Lecture Notes
Chem 51C
S. King

Chapter 28 Carbohydrates

Carbohydrates are the most abundant class of organic compounds in the plant world. They are synthesized by nearly all plants and animals, which use them to store energy and deliver it to the cells.

most living organisms:

**Starch, Glycogen and cellulose are all polymers of glucose**.

- Plants store energy by converting glucose to **starch**
- Animals store energy by converting glucose to **glycogen.**
- Plants use **cellulose** as structural material to support the weight of the plant.
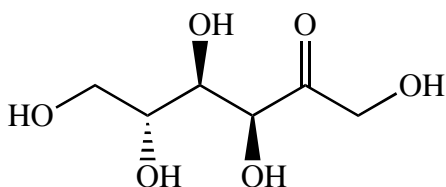
I. **Classification of Carbohydrates**

A. **Monosaccharides**

Monosaccharides are carbohydrates that cannot be broken down into simpler units by hydrolysis.
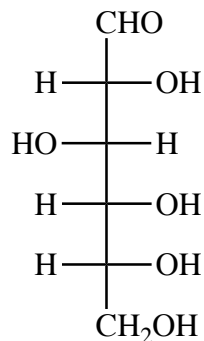
Example: Glucose & Fructose
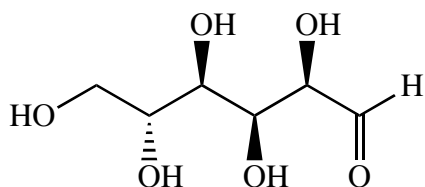
D-glucose
(open-chain
aldehyde form)

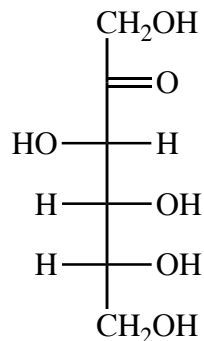**D-fructose**
(open-chain
ketone form)

A simpler way to designate the structure of monosaccharides is to use a **Fischer Projection**:

D-glucose

$$
\begin{array}{c}
\text{CHO} \\
\text{H} \!-\!\!-\!\!-\! \text{OH} \\
\text{HO} \!-\!\!-\!\!-\! \text{H} \\
\text{H} \!-\!\!-\!\!-\! \text{OH} \\
\text{H} \!-\!\!-\!\!-\! \text{OH} \\
\text{CH}_2\text{OH}
\end{array}
$$

D-fructose

$$
\begin{array}{c}
\text{CH}_2\text{OH} \\
=\!\!=\!\text{O} \\
\text{HO} \!-\!\!-\!\!-\! \text{H} \\
\text{H} \!-\!\!-\!\!-\! \text{OH} \\
\text{H} \!-\!\!-\!\!-\! \text{OH} \\
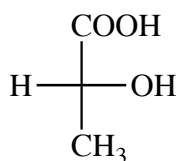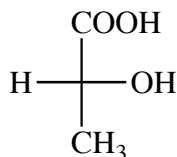\text{CH}_2\text{OH}
\end{array}
$$

- Most highly oxidized end carbon on top
- Horizontal lines are wedges   (project out toward the viewer)
- vertical lines are dashed lines   (project away from viewer)
- **NOT** <u>the same thing as a Lewis Structure</u>!

Rule of thumb for Fischer projections:

> In comparing Fischer Projections, you can rotate the drawing 180° *in* the plane of the paper. You *cannot* flip it over and you *cannot* rotate it by 90°.

Example:

$$
\begin{array}{c}
\text{COOH} \\
\text{H} \!-\!\!-\!\!-\! \text{OH} \\
\text{CH}_3
\end{array}
\qquad \longrightarrow
$$

$$
\begin{array}{c}
\text{COOH} \\
\text{H} \!-\!\!-\!\!-\! \text{OH} \\
\text{CH}_3
\end{array}
\qquad \longrightarrow
$$

```
     COOH
      |
H —————— OH                    ⟶
      |
     CH₃
```

B. Disaccharide

A disaccharide is a sugar that can be hydrolyzed to two monosaccharides:

C. Oligosaccharide

An oligosaccharide contains relatively few monsaccharide units.

D. Polysaccharide

Carbohydrates that can be hydrolyzed into many monosaccharide units.
They are naturally occuring polymers of monosacchardes.

Example: Cellulose, Starch
(Polysaccharides made up of glycogen D-glucose units. Vastly
different physical properties results from subtle differences in the
stereochemistry of the two polymers.)

II. Classification of Monosaccharides

Monosaccharides can be classified by three criteria:

1. Whether the sugar contains a ketone or an aldehyde group.

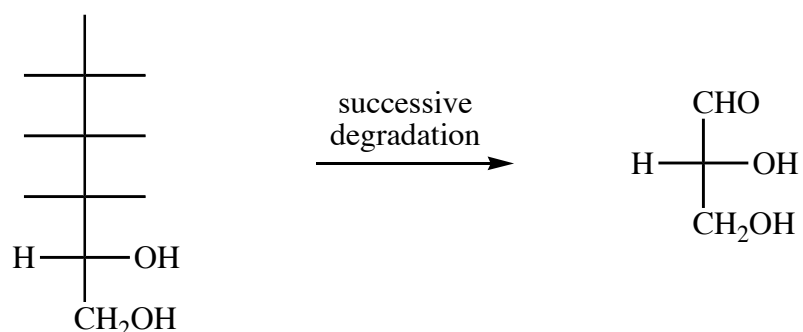2. The # carbons in the carbon chain:

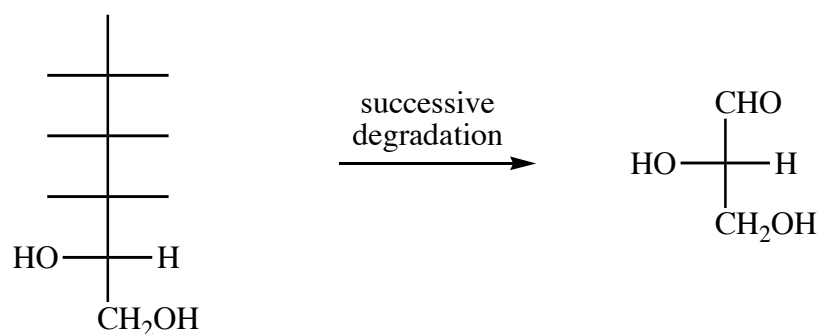|	
3 C's	4 C's
5 C's	6 C's
7 C's	

1 & 2 are often combined:

Example: glucose

3. The stereochemical configuration of the chiral carbon atom farthest from the carbonyl group. **D** or **L** is used to designate the configuration at this carbon atom.
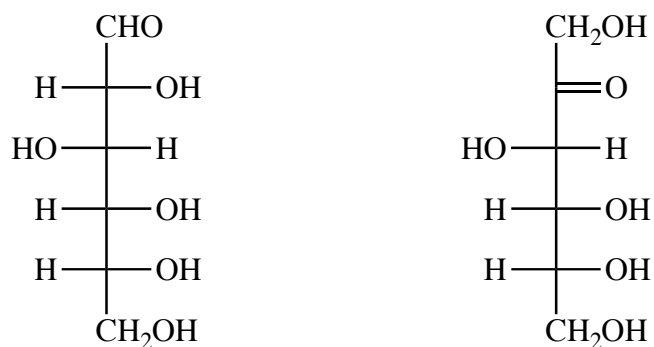
The D family of sugars:

H——OH
CH$_2$OH

successive degradation →

CHO
H——OH
CH$_2$OH

The L family of sugars:

HO——H
CH$_2$OH

successive degradation →

CHO
HO——H
CH$_2$OH

• The D or L configuration has nothing to do with whether the compound is dextrorotatory or levorotatory. This must be determined by experiment.
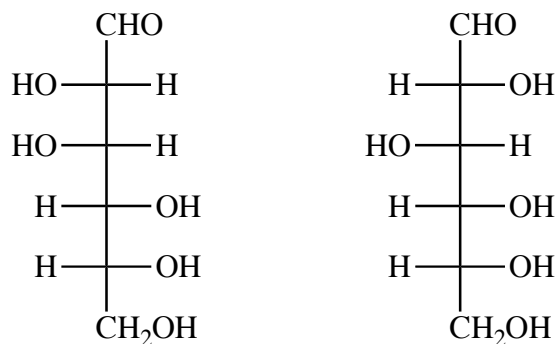
Example:

```
        CHO                          CH₂OH
   H ───── OH                    ═════ O
  HO ───── H                 HO ───── H
   H ───── OH                  H ───── OH
   H ───── OH                  H ───── OH
       CH₂OH                       CH₂OH
```

- The enantiomer of a D sugar is always the L sugar.

```
        CHO
  HO ───── H
   H ───── OH
       CH₂OH
```
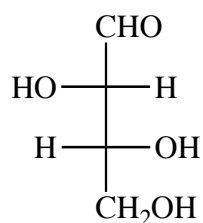
A. Epimers

Many of the common sugars are closely related to eachother, differing only in the stereochemistry at a single carbon atom. Sugars that differ only by the stereochemistry at a single carbon atom are **epimers** *(the carbon atom at which they differ is generally stated.)*

```
        CHO                          CHO
  HO ───── H                    H ───── OH
  HO ───── H                   HO ───── H
   H ───── OH                   H ───── OH
   H ───── OH                   H ───── OH
       CH₂OH                       CH₂OH
```

153

III. Cyclic Structures of Monosaccharides: Cyclic Hemiacetals

Recall: Hemiacetals are generally unstable and rarely isolated (the equilibrium favors aldehyde or ketone)
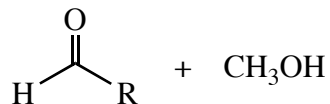
But cyclic hemiacetals are favored when a 5 or 6-membered ring can be formed.
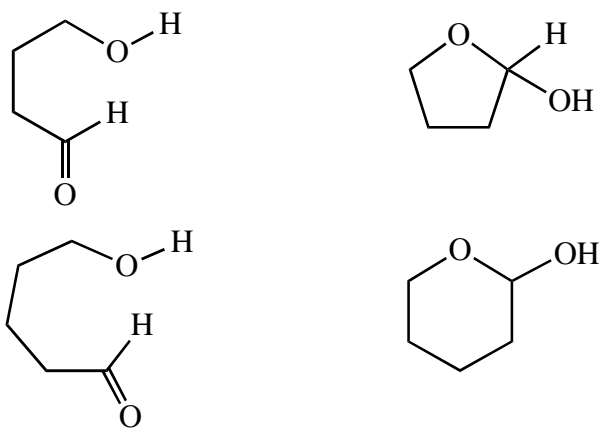

The same is true for aldoses and ketoses. They exist primarily as cyclic hemiacetals. Notice that for most sugars, both 5 or 6 membered rings are possible. The 6-membered ring is usually favored, although 5-membered cyclic acetals are also important.
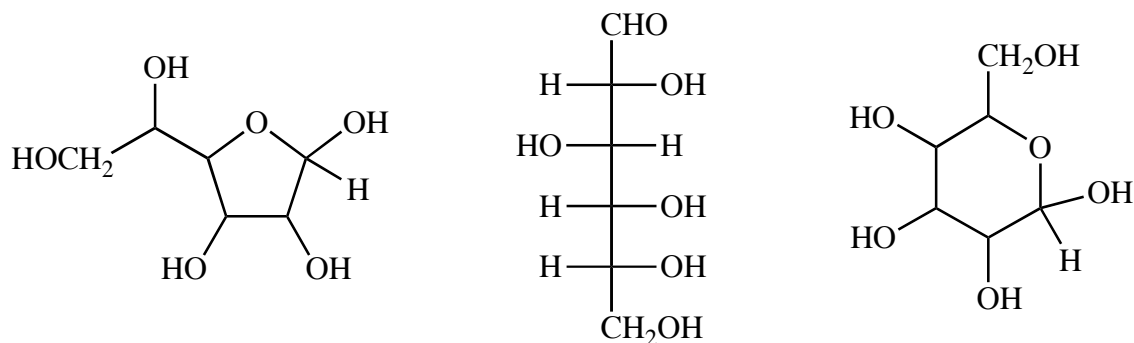
NOTE: Formation of the hemiacetal introduces a ***new stereocenter***. There are two possible configurations, α & β. The hemiacetal carbon is called an ***anomeric carbon***, and the two possible isomers are called ***anomers***.

The Cyclic Hemiacetal Form of Glucose
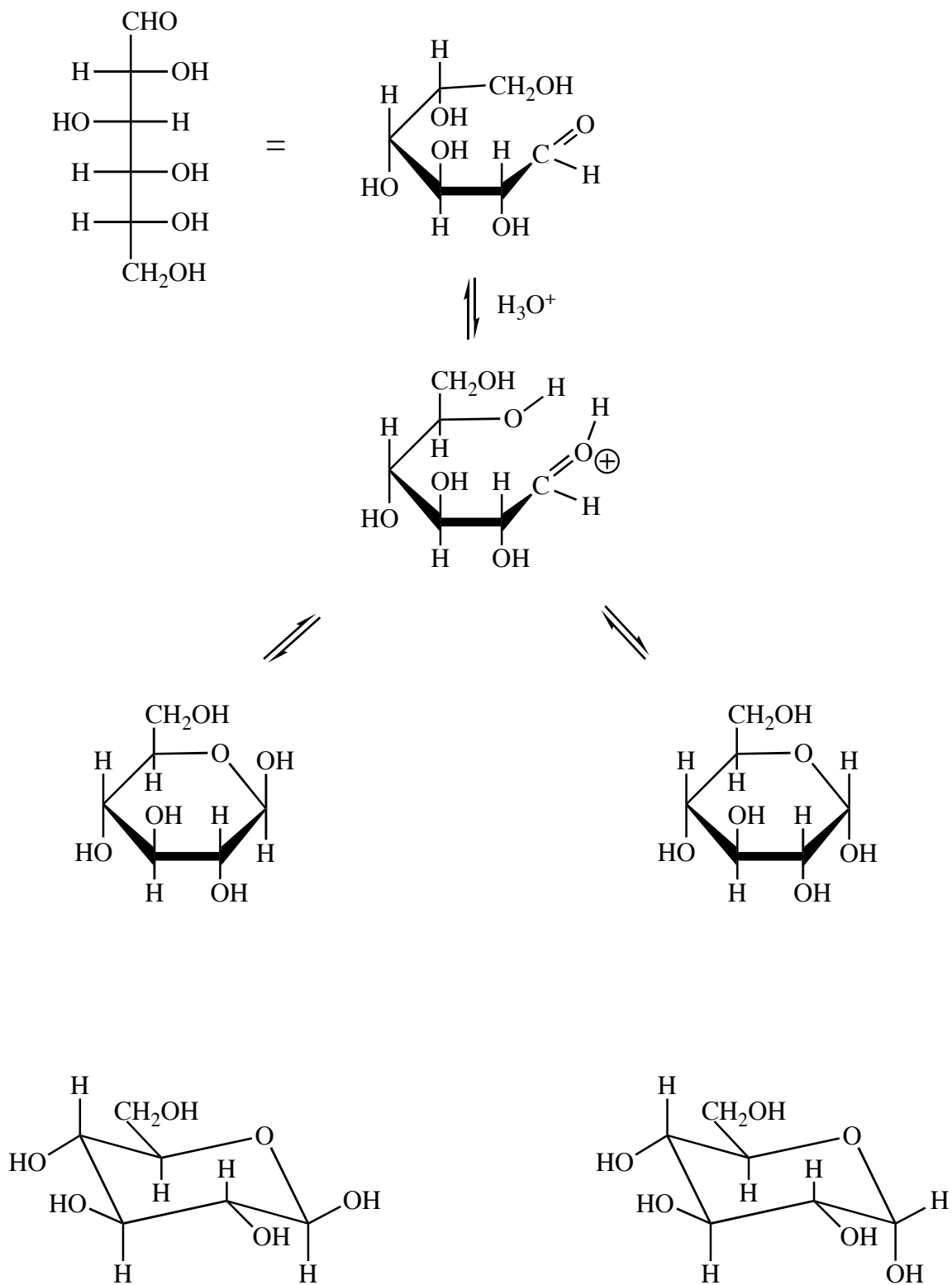
Drawing Cyclic Monosaccharides
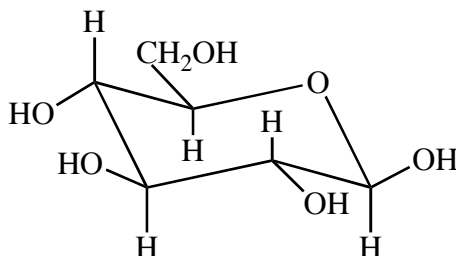
Haworth projection:

1. Mentally lay the Fischer projection on its right side. Groups that were on the right in the Fischer projection are down and the ones that were on the left are up.

2. Rotate the C4-C5 bond so that the C5 hydroxyl group can form a part of the ring. *For the D series sugars, this rotation puts the terminal -CH$_2$OH upward.*

3. Close the ring and draw the result. Always draw the Haworth projection with the ring oxygen in the back right hand corner, with C1 (the hemiacetal C) at the far right. The hydroxyl group at C1 can be either up or down. Sometimes this ambiguous stereochemistry is symbolized by a wavy line.
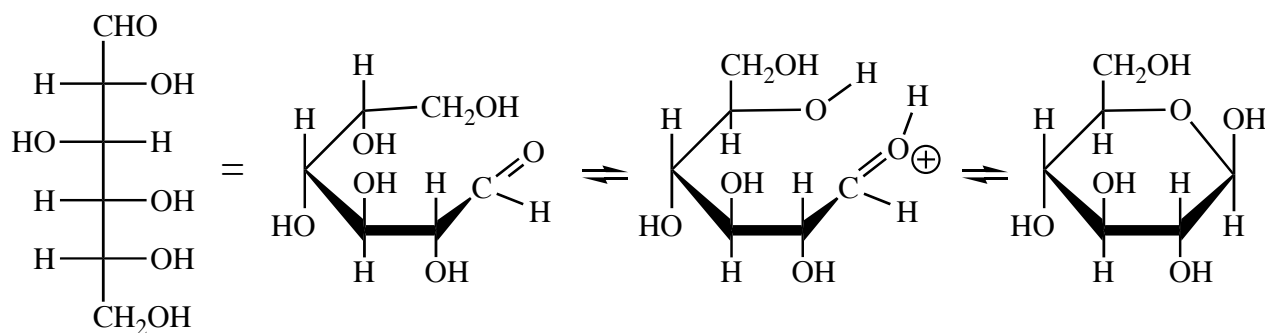
Chair conformation:

Chair conformations are easily drawn by recognizing the differences between the sugar in question and glucose.

1. Draw the chair conformation as shown below with the ring oxygen on the back right-hand corner and the hemiacetal carbon (C1) down.

2. In glucose, all the hydroxy groups are in the equatorial position.

3. To draw other common sugars, notice how they differ from glucose and make the appropriate changes.

Example: Draw the cyclic hemiacetal form of β-D-mannose, both as a chair conformation and as a Haworth projection. Mannose is the C2 epimer of glucose.

CHO

H———OH

HO———H

H———OH

H———OH

CH$_2$OH
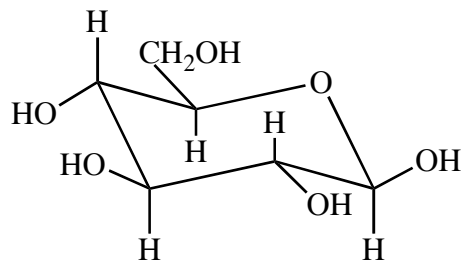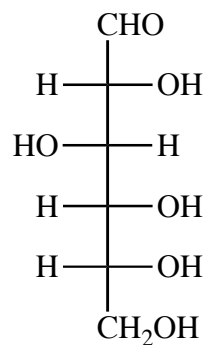
The 5-Membered Ring Cyclic Hemiacetal Form of Fructose

Not all sugars form 6-membered rings in their hemiacetal form. Many aldopentoses and ketohexoses form 5-membered rings.

CH$_2$OH
O
HO——H
H——OH
H——OH
CH$_2$OH

HOCH$_2$ O OH
H OH
H CH$_2$OH
OH H

HOCH$_2$ O CH$_2$OH
H OH
H OH
OH H
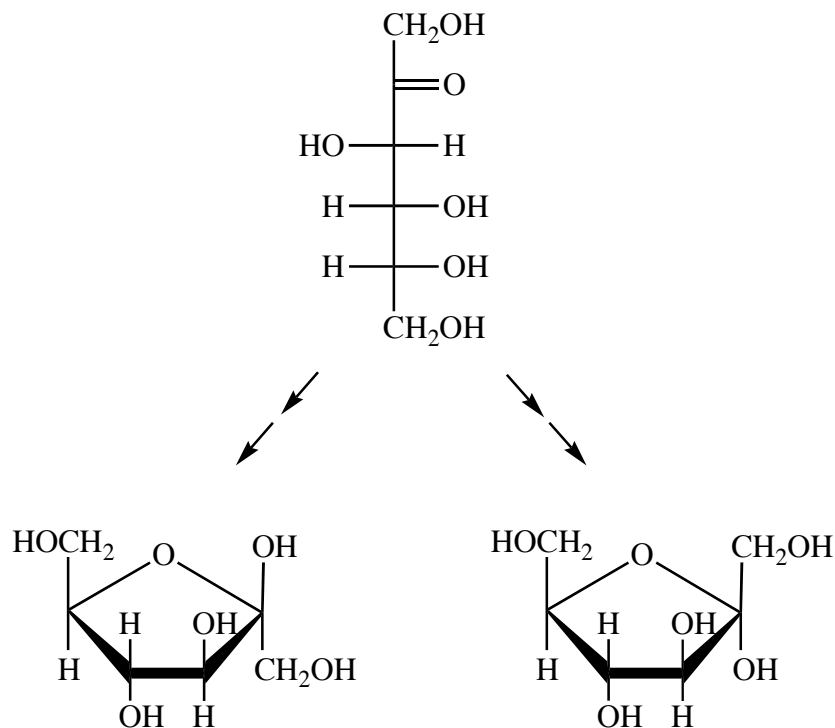
Drawing **5-membered Ring Cyclic Monosaccharides:**

1. Mentally lay the Fischer projection over on it's right hand side. Groups that were on the right are down and groups that are on the left are up.

2. Rotate the C4 - C5 bond so that the C5 -OH can form the ring.

3. Close the ring and draw the result. The ring oxygen should be at the top of the 5-membered ring.

IV. Properties of Anomers: Mutarotation

An aqueous solution of D-glucose contains an equilibrium mixture of α-D-gluco-
pyranose, β-D-glucopyranose, and the intermediate open chain form.

pure α anomer
m.p. = 146°C
$[\alpha] = +112.2°$

pure β anomer
m.p. = 150°C
$[\alpha] = +18.7°$
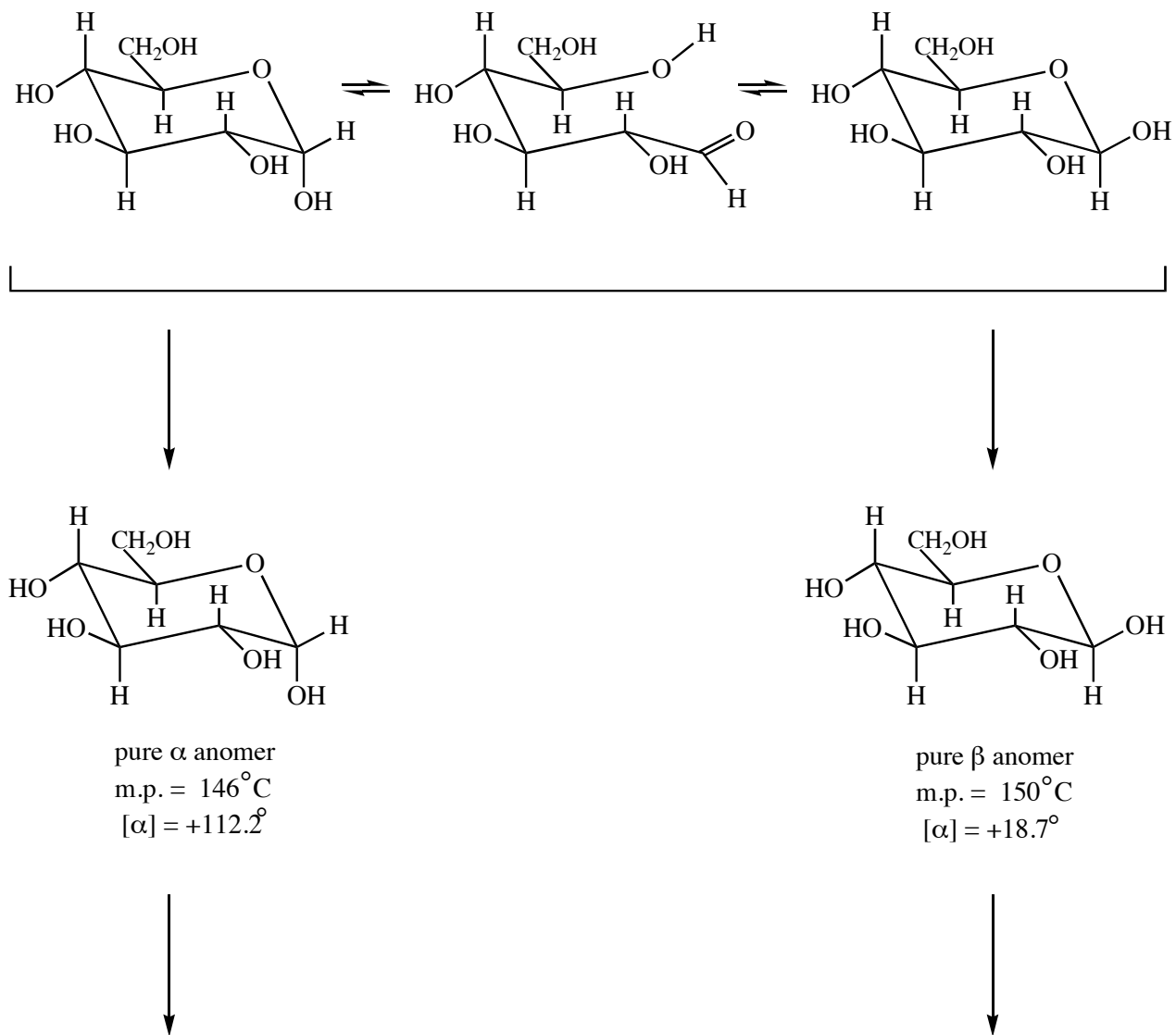
This change in specific rotations to a mutual value: *MUTAROTATION*

