Chem 112A: Second Midterm

October 30th, 2012

Please provide all answers in the space provided. You are not allowed to use a calculator for this exam, but you may use (previously disassembled) molecular model kits. Including the title page, there should be **8** total questions spread over **9** pages.

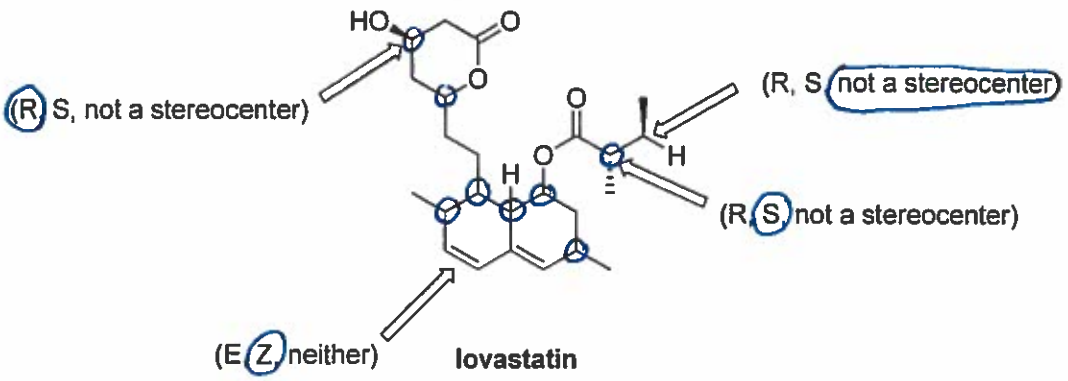
Name: Answer Key

GSI/Section: _____

Question	Points
1	_____ (28)
2	_____ (20)
3	_____ (18)
4	_____ (18)
5-6	_____ (20)
7	_____ (8)
8~~a~~ a-b	_____ (~~8~~)(8)
8~~b~~ c	_____ (~~8~~)(5)
TOTAL	_____ (125)

1. Lovastatin, a naturally occurring compound (initially isolated from the fungus *Aspergillus terreus*), was the first statin drug approved by the FDA for treatment of high LDL cholesterol. Like many natural products, the biosynthetic pathway leads to a single stereoisomer.

   a. Several sites are labeled with an arrow on the structure below. For each one, circle the appropriate stereochemical descriptor. (12 pt)



   b. Lovastatin contains several additional stereocenters, whose configuration is not depicted in this drawing. **Circle** all of the asymmetric carbon stereocenters (<u>not</u> including alkene carbons) in the structure above. (5 pt)

   c. Based on the number of asymmetric carbons (<u>not</u> including alkene stereochemistry) how many total stereoisomers of lovastatin are possible? Show your work. (2 pt)

$2^n = 2^8$ $n = 8$ stereocenters

   d. Lovastatin is provided to patients as a single stereoisomer, which (like many drugs) binds strongly to human plasma proteins in the bloodstream. (8 pt)

      i. Would you expect the enantiomer of lovastatin to have the same solubility in water as lovastatin? Yes

      ii. Would you expect a diastereomer of lovastatin to have the same solubility in water as lovastatin? No

      iii. Would you expect the enantiomer of lovastatin to have the same intermolecular interactions with plasma proteins as lovastatin? NO

      iv. Would you expect a diastereomer of lovastatin to have the same intermolecular interactions with plasma proteins as lovastatin? No

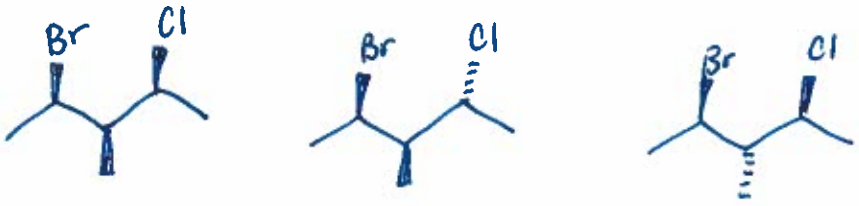
e. 1 pt "free credit"

Points earned 27 28

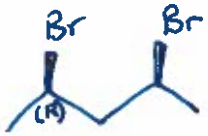
2. Draw pictures to match the following instructions. Make sure that when you draw stereocenters, you follow the conventions described in class. (20 pt)

   a. A chiral compound and its enantiomer.

   b. A set of three compounds which are all diastereomers of each other.



