COURSE : SC202 (CHEMISTRY)

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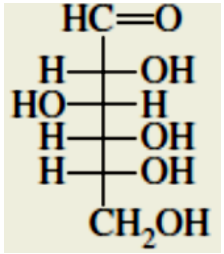
LECTURE-10

DATE: 30.1.2021

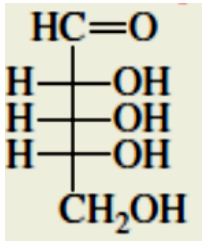
Carbohydrates

Carbohydrates are polyhydroxy aldehydes such as D-glucose, polyhydroxy ketones such as D-fructose, and compounds such as sucrose that can be hydrolyzed to polyhydroxy aldehydes or polyhydroxy ketones.

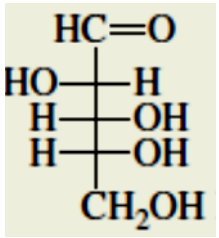
Most sugars have molecular formulas Cn (H_2O)m, suggesting that carbon atoms are combined in some way with water. In fact, the empirical formula of most simple sugars is C(H_2O) .



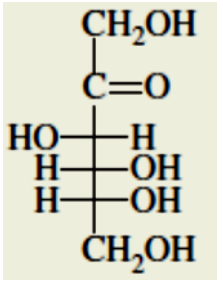
Glucose



Ribose



Arabinose

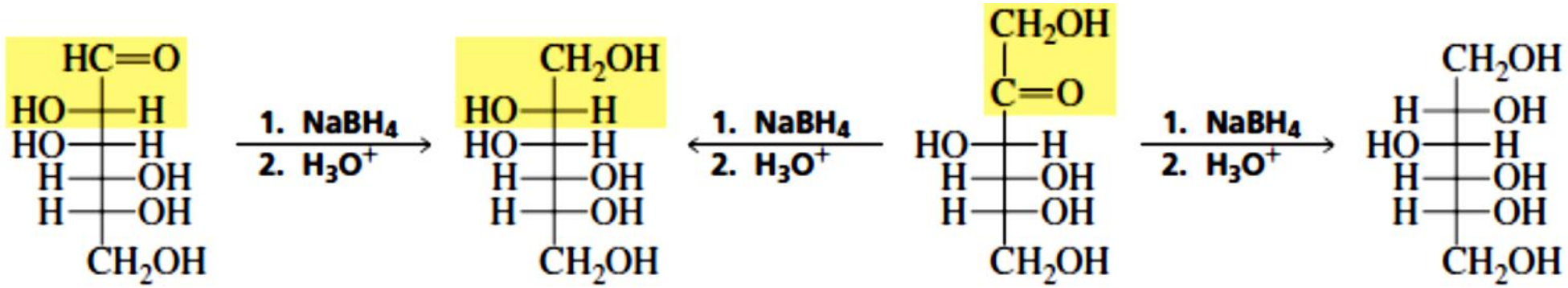


Fructose

Redox Reactions of Monosaccharides

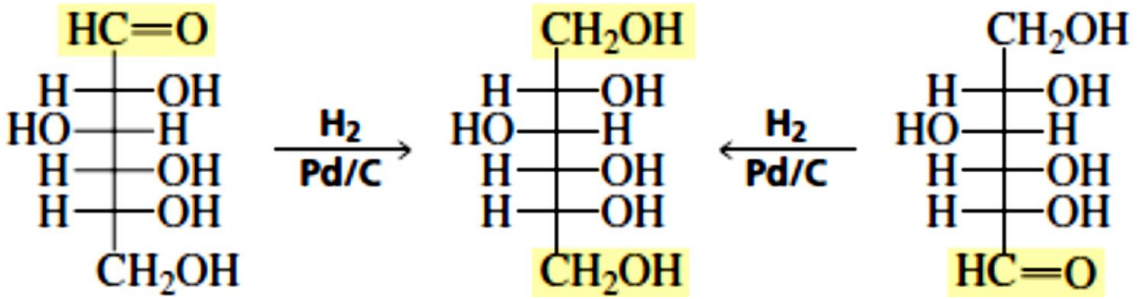
Reduction

The carbonyl group of aldoses and ketoses can be reduced by the usual carbonyl-group reducing agents like $NaBH_4$. The product of the reduction is a polyalcohol, known as an **alditol**. Reduction of an aldose forms one alditol. Reduction of a ketose forms two alditols because the reaction creates a new asymmetric carbon in the product.



D-mannose | D-mannitol, an alditol | D-fructose | D-glucitol, an alditol

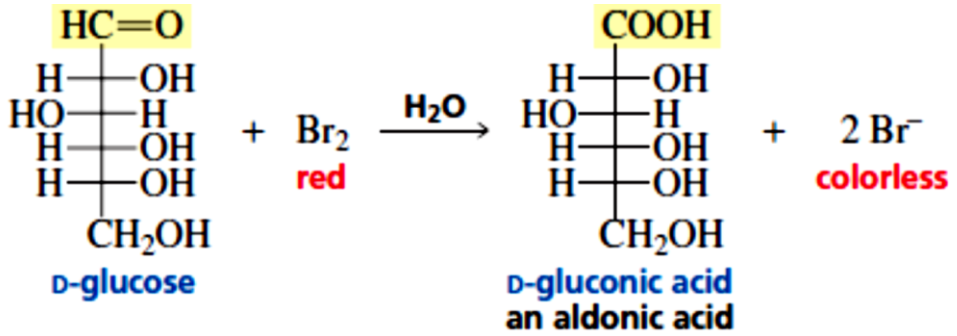
D-Glucitol—also called sorbitol—is about 60% as sweet as sucrose. It is found in plums, pears, cherries, and berries and is used as a sugar substitute in the manufacture of candy. D-Glucitol is also obtained from the reduction of either D-glucose or L-gulose.



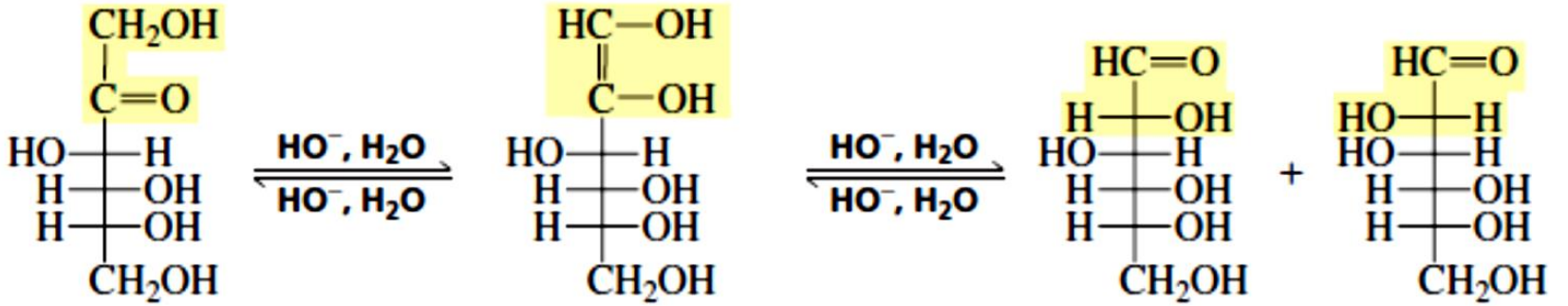
D-glucose | D-glucitol, an alditol | L-gulose, drawn upside down

Oxidation

1. Br_2 is a mild oxidizing agent and easily oxidizes the aldehyde group, but it cannot oxidize ketones or alcohols. Consequently, if a small amount of an aqueous solution of Br_2 is added to an unknown monosaccharide, the reddish-brown color will disappear if the monosaccharide is an aldose, but will persist if the monosaccharide is a ketose.



