**General Chemistry** 

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# **Organic Chemistry**

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## Introduction of Organic chemistry

**Organic chemistry:** - is the study of the structure, properties, composition, reactions, and preparation of carbon-containing compounds. Most organic compounds contain carbon and hydrogen which called hydrocarbons (alkane, alkene, alkyne and aromatic), but they may also include any number of other elements (e.g., nitrogen, oxygen, halogens, phosphorus, silicon, sulfur).

# Alkane

Alkanes: - are organic compounds that consist of single-bonded carbon and hydrogen atoms. The formula for *Alkanes is*  $C_nH_{2n+2}$ , subdivided into three groups – *chain alkanes*, *cycloalkanes, and the branched alkanes*.

# **Physical Properties of Alkanes**

- 1- The Solubility of Alkanes: due to very little difference of electronegativity between carbon and hydrogen and covalent nature of C-C bond or C-H bond, alkanes are generally non-polar molecules.
- 2- As the intermolecular Van Der Waals forces increase with the increase of the molecular size or the surface area of the molecule we observe: the boiling point of alkanes increases with increasing molecular weight, the straight-chain alkanes are observed to have a higher boiling point in comparison to their structural isomers.
- 3- The melting point of alkanes follows the same trend as their boiling point, that is, it increases with an increase in molecular weight.

# **Nomenclature of Alkanes**

The systematic name of an alkane is obtained using the following rules:

1- Determine the number of carbons in the longest continuous carbon chain. This chain is called the parent hydrocarbon.



2- The name of any alkyl substituent that hangs off the parent hydrocarbon is cited before the name of the parent hydrocarbon, together with a number to designate the carbon to which the alkyl substituent is attached. And it gives as lowest a number of the chain. The substituent's name and the name of the parent hydrocarbon are joined in one word, and there is a hyphen between the number and the substituent's name.

$^{1}_{CH_{3}CHCH_{2}CH_{2}CH_{2}CH_{3}}^{2}$	$^{6}_{CH_{3}CH_{2}CH_{2}CH_{2}CH_{2}CH_{2}CH_{2}CH_{3}}^{2}$
CH <sub>3</sub>	CH <sub>2</sub> CH <sub>3</sub>
2-methylpentane	3-ethylhexane
<sup>1</sup> CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> CH <sub>2</sub> C 4-isopt	$^{5}_{CHCH_{2}CH_{2}CH_{2}CH_{2}CH_{3}}$ $^{2}_{CHCH_{3}}$ $^{2}_{CH_{3}}$ $^{2}_{CH_{3}}$ ropyloctane

Alkyl groups naming Removing a hydrogen from an alkane results in an alkyl substituent (or an alkyl group). Alkyl substituents are named by replacing the "ane" ending of the alkane with "yl." The letter "R" is used to indicate any alkyl group.

methyl	СН <sub>3</sub> —
ethyl	CH <sub>3</sub> CH <sub>2</sub> —
propyl	CH <sub>3</sub> CH <sub>2</sub> CH <sub>2</sub> —
isopropyl	CH <sub>3</sub> CH—   CH <sub>3</sub>
	5
butyl	$CH_3CH_2CH_2CH_2$ —
isobutyl	CH <sub>3</sub> CHCH <sub>2</sub> —
	ĊH <sub>3</sub>

3- If more than one substituent is attached to the parent hydrocarbon, the chain is numbered in the direction that having a lowest number in the name of the compound. the substituents are listed in alphabetical order.

#### CH<sub>3</sub>CH<sub>2</sub>CHCH<sub>2</sub>CHCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub> | | CH<sub>3</sub> CH<sub>2</sub>CH<sub>3</sub> **5-ethyl-3-methyloctane** not **4-ethyl-6-methyloctane** because 3 < 4

4- If two or more substituents are the same, the prefixes "di," "tri," and "tetra" are used to indicate how many identical substituents the compound has. The numbers indicating the locations of the identical substituents are listed together, separated by commas.

 $\begin{array}{cccc} CH_3 & CH_3 & CH_3 \\ CH_3 CH_2 CHCH_2 CHCH_3 \\ & & & \\ CH_3 & CH_3 \\ \hline \\ \textbf{CH}_3 & CH_3 \\ \textbf{CH}_3 & CH_3 \\ \hline \\ \textbf{CH}_3 & CH_3$ 

5- When both directions lead to the same lowest number for one of the substituents, the direction is chosen that gives the lowest possible number to one of the remaining substituents

$$\begin{array}{ccccc} CH_3 & CH_3 & CH_2CH_3 \\ CH_3CCH_2CHCH_3 & CH_3CH_2CHCH_2 \\ CH_3 & CH_3 & CH_3 \\ CH_3 & CH_3 & CH_3 \\ \textbf{2,2,4-trimethylpentane} & \textbf{6-ethyl-3,4-dimethyloctane} \\ not & not \\ \textbf{2,4,4-trimethylpentane} \\ because 2 < 4 & \textbf{3-ethyl-5,6-dimethyloctane} \\ \textbf{because 4 < 5} \end{array}$$

Only if the same set of numbers is obtained in both directions does the first group cited get the lower number.





#### Nomenclature of Cycloalkanes

- ♦ Cycloalkanes are alkanes with their carbon atoms arranged in a ring.
- ✤ the general molecular formula for a cycloalkane is
- Cycloalkanes are named by adding the prefix "cyclo" to the alkane name that signifies the number of carbon atoms in the ring.



## **Reaction of Alkanes**

1- Combustion: - Complete combustion (given sufficient oxygen) of any hydrocarbon produces carbon dioxide and water. It is quite important that you can write properly balanced equations for these reactions, because they often come up as a part of thermochemistry calculations.

#### For example,

$$CH_4 + 2O_2 \longrightarrow CO_2 + 2H_2O_{\Delta_cH^\circ = -890 \text{ KJ/mol}}$$

minor

$$C_2H_6 + (7/2)O_2 \longrightarrow 2CO_2 + 3H_2O_{\Delta_cH^\circ} = -2875.84 \text{ KJ/mol}$$

2- Halogenation: - When the mixture of hydrocarbon and halogen is heated at 520-670 K in dark or is subjected to ultraviolet light at room temperature. a hydrogen of a hydrocarbon is replaced by an atom of halogen. For example,

 $CH_{3}-CH_{3} + Cl_{2} \xrightarrow{520-670K} CH_{3}-CH_{2}-Cl$   $CH_{3}-CH_{2}-CH_{2}-CH_{3} \xrightarrow{Cl_{2}} CH_{3}-CH_{2}-CH_{2}-CH_{3} + CH_{3}-CH_{2}-CH_{2}-CH_{2}-Cl$ 

Cl

## Alkene

*alkenes* are hydrocarbons with one or more carbon–carbon double bonds ( $R_2C=CR_2$ ) which have a general formula of  $C_nH_{2n}$ . Alkenes are extremely important in the chemical industry; the smallest form of alkene is ethene.

#### **Physical properties of Alkenes**

Alkenes are a form of unsaturated hydrocarbons. Physically alkenes are very similar to alkanes, they are <u>combustible</u>, <u>are colourless and non-polar</u>. Due to their physical structure, alkenes can have isomers. Isomeric alkenes are difficult to differentiate by boiling as they tend to have identical or extremely similar boiling points. Moreover, attributing to the carbon-carbon double bond, at room temperature, they are found in the gaseous state, the liquid state, as well as the solid state. Alkenes are insoluble in water, this is due to the fact that they have weak van der waal forces (van der waal forces are weak electric forces that deal with repulsion and attraction between atoms and molecules), however when alkenes come in contact with organic solvents, new van der waal forces come in place, making the alkenes soluble. The boiling point of alkenes is directly proportional to the molecular structure, the bigger the molecular chain higher the boiling point.

#### **Chemical Properties of Alkenes**

Chemically alkenes are highly reactive, this is due to the fact that they are unsaturated compounds. While alkenes and alkanes are both combustible, alkenes tend to be a lot more reactive in comparison to alkanes due to the fact that most of the chemical reactions that occur within alkenes do at the carbon-carbon double bonds. Alkenes usually go through three primary chemical reactions, firstly on the addition of hydrogen they become alkanes; on the addition of halogens, alkenes produce vicinal dihalides; and on the addition of hydrogen halides, the hydrogen attaches at the carbon-carbon double bond to whichever atom that is attached to more hydrogen atoms and the Halide ion attaches to whichever carbon atom has lesser hydrogen atom. This is known as the Markovnikov rule.

#### Nomenclature of alkene

- 1- Identify longest chain containing the alkene (both carbons)
- 2- Number carbons in chain so that double bond carbons have lowest possible numbers (if choice give sub lowest number) lowest possible numbers (if choice, give sub lowest number)
- 3- Name, number, and list substituents alphabetically as prefix like alkane nomenclature
- 4- Indicate position of alkene with number-followed by name of longest chain with suffix -ane replaced with -ene.



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# **Cycloalkene Nomenclature**

- 1- Alkene carbons by definition carbons 1 and 2. Give first substituent lowest possible number.
- 2- Name number and list substituents alphabetically as prefix like Name, number, and list substituents alphabetically as prefix like alkane nomenclature.
- 3- You do not need to indicate position of alkene with number, simply name ring size with prefix cyclo and followed suffix -ene.



1-Methylcyclohexene



1,4-Cyclohexadiene (New: Cyclohexa-1,4-diene)

#### 1,5-Dimethylcyclopentene

# Examples



# **Reaction of alkenes**

The functional group, C=C, allows alkenes to undergo addition reactions. The addition of these substances to an alkene proceeds by an ionic mechanism, with formation of the most stable carbocation. Therefore, it follows Markovnikov's Rule.

1- Addition of H<sub>2</sub> to alkene to form alkane

$$H_2C=CH_2 \xrightarrow{H_2} H_3C-CH_3$$



# Alkyne

Alkynes are an unsaturated hydrocarbon containing at least one carbon-carbon triple bond. Like other <u>hydrocarbons</u>, alkynes are generally hydrophobic. the general formula of alkynes  $C_nH_{2n-2}$ . Ethyne is more commonly known under the trivial name acetylene. It is the simplest of the alkynes, consisting of two carbon atoms connected by a triple bond, leaving each carbon able to bond to one hydrogen atom.

## **Physical properties of alkynes**

- 1- The physical properties of alkynes resemble those of hydrocarbons of similar shape and molecular weight.
- 2- Alkynes have low melting points and boiling points.
- 3- Melting point and boiling point increase as the number of carbons increases.
- 4- Alkynes are soluble in organic solvents and insoluble in water.

## Nomenclature of alkynes

- 1- Select the longest hydrocarbon chain, which is termed as parent/ root or base chain. In the case of alkynes, the chain which is having triple bond will be considered a Root or parent, or base chain. The name of the parent chain is termed with the help of IUPAC.
- 2- Start numbering the carbons in the longest carbon chain, in alkynes numbering will start from that end to which the triple bond is closest.
- 3- 1-alkyne will be referred to as terminal alkynes and other triple bonds present in the compound will be referred to as terminal alkynes.
- 4- After numbering, the next step is naming the compound, remembering that naming should be done according to alphabetical order.
- 5- For more than one same substituent group present in the same compound we have to use prefixes like di, tri, tetra, etc. For two, three, and four respectively.
- 6- Substituent groups that have triple bonds are known as alkynyl.
- 7- Compounds that contain both alkene and alkyne groups are known as alkyne. Numbering will start with a functional group that is closest to the terminal.
- 8- If both alkene and alkyne are at the same distance then, preference will be given to alkene.



Exercise: - Draw the structure of the following

- (1) 4-methyl-1-hexen-5-yne
- (2) 5-Isopropyloctyne
- (3) 1-Cyclobutyl-3-methyl-1-butyne

#### Reaction of alkynes

Alkynes undergo reactions that are similar to those of alkenes, except that they are capable of adding two molecules of a reagent for each triple bond present.

1- Addition reaction





#### **Complete Addition**

Alkyne may add hydrogen in the presence of suitable catalyst (pd, Pt,or Ni) similar to the case in alkenes. However, the hydrogenation cannot be stopped at alkene stage, and the final product is always an alkane.

$$-\mathbf{C} \equiv \mathbf{C} - \xrightarrow{2\mathbf{H}_2} - \xrightarrow{\mathbf{H}}_{\mathbf{C}} \xrightarrow{\mathbf{H}}_{\mathbf{H}} \xrightarrow{\mathbf{H}}_{\mathbf{H}}$$

#### Controlled addition Cis-alkene

Hydrogenation can be stopped at the intermediate alkene stage by the use of modified catalyst such as Lindlar Catalyst. As a result, this method affords a stereoselective synthesis of cis alkene from alkyne.



#### Controlled addition Trans-alkene

When we use Na; Sodium or Li; Lithium metal dissolved in NH3; liquid ammonia, we obtain trans alkene as product.



Alkynes react with halogens to yield tetra haloalkanes. Two molecules of the halogen (chlorine or bromine) add to the triple bond as follows:





Example





The addition of hydrogen chloride HCl, bromide HBr, or iodide HI to alkynes follows Markovnikov's rule.

The General Reaction If two moles of HX is added:

- 1- First halogen follows alkene hydrohalogenation regioselectivity rules, i.e; obeys Markovnikov's rule.
- 2- Second halogen goes on same carbon as first halogen; geminal dihalide.

3-



Although the reaction can usually be stopped after addition of 1 equivalent of HX to yield a vinylic halide, an excess of HX leads to formation of a dihalide product.

## Example





#### **Preparation of alkynes**

#### 1- Preparation of alkynes from calcium carbide:

At the industrial level, the synthesis of alkynes is done using calcium carbide. <u>Calcium Carbide</u> is prepared by heating quicklime (CaO) in the presence of coke (C). When calcium carbide is made to react with water, It results in the formation of <u>calcium hydroxide</u> and <u>acetylene</u>.

 $\begin{aligned} & \text{CaCO}_3 \rightarrow \text{CaO} + \text{CO}_2 \\ & \text{CaO} + 3\text{C} \rightarrow \text{CaC}_2 + \text{CO} \\ & \text{CaC}_2 + 2\text{H}_2\text{O} \rightarrow \text{Ca(OH)}_2 + \text{C}_2\text{H}_2 \end{aligned}$ 

2- Dehydrohalogenation of alkyl dihalides by using strong base

By treating vicinal dihalides with strong base (alcoholic KOH), followed by sodium amide (NaNH<sub>2</sub>), results in the formation of Alkyne.



### 3- Reaction of sodium Acetylide with Primary Alkyl Halides

- a- The acidic acetylenic hydrogens in acetylene or 1-alkynes can be replaced by certain metals to form salts Known as; metal acetylides.
- b- The reaction takes place with sodium; Na in liquid ammonia; NH3 or sodium amide (NaNH<sub>2</sub>) to form sodium acetylides.
- c- Sodium acetylides react with primary alkyl halides to yield higher alkynes.

$$H-C \equiv C-H \xrightarrow{Na}_{NH_{3}} H-C \equiv C: Na^{+} \xrightarrow{R'-X} H-C \equiv C-R'$$

$$R-C \equiv C-H \xrightarrow{Na}_{NH_{3}} R-C \equiv C: Na^{+} \xrightarrow{R'-X} R-C \equiv C-R'$$

$$Example$$

$$CH_{3}C \equiv CH + Na \xrightarrow{liq NH_{3}} CH_{3}C \equiv C: Na^{+} + CH_{3}CH_{2}Br$$

$$\downarrow$$

$$CH_{3}C \equiv CCH_{2}CH_{3} + NaBr \xrightarrow{Activate}_{Go to Settir}$$

# Alcohols

**Alcohols:** - are organic compounds of general formula R-OH (*Functional group of alcohols is hydroxyl group*). It may be regarded as derivatives of water in which one of the hydrogen atoms of water molecules (H-OH) has been replaced by an alkyl ( $-\mathbf{R}$ ) or substituted alkyl group. Alcohols may be open chain or cyclic.



# 1- Classification

Alcohols can be classified as primary, secondary, and tertiary alcohols, according to the kind of carbon-atom that bears (-OH) group.

ŎН	OH	ŎН
R-Ċ-H	R-Ċ-R	R-Ċ-R
Η̈́	Ĥ	Ŕ
Primary	Secondary	Tertiery
1 <sup>0</sup>	2°	3°

The different types of alcohols (primary, secondary, and tertiary) can be distinguished by using Lucas test.

- Tertiary alcohols turn turbid 2-3 minutes.
- Secondary alcohols turn turbid 5-15 minutes.
- In primary alcohols one layer appears.

#### Lucas test:

This test often provides classification information on alcohols and is used to distinguish between the different types of alcohols (primary, secondary, or tertiary). It depends on the formation of alkyl halides as second liquid phase. Tertiary alcohols are faster in the formation of conjugated halides than secondary alcohols. Primary alcohols and methanol do not react readily at room temperature and do not give two layers.



colourless T > room temperture

# 2- Nomenclature

There are two types of nomenclature: -

- a- *IUPAC name*: Alcohols are named by IUPAC name according to the following roles.
  - 1- Select as the parent structure the longest continuous carbon chain that contains the –OH group. Each name is derived by replacing the terminal –e of corresponding alkane by –ol.
  - 2- Indicate by the number of position of the –OH group in the parent chain, generally using the lowest possible number for this purpose.
  - 3- Indicate by numbers positions of the other groups attached to the parent chain.
  - 4- Numbering priority of substituted group is made according to alphabetic.



**b-** Common name:- is anther nomenclature of organic compounds.



# 3- Physical properties

Physical properties of alcohol can be explained by the following steps.

#### a- Boiling point

Alcohols generally have higher boiling points in comparison to other hydrocarbons having equal molecular masses. This is due to the presence of intermolecular hydrogen bonding between hydroxyl groups of alcohol molecules. For example, boiling point of Pentane is  $36 \,^{\circ}C$  (M.Wt= 72) while boiling point of Butanol is 118 (M.Wt= 74).



*Note*:- In general, the boiling point of alcohols increases with increase in the number of carbon atoms in the aliphatic carbon chain while the boiling point decreases with increase in branching in aliphatic carbon chains because the Van der Waals forces decreases with branching.

#### b-Solubility: -

The solubility of alcohol in water is governed by the hydroxyl group present. The hydroxyl group in alcohol is involved in the formation of intermolecular hydrogen bonding. Thus, hydrogen bonds are formed between water and alcohol molecules which make alcohol soluble in water. However, the alkyl group attached to the hydroxyl group is hydrophobic (Lipopholic) in nature. Thus, the solubility of alcohol decreases with the increase in the size of the alkyl group.



#### *c*- *The Acidity:* -

Alcohols react with strong bases such as sodium hydroxide, potassium hydroxide to form the corresponding alkoxide while react with strong acid to form oxoium. These reactions of alcohols indicate their acidic nature. The acidic nature of alcohol is due to the polarity of –OH bond. The acidity of alcohols decreases when an electron donating group is attached to the hydroxyl group as it increases the electron density on the oxygen atom and the acidic increase with withdrawing group. Thus, primary alcohols are generally more acidic than secondary and tertiary alcohols due to the presence of unshared electrons on the oxygen atom.



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# 4- Reactions of alcohols

The important reactions of alcohols are listed below: -

## a- Reaction with hydrogen halides

Alkyl halides are often synthesized from alcohols, in effect substituting a halogen atom for the hydroxyl group. Hydrochloric (HCl), hydrobromic (HBr), and hydroiodic (HI) acids are useful reagents for this substitution, giving their best yields with tertiary alcohols.

 $R-OH + HX \longrightarrow R-X + H_2O$ 

Example



Reactivity of HX: HI > HBr > HCl

Reactivity of ROH: allyl, benzyl  $> 3^{\circ} > 2^{\circ} > 1^{\circ}$ 

## **b-Reaction** with phosphorous trihalides

 $3R-OH+PX_3 \longrightarrow 3R-X+H_3PO_3$ 

Example



 $PX_3 = PBr_3, PI_3$ 

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#### c- Dehydration

Dehydration is a chemical process of removing water from the molecule. In the presence of strong acid, alcohol undergoes dehydration to yield the alkene. Dehydration may also refer as elimination reaction. In the dehydration reaction, -OH and -H are eliminated from the adjacent carbon atoms in the given alcohol to yield the alkene and water  $(H_2O)$ .

Reactivity of ROH:  $3^{\circ} > 2^{\circ} > 1^{\circ}$ 

Example



## d- Ester formation

Alcohol reacts with carboxylic acid to form ester by using acid as catalyst

$$R_1 - OH + R_2 - COOH \xrightarrow{\text{acid}} R_1 \xrightarrow{O} C \xrightarrow{R_2} + H_2O$$

$$\begin{array}{ccc} H_{2} & O \\ H_{3}C & O \\ OH + H_{3}C & OH \\ ethanol & acetic acid & ethyl acetate \end{array}$$

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#### e- Oxidation

The oxidation of an alcohol involves the loss of one or more hydrogen ( $\alpha$ -hydrogen) from the carbon bearing –OH group. The kind of the forming product is depended upon how many of this  $\alpha$ -hydrogen which the alcohol contains (primary, secondary or tertiary).

A primary alcohol contains two  $\alpha$ -hydrogens

A secondary alcohol contains one α-hydrogen

A tertiary alcohol contains no  $\alpha$ -hydrogen and is not oxidized.



# 5- Preparation of alcohols

Alcohols can be prepared by one of the methods outlined below.

#### a- Oxymercuration-demercuration.

Alkenes react with mercuric acetate in the presence of water to give hydroxylmercurial compounds which on reduction yield alcohols.

$$C = C + Hg(OAc)_2 + H_2O \longrightarrow -C - C - C - NaBH_4 \rightarrow -C - C - C - Markovnikov orientation OH HgOAc OH H$$

Example



#### b- Hydroboration-oxidation

With the reagent diborane  $(BH_3)_2$ , alkenes undergo hydroboration to yield alkylboranes  $(R_3B)$  which on oxidation give alcohols.

$$C = C \left( \begin{array}{c} (1) BH_3 . THF \\ \hline (2) H_2O_2 . NaOH \end{array} \right) \left( \begin{array}{c} | \\ -C \\ OH H \end{array} \right)$$

Example

$$H_{3}C \xrightarrow{H} CH_{2} \xrightarrow{(1) BH_{3}. THF} H_{3}C \xrightarrow{H_{2}} OH_{2} Addition, anti-Markovnikov orientation$$
Propene 1-Propanol

#### c- Grignard synthesis

The class of alcohol that is obtained from a Grignard synthesis depends on upon the type of carbonyl compound used: formaldehyde, HCHO, yields primary alcohols; other aldehydes, RCHO, yield secondary alcohols; and ketone, R<sub>2</sub>CO, yield tertiary alcohols.

A related synthesis utilizes ethylene oxide to make primary alcohols containing two more carbons than Grignard reagent.

 $C = O + R - MgX \longrightarrow - C - OMgX \xrightarrow{H_2O} - C - OH + Mg^{2+} + X^{-}$ 

#### d- Hydrolysis of alkyl halides (Nucleophilic Substitution)

Alkyl halide can be converted to alcohols by using water or hydroxide as the nucleophile.

R−X + KOH → R−OH + KI

Example



#### e- Hydroxylation (Formation 1,2-diols)

Hydroxylation of alkenes is the most important method for the synthesis of 1,2-diols, with the special feature of permitting stereochemical control by choice of the reagent.



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# **Problems**

1- Give IUPAC name of the following compounds.



- 2- How distinguish between the types of alcohols?
- 3- Prepare 1-propanol from chloroethane.
- 4- Explain physical properties of alcohols.

# **Aldehydes and Ketones**

Aldehydes are compounds of the general formula RCHO; Ketones are compounds of the general formula  $RR^-CO$ . The group R and  $R^-$  may be aliphatic or aromatic group.



R and  $R^- = Alkyl$  or aromatic group

Both aldehydes and ketones contain carbonyl group (C=O) and are often referred to collectively as **carbonyl group**. It is the carbonyl group that largely determines the chemistry of aldehydes and ketones. It is not surprising to find that the aldehydes and ketones resemble each other closely in most of their properties. However, there is a hydrogen atom attached to the carbonyl group of aldehydes, and there are two organic group attached to the carbonyl group of ketones. This difference in structure affects their properties.

# **1-Physical properties**

- All aldehydes and ketones are liquids except formaldehyde, which is a gas (boiling point = -21 <sup>o</sup>C) and benzophenone, which is a solid (melting point = 48 <sup>o</sup>C).
- The lower aldehydes and ketones are appreciably soluble in water (containing five or less carbon atoms), aromatic ones are insoluble in water, and all of them are soluble in organic solvents.
- They are colorless except <u>benzaldehyde</u>, which has a pale yellow color (due to oxidation) with a characteristic odor.
- The boiling points of aldehydes and ketones are lower than those of the alcohols from which they are derived. For example, isopropyl alcohol boils at 82.5 °C while its oxidation product, acetone, boils at 56 °C; ethanol boils at 78 °C, while its oxidation product, acetaldehyde, boils at 21 °C.
- Ignition: aliphatic aldehydes and ketones burn with a blue flame (without smoke) while aromatic ones burn with a smoky yellow flame.
- Aldehydes quite easily oxidized to carboxylic acid, whereas ketones are not oxidized.

# 2- Nomenclature

There are two types on nomenclature.

- a- **IUPAC**: Aldehydes and ketones are named by IUPAC name according to the following roles.
  - Select as the parent structure the longest continuous carbon chain that contains the C=O group. Each name is derived by replacing the terminal –e of corresponding alkane by al for aldehyde and none for ketone.
  - 2- Indicate by the number of position of the C=O group for ketone in the parent chain, generally using the lowest possible number for this purpose.
  - 3- Indicate by numbers positions of the other groups attached to the parent chain.
  - 4- Numbering priority of substituted group is made according to alphabetic.





# Distinguishing between aldehyde and ketone

The distinguishing between aldehydes and ketones are achieved by taking the fact that the aldehydes can be easily oxidized while ketones cannot. Two reagents can be used for this purpose, <u>Tollen's reagent or Fehling's reagent</u>. Only aldehydes give positive results with these two reagents.

#### a- Tollen's reagent

Tollen's reagent is the combination of silver nitrate solution with ammonium hydroxide in the presence of sodium hydroxide solution.

This a reagent gives silver mirror in the presence of aldehydes because the reaction between them involves the **oxidation of aldehydes** to corresponding carboxylic acid with an accompanying **reduction of silver ion** of this reagent to **silver element in the form of a silver mirror**. **General Chemistry** 

$$2AgNO_{3} + 2NaOH \longrightarrow 4g_{2}O + 2NaNO_{3} + H_{2}O$$

$$ppt$$

$$Ag_{2}O + 4NH_{4}OH \longrightarrow 2[Ag(NH_{3})_{2}OH] + 2H_{2}O$$

$$2[Ag(NH_{3})_{2}OH] + RCHO \longrightarrow RCOOH + 2Ag + 2H_{2}O$$
Silver mirror

#### **b- Fehling's reagent**

This test uses to distinguish between aldehydes and ketones. Only aldehydes can reduce Fehling's reagent (a deep blue solution) to give a <u>red cuprous oxide</u> <u>precipitate</u> Cu<sub>2</sub>O.

R–CHO	+ $2Cu^{+2}$ + NaOH	$\longrightarrow$ $\downarrow$ Cu <sub>2</sub> O + R–COONa + H <sub>2</sub> C		
Aldehyde	copper II	copper I oxide		
Dee	ep blue solution	red ppt.		

# **Reaction aldehyde and ketones**

The important reactions of aldehydes and ketones are listed below.

### a- Oxidation

1- Aldehyde can be oxidized by KMno<sub>4</sub> or Tollen's reagent into carboxylic acid.

$$R \xrightarrow{O} H \xrightarrow{KMnO_4} R \xrightarrow{O} OH$$

2- Methyl ketones

$$R \xrightarrow{O} CH_3 \xrightarrow{KOCI} R \xrightarrow{O} OH + CHCI_3$$

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#### **b- Reduction**

1- Reduction to alcohols

$$\xrightarrow{\mathsf{O}} H_2 + \mathsf{Ni}, \mathsf{Pt}, \mathsf{Pd} \longrightarrow -\overset{\mathsf{O}}{\mathsf{C}} - \overset{\mathsf{O}}{\mathsf{OF}}$$
or  $\mathsf{NaBH}_4$  then  $\mathsf{H}^+ \longrightarrow \overset{\mathsf{H}}{\mathsf{H}}$ 

2- Reduction to hydrocarbons



## c- Addition of Grignard reagent



#### d- Addition of cyanide (cyanohydrin formation)



#### e- Addition of alcohols (Acetal formation)

+ 2ROH 
$$\rightarrow$$
 + 2ROH  $\rightarrow$  -C-OR  
OR  
Acetal

# 6- Preparation aldehydes and ketones

### a- Preparation aldehydes

1- Oxidation of primary alcohols



#### 2- Oxidation methylbenzenes



3- Reduction of acid chlorides

$$R \xrightarrow{O} LiAlH_4(Bu-t)_3 \xrightarrow{O} R \xrightarrow{O} H$$

#### **b- Preparation** of ketones

1- Oxidation of secondary alcohols

$$R \xrightarrow{OH} \frac{CrO_3}{or K_2Cr_2O_7} R \xrightarrow{O} R$$

2- Friedel- Crafts acylation



3- Reduction of acid chlorides with organocopper compounds

$$R-MgX \xrightarrow{CuX} R^{-}Cu-Li \xrightarrow{R^{-}COCI} R^{-}R^{-}R^{-}$$

# **Problems**

5- Give IUPAC name of the following compounds.



- 6- How distinguish between aldehydes and ketones?
- 7- Prepare propanal from 1-propanol.
- 8- Explain physical properties of aldehyde and ketones.
- 9- Explain the mechanism of reaction of ketones with cyanide.

**General Chemistry** 

# Carboxylic acids

A Carboxylic Acid is an organic compound containing a carboxyl functional group. The *general formula of a carboxylic acid is R-COOH*, where COOH refers to the carboxyl group, and R refers to the rest of the molecule to which this group is attached. In this carboxyl group, there exists a carbon which shares a double bond with an oxygen atom and a single bond with a hydroxyl group.

#### 1- Properties of carboxylic acids

a- Carboxylic acids have higher melting and boiling points than the corresponding alcohols. This is because in a pure carboxylic acid, hydrogen bonding can occur between two molecules of acid to produce a dimer, making the van der Waals' forces stronger. Hence more energy is required to overcome these forces of attraction.



- b- Small carboxylic acids are soluble in water. This is because carboxylic acid is capable of forming hydrogen bond with water molecule. However, the solubility decreases as the number of carbon atoms increases. This is because the presence of long hydrocarbon tail disrupts the effectiveness of hydrogen bonding.
- c- In most cases, the equilibrium significantly favors the carboxylic acid with a Ka usually around 10<sup>-4</sup> or 10<sup>-5</sup>. In other words, the pKa of most carboxylic acids is between 4 and 5. Pka decrease by the substituent effects on acidity such as withdrawing group.



## 2-Nomenclature of carboxylic acid

In the IUPAC nomenclature of these compounds, the suffix <u>"-oic acid"</u> is assigned. The guidelines that must be followed in the IUPAC nomenclature of carboxylic acids are listed below.

- The suffix "e" in the name of the corresponding alkane is replaced with "oic acid".
- When the aliphatic chain contains only one carboxyl group, the carboxylic carbon is always numbered one. For example, CH<sub>3</sub>COOH is named as ethanoic acid.
- When the aliphatic chain contains more than one carboxyl group, the total number of carbon atoms is counted and the number of carboxyl groups is represented by Greek numeral prefixes such as "di-", "tri-", etc.
- A carboxylic acid is named by adding these prefixes and suffixes to the parent alkyl chain. Arabic numerals are used for indicating the positions of the carboxyl group.
- The name "carboxylic acid" or "carboxy" can also be assigned for a carboxyl substituent on a carbon chain. An example of such nomenclature is the name 2-carboxyfuran for the compound 2-Furoic acid.



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#### 3- Reaction of carboxylic acid

a- The Fischer Esterification

acid and alcohol  $\rightarrow$  ester and water

Example



#### b- Synthesis of Acid Chlorides

In the laboratory, carboxylic acids are converted into acid chlorides by treatment with thionyl chloride, SOCl<sub>2</sub>.





#### c- Conversion into acid anhydrides

Acid anhydrides can be derived from two molecules of carboxylic acid by heating to remove 1 equivalent of water. Because of the high temperatures needed, however, only acetic anhydride is commonly prepared this way.



Example



**General Chemistry** 

#### d- Conversion into amides

Carboxylic acid reacts with amines to form amide compound



## e- Reduction to yield primary alcohols

Carboxylic acids are reduced by LiAlH<sub>4</sub> to give primary alcohols.



## Example



# 4- Preparation of carboxylic acids

a- **Oxidation of substituted alkyl benzene:** with KMnO<sub>4</sub> or Na<sub>2</sub>Cr<sub>2</sub>O<sub>7</sub> gives a substituted benzoic acid. Both primary and secondary alkyl groups can be oxidized, but tertiary groups are not affected.



b-Oxidation of a primary alcohol or an aldehyde: yields a carboxylic acid. Primary alcohols are often oxidized with CrO<sub>3</sub> in aqueous acid, and aldehydes are similarly oxidized.



#### c- Carboxylation of Grignard reagents

Another method for preparing carboxylic acids is by reaction of a Grignard reagent with  $CO_2$  to yield a metal carboxylate, followed by protonation to give a carboxylic acid. This carboxylation reaction is usually carried out by bubbling a stream of dry CO2 gas through a solution of the Grignard reagent.

$$R - MgX \xrightarrow{1. CO_2} R \xrightarrow{O} C$$

Example



#### d- Hydrolysis of nitriles

Carboxylic acids can be prepared from nitriles on heating with aqueous acid or base by a mechanism. Since nitriles themselves are usually made by SN 2 reaction of a primary or secondary alkyl halide with CN<sup>-</sup>

# Amines

**Amines**: Amines are a group of organic compounds that are derived from ammonia (NH<sub>3</sub>) Figure (1), compounds that has a nitrogen atom connected with two hydrogen atoms (-NH<sub>2</sub>), and a single group of some other atoms for example (R).

## 1- Classification of Amines

Amines are classified by the number of organic compounds attached with the central nitrogen atom



## 2- Properties of amine

- a- The lower aliphatic amines with a fishy smell are gaseous in nature.
- b- Primary amines are liquids at room temperature containing three to four carbon atoms, whereas higher amines are solids.
- c- Aniline and other arylamines are normally colourless, but when stored open due to atmospheric oxidation, they get painted.
- d- Lower aliphatic amines can form water molecular hydrogen bonds, making them water-soluble.
- e- Increasing the size of the hydrophobic alkyl portion decreases the amine molar weight, resulting in a decrease in water solubility.

- f- As a product of hydrogen bonding between the nitrogen and the hydrogen of the other atom, primary and secondary amines are often involved in the intermolecular interaction.
- g- Due to the availability of two hydrogen atoms, the intermolecular association is more prominent in primary amines compared to secondary. Due to the absence of a free hydrogen atom for bonding, there is no intermolecular association in tertiary amines.

# **3-Nomenclature of amine**

Amines are named by specifying the alkyl groups attached to the nitrogen and adding the suffix – amine (Alkylamine).

CH<sub>3</sub>CH<sub>2</sub>NH<sub>2</sub> (CH<sub>3</sub>CH<sub>2</sub>)<sub>2</sub>NH (CH<sub>3</sub>CH<sub>2</sub>)<sub>3</sub>N triethylamine ethylamine diethylamine CH<sub>3</sub>CH<sub>3</sub> -CH<sub>2</sub>CH<sub>3</sub> (primary) (tertiary) (secondary) CH2CH3 Triethylamine Diphenylamine CH2NHCH3 CH<sub>3</sub>NH<sub>2</sub> CH\_NHCH\_CH\_ Benzylmethylamine Methylamine Ethylmethylamine CH. H.C CH3CH2NCH2CH3 CH<sub>3</sub>NHCH<sub>3</sub> Dimethylamine Diethylisopropylamine CH<sub>3</sub>CHCH<sub>3</sub> CH<sub>3</sub>CHCH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub> CH<sub>3</sub>CH<sub>2</sub>NH<sub>2</sub> CH<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub>  $NH_2$ NHCH<sub>3</sub> NH2 N-methyl-2-pentanamine propanamine 2-propanamine aminoethane 2-aminopentane  $NH_2$ CH<sub>3</sub>CHCH<sub>2</sub>CO<sub>2</sub>H H<sub>2</sub>NCH<sub>2</sub>CH<sub>2</sub>CCH<sub>2</sub>CH<sub>3</sub> 3-aminobutanoic acid 1-amino-3-pentanone

# **Aromatic hydrocarbons**

Aromatic compounds are chemical compounds that consist of conjugated planar ring systems accompanied by delocalized pi-electron clouds in place of individual alternating double and single bonds.

They are also called *aromatics or arenes*. The best examples are toluene and <u>benzene</u>. *Aromatics require satisfying Huckel's rule*. Plants and micro-organisms have an exclusive route to benzene-ring compounds. The great majority of aromatic compounds in nature, therefore, are produced by plants and micro-organisms, and animals are dependent upon plants for many aromatic compounds either directly or indirectly.

# **Carbohydrates**

Carbohydrates (which consist of the elements carbon, hydrogen, and oxygen) are organic compounds that contain large quantities of hydroxyl groups. It has the general formula (CnH2nOn). The simplest carbohydrates also contain either an aldehyde moiety or a ketone moiety.

# Function of carbohydrates

- 1- Source and storage of energy e.g. glucose and glycogen
- 2- Structural components e.g. skin, bone, cell
- 3- Ribose and deoxyribose are a component of RNA and DNA, respectively.
- 4- Involved in cell-cell interaction.
- 5- Their derivatives are drugs e.g. erythromycin.
- 6- Ascorbic acid, a derivative of carbohydrate is a water- soluble vitamin.

# Classification of carbohydrates

**Monosaccharides:** which contain in their structure one building unit. its classified to:

**\*Trioses:** which contains in its composition **three** carbon atoms, such as **gylceraldehyde**.

\*Tetroses: which contain in its composition four carbon atoms, such as erythrose.

\*Pentoses: which contains five carbon atoms, such as ribose.



Three most abundant disaccharides are:

\*Sucrose prevalent in sugar cane and sugar beets, is composed of glucose and fructose through an  $\alpha$  (1,2) -glycosidic bond



\*Lactose is found exclusively in the milk of mammals and consists of galactose and glucose in a  $\beta$ -(1,4) glycosidic bond



\*Maltose the major degradation product of starch, is composed of 2 glucose monomers in an  $\beta$ -(1,4) glycosidic bond.

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Sucrose and lactose are heterosaccharides.

Herefore a maltose is homosaccharide.

**Note: - Reducing sugar**: A molecule containing free carbonyl group that can reduce the indicators such as cupric ions reagent into cuprous ions. (Lactose and Mannose are reducing sugars while sucrose is not reducing sugar).

- 3- Oliogosaccharide: is a saccharide polymer containing a small number (typically three to ten) of component sugars, and is also known as simple sugars.
- 4- Polysaccharides: Most of the carbohydrates found in nature occur in the form of high molecular weight polymers called polysaccharides. The monomeric building blocks used to generate polysaccharides can be varied; in all cases, however, the predominant monosaccharide found in polysaccharides is D-glucose.
  - \* **Homopolysaccharides:** polysaccharides are composed of a single monosaccharide building block, they are termed.
  - \* **Heteropolysaccharides**: Polysaccharides composed of more than one type of monosaccharide are termed.
- **a- Glycogen**: Glycogen is the major form of stored carbohydrate in animals. This crucial molecule is a homopolymer of glucose in  $\alpha$ -(1,4) linkage; it is also highly branched, with  $\Box$ -(1,6) branch linkages occurring every 8-10 residues. Glycogen is a very compact structure that results from the coiling of the polymer chains. This compactness allows large amounts of carbon energy to be stored in a small volume, with little effect on cellular osmolarity.
- b- Starch: Starch is the major form of stored carbohydrate in plant cells. Its structure is identical to glycogen, except for a much lower degree of branching (about every 20-30 residues). Unbranched starch ( $\alpha$ -(1,4) linkage only) is called **amylase** (15-20%); branched starch ( $\alpha$ -(1,4) and  $\alpha$ -(1,6) linkages) is called **amylopectin**.

c- Cellulose: The main polysaccharide in plants. It is is a homopolymer of glucose in  $\beta$ -glycosidic linkages. d- Inulin: Present in Dahlias. Consists of fructose only.



e- Chitin: structural elements of invertebrates and in the exoskeleton of arthropods. It is poly (N-acetyl-D-glucosamine units) joined by  $\beta$  (1,4) linkages.

f- **Dextrin**: formed during the course of starch hydrolysis.

g- **Dextran:** A storage polysaccharide present in yeast and bacteria consists of glucose linked by  $(\alpha$ -(1,6) linkages and for branches  $(\alpha$ -(1,2)  $\alpha$ -(1,3) and  $\alpha$ -(1,4).



# Amino acids

#### Chemical Nature of the Amino Acids:

\*All peptides and polypeptides are polymers of alpha-amino acids.

\*There are 20  $\square$ -amino acids that are relevant to the make-up of mammalian proteins (see below).

@ Several other amino acids are found in the body free or in combined states (i.e. not associated with peptides or proteins). These non-protein associated amino acids perform specialized functions.

e.g. *γ-Aminobutyric acid (GABA)*: involved in neurotransmission of nerve pulses.

e.*g*  $\beta$ -*alanine* : Part of the structure of Coenzyme A.

@ Several of the amino acids found in proteins also serve functions distinct from the formation of peptides and proteins: *e.g. tyrosine in the formation of thyroid hormones and other example is glutamate acting as a neurotransmitter.* 

@ The  $\Box$ -amino acids in peptides and proteins (*excluding proline*) consist of a carboxylic acid (-COOH) and an amino (-NH<sub>2</sub>) functional group attached to the same tetrahedral carbon atom. This carbon is the  $\Box$ -carbon.

Distinct R-groups, that distinguish one amino acid from another, also are attached to the alpha-carbon (except in the case of glycine where the R-group is hydrogen). The fourth substitution on the tetrahedral  $\Box$ -carbon of amino acids is hydrogen.



Neutral formula Zwitterion formula Figure (1):General structure of amino acids. Neutral formula never found in the body.

#### Properties of amino acids

1- Crystalline amino acids are colourless,

2- odorless

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- 3- melt with decomposition at temperature more than (200 °C).
- 4- In aqueous solution amino acids exist predominantly in the form of zwitterion.

### Amino Acid Classifications

Each of the 20  $\Box$ -amino acids found in proteins can be distinguished by the R-group substitution on the  $\Box$ -carbon atom. There are two broad classes of amino acids based upon whether the R-group is <u>hydrophobic or hydrophilic</u>.

\* The hydrophobic amino acids tend to repel the aqueous environment and, therefore, reside predominantly in the interior of proteins. This class of amino acids does not ionize nor participate in the formation of H-bonds.

\* The hydrophilic amino acids tend to interact with the aqueous environment, are often involved in the formation of H-bonds and are predominantly found on the exterior surfaces proteins or in the reactive centers of enzymes.

Amino Acid	Symbol	Structure*	pK <sub>1</sub> (COOH)	pK <sub>2</sub> (NH <sub>2</sub> )	pK R Group
	A	mino Acids with Aliphatic R-Gro	oups		
Glycine	Gly - G	H-CH-COOH NH <sub>2</sub>	2.4	9.8	
Alanine	Ala - A	CH <sub>3</sub> -CH-COOH NH <sub>2</sub>	2.4	9.9	
Valine	Val - V	H <sub>3</sub> C <sub>C</sub> H-CH-COOH H <sub>3</sub> C NH <sub>2</sub>	2.2	9.7	
Leucine	Leu - L	$H_3C$ CH-CH <sub>2</sub> -CH-COOH H <sub>3</sub> C NH <sub>2</sub>	2.3	9.7	
Isoleucine	Ile - I	H <sub>3</sub> C~CH <sub>2</sub> ~CH-CH-COOH H <sub>3</sub> C NH <sub>2</sub>	2.3	9.8	

## **Table of** □-Amino Acids Found in Proteins

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	Non-Aroi	natic Amino Acids with Hydroxy	l R-Grouj	ps	
Serine	Ser - S	HO-CH <sub>2</sub> -CH-COOH NH <sub>2</sub>	2.2	9.2	~13
Threonine	Thr - T	H <sub>3</sub> C, CH-CH-COOH HO NH <sub>2</sub>	2.1	9.1	~13
	Amino	• Acids with Sulfur-Containing R	-Groups		
Cysteine	Cys - C	HS-CH <sub>2</sub> -CH-COOH NH <sub>2</sub>	1.9	10.8	8.3
Methionine	Met-M	H <sub>3</sub> C-S-(CH <sub>2</sub> ) <sub>2</sub> -CH-COOH NH <sub>2</sub>	2.1	9.3	
	А	cidic Amino Acids and their Ami	ides		
Aspartic Acid	Asp - D	HOOC-CH <sub>2</sub> -CH-COOH NH <sub>2</sub>	2.0	9.9	3.9
Asparagine	Asn - N	H <sub>2</sub> N-C-CH <sub>2</sub> -CH-COOH O NH <sub>2</sub>	2.1	8.8	
Glutamic Acid	Glu - E	HOOC-CH <sub>2</sub> -CH <sub>2</sub> -CH-COOH NH <sub>2</sub>	2.1	9.5	4.1
Glutamine	Gln - Q	H <sub>2</sub> N-C-CH <sub>2</sub> -CH <sub>2</sub> -CH-COOH O NH <sub>2</sub>	2.2	9.1	
Basic Amino Acids					
Arginine	Arg - R	$\begin{array}{c} H N - C H_2 - C H_2 - C H_2 - C H - C OOH \\ C = N H & N H_2 \\ N H_2 \end{array}$	1.8	9.0	12.
Lysine	Lys - K	H <sub>2</sub> N–(CH <sub>2</sub> ) <sub>4</sub> –CH–COOH NH <sub>2</sub>	2.2	9.2	10.8
TT	Lie L		1 8	0.2	6.0

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Amino Acids with Aromatic Rings					
Phenylalanine	Phe - F	CH2-CH2-CH-COOH NH2	2.2	9.2	
Tyrosine	Tyr - Y		2.2	9.1	10.1
Tryptophan	Trp-W	CH <sub>2</sub> -CH-COOH NH <sub>2</sub> H	2.4	9.4	
Imino Acids					
Proline	Pro - P	л соон н н	2.0	10.6	

\*Backbone of the amino acids is red, R-groups are black

**isoelectric point (pI):-** also referred to as the zwitterion's pH, is the pH value at which the molecule carries no electrical charge.



#### **Optical Properties of the Amino Acids**

A tetrahedral carbon atom with 4 distinct constituents is said to be **chiral**. The one amino <u>acid not exhibiting chirality is glycine</u>.

-Chirality describes the handedness of a molecule that is observable by the ability of a molecule to rotate the plane of polarized light either to the right (**dextrorotatory**) or to the left (**levorotatory**).

All of the amino acids in proteins exhibit the same absolute steric configuration as **L**-glyceraldehyde. Therefore, they are all L- $\Box$ -amino acids.

-D-amino acids are never found in proteins, although they exist in nature. D-amino acids are often found in polypetide antibiotics.



Figure: Isomers of amino acid. D-types never found in proteins

**Essential Amino Acids:** Obtained from diet because body cannot synthesize them: Phe, Trp, Val, Ile, Leu, Met, Lys, Thr.

Non Essential Amino Acids: All other Amino Acids body cannot synthesize them.

## The Peptide Bond

The simplest peptide, a **dipeptide**, contains a single peptide bond formed by the condensation of the carboxyl group of one amino acid with the amino group of the second with the concomitant elimination of water. Peptide bond formation is a condensation reaction leading to the polymerization of amino acids into peptides and proteins. Peptides are small consisting of few amino acids.

#### \*Importance of Peptides:

- 1. A number of hormones (e.g. Insulin) and some neurotransmitters are peptides.
- 2. Several antibiotics (e.g. Gramicidin and Valinomycin) are peptides.
- 3. Some antitumor agents are peptides (e.g.Bleomycin).

#-We started from amino group (N-terminal residue) from the left if we write the sequence of a.a. of P.P.Ch.



# Proteins

## **Protein Functions:**

- 1. Enzyme catalysis: e.g. All enzymes that catalyze cell reactions are proteins.
- 2. Transport and storage: Hemoglobin transport oxygen, Ferritin store iron.
- 3. Coordinated motions: e.g. muscles contain two motion proteins (myosin and actin)
- 4. Mechanical support: e.g. collagen (a fibrous protein)
- 5. Immune and Protection: e.g. Antibodies (immunoglobulin-A,-G,-M, and-E)
- 6. Control of growth and differentiation: e.g.(Hormones: insulin, growth hormone...)

# **Protein Structure**

Protein is a polymer of more than 100 amino acids. Each of them is called residue. There are 4 basic levels of structure in protein architecture: -



Figure-1. Levels of Structure in Proteins.

## **1-Protein Primary Structure**

The primary structure of peptides and proteins refers to the linear number and order (sequence) of the amino acids present.

#### 2-Protein Secondary Structure

The ordered array of amino acids in a protein confers regular conformational forms upon that protein. These conformations constitute the secondary structures of a protein.

@Two elements of secondary protein structure:

## A. The Alpha-Helix:

- The  $\alpha$ -helix is a common secondary structure encountered in proteins of the globular class.
- The formation of the  $\alpha$ -helix is spontaneous and is stabilized by H-bonding between amide nitrogen and carbonyl carbon of peptide bonds spaced <u>four</u> residues apart.
- helix makes one turn for every 3.6 amino acids, and the side chains of these amino acids project outward from the coiled backbone.

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Figure-2. α-helix Sheet Structure in Proteins

## **Pleated Sheets**:

• □-sheets are composed of 2 or more different regions of stretches of at least 5-10 amino acids. The folding and alignment of stretches of the polypeptide backbone aside one another to form □-sheets is stabilized by H-bonding between amide nitrogen and carbonyl carbon. Example; silk fibers protein



Figure-3. β-Pleated Sheet Structure in Proteins

Note: In general proteins fold into two broad classes of structure termed:

-globular proteins Globular proteins, the other major class, are soluble in aqueous media. In these proteins, the chains are folded so that the molecule as a whole is roughly spherical. Familiar examples include albumin. Serum albumin plays a major role in transporting fatty acids and maintaining a proper balance of osmotic pressures in the body. Hemoglobin and myoglobin, which are important for binding oxygen.

-fibrous proteins are insoluble in water and usually serve structural, connective, and protective functions. Examples of fibrous proteins are keratins, collagens, myosins, and elastins. Hair and the outer layer of skin are composed of keratin. Connective tissues contain collagen. Myosins are muscle proteins and are capable of contraction and extension. Elastins are found in ligaments and the elastic tissue of artery walls.

#### $Q/\Box$ Why $\Box$ -Sheets are said to be pleated $\Box$

 $\square$  This is due to positioning of the  $\square$ -carbons of the peptide bond which alternates above and below the plane of the sheet.

**@Types of**  $\square$  -Pleated Sheets: -  $\square$ -Sheets can be classified into parallel or antiparallel. Parallel beta pleated sheets have two polypeptide strands running in the same direction while antiparallel beta pleated sheets have two polypeptide strands running in the opposite directions.

#### **3-Tertiary Structure**

- The tertiary structure refers to the unique three-dimensional shape of the protein as a whole, which results from the folding and bending of the protein backbone.
- The interactions of different domains is governed by several forces: These include hydrogen bonding, hydrophobic interactions, electrostatic interactions and van der Waals forces.

#### **Forces Controlling Protein Structure**

- 1. **Ionic bonding**. Ionic bonds result from electrostatic attractions between positively and negatively charged side chains of amino acids. For example, the mutual attraction between an aspartic acid carboxylate ion and a lysine ammonium ion helps to maintain a particular folded area of a protein
- 2. Hydrogen Bonding: Polypeptides contain numerous proton donors and acceptors both in their backbone and in the R-groups of the amino acids. H-bonding, therefore, occurs not only within and between polypeptide chains but with the surrounding aqueous medium.
- **3. Hydrophobic Forces:** The hydrophobicity of certain amino acid R-groups tends to drive them away from the exterior of proteins and into the interior. This driving force restricts the available conformations into which a protein may fold.
- 4. Electrostatic Forces: Electrostatic forces are mainly of three types; chargecharge, charge-dipole and dipole-dipole.
- 5. Van der Waals Forces: There are both attractive and repulsive van der Waals forces that control protein folding.
- 6. **Disulfide bonds (Bridge):** The thiol of cysteine is able to form a disulfide bond with other cysteine in the same polypeptide chain in the Tertiary structure. For example; Ribonuclease A enzyme has 4 disulfide binds.



Figure-4. Four interactions stabilize the tertiary structure of a protein: (a) ionic bonding, (b) hydrogen bonding, (c) disulfide linkages, and (d) dispersion forces.

#### **4-Quaternary Structure:**

Proteins with multiple polypetide chains are termed **oligomeric** proteins. The structure formed by monomer-monomer interaction in an oligomeric protein is known as **quaternary structure**. e.g. Hemoglobin, the oxygen carrying protein of the blood, contains two  $\Box$  and two  $\Box$  subunits arranged with a quaternary structure in the form,  $\Box_2\Box_2$ . Hemoglobin is, therefore, a hetero-oligomeric protein.

#### **\*Complex Protein Structures**

I-glycoproteins: Proteins covalently associated with carbohydrates.

Proteins covalently conjugated with carbohydrates following the synthesis (**translation**) of proteins and are, therefore, termed (*post-translational modifications*).

-Glycoproteins are of two classes: (1) N-linked sugars are attached to the amide nitrogen of the R-group of asparagine (2) O-linked sugars are attached to the hydroxyl groups of either serine or threonine. they are extremely important glycoproteins found on the surface of erythrocytes. There are at least 100 blood group determinants, most of which are due to carbohydrate differences. The most common blood groups, A, B, and O.

**II-<u>lipoproteins</u>**: protein associated with lipid via <u>noncovalent</u> interactions are termed lipoproteins. Their major function in the body is to aid in the storage transport of lipid and cholesterol. Example: chylomicron, HDL, LDL, VLDL

## **Analysis of Protein Structure**

#### &&-Determination of Amino acid composition

## **I-Amino-Terminal Sequence Determination**:

There are three major chemical techniques for sequencing peptides and proteins from the N-terminus. These are the <u>Sanger, Dansyl chloride and Edman techniques</u>.

- 1. **Sanger's Reagent:** This sequencing technique utilizes the compound, 2,4dinitrofluorobenzene (DNF) which reacts with the N-terminal residue under alkaline conditions. The derivatized amino acid can be hydrolyzed and will be labeled with a dinitrobenzene group that imparts a yellow color to the amino acid. Separation of the modified amino acids (DNP-derivative) by <u>electrophoresis</u>.
- 2. **Dansyl chloride:** Like DNF, dansyl chloride reacts with the N-terminal residue under alkaline conditions. Analysis of the modified amino acids is carried out similarly to the Sanger method except that the dansylated amino acids are <u>detected by</u> <u>fluorescence</u>. This imparts <u>a higher sensitivity</u> into this technique over that of the Sanger method.
- 3. Edman degradation: This method utilizes phenylisothiocyanate to react with the N-terminal residue under alkaline conditions. The resultant phenylthiocarbamyl derivatized amino acid is hydrolyzed in anhydrous acid.



2,4-dinitrofluorobenzene

Dansyl chloride

phenylisothiocyanate

## **II-Protease Digestion**

Enzymes, *endopeptidases*, cleave at specific sites within the primary sequence of proteins. The resultant smaller peptides can be chromatographically separated and subjected to Edman degradation sequencing reactions. <u>Peptides longer than around 50 residues can not be sequenced completely by Edman degradation technique</u>.

\*For example, *Trypsin* specifically hydrolyze peptide bonds on the carboxylic sides of lysine, arginine and histidine. Other example is *Pepsin* cleaves peptide bonds in the aminoterminal side of the cyclic **amino acid** residues (tyrosine, phenylalanine, tryptophan and methionine).

Chymotrypsin hydrolyzes peptide bonds on the carboxylic sides of tyrosine, phenylalanine, tryptophan, valine and leucine.



#### **III-Carboxy-Terminal Sequence Determination**

*exopeptidases* enzymes have been identified that cleave peptides at the C-terminal residue which can then be analyzed chromatographically and compared to standard amino acids. This class of exopeptidases is called, *carboxypeptidases*. For example,

- 1- Carboxypeptidase A catalyzes hydrolysis of aromatic amino acids such as tyrosine, phenylalanine, tryptophan
- **2- Carboxypeptidase B** catalyzes hydrolysis of the basic amino acids such as lysine and arginine from the C-terminal end of polypeptides.
- 3- *Carboxypeptidase C* that cleaves all free C-terminal residues

Enzyme	Hydrolysis of bonds formed by carboxyl groups of
Pepsin	Phe, Tyr, Trp, Met
Trypsin	Arg, Lys
Chymotrypsin	Phe, Tyr, Trp, Val, Leu
Elastase	Ala, Gly, Ser
Carboxypeptidase A	C-terminal aromatic amino acid
Carboxypeptidase	C-terminal basic amino acid