Stereochemistry Part I – Monday Problem Questions 03.11.08

This first set of problem questions aims to recap some of the basics of nomentclature, terminology, techniques to view and physical effects involved in the stereochemical problems observed in organic synthesis.

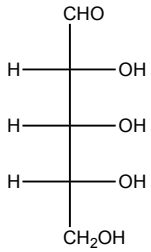
1. Nomenclature –

a) Give a one-line definition of –

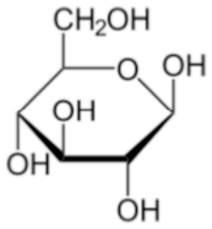
(i) Diastereoisomerism
(ii) Enantioisomerism

b) Using a suitable example, display the R- and S- nomenclature for stereoisomers.

c) Below is the Fischer projection of acyclic sugar ribose and cyclic hexose sugar β-D-glucopyranose.



ribose

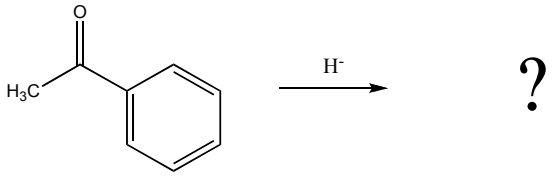


β-D-glucopyranose

(i) Which stereoisomer of ribose is this?
(ii) Using the sawhorse projection, convert this Fischer projection to the corresponding Natta projection and assign all stereocentres.
(iii) How many stereomers of ribose are there and what are there names?
(iv) What do the prefixes threo- and eryhtro- describe and can you draw the structure of the sugars of the same name?
(v) Draw β-D-glucopyranose in its conventional 3-D form and assign each stereocentre.

d) In the reduction of acetophenone, displayed below, there are two possible products.

(i) Using Re and Si nomenclature assign which face of approach gives which enantiomeric product.



2. Conformation-

a) Butane-

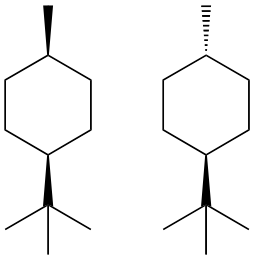
(i)Draw all possible conformations of butane and correlate these to the corresponding relative energy profile.
(ii) Label each conformation with the terms shown below –

- anticlinal
- synclinal
- gauche
- syn-periplanar
- anti-periplanar

b) Cyclohexane –

(i) Draw the Newman projection of cyclohexane.

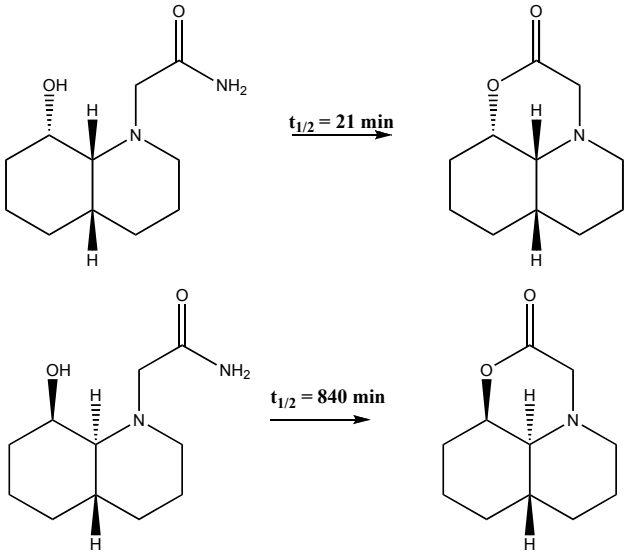
(ii) Draw the Natta projection of the di-substituted systems below; which conformation do these systems lie in?



c) Decalin-

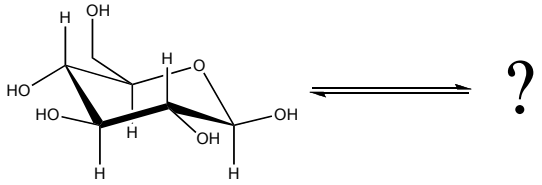
(i) Draw cis and trans fused decalin systems.

(ii) Explain the difference in rate observed in the amide cleavage reactions displayed below.



d) Anomeric Effect-

(i) β-D-glucopyranose, shown above and below, exists in another epimeric form.

