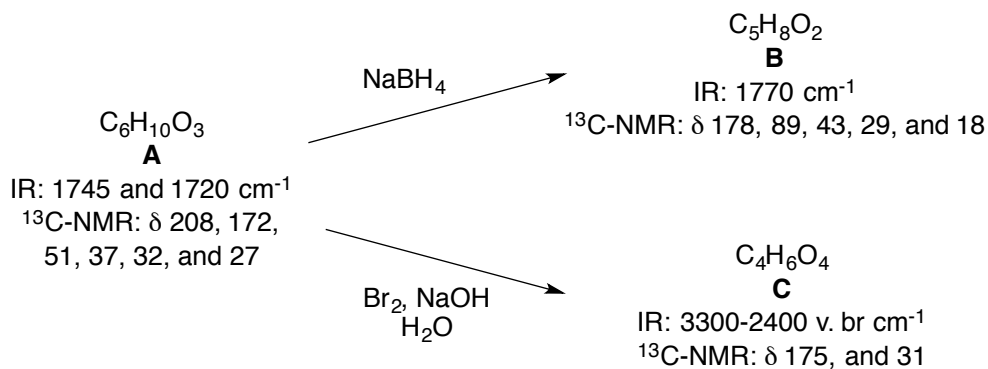


Renaud Group Exercise Set

Prepared by Nick Tappin
08/07/16

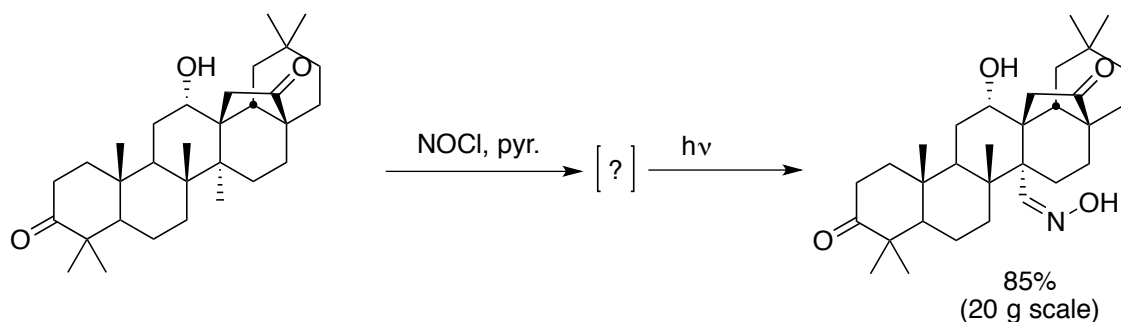
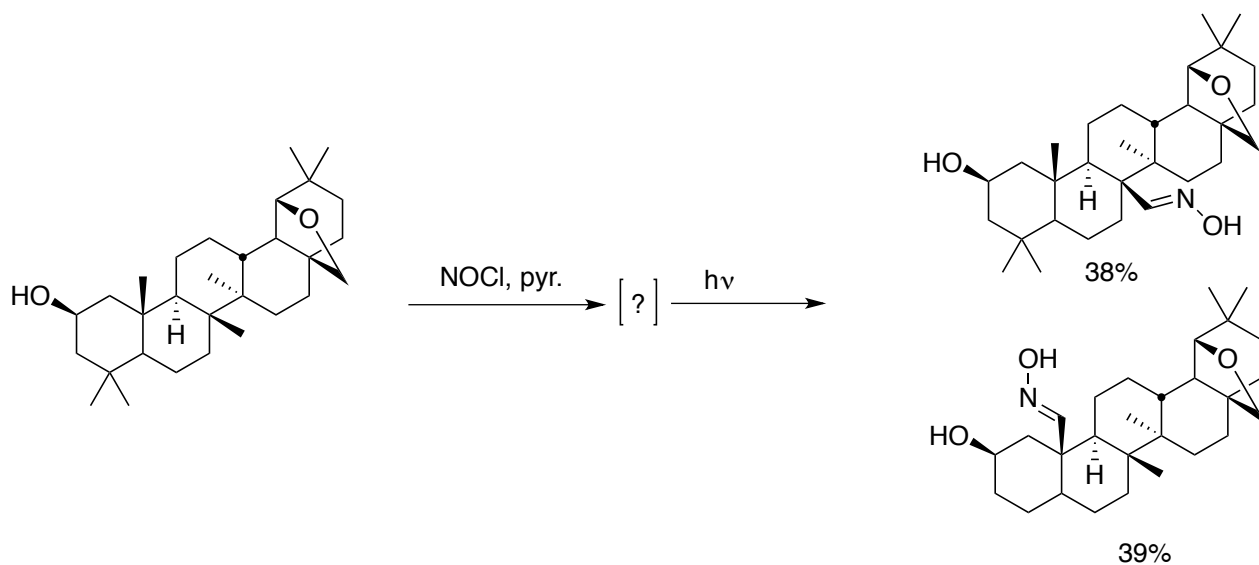
Spectroscopy

1. Deduce the structures for compounds **A**, **B**, and **C**



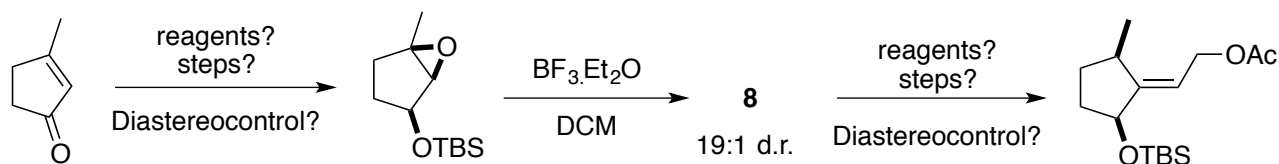
Mechanism

2. Propose a structure for the missing intermediates and rationalize the outcomes by use of mechanism. *Hint: draw the structures in 3-D.*



