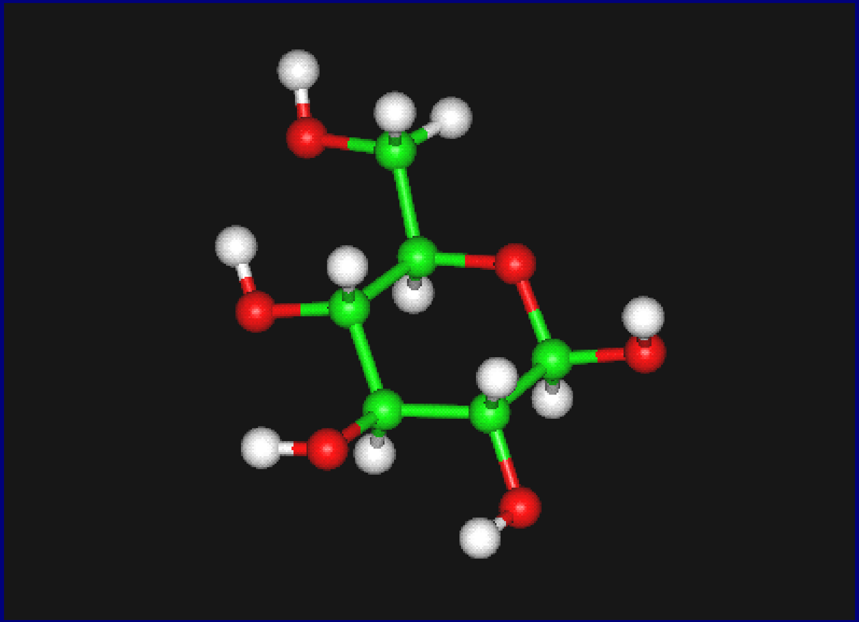
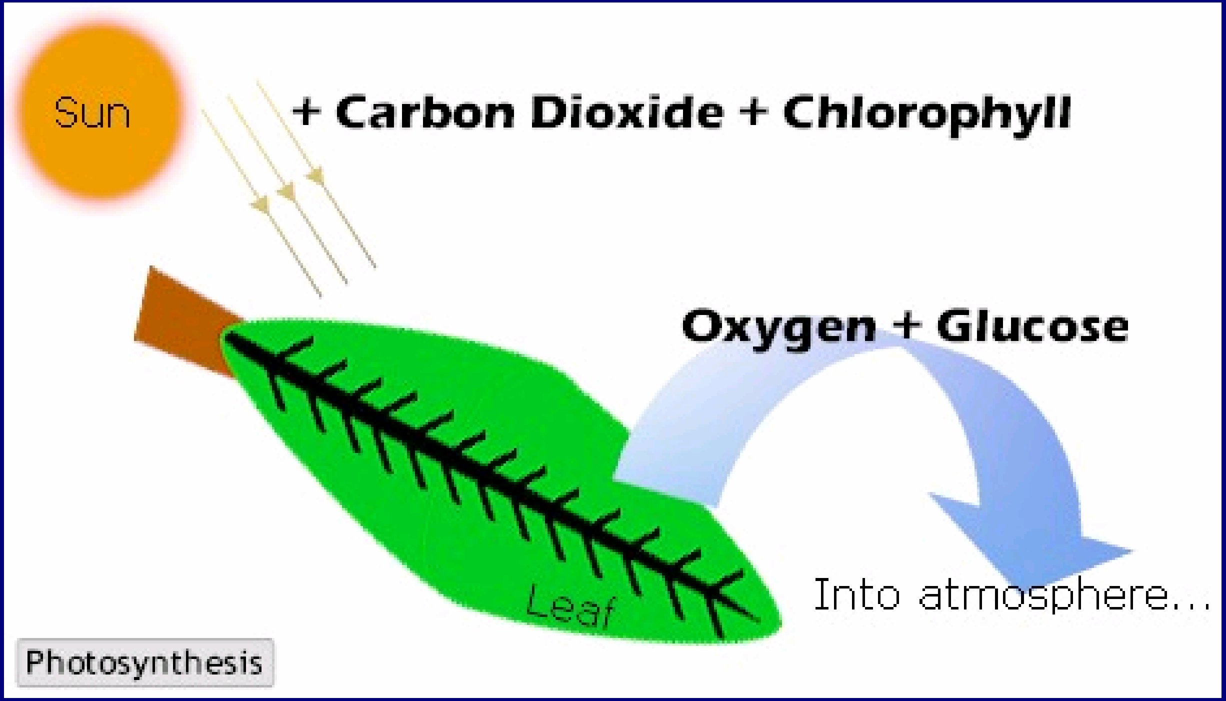
Chapter 24: Carbohydrates



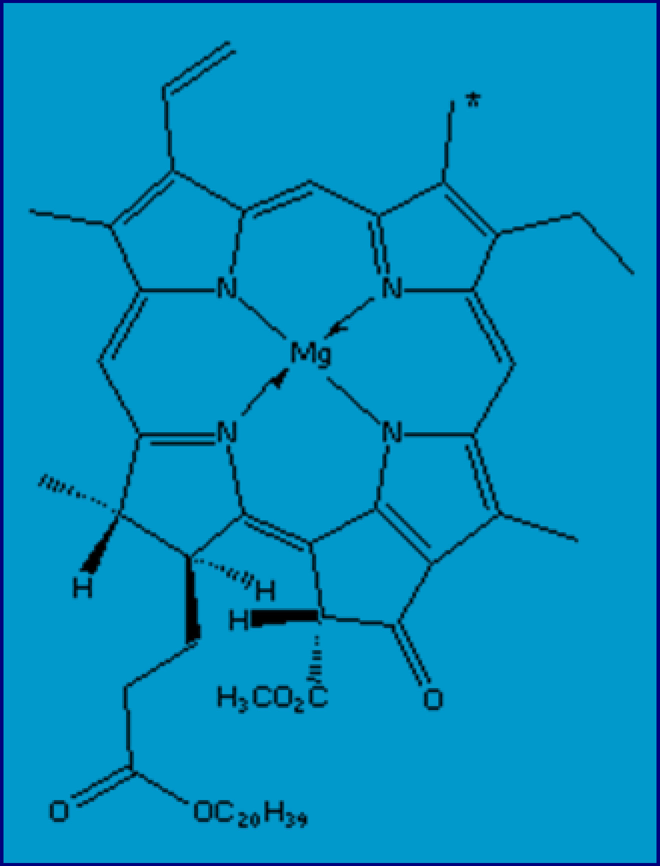
glucose

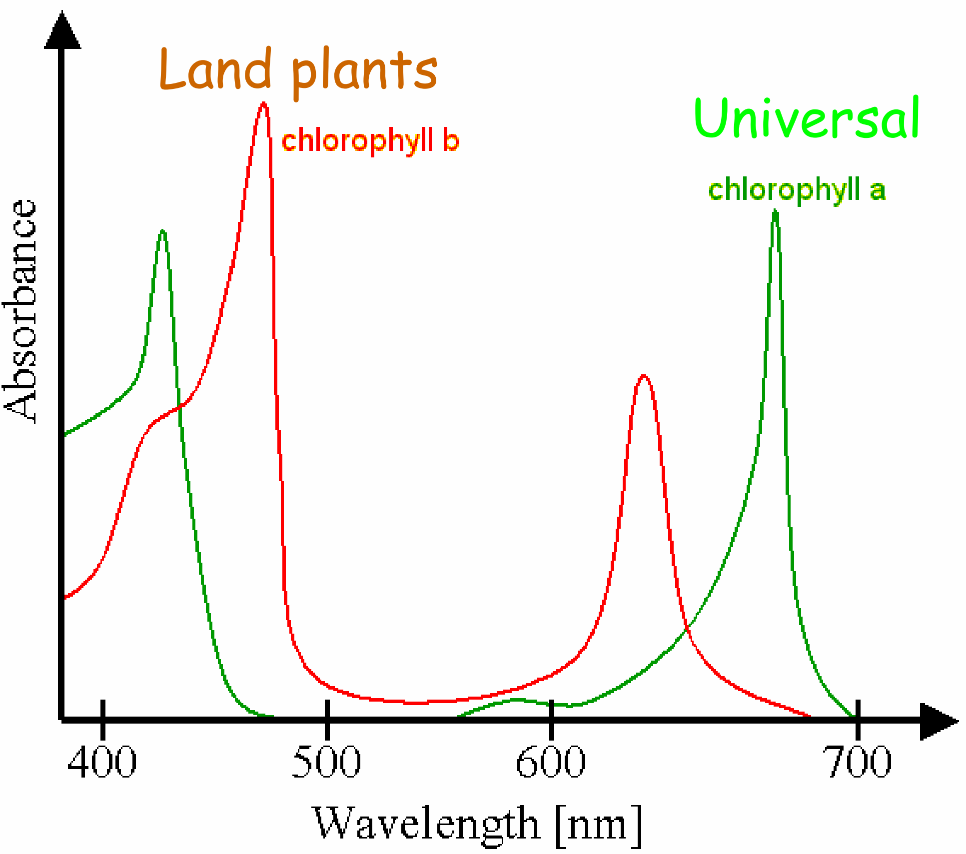
Photosynthesis: Energy storage



$$6\ CO_2 + 6\ H_2O \underset{\text{Metabolism}}{\overset{\text{Sun, chlorophyll}}{\rightleftharpoons}} C_6(H_2O)_6 + 6\ O_2$$

Glucose



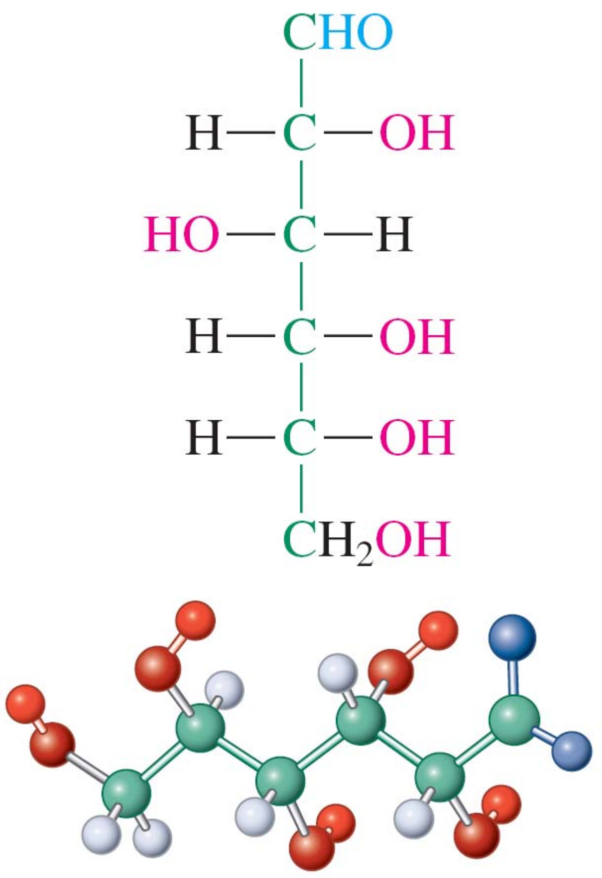


Chlorophyll

3% to 6% of the total incident solar radiation is used for chemical conversion of H_2O (oxidation to O_2) and CO_2 (reduction to glucose).

Carbohydrate = $C_n(H_2O)_n$

Hydrated carbon



Glucose

(An aldohexose)

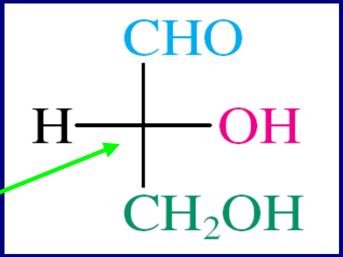
A pentahydroxyaldehyde

Carbohydrates occur in nature in nucleic acids, fats, cellulose, fibers, starch, "table sugar," antibiotics, and other biological molecules.

Naming

The simplest carbohydrates are the sugars or saccharides. They constitute polyhydroxy-aldehydes (aldoses) or -ketones (ketoses); they form oligomers by ether bridges (hence di-, tri-, tetrasaccharide, etc.).

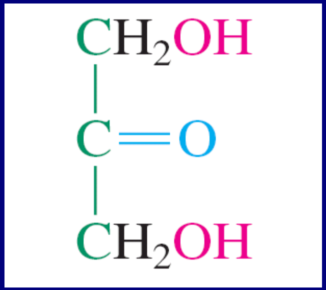
The simplest sugars, both $C_3(H_2O)_3$:



$$\mathrm{H}-\overset{\mathrm{CHO}}{\underset{\mathrm{CH_2OH}}{+}}-\mathrm{OH}$$

Chiral

2,3-Dihydroxypropanal
(Glyceraldehyde)
An aldotriose

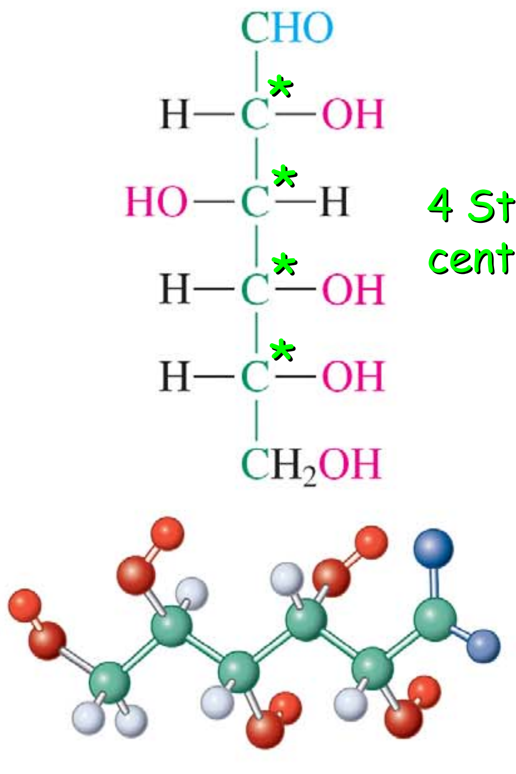


$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{C{=}O} \\ | \\ \mathrm{CH_2OH} \end{array}$$

1,3-Dihydroxyacetone
A ketotriose

Chain length: Triose, tetrose, pentose, etc.

Some important monosaccharides:

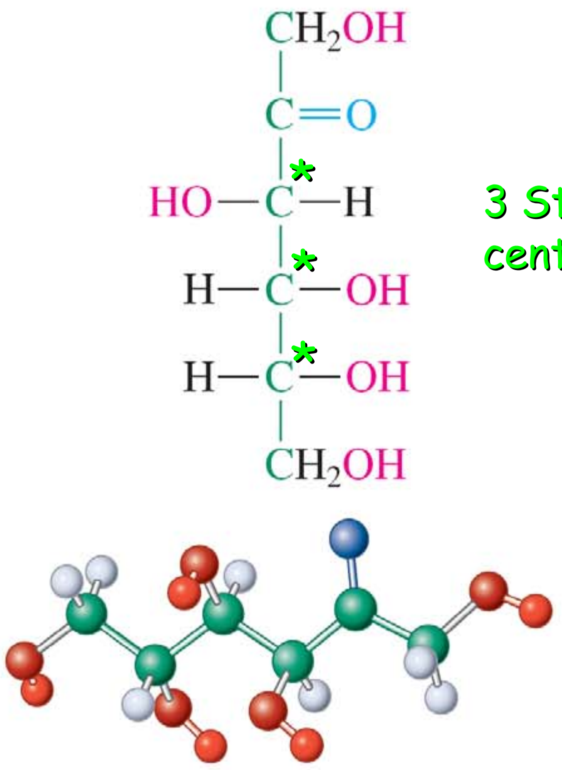


4 Stereo-centers

Glucose

(An aldohexose)

Dextrose, blood sugar, grape sugar

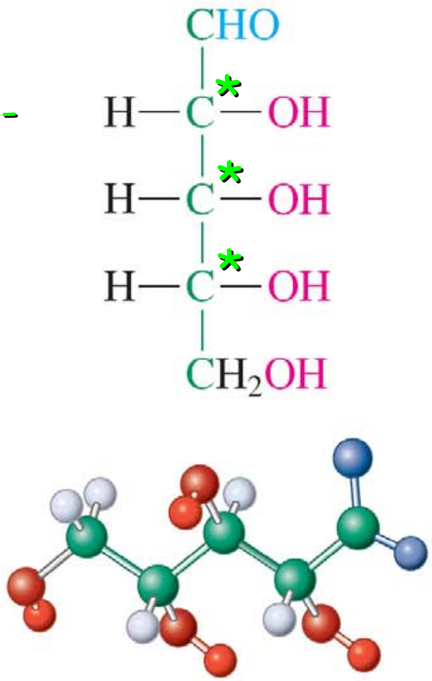


3 Stereo-centers

Fructose

(A ketohexose)

Sweetest natural sugar; fruits



Ribose

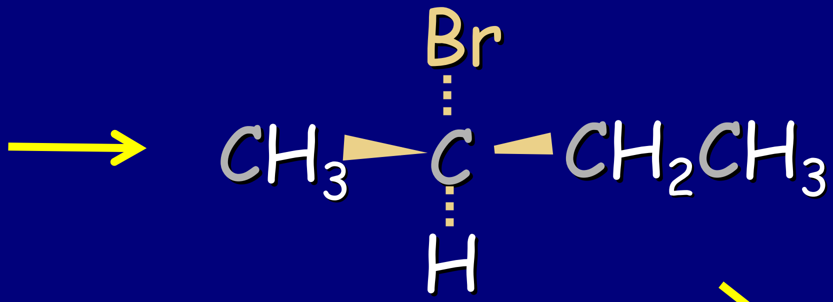
(An aldopentose)

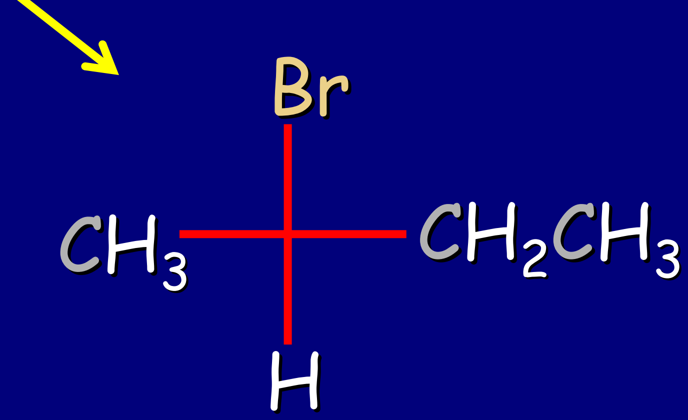
Ribonucleic acids

Fischer projections: Review chapter 5

Fischer Projection: A flat stencil

Eyes in the plane of the board

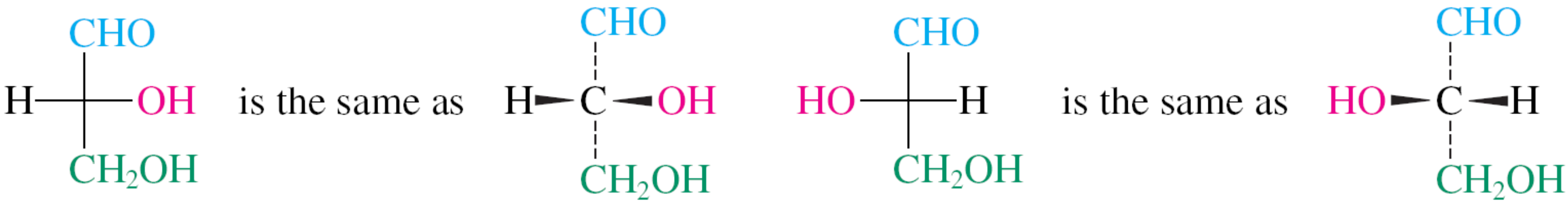




Rules reminder:
180 ° turn or double exchange leaves stereochemistry intact

Depending on your starting dashed-wedged line structure, several Fischer projections are possible for the same molecule.