2. Both aldoses and ketoses are oxidized to aldonic acids by Tollens reagent (Ag^+, NH_3, OH^-)so that reagent cannot be used to distinguish between aldoses and ketoses. Ketoses are oxidized because the reaction is carried out under basic conditions, and in a basic solution, ketoses are converted into aldoses by enolization



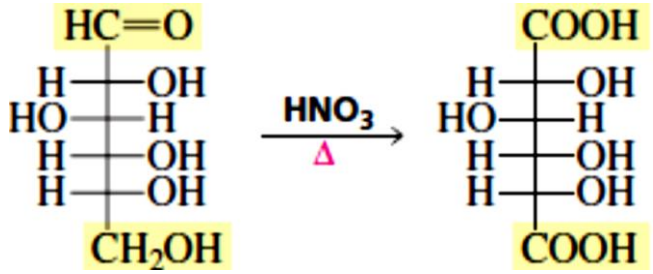
D-fructose
a ketose

enol of D-fructose
enol of D-glucose
enol of D-mannose

D-glucose
an aldose

D-mannose
an aldose

3. If a stronger oxidizing agent is used (such as HNO_3), one or more of the alcohol groups can be oxidized in addition to the aldehyde group. A primary alcohol is the one most easily oxidized. The product that is obtained is called an **aldaric acid**.

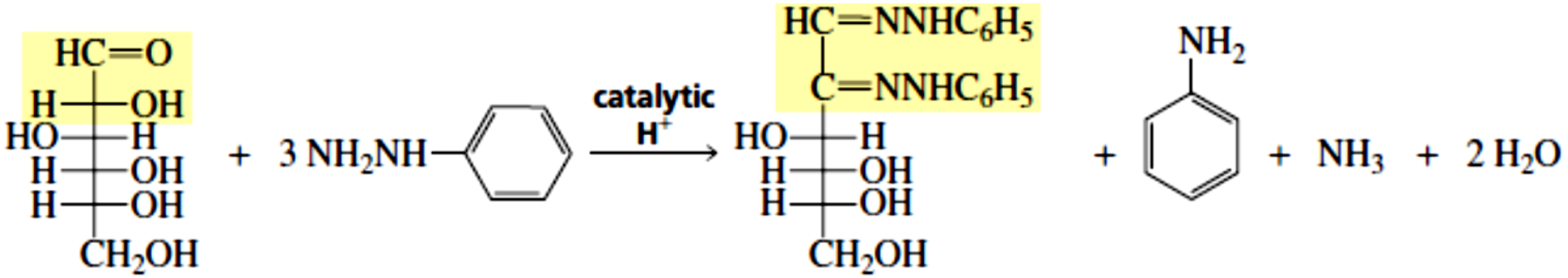


D-glucose D-glucaric acid(**an aldaric acid**)

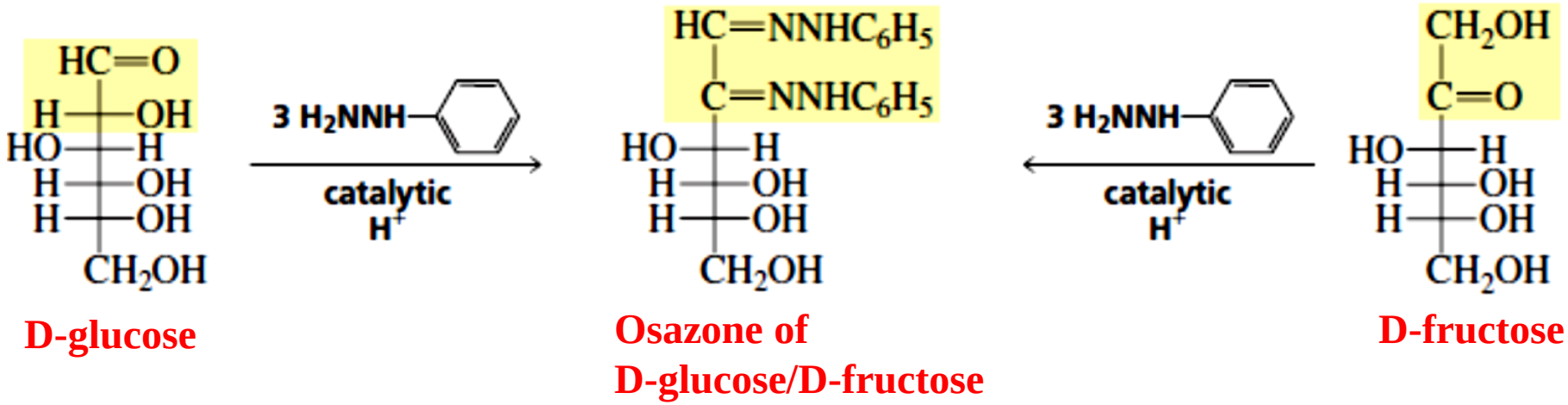
Aldoses reduce Tollens'reagent, as we would expect aldehydes to do. They also reduce Fehling's solution, an alkaline solution of cupric ion complexed with tartrate ion (or Benedict's solution, in which complexing is with citrate ion); the deep-blue color of the solution is discharged, and red cuprous oxide precipitates.

Osazone Formation

Aldoses and ketoses, in contrast, react with three equivalents of phenylhydrazine, forming osazones. One equivalent functions as an oxidizing agent and is reduced to aniline and ammonia. Two equivalents form imines with carbonyl groups. The reaction stops at this point, regardless of how much phenylhydrazine is present.

