النادي الطبي

Organic chemistry

Lec: 1-2-3

Done by: Alaa Alaiwah

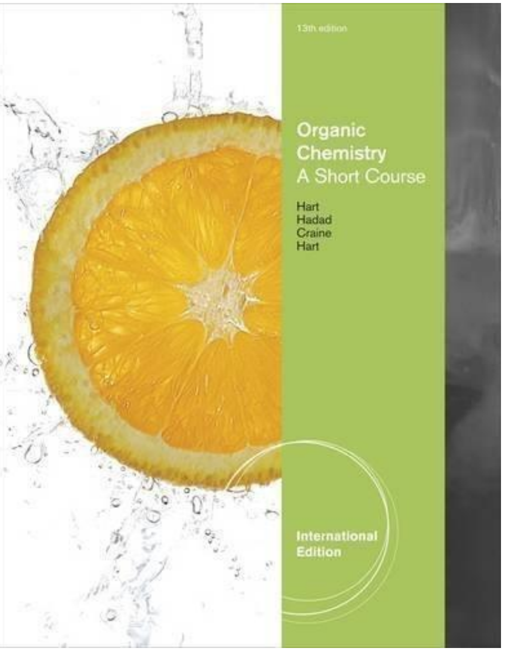
Chem 237 Basics of Organic Medicinal Chemistry

