CARBOHYDRATES OR SUGARS

- **A group of naturally occurring aldehydes / ketones, *formally* composed of C atoms and H_2O molecules in a ratio equal or close to 1 : 1**

general formula: $(CH_2O)_n$ ... or close

- **Immense biological importance of carbohydrates:**

blood group determinants
antigens, immune responses
cancer cell markers
energy storage & generation
nucleic acids, glycoproteins
materials & fibers
extracellular support matrices
genetic disease

SIMPLE SUGARS OR MONOSACCHARIDES

- **Carbohydrates of general formula $(CH_2O)_n$ $(3 \leq n \leq 9)$ that possess a structure based on a linear polyhydroxy aldehyde (aldoses) or polyhydroxy ketone (ketose)**

$HOCH_2–(CHOH)_x–CHO$ — an aldose

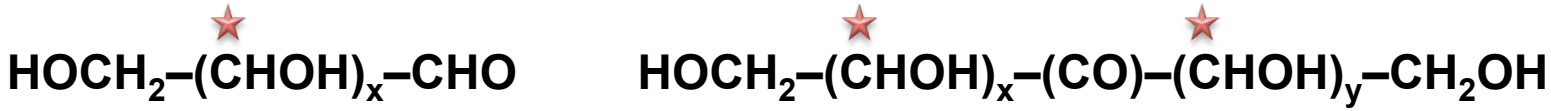
$HOCH_2–(CHOH)_x–(CO)–(CHOH)_y–CH_2OH$ — a ketose

- **Triose, tetrose, pentose, hexose, heptose, octose, nonose: a monosaccharide that incorporates a total of 3, 4, 5, 6, 7, 8 or 9 carbon atoms**

Note: most monosaccharides of biological importance contain 5 or 6 C atoms. Monosaccharides incorporating more that 6 C atoms are known, but they are rare, and rarity increases with an increasing number of C atoms.

STEREOISOMERISM IN MONOSACCHARIDES

- **Monosaccharides as chiral molecules due to the presence of multiple stereogenic centers**



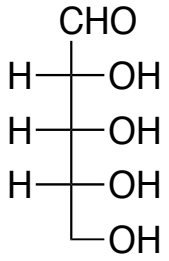
an aldose **a ketose**

- **Common ketoses of biological interest as compounds of the type** $HOCH_2–(CHOH)_x–(CO)–CH_2OH$

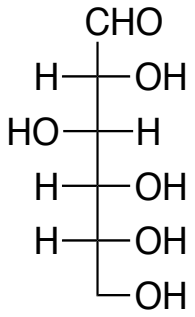
- **The vast majority of naturally occurring monosaccharides as chiral and enantiomerically pure substances**

REPRESENTATION OF MONOSACCHARIDES

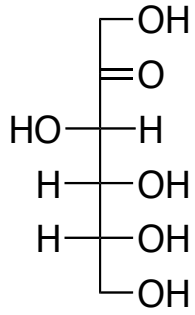
- **Frequent use of Fischer projections to represent monosaccharides; e.g.:**



ribose



glucose



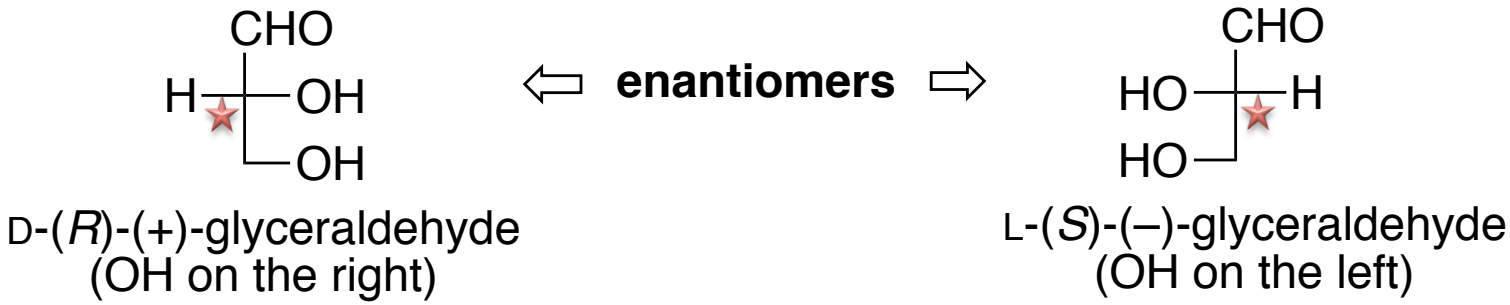
fructose

- **Ribose as a pentose; glucose and fructose as hexoses**

- **Ribose and glucose as aldoses; fructose as a ketose**

GLYCERALDEHYDE: THE SIMPLEST ALDOTRIOSE

- **D- and L-forms of glyceraldehyde:**

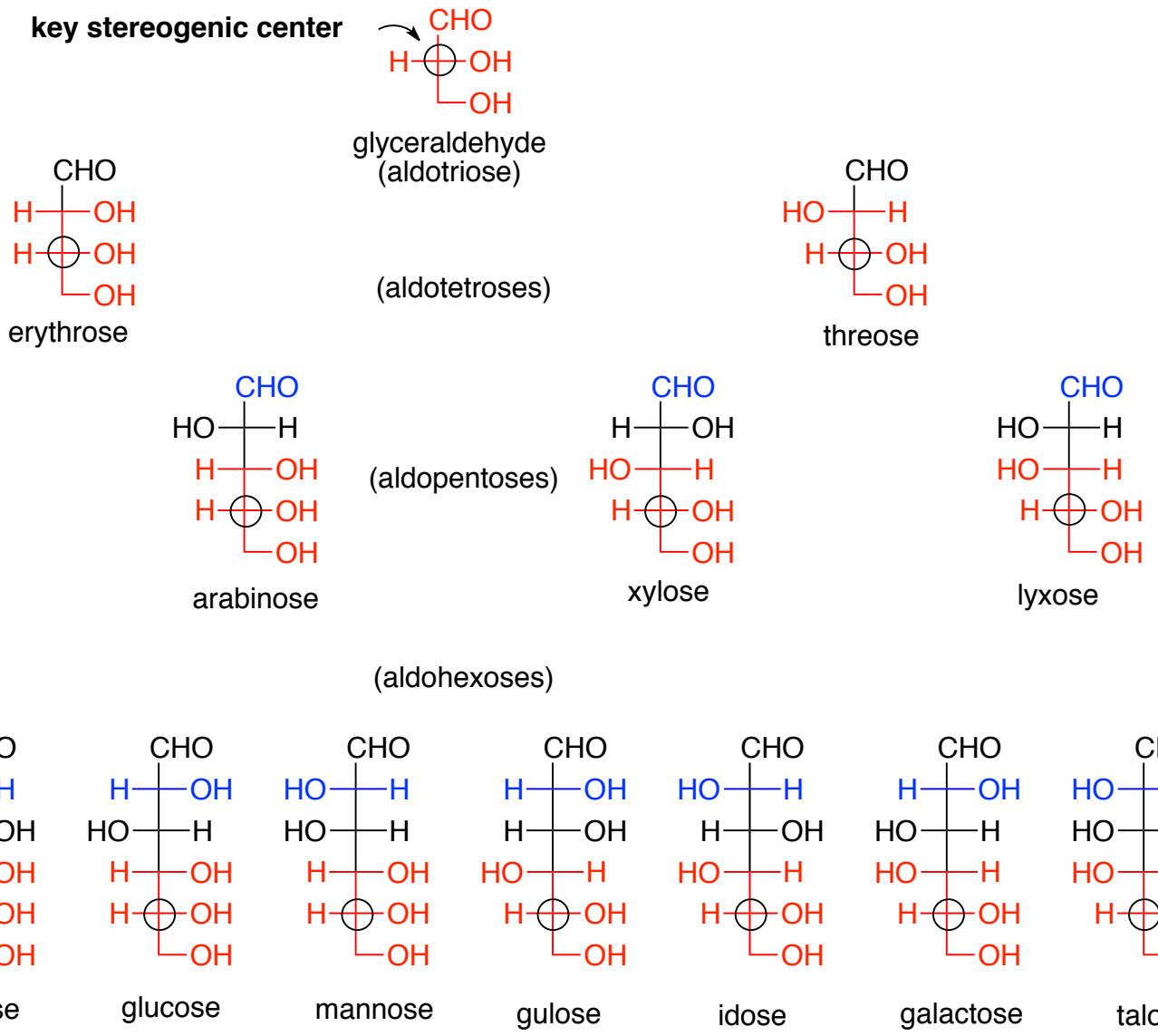


D-(*R*)-(+)-glyceraldehyde
(OH on the right)