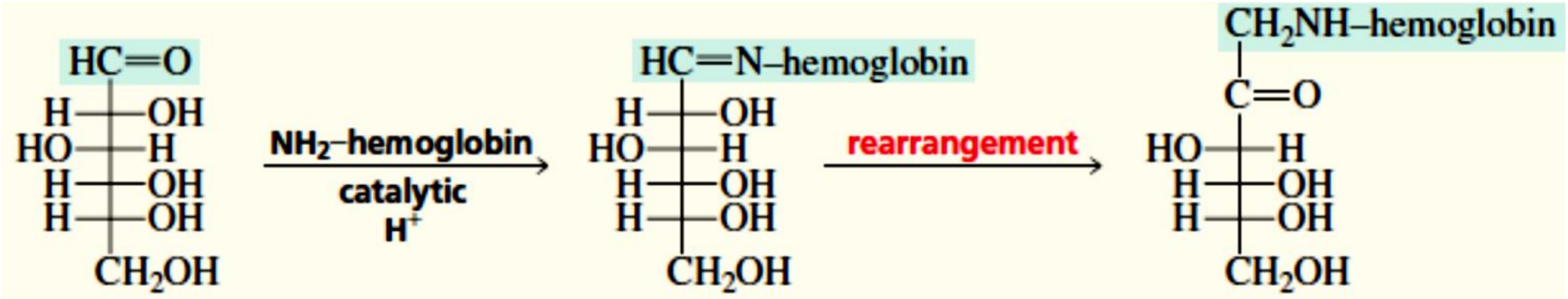


Osazone of D-glucose



D-glucose **Osazone of D-glucose/D-fructose** **D-fructose**

Measuring The Blood Glucose Levels of Diabetics

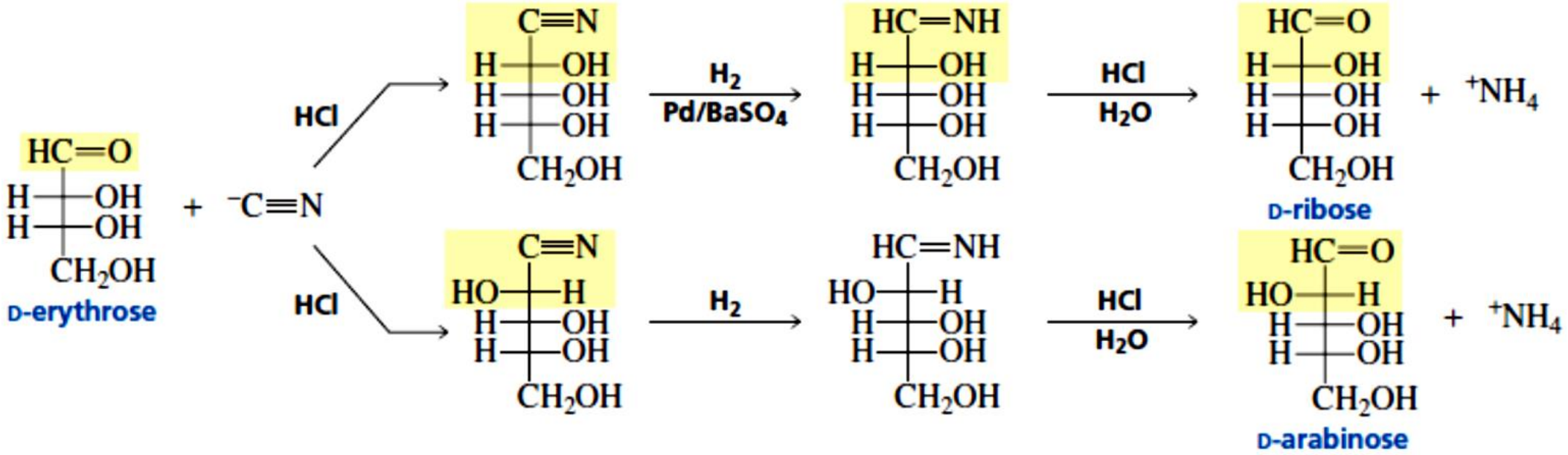


D-glucose **hemoglobin-A_{Ic}**

Glucose reacts with an amino group of hemoglobin to form an imine that subsequently undergoes an irreversible rearrangement to a more stable α-amino ketone known as hemoglobin-A_{Ic} .Measuring the hemoglobin-A_{Ic} level is a way to determine whether the blood glucose level of a diabetic is being controlled. Cataracts, a common complication in diabetics, are caused by the reaction of glucose with the NH_2 group of proteins in the lens of the eye. The arterial rigidity common in old age may be attributable to a similar reaction of glucose with the NH_2 group of proteins

Chain Elongation: The Kiliani–Fischer Synthesis

The carbon chain of an aldose can be increased by one carbon in a **Kiliani–Fischer synthesis**.

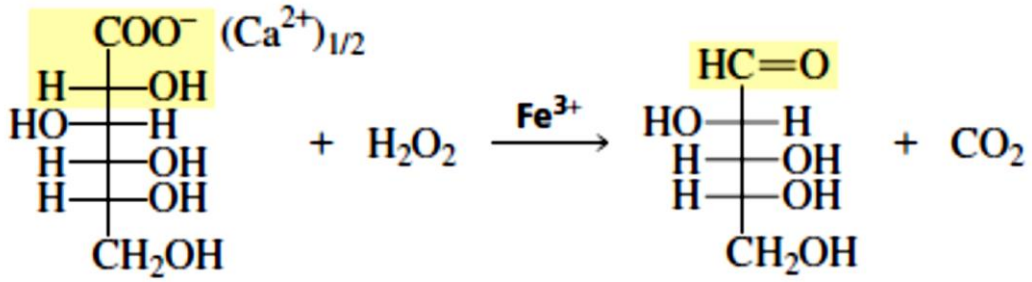


In the first step of the synthesis (the Kiliani portion), the aldose is treated with sodium cyanide and HCl. Addition of cyanide ion to the carbonyl group creates a new asymmetric carbon. Consequently, two cyanohydrins that differ only in configuration at C-2 are formed. The cyanohydrins are reduced to imines, using a partially deactivated palladium (on barium sulfate) catalyst so that the imines would not be further reduced to amines. The imines could then be hydrolyzed to aldoses

The Kiliani–Fischer synthesis leads to a pair of C-2 epimers.

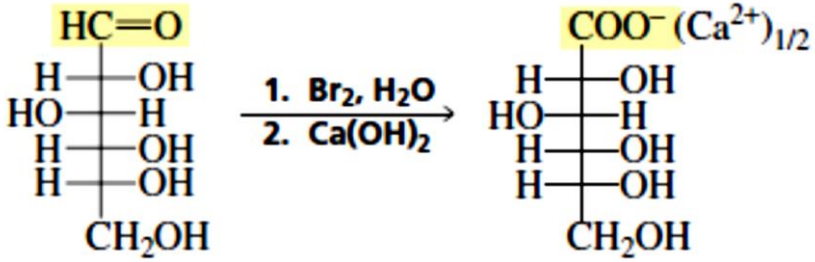
Chain Shortening: The Ruff Degradation

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.



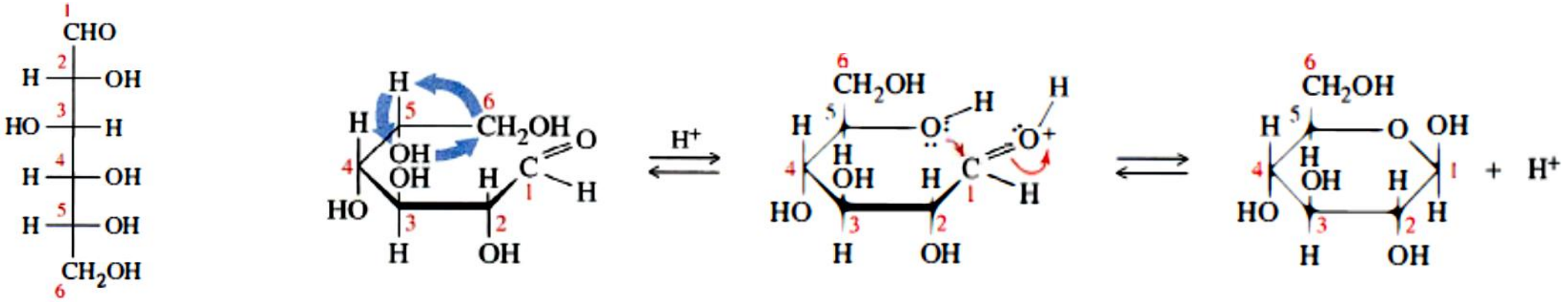
calcium D-gluconate **D-arabinose**

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

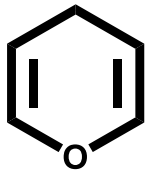


D-glucose **calcium D-gluconate**

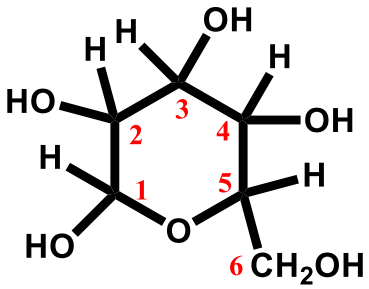
Pyranose and Furanose Names



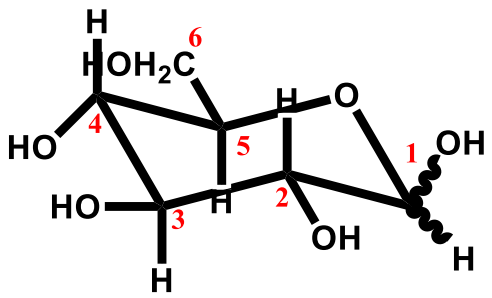
- Cyclic structures of monosaccharides are named according to their five- or six-membered rings.
- A six-membered cyclic hemiacetal is called a **pyranose**, derived from the name of the six-membered cyclic ether pyran.
- A five-membered cyclic hemiacetal is called a **furanose**, derived from the name of the five-membered cyclic ether furan.



