

# Chapter 25. Biomolecules: Carbohydrates

Based on McMurry's *Organic Chemistry*, 7<sup>th</sup> edition

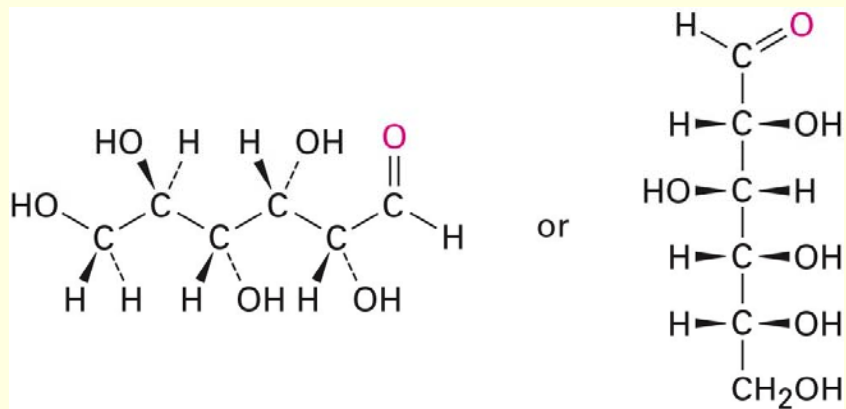
# Importance of Carbohydrates

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- Distributed widely in nature
- Key intermediates of metabolism (sugars)
- Structural components of plants (cellulose)
- Central to materials of industrial products: paper, lumber, fibers
- Key component of food sources: sugars, flour, vegetable fiber
- Contain OH groups on most carbons in linear chains or in rings

# Chemical Formula and Name

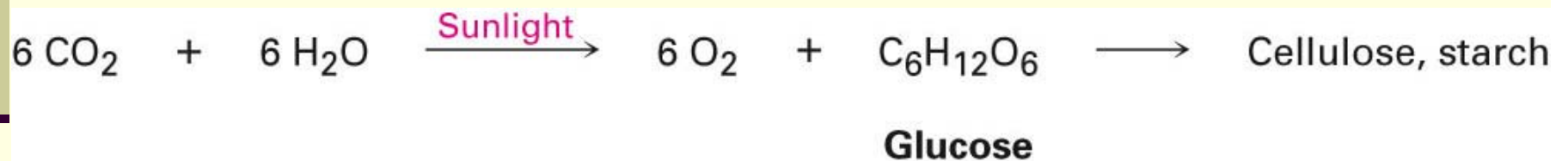
- Carbohydrates have roughly as many O's as C's (highly oxidized)
- Since H's are about connected to each H and O the empirical formulas are roughly  $(C(H_2O))_n$ 
  - Appears to be “carbon hydrate” from formula
- Current terminology: natural materials that contain many hydroxyls and other oxygen-containing groups



**Glucose (dextrose),  
a pentahydroxyhexanal**

# Sources

- Glucose is produced in plants through photosynthesis from  $\text{CO}_2$  and  $\text{H}_2\text{O}$
- Glucose is converted in plants to other small sugars and polymers (cellulose, starch)
- Dietary carbohydrates provide the major source of energy required by organisms



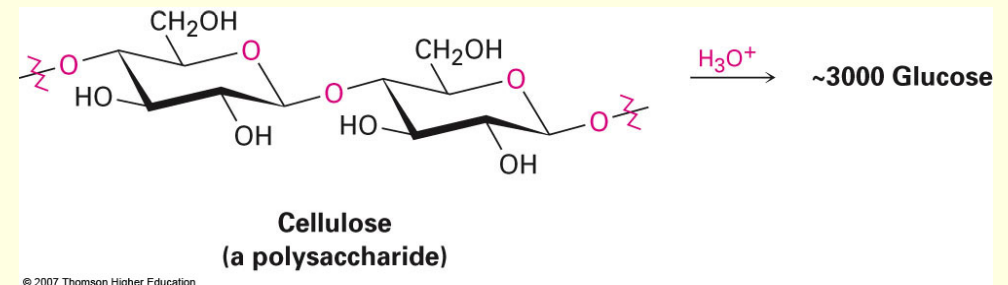
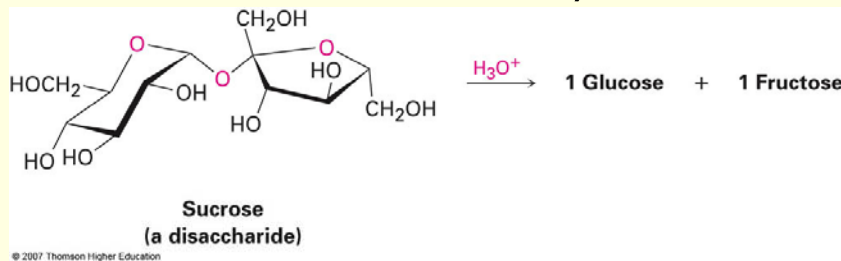
# Why this Chapter?

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- To see what the structures and 1° biological functions of carbohydrates are
- To have an introduction on how carbohydrates are biosynthesized and degraded in organisms

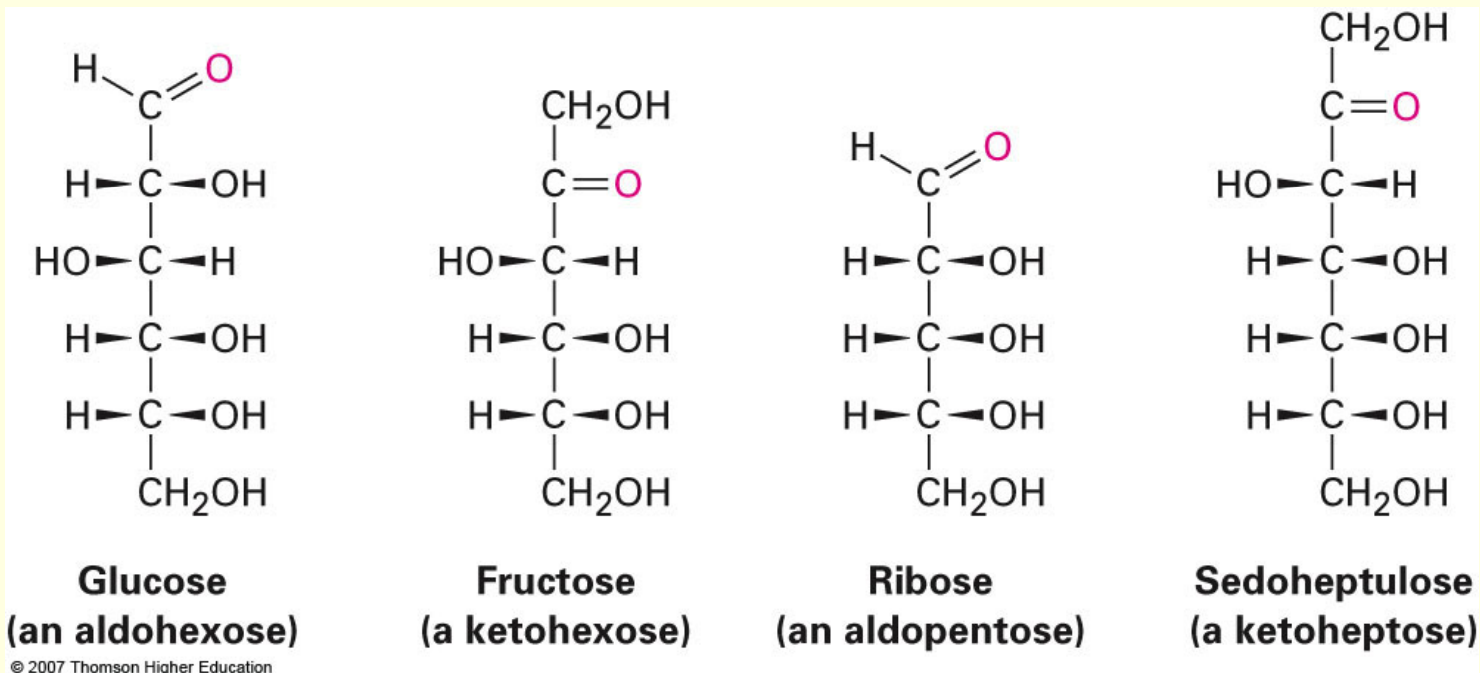
# 25.1 Classification of Carbohydrates

- Simple sugars (monosaccharides) can't be converted into smaller sugars by hydrolysis.
- Carbohydrates are made of two or more simple sugars connected as acetals (aldehyde and alcohol), oligosaccharides and polysaccharides
- Sucrose (table sugar): disaccharide from two monosaccharides (glucose linked to fructose),
- Cellulose is a polysaccharide of several thousand glucose units connected by acetal linkages (aldehyde and alcohol)



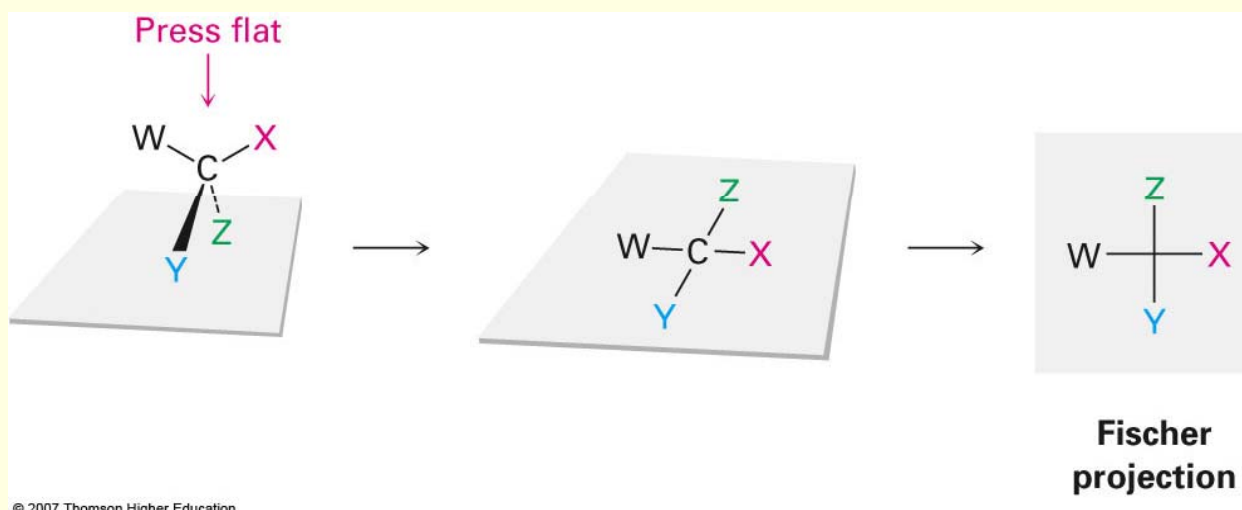
# Aldoses and Ketoses

- *aldo-* and *keto-* prefixes identify the nature of the carbonyl group
- *-ose* suffix designates a carbohydrate
- Number of C's in the monosaccharide indicated by root (-tri-, tetra-, penta-, hexa-)



