

CHE 3209 Natural Products

Carbohydrates -1

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 storage unit for solar energy.
- Most sugars have formula $\text{C}_n(\text{H}_2\text{O})_n$, “hydrate of carbon.”

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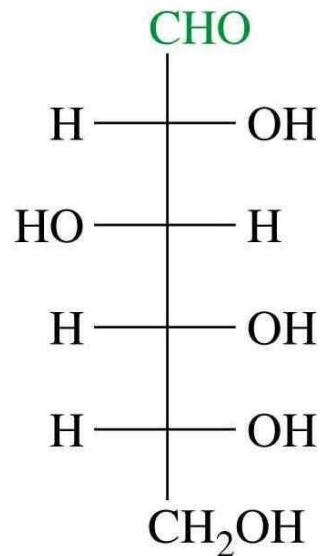
Classification of Carbohydrates

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

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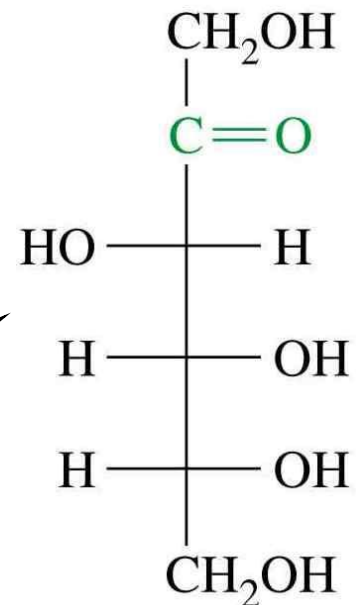
Monosaccharides

- Classified by:
 - aldose or ketose
 - number of carbons in chain
 - configuration of chiral carbon farthest from the carbonyl group



