

PHARMACEUTICAL ORGANIC CHEMISTRY"1"

MORPHINE ACADEMY

MORPHINE ACADEMY

Pharmaceutical Organic Chemistry-1

Chapter-1: Introduction



- The word Organic can be a biological or chemical term, in biology it means 0 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, \mathbf{O} 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 \mathbf{O} one constituent common to all was the element carbon.
- Organic chemistry is defined as the study of carbon/hydrogen-containing 0 compounds and their derivatives.

The Uniqueness of

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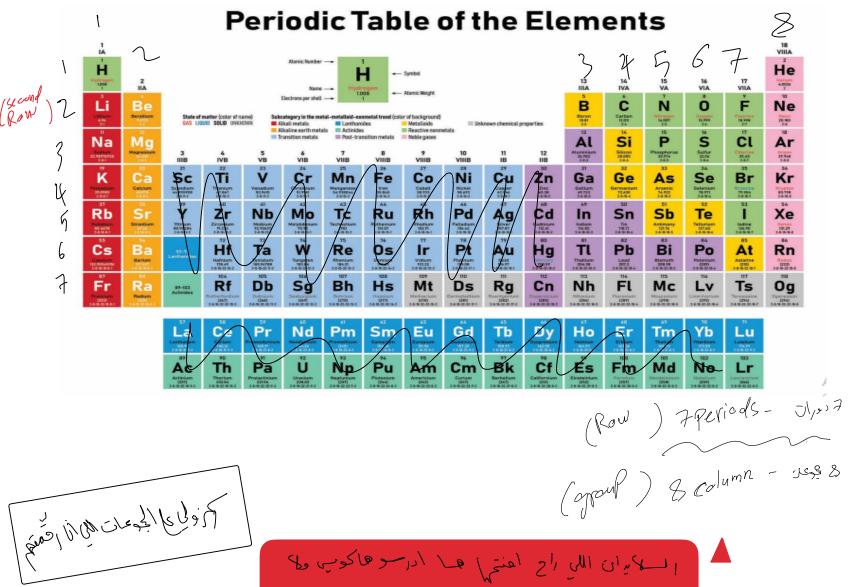
- o What is unique about the element carbon?
- o Why does it form so many compounds?
 - The answers lie
 - \rightarrow in The structure of the carbon atom.
 - > The **position** of *carbon* in the periodic table
- o These factors enable it to form strong bonds with
 - other carbon atoms
 - > and with other elements (hydrogen, oxygen, nitrogen, halogens,...etc).
- o Each organic compound has its own characteristic set of physical and chemical properties which depend on the structure of the molecule.

