CHIMICA ORGANICA I
con
LABORATORIO

Organizzazione

Docente:

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  - Tel.: 040 558 3919

Libri di testo

John McMurry
Chimica Organica
PICCIN-NUOVA LIBRARIA

D'Auria M.V.; Taglialatela Scafati O.; Zampella A.
Guida ragionata allo svolgimento di esercizi di chimica organica
LOGHIA

Brown W.H.; Foote, C.S.; Iverson, B.L.
Chimica Organica
EdiSES

Janice Gorzynski Smith
Organic Chemistry
McGraw-Hill

Vollhardt K. Peter; Schore Neil E.
Chimica organica
Zanichelli

Solomons T.W. Graham;
Fryhle Craig B.
Chimica organica
Zanichelli

Seyhan N. Ege
Chimica Organica: Struttura e reattività
Idelson-Gnocchi

ORGANIC CHEMISTRY = Chemistry of Carbon Compounds

Joseph Proust 1754-1826

The Inorganic World
Non-Living Entities
Rational Laws

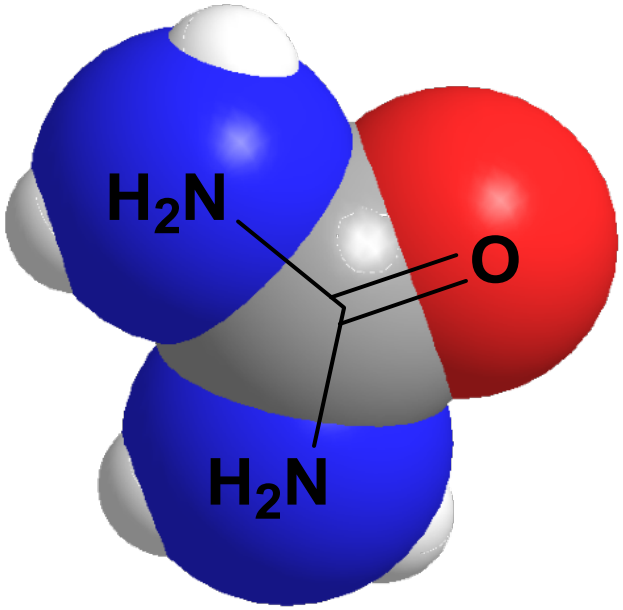
Organic World
Living Entities
Vital Spark

Inorganic Compounds:
Es. NH_3, H_2O
Definite Proportions

Organic World: Es. CH_4, C_2H_6, C_3H_8,
C_2H_4
C_2H_2
Similar properties but different proportions:
Vitalism!

1828: The End of Vitalism

Friedrich Woehler
1800-1882



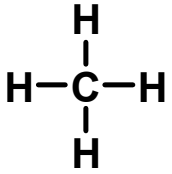
$$Pb(OCN)_2 + 2\ NH_4OH \longrightarrow Pb(OH)_2 + 2\ CO(NH_2)_2$$

Organic Compounds are Ubiquitous

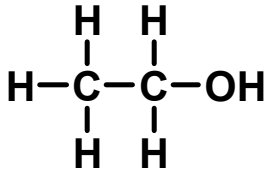
There are approximately 60.000.000 organic molecules.

- Biomolecules: c*arbohydrates, lipids, proteins and nucleic acids*.
- Materials: c*otton*, *paper*, *wood, leather, silk, wool, benzin, mineral oils*.
- Synthetic molecules and materials: *drugs, plastics, paints, dyes, artificial fibres, fertilizers, aromas, cosmetics, detergents, parfumes, sweeteners,* etc.

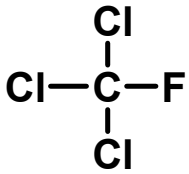
Organic Compounds



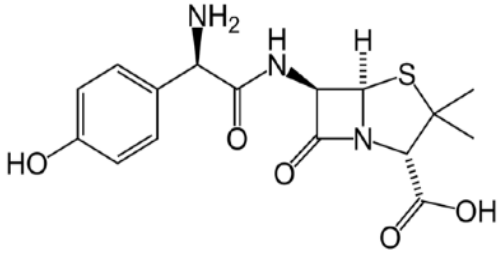
Methane



Ethanol

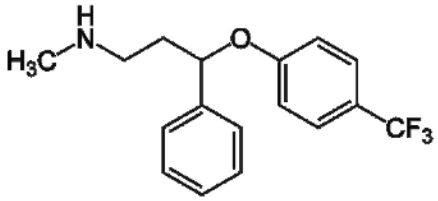


Trichlorofluoromethane



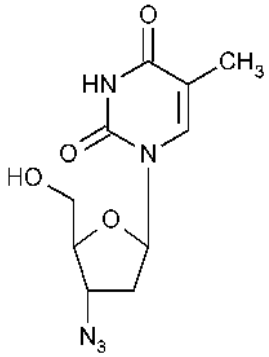
Amoxycillin

(2*S*,5*R*,6*R*)-6-(2-amino-2-(4-hidroxyphenyl)acetamido)-3,3-dimehyl-7-oxo-4-thia-1-azabiciclo[3.2.0]heptane-2-carboxylic acid



Fluoxetin
Prozac

N-methyl-3-phenyl-3-[4-(trifluoromethyl)phenoxy]propan-1-amine



AZT

3'-azido-3'-deoxythymidine

The Carbon Atom

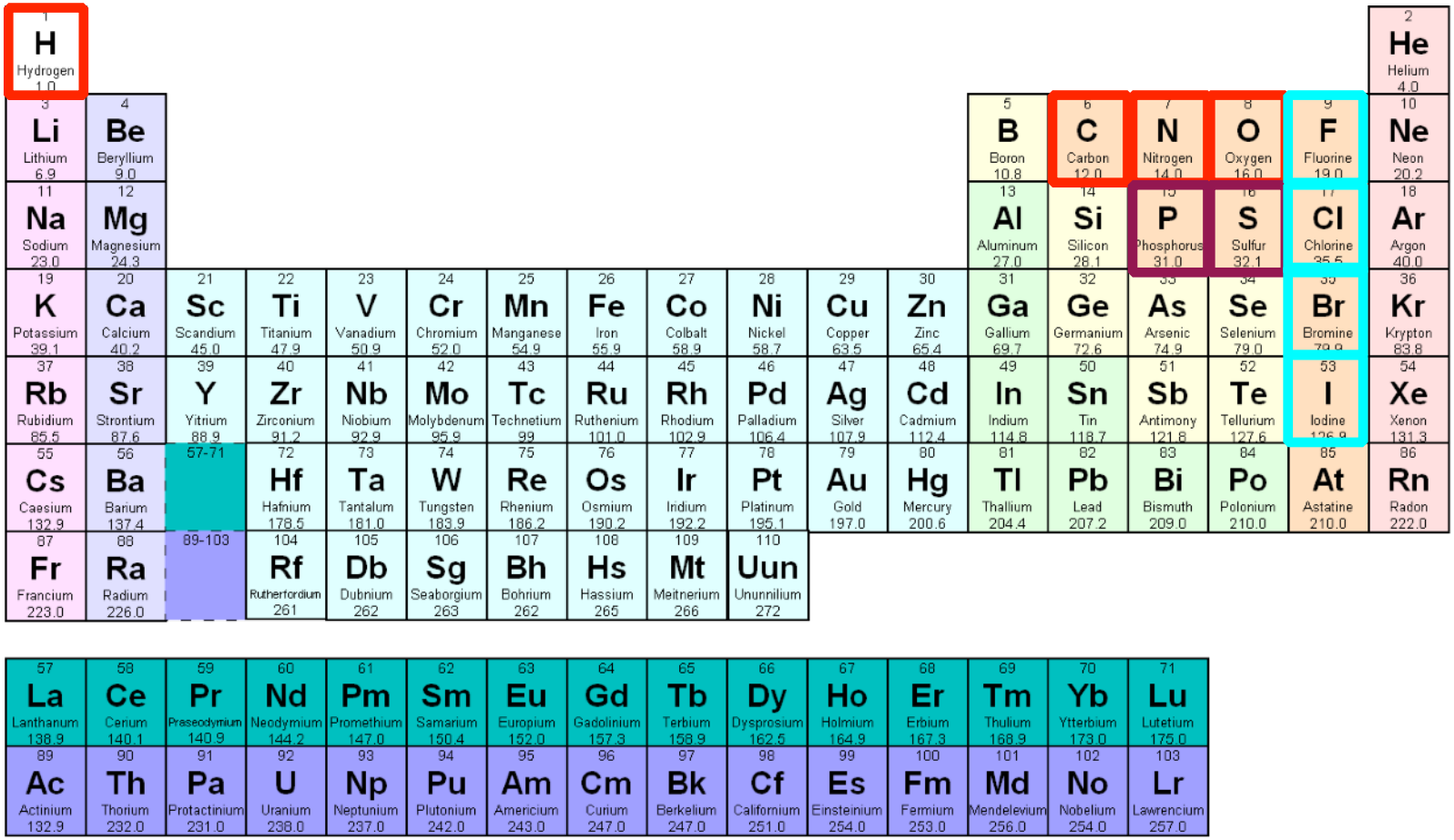
- Atomic Number: 6
- 2 Isotopes

  ^{12}C (98,9%): 6 protons, 6 neutrons

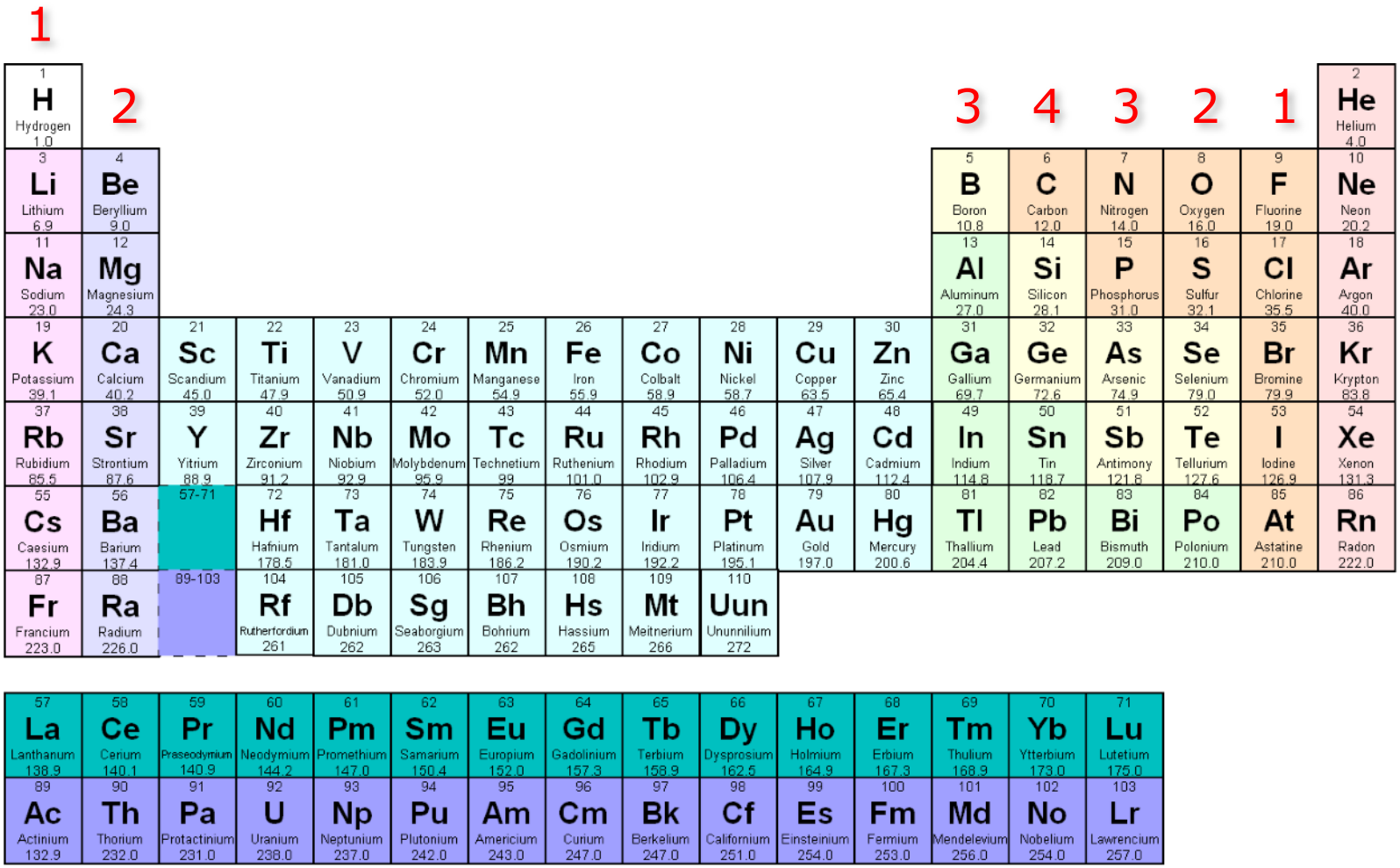
  ^{13}C (1,1%): 6 protons, 7 neutrons
- Electron Configuration: $1s^2$

  $2s^2\ 2p^2$

1. Carbon Forms Covalent Bonds With Many Other Elements



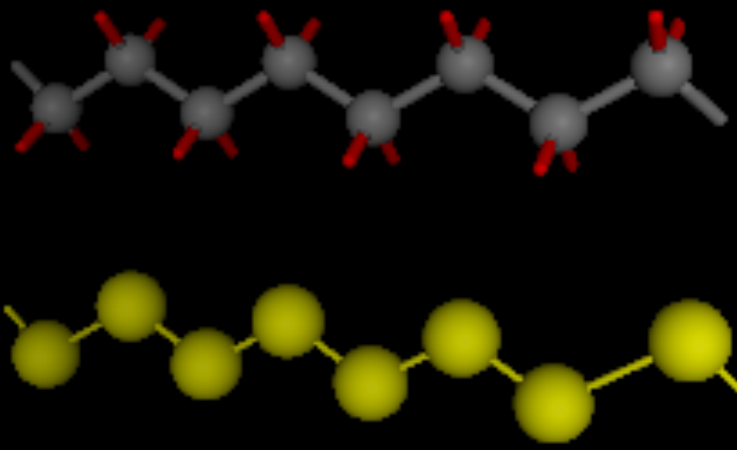
2. Carbon Is Tetravalent



3. Carbon Forms Very Strong Bonds

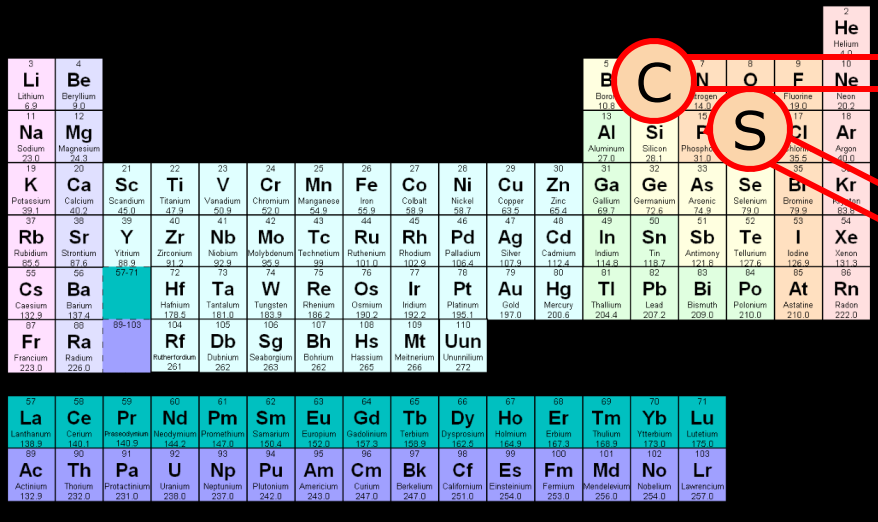
Bond	Bond Dissociation Energy (kJ/M)
C—C	360
C—H	400-550
C—O	350-400
C—N	360
N—N	250
O—O	180

4 Carbon forms chains



Energy (kJ/mol)

C-C	360
N-N	230-280
O-O	160-200



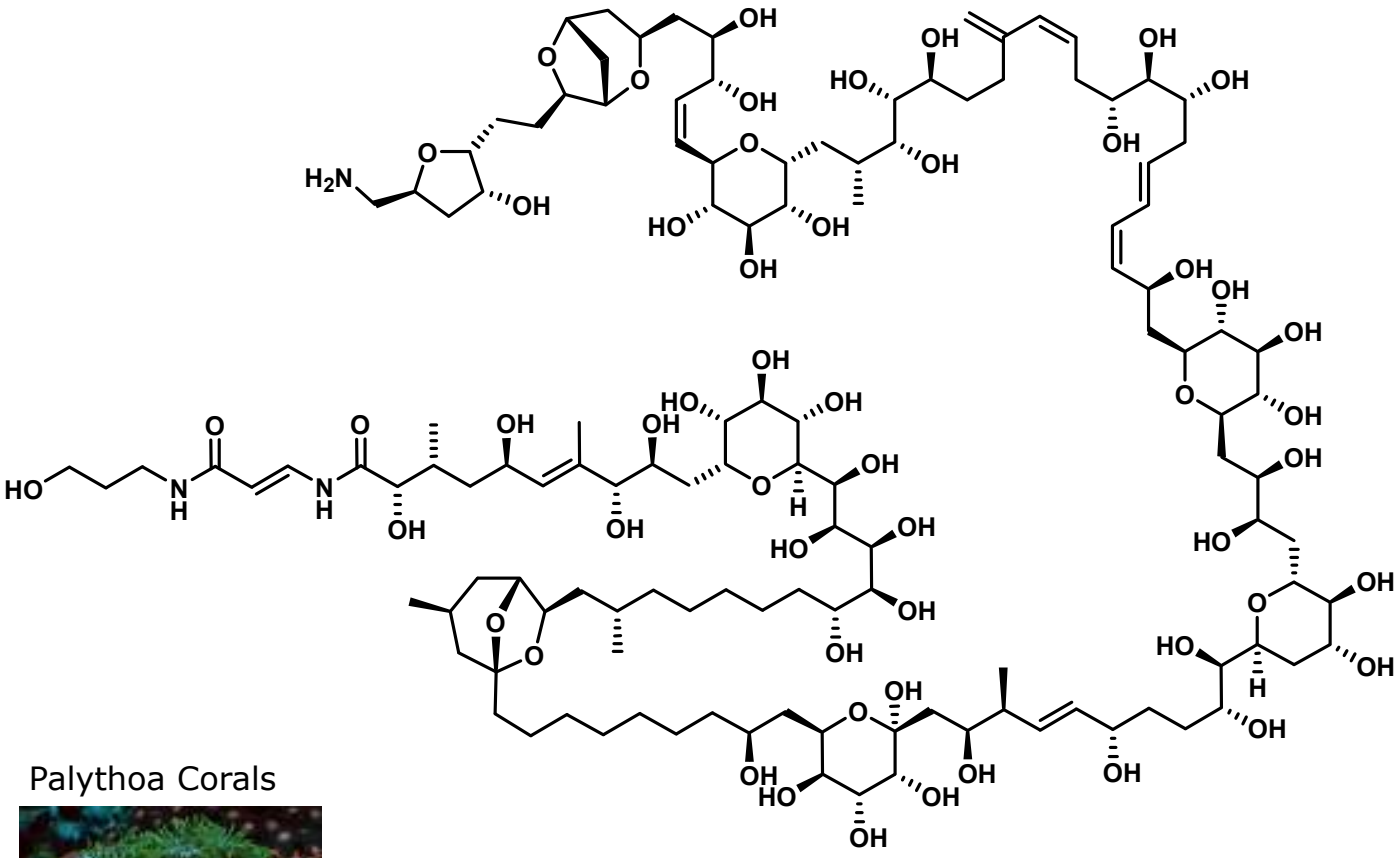
$2s^2 2p^2$

$3s^2 3p^4$

5. Carbon Forms Multiple Bonds

Bond	Bond Dissociation Energy (kJ/M)
C—C	360
C=C	700
C≡C	950
C—O	400
C=O	750
C—N	360
C=N	700
C≡N	950

Organic Compounds



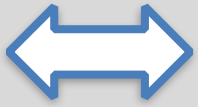
Palytoxin

Palythoa Corals

Lophozozymus pictor

Organic Chemistry

- Structure
- Reactivity
- *Structure* and *reactivity* are correlated.

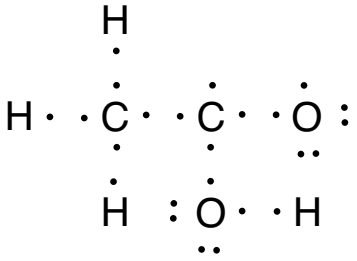
STRUCTURE  REACTIVITY

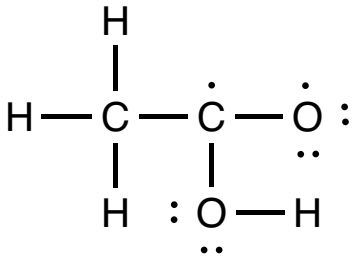
Goals

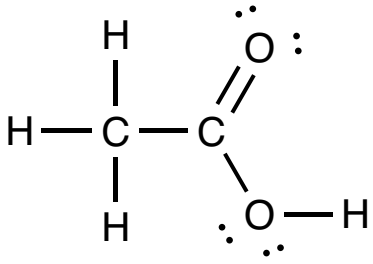
- Assign Structure and Name to Organic Compounds.
- Predict:
  - The tridimensional structure
  - The effects on reactivity (reaction rates and equilibrium constants)
- Design simple synthetic pathways
- Communicate with an appropriate language

Drawing molecules

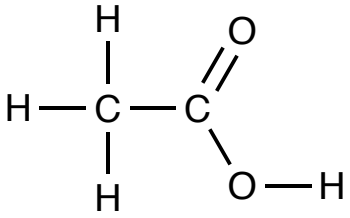
Acetic Acid



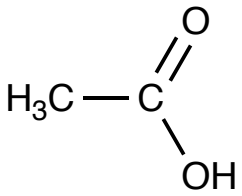




Lewis structures



Structural Formula

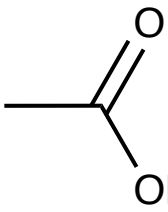


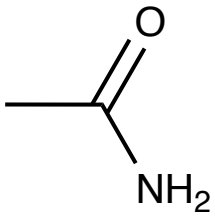
Condensed Formula

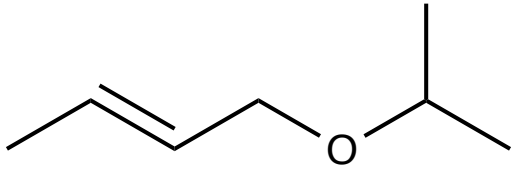
CH_3COOH

$C_2H_4O_2$

Empirical Formula

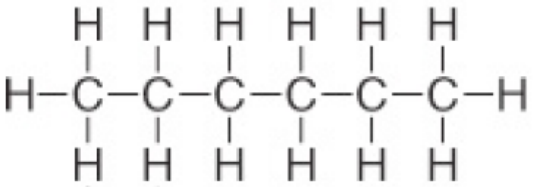


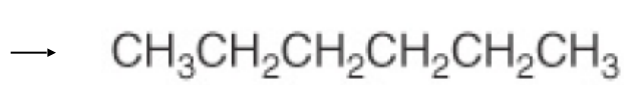


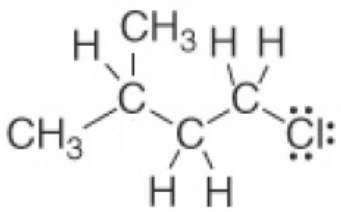


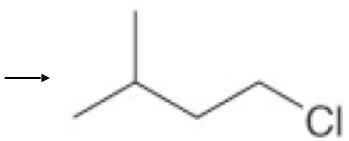
Skeletal Formula

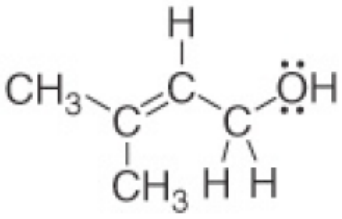
Examples

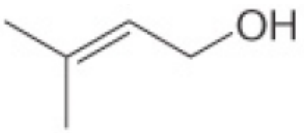


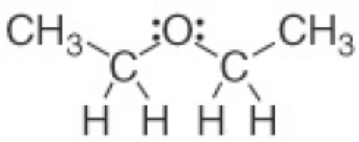


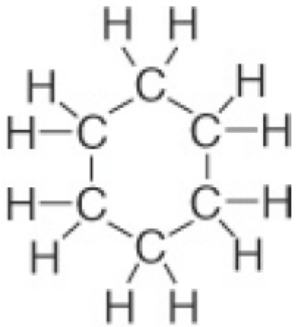




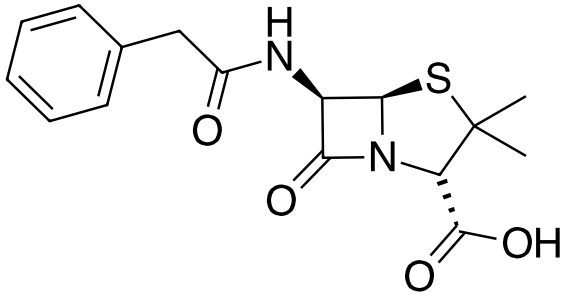




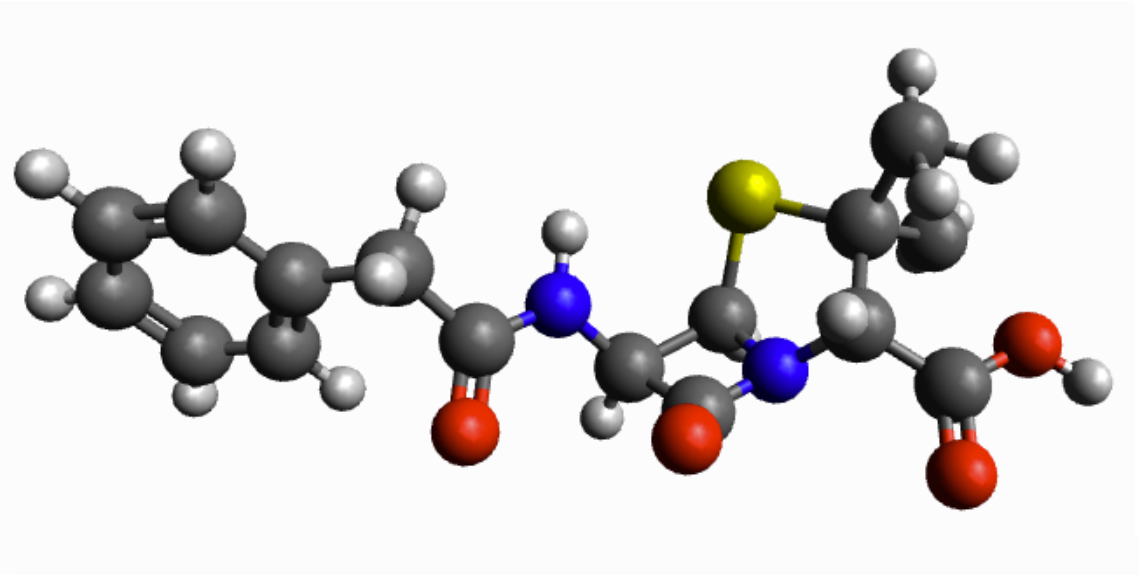


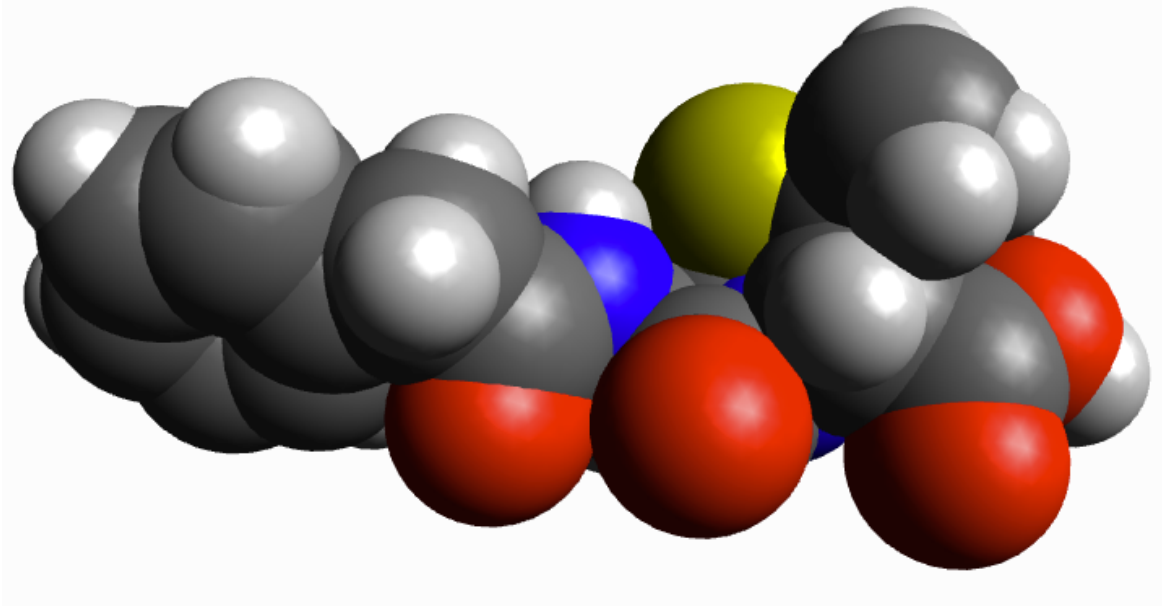


Molecular Models

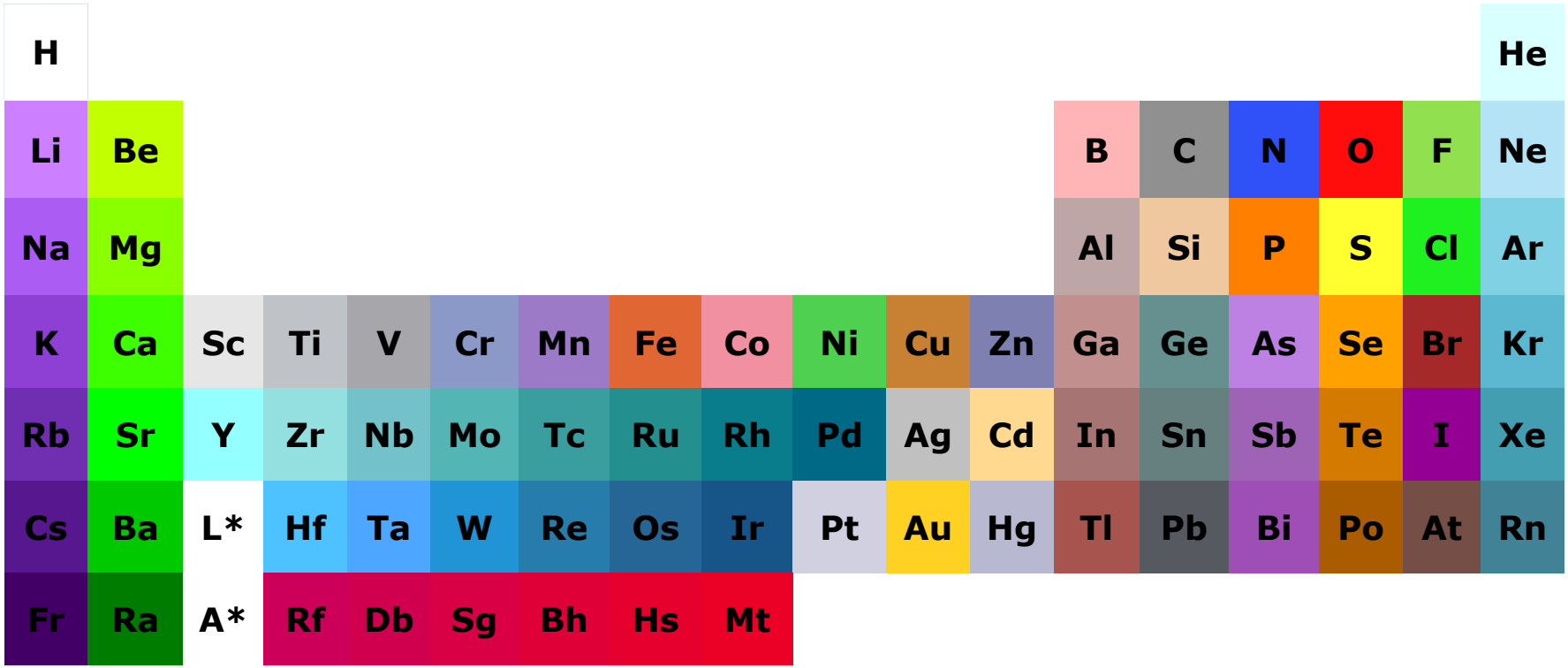


Benzylpenicillin
(penicillin G)



