Université Paris-Saclay | Faculté de Pharmacie

TU07 – Refresher training in organic chemsitry

Year 2024-2025

Course outline

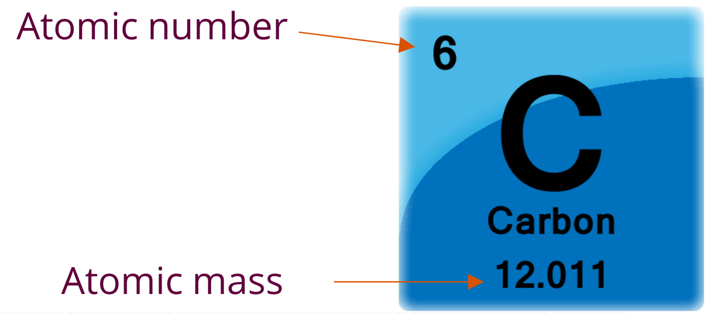
- Atoms and chemical bonds
  - Number of bonds around an atom
  - Types of chemical bonds
    - Covalent vs ionic
    - Single vs multiple
  - Impact of chemical bonds on structure
  - Functional groups

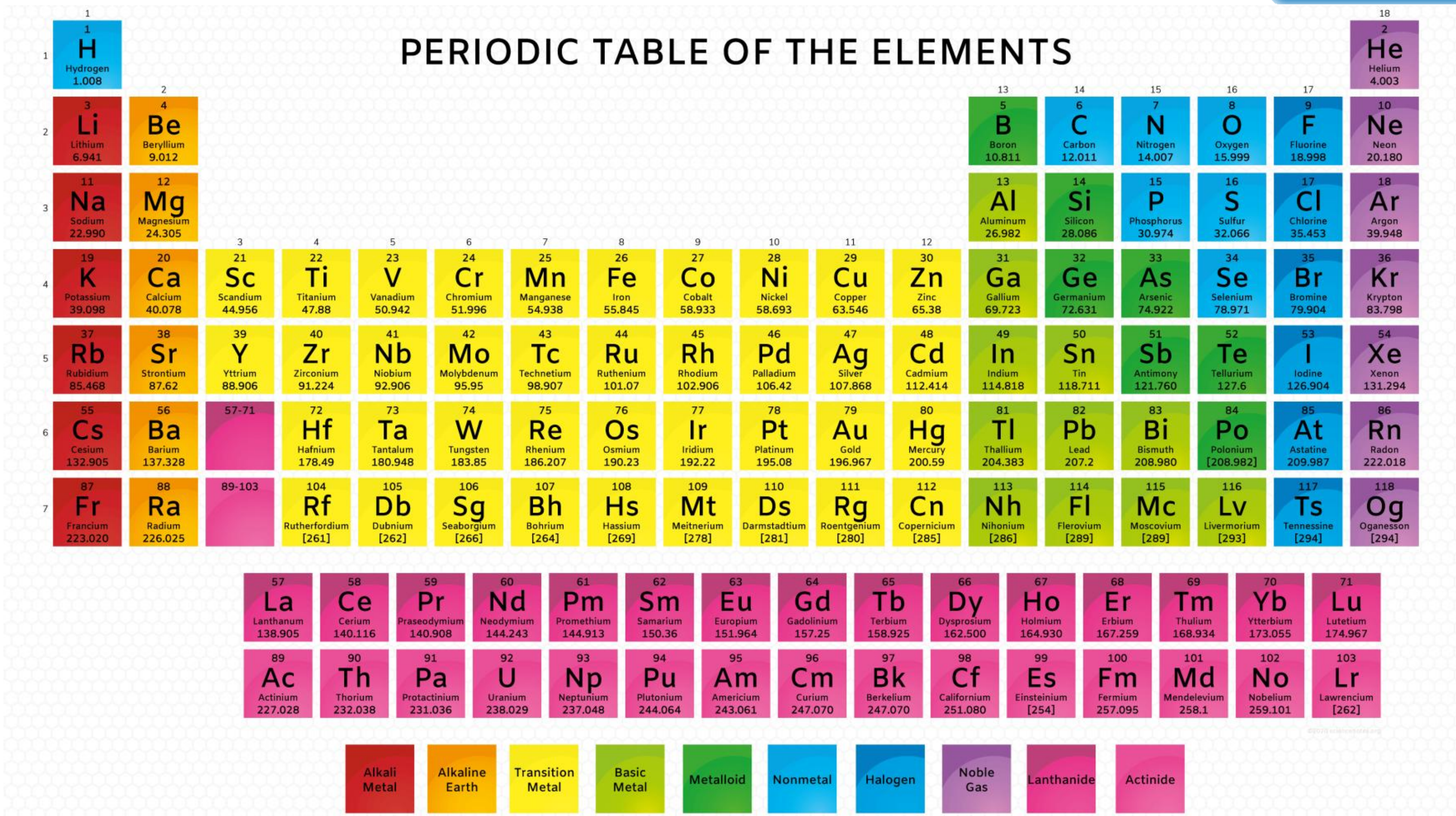
- Chemical reactivity
  - Nucleophile and electrophile
  - Bond polarisation
  - Inductive and mesomeric effects
  - Principal mechanisms

Atoms and chemical bonds

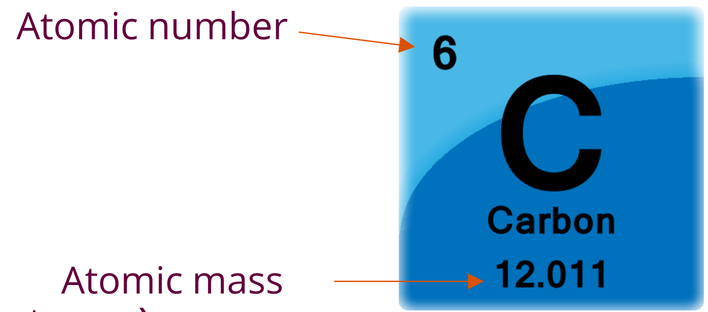
Organic chemistry is…

Carbon Chemistry!





Identity card of atoms



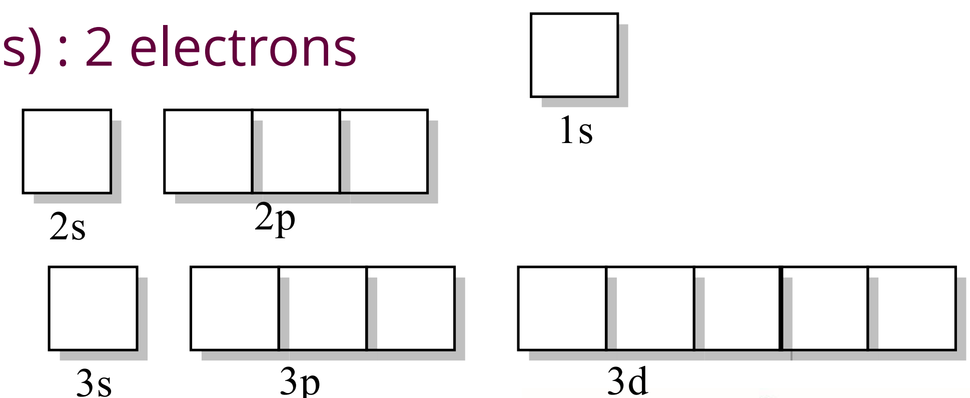
- Atomic number:

  positive charges (protons) = negative charges (electrons) in the nucleus

- Atomic mass:

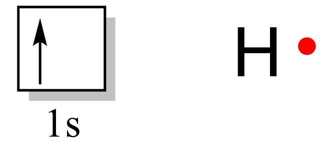
  positive (protons) and neutral (neutrons) charges in the nucleus

- Electrons occupy various core layers from K layer to M layer
  - K layer closest to the nucleus) : 2 electrons
  - L Layer : 8 electrons
  - M layer : 18 electrons



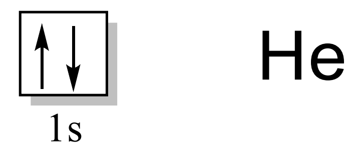
Atoms and chemical bonds

- Hydrogen (H): 1 electron
  1 chemical bond is allowed

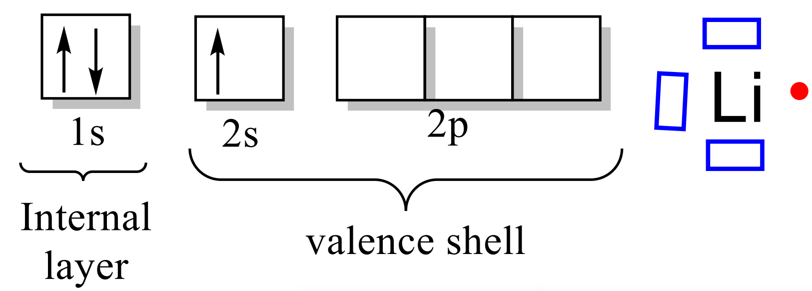


- Helium (He): 2 electrons

  Layer K is full ➤ noble gaz
  No chemical bond allowed



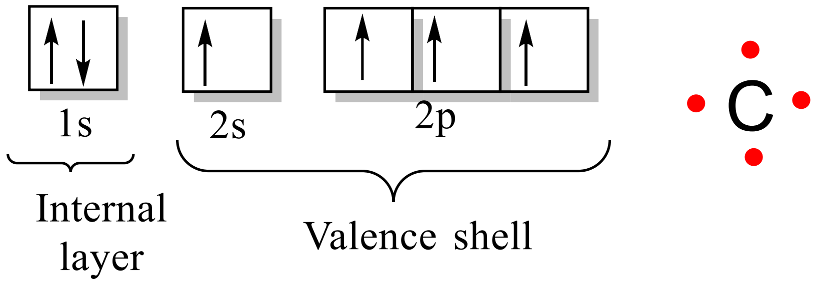
- Lithium (Li): 3 electrons
  1 chemical bond is allowed
  3 electron holes are present