- **Course description**

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

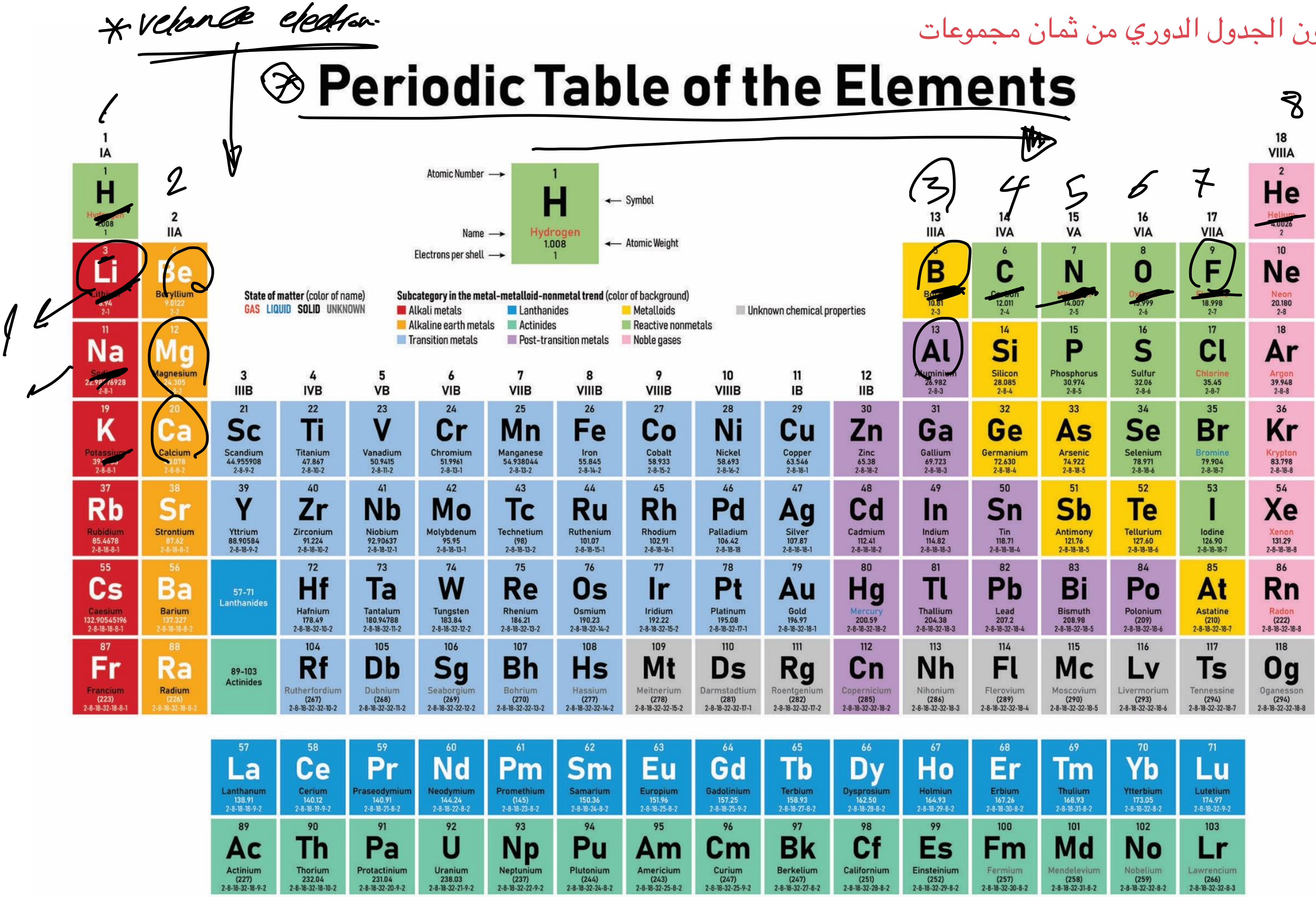
- **Texts**

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

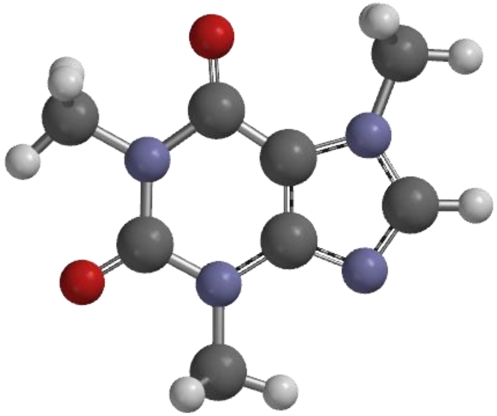


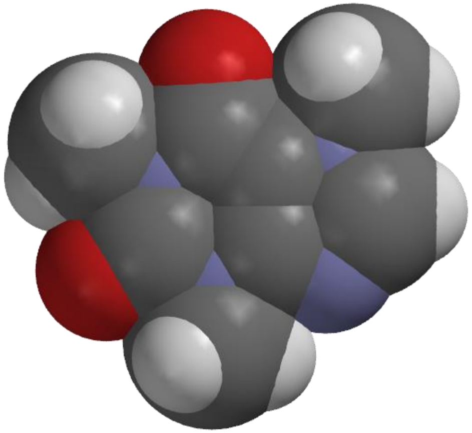
Dr. Eyad Younes

يتكون الجدول الدوري من ثمان مجموعات

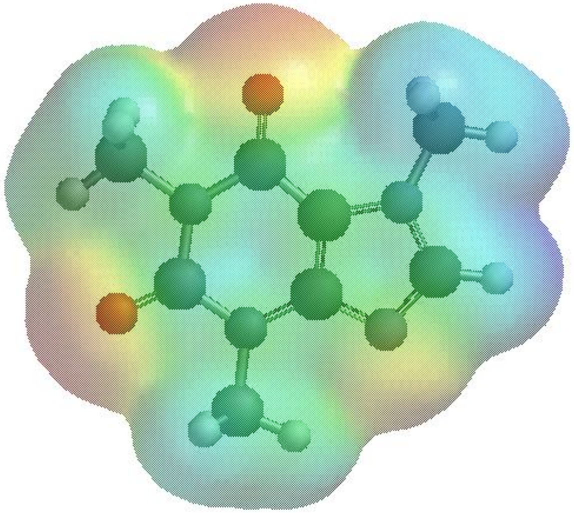


يفضل حفظ بعض العناصر المميزة في كل مجموعة



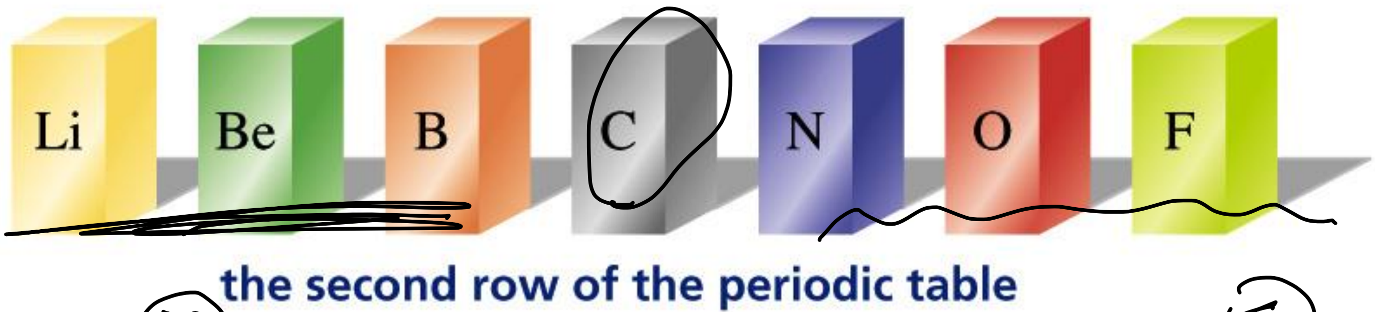


Chapter 1: Bonding and Isomerism



Organic Chemistry

- Organic compounds are compounds containing carbon



العناصر على جهة اليسار تميل
إلى إعطاء الإلكتروني

العناصر على جهة اليمين تميل
إلى كسب الكترونات

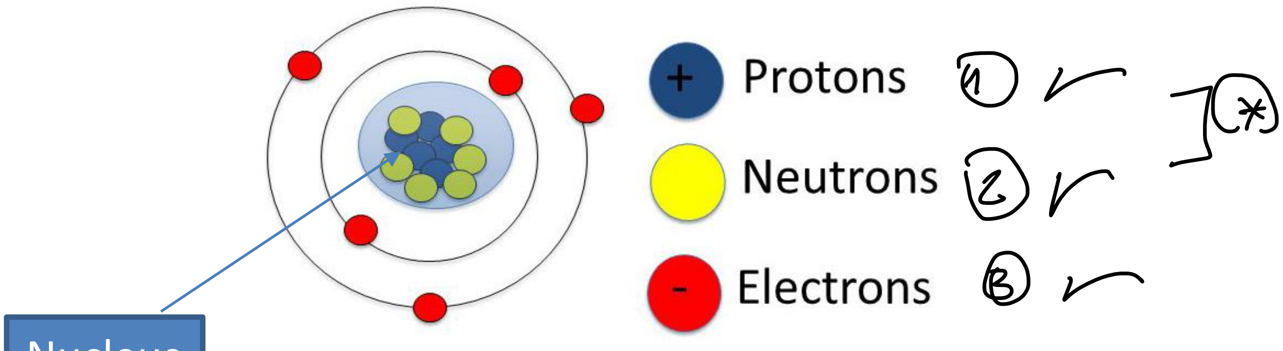
- Atoms to the left of carbon give up electrons.
- Atoms to the right of carbon accept electrons.
- Carbon shares electrons.

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. تعتبر الذرة اصغر الجزيئات الموجودة في كل عنصر وهي أساسية التفاعلات الكيميائية

- An atom consists of negatively charged electrons, positively charged protons, and neutral neutrons



The structure of an atom

- **Atomic number**: numbers of protons in its nucleus and it’s the number of electrons in the neutral atom. يعتبر العدد الذري عدد البروتينات الموجودة في النواة وأيضا عدد الإلكترونات ولكن في الذرة ال متعادله كهربائيا

- **Mass number**: the sum of the protons and neutrons of an atom.

(Protons and neutrons are ~1837 times the mass of an e^-) يعتبر العدد الكتلة لي مجموعة ال بروتونات والنيترونات الموجودة في الذرة

- Isotopes have the same atomic number but different mass numbers (^{12}C and ^{13}C)

النظائر المشعة تحتوي على نفس العدد الذري ولكن تختلف والعدد الكتلي

- 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.

ال shell تحوي على orbitals التي تترتب فيها الألكترونات

- Orbitals are grouped in shells .

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

Table 1.1 Distribution of Electrons in the First Four Shells That Surround the Nucleus

	First shell	Second shell	Third shell	Fourth shell
Atomic orbitals	*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:

$_6C$

كلما إقتربنا من المدارات كلما زادة الاستقرار وقلت الطاقة يعني ال s orbital بكون أكثر استقرار و أقل طاقة من orbital p

لها طريقتين للحساب اما رقم المجموعة أو عدد الإلكترونات في المدار الاخير يعني في shell الاخير

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	:Ö:
	^{6}C: ______		

Table 1.3 Valence Electrons of the First 18 Elements

Group	I	II	III	IV	V	VI	VII	VIII
	H·							He:
	Li·	·Be·	·Ḃ·	·Ċ·	·Ṅ:	·Ö:	:F̈:	:N̈e:
	Na·	·Mg·	·Ȧl·	·Ṡi·	·Ṗ:	·S̈:	:C̈l:	:Är:

• Chemical Bonds

جميع التفاعلات الكيميائية تكون بناءا على عدد الإلكترونات فيshell الاخير

1. Ionic Bonding

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

VE

$^{11}Na : [Ne]\,3s^1 \xrightarrow{-e} Na^{\oplus} : [Ne]$

$1s^2 / 2s^2p^6 / 3s^1$

$^{17}Cl : [Ne]\,3s^1\,3p^5 \xrightarrow{+e} Cl^{\ominus} : [Ar]$

VE

Na-Cl

تتميز الرابطة الأيونية بالتفاعل بين عنصرين أحدهما شحنة موجبة والآخر شحنة سالبة وتتكون بناءا على منح كامل للألكترونات من عنصر إلى آخر

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

الهدف الأساسي من هذه الرابطة وصول العناصر إلى الاستقرار والأقرب إلى مجموعة الثمانية يعني تحتوي على عدد الإلكترونات في المدار الاخير مكتمل

$Ca^{+2} \longrightarrow 2Cl$

لو كانت هذه الرابطة بين عنصر الكالسيوم وعنصر الكلور لازم يكون عنصرين الكلور لانه العنصر الواحد من الكلور قادر على اكتساب شحنة واحدة فقط والكالسيوم قادر على منح شحنتين لذلك عنصر الكالسيوم يعطي الألكترونات لعنصريين الكلور

2. Covalent Bonding

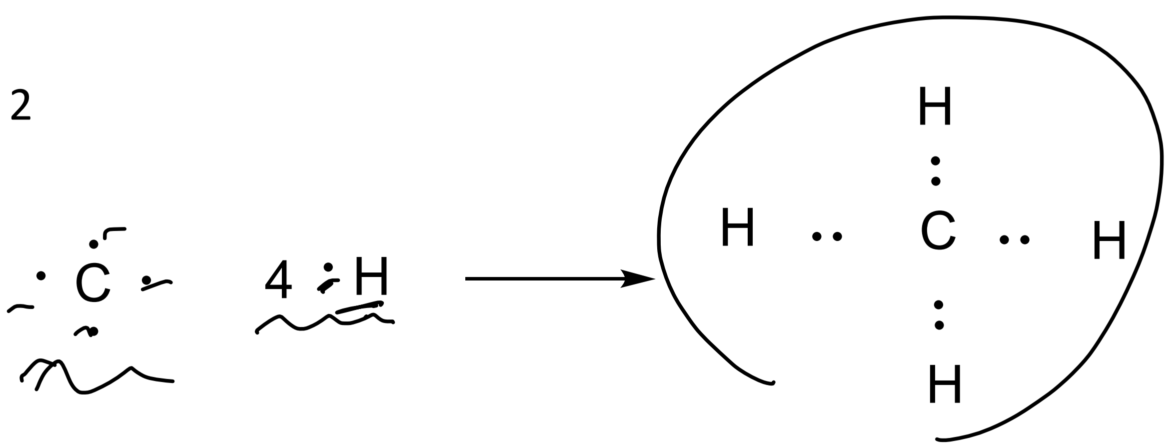
- Ionic bonds occur when an e^- is transferred between a metal and nonmetal.
- Covalent bonds are resulting from sharing e^-

$$2\,H\cdot \longrightarrow H\!:\!H$$

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

Example 2

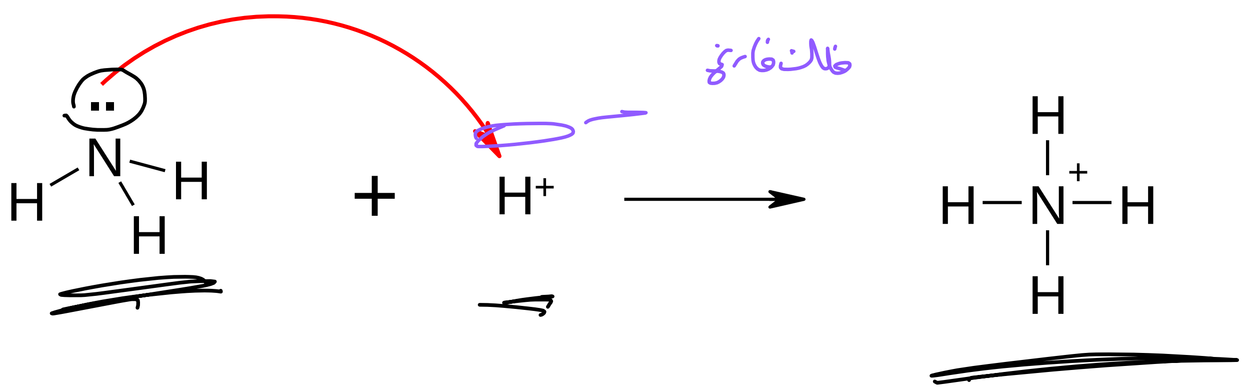


A second general version of a covalent bond is possible. This occurs when BOTH e^- come from one atom: a coordinate covalent bond

i.e.

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

هذه هي الرابطة التناسقيه وتكون بناءا على اتحاد بين مركب وعنصر أحدهما يقدم فلك فارغ والآخر يقدم زوج من الألكترونات غير الرابطة



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

TABLE 1.3 The Electronegativities of Selected Elements[a]

IA	IIA	IB	IIB	IIIA	IVA	VA	VIA	VIIA
H 2.1								
Li 1.0	Be 1.5			B 2.0	C 2.5	N 3.0	O 3.5	F 4.0
Na 0.9	Mg 1.2			Al 1.5	Si 1.8	P 2.1	S 2.5	Cl 3.0
K 0.8	Ca 1.0							Br 2.8
								I 2.5

increasing electronegativity →

increasing electronegativity ↑

[a]Electronegativity values are relative, not absolute. As a result, there are several scales of electronegativities. The electronegativities listed here are from the scale devised by Linus Pauling.