Q: How much α & β is there in the equilibrium mixture?
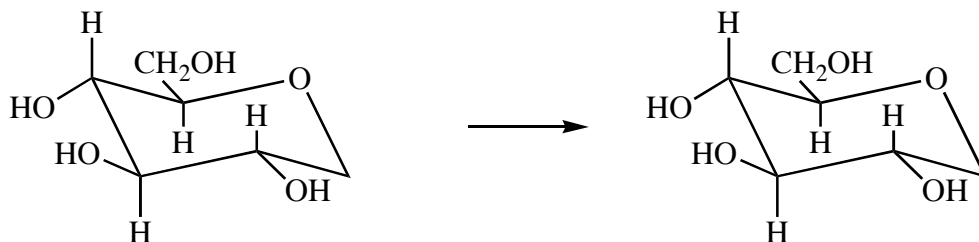*A:* This can be calculated as follows:

>   let **a** = fraction of glucose as α anomer
>   let **b** = fraction of glucose as β anomer

D-glucose can also cyclize to two furanose forms, but furanose forms constitute only 0.14% @ equilibrium:
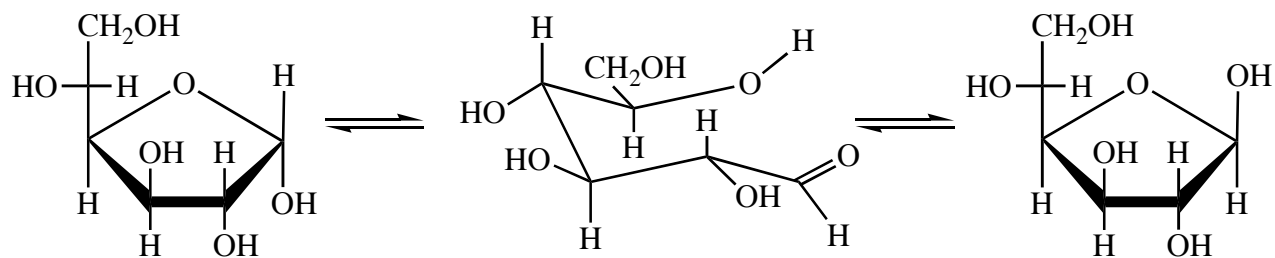
V. Reactions of Monosaccharides as Carbonyl Compounds

A. Formation of Gycosides:

Methyl glucopyranosides:

- do not undergo mutarotation
- are stable to base, but hydrolyze easily in acid solution

Mechanism:
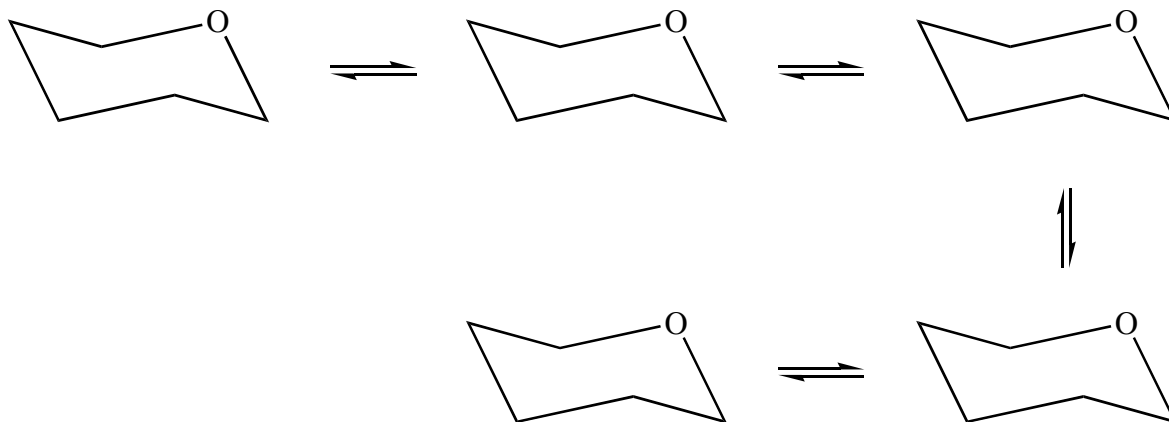
B. Hydrolysis of Glycosides

The mechanism for hydrolysis of glycosides is exactly the opposite of the mechanism for formation of glycosides!
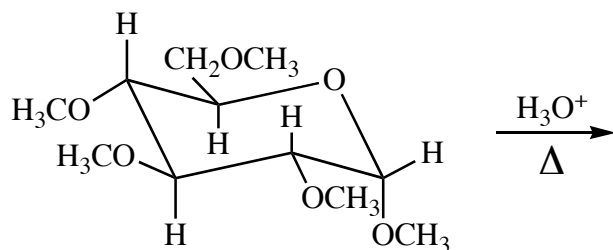
Mechanism:
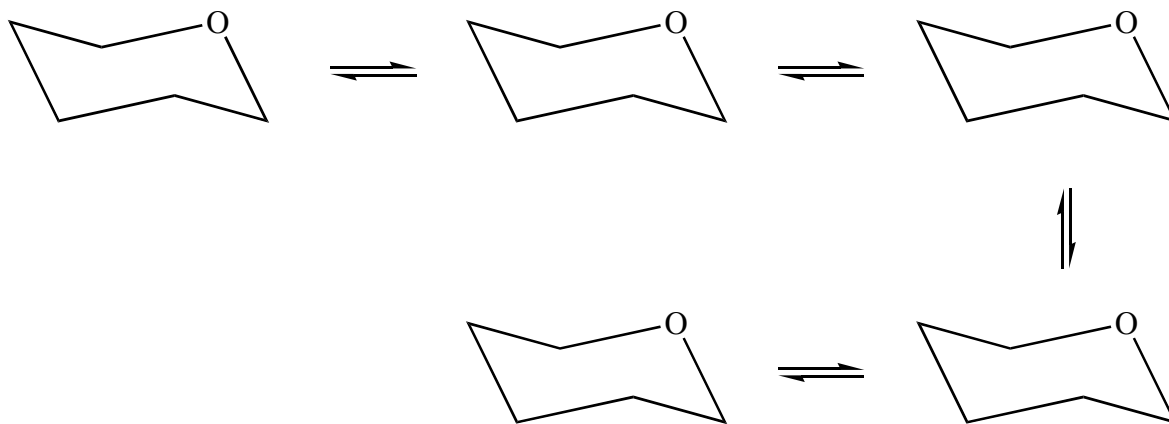
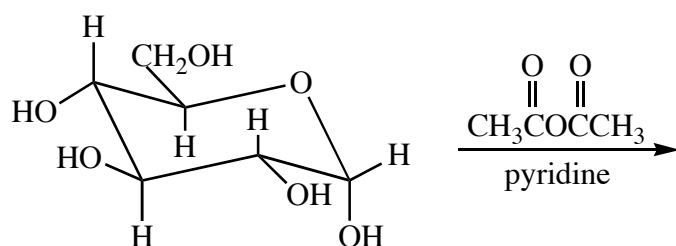## VI. Reactions of Monosaccharides as Alcohols

