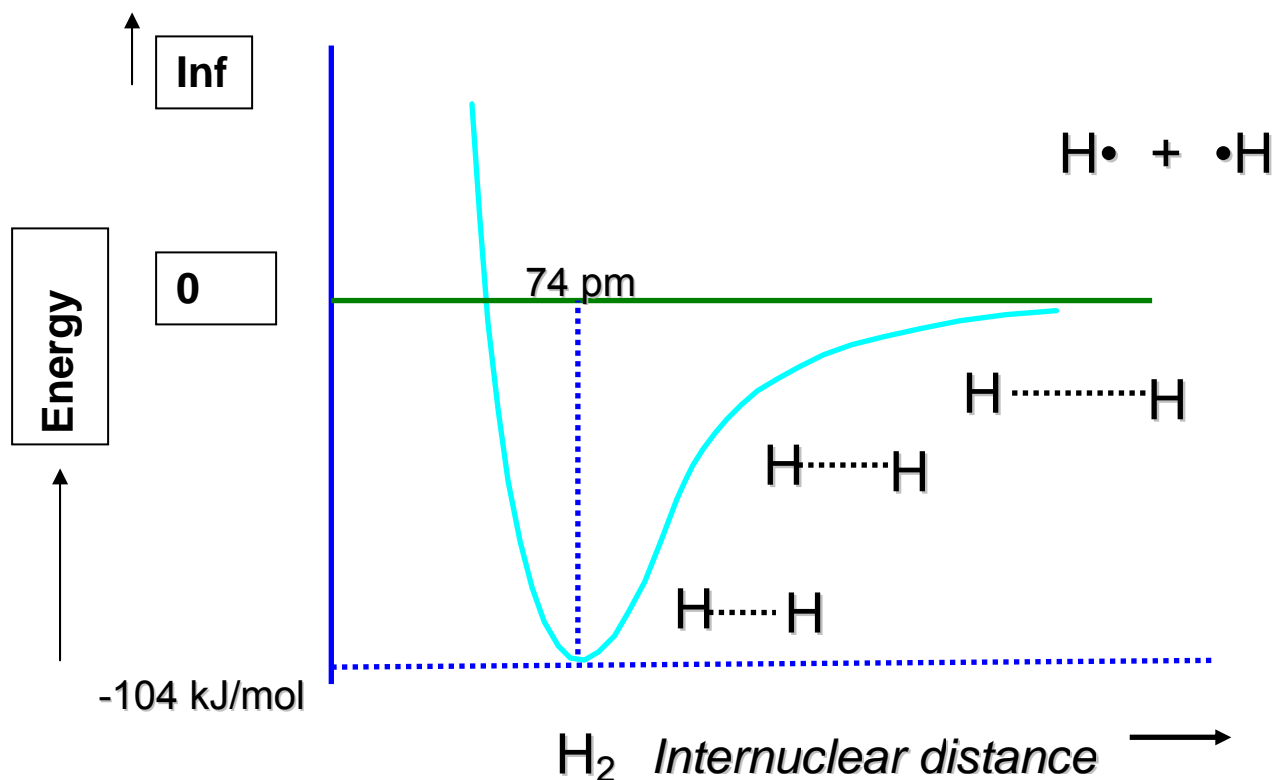
Systematic name	Ethane	Ethene	Ethyne
Hybrid orbitals of C	sp^3	sp^2	sp
Structural formula	$\text{H}_3\text{C}-\text{CH}_3$	$\text{H}_2\text{C}=\text{CH}_2$	$\text{H}-\text{C}\equiv\text{C}-\text{H}$
C-C Bondlength pm	154	134	120
C-H Bondlength pm	112	110	106
bond angle (H-C-C) $^\circ$	110	121	180
C-C BE kcal/mol	88	150	200
C-H BE kJcalmol	100	110	130

Indicate weak to strong. Indicate short to long?