Pyran

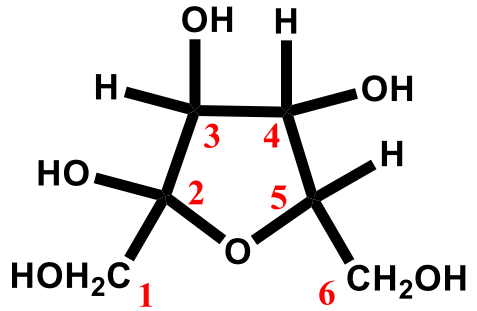


pyranose

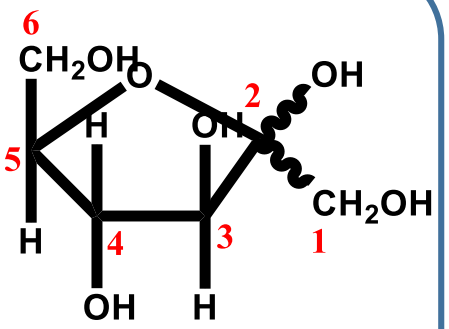


D-glucopyranose

Furan



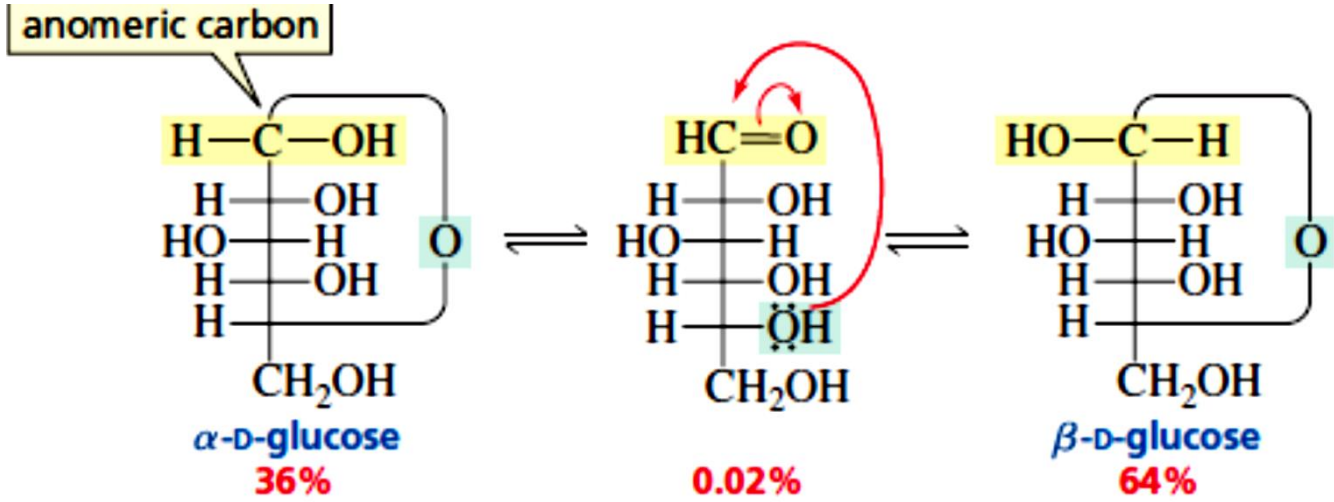
furanose



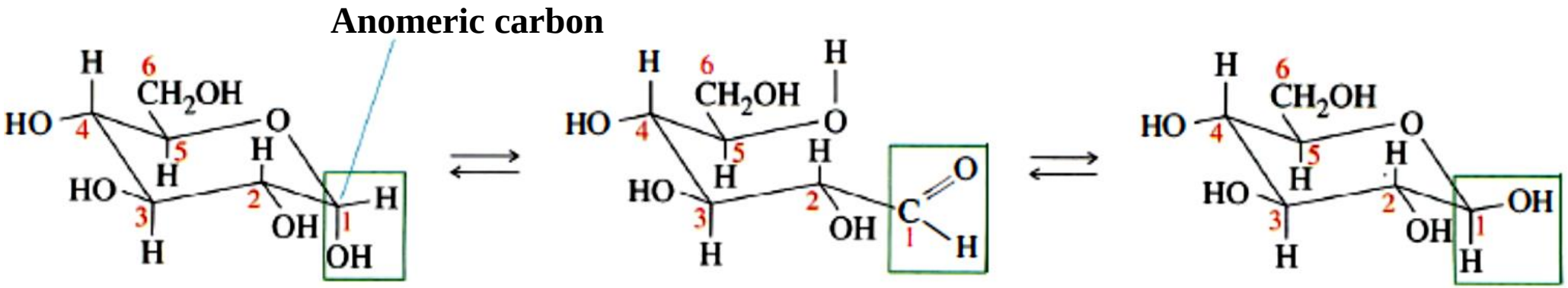
D-fructofuranose

Cyclic Structure of Monosaccharides

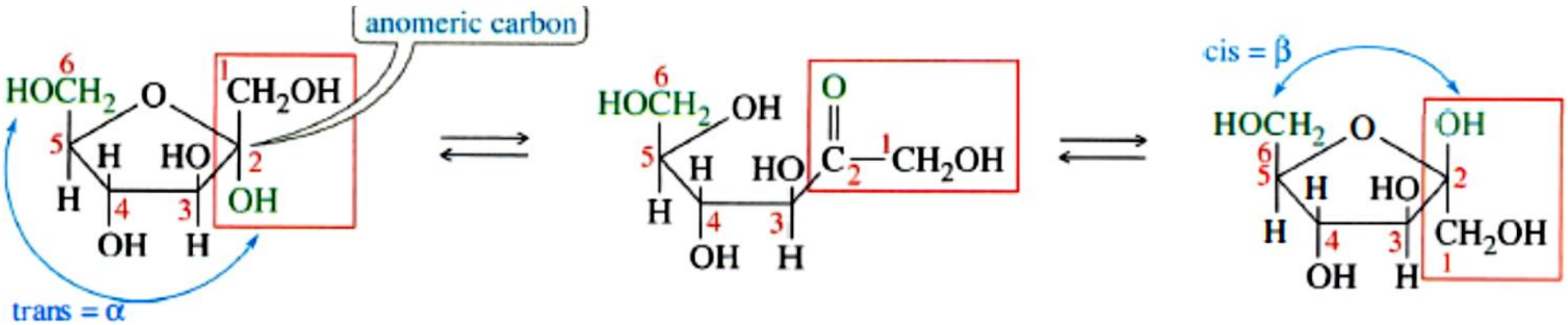
D-Glucose exists in three different forms: the open-chain form of D-glucose that we have been discussing and two cyclic forms— α-D-glucose and β-D-glucose.



- α-D-glucose and β-D-glucose are called **anomers**. **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.
- Anomers, like epimers, are a particular kind of diastereomers—they differ in configuration at only one carbon atom.
- In an aqueous solution, the open-chain compound is in equilibrium with the two cyclic hemiacetals. Formation of the cyclic hemiacetals proceeds nearly to completion (unlike formation of acyclic hemiacetals), so very little glucose exists in the open-chain form (about 0.02%). At equilibrium, there is almost twice as much β-D-glucose (64%) as α-D-glucose (36%).



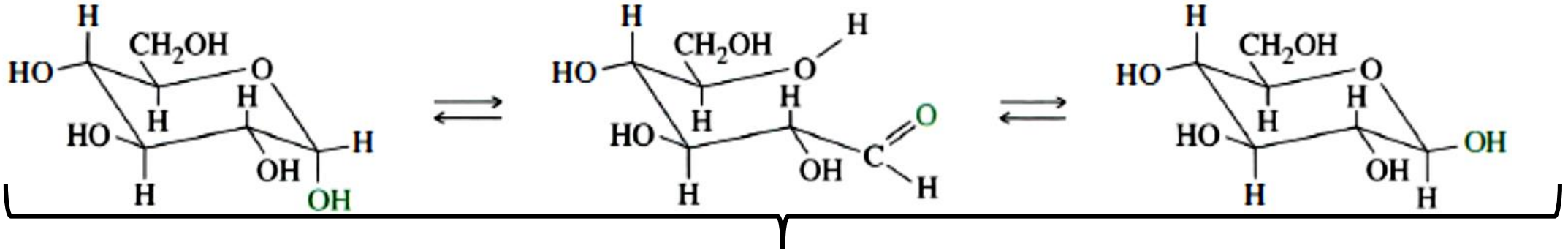
The anomer with the anomeric -OH group down (axial) is called the α(alpha) anomer, and the one with the anomeric -OH group up (equatorial) is called the β (beta) anomer.



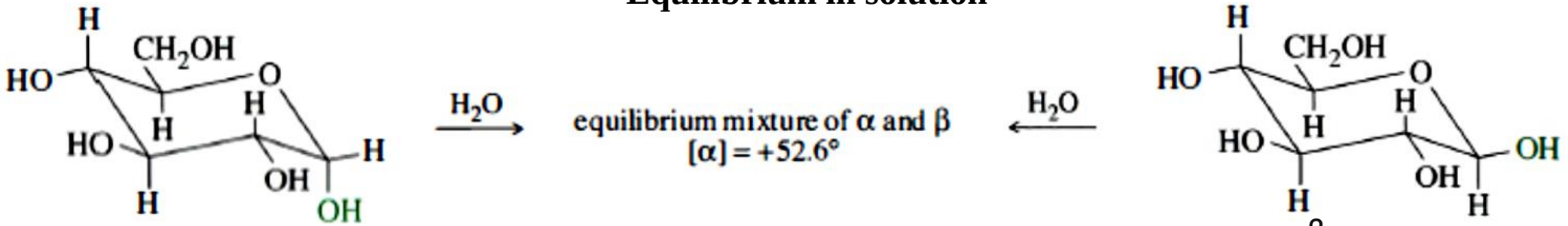
The α anomer of fructose has the anomeric -OH group down, trans to the terminal – CH_2OH group.
The β anomer has the anomeric hydroxyl group up, cis to the terminal - CH_2OH.

Mutarotation

When one of the pure glucose anomers dissolves in water, an interesting change in the specific rotation is observed. When the α anomer dissolves, its specific rotation gradually decreases from an initial value of + 112.2° to +52.6°. When the pure β anomer dissolves, its specific rotation gradually increases from + 18.7° to the same value of +52.6°. This change in rotation occurs because, in water, the hemiacetal opens to form the aldehyde and, when the aldehyde recyclizes, both α-D-glucose and β-D-glucose can be formed. Eventually, the three forms of glucose reach equilibrium concentrations. The specific rotation of the equilibrium mixture is +52.6°. A slow change in optical rotation to an equilibrium value is known as **mutarotation.**



Equilibrium in solution

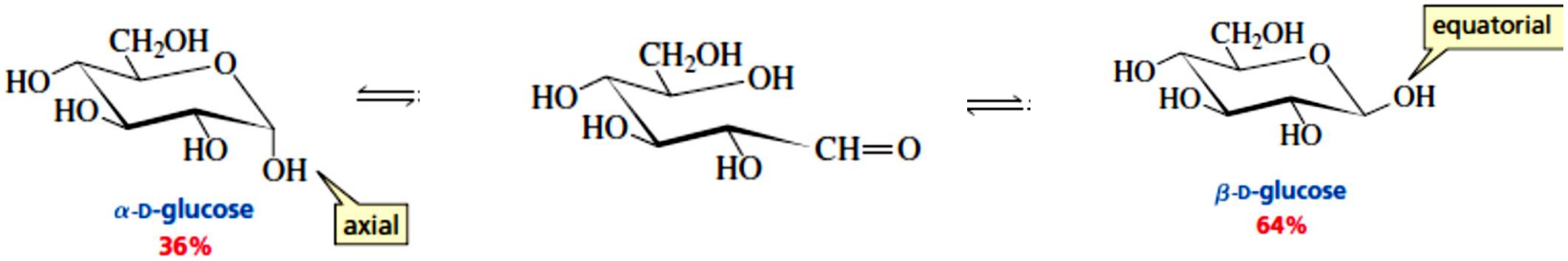


pure α anomer
mp 146°C, [α] = + 112.2°

pure β anomer
mp 146°C, [α] = + 18.7°

Why is there more β-D-glucose than α-D-glucose in an aqueous solution at equilibrium?

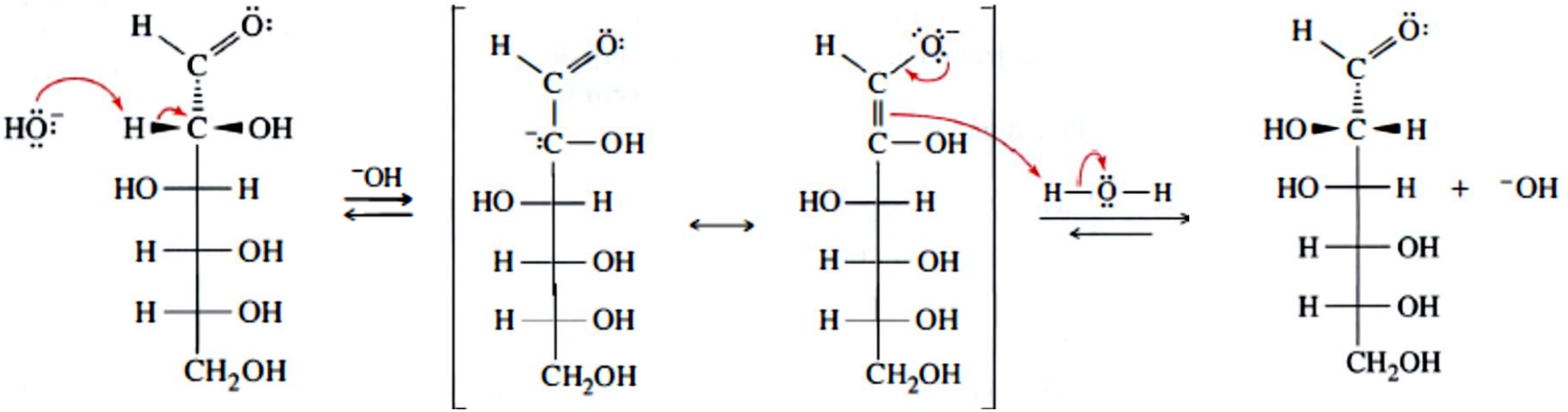
The OH group bonded to the anomeric carbon is in the equatorial position in β-Dglucose, whereas it is in the axial position in α-D-glucose. Therefore, β-D-glucose is more stable than α-D-glucose, so β-D-glucose predominates at equilibrium in an aqueous solution.



