COURSE : SC202 (CHEMISTRY)

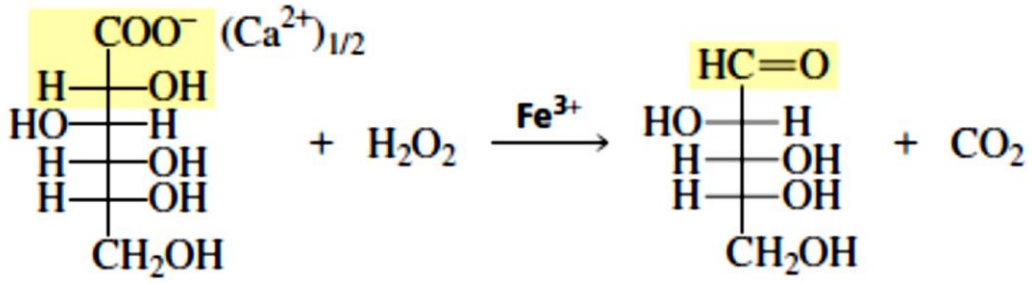
DR. SANGITA TALUKDAR

LECTURE-11

DATE: 1.2.2021

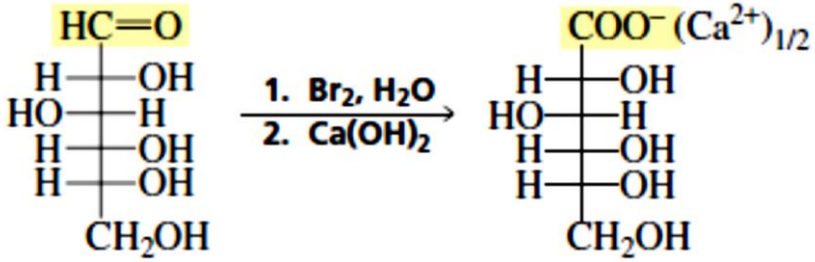
Chain Shortening: The Ruff Degradation

The **Ruff degradation** shortens an aldose chain by one carbon. In the Ruff degradation, the calcium salt of an aldonic acid is oxidized with hydrogen peroxide. Ferric ion catalyzes the oxidation reaction, which cleaves the bond between C-1 and C-2, forming CO_2 and an aldehyde.



calcium D-gluconate **D-arabinose**

The calcium salt of the aldonic acid necessary for the Ruff degradation is easily obtained by oxidizing an aldose with an aqueous solution of bromine and then adding calcium hydroxide to the reaction mixture

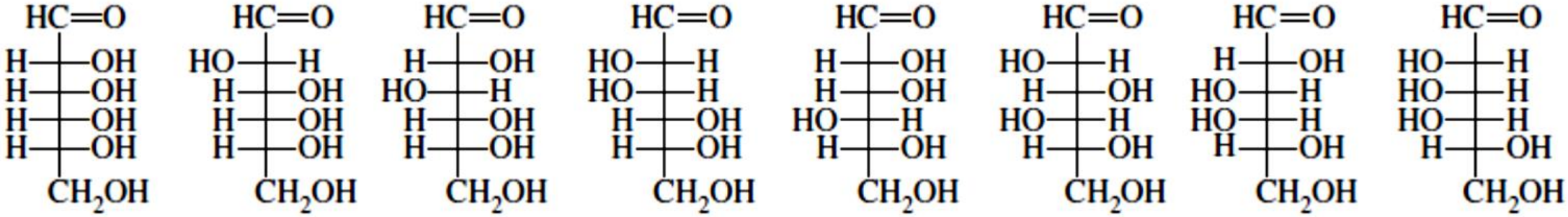


D-glucose **calcium D-gluconate**

Stereochemistry of Glucose: The Fischer Proof

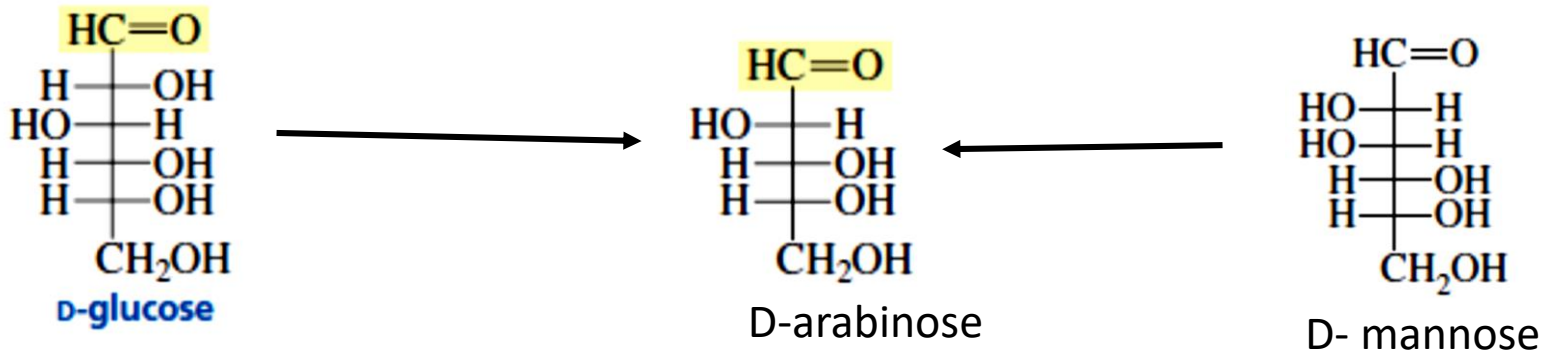
Emil Fischer determined the structures of glucose and the other aldohexoses in 1891, only 14 years after the tetrahedral structure of carbon had been proposed. Fischer received the Nobel Prize for this work in 1902. Much of Fischer's proof used the carbohydrate reactions we have studied, together with some clever reasoning about the symmetry and dissymmetry of the resulting products.

Fischer knew that D-glucose was an aldohexose, but 16 different structures can be written for an aldohexose. The 16 stereoisomers of the aldohexoses are actually eight pairs of enantiomers.



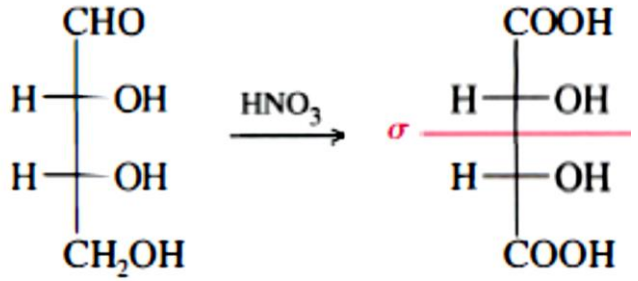
1 D-allose **2** D-altrose **3** D-glucose **4** D-mannose **5** D-gulose **6** D-idose **7** D-galactose **8** D-talose

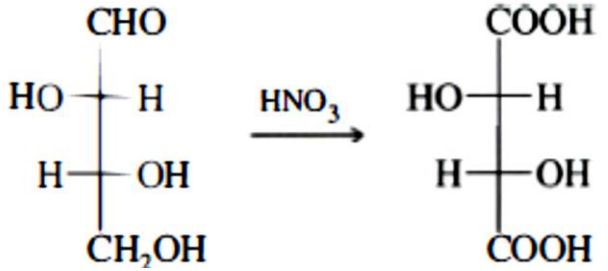
1.On Ruff degradation, glucose and mannose give the same aldopentose: D- (-) -arabinose.



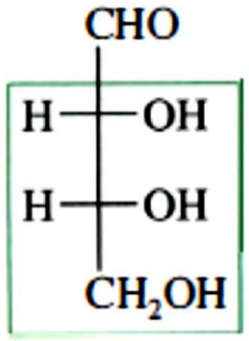
This clue suggests that glucose and mannose are C2 epimers

2. On Ruff degradation, D-(-)-arabinose gives the aldotetrose D-(-) -erythrose. Upon treatment with nitric acid, erythrose gives an optically inactive aldaric acid, meso-tartaric acid.