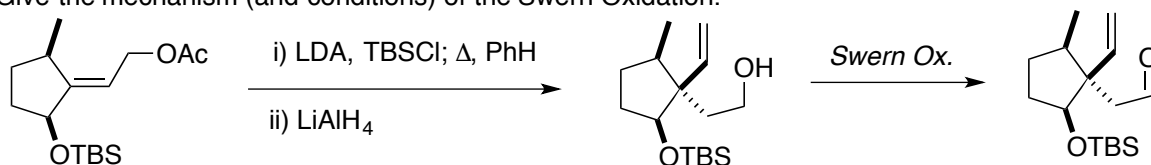
Synthesis

- Suggest how to effect the transformation from the methyl cyclopentenone to the epoxide.
- Propose missing compound **8**. Can you suggest a why one diastereoisomer is major?
- Suggest how to effect the transformation from **8** to the allylic acetate, rationalizing *E/Z* control.

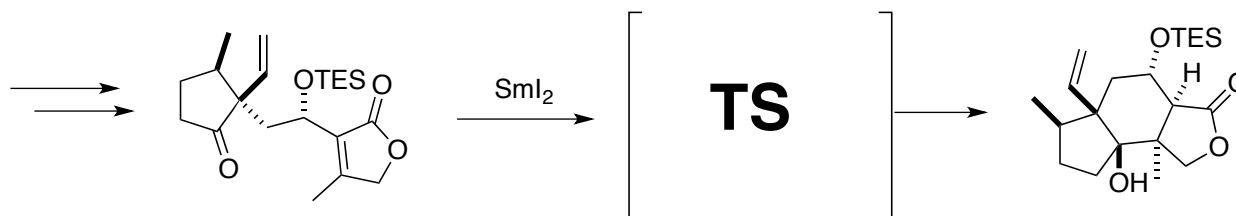


Mechanism

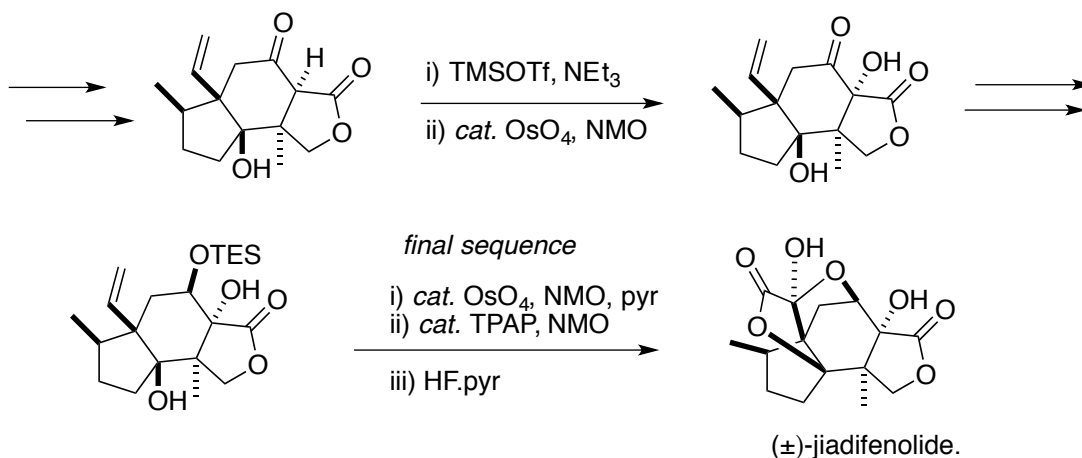
- Propose a mechanism from the allylic acetate to the β -vinyl carboxylic acid. Name this reaction. Rationalize the stereochemical outcome.
- Give the mechanism (and conditions) of the Swern Oxidation.



- Suggest a mechanism for the SmI_2 -mediated coupling. Attempt to justify the diastereoselectivity with use of a 3-D samarium-chelate TS. What could another TS look like and why does the reaction not proceed through that one?



- The synthesis of a tertiary alcohol is not always evident. Outline the hydroxylation reaction with OsO_4 briefly justifying chemoselectivity.
- Explain, with mechanisms, the final sequence to furnish the natural product (\pm)-jiadifenolide.

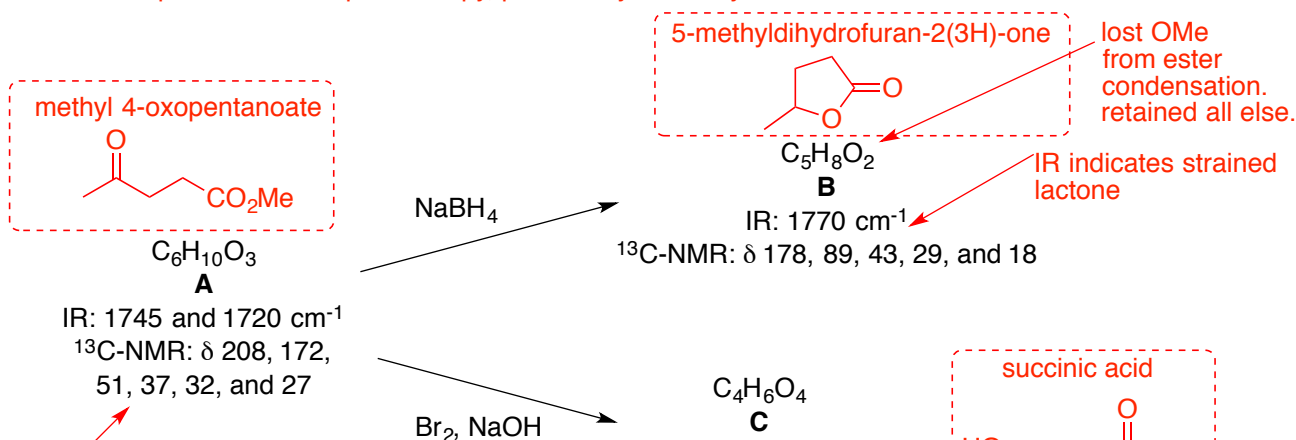


solutions

Prepared by Nick Tappin
08/07/16

Spectroscopy

Purpose: to remind/ practise some spectroscopy, particularly the utility of IR.



IR and ^{13}C indicates clearly two carbonyls, one a ketone and the other an ester (fits elemental, i.e. O_3). There are no upfield methylene shifts suggesting that all CH₂ units experience EW effect of carbonyls. Shift at 51 indicates adjacency to e-neg heteroatom.

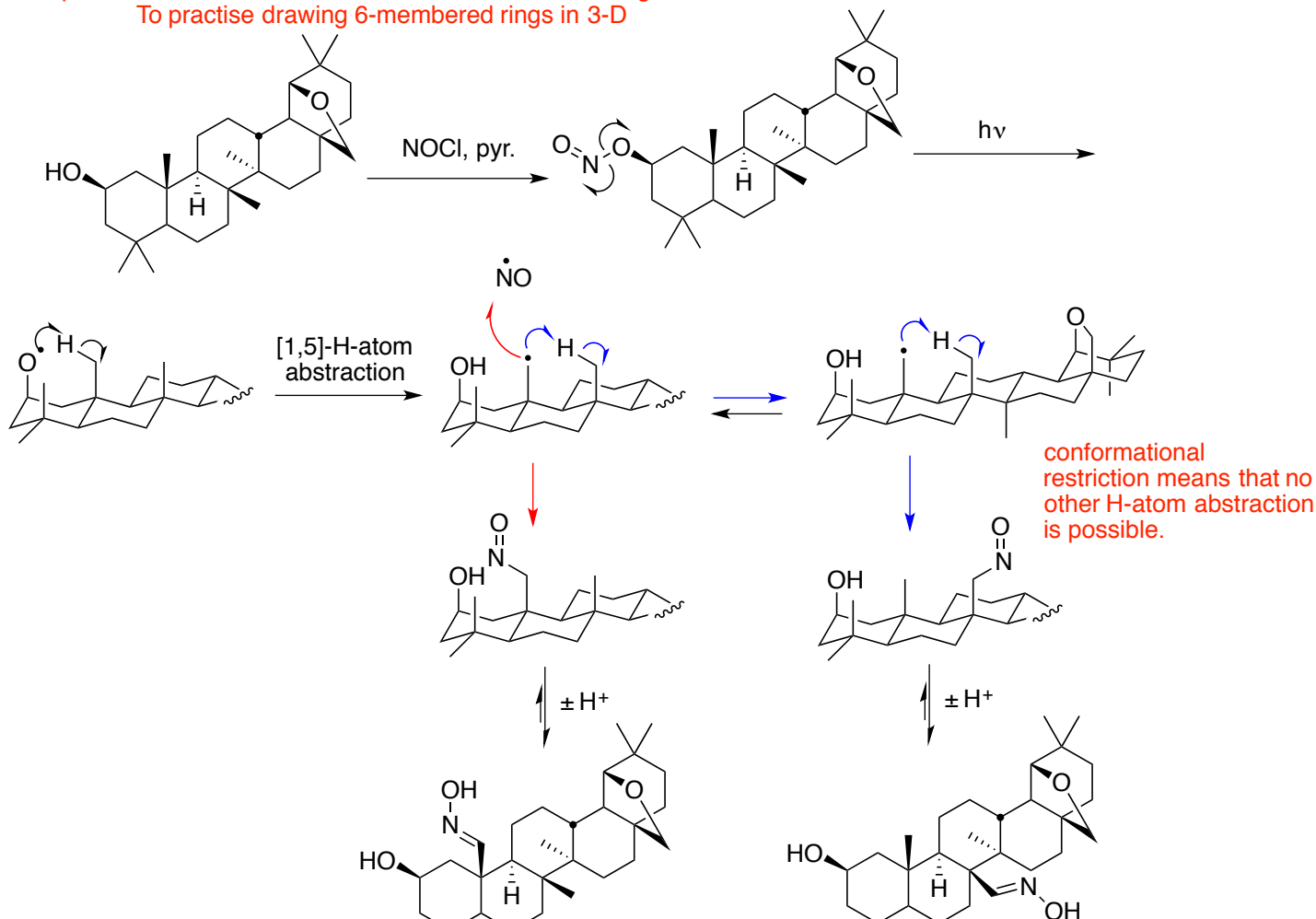
IR indicates loss of ester and ketone carbonyls and presence of a carboxylic acid. ^{13}C indicates a large gain in symmetry. One shift is a carbonyl of an ester or acid, other an α -carbonyl CH₂

adapted from pp 246, Spectroscopic methods in organic chemistry, 6th Ed., D. Williams, I. Fleming, McGraw-Hill, 2008

2. Barton Nitrile Ester Reaction

Purpose: To see another radical cascade reaction coming from the Barton lab.

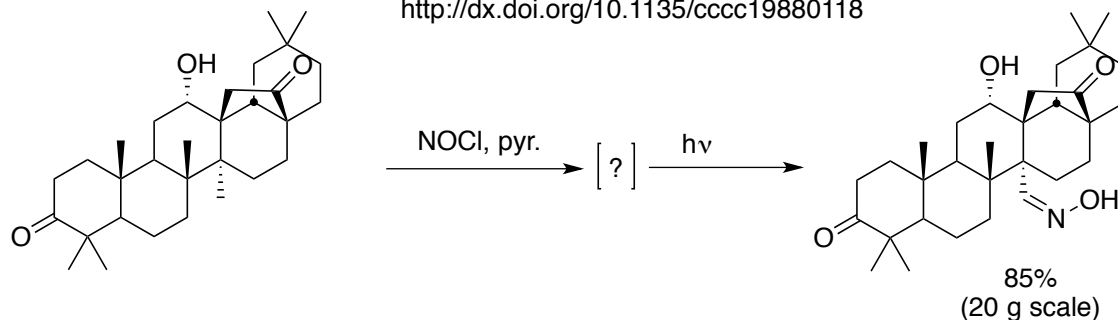
To practise drawing 6-membered rings in 3-D



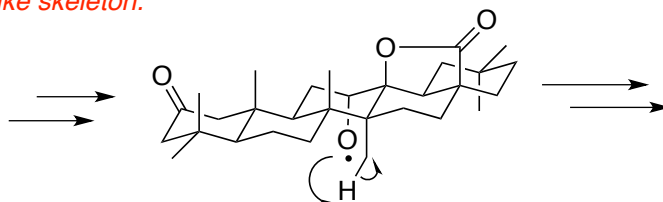


ratio of 1:1 since the reaction is fast and reversible and there is no particular stabilization of one radical or another.

Collect. Czech. Chem. Commun. 1988, 53, 118-131
<http://dx.doi.org/10.1135/cccc19880118>



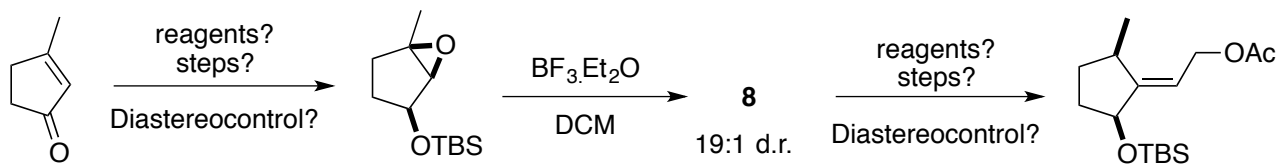
This is the same idea as above: H-atom abstraction from alkoxy radical to an axially orientated methyl group on a cholesterol-like skeleton.



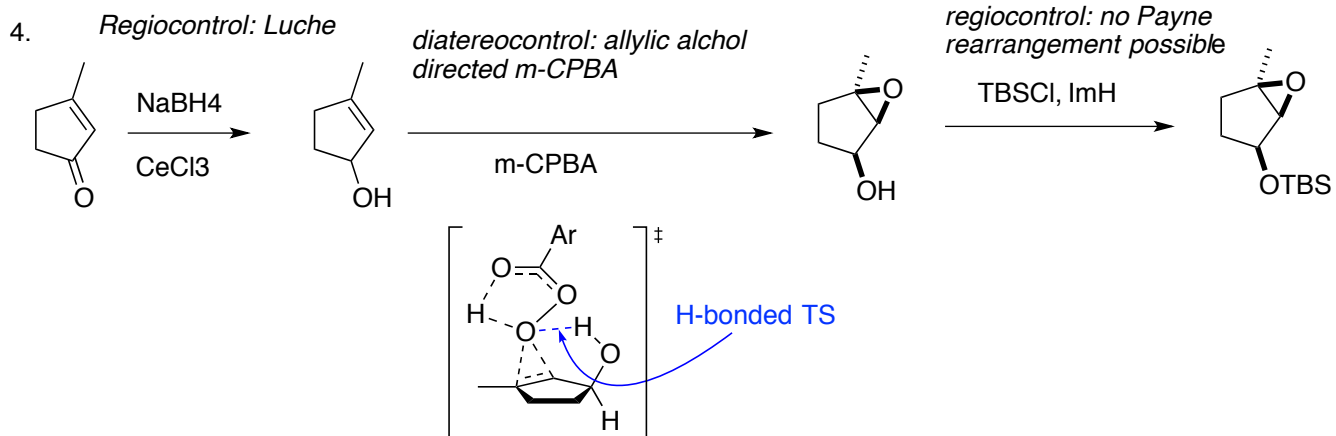
J. Org. Chem., 1997, 62 (4), pp 960–966
 DOI: 10.1021/jo9615864

Synthesis Paterson ACIE 2014, 53, 7288

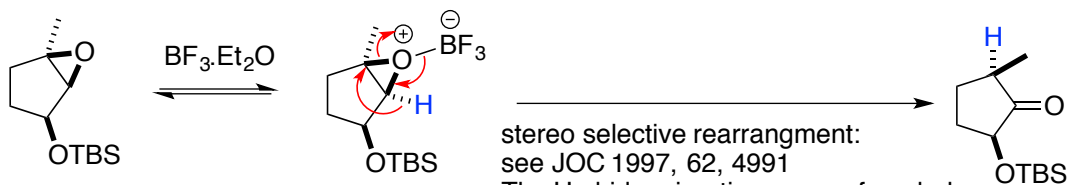
- Suggest how to effect the transformation from the methyl cyclopentenone to the epoxide.
- Propose missing compound **8**. Can you suggest a why one diastereoisomer is major?
- Suggest how to effect the transformation from **8** to the allylic acetate, rationalizing *E/Z* control.



Purpose: To think about some simple synthesis from very common SM, particularly how to control the outcomes (diastereoselective and regioselective).



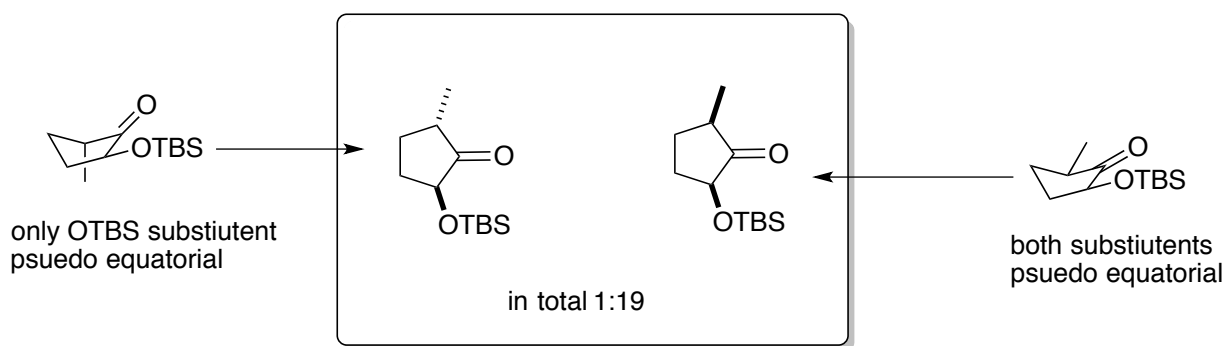
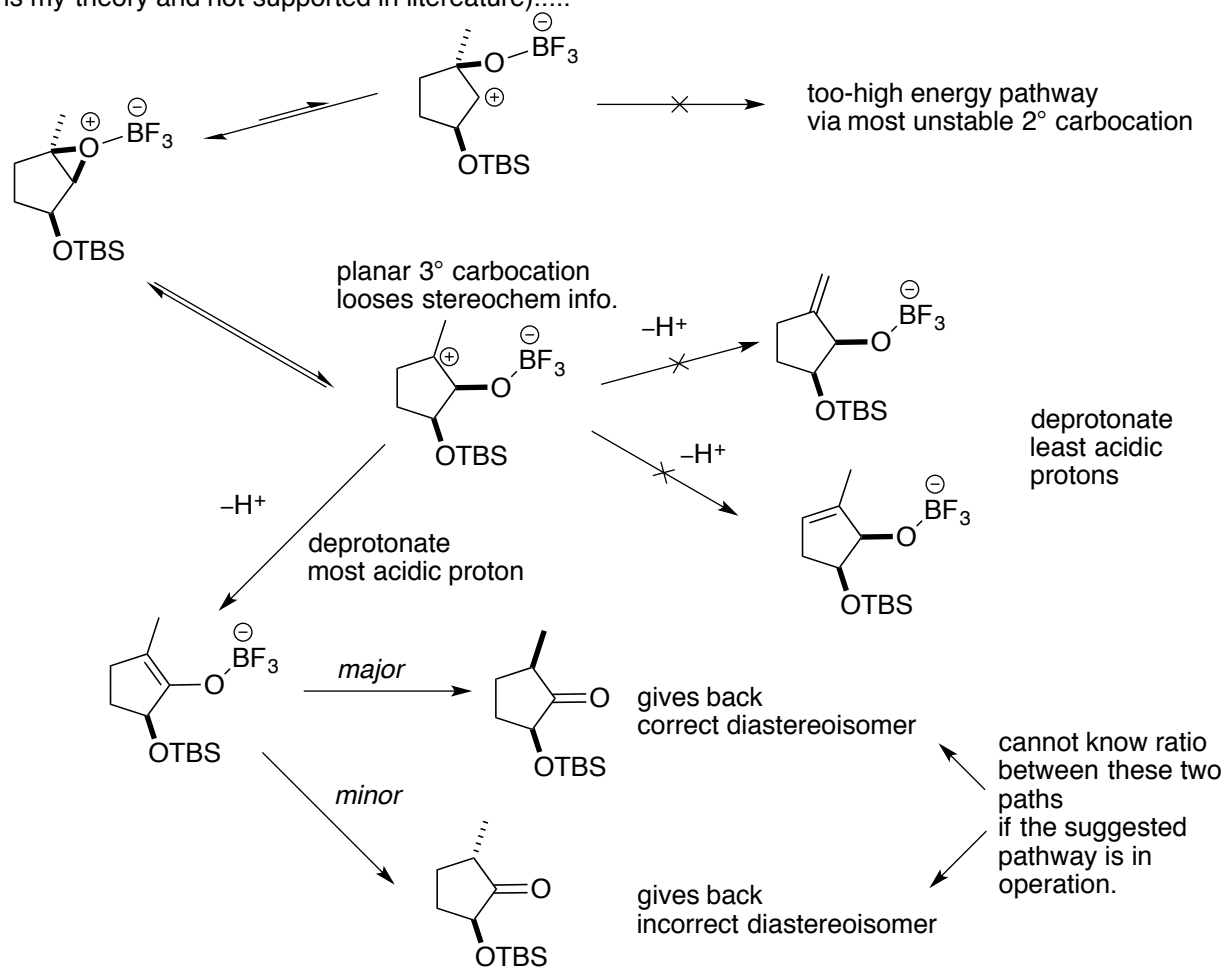
5.



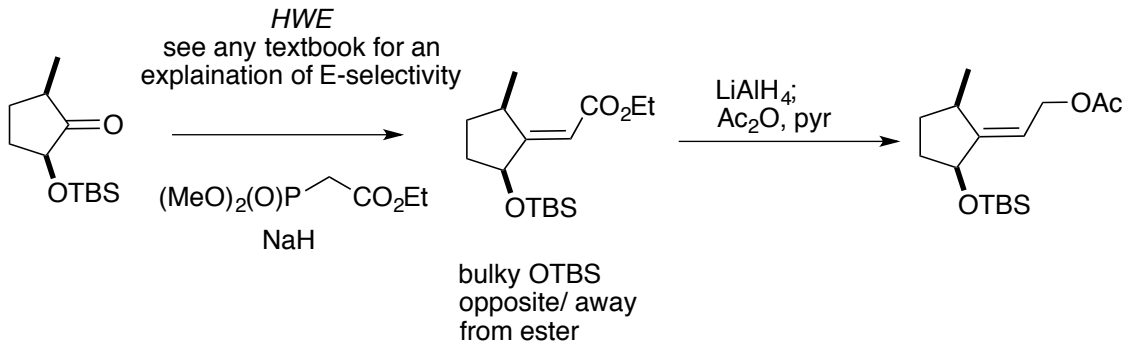
stereo selective rearrangement:
 see JOC 1997, 62, 4991
 The Hydride migration comes from below
 the epoxide, thus setting the
 stereochem at the methyl group

would be stereospecific,
 but have a d.r. 19:1
 which means a second
 pathway is in operation
 (see below)

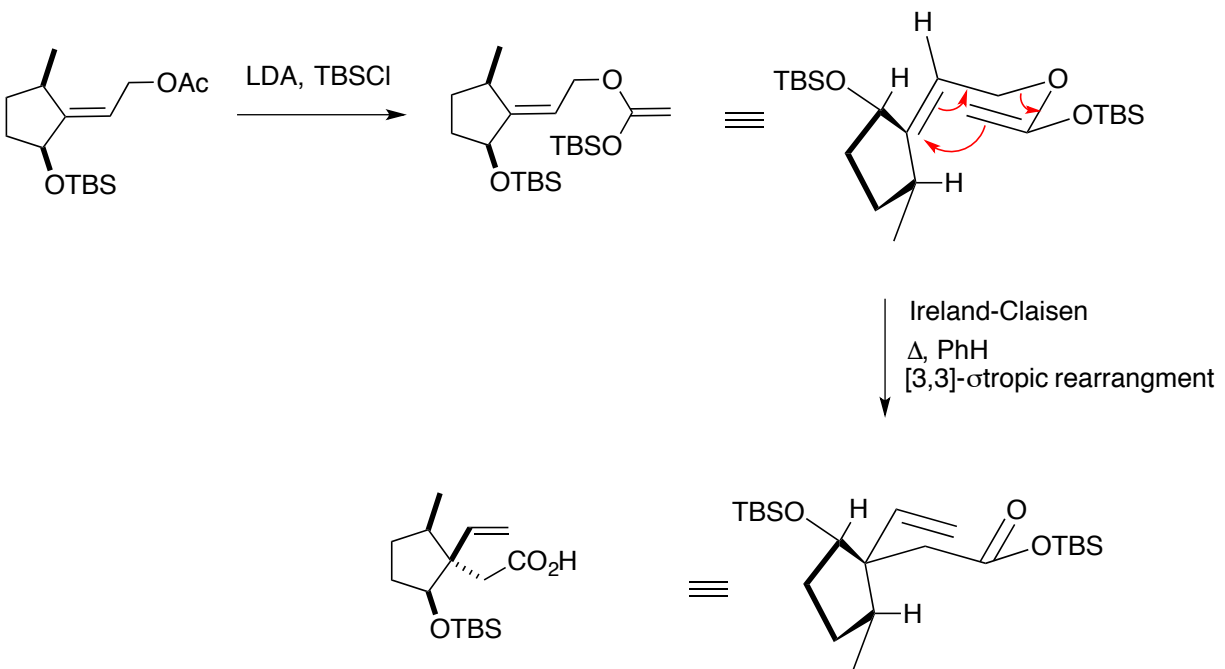
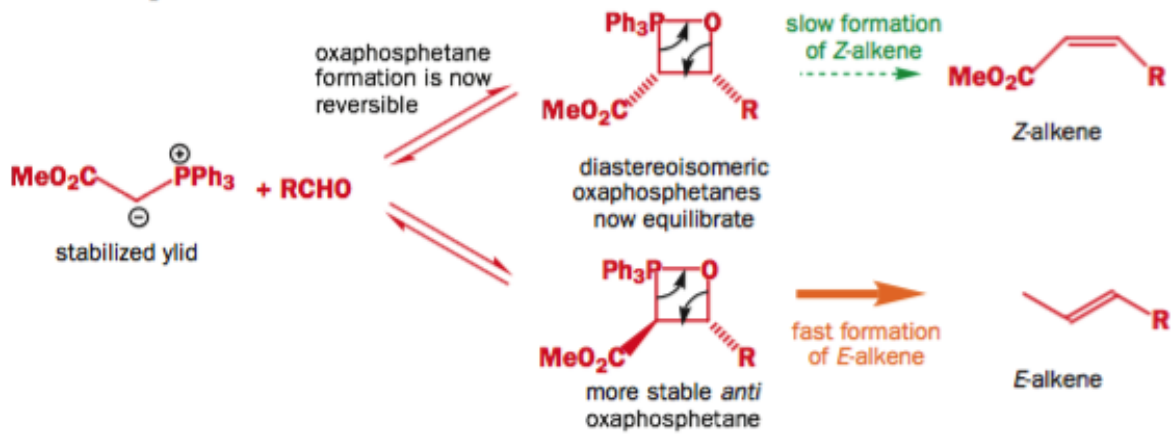
In order to explain the formation of the minor stereoisomer, or indeed to provide an alternative (possibly more likely) mechanism (this is my theory and not supported in literature).....



6.



E-alkene is produced.



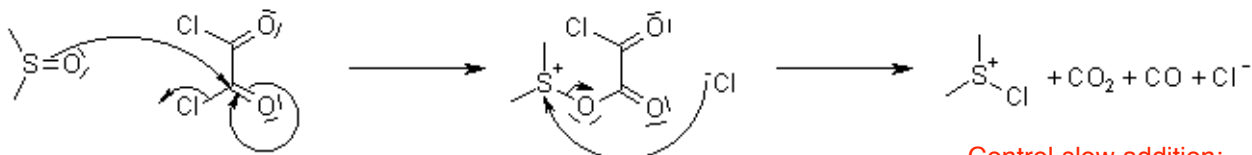
7. Swern Oxidation.

Purpose: To think more deeply about this common (and easy?) mechanism: to point out all details and how they make sense with the reaction conditions. To illustrate the pummerer rearrangement.

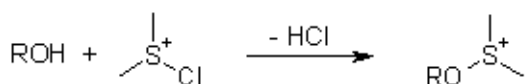
A good textbook will provide a complete mechanism.

Mechanism of the Swern Oxidation

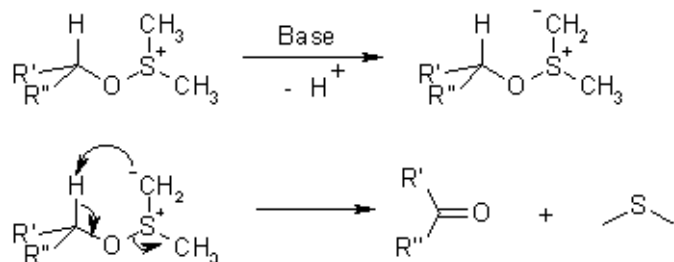
Dimethylchlorosulphonium ion is generated in situ from DMSO and oxalyl chloride.



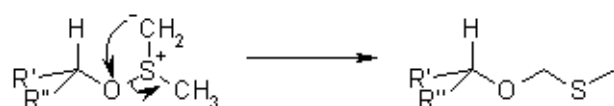
The reaction with an alcohol at -78°C leads to an alkoxysulphonium ion:



Deprotonation of this intermediate gives a sulphur ylide, which undergoes intramolecular deprotonation via a five-membered transition state to give the product and DMS (odour!):

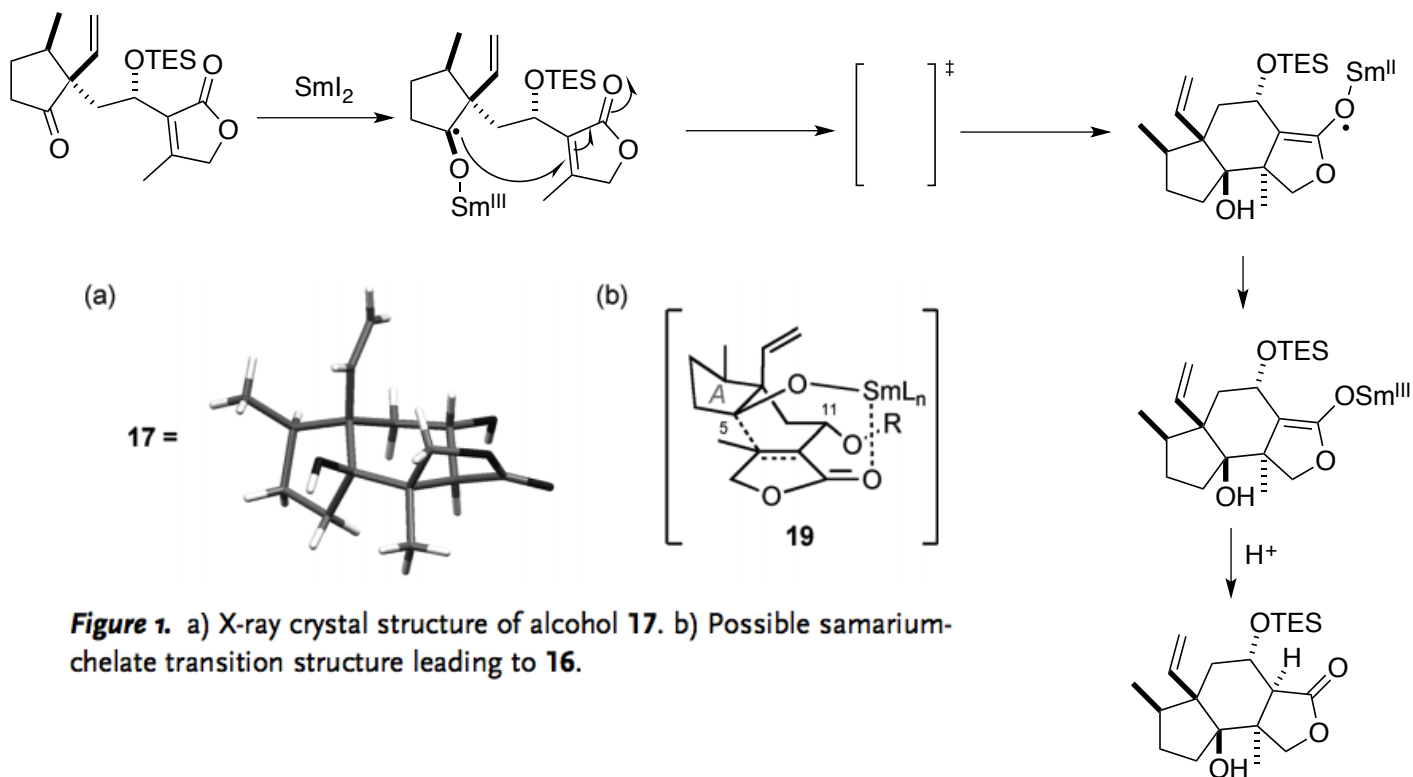


If the temperature is not kept near -78°C , mixed thioacetals may result:

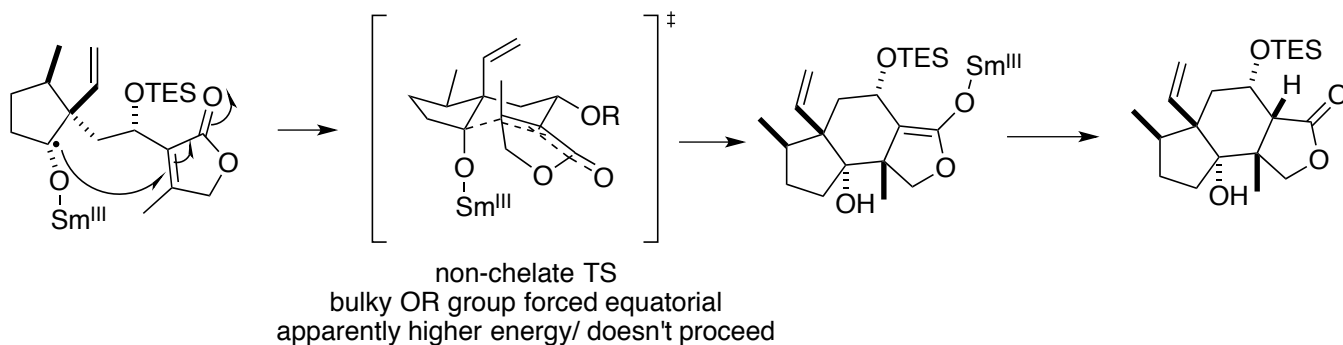


Control Temp:
Pummerer rearrangement above -60°C

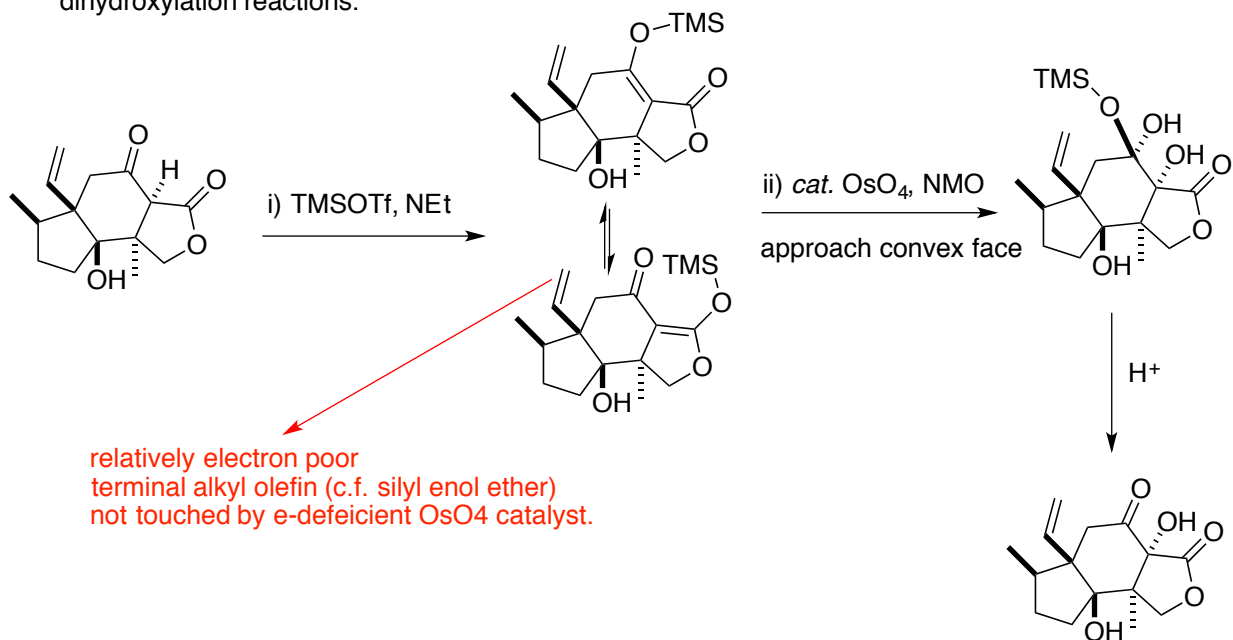
8. Purpose: to revisit (again) the SmI₂ reduction mechanism and see how it may be used on some exciting cyclization chemistry with an unsaturated lactone. To think about diastereomeric TSs.



alternatively....



9. Purpose: to remind about hemiketals and their instability to give back ketones. To think about chemoselective dihydroxylation reactions.



10. Purpose: to encourage thoughts about an astute and highly intelligent first disconnection that unveils two annulations by encompassing a ketalization under oxidative conditions. To see the use of an alkene as a latent diol/ reactive glyoxal.