A. Ether Formation

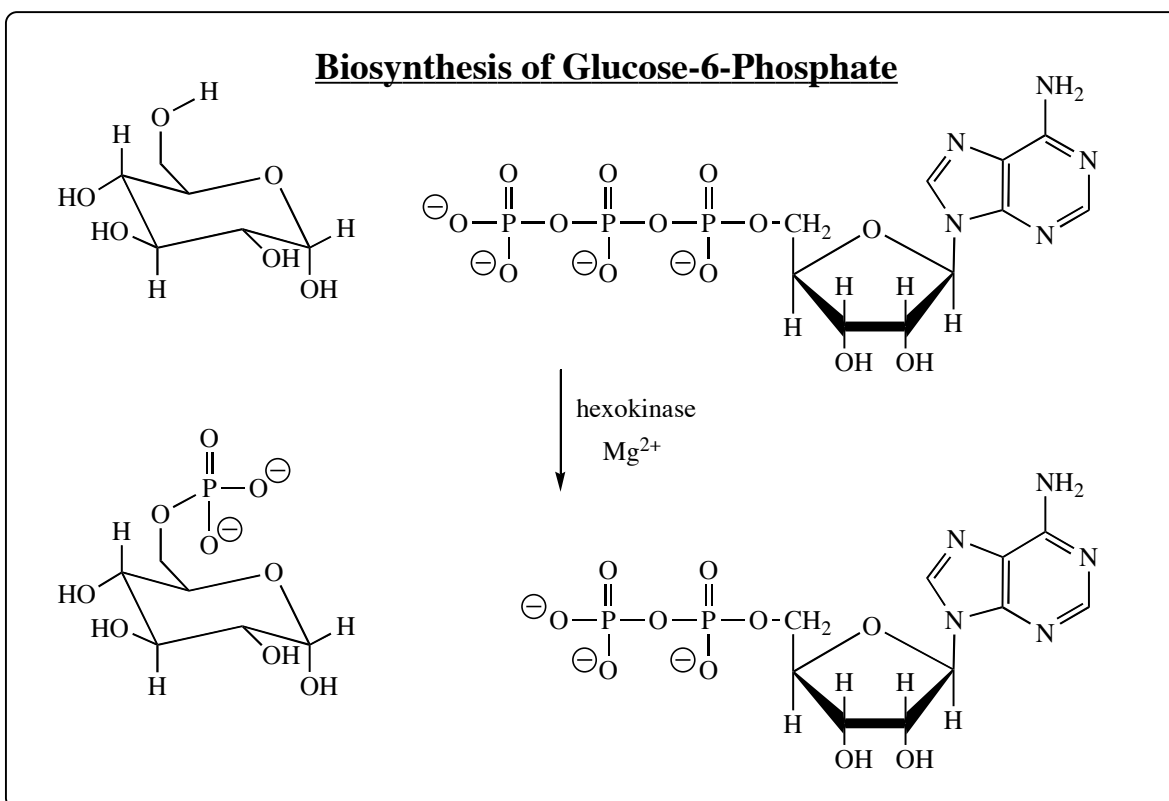Methyl ethers can be formed at all the -OH groups of a sugar with very reactive alkylating agents:
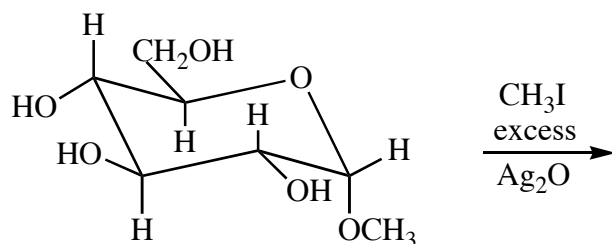
The methoxy group at the anomeric carbon *is* sensitive to acid hydrolysis:

$$\xrightarrow[\Delta]{H_3O^+}$$

B. Esterification: The OH groups of a sugar can also be esterified:

$$\xrightarrow[\text{pyridine}]{CH_3COCCH_3}$$

☞ *In biological systems, the most important esters of sugars are phosphate esters:*

Biosynthesis of Glucose-6-Phosphate

hexokinase
Mg^{2+}

VII. Oxidation Reactions of Sugars

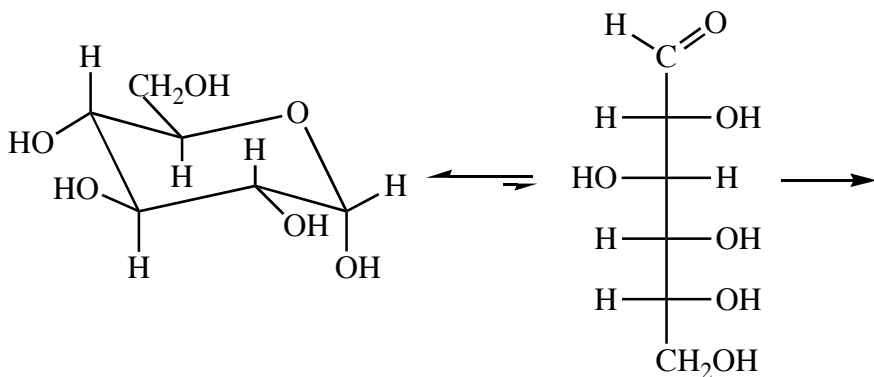**Reducing Sugars**: Sugars that are easily oxidized by mild oxidizing agents.

Non-reducing sugars: Not easily oxidized - The carbonyl group is tied up in an acetal linkage.

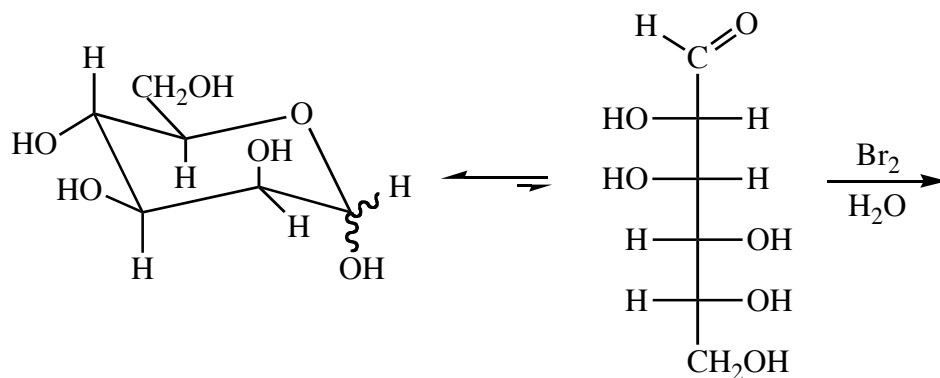**Examples:** methyl β-D-glucopyranoside & sucrose
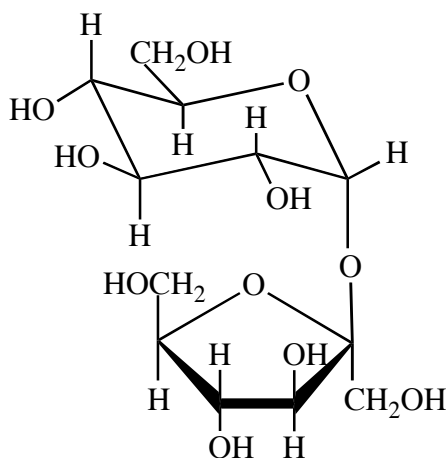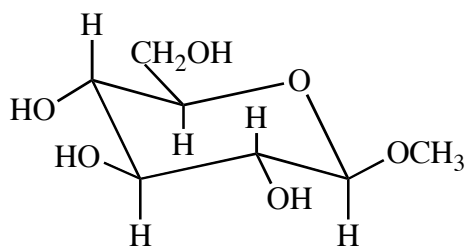
A. Oxidizing Agents:

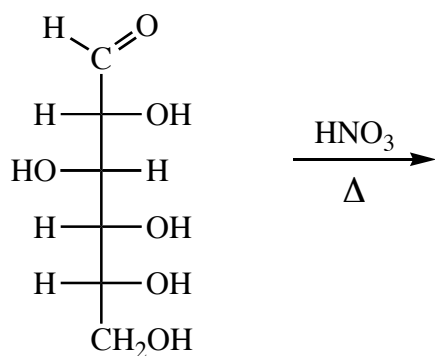**1. Tollen's Reagent (Tollen's Test):** Oxidizes aldoses to aldonic acids.

2. **Bromine/H₂O:** Also oxidizes aldoses to aldonic acids.

$$\ce{H-C(=O)} \quad\text{(Fischer projection)}$$

HO—	—H
HO—	—H
H—	—OH
H—	—OH
	CH₂OH

$\xrightarrow[\text{H}_2\text{O}]{\text{Br}_2}$

3. **Nitric Acid**

This is a stronger oxidizing agent, and it oxidizes both ends of the chain to a dicarboxylic acid, known as an **aldaric acid**.