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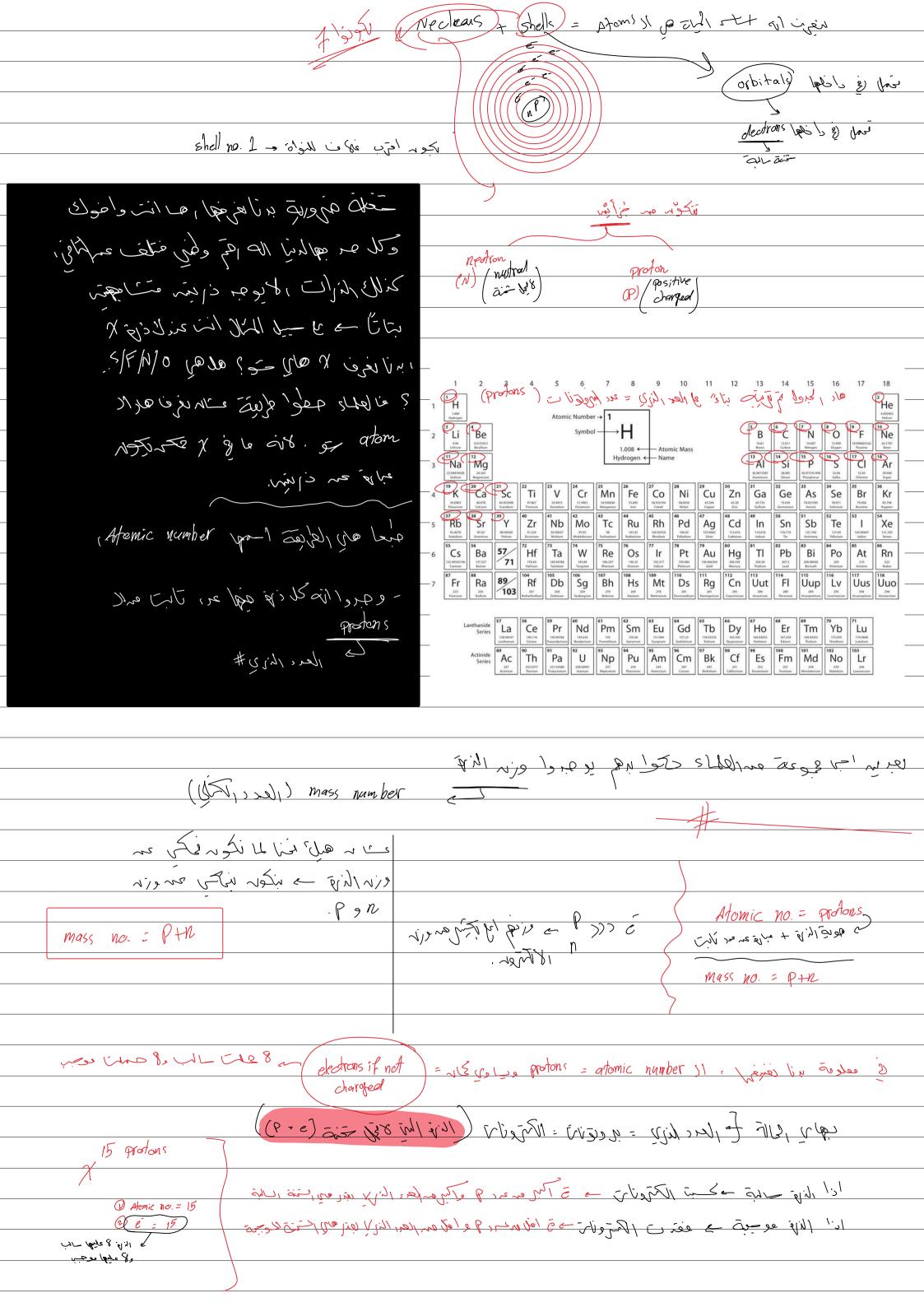
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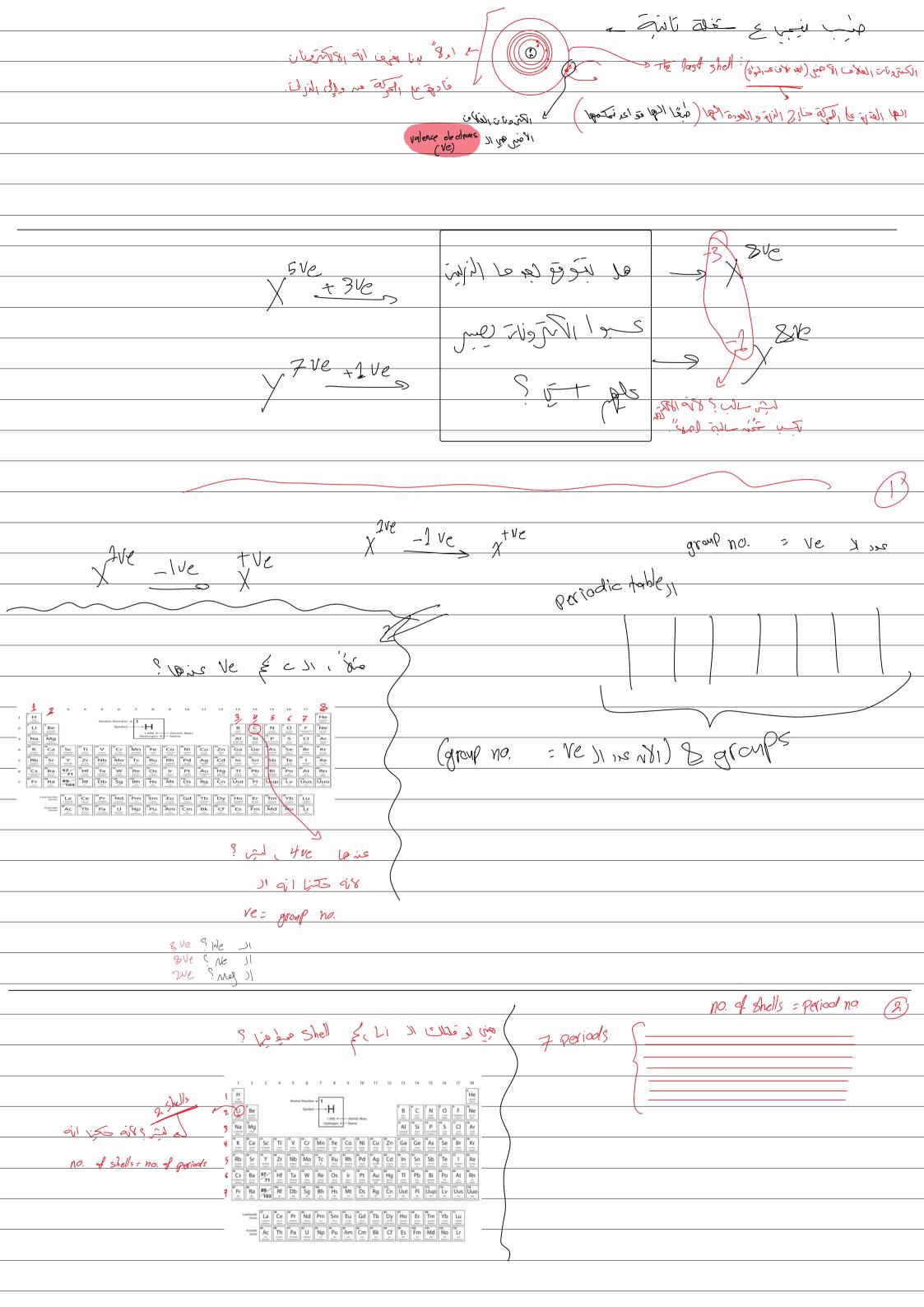
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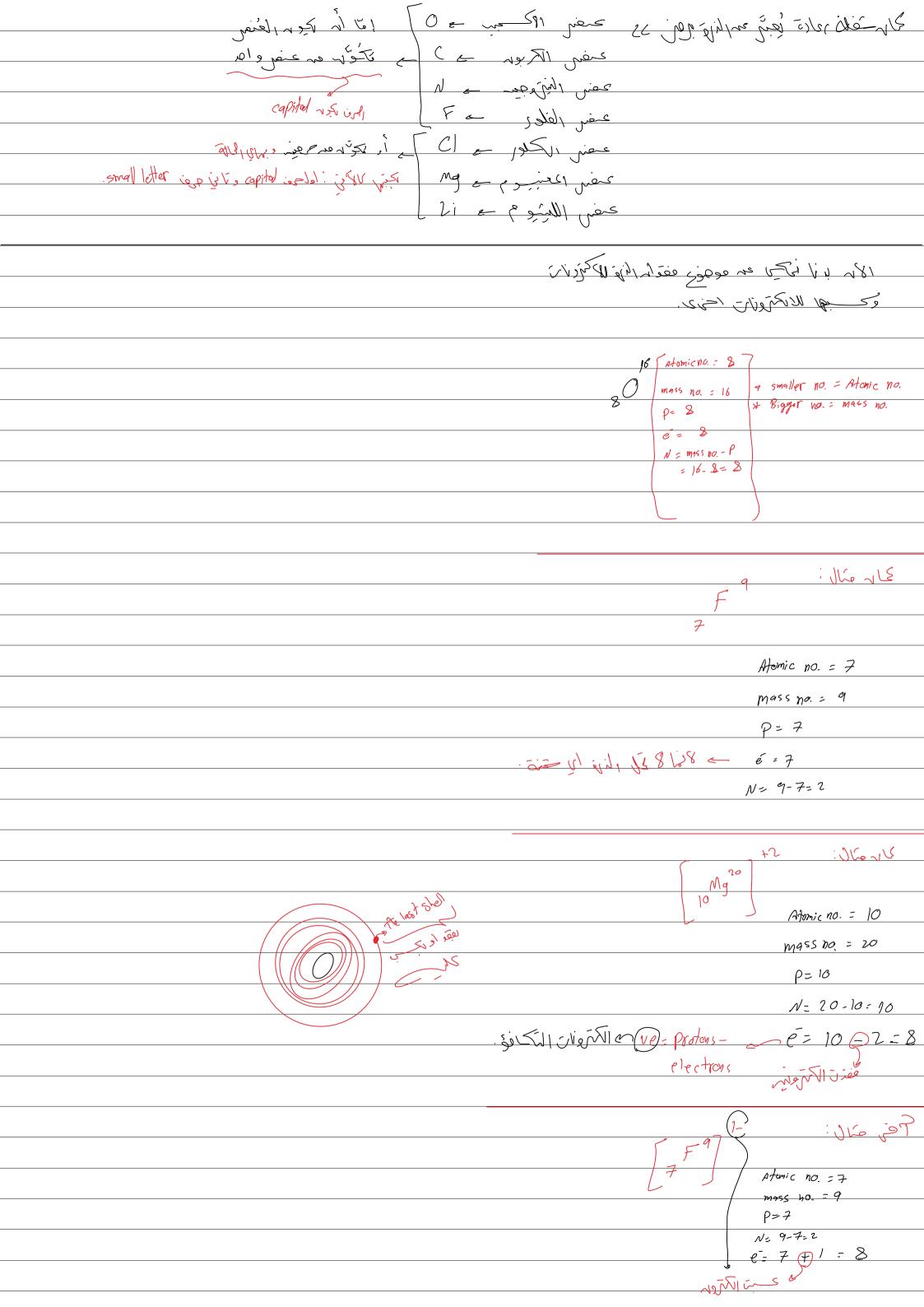