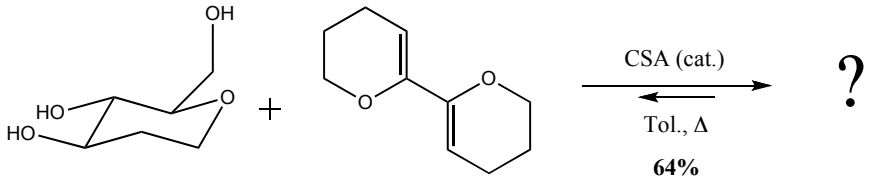


(ii) What is the other form?

(iii) What is an epimer?

(iv) The other epimeric form is a special type of epimer, what is it called and what is the interconversion process called?
(v) In aqueous solution this interconversion happens readily, estimate the ratio of epimers and justify for estimation.

(v) The anomeric effect can be held responsible for the selective protection of di-equitorial 1,2-diols, as present in the process below. What are the possible diastereomeric products and which is the only product formed in physical practice?

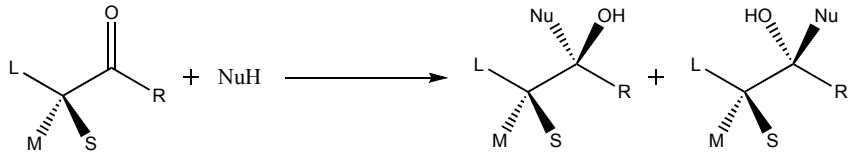


Stereochemistry Part II – Monday Problem Questions 16.11.09

These final questions aim to introduce a final couple of reactivity models and the investigate some key stereoselective steps from natural product synthesis.

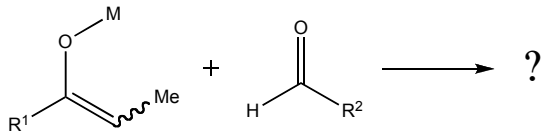
1. Asymmetric Induction –

Using the model reaction below to describe the Cram and Felkin-Ahn models for nucleophilic addition to aldehydes and ketones and explain which is the major diastereomer formed.

