KJM3200/KJM4200, spring 2007

Problem set 4 (for discussion on May 23, 2007)

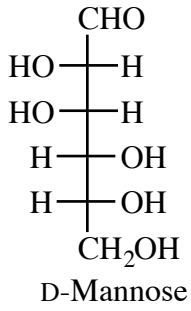
Exercise 1

a) D-mannose is shown below

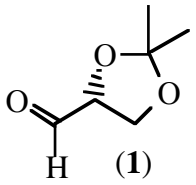
i) D-Mannose is an aldohexose. Explain.

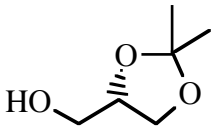
ii) Draw L-mannose.

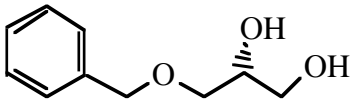
iii) D-Mannose can exist as both α- and β-D-mannopyranose. Draw the β-form.

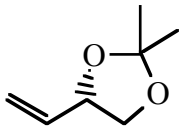


D-Mannose


(**1**)

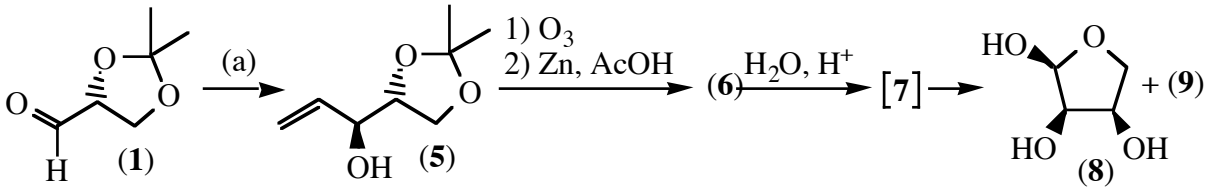

(**2**)


(**3**)


(**4**)

b) The chiral aldehyde **1** can be synthesized from D-mannose. How can compounds **2** – **4** be synthesized from **1**? (Show also synthetic intermediates)

c) Compound **8** is available from **1**. Show reagents used in (a) and the structures of intermediates **6** and **7**. Compound **7** is not a stable intermediate and will go directly to **8** and **9** under these reaction conditions. **9** is an isomer of **8**. Show structure of **9**, What kind of isomers are **8** and **9**? In the first step, the yield of **5** is modest. An other compound with the same molecular formula as **5** is formed in almost equal amounts, explain.



(**1**) (**5**) (**6**) (**8**)

Exercise 2

Draw a Fisher projection of (2*R*,3*S*,4*R*,5*S*,6*S*)-2,3,4,5,6,7-hexahydroxyheptanal. Is this a D- or L sugar? The hexose is subjected to a Wohl degradation. Suggest a mechanism for the reaction and draw the Fisher projection of the product. What will be the more stable chair conformation of the pyranose form of the product? What will be the major pyranose anomer? Finally, suggest a way to protect all the hydroxy groups of the product. How can the protecting groups be easily removed again?

Exercise 3

Propose a synthesis of racemic phenylalanin (Phe) from benzene. Show how the dipeptide Phe-Gly could be made using appropriate protecting groups and reagents.

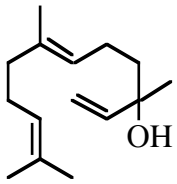
Exercise 4 (Try to answer the question without looking up the structure of γ-bisabolen)

a) The natural product γ-bisabolen has the molecular formula $C_{15}H_{24}$. Catalytical hydrogentation (H_2-gas, Pt-cat., AcOH) of γ-bisabolen gives comp. **A** ($C_{15}H_{30}$). How many unsaturations are there in γ-bisabolen, and how many of these are rings.

b) In cyclohexane γ-bisabolen may be reduced to **B** $C_{15}H_{28}$). Ozonolysis of **B** gives 6-methyl-2-heptanone and 4-methyl cyclohexanone. Draw **B**.

