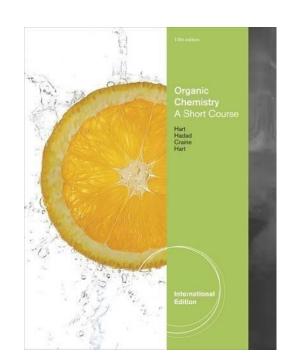
Chem 237 Basics of Organic Medicinal Chemistry

Course description

This is the first year organic chemistry course, introducing basic concepts and principles of organic chemistry (chapters 1-11).

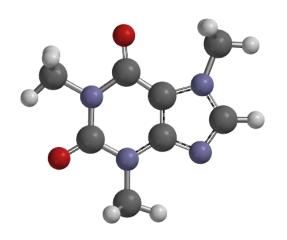
Texts

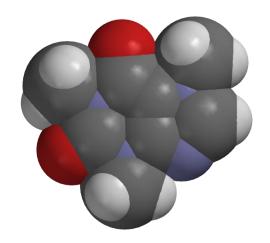
Hart, Craine, Hart and Hadad, Organic Chemistry, A Short Course,13th Edition (Brooks/Cole, Cengage Learning, CA 94002-3098 USA, 2012).



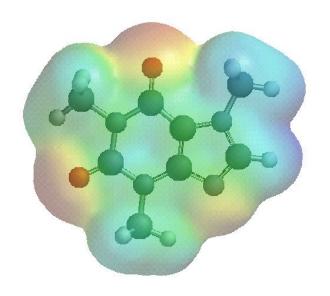
Periodic Table of the Elements

1 IA 1 Hydrogen 1008	2 IIA				Atomic Number	→ Hydr	ogen	· Symbol · Atomic Weight				13 IIIA	14 IVA	15 VA	16 VIA	17 VIIA	18 VIIIA 2 He Helium 4,0026
3 Lithium 6.94 2-1	Beryllium Politic Beryllium P								Oxygen 15,999 2-6	9 Fluorine 18.998 2-7 17	Ne Neon 20.180 2-8						
Sodium 22,987/6928 2-8-1	Mg Magnesium 24:305 2-8-2 20	3 IIIB	4 IVB	5 VB 23	6 VIB	7 VIIB	8 VIIIB	9 VIIIB	10 VIIIB	11 IB 29	12 IIB 30	Aluminium 26.982 2-8-3	Silicon 28.085 2-8-4	Phosphorus 30,974 2-8-5	Sulfur 32.06 2-8-6	Chlorine 35.45 2-8-7	Argon 39,948 2-8-8
Potassium 39,0983 2-8-8-1	Calcium 40.078 2-8-8-2	Sc Scandium 44.955908 2-8-9-2 39	Titanium 47.867 2-8-10-2	Vanadium 50,9415 2-8-11-2	Cr Chromium 51,9961 2-8-13-1 42	Mn Manganese 54.938044 2-8-13-2	Fe Iron 55.845 2-8-14-2	Co Cobalt 58,933 2-8-15-2	Nickel 58.693 2-8-16-2	Cu Copper 63.546 2-8-18-1	Zn Zinc 65,38 2-8-18-2	Gallium 69.723 2-8-18-3	Ge Germanium 72.630 2-8-18-4	As Arsenic 74,922 2-8-18-5	Se Selenium 78.971 2-8-18-6	Bromine 79,904 2-8-18-7	Krypton 83.798 2.8-18-8
Rb Rubidium 85.4678 2-8-18-8-1	Sr Strontium 87.62 2-8-18-8-2	Yttrium 88.90584 2-8-18-9-2	Zr Zirconium 91.224 2-8-18-10-2	Niobium 92.90637 2-8-18-12-1	Molybdenum 95,95 2-8-18-13-1 74	Technetium (98) 2-8-18-13-2	Ru Ruthenium 101.07 2-8-18-15-1 76	Rhodium 102.91 2-8-18-16-1	Pd Palladium 106.42 2-8-18-18	Ag Silver 107.87 2-8-18-18-1	Cd Cadmium 112.41 2-8-18-18-2	Indium 114.82 2-8-18-18-3	Sn Tin 118.71 2-8-18-18-4 82	Sb Antimony 121.76 2-8-18-18-5	Tellurium 127.60 2-8-18-18-6	lodine 126.90 2-8-18-18-7	Xe Xenon 131.29 2-8-16-18-8
Cs Caesium 132,90545196 2-8-18-18-8-1	Ba Barium 137,327 2-8-18-18-8-2	57-71 Lanthanides	Hafnium 178.49 2-8-18-32-10-2	Tantalum 180.94788 2-8-18-32-11-2	Tungsten 183.84 2-8-18-32-12-2	Re Rhenium 186.21 2-8-18-32-13-2	Osmium 190.23 2-8-18-32-14-2	Iridium 192.22 2-8-18-32-15-2	Pt Platinum 195.08 2-8-18-32-17-1	Gold 196.97 2-8-18-32-18-1	Mercury 200.59 2-8-18-32-18-2	Thallium 204.38 2-8-18-32-18-3	Pb Lead 207.2 2-8-18-32-18-4	Bi Bismuth 208.98 2-8-18-32-18-5	Po Polonium (209) 2-8-18-32-18-6	Astatine (210) 2-8-18-32-18-7	Rn (222) 2-8-18-32-18-8
Francium (223) 2-8-19-32-18-8-1	Radium (226) 2-8-18-32-18-8-2	89-103 Actinides	Rf Rutherfordium (267) 2-8-18-32-32-10-2	Db Dubnium (268) 2-8-18-32-32-11-2	Sg Seaborgium (269) 2-8-18-32-32-12-2	Bh Bohrium (270) 2-8-18-32-32-13-2	Hs Hassium (277) 2-8-18-32-32-14-2	Mt Meitnerium (278) 2-8-18-32-32-15-2	Ds Darmstadtium (281) 2-8-18-32-32-17-1	Rg Roentgenium (282) 2-8-18-32-32-17-2	Cn Copernicium (285) 2-8-18-32-32-18-2	Nh Nihonium (286) 2-8-18-32-32-18-3	Flerovium (289) 2-8-18-32-32-18-4	Moscovium (290) 2-8-18-32-32-18-5	Livermorium (293) 2-8-18-32-32-18-6	Ts Tennessine (294) 2-8-18-32-32-18-7	Og Oganesson (294) 2-8-18-32-32-18-8
		57 La Lanthanum 138.91 2-8-18-18-9-2	58 Ce Cerium 140.12 2-8-13-17-9-2	59 Pr Praseodymium 140.91 2-8-18-21-8-2	Neodymium 144.24 2-8-18-72-8-2	Promethium (145) 2-8-18-23-8-2	502 Sm Samarium 150.36 2-8-18-74-8-2	63 Eu Europium 151.96 2-8-18-25-8-2	64 Gd Gadotinium 157.25 2-8-18-25-9-2	65 Tb Terbium 158.93 2-8-18-27-8-2	Dy Dysprosium 162.50 2-8-18-23-8-2	67 Ho Holmiun 164,93 2-8-18-27-8-2	68 Er Erbium 167.26 2-8-18-30-8-2	69 Tm Thulium 168,93 2-8-18-31-8-2	70 Yb Ytterbium 173.05 2-8-18-32-8-2	71 Lu Lutetium 174.97 2-8-18-32-9-2	
		Ac Actinium (227)	70 Th Thorium 232.04	Protactinium 231.04	92 U Uranium 238.03	Np Neptunium (237)	Plutonium (244)	Am Americium (243)	Cm Curium (247)	97 Bk Berkelium (247)	Cf Californium (251)	99 Es Einsteinium (252)	Fermium (257)	Md Mendelevium (258)	Nobelium (259)	Lr Lawrencium (266)	



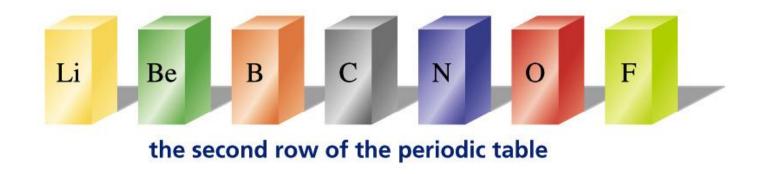


Chapter 1: Bonding and Isomerism



Organic Chemistry

Organic compounds are compounds containing carbon

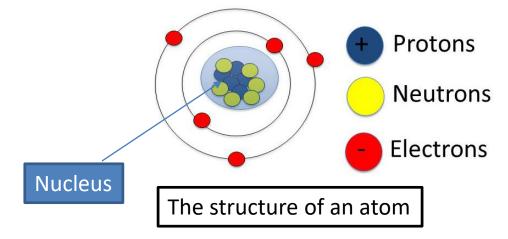


- Atoms to the left of carbon give up electrons.
- Atoms to the right of carbon accept electrons.
- Carbon shares electrons.

