SRINIVASAN COLLEGE OF ARTS AND SCIENCE

PERAMBALUR-621212

(Affiliated to Bharathidasn University-Tiruchirappalli)

DEPARTMENT OF CHEMISTRY

COURSE MATERIAL

COURSE : UG

SUBJECT : ORGANIC CHEMISTRY II

SUBJECT CODE : 16SCCCH8

SEMESTER : EVEN SEM

SYLLABUS

S.NO	UNIT	PAGE NO
1	**CHEMISTRY OF CARBOHYDRATES**	**5-21**
2	**CHEMISTRY OF PROTEINS AND VITAMINS**	**22-43**
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4	**MOLECULAR REARRANGEMENTS**	**63-77**
5	**ORGANIC SPECTROSCOPY**	**78-100**

SYLLABUS

ORGANIC CHEMISTRY II

OBJECTIVES

1. To learn the chemistry of carbohydrates, proteins, vitamins, alkaloids and terpenoids.
2. To understand the rearrangements and spectroscopy techniques for the elucidation of structures.

UNIT I CHEMISTRY OF CARBOHYDRATES

1.1 Carbohydrate - classification, properties of mono saccharides (glucose and fructose), structure and configuration of mono saccharides, interconversion.
1.2 Ascending and descending series, muta rotation, epimerization- cyclic structure - determination of size of sugar rings.
1.3 Disaccharides - sucrose, maltose - structure elucidation - polysaccharide - starch and cellulose (elementary treatment).

UNIT II CHEMISTRY OF PROTEINS AND VITAMINS

2.1 Amino acids – Zwitter ion – isoeletric point - general methods of preparation and reactions of amino acids. Peptides - Peptide linkages – proteins - classification of proteins.
2.2 Structure of proteins - primary structure - end group analysis - Edman method - secondary structure - tertiary structure - denaturation - colour reactions of proteins.
2.3 Nucleic acids - elementary treatment of DNA and RNA - Vitamins - classification, structure and biological importance of vitamins A, B_1, B_2, B_6, B_{12} and C.

UNIT III CHEMISTRY OF ALKALOIDS AND TERPENOIDS

3.1 Chemistry of natural products - alkaloids – classification, isolation - methods for synthesis of coniine, piperine, nicotine and quinine.
3.2 Terpenoids - classification - isoprene, special isoprene rule, methods for synthesis of citral, limonene, menthol, camphor.

UNIT IV MOLECULAR REARRANGEMENTS

4.1 Molecular rearrangements - types of rearrangement (nucleophilic and electrophilic) – mechanism with evidence for the following re-arrangements: pinacol – pinacolone.
4.2 Benzil - benzilic acid, benzidine, Claisen, Fries, Hofmann. Curtius, Lossen, Beckmann and dienone – phenol rearrangements.

UNIT V ORGANIC SPECTROSCOPY

5.1 UV - VIS spectroscopy - types of electronic transitions – Instrumentation- solvent effects on λ max - Woodward - Fieser rules for calculation of λ max : dienes only – bathochromic shift and hypsochromic shift.

5.2IR spectroscopy - number and types of fundamental vibrations – selection rulesmodes of vibrations and their energies. Instrumentation - position of IR absorption frequencies for functional groups like aldehyde, ketone, alcohol, acid, amine and amide.

5.3 NMR spectroscopy - principle - chemical shift- factors affecting the chemical shift - inductive effect and hydrogen bonding - TMS, delta scales, splitting of signals - spin-spin coupling, NMR spectrum of EtOH, n -propyl bromide and isopropyl bromide.

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UNIT I

CHEMISTRY OF CARBOHYDRATES

Carbohydrate:

Carbohydrates, also known as saccharides or carbs, are sugars or starches. They are a major food source and a key form of energy for most organisms.

They consist of carbon, hydrogen, and oxygen atoms.

Two basic compounds make up carbohydrates:

Aldehydes: These are double-bonded carbon and oxygen atoms, plus a hydrogen atom.

Ketones: These are double-bonded carbon and oxygen atoms, plus two additional carbon atoms.

Carbs can combine together to form polymers, or chains.

These polymers can function as:

- long-term food storage molecules
- protective membranes for organisms and cells
- the main structural support for plants
- Most organic matter on earth is made up of carbohydrates. They are involved in many aspects of life.

Classification:

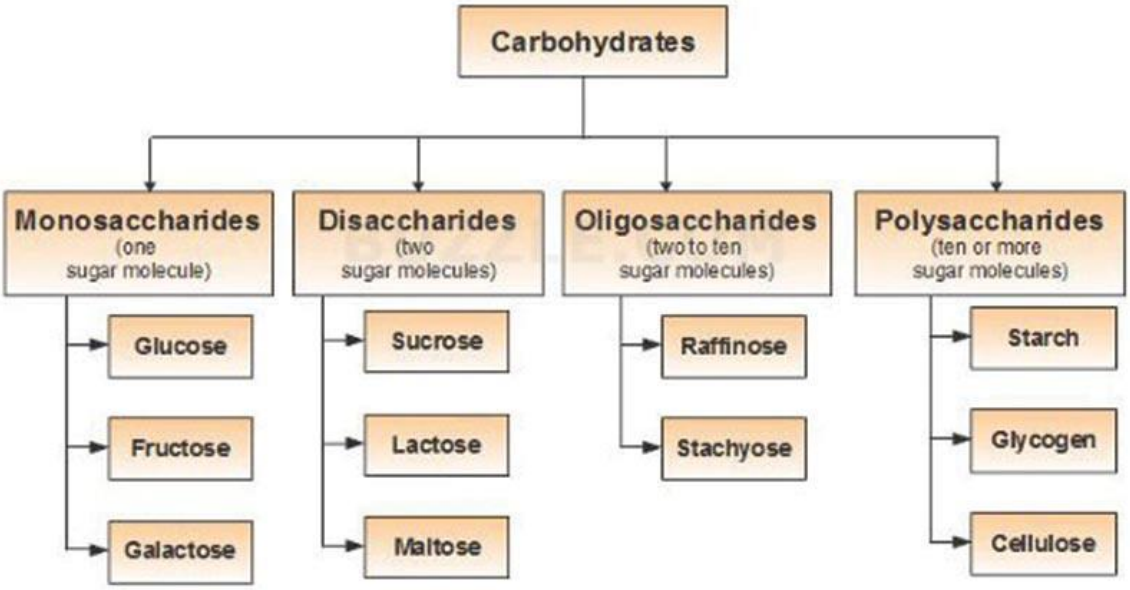
There are various types of carbohydrate. They include:

Monosaccharides

Disaccharides

Oligosaccharides

Polysaccharides



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Monosaccharides

This is the smallest possible sugar unit. Examples include glucose, galactose, or fructose. Glucose is a major source of energy for a cell. “Blood sugar” means “glucose in the blood.”

In human nutrition, these include:

- galactose, most readily available in milk and dairy products
- fructose, mostly in vegetables and fruit

Disaccharides

Disaccharides are two monosaccharide molecules bonded together, for example, lactose, maltose, and sucrose.

Bonding one glucose molecule with a galactose molecule produces lactose. Lactose is commonly found in milk.

Bonding one glucose molecule with a fructose molecule, produces a sucrose molecule.

Sucrose is found in table sugar. It is often results from photosynthesis, when sunlight absorbed by chlorophyll reacts with other compounds in plants.

Polysaccharides

Different polysaccharides act as food stores in plants and animals. They also play a structural role in the plant cell wall and the tough outer skeleton of insects.

Polysaccharides are a chain of two or more monosaccharides.

The chain may be:

- branched, so that the molecule looks like a tree with branches and twigs
- unbranched, where the molecule is a straight line

Polysaccharide molecule chains may consist of hundreds or thousands of monosaccharides.

Glycogen is a polysaccharide that humans and animals store in the liver and muscles.

Starches are glucose polymers that are made up of amylose and amylopectin. Rich sources include potatoes, rice, and wheat. Starches are not water soluble. Humans and animals digest them using amylase enzymes.

Cellulose is one of the main structural constituents of plants. Wood, paper, and cotton are mostly made of cellulose.

Properties of Mono Saccharides:

- **Stereoisomerism** – Compound shaving the same structural formula but they differ in spatial configuration. Example: Glucose has two isomers with respect to the penultimate carbon atom. They are D-glucose and L-glucose.
- **Optical Activity** – It is the rotation of plane-polarized light forming (+) glucose and (-) glucose.
- **Diastereo isomers** – It the configurational changes with regard to C2, C3, or C4 in glucose. Example: Mannose, galactose.
- **Annomerism** – It is the spatial configuration with respect to the first carbon atom in aldoses and second carbon atom in ketoses.
- Most monosaccharides have a sweet taste (fructose is sweetest; 73% sweeter than sucrose).
- They are solids at room temperature.
- They are extremely soluble in water: – Despite their high molecular weights, the presence of large numbers of OH groups make the monosaccharides much more water-soluble than most molecules of similar MW.
- Glucose can dissolve in minute amounts of water to make a syrup (1 g / 1 ml H_2O).
- Simplest group of carbohydrates and often called simple sugars since they cannot be further hydrolyzed.
- Colorless, crystalline solid which are soluble in water and insoluble in a non-polar solvent.
- These are compound which possesses a free aldehyde or ketone group.

- The general formula is $C_n(H2O)_n$or $C_nH_{2n}O_n$.
- They are classified according to the number of carbon atoms they contain and also on the basis of the functional group present.
- The monosaccharides thus with 3,4,5,6,7… carbons are called trioses, tetroses, pentoses, hexoses, heptoses, etc., and also as aldoses or ketoses depending upon whether they contain aldehyde or ketone group.
- Examples: **Glucose, Fructose, Erythrulose, Ribulose.**

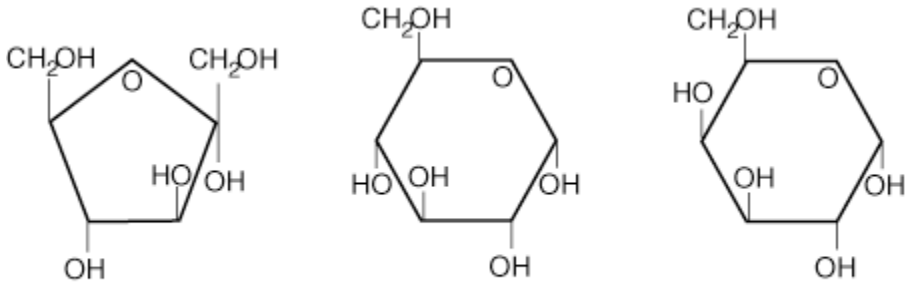
Structure and Configuration of Mono Saccharides:

Carbohydrates, one type of macromolecule, especially when it comes to what we eat. To lose weight, some individuals adhere to "low-carb" diets. Athletes, in contrast, often "carb-load" before important competitions to ensure that they have enough energy to compete at a high level. Carbohydrates are, in fact, an essential part of our diet; grains, fruits, and vegetables are all natural sources of carbohydrates. Carbohydrates provide energy to the body, particularly through glucose, a simple sugar that is a component of starch and an ingredient in many staple foods. Carbohydrates also have other important functions in humans, animals, and plants.

Carbohydrates can be represented by the stoichiometric formula $(CH_2O)n$, where n is the number of carbons in the molecule. In other words, the ratio of carbon to hydrogen to oxygen is 1:2:1 in carbohydrate molecules. This formula also explains the origin of the term "carbohydrate": the components are carbon ("carbo") and the components of water (hence, "hydrate"). Carbohydrates are classified into three subtypes: monosaccharides, disaccharides, and polysaccharides.

Monosaccharides

Monosaccharides (*mono–* = "one"; *sacchar–* = "sweet") are simple sugars, the most common of which is glucose. In monosaccharides, the number of carbons usually ranges from three to seven. Most monosaccharide names end with the suffix *–ose*. If the sugar has an aldehyde group (the functional group with the structure R-CHO), it is known as an aldose, and if it has a ketone group (the functional group with the structure RC(=O)R′), it is known as a ketose. Depending on the number of carbons in the sugar, they also may be known as trioses (three carbons), pentoses (five carbons), and or hexoses (six carbons). See Figure 1 for an illustration of the monosaccharides.



Fructose Glucose Galactose

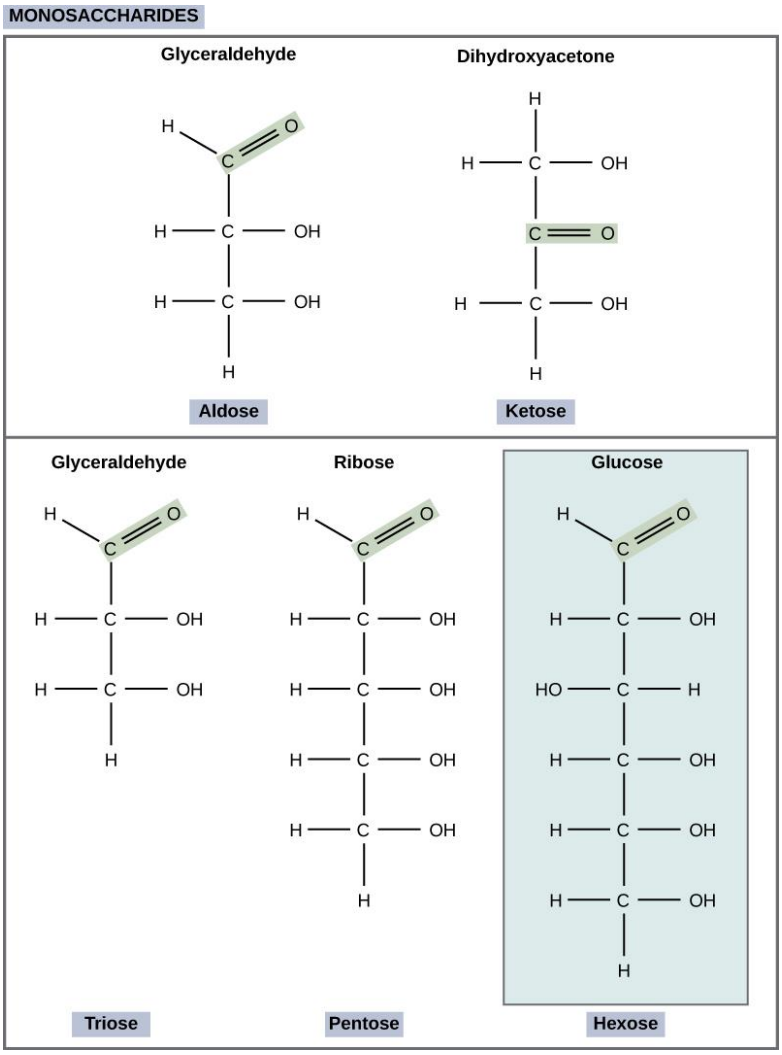


Figure 1. Monosaccharides are classified based on the position of their carbonyl group and the number of carbons in the backbone. Aldoses have a carbonyl group (indicated in green) at the end of the carbon chain, and ketoses have a carbonyl group in the middle of the carbon chain. Trioses, pentoses, and hexoses have three, five, and six carbon backbones, respectively.

The chemical formula for glucose is $C_6H_{12}O_6$. In humans, glucose is an important source of energy. During cellular respiration, energy is released from glucose, and that energy is used to help make adenosine triphosphate (ATP). Plants synthesize glucose using carbon dioxide and water, and glucose in turn is used for energy requirements for the plant. Excess glucose is often stored as starch that is catabolized (the breakdown of larger molecules by cells) by humans and other animals that feed on plants.

Galactose and fructose are other common monosaccharides — galactose is found in milk sugars and fructose is found in fruit sugars. Although glucose, galactose, and fructose all have the same chemical formula ($C_6H_{12}O_6$), they differ structurally and chemically (and are known as isomers) because of the different arrangement of functional groups around the asymmetric carbon; all of these monosaccharides have more than one asymmetric carbon (Figure 2).

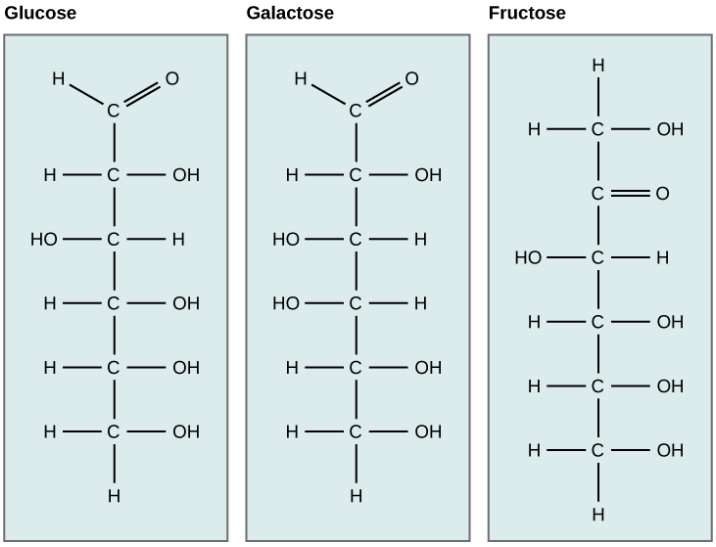


Figure 2. Glucose, galactose, and fructose are all hexoses. They are structural isomers, meaning they have the same chemical formula ($C_6H_{12}O_6$) but a different arrangement of atoms.

Monosaccharides can exist as a linear chain or as ring-shaped molecules; in aqueous solutions they are usually found in ring forms (Figure 3). Glucose in a ring form can have two different arrangements of the hydroxyl group (−OH) around the anomeric carbon (carbon 1 that becomes asymmetric in the process of ring formation). If the hydroxyl group is below carbon number 1 in the sugar, it is said to be in the alpha (α) position, and if it is above the plane, it is said to be in the beta (β) position.

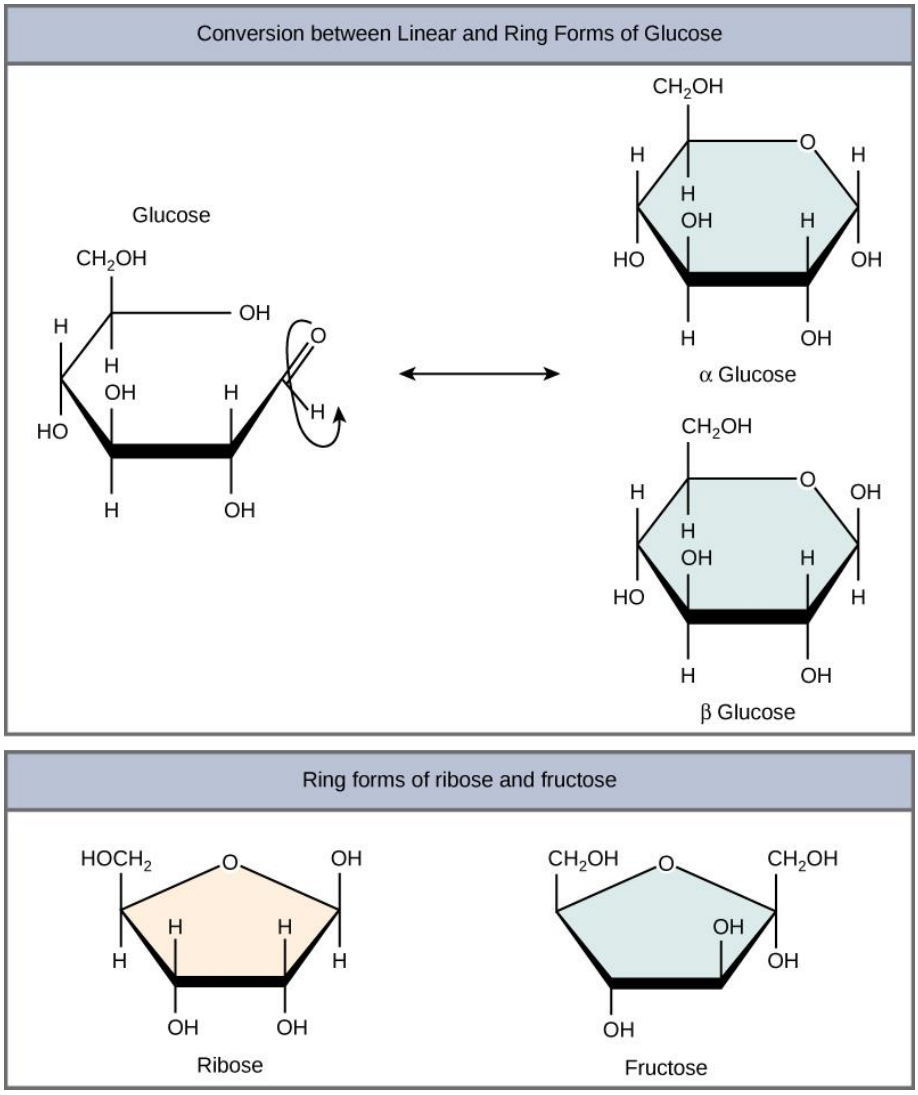
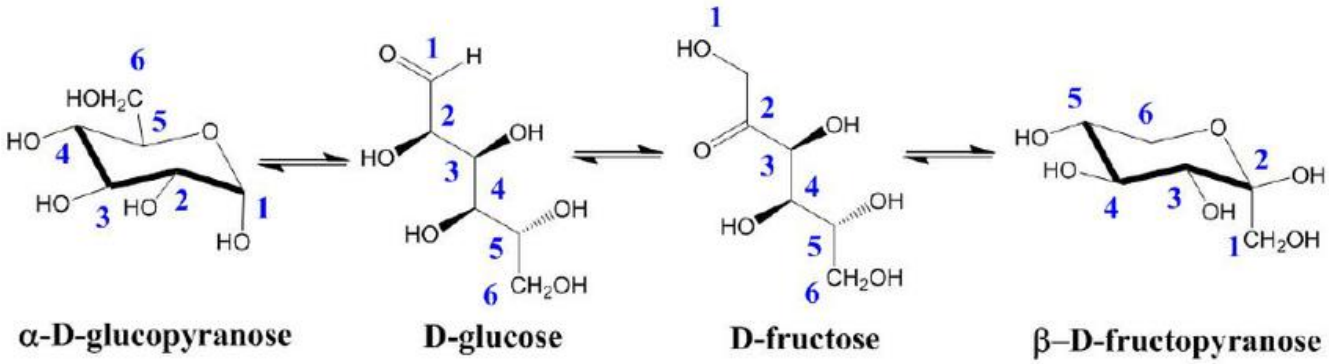


Figure 3. Five and six carbon monosaccharides exist in equilibrium between linear and ring forms. When the ring forms, the side chain it closes on is locked into an α or β position. Fructose and ribose also form rings, although they form five-membered rings as opposed to the six-membered ring of glucose.

Interconversion:

Conversion of D-glucose to D-fructose by interconversion. the complete reaction cat- alyzed by is believed to involve three major steps:

(1) ring opening, (2) isomerization, and (3) ring closure.



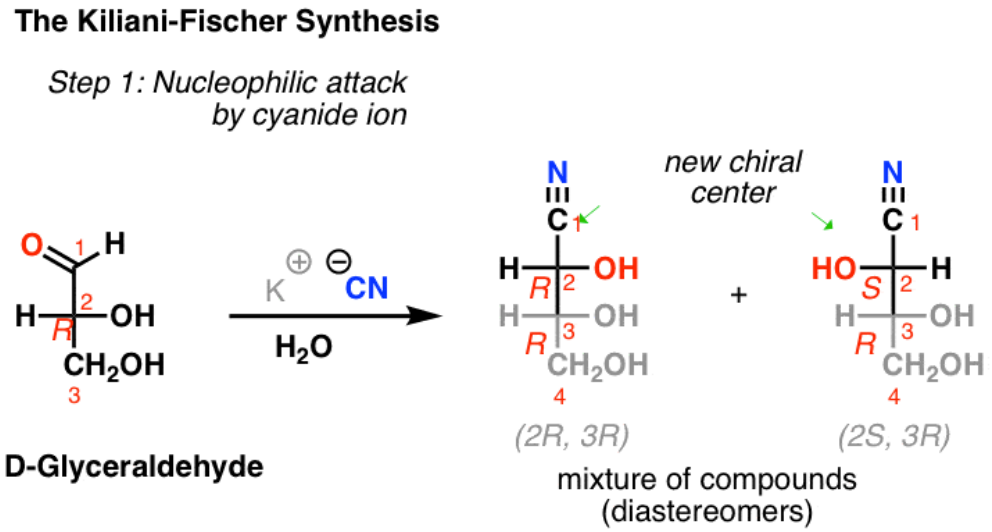
Ascending and descending series:

The Kiliani-Fischer Synthesis

This very same reaction can be used to extend the carbon chain of a very prominent class of aldehydes: **aldoses** .For example, take the simplest sugar, the three-carbon aldose glyceraldehyde (below, show D-glyceraldehyde).

As with the example above, attack of cyanide ion on the aldehyde results in a cyanohydrin, extending the length of the longest carbon chain from three to four. It also creates a new stereocenter, giving rise to a mixture of products with (*R)* and *(S)* configurations.

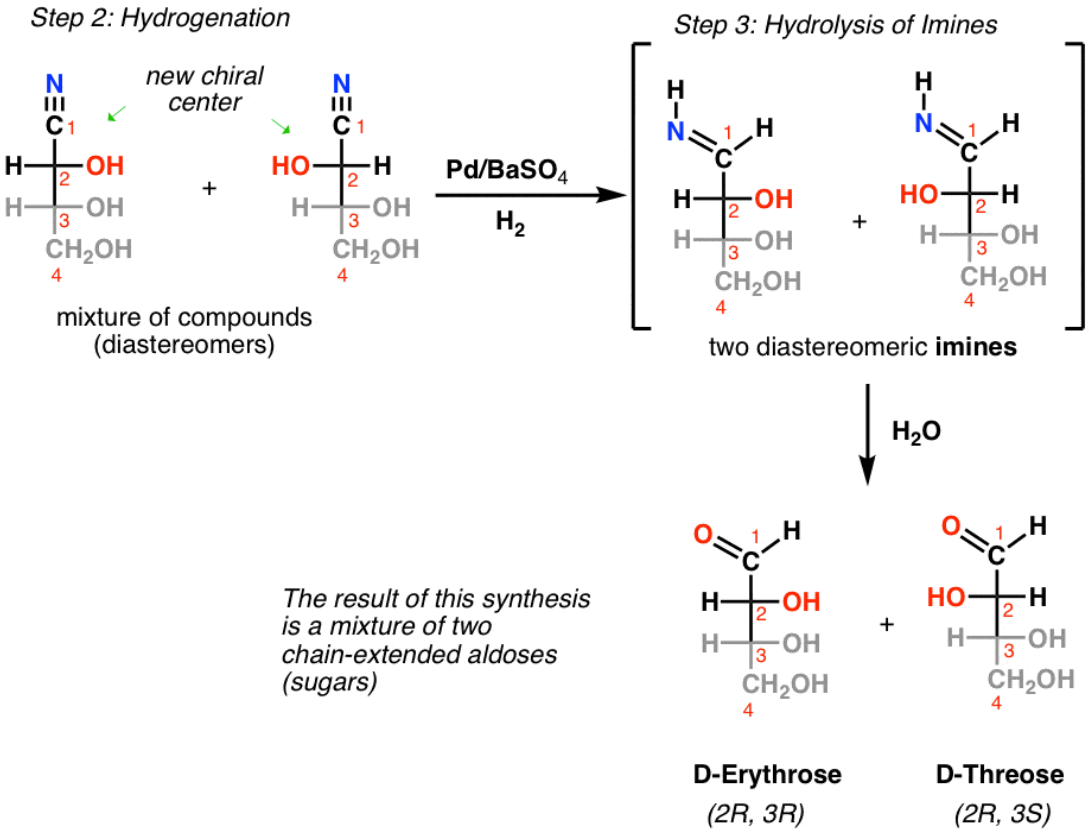
Since the stereocenter at the C-3 carbon (*R*) remains unchanged by this process, in the absence of any chiral reagents this process results in a mixture of diastereomers: (*2R, 3R*) and (*2S, 3R*).



Reduction and Hydrolysis Converts the Nitrile into an Aldehyde

While these cyanohydrins can be hydrolyzed to carboxylic acids (with aqueous acid), it's often more useful to adopt the process for the creating of a new aldose.

Using a poisoned catalyst ($Pd/BaSO_4$) in the presence of hydrogen gas (H_2) will reduce the nitrile to an **imine**. In the presence of water, the imine will then be rapidly hydrolyzed to an aldehyde.



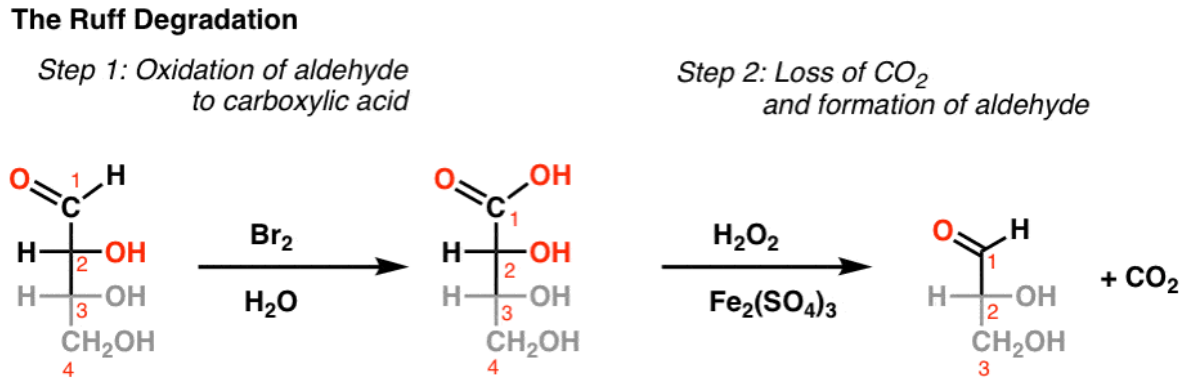
The result is an extension of a sugar by one carbon (as a mixture). For example, application of this procedure to D-glyceraldehyde results in the two diastereomers D-erythrose (2R, 3R) and D-threose (2R, 3S). (*Since these two diastereomers only differ in the configuration at a single carbon, they are often called "epimers".)*

The Ruff Degradation

It's also possible to go in the *reverse* direction, where an aldose is **reduced** in length by one carbon.