كلما قلة حجم النواة كلما كانت سلبية العناصر أعلى واكبر والعناصر التي تكون أقل حجما وتتكون أعلى الجدول الدوري من جهة اليمين

Covalent bonds can be classified as

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

Examples C-C C-H

B. Polar covalent bond (Δ EN = 0.5 – 1.9)

O–H N–H A polar bond has a negative end and a positive end

dipole moment (D) = μ = *e* x *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

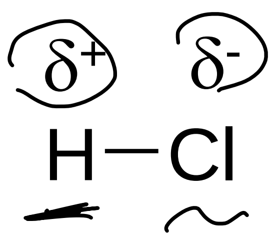
Bond	Dipole moment (D)	Bond	Dipole moment (D)
H—C	0.4	C—C	0
H—N	1.3	C—N	0.2
H—O	1.5	C—O	0.7
H—F	1.7	C—F	1.6
H—Cl	1.1	C—Cl	1.5
H—Br	0.8	C—Br	1.4
H—I	0.4	C—I	1.2

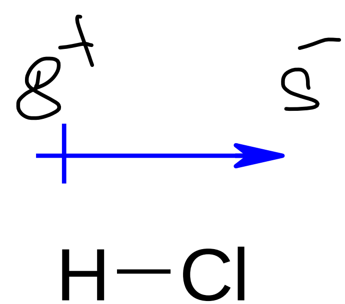
if The Δ EN increases the polarity increases

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

Bond Polarity & Electronegativity (cont'd)

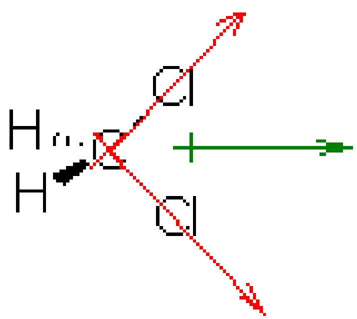
The result of polar covalent bonding is that the e^- pair spend more time near the more EN atom. This means it will acquire a permanent excess negative charge. The other atom acquires a permanent excess positive charge. This is indicated by a δ^+ or δ^- (where δ means a "partial charge") or a dipole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





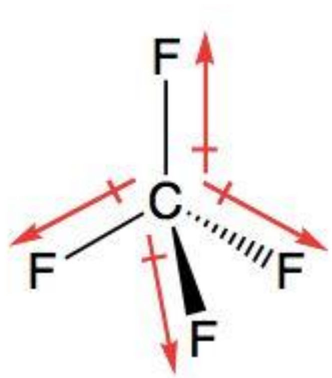
Bond Polarity & Electronegativity (cont'd)

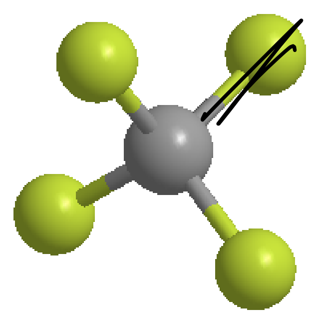
The more polar the molecule the stronger the dipole moment. The molecular dipole moment is the vector sum of the bond moments, *i.e.*



Net dipole moment

ممكن أن تكون الرابطة بين الذرة المركزية و العنصر polar ولكن محصله الروابط للمركب كامل تكون non polar والعكس صحيح





Net dipole moment =0

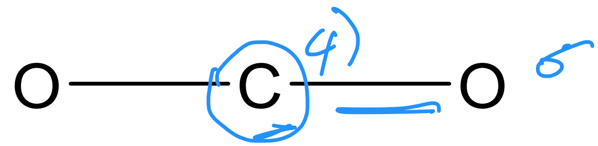
Lewis Structures It only deals with VE

Procedure for obtaining good Lewis structures: eg. CO_2

1) determine total number of valence shell e^- (including ionic charge if present).

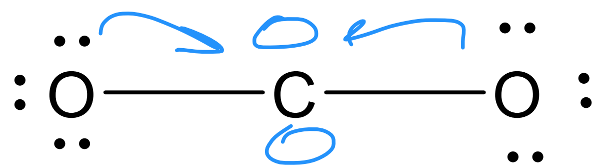
$CO_2 = 4+2(6) = 16.$

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.

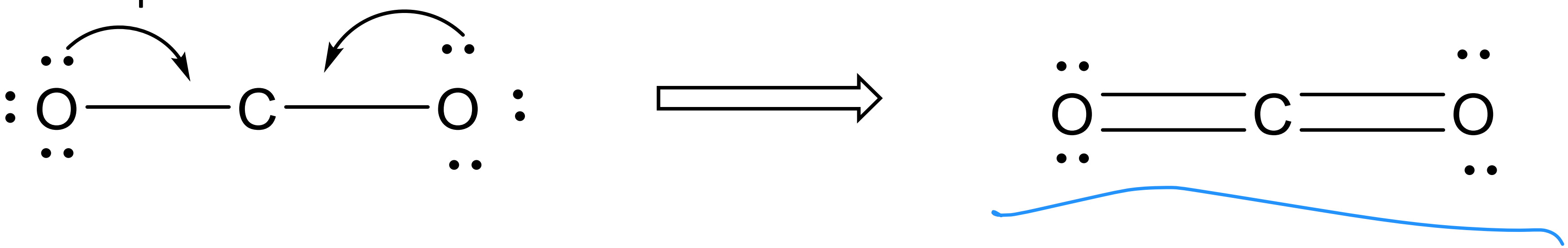


3) determine number of remaining e^-. complete the octet of the terminal atoms.

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)

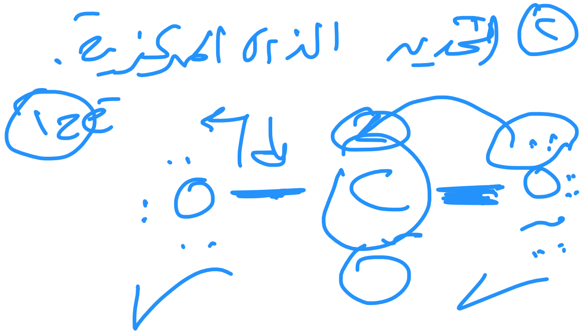
For O 6-6 =0

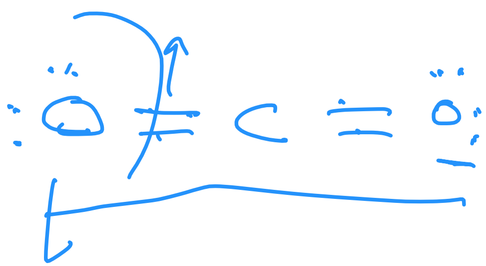
For C   4-4 =0

* CO_2: $4 + 2(6) = 16 = VE$

① VE الحساب

② التحديد الذرة المركزية.





$VE - 6 - 6 = 0$

$(4) - 4 = 0$

$6 - 6 = 0$

ثابت الكلي ← $0 = 0 + 0 + 0$

formal charge.

① ✗ (1-)

Ex: NO_3^-

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

24 = VE

① 6 − 6 = 0

② 6 − 7 = −1

③ 6 − 7 = −1

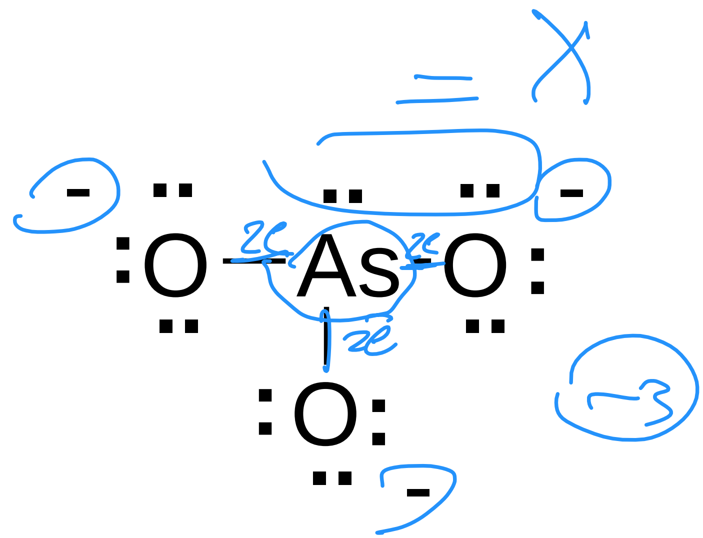
④ 5 − 4 = +1

total formal charge = 0 −1 −1 +1 = −1

Lewis Structures (other examples)

Example 2: AsO_3^{3-}

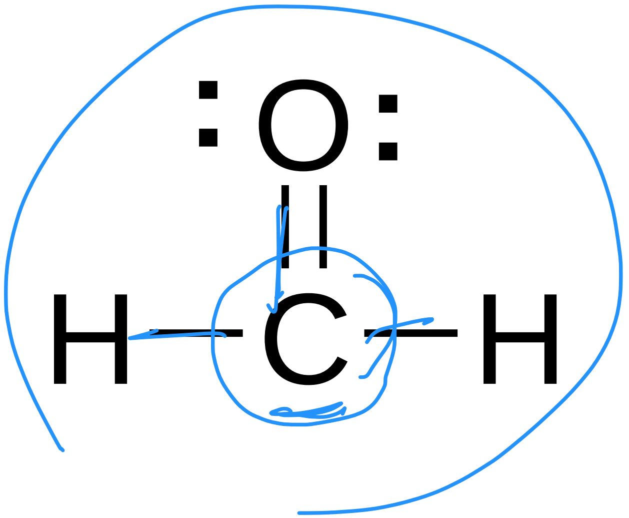
1) # e^-: 5 + 3(6) + 3 = 26
2) form 3 single bonds
3) 20 e^- remain
4) O needs 6, As needs 2
5) All octets
6) Formal charges



