1 Carbohydrate

Carbohydrate: Hydrates of carbon, general formula $C_x(H_2O)_y$,
but formaldehyde, CH_2O; acetic acid, $C_2(H_2O)_2$ are not carbohydrate
and
ribose, $C_5H_{10}O_4$ is carbohydrate.

Carbohydrate: optically active polyhydroxy ketone or aldehyde, or substance that yield these on hydrolysis.

Nomenclature

Classification

Monosaccharides:

Glycoaldehyde $HOCH_2CHO$ optical inactivity.

1. **Triose**
   i. Aldotetrose; glyceraldehyde, $C_3H_6O_3$, one Chiral carbon (2^n) optically active D- and L- forms, standards
   ii. Ketotetrose; dihydroxyacetone, optically inactive

2. **Tetrose**
   i. Aldotetrose; 2 asymmetric carbon,, four forms, D- and L-erythrose and D and L-threose
   ii. ketotetrose; erythrulose, optically active D- and L- forms

3. **Pentose**
   i. Aldopentose; 3 assymetric carbon, 8 forms, D- and L- forms of arabinose, xylose, ribose, lyxose. 2-deoxyribose is related to ribose
   ii. Ketopentose: 2assymmetric carbon, 4 forms, D- and L- forms of ribulose and xylulose

4. **Hexose**
   i. Aldohexose: 4 assymmetric carbon, 16 forms, D- and L- forms of glucose, mannose, galactose, allose, gulose, altrose, idose, talose
   ii. ketohexose; 3 asymmetric carbons, 8 forms, D- and L- forms of fructose, sorbose, tagatose, psicose

D-(+)Glucose

Structure elucidation

- Molecular formula; $C_6H_{12}O_6$
- With acetic anhydride gives penta-acetate. 5 -OH
- With hydroxylamine give oxime. carbonyl group
- By oxidation with Br_2 gives Petahydroxy Gluconic acid. carbonyl is aldehyde
- Reduction with HI, red P gave n-hexane. six carbons in straight chain.

So the structure is $CH(O)\text{-}(CH(OH))_4\text{-}CH_2OH$

confirmation of structure by synthesis

D-(-)-Fructose

Reactions of glucose and fructose

Osazone formation

Epimerization: inter conversion of epimers

Glucose + Bromine water → Gluconic acid
$CH(O)\text{-}HC(OH)\text{-} + Br_2 \rightarrow COOH\text{-}HC(OH)\text{-}$

Gluconic acid + pyridine → gluconate salt
$COOH\text{-}HC(OH)\text{-} + C_5H_5N \overset{\rightarrow}{\leftarrow} COO^-\text{-}HC(OH)\text{-}$

$COO^-\text{-}HC(OH)\text{-} \overset{\rightarrow}{\leftarrow} COO^-\text{-}{}^-C(OH)\text{-} + H^+$ (deprotonation)

$COO^-\text{-}{}^-C(OH)\text{-} \leftrightarrow C(O^-)(O^-)=C(OH)\text{-}$ (resonance)

$C(O^-)(O^-)=C(OH)\text{-} + H^+ \overset{\rightarrow}{\leftarrow} COO^-\text{-}(OH)C(H)\text{-}$ (Mannoate

$COO^-\text{-}(OH)C(H)\text{-} + H^+ \rightarrow COOH\text{-}(OH)C(H)\text{-}$ Mannoic acid

$COOH\text{-}(OH)C(H)\text{-}$ Na/Hg → $CHO\text{-}(OH)C(H)\text{-}$ Mannose

Disaccharides

1.1 Classification

Based on crystallinity

Sugars; crystalline, sweet and water soluble

monosaccharides: Cannot be hydrolysed in smaller molecule.

oligosaccharides: yields 2-10 monosaccharide molecule on hydrolysed

Polysaccharides; non-crystalline, not sweet, insoluble in water yield large number of monosaccharides

1.2 Nomenclature

Suffix; -ose; if aldehydic; aldose and if ketonic; ketose

with number of carbon i.e. pentose, hexose etc.

1.3 Monosaccharides

1.3.1 Glucose

1.3.1.1 Occurrence

Occurrence: fruits, honey

Source: hydrolysis of starch

1.3.1.2 Properties

Optically activity; dextrorotary so also called dextrose,

m. p. 146°C,

Taste; sweet

1.3.1.3 Structure determination

Molecular formula; $C_6H_{12}O_6$

With acetic anhydride gives penta-acetate. 5 -OH

With hydroxylamine give oxime. carbonyl group

By oxidation with Br_2 gives Petahydroxy Gluconic acid. carbonyl is aldehyde

Reduction with HI, red P gave n-hexane. six carbons in straight chain.