Most sugars are chiral and occur enantiomerically pure. Simplest case, one stereocenter:



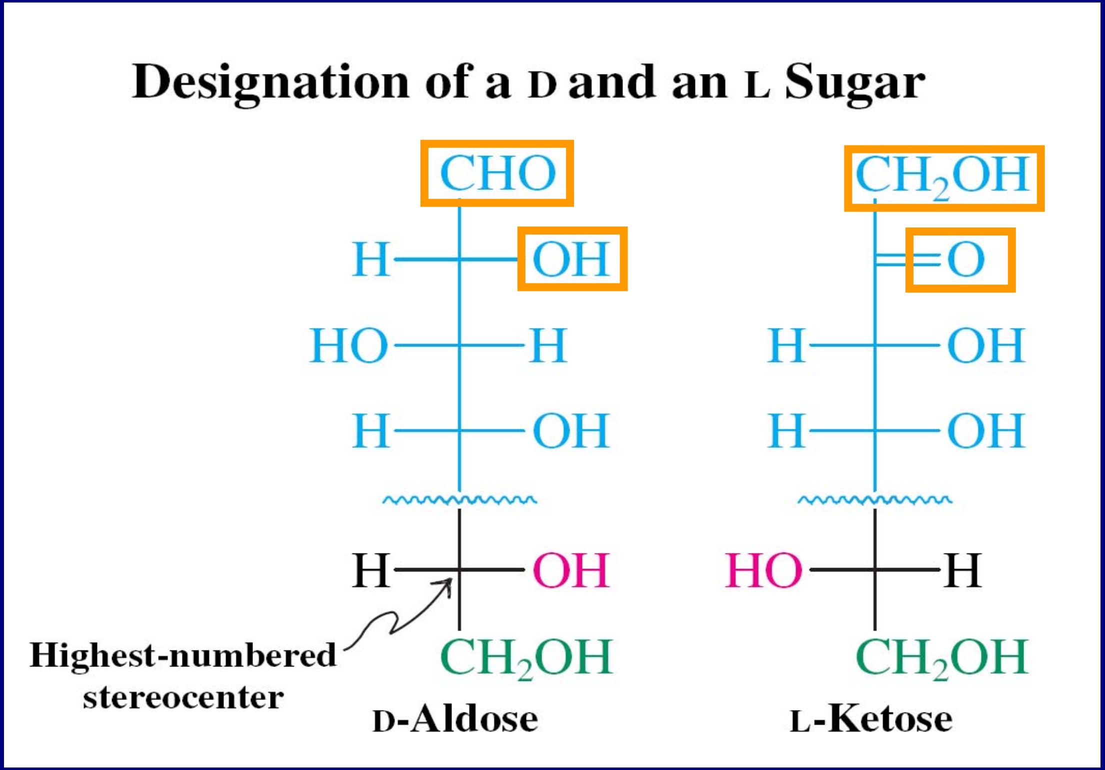
(*R*)-(+)-2,3-Dihydroxypropanal
[D-(+)-Glyceraldehyde]
($[\alpha]_D^{25°C} = +8.7$)

(*S*)-(−)-2,3-Dihydroxypropanal
[L-(−)-Glyceraldehyde]
($[\alpha]_D^{25°C} = -8.7$)

D and L is an older nomenclature (predates the knowledge of the absolute configuration of glyceraldehyde). The dextrorotatory enantiomer was called D, the other L. Later, D was found to be *R*, L therefore *S*.

Almost all natural sugars have stereocenter furthest away from carbonyl (drawn at the bottom) with the same absolute configuration as D-glyceraldehyde: "D-sugars"

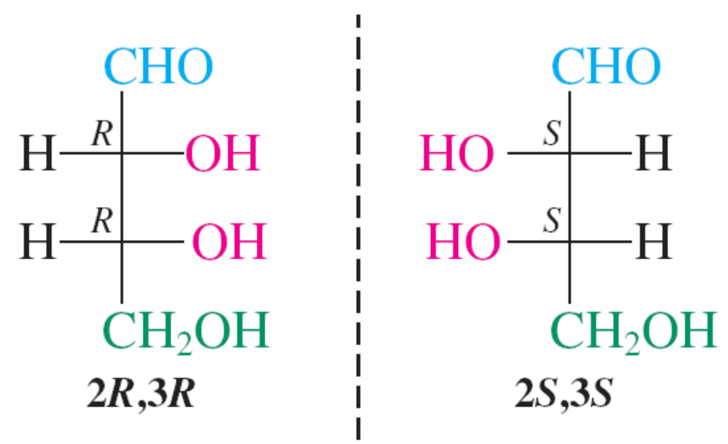
Designation of a D and an L Sugar



Natural

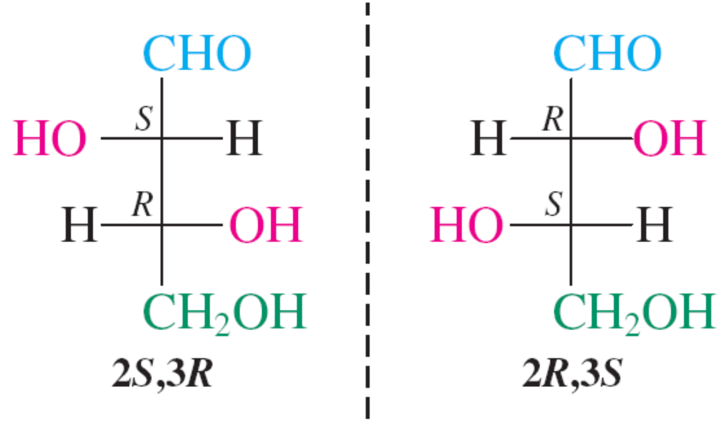
Unnatural

Rules for arranging the Fischer stencil: Carbonyl on top, places bottom C*OH on the right in the D sugars.



D-Erythrose

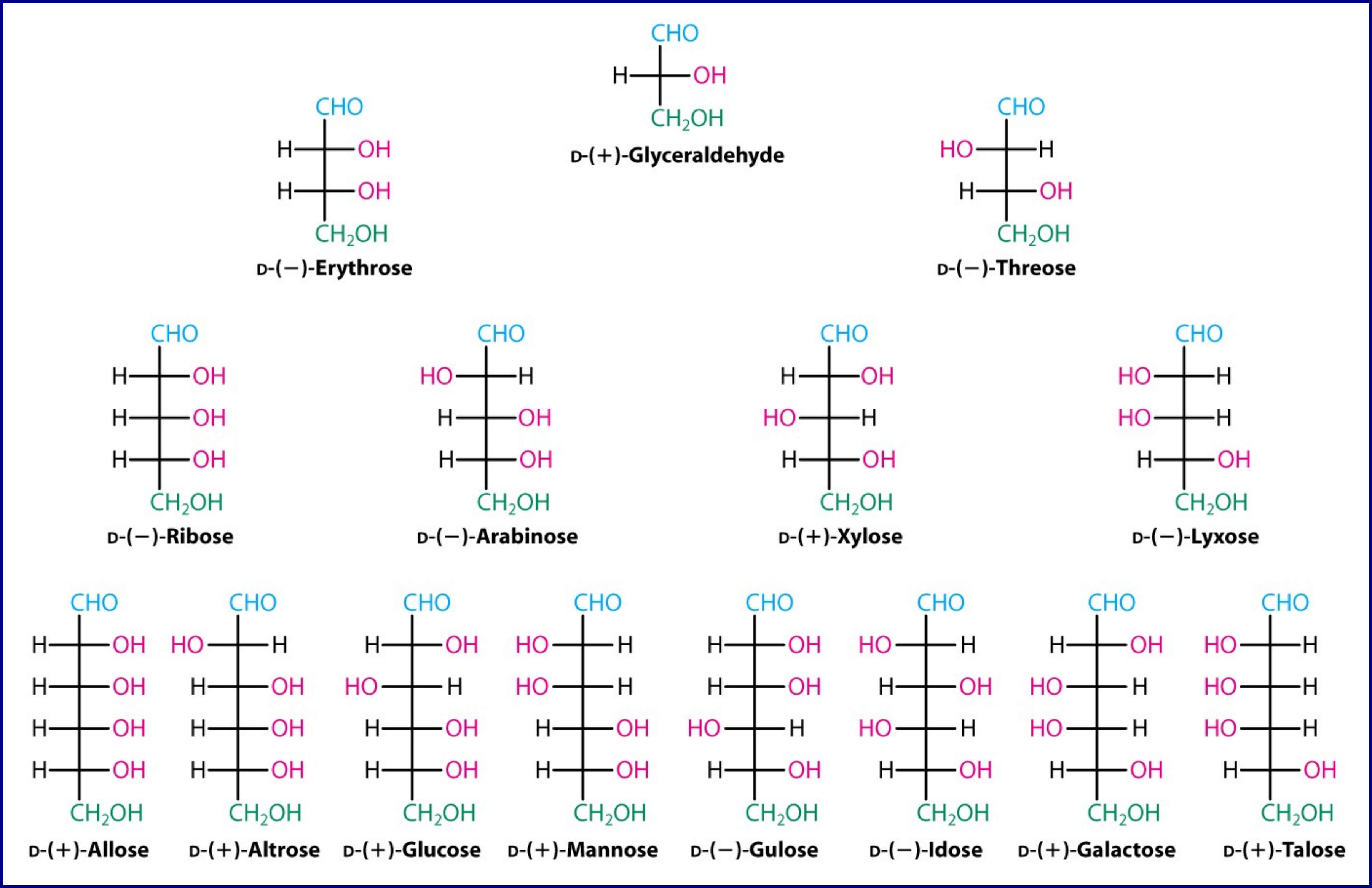
L-Erythrose



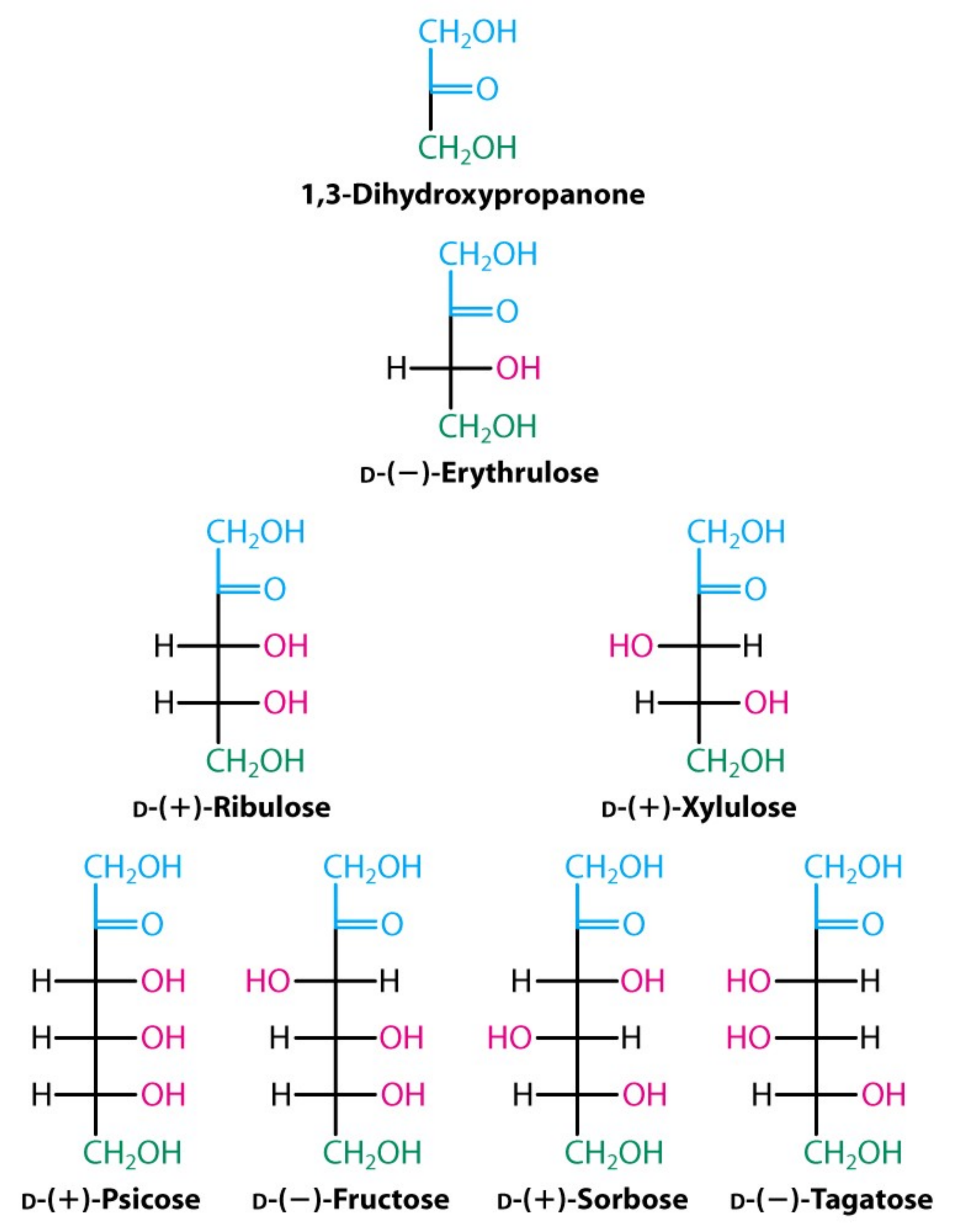
D-Threose

L-Threose

The Family of Natural Aldoses

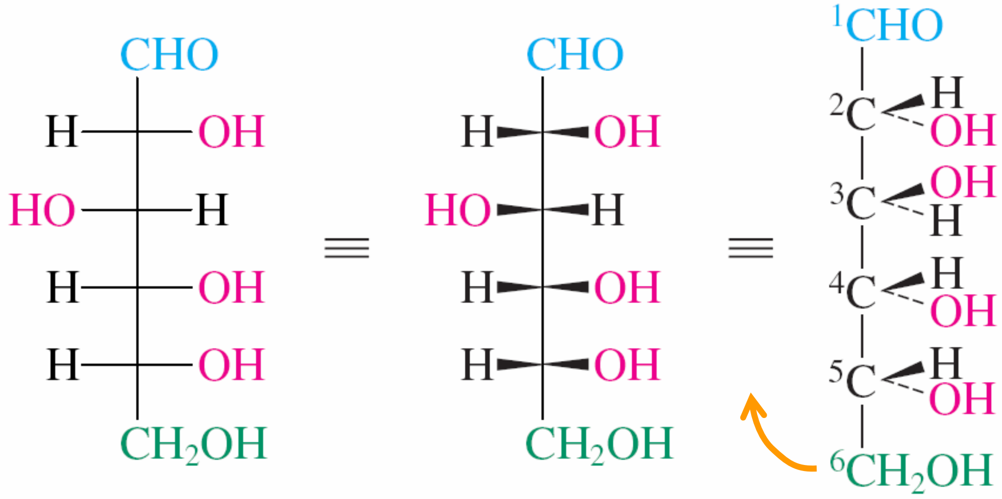


The Family of Natural Ketoses

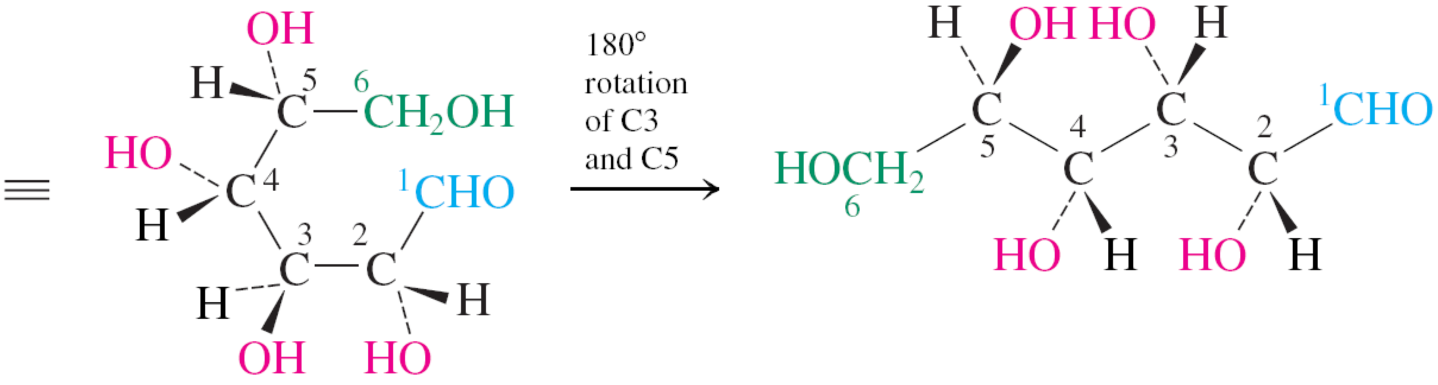


Fischer Projections and Dashed-Wedged Line Structures

Recall: Fischer projections represent an unrealistic model of the molecule: All eclipsed; carbon chain “curves”. It’s usefulness is in stereochemical bookkeeping.