Lewis Structures (cont'd)

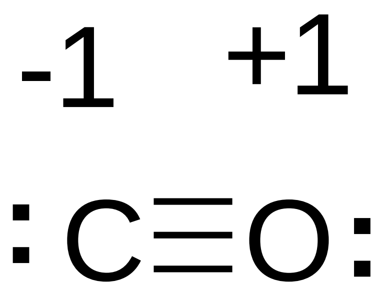
Example 3: CH_2O

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



Lewis Structures (cont’d)

Example 4: CO



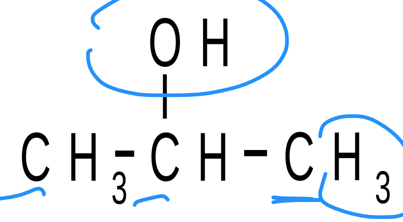
1) # e^-: 4 + 6 = 10
2) try 1 single bond
3) 8 e^- remain
4) C needs 6 as does O short 4 e^-
5) Share 4 more e^- - triple bond
6) Octets
7) Formal charges

1.8 Isomers

Structural or **constitutional** isomers have same molecular formula but different structural formula.
They have different physical and chemical properties:

$CH_3-CH_2-CH_2-O-H$

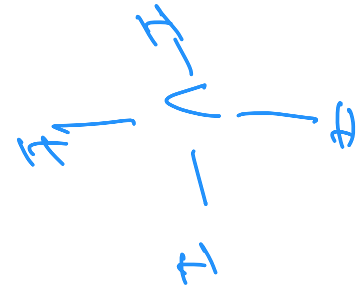
1-propanol
(bp 97.4 C)



2-propanol
(bp 82.4 C)

1.9 Writing Structural Formulas

write out all possible structural formulas that correspond to the molecular formula C_5H_{12}.

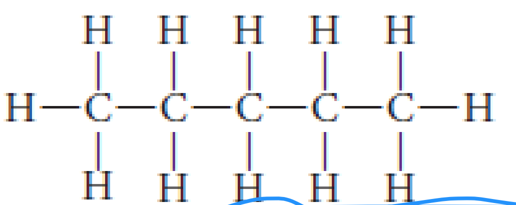


C - C - C -C - C

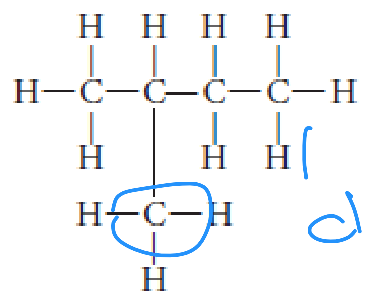
Continuous chain ①

C - C -C – C
C

② Branched chain



pentane, bp 36°C



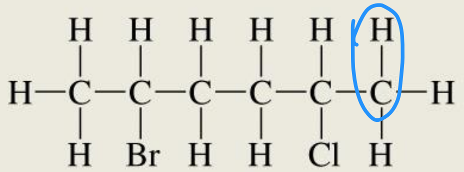
2-methylbutane, bp 28°C
(isopentane)

C forms 4 covalent bonds

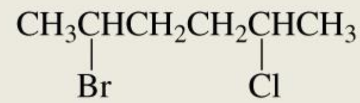
Dash formula

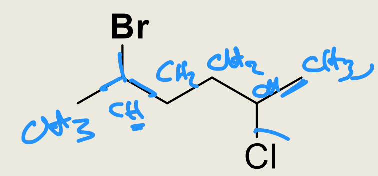
Kekul structur e	Condensed structures	Bond line formula

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

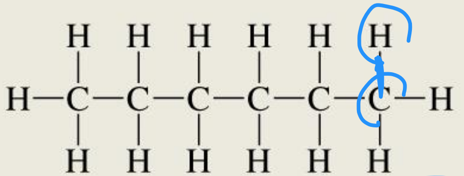


$CH_3CHBrCH_2CH_2CHClCH_3$ or

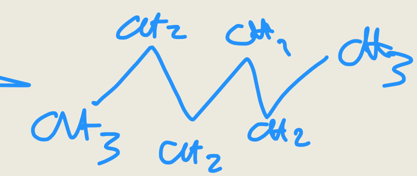




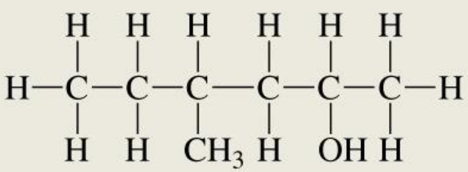
Repeating CH_2 groups can be shown in parentheses.



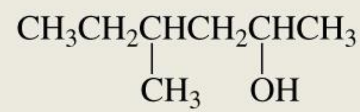
$CH_3CH_2CH_2CH_2CH_2CH_3$ or $CH_3(CH_2)_4CH_3$

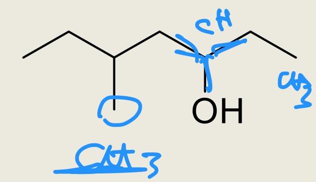


Groups bonded to a carbon can be shown (in parentheses) to the right of the carbon, or hanging from the carbon.

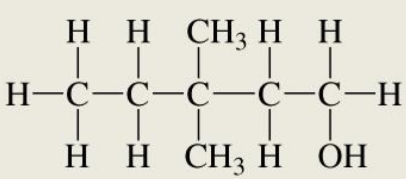


$CH_3CH_2CH(CH_3)CH_2CH(OH)CH_3$ or

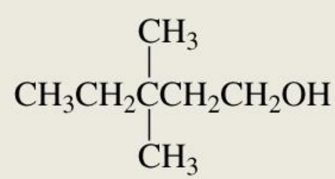


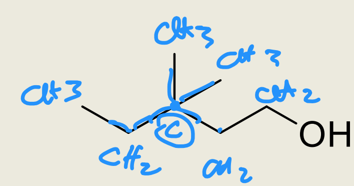


Groups bonded to the far-right carbon are not put in parentheses.

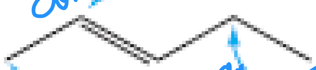


$CH_3CH_2C(CH_3)_2CH_2CH_2OH$ or





$CH_3CH{=}CHCH_2CH_3$

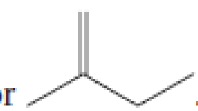


Three line segments emanate from this point; therefore, this carbon has one hydrogen (4 − 3 = 1) attached to it.

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.

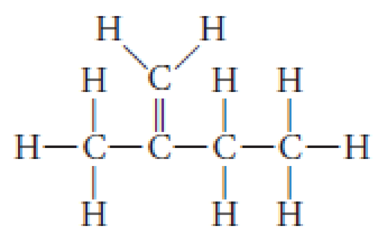
EXAMPLE 1.12

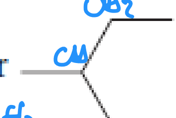
Write a more detailed structural formula for  .

