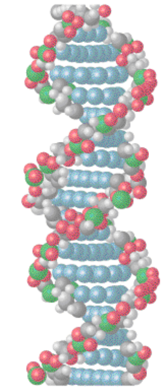


Organic Chemistry, 7th Edition

L. G. Wade, Jr.

Chapter 23

Carbohydrates and Nucleic Acids

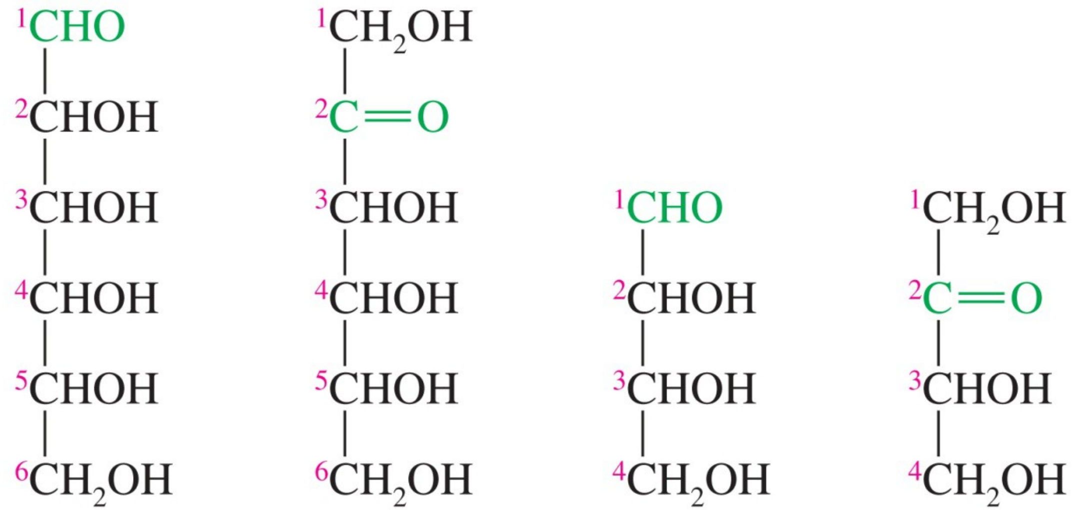
Carbohydrates

- Synthesized by plants using sunlight to convert CO_2 and H_2O to glucose and O_2.
- Polymers include starch and cellulose.
- Starch is a storage unit for solar energy.
- Most sugars have formula $C_n(H_2O)_n$, "hydrate of carbon."

Classification of Carbohydrates

- Monosaccharides or simple sugars:
  - polyhydroxyaldehydes or aldoses
  - polyhydroxyketones or ketoses
- Disaccharides can be hydrolyzed to two monosaccharides.
- Polysaccharides hydrolyze to many monosaccharide units. For example, starch and cellulose have > 1000 glucose units.

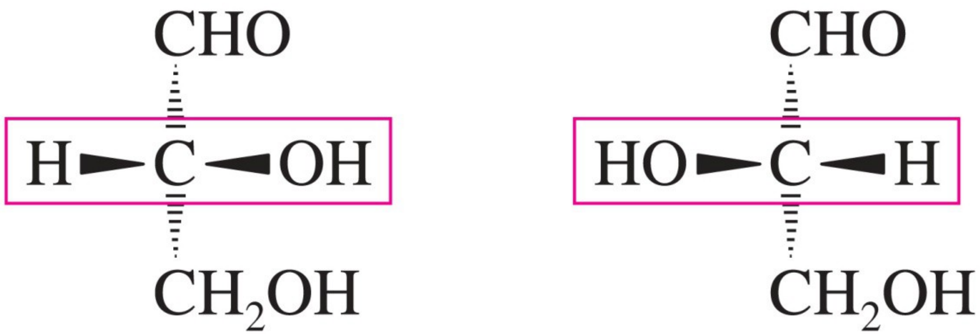
Monosaccharides



an aldohexose a ketohexose an aldotetrose a ketotetrose

- Classified using three criteria:
  - If it contains a ketone or an aldehyde group.
  - Number of carbons in the chain.
  - Configuration of the asymmetric carbon farthest from the carbonyl group.

(+) and (-)-Glyceraldehydes

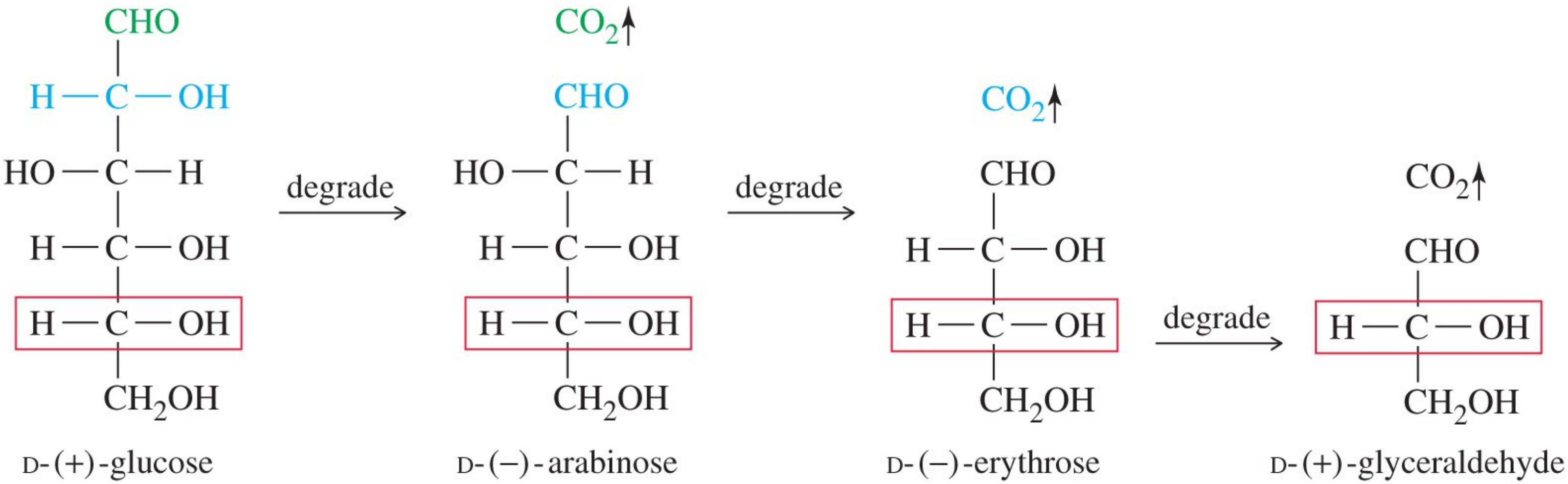


(+)-glyceraldehyde
D series of sugars

(−)-glyceraldehyde
L series of sugars

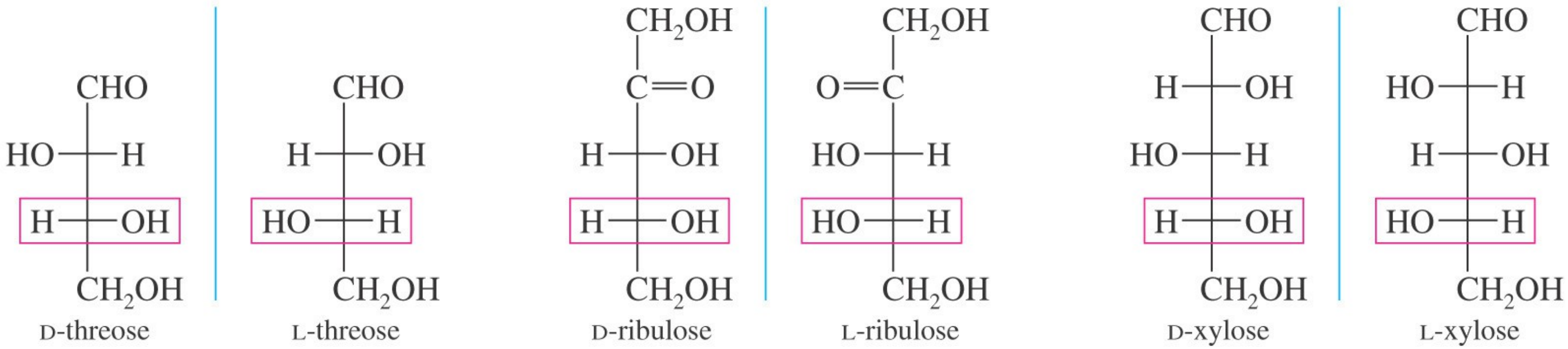
- The (+) enantiomer of glyceraldehyde has its OH group on the right of the Fischer projection.
- The (-) enantiomer of glyceraldehyde has its OH group on the left of the Fischer projection.

Degradation of D and L Sugars



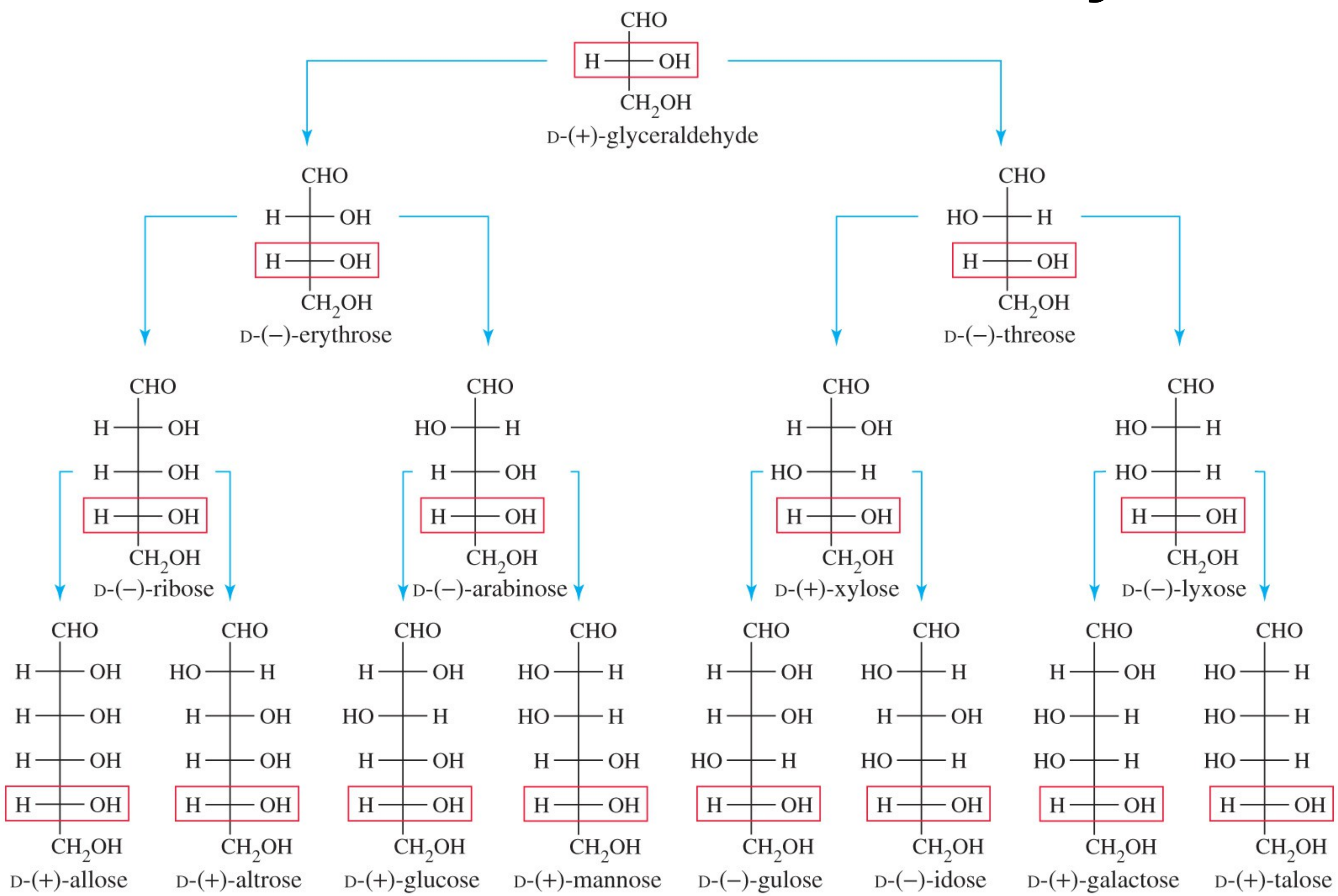
- Fischer–Rosanoff Convention
- D sugars can be degraded to the dextrorotatory (+) form of glyceraldehyde.
- L sugars can be degraded to the levorotatory (-) form of glyceraldehyde.

D and L Series of Sugars

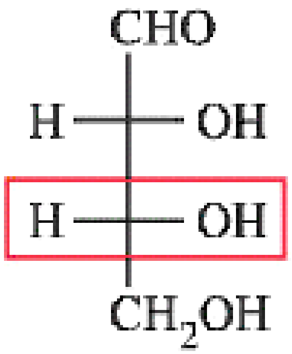


- Sugars of the D series have the OH group of the bottom asymmetric carbon on the right in the Fischer projection.
- Sugars of the L series, in contrast, have the OH group of the bottom asymmetric carbon on the left.