Fischer projection

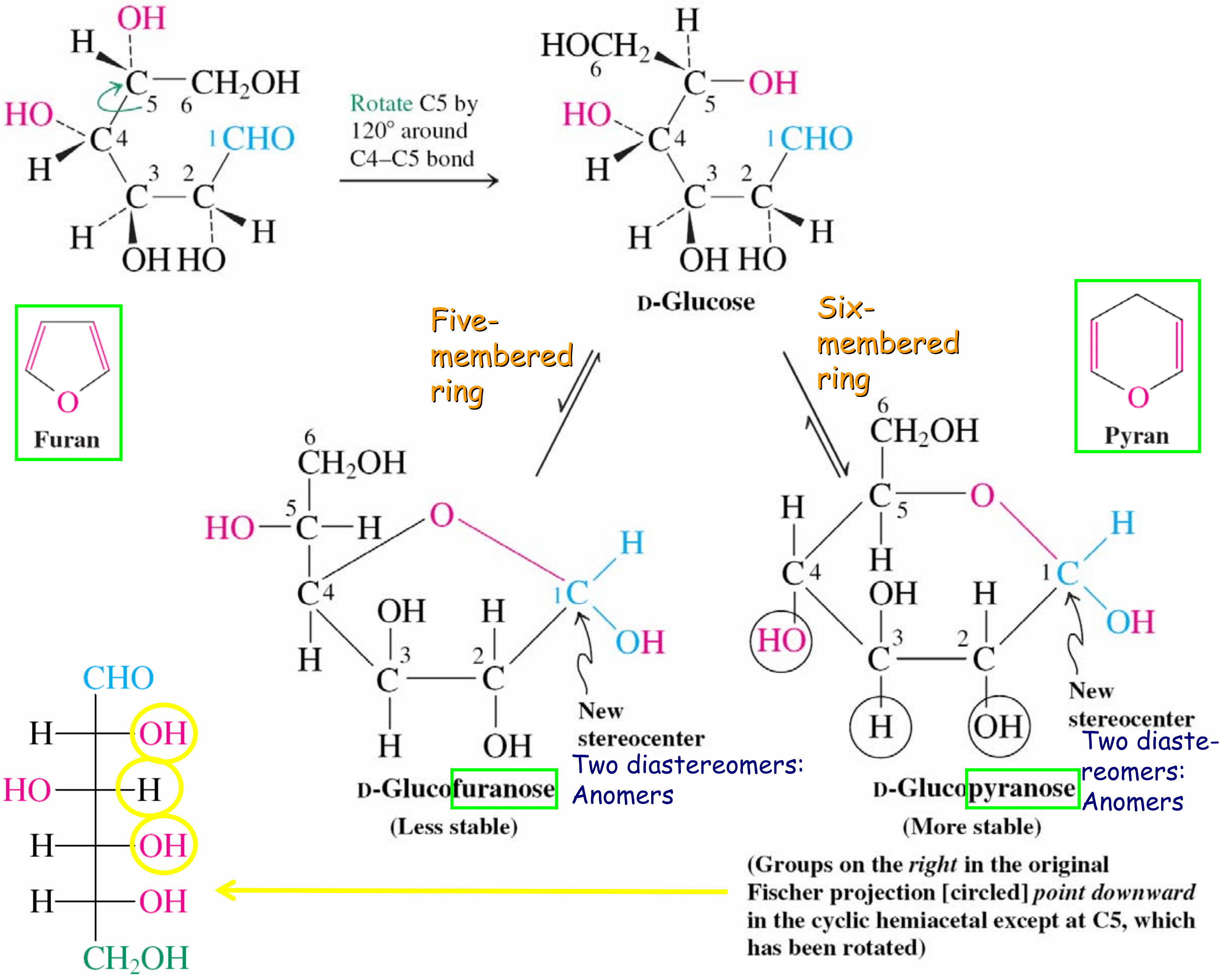


All-eclipsed dashed-wedged line structure

D-Glucose

All-staggered dashed-wedged line structure

Cyclic Hemiacetal Formation by Glucose



Rotate C5 by 120° around C4–C5 bond

D-Glucose

Furan

Pyran

New stereocenter

D-Glucofuranose

(Less stable)

Two diastereomers: Anomers

New stereocenter

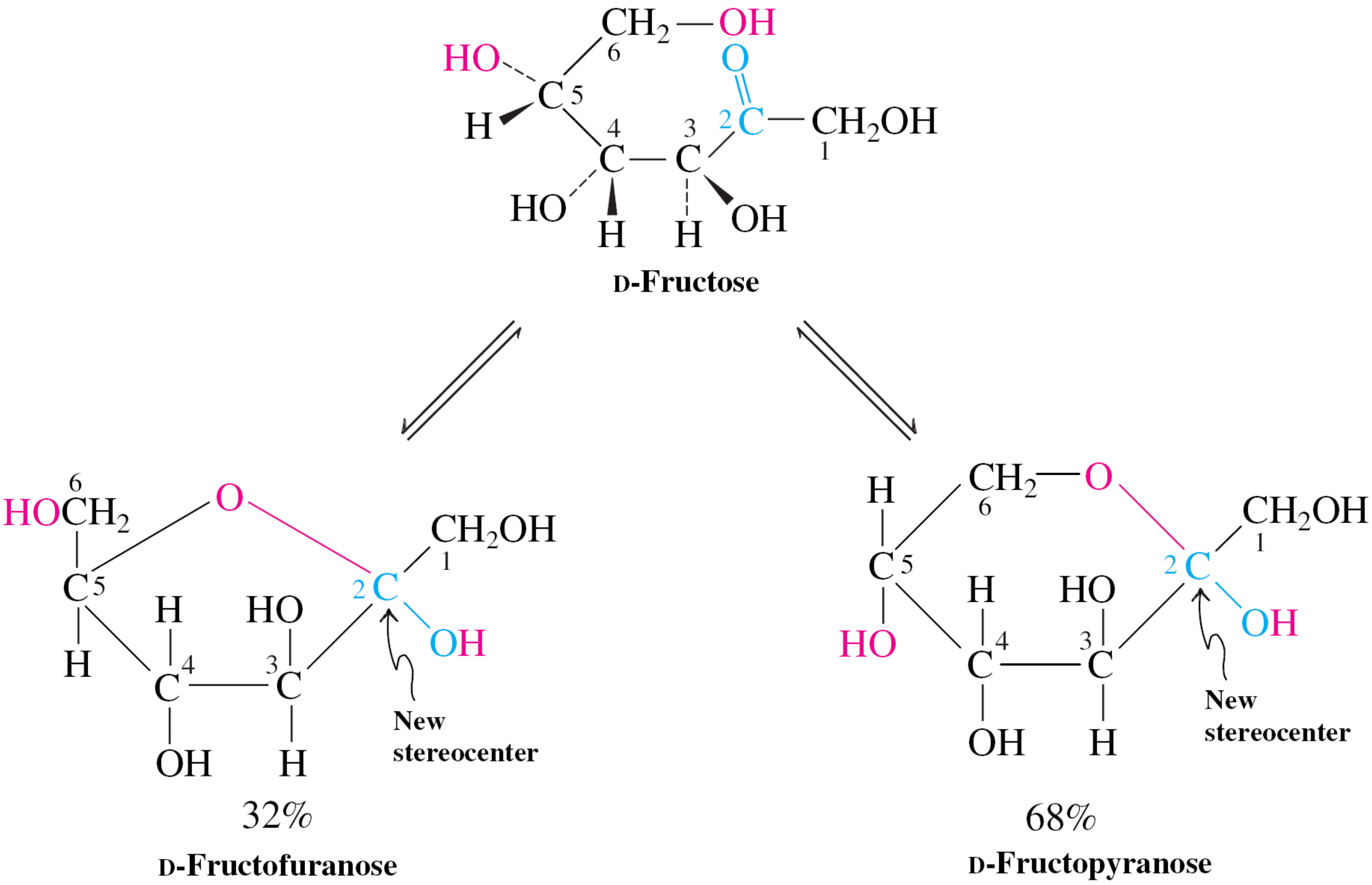
D-Glucopyranose

(More stable)

Two diastereomers: Anomers

(Groups on the *right* in the original Fischer projection [circled] *point downward* in the cyclic hemiacetal except at C5, which has been rotated)

Cyclic Hemiacetal Formation by Fructose



D-Fructose

D-Fructofuranose

32%

D-Fructopyranose

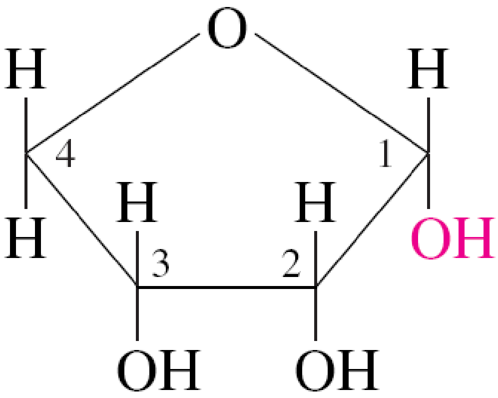
68%

New stereocenter

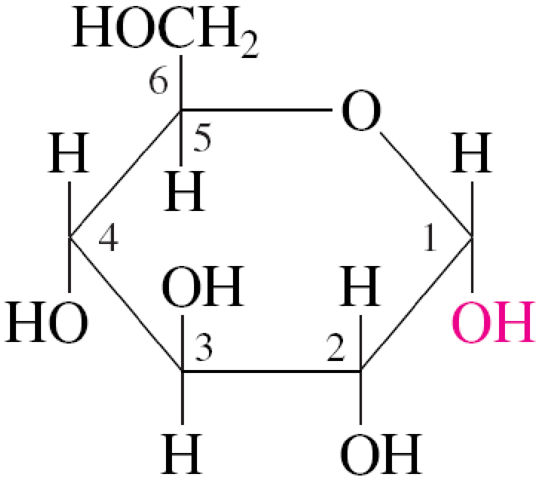
New stereocenter

Haworth Structures

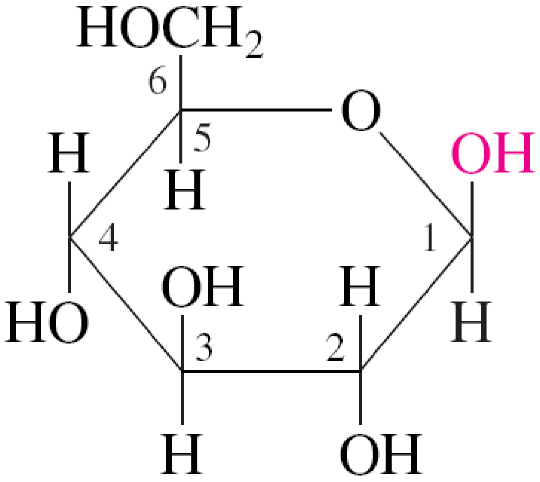
Groups that lie on the *right* in the Fischer projection point *downward* in the Haworth projection.



α-D-(−)-Erythrofuranose



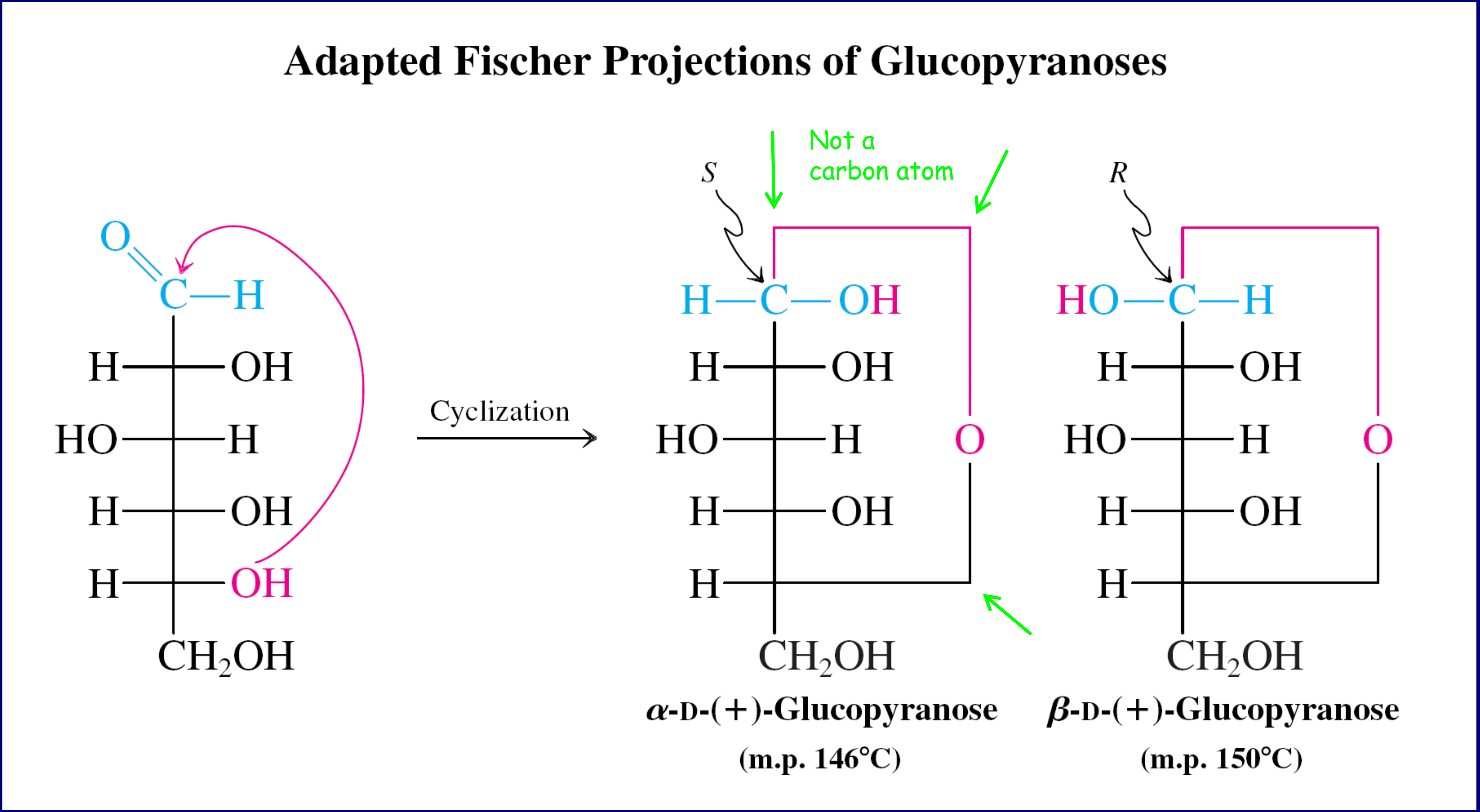
α-D-(+)-Glucopyranose



β-D-(+)-Glucopyranose

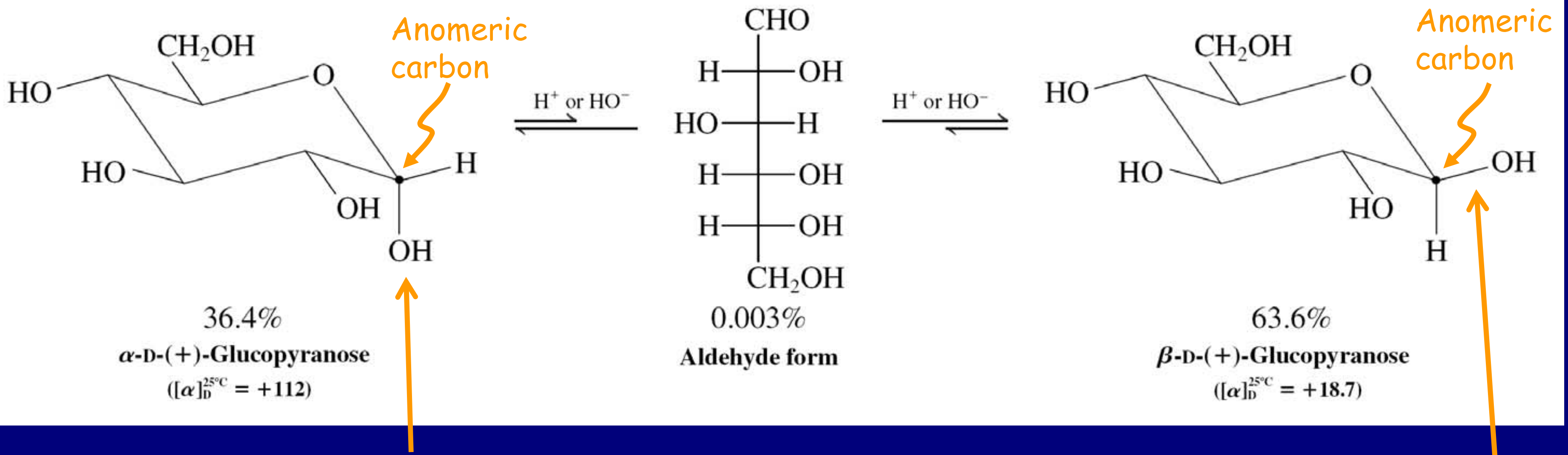
At the anomeric carbon: OH down is called the α-anomer, OH up is called the β-anomer.

Other ways of drawing cyclic structures:



Best are conformational pictures:

Interconversion of Open-Chain and Pyranose Forms of D-Glucose



Anomeric carbon

Anomeric carbon

36.4%
α-D-(+)-Glucopyranose
($[\alpha]_D^{25°C} = +112$)

0.003%
Aldehyde form

63.6%
β-D-(+)-Glucopyranose
($[\alpha]_D^{25°C} = +18.7$)

OH down: α-Anomer; crystallizes

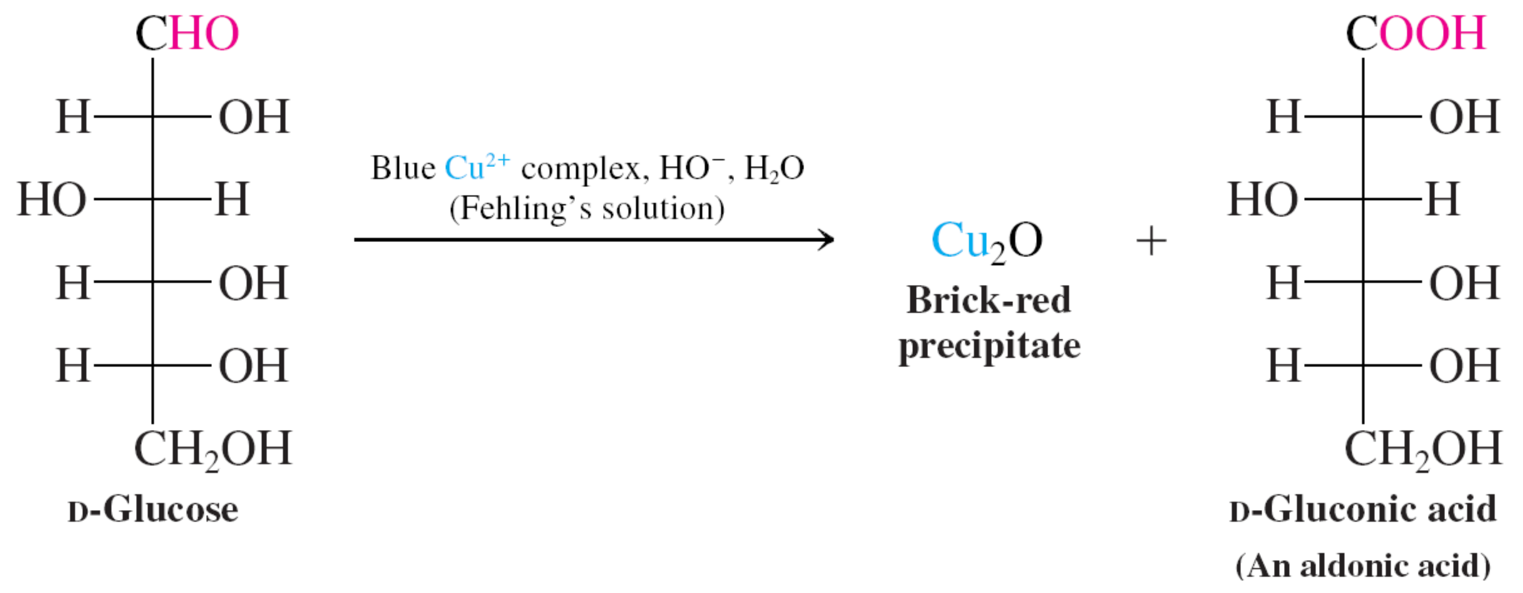
OH up: β-Anomer; more stable because all-equatorial

Mutarotation: Change in observed optical rotation when a sugar molecule equilibrates with its anomer.