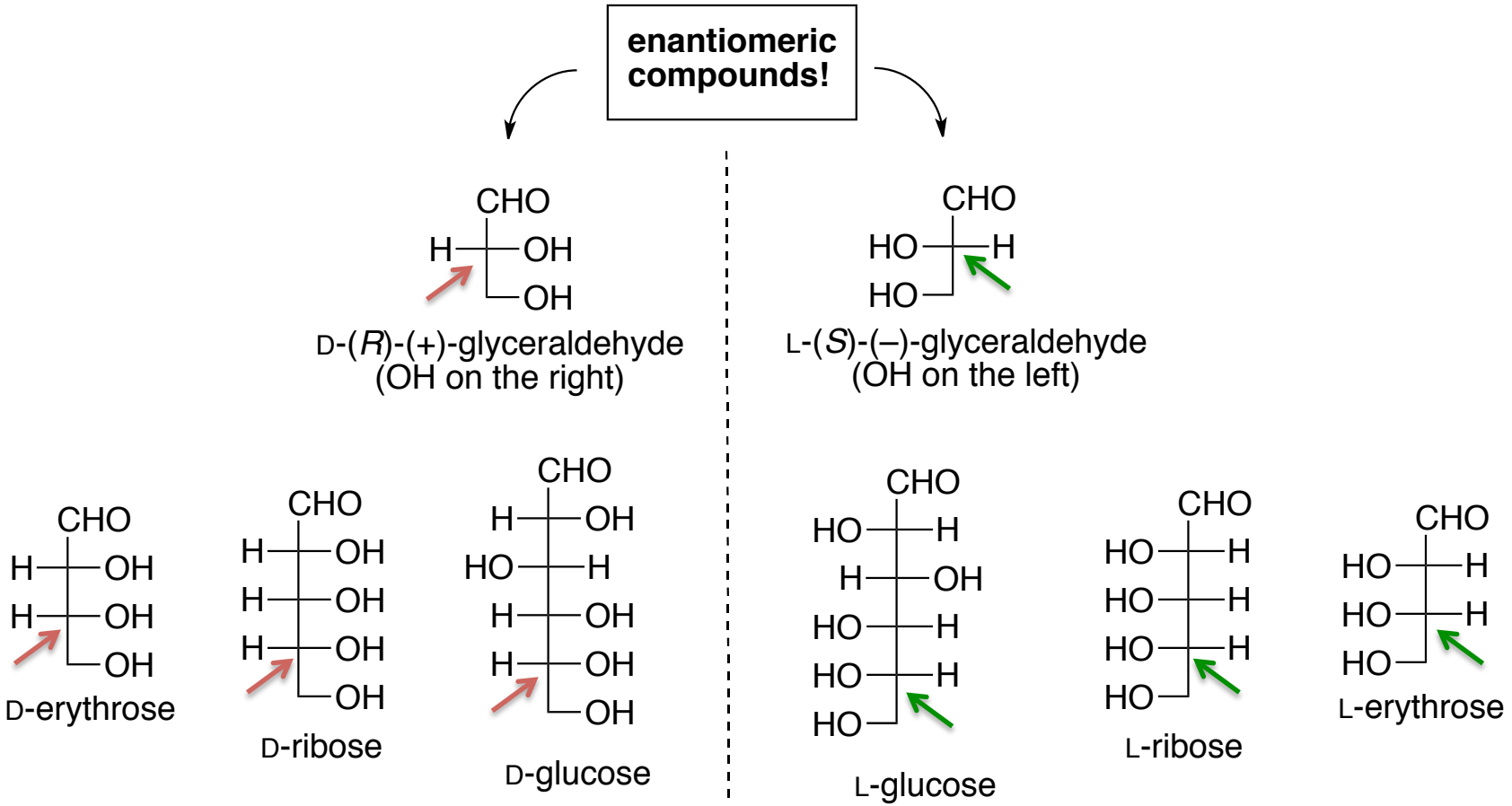
L-(*S*)-(–)-glyceraldehyde
(OH on the left)

- **D-Glyceraldehyde as the formal progenitor of all common monosaccharides**

STEREOCHEMICAL PROGENY OF COMMON ALDOSES



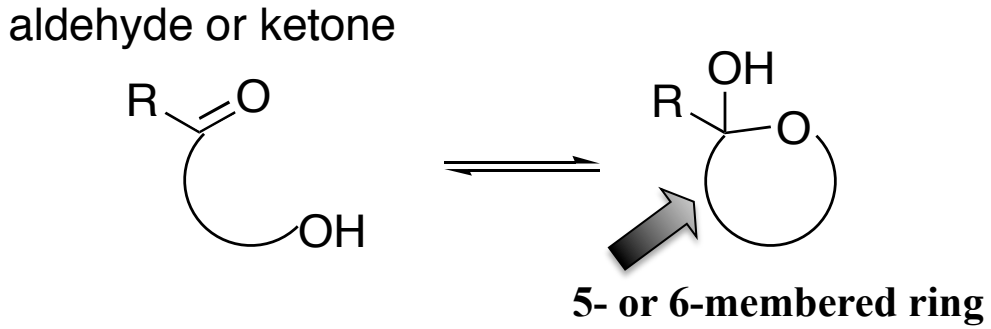
D- AND L-MONOSACCHARIDES



- **Most natural monosaccharides belong to the D-stereochemical series. The much rarer L-sugars are produced primarily by fungal or microbial organisms for specialized purposes**

STRUCTURE OF MONOSACCHARIDES: FORMATION OF HEMIACETALS

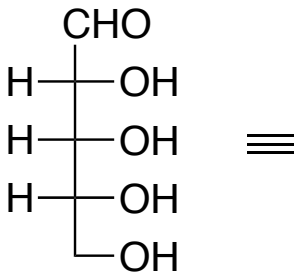
- **Molecules incorporating both an alcohol and an aldehyde or ketone functionality tend to exist as cyclic hemiacetals — *if a 5- or 6-membered ring can thus be formed*; e.g.:**



HEMIACETAL FORMS OF D-RIBOSE AND D-GLUCOSE

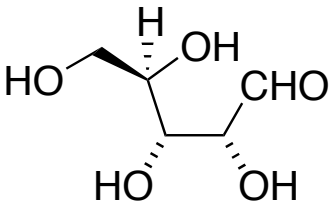
wavy line means that either configuration is possible

Ribose (building block of RNA):



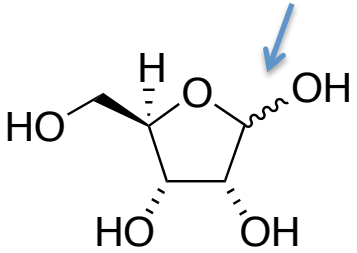
Fischer projection of D-ribose

≡



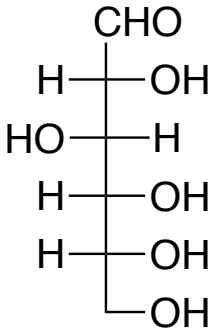
aldehyde (carbonyl) form of D-ribose

⇌



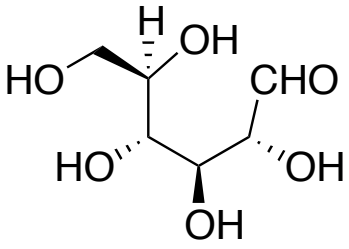
common hemiacetal form of D-ribose (preferred)

Glucose:



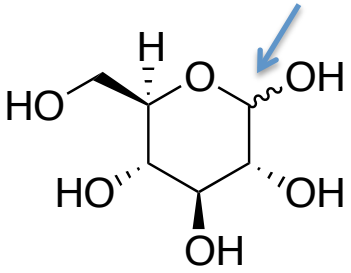
Fischer projection of D-glucose

≡



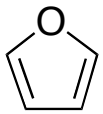
aldehyde (carbonyl) form of D-glucose

⇌

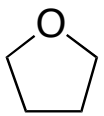


common hemiacetal form of D-glucose (preferred)

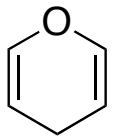
FURANOSE AND PYRANOSE FORMS OF MONOSACCHARIDES



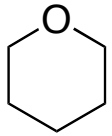
furan



tetrahydrofuran

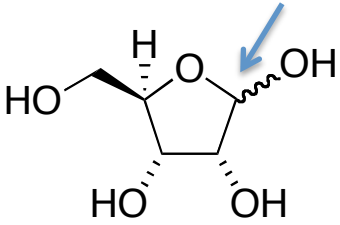


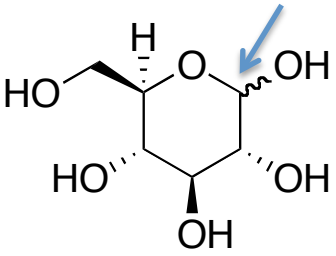
pyran



tetrahydropyran

furanose form of D-ribose ("D-ribofuranose")



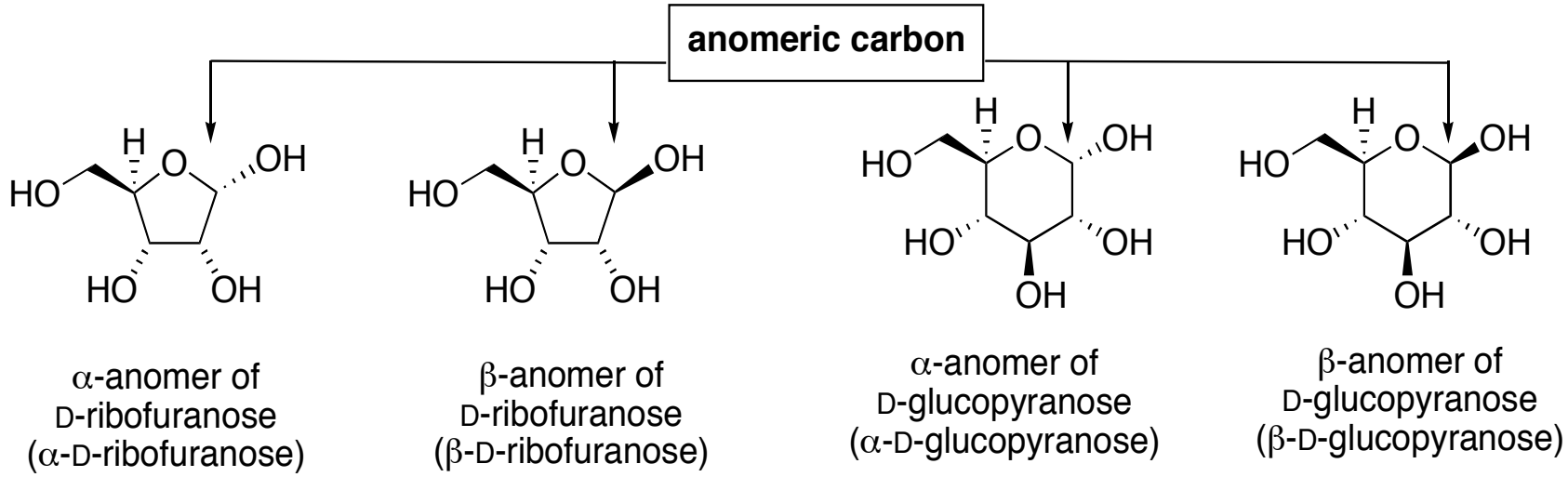


pyranose form of D-glucose ("D-glucopyranose")

