Pharmaceutical Organic Chemistry-1

Chapter-1: Introduction

Organic Chemistry: Definition

- The word Organic can be a biological or chemical term, in biology 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 *the study of carbon/hydrogen-containing compounds and their derivatives.*

The Uniqueness of Carbon

- **What is unique about the element *carbon*?**
- **Why does it form so many compounds?**

  The answers lie in

  - **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**
  - **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*.**

Atomic Structure

- **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*).

- **Atom is electrically neutral.**

    i.e. Number of electrons = Number of protons

- **Atomic number of an element is the number of protons.**

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)

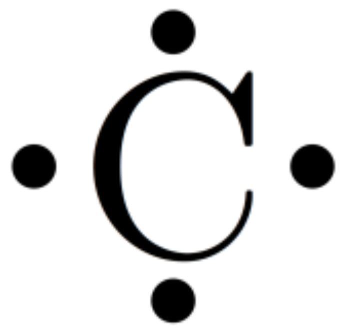
  6 electrons are distributed about the nucleus as

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

Atomic Structure

Valance Electrons: Electron-Dot Structures

- **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.



Chemical Bonding

- **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.

Chemical Bonding

When two atoms combine together

Of the same element they form a molecule of element

Ex:

$O + O \rightarrow O_2$

Oxygen atom | Oxygen atom | Oxygen molecule

Of different elements they form a molecule of compound.

Ex:

$Na + Cl \rightarrow NaCl$

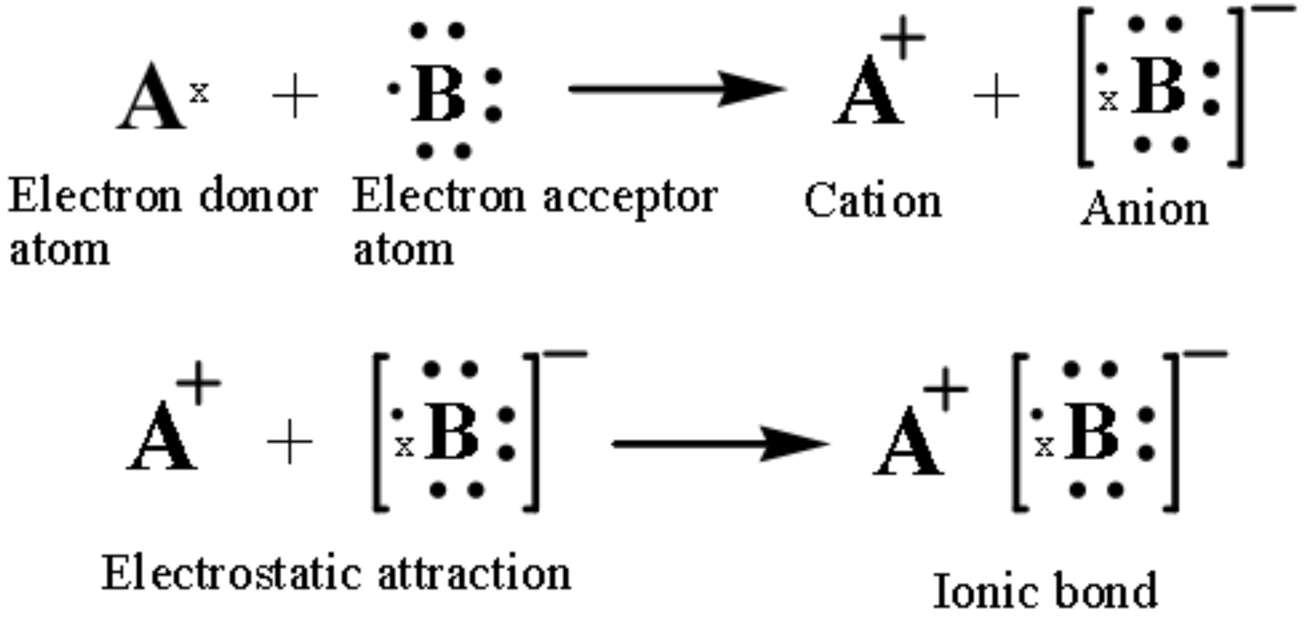
Sodium atom | Chlorine atom | Sodium chloride molecule

Covalent Bonds	*Ionic Bonds*

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.



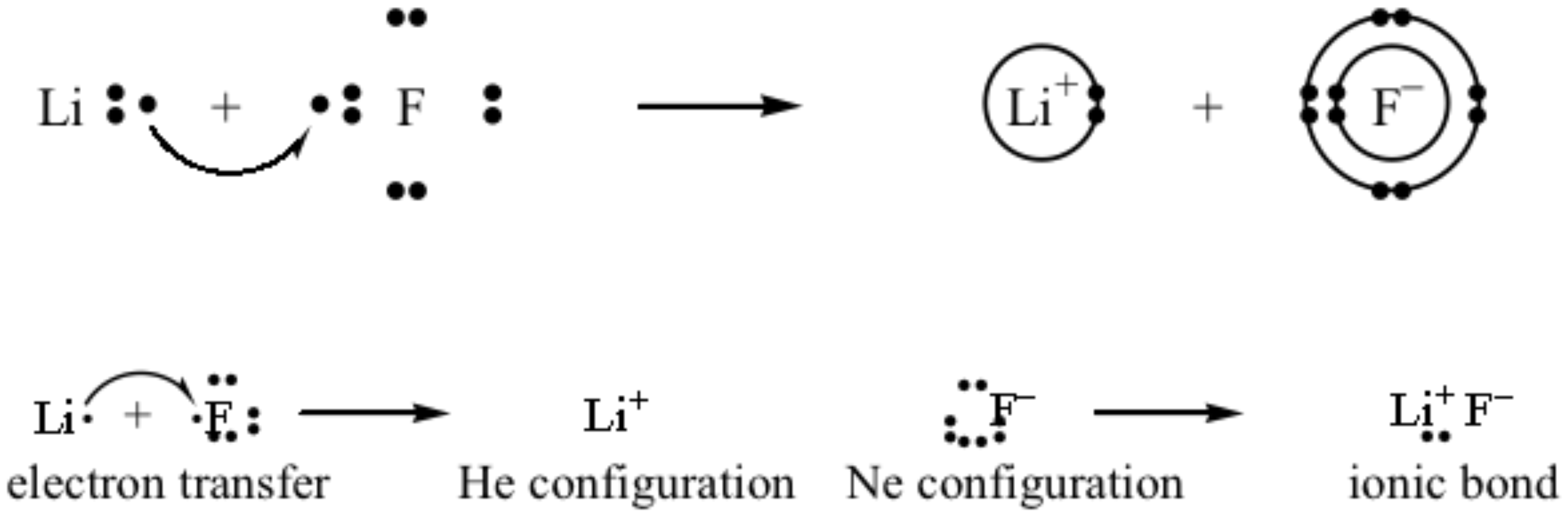
- The majority of ionic compounds are *inorganic substances*.

Electronegativity Measures The Ability of An Atom To Attract Electrons

Increasing electronegativity

							H
							2.1
F	**O**	**N**	**C**	**B**		**Be**	**Li**
4	3.5	3	2.5	2		1.5	1
Cl	**S**	**P**	**Si**	**Al**		**Mg**	**Na**
3	2.5	2.1	1.8	1.5		1.2	0.9
Br							**K**
2.8							0.8

Decreasing electronegativity



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.

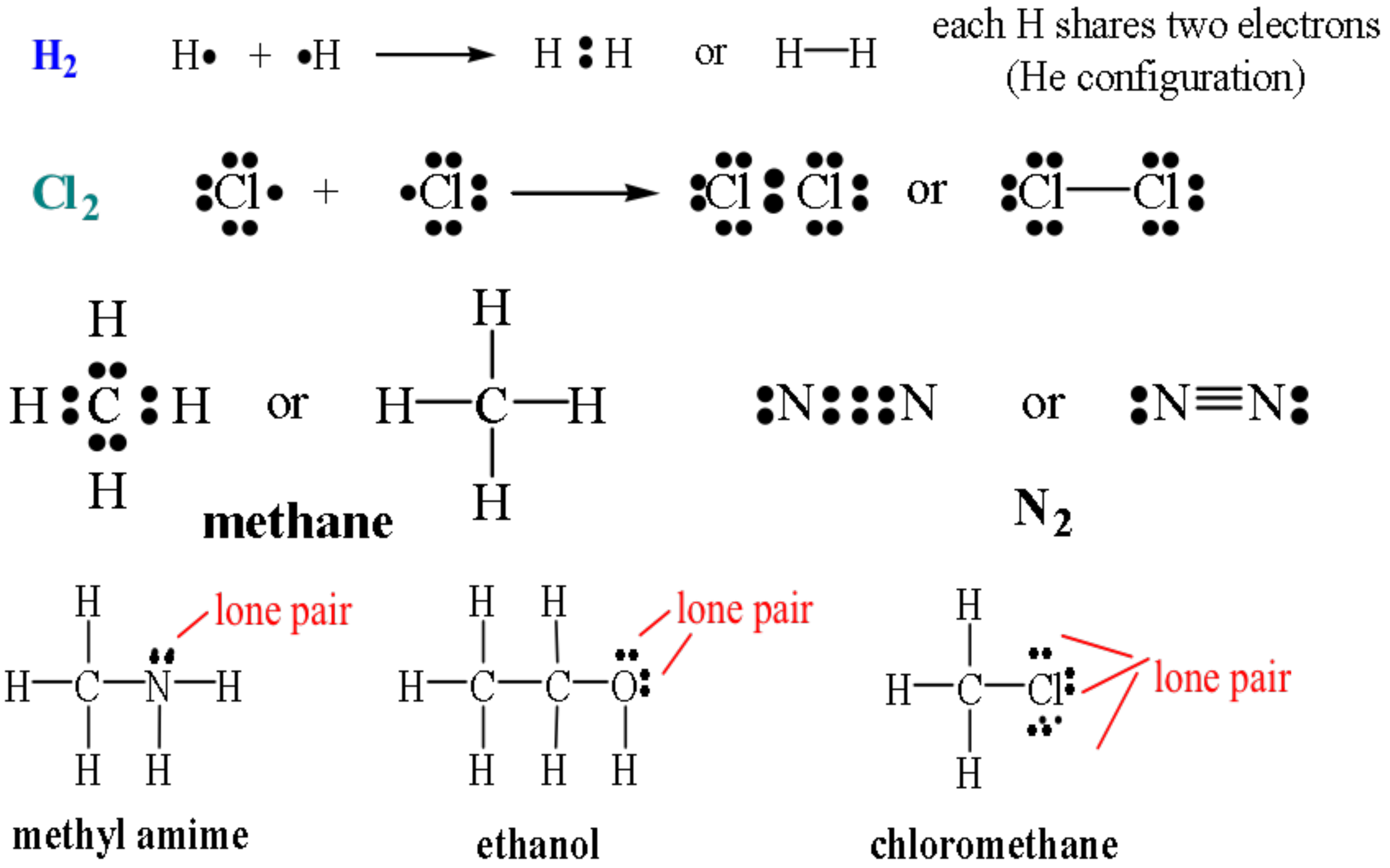
- Covalent bond

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



B) Covalent Bonds

- In molecules that consist of **two like atoms**;

  the bonding electrons are shared equally

  (both atoms have the same electronegativity).

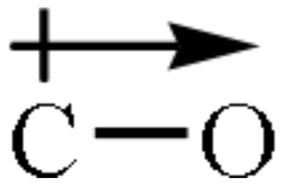
- When **two unlike atoms**;

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

A) Polar Covalent Bond

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

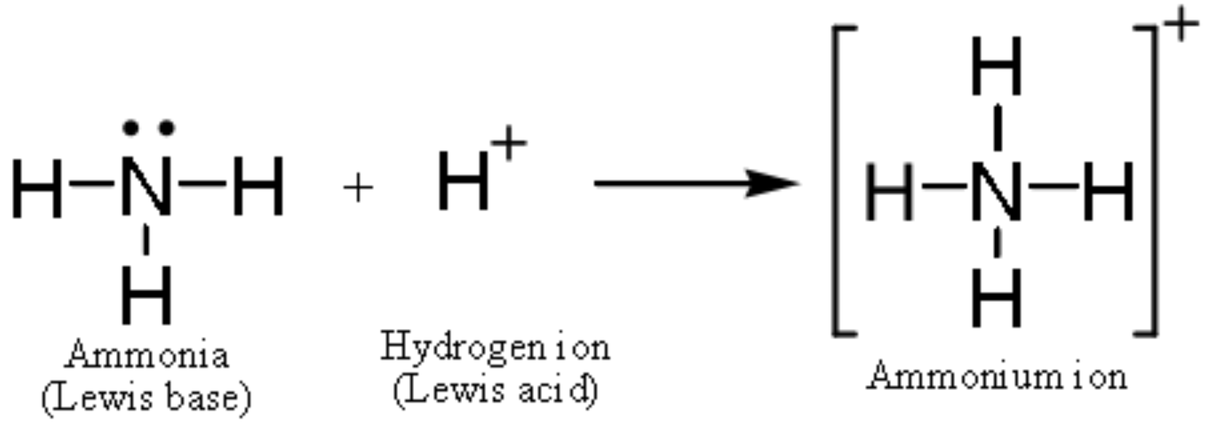
➤ **The more electronegative atom assumes a partial negative charge and the less electronegative atom assumes a partial positive charge.**



or $\overset{\delta+}{C}-\overset{\delta-}{O}$

B) Coordinate Covalent Bonds

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

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.***

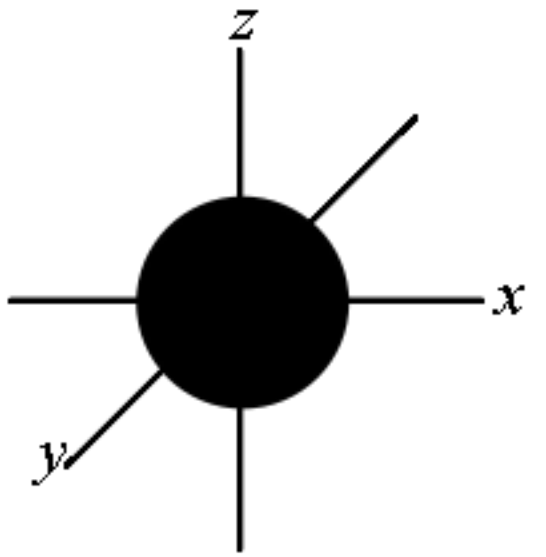
Element	Number of valence electrons	Number of electrons in filled valence shell	Covalence number
H	1	2	1
C	4	8	4
N	5	8	3
O	6	8	2
F, Cl, Br, I	7	8	1

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 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.**



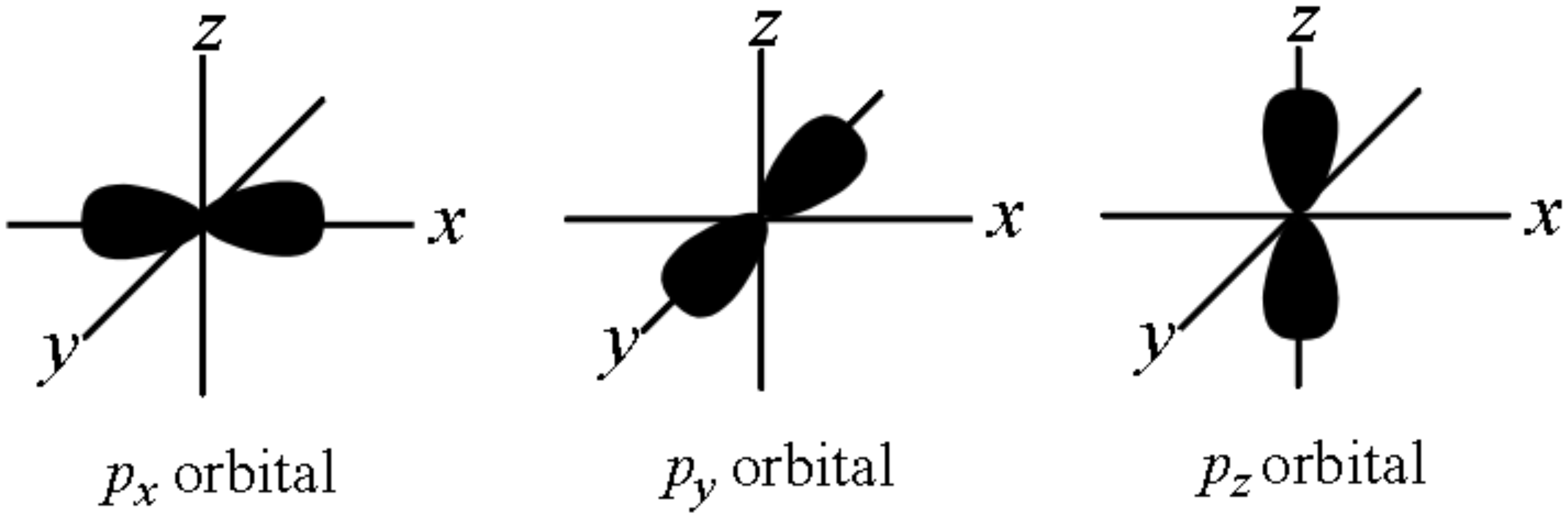
s orbital

Shapes of Organic Molecules: Orbital Picture of Covalent Bond

Atomic Orbitals

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

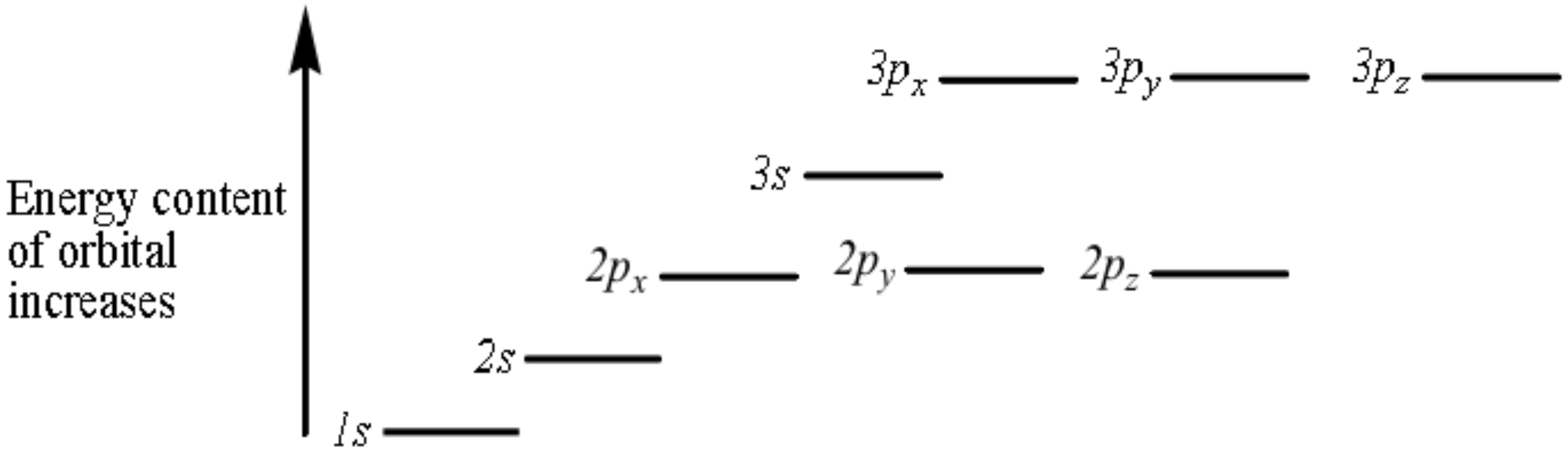
- **Each *p* orbital is oriented along one of three perpendicular coordinate axes (in the *x, y, or z* direction).**



Shapes of Organic Molecules: Orbital Picture of Covalent Bond

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.

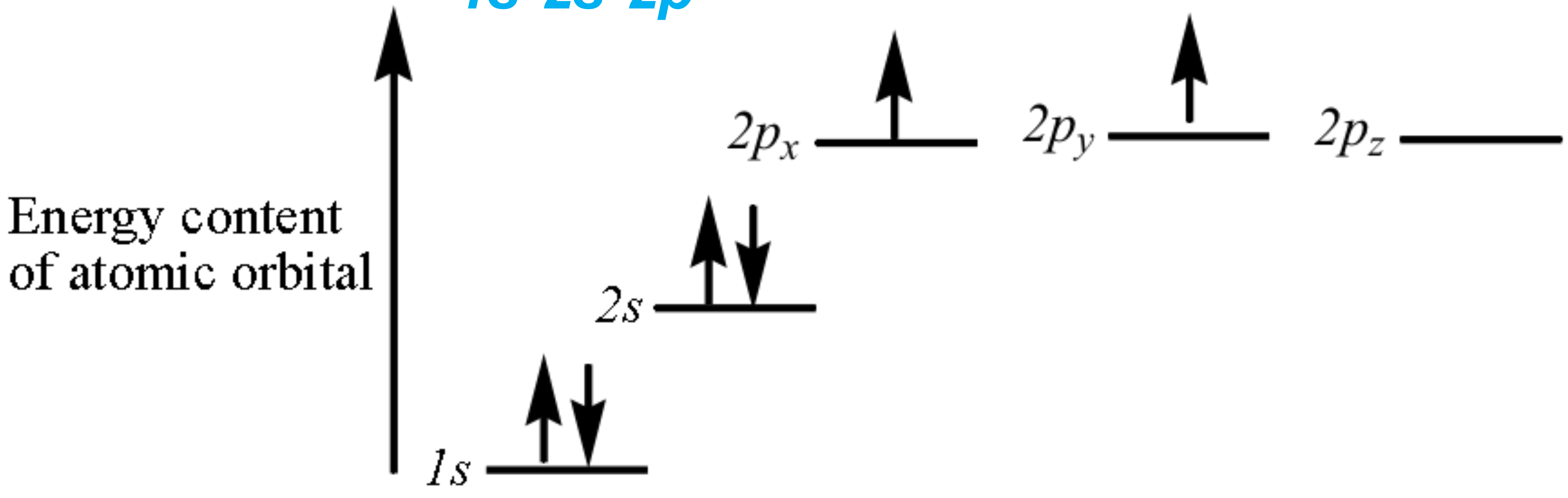
  (2) Electrons fill orbitals of lower energy first.

  (3) No orbital is filled by 2 electrons until all the orbitals of equal energy have at least one electron.

Shapes of Organic Molecules: Orbital Picture of Covalent Bond

Atomic Orbitals

- The electronic configuration of carbon (atomic number 6) can be represented as
  $1s^2 2s^2 sp^1{}_x 2p^1{}_y$ or
  $1s^2 2s^2 2p^2$



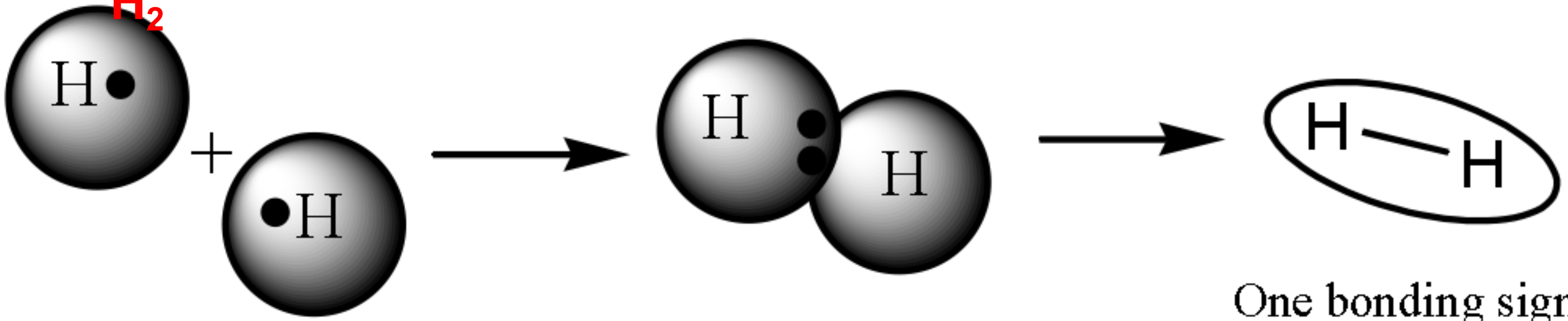
Energy level diagram for carbon.