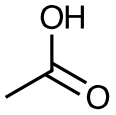


Element Coloring Scheme



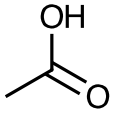
Line Notations

SMILES (**S**implified **M**olecular **I**nput **L**ine **E**ntry **S**ystem)



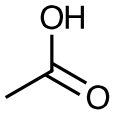
CC(=O)O

InChI (**In**ternational **Ch**emical **I**dentifier)



InChI=1S/C2H4O2/c1-2(3)4/h1H3,(H,3,4)

InChIKey (A hashed version of InChI)



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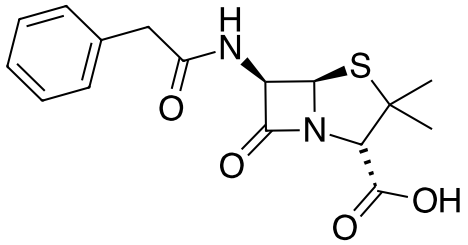


NIH molecular editor

SMILES: CC(=O)[C@@H]3C2C(=O)[C@@H](NC(=O)Cc1ccccc1)[C@H]2SC3(C)C

InChI: InChI=1S/C18H21NO3S/c1-10(20)14-13-16(22)15(17(13)23-18(14,2)3)19-12(21)9-11-7-5-4-6-8-11/h4-8,13-15,17H,9H2,1-3H3,(H,19,21)/t13?,14-,15-,17+/m1/s1

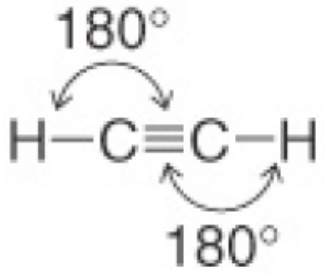
InChIKey: SOQSAIZEYNYYAA-LZMBWQIGSA-N

Atomic Structure and Bonding

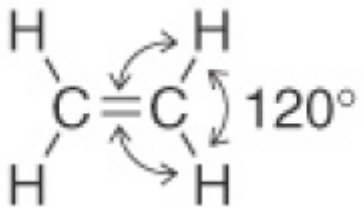
Chapter 1
Organic Chemistry, *8th Edition*
John McMurry

Geometry – VSEPR Theory

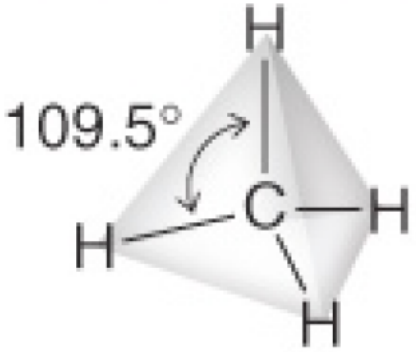
Number of groups	Geometry	Angle
2	linear	180°
3	trigonal planar	120°
4	tetrahedral	109.5°



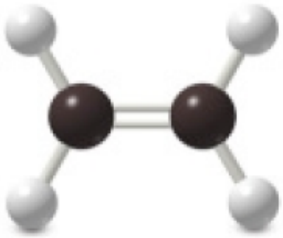
acetylene

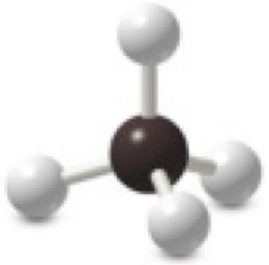


ethylene



methane





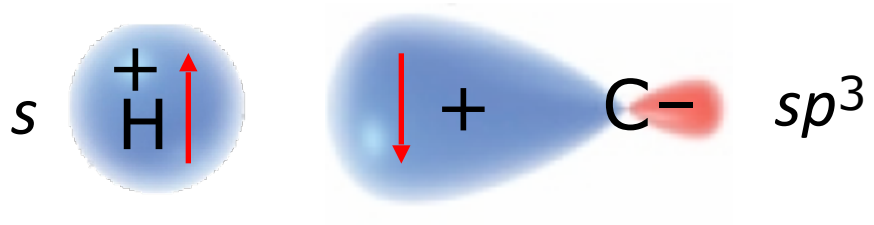
Energies of Multiple Bonds

Bond	Bond Dissociation Energy (kJ/M)
C—C	360
C=C	700
C≡C	950
C—O	400
C=O	750
C—N	360
C=N	700
C≡N	950

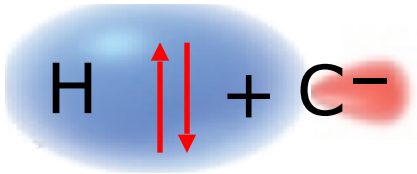
The Lewis model is not adequate!

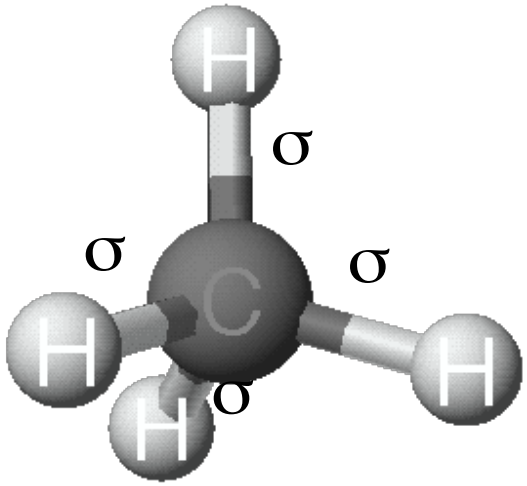
Methane

The overlap of a half-full *1s* orbital of hydrogen with a half-full sp^3 orbital of carbon bond gives a **σ** orbital.

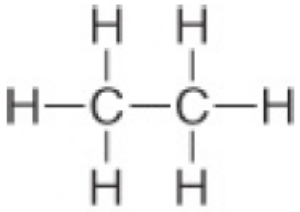


σ C–H

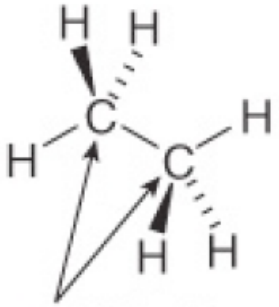




Ethane

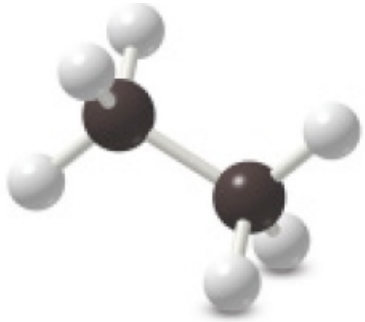


ethane

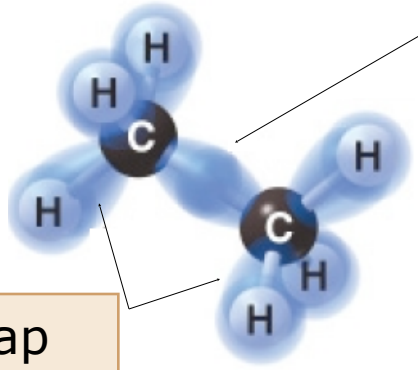


tetrahedral sp^3 C

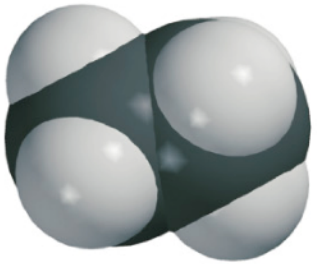
=

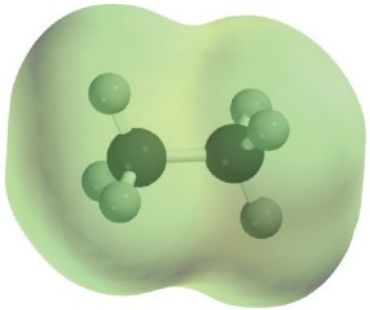


Two sp^3 hybrids overlap giving the C–C σ bond

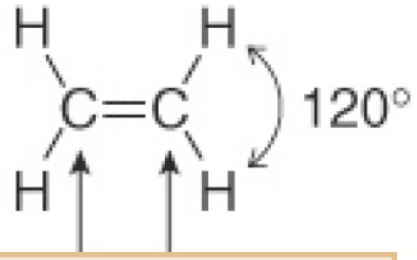


sp^3 hybrids on C overlap with *1s* orbitals on H giving the C-H σ bonds.