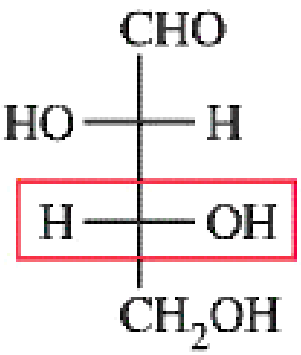
The D Aldose Family



Erythrose and Threose



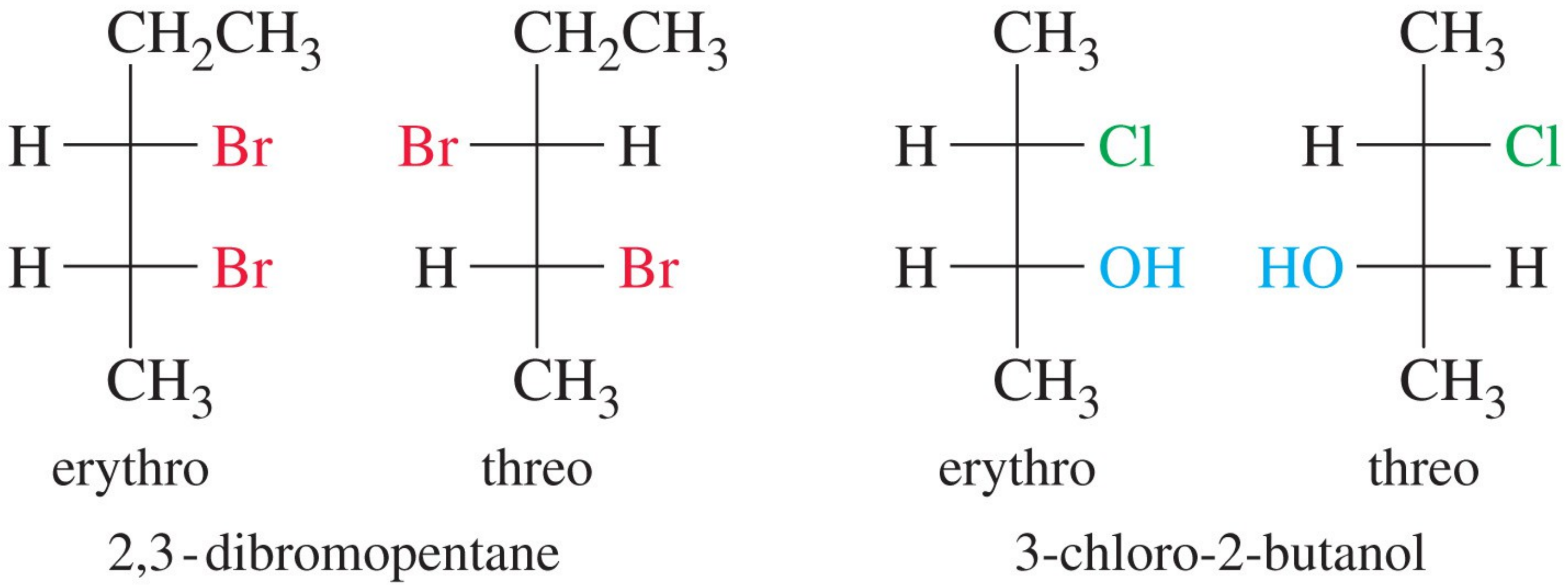
D-(-)-*erythrose*



D-(-)-*threose*

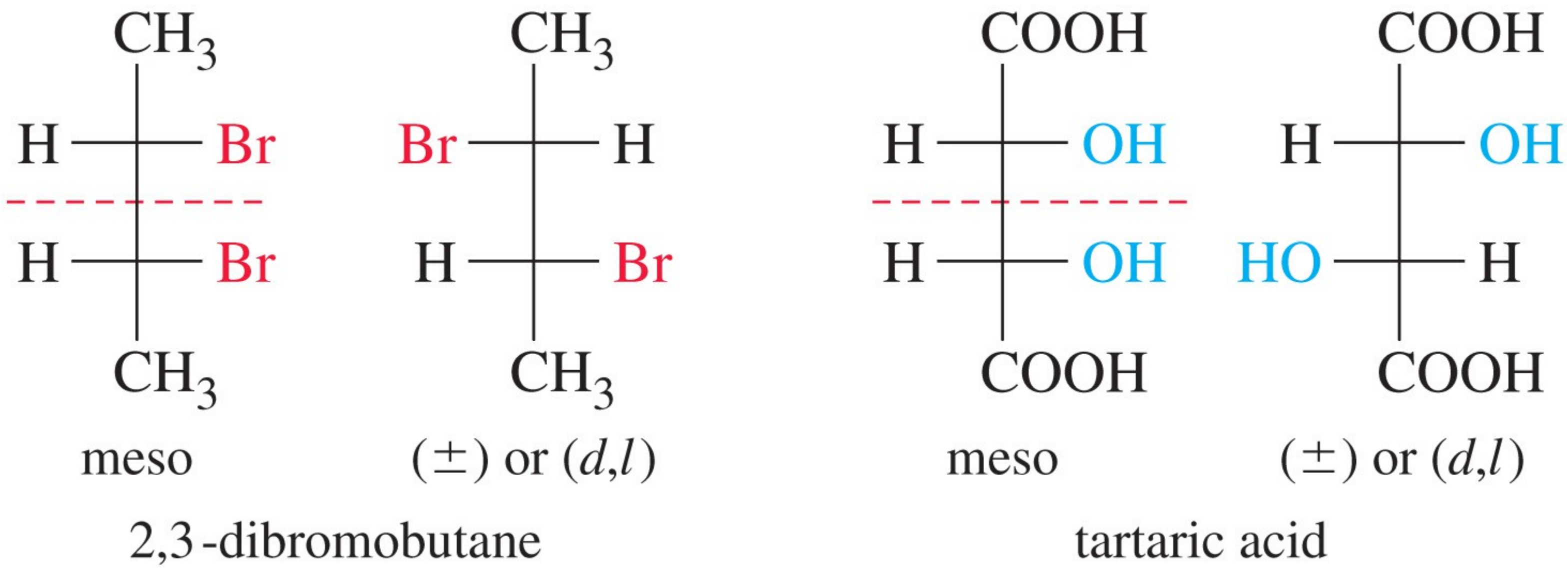
- ***Erythrose*** is an aldotetrose with the OH groups of its two asymmetric carbons on the same side of the Fischer projection.
- ***Threose*** is the diastereomer with the OH groups on opposite sides of the Fischer projection.

Erythro and Threo Diastereomers



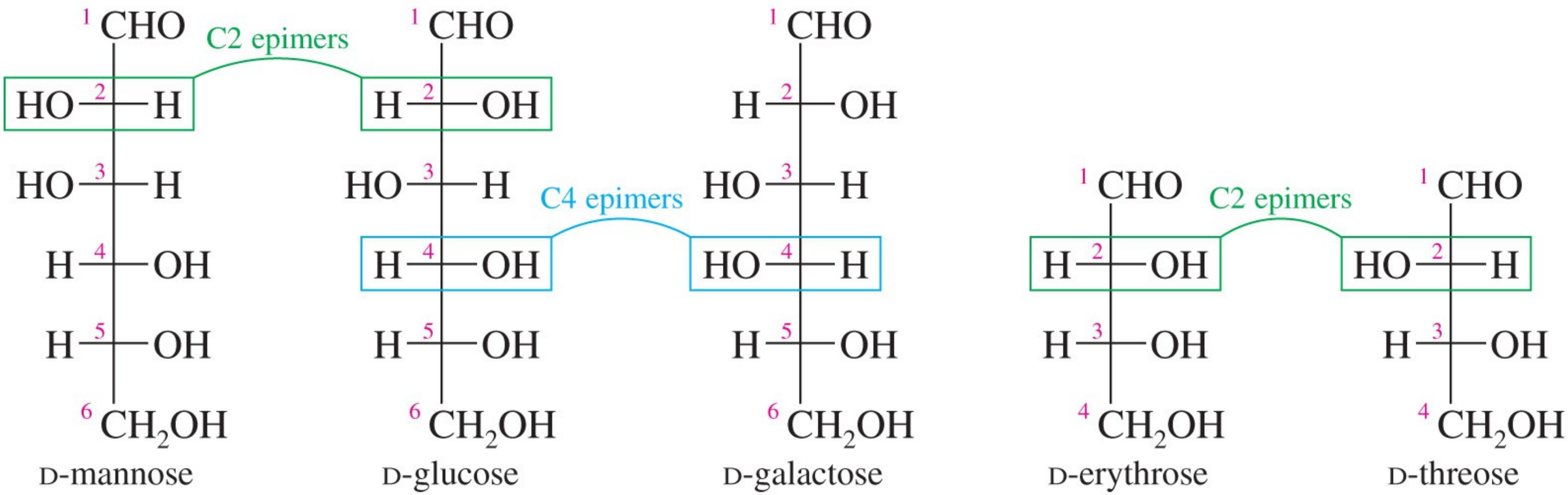
- Erythro diastereomers have similar groups on the same side of the Fischer projection.
- Threo diastereomers have similar groups on opposite sides of the Fischer projection.

Symmetric Molecules



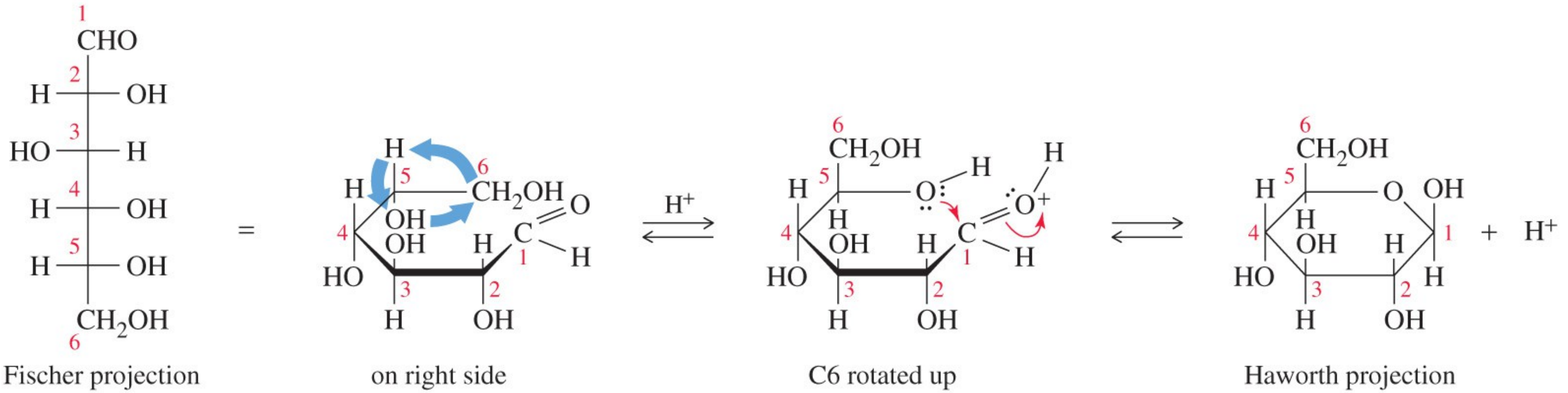
- Erythro and threo are not used on molecules with similar ends.
- For symmetric molecules, the terms *meso* and *(d,l)* are used.

Epimers



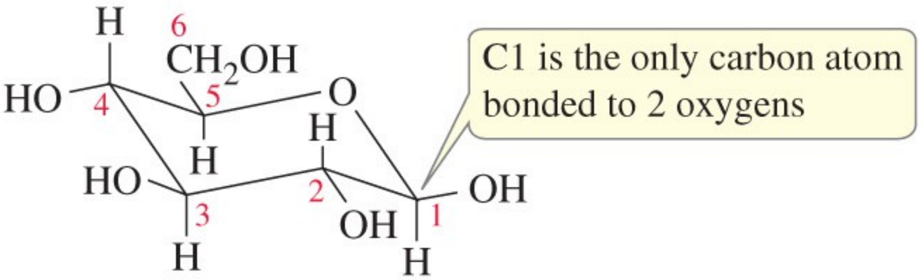
- Sugars that differ only in their stereochemistry at a single carbon.
- The carbon at which the stereochemistry differs is usually specified.

Cyclic Structure for Glucose

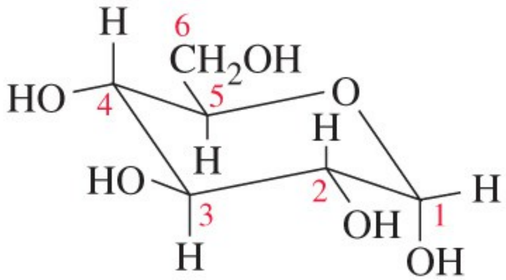


- Glucose exists almost entirely as its cyclic hemiacetal form.
- Five- or six-membered ring hemiacetals are more stable than their open-chain forms.
- The Haworth projection, although widely used, may give the impression of the ring being flat.

Chair Conformation for Glucose



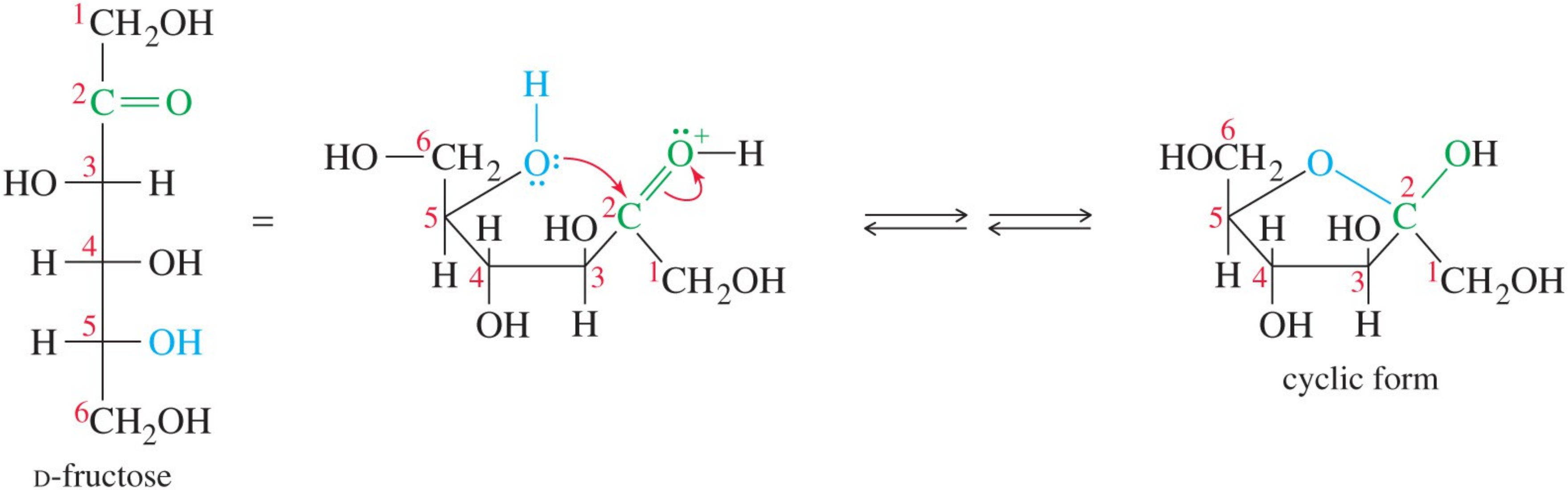
chair conformation (all substituents equatorial)



chair conformation (OH on C1 axial)

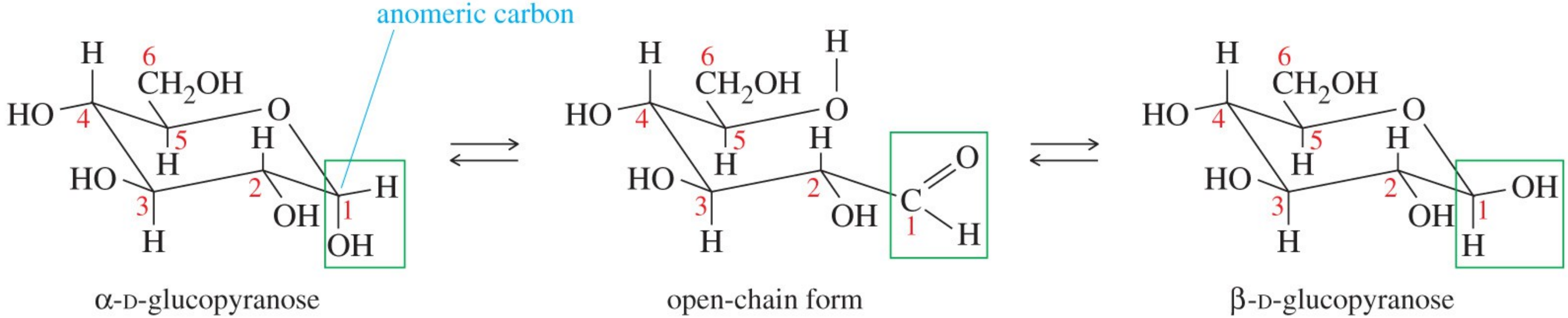
- The chair conformations give a more accurate representation of glucose.
- Glucose exists almost entirely as its cyclic hemiacetal form.

Cyclic Structure for Fructose



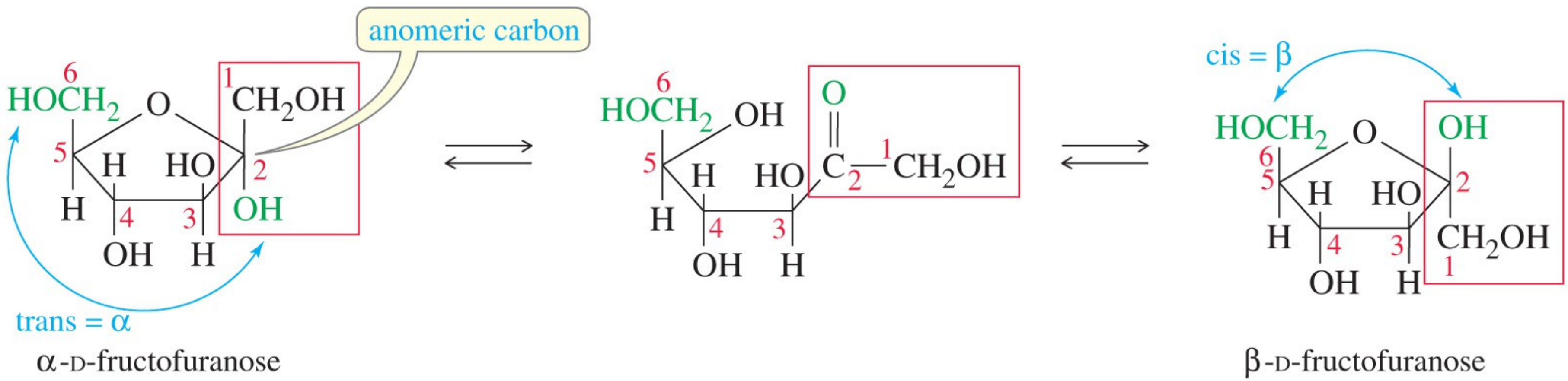
- Cyclic hemiacetal formed by reaction of C═O at C2 with —OH at C5.
- Since five-membered rings are not puckered as much as six-membered rings, they are usually depicted as flat Haworth projections.