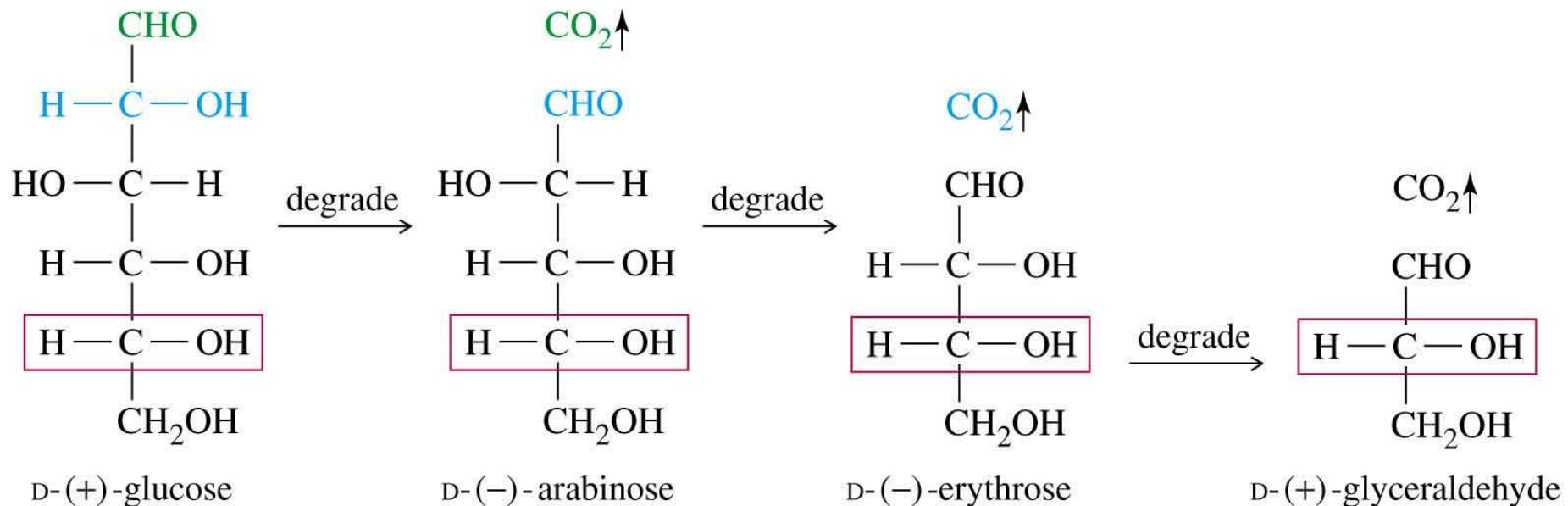
glucose, a
D-aldohexose

fructose, a
D-ketohexose

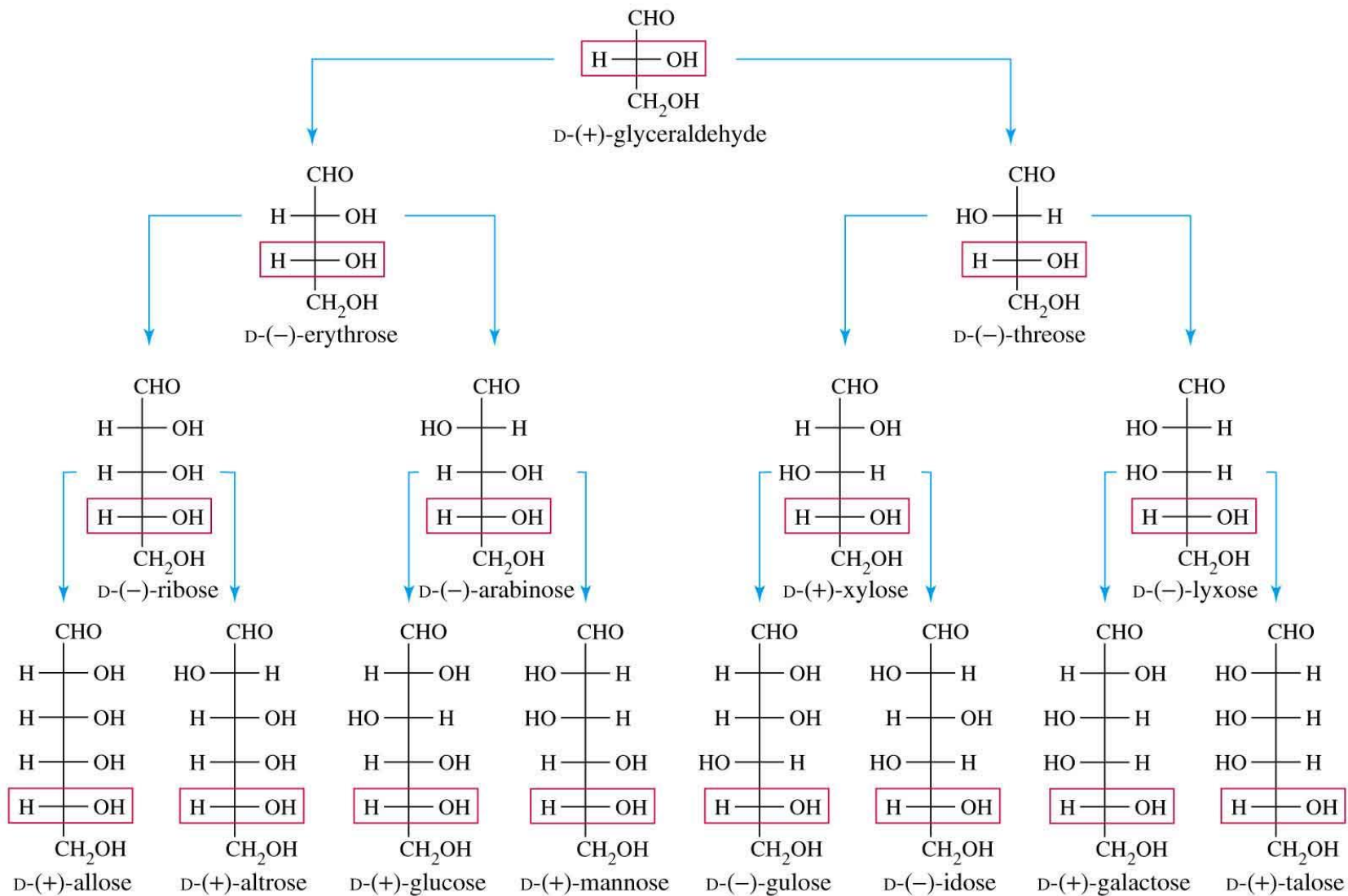


D and L Sugars

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

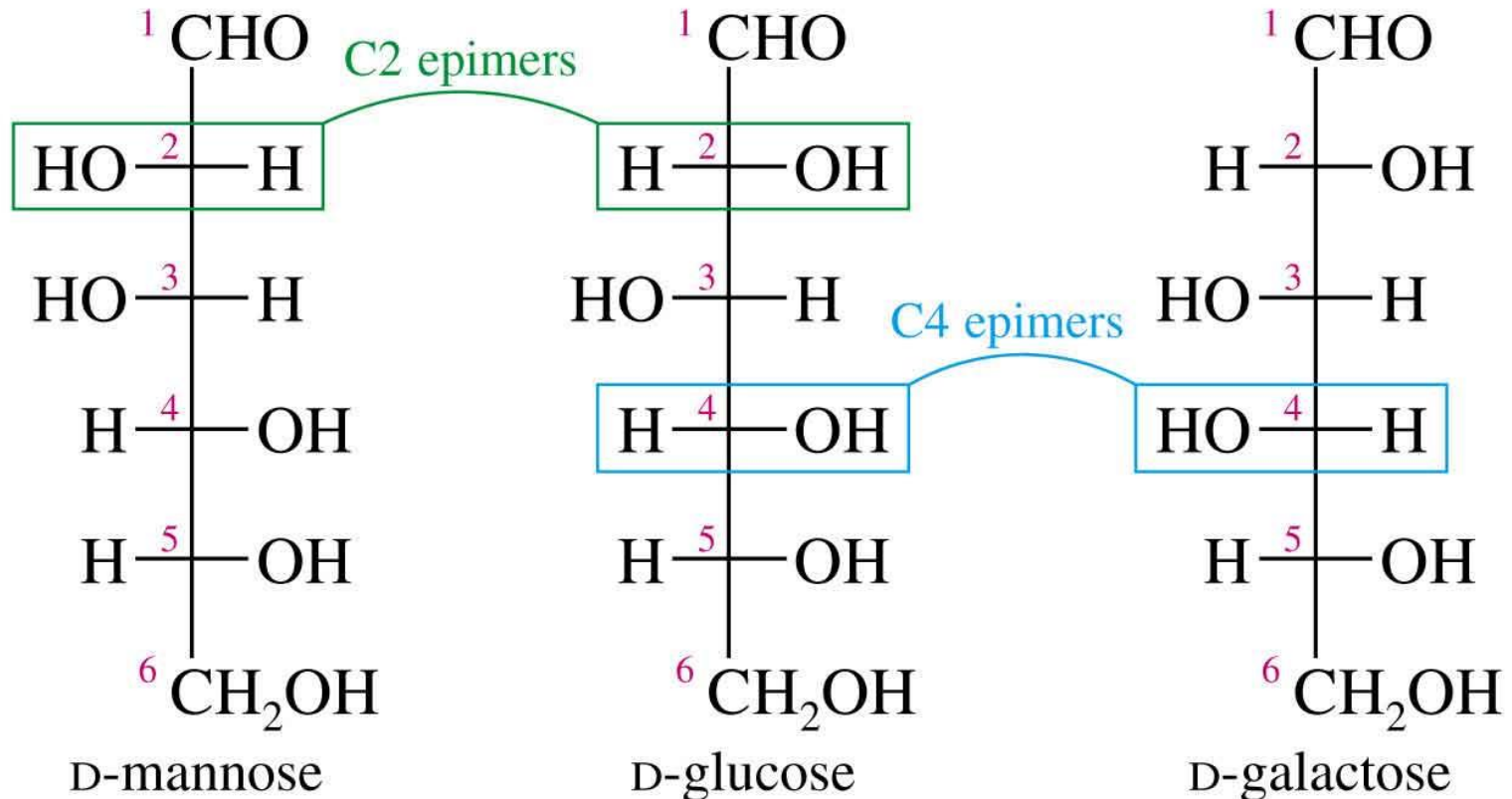


The D Aldose Family



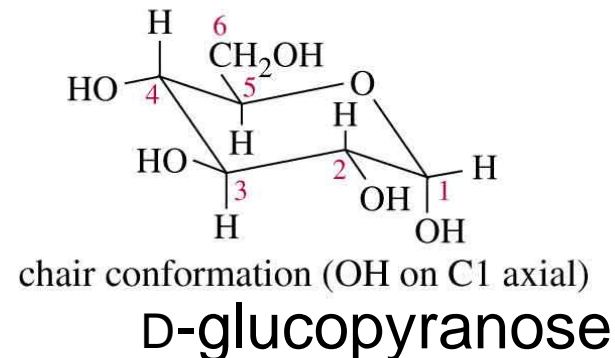
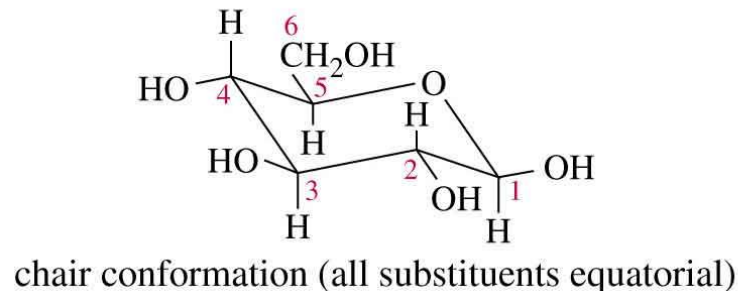
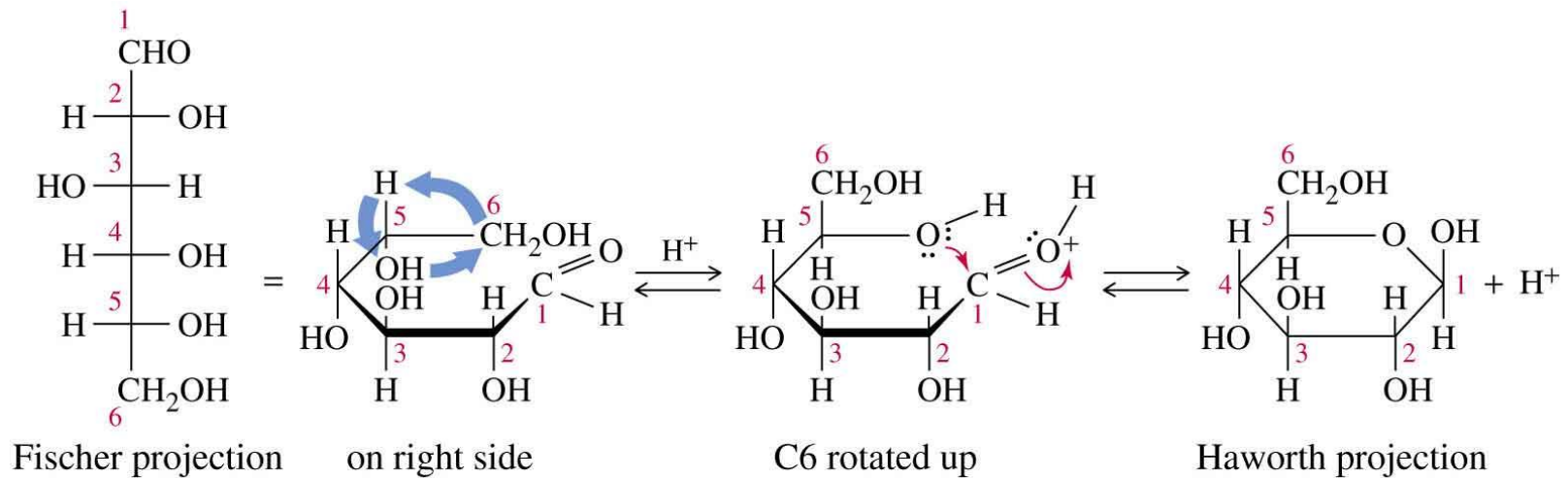
Epimers

Sugars that differ only in their stereochemistry at a single carbon (differ in configuration at one chiral center).

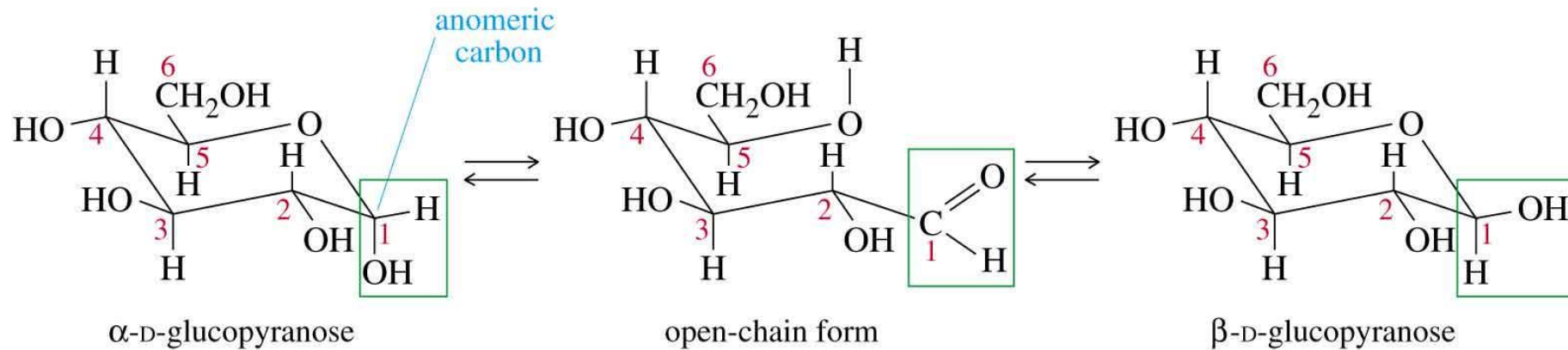


Cyclic Structure for Glucose

Glucose cyclic hemiacetal formed by reaction of -CHO with -OH on C5.