Bonding and Isomerism

1.1 How Electrons Are Arranged in Atoms

- An atom is: the *smallest particle* of an element that retains all of the chemical properties of that element.
- •An atom consists of negatively charged electrons, positively charged protons, and neutral neutrons



- **Atomic number**: numbers of protons in its nucleus and it's the number of electrons in the neutral atom.
- Mass number: the sum of the protons and neutrons of an atom. (Protons and neutrons are ~1837 times the mass of an e⁻)
- •Isotopes have the same atomic number but different mass numbers (¹²C and ¹³C)

- Electrons are located in atomic orbitals (S, P, d, f).
- Orbitals tell us the energy of the electron and the volume of space around the nucleus where an electron is most likely to be found.
- Orbitals are grouped in shells.

Each orbital can hold a maximum of 2e⁻ and the two electrons have opposite spin

Table 1.1	Table 1.1 Distribution of Electrons in the First Four Shells That Surround the Nucleus							
		First shell	Second shell	Third shell	Fourth shell			
Atomic orb	oitals	S	s, p	s, p, d	s, p, d, f			
Number of atomic orbitals		1	1, 3	1, 3, 5	1, 3, 5, 7			
Maximum	number of electrons	2	8	18	32			

Example:

¹H:

6C

Valence electrons (VE) are located in the outermost shell. They are involved in chemical reactions.

VE = Group number

	VE	Lewis symbol of atom
Examples: ¹ H: Is ¹	1	H·
⁸ O: IS ² 2S ² 2P ⁴	6	 :
⁶ C:		

Group		II	Ш	IV	V	VI	VII	VIII
	Н٠							He:
	Li•	· Be·	• B •	· ċ ·	· N:	• 0:	:F:	: Ne
	Na ·	· Mg ·	• ΔI •	· Si ·	. D ·	·S:	: Cl :	: Ar :

Chemical Bonds

1. lonic Bonding

An ionic bond is an electrostatic attraction between positive & negative ions resulting from e- transfer.

¹¹Na : [Ne] 3s¹
$$\xrightarrow{-e}$$
 Na : [Ne]

¹⁷Cl: [Ne] 3s¹ 3p⁵ $\xrightarrow{+e}$ Cl : [Ar]

Na-Cl

The resulting e⁻ configuration of both ions are those of the nearest noble gas, Ne and Ar respectively, both satisfy the octet rule.

2. Covalent Bonding

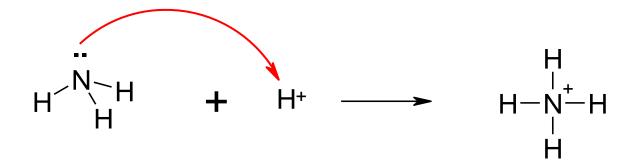
- Ionic bonds occur when an e⁻ is transferred between a metal and nonmetal.
- Covalent bonds are resulting from sharing e

The result is both atoms have a [He] e⁻ configuration, i.e.

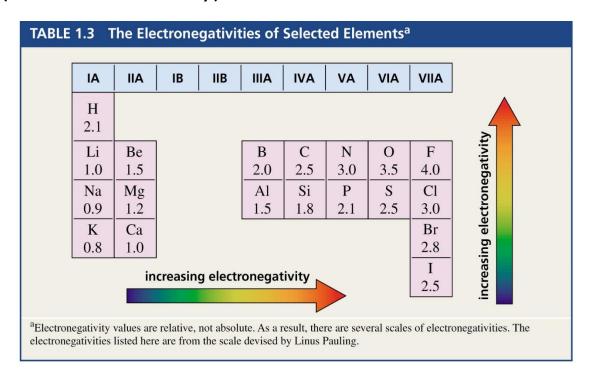
The bond is commonly display as a line rather than a pair of $e^{-}(:)$, *i.e.* H - H rather than H: H

A second general version of a covalent bond is possible. This occurs when BOTH e⁻ come from one atom: a coordinate covalent bond *i.e.*

$$NH_3 + H^+ \rightarrow NH_4^+$$



Electronegativity (EN): measures the tendency of an atom to attract a shared pair of electrons (or electron density).