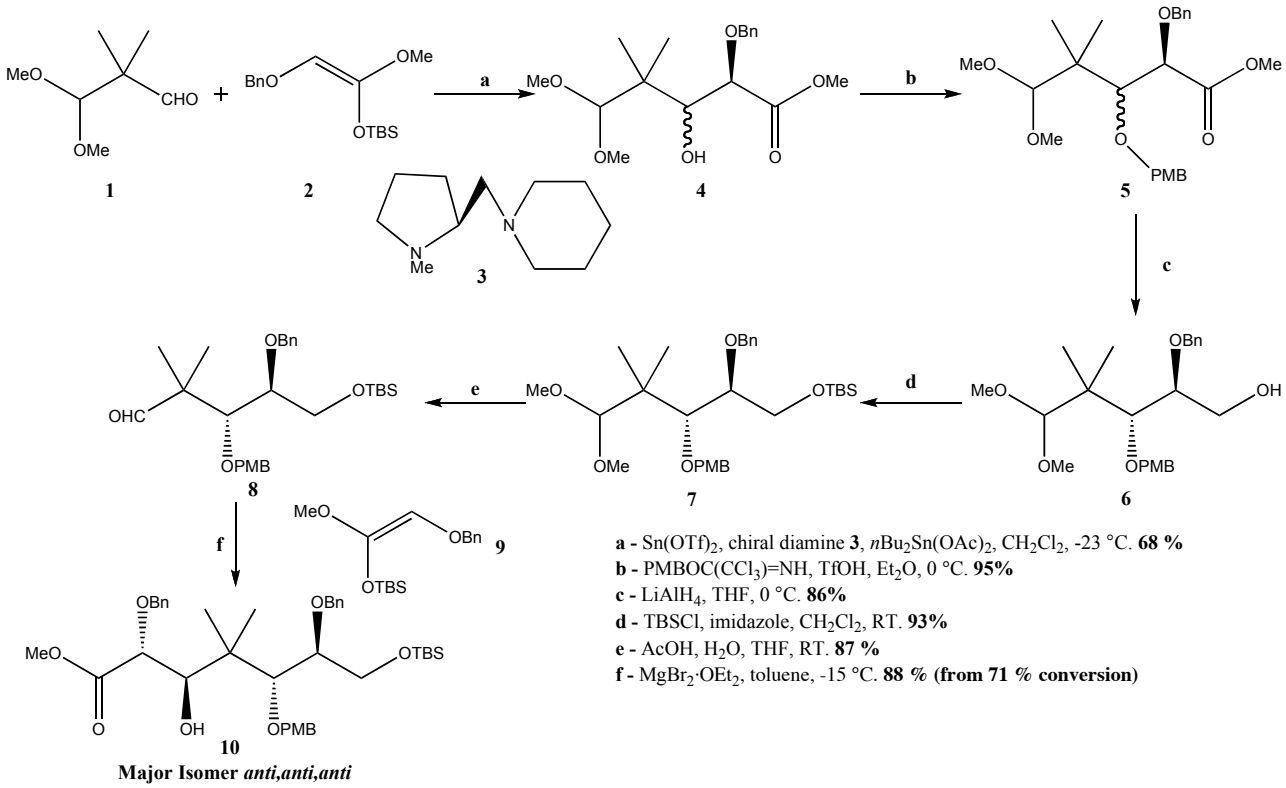


2. Aldol Reaction –

(a) Illustrate all possible transitions states and therefore predict the major products of the model aldol reaction below.



(b) Below is a short section from Mukaiyama's synthesis of Taxol.



(i) Give reaction mechanisms for steps a-f

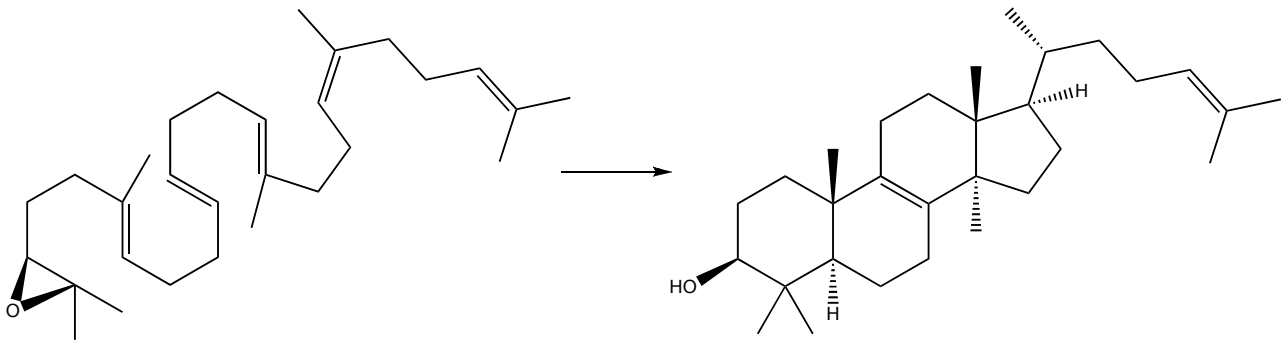
and

(ii) Predict the major stereoisomer of Aldol reaction product **5**.

(iii) Explain the 81(anti,anti,anti):19(syn,anti,anti) ratio of Mukaiyama-Aldol reaction product **10** including why the other 2 steroisomers where not observed.

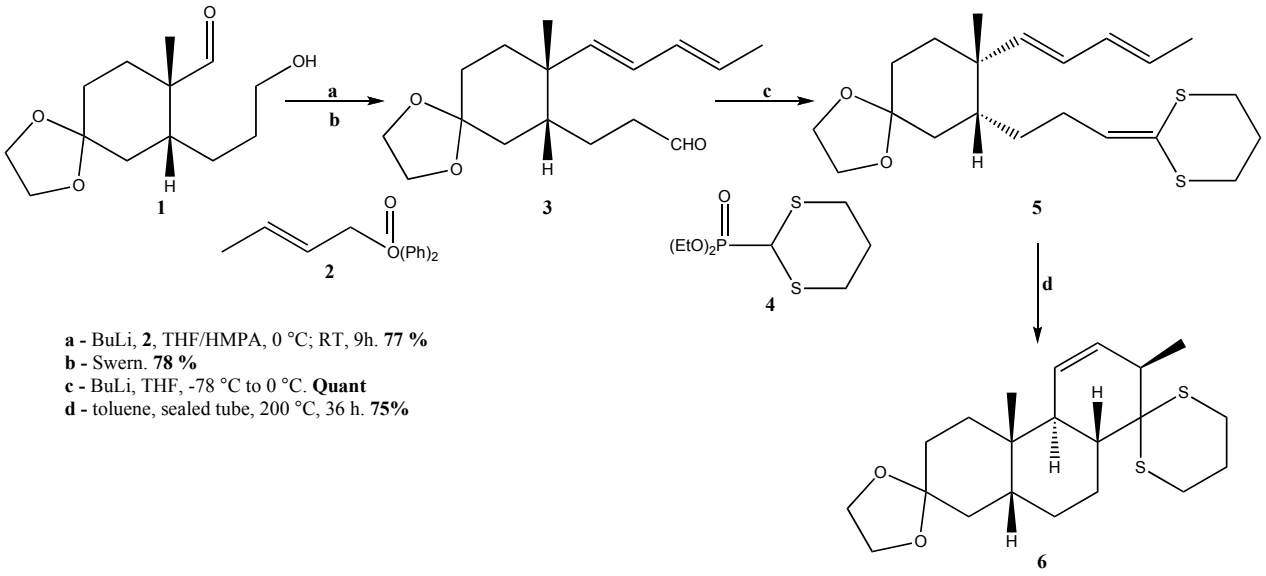
3. Biosynthesis –

Draw the cyclic transitions states for the biosynthetic transformation of 2,3-oxidosqualene to lanosterol to justify the observed sterochemistry observed in the steroid product (shown below).



4. Diels-Alder Reaction –

In Stork's synthesis of (+)-Digitoxin (1996) he uses a intramolecular Diels-Alder reaction a the key steroid core forming step (Below).



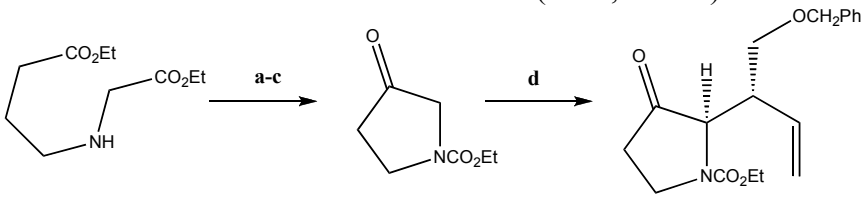
a - BuLi, **2**, THF/HMPA, 0 °C; RT, 9h. **77 %**
b - Swern. **78 %**
c - BuLi, THF, -78 °C to 0 °C. **Quant**
d - toluene, sealed tube, 200 °C, 36 h. **75%**

(i) Give reactions mechanisms for steps **a-d**.
(ii) Illustrate the cyclic transition state in the [4+2] cycloaddition to form **6**.

5. Rearrangements –

(a) [3,3] sigmatropic rearrangement

Oshawa et al. used the [3,3]sigmatropic rearrangement as a key step in the synthesis of the pyrrolizidine skeleton of Retronecine and Turneforcedine (1983, Below).



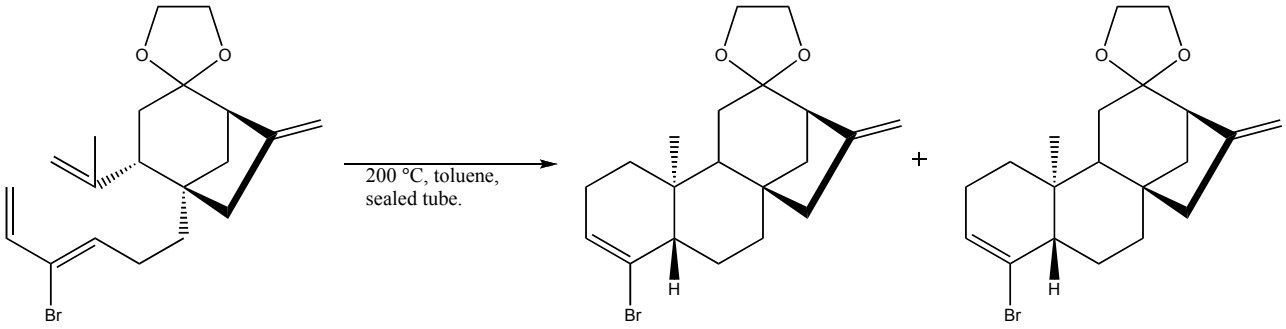
a - $ClCO_2Et$, K_2CO_3, $CHCl_3$.
b - NaOEt, benzene.
c - 10 % H_2SO_4, EtOH. **59 % over 3 steps**
d - allyl alcohol, CSA, xylene, Na_2SO_4, Δ, 20 h. **86 % (Based on 27 % conversion)**

(a) Give reaction mechanisms for steps a-d.
(b) Draw the transition state for the rearrangement which leads to production of **3** with total regio- and stereo- control.

AND FINALLY!!!

(b) Cope rearrangment

Toyota *et al.* used a Cope variant as the key stereocentre forming step in the synthesis of diterpenoid 'Methyl Atis-16-en-19-oate (Below).



(i) Draw the transition state for both products and justify which was the major isomer observed by the big man Toyota himself.