Reactions of Sugars

1. Oxidation

a. CHO → COOH (aldose → aldonic acid)



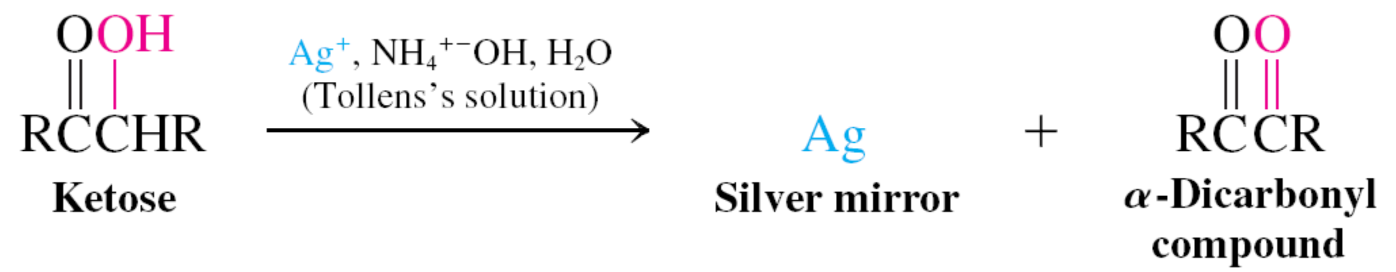
D-Glucose

Brick-red precipitate

D-Gluconic acid

(An aldonic acid)

b. α-Hydroxy group of ketoses → α-dicarbonyl



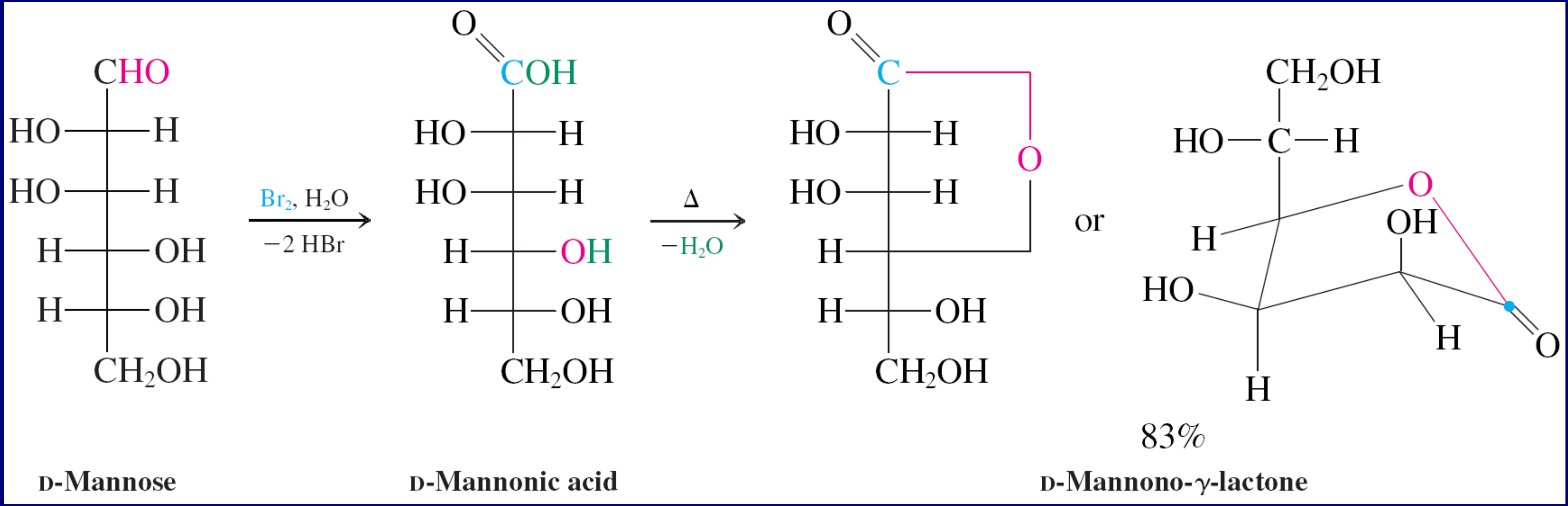
Ketose

Silver mirror

α-Dicarbonyl compound

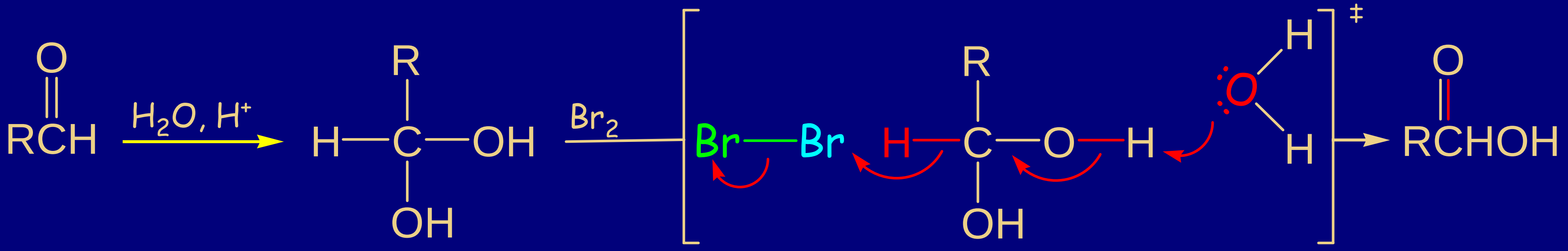
Tests for "reducing" sugars; all ordinary saccharides are reducing.

Large scale preparation of aldonic acids: Br_2, H_2O

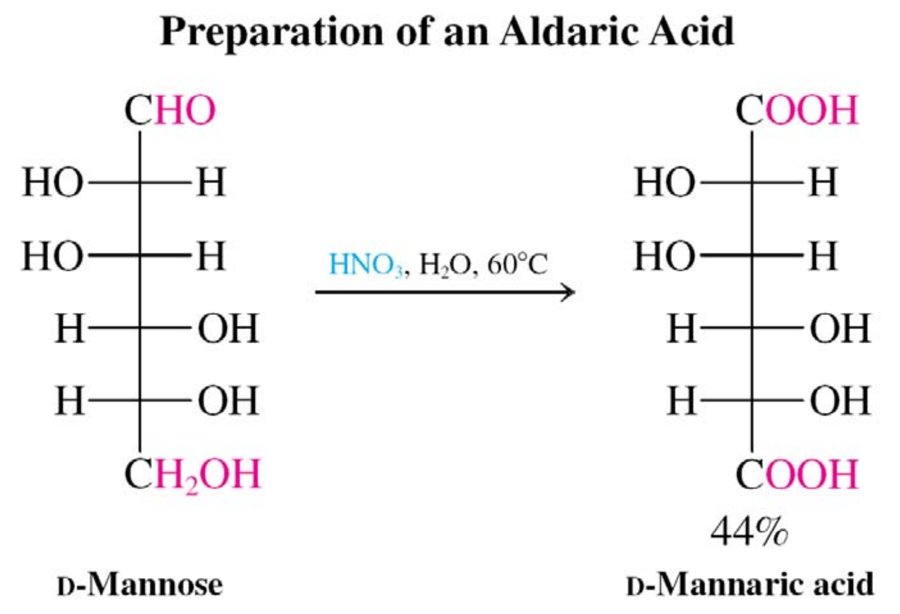


Dehydration gives lactones, typically five-membered (γ- lactones).

Mechanism of bromine oxidation:



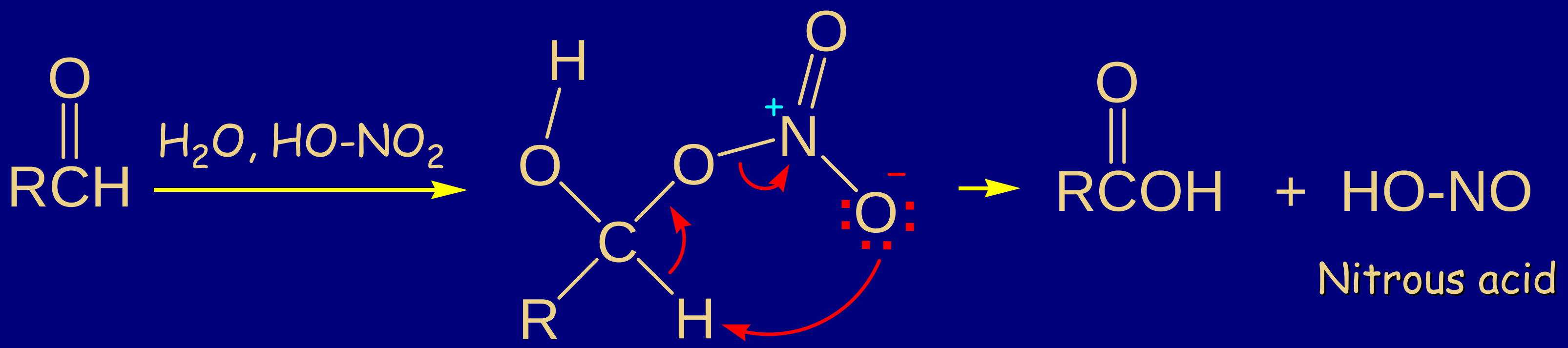
c. Oxidation of both ends of aldoses → aldaric acid



Preparation of an Aldaric Acid

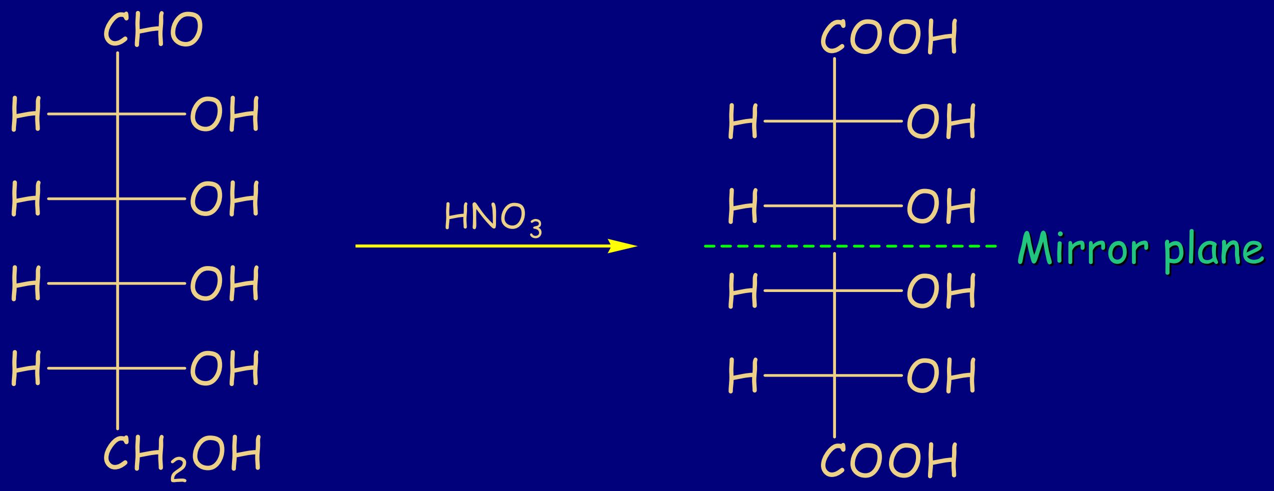
Note selectivity of nitric acid: Picks on primary OH function (after oxidizing the formyl group): Less hindered.

Mechanism:



Nitrous acid

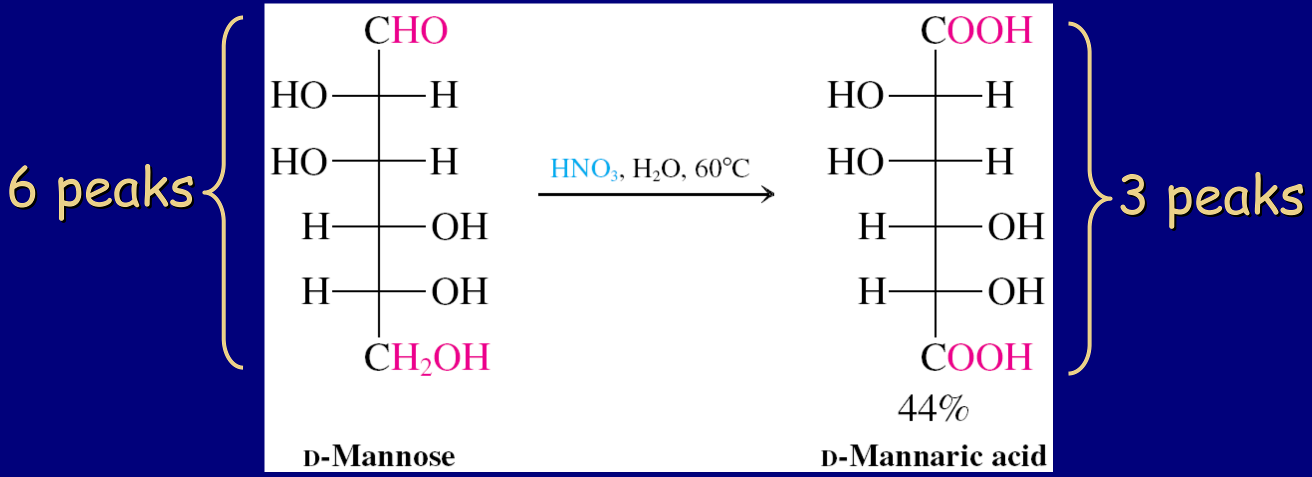
For some sugars, this oxidation may give meso (achiral) aldaric acid. Can be used for proof of stereochemistry.



D-(+)-Allose

Allaric acid (meso)

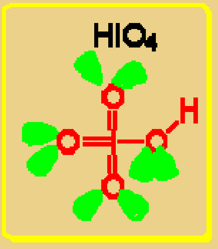
Symmetry becomes obvious also in NMR, e.g. ^{13}C NMR:



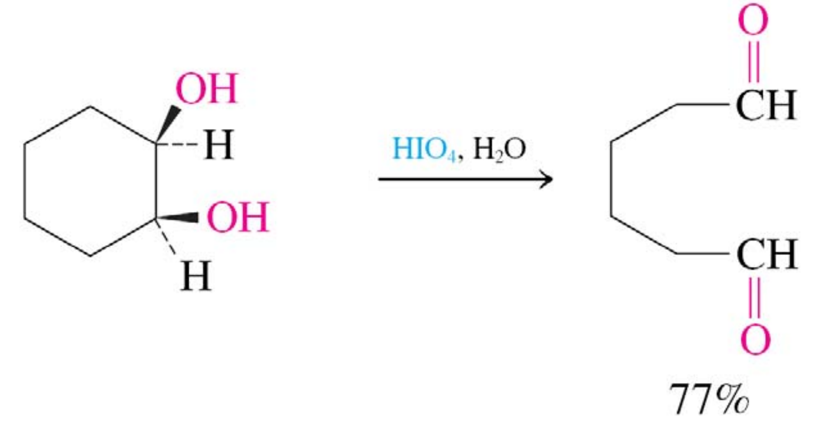
D-Mannose

D-Mannaric acid

d. Oxidative cleavage: HIO_4



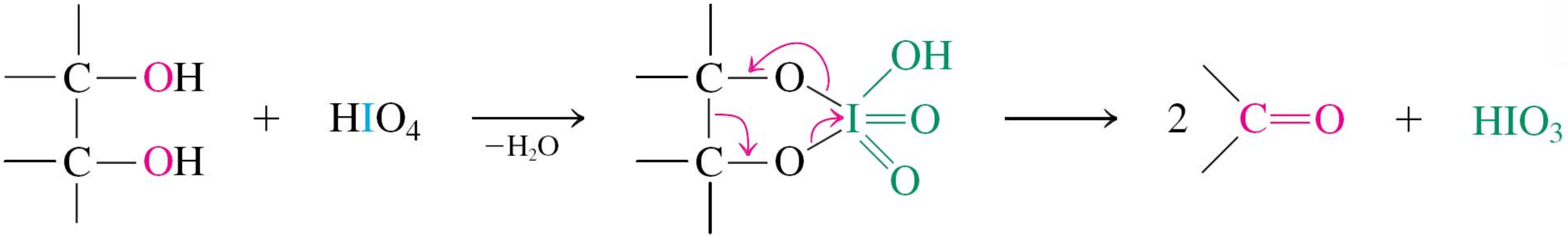
This reagent causes the rupture of vicinal diols to dialdehydes. How?



cis-1,2-Cyclohexanediol

Hexanedial

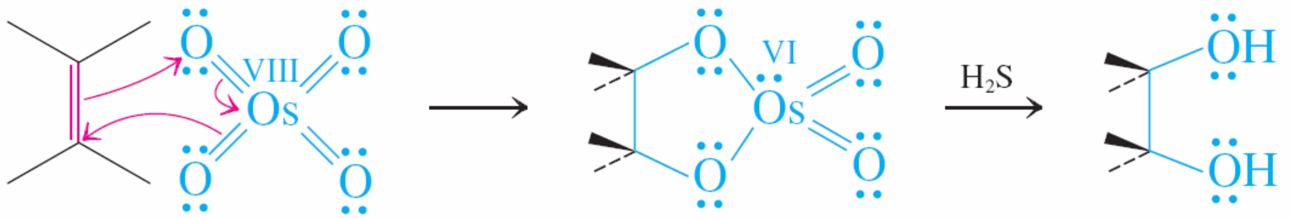
Mechanism of Periodic Acid Cleavage of Vicinal Diols



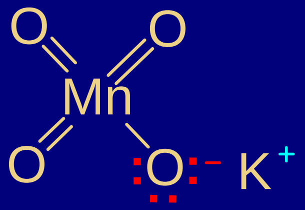
Cyclic periodate ester

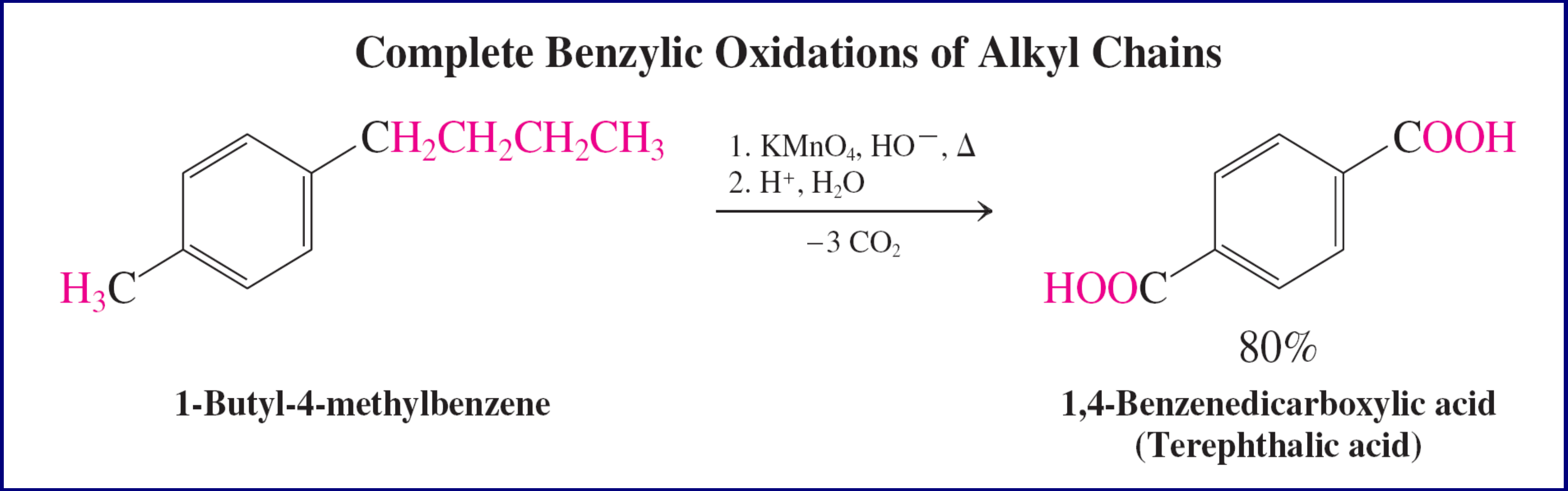
Does this ring a bell? Remember OsO_4 oxidation of alkenes to vicinal diols: Cleaves “half” a double bond.

Mechanism of the Osmium Tetroxide Oxidation of Alkenes



HIO_4 does the same to a single bond (bearing OHs). Similarly: Remember benzylic oxidation of alkylbenzenes to benzenecarboxylic acids by basic $KMnO_4$.



