

PHARMACEUTICAL ORGANIC CHEMISTRY"1"

MORPHINE ACADEMY

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Pharmaceutical Organic Chemistry-1

Chapter-1: Introduction



Organic Chemistry: Definition

المادة العضوية بالنسبة النا في الكيمياء هي الكائنات الحية التي تحتوي على العنصر الاساسي و هو الكربون

- The word <u>Organic</u> can be a biological or chemical term, in <u>biology</u> it means anything that is living or has lived. The opposite is Non-Organic.
- Organic Chemistry is unique in that it deals with vast numbers of substances, both natural and synthetic.

The clothes, the petroleum products, the paper, rubber, wood, plastics, paint, cosmetics, insecticides, and drugs

- But, from the chemical makeup of organic compounds, it was recognized that one constituent common to all was the element carbon.
- Organic chemistry is defined as <u>the study of carbon/hydrogen-containing compounds</u> and their derivatives.

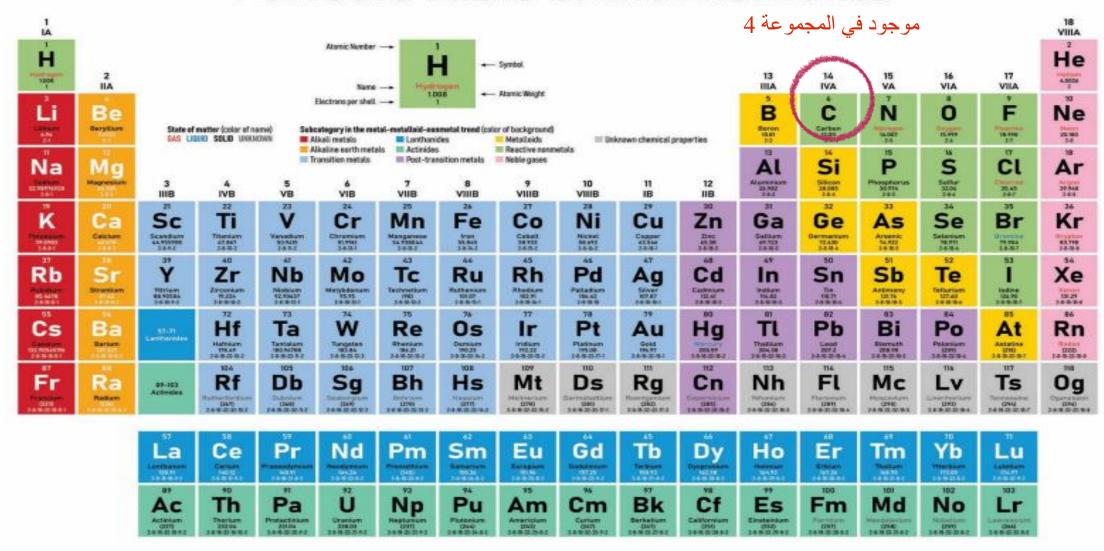
The Uniqueness of Carbon

- What is unique about the element carbon?
- Owhy does it form so many compounds?
 - The answers lie in

يتميز الكربون ؟

- The structure of the *carbon* atom.
- > The position of carbon in the periodic table.
- These factors enable it to form strong bonds with
 - other carbon atoms
 وصفات الكربون بتتغير بناءً على ارتباطه بالذرات الإخرى
 - > and with other elements (hydrogen, oxygen, nitrogen, halogens,...etc).
- Each organic compound has its own characteristic set of physical and chemical properties which depend on the structure of the molecule.

Periodic Table of the Elements



Organic compounds are compounds containing carbon



المجموعات 1/2/3 يفقدوا الالكترونات وبصير عليهم شحنة موجبة

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

Atomic Structure

- Atoms consist of three main particles: <u>neutrons</u> (have no charge), <u>protons</u> (positively charged) and <u>electrons</u> (negatively charged).
 - Neutrons and protons are found in the nucleus.
 - > Electrons are found outside the nucleus.

Electrons are distributed around the nucleus in successive shells (principal energy levels). بكونوا electrons عشان بيناتهم شحنات سالبة ويتنافروا مع بعض

Atom is electrically neutral.

i.e. Number of electrons = Number of protons والي هو بناءً عليه بنرتب العناصر في الجدول الدوري

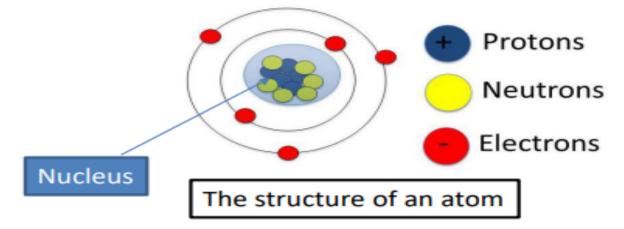
Atomic number of an element is the <u>number of protons</u>.

Or <u>number of eletrons in neutral atom</u> الذرة المتعادلة

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 <u>same atomic number</u> but <u>different mass numbers</u> (¹²C and ¹³C)

Atomic Structure

- The energy levels are designated by capital letters (K, L, M, N, ..) or whole numbers (n).
- The maximum capacity of a shell = $2n^2$ electrons.

n = number of the energy level.

For example, the element carbon (atomic number 6)

6 electrons are distributed about the nucleus as

Shell	K	L	M	N
Number of electrons	2	4	0	0

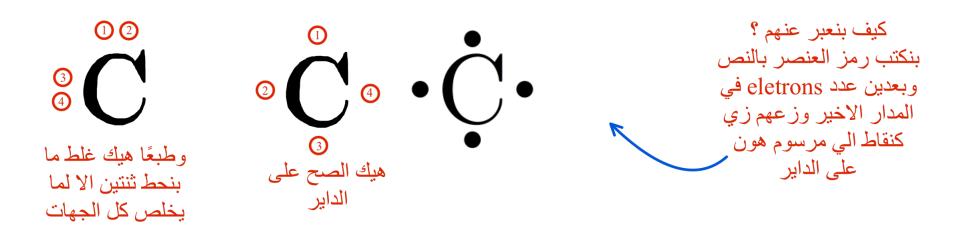
Atomic Structure

الكترونات التكافؤ الموجودة في المدار الاخير

Valance Electrons: Electron-Dot Structures

احنا بنهتم بهذه electrons عشان هي الي بتتفاعل مع العناصر الثانية

- Valance Electrons are those electrons located in the outermost energy level (the valance shell).
- Electron-dot structures
 - > The symbol of the element represents the core of the atom.
 - > The valance electrons are shown as dots around the symbol.



طبعًا صعب جدًا ان يكون element بالصيغة الحرة ومش element مرتبط مع مركبات مرتبط مع مركبات مع مركبات .

عشان المركبات تسعى انها تكون تشبه الغازات النبيلة وتكون مستقرة و بكون المدار الاخير شبعان ما بكسب و لا بفقد

In 1916 G.N. Lewis pointed out that:

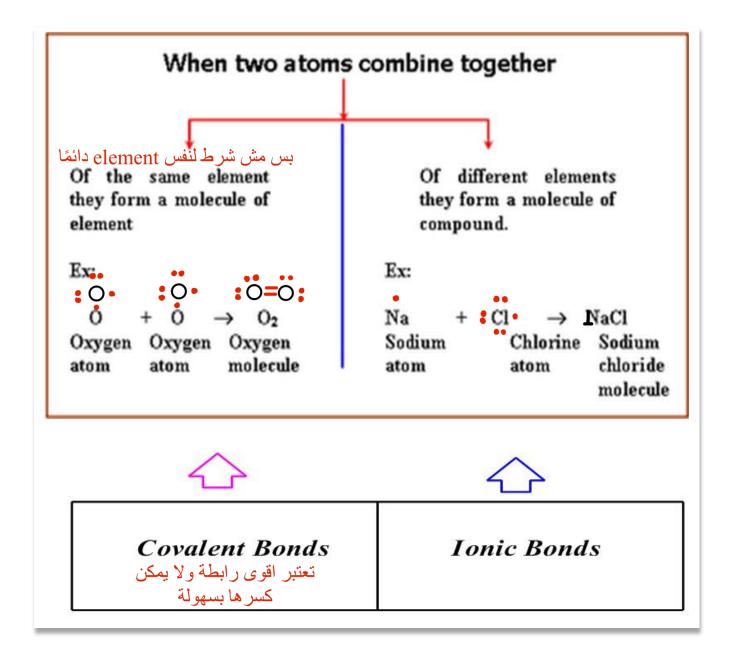
The noble gases were stable elements and he described their lack of reactivity to their having their valence shells filled with electrons.

- 2 electrons in case of helium.
- > 8 electrons for the other noble gases.
- According to Lewis,

in interacting with one another atoms can achieve a greater degree of stability

by rearrangement of the valence electrons

to acquire the outer-shell structure of the closest noble gas in the periodic table.



A) Ionic Bonds

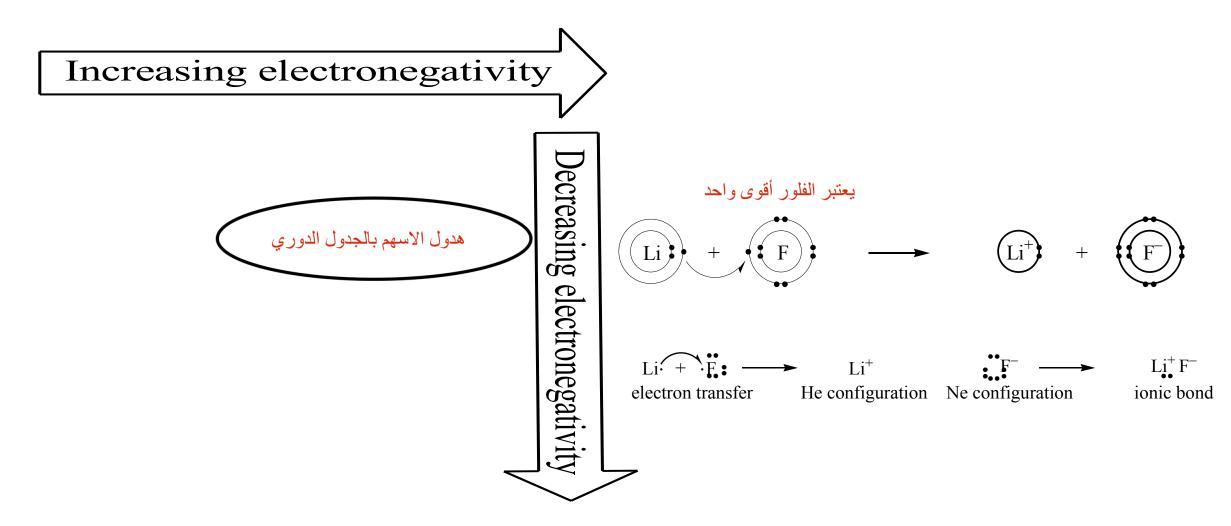
- Elements at the left of the periodic table give up their valance electrons and become +ve charged ions (cations).
- Elements at the right of the periodic table gain the electrons and become -ve charged ions (anions).
- Ionic bond

The electrostatic force of attraction between oppositely charged ions.

$$\mathbf{A}^{\times} + \mathbf{B} : \longrightarrow \mathbf{A}^{+} + \begin{bmatrix} \mathbf{x} \mathbf{B} : \end{bmatrix}^{-}$$
Electron donor atom atom
$$\mathbf{A}^{+} + \begin{bmatrix} \mathbf{x} \mathbf{B} : \end{bmatrix}^{-} \longrightarrow \mathbf{A}^{+} \begin{bmatrix} \mathbf{x} \mathbf{B} : \end{bmatrix}^{-}$$
Electrostatic attraction Ionic bond

The majority of ionic compounds are inorganic substances.

Electronegativity Measures The Ability of An Atom To Attract Electrons



B) Covalent Bonds

 Elements that are close to each other in the periodic table attain the stable noble gas configuration

by sharing valence electrons between them.

Covalent bond

The chemical bond formed when two atoms share one pair of electrons.

 A shared electron pair between two atoms or single covalent bond, will be represented by a dash (-).

B) Covalent Bonds

Examples

H₂ H• +•H
$$\longrightarrow$$
 H:H or H—H $\stackrel{\text{each H shares two electrons}}{\text{(He configuration)}}$

Cl₂ :Cl• +•Cl: \longrightarrow :Cl•Cl: or :Cl—Cl:

H

H:C : H or H—C—H

methane

N₂

H

lone pair

H

H

lone pair

H

H

chloromethane

ethanol

chloromethane

B) Covalent Bonds

- In molecules that consist of two like atoms;
 the bonding electrons are shared equally
 (both atoms have the same electronegativity).
- When two unlike atoms;

the bonding electrons are no longer shared equally (shared unequally).

A) Polar Covalent Bond

الكربون في المجموعة 4 والاكسجين في المجموعة 6 يعني مين بحب electrons أكثر ؟ هو الأكسجين حسب المجدول الدوري والي حكينا فوق ، يعني بيكون electron اكثر وبسحبهم يعني فترة بقاء electron عند الاكسجين اكثر بلحظات معينة

A bond, in which an electron pair is shared unequally.

> The more electronegative atom assumes a partial negative charge and the less electronegative atom assumes a partial positive charge.

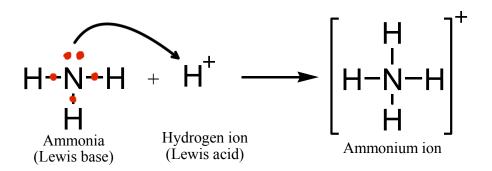
$$\leftarrow$$
 δ + δ - C or C \leftarrow O

التناسقية

B) Coordinate Covalent Bonds

هسا في covelent bond العادية او poler بيكون في تشارك بين الذرات في covelent bond بيكون electrons من ذرة وحدة

- There are molecules in which one atom supplies both electrons to another atom in the formation of a covalent bond.
- For example;



Lewis base

The species that furnishes the electron pair to form a coordinate covalent bond.

lewis الى element الى قدم زوج electrons هو قاعدة element

Lewis acid

The species that accepts the electron pair to complete its valance shell.

اما الي استقبل زوج electrons هو حمض lewis

- 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. بهمنا كثير الحجم عشان يعني لما نحط المركبات الاخرى بدنا نعرف كم رح ياخذ مساحة حسب المركبات الاخرى الموجودة ورح يغير لنا الكثافة ورح يدخل في المستقبلات او لأ
- Orbitals are grouped in shells.

يعني ما بزبط اعبي في المدار الواحد أكثر من 2 من electrons وطبعا بكونوا بدوروا عكس بعض عشان في بينهم تنافر 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 orl	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		

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

VE = Group number

VE - Group Humber	VE	Lewis symbol of atom
Examples: ¹H: Is¹	1	H·
⁸ O: IS ² 2S ² 2P ⁴	6	
6C : $1S^2 2S^2 2P^2$		

Group	- 1	II	III	IV	V	VI	VII	VIII
	Н٠							He:
	Li•	Be•	·B·	٠ċ٠	· N :	· ö :	:F:	:Ne:
	Na ·	Ma.	·Al·	. ci .			• 61 •	: Ar :

How Many Bonds to an Atom? Covalence Number

The number of covalent bonds that an atom can form with other atoms.

i.e. the covalence number is equal to the number of electrons needed to fill its valance shell.

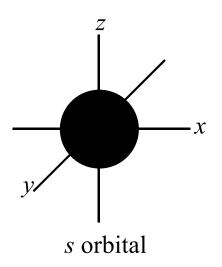
Element	Number of valence electrons	Number of electrons in filled valence shell	Covalence number
Н	1	2	1
C	4	8	4
N	5	8	3
0	6	8	2
F, Cl, Br, I	7	8	1

Atomic Orbitals

- An atomic orbital represents a specific region in space in which an electron is most likely to be found.
- Atomic orbitals are designated in the order in which they are filled by the letters s, p, d, and f.
 - Examples: K shell has only one 1s orbital.

L shell has one 2s and three 2p $(2p_x, 2p_y)$ and $2p_z$.

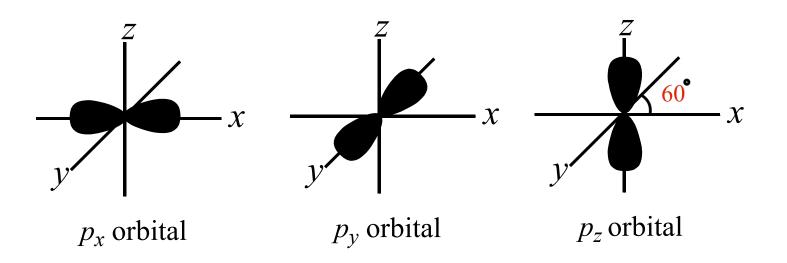
 An s orbital is spherically shaped electron cloud with the atom's nucleus and its center.



Atomic Orbitals

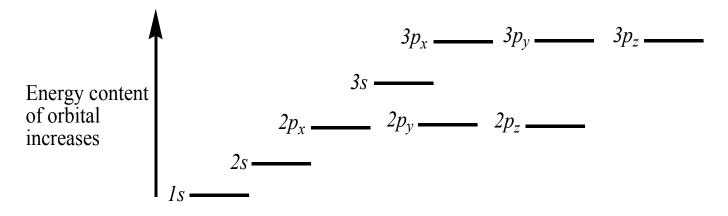
- O A p orbital is a dumbbell-shaped electron cloud with the nucleus between the two lobes.

 Representation of the image of the strong electrons lobes.
- Each p orbital is oriented along one of three perpendicular coordinate axes (in the x, y, or z direction).



Atomic Orbitals

An energy level diagram of atomic orbitals.

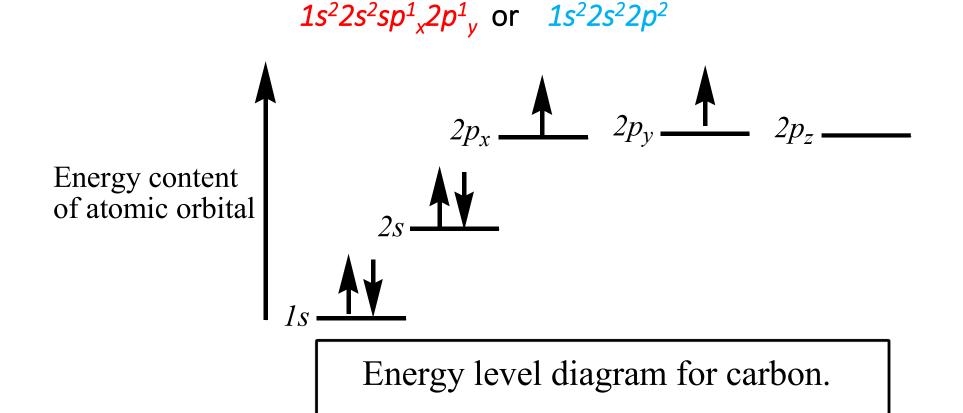


- When filling the atomic orbitals, keep in mind that
 - (1) An atomic orbital contain no more 2 electrons.
 - (2) Electrons fill orbitals of lower energy first.
 - (3) No orbital is filled by 2 electrons until all the orbitals of equal energy have at least one electron.

 Least one electrons على كل orbital في shell وبعدين بترجع بتعبى من اول وجديد electrons على كل orbital على كل orbital وبعدين بترجع بتعبى من اول وجديد

Atomic Orbitals

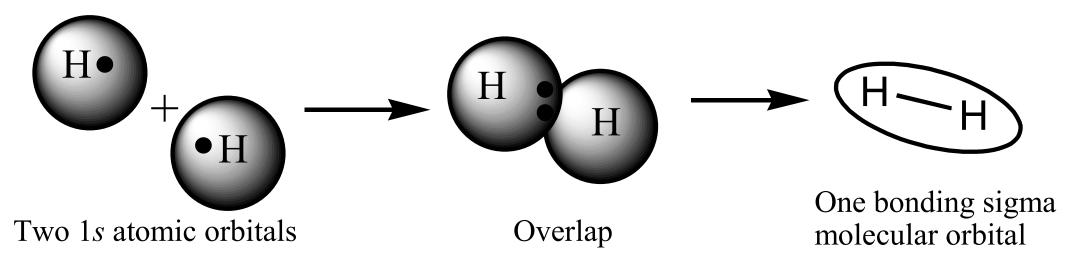
The electronic configuration of carbon (atomic number 6) can be represented as



Molecular Orbitals

- A covalent bond consists of the overlap between two atomic orbitals to form a molecular orbital.
- Example:

Molecular orbital of H₂



Molecular Orbitals

- رابطة احادية
- O Sigma bonds (σ bonds) can be formed from
 - The overlap of two s atomic orbitals.
 - The end-on overlap of two p atomic orbitals.
 - \triangleright The overlap of two an s atomic orbital with a p atomic orbital.
- وابطة ثنائية opi bonds (π bonds) can be formed from the side-side overlap between two p atomic orbitals.

Bond Energy and Bond Length

A molecule is more stable than the isolated constituent atoms.

This stability is apparent in the release of energy during the formation of the molecular bond.

- Heat of formation (bond energy)
 The amount of energy released when a bond is formed.
- Bond dissociation energy

The amount of energy that must be absorbed to break a bond.

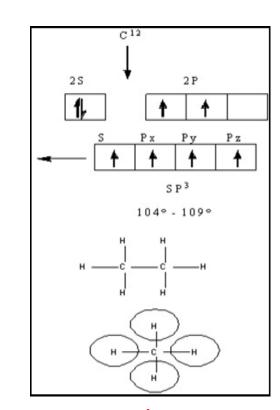
Bond length

The distance between nuclei in the molecular structure.

Hybridization (Alkanes sp³)

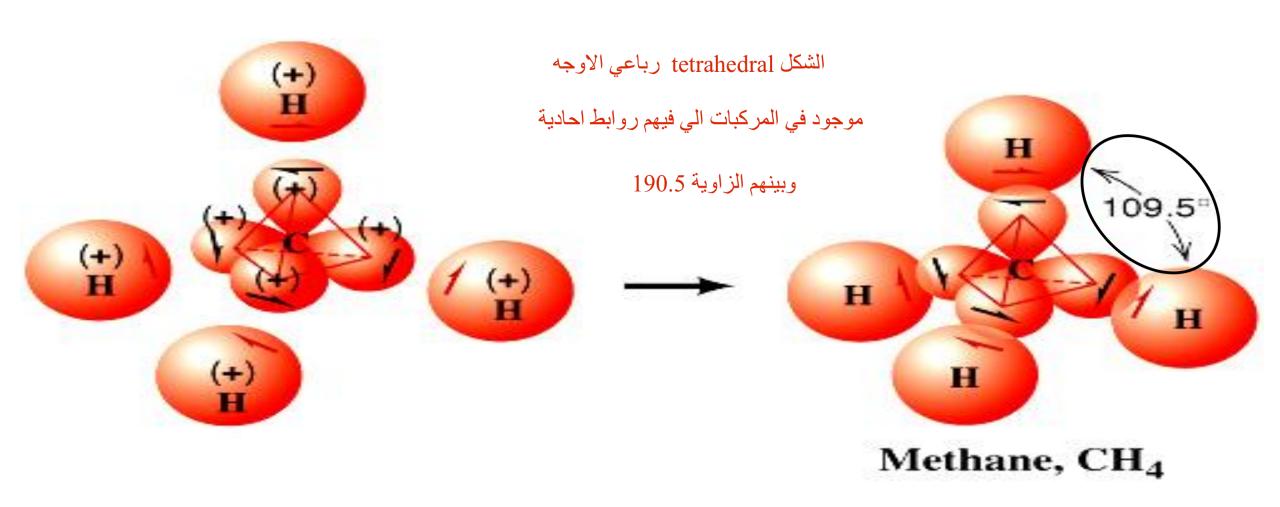
1s + 3p

- o In the case of alkanes sp^3 , the three 2p orbitals of the carbon atom are combined with its 2s orbital to form four new orbitals called " sp^3 " hybrid orbitals.
- Four hybrid orbitals were required since there are four atoms attached to the central carbon atom.
- \circ These new orbitals will have an energy slightly above the 2s orbital and below the 2p orbitals as shown in the following illustration.
- Notice that no change occurred with the 1s orbital.



Methane

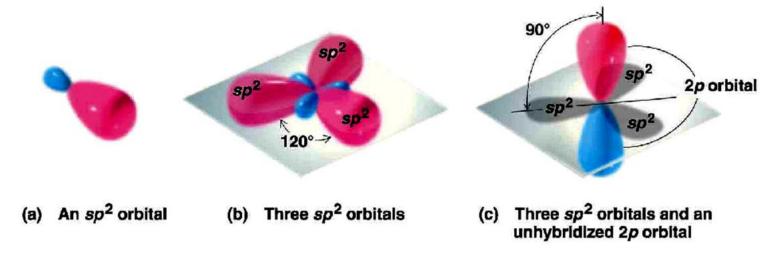
Hybridization (Alkanes sp³)



موجود في المركبات الي فيهم روابط ثنائية يعني (Alkenes sp²) المركبات الي فيهم روابط ثنائية يعني

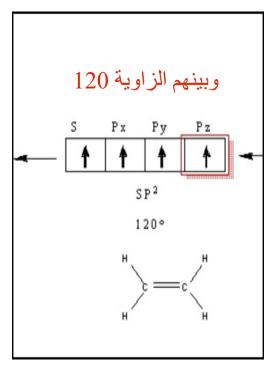
o In the case of alkenes sp^2 , the 2s orbital is combined with only two of the 2p orbitals (since we only need three hybrid orbitals for the three groups. thinking of groups as atoms and nonbonding pairs) forming three hybrid orbitals called sp2 hybrid orbitals.

- The other p-orbital remains unhybridized and is at right angles to the trigonal planar arrangement of the hybrid orbitals.
- The trigonal planar arrangement has bond angles of 120°.



الشكل trigonal ثلاثي الاوجه

sigma bond and pi bond



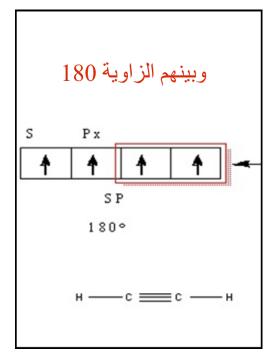
Ethene (Ethylene)

Hybridization (Alkynes sp)

1s + 1p

موجود في المركبات الي فيهم روابط ثلاثية الشكل linear ثنائي الاوجه

- In the case of alkynes sp, the 2s orbital is combined with only one of the 2p orbitals to yield two sp hybrid orbitals.
- The two hybrid orbitals will be arranged as far apart as possible from each other with the result being a linear arrangement.
- O The two unhybridized p-orbitals stay in their respective positions (at right angles to each other) and perpendicular to the linear molecule (180°).



Ethyne (Acetylene)

Formal Charge

Formal Charge: is the net charge on each atoms of the molecule or ion. (which contain a covalent bond only)

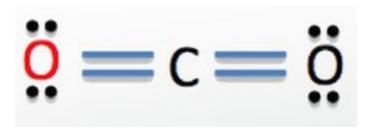
How to calculate the Formal Charge (FC):

FC =
$$\frac{\text{Valence e}^{-}}{\text{in Free Atom}}$$
 - $\frac{\text{Total}}{\text{Nonbonding e}^{-}}$ + $\frac{\text{Bonding e}^{-}}{2}$

Example: calculate the formal charge of CO2

FC for
$$O = 6 - (4 + 4/2) = 0$$

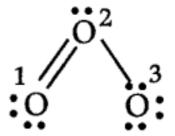
FC for
$$C = 4 - (0 + 8/2) = 0$$



Example:

Formal Charge

Lewis structure of O_3 is

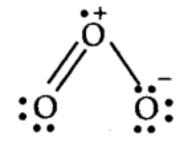


Formal charge on O(1) = 6 -
$$(4 + \frac{4}{2})$$
 = 0

Formal charge on O(2) =
$$6 - (2 + \frac{6}{2}) = + 1$$

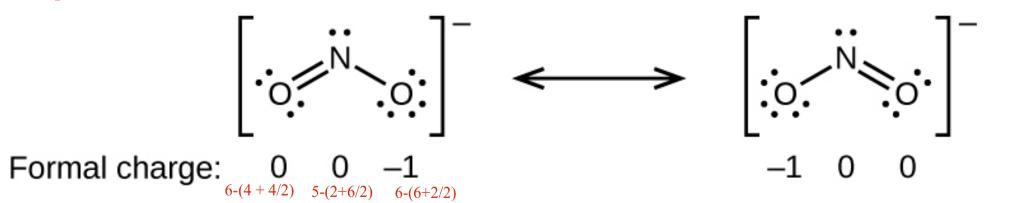
Formal charge on O(3) = 6 -
$$(6 + \frac{2}{2}) = -1$$

Hence we represent O₃ along with formal charges as follows.



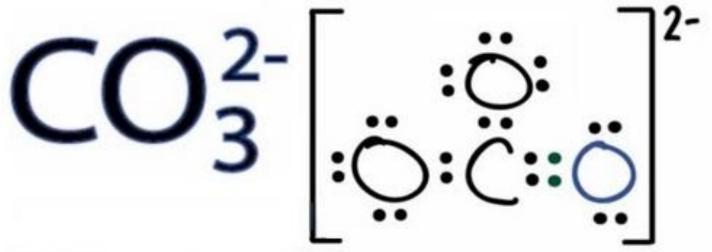
Formal Charge

Example:



Formal Charge

Example:



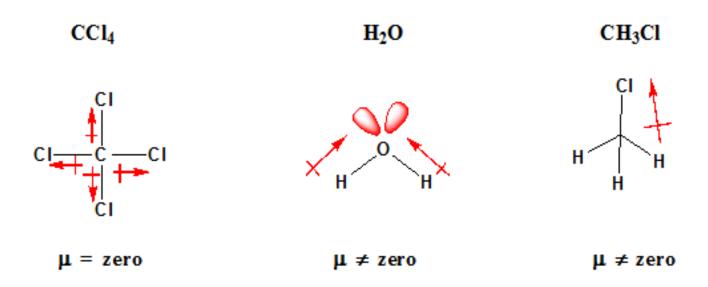
Inductive Effect

- Inductive effect can be defined as the permanent displacement of electrons forming a covalent bond (sigma σ bonds) towards the more electronegative element or group
 بأنه الإزاحة الدائمة للإلكترونات التي تشكل رابطة تساهمية نحو العنصر أو المجموعة الأكثر كهرسلبية.
- The inductive effect is represented by the symbol, the arrow pointing towards the more electronegative element or group of elements.
 - (+ I) effect if the substituent electron-donating

Electron-donating substituents (+I): -CH₃, -C₂H₅,.... Electron-withdrawing substituents (-I): -NO₂, -CN, -SO₃H, COOH, COOR, NH₂, OH, OCH₃

Bond Polarity and Dipole Moment (µ)

- Dipole moment (depends on the inductive effect).
- A bond with the electrons shared equally between two atoms is called a nonpolar bond like in CI-CI and C-C bond in ethane.
- A bond with the electrons shared unequally between two different elements is called a polar bond like in H-Cl and H-O bond.
- The bond polarity is measured by its dipole moment (µ).
- O Dipole moment (μ) defined to be the amount of charge separation ($+\delta$ and $-\delta$) multiplied by the bond length.

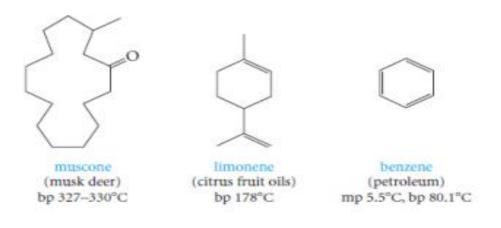


1.17: Classification According to Molecular Framework

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.

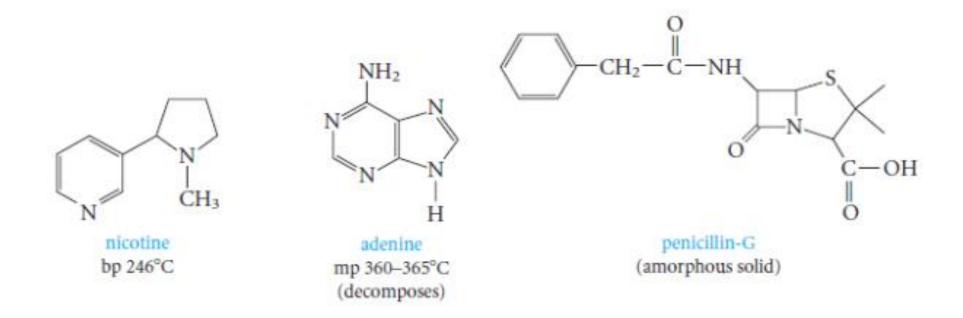
1.17b: Carbocyclic Compounds: contain rings of carbon atoms



اطمنوا الاشكال مش حفظ #منقول من الدكتورة



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.

	Structure	Class of compound	Specific example	Common name of the specific example
A. Functional groups that are a part of the molecular framework		alkane	СН ₃ —СН 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	-ф-он	alcohol	CH ₃ CH ₂ OH	ethyl alcohol, found in beer, wines, and liquors
	-¢-o-¢-	ether	CH ₃ CH ₂ OCH ₂ CH ₃	diethyl ether, once a common anesthetic

Table 1.6 continued				10
	Structure	Class of compound	Specific example	Common name of the specific example
2. With carbon-oxygen double bonds*	_2-н	aldehyde	CH ₂ =0	formaldehyde, used to preserve biological specimens
		ketone	сн _з ссн _з	acetone, a solvent for varnish and rubber cement
3. With single and double carbon—oxygen bonds	—c—он	carboxylic acid	снэс—он	acetic acid, a component of vinegar
	-ç-o-¢-	ester	O CH₃C — OCH₂CH₃	ethyl acetate, a solvent for nail polish and model airplane glue
C. Functional groups containing nitrogen**	-¢-NH=	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	_с_мн _{>}	primary amide	H-C-NH2	formamide, a softener for paper
E. Functional group with halogen	—x	alkyl or aryl halide	CH ₃ CI	methyl chloride, refrigerant and local anesthetic
F. Functional groups containing sulfur	— с —sн	thiol (also called mercaptan)	CH ₃ SH	methanethiol, has the odor of rotten cabbage
		thioether (also called sulfide)	(CH ₂ =CHCH ₂) ₂ S	diallyl sulfide, has the odor of garlic

Functional Groups

Functional Group is a reactive portion of an organic molecule, an atom, or a group of atoms that confers on the whole molecule its characteristic properties.

Class	General formula	Functional group	Specific
Alkane	RH	C – C (single bond)	$H_3C - CH_3$
Alkene	$R - CH = CH_2$	C = C (double bond)	$H_2C = CH_2$
Alkyne	R-C≡CH	c≡c (triple bond)	нс≡сн
Alkyl halide	RX	-X (X = F, Cl, Br, I)	H ₃ C - Cl
Alcohol	R – OH	-OH	H ₃ C - OH
Ether	R – O –R'	- C- O – C -	$H_3C - O - CH_3$
Aldehyde	0 R-C-H 0	О —Ё–Н	О H-С-H, H ₃ C-С-H О Н ₃ C-С-СН ₃
Ketone	O R-C-R	— С–H - С–С–С–	O H ₃ C-Č-CH ₃
Carboxylic acid	О R-С-ОН	' о ' —Ё-он	O O O O O
Ester	0 r -C-or	o —ċ-or	O H-Ö-OCH ₃ O H ₃ C-Ö-OCH ₃
Amine	R – NH ₂	$-\overset{I}{C}-NH_2$	H ₃ C – NH ₂

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.

H-C-C-C-C-H CH₃CHBrCH₂CH₂CHClCH₃ or CH₃CHCH₂CH₂CHCH₃
H Br H H Cl H CH₃CHBrCH₂CHClCH₃ or CH₃CHCH₂CH₂CHCH₃

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.

H-C-C-C-C-C-H $CH_3CH_2CH(CH_3)CH_2CH(OH)CH_3$ or $CH_3CH_2CHCH_2CHCH_3$ CH₃ OH

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

CH₃ CH₃CH₂C(CH₃)₂CH₂CH₂OH or CH₃CH₂CCH₂CH₂OH CH₃