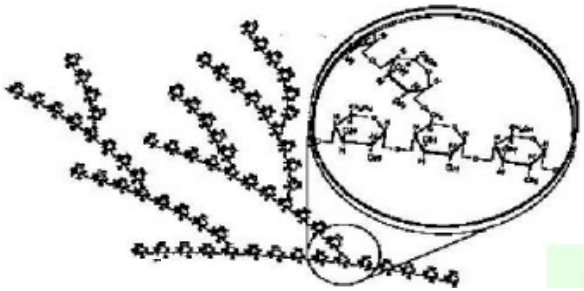
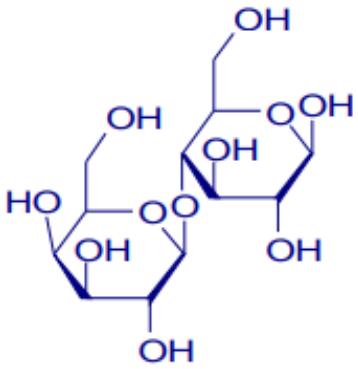
Introduction to Natural Product

- A chemical substance produced by a living organism;
- It is used commonly in reference to chemical substances found in nature that have distinctive pharmacological effects.
- Main Classes of Natural Products: -
  - ✓ Carbohydrates ;
  - ✓ Lipids ;
  - ✓ Proteins ;
  - ✓ Nucleic Acid.
- Carbohydrates-A broad category of chemical compounds, also referred as Sugars.
- ✓ The most abundant class of bio-organic molecules on

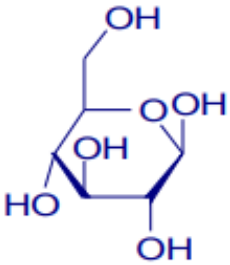
Carbohydrates…??

- ✓ Although relatively low in human, it constitute about 75% by mass of dry plant materials.
- ➢ Main functions: Energy storage, structure element , source of carbon of the biosynthesis of other substances, “Markers” on cell surface for cell-cell recognition. Se structures

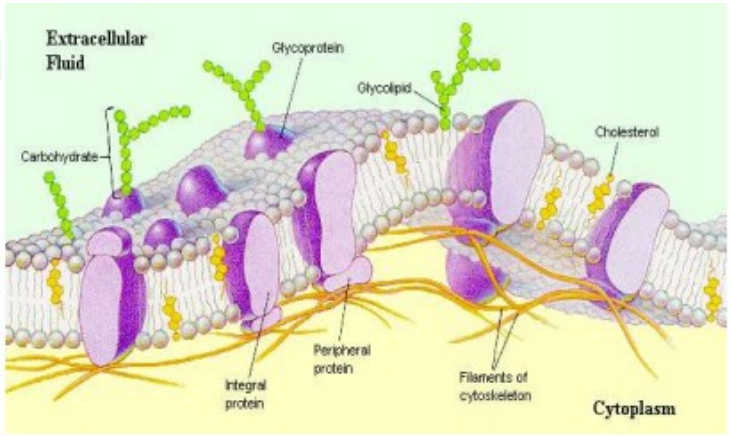




Lactose

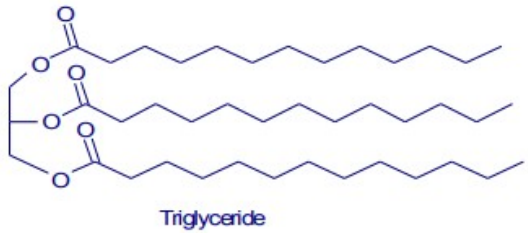


Glucose



Lipids

- A broad category of chemical compounds, also referred as Fat.
- Most of those products are non polar fat, oil, or wax that does not (or poorly) dissolves in water.
- Main functions: Main component of cells membrane, energ cells (horm

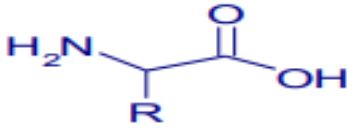


Proteins

- A broad category of chemical compounds composed of amino acids. It includes Aminoacids, polypetides, Enzymes.
- Main functions:

✓ Very large variety of functions, from maintenance or repairing of existing tissues and

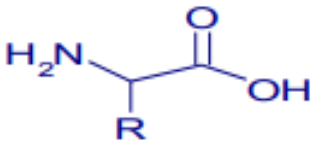
✓ synthesis of new ones to the catalysis of all the bio-chemical reactions that take place in a living organism (Enzymes).Functiona



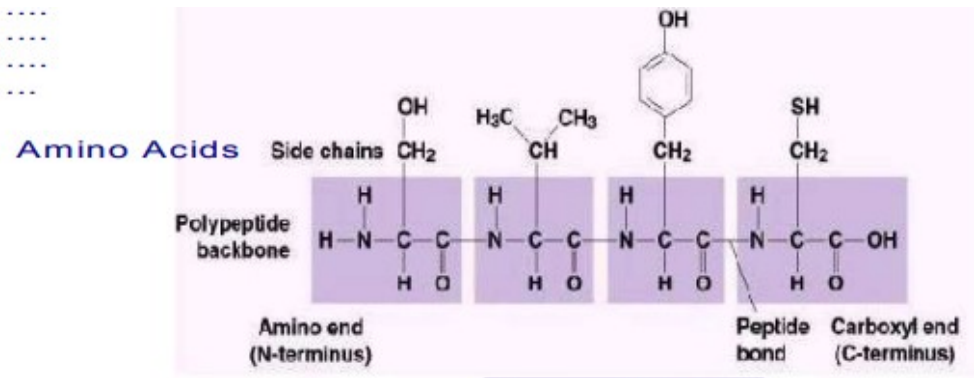
cids;

R = CH_2SH : Cys
R = CH_3 : Ala
R = CH_2COOH : Asp
R = $(CH_2)_4NH_2$: Lys

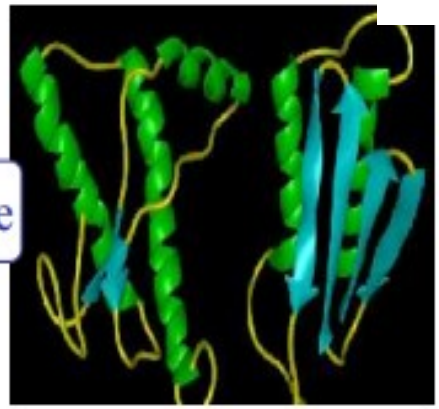
From Aminoacids...;



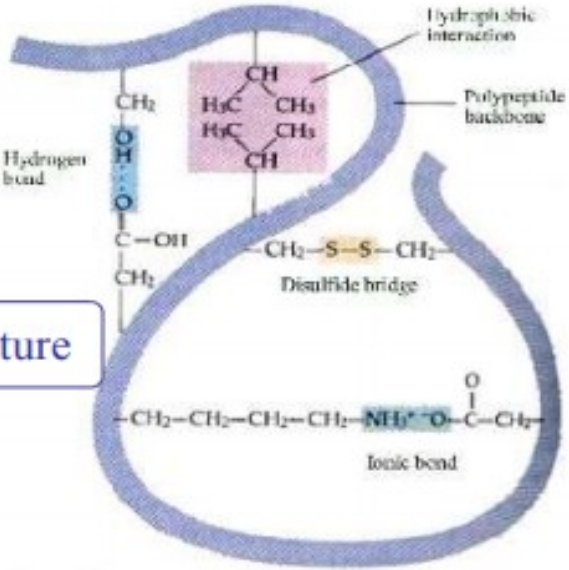
R = CH_2SH : Cys
R = CH_3 : Ala
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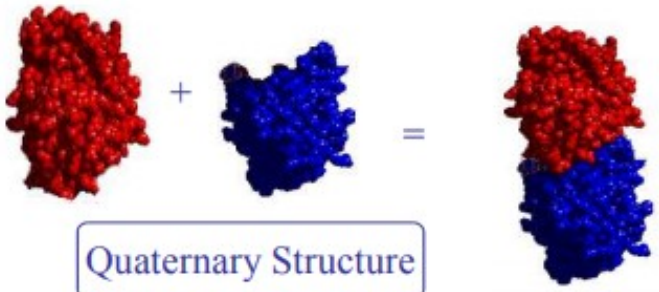
Primary Structure



Secondary Structure



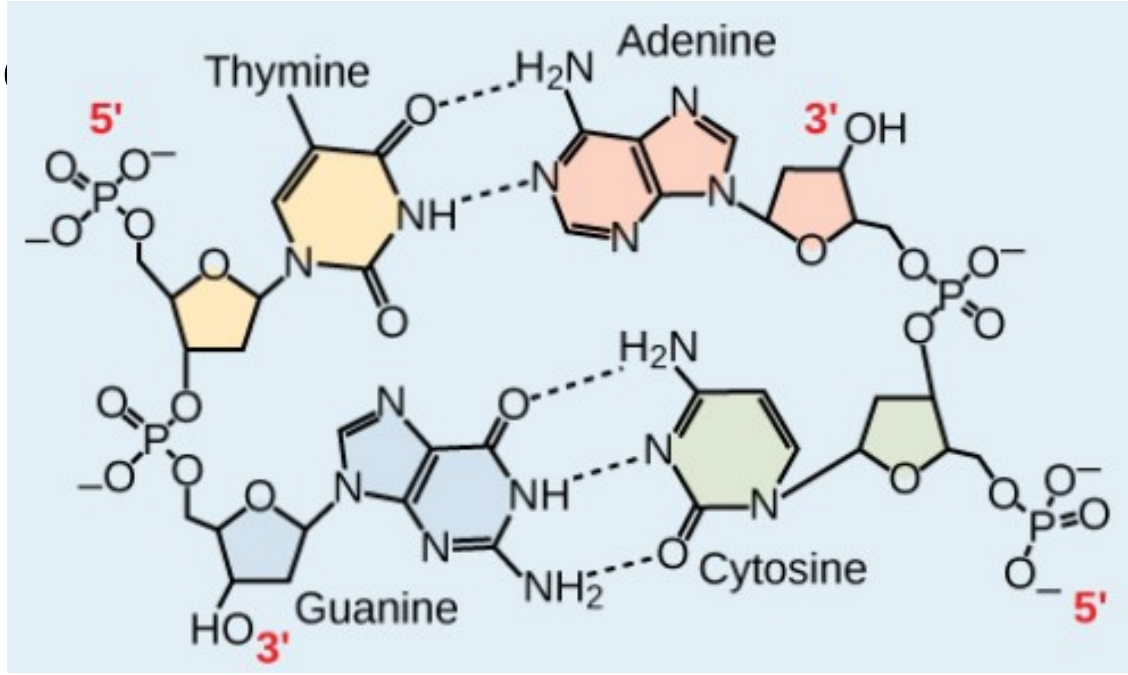
Tertiary Structure



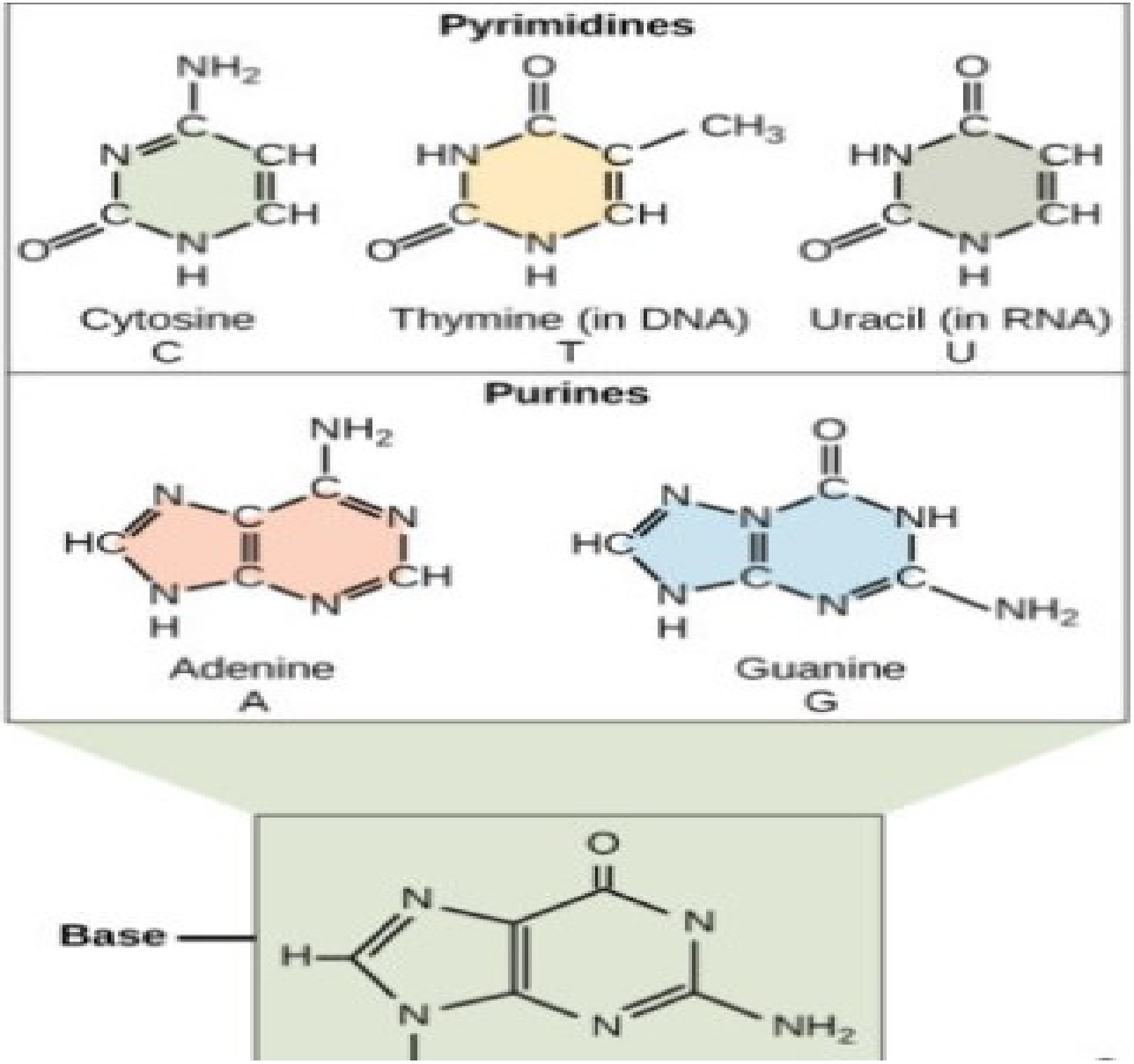
Quaternary Structure

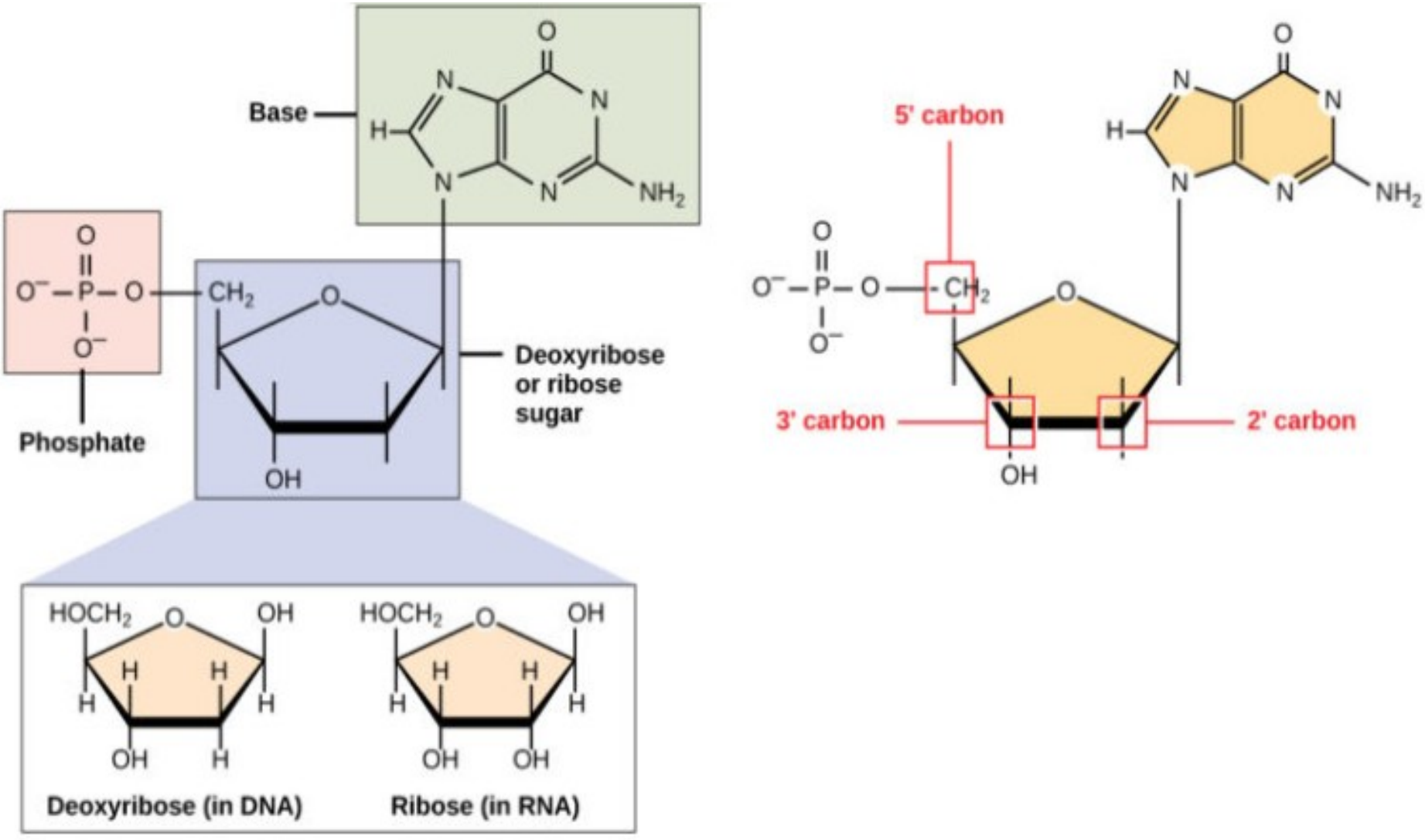
Nucleic Acids

- A category of complex chemical compounds involved in the transmition of genetic information (DNA) and its transfer as information to the cell (RNA).
- Main functions: Genetic information, some simple nucleotides acts as source of energy for chemical reacti



Structural determination!




Base
Phosphate
Deoxyribose or ribose sugar
5' carbon
3' carbon
2' carbon
Deoxyribose (in DNA)
Ribose (in RNA)

Further Illustration;

- The nitrogenous bases, important components of nucleotides, are organic molecules and are so named because they contain carbon and nitrogen. They are bases because they contain an amino group that has the potential of binding an extra hydrogen, and thus, decreases the hydrogen ion concentration in its environment, making it more basic. Each nucleotide in DNA contains one of four possible nitrogenous bases: adenine (A), guanine (G) cytosine (C), and thymine (T). RNA nucleotides also contain one of four possible

Cont'd...

- Adenine and guanine are classified as **purines**. The primary structure of a purine is two carbon-nitrogen rings.
- Cytosine, thymine, and uracil are classified as **pyrimidines** which have a single carbon-nitrogen ring as their primary structure (above figure).
- Each of these basic carbon-nitrogen rings has different functional groups attached to it.
- In molecular biology shorthand, the nitrogenous bases are simply known by their symbols A, T, G, C, and U. DNA contains A, T, G, and C whereas RNA contains A, U,

Cont'd...

- The pentose sugar in DNA is deoxyribose, and in RNA, the sugar is ribose (above figure).
- The difference between the sugars is the presence of the hydroxyl group on the second carbon of the ribose and hydrogen on the second carbon of the deoxyribose.
- The carbon atoms of the sugar molecule are numbered as 1′, 2′, 3′, 4′, and 5′ (1′ is read as "one prime").
- The phosphate residue is attached to the hydroxyl group of the 5′ carbon of one sugar and the hydroxyl group of the 3′ carbon of the sugar of the next nucleotide, which forms a 5′–3′ **phosphodiester** linkage.

Cont'd...

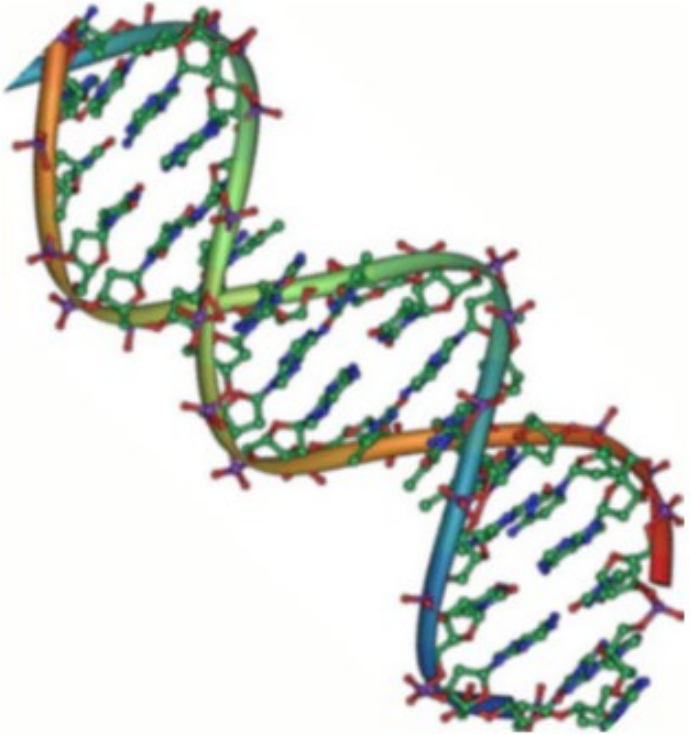
- The phosphodiester linkage is not formed by simple dehydration reaction like the other linkages connecting monomers in macromolecules: its formation involves the removal of two phosphate groups.
- A polynucleotide may have thousands of such phosphodiester linkages.

✓ **DNA Double-Helix Structure**

- DNA has a double-helix structure (Figure 2). The sugar and phosphate lie on the outside of the helix, forming the backbone of the DNA.

Cont'd...

- The nitrogenous bases are stacked in the interior, like the steps of a staircase, in pairs; the pairs are bound to each other by hydrogen bonds. Every base pair in the double helix is separated from the next base pair by



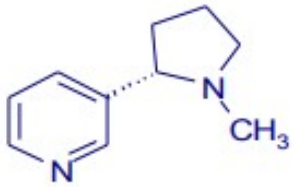
  - ✓ DNA is an antiparallel double helix. The phosphate backbone (the curvy lines) is on the outside, and the bases are on the inside. Each base interacts with a base from the opposing

Metabolism

- is the sum of all the chemical reactions that take place in a living organism.
- ✓ Primary Metabolism: All the chemical reactions necessary for the live of the organism by itself. All the chemical products involved in the Primary Metabolism.
- ✓ Secondary Metabolites: All the chemical products that are produced by the living organism but are NOT involved in the primary metabolism.
- ✓ Not necessary for the live of the organism by itself but usefull for interaction with others (chemical communication, chemical defences).

For instance, Tobacco Plant



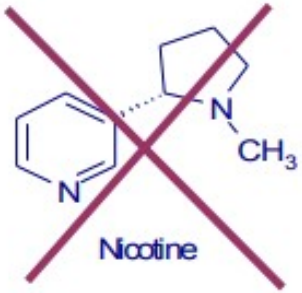


Nicotine







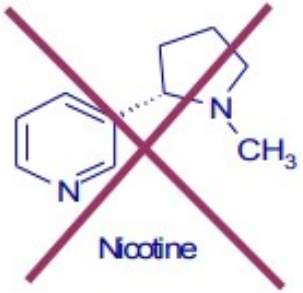


Nicotine









Nicotine



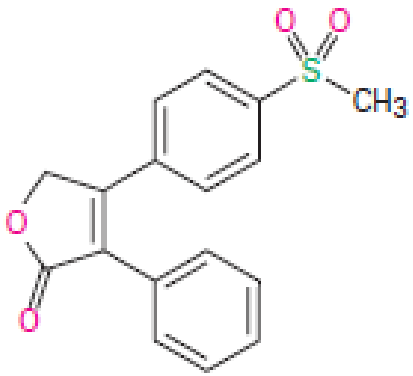


- **Points for discussion: *Over view!!***
  - ✓ ***What is organic chemistry?***
  - ✓ ***Why we study it?***
  - ✓ ***Where its source? How we get it?***

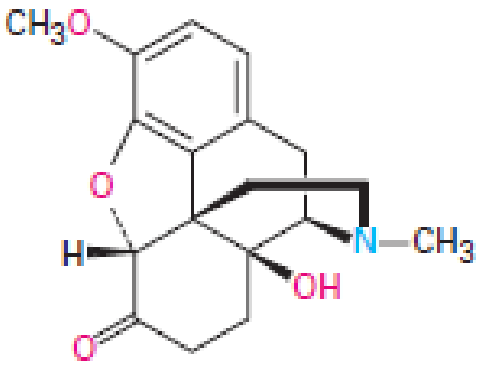
- Every living organisms were/are made up of *organic chemicals*; *How and Why*? *For instance*;
  - ✓ the *proteins* w/c make up our *hair, skin, muscles, etc*;
  - ✓ the *DNA* w/c controls our *genetic heritage*;
  - ✓ the *foods* w/c *nourish* us! and
  - ✓ the *medicines* w/c we *heal*!!!

Introduction,...

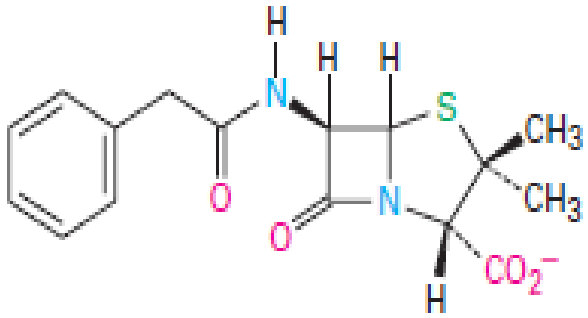
- So; anyone with a curiosity about *life and living things*,
- anyone who wants to be a parts of many exciting developments,
- now happening in *medicines and biological sciences*, must understanding first about organic chemistry!!
- *Look the following drawing structures those might be a familiar with their NOMENCLATURE!!*



Rofecoxib
(Vioxx)

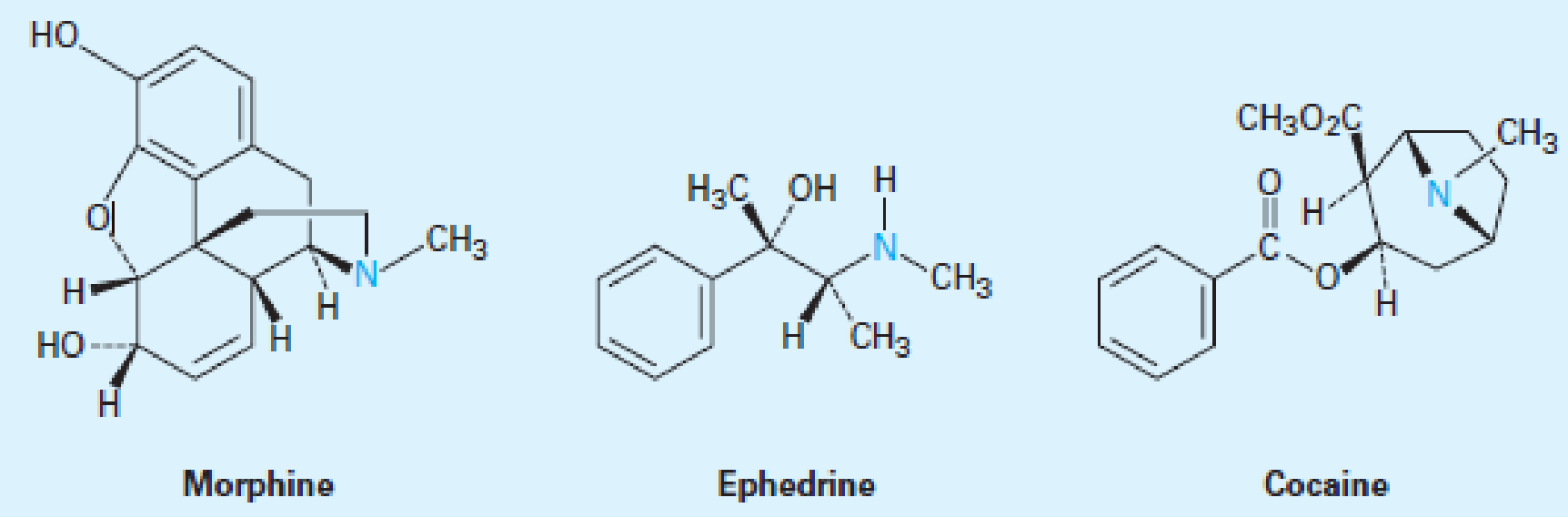


Oxycodone
(OxyContin)



Benzylpenicillin

Some alkaloids have biological properties!



✓Morphine, an analgesic agent, is obtained from the *opium poppy* *Papaver somniferum*.

✓*Ephedrine, a bronchodilator, decongestant, and appetite suppressant,* is obtained from the *Chinese plant Ephed*

Cocaine...,

- Cocaine, both an anesthetic and a stimulant, is obtained from the coca bush *Erythroxylon coca*, *endemic to the upland* rain forest areas of central South America.
- a small amount of cocaine in the original Coca-Cola recipe, although it was removed.
- Cocaine itself is no longer used as a medicine because it is too addictive, but its anesthetic



History of Organic Chemistry

- The foundations of organic chemistry:
  - ✓ date from the mid-1700s,
  - ✓ when chemistry was developing from an *alchemist's art* into a modern science.
- Little was known about chemistry and the behavior of the "organic" substances w/c isolated from plants and animals seemed different from "inorganic" substances
- physico-chemical aspect of Organic compounds were :
  - ✓ low-melting solids;
  - ✓ usually more difficult to isolate, purify,
  - ✓ work with high-melting inorganic compounds.

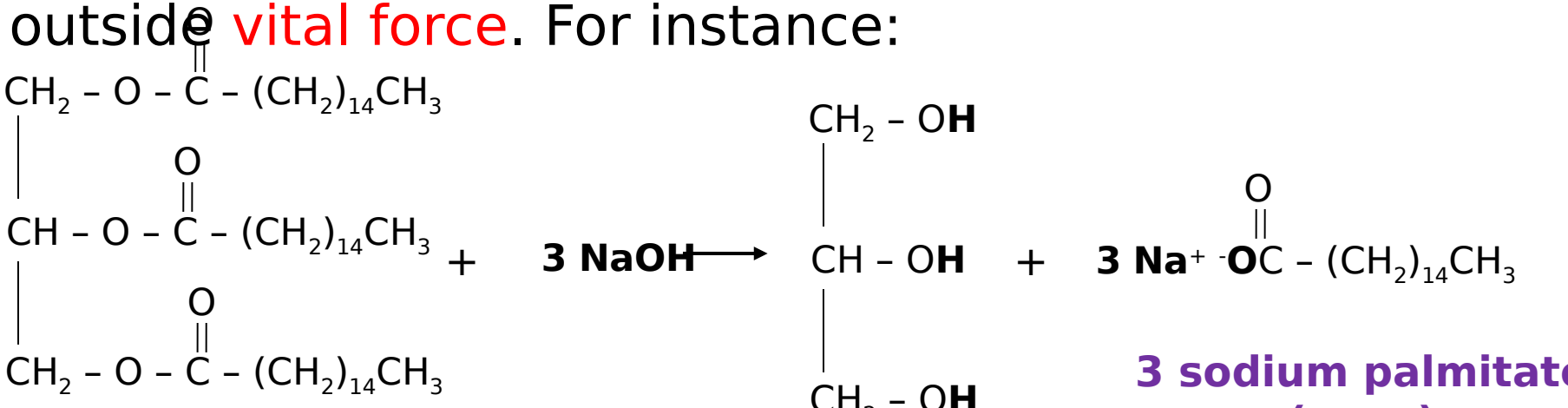
Cont'd...,

- To many chemists, the simplest explanation for the difference in behavior between organic and inorganic compounds;
  - ✓ was that organic compounds contained a peculiar

- Because of this vital force, chemists believed, organic compounds could not be prepared and manipulated in the laboratory as could inorganic compounds.
- As early as 1816, however, this vitalistic theory received a heavy blow when **Michel Chevreul** found that
  - ✓ Alkali with Animal fat yields Soap;

Cont'd...,

- ✓Then, it could be separated into several pure organic compounds, *fatty acids.*
- ➢*This indicates that, one organic substance (fat) was* converted into others (fatty acids plus glycerin) without the intervention of an outside vital force. For instance:



glyceryl tripalmitate (tripalmitin)

glycerol

3 sodium palmitate (soap)

Cont'd...,

- Little more than a decade later, the vitalistic theory suffered;
- For instance:

Friedrich Wöhler (1828)



- He had discovered the conversion of the "inorganic" into possible reac

$$AgCNO(aq) + NH_4Cl(aq) \rightarrow AgCl(s) + NH_4CNO(aq)$$

$$NH_4CNO\,(aq) \xrightarrow{\text{evaporation}} H_2N-\overset{\overset{O}{\|}}{C}-H_2N\,(s)$$

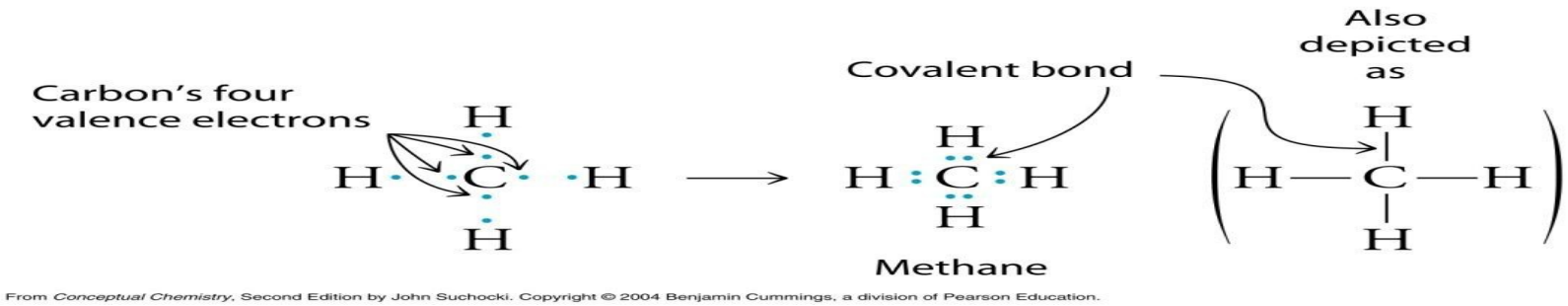
Urea

Cont'd...,

- By the mid-1800s, the weight of evidence was clearly against the vitalistic theory and
- it was clear that there was no fundamental difference between organic and inorganic compounds.
- The same fundamental principles explain the behaviors of all substances, regardless of origin or complexity.
- The only distinguishing characteristic of organic chemicals is that all contain the element carbon.
- Therefore, Organic chemistry, then, is the study of carbon compounds.
- But why is carbon SPECIAL?

why is carbon SPECIAL???

- Because: it starts from carbon's electronic structure;
  - ✓ Its consequent position in the periodic table.
  - ✓ As a group IVA element, carbon can share 4v e-s
  - ✓ form four strong covalent bonds.



From *Conceptual Chemistry*, Second Edition by John Suchocki. Copyright © 2004 Benjamin Cummings, a division of Pearson Education.

  - ✓ Furthermore, carbon atoms can bond to one another, forming long chains and rings.

- Carbon, alone of all elements, is able to form an immense diversity of compounds.

- from the simple CH_4, with one carbon atom, to the staggeringly complex DNA, which can have more than *100 million carbons*.
- Not all carbon compounds are derived from living organisms.
- Modern chemists have developed a remarkably sophisticated ability to design and synthesize new organic compounds in the laboratory. Eg. medicines, dyes, polymers, and other host of substances.
- Hence, the study of organic chemistry, although complex, is very interesting, and begins here with an introduction of the theory of chemical bonding.

The Chemical Bond, then what?

➢Atomic Theory

✓The atomic theory of electrons began in the early 1900s and gained acceptance around 1926;

✓After *Heisenberg and Schroedinger* found mathematical solutions to the electronic energy levels found in atoms;

✓the field is now called quantum mechanics.

➢Electrons exist in energy levels(i.e., shell) that surround the nucleus of the atom and within shells there is, sub-shells or orbitals., w/c contains a no. of electrons.

➢The energy of these levels increases as they get farther from the nucleus.

For Instance!

	Orbitals				
Shell	s	p	d	f	Total Electrons Possible
1	1				2
2	2	3			8
3	3	3	5		18
4	1	3	5	7	32

- According to *Aufbau Principle*; Electrons fill the lower energy levels first until all of the electrons are used.
- An element contains the number of electrons equal to its atomic number.
- Eg. for the first and second row elements the electron configurations are relatively simple.

Illustration I

Element (atomic number)	Electron Configuration
H (1)	$1s^1$ (1st shell, s orbital, one electron)
He (2)	$1s^2$
Li (3)	$1s^2, 2s^1$

Home work??

1)What about orbitals?

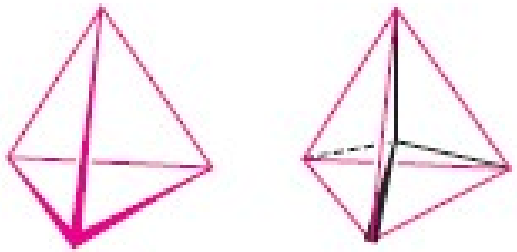
2)What about the electrons?

3)How are they distributed in an atom?

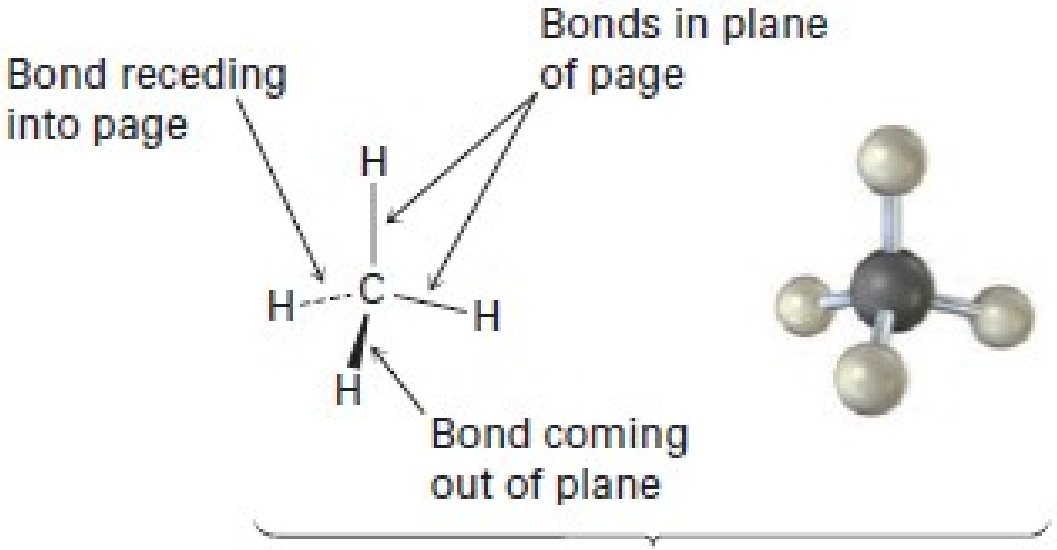
- By the mid-1800s, the new science of chemistry was developing rapidly;
- chemists had begun to investigate the forces holding molecules together.
- In 1858, August Kekulé and Archibald Couper independently proposed that, in all organic compounds, carbon is *tetravalent;*
- Which always forms four bonds when it joins other elements to form chemical compounds.
- A representation of tetrahedral carbon atom and the solid lines represent bonds in the plane of the paper,

Cont'd...,

- the heavy wedged line represents a bond coming out of the plane of the page, and
- the dashed line represents a bond going back behind the plane of the page.



A regular tetrahedron

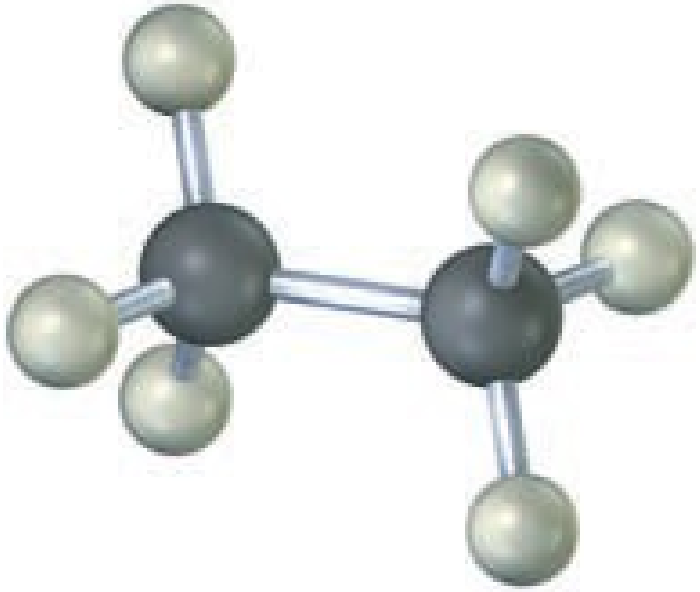


A tetrahedral carbon atom

Problem

1)Draw a molecule of chloromethane, CH_3Cl, using solid, wedged, and dashed lines to show its tetrahedral geometry.

2)Convert the following molecular model of ethane, C_2H_6, into a structure that uses wedged, normal and dashed lines to represent three-dimensionality.



The Nature of Chemical Bonds

Brain Storm!

✓Why do atoms bond together?

✓ How can bonds be described electronically?

Reflection 1

✓atoms bond together because the compound that results is more stable and lower in energy than the separate atoms.

✓Energy (as heat) is always released and flows *out of the* chemical system when a bond forms.

✓Conversely, energy must be put into the system to break a bond.

✓Making bonds always releases energy, and breaking

Reflection 2

electronic properties of atoms.

- ✓eight electrons an electron *octet in* an atom's outermost shell, or valence shell,
- ✓impart special stability to the noble-gas elements in group VIIIA of the periodic table: Ne (2, 8); *Ar (2, 8, 8); Kr (2, 8, 18, 8).*
- ✓Hence, the alkali metals, w/c achieves a noble gas configuration by losing the single s electron from their valence shell to form a cation;
- ✓while the halogens also achieves a noble gas configuration by gaining a p *electron to fill their* valence shell and form an anion.

Electronic nature…,

✓For instance; the resultant ions are held together in compounds like Na^+ Cl^- by an electrostatic attraction, i.e., an *ionic bond*

Home work !

➢How, do elements makes chemical bonding near the middle and right hand side of the periodic table form bonds?

➢**What was/is the fundamental concept of electron-dot structures in the sense of covalent bond?**

Bonding in carbon compounds

➢Valence Bond Theory

✓How does electron sharing lead to bonding between atoms?

➢According to valence bond theory, a covalent bond forms when two atoms approach each other closely and,

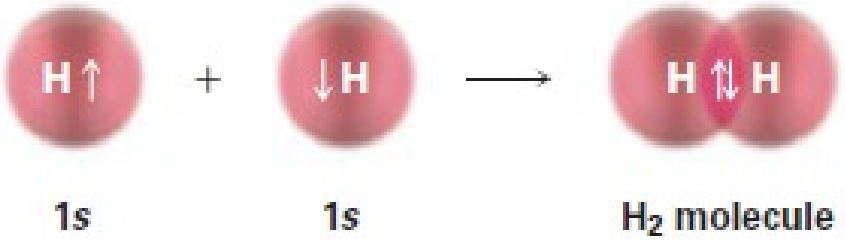
➢a singly occupied orbital on one atom *overlaps a singly occupied*

➢The electrons are now paired in the overlapping orbitals orbital on the other atom.

and are attracted to the nuclei of both atoms, thus bonding the atoms together.

Illustration 1

- In the H_2 molecule, the H-H bond results from the overlap of two singly occupied hydrogen 1*s* orbitals.



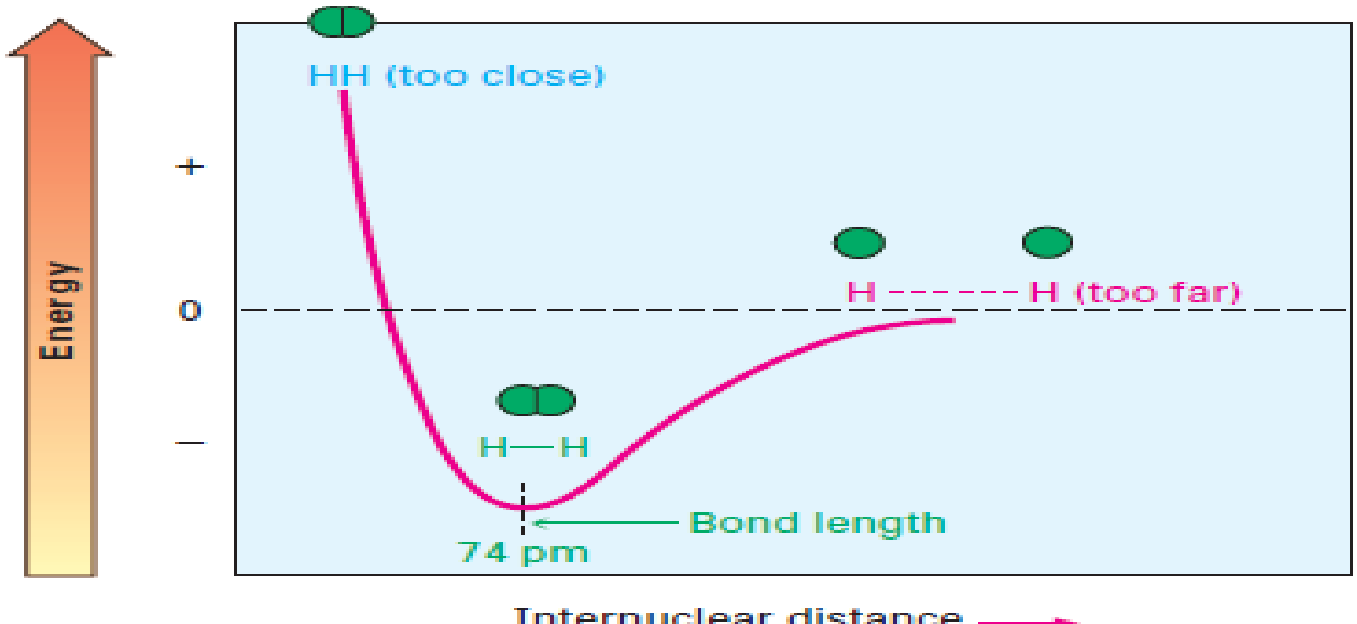
- During the bond-forming reaction $2H^{\cdot} \rightarrow H_2$, 436 kJ/mol (104 kcal/mol) of energy is released.
- Because the product H_2 molecule has 436 kJ/mol less energy than the starting $2H^{\cdot}$ atoms,
- This show that the product is *more stable* than the reactant and the new H-H bond has a bond strength of

Cont'd…,

- In other words, we would have to put 436 kJ/mol of energy *into* the H-H bond to break the H_2 molecule apart into two H atoms.
  - ✓ How close are the two nuclei in the H_2 molecule?
- If they are too close, they will repel each other because both are positively charged, yet if they are too far apart, they won't be able to share the bonding electrons
- Thus, there is an optimum distance between nuclei that leads to maximum stability in the ff. figure and called the **bond length,** with **74 pm** in the H_2 molecule.

Diagrammatically…,

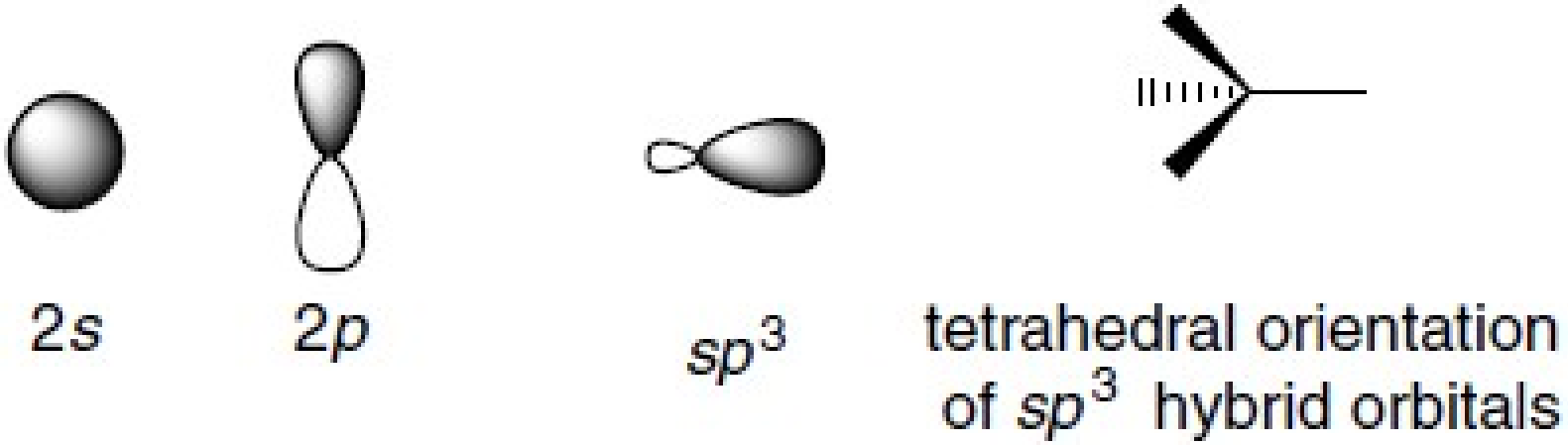
- Every covalent bond has both a characteristic bond strength and bond length.
- ✓Consider A plot of energy versus inter-nuclear distance for two hydrogen atoms.
- ✓The distance at the minimum energy point is the bond lengtl



Orbital Hybridizations

- Qualitative application of VB theory to molecules containing second-row elements such as C, N_2 and O_2 involves the concept of *hybridization and* which was developed by Linus Pauling.
- The atomic orbitals of the second-row elements include:
  - ✓ the spherically *symmetric 2s* and the three *2p orbitals*,
  - ✓ which are oriented perpendicularly to one another,
  - ✓ is equivalent to four sp^3 orbitals,
  - ✓ directed toward the corners of a tetrahedron,
  - ✓ *sp^3 hybrid orbitals*.
- For example, in CH_4, these orbitals overlap with hydrogen 1s orbitals to form sigma bonds.

Diagrammatical Illustration



- The VB description of CH_4, NH_3 and H_2O predicts tetrahedral geometry. **How?**
- The hybridization concept can be readily applied to molecules with double and triple bonds,
- Second-row elements are described as having sp2 or *sp* orbitals, resulting from hybridization of the s orbital with two or one p orbitals, respectively.

Cont'd...,

- The double and triple bonds are conceived as arising from the overlap of the unhybridized p orbitals on adjacent atoms.
- These bonds have a nodal p i bonds.
- Because the overlap is not as effective as for sp3 orbitals, these bonds are somewhat weaker than sigma bonds.



trigonal orientation of sp^2 hybrid orbitals

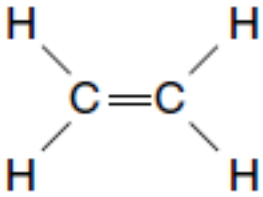


digonal orientation of *sp* hybrid orbitals

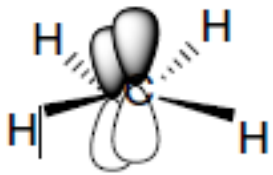
- The prototypical hydrocarbon examples of sp2 and *sp hybridization are ethene* and ethyne, respectively.

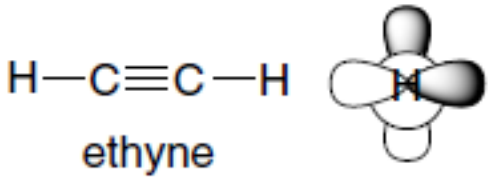
Possible Explanation,

- The total electron density between the carbon atoms in these molecules is the sum from the pi and sigma bonds.
- For ethene, the electron density is somewhat elliptical, because the component is not cylindrically symmetrical.
- For C_2H_4, the combination of the two bonds restores cylindrical symmetry. The electron density contours for ethene are depicted in Fig. below, w/c shows the highest density near the nuclei, but with net accumulation of electron den



ethene



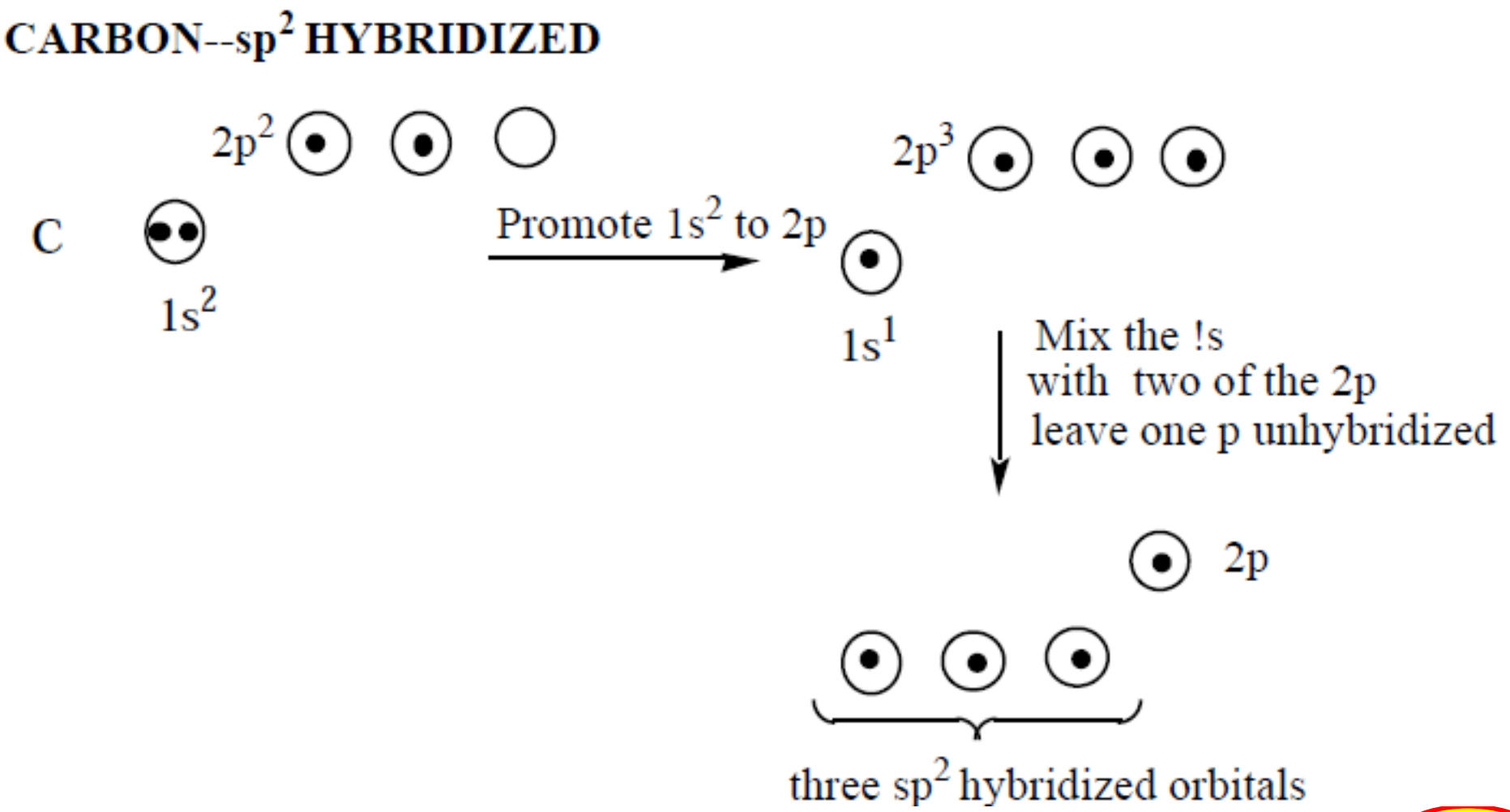


ethyne

Further Illustration

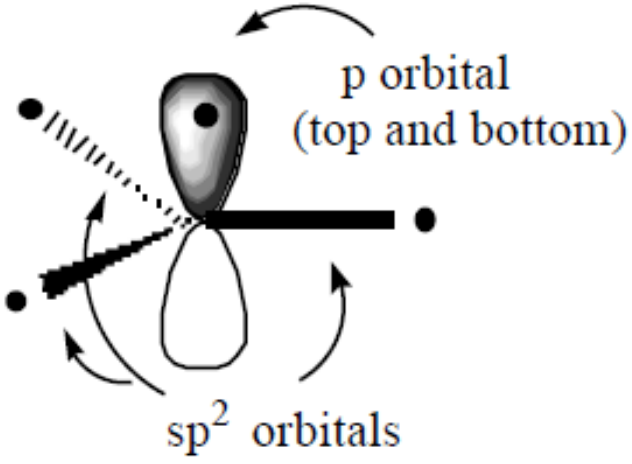
- The combination of two of the sp^2 hybridized carbon atom leads to two carbon atoms being joined by overlap of sp^2 orbitals to form a C-C single bond, and
- the side-to-side overlap of the p orbitals to form another bond known as a **pi (π)**bond.
- In the molecule of ethene shown below there are a total of 5 sigma bonds and one pi bond.
- As a result of the bonding in an ethene'
  - ✓the molecule is planar
  - ✓ bond angles of 120° and a C=C bond length that is longer than the C-H bond length.

For instance:



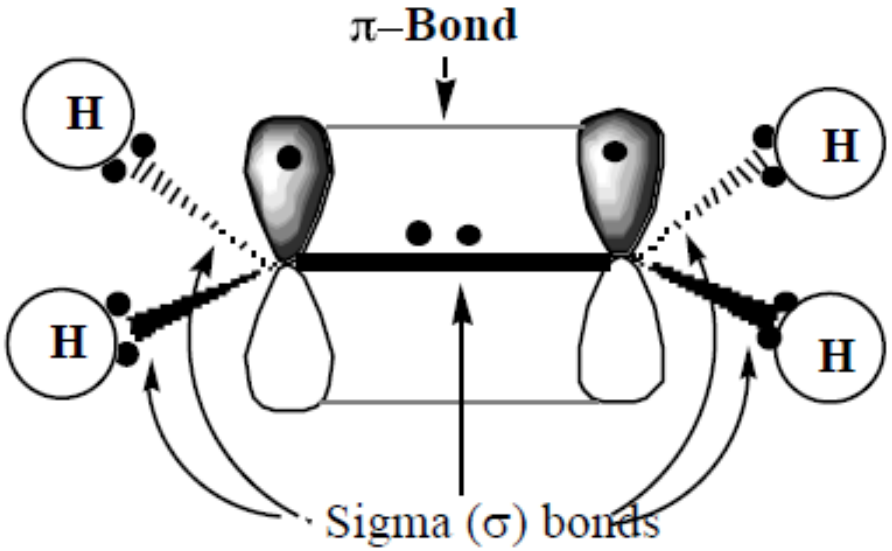
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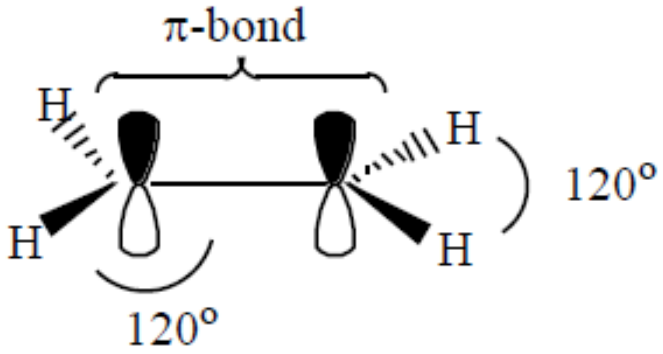
ETHENE $CH_2=CH_2$



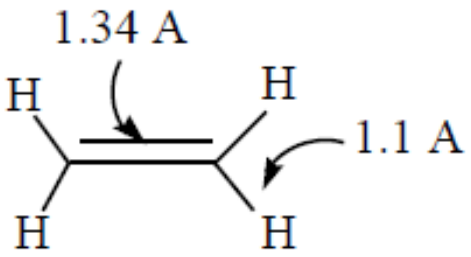
sp^2 hybridized carbon

(top and bottom forms one π-bond





sp^2 hybrid



planar

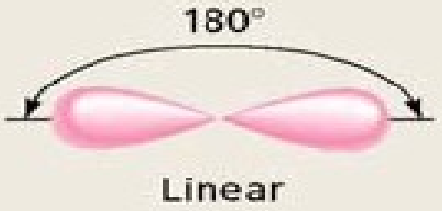
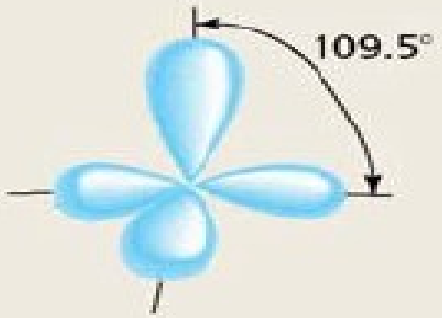
Cont'd...,

- Besides, when carbon forms a bond with an EN atom such as O_2, N_2, S or a halogen, the bond is a polar covalent bond with the electrons of the bond residing closer to the EN atom.

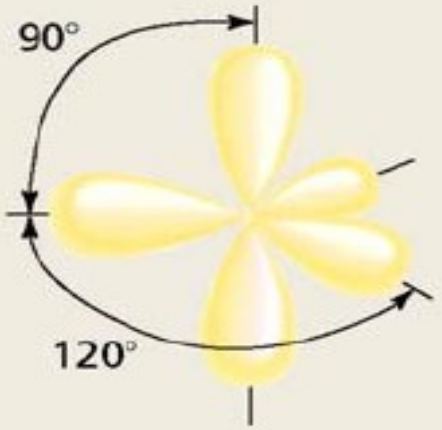
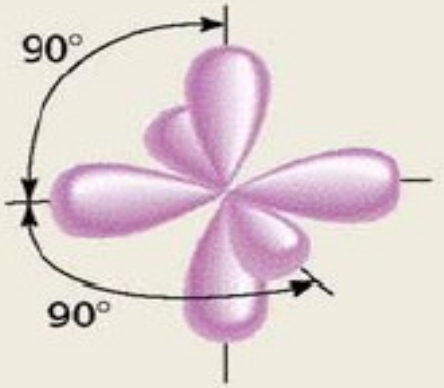
Home Work!

- ✓ **Discuss the hybridization of the C-C Triple Bond and states other parameters; For example C_2H_2,** $BeCl_2$
- ✓ Describe the hybridization state of phosphorus in PBr_5 , SF_6

Summary

Pure Atomic Orbitals of the Central Atom	Hybridization of the Central Atom	Number of Hybrid Orbitals	Shape of Hybrid Orbitals	Examples
s, p	*sp*	2	 Linear	$BeCl_2$
s, p, p	sp^2	3	 Planar	BF_3
s, p, p, p	sp^3	4		CH_4, NH_4^+

Cont'd...,

s, p, p, p, d	sp^3d	5	 Trigonal bipyramidal	PCl_5
s, p, p, p, d, d	sp^3d^2	6	 Octahedral	SF_6

Molecular Orbital Concept

- Molecular orbital (MO) theory is an alternative way of describing molecular structure and electron density.
- It also depicts covalent bond formation as arising from a mathematical combination of atomic orbitals (wave functions) on different atoms;
- *because they belong to the* entire *molecule rather than to an individual atom.*
- It explains again a region of space in a *molecule where electrons are most likely to be found.*

Reading Assignment!

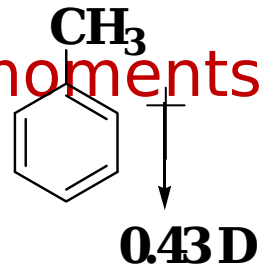
The Hückel MO Method

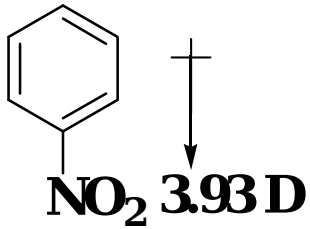
Factors influencing electron availability

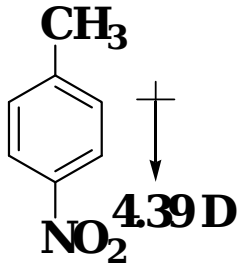
- Inductive Effect;
- Resonance /Mesomeric Effect;
- Steric Effect;
- Electromeric Effect;
- Hyperconjugative Effect;
- Tautomerism;

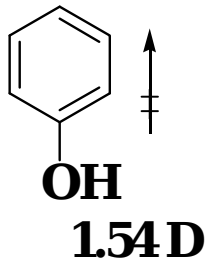
Dipole moment, *why!?*

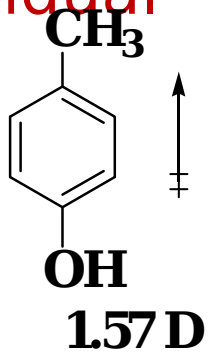
- The ***dipole moment*** is a property of the molecule that results from charge separations.
- However, it is not possible to measure the dipole moment of an individual bond within a molecule;
- It can measure only the total moment of the molecule, which is the vectorial sum of the individual bond moments











The arrow points to the negative parts of molecule!

Cont'd...,

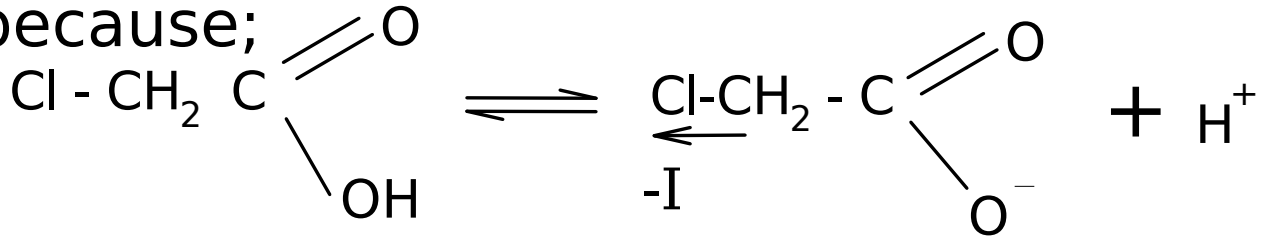
- In a simple molecule, it is the relative EN of the two atoms that are the major factor.
- EN is the tenancy of an atom to pull electrons towards it;
- Eg. a molecule such methanol the oxygen pulls electrons away from the carbon making the carbon electron deficient.
- This case also in more complicated structures however there are also resonance effects to take into account.
- For example in a C_6H_6 ring with an EDG by drawing the resonance structures you can place positive charges on different positions on the ring.

Inductive effect

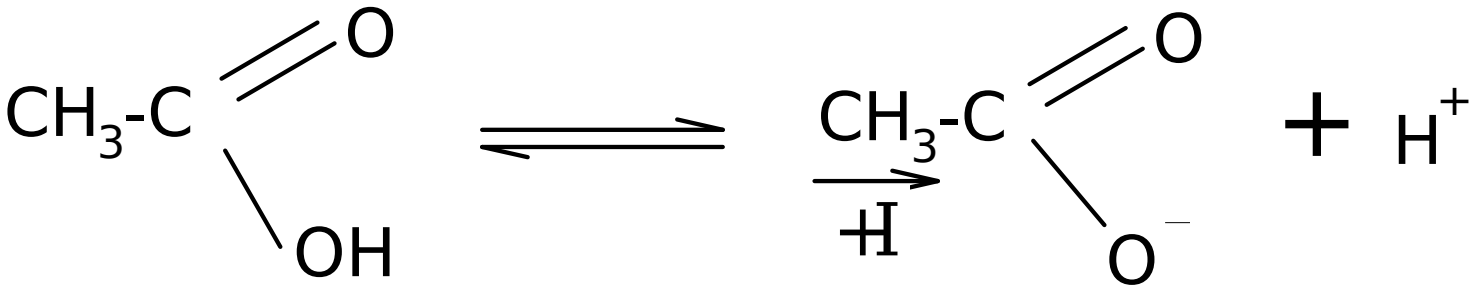
- It is experimentally observed effect of the transmission of unequal sharing of the bonding electron through a chain of atoms in a molecule, leading to a permanent dipole in a bond;
- It is present in a σ bond w/c opposed to electromeric effect; which is present on a π bond.
- For instance, halides are EWG, and all alkyls are EDG.
- If the EN atom (missing an electron, i.e. having a +ve) is then joined to a chain of atoms, usually carbon;
- the +ve is relayed to the other atoms in the chain and is the EW inductive effect, w/c is ***-I*** effect. Eg. R groups tend to donate electrons, leading to the inductive effect

For instance

- ✓ Chloroacetic acid is a stronger acid than acetic acid because;



$K_a = 1.4 \times 10^{-3}$



$K_a = 1.75 \times 10^{-5}$

➢ Depending on the strength of EWD or EDG, it is classified into:

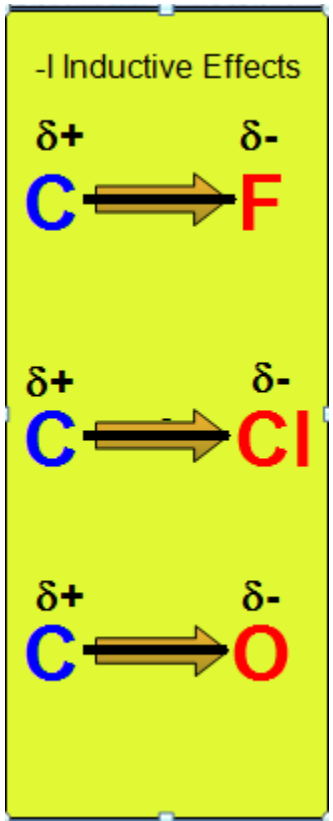
i) + I effect– electron donating gro

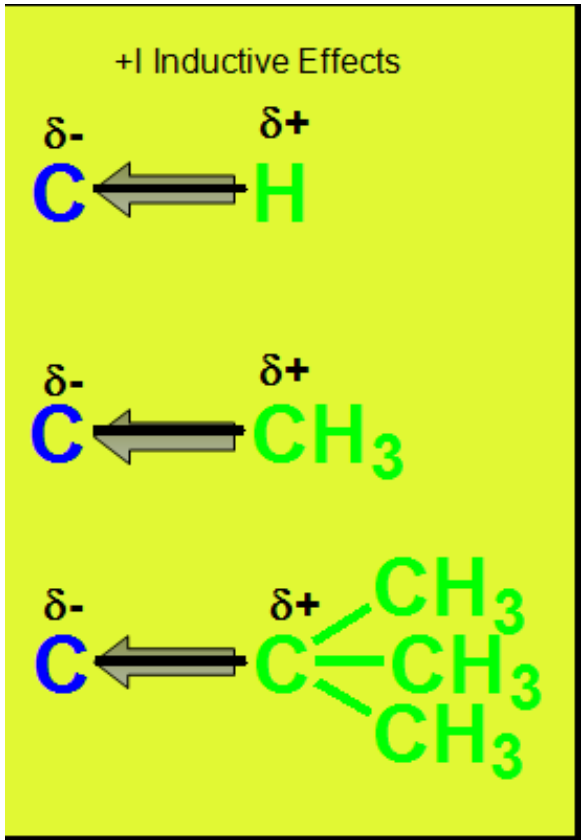
ii) Negative Inductive effect (-I)

- It is EWD groups or atoms such as

NH_4^+,NO_2,CN,SO_3H,CHO,CO,COOH,F,Cl,Br,I,OH etc

Generally, Bond Polarisation and Inductive Effects





Question (1)

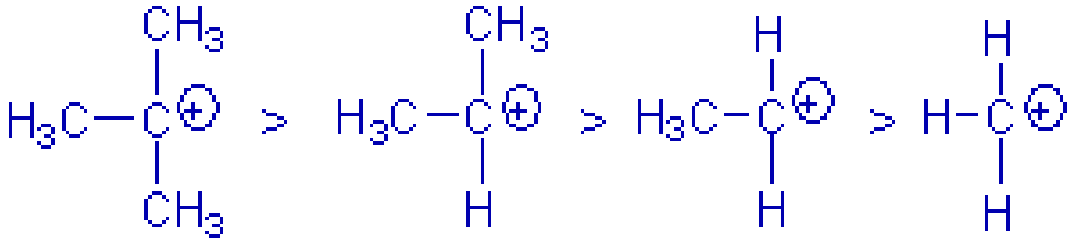
- Why alkyl groups are showing positive inductive effect?

✓Application of Inductive effects!

- Stability of carbonium ions:

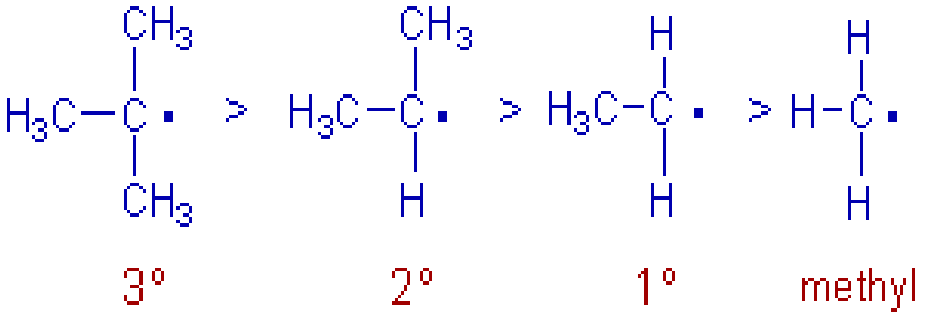
✓It increases with increases in number of alkyl group due to their + I effect;

✓The alkyl group release an electrons to carbon, bearing positive charge and thus stabilizes the ions.



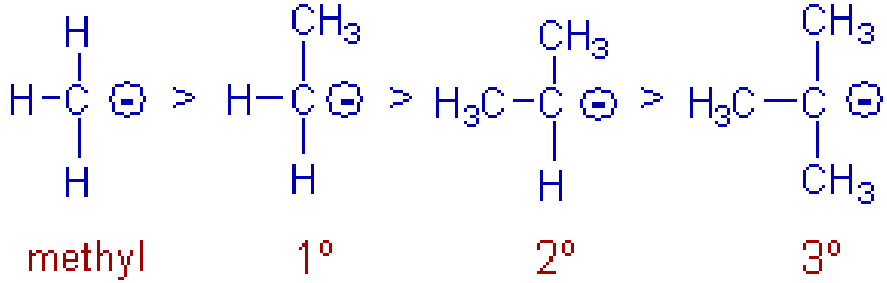
➢Stability of free radicals

✓In the same way, the stability of free radicals increases with increases in number of alkyl groups



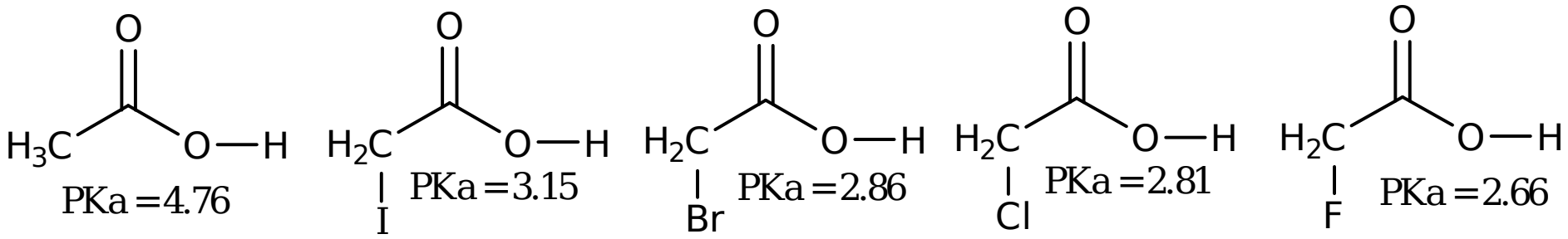
➢Stability of carbanions;

✓However it is decreases as the number of alkyl groups increases; since the electro donating alkyl groups destabilize the carbanions by increasing electron density.



Acidity and basicity Strength

- EWG groups (-I) decreases the +ve charges on the carboxylate ions and thus by stabilize it.
- Hence the acidity strength increase when –I is present; but +I decreases acidity.

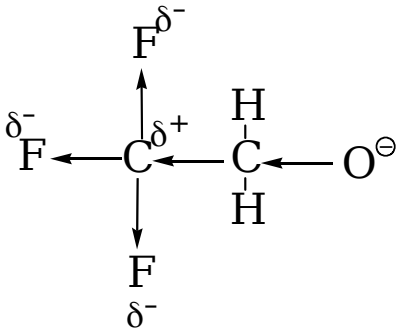


- The reason for the increased acidity of the above compounds is that the EN of halogen atoms stabilize the negatively charged conjugate base.

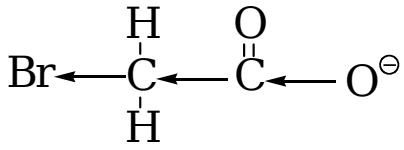
In addition,



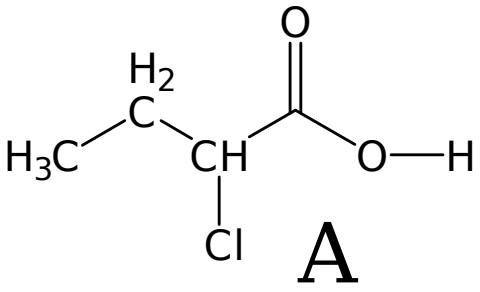
No additional electronegativity atoms stabilize the conjugated base



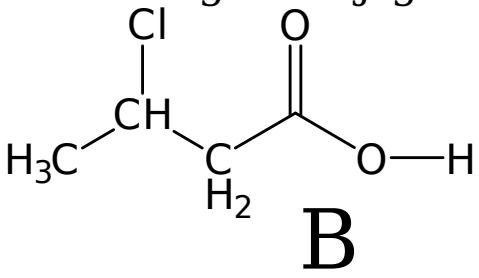
CF_3 withdraws electron density, stabilizing the conjugate base



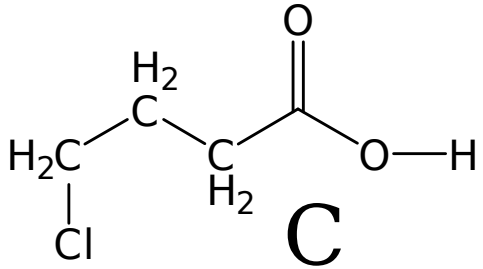
inductive electron withdrawal



A



B

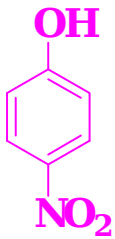


C

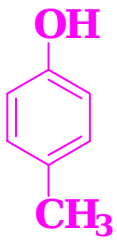
Acidity in increasing order A >B >C

➢Question (2)

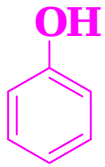
✓**Order the following structure based on the increasing acidity**



(A)



(B)

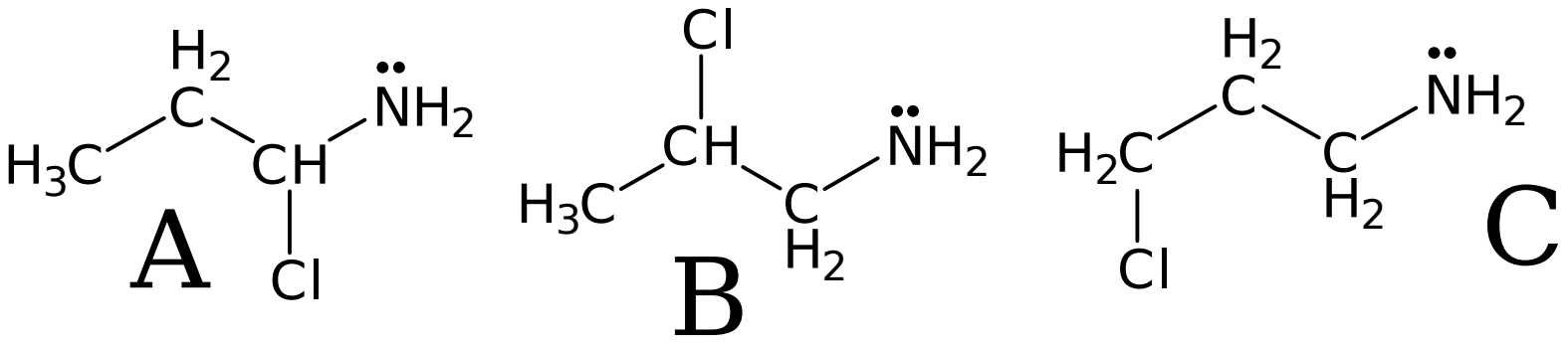


(C)

Strength of Base!

- EDG like alkyl groups increase the basic strength of amines; whereas EWD groups like Aryl groups decrease the strength of basic natures.
- Thus, alkyl amines are stronger Lewis base than NH_3, and aryl amines are weaker than NH_3. For instance (1) CH_3NH_2, NH_3,$C_6H_5NH_2$.

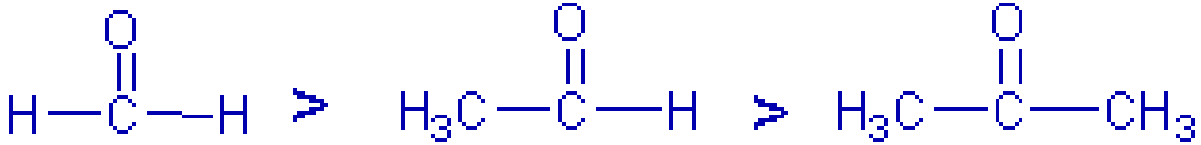
(2)



Basic character A <B <C

Reactivity of carbonyl groups!

- The +I groups increases the electron density at carbonyl groups.
- ✓ Hence their reactivity towards NU^- decreases.
- For instance: formaldehyde is more reactive than acetaldel



lic addition reactions

- **Question (3)**
- ✓ **Why Inductive effect is less influencing than other effects like resonance effects and hyperconjugation effects? Support your an**

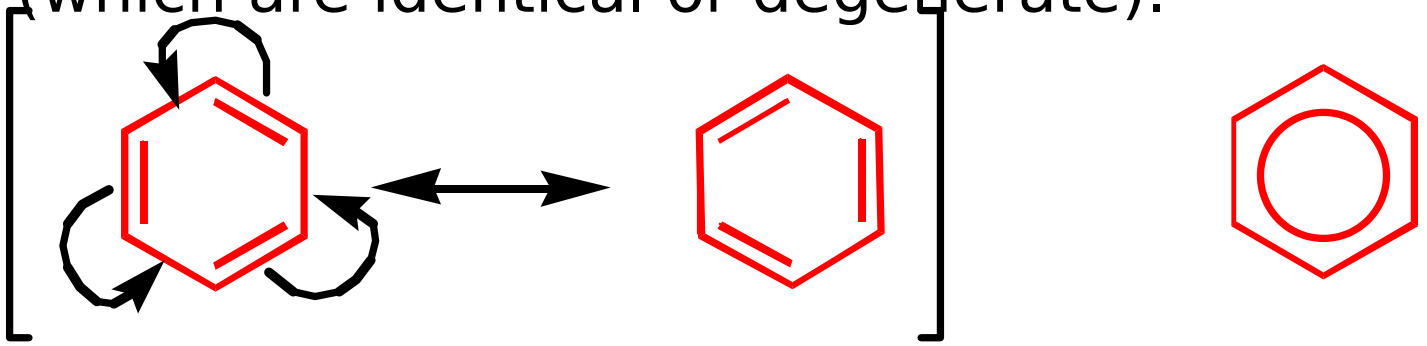
Resonance Effects

- The representation of structure of a molecules;
- It is weighted average of two or more hypothetical structures;
- with only differ by arrangement of electrons but with same positions for atoms.
- Bonding or sharing of electrons between more than two atoms (nuclei)
- The compounds contain one or more bonding orbitals that are not restricted to two atoms,
- but that are spread out over three or more and such bonding is ***delocalized.***

Illustration (1)

Resonance Structures of Benzene

- The 6 π-electrons are able to flow (or resonate) continually around the π -molecular orbital;
- W/c formed from the six pi atomic orbitals on each of the 6 carbon atoms on the ring structure.
- This is represented by the two resonance structures below (which are identical or degenerate).



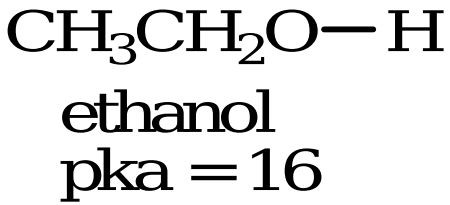
The π-electrons are referred to as being

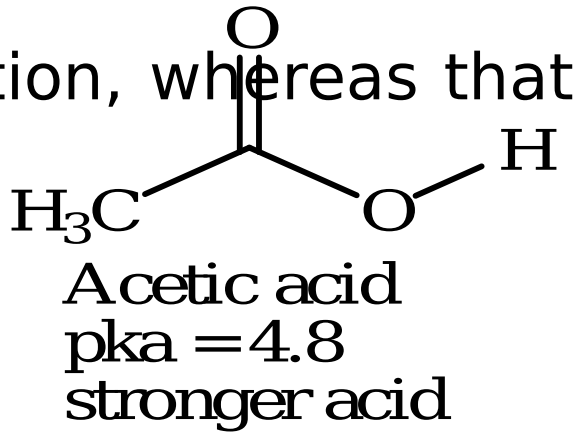
Comparison;...?

- This flow of electrons leads to a very stable electronic structure,
- which accounts for benzenes low reactivity relative to alkenes.
- This stability is referred to as the *Resonance Stabilization Energy.*

✓When the conjugate bases of the two species are compared,

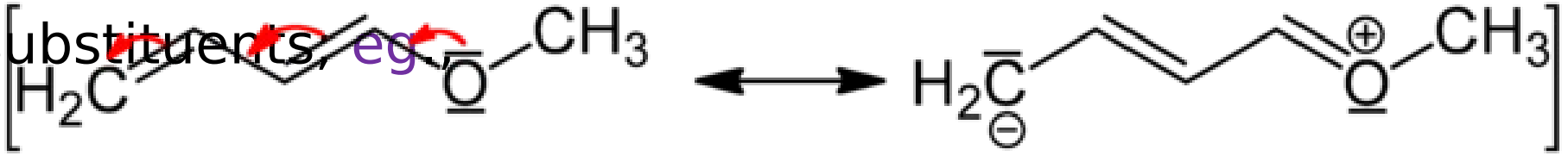
✓it is evident that the conjugate base of acetic acid performs resonance stabilization, whereas that of ethanol does not





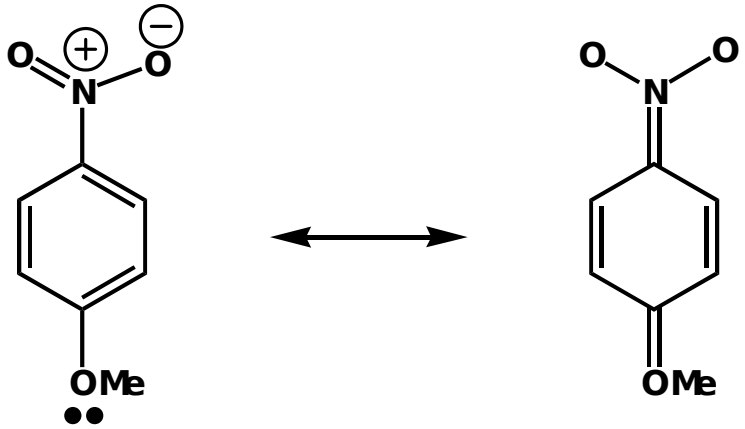
Resonance/mesomeric effect

- mesomeric effect is a property of substituents or functional groups in a chemical compound.
- The effect is used in a qualitative way and describes the electron withdrawing or releasing properties of substituents, eg



Question 1: Resonances

- On structure A draw on the arrows that lead to the bonding in the resonance structure B; place charges

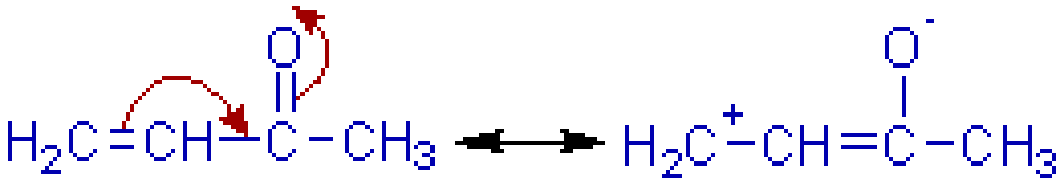


A B

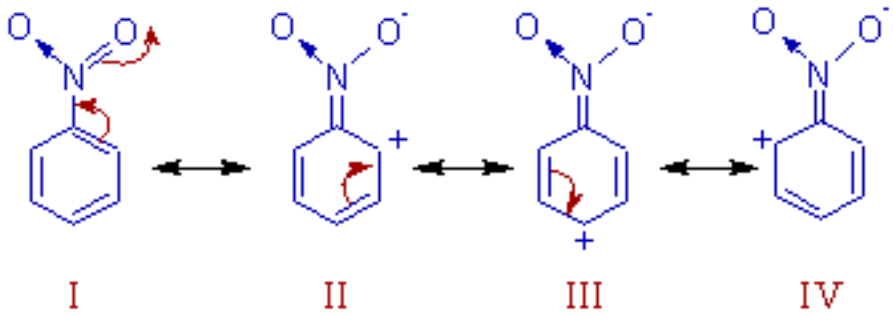
Types of Mesomeric effects

- The mesomeric effect is negative (**–M**) when the substituent is an electron-withdrawing groups.
- The electron density on the rest of molecular entity is decreased due to th

E.g. $-NO_2$, Carbony group (C=O), $-C\equiv N$, $-COOH$, $-SO_3H$ etc.

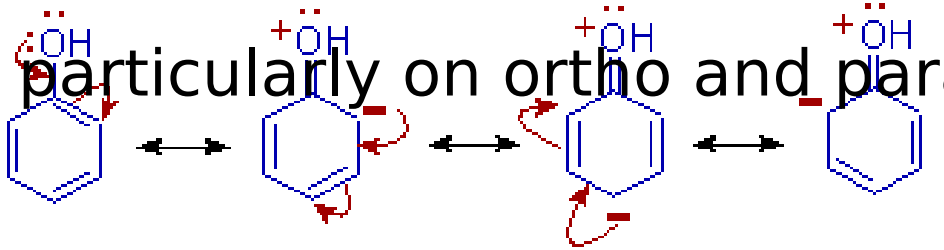


- Moreover; In nitro groups, $-NO_2$; in nitrobenzene, show s –M effect due to delocalization of conjugated n electrons as shown bel



Positive resonance/mesomeric effect

- The groups show +ve mesomeric effect when they release electrons to the rest of molecule by delocalization.
- Due to this effect, the electron density on the rest of the molecule entity is increased. Eg. -OH,-OR,-SH,-SR,-NH_2,-NR_2,etc
- In phenol, the –OH group shows +M effect due to delocalization of lone pair on oxygen atom towards to the ring.
- Thus the electron density on the benzene ring is increased particularly on ortho and para positions.

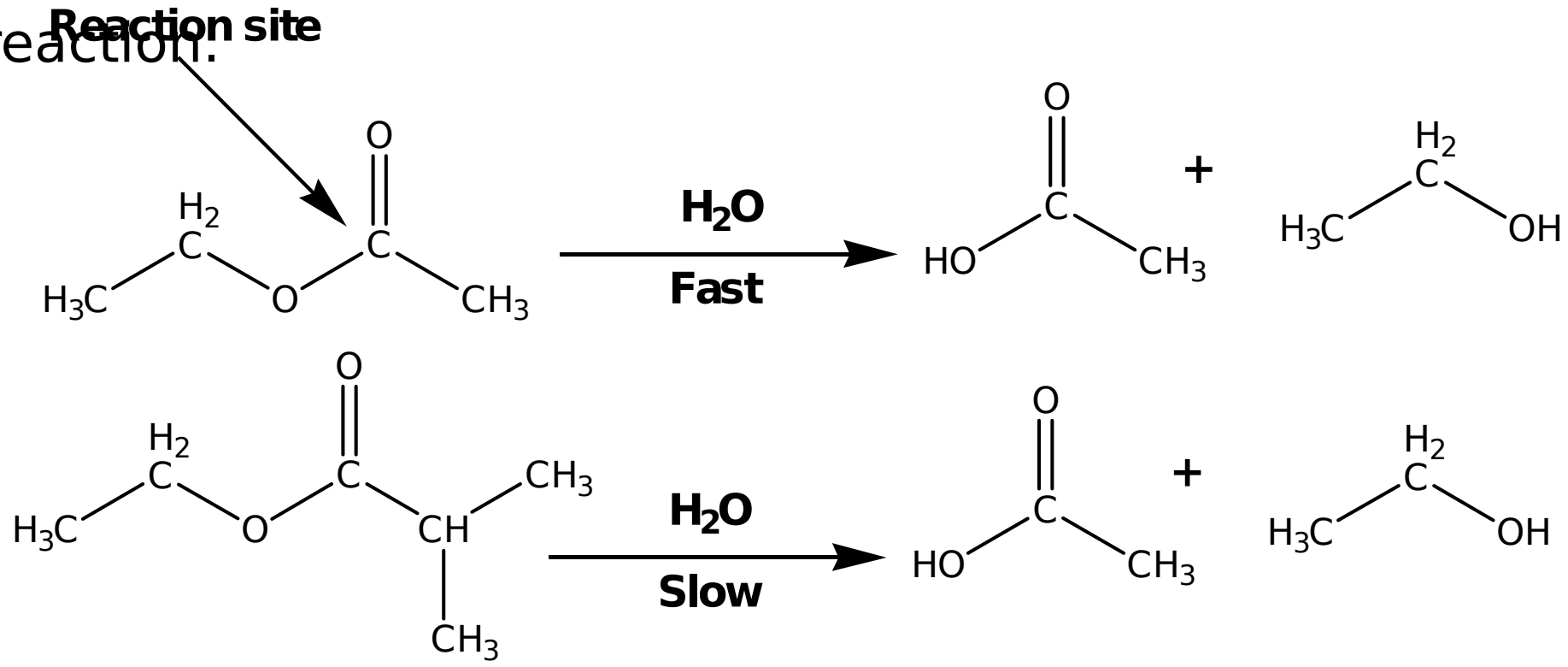


Steric effects

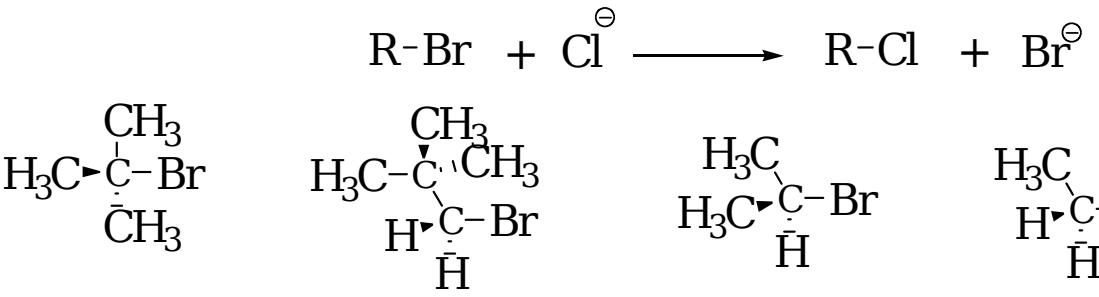
- **Steric effects** are nonbonding interactions that influence the shape (conformation) and reactivity of ions and molecules.
- Steric effects complement electronic effects, which usually dictate shape and reactivity.
- It results from repulsive forces between overlapping e-s clouds.
- Steric effects are essentially repulsive forces within a non-bonding effect, where certain atoms or molecules will essentially want to take themselves apart.
- Once taken apart these molecules essentially repel themselves; If they repel themselves enough they can

Steric effects…,

- The size of the atom(s) that attached near to the reactive site can also affect the reactive site;
- Larger group will hinder the substrate from making of reaction.



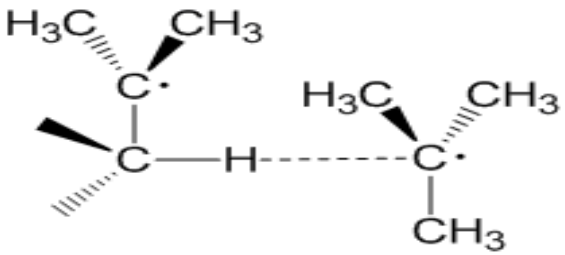
Reaction progress



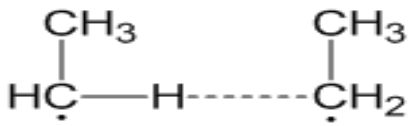
- **Steric hindrance** is a consequence of steric effects and it is the slowing of chemical reactions due to steric bulk.
- It is usually manifested in intermolecular reactions, whereas discussion of steric effects often focus on intramolecular interactions.
- Steric hindrance between adjacent groups can also affect torsional bond angles.

Reflection!

- Steric effect is the influence of the spatial configuration of reacting substances upon the rate, nature, and extent of reaction.
- The sizes, shapes of atoms and molecules, the electrical charge distribution, and the geometry of bond angles influence the courses of chemical reactions.
- For instance: molecules with large steric effects typically only exist for an extremely short period of time as intermediates. but smaller steric effects are more associated

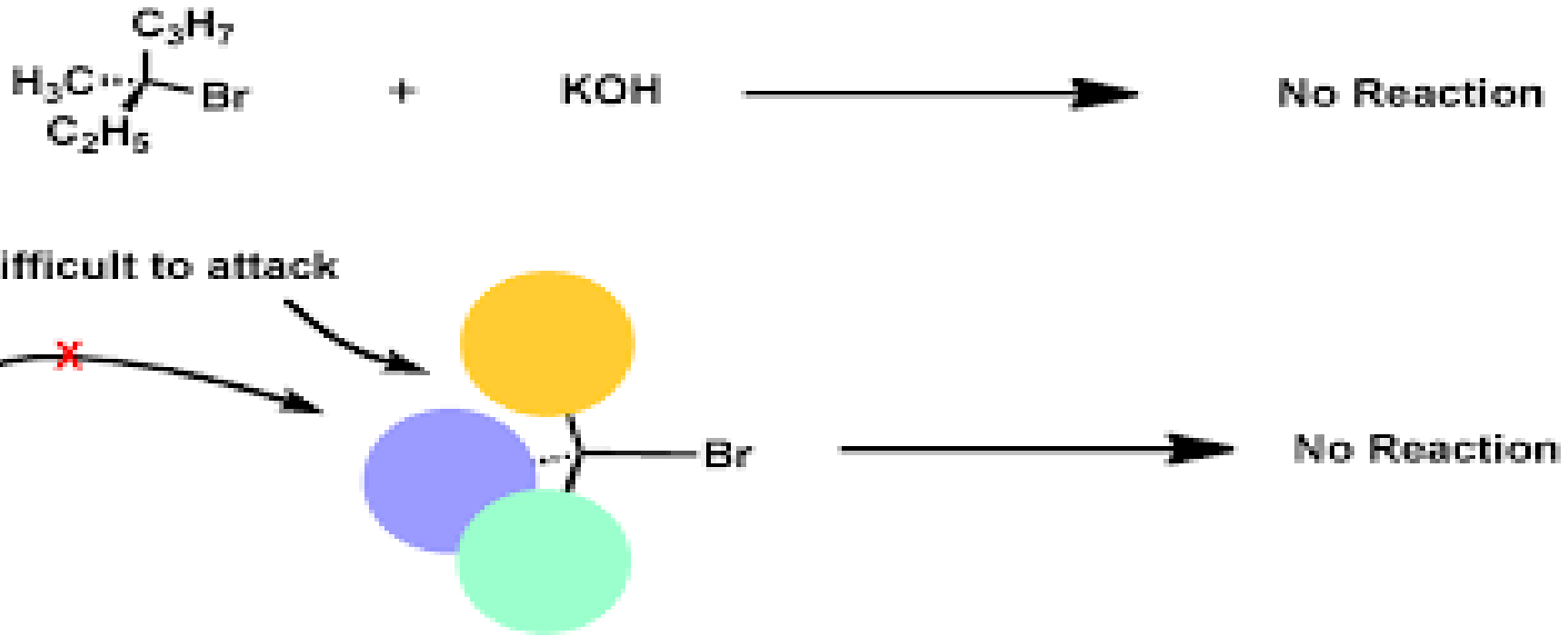


More Sterically Hindered



Less Sterically Hindered

Illustration 1



- In the above example, its not possible for a bigger nucleophile OH^- to attack at central atom and give SN^2 reaction.
- Because of the presence of bulky groups OH- RADI

Types
Steric hindrance

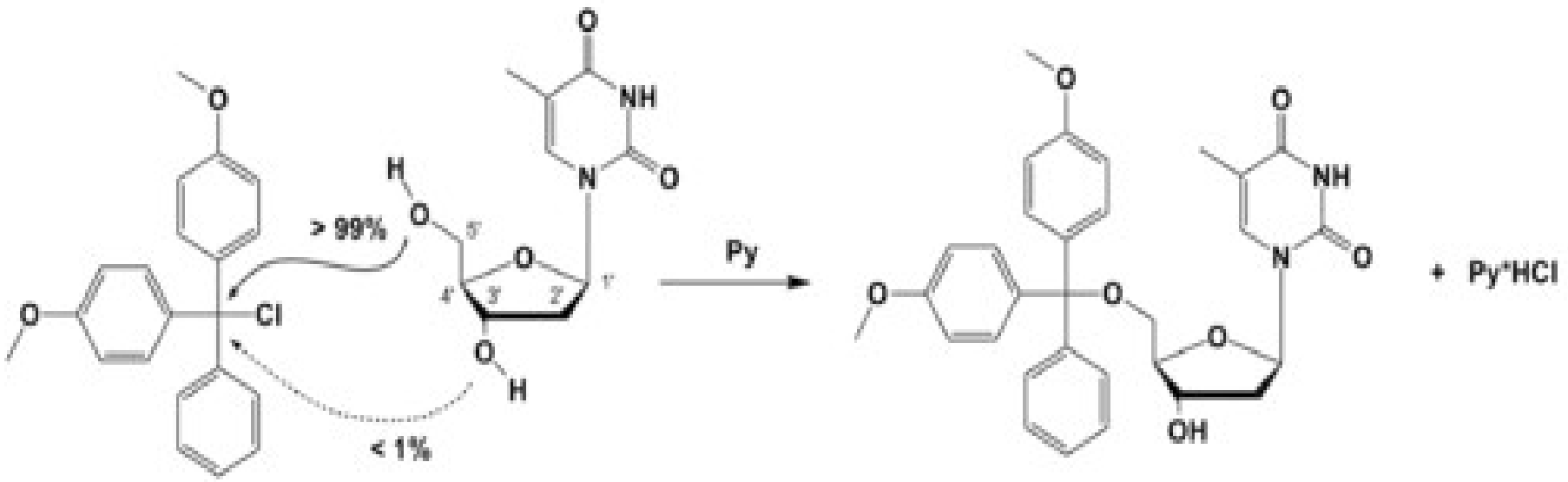
- Steric hindrance occurs when the large size of groups within a molecule prevents chemical reactions that are observed in related molecules with smaller groups.
- Although steric hindrance is sometimes a problem (it prevents with tertiary substrates from taking place) it can also be a very useful tool;
- and is often exploited by chemists to change the reactivity pattern of a molecule:
- by stopping unwanted side-reactions (**steric protection**) or
- by leading to a preference for one stereochem

Cont'd

- Steric hindrance between adjacent groups can also restrict torsional bond angles.
- However, hyperconjugation has been suggested as an explanation for the preference of the staggered conformation of ethane because the steric hindrance of the small. For instance;

- Regioselective dimethoxytritylation of the primary 5'-hydroxyl group of thymidine in the presence of a free secondary 3'-hydroxy group as a result of steric hindrance due to the dimethoxytrityl group and the ribose ring (Py = pyridine)

Structural illustration!



Other steric effects

➢**Steric shielding** occurs when a charged group on a molecule is seemingly weakened or spatially shielded by less charged (or oppositely charged) atoms, including counterions in solution (Debye shielding).

Cont'd...

- In some cases, for an atom to interact with sterically shielded atoms, it would have to approach from a vicinity where there is less shielding, thus controlling where and from what direction a molecular interaction can take place.
- **Steric attraction** occurs when molecules have shapes or geometries that are optimized for interaction with one another.
- **Chain crossing:**
  - In these cases, molecules will react with each other most often in specific arrangements.
  - A chain, ring, or a set of rings cannot change from one conformation to another if it would require a chain.

Cont'd…

- ✓This effect, or lack of, is responsible for the shape of catenanes and molecular knots.
- ➢**Steric repulsions** between different parts of a molecular system were found to be of key importance in governing the direction of transition-metal-mediated transformations and catalysis.
- ➢Steric effects can even induce a mechanism switch in the catalytic reaction.
- ➢Steric repulsion is also largely responsible for the stabilizing of colloids by coating the surface with a polymer, can also cause bond length shortening, steric deshielding of proton resonance and compres

Cont'd…

- **Steric inhibition of resonance** is present only in benzene rings.

✓The presence of any group at the ortho position in benzoic acid will throw the carboxylic acid group out of the plane, and

✓thus its mesomeric connection with the benzene ring disappear.

✓This means that ortho-substituted benzoic acids are stronger than meta- and para-substituted benzoic acids.

Significance!!!

- ✓Understanding steric effects is critical to chemistry, biochemistry and pharmacology.
- ✓In organic chemistry, steric effects are nearly universal and affect the rates and activation energies of most chemical reactions to varying degrees.
- ✓Steric effects often dictate reaction pathways in organic synthesis because there are fewer configurations in which molecules can collide and successfully react.
- ✓In surface chemistry, steric effects manifest in an entropic contribution to the overall Gibbs energy.

✓Hence, colloidal stability can be obtained by steric shielding from polymers, often made possible via block co-polymer adsorption or grafting polymer onto charged nanoparticles.

✓This spatial shielding effect is large-scale in comparison to Debye shielding due to the size of the attached polymer strands.

✓In biochemistry, steric effects are often exploited in naturally occurring molecules such as enzymes, where the catalytic site may be buried within a large protein structure.

Significance…,

- ✓In pharmacology, steric effects determine how and at what rate a drug will interact with its target bio-molecules.
- ✓Finally, organic chemical example of stereochemistry of ketonization of enols and enolates where diastereoselectivity results from steric hindrance.

Question 3

1) Compare and contrast Inductive and Mesomeric effects.
2) State the use of Steric effects and support your answer with example!

Functional groups in organic chemistry

➢Points for discussion!

✓A functional groups, What is it?

✓How it stated?, What is its application?

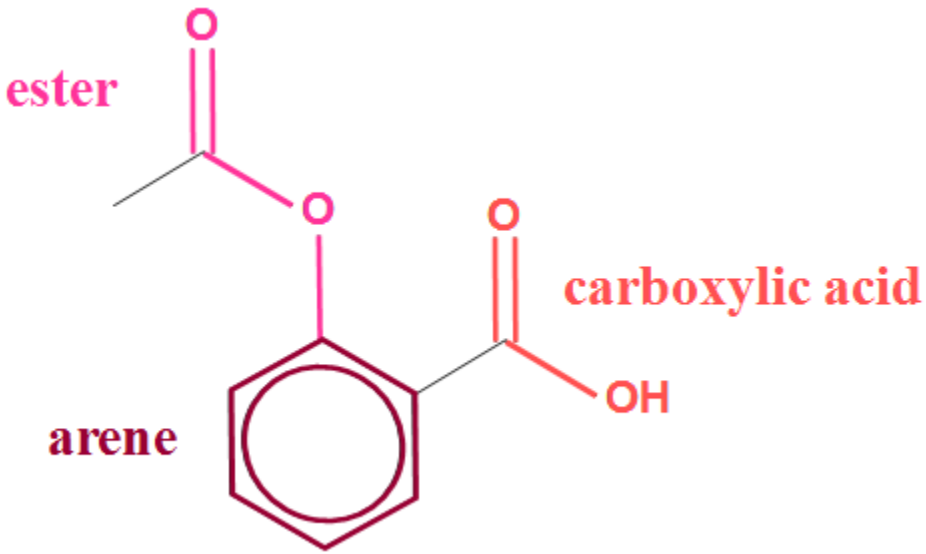
✓Why classification of organic cpd. is important?

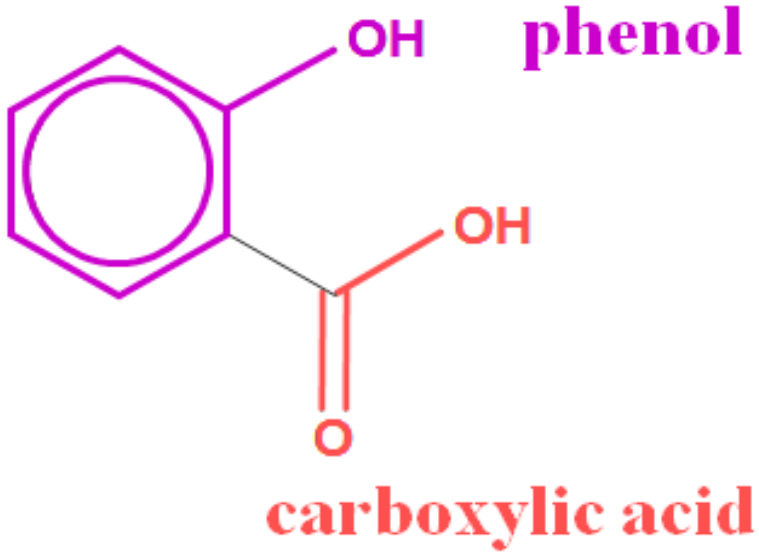
➢A functional group is a portion of a molecule that is a recognizable/classified group of bound atoms.

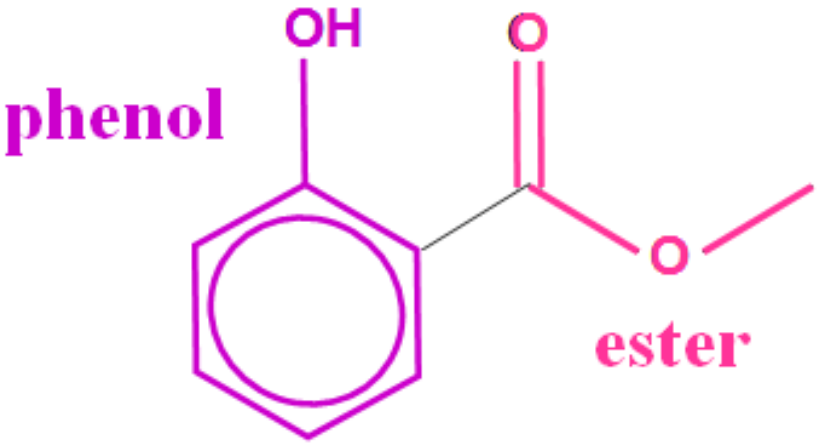
✓In organic chemistry it is very common to see molecules comprised mainly of a carbon backbone with functional groups attached to the chain.

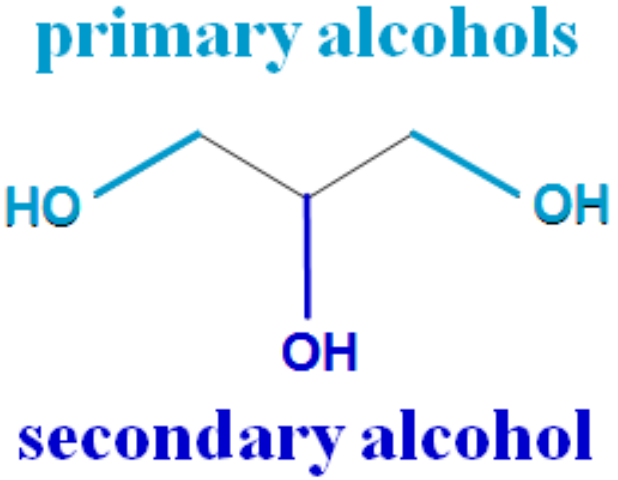
✓The functional group gives the molecule its chemical reactivity, regardless of what molecule contains it.

For instance;









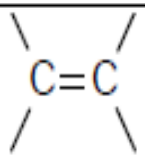
Important Reason;

- Classification of functional groups is important for three reasons:
  - ✓they are the units by w/c organic compounds divide into classes;
  - ✓they are sites of characteristic chemical reactions and particular functional group, in all compounds that contain it, undergoes the same types of chemical reactions;
  - ✓functional groups serve as a basis for naming organic compounds.

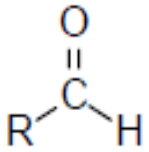
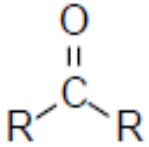
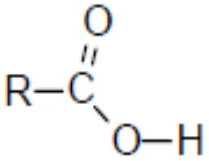
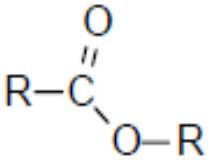
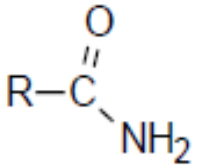
Question (1)

- ✓Is there any significance advantage which functional group has contribution on physical properties?

Common functional groups

Functional Group	Compound	Prefix/Suffix	Example	IUPAC Name (Common Name)
R-H	alkane	-ane	CH_3CH_3	ethane
	alkene	-ene	$H_2C{=}CH_2$	ethene (ethylene)
—C≡C—	alkyne	-yne	HC≡CH	ethyne (acetylene)
R-X	haloalkane	halo-	CH_3Cl	chloromethane
R-OH	alcohol	-ol (hydroxy-)	CH_3OH	methanol
$R\text{-}NH_2$	amine	-amine (amino-)	$CH_3CH_2NH_2$	ethylamine aminoethane
R-O-R	ether	ether (alkoxy-)	CH_3OCH_3	dimethyl ether

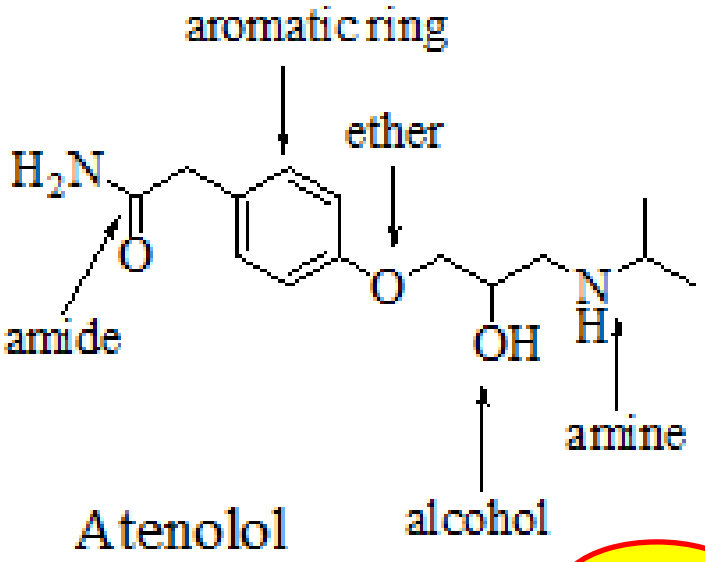
Cont'd...;

	aldehyde	-al	CH_3CH (O)	ethanal (acetaldeyde)
	ketone	-one	CH_3CCH_3 (O)	propanone (acetone)
	carboxylic acid	-oic acid	CH_3COH (O)	ethanoic acid (acetic acid)
	ester	-oate	CH_3COCH_3 (O)	methyl ethanoate (methyl acetate)
	amide	-amide	CH_3CNH_2 (O)	ethanamide (acetamide)

R = alkyl group, an unfunctionalized saturated chain; X = halogen

In Summary!

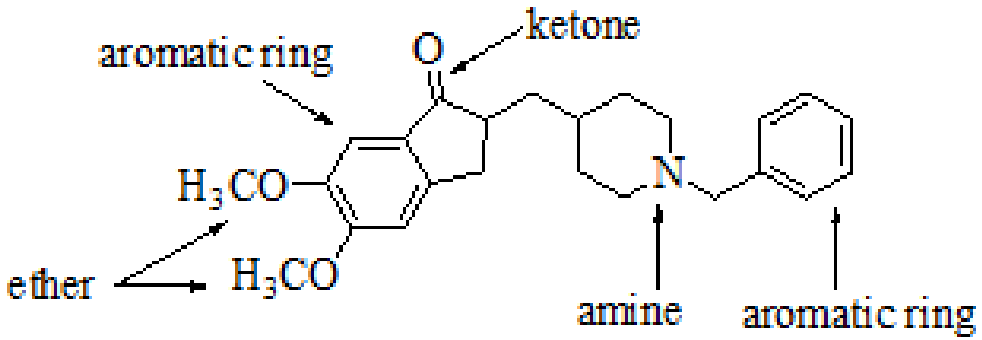
- **An overview of functional groups, it has subdivision into:**
  - ✓ Hydrocarbons;
  - ✓ Compounds containing a C – Z σ bonds; Z = EN and
  - ✓ Compounds containing a C=O group.
- Besides, Atenolol and donepezil are examples of useful drugs that contain a variety of functional groups.
- Hence, Atenolol is a blocker, a group of drugs used to treat



Atenolol

Cont'd...,

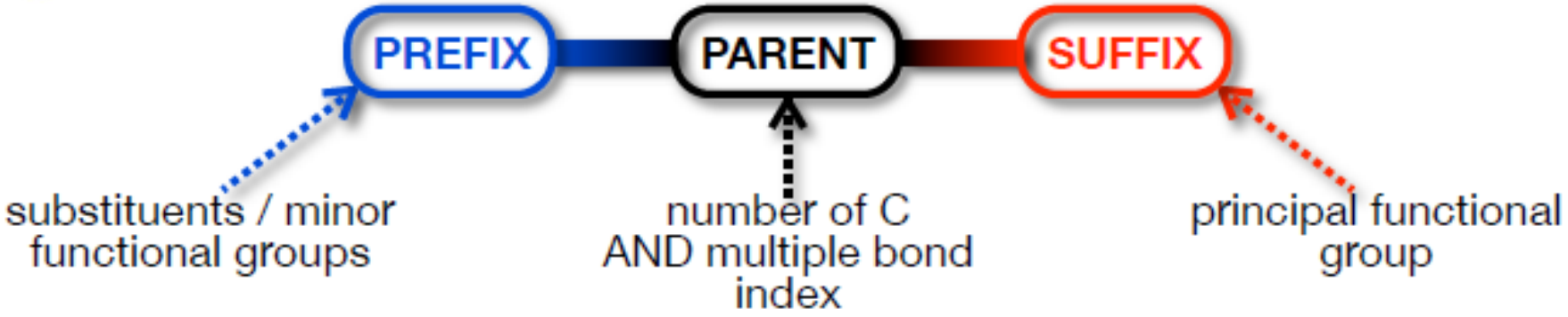
- Donepezil, sold under the trade name Aricept, is used to treat mild to moderate dementia associated with Alzheimer



Donepezil

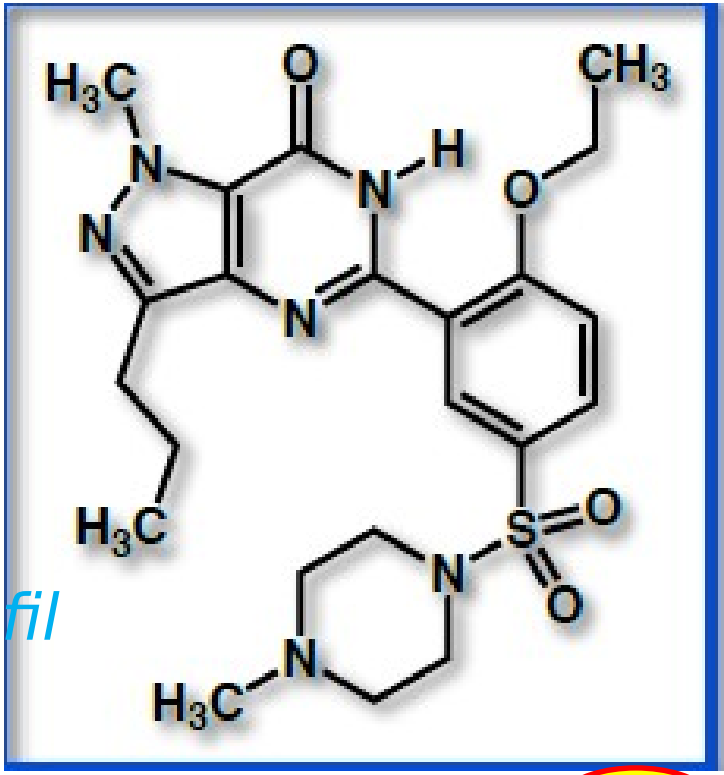
- Nomenclature of organic Compounds:
  - ✓ It is based on the their functional groups!
- To write and interpret IUPAC names for small, simple molecules
- Identify some common functional groups found

Systematic (IUPAC) naming



For instance:

✓The IUPAC Name of ?

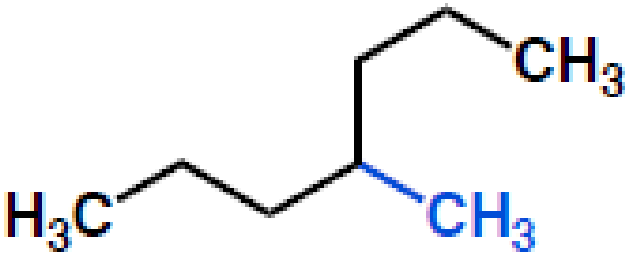


But the its common name is *sildenafil*

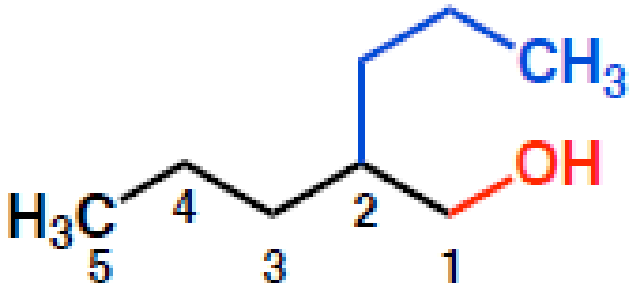
viagra) its trade name;

Nomenclature rules

1. **Parent** - root derived from number of carbon in longest un-branched chain containing functional group;

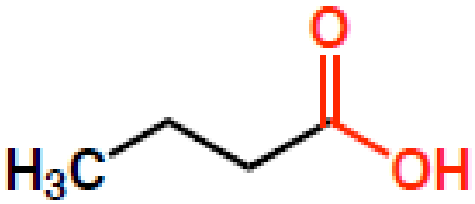


4-methylheptane

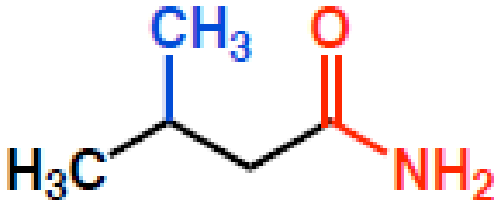


2-propyl-1-pentanol

2. Suffix - basic name derived by adding ending of major functional group.



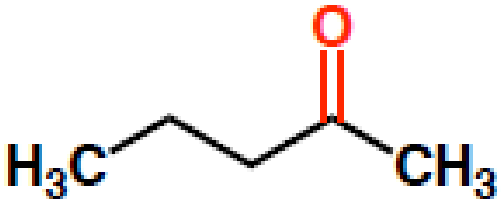
butanoic acid



3-methylbutanamide

Rules...,

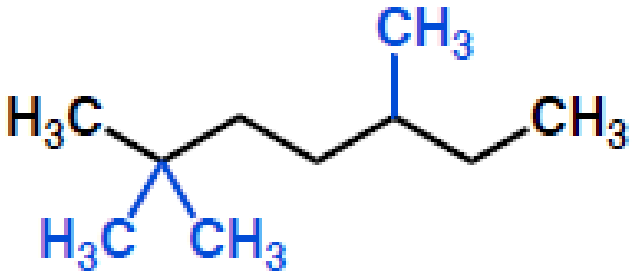
3. Position - position of FG denoted by Arabic numeral placed before whole name or just before ending;



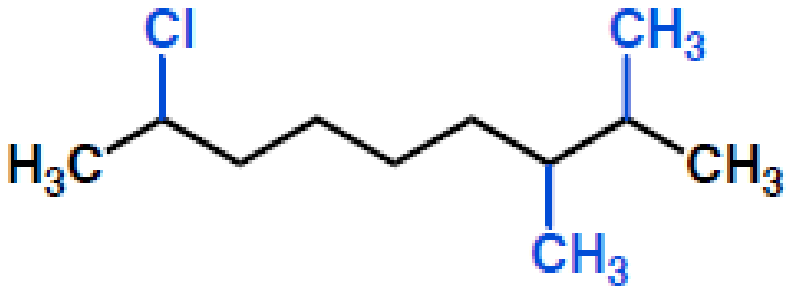
2-pentanone
pentan-2-one
NOT 4-pentanone

✓Numbering achieves lowest number for FG.

4. Prefix - substituents are designated by prefix & Arabic number indicating position (lowest possible numbering),



2,2,5-trimethylheptane
NOT 3,6,6-trimethylheptane

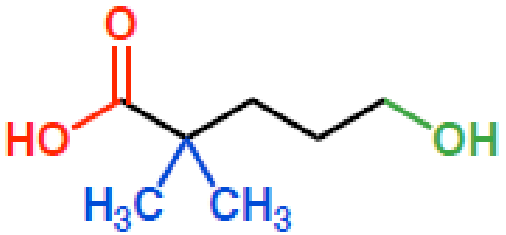


8-chloro-2,3-dimethylnonane
NOT 2-chloro-7,8-dimethylnonane

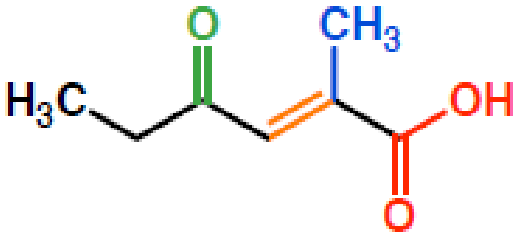
Rules…,

5. FG - if more than one FG name & number based on principle FG; then List of priorities given in course notes;

✓Multiple bonds are added to parent (end), all others are pr



5-hydroxy-2,2-dimethylpentanoic acid



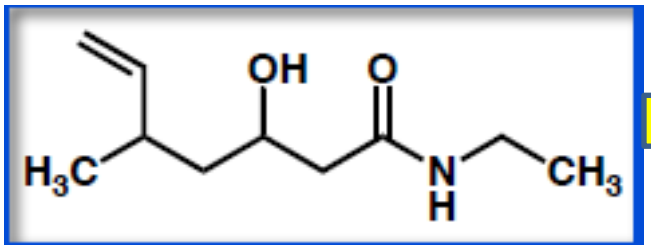
2-methyl-4-oxohex-2-enoic acid

6. Minor FG - halo-, nitro- (-NO_2), nitroso- (-NO) & azo- (-N_2-) are considered substituents & not FG for nomenclature only;

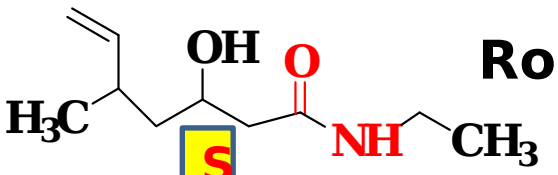
7. Order - substituents are written in alphabetical order.

Examples(1) structure to name

A)



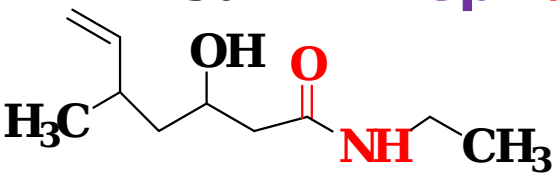
Step 1



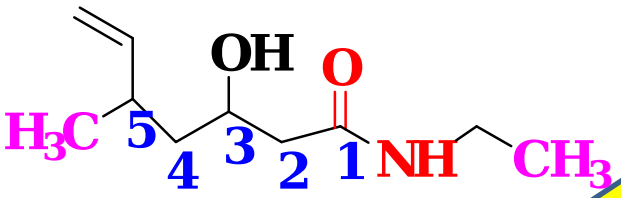
Root: hept

Step 2

suffix: hept amide

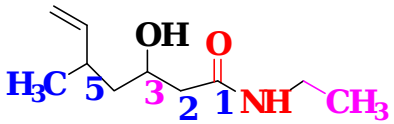


Step 3



Multiple bond index:

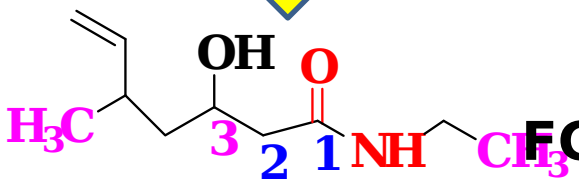
hept 6-enamide



N-ethyl-3-hydroxy 5-methylhept 6-enamide

Step 4

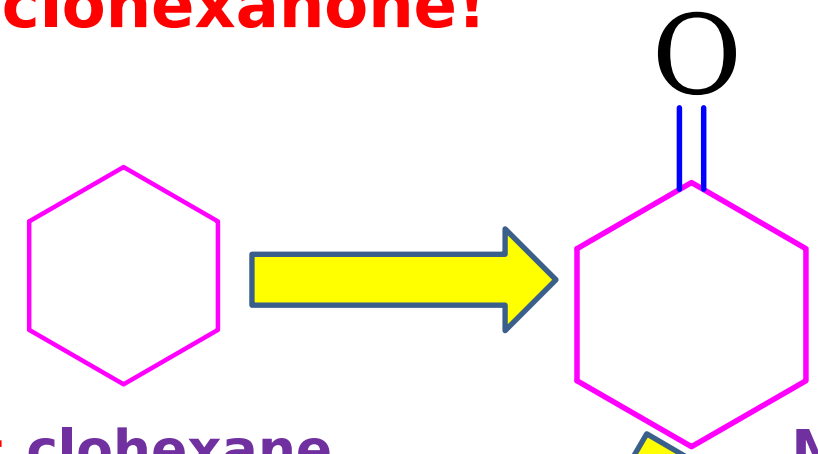
Step 5



FG: 3-hydroxy hept 6-enamide

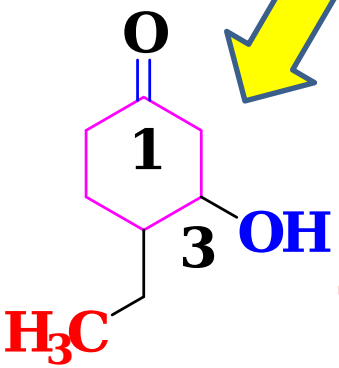
Examples (2) name to structure

✓Draw the structure for **4-ethyl-3-hydroxycyclohexanone!**



the root: **clohexane**

Major FG: cyclohexanone

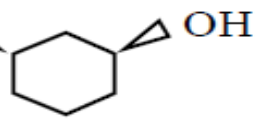


4-ethyl-3-hydroxycyclohexanone

Exercise (1)

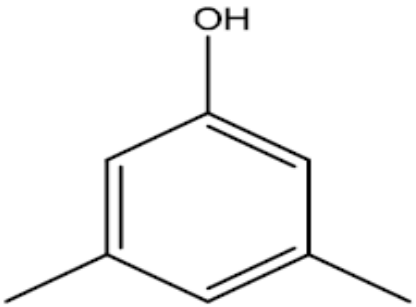
) Name each of the following compounds

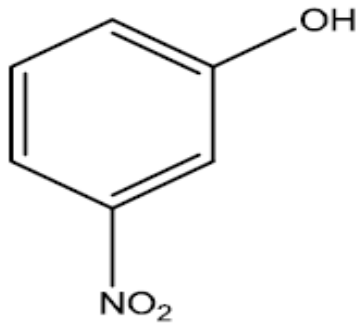
a) $HOCH_2CH(CH_3)_2$

b) CH_3CH_2O  OH

c) $CH_3CH_2CH(CH_3)C(OH)CH_2CH_3$ with $CH(CH_3)_2$ attached to the C

d) 

e) 

f) 

B) Draw the structure of each of the following compounds

i) 2-methoxy-5-methylheptane

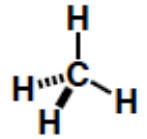
ii) 3-*tert-butyl-4-methylcyclohexanol*

iii) 2,4,6-trimethoxyphenol

Alkanes

- Saturated hydrocarbons - contain only C & H and no multiple bonds with C_nH_{2n+2} chemical formula.

✓ For instance



methane
CH_4



propane
C_3H_8

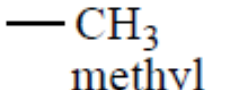


pentane
C_5H_{12}

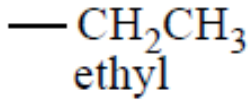


cyclopentane
C_5H_{10}

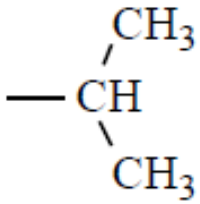
- Common alkyl groups w/c replace "ane" ending of alkane name with "yl".
- Alternate names for complex substituents are given in brack



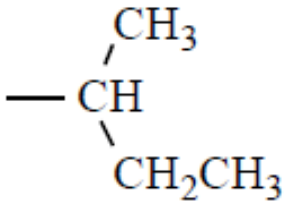
— CH_3
methyl



— CH_2CH_3
ethyl



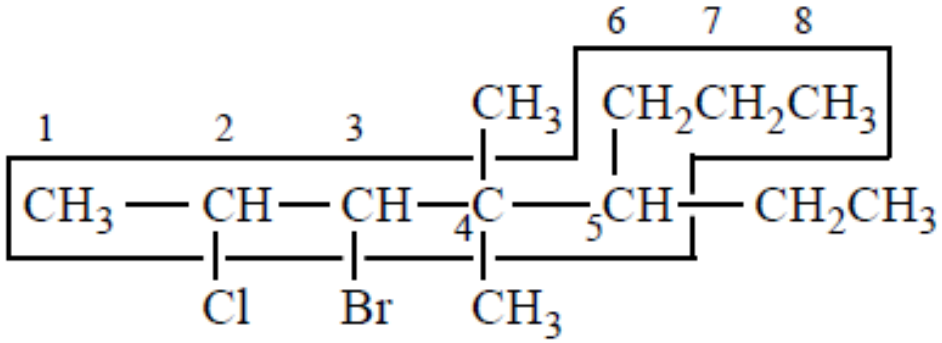
isopropyl
[1-methylethyl]



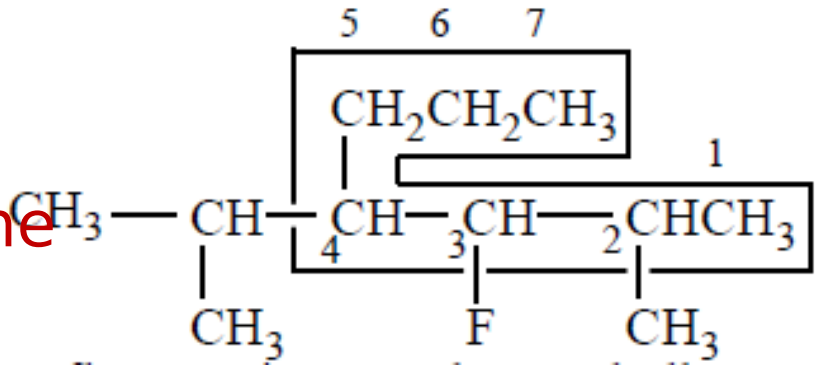
sec-butyl
[1-methylpropyl]

aming Substituted Alkanes and CycloalkanesGroup

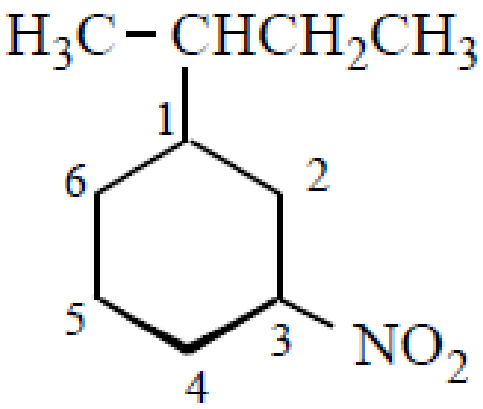
- ✓IUPAC Nomenclature



3-bromo-2-chloro-5-ethyl-4,4-dimethyloctane



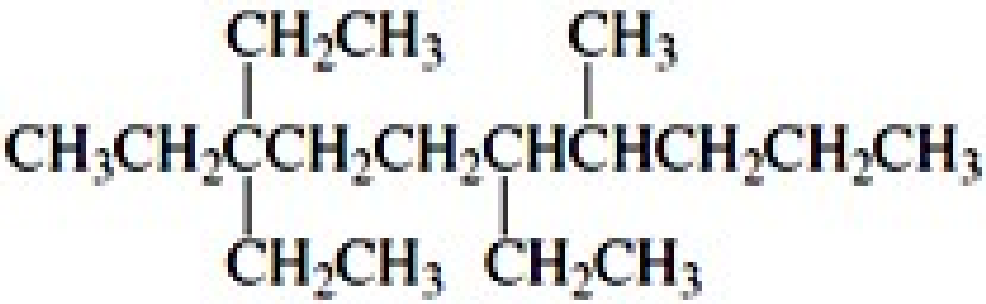
-fluoro-4-isopropyl-2-methylheptane

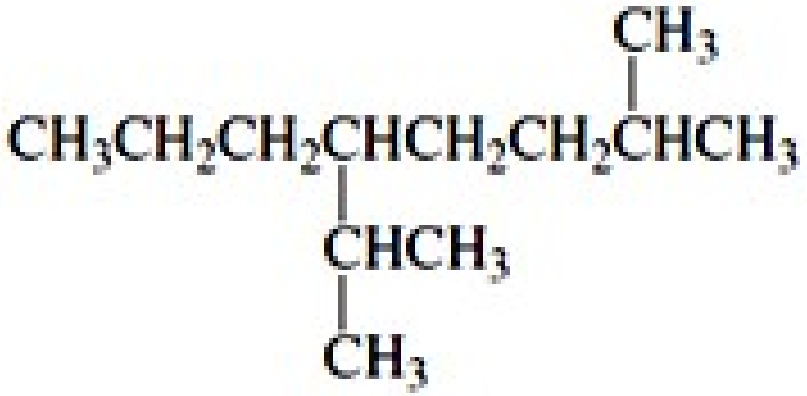


1-*sec-butyl-3-nitrocyclohexane*

Exercise (2)

A) The IUPAC name of





B) Draw the structure of

i) 4-isopropyl-2,4,5-trimethylheptane

ii) 4-isobutyl-2,5-dimethyloctane

iii) 6-ethyl-2,3-dimethylnonane

Nomenclature and physical properties of some Alkanes

Number of carbons	Molecular formula	Name	Condensed structure	Boiling point (°C)	Melting point (°C)	Density (g/mL)
1	CH_4	Methane	CH_4	-16.7	-182.5	-
2	C_2H_6	Ethane	CH_3CH_3	-88.6	-183.3	-
3	C_3H_8	Propane	$CH_3CH_2CH_3$	-42.1	-187.7	-
4	C_4H_{10}	Butane	$CH_3CH_2CH_2CH_3$	-0.5	-138.3	-
5	C_5H_{12}	Pentane	$CH_3(CH_2)_3CH_3$	36	-129.8	0.5572
6	C_6H_{14}	Hexane	$CH_3(CH_2)_4CH_3$	68.7	-95.3	0.6603
7	C_7H_{16}	Heptanes	$CH_3(CH_2)_5CH_3$	98.4	-90.6	0.6837
8	C_8H_{18}	Octane	$CH_3(CH_2)_6CH_3$	127.7	-56.8	0.7026
9	C_9H_{20}	Nonane	$CH_3(CH_2)_7CH_3$	150.8	-53.5	0.7177
10	$C_{10}H_{22}$	Decane	$CH3(CH2)_8CH_3$	174.0	-29.7	0.7299
11	$C_{11}H_{24}$	Undecane	$CH_3(CH_2)_9CH_3$	195.8	-25.6	0.7402
12	$C_{12}H_{26}$	Dodecane	$CH_3(CH_2)_{10}CH_3$	216.3	-9.6	0.7487
13	$C_{13}H_{28}$	Tridecane	$CH_3(CH_2)_{11}CH_3$	235.4	-5.5	0.7

Chemical properties of Alkane

) Combustion reaction

$$C_nH_{2n+2} + \left(\frac{3n+1}{2}\right)O_2 \rightarrow nCO_2 + (n+1)H_2O + \text{heat}$$

Example

$$C_3H_8 + 5O_2 \rightarrow 3CO_2 + 4H_2O + 2299\ kJ$$

Substitution reaction

✓reaction that involves the replacement of one atom or a group of atoms by another atom or group of atoms.

Example $CH_4(g) + Cl_2(g) \rightarrow CH_3Cl(g) + HCl(g)$

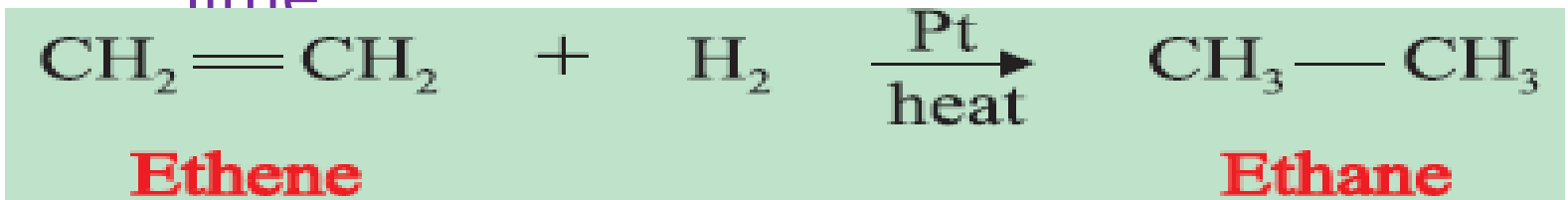
Elimination reaction $CH_3CH_3 \xrightarrow{600\text{-}800^\circ C} CH_2=CH_2 + H_2$

Ethane — Ethene

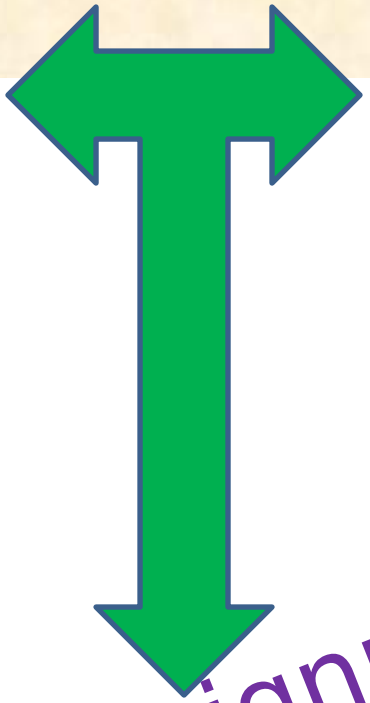
Preparation of Alkanes

- Industrially, Alkanes are the major constituents of petroleum, Coal and natural gas.
- They are mainly obtained by fractional distillation of petroleum.
- Alkanes can also be prepared in the laboratory and some methods of their preparation are as follows:
  - ✓ Hydrogenation of alkenes with a metal catalyst.
  - ✓ Wûrtz Synthesis (*reaction).*
  - ✓ Heating sodium salt of an organic acid with soda lime

For instance, the first method is better applicable than the oth



Alkenes and Alkynes!

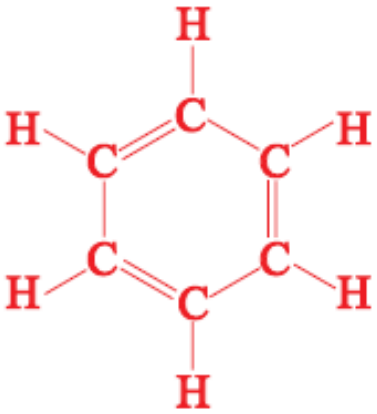


- Reading Assignment!!!

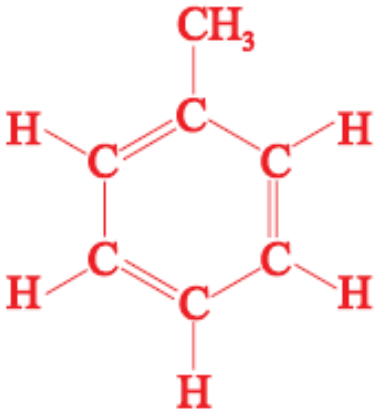
Aromatic hydrocarbons

- The term aromatic is derived from the word ‘aroma’ meaning pleasant smell;
- which was originally used to describe naturally occurring compounds with pleasant smells.
- Aromatic hydrocarbons are generally obtained from petroleum and coal tar.
- They are a group of hydrocarbons characterized by the presence of a benzene ring or related structures.
- Aromatic” compounds are those derived from benzene and similar ring systems.

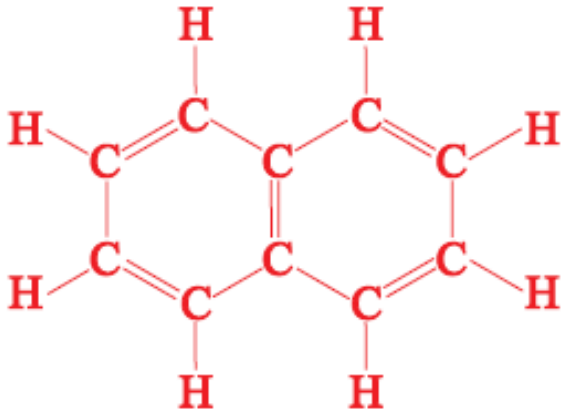
For example;



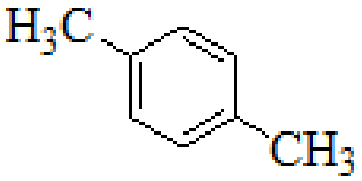
Benzene



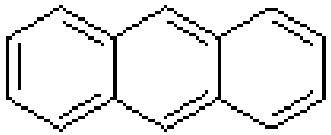
Methyl benzene
(Toluene)



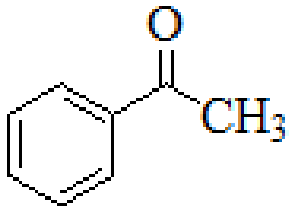
Naphthalene



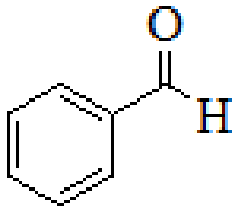
Para-xylene



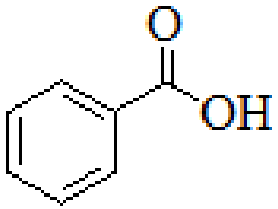
Anthracene



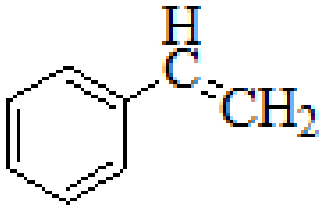
Acetophenone



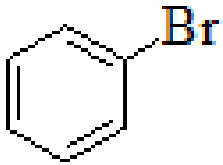
Benzaldehyde



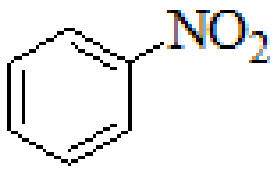
Benzoic acid



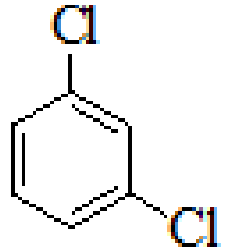
Styrene



Bromobenzene

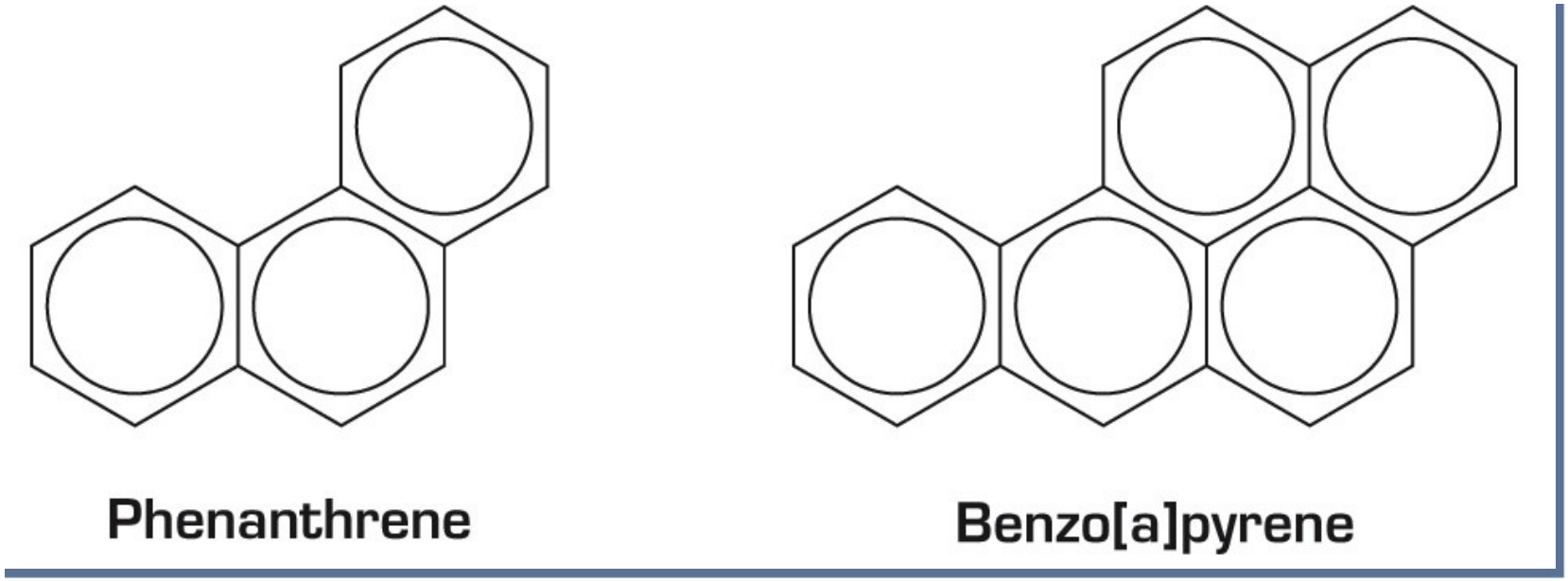


Nitrobenzene



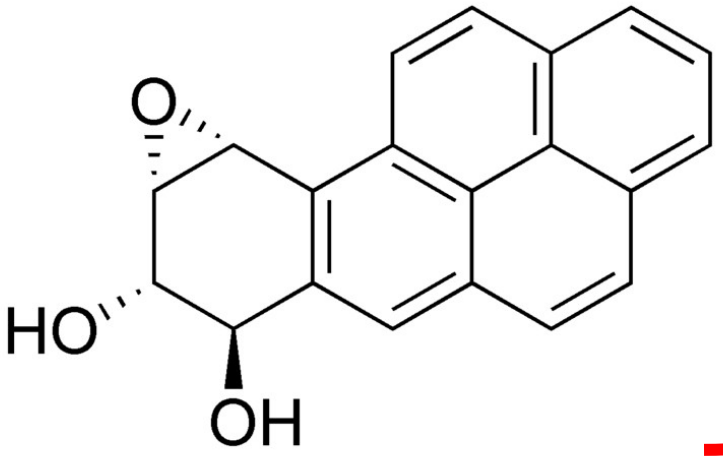
m-Chlorobenzene

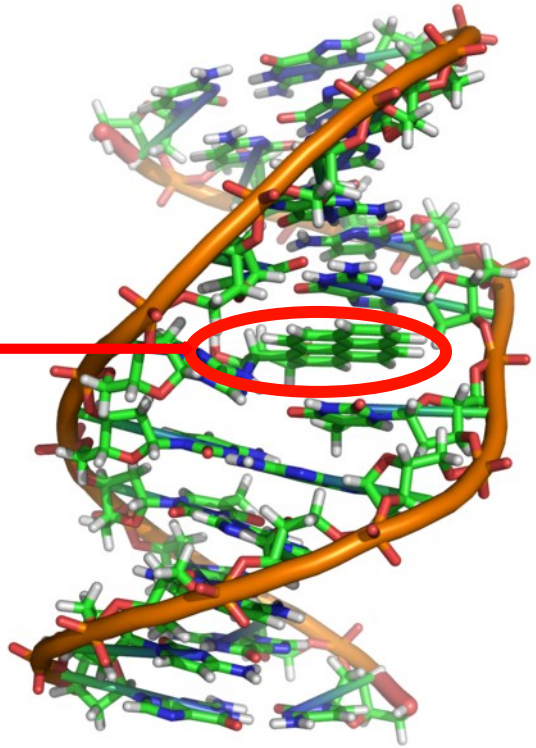
Ar- cpds can contain multiple aromatic rings



✓Benzo(a)pyrene found in tobacco smoke is converted to carcinogenic products in the liver.

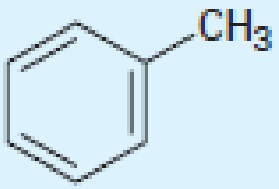
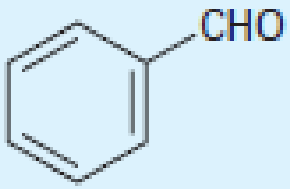
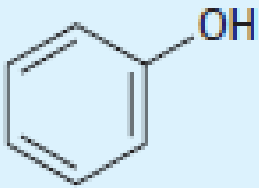
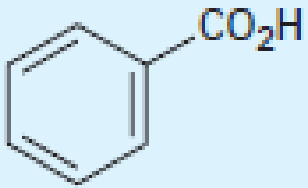
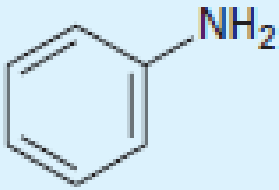
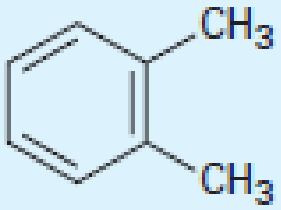
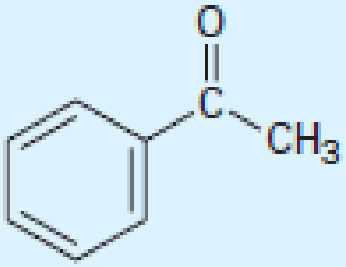
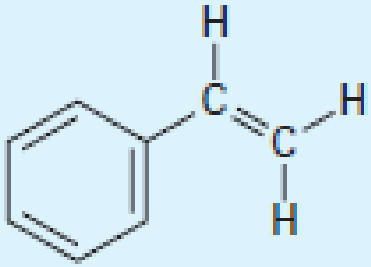
For instance, its health effects!





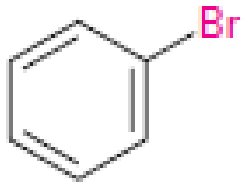
DNA and cause mutations

Common Names of Some Aromatic Compounds

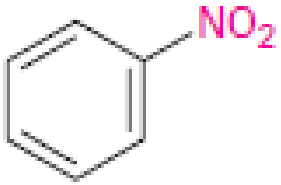
Structure	Name	Structure	Name
	Toluene (bp 111 °C)		Benzaldehyde (bp 178 °C)
	Phenol (mp 43 °C)		Benzoic acid (mp 122 °C)
	Aniline (bp 184 °C)		ortho-Xylene (bp 144 °C)
	Acetophenone (mp 21 °C)		Styrene (bp 145 °C)

IUPAC Name of Aromatic Cpds

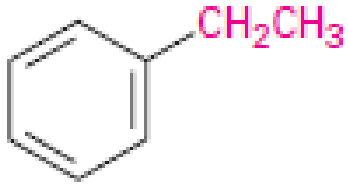
✓Monosubstituted benzenes are systematically named in the same manner as other hydrocarbons, with *-benzene as the parent name. For example!*



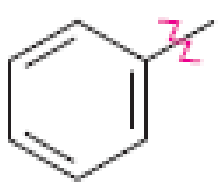
Bromobenzene



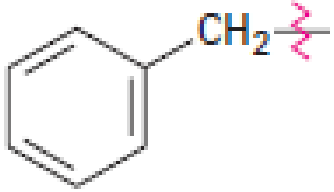
Nitrobenzene



Ethylbenzene



A phenyl group



A benzyl group

✓But for disubstituted benzenes are named using one of the

prefixes *ortho- (o), meta- (m), or para- (p).*

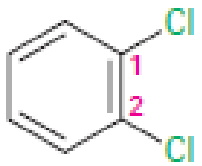
Naming, Aromatic Cpds!

✓*An ortho-disubstituted benzene has its two substituents* in a 1,2 relationship on the ring;

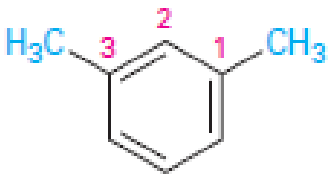
✓a meta-disubstituted benzene has its two substituents in a 1,3 relationship; and

✓a para-disubstituted benzene has its substituents in a 1,4 relationship

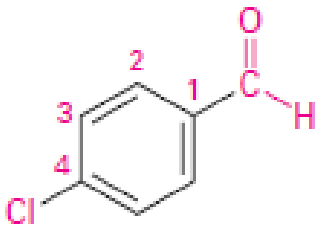
For instance



ortho-Dichlorobenzene
1,2 disubstituted



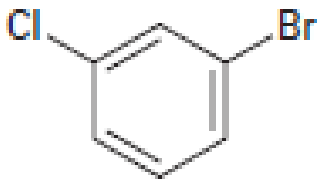
meta-Dimethylbenzene
(*meta*-xylene)
1,3 disubstituted

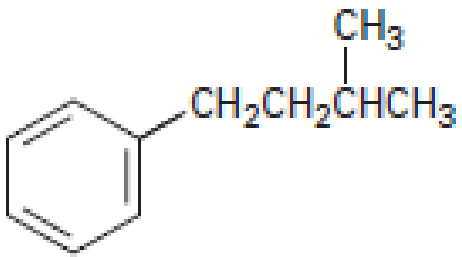


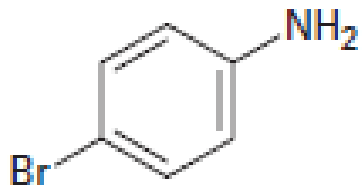
para-Chlorobenzaldehyde
1,4 disubstituted

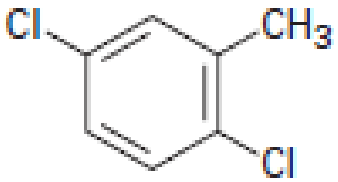
Exercise (1)

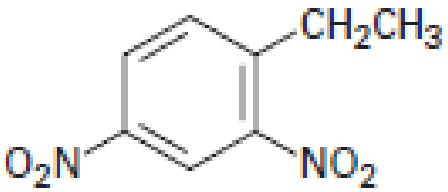
- Give IUPAC names for the following compounds

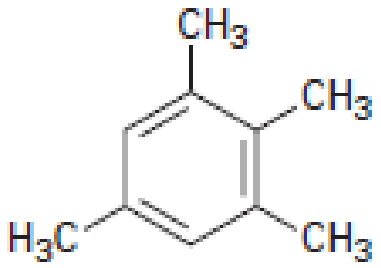
(a) 

(b) 

(c) 

(d) 

(e) 

(f) 

- Draw structures corresponding to the following IUPAC names:

(a)p-Bromochlorobenzene (b) p-Bromotoluene

(c) m-Chloroaniline (d) 1-Chloro-3,5-dimethylbenzene

Alcohols, Ethers and Epoxides

➢Alcohols, ethers and epoxides are three functional groups that contain carbon–oxygen sigma bonds.



alcohol



ether



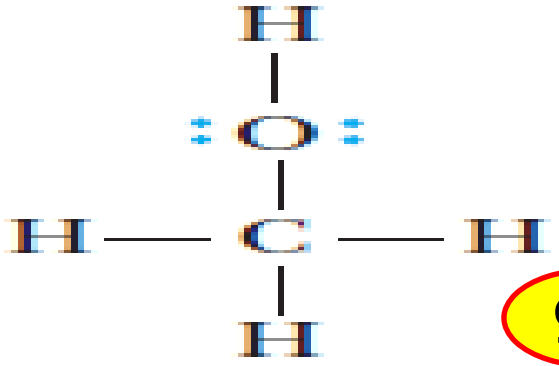
epoxide

❖Alcohols

✓It contains a hydroxyl group (OH group) bonded to sp^3 hybridized carbon atom.

✓The oxygen atom of an alcohol is also *sp3 hybridized*.

✓*Two sp3 hybrid orbitals of oxygen form sigma bonds to atoms of carbon and*

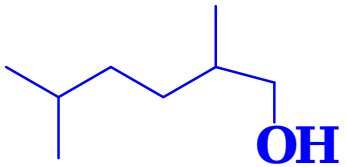


Main category of Alcohol

- Depending on the no. of –OH groups, alcohols are generally categorized as monohydric, dihydric and trihydric.
  - ✓ Monohydric alcohols

CH_3CH_2OH

Ethanol

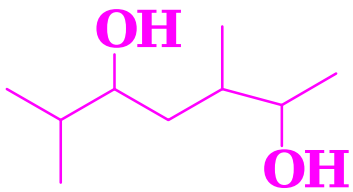


2, 5-dimethylhexanol

- ✓ **Dihydric alcohols**

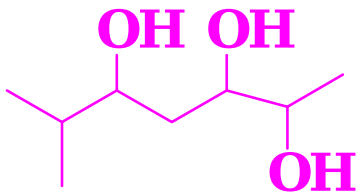


Ethan-1,2-diol (ethylene glycol)



3, 6-dimethylheptan-2,5-diol

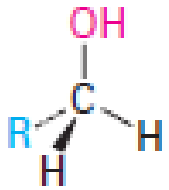
- ✓ **Trihydric alcohols**



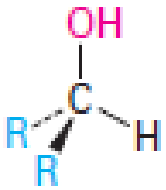
6-methylheptan-2,3,5-triol

Classification of Monohydric Alcohol

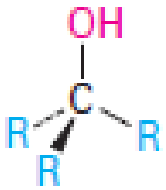
✓Depending on the number of carbon substituents bonded to the OH-bearing carbon; it classified as primary (1°), secondary (2°), or tertiary (3°).



A primary (1°) alcohol



A secondary (2°) alcohol

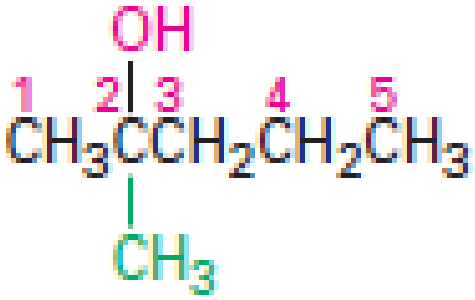


A tertiary (3°) alcohol

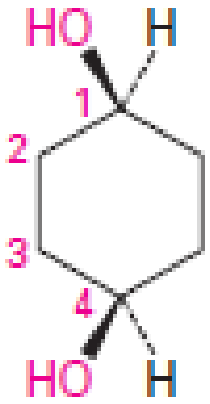
✓The nomenclatures of alcohols that derive the IUPAC names in the same manner as alkanes; the exception is the ending of the parent alkane is changed from *-e to -ol*.

✓Number the alkane chain beginning at the end; nearer the hydroxyl group.

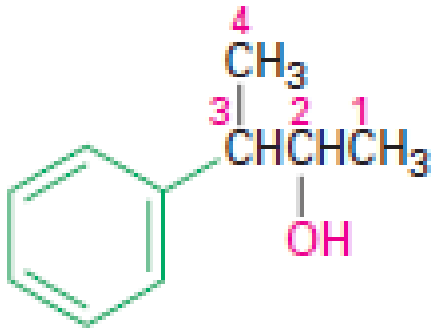
For instance;



2-Methylpentan-2-ol



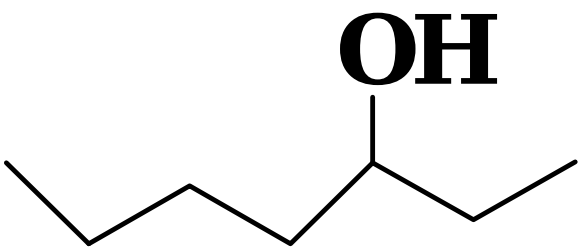
cis-Cyclohexane-1,4-diol

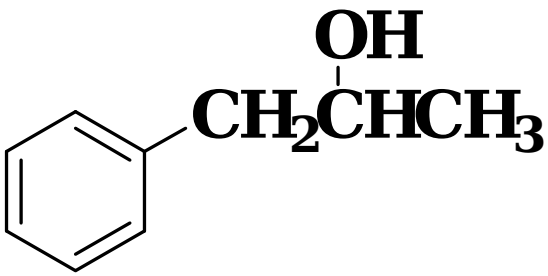


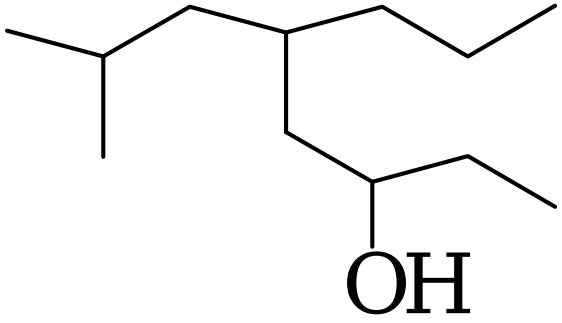
3-Phenylbutan-2-ol

Question (1)

✓**Provide the IUPAC name of the following given structures**







Physical Properties of Alcohols

Activity!

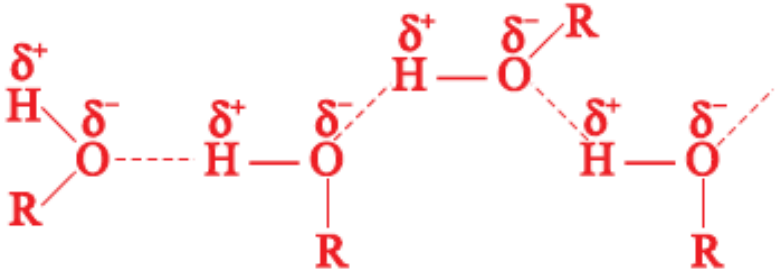
- ✓Why do alcohols have higher boiling points than the corresponding hydrocarbons?
- ✓Why boiling points of dihydric and trihydric alcohols are higher than those of monohydric alcohols of comparable molecular size?
- ✓Lower alcohols, like methanol and ethanol, are miscible with H_2O in all proportions, while higher hydrocarbons are not so. Explain.
- ✓Based on the *b.pt. of* H_2O, *and* CH_3OH, in which one would you expect to observe a greater degree

Polarity, B.Pt. and M.Pt. natures!

✓The –OH in an alcohol is polar due to the high EN of oxygen.

➢**Hydrogen bonding:**

✓As a result, there is significan **between molecules of an alcohol** alcohols



❖Due to the hydrogen bonding in alcohols;

✓have higher m.pt. and b.pt. than hydrocarbons of comparable molecular size.

✓Even it is also the *cause* for lower members to be liquids at room temperature.

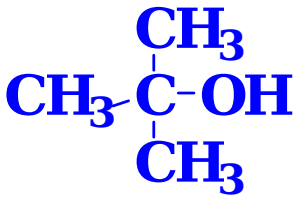
✓Straight-chain alcohol has more b.pt. than that of its Branched isomeric

For Example

$CH_3CH_2CH_2CH_2OH$

Butanol; b.pt 117.7 ^0C

While



tert-Butanol; b.pt. 82.5 ^0C

Solubility of Alcohol

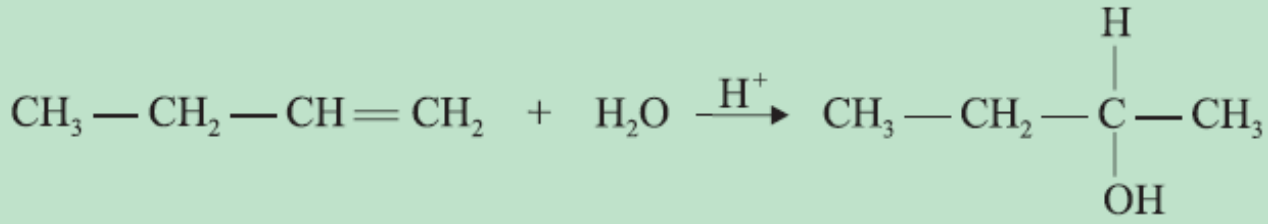
- ✓The first three alcohols, CH_3OH,CH_3CH_2OH and $CH_3CH_2CH_2OH$ are miscible with water in all proportions;
- ✓while the solubility in water decreases with increasing carbon number.
- ✓The water solubilities of dihydric and trihydric alcohols are higher than monohydric alcohols of similar mo

Preparation of Alcohols

➢The general laboratory methods for alcohols preparation are:

i) **Acid**

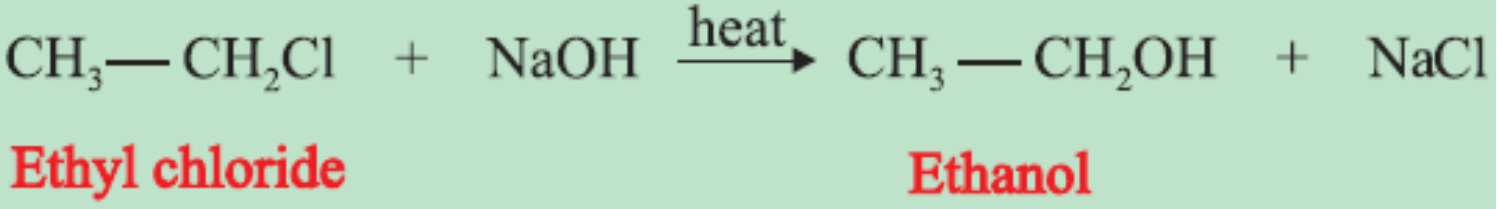
Example



ii) Hydrolysis of alkyl halides:

✓Warming alkyl halides with sodium hydroxide forms alcol

Example



Preparation of Alcohols,…

iii) Hydrolysis of Esters:

✓Heating esters with potassium hydroxide produce alc

Example

$$CH_3COOCH_2CH_3 + KOH \xrightarrow{heat} CH_3COOK + CH_3CH_2OH$$

Ethyl acetate — Ethanol

❖**Industrial preparation of Alcohol**

ermentation of carbohydrates such as sugar,

$$C_{12}H_{22}O_{11} + H_2O \xrightarrow{invertase} C_6H_{12}O_6 + C_6H_{12}O_6$$

Sucrose — Glucose — Fructose

Example

$$C_6H_{12}O_6 \longrightarrow 2CH_3CH_2OH + 2CO_2$$

Glucose — Ethanol

Exercise (1)

Write the products in the following chemical reaction:

i) $CH_3CH_2CH_2Cl + KOH \xrightarrow[Heat]{}$

ii) $CH_3COOCH_2CH_3 + KOH \longrightarrow$

iii) $C_6H_{12}O_6 \xrightarrow{Zymase}$

iv) $CH_2{=}CH_2\,(g) + H_2O\,(g) \xrightarrow[573\ k/60\ atm]{H_3PO_4}$

Chemical Properties of Alcohols

- ✓Why alcoholic beverages such as "Tela", "Tej", beer and wine turn sour if they are not properly stored?
- ✓What types of reactions do alcohols undergo?
- ✓Alcohols contain a hydrocarbon group and a functional group (–OH) and which part of alcohols is responsible for chemical reactions?

➢Reactions of alcohols may involve:

- ✓ the bond cleavage of the (— O — H) and
- ✓the bond cleavage of the (— C — O) bond.

Rxns involving the –O–H bond cleavage

a) Alcohols react with strongly electropositive metals;

Example

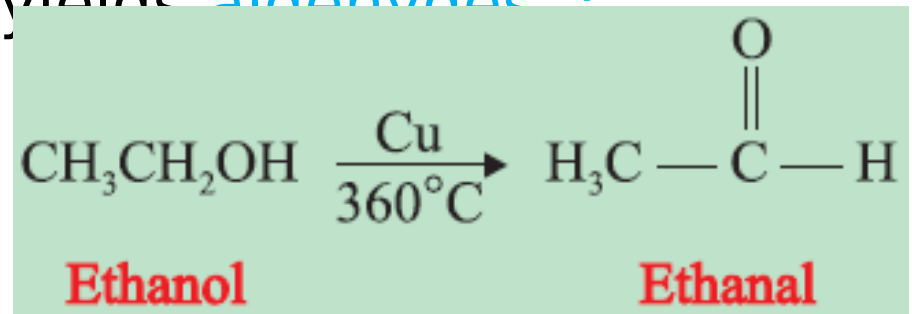


Ethanol — Sodium ethoxide

Oxidation of alcohols,
he reactions is depend on the nature of Oxidizing age

i) Oxidation of 1^0 alcohols in the presence of mild oxidizing agents yields aldehydes ;

❖For instance



Ethanol — Ethanal

Using strong Oxidizing agents

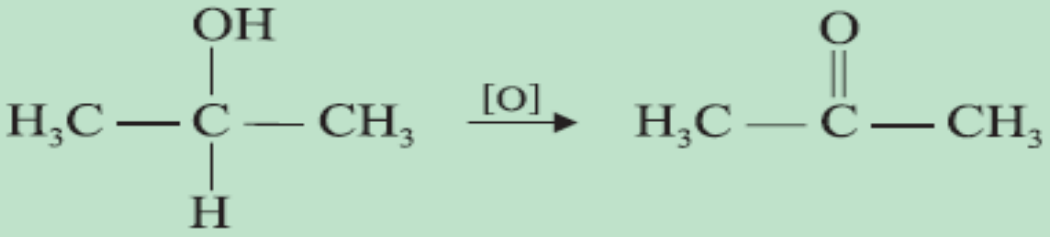
✓Strong oxidizing agents, such as acidified $KMnO_4$ or $K_2Cr_2O_7$ and CrO_3 in H_2SO_4, oxidize primary alcohol first to aldehydes, then to carboxylic acids

Example



) Oxidation of 2^0 alcohols yields ketones

Example

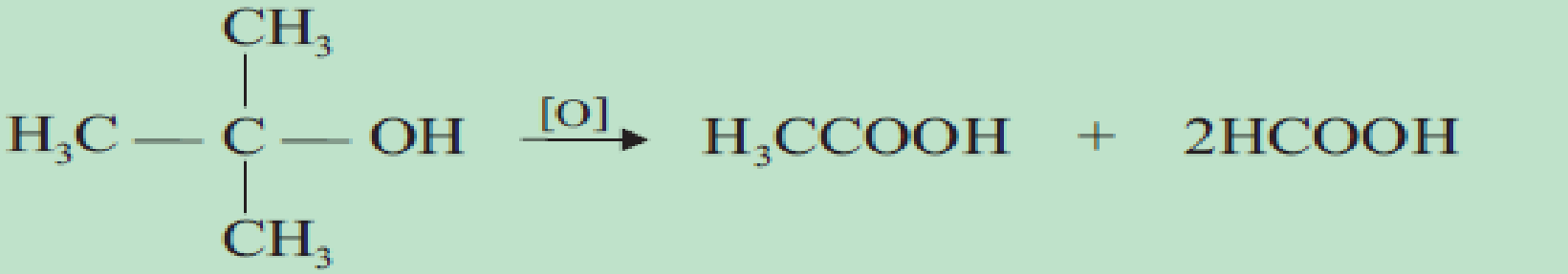


Oxidations of Alcohol,...

