Aalto University
School of Chemical
Technology

CHEM-E1150
BIOMASS PRETREATMENT AND FRACTIONATION

CARBOHYDRATE CHEMISTRY

Herbert Sixta, 2018

Learning Outcomes

1. Structure and stereochemistry of monosaccharides
2. Nomenclature of monosaccharides
3. Important monosaccharides in wood chemistry
4. Reactions of monosaccharides
5. Oligosaccharides

Definition of Carbohydrates

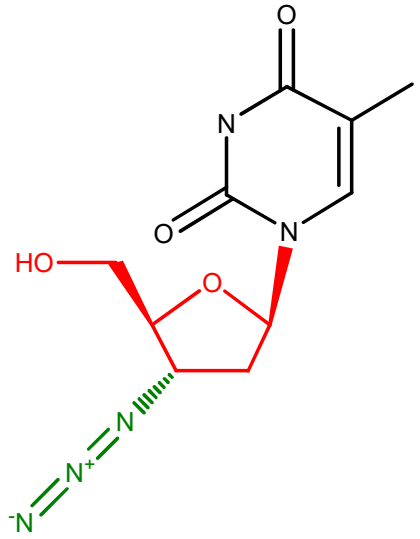
- ***Polyhydroxycarbonyls*** **→simplest sugars:** $C_n(H_2O)_n$
- Most abundant biomacromolecule on earth: 2x10^{11} t annually, 90% from trees.
- Sugars are the building blocks of carbohydrates
- Insoluble sugars function as structural material in the cell walls of plants and bacteria: **Oligo**- and **Polysaccharides**
- **Glycoproteins:** sugars attached to proteins.
- **Glycolipids:** sugars attached to lipids.

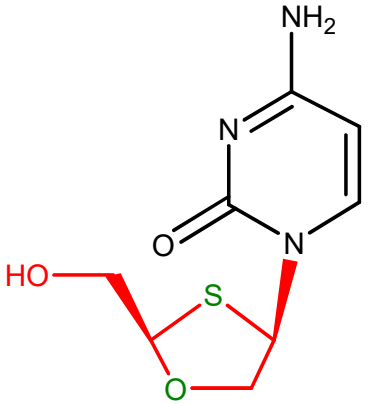
Cell recognition process

…..involves specific carbohydrates

AZT (Azidothymidin) works by selectively inhibiting HIV's reverse transcriptase, the enzyme that the virus uses to make a DNA copy of its RNA.

The azido group increases the lipophilic nature of AZT, allowing better penetretation into cells



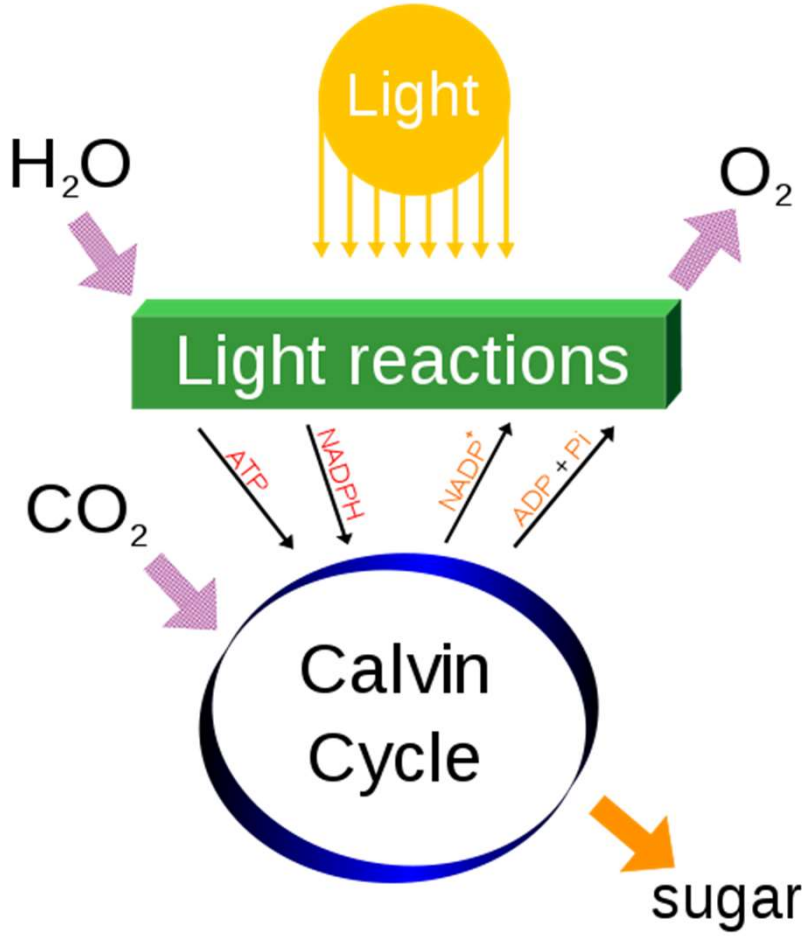


3-TC
lamivudine
4-amino-1-((2R,4R)-2-(hydroxymethyl)-1,3-oxathiolan-4-yl)pyrimidin-2(1H)-one

Lamivudine, GlaxoSmith, is a potent nucleoside, reverse transcriptase inhibitor, used for the treatment of **HIV** and **hepatitits B**.

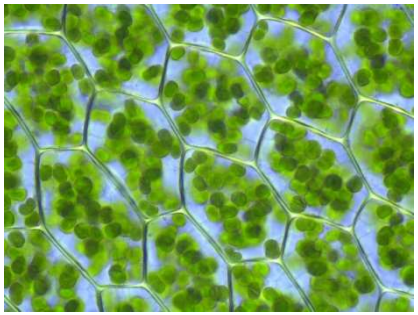
Developed in 1964 by Jerome P Horwitz as anti cancer (unsuccessful); however, 20 years later the inhibiting effect of the reverse transcriptase was shown; bought by GlaxoSmithKline

Photosynthesis



CO_2 is converted to sugars ~ Carbon fixation (reduction).

Plants usually convert light into chemical energy with a photosynthetic efficiency of 3–6%.



Chloroplasts

Hermann Emil Fischer

Nobel Prize (2nd) for Chemistry in 1902.

Elucidation of the structure of sugars:

- Fischer projection
- Reduction and oxidation of sugars.
- Reaction with phenylhydrazine to phenylhydrazone and osazones.

Van't Hoff

Learning Outcomes

1. **Structure and stereochemistry of monosaccharides**
2. Nomenclature of monosaccharides
3. Important monosaccharides in wood chemistry
4. Reactions of monosaccharides
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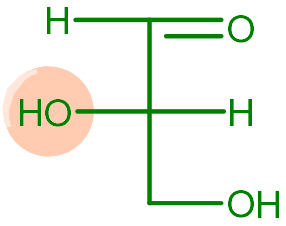
Structure of Monosaccharides

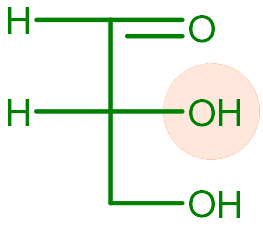
Smallest carbohydrate unit consists of 3 C-atoms.

Aldoses



L-Glyceraldehyde

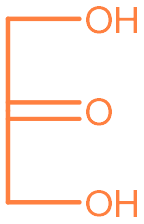
$[\alpha]^{25}_{D} = 8.7°$



D-Glyceraldehyde

$[\alpha]^{25}_{D} = -8.7°$

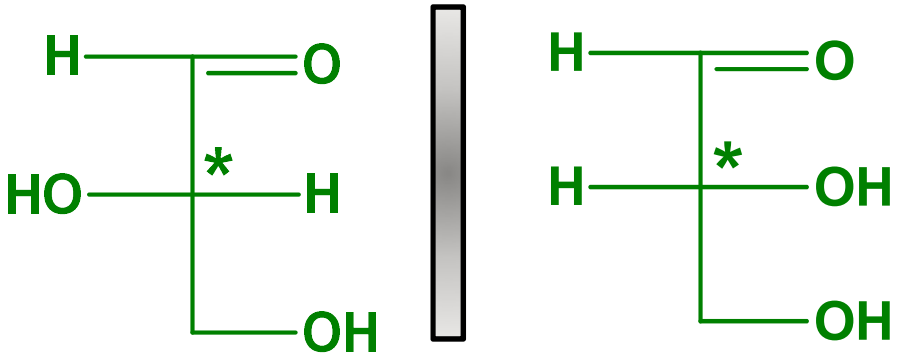
Ketose



1,3-Dihydroxyacetone

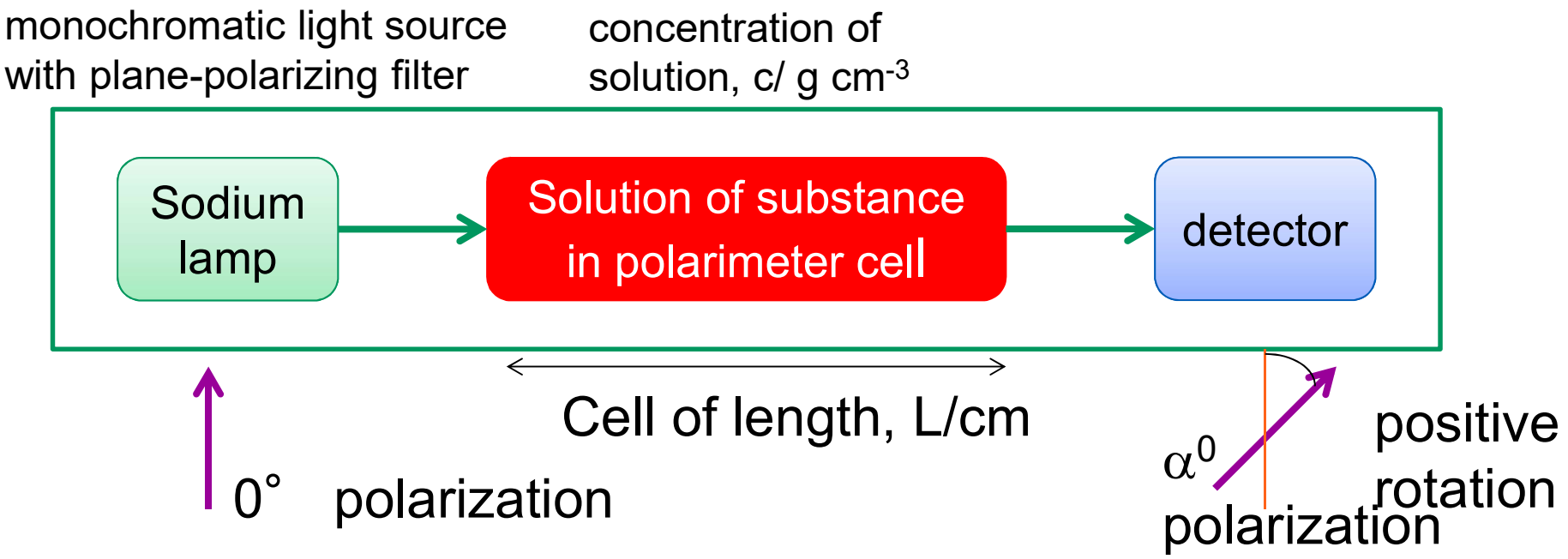
Most of the naturally occuring carbohydrates have the **D-conformation** (Fischer)

Chirality of Sugars



- Molecule with a **tetrahedral C-atom** carrying **4 different groups** is **chiral** or **stereogenic** (*).
- Any structure that has no plane of symmetry can exist as two mirror-image forms (***enantiomers***).
- **Enantiomers** rotate plane-polarized light
- **n** (number of) chiral centers result in 2^n stereoisomers and $2^{(n-1)}$ pairs of enantiomers.

Optical Activity - Polarimeter

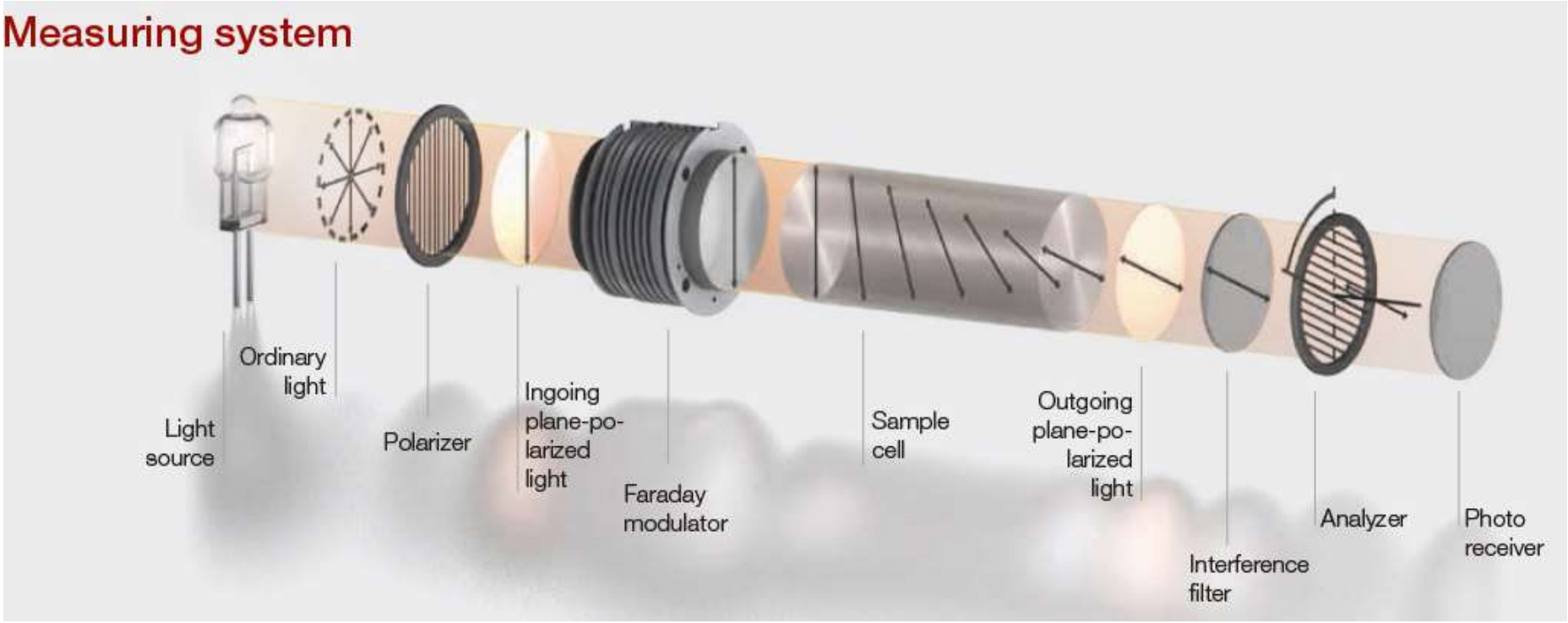


Specific rotation at 20°C, λ = 589 nm.

By dividing α by the path length L (in dm) and the concentration c (in g cm^{-3}) we get a value, $[\alpha]_D$, which is specific to the compound in question.

$$[\propto]_D^{20} = \frac{\propto}{c \cdot L}$$

Polarimeter



http://en.wikipedia.org/wiki/Polarimeter

Enantiomers

(+) enantiomers rotate plane-polarized light to the right

(-) enantiomers rotate plane-polzarized light to the left

D, L-enantiomers

- Glyceraldehyde was labelled **D** (dextro, (+)-enantiomer) and **L** (laevo, (-)-enantiomer).
- Any enantiomerically pure compound that could be related to D-(+)-glyceraldehyde was labelled D (and vice-versa)
- **Very laborous process. Thus, no more in use**; **instead R/S**

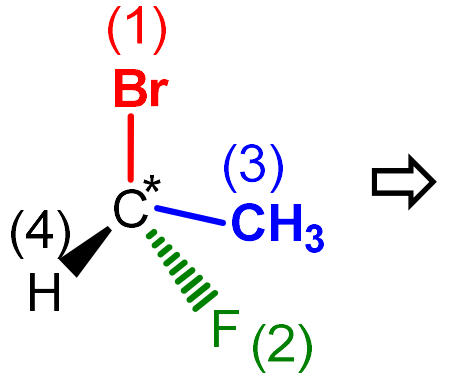
R- and S-Configuration

1. Assign a priority number to each substituent at the chiral centre, **higher atomic numbers get higher priority**.
2. Arrange a molecule so that the **lowest priority (H) is pointing away from you**.
3. Moving in a clockwise manner denotes **R**, in an anticlock-wise manner, assign the label **L** to the chiral centre.

CAHN-INGOLD-PRELOG Priority Scale:

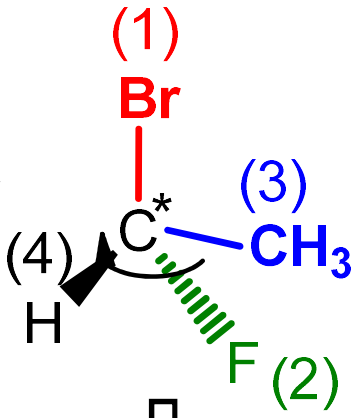
–I > –Cl > –S–CH_3 > **–SH** > –F > **–O–CH_3 > –OH >** –N_3 > –N $(CH_3)_2$ > –NH–C_6H_5 > **–NH_2 > –COOH > –$CONH_2$** > **–CHO > –CH_2OH** > –CD_3 > –CD_2H > –CDH_2 > **–CH_3** > –D > **–H**

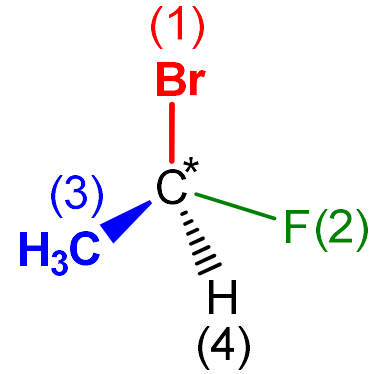
R- and S-Configuration

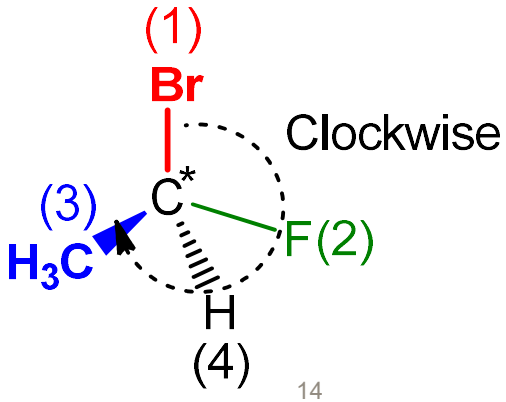


1-Bromo-1-Fluoroethane

Lowest priority atom, H, has to point behind the plane:
Thus, rotate the molecule ~120° to the right

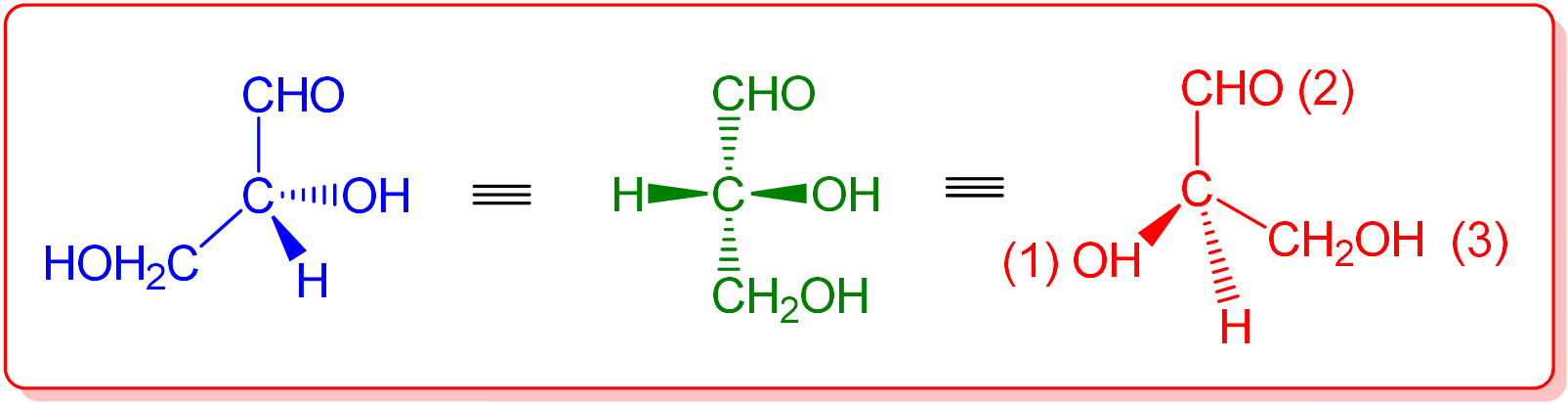






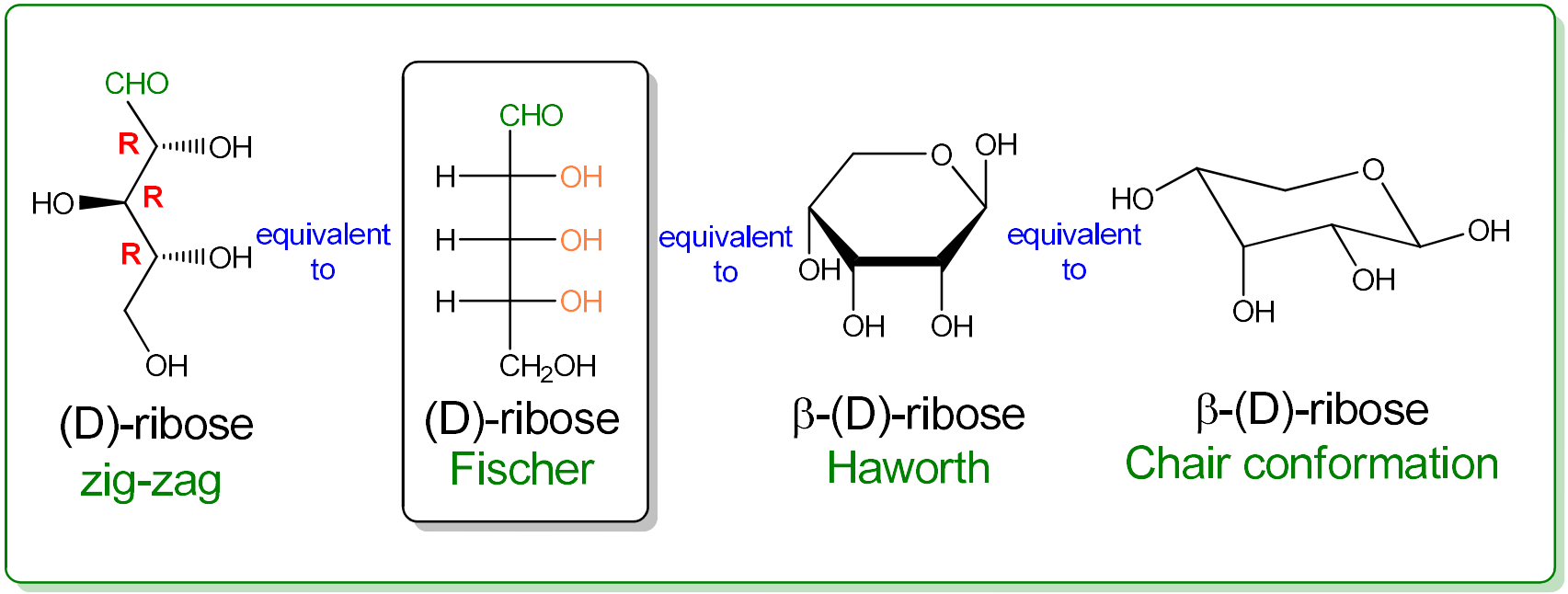
(R)-1-Bromo-1-Fluoroethane

Fischer projection



(R)-2,3-dihydroxypropanal

Fischer projection



Lowest numbered atom is positioned up the chain, numbering proceeds down the chain.

Penultimate-C of D-sugars is depicted with OH group on the right.

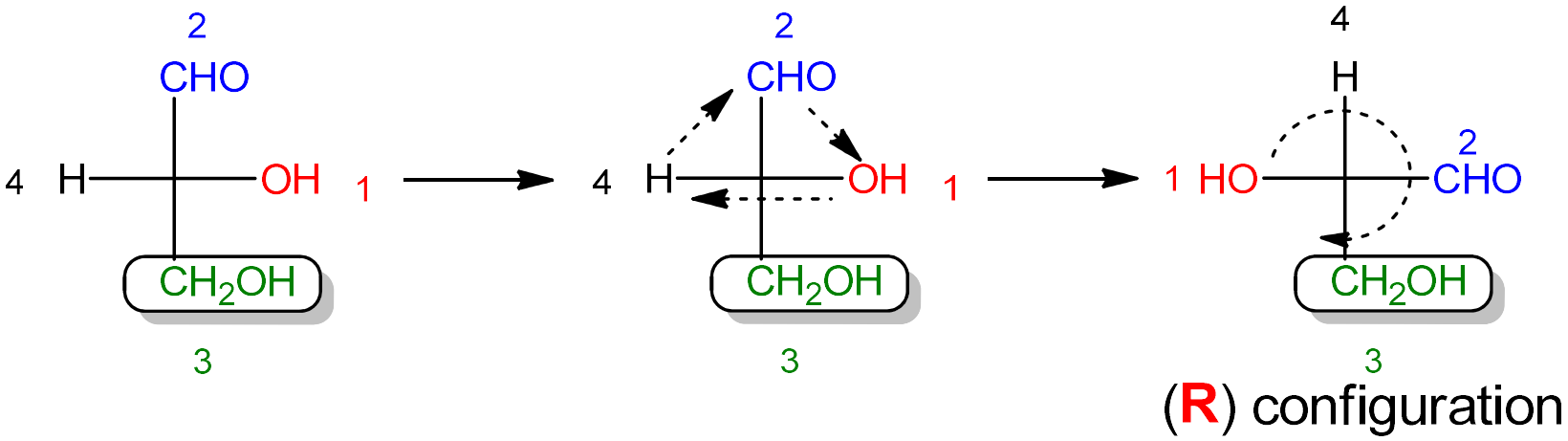
OH group located **left in Fischer** projection, translates to **upward in the Haworth / chair**

Rules for determining R/S configuration from Fischer projection

1. Draw the molecule in a Fischer projection
2. Exchange any 3 groups in sequence around a chiral center while holding 1 group in place
3. Place the group with the lowest priority at the top (or bottom) of the Fischer projection
4. Draw a curved arrow on the page pointing from 1→2→3 (ignore 4) according to the **Cahn-Ingold-Prelog** priority rules (CIP) [atomic number, molar mass,..]

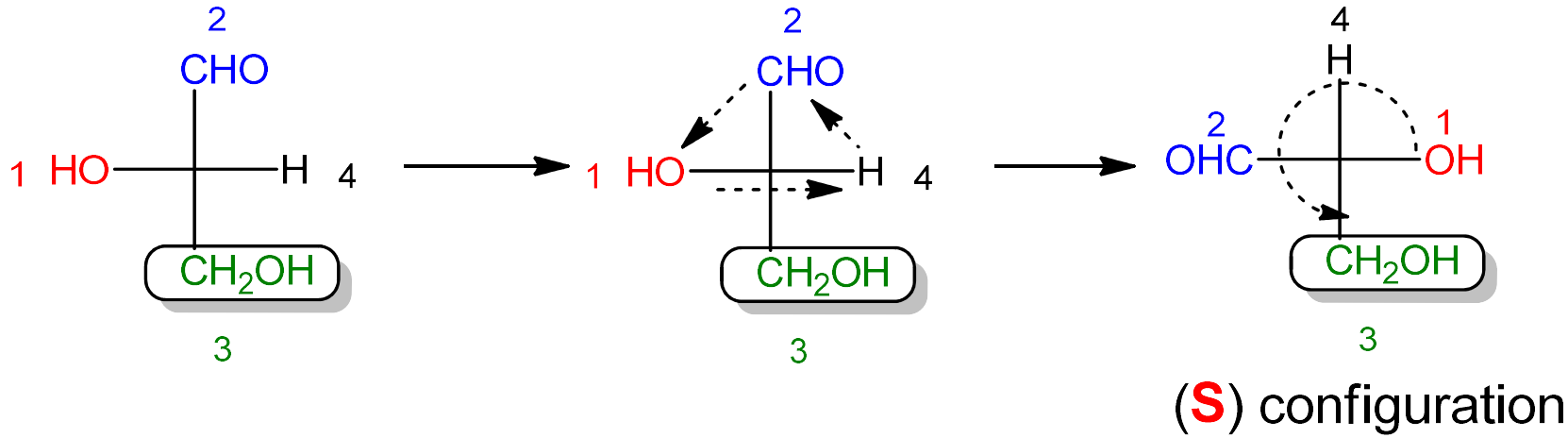
Example for determining R/S configuration from Fischer projection

D-Glyceraldehyde



Example for determining R/S configuration from Fischer projection

L-Glyceraldehyde



(**S**) configuration

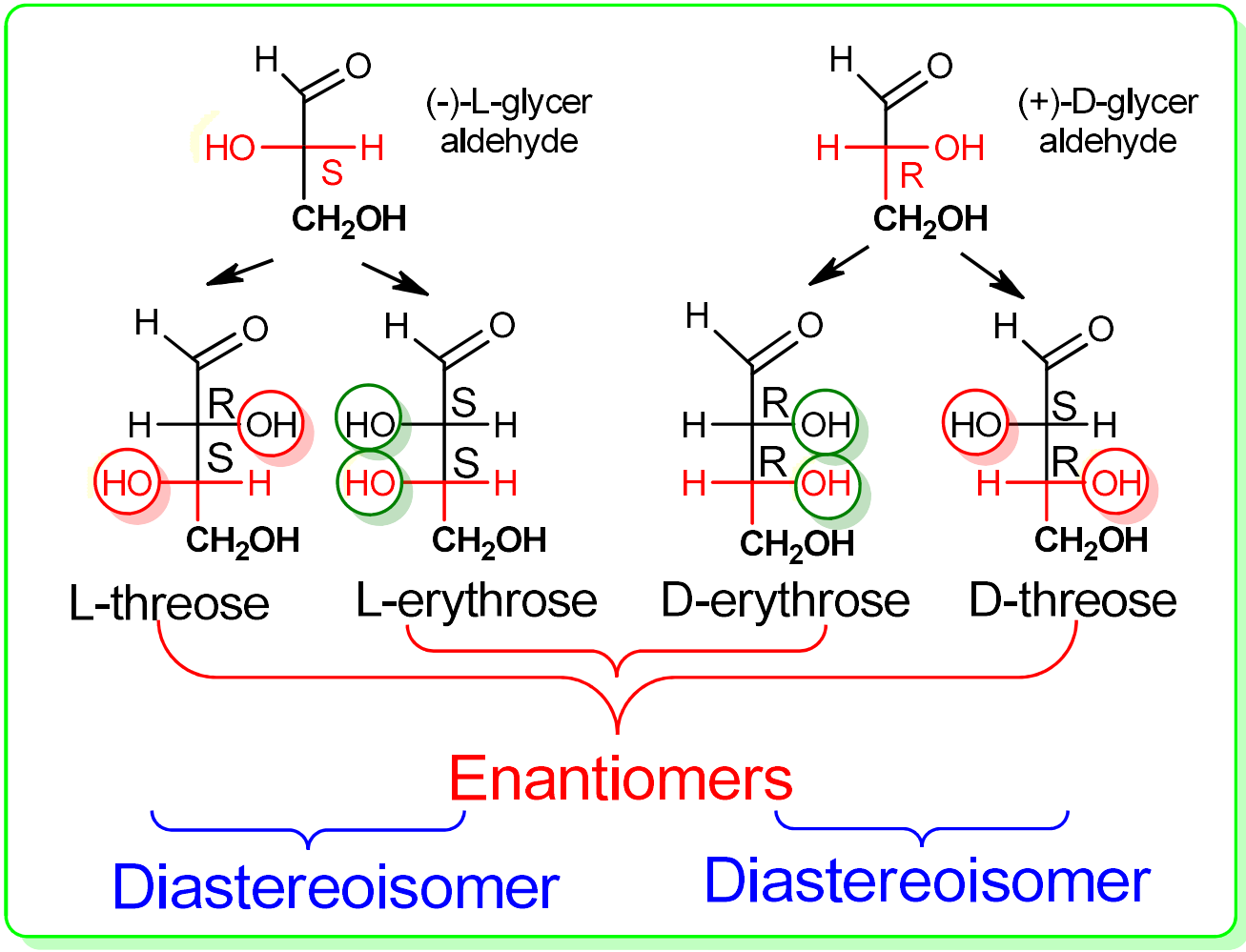
Diastereoisomers vs Enantiomers

Two enantiomers are chemically identical,

while diastereoisomers

differ in their physical and chemical properties

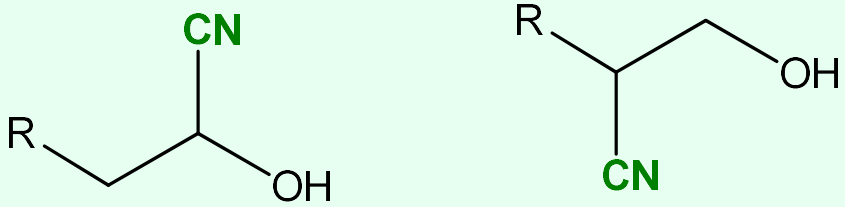
Diastereoisomers vs Enantiomers



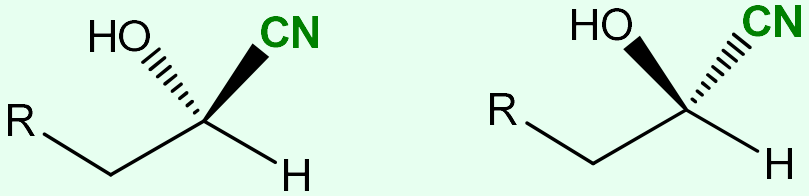
Diastereoisomers vs Enantiomers

Stereoisomers vs. Constitutional Isomers

Constitutional Isomers: **Connectivity is different**

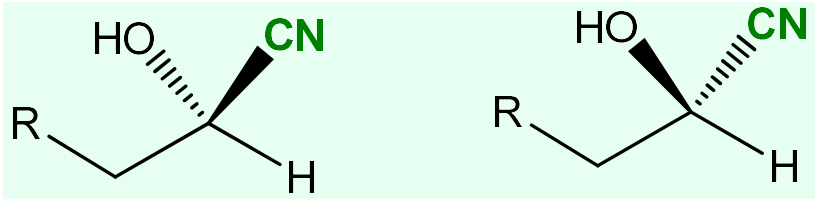


Stereoisomers: Connectivity of atoms is **the same**

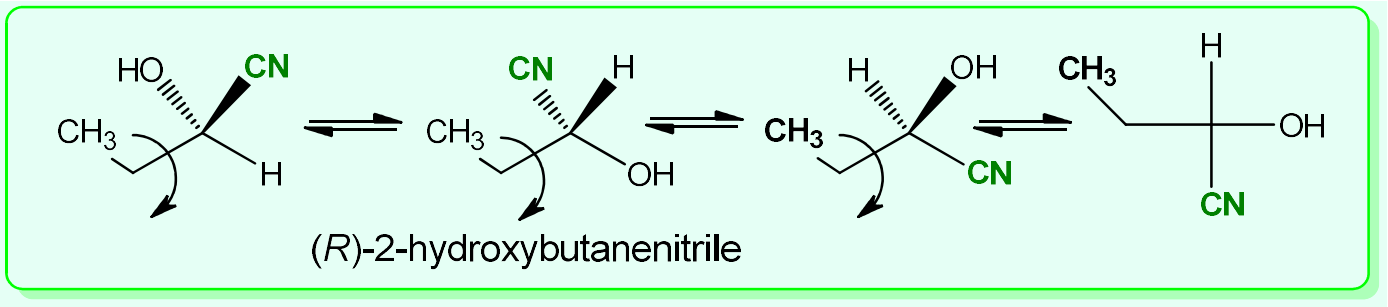


Configuration vs. Conformation

Configuration: going from one enantiomer to the other requires a bond to be broken



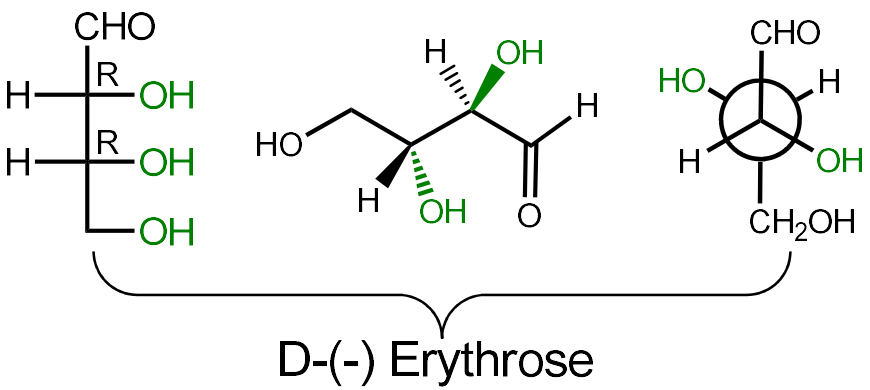
Conformation: Same molecule, **interconvertable by rotating about bonds**, but not breaking them.



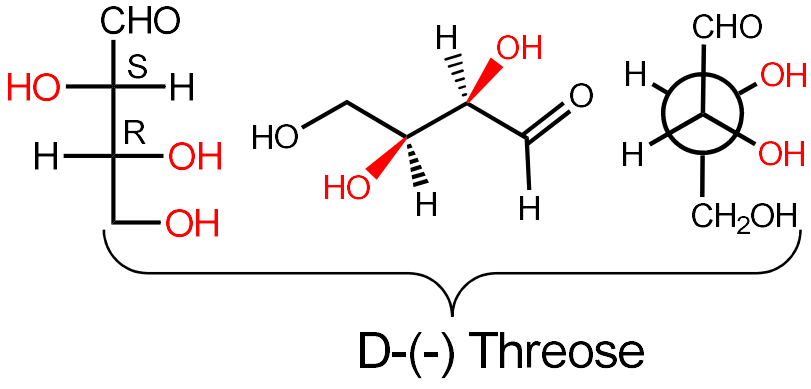
Aldehyde cyanohydrin

Erythro and Threo

D-*erythro* („E“) and D-*threo* („T“) terms for diastereoisomers with two adjacent chiral carbons, without symmetric ends. For symmetric molecules, use *meso*



D-(-) Erythrose



D-(-) Threose

	zig-zag	Fischer
erythro	opposite side (anti)	same side (syn)
threo	same side (syn)	opposite side (anti)

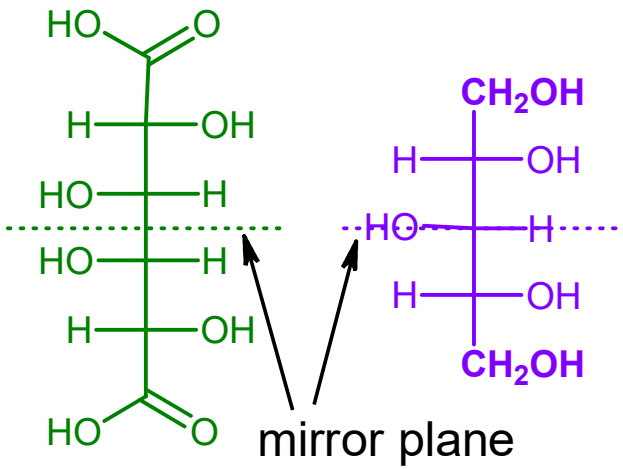
Optical inactive systems

Racemic mixture:

Mixture of two enantiomers in equal proportions

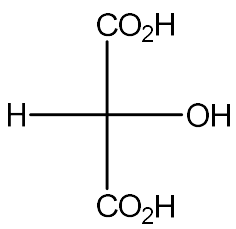
Meso-compounds: internal symmetry

galactaric acid xylitol

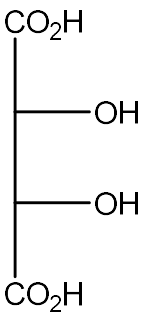


Question

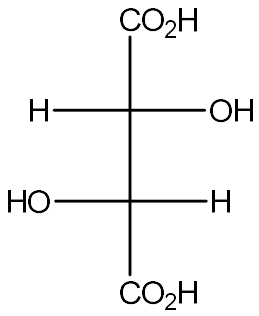
Which of the following aldaric acids are optically active?



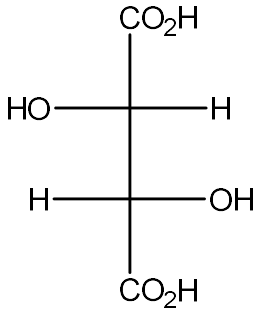
A



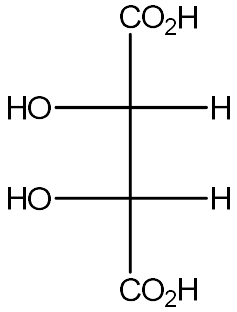
B



C

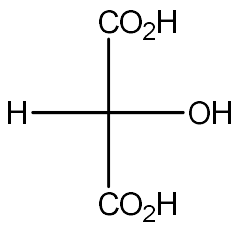


D



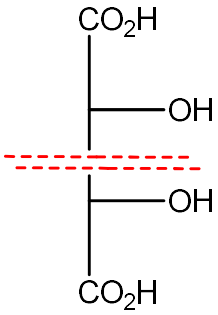
E

Answer



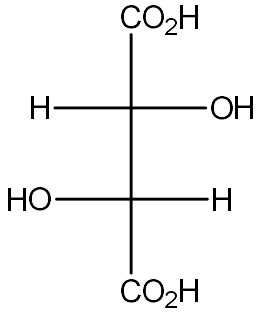
A

no stereocenter



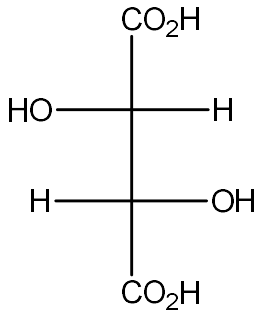
B

meso



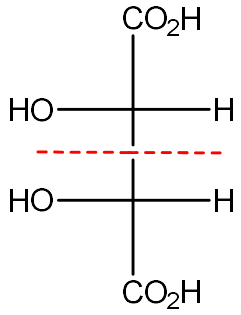
C

R,R



D

S,S

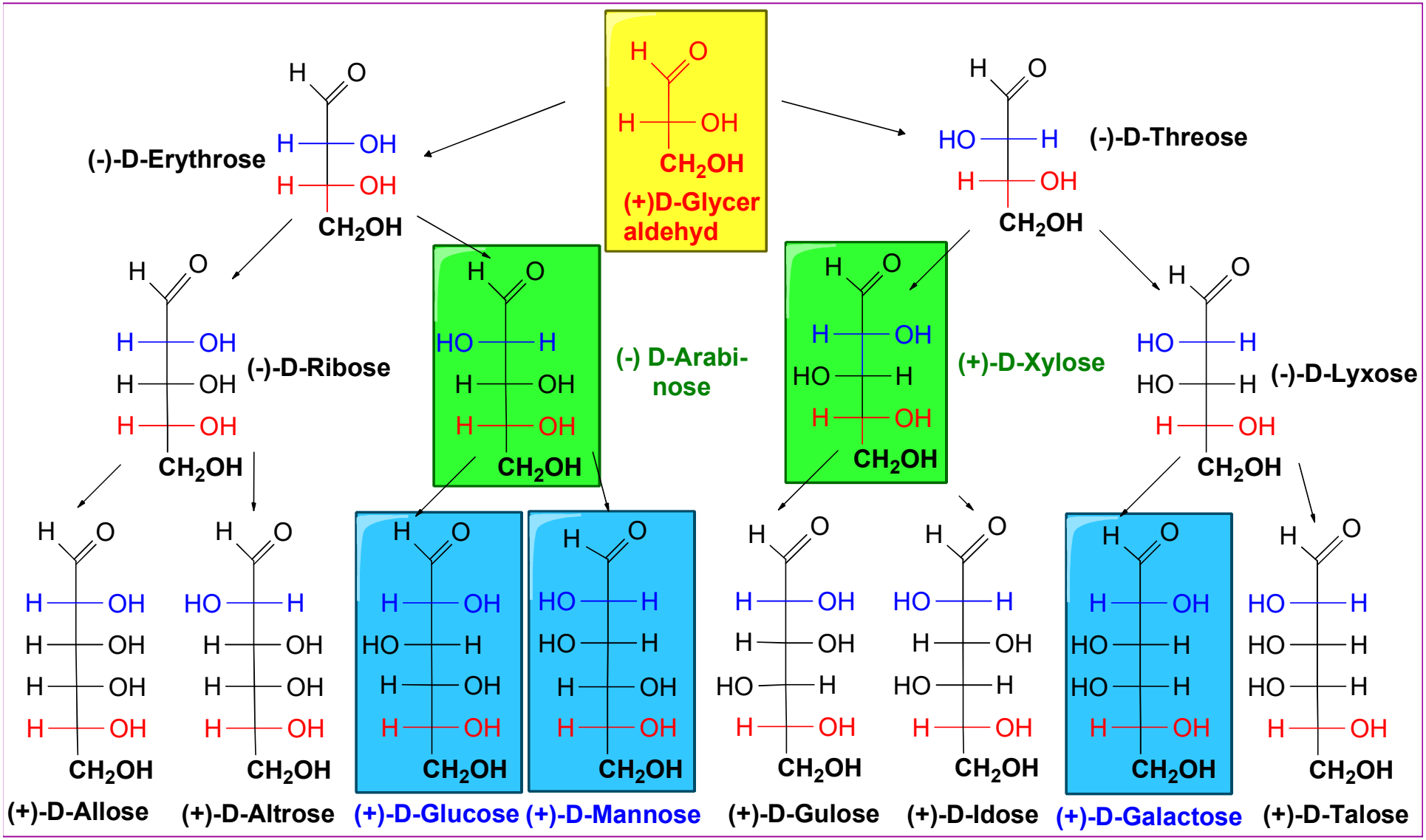


E

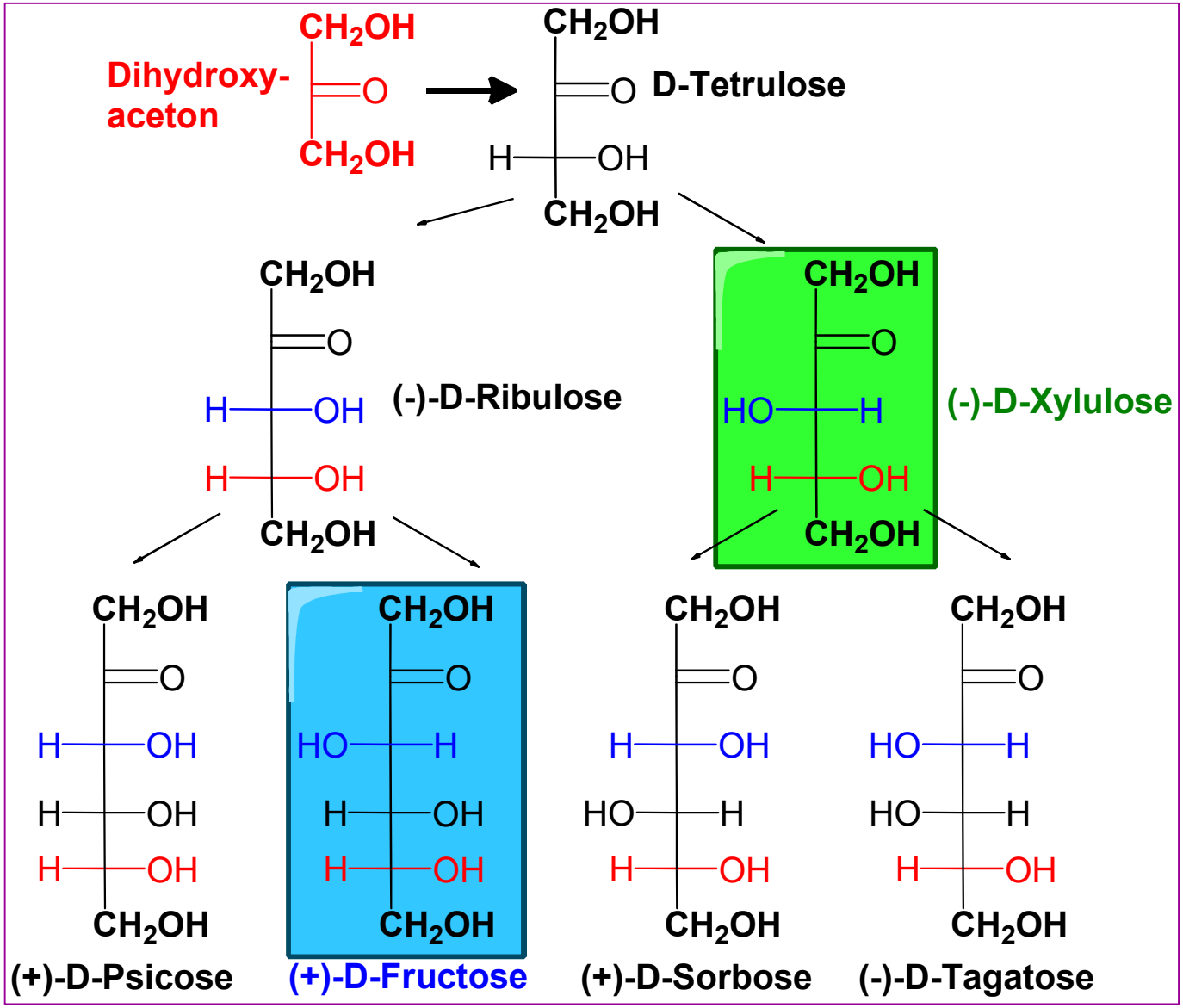
meso

C and D

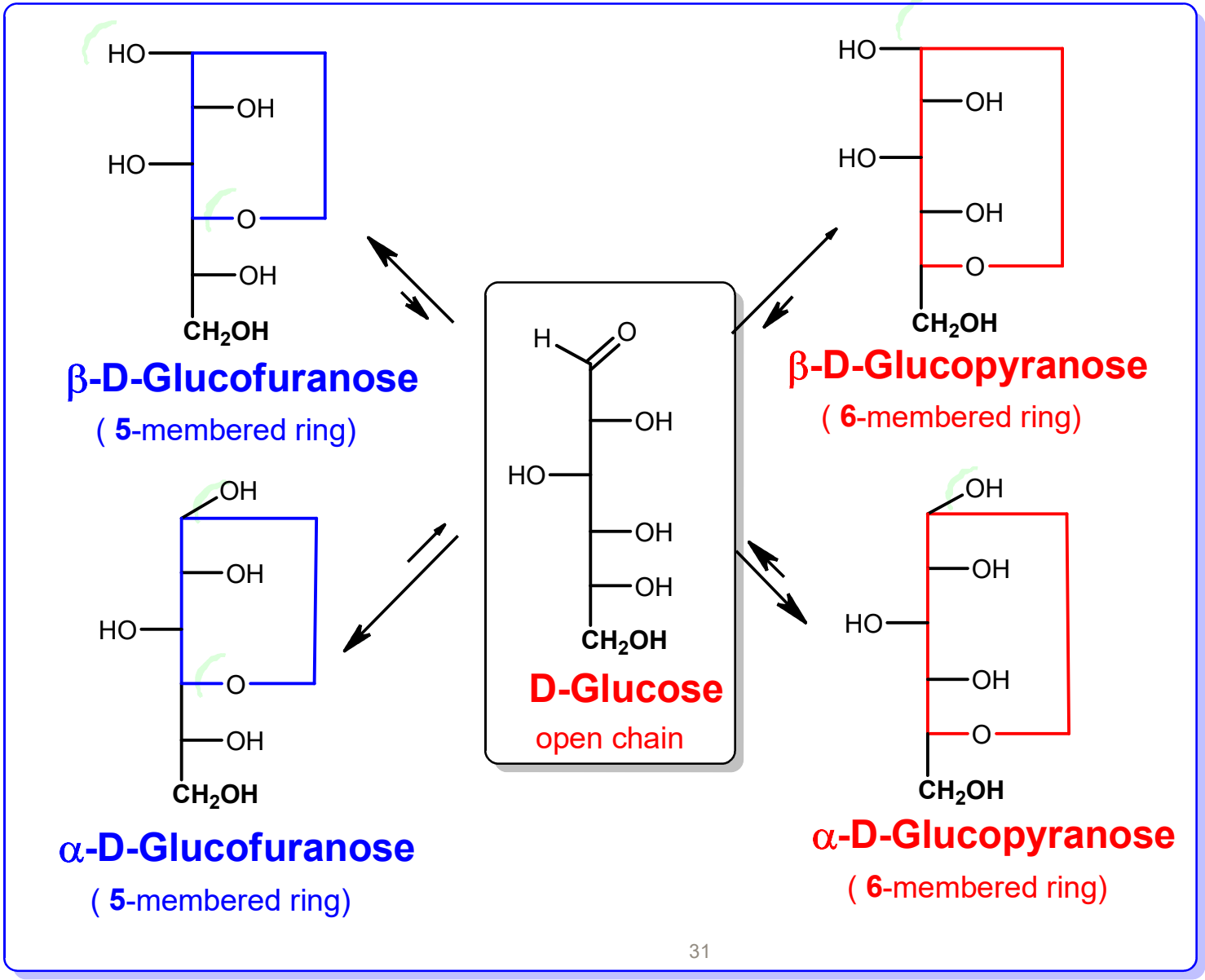
Acyclic Forms of D-Aldoses



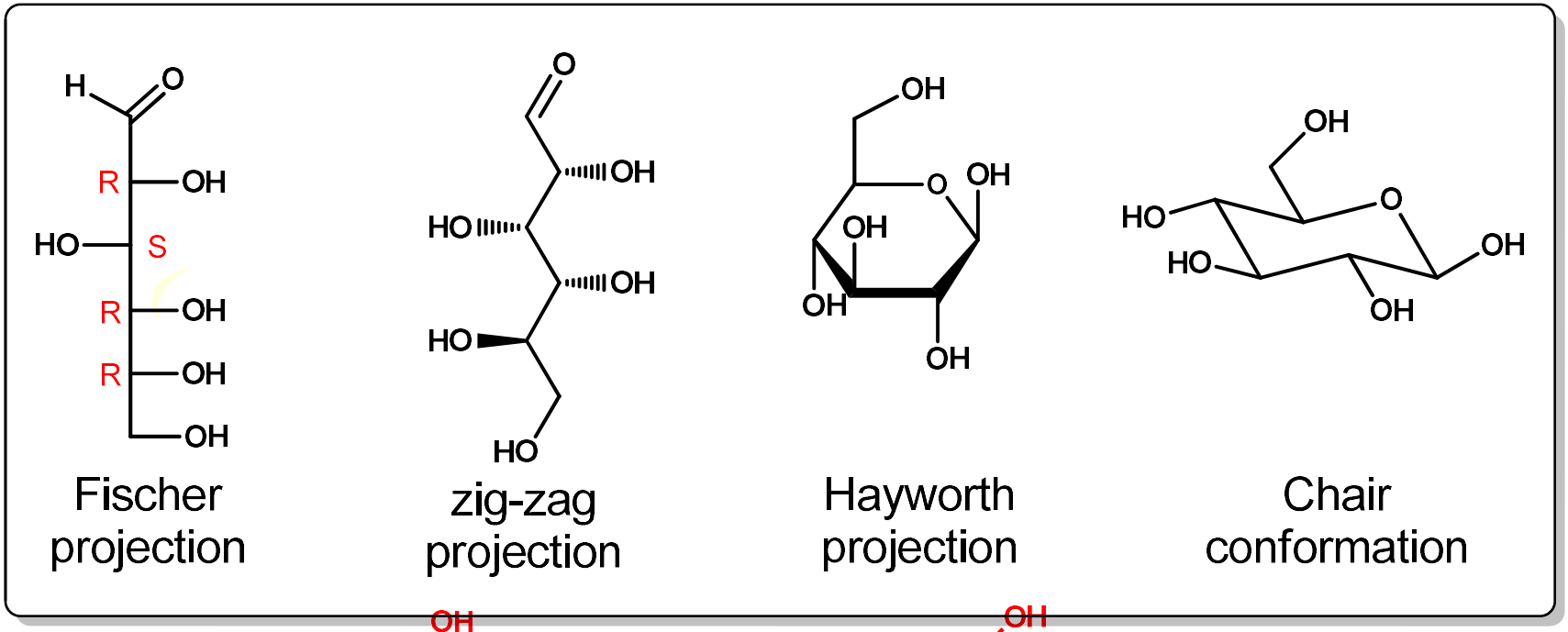
Acyclic Forms of Ketoses

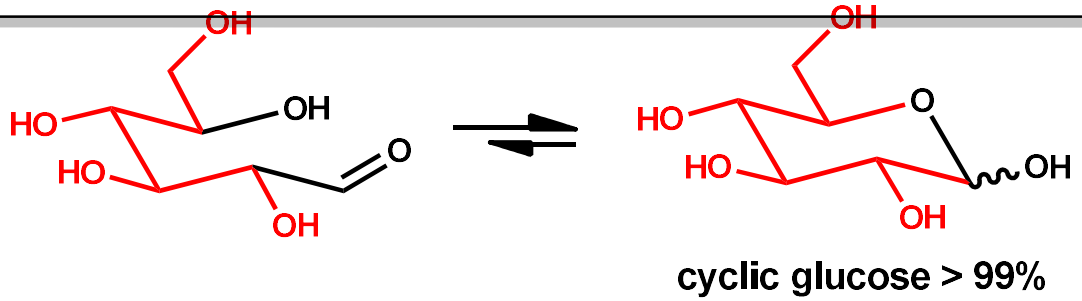


Formation of cyclic hemiacetals



Glucose structures

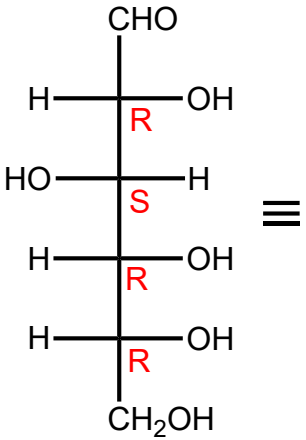




cyclic glucose > 99%

R/S of Glucose

D-Glucose



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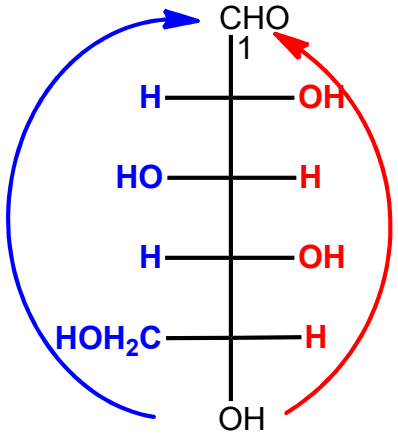
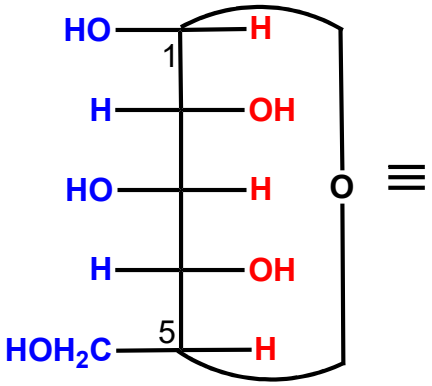