## 25.2 Depicting Carbohydrate Stereochemistry: Fischer Projections

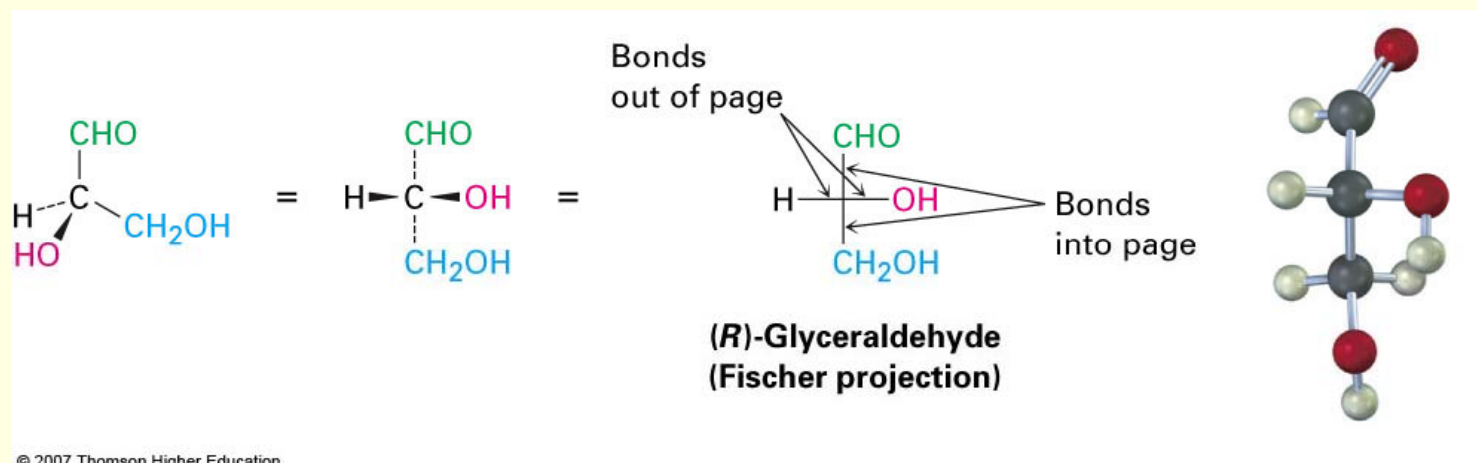
- Carbohydrates have multiple chirality centers and common sets of atoms
- A chirality center C is projected into the plane of the paper and other groups are horizontal or vertical lines
- Groups forward from paper are always in horizontal line. The oxidized end of the molecule is always higher on the page (“up”)
- The “projection” can be seen with molecular models





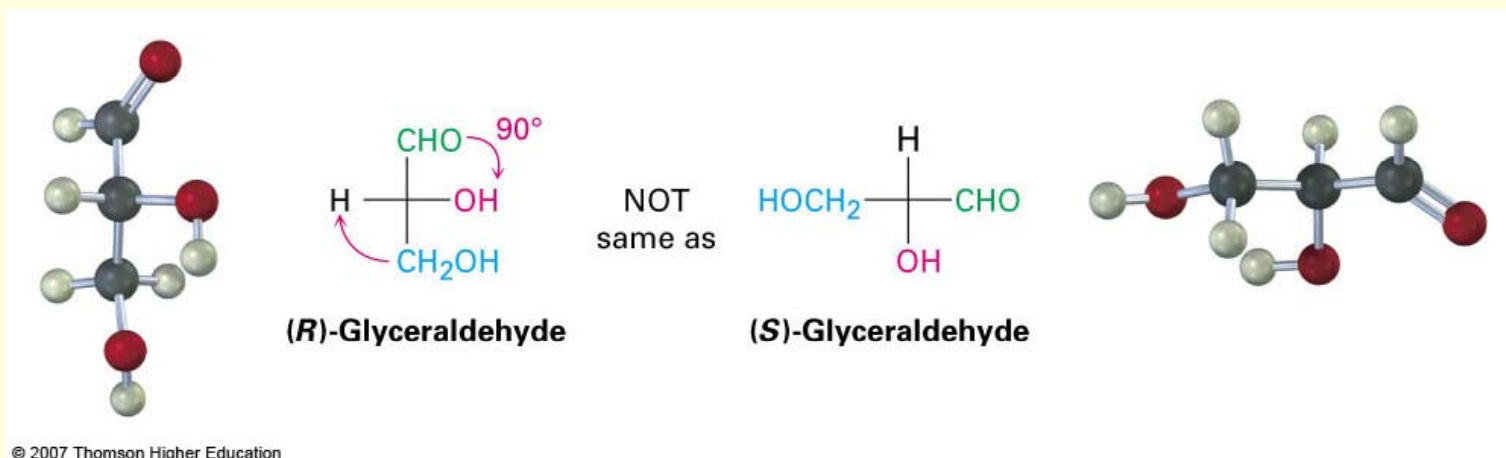
# Stereochemical Reference

- The reference compounds are the two enantiomers of glyceraldehyde,  $C_3H_6O_3$
- A compound is “D” if the hydroxyl group at the chirality center farthest from the oxidized end of the sugar is on the right or “L” if it is on the left.
- D-glyceraldehyde is (*R*)-2,3-dihydroxypropanal
- L-glyceraldehyde is (*S*)-2,3-dihydroxypropanal



# Working With Fischer Projections

- If groups are not in corresponding positions, they can be exchanged three at a time in rotation – work with molecular models to see how this is done
- The entire structure may only be rotated by  $180^\circ$
- While R, S designations can be deduced from Fischer projections (with practice), it is best to make molecular models from the projected structure and work with the model

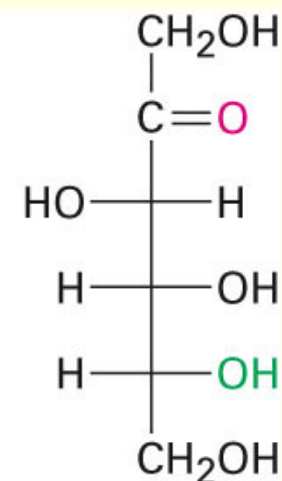
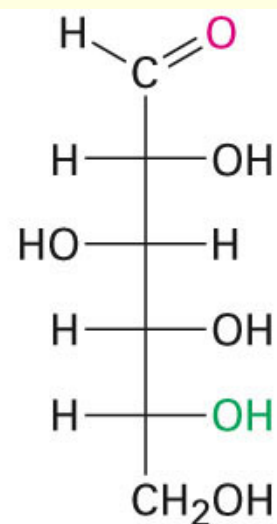
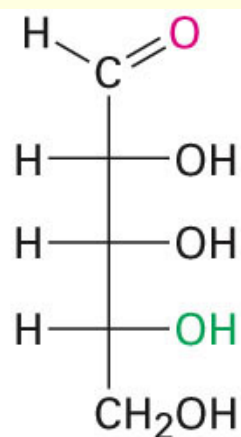
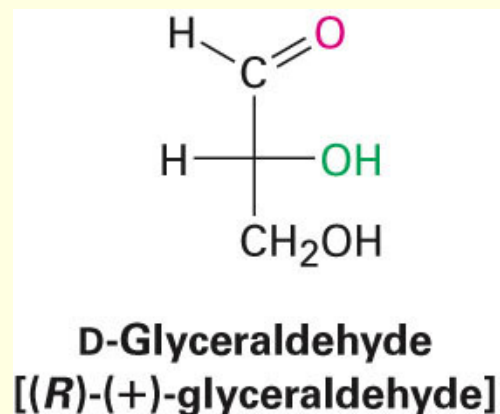


## 25.3 D, L Sugars

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- Glyceraldehyde exists as two enantiomers, first identified by their opposite rotation of plane polarized light
- Naturally occurring glyceraldehyde rotates plane-polarized light in a clockwise direction, denoted (+) and is designated “(+)-glyceraldehyde”
- The enantiomer gives the opposite rotation and has a (-) or “l” (levorotatory) prefix
- The direction of rotation of light does not correlate to any structural feature

# Naturally Occurring D Sugars



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## 25.4 Configurations of the Aldoses

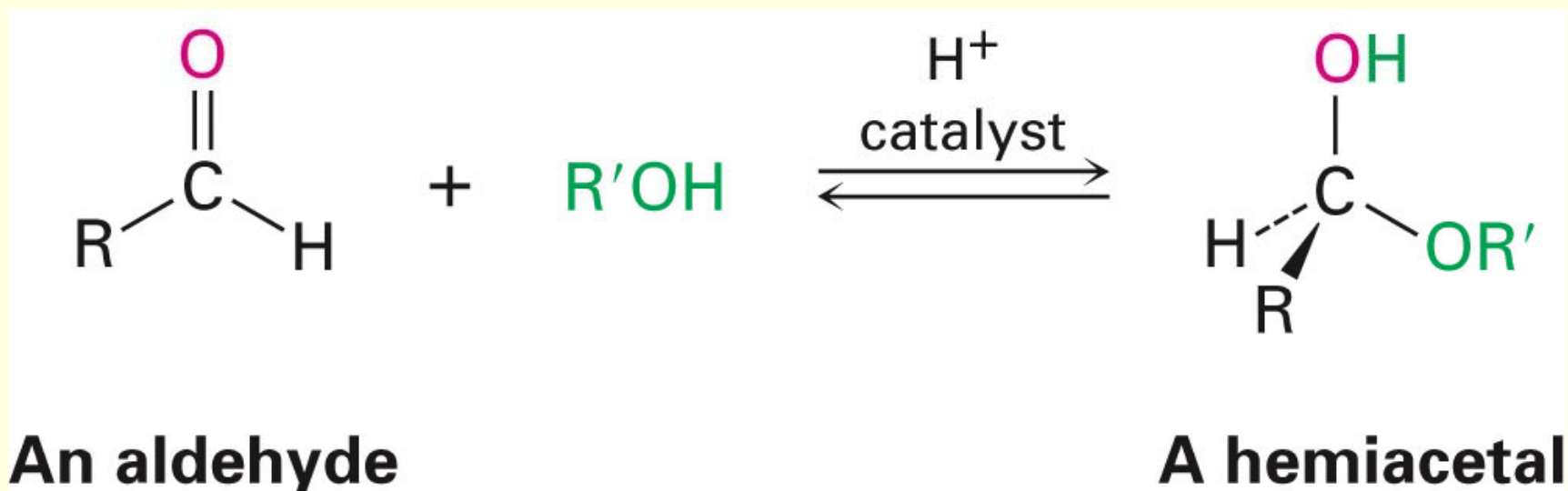
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- Stereoisomeric aldoses are distinguished by trivial names, rather than by systematic designations
- Enantiomers have the same names but different D,L prefixes
- *R,S* designations are difficult to work with when there are multiple similar chirality centers
- Systematic methods for drawing and recalling structures are based on the use of Fischer projections

- 
- **Aldotetroses** have two chirality centers
  - There are 4 stereoisomeric aldotetroses, two pairs of enantiomers: *erythrose* and *threose*
  - D-erythrose is a diastereomer of D-threose and L-threose
  - **Aldopentoses** have three chirality centers and  $2^3 = 8$  stereoisomers, four pairs of enantiomers: *ribose*, *arabinose*, *xylose*, and *lyxose*

## 25.5 Cyclic Structures of Monosaccharides: Anomers

- Alcohols add reversibly to aldehydes and ketones, forming hemiacetals



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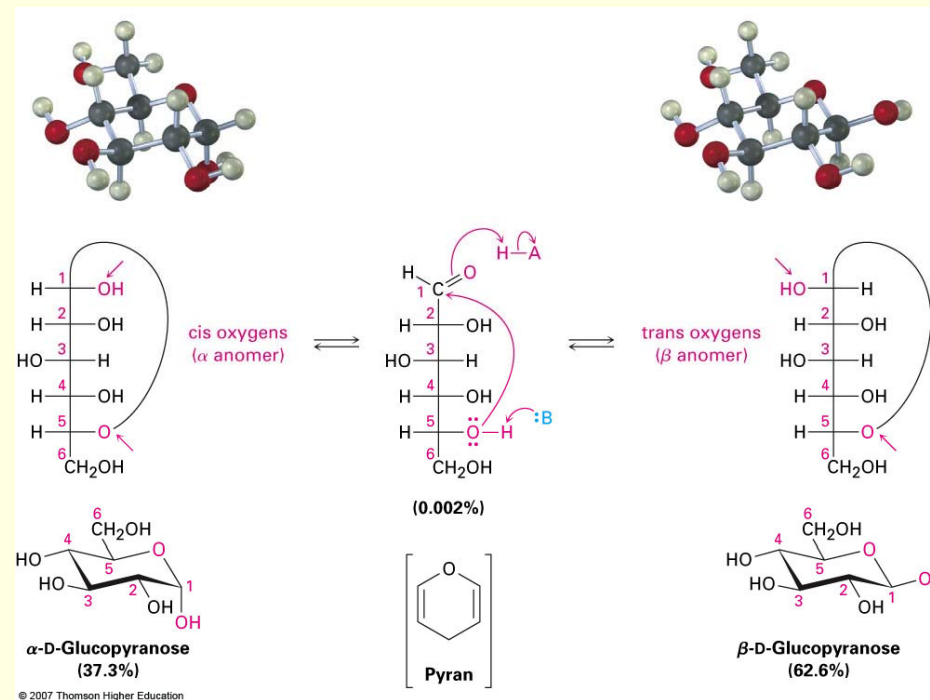
# Internal Hemiacetals of Sugars

- Intramolecular nucleophilic addition creates cyclic hemiacetals in sugars
- Five- and six-membered cyclic hemiacetals are particularly stable
- Five-membered rings are furanoses. Six-membered are pyranoses
- Formation of the cyclic hemiacetal creates an additional chirality center giving two diastereomeric forms, designated  $\alpha$  and  $\beta$
- These diastereomers are called anomers
- The designation  $\alpha$  indicates that the OH at the anomeric center is on the same side of the Fischer projection structure as hydroxyl that designates whether the structure is D or L



# Converting to Proper Structures

- The Fischer projection structures must be redrawn to consider real bond lengths, and you also see the “Pyran” form
- Pyranose rings have a chair-like geometry with axial and equatorial substituents
- Rings are usually drawn placing the hemiacetal oxygen atom at the right rear



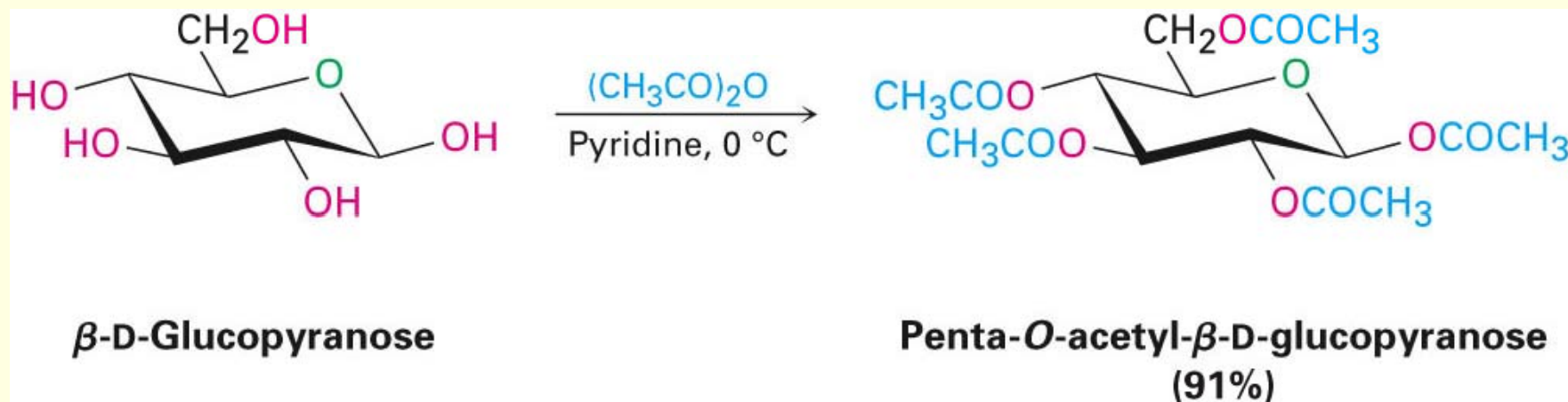
# Monosaccharide Anomers: Mutarotation

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- The two anomers of D-glucopyranose can be crystallized and purified
  - $\alpha$ -D-glucopyranose melts at  $146^\circ$  and its specific rotation,  $[\alpha]^D = 112.2^\circ$ ;
  - $\beta$ -D-glucopyranose melts at  $148\text{--}155^\circ\text{C}$  with a specific rotation of  $[\alpha]^D = 18.7^\circ$
- Rotation of solutions of either pure anomer slowly changes due to slow conversion of the pure anomers into a 37:63 equilibrium mixture of  $\alpha$ : $\beta$  called mutarotation

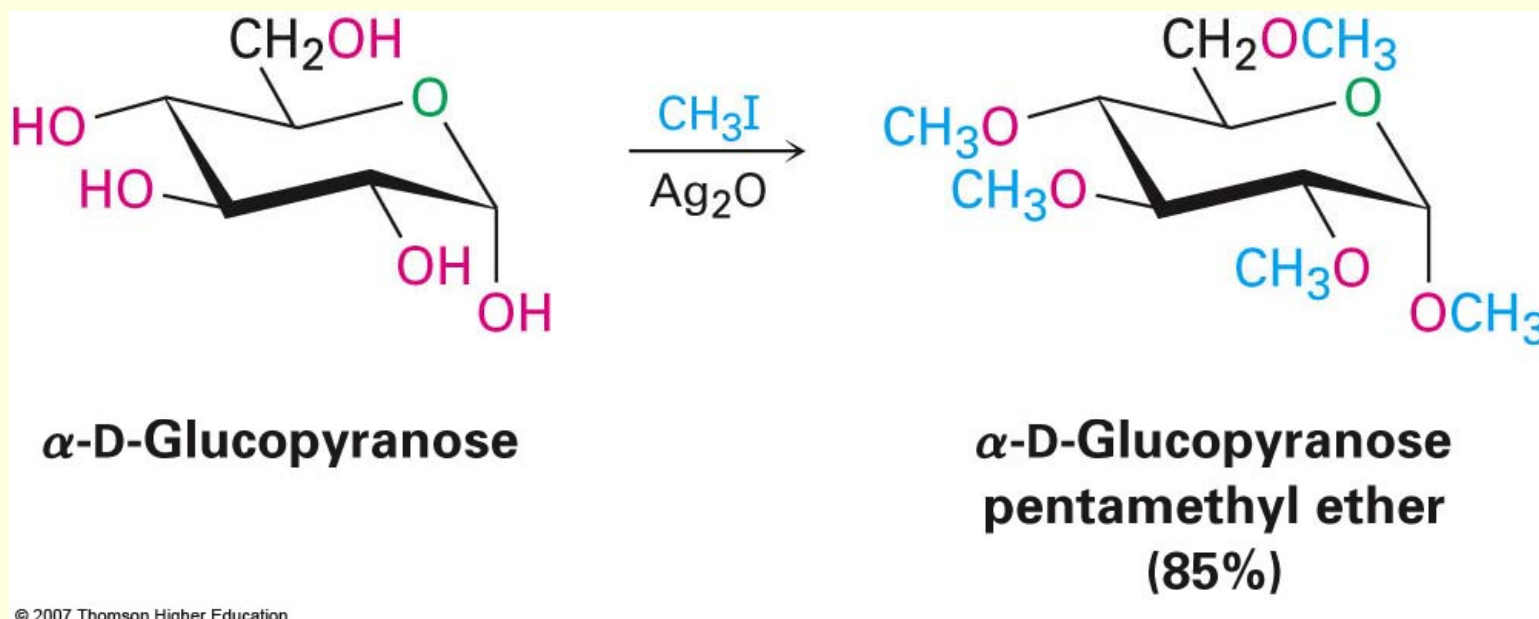
## 25.6 Reactions of Monosaccharides

- —OH groups can be converted into esters and ethers, which are often easier to work with than the free sugars and are soluble in organic solvents.
  - Esterification by treating with an acid chloride or acid anhydride in the presence of a base
  - All —OH groups react



# Ethers

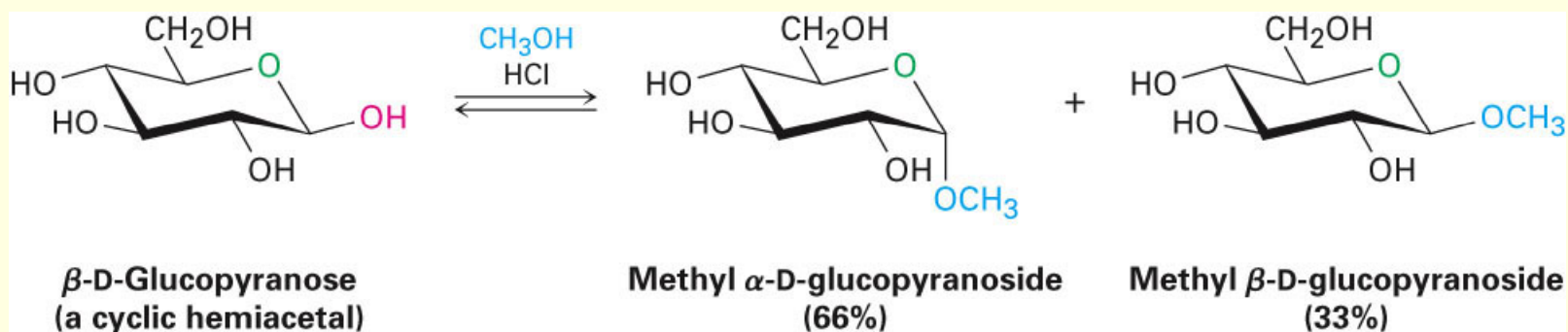
- Treatment with an alkyl halide in the presence of base—the Williamson ether synthesis
- Use silver oxide as a catalyst with base-sensitive compounds



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# Glycoside Formation

- Treatment of a monosaccharide hemiacetal with an alcohol and an acid catalyst yields an acetal in which the anomeric —OH has been replaced by an —OR group
  - $\beta$ -D-glucopyranose with methanol and acid gives a mixture of  $\alpha$  and  $\beta$  methyl D-glucopyranosides



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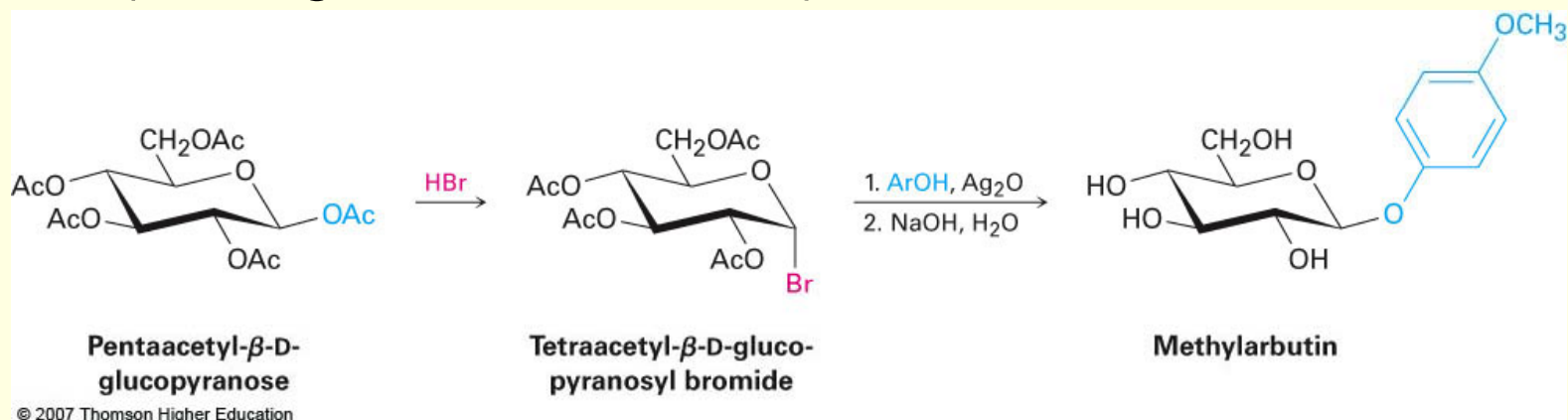
# Glycosides

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- Carbohydrate acetals are named by first citing the alkyl group and then replacing the *-ose* ending of the sugar with *-oside*
- Stable in water, requiring acid for hydrolysis

