Advanced Organic Chemistry: Synthesis Name:_____
CHEM 311/511
Final Exam
Monday, December 14, 2009
Wednesday, December 16, 2009

Review each question carefully before answering and 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. Maximum credit will be given for answers that correctly address stereochemical considerations in a particular reaction. Don't forget to include formal charges when appropriate.

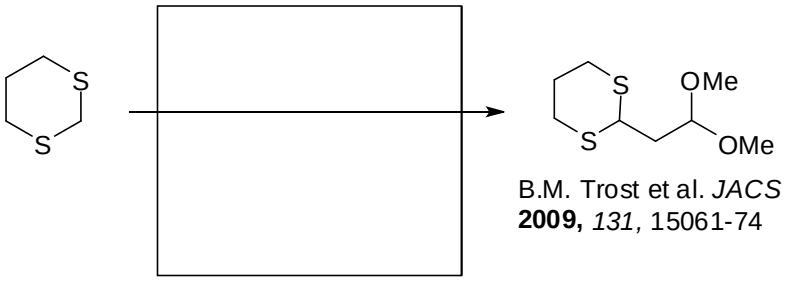
You may use models to assist in determining answers. You should use scrap paper to work out problems before entering your final answer on the exam sheets. In addition, feel free to use the back side of the exam sheets for scrap. If necessary, you may enter exam answers on the back side of the exam sheets,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

Graduate students:
Complete 10 of 12 boxes in question 1 (40 pts.)
Complete six of eight parts in questions 2 and 3. (60 pts.)
Complete two retrosynthetic examples in question 4. (20 pts.)
Offer two examples for each part of question 5. (30 pts.)

Undergraduate students:
Complete 8 of 12 boxes in question 1 (40 pts.)
Complete five of eight parts in questions 2 and 3. (60 pts.)
Complete one retrosynthetic example in question 4. (20 pts.)
Offer one example for each part of question 5. (30 pts.)

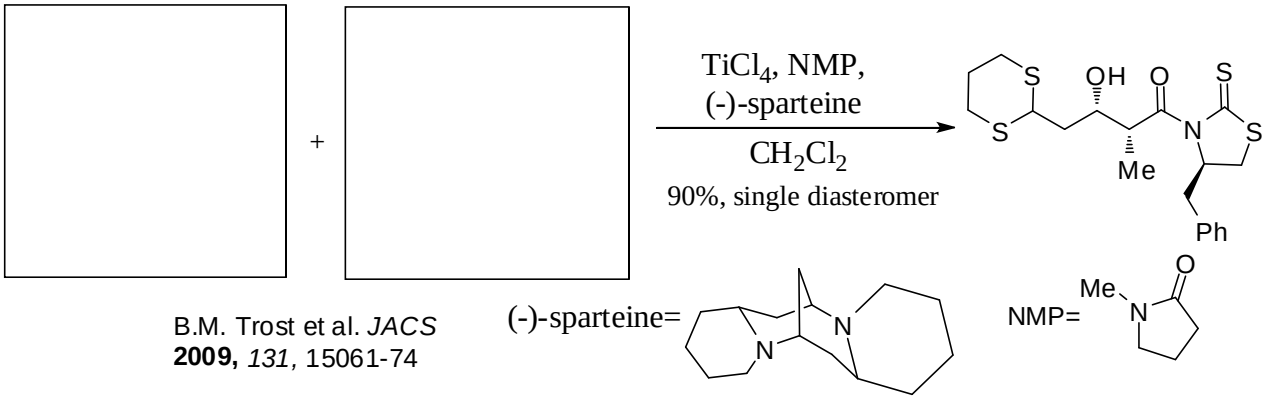
1. Box questions. Provide the necessary information, products or reagents, to complete the following reactions. Undergraduates complete eight of the twelve boxes and graduate students complete ten of twelve. (40 pts.)

a)



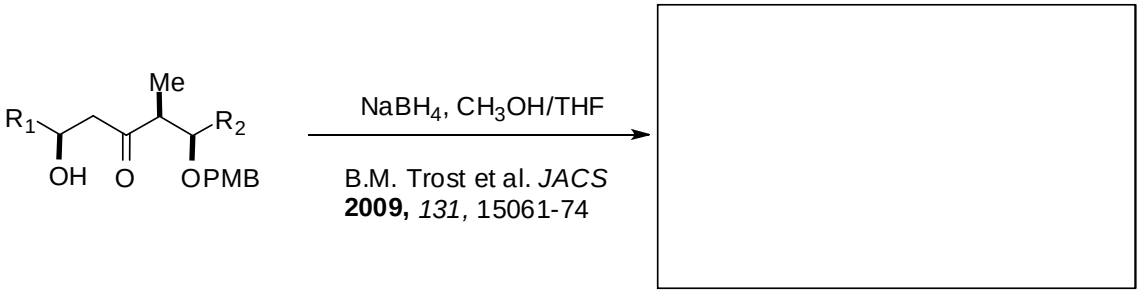
B.M. Trost et al. *JACS* **2009,** *131,* 15061-74

b)