Solution

$$CH_3-\underset{}{C}(=CH_2)-CH_2-CH_3$$

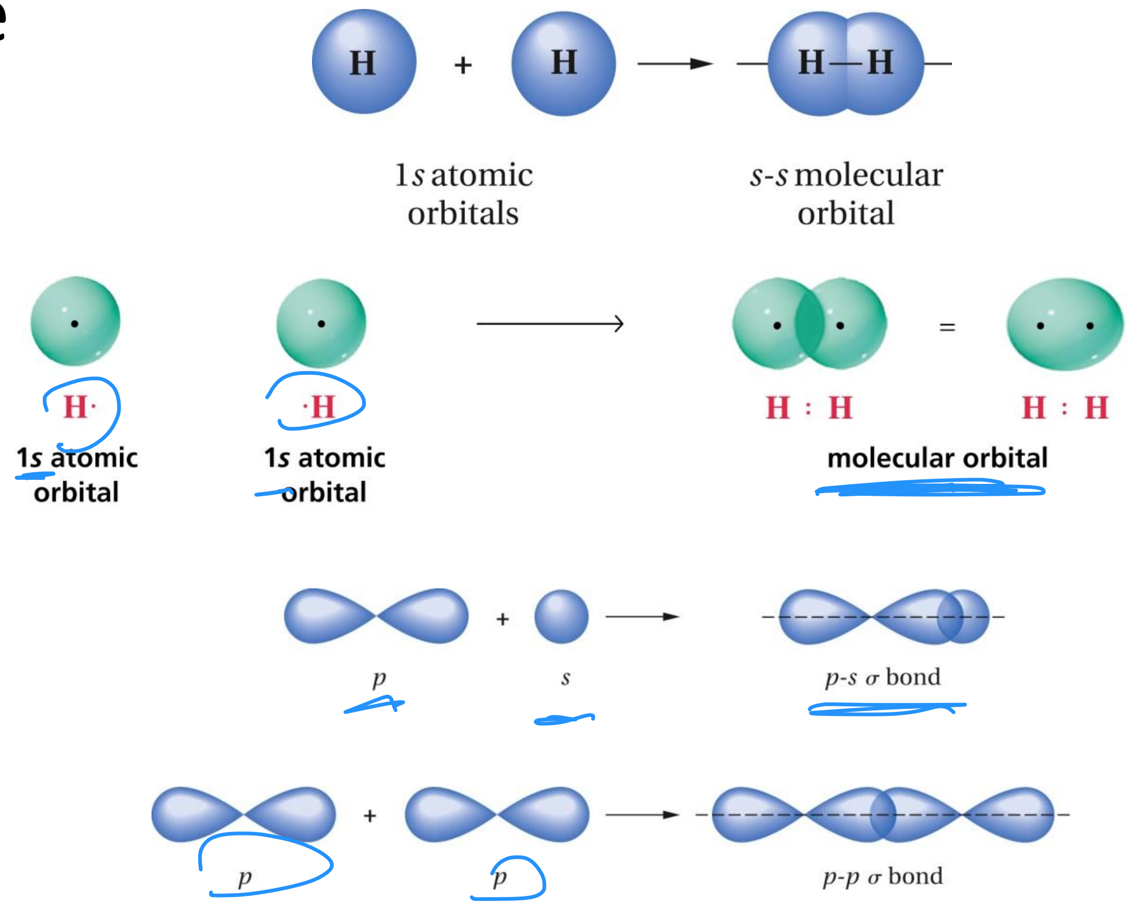
or



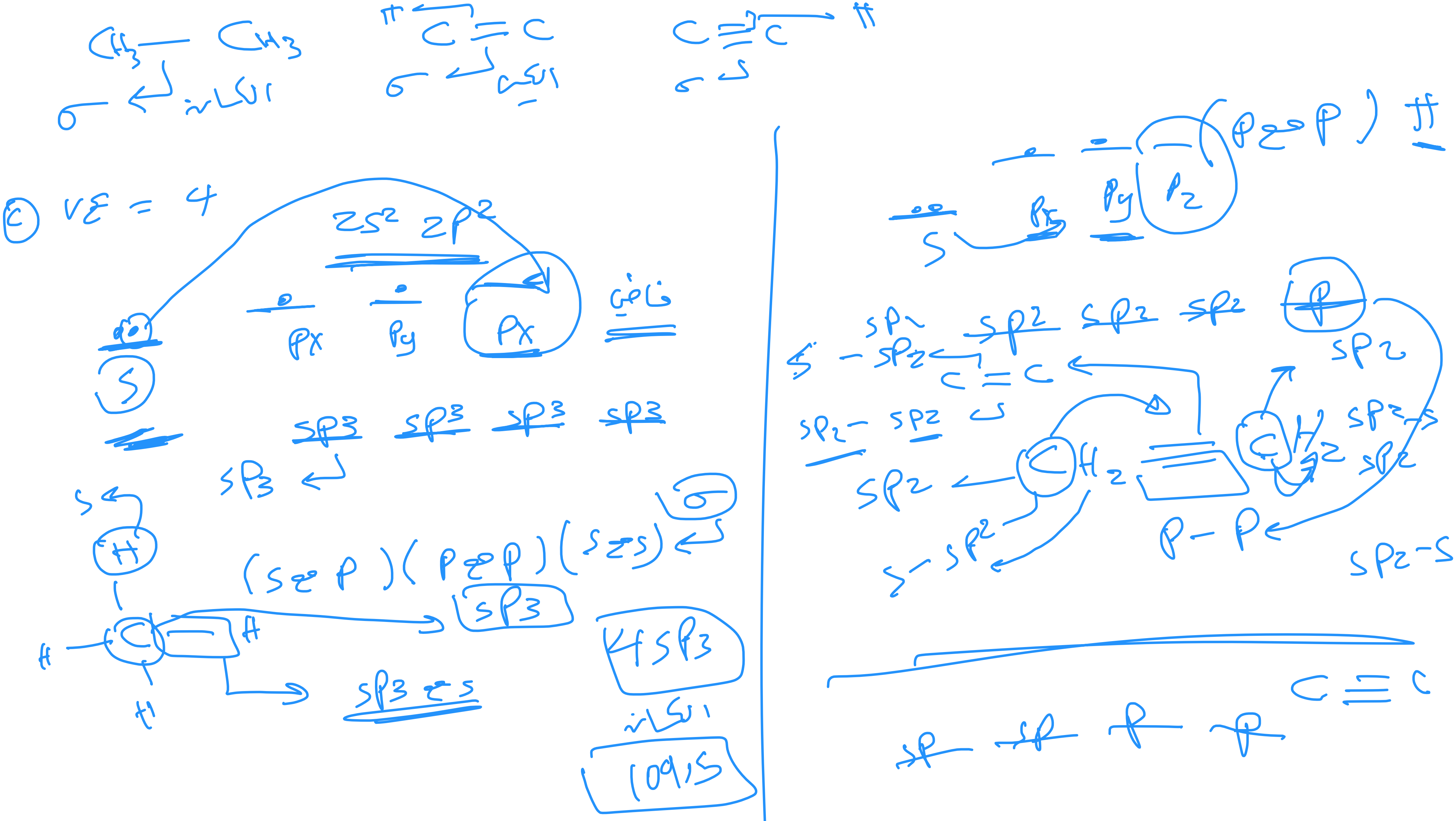
PROBLEM 1.23 Write a more detailed structural formula for  .

1.14 The Orbital View of Bonding; the Sigma Bond

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



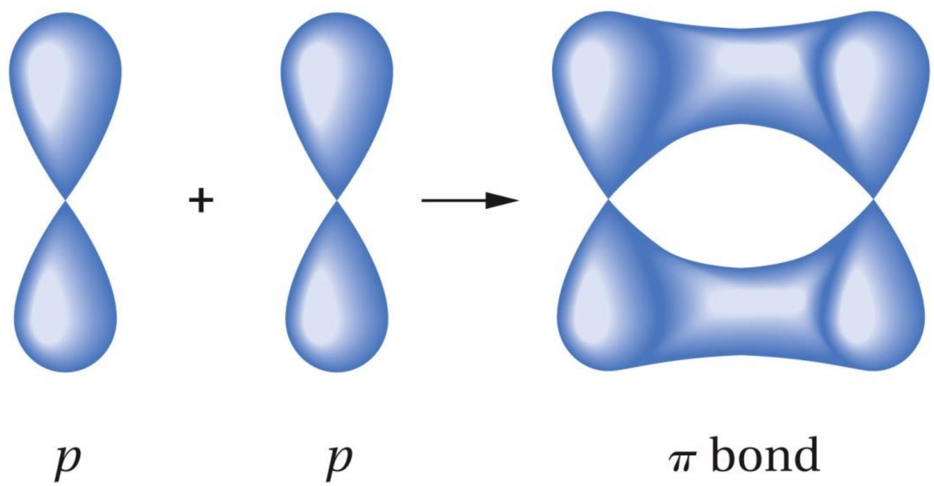
Orbitals approach each other in a **head to head** fashion


CH3 — CH3
σ
π
C = C
C ≡ C
VE = 4
2s2 2p2
Px
Py
Pz
s
sp3 sp3 sp3 sp3
sp3
(s ≥ p)(p ≥ p)(s ≥ s)
H
C
4 sp3
sp3 ≥ s
109.5
sp2 sp2 sp2 sp2
C = C
CH2
p - p
sp2 - s
C ≡ C
sp sp p p

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

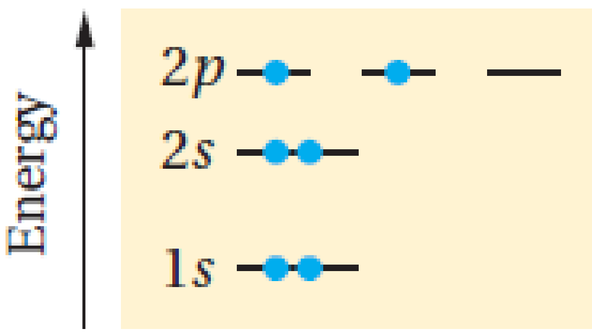
There is one other type of bond, a pi (π) bond. In contrast to a sigma bond the e^- density in a pi bond is not located on the internuclear axis, but rather on either "side" of it.

π bonds are formed by the **side to side overlap** of 2 "p" orbitals



Carbon sp^3 Hybrid Orbitals

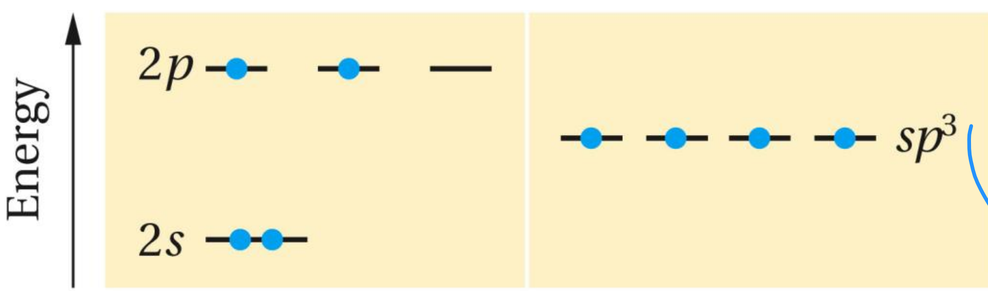
$^{6}C: 1S^2\ 2S^2\ 2P^2$



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

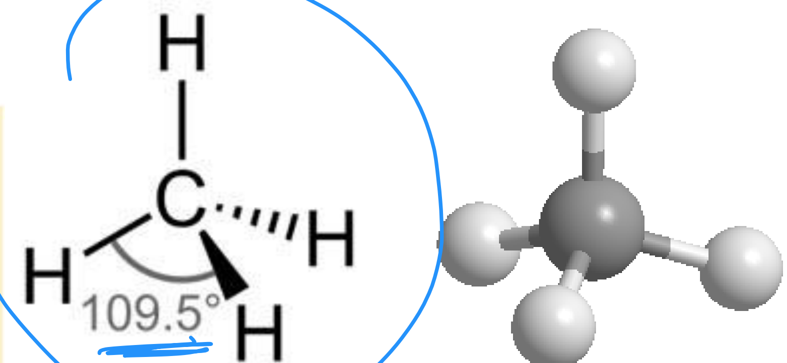
Q: Should the carbon form only two bonds !!!

A: We know from experience that carbon usually forms *four* single bonds, and often these bonds are all equivalent, as in CH_4



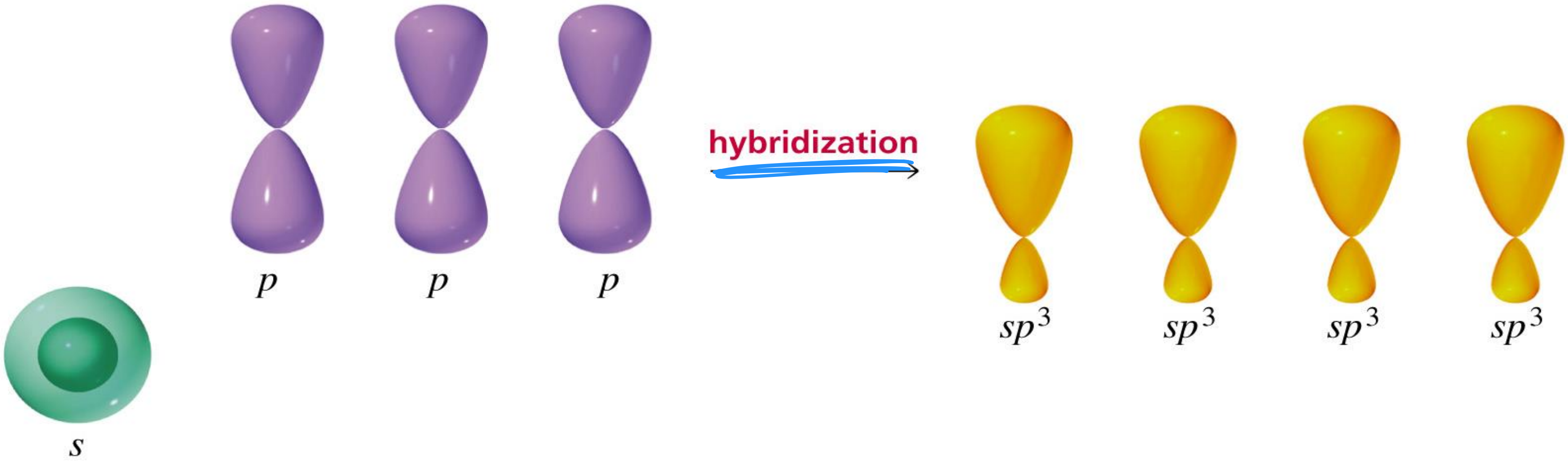
Atomic orbitals of carbon

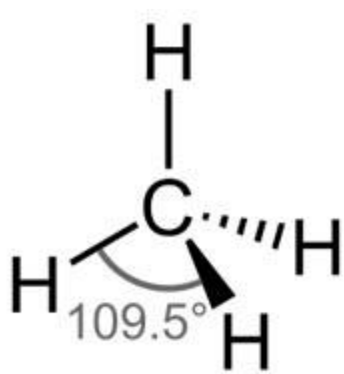
Four equivalent sp^3 hybrid orbitals

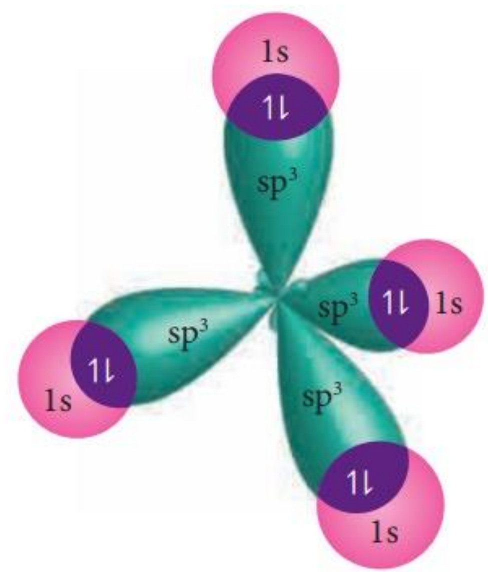


3D Structure of Methane Molecule

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

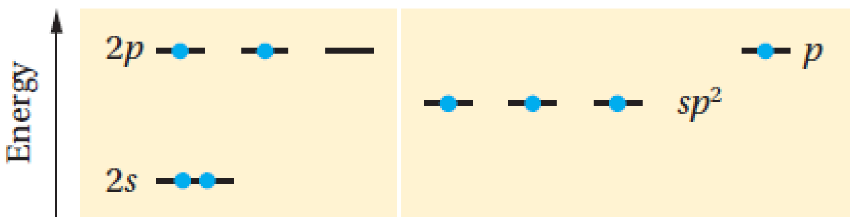






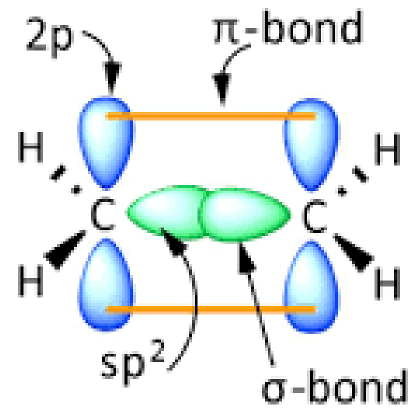
SP^2-Hybridized orbitals

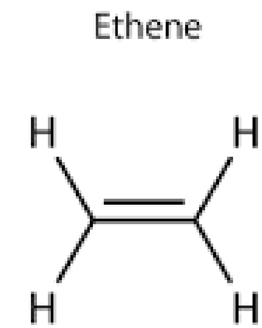
One part *s* and two parts *p* in character and are directed toward the three vertices of an equilateral triangle.

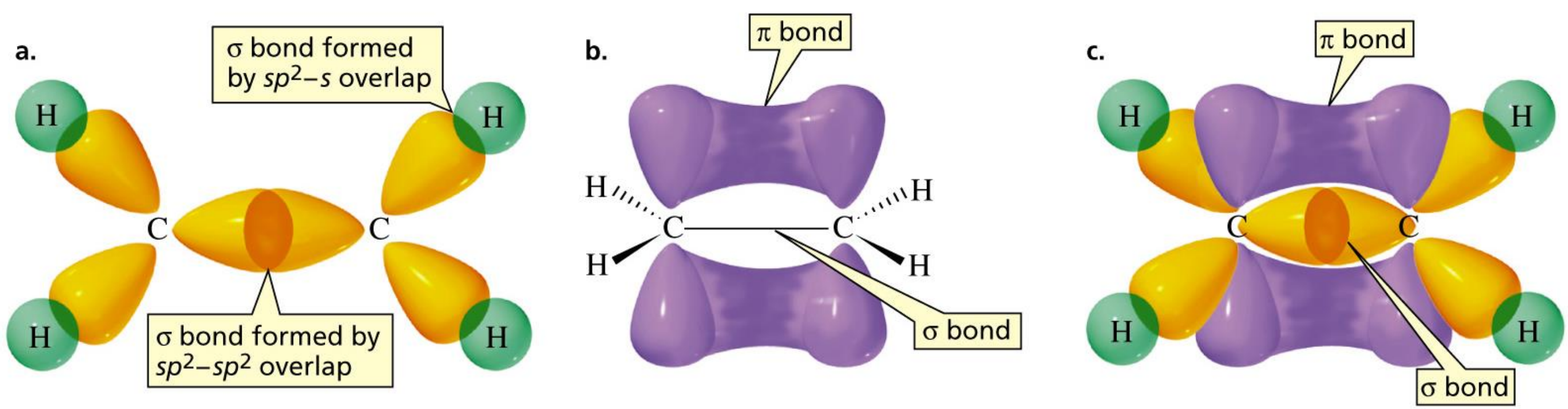


Atomic orbitals of carbon

The 2*s* and two 2*p* orbitals are combined to form three hybrid sp^2 orbitals, leaving one electron still in a *p* orbital.