Covalent bonds can be classified as

A. Nonpolar covalent bond (\triangle EN = 0-0.5)

Examples C-C C-H

B. Polar covalent bond (\triangle EN = 0.5 1.9)



N - H

A polar bond has a negative end and a positive end

dipole moment (D) = $\mu = e \times d$

(e): magnitude of the charge on the atom

(d): distance between the two charges

Table 1.4	The Dipole Moments of Some Commonly Encountered Bonds						
Bond	Dipole moment (D)	Bond	Dipole moment (D)				
н-с	0.4	C-C	0				
H-N	1.3	C-N	0.2				
н—о	1.5	C-O	0.7				
H—F	1.7	C-F	1.6				
H—Cl	1.1	C—Cl	1.5				
H—Br	0.8	C—Br	1.4				
H—I	0.4	C—I	1.2				

if The Δ EN increases the polarity increases

Note: If Δ EN is more than 1.9then the bond is ionic Ex: Li-F

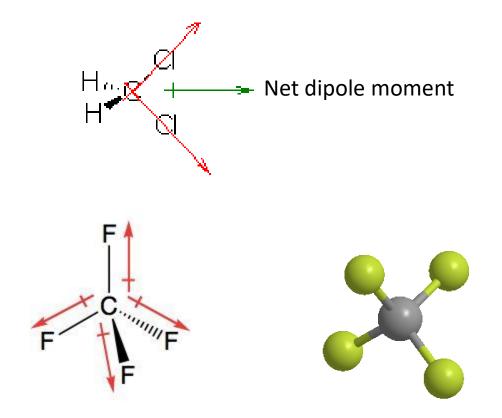
Bond Polarity & Electronegativity (cont'd)

The result of polar covalent bonding is that the e⁻ pair spend more time near the more EN atom. This means it will acquire a permanent excess negative charge. The other atom acquires a permanent excess positive charge. This is indicated by a δ^+ or δ^- (where δ means a "partial charge") or a dipole arrow which points from the positive end of the bond to the negative end.

$$\delta^+$$
 δ^- H-Cl

Bond Polarity & Electronegativity (cont'd)

The more polar the molecule the stronger the dipole moment. The molecular dipole moment is the vector sum of the bond moments, i.e.



Net dipole moment =0

Lewis Structures It only deals with VE

Procedure for obtaining good Lewis structures: eg. CO₂

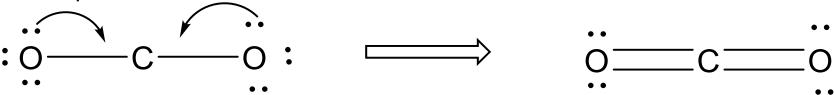
- 1) determine total number of valence shell e^{-} (including ionic charge if present). $CO_2 = 4+2(6) = 16$.
- 2) Chose a cental atom and draw a skeleton of the molecule connected with single bonds. (the central **atom** is usually the **least electronegative element** in the **molecule** or **ion**; hydrogen and the halogens are usually terminal.

$$0$$
— C — C

3) determine number of remaining e⁻. complete the octet of the terminal atoms.

$$16 - 4 = 12$$

4) Complete the octet Use lone pair e⁻ from terminal atoms to create multiple bonds.



5) determine the formal charges of all atoms.

Formal charge = number of valence electrons – (number of lone pair electrons +1/2 number of bonding electrons)

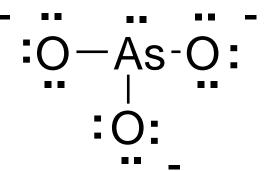
Ex: NO₃

1. VE= 5+6*3+1 =24

Lewis Structures (other examples)

Example 2: AsO₃³-

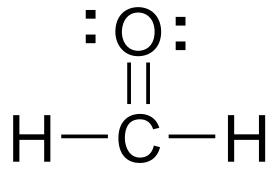
- 1) $\# e^{-}$: 5 + 3(6) + 3 = 26
- 2) form 3 single bonds
- 3) 20 e⁻ remain
- 4) O needs 6, As needs 2
- 5) All octets
- 6) Formal charges



Lewis Structures (cont'd)

Example 3: CH₂O

- 1) $\# e^{-}$: 4 + 2(1) + 6 = 12
- 2) try 3 single bonds
- 3) 6 e⁻ remain
- 4) O 6 but C?
- Form a double bond
- 6) Both O & C octets
- 7) Formal charges



Lewis Structures (cont'd)

Example 4: CO

- 1) $\# e^{-}$: 4 + 6 = 10
- 2) try 1 single bond
- 3) 8 e⁻ remain
- 4) C needs 6 as does O short 4 e⁻
- 5) Share 4 more e⁻ triple bond
- 6) Octets
- 7) Formal charges

- -1 +1
- :C≡O:

1.8 Isomers

Structural or **constitutional** isomers have same molecular formula but different structural formula.

They have different physical and chemical properties:

$$CH_{3}-CH_{2}-CH_{2}-O-H$$
 $CH_{3}-CH_{2}-CH_{2}-O-H$
 $CH_{3}-CH_{2}-CH_{3}-CH_{3}-CH_{3}$
 $CH_{3}-CH_{2}-CH_{3}-CH_{3}-CH_{3}$
 $CH_{3}-CH_{2}-CH_{3$

1.9 Writing Structural Formulas

write out all possible structural formulas that correspond to the molecular formula C₅H₁₂.

Continuous chain

$$C - C - C - C$$

Branched chain

2-methylbutane, bp 28°C (isopentane)

C forms 4 covalent bonds

Dash formula

Kekul structur e

Condensed structures

Bond line formula

Atoms bonded to a carbon are shown to the right of the carbon. Atoms other than H can be shown hanging from the carbon.

CH₃CHBrCH₂CH₂CHClCH₃ or CH₃CHCH₂CH₂CHCH₃ Br

Repeating CH₂ groups can be shown in parentheses.

Groups bonded to a carbon can be shown (in parentheses) to the right of the carbon, or hanging from the carbon.

Groups bonded to the far-right carbon are not put in parentheses.

CH₃ CH₃CH₂C(CH₃)₂CH₂CH₂OH or CH₃CH₂CCH₂CH₂OH CH₃

CH₃CH=CHCH₂CH₃

Three line segments emanate from this point; therefore, this carbon has one hydrogen (4 - 3 = 1) attached to it.

-Two line segments emanate from this point; therefore, this carbon has two hydrogens (4 - 2 = 2) attached to it.

One line segment emanates from this point; therefore, this carbon has three hydrogens (4 - 1 = 3) attached to it.

EXAMPLE 1.12

Write a more detailed structural formula for

Solution

$$CH_{2}$$
 H C H H CH_{3} — C — CH_{2} — CH_{3} or H — C — C — C — C — H

PROBLEM 1.23 Write a more detailed structural formula for —

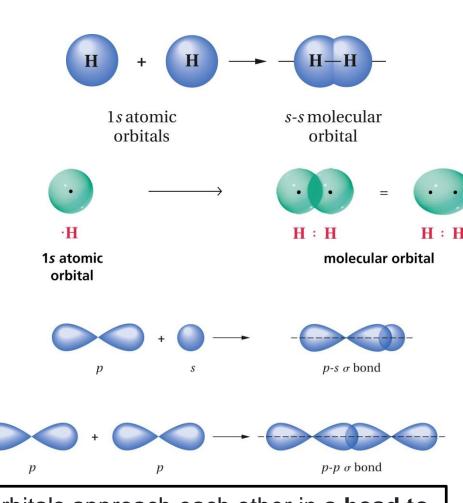
1.14 The Orbital View of Bonding; the Sigma Bond

H.

1s atomic

orbital

Sigma (σ) bonds: are characterized by a region of high e-density along the internuclear axis.



Orbitals approach each other in a **head to head** fashion

1.14 The Orbital View of Bonding; the pi (π) bond

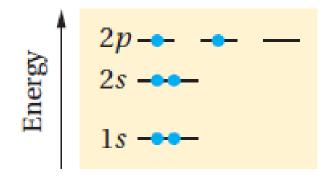
There is one other type of bond, a pi (π) bond. In contrast to a sigma bond the e⁻ density in a pi bond is not located on the internuclear axis, but rather on either "side" of it.

 π bonds are formed by the <u>side to side overlap</u> of 2 "p"

orbitals

Carbon sp³ Hybrid Orbitals

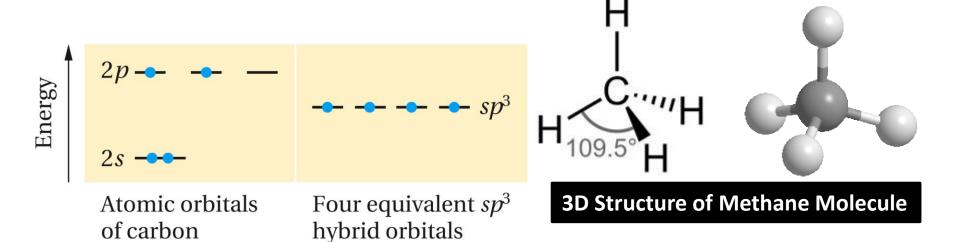
⁶C: 1S² 2S² 2P²



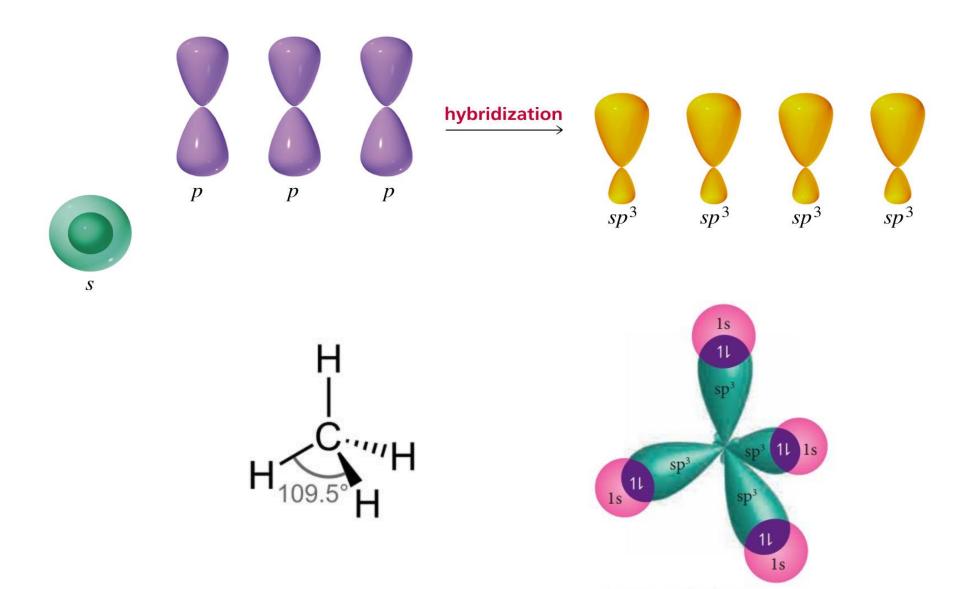
Distribution of the six electrons in a carbon atom. Each dot stands for an electron.

Q: Should the carbon form only two bonds !!!

A: We know from experience that carbon usually forms *four* single bonds, and often these bonds are all equivalent, as in CH₄

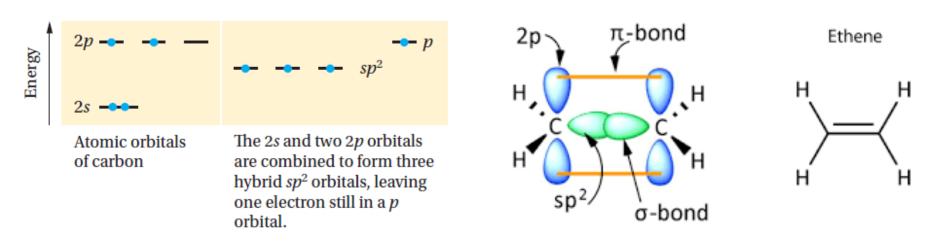


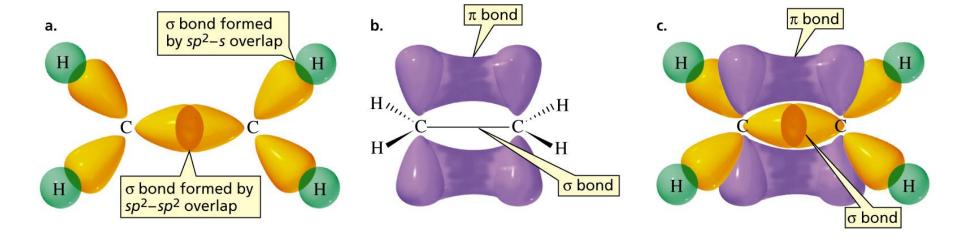
Mix or combine the four atomic orbitals of the valence shell to form four identical hybrid orbitals



SP²-Hybridized orbitals

One part s and two parts p in character and are directed toward the three vertices of an equilateral triangle.

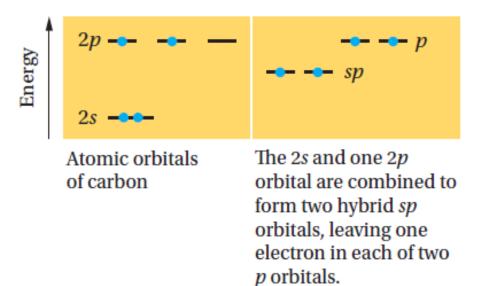




SP-Hybridized orbitals

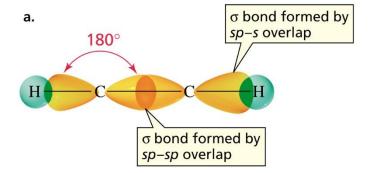
Bonding in Ethyne: A Triple Bond

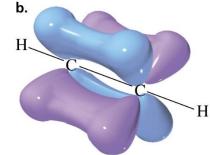
• A triple bond consists of one σ bond and two π bonds



H = -H

sp orbitals forms a sigma bond between the two carbons, and lateral overlap of the properly aligned p orbitals forms two pi bonds





Valence Bond Theory (cont'd)

Orbitals are combined in various portions to make equivalent hybrid orbitals, i.e.

AOs(#(s, p))	hybrid	Angle	orientation
1, 1	2 sp	180° line	ear
1, 2	3 sp^2	120° trig	gonal planar
1, 3	4 sp^3	109° tet	rahedral

1.12 Resonance

There are molecules (or ions) for which more than one correct Lewis structure can be drawn, these equivalent Lewis structures are resonance structures.

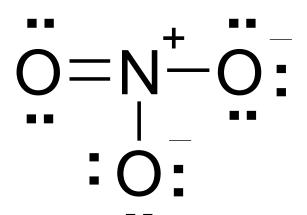
The assumption in these diagrams is that the <u>atom</u> <u>positions do not change</u>, we are only allowed to change the distribution of e⁻, *i.e.* the bonds and lone pairs.

Lewis structures do not always explain properties of molecules. Resonance theory is a second layered approach.

Resonance (cont'd)

Example 1: NO₃

- 1) $\# e^{-}$: 5 + 3(6) + 1 = 24
- 2) try 3 single bonds
- 3) 18 e⁻ remain
- 4) Each O needs 6, leave 2 short
- 5) Share 1 pair but which one?
- 6) Pick one O, octets
- 7) Formal chargall es



Resonance (cont'd)

Example 1: NO₃ (cont'd)

Depending on your choice of the double bond to oxygen, there are three possible structures differing in the location of the double bond and charges on the oxygen.

$$O = N^{+} - O$$
:
 $O = N^{+} - O$:
 $O =$

In real the structure is hybrid of all (A, B and C)

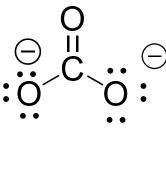
A resonance hybrid

The Lewis structure can be converted to other by changing the position of electrons

Rules for drawing resonance structures:

- 1) Electrons only can be oved (lone pair / π electrons)
- 2) Electrons move toward SP/ SP² hybridized atom only.

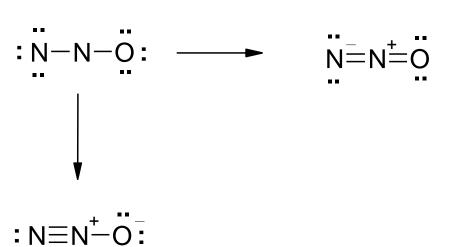
Examples: Write a second resonance structure for the following compounds?



Resonance (cont'd)

Example 2: N₂O

- 1) $\# e^{-}$: 2(5) + 6 = 16
- 2) try 2 single bonds
- 3) 12 e⁻ remain
- 4) 16 e- for octets 4 short
- 5) Options 2 double bonds, 1 triple & 1 single
- 6) Octets
- 7) Formal charges
- 8) Which is better and why?

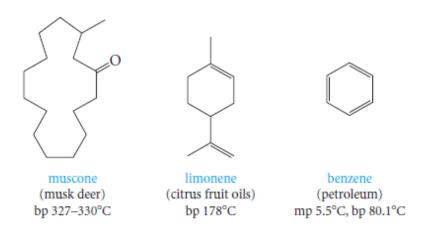


1.17: Classification According to Molecular Framework

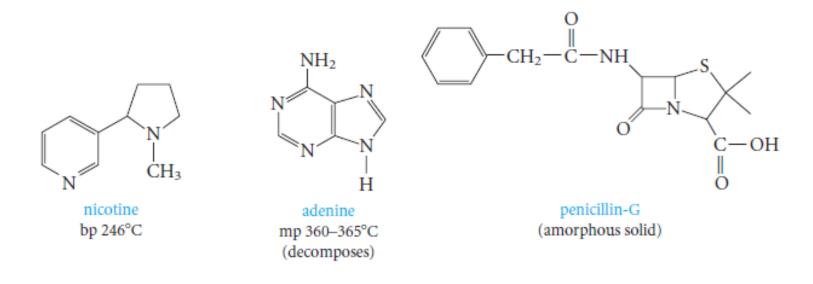
➤ The three main classes of molecular frameworks for organic structures are acyclic, carbocyclic, and heterocyclic compounds.

1.17.a Acyclic Compounds (*not cyclic*): contain chains that may be unbranched or branched.

1.17b: Carbocyclic Compounds: contain rings of carbon atoms



1.17.c Heterocyclic Compounds (In heterocyclic compounds, at least one atom in the ring must be a heteroatom, an atom that is *not* carbon: *eg*. N, O,S...)



Classification According to Functional Group

A functional group is an arrangement of atoms with distinctive **physical** and **chemical** properties.

Table 1.6 — The Main Functional Groups							
	Structure	Class of compound	Specific example	Common name of the specific example			
A. Functional groups that are a part of the molecular framework	-c-c-	alkane	CH ₃ —CH ₃	ethane, a component of natural gas			
)c=c(alkene	CH ₂ =CH ₂	ethylene, used to make polyethylene			
	—C = C—	alkyne	HC≡CH	acetylene, used in welding			
		arene		benzene, raw material for polystyrene and phenol			
B. Functional groups containing oxygen							
With carbon–oxygen single bonds	-c-он	alcohol	CH ₃ CH ₂ OH	ethyl alcohol, found in beer, wines, and liquors			
	-c-o-c-	ether	CH ₃ CH ₂ OCH ₂ CH ₃	diethyl ether, once a common anesthetic			

	Structure	Class of compound	Specific example	Common name of the specific example
2. With carbon—oxygen double bonds*	о - - - -	aldehyde	CH ₂ =0	formaldehyde, used to preserve biological specimens
	-c-c-c-	ketone	O ∥ CH₃CCH₃	acetone, a solvent for varnish and rubber cement
3. With single and double carbon–oxygen bonds	о сон	carboxylic acid	O ∥ CH₃C—OH	acetic acid, a component of vinegar
	-c-o-c-	ester	O ∥ CH₃C—OCH₂CH₃	ethyl acetate, a solvent for nail polish and model airplane glue
C. Functional groups containing nitrogen**	-C-NH ₂	primary amine	CH ₃ CH ₂ NH ₂	ethylamine, smells like ammonia
	—C≡N	nitrile	CH ₂ =CH−C≡N	acrylonitrile, raw material for making Orlon
D. Functional group with oxygen and nitrogen	O 	primary amide	O ∥ H— C—NH₂	formamide, a softener for paper
E. Functional group with halogen	—х	alkyl or aryl halide	CH₃CI	methyl chloride, refrigerant and local anesthetic
F. Functional groups containing sulfur [†]	_с_sн	thiol (also called mercaptan)	CH₃SH	methanethiol, has the odor of rotten cabbage
	-c-s-c-	thioether (also called sulfide)	(CH ₂ =CHCH ₂) ₂ S	diallyl sulfide, has the odor of garlic

Ex. What functional groups can you find in the following natural products?