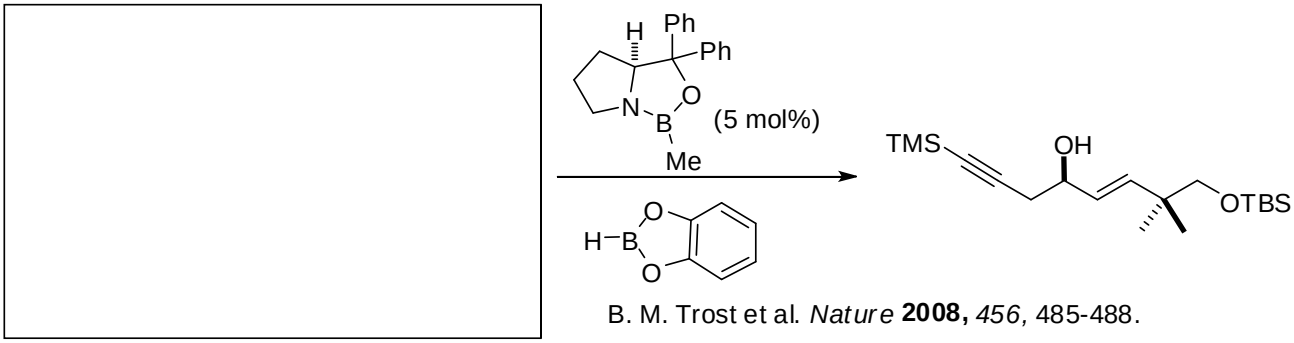
B.M. Trost et al. *JACS* **2009,** *131,* 15061-74

c)



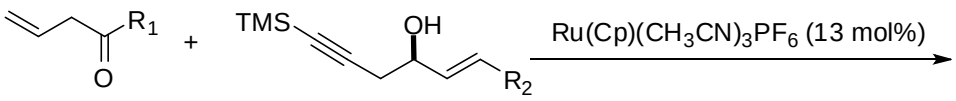
B.M. Trost et al. *JACS* **2009,** *131,* 15061-74

d)



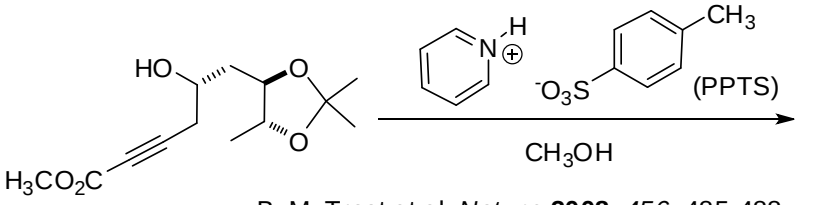
B. M. Trost et al. *Nature* **2008,** *456,* 485-488.

e)



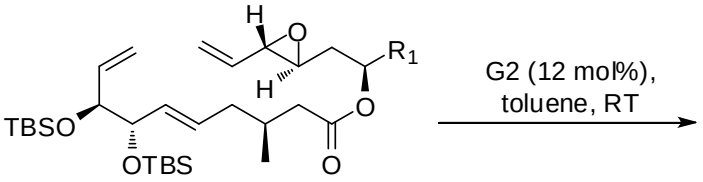
B. M. Trost et al. *Nature* **2008,** *456,* 485-488.

f)



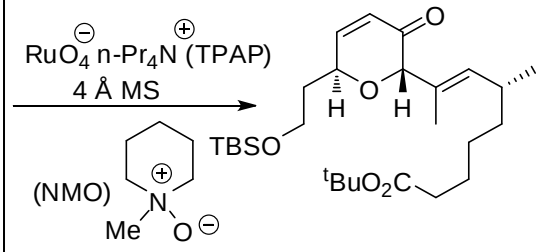
B. M. Trost et al. *Nature* **2008,** *456,* 485-488.

g)



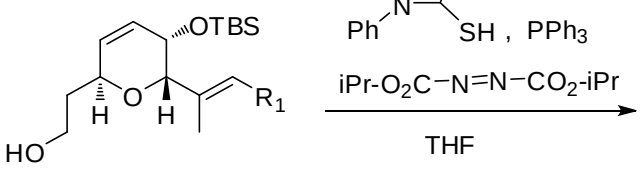
C. Nevado et al. *Angew. Chem. Int. Ed.* **2009,** *48,* 8780-8783.

h)



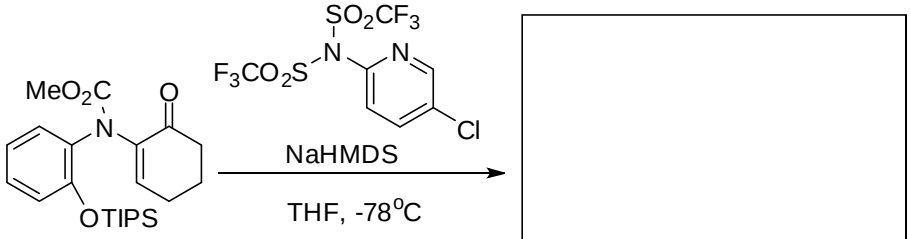
A. B. Smith, III, et al. *JACS* **2009,** *131,* 12109-11

i)



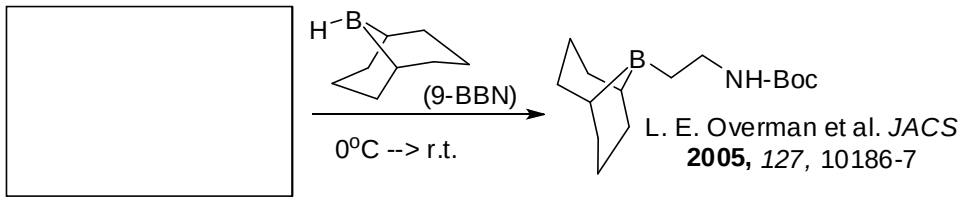
A. B. Smith, III, et al. *JACS* **2009,** *131,* 12109-11

j)



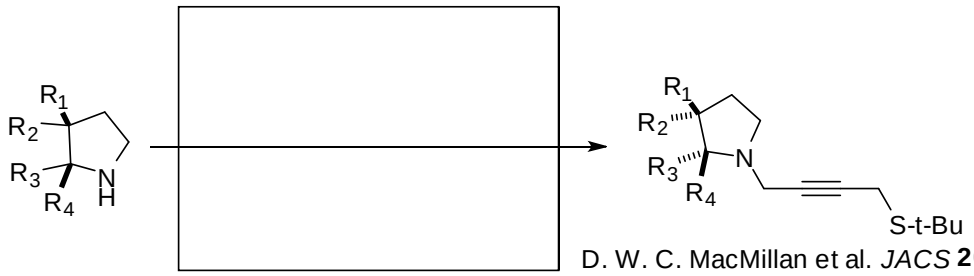
L. E. Overman et al. *JACS* (89 %)
2005, *127,* 10186-7

k)



L. E. Overman et al. *JACS*
2005, *127,* 10186-7

l)

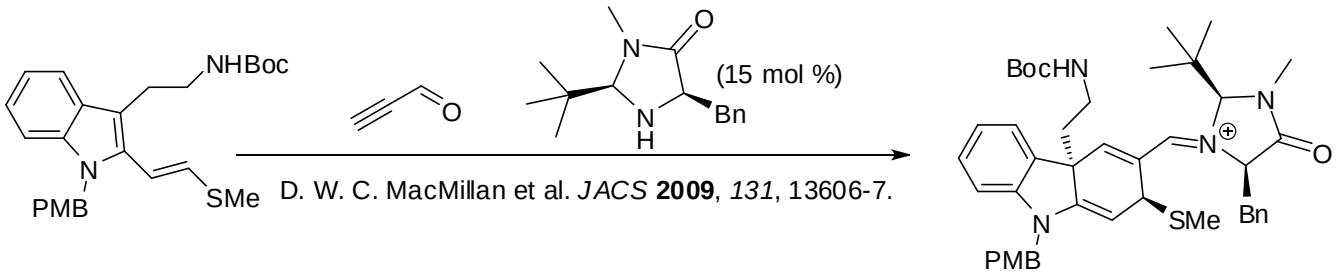


D. W. C. MacMillan et al. *JACS* **2009**, *131*, 13606-7.

Questions 2 and 3: Undergraduate students must answer five of eight parts and at least two from each section. Graduates students must answer six of eight parts. (60 pts. total)

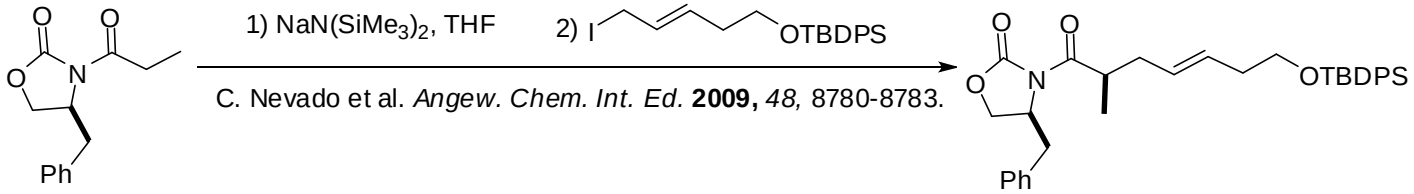
2. Mechanism questions. Provide the mechanism of the reactions shown. Use curved arrow electron flow conventions and show all key intermediates. (30 pts.)

a)



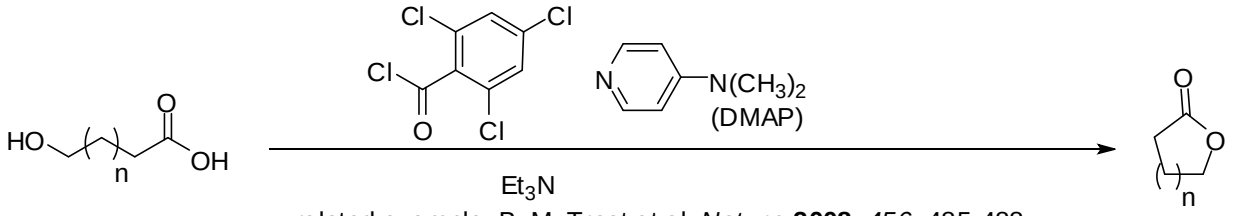
D. W. C. MacMillan et al. *JACS* **2009**, *131*, 13606-7.

b) Show the mechanism of the following alkylation reaction.



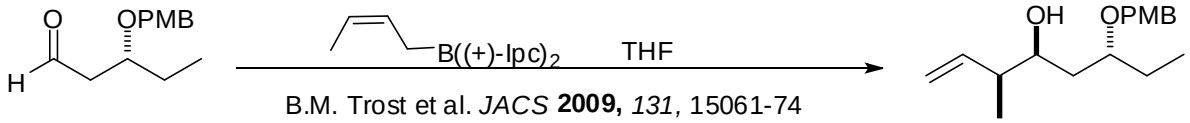
C. Nevado et al. *Angew. Chem. Int. Ed.* **2009,** *48,* 8780-8783.

c) Draw the mechanism of the macrolactonization process shown below.

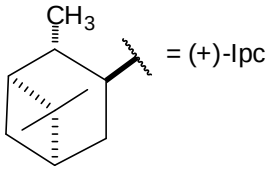


related example: B. M. Trost et al. *Nature* **2008,** *456,* 485-488.

d) Draw the mechanism and transition state of the following reaction. Do not be concerned with explaining the stereochemistry. Hint: the transition state is the same as the boron enolate aldol reactions discussed earlier in the semester.

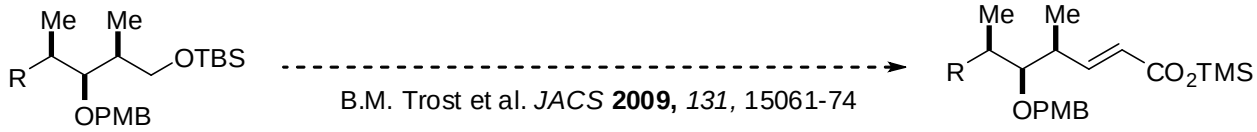


B.M. Trost et al. *JACS* **2009,** *131,* 15061-74



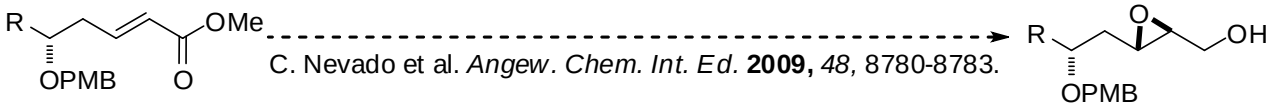
3. Synthesis questions. Provide a series of synthetic reactions to transform the starting material to the product shown. All syntheses can be completed in three or fewer steps.

a)