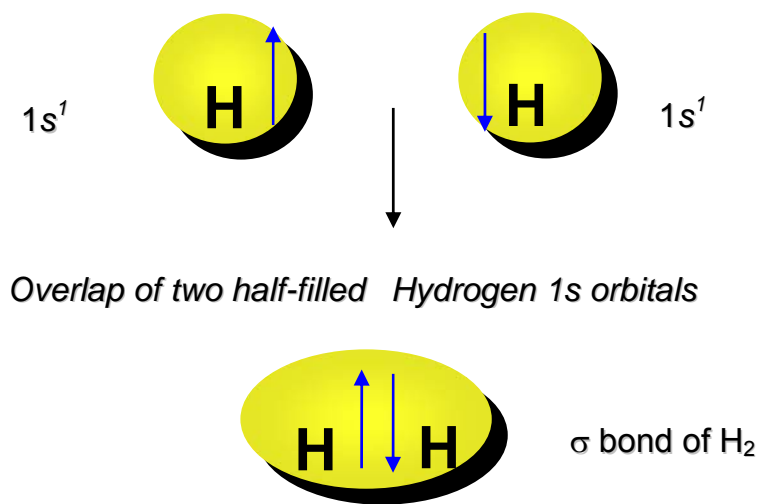


More in depth picture of bonding

Imagine what happens when 2 H[•] atoms come together from infinite distance in space.



Valence Bond Model of Molecular Bonding



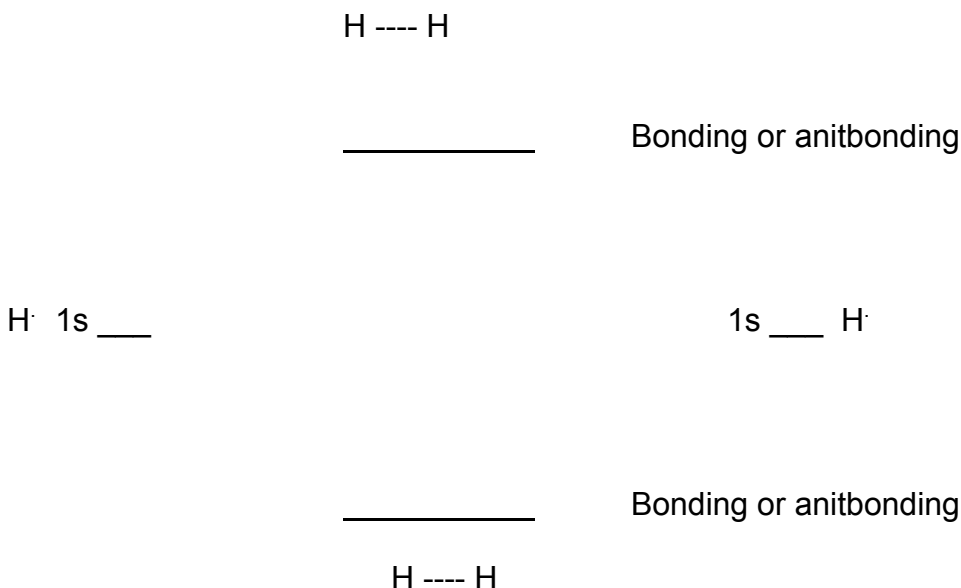
Hybrid orbitals are very useful and are in the common language of organic chemistry. Valence bond orbitals are simple to understand. But neither of these models are mathematically correct. So, we need a better model.