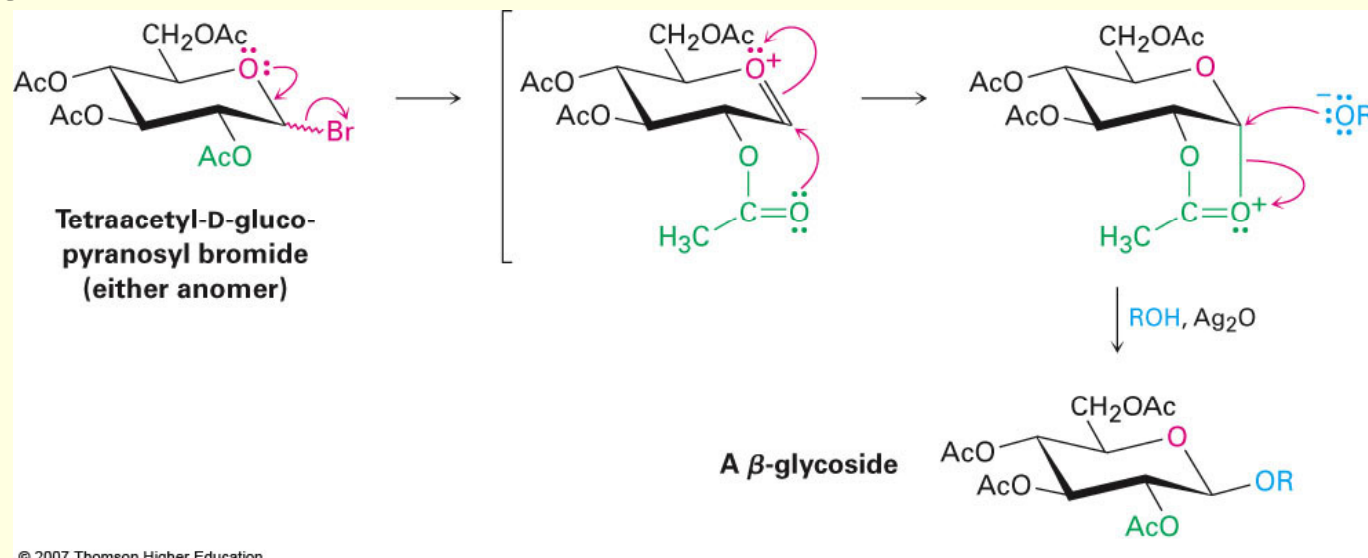
# Selective Formation of C1-Acetal

- Synthesis requires distinguishing the numerous —OH groups
- Treatment of glucose pentaacetate with HBr converts anomeric OH to Br
- Addition of alcohol (with  $\text{Ag}_2\text{O}$ ) gives a  $\beta$  glycoside (Koenigs–Knorr reaction)



# Koenigs-Knorr Reaction Mechanism

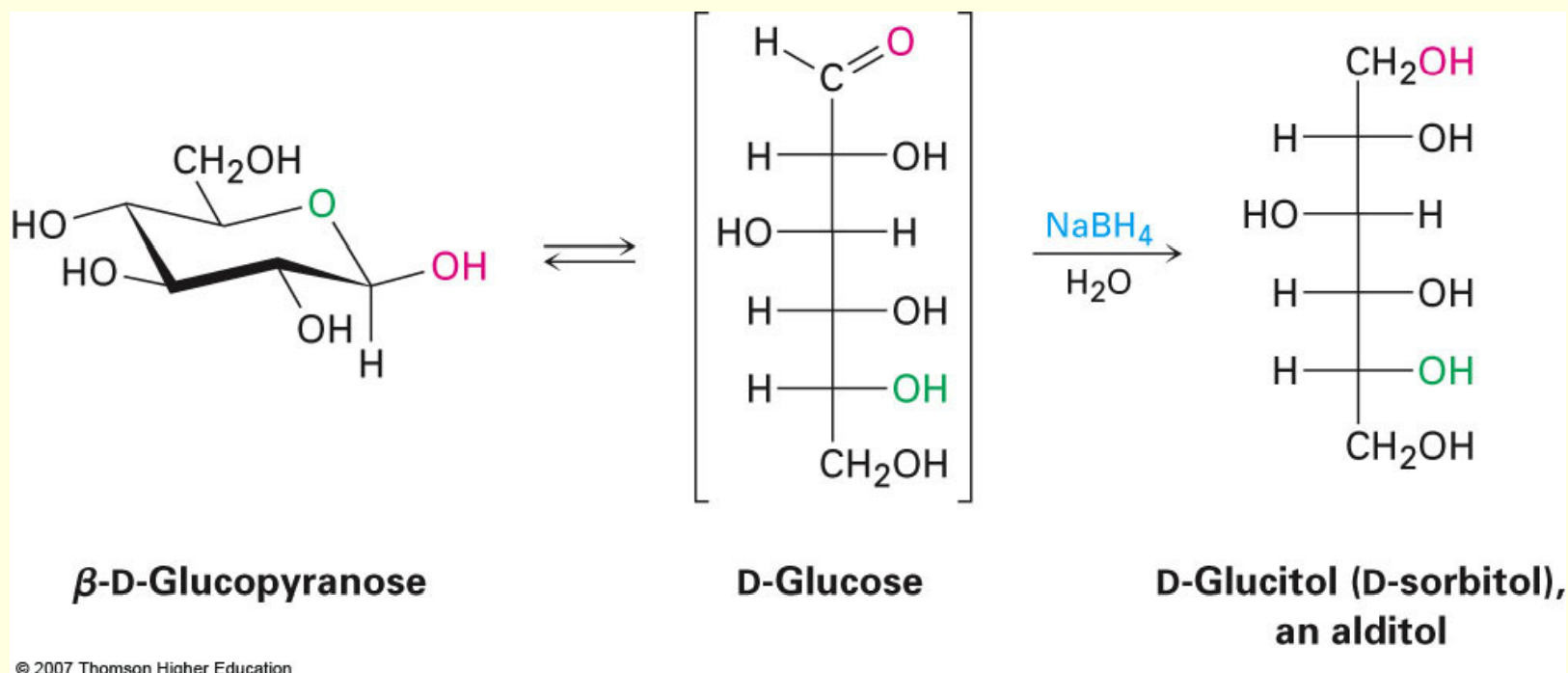
- $\alpha$  and  $\beta$  anomers of tetraacetyl-D-glucopyranosyl bromide give  $\beta$ -glycoside
- Suggests either bromide leaves and cation is stabilized by neighboring acetyl nucleophile from  $\alpha$  side
- Incoming alcohol displaces acetyl oxygen to give  $\beta$  glycoside





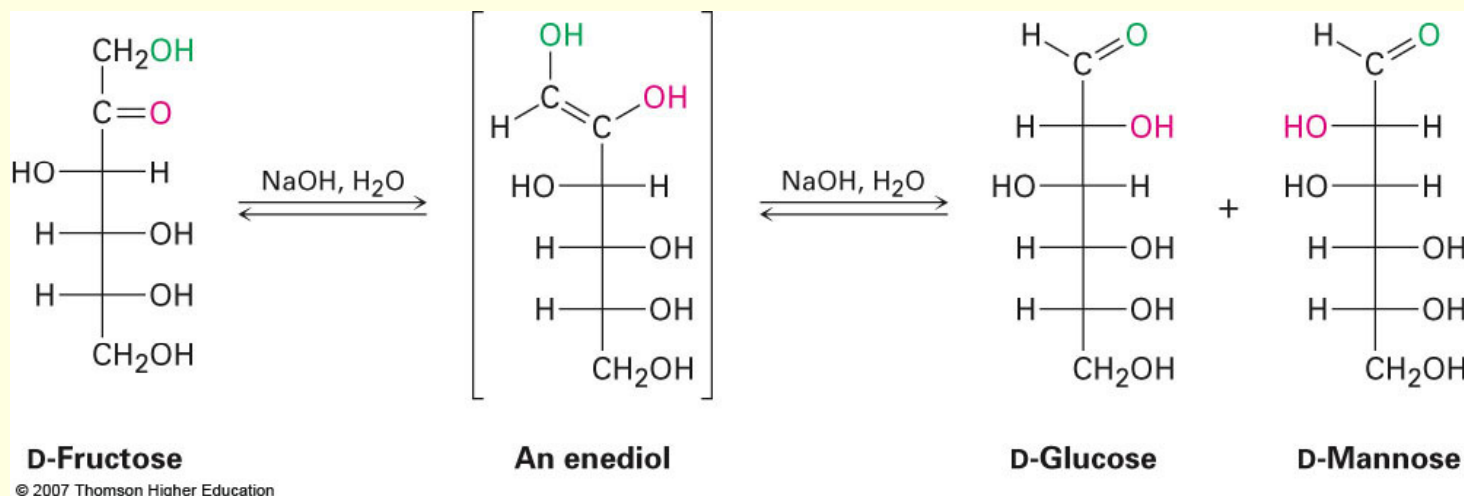
# Reduction of Monosaccharides

- Treatment of an aldose or ketose with  $\text{NaBH}_4$  reduces it to a polyalcohol (alditol)
- Reaction via the open-chain form in the aldehyde/ketone hemiacetal equilibrium



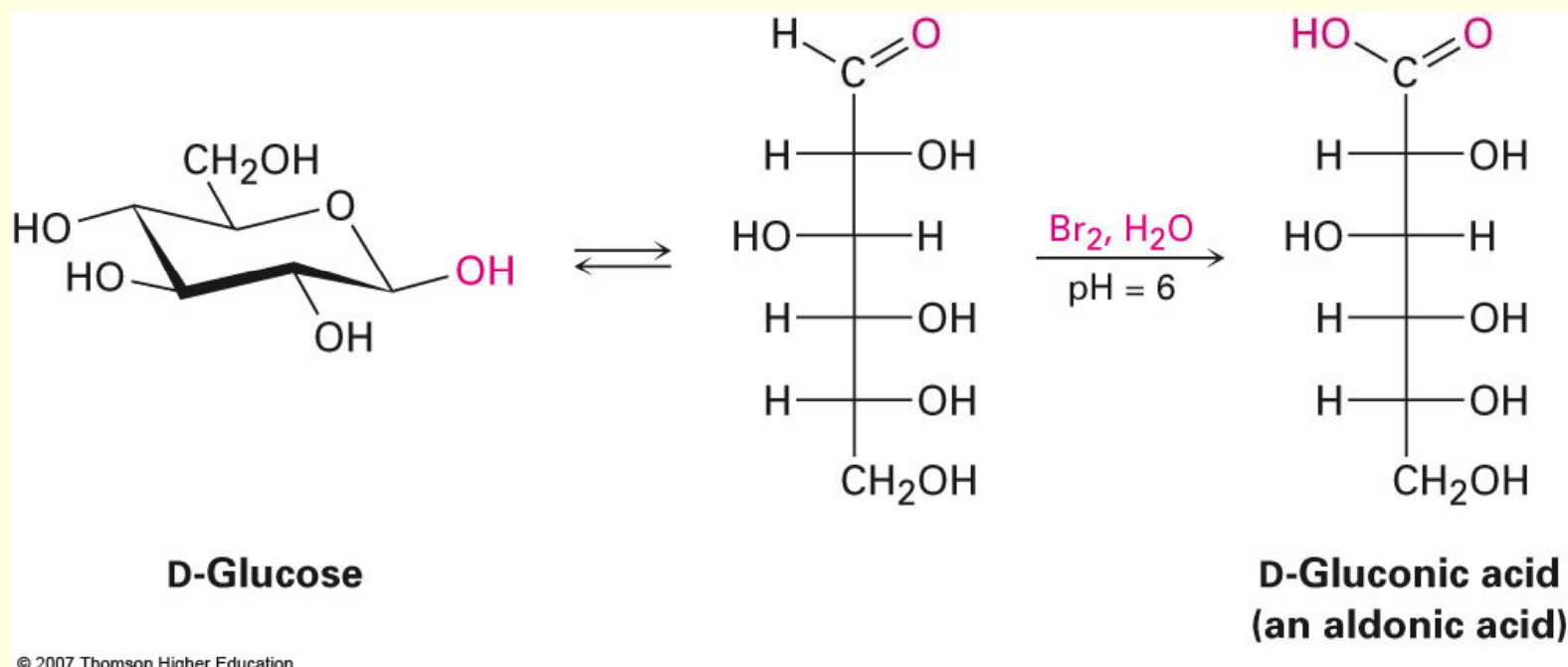
# Oxidation of Monosaccharides

- Aldoses are easily oxidized to carboxylic acids by: Tollens' reagent ( $\text{Ag}^+$ ,  $\text{NH}_3$ ), Fehling's reagent ( $\text{Cu}^{2+}$ , sodium tartrate), Benedict's reagent ( $\text{Cu}^{2+}$  sodium citrate)
  - Oxidations generate metal mirrors; serve as tests for “reducing” sugars (produce metallic mirrors)
- Ketoses are reducing sugars if they can isomerize to aldoses



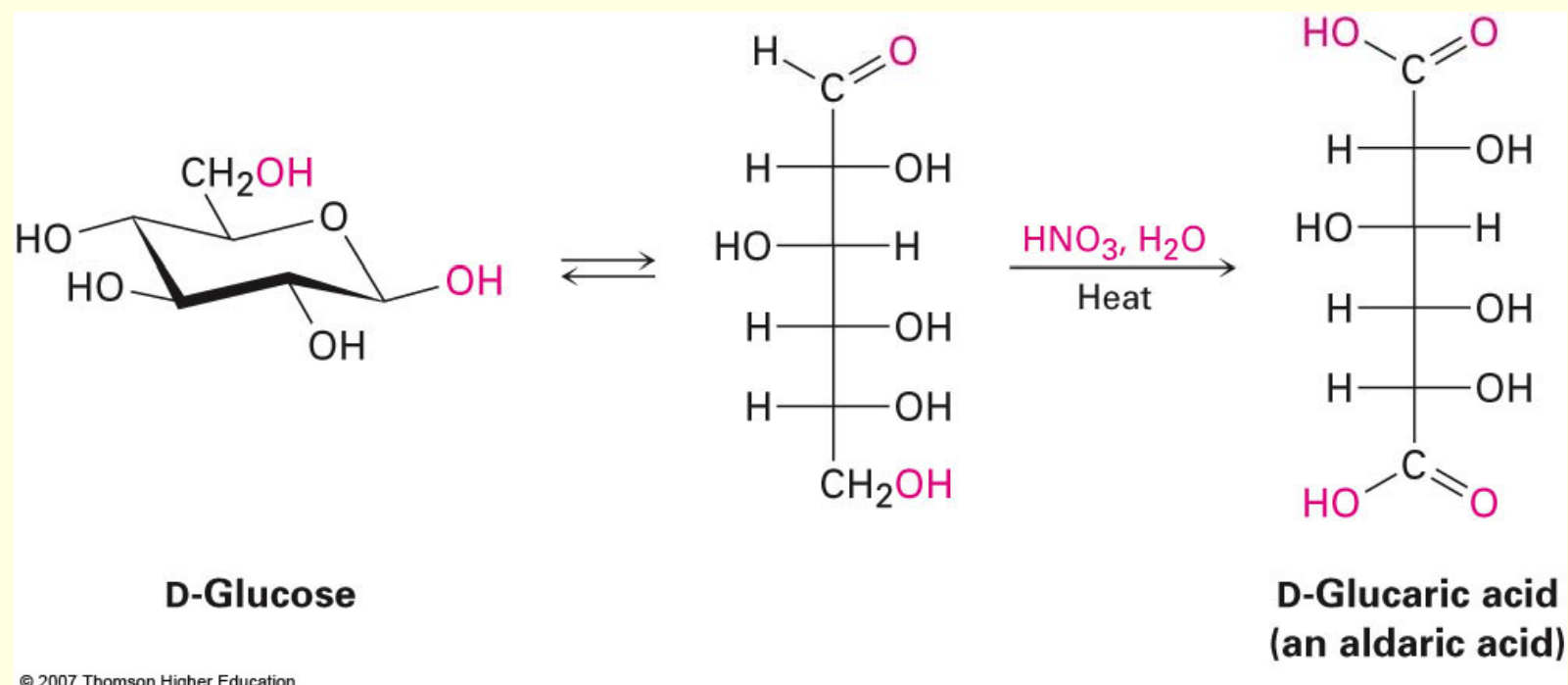
# Oxidation of Monosaccharides with Bromine

- $\text{Br}_2$  in water is an effective oxidizing reagent for converting aldoses to carboxylic acid, called aldonic acids (the metal reagents are for analysis only)



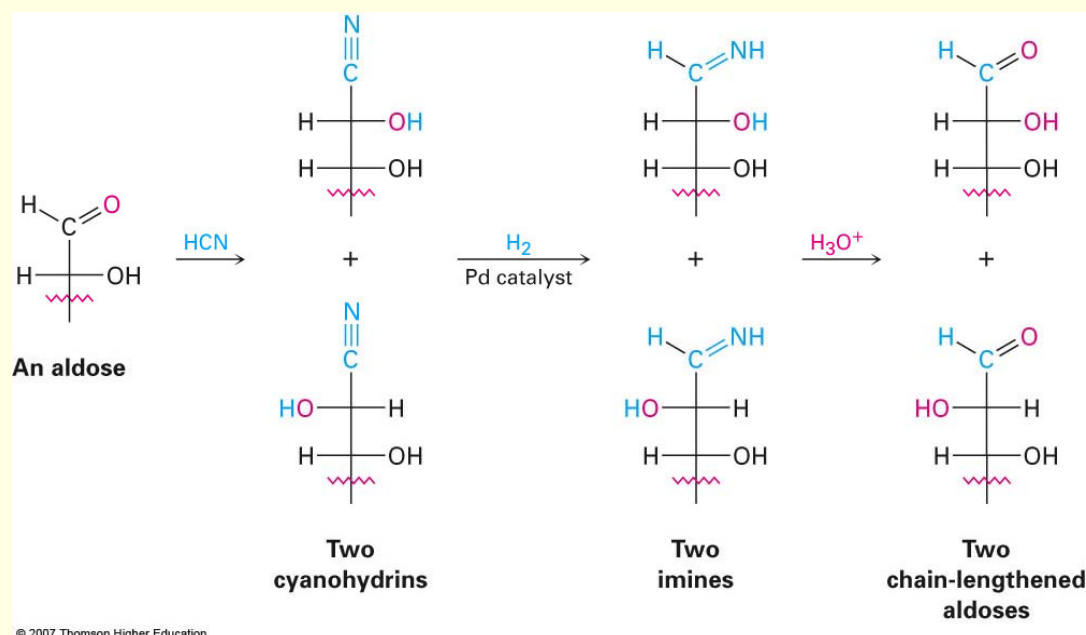
# Formation of Dicarboxylic Acids

- Warm dilute  $\text{HNO}_3$  oxidizes aldoses to dicarboxylic acids, called aldaric acids
- The  $\text{—CHO}$  group and the terminal  $\text{—CH}_2\text{OH}$  group are oxidized to  $\text{COOH}$



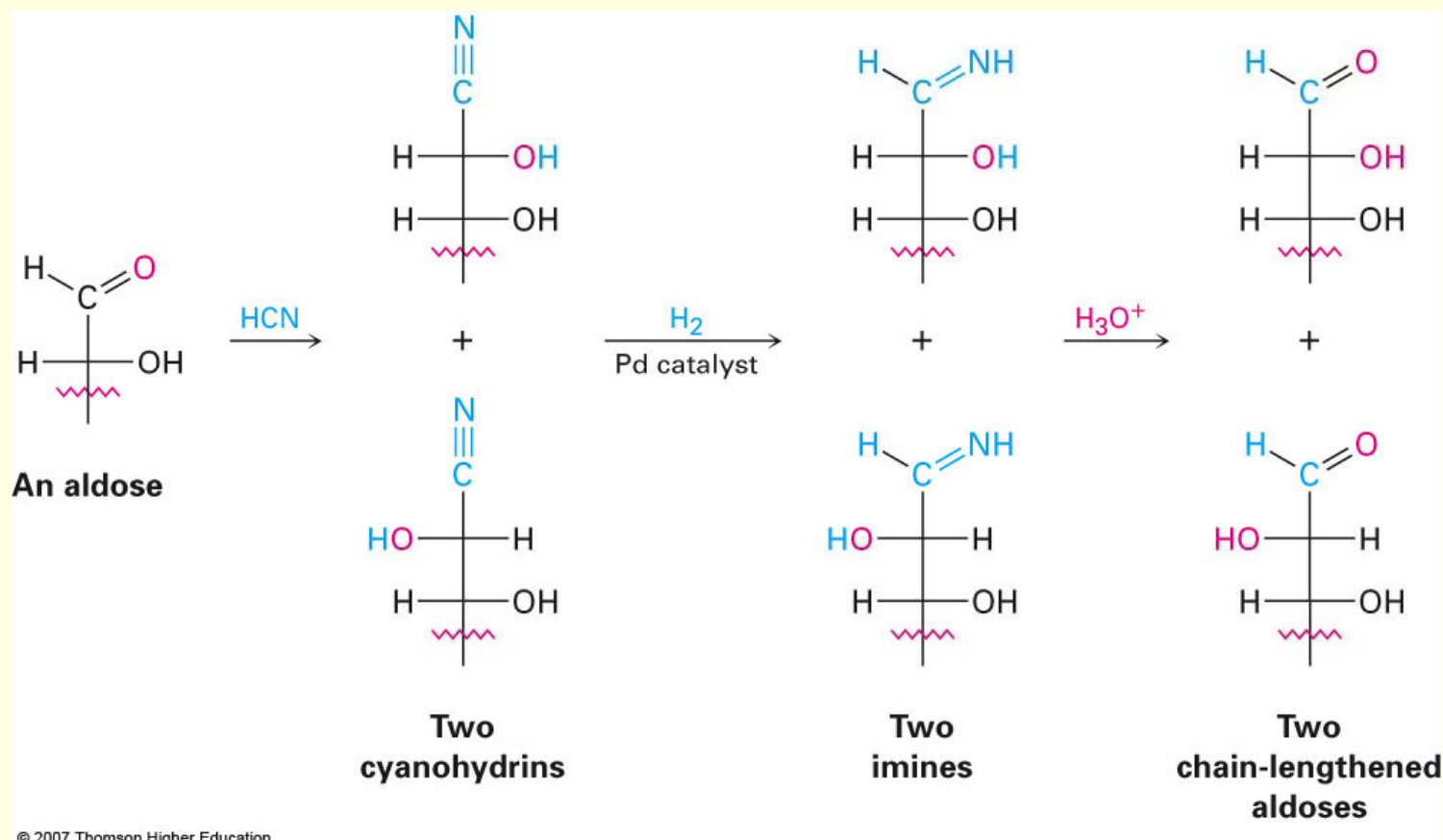
# Chain Lengthening: The Kiliani–Fischer Synthesis

- Lengthening aldose chain by one  $\text{CH}(\text{OH})$ , an aldopentose is converted into an aldohexose
- Aldoses form cyanohydrins with  $\text{HCN}$ 
  - Follow by hydrolysis, ester formation, reduction
- Modern improvement: reduce nitrile over a palladium catalyst, yielding an imine intermediate that is hydrolyzed to an aldehyde