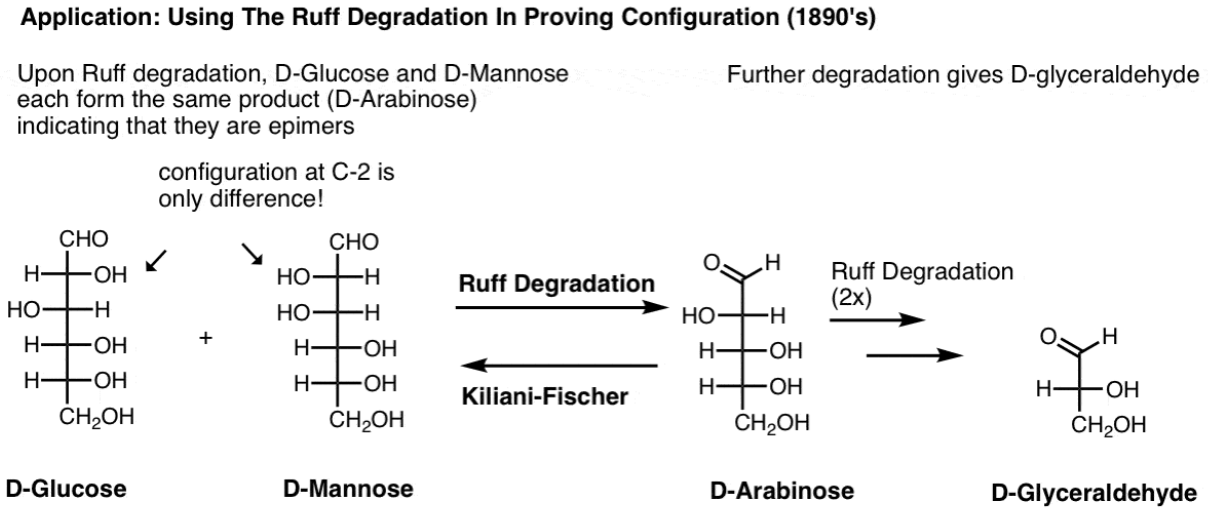
In the first step, the aldehyde is selectively oxidized to a carboxylic acid by bromine (Br_2) and water. *Note that the secondary and primary alcohols are not oxidized here!*

The next step involves adding an iron (III) salt [$Fe_2(SO_4)_3$] with hydrogen peroxide, which involves the loss of carbon dioxide and oxidation of the adjacent C_2-OH to an aldehyde:



Most courses don't generally go into the weeds as far as the mechanistic details, but we'll have a stab at the Br_2/H_2O reaction down in the endnotes.

Fischer was able to show that D-glucose and D-mannose each formed the same product upon Ruff degradation (D-arabinose) indicating them to have opposite configurations at C-2 (epimers). Further Ruff degradations gave D-glyceraldehyde, which established the stereochemistry of the chiral center on C-5.



Muta Rotation:

Mutarotation refers to the change in specific rotation over time due to a change between isomers. 'Muta' means 'change', so it literally means a change in rotation.

The specific rotation of a molecule never changes, but the specific rotation of the entire solution can change. This is because the molecule can change between isomers in some cases (such as with glucose).

Let's look at what happens when we put pure alpha-D-Glucose into water and measure the specific rotation over time. At first, it starts out at 112° just as we would expect, but it slowly starts to change until it reaches 52.5° .

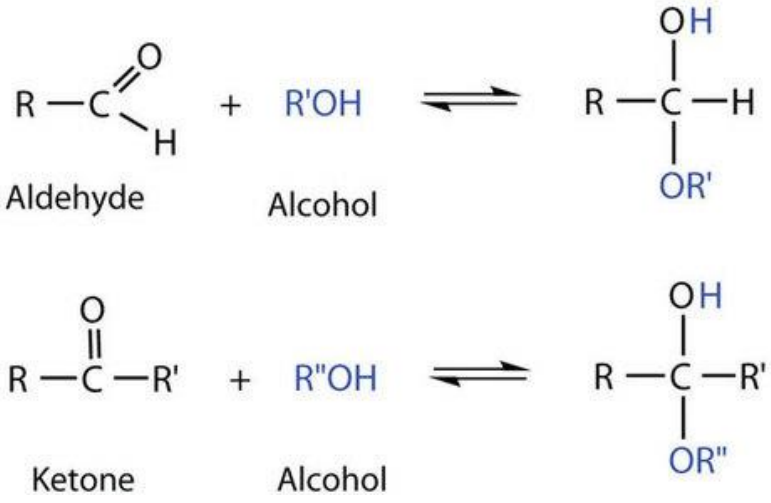
Now, let's look at what happens when we put pure beta-D-Glucose into water and measure the specific rotation over time. Once again, it starts out where we would expect it at 18.7°, but it slowly changes until it also reaches 52.5°.

Epimerization:

Epimerization is a chemical process where an epimer is converted to its chiral counterpart.It can happen in condensed tannins depolymerisation reactions. Epimerisation can be spontaneous (generally a slow process), or catalyzed by enzymes, e.g. the epimerization between the sugars *N*-acetylglucosamine and *N*-acetylmannosamine, which is catalyzed by renin-binding protein.

Cyclic Structure -Determination of Size of Sugar Rings:

So far we have represented monosaccharides as linear molecules, but many of them also adopt cyclic structures. This conversion occurs because of the ability of aldehydes and ketones to react with alcohols:



You might wonder why the aldehyde reacts with the OH group on the fifth carbon atom rather than the OH group on the second carbon atom next to it. Recall that cyclic alkanes containing five or six carbon atoms in the ring are the most stable. The same is true for monosaccharides that form cyclic structures: rings consisting of five or six carbon atoms are the most stable.

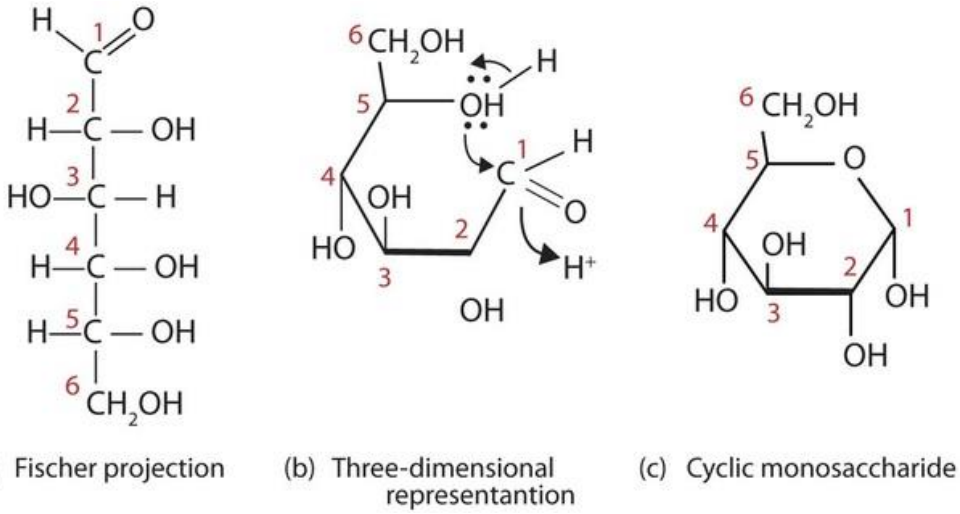


Figure1: Cyclization of D-Glucose. D-Glucose can be represented with a Fischer projection (a) or three dimensionally (b). By reacting the OH group on the fifth carbon atom with the aldehyde group, the cyclic monosaccharide (c) is produced.

When a straight-chain monosaccharide, such as any of the structures shown in Figure, forms a cyclic structure, the carbonyl oxygen atom may be pushed either up or down, giving rise to two stereoisomers, as shown in Figure.2.

The structure shown on the left side of Figure 2, with the OH group on the first carbon atom projected downward, represent what is called the *alpha (α) form*. The structures on the right side, with the OH group on the first carbon atom pointed upward, is the *beta (β) form*. These two stereoisomers of a cyclic monosaccharide are known as anomers; they differ in structure around the anomeric carbon—that is, the carbon atom that was the carbonyl carbon atom in the straight-chain form.

It is possible to obtain a sample of crystalline glucose in which all the molecules have the α structure or all have the β structure. The α form melts at 146°C and has a specific rotation of +112°, while the β form melts at 150°C and has a specific rotation of +18.7°. When the sample is dissolved in water, however, a mixture is soon produced containing both anomers as well as the straight-chain form, in dynamic equilibrium (part (a) of Figure.2

You can start with a pure crystalline sample of glucose consisting entirely of either anomer, but as soon as the molecules dissolve in water, they open to form the carbonyl group and then reclose to form either the α or the β anomer.

The opening and closing repeats continuously in an ongoing interconversion between anomeric forms and is referred to as mutarotation (Latin *mutare*, meaning "to change"). At equilibrium, the mixture consists of about 36% α-D-glucose, 64% β-D-glucose, and less than 0.02% of the open-chain aldehyde form. The observed rotation of this solution is +52.7°.

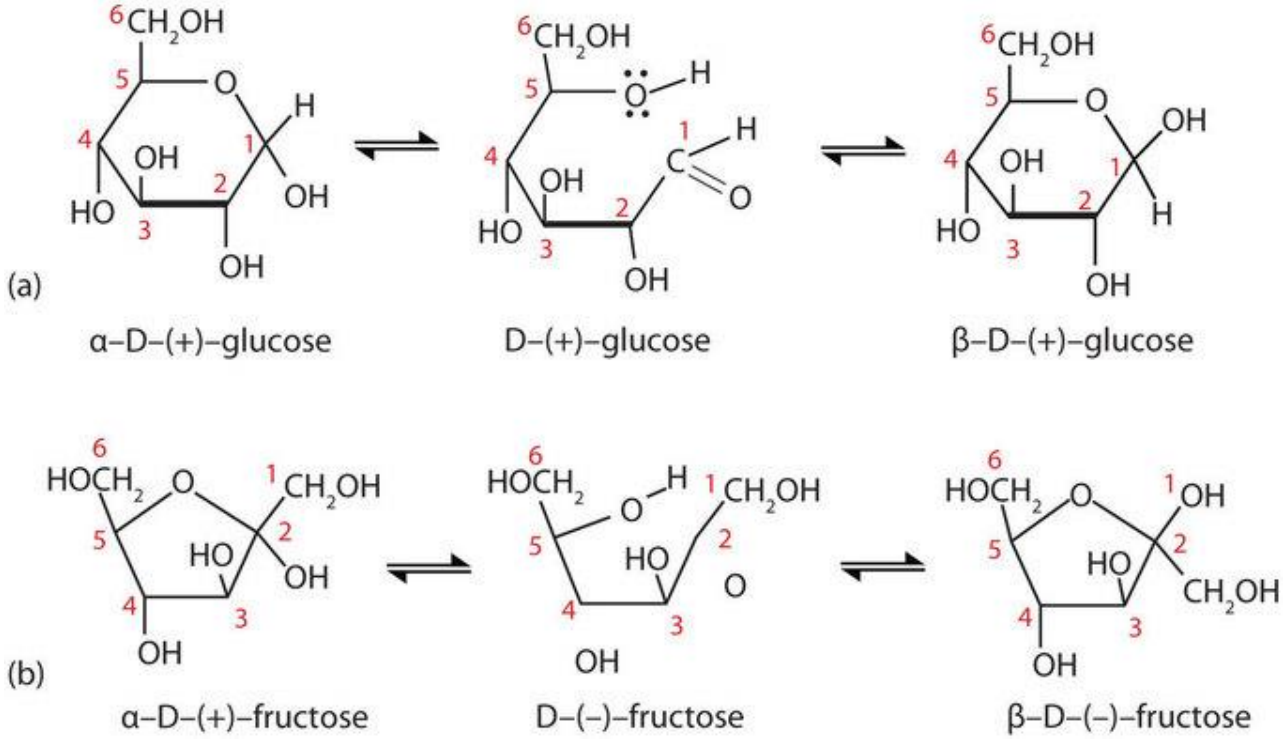


Figure 2: Monosaccharides. In an aqueous solution, monosaccharides exist as an equilibrium mixture of three forms. The interconversion between the forms is known as *mutarotation*, which is shown for D-glucose (a) and D-fructose (b).

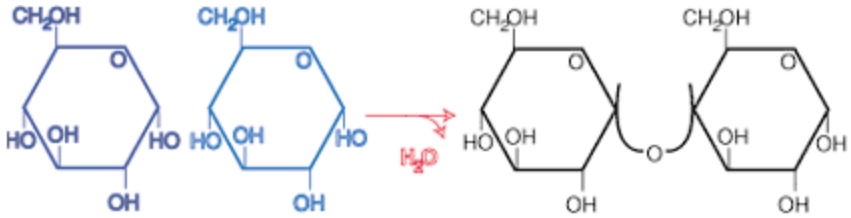
Even though only a small percentage of the molecules are in the open-chain aldehyde form at any time, the solution will nevertheless exhibit the characteristic reactions of an aldehyde. As the small amount of free aldehyde is used up in a reaction, there is a shift in the equilibrium to yield more aldehyde. Thus, *all* the molecules may eventually react, even though very little free aldehyde is present at a time.

The cyclic forms of sugars are depicted using a convention first suggested by Walter N. Haworth, an English chemist. The molecules are drawn as planar hexagons with a darkened edge representing the side facing toward the viewer. The structure is simplified to show only the functional groups attached to the carbon atoms. Any group written to the right in a Fischer projection appears below the plane of the ring in a Haworth projection, and any group written to the left in a Fischer projection appears above the plane in a Haworth projection.

The difference between the α and the β forms of sugars may seem trivial, but such structural differences are often crucial in biochemical reactions. This explains why we can get energy from the starch in potatoes and other plants but not from cellulose, even though both starch and cellulose are polysaccharides composed of glucose molecules linked together.

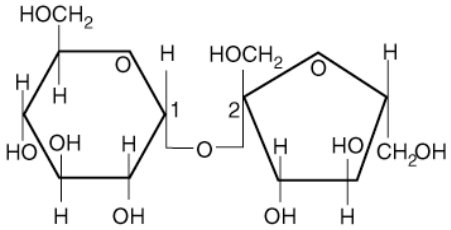
Disaccharides:

Disaccharides, meaning "two sugars", are commonly found in nature as sucrose, lactose and maltose. They are formed by a condensation reaction where one molecule of water condenses or is released during the joining of two monosaccharides. The type of bond that is formed between the two sugars is called a glycosidic bond.



Sucrose:

Sucrose is found in common table sugar and is composed of glucose and fructose linked via a 1-2 alpha glycosidic bond.



preservative because it has no "reducing end" or reactive group like the other sugars. Because glucose is joined to the carbon atom labeled number two on fructose, neither monosaccharide is able to open or react with other compounds in solution. It is for this reason that sucrose is an excellent natural preservative and is found in many jarred foods including jams. Other natural sources of sucrose are found in plants such as sugar cane, sugar beets, and maple syrup.

Maltose:

Maltose is the final disaccharide and consists of two glucose molecules joined by an alpha glycosidic bond. Maltose is an interesting compound because of its use in alcohol production. Through a process called fermentation, glucose, maltose and other sugars are converted to ethanol by yeast cells in the absence of oxygen. Through an analogous process, muscle cells convert glucose into lactic acid to obtain energy while the body operates under anaerobic conditions. Although maltose is uncommon in nature, it can be formed through the breakdown of starch by the enzymes of the mouth.

Structure Elucidation:

Polysaccharide:

Polysaccharides or complex carbohydrates are usually monomers and consist of thousands of repeating glucose units. Naturally, they allow for the storage of large quantities of glucose. Starch is the major storage form of carbohydrate in plants and has two different types: amylose and amylopectin. Although digestible alpha glycoisidic bonds link both types of starch, each type is unique in their branching of glucose. While amylose is a straight chain polymer, amylopectin is highly branched. These differences account for the fact that amylopectin can form stable starch gels which are able to retain water while amylose is unable to do so. Therefore, amylopectin is often used by manufacturers to produce many different kinds of thick sauces and gravies. Sources of starch include potatoes, beans, bread, pasta, rice and other bread products.

Like amylopectin, glycogen is a highly branched polymer of glucose that is the main storage form of carbohydrate in humans. The main chain of the structure is composed of alpha 1, 4 glycosidic bonds, while alpha 1,6 glycosidic bonds give rise to the branch points of the polymer (figure 5). Glycogen is stored in the liver and muscle where it is synthesized and degraded depending upon the energy requirements of the body.

Indigestible forms of polysaccharides are known as dietary fiber and come in many different forms including cellulose, hemicellulose, pectin, gum and mucilage. Cellulose is by far the most abundant biochemical compound on the earth because it forms part of the structure of many plants. It is unique among polysaccharides in that it forms intramolecular hydrogen bonds between adjacent glucose units as well as beta 1,4 glycosidic bonds present in other carbohydrates. These special bonding characteristics allow cellulose to form long, straight chains of glucose and give it strength and rigidity that many plants require for proper growth. Cellulose and most forms of hemicellulose are insoluble fibers while pectin, gum and mucilage are all soluble fibers and readily dissolve or swell when mixed with water.

Starch:

Starch is the stored form of sugars in plants and is made up of a mixture of amylose and amylopectin (both polymers of glucose). Plants are able to synthesize glucose, and the excess glucose, beyond the plant's immediate energy needs, is stored as starch in different plant parts, including roots and seeds. The starch in the seeds provides food for the embryo as it germinates and can also act as a source of food for humans and animals. The starch that is consumed by humans is broken down by enzymes, such as salivary amylases, into smaller molecules, such as maltose and glucose. The cells can then absorb the glucose.

Starch is made up of glucose monomers that are joined by α 1-4 or α 1-6 glycosidic bonds. The numbers 1-4 and 1-6 refer to the carbon number of the two residues that have joined to form the bond. As illustrated in Figure 6, amylose is starch formed by unbranched chains of glucose monomers (only α 1-4 linkages), whereas amylopectin is a branched polysaccharide (α 1-6 linkages at the branch points).

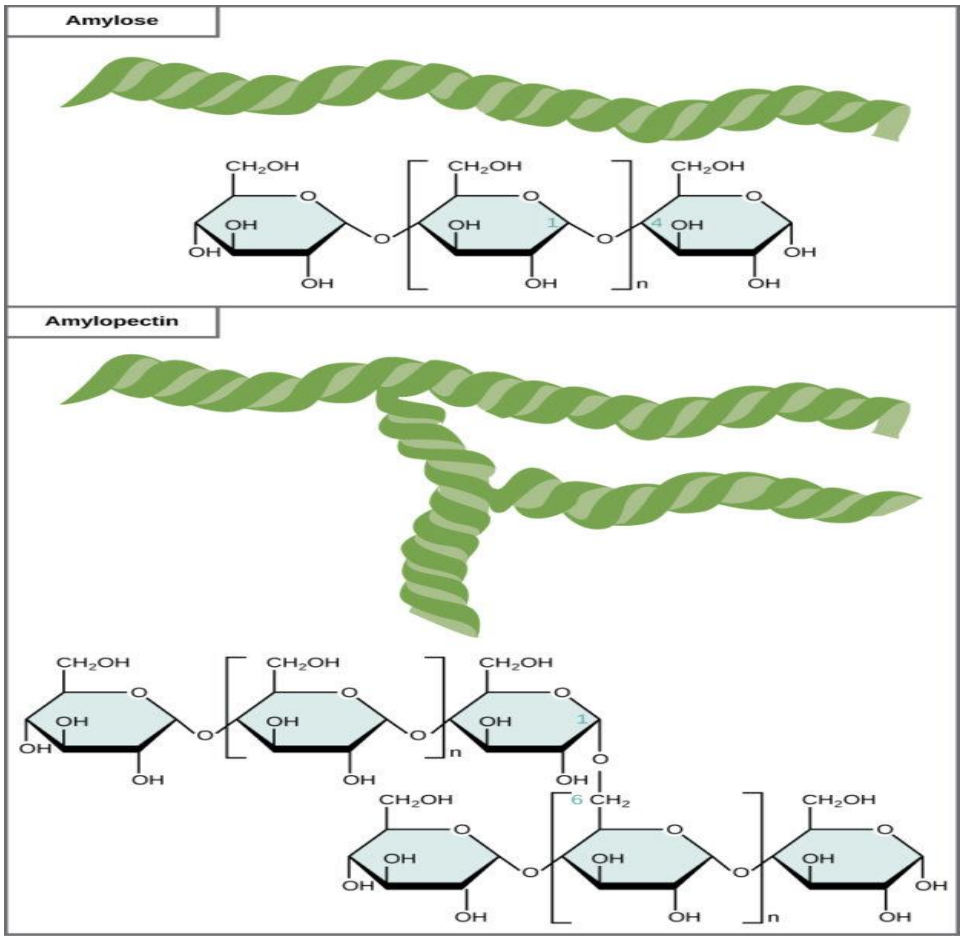


Figure . Amylose and amylopectin are two different forms of starch. Amylose is composed of unbranched chains of glucose monomers connected by α 1,4 glycosidic linkages.

Amylopectin is composed of branched chains of glucose monomers connected by α 1,4 and α 1,6 glycosidic linkages. Because of the way the subunits are joined, the glucose chains have a helical structure. Glycogen (not shown) is similar in structure to amylopectin but more highly branched.

Cellulose:

Cellulose is the most abundant natural biopolymer. The cell wall of plants is mostly made of cellulose; this provides structural support to the cell. Wood and paper are mostly cellulosic in nature. Cellulose is made up of glucose monomers that are linked by β 1-4 glycosidic bonds (Figure).

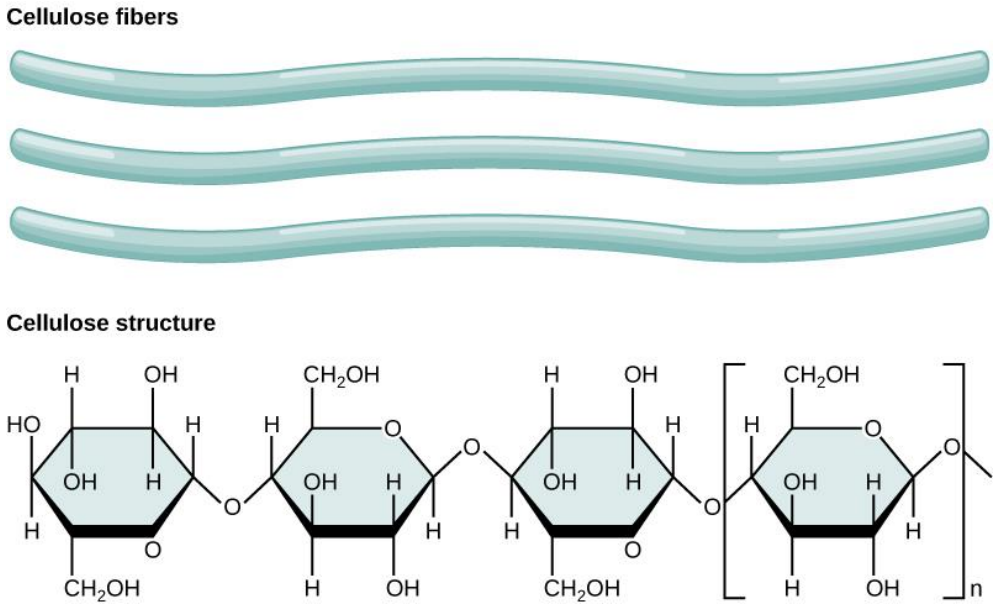


Figure . In cellulose, glucose monomers are linked in unbranched chains by β 1-4 glycosidic linkages. Because of the way the glucose subunits are joined, every glucose monomer is flipped relative to the next one resulting in a linear, fibrous structure.

As shown in Figure , every other glucose monomer in cellulose is flipped over, and the monomers are packed tightly as extended long chains. This gives cellulose its rigidity and high tensile strength—which is so important to plant cells. While the β 1-4 linkage cannot be broken down by human digestive enzymes, herbivores such as cows, koalas, buffalos, and horses are able, with the help of the specialized flora in their stomach, to digest plant material that is rich in cellulose and use it as a food source.

In these animals, certain species of bacteria and protists reside in the rumen (part of the digestive system of herbivores) and secrete the enzyme cellulase. The appendix of grazing animals also contains bacteria that digest cellulose, giving it an important role in the digestive systems of ruminants. Cellulases can break down cellulose into glucose monomers that can be used as an energy source by the animal. Termites are also able to break down cellulose because of the presence of other organisms in their bodies that secrete cellulases.

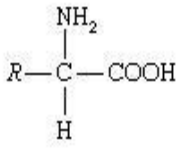
UNIT II

CHEMISTRY OF PROTEINS AND VITAMINS

Amino acids:

Amino acid, any of a group of organic molecules that consist of a basic amino group ($-NH_2$), an acidic carboxyl group (−COOH), and an organic *R* group (or side chain) that is unique to each amino acid.

The term *amino acid* is short for *α-amino [alpha-amino] carboxylic acid*. Each molecule contains a central carbon (C) atom, called the α-carbon, to which both an amino and a carboxyl group are attached. The remaining two bonds of the α-carbon atom are generally satisfied by a hydrogen (H) atom and the *R* group. The formula of a general amino acid is:



Simple structure of amino acids

Zwitter Ion:

A zwitterion is a molecule with functional groups, of which at least one has a positive and one has a negative electrical charge. The net charge of the entire molecule is zero. Amino acids are the best-known examples of zwitterions. They contain an amine group (basic) and a carboxylic group (acidic). The -NH2 group is the stronger base, and so it picks up H+ from the -COOH group to leave a zwitterion. The (neutral) zwitterion is the usual form amino acids exist in solution.

Isoeletric Point:

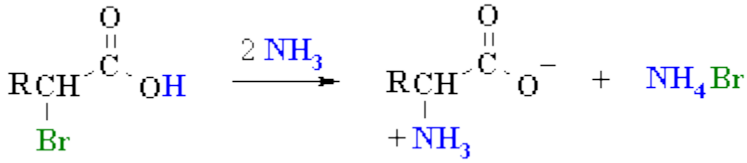
The isoelectric point (pI, pH(I), IEP), is the pH at which a molecule carries no net electrical charge or is electrically neutral in the statistical mean.

The net charge on the molecule is affected by pH of its surrounding environment and can become more positively or negatively charged due to the gain or loss, respectively, of protons (H+).

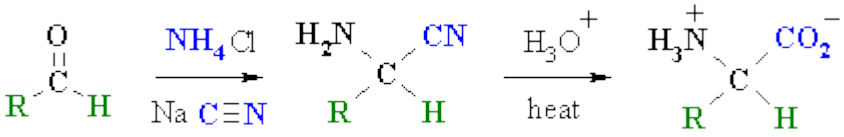
General Methods of Preparation:

There are several ways in which α-amino acids can be synthesised using reactions we have already encountered:

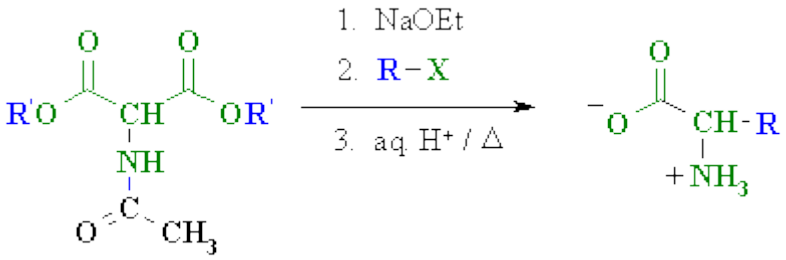
- Nucleophilic substitution of α-halocarboxylic acids



- Strecker synthesis



- Alkylation of an acetamidomalonae



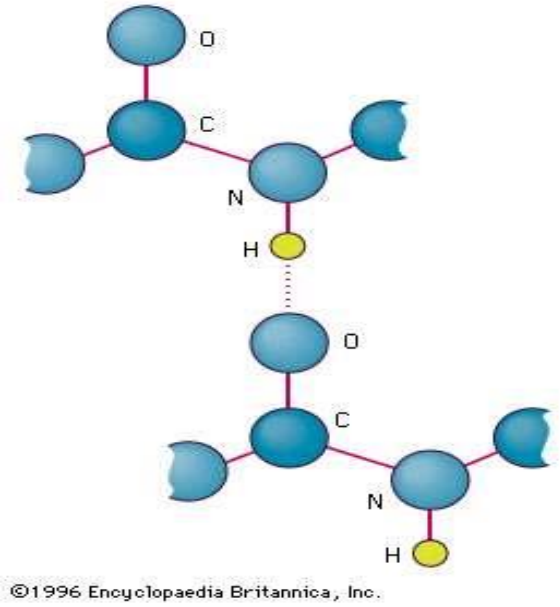
Reactions of Amino Acids:

Amino acids via their various chemical functionalities (carboxyls, amino, and *R* groups) can undergo numerous chemical reactions. Two reactions (peptide bond and cysteine oxidation) are of particular importance because of their effect on protein structure.