Anomers of Glucose



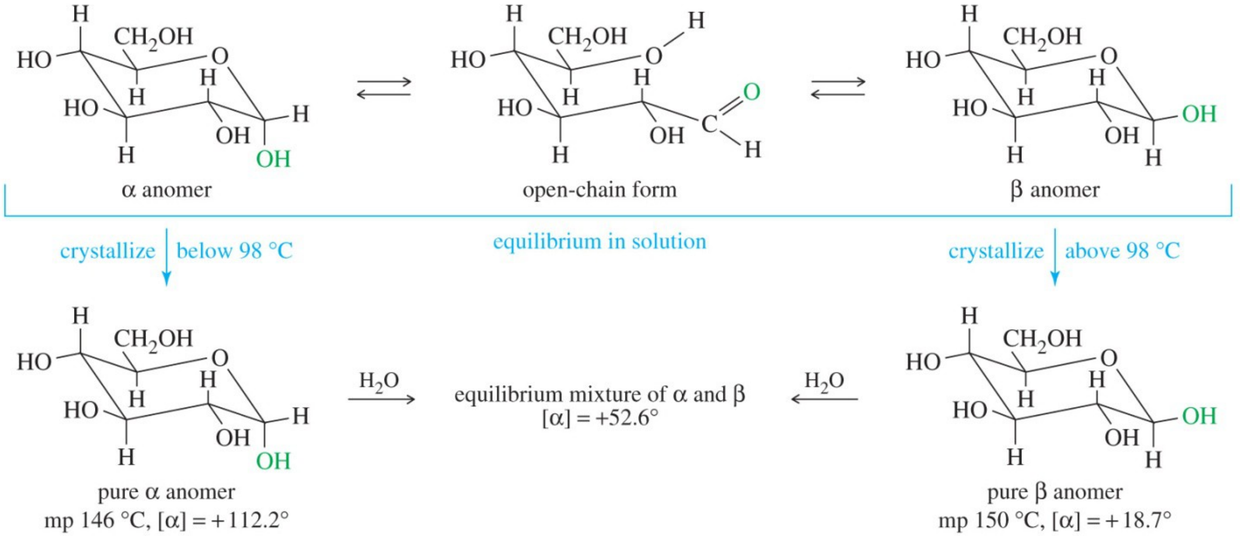
- The hydroxyl group on the anomeric (hemiacetal) carbon is down (axial) in the *α* anomer and up (equatorial) in the *β* anomer.
- The *β* anomer of glucose has all its substituents in equatorial positions.
- The hemiacetal carbon is called the anomeric carbon, easily identified as the only carbon atom bonded to two oxygens.

Anomers of Fructose



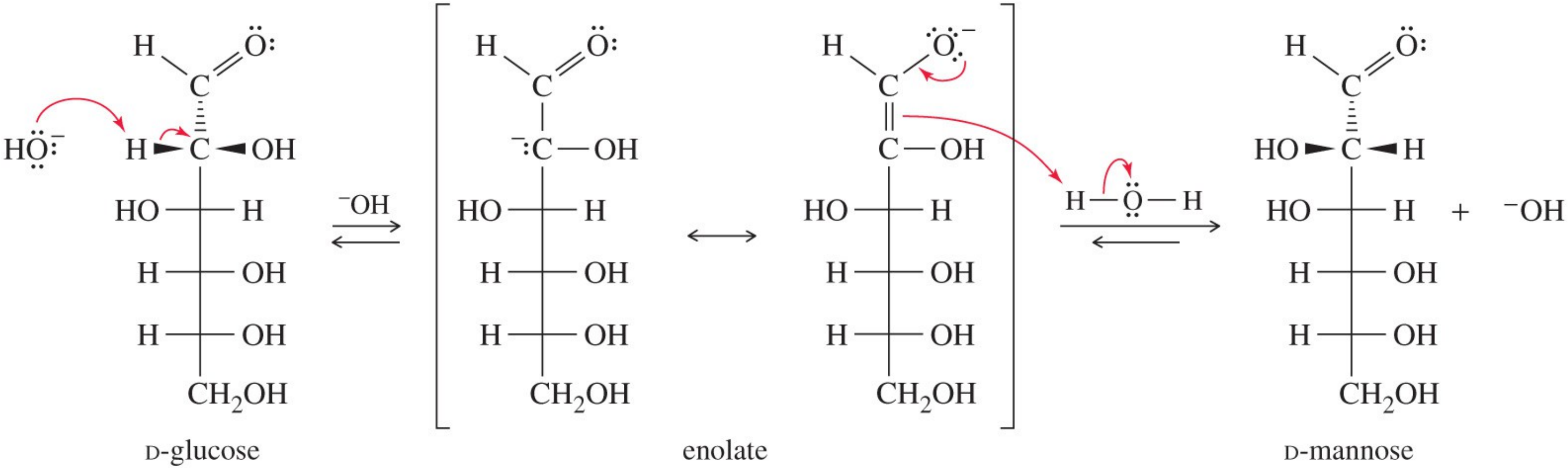
- The anomer of fructose has the anomeric —OH group down, trans to the terminal —CH_2OH group.
- The anomer has the anomeric —OH group up, cis to the terminal —CH_2OH.

Mutarotation



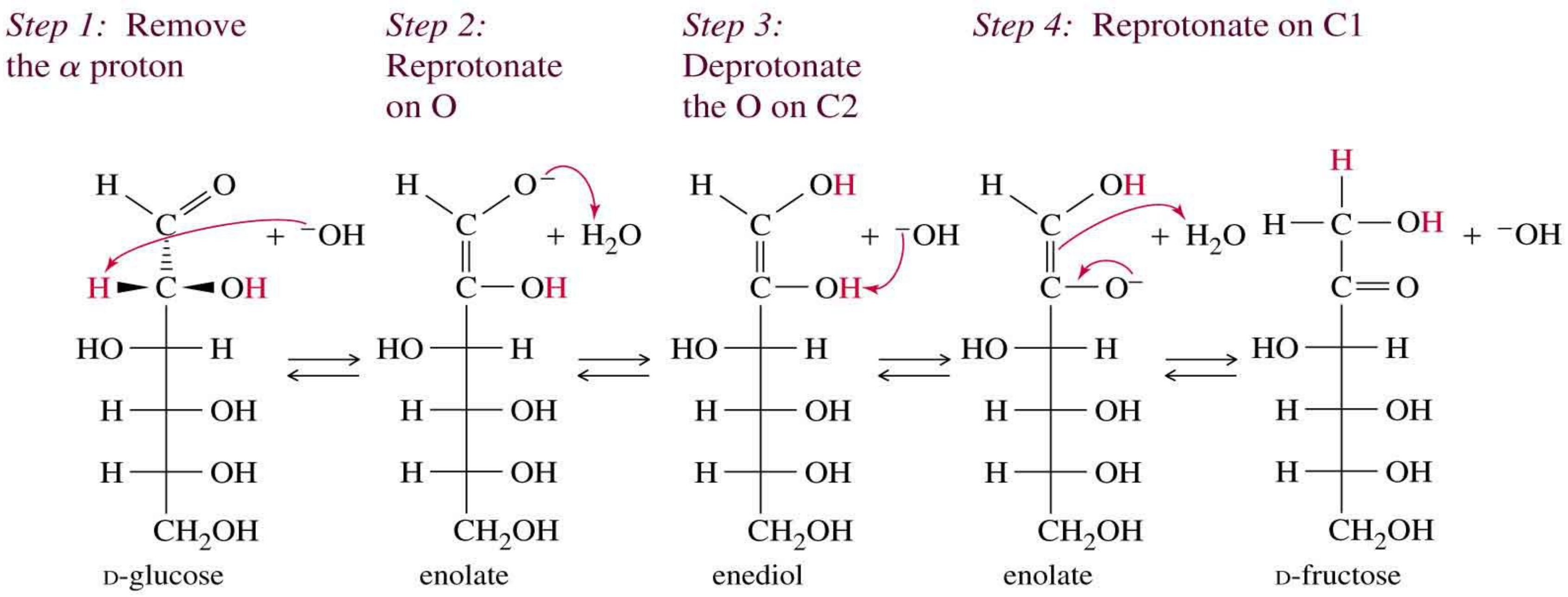
- An aqueous solution of D-glucose contains an equilibrium mixture of *α*-D-glucopyranose, *β*-D-glycopyranose, and the intermediate open-chain form.
- Crystallization below 98°C gives the *α* anomer, and crystallization above 98°C gives the *β* anomer.

Base-Catalyzed Epimerization of Glucose



- Under basic conditions, stereochemistry is lost at the carbon atom next to the carbonyl group.
- The enolate intermediate is not chiral, so reprotonation can produce either stereoisomer.
- Because a mixture of epimers results, this stereochemical change is called ***epimerization***.

Enediol Rearrangement

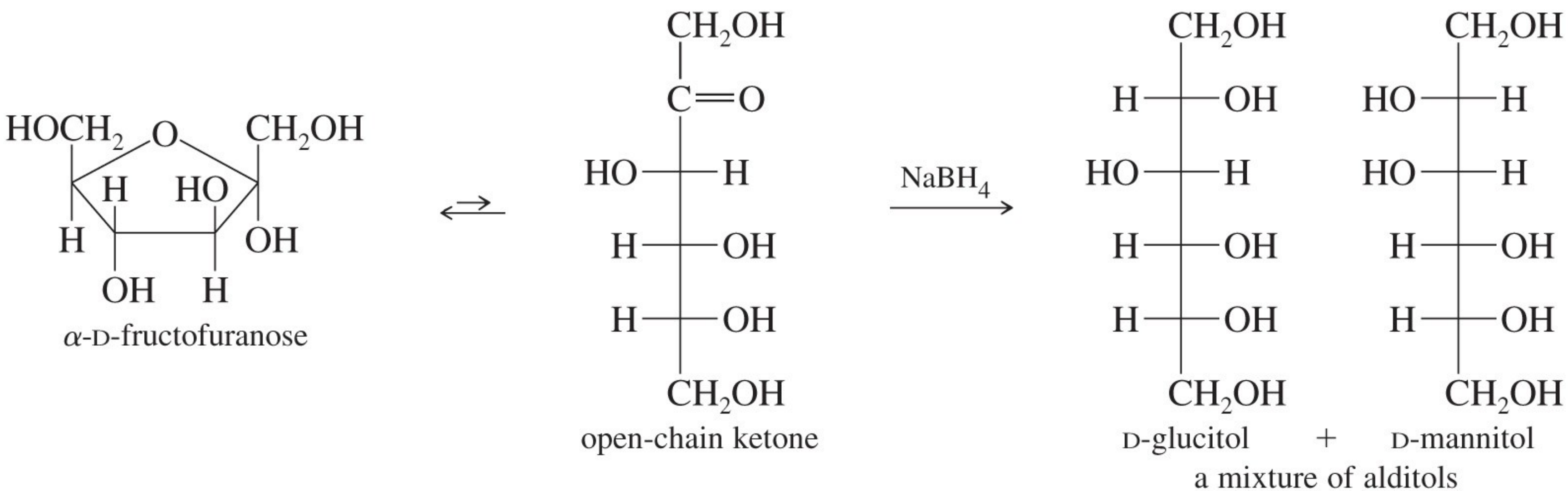


- In base, the position of the carbonyl can shift.
- Chemists use acidic or neutral solutions of sugars to prevent this rearrangement.

Reduction of Simple Sugars

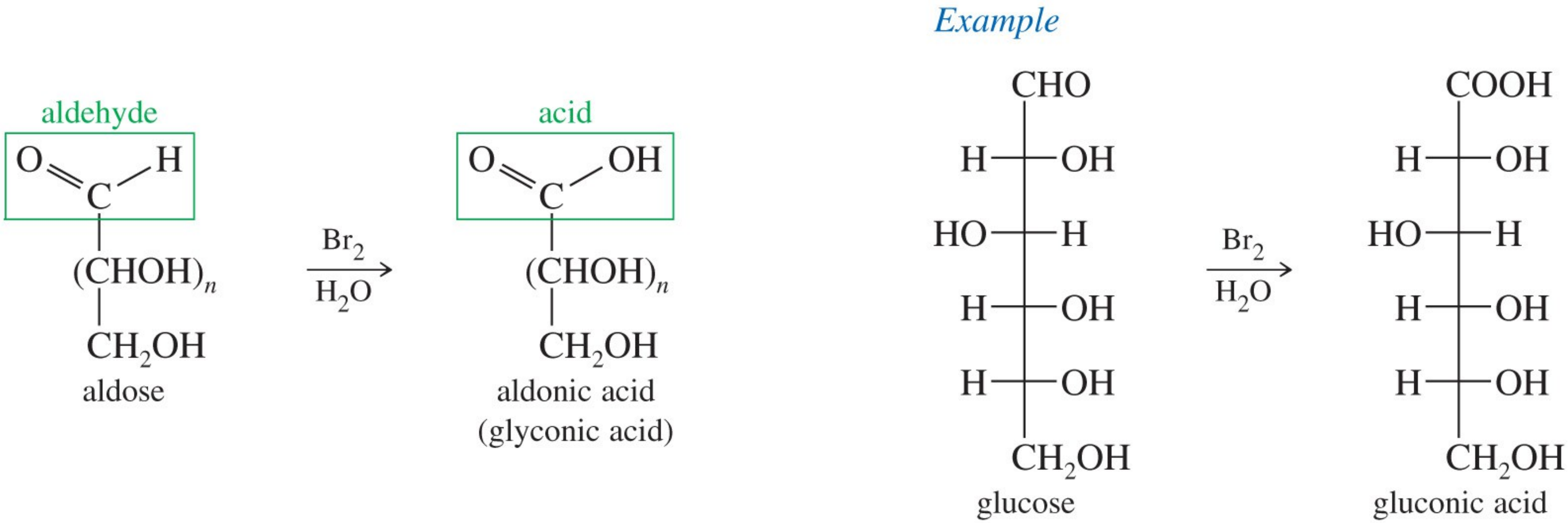
- C═O of aldoses or ketoses can be reduced to C—OH by $NaBH_4$ or H_2/Ni.
- Name the sugar alcohol by adding *-itol* to the root name of the sugar.
- Reduction of D-glucose produces D-glucitol, commonly called D-sorbitol.
- Reduction of D-fructose produces a mixture of D-glucitol and D-mannitol.

Reduction of Fructose



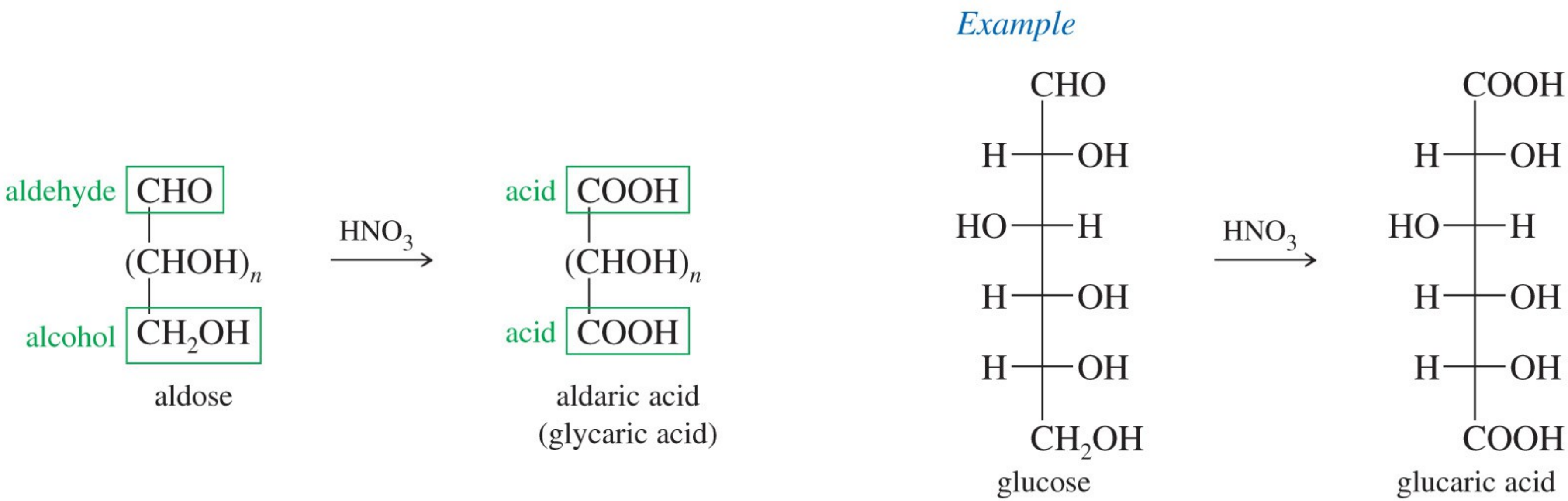
- Reduction of fructose creates a new asymmetric carbon atom, which can have either configuration.
- The products are a mixture of glucitol and mannitol.

Oxidation by Bromine



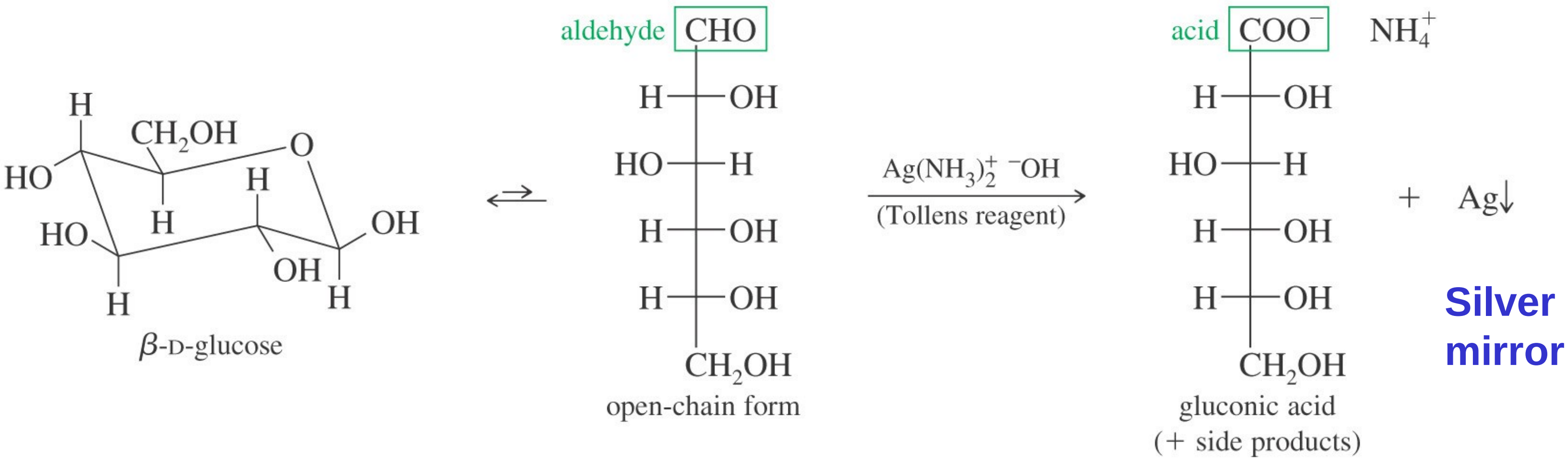
- Bromine water oxidizes the aldehyde group of an aldose to a carboxylic acid.
- Bromine in water is used for this oxidation because it does not oxidize the alcohol groups of the sugar and it does not oxidize ketoses.

Nitric Acid Oxidation



- Nitric acid is a stronger oxidizing agent than bromine, oxidizing both the aldehyde group and the terminal —CH_2OH group of an aldose to a carboxylic acid.

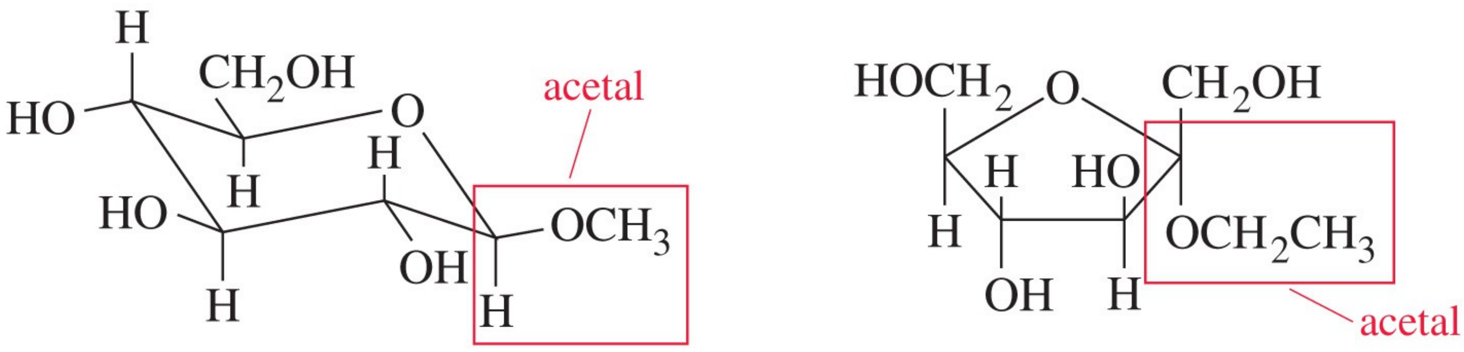
Oxidation by Tollens Reagent



- Aldoses have an aldehyde group, which reacts with Tollens reagent to give an aldonic acid and a silver mirror.
- Sugars that reduce Tollens reagent to give a silver mirror are called ***reducing sugars***.
- Tollens test is used as a qualitative test for the identification of aldehydes.

Nonreducing Sugars

Examples of nonreducing sugars

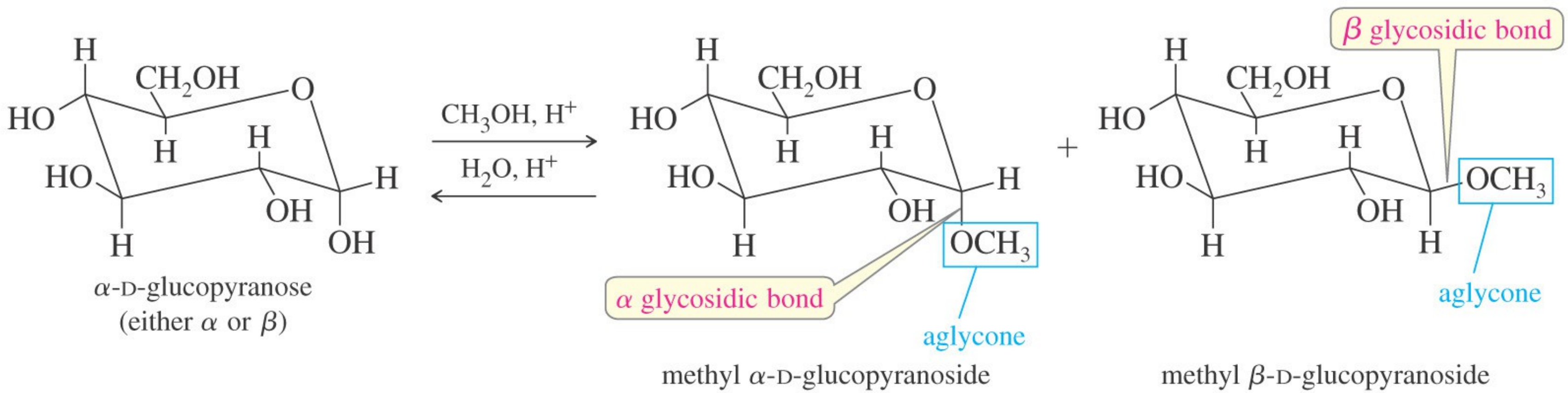


methyl β-D-glucopyranoside
(or methyl β-D-glucoside)

ethyl α-D-fructofuranoside
(or ethyl α-D-fructoside)

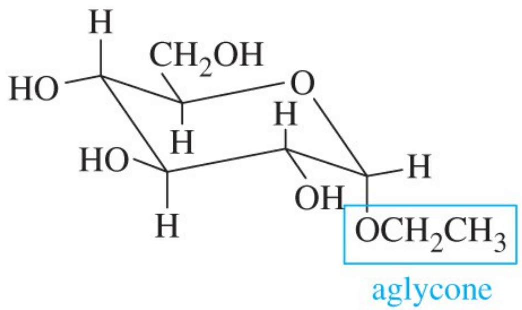
- Glycosides are acetals, stable in base, so they do not react with Tollens reagent.
- Disaccharides and polysaccharides are also acetals, nonreducing sugars.

Formation of Glycosides

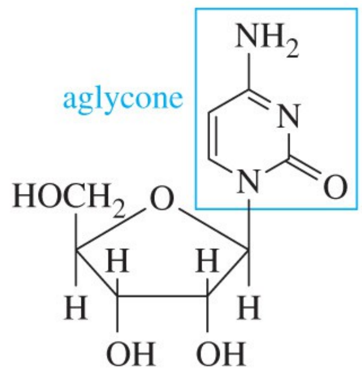


- React the sugar with alcohol in acid.
- Since the open-chain sugar is in equilibrium with its - and -hemiacetal, both anomers of the acetal are formed.
- *Aglycone* is the term used for the group bonded to the anomeric carbon.

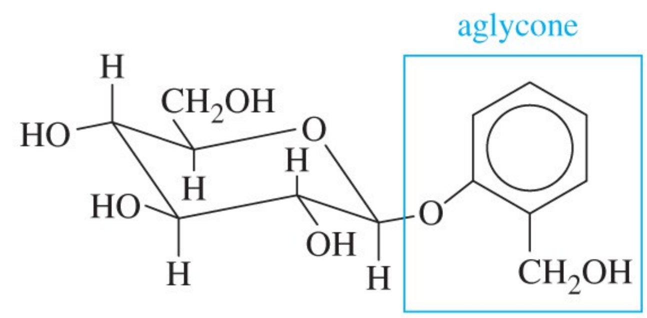
Aglycones



ethyl α-D-glucopyranoside



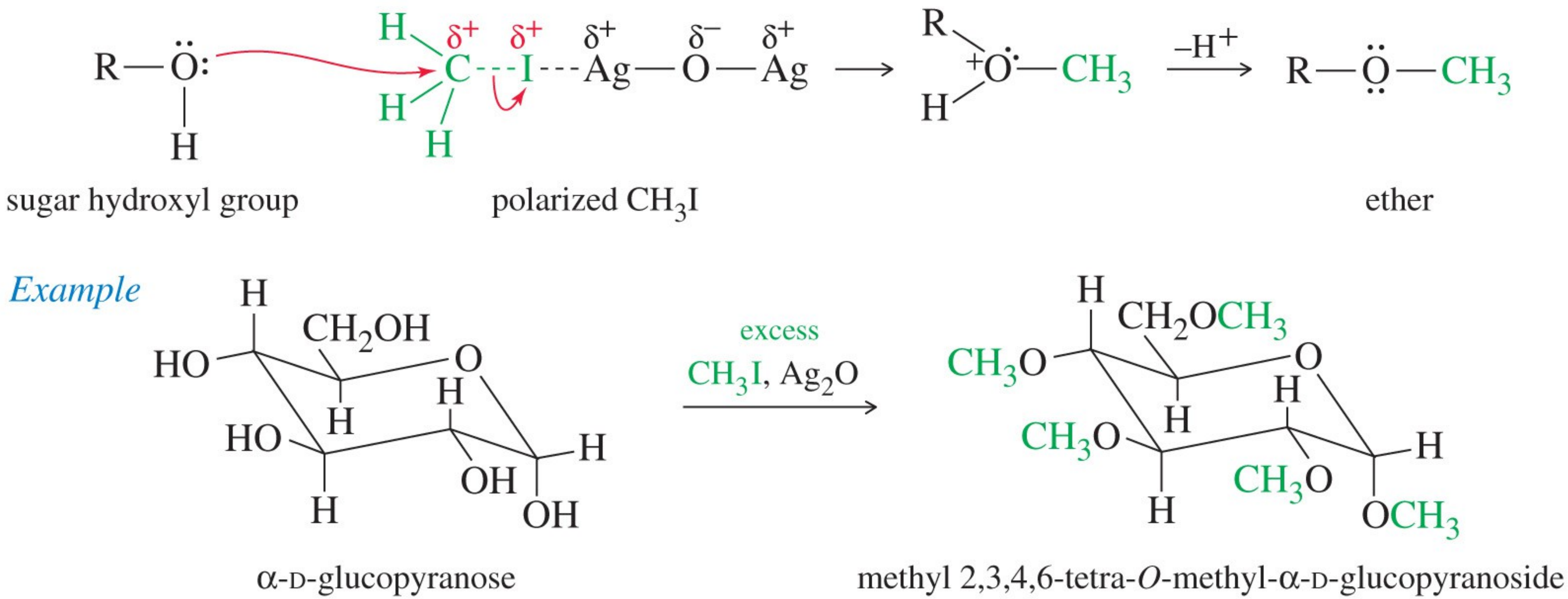
cytidine, a nucleoside (Section 23-21)



salicin, from willow bark

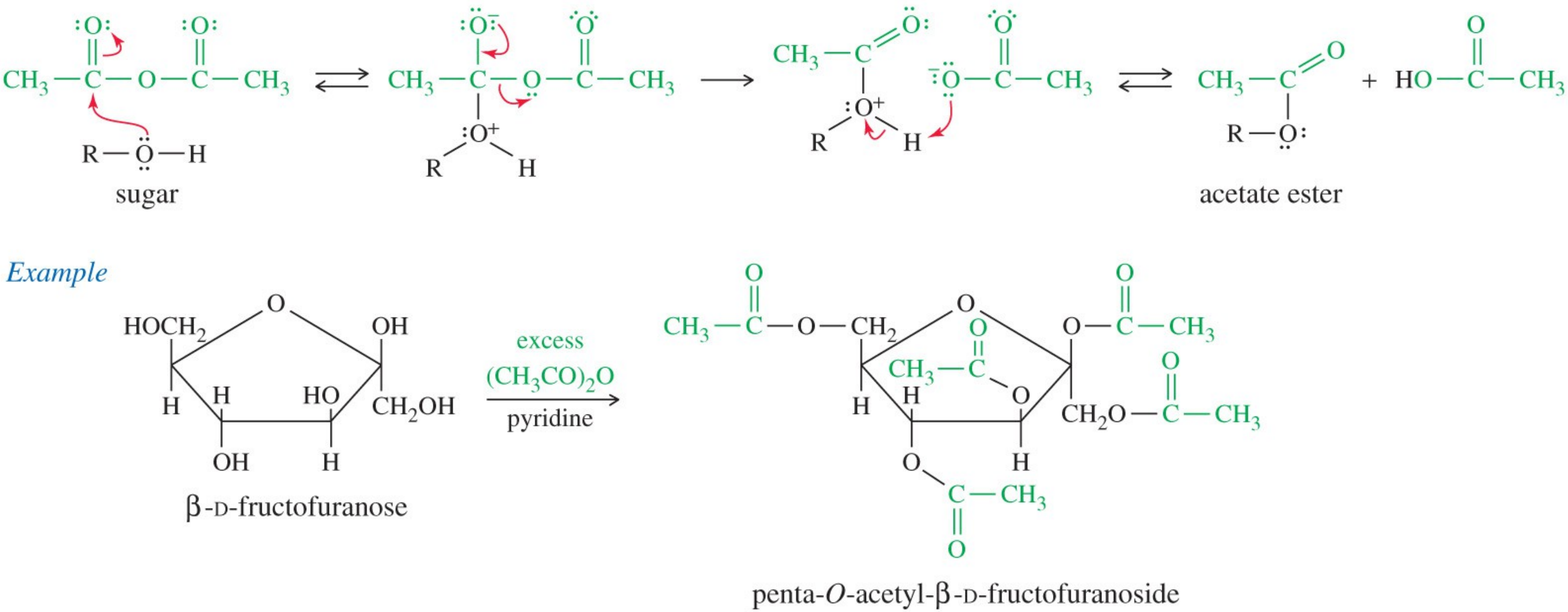
- The group bonded to the anomeric carbon of a glycoside is called an ***aglycone***.
- Some aglycones are bonded through an oxygen atom (a true acetal), and others are bonded through other atoms such as nitrogen.

Methyl Ether Formation



- Reaction of the sugar with methyl iodide and silver oxide will convert the hydroxides to methyl ethers.
- The methylated sugar is stable in base.

Acetate Ester Formation

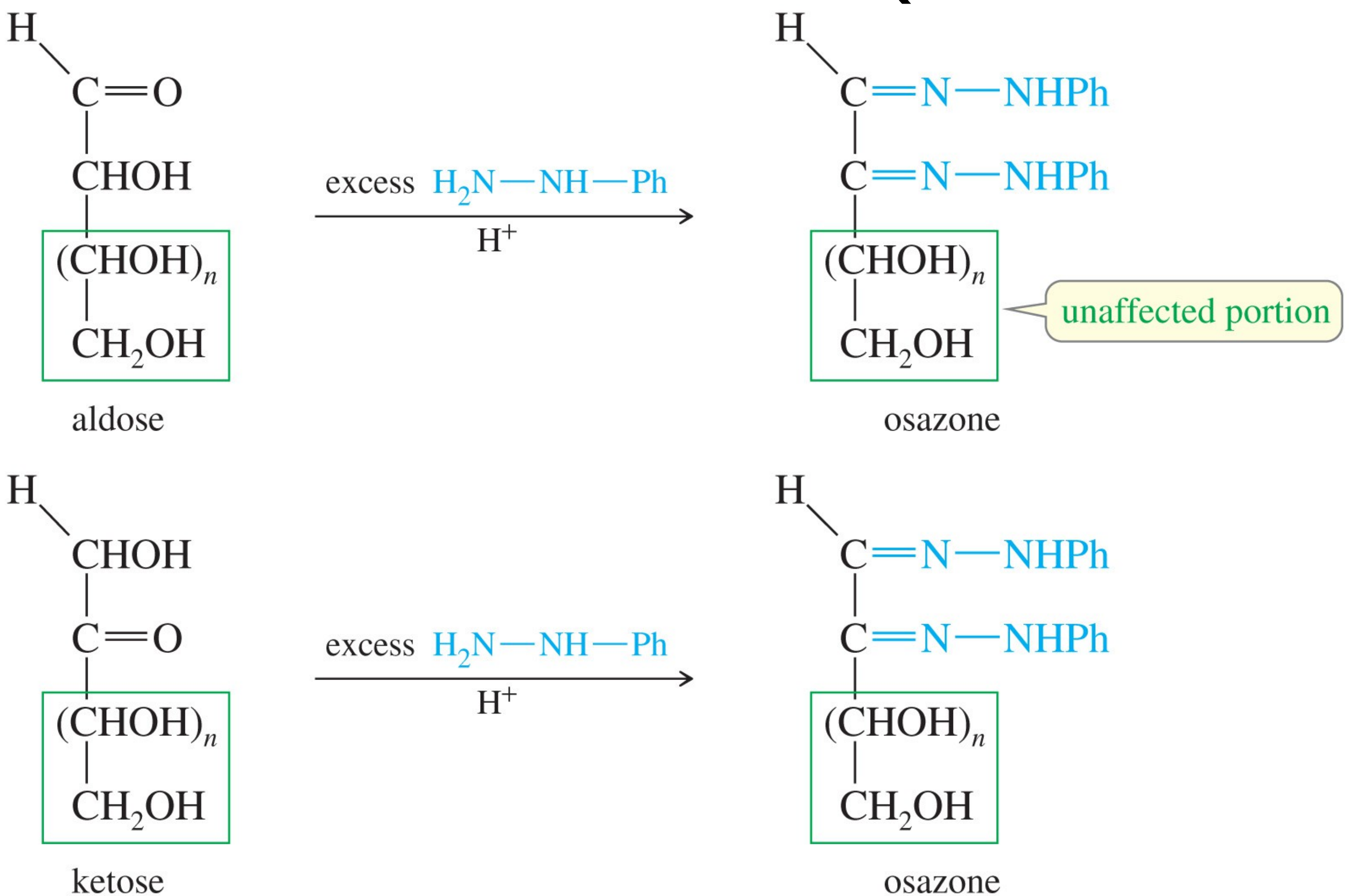


- Acetic anhydride with pyridine catalyst converts all the oxygens to acetate esters.
- Esters are readily crystallized and purified.

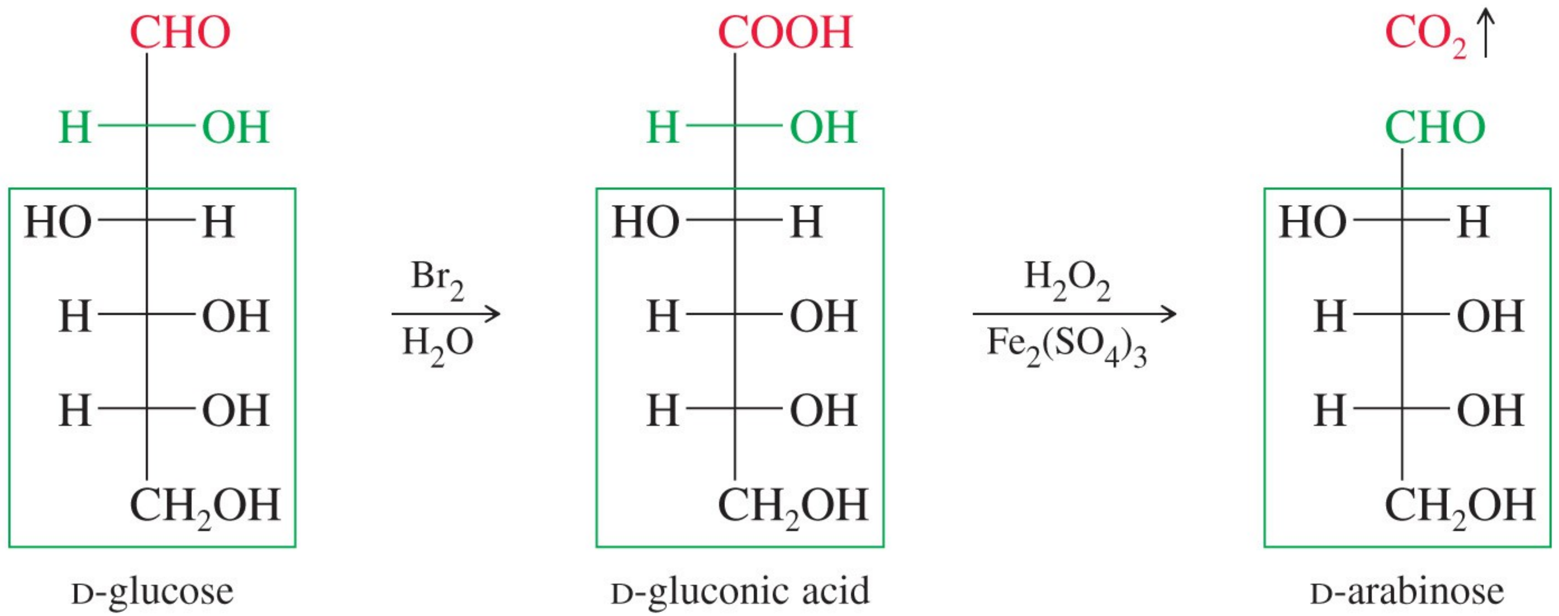
Osazone Formation

- Most osazones are easily crystallized and exhibit sharp melting points.
- Melting points of osazone derivatives provide valuable clues for the identification and comparison of sugars.
- Two molecules of phenylhydrazine condense with each molecule of the sugar to give an osazone, in which both C1 and C2 have been converted to phenylhydrazones.

Osazone Formation (Continued)

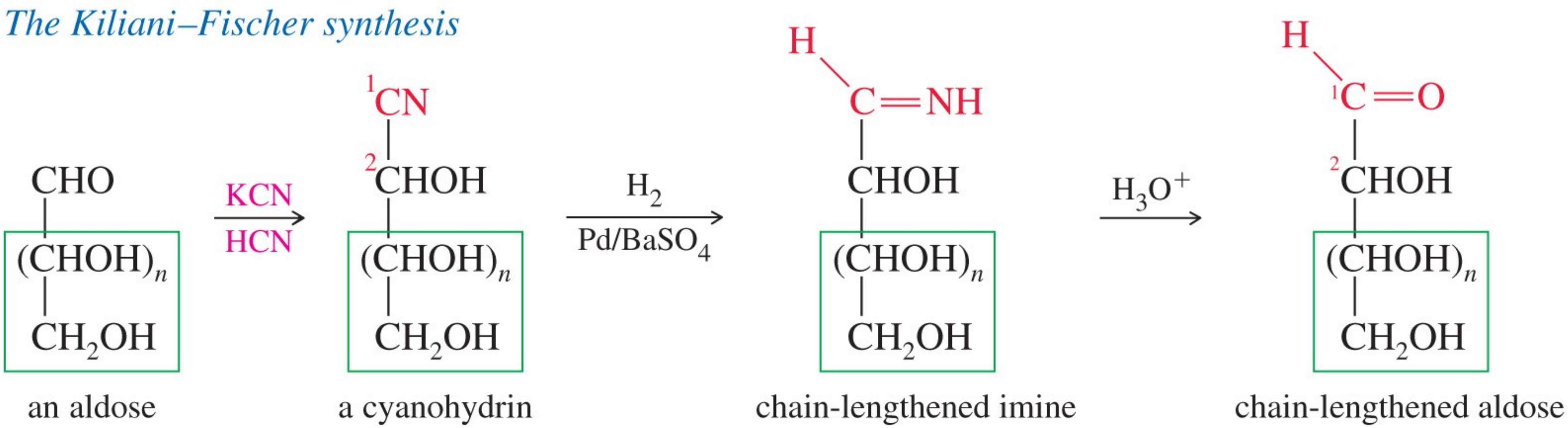


Ruff Degradation



- The Ruff degradation is a two-step process that begins with the bromine water oxidation of the aldose to its aldonic acid.
- Treatment of the aldonic acid with hydrogen peroxide and ferric sulfate oxidizes the carboxyl group to CO_2 and gives an aldose with one less carbon atom.

Kiliani–Fischer Synthesis

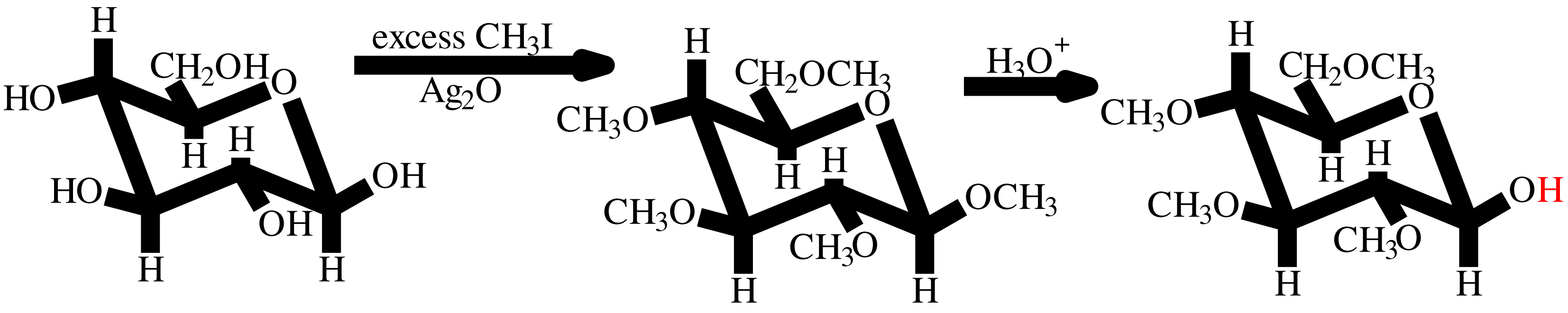


- The Kiliani–Fischer synthesis lengthens an aldose carbon chain by adding one carbon atom to the aldehyde end of the aldose.
- This synthesis is useful both for determining the structure of existing sugars and for synthesizing new sugars.

Fischer's Proof

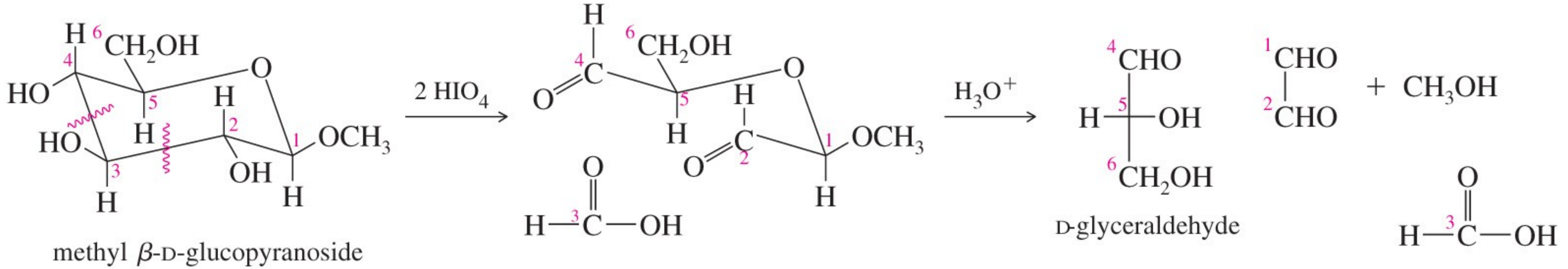
- Emil Fischer determined the configuration around each chiral carbon in D-glucose in 1891, using Ruff degradation and oxidation reactions.
- He assumed that the —OH is on the right in the Fischer projection for D-glyceraldehyde.
- This guess turned out to be correct!

Determination of Ring Size



- Haworth determined the pyranose structure of glucose in 1926.
- The anomeric carbon can be found by complete methylation of the —OHs, then hydrolysis of the acetal methyl group.

Periodic Acid Cleavage of Carbohydrates

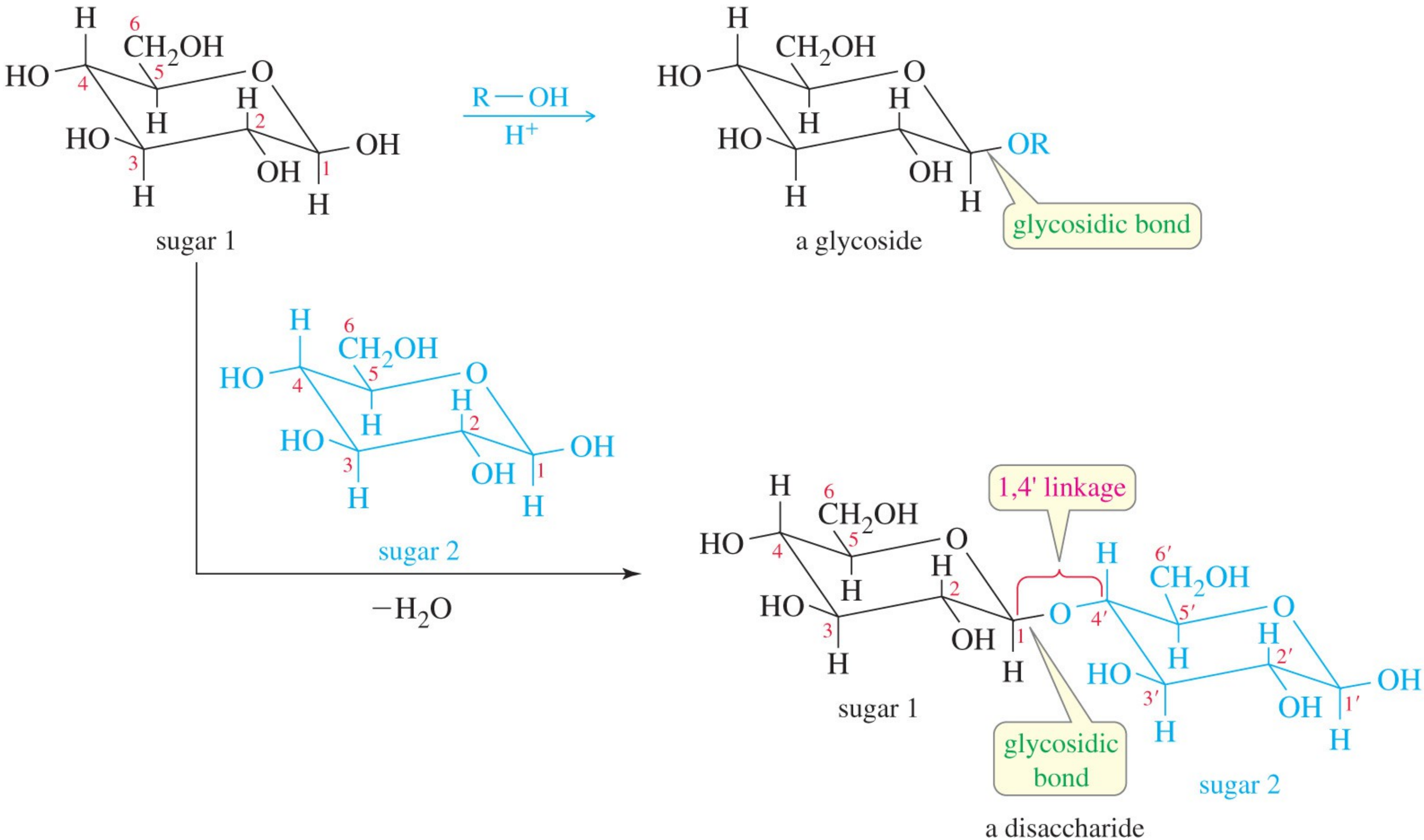


- Periodic acid cleaves vicinal diols to give two carbonyl compounds.
- Separation and identification of the products determine the size of the ring.

Disaccharides

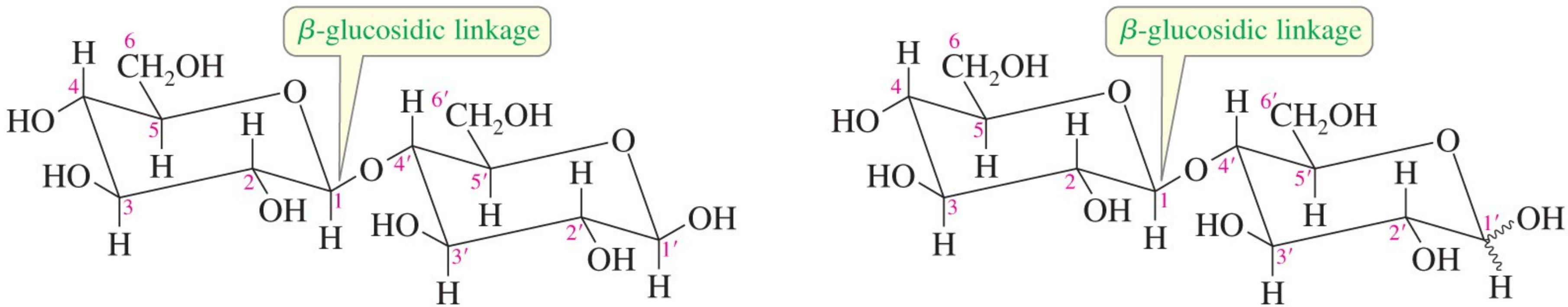
- Three naturally occurring glycosidic linkages:
  - 1-4' link: The anomeric carbon is bonded to oxygen on C4 of second sugar.
  - 1-6' link: The anomeric carbon is bonded to oxygen on C6 of second sugar.
  - 1-1' link: The anomeric carbons of the two sugars are bonded through an oxygen.

Disaccharides (Continued)



A -1-4’ Glycosidic Linkage

Cellobiose, 4-O-(β-D-glucopyranosyl)-β-D-glucopyranose or 4-O-(β-D-glucopyranosyl)-D-glucopyranose

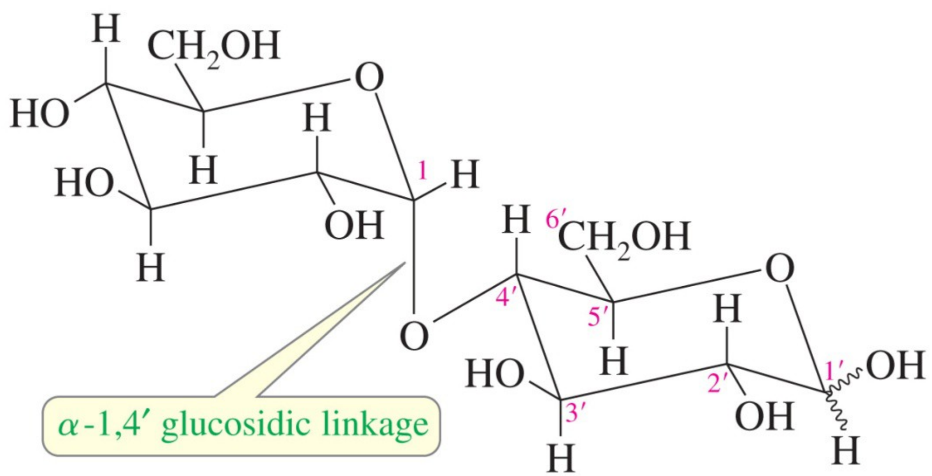


Two alternative ways of drawing and naming cellobiose

- In cellobiose, the anomeric carbon of one glucose unit is linked through an equatorial ( ) carbon-oxygen bond to C4 of another glucose unit.
- This is called a ***-1-4’ glycosidic linkage***.

An -1,4’ Glucosidic Linkage

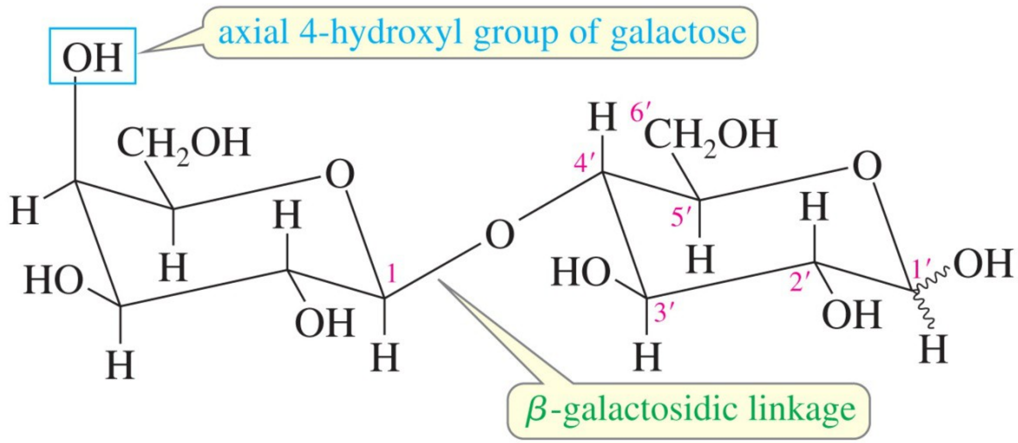
Maltose, 4-O-(α-D-glucopyranosyl)-D-glucopyranose



- Maltose contains a 1,4’ glucosidic linkage between the two glucose units.
- The monosaccharides in maltose are joined together by the axial position of C1 and the equatorial position of C4'.

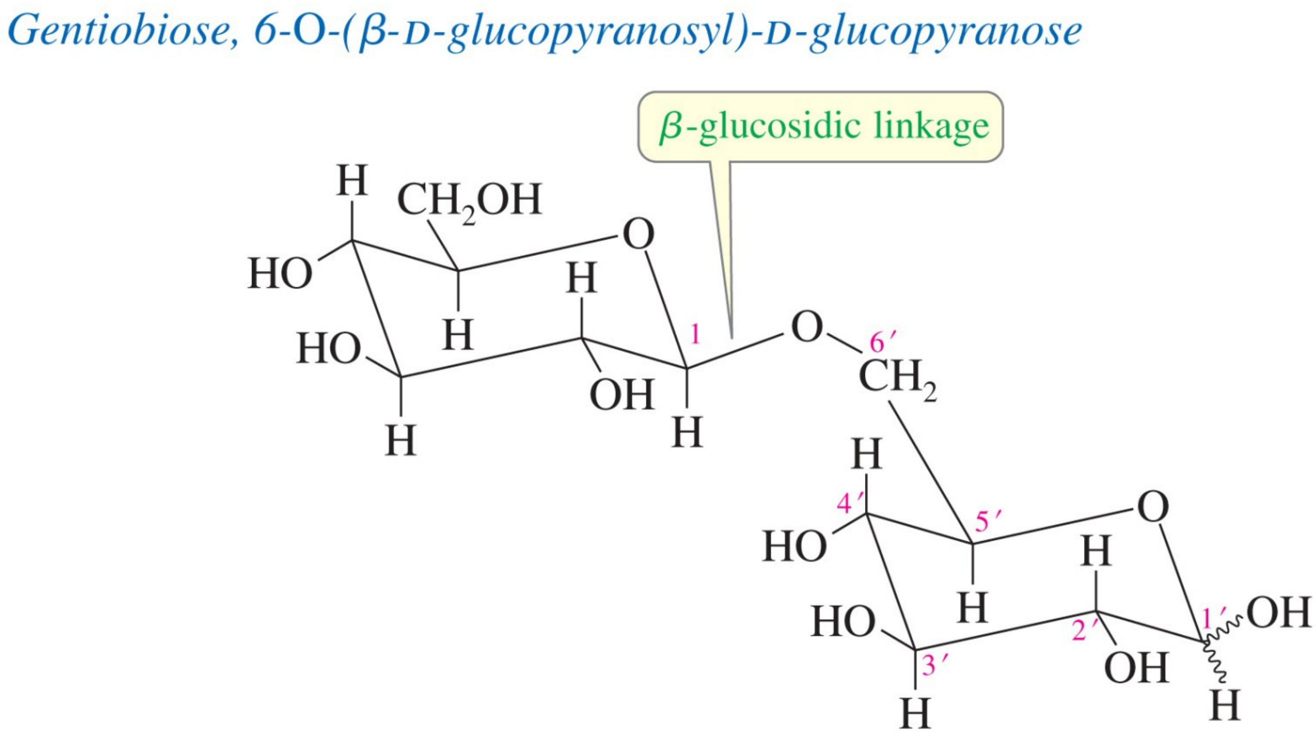
Lactose: A   -1,4' Galactosidic Linkage

Lactose, 4-O-(β-D-galactopyranosyl)-D-glucopyranose



- Lactose is composed of one galactose unit and one glucose unit.
- The two rings are linked by a   -1,4’ glycosidic bond of the galactose acetal to the 4-position on the glucose ring: a   ***-1,4’ galactosidic linkage***.

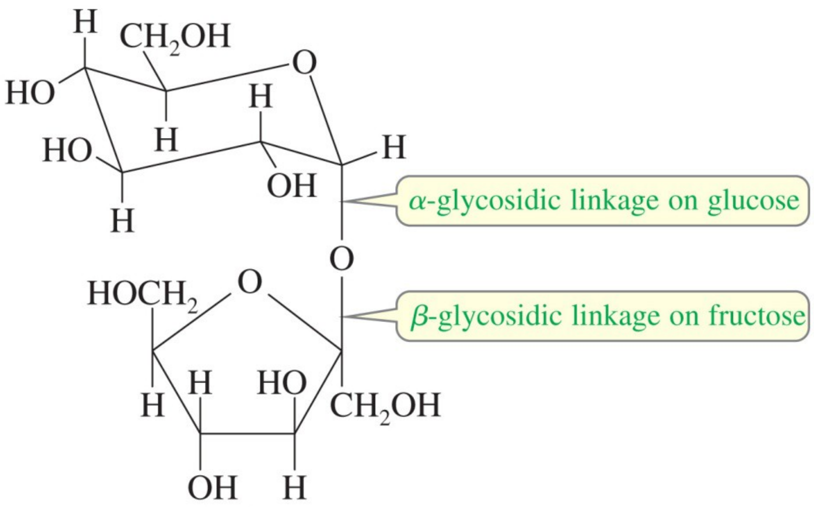
Gentiobiose



- Two glucose units linked 1,6’.
- Rare for disaccharides, but commonly seen as branch point in carbohydrates.

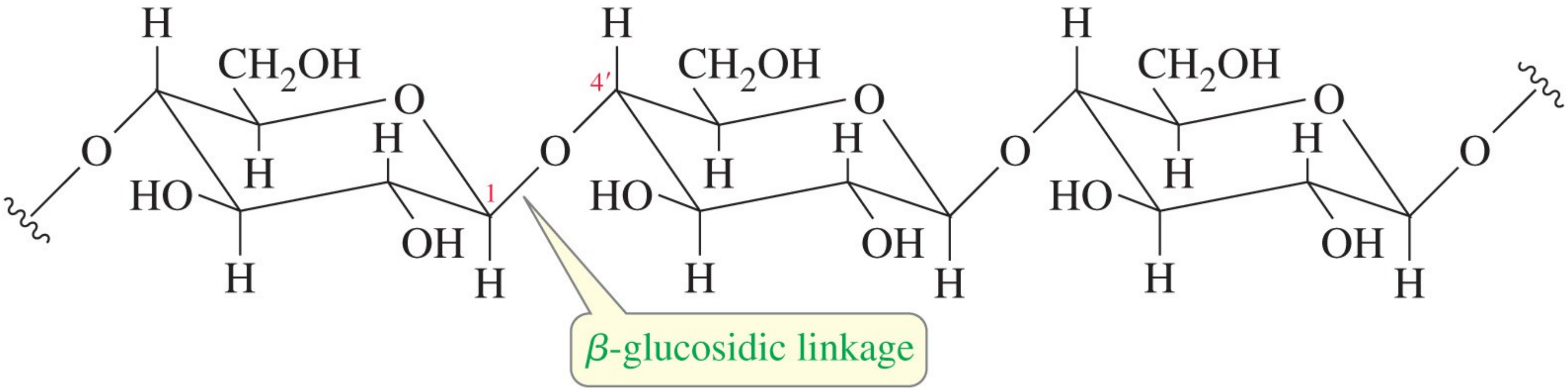
Sucrose: Linkage of Two Anomeric Carbons

Sucrose, α-D-glucopyranosyl-β-D-fructofuranoside
(or β-D-fructofuranosyl-α-D-glucopyranoside)



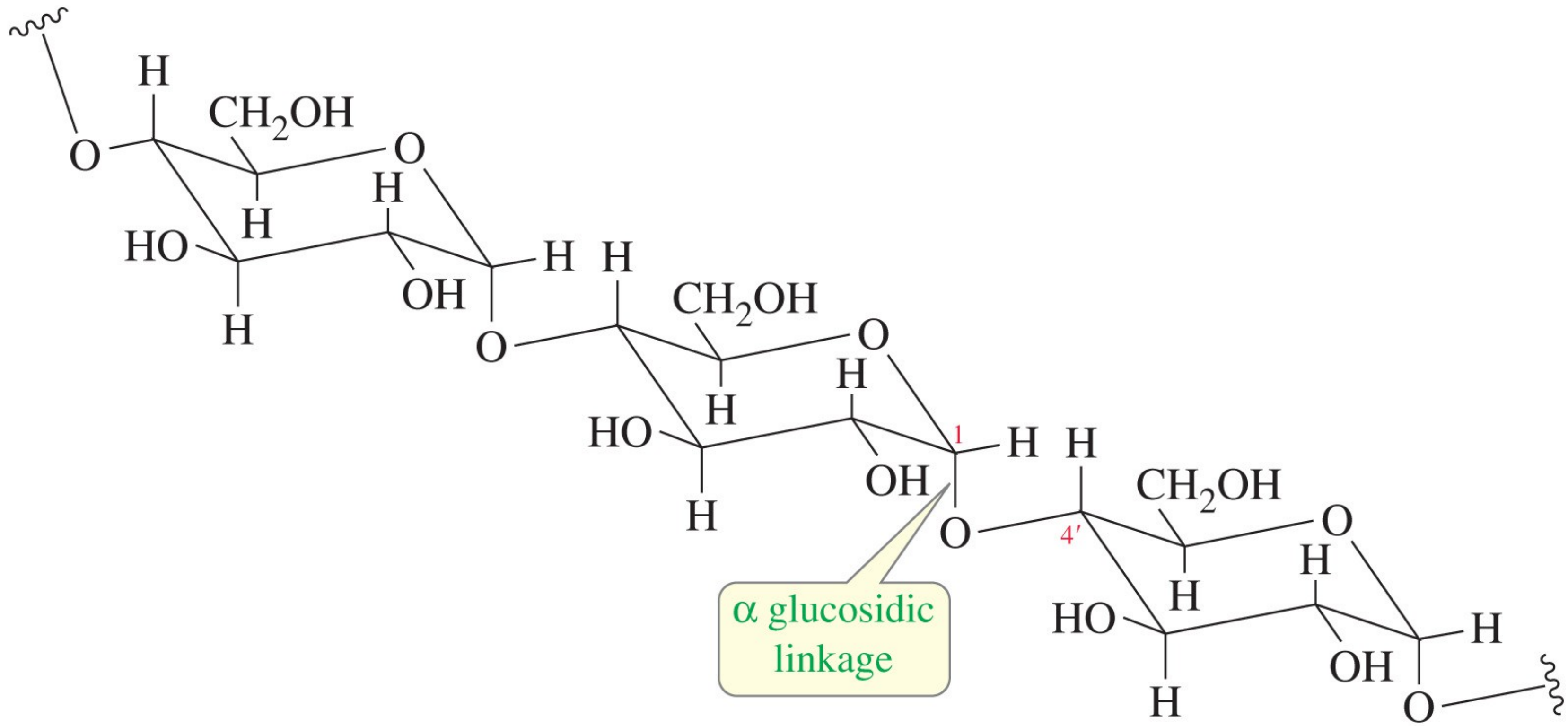
- Some sugars are joined by a direct glycosidic linkage between their anomeric carbon atoms: a 1,1' linkage.

Cellulose



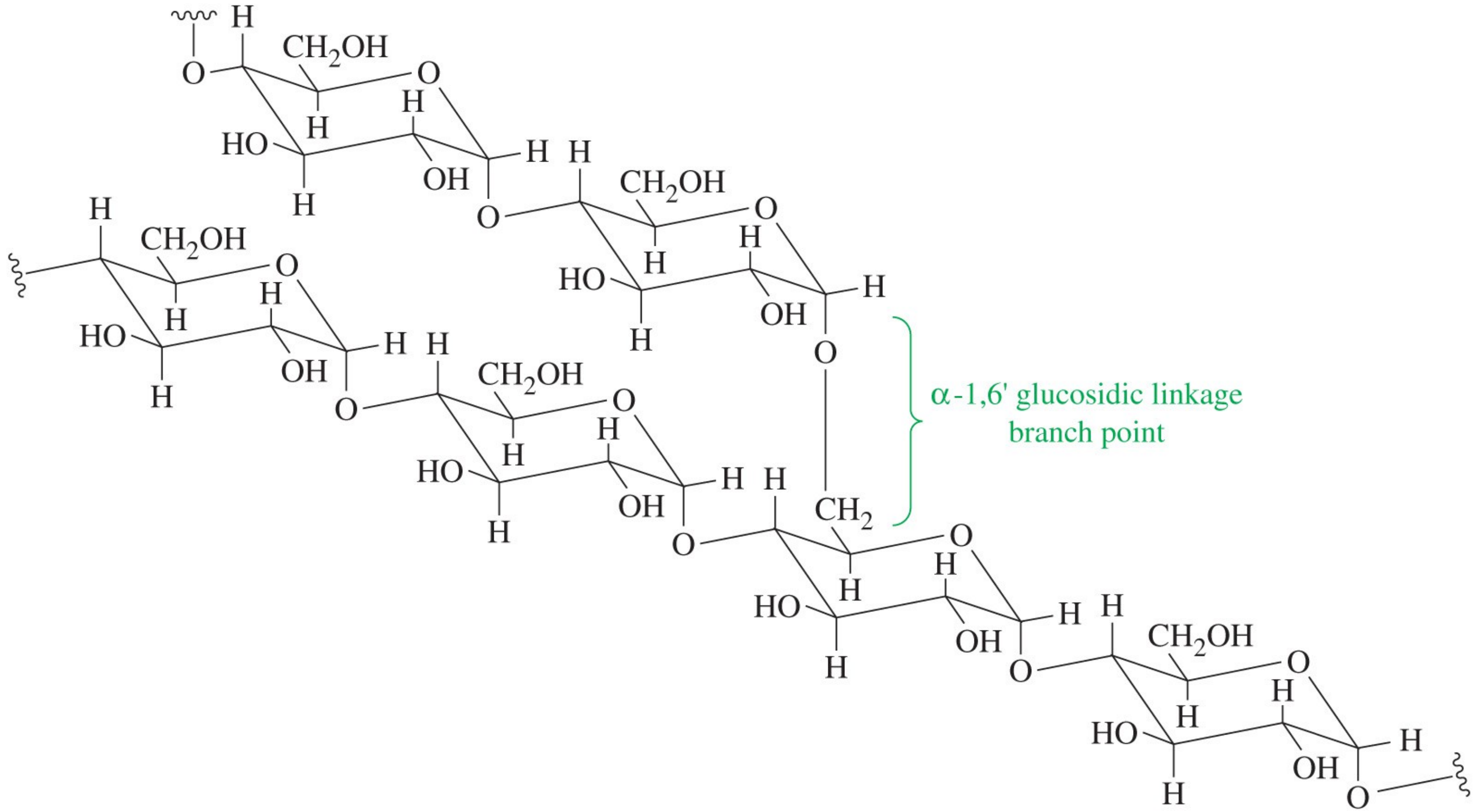
- Cellulose is a -1,4’ polymer of D-glucose, systematically named poly(1,4’-O- -D-glucopyranoside).
- Cellulose is the most abundant organic material.
- It is synthesized by plants as a structural material to support the weight of the plant.

Amylose



- Amylose is an -1,4’ polymer of glucose, systematically named poly(1,4’-O- -D-glucopyranoside).

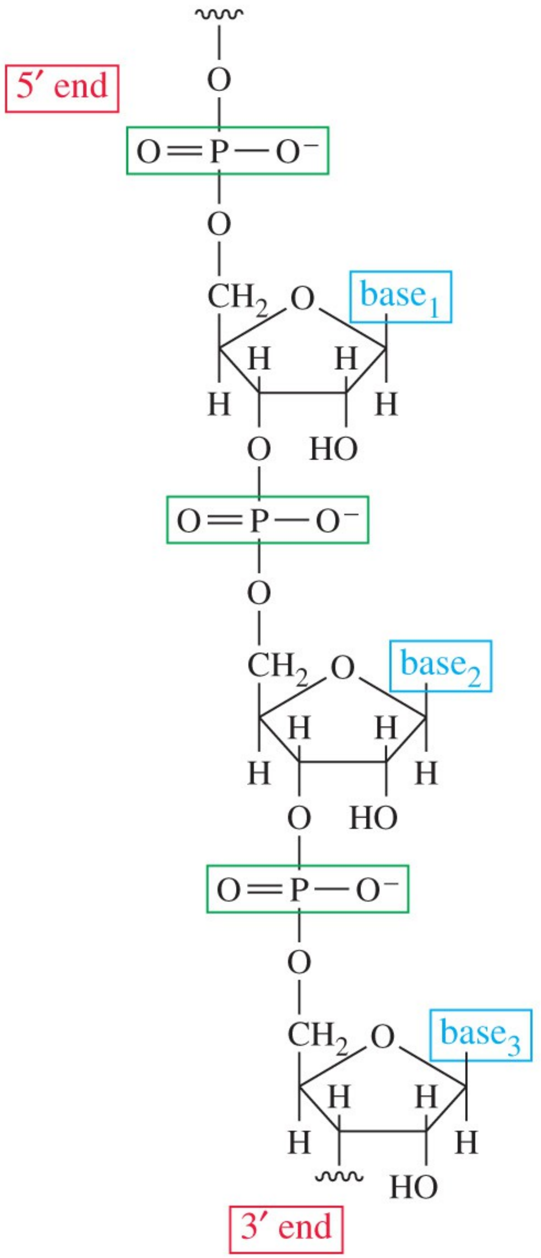
Amylopectin



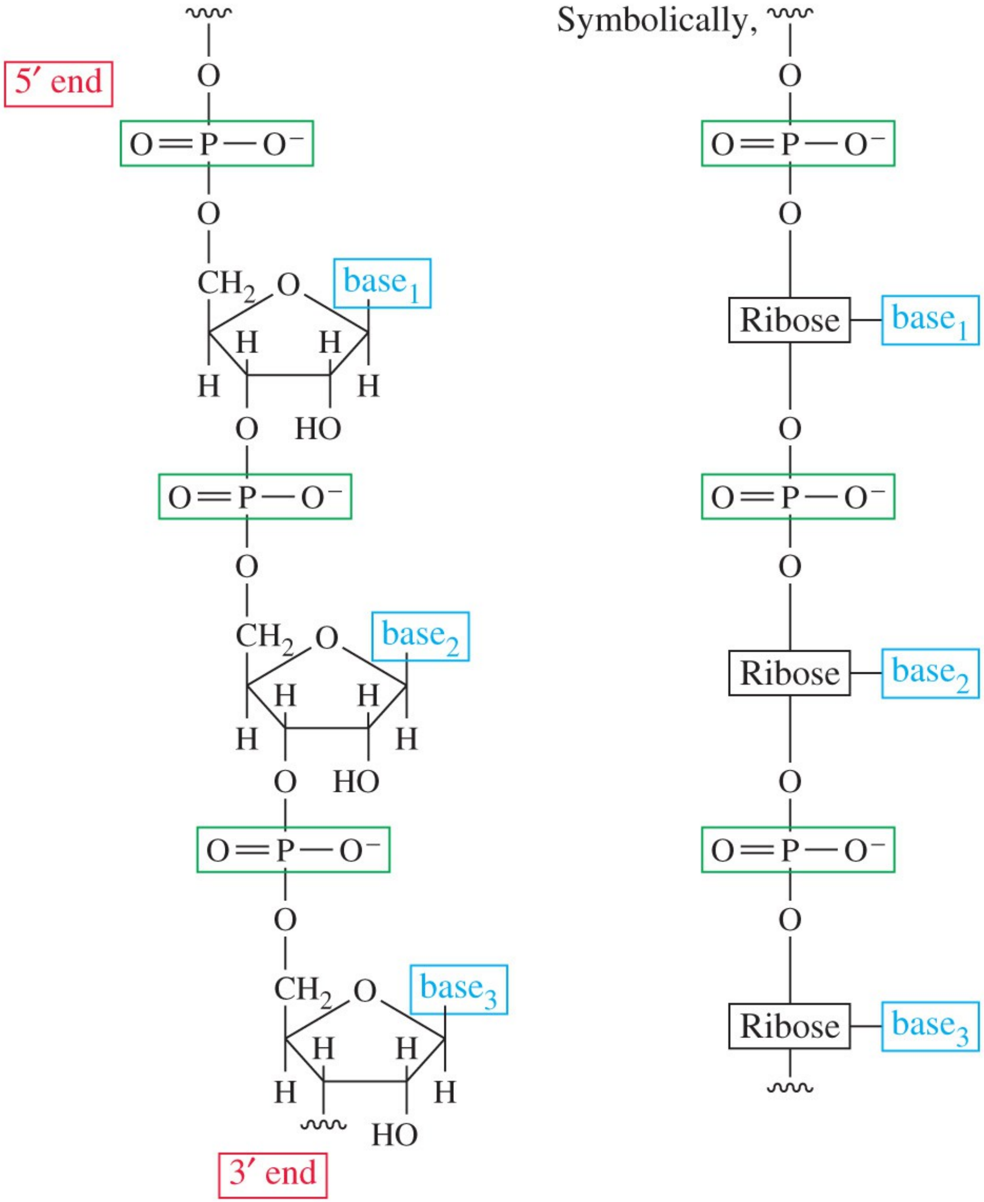
- Amylopectin is a branched -1,6’ polymer of glucose.

Nucleic Acids

- Polymer of ribofuranoside rings linked by phosphate ester groups.
- Each ribose is bonded to a base.
- Ribonucleic acid (RNA)
- Deoxyribonucleic acid (DNA)

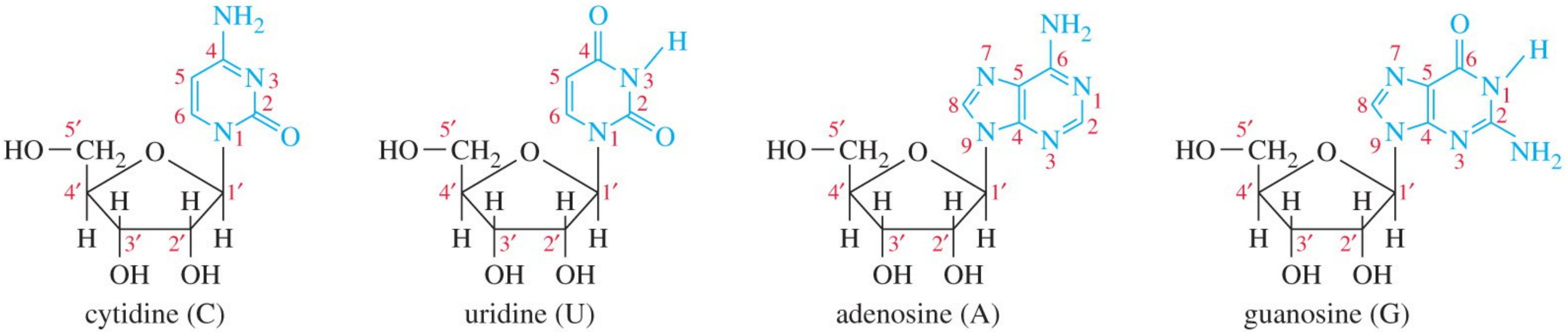


RNA Polymer



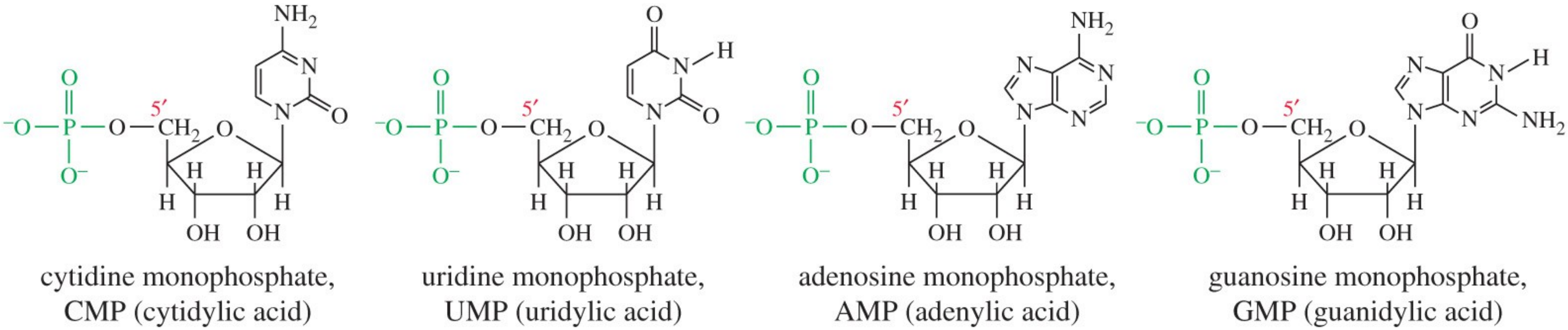
- Nucleic acids are assembled on a backbone made up of ribofuranoside units linked by phosphate esters.

