ORGANIC CHEMISTRY-I

CARBOHYDRATES (UNIT-I)

BCH52

B.SC CHEMISTRY- III YEAR

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ORGANIC CHEMISTRY-I
Unit-I: CARBOHYDRATES

INTRODUCTION

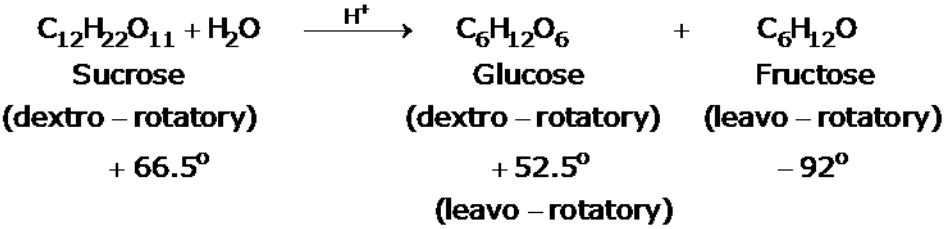
Carbohydrates are the most abundant class of organic compounds in the plant world.

They are synthesized by nearly all plants and animals, which use them to store energy and deliver it to the cells.

What are carbohydrates?

The carbohydrates are a group of naturally occurring carbonyl compounds (aldehydes or ketones) that also contain several hydroxyl groups. It may also include their derivatives which produce such compounds on hydrolysis. They are the most abundant organic molecules in nature and also referred to as "saccharides". The carbohydrates which are soluble in water and sweet in taste are called as "sugars".

The hydrolysis of sucrose in presence of a mineral acid takes place according to the equation. The hydrolysis of sucrose in presence of a mineral acid takes place according to the equation.



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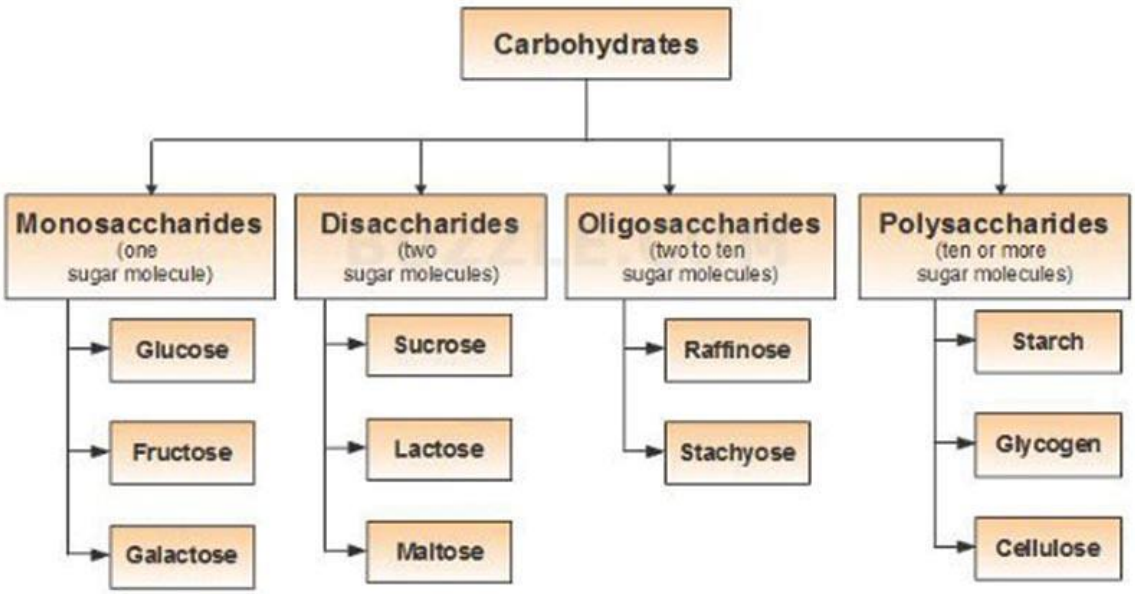
Structure of carbohydrates

Carbohydrates consist of carbon, hydrogen, and oxygen. The general empirical structure for carbohydrates is $(CH_2O)_n$. They are organic compounds organized in the form of aldehydes or ketones with multiple hydroxyl groups coming off the

carbon chain. The building blocks of all carbohydrates are simple sugars called monosaccharides. A monosaccharide can be a polyhydroxy aldehyde (aldose) or a polyhydroxy ketone (ketose).
The carbohydrates can be structurally represented in any of the three forms:

- Open chain structure.
- Hemi-acetal structure.
- Haworth structure.
- **Open chain structure** – It is the long straight-chain form of carbohydrates.
- **Hemi-acetal structure** – Here the 1st carbon of the glucose condenses with the -OH group of the 5th carbon to form a ring structure.
- **Haworth structure** – It is the presence of the pyranose ring structure.

CLASSISSIFICATION OF CARBOHYDRATES



Carbohydrates are classified into following-:

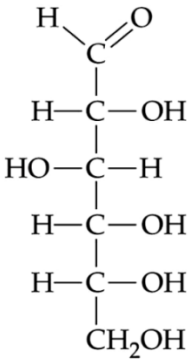
Monosaccharides – carbohydrates that cannot be hydrolyzed to simpler carbohydrates; eg. Glucose or fructose.

Disaccharides – carbohydrates that can be hydrolyzed into two monosaccharide units; eg. Sucrose, which is hydrolyzed into glucose and fructose.

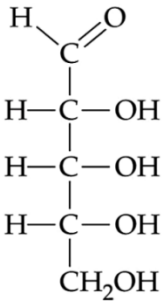
Oligosaccharides – carbohydrates that can be hydrolyzed into a few monosaccharide units.

Polysaccharides – carbohydrates that are are polymeric sugars; eg Starch or cellulose.

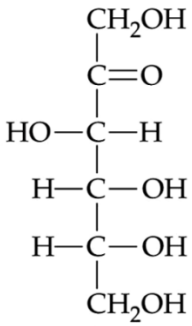
- sugars; eg Starch or cellulose.**Monosaccharides** contain a single polyhydroxy aldehyde or ketone unit (*saccharo* is Greek for "sugar") (e.g., glucose, fructose).



Glucose, an aldohexose (monomer for starch and cellulose; major source of energy)



Ribose, an aldopentose (a component of ATP, coenzymes, and RNA)



Fructose, a ketohexose (present in corn syrup and fruit)

- **Disaccharides** consist of two monosaccharide units linked together by a covalent bond (e.g., sucrose).
- **Oligosaccharides** contain from 3 to 10 monosaccharide units (e.g., raffinose).
- **Polysaccharides** contain very long chains of hundreds or thousands of monosaccharide units, which may be either in straight or branched chains (e.g., cellulose, glycogen, starch).

Reducing and Non-reducing sugars

Carbohydrates are generally sweet in taste and hence referred to as sugars.

Reducing sugars: Aldehydes and keto groups have reducing character and reduce Tollens reagent and Fehling's (Benedict's) solution. Carbohydrates containing free aldehyde and keto functional group are thus reducing sugars. Example: Glucose, lactose.

Non-reducing sugars: If the groups are not free, then they do not reduce Tollens reagent and Fehling's solution and are, therefore, classified as Non-reducing sugars. Example: Maltose, sucrose.

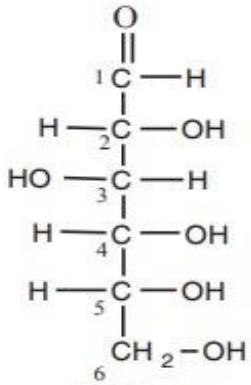
PROPERTIES OF MONOSACCHARIDES

Physical properties of monosaccharides

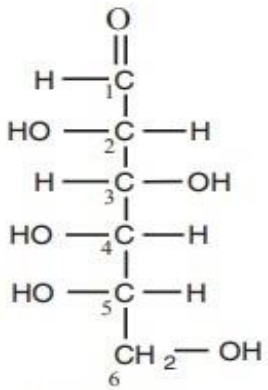
Monosaccharides are colourless and crystalline compounds. They are readily soluble in water. They have sweet taste.

Stereo isomerism

D-glucose and L-glucose are mirror images of each other.



D-Glucose

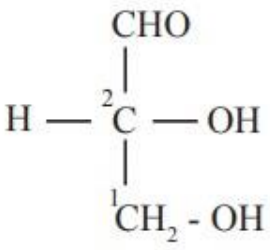


L-Glucose

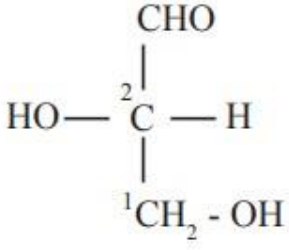
The presence of asymmetric carbon atoms in a compound give rise to the formation of isomers of that compound. Such compound which are identical in composition and differs only in spatial configuration are called "stereo isomers''. For example glucose can exist in two forms as shown below.

D-series and L-series

The orientation of the H and OH groups around the carbon atom just adjacent to the terminal primary alcohol carbon, eg. C_5 in glucose determines the series. The D and L forms of glyceraldehyde are given below.



D-Glyceraldehyde

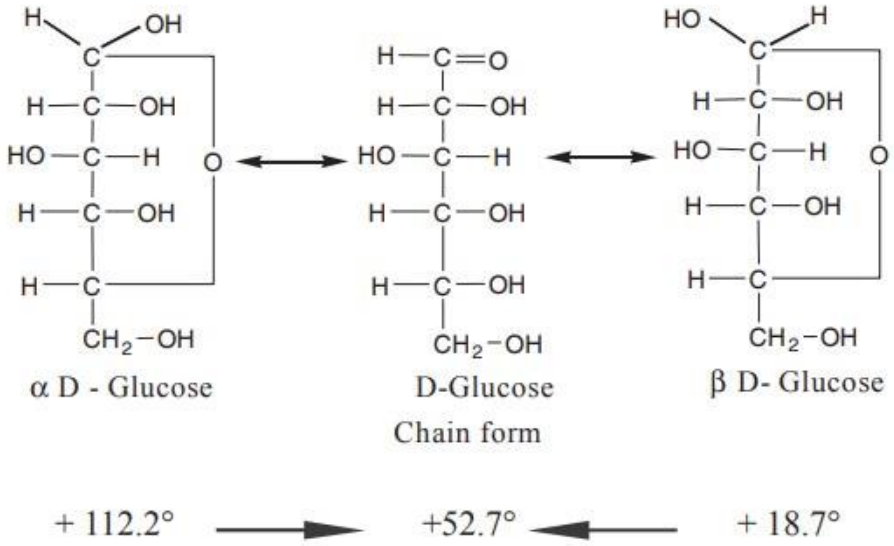


L-Glyceraldehyde

when the -OH group of this C_2 is at the right, it belongs to D-series, when the -OH group is on the left it belongs to L-series.

5. Mutarotation

When an aldohexose is first dissolved in water and the solution is kept in optical path and plane polarised light is passed, the initial optical rotation shown by the sugar gradually changes until a constant fixed rotation characteristic of the sugar is reached. This phenomenon of change of rotation is called as "Mutarotation".



The mutarotation is due to the existence of two optical isomers of glucose, namely a, D glucose with a specific rotation +112.2° and b, D glucose with a specific rotation +18.7° α and β isomers are called as anomers and the carbon atom responsible for this is the anomeric carbon atom. Anomers are isomers differing in configuration of a particular carbon atom alone.

A freshly prepared aqueous solution of α, D glucose has a specific rotation of +112.2°. When this solution is allowed to stand, the rotation falls to 52.7° and remains constant at this value. This gradual change in specific rotation is called mutarotation. The value of mutarotation for α, D-glucose is +59.5°. (+112.2°) - (52.7°) = +59.5°. A freshly prepared solution of b, D glucose has a rotation value of 18.7°. It also gradually increases and reaches the same final value of + 52.7°.

The general formula for a **monosaccharide** is (CH_2On), where n can be any number greater than two. For example, if nn is 6, then the formula can be written $C_6H_{12}O_6$. This is the formula for the monosaccharide glucose. Another monosaccharide, fructose, has the same chemical formula as glucose, but the atoms are arranged differently. Carbohydrates have many isomers because of the arrangement of the −OH−OH groups in their structures. Compare the glucose and

fructose molecules in the figure below. Can you identify their differences? The only differences are the positions of some of the atoms. These differences affect the properties of the two monosaccharides.

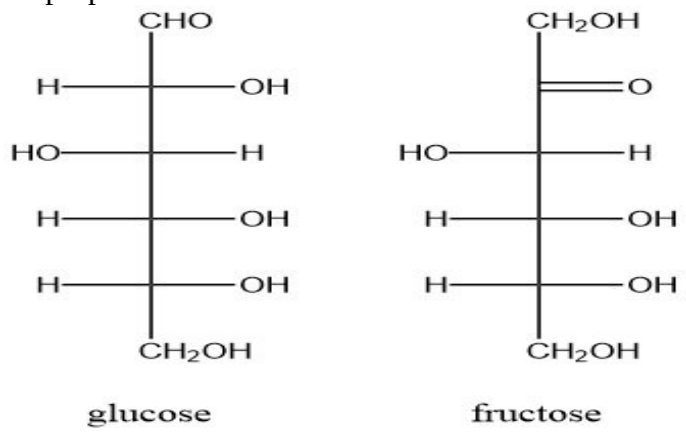


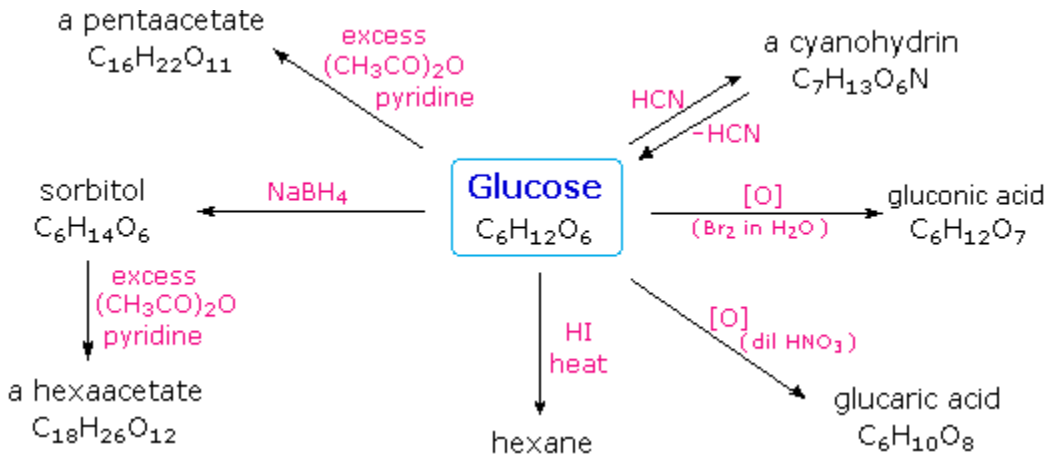
Figure 5.2.1: Structures of glucose and fructose.

Monosaccharides can be classified by the number of carbon atoms they contain: diose (2), triose (3), tetrose (4), pentose (5), hexose (6), heptose (7), and so on. They can also be classified based on whether or not they contain an aldehyde (aldose) or ketone (ketose). We can also combine these two designations to refer to classes of carbohydrates. For example, an aldohexose is a carbohydrate (indicated by the *-ose* ending) with six carbons (*hex*) and an aldehyde group (*aldo*). A ketopentose is a carbohydrate with a ketone and 5 carbons. Both glucose and fructose are hexoses because they contain six carbons but glucose is an aldohexose while fructose (also known as "fruit sugar") is a ketohexose. Other common monosaccharides include galactose (part of lactose), xylose ("wood sugar"), ribose (in RNA), and deoxyribose (in DNA).

Chemical properties

1. Glucose

Carbohydrates have been given non-systematic names, although the suffix **ose** is generally used. The most common carbohydrate is **glucose** ($C_6H_{12}O_6$). Applying the terms defined above, glucose is a monosaccharide, an aldohexose (note that the function and size classifications are combined in one word) and a reducing sugar. The general structure of glucose and many other aldohexoses was established by simple chemical reactions. The following diagram illustrates the kind of evidence considered, although some of the reagents shown here are different from those used by the original scientists.



Hot hydriodic acid (HI) was often used to reductively remove oxygen functional groups from a molecule, and in the case of glucose this treatment gave hexane (in low yield). From this it was concluded that the six carbons are in an unbranched chain. The presence of an aldehyde carbonyl group was deduced from cyanohydrin formation, its reduction to the hexa-alcohol sorbitol, also called glucitol, and mild oxidation to the mono-carboxylic acid, glucuronic acid. Somewhat stronger oxidation by dilute nitric acid gave the diacid, glucaric acid, supporting the proposal of a six-carbon chain. The five oxygens remaining in glucose after the aldehyde was accounted for were thought to be in hydroxyl groups, since a penta-acetate derivative could be made. These hydroxyl groups were assigned, one each, to the last five carbon atoms, because geminal hydroxyl groups are normally unstable relative to the carbonyl compound formed by loss of water. By clicking on the above diagram, it will change to display the suggested products and the gross structure of glucose. The four middle carbon atoms in the glucose chain are centers of chirality and are colored red. Glucose and other saccharides are extensively cleaved by periodic acid, thanks to the abundance of vicinal diol moieties in their structure. This oxidative cleavage, known as the **Malaprade reaction** is particularly useful for the analysis of selective O-substituted derivatives of saccharides, since ether functions do not react. The stoichiometry of aldohexose cleavage is shown in the following equation.

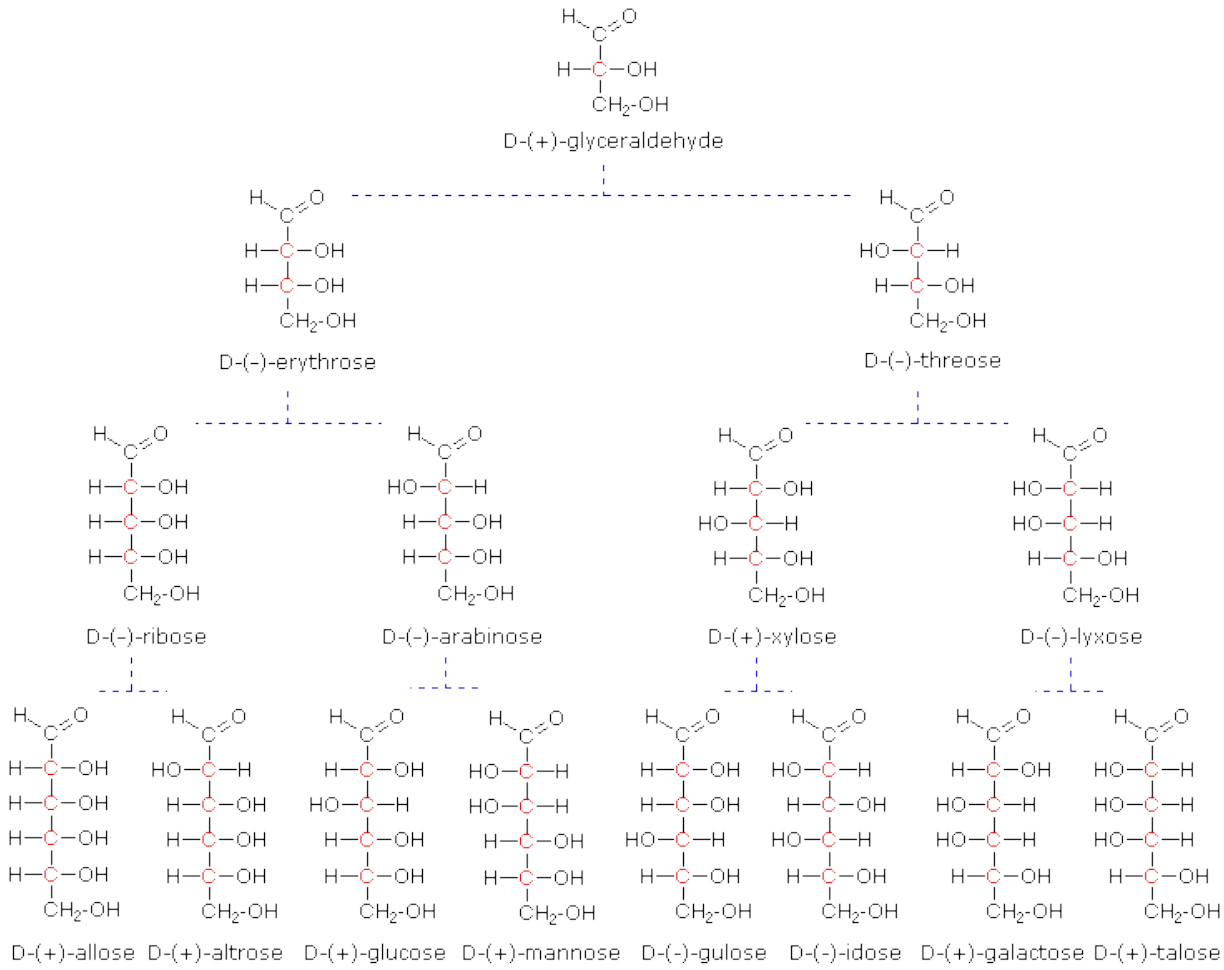
$$HOCH_2(CHOH)_4CHO + 5\ HIO_4 \longrightarrow H_2C{=}O + 5\ HCO_2H + 5\ HIO_3$$

The Configuration of Glucose

The four chiral centers in glucose indicate there may be as many as sixteen (2^4) stereoisomers having this constitution. These would exist as eight diastereomeric pairs of enantiomers, and the initial challenge was to determine which of the eight corresponded to glucose. This challenge was accepted and met in 1891 by the German chemist Emil Fischer. His successful negotiation of the stereochemical maze presented by the aldohexoses was a logical tour de force, and it is fitting that he received the 1902 Nobel Prize for chemistry for this accomplishment. One of the first tasks faced by Fischer was to devise a method of representing the configuration of each chiral center in an unambiguous manner. To this end, he invented a simple technique for drawing chains of chiral centers, that we now call the Fischer projection formula. Click on this link for a review.

At the time Fischer undertook the glucose project it was not possible to establish the **absolute configuration** of an enantiomer. Consequently, Fischer made an arbitrary choice for (+)-glucose and established a network of related aldose configurations that he called the **D**-family. The mirror images of these configurations were then designated the **L**-family of aldoses. To illustrate using present day knowledge, Fischer projection formulas and names for the D-aldose family (three to six-carbon atoms) are shown below, with the asymmetric carbon atoms (chiral centers) colored red. The last chiral center in an aldose chain (farthest from the aldehyde group) was chosen by Fischer as the D / L designator site. If the hydroxyl group in the projection formula pointed to the right, it was defined as a member of the D-family. A left directed hydroxyl group (the mirror image) then represented the L-family. Fischer's initial assignment of the D-configuration had a 50:50 chance of being right, but all his subsequent conclusions concerning the relative configurations of various aldoses were soundly based. In 1951 x-ray fluorescence studies of (+)-tartaric acid, carried out in the Netherlands by Johannes Martin Bijvoet (pronounced "buy foot"), proved that Fischer's choice was correct.

It is important to recognize that the sign of a compound's specific rotation (an experimental number) does not correlate with its configuration (D or L). It is a simple matter to measure an optical rotation with a polarimeter. Determining an absolute configuration usually requires chemical interconversion with known compounds by stereospecific reaction paths.



Models of representative aldoses may be examined by clicking on the Fischer formulas for glyceraldehyde, erythrose, threose, ribose, arabinose, allose, altrose, glucose or mannose in the above diagram.

2. Important Reactions

Emil Fischer made use of several key reactions in the course of his carbohydrate studies. These are described here, together with the information that each delivers.

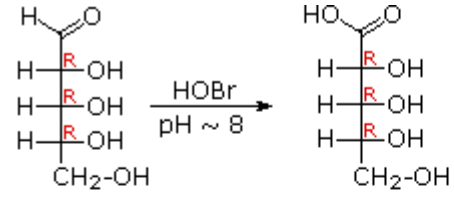
Oxidation

As noted above, sugars may be classified as **reducing** or **non-reducing** based on their reactivity with Tollens', Benedict's or Fehling's reagents. If a sugar is oxidized by these reagents it is called **reducing**, since the oxidant ($Ag^{(+)}$ or $Cu^{(+2)}$) is reduced in the reaction, as evidenced by formation of a silver mirror or

precipitation of cuprous oxide. The Tollens' test is commonly used to detect aldehyde functions; and because of the facile interconversion of ketoses and aldoses under the basic conditions of this test, ketoses such as fructose also react and are classified as reducing sugars.

When the aldehyde function of an aldose is oxidized to a carboxylic acid the product is called an **aldonic acid**. Because of the 2º hydroxyl functions that are also present in these compounds, a mild oxidizing agent such as hypobromite must be used for this conversion (equation 1). If both ends of an aldose chain are oxidized to carboxylic acids the product is called an **aldaric acid**. By converting an aldose to its corresponding aldaric acid derivative, the ends of the chain become identical (this could also be accomplished by reducing the aldehyde to CH_2OH, as noted below). Such an operation will disclose any latent symmetry in the remaining molecule. Thus, ribose, xylose, allose and galactose yield achiral aldaric acids which are, of course, not optically active. The ribose oxidation is shown in equation 2 below.

1.



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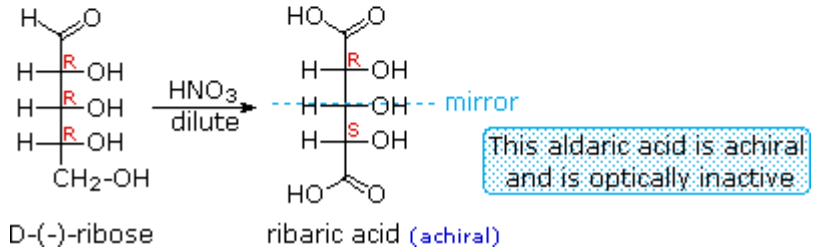

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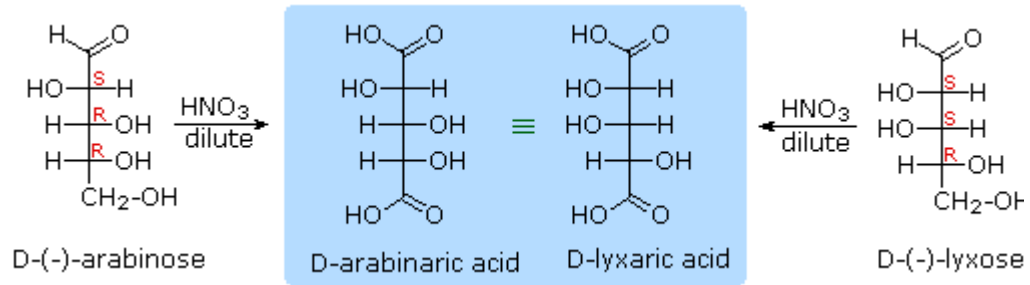


Other aldose sugars may give identical chiral aldaric acid products, implying a unique configurational relationship. The examples of arabinose and lyxose shown in equation 3 above illustrate this result. Remember, a Fischer projection formula may be rotated by 180º in the plane of projection without changing its configuration.

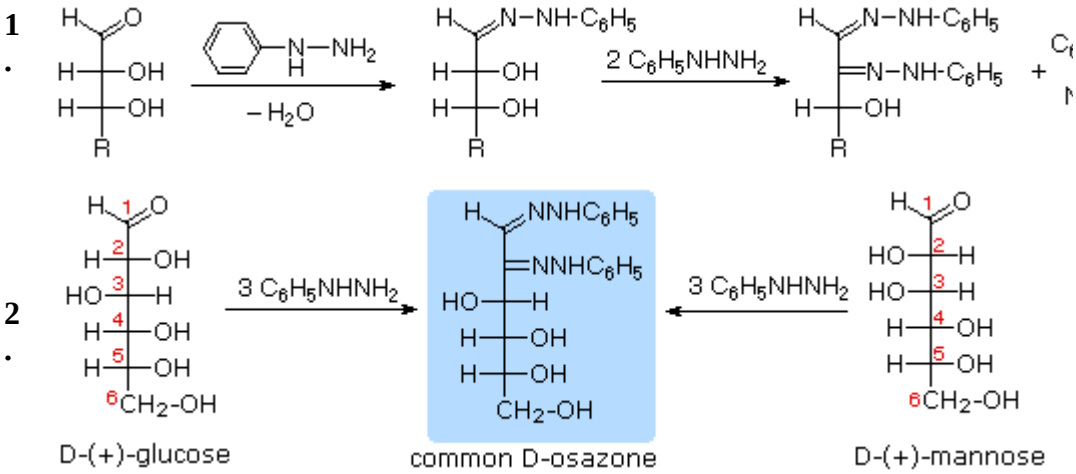
Reduction

Sodium borohydride reduction of an aldose makes the ends of the resulting **alditol** chain identical, $HOCH_2(CHOH)_nCH_2OH$, thereby accomplishing the same configurational change produced by oxidation to an aldaric acid. Thus, allitol and galactitol from reduction of allose and galactose are achiral, and altrose and talose are reduced to the same chiral alditol. A summary of these redox reactions, and derivative nomenclature is given in the following table.

Derivatives of $HOCH_2(CHOH)_nCHO$

HOBr Oxidation	——>	$HOCH_2(CHOH)_nCO_2H$ an Aldonic Acid
HNO_3 Oxidation	——>	$H_2OC(CHOH)_nCO_2H$ an Aldaric Acid
$NaBH_4$ Reduction	——>	$HOCH_2(CHOH)_nCH_2OH$ an Alditol

Osazone Formation

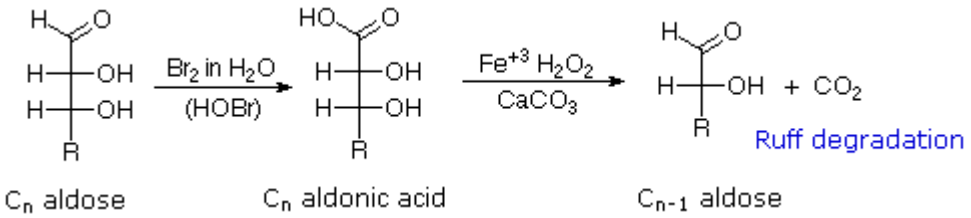


The osazone reaction was developed and used by Emil Fischer to identify aldose sugars differing in configuration only at the alpha-carbon. The upper equation

shows the general form of the osazone reaction, which effects an alpha-carbon oxidation with formation of a bis-phenylhydrazone, known as an osazone. Application of the osazone reaction to D-glucose and D-mannose demonstrates that these compounds differ in configuration only at C-2.

Chain Shortening and Lengthening

1.



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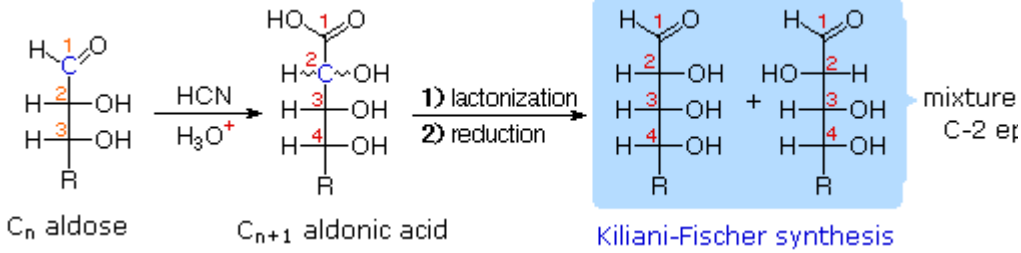


These two procedures permit an aldose of a given size to be related to homologous smaller and larger aldoses. The importance of these relationships may be seen in the array of aldose structurespresented earlier, where the structural connections are given by the dashed blue lines. Thus Ruff degradation of the pentose arabinose gives the tetrose erythrose. Working in the opposite direction, a Kiliani-Fischer synthesis applied to arabinose gives a mixture of glucose and mannose. An alternative chain shortening procedure known as the Wohl degradation is essentially the reverse of the Kiliani-Fischer synthesis.

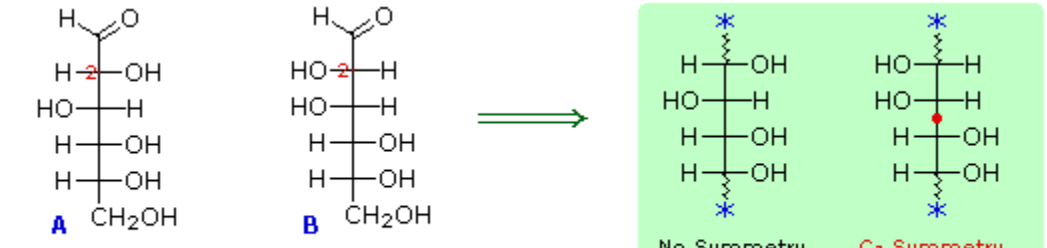
Using these reactions we can now follow Fischer's train of logic in assigning the configuration of D-glucose.

Ribose and arabinose (two well known pentoses) both gave erythrose on Ruff degradation. As expected, Kiliani-Fischer synthesis applied to erythrose gave a mixture of ribose and arabinose.

Oxidation of erythrose gave an achiral (optically inactive) aldaric acid. This defines the configuration of erythrose.

Oxidation of ribose gave an achiral (optically inactive) aldaric acid. This defines the configuration of both ribose and arabinose. Ruff shortening of glucose gave arabinose, and Kiliani-Fischer synthesis applied to arabinose gave a mixture of glucose and mannose. Glucose and mannose are therefore epimers at C-2, a fact confirmed by the common product from their osazone reactions. A pair of structures for these epimers can be written, but which is glucose and which is mannose?

In order to determine which of these epimers was glucose, Fischer made use of the inherent C_2 symmetry in the four-carbon dissymmetric core of one epimer (**B**). This is shown in the following diagram by a red dot where the symmetry axis passes through the projection formula. Because of this symmetry, if the aldehyde and 1°-alcohol functions at the ends of the chain are exchanged, epimer **B** would be unchanged; whereas **A** would be converted to a different compound. By clicking on the diagram, the consequences of such an exchange will be displayed.



A pair of C-2 epimers.
One is glucose, the other is mannose.

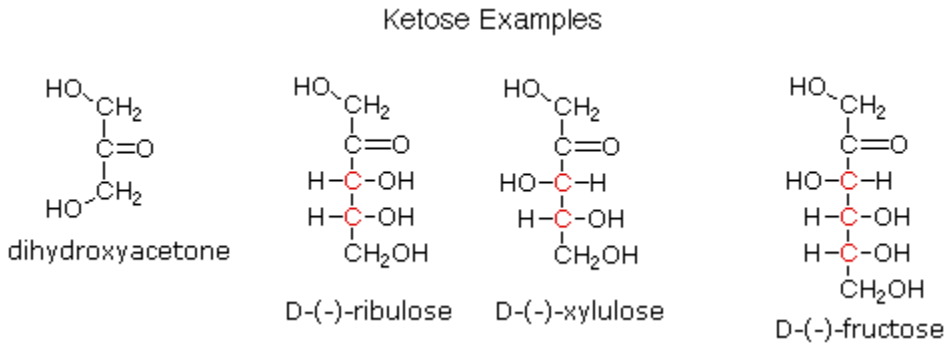
Four-Carbon Dissymmetric Core

Fischer looked for and discovered a second aldohexose that represented the end group exchange for the epimer lacking the latent C_2 symmetry (**A**). This compound was L-(+)-gulose, and its exchange relationship to D-(+)-glucose was demonstrated by oxidation to a common aldaric acid product. Equations for this operation will be displayed by clicking again on the above diagram. The remaining epimer is therefore mannose.

3. Ketoses

If a monosaccharide has a carbonyl function on one of the inner atoms of the carbon chain it is classified as a **ketose**. Dihydroxyacetone may not be a sugar, but it is included as the ketose analog of glyceraldehyde. The carbonyl group is commonly found at C-2, as illustrated by the following examples (chiral centers are colored red). As expected, the carbonyl function of a ketose may be reduced by sodium borohydride, usually to a mixture of epimeric products. D-Fructose, the sweetest of the common natural sugars, is for example reduced to a mixture of D-glucitol (sorbitol) and D-mannitol, named after the aldohexoses from which

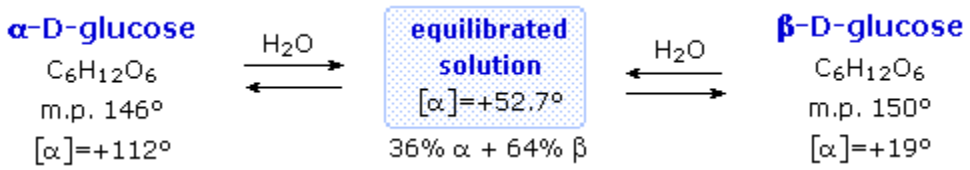
they may also be obtained by analogous reduction. Mannitol is itself a common natural carbohydrate.
Although the ketoses are distinct isomers of the aldose monosaccharides, the chemistry of both classes is linked due to their facile interconversion in the presence of acid or base catalysts. This interconversion, and the corresponding epimerization at sites alpha to the carbonyl functions, occurs by way of an **enediol** tautomeric intermediate. By clicking on the diagram, an equation illustrating these isomerizations will be displayed.



Because of base-catalyzed isomerizations of this kind, the Tollens' reagent is not useful for distinguishing aldoses from ketoses or for specific oxidation of aldoses to the corresponding aldonic acids. Oxidation by HOBr is preferred for the latter conversion.

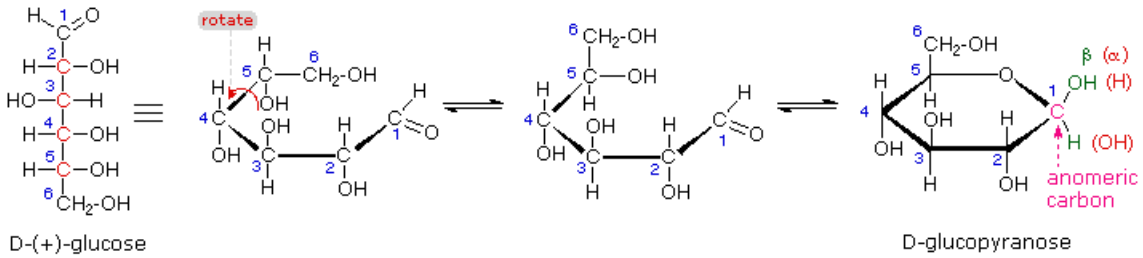
4. Anomeric Forms of Glucose

Fischer's brilliant elucidation of the configuration of glucose did not remove all uncertainty concerning its structure. Two different crystalline forms of glucose were reported in 1895. Each of these gave all the characteristic reactions of glucose, and when dissolved in water equilibrated to the same mixture. This equilibration takes place over a period of many minutes, and the change in optical activity that occurs is called **mutarotation**. These facts are summarized in the diagram below.



When glucose was converted to its pentamethyl ether (reaction with excess CH_3I & AgOH), two different isomers were isolated, and neither exhibited the expected aldehyde reactions. Acid-catalyzed hydrolysis of the pentamethyl ether derivatives, however, gave a tetramethyl derivative that was oxidized by Tollen's reagent and reduced by sodium borohydride, as expected for an aldehyde. These reactions will be displayed above by clicking on the diagram.

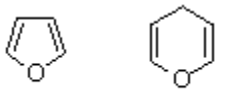
The search for scientific truth often proceeds in stages, and the structural elucidation of glucose serves as a good example. It should be clear from the new evidence presented above, that the open chain pentahydroxyhexanal structure drawn above must be modified. Somehow a new stereogenic center must be created, and the aldehyde must be deactivated in the pentamethyl derivative. A simple solution to this dilemma is achieved by converting the open aldehyde structure for glucose into a cyclic hemiacetal, called a **glucopyranose**, as shown in the following diagram. The linear aldehyde is tipped on its side, and rotation about the C4-C5 bond brings the C5-hydroxyl function close to the aldehyde carbon. For ease of viewing, the six-membered hemiacetal structure is drawn as a flat hexagon, but it actually assumes a chair conformation. The hemiacetal carbon atom (C-1) becomes a new stereogenic center, commonly referred to as the **anomeric carbon**, and the α and β-isomers are called **anomers**.



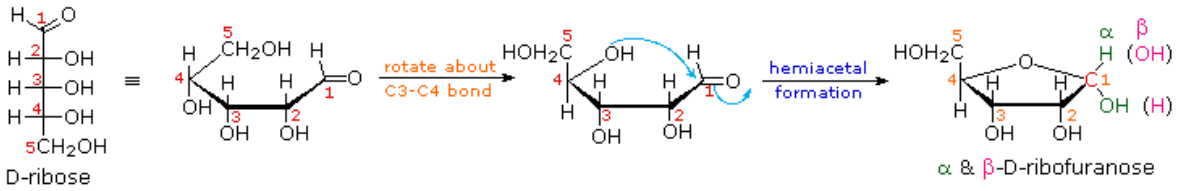
We can now consider how this modification of the glucose structure accounts for the puzzling facts noted above. First, we know that hemiacetals are in equilibrium with their carbonyl and alcohol components when in solution. Consequently, fresh solutions of either alpha or beta-glucose crystals in water should establish an equilibrium mixture of both anomers, plus the open chain chain form. This will be shown above by clicking on the diagram. Note that despite the very low concentration of the open chain aldehyde in this mixture, typical chemical reactions of aldehydes take place rapidly.
Second, a pentamethyl ether derivative of the pyranose structure converts the hemiacetal function to an acetal. Acetals are stable to base, so this product should

not react with Tollen's reagent or be reduced by sodium borohydride. Acid hydrolysis of acetals regenerates the carbonyl and alcohol components, and in the case of the glucose derivative this will be a tetramethyl ether of the pyranose hemiacetal. This compound will, of course, undergo typical aldehyde reactions. By clicking on the diagram a second time this relationship will be displayed above.

5. Cyclic Forms of Monosaccharides

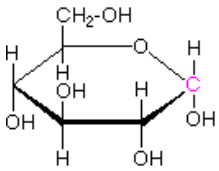


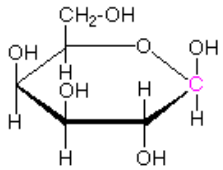
As noted above, the preferred structural form of many monosaccharides may be that of a cyclic hemiacetal. Five and six-membered rings are favored over other ring sizes because of their low angle and eclipsing strain. Cyclic structures of this kind are termed **furanose** (five-membered) or **pyranose** (six-membered), reflecting the ring size relationship to the common heterocyclic compounds furan and pyran shown on the right. Ribose, an important aldopentose, commonly adopts a furanose structure, as shown in the following illustration. By convention for the D-family, the five-membered furanose ring is drawn in an edgewise projection with the ring oxygen positioned away from the viewer. The anomeric carbon atom (colored red here) is placed on the right. **The upper bond to this carbon is defined as beta, the lower bond then is alpha**. Click on the following diagram to see a model of β-D-ribofuranose.

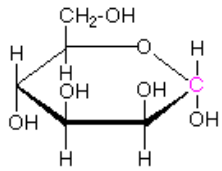


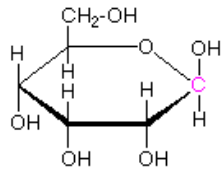
The cyclic pyranose forms of various monosaccharides are often drawn in a flat projection known as a **Haworth formula**, after the British chemist, Norman Haworth. As with the furanose ring, the anomeric carbon is placed on the right with the ring oxygen to the back of the edgewise view. In the D-family, the alpha and beta bonds have the same orientation defined for the furanose ring (beta is up & alpha is down). These Haworth formulas are convenient for displaying stereochemical relationships, but do not represent the true shape of the molecules. We know that these molecules are actually puckered in a fashion we call a chair conformation. Examples of four typical pyranose structures are shown below, both as Haworth projections and as the more representative chair conformers. The anomeric carbons are colored red.

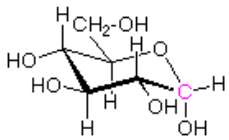
Examples of Some Pyranose Forms of Hexoses

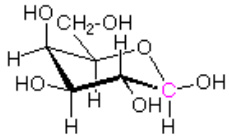

α-D-glucopyranose

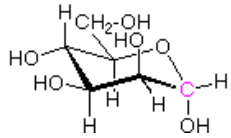

β-D-galactopyranose

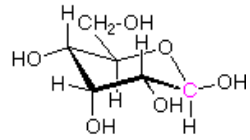

α-D-mannopyranose


β-D-allopyranose









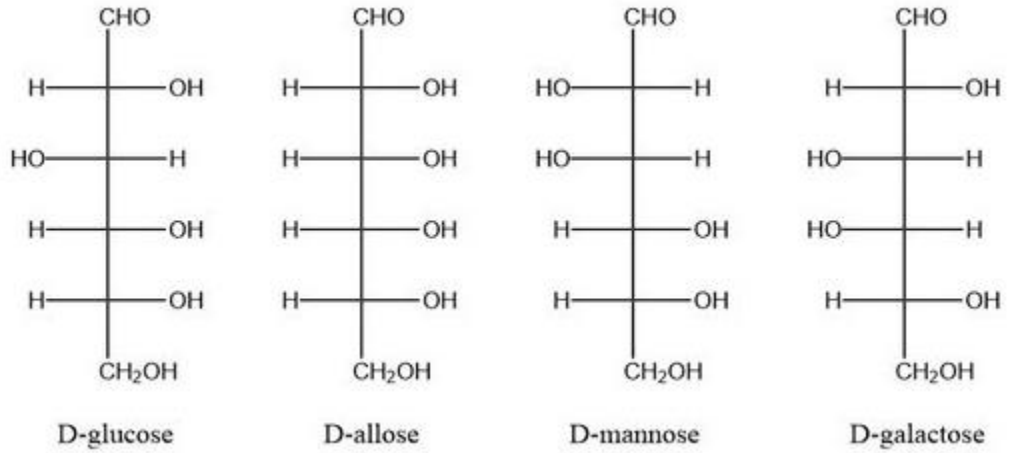
The size of the cyclic hemiacetal ring adopted by a given sugar is not constant, but may vary with substituents and other structural features. Aldolhexoses usually form pyranose rings and their pentose homologs tend to prefer the furanose form, but there are many counter examples. The formation of acetal derivatives illustrates how subtle changes may alter this selectivity. By clicking on the above diagram. the display will change to illustrate this. A pyranose structure for D-glucose is drawn in the rose-shaded box on the left. Acetal derivatives have been prepared by acid-catalyzed reactions with benzaldehyde and acetone. As a rule, benzaldehyde forms six-membered cyclic acetals, whereas acetone prefers to form five-membered acetals. The top equation shows the formation and some reactions of the 4,6-O-benzylidene acetal, a commonly employed protective group. A methyl glycoside derivative of this compound (see below) leaves the C-2 and C-3 hydroxyl groups exposed to reactions such as the periodic acid cleavage, shown as the last step. The formation of an isopropylidene acetal at C-1 and C-2, center structure, leaves the C-3 hydroxyl as the only unprotected function. Selective oxidation to a ketone is then possible. Finally, direct di-O-isopropylidene derivatization of glucose by reaction with excess acetone results in a change to a furanose structure in which the C-3 hydroxyl is again unprotected. However, the same reaction with D-galactose, shown in the blue-shaded box, produces a pyranose product in which the C-6 hydroxyl is unprotected. Both derivatives do not react with Tollens' reagent. This difference in behavior is attributed to the cis-orientation of the C-3 and C-4 hydroxyl groups in galactose, which permits formation of a less strained five-membered cyclic acetal, compared with the trans-C-3 and C-4 hydroxyl groups in glucose. Derivatizations of this kind permit selective reactions to be conducted at different locations in these highly functionalized molecules.

Fischer Projections

There are several ways to draw the structure of carbohydrate molecules. The Fischer projection (straight chain) makes it appear that the molecule is flat but it is a three-dimensional molecule. Although we will not be concerned with the 3D orientation, know that the arrangement in the Fischer projection does provide information about the orientation of atoms around each carbon atom.

These projections simplify the drawing of molecules yet retain important information about the arrangement of atoms within the structure. The figure below shows the Fischer projections for the enantiomers (non-superimposable mirror images) of ephedrine and pseudoephedrine. While it may appear that the molecules are the same, they are not because the Fischer projection does not explicitly show the three-dimensional geometry of the molecule.

Fischer projections provide an easy way to distinguish among the many, similar carbohydrate molecules that exist. For example, there are sixteen aldohexoses (see figure below). Note the different patterns of the −OH−OH bonds on the left and right sides of the Fischer projection for each. Changing the orientation of one or more of the −OH−OH groups changes the identity of the molecule.



Four of the sixteen aldohexoses

Each carbohydrate molecule also has an enantiomer and the two are designated as the D- and L- versions of the compound. The designation is based on the orientation of the −OH−OH group on the chiral carbon farthest from the aldehyde or ketone. The structures of D-glucose and L-glucose are shown in the figure below. The orientation of all −OH−OH groups are reversed but only the arrangement of at the carbon indicated by the arrow determines whether the sugar is a D-sugar with the −OH−OH group on the right or an L-sugar with the −OH−OH group on the left.

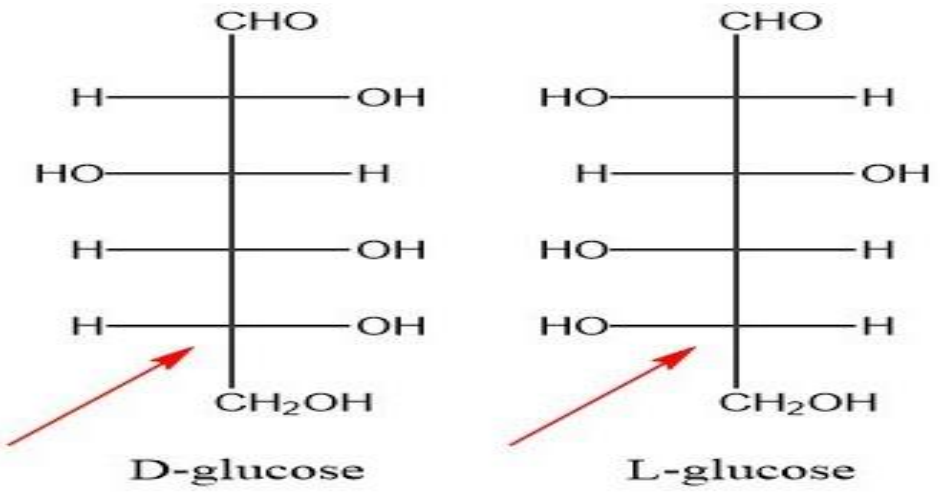
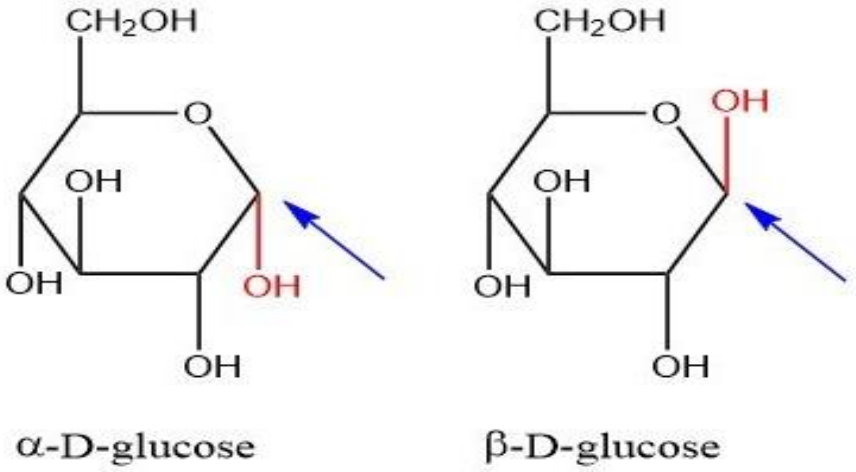


Figure 5.2.4: D-glucose and L-glucose are mirror images of one another.

Haworth Structures

Like Fischer projections, the Haworth structures provide information about a molecule's three-dimensional structure without explicitly showing it in the drawing. Carbohydrates are present in the body in both the chain and ring forms with the latter being more common. Haworth projections provide a simple way to display the ring structures and may or may not show the hydrogen atoms attached to each carbon. Remember, every carbon has four bonds so hydrogens are implied when the structure does not show all four bonds. When the cyclic monosaccharide forms, there are two versions that can form, called αα (alpha\) and ββ (beta) (see figure below). The arrow in the figure indicates the **anomeric** carbon which it the location where the ring forms and where the orientation of the −OH−OH group can change. The orientation of the other −OH−OH groups are fixed because they are determined by the orientation of the −OH−OH groups in the particular monosaccharide (compare to the orientation of the −OH−OH groups on the left and right sides of the Fischer projections). Each monosaccharide can exist in either αα or ββ form and the two forms will interconvert as the ring opens and closes. The αα form occurs when the −OH−OH group on the anomeric carbon is pointing down and the ββ version exists when the −OH−OH group on the anomeric carbon is pointing up.



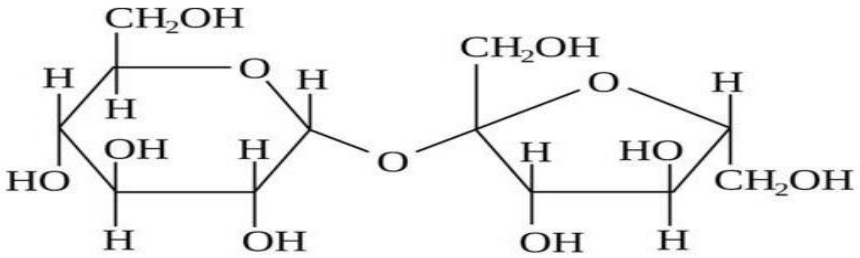
α-D-glucose β-D-glucose

Figure 5.2.5: The cyclic forms of carbohydrates can interconvert between the alpha and beta forms.

DISACCHARIDES

If two monosaccharides bond together, they form a carbohydrate called a **disaccharide**. Two monosaccharides will bond together through a dehydration reaction, in which a water molecule is lost. A dehydration reaction is a **condensation reaction**, a chemical reaction in which two molecules combine to form one single molecule, losing a small molecule in the process. In the dehydration reaction, this small molecule is water. The bond between two monosaccharides is known as a **glycosidic bond**.

An example of a disaccharide is sucrose (table sugar), which consists of the monosaccharides glucose and fructose (see figure below). Other common disaccharides include lactose ("milk sugar") and maltose. Monosaccharides and disaccharides are also called *simple sugars*. They provide the major source of energy to living cells.



KEY: C = Carbon, H = Hydrogen, O = Oxygen

NOTE: Each unlabeled point where lines intersect represents another carbon atom.

Sucrose molecule. This sucrose molecule is a disaccharide. It is made up of two monosaccharides: glucose on the left and fructose on the right.

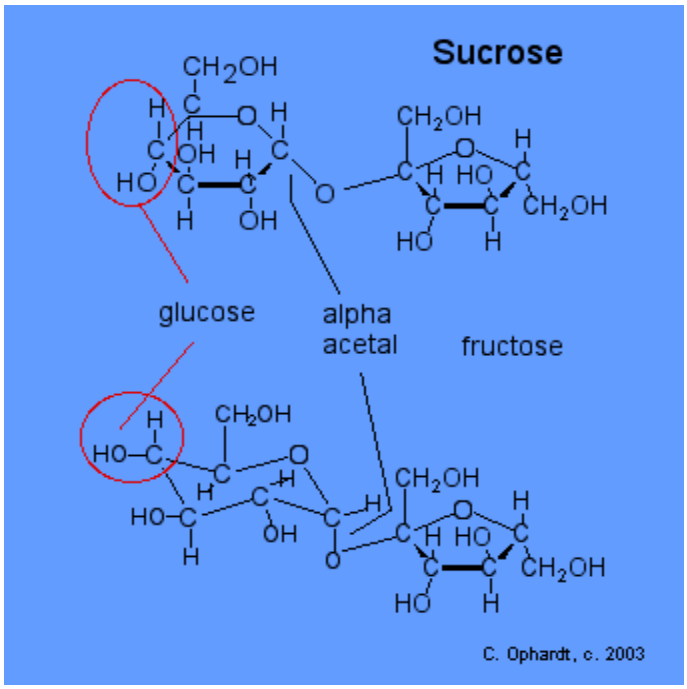
As a result of these different orientations, we can have four forms of each monosaccharide. For example, glucose can exist as αα-D-glucose, αα-L-glucose, ββ-D-glucose, or ββ-L-glucose. While the αα and ββ forms can interconvert, the same cannot be said for D and L versions. Naturally occurring monosaccharides are in the D version, called "D sugars". The arrangement within the D or L form is fixed and they cannot interconvert.

SUCROSE

Sucrose or table sugar is obtained from sugar cane or sugar beets. Sucrose is made from glucose and fructose units. The glucose and fructose units are joined by an acetal oxygen bridge in the alpha orientation. The structure is easy to recognize because it contains the six member ring of glucose and the five member ring of fructose.

Introduction

To recognize glucose look for the horizontal projection of the -OH on carbon #4. The alpha acetal is is really part of a double acetal, since the two monosaccharides are joined at the hemiacetal of glucose and the hemiketal of the fructose. There are no hemiacetals remaining in the sucrose and therefore sucrose is a *non-reducing sugar*.



SUGAR PROCESSING

Sugar or more specifically sucrose is a carbohydrate that occurs naturally in every fruit and vegetable. It is the major product of photosynthesis, the process by which plants transform the sun's energy into food. Sugar occurs in greatest quantities in sugar cane and sugar beets from which it is separated for commercial use.

In the first stage of processing the natural sugar stored in the cane stalk or beet root is separated from the rest of the plant material by physical methods. For sugar cane, this is accomplished by:

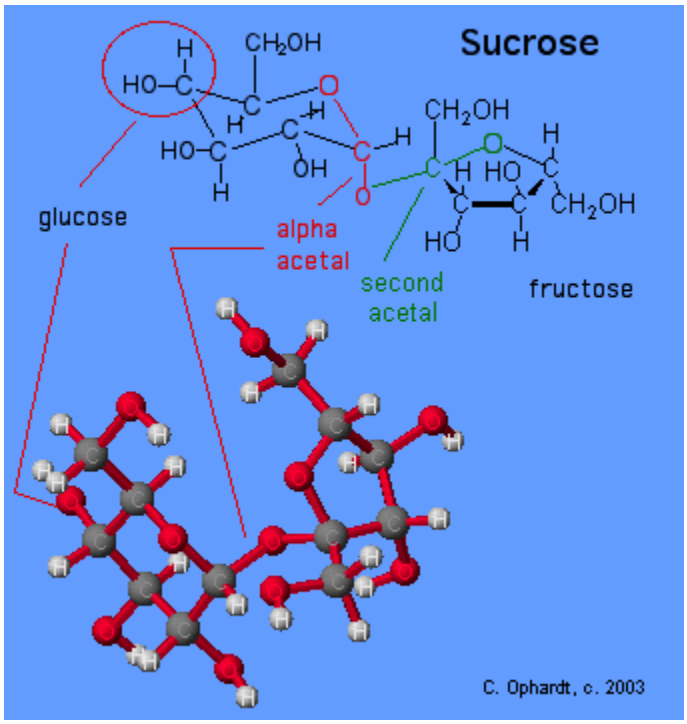
1. pressing the cane to extract the juice containing the sugar
2. boiling the juice until it begins to thicken and sugar begins to crystallize
3. spinning the sugar crystals in a centrifuge to remove the syrup, producing raw sugar; the raw sugar still contains many impurities
4. shipping the raw sugar to a refinery where it is washed and filtered to remove remaining non-sugar ingredients and color
5. crystallizing, drying and packaging the refined sugar.

Beet sugar processing is similar, but it is done in one continuous process without the raw sugar stage. The sugar beets are washed, sliced and soaked in hot water to separate the sugar-containing juice from the beet fiber. The sugar-laden juice is purified, filtered, concentrated and dried in a series of steps similar to cane sugar processing.

Acetal Functional Group

Carbon # 1 (red on left) is called the **anomeric carbon** and is the center of an acetal functional group. A carbon that has two ether oxygens attached is an acetal. The **Alpha position** is defined as the ether oxygen being on the opposite side of the ring as the C # 6. In the chair structure this results in a **down projection**. This is the same definition as the -OH in a hemiacetal.

A second acetal grouping is defined by the green atoms. This result because the the formation reaction of the disaccharide is between the hemiacetal of glucose and the hemiketal of the fructose.



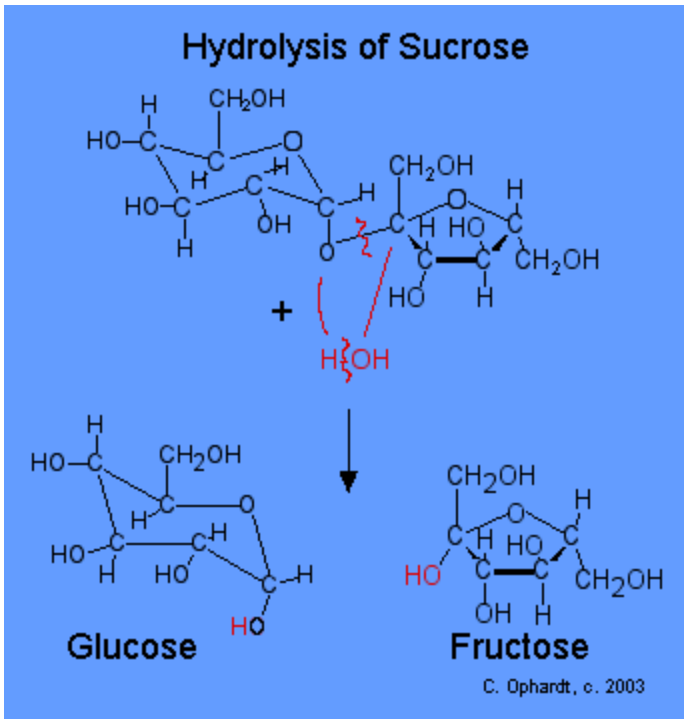
Sucrose

Invert Sugar

When sucrose is hydrolyzed it forms a 1:1 mixture of glucose and fructose. This mixture is the main ingredient in honey. It is called invert sugar because the angle of the specific rotation of the plain polarized light changes from a positive to a negative value due to the presence of the optical isomers of the mixture of glucose and fructose sugars.

Hydrolysis of Sucrose

In the hydrolysis of any di- or poly saccharide, a water molecule helps to break the acetal bond as shown in red. The acetal bond is broken, the H from the water is added to the oxygen on the glucose. The -OH is then added to the carbon on the fructose.



Hydrolosis of Sucrose

MALTOSE

Maltose occurs to a limited extent in sprouting grain. It is formed most often by the partial hydrolysis of starch and glycogen. In the manufacture of beer, maltose is liberated by the action of malt (germinating barley) on starch; for this reason, it is often referred to as *malt sugar*. Maltose is about 30% as sweet as sucrose. The human body is unable to metabolize maltose or any other disaccharide directly from the diet because the molecules are too large to pass through the cell membranes of the intestinal wall. Therefore, an ingested disaccharide must first be broken down by hydrolysis into its two constituent monosaccharide units. In the body, such hydrolysis reactions are catalyzed by enzymes such as *maltase*. The same reactions can be carried out in the laboratory with dilute acid as a catalyst, although in that case the rate is much slower, and high temperatures are required. Whether it occurs in the body or a glass beaker, the hydrolysis of maltose produces two molecules of D-glucose.

Maltose is a reducing sugar. Thus, its two glucose molecules must be linked in such a way as to leave one anomeric carbon that can open to form an aldehyde group. The glucose units in maltose are joined in a *head-to-tail* fashion through an α-linkage from the first carbon atom of one glucose molecule to the fourth carbon atom of the second glucose molecule (that is, an α-1,4-glycosidic linkage; see Figure 1). The bond from the anomeric carbon of the first monosaccharide unit is directed downward, which is why this is known as an α-glycosidic linkage. The OH group on the anomeric carbon of the second glucose can be in either the α or the β position, as shown in Figure 1.

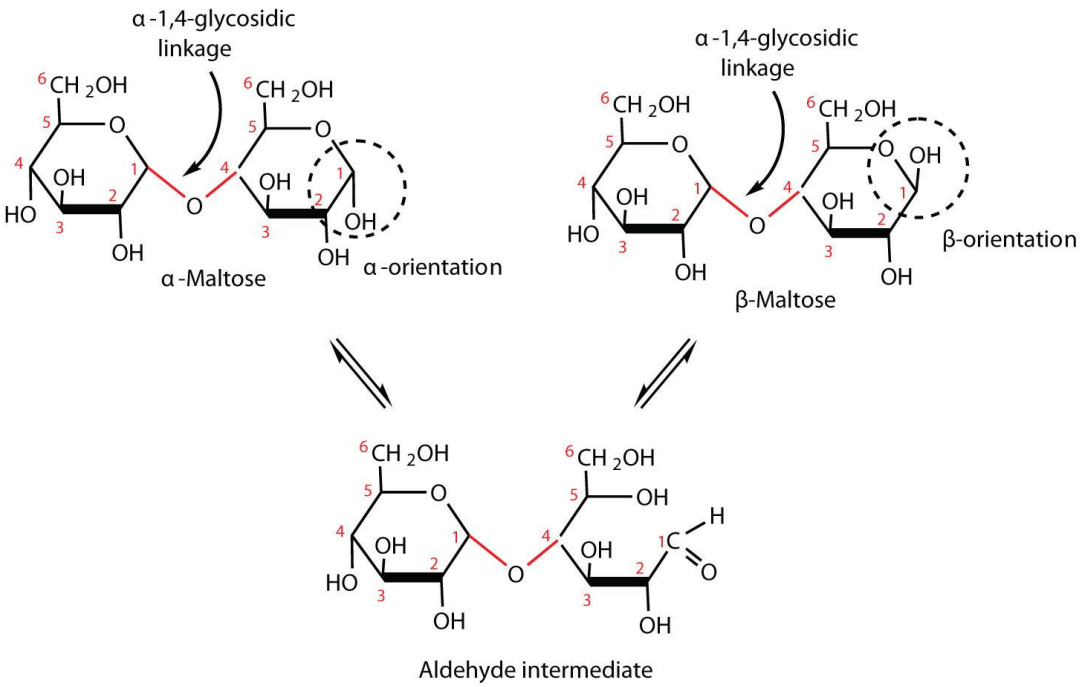


Figure 1 *An Equilibrium Mixture of Maltose Isomers*

POLYSACCHARIDES
STARCH

Starch is the most important source of carbohydrates in the human diet and accounts for more than 50% of our carbohydrate intake. It occurs in plants in the form of granules, and these are particularly abundant in seeds (especially the cereal grains) and tubers, where they serve as a storage form of carbohydrates. The breakdown of starch to glucose nourishes the plant during periods of reduced photosynthetic activity. We often think of potatoes as a "starchy" food, yet other plants contain a much greater percentage of starch (potatoes 15%, wheat 55%, corn 65%, and rice 75%). Commercial starch is a white powder.

Starch is a mixture of two polymers: amylose and amylopectin. Natural starches consist of about 10%–30% amylase and 70%–90% amylopectin. Amylose is a linear polysaccharide composed entirely of D-glucose units joined by the α-1,4-glycosidic linkages we saw in maltose (part (a) of Figure 5.1.1). Experimental evidence indicates that amylose is not a straight chain of glucose units but instead is coiled like a spring, with six glucose monomers per turn (part (b) of Figure 5.1.1). When coiled in this fashion, amylose has just enough room in its core to accommodate an iodine molecule. The characteristic blue-violet color that appears when starch is treated with iodine is due to the formation of the amylose-iodine complex. This color test is sensitive enough to detect even minute amounts of starch in solution.

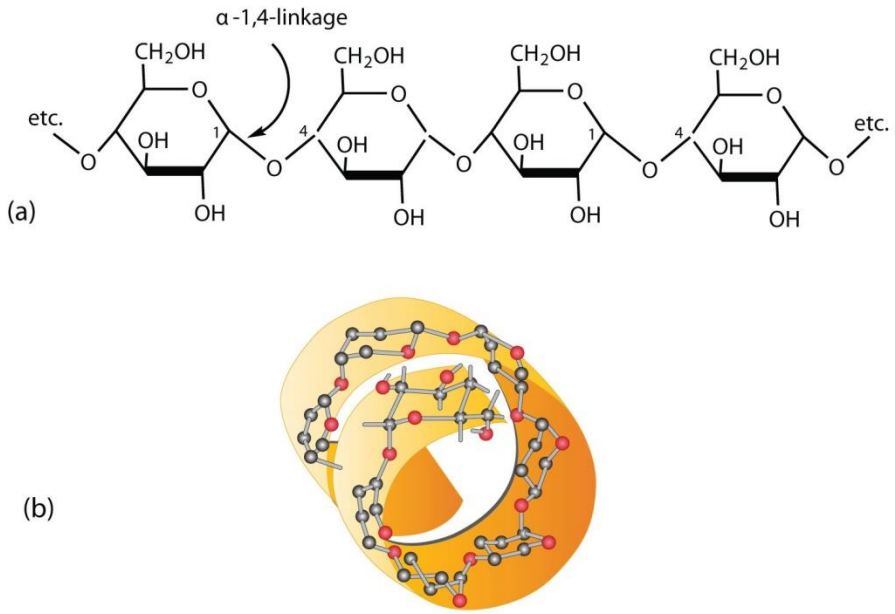


Figure 5.1.1: *Amylose. (a) Amylose is a linear chain of α-D-glucose units joined together by α-1,4-glycosidic bonds. (b) Because of hydrogen bonding, amylose acquires a spiral structure that contains six glucose units per turn*

Amylopectin is a branched-chain polysaccharide composed of glucose units linked primarily by α-1,4-glycosidic bonds but with occasional α-1,6-glycosidic bonds, which are responsible for the branching. A molecule of amylopectin may contain many thousands of glucose units with branch points occurring about every 25–30 units (Figure 5.1.2). The helical structure of amylopectin is disrupted by the branching of the chain, so instead of the deep blue-violet color amylose gives with iodine, amylopectin produces a less intense reddish brown.

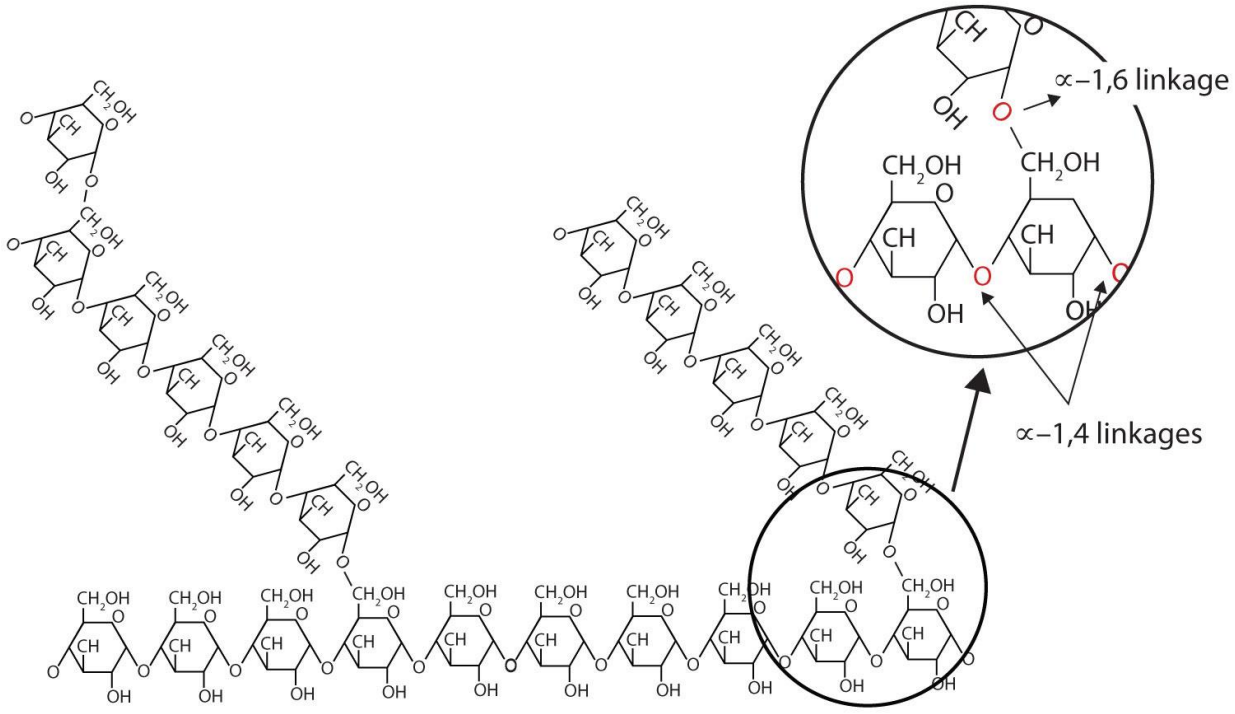
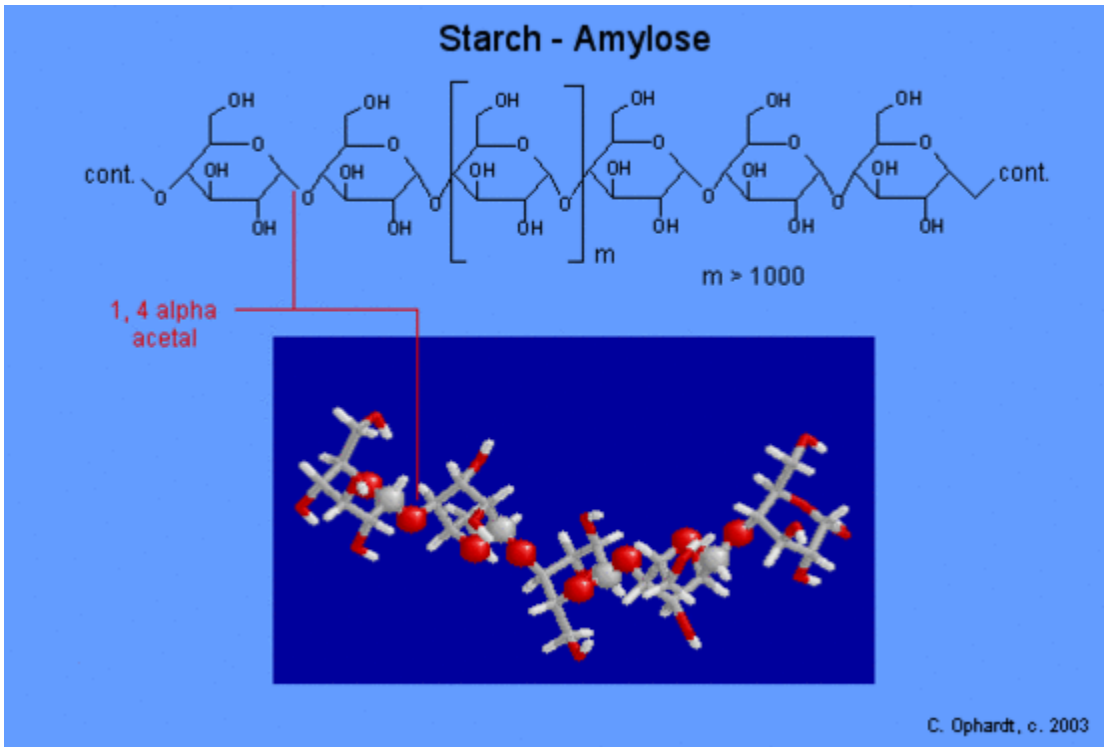


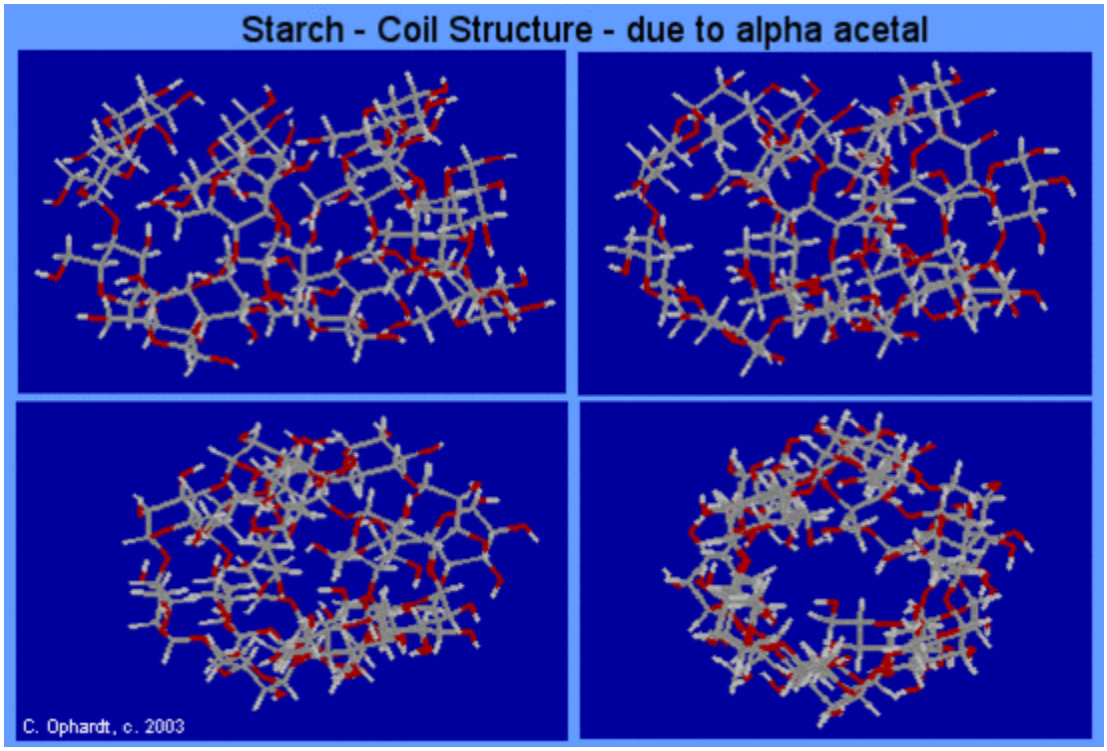
***Figure 5.1.2**: Representation of the Branching in Amylopectin and Glycogen. Both amylopectin and glycogen contain branch points that are linked through α-1,6-linkages. These branch points occur more often in glycogen.*



Amylose forms a colloidal dispersion in hot water, while amylopectin is soluble it is demanding of more extensive heating than amylose. The structure of amylose consists of long polymer chains of glucose units connected by an **alpha acetal** linkage. The graphic on the left shows a very small portion of an amylose chain. All of the monomer units are alpha -D-glucose, and all the alpha acetal links connect C #1 of one glucose and C #4 of the next glucose.

Acetal Functional Group

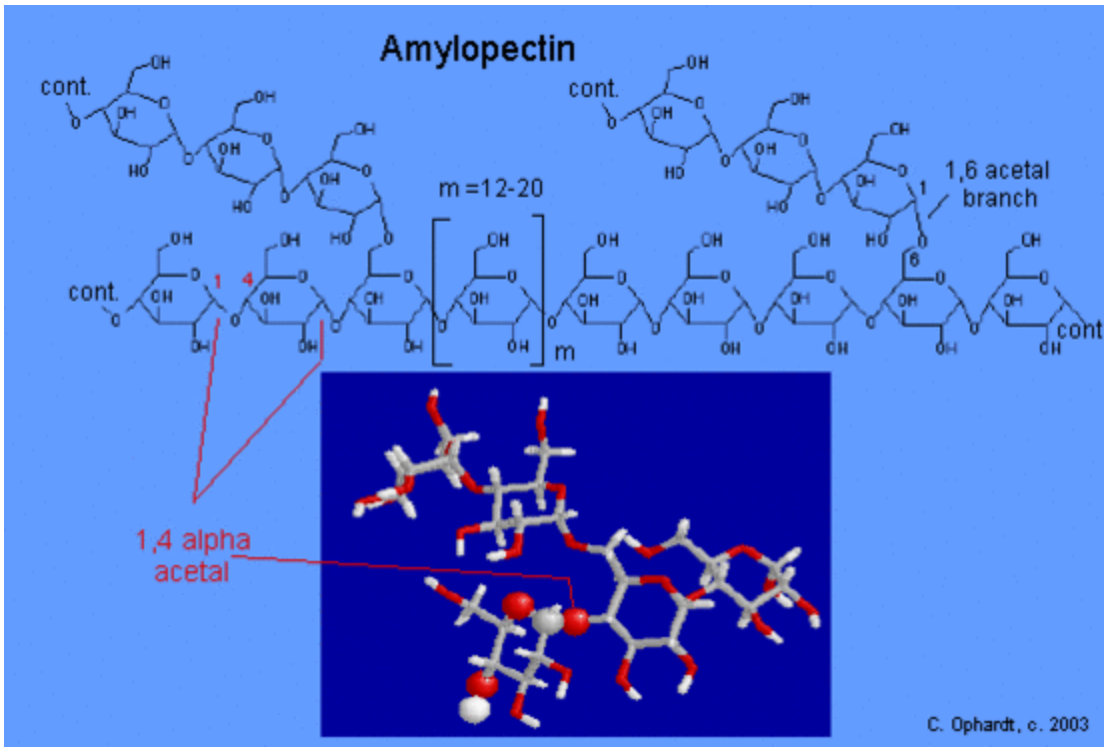
Carbon # 1 is called the **anomeric carbon** and is the center of an acetal functional group. A carbon that has two ether oxygens attached is an acetal. The **Alpha position** is defined as the ether oxygen being on the opposite side of the ring as the C # 6. In the chair structure this results in a **downward projection**. This is the same definition as the -OH in a hemiacetal.



As a result of the bond angles in the alpha acetal linkage, amylose actually forms a spiral much like a coiled spring. Amylose is responsible for the formation of a deep blue color in the presence of iodine, which slips inside of the amylose coil.

Amylopectin

The graphic on the left shows very small portion of an amylopectin-type structure showing two branch points [drawn closer together than they should be]. The acetal linkages are alpha connecting C #1 of one glucose to C #4 of the next glucose.



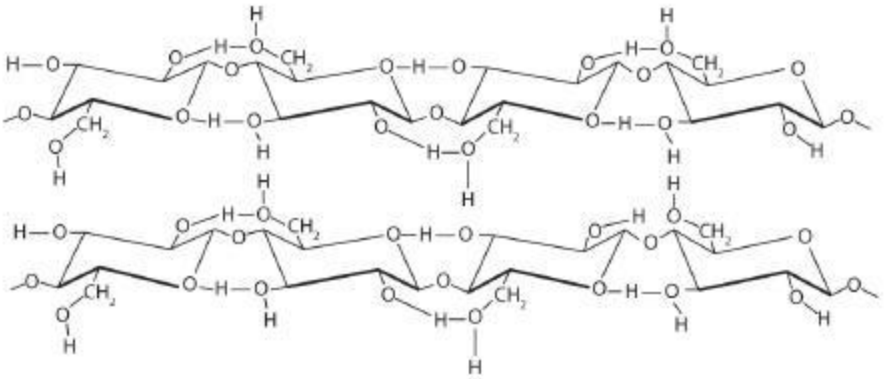
The branches are formed by linking C #1 to a C #6 through an acetal linkages. Amylopectin has 12-20 glucose units between the branches. Natural starches are mixtures of amylose and amylopectin. In glycogen, the branches occur at intervals of 8-10 glucose units, while in amylopectin the branches are separated by 10-12 glucose units.

CELLULOSE

Cellulose, a fibrous carbohydrate found in all plants, is the structural component of plant cell walls. Because the earth is covered with vegetation, cellulose is the most abundant of all carbohydrates, accounting for over 50% of all the carbon found in the vegetable kingdom. Cotton fibrils and filter paper are almost entirely cellulose (about 95%), wood is about 50% cellulose, and the dry weight of leaves is about 10%–20% cellulose. The largest use of cellulose is in the manufacture of paper and paper products. Although the use of noncellulose synthetic fibers is increasing, rayon (made from cellulose) and cotton still account for over 70% of textile production.

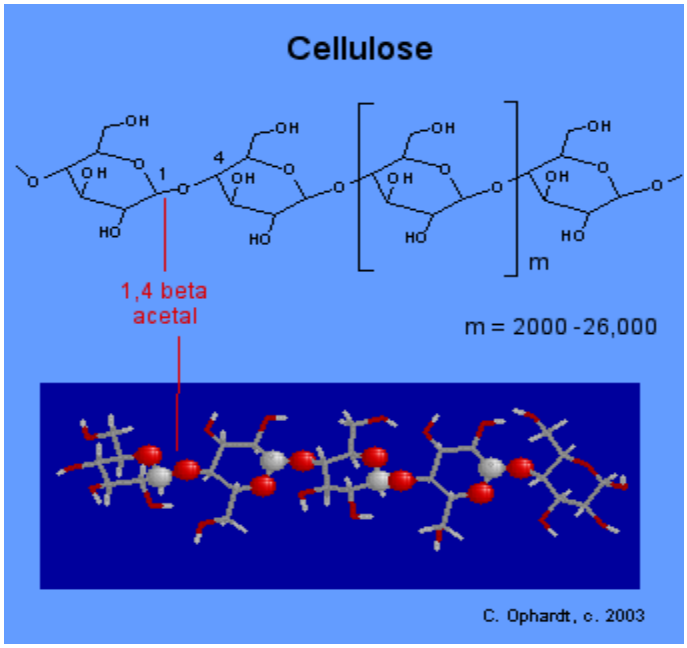
Like amylose, cellulose is a linear polymer of glucose. It differs, however, in that the glucose units are joined by β-1,4-glycosidic linkages, producing a more extended structure than amylose (part (a) of Figure 5.1.3). This extreme linearity allows a great deal of hydrogen bonding between OH groups on adjacent chains, causing them to pack closely into fibers (part (b) of Figure 5.1.3). As a result, cellulose exhibits little interaction with water or any other solvent. Cotton and wood, for example, are completely insoluble in water and have considerable mechanical strength. Because cellulose does not have a helical structure, it does not bind to iodine to form a colored product.

(a)



(b)

Figure 5.1.3*: Cellulose. (a) There is extensive hydrogen bonding in the structure of cellulose. (b) In this electron micrograph of the cell wall of an alga, the wall consists of successive layers of cellulose fibers in parallel arrangement.*



Animals such as cows, horses, sheep, goats, and termites have symbiotic bacteria in the intestinal tract. These symbiotic bacteria possess the necessary enzymes to digest cellulose in the GI tract. They have the required enzymes for the breakdown or hydrolysis of the cellulose; the animals do not, not even termites, have the correct enzymes. No vertebrate can digest cellulose directly.

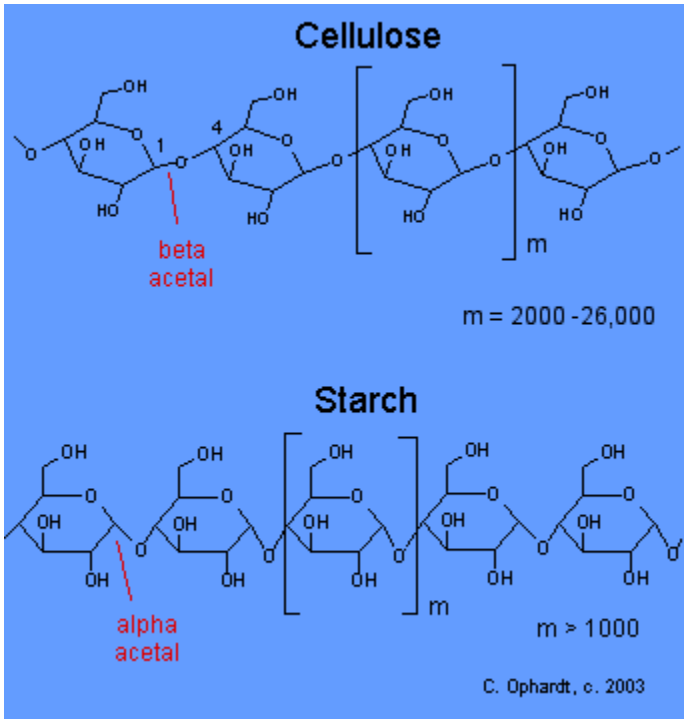
Even though we cannot digest cellulose, we find many uses for it including: Wood for building; paper products; cotton, linen, and rayon for clothes; nitrocellulose for explosives; cellulose acetate for films. The structure of cellulose consists of long polymer chains of glucose units connected by a beta acetal linkage. The graphic on the left shows a very small portion of a cellulose chain. All of the monomer units are beta-D-glucose, and all the beta acetal links connect C # 1 of one glucose to C # 4 of the next glucose.

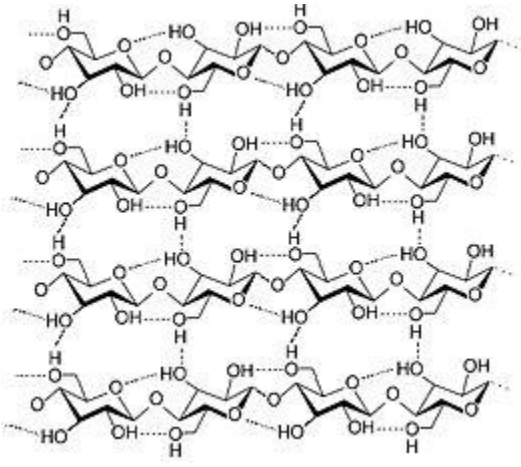
Acetal Functional Group

Carbon # 1 is called the anomeric carbon and is the center of an acetal functional group. A carbon that has two ether oxygens attached is an acetal. The Beta position is defined as the ether oxygen being on the same side of the ring as the C # 6. In the chair structure this results in a horizontal or up projection. This is the same definition as the -OH in a hemiacetal.

Compare Cellulose and Starch Structures

Cellulose: Beta glucose is the monomer unit in cellulose. As a result of the bond angles in the beta acetal linkage, cellulose is mostly a linear chain. Starch: Alpha glucose is the monomer unit in starch. As a result of the bond angles in the alpha acetal linkage, starch-amylose actually forms a spiral much like a coiled spring.





Cellulose yields D-glucose after complete acid hydrolysis, yet humans are unable to metabolize cellulose as a source of glucose. Our digestive juices lack enzymes that can hydrolyze the β-glycosidic linkages found in cellulose, so although we can eat potatoes, we cannot eat grass. However, certain microorganisms can digest cellulose because they make the enzyme cellulase, which catalyzes the hydrolysis of cellulose. The presence of these microorganisms in the digestive tracts of herbivorous animals (such as cows, horses, and sheep) allows these animals to degrade the cellulose from plant material into glucose for energy. Termites also contain cellulase-secreting microorganisms and thus can subsist on a wood diet. This example once again demonstrates the extreme stereospecificity of biochemical processes.

REFERENCES

1. Morrison, R.T. & Boyd, R.N. (1992) Organic Chemistry, 6th edn, Benjamin Cummings, San Francisco. Chapters 34 and 35 cover the structure, stereochemistry, nomenclature, and chemical reactions of carbohydrates.