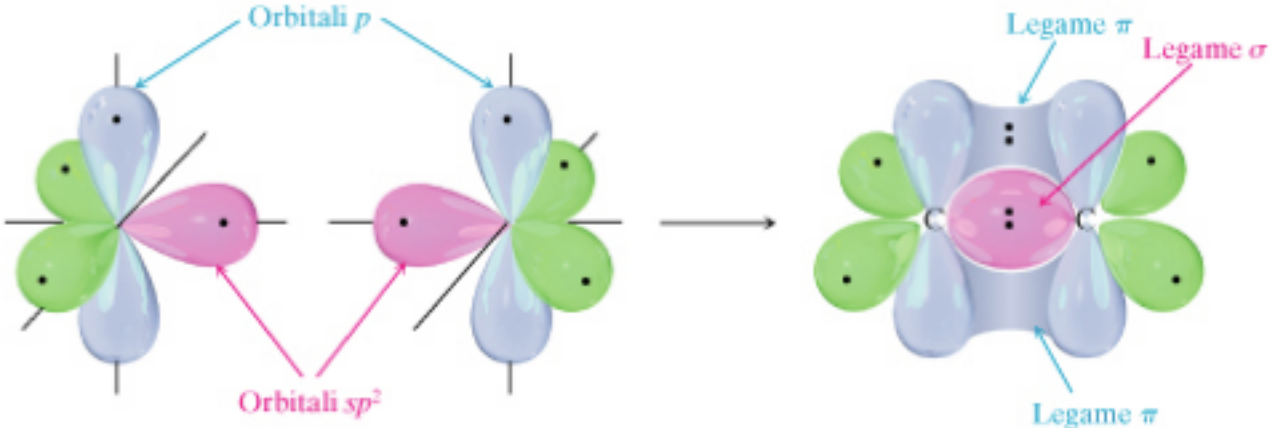




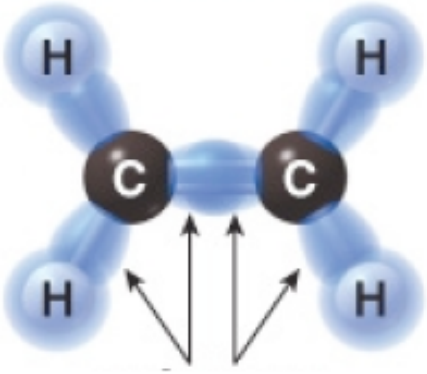
Ethylene C_2H_4



3 groups around C
C atoms are *sp*²

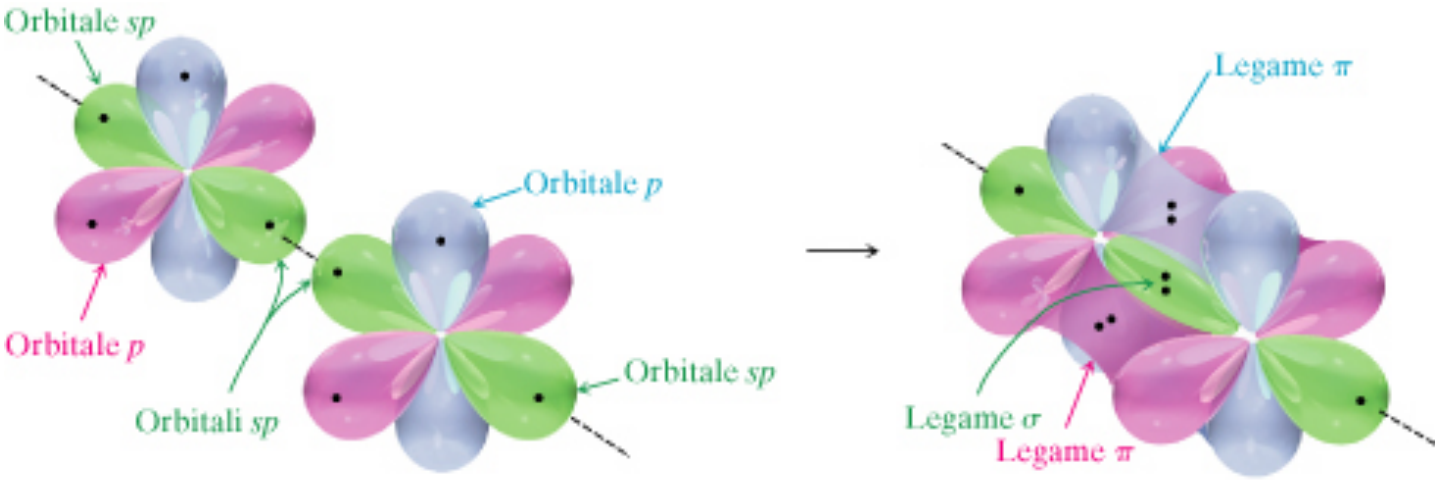


C-C double bond

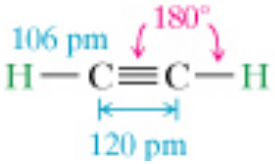


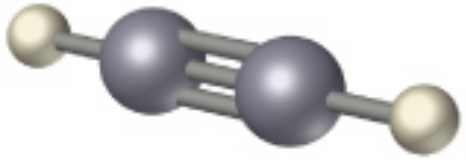
*Sp*² hybrids

Acetylene C_2H_2



C-C triple bond





Polar Bonds
Intermolecular Interactions
Delocalised Bonds

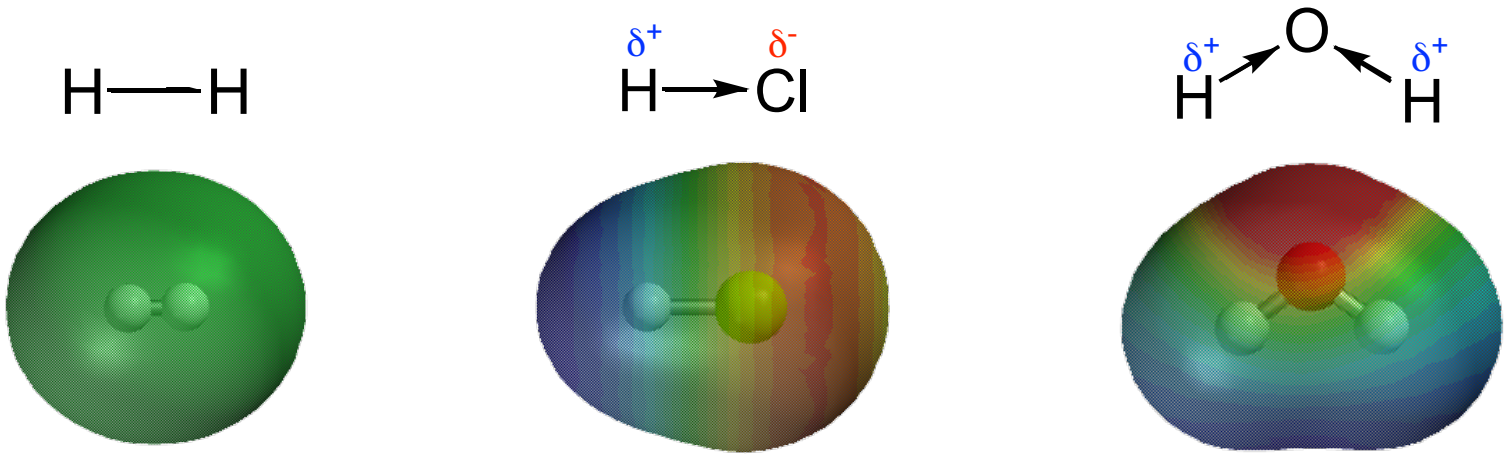
Chapter 2

Organic Chemistry, *8th Edition*

John E. McMurry

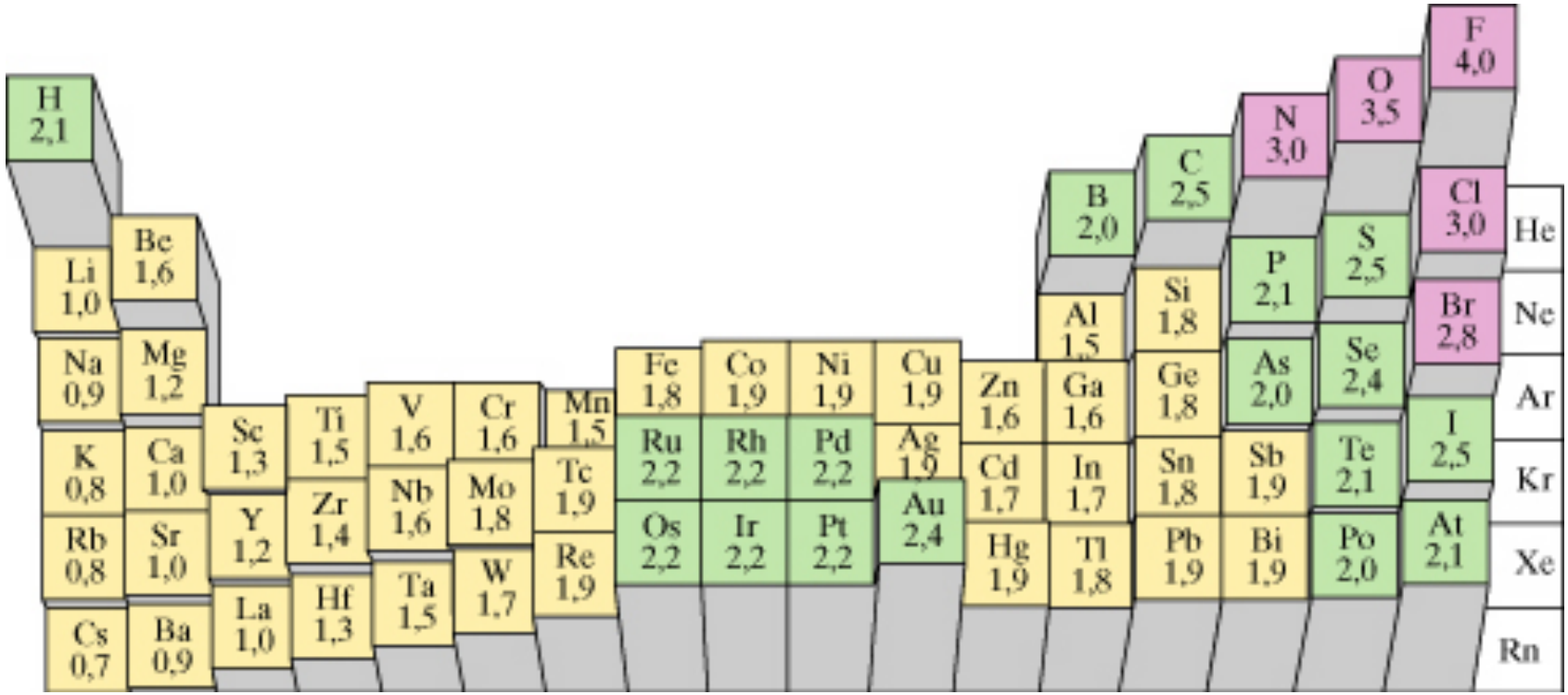
Polar Covalent Bonds

- In polar bonds, bonding electrons are attracted towards the more electronegative atom.



- The higher the electronegativity difference, the higher the polar character of a covalent bond.
  - $\Delta X > 1.9 \Rightarrow$ ionic bond
  - $\Delta X < 0.5 \Rightarrow$ covalent bond
  - $\Delta X = 0.5 - 1.9 \Rightarrow$ polar covalent bond

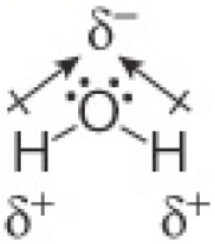
Pauling's Electronegativities

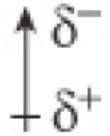


Dipole Moments

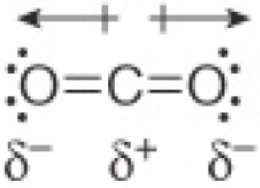
- Polar molecules have one or more polar bonds.

Es. H_2O

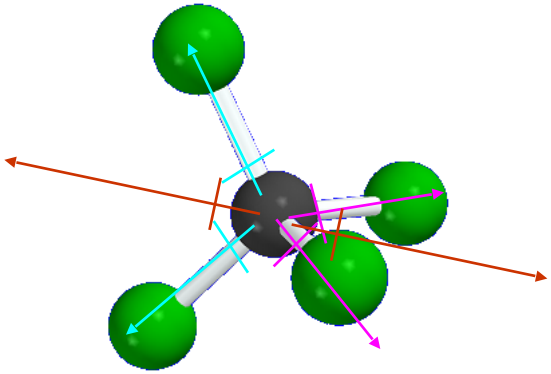




- Apolar molecules either do not have polar bonds or have polar bonds whose dipoles cancell each other. E.g. CO_2

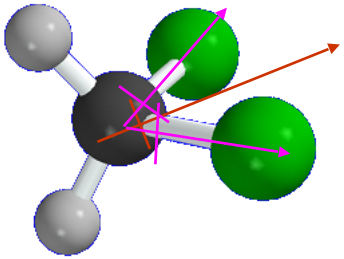


CCl_4 μ = 0 D



Dipoles cancel

CH_2Cl_2 μ = 1.62 D



Dipoles add

Intermolecular interactions

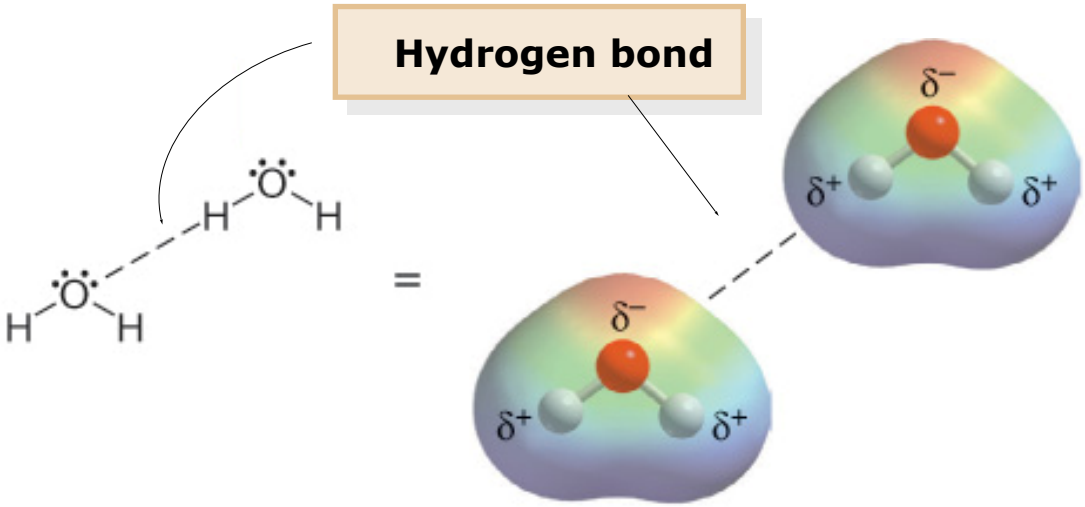
- Intermolecular interactions are also called non-covalent or non-bonded interactions.

- Intermolecular interactions depend on the type and number of functional groups.

- In neutral molecules there are three main types of intermolecular interactions.
  - Vand der Waals interactions (London dispersion forces) – VDW
  - Dipole-dipole interactions – DD
  - Hydrogen bonds– HB

The Hydrogen Bond

- The hydrogen bond is an electrostatic interaction betweeen a O-H or N-H group and a lone pair on O or N.

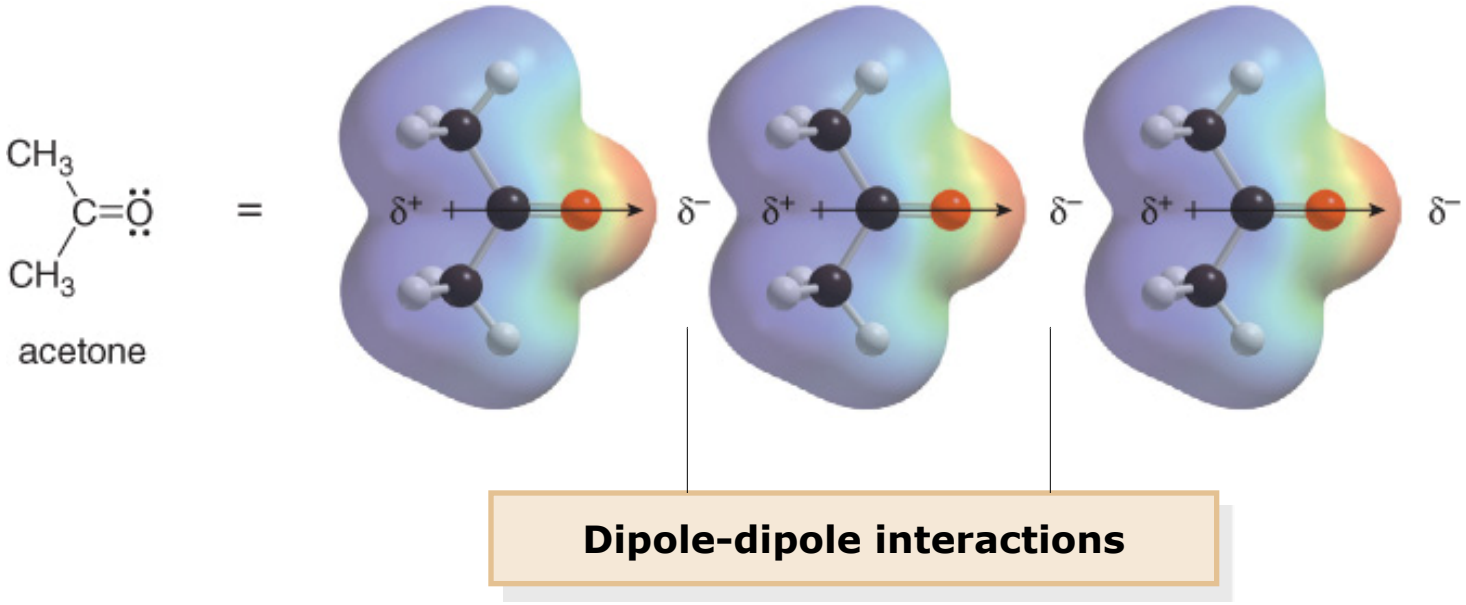


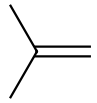
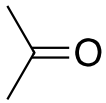
The Hydrogen Bond

	MW	***b.p. (°C)***	***H-bond***
H_3C-CH_3	***30***	***-89***	***none***
H_3C-NH_2	***31***	***-6***	***weak***
H_3C-OH	***32***	***65***	***strong***

Dipole-Dipole Interactions

- Dipole-dipole interactions are attraction forces between the permanent dipoles of two molecules.

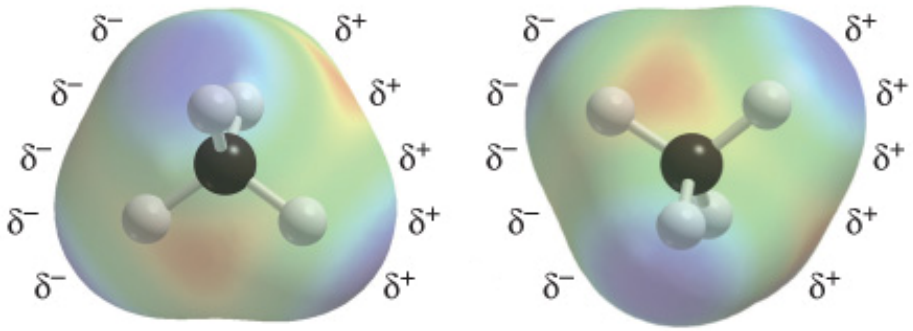


	MW	*b.p. (°C)*
	***56***	***-5***
	***58***	***56***

Van der Waals (London) Forces

- VdW forces are weak interactions originating from temporary variations of the molecule's electron density distribution.
- They are the only attractive forces in apolar molecules.

Van der Waals interactions between two CH_4 molecules

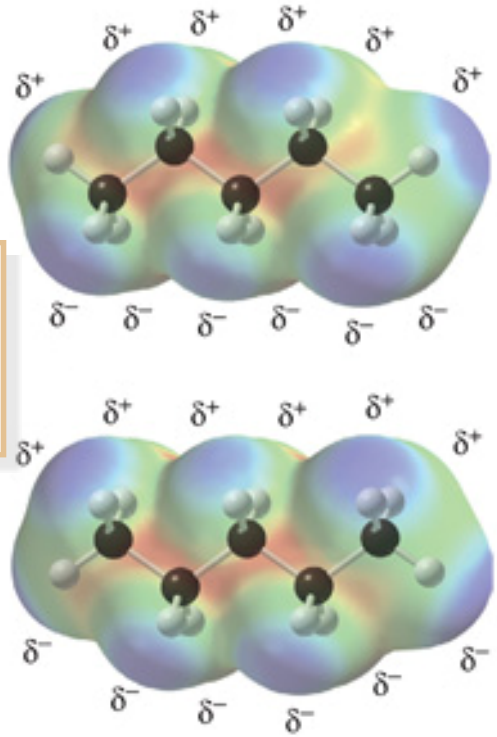


Dipoles generated by a temporay asymmetry in the electron density

Van der Waals (London) Forces

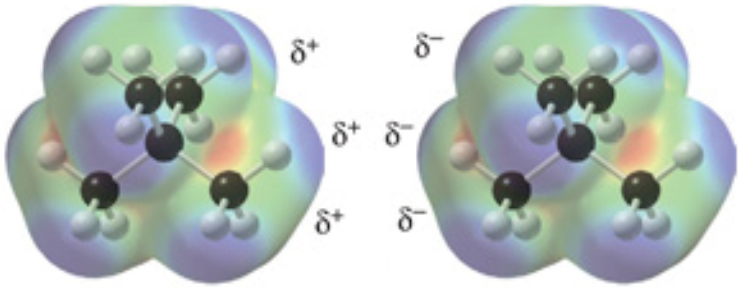
- Van der Waals interactions are present in all molecules.
- The larger the surface area, the larger the attractive force between two molecules, and the stronger the intermolecular forces.

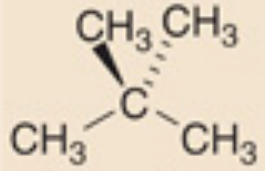
Long, cylindrical molecules:
stronger interactions



$CH_3CH_2CH_2CH_2CH_3$
n-pentane
b.p. 36 °C

Compact, spherical molecules:
weaker interactions





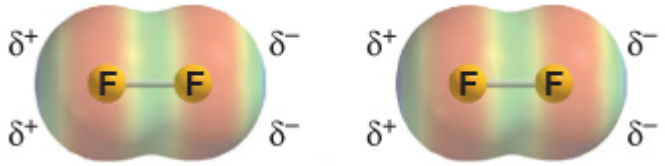
neopentane
b.p. 10 °C

Van der Waals (London) Forces

- VdW forces depend on polarizability.
- Larger atoms, like iodine, which have more loosely held valence electrons, are more polarizable than smaller atoms like fluorine, which have more tightly held electrons

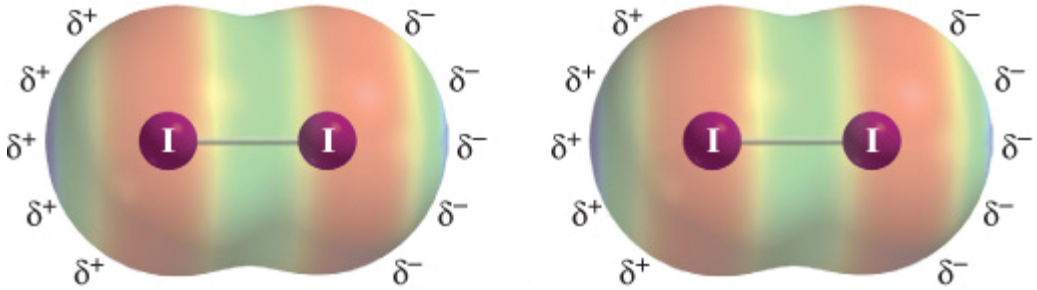
Small atoms: lower polarizability

Weak interaction



Large atoms: higher polarizability

Stronger interaction



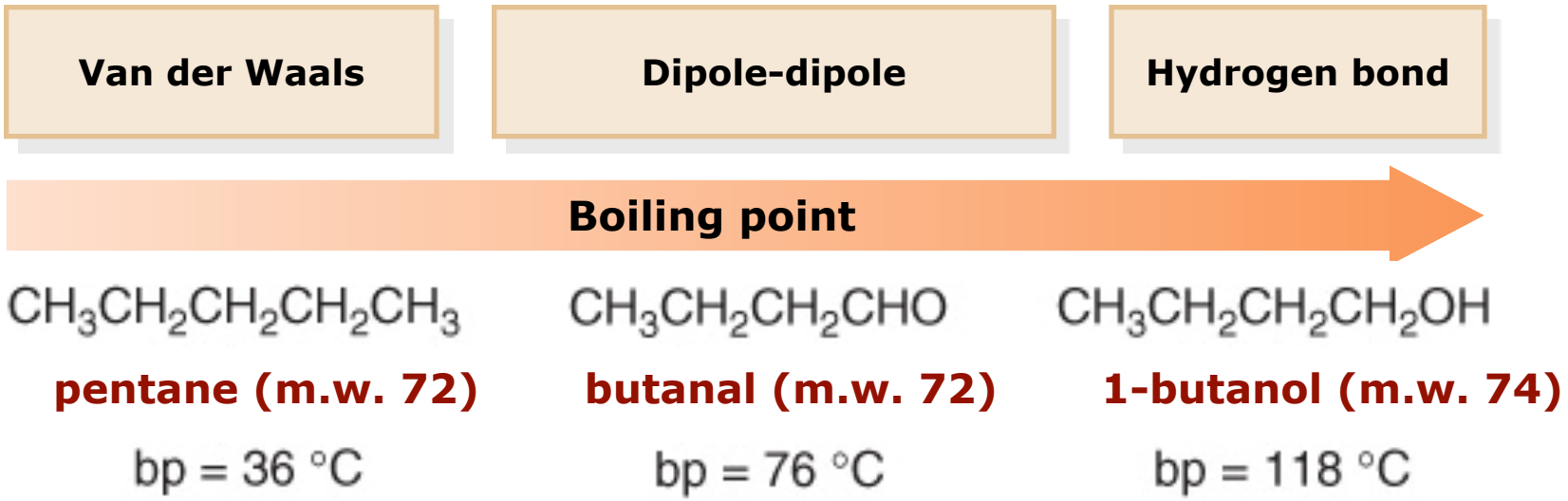
Summary

Interaction	Relative strength	Present in	Examples
Van der Waals VDW	Very weak	All molecules	$CH_3CH_2CH_2CH_2CH_3$ $CH_3CH_2CH_2CHO$ $CH_3CH_2CH_2CH_2OH$
Dipole-dipole DD	weak	Permanent dipoles	$CH_3CH_2CH_2CHO$ $CH_3CH_2CH_2CH_2OH$
Hydrogen bond HB	strong	Molecules with OH, NH, funct. groups	$CH_3CH_2CH_2CH_2OH$
ionic	Very strong	Ionic compounds	NaCl, LiF

Polar molecules interact strongly than apolar ones.

Boiling Point

- The boiling point is the temperature at which the vapor pressure of a liquid is equal to the external pressure.
- Energy is required to break intermolecular interactions.
- The higher the intermolecular interactions, the higher the b.p..
- Compounds with similar M.W.:



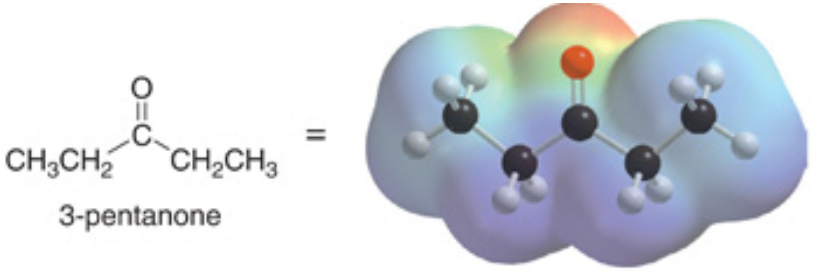
Boiling Point

b.p. = 42 °C

I is more polarizable

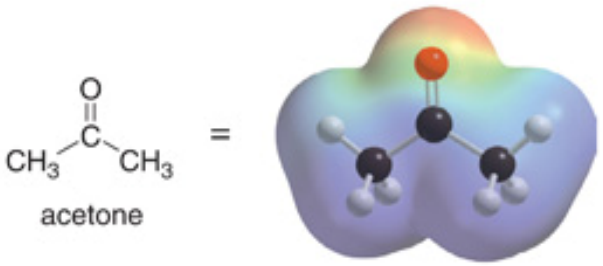
b.p. = –78 °C

Smaller F has a low polarizability



b.p. = 102 °C

Larger surface area

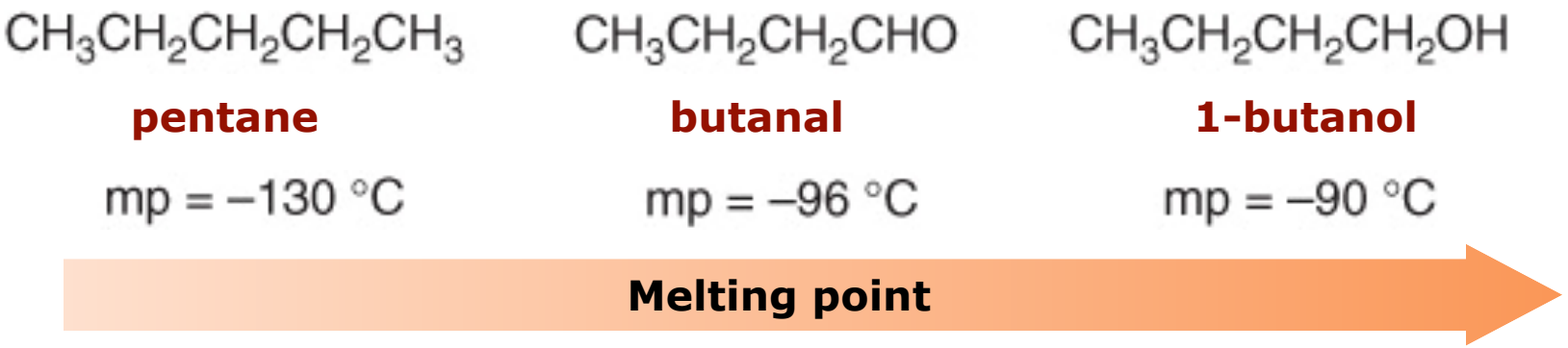


b.p. = 56 °C

Smaller surface area

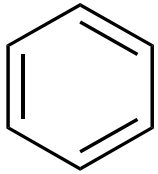
Melting Point

- M.p. and b.p. follow the same trend.

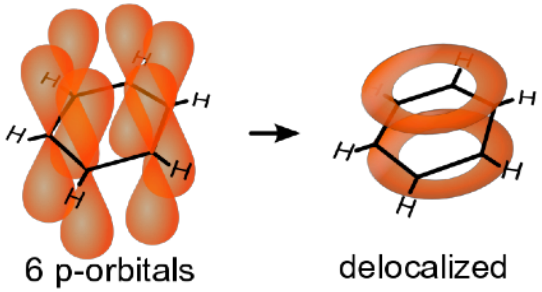


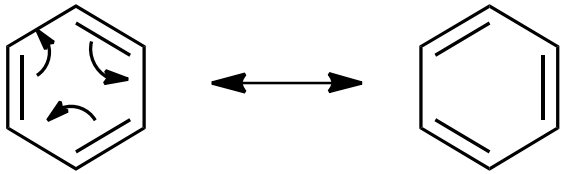
Resonance - Delocalized Bonds

Benzene (C_6H_6)

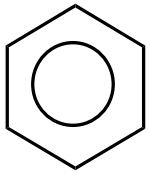


Very stabile
6 identical C-C bonds

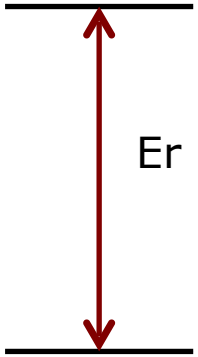


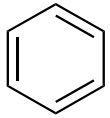


Resonance structures



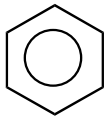
Resonance
hybrid





6 localized
π electrons

Er = 150.7 kJ/mol
(36 kcal/mol)



6 delocalized
π electrons

Resonance

1. Resonance structures are not real. No single resonance structure can adequately represent the real structure of a species with delocalized electrons.
2. Resonance structures are not isomers. They only differ in the distribution of electrons not in the disposition of the nuclei.
3. Resonance structures are not in equilibrium.

Acids and Bases
Electrophiles and Nucleophiles
Organic Reaction Mechanisms

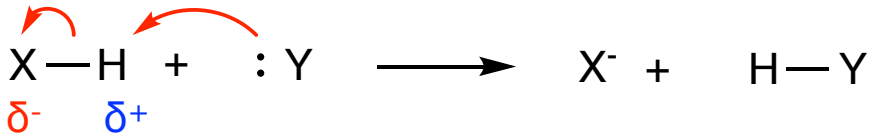
Chapters 2 & 6

Organic Chemistry, *8th Edition*

John McMurry

Brønsted-Lowry Acids and Bases

- An acid-base reaction is a proton transfer reaction



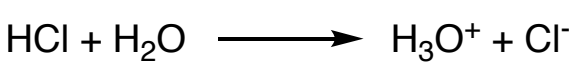
- Acids donate protons to an acceptor

  All Brønsted-Lowry acids contain a polar X-H bond.

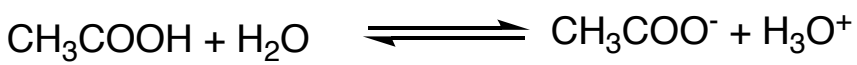
  (X=O, Halogens)

- Bases accept protons from a donor

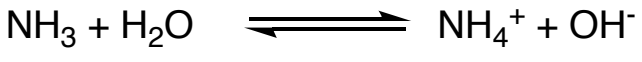
  All Brønsted-Lowry bases contain a lone pair.



strong acid



weak acid



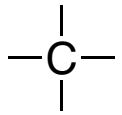
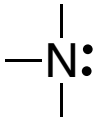
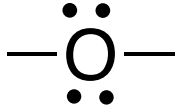
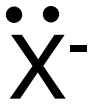
weak acid

Organic Acids

Element	Electronegativity	Bond	Acidity
H	2.1		
C	2.5	C-H	NO
N	3.0	N-H	NO
O	3.5	O-H	YES

Formula	Name	K_a	pK_a	acidity
R-OH	alcohols	$<10^{-15}$	> 15	less than H_2O
Ar-OH	phenols	10^{-9}	9	slightly dissociated
R-COOH	carboxylic acids	$> 10^{-5}$	> 5	more dissociated

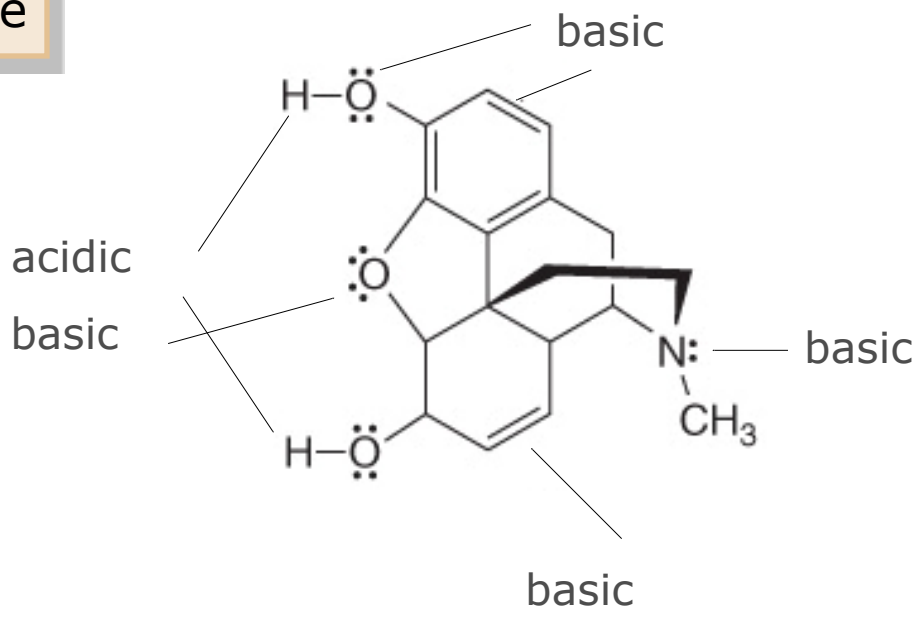
Organic Bases

Group	electron pairs	electronegativity	Basicity
	NO	-	NO
	1	3.0	YES
	2	3.5	WEAK
	at least 1		STRONG

Brønsted-Lowry Acids and Bases

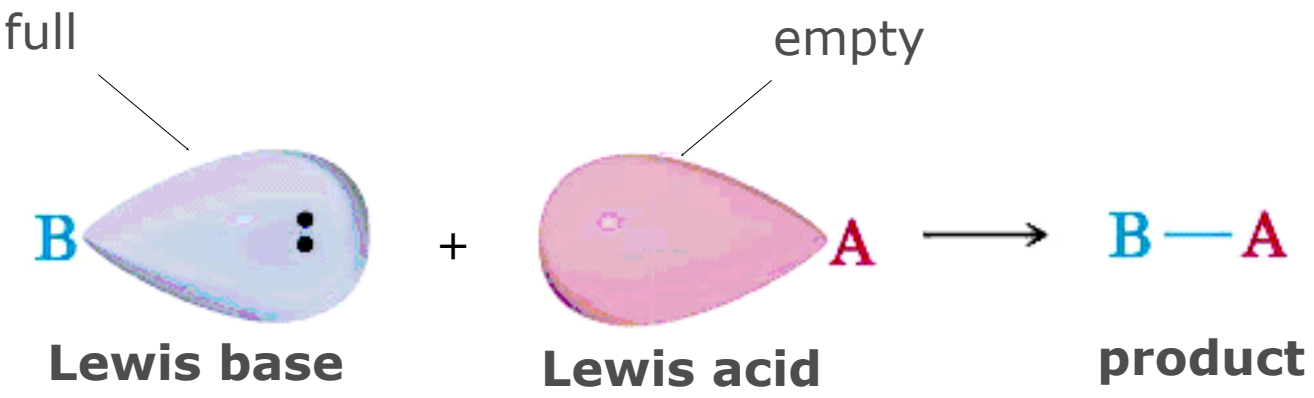
- Certain molecules can behave both as acids and bases.