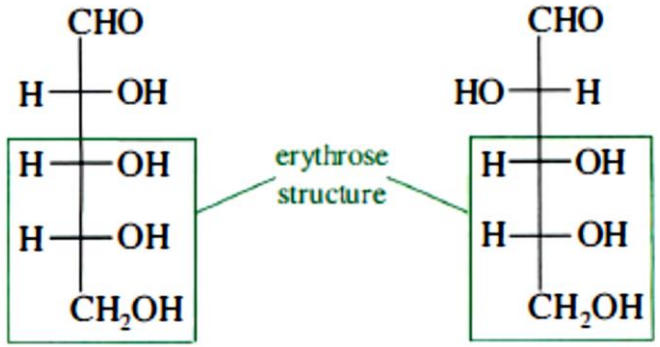




Because oxidation of D-erythrose gives an optically inactive aldaric acid, erythrose must correspond to structure I.

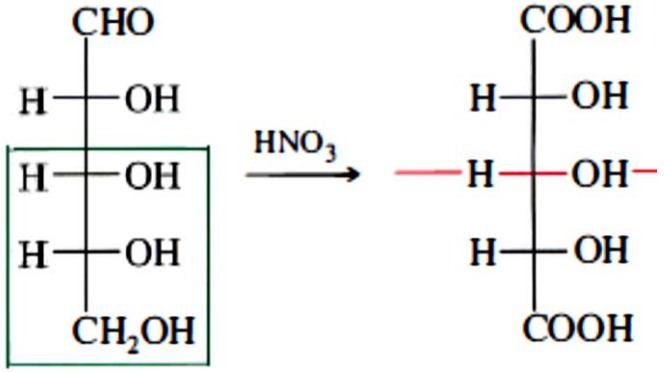


D-(-)-erythrose

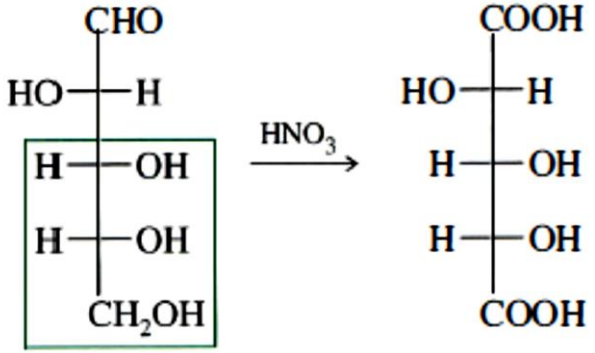


possible structures of D-(-)-arabinose

3.On oxidation with nitric acid, D-(-)-arabinose gives an optically active aldaric acid.



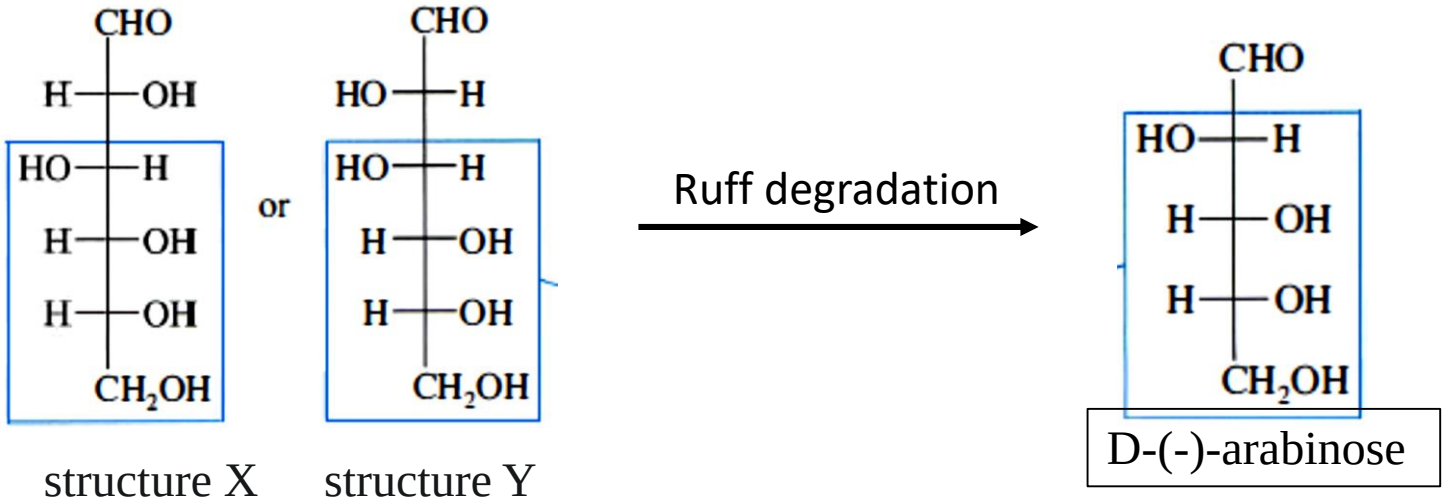
structure A optically inactive aldaric acid



structure B optically active aldaric acid

D-(-)-arabinose

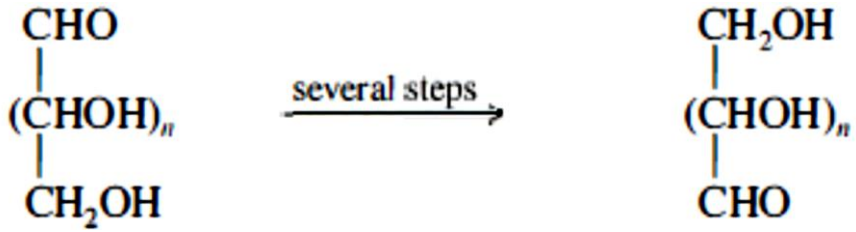
Since glucose and mannose degrade to arabinose, structures X and Y shown below must be glucose and mannose. At this point, however, it is impossible to tell which structure is glucose and which is mannose.

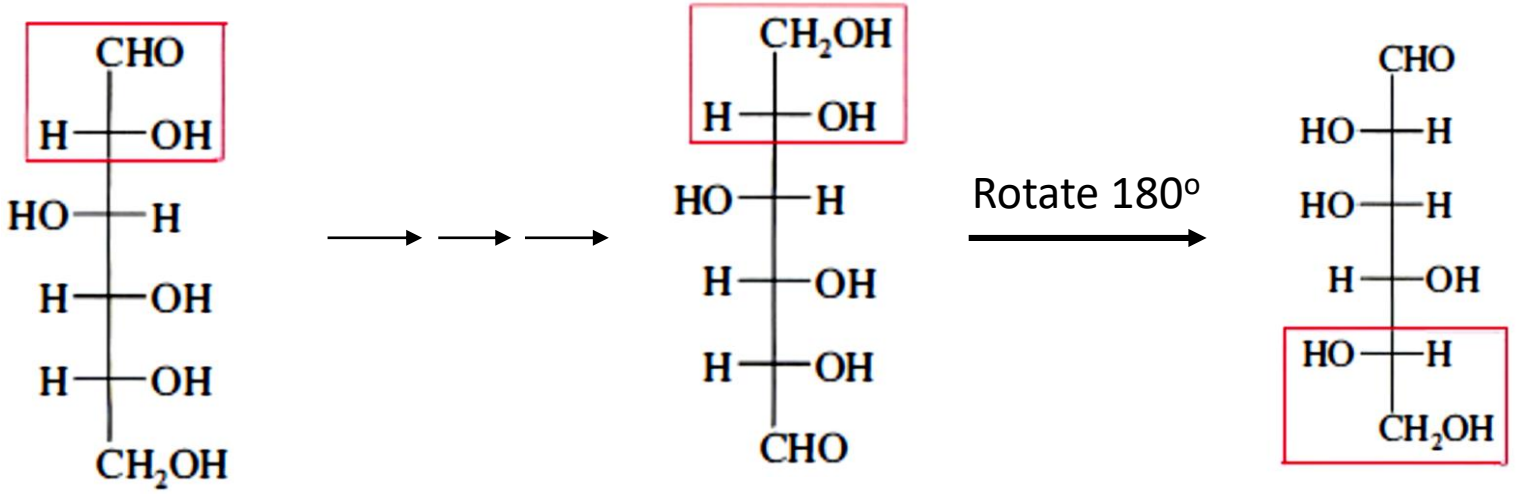


structure X structure Y

4. When the -CHO and - CH_2OH groups of D-mannose are interchanged, the product is still D-mannose. When the -CHO and - CH_2OH groups of D-glucose are interchanged, the product is an unnatural L sugar.

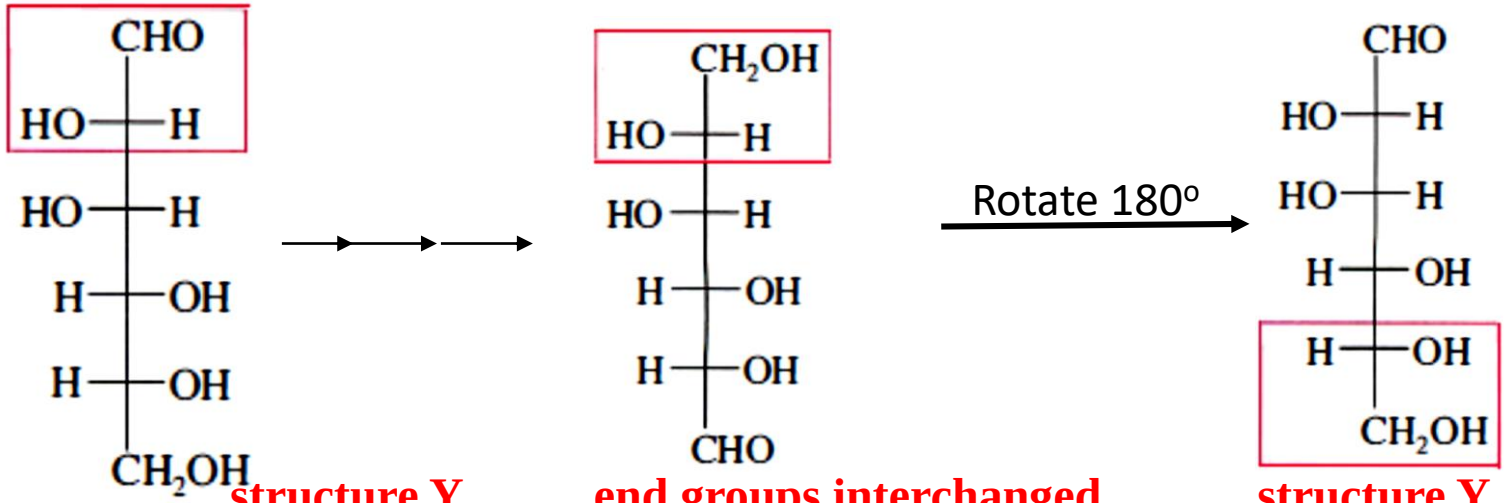
Fischer had developed a clever method for converting the aldehyde group of an aldose to an alcohol while converting the terminal alcohol group to an aldehyde. In effect,this synthesis interchanges the two end groups of the aldose chain.





structure X (D-glucose) **end groups interchanged** **an L sugar (L-gulose)**

If the two end groups of structure X are interchanged, we can rotate a Fischer projection by 180°; when we do that, it becomes clear that the product is an unusual sugar of the L series (L-gulose). Structure X must be D-glucose.

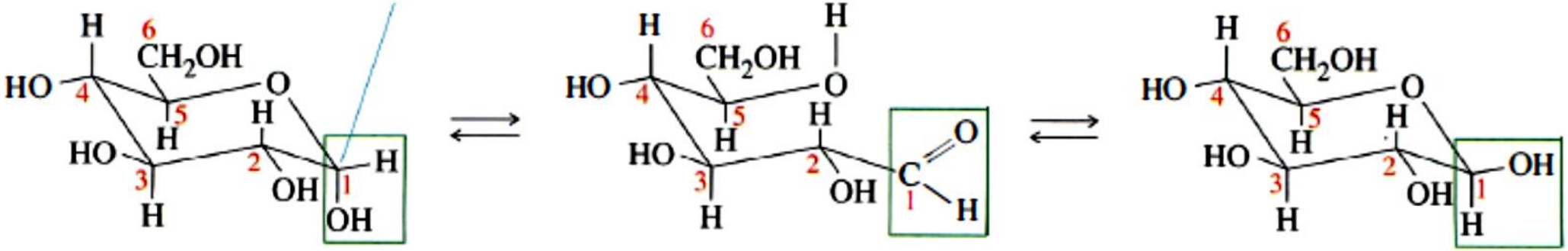


structure Y (D-mannose) **end groups interchanged** **structure Y (D-mannose)**

Cyclic Structure of Monosaccharides

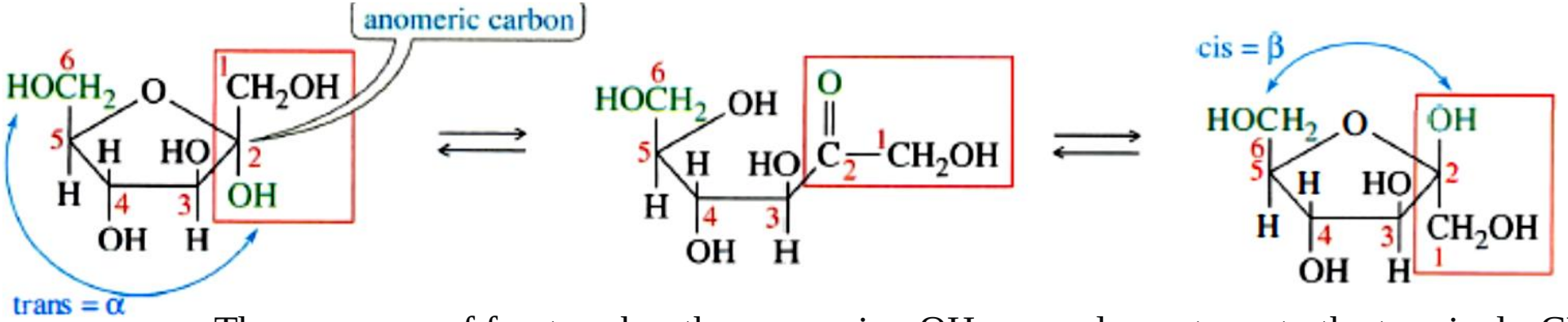
Anomers are two sugars that differ in configuration only at the carbon that was the carbonyl carbon in the open-chain form. This carbon is called the **anomeric carbon**. The prefixes α and β denote the configuration about the anomeric carbon

Anomeric carbon



α -D-glucopyranose open chain form β -D-glucopyranose

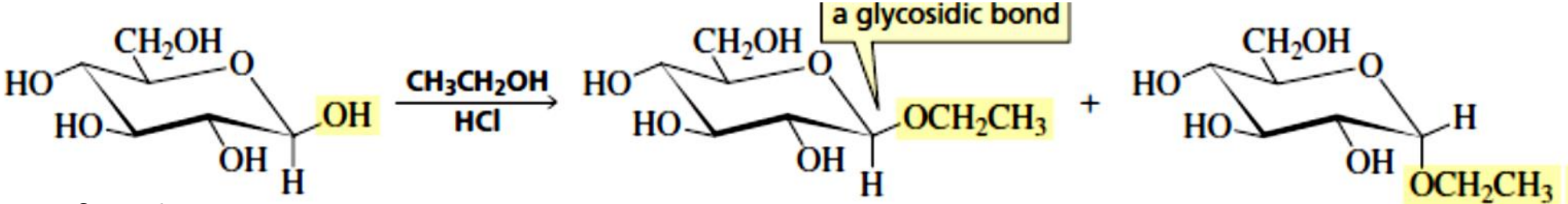
The anomers of glucose. The hydroxyl group on the anomeric (hemiacetal) carbon is down (axial) in the α anomer and up (equatorial) in the β anomer.



The α anomer of fructose has the anomeric - OH group down, trans to the terminal - CH_20H group.
The β anomer has the anomeric hydroxyl group up, cis to the terminal - CH_20H.

Formation of Glycosides

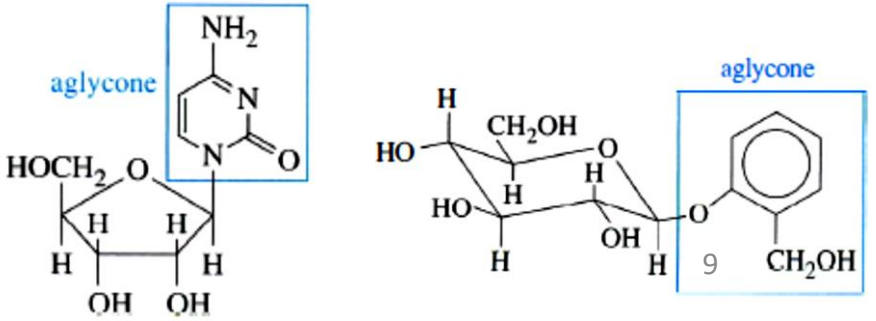
The cyclic hemiacetal (or hemiketal) formed by a monosaccharide can react with an alcohol to form an acetal (or ketal). The acetal (or ketal) of a sugar is called a **glycoside**, and the bond between the anomeric carbon and the alkoxy oxygen is called a **glycosidic bond**. Glycosides are named by replacing the "e" ending of the sugar's name with "ide." Thus, a glycoside of glucose is a glucoside, a glycoside of galactose is a galactoside, etc.



β-D-glucose ethyl β-D-glucose ethyl α-D-glucose

The OH group bonded to the anomeric carbon becomes protonated in the acidic solution, and a lone pair on the ring oxygen helps expel a molecule of water. The anomeric carbon in the resulting oxocarbenium ion is sp^2 hybridized, so that part of the molecule is planar. (An **oxocarbenium ion** has a positive charge that is shared by a carbon and an oxygen.) When the alcohol comes in from the top of the plane, the β-glycoside is formed; when the alcohol comes in from the bottom of the plane, the α-glycoside is formed.

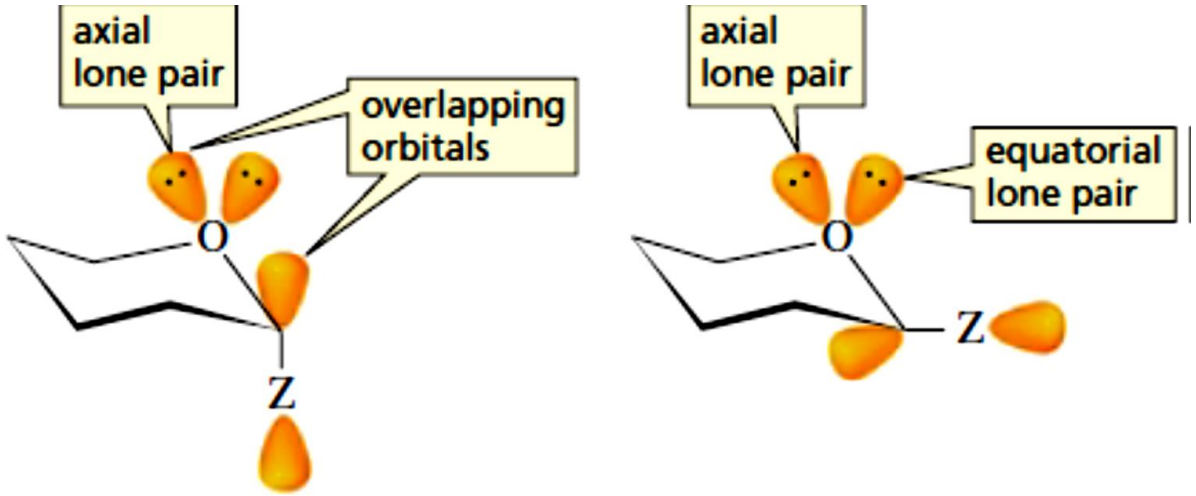
An **aglycone** is the group bonded to the anomeric carbon atom of a glycoside



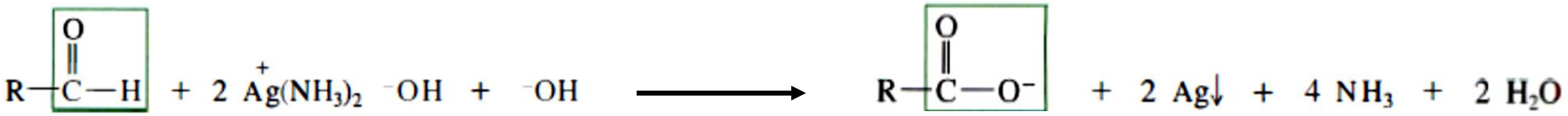
The Anomeric Effect

When glucose reacts with an alcohol to form a glucoside, the major product becomes the α-glucoside. Since acetal formation is reversible, the α-glucoside must be more stable than the β-glucoside.The preference of certain substituents bonded to the anomeric carbon for the axial position is called the **anomeric effect.**

What is responsible for the anomeric effect?
The C-Z bond has a σ* antibonding orbital. If one of the ring oxygen's lone pairs is in an orbital that is parallel to the σ* antibonding orbital, the molecule can be stabilized by electron density from oxygen moving into the σ* orbital. The orbital containing the axial lone pair of the ring oxygen can overlap the σ* orbital only if the substituent is axial. If the substituent is equatorial, neither of the orbitals that contain a lone pair is aligned correctly for overlap. As a result of overlap between the lone pair and the σ* orbital, the C-Z bond is longer and weaker and the C-O bond within the ring is shorter and stronger than normal.



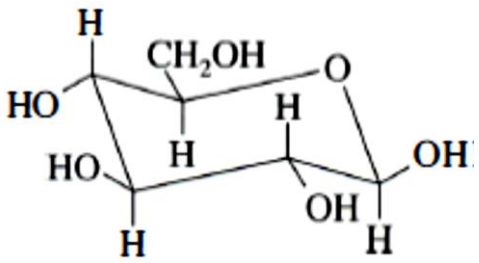
Reducing and Nonreducing Sugars



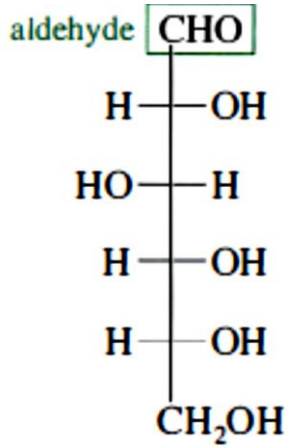
Tollens reagent

oxidized acid anion

reduced silver mirror

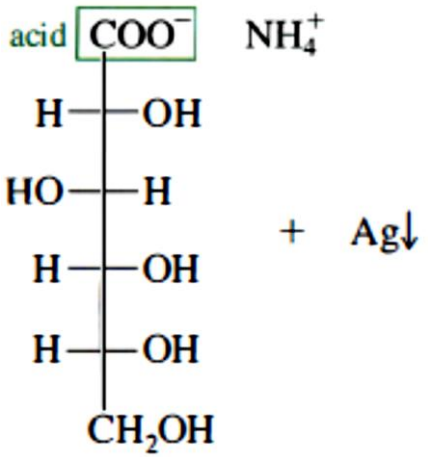


β-D-glucose



Open chain form

Tollens reagent

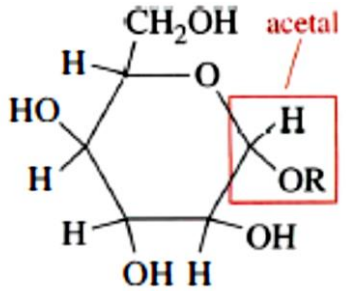


+ Ag↓

Gluconic acid

Hemiacetals (or hemiketals) are in equilibrium with the open-chain sugars in aqueous solution. So as long as a sugar has an aldehyde, a ketone, a hemiacetal, or a hemiketal group, it is able to reduce an oxidizing agent and therefore is classified as a **reducing sugar**.

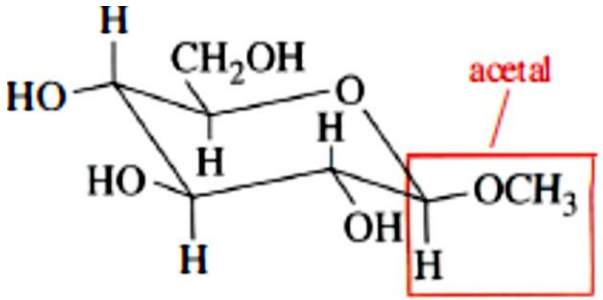
Glycosides are acetals (or ketals), they are not in equilibrium with the openchain aldehyde (or ketone) in neutral or basic aqueous solutions. Because they are not in equilibrium with a compound with a carbonyl group, they cannot be oxidized by reagents such as Ag^+ or Br_2. Glycosides, therefore, are nonreducing sugars—they cannot reduce Ag^+ or Br_2.



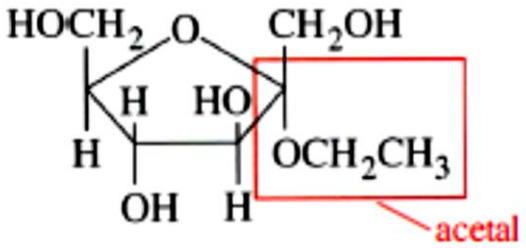
Tollens reagent → No reaction

glycoside

Examples of nonreducing sugars



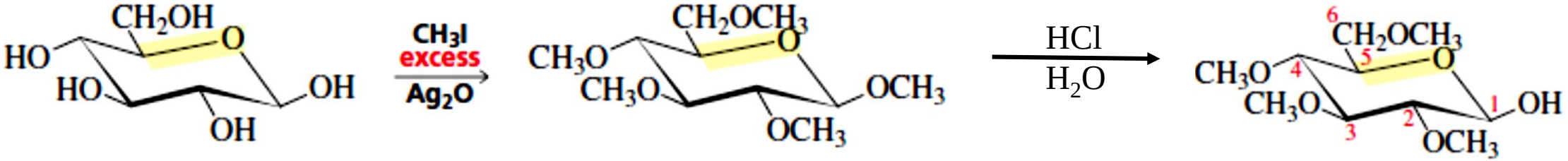
Methyl β-D-glucopyranoside



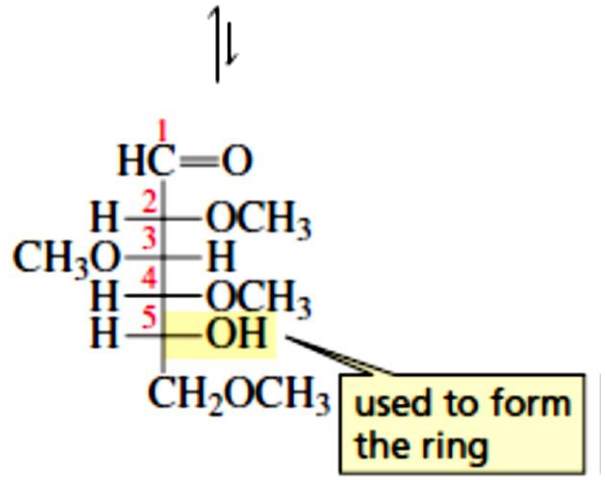
ethyl α-D-fructofuranoside

Determination of Ring Size

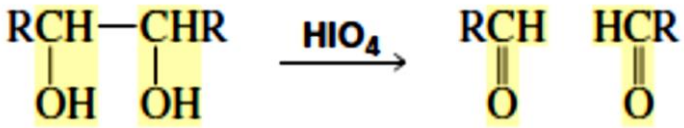
In the first procedure, treatment of the monosaccharide with excess methyl iodide and silver oxide converts all the OH groups to groups OCH_3. Acid-catalyzed hydrolysis of the acetal then forms a hemiacetal, which is in equilibrium with its openchain form. The size of the ring can be determined from the structure of the open-chain form because the sole OH group is the one that had formed the cyclic hemiacetal.



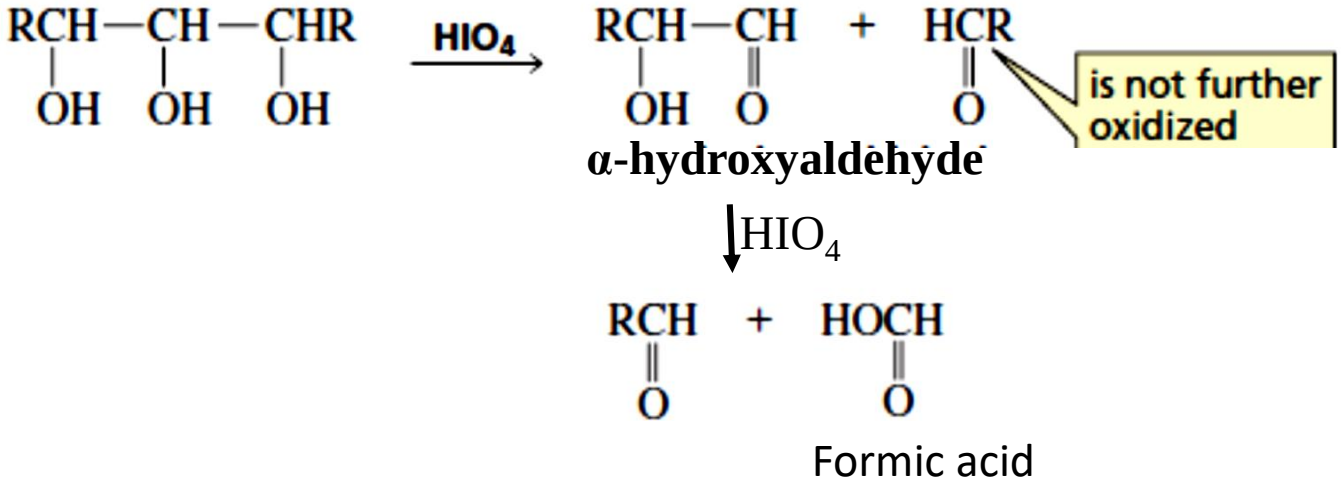
acetal hemiacetal



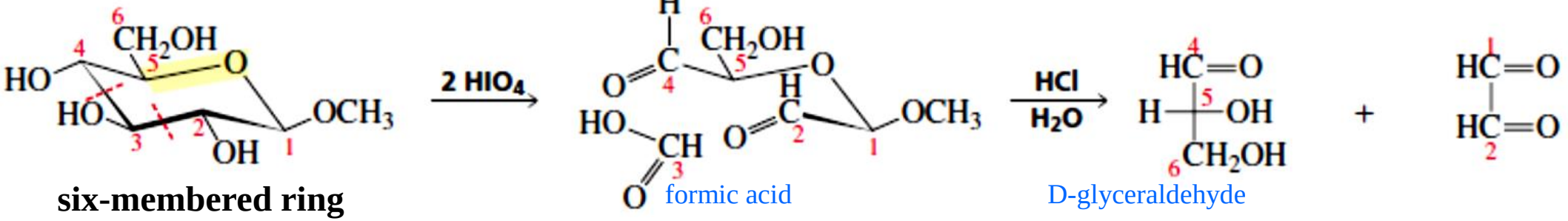
In the second procedure used to determine a monosaccharide's ring size, an acetal of the monosaccharide is oxidized with excess periodic acid.