Anomeric position or anomeric carbon: the one sustaining the hemiacetal function (arrows above)

POSSIBLE EXISTENCE OF TWO DIASTEREOMERS OF THE HEMIACETAL FORM OF A MONOSACCHARIDE

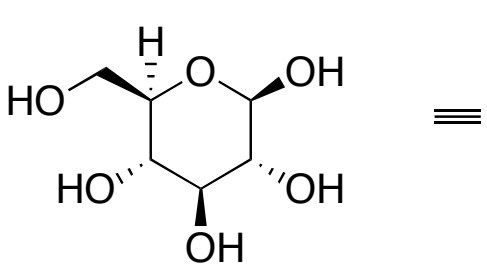
alpha- and beta-anomers of a monosaccharide



alpha-anomer: the OH group of the hemiacetal moiety is *trans* relative to the CH_2OH group on the carbon that defines the D / L series

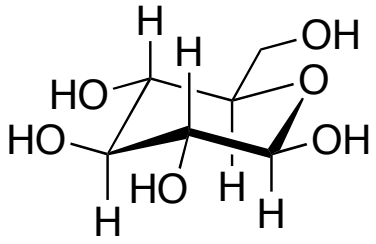
beta-anomer: the OH group of the hemiacetal moiety is *cis* relative to the CH_2OH group on the carbon that defines the D / L series

CONFORMATIONS OF PYRANOSES; e.g., GLUCOSE



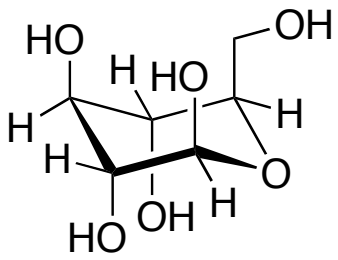
β-D-glucopyranose

≡

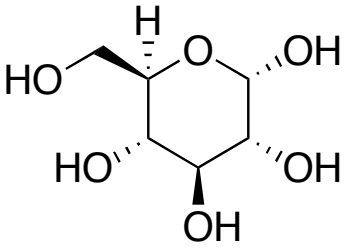


all equatorial:
favored

⇌

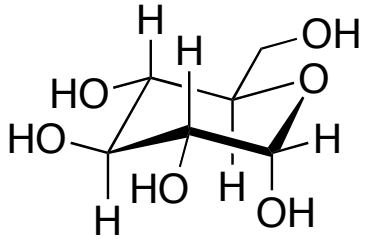


A-value of OH < 1.0 kcal/mol
A-value of $CH_2OH \approx 2$ kcal/mol



α-D-glucopyranose

≡



all but 1 OH equatorial:
favored

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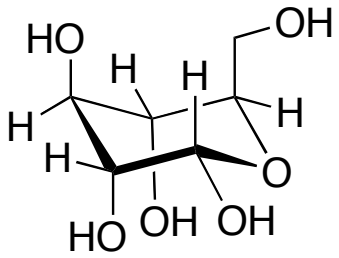
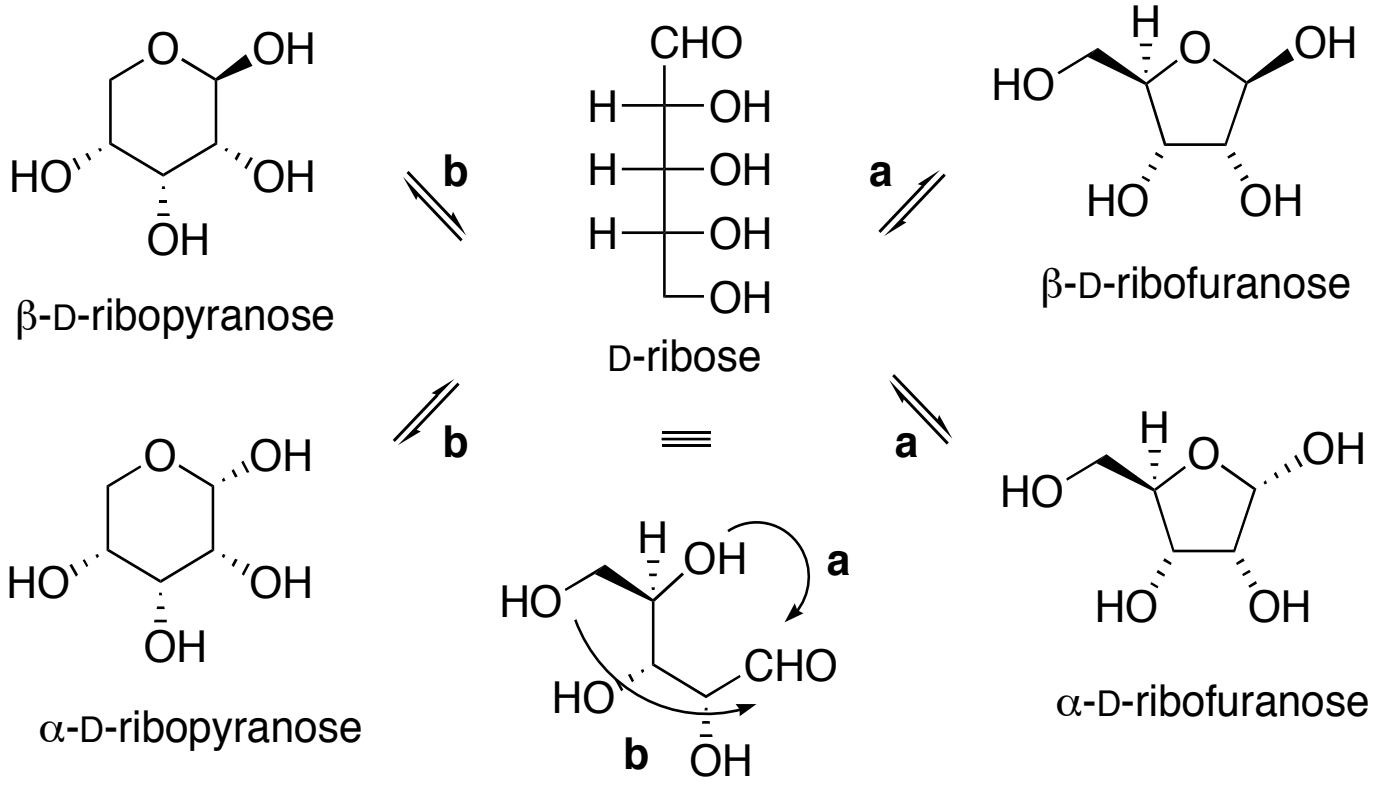