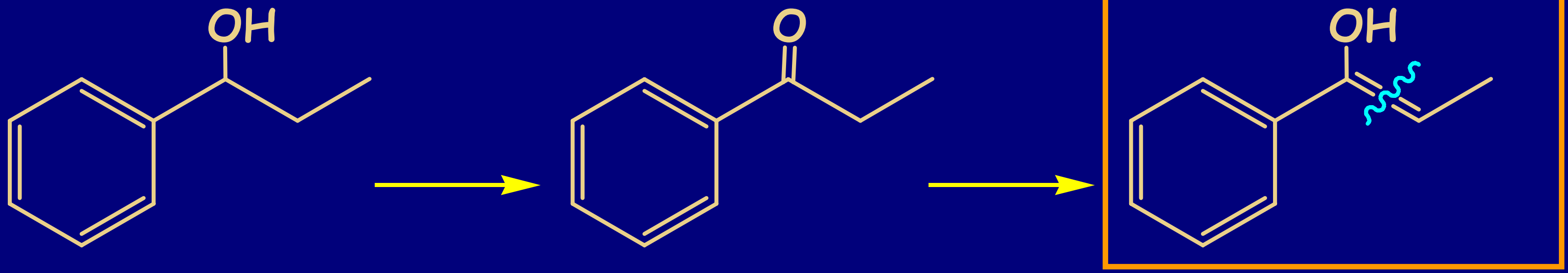


Complete Benzylic Oxidations of Alkyl Chains

1-Butyl-4-methylbenzene

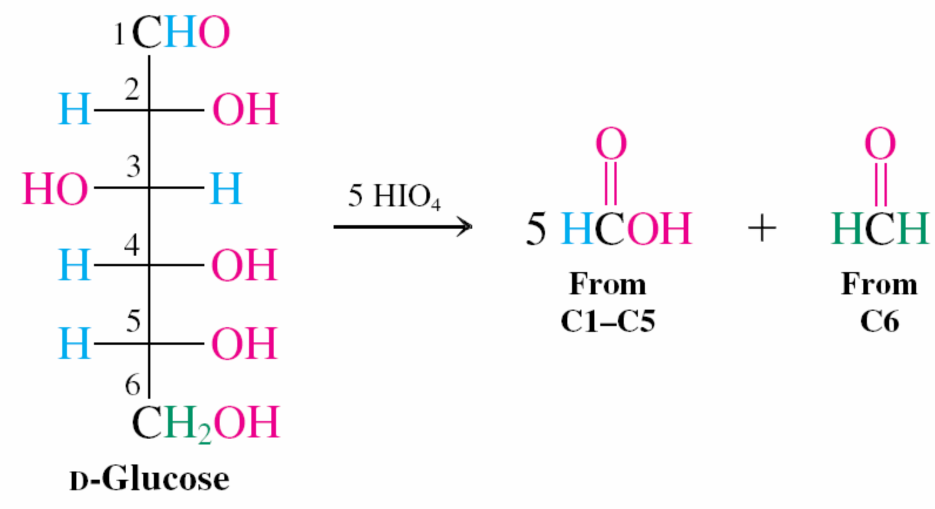
1,4-Benzenedicarboxylic acid
(Terephthalic acid)

- C-C bond broken via:

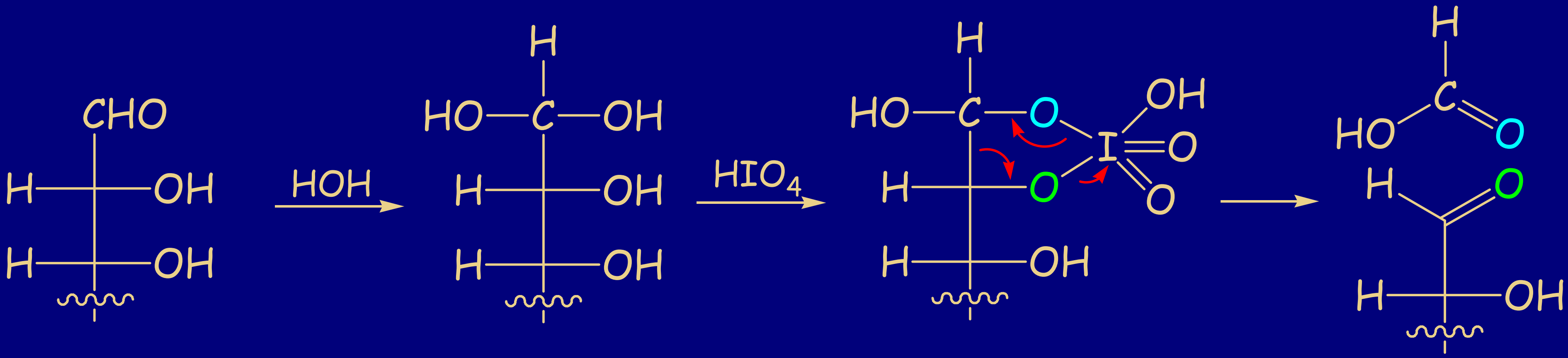


$KMnO_4$ does both the OsO_4-type and HIO_4-type oxidations sequentially in the same reaction step.

How does this work for sugars? Leads to complete degradation of the carbon chain.

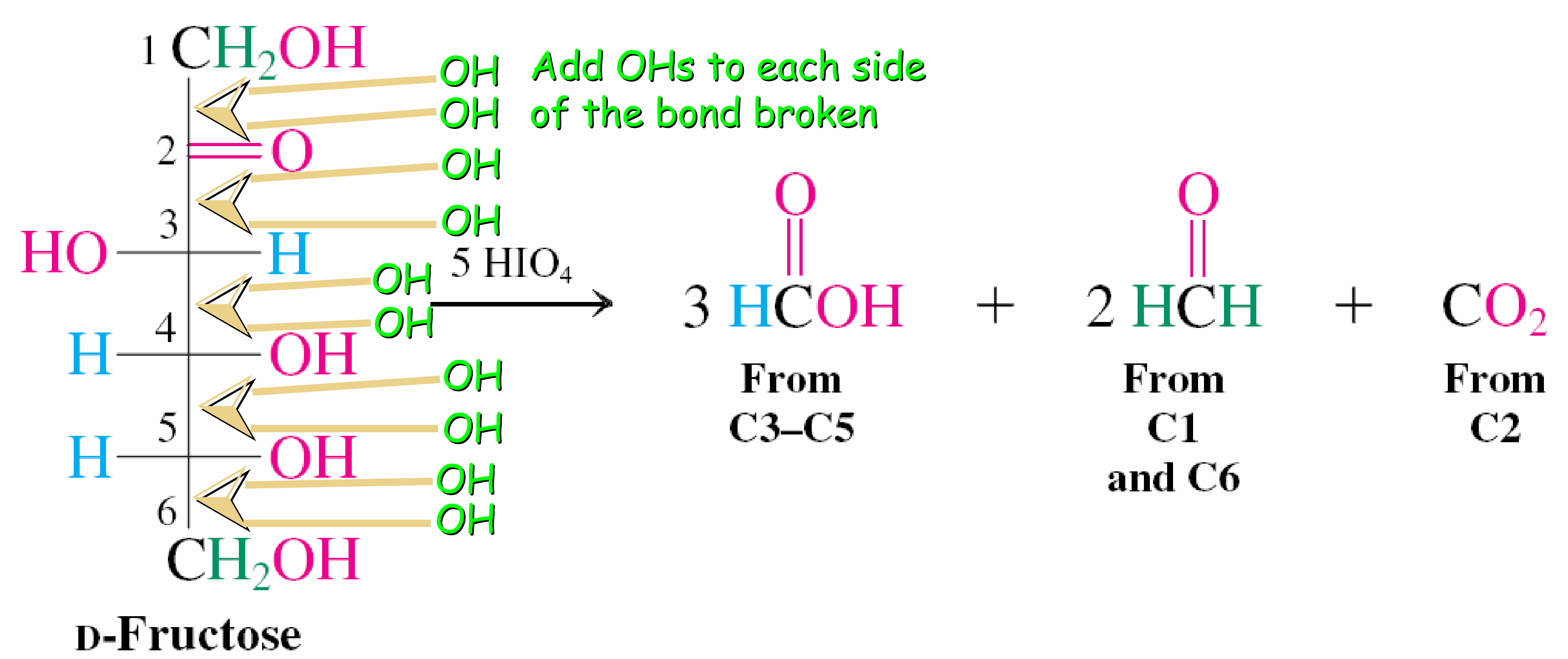


D-Glucose



Note: Each carbon fragment retains the same number of attached hydrogen atoms as were present in the original sugar.

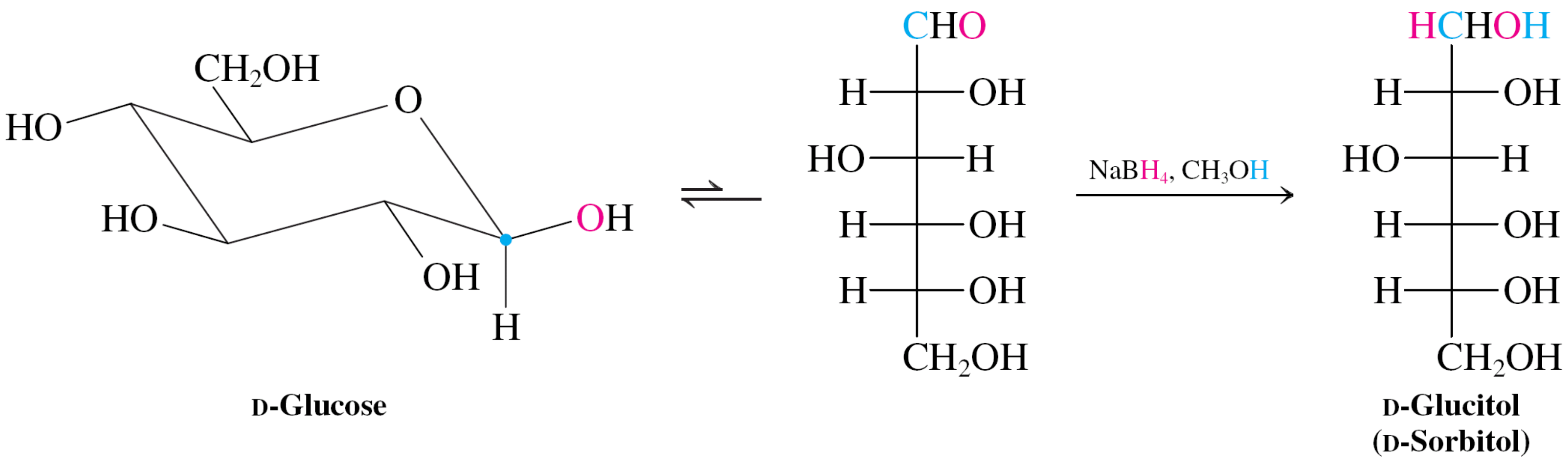
Another way to think about this is as a "dihydroxylative" cleavage of each chain C-C bond, e.g. fructose:



Note: Each carbon fragment retains the same number of attached hydrogen atoms as were present in the original sugar.

2. Reduction to alditols

Preparation of an Alditol

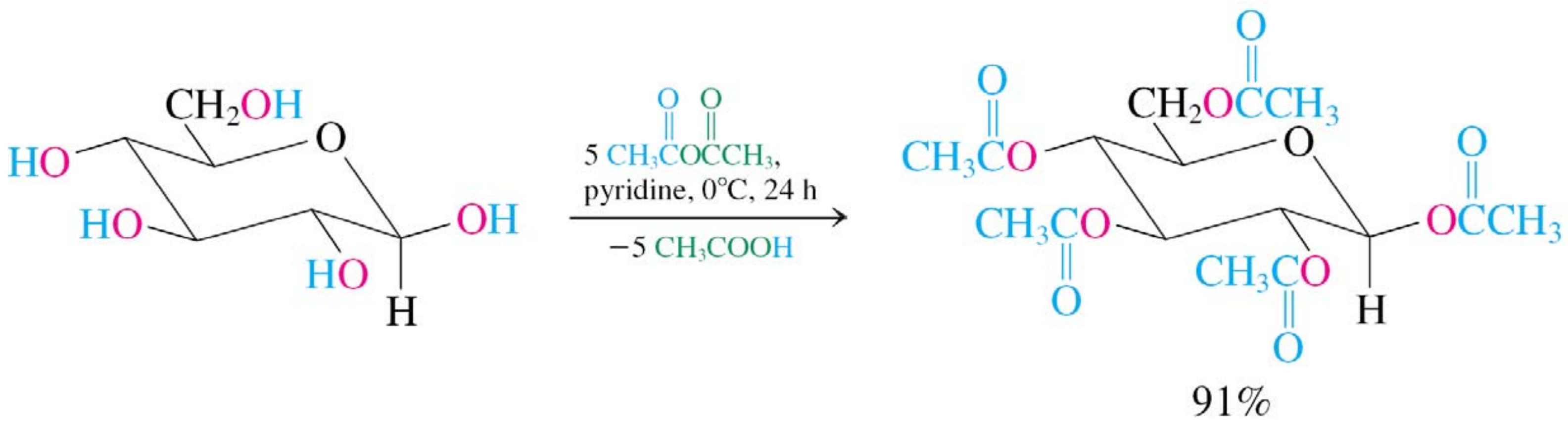


Note: Just as in the oxidation to aldaric acids, reduction may symmetrize the sugar.

Sorbitol (“sugar alcohol”) is used as artificial sweetener in diet foods: 2.6 cal/g per versus 4 cal/g for normal sugar. Sorbitol also occurs naturally in many stone fruits.

3. Esters and Ethers: Protection

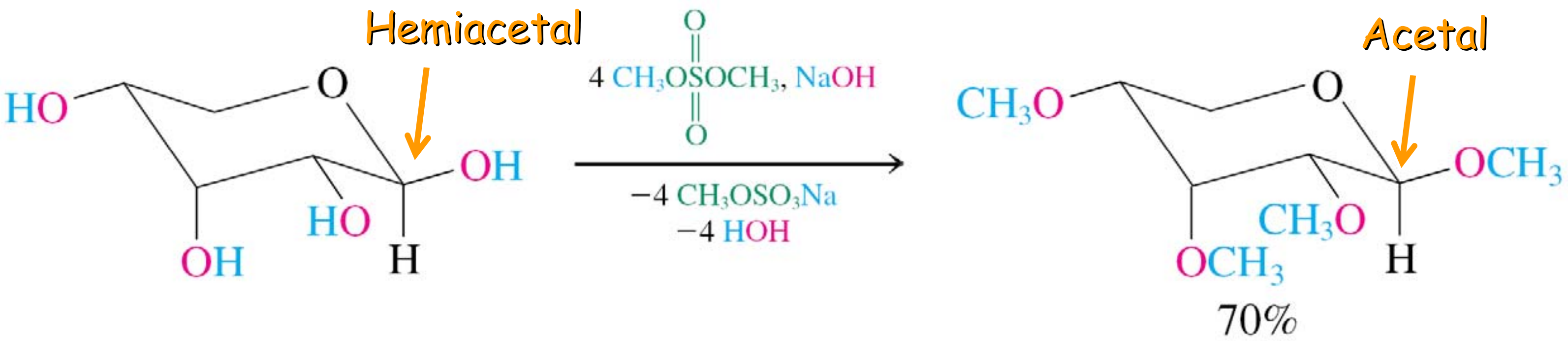
Complete Esterification of Glucose



β-D-Glucopyranose

β-D-Glucopyranose pentaacetate

Complete Methylation of a Pyranose



Hemiacetal

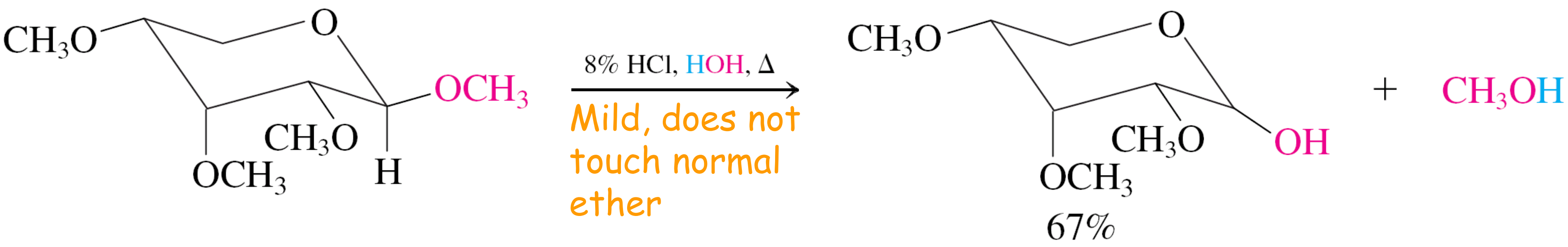
Acetal

β-D-Ribopyranose

β-D-Ribopyranose tetramethyl ether

Acetal function can be deprotected selectively

Selective Hydrolysis of a Sugar Acetal



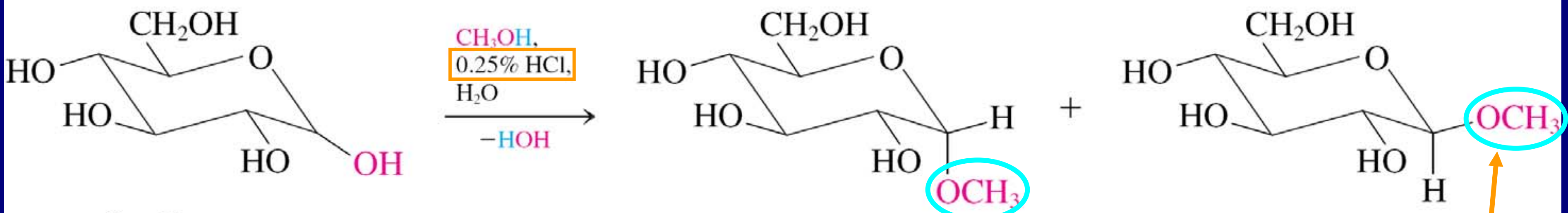
Mild, does not touch normal ether

D-Ribopyranose trimethyl ether

(Mixture of α and β forms)

Alternative exploitation of the special reactivity of the (hemi)acetal function: Turn it into an acetal, called glycoside for sugars.

Selective Preparation of a Glycoside (Sugar Acetal)



α- or β-D-Glucopyranose

Methyl α-D-glucopyranoside

(m.p. 166°C, $[\alpha]_D^{25°C} = +158$)

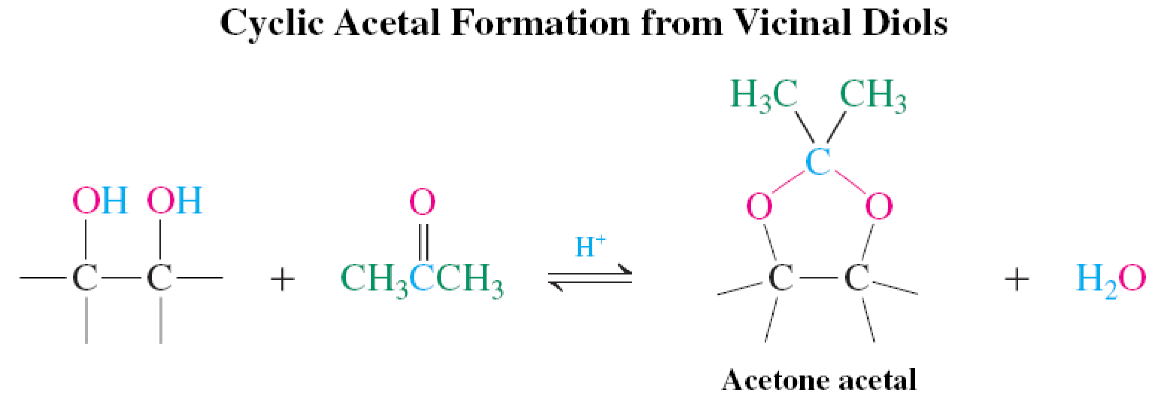
Methyl β-D-glucopyranoside

(m.p. 105°C, $[\alpha]_D^{25°C} = -33$)

Protection of anomeric carbon → no mutarotation, no aldehyde oxidation (i.e. does not behave as reducing sugar), no reduction.