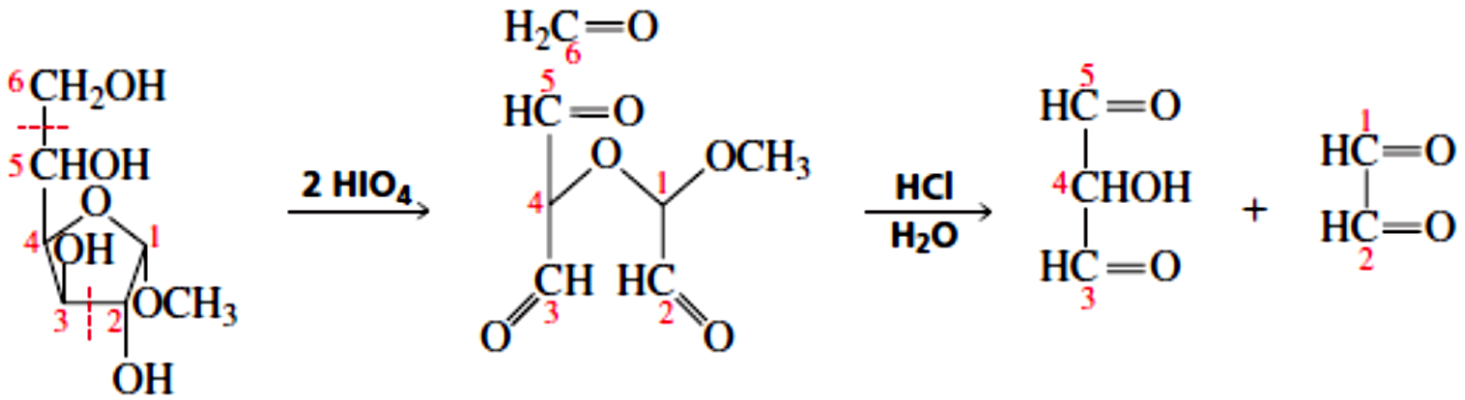
The α-hydroxyaldehyde formed when periodic acid cleaves a 1,2,3-diol is further oxidized to formic acid and another aldehyde.



The products obtained from periodate cleavage of a six-membered-ring acetal are different from those obtained from cleavage of a five-membered-ring acetal.



six-membered ring

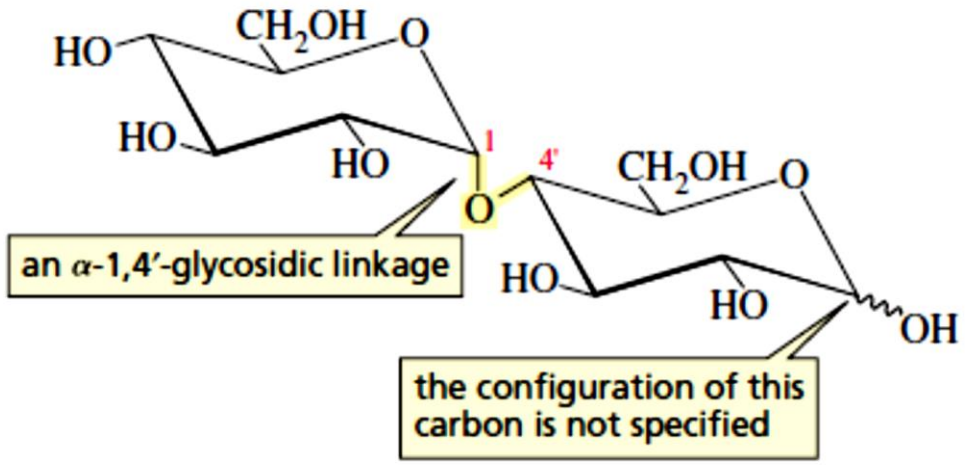


five-membered ring

Disaccharides

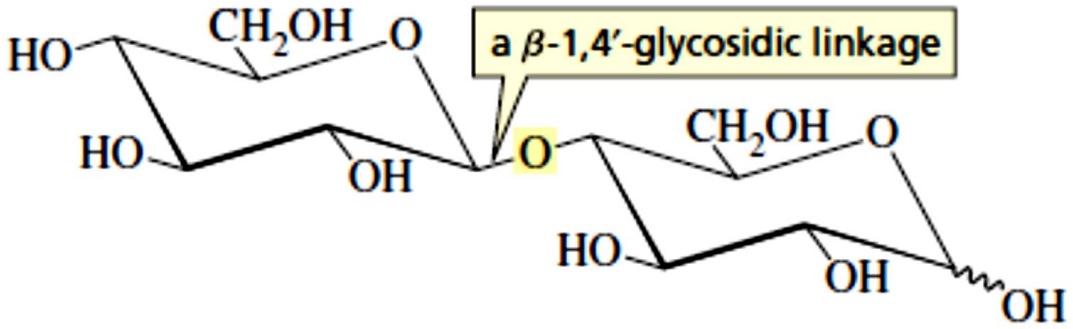
Disaccharides are compounds consisting of two monosaccharide subunits hooked together by an acetal linkage. For example, maltose is a disaccharide obtained from the hydrolysis of starch. It contains two D-glucose subunits hooked together by an acetal linkage. This particular acetal linkage is called an **α-1,4'-glycosidic linkage.** The linkage is between C-1 of one sugar subunit and C-4 of the other. The "prime" superscript indicates that C-4 is not in the same ring as C-1. The linkage is an **α-1,4'-glycosidic linkage** linkage because the oxygen atom involved in the glycosidic linkage is in the **α-position.**

.



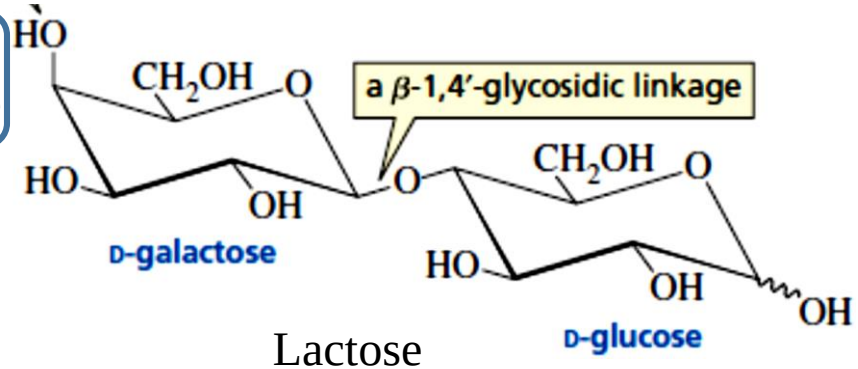
In α-maltose the OH group bonded to this anomeric carbon is in the axial position. In β-maltose the OH group is in the equatorial position. Because maltose can exist in both α and β forms, mutarotation occurs when crystals of one form are dissolved in a solvent. Maltose is a reducing sugar because the right-hand subunit is a hemiacetal and therefore is in equilibrium with the open-chain aldehyde that is easily oxidized.

- **Cellobiose**, a disaccharide obtained from the hydrolysis of cellulose, also contains two D-glucose subunits. Cellobiose differs from maltose in that the two glucose subunits are hooked together by a **α-1,4' glycosidic linkage.**
- Like maltose, cellobiose exists in both α and β forms because the OH group bonded to the anomeric carbon not involved in acetal formation can be in either the axial position (in α cellobiose) or the equatorial position (in β cellobiose).
- Cellobiose is a reducing sugar because the subunit on the right is a hemiacetal



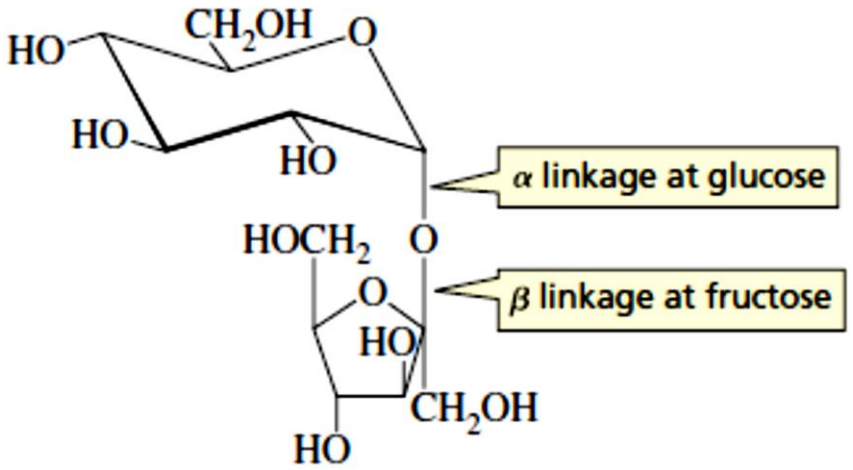
- Lactose is a disaccharide found in milk. One of the subunits of lactose is D-galactose, and the other is D-glucose.
- The D-galactose subunit is an acetal, and the D-glucose subunit is a hemiacetal. The subunits are joined through a **β-1,4' glycosidic linkage** linkage.
- Because one of the subunits is a hemiacetal, lactose is a reducing sugar and undergoes mutarotation.

D-galactose is a C-4 epimer of D-glucose



Lactose

- Sucrose consists of a D-glucose subunit and a D-fructose subunit linked by a glycosidic bond between C-1 of glucose (in the α-position) and C-2 of fructose (in the β-position).
- Sucrose is not a reducing sugar and does not exhibit mutarotation because the glycosidic bond is between the anomeric carbon of glucose and the anomeric carbon of fructose. Sucrose, therefore, does not have a hemiacetal or hemiketal group, so it is not in equilibrium with the readily oxidized open-chain aldehyde or ketone form in aqueous solution.

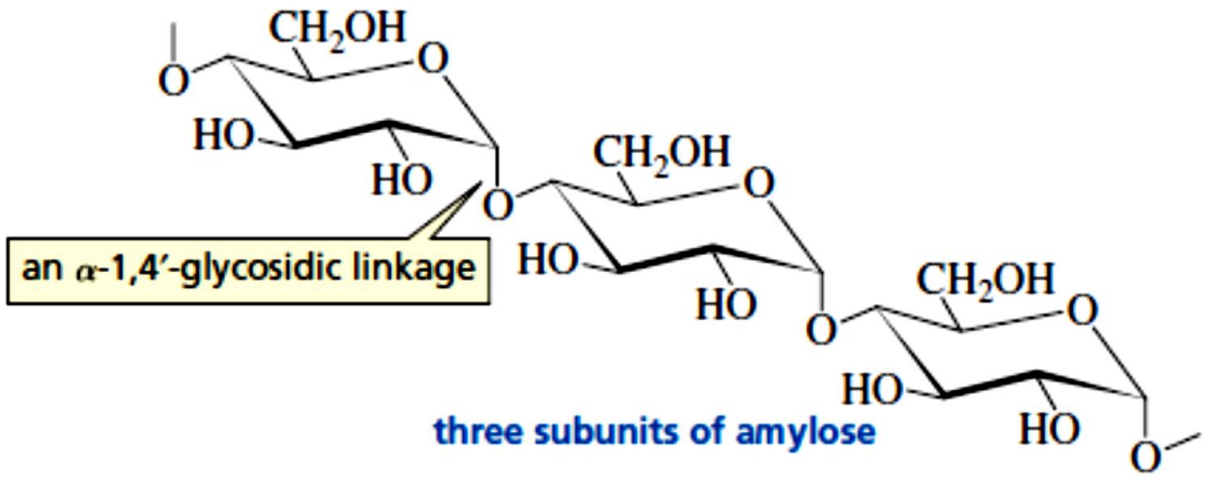


Sucrose has a specific rotation of +66.5^{o} . When it is hydrolyzed, the resulting equimolar mixture of glucose and fructose has a specific rotation of -22.0^{o}. Because the sign of the rotation changes when sucrose is hydrolyzed, a (1:1)mixture of glucose and fructose is called *invert sugar*. The enzyme that catalyzes the hydrolysis of sucrose is called *invertase*

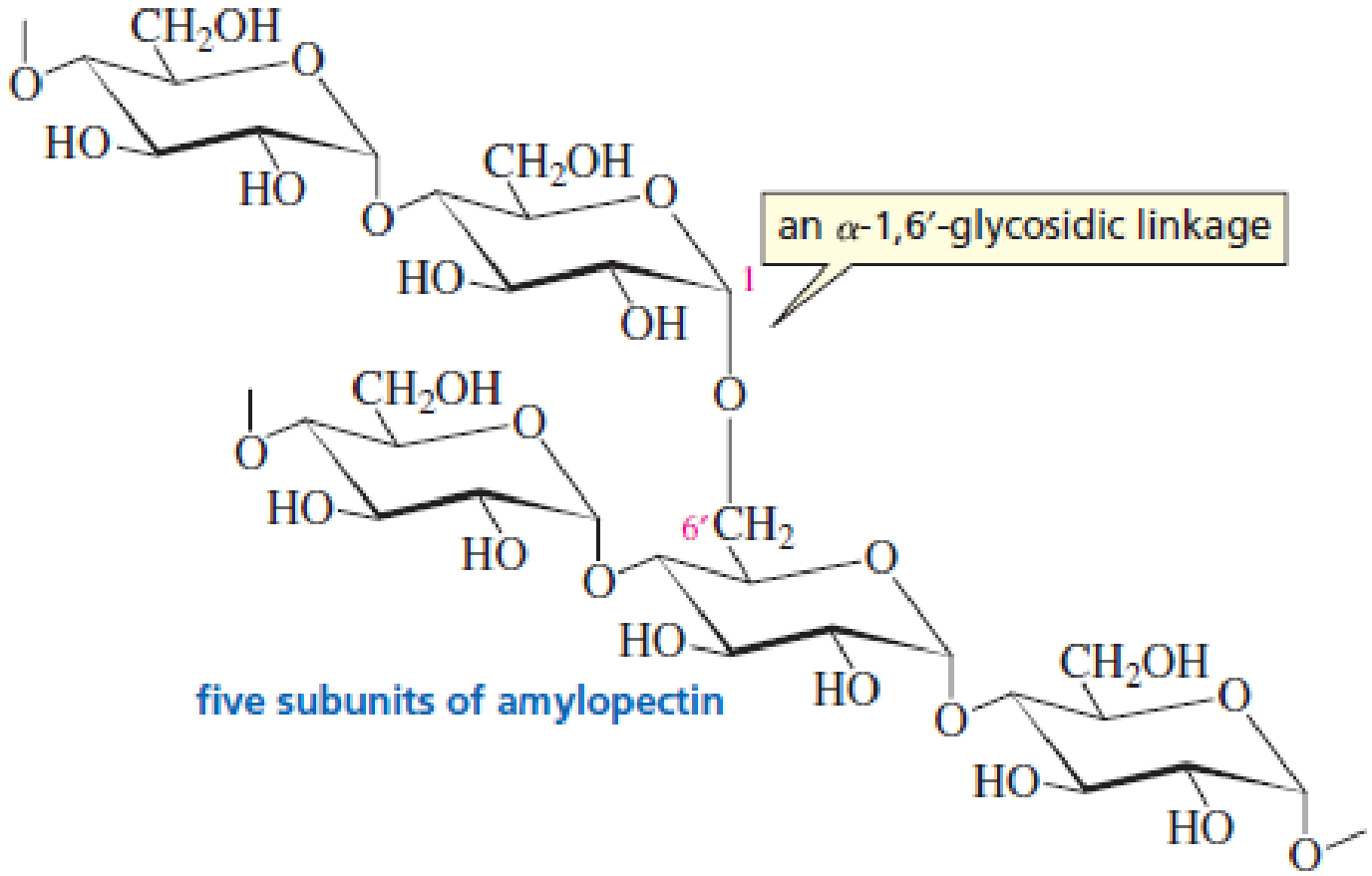
Polysaccharides

Polysaccharides contain as few as 10 or as many as several thousand monosaccharide units joined together by glycosidic linkages.The most common polysaccharides are **starch and cellulose**

