Carbohydrates – A Classic Tale of Fischer
May 20, 2013

Emil Fischer
Nobel Laureate #2
Chemistry, 1902

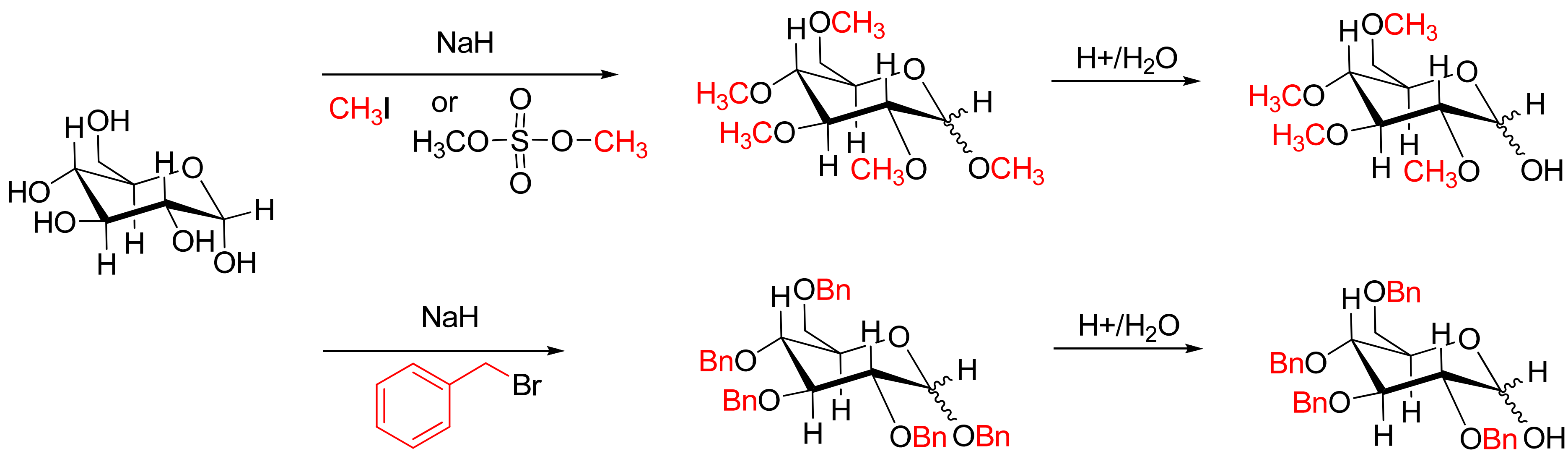
- Some reactions of carbohydrates (etherification, esterification, acetalization, oxidation reactions, periodate cleavage).
- Fischer's proof of the structure of glucose.

Announcements

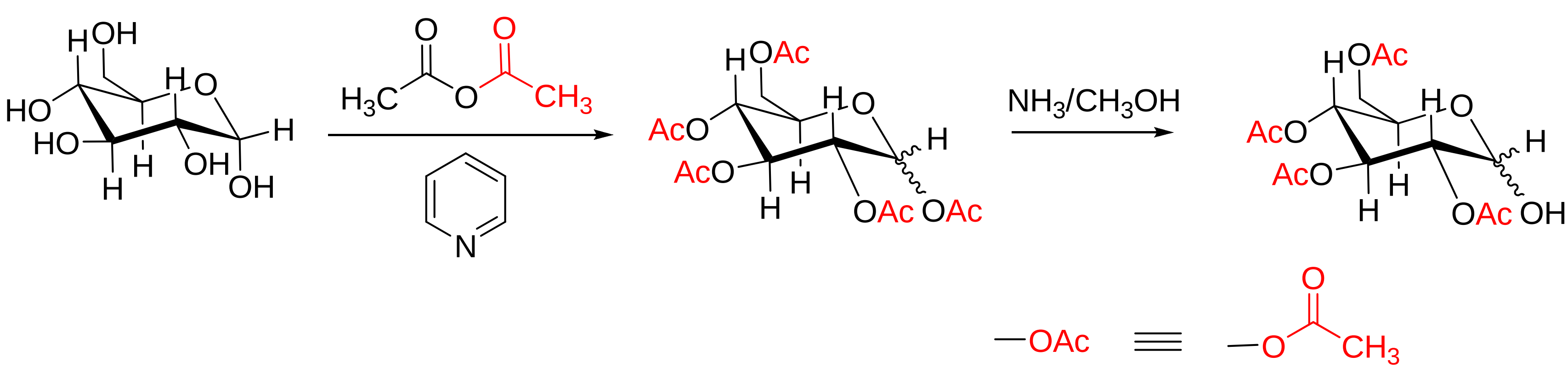
TA Office Hours: Mon 7-8 pm: Rob Craig - 302 Schlinger (x4056); Tue 3-4 pm: Kelly Kim - 302 Schlinger (x4047); Tue 7-8 pm: Corey Reeves - 302 Schlinger (x4056); Wed 5-6 pm: Adam Boynton - 139 Noyes (x3202); Wed 8-9 pm: Ben Suslick (UTA) - Lloyd Lounge; Thu 8-9 pm: Evan Zhao (UTA) - Fleming Lounge; Thu 9-10 pm: Crystal Chu - 202 Schlinger (x3634); Sun 3-4 pm: Chung Wan Lee - 302 Schlinger (x4056).

Suggested Problems for Chapter 24: 24.39(a,c,e,g), 24.40, 24.42, 24.45, 24.46, 24.50, 24.54, 24.57, 24.60.

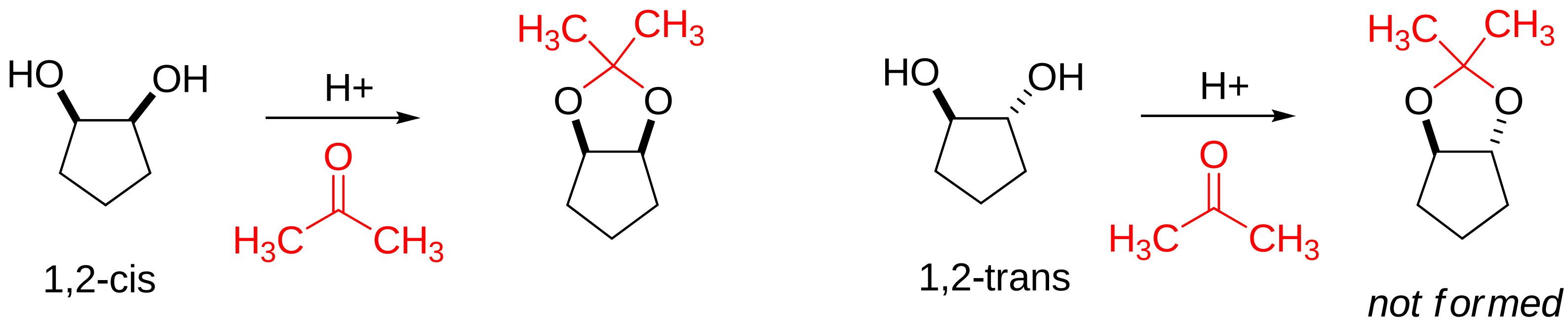
Etherification Reactions:



