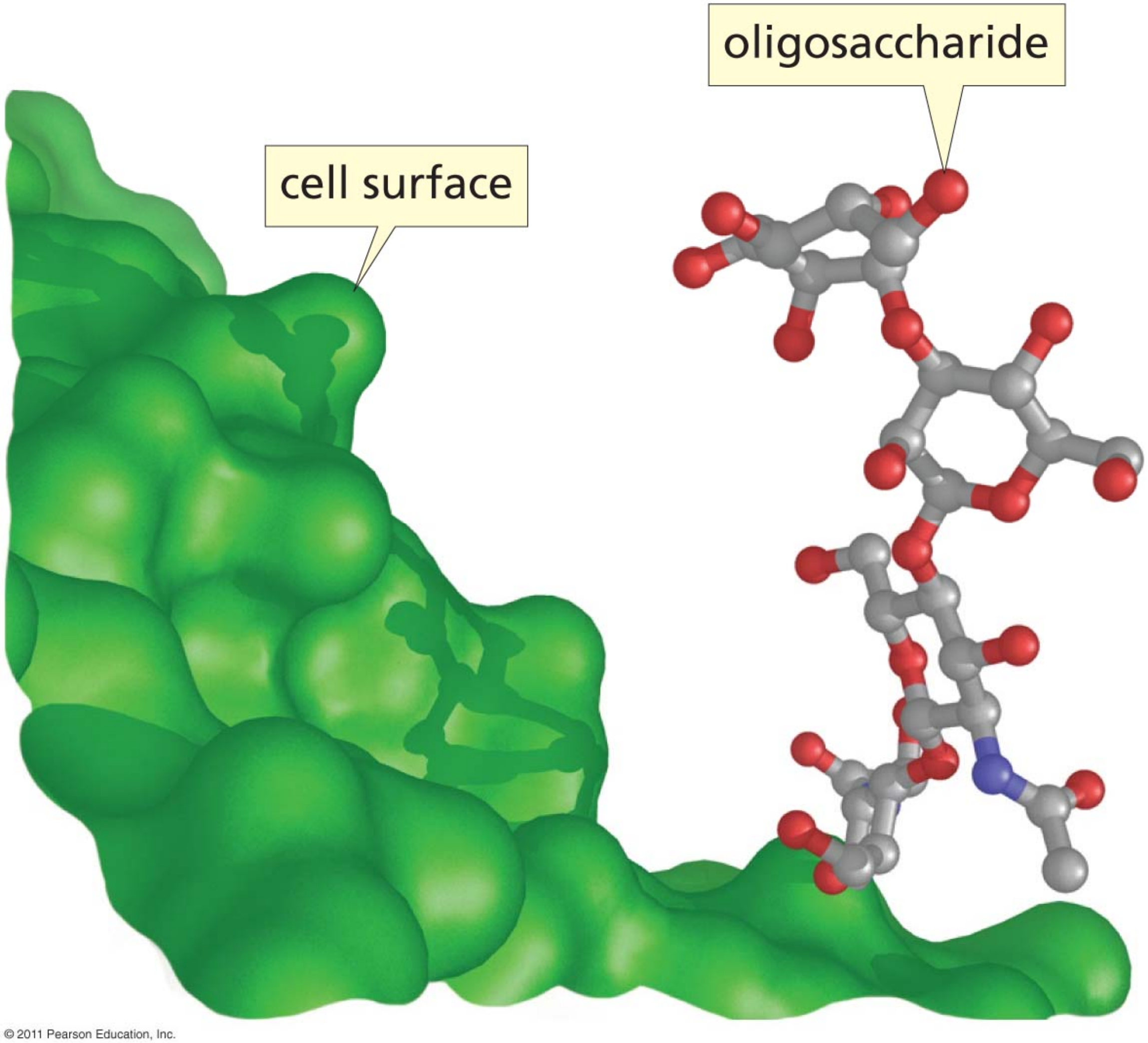
Organic Chemistry

6th Edition

Paula Yurkanis Bruice

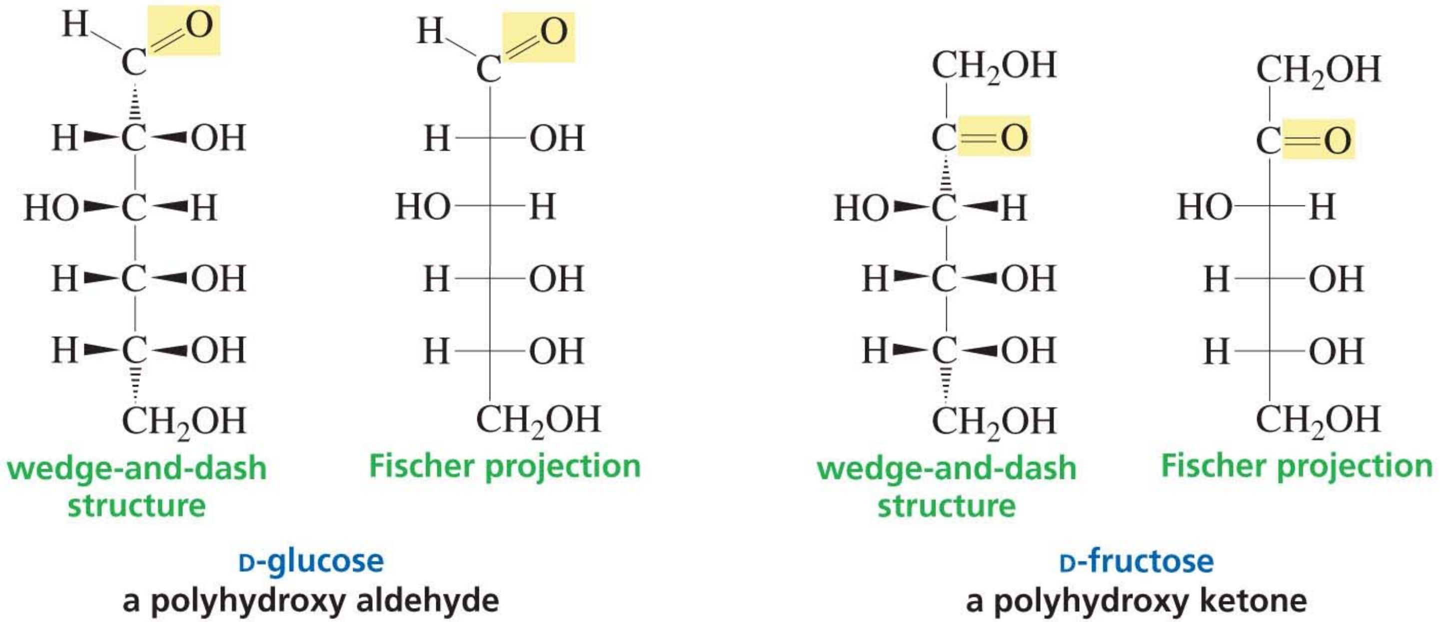


Chapter 22

The Organic Chemistry of Carbohydrates

Carbohydrates

- General molecular formula is $C_n(H_2O)_n$.
- Structurally, are polyhydroxy aldehydes or ketones.
- The most abundant carbohydrate in nature is glucose.



wedge-and-dash structure

Fischer projection

wedge-and-dash structure

Fischer projection

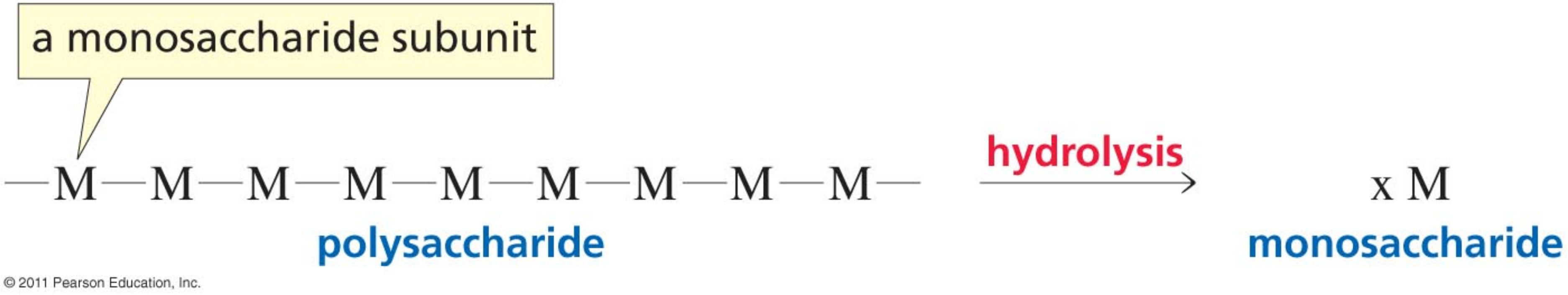
D-glucose
a polyhydroxy aldehyde

D-fructose
a polyhydroxy ketone

Simple carbohydrates are monosaccharides

Complex carbohydrates contain two or more sugar units linked together:

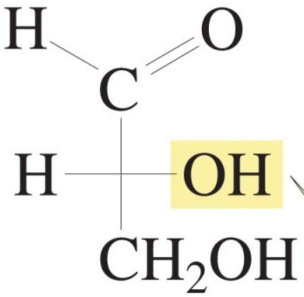
- Disaccharides
- Oligosaccharides
- Polysaccharides



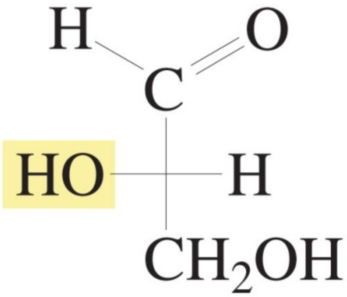
Polyhydroxy aldehydes are aldoses

Polyhydroxy ketones are ketoses

D and L notations are used to describe the configurations of carbohydrates:

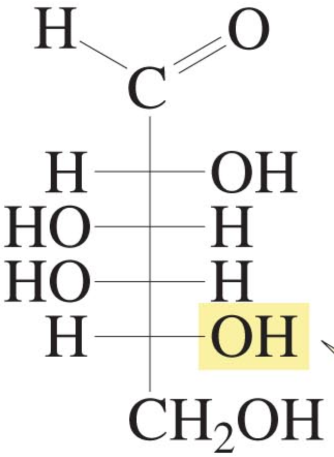


D-glyceraldehyde



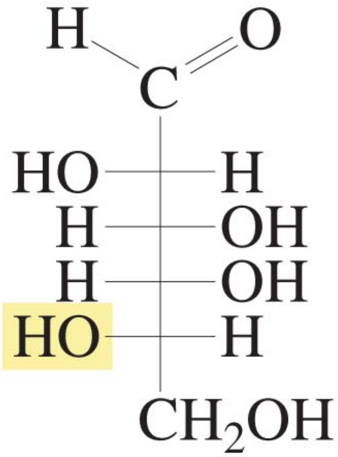
L-glyceraldehyde

the OH group
is on the right



D-galactose

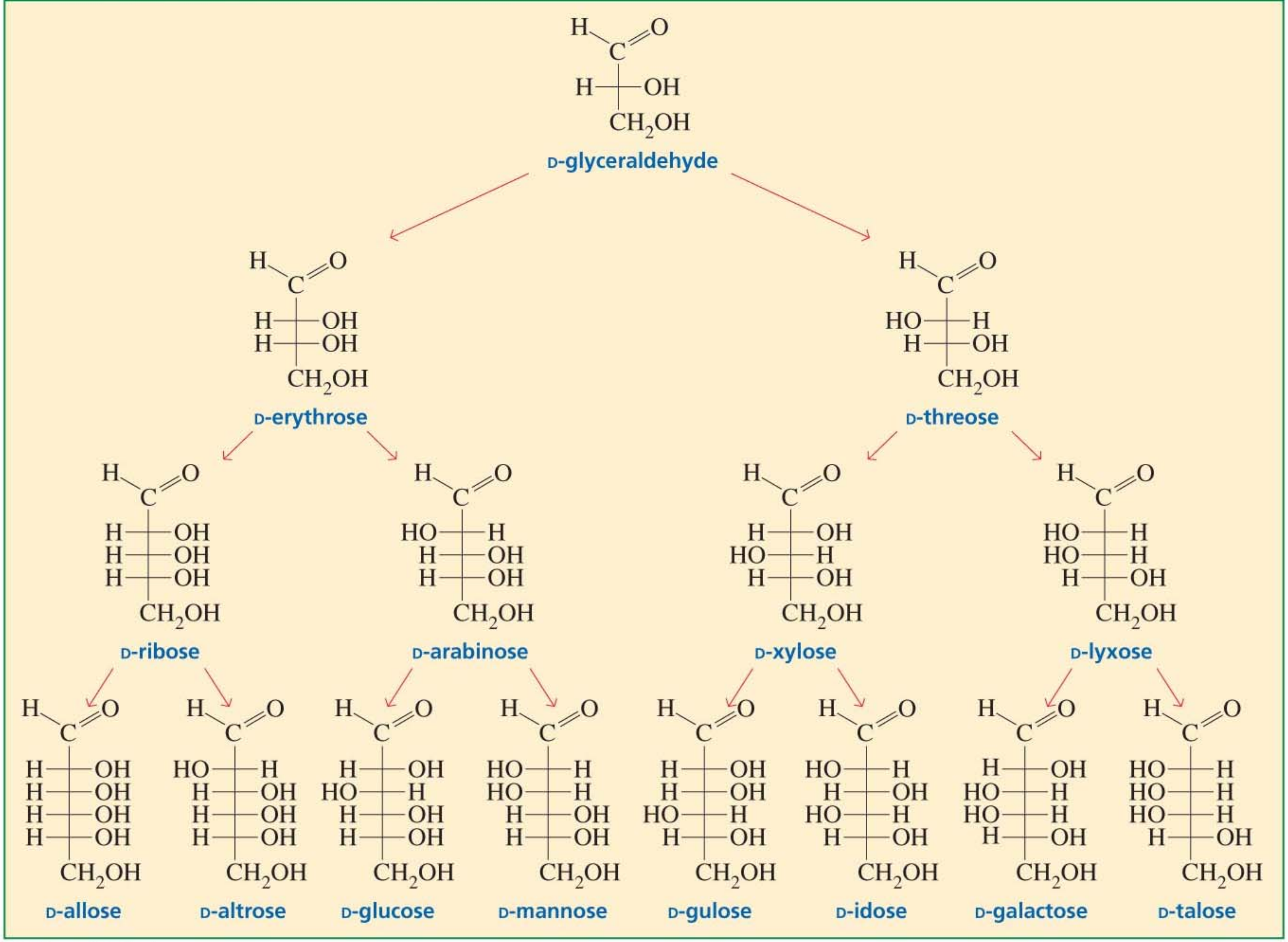
the OH group
is on the right



L-galactose

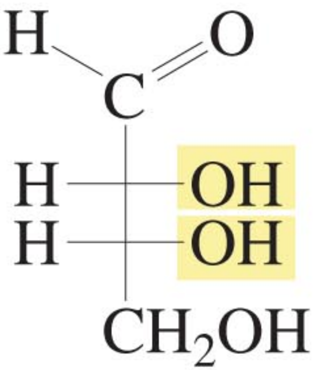
mirror image of D-galactose

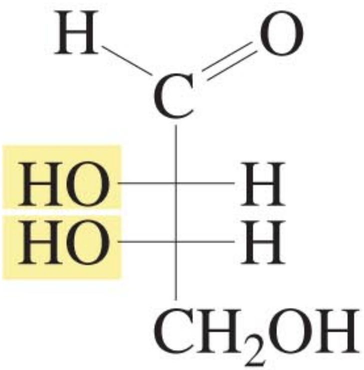
Table 22.1 Configurations of the D-Aldoses

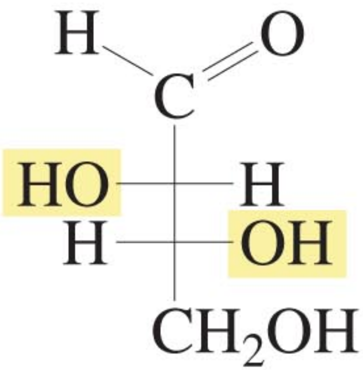


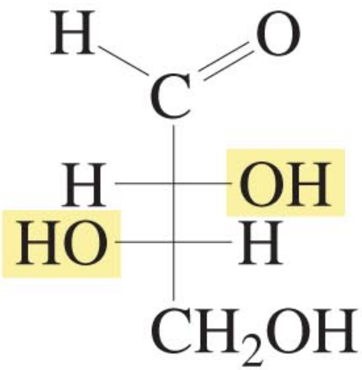
Configurations of Aldoses

Aldotetroses have two asymmetric centers and four stereoisomers:


D-erythrose


L-erythrose


D-threose


L-threose

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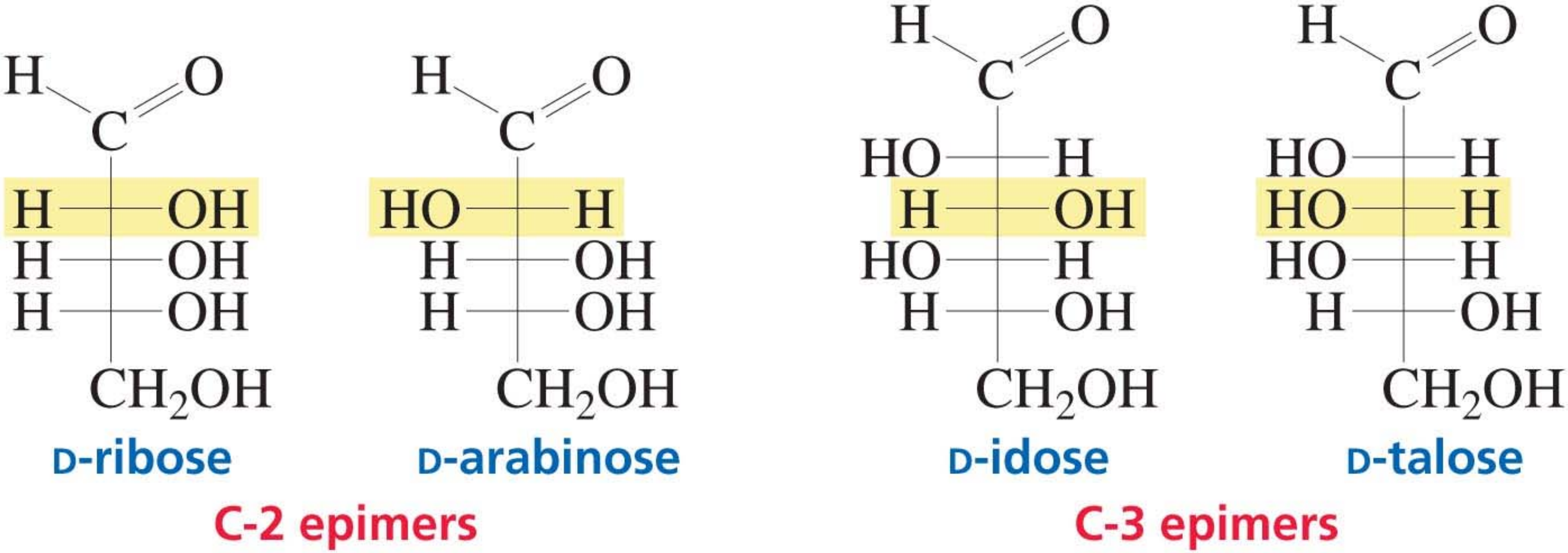
Aldopentoses have three asymmetric centers and eight stereoisomers

Aldohexoses have four asymmetric centers and 16 stereoisomers

Diastereomers that differ in configuration at only one asymmetric center are called epimers:



D-ribose D-arabinose

C-2 epimers

D-idose D-talose

C-3 epimers

D-Mannose is the C-2 epimer of D-glucose

D-Galactose is the C-4 epimer of D-glucose

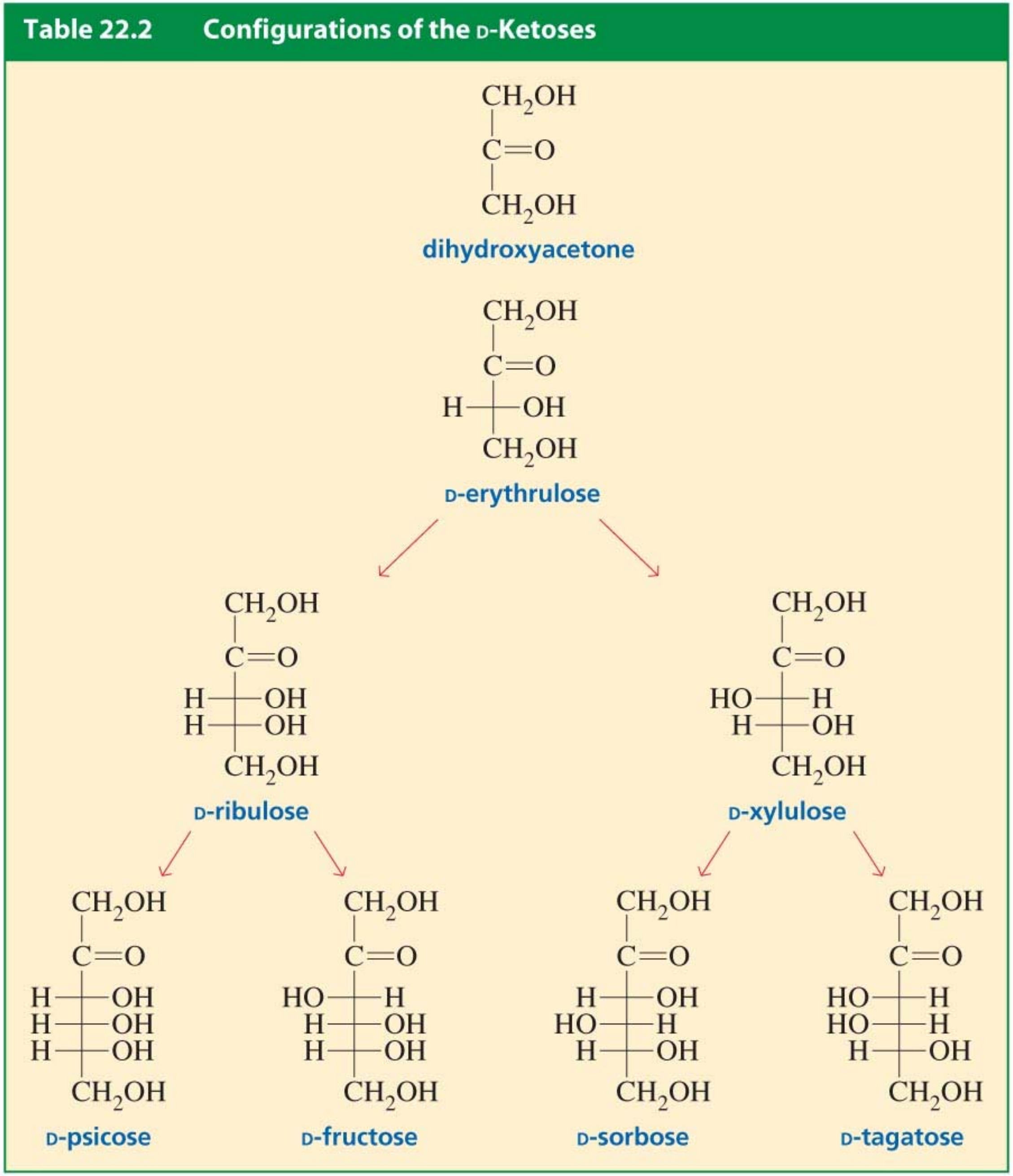
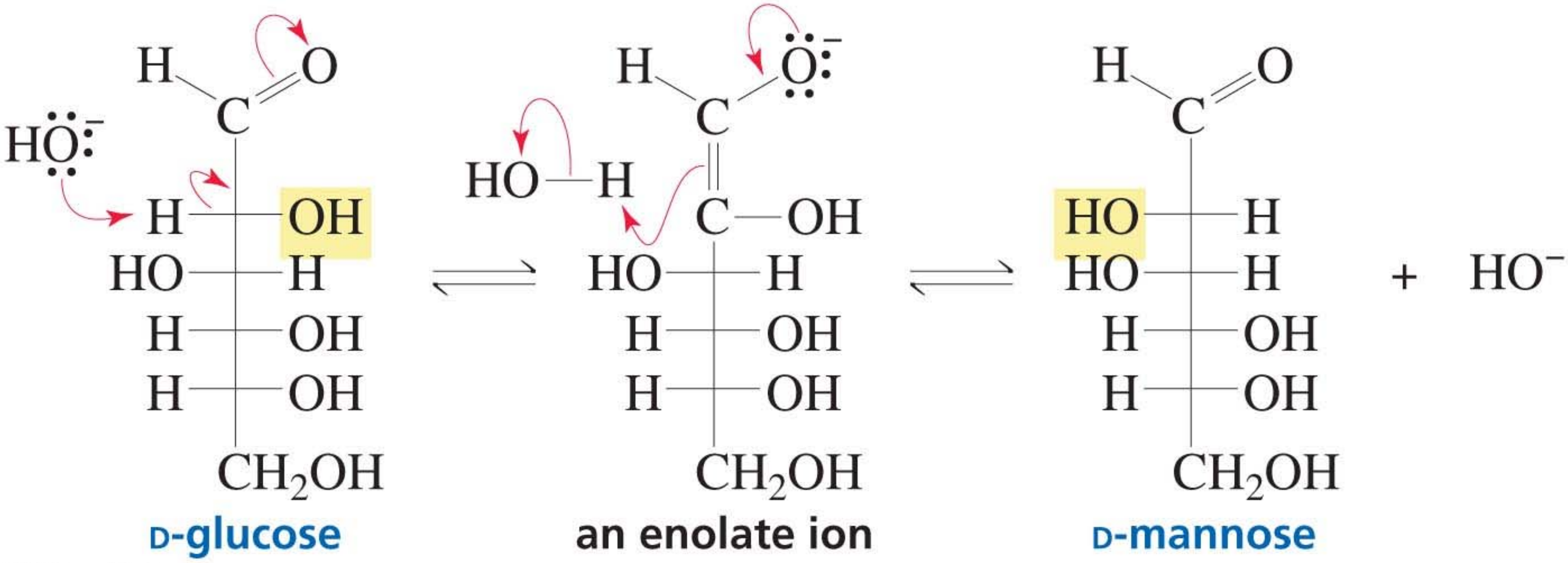


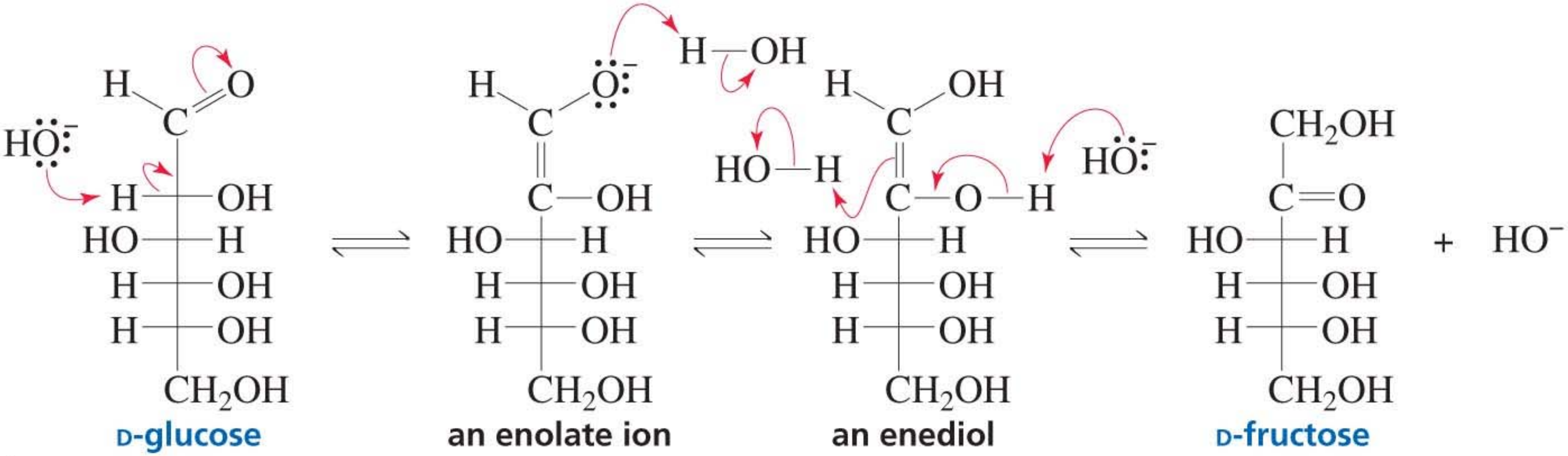
Table 22.2 Configurations of the D-Ketoses

- **A ketose has one fewer asymmetric center than an aldose.**
- **Therefore, ketoses have fewer stereoisomers than aldoses.**
- **Naturally occurring ketoses have the ketone group in the 2-position.**

Mechanism for the base-catalyzed epimerization of a monosaccharide:

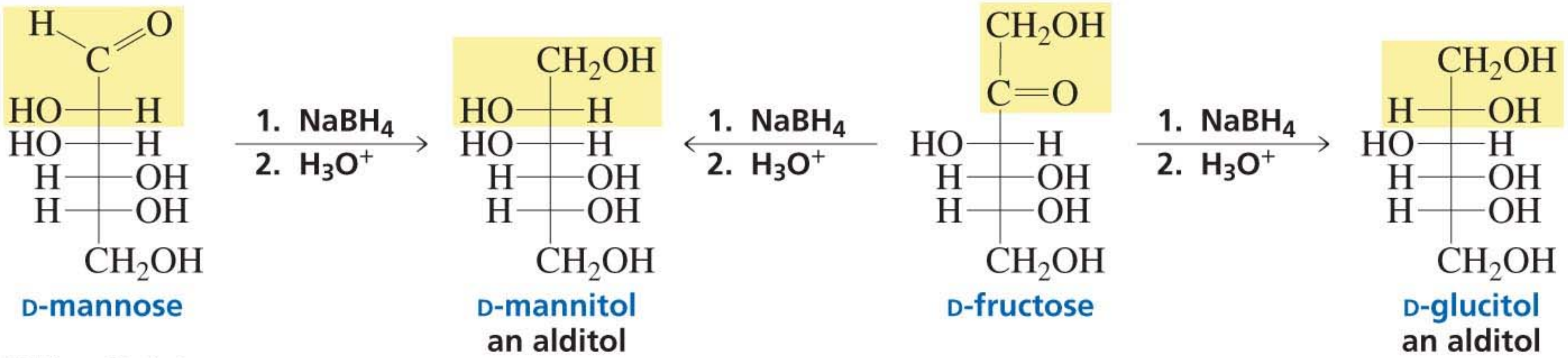


Mechanism for the base-catalyzed enediol rearrangement of a monosaccharide:



Redox Reactions of Monosaccharides

The carbonyl of aldoses and ketoses can be reduced by the carbonyl-group reducing agents:



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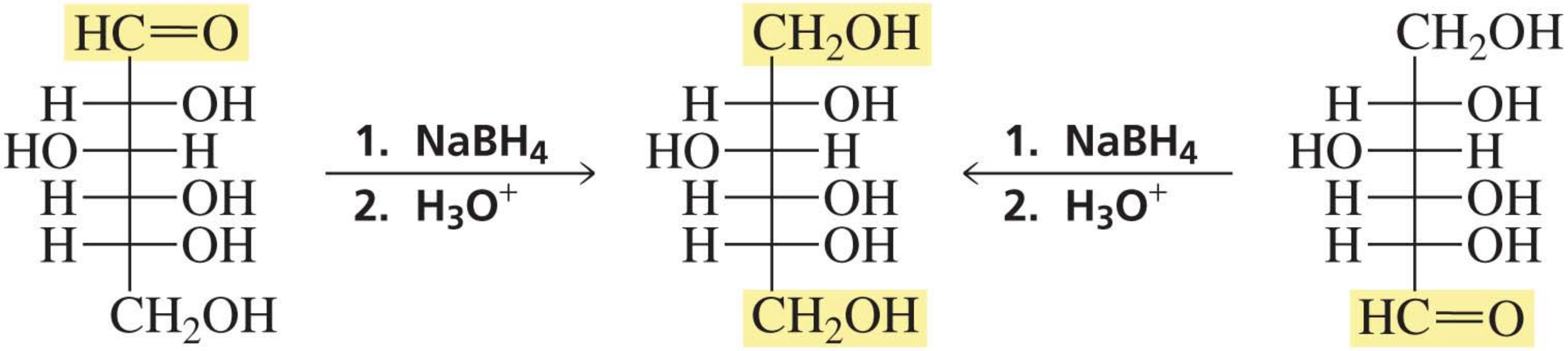


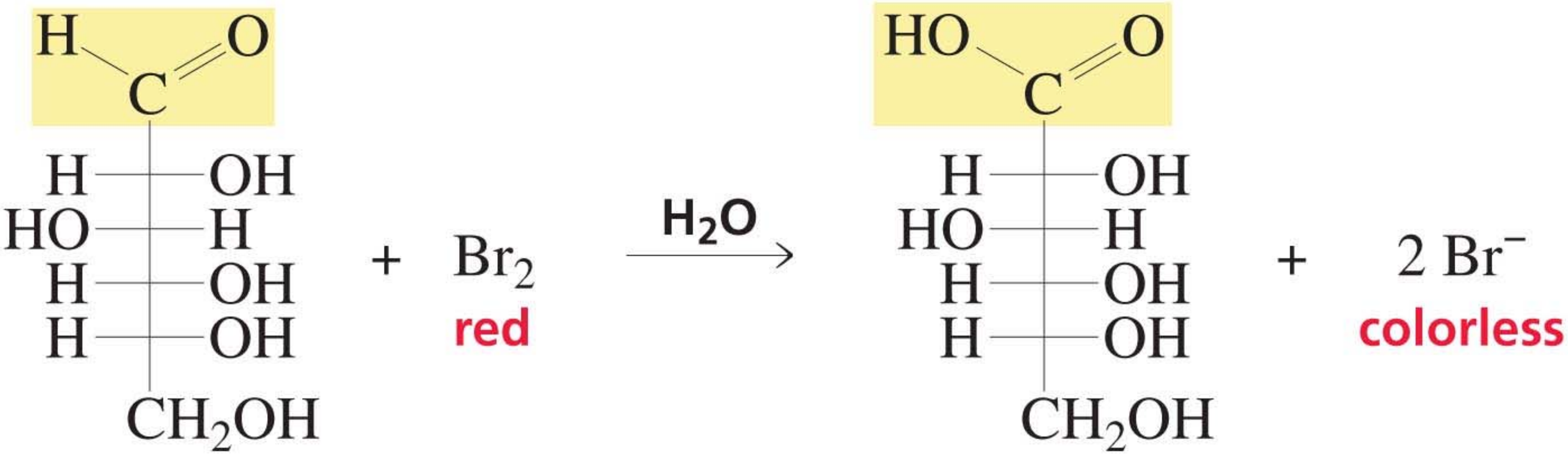
D-glucose

D-glucitol
an alditol

L-gulose
drawn upside down

Oxidation

The aldehyde groups can be oxidized by Br_2

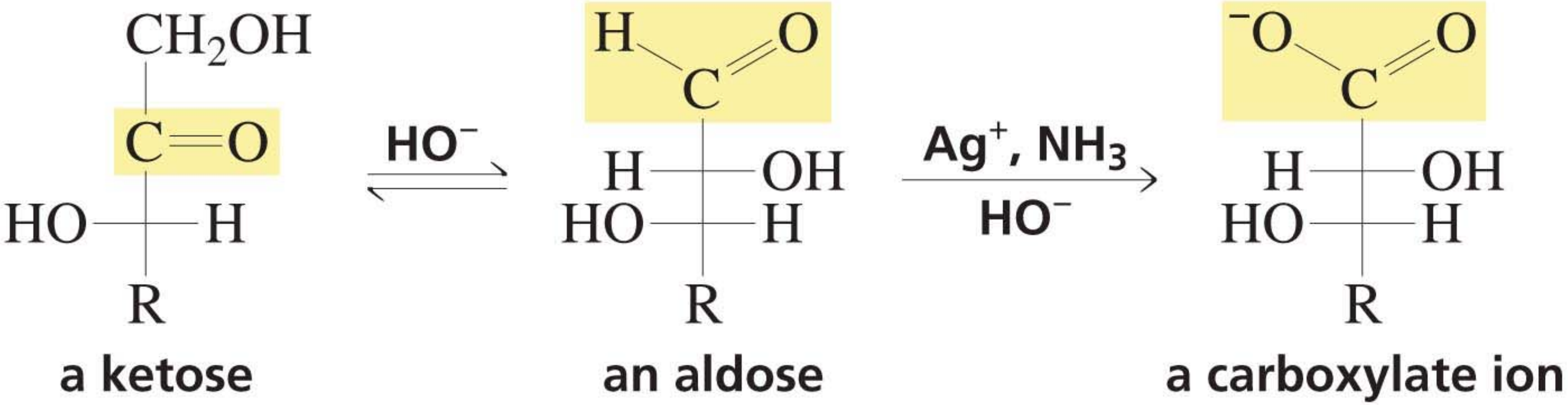


D-glucose

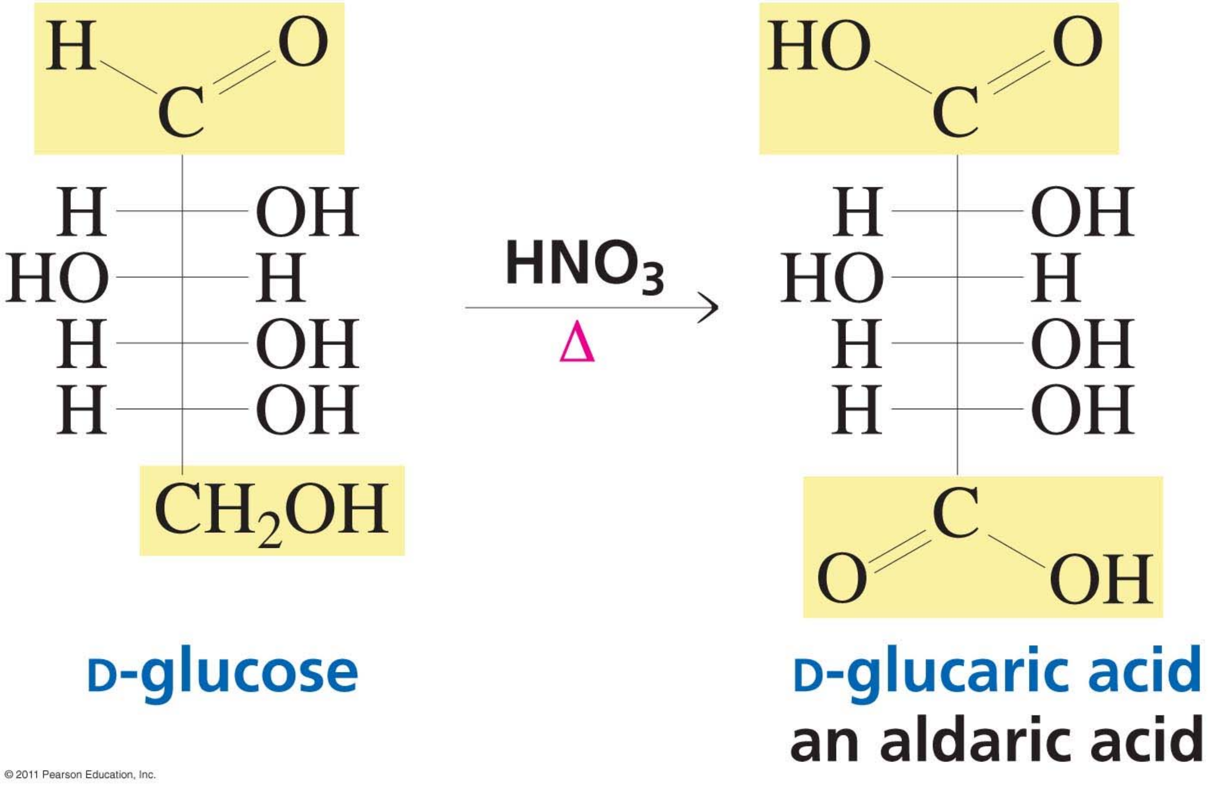
D-gluconic acid
an aldonic acid

Ketones and alcohols cannot be oxidized by Br_2

Both aldoses and ketoses are oxidized to aldonic acids by Tollens reagent:



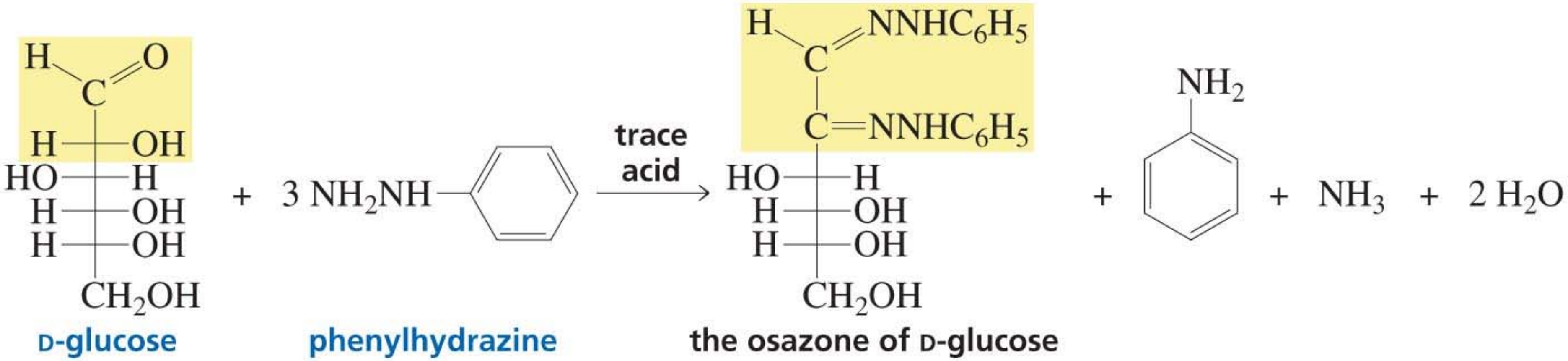
A strong oxidizing agent such as HNO_3 can oxidize both the aldehyde and the alcohol groups:



A primary alcohol is the one most easily oxidized

Osazone Formation

Aldoses and ketoses react with three equivalents of phenylhydrazine to form osazones:



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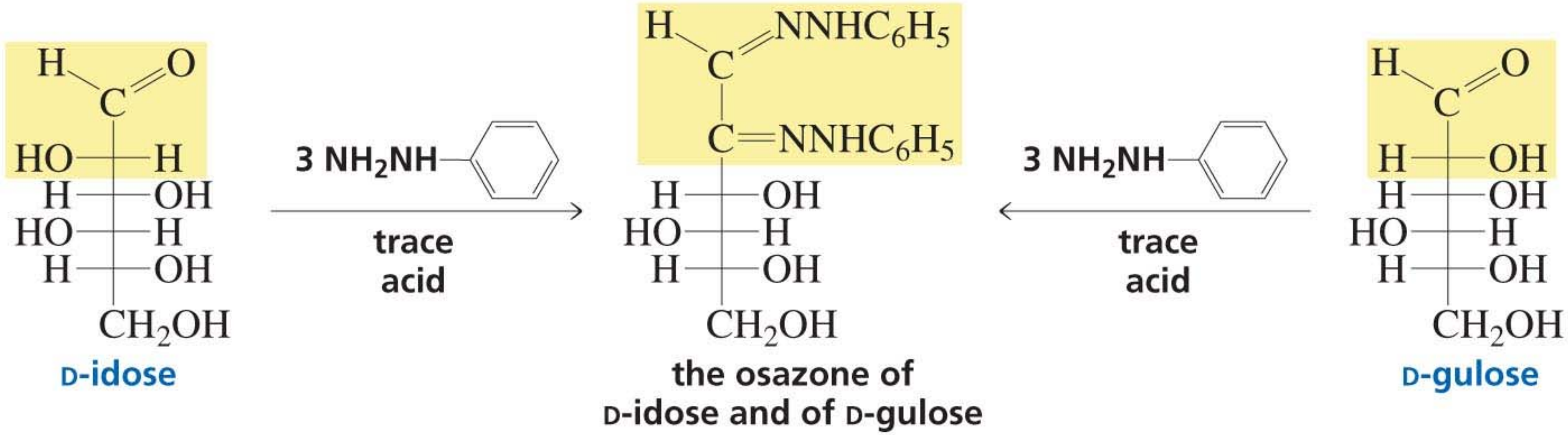
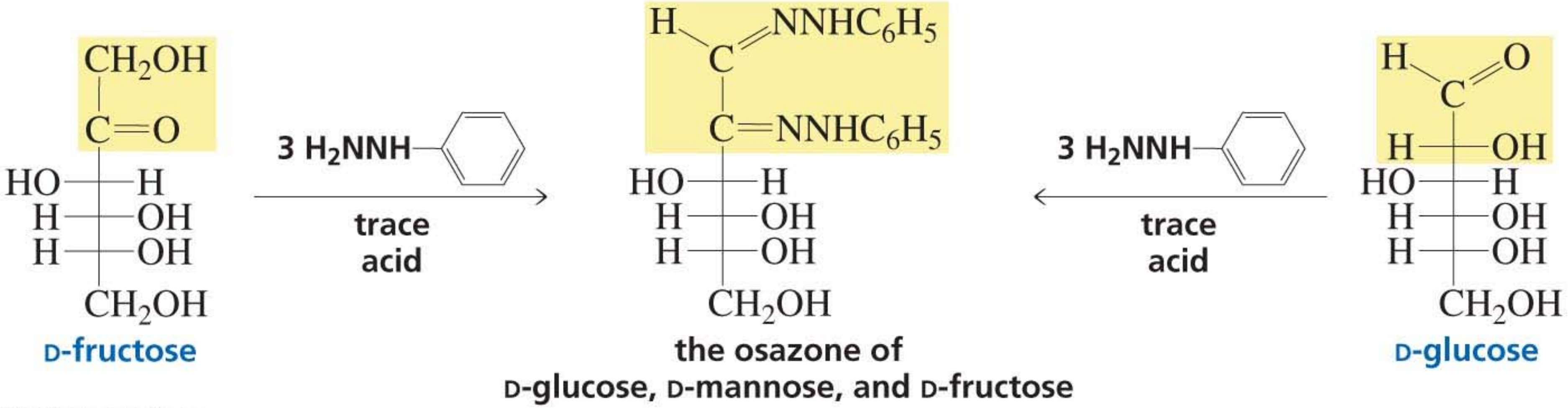
The C-2 epimers of aldoses form identical osazones…



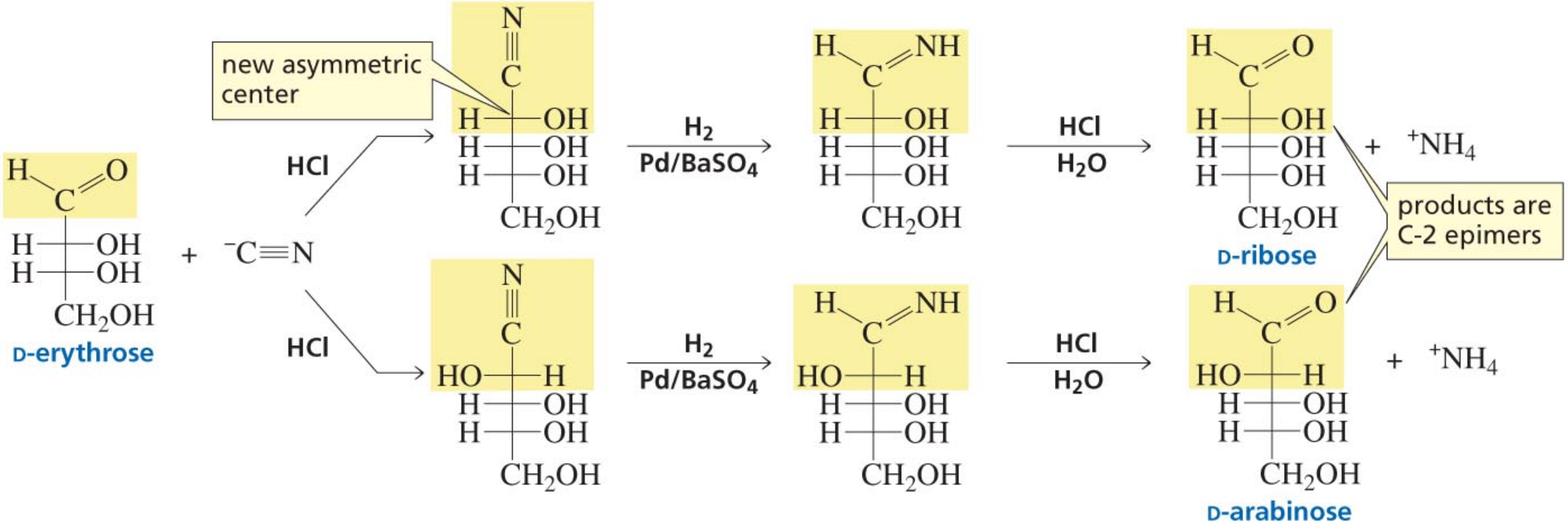
…because the configuration of the C-2 carbon is lost during osazone formation

The C-1 and C-2 carbons of ketoses also react with phenylhydrazine:



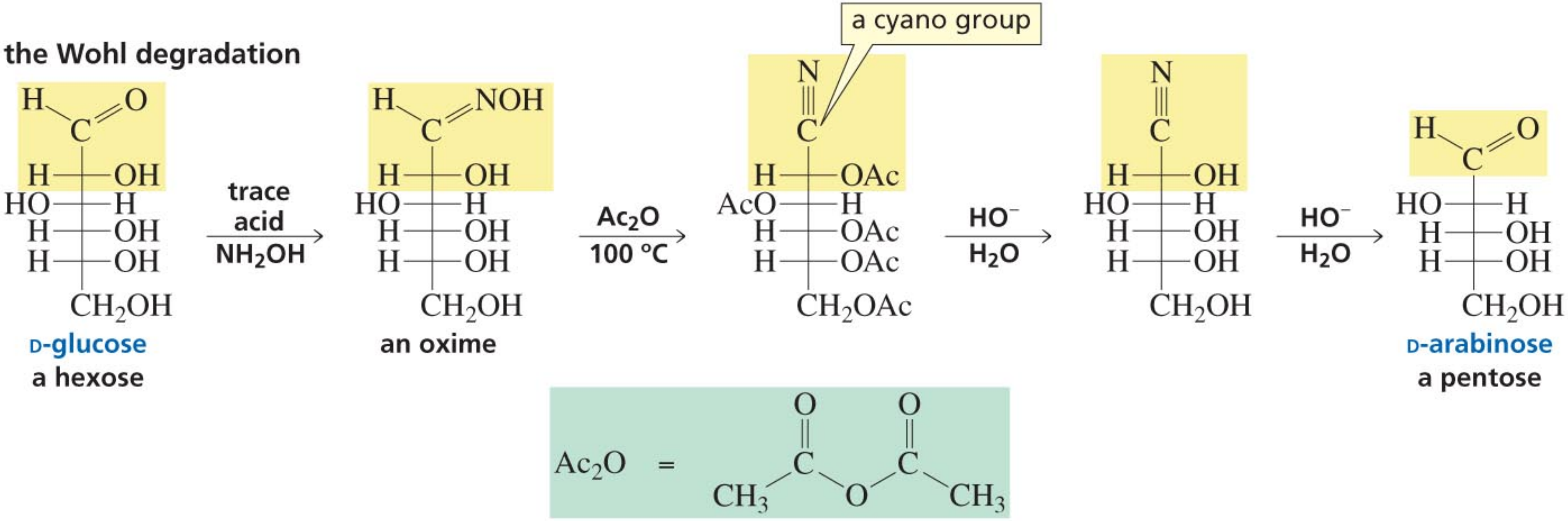
The carbon chain of an aldose can be increased by one carbon in a Kiliani–Fischer synthesis:

the modified Kiliani–Fischer synthesis

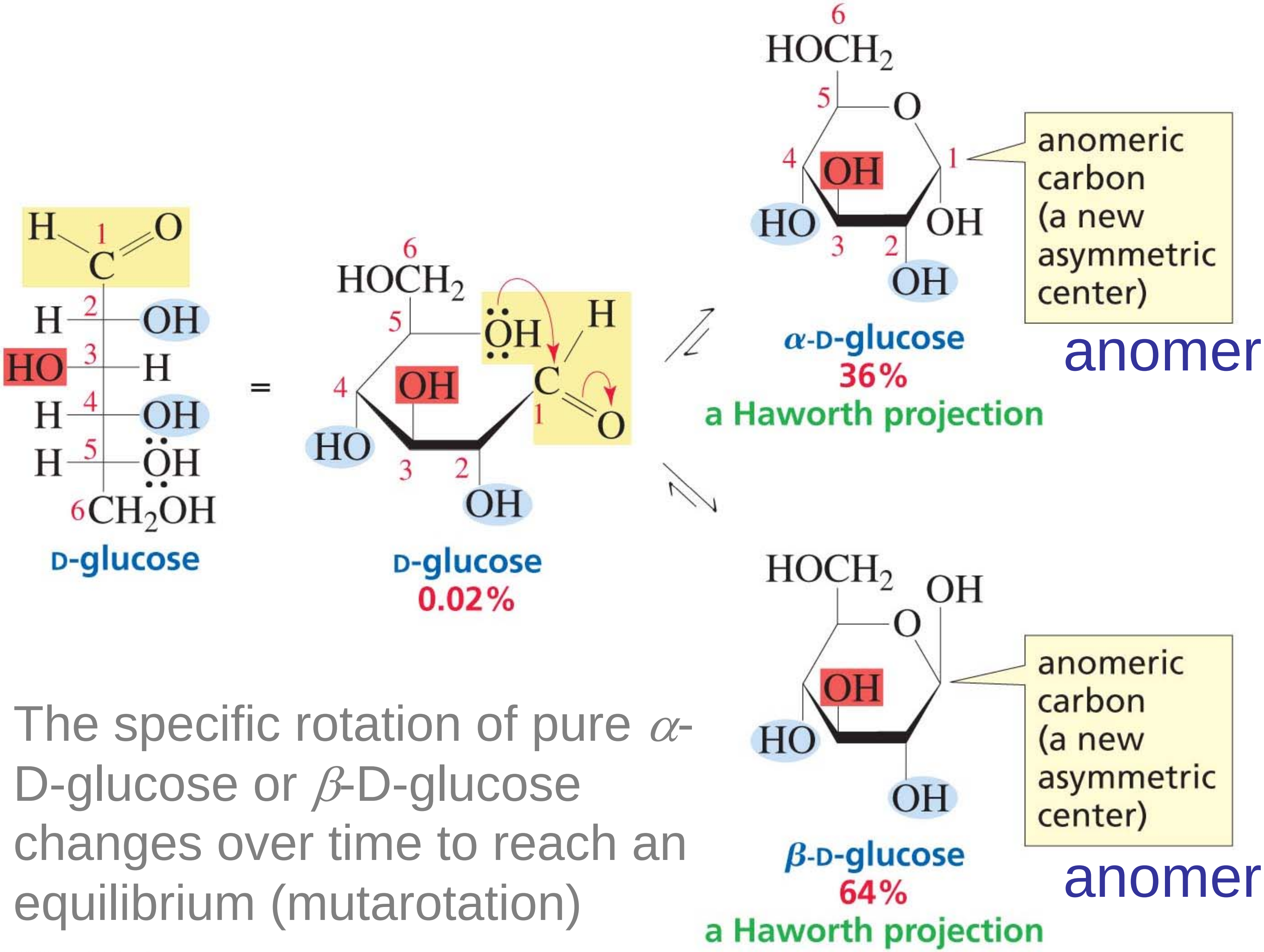


This reaction leads to a pair of C-2 epimers

The Wohl degradation shortens an aldose chain by one carbon:



D-Glucose exists in three different forms:



D-glucose

D-glucose
0.02%

α-D-glucose
36%
a Haworth projection

anomeric carbon (a new asymmetric center)

anomer

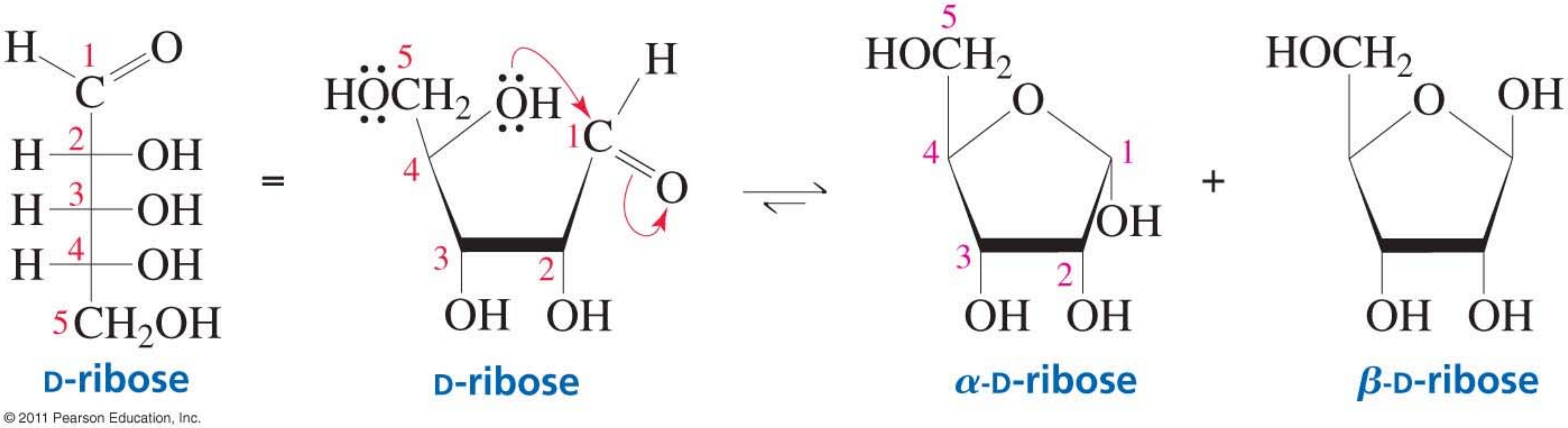
β-D-glucose
64%
a Haworth projection

anomeric carbon (a new asymmetric center)

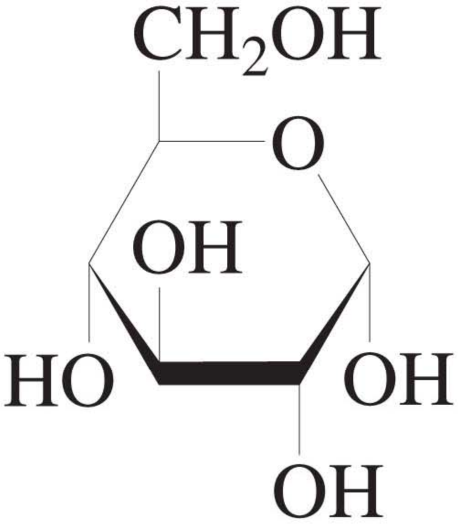
anomer

The specific rotation of pure α-D-glucose or β-D-glucose changes over time to reach an equilibrium (mutarotation)

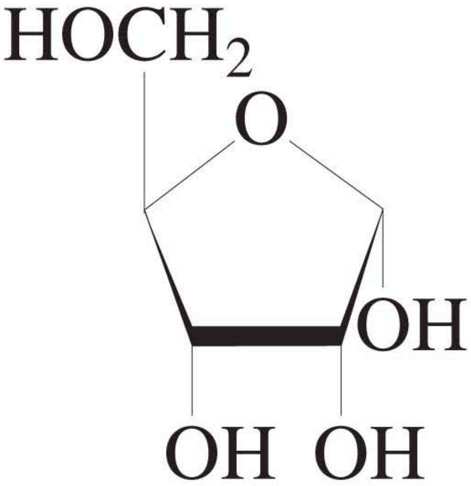
If an aldose can form a five- or six-membered ring, it will exist predominantly as a cyclic hemiacetal:



- Six-membered rings are called pyranoses.
- Five-membered rings are called furanoses.
- The prefix α- indicates the configuration about the anomeric carbon.

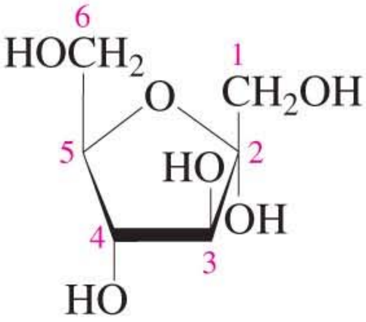


α-D-glucose
α-D-glucopyranose



α-D-ribose
α-D-ribofuranose

Ketoses also exist predominantly in cyclic forms:



α-D-fructofuranose

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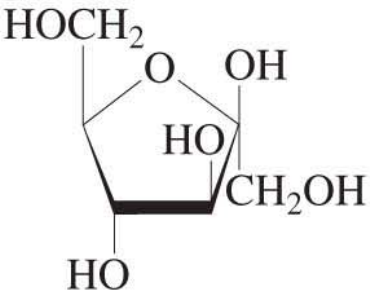
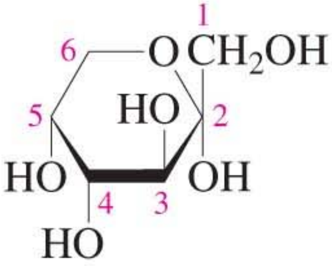
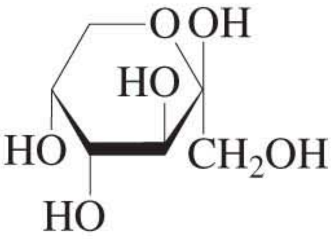


β-D-fructofuranose

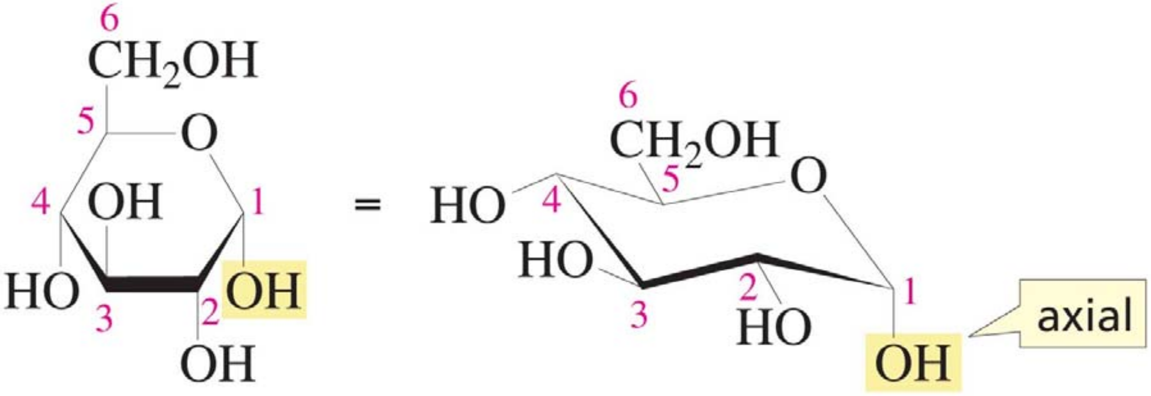


α-D-fructopyranose

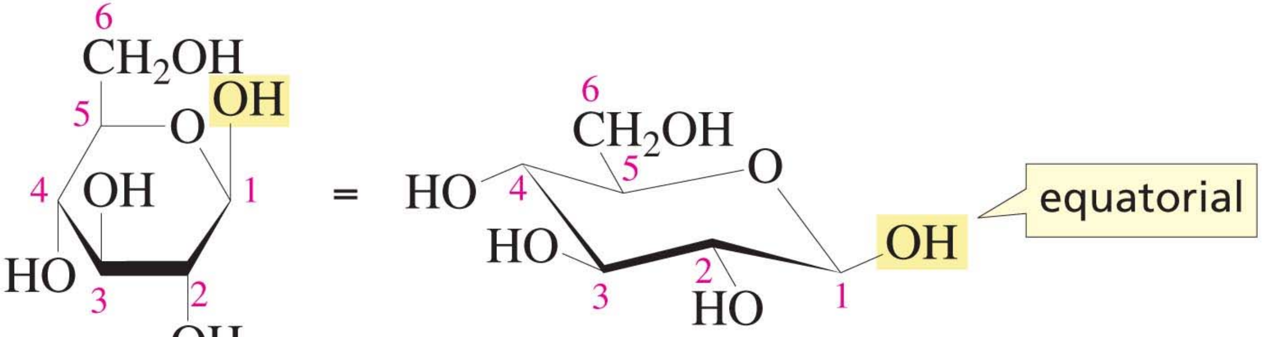


β-D-fructopyranose

β-D-Glucose is the most stable of all aldohexoses and predominates at equilibrium:



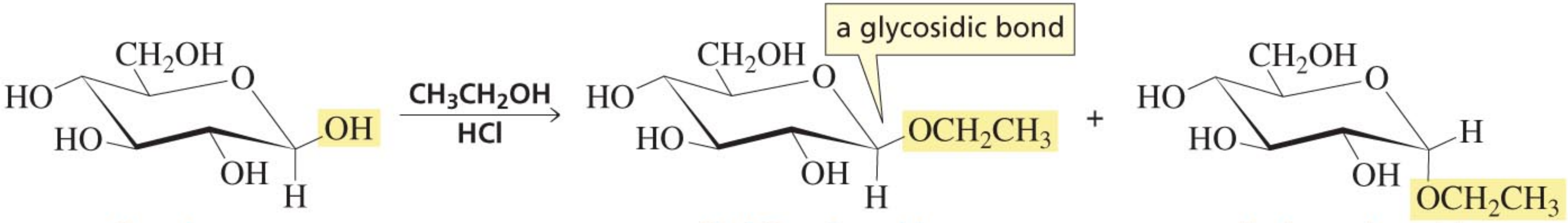
α-D-glucose chair conformer



β-D-glucose chair conformer

Formation of Glycosides

The acetal (or ketal) of a sugar is called a glycoside:



a glycosidic bond

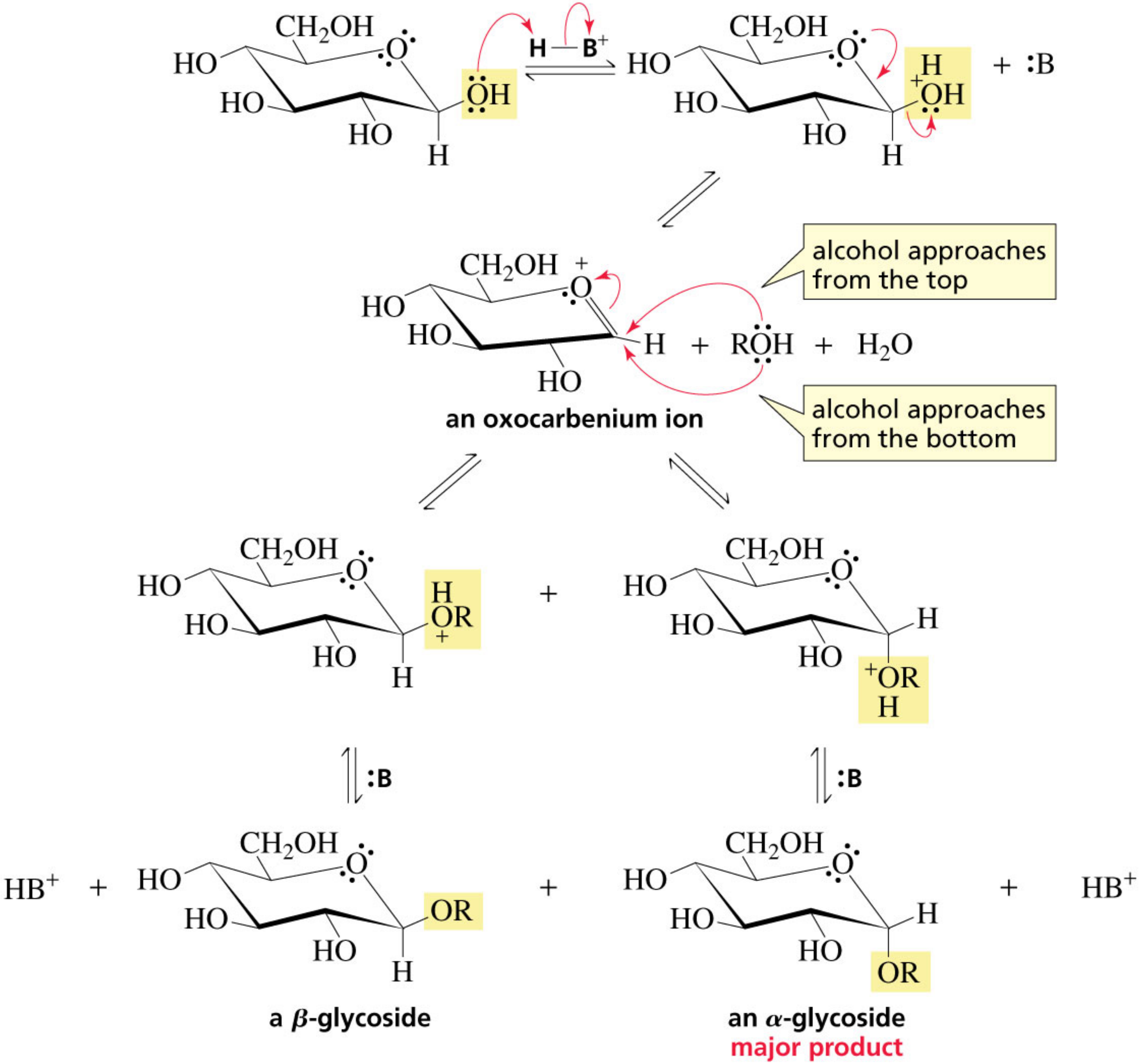
β-D-glucose
β-D-glucopyranose

ethyl β-D-glucoside
ethyl β-D-glucopyranoside

acetal

ethyl α-D-glucoside
ethyl α-D-glucopyranoside

Mechanism for glycoside formation



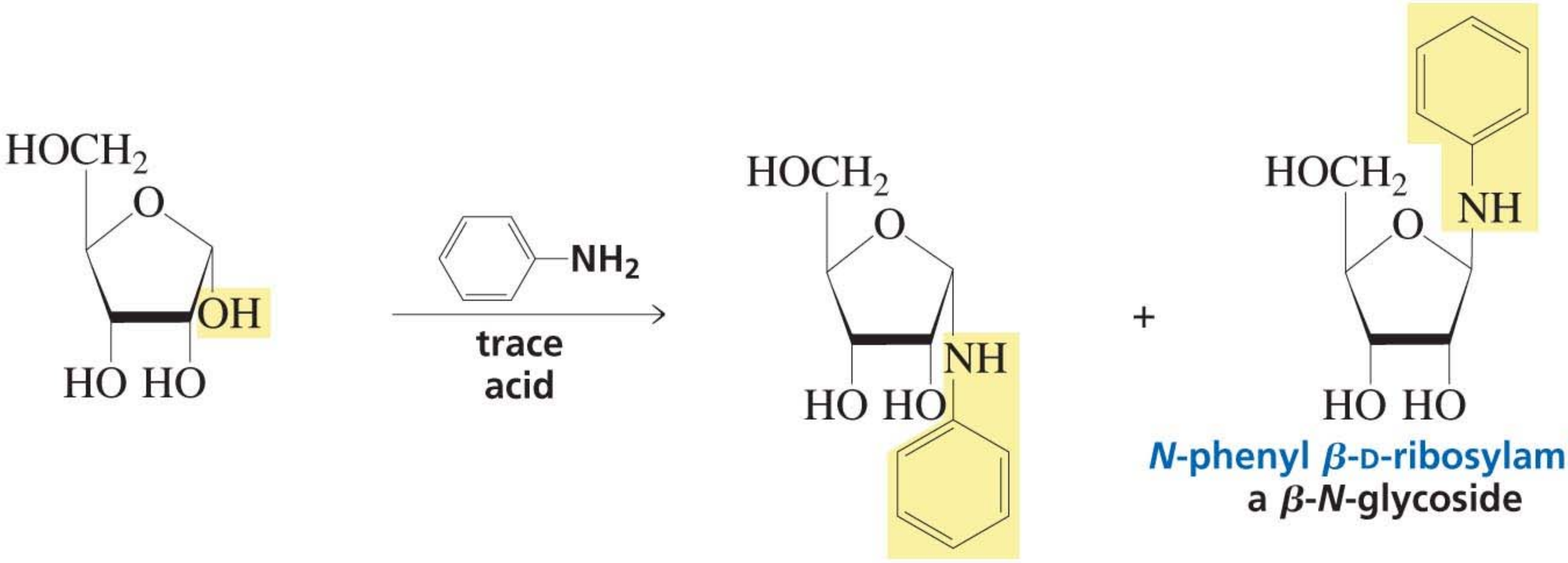
alcohol approaches from the top

alcohol approaches from the bottom

a *β*-glycoside

an *α*-glycoside
major product

Formation of an *N*-Glycoside

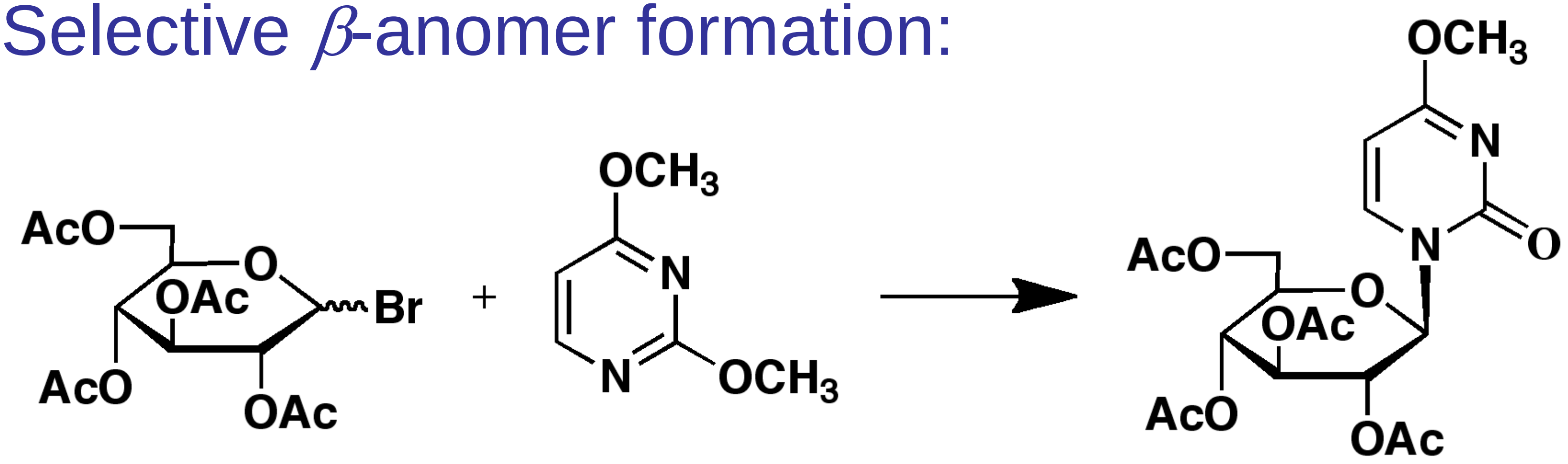


N-phenyl β-D-ribosylamine
a β-*N*-glycoside

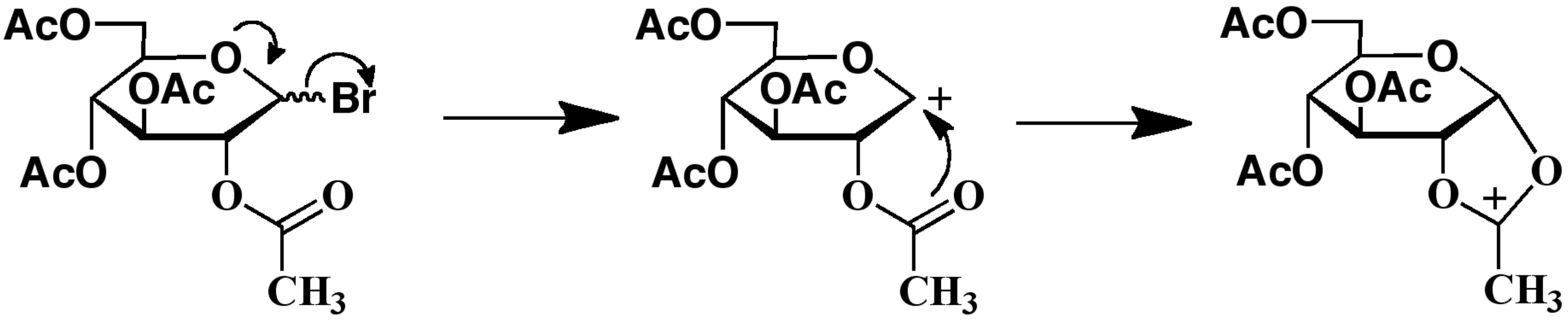
N-phenyl α-D-ribosylamine
an α-*N*-glycoside

Hilbert–Johnson Reaction

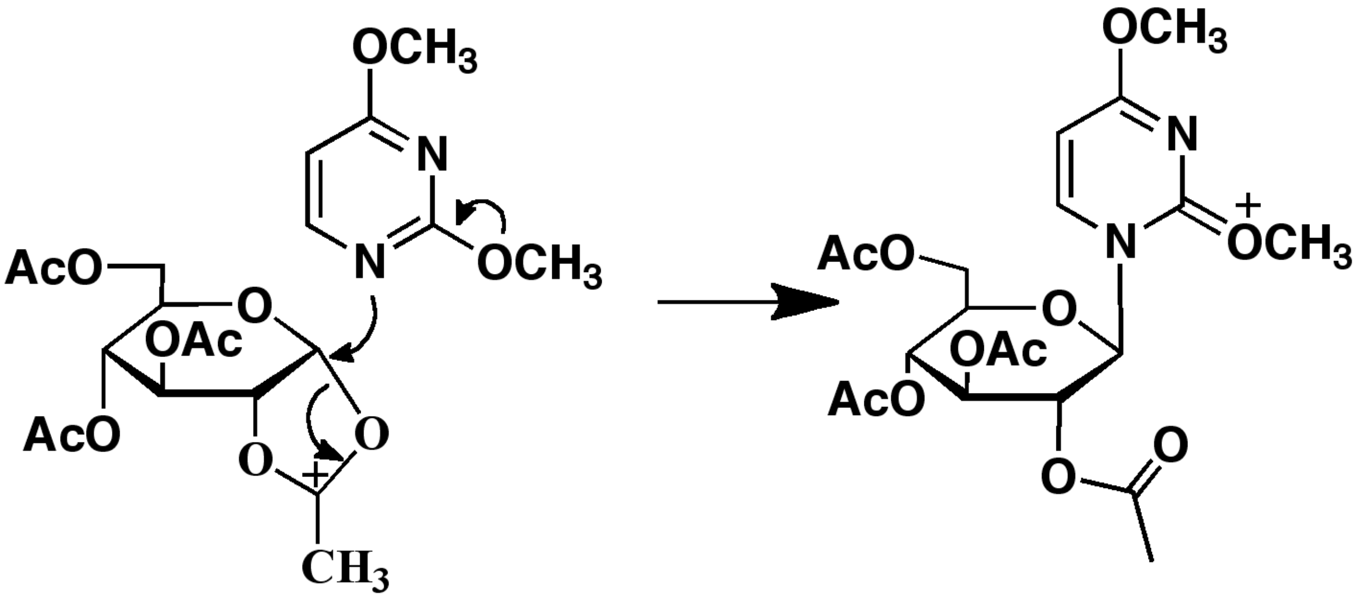
Selective *β*-anomer formation:



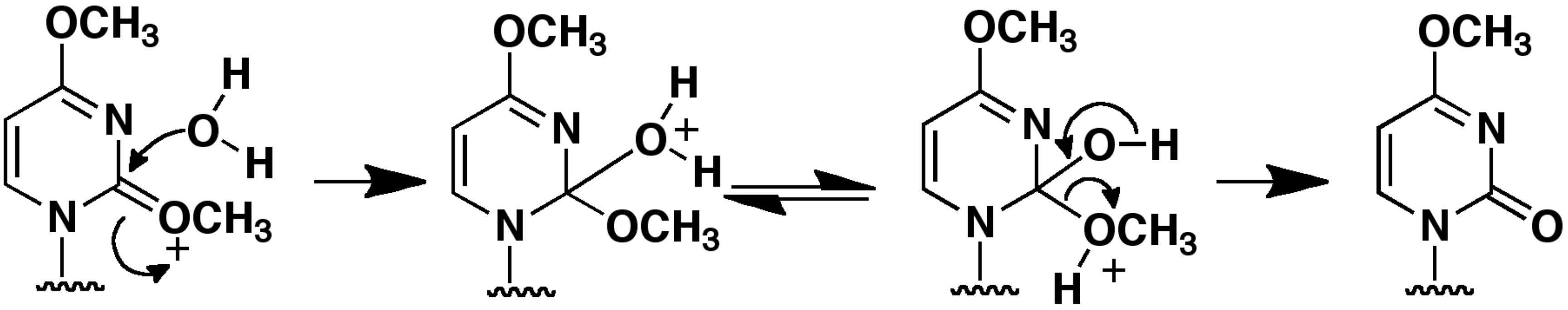
Oxocarbocation formation:



β-Nucleophilic attack:

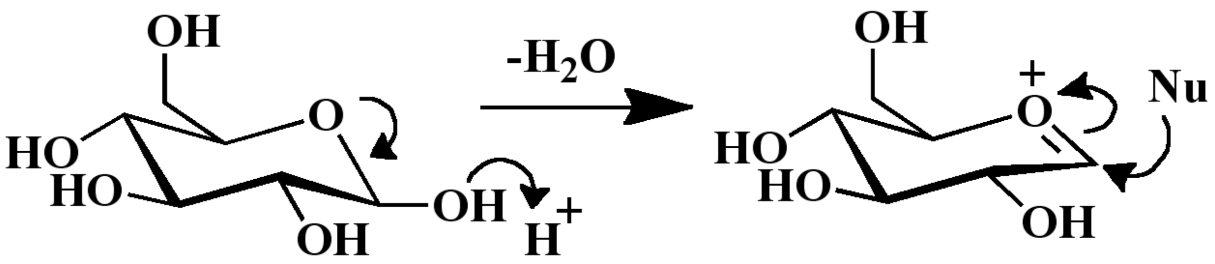


Hydrolysis:



Glycoside Formation in Diabetes

Glucose can form glycosides with amine groups on hemoglobin

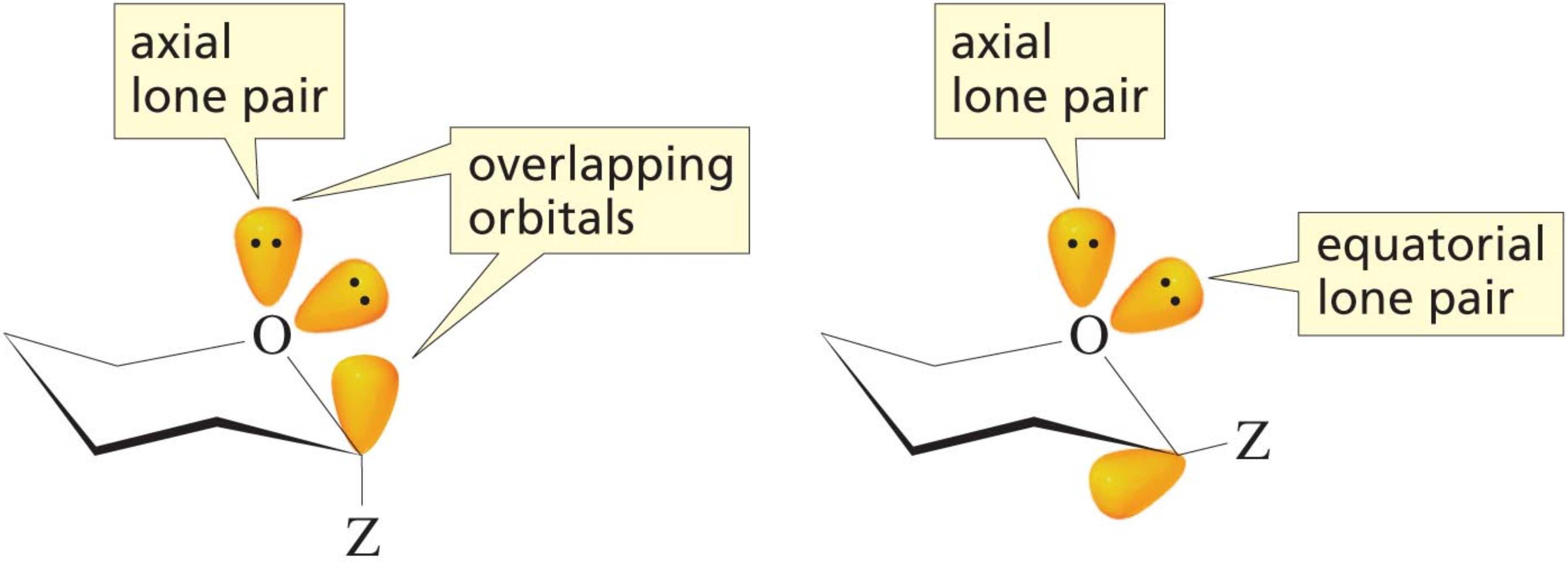


Glycated hemoglobin test:

- **Without diabetes, 5.5 to 9% glycated hemoglobin**
- **With diabetes, 10.9 to 15.5% glycated hemoglobin**

The Anomeric Effect

The preference of certain substituents bonded to the anomeric carbon for the axial position is called the anomeric effect:



Reducing and Nonreducing Sugars

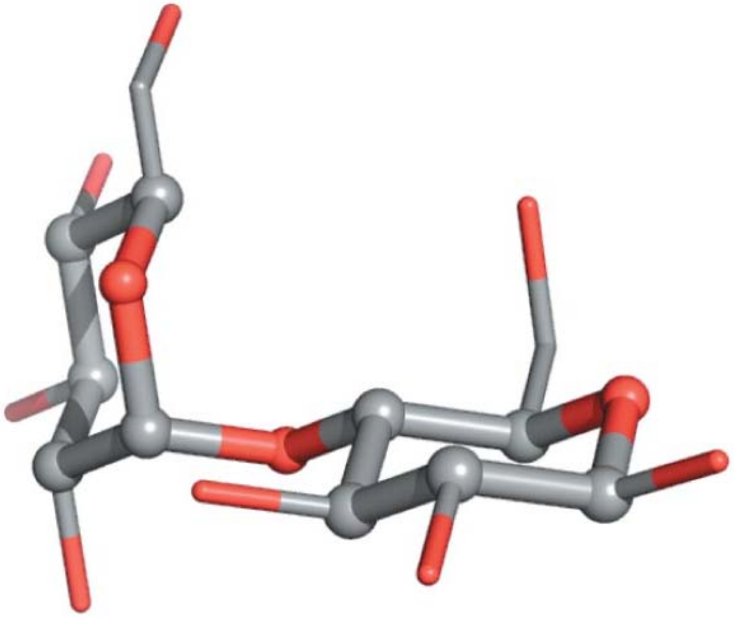
A sugar with an aldehyde, a ketone, a hemiacetal, or a hemiketal group is a reducing sugar

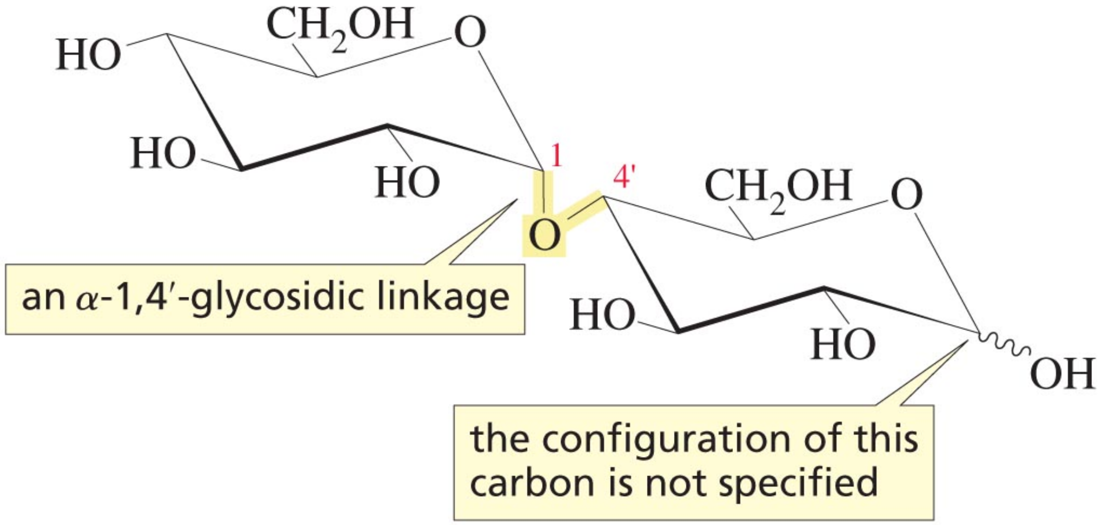
A sugar without one of these groups is a nonreducing sugar

Nonreducing sugars cannot reduce Ag^+ or Br_2

Disaccharides

Composed of **two** monosaccharide subunits linked together by an **acetal** linkage:



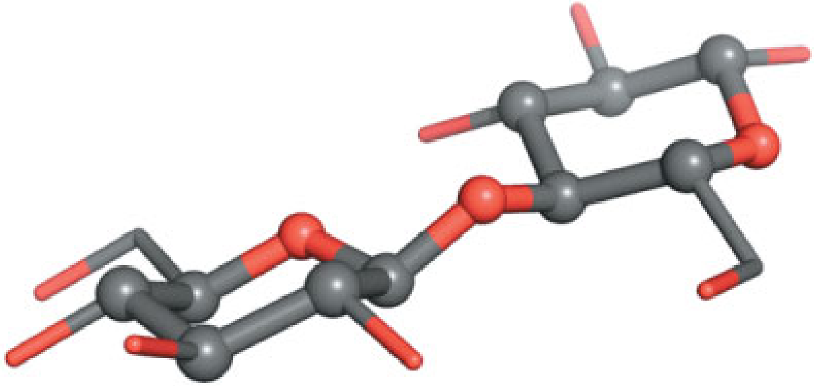


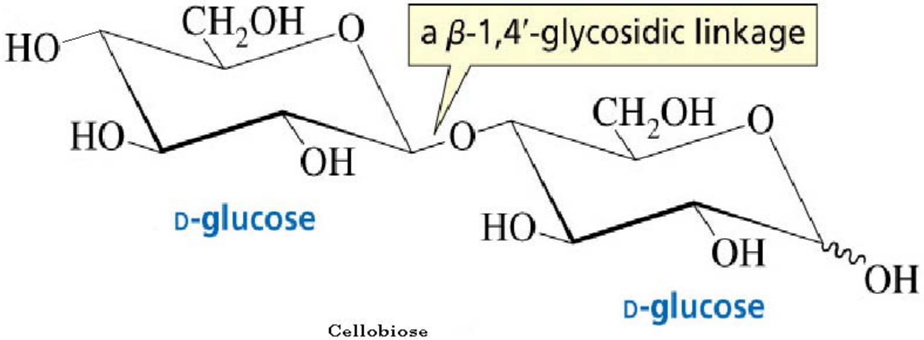
maltose

In maltose, the OH group bonded to the anomeric carbon is axial, ***hence the 'α' in the linkage descriptor***

Maltose is a reducing sugar

In cellobiose, the two subunits are linked together by a ***β*-1,4′-glycosidic linkage**



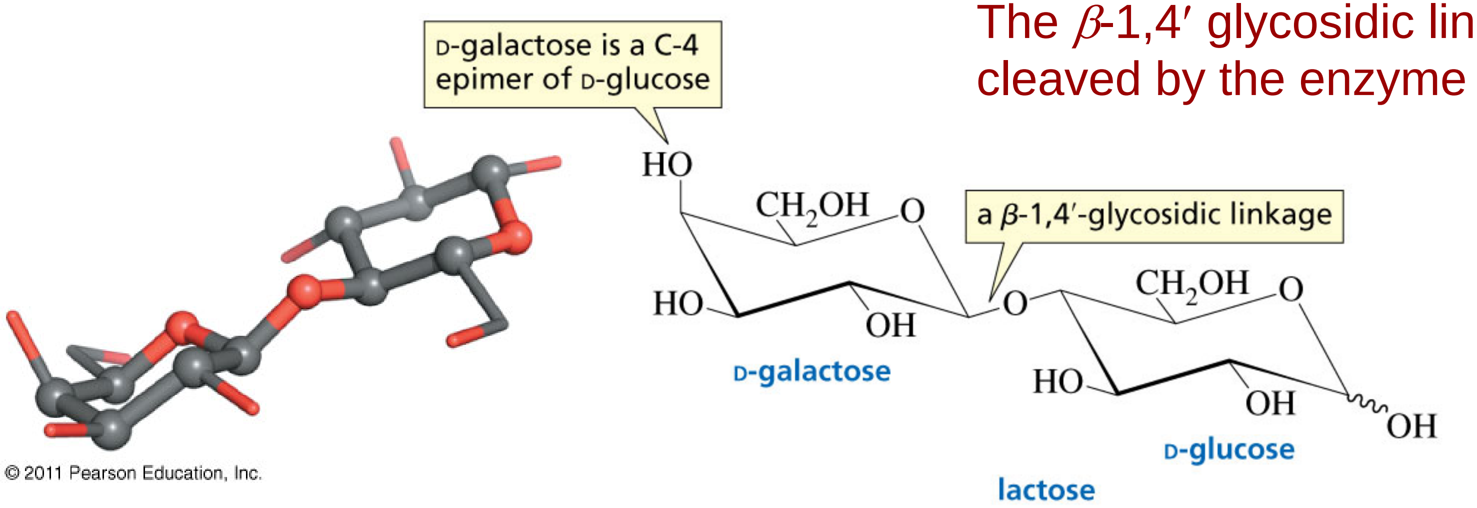


Cellobiose

Cellobiose is a reducing sugar

In lactose, the two different subunits are joined by a *β*-1,4′-glycosidic linkage

The *β*-1,4′ glycosidic linkage is cleaved by the enzyme lactase



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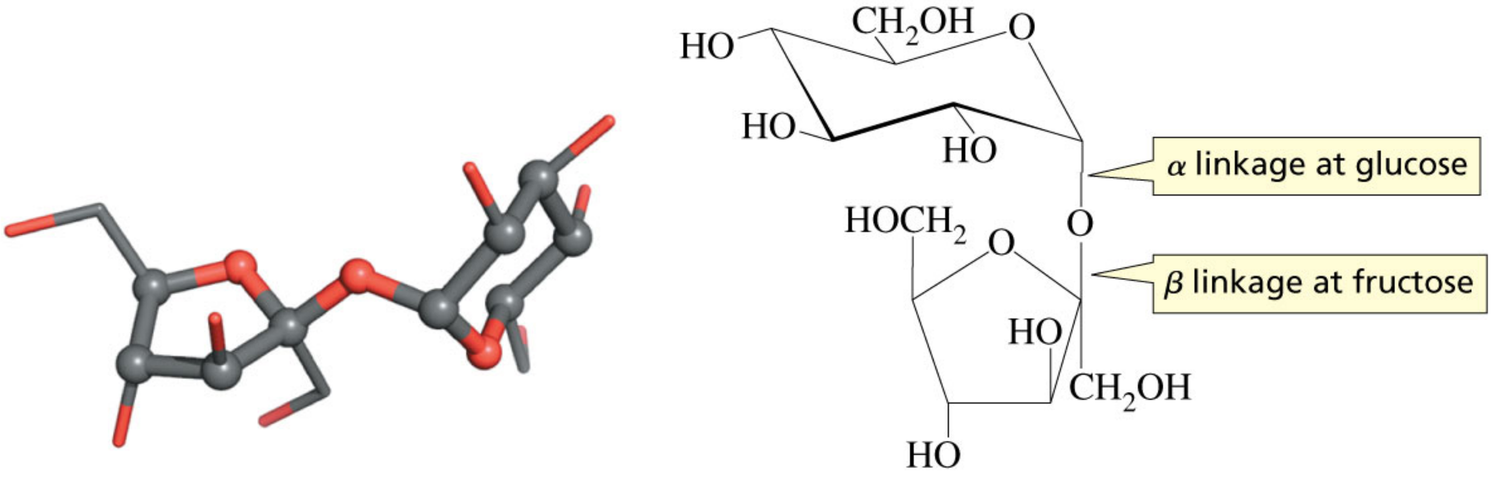
Without lactase, lactose is turned into gases by flora in the lower bowel, producing flatulence and bloating

Lactose is a reducing sugar and undergoes mutarotation

Sucrose: The most common disaccharide



sucrose

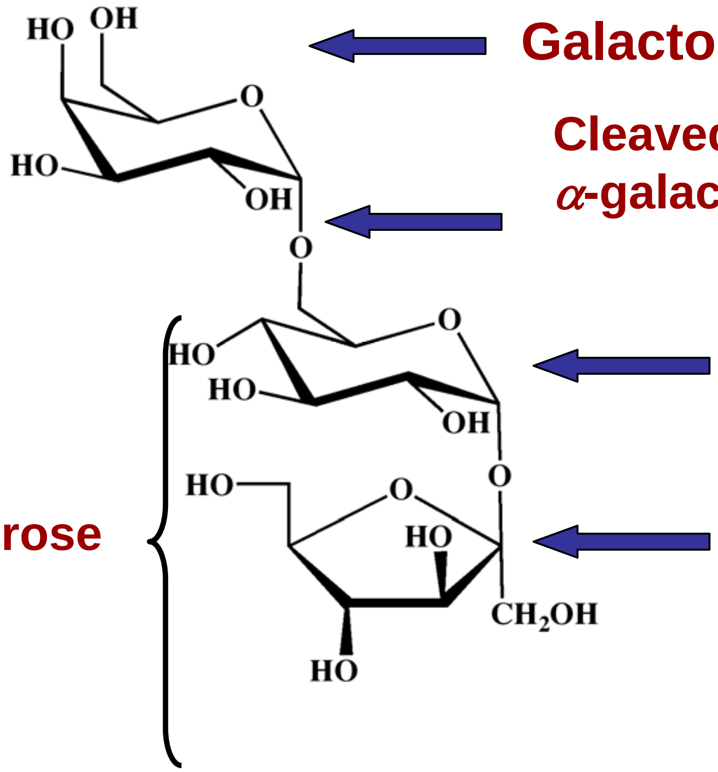
Sucrose is not a reducing sugar and does not exhibit mutarotation

$$\text{Sucrose } [\alpha]_D = +66.5\,^{o} \xrightarrow[\text{H}_2\text{O}]{\text{hydrolysis}} \text{Glucose + fructose (1:1) } [\alpha]_D = -22.0\,^{o}$$

Hence also called ‘invert sugar’. Bees have invertase

How Does Beano Work?