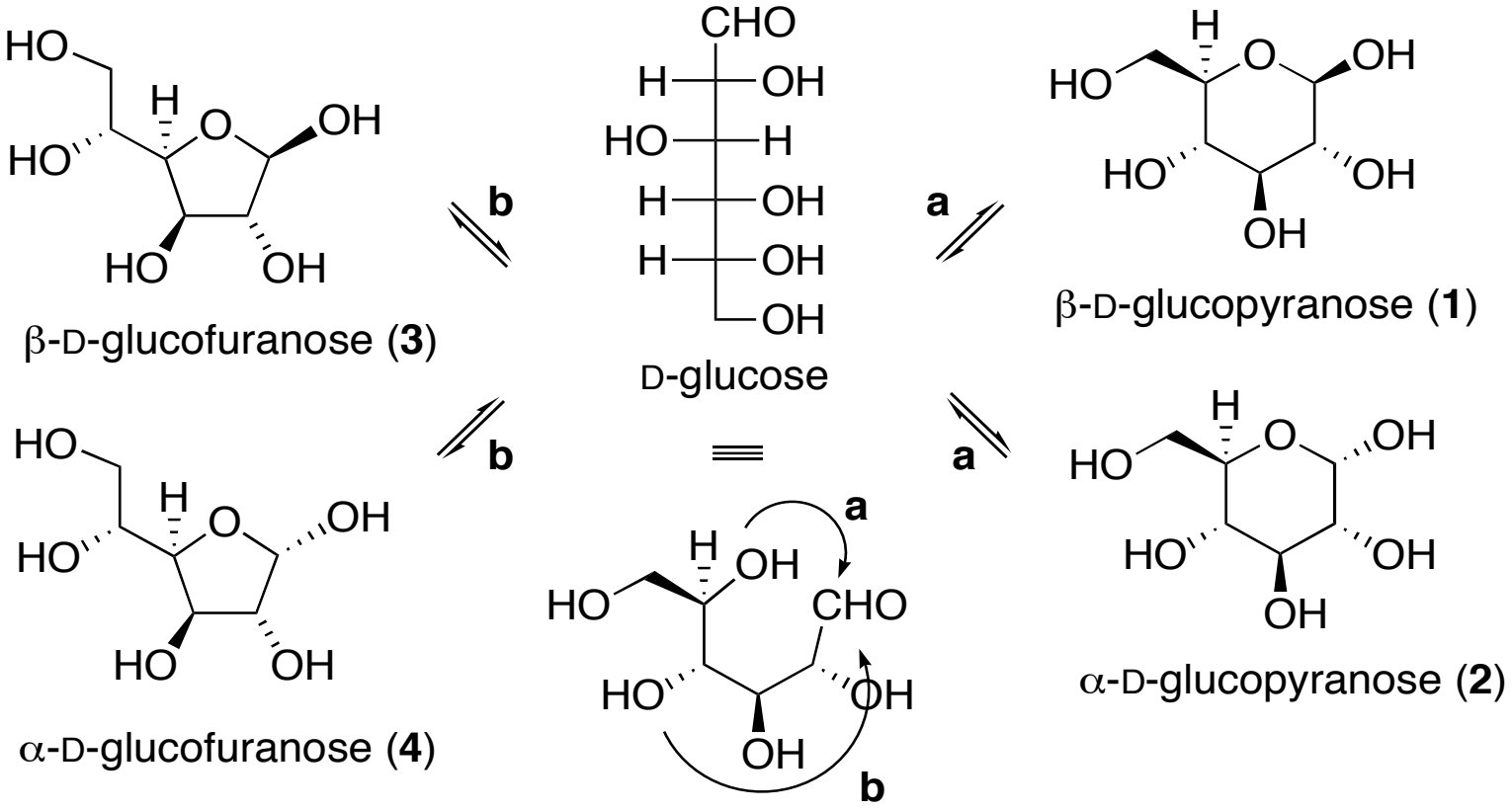
under appropriate conditions, it is possible to obtain pure α-D-glucopyranose or pure β-D-glucopyranose (crystallization). These two anomeric forms of glucopyranose, being diastereomeric, differ in solubility, melting point (146 °C for the α-anomer, 150 °C for the β-anomer), and optical rotation ($[a]_D^{25}$ = +112° for the α-anomer, + 19° for the β-anomer).

INTERCONVERSION OF PYRANOSE AND FURANOSE FORMS AND OF α- and β-ANOMERS: RIBOSE



all forms will be present at equilibrium in a solution of ribose, although one especially thermodynamically favorable form may be the dominant (or even the exclusive) species (β-D-ribofuranose in the this case)

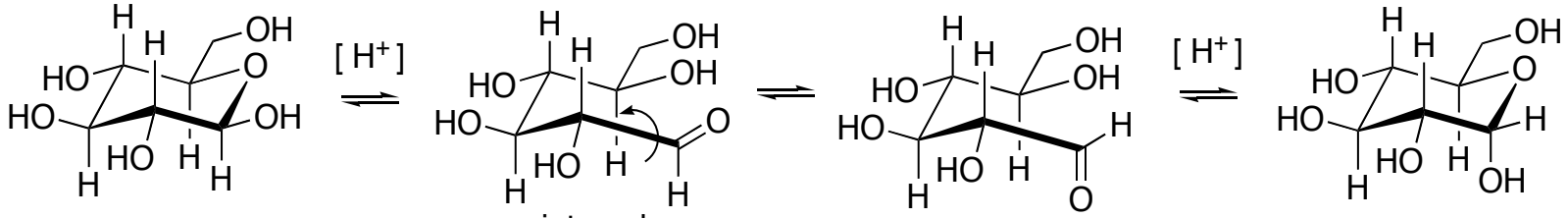
INTERCONVERSION OF PYRANOSE AND FURANOSE FORMS AND OF α- and β-ANOMERS: GLUCOSE



at equilibrium in H_2O: **1** ≈ 64%; **2** ≈ 36%; **3** + **4** < 1%

MUTAROTATION OF MONOSACCHARIDES: THE CASE OF GLUCOSE

if one prepares an aqueous solution of either pure anomer of glucose, and one measures the specific optical rotation of the solution over time, one observes that the rotation of a solution of pure α-anomer, initially equal to +112°, *drops* to a final value of ca. +53°, while that of a solution of pure β-anomer, initially equal to +19°, *increases* to a final value of ca. +53°.



β-D-glucopyranose

m.p. 150 °C

$[\alpha]_D$ = + 19°

α-D-glucopyranose

m.p. 146 °C

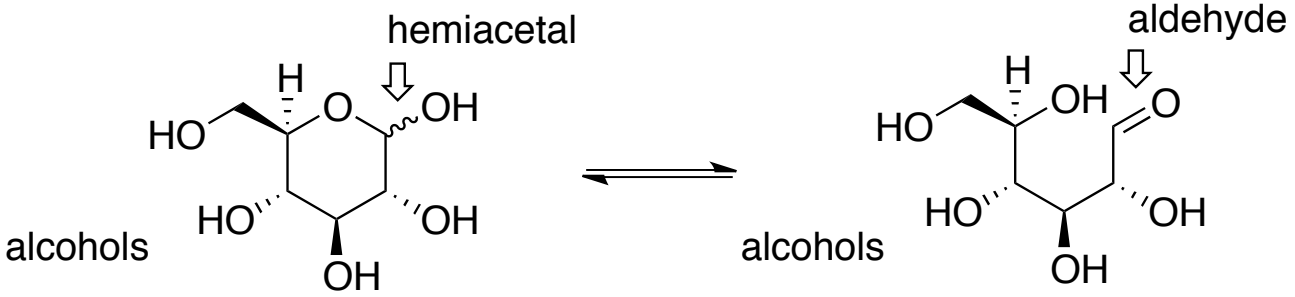
$[\alpha]_D$ = + 112°

This phenomenon is termed *mutarotation* (="rotation change") and it is due to equilibration of the anomers. At equilibrium, the solution contains a mixture of ca. 64% of β-anomer (all equatorial, more stable) and ca. 36% of α-anomer:

(0.64 x 19°) + (0.36 x 112°) = 12.2° + 40.3° = +52.5°

CHEMICAL REACTIVITY OF CARBOHYDRATES

carbohydrates contain both OH and C=O groups (often "masked" as hemiacetals); therefore, their reactivity will parallel that of alcohols, hemiacetals, and C=O compounds:

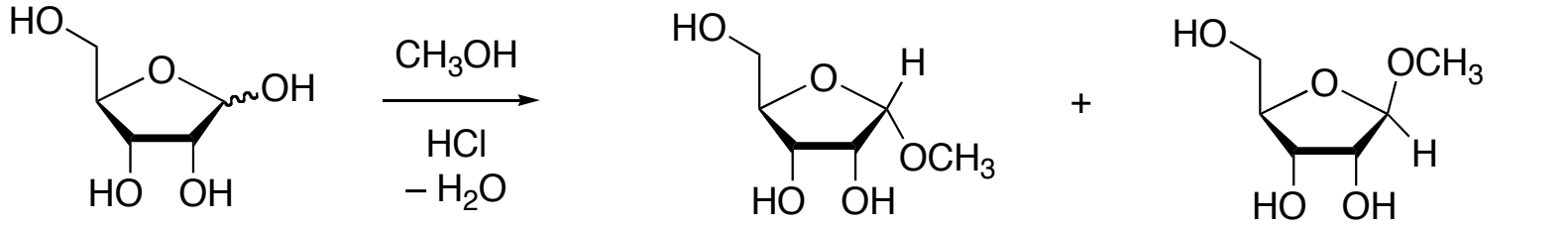


α- or β-glucopyranose

open form of glucose

FORMATION OF GLYCOSIDES OF MONOSACCHARIDES

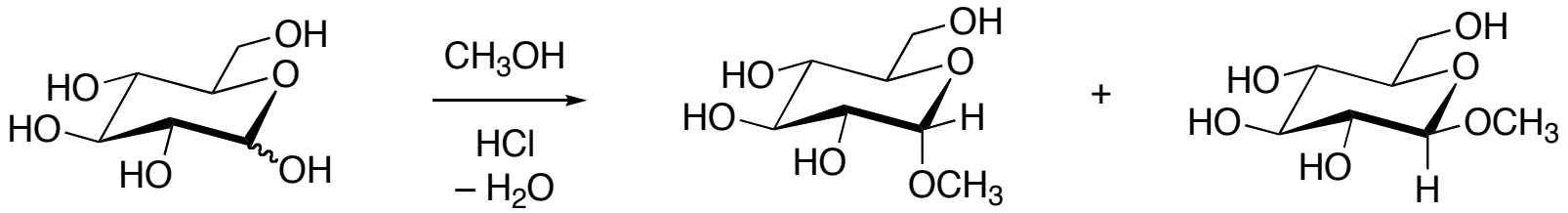
much like a hemiacetal will react with an alcohol under acidic conditions to form an acetal, so a monosaccharide will react under the same conditions to form an acetal termed a *glycoside* (riboside, glucoside, ….)



