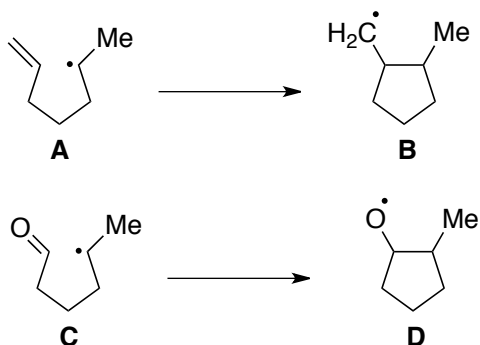


CEM 852 Exam-1

February 11, 2017

This exam consists of 5 pages. Please make certain that your exam has all of the necessary pages. Total points possible for this exam are 100. In answering your questions, please write legibly and draw all structures clearly. Write all your answers in the exam booklets. Good luck.

- I. The radical cyclization of **A** to **B** proceeds smoothly, even though the reaction starts with a secondary carbon radical and ends with a less stable primary carbon radical. In contrast the radical cyclization of **C** to **D** is not a facile process. Explain. (5 pts)



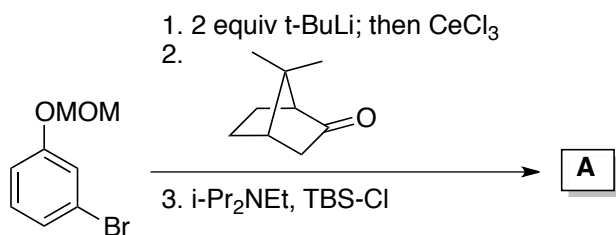
- II. Using words or chemical examples, define the following terms: (a) the Curtin-Hammett principle, (b) chemoselectivity, (c) double diastereodifferentiation, and (d) the Ireland model for ester E-enolate formation. (16 pts)

- III. Provide an example of an optically active (*R*)-allene. (2 pts)

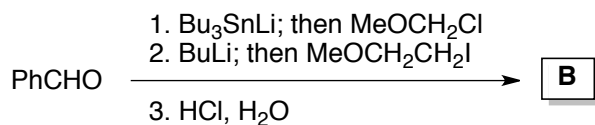
- IV. Illustrate the use of a ketene synthon in a [4+2] cyclization, including any post-Diels-Alder modifications. (3 pts)

- V. Provide the product or products of the reactions outlined below. Show all intermediate compounds and be sure to indicate the product's relative or absolute stereochemistry. For reactions where multiple products are possible, be sure to indicate the major and minor species. (30 pts)

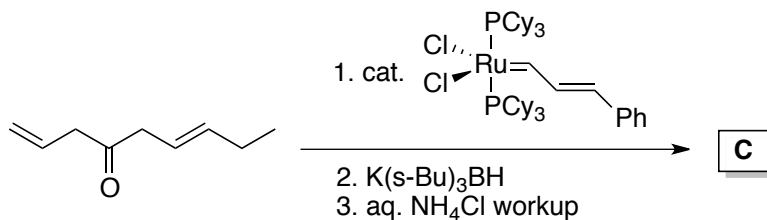
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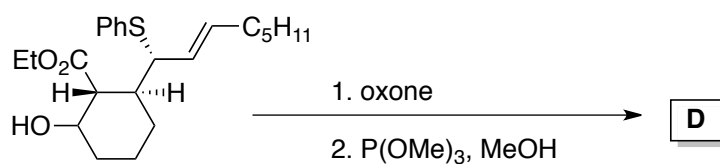
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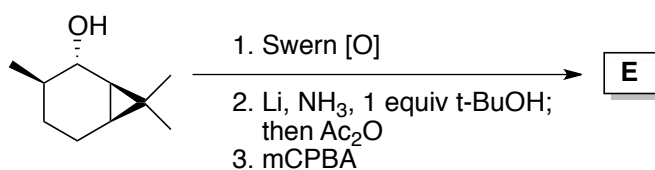
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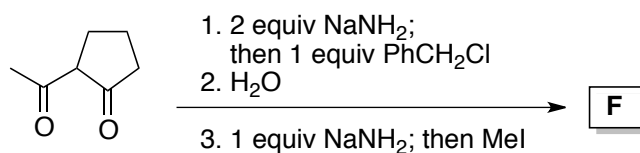
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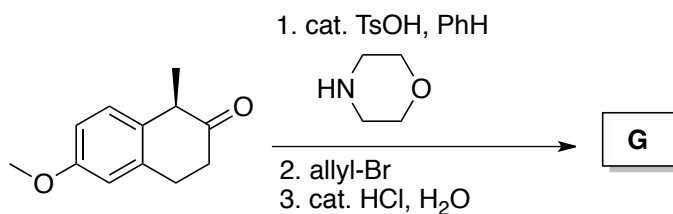
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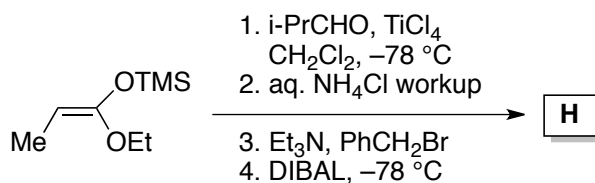
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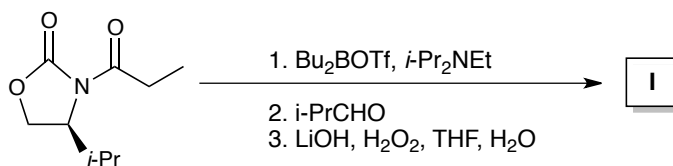
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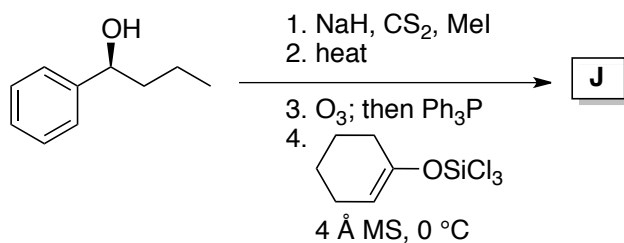
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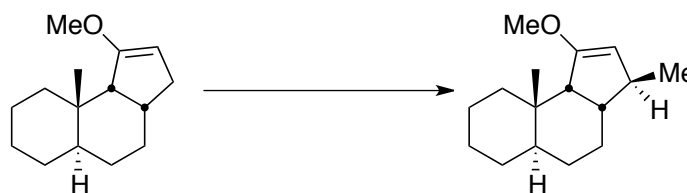


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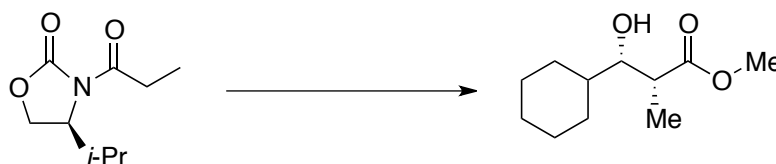


VI. Provide conditions that will effect the transformations outlined below. Some of these conversions will require more than one reaction, so be sure to show all intermediate compounds. (18 pts)

1.



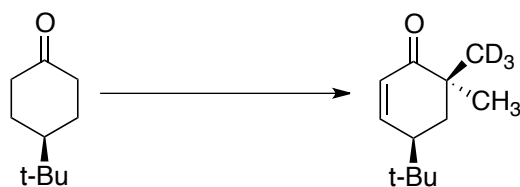
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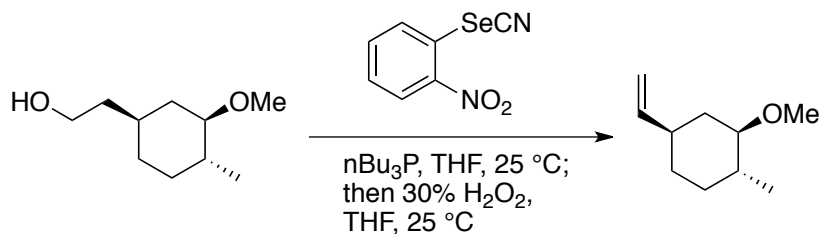
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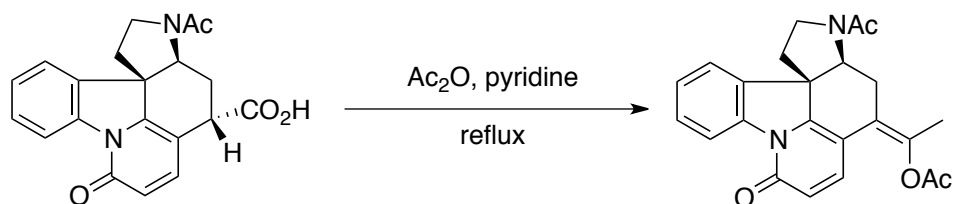
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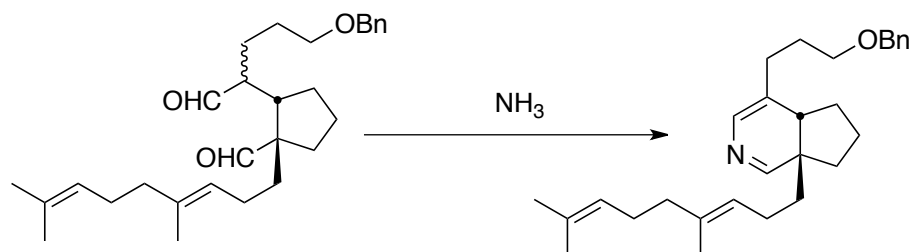
VII. Provide a complete arrow (electron) pushing mechanism for the following transformation. (Note: you don't have to show the mechanism for the H_2O_2 oxidation) (6 pts)