The trisaccharide raffinose is found in beans and a variety of grains and vegetables



Galactose

Cleaved by α-galactosidase (α-GAL)

Glucose

Fructose

Sucrose

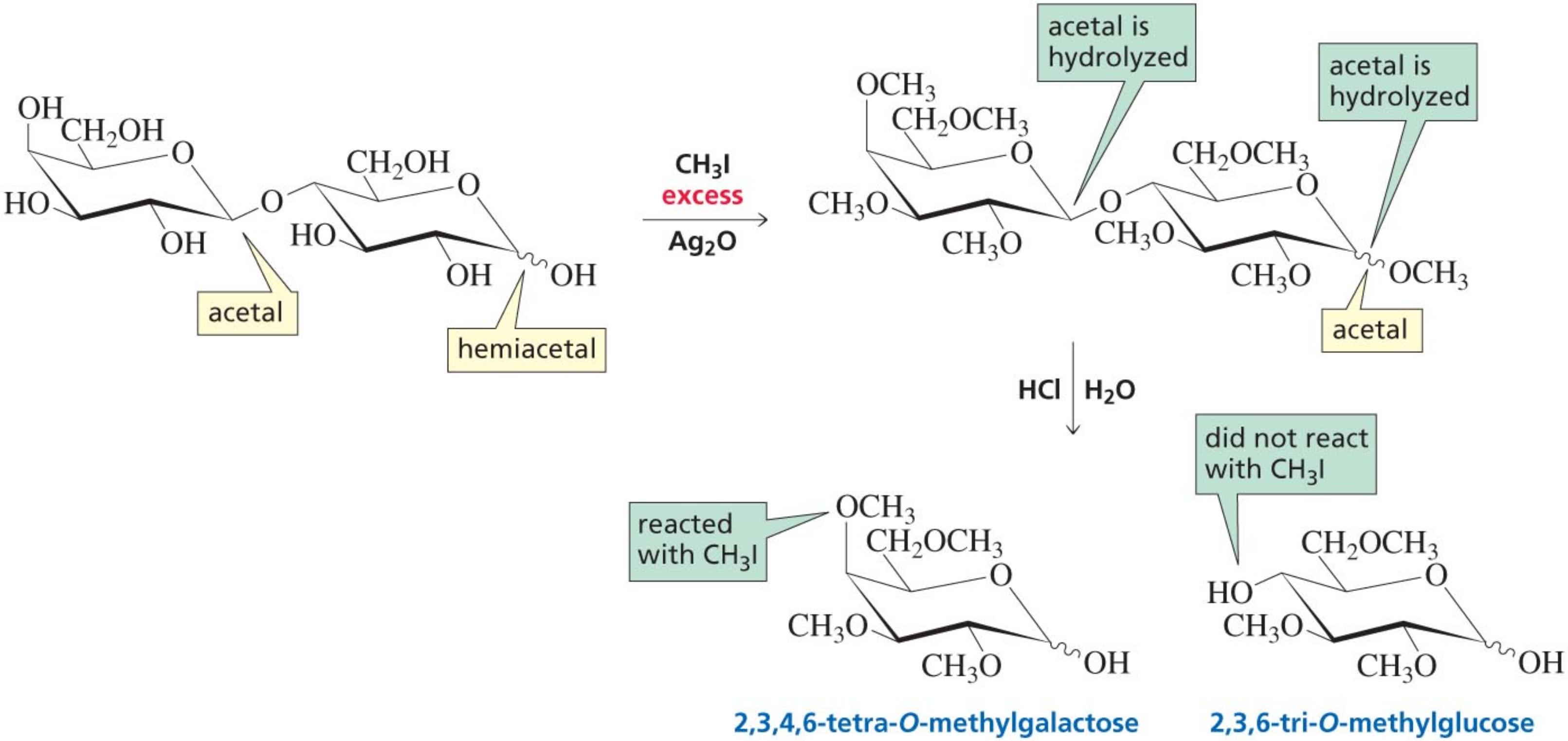
- **α-GAL is not in the human digestive tract.**
- **Raffinose is not cleaved to sucrose and galactose.**
- **Lower gut flora converts raffinose to gases; flatulence results.**

Beano contains fungal α-GAL that cleaves raffinose and other polysaccharides

Determination of disaccharide structure (sequence)

Consider lactose: disaccharide containing galactose and glucose

How are they linked?



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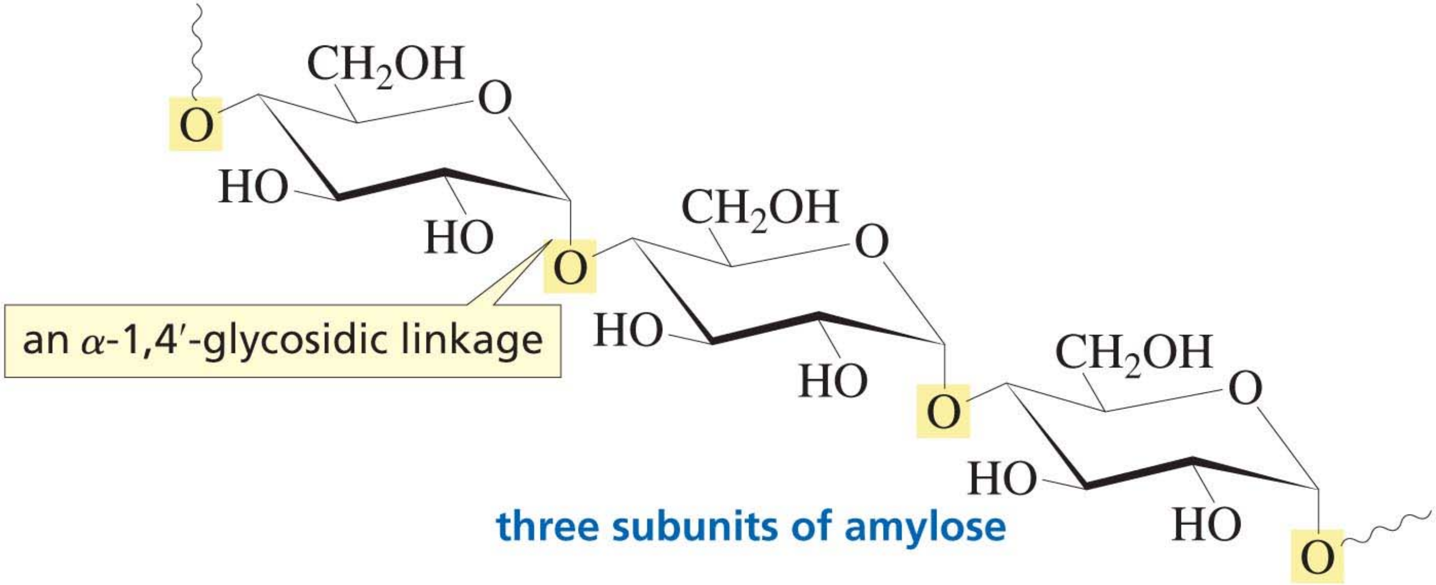
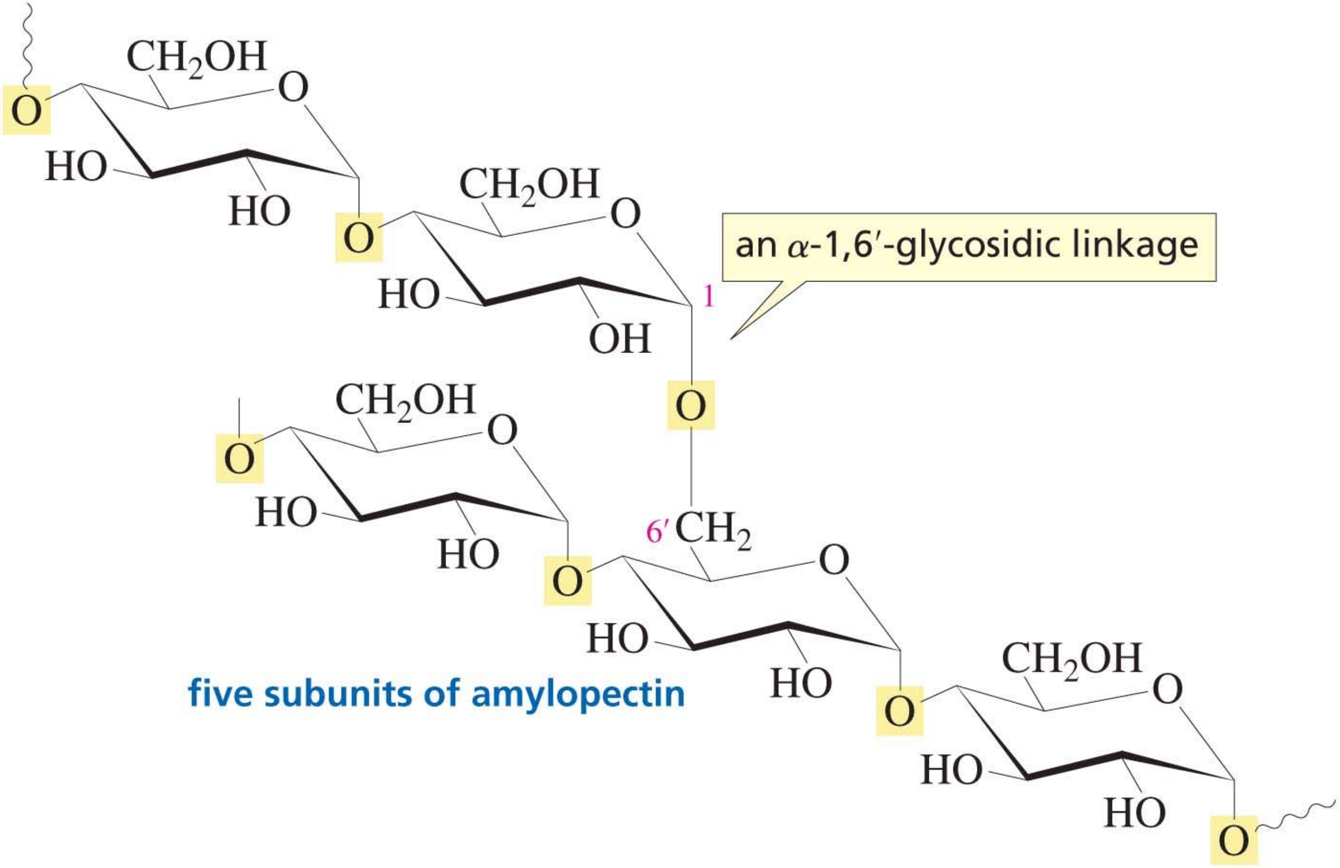
Polysaccharides

Amylose is a component of starch:



three subunits of amylose

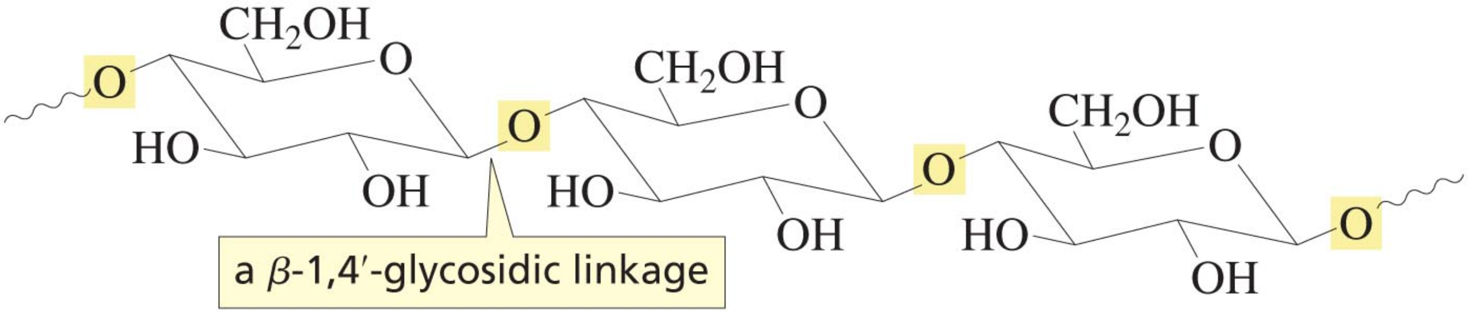
Amylopectin is another polysaccharide component of starch that has a branched structure:



an α-1,6′-glycosidic linkage

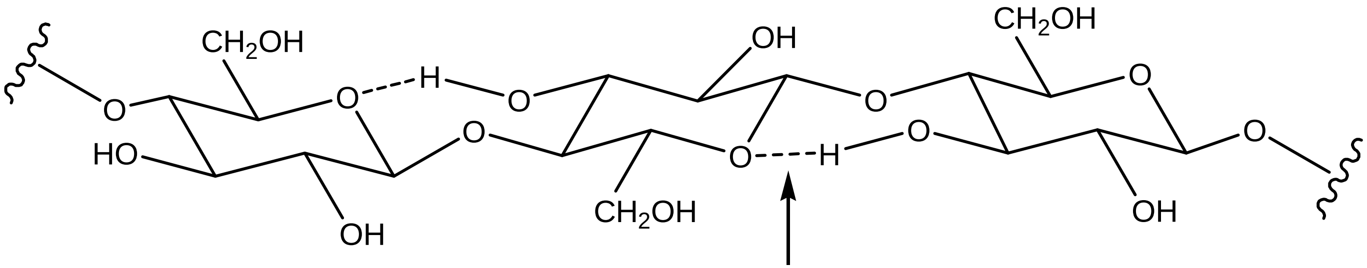
five subunits of amylopectin

Cellulose is the structural material of higher plants:



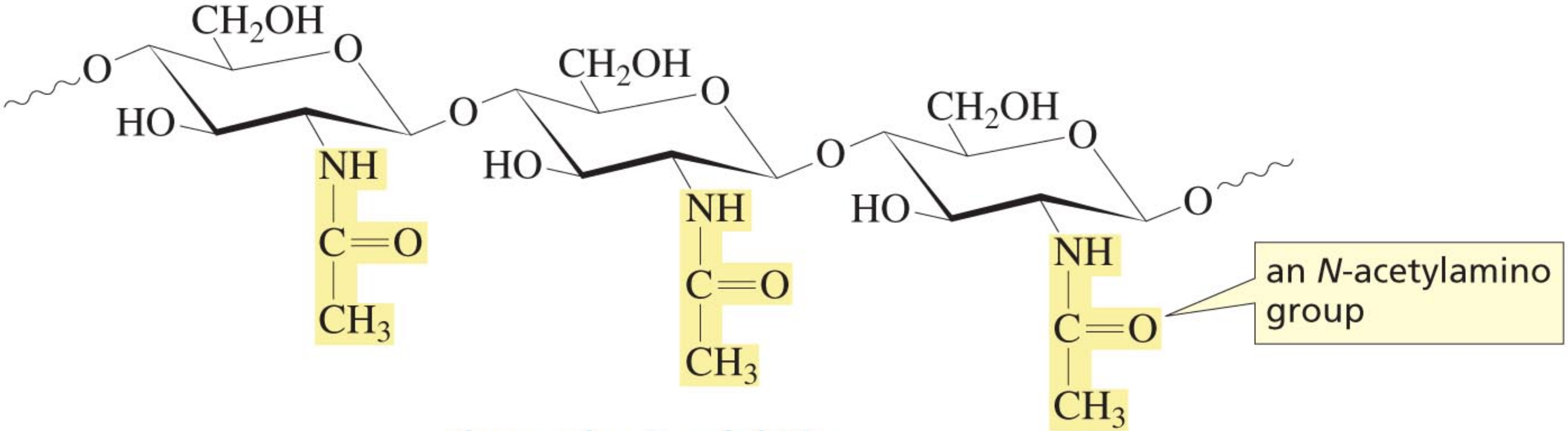
three subunits of cellulose

α-1,4′-Glycosidic linkages are easier to hydrolyze than β-1,4′-glycosidic linkages because of the ***anomeric effect***



intramolecular hydrogen bond

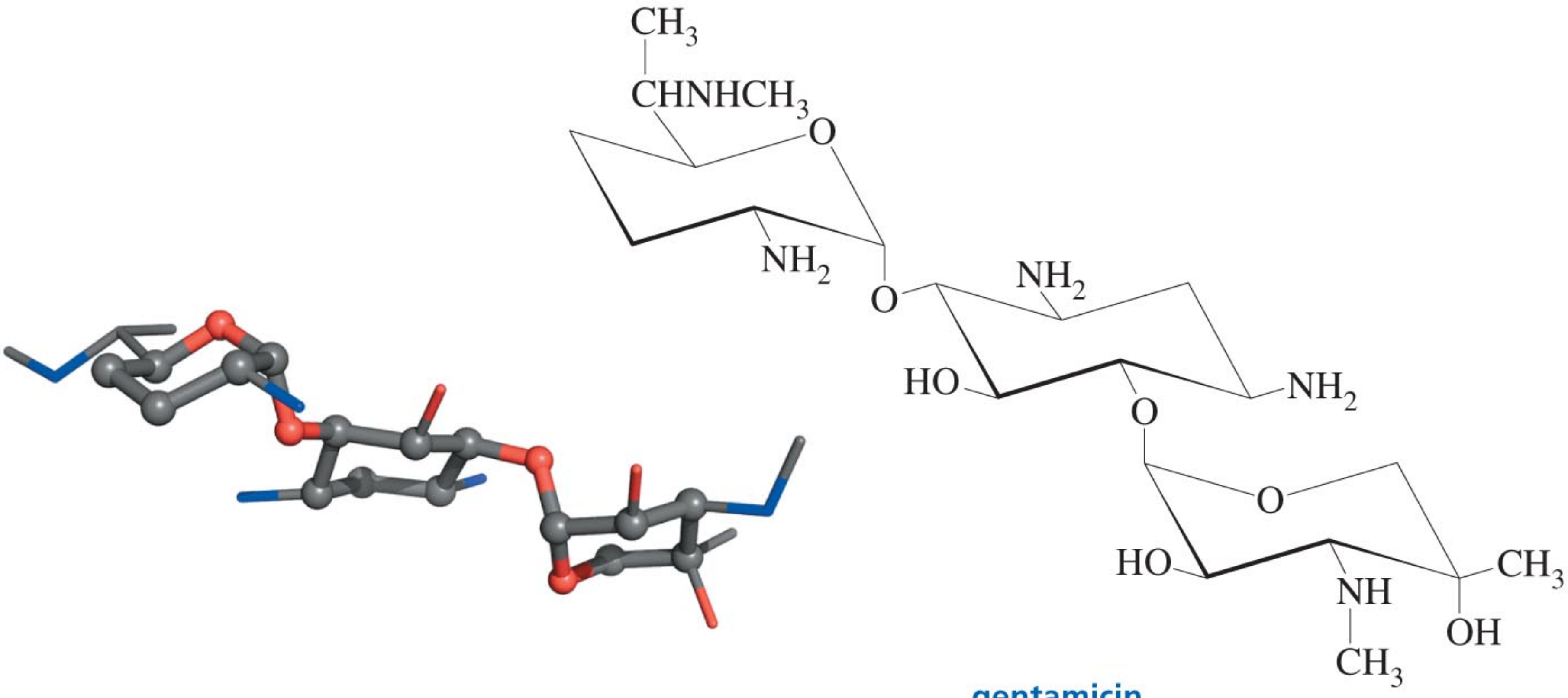
Chitin: The structural component of the shells of crustaceans



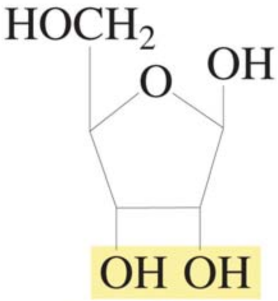
an *N*-acetylamino group

three subunits of chitin

Naturally occuring derivatives of carbohydrates



gentamicin
an antibiotic



β-D-ribose

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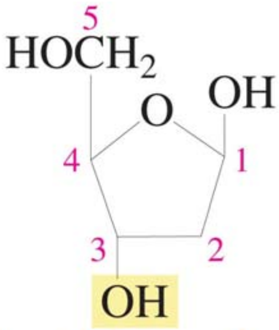
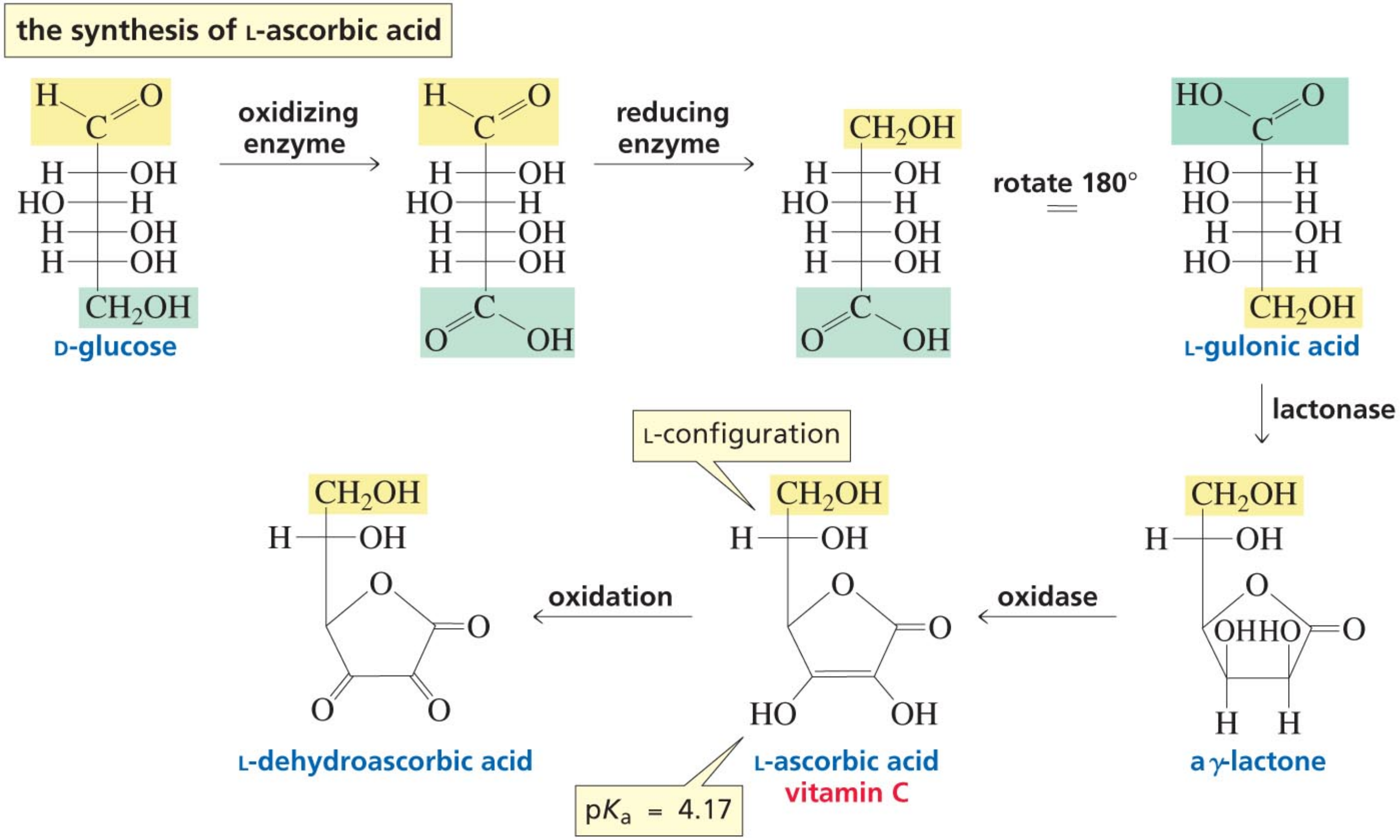


β-D-2-deoxyribose

D-Ribose is the sugar component of ribonucleic acid

D-2-Deoxyribose is the sugar component of deoxyribonucleic acid

Vitamin C (L-ascorbic acid) is synthesized from D-glucose



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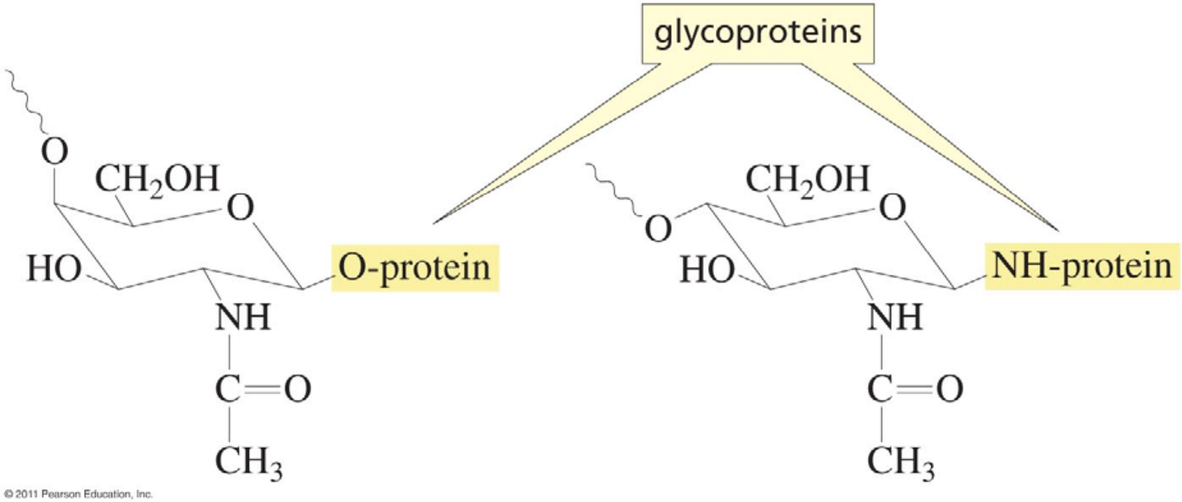
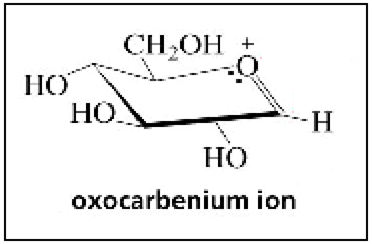
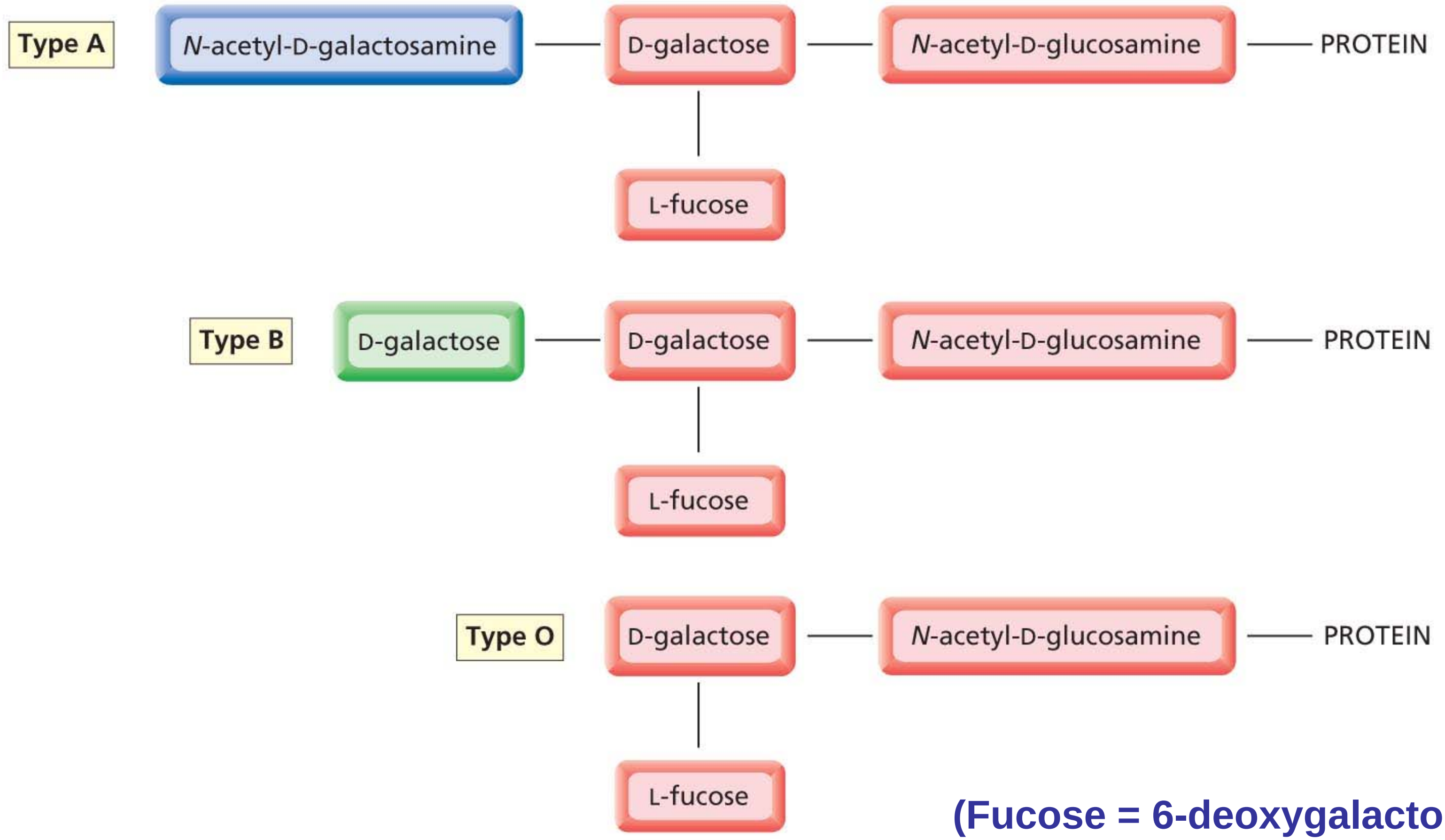
Proteins bonded to oligosaccharides are called **glycoproteins**





Blood type is determined by the sugar bound to the protein on the surface of red blood cells



Type A N-acetyl-D-galactosamine — D-galactose — N-acetyl-D-glucosamine — PROTEIN
L-fucose

Type B D-galactose — D-galactose — N-acetyl-D-glucosamine — PROTEIN
L-fucose

Type O D-galactose — N-acetyl-D-glucosamine — PROTEIN
L-fucose

(Fucose = 6-deoxygalactose)

nature
biotechnology

Bacterial glycosidases for the production of universal red blood cells

Qiyong P Liu[1,9], Gerlind Sulzenbacher[2,9], Huaiping Yuan[1], Eric P Bennett[3], Greg Pietz[1,3], Kristen Saunders[1], Jean Spence[1], Edward Nudelman[1], Steven B Levery[4], Thayer White[1], John M Neveu[5], William S Lane[5], Yves Bourne[2], Martin L Olsson[6,7], Bernard Henrissat[2] & Henrik Clausen[3,8]

Enzymatic removal of blood group ABO antigens to develop universal red blood cells (RBCs) was a pioneering vision originally proposed more than 25 years ago. Although the feasibility of this approach was demonstrated in clinical trials for group B RBCs, a major obstacle in translating this technology to clinical practice has been the lack of efficient glycosidase enzymes. Here we report two bacterial glycosidase gene families that provide enzymes capable of efficient removal of A and B antigens at neutral pH with low consumption of recombinant enzymes. The crystal structure of a member of the α-*N*-acetylgalactosaminidase family reveals an unusual catalytic mechanism involving NAD$^+$. The enzymatic conversion processes we describe hold promise for achieving the goal of producing universal RBCs, which would improve the blood supply while enhancing the safety of clinical transfusions.

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