So, the structure is $CH(O)-(CH(OH))_4-CH_2OH$

confirmation of structure by synthesis

1.3.2 Fructose

1.3.2.1 Occurrence

Occurrence: fruits, honey

Source: hydrolysis of inulin found in dahlia tuber

optically activity; dextrorotary so also called dextrose, m.p. 102°C

1.3.2.2 Structure determination

- Molecular formula; $C_6H_{12}O_6$
- With acetic anhydride gives penta-acetate. 5 -OH

- With hydroxylamine give oxime. carbonyl group
- No reaction with Br_2. carbonyl is not aldehyde
- By oxidation with HNO_3 gives trihydroxyglutarate (COOH-CHOH-CHOH-CHOH-COOH) tartaric acid (COOH-CHOH-CHOH-COOH) and glycollic acid ($CH_2OHCOOH$). Since product is fragments of original molecule, carbonyl is ketonic
- By reduction with HI, red P gave n-hexane. Six carbon in straight chain.
- Ascending series by Kiliani reaction and reducing the product 2-methylhexanoic acid is obtained. So ketonic group is adjacent to terminal carbon.

So the structure is $CH_2(OH)\text{-}CO\text{-}(CH(OH))_3\text{-}CH_2OH$
confirmation by synthesis

1.4 Ring structure

Evidences

Glucose did not give Schiff's reaction. does not form bisulphite compound. so aldehyde is not free
Mutarotation

Ring size determination
Periodic acid oxidation

$RCHOH\text{-}CHOHR' + HIO_4 \rightarrow RCHO + R'CHO$
$RCHOH\text{-}CHOH\text{-}CHOHR' + 2\ HIO_4 \rightarrow RCHO + HCOOH + R'CHO$

also

$RCHOH\text{-}CHO + HIO_4 \rightarrow RCHO + HCOOH$

$RCOCHOHR' + HIO_4 \rightarrow RCOOH + R'CHO$

number of moles periodic acid consumed is indicative of the number of neighbouring hydroxyl
free aldose is completely broken by periodic acid.

Glucose + MeOH + HCl → methyl glucoside. It is not completely broken down by periodic acid.

Glucose + $2HIO_4$ periodic acid oxidation → di aldehyde +1 HCOOH

2 molecules of periodic acid used so 3 neighbouring -OH
6 membered or pyranose ring

1.4.1 Fischer and Haworth representation

Fischer projection

all the carbon in a straight chain
carbonyl at the top and designated C1 in aldose and C2 in Ketose
D and L refers to the configuration at C5
horizontal lines are projecting above the plane and vertical below
in ring form right side OH on C1 is α and left side is β.
hemiacetal is formed between carbonyl and -OH C5.

Haworth projection six-member planar ring

Conversion of Fischer to Haworth
Walden inversion at C5 between H and hemiacetal bond. Configuration is inverted
Walden inversion of hemiacetal on C5 bond with C6. Configuration is restored.
All the left side groups are projected on top and right side below the ring.

1.5 Mutarotation

Mutarotation
when a substance is dissolved in solution optical rotatory power changes until it reaches a constant value. Specific rotation of fresh solution of glucose +111º. after equilibration +52.5º.
Tollen (1883) ring stricture by hemiacetal formation with C-4 or C-5 -OH. Generation of new chiral center. two forms *viz* α and β anomer.
Both form isolated by Tarnet (1895).
Haworth (1926) glucose is 6-member planar ring pyranose ring.
Reeves (1950) chair like conformation with glyosidic hydroxyl in axial form in α form and in equatorial form in β form. stability of equatorial is more so β is predominant,

α anomer: m.p. 146°C Specific rotation +111º, crystallized from cold solution.
β anomer: m.p. 148°C Specific rotation +19.2º, crystallized from hot solution.
Mechanism

α ⇄ open chain structure ⇄ β
Equilibrium is reached faster with heat or base catalyst.

1.6 Osazone formation

(Fischer, 1884)
aldehyde/ ketone + phenylhydrazine → phenylhydrazone

Aldose/ ketose + excess of phenylhydrazine → Osazone + aniline + ammonia

$CH(O)-CH(OH)- + 3\ PhNHNH_2 \rightarrow CH(=NNHPh)-C(=NNHPh)-$
$CH_2(OH)-CO- + 3\ PhNHNH_2 \rightarrow CH(=NNHPh)-C(=NNHPh)-$

Mechanism Waygand (1940)
Aldose/ ketose + phenylhydrazine → phenylhydrazone

$CH(O)-CH(OH)- + 3\ PhNHNH_2 \rightarrow CH(=NNHPh)-C(OH)-$

$CH_2(OH)$-CO- + 3 $PhNHNH_2$ → CH(OH)-C(=NNHPh)-

phenylhydrazone → Amadori reaarrangement → rearranged phenylhydrazone + aniline

CH(=NNHPh)-C(OH)- → CH(=NH)-C(O)- + $PhNH_2$
CH(OH)-C(=NNHPh)- → CH(O)-C(=NH)- + $PhNH_2$

Rearranged phenylhydrazone + 2 phenylhydrazine → Osazone
CH(=NH)-C(O)- + $PhNHNH_2$ → CH(=NH)-C(=NNHPh)- + H_2O
CH(O)-C(=NH)- + $PhNHNH_2$ → CH(=NNHPh)-C(=NH)- + H_2O

CH(=NH)-C(=NNHPh)- + $PhNHNH_2$ → CH(=NNHPh)-C(=NNHPh)- + NH_3
CH(=NNHPh)-C(=NH)- + $PhNHNH_2$ → CH(=NNHPh)-C(=NNHPh)- + NH_3

In glucose, during Amadori rearrangement, α-hydroxyl group gets oxidized to carbonyl, it could have further oxidize β-hydroxyl too but does not because osazone gets chelated by ring formation through internal H-bond

CH(=NNH*Ph)-C(=N*NHPh)- in solid
[-$O^{\#}$]-CH(NH*NHPh)-C(N=N*HPh)-$(CHOH)_2$-CH-[$O^{\#}$]-CH_2OH in ring form

Osazone are crystalline. used for characterizing sugar,

Osone formation
CH(=NNHPh)-C(=NNHPh)- +HCl → CH(=O)-C(=O)

Osone +CuSO4 → crystalline Complexes with sharp melting point

Glucose and fructose form same osazones; so they have similar configuration in rest of the 4 carbon
Aldose which give same osazone are called epimers. They differ only in their α-carbon configuration. eg glucose and mannose

1.7 Interconversion

1.7.1 Aldose to ketose

Aldose → Osazone
Osazone + Zn + HCl → Ketose

1.7.2 Ketose to aldose

ketose +H_2/Ni → polyhydric alcohol

polyhydric alcohol + HNO_3 → aldonic acid
aldonic acid +heat → lactone
lactone + Na/Hg + HCl → Aldose

1.7.3 Lower homologue to higher

Killiani Method

-CH(OH)-CH(OH)-CHO + HCN → -CH(OH)-CH(OH)-CH(OH)CN
new chiral centre, two isomers possible one predominated, due to diastereoselectivity

-CH(OH)-CH(OH)-CH(OH)CN + aq. $Ba(OH)_2$ → -CH(OH)-CH(OH)-CH(OH)COO^-

-CH(OH)-CH(OH)-CH(OH)COO^- + H^+ → -CH(OH)-CH(OH)-CH(OH)COOH

-CH(OH)-CH(OH)-CH(OH)COOH → -CH[O-]-CH(OH)-CH(OH)CO[O-] Lactone

-CH[O-]-CH(OH)-CH(OH)CO[O-] + Na/Hg +H_2SO_4 → -CH(OH)-CH(OH)-CH(OH)-CHO

Snowden Method

-CHO + CH_3NO_2 + 2 CH_3ONa → -CH(OH)-CH=NO_2Na + 2 CH_3OH

-CH(OH)-CH=NO_2Na + H^+/H_2O → -CH(OH)-CH=O

1.7.4 Higher homologue to lower

Wohl's method

-CH(OH)-CH=O + NH_2OH → -CH(OH)-CH=N-OH

-CH(OH)-CH=N-OH + Ac_2O → -CH(OAc)-CH=N-OAc

-CH(OAc)-CH=N-OAc +Na_2CO_3 → -CH(OAc)-CN

-CH(OAc)-CN + AgOH → -CHO + AgCN

Ruffs method

-CH(OH)-CH=O + Br_2/H_2O → -CH(OH)-COOH

-CH(OH)-COOH +$Ca2^+$ → $(-CH(OH)-COO)_2Ca$

$(-CH(OH)-COO)_2Ca$ + H_2O_2 +Fe^{2+} → -CHO +CO_2 decarboxylation of α-hydroxyacid

1.8 Disaccharide

Def: Consists of two monosaccharides.

Depending on reducing property two types 1. Reducing 2. non-reducing

Reducing when anomeric hydroxyl is free. e.g maltose, cellobiose

Non-reducing when anomeric hydroxyl is used in glycosidic bond formation. e.g sucrose

Sucrose, $C_{12}H_{22}O_{11}$

Chemical property

non-reducing, no reaction with Fehling solution, no formation of osasone and do not show mutarotation

Sucrose Source: cane, sweet potato

Crystalline form sugar, m.p. 180°C

Noncrystalline syrup form mollases

Constituent: Made of α-D-(+)-glucopyranoside and β-D-(-)-fructofuranoside. *free molecule of*

fructose is pyranoside.

Optical property: Dextrarotatory +66°, when hydrolysed fructose had more (-) rotation than of the (+) of glucose so there is inversion of rotation in the mixture. The mixture is known as invert sugar.