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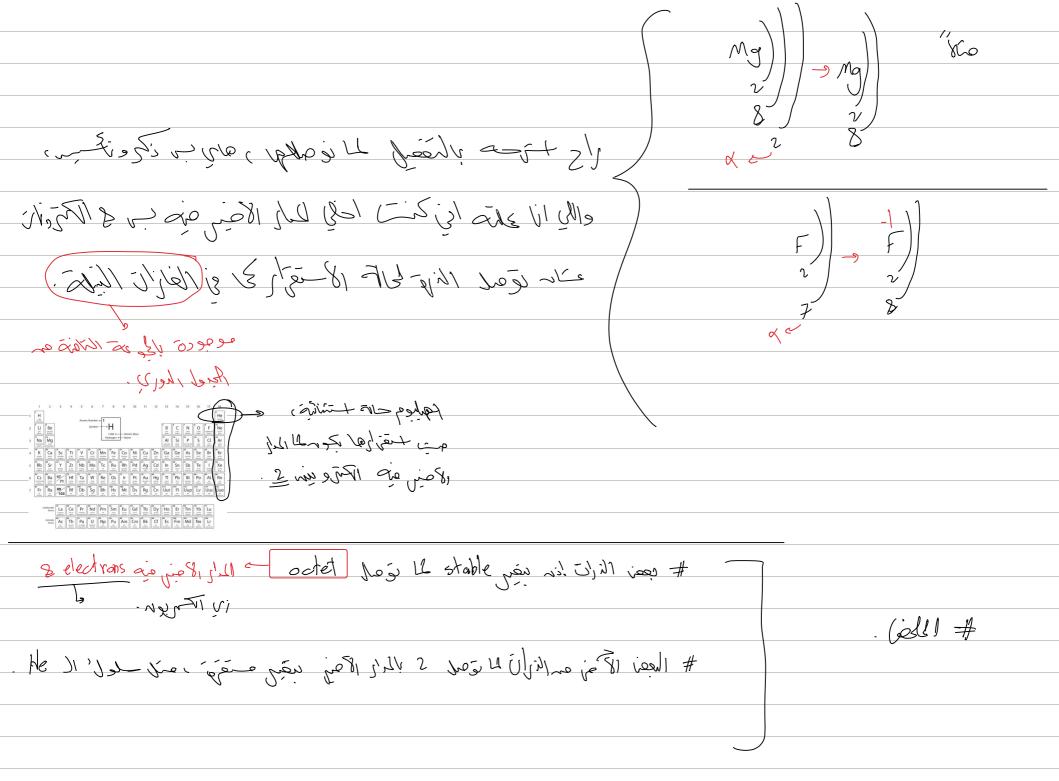
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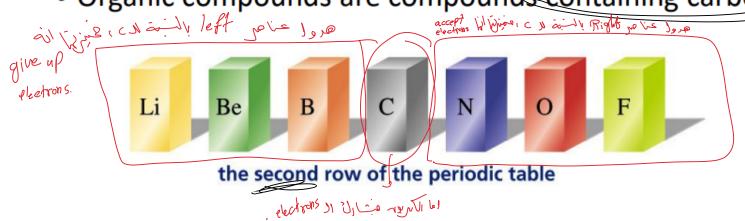
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Organic compounds are compounds containing carbon



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

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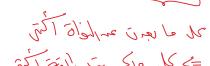
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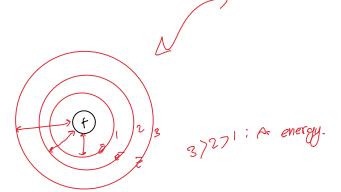
Structure

- O Atoms consist of three main particles: neutrons (have no charge), protons (positively charged) and electrons (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).

- o **Atom** is electrically neutral.
 - i.e. Number of electrons = Number of protons
- o Atomic number of an element is the number of protons.

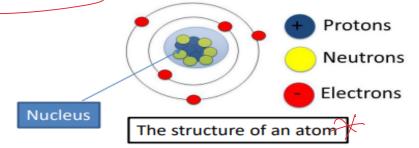




Bonding and Isomerism

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 (120 and 130)

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Atomic



Structure

- The energy levels are designated by capital letters (K, L, M, N, ...) or whole 0 numbers (n).
- The maximum capacity of a shell = 2n2 electrons. 0

n = number of the energy level.

For example, the element carbon (atomic number 6) 0

6 electrons are distributed about the nucleus as

Shell

Number of electrons

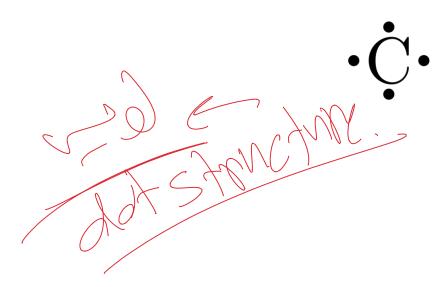
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Atomic

Structure

Valance Electrons: Electron-Dot

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



Chemical Bonding

o In 1916 G.N. Lewis pointed out that:

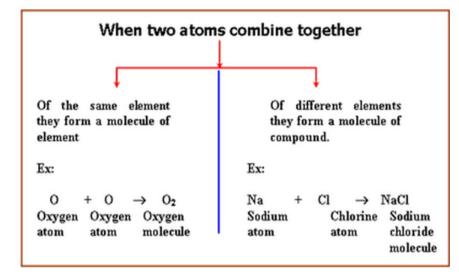
The noble gases were stable elements and he described their lack of reactivity to their having their valence shells filled with electrons.

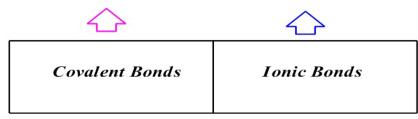
- > 2 electrons in case of helium.
- > 8 electrons for the other noble gases.
- o According to Lewis,

in interacting with one another atoms can achieve a greater degree of stability rearrangement of the valence electrons

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

Chemical Bonding





A) Ionic Bonding

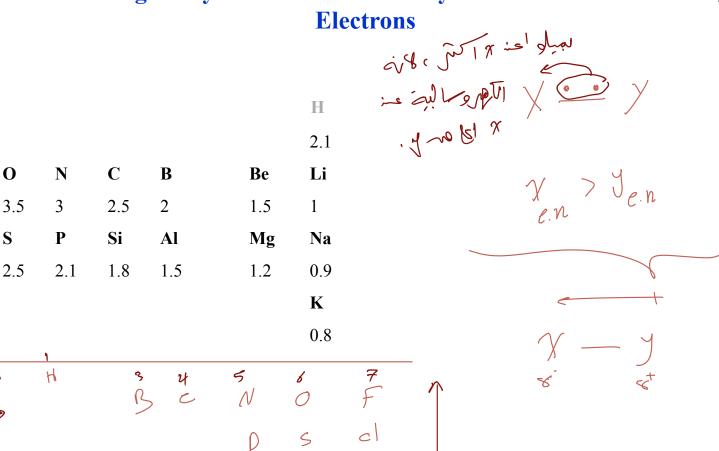
- o Elements at the left of the periodic table give up their valance electrons and become +ve charged ions (cations).
- o Elements at the right of the periodic table gain the electrons and become charged ions (anions).
- o Ionic bond

The electrostatic force of attraction between oppositely charged ions.

o The majority of ionic compounds are *inorganic substances*.