α- or β-D-ribofuranose

α-methyl-D-ribofuranoside

β-methyl-D-ribofuranoside



α- or β-D-glucopyranose

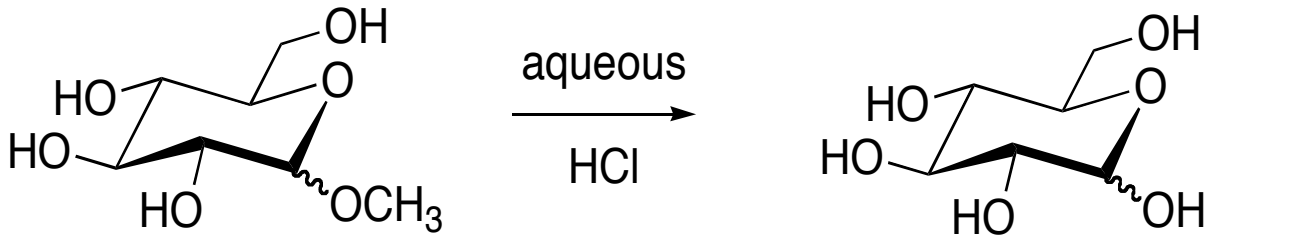
α-methyl-D-glucopyranoside

β-methyl-D-glucopyranoside

note: the mechanism of these reactions is analogous to that seen earlier for simpler hemiacetals

HYDROLYSIS OF GLYCOSIDES IN AQUEOUS ACID

much like an acetal undergoes hydrolysis in aqueous acid, so a glycoside can be hydrolyzed back to a "free" sugar under aqueous acidic conditions

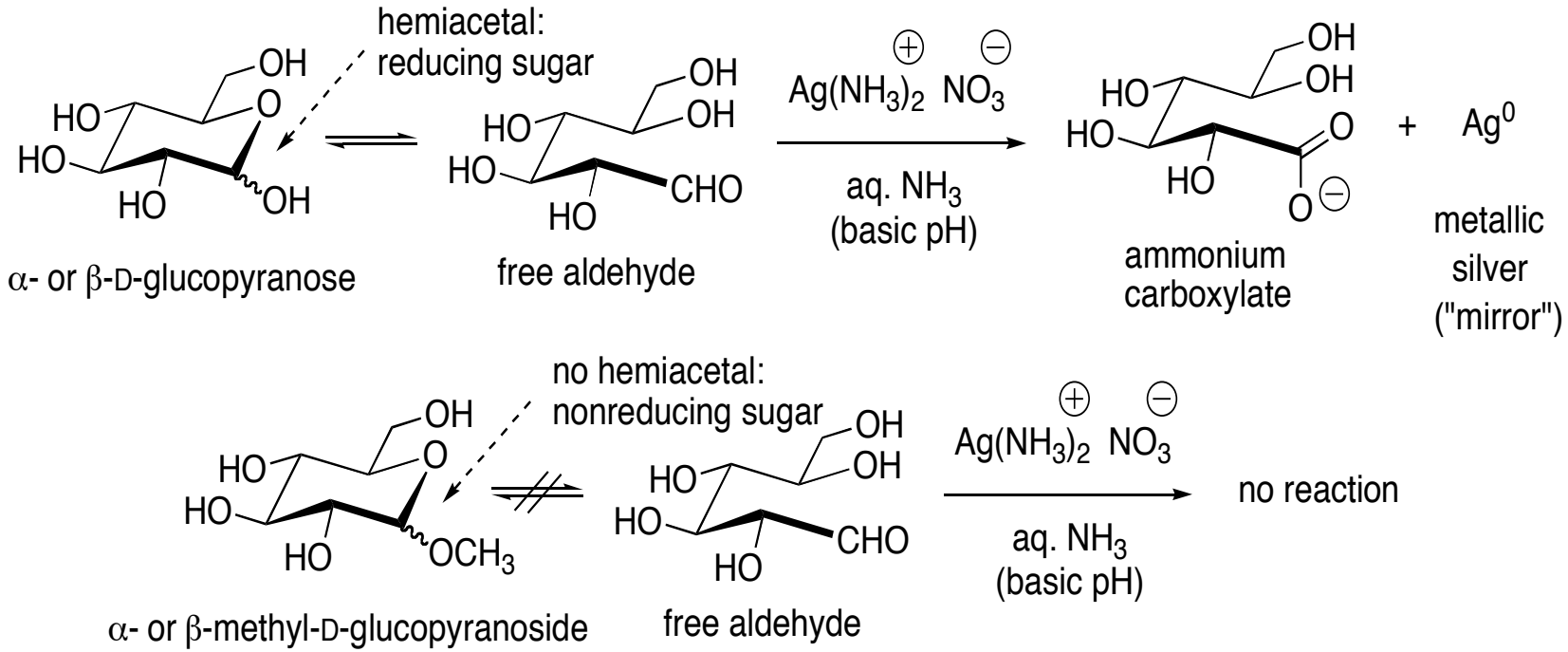


α- or β-methyl-D-glucopyranoside

α- and β-D-glucopyranoses

note: the mechanism of this reaction is analogous to that seen earlier for simpler acetals

REDUCING AND NON-REDUCING SUGARS: THE TOLLENS TEST

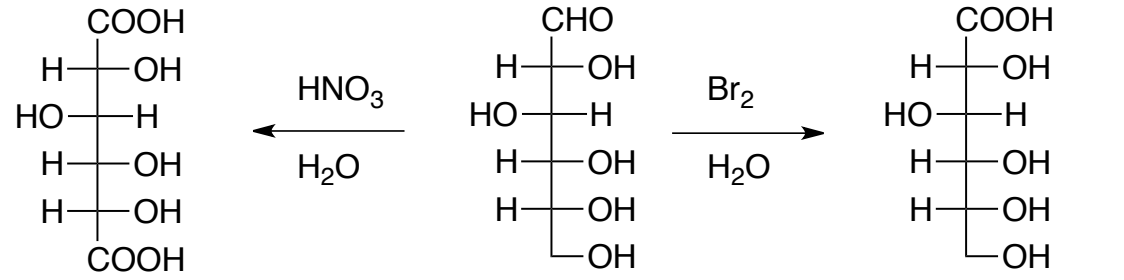


reminder: an acetal is stable in the presence of bases, even strong ones like carbanions
note: the mechanism of the Tollens reaction is complex and will not be discussed in CHEM 203

importance of the Tollens test in the structural elucidation of natually occurring carbohydrates

REDOX CHEMISTRY OF ALDOSES

- **Oxidation to aldonic or aldaric acids**

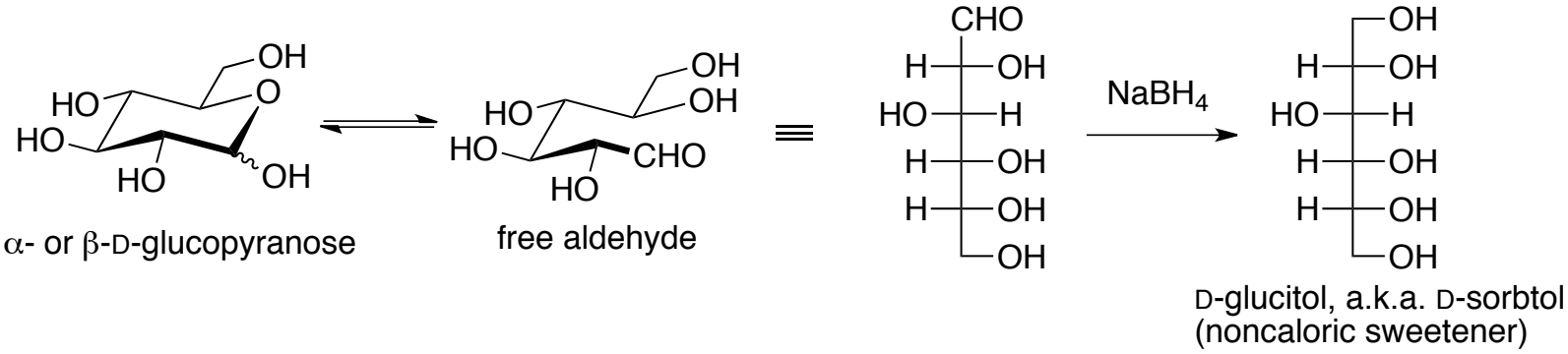


D-glucaric acid: an **aldaric** acid

D-glucose

D-gluconic acid: an **aldonic** acid

- **Reductions to alditols**

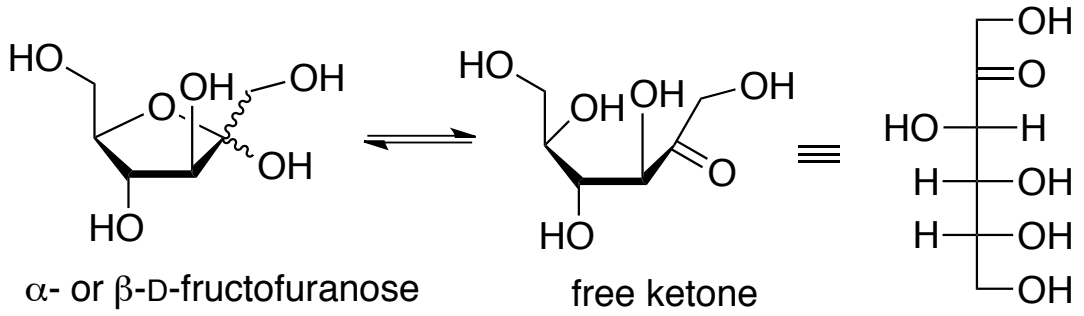


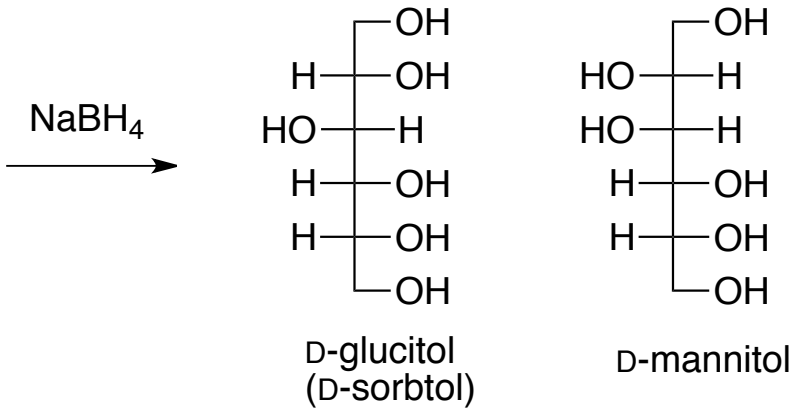
α- or β-D-glucopyranose

free aldehyde

D-glucitol, a.k.a. D-sorbtol (noncaloric sweetener)