Peptide bond formation:

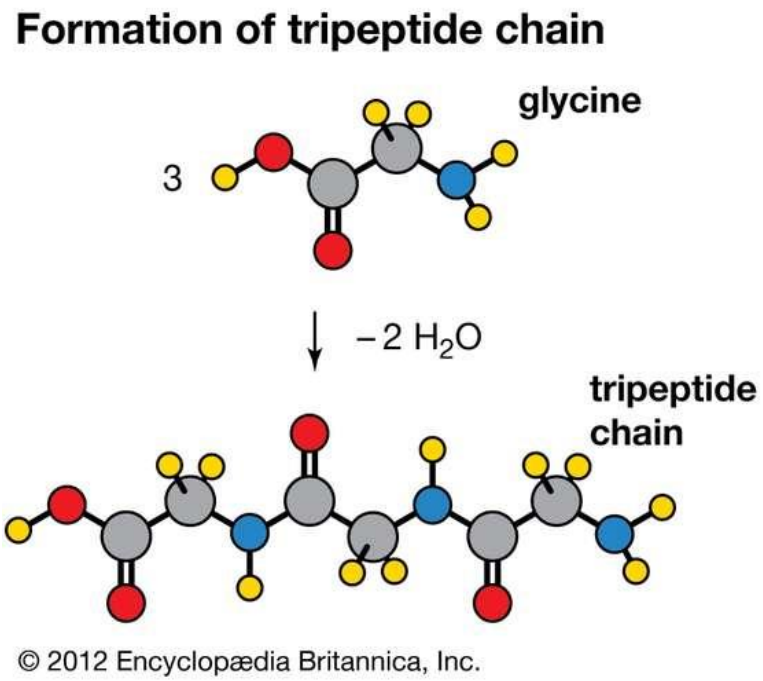
Amino acids can be linked by a condensation reaction in which an —OH is lost from the carboxyl group of one amino acid along with a hydrogen from the amino group of a second, forming a molecule of water and leaving the two amino acids linked via an amide—called, in this case, a peptide bond. At the turn of the 20th century, German chemist Emil Fischer first proposed this linking together of amino acids. Note that when individual amino acids are combined to form proteins, their carboxyl and amino groups are no longer able to act as acids or bases, since they have reacted to form the peptide bond. Therefore, the acid-base properties of

proteins are dependent upon the overall ionization characteristics of the individual *R* groups of the component amino acids.



The linking of atoms in a peptide bond.

Amino acids joined by a series of peptide bonds are said to constitute a peptide. After they are incorporated into a peptide, the individual amino acids are referred to as amino acid residues. Small polymers of amino acids (fewer than 50) are called oligopeptides, while larger ones (more than 50) are referred to as polypeptides. Hence, a protein molecule is a polypeptide chain composed of many amino acid residues, with each residue joined to the next by a peptide bond. The lengths for different proteins range from a few dozen to thousands of amino acids, and each protein contains different relative proportions of the 20 standard amino acids.



Cysteine oxidation:

Cysteine, Sulfur-containing nonessential amino acid. In peptides and proteins, the sulfur atoms of two cysteine molecules are bonded to each other to make cystine, another amino acid. The bonded sulfur atoms form a disulfide bridge, a principal factor in the shape and function of skeletal and connective tissue proteins and in the great stability of structural proteins such as keratin.

The thiol (sulfur-containing) group of cysteine is highly reactive. The most common reaction of this group is a reversible oxidation that forms a disulfide. Oxidation of two molecules of cysteine forms cystine, a molecule that contains a disulfide bond. When two cysteine residues in a protein form such a bond, it is referred to as a disulfide bridge. Disulfide bridges are a common mechanism used in nature to stabilize many proteins. Such disulfide bridges are often found among extracellular proteins that are secreted from cells. In eukaryotic organisms, formation of disulfide bridges occurs within the organelle called the endoplasmic reticulum.

In extracellular fluids (such as blood), the sulfhydryl groups of cysteine are rapidly oxidized to form cystine. In a genetic disorder known as cystinuria, there is a defect that results in excessive excretion of cystine into the urine. Because cystine is the least soluble of the amino acids, crystallization of the excreted cystine results in formation of calculi—more commonly known as "stones"—in the kidney, ureter, or urinary bladder. The stones may cause intense pain, infection, and blood in the urine. Medical intervention often involves the administration of d-penicillamine. Penicillamine works by forming a complex with cystine; this complex is 50 times more water-soluble than cystine alone.

Ninhydrin test

When 1 ml of Ninhydrin solution is added to 1 ml protein solution and heated, formation of a violet colour indicates the presence of ?-amino acids.

Xanthoproteic test

The xanthoproteic test is performed for the detection of aromatic amino acids (tyrosine, tryptophan, and phenylalanine) in a protein solution. Nitration of benzoid radicals present in the amino acid chain occurs due to reaction with nitric acid, giving the solution yellow colouration.

Reaction with Sanger's reagent

Sanger's reagent (1-fluoro-2, 4-dinitrobenzene) reacts with free amino group in the peptide chain in mild alkaline medium under cold conditions.

Reaction with nitrous acid

Nitrous acid reacts with the amino group to liberate nitrogen and form the corresponding hydroxyl.

Peptides:

Peptides are short strings of amino acids, typically comprising 2–50 amino acids. Amino acids are also the building blocks of proteins, but proteins contain more.

Peptides may be easier for the body to absorb than proteins because they are smaller and more broken down than proteins. They can more easily penetrate the skin and intestines, which helps them to enter the bloodstream more quickly.

The peptides in supplements may come from plant or animal sources of protein, including:

- eggs
- milk
- meat
- fish and shellfish
- beans and lentils
- soy
- oats
- flaxseed
- hemp seeds
- wheat

Scientists are most interested in bioactive peptides, or those that have a beneficial effect on the body and may positively impact human health.

Different bioactive peptides have different properties. The effects they have on the body depend on the sequence of amino acids they contain.

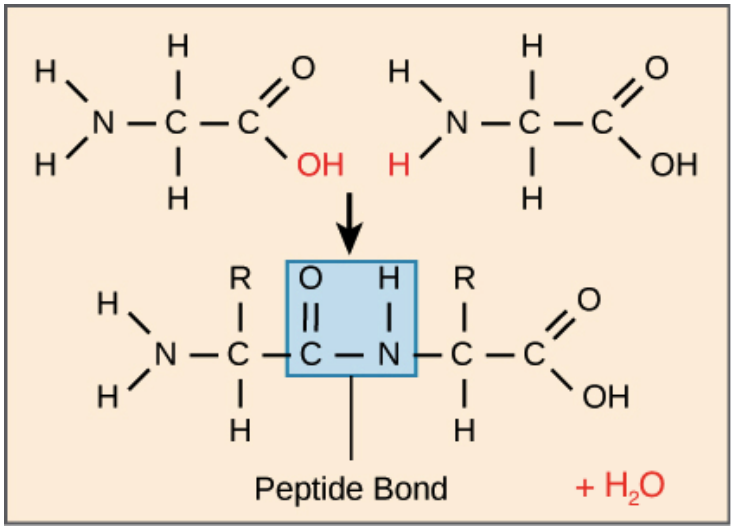
Some of the most common peptide supplements available are:

- Collagen peptides, which may benefit skin health and reverse the effects of aging.
- Creatine peptides, which may build strength and muscle mass.

Some people may take other peptides and peptide hormones to enhance athletic activity. However, the World Anti-Doping Agency have banned many of these, including follistatin, a peptide that increases muscle growth.

Peptide Linkages:

Proteins are made up of amino acids, which are joined by peptide linkages. Although there are only 20 different naturally occurring amino acids, various combinations of these form the thousands of proteins used in metabolism.



All amino acids have a similar structure. There is a central carbon atom, called the alpha-carbon, which is bonded to an amino group on one side and a carboxyl group on the other. Also bonded to the alpha-carbon is a side chain—one of 20 different chemical groups—that gives each amino acid its unique identity and function. However, the backbone of an amino acid consists solely of the alpha-carbon, the amino group, and the carboxyl group, and this is the same for all amino acids.

The amino group consists of a nitrogen atom bonded to two hydrogenatoms: HNH. The carboxyl group is a carbon bonded to an alcohol group (—OH) and double bonded to an oxygen.

This structure, O = COH, is called a carboxylic acid group.

Proteins are constructed from amino acids that are assembled by the formation of peptide bonds. The amino group of one amino acid bonds with the carboxyl group of another, eliminating one

watermolecule (HOH). The bond between the two amino acids consists of a nitrogen with one hydrogen bonded to a carbon with a double bonded oxygen: HNC = O.

This simple structure, the peptide bond, is the basis of all the enzymes and proteins that make life possible.

Proteins:

The **proteins** are the **cellular macromolecules** most abundant constituting 60% of the dry weight of cells. They consist of one or more **polypeptide chains** and has a **molecular weight greater than 10,000** . They have a *unique and diverse structure* . The polypeptide chains fold more or less heavily on themselves inducing a large number of different three-dimensional structures.

Polymeric compounds the monomeric units of which is amino acid.

Classification of Proteins:

i)SimpleProteins

ii)ConjugatedProteins

iii) Derived proteins

Biological Role of Protien:

(1) Membrane Proteins:

Proteins and lipids form the major structural components of cell membrane. The membrane associated proteins consists of intrinsic proteins and extrinsic proteins. Many enzymes and enzyme systems are associated with membrane proteins i.e. components of electron transport system.

(2) Enzymes:

Enzymes are proteins produced within an organism which are capable of catalyzing specific catalytic reactions. They are biocatalysts which influence the rate f a chemical reaction, usually without undergoing any change themselves.

(3) Hormones:

Several hormones are peptides and proteins. They play an important role in the regulation of metabolic reactions.

(4) Blood Proteins:

The blood proteins include plasma proteins and haemoglobin.

(a) Plasma proteins are mainly albumin, globulins and fibrinogen. Albumin maintains the colloid osmotic pressure of plasma and transport materials. Globulins inhibit proteolytic enzymes, and helps to immunosystem of the body. Fibrinogen helps in blood clotting. Lipoproteins are concerned with transport of fat in blood.

(b) Haemoglobin is a conjugated protein consisting ofglobin and haeme. Haemoglobin carries oxygen in the form of oxyhaemoglobin in blood.

(5) Antibodies:

Some antibodies like gramicidin S, tyrocidin and penicillin G are peptides.

(6) Nucleoproteins:

These are conjugated proteins of cell nuclei.

(7) Multiple Protein Assemblies:

These contain several compounds which together from a functional unit.

(a) Collagen: A fibrous proteins found in many connective tissue.

(b) Flagella: Microtubules of flagella are made up of tubules.

Structure of Proteins:

The four levels of protein structure are distinguished from one another by the degree of complexity in the polypeptide chain. A single protein molecule may contain one or more of the protein structure types: primary, secondary, tertiary, and quaternary structure.

1. Primary Structure:

Primary Structure describes the unique order in which amino acids are linked together to form a protein. Proteins are constructed from a set of 20 amino acids. Generally, amino acids have the following structural properties:

A carbon (the alpha carbon) bonded to the four groups below:

A hydrogen atom (H)

A Carboxyl group (-COOH)

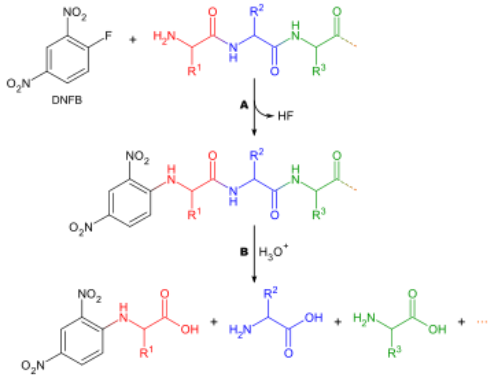
An Amino group (-NH2)

A "variable" group or "R" group

All amino acids have the alpha carbon bonded to a hydrogen atom, carboxyl group, and an amino group. The "R" group varies among amino acids and determines the differences between these protein monomers. The amino acid sequence of a protein is determined by the information found in the cellular genetic code. The order of amino acids in a polypeptide chain is unique and specific to a particular protein. Altering a single amino acid causes a gene mutation, which most often results in a non-functioning protein.

End Group Analysis

N-terminal amino acid analysis:



Sanger's method of peptide end-group analysis: **A** derivatization of *N*-terminal end with Sanger's reagent (DNFB), **B** total acid hydrolysis of the dinitrophenyl peptide

Determining which amino acid forms the *N*-terminus of a peptide chain is useful for two reasons: to aid the ordering of individual peptide fragments' sequences into a whole chain, and because the first round of Edman degradation is often contaminated by impurities and therefore does not give an accurate determination of the *N*-terminal amino acid.

A generalised method for *N*-terminal amino acid analysis follows:

1. React the peptide with a reagent that will selectively label the terminal amino acid.
2. Hydrolyse the protein.
3. Determine the amino acid by chromatography and comparison with standards.

C-terminal amino acid analysis:

The number of methods available for C-terminal amino acid analysis is much smaller than the number of available methods of N-terminal analysis. The most common method is to add carboxypeptidases to a solution of the protein, take samples at regular intervals, and determine the terminal amino acid by analysing a plot of amino acid concentrations against time. This method will be very useful in the case of polypeptides and protein-blocked N termini. C-terminal sequencing would greatly help in verifying the primary structures of proteins predicted from DNA sequences and to detect any postranslational processing of gene products from known codon sequences.

Edman method

The Edman degradation is a very important reaction for protein sequencing, because it allows the ordered amino acid composition of a protein to be discovered. Automated Edman sequencers are now in widespread use, and are able to sequence peptides up to approximately 50 amino acids long. A reaction scheme for sequencing a protein by the Edman degradation follows; some of the steps are elaborated on subsequently.

1. Break any disulfide bridges in the protein with a reducing agent like 2-mercaptoethanol. A protecting group such as iodoacetic acid may be necessary to prevent the bonds from re-forming.
2. Separate and purify the individual chains of the protein complex, if there are more than one.
3. Determine the amino acid composition of each chain.
4. Determine the terminal amino acids of each chain.
5. Break each chain into fragments under 50 amino acids long.
6. Separate and purify the fragments.

7. Determine the sequence of each fragment.
8. Repeat with a different pattern of cleavage.
9. Construct the sequence of the overall protein

2. Secondary Structure

Secondary Structure refers to the coiling or folding of a polypeptide chain that gives the protein its 3-D shape.

There are two types of secondary structures observed in proteins.

1.One type is the alpha (hlix structure. This structure resembles a coiled spring and is secured by hydrogen bonding in the polypeptide chain.

2.The second type of secondary structure in proteins is the beta pleated sheet. This structure appears to be folded or pleated and is held together by hydrogen bonding between polypeptide units of the folded chain that lie adjacent to one another.

3. Tertiary Structure :

Tertiary Structure refers to the comprehensive 3-D structure of the polypeptide chain of a protein. There are several types of bonds and forces that hold a protein in its tertiary structure.

Hydrophobic interactions greatly contribute to the folding and shaping of a protein. The "R" group of the amino acid is either hydrophobic or hydrophilic.

Hydrogen bonding in the polypeptide chain and between amino acid "R" groups helps to stabilize protein structure by holding the protein in the shape established by the hydrophobic interactions.

Due to protein folding, ionic bonding can occur between the positively and negatively charged "R" groups that come in close contact with one another.

4. Quaternary Structure

Quaternary Structure refers to the structure of a protein macromolecule formed by interactions between multiple polypeptide chains.

Each polypeptide chain is referred to as a subunit. Proteins with quaternary structure may consist of more than one of the same type of protein subunit. They may also be composed of different subunits.

Hemoglobin is an example of a protein with quaternary structure. Hemoglobin, found in the blood, is an iron-containing protein that binds oxygen molecules. It contains four subunits: two alpha subunits and two beta subunits.

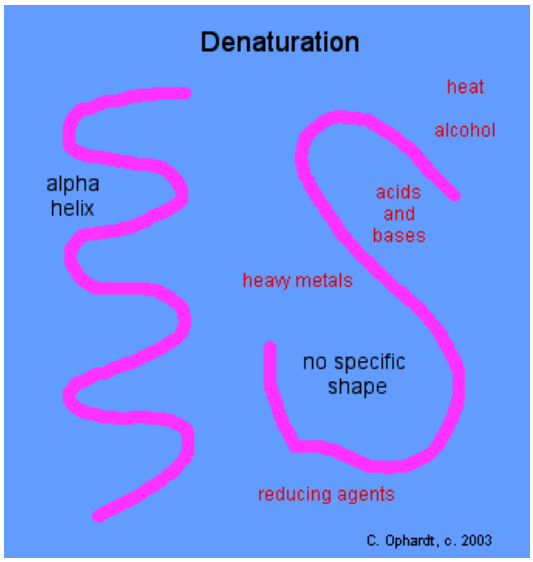
Denaturation:

Proteins involves the disruption and possible destruction of both the secondary and tertiary structures. Since denaturation reactions are not strong enough to break the peptide bonds, the primary structure (sequence of amino acids) remains the same after a denaturation process. Denaturation disrupts the normal alpha-helix and beta sheets in a protein and uncoils it into a random shape.

Denaturation occurs because the bonding interactions responsible for the secondary structure (hydrogen bonds to amides) and tertiary structure are disrupted.

In tertiary structure there are four types of bonding interactions between "side chains" including: hydrogen bonding, salt bridges, disulfide bonds, and non-polar hydrophobic interactions. which may be disrupted. Therefore, a variety of reagents and conditions can cause denaturation.

The most common observation in the denaturation process is the precipitation or coagulation of the protein.



Colour Reactions of Proteins:

a) Xanthoproteic reaction

The addition of concentrated nitric acid to protein solutions generally causes the formation of a white precipitate which turns yellow upon heating, the colour becoming orange when the solution is made alkaline. Insoluble proteins are turned yellow and orange on the surface. The xanthoproteic reaction is due to nitration of the phenyl rings present in tyrosine, phenylalanine, and tryptophan to give yellow nitrosubstitution products, which become orange-coloured upon the addition of alkali. Most proteins give the xanthoproteic reaction.

b) Biuret Reaction

When protein solutions are made strongly alkaline with sodium or potassium hydroxide and when very dilute copper sulphate is added, a purplish to pinkish violet is obtained, the colour depending upon the complexity of protein. Proteins give a purplish violet colour while proteoses and peptones give a pink colour. Peptides give a very light pink colour and gelatin gives a blue colour. This biuret reaction is used as a test for the presence of proteins in biological materials. It is also used as an excellent method for the quantitative estimation of proteins.

Nucleic Acids:

Nucleic acids are composed of **nucleotide** monomers linked together. Nucleotides have three parts:

- **A Nitrogenous Base**
- **A Five-Carbon (Pentose) Sugar**
- **A Phosphate Group**

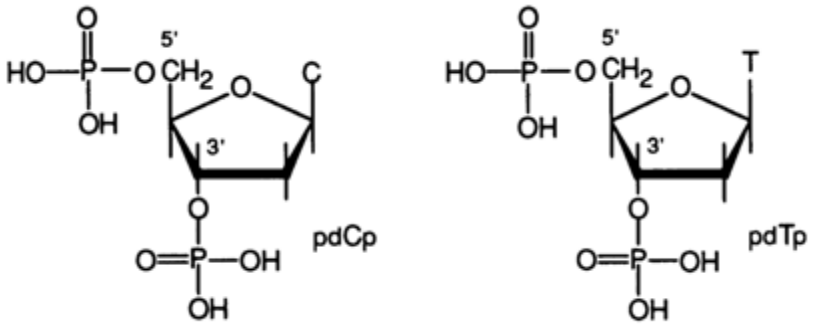
Elementary Treatment of DNA And RNA:

DNA is the cellular molecule that contains instructions for the performance of all cell functions. When a cell divides, its DNA is copied and passed from one cell generation to the next generation. DNA is organized into chromosomes and found within the nucleus of our cells. It contains the "programmatic instructions" for cellular activities. When organisms produce offspring, these instructions in are passed down through DNA.

- DNA commonly exists as a double stranded molecule with a twisted double helix shape. DNA is composed of a phosphate-deoxyribose sugar backbone and the four **nitrogenous bases: adenine (A), guanine (G), cytosine (C), and thymine (T)**. In double stranded DNA, adenine pairs with thymine **(A-T)** and guanine pairs with cytosine (**G-C)**.

Internucteotide Linkage In DNA:

Chemical hydrolysis of DNA as a method for degrading the polymer to establish the nature of internucleotide linkage has turned out to be useless for all practical purposes. DNA is not hydrolysed at alkaline pH values, which is quite consistent with the assumption that the internucleotide linkage is phosphodiester in nature (the stability of dialkylphosphates in alkaline media has already been discussed). When treated with acid even under mild conditions, DNA is hydrolysed both at phosphodiester bonds and at N-glycosidic bonds formed by purine bases. Consequently, hydrolysis of the polymer does not yield consistent results, yet it has been possible to isolate, among products of acid DNA hydrolysis, diphosphates of pyrimidine deoxynucleosides, which are identical with synthetic deoxycytidine and deoxythymidine 3',5'-diphosphates:

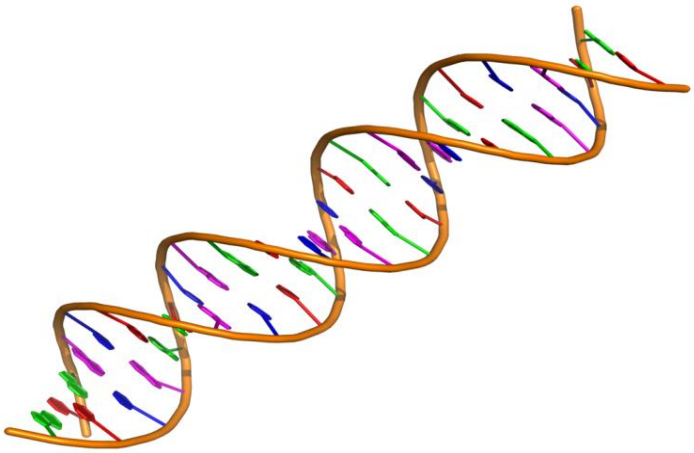


Nucleic Acid Double Helix:

In molecular biology, the term **double helix** refers to the structure formed by double-stranded molecules of nucleic acids such as DNA. The double helical structure of a nucleic acid complex arises as a consequence of its secondary structure, and is a fundamental component in determining its tertiary structure.

The DNA double helix biopolymer of nucleic acid, held together by nucleotides which base pair together. In B-DNA, the most common double helical structure found in nature, the double helix is right-handed with about 10–10.5 base pairs per turn.

The double helix structure of DNA contains a *major groove* and *minor groove*. In B-DNA the major groove is wider than the minor groove.Given the difference in widths of the major groove and minor groove, many proteins which bind to B-DNA do so through the wider major groove.



Vitamins:

A vitamin is an essential compound of **organic** molecules that cannot be synthesized in the **body** but acquired through the **diet** that the person intakes. It is taken in sufficiently small amounts and is **beneficial** in many **metabolic processes** of the body.

There are **two main types of vitamins**; **fat-soluble vitamins** (**Vitamins A, D, E, and K**) and **water-soluble vitamins** (**Vitamins B and C**). As the names suggest, fat-soluble vitamins are stored in the **fatty tissues** and can be stored in the body for longer periods of time to be eventually consumed up later while the water-soluble vitamins cannotbe stored in the body as they are excreted out in the urine by the excretory system and need to be taken regularly.

Classification:

Vitamin A

This vitamin is important for a better **eyesight** and an **improved immune system.** It also promotes **healthy skin**, maintenance of different organs, **healthy growth of muscle tissues** and a healthy **reproductive system**.it is found in **eggs, fish** and different **milk products**. If the vitamin A is not present in sufficient amount, it could lead to a **disease** known as xerophthalmia.

Vitamin B

This is a diverse form of vitamin and further divided into **B1, B2, B3, B5, B6, and B12.** It is important in maintaining **nerve cell function**, producing RBC's, **synthesizing fats** and carbohydrates into energy and potentially producing **cholesterol**, different kinds of **hormones** and also aiding in the replication of **DNA**. It is found in **bread, liver, eggs, beans, nuts, fish** and many **fruits and vegetables**. The deficiency of the said vitamin could lead to weakness, disturbance in the gastrointestinaltract, fatigue, nausea, dermatitis etc.

Vitamin C

It is an **anti-oxidant** i.e it produces an inhibiting effect onthe aging process. It is also responsible for the healing of injuries by producing collagen eventually leading up to a better **immune system** and the formation of **iron** which is an essential component in driving the oxygen into different parts of the body. It is found in **citrus fruits** and many vegetables like **Brussels, tomatoes, potatoes, spinach, andcabbage** etc. Its deficiency in the body could lead to scurvy or **anemia**.

Vitamin D

It is an **essential vitamin** that can be obtained from the **sunlight** and helps in the growth of **bone tissues** by absorbing the calcium from different sources. The deficiency of vitamin D can lead to **osteoporosis**. Vitamin D can be acquired through the external environment but since many people work indoors, it can be consumed through other sources. It is found in fish, dairy products like yoghurt, cheese and milk and fish oils.

Vitamin E

It is also a type of **anti-oxidant** and also helps the body to produce **better defense against diseases**. It is found in **wheat, margarine, nuts, oils, corn** etc. Its deficiency could lead to neuropathy and breakdown of the red blood cells in the body.

Vitamin K

It is the main factor that helps in the **coagulation of blood.** It is found in leafy and **green vegetables** like **cabbages, kale, spinach, broccoli** etc. The deficiency of Vitamin K can lead to serious internal bleeding and internal clot formation.

To conclude the article, there are many **uses of vitamins** and they are considered to be **vital for the body** as they play a much significant part in the **metabolism and immunity of the body** of a living organism. That is why one should take foods which are high in vitamins because they cannot be directly produced in the body and their deficiency could lead to a number of diseases which may become harmful in the future.

Structure and Biological Importance of Vitamins A, B1, B2, B6, B12 and C.

Vitamin A:

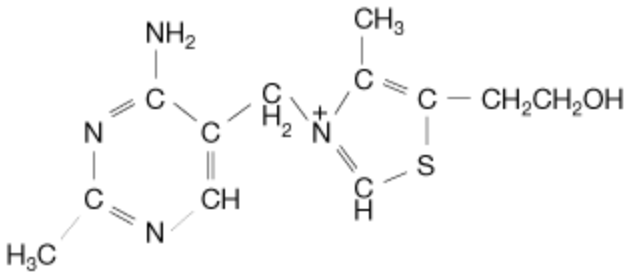
Vitamin A, also called **retinol**, a fat-soluble alcohol, most abundant in fatty fish and especially in fish-liver oils. Vitamin A is also found in milk fat, eggs, and liver; synthetic vitamin A is added to margarine. Vitamin A is not present in plants, but many vegetables and fruits contain one or more of a class of pigments that can be converted to vitamin A in the body; of these pigments, beta-carotene (provitamin A) is an excellent source of vitamin activity.

Vitamin A is readily destroyed upon exposure to heat, light, or air. The vitamin, which functions directly in vision, is converted into retinaldehyde, a component of a light-sensitive pigment called rhodopsin (visual purple), which is present in the retina of the eye. In the form of retinoic acid combined with specific proteins, it also functions in the regulation of embryonic development and growth. Retinoic acid is also essential for maintenance of the epithelial tissues (the skin and the mucous membranes lining the internal body surfaces), for sperm formation, and for proper functioning of the immune system.

Vitamin B1:

Thiamin, also spelled **thiamine**, also called **vitamin B_1**, water-soluble organic compound that is necessary for carbohydrate metabolism in both plants and animals. It carries out these functions in its active form, as a component of the coenzyme thiamin pyrophosphate. Thiamin deficiency results in beriberi, a disease characterized by multiple neuritis (lesions of nerves), general debility, and heart failure.

The chemical structure is as follows:

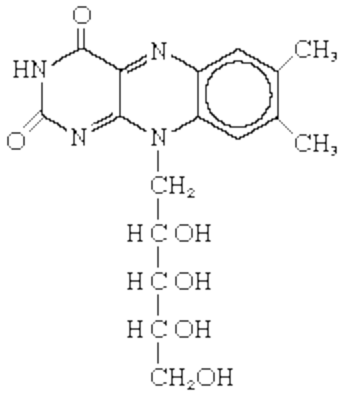


Thiamin

Thiamin is found most abundantly in cereal grains and in certain other seeds. In many countries, white rice and white wheat flour are now fortified with synthetic thiamin. Pork is one of the richest animal sources. The recommended daily intake of thiamin is 1.0 to 1.4 mg (1 mg = 0.001 gram) for adult humans.

Vitamin B2:

Riboflavin, also called **vitamin B_2**, a yellow, water-soluble organic compound that occurs abundantly in whey (the watery part of milk) and in egg white. An essential nutrient for animals, it can be synthesized by green plants and by most bacteria and fungi. The greenish yellow fluorescence of whey and egg white is caused by the presence of riboflavin, It has the following chemical structure:



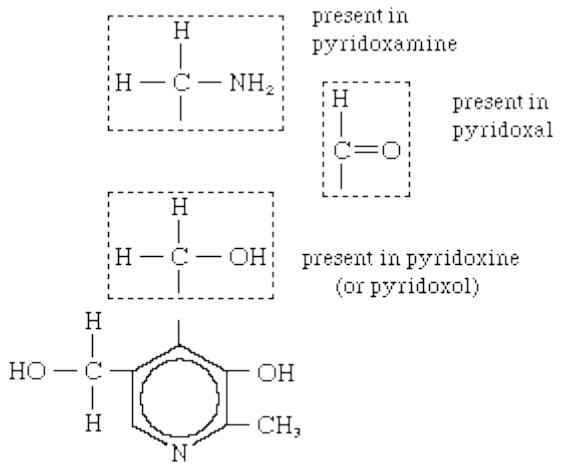
Vitamin B_2 (riboflavin)

Riboflavin functions as part of metabolic systems concerned with the oxidation of carbohydrates and amino acids, the constituents of proteins. Like thiamin (vitamin B_1), it is active not in the free form but in more complex compounds known as coenzymes, such as flavin mononucleotide (FMN) and flavin adenine dinucleotide (FAD), or flavoprotein. Riboflavin is widely distributed in both plants and animals, but its abundance varies considerably. Milk, eggs, leafy vegetables, kidney, and liver are good dietary sources.

A dietary lack of riboflavin is characterized by variable symptoms that may include reddening of the lips with cracks at the corners of the mouth (cheilosis); inflammation of the tongue (glossitis); ocular disturbances, such as vascularization of the eyeball with eyestrain and abnormal intolerance of light; and a greasy, scaly inflammation of the skin. Some disagreement persists as to the characteristic syndrome of riboflavin deficiency in humans because it tends to be associated with a deficiency of other vitamins, notably niacin.

Vitamin B6:

Vitamin B_6, water-soluble organic compound that is an essential micronutrient for microorganisms and animals. It occurs in three forms: pyridoxine (or pyridoxol), pyridoxal, and pyridoxamine. Pyridoxal and pyridoxamine, the vitamin B_6 activity in animal tissues. Vitamin B_6 is widely distributed in foodstuffs and is particularly abundant in cereal grains, meats, nuts, and some fruits and vegetables. The chemical structure of the vitamin B_6 family is as follows:



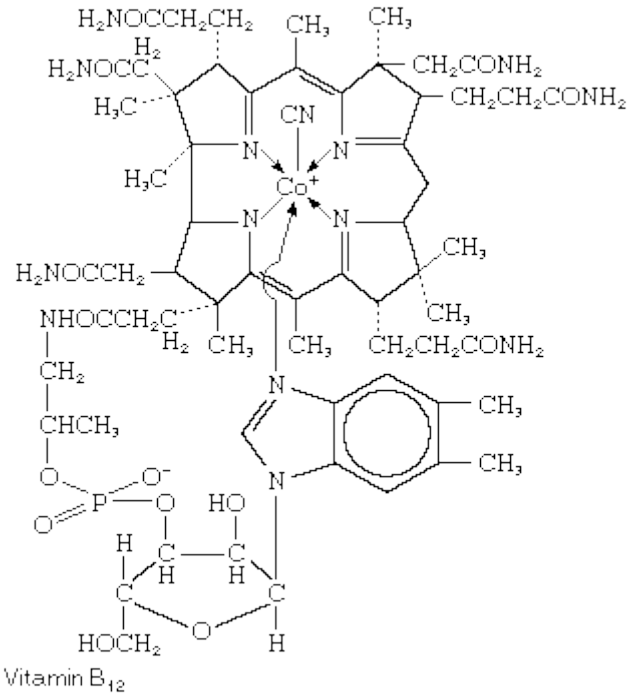
Vitamin B_6 (pyridoxine), the pyridoxine family of vitamins

Vitamin B_6 is active in its coenzyme form of pyridoxol phosphate and functions in the formation and breakdown of amino acids, and hence indirectly of protein, and in the regulation of blood glucose levels. It is also involved in the synthesis of the neurotransmitters serotonin and norepinephrine and of heme (a molecular constituent of hemoglobin) and in the conversion of the amino acid tryptophan to the vitamin niacin.

No human disease has been found to be caused by a deficiency of vitamin B_6 in the diet, although certain metabolic disorders respond to its administration. However, a long-term deficiency of the vitamin can cause symptoms such as dermatitis, mental depression, confusion, or convulsions. In experimental animals, vitamin B_6 deficiency produces skin lesions that depend to some extent on the other constituents of the diet; e.g., the lesions in rats may not appear if certain fats are present in the food.

Vitamin B12:

Vitamin B_{12}, a complex water-soluble organic compound that is essential to a number of microorganisms and animals, including humans. Vitamin B_{12} aids in the development of red blood cells in higher animals. The vitamin, which is unique in that it contains a metallic ion, cobalt, has a complex chemical structure as shown:

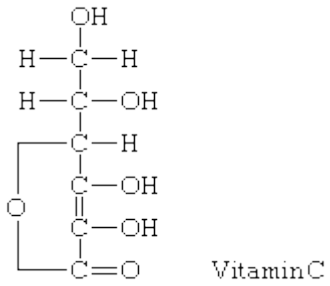


Vitamin B_{12} is involved in cellular metabolism in two active coenzyme forms—methylcobalamin and 5-deoxyadenosylcobalamin. Vitamin B_{12} cooperates with folic acid (folate) in the synthesis of deoxyribonucleic acid (DNA). A deficiency of either compound leads to disordered production of DNA and, hence, to the impaired production of red blood cells. Vitamin B_{12} also has a separate biochemical role, unrelated to folic acid, in the synthesis of fatty acids in the myelin sheath that surrounds nerve cells.

Vitamin C:

Vitamin C, also called **ascorbic acid**, water-soluble, carbohydrate-like substance that is involved in certain metabolic processes of animals. Although most animals can synthesize vitamin C, it is necessary in the diet of some, including humans and other primates, in order to prevent scurvy, a disease characterized by soreness and stiffness of the joints and lower extremities, rigidity, swollen and bloody gums, and hemorrhages in the tissues of the body.

Vitamin C is essential for the synthesis of collagen, a protein important in the formation of connective tissue and in wound healing. It acts as an antioxidant, protecting against damage by reactive molecules called free radicals. The vitamin also helps in stimulating the immune system. It has been shown in animal trials that vitamin C has some anticarcinogenic activity.



Vitamin C

Relatively large amounts of vitamin C are required—for instance, an adult man is said to need about 70 mg (1 mg = 0.001 gram) per day. Citrus fruits and fresh vegetables are the best dietary sources of the vitamin. Because vitamin C is easily destroyed by reactions with oxygen, especially in neutral or alkaline solution or at elevated temperatures, it is difficult to preserve in foods. The vitamin is added to certain fruits to prevent browning.

UNIT III

CHEMISTRY OF ALKALOIDS AND TERPENOIDS

Chemistry of Natural Products:

A **natural product** is a chemical compound or substance produced by a living organism—that is, found in nature. In the broadest sense, natural products include any substance produced by life.

Natural products can also be prepared by chemical synthesis (both semisynthesis and total synthesis) and have played a central role in the development of the field of organic chemistry by providing challenging synthetic targets.

The term natural product has also been extended for commercial purposes to refer to cosmetics, dietary supplements, and foods produced from natural sources without added artificial ingredients

Alkaloids:

Any of a class of naturally occurring organic nitrogen-containing bases. Alkaloids have diverse and important physiological effects on humans and other animals. Well-known alkaloids include morphine, strychnine, quinine, ephedrine, and nicotine.

The chemical structures of alkaloids are extremely variable. Generally, an alkaloid contains at least one nitrogen atom in an amine-type structure—i.e., one derived from ammonia by replacing hydrogen atoms with hydrogen-carbon groups called hydrocarbons.

This or another nitrogen atom can be active as a base in acid-base reactions. The name alkaloid (“alkali-like”) was originally applied to the substances because, like the inorganic alkalis, they react with acids to form salts.

Most alkaloids have one or more of their nitrogen atoms as part of a ring of atoms, frequently called a cyclic system. Alkaloid names generally end in the suffix -ine, a reference to their chemical classification as amines. In their pure form most alkaloids are colourless, nonvolatile, crystalline solids. They also tend to have a bitter taste.

Classification:

Compared with most other classes of natural compounds, alkaloids are characterized by a great structural diversity. There is no uniform classification. Initially, when knowledge of chemical structures was lacking, botanical classification of the source plants was relied on. This classification is now considered obsolete.

More recent classifications are based on similarity of the carbon skeleton (*e.g.*, indole-, isoquinoline-, and pyridine-like) or biochemical precursor (ornithine, lysine, tyrosine, tryptophan, etc.). However, they require compromises in borderline cases; for example, nicotine contains a pyridine fragment from nicotinamide and a pyrrolidine part from ornithine and therefore can be assigned to both classes.

Alkaloids are often divided into the following major groups:

1. "True alkaloids" contain nitrogen in the heterocycle and originate from amino acids. Their characteristic examples are atropine, nicotine, and morphine. This group also includes some alkaloids that besides the nitrogen heterocycle contain terpene (*e.g.*, evonine) or peptide fragments (*e.g.* ergotamine). The piperidine alkaloids coniine and coniceine may be regarded as true alkaloids (rather than pseudoalkaloids: see below) although they do not originate from amino acids.
2. "Protoalkaloids", which contain nitrogen (but not the nitrogen heterocycle) and also originate from amino acids. Examples include mescaline, adrenaline and ephedrine.
3. Polyamine alkaloids – derivatives of putrescine, spermidine, and spermine.
4. Peptide and cyclopeptide alkaloids.
5. Pseudoalkaloids – alkaloid-like compounds that do not originate from amino acids.[48] This group includes terpene-like and steroid-like alkaloids, as well as purine-like alkaloids such as caffeine, theobromine, theacrine and theophylline. Some authors classify as pseudoalkaloids such compounds such as ephedrine and cathinone. Those originate from the amino acid phenylalanine, but acquire their nitrogen atom not from the amino acid but through transamination.

Some alkaloids do not have the carbon skeleton characteristic of their group. So, galanthamine and homoaporphines do not contain isoquinoline fragment, but are, in general, attributed to isoquinoline alkaloids.

Isolation:

Most plants contain several alkaloids. Their mixture is extracted first and then individual alkaloids are separated. Plants are thoroughly ground before extraction. Most alkaloids are present in the raw plants in the form of salts of organic acids.

The extracted alkaloids may remain salts or change into bases. Base extraction is achieved by processing the raw material with alkaline solutions and extracting the alkaloid bases with organic solvents, such as 1,2-dichloroethane, chloroform, diethyl ether or benzene. Then, the impurities are dissolved by weak acids; this converts alkaloid bases into salts that are washed away with water.

The Process of Extraction of Alkaloids from Plants are listed below:
Process -A:
The powder material is moistened with water and mixed with lime, which combined with acids, tannins and other phenolic substances and set free alkaloids (if they exist in the plant as salts). Extraction is then carried out with organic solvent such as ether or petroleum spirit. The concentrated organic liquid is then shaken with aqueous acid and allowed and to separate.

Alkaloidal salt are now in the aqueous liquid, while many impurities remain behind in the organic liquid.

Process-B:
The powder material is extracted with water or aqueous alcohol containing dilute acid. Pigment and unsaturated materials are removed by shaking with chloroform or other organic solvents.

The free alkaloids are then precipitated by the addition of excess sodium bicarbonate or ammonia and separated by filtration or by extraction with organic solvent.

Large-scale extractions based on the above principles are sometime done in the field and the crude mixtures of alkaloids afterward sent to a factory for separation and purification.

The separation and final purification of a mixture of alkaloids may sometimes be done by fractional precipitation or by fractional crystallization of salt such as oxalate, tartrate or pirate. Chromatographic methods are particularly suitable if the mixture is a complex one and if small quantities of alkaloids will office. Volatile liquid alkaloids such as nicotine and coniine are most conveniently isolated by distillation. An aqueous extract is made alkaline with caustic soda or sodium carbonate and alkaloid distilled off in steam. Nicotine is important insecticide, and large quantity of it are prepared those part of the tobacco plant which cannot be used for tobacco manufacture.

Methods For Synthesis of Coniine:

Coniine refers to a poisonous chemical compound, an alkaloid present in and isolable from poison hemlock (*Conium maculatum*), where its presence has been a source of significant economic, medical, and historico-cultural interest; coniine is also produced by the yellow pitcher plant (*Sarracenia flava*)

D-(*S*)-Coniine has since been determined to be a colorless alkaline liquid, with a penetrating odour and a burning taste; has D^{0° 0.8626 and D^{19° 0.8438, refractive index $n^{23^\circ}{}_D$ 1.4505, and is dextrorotatory, $[\alpha]^{19^\circ}{}_D$ +15.7°.L-(*R*)-Coniine has $[\alpha]^{21^\circ}{}_D$ 15° and in other respects resembles its D-isomer.

But the salts have slightly different melting points; the platinichloride has mp. 160 °C (Löffler and Friedrich report 175 °C), the aurichloride mp. 59 °C.

Solubility:

Coniine is slightly soluble (1 in 90) in cold water, less so in hot water, so that a clear cold solution becomes turbid when warmed. On the other hand, the base dissolves about 25% of water at room temperature.

It mixes with alcohol in all proportions, is readily soluble in ether and most organic solvents. Coniine dissolves in carbon disulfide, forming a complex thiocarbamate.

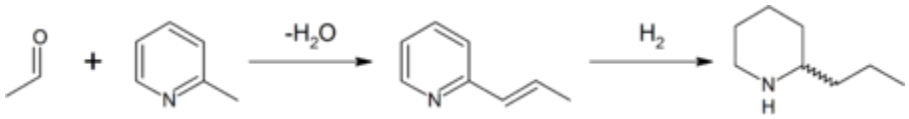
Crystallization

Coniine solidifies into a soft crystalline mass at −2 °C. It slowly oxidizes in the air. The salts crystallize well and are soluble in water or alcohol. crystallizes on standing, mp. 77 °C. The picrate forms small yellow needles, mp. 75 °C, from hot water. The 2,4-dinitrobenzoyl- and 3,5-dinitrobenzoyl-derivates have mps. 139.0–139.5 °C and 108–9 °C respectively. The precipitate afforded by potassium cadmium iodide solution is crystalline, mp. 118 °C, while that given by nicotine with this reagent is amorphous.

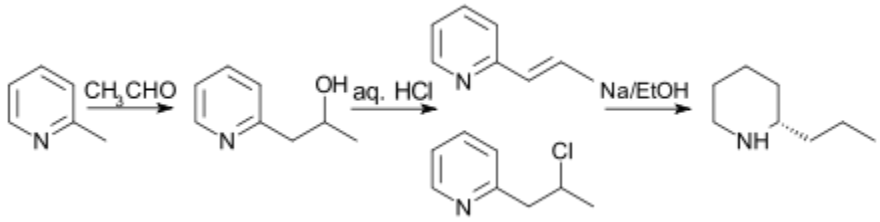
Synthesis

N-methylpyridine, as its iodide salt, was isomerised at 250 °C to obtain 2-methylpyridine (α-picoline). Reaction of this, with the cyclic trimer of acetaldehyde, paraldehyde, in the presence of a base gave 2-propenylpyridine via a Knoevenagel condensation.

This intermediate was reduced with metallic sodium in ethanol or by hydrogen gas (as shown to provide racemic (±) coniine. Enantiopure coniine was then obtained by a chiral resolution, specifically, fractional crystallisation of the diastereomeric (+)-tartaric acid salt.



The initial reaction, however, gives a poor yield and was improved by interaction of the two reagents at 150 °C in sealed tubes to give methyl-2-picolylalkyne, which was then heated at 185 °C with hydrochloric acid for 10 hours, producing a mixture of 2-propenylpyridine and 2-chloropropylpyridine. This mixture was reduced to *rac*-coniine by sodium in ethanol.

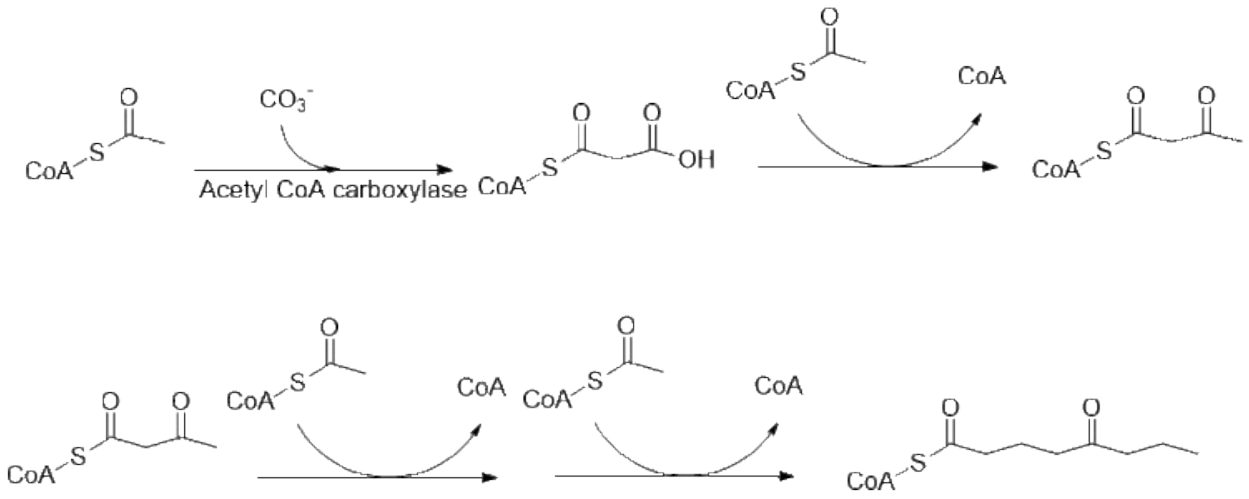


Biosynthesis

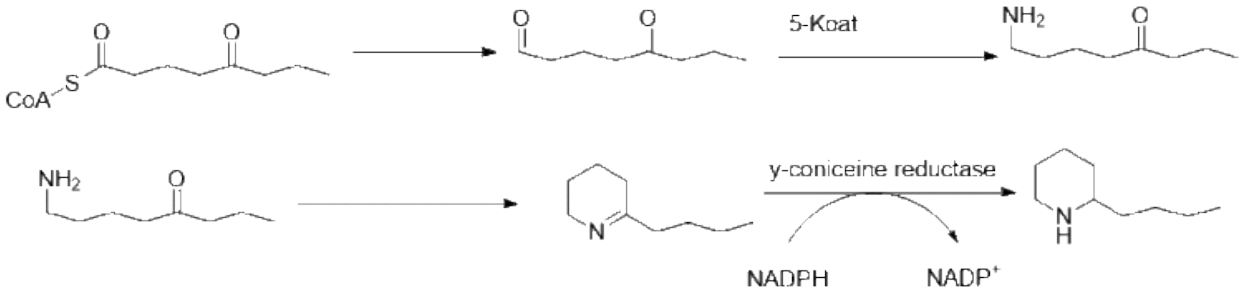
The complete biosynthesis of coniine is still being investigated. While the exact mechanism is still to be determined, much of the pathway has been elucidated.

Originally thought to use 4 acetyl groups as feed compounds for the polyketide synthase that forms coniine, recent work has led to the conclusion that two malonyl and a butyryl CoA are what is coupled together before further operations are performed to finally form coniine.

Initially, acetate is converted to acetyl-CoA, some of which is also used to form malonyl CoA. An acetyl CoA is further elongated using malonyl-CoA by fatty acid synthase to form butyryl-CoA.



Further elongation of butyryl-CoA using 2 malonyl-CoA forms 5-ketooctanal. Ketooctanal then undergoes transamination using alanine:5-keto-octanal aminotransferase. The amine then spontaneously cyclizes and is dehydrated to form the coniine precursor γ–coniceine. This is then reduced using NADPH dependent y-coniceine reductase to form coniine.



.Piperine:

Piperine, along with its isomer chavicine, is the alkaloid responsible for the pungency of black pepper and long pepper. It has been used in some forms of traditional medicine.

Preparation

Piperine is extracted from black pepper using dichloromethane. Aqueous hydrotropes can be used in the extraction to result in high yield and selectivity.

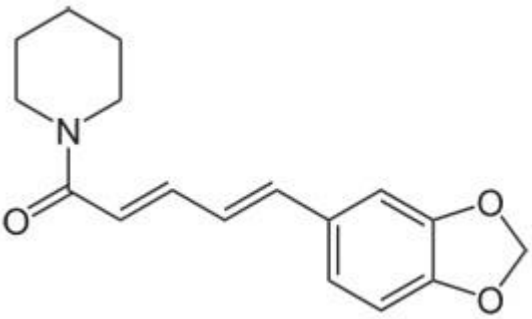
The amount of piperine varies from 1–2% in long pepper, to 5–10% in commercial white and black peppers. Further, it may be prepared by treating the solvent-free residue from an alcoholic extract of black pepper, with a solution of potassium hydroxide to remove resin (said to contain chavicine, an isomer of piperine) and solution of the washed, insoluble residue in warm alcohol, from which the alkaloid crystallises on cooling.

Piperine Molecule in Black Pepper

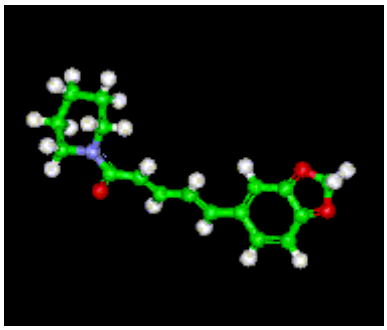
Piperine s the alkaloid responsible for the pungency of **black pepper** and long pepper, along with chavicine (an isomer of piperine). It has also been used in some forms of traditional medicine and as an insecticide.

Piperine forms monoclinic needles, is slightly soluble in water ,the solution in alcohol has a pepper-like taste.

It yields salts only with strong acids.



Piperine Chemical Structure



Ball and Stick Model of Piperine

Nicotine:

Nicotine is a stimulant and potent parasympathomimetic alkaloid that is naturally produced in the nightshade family of plants. It is used for smoking cessation to relieve withdrawal symptoms. Nicotine acts as a receptor agonist at most nicotinic acetylcholine receptors , except at two nicotinic receptor subunits where it acts as a receptor antagonis.

Biosynthesis:

The biosynthetic pathway of nicotine involves a coupling reaction between the two cyclic structures that comprise nicotine. Metabolic studies show that the pyridine ring of nicotine is derived from niacin (nicotinic acid) while the pyrrolidine is derived from *N*-methyl-Δ^1-

pyrrollidium cation. Biosynthesis of the two component structures proceeds via two independent syntheses, the NAD pathway for niacin and the tropane pathway for *N*-methyl-Δ^1-pyrrollidium cation.

The NAD pathway in the genus *Nicotiana* begins with the oxidation of aspartic acid into α-imino succinate by aspartate oxidase (AO). This is followed by a condensation with glyceraldehyde-3-phosphate and a cyclization catalyzed by quinolinate synthase (QS) to give quinolinic acid. Quinolinic acid then reacts with phosphoriboxyl pyrophosphate catalyzed by quinolinic acid phosphoribosyl transferase (QPT) to form niacin mononucleotide (NaMN). The reaction now proceeds via the NAD salvage cycle to produce niacin via the conversion of nicotinamide by the enzyme nicotinamidase.

The *N*-methyl-Δ^1-pyrrollidium cation used in the synthesis of nicotine is an intermediate in the synthesis of tropane-derived alkaloids. Biosynthesis begins with decarboxylation of ornithine by ornithine decarboxylase (ODC) to produce putrescine. Putrescine is then converted into *N*-methyl putrescine via methylation by SAM catalyzed by putrescine *N*-methyltransferase (PMT). *N*-methylputrescine then undergoes deamination into 4-methylaminobutanal by the *N*-methylputrescine oxidase (MPO) enzyme, 4-methylaminobutanal then spontaneously cyclize into *N*-methyl-Δ^1-pyrrollidium cation.

The final step in the synthesis of nicotine is the coupling between *N*-methyl-Δ^1-pyrrollidium cation and niacin. Although studies conclude some form of coupling between the two component structures, the definite process and mechanism remains undetermined. The current agreed theory involves the conversion of niacin into 2,5-dihydropyridine through 3,6-dihydronicotinic acid. The 2,5-dihydropyridine intermediate would then react with *N*-methyl-Δ^1-pyrrollidium cation to form enantiomerically pure (−)-nicotine.

Uses:

Medical

The primary therapeutic use of nicotine is treating nicotine dependence to eliminate smoking and the damage it does to health.

Controlled levels of nicotine are given to patients through gums, dermal patches, lozenges, inhalers, electronic/substitute cigarettes or nasal sprays to wean them off their dependence.

Combining nicotine patch use with a faster acting nicotine replacement, like gum or spray, improves the odds of treatment success. 4 mg versus 2 mg nicotine gum also increase the chances of success.

Pesticide

Nicotine has been used as an insecticide . Foods are imported from countries in which nicotine pesticides are allowed, such as China, but foods may not exceed maximum nicotine levels.

Neonicotinoids, which are derived from and structurally similar to nicotine, are widely used as agricultural and veterinary pesticides.

In nicotine-producing plants, nicotine functions as an antiherbivory chemical; consequently, nicotine has been widely used as an insecticide, and neonicotinoids, such as imidacloprid, are widely used.

Quinine:

Quinine is a medication used to treat malaria and babesiosis. This includes the treatment of malaria due to *Plasmodium falciparum* that is resistant to chloroquine when artesunate is not available. While used for restless legs syndrome, it is not recommended for this purpose due to the risk of side effects.

It can be taken by mouth or used intravenously. Malaria resistance to quinine occurs in certain areas of the world. Quinine is also the ingredient in tonic water that gives it its bitter taste.

Common side effects include headache, ringing in the ears, trouble seeing, and sweating.

More severe side effects include deafness, low blood platelets, and an irregular heartbeat. Use can make one more prone to sunburn. While it is unclear if use during pregnancy causes harm to the baby, use to treat malaria during pregnancy is still recommended. Quinine is an alkaloid, a naturally occurring chemical compound. How it works as a medicine is not entirely clear.

Synthesis

Cinchona trees remain the only economically practical source of quinine.

Biosynthesis

In the first step of quinine biosynthesis, the enzyme strictosidine synthase catalyzes a stereoselective Pictet–Spengler reaction between tryptamine and secologanin to yield strictosidine. Suitable modification of strictosidine leads to an aldehyde. Hydrolysis and decarboxylation would initially remove one carbon from the iridoid portion and produce corynantheal.

Then the tryptamine side-chain were cleaved adjacent to the nitrogen, and this nitrogen was then bonded to the acetaldehyde function to yield cinchonaminal.

Ring opening in the indole heterocyclic ring could generate new amine and keto functions. The new quinoline heterocycle would then be formed by combining this amine with the aldehyde produced in the tryptamine side-chain cleavage, giving cinchonidinone.

For the last step, hydroxylation and methylation gives quinine.

Uses:

Medical

Quinine was frequently prescribed as an off-label treatment for leg cramps at night, but this has become less common due to a warning from the US Food and Drug Administration (FDA) that such practice is associated with life-threatening side effects.

Available forms

Quinine is a basic amine and is usually provided as a salt. Various existing preparations include the hydrochloride, dihydrochloride, sulfate, bisulfate and gluconate. In the United States, quinine sulfate is commercially available in 324-mg tablets under the brand name Qualaquin.

All quinine salts may be given orally or intravenously (IV); quinine gluconate may also be given intramuscularly (IM) or rectally (PR). The main problem with the rectal route is that the dose can be expelled before it is completely absorbed; in practice, this is corrected by giving a further half dose. No injectable preparation of quinine is licensed in the US; quinidine is used instead.

Terpenoids:

The **terpenoids** , sometimes called **isoprenoids**, are a large and diverse class of naturally occurring organic chemicals derived from terpenes. Most are multicyclic structures with oxygen-containing functional groups. About 60% of known natural products are terpenoids.Although sometimes used interchangeably with "terpenes", terpenoids contain additional functional groups, usually O-containing.Terpenes are hydrocarbons.

Classification:

Terpenoids are modified terpenes, wherein methyl groups have been moved or removed, or oxygen atoms added. (Some authors use the term "terpene" more broadly, to include the terpenoids.) Just like terpenes, the terpenoids can be classified according to the number of isoprene units that comprise the parent terpene:

- Hemiterpenoids, 1 isoprene unit (5 carbons)
- Monoterpenoids, 2 isoprene units (10C, i.e., derived from monoterpenes)
- Sesquiterpenoids, 3 isoprene units (15C, i.e., derived from sesquiterpenes)
- Diterpenoids, 4 isoprene units (20C, i.e., derived from diterpenes). ginkgolides.
- Sesterterpenoids, 5 isoprene units (25C, i.e., derived from sesterterpenes).
- Triterpenoids, 6 isoprene units (30C, i.e., derived from triterpenes). Example: sterols.
- Tetraterpenoids, 8 isoprene units (40C, i.e., derived from tetraterpenes). Example: carotenoids)
- Polyterpenoid with a larger number of isoprene units

Terpenoids can also be classified according to the number of cyclic structures they contain. The Salkowski test can be used to identify the presence of terpenoids.

Isoprene:

Isoprene, or **2-methyl-1,3-butadiene**, is a common organic compound with the formula $CH_2=C(CH_3)-CH=CH_2$. In its pure form it is a colorless volatile liquid.

Isoprene is an unsaturated hydrocarbon. It is produced by many plants and animals (including humans) and its polymers are the main component of natural rubber. It from thermal decomposition (pyrolysis) of natural rubber; he correctly deduced the empirical formula C_5H_8.

Biological roles

Isoprene emission appears to be a mechanism that trees use to combat abiotic stresses. In particular, isoprene has been shown to protect against moderate heat stress (around 40 °C).

It may also protect plants against large fluctuations in leaf temperature. Isoprene is incorporated into and helps stabilize cell membranes in response to heat stress.

Isoprene also confers resistance to reactive oxygen species.The amount of isoprene released from isoprene-emitting vegetation depends on leaf mass, leaf area, light (particularly photosynthetic photon flux density, or PPFD) and leaf temperature.

Thus, during the night, little isoprene is emitted from tree leaves, whereas daytime emissions are expected to be substantial during hot and sunny days, up to 25 μg/(g dry-leaf-weight)/hour in many oak species.

Special Isoprene Rule:

Formally, in biosynthesis of terpenes, two or more isoprene molecules are linked to one another. Linking between two isoprene molecules could occur in three ways, given that the head and the tail of the molecule are primarily involved in the linking:

1-1 Linkage

The head of one isoprene molecule could link with the head of another isoprene molecule.

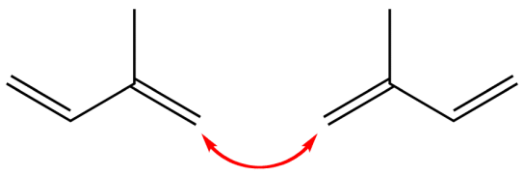


Figure 1: *This link is called a head-to-head or 1-1 link.*

1-4 Linkage

The head of one isoprene molecule could link with the tail of another isoprene molecule.

