Ring Synthesis and Carbohydrates

Reading: Your lecture notes should be very useful for this topic. All the main texts carry a decent section on this aspect of organic chemistry, particularly Carey & Sundberg, Clayden and March and the following:

i) Martin Grossel, "Alicyclic Chemistry", Oxford Chemistry Primer No 54.

ii) McQuillan and Baird, "Alicyclic Chemistry" (Cambridge University Press, 2nd Edition)

iii) Davis and Fairbanks, “Carbohydrate Chemistry” Oxford Chemistry Primer No 99

Topics for notes:

Ring Synthesis

Make a brief summary of the possible synthetic approaches to cyclic systems. Make sure that you can draw mechanisms where needed.

i) Cyclopropanes

e.g. Carbene addition, sulfur ylides, Simmons-Smith, alkylations.

ii) Cyclobutanes

e.g. Thermal/photochemical [2+2] cycloaddition, malonic ester synthesis, ring expansion.

iii) Cyclopentanes, cyclohexanes and cycloheptenes.

e.g. Diels Alder, Birch reduction, Robinson ring annelation, cycloadditions. Ring closure reactions e.g. Thorpe-Ziegler, Dieckmann (and Claisen) condensations, acyloin (and TMSCI modification), alkylations, radical cyclisations etc.

iv) Medium (7-12) and Large Rings (>12)

e.g. Acyloin reaction, use of ring expansion and fragmentation reactions, metal template: eg Nickel(II) for cyclooctatetraene, and butadiene oligomerisations to give cyclooctadiene and cyclodecatriene.

v) Ring Expansion and Contraction and Ring Cleavage Reactions.

e.g. Ring enlargements: diazomethane on ketone, cycloaddition and electrocyclic ring opening of the bicyclic adducts. Ring contractions: Favorskii, Ramberg Buckland, Wolff rearrangement of diazoketones. Ring cleavages of bicyclic compounds: synthesis of cyclodecane derivatives by cleavage of central bonds in decalin systems.

Reactions: effect of ring size on rates and positions of equilibria; strain in rings and the consequences in reactions, e.g. ring opening of 3 and 4 membered rings; opening of cyclopropanes (anionic) cyclopropyl and cyclobutyl halides to allyl and homoallyl ions (cationic). Ease of cyclisation (of acyclics) vs. ring size (enthalpy / entropy / yield); Baldwin’s rules. Transannular reactions; ring opening and closing reactions such as the reverse Claisen and Aldol reactions.

Carbohydrates

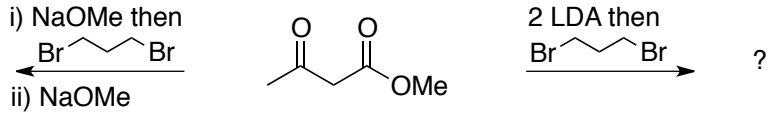
Structure: Cyclic and acyclic forms, equilibrium between these. The anomeric effect, mutarotation.

Reactions: Protection and selective functionalisation of the different hydroxyl groups. This part of the tutorial mostly concentrates on the chemistry of acetals and related functional groups, and on recognising that much of this is about how to protect an alcohol, diol or an aldehyde. This is a good introduction to protecting group chemistry. For any protecting group situation - How do you put it on? Will it stay on? What is it stable to? How do you get it off? The answer to most of these involve acid, base, oxidation and reduction.

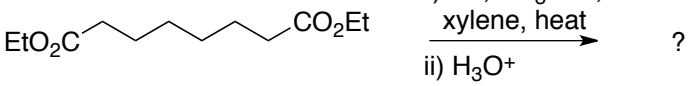
Further reactions at the anomeric centre, NGP effects, Fischer glycosidation. Be aware of examples of umpolung chemistry using the equivalent of formaldehyde anion as nucleophile [to ascend] and leaving group [to come down the series].

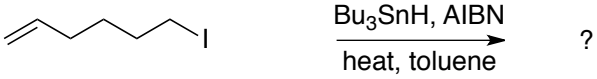
Tutorial Problems

1. Predict products, and provide mechanisms for the following reactions:

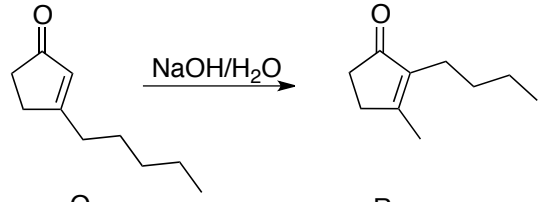
a) ? 

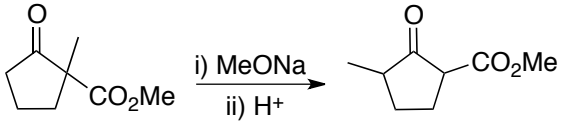
b) 

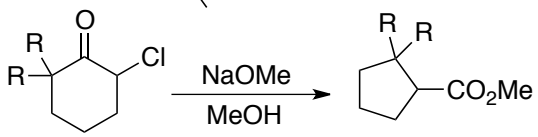
c) 

d) 

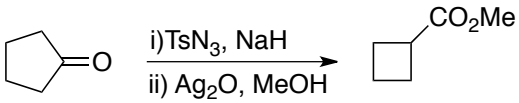
2. Provide mechanisms for the following transformations

a) 

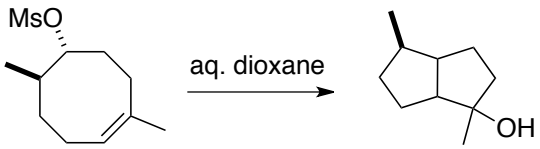
b) 

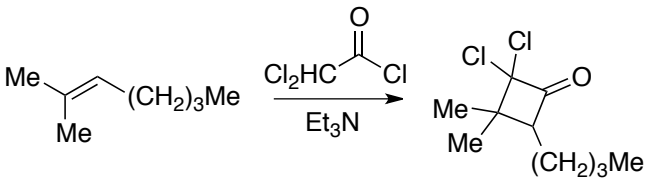
c) 

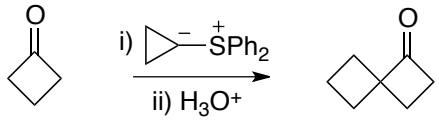
R = H, Me

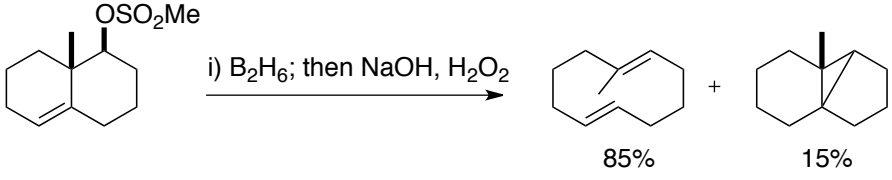
d) 

e) 

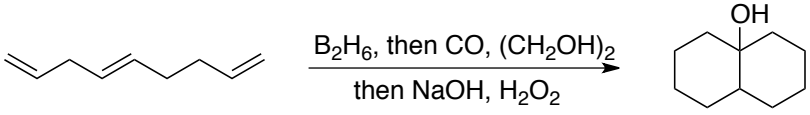
f) 

g) 

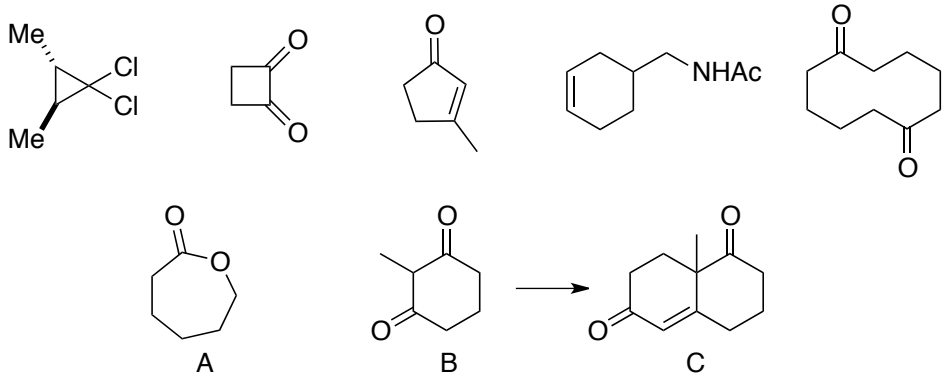
h) 

i) 