Reactions of Monosaccharides: Side Reactions in Base

One of the most important aspects of sugar chemistry is the inability, in most cases, to use basic reagents because they cause unwanted side reactions. Two common base-catalyzed side reactions are **epimerization and enediol rearrangement.**

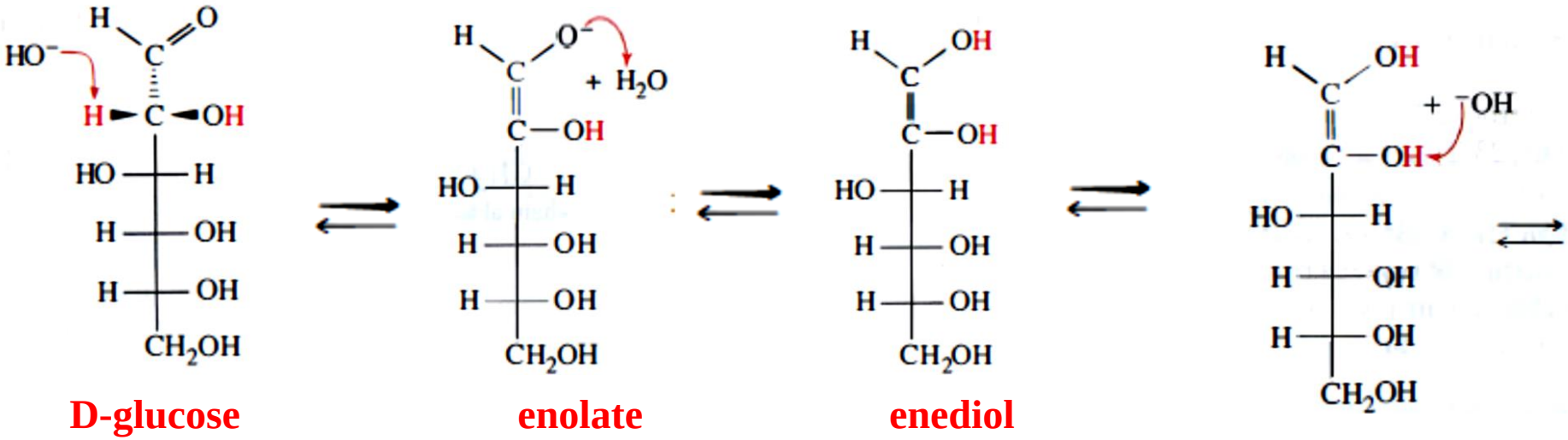
Base-Catalyzed Epimerization of Glucose

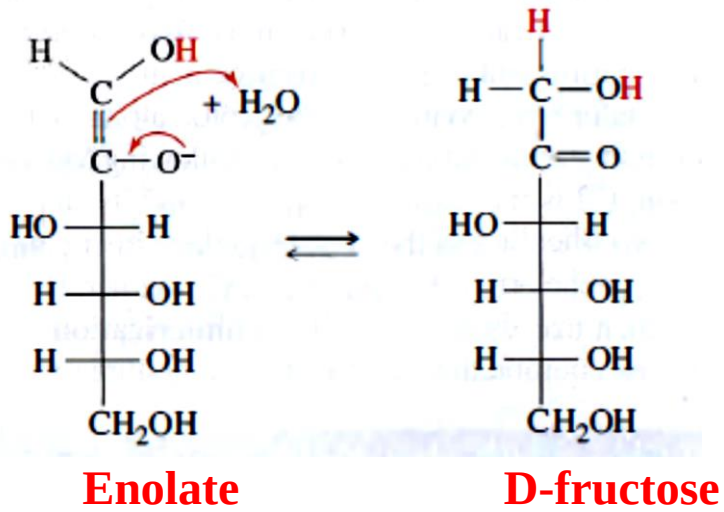


D-glucose **enolate** **D-mannose**

Under basic conditions, the proton alpha to the aldehyde (or ketone) carbonyl group is reversibly removed. In the resulting enolate ion, C2 is no longer asymmetric, and its stereochemistry is lost. Reprotonation can occur on either face of the enol ate, giving either configuration. The result is an equiliblium mixture of the original sugar and its C2 epimer. Because a mixture of epimers results, this stereochemical change is called **epimerization**.

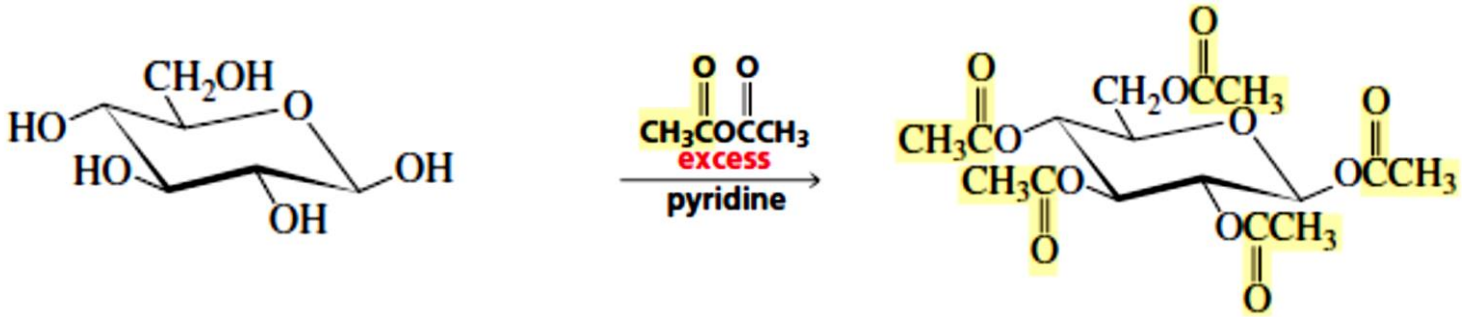
Another base-catalyzed side reaction is the **enediol rearrangement**, which moves the carbonyl group up and down the chain. If the enolate ion (formed by removal of a proton on C2) reprotonates on the C l oxygen, an enediol intermediate results. Removal of a proton from the C2 oxygen and reprotonation on C l gives fructose, a ketose.





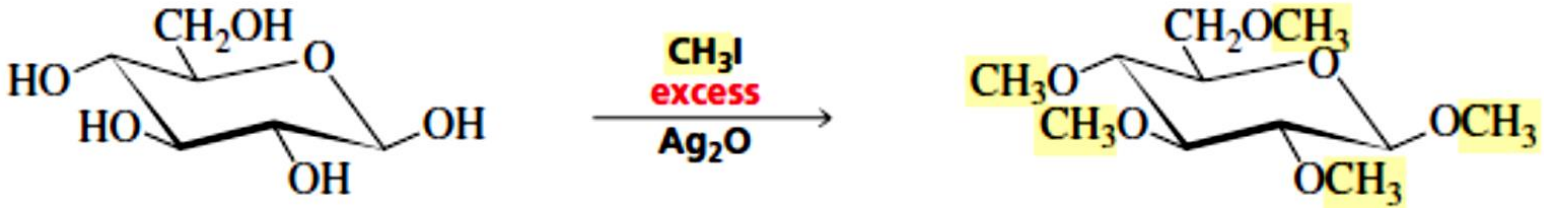
Acylation and Alkylation of Monosaccharides

The OH groups of monosaccharides show the chemistry typical of alcohols. For example, they react with acetyl chloride or acetic anhydride to form esters



penta-*O*-acetyl- β-D-glucose

The OH groups also react with methyl iodide/silver oxide to form ethers. The OH group is a relatively poor nucleophile, so silver oxide is used to increase the leaving tendency of the iodide ion in the S_N2 reaction.