C-1 is **not** a chiralic center



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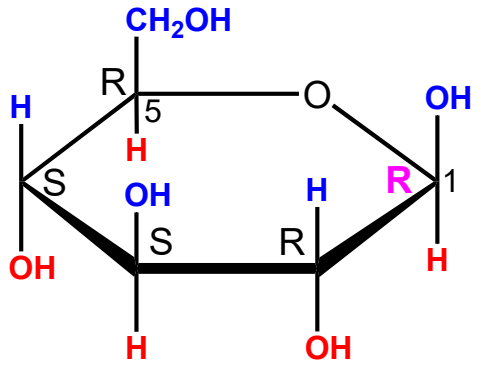
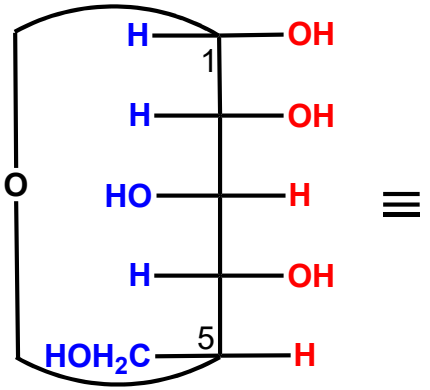


β-D-Glucopyranose

C-1 is a chiralic center



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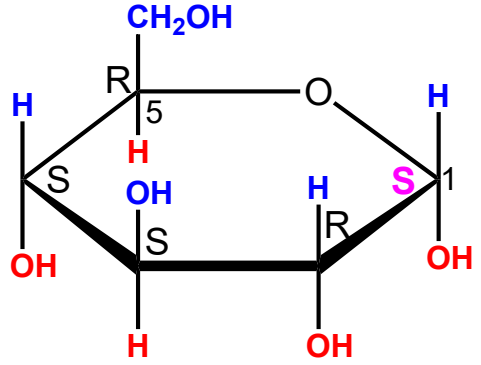
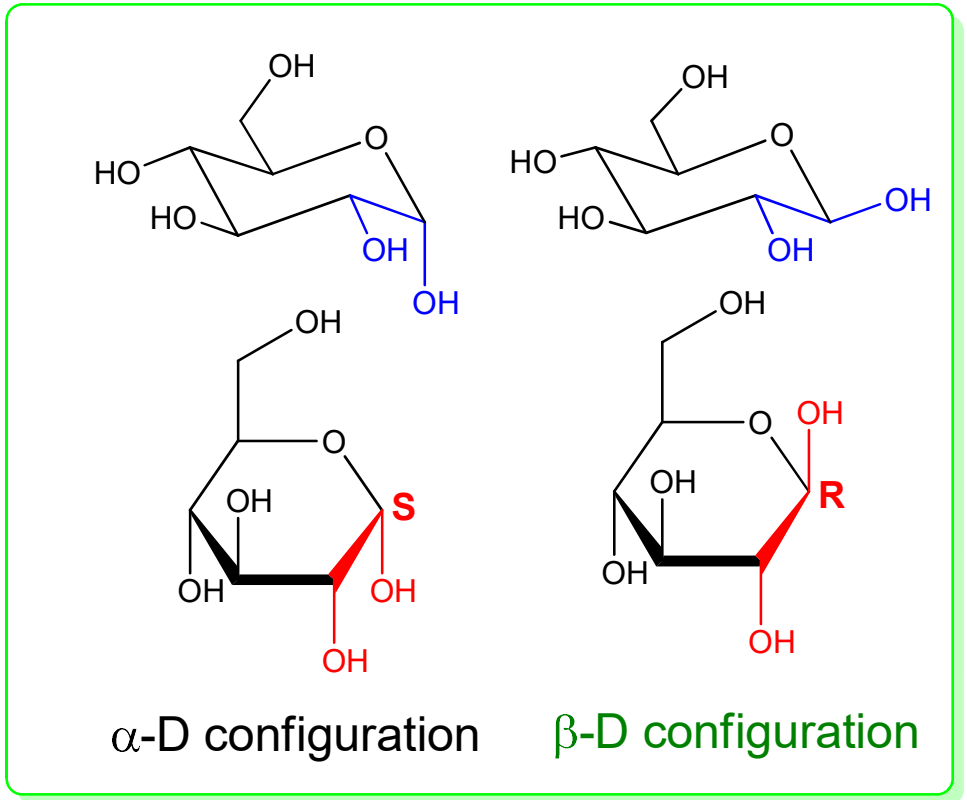


α-D-Glucopyranose

The anomeric configuration



D-series:

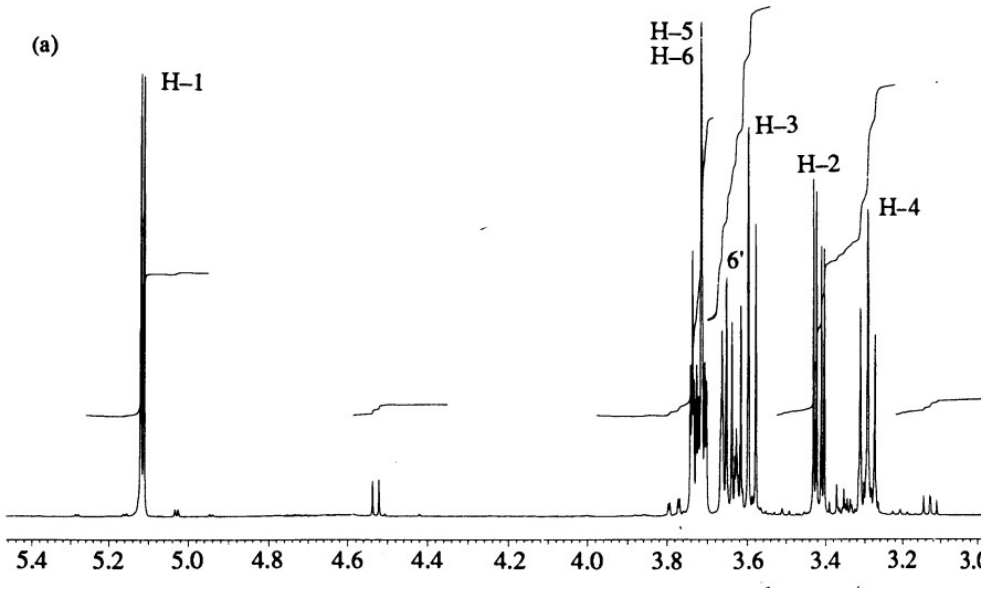
α-anomers: OH projecting downwards

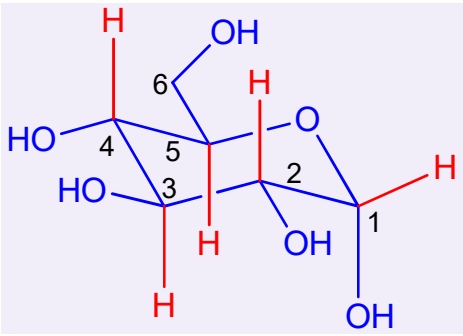
β-anomers: OH projecting upwards.

α- and β-anomers are diastereoisomers

^{1}H-NMR of α-D-glucopyranose

Dissolved in D_2O



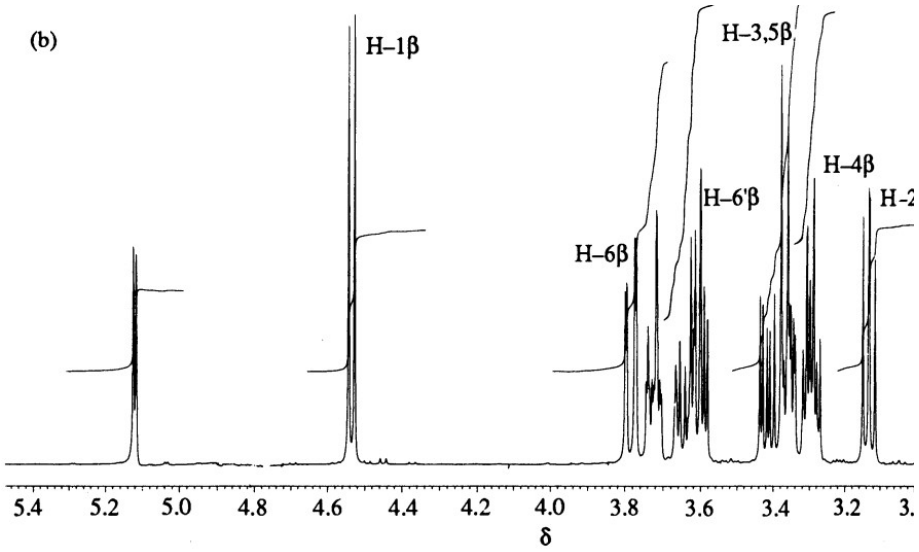


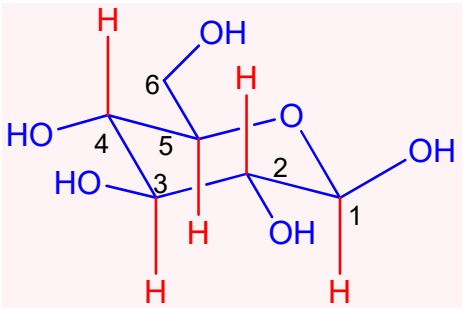
Anomeric H → **downfield shift due to the deshielding effect of the ring-O, appears as a doublet, coupling with H-2: δ 5.12 ppm, doublet (J = 3.6 Hz)**

Ring → **δ 3.3, 3.4, 3.6 ppm large splittings (10 Hz), characteristic of axial protons having axial neighbouring protons**

^{1}H-NMR of α/β-D-glucopyranose

Dissolved in D_2O





Isomerization after a few hours: 60% β

Anomeric → **4.53 ppm ~ 0.6 ppm upfield relative to H-1 of α-anomer, doublet with J = 7.8 Hz***

Ring-Hs→ **δ 3.13, 3.78 ppm**

*axial-H1 / axial-H2: due to influence of ring-O, J is smaller than 10 Hz

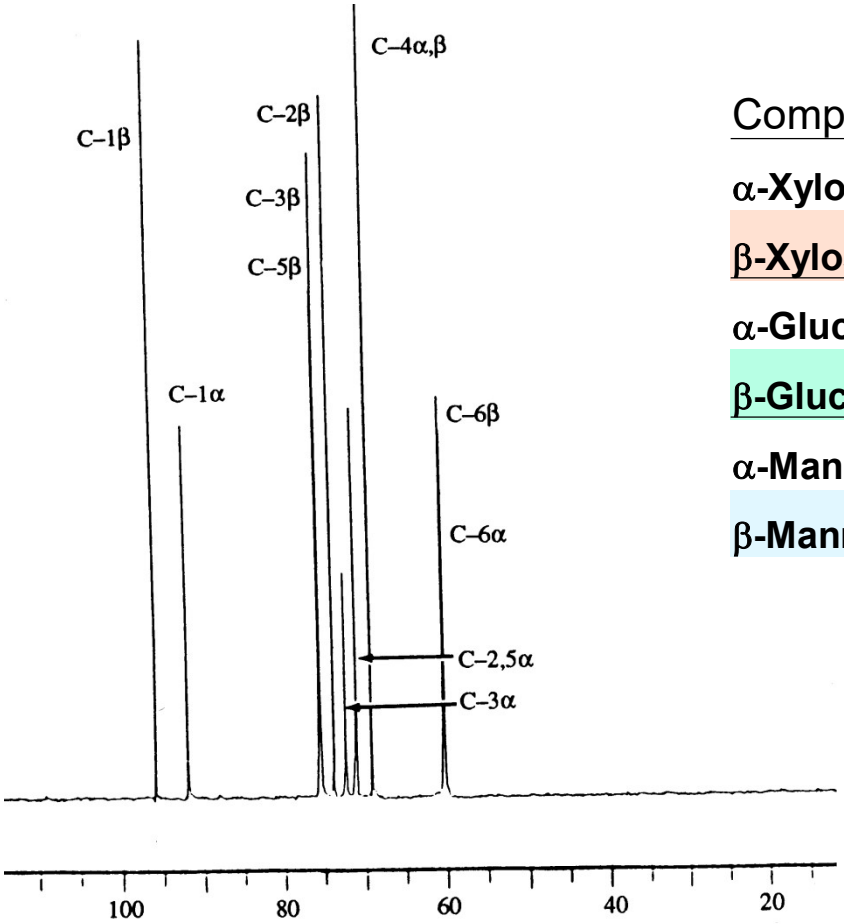
^{1}H-Chemical shifts of aldopyranoses

Compound		H-1	H-2	H-3	H-4	H-5	H-5'	H-6	H-6'
α-Xylose	δ, ppm	5,09	3,42	3,48	3,52	3,58	3,57		
	J, Hz	3,6	9,0	9,0		7,5	7,5		
β-Xylose	δ, ppm	4,47	3,14	3,33	3,51	3,82	3,22		
	J, Hz	7,8	9,2	9,0		5,6	10,5		
α-Glucose	δ, ppm	5,09	3,41	3,61	3,29	3,72		3,72	3,63
	J, Hz	3,6	9,5	9,5	9,5			2,8	5,7
β-Glucose	δ, ppm	4,51	3,13	3,37	3,3	3,35		3,75	3,6
	J, Hz	7,8	9,5	9,5	9,5			2,8	5,7
α-Mannose	δ, ppm	5,05	3,79	3,72	3,52	3,7		3,74	3,63
	J, Hz	1,8	3,8	10,0	9,8			2,8	6,8
β-Mannose	δ, ppm	4,77	3,85	3,53	3,44	3,25		3,74	3,6
	J, Hz	1,5	3,8	10,0	9,8			2,8	6,8
α-Galactose	δ, ppm	5,16	3,72	3,77	3,9	4		3,7	3,62
	J, Hz	3,8	10,0	3,8	1,0			6,4	6,4
β-Galactose	δ, ppm	4,48	3,41	3,56	3,84	3,61		3,7	3,62
	J, Hz	8,0	10,0	3,8	1,0			3,8	7,8

^{13}C-NMR of α,β-D-glucopyranose

No resonances for an aldehyde group

Dissolved in D_2O



Compound		C-1	C-2	C-3	C-4	C-5	C-6
α-Xylose	δ, ppm	93,1	72,5	73,9	70,4	61,9	
β-Xylose	δ, ppm	97,5	75,1	76,8	70,2	66,1	
α-Glucose	δ, ppm	92,9	72,5	73,8	70,6	72,3	61,6
β-Glucose	δ, ppm	96,7	75,1	76,7	70,6	76,8	61,7
α-Mannose	δ, ppm	95,0	71,7	71,3	68,0	73,4	62,1
β-Mannose	δ, ppm	94,6	72,3	74,1	67,8	77,2	62,1

Mutarotation

On dissolution of each crystalline, reducing sugar in water, the hemiacetal ring opens and forms conformers.

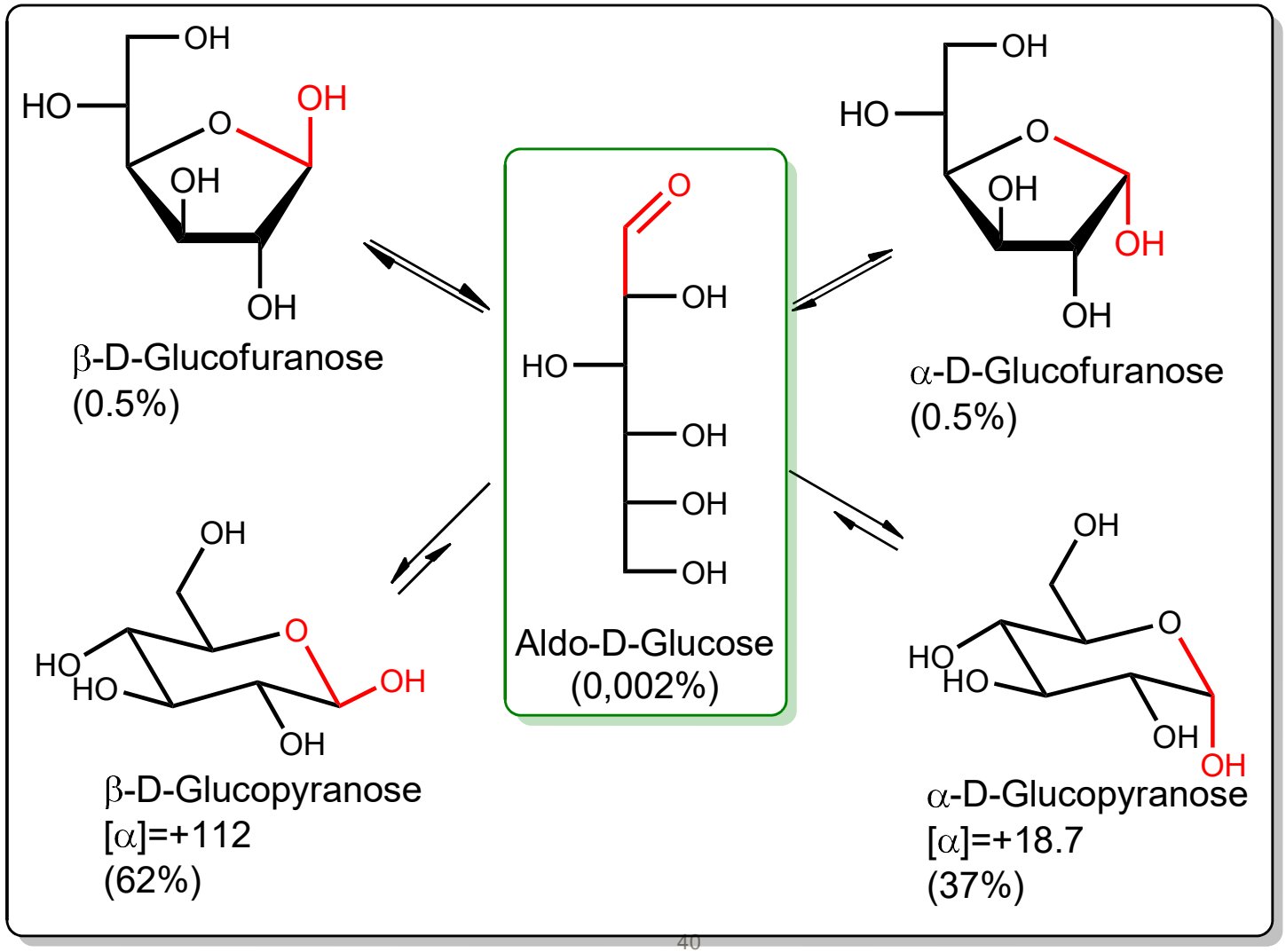
Equilibrium accompanied by a change in optical rotation, known as **mutarotation**.

Mutarotation of D-glucose leads to a mixture of **α- and β-pyranoses and -furanoses**.

Specific rotation keeps changing until an equilibrium value of +52.7° is reached after 3 h.

Mutarotation

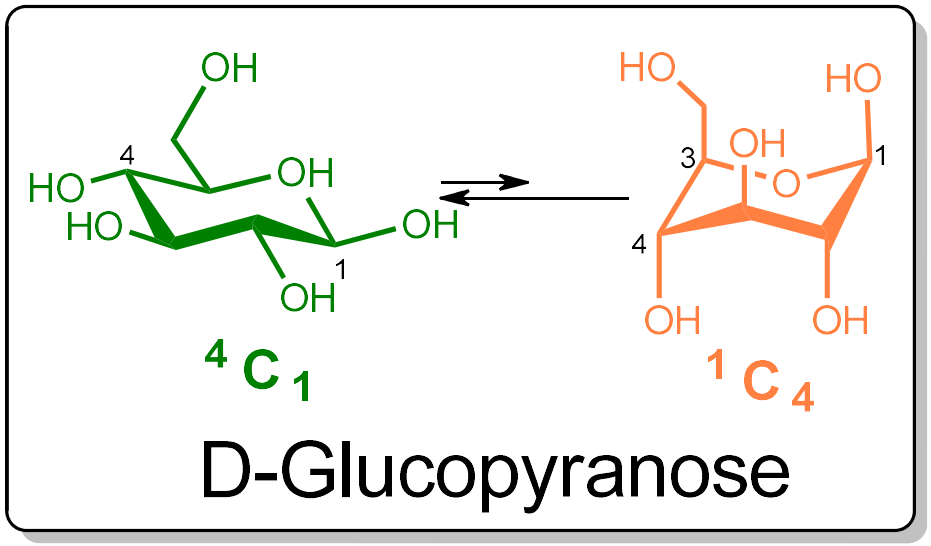
Base- and acid catalyzed



Conformations of Pyranoses

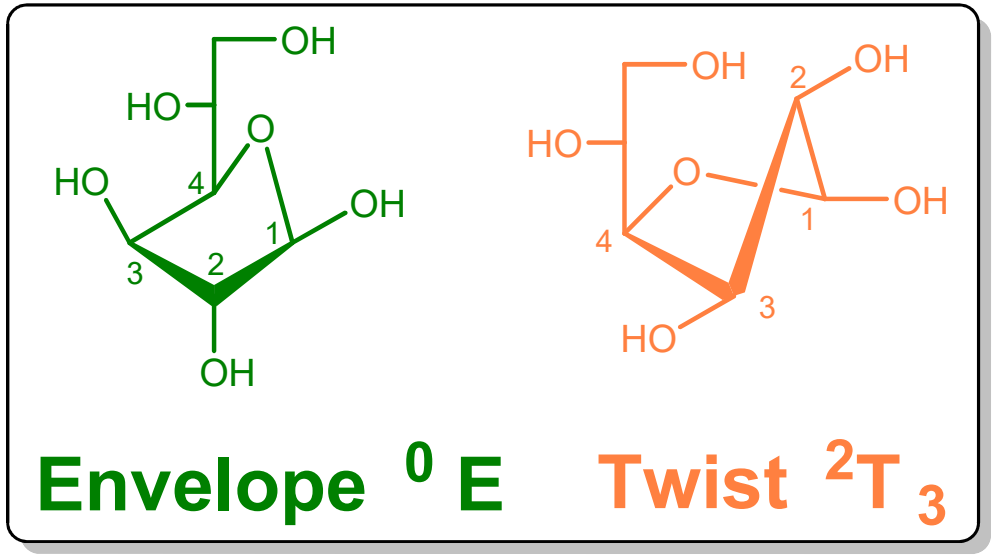
Two possible chair conformations.

$^{1}C_{4}$ conformation is unfavored compared to $^{4}C_{1}$ because of van der Waals repulsion of the 1,3 diaxially positioned ring substituents: ΔE = 25 kJ/mol



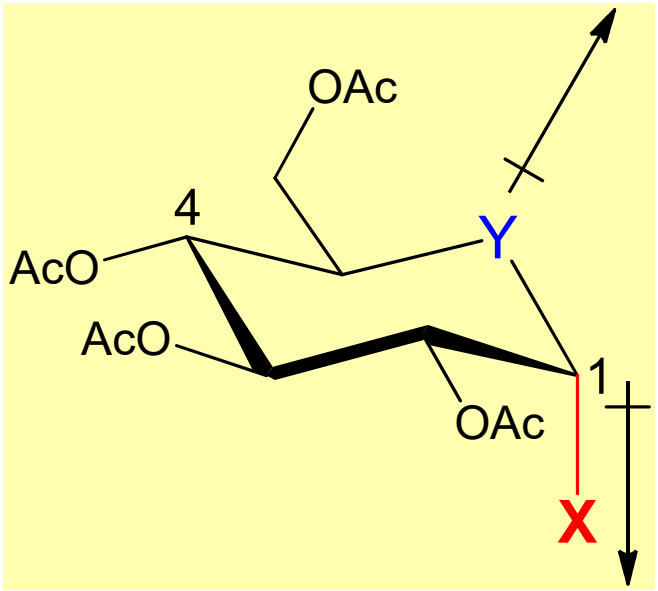
Conformations of Furanoses

- Non-planar
- **Envelope (E):** $^{1}E,E_{1},^{2}E,E_{2},^{3}E,E_{3},^{4}E,E_{4},^{0}E,E_{0}$
- **Twist (T):** $^{0}T_{1},^{1}T_{0},^{1}T_{2},^{2}T_{1},^{2}T_{3},^{3}T_{2},^{3}T_{4},^{4}T_{3},^{4}T_{0},^{0}T_{4}$



The anomeric effect*

Electronegative groups (**X**) at the anomeric centre stabilize the sterically unfavored axial position.



*R. Lemieux

The anomeric effect*

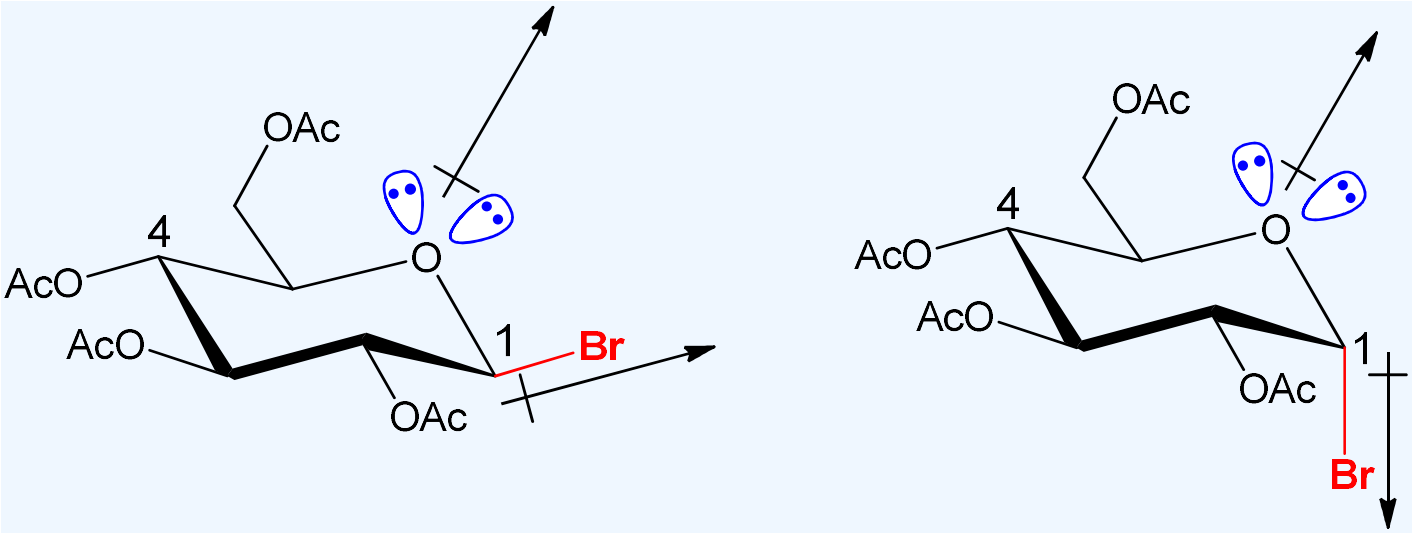
Explained by dipol-dipol interaction. One dipole arises from the two lone e^--pairs of the ring-O (Y).

The other dipole points along the polarized bond between anomeric C and its bound X.

Anomeric configurations, where the two dipoles partially neutralize each other are favored

*R. Lemieux

The anomeric effect



Anomeric effect favors the axial conformation.

In the case of acetobromoglucose the β-anomer is unknown.

The anomeric effect

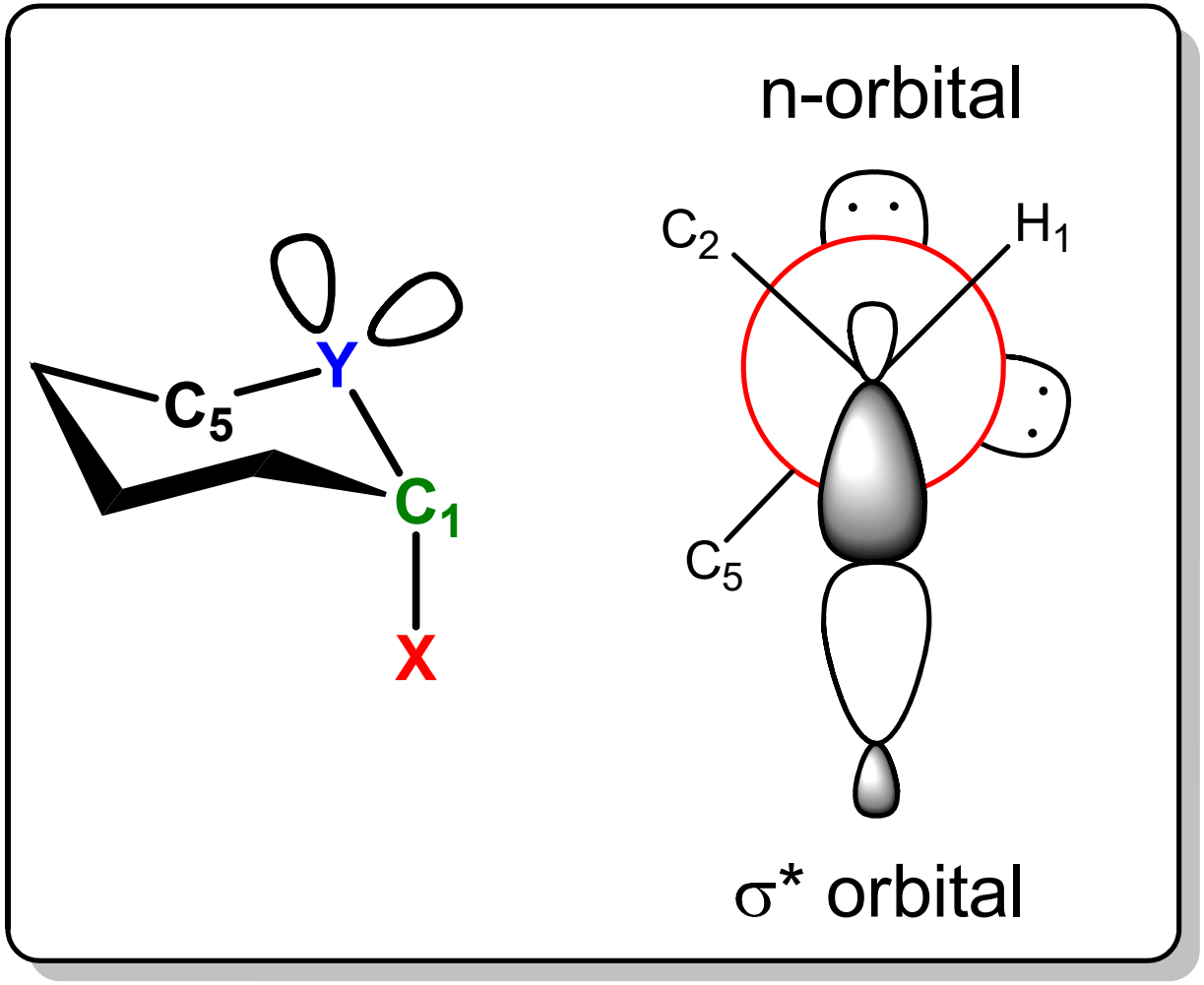
Stereoelectronic effect:

Lone pair of e^- located in the n-orbital of Y overlaps with the antibonding σ^*-orbital of the C-X bond.

Energy favorable delocalization of nonbonding $\mathbf{e}^-$ only possible with an antiperiplanar arrangement.

When C-2 is equatorial (glucose), the anomeric effect is weakened, when C-2 is axial (mannose), it is enhanced.

The anomeric effect

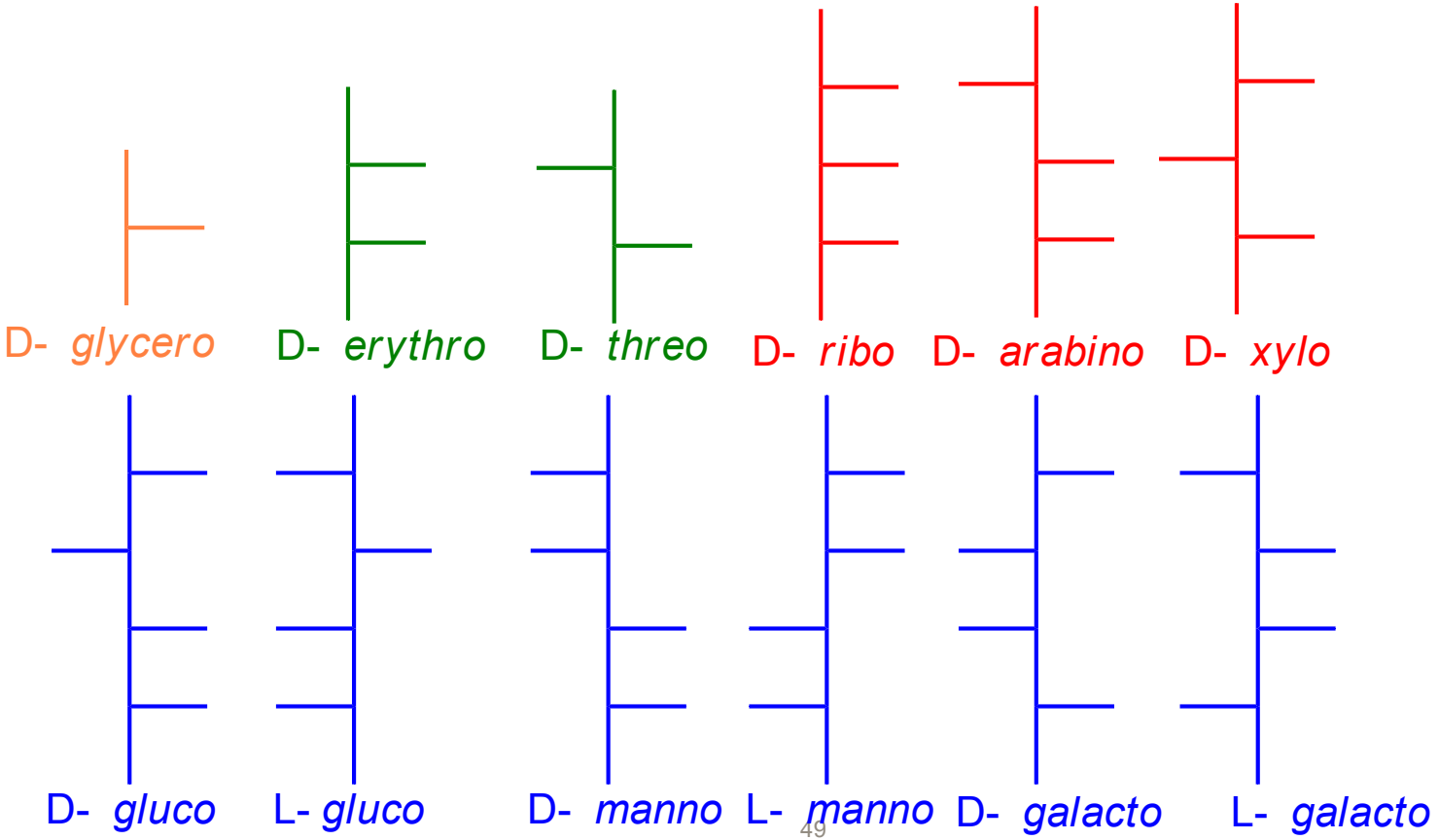


Learning Outcomes

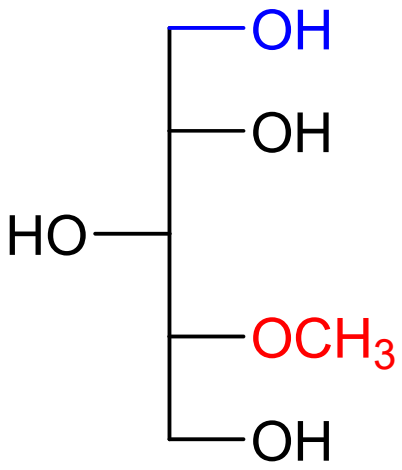
1. Structure and stereochemistry of monosaccharides
2. **Nomenclature of monosaccharides**
3. Important monosaccharides in wood chemistry
4. Reactions of monosaccharides
5. Oligosaccharides

Nomenclature of monosaccharides

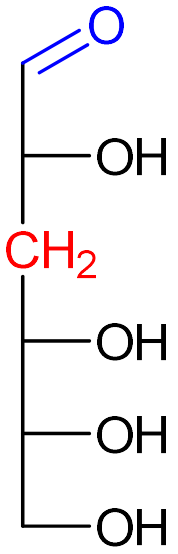
- Prefix ”deoxy”
- Prefix ”substituent”, *e.g.* 4-O-methyl, 3-bromo,…
- Trivial names until six carbon sugars: *xylo*-, *gluco*-,



Nomenclature of monosaccharides



4-*O*-Methyl-D-xylitol

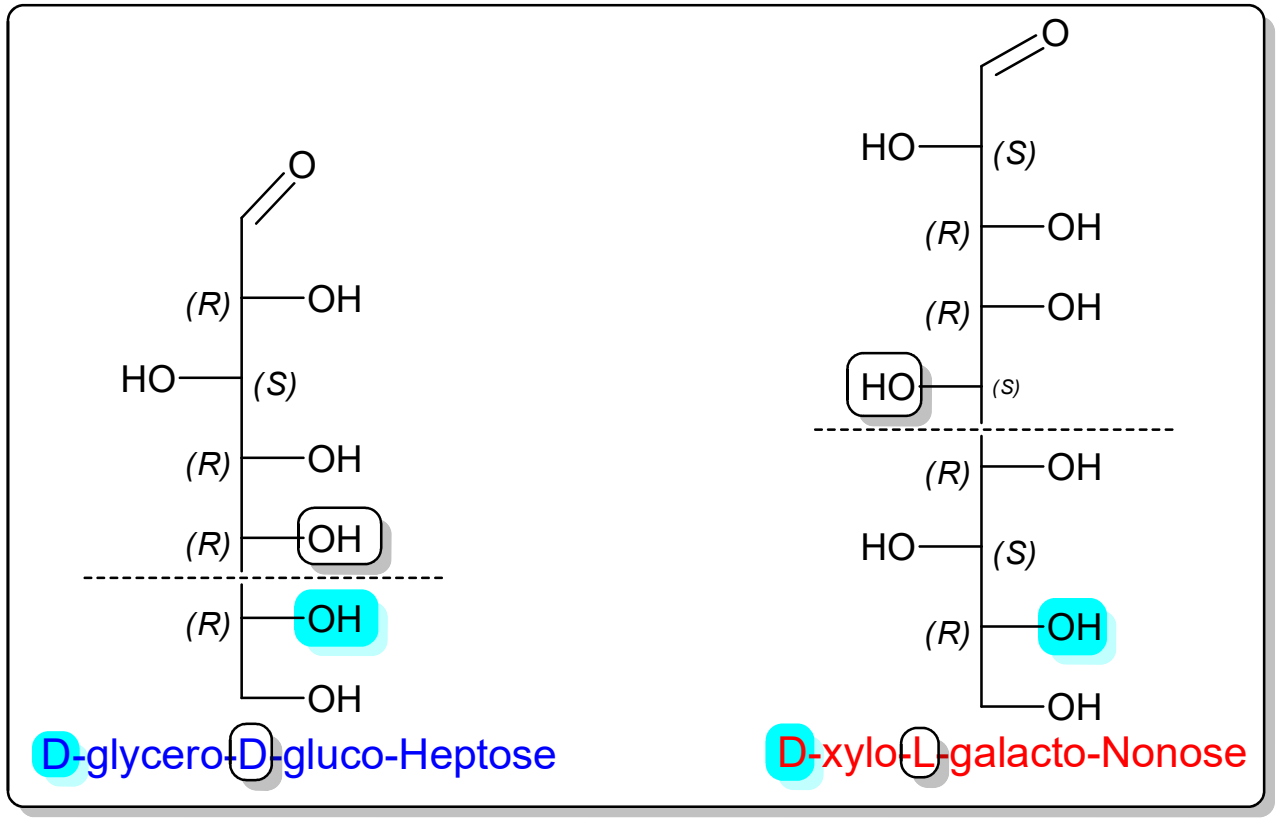


3-Deoxy-D-*ribo*-hexose

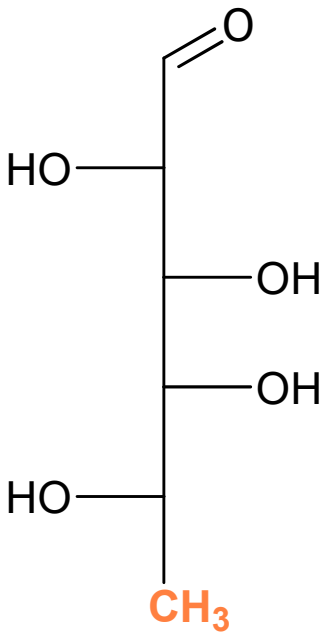
>6 C-atom monosaccharides

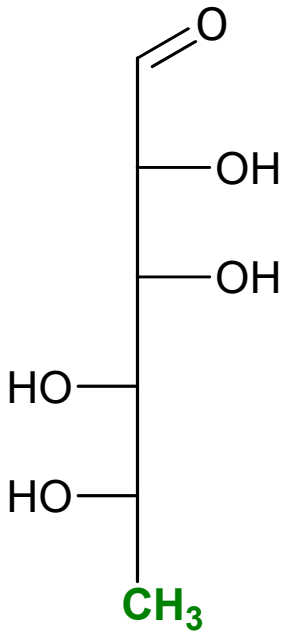
By adding 2 or more configurational prefixes to the stem name.

Prefix, relating to the group of C-atoms farthest from C-1 is cited first



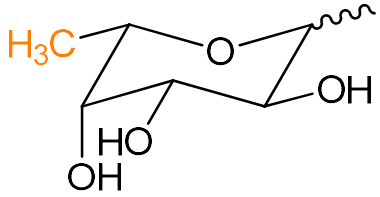
Deoxygenated sugars

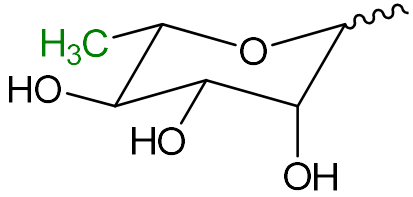




OH-replaced by H:
deoxy

Most abundant *deoxy* sugars are **L-Fucose** and **L-Rhamnose**



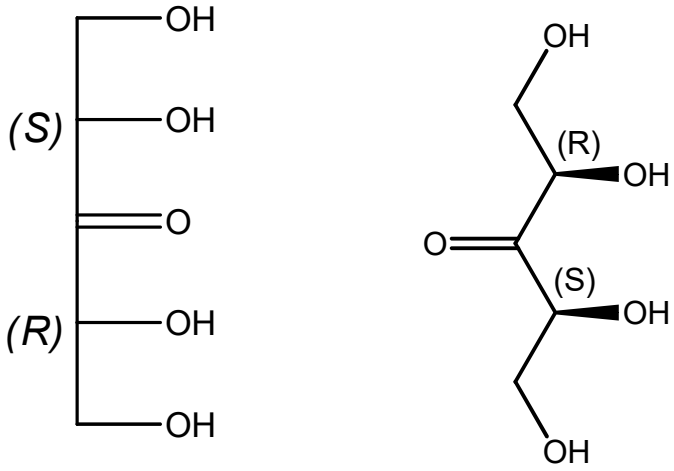


L-Fucose
6-Deoxy-L-galacto-pyranose

L-Rhamnose
6-Deoxy-L-manno-pyranose

Ketoses

ULOSE implies *KETOSE*



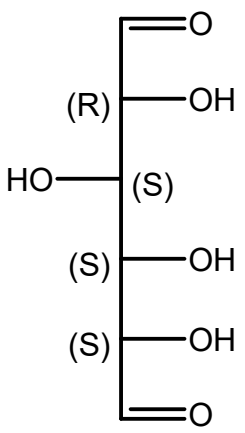
erythro-pent-3-ulose

(2R,4S)-1,2,4,5-tetrahydroxypentan-3-one

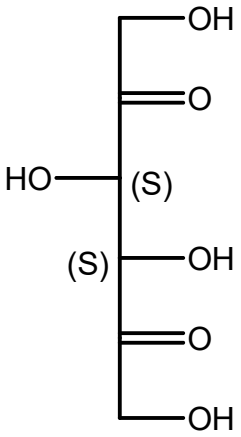
Dicarbonyl Compounds

Dialdehyde derivatives of aldoses are ”dialdoses”.

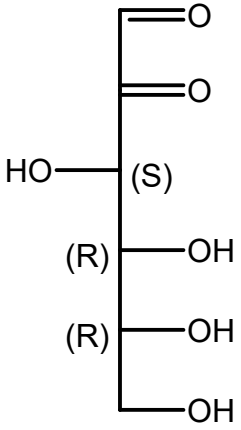
When such compounds have to be described in cyclic forms, the carbonyl goup involved in ring formation must be specified.



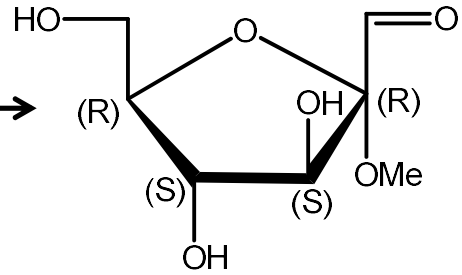
D-*gluco*-hexodialdose



D-*threo*-hexo-2,5-diulose



D-*arabino*-hexos-2-ulose

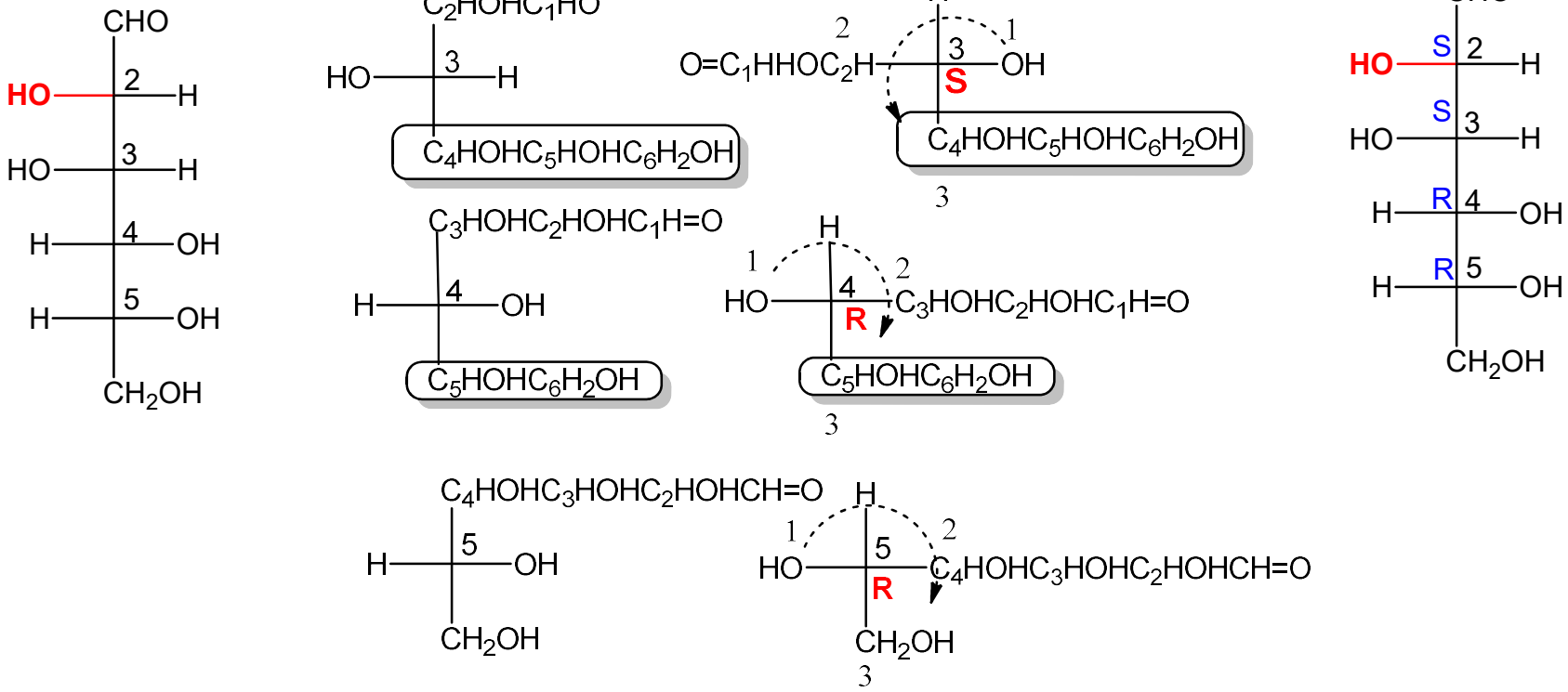


Methyl-α-D-*arabino*-hexos-2-ulo-2,5-furanoside

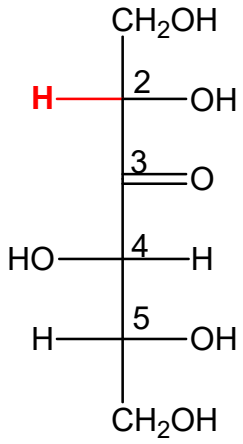
Ring closure involving O-5 and the ketonic group

Stereochemistry

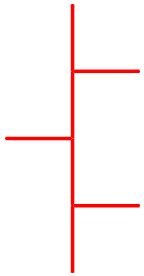
3. Describe the configuration of the chiral centers of the following molecule by the Cahn-Ingold-Prelog Convention



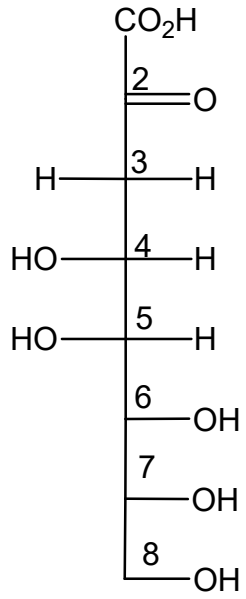
Nomenclature



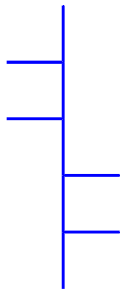
D-xylo-hex-3-ulose or
D-xylo-hexulose



D- *xylo*



KdO=Ketodeoxyoctonic acid
3-deoxy-D-manno-oct-2-ulosonic acid



D- *manno*

Learning Outcomes

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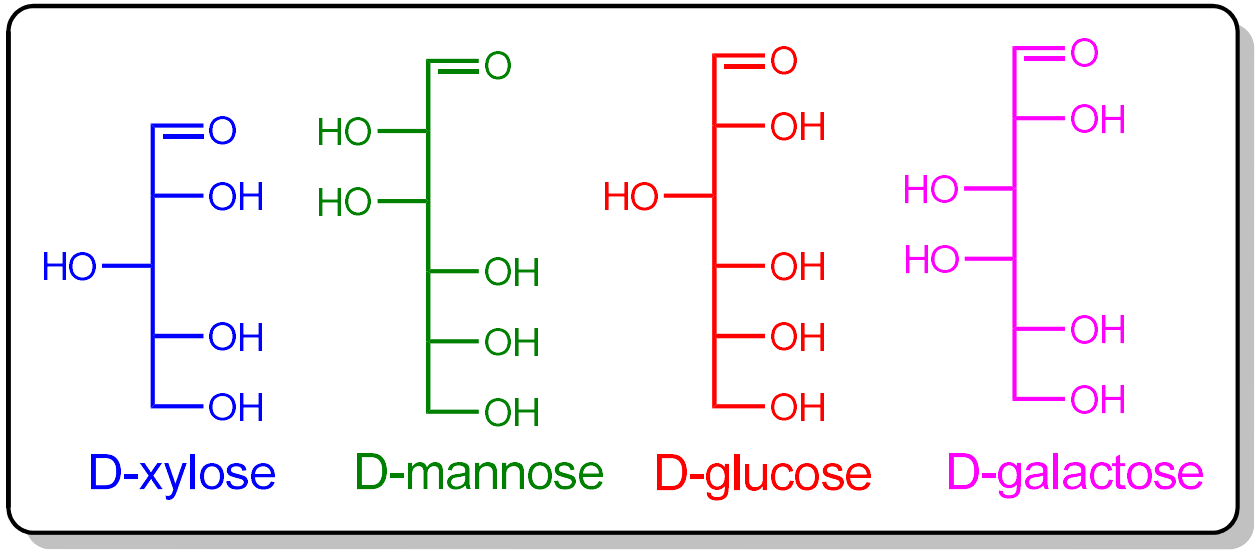
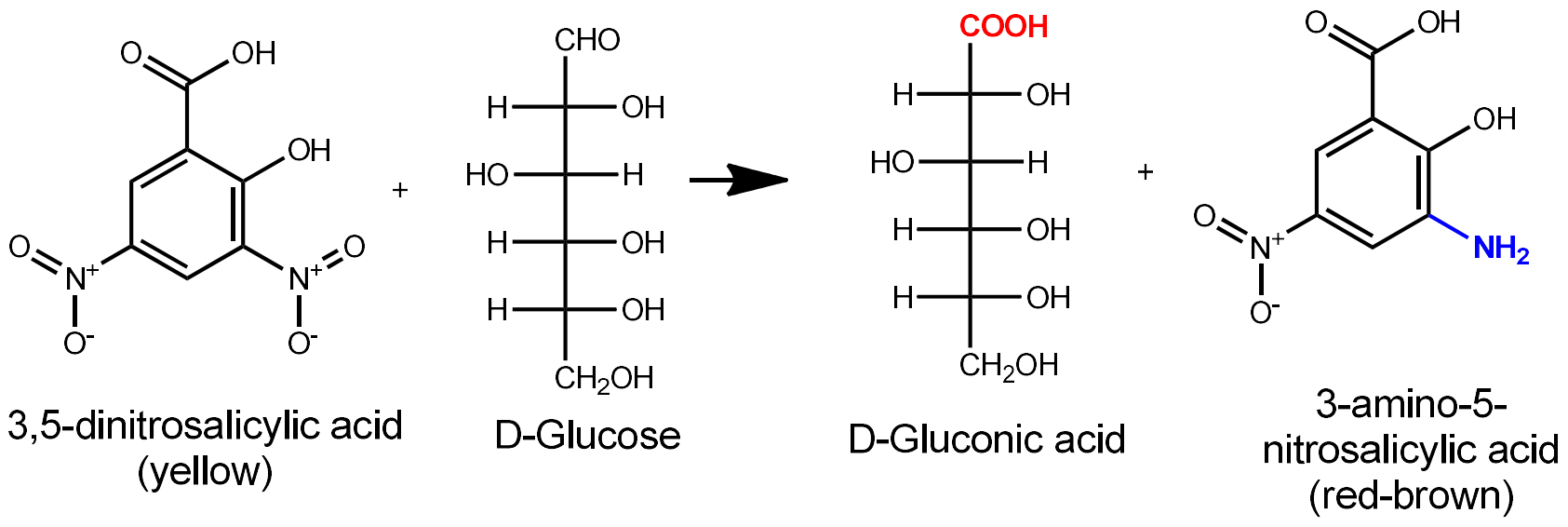
Aldoses – Reducing Sugars



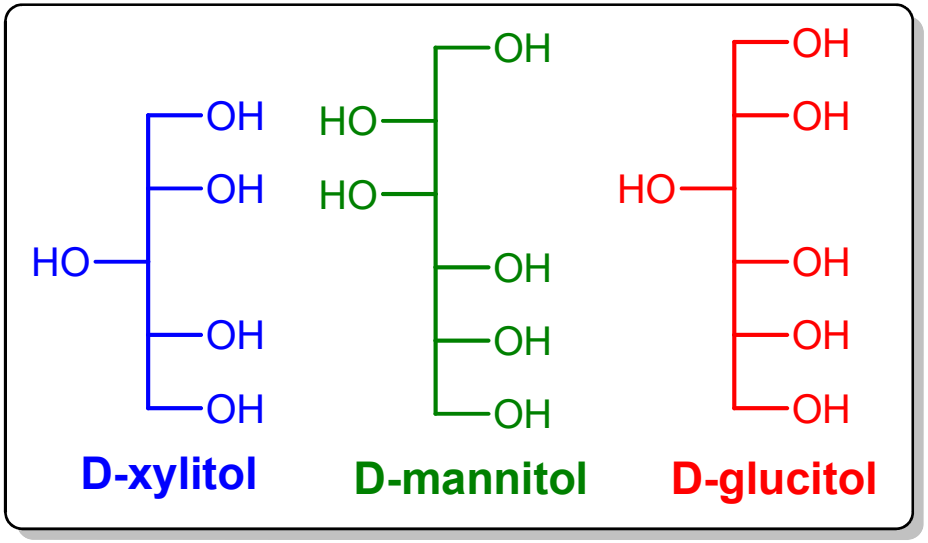
- D-xylose is not metabolized by humans
- D-mannose might prevent certain kinds of bacteria from sticking to the walls of the urinary tract and causing infection
- D-glucose is a ubiquitous fuel in biology. Through aerobic respiration it provides 16 kJ/g.
- D-galactose is found in dairy products. It is synthesized by the body where it forms glycolipids and glycoproteins.

Detection of reducing sugars by calorimetry

The reducing sugars reduce **3,5-dinitrosalicylic acid**, DNSA, to 3-amino-5-nitrosalicylic acid



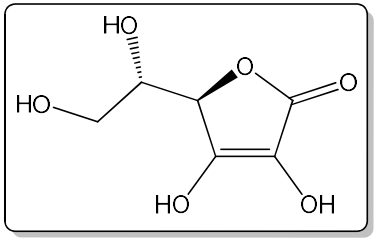
Alditols



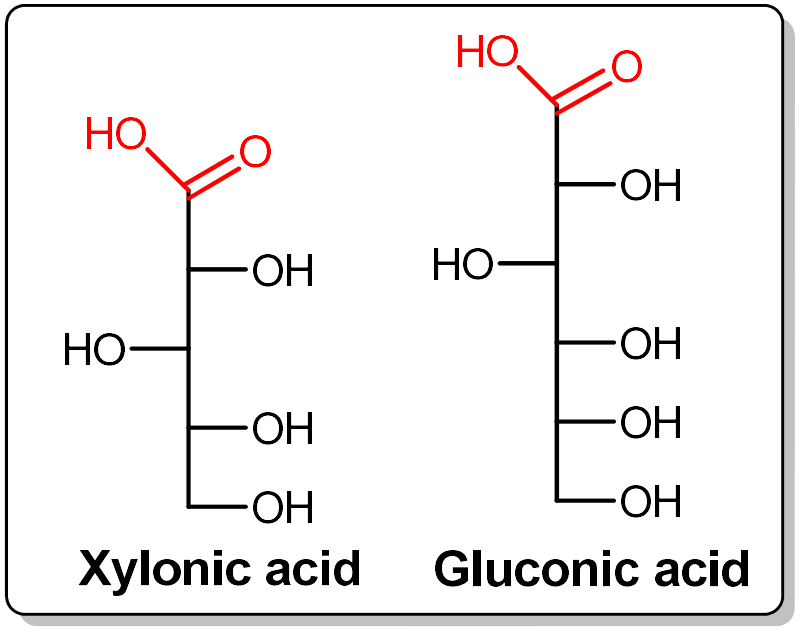
Aldehyde reduced to alcoholic function.

Low-calorific sugars; diabetic sugar, non-cariogenic;

D-glucitol (D-sorbit) starting material for **Vitamin C** synthesis

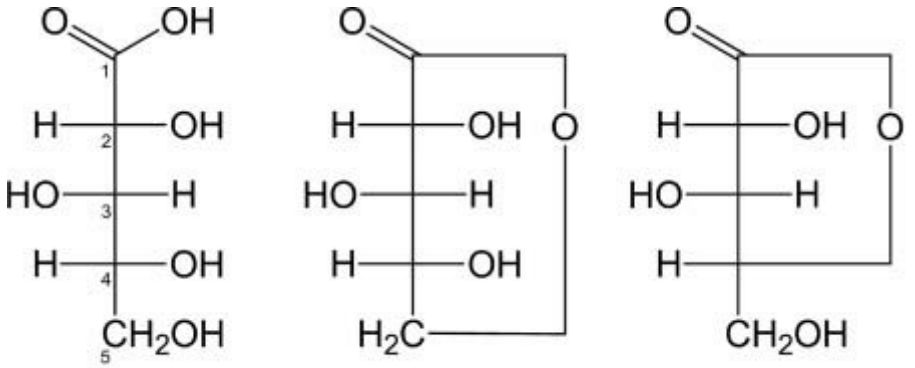


Aldonic acids



Oxidation of reducing end (C-1) to carboxylic group

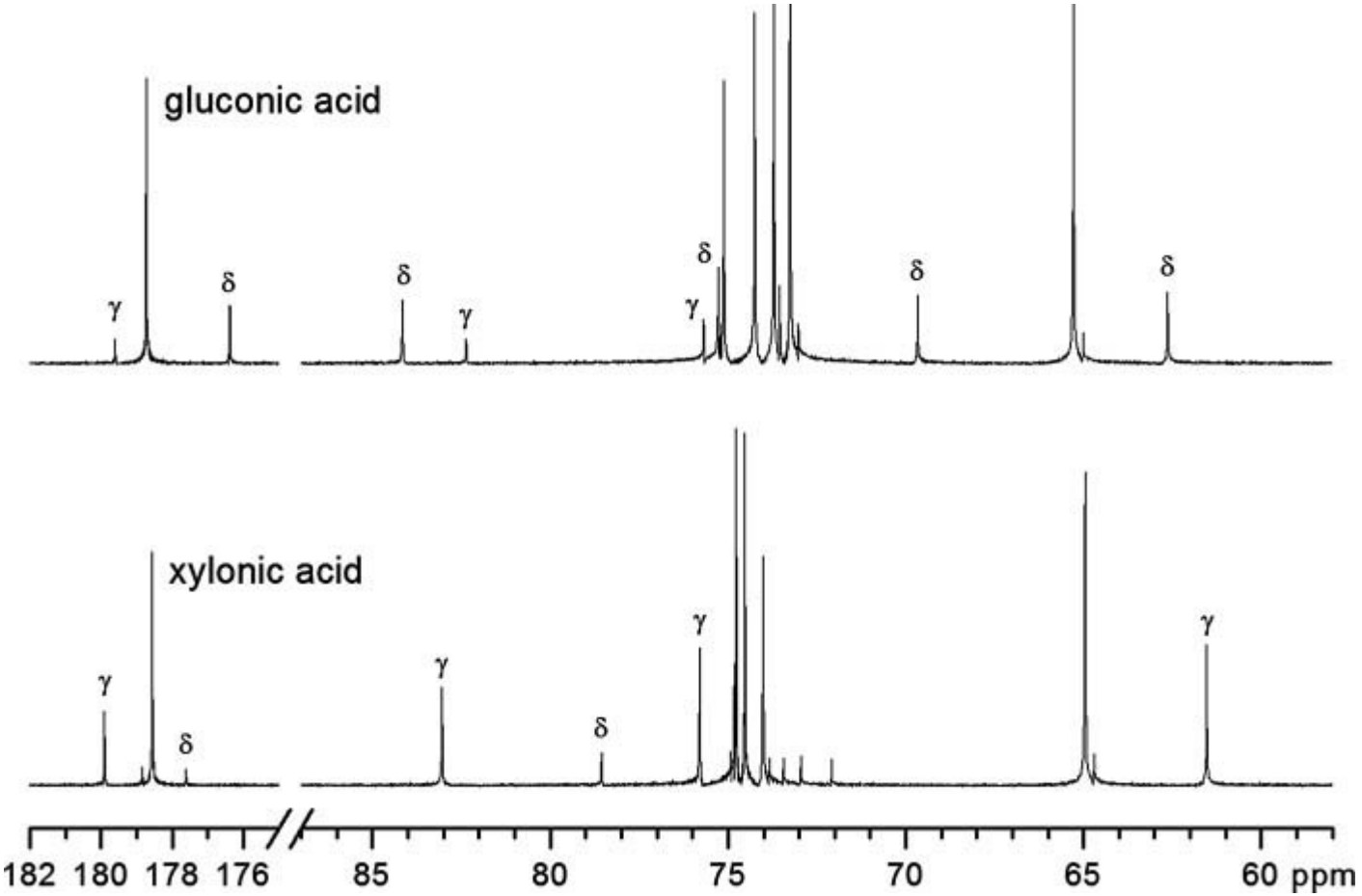
Xylonic acid



- In acidic aqueous solutions the xylonic acid/xylonate equilibrium is coupled with the formation of the *γ*- and *δ*-lactones.
- The *γ*-lactone is formed more readily, whereas the *δ*-lactone can only be observed in traces at very low pH values (<2.5).
- By means of ^{13}C NMR, both the lactone hydrolization constant and the acid dissociation constant could be determined (KL = 4.08, pKa_1 = 3.65).
- Further, a second deprotonation of one of the hydroxyl groups could be observed at very high pH (pKa_2 = 13.3)

Hummel, M. et al. 2010. **J. Carbohydr. Chem**. 29, 416-428

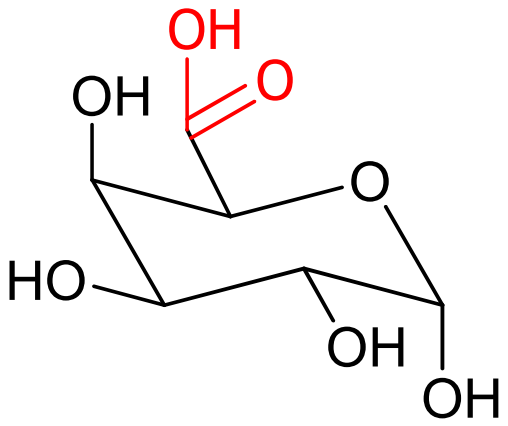
^{13}C-NMR spectra of Xylonic acid



^{13}C NMR spectra of gluconic (pH 2.63) and xylonic acid (pH 2.16). Gluconic acid forms the *δ*-lactone more readily, whereas the *γ* -lactone predominates in acidic solutions of xylonic acids (the lactone peaks where assigned according to Zhang et al.)

Hummel, M. et al. 2010. **J. Carbohydr. Chem**. 29, 416-428

Uronic acids

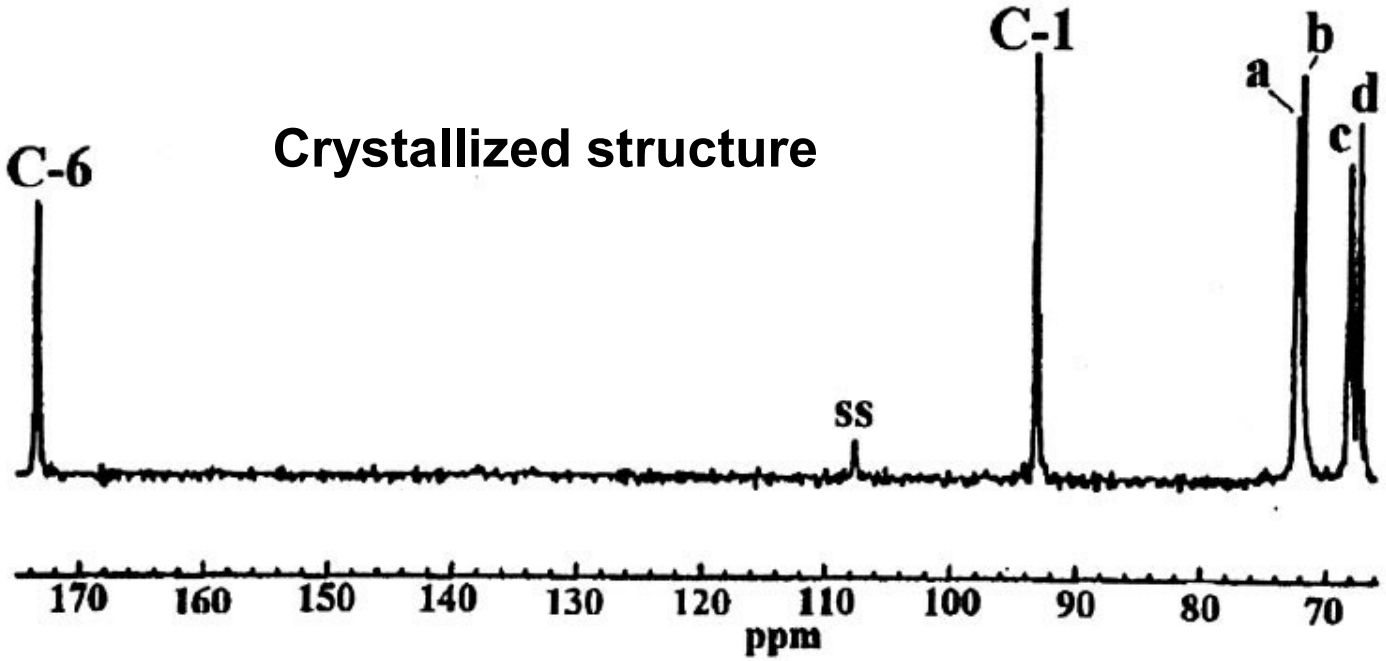


α-D-Galacturonic acid

Oxidation of primary alcohol at C-6 to a carboxylic group.

In the human body many wastes are excreted in the urine as their glucoronate salts

^{13}C CPMAS NMR of α-D-galacturonic acid



C-1	C-2	C-3	C-4	C-5	C-6
93.76	69.46	70.67	72.17	72.63	176.84
C-1	d	c	b	a	C-6

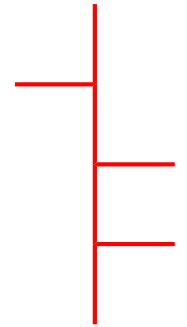
Carbohydrate Research 330 (2001) 391-399

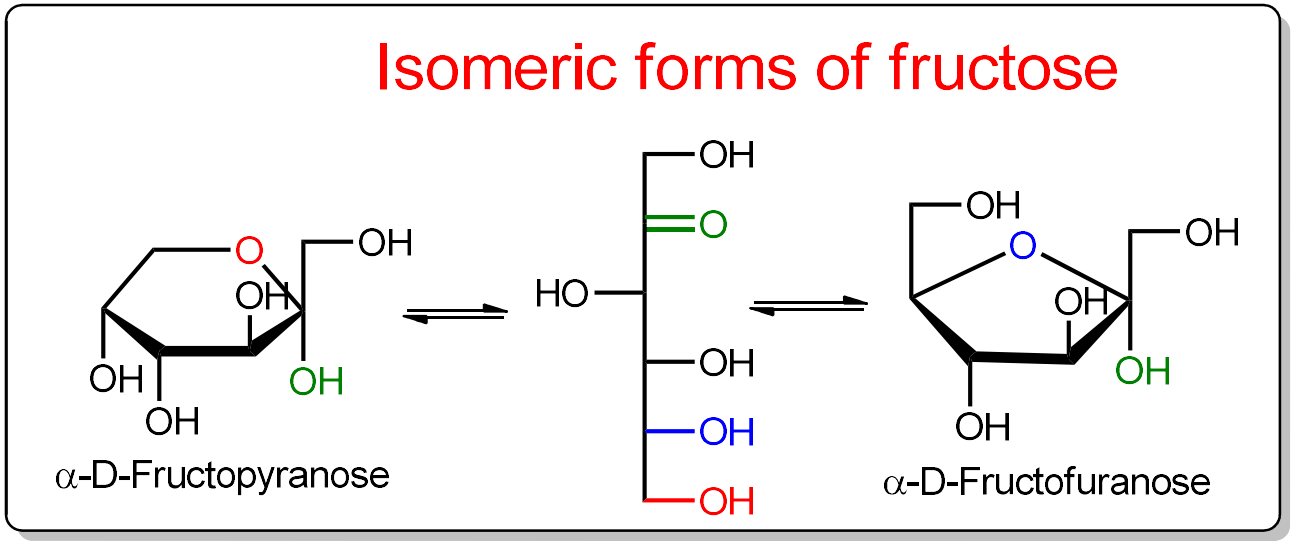
Ketoses - Fructose

Nomenclature according to the position of the carbonylic group (2-, 3-).

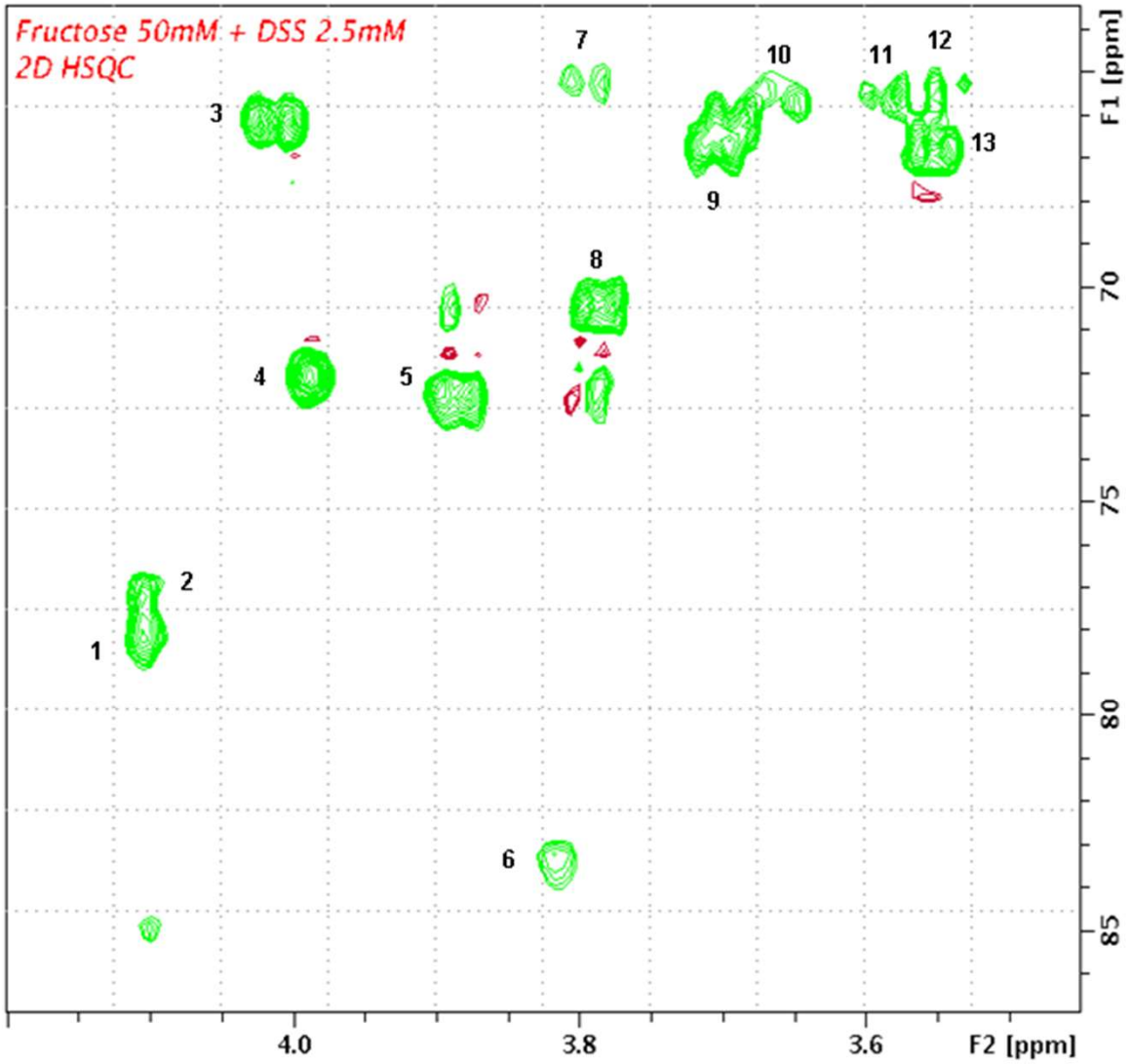
Suffix ”**ose**” replaced by”**ulose**”

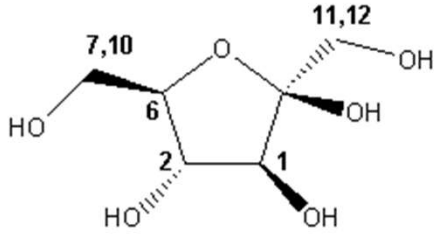
Fructose is a 2-hexulose, **D-*arabino*-2-hexulose**



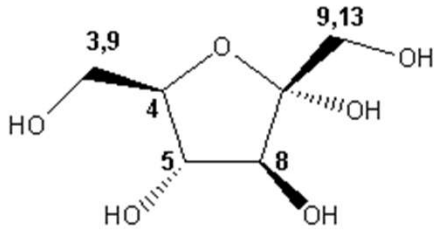


2D HSQC-NMR of fructose





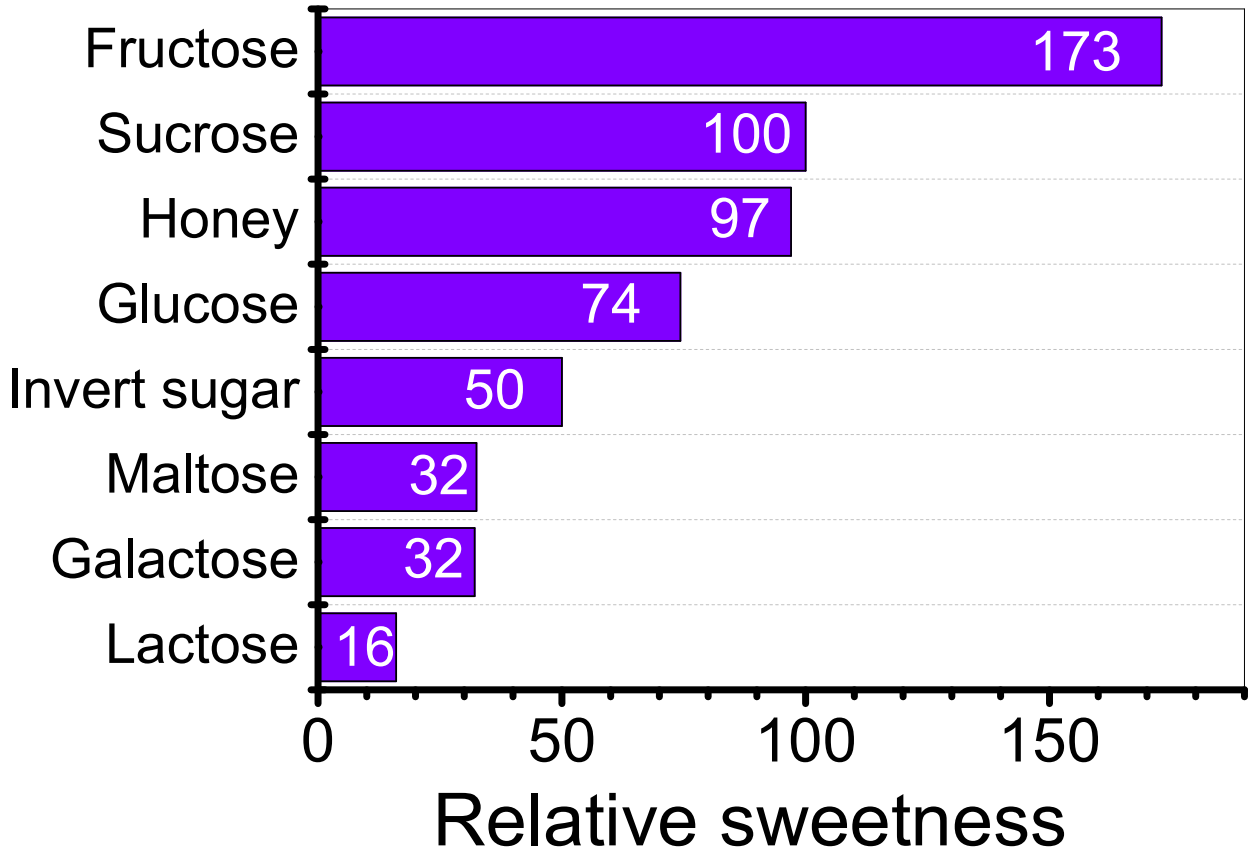
α - D - Fructose



β - D - Fructose

#	F2[ppm]	F1[ppm]	Intensity
1	4.1055	78.2044	2332524.00
2	4.1057	77.4277	
3	4.0141	66.1200	809528.00
4	3.9871	72.1456	8112020.00
5	3.8856	72.5344	2209896.00
6	3.8189	83.5814	
7	3.8009	65.3592	
8	3.7858	70.4286	2028992.00
9	3.6995	66.4439	3119692.00
10	3.6659	65.5982	
11	3.5895	65.5982	
12	3.5423	65.4190	
13	3.5523	66.8327	1497976.00

Relative sweetness of sugars



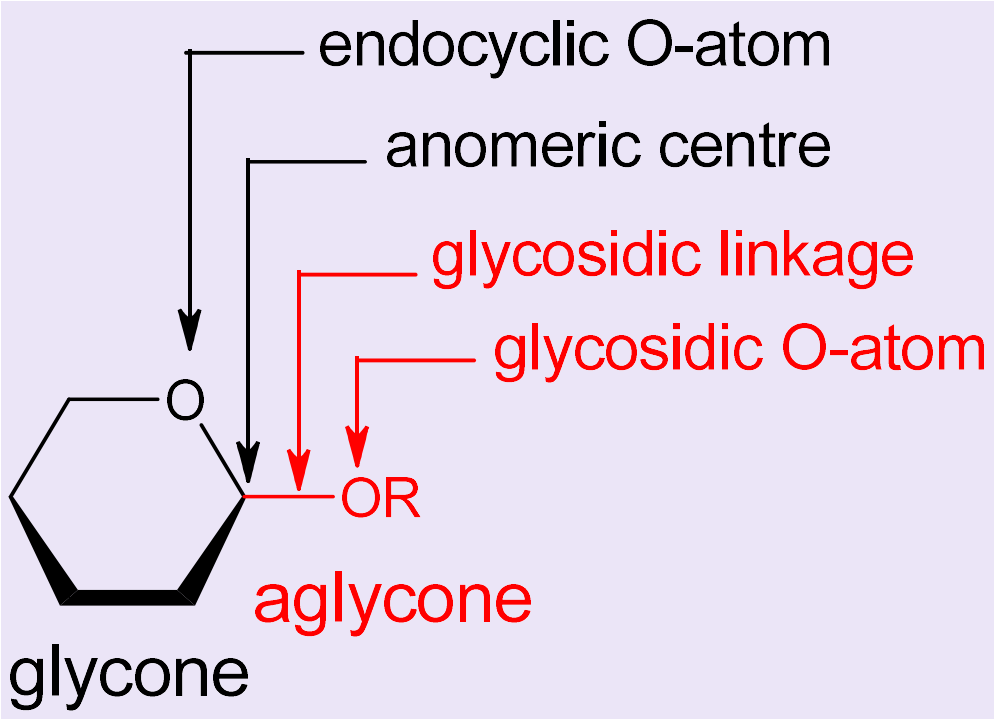
Learning Outcomes

1. Structure and stereochemistry of monosaccharides
2. Nomenclature of monosaccharides
3. Important monosaccharides in wood chemistry
4. **Reactions of monosaccharides**
5. Oligosaccharides

Reactions of free sugars

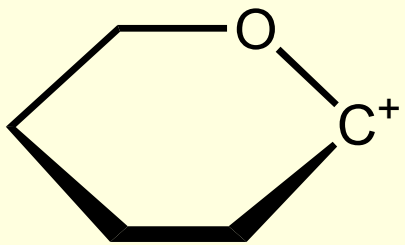
- O-Glycosides
- Reactions with nitrogen-nucleophiles
- Reactions with carbon-nucleophiles
- Reductions
- Oxidations
- Reactions with bases
- Reactions with acids

O-Glycoside



A glycoside is a cyclic acetal, with a **glycone** and an **aglycone** bound to it at the anomeric centre.

O-Glycoside



electrophilic
glycosyl donor

$RO^{\ominus}$

nucleophilic
glycosyl acceptor

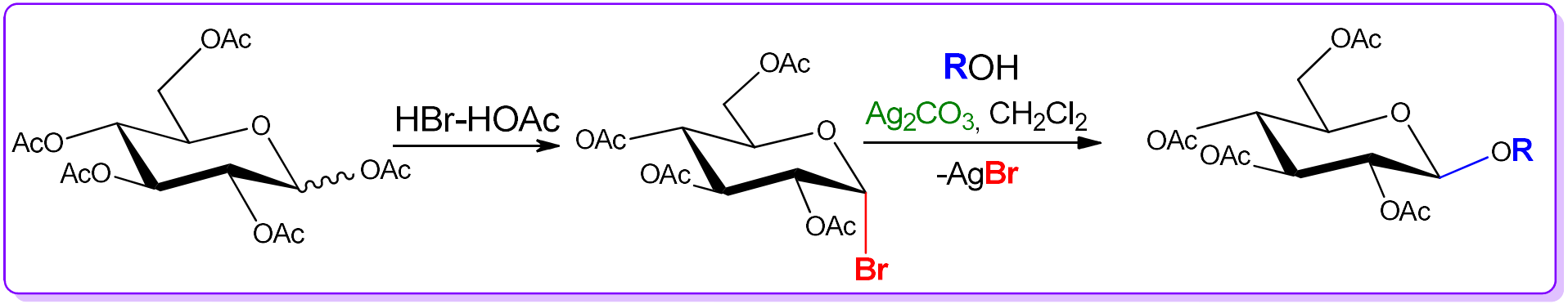
Oligosaccharide synthesis requires:

Leaving group in glycosyl donor (L=OAc, Br,..) and activator ($BF_3.Et_2O$, Ag_2CO_3,..)

Glycosylation reactions

- Koenigs-Knorr type reactions
- Trichloro**acetimidate** method

Koenigs-Knorr method

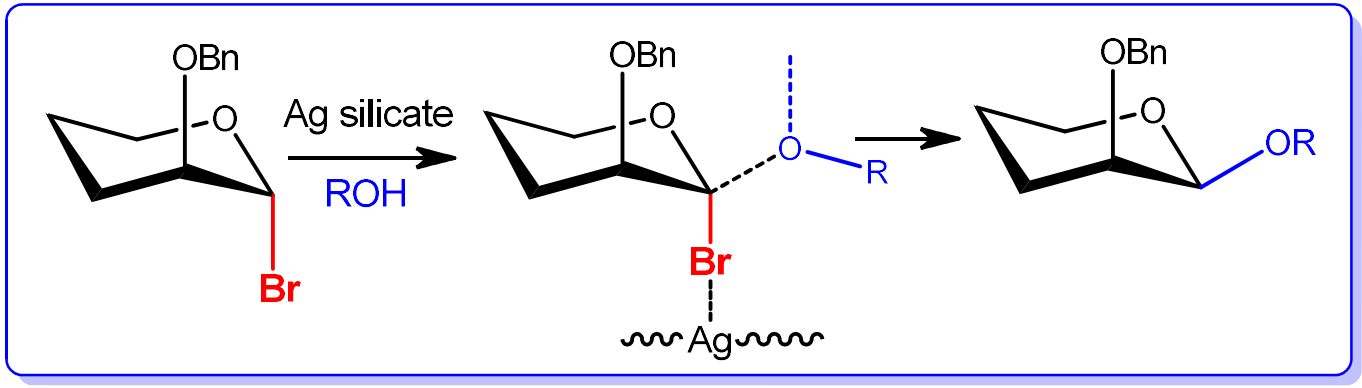


Exclusively **1,2-trans glycoside.**

Participating protecting groups at the **2-position** is denoted as **anchimeric assistance**.

Wilhelm Koenigs, Eduard Knorr. *Berichte der Deutschen Chemischen Gesellschaft zu Berlin* **34** (1901) 957

Koenigs-Knorr method



Reaction occurs at the surface of Ag_2CO_3, thus shielding the α-face of the sugar.

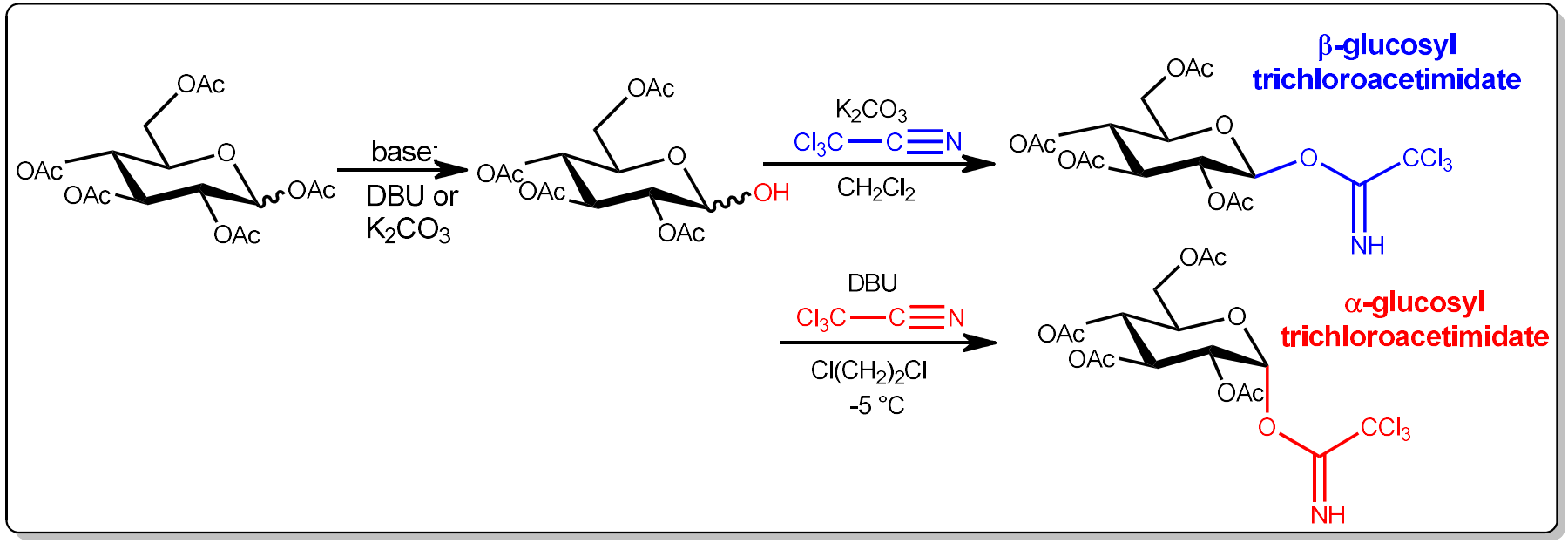
Glycosyl donors: glycoside bromide.

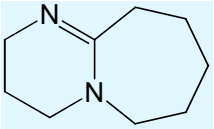
Promotors: silver salts.

Wilhelm Koenigs, Eduard Knorr. *Berichte der Deutschen Chemischen Gesellschaft zu Berlin* **34** (1901) 957

Trichloro**acetimidate** method

Glycosyl trichloroacetimidates are **strong** **glycosyl donors**, activated by Lewis acid catalysts, as $BF_3.Et_2O$





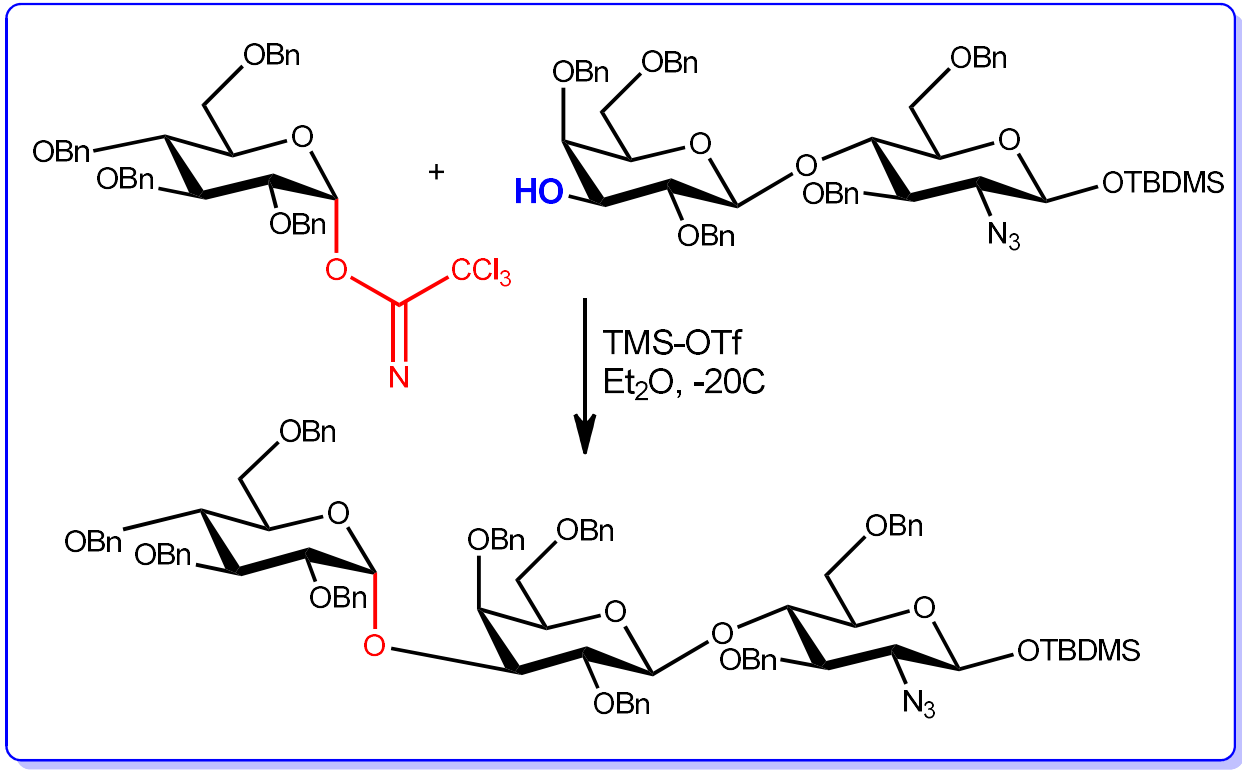
DBU

Schmidt, R.R., Michel, J. J *Angew. Chem.* 1980, **92**, 763-764.

trichloracetonitrile

Synthesis of an α-glycoside

The trisaccharide shows a tumor-associated antigen structure



TMS-Otf (Trimethylsilyl trifluoromethanesulfonate ≈ triflate) strong acid catalyst. TBDMS: tert-butyldimethylsilyl ether

G. Grundler, R.R. Schmidt, *Liebigs Ann. Chem*. 1826, **1984**

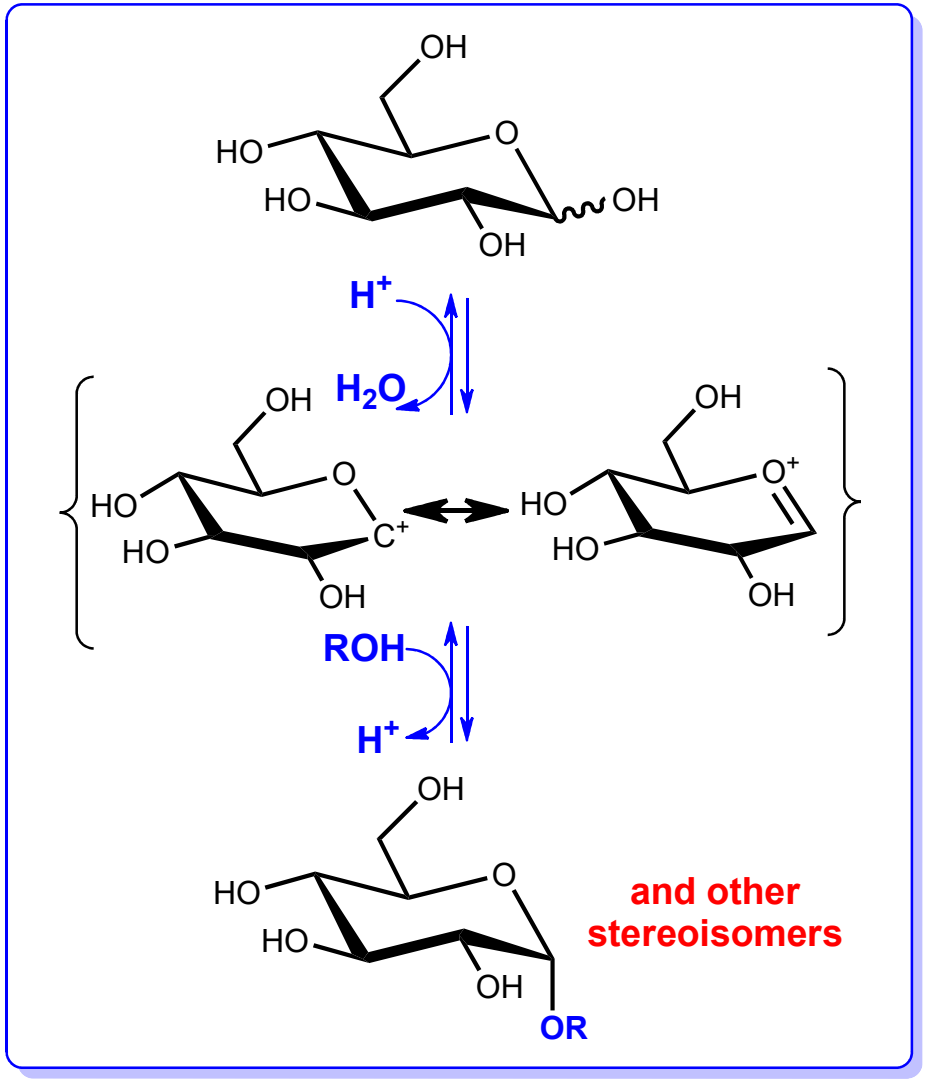
Fischer glycosidation – Acetal Formation

Acid-catalyzed (ion exchange resin) reaction of cyclic hemiacetal (**free sugar**) **with excess alcohol** to shift the equilibrium towards the product.

Mixture of stereoisomeric glycosides:
main product goverened by the anomeric effect.

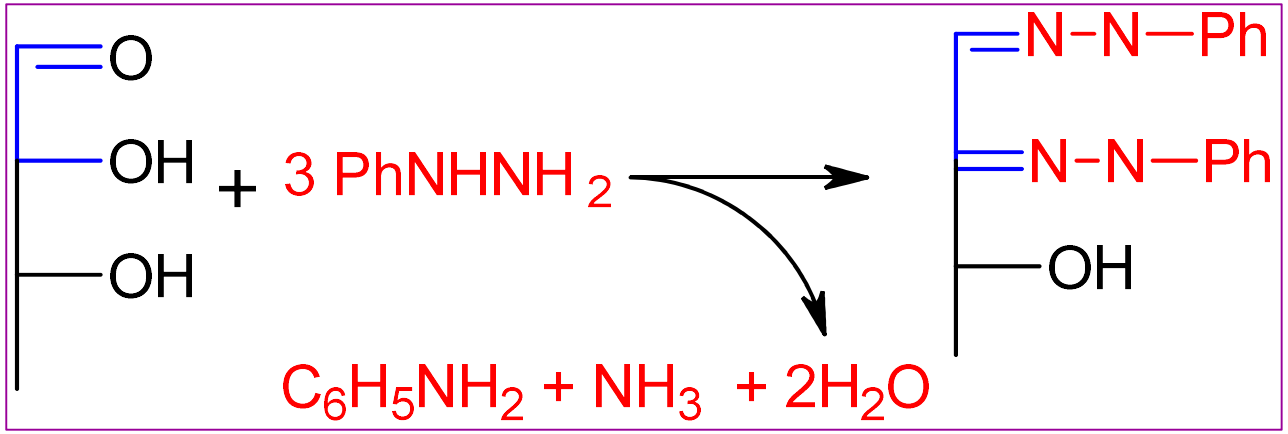
E. Fischer. *Ber der deutschen Chem Gesellschaft* 26(3), **1893**, 2400

Fischer glycosidation – Acetal Formation



E. Fischer. *Ber der deutschen Chem Gesellschaft* 26(3), **1893**, 2400

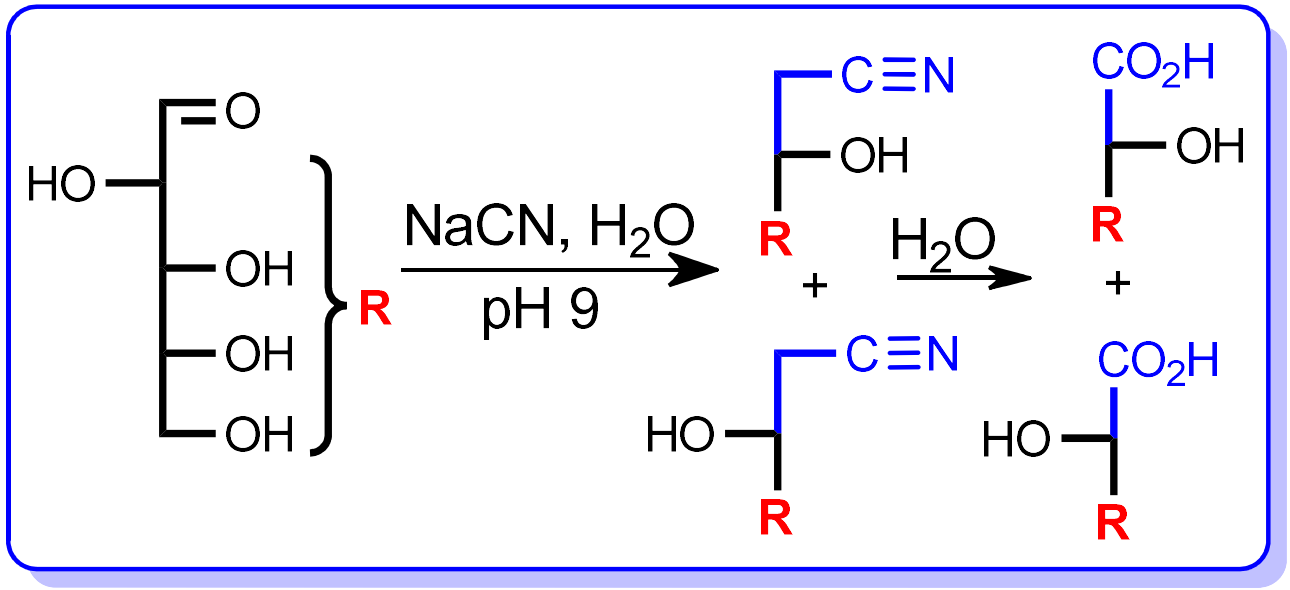
Reactions with nitrogen-nucleophiles



α-Hydroxy aldehydes, ketones and α-dicarbonyls give water insoluble highly crystalline **osazones** (Fischer, 1884).

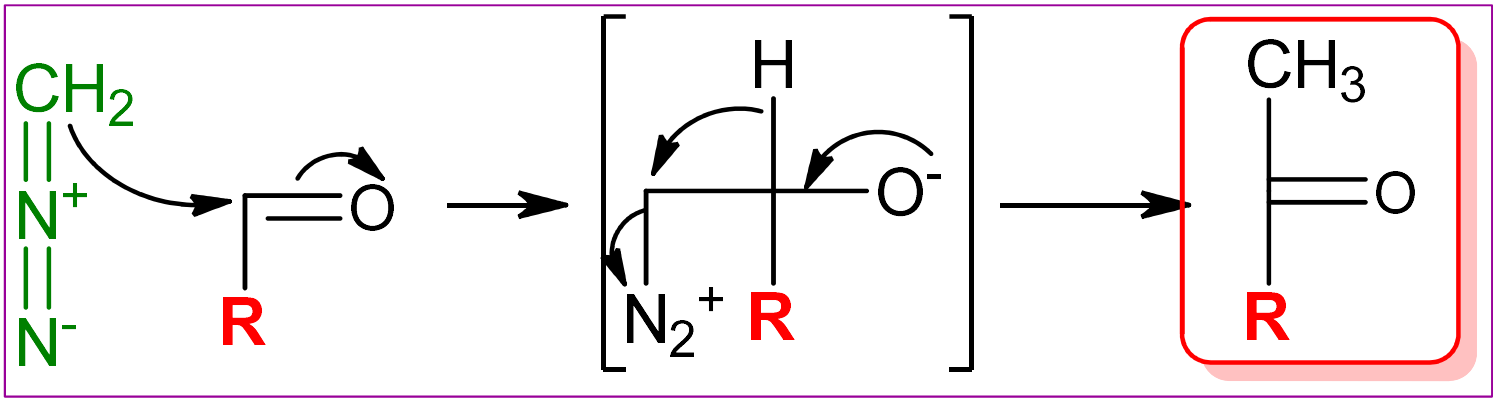
D-glucose und D-mannose give identical **osazones**, since they possess no asymmetry at C-1 and C-2. Thus, the aldoses are epimers.

Kiliani Fischer - Cyanohydrins



Kiliani Fischer: D-ara->D-gluconic and D-mannonic acids

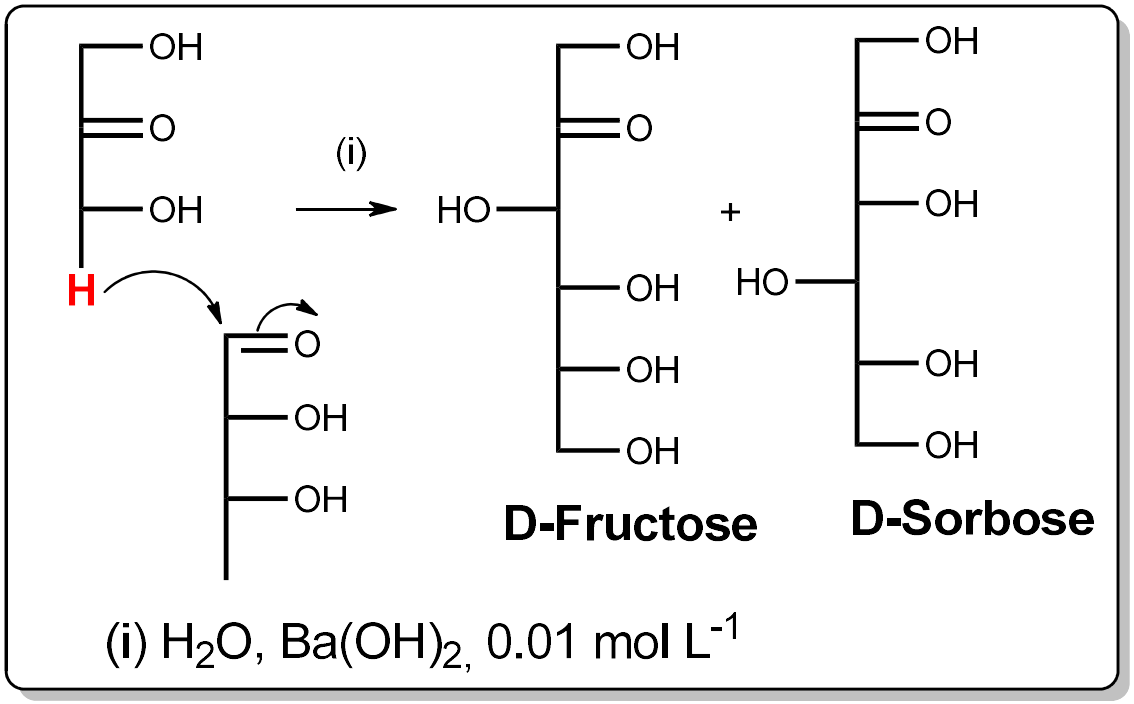
Diazomethane



Nucleophilic carbon attacks carbonyl group.

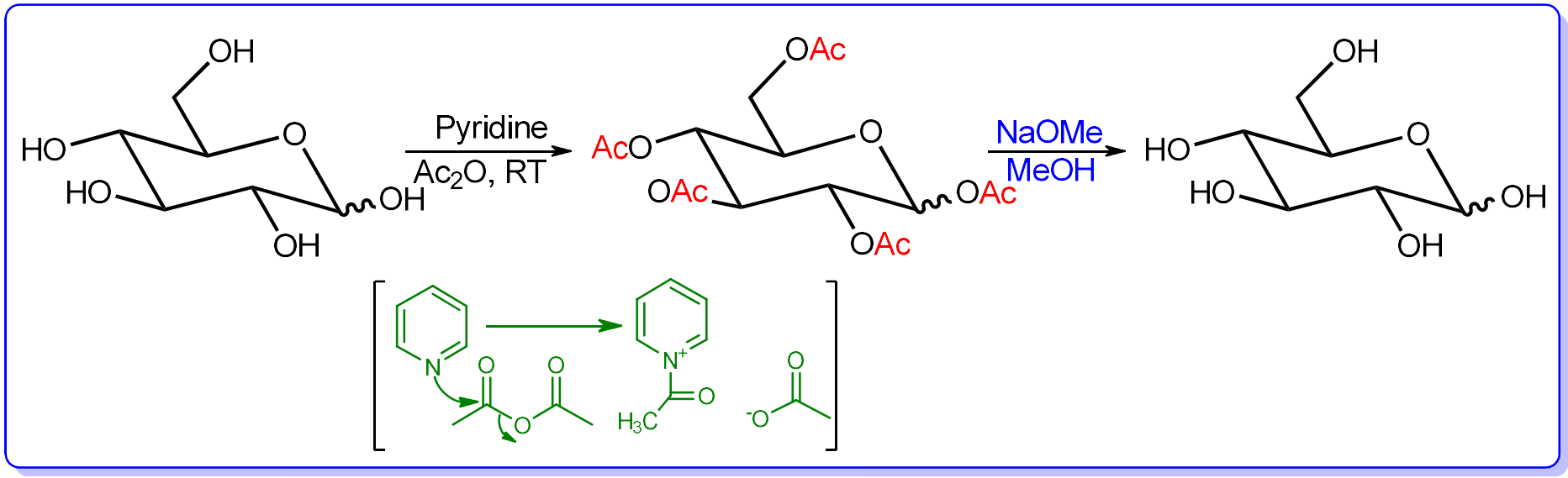
Used to extend the carbon chains of aldoses

Aldol condensation



Treatment of **D-glycerinaldehyde** and **1,3-dihydroxyacetone** with barium hydroxide results in a mixture of D-fructose and and D-sorbose in almost quantitative yield.

Acetylation, Deacetylation



Sugar dissolved in pyridine, addition of acetic anhydride, mixture stirred at RT.

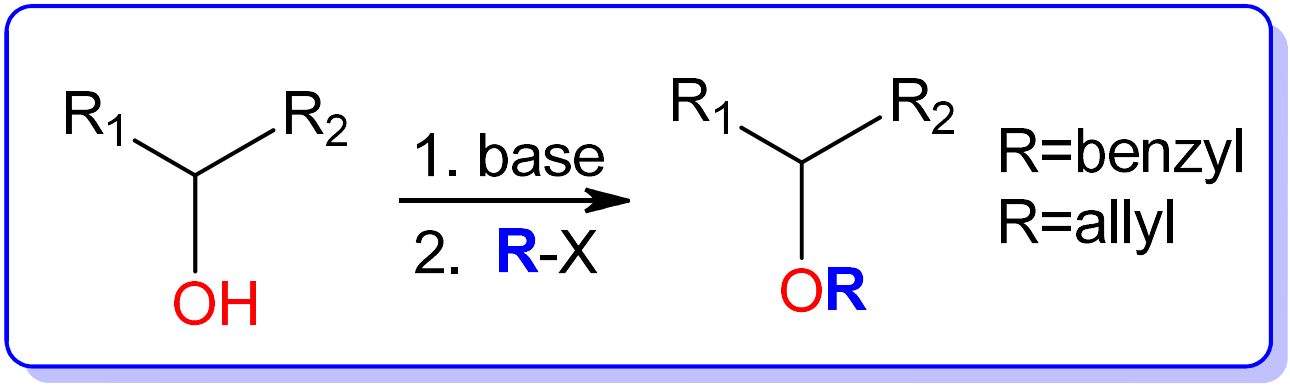
Deprotection by the **Zemplén method**, using **Na^+ methanolate$^-$** in methanol.

Ether protecting groups

Alkyl ethers resistant to strong bases and acids:
Ether protection always **before esterification**.

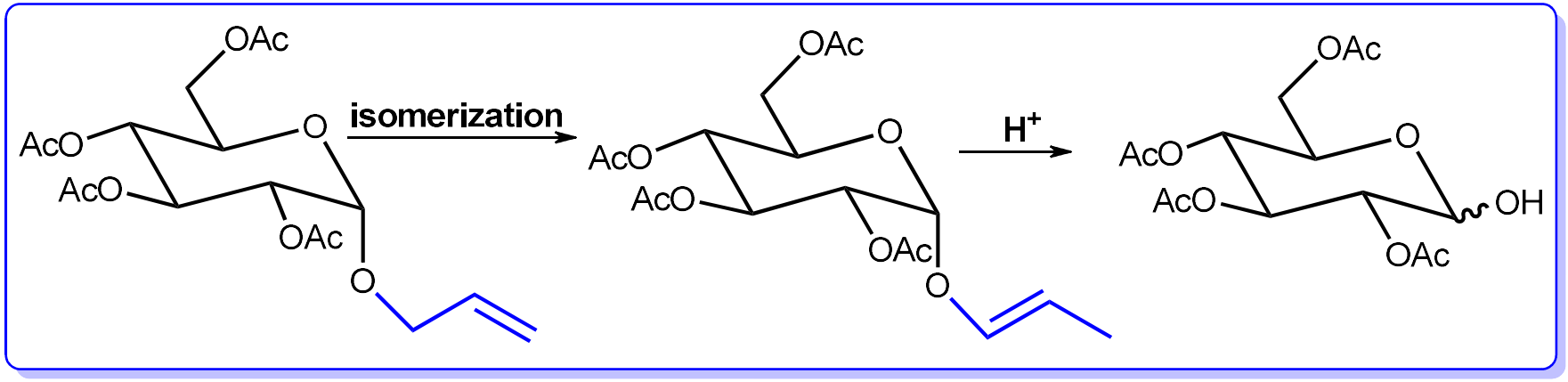
Benzyl- and vinyl ethers used as protecting group.

Williamson synthesis: NaOH in polar aprotic solvent (DMF) + alkylhalide.



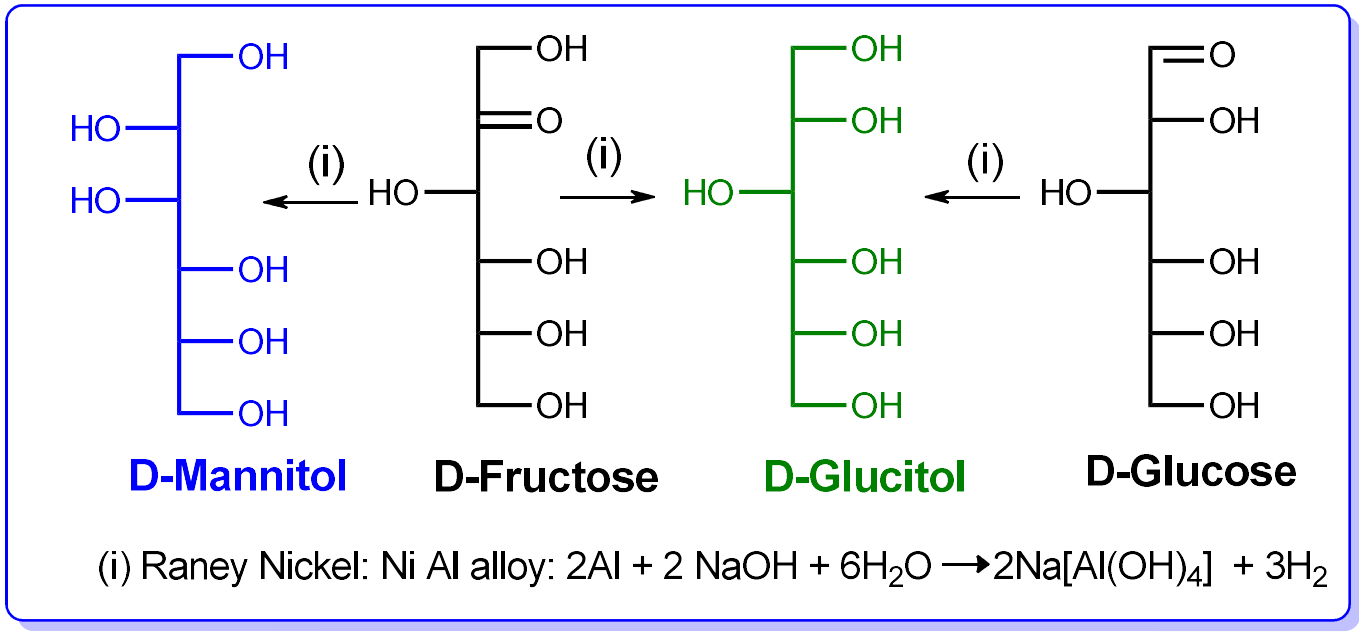
Allyl ethers

Introduced under the same conditions as benzyl ethers, but easier to remove*. For deprotection, allyl group is isomerized, employing metal catalyst. Then labile enolether is hydrolysed under mild acidic conditions.



*Benzyl ethers require for removal catalytic hydration: Pd-C, p_{H2} = 100 bar

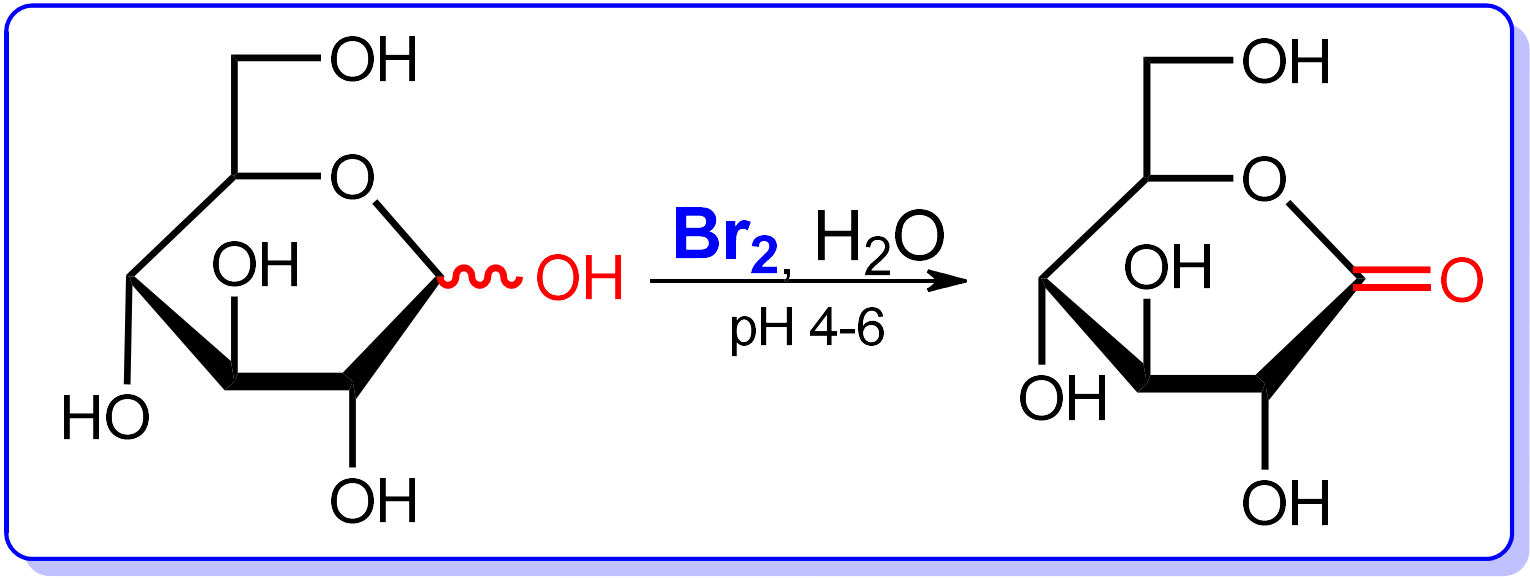
Reductions to alditols



Aldoses give one product, ketoses give two:
D-fructose produces D-mannitol and D-glucitol.

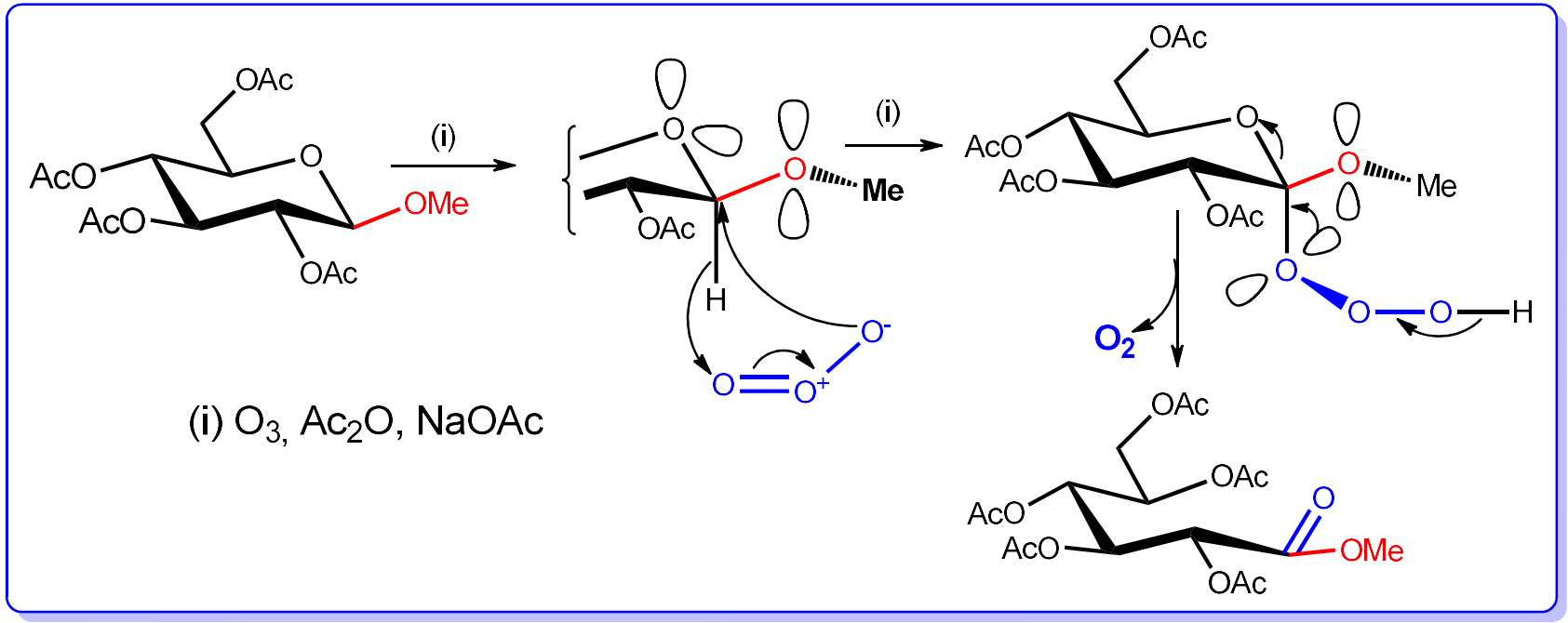
The reduction typically occurs with **Raney Nickel**.

Oxidation to aldonic acids



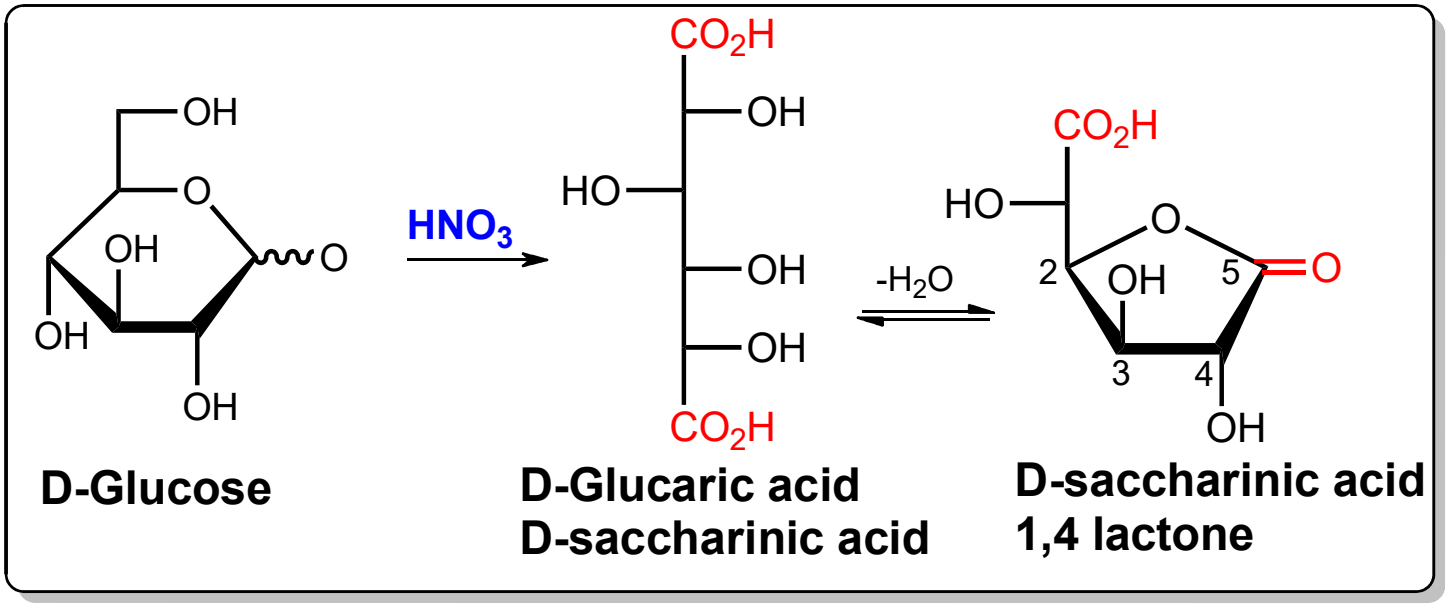
β-anomer reacts 250 times faster than the α-form at pH5.

Oxidation to aldonic acids with ozone



- Abstraction of H from C-1 because lone pair orbitals on both Os bonded to C-1 can be arranged antiperiplanar to the C-H bond
- Oxidation proceeds under strict stereoelectronic control

Oxidation to aldaric acid

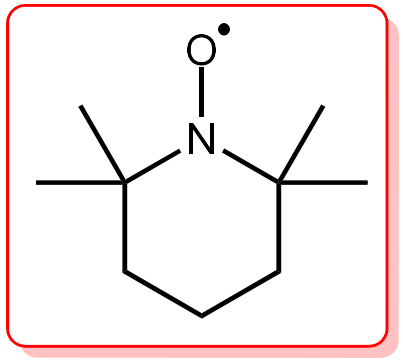


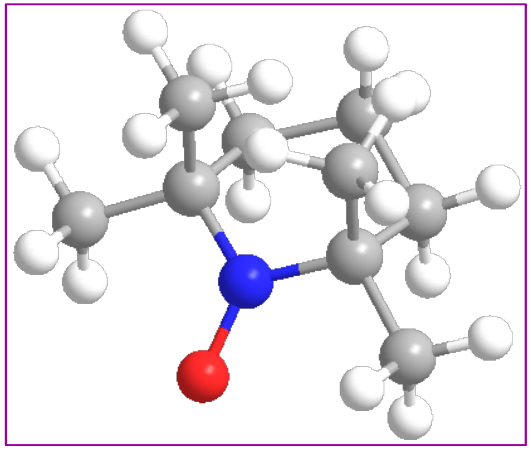
Ca^{2+} D-glucarate found in human body, vegetables and fruits.

Inhibts β-glucuronidase, leads to detoxification, removal of fat-soluble toxins are removed.

TEMPO Oxidation

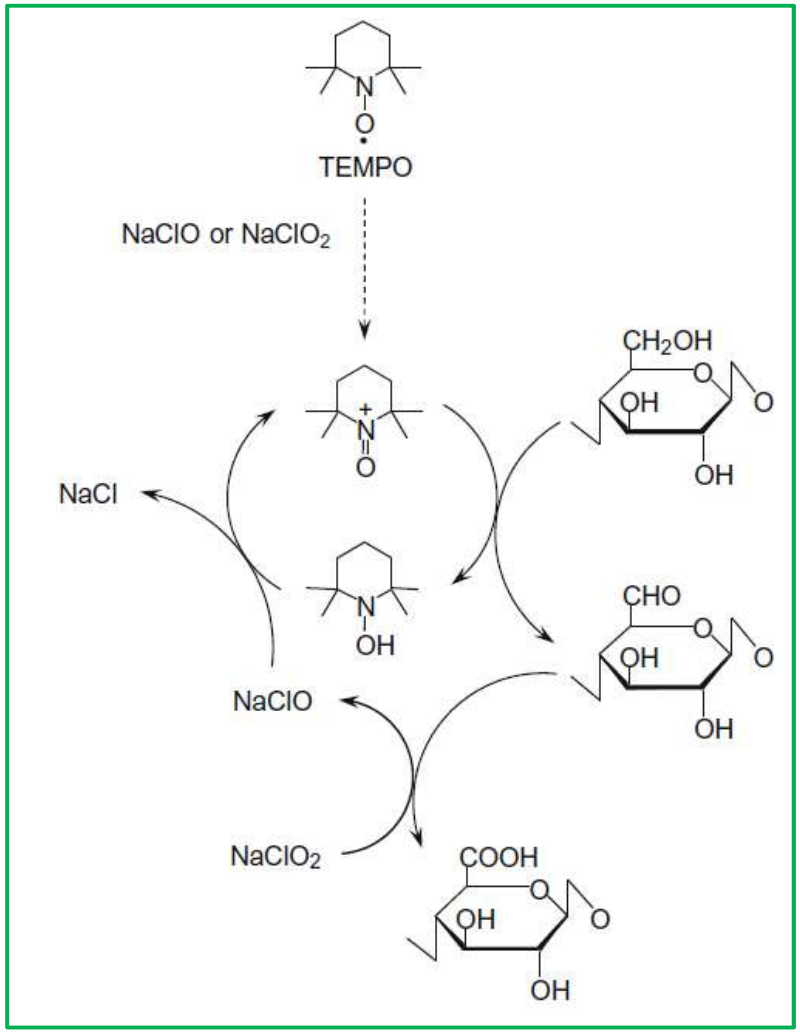
- 2,2,6,6-tetramethylpiperidine-1-oxyl
- Selective oxidant.
- Previously applied under alkaline conditions (NaBr), lately under neutral conditions ($NaClO_2$)





A. Isogai

Mechanism of TEMPO Oxidation



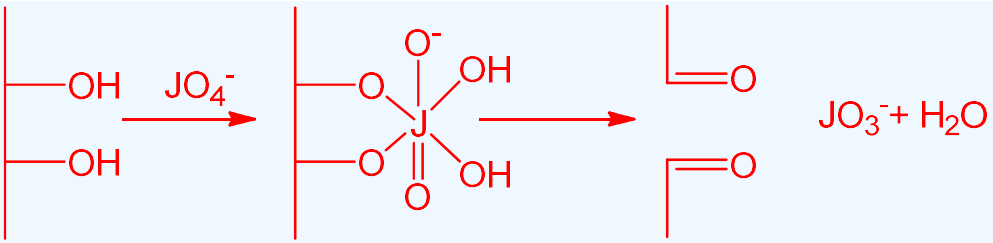
- Aqueous media at pH 3-7
- Highly regioselective at C6-OH.
- Proceeds under mild conditions (20-80° C, 2-24h)
- Little depolymerization

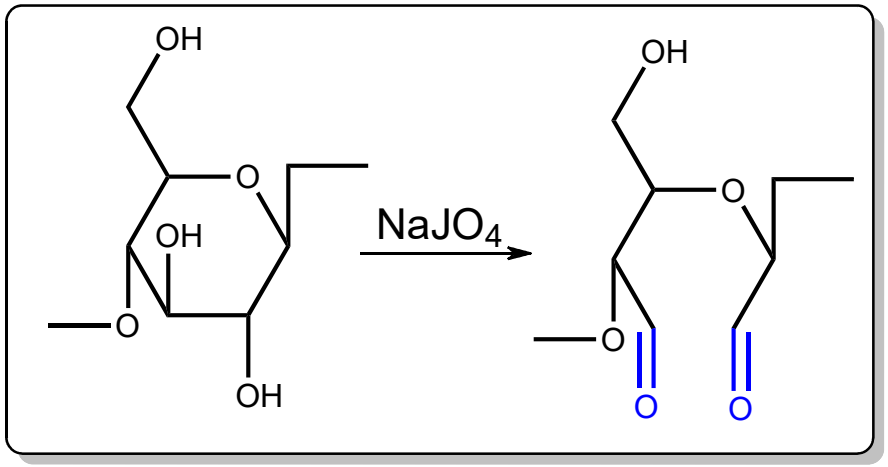
T. Saito et al. J Wood Sci. 56:227-232 (2010)

Periodate Oxidation of Cellulose

- Highly selective oxidative cleavage of C2-C3-bond of carbohydrates (cellulose) with $NaJO_4$ to the dialdehydes.

- Cotton: 4-120 h, 0.1 – 0.4 M $NaJO_4$





S. Vicini et al. *Thermochimica Acta* (2004)

Reactions with bases

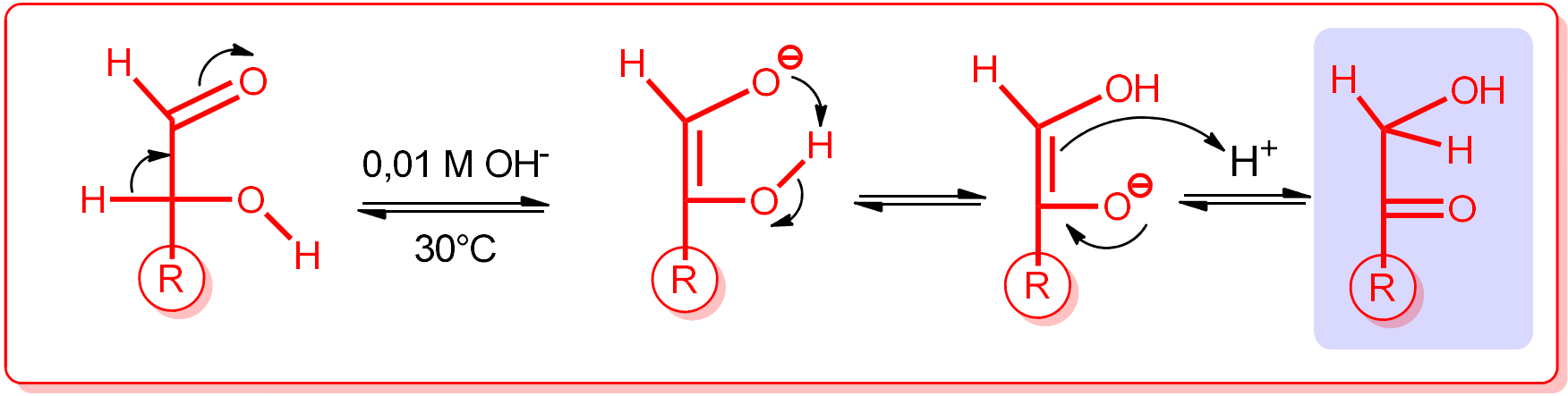
1. Epimerizations, aldose-ketose isomerization

   (Lobry de Bruyn-van Ekenstein)

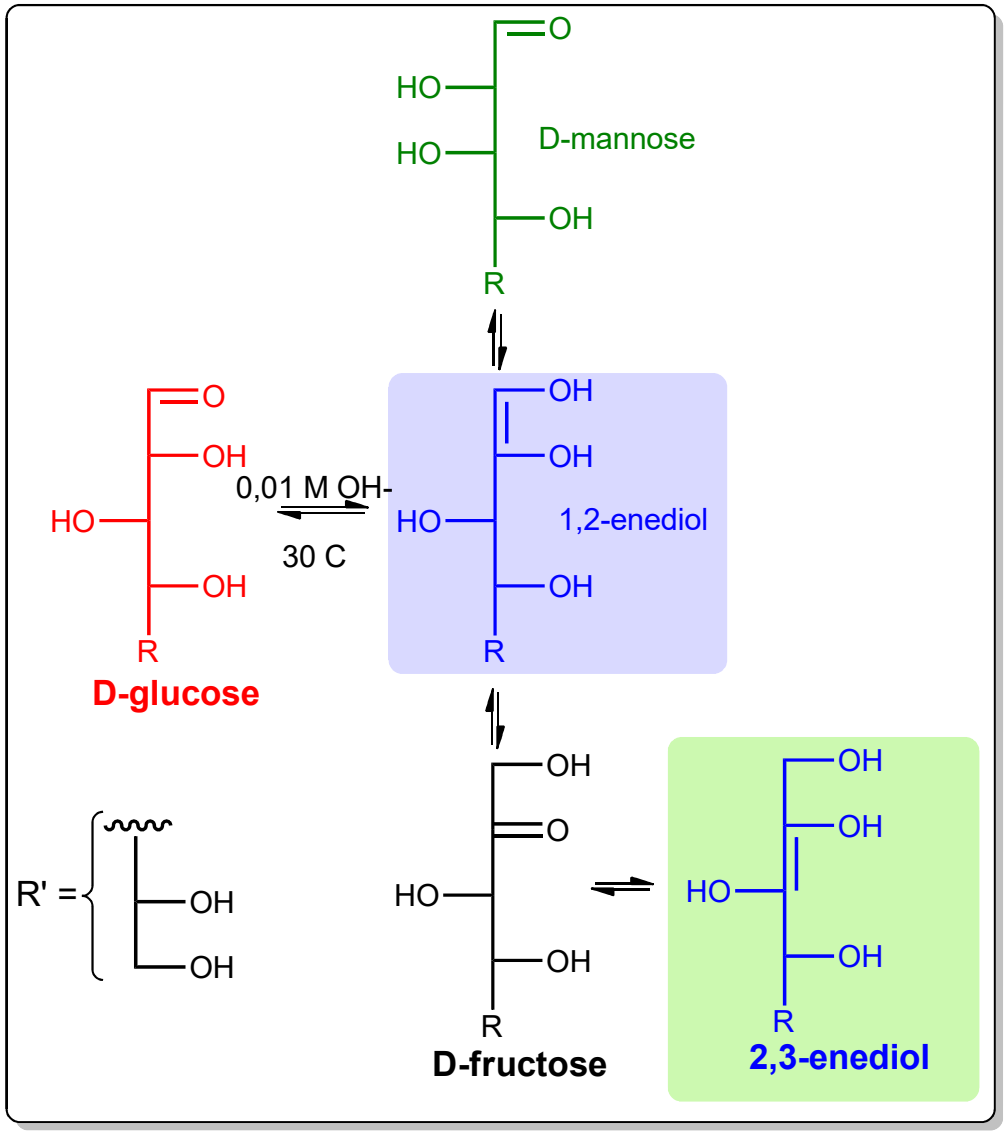
2. β-elimination (saccharinic acid formation)

3. Retroaldol reactions

Lobry de Bruyn-van Ekenstein rearrangement



Lobry de Bruyn-van Ekenstein rearrangement



D-Glucose epimerizes into D-fructose (28%) and D-mannose (3%)*.

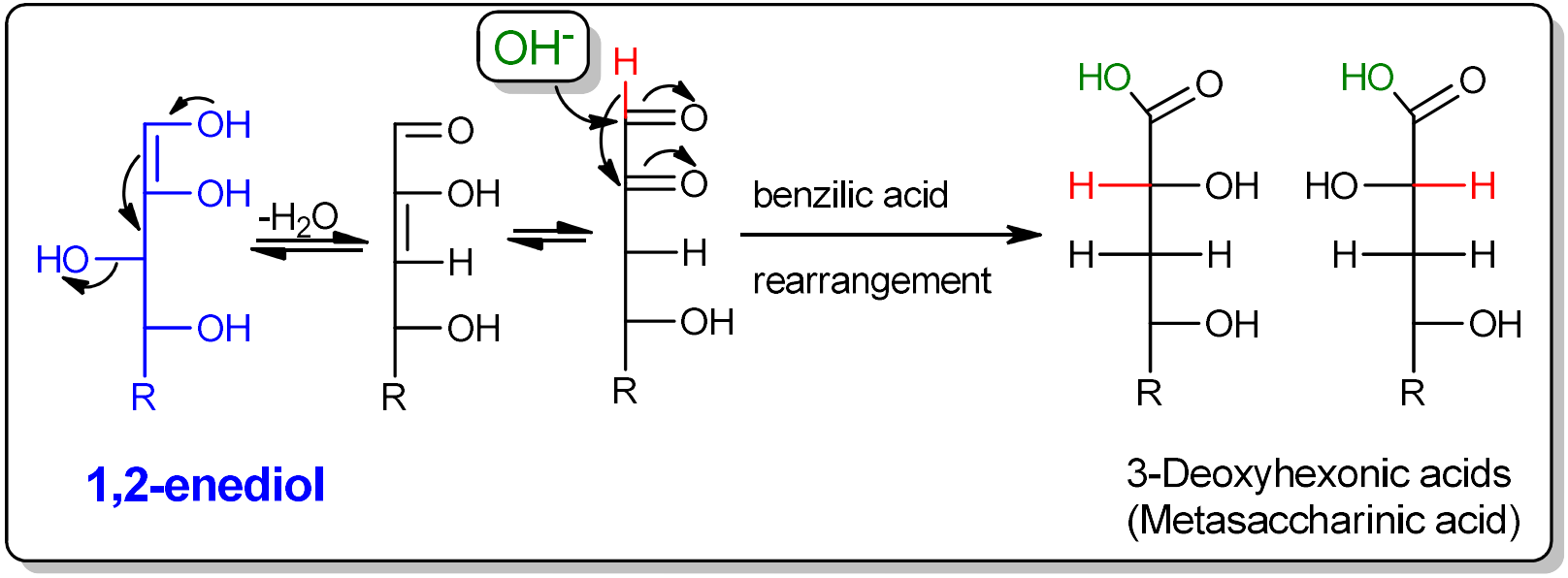
The interconversion occurs via **enediol** formation.

*0.01 M NaOH, 35° C for 100 h

Saccharinic acid formation

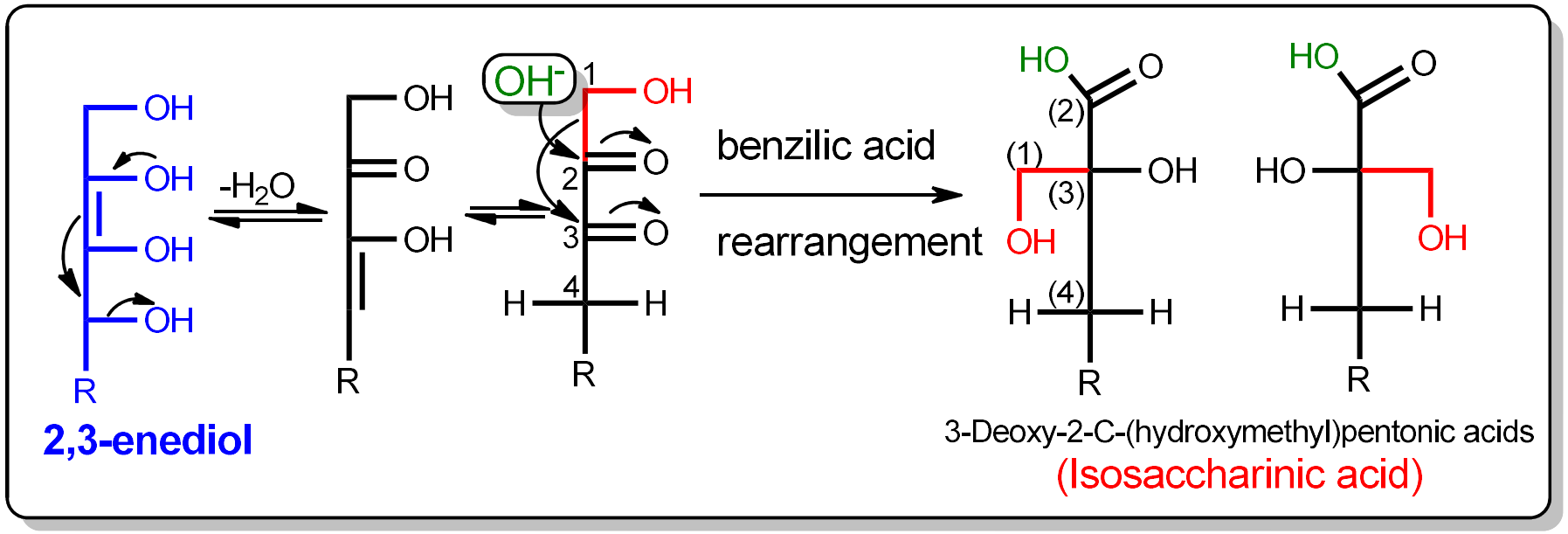
More concentrated basic solutions > 0.27 OH^-

1. β-elimination from an enediol
2. Benzilic acid rearrangement
3. Leaving group OH^-. If O-3 carries an alkyl or acyl substituent, elimination is easier



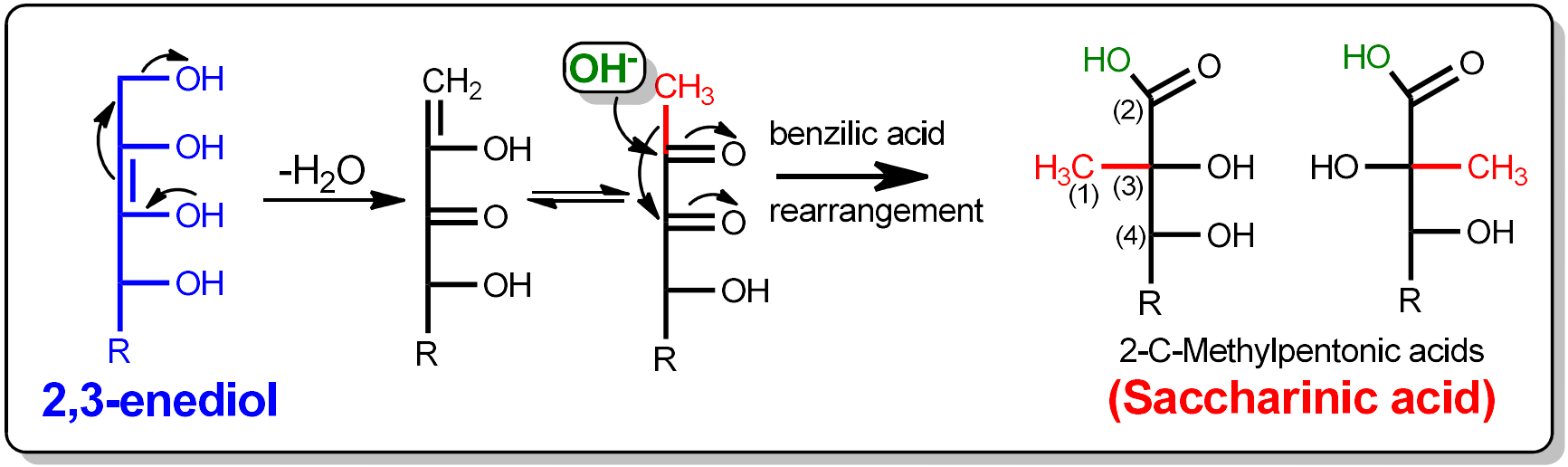
Saccharinic acid formation

2,3-endiol as initial substrate (1)



Saccharinic acid formation

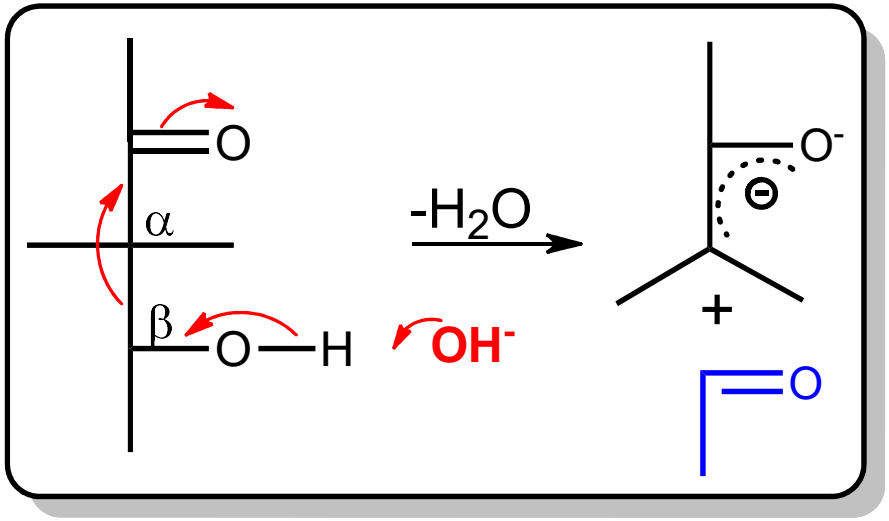
2,3-endiol as initial substrate (2)



Retroaldol reaction

Prolonged treatment of hexoses with moderately concentrated aqueous base yields **three-carbon fragments.**

- 2-OH propionaldehyde,
- pyruvic acid,
- dihydroxyacetone



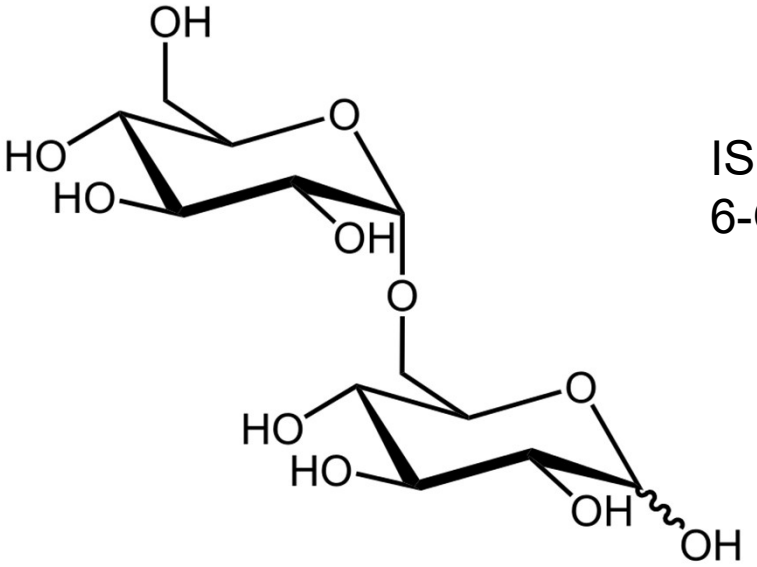
Reactions with acids

1. Reversion and anhydride formation
2. Formation of furans

Reversion*

D-Glucose is heated in 0.15 mol/L H_2SO_4.
About 0.1% of **isomaltose** is produced.

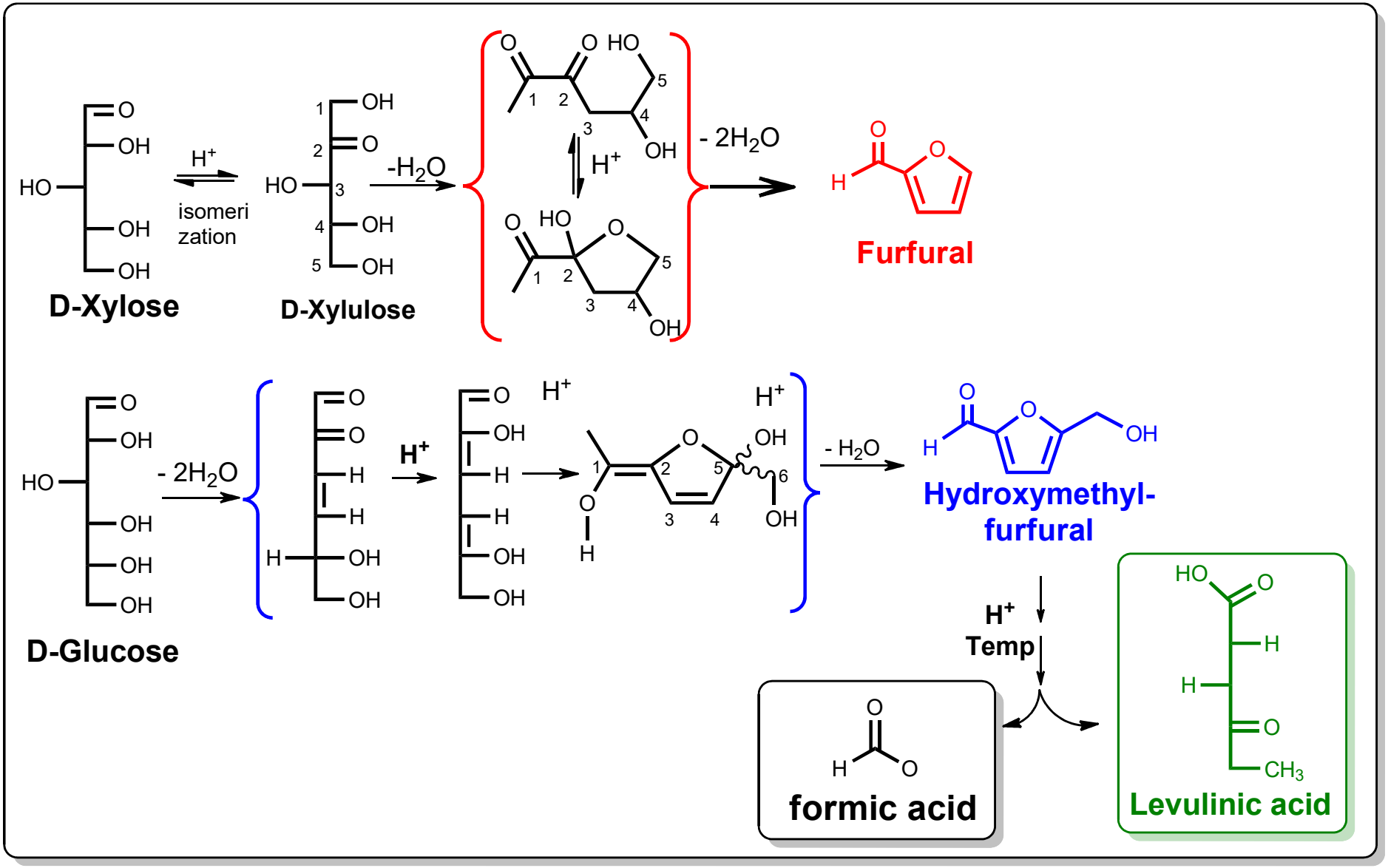
Attack of primary-OH of one glucose molecule upon the anomeric carbon of another.



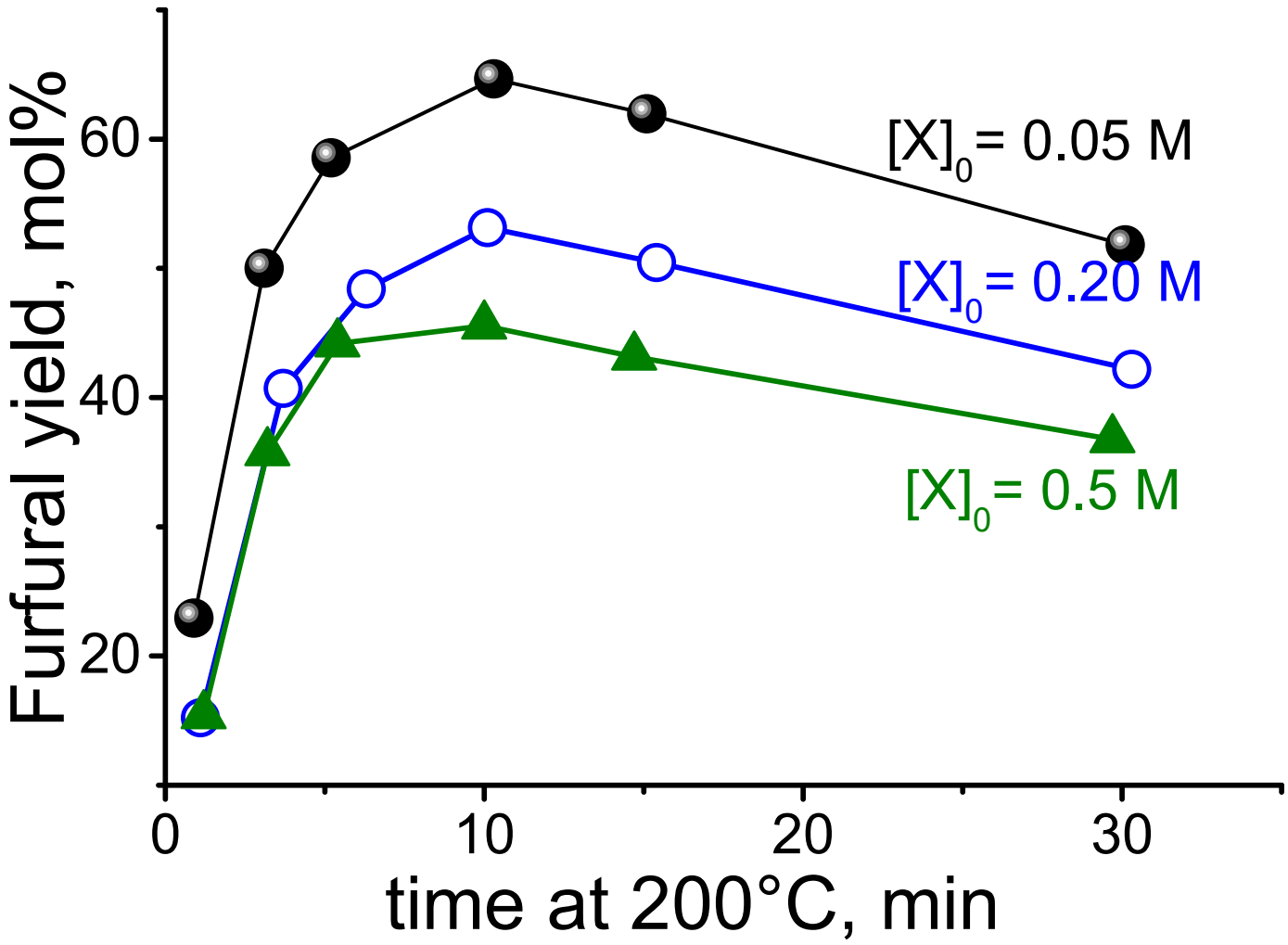
ISOMALTOSE
6-O-α-D-glucopyranosyl-D-glucose

*caramelization

Hydroxymethylfurfural, Furfural



Furfural from xylose



M. Lara, 2011

Learning Outcomes

1. Structure and stereochemistry of monosaccharides
2. Nomenclature of monosaccharides
3. Important monosaccharides in wood chemistry
4. Reactions of monosaccharides
5. **Oligosaccharides**

Oligosaccharides

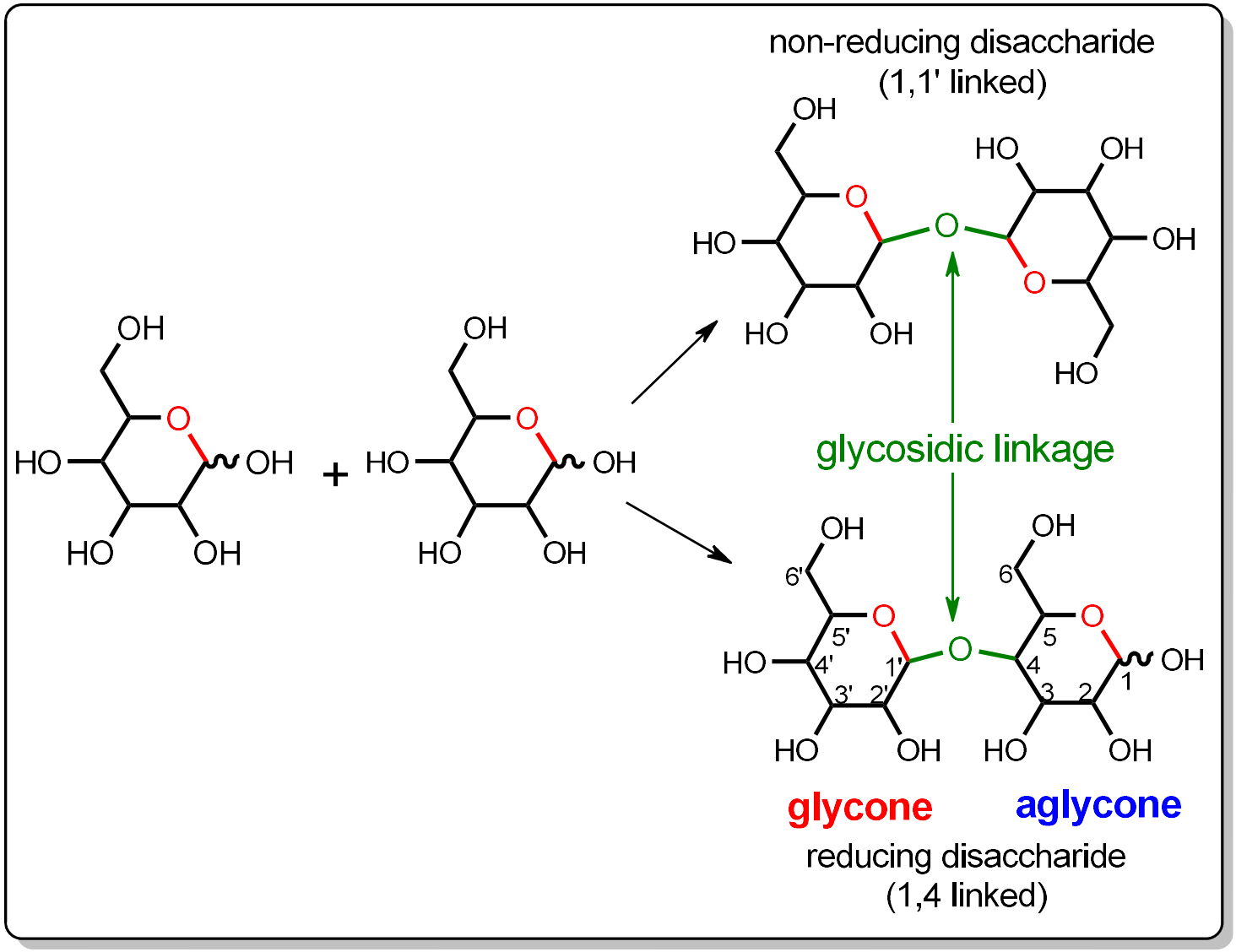
Linking monosaccharides via glycosidic bonds leads to the formation of oligosaccharides.

The part at the **reducing end** is called **aglycone**, the remaining portion the **glycone** part.

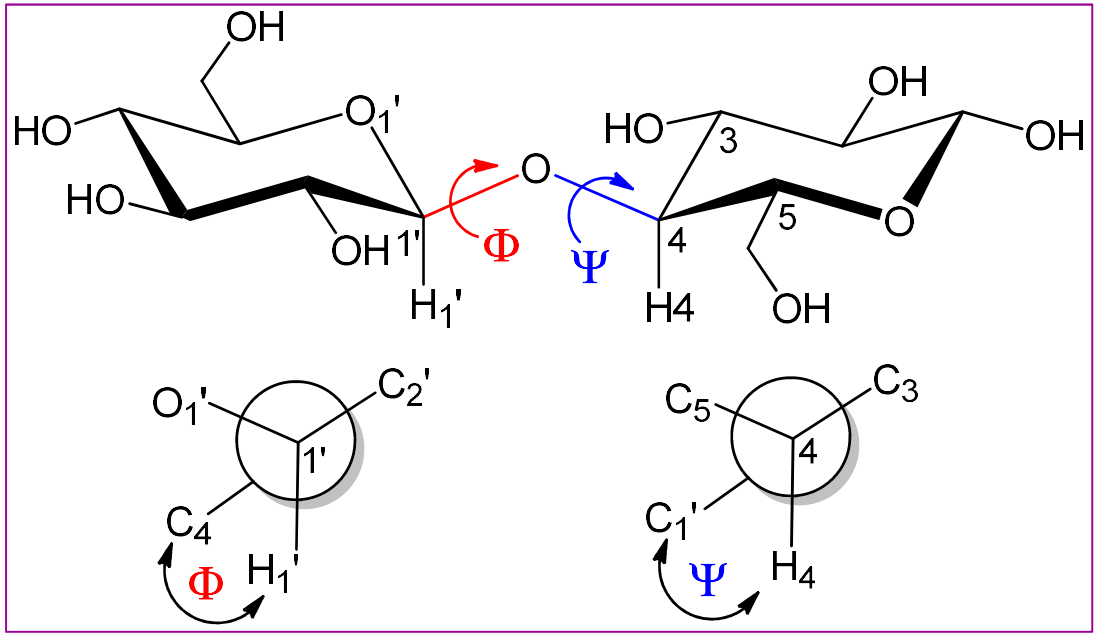
Nomenclature: the non-reducing element is given the suffix ”-yl”:

Lactose = β-D-galactopyranosyl-(1->4)-D-glucopyranose.

Oligosaccharides (OS)



Conformational properties of OS

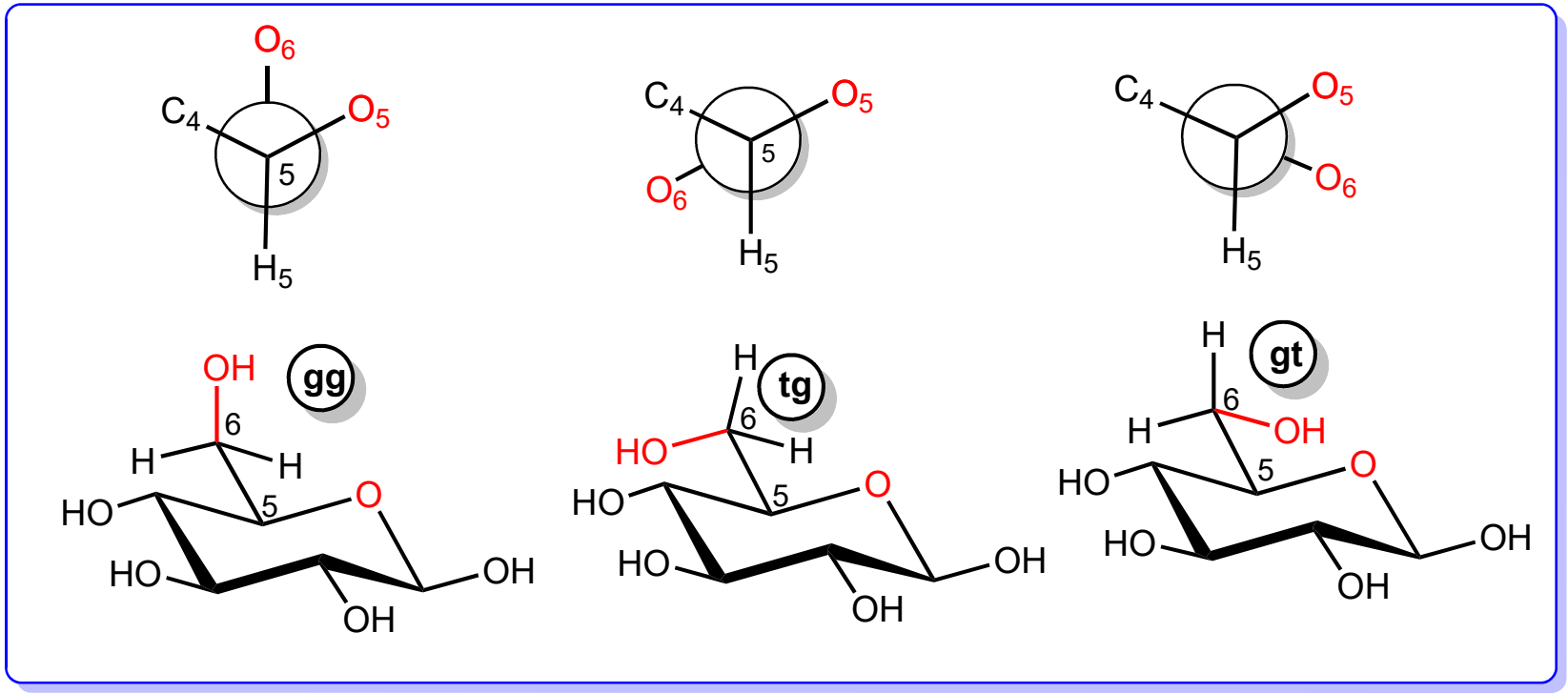


Two dihedral angles ϕ und ψ, important to assign stereochemistry of a glycosidic link, i.e. 1→1, 1→2, 1→3, **1→4**, linkages.

The ϕ angle: H1'-C1'-O-C(aglycone) fragment,

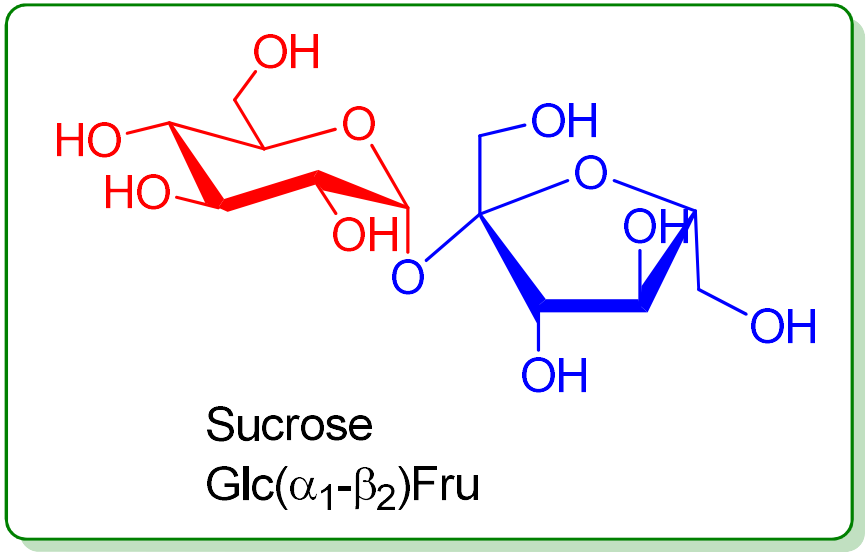
The ψ angle: C1'-O-C(aglycone)-H(aglycone) fragment.

Conformation of hydroxymethyl group



The three most common conformations of the C5-C6 fragment are the staggered conformations, **gg** (gauche-gauche), **gt** (gauche-trans) and **tg** (trans-gauche) of the dihedral angles O5-C5-C6-O6 and C4-C5-C6-O6

Saccharose (sucrose)

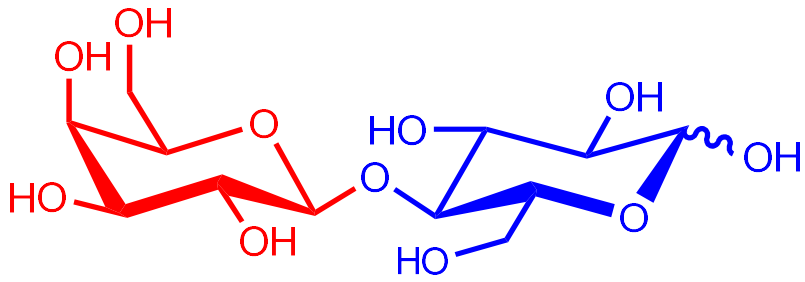


β-(2*S*,3*S*,4*S*,5*R*)-fructofuranosyl-
α-(1*R*,2*R*,3*S*,4*S*,5*R*)-glucopyranoside

Non-reducing sugar. Hydrolysis results in the inversion of the optical rotation -> **Invert sugar**

$$\boldsymbol{S([\alpha]_D + 66.5°) \rightarrow G([\alpha]_D + 52°) + F([\alpha]_D - 92°)}$$

Lactose



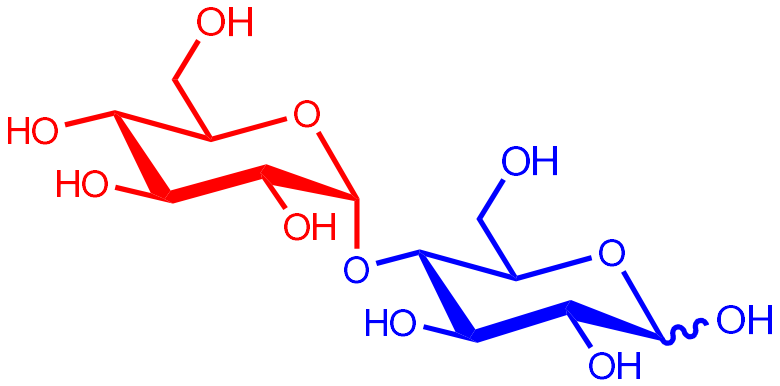
Lactose
Gal(β1-4)Glc

β-D-galactopyranosyl-(1→4)-D-glucose

Lactose is naturally occuring in milks of mammals. (human milk 5-8%, cow milk 4-6%).

Lactose is a reducing sugar, forms an osazone and crystalline α and β-forms ($[\alpha]_D$ +90° bzw. $[\alpha]_D$+35°).

Maltose

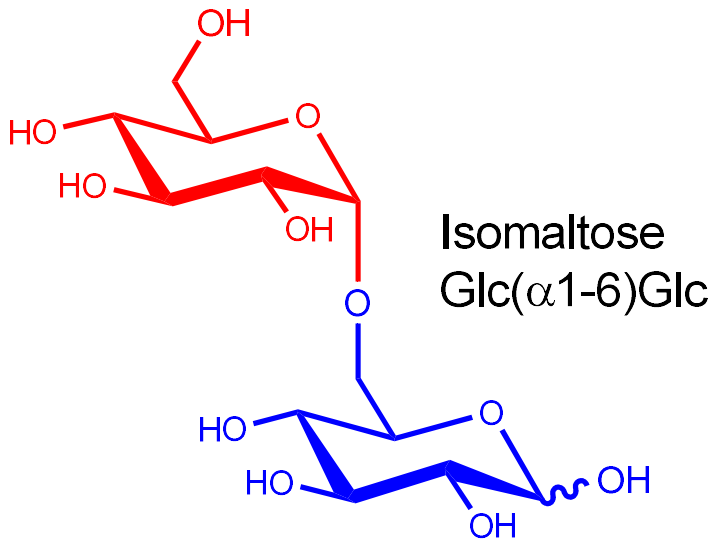


Maltose
Glc(α1-4)Glc

4-*O*-α-D-Glucopyranosyl-D-glucose

Enzymatic hydrolysis (amylase) of starch. Maltase breaks maltose down to two glucose molecules. Tastes about half as sweet as glucose.

Isomaltose



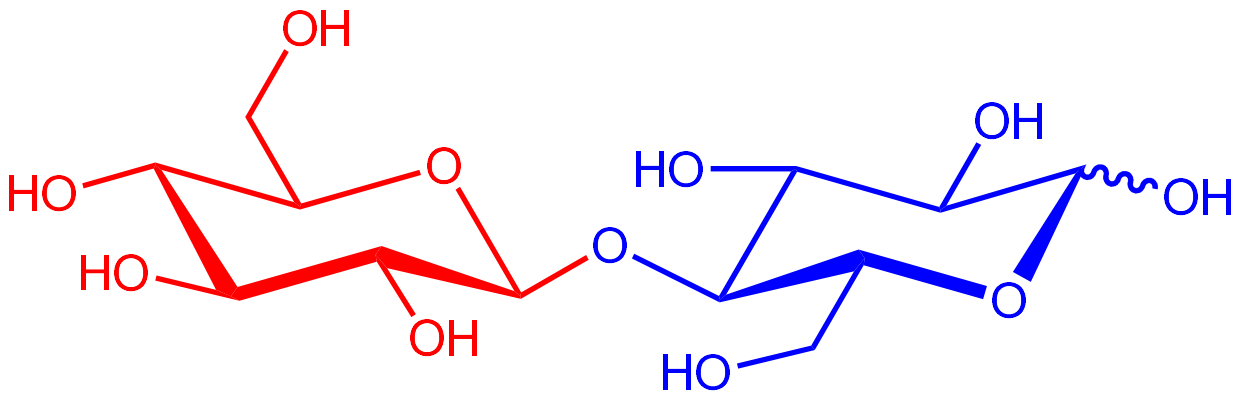
Isomaltose
Glc(α1-6)Glc

6-*O*-α-D-Glucopyranosyl-D-glucopyranose

Reducing sugar; α-(1-6)-linkage;

transglucosidase produces isomaltose from maltose syrup.

Cellobiose



Cellobiose
Glc(β1-4)Glc

Reducing sugar, consists of two glucose molecules. It can be obtained by enzymatic or acidic hydrolysis of cellulose

Cyclodextrine

Cyclic OS.

Available from starch using cyclodextrin glucotransferase (CGTases), amylolytic enzymes produced by *Bacillus macerans*

The most common and commercially available cyclodextrins consist of **six**, **seven** and eight glucose units, α-, β- und γ-cyclodextrines.

Cyclodextrine

Conical molecules, with well defined cavities, **hydrophilic exteriors**, and more **hydrophobic interiors.**

Hydrophobic compounds entrapped in the cavities→**drug delivery system**