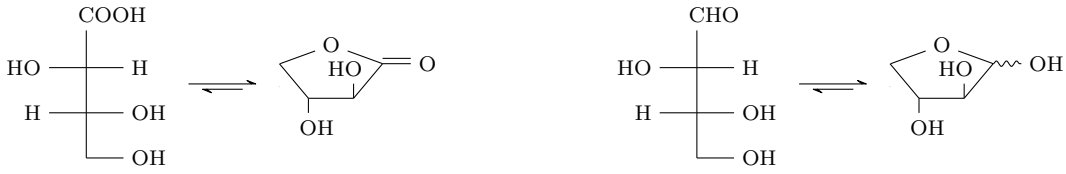
Week 9

Intro to Biological Molecules

9.1 Carbohydrates 2

5/24:

- Today's lecture content in Solomons et al. (2016).
  - Today: Sections 22.3-22.4, 22.6-22.7 and 22.9A-22.9B. Read Sections 22.10-22.11.
  - Next time: Sections 25.1-25.2, 25.4-25.5, 24.11, and more.
  - Practice problems: 22.20, 22.31, and 22.43.
- Final exam info.
  - The final exam will be 2.2 times longer than the midterm (so slightly more than twice as many problems).
  - This should help us as we won't lose so many points if we can't get a mechanism this way.
  - The final is cumulative, though Tang will try to test more on new content.
  - The practice exam is almost as hard as the real final exam.
- Review of last lecture.
  - In the Kiliani-Fischer synthesis, the carboxylic acid intermediate can cyclize into a lactone and the final product can cyclize into a sugar.



(a) Intermediate 2. (b) Product.

Figure 9.1: Extra Kiliani-Fischer cyclizations.

  - D-threose is now used in biology to mimic ribose.
- Today, we will cover the following.

II. Reactions.

B. Mutarotation.

C. Glycosides.

D. Oxidation/degradation.

- Differences between α-D-glucopyranose and β-D-glucapyranose.

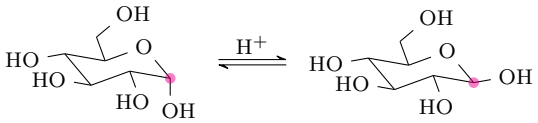
$$\text{MP}_\alpha = 146\,^\circ\text{C} \qquad [\alpha]_\alpha = \pm 112.2^\circ$$
$$\text{MP}_\beta = 150\,^\circ\text{C} \qquad [\alpha]_\beta = \pm 18.7^\circ$$

  - The **anomers** differ in their melting point (MP) and optical rotation ($[\alpha]$).

- Crystallization of a D-glucose solution at different temperatures can isolate either one of them.
  - α can be crystallized at room temperature; β can be crystallized at 100 °C.

- If the α and β anomers (in any proportion) are added to H_2O, over time, the optical rotation tends toward 52.6°.
  - This is because of **mutarotation**, which will always make the $\beta : \alpha$ ratio tend to 64 : 36.
  - If we now take a weighted average of the specific rotations of the pure anomers, we will get approximately 52.6°.

- General form.



  - We use an acid catalyst to simplify the mechanism, but it may not be necessary?

- Mechanism.

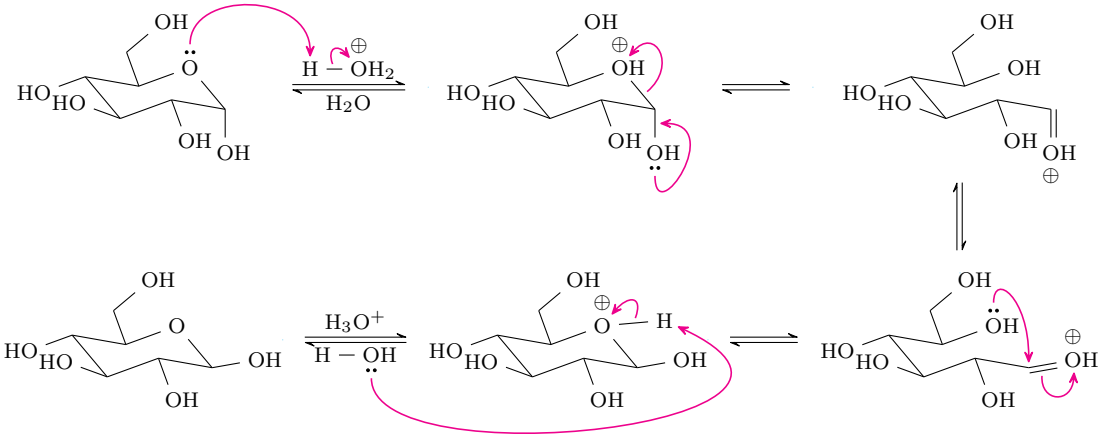


Figure 9.2: Mutarotation mechanism.

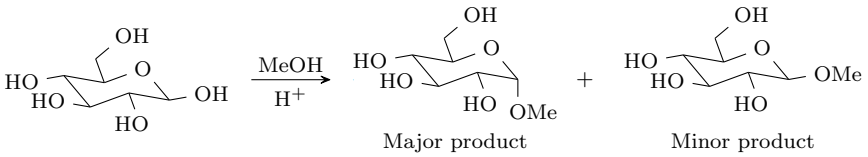
  - When we recyclize, we can form either anomer once again.
  - Note that if we lose a proton from the second intermediate, we can create the linear form of glucose.

- Key: Rapid interconversion of the α, β forms.

- The equatorial, β anomer is not always energetically preferred.
  - For example, α-D-mannose (or α-D-mannopyranose) is preferable to β-D-mannose (or β-D-mannopyranose).
  - The mechanism is not fully understood, but the current assumption is that on the α-anomer, the σ^* orbital of the axial C−O bond accepts electrons from the oxo lone pair via hyperconjugation in a stabilizing fashion.

  - α or β case-by-case prediction is not testable material.

- **Glycoside**: A cyclic acetal/ketal of a sugar.
- Glycoside formation.
- General form.



  - We notably do not form the open hemiacetal from the open form of a sugar.
  - The two anomers of the product are called **methyl α-D-glucopyranoside** (major) and **methyl β-D-glucopyranoside** (minor).

- Mechanism.

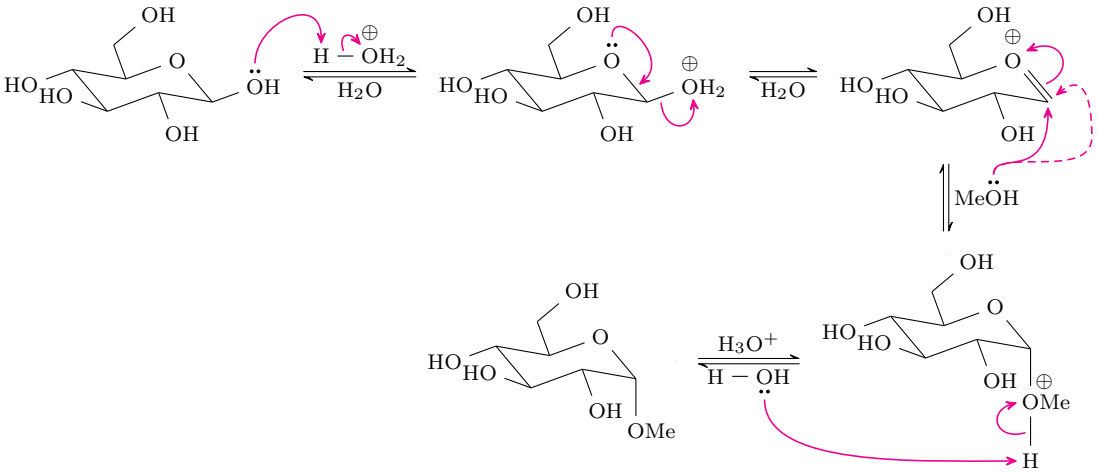
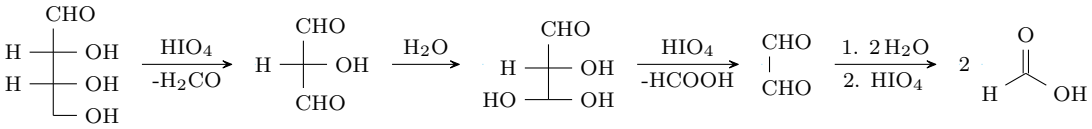


Figure 9.3: Glycoside formation mechanism.

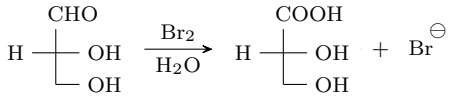
  - Note that the mechanism is symmetric for α-D-glucose.
  - Which anomer of the product is formed depends on the side from which the MeOH nucleophile attacks. Indeed, if we use the dashed attack in step 3 instead of the solid attack, we will get the β product.

- Note that mutarotation and glycoside formation proceed through different intermediates.
  - We use the mutarotation intermediate because it is much likelier to form in water. The glycoside formation one is just what we need for glycoside formation to proceed, so we have no choice but to go through it.
- Oxidation/degradation.
- Periodic acid.
- Consider periodic acid (HIO_4).
  - Recall diol cleavage (see Figure 1.3).
- General form.



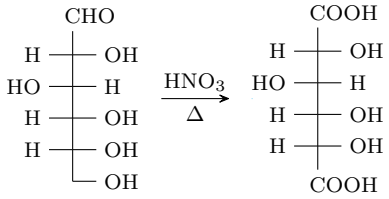
  - Applying it to sugars cleaves repeatedly.
  - We get formic acid and formaldehyde in multiple equivalents?
  - We have to see aldehydes as hydrates here.

- Tang works through D-fructose as an example.
- Bromine water.
- General form.



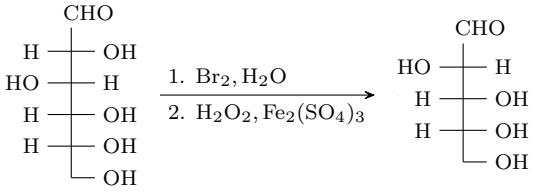
  - This is a good, mild way to convert aldehydes to carboxylic acids.

- Mechanism. *picture; email Tang.*
- Nitric acid and heat.
- General form.



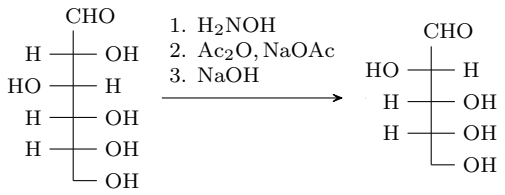
  - The product is **glucaric acid**.

- Mechanism. *picture; email Tang.*
- Ruff degradation.
- General form.



  - Read 22.11 for ??
  - The first step is bromine water again.
  - The second step is the exact opposite of Kiliani-Fischer synthesis.

- Mechanism. *picture; Google it.*
- Wohl degradiation.
- General form.



  - The reactant is hydroxylamine and forms an oxime.
  - Ac_2O is acetic anhydride very reactive.
  - The product is **D-arabinose**.

- Mechanism.
  - Essentially, we form an oxime from the top aldehyde.
  - Then we turn the hydroxyl portion of the oxime into AcO, a good leaving group. AcO^- engages in an E2 elimination on the oxime hydrogen, forming a cyano group.
  - Base then eliminates the cyano group, giving us an aldehyde one carbon down.
- What Tang expects us to know from Chapter 22.
  - The mechanisms she showed us (only a few).
  - No synthesis problems with sugars.
    - Tang has shown us some good reactions, but modern sugar synthesis does not use any of these reactions; these are all decades old.
    - Modern sugar chemistry is very hard; these reactions are just classic ones.