Morphine



Lewis Acids and Bases

- A Lewis acid accepts an electron pair from a donor. Lewis acids have a low energy empty orbital.
- A Lewis base donates an electron pair to an acceptor. Lewis bases have a high energy full orbital (lone pair or π bonds).



Lewis Acids and Bases

- All Brønsted-Lowry acids are Lewis acids. Not all Lewis acids are Brønsted-Lowry acids.
- Only species with ionizable protons are Brønsted-Lowry acids. Any electron acceptor is a L.A.

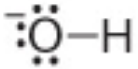
H_2O CH_3OH

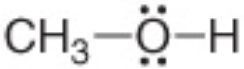
Brønsted-Lowry and Lewis acids

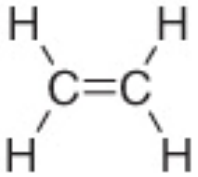
BF_3 $AlCl_3$

Lewis acids

- All Brønsted-Lowry bases are also Lewis bases. They must have either a lone pair or a π bond.

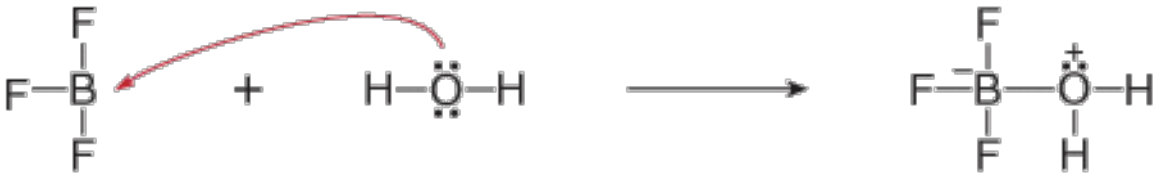






Reactions Between Lewis Acids and Bases

- Organic reactions can in most cases be described as reactions between electron poor species (Lewis acids) and electron rich species (Lewis bases).
- The electron poor species (Lewis acid) is called electrophile.
- The electron rich species (Lewis base) is called nucleophile.
- The movement of electrons is indicated with curved arrows.

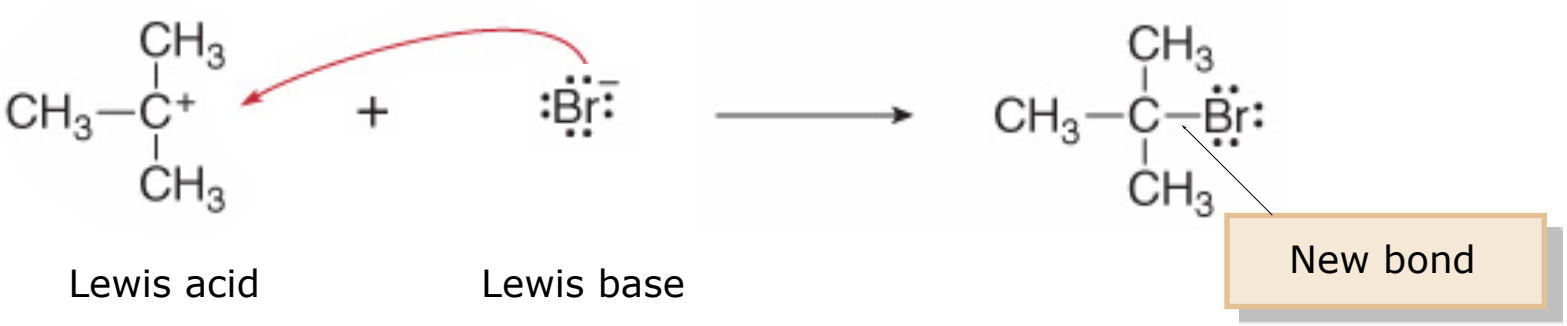


Lewis acid — Lewis base

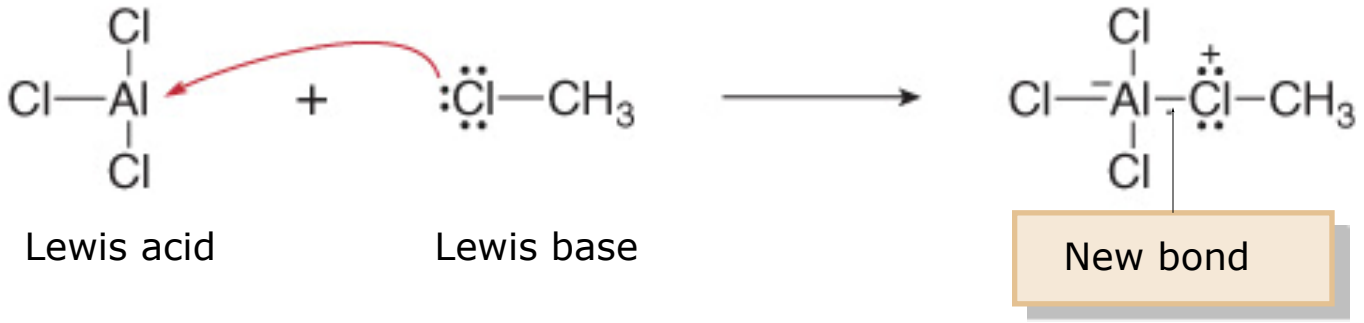
electrophile — nucleophile

Electrophiles and Nucleophiles

electrophile nucleophile



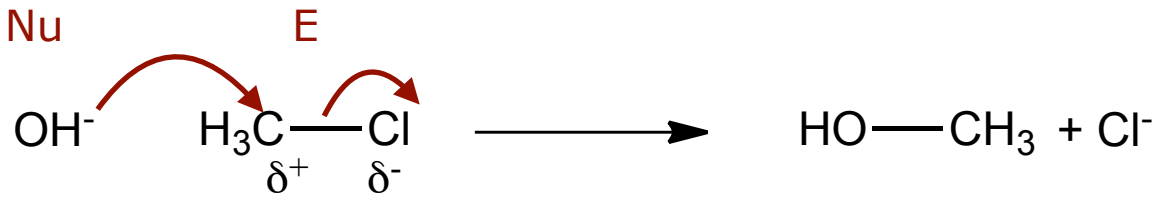
Lewis acid Lewis base

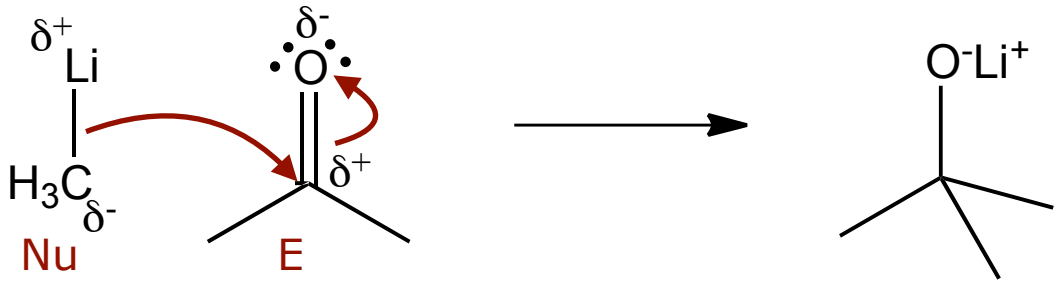


Lewis acid Lewis base

Electrophiles and Nucleophiles

- Nucleophiles and electrophiles may also contain polar bonds





Organic Reactions

- Type of reaction (bond breaking/bond formation):
  - substitution
  - addition
  - elimination
  - rearrangement/transposition
- Mechanism = movement of electrons:
  - ionic (polar)
  - radicalic
  - pericyclic

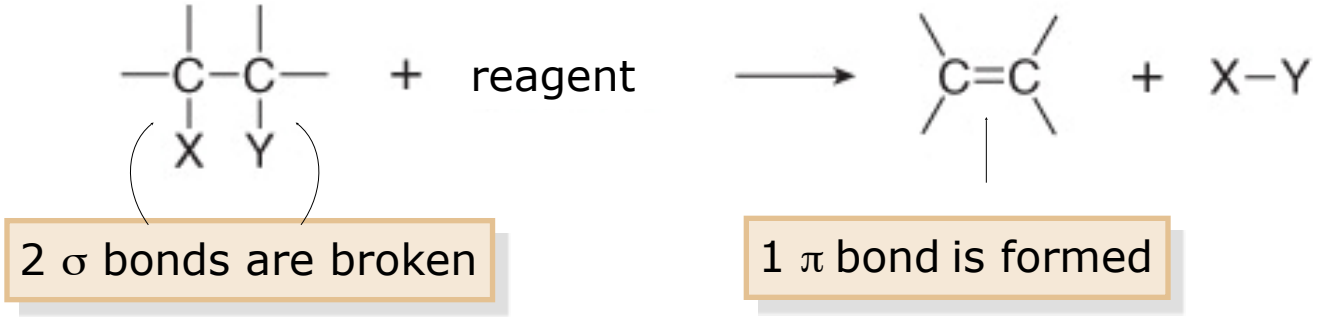
Substitutions

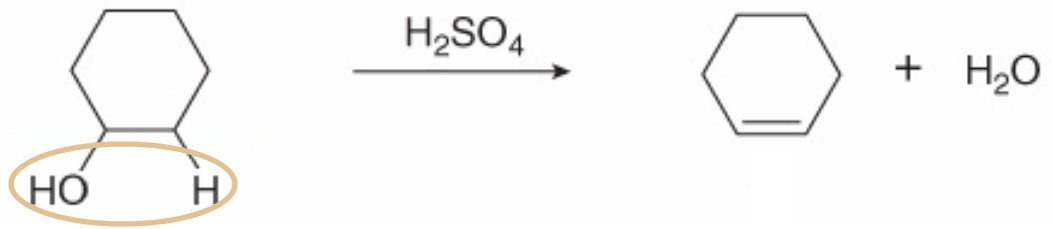
- In a general substitution reaction, an atom or group Y replaces an atom or group Z at carbon.
- Substitutions involve breaking and forming σ bonds.

Y replaces Z

Eliminations

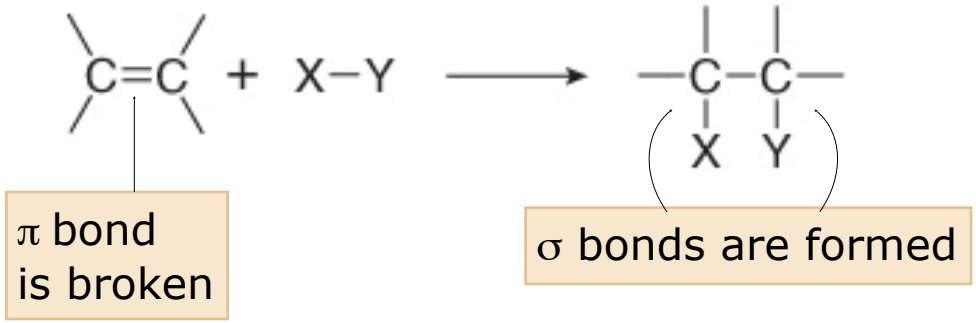
- In an elimination reaction two σ bonds are broken and one π bond is formed.

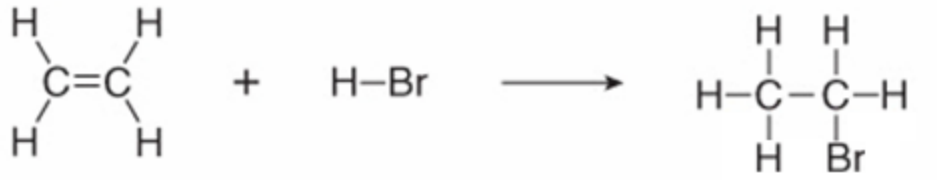


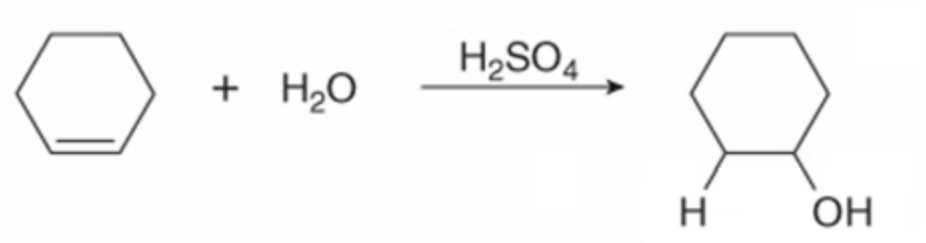


Additions

- In an addition reaction a π bond is broken and two new σ bond are formed.



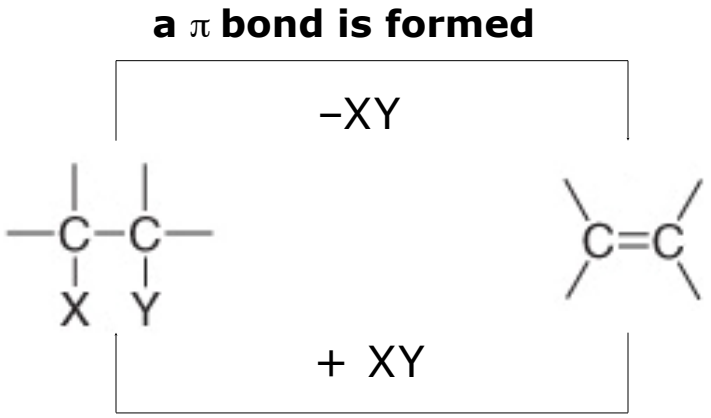




Additions and Eliminations

- Eliminations are the inverse of additions. A π bond is formed in eliminations and a π bond is broken in additions.

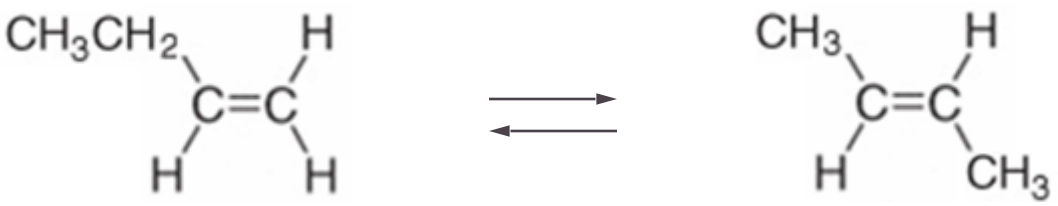
Elimination



Addition

Rearrangements or Transpositions

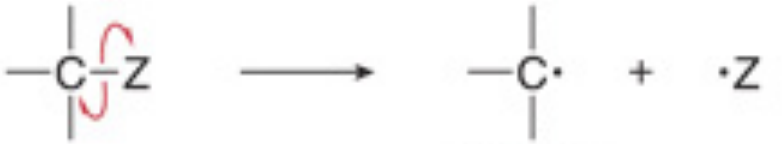
- In a rearrangement or transposition the bonding pattern of a single reagent changes giving a constitutional isomer.



1-butene 2-butene

Bond Breaking

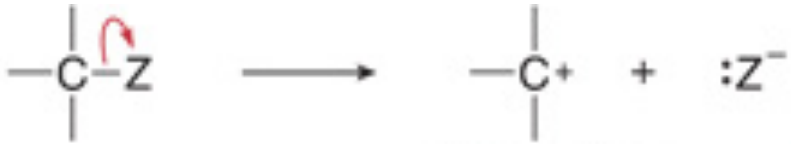
Omolysis



Radical

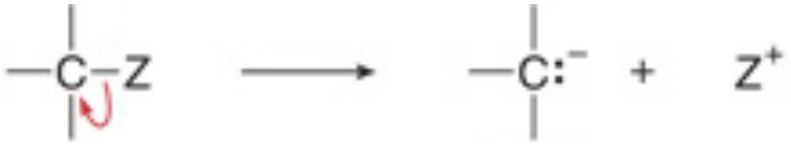
radicals are formed in *radical (omolitic) reactions*

Heterolysis



Carbocation

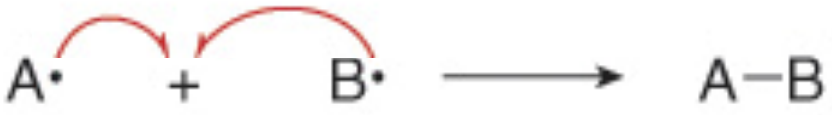
ions are formed or react in *polar (ionic) reactions*



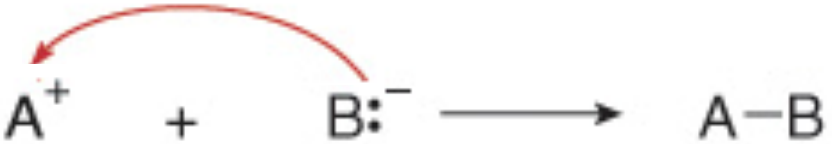
Carbanion

Bond Formation

- A new bond can be formed in two ways:
  - From two radicals each contributing a single electron.



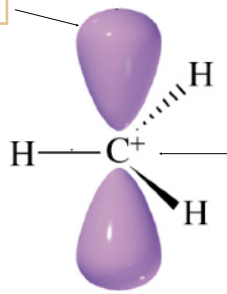
  - From a nucleophile contributing an electron pair and an electrophile accepting the electron pair. Nu and E may be ions or neutral molecules



Energy is released in the formation of a bond

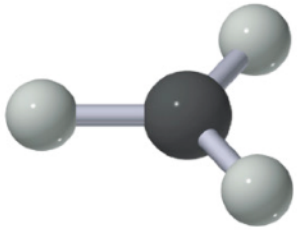
Carbocations, Carbanions, Radicals

empty *p* orbital

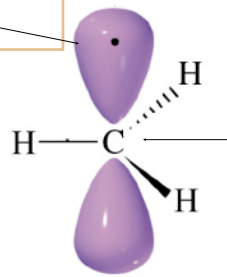


C *sp*² planar

$^{+}CH_3$

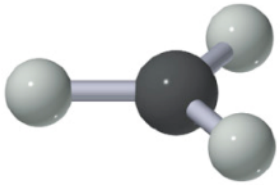


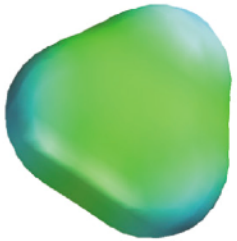
Singly occupied *p* orbital



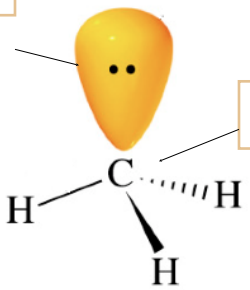
C *sp*² planar

$\cdot CH_3$



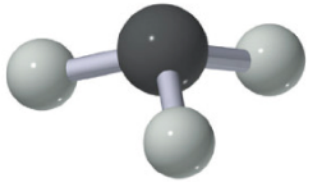


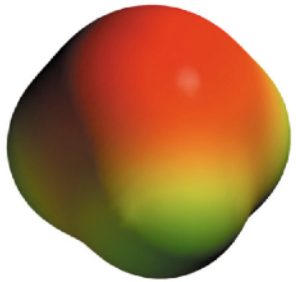
lone pair *sp*³



C *sp*³ tetrahedral

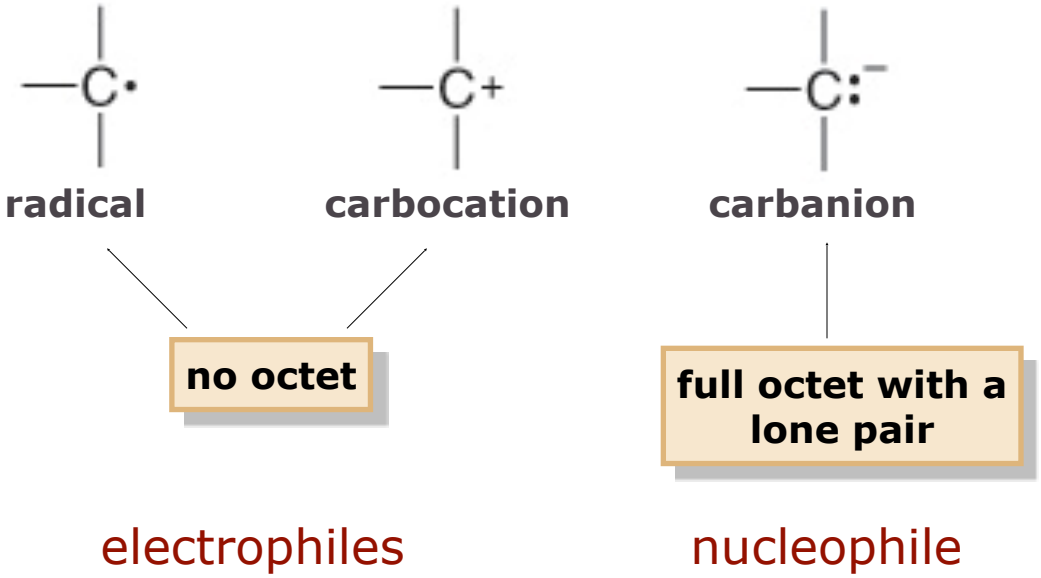
$\bar{:}CH_3$





Carbocations, Carbanions, Radicals

- Radicals and carbocations are electrophiles because the carbon atom does not have a full octet.
- Carbanions are nucleophiles because the carbon atom has a lone pair.

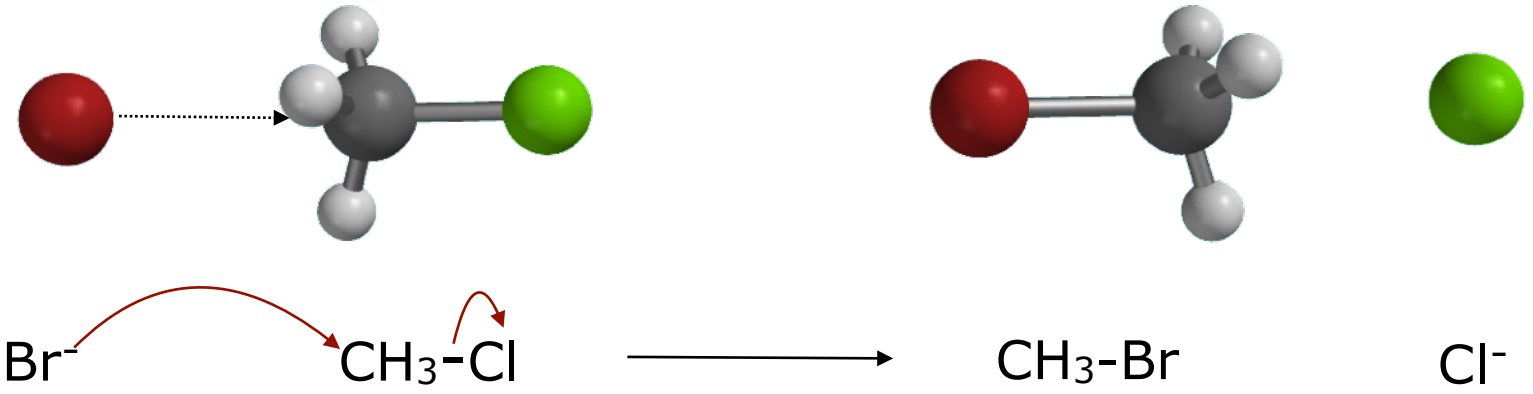


A Reaction Mechanism……

- Accounts for all reagents and products and their ratios.
- Describes in which order bonds are broken and formed and the rates of individual steps.
- In a *concerted reaction* reagents are directly converted into products in a single step.

- A multistep reaction involves the formation of one or more reactive intermediates.

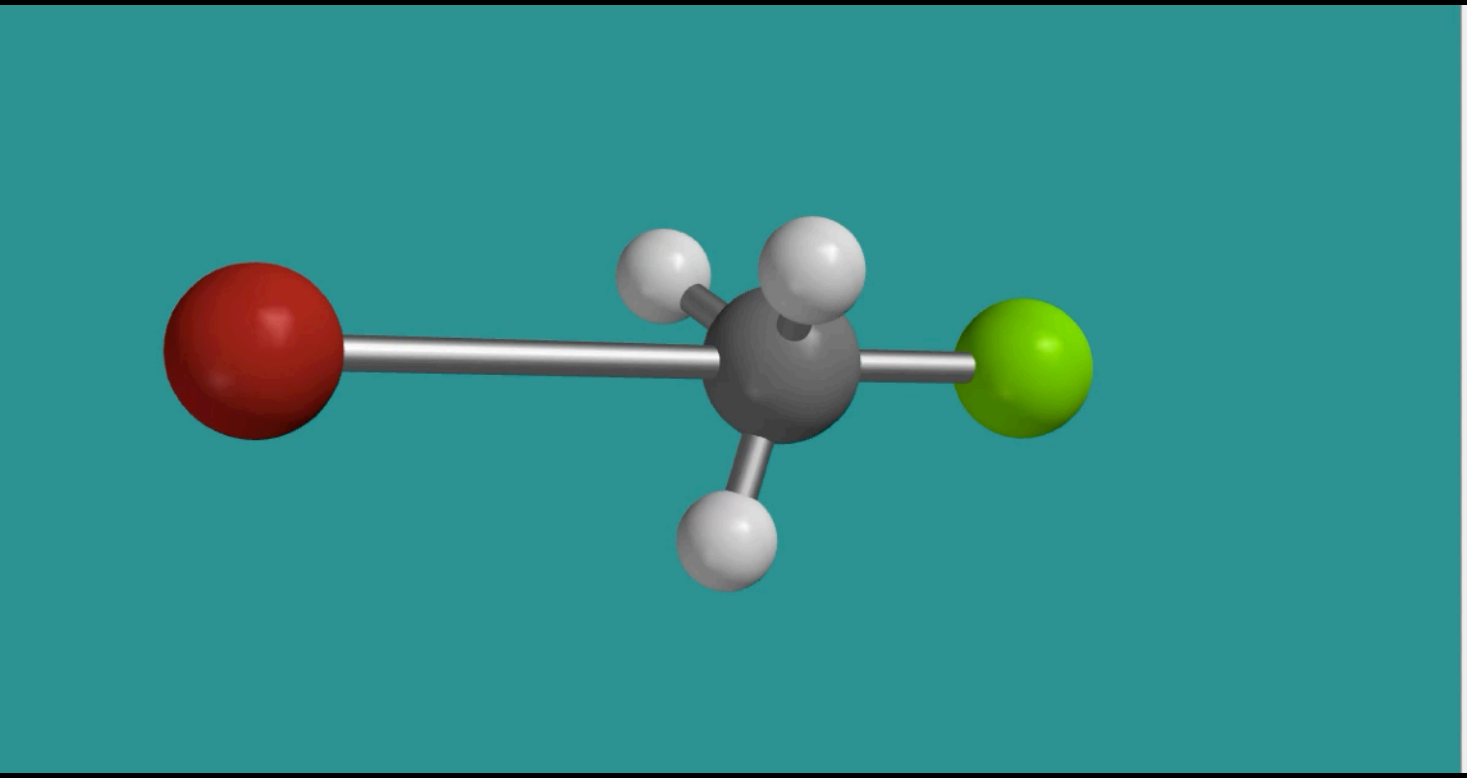
Transition State Theory and Collisional Theory

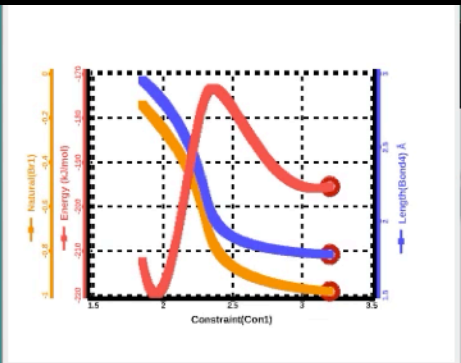


- Collisional theory: rigid collision between reacting species.

- Transition state theory: continuous deformation of reagent structure into product structure

Transition State Theory





Transition State Theory - Energy Diagrams

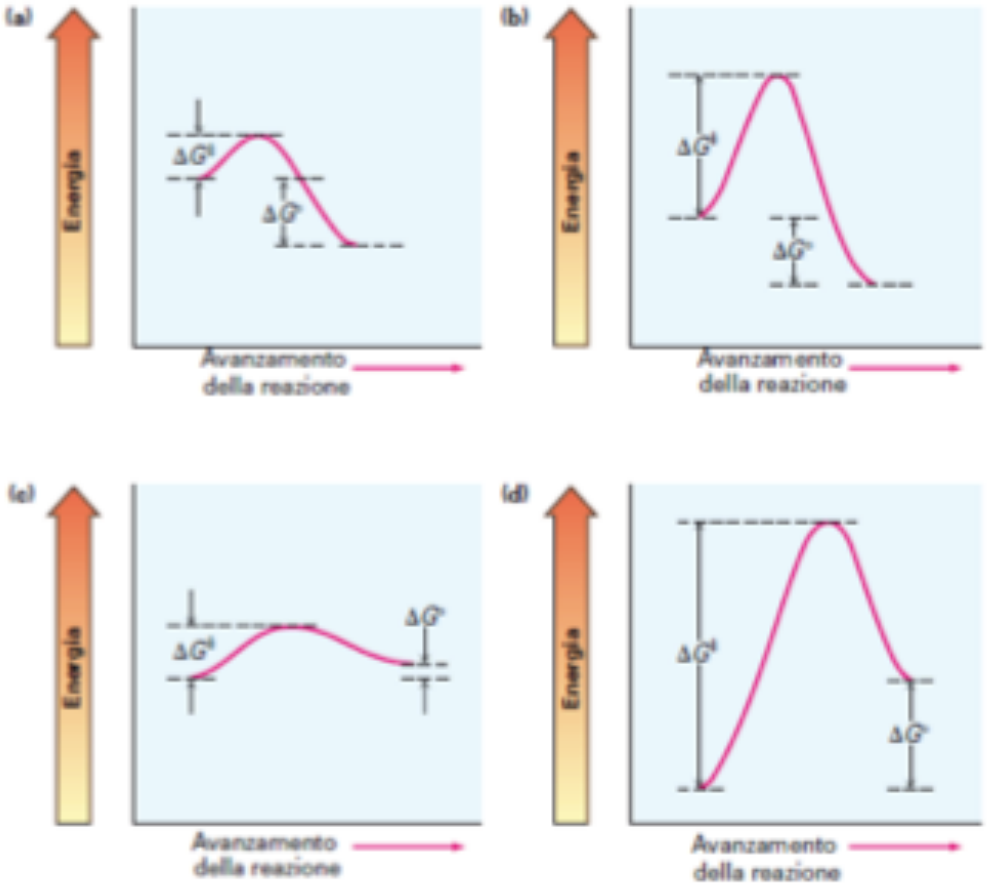
- The activation energy $\Delta G^{\neq}$ is the energy required for a reaction to take place.
- $\Delta G^{\neq} = \Delta H^{\neq} - T\Delta S^{\#}$
- $\Delta G^{\neq}$ is correlated with the reaction's rate constant.

Eyring equation:

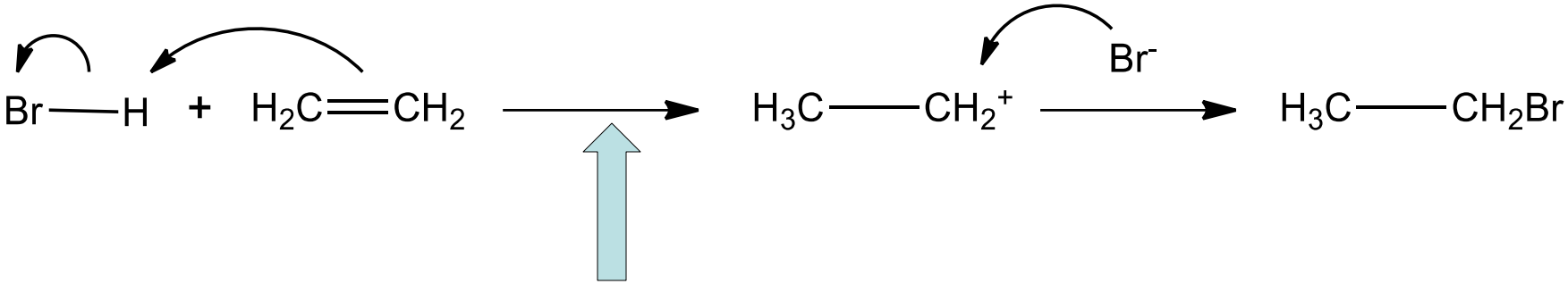
$$k = \frac{k_B T}{h} e^{-\frac{\Delta G^{\#}}{RT}}$$

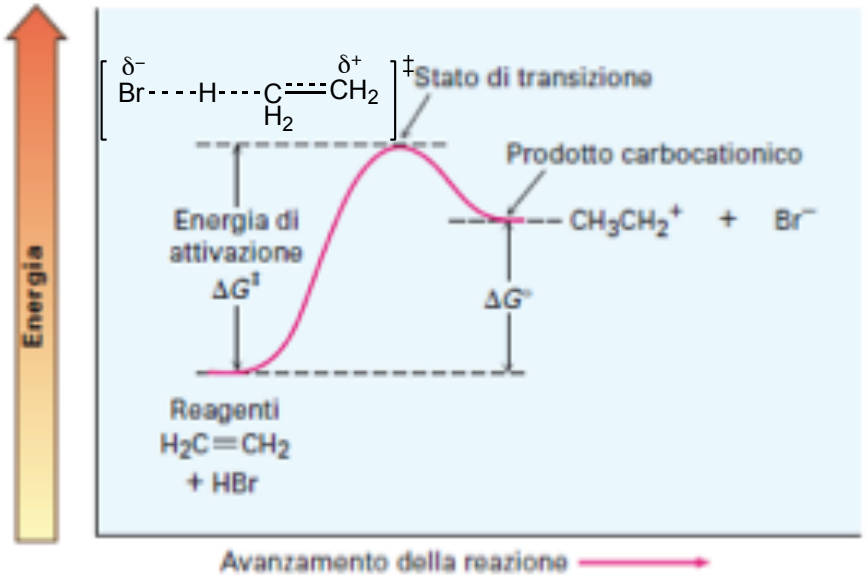
- The transition state structure is intermediate between the structures of reagents and products. In the transition state there are partial bonds and partial charges (if the mechanism is ionic).
- Transition states are represented in brackets with the $^{\#}$ symbol.

Energy Diagrams



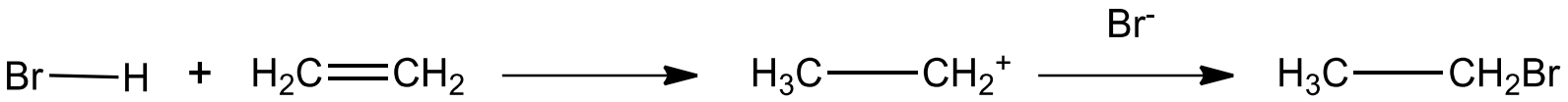
Energy Diagrams

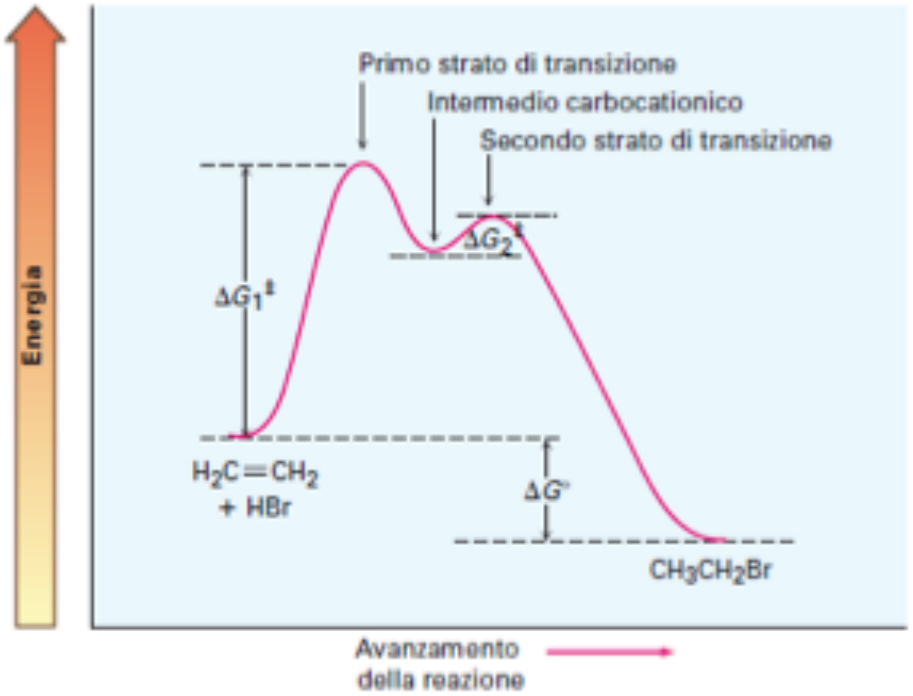




Energy Diagrams

Complete energy diagram for the two-step reaction:





Functional Groups

Chapter 3.1
Organic Chemistry, *8th Edition*
J. McMurry

Functional Groups

Organic Residue (Radical)

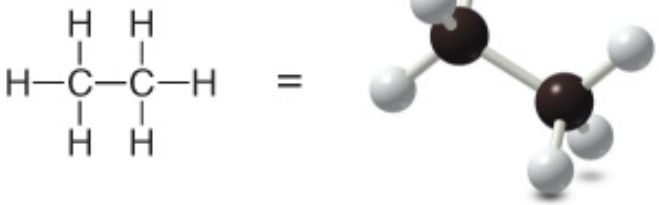
(from a hydrocarbon)

Functional Group

(heteroatom or group of atoms containing one ore or more heteroatoms)

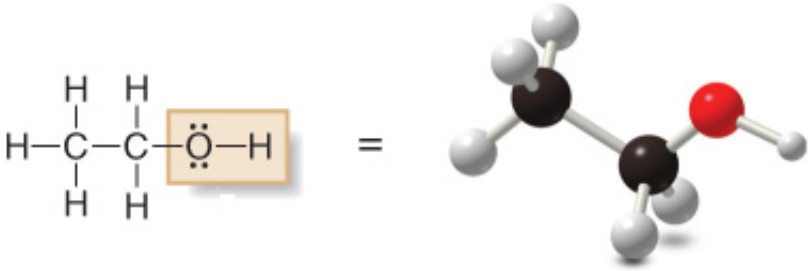
A functional group is an atom or a group of atoms all or in part # than C with specific and well defined physico-chemical properties.

Functional Groups



- Only C—C and C—H bonds
- No functional groups

- Does not posses polar bond or π bonds: very unreactive.
- Gas at NTP
- Insoluble in water



- OH functional groups

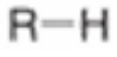
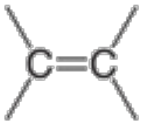
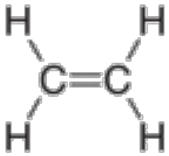
- Polar C-O and O-H bonds
- Lone pair on O
- Reacts with electrophiles
- Reacts with strong bases
- Liquid at NTP
- Soluble in water

Functional Groups

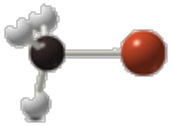
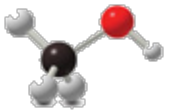
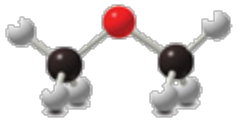
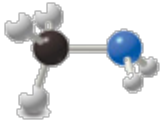
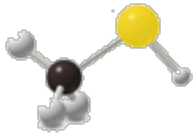
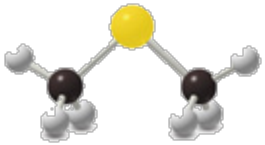
1. Define a class of compounds
   - Compounds belonging to the same class have similar properties and reactivity.
2. Are frequently the reaction site
   - Define the reactivity of a molecule
3. Determine the name
   - For example all ketones have the suffix –one:
     - acetone
     - cyclopropanone
     - cortisone

Hydrocarbons

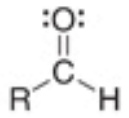
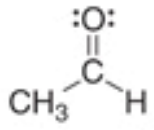
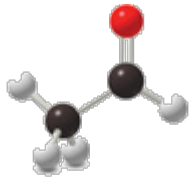
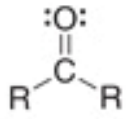
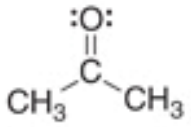
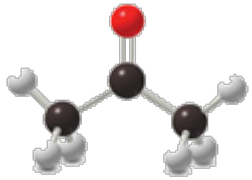
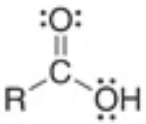
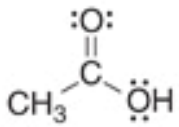
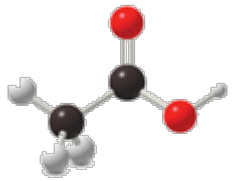
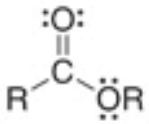
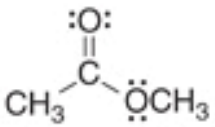
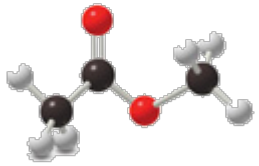
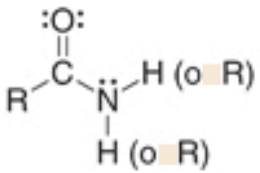
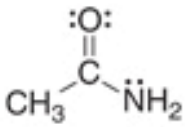
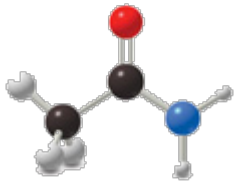
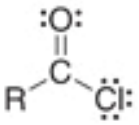
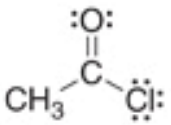
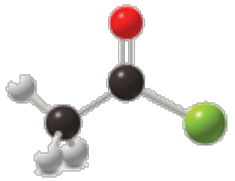
- Hydrocarbons possess only C–C e C–H bonds.
  - aliphatic (alkanes, alkenes, alkynes) and aromatic.

Hydrocarbon	General	Example	Functional
Alkanes			-----
Alkenes			Double bond
Alkynes			Triple bond
Aromatics			Aromatic ring

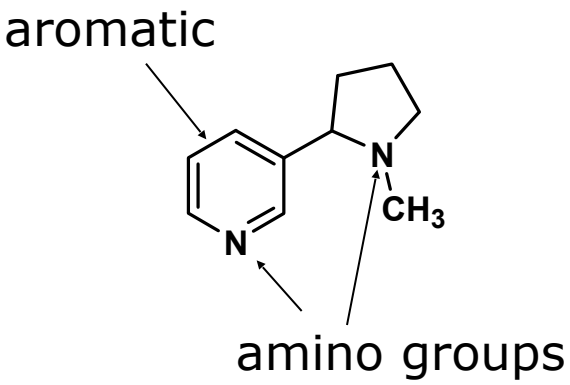
Functional Groups Containing C–Y σ bonds

Class Name	Structure	Example	3D Structure	Functional Group
Alkyl Halide	R–X: (X=F, Cl, Br, I)	CH_3–Br:		–X halo
Alcohol	R–OH	CH_3–OH		–OH hydroxy
Ether	R–O–R	CH_3–O–CH_3		–OR alcoxy
Amine	R–NH_2 o R_2NH or R_3N	CH_3–NH_2		–NH_2 amino
Thiol	R–SH	CH_3–SH		–SH mercapto
Sulfide	R–S–R	CH_3–S–CH_3		–SR alkylthio

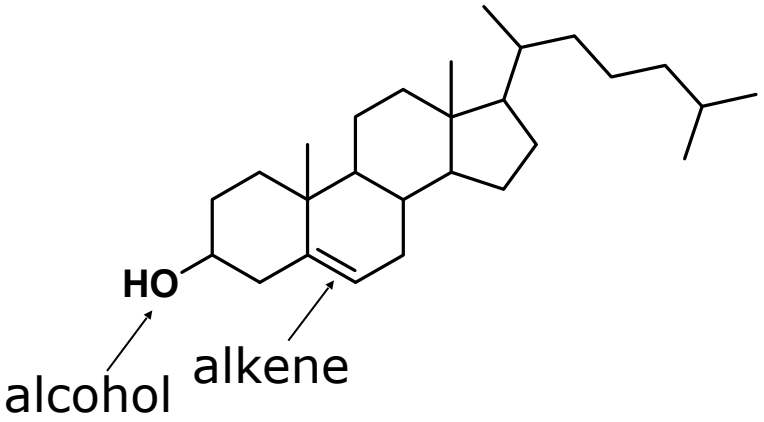
Functional Groups Containing The C=O Bond

Class Name	Structure	Example	3D Structure	Functional Group
Aldehyde				H–C=O formyl
Ketone				C=O carbonyl
Carboxylic Acid				–COOH carboxylate
Ester				–COOR
Amide				$-CONH_2$ –CONHR $-CONR_2$
Acid Chloride				–COCl

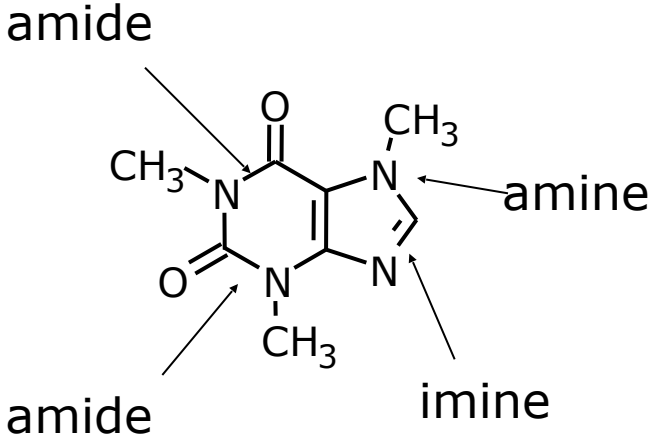
Polyfunctional Molecules



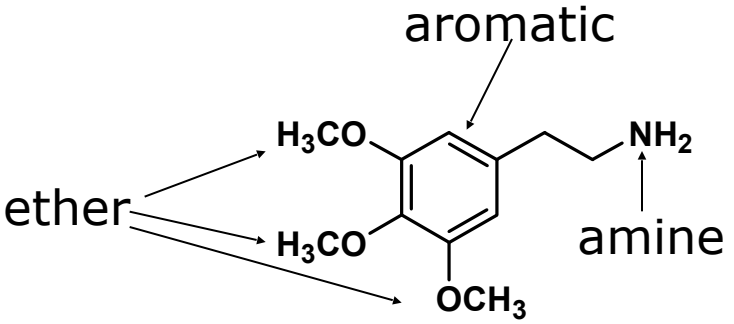
nicotine



cholesterol



caffein



mescalin