VIII. Provide a complete arrow (electron) pushing mechanism for the following transformation. (6 pts)

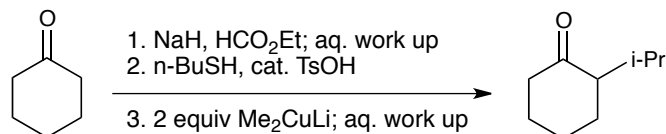


IX. Provide a complete arrow (electron) pushing mechanism for the following transformation. (6 pts)



X. The alkylation of the LDA formed enolate of cyclohexanone with isopropyl iodide can be problematic, often regenerating the cyclohexanone and propylene. Provide a mechanism that explains this problematic observation (2 pts)

XI. The Scheme below shows a three-step process that provides 2-isopropylcyclohexanone in high yield. Provide a complete arrow (electron) pushing mechanism for that transformation (6 pts)



Bonus Question: (2 pts) Today is my daughter's birthday. Famous people born on February 11, include Jennifer Aniston, Thomas Edison, and of course the rapper Nasty C. I couldn't find any famous chemists born on her birthday, BUT I share a birthday with the "father of chemistry and uncle of the Earl of Cork". Who is he?

- (a) Robert Boyle
- (b) John Dalton
- (c) Michael Faraday
- (d) Joseph Priestly
- (e) Ned Brainard

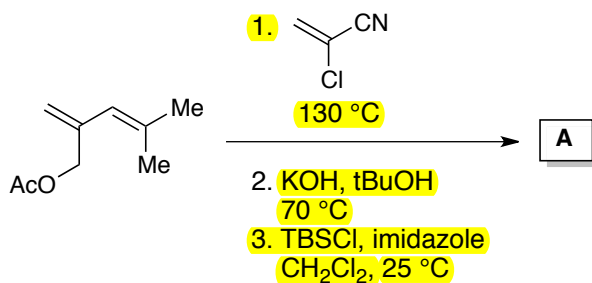
CEM 852 Exam-2

March 25, 2017

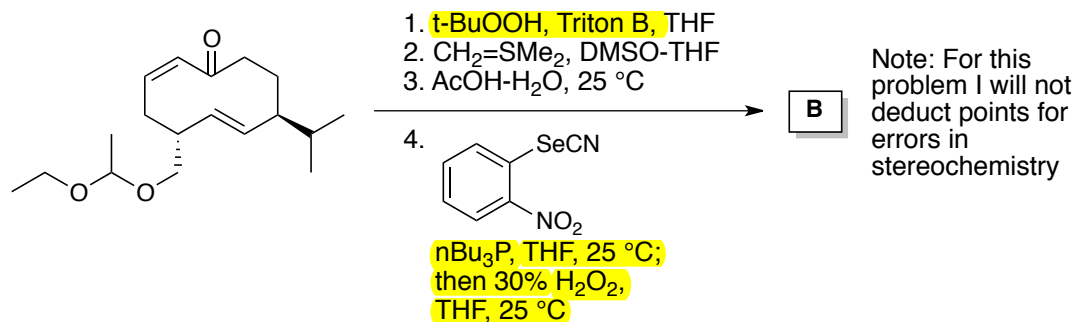
This exam consists of 6 pages. Please make certain that your exam has all of the necessary pages. Total points possible for this exam are 100. In answering your questions, please write legibly and draw all structures clearly. Write all your answers in the exam booklets. Good luck.

- I. Illustrate the use of a ketene synthon in a [4+2] cyclization, including any post-Diels-Alder modifications. (3 pts)
- II. Provide examples of the following name reactions: (a) Baylis-Hillman reaction, (b) Eschenmoser-Claisen rearrangement, (c) Paterno-Büchi reaction, (d) Sakurai reaction, (e) Sharpless epoxidation. (10 pts)
- III. Provide the product or products of the reactions outlined below. Show all intermediate compounds and be sure to indicate the product's relative or absolute stereochemistry. For reactions where multiple products are possible, be sure to indicate the major and minor species. (27 pts)

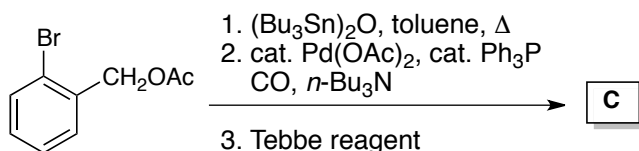
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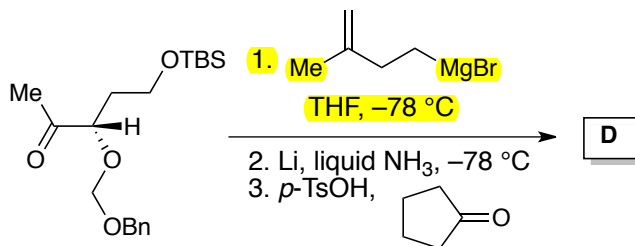
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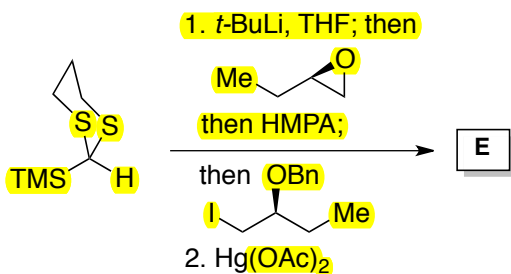
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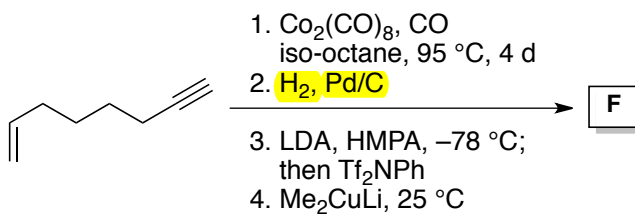
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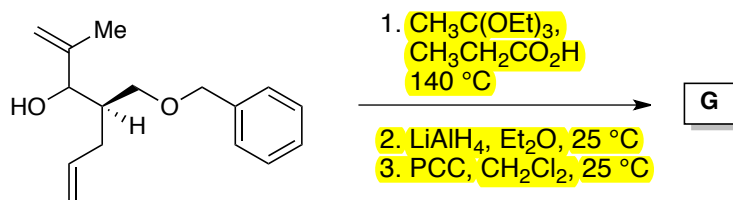
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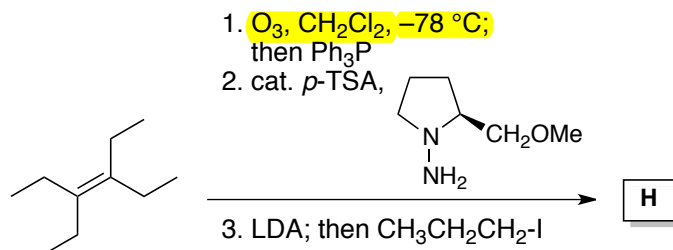
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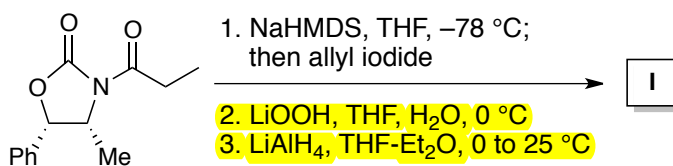
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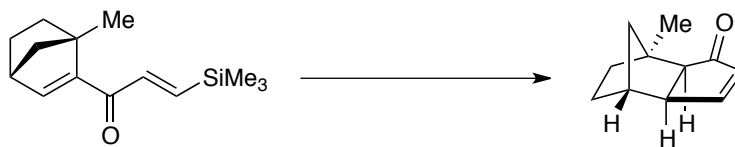


9.



IV. Provide conditions that will enable the transformations outlined below. Some of these conversions will require more than one reaction, so be sure to show all intermediate compounds. (15 pts)

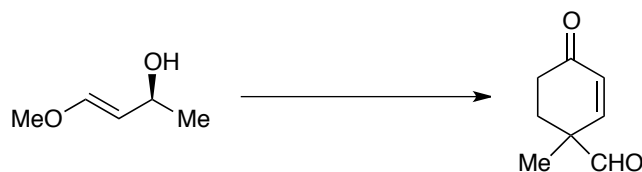
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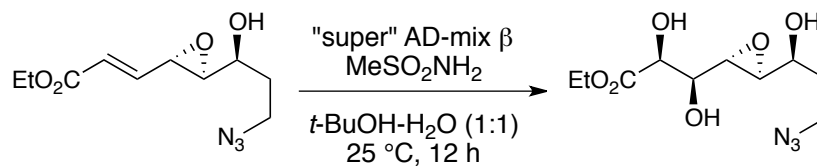
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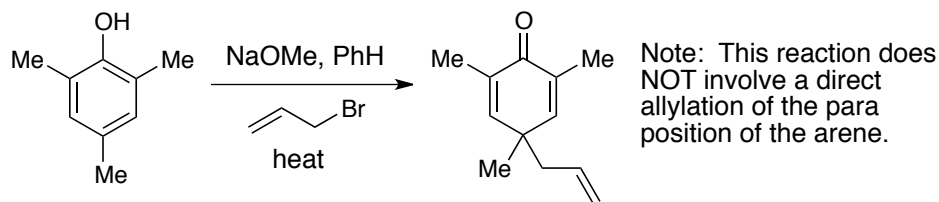
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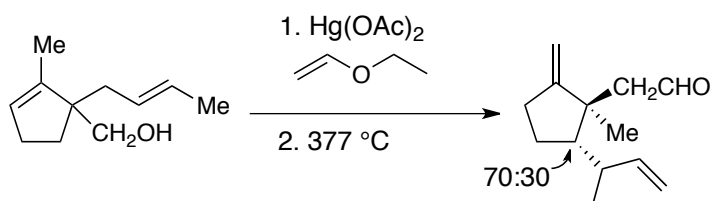
V. The Sharpless asymmetric dihydroxylation traditional employs AD-mix α or AD-mix β . "Super" AD-mix β consists of $K_3Fe(CN)_6$, K_2CO_3 , $(DHQD)_2PHAL$, $K_2OsO_2(OH)_4$ in a molar ratio of 3.0:3.0:0.1:0.01. Describe the role of each of these "Super" AD-mix β components. (3 pts)



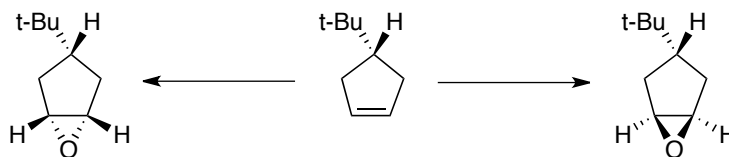
- VI. Provide a complete arrow (electron) pushing mechanism for the following transformation. (3 pts)



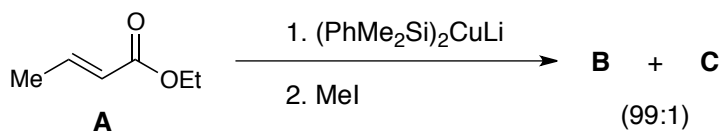
- VII. Provide a complete arrow (electron) pushing mechanism for the following transformation. (6 pts)



- VIII. Provide the two sets of conditions that will convert 4-*t*-butylcyclopentene into the two stereocomplementary epoxides shown below. (4 pts)

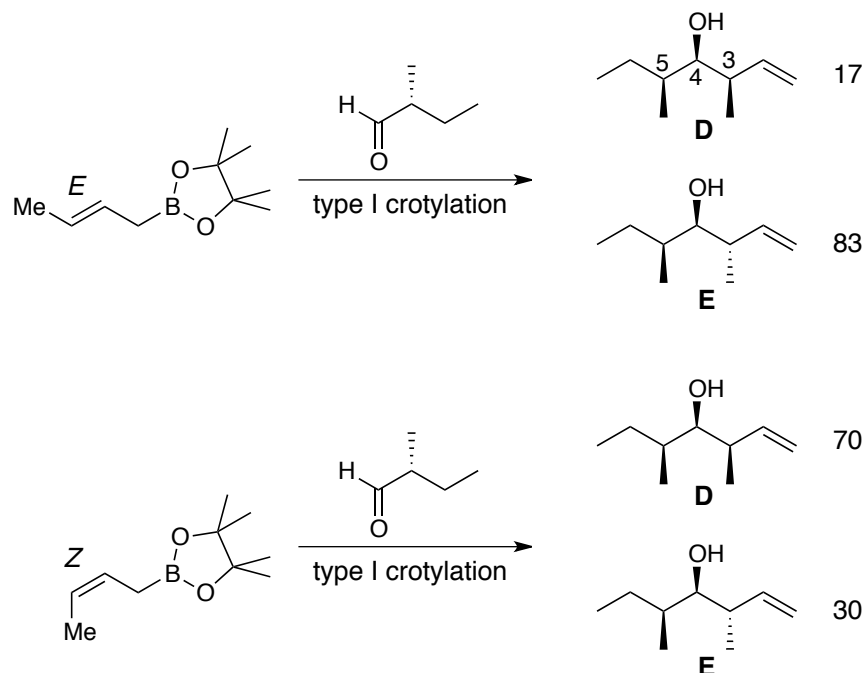


- IXa. The cuprate addition of $(\text{PhMe}_2\text{Si})_2\text{CuLi}$ to trans-crotonate **A** followed by trapping with MeI affords compounds **B** and **C** in a ratio of 99:1 (82% yield). The relative diastereoselectivity can be explained by a minimization of A(1,3) allylic strain in the intermediate ester enolate. Provide the structures of **B** and **C** and illustrate the conformation of the ester enolate that minimizes its A(1,3) allylic strain. (Hint: In the reactive conformation the Si-group is the “large” group.) (6 pts)



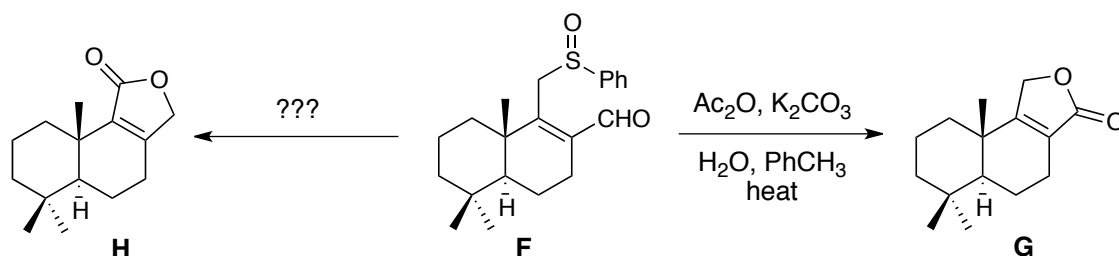
- IXb. The authors of the above work also offer an alternative explanation for the observed diastereoselectivity. This alternate explanation involves a cyclic intermediate. Base on this information and your CEM 850 knowledge of the properties/reactivity of silanes propose a cyclic intermediate that would also afford the same sense of relative diastereoselection. (2 pts)

- X. A type I crotylation of optically active 2-methylbutanal affords homoallylic alcohols **D** and **E**. Using the *E*-boronate affords **D** and **E** in a ratio of 17:83. In contrast, the *Z*-boronate affords **D** and **E** in a ratio of 70:30.



- (a) Explain why the *E*-boronate favors formation of the 3,4-anti product, while the *Z*-boronate favors formation of the 3,4-syn product. (6 pts)
- (b) Explain why the 4,5-syn products are always favored. (3 pts)
- (c) Explain why reaction of the *Z*-boronate is less selective (70:30) towards its major product than the *E*-boronate is towards its major product (83:17). (3 pts)

- XIa. We learned about the Pummerer reaction during the “Classics” presentation of Schreiber’s asteltoxin synthesis. An interesting application of a Pummerer-like reaction is that which can be carried out on sulfoxide **F** to afford lactone **G**. Provide a complete arrow (electron) pushing mechanism for that transformation. (6 pts)



- XIb. How would you alter the reaction conditions to enable the conversion of sulfoxide **F** to lactone **H**? (Hint: I would do this by modifying the Pummerer conditions used above and then reacting that product with aqueous HgCl_2) (3 pts)

Bonus Question: (2 pts) Curiously, Rudolf Pummerer probably did not discover the rearrangement that bears his name. Indeed, closely-related reactions were reported by Fromm & Achert and by Smythe before Pummerer's first papers on the subject were published in 1909 and 1910. In fact, a short biography of Pummerer that appeared in a 1951 issue of the *Journal of Chemical Education* doesn't even mention the reaction, but rather lists the Sandmeyer indigo process, the formation of lewlic acid from glucose, and the dehydrogenation of phenols as being among his notable accomplishments. The omission of what today we know as the Pummerer rearrangement was most certainly due to the reaction being rarely practiced until the 1960s. Nonetheless, the author of the *Journal of Chemical Education* article did note that Pummerer was an award-winning sports star. At what sport did Pummerer excel?

- (a) tennis
- (b) speed skating
- (c) ski jumping
- (d) handball
- (e) dodgeball

CEM 852 Final Exam

May 3, 2017

This exam consists of 7 pages. Please make certain that your exam has all of the necessary pages. Total points possible for this exam are 150. In answering your questions, please write legibly and draw all structures clearly. Write all your answers in the exam booklets. Good luck.

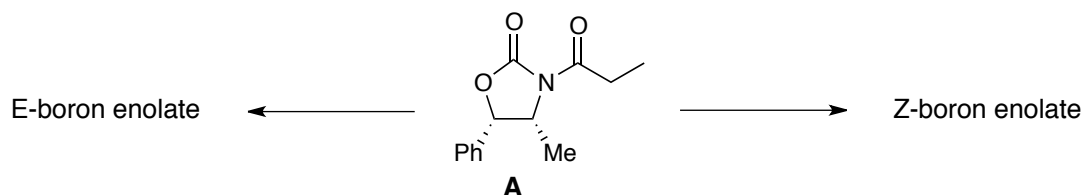
I. Provide the pKa's of the most acidic proton on following solvents within 2 pKa units. (10 pts)

- | | |
|----------------------|------------------|
| 1. acetic acid | 6. DMSO |
| 2. acetone | 7. ethanol |
| 3. acetonitrile | 8. ethyl acetate |
| 4. <i>t</i> -butanol | 9. toluene |
| 5. diisopropylamine | 10. water |

II. Explain, describe, or illustrate each of the following: (15 pts)

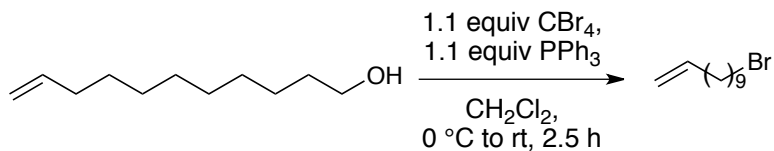
1. the Bürgi-Dunitz angle
2. the Felkin-Ahn model
3. matched/mismatched diastereoselectivity
4. the Sharpless epoxidation mnemonic
5. a Zimmerman-Traxler transition state

III. Provide conditions to convert Evans' oxazolidinone A into its *E*- and *Z*-boron enolates. Be sure to draw the *E*- and *Z*-boron enolates. (8 pts)

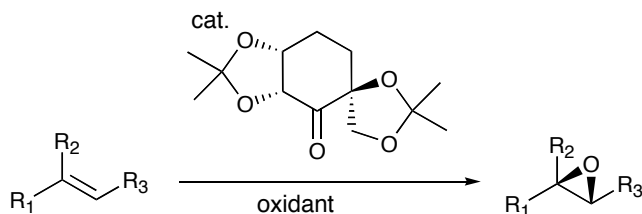


IV. Provide the name associated with each of the name reactions shown below. (15 pts).

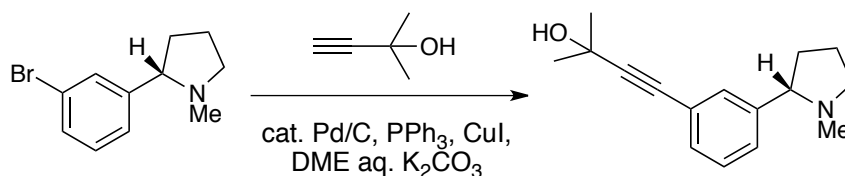
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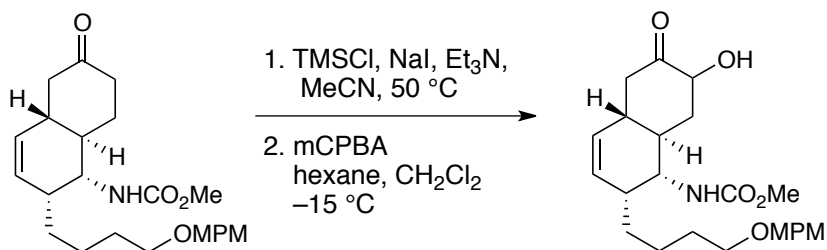
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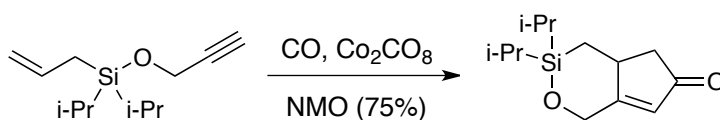
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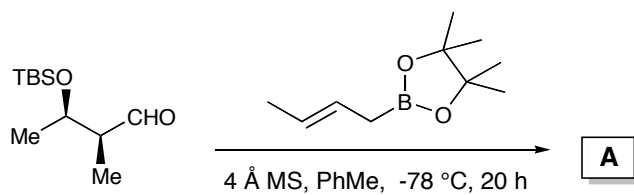


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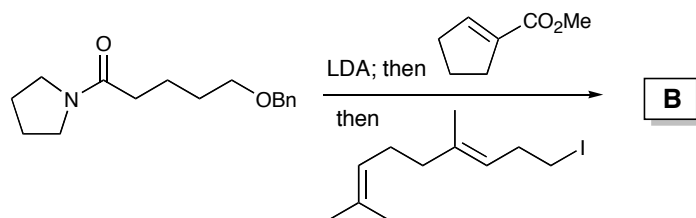


V. Provide the product or products of the reactions outlined below. Show all intermediate compounds and be sure to indicate the product's relative or absolute stereochemistry. For reactions where multiple products are possible, be sure to indicate the major and minor species. (40 pts)

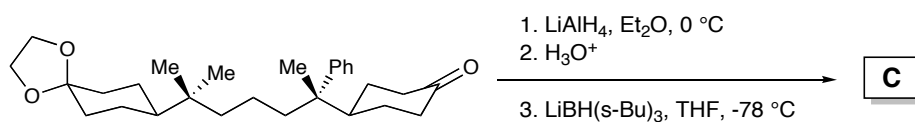
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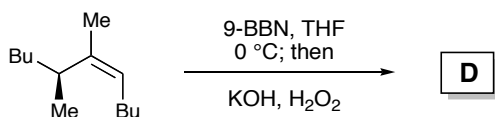
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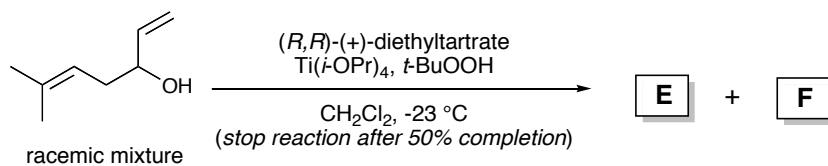
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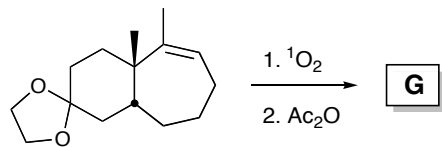
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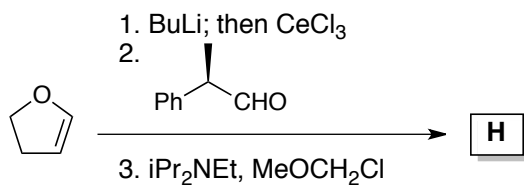
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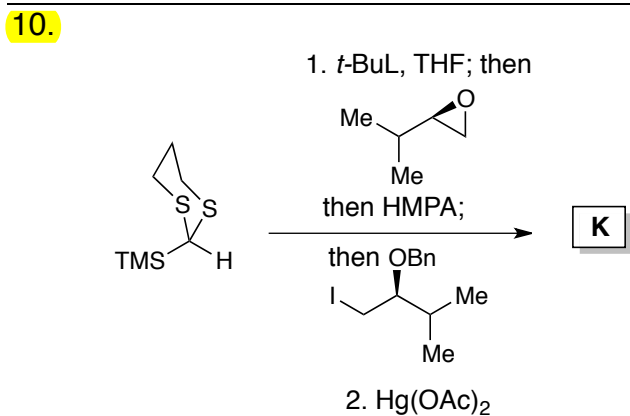
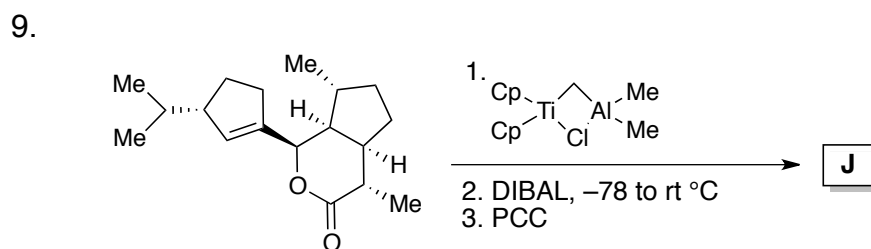
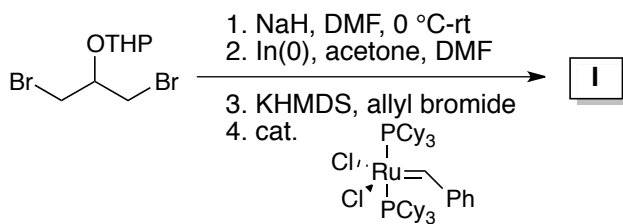
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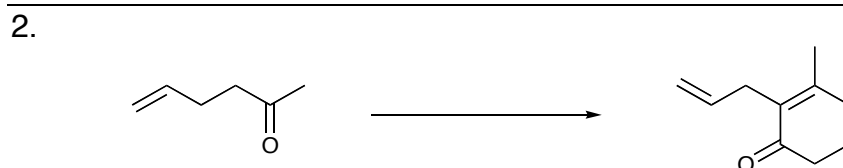
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8.



VI. Provide conditions that will effect the transformations outlined below. Some of these conversions will require more than one reaction, so be sure to show all intermediate compounds. (20 pts)



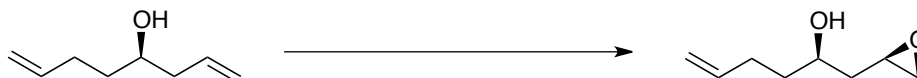
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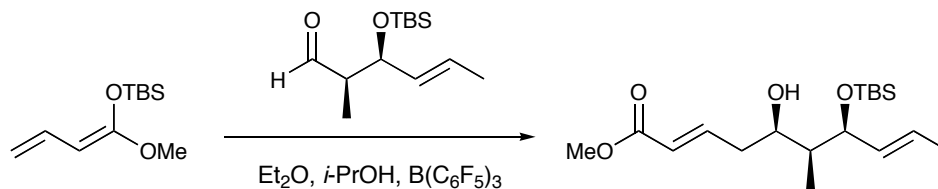
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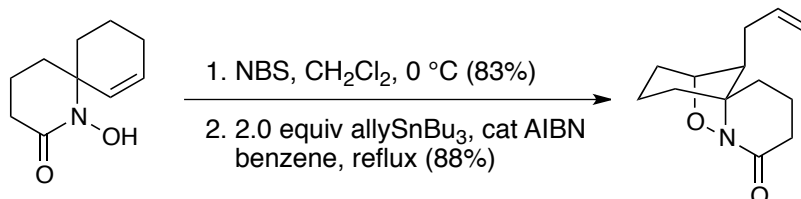
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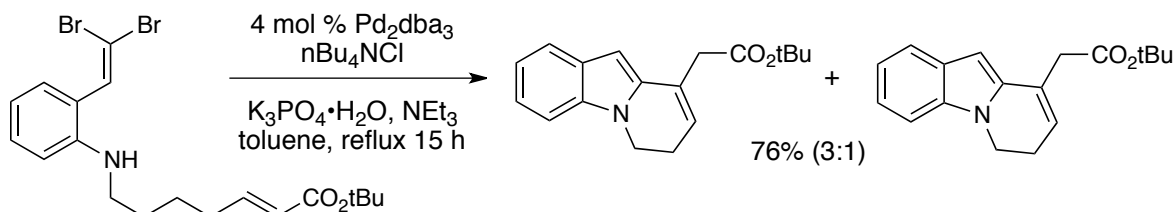
VIII. An example of the vinylogous Mukaiyama Aldol is shown below. Provide an explanation for the observed stereochemical outcome of that reaction. (6 pts)



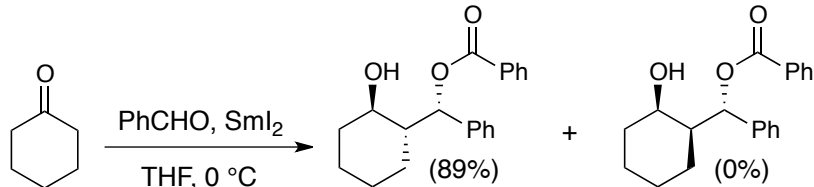
X. Provide a detailed arrow pushing mechanism for the reaction sequence below. For the first step, you may simply consider NBS as a source of "Br⁺". For the second step be sure your mechanism explains the role of AIBN and how the reaction propagates. (10 pts)



XI. For the reaction shown below, illustrate the catalytic cycle indicating all Pd bearing intermediates. (12 pts)

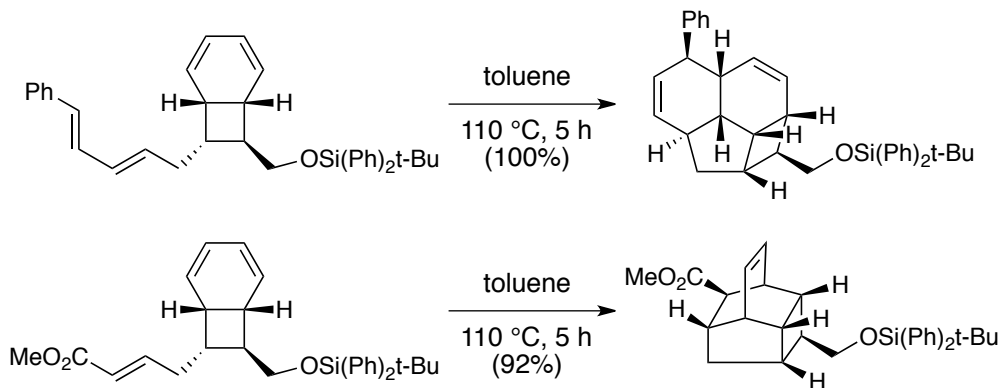


XII. Reaction of cyclohexanone, benzaldehyde, and samarium iodide exclusively affords the 1,2-syn-1,3-anti-product and none of the 1,2-anti-1,3-anti-product is observed.



The reaction is thought to proceed via a Sm mediated aldol, followed by an Evans-Tischenko reaction. Curiously, by adjusting the stoichiometry and stopping the reaction at low conversion, the 1,2-anti-aldol product predominates. Owing to this they suggest that this is an example of Le Chatelier's principle, with the relative rates of Evans-Tischenko reaction driving the equilibrium. Provide arrow pushing mechanisms for the Evans-Tischenko reaction on both the syn and anti aldolates. Why would one be favored over the other? (Hint: think about cyclohexanone reductions.) (12 pts)

XIII. Provide detailed arrow pushing mechanisms for two complementary reactions shown below. (10 pts)



Bonus Question: (2 pts) It appears the US Presidential election will pit Donald Trump vs. Hillary Clinton. Thus the US may see its first female President or it's first President to have been inducted into the World Wrestling Entertainment Hall of Fame, we will once again not see a chemist as President. History though has occasionally seen chemists rise to high political office, albeit not without the occasional controversy. Which chemist/political figure had the dubious distinction of being thrown out of a chemistry exam for cheating.

- Former Vice Prime Minister of Romania, Elena Ceausescu
- Princess of Thailand, HRH Princess Chulabhorn
- Former Massachusetts State Assemblyman, William S. Clark
- Former Prime Minister of the United Kingdom, Margaret Thatcher

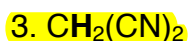
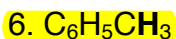
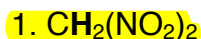
e. Fictional President in the 1973 film *Escape from the Planet of the Apes*, Matthew Williams

CEM 852 Final Exam

May 4, 2016

This exam consists of 7 pages. Please make certain that your exam has all of the necessary pages. Total points possible for this exam are 150. In answering your questions, please write legibly and draw all structures clearly. Write all your answers in the exam booklets. Good luck.

I. For the following compounds provide the pKa's of the hydrogen in **bold** within 2 pKa units. (10 pts)



II. Explain, describe, or illustrate each of the following: (15 pts)

1. kinetic resolution

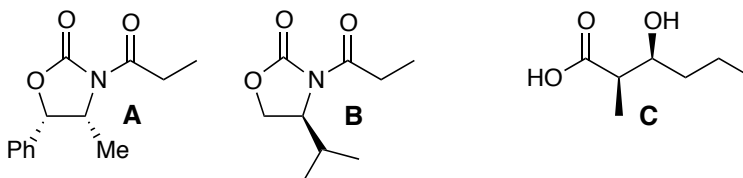
2. a syn-pentane interaction

3. double diastereodifferentiation

4. organocatalysis

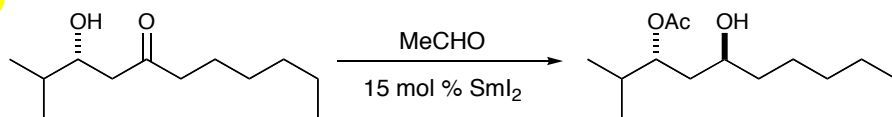
5. an outersphere mechanism (as coined by Noyori)

III. Which Evans' oxazolidinone should one use to form **C** in high enantiomeric excess? Explain your choice by illustrating a Zimmerman-Traxler transition structure that employs the oxazolidinone of your choosing. (6 pts)

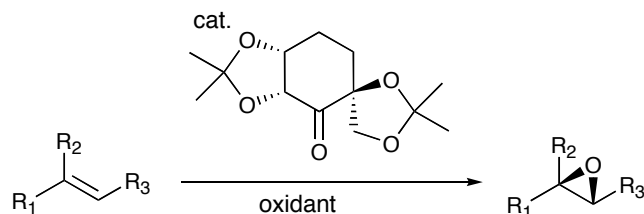


IV. Provide the name associated with each of the name reactions shown below. (10 pts).

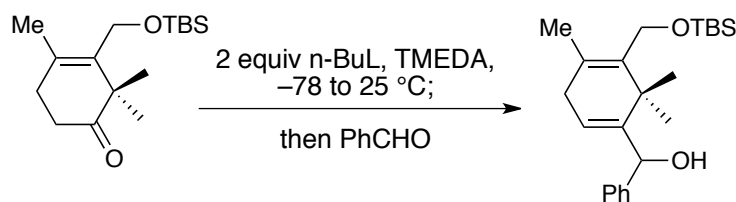
1.



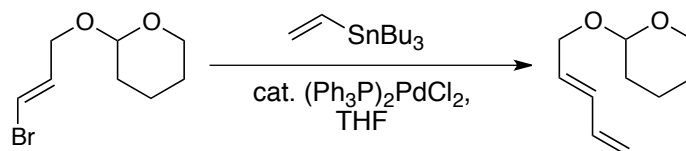
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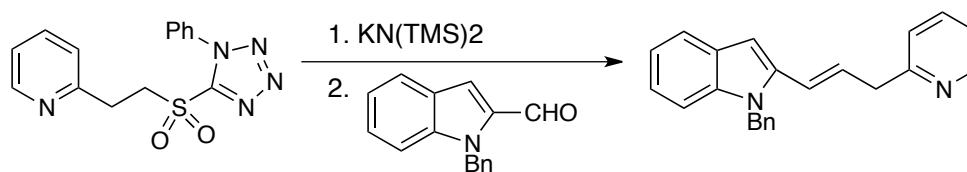
3.



4.

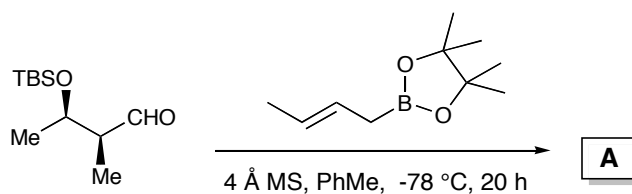


5.

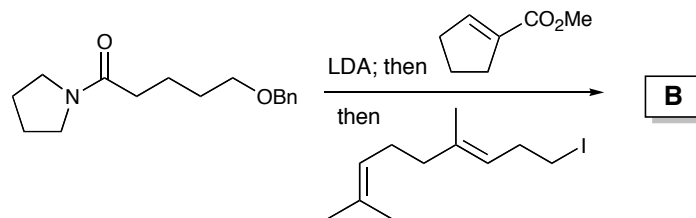


V. Provide the product or products of the reactions outlined below. Show all intermediate compounds and be sure to indicate the product's relative or absolute stereochemistry. For reactions where multiple products are possible, be sure to indicate the major and minor species. (40 pts)

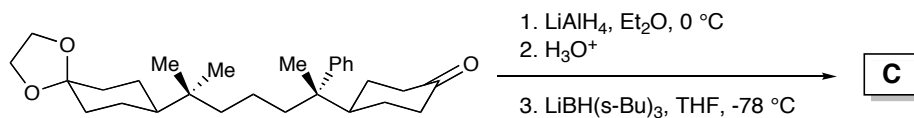
1.



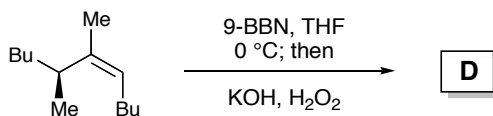
2.



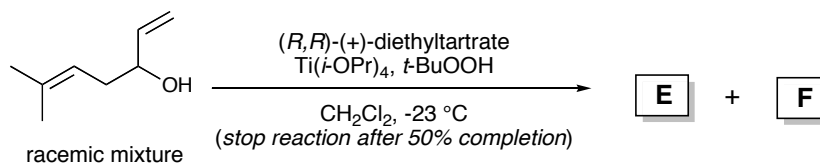
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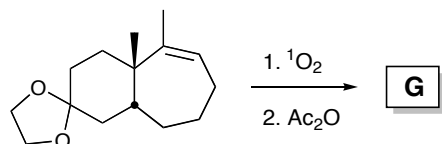
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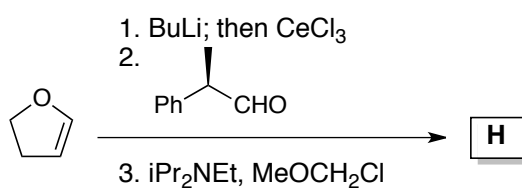
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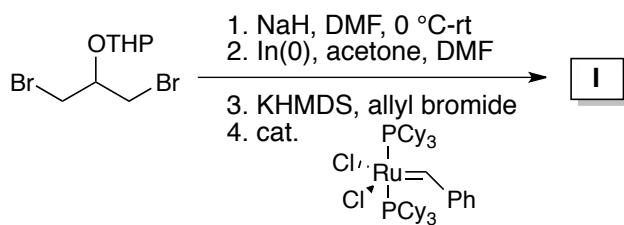
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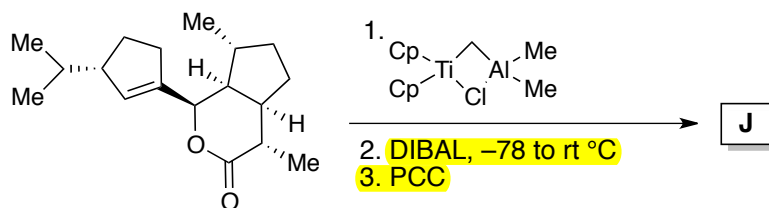
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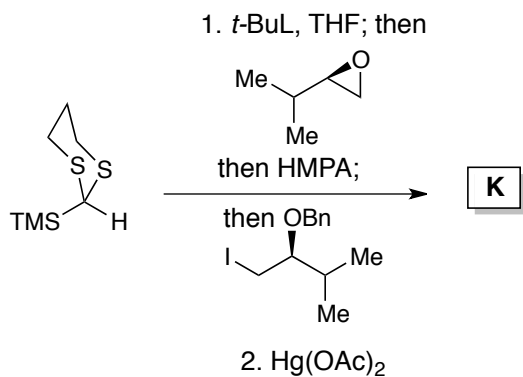
8.



9.



10.

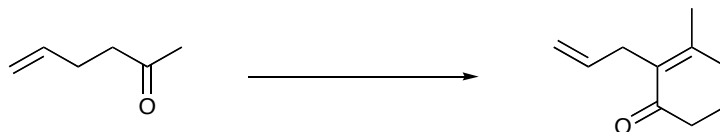


VI. Provide conditions that will effect the transformations outlined below. Some of these conversions will require more than one reaction, so be sure to show all intermediate compounds. (20 pts)

1.



2.



3.



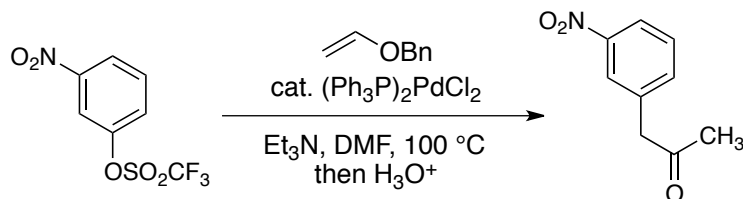
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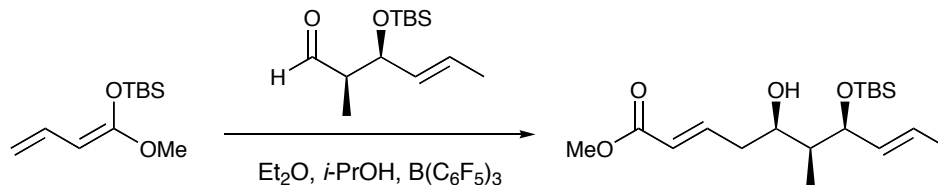
5.



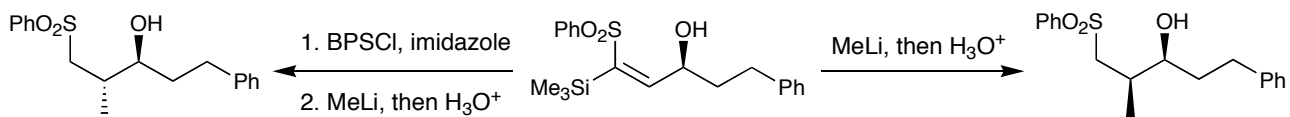
VII. Illustrate the catalytic cycle for the reaction below. (6 pts)



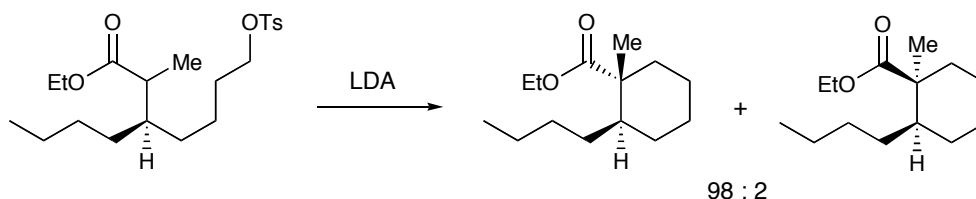
VIII. An example of the vinylogous Mukaiyama Aldol is shown below. Provide an explanation for the observed stereochemical outcome of that reaction. (6 pts)



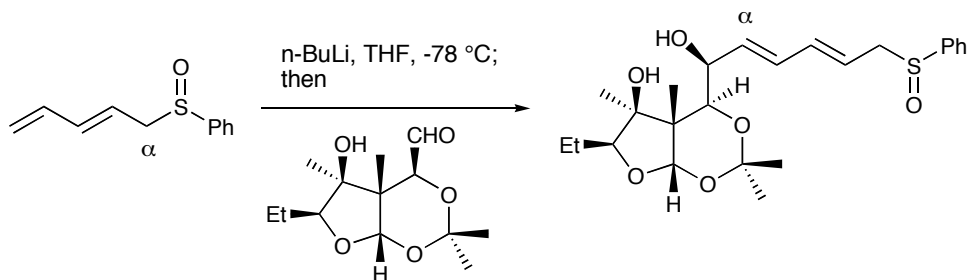
IX. When the alcohol shown below reacts with MeLi the (*R*)-isomer is formed. When that same alcohol is protected as a tert-butyldiphenylsilyl ether the reaction with MeLi affords the (*S*)-isomer. Using Felkin-Ahn-like models explain these observations. (6 pts)



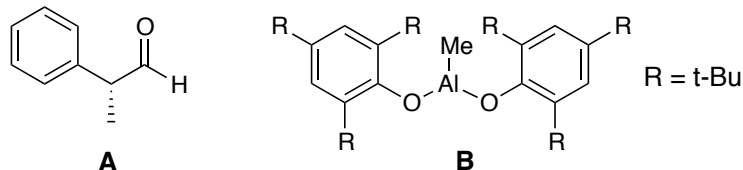
X. For the reaction shown below explain the stereochemical outcome. (6 pts)



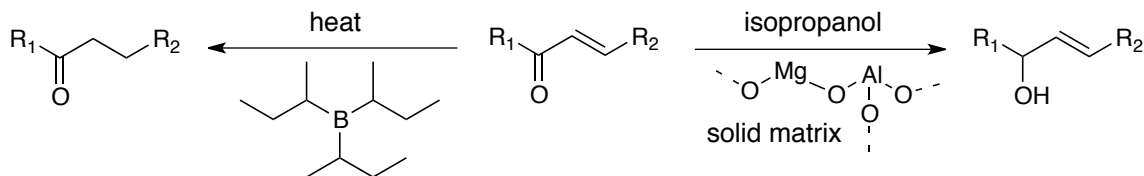
- XI. In the reaction shown below, the deprotonated α -carbon of the sulfoxide reacts with the aldehyde, before 2,3-sigmatropic rearrangements leads to the final product. Give a *detailed* mechanistic account of that reaction sequence. (10 pts)



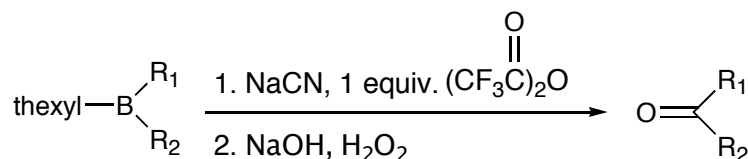
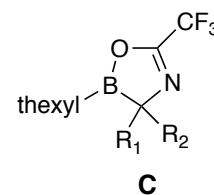
- XII. Reaction of aldehyde **A** with EtMgBr at $-78\text{ }^\circ\text{C}$ affords an 81/16 ratio of the Cram to anti-Cram products. However if a bis(alkylphenoxy)aluminum salt (e.g. **B**) is added prior to the addition of the EtMgBr the anti-Cram product predominates by a ratio of 80/20. Explain (5 pts)



- XIII. Provide a mechanistic rationale for two complementary regiochemical hydride reductions shown below (Hint: Think about the origin of the hydride). (10 pts)



- XIV. In class we saw how reacting the appropriate trialkylborane with carbon monoxide could afford ketones. Toxicity and handling issues with CO inspired development of the Pelter modification to the CO reaction (shown below). Step one of this reaction sequence involves the generation of a heterocyclic boron containing species. Provide a complete arrow (electron) pushing mechanism for the Pelter modification. (Hint: compound **C** is the product of step 1). (10 pts)



Bonus Question: (2 pts) It appears the US Presidential election will pit Donald Trump vs. Hillary Clinton. Thus the US may see its first female President or its first President to have been inducted into the World Wrestling Entertainment Hall of Fame, we will once again not see a chemist as President. History though has occasionally seen chemists rise to high political office, albeit not without the occasional controversy. Which chemist/political figure had the dubious distinction of being thrown out of a chemistry exam for cheating.

- a. Former Vice Prime Minister of Romania, Elena Ceausescu
- b. Princess of Thailand, HRH Princess Chulabhorn
- c. Former Massachusetts State Assemblyman, William S. Clark
- d. Former Prime Minister of the United Kingdom, Margaret Thatcher
- e. Fictional President in the 1973 film *Escape from the Planet of the Apes*, Matthew Williams

CEM 852 Final Exam

May 6, 2015

This exam consists of 7 pages. Please make certain that your exam has all of the necessary pages. Total points possible for this exam are 150. In answering your questions, please write legibly and draw all structures clearly. Write all your answers in the exam booklets. Good luck.

I. For the following compounds provide their pKa's within 2 pKa units. (5 pts)

1. acetone

2. diacetylacetone

3. dimethylsulfoxide

4. dimethylsulfone

5. nitromethane

II. Explain, describe, or illustrate each of the following: (15 pts)

1. 60% ee

2. a lipase hydrolysis

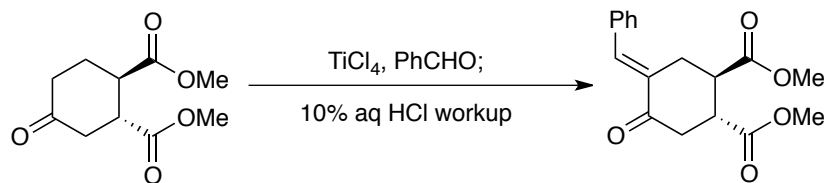
3. a synthon

4. a Felkin-Ahn reduction

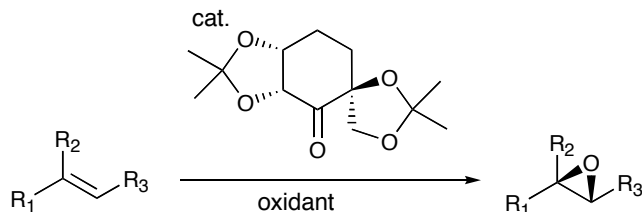
5. a mismatched Sharpless epoxidation

III. Provide the name associated with each of the name reactions shown below. (10 pts).

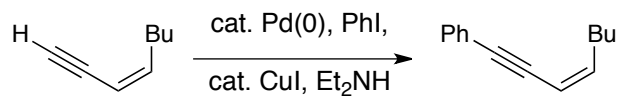
1.



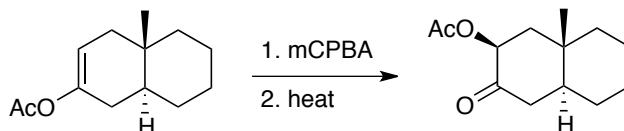
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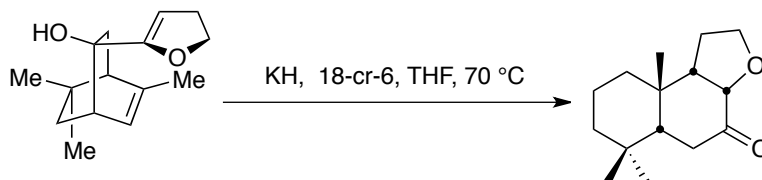
3.



4.

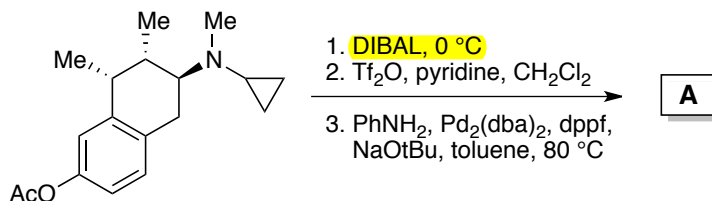


5.

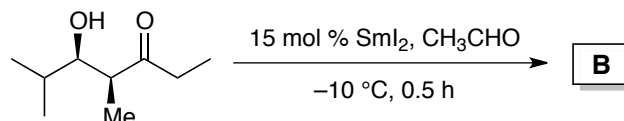


IV. Provide the product or products of the reactions outlined below. Show all intermediate compounds and be sure to indicate the product's relative or absolute stereochemistry. For reactions where multiple products are possible, be sure to indicate the major and minor species. (30 pts)

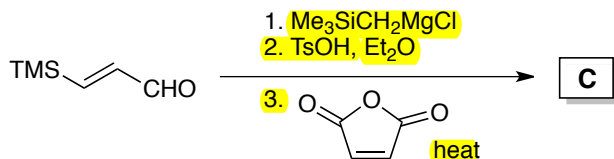
1.



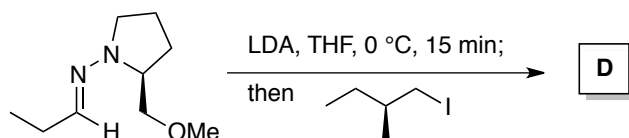
2.



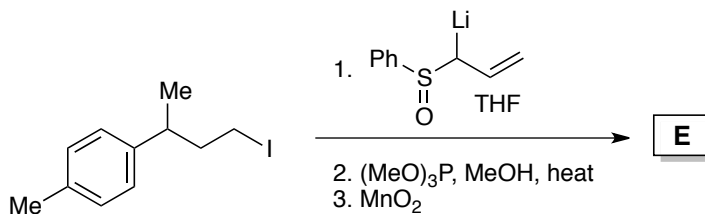
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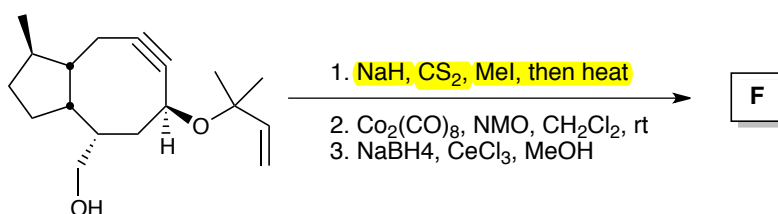
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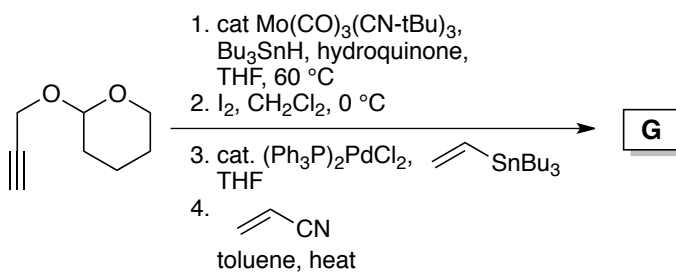
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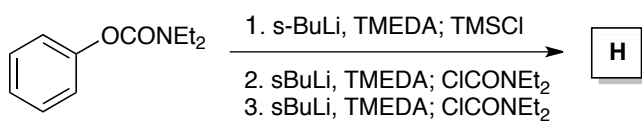
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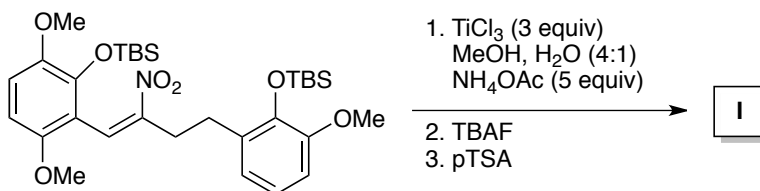
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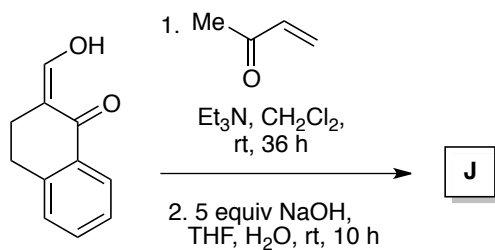
8.



9.



10.



V. Provide conditions that will effect the transformations outlined below. Some of these conversions will require more than one reaction, so be sure to show all intermediate compounds. (24 pts)

1.



2.



3.



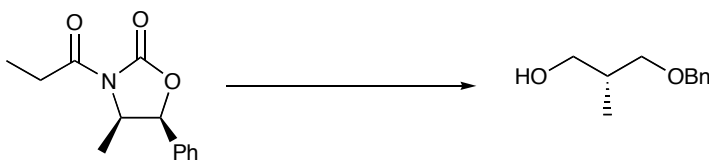
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5.



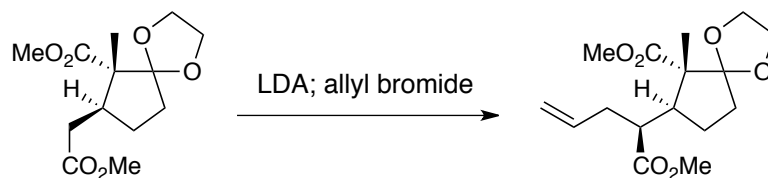
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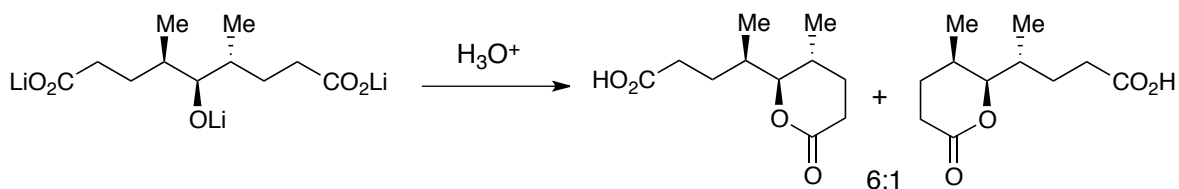
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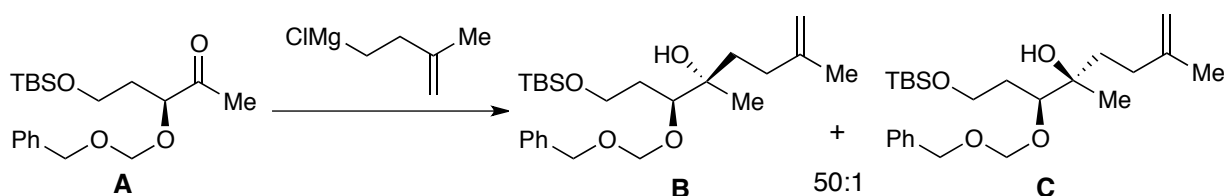
VI. The stereoselectivity of the reaction below arises from the minimization of A(1,3) strain in the transition structure leading to the major product. Illustrate this. (5 pts)



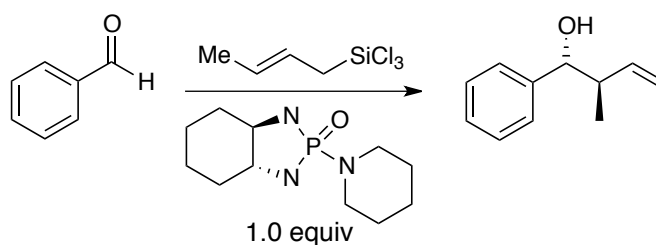
VII. The stereoselectivity of the reaction below arises from the minimization of syn pentane interactions in the transition structure leading to the major product. Illustrate this. (5 pts)



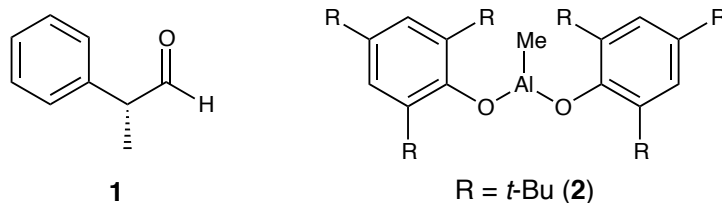
VIII. Explain the stereoselectivity observed for the reaction below (5 pts). Using the same starting ketone (**A**), provide a practical (i.e. selective) synthesis that would afford **C** as the major product (you may use more than one step) (5 pts).



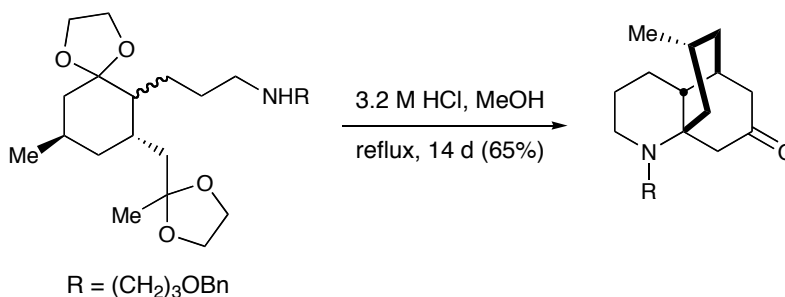
IX. The asymmetric reaction below is thought to proceed through a boat transition structure and exhibits a positive non-linear effect. What is a positive non-linear effect (3 pts)? Offer an explanation for this positive non-linear effect (10 pts). (Note: you do not have to explain the absolute stereochemical outcome.)



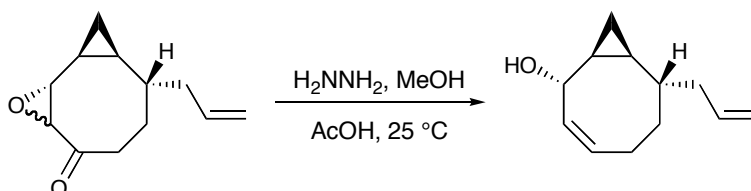
- X. Reaction of aldehyde **1** with EtMgBr at $-78\text{ }^{\circ}\text{C}$ affords an 81/16 ratio of the Felkin to anti-Felkin products. However if a bis(alkylphenoxy)aluminum salt (e.g. **2**) is added prior to the addition of the EtMgBr the anti-Felkin product predominates by a ratio of 80/20. Explain. (5 pts)



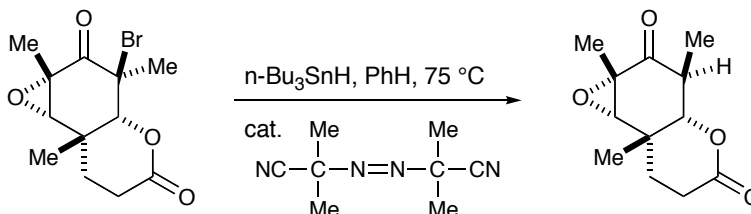
- XI. Give a *detailed* mechanistic account of the following reaction sequence. (10 pts)



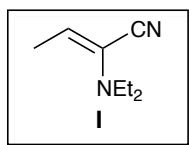
- XII. A variation of the Shapiro reaction is the Wharton rearrangement, an example of which is shown below. Provide a complete arrow (electron) pushing mechanism for the Wharton rearrangement. (10 pts)



- XIII. Give a *detailed* mechanistic account of the following reaction sequence. (5 pts)



IX. Give an example that illustrates how compound I can be viewed as a synthon for C–C–CO₂H (3 pts)



Bonus Question: During the synthesis presentations we mentioned Columbia's Gilbert Stork. Here is a question about another Columbia chemist. After earning a degree in chemistry from Atlanta University, he moved to New York and began post-graduate work at Columbia University. Soon though he also began to pursue his other passion, jazz. As leader of the first great jazz big band, his ability to spot talent was legendary. Indeed he hired many future jazz greats including an up and coming trumpet player named Louis Armstrong. Who was he?

- a. Fletcher Henderson
- b. Earl Hines
- c. Johnny St. Cyr
- d. Kid Ory
- e. Kid Rock