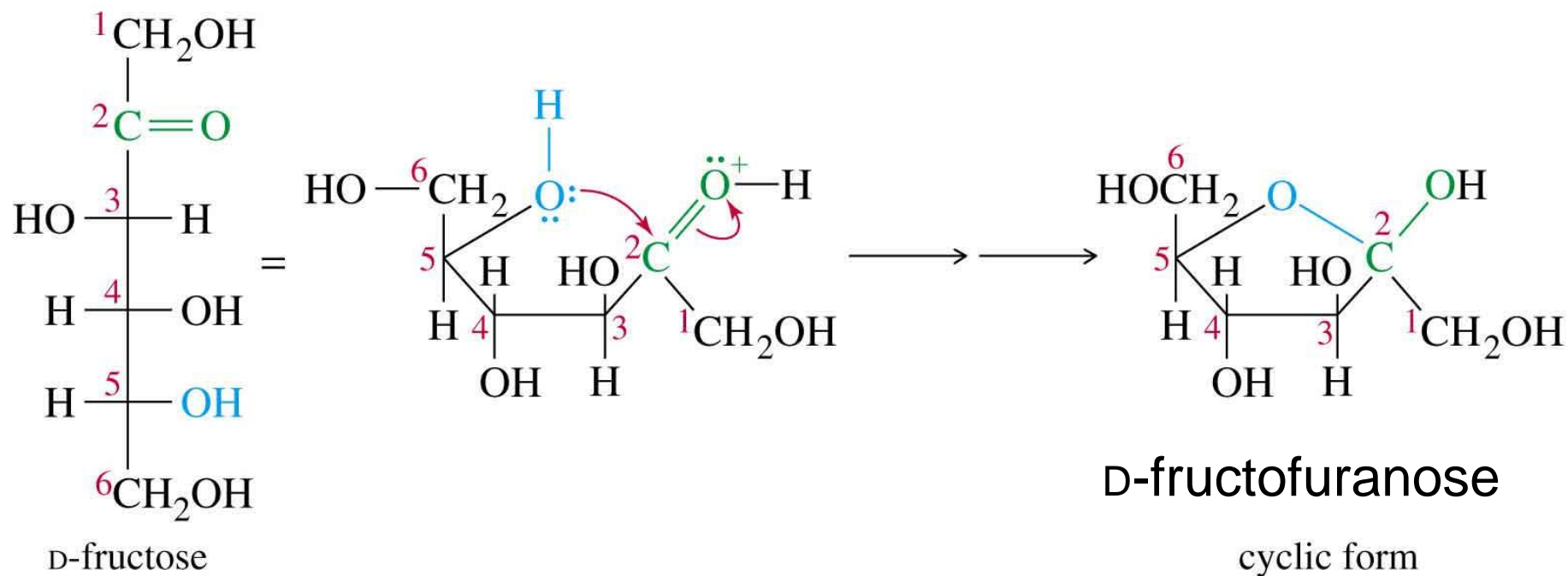


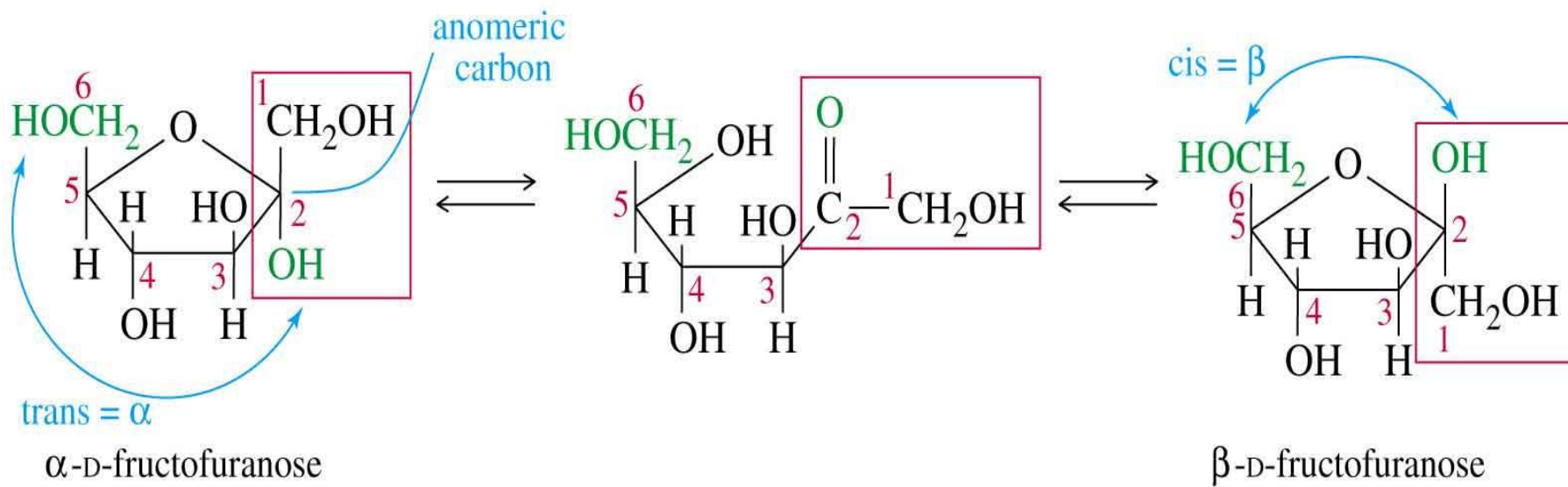
Anomers



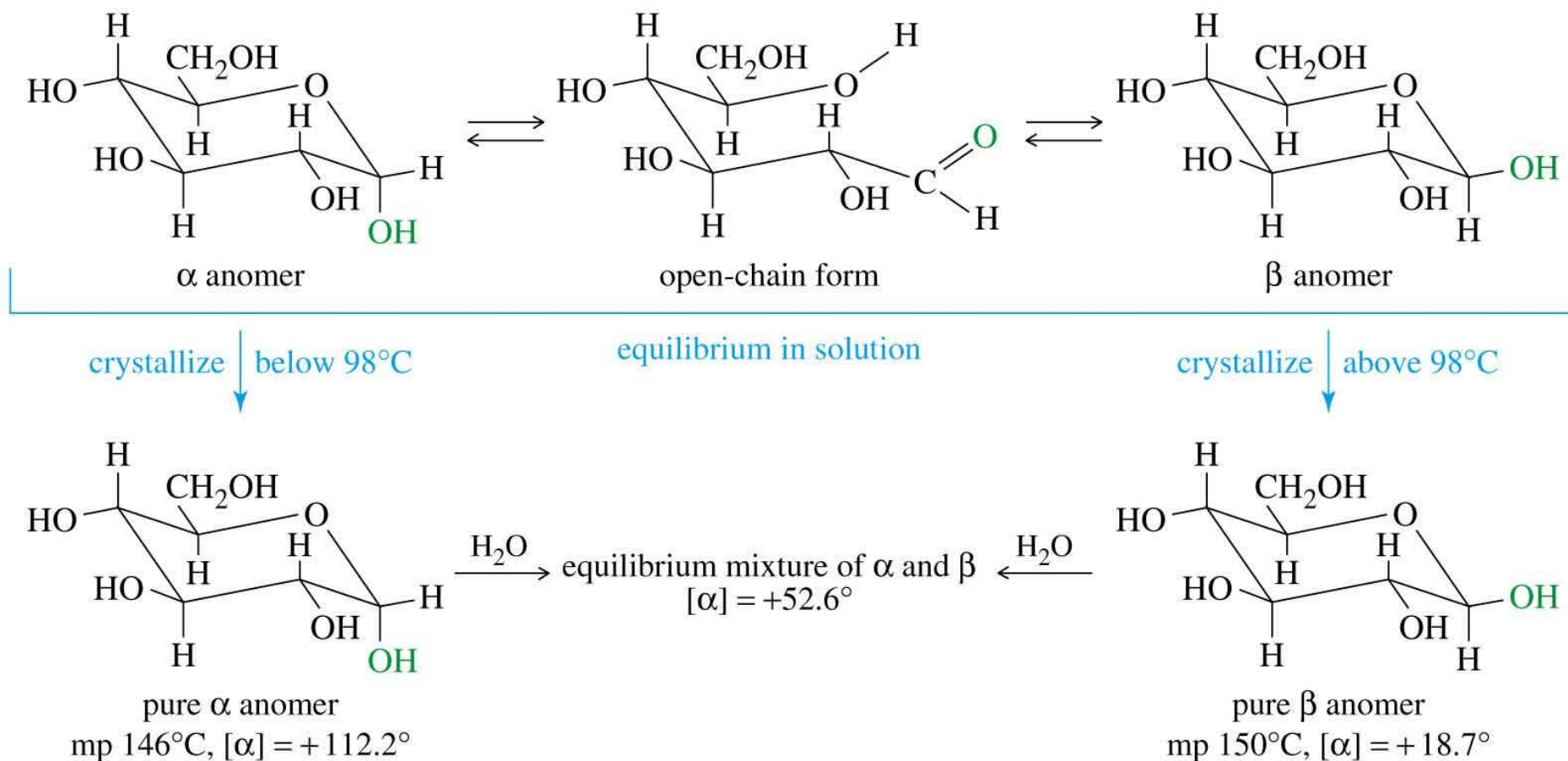
Cyclic Structure for Fructose

Cyclic hemiacetal formed by reaction of C=O at C2 with -OH at C5.



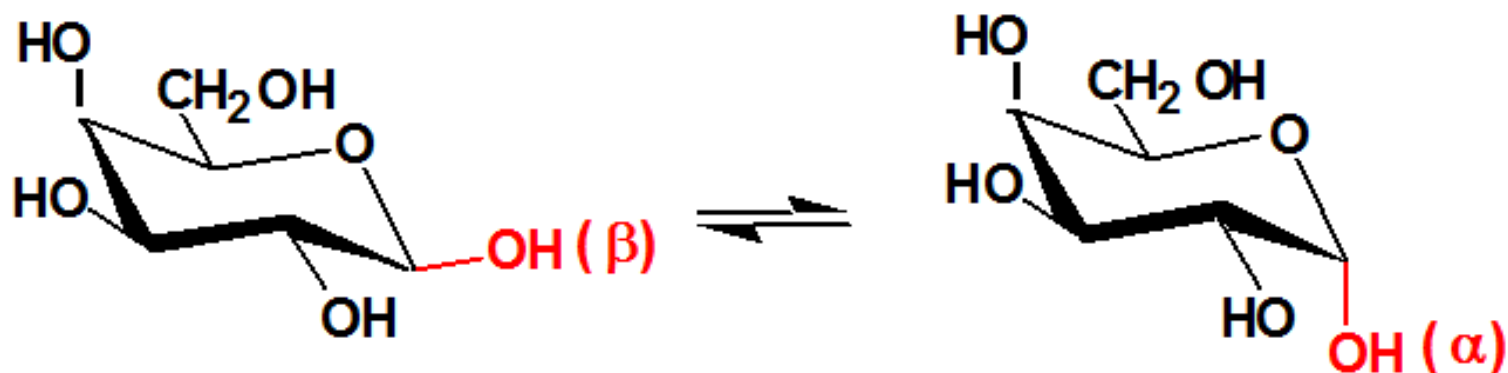


Mutarotation



Glucose also called dextrose ; dextrorotatory.