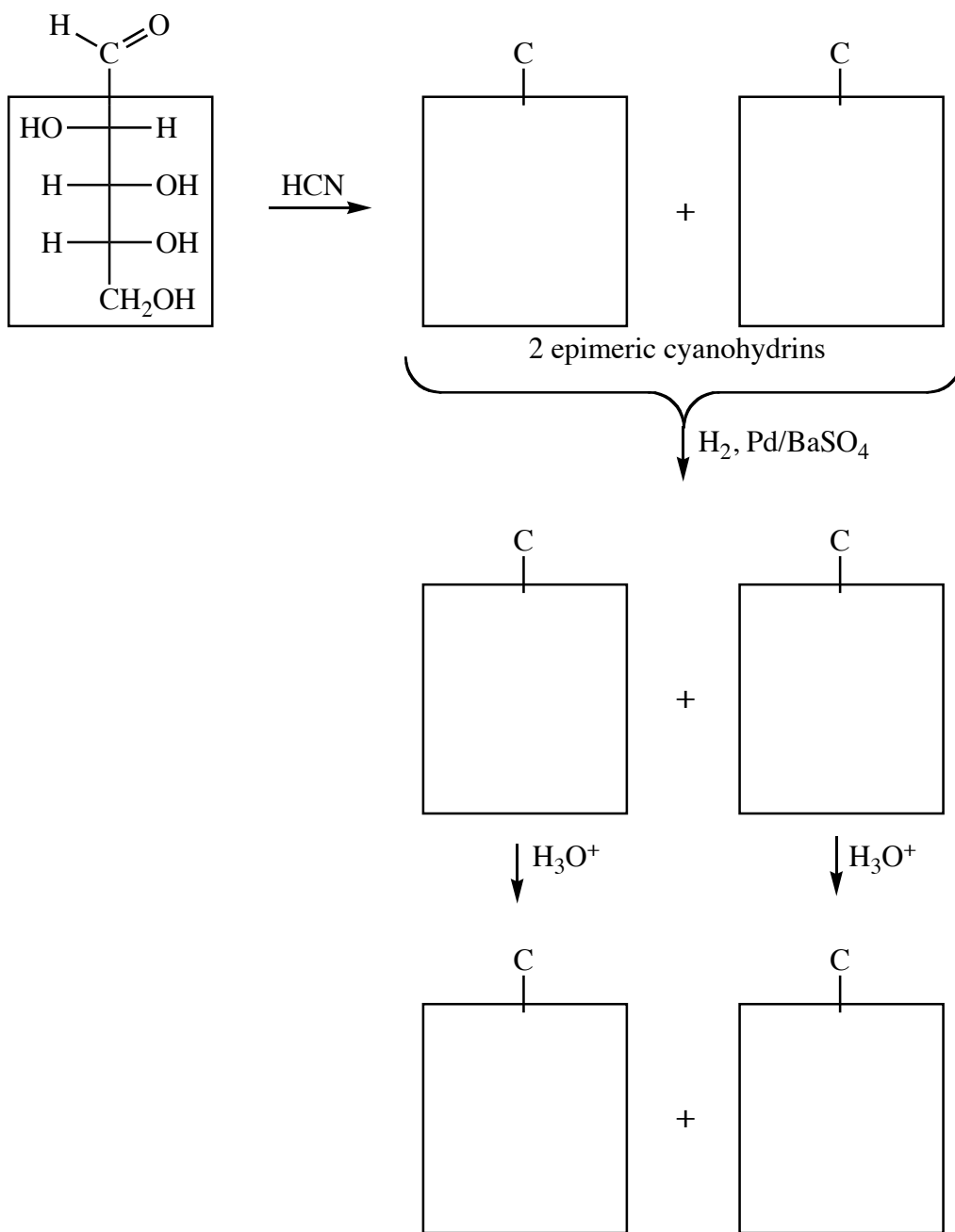|	
H—	—OH
HO—	—H
H—	—OH
H—	—OH
	CH₂OH

$\xrightarrow[\Delta]{\text{HNO}_3}$

- 2° alcohols are slow to oxidize. HNO₃ only oxidizes 1° alcohols & aldehydes.

VIII. Lengthening and Shortening Chains in Carbohydrates

A. The Kiliani Fischer Synthesis

The Kiliani Fischer Synthesis lengthens an aldose carbon chain by adding one carbon atom to the aldehyde end of the aldose.

$$\underset{\text{H}}{}\overset{\text{O}}{\underset{}{\text{C}}}$$

HO————H

H————OH

H————OH

CH$_2$OH

$\xrightarrow{\text{HCN}}$

C

\+

C

2 epimeric cyanohydrins

$\downarrow$ H$_2$, Pd/BaSO$_4$

C

\+

C

$\downarrow$ H$_3$O$^+$ $\downarrow$ H$_3$O$^+$

C

\+

C

B. The Ruff Degradation

Ruff degradation can be used to shorten the chain of an aldose by one carbon.

CHO
H——OH
H——OH
H——OH
CH$_2$OH

$\xrightarrow{\text{1. Br}_2/\text{H}_2\text{O} \\ \text{2. Ca(OH)}_2}$
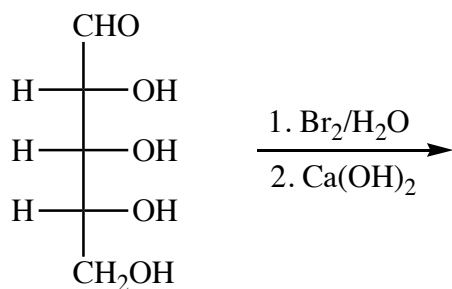
D-Ribose

• The Ruff Degradation can be used in structure determination.

Example: D-Altrose is an aldohexose. Ruff degradation of D-altrose gives the same aldopentose as does degradation of D-allose, the C-3 epimer of glucose. Give the structure of D-altrose.

IX. Reduction Reactions of Sugars: NaBH$_4$ reduces aldoses to alditols.

H—C=O
H——OH
HO——H
H——OH
CH$_2$OH

$\xrightarrow{\text{1. NaBH}_4 \\ \text{2. H}_3\text{O}^+}$
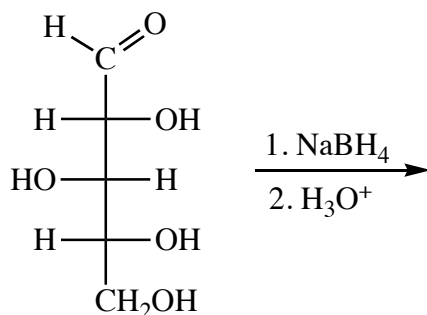
X. Disaccharides

anomeric carbon of sugar + R-OH → acetal (glycoside)

If ROH is another sugar → disaccharide (composed of two monosaccharide units)

In naturally occurring disaccharides, there are three principal glycosidic bonding arrangements:

1. **a 1,4' link** The anomeric carbon (C1) is bonded to the O atom on C4 of the second sugar to form a disaccharide. The prime symbol (') in (1,4') indicates that C4 is on the second sugar.

2. **a 1,6' link** The anomeric carbon (C1) is bonded to the O atom on C6 of the second sugar.

3. **a 1,1' link** The anomeric carbon of the first sugar is bonded through an O atom to the anomeric C of the second sugar.

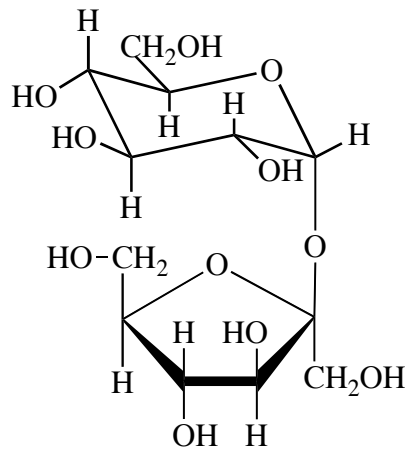**Lactose**: a β-1,4' galactosidic linkage between galactose and glucose
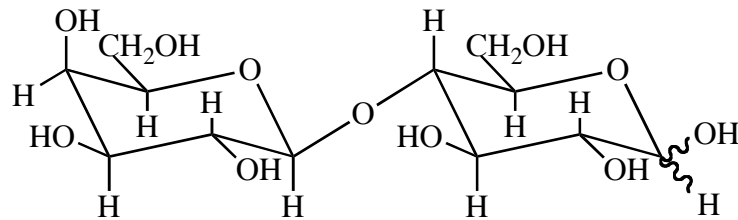
Maltose: an α-1,4' glucosidic linkage between two glucose units.
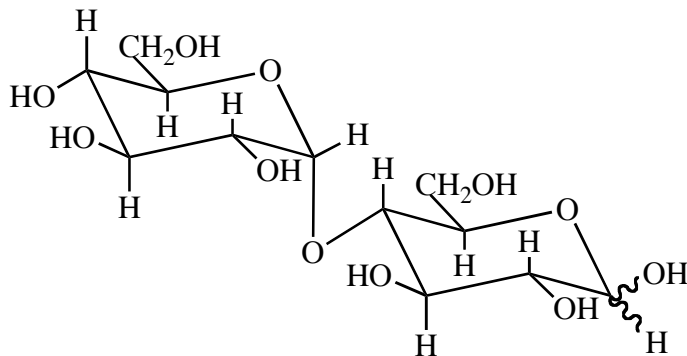
Gentiobiose: a β-1,6' glucosidic linkage between two glucose units. (the 1,6' linkage is rare in disaccharides but common as branch points in polysaccharides.)
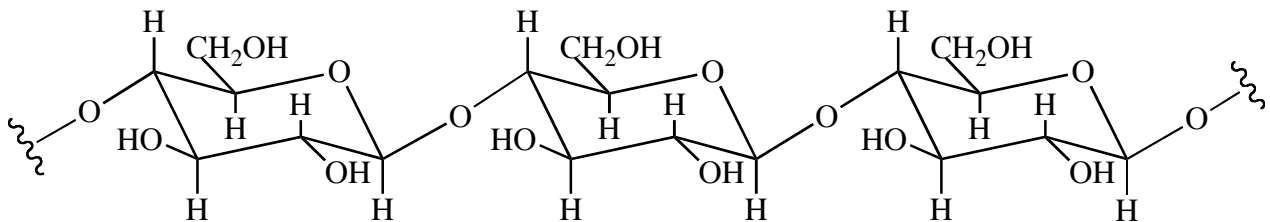
H
CH₂OH
HO
O
HO   H   H
OH
O—CH₂
H   OH   OH HO
O
HO   H   H
OH
OH
H   H
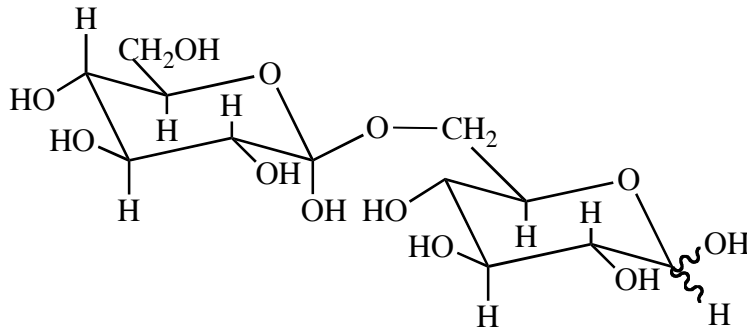
Sucrose: a 1,1' glycosidic linkage between glucose and fructose.