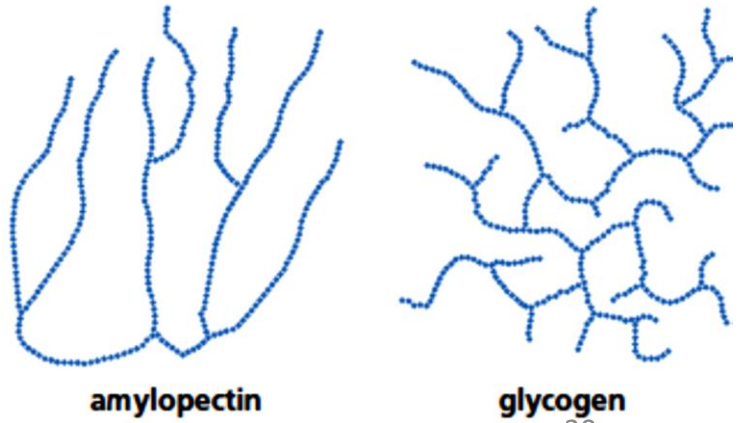
Starch is a mixture of two different polysaccharides: amylose (about 20%) and amylopectin (about 80%). Amylose is composed of unbranched chains of D-glucose units joined by α-1,4'- glycosidic linkages.



Amylopectin is a branched polysaccharide. Like amylose, it is composed of chains of D-glucose units joined by α-1,4'-glycosidic linkages. Unlike amylose, however, amylopectin also contains α-1,6'- glycosidic linkages. These linkages create the branches in the polysaccharide

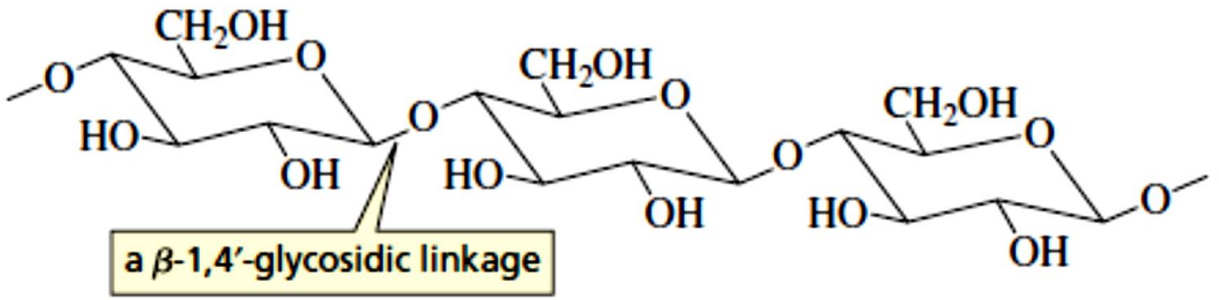


Animals store their excess glucose in a polysaccharide known as glycogen. Glycogen has a structure similar to that of amylopectin, but glycogen has more branches. The branch points in glycogen occur about every 10 residues, whereas those in amylopectin occur about every 25 residues. The high degree of branching in glycogen has important physiological effects. When the body needs energy, many individualglucose units can be simultaneously removed from the ends of many branches.



Cellulose is the structural material of higher plants. Cotton, for example, is composed of about 90% cellulose, and wood is about 50% cellulose.

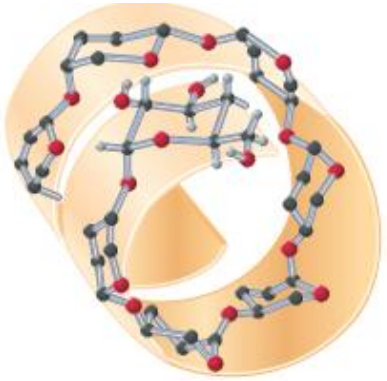
Like amylose, cellulose is composed of unbranched chains of D-glucose units. Unlike amylose, however,the glucose units in cellulose are joined by β-1,4'- glycosidic linkages rather than by α-1,4'- glycosidic linkages.



α-1,4'- glycosidic linkages are easier to hydrolyze than β-1,4'- glycosidic linkages because of the anomeric effect that weakens the bond to the anomeric carbon. All mammals have the enzyme (α-glucosidase) that hydrolyzes the α-1,4'- glycosidic linkages that join glucose units, but they do not have the enzyme (β-glucosidase) that hydrolyzes linkages. As a result, mammals *cannot* obtain the glucose they need by eating cellulose. However, bacteria that possess β-glucosidase inhabit the digestive tracts of grazing animals, so cows can eat grass and horses can eat hay to meet their nutritional requirements for glucose.

The different glycosidic linkages in starch and cellulose give these compounds very different physical properties.

- The α-linkages in starch cause amylose to form a helix that promotes hydrogen bonding of its OH groups to water molecules. As a result, starch is soluble in water.
- On the other hand, the β-linkages in cellulose promote the formation of intramolecular hydrogen bonds. Consequently, these molecules line up in linear arrays, and intermolecular hydrogen bonds form between adjacent chains. These large aggregatescause cellulose to be insoluble in water.



The α-1,4’ -glycosidic linkages in amylose cause it to form a lefthanded helix. Many of its OH groups form hydrogen bonds with water molecules

Strands of cellulose in a plant fiber

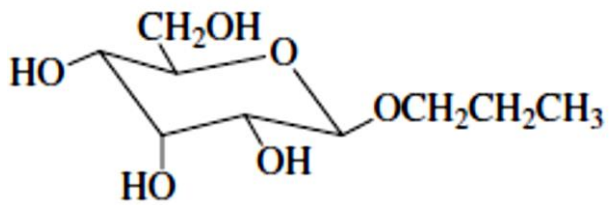
Problem 1: Aldohexoses A and B form the same osazone. A is oxidized by nitric acid to an optically active aldaric acid, and B is oxidized to an optically inactive aldaric acid. Ruff degradation of either A or B forms aldopentose C, which is oxidized by nitric acid to an optically active aldaric acid. Ruff degradation of C forms D, which is oxidized by nitric acid to an optically active aldaric acid. Ruff degradation of D forms (+)-glyceraldehyde. Identify A, B, C, and D.

The bottom-most asymmetric carbon in D must have the OH group on the right because D is degraded to (+)-glyceraldehyde. D must be D-threose, since D is oxidized to an optically active aldaric acid. The two bottom-most asymmetric carbons in C and D have the same configuration because C is degraded to D. C must be D-lyxose, since it is oxidized to an optically active aldaric acid. A and B, therefore, must be D-galactose and D-talose. Because A is oxidized to an optically active aldaric acid, it must be D-talose and B must be D-galactose.

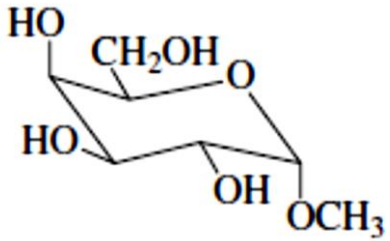
Problem 2: On treatment with phenylhydrazine, aldohexoses A and B give the same osazone. On treatment with warm nitric acid, A gives an optically inactive aldaric acid, but sugar B gives an optically active aldaric acid. Sugars A and B are both degraded to aldopentose C, which gives an optically active aldaric acid on treatment with nitric acid. Aldopentose C is degraded to aldotetrose D, which gives optically active tartaric acid when it is treated with nitric acid. Aldotetrose D is degraded to (+)-glyceraldehyde. Deduce the structures of sugars A, B, C, and D.

Problem 3: Name the following compounds, and indicate whether each is a reducing sugar or a nonreducing sugar:

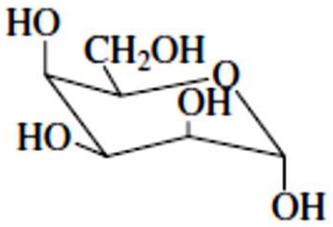
a.



b.



c.



d.