Chemical

Electronegativity Measures The Ability of An Atom To Abouting **Electrons**

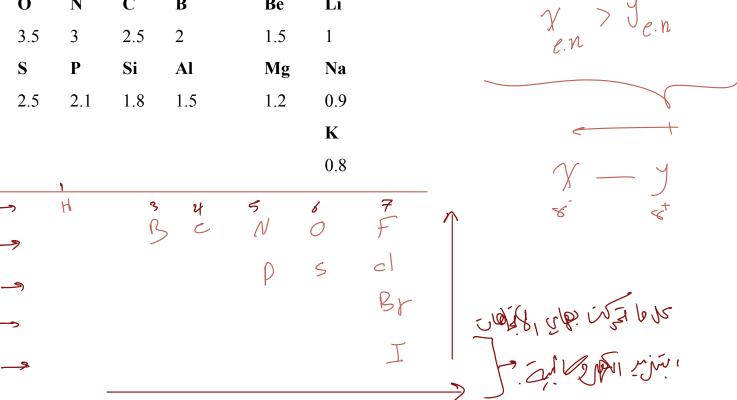


F

Cl

Br

2.8



Chemical **Bonding**

B) Covalent **Bonds**

Elements that are close to each other in the periodic table attain the stable 0 noble gas configuration

by sharing valence electrons between

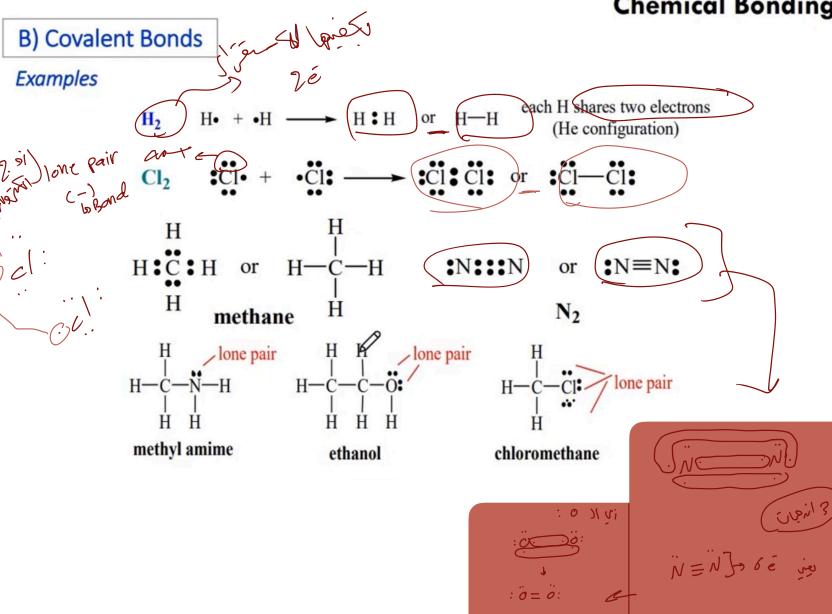
Covalent bond 0

> 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 0 represented by a dash (-).

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Chemical Bonding



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B) Covalent Bonds

Bond:

Bond:

Bond:

Covalent Bonds

Bond:

Covalent Bonds

Chemical Bonding

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

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

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

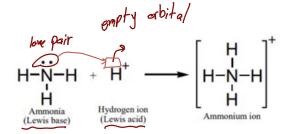
electronegative atom assumes a partial positive charge.

+8 & C=N

Chemical Bonding

B) Coordinate Covalent

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



o Lewis base

The species that <u>furnishes</u> the electron pair to form a coordinate covalent bond.

o Lewis acid

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

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.

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

mat Junouna the	ivacieus			
	First shell	Second shell	Third shell	Fourth shell
Atomic orbitals 14 الكترويية	و موا	2 6=8 S, p	s, p, d	$\frac{2}{s, p, d, f} = 3$
Number of atomic orbitals	1	1, 3	1, 3, 5	1, 3, 5, 7
Maximum number of electrons	2	8	18	32
	S-3) number of aformic or hidred			18
	A-	25 /	11/	

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

VE = Group number

VE Lewis symbol of atom

Examples: 1 H: 1 I 8 O: 1 IS 2 2S 2 2P 4 I 6 C:

Table 1.3 — Valence Electrons of the First 18 Elements							
Group	II	Ш	IV	V	VI	VII	VIII
H Li Na	Be·	·B·	· ċ · ·	·N: ·P:	·0:	:F:	He: :Ne: :Ar:
			•		;	; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ; ;	

How Many Bonds to an Atom? Covalence Number Bonding

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			Covalence	
		in filled	valence shell	number		
H	1	2	1			
\mathbf{C}	4	8	4			
N	5	8	3			
O	6	8	2			
F. Cl	. Rr. I	7	8	1		

Shapes of Organic Molecules: Orbital Picture of Covalent Bonds

Atomic

- **Orbitals** An atomic orbital represents a specific region in space in which an electron is most 0 likely to be found.
- **Atomic orbitals** are designated in the order in which they are filled by the letters 0 s, p, d, and f.

A shell has only one 1s orbital.

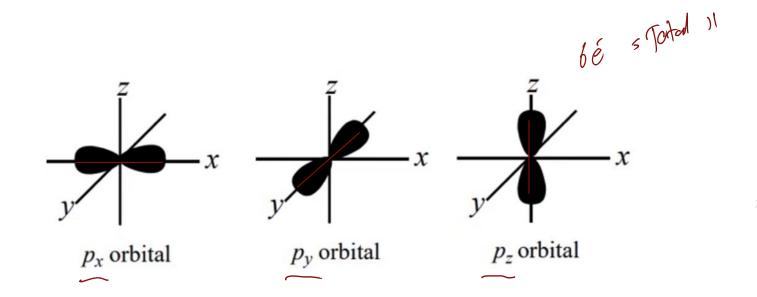
* L shell has one 2s and three 2p (2px, 2py and 2pz).

Sois shell is shell is shell if shell is shell if

An s orbital is spherically shaped electron cloud with the 0 atom's nucleus and its center.

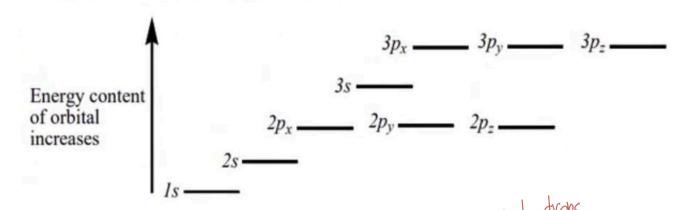
Shapes of Organic Molecules: Orbital Picture of Covalent Bonds

- Atomic Orbitals
- o A p orbital is a dumbbell-shaped electron cloud with the nucleus between the two lobes.
- o Each p orbital is oriented along one of three perpendicular coordinate axes (in the x, y, or z direction).



An energy level diagram of atomic orbitals.

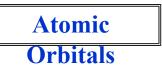
Atomic Orbitals



- 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.

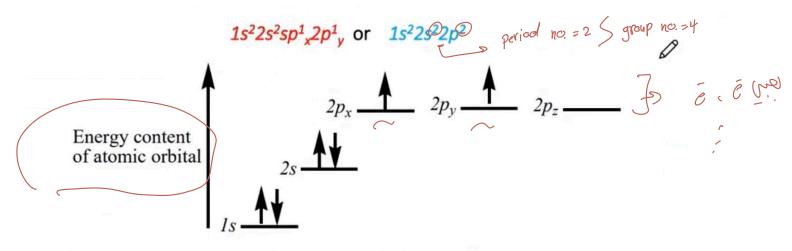
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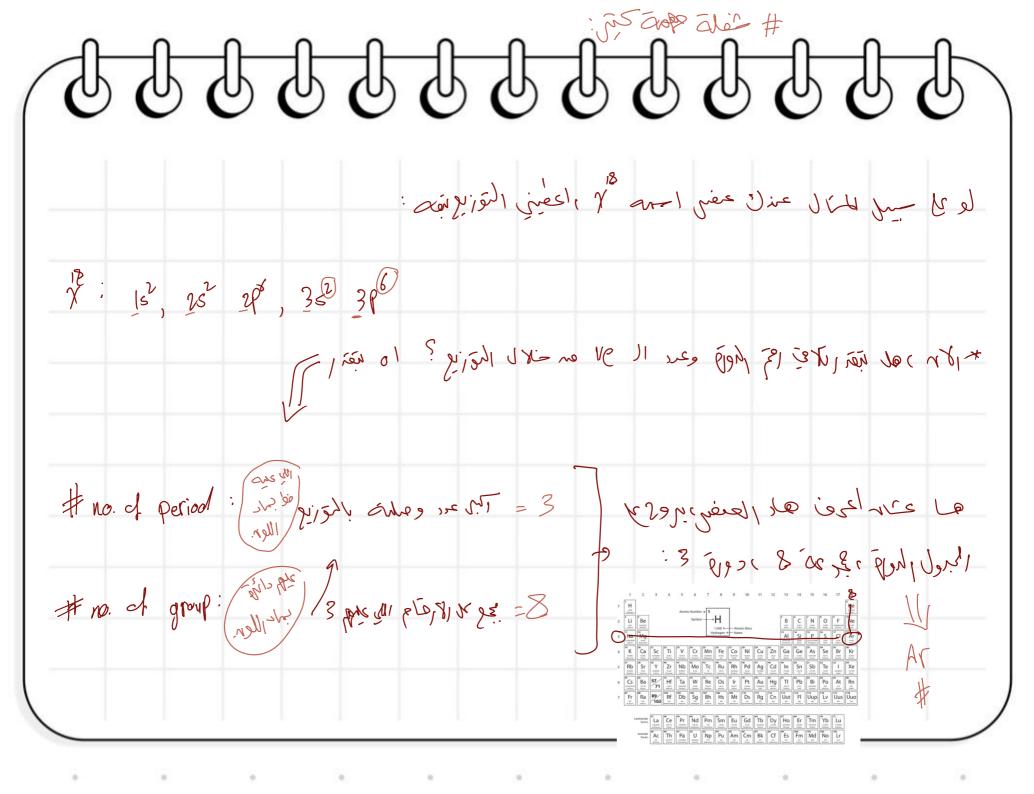


Shapes of Organic Molecules: Orbital Picture of Covalent Bonds

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



Energy level diagram for carbon.

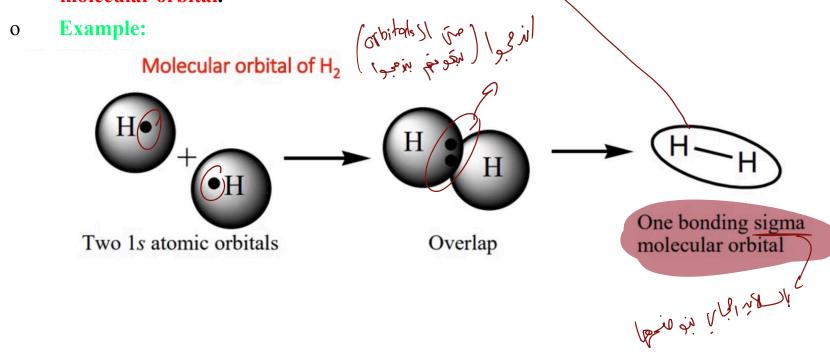


Shapes of Organic Molecules: Orbital Picture of Covalent

Bonds

Molecular Orbitals

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



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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.

o **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.

o **Bond length**

The distance between nuclei in the molecular structure.

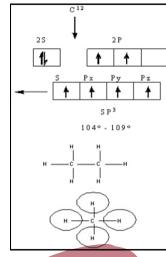
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- o In the case of **alkanes** *sp3*, the three *2p* orbitals of the carbon atom are combined with its *2s* orbital to form four new orbitals called "*sp3*" hybrid orbitals.
- o Four hybrid orbitals were required since there are four atoms attached to the central carbon atom.
- o These new orbitals will have an energy slightly above the 2s orbital and below the 2p orbitals as shown in the following illustration.
- o Notice that no change occurred with the *1s* orbital.
- Regular tetrahedron with all H-C-H bond angles of 109.5°.



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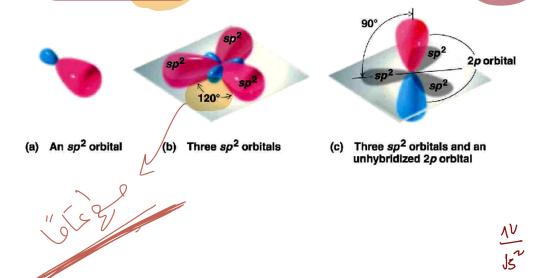


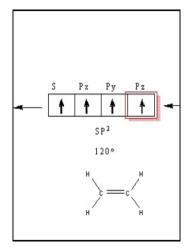
Hybridization (Alkanes *sp3*) STetrahedron (109.5°) H (+)(+)H Methane, CH₄ # Wip 1801 Sid / LIP 1868: $\frac{1V}{2S} \qquad \frac{1}{2\ell} - \frac{1}{R^3} \qquad \frac{1}{2} - \frac{1}{R^3} \qquad \frac{1}{2} - \frac{1}{2} \qquad \frac{1}{2} = \frac{1}{2} - \frac{1}{2} \qquad \frac{1}{2} = \frac{1}{2}$ 503 (= single local of X Tools - 25 9) IL +

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Hybridization (Alkenes

- o In the case of **alkenes** sp2, 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 non-bonding pairs) forming three hybrid orbitals called sp2 hybrid orbitals.
- o The other *p*-orbital remains unhybridized and is at right angles to the trigonal planar arrangement of the hybrid orbitals.
- o The trigonal planar arrangement has bond angles of 120°.



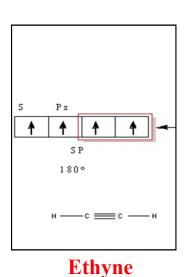


Ethene (Ethylene

$$-\frac{1}{2} - \frac{1}{6}$$

Hybridization (Alkynes = sp)

- 4-C=C-4
- o 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.
- The two unhybridized p-orbitals stay in their respective positions (at right angles to each other) and perpendicular to the **linear** molecule (180 \square).



(Acetylene) $\frac{1}{2}$

SP3	le le sinelle	55 Xis 4 5P ³	75% = P =================================	109.5°	Tetrahedral
SPZ	a least one double wond	SP2 etail 3 Prolosing	76% = P zi	120°	planar
SP	2 double bond or = bond	other 95 eother 9	50% = 5 and	120°	linear.

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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 =
$$\frac{\text{Valence e}^{-}}{\text{in Free Atom}} - \left(\frac{\text{Total}}{\text{Nonbonding e}^{-}} + \frac{\text{Bonding e}^{-}}{2}\right)$$

$$= \frac{\text{Ve - (dots + lines)}}{2}$$
Example: calculate the formal charge of CO2

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

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

$$H_{2Q} = Ve - (dots + lines)$$
 $H_{2Q} = Ve - (dots + lines)$
 $H_{2Q} = Ve - (dots + lines)$

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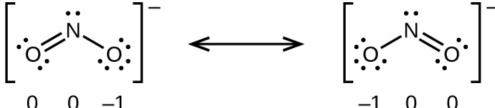
Example Formal Lewis structure of O_3 is 1900 ag : es es : Vèri. ا کارزی ی تیکچید Formal charge on O(1) = 6 - $(4 + \frac{4}{2})$ Formal charge on O(2) = $6 - (2 + \frac{6}{2}) = + 1$ Formal charge on O(3) = 6 - $(6 + \frac{2}{2}) = -1$ lence we represent O₃ along with formal charges as follows. له لو مقنا القانوب بالله الاحبر ، الاجعال الد الاحبير المحري ببطاع علم شخنه موجيت (+) والأفراف سالبة (-).

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Formal Charge

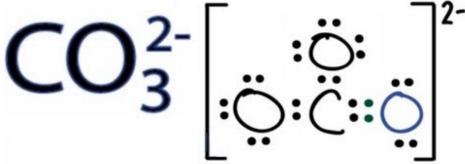
Example



Formal charge: 0 0 -1

Example

Formal Charge



Formal Charge	=	Valence	-	NonBondin Val Electron		Bonding Elec	trons		
C	=	4	-	0	-	8/2	=	0	
0	=	6	-	6	-	2/2	=	-1	
0	=	6	_	4	_	4/2	=	0	

Inductive

- o Inductive effect can be defined as Extremanent displacement of electrons forming a covalent bond ($\underline{\text{sigma } \sigma \text{ bonds}}$) towards the more electronegative element or group.
- The inductive effect is represented by the symbol, the arrow pointing towards the more electronegative element or group of elements.

Electron-withdrawing substituents (-I): -NO2, -CN, -SO3H, COOH, COOR, NH2,

OH, OCH3

H3C—CI

H3C—CI

H C C CI

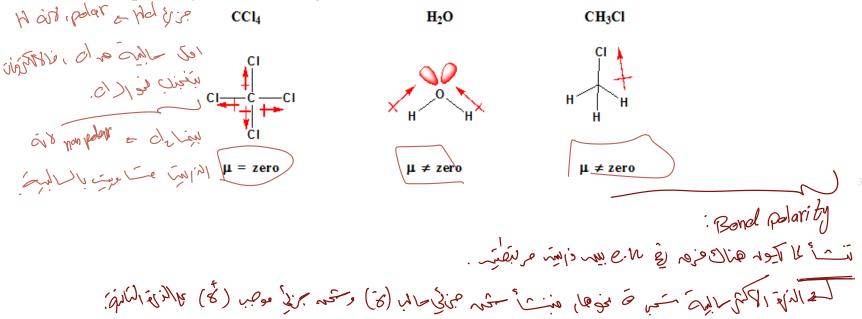
H C C CI

Electron-donating substituents (+D): -CH3, -C2H5,....

Electron-withdrawing substituents (-D): NO2 CN SO2H COOK COOK NICE

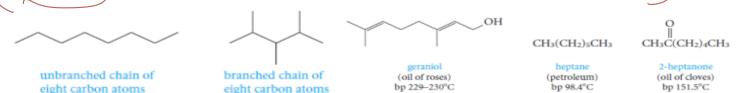
Bond Polarity and Dipole Moment o Dipole moment (depends on the inductive) effect).

- o A bond with the electrons shared equally between two atoms is called a **nonpolar bond** like in Cl-Cl and C-C bond in ethane.
- o A bond with the electrons shared unequally between two different elements is called a **polar bond**.
- o 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.

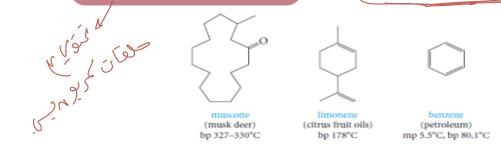


1.17: Classification According to Molecular Framework

- > 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



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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...)

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Classification According to Functional Group

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

Table 1.6 — The Main F	unctional Groups			
	Structure	Class of compound	Specific example	Common name of the specific example
A. Functional groups that are a part of the molecular framework		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	— <mark>С</mark> —он	alcohol	CH₃CH₂OH	ethyl alcohol, found in beer, wines, and liquors
	-ç-o-ç-	ether	CH ₃ CH ₂ OCH ₂ CH 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*	о _е_н	aldehyde	CH ₂ =O	formaldehyde, used to preserve biological specimens
	-ç-c-ç-	ketone	о сн₃ссн₃	acetone, a solvent for varnish and rubber cement
3. With single and double carbon–oxygen bonds	о —с—он	carboxylic acid	он₃с—он	acetic acid, a component of vinegar
	-c-o-d-	ester	о 	ethyl acetate, a solvent for nail polish and model airplane glue
C. Functional groups containing nitrogen**	-¢-NH₂	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	О 	primary amide	O H— C—NH ₂	formamide, a softener for paper
E. Functional group with halogen	—x	alkyl or aryl halide	CH₃CI	methyl chloride, refrigerant and local anesthetic
F. Functional groups containing sulfur [†]	— <mark>С</mark> — S H	thiol (also called mercaptan)	CH₃SH	methanethiol, has the odor of rotten cabbage
	-ç-s-ç-	thioether (also called sulfide)	(CH ₂ =CHCH ₂) ₂ S	diallyl sulfide, has the odor of garlic

Functional Groups

R-NH2

Amine

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)	H3C – CH3
Alkene	R - CH = CH2	C = C (double bond)	H2C = CH2
Alkvne		(triple bond)	
Alkvl halide	RX	-X (X = F. Cl. Br. I)	H3C - Cl
Alcohol	R – OH	-OH	H3C - OH
Ether	R - O - R	- C- O - C -	H3C - O - CH3
Aldehvde			
Ketone			
Carboxylic acid			
Ester			

H3C - NH2

Kekul structure 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.

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.

الفئة	المجموعة	الصيغة العامة		مثال	الميزة الرئيسية
ألكان	C-C	R-CH₃	CH₃−CH₃		روابط مفردة – خاملة نسبيًا
ألكين	C=C	R-CH=CH₂	CH₂=CH₂		تفاعلية عالية
ألكاين	C≡C	R-C≡CH	HC≡CH		تفاعلات إضافة
كحول	-OH	R-OH	CH₃CH₂OH		قطبي – يذوب بالماء
إيثر	-O-	R-O-R'	CH₃CH₂OCH₂C	H₃	مذیب عضوي جید
ألدهيد	-CHO	R-CHO	НСНО		مؤكسد بسهولة
كيتون	>C=O	R-CO-R'	CH₃COCH₃		مذيب عضوي قوي
حمض كربوكسيلي	-COOH	R-COOH	CH₃COOH		حمضي جدًا
إستر	-COOR	R-COOR'	CH₃COOCH₃		رائحة عطرية
أمين	−NH₂	R−NH₂	CH₃NH₂		أساسي (قاعدة عضوية)
أميد	-CONH ₂	R–CONH₂	CH₃CONH₂		رابطة قوية جدًا