H
CH₂OH
HO
O
HO   H   H
OH   H
H
O
HO-CH₂   O
H   HO
H   CH₂OH
OH   H

XI. Polysaccharides

A. Cellulose (polymer of D-glucose with β-1,4' linkage)

H
CH₂OH
O
O   HO   H   H   O   H   CH₂OH   O   HO   H   H   O   H   CH₂OH   O   HO   H   H   O
OH   H
H   H

Note: Humans and other mammals cannot digest cellulose because we lack the β-glucosidase enzyme necessary to digest the β-glucosidic linkage. β-Glucosidase is synthesized only by bacteria such as the digestive bacteria of ruminants & termites. When a cow eats hay, these bacteria digest about 20 to 30% of the cellulose to digestable carbohydrates. All animals produce α-glucosidase, however, and can hydrolyze the α-glucosidic linkage of sucrose.

B. Starches: Amylose, Amylopectin & Glycogen (polymer of D-glucose with α-1,4' linkage)

Amylose & Amylopectin
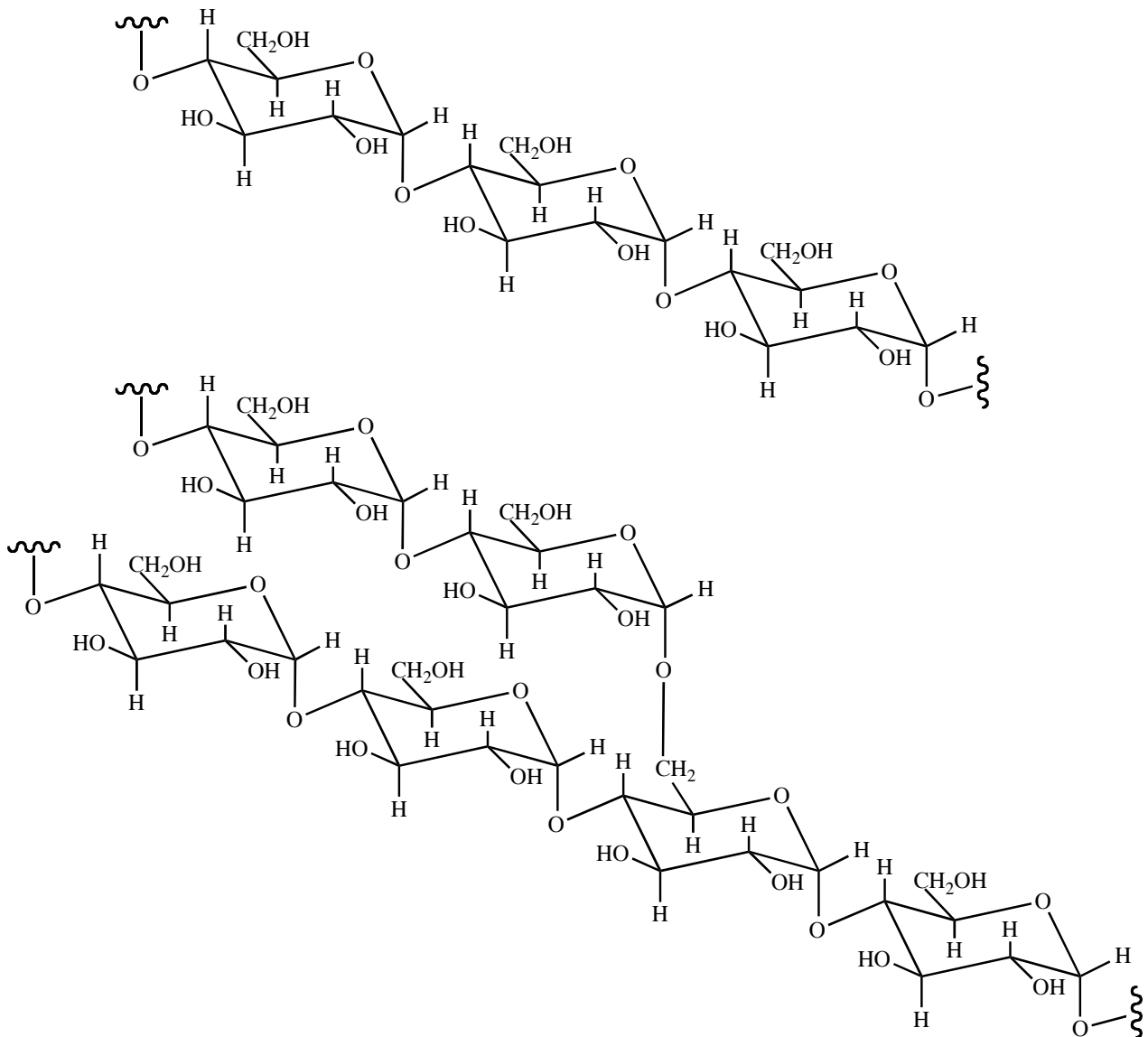
glycogen (similar to amylopectin but with much more branching)

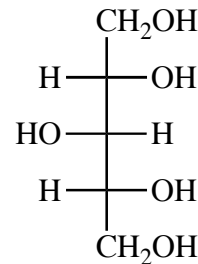## XII. Sweeteners, Fats, and Drugs Derived from Sugars
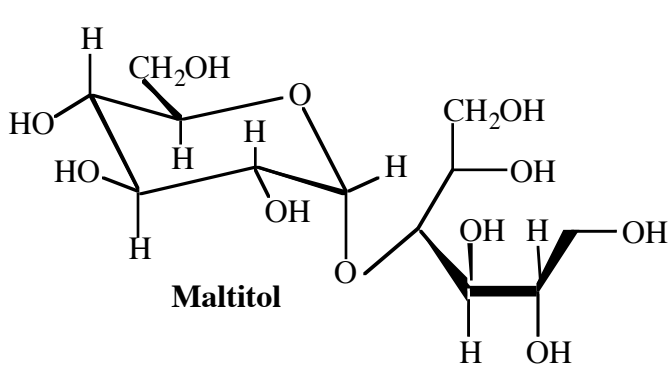
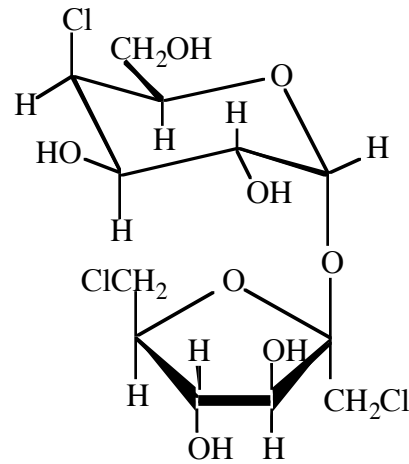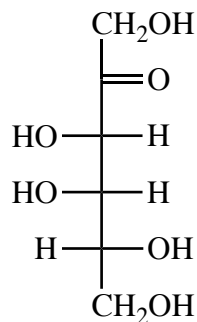Low calorie and no calorie sweeteners:

D-glucitol

CH_2OH
H —— OH
HO —— H
H —— OH
H —— OH
CH_2OH

D-mannitol

CH_2OH
HO —— H
HO —— H
H —— OH
H —— OH
CH_2OH

D-xylitol

CH_2OH
H —— OH
HO —— H
H —— OH
CH_2OH
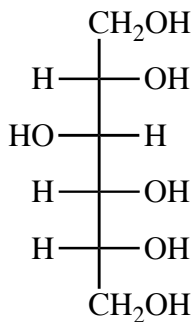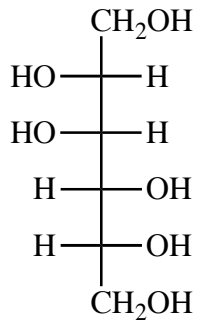
Maltitol

Sucralose (Spenda®)

D-Tagatose

CH_2OH
═O
HO —— H
HO —— H
H —— OH
CH_2OH
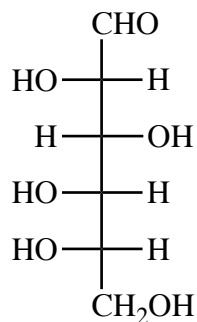
The Holy Grail: L-glucose

CHO
HO —— H
H —— OH
HO —— H
HO —— H
CH_2OH
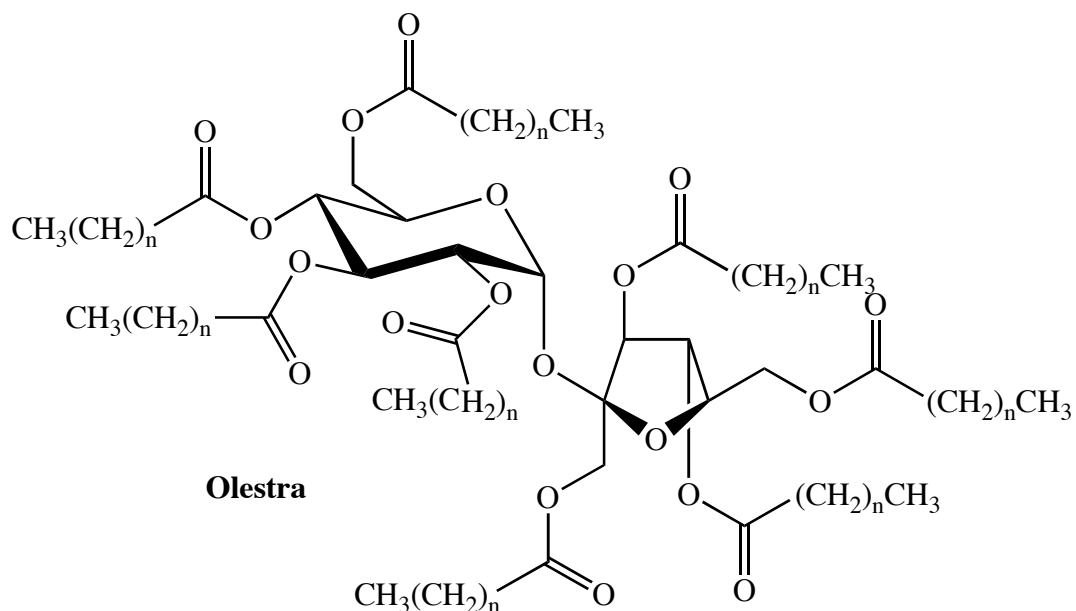
Problems w/ artificial sweeteners:

- Digestive issues
- They alter the brain's taste and response signaling, with potential long-term health implications.

Olestra

- **Olestra** is made by esterifying all the OH groups of sucrose with fatty acids obtained from cottonseed and soybean oil. The ester linkages of **Olestra** are too hindered to be hydrolyzed by dietary enzymes, and thus it is not digested.

Amygdalin

mild hydrolysis
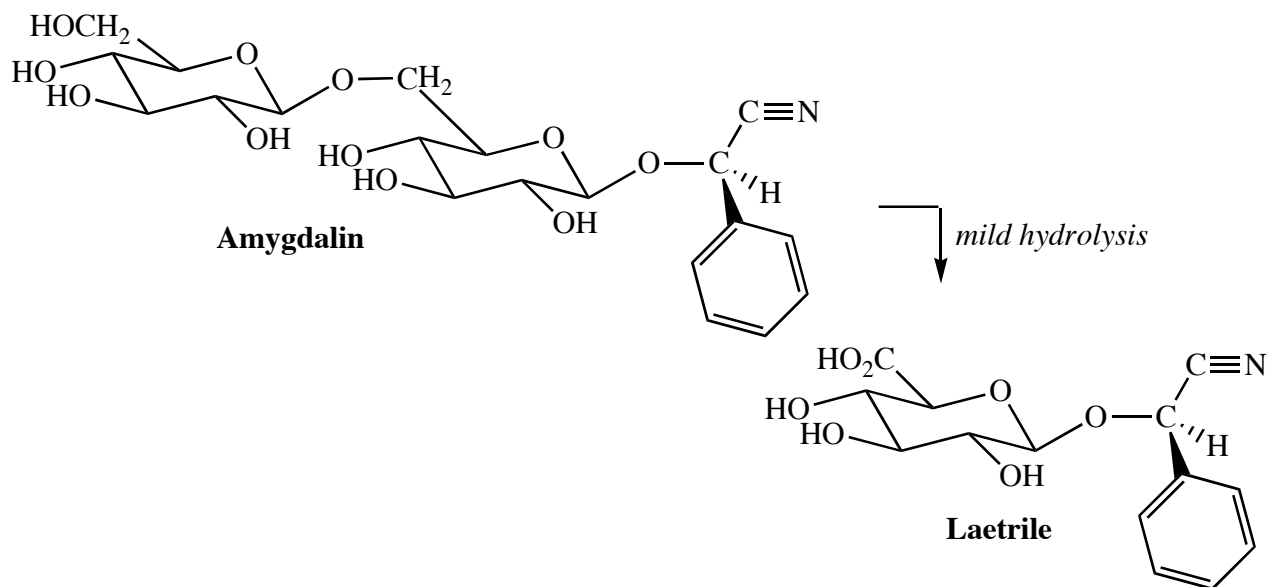
Laetrile

- **Amygdalin** is a disaccharide derivative found in the seeds of foods such as cherries, peaches, and apricots. When Amygdalin is carefully hydrolyzed at low temperature, and the product is oxidized, **Laetrile** is formed.
- **Laetrile** was a popular alternative cancer treatment in the 1970's and has since been proven ineffective. It is an example of a cyanogenic glycoside, compounds that are potentially toxic because they liberate hydrogen cyanide on enzymatic or acid-catalyzed hydrolysis.

172

XV. Amino Sugars

Amino sugars contain an –NH$_2$ group instead of an –OH group at a non-anomeric carbon. The most common amino sugar in nature is D-glucosamine:
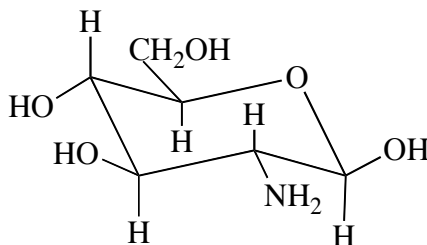

- D-glucosamine is derived from D-glucose by replacing the OH at C-2 with NH$_2$.
- D-glucosamine is widely used in combination with chondroitin to treat osteoarthritis. It is thought to promote the repair of deteriorating cartilage.

XVI. N-Glycosides

N-glycosides are formed when a monosaccharide is reacted with an amine in the presence of mild acid.
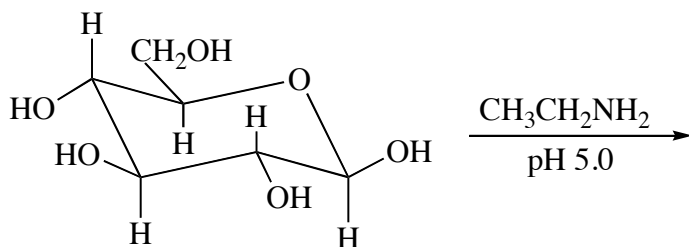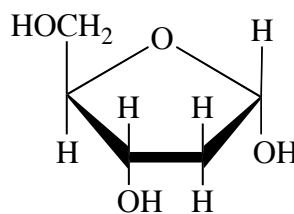

The N-glycosides of two sugars, D-ribose and 2-deoxy-D-ribose, are particularly noteworthy:
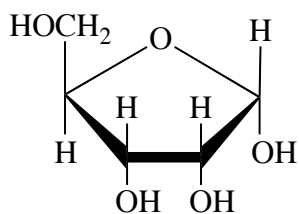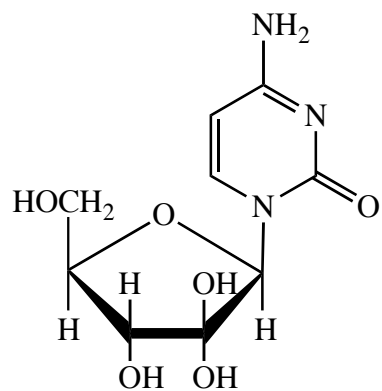

D-ribose

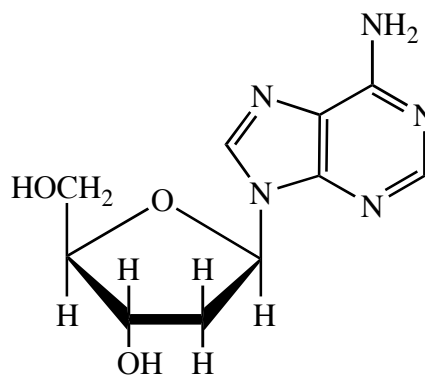*reacts with purine or pyrimidine*
base to form a ribonucleoside

2-deoxy-D-ribose

reacts with purine or pyrimidine
base to form a deoxyribonucleoside.

Two N-glycosides of D-ribose and 2-deoxy-D-ribose:

a ribonucleoside

a deoxyribonucleoside