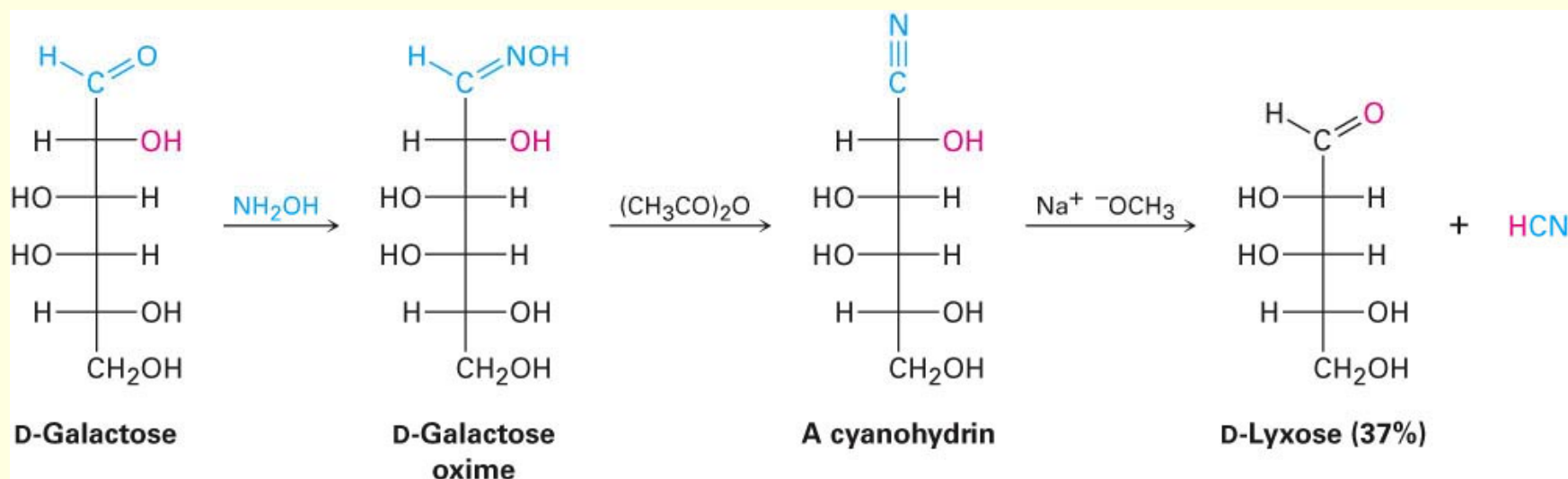
# Stereoisomers from Kiliani-Fischer Synthesis

- Cyanohydrin is formed as a mixture of stereoisomers at the new chirality center, resulting in two aldoses



# Chain Shortening: The Wohl Degradation

- Shortens aldose chain by one  $\text{CH}_2\text{OH}$



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## 25.7 The Eight Essential Monosaccharides

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- Cells need eight monosaccharides for proper functioning
- More energetically efficient to obtain these from environment
- Include L-fucose, D-galactose, D-glucose, D-mannose, N-acetyl-D-glucosamine, N-acetyl-D-galactosamine, D-xylose, N-acetyl-D-neuraminic acid

See Figure 25.9



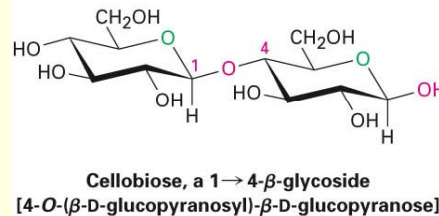
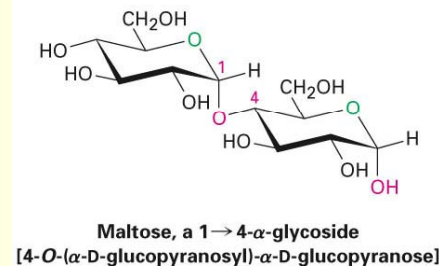
## 25.8 Disaccharides

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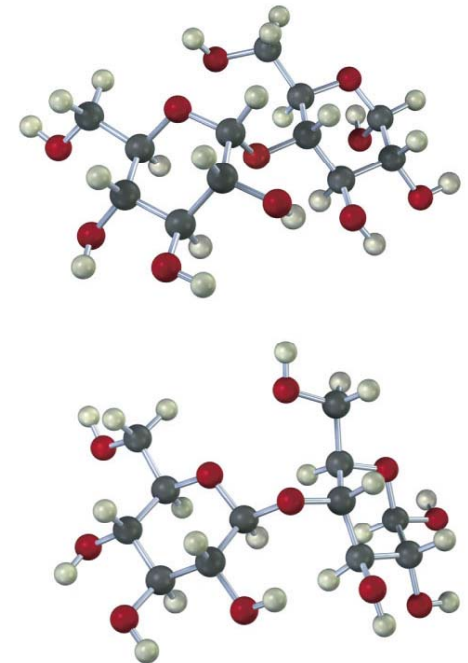
- A disaccharide combines a hydroxyl of one monosaccharide in an acetal linkage with another
- A glycosidic bond between C1 of the first sugar ( $\alpha$  or  $\beta$ ) and the —OH at C4 of the second sugar is particularly common (a 1,4' link)

# Maltose and Cellobiose

- Maltose: two D-glucopyranose units with a 1,4'- $\alpha$ -glycoside bond (from starch hydrolysis)
- Cellobiose: two D-glucopyranose units with a 1,4'- $\beta$ -glycoside bond (from cellulose hydrolysis)

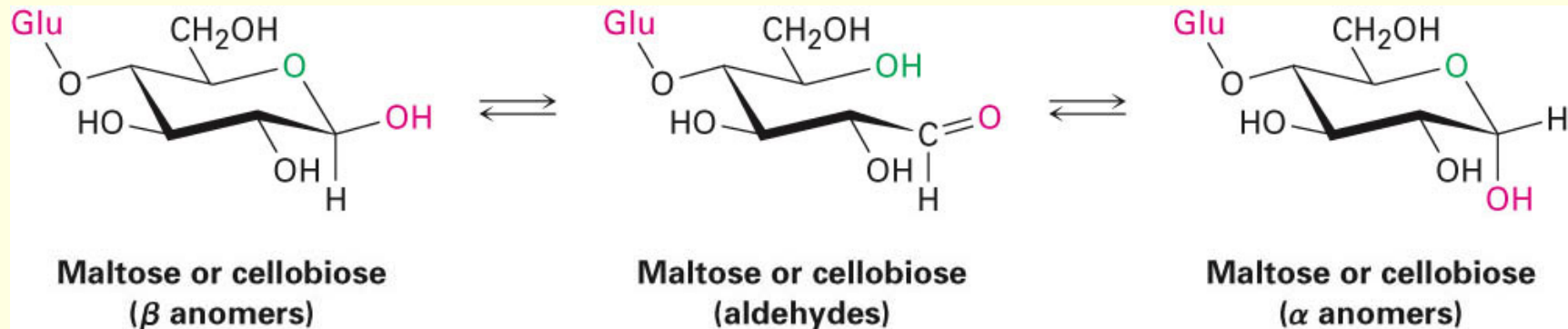


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# Hemiacetals in Disaccharides

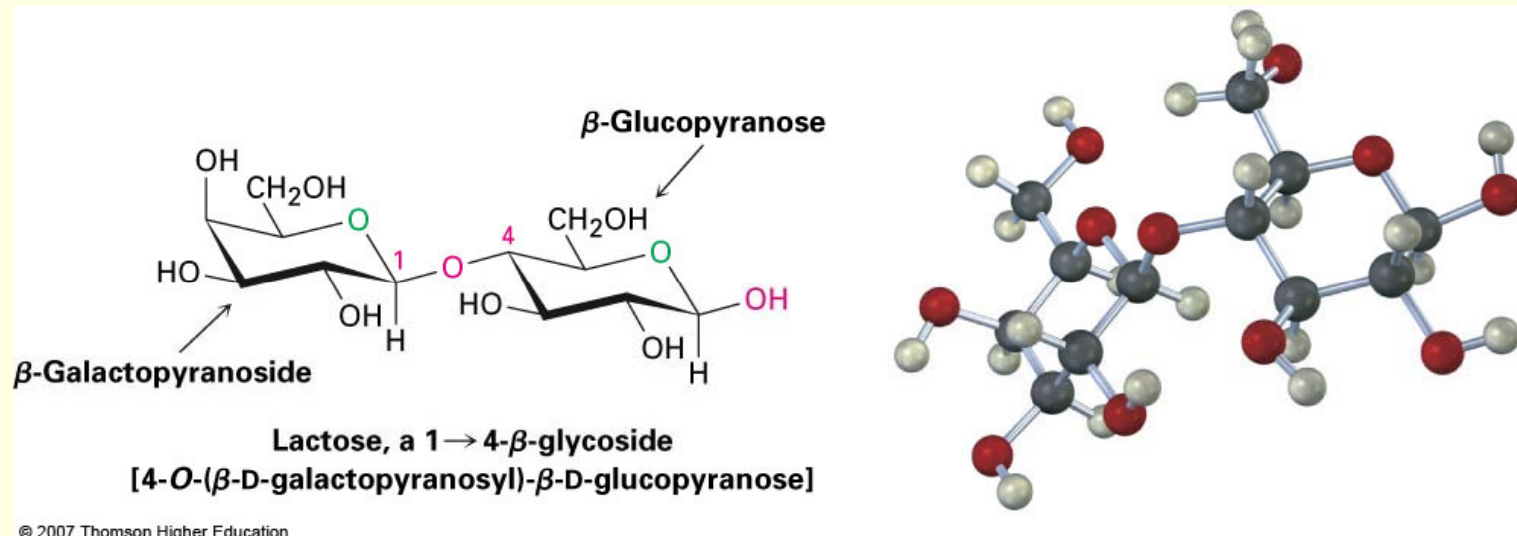
- Maltose and cellobiose are both reducing sugars
- The  $\alpha$  and  $\beta$  anomers equilibrate, causing mutarotation



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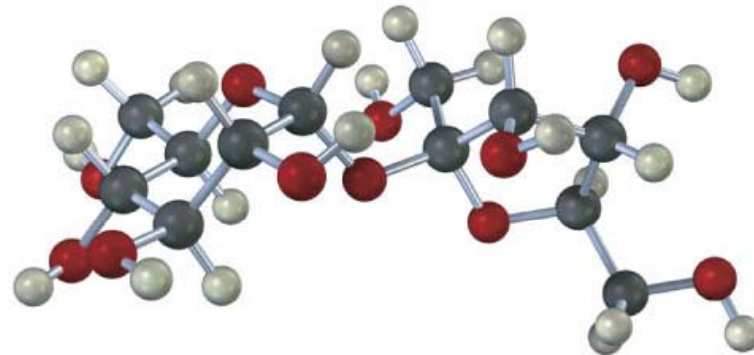
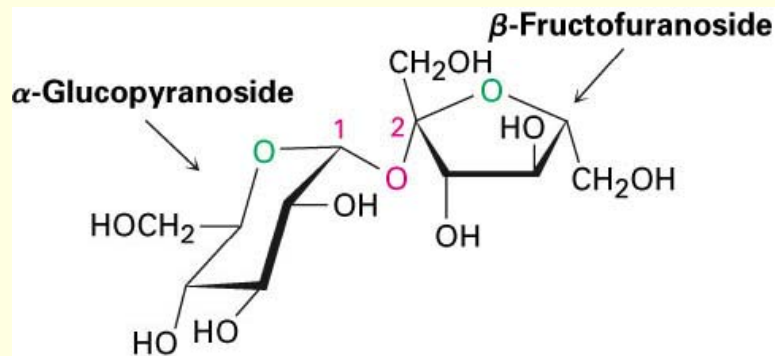
# Lactose

- A disaccharide that occurs naturally in milk
- Lactose is a reducing sugar. It exhibits mutarotation
- It is 1,4'- $\beta$ -D-galactopyranosyl-D-glucopyranoside
- The structure is cleaved in digestion to glucose and galactose



# Sucrose

- “Table Sugar” is pure sucrose, a disaccharide that hydrolyzes to glucose and fructose
- Not a reducing sugar and does not undergo mutarotation (not a hemiacetal)
- Connected as acetal from both anomeric carbons (aldehyde to ketone)



**Sucrose, a 1 $\rightarrow$ 2-glycoside**

**[2-O-( $\alpha$ -D-glucopyranosyl)- $\beta$ -D-fructofuranoside]**

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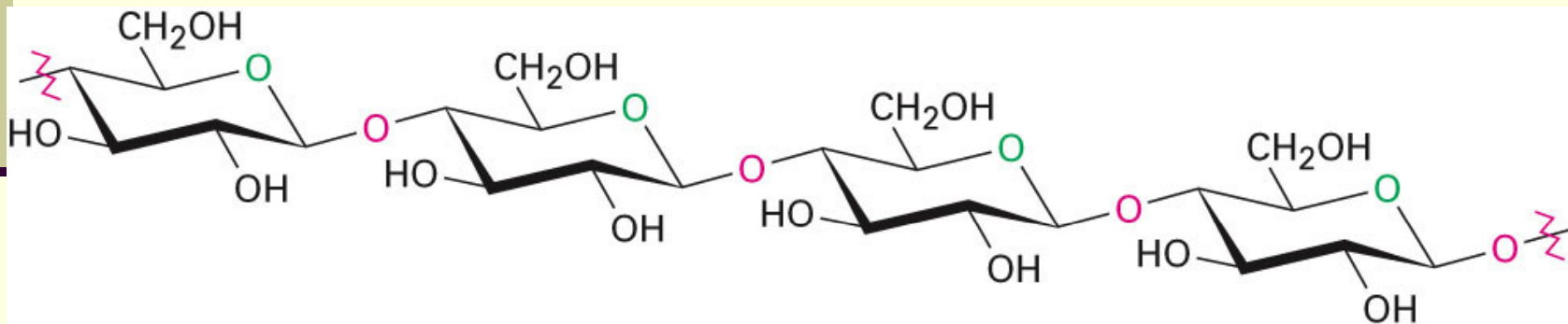
## 25.9 Polysaccharides and Their Synthesis