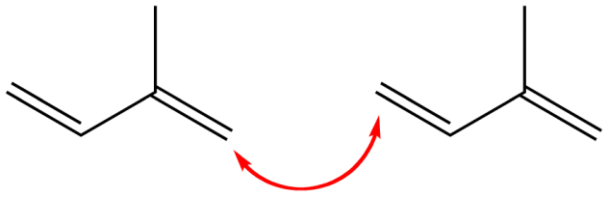


***Figure 2**: This link is called a head-to-tail or 1-4 link.*

4-4 Linkage

The tail of one isoprene molecule could link with the tail of another isoprene molecule.

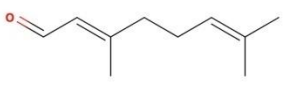
***Figure 3**: This link is called a tail-to-tail or 4-4 link.*

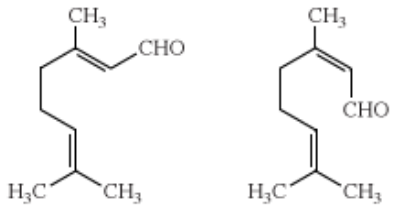
Cyclic terpenes also contain links that are neither 1-1, 1-4, nor 4-4, which are called *crosslinks*.

Methods For Synthesis

Citral:

Citral is different from other terpenoids in that it is actually a pair of isomers connected by a double bond; geranial (citral A) and neral (citral B). Often citral will be referred to as one of its two isomers–more commonly geranial–or as lemonal. Citral is found naturally in varying citrus such as lemon, orange, and lime. This terpenoid is also found in lemongrass and lemon balm. Citral is credited with giving specific citrus and grass their lemony scent.





geranial (citral a) neral (citral b)

Lemongrass oil contains 70–80 percent citral, which may be isolated by distillation. Other natural sources include the oils of verbena and citronella. Citral can be synthesized from myrcene. Ionone and methylionone, made from citral, are used in perfumery; ionone is also converted into synthetic vitamin A.

Properties

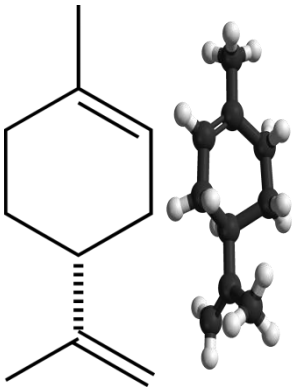
- Color: Clear to pale yellow
- Consistency: Liquid
- Odor: Strong lemon
- Taste: Lemon
- Boiling point: 229ºC
- Flash point: >93.1ºC
- Solubility: In water, 1.34X10+3 mg/L at 27ºC
- Formula: C10H16O
- Density: 0.891-.897 g/cm3 at 15ºC
- Molecular Weight: 152.237 g/mol

Limonene:

Limonene is a colorless liquid aliphatic hydrocarbon classified as a cyclic monoterpene, and is the major component in the oil of citrus fruit peels.

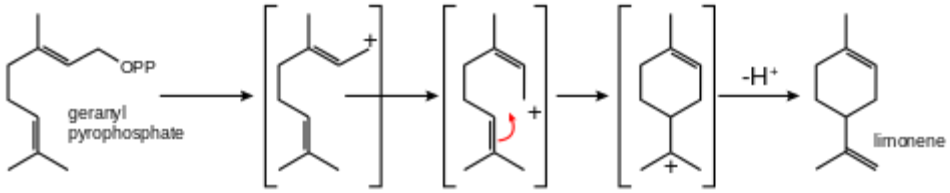
The D-isomer, occurring more commonly in nature as the fragrance of oranges, is a flavoring agent in food manufacturing.It is also used in chemical synthesis as a precursor to carvone and as a renewables-based solvent in cleaning products.

The less common L-isomer is found in mint oils and has a piny, turpentine-like odor. The compound is one of the main volatile monoterpenes found in the resin of conifers, particularly in the Pinaceae, and of orange oil.



Biosynthesis

In nature, limonene is formed from geranyl pyrophosphate, via cyclization of a neryl carbocation or its equivalent as shown. The final step involves loss of a proton from the cation to form the alkene.



The most widely practiced conversion of limonene is to carvone. The three-step reaction begins with the regioselective addition of nitrosyl chloride across the trisubstituted double bond. This species is then converted to the oxime with a base, and the hydroxylamine is removed to give the ketone-containing carvone.

Limonene is a chemical found in the peels of citrus fruits and in other plants. It is used to make medicine.

Limonene is used for obesity, cancer, and bronchitis, but there is no good scientific evidence to support these uses.

Uses:

In foods, beverages, and chewing gum, limonene is used as a flavoring.

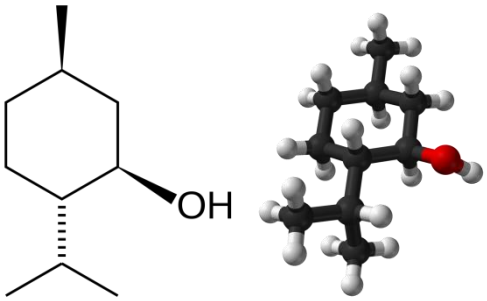
In pharmaceuticals, limonene is added to help medicinal ointments and creams penetrate the skin.

In manufacturing, limonene is used as a fragrance, cleaner (solvent), and as an ingredient in household cleaning products, cosmetics, and personal hygiene products.

- **Cancer.** One form of limonene (D-limonene) seems to build up in tumors in people with advanced cancer when it is taken by mouth. The high levels of limonene in the tumors may slow down the progress of the cancer, but their effect on the person's survival is uncertain.
- **Obesity.**
- **Short-term swelling (inflammation) of the airways in the lungs (acute bronchitis).**

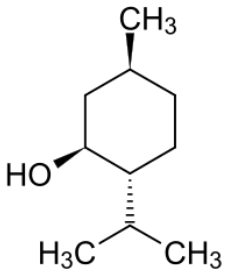
Menthol:

Menthol is an organic compound made synthetically or obtained from the oils of corn mint, peppermint, or other mints. It is a waxy, crystalline substance, clear or white in color, which is solid at room temperature and melts slightly above.

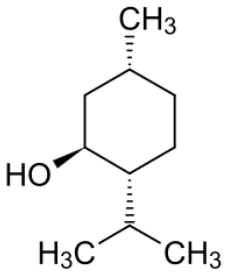


Structure

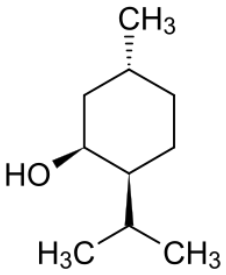
(+)-Menthol



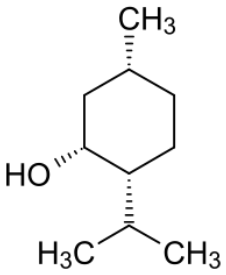
(+)-Isomenthol



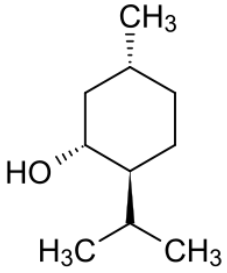
(+)-Neomenthol



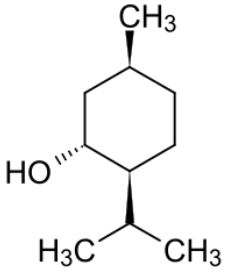
(+)-Neoisomenthol



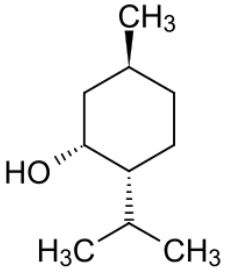
(-)-Menthol



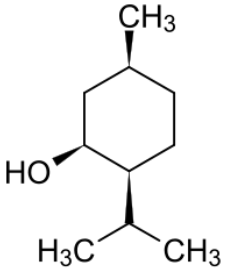
(-)-Isomenthol



(-)-Neomenthol

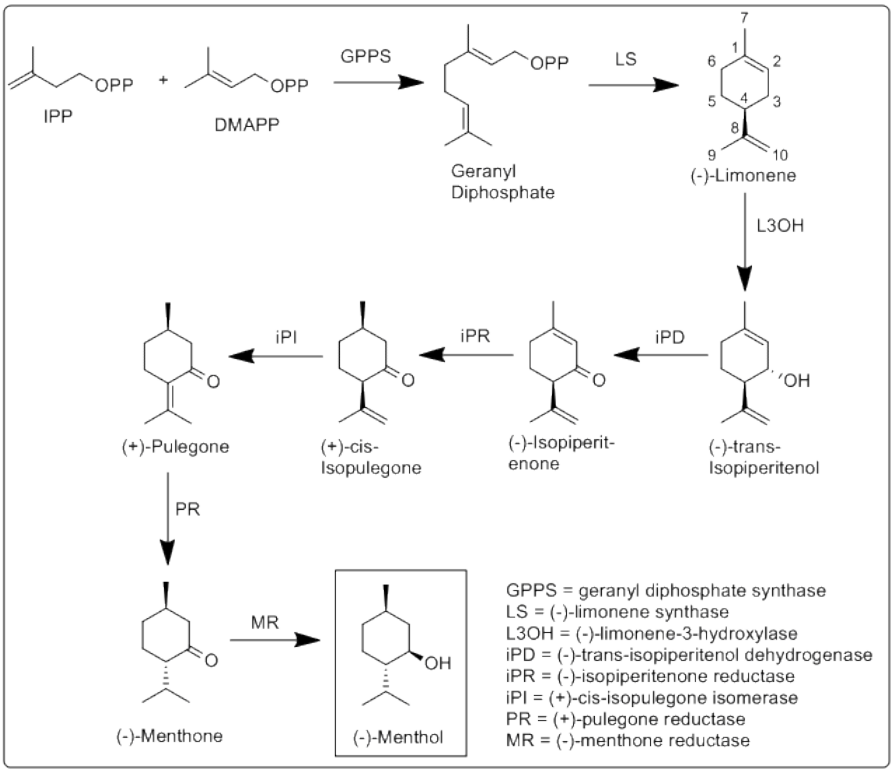


(-)-Neoisomenthol



Biosynthesis

The biosynthesis of menthol has been investigated in *Mentha* × *piperita* and the enzymes involved in have been identified and characterized. It begins with the synthesis of the terpene limonene, followed by hydroxylation, and then several reduction and isomerization steps.



Menthol is either manmade or made from the extracts of mint oil. Menthol provides a cooling sensation when applied to the skin or other tissues (such as the tongue, gums, or inside the cheeks).

Menthol topical oral mucous membrane (for use inside the mouth) is used to treat minor sore throat pain, or mouth irritation caused by a canker sore.

Uses:

Menthol topical may also be used for purposes not listed in this medication guide.

Follow all directions on your medicine label and package. Tell each of your healthcare providers about all your medical conditions, allergies, and all medicines you use.

You should not use this medicine if you are allergic to menthol.

Ask a doctor or pharmacist if it is safe for you to use this medicine if you have other medical conditions, especially:

Side Effect

- Cough with mucus;
- Cough caused by smoking, emphysema, or chronic bronchitis;
- a Aore throat with fever, headache, swelling, skin rash, or nausea and vomiting.

A menthol lozenge may contain glucose (sugar) or phenylalanine. Talk to your doctor before using this medicine if you have diabetes or phenylketonuria (PKU).

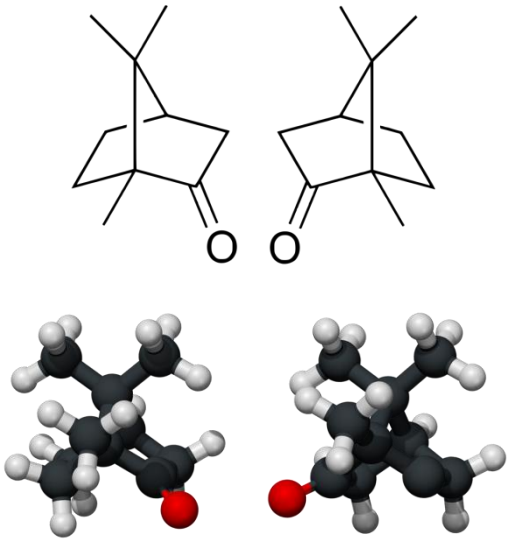
Camphor:

Camphor s a waxy, flammable, transparent solid with a strong aroma.

It is a terpenoid with the chemical formula $C_{10}H_{16}O$.

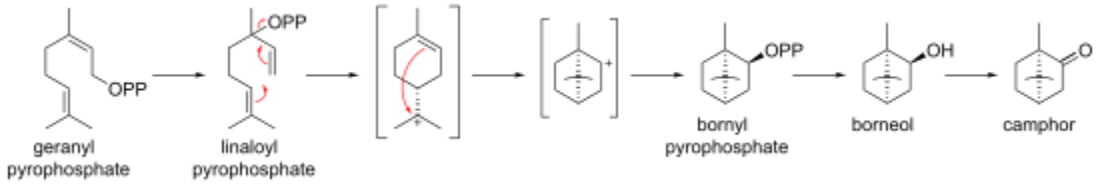
It is found in the wood of the **camphor laurel** (*Cinnamomum camphora*), a large evergreen tree and also of the unrelated *kapur tree*, a tall timber tree from the same region. It also occurs in some other related trees in the laurel family, notably *Ocotea usambarensis*. Rosemary leaves (*Rosmarinus officinalis*) contain 0.05 to 0.5% camphor,while camphorweed (*Heterotheca*) contains some 5%.

A major source of camphor in Asia is camphor basil (the parent of African blue basil). Camphor can also be synthetically produced from oil of turpentine.



Biosynthesis

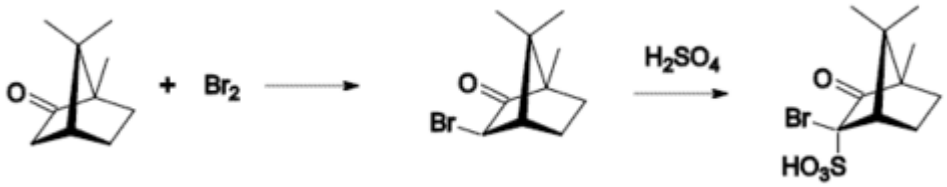
n biosynthesis, camphor is produced from geranyl pyrophosphate, via cyclisation of linaloyl pyrophosphate to bornyl pyrophosphate, followed by hydrolysis to borneol and oxidation to camphor.



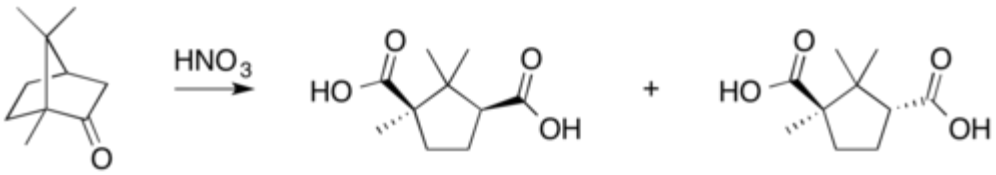
Reactions

Typical camphor reactions are

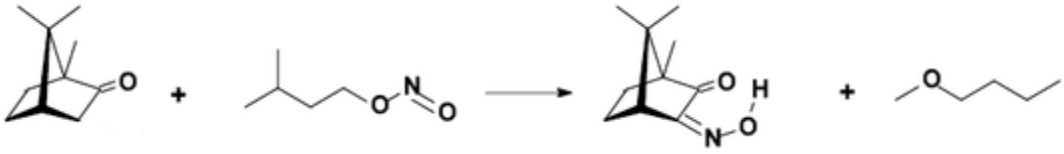
- bromination,



- oxidation with nitric acid,



- conversion to isonitrosocamphor.



Camphor can also be reduced to isoborneol using sodium borohydride.

Uses:

Plastics

The first significant manmade plastics were low-nitrogen (or "soluble") nitrocellulose (pyroxylin) plastics. In the early decades of the plastics industry, camphor was used in immense quantities[11]:130 as the plasticizer that creates celluloid from nitrocellulose, in nitrocellulose lacquers and other plastics and lacquers.

Pest deterrent and preservative

Camphor is believed to be toxic to insects and is thus sometimes used as a repellent.[s] Camphor is used as an alternative to mothballs. Camphor crystals are sometimes used to prevent damage to insect collections by other small insects. It is kept in clothes used on special occasions and festivals, and also in cupboard corners as a cockroach repellent. The smoke of camphor crystal or camphor incense sticks can be used as an environmentally-friendly mosquito repellent.

Recent studies have indicated that camphor essential oil can be used as an effective fumigant against red fire ants, as it affects the attacking, climbing, and feeding behavior of major and minor workers.

Camphor is also used as an antimicrobial substance. In embalming, camphor oil was one of the ingredients used by ancient Egyptians for mummification.

Solid camphor releases fumes that form a rust-preventative coating and is therefore stored in tool chests to protect tools against rust.

Perfume

Camphor was a common perfume ingredient, according to the Perfume Handbook. The Chinese referred to the best camphor as "dragon's brain perfume," due to its "pungent and portentous aroma" and "centuries of uncertainty over its provenance and mode of origin."

UNIT IV

MOLECULAR REARRANGEMENTS

Molecular Rearrangements :

Migration of one group from one atom to another within the molecule

Generally the migrating group never leaves the molecule

Types of rearrangement :

There are five types of skeletal rearrangements-

1. Electron deficient skeletal rearrangement

2. Electron rich skeletal rearrangement

3. Radical rearrangement

4. Rearrangements on an aromatic ring

5. Sigmatropic rearrangement

Mechanism of pinacol – pinacolone:

Pinacol Pinacolone rearrangement is a very important process in organic chemistry for the conversion of 1,2 diols into carbonyl compounds containing a carbon oxygen double bond. This is done via a 1,2-migration which takes place under acyl conditions.

The pinacol pinacolone rearrangement process takes place via a 1,2-rearrangement as discussed earlier. This rearrangement involves the shift of two adjacent atoms. This reaction is a result of the work of the German chemist William Rudolph Fittig who first described it in the year 1860.

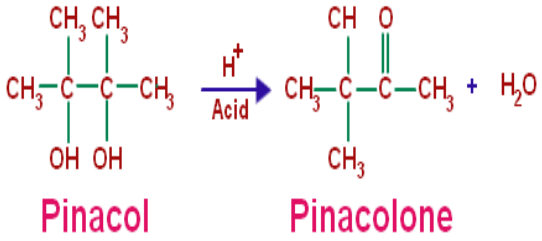
Pinacol and Pinacolone

Pinacol is a compound which has two hydroxyl groups, each attached to a vicinal carbon atom. It is a solid organic compound which is white in colour.

The IUPAC name of Pinacolone is 3,3-dimethyl-2-butanone. Pinacolone is a very important ketone. It has a peppermint like or camphor like odour and appears to be a colorless liquid.

Pinacol Pinacolone Reaction

The pinacol pinacolone rearrangement proceeds through the formation of an intermediate which is positively charged. The methyl group in this intermediate proceeds to migrate from one carbon to another. This reaction can be given by:



Pinacol Pinacolone Rearrangement Mechanism

The Pinacol Pinacolone rearrangement mechanism proceeds via four steps. Each of these steps are explained below.

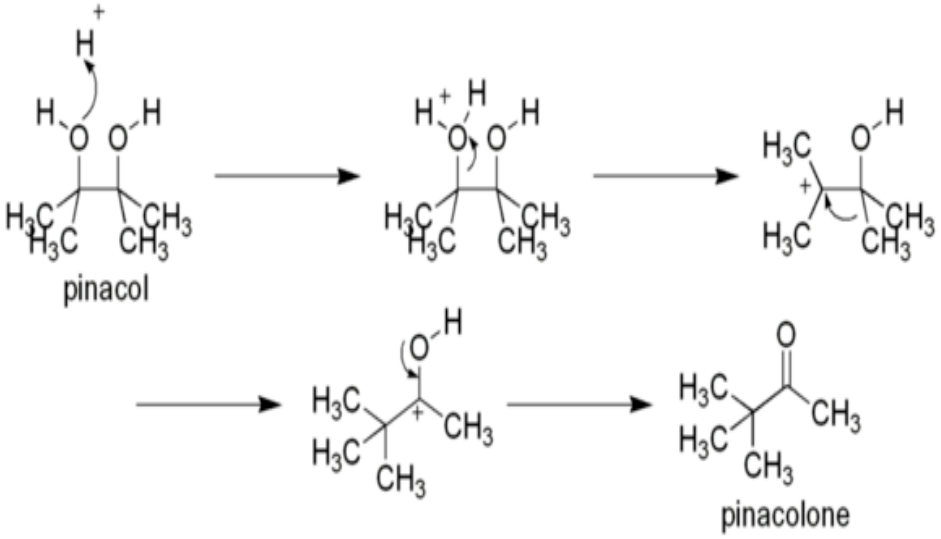
Step 1: Since the reaction is carried out in an acidic medium, the hydroxide group of the pinacol is protonated by the acid.

Step 2: Water is now removed from the compound, leaving behind a carbocation. This carbocation is tertiary and therefore stable.

Step 3: The methyl group shifts to the positively charged carbon in a rearrangement of the compound.

Step 4: The oxygen atom which is doubly bonded to the carbon is now deprotonated, giving rise to the required pinacolone.

This reaction mechanism can be illustrated as:



Thus, the required Pinacolone product is generated. It is important to note that this rearrangement is regioselective in nature. The rearrangement of the more stable carbocation yields the major product.

Uses of Pinacolone

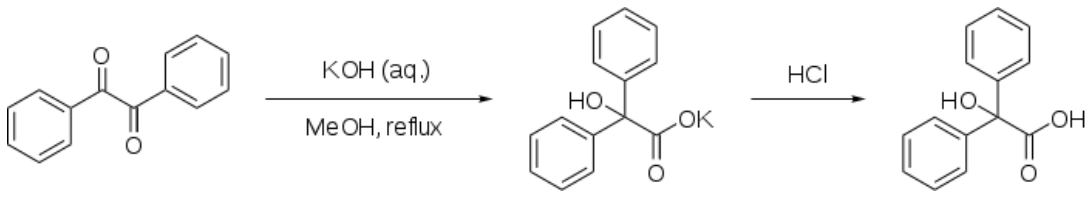
The uses of the pinacolone product produced from the pinacol pinacolone rearrangement include:

- Pinacolone is used in Pesticides, Fungicides, and Herbicides.
- Pinacolone is used to prepare the cyanoguanidine drug – pinacidil.
- Another drug use of Pinacolone is its use in Stiripentol, which is used to treat epilepsy.
- Pinacolone is used to produce triadimefon which is used to control fungal diseases in agriculture.

The primary applications of pinacolone are in the drug industry.

Benzil - benzilic acid:

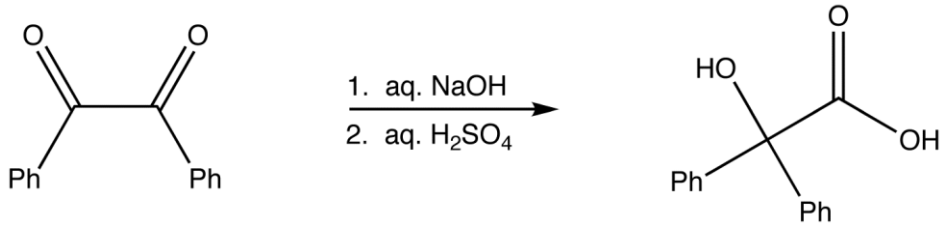
The **benzilic acid rearrangement** is formally the 1,2-rearrangement of 1,2-diketones to form α-hydroxy–carboxylic acids using a base. This reaction receives its name from the reaction of benzil with potassium hydroxide to form benzilic acid.



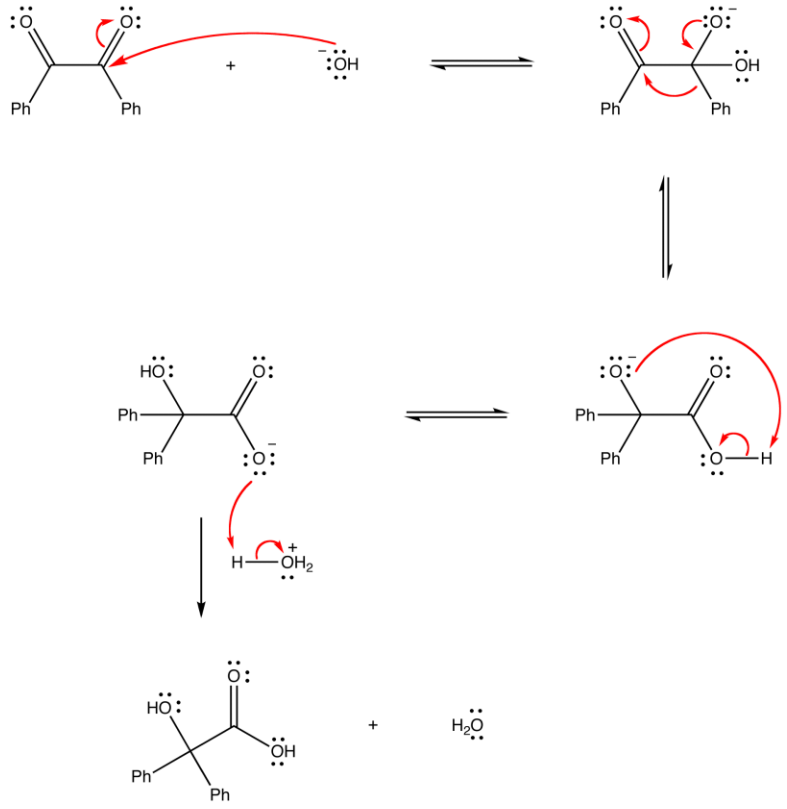
The reaction has been shown to work in aromatic, semi-aromatic, aliphatic, and heterocyclic substrates. The reaction works best when the ketone functional groups have no adjacent

enolizable protons, as this allows aldol condensation to compete. The reaction is formally a ring contraction when used on cyclic diketones. It has been found that aryl groups more readily migrate than alkyl groups, and that aryl groups with electron-withdrawing groups migrate the fastest.

eg:



Mechanism:

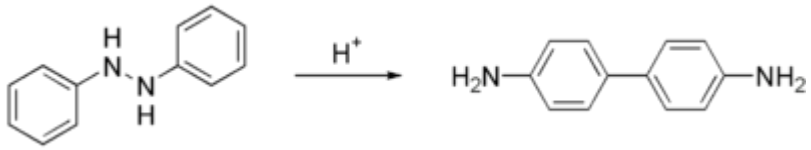


Benzidine:

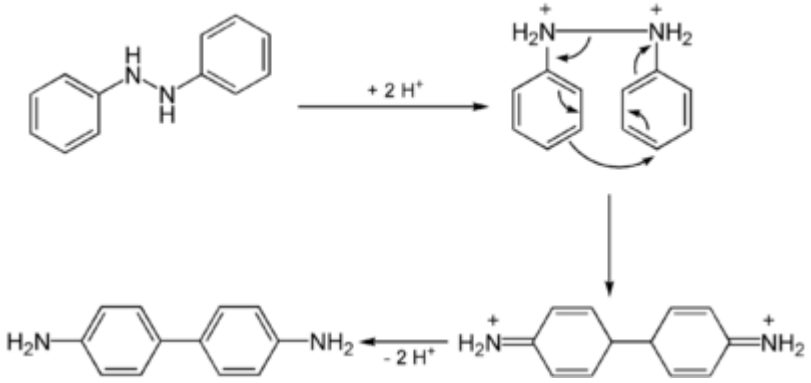
Benzidine (trivial name), also called **1,1'-biphenyl-4,4'-diamine** (systematic name), is an organic compound with the formula $(C_6H_4NH_2)_2$. It is an aromatic amine. It is a component of a test for cyanide. Related derivatives are used in the production of dyes. Benzidine has been linked to bladder and pancreatic cancer.

Mechanism:

Benzidine is prepared in a two step process from nitrobenzene. First, the nitrobenzene is converted to 1,2-diphenylhydrazine, usually using iron powder as the reducing agent. Treatment of this hydrazine with mineral acids induces a rearrangement reaction to 4,4'-benzidine. Smaller amounts of other isomers are also formed. The **benzidine rearrangement**, which proceeds intramolecularly, is a classic mechanistic puzzle in organic chemistry.



The conversion is described as a [5,5]sigmatropic reaction.



In terms of its physical properties, 4,4'-benzidine is poorly soluble in cold water but can be recrystallized from hot water, where it crystallises as the monohydrate. It is dibasic, the deprotonated species has K_a values of 9.3×10^{-10} and 5.6×10^{-11}. Its solutions react with oxidizing agents to give deeply coloured quinone-related derivatives.

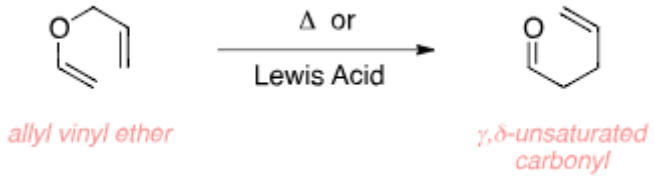
Claisen Rearrangements:

Claisen rearrangement is an organic chemical reaction that offers a ***powerful method in the formation of carbon-carbon bonds***. The reactant of this reaction – allyl vinyl ether, is converted into a gamma, delta-unsaturated carbonyl compound when subjected to heat or a Lewis acid.

The Claisen rearrangement reaction is named after its discoverer, the **German chemist Rainer Ludwig Claisen**, who discovered it in 1912. This reaction belongs to the ***"sigmatropic rearrangement"*** category of reactions wherein the mechanism of the reaction is concerted (i.e. all the bonds break and form simultaneously).

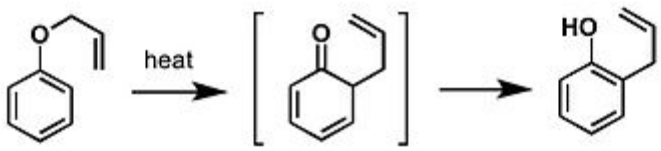
An interesting fact about this reaction is that it was the first ever recorded example of a [3,3]-sigmatropic rearrangement reaction.

An example for the Claisen rearrangement reaction of an allyl vinyl ether is given below.



Claisen Rearrangement Example for Allyl Vinyl Ether

The reaction can also be performed with allyl phenyl ethers. In this rearrangement, the regioselectivity is affected by the meta-substitution. The [3,3]-sigmatropic rearrangement of the allyl phenyl ether gives an intermediate. This intermediate now undergoes tautomerization to give a phenol which is substituted at the ortho position. An example for the [3,3]-sigmatropic rearrangement of an allyl phenyl ether is given below.



Claisen Rearrangement Example for Allyl Phenyl Ethers

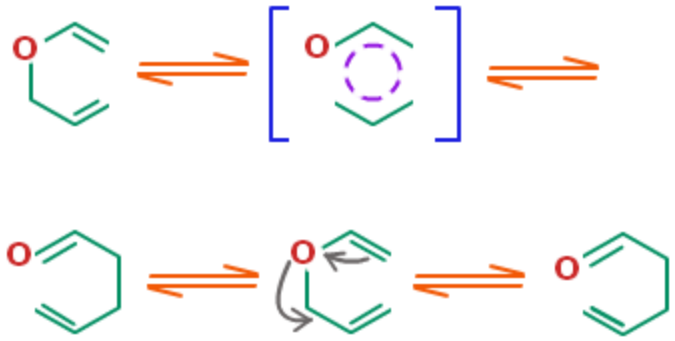
Mechanism of Claisen Rearrangement

This rearrangement reaction has an exothermic nature. As discussed earlier, the reaction ***mechanism is concerted.*** The ***reaction kinetics of this rearrangement reaction is of the first order.*** The reaction is accelerated by polar solvents. Hydrogen-bonding solvents provide further acceleration of reaction speed and greater rate constants.

1. Allyl Vinyl Ethers

Here, heat is the catalyst of the reaction. When the allyl vinyl ether is subjected to heat, it ***forms a transition state***. Now, a [3,3]-sigmatropic rearrangement takes place leading to the formation of the required gamma,delta-unsaturated carbonyl compound product.

This mechanism is illustrated below.

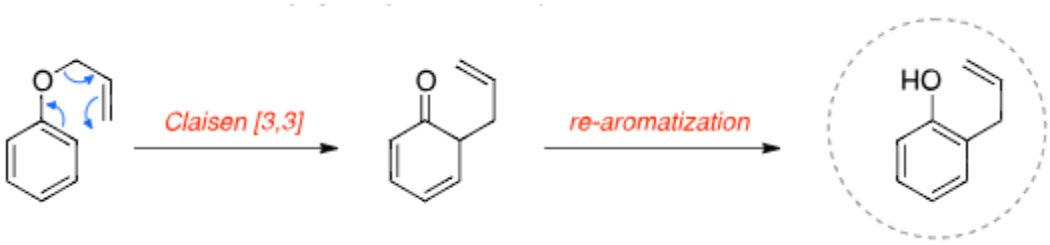


Claisen Rearrangement Mechanism Allyl Vinyl Ether

2. Allyl Phenyl Ethers

The electrons are pushed around the six-membered ring in an electrocyclic process. The resulting dienone now undergoes ***tautomerization to give its aromatic enol form***. This form is more stable than the dienone form. The required compound is therefore formed.

This mechanism can be illustrated as follows.



Claisen Rearrangement Mechanism Allyl Phenyl Ethers

Thus, the required gamma,delta-unsaturated carbonyl compounds are generated from the Claisen rearrangement of allyl vinyl ethers or allyl phenyl ethers.

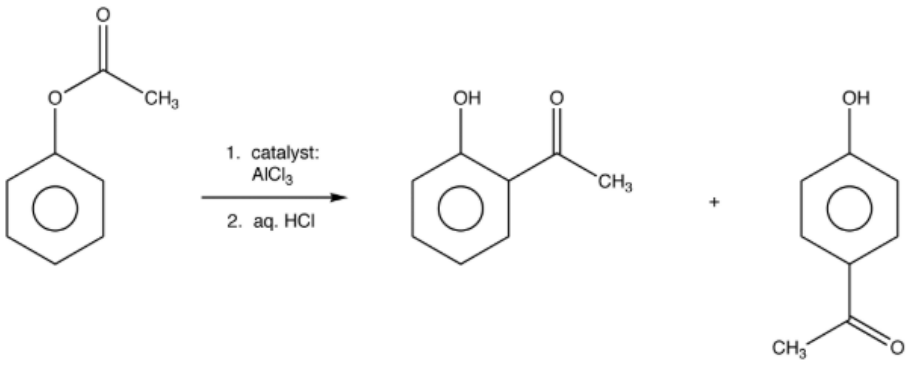
Variations of Claisen Rearrangement

In addition to the classical allyl vinyl ether rearrangement, several variations have been developed which improve the synthetic value of the Claisen rearrangement with respect to the preparation of the parent compounds, reaction conditions and stereoselectivity.

Fries Rearrangements:

Fries Rearrangement is an organic rearrangement reaction in which an aryl ester is transformed into a hydroxy aryl ketone with the help of a Lewis acid catalyst and an aqueous acid. In this reaction, an acyl group belonging to the phenolic ester migrates to the aryl ring. It is important to

note that Fries rearrangement is ortho and para selective, i.e. the acyl group attaches itself at the ortho or para positions of the aryl ring. The selectivity of the reaction can be directed by modifying the reaction conditions (such as the temperature under which the reaction is conducted, or the solvent used in the reaction).



Fries Rearrangement

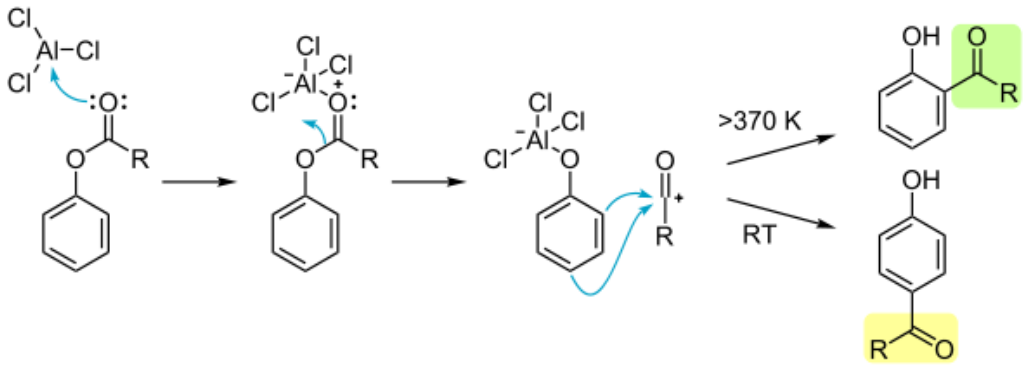
An illustration detailing the Fries rearrangement undergone by phenyl acetate (acetoxy benzene) is provided above. Note that the products feature ortho and para migrations of the acyl group.

Fries Rearrangement Mechanism

Initially, the carbonyl oxygen belonging to the acyl group forms a complex with the Lewis acid catalyst (usually $AlCl_3$). The formation of the complex with the carbonyl oxygen is favoured over the complexation of the phenolic oxygen since the carbonyl oxygen is richer in electrons and is, therefore, a better Lewis base.

Now, the bond between the phenolic oxygen and the acyl complex becomes polarized, resulting in the rearrangement of the $AlCl_3$ bond to the phenolic oxygen. This results in the generation of an acylium carbocation.

The acylium carbocation goes on to attack the aromatic ring via an electrophilic aromatic substitution reaction. It is important to note that the orientation of this electrophilic aromatic substitution is temperature-dependent. Low reaction temperatures favour substitutions at the para position and relatively high temperatures favour ortho substitution.



Mechanism of Fries Rearrangement

The mechanism of the Fries rearrangement reaction is illustrated above. The use of a non-polar solvent in this reaction also favours the formation of ortho-substituted products. Highly polar solvents favour para substitution in this reaction.

Limitations of Fries Rearrangement

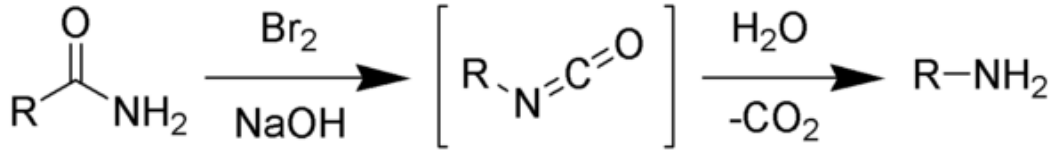
The key limitations of Fries rearrangement are listed below.

- Owing to its relatively harsh reaction conditions, only esters with relatively stable acyl components can be used in this reaction.
- Low yields are obtained when heavily substituted acyl components exist.
- The presence of deactivating or meta-directing groups on the aromatic ring results in low yields.

Hofmann Rearrangements:

Hofmann rearrangement, also known as Hofmann degradation is the reaction of a primary amide with a halogen (chlorine or bromine) in strongly basic (sodium or potassium hydroxide) aqueous medium, which converts the amide to a primary amine. For example:

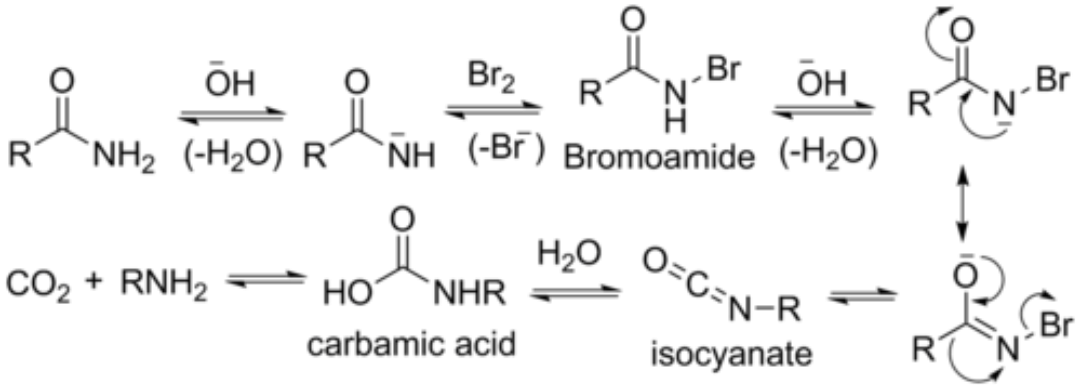
The organic reaction of a primary amide to a primary amine with one fewer carbon atom.



The Hofmann rearrangement.

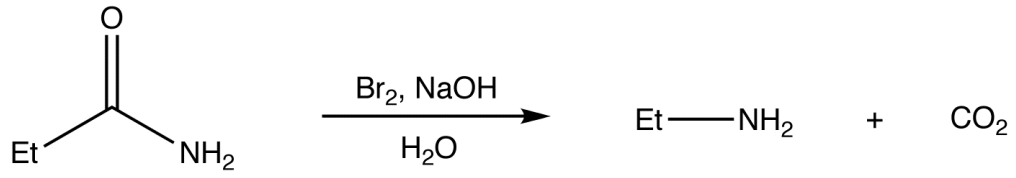
The reaction of bromine with sodium hydroxide forms sodium hypobromite *in situ*, which transforms the primary amide into an intermediate isocyanate. The formation of an intermediate nitrene is not possible because it implies also the formation of a hydroxamic acid as a byproduct,

which has never been observed. The intermediate isocyanate is hydrolyzed to a primary amine, giving off carbon dioxide.

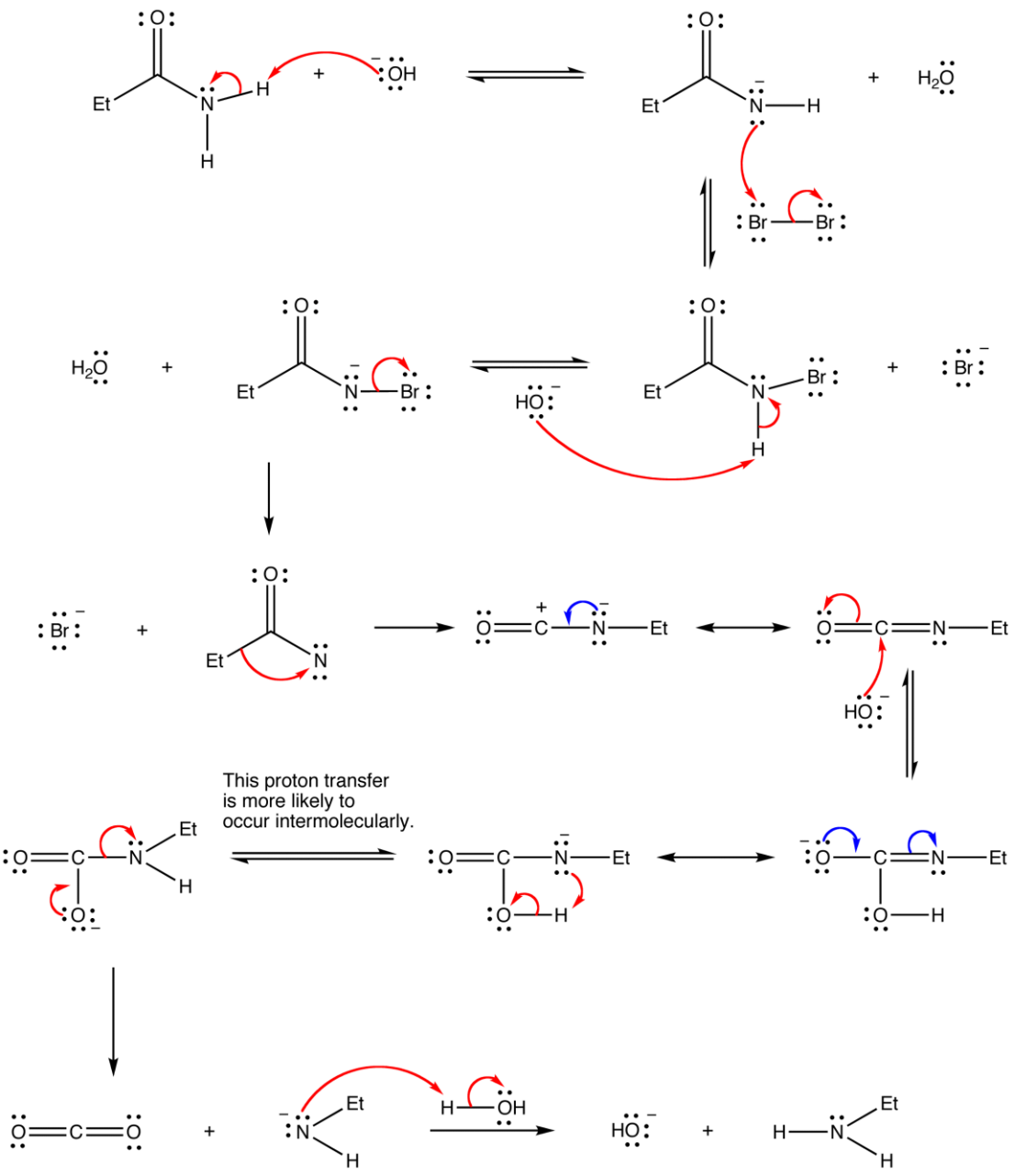


1. Base abstracts an acidic N-H proton, yielding an anion.
2. The anion reacts with bromine in an α-substitution reaction to give an *N*-bromoamide.
3. Base abstraction of the remaining amide proton gives a bromoamide anion.
4. The bromoamide anion rearranges as the R group attached to the carbonyl carbon migrates to nitrogen at the same time the bromide ion leaves, giving an isocyanate.
5. The isocyanate adds water in a nucleophilic addition step to yield a carbamic acid (aka urethane).
6. The carbamic acid spontaneously loses CO_2, yielding the amine product.

Another Reaction:

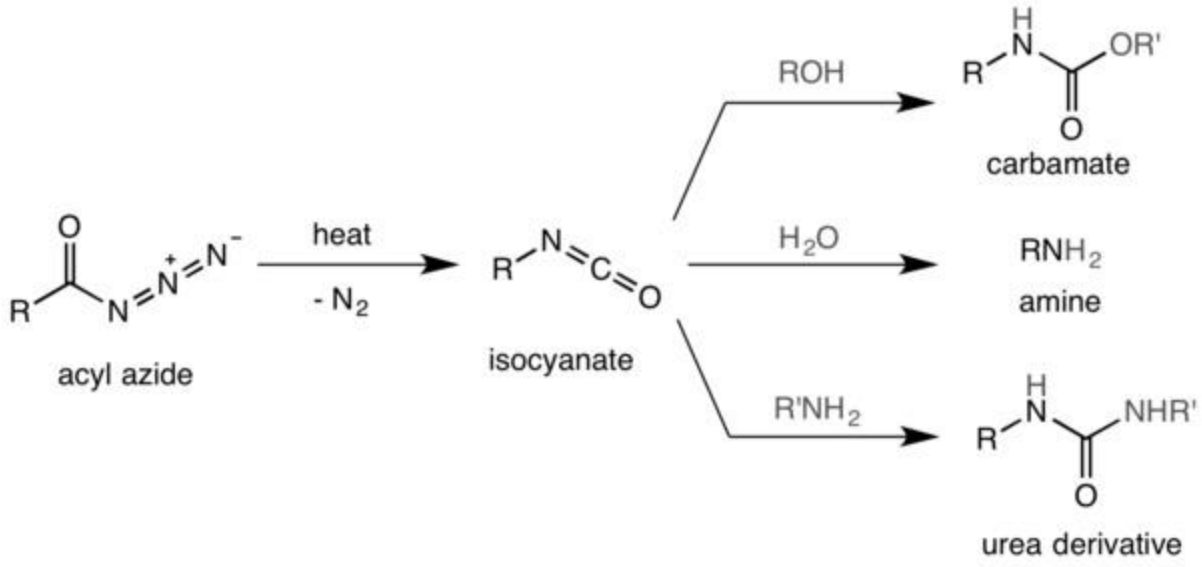


Mechanism:



Curtius Rearrangements:

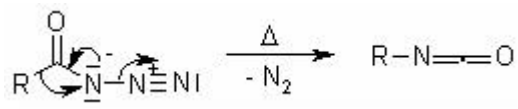
Curtius Rearrangement is also called Curtius degradation or Curtius reaction. Curtius Rearrangement is a thermal decomposition of acyl acid to form isocyanate with a loss of nitrogen as stated by Theodor Curtius in the year 1885. It is also known as Curtius degradation or Curtius reaction. This reaction is identical to Schmidt Reaction.

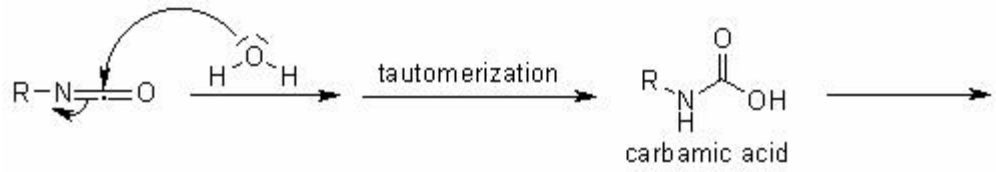


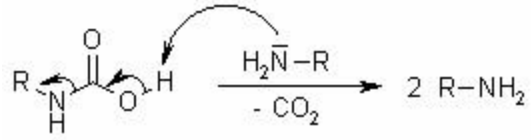
Isocyanates are subjected to attack by various nucleophiles namely alcohols, water, and amines which in turn outputs urea derivative or carbamate and essential amines.

Mechanism of Curtius Rearrangement

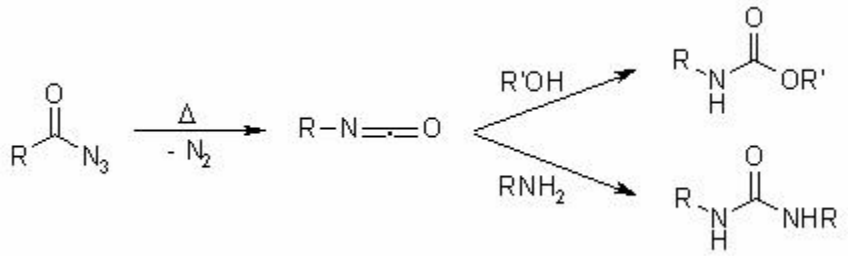
- Acyl azide preparation
- Decomposition
- Reacts with water to form an unstable carbamic acid derivative. It further undergoes spontaneous decarboxylation.





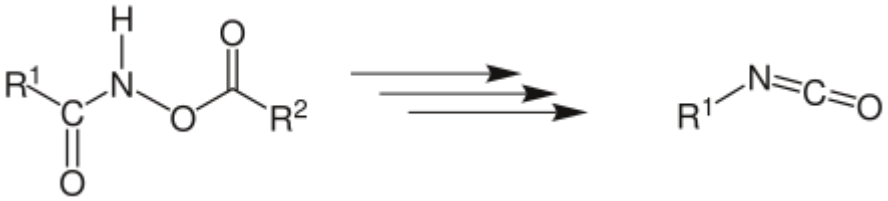


- Isocyanates are versatile starting materials. Isocyanates play a vital role in polymerization work and in the derivatization of biomacromolecules.



Lossen Rearrangements:

The **Lossen rearrangement** is the conversion of a hydroxamate ester to an isocyanate. Typically O-acyl, sulfonyl, or phosphoryl O-derivative are employed.[1][2]The isocyanate can be used further to generate ureas in the presence of amines or generate amines in the presence of H_2O.

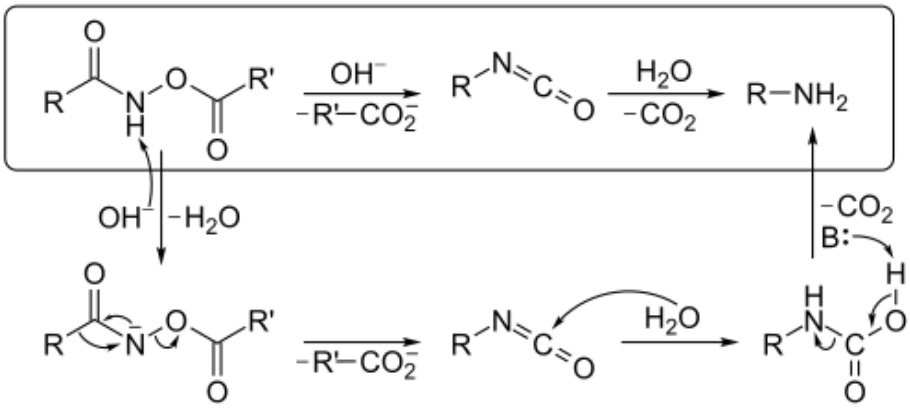


Mechanism:

The mechanism below begins with an O-acylated hydroxamic acid derivative that is treated with base to form an isocyanate that generates an amine and CO_2 gas in the presence of H_2O.

The hydroxamic acid derivative is first converted to its conjugate base by abstraction of a hydrogen by a base.

Spontaneous rearrangement kicks off a carboxylate anion to produce the isocyanate intermediate. The isocyanate in the presence H_2O hydrolyzes and then decarboxylation via abstraction of a hydrogen by a base generates an amine and CO_2 gas.



Hydroxamic acids are commonly synthesized from their corresponding esters

Beckmann Rearrangements:

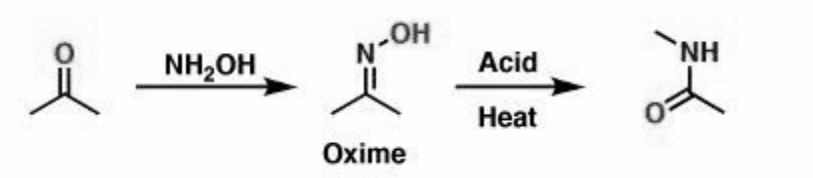
The Beckmann Rearrangement is a reaction of the oximes that can bring about either nitriles or amides, contingent upon the beginning material. These Oximes that obtained from the ketones develop into amides; oximes got from the aldehydes shape into nitriles.

The Beckmann Rearrangement process is a natural reaction that is useful in changing an oxime to that of an amide under some acidic conditions. The reaction eventually starts by the process of protonation of the alcohol group gather shaping a preferred leaving group.

The R group transition to that of the leaving species then moves to the nitrogen, bringing about a carbocation and the arrival of a water particle. The water atom attacks the carbocation, and after the process of deprotonation and tautomerization, the amide is obtained.

In simple, Beckmann Rearrangement is a reaction where oxime is changed over to an amide. The oxime is processed by treating an aldehyde or a ketone with hydroxylamine. This Beckmann Rearrangement reaction, named after Ernst Otto Beckmann, a German scientist.

Mechanism:



The process of Beckmann Rearrangement is as shown below-

1. The oxime is shaped when cyclohexanone responds with the hydroxylamine.

2. The Protonation of hydroxyl of oxime happens after the change of the alkyl substituent “trans” to the nitrogen

3. At the same time, the N-O bond is severed with the expulsion of water.

4. Later, Isomerization process happens which protonates the molecule of nitrogen and then prompts to the production of amine.

Applications:

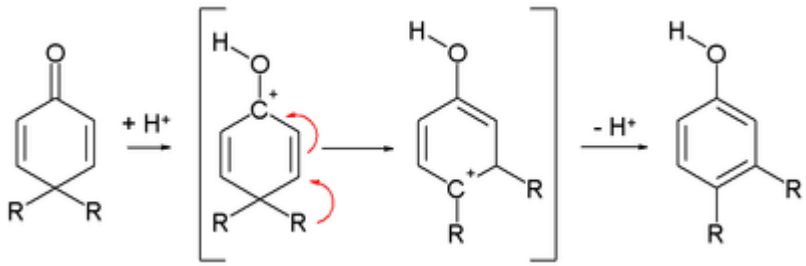
Some of the uses of this reaction are as below-

- It is used in the industries for the synthesis of paracetamol. This integration is achieved by the process of conversion of a ketone to ketoxime with the help of hydroxylamine.
- It is mainly used in the synthesis of various steroids and drugs
- The Beckmann Rearrangement synthesis is helpful in the production of some of the chloro bicyclic lactams.

Dienone – Phenol Rearrangements:

A **dienone** is a class of organic compounds that are formally "derived from diene compounds by conversion of a –CH2– groups into –C(=O)– group .", resulting in "a conjugated structure". The class includes some heterocyclic compounds.

Rearrangement reaction of 6-membered cyclic dienones generate phenols through the **dienone phenol rearrangement**:



UNIT V

ORGANIC SPECTROSCOPY

Uv - Vis Spectroscopy:

Ultraviolet–visible spectroscopy or **ultraviolet-visible spectrophotometry** (**UV-Vis** or **UV/Vis**) refers to absorption spectroscopy or reflectance spectroscopy in the ultraviolet-visible spectral region. This means it uses light in the visible and adjacent (near-UV and near-infrared [NIR]) ranges. The absorption or reflectance in the visible range directly affects the perceived color of the chemicals involved. In this region of the electromagnetic spectrum, molecules undergo electronic transitions. This technique is complementary to fluorescence spectroscopy, in that fluorescence deals with transitions from the excited state to the ground state, while absorption measures transitions from the ground state to the excited state.

Types of Electronic Transitions:

Molecules containing π-electrons or non-bonding electrons (n-electrons) can absorb the energy in the form of ultraviolet or visible light to excite these electrons to higher anti-bonding molecular orbitals The more easily excited the electrons (i.e. lower energy gap between the HOMO and the LUMO), the longer the wavelength of light it can absorb)

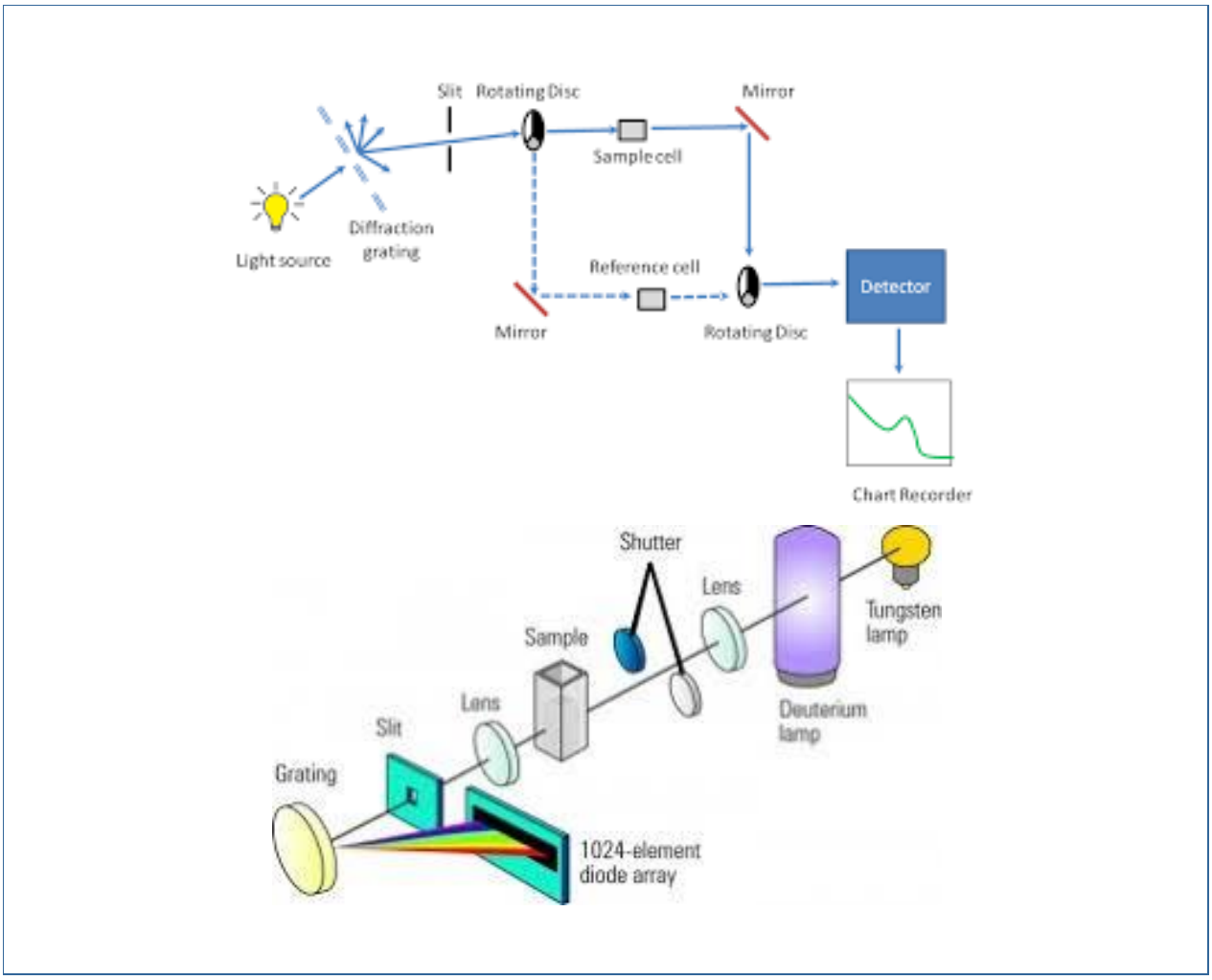
Instrumentation:

There are three types of absorbance instruments used to collect UV-vis spectra:

1. 1) Single beam spectrometer.
2. 2) Double beam spectrometer.
3. 3) Simultaneous spectrometer.

All of these instruments have a light source (usually a deuterium or tungsten lamp), a sample holder and a detector, but some have a filter for selecting one wavelength at a time. The single beam instrument (Figure) has a filter or a monochromator between the source and the sample to analyze one wavelength at a time. The double beam instrument (Figure) has a single source and a monochromator and then there is a splitter and a series of mirrors to get the beam to a reference sample and the sample to be analyzed, this allows for more accurate readings. In contrast, the simultaneous instrument (Figure) does not have a monochromator between the sample and the source; instead, it has a diode array detector that allows the instrument to simultaneously detect

the absorbance at all wavelengths. The simultaneous instrument is usually much faster and more efficient, but all of these types of spectrometers work well.



Solvent Effects on Λ Max:

Chloroform-d ($CDCl_3$) is the most common solvent for nmr measurements, thanks to its good solubilizing character and relative unreactive nature (except for 1º and 2º-amines). As noted earlier, other deuterium labeled compounds, such as deuterium oxide (D_2O), benzene-d6 (C_6D_6), acetone-d6 (CD_3COCD_3) and DMSO-d6 (CD_3SOCD_3) are also available for use as nmr solvents. Because some of these solvents have π-electron functions and/or may serve as hydrogen bonding partners, the chemical shifts of different groups of protons may change depending on the solvent being used. The following table gives a few examples, obtained with dilute solutions at 300 MHz.

Some Typical ^1H Chemical Shifts (δ values) in Selected Solvents

Solvent Compound	$CDCl_3$	C_6D_6	CD_3COCD_3	CD_3SOCD_3	$CD_3C{\equiv}N$	D_2O
$(CH_3)_3C–O–CH_3$ $C–CH_3$ $O–CH_3$	 1.19 3.22	 1.07 3.04	 1.13 3.13	 1.11 3.03	 1.14 3.13	 1.21 3.22
$(CH_3)_3C–O–H$ $C–CH_3$ $O–H$	 1.26 1.65	 1.05 1.55	 1.18 3.10	 1.11 4.19	 1.16 2.18	 --- ---
$C_6H_5CH_3$ CH_3 C_6H_5	 2.36 7.15-7.20	 2.11 7.00-7.10	 2.32 7.10-7.20	 2.30 7.10-7.15	 2.33 7.15-7.30	 --- ---
$(CH_3)_2C=O$	2.17	1.55	2.09	2.09	2.08	2.22

For most of the above resonance signals and solvents the changes are minor, being on the order of ±0.1 ppm. However, two cases result in more extreme changes and these have provided useful applications in structure determination. First, spectra taken in benzene-d_6 generally show small upfield shifts of most C–H signals, but in the case of acetone this shift is about five times larger than normal. Further study has shown that carbonyl groups form weak π–π collision complexes with benzene rings, that persist long enough to exert a significant shielding influence on nearby groups. In the case of substituted cyclohexanones, axial α-methyl groups are shifted upfield by 0.2 to 0.3 ppm; whereas equatorial methyls are slightly deshielded (shift downfield by about 0.05 ppm). These changes are all relative to the corresponding chloroform spectra.

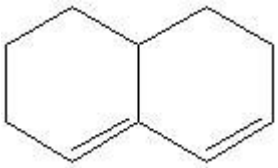
The second noteworthy change is seen in the spectrum of tert-butanol in DMSO, where the hydroxyl proton is shifted 2.5 ppm down-field from where it is found in dilute chloroform solution. This is due to strong hydrogen bonding of the alcohol O–H to the sulfoxide oxygen, which not only de-shields the hydroxyl proton, but secures it from very rapid exchange reactions that prevent the display of spin-spin splitting. Similar but weaker hydrogen bonds are formed to the carbonyl oxygen of acetone and the nitrogen of acetonitrile. A useful application of this phenomenon is described elsewhere in this text.

Woodward - Fieser Rules for Calculation of Λ Max Dienes:

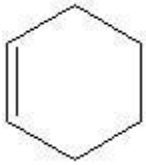
Each type of diene or triene system is having a certain fixed value at which absorption takes place; this constitutes the ***Base value or Parent value***. The contribution made by various alkyl substituents or ring residue, double bond extending conjugation and polar groups such as –Cl, -Br etc are added to the basic value to obtain λ_{max} for a particular compound.

a) **Homoannular Diene:-** Cyclic diene having conjugated double bonds in same ring.

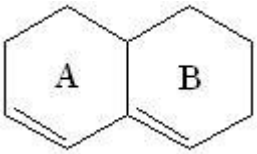
b) Heteroannular Diene:- Cyclic diene having conjugated double bonds in different rings.



b) **Endocyclic double bond:-** Double bond present in a ring.



c) **Exocyclic double bond: -** Double bond in which one of the doubly bonded atoms is a part of a ring system.



Here Ring A has one exocyclic and endocyclic double bond. Ring B has only one endocyclic double bond.

Conjugated Diene Correlations:

i) Base value for homoannular diene = 253 nm

ii) Base value for heteroannular diene = 214 nm

iii) Alkyl substituent or Ring residue attached to the parent diene = 5 nm

iv) Double bond extending conjugation = 30 nm

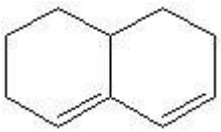
v) Exocyclic double bonds = 5 nm

vi) Polar groups: a) -OAc = 0 nm

b) -OAlkyl = 6 nm

c) -Cl, -Br = 5 nm

Eg:



Base value = 214 nm

Ring residue = 3 x 5 = 15 nm

Exocyclic double bond = 1 x 5 = 5 nm

λ_{max} = 214 + 15 + 5 = 234 nm

Bathochromic Shift:

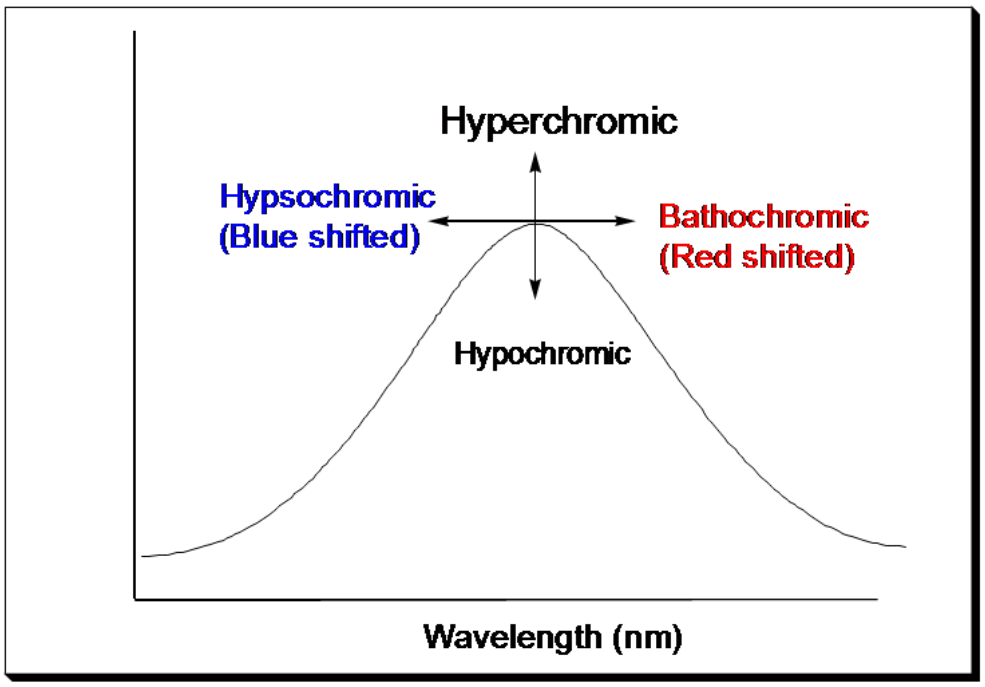
Bathochromic shift is a change of spectral band position in the absorption, reflectance, transmittance, or emission spectrum of a molecule to a longer wavelength (lower frequency).Because the red color in the visible spectrum has a longer wavelength than most other colors, the effect is also commonly called a ***red shift***.

Hypsochromic shift is a change to shorter wavelength (higher frequency).

Conditions

It can occur because of a change in environmental conditions: for example, a change in solvent polarity will result in solvatochromism.

A series of structurally-related molecules in a substitution series can also show a bathochromic shift. Bathochromic shift is a phenomenon seen in *molecular* spectra, not *atomic* spectra; it is thus more common to speak of the movement of the peaks in the spectrum rather than lines. where is the wavelength of the spectral peak of interest and



Detection

Bathochromic shift is typically demonstrated using a spectrophotometer, colorimeter, or spectroradiometer.

Hypsochromic Shift:

Hypsochromic shift is a change of spectral band position in the absorption, reflectance, transmittance, or emission spectrum of a molecule to a shorter wavelength (higher frequency). Because the blue color in the visible spectrum has a shorter wavelength than most other colors, this effect is also commonly called a **blue shift**.

This can occur because of a change in environmental conditions: for example, a change in solvent polarity will result in solvatochromism. A series of structurally related molecules in a substitution series can also show a hypsochromic shift. Hypsochromic shift is a phenomenon seen in *molecular* spectra, not *atomic* spectra - it is thus more common to speak of the movement of the peaks in the spectrum rather than lines.

IR Spectroscopy:

The IR spectroscopy theory utilizes the concept that molecules tend to absorb specific frequencies of light that are characteristic of the corresponding structure of the molecules. The energies are reliant on the shape of the molecular surfaces, the associated vibronic coupling, and the mass corresponding to the atoms.

For instance, the molecule can absorb the energy contained in the incident light and the result is a faster rotation or a more pronounced vibration.

Number and Types of Fundamental Vibrations:

The IR spectroscopy theory utilizes the concept that molecules tend to absorb specific frequencies of light that are characteristic of the corresponding structure of the molecules. The energies are reliant on the shape of the molecular surfaces, the associated vibronic coupling, and the mass corresponding to the atoms.

For instance, the molecule can absorb the energy contained in the incident light and the result is a faster rotation or a more pronounced vibration.

In order for a vibrational mode in a molecule to be "IR active," it must be associated with changes in the permanent dipole.

A molecule can vibrate in many ways, and each way is called a *vibrational mode.* Linear molecules have 3N–5 degrees of vibrational modes whereas nonlinear molecules have 3N–6 degrees of vibrational modes (also called vibrational degrees of freedom). As an example H_2O, a non-linear molecule, will have 3×3–6 = 3 degrees of vibrational freedom, or modes.

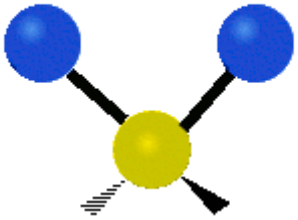
Simple diatomic molecules have only one bond and only one vibrational band. If the molecule is symmetrical, e.g. N_2, the band is not observed in the IR spectrum, but only in the Raman spectrum. Unsymmetrical diatomic molecules, e.g. CO, absorb in the IR spectrum. More complex molecules have many bonds, and their vibrational spectra are correspondingly more complex, i.e. big molecules have many peaks in their IR spectra.

The atoms in a CH_2 group, commonly found in organic compounds, can vibrate in six different ways: **symmetric and antisymmetric stretching**,**scissoring**, **rocking**, **wagging** and **twisting**:

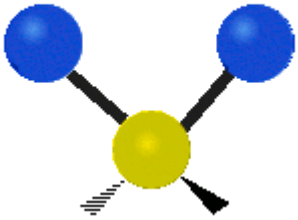
Modes of Vibrations and Their Energies:

A molecule has translational and rotational motion as a whole while each atom has it's own motion. The vibrational modes can be IR or Raman active. For a mode to be observed in the IR spectrum, changes must occur in the permanent dipole (i.e. not diatomic molecules). Diatomic molecules are observed in the Raman spectra but not in the IR spectra. This is due to the fact that diatomic molecules have one band and no permanent dipole, and therefore one single vibration. An example of this would be O_2 or N_2. However, unsymmetric diatomic molecules (i.e. CN) do absorb in the IR spectra. Polyatomic molecules undergo more complex vibrations that can be summed or resolved into normal modes of vibration.

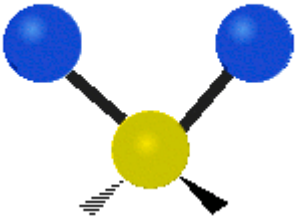
Symmetric Stretching



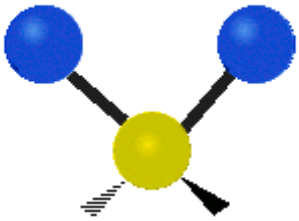
Asymmetric Stretching



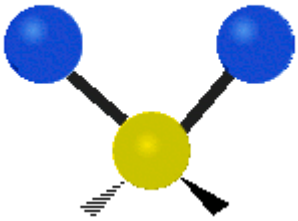
Wagging



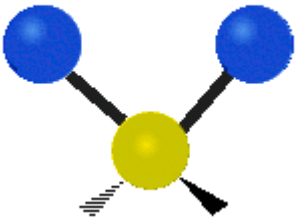
Twisting



Scissoring



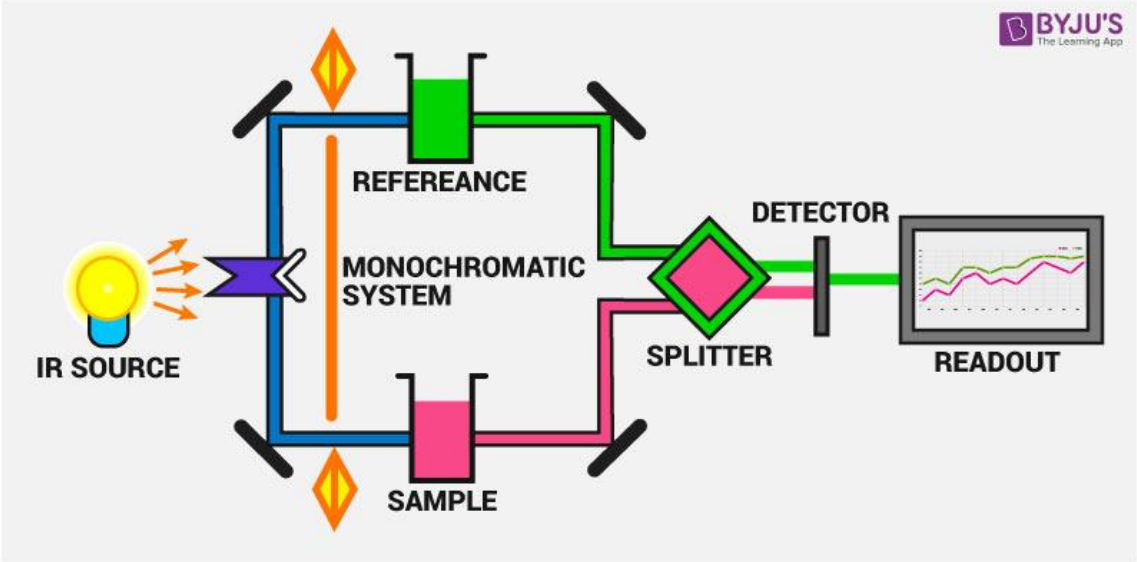
Rocking



Selection Rules:

Instrumentation:

The instrumentation of infrared spectroscopy is illustrated below. First, a beam of IR light from the source is split into two and passed through the reference ant the sample respectively.



Now, both of these beams are reflected to pass through a splitter and then through a detector. Finally, the required reading is printed out after the processor deciphers the data passed through the detector.

Samples in Infrared Spectroscopy

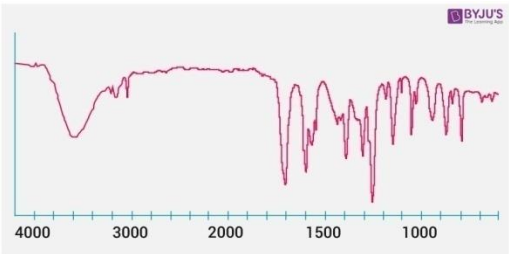
The samples used in IR spectroscopy can be either in the solid, liquid, or gaseous state.

- Solid samples can be prepared by crushing the sample with a mulling agent which has an oily texture. A thin layer of this mull can now be applied on a salt plate to be measured.
- Liquid samples are generally kept between two salt plates and measured since the plates are transparent to IR light. Salt plates can be made up of sodium chloride, calcium fluoride, or even potassium bromide.
- Since the concentration of gaseous samples can be in parts per million, the sample cell must have a relatively long pathlength, i.e. light must travel for a relatively long distance in the sample cell.

Thus, samples of multiple physical states can be used in Infrared Spectroscopy.

Graph of the IR spectrum

Given below is a sample of typical Infrared Absorption Frequencies.



Thus, IR spectroscopy involves the collection of absorption information and its analysis in the form of a spectrum. To learn more about similar topics, download the free BYJU's app from the Google Play store.

Position of IR absorption Frequencies for Functional Groups:

Infrared spectroscopy is the study of the interaction of infrared light with matter. The fundamental measurement obtained in infrared spectroscopy is an infrared spectrum, which is a plot of measured infrared intensity versus wavelength (or frequency) of light.

In infrared spectroscopy, units called wavenumbers are normally used to denote different types of light. The frequency, wavelength, and wavenumber are related to each other via the following equation:

$c = \nu\lambda$

c = the speed of light (cm/sec)
ν = frequency in Hertz (sec^{-1})
λ = wavelength in cm

$W = 1/\lambda$

W = wavenumber in cm^{-1}
λ = wavelength in cm

These equations show that light waves may be described by their frequency, wavelength or wavenumber. Here, we typically refer to light waves by their wavenumber, however it will be more convenient to refer to a light wave's frequency or wavelength. The wavenumber of several different types of light are shown in table 1.

>14,000 cm^{-1} Visible UV & X-rays	14,000 to 4000cm^{-1} Near Infrared	4000 to 400cm^{-1} Mid Infrared	400 to 4cm^{-1} Far Infrared	< 4cm^{-1} Microwaves Radio Waves
← Higher Wavenumber				Lower Wavenumber →
← Higher Frequency				Lower Frequency →
← Higher Energy				Lower Energy →
← Shorter Wavelength				Longer Wavelength →

Frequencies for Aldehyde ,Ketone, Alcohol,Acid:

Alcohols have IR absorptions associated with both the O-H and the C-O stretching vibrations.

- O–H stretch, hydrogen bonded 3500-3200 cm^{-1}
- C–O stretch 1260-1050 cm^{-1} (s)

Figure 1 shows the spectrum of ethanol. Note the very broad, strong band of the O–H stretch.

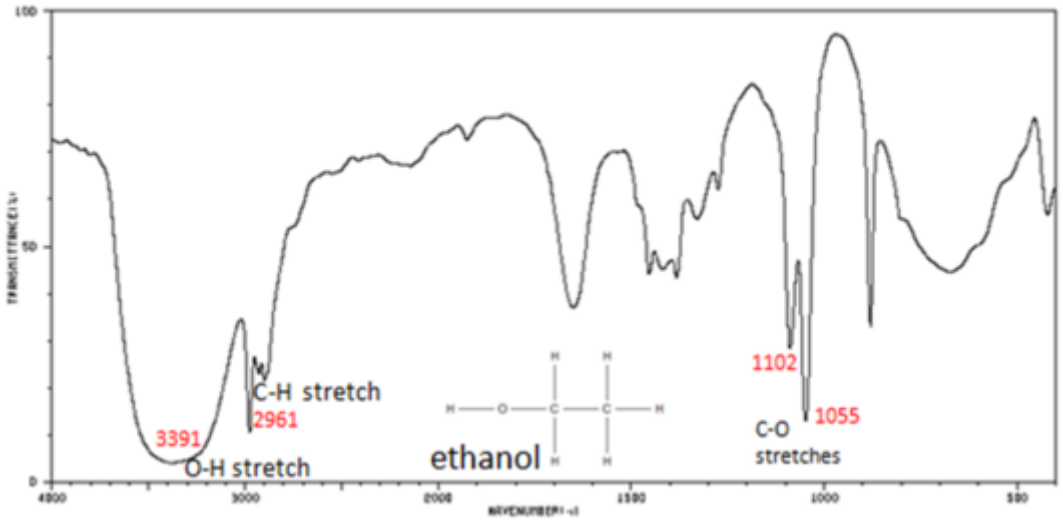


Figure 1 Infrared Spectrum of Ethanol

The carbonyl stretching vibration band C=O of saturated aliphatic ketones appears:

C=O stretch - aliphatic ketones 1715 cm^{-1}

Unsaturated ketones 1685-1666 cm^{-1}

Figure 2 shows the spectrum of 2-butanone. This is a saturated ketone, and the C=O band appears at 1715.

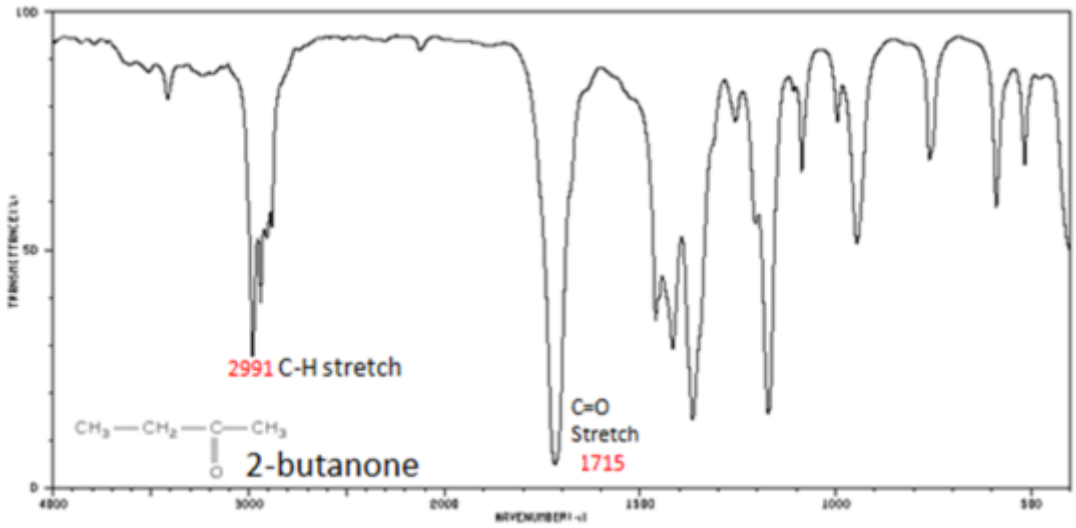


Figure 2Infrared Spectrum of 2-Butanone

If a compound is suspected to be an aldehyde, a peak always appears around 2720 cm^{-1} which often appears as a shoulder-type peak just to the right of the alkyl C–H stretches.

- H–C=O stretch 2830-2695 cm^{-1}
- C=O stretch:
  - aliphatic aldehydes 1740-1720 cm^{-1}
  - alpha, beta-unsaturated aldehydes 1710-1685 cm^{-1}

Figure 3shows the spectrum of butyraldehyde.

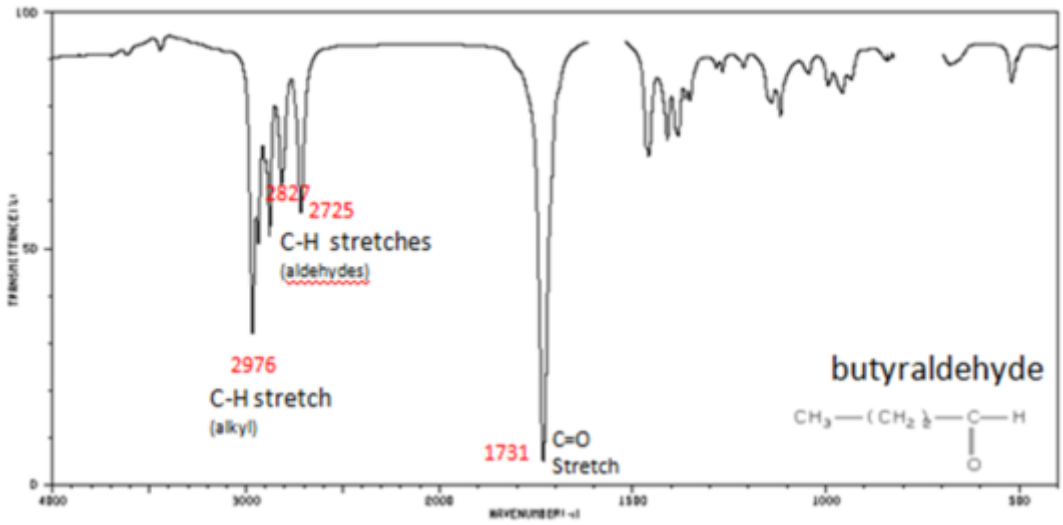


Figure3 Infrared Spectrum of Butyraldehyde

The carbonyl stretch C=O of esters appears:

- C=O stretch
  - aliphatic from 1750-1735 cm^{-1}
  - unsaturated from 1730-1715 cm^{-1}
- C–O stretch from 1300-1000 cm^{-1}

Figure 4 shows the spectrum of ethyl benzoate.

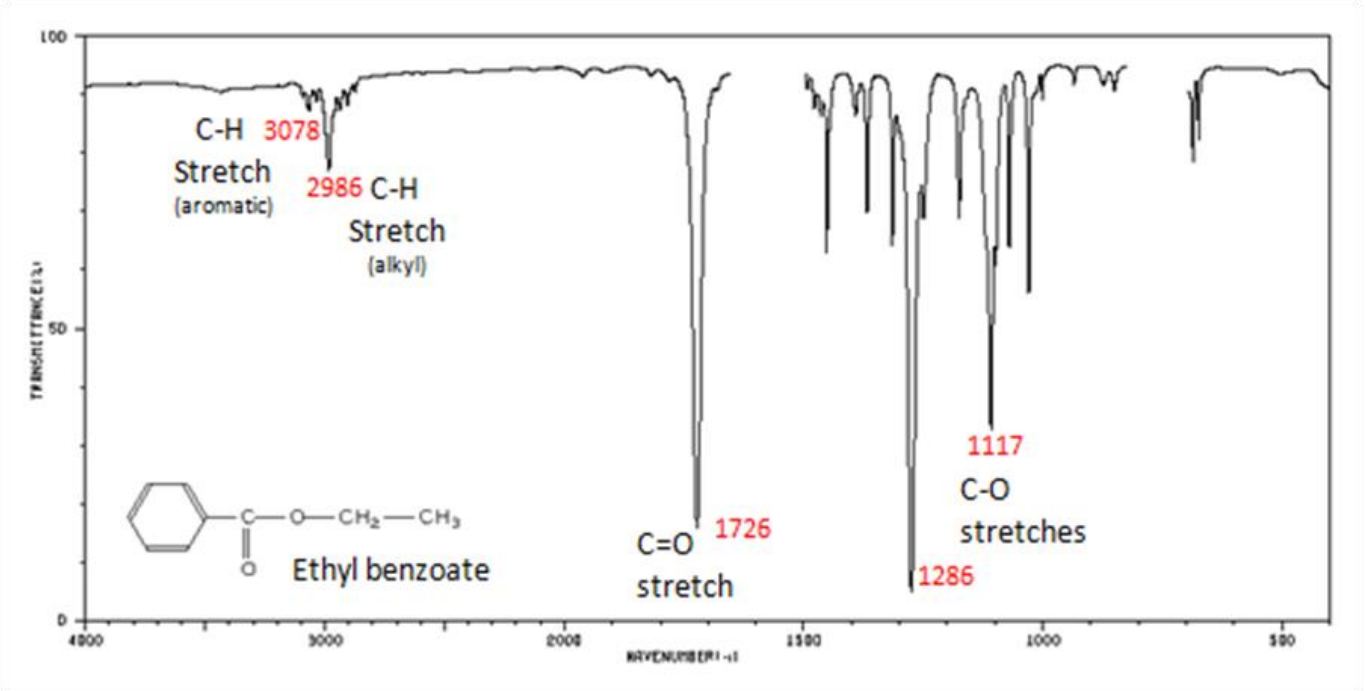


Figure 4 Infrared Spectrum of Ethyl benzoate

The carbonyl stretch C=O of a carboxylic acid appears as an intense band from 1760-1690 cm^{-1}. The exact position of this broad band depends on whether the carboxylic acid is saturated or unsaturated, dimerized, or has internal hydrogen bonding.

- O–H stretch from 3300-2500 cm^{-1}
- C=O stretch from 1760-1690 cm^{-1}
- C–O stretch from 1320-1210 cm^{-1}
- O–H bend from 1440-1395 and 950-910 cm^{-1}

Figure 5 shows the spectrum of hexanoic acid.

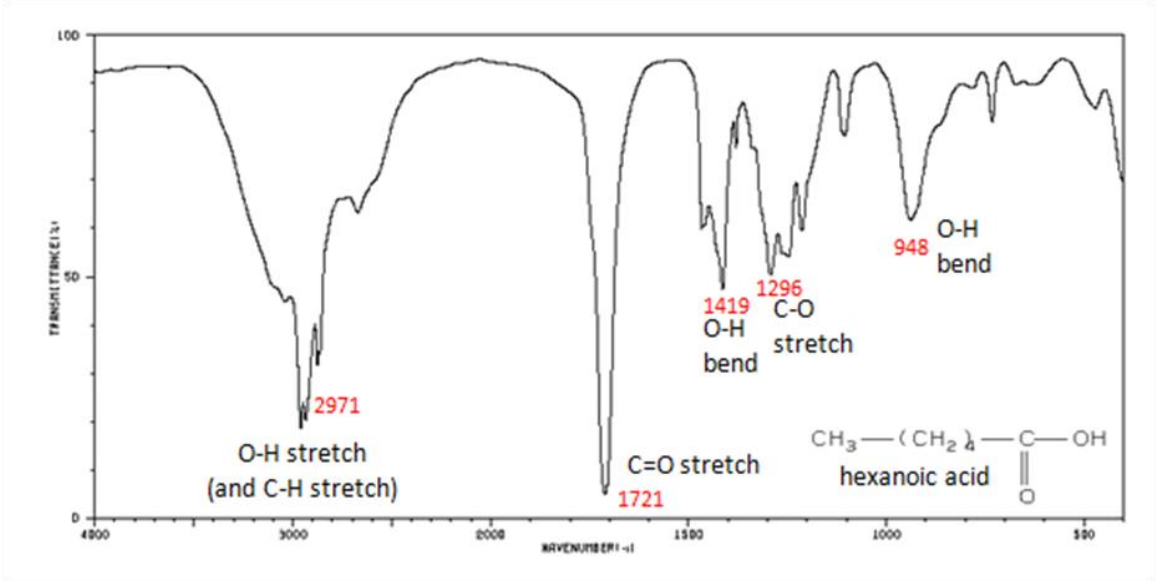


Figure 5 spectrum of hexanoic acid

Frequencies for Amine, Amide:

- N–O asymmetric stretch from 1550-1475 cm^{-1}
- N–O symmetric stretch from 1360-1290 cm^{-1}

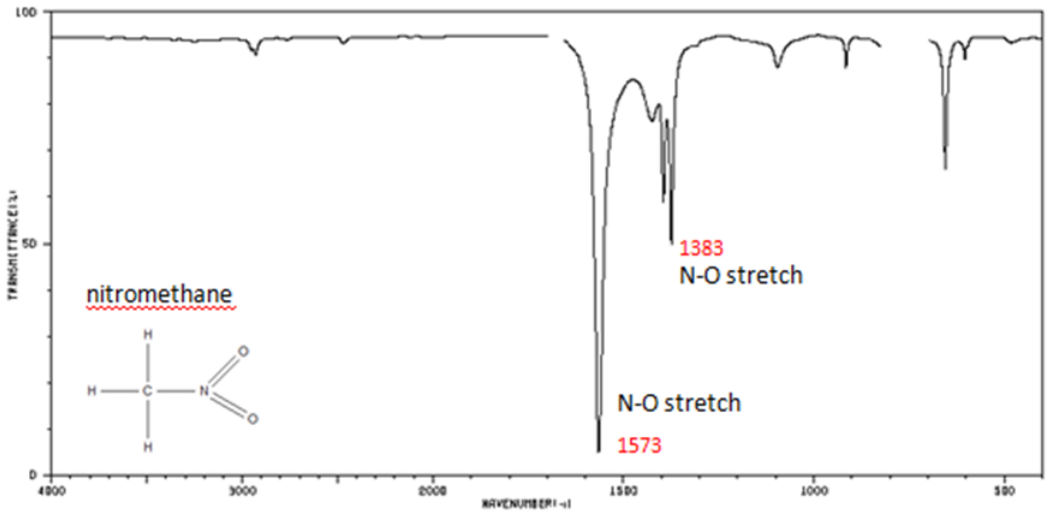


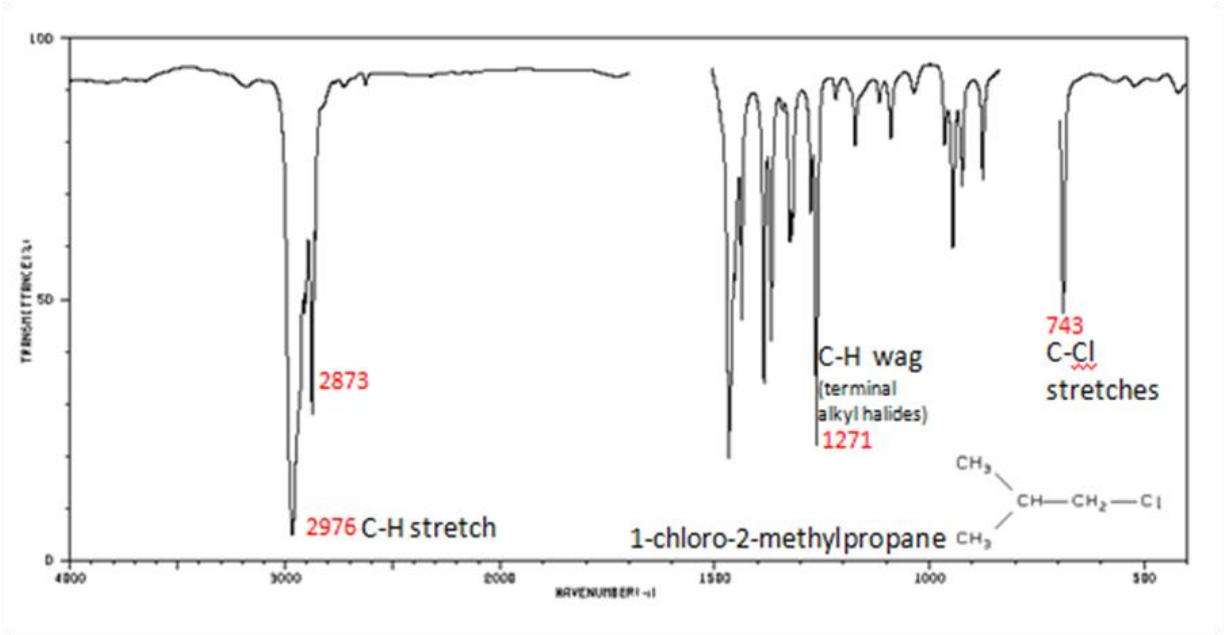
Figure 6 Infrared Spectrum of Nitomethane

Organic Compounds Containing Halogens

Alkyl halides are compounds that have a C–X bond, where X is a halogen: bromine, chlorine, fluorene, or iodine.

- C–H wag (-CH_2X) from 1300-1150 cm^{-1}
- C–X stretches (general) from 850-515 cm^{-1}
    - C–Cl stretch 850-550 cm^{-1}
    - C–Br stretch 690-515 cm^{-1}

The spectrum of 1-chloro-2-methylpropane are shown below.



Infrared Spectrum of 1-chloro-2-methylpropane

For more Infrared spectra Spectral database of organic molecules is introduced to use free database. Also, the infrared spectroscopy correlation tableis linked on bottom of page to find other assigned IR peaks.

NMR Spectroscopy:

NMR Spectroscopy is abbreviated as ***Nuclear Magnetic Resonance spectroscopy.***

Nuclear magnetic resonance (NMR) spectroscopy is the study of molecules by recording the interaction of radiofrequency (Rf) electromagnetic radiations with the nuclei of molecules placed in a strong magnetic field.

Zeeman first observed the strange behavior of certain nuclei when subjected to a strong magnetic field at the end of the nineteenth century, but the practical use of the so-called ***"Zeeman effect"*** was only made in the 1950s when NMR spectrometers became commercially available.

It is a research technique that exploits the magnetic properties of certain atomic nuclei. The NMR spectroscopy determines the physical and chemical properties of atoms or molecules.

Principle:

- All nuclei are electrically charged and many have spin.
- Transfer of energy is possible from base energy to higher energy levels when an external magnetic field is applied.
- The transfer of energy occurs at a wavelength that coincides with the radio frequency.
- Also, energy is emitted at the same frequency when the spin comes back to its base level.
- Therefore, by measuring the signal which matches this transfer the processing of the NMR spectrum for the concerned nucleus is yield.

Chemical Shift:

A spinning charge generates a magnetic field that results in a magnetic moment proportional to the spin. In the presence of an external magnetic field, two spin states exist; one spin up and one spin down, where one aligns with the magnetic field and the other opposes it.

In nuclear magnetic resonance (NMR) spectroscopy, the **chemical shift** is the resonant frequency of a nucleus relative to a standard in a magnetic field. Often the position and number of chemical shifts are diagnostic of the structure of a molecule.Chemical shifts are also used to describe signals in other forms of spectroscopy such as photoemission spectroscopy.

Some atomic nuclei possess a magnetic moment (nuclear spin), which gives rise to different energy levels and resonance frequencies in a magnetic field.

The total magnetic field experienced by a nucleus includes local magnetic fields induced by currents of electrons in the molecular orbitals (note that electrons have a magnetic moment themselves).

The electron distribution of the same type of nucleus (e.g. ^{1}H, ^{13}C, ^{15}N) usually varies according to the local geometry (binding partners, bond lengths, angles between bonds, and so on), and with it the local magnetic field at each nucleus.

This is reflected in the spin energy levels (and resonance frequencies). The variations of nuclear magnetic resonance frequencies of the same kind of nucleus, due to variations in the electron distribution, is called the chemical shift. The size of the chemical shift is given with respect to a reference frequency or reference sample (see also chemical shift referencing), usually a molecule with a barely distorted electron distribution.

Factors affecting the Chemical Shift:

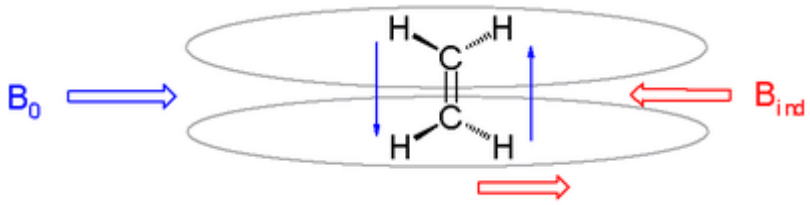
Important factors influencing chemical shift are electron density, electronegativity of neighboring groups and anisotropic induced magnetic field effects.

Electron density shields a nucleus from the external field. For example, in proton NMR the electron-poor tropylium ion has its protons downfield at 9.17 ppm, those of the electron-rich

cyclooctatetraenyl anion move upfield to 6.75 ppm and its dianion even more upfield to 5.56 ppm.

A nucleus in the vicinity of an electronegative atom experiences reduced electron density and the nucleus is therefore deshielded. In proton NMR of methyl halides (CH_3X) the chemical shift of the methyl protons increase in the order I < Br < Cl < F from 2.16 ppm to 4.26 ppm reflecting this trend. In carbon NMR the chemical shift of the carbon nuclei increase in the same order from around −10 ppm to 70 ppm. Also when the electronegative atom is removed further away the effect diminishes until it can be observed no longer.

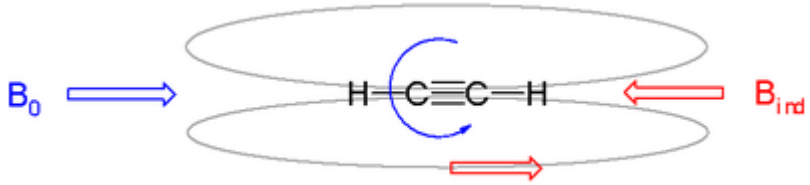
Anisotropic induced magnetic field effects are the result of a local induced magnetic field experienced by a nucleus resulting from circulating electrons that can either be paramagnetic when it is parallel to the applied field or diamagnetic when it is opposed to it. It is observed in alkenes where the double bond is oriented perpendicular to the external field with pi electrons likewise circulating at right angles. The induced magnetic field lines are parallel to the external field at the location of the alkene protons which therefore shift downfield to a 4.5 ppm to 7.5 ppm range. The three-dimensional space where a diamagnetic shift is called the shielding zone with a cone-like shape aligned with the external field.



Induced magnetic field of alkenes in external magnetic fields, field lines in grey.

The protons in aromatic compounds are shifted downfield even further with a signal for benzene at 7.73 ppm as a consequence of a diamagnetic ring current.

Alkyne protons by contrast resonate at high field in a 2–3 ppm range. For alkynes the most effective orientation is the external field in parallel with electrons circulation around the triple bond. In this way the acetylenic protons are located in the cone-shaped shielding zone hence the upfield shift.

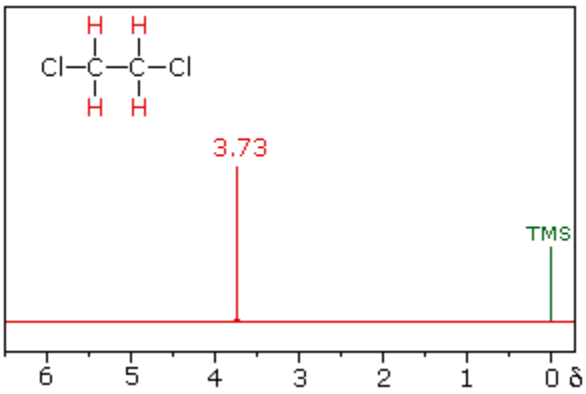


Induced magnetic field of alkynes in external magnetic fields, field lines in grey.

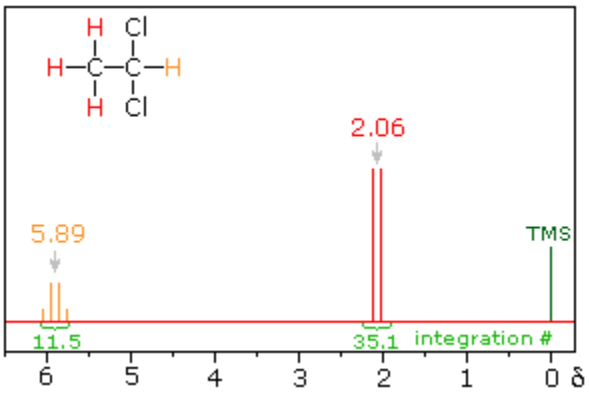
Inductive Effect:

Hydrogen Bonding: TMS, Delta Scales, Splitting of Signals - Spin-Spin Coupling:

The nmr spectrum of 1,1-dichloroethane (below right) is more complicated than we might have expected from the previous examples. Unlike its 1,2-dichloro-isomer (below left), which displays a single resonance signal from the four structurally equivalent hydrogens, the two signals from the different hydrogens are split into close groupings of two or more resonances. This is a common feature in the spectra of compounds having different sets of hydrogen atoms bonded to adjacent carbon atoms. The signal splitting in proton spectra is usually small, ranging from fractions of a Hz to as much as 18 Hz, and is designated as J (referred to as the coupling constant). In the 1,1-dichloroethane example all the coupling constants are 6.0 Hz, as illustrated by clicking on the spectrum.

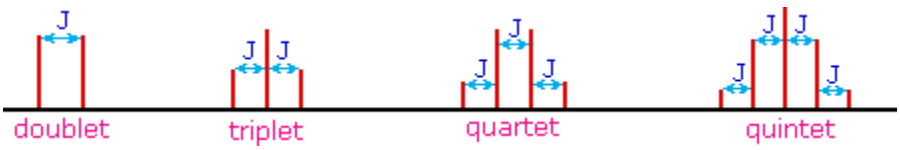


1,2-dichloroethane



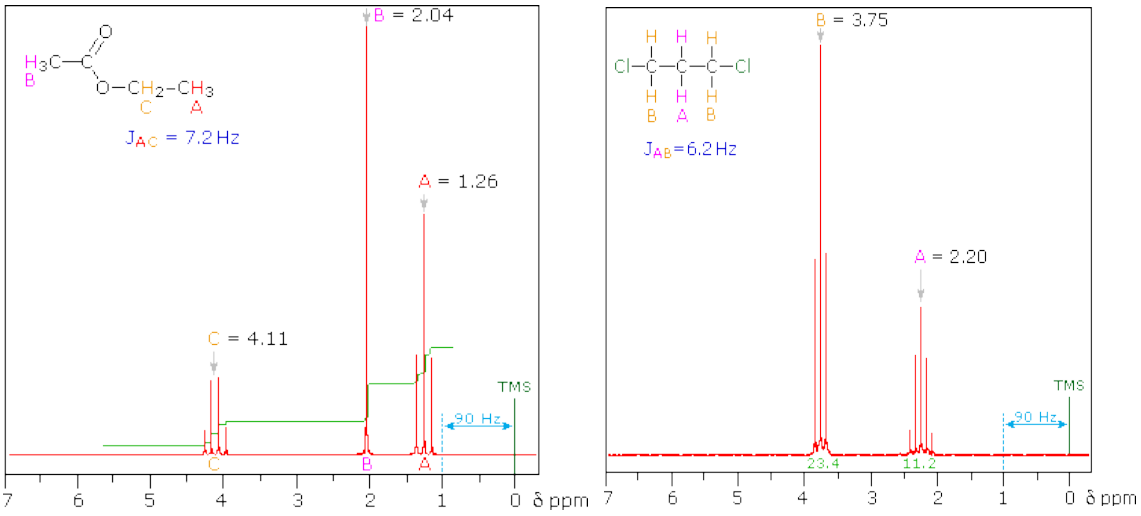
1,1-dichloroethane

The splitting patterns found in various spectra are easily recognized, provided the chemical shifts of the different sets of hydrogen that generate the signals differ by two or more ppm. The patterns are symmetrically distributed on both sides of the proton chemical shift, and the central lines are always stronger than the outer lines. The most commonly observed patterns have been given descriptive names, such as doublet (two equal intensity signals), triplet (three signals with an intensity ratio of 1:2:1) and quartet (a set of four signals with intensities of 1:3:3:1). Four such patterns are displayed in the following illustration. The line separation is always constant within a given multiplet, and is called the coupling constant (J). The magnitude of J, usually given in units of Hz, is magnetic field independent.

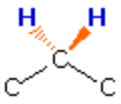


The splitting patterns shown above display the ideal or "First-Order" arrangement of lines. This is usually observed if the spin-coupled nuclei have very different chemical shifts (i.e. $\Delta\nu$ is large compared

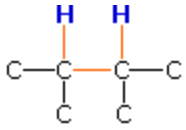
to J). If the coupled nuclei have similar chemical shifts, the splitting patterns are distorted (second order behavior). In fact, signal splitting disappears if the chemical shifts are the same. Two examples that exhibit minor 2nd order distortion are shown below (both are taken at a frequency of 90 MHz). The ethyl acetate spectrum on the left displays the typical quartet and triplet of a substituted ethyl group. The spectrum of 1,3-dichloropropane on the right demonstrates that equivalent sets of hydrogens may combine their influence on a second, symmetrically located set.
Even though the chemical shift difference between the A and B protons in the 1,3-dichloroethane spectrum is fairly large (140 Hz) compared with the coupling constant (6.2 Hz), some distortion of the splitting patterns is evident. The line intensities closest to the chemical shift of the coupled partner are enhanced. Thus the B set triplet lines closest to A are increased, and the A quintet lines nearest B are likewise stronger. A smaller distortion of this kind is visible for the A and C couplings in the ethyl acetate spectrum.



What causes this signal splitting, and what useful information can be obtained from it ? If an atom under examination is perturbed or influenced by a nearby nuclear spin (or set of spins), the observed nucleus responds to such influences, and its response is manifested in its resonance signal. This spin-coupling is transmitted through the connecting bonds, and it functions in both directions. Thus, when the perturbing nucleus becomes the observed nucleus, it also exhibits signal splitting with the same J. For spin-coupling to be observed, the sets of interacting nuclei must be bonded in relatively close proximity (e.g. vicinal and geminal locations), or be oriented in certain optimal and rigid configurations. Some spectroscopists place a number before the symbol J to designate the number of bonds linking the coupled nuclei (colored orange below). Using this terminology, a vicinal coupling constant is ^{3}J and a geminal constant is ^{2}J.



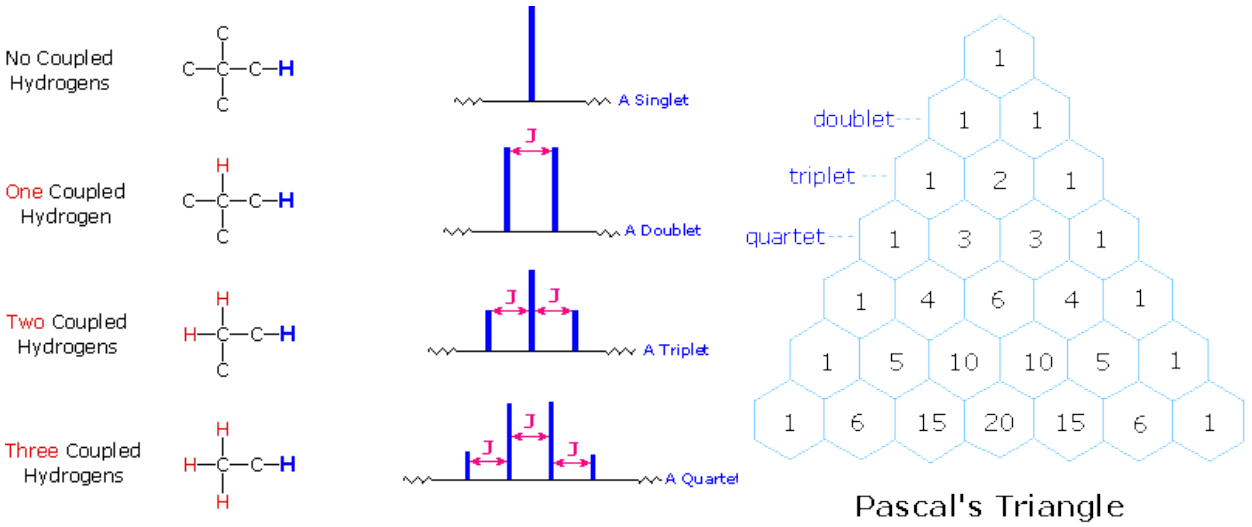
Geminal Hydrogens



Vicinal Hydrogens

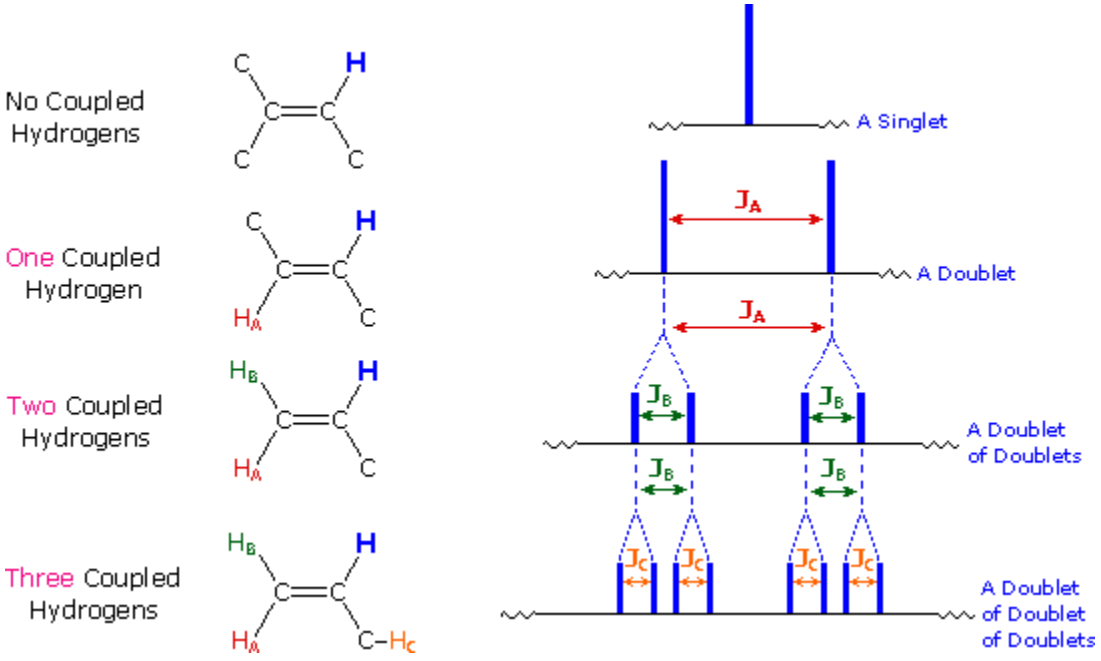
The following general rules summarize important requirements and characteristics for spin 1/2 nuclei :

1) Nuclei having the same chemical shift (called isochronous) do not exhibit spin-splitting. They may actually be spin-coupled, but the splitting cannot be observed directly.
2) Nuclei separated by three or fewer bonds (e.g. vicinal and geminalnuclei) will usually be spin-coupled and will show mutual spin-splitting of the resonance signals (same J's), provided they have different chemical shifts. Longer-range coupling may be observed in molecules having rigid configurations of atoms.
3) The magnitude of the observed spin-splitting depends on many factors and is given by the coupling constant J (units of Hz). J is the same for both partners in a spin-splitting interaction and is independent of the external magnetic field strength.
4) The splitting pattern of a given nucleus (or set of equivalent nuclei) can be predicted by the n+1 rule, where n is the number of neighboring spin-coupled nuclei with the same (or very similar) Js. If there are 2 neighboring, spin-coupled, nuclei the observed signal is a triplet (2+1=3); if there are three spin-coupled neighbors the signal is a quartet (3+1=4). In all cases the central line(s) of the splitting pattern are stronger than those on the periphery. The intensity ratio of these lines is given by the numbers in Pascal's triangle. Thus a doublet has 1:1 or equal intensities, a triplet has an intensity ratio of 1:2:1, a quartet 1:3:3:1 etc. To see how the numbers in Pascal's triangle are related to the Fibonacci series click on the diagram.



If a given nucleus is spin-coupled to two or more sets of neighboring nuclei by different J values, the n+1 rule does not predict the entire splitting pattern. Instead, the splitting due to one J set is added to that

expected from the other J sets. Bear in mind that there may be fortuitous coincidence of some lines if a smaller J is a factor of a larger J.



Magnitude of Some Typical Coupling Constants

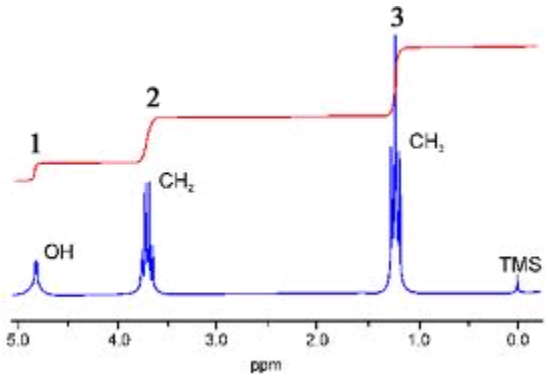
Structural Type	J (Hz)
H–C–(C)$_n$–C–H	0 (unless in a rigid ideal orientation)
H_3C-CH_2-X	6 to 8
H_3C, CH–X, H_3C	5 to 7
H–C(X)–C(Y)–H	2 to 12 (depends on dihedral angle and the nature of X and Y)
C(H)–C(=O)–H	0.5 to 3
C(H)(H)	12 to 15 (must be diastereotopic)

Structural Type	J (Hz)
H–C=C–H	12 to 18
H, H on C=C	7 to 12
H–C=C, H	0.5 to 3
H–C=C–C–H	3 to 11 (depends on dihedral angle)
H–C–C≡C–H	2 to 3
H on benzene	o 6 to 9 m 1 to 3 p 0 to 1

Spin 1/2 nuclei include ^{1}H, ^{13}C, ^{19}F & ^{31}P. The spin-coupling interactions described above may occur between similar or dissimilar nuclei. If, for example, a ^{19}F is spin-coupled to a ^{1}H, both nuclei will appear as doublets having the same J constant. Spin coupling with nuclei having spin other than 1/2 is more complex and will not be discussed here.

NMR Spectrum Of EtoH:

In the ^{1}H NMR spectrum, the amount of radiation absorbed for each chemical shift is proportional to the number of nuclei in that environment. This is extremely helpful when combined with an analysis of the number of equivalent nuclei and their chemical shifts.



The NMR spectrometer calculates the area of each peak in the spectrum ("integration"). (The bands in NMR spectra are usually so narrow that the height of the peak is usually a good enough guide.) The spectrum displayed by the spectrometer shows the integral and the ratio of the peak areas.

The ^{1}H NMR spectrum of ethanol is shown below with the integral line shown in orange.

There are 3 ^{1}H environments in ethanol,CH_3CH_2OH, due to the 3 H in the CH_3 group, 2 H in the CH_2 group and 1 H on the OH group. There are therefore 3 signals in the spectrum with relative areas of 3 : 2 : 1.

Notice that the integration is over each *set* of lines as each signal is split by coupling.

The integration usually gives the *relative* areas of the signals.

Integrals are not normally displayed on ^{13}C NMR spectra and the peak heights are not a reliable indicator of the number of nuclei in each environment. This is a consequence of the way in which ^{13}C NMR is recorded. As ^{13}C is only 1% abundant, the NMR signal is extremely weak and is barely noticeable above the noise. As a consequence, the spectrometer re-scans the spectrum many times and adds them together so that the true signals grow but any random noise averages to zero. The time between scans is quite short and means that not all nuclei have had a chance to 'relax' (i.e. realign their spin with the magnetic field) before the next scan is recorded. Such nuclei are unable to absorb for this scan.