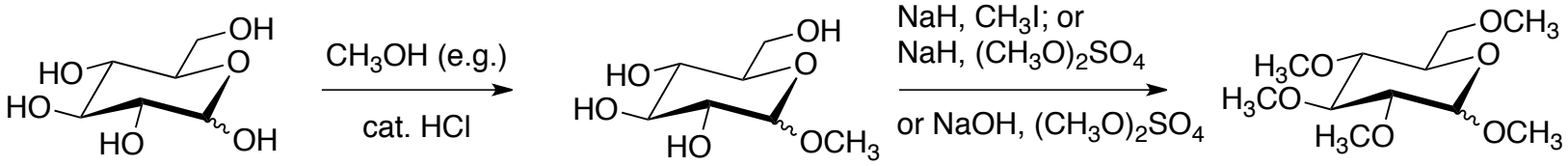
REDUCTION OF KETOSES: FORMATION OF DIASTEREOMERIC ALDITOLS





FORMATION OF ETHERS BY WILLIAMSON REACTION

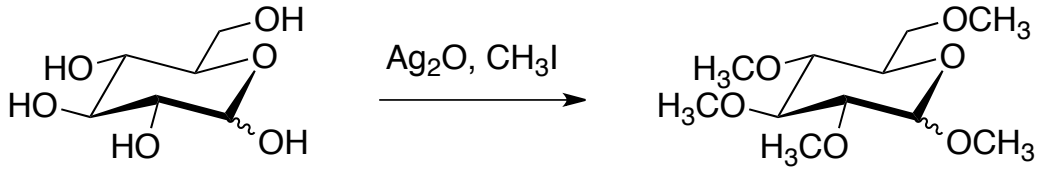
- **Reducing sugars are generally poor substrates for the Williamson reaction and must first be converted into glycosides:**



α- or β-D-glucopyranose

α- or β-methyl-D-glucopyranoside

- **Mild modification of the Williamson reaction:**



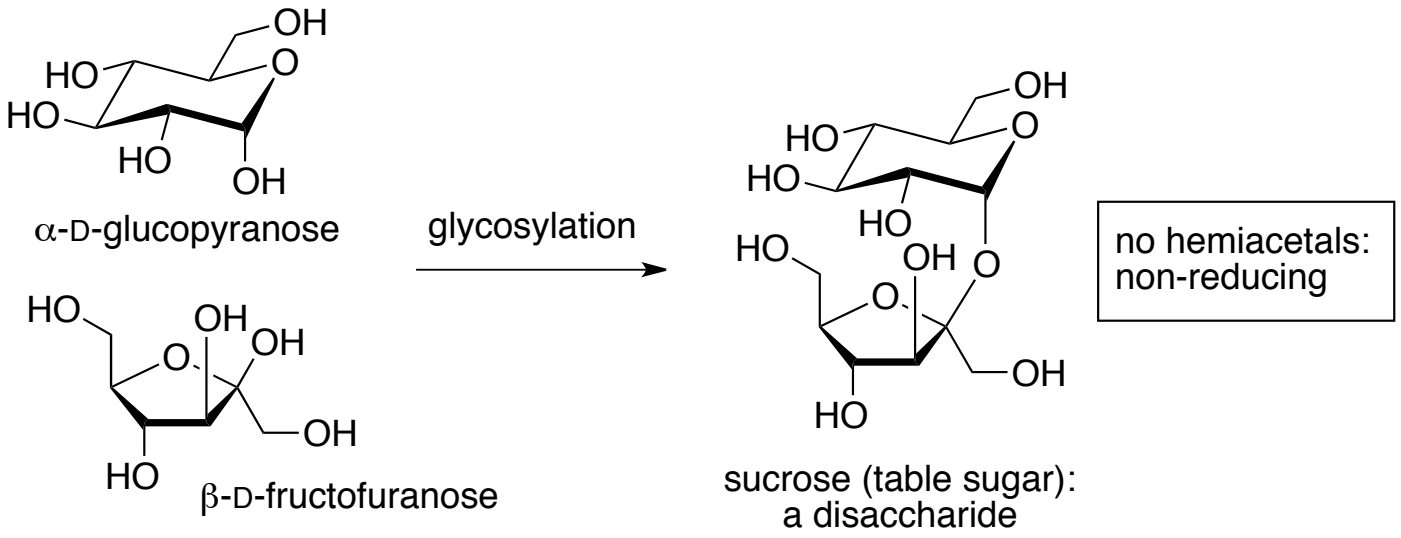
α- or β-D-glucopyranose

POLYSACCHARIDES OR COMPLEX SUGARS

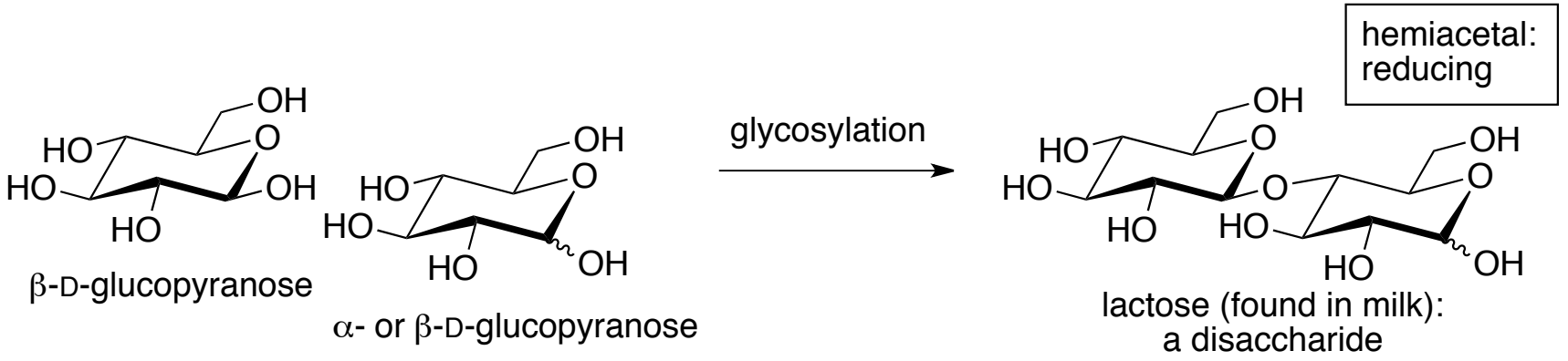
- **Polysaccharides or complex sugars are polymers of monosaccharides arising through glycosylation of a monosaccharide with another monosaccharide**

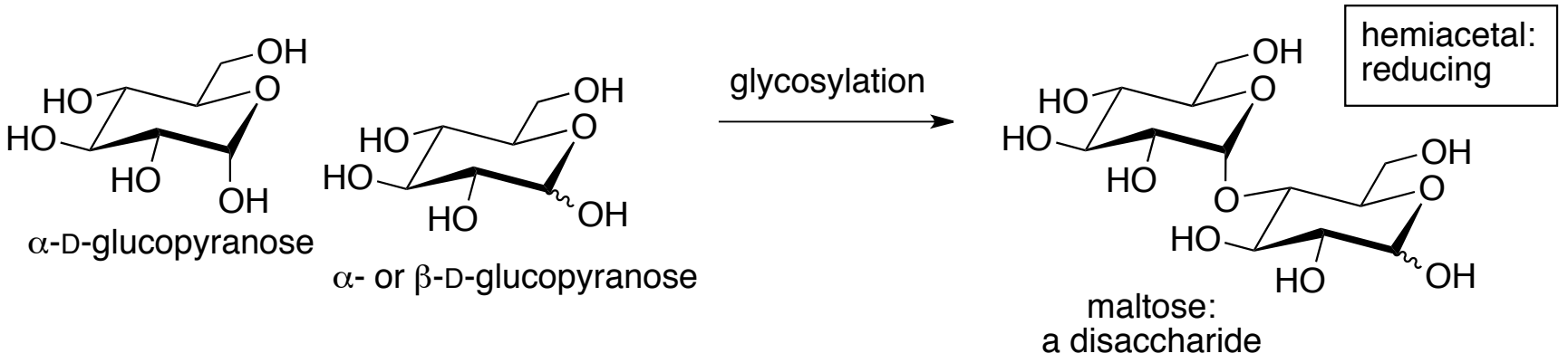
- **Disaccharides, trisaccharides, … oligosaccharides ("a few" saccharides, typically 2-10 saccharide units), polysaccharides (more than ≈ 10 saccharide units)**

- **Important disaccharides: sucrose, lactose, maltose:**

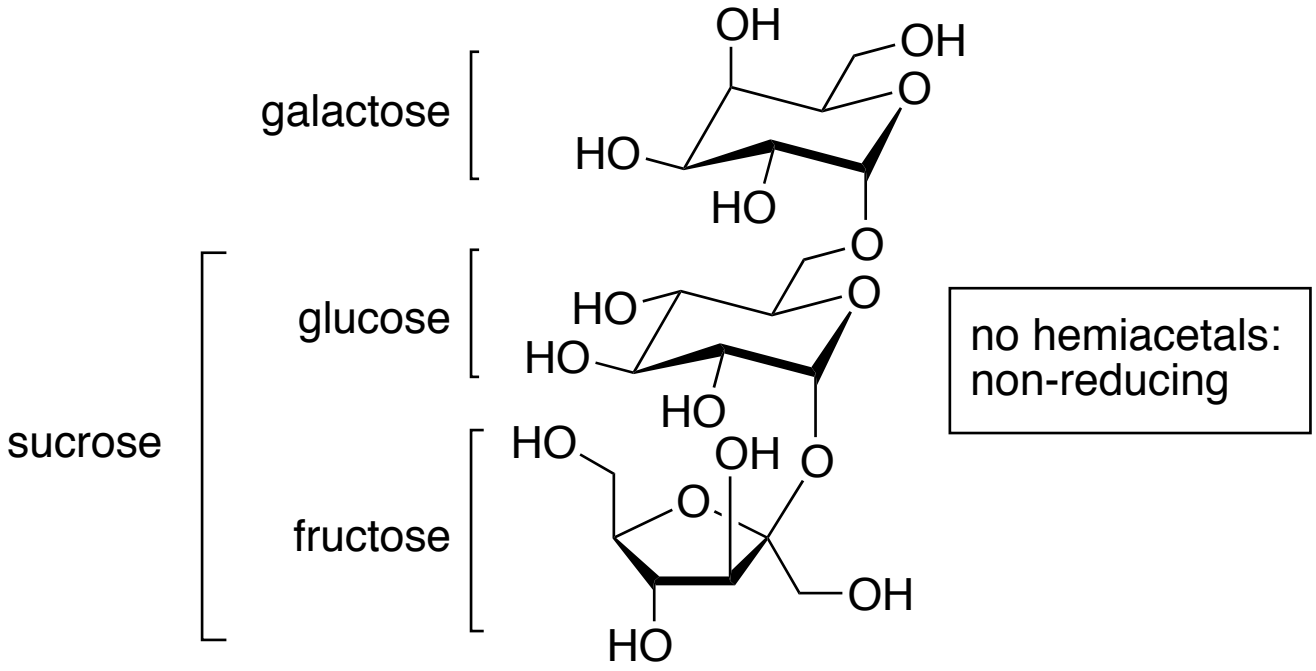


IMPORTANT DISACCHARIDES: LACTOSE & MALTOSE





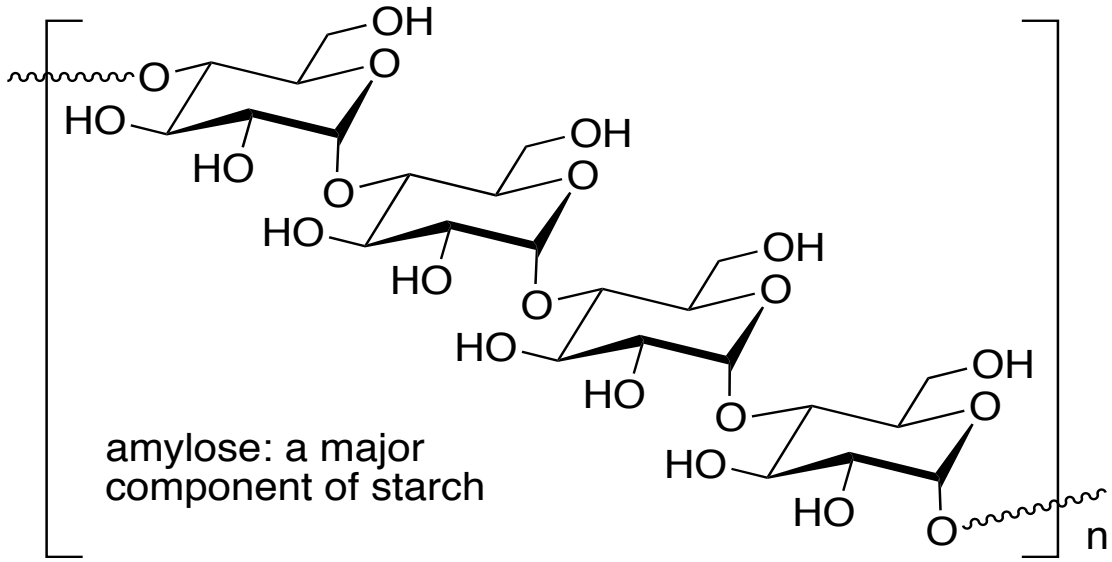
A TRISACCHARIDE: RAFFINOSE



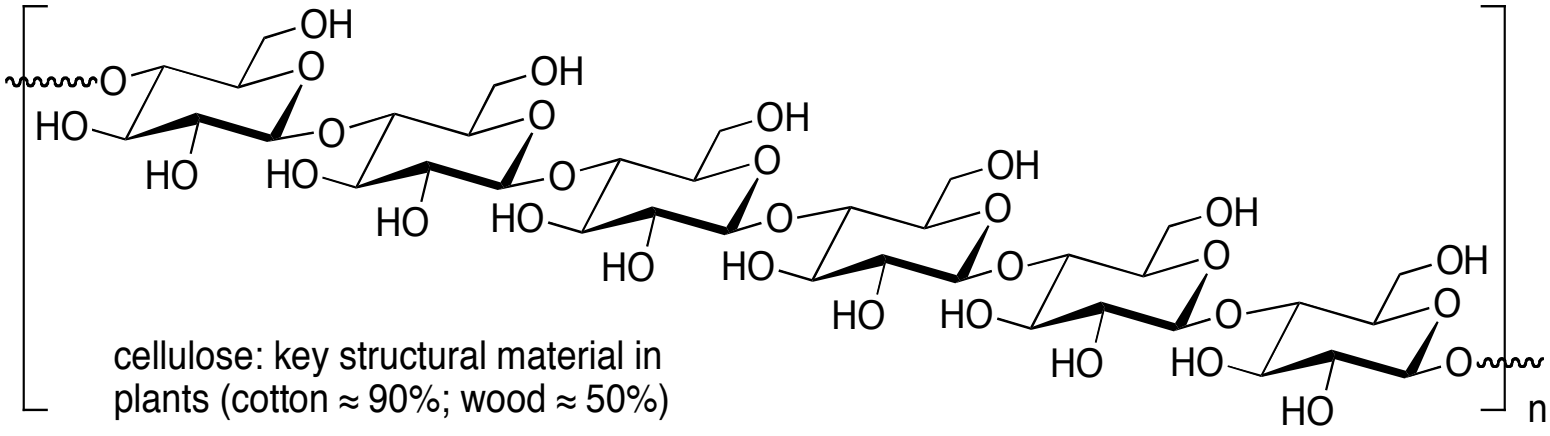
- **abundant in beans, broccoli, cabbage ,…**
- **indigestible to humans**
- **readily fermented by microorganism colonizing the human intestine**