Molecular Orbitals

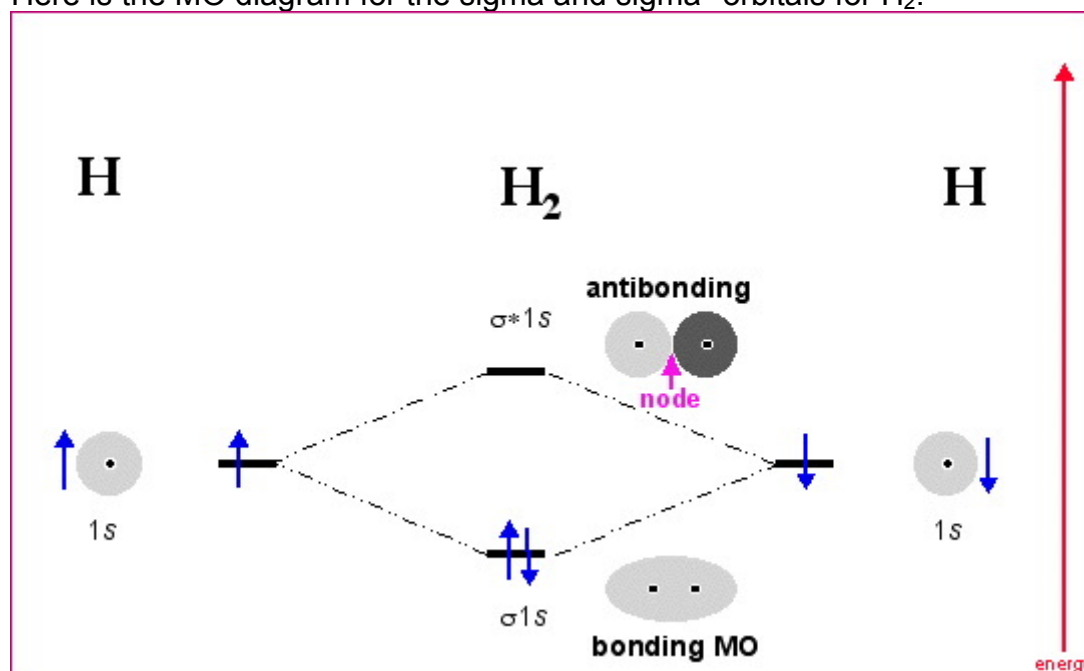
Atomic orbitals come together to make molecular orbitals. Here are some basic rules:

1. Start with the atomic orbitals and electrons.
2. Sum of atomic orbitals and the # of electrons. For every atomic orbital, there is a Molecular orbital. # of electrons in the molecule = # of electrons from atoms
3. Build the orbitals from most stable to least stable from bottom up.
4. Fill the electrons in the orbitals according to Hund's Rule using Pauli Exclusion Principle..
5. For neutral even number electron systems, there are as many filled orbitals as unfilled.

Construct an MO picture of H₂. Label the new orbitals drawn.



Here is the MO diagram for the sigma and sigma* orbitals for H₂.



Graphic from: http://www.meta-synthesis.com/webbook/39_diatomics/diatomics.html

Meaning of MO diagrams

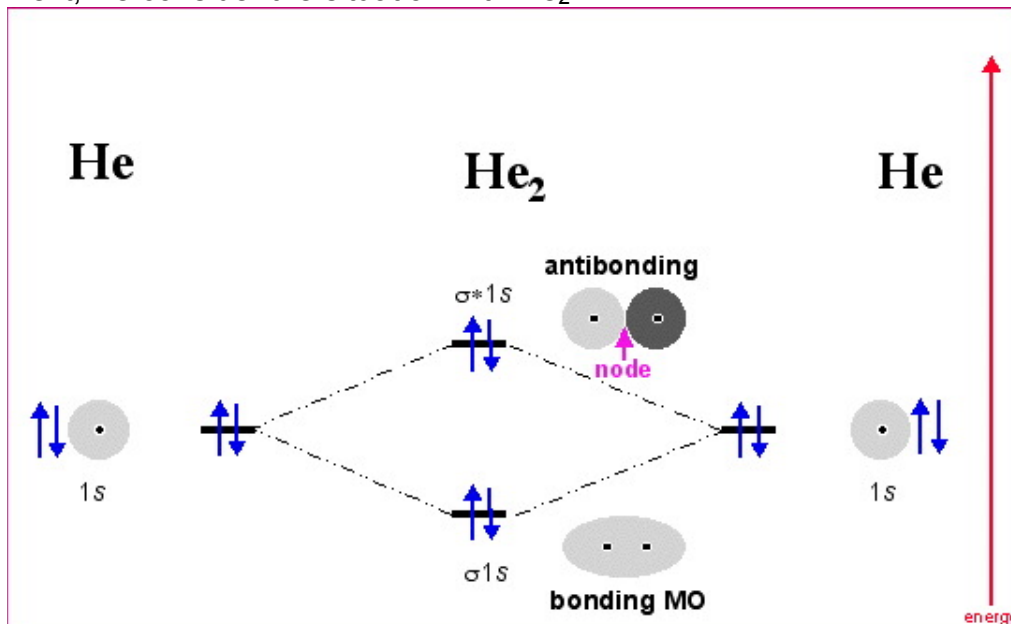
Bond order.

The bond order is based on the number of bonding orbitals (pi and sigma) minus the number of antibonding orbitals (pi* or sigma*).

H₂ has a bond order = _____.

Is H₂ a stable molecule? Why or why not?

Next, we consider the situation with He₂.

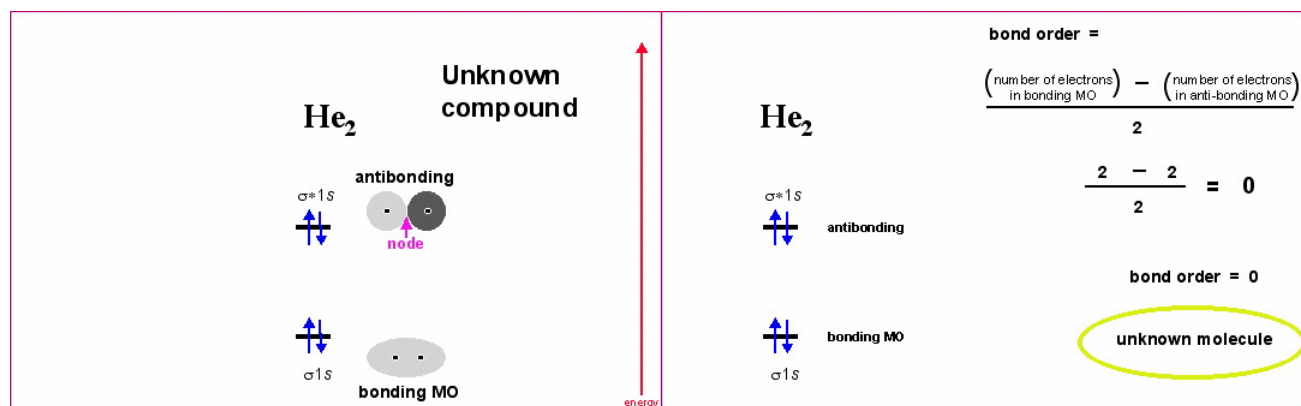


Graphic from: http://www.meta-synthesis.com/webbook/39_diatomics/diatomics.html

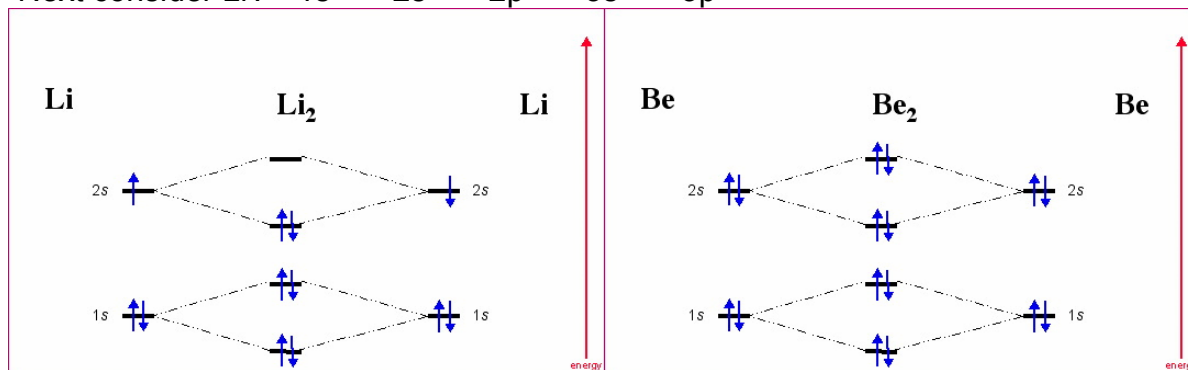
What is the bond order for He₂? _____

Is He₂ predicted to be stable or not?