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- Complex carbohydrates in which very many simple sugars are linked
- Cellulose and starch are the two most widely occurring polysaccharides

# Cellulose

- Consists of thousands of D-glucopyranosyl 1,4'- $\beta$ -glucopyranosides as in cellobiose
- Cellulose molecules form a large aggregate structures held together by hydrogen bonds
- Cellulose is the main component of wood and plant fiber

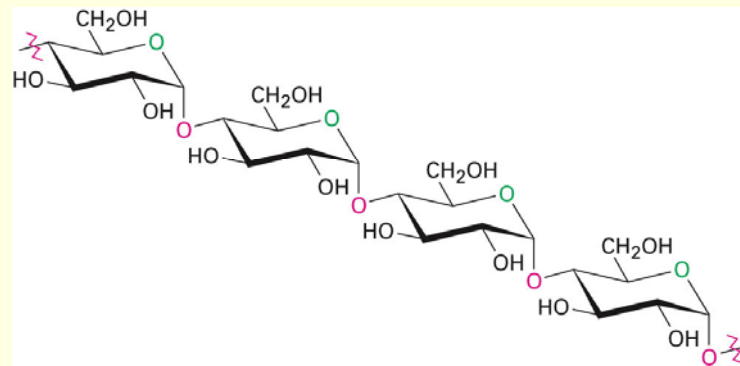


**Cellulose, a 1→4-O-( $\beta$ -D-glucopyranoside) polymer**

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# Starch and Glycogen

- Starch is a 1,4'- $\alpha$ -glucopyranosyl-glucopyranoside polymer
- It is digested into glucose
- There are two components
  - *amylose*, insoluble in water – 20% of starch
    - 1,4'- $\alpha$ -glycoside polymer
  - *amylopectin*, soluble in water – 80% of starch



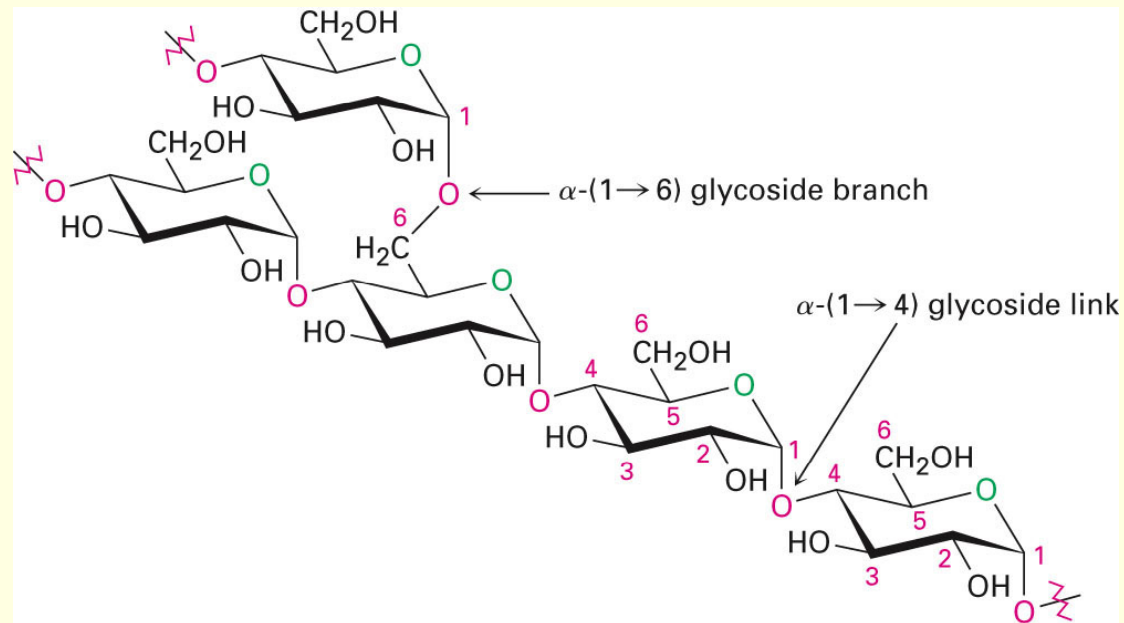
Amylose, a 1→4- $O$ -( $\alpha$ -D-glucopyranoside) polymer

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# Amylopectin

- More complex in structure than amylose
- Has 1,6'- $\alpha$ -glycoside branches approximately every 25 glucose units in addition to 1,4'- $\alpha$ -links

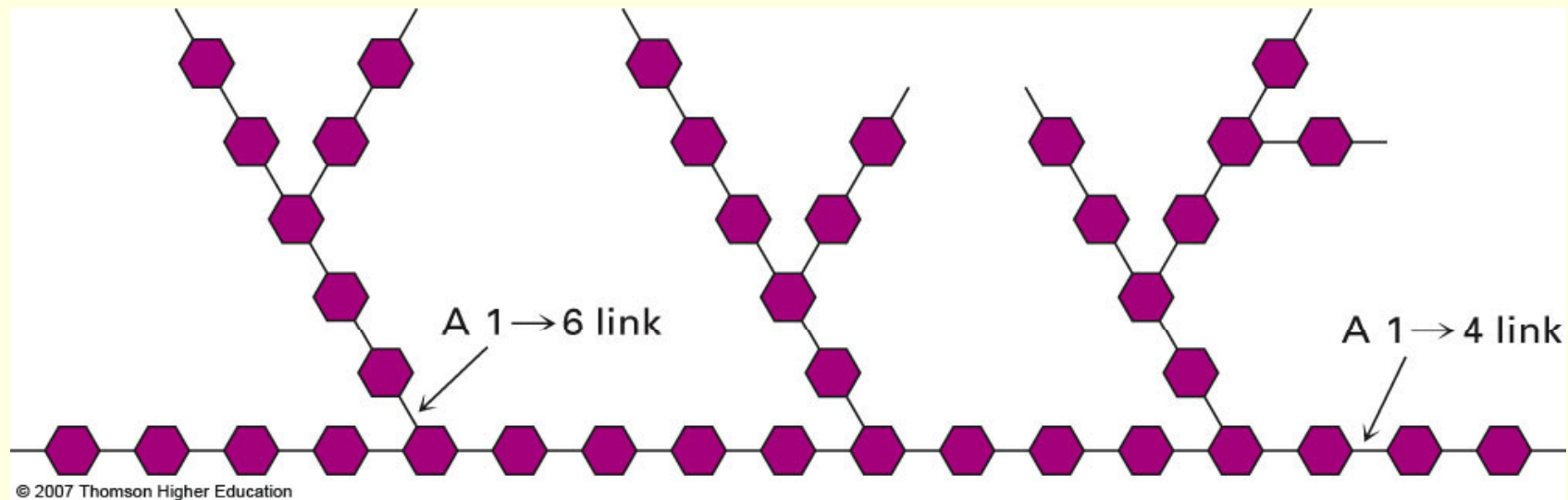


**Amylopectin:  $\alpha$ -(1 $\rightarrow$ 4) links  
with  $\alpha$ -(1 $\rightarrow$ 6) branches**

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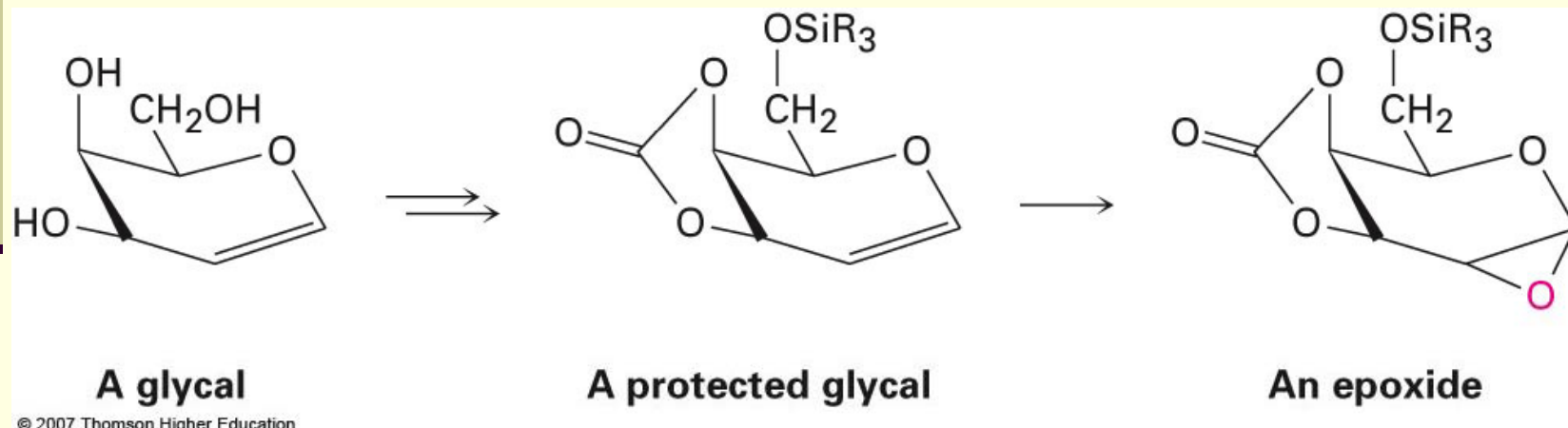
# Glycogen

- A polysaccharide that serves the same energy storage function in animals that starch serves in plants
- Highly branched and larger than amylopectin—up to 100,000 glucose units



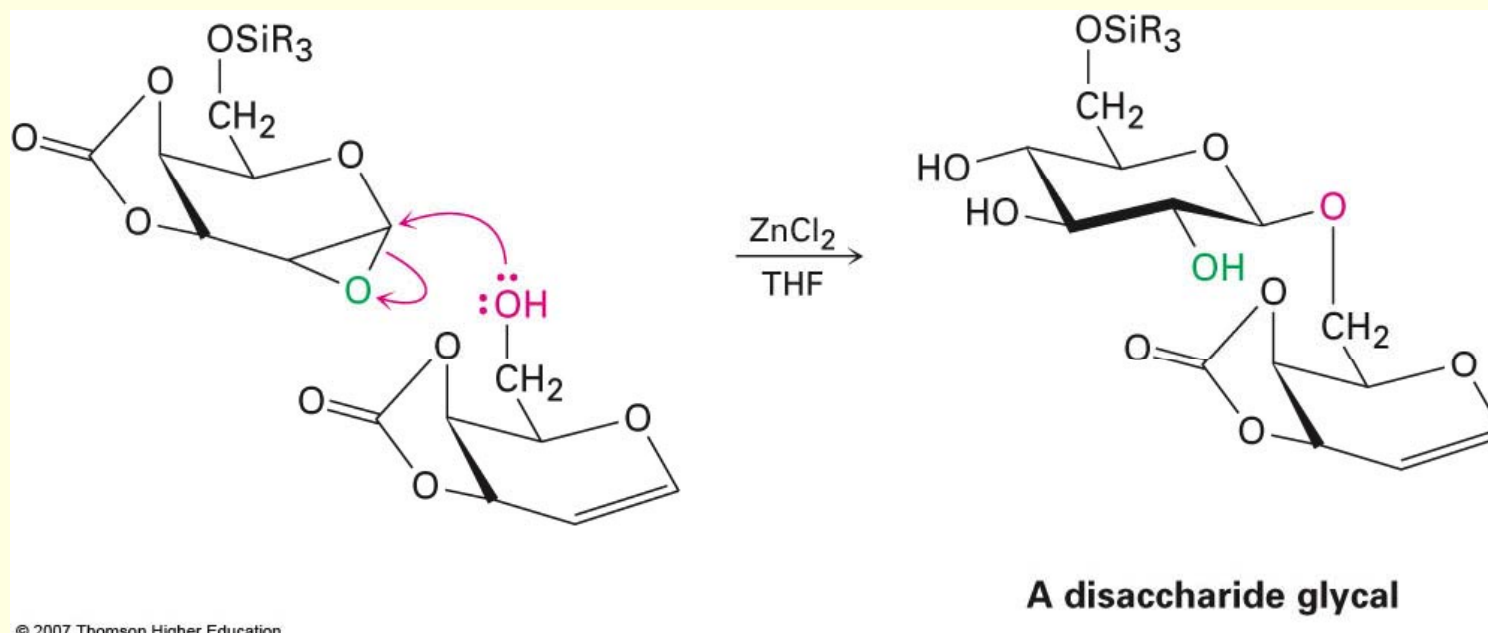
# Synthesis of Polysaccharides – via Glycals

- Difficult to do efficiently, due to many —OH groups
- Glycal assembly is one approach to being selective
- Protect C6 —OH as silyl ether, C3—OH and C4—OH as cyclic carbonate
- Glycal C=C is converted to epoxide



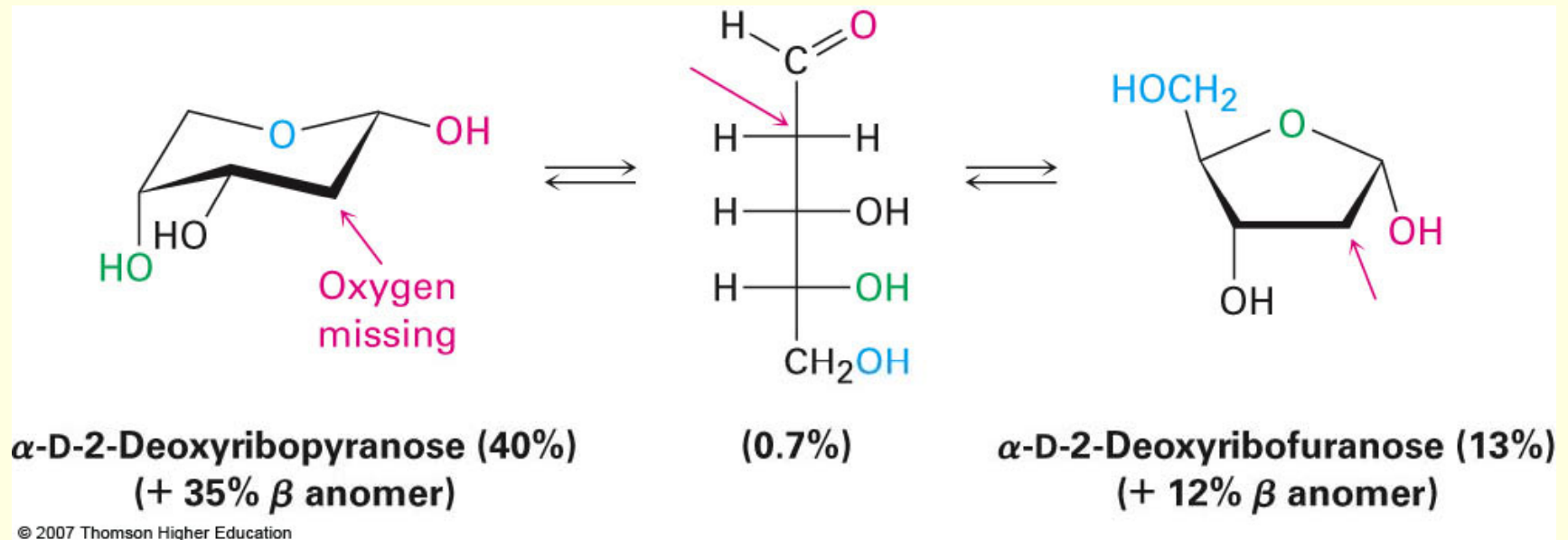
# Glycal Coupling

- React glycal epoxide with a second glycal having a free —OH (with  $\text{ZnCl}_2$  catalyst) yields a disaccharide
- The disaccharide is a glycal, so it can be epoxidized and coupled again to yield a trisaccharide, and then extended



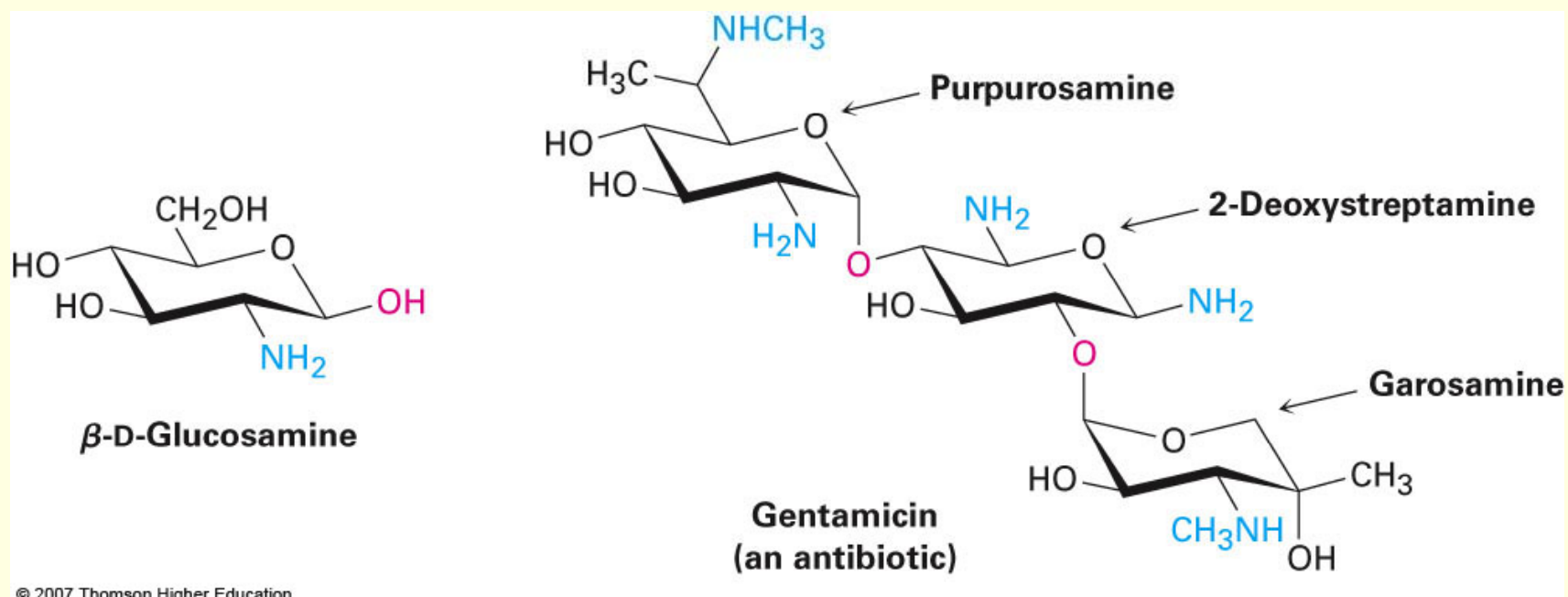
## 25.10 Some Other Important Carbohydrates

- Deoxy sugars have an —OH group is replaced by an —H.
  - Derivatives of 2-deoxyribose are the fundamental units of DNA (deoxyribonucleic acid)



# Amino Sugars

- —OH group is replaced by an —NH<sub>2</sub>
- Amino sugars are found in antibiotics such as streptomycin and gentamicin

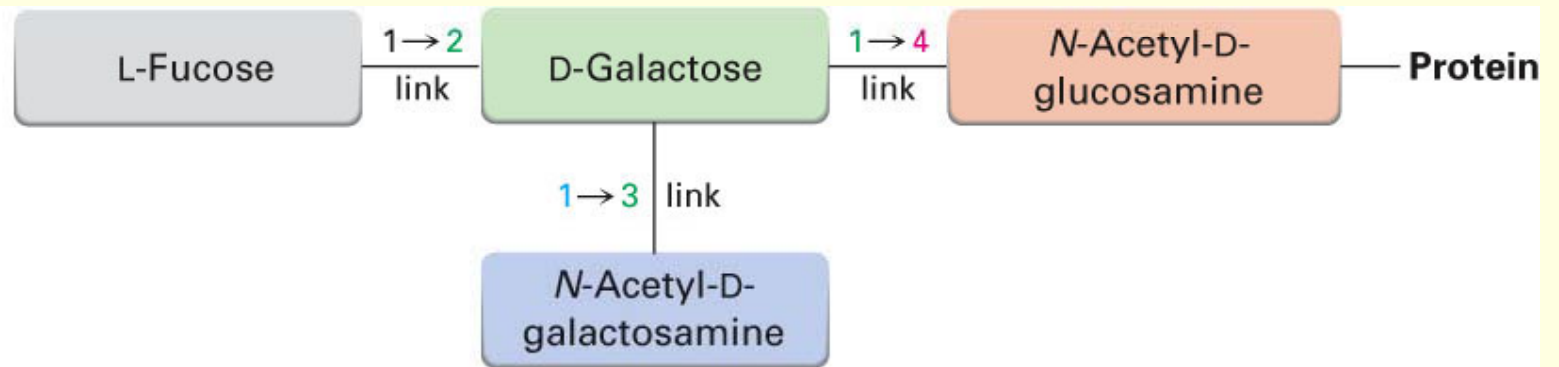


## 25.11 Cell-Surface Carbohydrates and Carbohydrate Vaccines

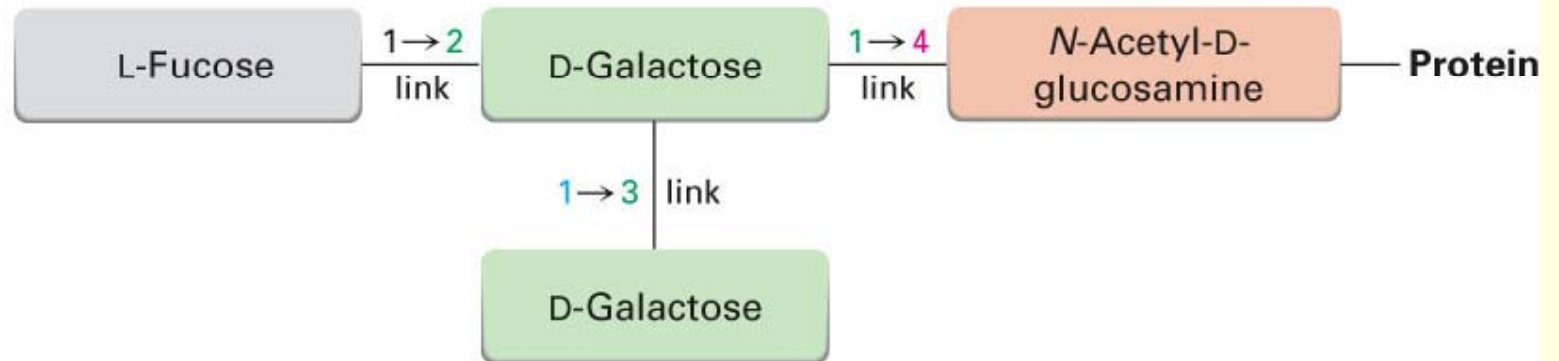
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- Polysaccharides are centrally involved in cell–cell recognition - how one type of cell distinguishes itself from another
- Small polysaccharide chains, covalently bound by glycosidic links to hydroxyl groups on proteins (*glycoproteins*), act as biochemical markers on cell surfaces, determining such things as blood type

### Blood group A



### Blood group B



### Blood group O

