Mid-term ROC 2013-2014

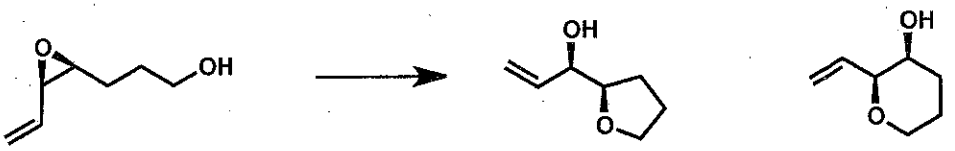
Friday, December 6th, 2013

Problem 1

A) When the *trans* and *cis* epoxides **1** and **2** are treated under identical conditions (0.1 equivalents of camphorsulfonic acid in DCM) the ratio of the cyclic reaction products differs significantly. Explain the "relative" outcome of these experiments.

1 **2** **3**

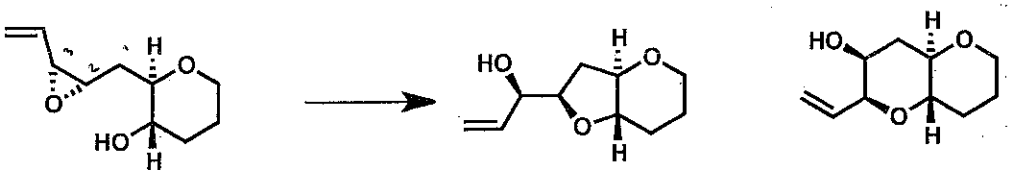
0 : 100



4 **5** **6**

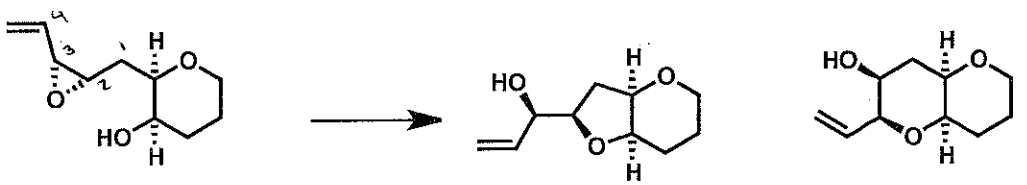
56 : 44

B) If the epoxide and alcohol are appended to a ring system, as in compounds **7** and **10**, the ratio of the cyclic products is different yet again. Why do we get more of the 6-ring product **9** when we start from **7**, in comparison to the reaction starting with acyclic epoxy alcohol **4**? Why do we only get the 5-membered ring product if we start from **10**?



7 **8** **9**

25 : 75



10 **11** **12**

100 : 0

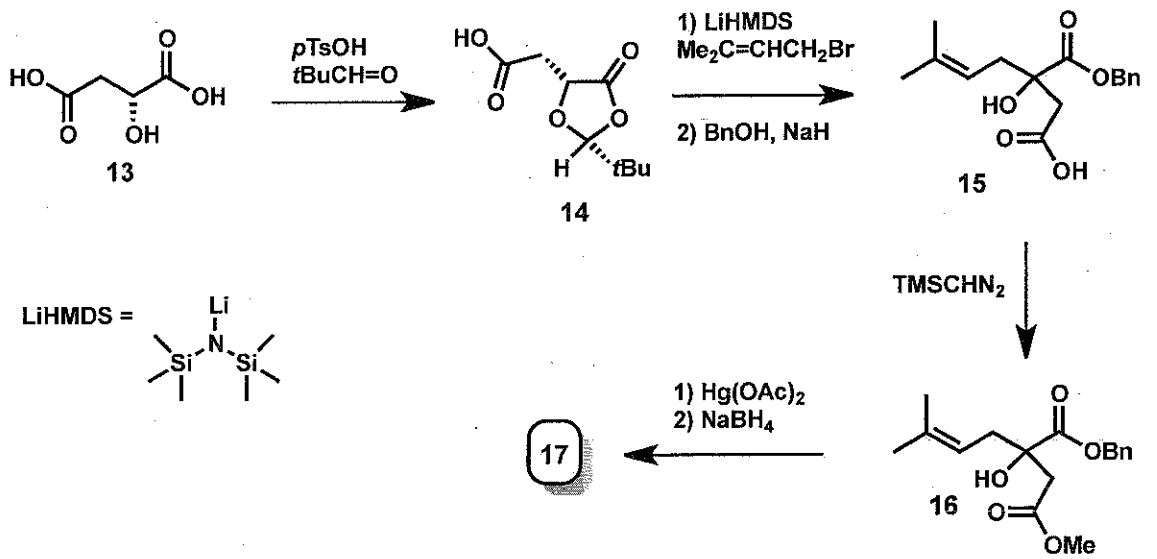
Problem 2

Depicted below is part of a synthesis towards anhydroharringtonine, an alkaloid with anti cancer potency. The synthesis below is a beautiful illustration of so-called "self-reproduction of chirality".

A) Provide the mechanism for the transformation of di-acid **13** into **14**.

B) Next acid **14** is treated with LiHMDS and prenylbromide to create a quarternary carbon atom on the 5-membered ring. Ensuing reaction with benzyl alcohol and NaH leads to product **15**. Provide the mechanisms of the reactions leading to product **15** from **14**. Why are two equivalents of LiHMDS required? Provide the stereochemistry of the newly formed quarternary C-atom and a rationale for the stereoselectivity.

C) After methylation of the free carboxylic acid, alkene **16** is treated with $Hg(OAc)_2$ and subsequently with $NaBH_4$. Provide the structure of compound **17**, including stereochemistry and a rationale for this stereoselectivity.



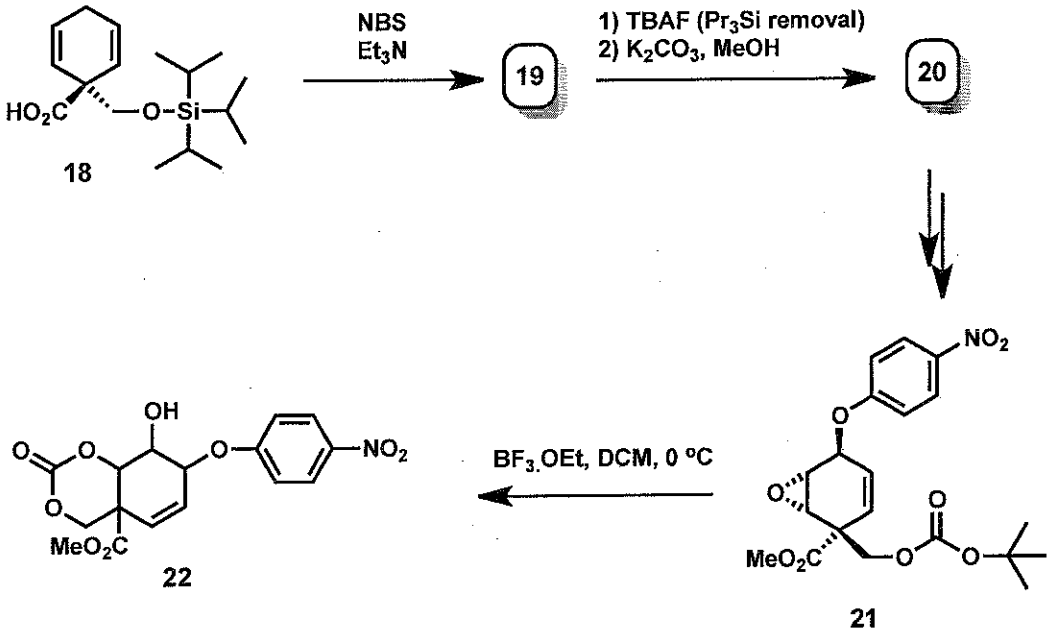
Problem 3

Below part of a synthesis of sphingofungin E, an immunosupressive agent, is depicted.

A) Diene **18** is treated with NBS and a base to give bicyle **19**. Give the structure of **19** and the mechanism of its formation. Account for the stereochemistry in the reaction.

B) After removal of the tri-*iso*-propylsilyl group from **19**, the compound is treated with a mild base in MeOH to give another bicycle, **20**. Give the structure of bicylce **20** along with the mechanism of its formation and a rationale for the observed stereochemistry.

C) After a couple of steps **20** is transformed into **21**. This compound is treated with a Lewis acid to give yet another bicylce. Give a mechanism for the formation of bicycle **22** and predict the stereochemistry of all chiral centers using this mechanism.

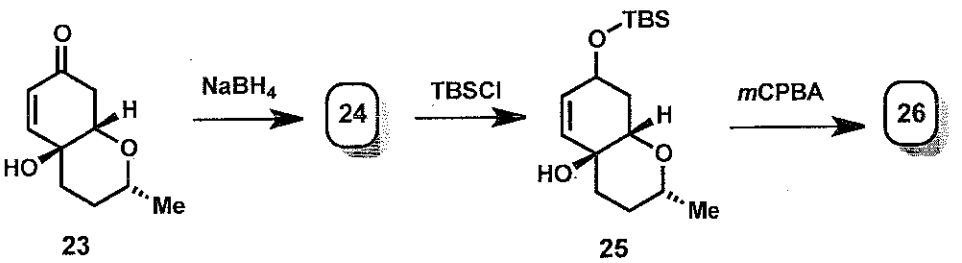


Problem 4

A part of a synthesis of cephalosporolide B is depicted below. Stereoselective reduction of **23** leads to alcohol **24**, which after protection is treated with *m*CPBA to give **26**.

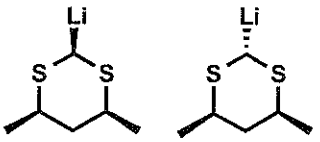
A) Which diastereomer is formed in the reduction of **23**? Explain.

B) Give the structure of compound **26** and account for the observed stereoselectivity.



Problem 5

Which diastereomer of the lithiated thioacetal below is more stable **27** or **28**. Justify your answer.



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