The MO diagram for He₂⁺⁺

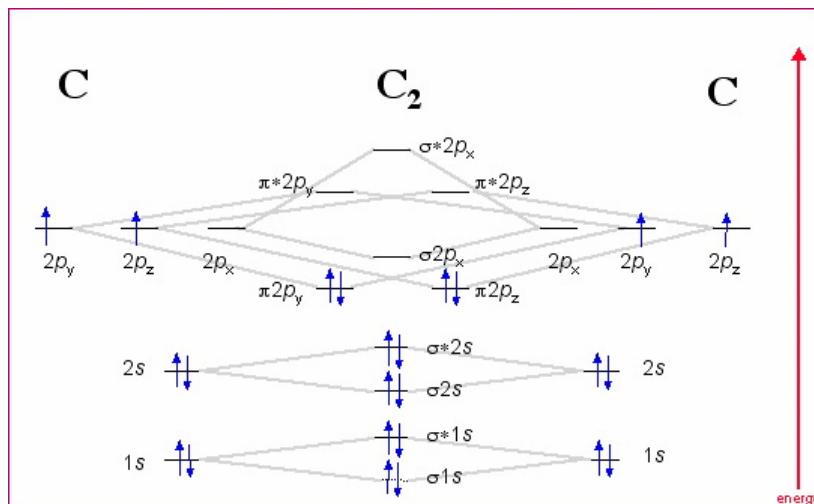
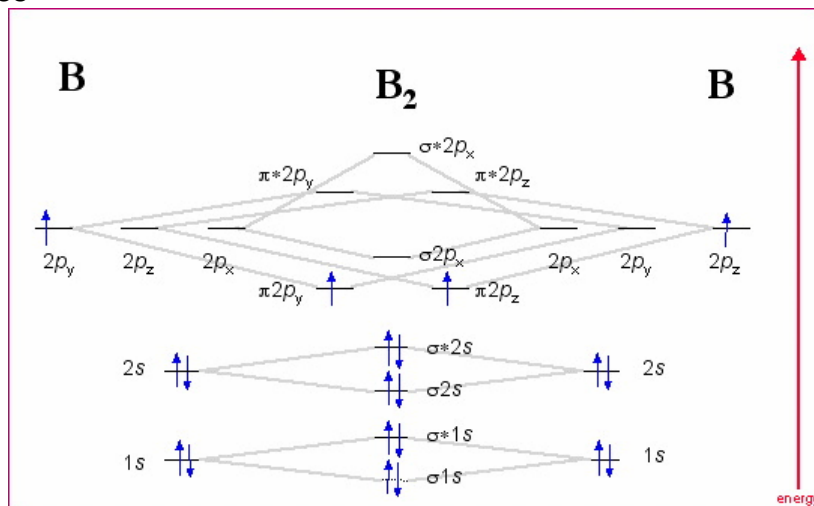


