

**Reactivity in Organic Chemistry Exam**

**Monday 30-01-2017**

**14:00-17:00**

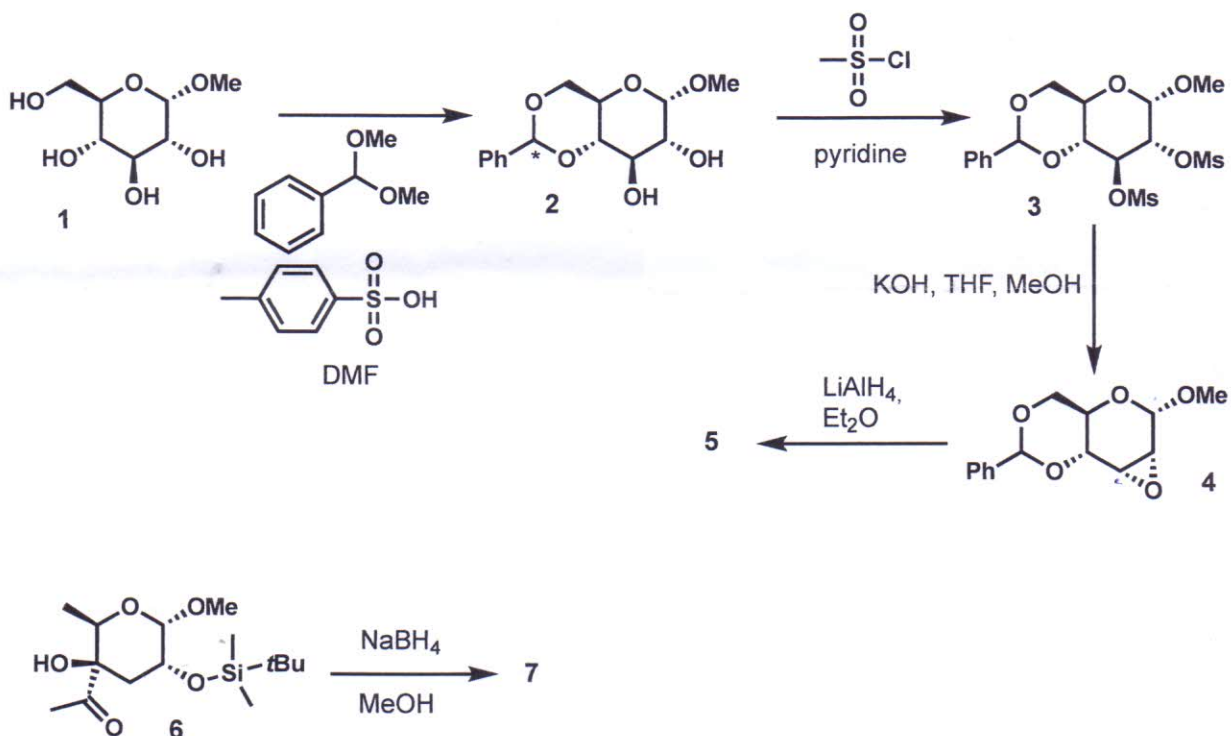
Provide every answer sheet with your  
**name** and **student number**

**Indicate how many answer sheets are handed in**

### Problem 1 (35 points)

During the synthesis of caryophyllose, a rare mycobacterial carbohydrate the following transformations are executed.

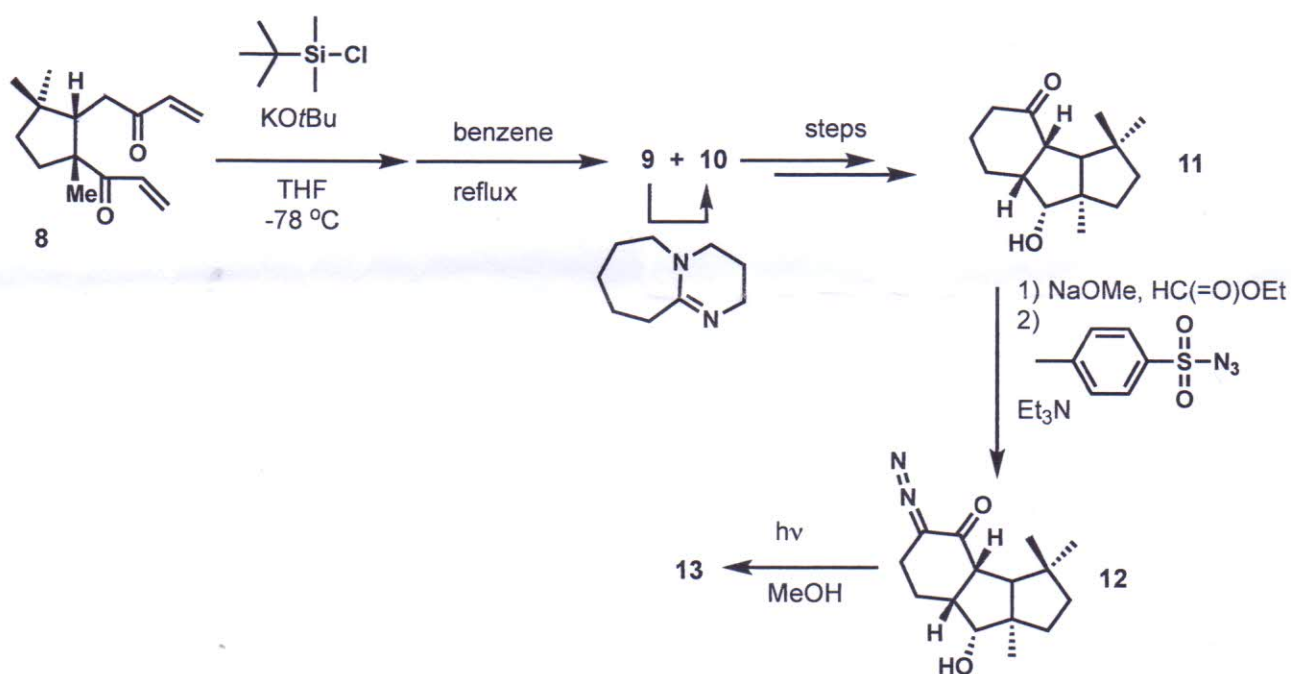
- When tetraol **1** is treated with benzaldehyde dimethylacetal and a catalytic amount of *para*-toluenesulfonic acid in DMF bicyclic **2** is formed. Give the mechanism of this reaction and explain which stereoisomer is formed (indicated with an asterisk (\*)). Explain the regioselectivity of this reaction.
- Next dimesylate **3** is generated from diol **2**. This dimesylate is treated with KOH to give epoxide **4**. Provide a mechanism for this transformation.
- Epoxide **4** is treated with  $\text{LiAlH}_4$ . Provide the structure of compound **5** and give the mechanism of its formation (including stereochemistry).
- To form another part of the caryophyllose molecule ketone **6** was treated with  $\text{NaBH}_4$  to give a diol **7**. Give the mechanism of the reaction and explain which major diastereomer of **7** is formed.



## Problem 2 (25 points)

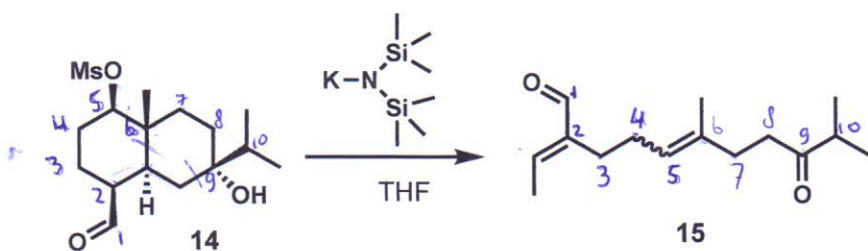
Below part of a synthesis of a Capnellene is depicted.

- A) Cyclopentane **8** is treated with TBDMS-Cl and KOtBu ( $\pm 1$  equivalent) to give an intermediate that was taken up in benzene and refluxed to give a mixture of two compounds **9** and **10**. Upon treatment of this mixture with DBU, **9** could be transformed into **10**. Provide the mechanism of the reactions leading from **8** to **9** and **10** and the reaction from **9** to **10**. Explain the stereochemical course of the reaction.
- B) After a few steps ketone **11** is obtained and this ketone is treated with NaOMe and Ethylformate and subsequently with tosylazide to give **12**. Give the mechanism of the reactions leading from **11** to **12**.
- C) Next **12** is irradiated with UV light in methanol to give methyl ester **13**. Provide the structure of compound **13** and the mechanism of its formation.



### Problem 3 (10 points)

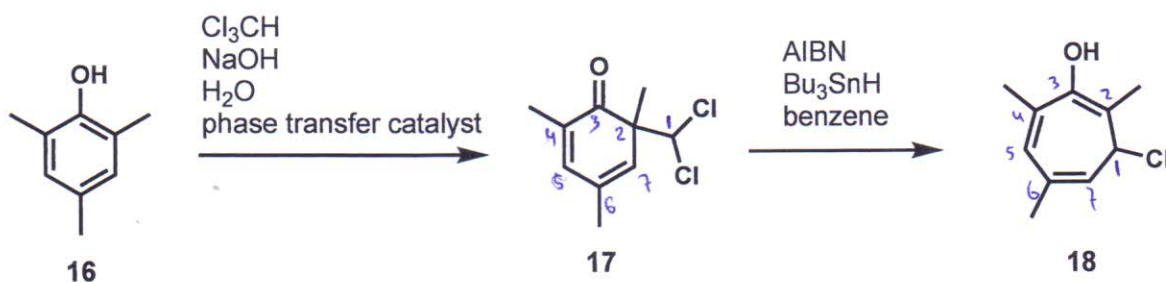
Upon treatment of **14** with KHMDS the linear dicarbonyl compound **15** was obtained. Provide the mechanism of the reaction that leads from **14** to **15** and show how the stereochemistry (*E* or *Z*) of the central double bond is determined.



### Problem 4 (20 points)

Below the synthesis of a tropone is depicted.

- In the first step phenol **16** is heated in a biphasic mixture of chloroform and aqueous NaOH to transform **16** into **17**. Give the mechanism of this transformation.
- Next the dichloride **17** is heated in benzene in the presence of  $\text{Bu}_3\text{SnH}$  and a catalytic amount of AIBN to give seven membered ring **18**. Provide a mechanism for this transformation.



**Problem 5 (10 points)**

Oleocathal is a compound found in extra vergine olive oil that has similar biological activity as ibuprofen. A step of the formal total synthesis of this compound is depicted below.

Provide the structure of ethyl ester **20** (including stereochemistry) and the mechanism of its formation from alcohol **19**.