yes, raffinose is the culprit

KEY POLYSACCHARIDES: AMYLOSE AND CELLULOSE

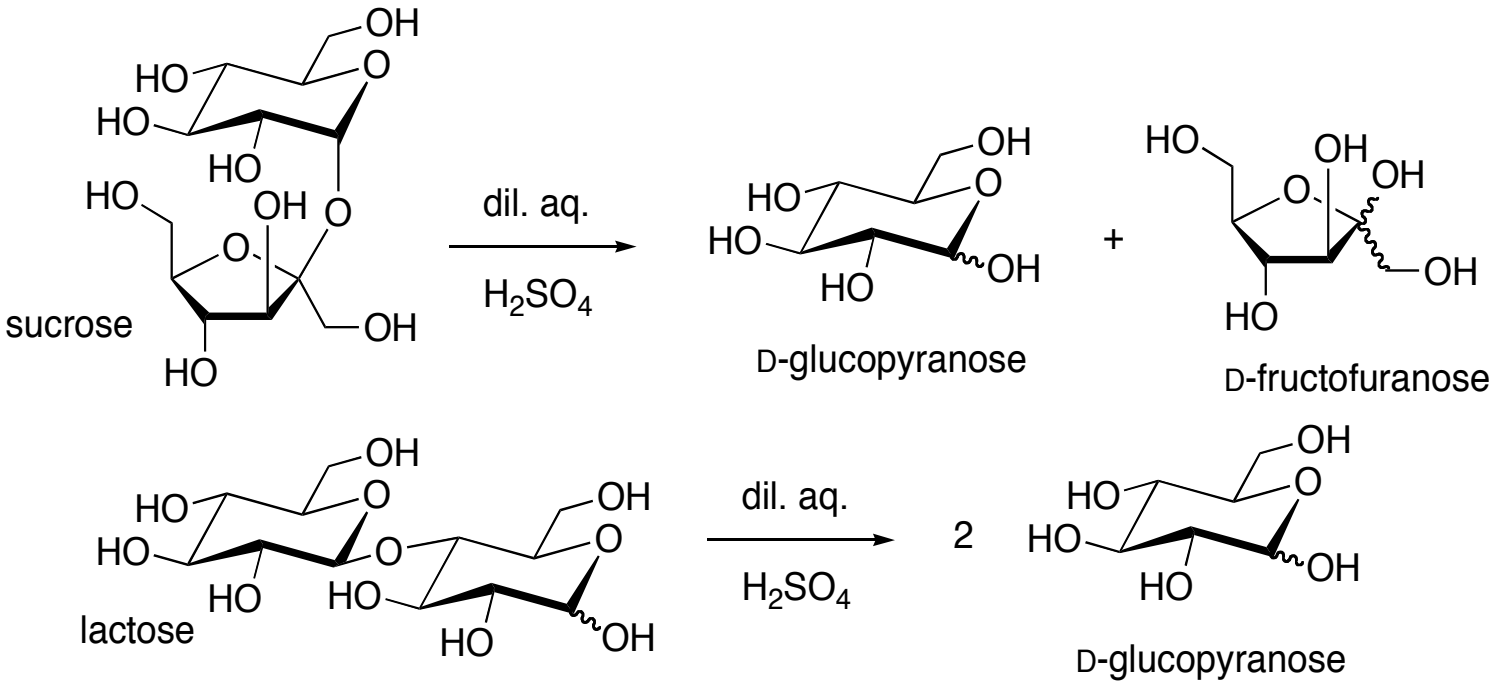


amylose: a major component of starch



cellulose: key structural material in plants (cotton ≈ 90%; wood ≈ 50%)

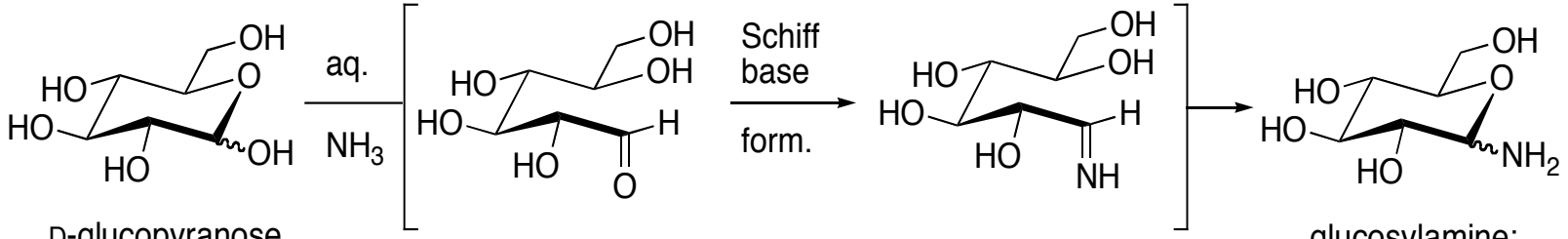
ACIDIC HYDROLYSIS OF POLYSACCHARIDES



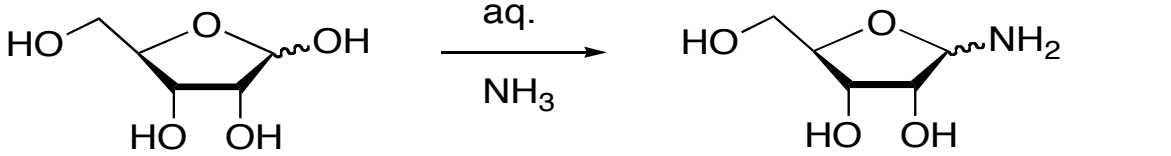
a polysaccharide can be hydrolyzed to simpler carbohydrates (ultimately, to free monosaccharides) with dilute aqueous acid (hydrolysis of the acetal functions), while a monosaccharide cannot be converted to simpler sugars under the same conditions

FORMATION OF GLYCOSYLAMINES

- **a free monosaccharide reacts with aqueous ammonia to yield a *glycosylamine***

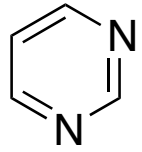


likewise:

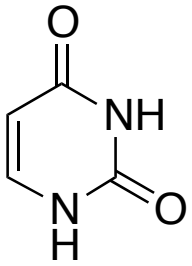


- **relevance of glycosylamines to nucleic acid chemistry . . .**

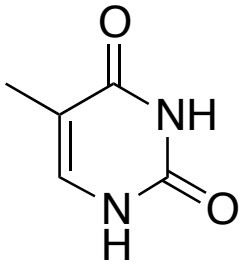
PYRIMIDINE AND PURINE: HETEROCYCLES OF LIFE



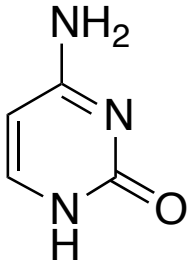
pyrimidine



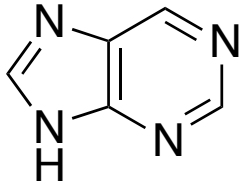
uracil



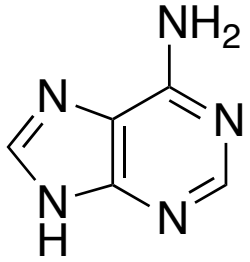
thymine



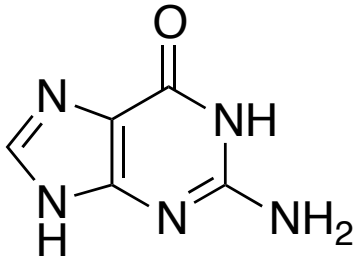
cytosine



purine

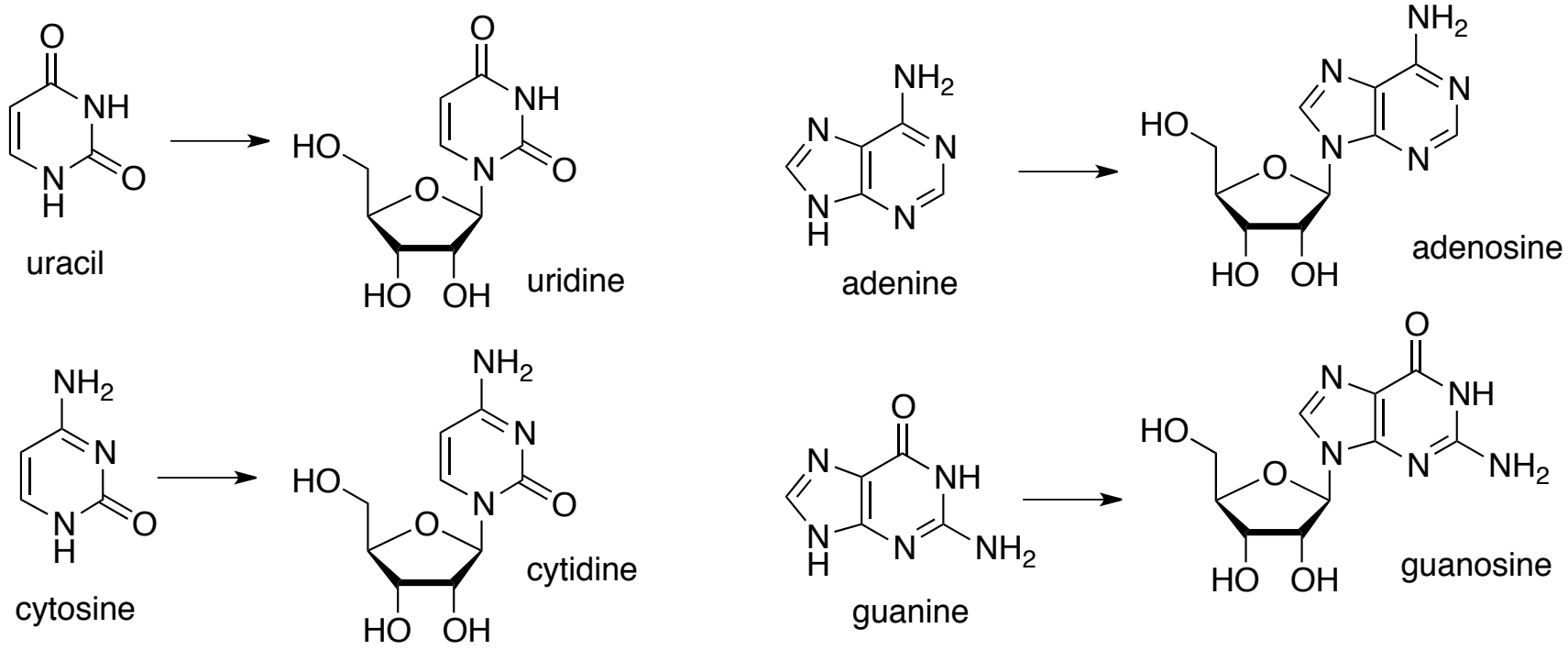


adenine



guanine

RIBONUCLEOTIDES: COMPONENTS OF RNA



2-DESOXYRIBONUCLEOTIDES: COMPONENTS OF DNA