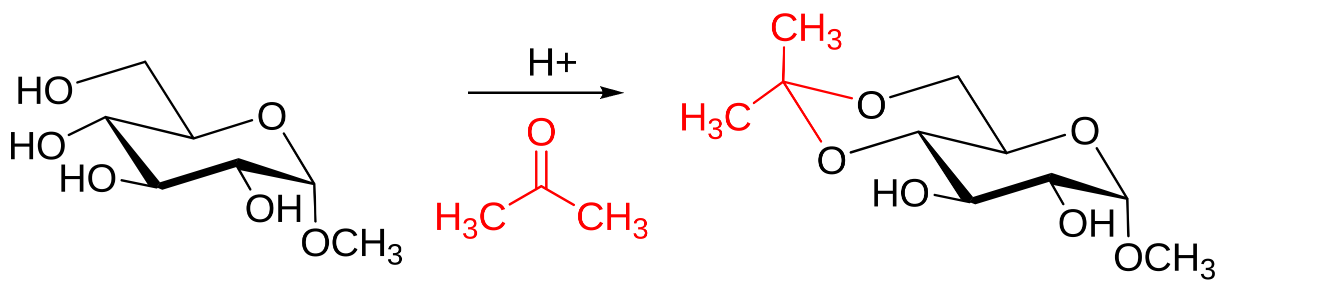
Esterification Reaction:



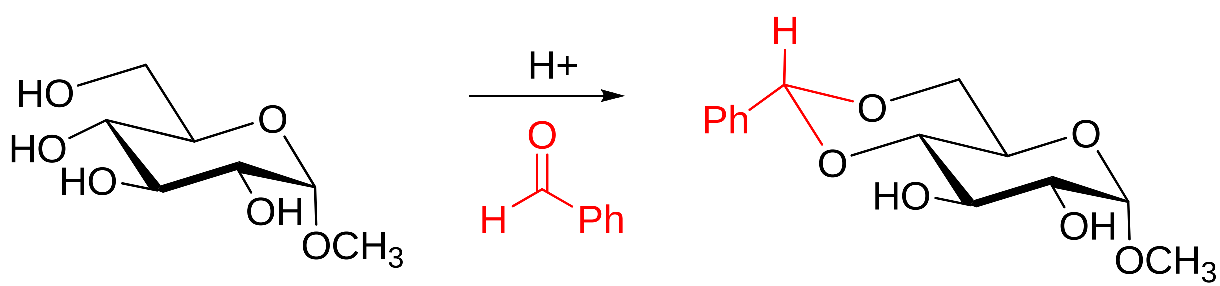
Ketal-forming Reactions:



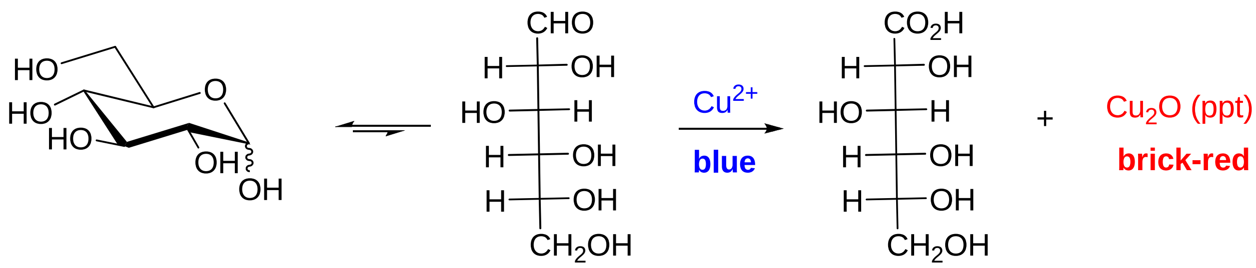
Ketal example w/ glucose:

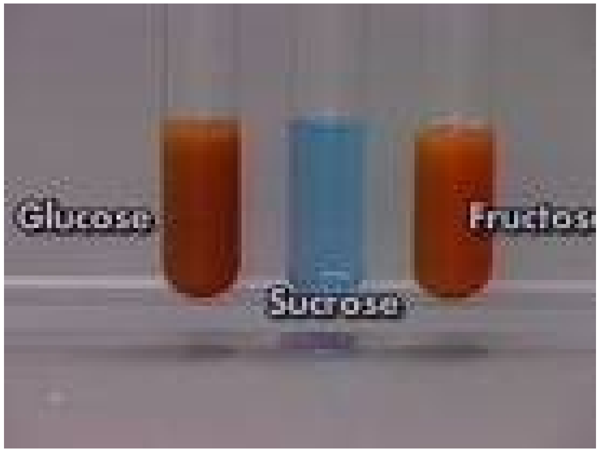


Acetal example w/ glucose:

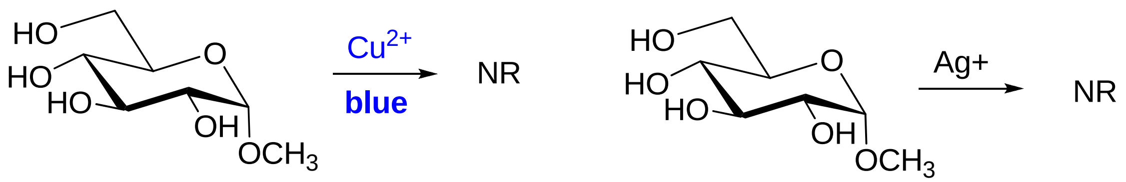


Detection of a Reducing Sugar via Benedict's Reagent

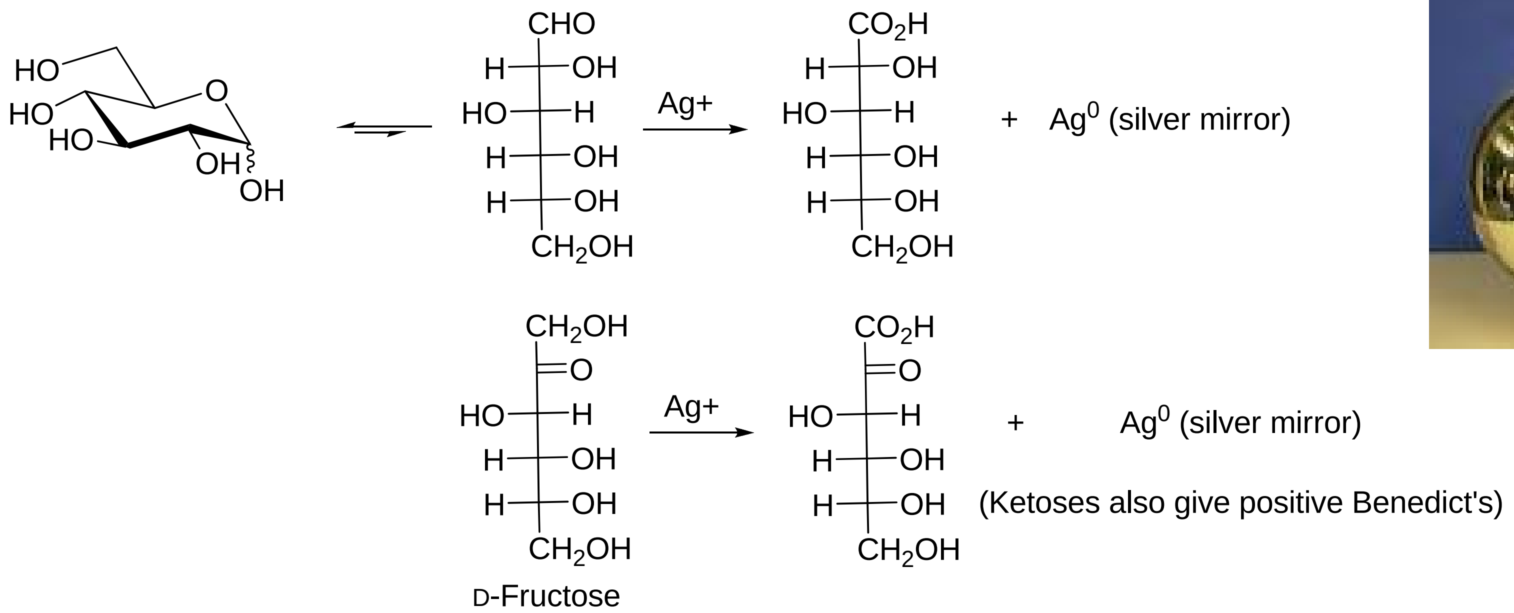




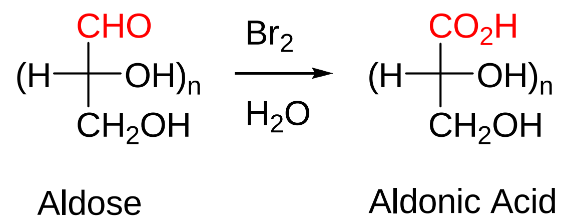
An Example of a Negative Benedict's or Tollen's Test with a Non-Reducing Sugar

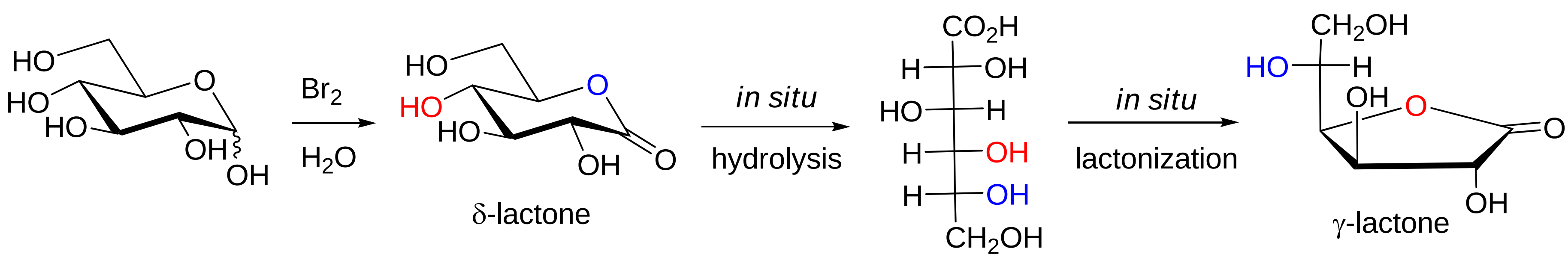


Detection of a Reducing Sugar via Tollens's Reagent

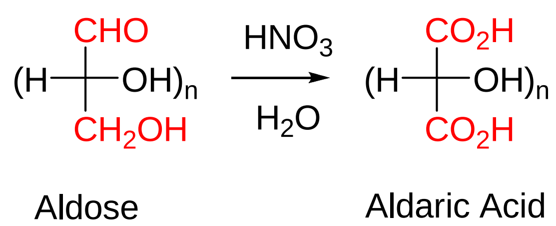


Oxidation of Aldoses with Bromine Water:



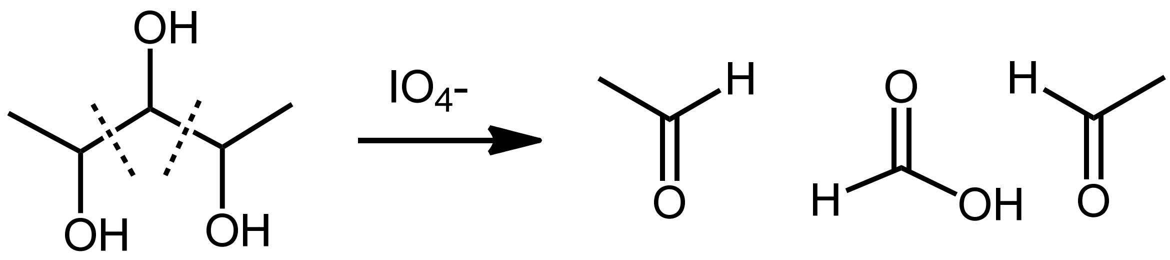


Oxidation of Aldoses with Dilute Nitric Acid:

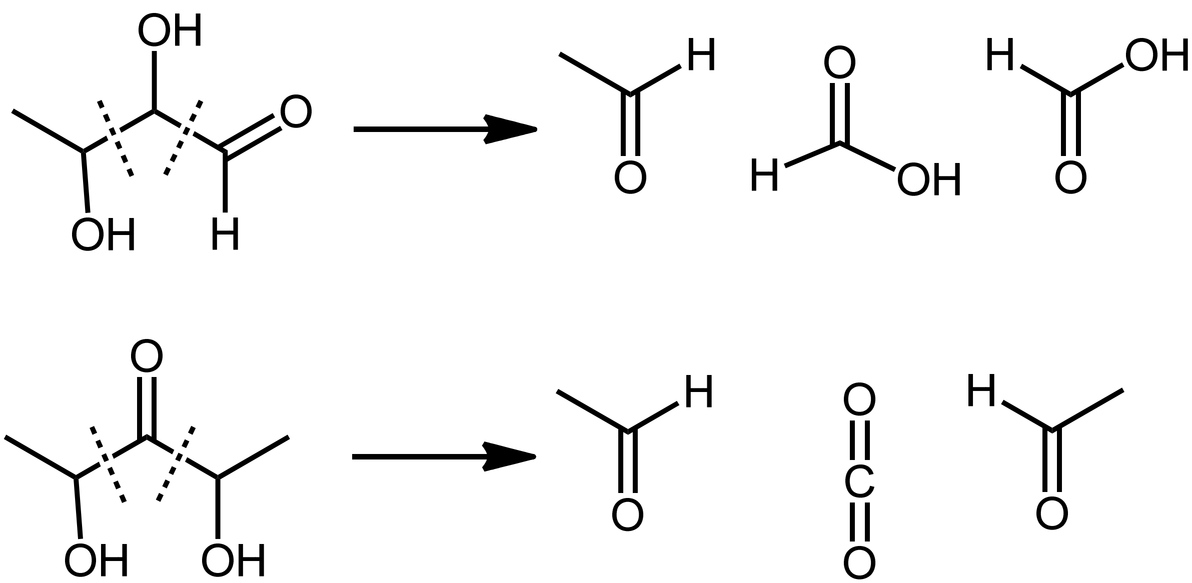


Periodate Cleavage Products

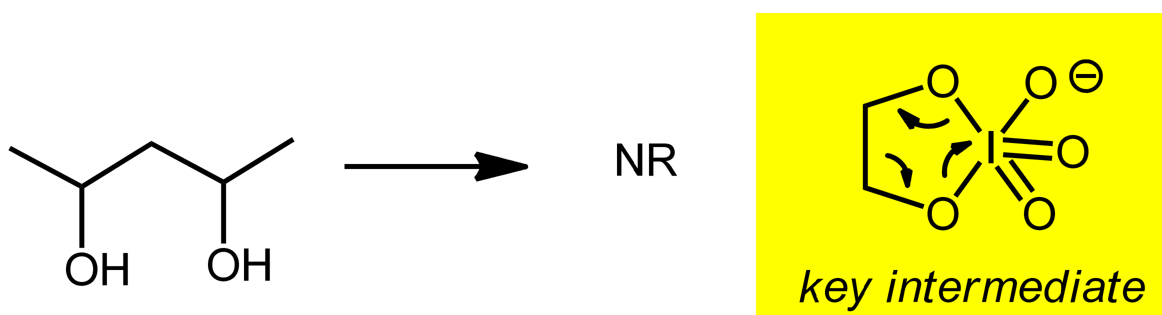
1.



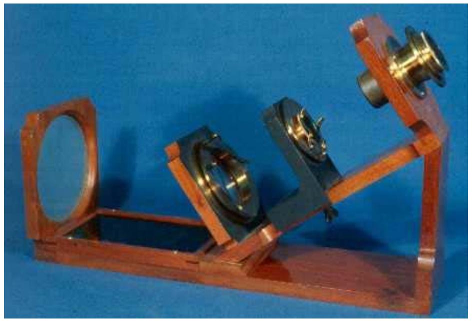
2.



3.

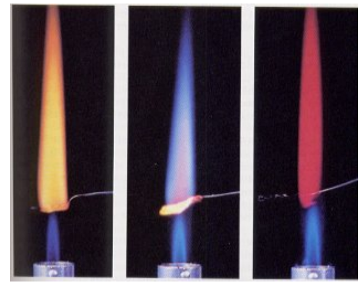


What tools did Fischer have at his disposal during his work on the sugars (1888-1894)?



polarimeter, sold for $20 to $45 in 1887

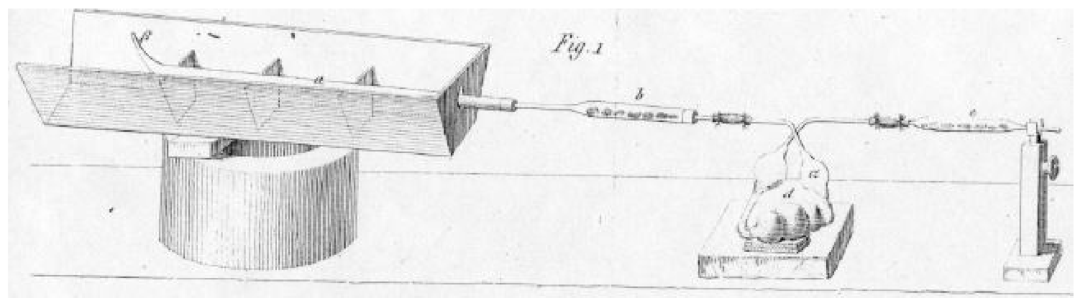
m.p. apparatus, admittedly this one is a bit too modern



flame tests to characterize atomic emission; the Bunsen burner was developed in 1955

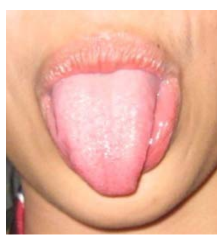
analytical balance (this is actually a 1927 model)

phenolphthalein (1877) and other acid-base indicators, note that the pH scale wasn't developed until 1909



Liebig's combustion apparatus (1831) for estimating C, H, and O analysis; techniques for analyzing N (1834), S, and halogens (1843)

You, of course, were encouraged to taste everything!



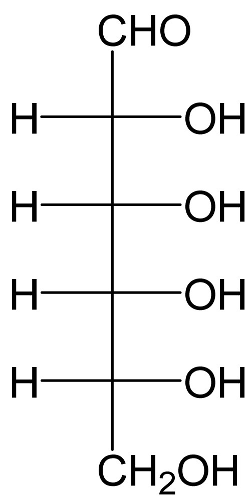
Use of precipitating reagents and titrations were common. Chromatography as a separation technique was first reported in the mid-1800's but was really developed in the 1930's

No IR (1900)
No MS (1897-1911)
No UV (1940)
No NMR (1945)
No GC (1953)

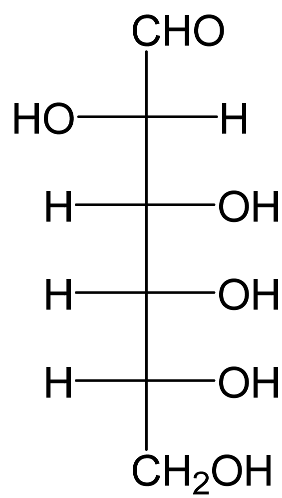
Approximate timeframes that these techniques were first being developed

although Beer's law known since 1852

The 5R or D Aldohexoses



1



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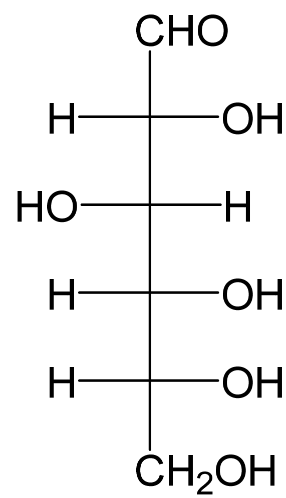

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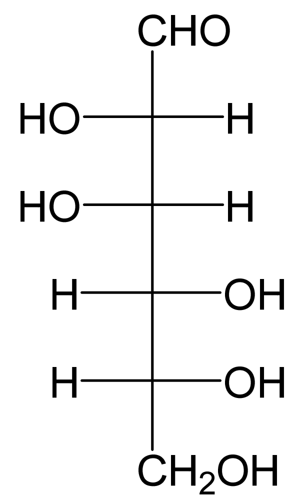

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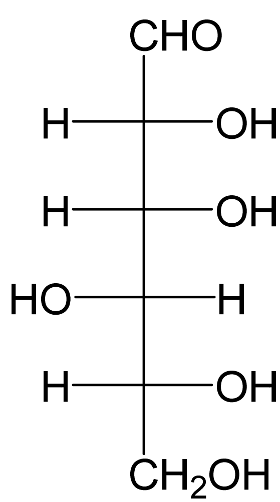

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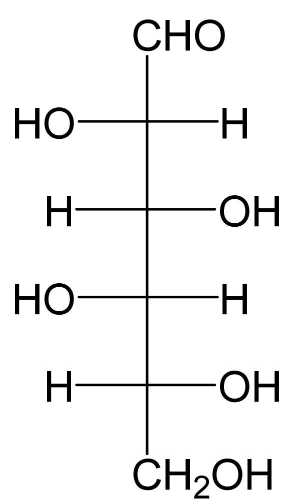

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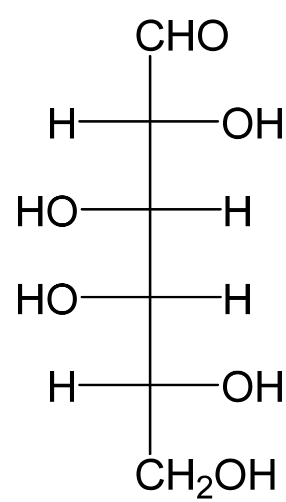

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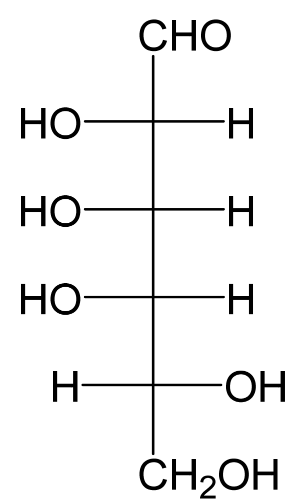

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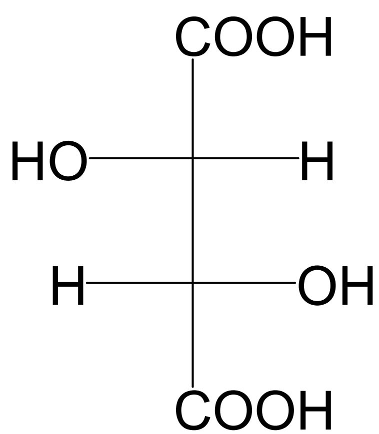
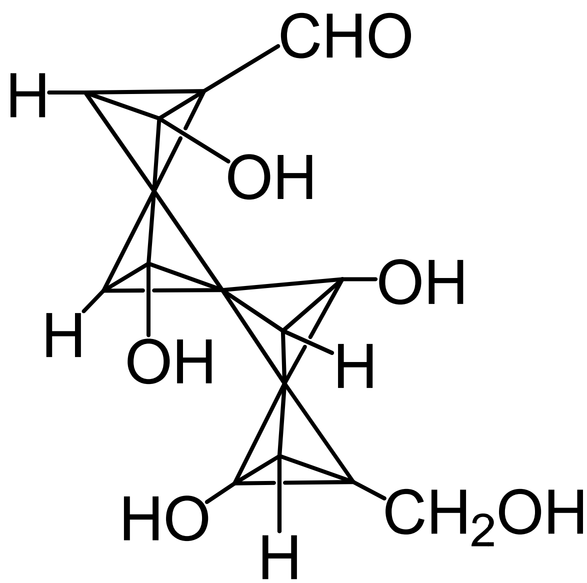
1. Fischer arbitrarily wrote down what is now called the D series. He had no way of assigning the absolute configuration and therefore discarded the mirror image forms of those shown above. In 1954, Bijvoet's special X-ray crystal structure analysis of D-tartaric acid revealed that Fischer had in fact made the correct assignment (D or *R* according to the CIP nomenclature).



D-Tartaric Acid (Structure not assigned until 1954)

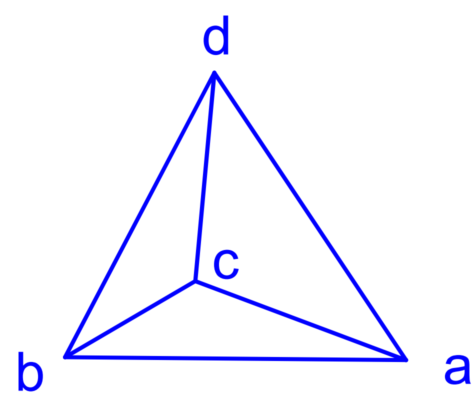
"All previous observations in the sugar group are in such complete agreement with the theory of the asymmetric carbon atom that the use of this theory as a basis for the classification of these substances seems justifiable"



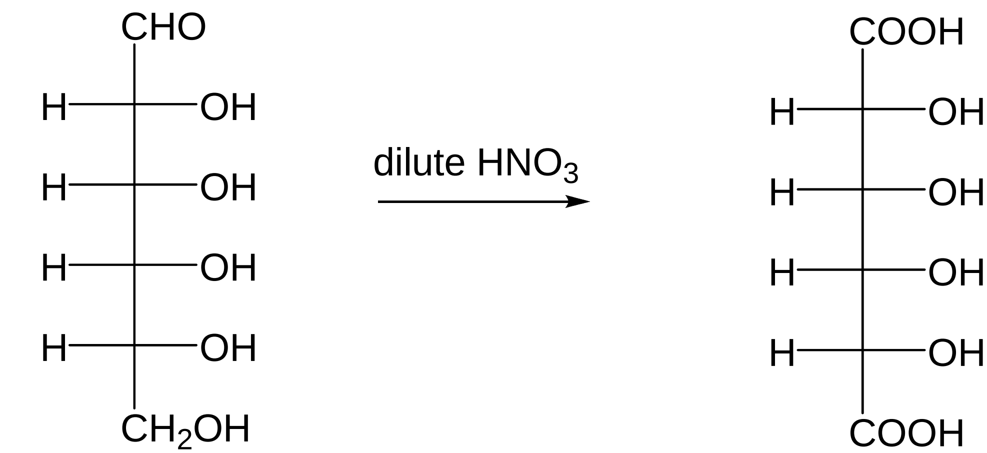
- Emil Fischer (1891)

van't Hoff and LeBel (1874):

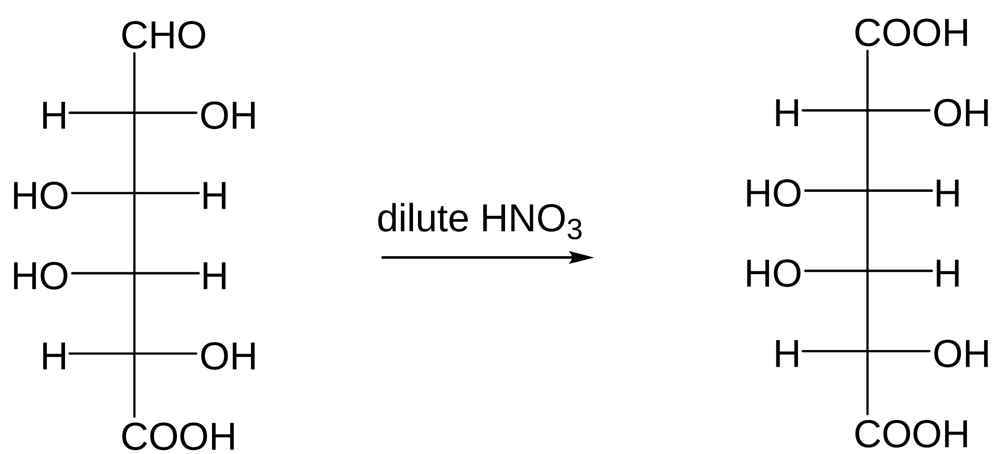
Proposed the case for enantiomerism for C_{abcd}: the tetrahedral carbon atom.



2. Both D-glucose and D-mannose are oxidized to optically active saccharic acids, eliminating structures **1** and **7**, which give meso structures:



1



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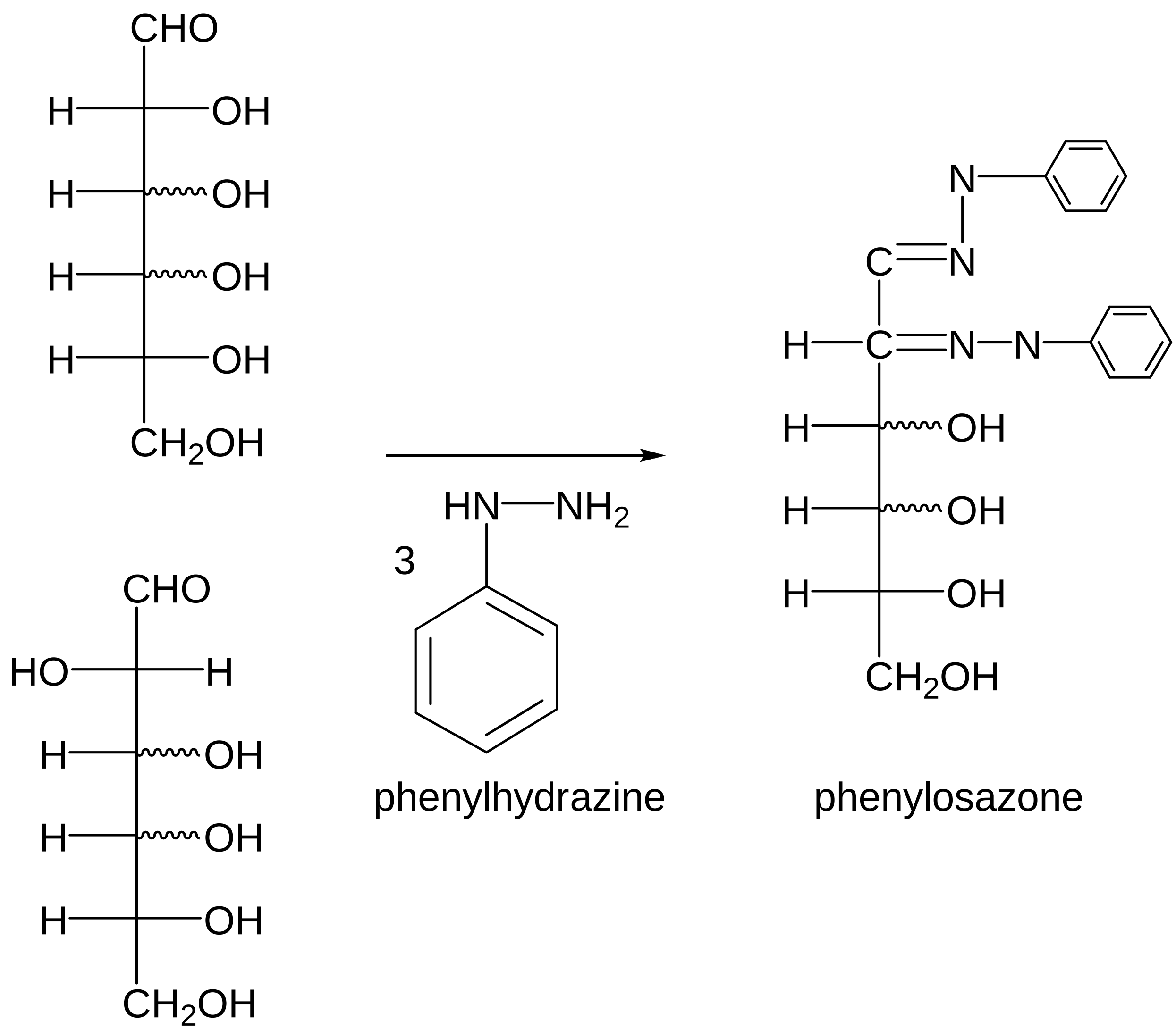
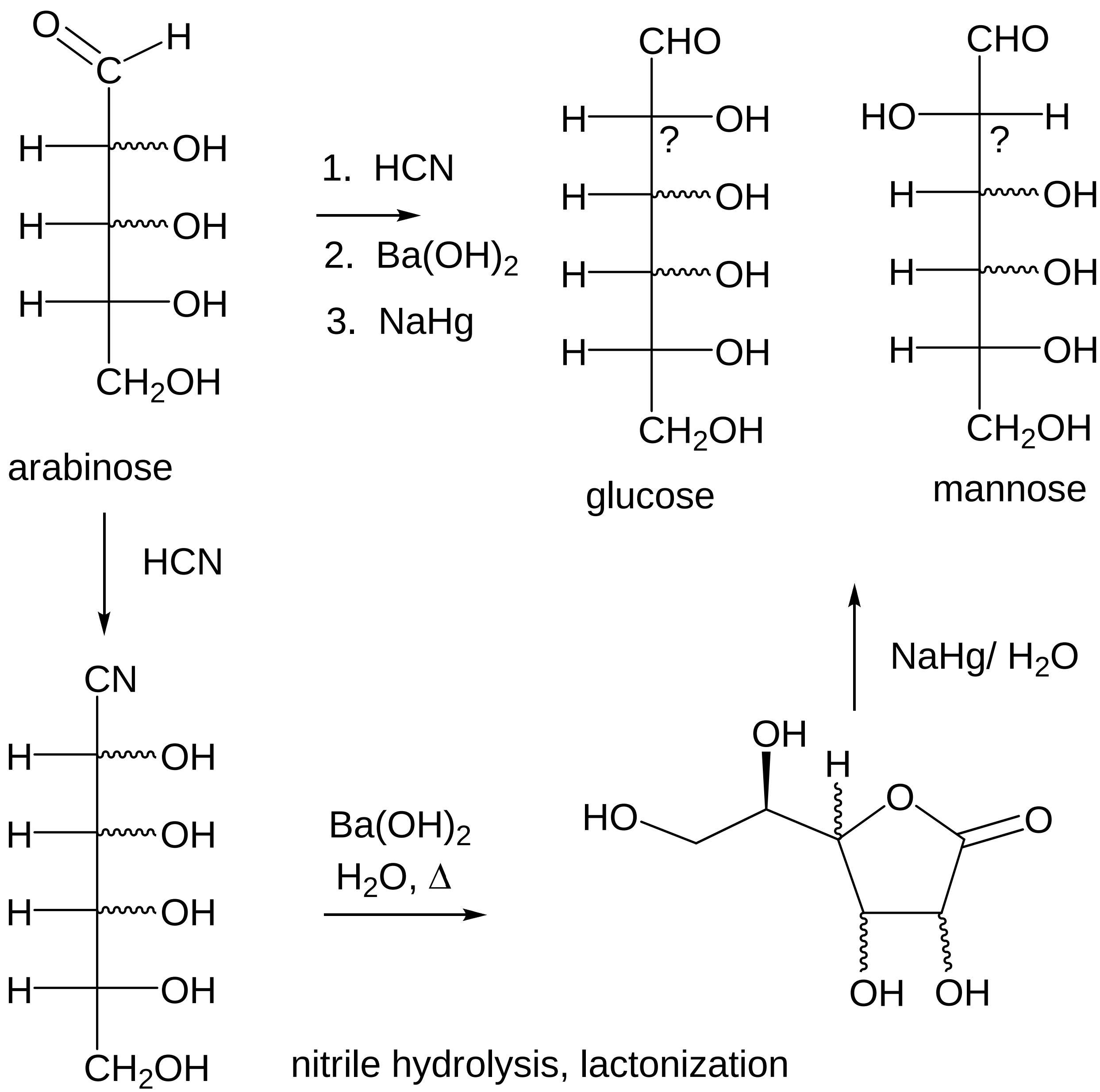
3. Both D-glucose and D-mannose give the same osazone, therefore, these two compounds differ only at C.2. Glucose and mannose must be **1** and **2**, **3** and **4**, **5** and **6**, or **7** and **8**. Based upon the nitric acid oxidation data, glucose and mannose must be **3** and **4** or **5** and **6**.

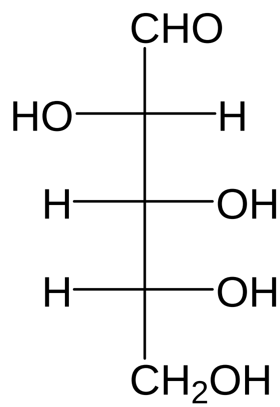


4. Kiliani-Fischer chain extension of the aldopentose D-arabinose yields both glucose and mannose.



What is the structure of arabinose?

either



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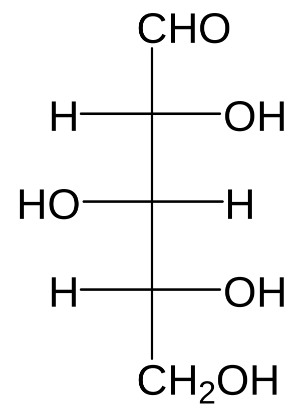
or



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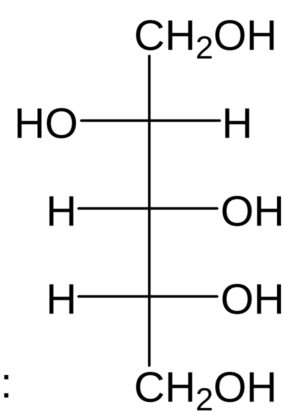
Based upon the Kiliani-Fischer chain extension data.

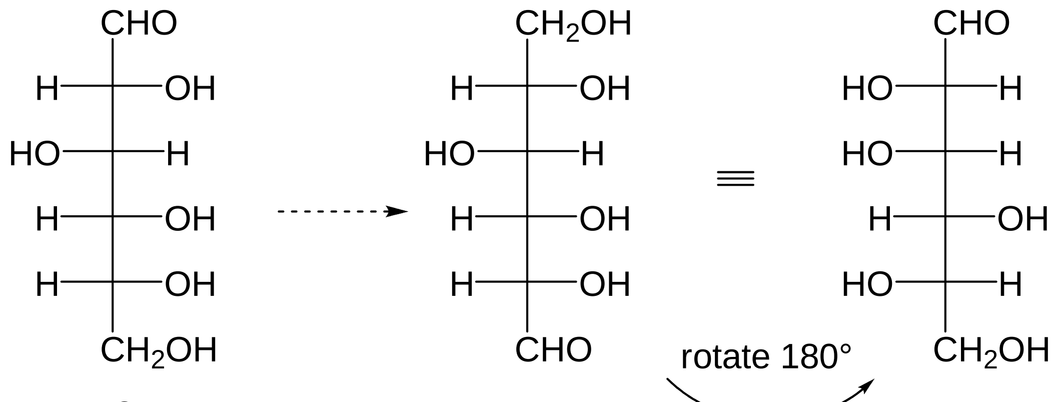
Arabinose $\xrightarrow{\text{reduction}}$ Arabinitol (optically active)

Conclusion: Arabinose must be **9**

Arabinitol:



5. With this information, **3** or **4** could be glucose. To choose between them, Fischer employed a chemical method he had devised to interchange the two ends of an aldose chain. The method is "fairly involved".



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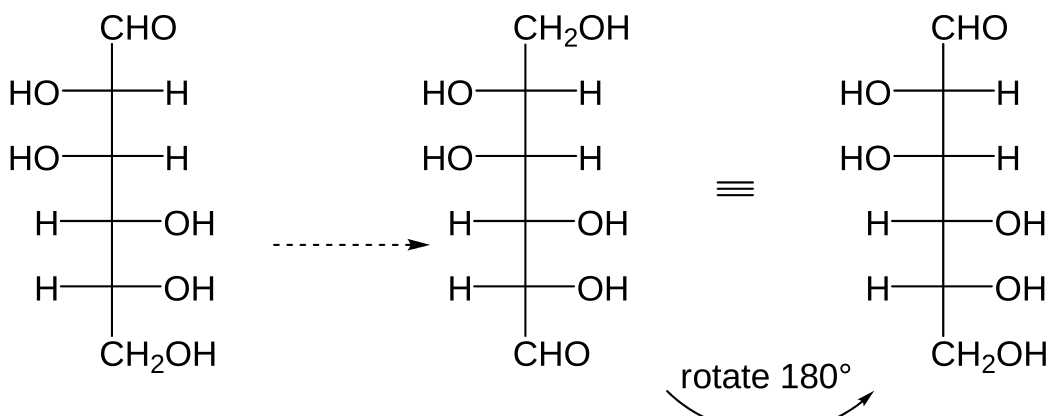

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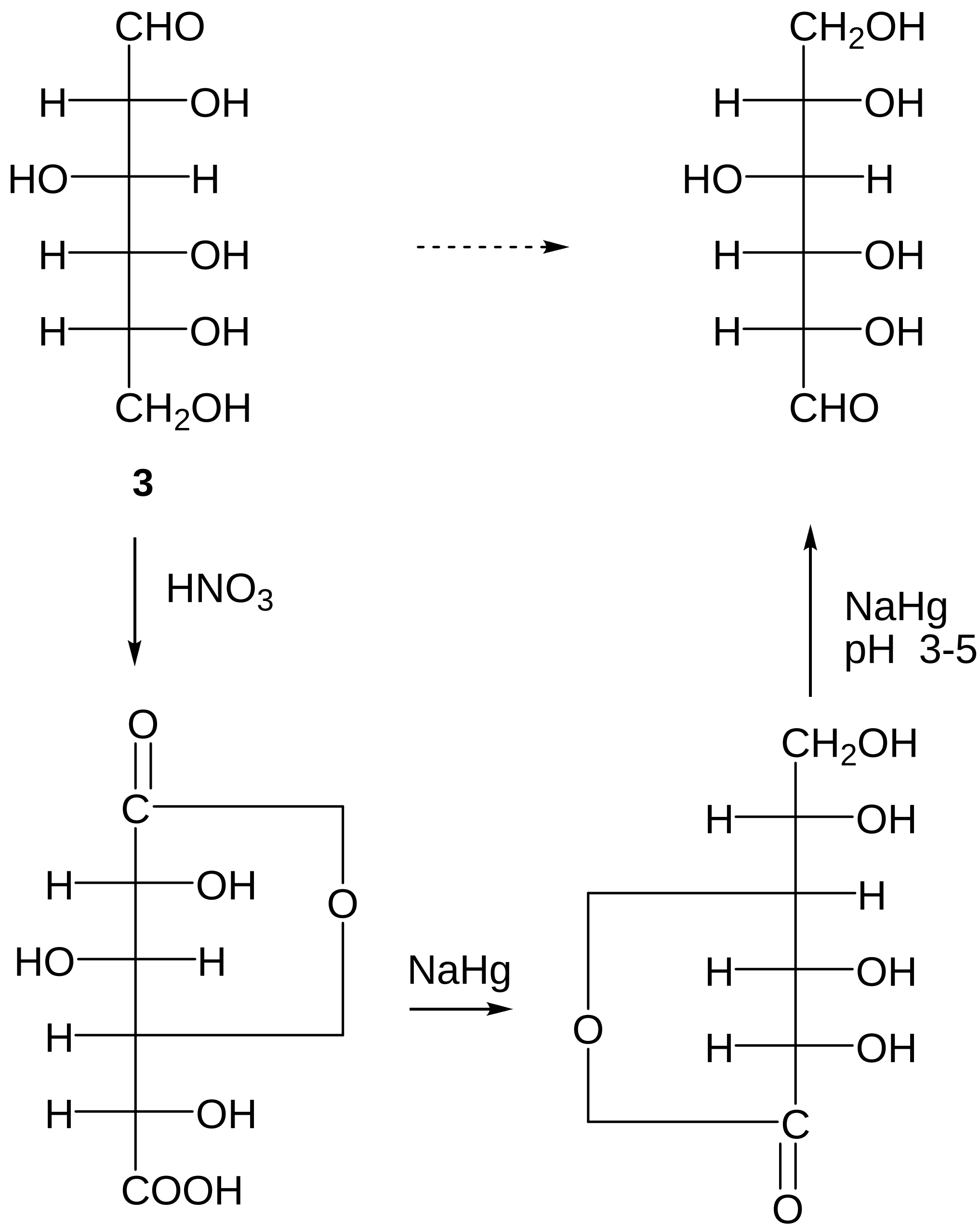
In compound **3**, C-1/C-6 interchange gives a different aldohexose.

In compound **4**, C-1/C-6 interchange gives the same aldohexose.

Fischer applied his method to glucose and discovered that a different aldohexose was produced, therefore structure **3** was glucose, structure **4** was mannose.

How did Fischer interchange two ends of an aldohexose?



Ruff Degradation: