

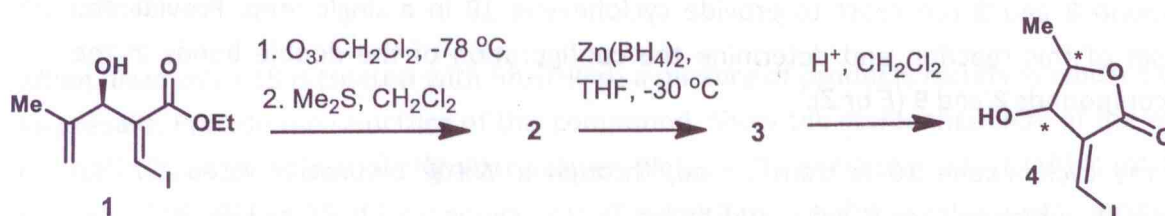
Exam Reactivity in Organic Chemistry (ROC) 2012-2013

January 31st 2013, 14:00 – 17:00

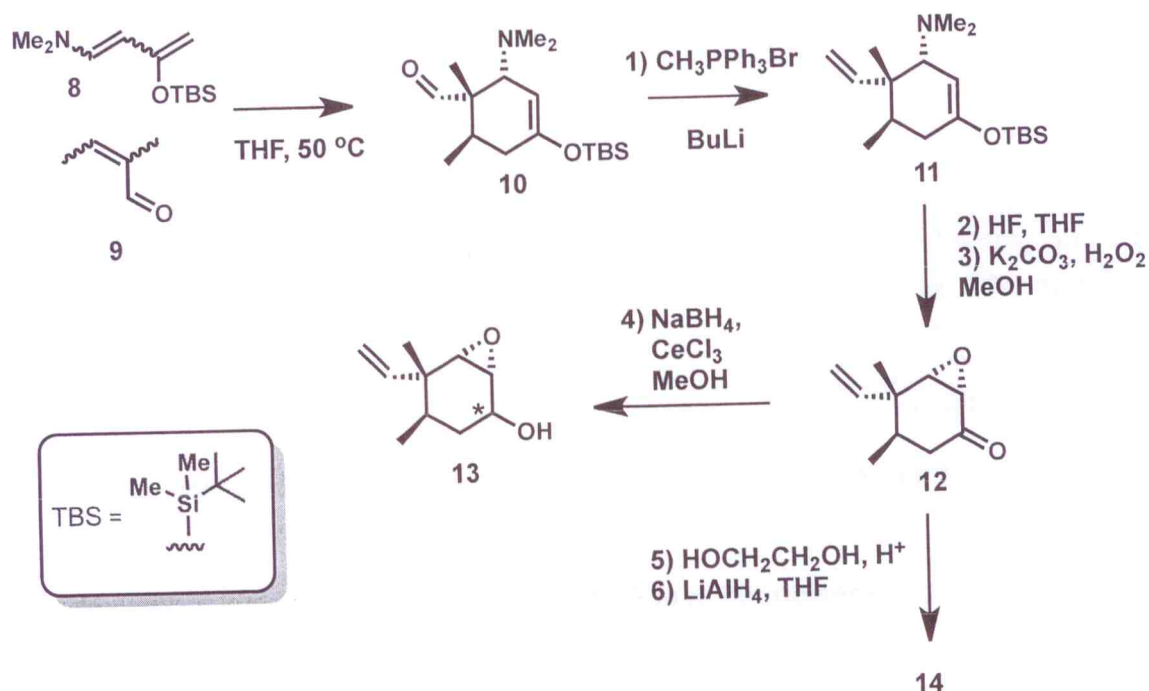
Problem 1

Compound **1** was treated with ozone and upon reductive work-up product **2** was formed. Hydride reduction of **2** gave **3**. Subsequent treatment of **3** with acid under anhydrous conditions led to 5-membered lactone **4**.

- Draw the structure of **2**.
- Give the mechanism of the conversion of **2** into **3** and predict the stereochemistry of the product **3**.
- Give the mechanism for the transformation of **3** into **4**. Show the absolute configuration of **4**.
- Another lactone could conceivably be formed upon the treatment of **3** with acid. Explain briefly why **4** is formed preferentially.



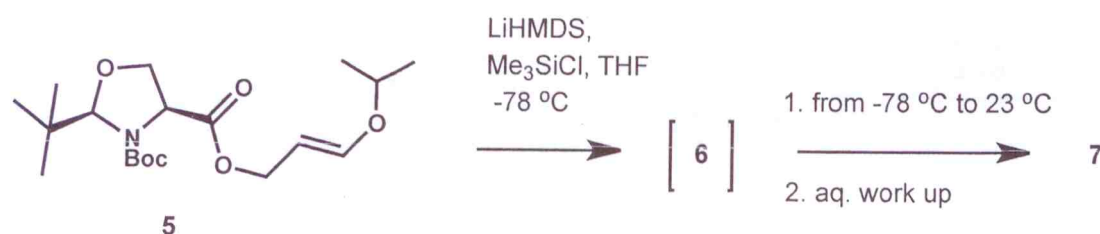
Problem 2



- Compound **8** and **9** can react to provide cyclohexene **10** in a single step. Provide the mechanism of this reaction and determine the configuration of the double bonds in the starting compounds **8** and **9** (*E* or *Z*).
- Next the cyclohexene **10** is transformed, through a Wittig olefination (step 1), into compound **11**, which in turn is subjected to a two-step sequence (2: HF in THF; 3: K_2CO_3 , H_2O_2 in MeOH) to provide **12**. Give the mechanism of these two steps (2 and 3).
- Compound **12** is then transformed, under so-called Luche conditions (step 4), into alcohol **13**. Predict the stereochemistry of the newly formed stereocenter, indicated with an asterisk (*).
- In an alternative sequence epoxide **12** is converted into **14** in two steps (5 and 6). Provide the mechanism of these two steps (5 and 6) and predict the structure of **14**, including stereochemistry.

Problem 3

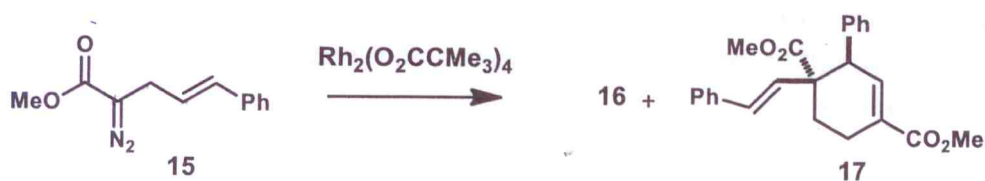
A derivative of serine **5** gave intermediate **6** (not isolated) upon treatment with strong non-nucleophilic base LiHMDS at low temperature. Compound **6** rearranged at higher temperature and product **7** was isolated as a single stereoisomer, after aqueous work-up.



- Provide the structure of **6** including all aspects of stereochemistry.
- Give the structure of **7**. Provide the mechanism of the formation of **7** from **6**. Predict the stereochemistry of the product **7** by analyzing the relevant transition states.

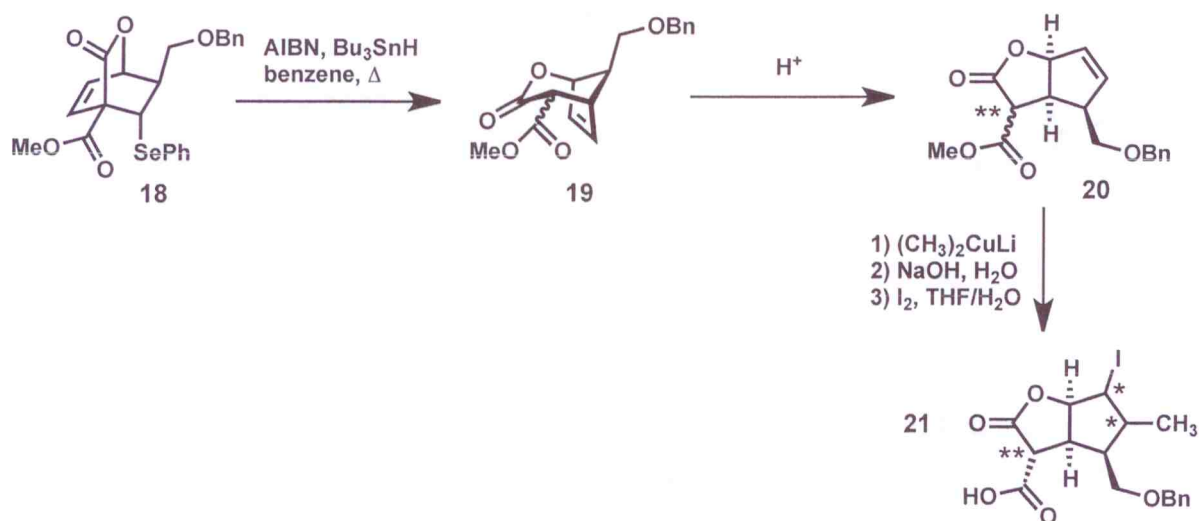
Problem 4

When diazo ester **15** is treated with Rh₂(OPiv)₄ a mixture of products results in which bicycle **16** prevails. Provide the structure of this compound. Show the stereochemistry of the newly formed chiral centers and justify your answer. Next to **16**, another product (**17**) is isolated, which was formed in a Diels-Alder reaction. Provide a reasonable reaction mechanism that accounts for the formation of this product from **15**.



Problem 5

Gelsemiol is a natural product that induces neurite outgrowth and part of a synthesis towards this compound is depicted below.



a) In the first step, bridged selenoether **18** is treated with AIBN and Bu_3SnH in refluxing benzene to provide rearranged product **19**. Provide a mechanism for this transformation (Hint: the rearrangement proceeds via a higher energy intermediate). Explain why a mixture of *R*- and *S*-epimers is formed at the carbon atom indicated with a double asterisk (**).

b) In the next step the product is treated with silica gel (mild acid) to provide bicycle **20**. Provide a mechanism for this transformation.

c) In a three-step sequence bicycle **20** is decorated with both a methyl group and an iodine atom to give product **21**. First **20** is treated with a methyl cuprate (a soft nucleophile). Next, the resulting compound is exposed to NaOH to give a product that was treated with I_2 in $\text{THF}/\text{H}_2\text{O}$ (after careful neutralization).

Provide the mechanism of the reactions leading to **21** from **20**.

Predict the stereochemistry of the carbon atoms indicated with an asterisk (*).

In the process a single epimer of **21** at the chiral center indicated with a double asterisk (**) is formed. Explain.