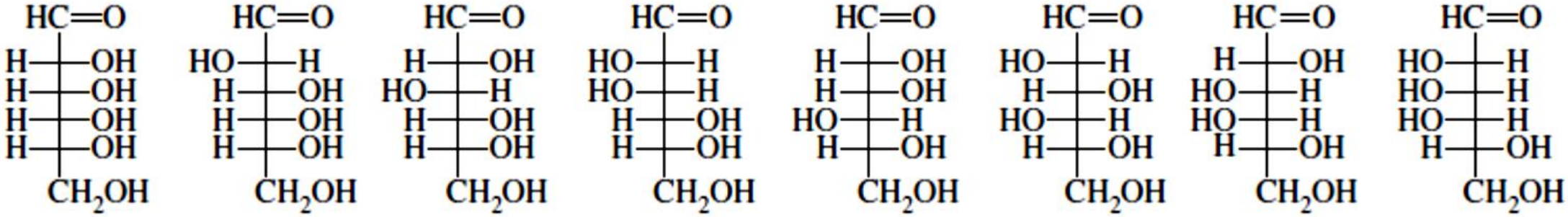


methyl tetra-*O*-methyl- β-D-glucoside

Stereochemistry of Glucose: The Fischer Proof

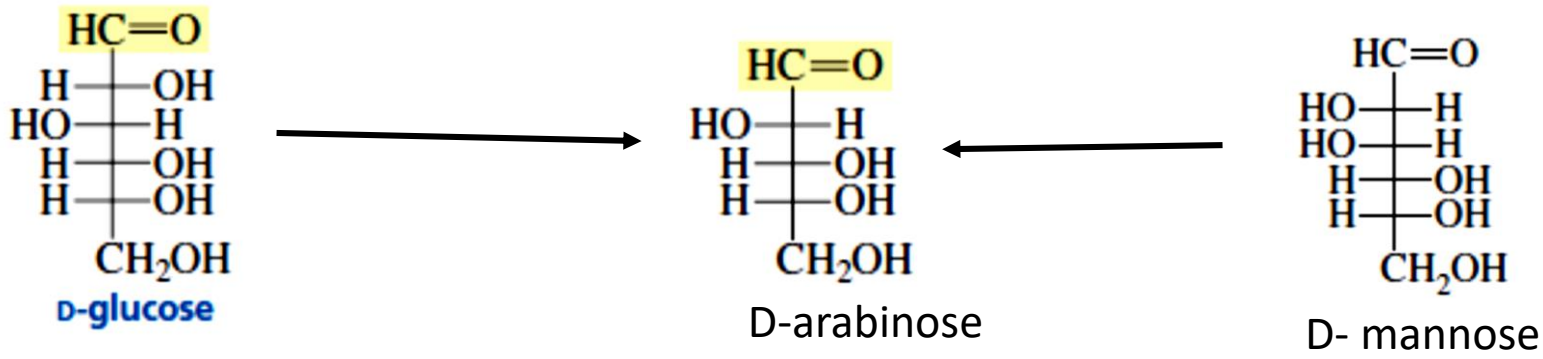
Emil Fischer determined the structures of glucose and the other aldohexoses in 1891, only 14 years after the tetrahedral structure of carbon had been proposed. Fischer received the Nobel Prize for this work in 1902. Much of Fischer's proof used the carbohydrate reactions we have studied, together with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



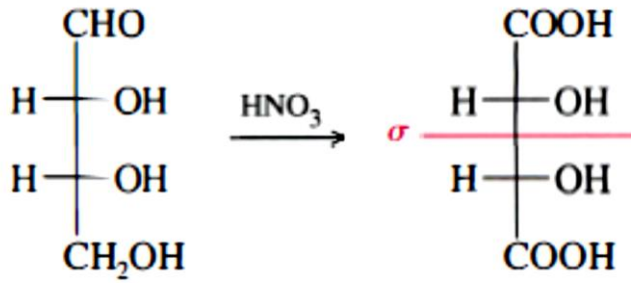
1 D-allose **2** D-altrose **3** D-glucose **4** D-mannose **5** D-gulose **6** D-idose **7** D-galactose **8** D-talose

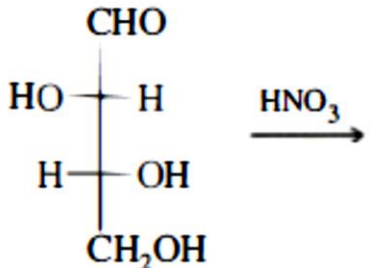
1.On Ruff degradation, glucose and mannose give the same aldopentose: D- (-) -arabinose.

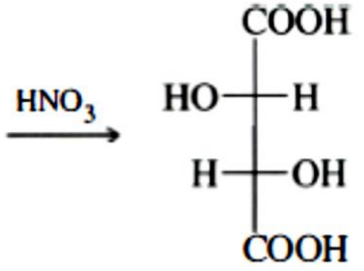


This clue suggests that glucose and mannose are C2 epimers

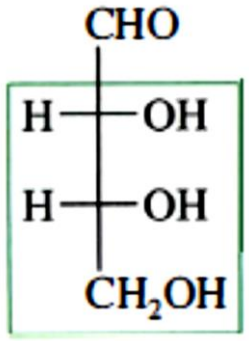
2. On Ruff degradation, D-(-)-arabinose gives the aldotetrose D-(-) -erythrose. Upon treatment with nitric acid, erythrose gives an optically inactive aldaric acid, meso-tartaric acid.



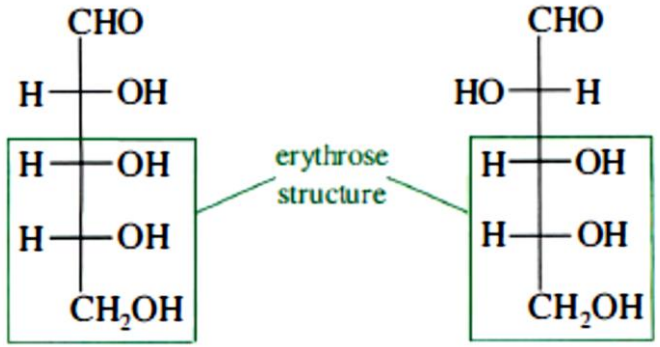




Because oxidation of D-erythrose gives an optically inactive aldaric acid, erythrose must correspond to structure I.

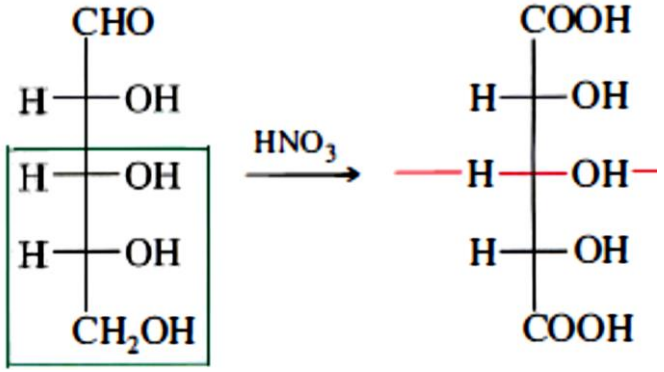


D-(-)-erythrose

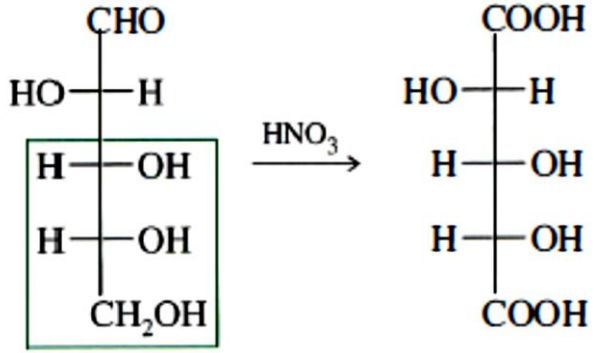


possible structures of D-(-)-arabinose

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



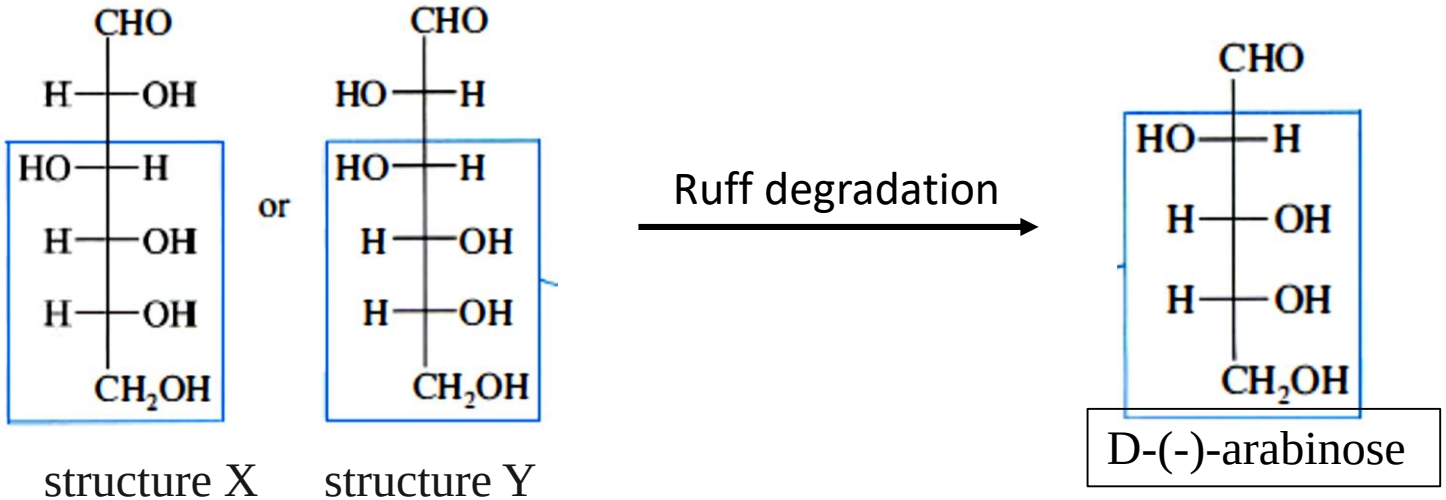
structure A optically inactive aldaric acid



structure B optically active aldaric acid

D-(-)-arabinose

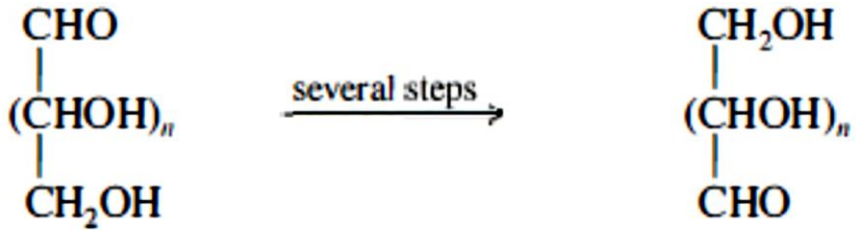
Since glucose and mannose degrade to arabinose, structures X and Y shown below must be glucose and mannose. At this point, however, it is impossible to tell which structure is glucose and which is mannose.

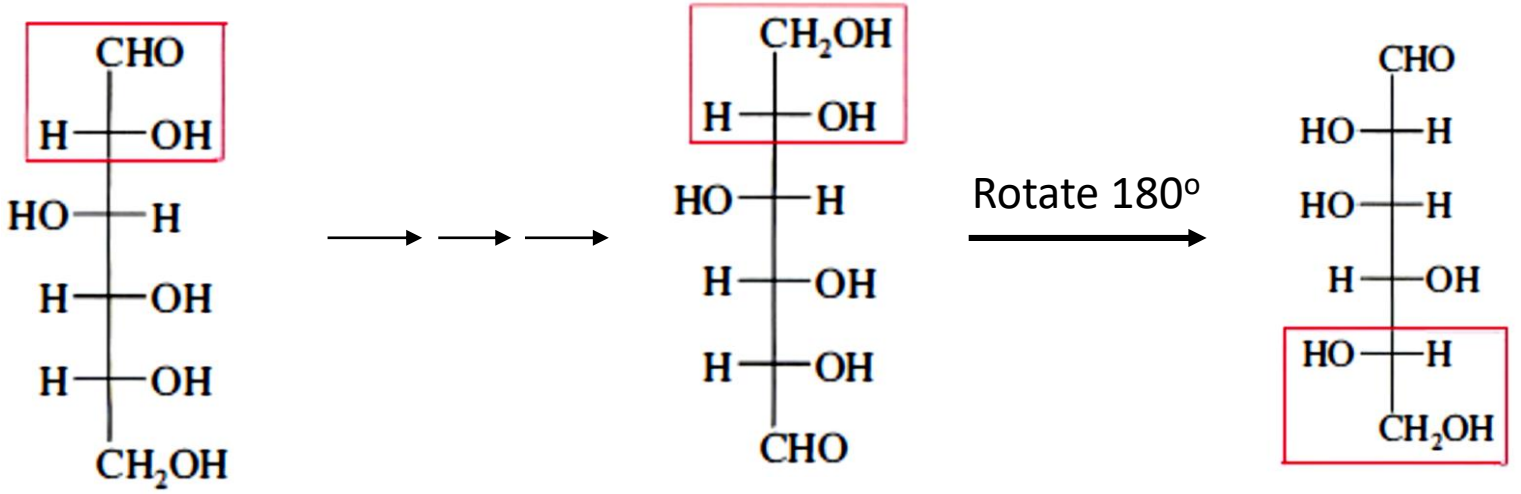


structure X structure Y

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.

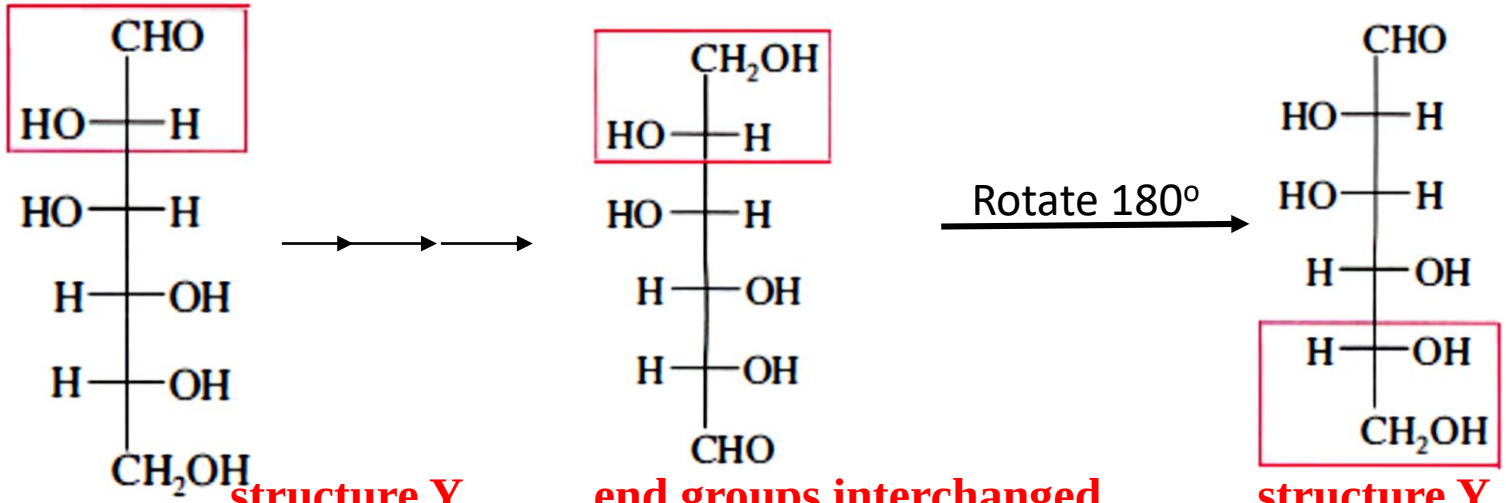
Fischer had developed a clever method for converting the aldehyde group of an aldose to an alcohol while converting the terminal alcohol group to an aldehyde. In effect,this synthesis interchanges the two end groups of the aldose chain.





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)**

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.