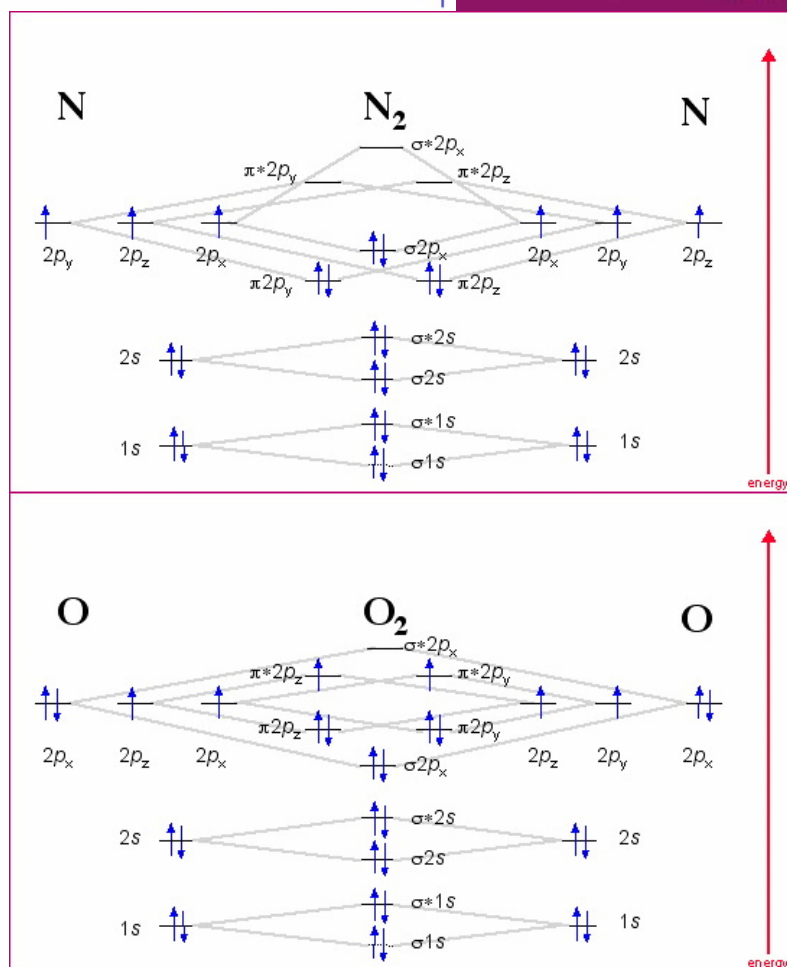
