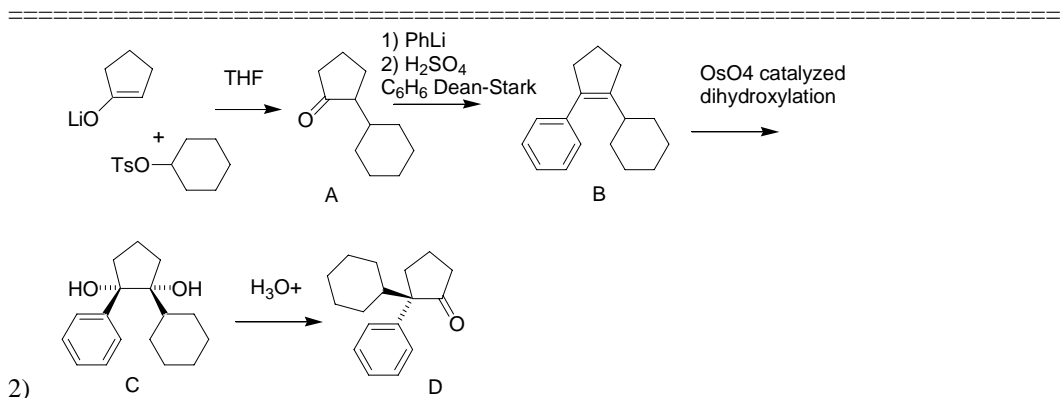
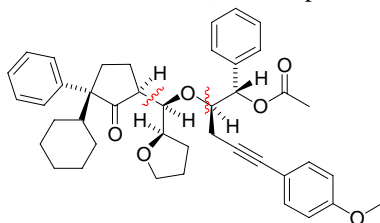


Key

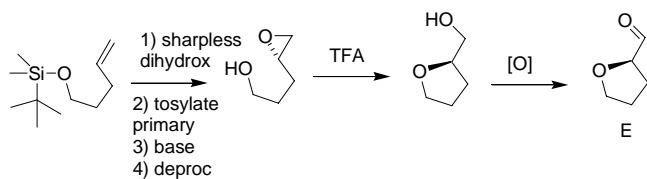
U. of Kentucky Chemistry 535 Synthetic Organic Chemistry Spring 2004

Final Exam (open notes)

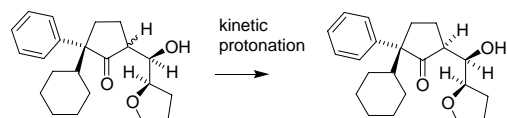
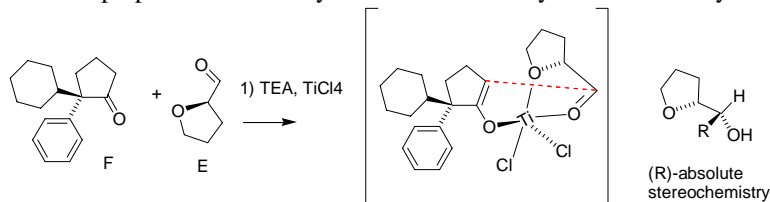
- 1) There was more than one way to solve this problem. I am picking the two bonds shown in the figure below as the two strategic bonds in my synthetic plan. Disconnections of these bonds are 'strategic'/advantageous for the following reason.
- \* The first disconnection is an aldol retron. This allows me to control stereochemistry at the position  $\alpha$  to the ketone in a variety of ways including kinetic protonation. The aldol will allow some control of the asymmetric carbinol carbon atom next to the  $\alpha$  to the ketone carbon atom.
  - \* The second disconnection forms an ether. The stereochemistry of this carbinol atom will be controlled by the  $S_N2$  reaction. I should be able to control the stereochemistry of the  $S_N2$  electrophile because it will be a 1,2-diol. We have discussed these in detail.



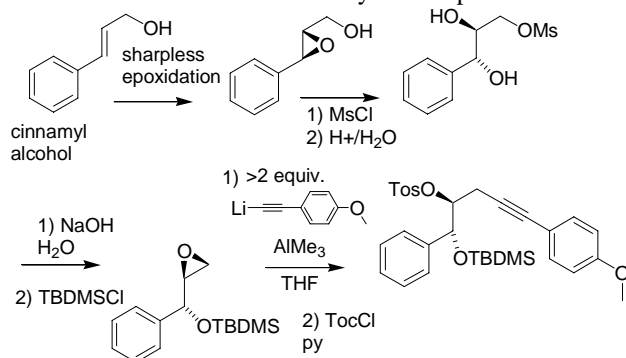
- 2)
- The first reaction will likely be of moderate yield, but that is ok since the starting materials are cheap. Enolate alkylation is probably best done with enamine chemistry. In any case the first reaction probably is not trivial. I would do a literature search for 2-cyclohexylcyclopentanone.
  - The 1,2-addition of phenyllithium to the cyclopentanone **A** would likely be assisted by the inclusion of  $CeCl_3$ .
  - To drive the elimination to completion to get **B** I want to remove water. This can be accomplished with a benzene azeotrope.
  - In the synthesis of **C** I might try to asymmetrically add OH, but this is probably doomed to failure. I will likely not get very good ee% due to limitations of the scope of this reaction. There is a size difference between Ph and cyclohexyl but it will not translate well to optically pure diol. I would likely make **C** without worrying about the chirality and resolve the diol.
  - With optically pure diol **C** I will rearrange via pinacol to **D** via. The Ph group has a greater migratory aptitude. It will stay on the same side of the five-membered ring.



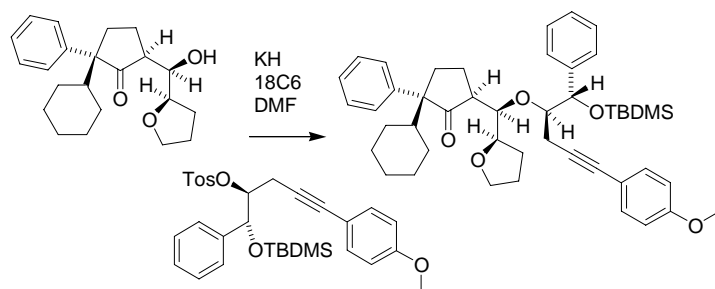
- The preparation of aldehyde E should be fairly trivial. I will try this method.



- With Ti-mediation enolization I will probably get the desired R absolute stereochemistry in the aldol addition. However the absolute stereochemistry at the quaternary center will not be controlled. To do so I will try kinetic protonation.



- The synthesis of the last portion of the molecule is outlined above. At the end of the procedure I have two secondary carbinol functionalities. I want to selectively protect one of them so the other can be selectively activated.
- I need (S) carbinol because it is going to invert in the S<sub>N</sub>2 reaction.



\* Deprotection and esterification complete the synthesis.