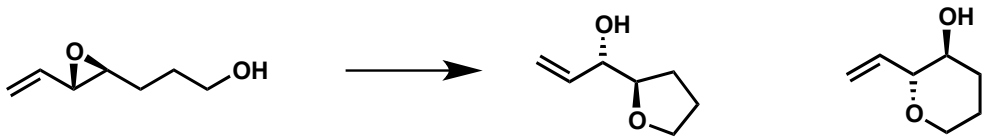
Mid-term ROC 2017-2018

Friday, December 7th, 2017

Available time: 2 hours

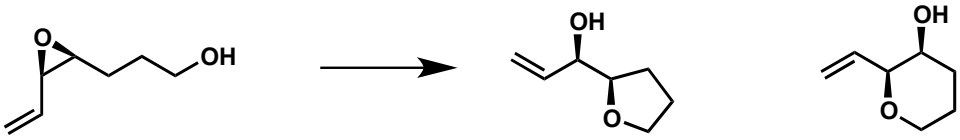
Problem 1 (20 points)

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**

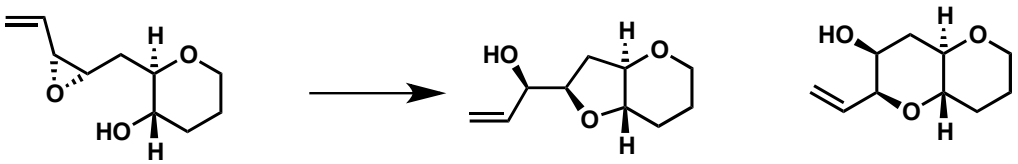
0 : 100



4 **5** **6**

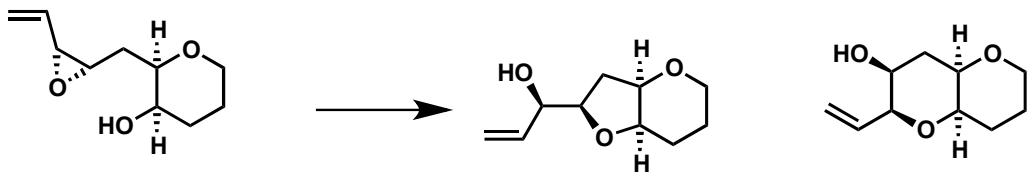
56 : 44

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

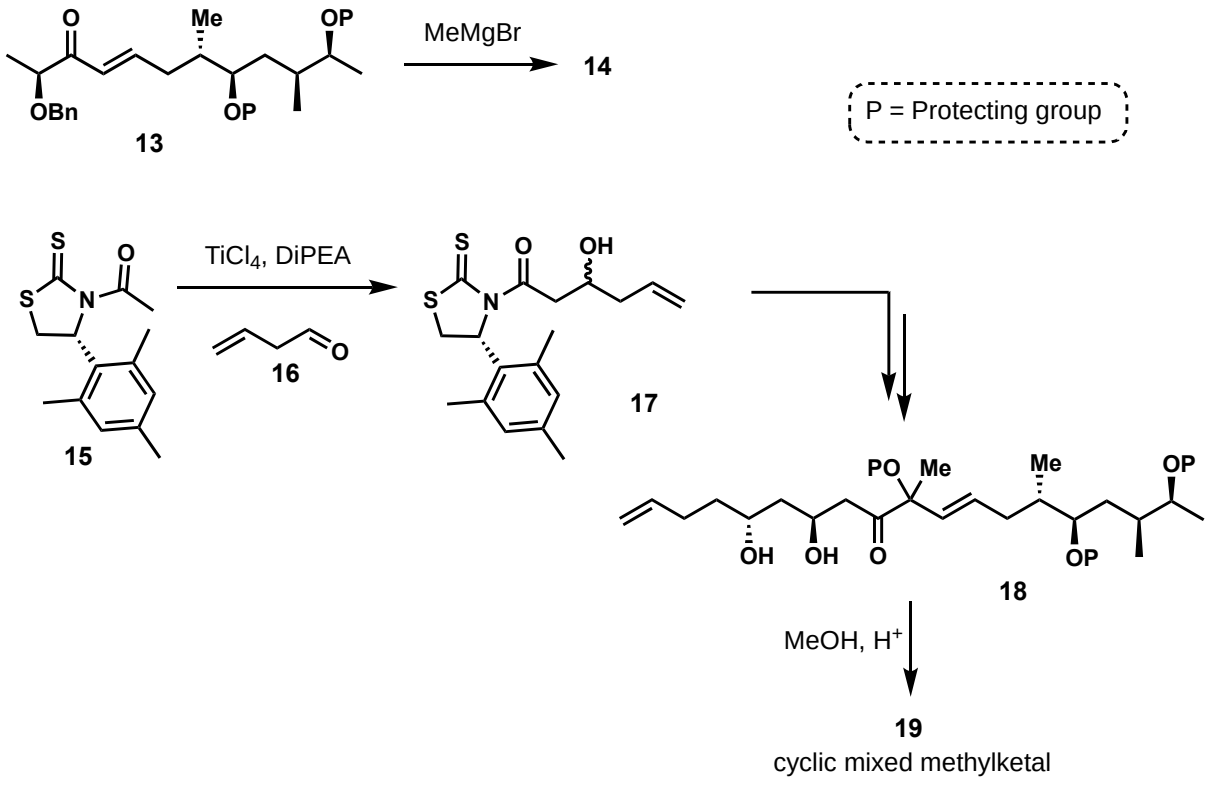
Problem 2 (60 points)

Depicted below is part of the synthesis of Iriomoteolide 1a, which is a metabolite found in an deep sea organism displaying promising anti-cancer and anti-viral activity.

A) When compound **13** is treated with MeMgBr a quarternary stereocenter is stereoselectively created. Provide the structure of compound **14** and account for the stereoselectivity in the addition reaction.

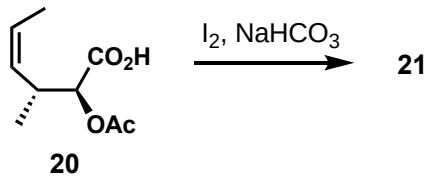
B) To construct another part of Iriomoteolide 1a, a Titanium enolate was generated from acyl thiazolidinethione **15** and reacted with butenal **16**. The chiral auxiliary used in this reaction (the thiazolidinethione) has been designed such that the C=S moiety complexes with the Ti ion in the transition state. Predict the chirality of the newly formed chiral center using an analysis of plausible transition states.

C) After a few steps, linear ketone **18** is obtained, which upon treatment with acid in MeOH cyclizes to give a single diastereomer of the cyclic ketal **19**. Provide the mechanism of the ring closing reaction, and account for the stereoselectivity observed in this reaction (which proceeds "under thermodynamic control").



Problem 3 (20 points)

Treatment of compound **20** with I_2 under mild basic conditions provides the cyclic compound **21** in a stereoselective manner. Provide the structure of compound **21** and give the mechanism of its formation. Account for the observed stereoselectivity.



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