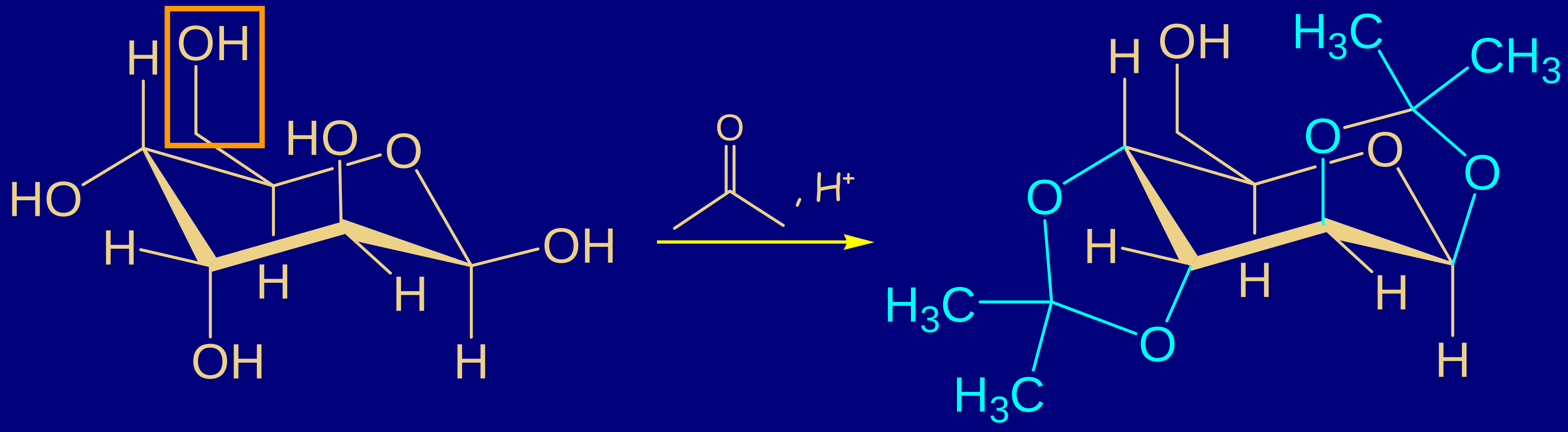
Protection as cyclic acetals

Recall:



Cyclic Acetal Formation from Vicinal Diols

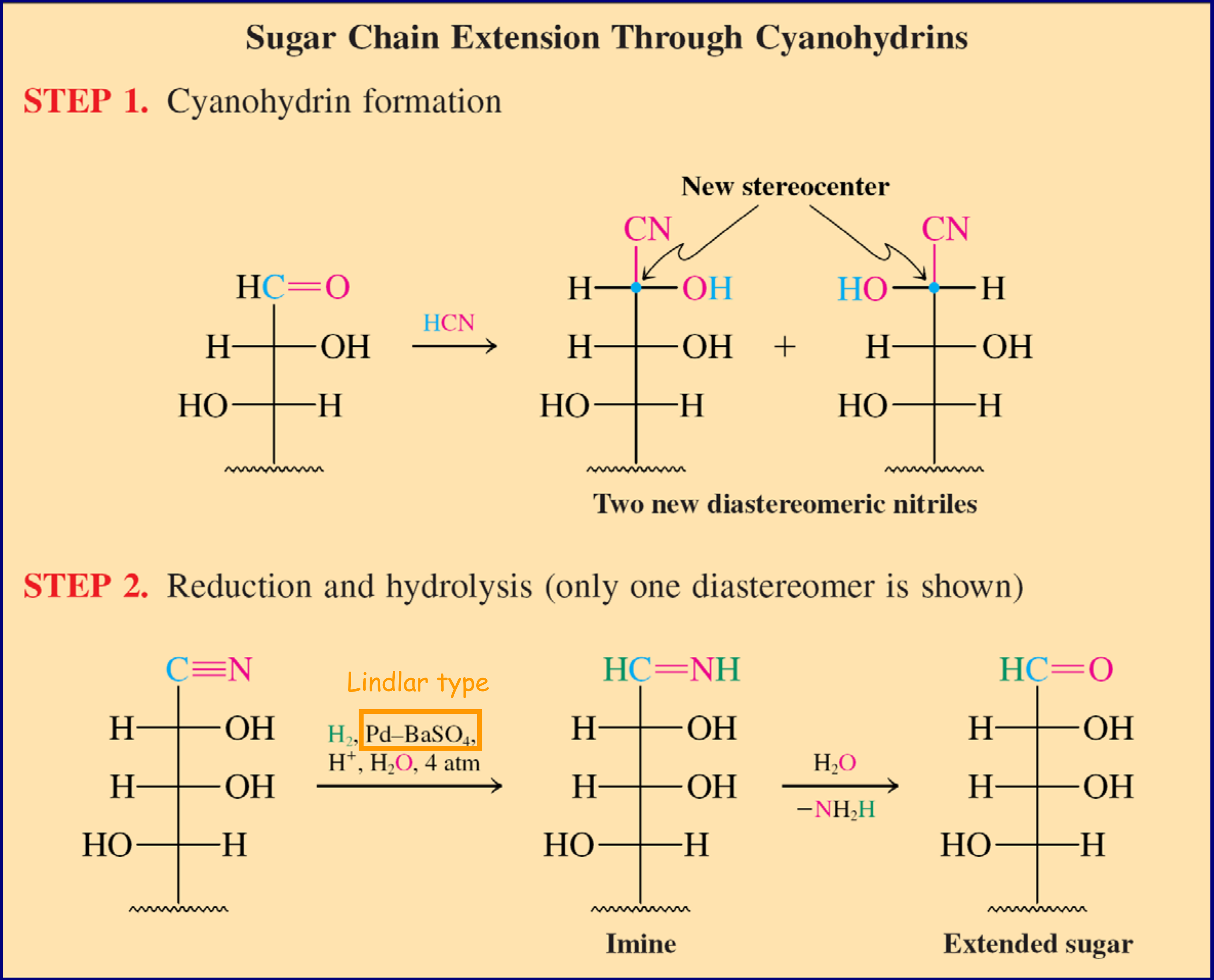
-CH_2OH often not engaged: Flexibility makes entropy of acetal formation worse ↓



β-D-Altrose

β-D-Altrose bisacetonide

4. Kiliani-Fischer Extension (Modified)



Sugar Chain Extension Through Cyanohydrins

STEP 1. Cyanohydrin formation

Two new diastereomeric nitriles

STEP 2. Reduction and hydrolysis (only one diastereomer is shown)

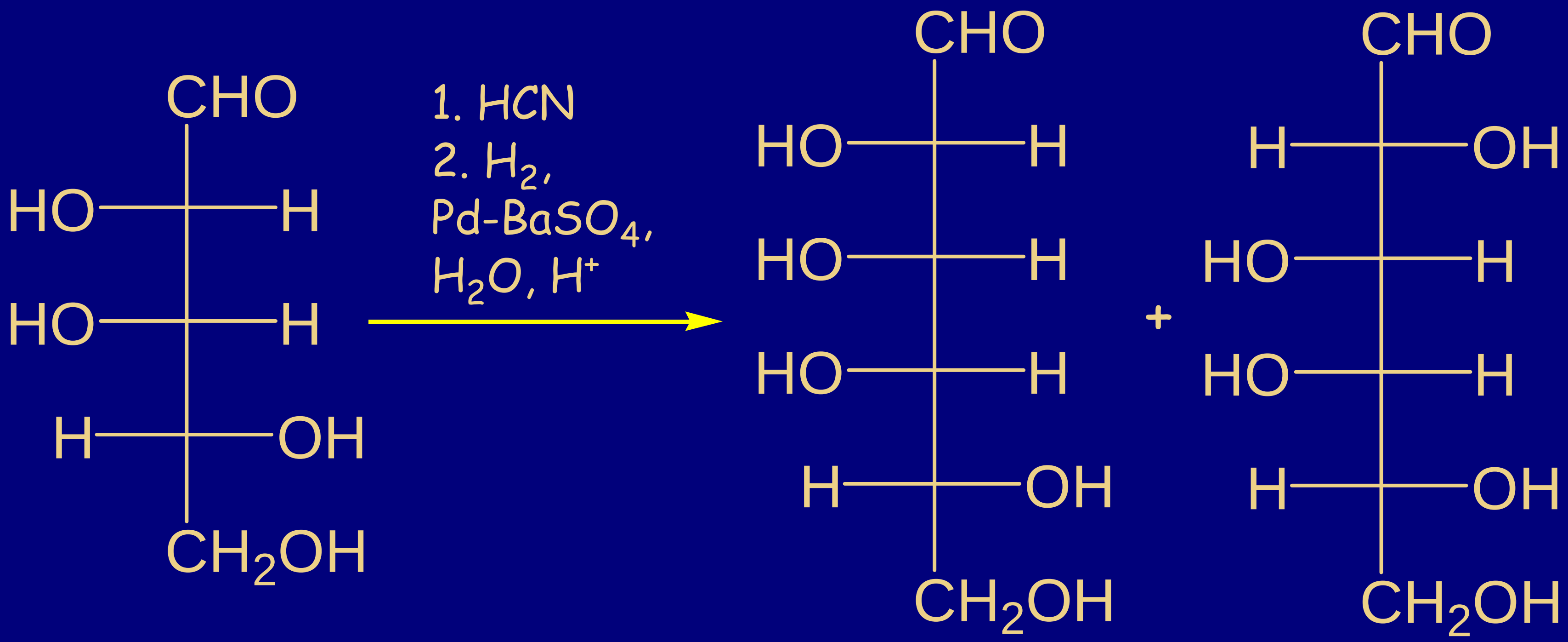
Imine

Extended sugar

Heinrich Kiliani
1855 - 1945

Emil Fischer
1852-1919

Example:



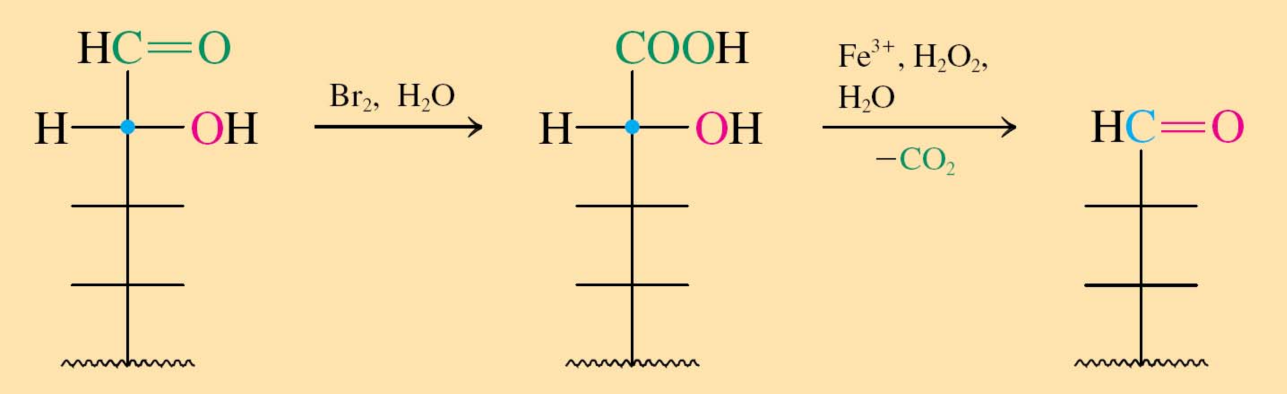
1. HCN
2. H_2,
Pd-$BaSO_4$,
H_2O, H^+

D-Lyxose

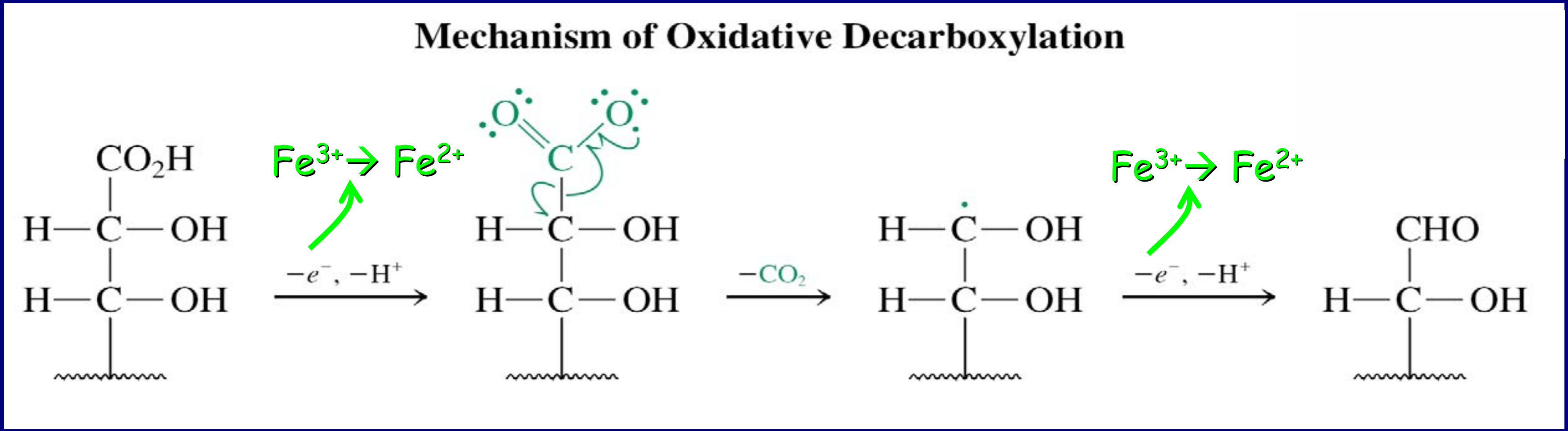
D-Talose

D-Galactose

5. Ruff Degradation



Note: Both diastereomers (*R* or *S* at the top stereocenter) degrade to the same lower sugar.

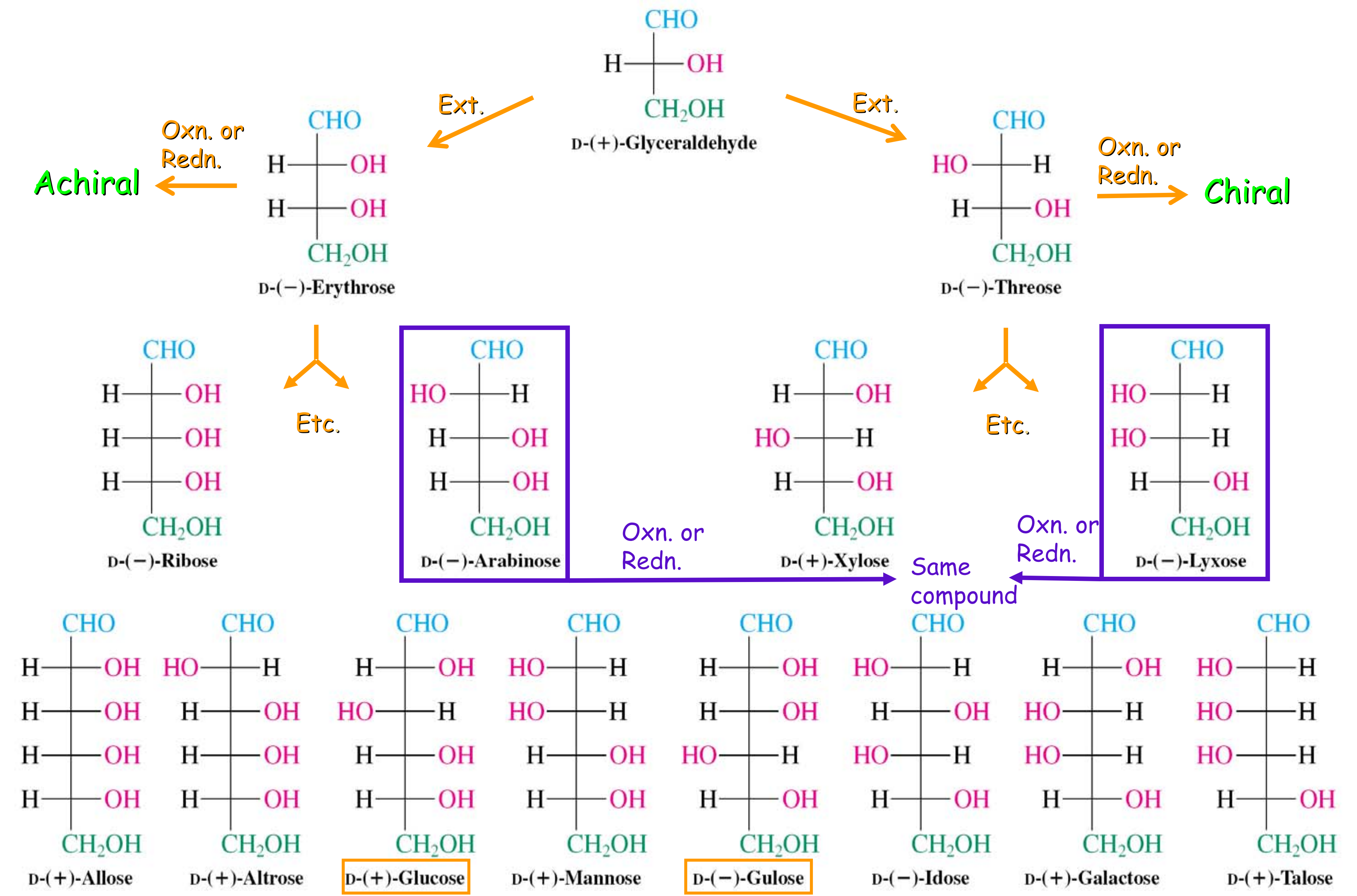

Mechanism of Oxidative Decarboxylation

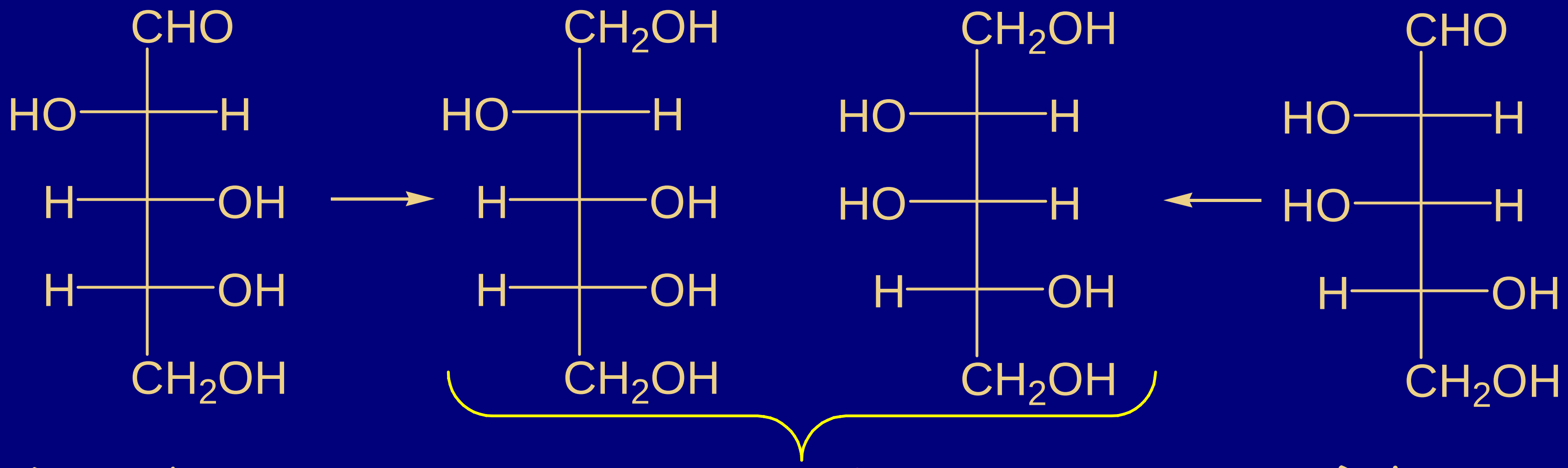
Structure Determination of Sugars- The Fischer Proof

Logical combination of

1. Sugar extension → 2 diastereomers
2. Sugar degradation: 2 Diastereomers give same sugar)
3. Sugar symmetrization via aldaric acids or alditols
4. Recognition of intricate stereochemical relationships

A glimpse at the logic:

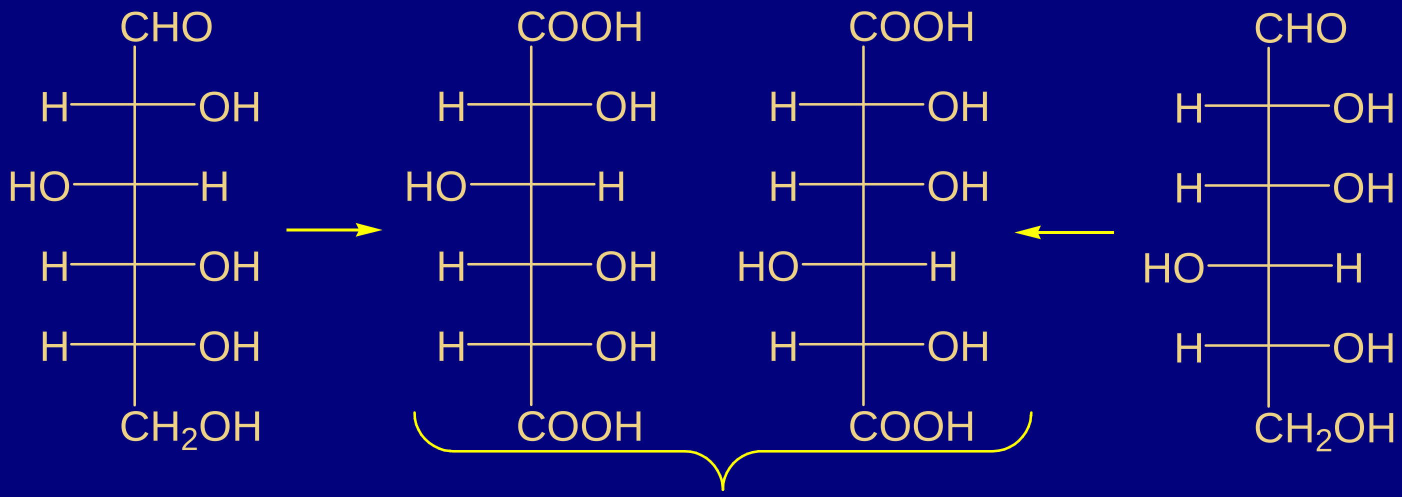




D-Arabinose

Same!

D-Lyxose



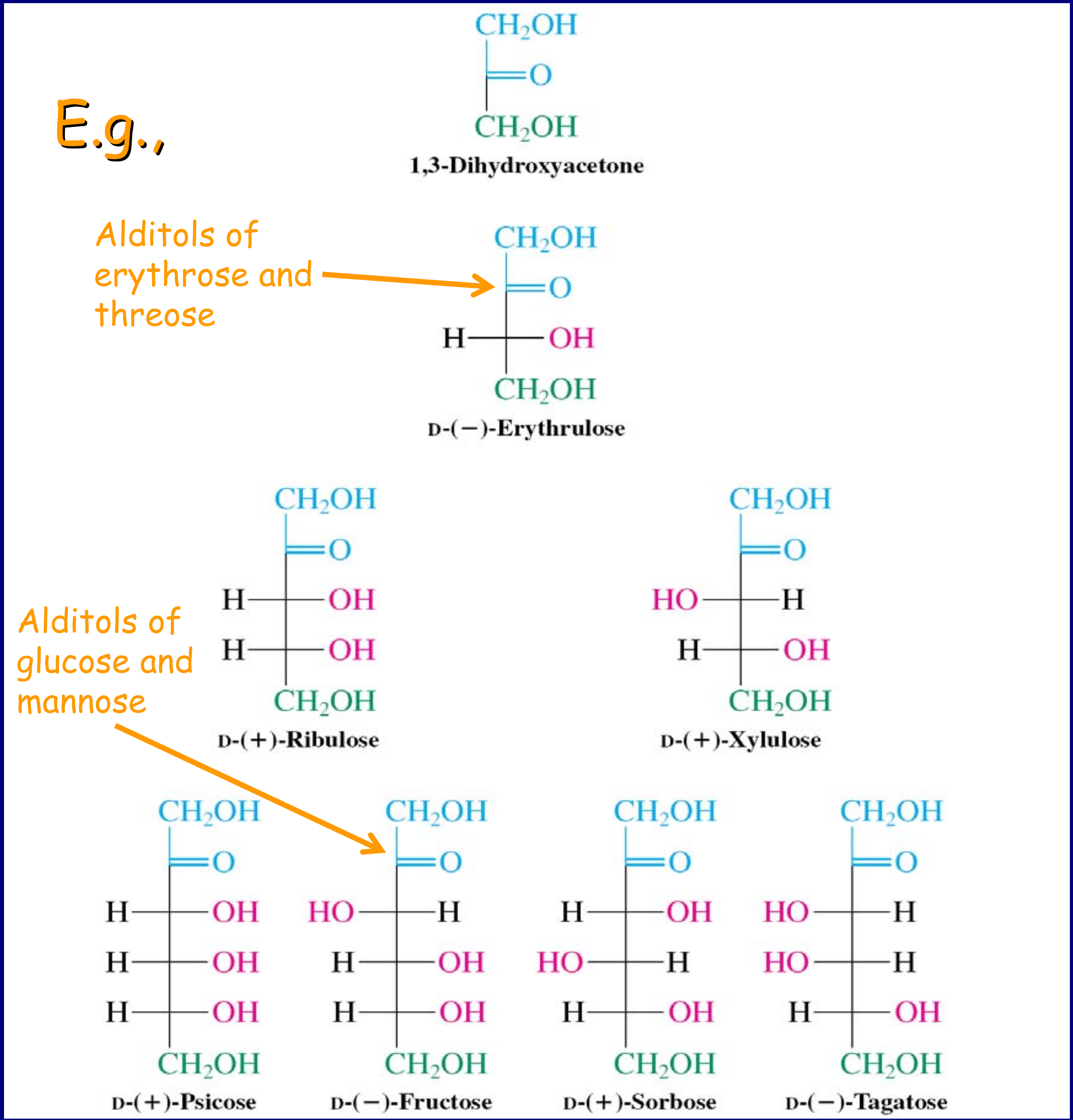
D-Glucaric acid

D-Gularic acid

Enantiomers

D-Ketoses correlate with alditols by reduction

E.g.,



Alditols of erythrose and threose

Alditols of glucose and mannose

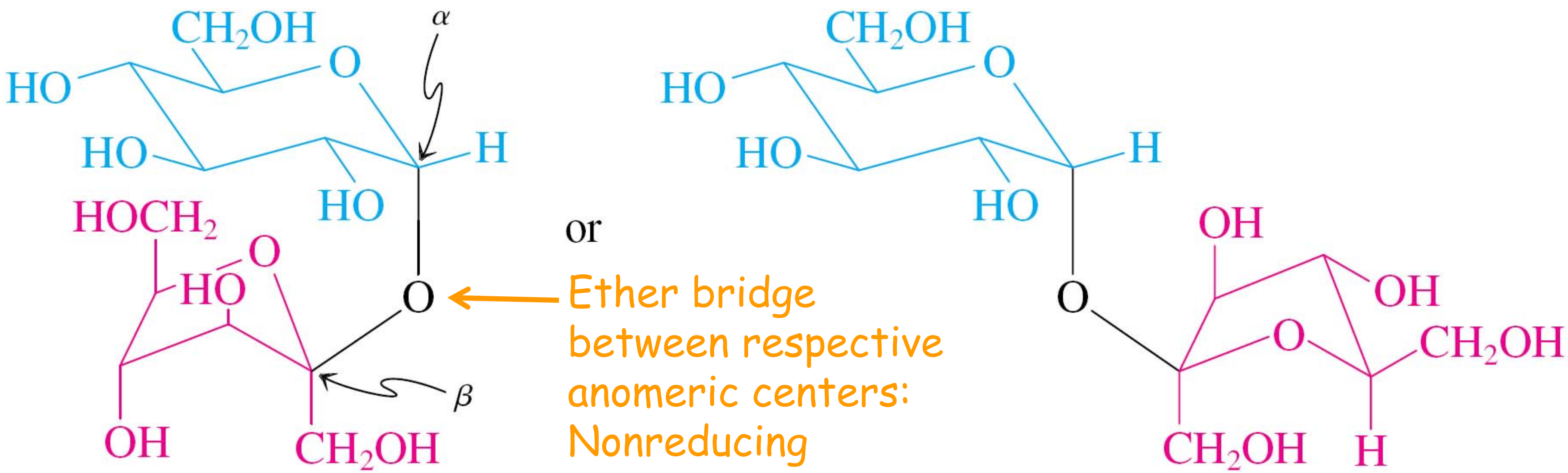
Again, potential symmetrization helps in structural assignment

Di- and Higher Saccharides

Sucrose: Disaccharide derived from glucose and fructose

"Table sugar"

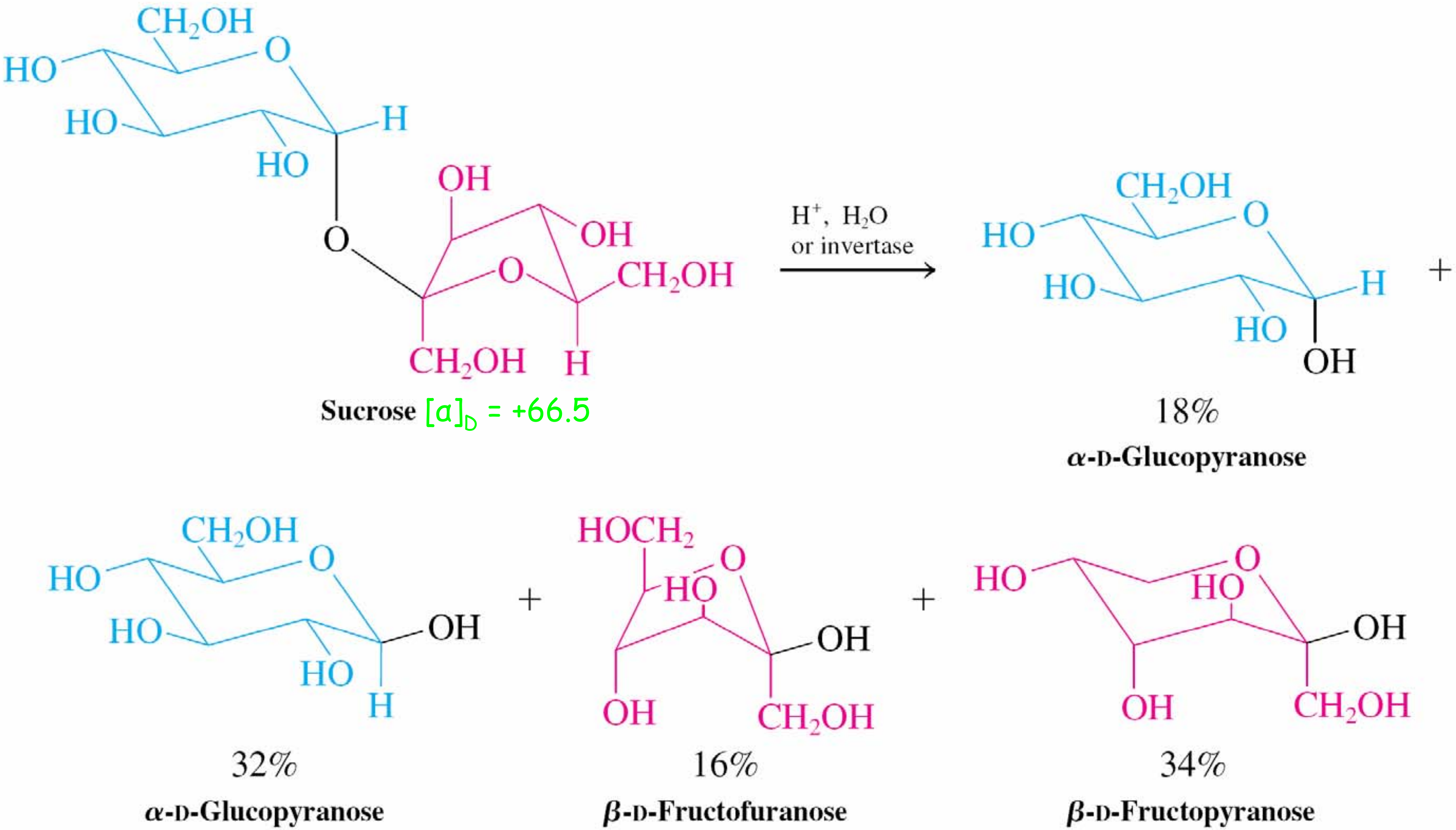
150 lb/ person/ year



Ether bridge between respective anomeric centers: Nonreducing

Sucrose, an α-D-glucopyranosyl-β-D-fructofuranose

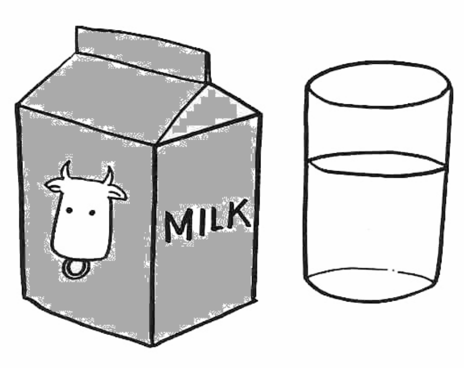
Inversion of Sucrose

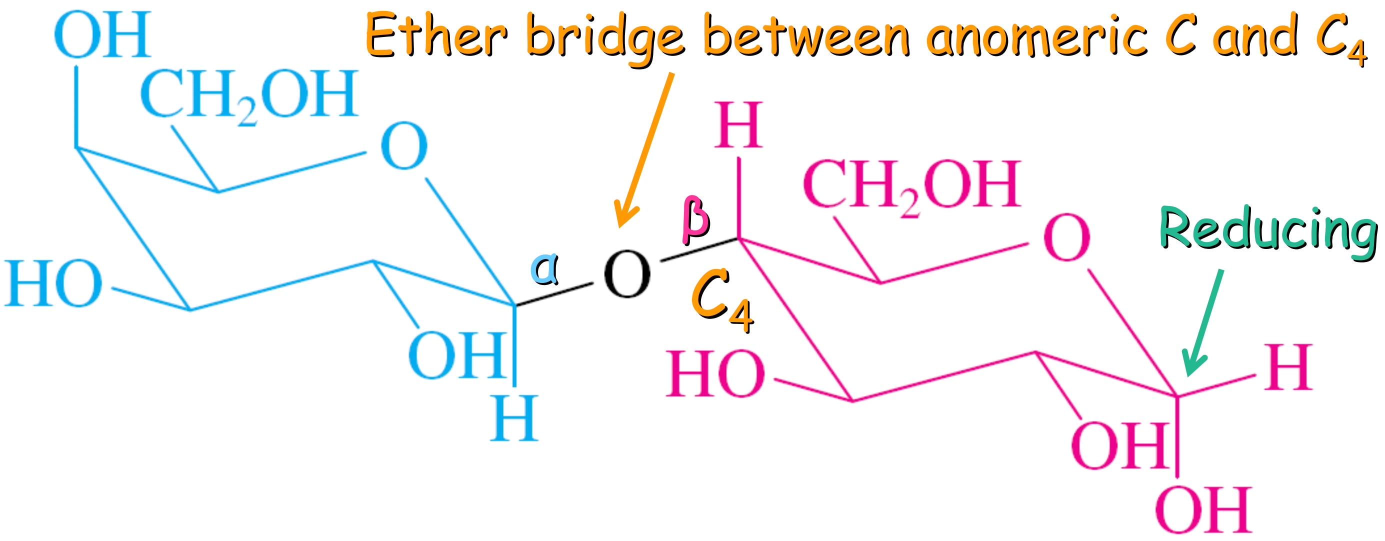


Sucrose $[\alpha]_D = +66.5$

$[\alpha]_D = -20$

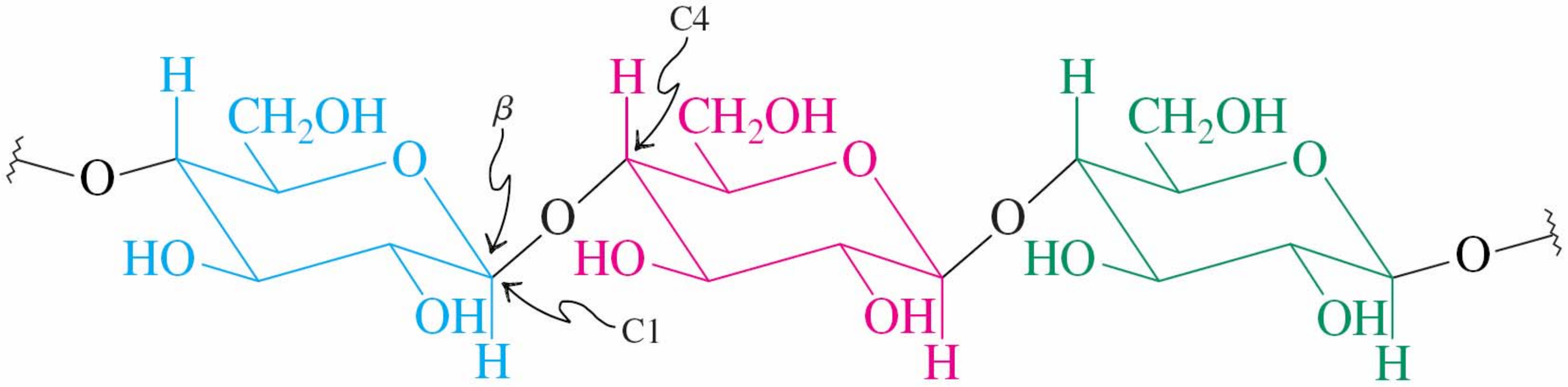
Lactose (milk sugar)





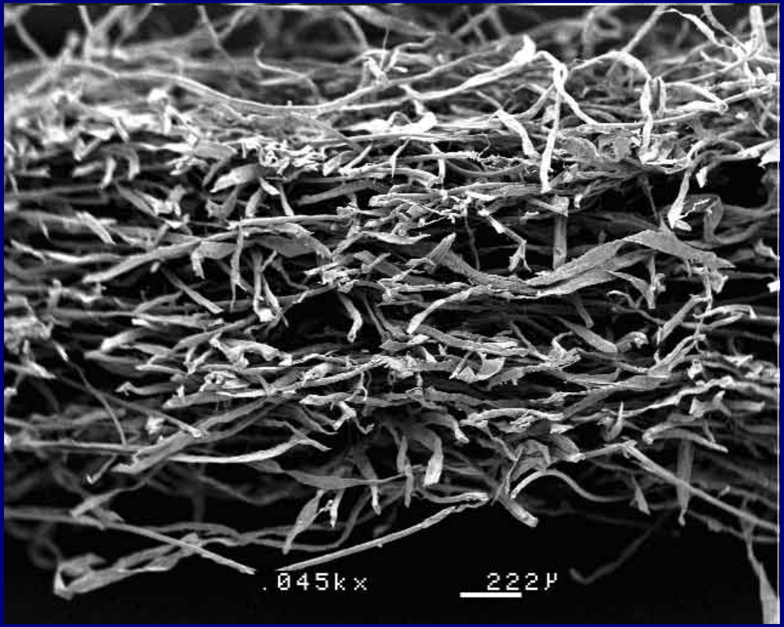
Crystalline α-lactose, a β-D-galactopyranosyl-α-D-glucopyranose

Cellulose: Sugar Polymer



Cellulose

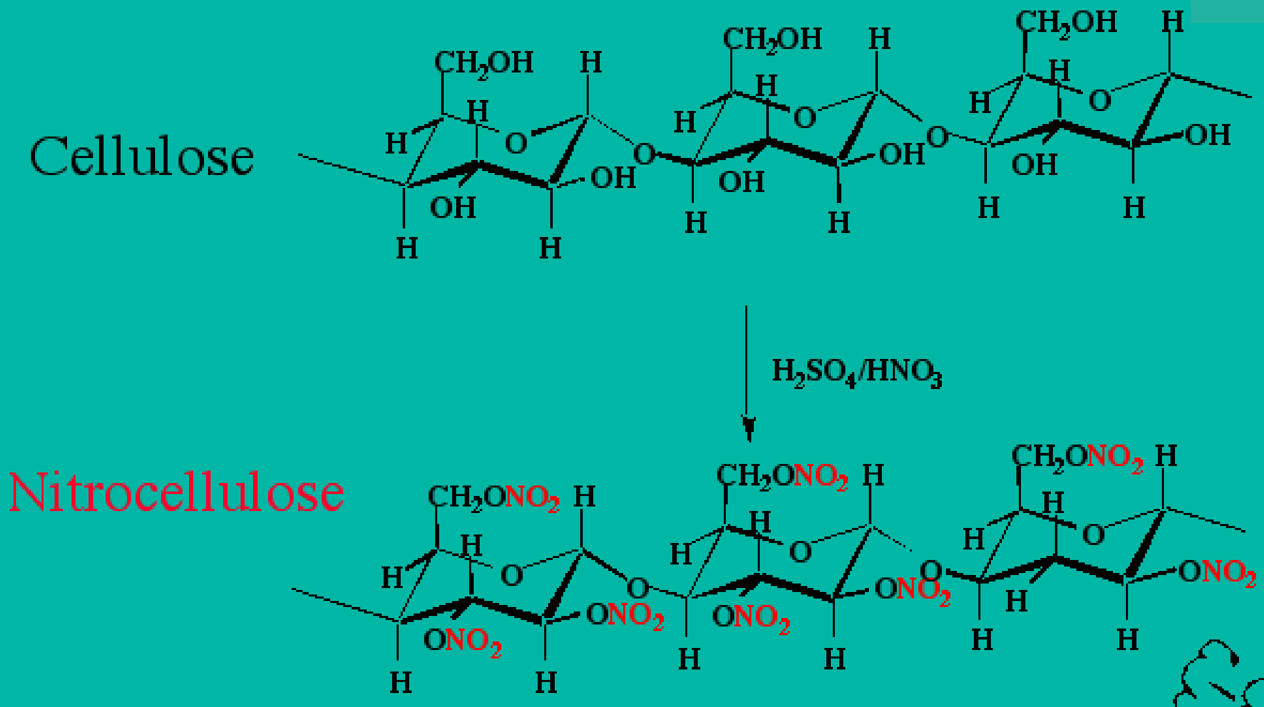
Molecular weight 500,000 (~3000 units) 1 unit = 178 molecular weight. Used in cell wall material: Rigid structure due to multiple hydrogen bonds.

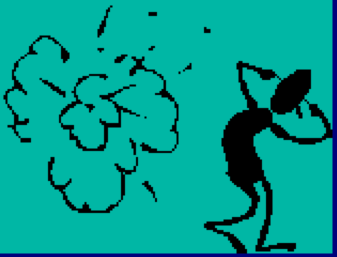


Nitrocellulose: Explosive

Major component of smokeless gunpowder (guncotton); used in photographic film.

Nitrocellulose



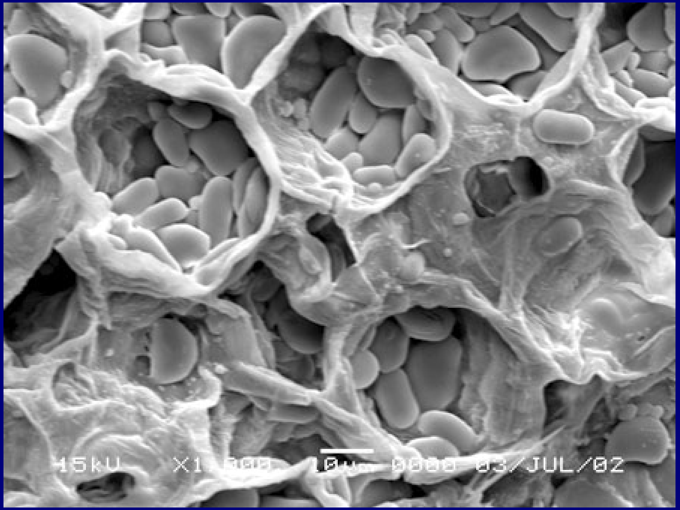


Christian F. Schönbein
1799-1868

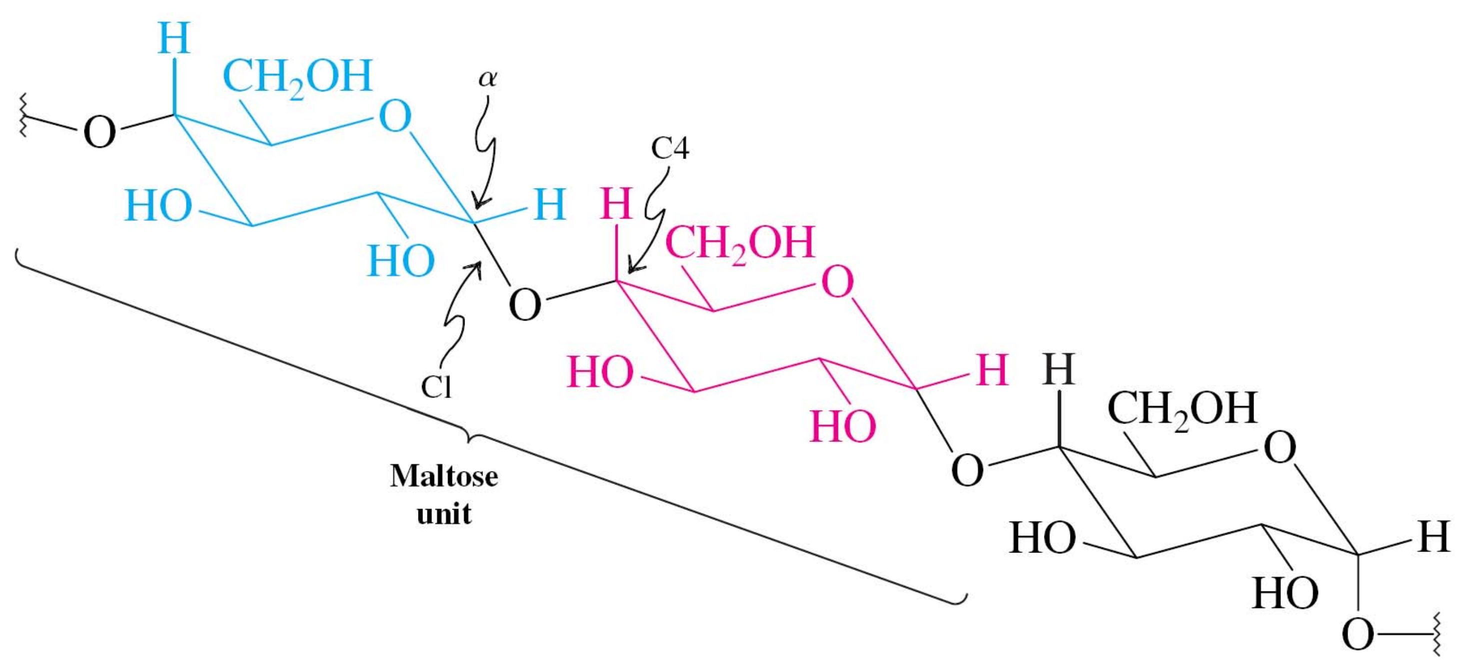
Henri Braconnot:
1832: HNO_3 + starch
Théophile-Jules Pelouze:
1838: HNO_3 + paper

Starch: Polyglucose with α–acetal links

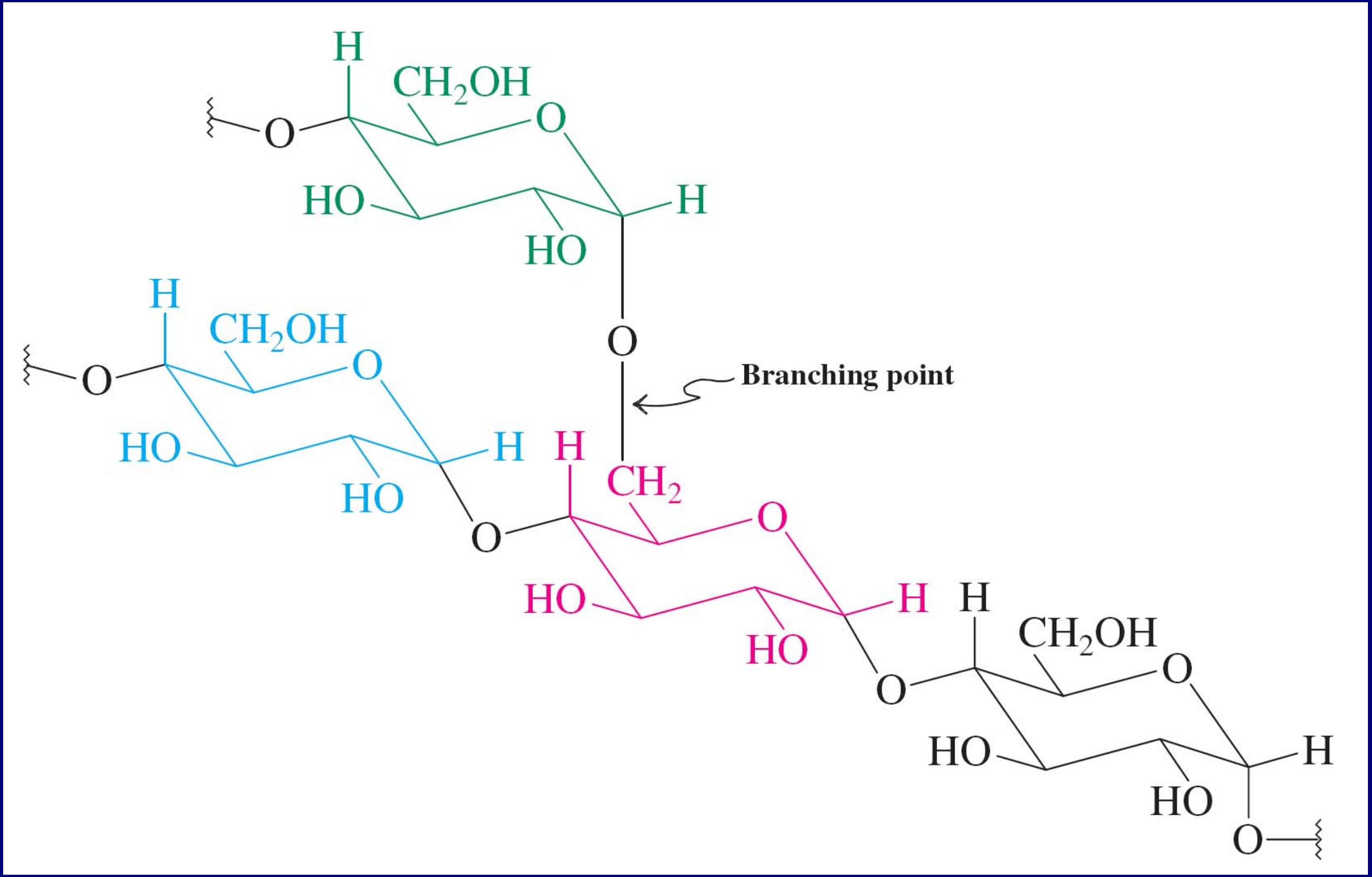
Constitutes fuel reserve in plants: Corn, potatoes, wheat (bread), rice. Hydrolyzes to glucose (sweat taste of bread in mouth). Two major components:



Amylose

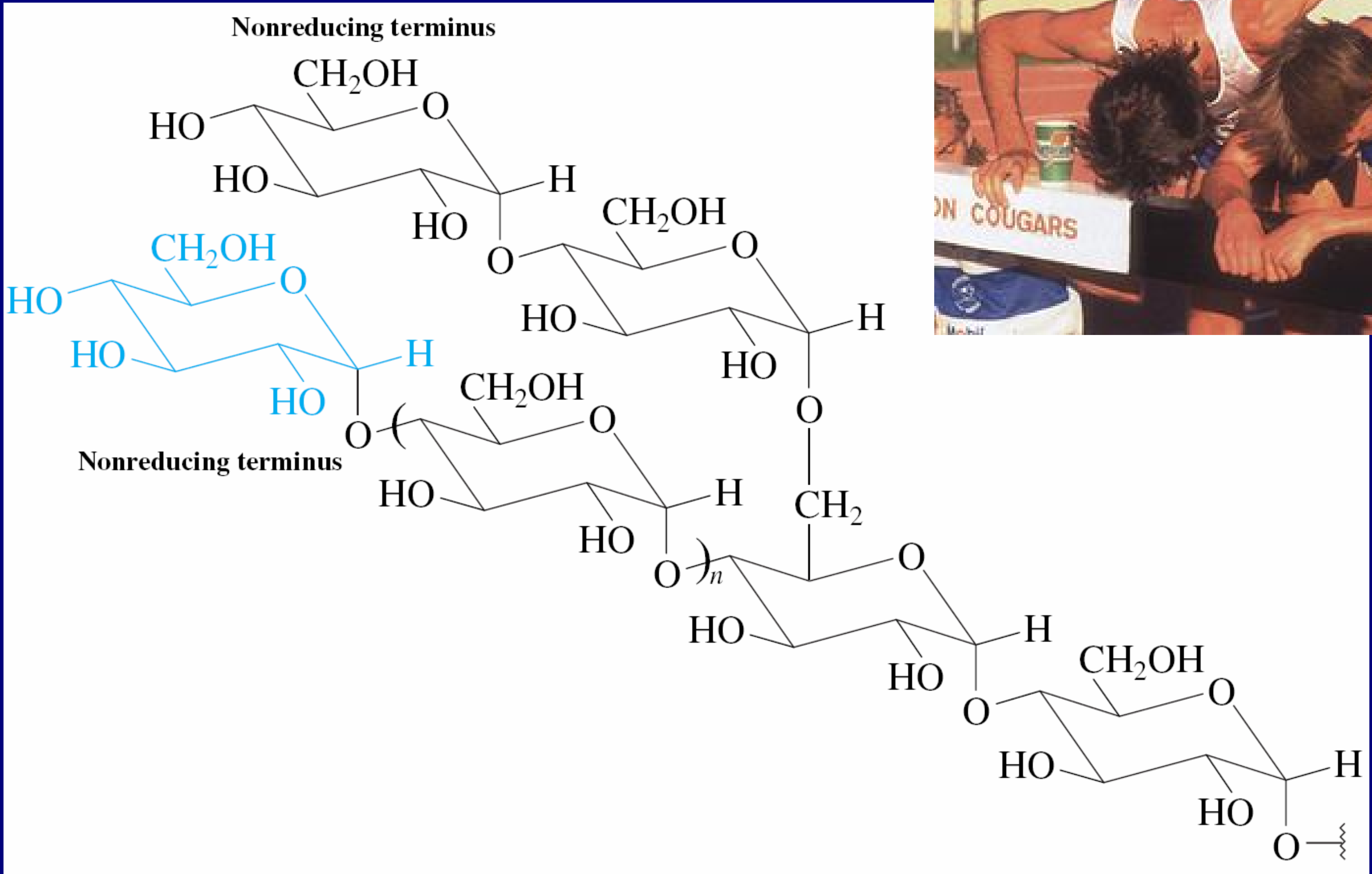


Amylopectin (has branches)



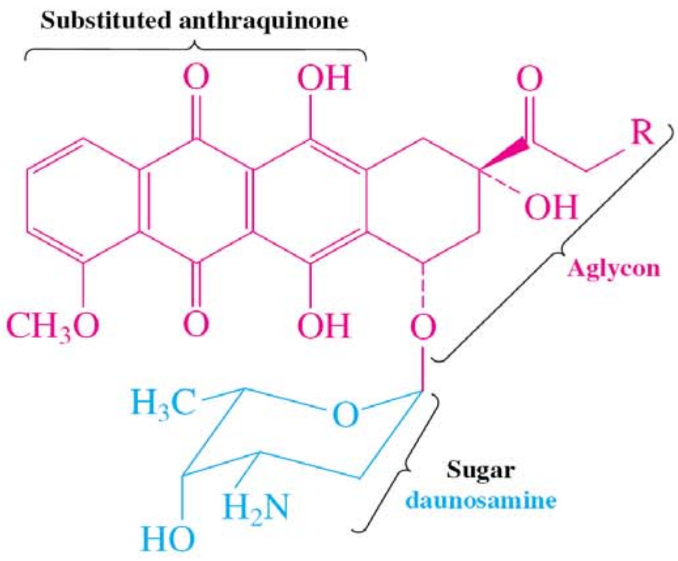
Human Fuel Tank: Glycogen

Provides immediate glucose during strain

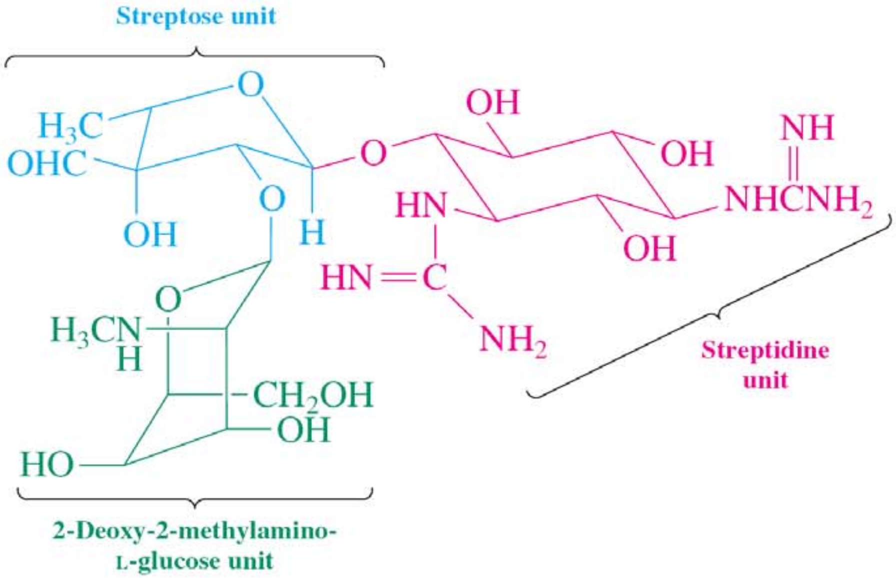


MW = 100 million

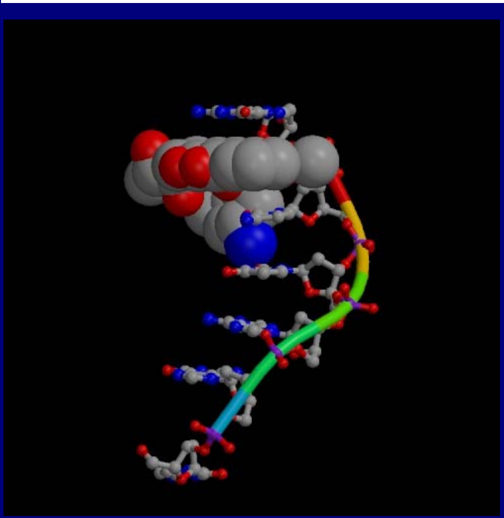
Sugars as water solubilizing groups in nature: Anthracycline anticancer agents and antibiotics



Adriamycin (R = OH)
Daunomycin (R = H)



Streptomycin



Anthracycline intercalates into DNA: Kills (tumor) cells

Streptomycin binds to the ribosome, causes misreading of genetic information