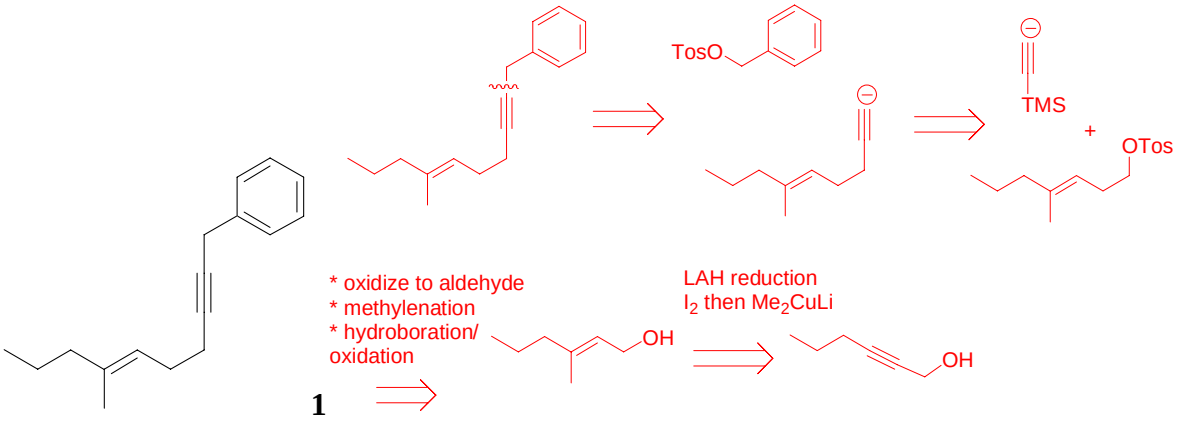
U. of Kentucky Chemistry 535 Synthetic Organic Chemistry Spring 2004
Midterm Exam: KEY!

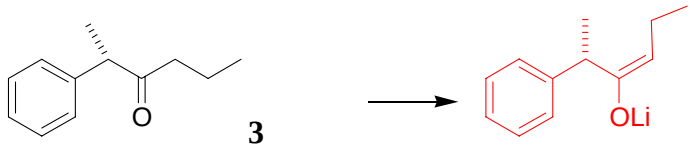
REMEMBER RETROSYNTHESES USE SYNTHONS

1. (15 pts.) Devise a stereocontrolled, convergent route to ene-yne **1**. Show a retrosynthetic analysis that leaves no doubt for the reader that you can make the molecule. You may start with molecules containing no less than ***seven*** carbon atoms.



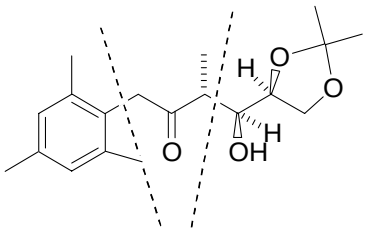
2. (10 pts.) Explain how you are controlling the stereochemistry above in the synthesis of **1** with a few words.

___The challenging bit to the synthesis of **1** is the stereoselective construction of the trisubstituted alkene. Above the stereochemistry is being controlled by propensity of the organo aluminate to iodinate then alkylate stereoselectively. _



The hindered base selectively deprotonates at the least hindered site. The E-enolate is favored as the kinetic product due to the six-membered t-state of the deprotonation.

3. (15 pts.) Predict the major product of the reaction of compound 3 with LDA at -40 °C. Stereochemistry is important in your answer.



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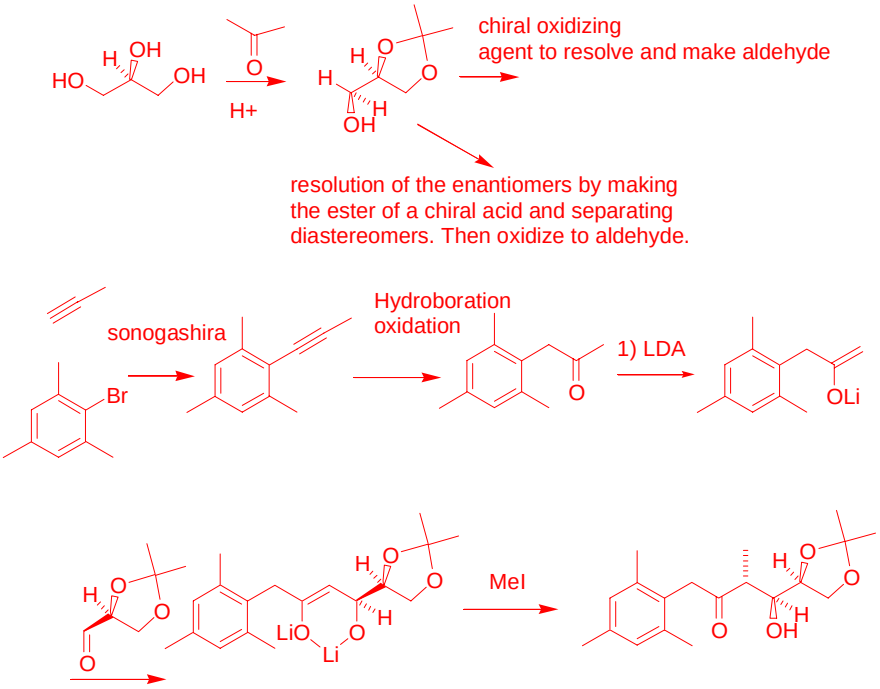
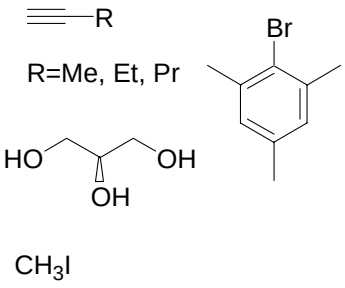
4. (20 pts.) Sketch out a forward *enantiospecific* synthesis of **4** that constructs the bonds indicated by the dotted lines. If you don't know how to do a certain step, use descriptions instead of reagents over the arrows, but be as specific as possible. For example words like 'oxidation' or 'resolution' above an arrow might win you points.

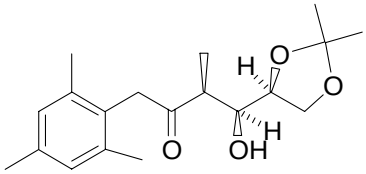


If there are rough spots in your synthesis make little notes at these points to let me know what you are worrying about.



The starting materials at left are hints for problem 4. You also might want to consider the following possibilities: Sonogashira coupling, enolate alkylation, diol protection, aldol reaction, resolution of enantiomers, hydroboration/ oxidation of alkynes.

If you see other possibilities to synthesize **4**, feel free to try them; however, you must form the bonds indicated.



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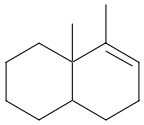
5. (10 pts.) How would your answer to problem 4 change if you were asked to construct the epimer of **4** shown in structure **5**?

The syn aldol is easier to get. In my synthesis above I would used butyne instead of propyne in the Sonogashira coupling. I would make the E-enolate of the ketone kinetically. The aldol reaction would be the last step to get target structure **5**.



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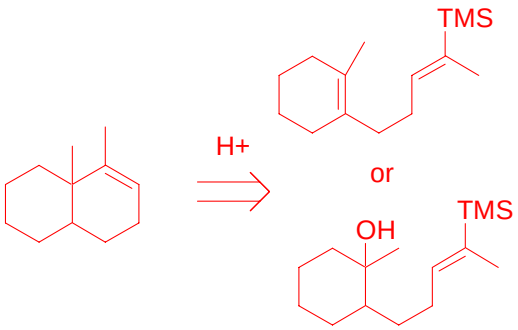
6. (10 pts.) Consider the carbon skeleton of the molecule above and outline a retrosynthesis for it using a cationic cyclization approach. All you need is one retroarrow and a suggested starting material. This was a homework problem.



One of these should work.