Cytidine, Uridine, Adenosine, and Guanosine



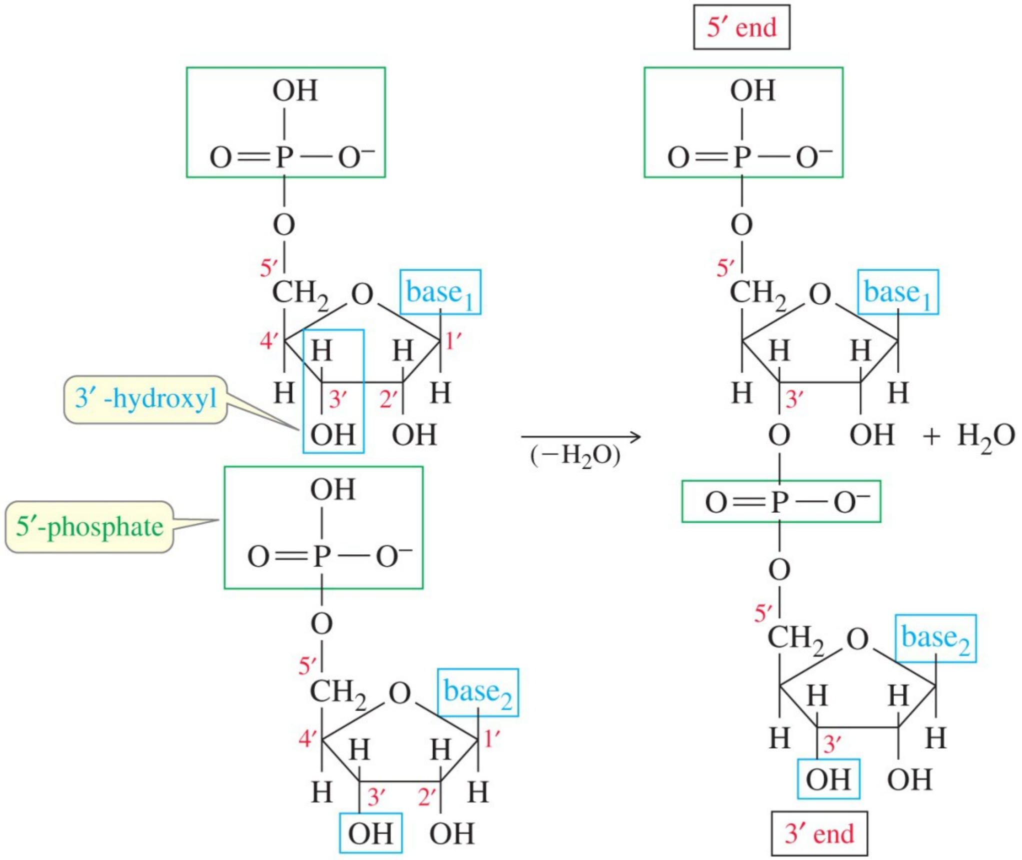
- Ribonucleosides are components of RNA based on glycosides of the furanose form of D-ribose.

Common Ribonucleotides



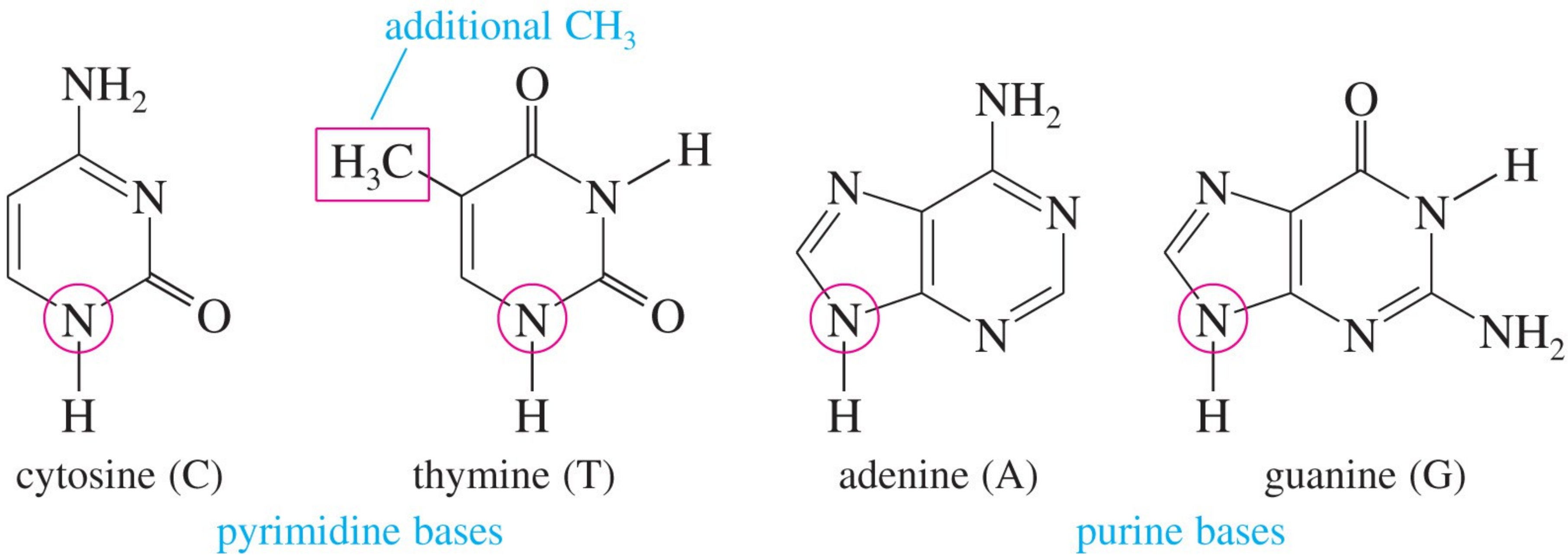
- Ribonucleosides esterified by phosphoric acid at their 5'-position, the —CH_2OH at the end of the ribose chain.
- Ribonucleosides are joined together by phosphate ester linkages.

Phosphate Linkages



- A molecule of RNA always has two ends (unless it is in the form of a large ring); one end has a free 3' group, and the other end has a free 5' group.

DNA Bases



- The four common bases of DNA are cytosine, thymine, adenine, and guanine.

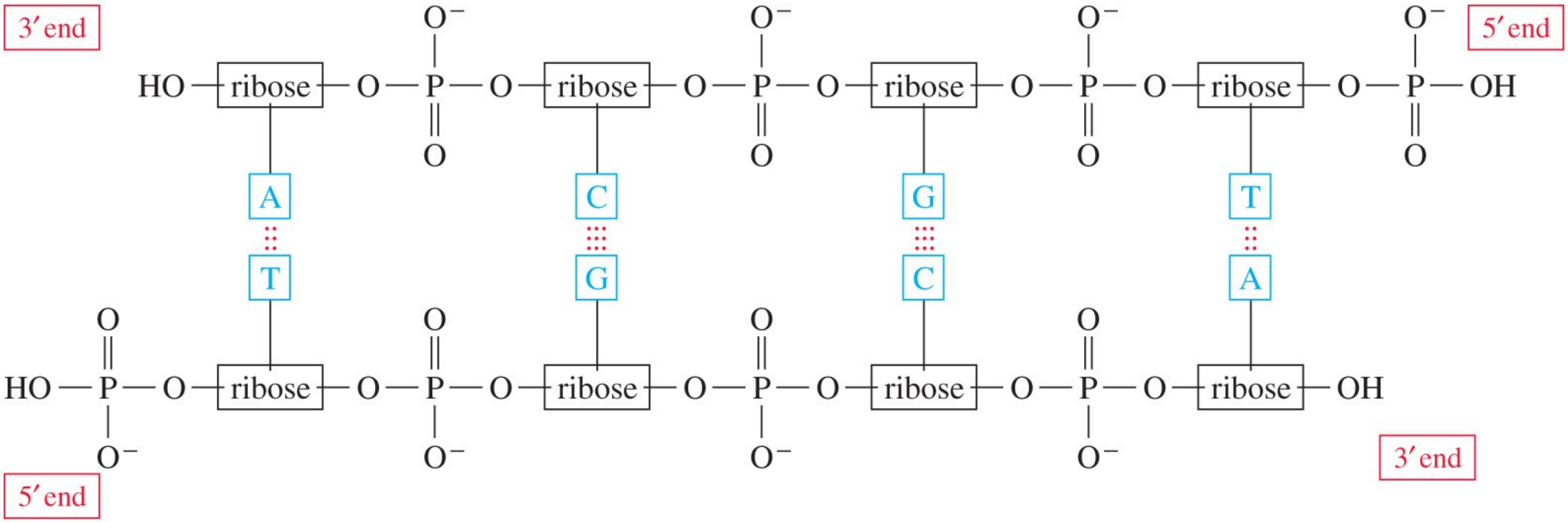
Structure of DNA

- -D-2-deoxyribofuranose is the sugar.
- Heterocyclic bases are cytosine, thymine (instead of uracil), adenine, and guanine.
- Linked by phosphate ester groups to form the primary structure.

Base Pairing in DNA and RNA

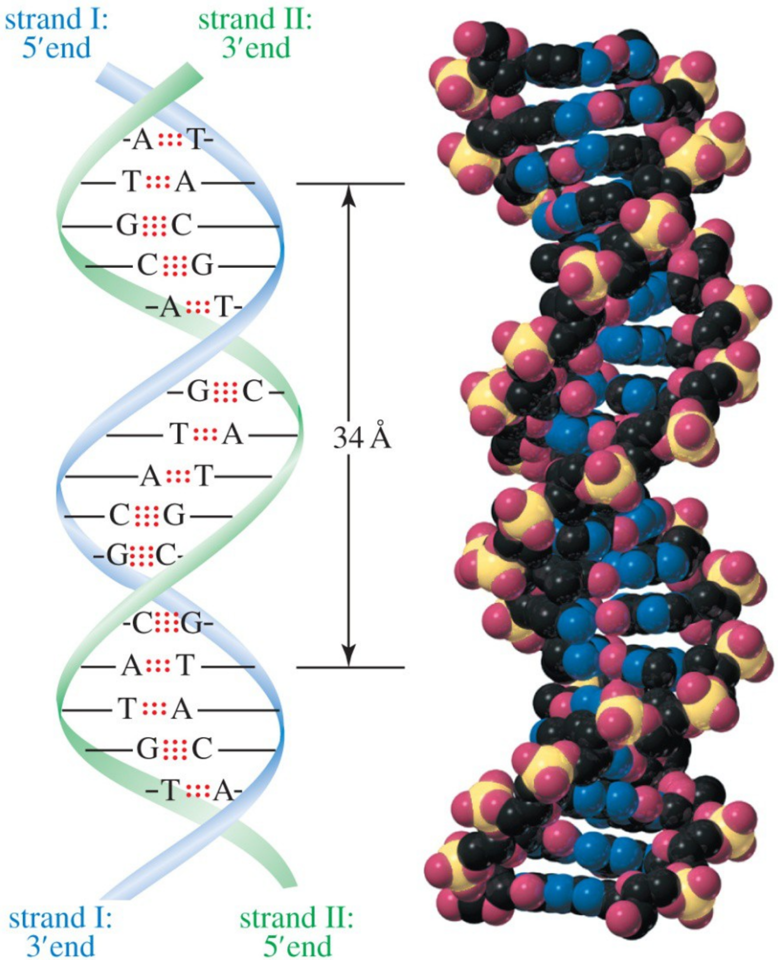
- Each purine forms a stable hydrogen-bonded pair with a specific pyrimidine base.
- Guanine hydrogen-bonds to cytosine in three places; adenine hydrogen-bonds to thymine in two places.

Antiparallel Strands of DNA



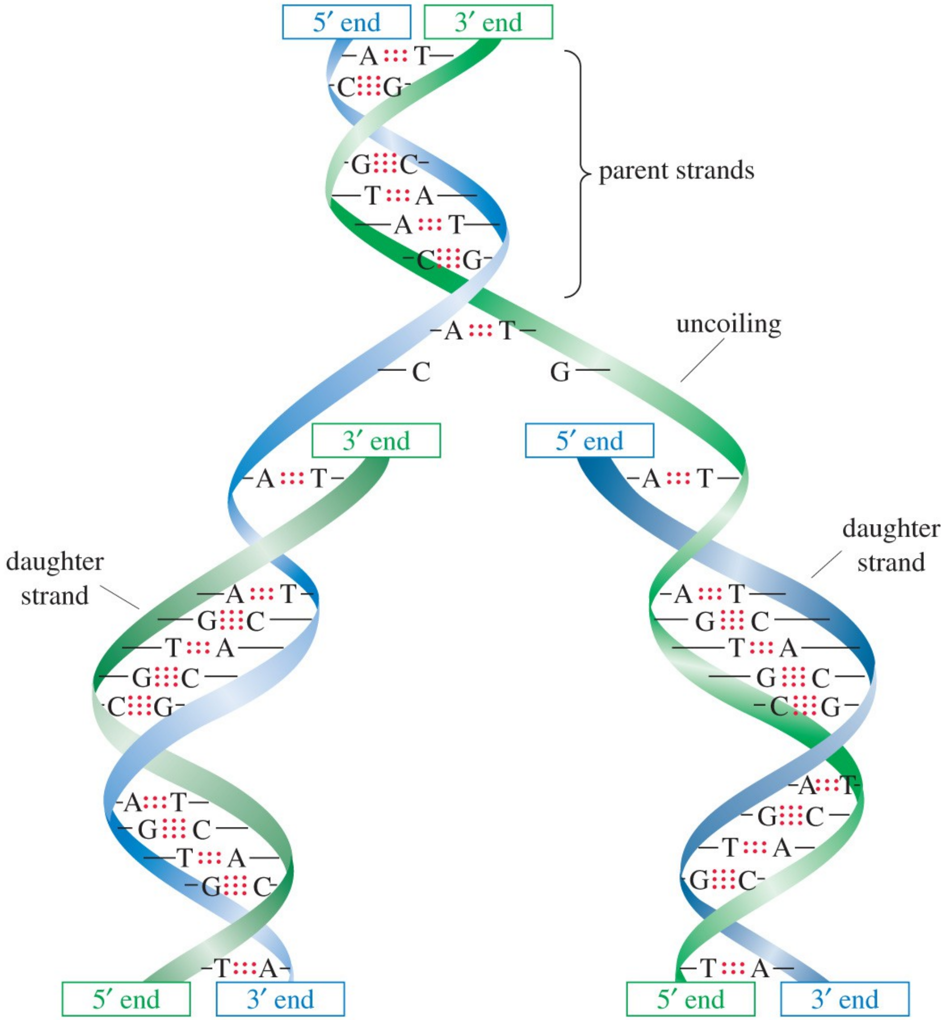
- DNA usually consists of two complementary strands, with all the base pairs hydrogen-bonded together.
- The two strands are antiparallel, running in opposite directions.

The Double Helix



- Two complementary strands are joined by hydrogen bonds between the base pairs.
- This double strand coils into a helical arrangement. Described by Watson and Crick in 1953.

Replication



Additional Nucleotides

- Adenosine monophosphate (AMP), a regulatory hormone.
- Nicotinamide adenine dinucleotide (NAD), a coenzyme.
- Adenosine triphosphate (ATP), an energy source.