Atoms and chemical bonds

- Carbone (C): 6 electrons

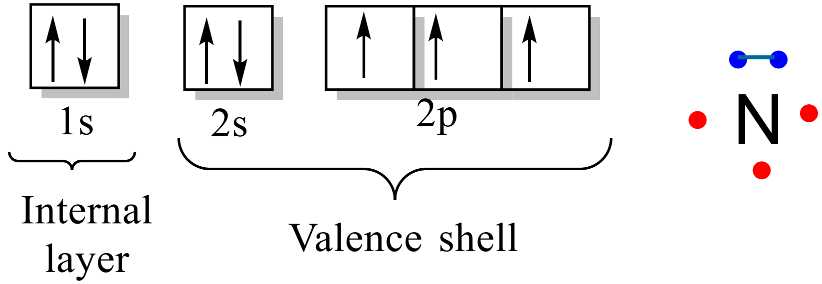
    4 chemical bonds are allowed



- Nitrogen (N): 7 electrons

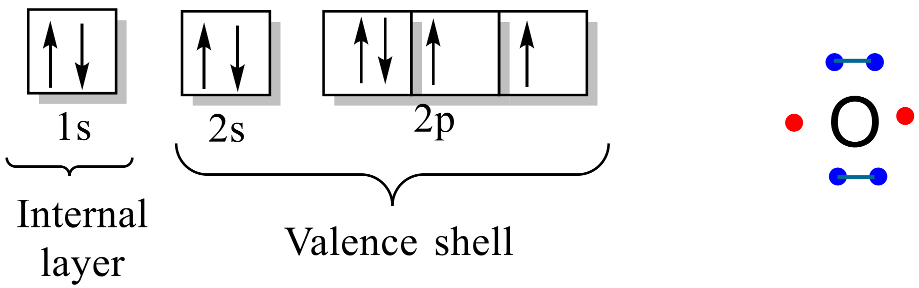
    3 chemical bonds are allowed

    1 lone pair is present

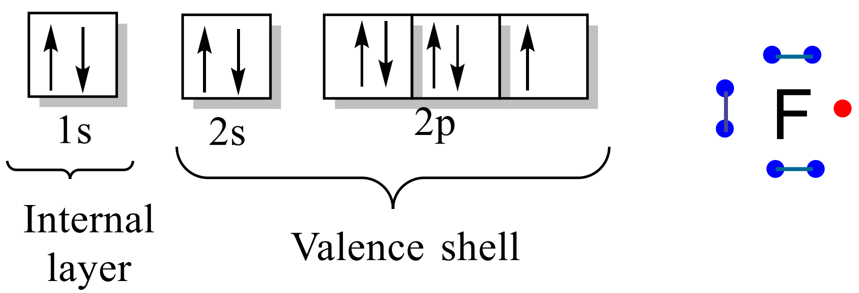


Atoms and chemical bonds

- Oxygen (O): 8 electrons



- Fluorine (F): 9 electrons



Types of chemical bonds

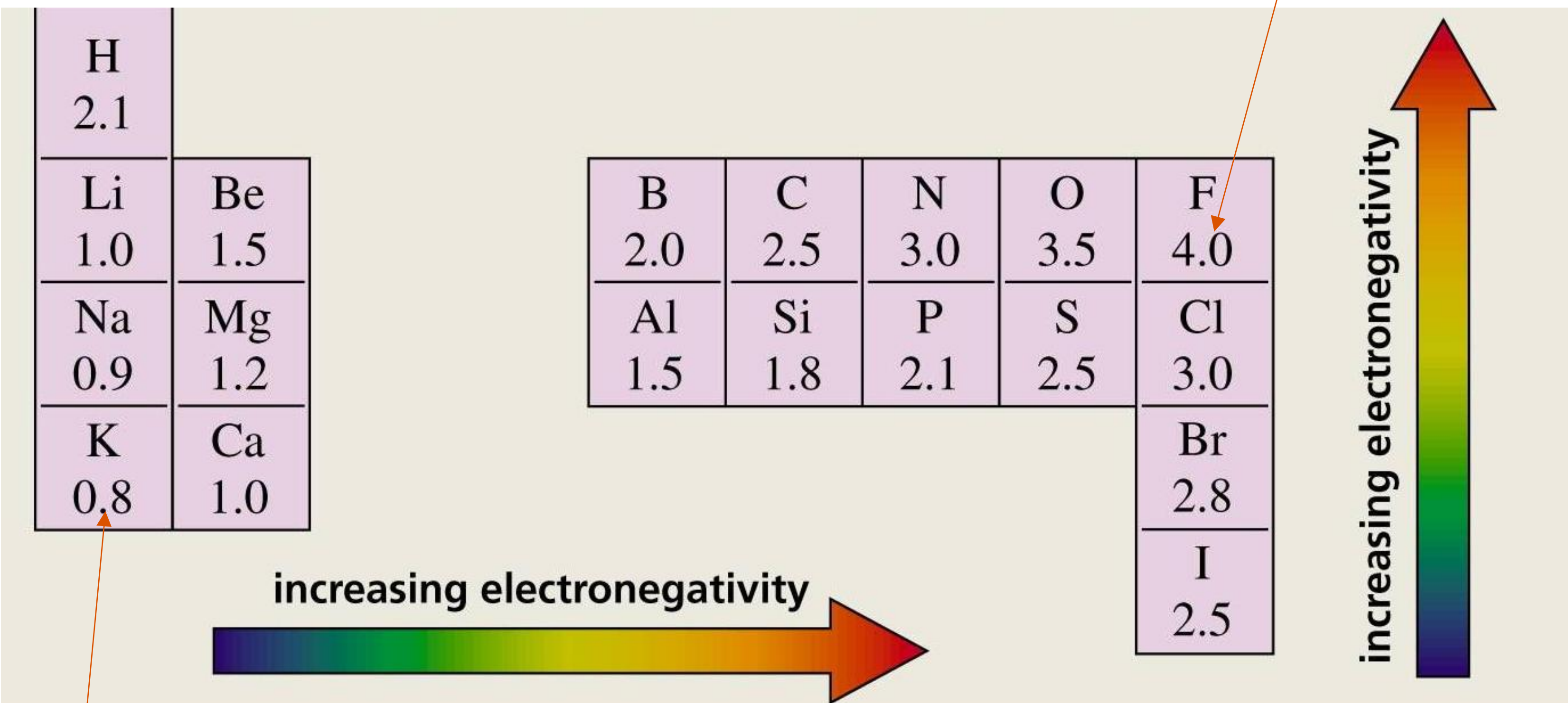
- Chemical bond = lasting attraction between two atoms by means of two electrons

- The type of chemical bonds is dependent of the electronegativities of the two atoms (ability of an atom to attract electrons)

Types of chemical bonds

Electronegativity based on the Pauling scale

The most electronegative



The less electronegative

Tricks for the two lines: **H**appy **He**ctor **Li**kes **Be**er **B**ut **C**ould **N**ot **O**btain **F**ood, **Ne**ver!

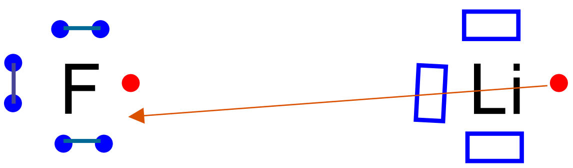
Types of chemical bonds

- Chemical bond = lasting attraction between two atoms by means of two electrons

Ionic bond: chemical bond involving the transfer of one electron from one atom to the other. Concerns atoms possessing very different electronegativities

Fluorine electronegativity : 4,0 ⇨strong attraction of electrons

Lithium electronegativity : 1,0



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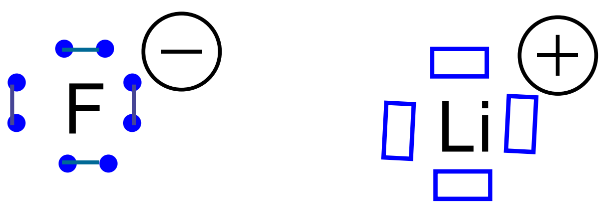
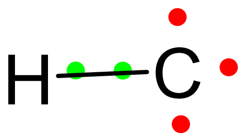
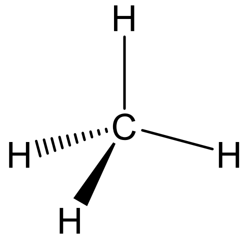


Types of chemical bonds

Pure covalent bond: sharing of two electrons from two atoms possessing similar electronegativities

- Carbon electronegativity : 2,5
- Hydrogen electronegativity : 2,1

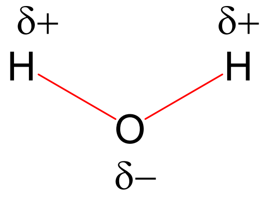


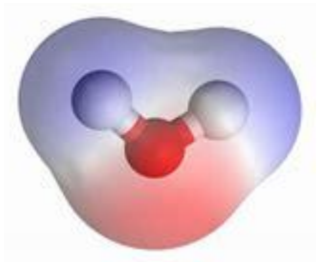


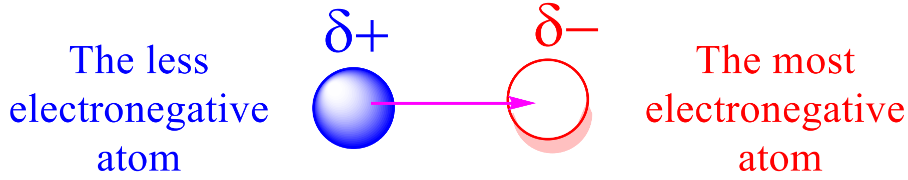
Polar covalent bond: covalent bond with a partial ionic caracter => Polarized bond

Oxygen electronegativity : 3,5

Hydrogen electronegativity : 2,1







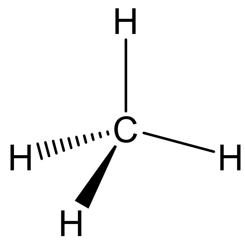
Type of chemical bonds - Exercise

- By considering the atom electronegativity, indicate the bond polarisation. Represent also the lone pairs and electron holes present on the atoms. Is the bond a covalent or a ionic one?

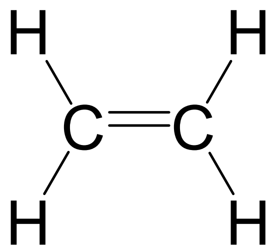
$H-F$	$EtO-H$	Et_2N-CH_3
$(H_3C)_3C-Cl$	H_3C-MgI	H_2N-Li

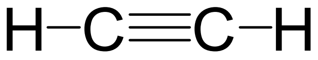
Single and multiple bonds

- When the two atoms share two electrons (one on each atom), you have a single bond.



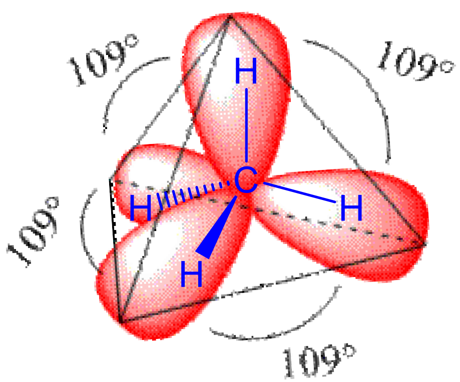
- When the two atoms share four/six electrons (two/three on each atom), you have a double/triple bond.