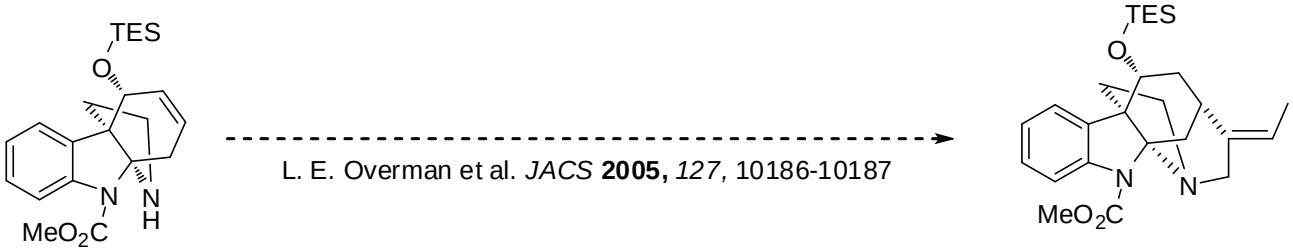


B.M. Trost et al. *JACS* **2009,** *131,* 15061-74

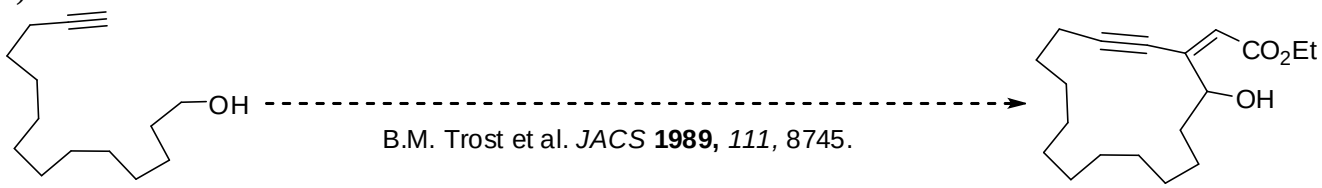
b)


R
OMe
OPMB
O
C. Nevado et al. *Angew. Chem. Int. Ed.* **2009,** *48,* 8780-8783.
R
O
OH
OPMB

c)

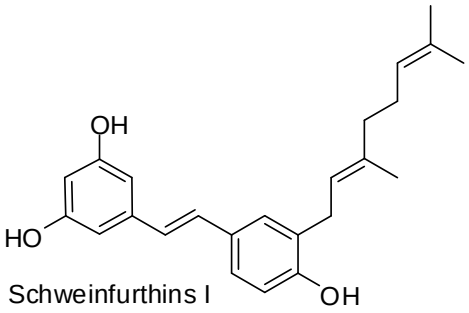

TES
O
N
N
H
MeO_2C
L. E. Overman et al. *JACS* **2005,** *127,* 10186-10187
TES
O
N
N
MeO_2C

d)


OH
B.M. Trost et al. *JACS* **1989,** *111,* 8745.
CO_2Et
OH

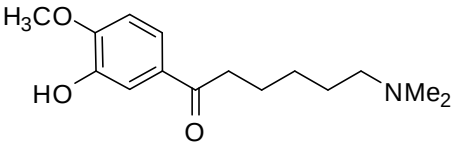
4. Retrosynthetic analysis. Provide a brief retrosynthetic plan for the following molecules. You should suggest one or two key bonds that might be central to the construction of these molecules. Include the structures of key intermediates. You should provide key reagents or name the reactions that will be used. Use protecting groups on your intermediates if one is required. Undergraduates must complete one retrosynthesis and graduate students must complete two. (20 pts.)

a)



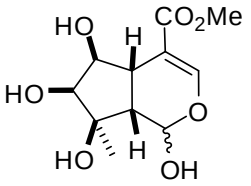
Schweinfurthins I
(reported in *J. Nat. Prod*. **2009** *ASAP*)

b)



Ficuseptamine B
(reported in *J. Nat. Prod.* **2009** *ASAP*)

c)



Lamiridosins A/B
(reported in *J. Nat. Prod.* **2009** *ASAP)*

5. Selectivity in synthetic chemistry. Complex molecule synthesis requires useful reactions to demonstrate selectivity, either chemo-, regio- or stereoselectivity. Undergraduate students show one example of each form of selectivity or site an example of each form used on this exam. Graduate students must show two examples of each form of selectivity. Both students must briefly explain the chemical basis of the selectivity if it is known. (30 pts.)

a) chemoselectivity example:

b) regioselectivity example:

c) stereoselectivity example: