Advanced Organic Chemistry (CHE 311/511)
First Mid-term Examination
Oct. 11, 2007
Prof. W. P. Malachowski

Name: Dwight Schrute

Read each question carefully before answering. Be certain you understand everything the question is requesting. Do the easy questions first. If questions appear confusing or exceedingly complex, then you may need to rethink the question. Keep in mind the intended examination topics.

In organic chemistry, hand-drawn pictures convey specific information. Be sure the drawing you have made conveys the essential information required to answer the question. Make certain that three-dimensional pictures display the correct atom arrangements. Don't forget to include formal charges when appropriate.

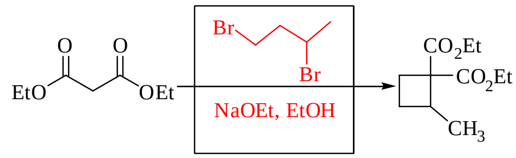
You may use models to assist in determining answers. You may use scrap paper to work out problems before entering your final answer on the exam sheets. In addition, feel free to use the back side of the exam sheets for scrap. If necessary, you may enter exam answers on the back side of the exam sheets, however you must clearly indicate which problems are located on the back of the exam pages.

Graduate students must do all questions on the exam. There are a total of 105 points for graduate students.
Undergraduate students only need to complete 14 of 17 boxes on question 1 and choose two of three questions among 6, 7a and 7b. There are a total of 90 points for undergraduate students.

.

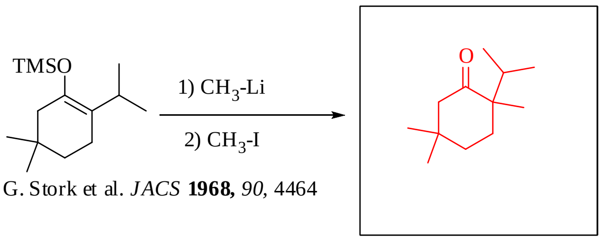
1. Provide the necessary infomation (product, reagent or starting material) to complete the following reactions. Undergraduates only need to fill in 14 of 17 boxes. Graduate students must do fill in all the boxes. (3 pts. each)

a)



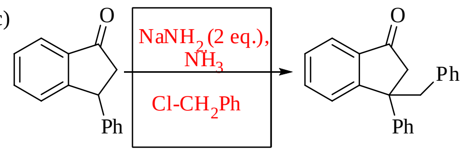
J. E. Baldwin and R. C. Burrell *JOC* **2000**, *65*, 7139

b)



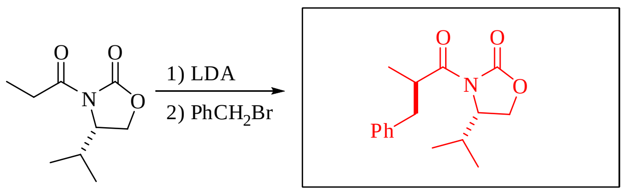
G. Stork et al. *JACS* **1968,** *90*, 4464

c)



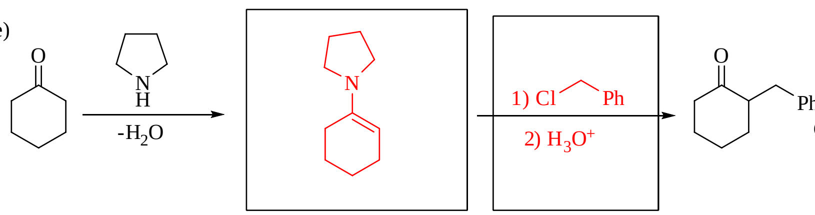
C. R. Hauser et al. *JOC* **1964,** *29*, 1394

d)



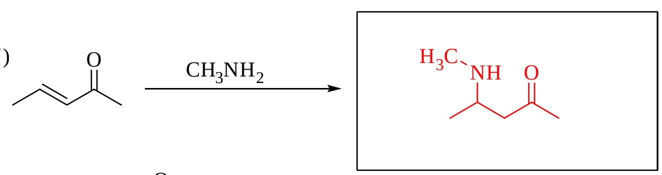
D. A. Evans et al. *JACS* **1982,** *104*, 1737

e)



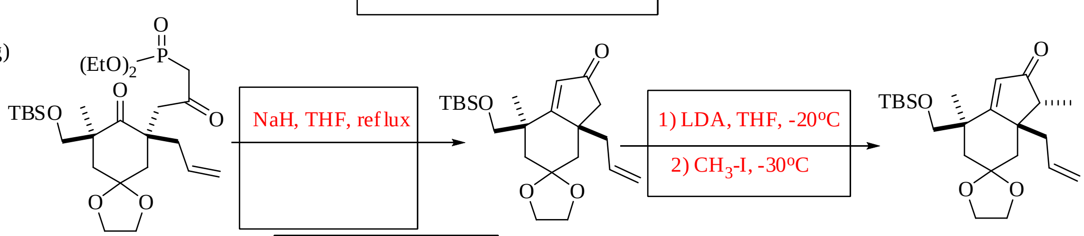
G. Stork et al. *JACS*, **1963**, *85*, 207

f)

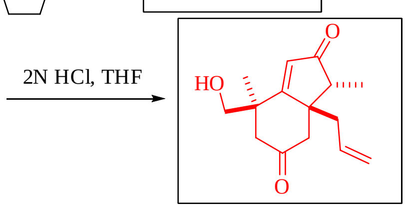


R. Lukes et al. *Coll. Czech. Chem. Commun.* **1960**, *25*, 2179

g)

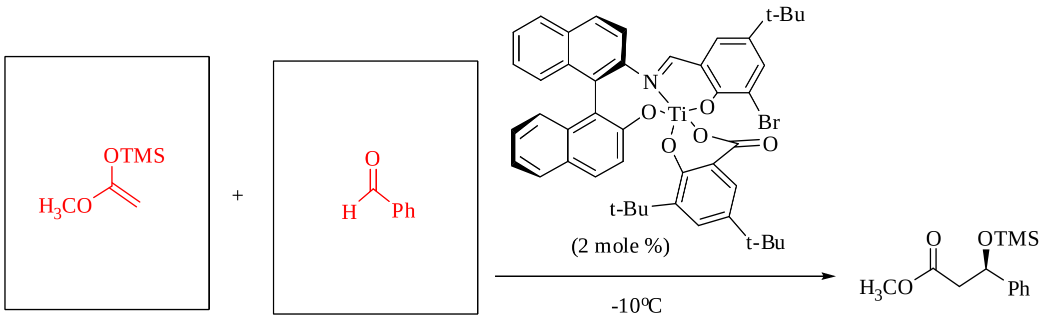


S. J. Danishefsky et al. *JACS* **2006,** *128*, 1016



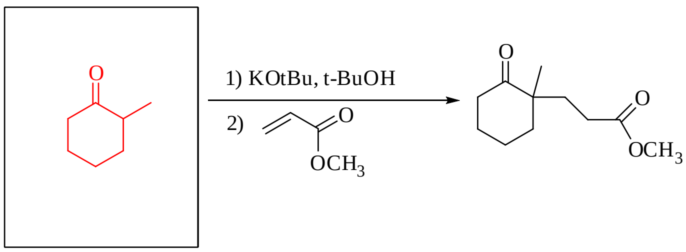
30 total points

h)



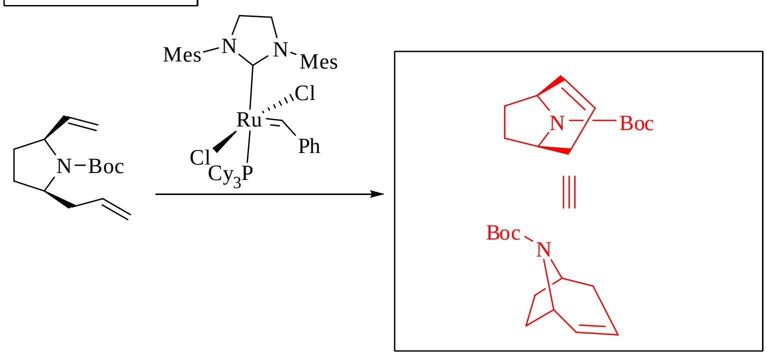
E. Carreira et al. *JACS* **1994**, *116*, 8837

i)



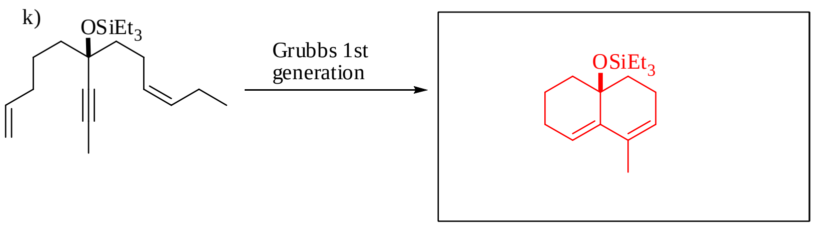
H. O. House, B. M. Trost et al. *JOC* **1966,** *31*, 646

j)



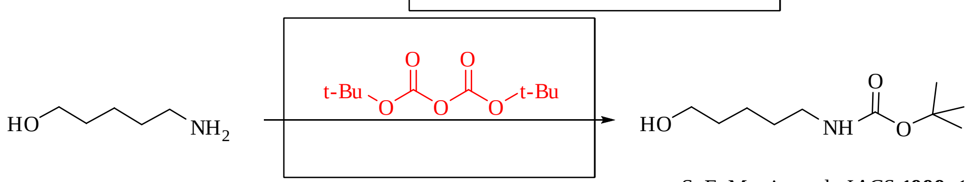
V. Aggarawal et al. *Org. Lett*. **2004**, *6*, 1469

k)

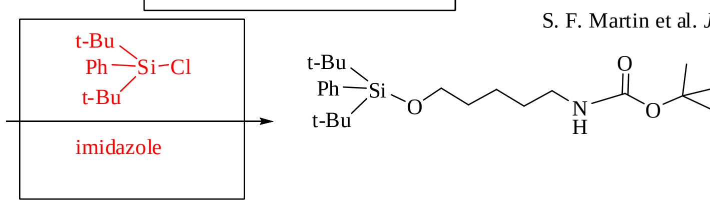


R. H. Grubbs et al. *JOC* **1996,** *61*, 1073

l)

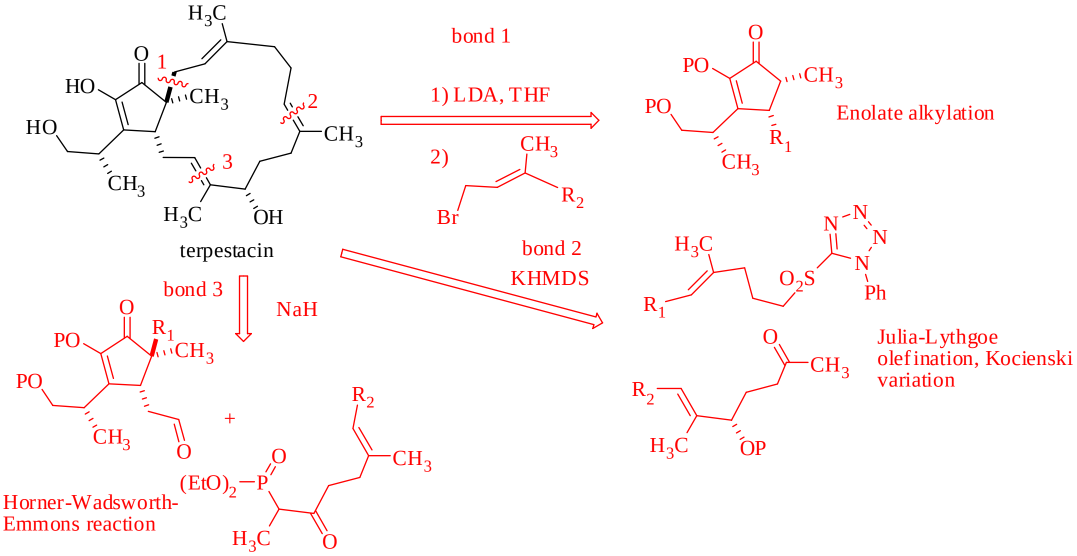


S. F. Martin et al. *JACS* **1999,** *121*, 866

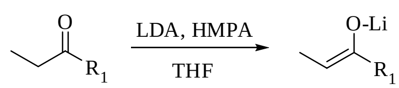


21 total points

2. The sesterterpene natural product terpestacin was first isolated in 1993 from a fungi and has demonstrated potent activity in assays for HIV and cancer treatment. Devise a retrosynthetic plan for the synthesis of terpestacin. Choose two key bond disconnections that you would use in a total synthesis of terpestacin and suggest reactions to form these bonds. You should show the starting materials (in abbreviated form) and reagents. These reactions must not be the same type of reaction. You should be conscious of when protecting groups will be necessary and use a 'P' on the group to be blocked. (8 pts.)

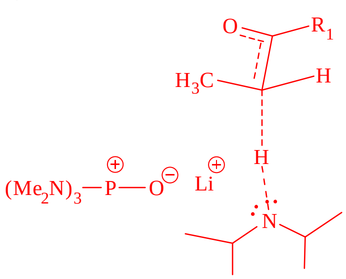


3. The stereoselective formation of an enolate from a carbonyl compound is an important step in controlling subsequent enolate reaction stereoselectivity. Shown below is an example of stereoselective enolate formation.



a) What is the stereochemistry of the enolate shown? (2 pts.) Z

b) Draw the transition state that rationalizes this outcome and explain why this transition state is favored. (6 pts.)



CH_3 and R_1 groups on opposite side limit steric strain .

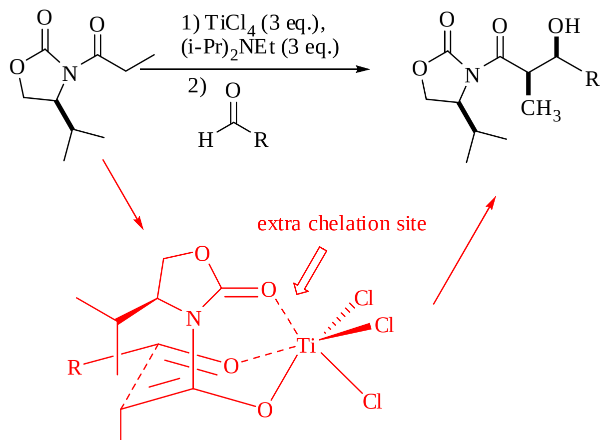
c) Is this enolate product considered the (circle one) **thermodynamic** or **kinetic** enolate? (2 pts.)

d) One early trick used by synthetic chemists to obtain this enolate stereoselectively was to employ very bulky R_1 groups. In these cases the particular base or additives had little effect. Why would this change in R_1 afford a high level of stereoselectivity for this enolate? (4 pts.)

A bulky R_1 group would make the E enolate even less stable due to steric interactions between the CH_3 group and the R_1 group.

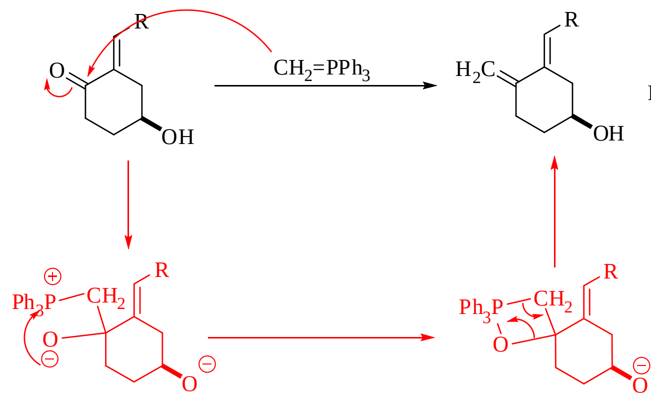
_____ 22 total pts.

4. Draw the transition state for the following reaction. (6 pts.)



J. Org. Chem. **1991,** *56*, 5747

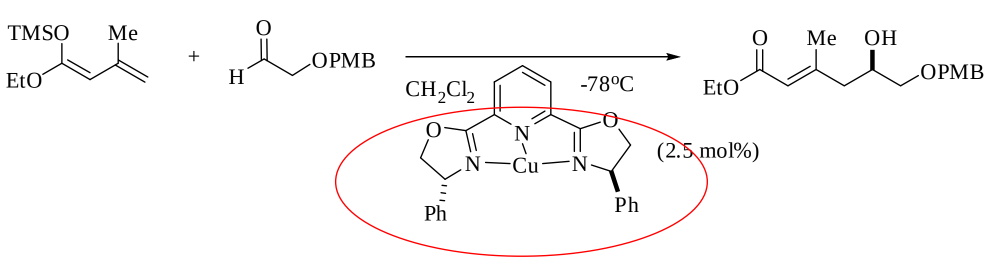
5. Draw a mechanism for the reaction shown below. (8 pts.)



Inhoffen et al. *Chem. Ber.* **1958,** *91*, 2309

For questions 6, 7a and 7b, undergraduates can answer any two of the three. Graduate students must answer all three.

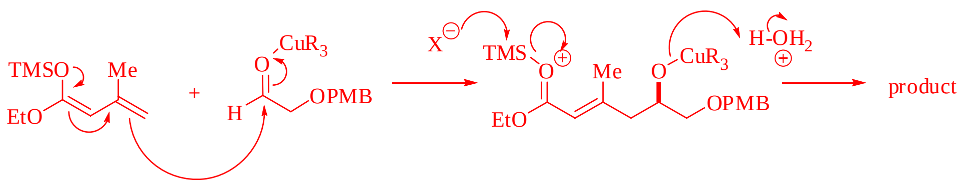
6. The reaction below was featured in a total synthesis of callipeltoside A by D. A. Evans and co-workers. (*JACS*, **2002,** *124*, 5654). It has elements similar to several reactions that we talked about in class.



a) Circle the group responsible for the enantioselectivity seen in the product. (2 pts.)

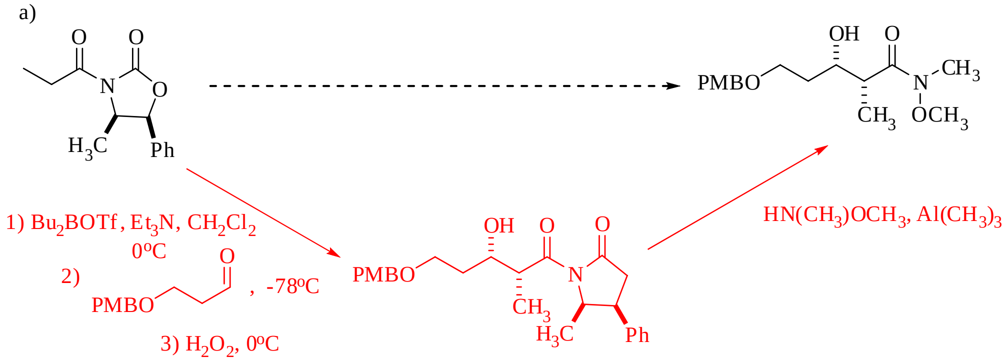
16 total pts.

b) Propose a mechanism for the reaction. You can abbreviate structures. (Hint: this is a Mukaiyama aldol reaction) (4 pts.)



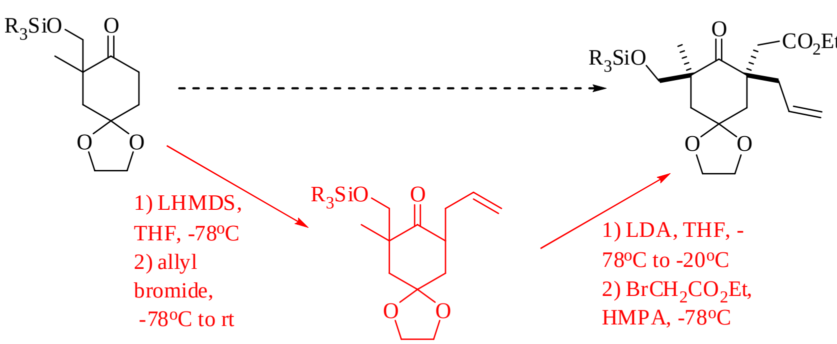
7. Provide a series of synthetic reactions to transform the starting material to the product shown. (6 pts. each)

a)



D. A. Evans et al. *JACS* **1990,** *112,* 7001

b)



relative stereocontrol only

S. J. Danishefsky et al. *JACS* **2006,** *128,* 1016

16 total points