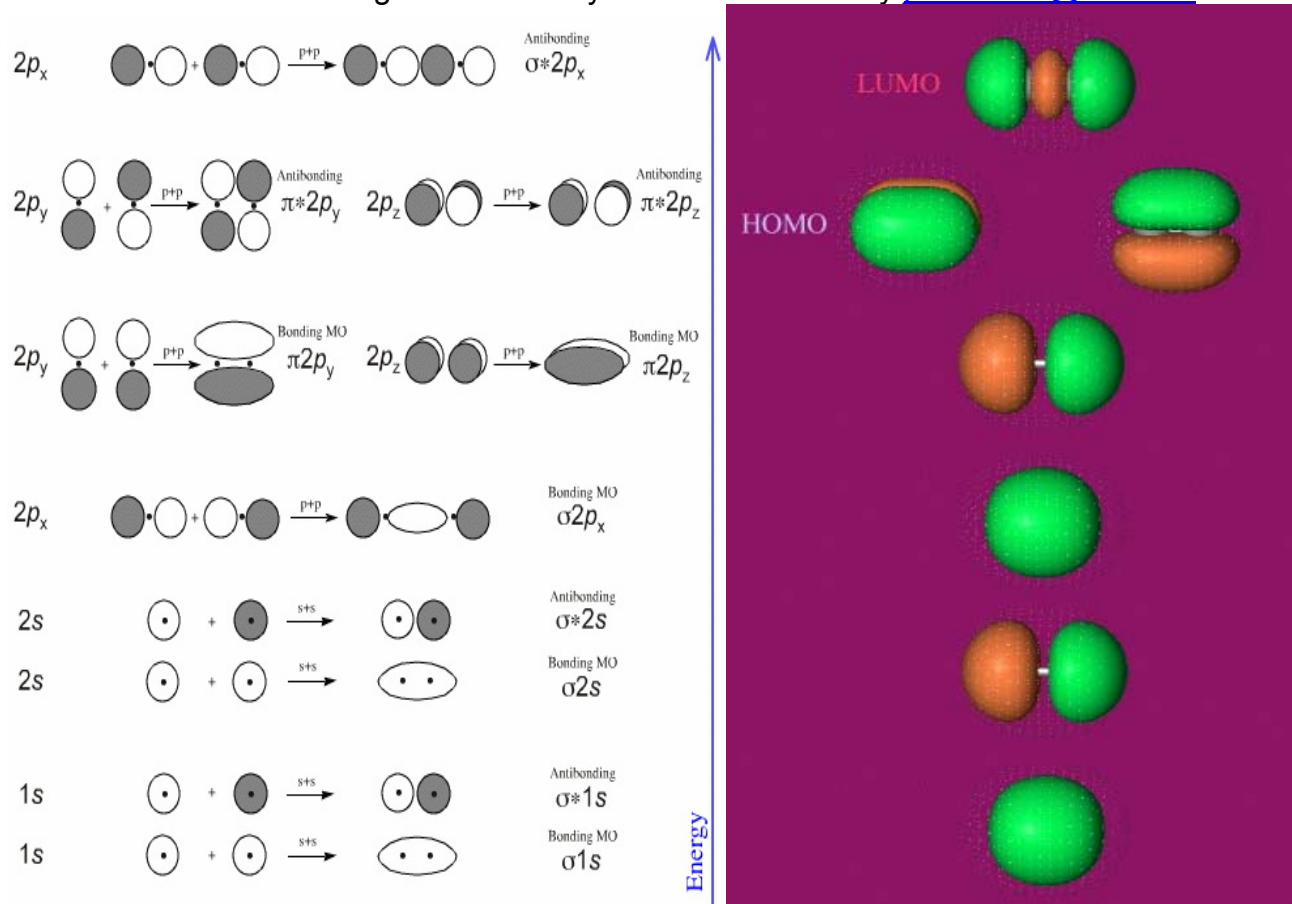
Next consider Li. 1s 2s 2p 3s 3p



What is the bond order for Li_2 ? _____ Is Li_2 predicted to be stable or not?
 What is the bond order for Be_2 ? _____ Is Be_2 predicted to be stable or not?
 Which molecule is more stable?

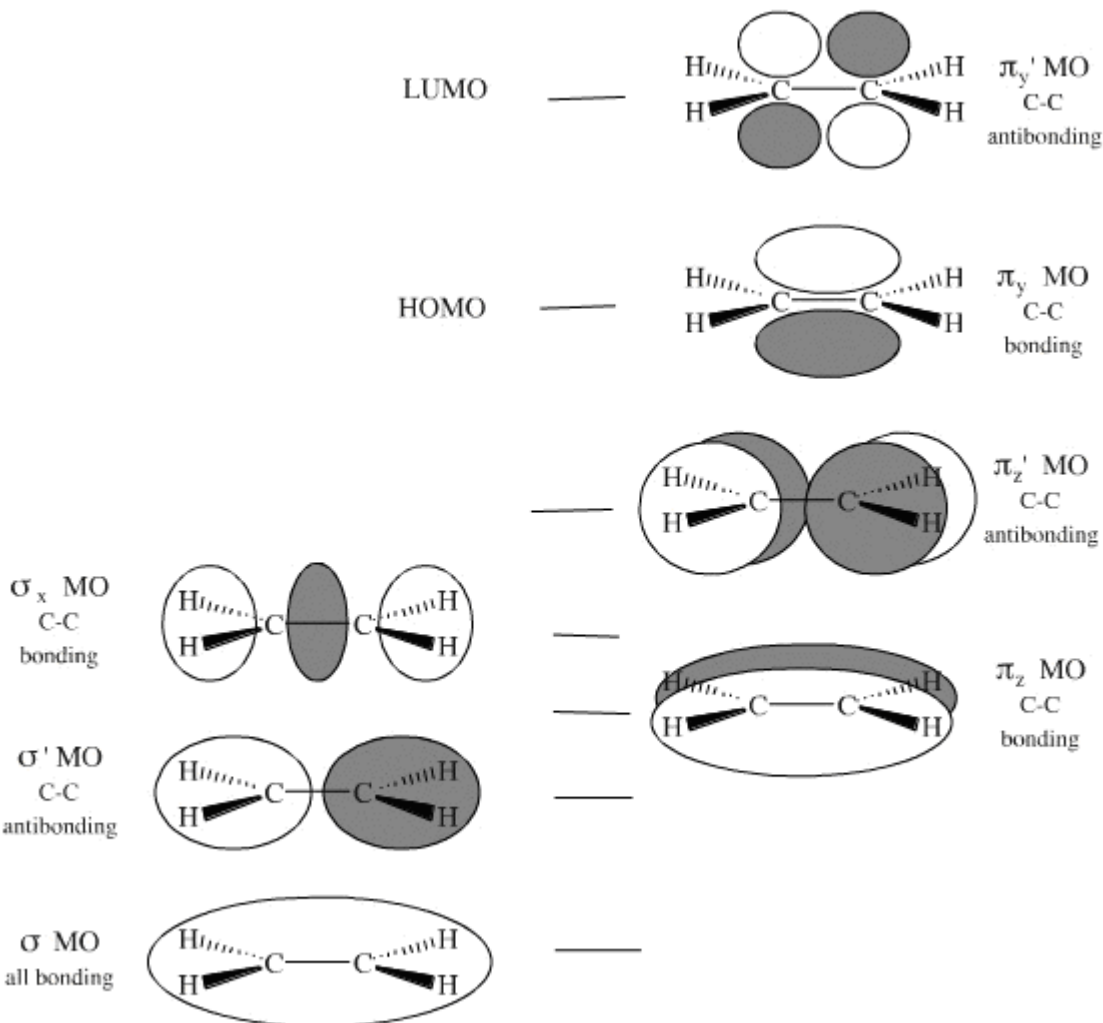
Magnetic Properties





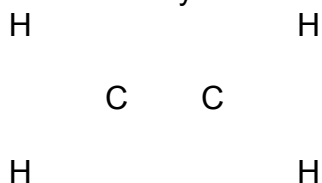
Putting it all together. Sigma and Pi Ethylene can be analyzed in the same manner. For molecules with p orbitals, the highest energy occupied molecular orbital (HOMO) is always a pi orbital and lowest energy unoccupied orbital (LUMO) is always pi*. There are many orbitals too stable to react. The reactive orbitals are classified as HOMO and LUMO.

How many orbitals are left out. Are they bonding?



Graphic modified from: http://www.meta-synthesis.com/webbook/39_diatomics/diatomics.html

Draw the Lewis Structure for ethylene.



How many sigma bonds?

How many pi bonds?

How do the VB and MO analyses differ?

Summaries

1. Learn the functional groups. Make notecards. Review functional groups 2 times a week.
2. Have a clear idea of the difference of s and p orbitals in shape and energy.
3. Memorize the valence rules for neutral and charged atoms in the tables on pps.5-6.
4. Be able to draw simple Lewis Structures for neutral and charged molecules.
5. Have a clear idea of the difference of sigma and pi orbitals in shape and energy.
6. Be able to recognize and construct hybrid orbitals on 2nd row elements.
7. Based on a Lewis structure, be able to determine the hybridization of atoms.
8. Rationalize how the properties of simple C-H compounds correspond to hybridization
9. Understand the difference between the valence bond and the molecular orbital model.
10. Be able to draw a simple molecular orbital structure of diatomic molecules.
11. Be able to assign sigma and pi orbitals from shapes and pictures.
12. Be able to predict the bond order of molecules and interpret the stability or instability of the bonds
13. Work problems from the back of the chapter 1:
1.21-1.48 (if it gets too tedious, skip some of the multipart –a,b,c,etc.-)