

25.17  
Carbohydrate Structure  
Determination

# *Carbohydrate Structure Determination*

Spectroscopy

X-Ray Crystallography

Chemical Tests

once used extensively; now superceded by spectroscopic methods and x-ray crystallography

reactions of carbohydrates can involve either open-chain form, furanose, or pyranose form

25.18  
Reduction of Carbohydrates

## *Reduction of Carbohydrates*

Carbonyl group of open-chain form is reduced to an alcohol.

Product is called an alditol.

Alditol lacks a carbonyl group so cannot cyclize to a hemiacetal.

## Reduction of D-Galactose

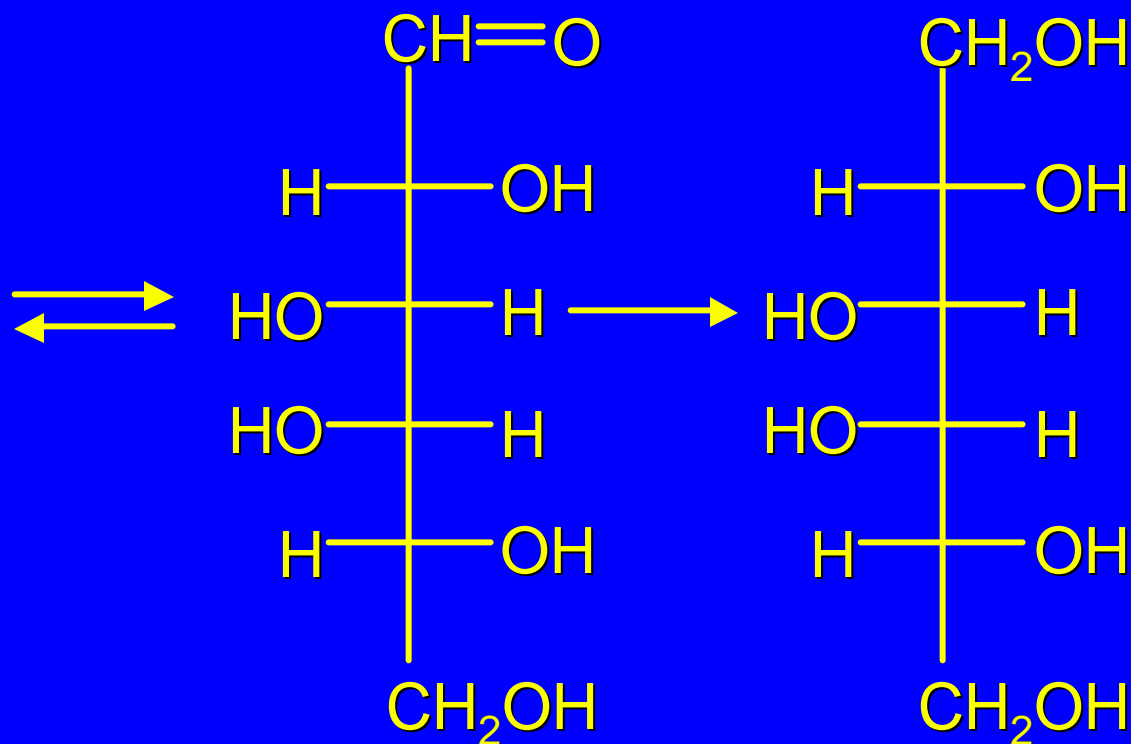
reducing agent:  $\text{NaBH}_4$ ,  $\text{H}_2\text{O}$   
(catalytic hydrogenation can also be used)

$\alpha$ -D-galactofuranose

$\beta$ -D-galactofuranose

$\alpha$ -D-galactopyranose

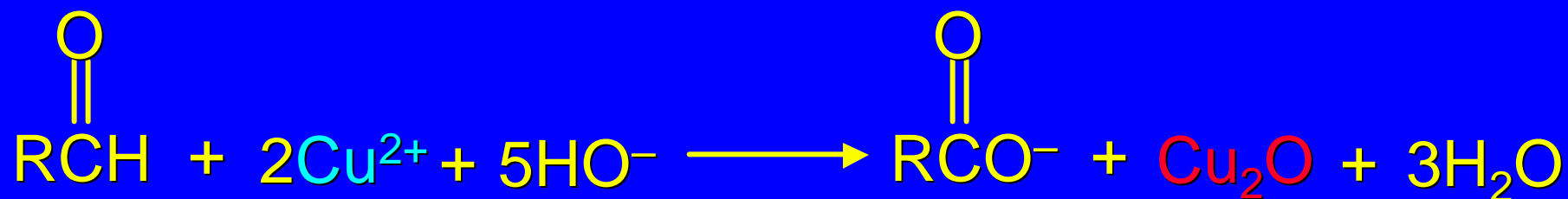
$\beta$ -D-galactopyranose



D-Galactitol (90%)

25.19  
Oxidation of Carbohydrates

## *Benedict's Reagent*



Benedict's reagent is a solution of the citrate complex of  $\text{CuSO}_4$  in water. It is used as a test for "reducing sugars."  $\text{Cu}^{2+}$  is a weak oxidizing agent.

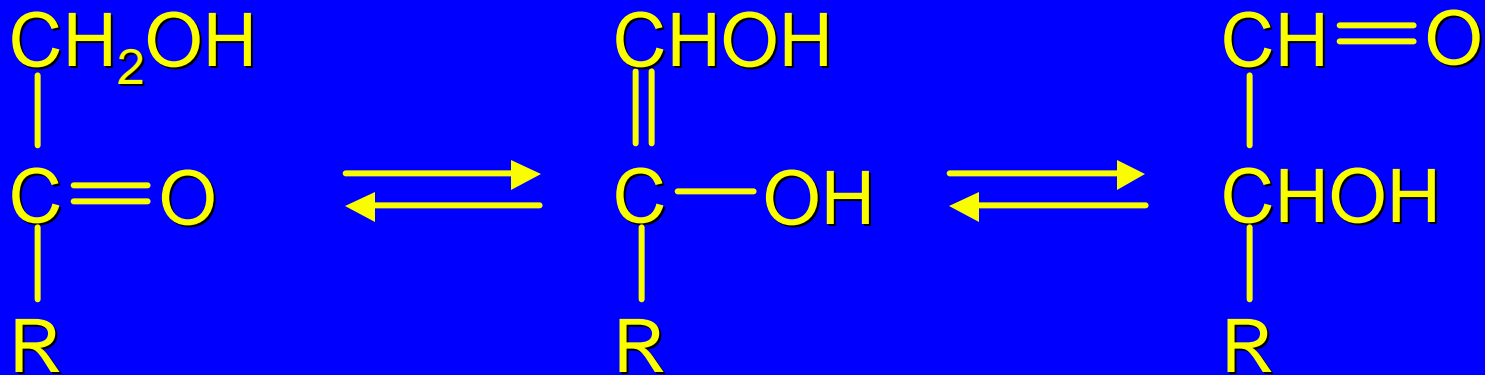
A reducing sugar is one which has an aldehyde function, or is in equilibrium with one that does.

A positive test is the formation of a red precipitate of  $\text{Cu}_2\text{O}$ .

## Examples of Reducing Sugars

Aldoses: because they have an aldehyde function in their open-chain form.

Ketoses: because enolization establishes an equilibrium with an aldose.