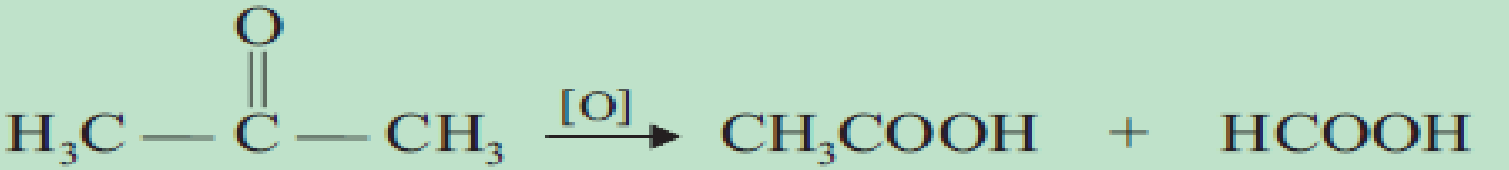
iii) Tertiary alcohols and ketones are generally resistant to oxidation.

✓However, they can undergo oxidation under drastic conditions to form a mixture of carboxylic acids.

Examples



3°alcohol Ethanoic acid Methanoic acid

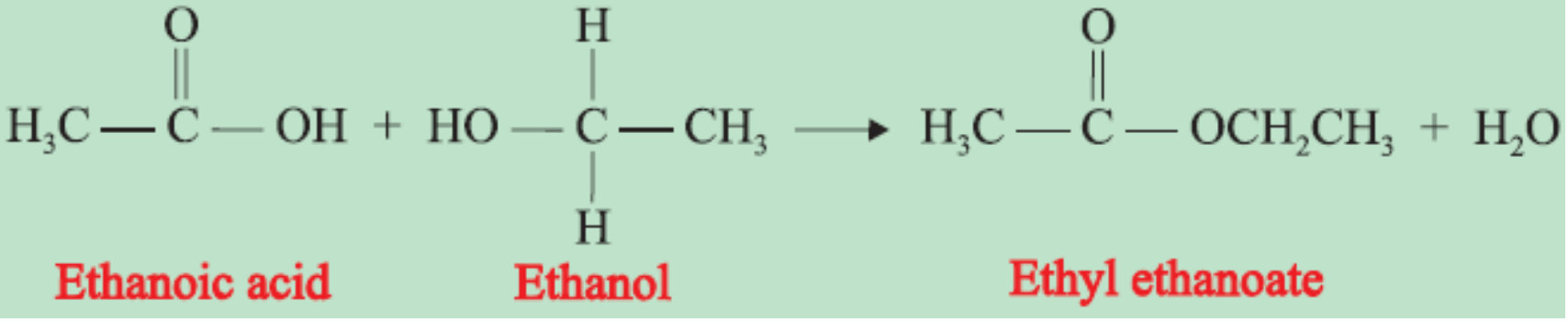


Propanone (ketone) Ethanoic acid Methanoic acid

c) Esterifications reaction

- ✓Carboxylic acids react with alcohols to form esters.

Example

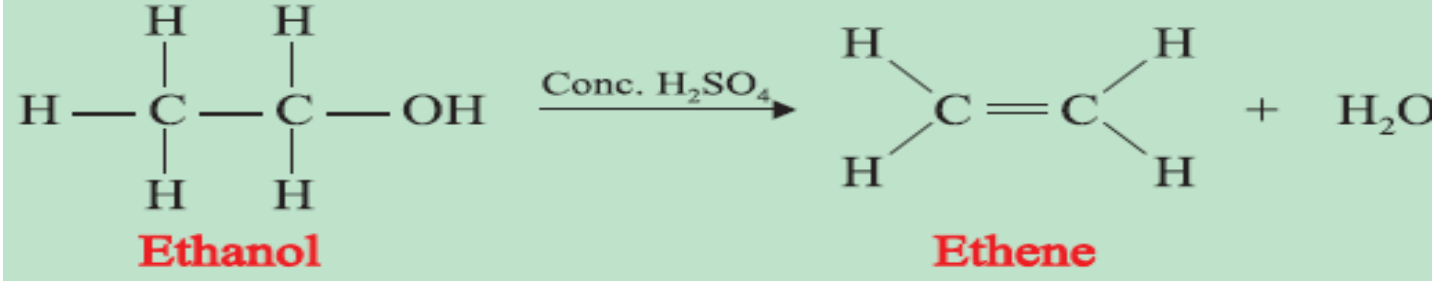


- ❖The reactions involving the – C – O bond cleavage.

a) Dehydration of alcohols

- ✓H_2SO_4 act as dehydrating agents

Example



Rxn involving the – C – O bond cleavages

b) Rxn of alcohols with hydrogen halides produce alkyl halides

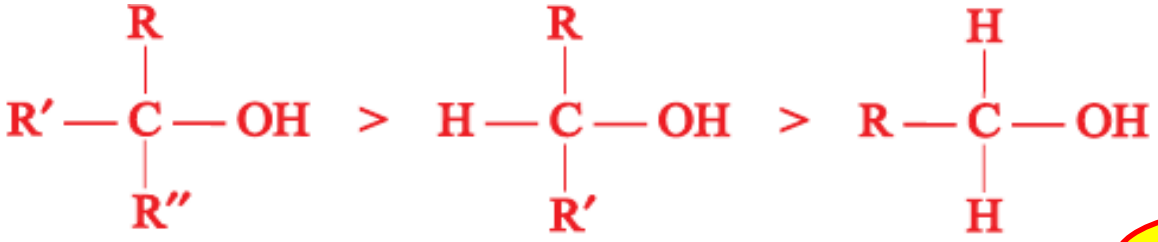
Example



Ethanol — Ethyl chloride (1-chloroethane)

❖Be remind!

✓The overall tendency of alcohols to undergo dehydration is in the following

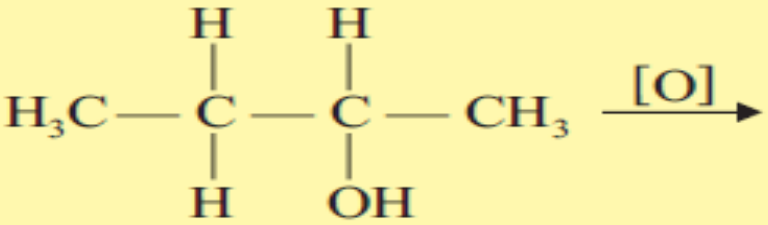


Tertiary alcohol — Secondary alcohol — Primary alcoh

Exercise (2)

1. Write the general structural formulas for aldehydes and ketones.
2. What structural difference do you see between aldehydes and ketones?
3. Write the general structural formulas for carboxylic acids and esters.
4. Which functional group characterizes alcohols?
5. Complete the following chemical reactions

a $CH_3CH_2CH_2OH \xrightarrow{[O]}$

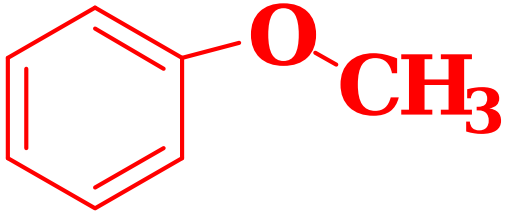
b 

c $CH_3CH_2COOH + CH_3CH_2OH \xrightarrow{H^+}$

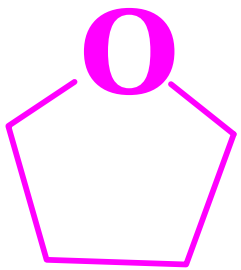
Ethers, then what?

- ✓Ethers (R-O-R'**),** like the alcohols and are also organic derivatives of H_2O;
- ✓W/c have two alkyl groups bonded to an oxygen atom.
- ✓It is symmetrical if the two alkyl groups are the same, and unsymmetrical if they are different.
- ✓Perhaps the most well-known ether is diethyl ether; $CH_3CH_2OCH_2CH_3$
- ✓which has a long history of medicinal use as an anesthetic and industrial use as a solvent.

Its uses,...



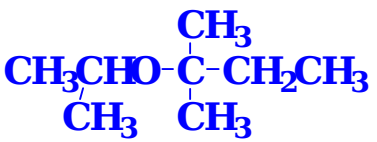
- ✓ ethers also include anisole, a pleasant-smelling aromatic ether used in perfumery.
- ✓ Tetrahydrofuran (THF), a cyclic ether often used as a solvent.



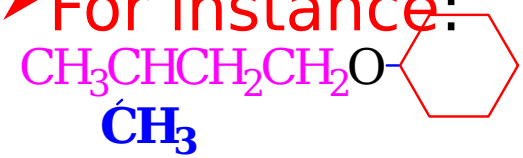
- ➢ The common name of an ether consists of the 2R substituents (in alphabetical order) w/c followed by the word ether.
- ➢ For instance:



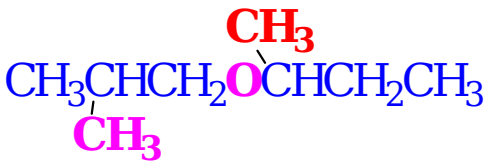
Ethyl methyl ether



tert-pentyl isopropylether



cyclohexyl isopentyl ether



isobutyl,sec-butylether

The IUPAC naming system

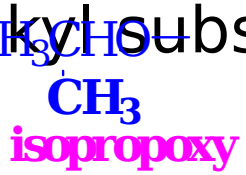
- ✓The names of an ether as an alkane with an RO substituent.
- ✓The substituents are named by replacing the "yl"' ending in the name of the alkyl substituent with "oxy"



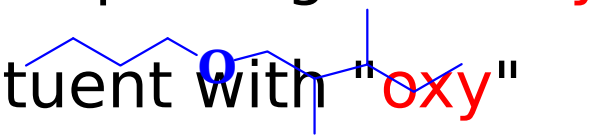
methoxy



ethoxy



isopropoxy

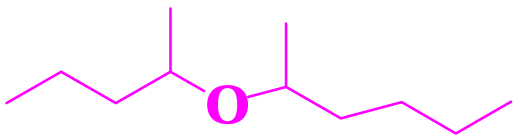


1-butoxy-2,3-dimethyl pentane

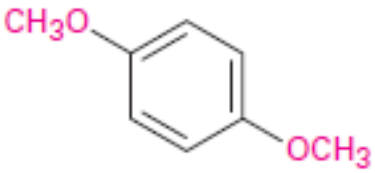
xercise (1)

Name the IUPAC system of the following structures.

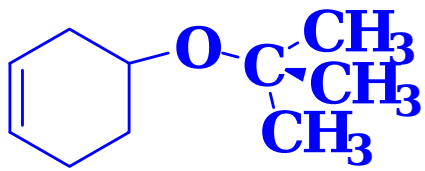
a)



b)

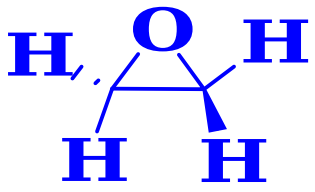


c)



Epoxides or oxiranes,

- ✓ one group of cyclic ethers;
- ✓ w/c different from open-chain ethers;
- ✓ are the three-membered-ring compounds.



Ethylene Oxide

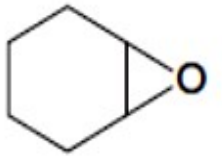
- ✓ Ethylene oxide, (epoxide), is an intermediate in the manufacture of ethylene glycol, used for automobile antifreeze, and polyester polymers.
- ✓ the name ethylene oxide *is* not a systematic one because the

–ene ending.

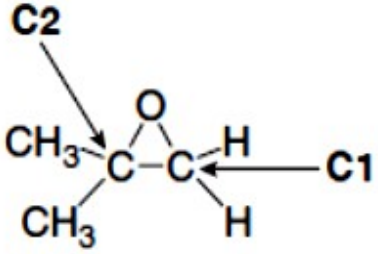
- ✓ The name is frequently used, however, ethylene oxide is

For instance

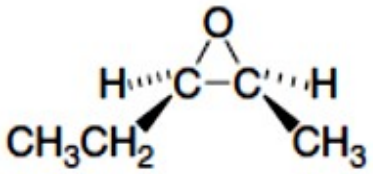
✓Epoxides are named in three different ways, epoxyalkanes, oxiranes, or alkene oxides.



1,2-epoxycyclohexane



1,2-epoxy-2-methylpropane



cis-2,3-epoxypentane

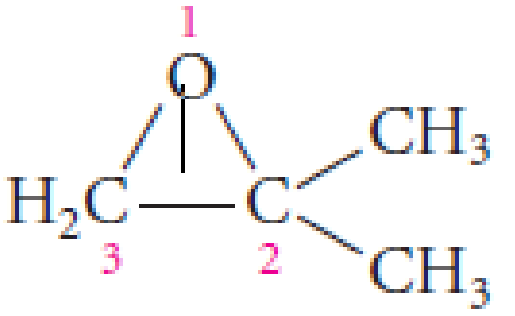
✓Epoxides bonded to a chain of carbon atoms can also be named as derivatives of oxirane;

✓the simplest epoxide having two carbons and one oxygen atom in a ring

✓Oxirane is the parent compound of a special class of heterocyclic ethers.

Labeling the epoxide,...

✓The atoms of the epoxide ring are numbered consecutively, with the oxygen receiving the number 1 regardless of the substituents present.



2,2-dimethyloxirane

Exercise (1)

i) Give a substitutive name for each of the following compounds

A) $(CH_3)_3C–O–CH_3$ B) $H_3CH_2C–O–CH_2CH_2OH$

ii) Draw the structure of each of the following compounds.

(a) ethyl propyl ether (b) dicyclohexyl ether

Basic Application of Epoxide

✓Although epoxides occur less widely in natural products than alcohols or ethers.

➢recently introduced drugs that contain an epoxide are eplerenone and tiotropium bromide.

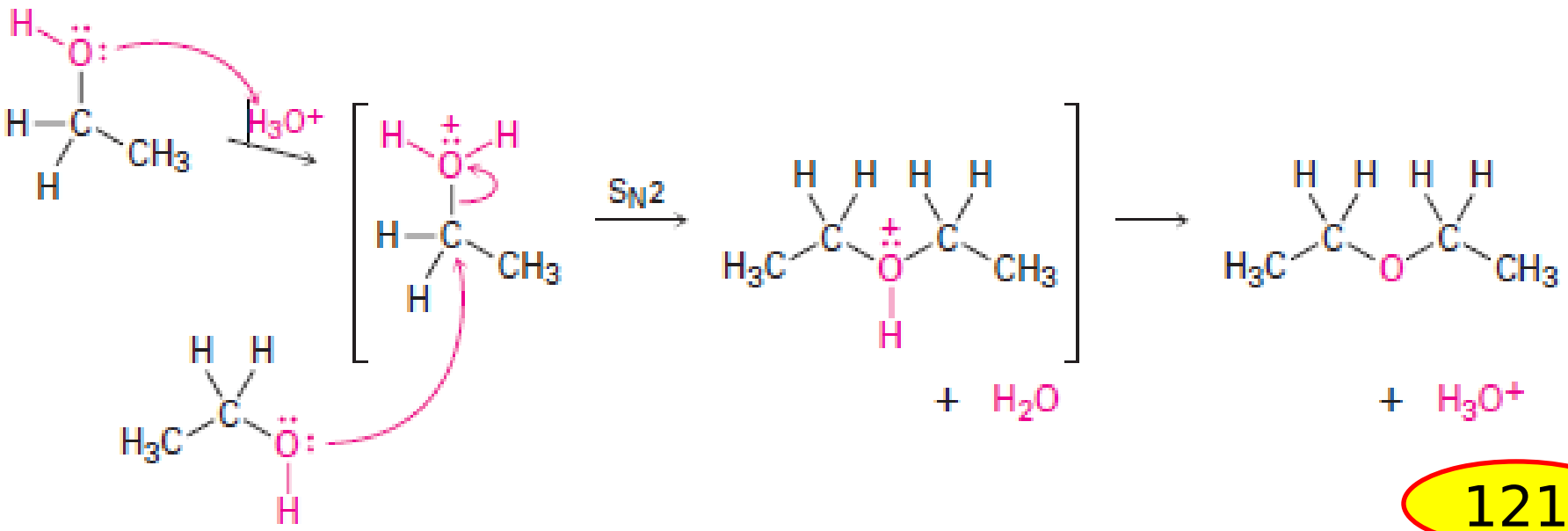
➢Eplerenone (trade name Inspra) is prescribed to reduce cardiovascular risk in patients.

➢Tiotropium bromide (trade name Spiriva) is a long-acting bronchodilator used to treat the chronic obstructive pulmonary disease of smokers.

Preparation of ethers and epoxides

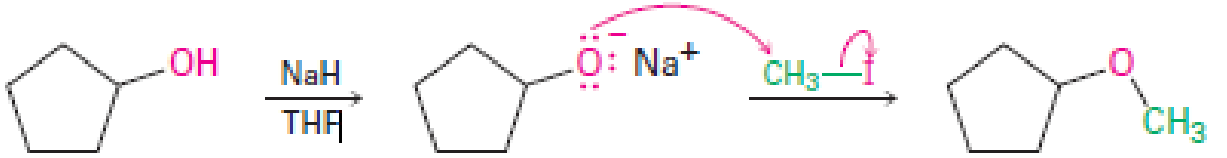
✓Diethyl ether and other simple symmetrical ethers are prepared industrially by the H_2SO_4 catalyzed reaction of alcohols.

➢The reaction occurs by S_N2 displacement of H_2O from a protonated ethanol molecule by the oxygen atom of a



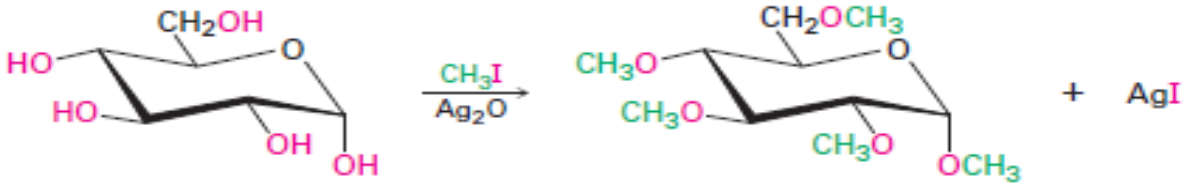
The Williamson Ether Synthesis

- Like alcohols; ethers are both common products of nucleophilic substitution.
- The method is an alkoxide ion reacts with a primary alkyl halide or tosylate in an S_N2 reaction. Example;



Cyclopentanol | Alkoxide ion | Cyclopentyl methyl ether (74%)

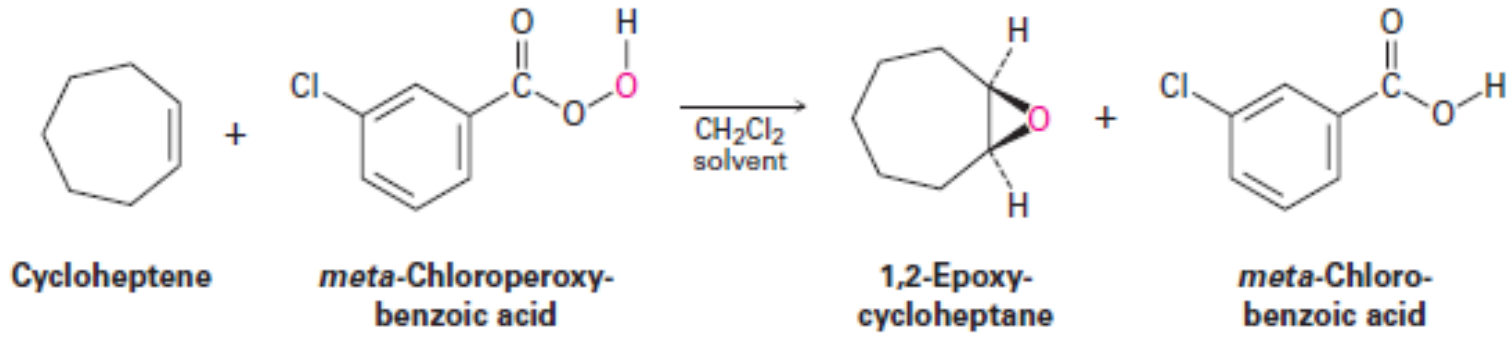
- Another useful variations of Williamson synthesis also involves with Ag_2O, as a mild base rather than NaH.



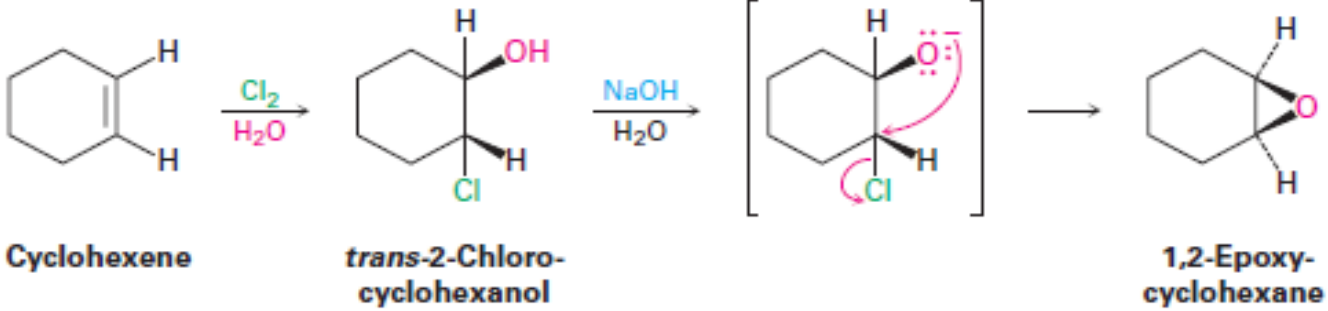
α-D-Glucose | α-D-Glucose pentamethyl ether (85%)

Epoxide synthesize

- In the laboratory, epoxides are usually prepared by treatment of an alkene with a peroxyacid (RCO_3H), typically *m-chlorc*



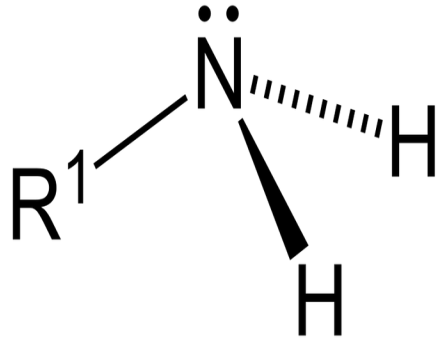
- Epoxides can also be prepared from halohydrins, themselves produced by electrophilic addition of HO-X to alkenes.

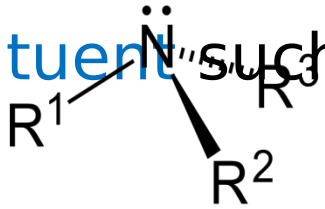


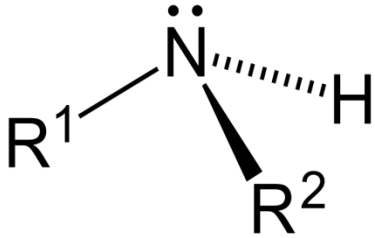
Amines

✓In organic chemistry, amines are compounds that contain a basic nitrogen atom with a lone pair.

✓It is formally derivative of NH_3, where in one or more hydrogen atoms have been replaced by a substituent such as an alkyl or aryl group.





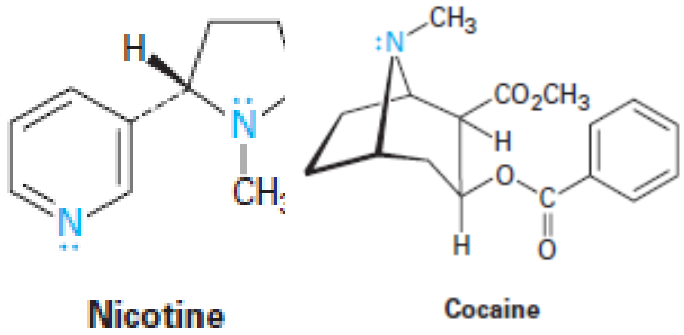


➢Amines occur widely in all living organisms.

✓Trimethylamine, for instance, occurs in animal tissues and is partially responsible for the distinctive odor o

Occurrence of Amine,...

✓nicotine is found in tobacco; and cocaine is a stimulant found in the leaves of the South American coca bush.

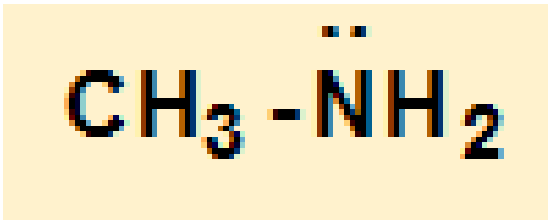


✓In addition, amino acids are the building blocks from which all proteins are made, and cyclic amine bases are constituents of nucleic acids.

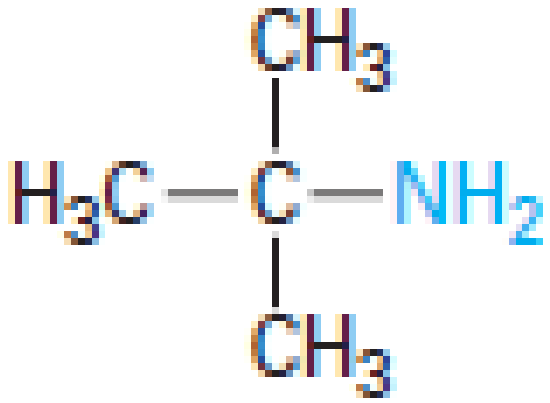
Structure & Classification

➢Amines can be classified according to the nature and number of substituents on nitrogen.

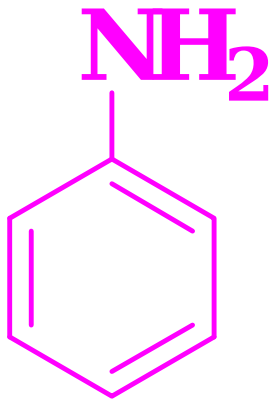
i) Primary (1°) amines**:** 1° amines arise when one of three hydrogen atoms in ammonia is replaced by an alkyl or aromatic group,



methylamine



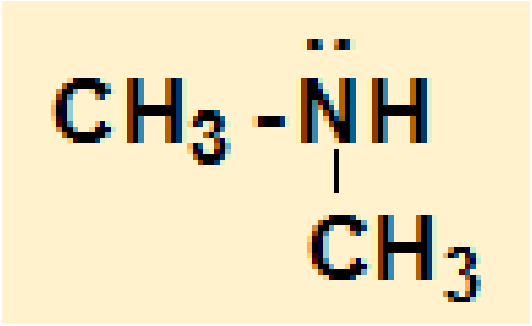
tert-Butylamine



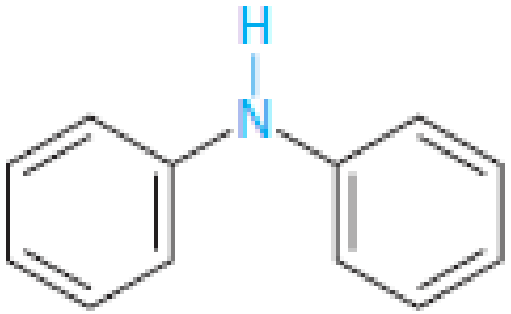
aniline

ii) Secondary (2°) amines

✓**2°** amines have two organic substituents (alkyl, aryl or both) bound to the nitrogen together with one hydrogen.



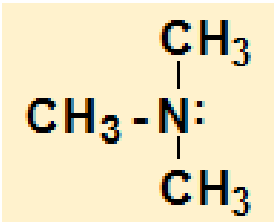
Dimethylamine



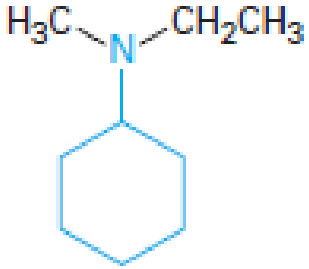
Diphenylamine

iii) Tertiary (3°) amines

✓In **3°**amine, nitrogen has three organic substituents



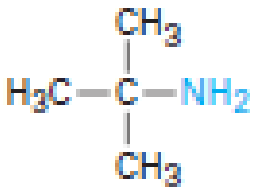
Trimethylamine



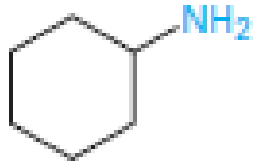
N-Ethyl-N-methylcyclohexylamine

Naming of Amines

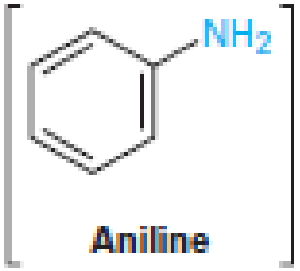
- Primary amines are named in the IUPAC system;
- For simple amines, the suffix -amine is added to the name of the alkyl substitu
- For example; phenylamine, $C_6H_5NH_2$, has the common name *aniline*.



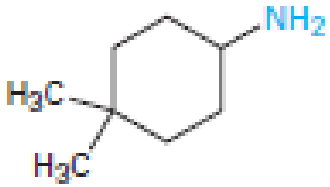
tert-Butylamine



Cyclohexylamine



Aniline



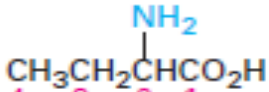
4,4-Dimethylcyclohexanamine

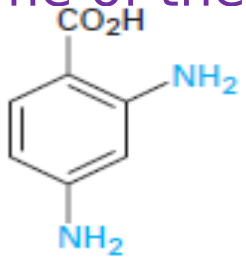
$H_2NCH_2CH_2CH_2CH_2NH_2$

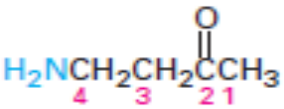
1,4-Butanediamine

Exercise 1

- Give the IUPAC Name of the ff.

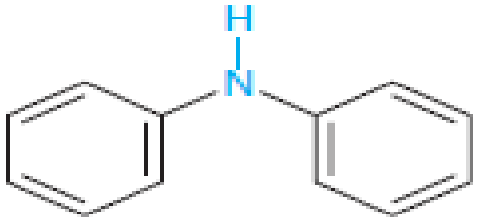




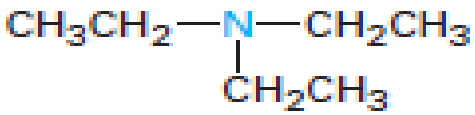


Secondary and Tertiary Amines

- Symmetrical secondary and tertiary amines are named by adding the prefix *di-* or *tri-* to the alkyl group.

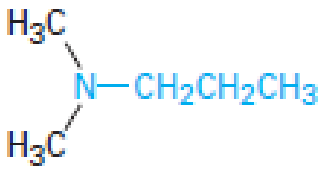


Diphenylamine

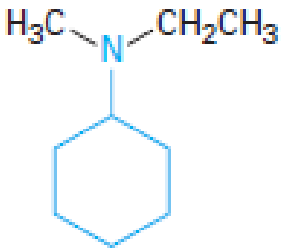


Triethylamine

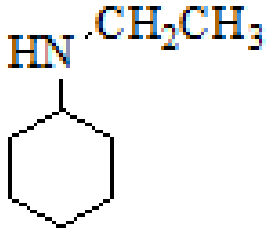
- Unsymmetrical substituted secondary and tertiary amines are named as N-substituted primary amines.
- For example:



***N,N*-Dimethylpropylamine**

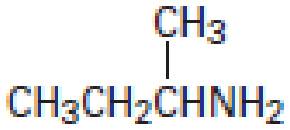


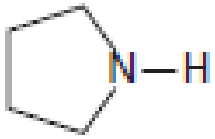
***N*-Ethyl-*N*-methylcyclohexylamine**

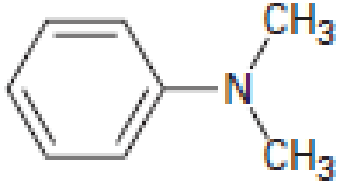


N-Ethylcyclohexanamine

(1) Classify each of the following compounds as either a primary, secondary, or tertiary amine:

(a) 

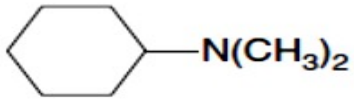
(b) 

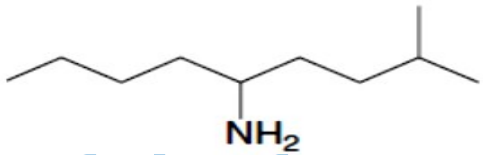
(c) 

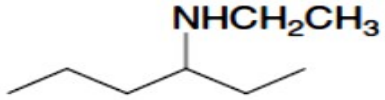
(2) Name each amine

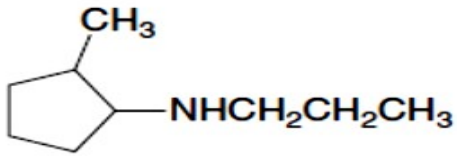
a. $CH_3CH_2CH(NH_2)CH_3$

b. $(CH_3CH_2CH_2CH_2)_2NH$

c. 

d. 

e. 

f. 

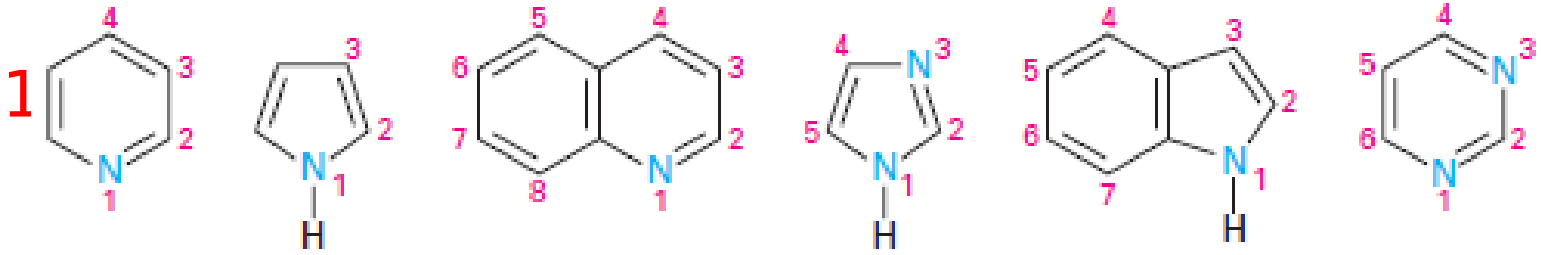
(3) Draw structures of the following compounds

(a) A secondary amine with one isopropyl group;

(b) A tertiary amine with one phenyl group and one ethyl group;

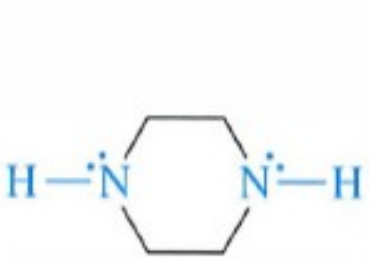
Heterocyclic amines

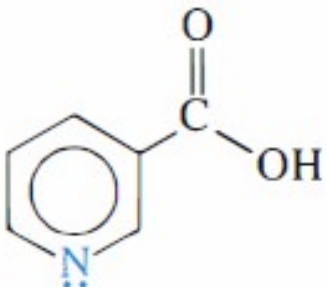
- ✓compounds in which the N atom occurs as part of a ring,
- ✓each different heterocyclic ring system has its own parent name.
- ✓For instance:
- ✓The heterocyclic N atom is always numbered as position 1

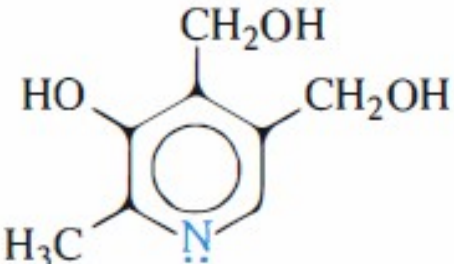


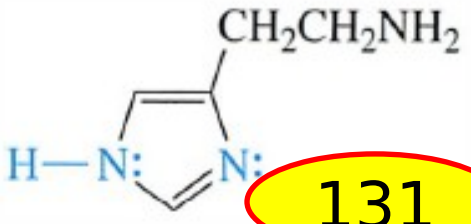
Pyridine Pyrrole Quinoline Imidazole Indole Pyrimidine

Exercise (1) Name the following heterocyclic ring of N atom.









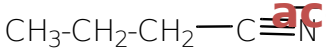
Nitriles

✓Nitrile is compounds that contain a $-C\equiv N$ functional group

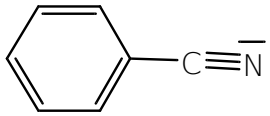
✓It is analogous to carboxylic acids in w/c both have a carbon atom with three bonds to an EN atom and both contain a *pi bond*.



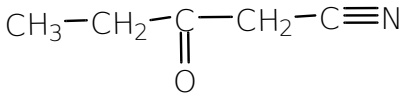
ethanonitrile, acetonitrile



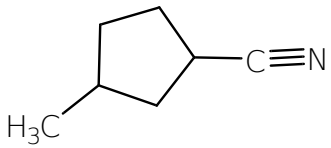
butannitrile



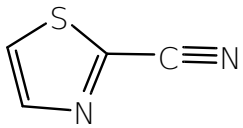
benzonitrile, benzoic acid nitrile



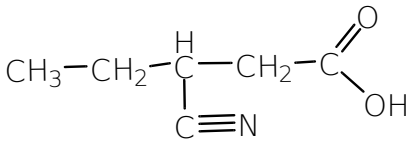
3-oxo-pentannitrile



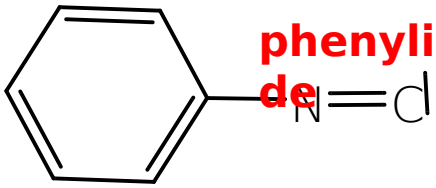
3-methylcyclopentane carbonitrile



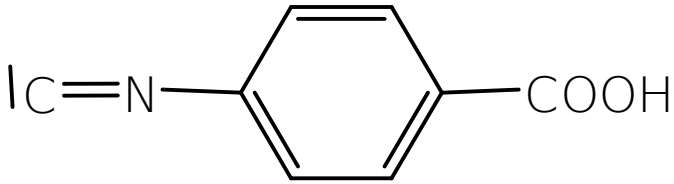
thiazole-2-carbonitrile



3-cyano-pentanoic acid



phenylisocyanide



4-isocyanobenzoic acid

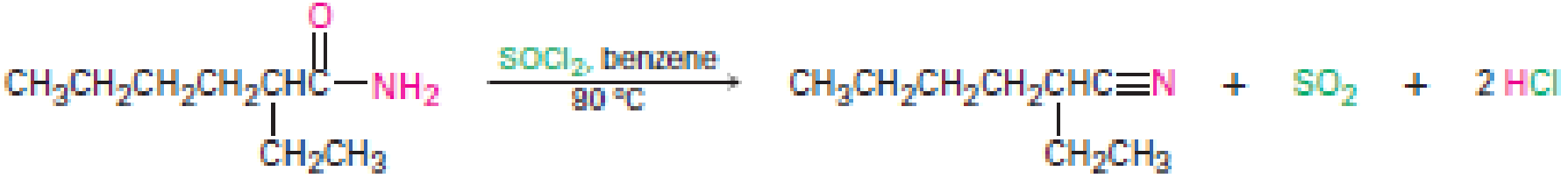
Preparation of nitriles

✓The simplest method of nitrile preparation is the SN^2 reaction of CN^- with a primary or secondary alkyl halide.

$$CH_3CH_2CH_2Br + CN^- \longrightarrow CH_3CH_2CH_2CN + Br^-$$

✓Another method for preparing nitriles is by dehydration of a primary amide, $RCONH_2$.

✓Thionyl chloride is often used for the reaction, although other dehydrating agents such as $POCl_3$ also work.

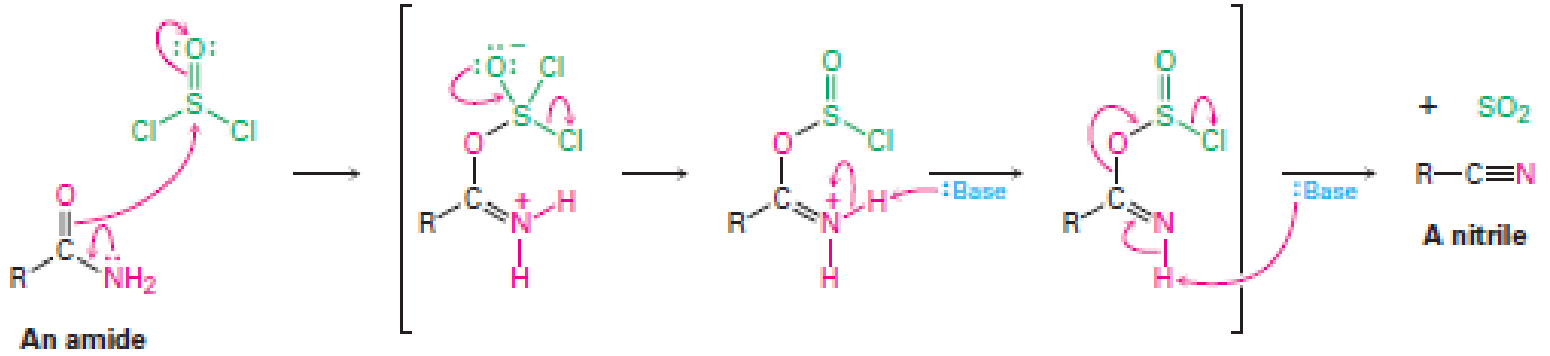


2-Ethylhexanamide

2-Ethylhexanenitrile (94%)

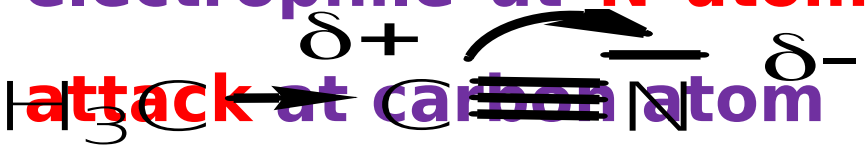
Possible mechanism

✓The dehydration occurs by initial reaction of $SOCl_2$ on the nucleophilic amide oxygen atom, followed by deprotonation and a subsequent E2 like elimination rea

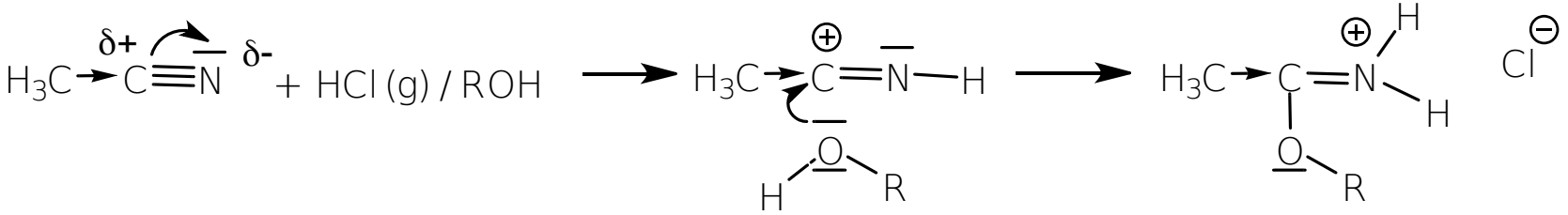


REACTIVITY of Nitriles

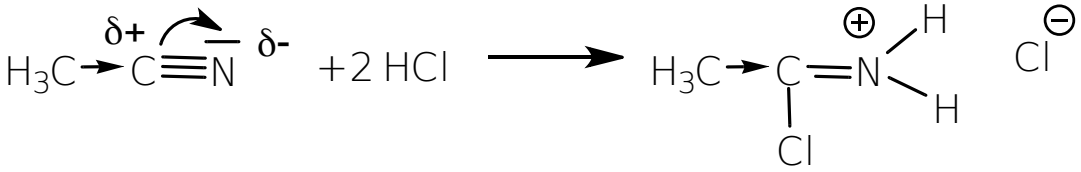
1)activation of the triple bond by the attack of electrophile at N atom followed by nucleophilic attack at carbon atom



For Examples

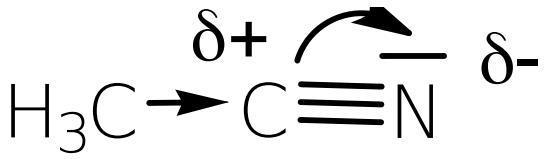


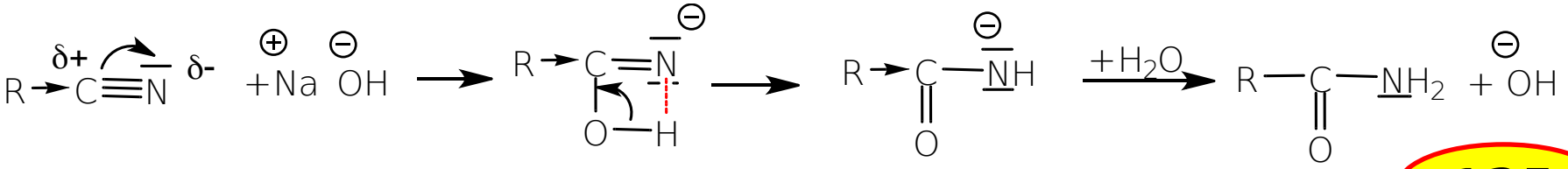
iminoether hydrochloride

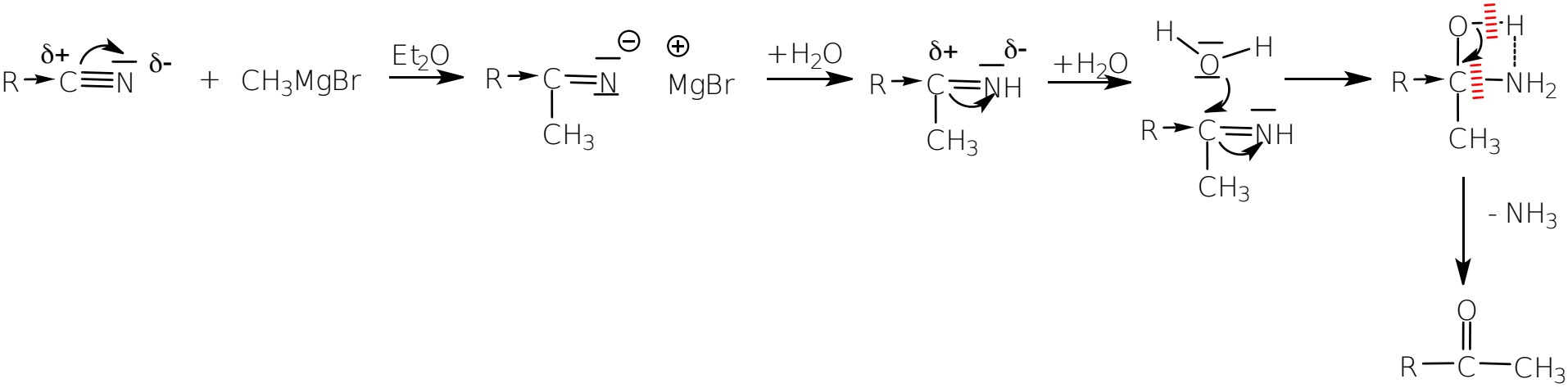


iminochloride hydrochloride

2) a strong nucleophile is able to attack carbon atom directly

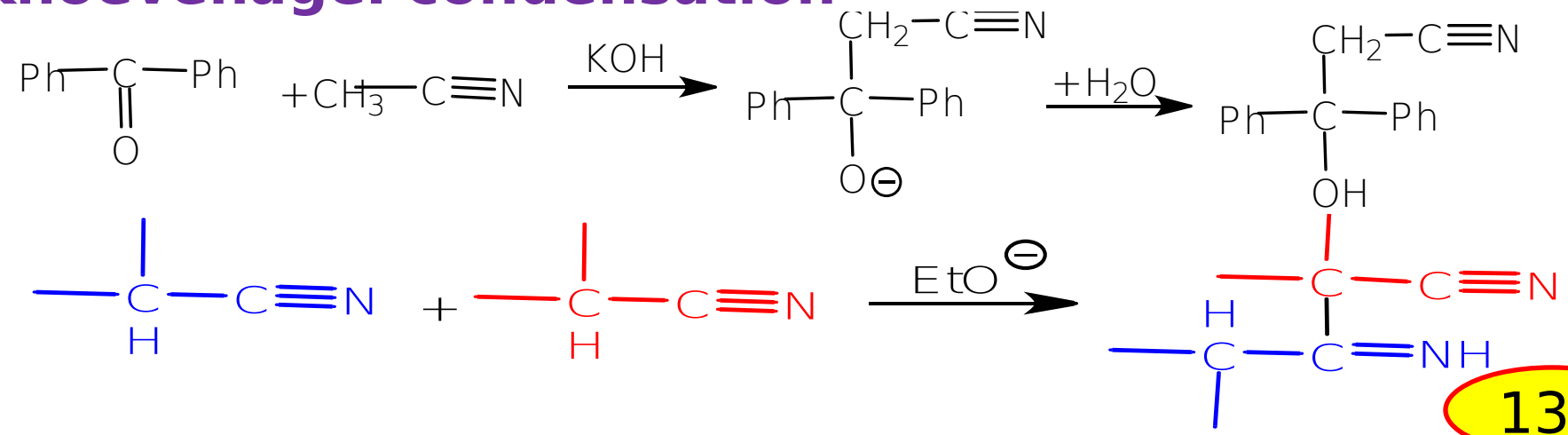






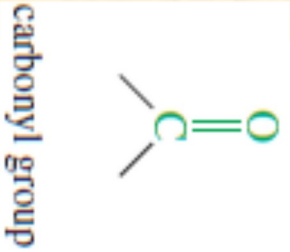
3) acidic hydrogen atom in a-position

✓condensation with aldehydes and ketones Knoevenagel condensation



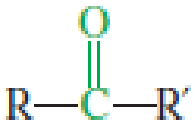
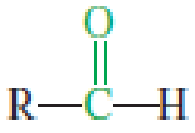
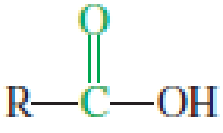
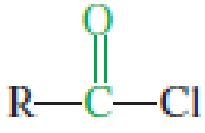
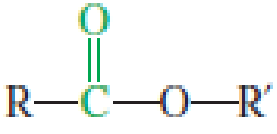
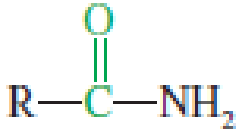
Aldehyde and ketones

- ✓Both are the simplest carbonyl compounds



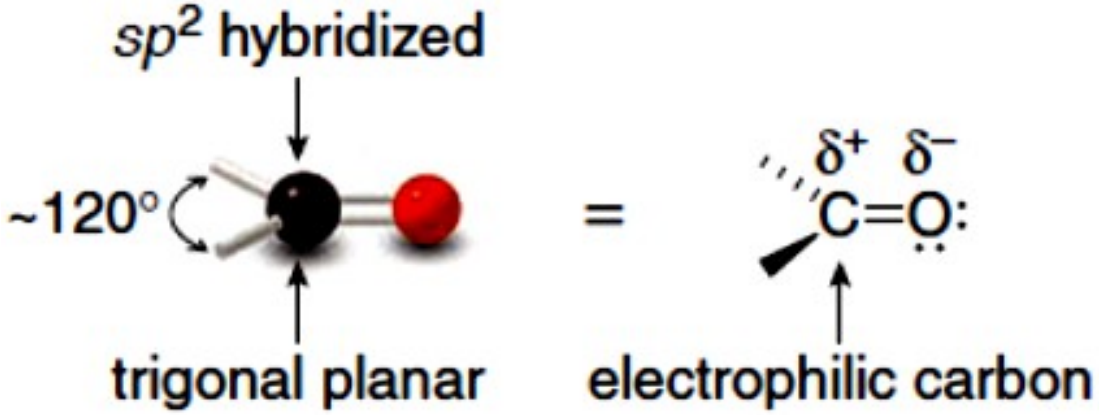
- ✓Many play important roles in biological processes.
- ✓ Hormones, vitamins, amino acids, drugs, and flavorings are just a few of the carbonyl compounds that affect us daily.

Common Classes of Carbonyl Compounds

Class	General Formula	Class	General Formula
ketones		aldehydes	
carboxylic acids		acid chlorides	
esters		amides	

Possible Structures of Carbonyl Groups

✓Two structural features determine the chemistry and properties of aldehydes and ketones.



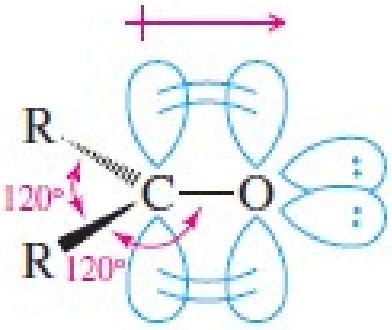
✓The carbonyl group is sp^2 hybridized and trigonal planar, making it relatively uncrowded.

✓The EN atom polarizes the carbonyl group, making the carbonyl carbon electrophilic.

✓As a result, aldehydes and ketones react with

Exceptional View

✓The double bond between carbon and oxygen is similar to an alkene double bond, except that the carbonyl double bond is shorter, stronger, and polarized.



	length	*energy*
ketone C═O bond	1.23 Å	745 kJ/mol (178 kcal/mol)
alkene C═C bond	1.34 Å	611 kJ/mol (146 kcal/mol)

✓The double bond of the carbonyl group has a large dipole moment because oxygen is more EN than carbon, and the bonding electrons are not shared equally.

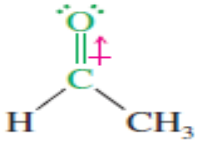
Electronic transition

✓In particular, the less tightly held pi electrons are pulled more strongly toward the oxygen atom,

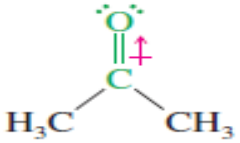
✓giving ketones and aldehydes larger dipole moments than most alkyl halides



✓The first resonance form is more important because it involves more bonds and less charge separation.

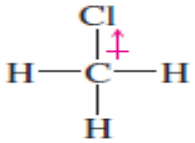


μ = 2.7 D
acetaldehyde

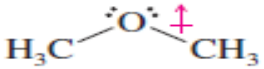


μ = 2.9 D
acetone

Compare with:



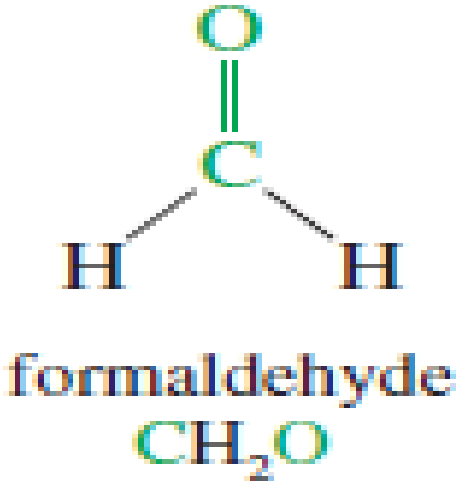
μ = 1.9 D
chloromethane



μ = 1.30 D
dimethyl ether

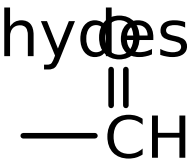
aldehyde

✓It has one alkyl (or aryl) group and one hydrogen atom bonded to the carbonyl carbon atom.



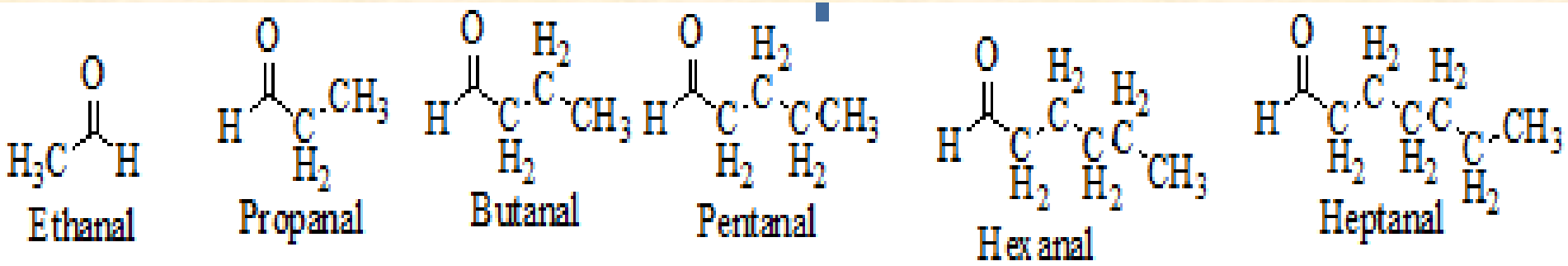
Eg., Formaldehyde is the simplest aldehyde, with two hydrogen atoms bonded to the carbonyl group.

✓The longest continuous chain that contains the group provides the base name for aldehydes



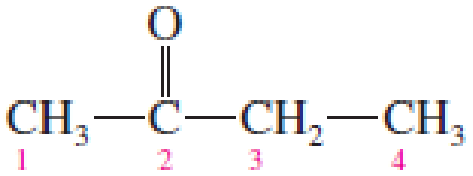
✓The *-e* ending of the corresponding alkane name is replaced by *-al*, and substituents are specified in the usual

Example

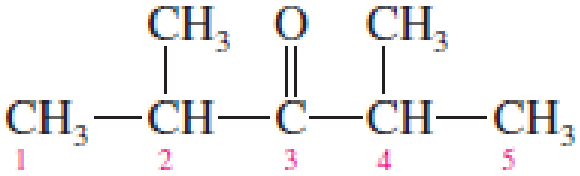


IUPAC Names

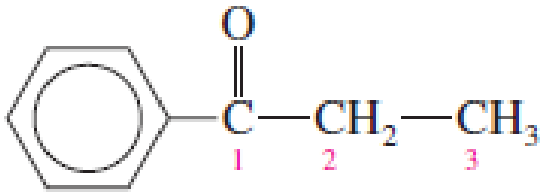
✓Systematic names of ketones are derived by replacing the final -*e in* the alkane name with –*one and the "alkane" name becomes "alkanone."*



2-butanone
butan-2-one

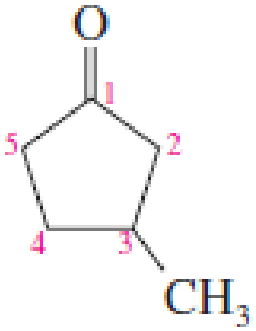


2,4-dimethyl-3-pentanone
2,4-dimethylpentan-3-one

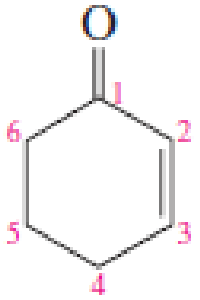


1-phenyl-1-propanone
1-phenylpropan-1-one

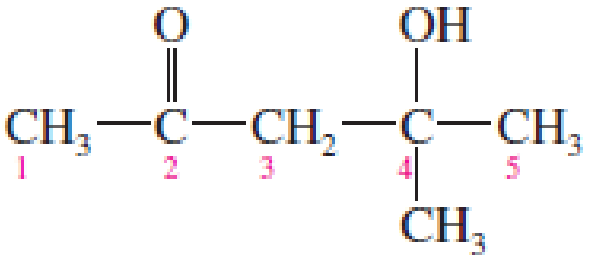
For instance;



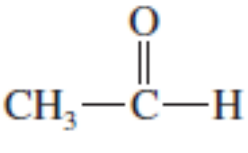
3-methylcyclopentanone



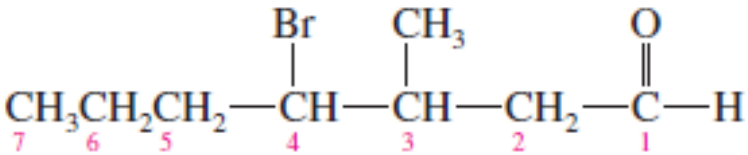
2-cyclohexenone
cyclohex-2-en-1-one



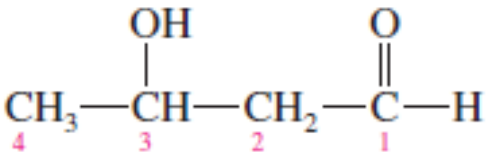
4-hydroxy-4-methyl-2-pentanone
4-hydroxy-4-methylpentan-2-one



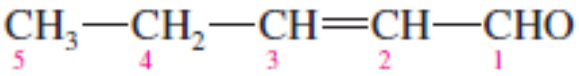
ethanal



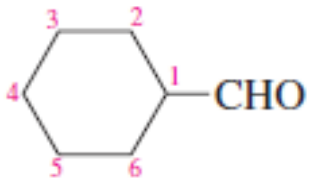
4-bromo-3-methylheptanal



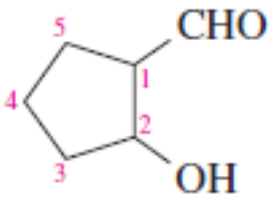
3-hydroxybutanal



2-pentenal
pent-2-enal



cyclohexanecarbaldehyde

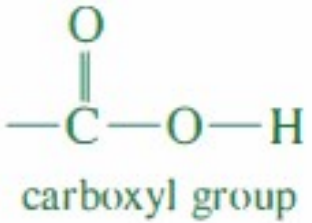


2-hydroxycyclopentane-1-carbaldehyde

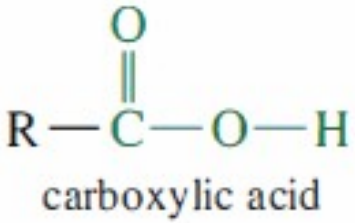
Carboxylic acids

✓The combination of a carbonyl group and a hydroxyl on the same carbon atom is called a carboxyl group.

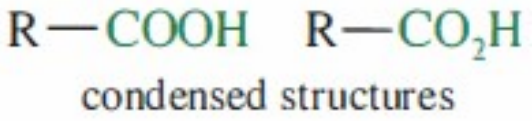
✓So, Compounds containing the carboxyl group are distinctly acidic and are called carboxylic acids.



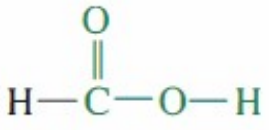
carboxyl group



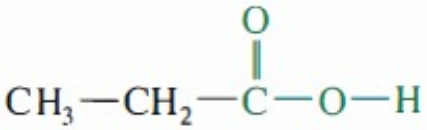
carboxylic acid



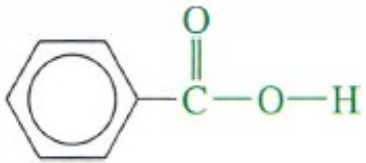
condensed structures



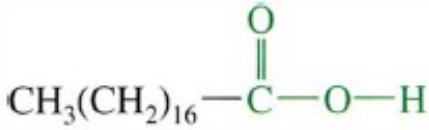
formic acid



propionic acid
(an aliphatic acid)



benzoic acid
(an aromatic acid)



stearic acid
(a fatty acid)

✓A carboxylic acid donates protons by heterolytic cleavage of the acidic O - H bond to give a proton

Nomenclature of Carboxylic Acids

- ✓Several aliphatic carboxylic acids have been known for hundreds of years, and their common names reflect their historical sources.
- ✓Formic acid; formica in Latin; was extracted from ants:.
- ✓Acetic acid; acetum ("sour") in Latin w/c was isolated from vinegar.
- ✓Propionic acid; derived from the Greek protos pion ("first fat") was considered to be the first fatty acid.
- ✓Butyric acid results from the oxidation of butyraldehyde.

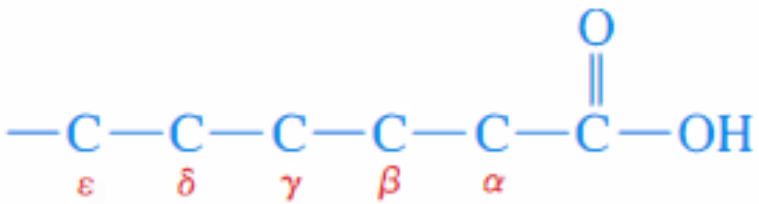
Physical Properties of Some Carboxylic Acids

IUPAC Name	Common Name	Formula	mp (°C)	bp (°C)	Solubility (g/100 g H_2O)
methanoic	formic	$HCOOH$	8	101	∞ (miscible)
ethanoic	acetic	CH_3COOH	17	118	∞
propanoic	propionic	CH_3CH_2COOH	−21	141	∞
2-propenoic	acrylic	$H_2C{=}CH{-}COOH$	14	141	∞
butanoic	butyric	$CH_3(CH_2)_2COOH$	−6	163	∞
2-methylpropanoic	isobutyric	$(CH_3)_2CHCOOH$	−46	155	23.0
trans-2-butenoic	crotonic	$CH_3{-}CH{=}CH{-}COOH$	71	185	8.6
pentanoic	valeric	$CH_3(CH_2)_3COOH$	−34	186	3.7
3-methylbutanoic	isovaleric	$(CH_3)_2CHCH_2COOH$	−29	177	5.0
2,2-dimethylpropanoic	pivalic	$(CH_3)_3C{-}COOH$	35	164	2.5
hexanoic	caproic	$CH_3(CH_2)_4COOH$	−4	206	1.0
octanoic	caprylic	$CH_3(CH_2)_6COOH$	16	240	0.7
decanoic	capric	$CH_3(CH_2)_8COOH$	31	269	0.2
dodecanoic	lauric	$CH_3(CH_2)_{10}COOH$	44		i
tetradecanoic	myristic	$CH_3(CH_2)_{12}COOH$	54		i
hexadecanoic	palmitic	$CH_3(CH_2)_{14}COOH$	63		i
octadecanoic	stearic	$CH_3(CH_2)_{16}COOH$	72		i
cis-9-octadecenoic	oleic	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	16		i
cis,cis-9,12-octadecadienoic	linoleic	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	−5		i

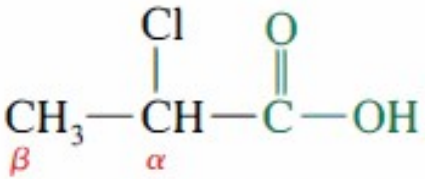
Additionally,...

✓Besides, in common names, the positions of substituents are named using Greek letters.

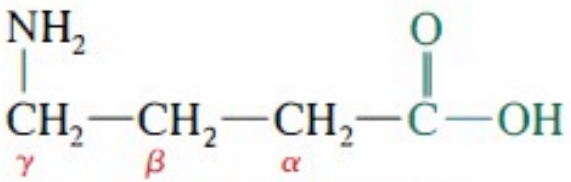
✓Notice that the lettering begins with the carbon atom adjacent to the carboxyl carbon, the α carbon.



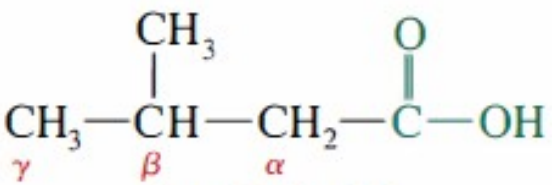
For instance.;



α-chloropropionic acid



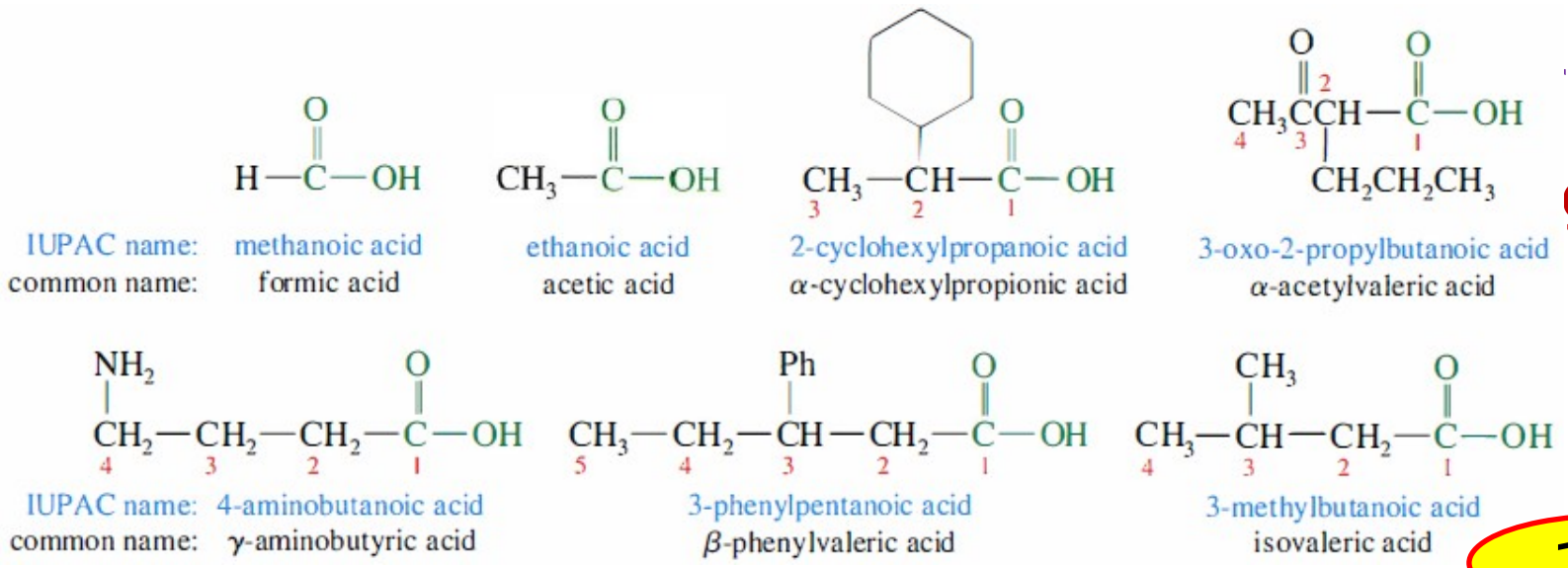
γ-aminobutyric acid



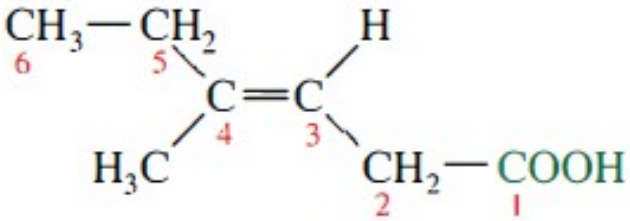
isovaleric acid
(β-methylbutyric acid)

IUPAC Names

- ✓Its nomenclature uses the name of the *alkane* that corresponds to the longest continuous chain of carbon atoms.
- ✓The final *-e* in the *alkane* name is replaced by the suffix *-oic acid*.
- ✓Th boxyl carb g the chai

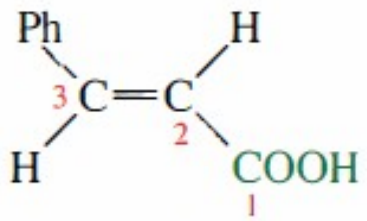


For Unsaturated acids;...



IUPAC name: (*E*)-4-methyl-3-hexenoic acid

new IUPAC name: (*E*)-4-methylhex-3-enoic acid

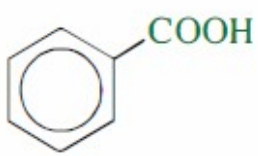


trans-3-phenyl-2-propenoic acid

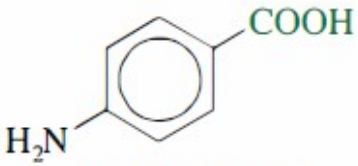
(*E*)-3-phenylprop-2-enoic acid

(cinnamic acid)

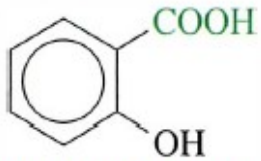
✓For Aromatic acids of the form Ar- COOH



benzoic acid

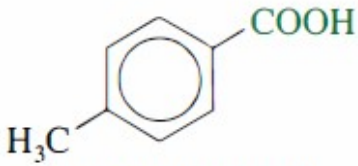


p-aminobenzoic acid



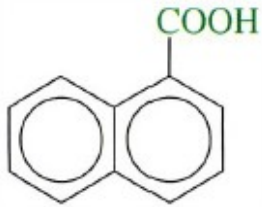
o-hydroxybenzoic acid

(salicyclic acid)

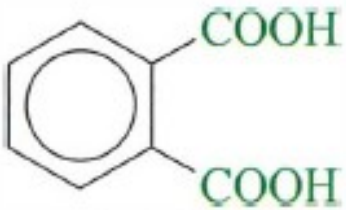


p-methylbenzoic acid

(*p*-toluic acid)

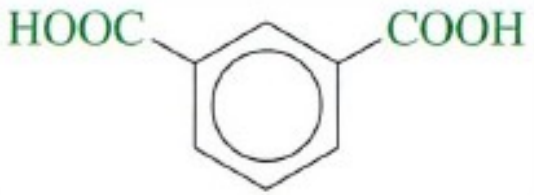


α-naphthoic acid



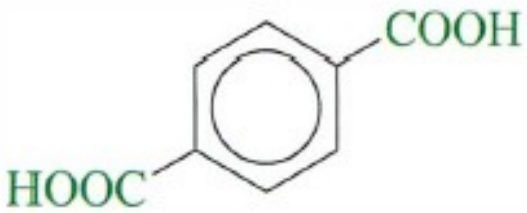
o-phthalic acid

phthalic acid



m-phthalic acid

isophthalic acid

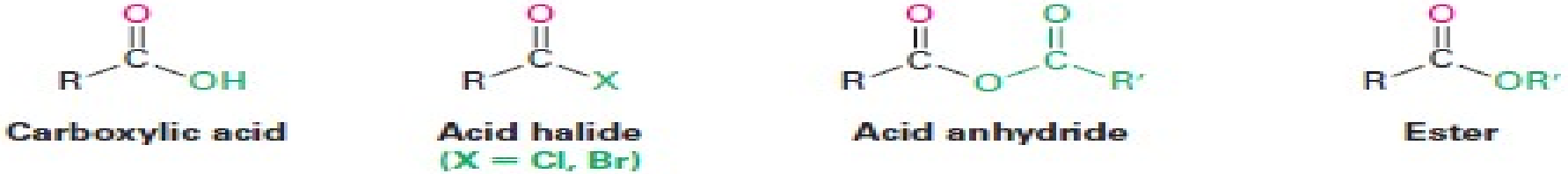


p-phthalic acid

terephthalic acid

Carboxylic Acid Derivatives

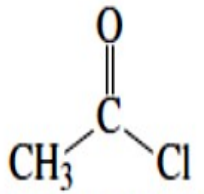
- ✓Carboxylic acid derivatives are compounds with functional groups that can be converted to carboxylic acids by a simple acidic or basic hydrolysis.
- ✓For instance; esters, amides, acid halides and acid anhydrides
- ✓Acyl halides and acid anhydrides are used only in the laboratory, but esters and amides are common in both laboratory and biological chemistry.



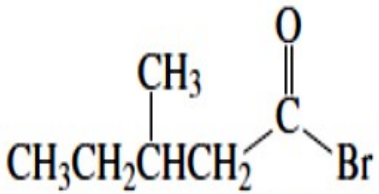
✓Acyl halides are compounds that have a halogen atom in place of the OH group of a carboxylic acid.

✓The most common acyl halides are acyl chlorides and acyl bromides.

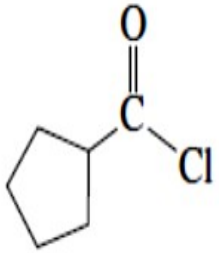
✓Acyl halides are named by using the acid name and replacing “ic acid” with “yl chloride” (or “yl bromide”). For e



systematic name: ethanoyl chloride
common name: acetyl chloride



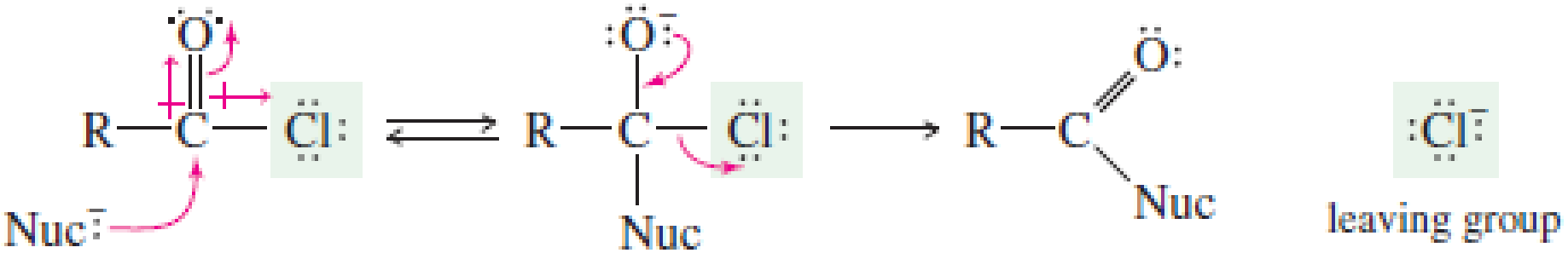
3-methylpentanoyl bromide
β-methylvaleryl bromide



cyclopentanecarbonyl chloride

Chemical reactions

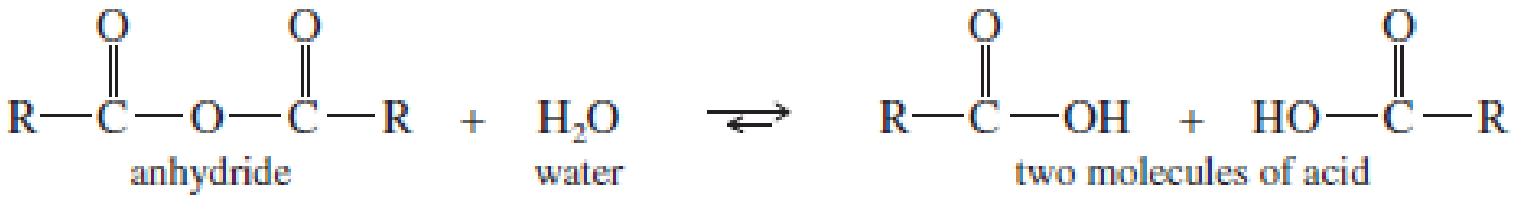
- ✓The halogen atom of an acyl halide inductively withdraws electron density from the carbonyl carbon;
- ✓W/c enhancing its electrophilic nature and making acyl halides particularly reactive toward nucleophilic acyl substitution.
- ✓The halide ion also serves as a good leaving group.



Acid Anhydrides

✓Anhydride means without H_2O and contains 2 molecules of an acid, with loss of a molecule of water.

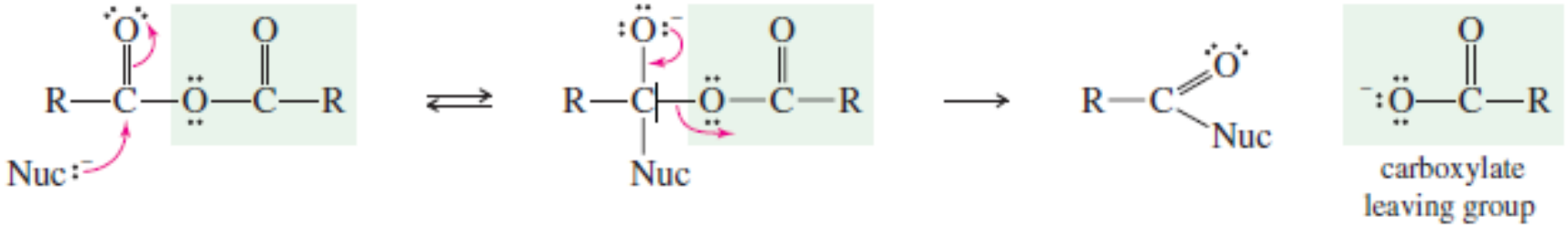
✓Addition of water to an anhydride regenerates two molecules of the carboxylic acid. Eg



✓Like acid halides, anhydrides are activated derivatives of carboxylic acids, although anhydrides are not as reactive as acid halides. Thus, in an acid chloride, the Cl atom activates the carbonyl group and serves as a leaving group.

✓In anhydride, the carboxylate group serves

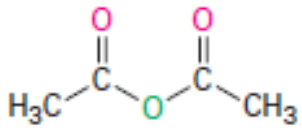
For instance;



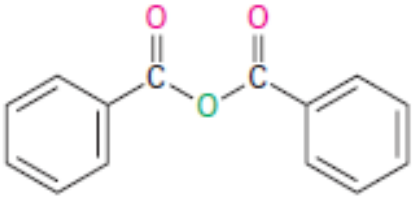
- ✓Half of an anhydride's acid units are lost as leaving groups.
- ✓If the acid is expensive, it is not use the anhydride as an activated form to make a derivative.
- ✓The acid chloride is a more efficient alternative, using chloride as the leaving group.
- ✓Anhydrides are used primarily when the necessary anhydride is cheap and readily available, like

Structural Comparison

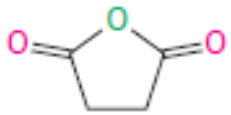
✓Symmetrical anhydrides of unsubstituted monocarboxylic acids and cyclic anhydrides of dicarboxylic acids are named by replacing the word *acid* *with anh*



Acetic anhydride

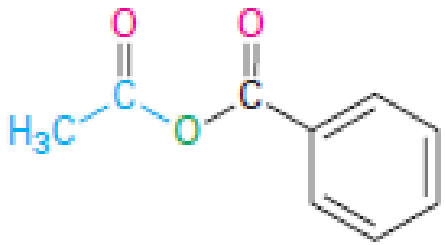


Benzoic anhydride



Succinic anhydride

✓Unsymmetrical anhydrides; w/c prepared from two different carboxylic acids are named by citing the two acids alphabetically and then adding *anhydride*



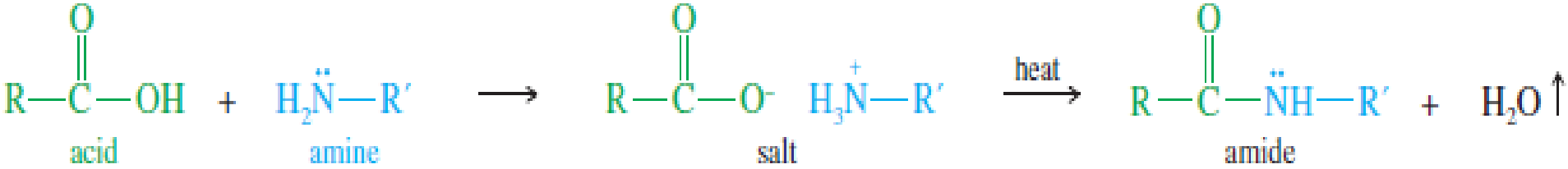
Acetic benzoic anhydride

Amides

- ✓It composites of a carboxylic acid and NH_3 or an amine.

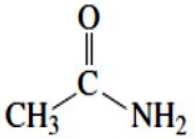
An acid reacts with an amine to form an ammonium carboxylate salt.

- ✓When this salt is heated to well above 100 °C, water is

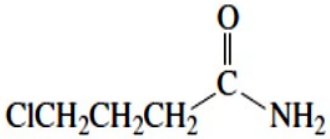


- ✓Hence, it has an NH_2, NHR, NR_2 or group in place of the OH group of a carboxylic acid.
- ✓Amides are named by using the acid name, replacing "oic acid" or "ic acid" with "amide.''

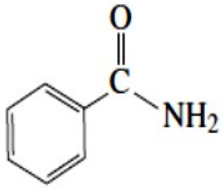
For instance;



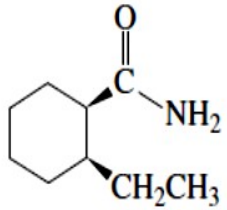
systematic name: ethanamide
common name: acetamide



4-chlorobutanamide
γ-chlorobutyramide

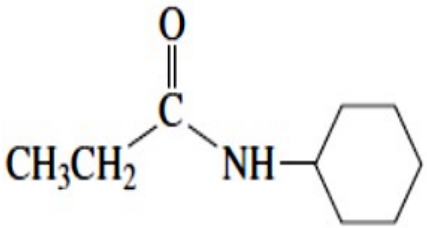


benzenecarboxamide
benzamide

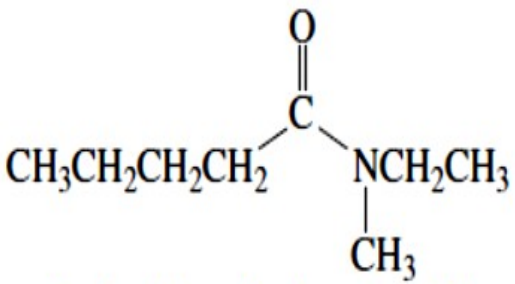


cis-2-ethylcyclohexanecarboxamide

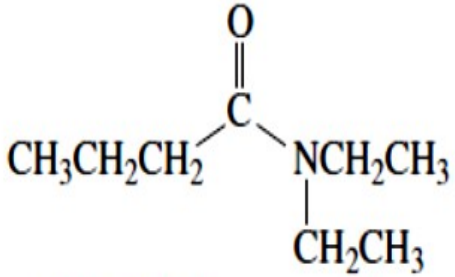
✓If a substituent is bonded to the nitrogen, the name of the substituent is stated first (if there is more than one substituent bonded to the nitrogen, they are stated alphabetically), followed by the name of the amide.



N-cyclohexylpropanamide



N-ethyl-*N*-methylpentanamide



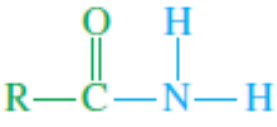
N,*N*-diethylbutanamide

Classification of Amides

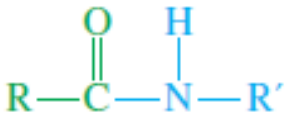
i) primary amide; there is only one carbon atom bonded to the amide nitrogen.

ii) secondary amide or an *N-substituted amide* ; *a*n amide with an alkyl group on nitrogen.

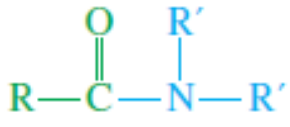
iii) tertiary amides or *N,N-disubstituted amides*; *a*mides with two alkyl groups on the amide nitrogen, *For instance*:



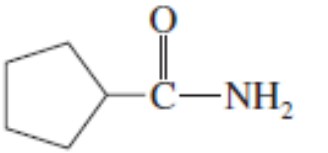
primary amide



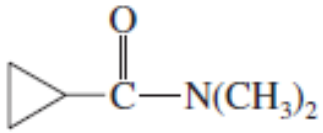
secondary amide
(*N*-substituted amide)



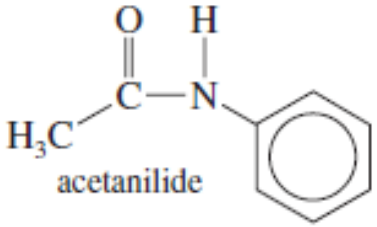
tertiary amide
(*N*,*N*-disubstituted amide)



cyclopentanecarboxamide



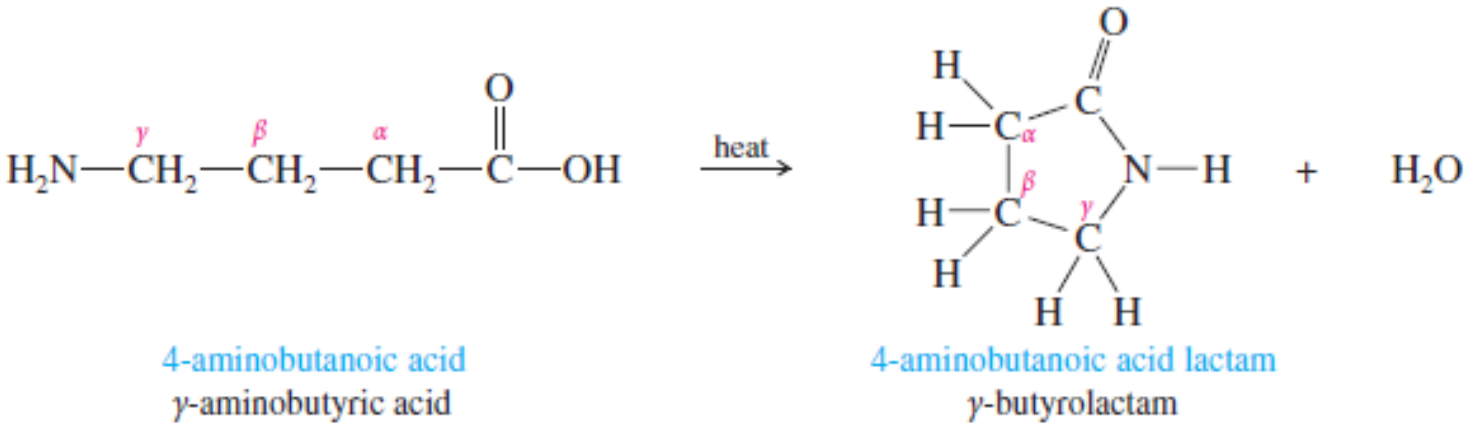
N,*N*-dimethylcyclopropanecarboxamide



acetanilide

Lactams; Cyclic amides

✓Lactams are formed from amino acids, where the amino group and the carboxyl group have joined to form an amide



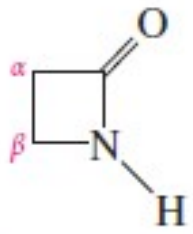
4-aminobutanoic acid
γ-aminobutyric acid

4-aminobutanoic acid lactam
γ-butyrolactam

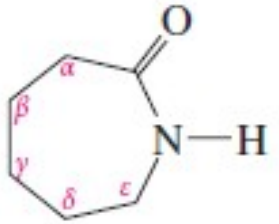
✓Lactams are named like lactones, by adding the term lactam at the end of the IUPAC name of the parent acid.

✓Common names of lactams are formed by changing the *-ic acid* ending of the amino acid to *-olactam*.

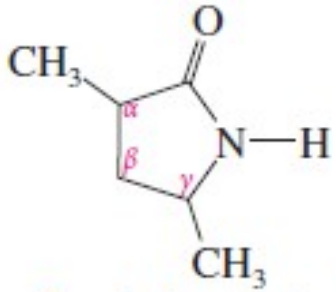
For example:



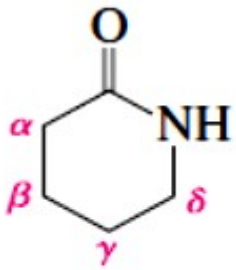
3-aminopropanoic acid lactam
β-propiolactam



6-aminohexanoic acid lactam
ε-caprolactam



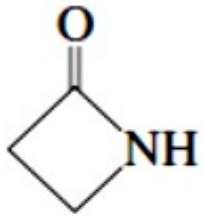
4-amino-2-methylpentanoic acid lactam
α-methyl-γ-valerolactam



2-azacyclohexanone
δ-valerolactam



2-azacyclopentanone
γ-butyrolactam



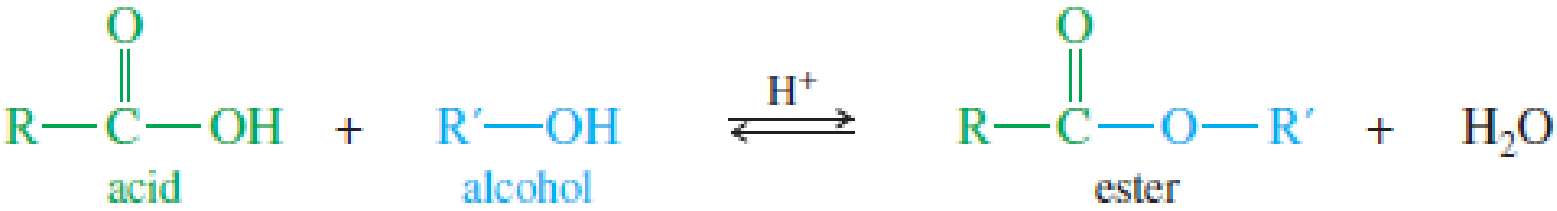
2-azacyclobutanone
β-propiolactam

✓In systematic nomenclature ‘’aza’’ is used to designate the nitrogen atom.

Esters of Carboxylic Acids

✓Esters are carboxylic acid derivatives in which the hydroxyl group -OH is replaced by an alkoxy group (-OR) .

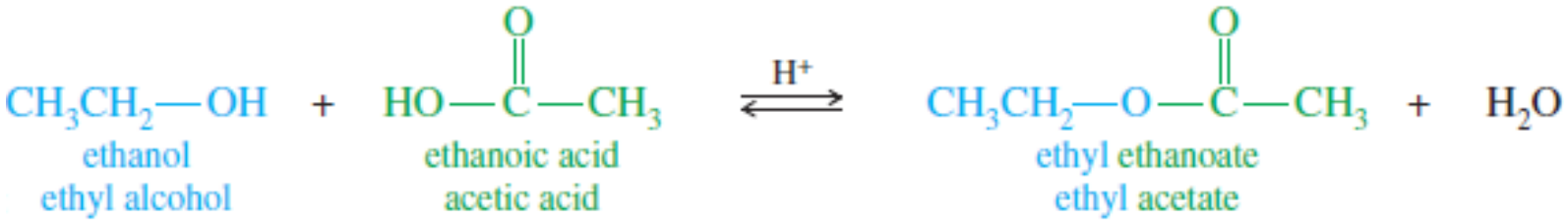
✓It is a combination of a carboxylic acid and an alcohol, with loss of a molecule of water. *Eg.*



✓The names of esters consist of two words that reflect their composite structure and the 1st word is derived from the *alkyl group of the alcohol* and the *2nd word from the carboxylate group of the carboxylic acid*.

Nomenclatures; esters

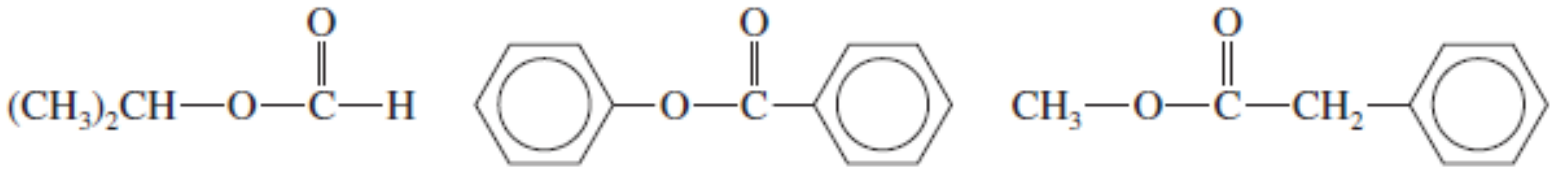
- ✓The IUPAC name is derived from the IUPAC names of the alkyl group and the carboxylate, and
- ✓the common name is derived from the common names of e



ethanol
ethyl alcohol

ethanoic acid
acetic acid

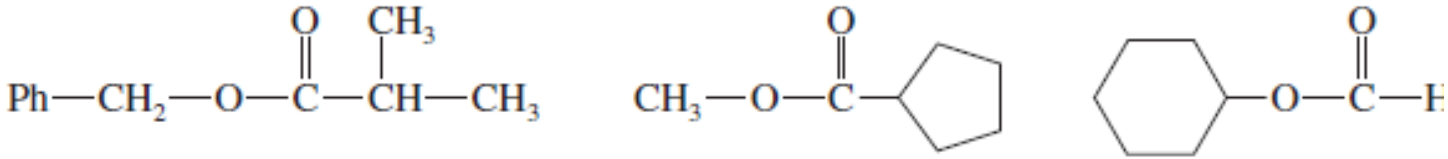
ethyl ethanoate
ethyl acetate



1-methylethyl methanoate
isopropyl formate

phenyl benzoate
phenyl benzoate

methyl 2-phenylethanoate
methyl phenylacetate



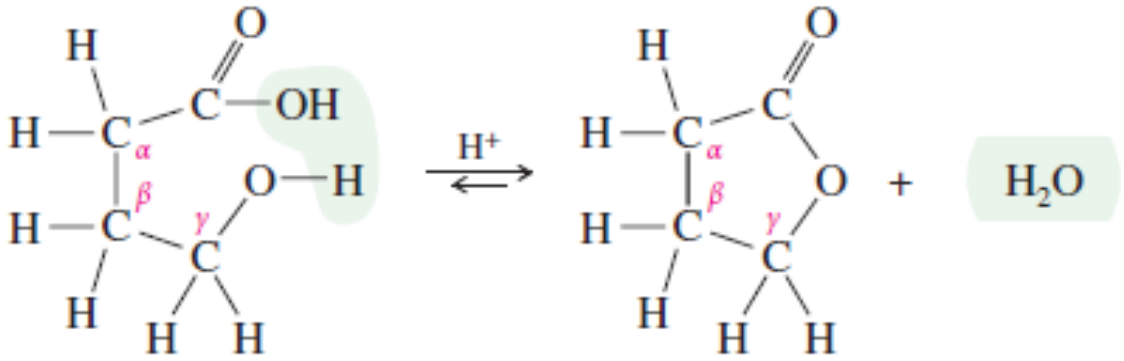
benzyl 2-methylpropanoate
benzyl isobutyrate

methyl cyclopentanecarboxylate
methyl cyclopentanecarboxylate

cyclohexyl methanoate
cyclohexyl formate

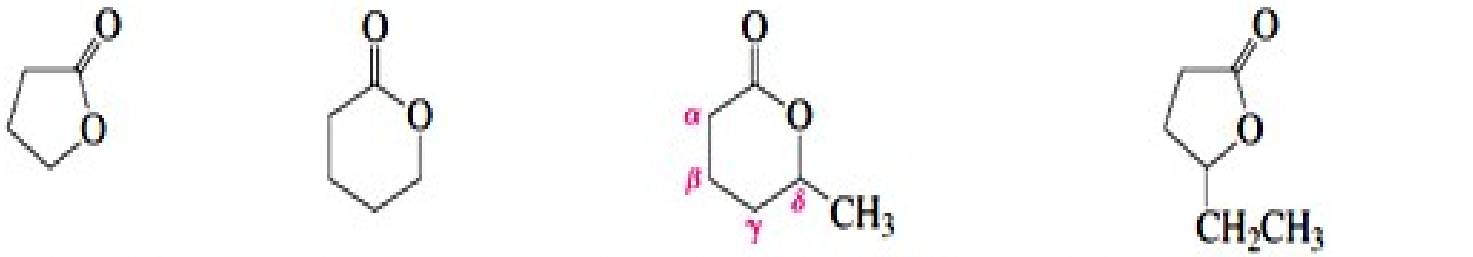
Lactones: Cyclic Esters

✓A lactone is formed from an open chain hydroxy acid in which the hydroxyl group has reacted with the acid group to form an ϵ



4-hydroxybutanoic acid
γ-hydroxybutyric acid

4-hydroxybutanoic acid lactone
γ-butyrolactone



2-oxacyclopentanone
γ-butyrolactone

2-oxacyclohexanone
δ-valerolactone

3-methyl-2-oxacyclohexanone
δ-caprolactone

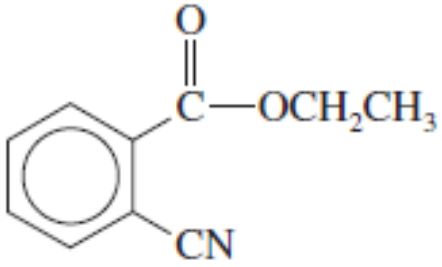
3-ethyl-2-oxacyclopentanone
γ-caprolactone

Summary

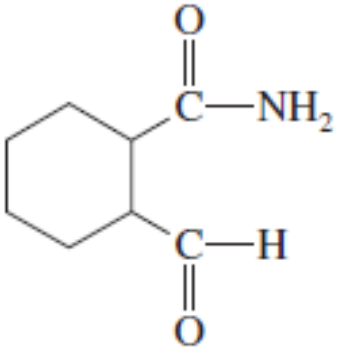
✓With all the different functional groups we have studied, it is not always obvious which functional group of a multifunctional compound is the "main" one and which groups should be named as substituents.

acid > ester > amide > nitrile > aldehyde > ketone > alcohol > amine > alkene, alkyne

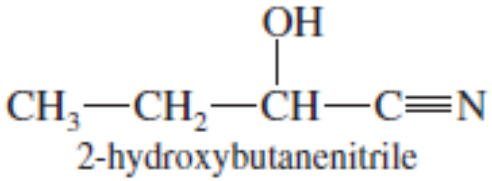
✓So, it summarizes these priorities, together with the suffixes used for main groups and the prefixes used for su



ethyl *o*-cyanobenzoate



2-formylcyclohexanecarboxamide



2-hydroxybutanenitrile

Exercise (1)

i) Name the following carboxylic acid derivatives, giving both a common name and an IUPAC name where possible.

(a) $PhCOOCH_2CH(CH_3)_2$

(b) $PhOCHO$

(c) $PhCH(CH_3)COOCH_3$

(d) $PhNHCOCH_2CH(CH_3)_2$

(e) $CH_3CONHCH_2Ph$

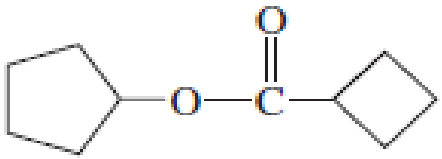
(f) $CH_3CH(OH)CH_2CN$

(g) $(CH_3)_2CHCH_2COBr$

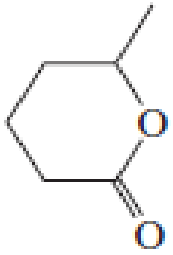
(h) $Cl_2CHCOCl$

(i) $(CH_3)_2CHCOOCHO$

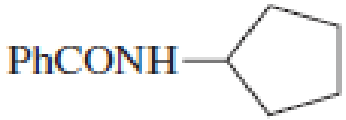
(j)



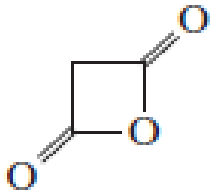
(k)



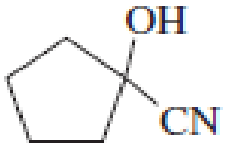
(l)



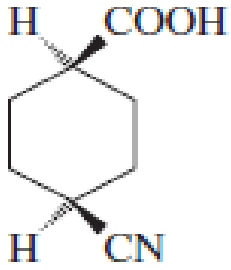
(m)



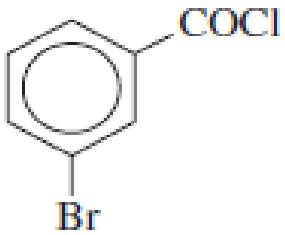
(n)



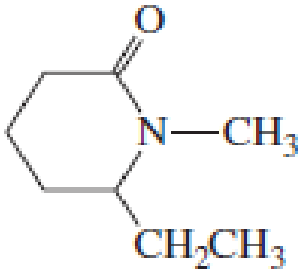
(o)



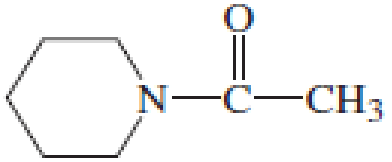
(p)



(q)



(r)



(*Hint:* Named as a piperidine derivative.)