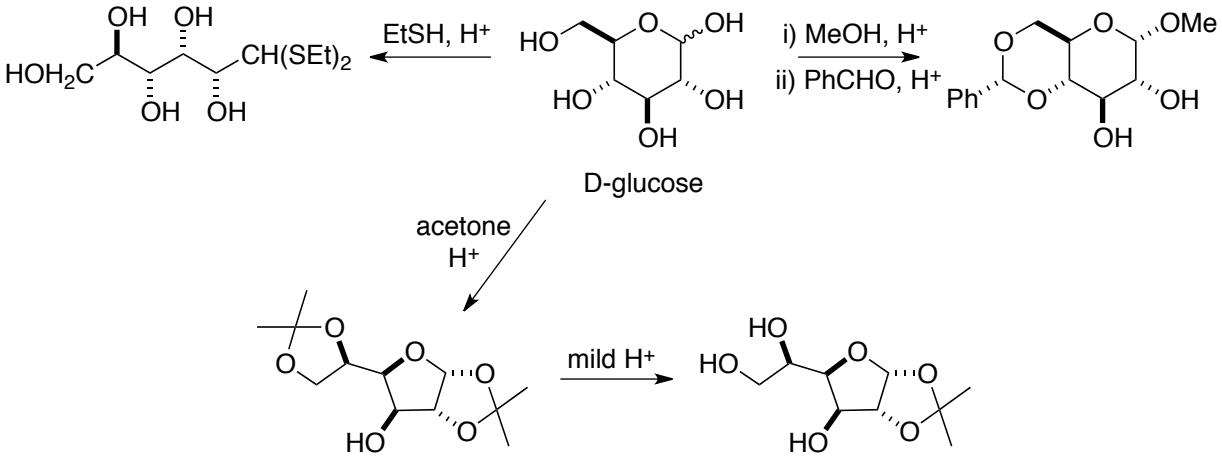
85% 15%

j) 

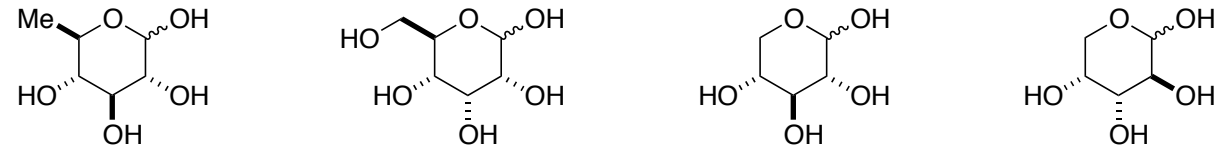
3. a) Suggest syntheses for the following 5 compounds (you can use either acyclic or aromatic starting materials). b) Suggest a synthesis of **A** from cyclohexanone and a synthesis of **C** from **B**.



4. a) Explain with mechanistic reasoning the following reactions of D-glucose:

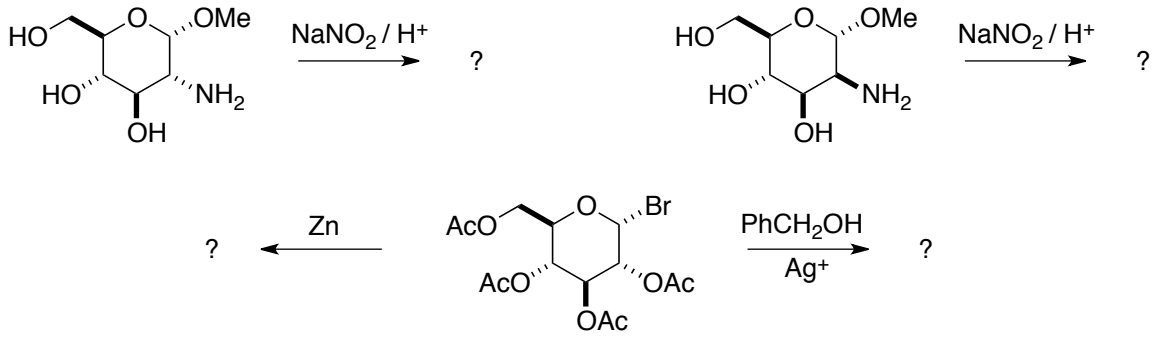


b) Considering the protecting strategies in part a) suggest syntheses of the following compounds from D-glucose:



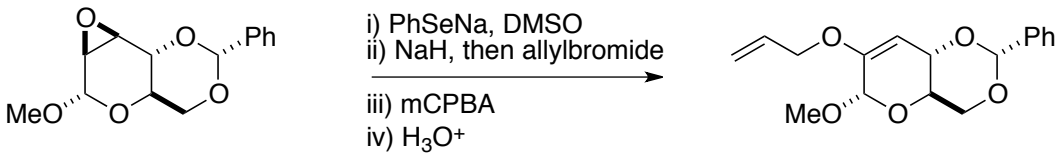
6-deoxy-D-glucose D-allose D-xylose D-arabinose

c) Identify the products of the following reactions:

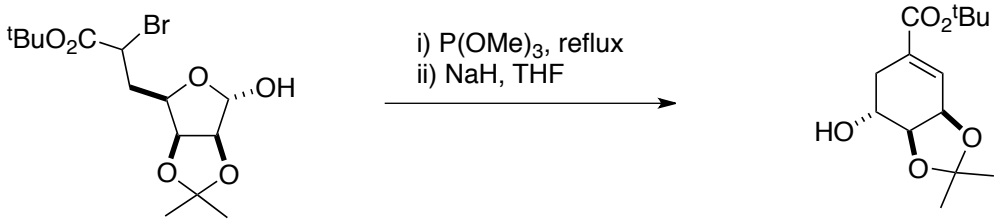


5. Give mechanisms for the following transformations:

a)



b)



c)