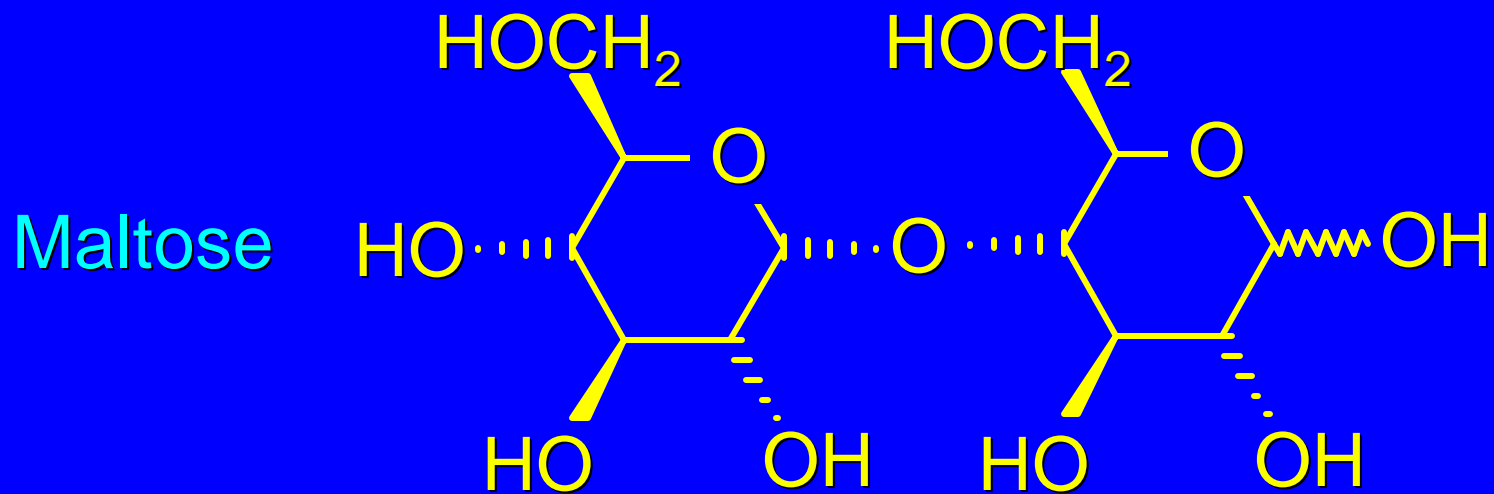


oxidized by  $\text{Cu}^{2+}$



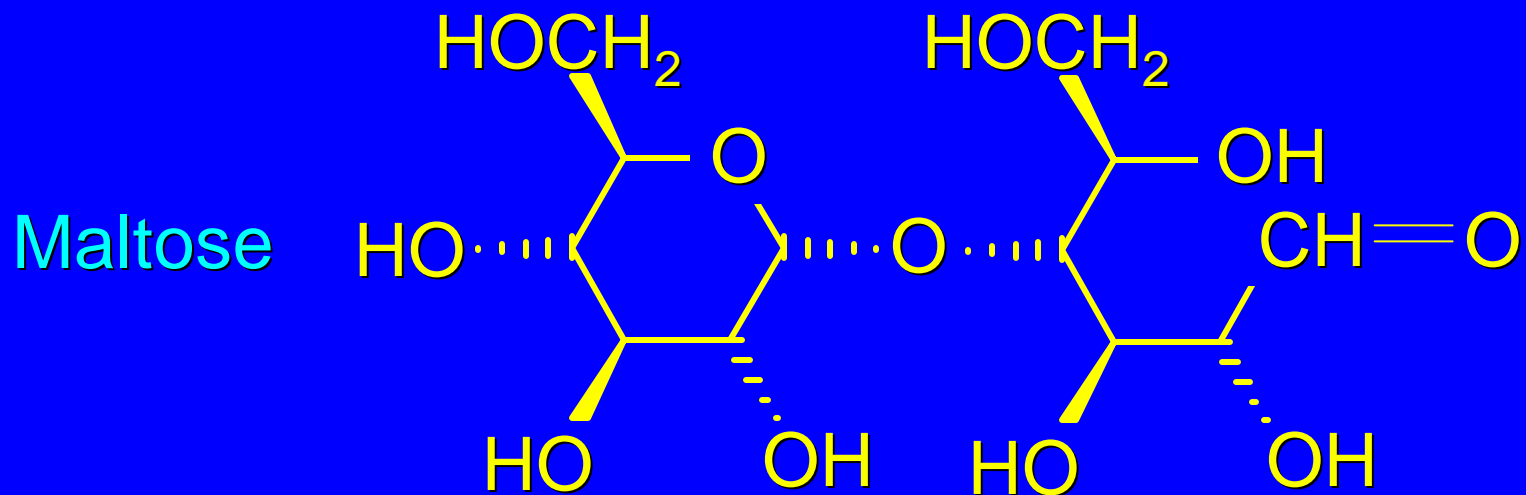
## *Examples of Reducing Sugars*

Disaccharides that have a free hemiacetal function.



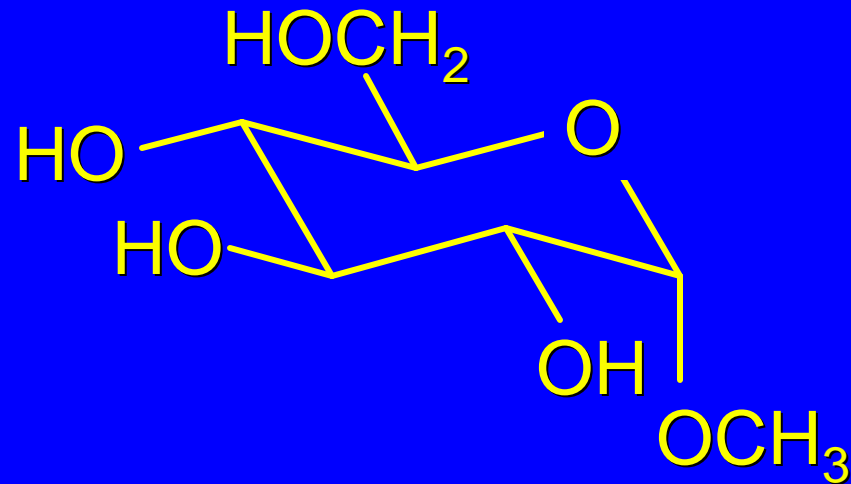
## Examples of Reducing Sugars

Disaccharides that have a free hemiacetal function.



oxidized by  $\text{Cu}^{2+}$

*Glycosides are not reducing sugars*



Methyl  $\alpha$ -D-glucopyranoside lacks a free hemiacetal function; cannot be in equilibrium with a species having an aldehyde function

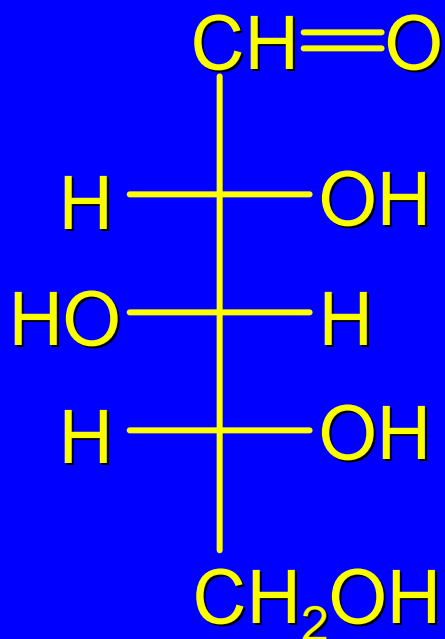
## *Oxidation of Reducing Sugars*

The compounds formed on oxidation of reducing sugars are called aldonic acids.

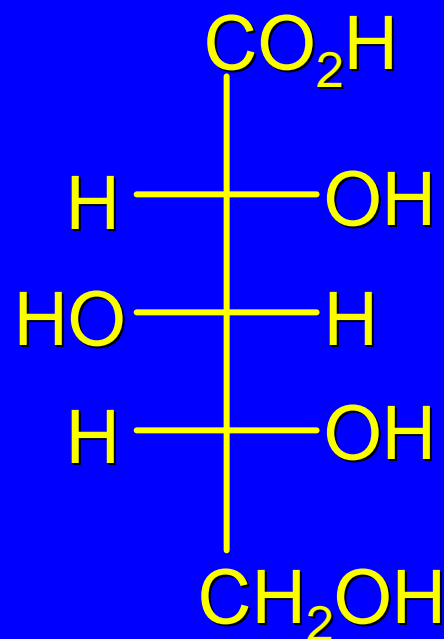
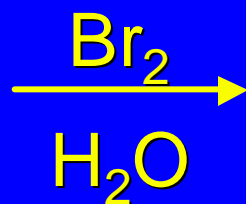
Aldonic acids exist as lactones when 5- or 6-membered rings can form.

A standard method for preparing aldonic acids uses  $\text{Br}_2$  as the oxidizing agent.

## Oxidation of D-Xylose

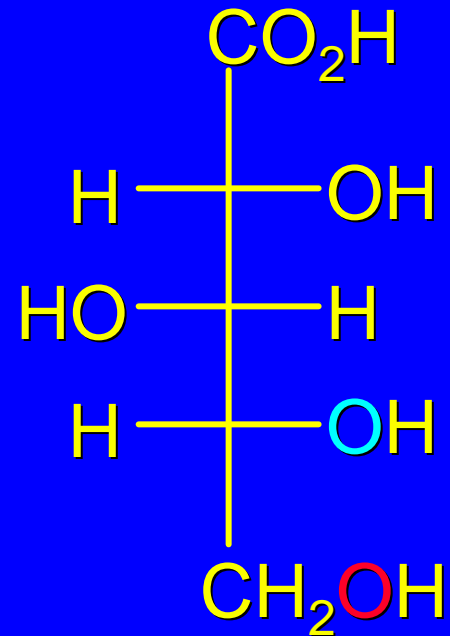
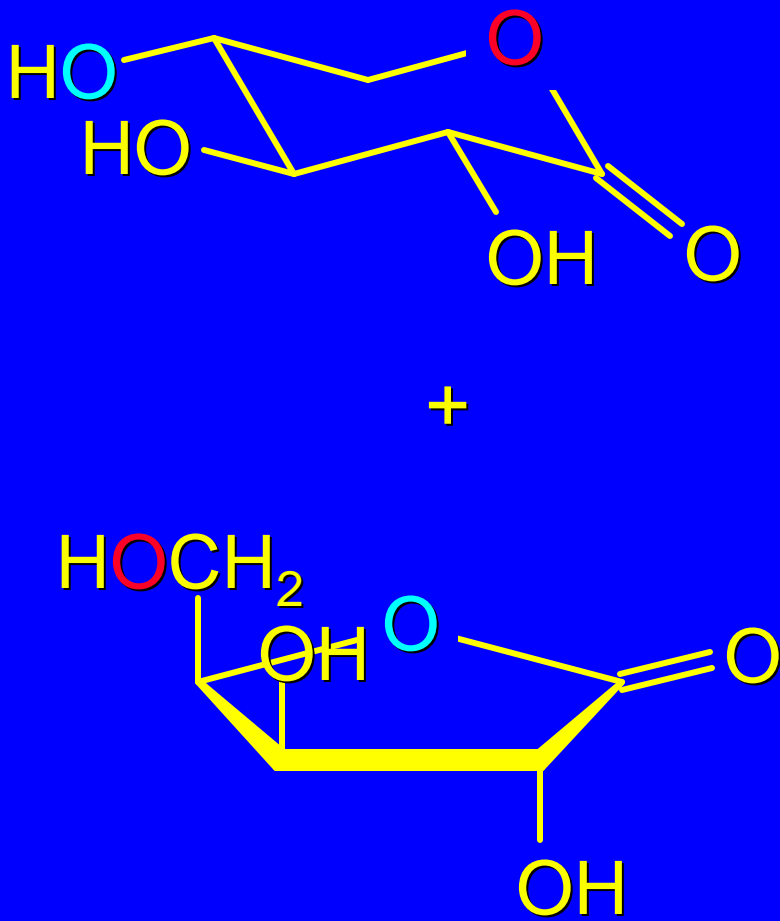


D-Xylose



D-Xylonic acid (90%)

## Oxidation of D-Xylose



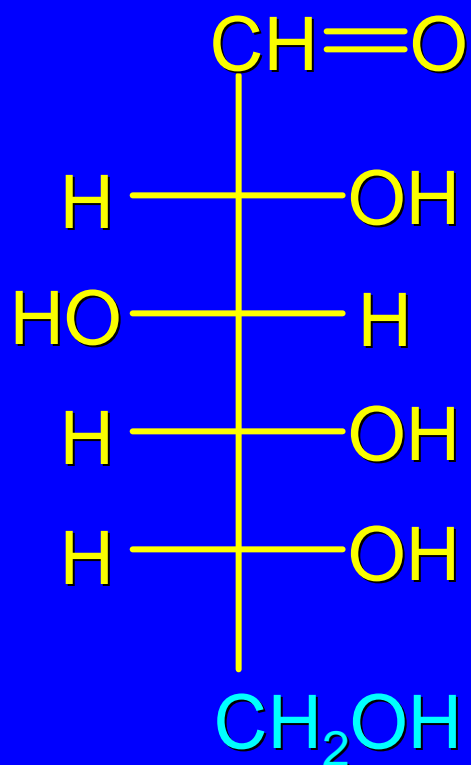
D-Xylonic acid (90%)

## *Nitric Acid Oxidation*

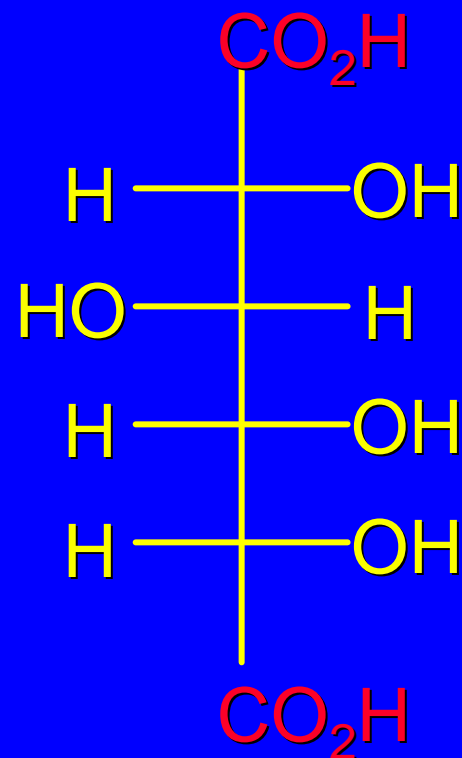
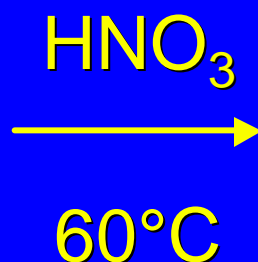
Nitric acid oxidizes both the aldehyde function and the terminal  $\text{CH}_2\text{OH}$  of an aldose to  $\text{CO}_2\text{H}$ .

The products of such oxidations are called aldaric acids.

## Nitric Acid Oxidation



D-Glucose

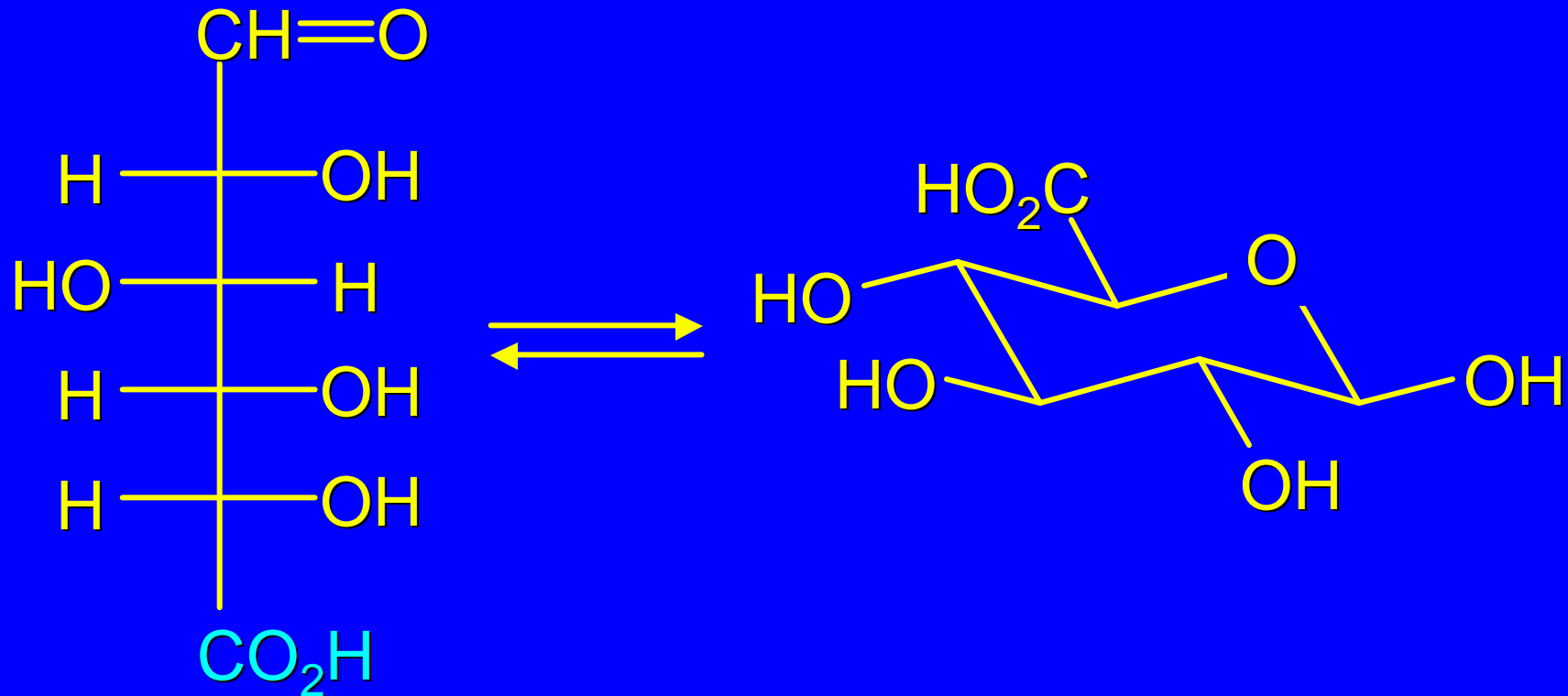


D-Glucaric acid (41%)



## *Uronic Acids*

Uronic acids contain both an aldehyde and a terminal  $\text{CO}_2\text{H}$  function.



D-Glucuronic acid

25.20

Cyanohydrin Formation and  
Carbohydrate Chain Extension

## *Extending the Carbohydrate Chain*

Carbohydrate chains can be extended by using cyanohydrin formation as the key step in C—C bond-making.

The classical version of this method is called the Kiliani-Fischer synthesis. The following example is a more modern modification.

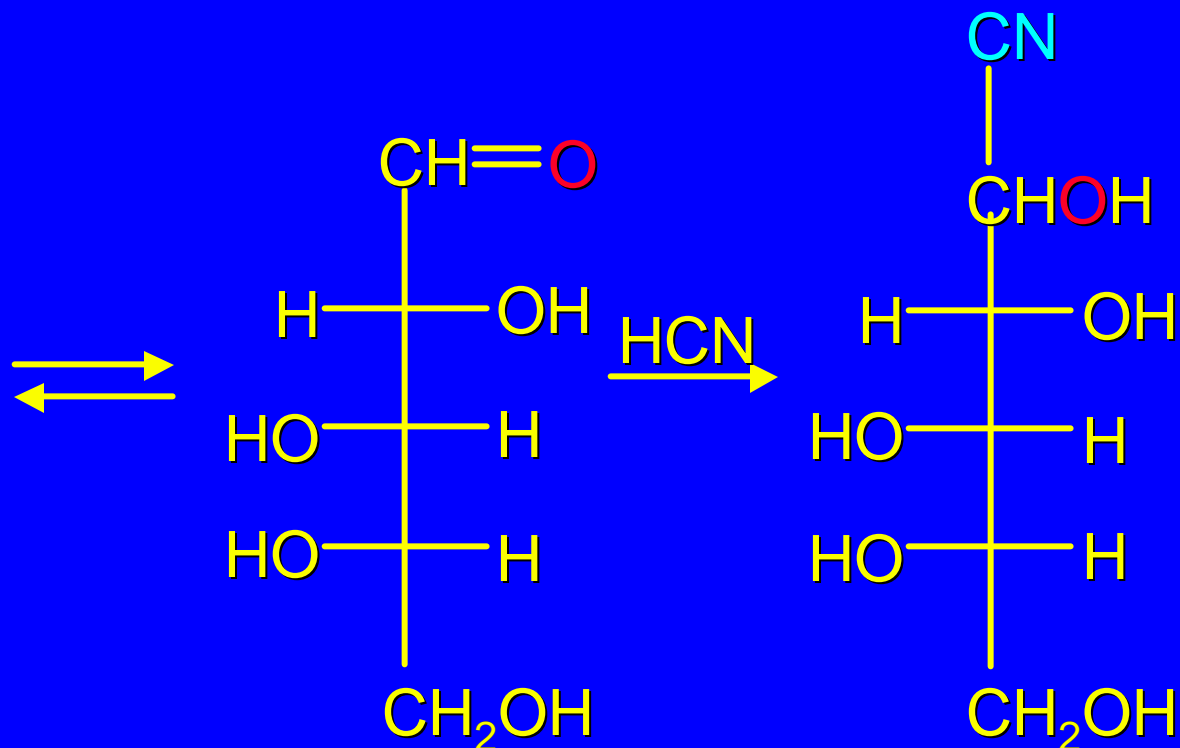
## Extending the Carbohydrate Chain

$\alpha$ -L-arabinofuranose

$\beta$ -L-arabinofuranose

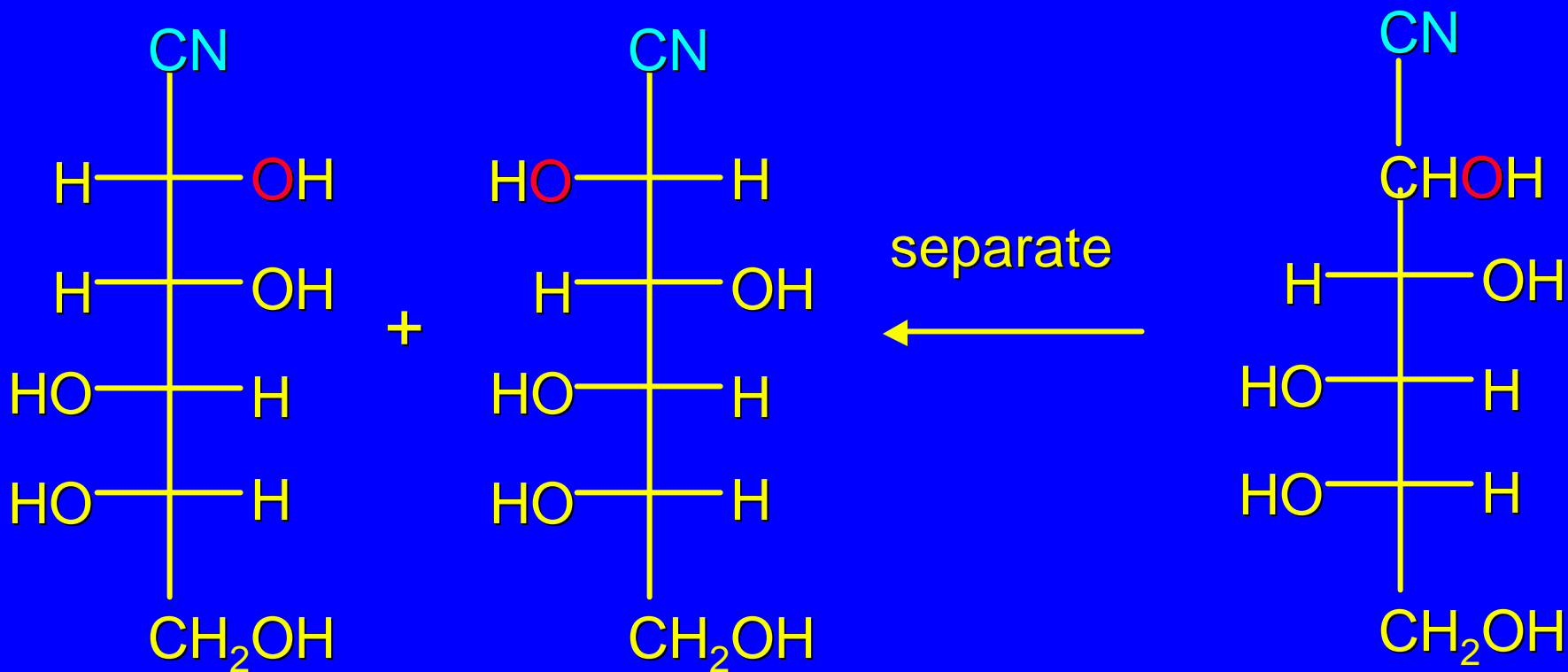
$\alpha$ -L-arabinopyranose

$\beta$ -L-arabinopyranose



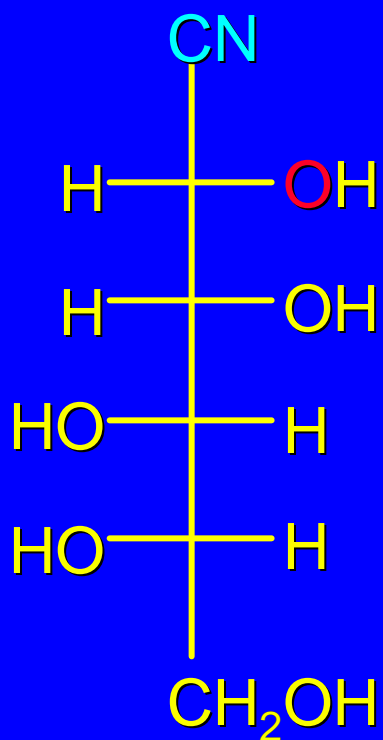
the resulting cyanohydrin is a mixture of two stereoisomers that differ in configuration at C-2; these two diastereomers are separated in the next step

## Extending the Carbohydrate Chain

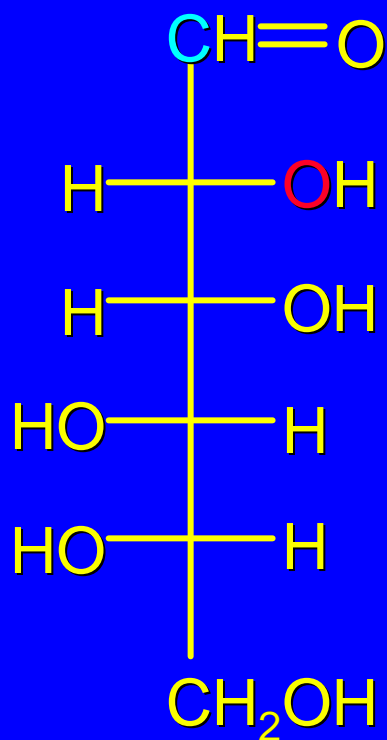
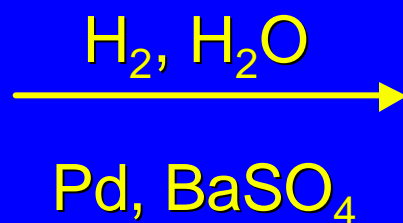


L-Mannonitrile    L-Glucononitrile

## Extending the Carbohydrate Chain

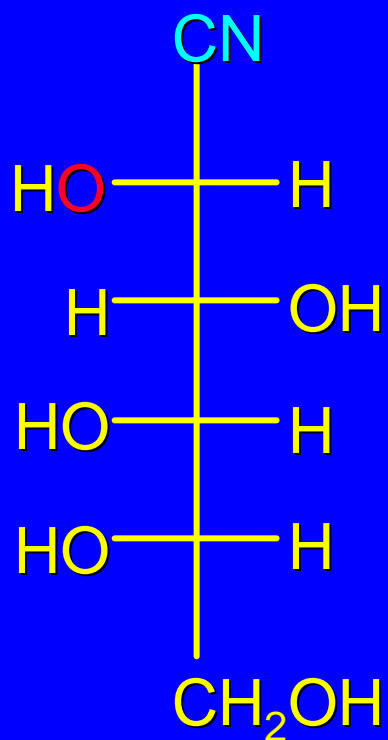


L-Mannonitrile

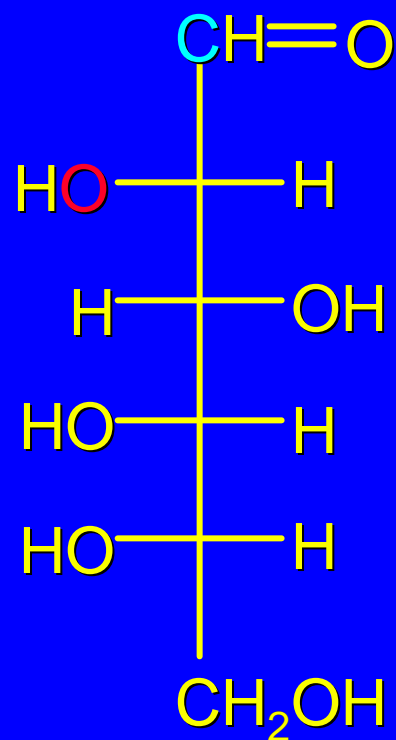
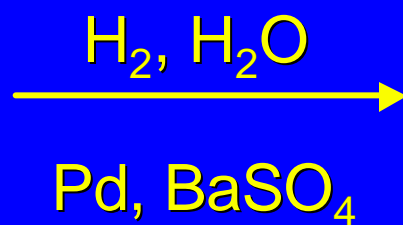


L-Mannose  
(56% from L-arabinose)

*Likewise...*



L-Glucononitrile



L-Glucose  
(26% from L-arabinose)

25.21

Epimerization, Isomerization, and  
Retro-Aldol Reactions of  
Carbohydrates



## *Enol Forms of Carbohydrates*

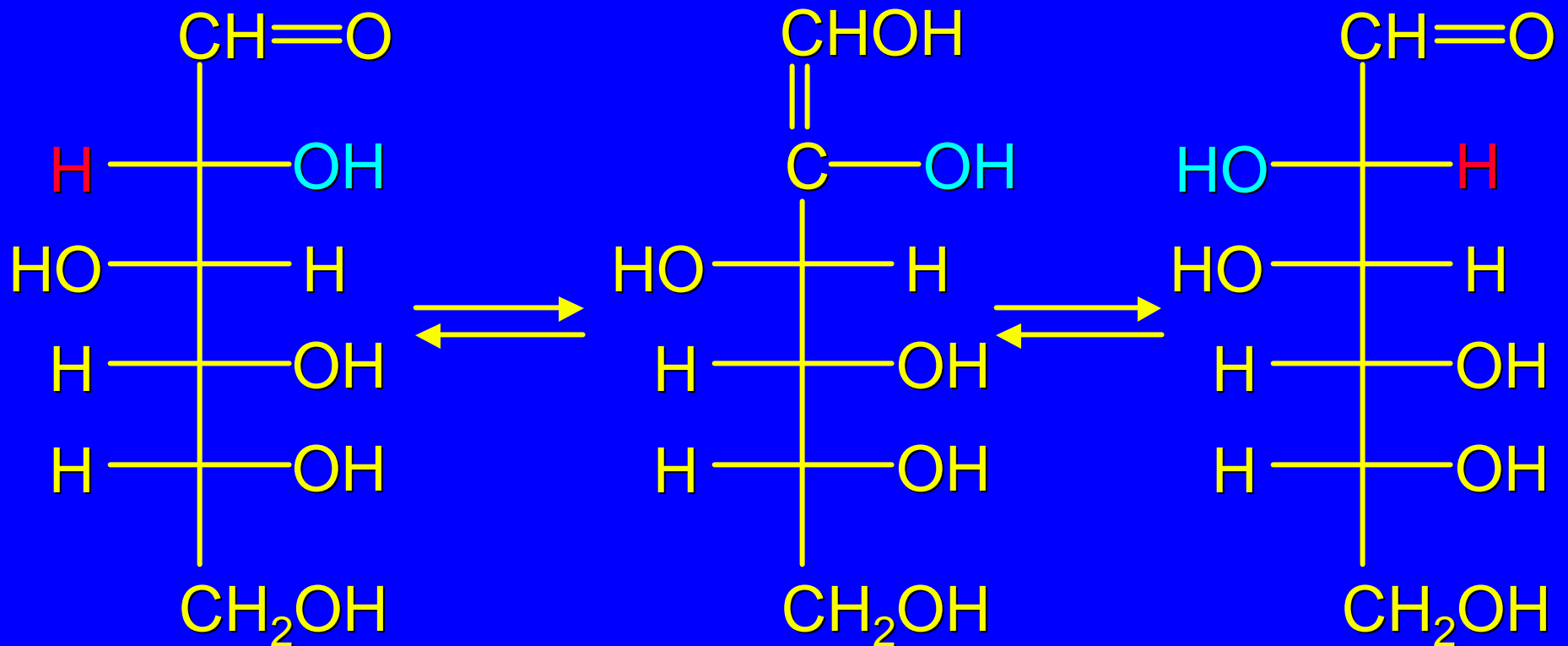
Enolization of an aldose scrambles the stereochemistry at C-2.

This process is called *epimerization*.

Diastereomers that differ in stereochemistry at only one of their stereogenic centers are called epimers.

D-Glucose and D-mannose, for example, are epimers.

## Epimerization



D-Glucose

Enediol

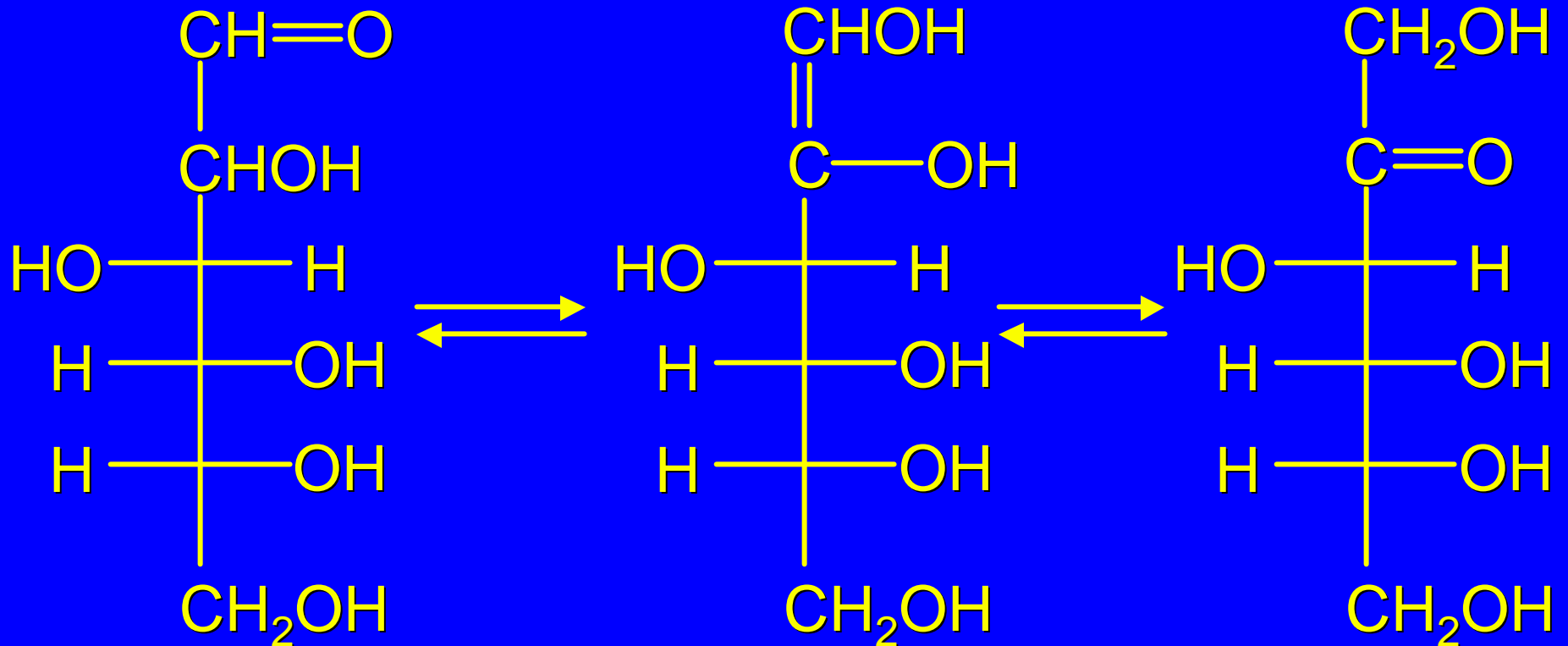
D-Mannose

This equilibration can be catalyzed by hydroxide ion.

## *Enol Forms of Carbohydrates*

The enediol intermediate on the preceding slide can undergo a second reaction. It can lead to the conversion of D-glucose or D-mannose (aldoses) to D-fructose (ketose).

# Isomerization



D-Glucose or  
D-Mannose

Enediol

D-Fructose

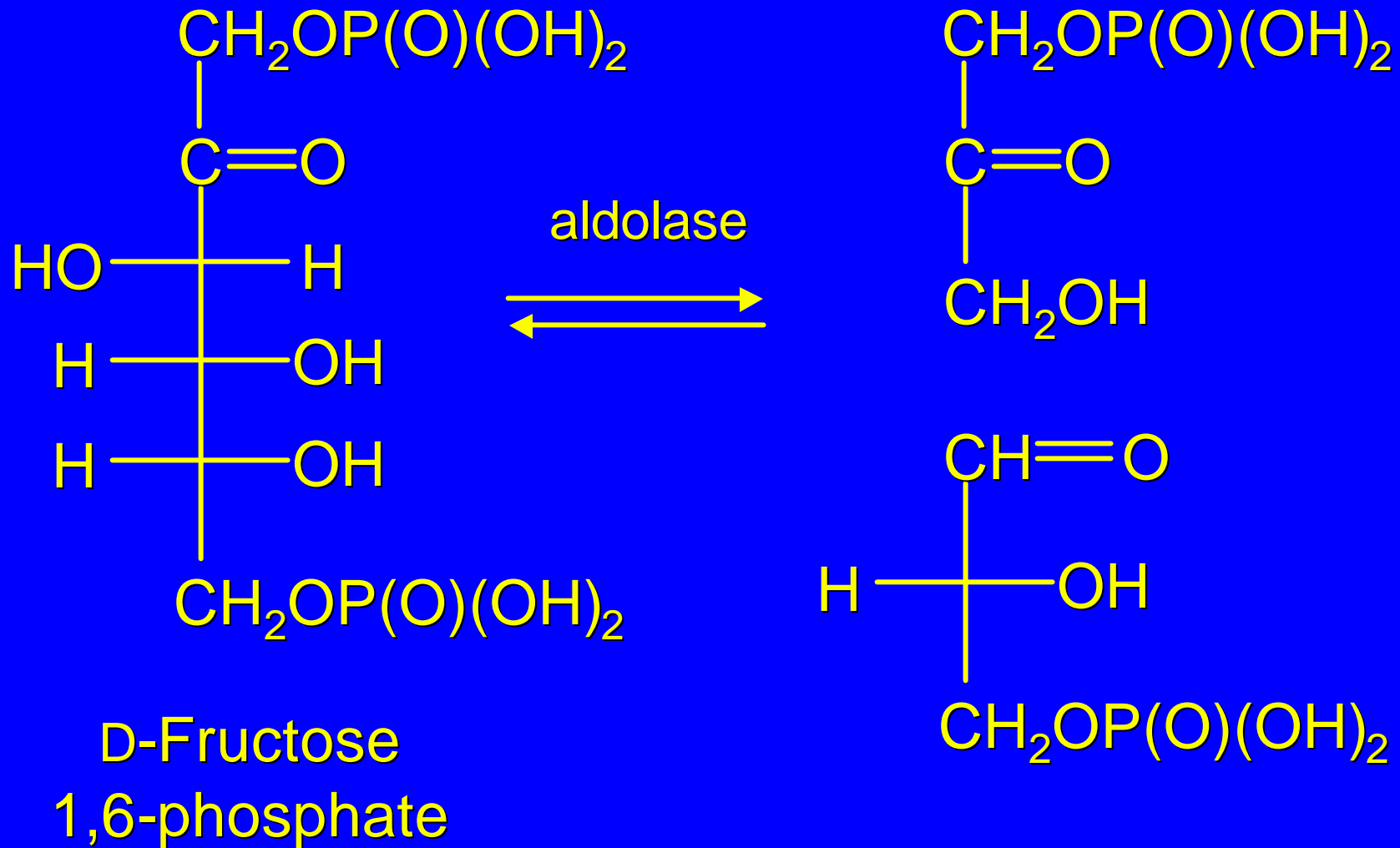
## *Retro-Aldol Cleavage*

The D-fructose 6-phosphate formed according to the preceding slide undergoes phosphorylation of its free  $\text{CH}_2\text{OH}$  group to give D-fructose 1,6-diphosphate.

D-Fructose 1,6-diphosphate is cleaved to two 3-carbon products by a reverse aldol reaction.

This *retro-aldol* cleavage is catalyzed by the enzyme *aldolase*.

# Isomerization



25.22

Acylation and Alkylation of  
Hydroxyl Groups in Carbohydrates

## *Reactivity of Hydroxyl Groups in Carbohydrates*

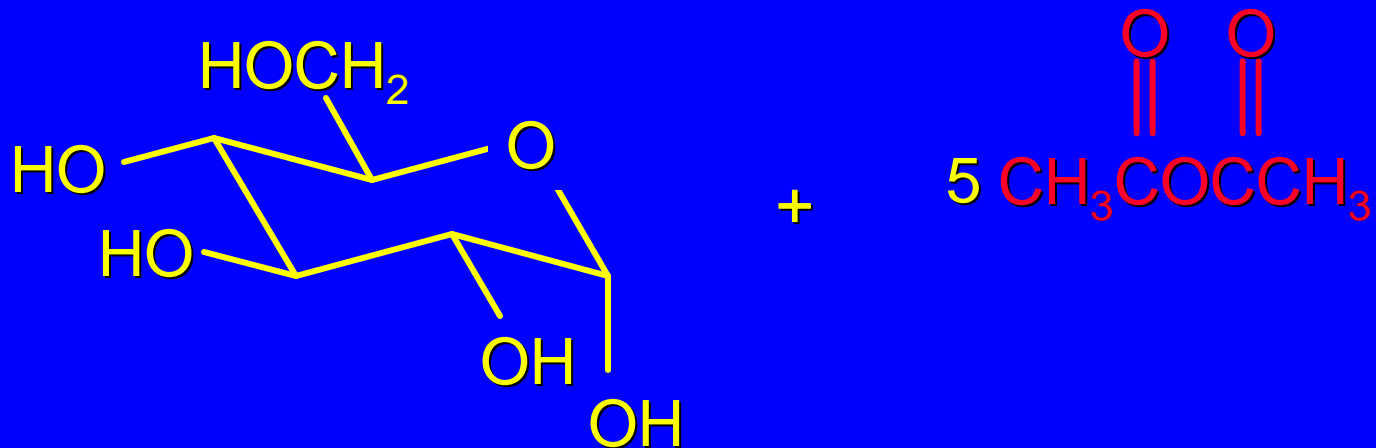
Hydroxyl groups in carbohydrates undergo reactions typical of alcohols.

acylation

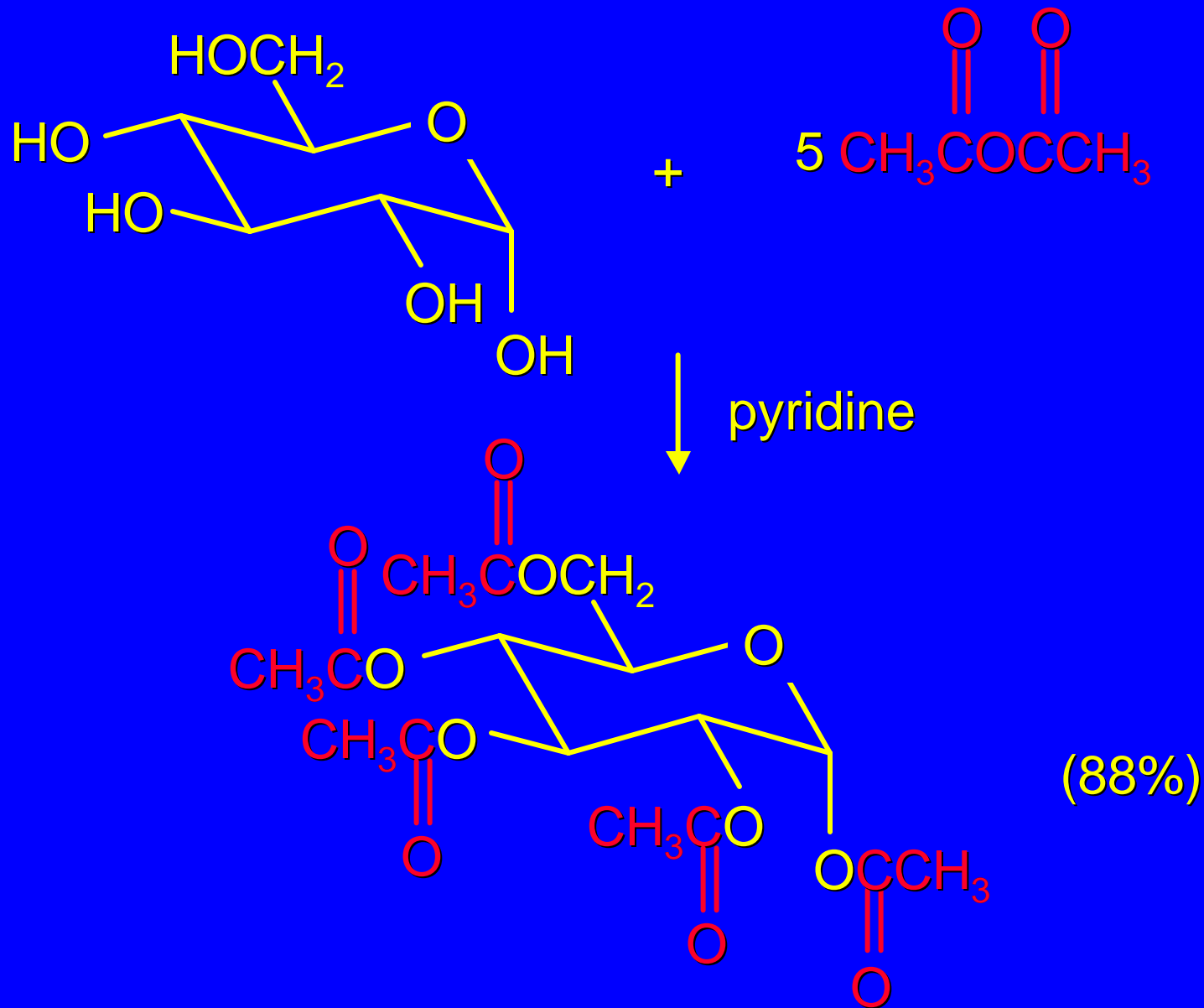
alkylation



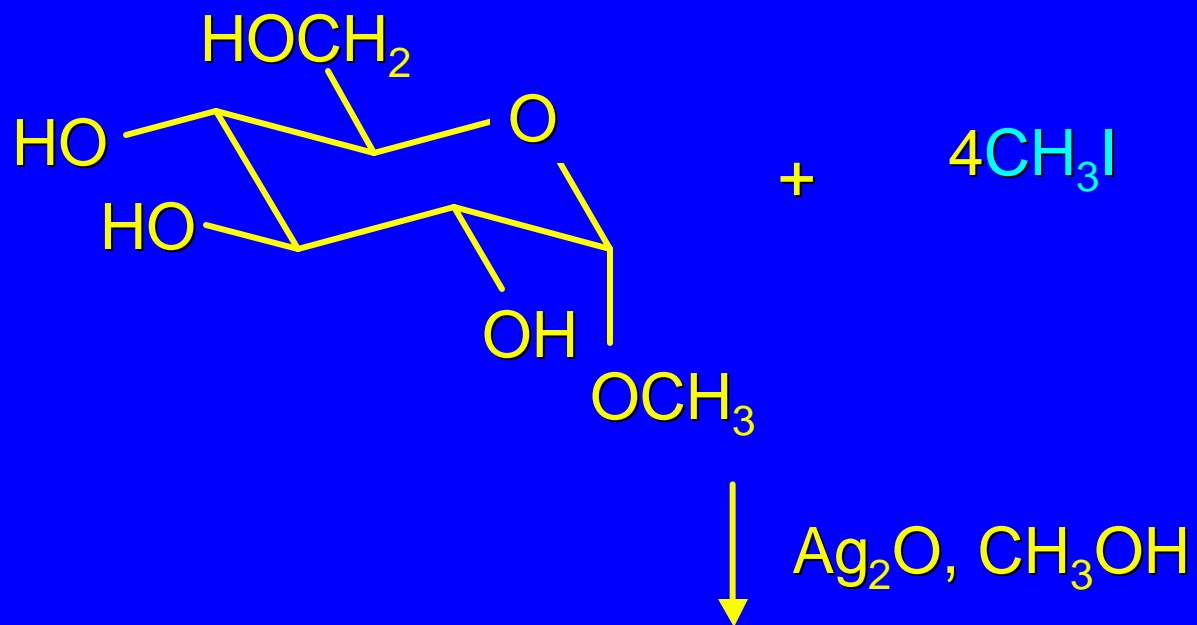
*Example: Acylation of  $\alpha$ -D-glucopyranose*



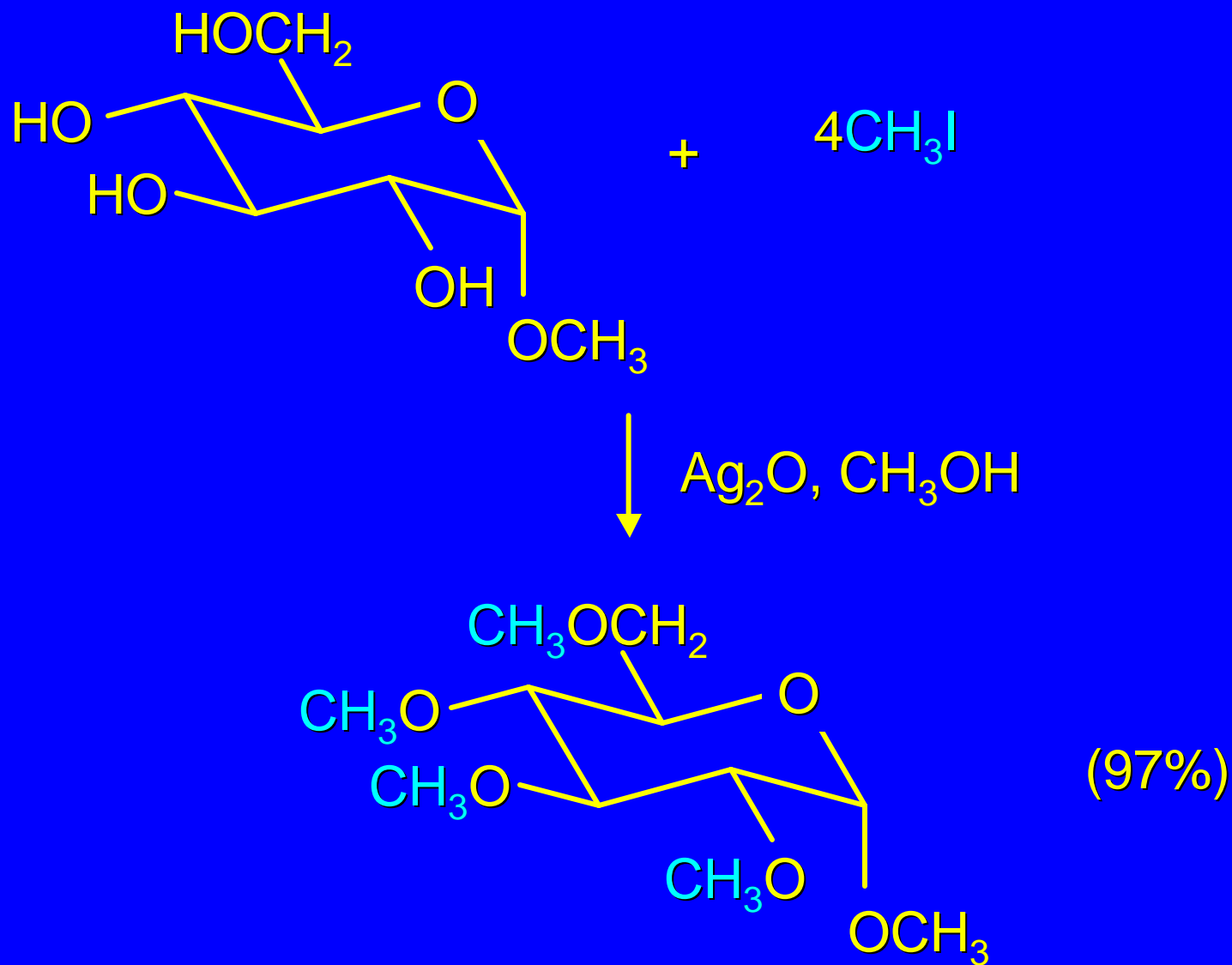
## Example: *Acylation of $\alpha$ -D-glucopyranose*



*Example: Alkylation of methyl  $\alpha$ -D-glucopyranoside*

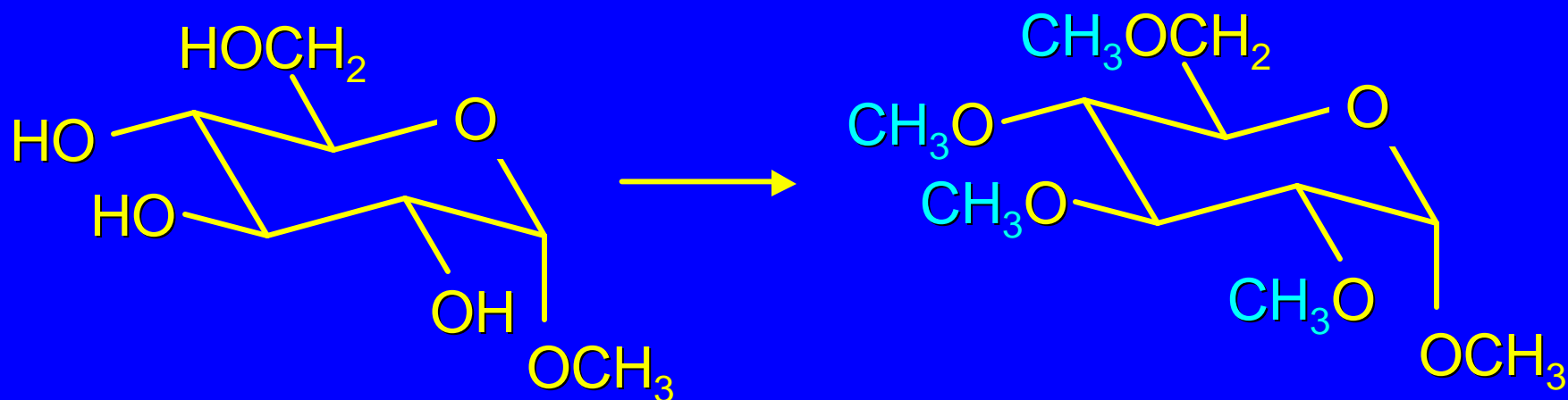


*Example: Alkylation of methyl  $\alpha$ -D-glucopyranoside*



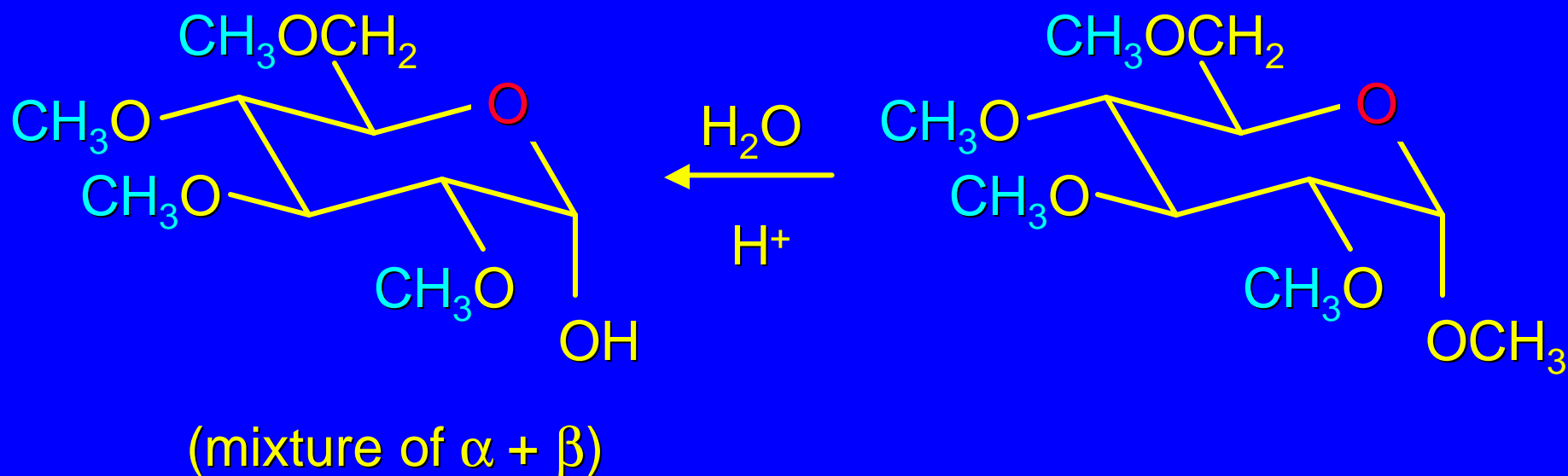
## *Classical Method for Ring Size*

Ring sizes (furanose or pyranose) have been determined using alkylation as a key step.



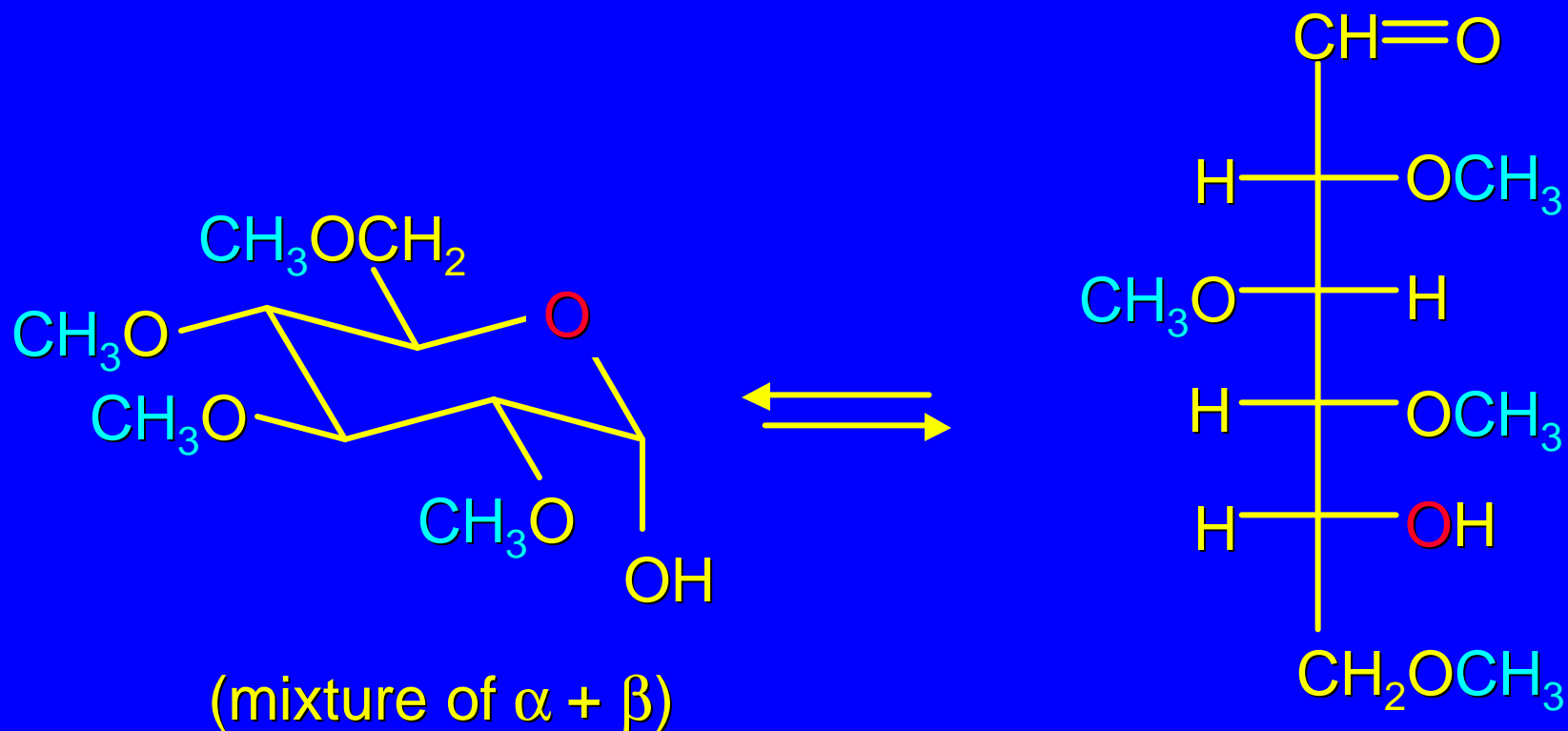
## Classical Method for Ring Size

Ring sizes (furanose or pyranose) have been determined using alkylation as a key step.



## Classical Method for Ring Size

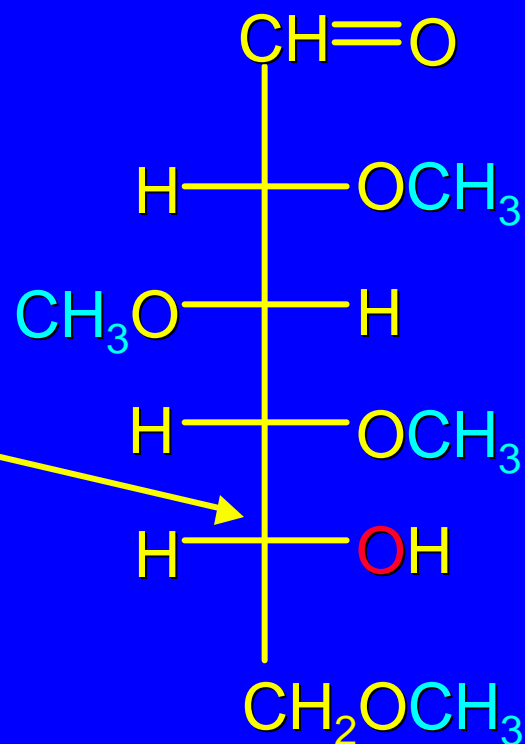
Ring sizes (furanose or pyranose) have been determined using alkylation as a key step.



## Classical Method for Ring Size

Ring sizes (furanose or pyranose) have been determined using alkylation as a key step.

This carbon has OH instead of OCH<sub>3</sub>. Therefore, its O was the oxygen in the ring.

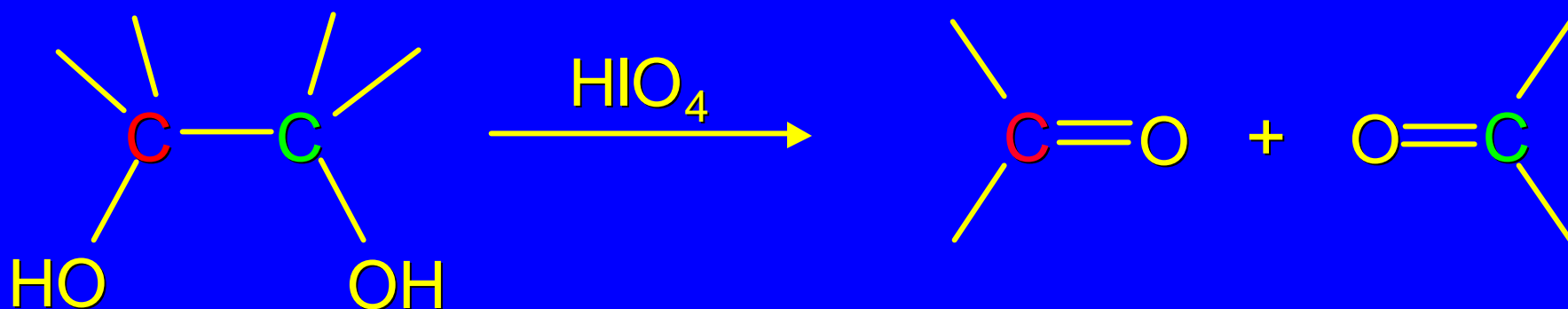




25.23  
Periodic Acid Oxidation of  
Carbohydrates

## *Recall Periodic Acid Oxidation*

Section 15.12: Vicinal diols are cleaved by  $\text{HIO}_4$ .

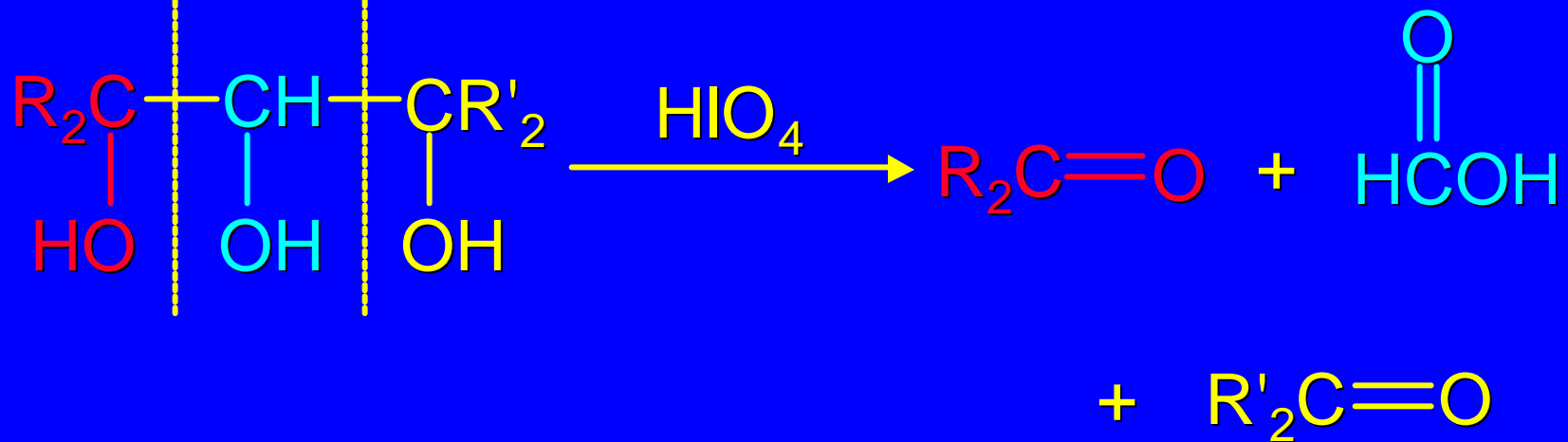


Cleavage of a vicinal diol consumes 1 mol of  $\text{HIO}_4$ .



*Also Cleaved by HIO<sub>4</sub>*

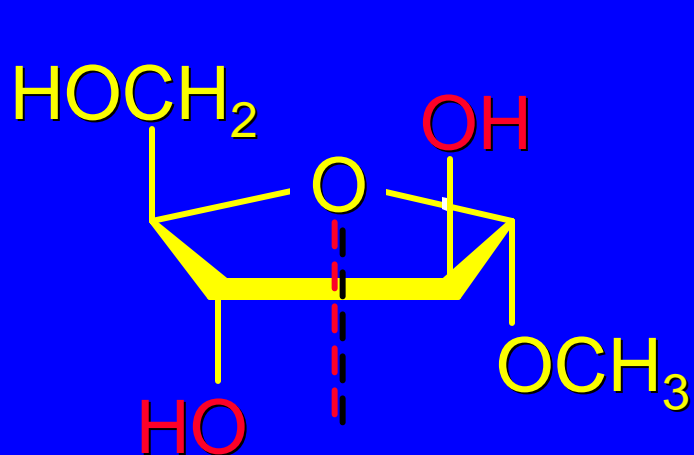
Compounds that contain three contiguous carbons bearing OH groups



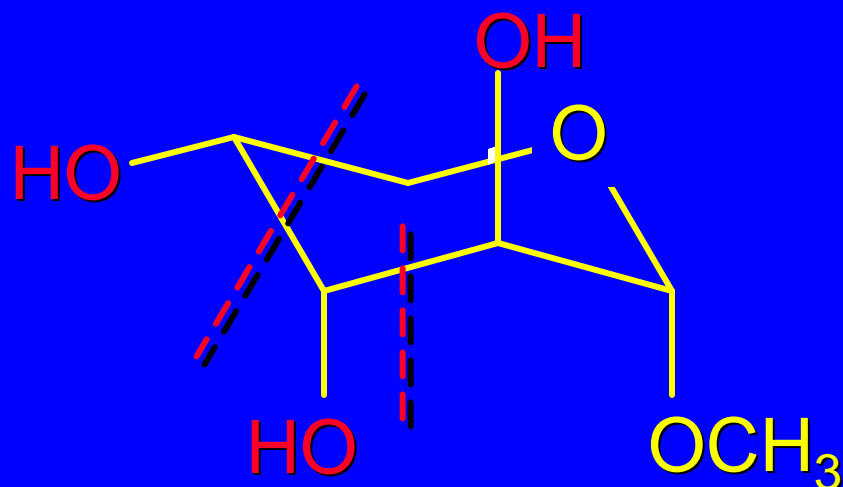
2 mol of HIO<sub>4</sub> are consumed. 1 mole of formic acid is produced.

## Structure Determination Using $\text{HIO}_4$

Distinguish between furanose and pyranose forms of methyl arabinoside



2 vicinal OH groups;  
consumes 1 mol of  $\text{HIO}_4$



3 vicinal OH groups;  
consumes 2 mol of  $\text{HIO}_4$