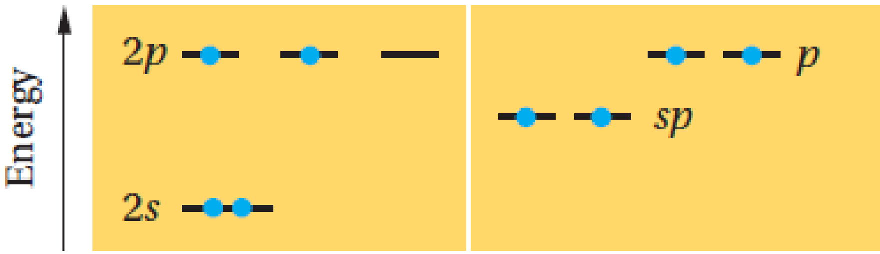




SP-Hybridized orbitals

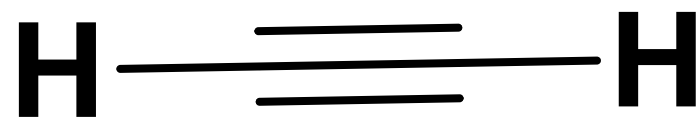
Bonding in Ethyne: **A Triple Bond**

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

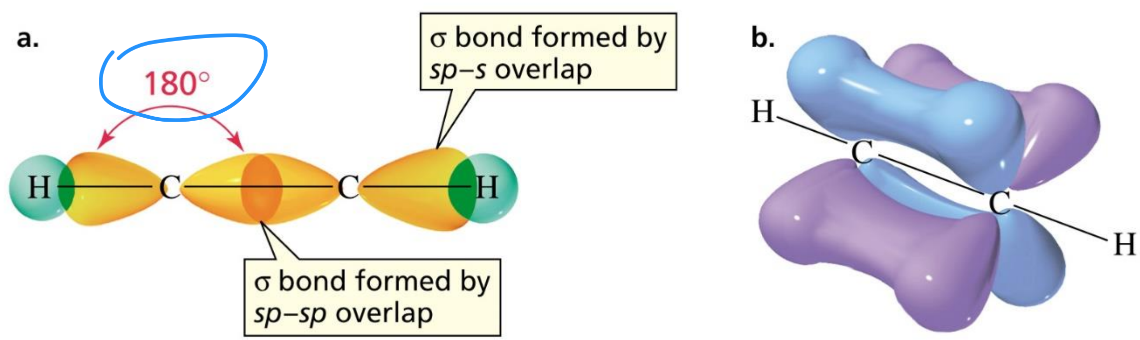


Atomic orbitals of carbon

The 2*s* and one 2*p* orbital are combined to form two hybrid *sp* orbitals, leaving one electron in each of two *p* orbitals.



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^o	linear
1, 2	3 sp^2	120^o	trigonal planar
1, 3	4 sp^3	109^o	tetrahedral

1.12 Resonance

اكثر من تعبير صحيح للمركب الواحد بشرط أن يكون النقل للالكترونات أو الروابط مع بقاء الذرات ثابتة في مكانها الأصلي

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 atom positions do not change, 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.

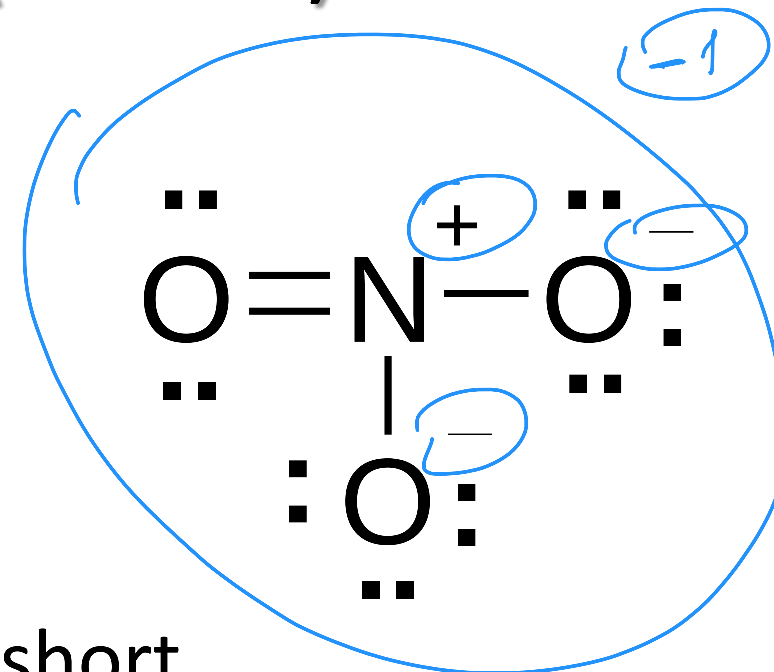
* resonance تكون موجودة فقط في الروابط الثنائية او الثلاثية يعني تهجين الذرة (c) تكون sp او sp2 .

* sp3 لا يوجد لها resonance على الإطلاق.

Resonance (cont'd)

Example 1: NO_3^-

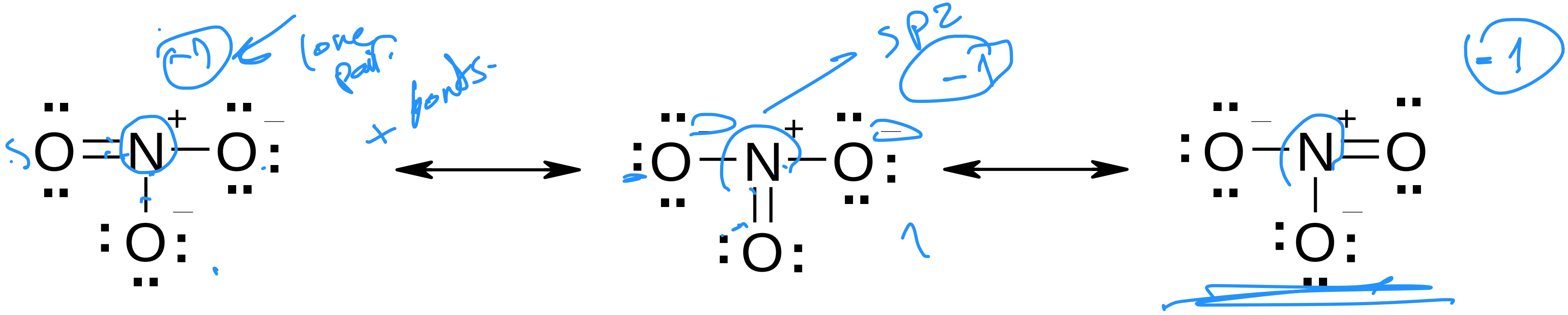
1) # e^-: 5 + 3(6) + 1 = 24
2) try 3 single bonds
3) 18 e^- remain
4) Each O needs 6, leave 2 short
5) Share 1 pair but which one?
6) Pick one O, octets
7) Formal chargall es



Resonance (cont'd)

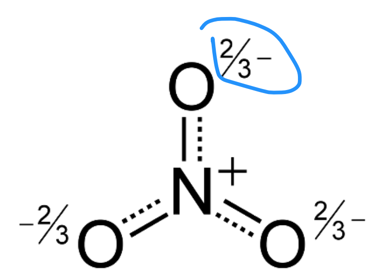
Example 1: NO_3^- (cont'd)

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.



A B C

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



A **resonance hybrid**

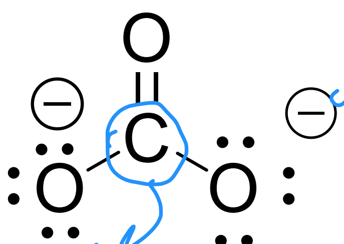
The Lewis structure can be converted to other by changing the position of electrons

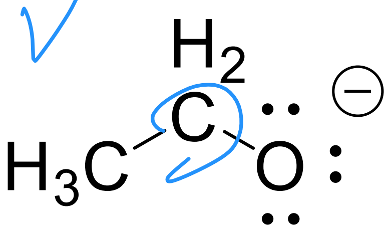
Rules for drawing resonance structures :

1) Electrons only can be oved (lone pair / π electrons)

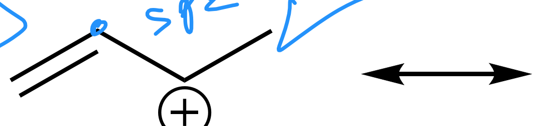
2) Electrons move toward SP/ SP^2 hybridized atom only.

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





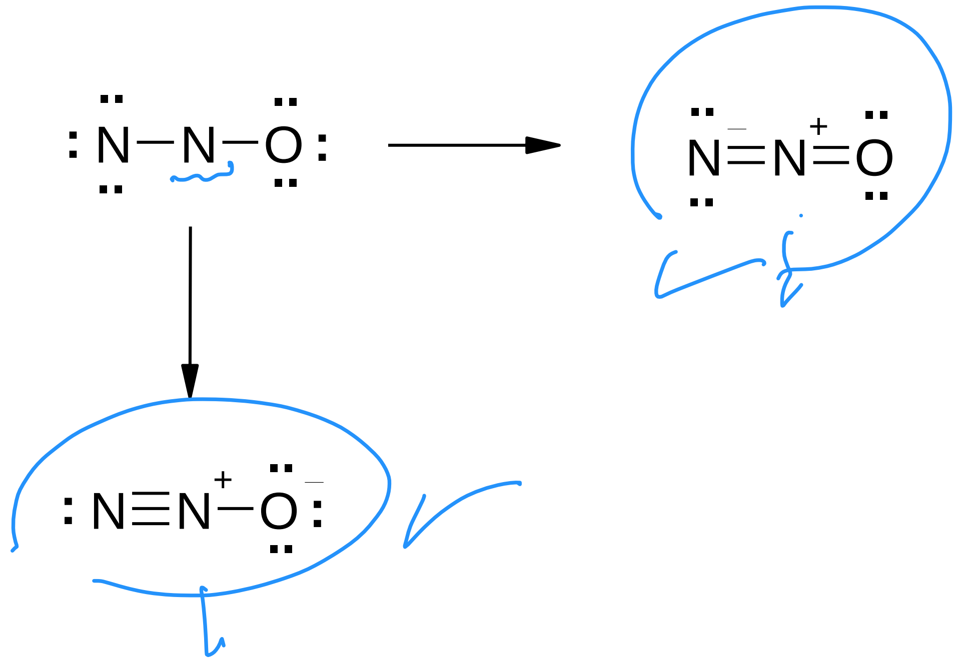
Exercise



Resonance (cont'd)

Example 2: N_2O

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?

