

**Advanced Organic Chemistry (CHE 311/511)**  
**Final Examination**  
**Dec. 17-21, 2007**  
**Prof. W. P. Malachowski**

Name: Saint Nicolaous

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. The exam has a total of nine pages and seven questions.

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:

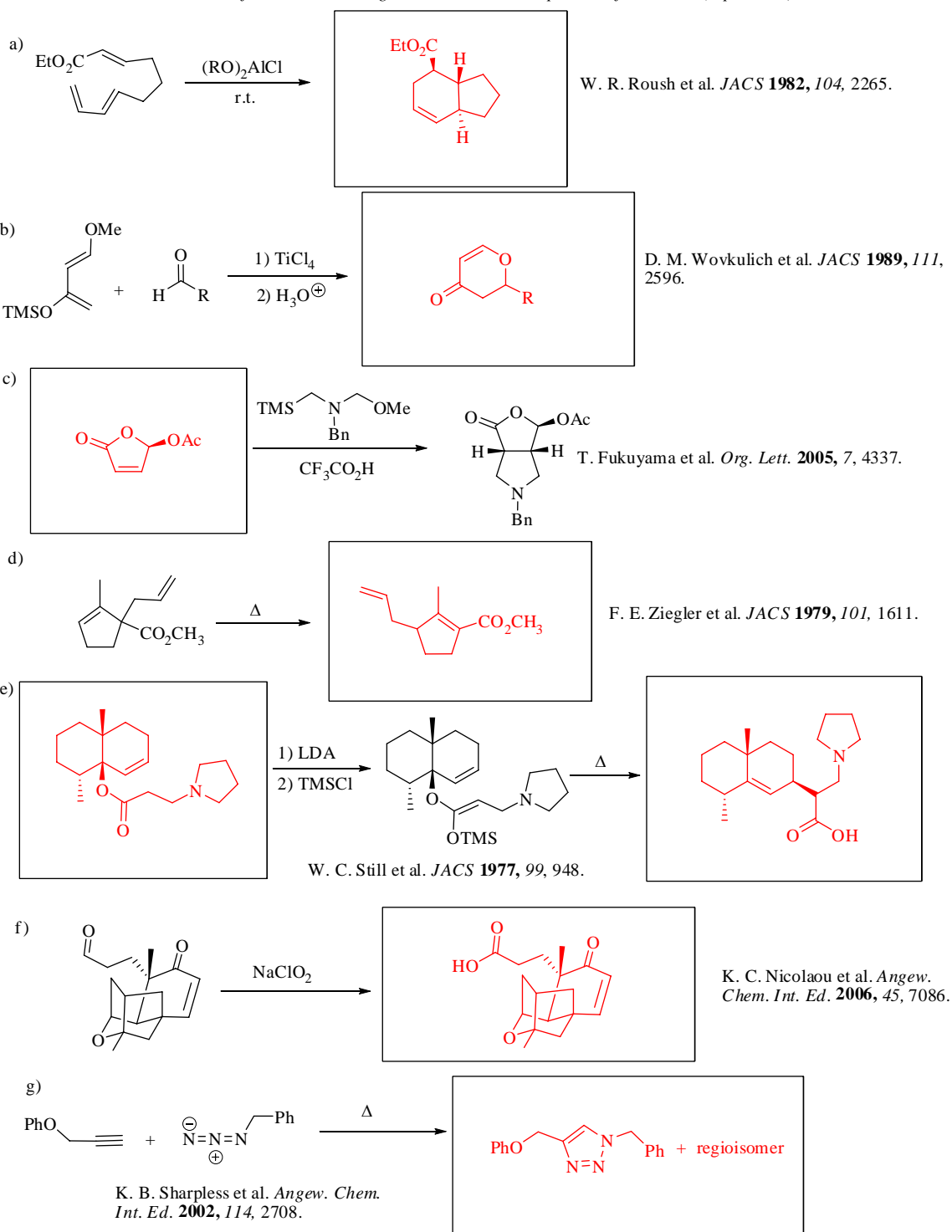
*Complete 12 of 16 boxes in question 1 (4 pts. each)*  
*Complete questions 2 and 3. (54 pts.)*  
*Complete six of eight parts in questions 4 and 5. (12 pts. each)*  
*Total points: 174*

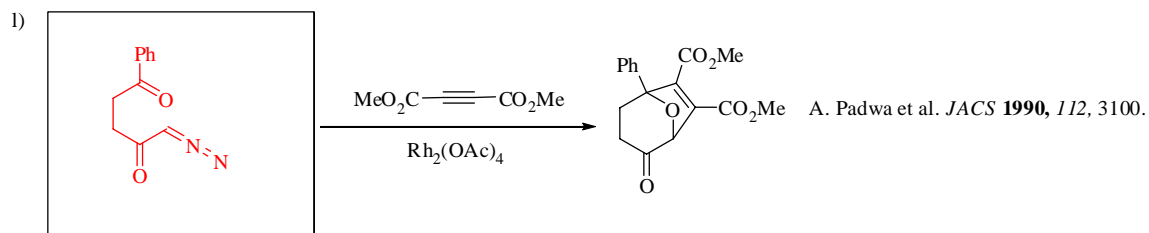
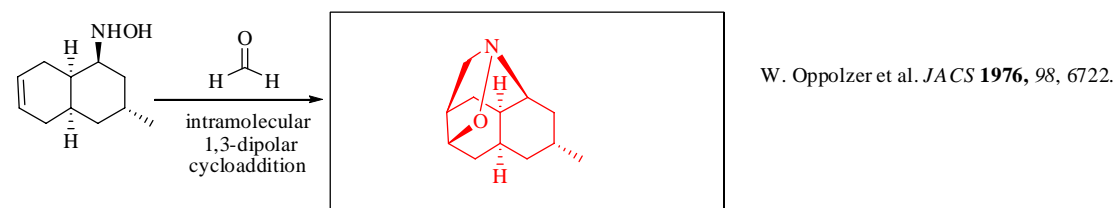
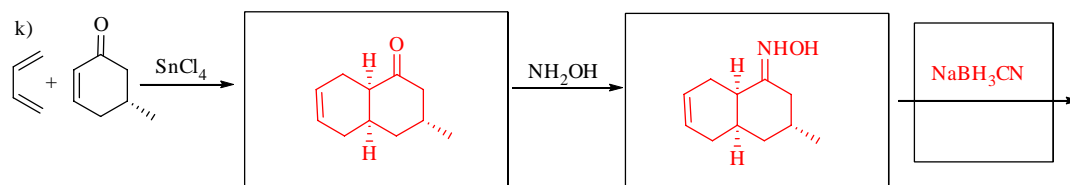
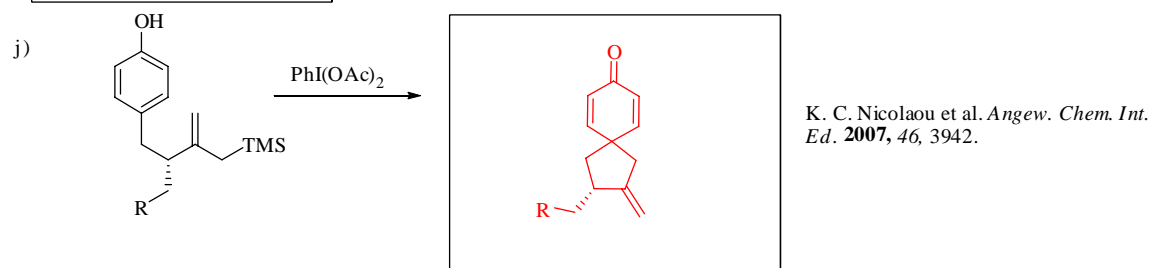
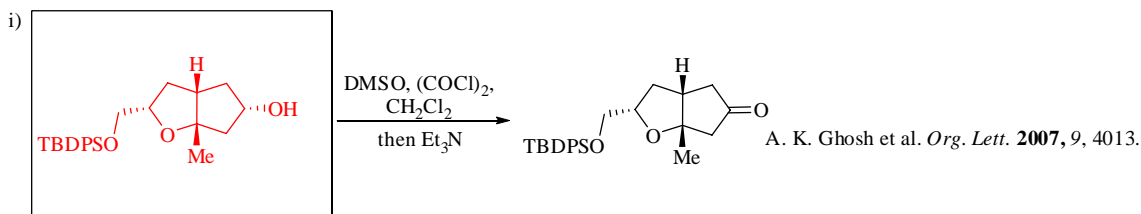
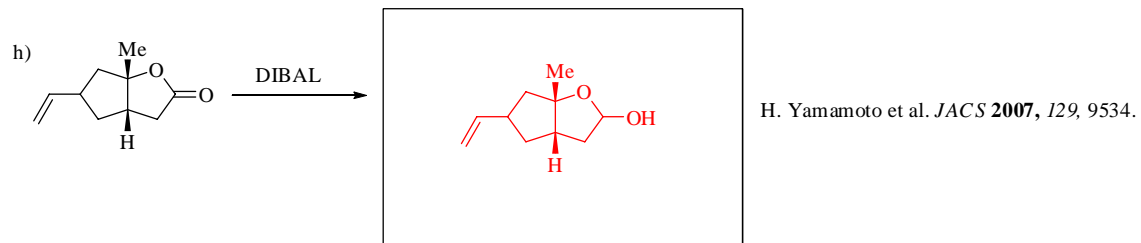
Undergraduate students:

*Complete 10 of 16 boxes in question 1 (4 pts. each)*  
*Complete questions 2 and 3. (54 pts.)*  
*Complete five of eight parts in questions 4 and 5. (12 pts. each)*  
*Total points: 154*

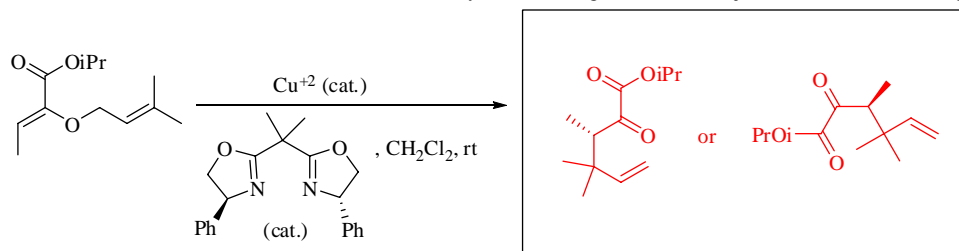
Bonus points: *If my meds are working when I grade the exam, there will be up to 10 bonus points be awarded for additional correct answers.*

1. Provide the necessary information (product, reagent or starting material) to complete the following reactions.  
 Graduate students must do 12 of 16 boxes. Undergraduates need to complete 10 of 16 boxes. (4 pts. each)





2. Unfortunately, we didn't have time to talk about catalytic enantioselective [3,3]-sigmatropic rearrangements, but it's your lucky day! I'm going to give you an opportunity to answer a question about the subject on the final exam. A few years ago Martin Hiersemann and co-workers reported the first example of a catalytic enantioselective sigmatropic rearrangement in *Angewandte Chemie International Edition* (2001, 40, 4700). Based on your knowledge of related subjects answer the following questions.



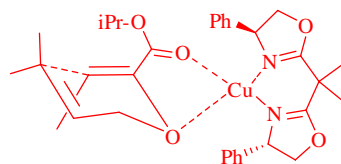
- a) Draw the product of the reaction in the box to the right. The new stereocenter in the major product of the reaction has an S configuration. Make sure your product reflects this outcome. (6 pts.)
- b) Draw the transition state of the reaction in the space below. Keep in mind this should be the thermodynamically most favorable transition state. FOR THIS QUESTION YOU CAN IGNORE THE CATALYST. (6 pts.)



- c) On the transition state drawn above, draw the electron flow arrows to convert your transition state to your product. (3 pts.)
- d) What is the common name given to this type of [3,3]-sigmatropic rearrangement? (2 pts.) **Claisen rearrangement**
- e) This reaction is thermodynamically favorable. Why? (2 pts.)

**The reaction converts one alkene into a stronger (thermodynamically more stable) carbonyl bond.**

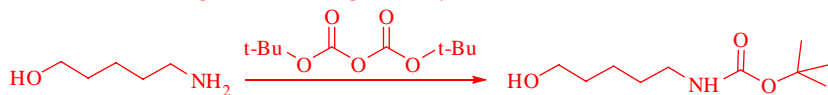
- f) Based on our discussions of similar enantioselective catalysts, propose a catalyst interaction with the transition state structure drawn above. **Hint:** use the most electron rich sterically accessible Lewis basic sites on the substrate to coordinate the Lewis acid reagent. (5 pts.)



3. Throughout the course, we discussed examples of chemo-, regio- and stereoselective reactions. Show one example of each type of reaction and briefly describe why the process is selective. You do not need an exact literature example, but you should show a structure that illustrates your point. You should show the reagents and draw the product. (30 pts.)

1) Example of a chemoselective reaction

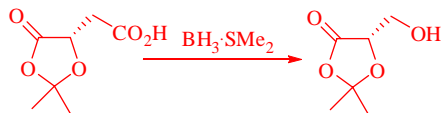
a) From exam 1: *amine protection in the presence of an alcohol*



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

Reason: amines are much better Nu's than alcohols.

b) From lecture notes: *borane reduction of carboxylic acid in the presence of the more electrophilic lactone.*

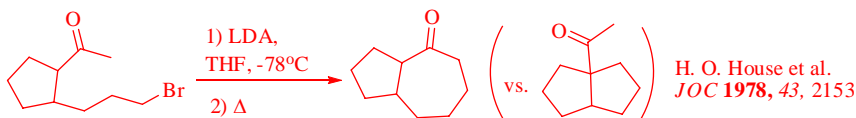


W. C. Still et al. *JACS* **1980**, *102*, 2117.

Reason: carboxylic acid loses proton and the resulting oxyanion bonds with boron. Ester/lactone can't lose a proton and bond with boron.

2) Example of a regioselective reaction

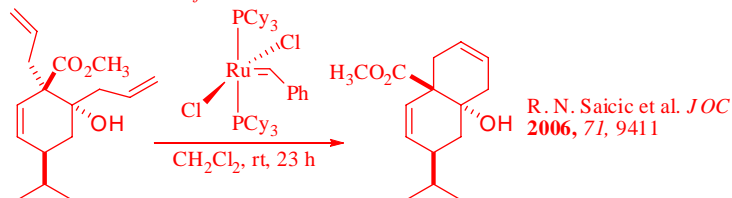
a) From PS 1: *selective enolate formation and reaction*



H. O. House et al. *JOC* **1978**, *43*, 2153

Reason: bulky LDA removes less hindered alpha proton, leading to formation of cycloheptanone instead of acetyl-cyclopentane ring.

b) From PS 3: *selective olefin metathesis*

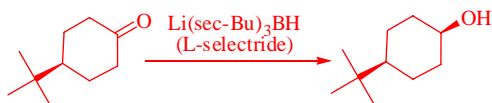


R. N. Saicic et al. *JOC* **2006**, *71*, 9411

Reason: terminal olefins react faster because they are less hindered and they form the more thermodynamically stable cyclohexene ring.

3) Example of a stereoselective reaction

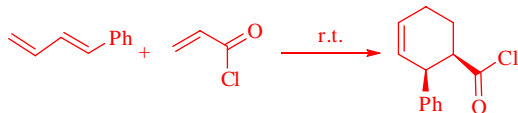
a) From exam 2: *borohydride reduction of a ketone*



H. C. Brown et al. *JACS* **1972**, *94*, 7159.

Reason: highly bulky L-selectride must approach ketone from less hindered equatorial direction leading to an axial alcohol.

b) From exam 2: *Diels-Alder reaction*

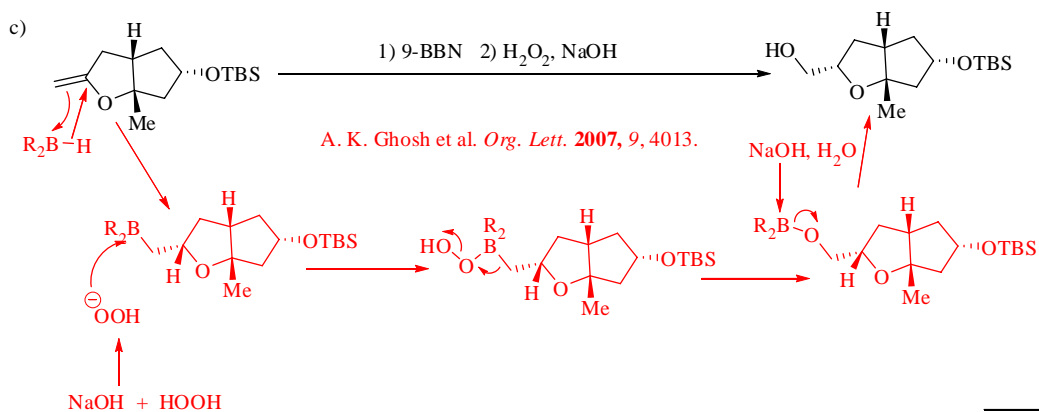
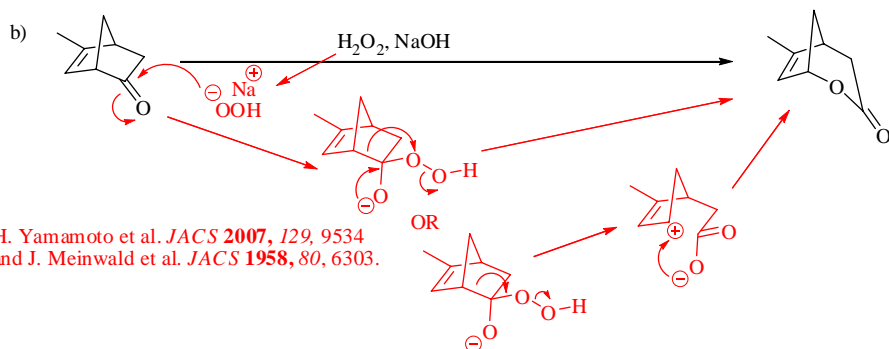
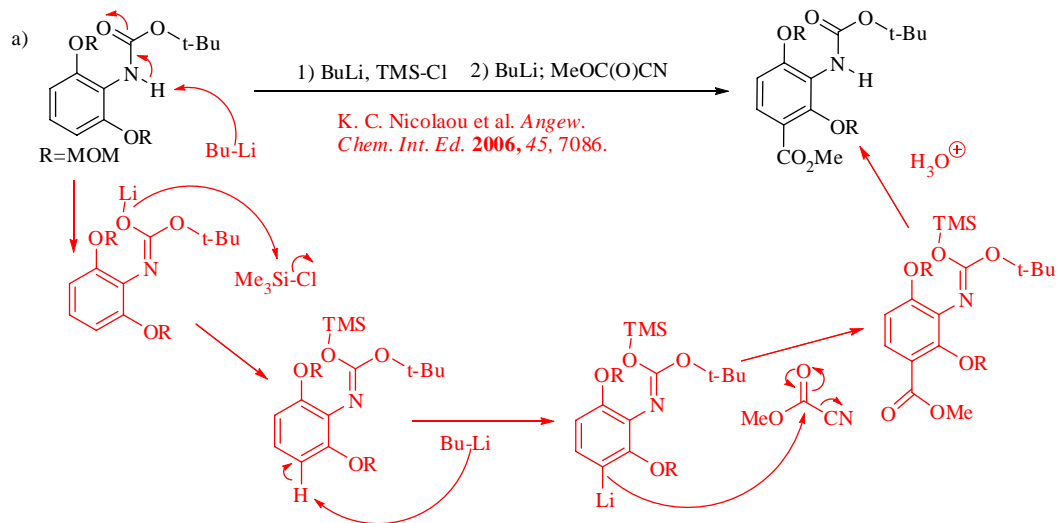


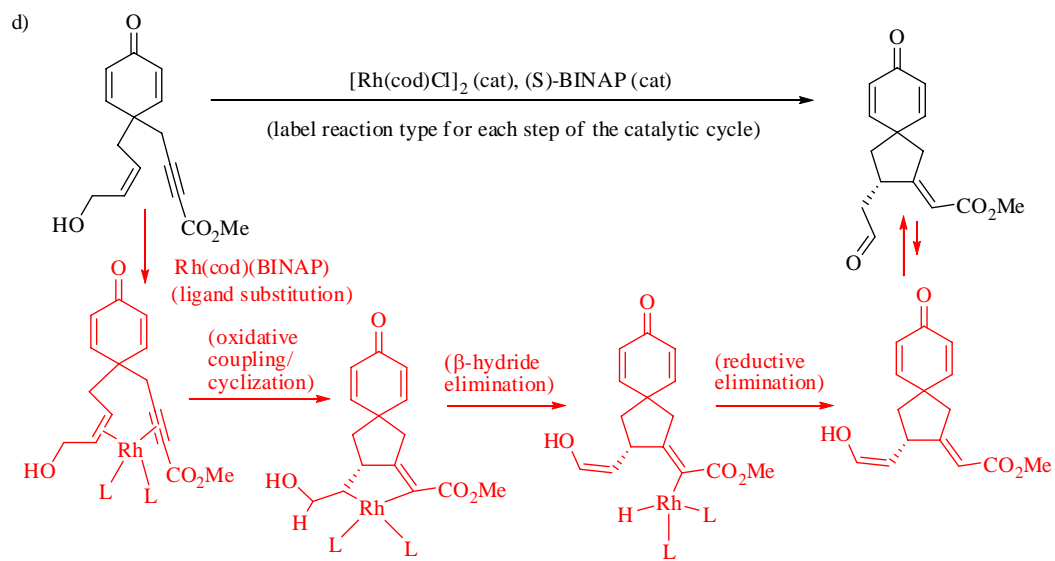
J. S. Meek et al. *JACS* **1952**, *74*, 2669.

Reason: Diels-Alder reaction favors an endo transition state due to secondary orbital overlap interactions between C-2 in diene and C-1 in acryloyl chloride.

The following two questions, 4 and 5, have four parts each. Undergraduate students must answer five of the eight parts and at least two from each section. Graduate students must answer six of eight parts. (12 pts. each)

4. Propose a mechanism for the following reactions.





5. Provide a series of synthetic reactions to transform the starting material to the product shown.