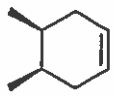
   c. An achiral compound which contains a stereocenter with R configuration.



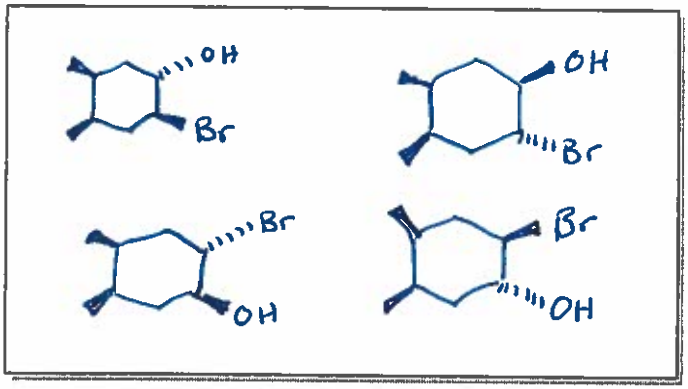
   d. A pair of compounds which are constitutional isomers of each other.

Points earned_____

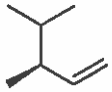
3. Draw the product(s) for each of the following reactions. (*Note: Explicitly draw each stereoisomer that could form. Duplicate answers (identical compounds) will cancel credit for correct answers.* (18 pt)



Br_2, H_2O →

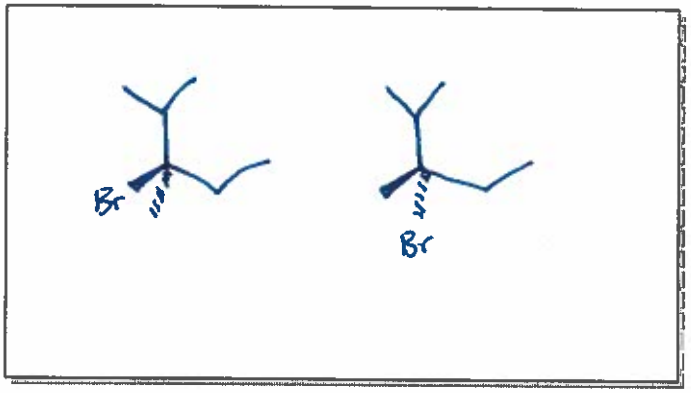


5 pt

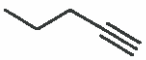


HBr

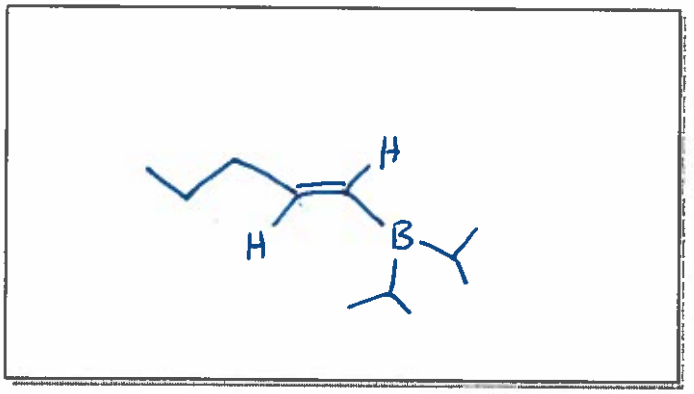
(H⊖ shift)



5 pt



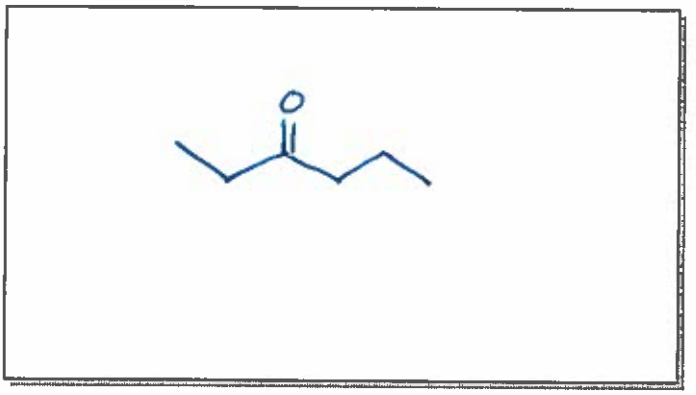
iPr_2BH (1 equiv.) →



4 pt

1. $Hg(OAc)_2$, H_2O →

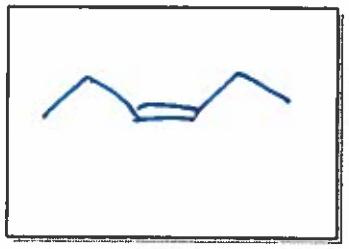
2. $NaBH_4$, NaOH



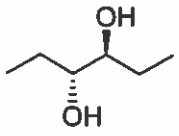
4 pt

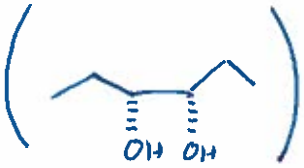
Points earned_____

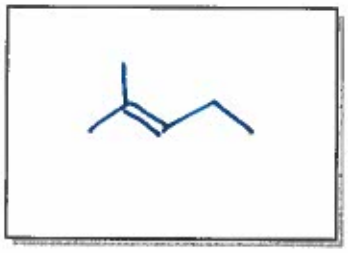
4. Propose an **alkene** starting material and the necessary reagent(s) to regioselectively and stereoselectively synthesize each of the following compounds. Use no more than two steps for each synthesis. (18 pt)



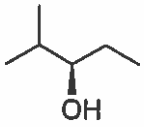
OsO_4, H_2O



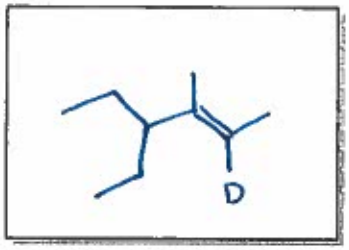




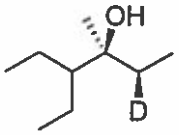
1. BH_3
2. H_2O_2, NaOH



(racemic)

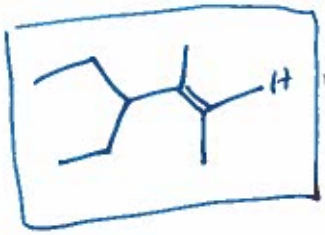


1. $Hg(OAc)_2$, H_2O
2. $NaBH_4$, NaOH



(racemic)

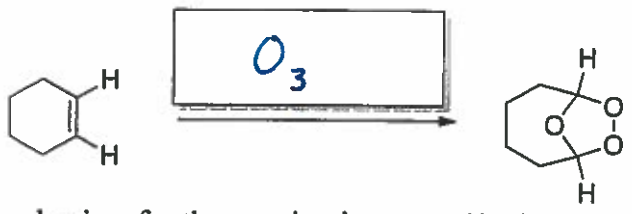
Or



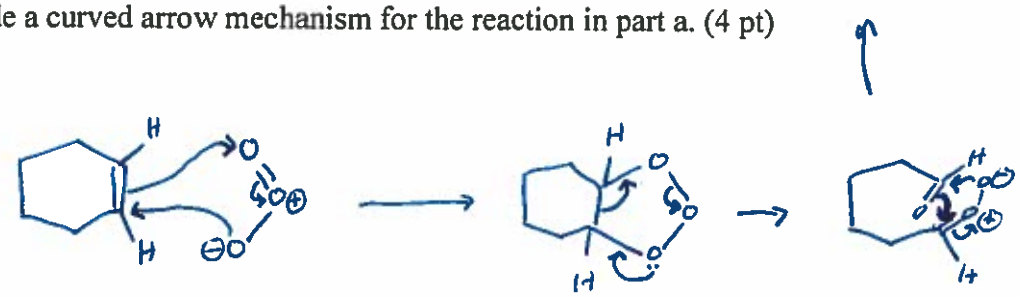
1. $Hg(OAc)_2$, H_2O
2. $NaBD_4$, NaOH

Points earned_____

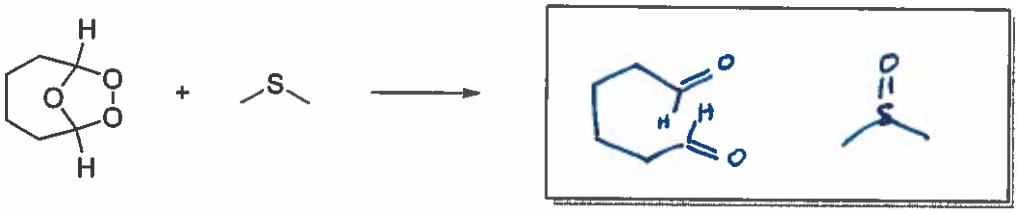
5. a. Provide reagent(s) for the following reaction: (4 pt)



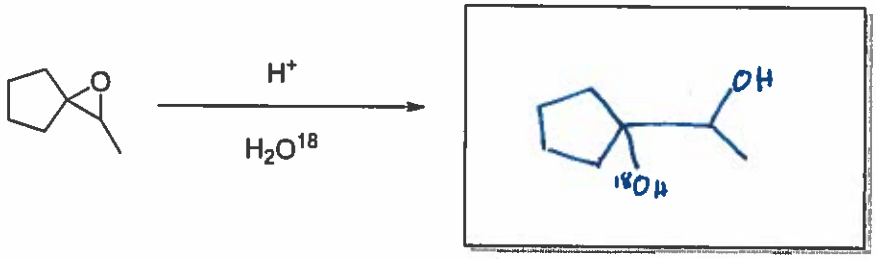
b. Provide a curved arrow mechanism for the reaction in part a. (4 pt)



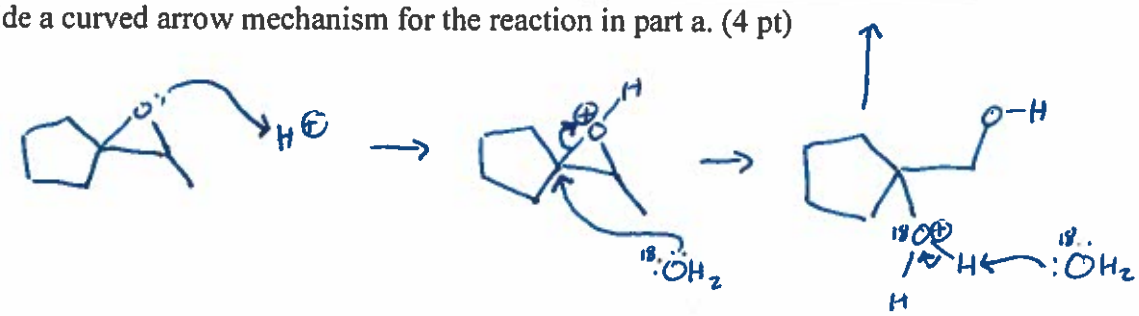
c. Provide the products of the following reaction. Make sure this reaction scheme is balanced: (4 pt)



6. a. Predict the product of the following transformation, indicating isotopic substitution (^{18}O) where appropriate: (4 pt)

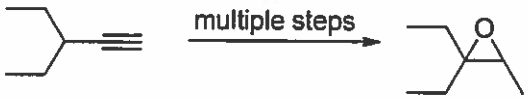


b. Provide a curved arrow mechanism for the reaction in part a. (4 pt)

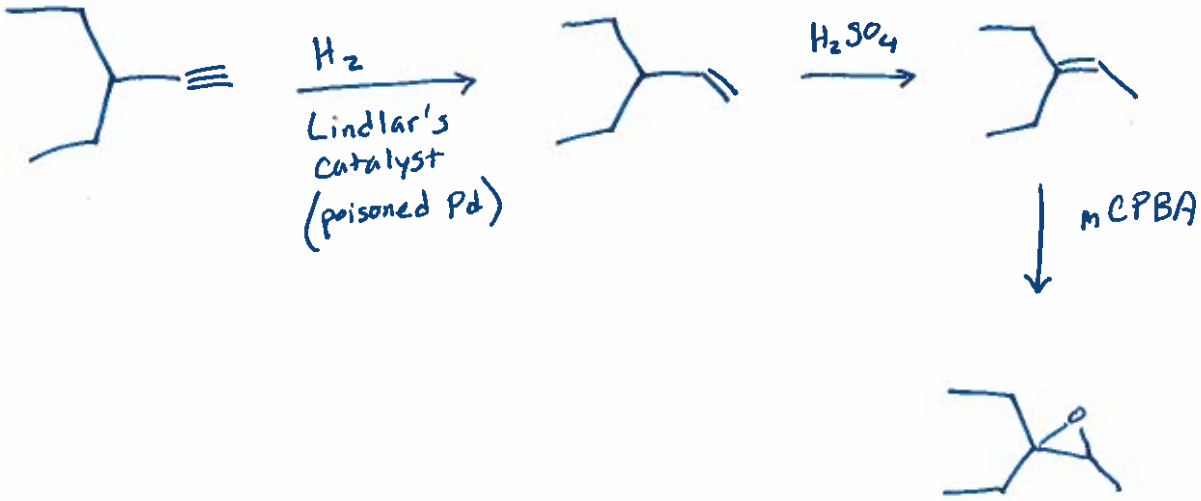


Points earned_____

7. Provide reagents that will accomplish the following transformation. (8 pt)



Your answer should be in the following format such that the final isolable product is the desired structure shown on the right above. You do not need to show mechanisms for your transformation(s).

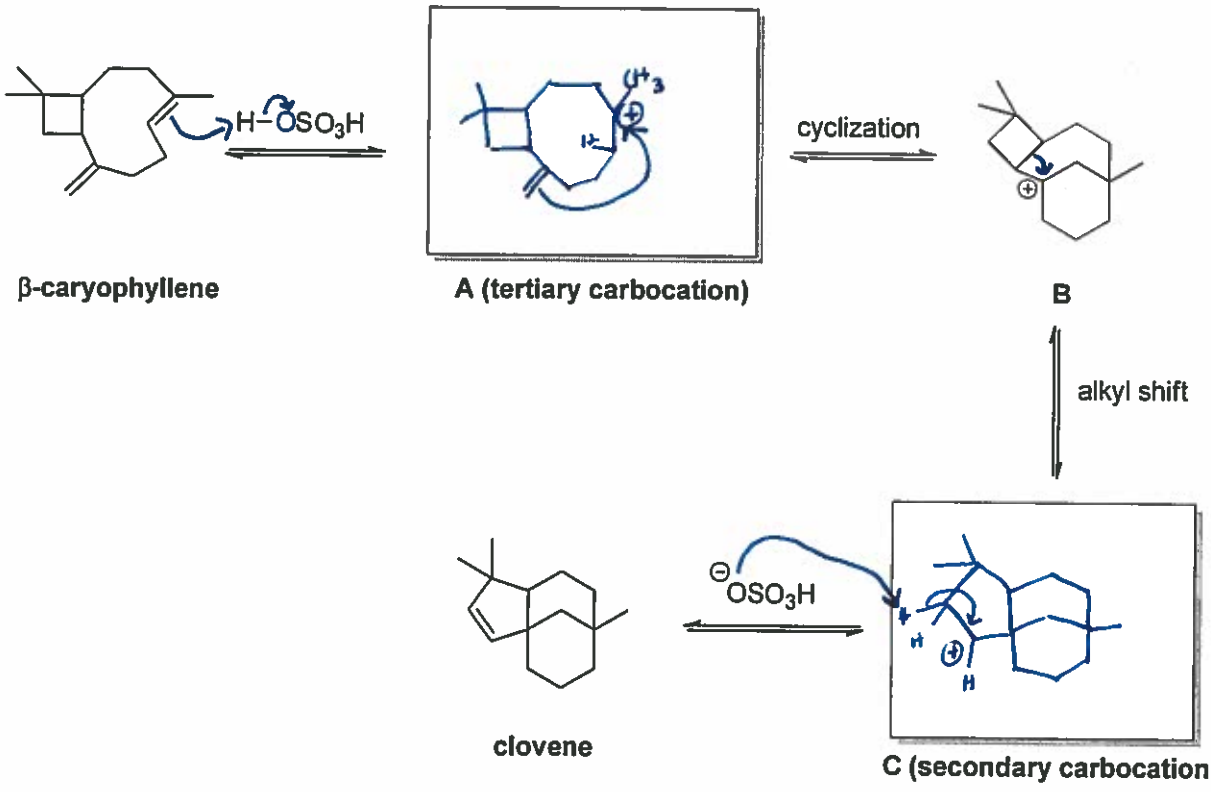


Points earned_____

8. β-Caryophyllene is a sesquiterpene natural product that is found in the essential oils from a number of plant sources, including cannabis, cloves, cinnamon, and black pepper. In a study of the mechanism and products of acid-catalyzed rearrangement of β-caryophyllene,[1] Fitjer and coworkers reported that reaction with excess sulfuric acid in diethyl ether leads to a complex mixture of products whose composition changes over time.

β-caryophyllene

a. Clovene is one of the products from this acid-catalyzed rearrangement of β-caryophyllene. **Fill in the boxes** below and **add curved arrows** to complete this mechanism. (6 pt)



β-caryophyllene | A (tertiary carbocation) | B | clovene | C (secondary carbocation)

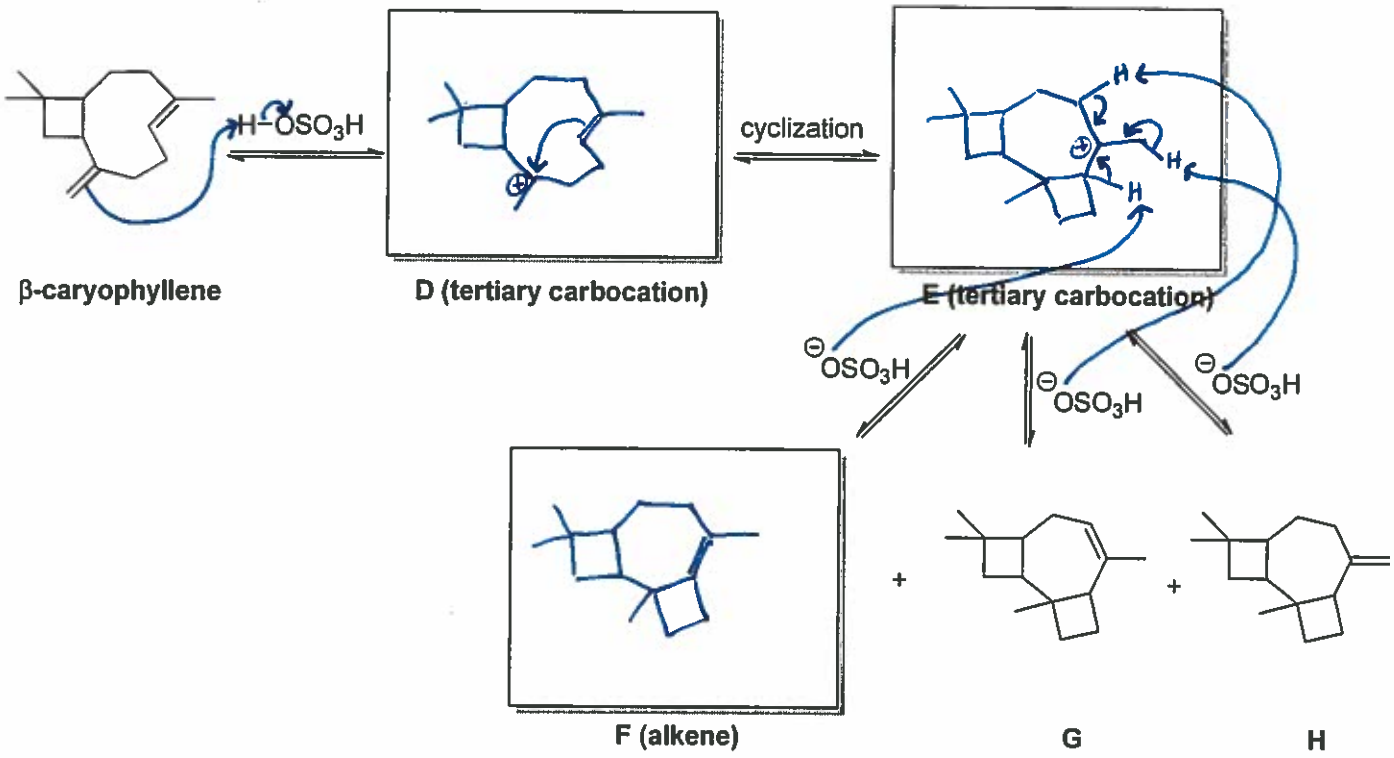
b. What is the driving force for the carbocation rearrangement of B to C? (2 pt)

ring strain (4-membered ring)

[1] *J. Am. Chem. Soc.* **1995**, *117*, 9180-9189.

Points earned_____

c. Three other products from the acid-catalyzed rearrangement of β-caryophyllene are alkenes F, G, and H, each of which can be formed by deprotonation of intermediate E. **Fill in the boxes** below and **add curved arrows** to complete this mechanism. (5 pt)



Points earned 5