c) Ozonolysis of B followed by oxidative work up gives among other things acetone and 4-oxopentanoic acid. Formic acid is not a product. Draw possible structures of γ-bisabolen

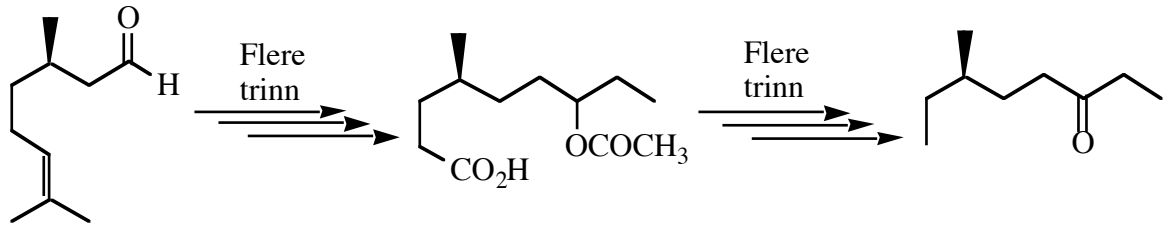
d) γ-Bisabolen can be formed from the natural product nerolidol. Suggest a mechanism and the structure for γ-bisabolen



Nerolidol

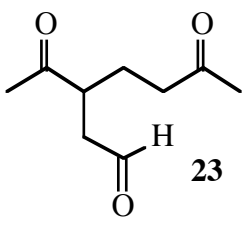
Exercise 5 (Try to answer the question without looking up the structure of limonene)

a) The natural product (+) citronellal has been used in the synthesis of the pheromone **22**. Explain how (+) citronellal can be converted to the intermediate **21**.



(+) Citronellal **21** **22**

b) The molecular formula of limonene is $C_{10}H_{16}$. When limonene is reacted with H2-gas in the presence of a Pt-catalyst a compound with the molecular formula $C_{10}H_{20}$is formed. Ozonolysis of racemic limonene followed by treatment with Zn/AcOH, gives compounds **23** and **24**. 1H NMR of limonene shows 3 vinylic hydrogens. One of these is not coupling with any of the other vinylic hydrogens, but with hydrogens in the alkyl-area. Show possible structures of limonene



23

CH_2O

24

e) (±) Limonene can be synthesized by a reaction between 3-buten-2-one and a diene followed by a Wittig reaction. Explain.

Exercise 6

Peptide **X** is widely distributed in the body. You have the following information about **X**:

- Vigorous acidic hydrolysis gives Arg, Glu (2), Gly, Leu, Lys. Met, Phe (2), Pro (2)
- Enzymatic hydrolysis gives Arg, Gln (2), Gly, Leu, Lys. Met, Phe (2), Pro (2)
- When **X** is treated with phenylisothiocyanate, phenylthiohydantoins derived from Arg, Pro, Lys and Pro can be obtained in that order
- Incubation of **X** with chymotrypsin gives peptides **A** and **B**.
- Peptide **A** contains Arg, Gln (2), Lys, Phe, Pro (2). Degradation with Edmans reagent gives the same phenylthiohydantoins derived from intact **X**. Carboxypeptidase releases first Phe, then Gln
- Peptide B reacts with phenylisothiocyanate to give phenylthiohydantoins derived from Phe,Gly and Leu in that order
- Peptide **X** is strongly basic, pI above 8.9. No amino acids are released when **X** is incubated with carboxypeptidase.
- If **X** is treated with 0.03 M HCL at 110 ºC, for 8-12 h (a method that cleaves carboxylic acid amides bonds but leave most peptide bonds untouched) peptide **C** is formed. Peptide C reacts with carboxypeptidase to give Gly, Met, Leu and Phe. The order in which these AA were released is not known

a) What is the N-terminal AA in **X**?
b) What is the C-terminal AA in **X**?
c) What is the sequence of AAs in peptide **A**?
d) What is the sequence of AAs in peptide **B**?
e) What is the complete structure of peptide **B**?
f) What is the sequence of AAs in peptide **C**?
g) What is the structure of **X**?