Shapes of Organic Molecules: Orbital Picture of Covalent Bond

Molecular Orbitals

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

Molecular orbital of H_2



Two 1*s* atomic orbitals

Overlap

One bonding sigma molecular orbital

Shapes of Organic Molecules: Orbital Picture of Covalent Bond

Molecular Orbitals

- **Sigma bonds (σ bonds) can be formed from**
  - **The overlap of two *s* atomic orbitals.**
  - **The end-on overlap of two *p* atomic orbitals.**
  - **The overlap of two an *s* atomic orbital with a *p* atomic orbital.**
- **pi 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**

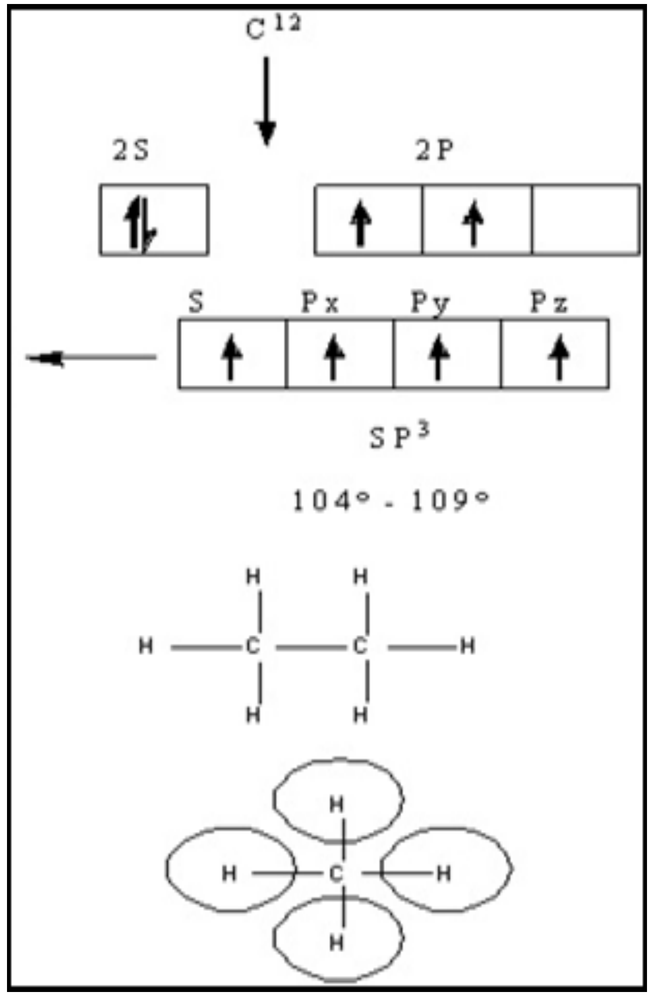
  The amount of energy that must be absorbed to break a bond.

- **Bond length**

  The distance between nuclei in the molecular structure.

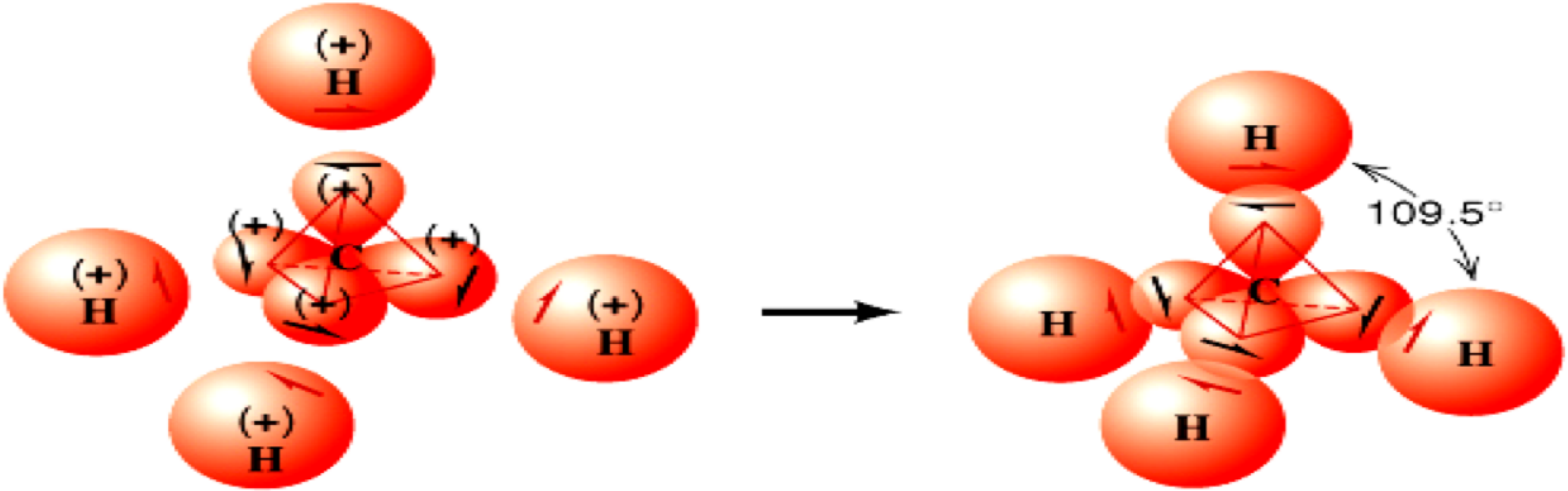
Hybridization (Alkanes *sp³*)

- 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.
- Four hybrid orbitals were required since there are four atoms attached to the central carbon atom.
- 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.
- **Regular tetrahedron with all H-C-H bond angles of 109.5º.**



Methane

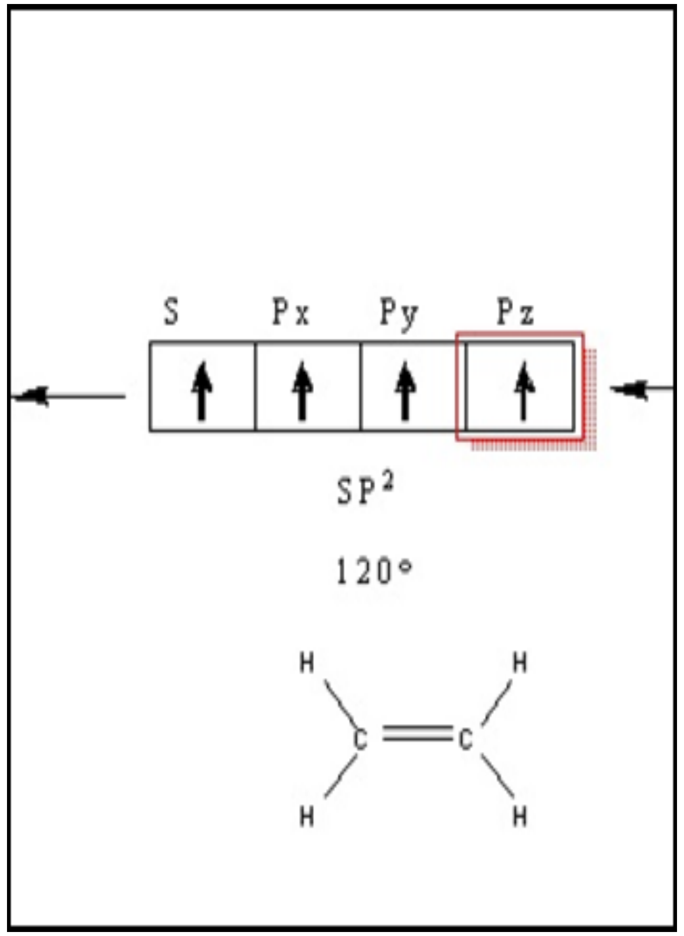
Hybridization (Alkanes *sp*³



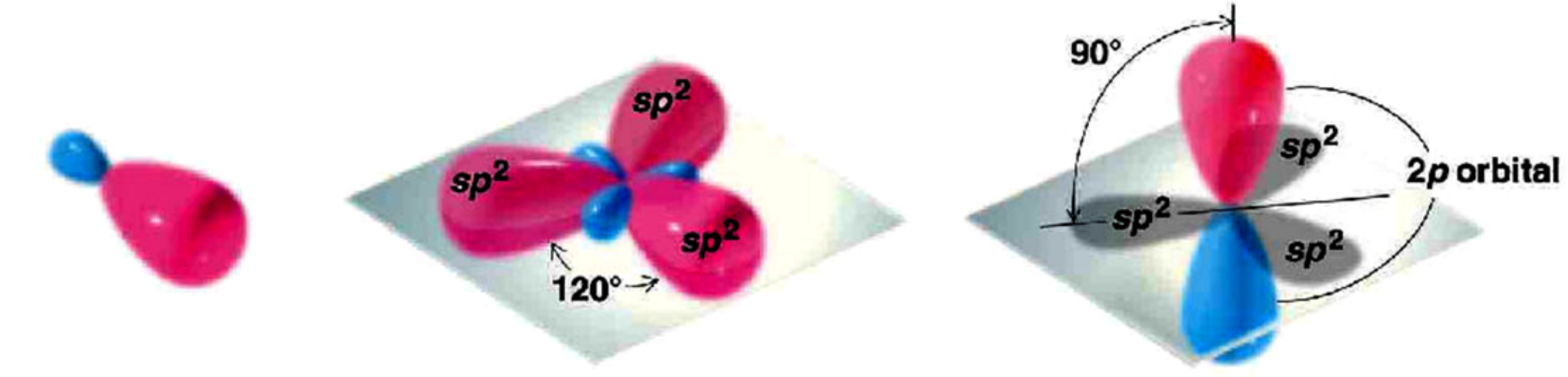
Methane, CH_4

Hybridization (Alkenes sp^2)

- 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 non-bonding pairs*) forming three hybrid orbitals called sp^2 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**



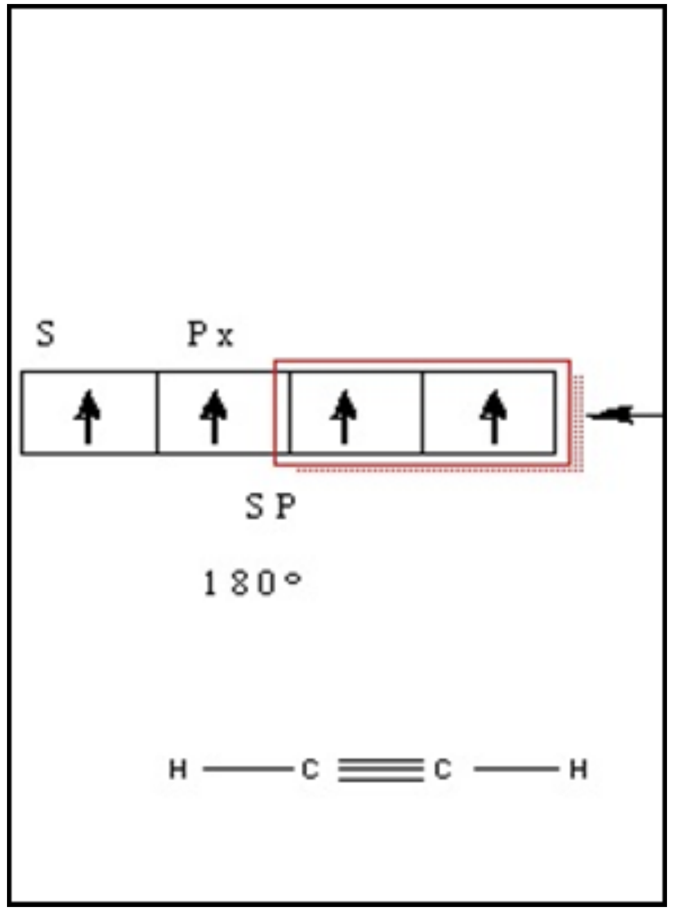
Ethene *(Ethylene)*



(a) An sp^2 orbital (b) Three sp^2 orbitals (c) Three sp^2 orbitals and an unhybridized $2p$ orbital

Hybridization (Alkynes *sp*)

- 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°).**



Ethyne *(Acetylene)*

Formal Charge

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

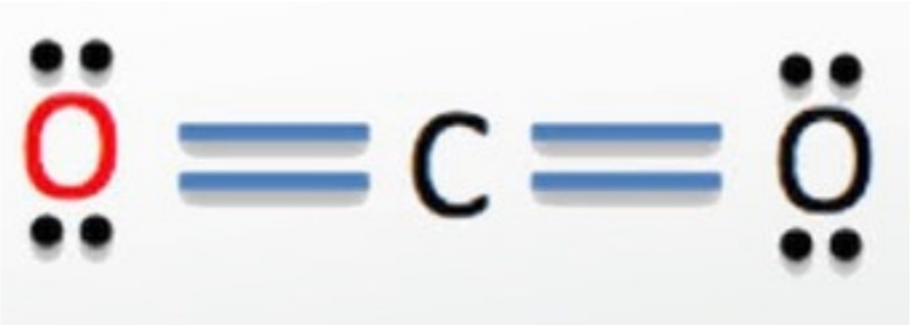
How to calculate the Formal Charge (FC):

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

Example: calculate the formal charge of CO2

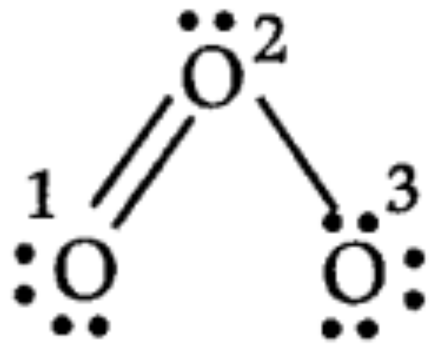
FC for O= 6-(4+4/2)=0

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



Example:

Lewis structure of O_3 is

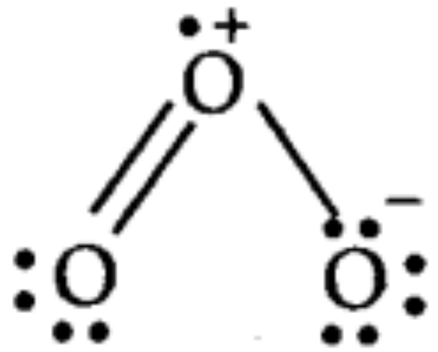


Formal charge on O(1) $= 6 - (4 + \frac{4}{2}) = 0$

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

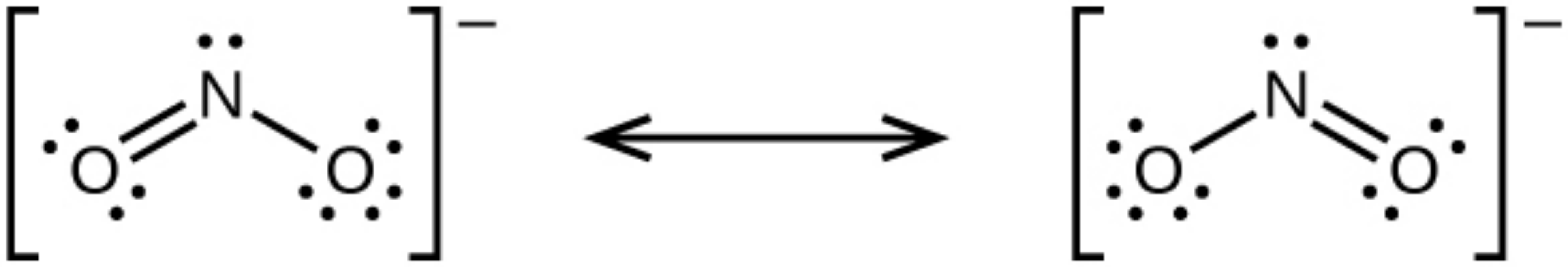
Formal charge on O(3) $= 6 - (6 + \frac{2}{2}) = -1$

Hence we represent O_3 along with formal charges as follows.



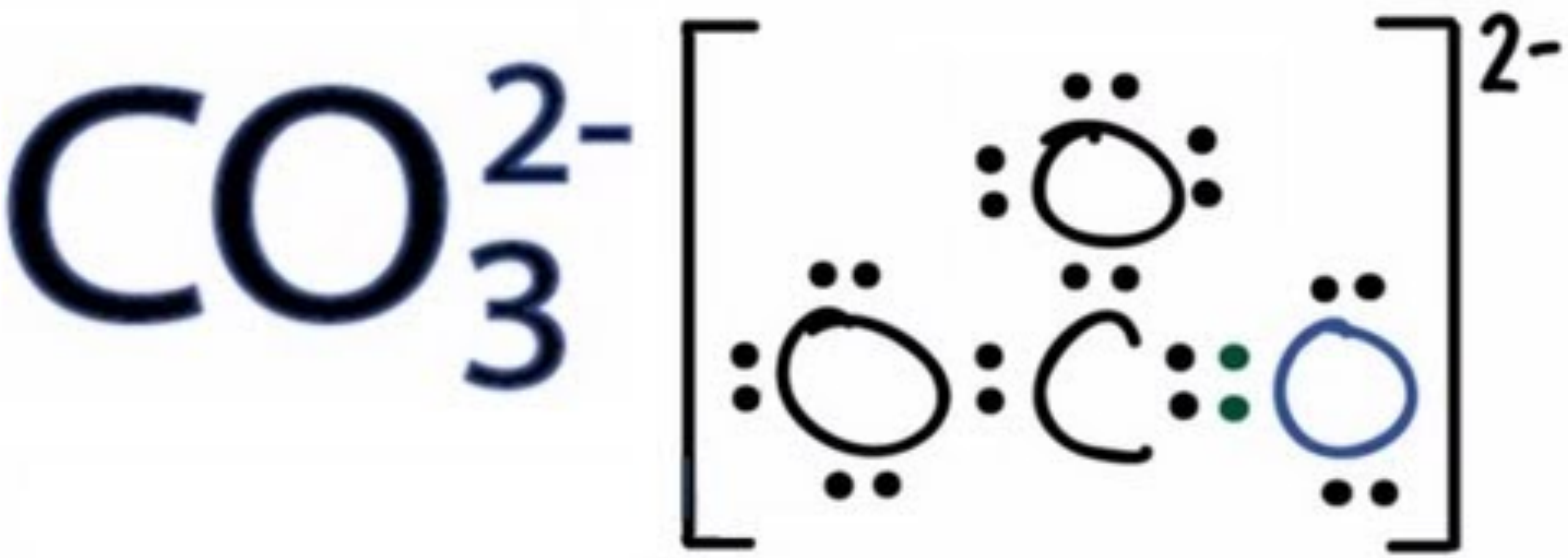
Formal Charg

Example:



Formal charge: 0 0 –1 –1 0 0

Example:



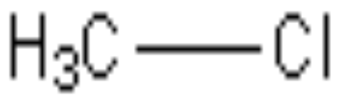
Formal Charge	=	Valence Electrons	-	NonBonding Val Electrons	-	$\frac{\text{Bonding Electrons}}{2}$		
C	=	4	-	0	-	8/2	=	0
O	=	6	-	6	-	2/2	=	-1
O	=	6	-	4	-	4/2	=	0

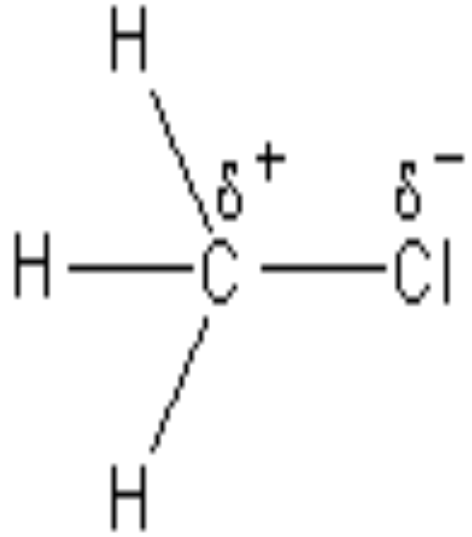
Inductive Effect

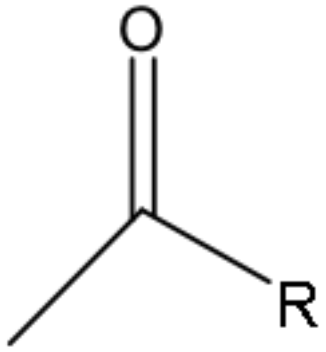
- **Inductive effect** can be defined as ***the permanent displacement of electrons forming a covalent bond (sigma σ bonds) towards the more electronegative element or group***.
- **The inductive effect is represented by the symbol, the arrow pointing towards the more electronegative element or group of elements.**

  (+ I) effect if the substituent electron-donating

  (- I) effect if the substituent electron-withdrawing





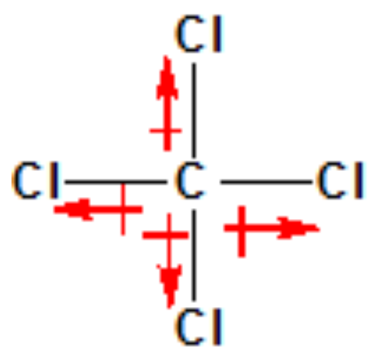


Electron-donating substituents (+I): $-CH_3$, $-C_2H_5$,….
Electron-withdrawing substituents (-I): $-NO_2$, -CN, $-SO_3H$, COOH, COOR, NH_2, OH, OCH_3

Bond Polarity and Dipole Moment (μ)

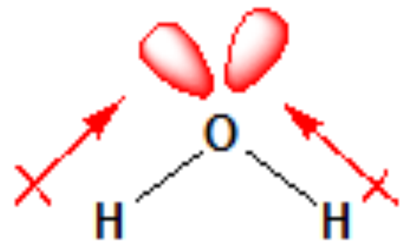
- **Dipole moment** (depends on the inductive effect).
- A bond with the electrons shared equally between two atoms is called a **nonpolar bond** like in Cl-Cl and C-C bond in ethane.
- A bond with the electrons shared unequally between two different elements is called a **polar bond**.
- The **bond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

CCl_4



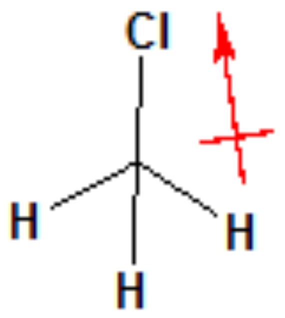
μ = zero

H_2O



$\mu \neq$ zero

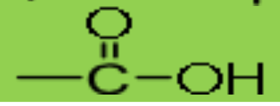
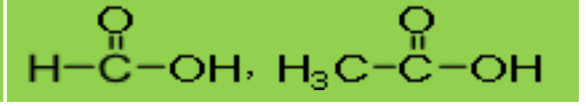
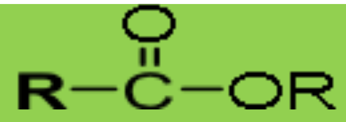
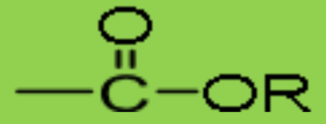
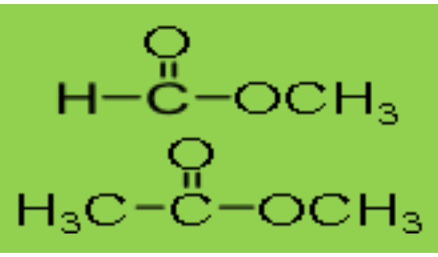
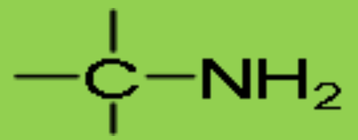
CH_3Cl



$\mu \neq$ zero

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	$R—C \equiv CH$	$C \equiv C$ (triple bond)	$HC \equiv CH$
Alkyl halide	RX	-X (X = F, Cl, Br, I)	H_3C - Cl
Alcohol	R – OH	-OH	H_3C - OH
Ether	R – O –R’	- C- O – C -	$H_3C – O – CH_3$
Aldehyde			
Ketone			
Carboxylic acid			
Ester			
Amine	$R – NH_2$		$H_3C – NH_2$