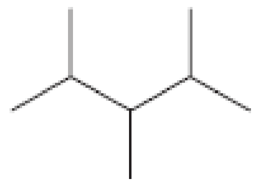


1.17: Classification According to Molecular Framework

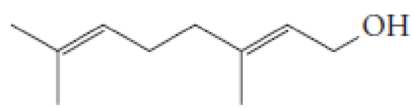
- The three main classes of molecular frameworks for organic structures are **acyclic**, **carbocyclic**, and **heterocyclic** compounds.

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

unbranched chain of eight carbon atoms



branched chain of eight carbon atoms



geraniol
(oil of roses)
bp 229–230°C

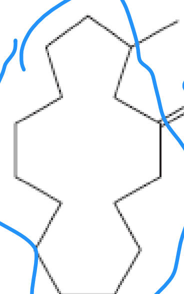
$CH_3(CH_2)_5CH_3$

heptane
(petroleum)
bp 98.4°C

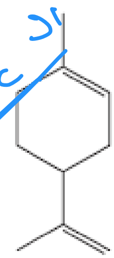
$CH_3C(=O)(CH_2)_4CH_3$

2-heptanone
(oil of cloves)
bp 151.5°C

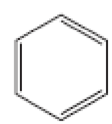
1.17b: Carbocyclic Compounds: contain rings of carbon atoms



muscone
(musk deer)
bp 327–330°C

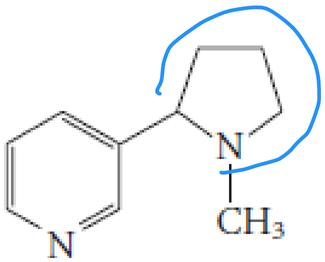


limonene
(citrus fruit oils)
bp 178°C

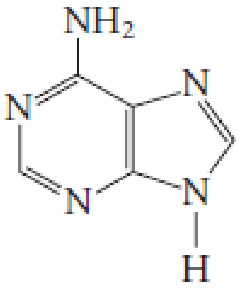


benzene
(petroleum)
mp 5.5°C, bp 80.1°C

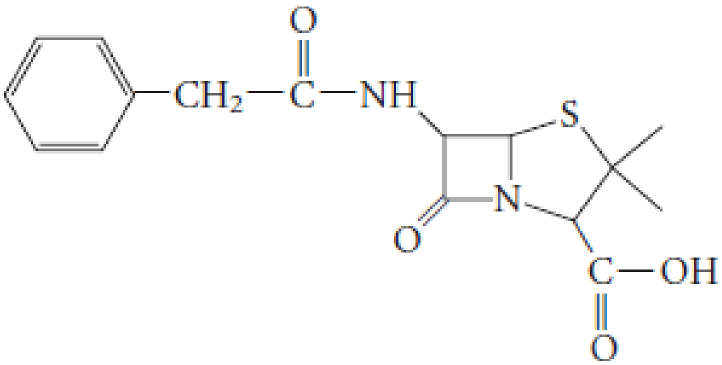
1.17.c Heterocyclic Compounds (In heterocyclic compounds, at least one atom in the ring must be a heteroatom, an atom that is *not* carbon: *eg*. N, O,S...)



nicotine
bp 246°C



adenine
mp 360–365°C
(decomposes)



penicillin-G
(amorphous solid)

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

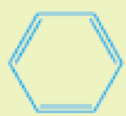
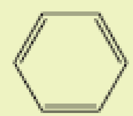
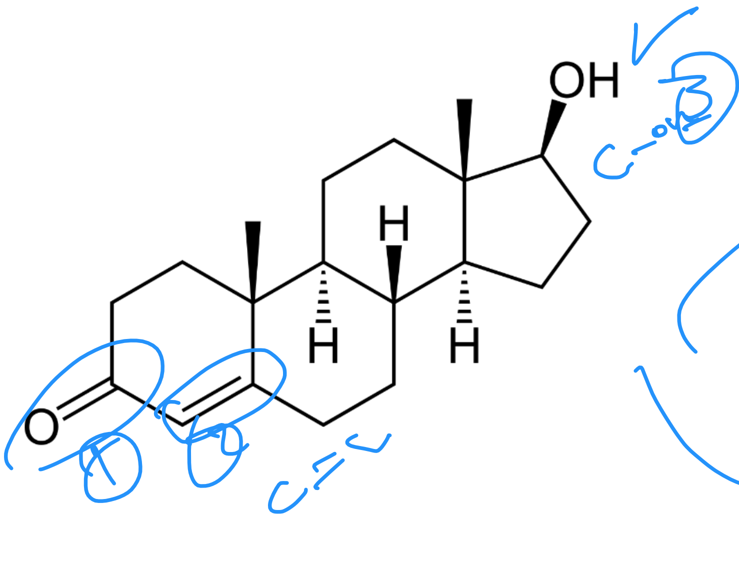
	Structure	Class of compound	Specific example	Common name of the specific example
A. Functional groups that are a part of the molecular framework	—C—C—	alkane	$CH_3—CH_3$	ethane, a component of natural gas
	C=C	alkene	$CH_2=CH_2$	ethylene, used to make polyethylene
	—C≡C—	alkyne	HC≡CH	acetylene, used in welding
		arene		benzene, raw material for polystyrene and phenol
B. Functional groups containing oxygen				
1. With carbon–oxygen single bonds	—C—OH	alcohol	CH_3CH_2OH	ethyl alcohol, found in beer, wines, and liquors
	—C—O—C—	ether	$CH_3CH_2OCH_2CH_3$	diethyl ether, once a common anesthetic

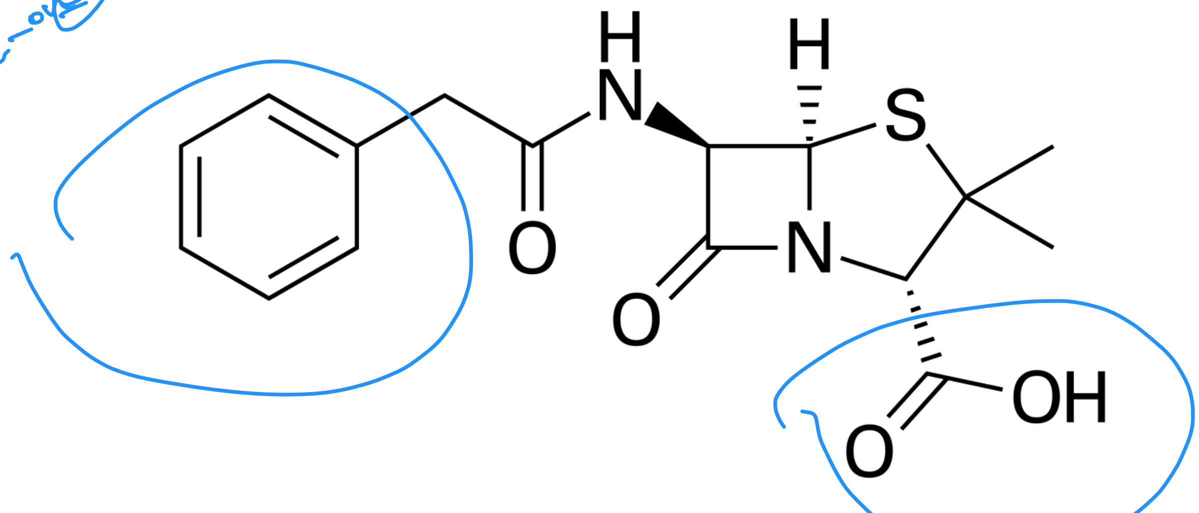
Table 1.6 — continued

	Structure	Class of compound	Specific example	Common name of the specific example
*2. With carbon–oxygen double bonds**	$-\overset{\overset{O}{\|}}{C}-H$	aldehyde	$CH_2{=}O$	formaldehyde, used to preserve biological specimens
	$-\overset{\|}{\underset{\|}{C}}-\overset{\overset{O}{\|}}{C}-\overset{\|}{\underset{\|}{C}}-$	ketone	$CH_3\overset{\overset{O}{\|}}{C}CH_3$	acetone, a solvent for varnish and rubber cement
3. With single and double carbon–oxygen bonds	$-\overset{\overset{O}{\|}}{C}-OH$	carboxylic acid	$CH_3\overset{\overset{O}{\|}}{C}-OH$	acetic acid, a component of vinegar
	$-\overset{\overset{O}{\|}}{C}-O-\overset{\|}{\underset{\|}{C}}-$	ester	$CH_3\overset{\overset{O}{\|}}{C}-OCH_2CH_3$	ethyl acetate, a solvent for nail polish and model airplane glue
*C. Functional groups containing nitrogen***	$-\overset{\|}{\underset{\|}{C}}-NH_2$	primary amine	$CH_3CH_2NH_2$	ethylamine, smells like ammonia
	$-C{\equiv}N$	nitrile	$CH_2{=}CH-C{\equiv}N$	acrylonitrile, raw material for making Orlon
D. Functional group with oxygen and nitrogen	$-\overset{\overset{O}{\|}}{C}-NH_2$	primary amide	$H-\overset{\overset{O}{\|}}{C}-NH_2$	formamide, a softener for paper
E. Functional group with halogen	$-X$	alkyl or aryl halide	CH_3Cl	methyl chloride, refrigerant and local anesthetic
F. Functional groups containing sulfur†	$-\overset{\|}{\underset{\|}{C}}-SH$	thiol (also called mercaptan)	CH_3SH	methanethiol, has the odor of rotten cabbage
	$-\overset{\|}{\underset{\|}{C}}-S-\overset{\|}{\underset{\|}{C}}-$	thioether (also called sulfide)	$(CH_2{=}CHCH_2)_2S$	diallyl sulfide, has the odor of garlic

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



testosterone



penicillin-G