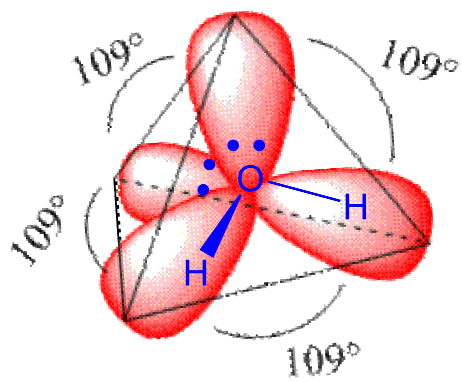


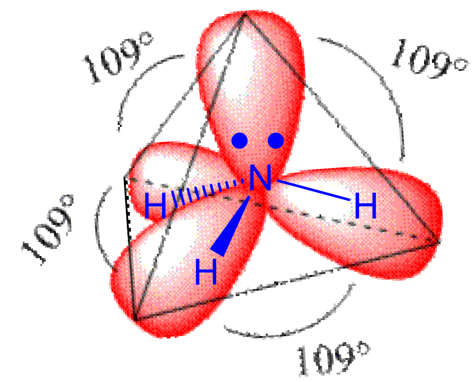


Impact of bonds on chemical structures

- An atom possesses a tetrahedral structure if he has around it 4 atoms and/or lone pairs
  - Only single bonds and lone pairs
  - Free rotation about single bonds

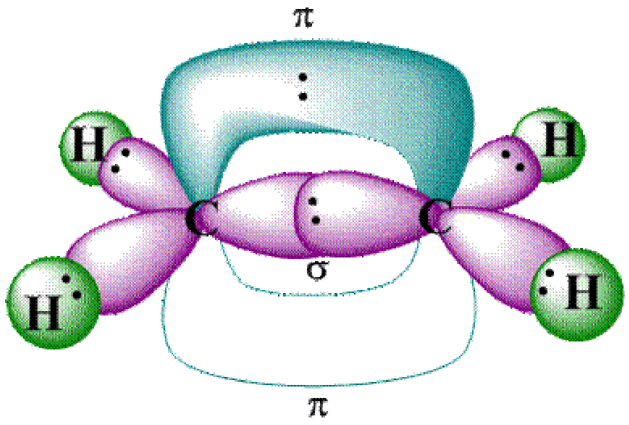


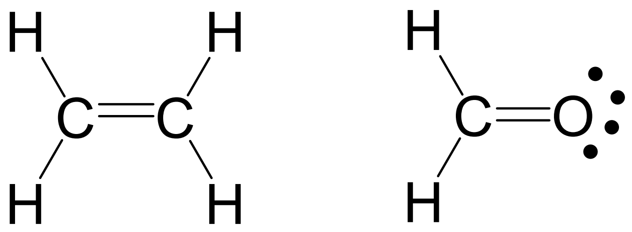




Impact of bonds on chemical structures

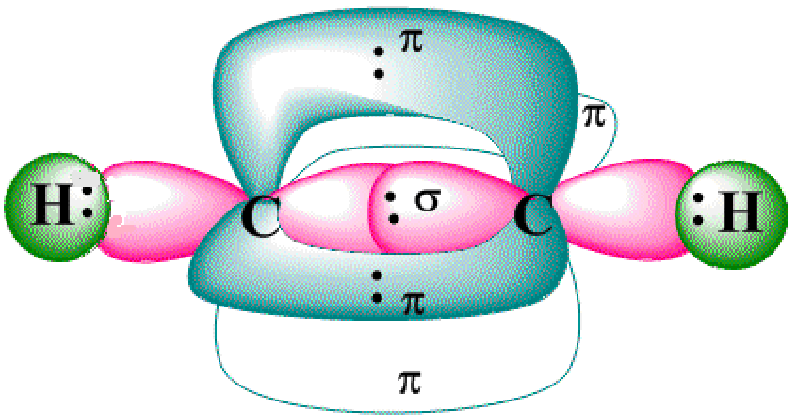
- An atom possesses a trigonal (plane) structure if he has around it 3 atoms and/or lone pairs
    - One double bond must be present
    - No free rotation about double bonds (rigid structure)





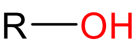
Impact of bonds on chemical structures

- An atom possesses a linear structure if he has around it 2 atoms and/or lone pairs
    - A triple bond must be present
    - No free rotation about double bonds (rigid structure)

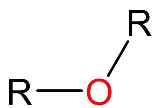


Functional groups

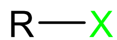
Monovalent functions



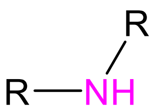
Alcohol



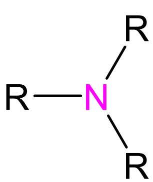
Ether

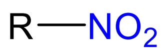


Halogen (Cl, F, I, Br)



Amine

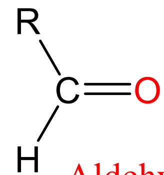




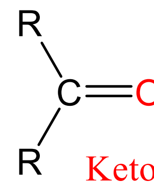
Nitro

Organometallic (Na, Li, MgCl)

Divalent Functions

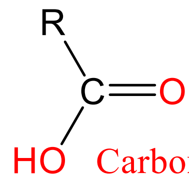


Aldehyde

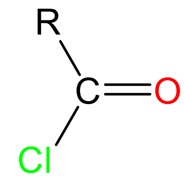


Ketone

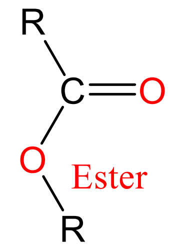
Trivalent Functions



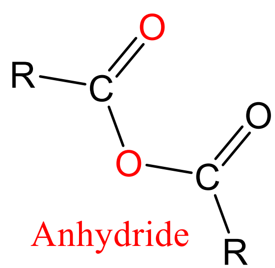
Carboxylic acid



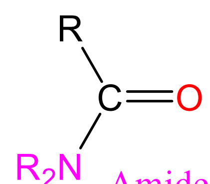
Acyl chloride



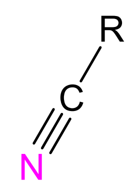
Ester



Anhydride



Amide



Nitrile

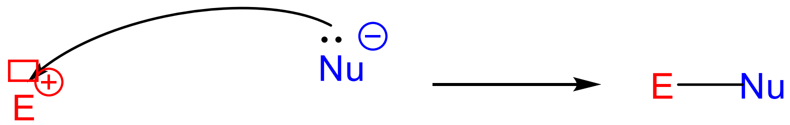
Chemical reactivity

Chemical reactivity

- Nucleophiles and electrophiles

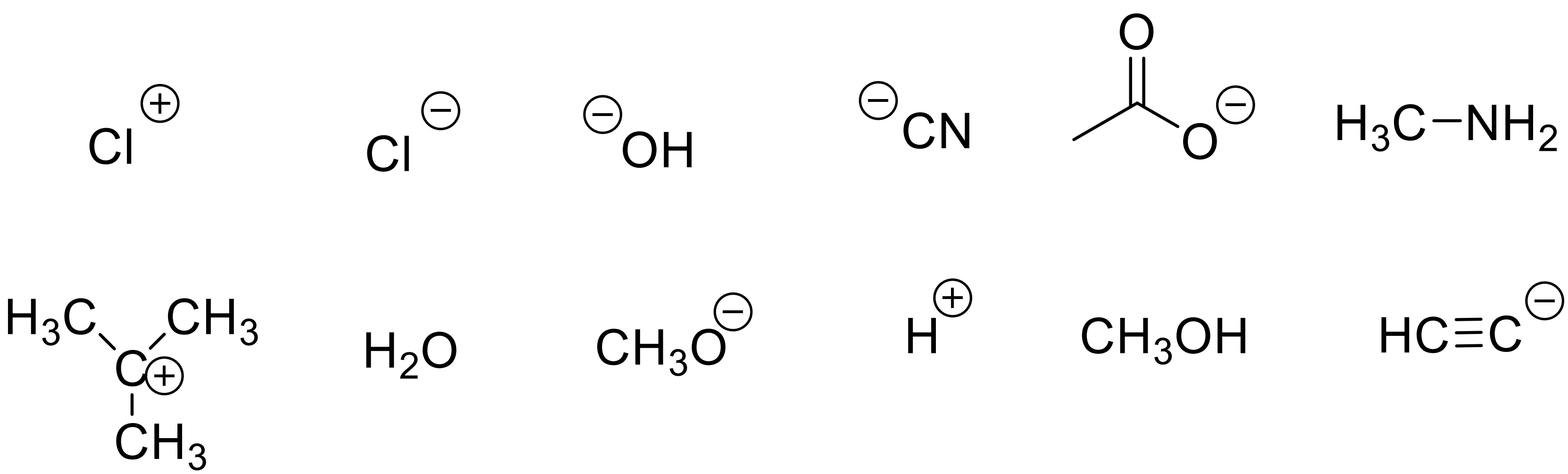
  - A nucleophile is an atom or atoms group possessing a lone pair (eventually with a negative charge). He reacts with electrophiles.

  - An electrophile is an atom or atoms group possessing a hole (eventually with a positive charge or a partial positive charge in the case of carbon). He reacts with nucleophiles.



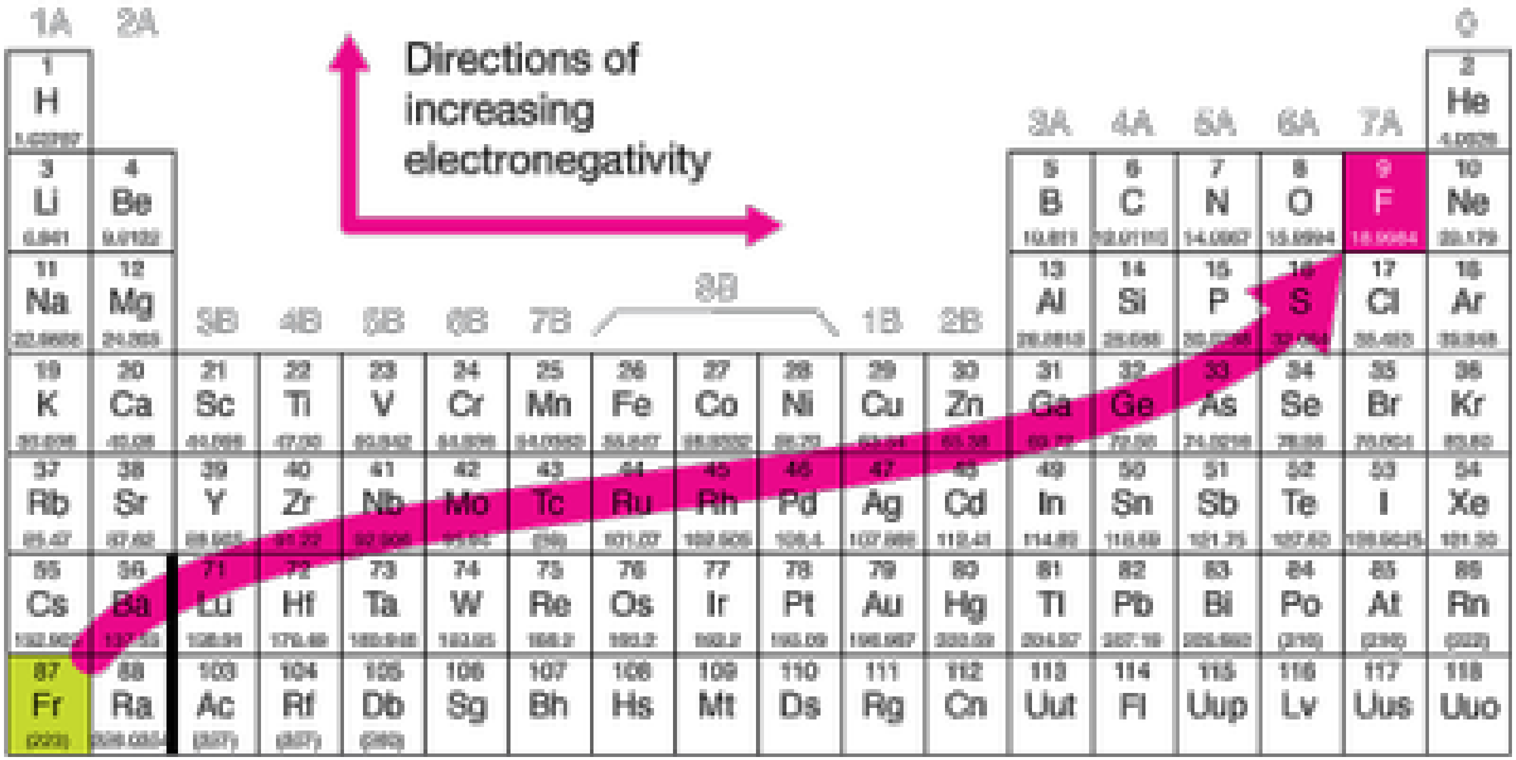
Chemical reactivity

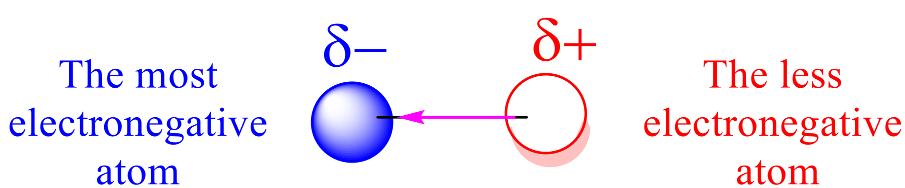
- Exercice: Represent the lone pairs and electron holes present on the atoms then categorize these compounds as nucleophile or electrophile. Indicate which atom is concerned.



Chemical reactivity

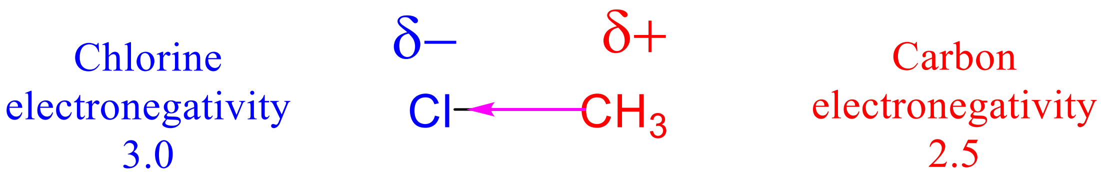
- In complex structures, it depends on the chemical bond polarization and substituants



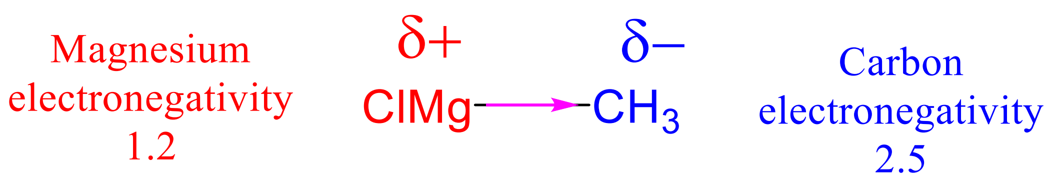


Chemical reactivity

- Electronic effect of substituants – Inductive effect
  - Concerns the bond polarization and the impact on the adjacent bonds. The effect is defined relative to a bond formed with a carbon atom.
    - Electro-withdrawing effect –I: When an atom or a group of atoms attracts the electrons of the bond



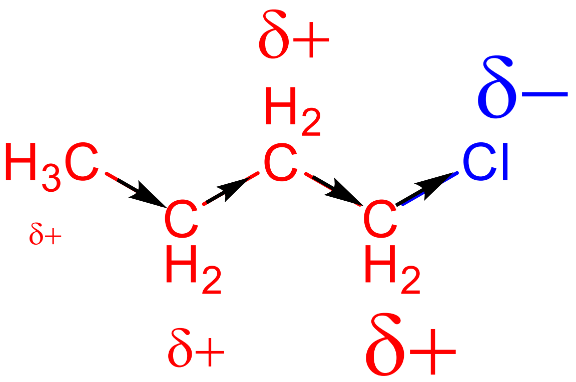
    - Electro-donating effect +I: When an atom or a group of atoms repels the electrons of the bond



Chemical reactivity

- Electronic effect of substituants – Inductive effect

  - The inductive effect is transferred through the single bonds but declined rapidly with the distance



Chemical reactivity

- Exercise: Determine if these substituents possess a +I or a –I effect???

$-NR_2$	$-NO_2$	-OR
-Halogens	-COR	-Alkyl
-CN	-COOR	$-CONR_2$
-Na	-Li	

Chemical reactivity

- Electronic effect of substituants – Inductive effect

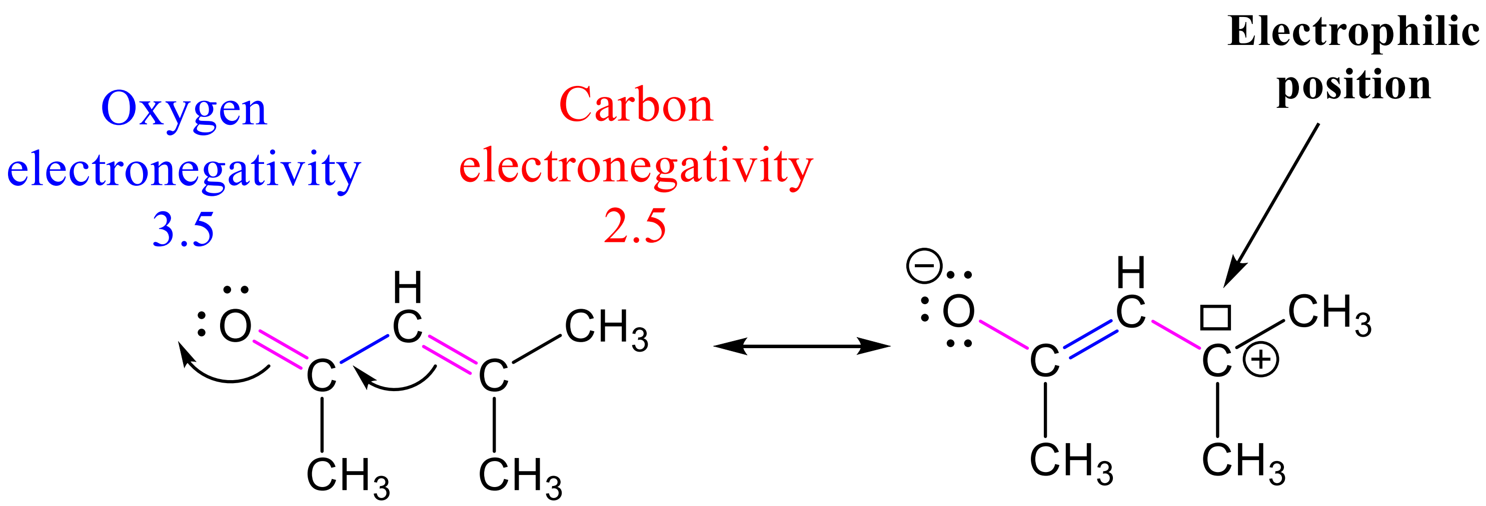
-I			+I		
$-NO_2$	-COR			-Alkyl	
-CN	-COOR	$-CONR_2$	-Na		-MgCl
$-NR_2$	-OR			-Li	
-SR	-Halogènes				

Chemical reactivity

- Electronic effect of substituants – mesomeric effect
  - Concerns the delocalization of the π electrons in a molecule ie the lone pairs, electron holes and π bonds (in multiple bonds)
  - The mesomeric effect can only take place when there is one single bond (and only one) between two π electrons:
    - π bond - σ bond - π bond
    - lone pair - σ bond - π bond
    - Electron hole - σ bond - π bond (or lone pair)
  - Mesomeric effects are superior to inductive effects

Chemical reactivity

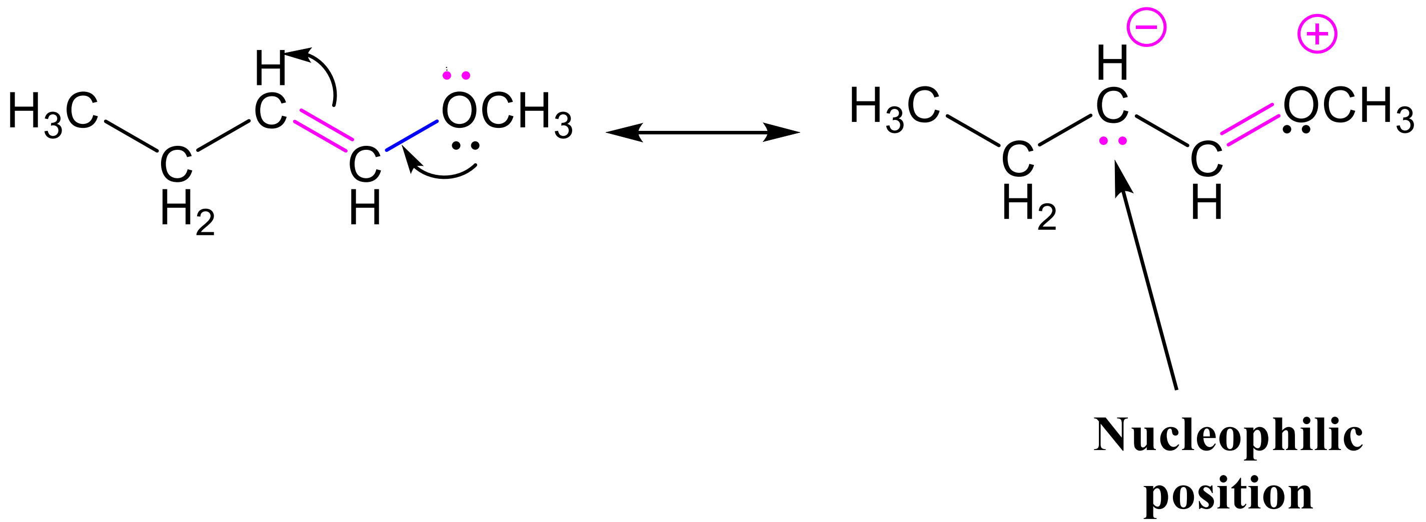
- Electronic effect of substituants – mesomeric effect
  - When you have a π **bond - σ bond - π bond**, the electrons are displaced from the less electronegative atom to the most negative atom



Chemical reactivity

- Electronic effect of substituants – mesomeric effect

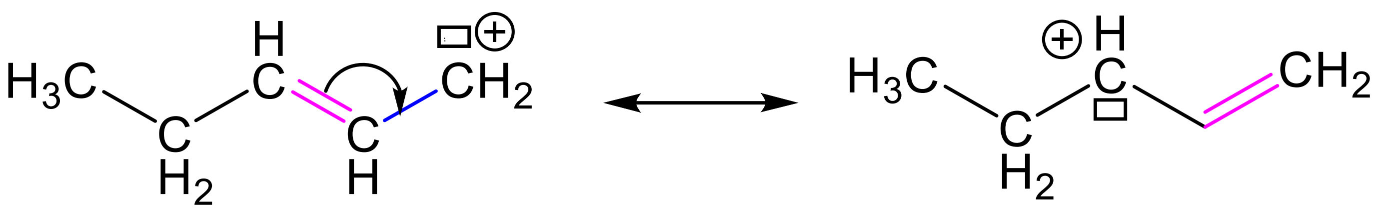
  - When you have a **lone pair - σ bond - π bond**, the electrons are displaced from the lone pair in direction to to the π bond



Chemical reactivity

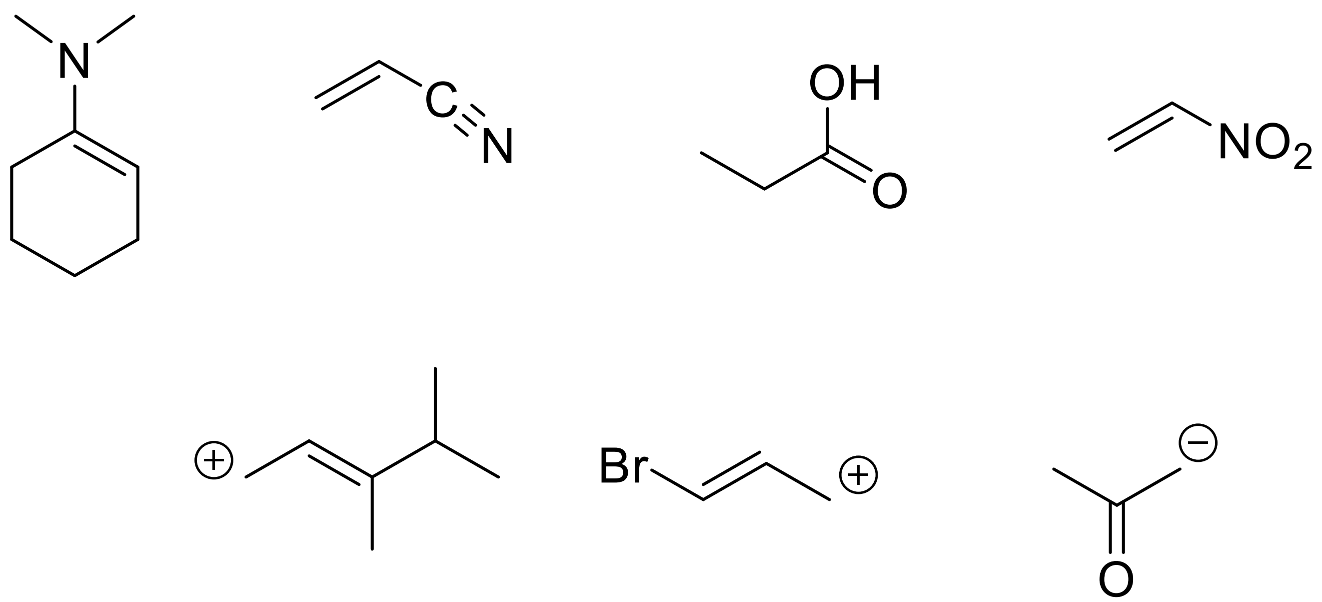
- Electronic effect of substituants – mesomeric effect

  - When you have an electron **hole- σ bond - π bond** (or **lone pair**), the electrons are displaced from the π bond in direction to to the electron hole



Chemical reactivity

- Exercise: For each compound represent the mesomeric forms. Then identify the electrophilic or nucleophilic atoms of the compounds



Chemical reactivity

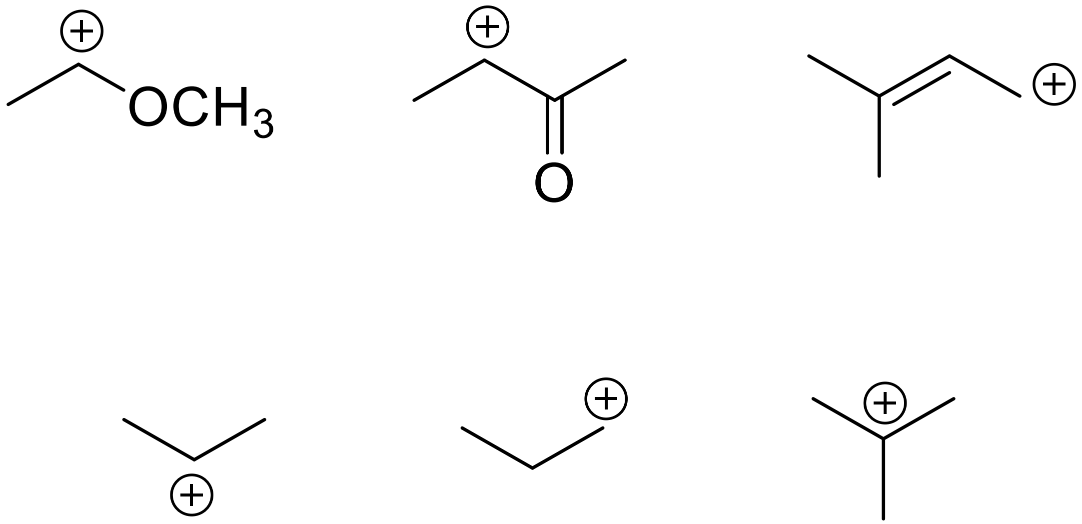
- Electronic effect of substituants – mesomeric effect

-M			+M	
$-NO_2$	-COR		$-NR_2$	-OR
-CN	-COOR	$-CONR_2$	-SR	-Halogènes

The inductive effects and the mesomeric effects explain the stability and the reactivity of organic molecules

Chemical reactivity

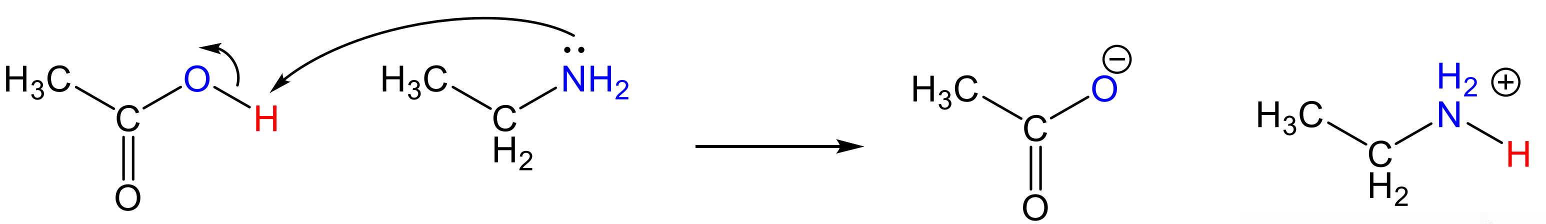
- Exercise: Thanks to the inductive and/or mesomeric effects, classify this carbocation from the less stable to the most stable.



Chemical reactivity

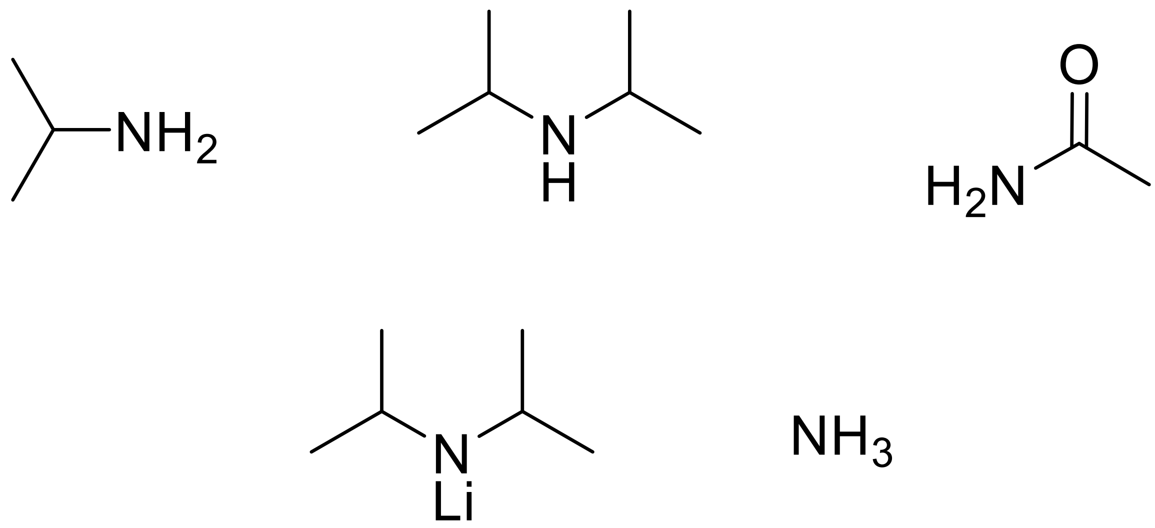
- Acids and bases

  - Acid: molecule able to give a proton (H^+)
  - Base: molecule able to catch a proton
  - An acid/base pair is defined by its pKa.
    - When pH<pKa the acid form is predominant
    - When pH>pKa the basic form is predominant
  - Acid-base reaction: displacement of the proton from the acid function to the basic one



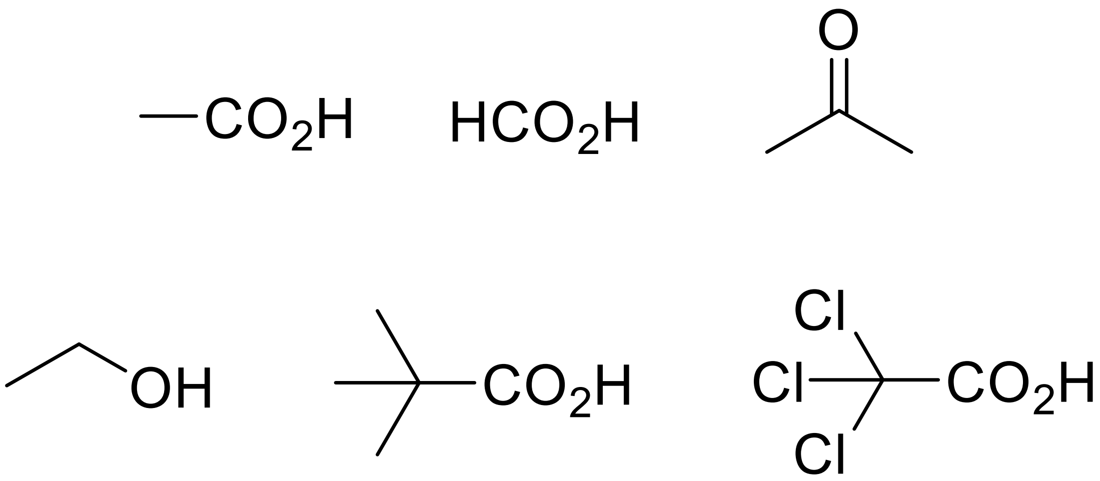
Chemical reactivity

- Exercise: Thanks to the inductive and/or mesomeric effects, classify these nitrogen functions from the less basic to the most basic.



Chemical reactivity

- Exercise: Thanks to the inductive and/or mesomeric effects, classify these molecules from the less acid to the most acid.



Principal mechanisms

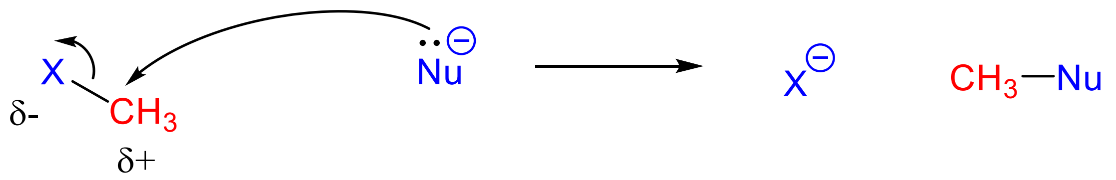
- Nucleophilic substitution
  - When the carbon has only single bonds
  - A nucleophile (Nu) attacks the electrophilic carbon (δ+) And causes the departure of the leaving group X^-

    The nucleophile can be for example:

    - an amine
    - an alcohol

    The leaving group is in general:

    - water
    - an halide (Cl^-, Br^-, I^-)

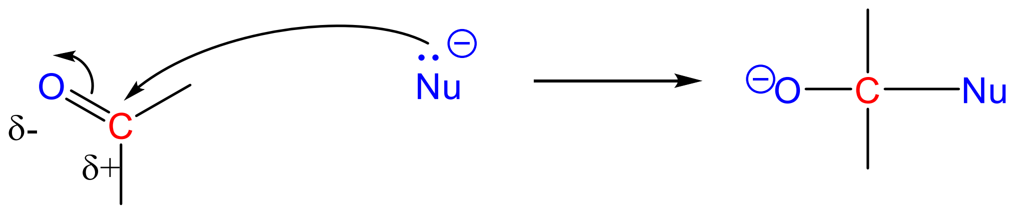


Principal mechanisms

- Nucleophilic Addition
  - When the carbon possesses a double bond.
  - A nucleophile (Nu) attacks the electrophilic carbon (δ+) and the two electrons of the π bond are sent as a supplementary lone pair on the oxygen (δ$^-$) for example (π bond is more fragile than σ bond)

    The nucleophile can be for example:

    - an amine
    - an alcohol (or water)



Principal mechanisms

- Nucleophilic addition/leaving group departure
  - When the carbon possesses a double bond and a leaving group.
  - A nucleophile (Nu) attacks the electrophilic carbon (δ+) and the two electrons of the π bond are sent as a supplementary lone pair on the oxygen (δ-)
  - In a second step the lone pair of the owygen creates a new double bond and causes the departure of the leaving group.