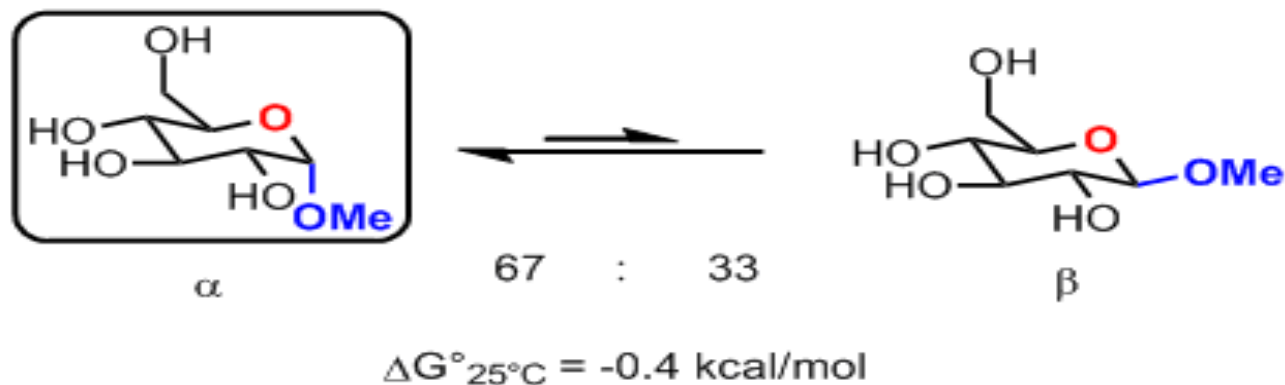
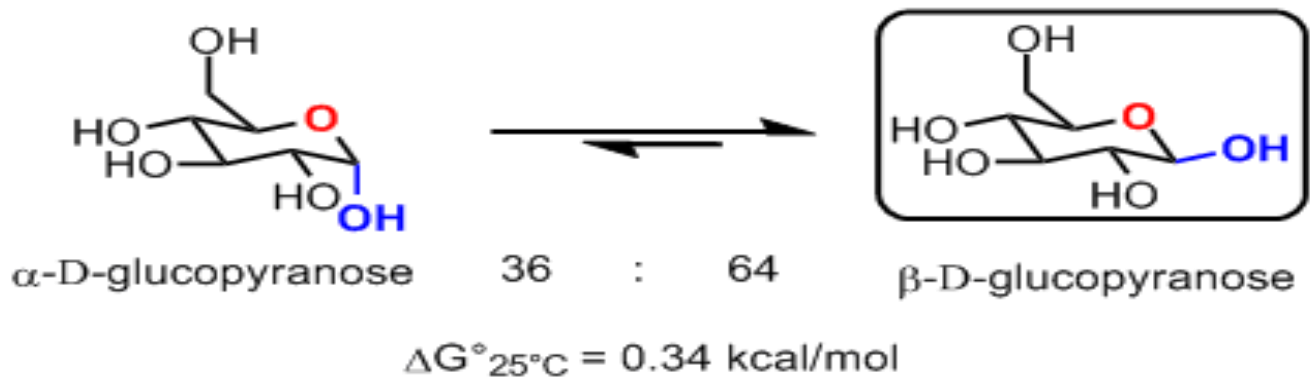
Monosaccharide	$[\alpha]$	$[\alpha]$ after Mutarotation	% Present at Equilibrium
α -D-glucose	+112.0	+52.7	36
β -D-glucose	+18.7	+52.7	64
α -D-galactose	+150.7	+80.2	28
β -D-galactose	+52.8	+80.2	72



D- Galactopyranose

Anomeric effect

- For unsubstituted glucopyranose, the β isomer is the lowest-energy isomer, and the α isomer is disfavored at a ratio of about 64:36.
- When the hydroxyl group at the acetal position is changed to a methoxy group, then the α isomer is the lowest-energy isomer at a ratio of about 67:33 – the selectivity reverse



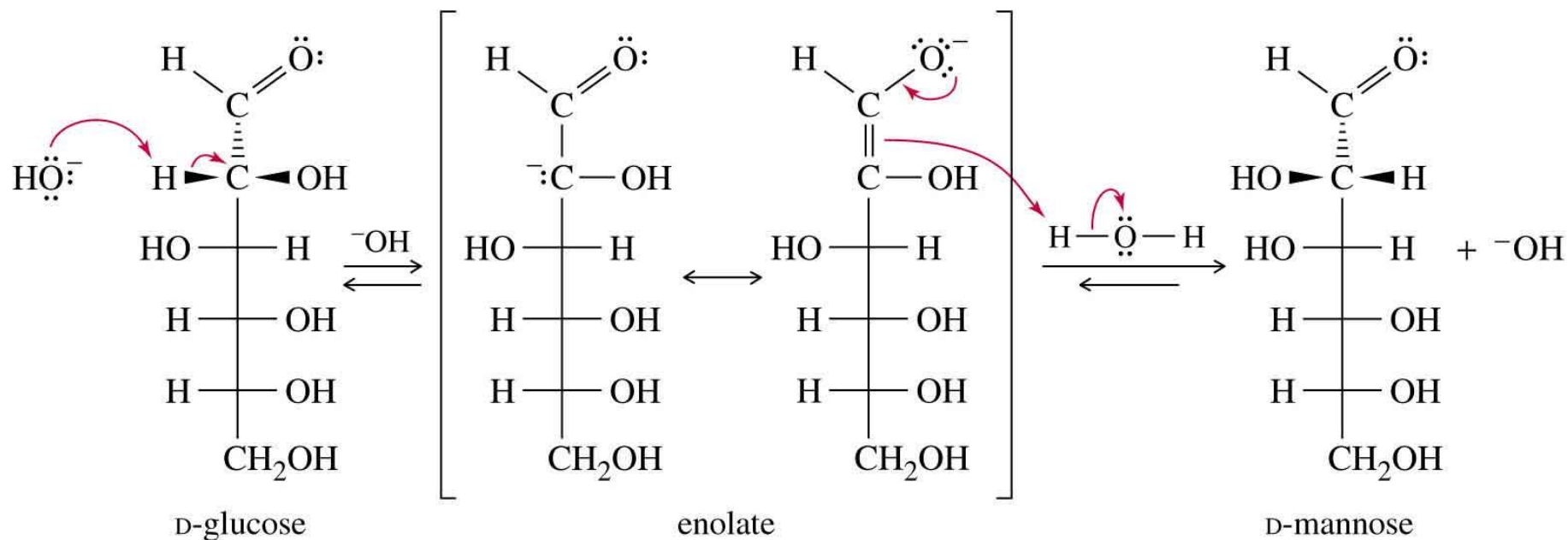
Reactions of Monosaccharides

1. Base Catalise Epimerization

In base, H on C2 may be removed to form enolate ion. Reprotonation may change the stereochemistry of C2.

Abstraction of the α proton

Reprotonation



2. Enediol Rearrangement

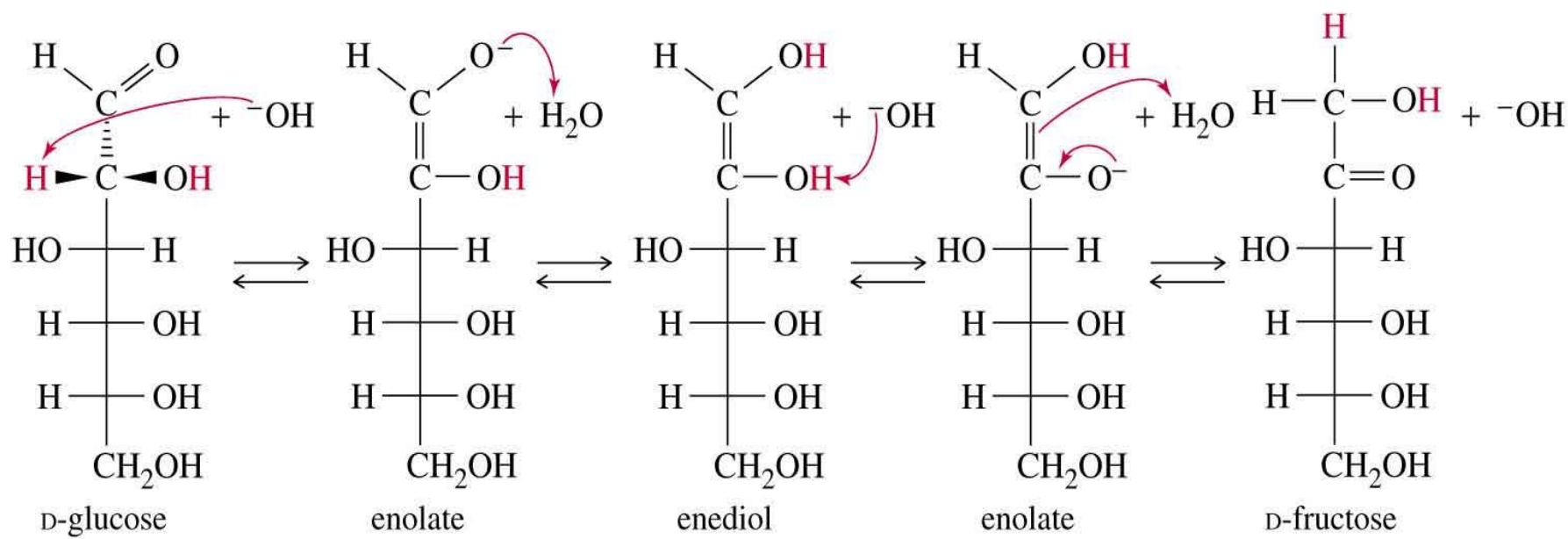
In base, the position of the C=O can be shift.

Step 1: Remove the α proton

Step 2: Reprotonate on O

Step 3: Deprotonate the O on C2

Step 4: Reprotonate on C1



- By using a base, a glucose solution can be changed either Mannose or Fructose or both. It can be known as a mixture of glucose, mannose and fructose.
- Acidic or neutral solutions of sugars can be used to prevent the reaction.

3. Reduction reactions

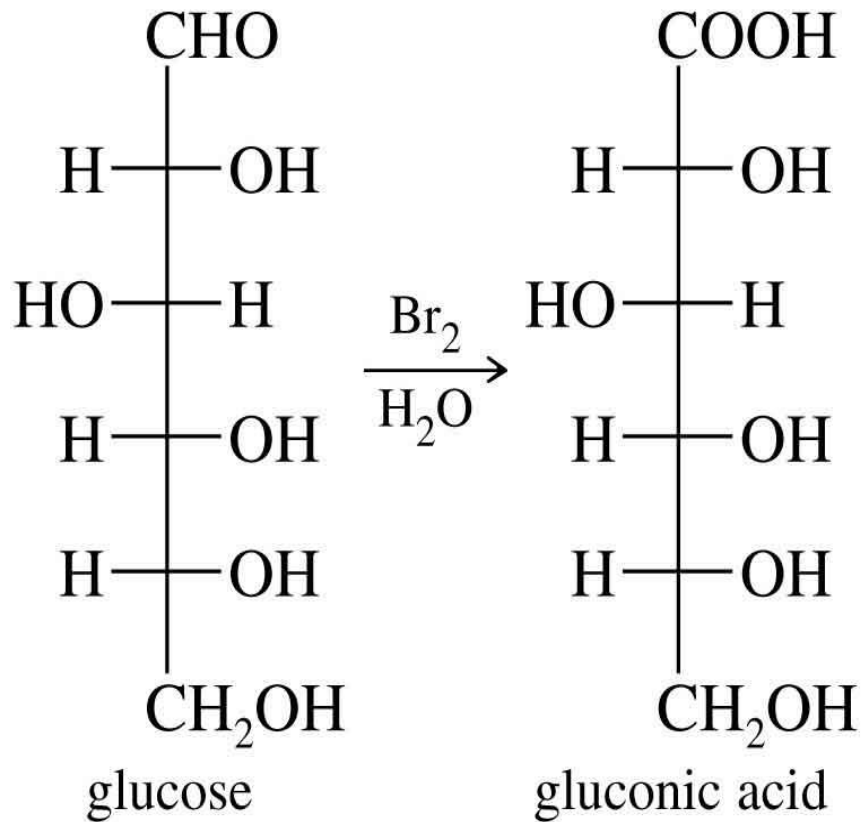
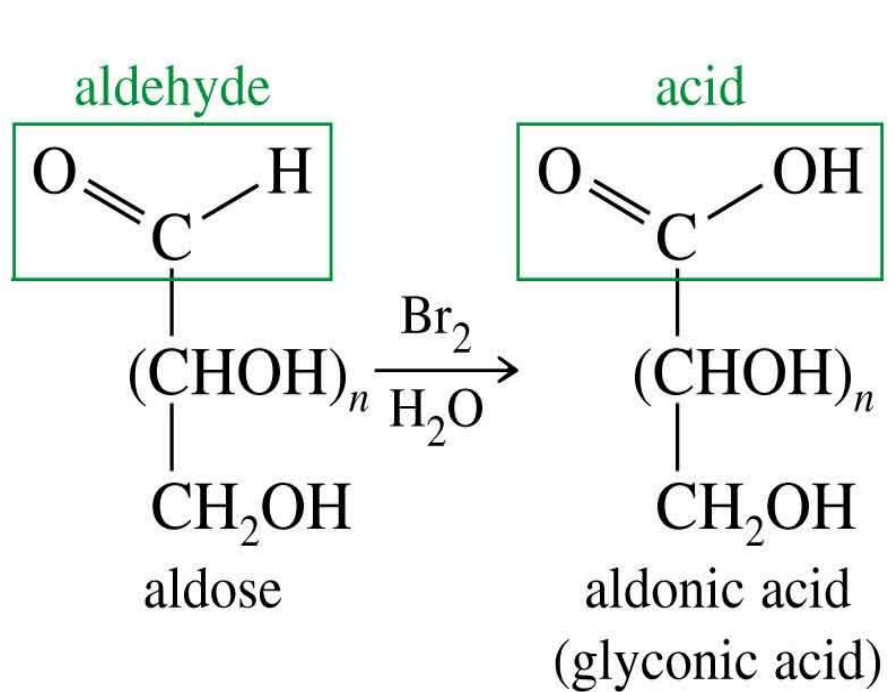
- C=O of aldoses or ketoses can be reduced to C-OH by NaBH_4 or H_2/Ni .
- Name the sugar alcohol by adding *-itol* to the root name of the sugar.
- Reduction of D-glucose produces D-glucitol, commonly called D-sorbitol.
- Reduction of D-fructose produces a mixture of D-glucitol and D-mannitol

(reactions.....)

4. Oxidation by Bromine

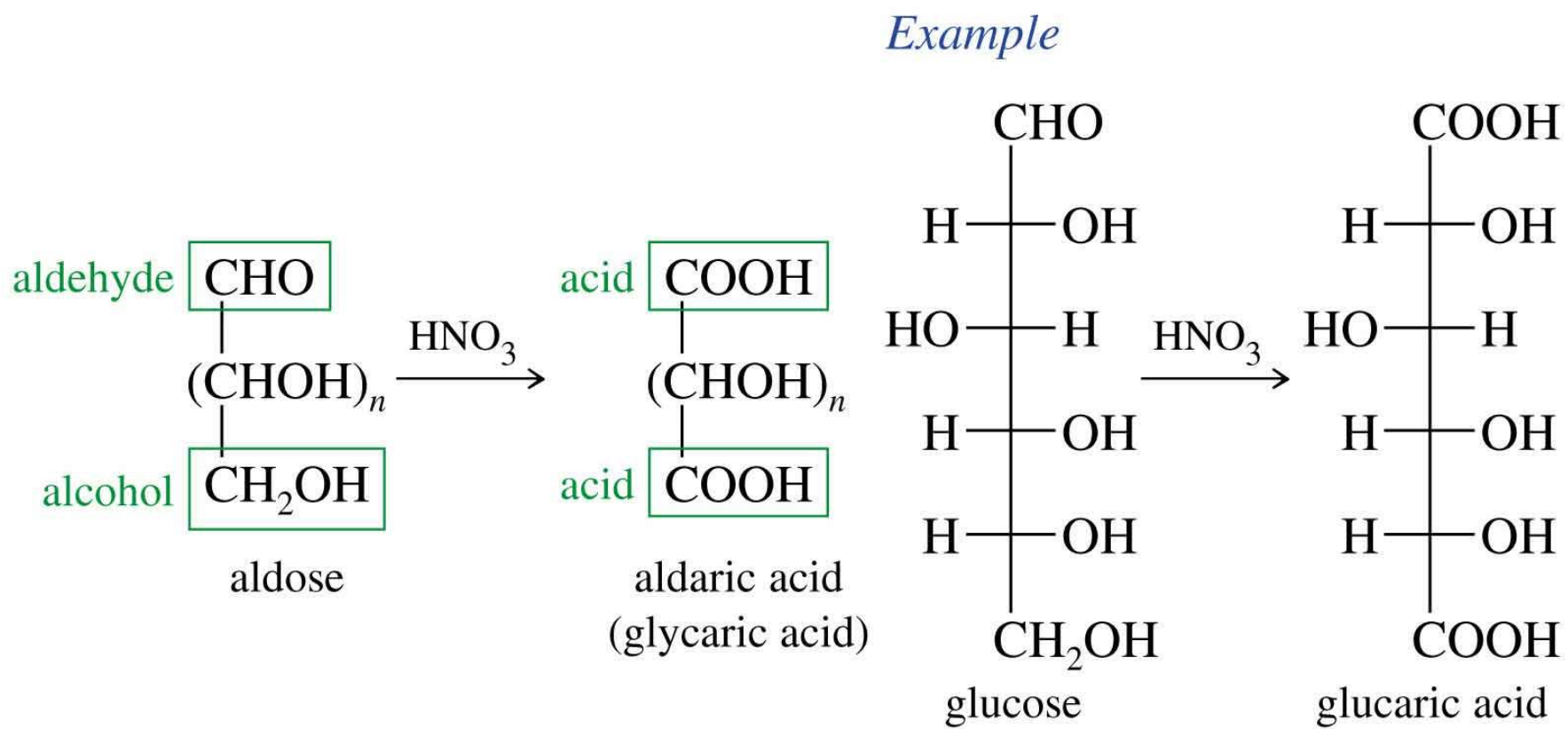
Bromine water oxidizes aldehyde, but not ketone or alcohol; forms aldonic acid. Open chain not stable, form cyclic structures (lactone)

Example



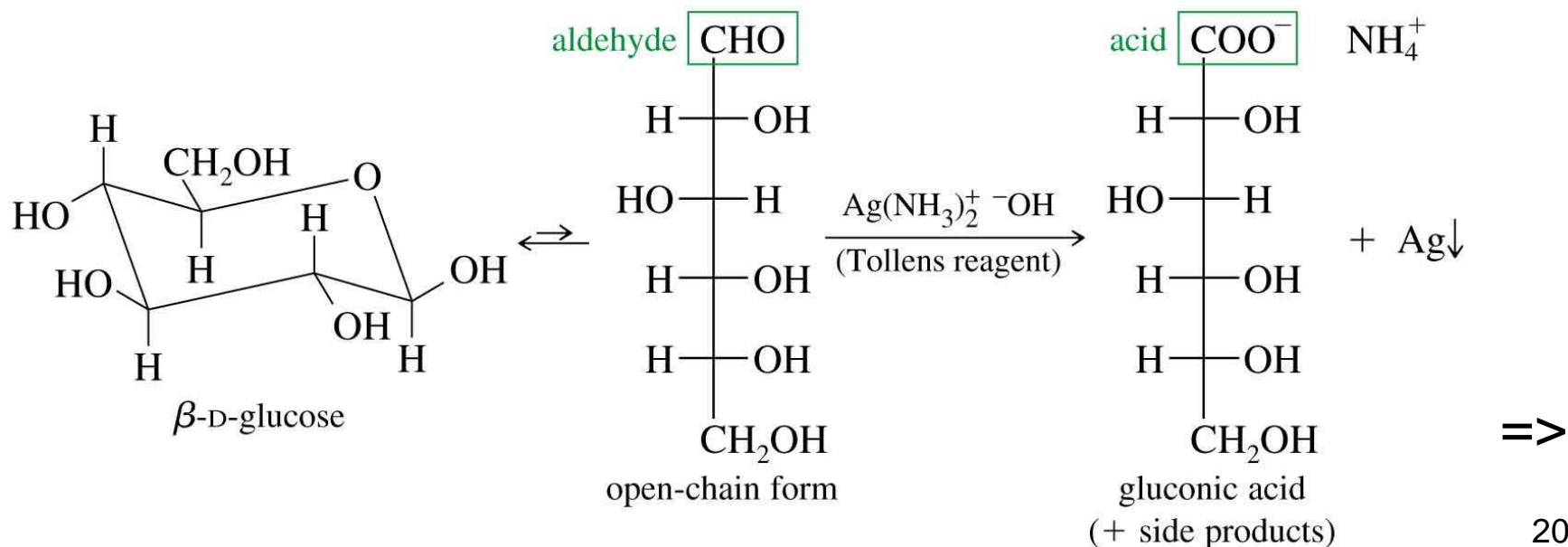
5. Oxidation with Nitric Acid

Nitric acid oxidizes the aldehyde and the terminal alcohol (primary alcohols) ; forms aldaric acid (dicarboxylic acid). Some times produce double lactones



Oxidation by Tollens Reagent

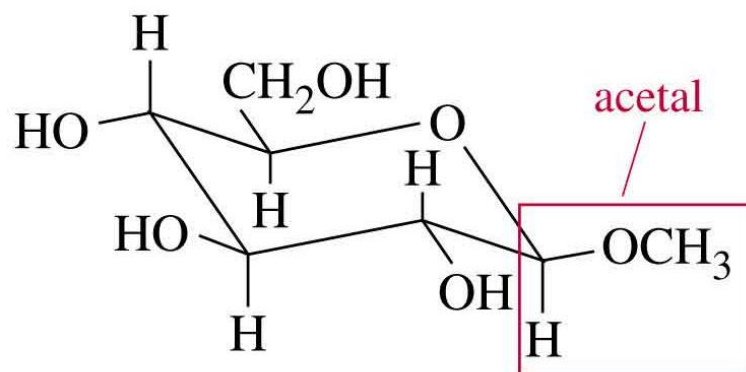
- Tollens reagent reacts with aldehyde, but the base promotes enediol rearrangements, so ketoses react too.
- Sugars that give a silver mirror with Tollens are called reducing sugars.



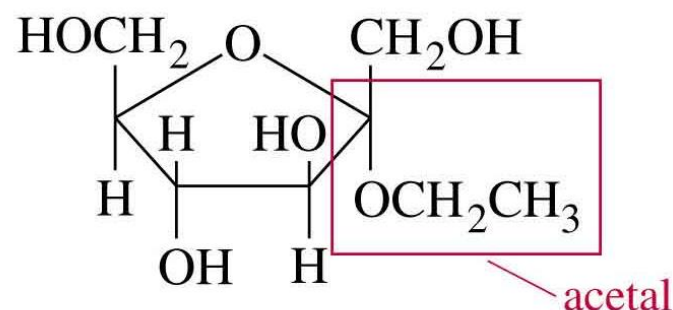
Nonreducing Sugars

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

Examples of nonreducing sugars



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

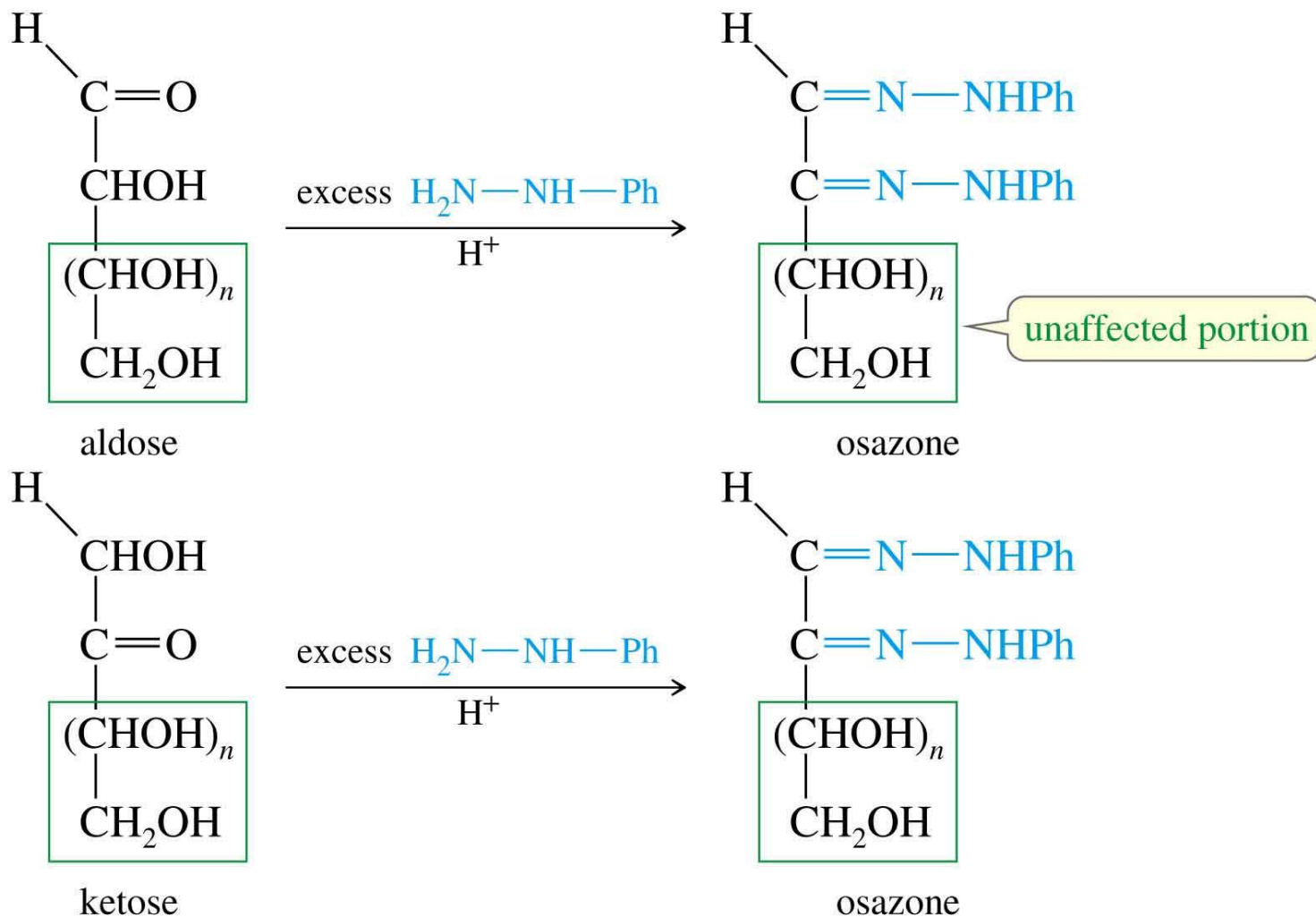


ethyl α-D-fructofuranoside
(or ethyl α-D-fructoside)

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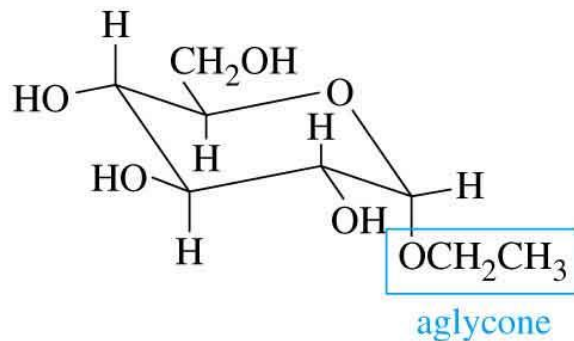
Osazone Formation

Both C1 and C2 react with phenylhydrazine.

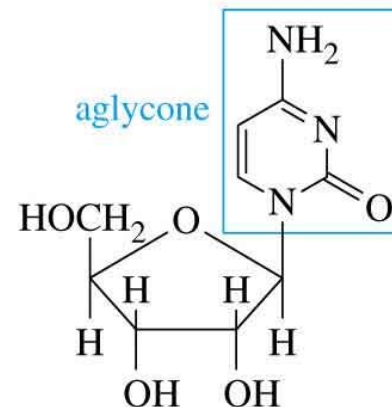


Formation of Glycosides

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



ethyl α -D-glucopyranoside

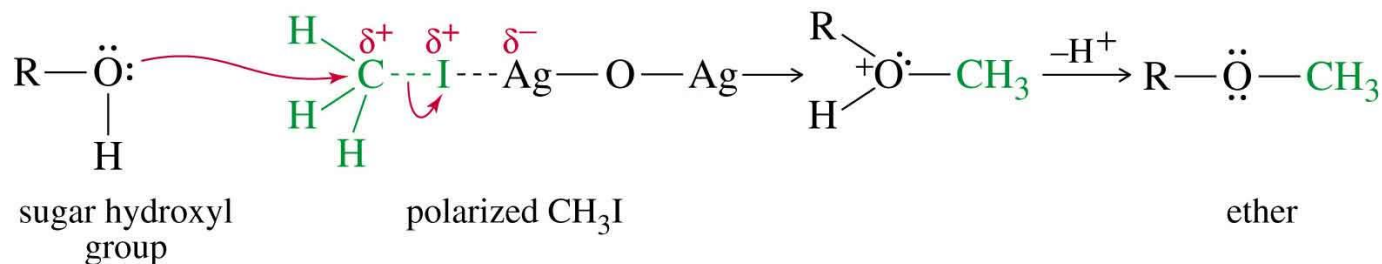


cytidine, a nucleoside (Section 23-21)

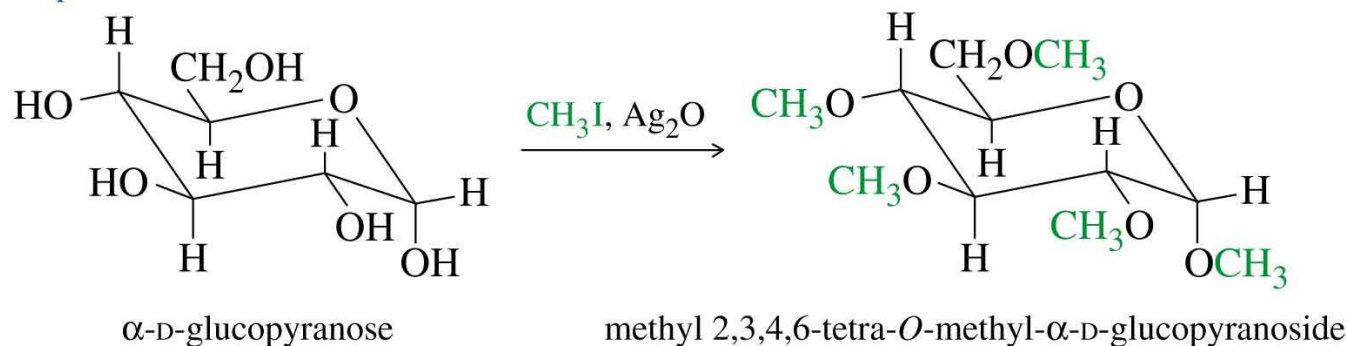
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Ether Formation

- Sugars are difficult to recrystallize from water because of their high solubility.
- Convert all -OH groups to -OR, using a modified Williamson synthesis, after converting sugar to acetal, stable in base.



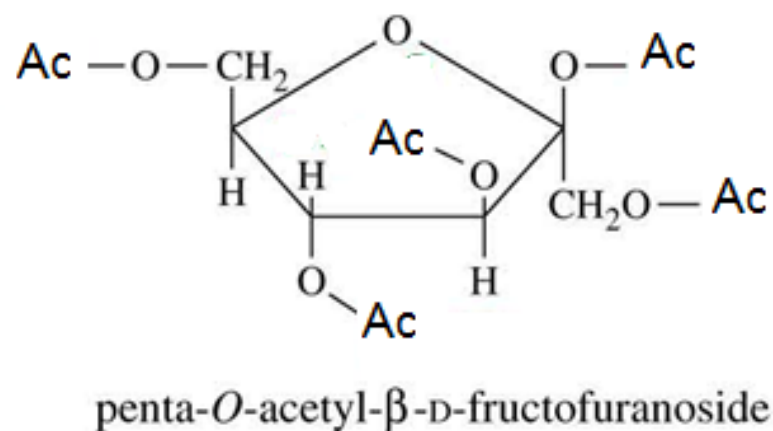
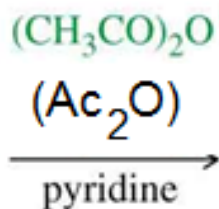
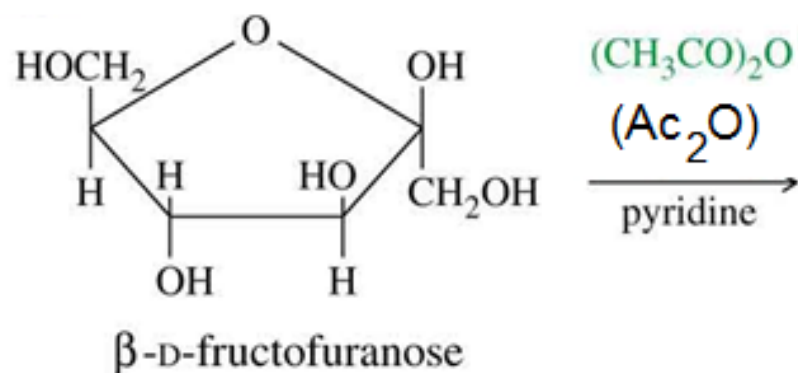
Example



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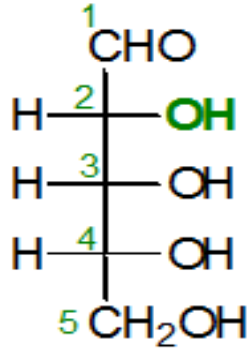
Ester Formation

Acetic anhydride with pyridine catalyst converts all the oxygens to acetate esters.

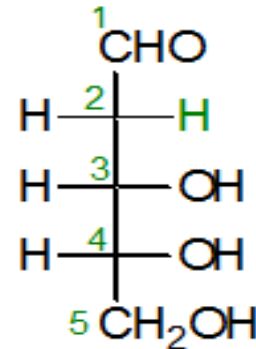


Deoxy Sugars.

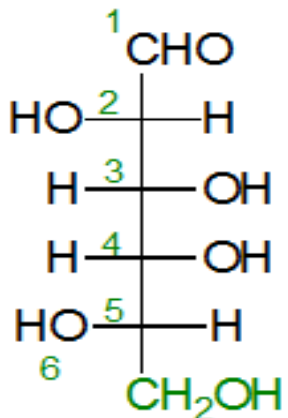
Sugars that are missing a hydroxy group.



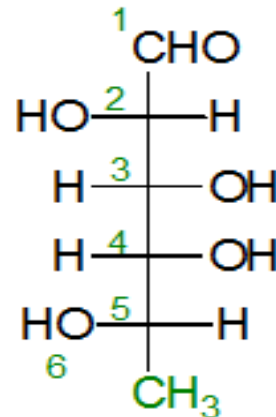
D-ribose



2-Deoxy-D-ribose



L-Galactose



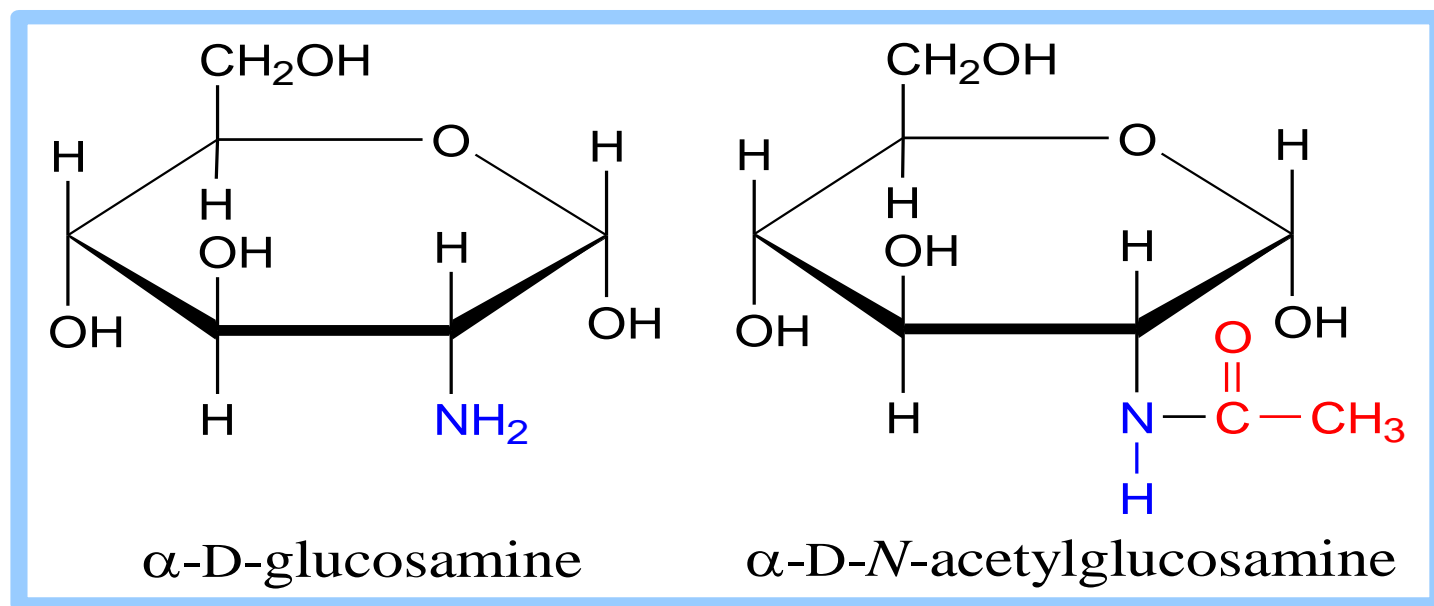
6-Deoxy-L-Galactose
(fucose)

Preparation.

Amino sugars

Amino sugar - an amino group substitutes for a hydroxyl.

The amino group may be **acetylated**, as in *N*-acetylglucosamine.

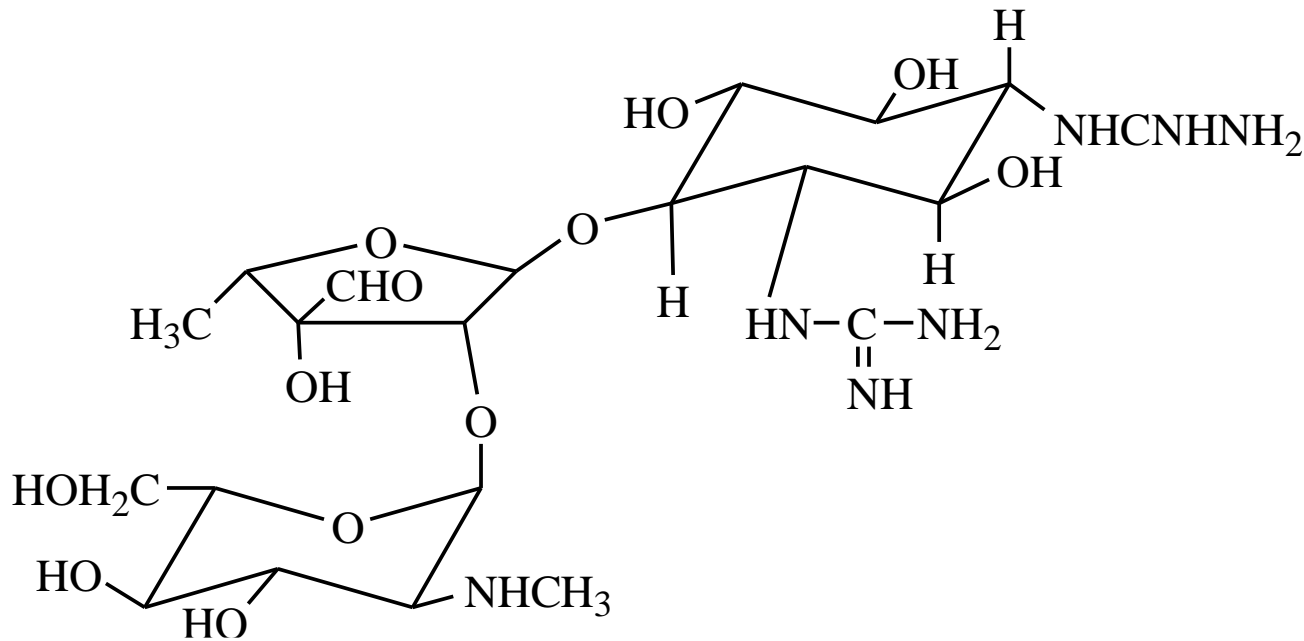


Amino sugars can be synthesized from suitably blocked sugars of SN2 type reaction of free hydroxyl group. Since OH⁻ is not really a good leaving group, it is converted into a better leaving group, generally p-Toluene sulfonyl group. The use of polar aprotic solvent like DMF with NH₃ to complete the reaction. (reaction....)

CARBOHYDRATE ANTIBIOTICS

Streptomycin: isolation of the carbohydrate antibiotic.

Streptomycin is made up of the following three subunits:



Other members of this family are antibiotics called kanamycins, neomycins, and gentamicins. All are based on an amino cyclitol linked to one or more amino sugars. The glycosidic linkage is nearly always α .

Thio Sugars

Synthesis of 6 thio-6-deoxy sugars can be achieved by displacement of 6-pToluene sulfonyloxy group of the suitably blocked sugar with thioxide anion (RS^-) in DMF

(reaction -1)

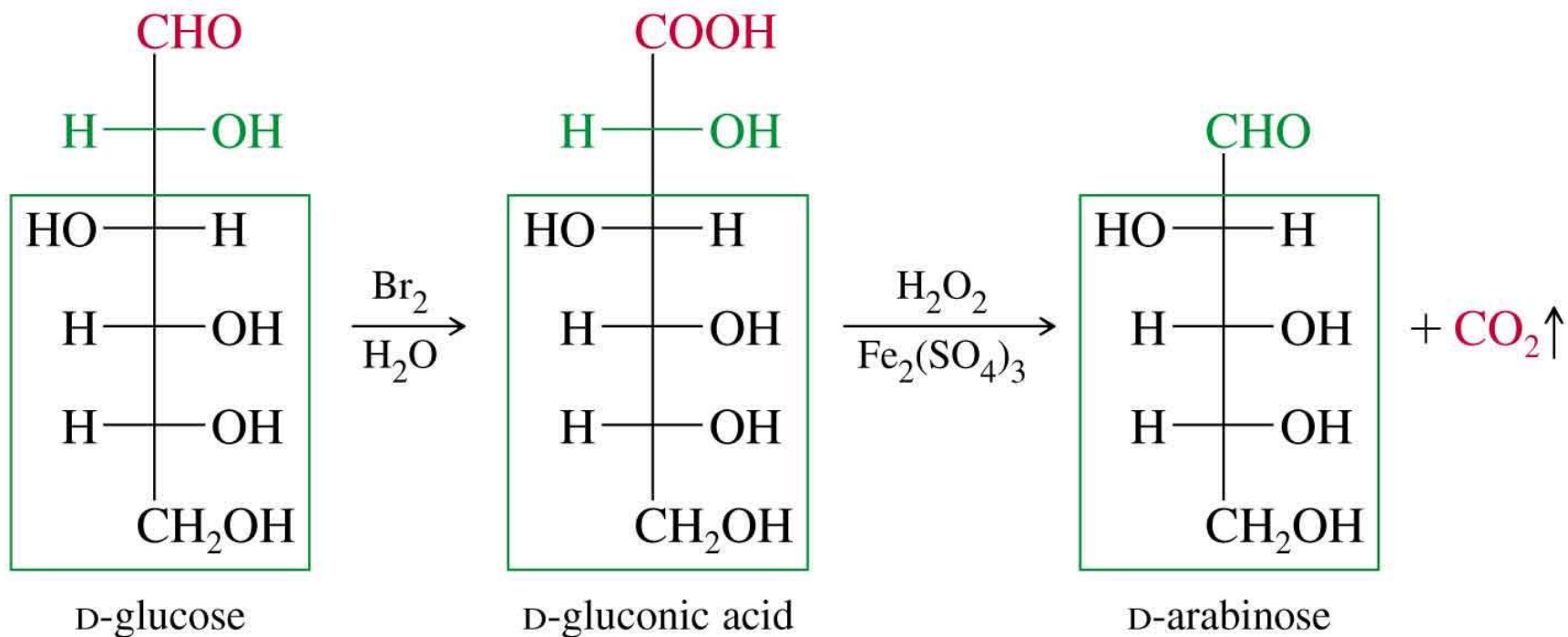
Displacement of p-Toluene sulfonyloxy group by thiocynate ($-\text{SCN}$) ion in acetone followed by hydrogenolysis, resulting thiocynate derivative.

(reaction -2)

Chain shortening Reaction

Ruff Degradation

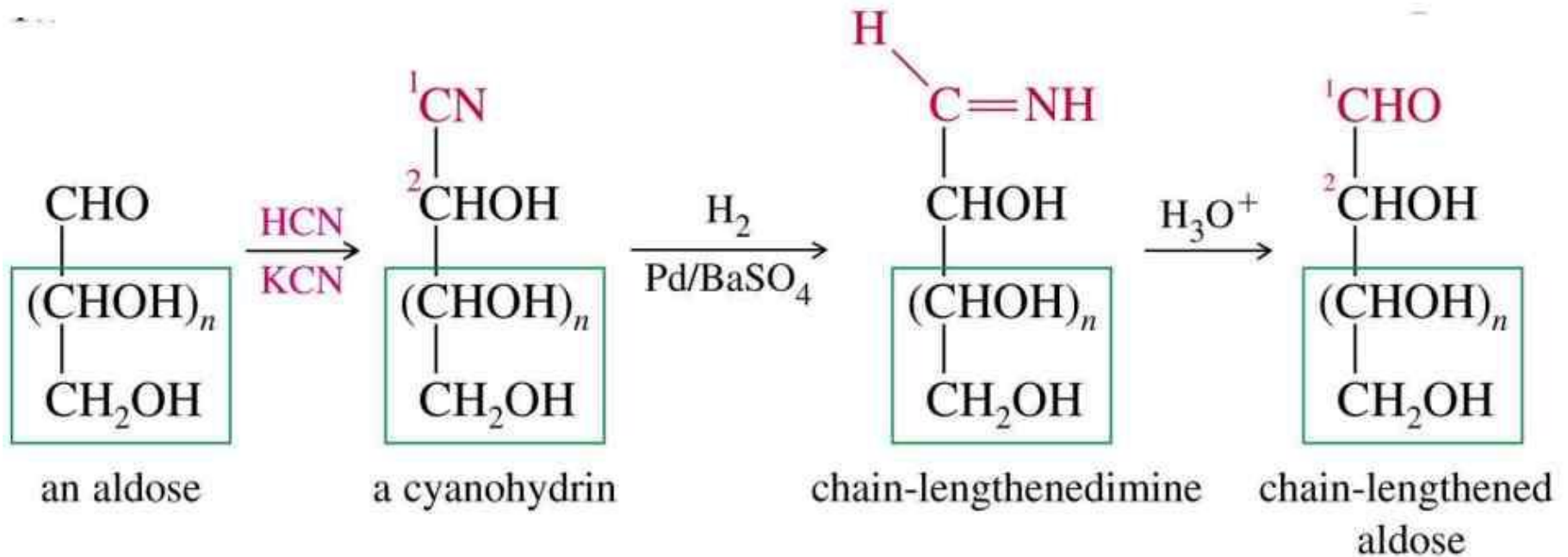
Aldose chain is shortened by oxidizing the aldehyde to -COOH, then decarboxylation. Degradation upto 3 carbons



Chain lengthening Reaction

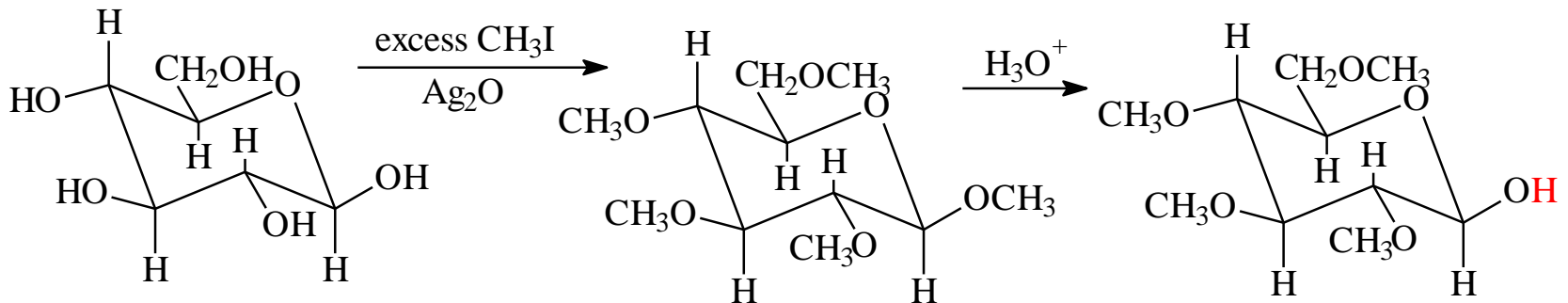
Kiliani-Fischer Synthesis

- This process lengthens the aldose chain.
- A mixture of C2 epimers is formed.



Determination of Ring Size

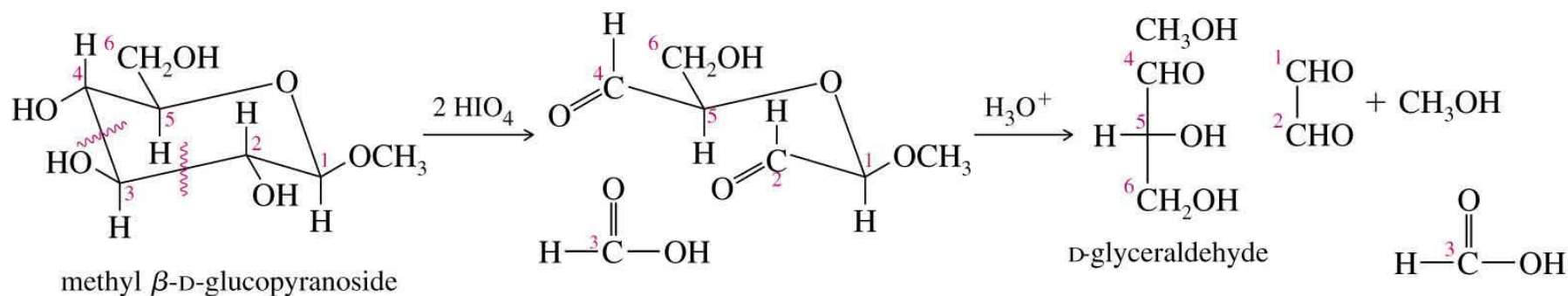
- Haworth determined the pyranose structure of glucose in 1926.
- The anomeric carbon can be found by methylation of the -OH's, then hydrolysis.



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Periodic Acid Cleavage

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

 \Rightarrow