CEM 852 Exam-2

April 2, 2005

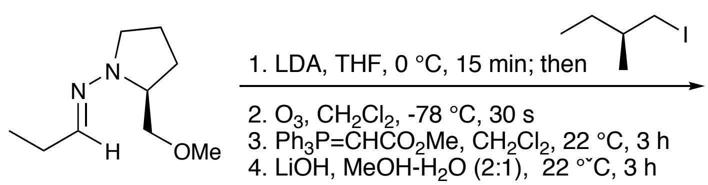
This exam consists of 5 pages. Please write ALL your answers in the answer books. Please write legibly and draw all structures clearly. Good luck.

1. Provide examples of the following name reactions: (12 pts)
   a. Nozaki-Hiyama-Kishi coupling
   b. Glaser coupling
   c. aza-Prins cyclization
   d. Paterno-Büchi reaction

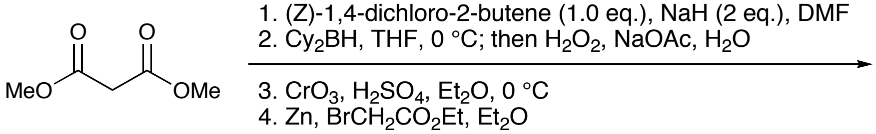
2. Provide a <u>brief</u> written description of the role played by each of the following reagents typically employed in the Sharpless asymmetric dihydroxylation: (3 pts)
   a. $K_2OsO_2(OH)_4$
   b. $K_3Fe(CN)_6$
   c. $MeSO_2NH_2$

3. 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, indicate the major and minor species. (28 pts)

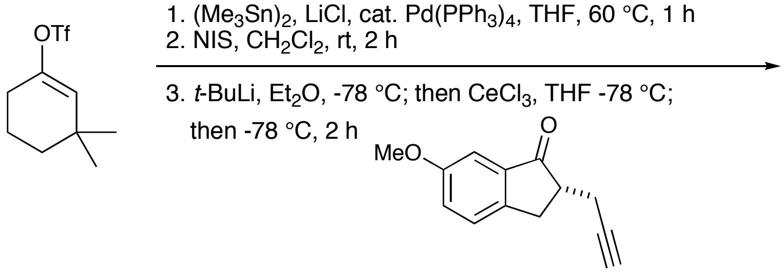
(a)



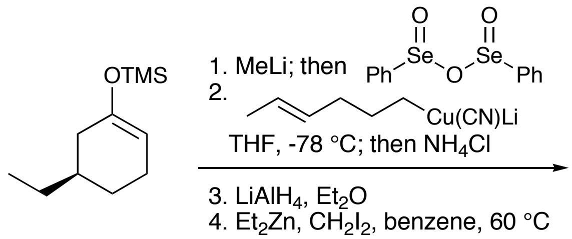
(b)



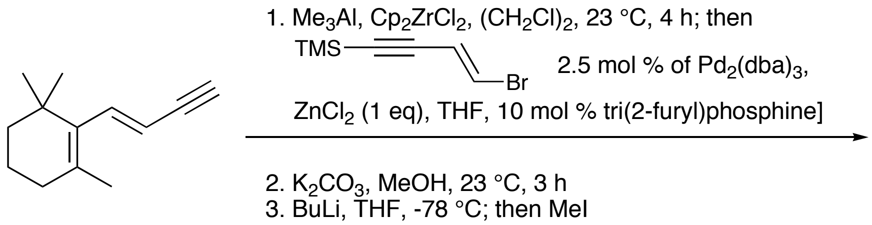
(c)



(d)



(e)



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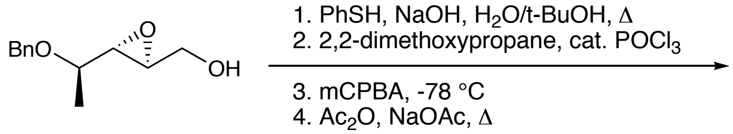

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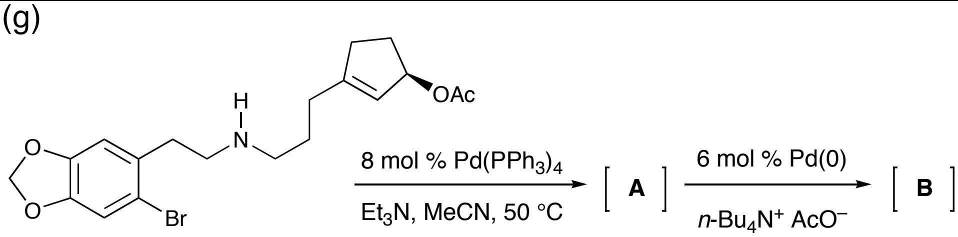
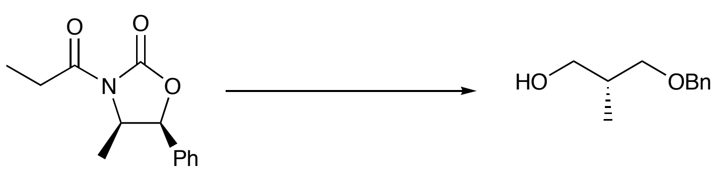


4. Provide the reagents necessary to convert the starting material to the product. Most of these transformations will require more than one step. Be sure to consider the product's relative or absolute stereochemistry. To maximize your chances at partial credit, it is recommended that you show all intermediate compounds. (28 pts)

(a)



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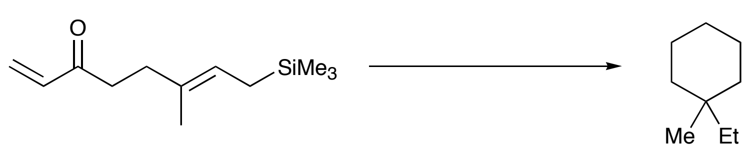

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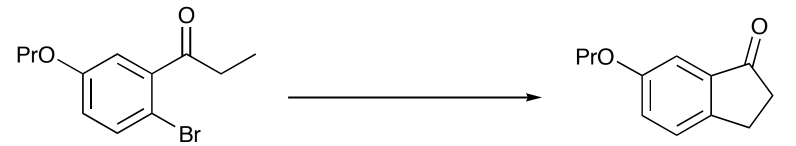

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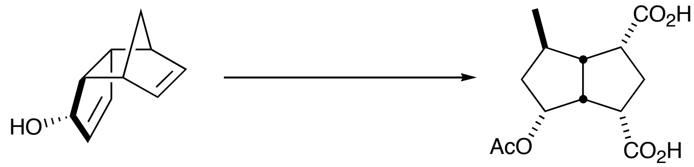

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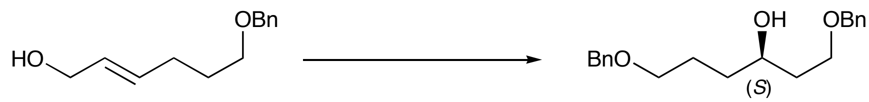

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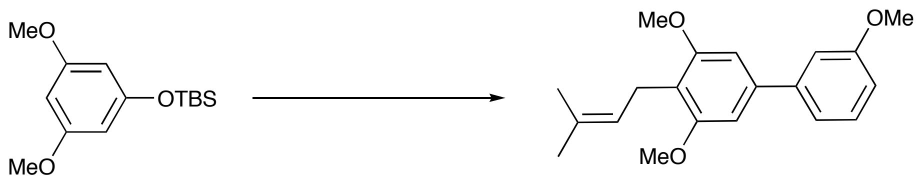
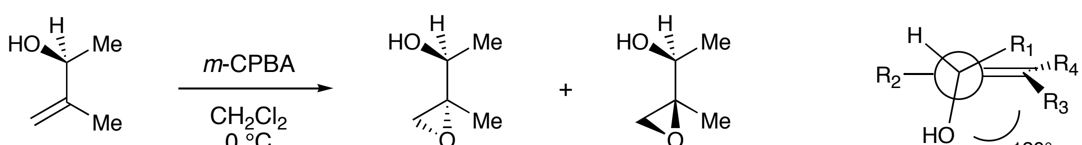
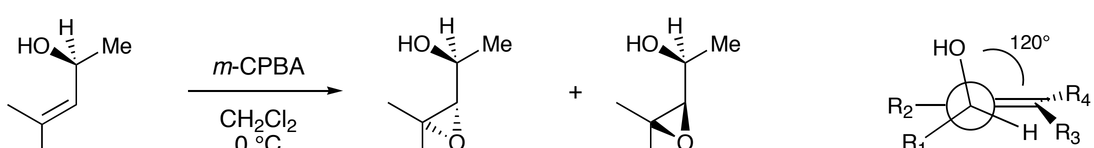


g)

5. Reactions of **A** and **B** with mCPBA are complementary with regards to the direction of epoxidation. This can be explained by considering A-strain combined with the putative 120° "olefin-hydroxyl bite angle." Thus, compound **A** prefers reactive conformation **I** while **B** reacts via conformation **II** during its mCPBA epoxidation. An examination of **I** and **II** can also explain why the mCPBA epoxidation of **B** is more selective that that of **A**. Please explain. (5 pts)



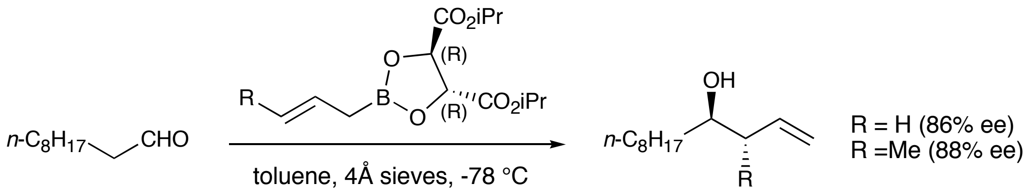
A 80 20 **I**



B 4 96 **II**

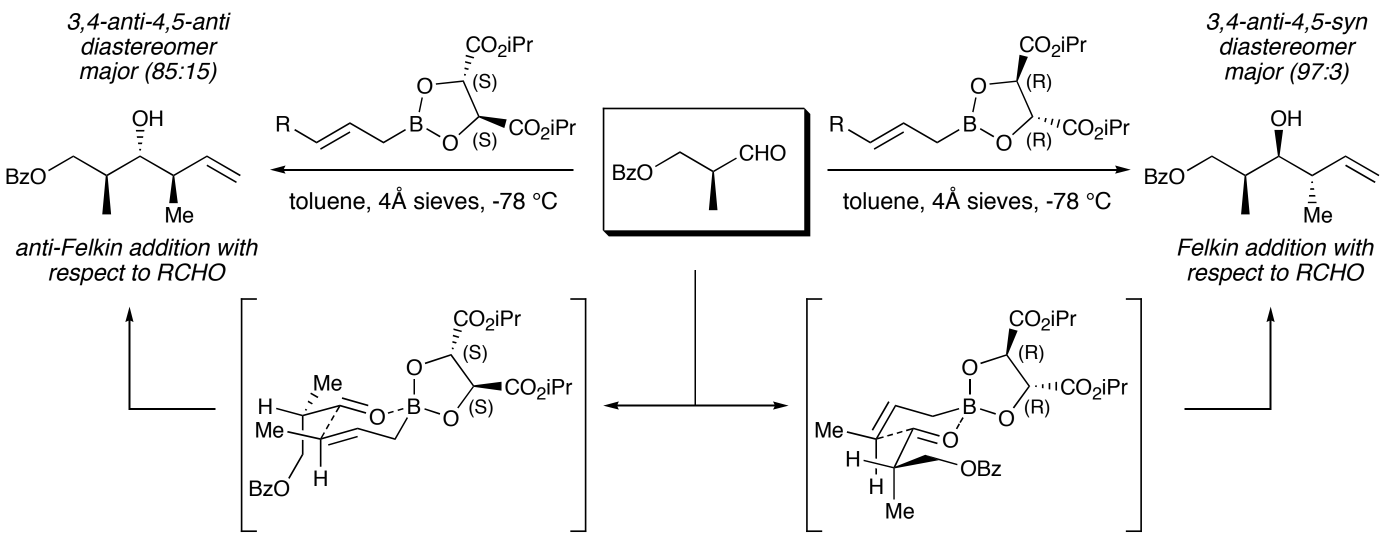
6. As shown in Scheme 1, allyl or (*E*)-crotylboration with the **R,R** tartrate derived reagents react at the ***Si*** face of simple aliphatic or aryl aldehydes to give the corresponding homoallylic alcohols. In a related fashion the **S,S** tartrate derived boronates react at the ***Re*** face (not shown).

Scheme 1.



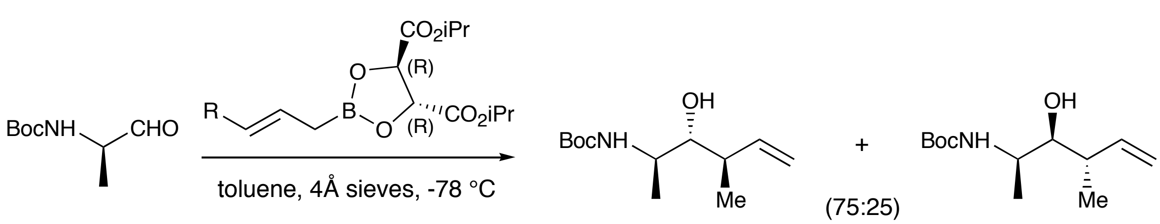
Similarly the (**R,R**)-(*E*)-crotylboronate reacts at the ***Si*** face of the optically active aldehyde shown in Scheme 2. In this case, *Si* face attack also corresponds to a Felkin approach and affords a high degree of stereocontrol (97:3). As expected the (**S,S**)-(*E*)-crotylboronate preferentially attacks the ***Re*** face, but as this approach is anti-Felkin a loss of selectivity is seen.

Scheme 2.

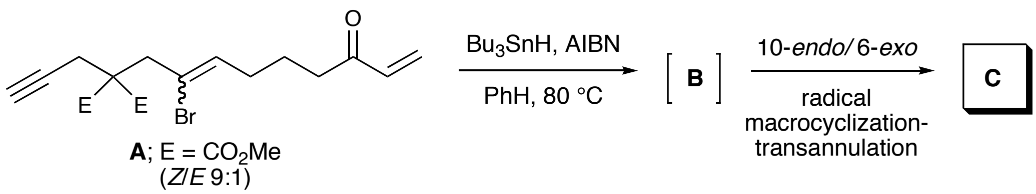


In contrast to the examples above, reaction of the alanine derived aldehyde with the (**R,R**)-(*E*)-crotylboronate proceeds with ***Re*** face attack to give as the major product the anti-Felkin product shown in Scheme 3. Explain this somewhat surprising result. (8 pts).

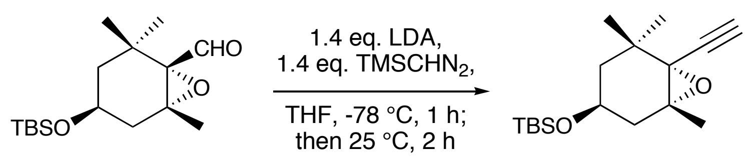
Scheme 3.



7. Treatment of halide **A** with Bu_3SnH results in a 5-*exo-dig* radical cyclization to give intermediate **B**, which is capable of undergoing a 10-*endo-trig*/6-*exo-trig* radical macrocyclization-transannulation process to afford **C**. ^{1}H-NMR of **C** reveals that this compound has no vinyl protons. Provide the structures of **B** (2 pts) and **C** (3 pts).

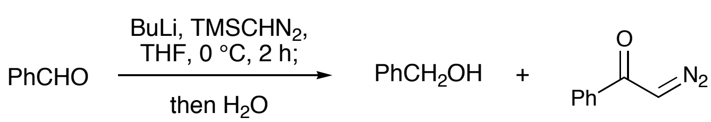


8. The Colvin rearrangement is a method to convert aldehydes to alkynes. Provide a complete arrow (electron) pushing mechanism for this transformation. (Note: A ^{1}H-NMR of $TMSCHN_2$ shows two peaks one of which is at 2.2 ppm and the other at ca. 0 ppm.) (6 pts)

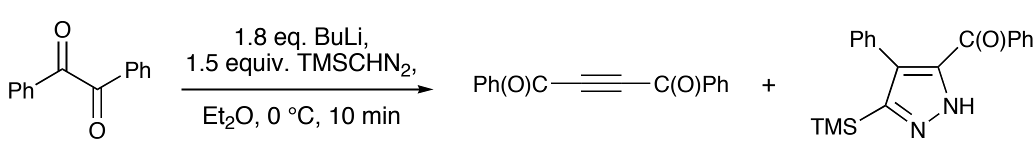


9. While the Colvin rearrangement above works well, other substrates are known to give unwanted side products. For example benzaldehyde does not rearrange to phenylethyne but instead gives benzyl alcohol and α-diazoacetophenone (Scheme 4). In another example, benzil undergoes the desired transformation, but the product is accompanied by significant amounts of pyrazole (Scheme 5). Provide a complete arrow (electron) pushing mechanism for the formation of **either** the pyrazole or the benzyl alcohol. (5 pts)

Scheme 4.



Scheme 5.



Bonus Question: In a few hours MSU will take to the court for a semi final game in this year's NCAA men's basketball championship. For a 3-point play name one organic chemistry faculty member from each of the other three final four schools: Illinois (Urbana-Champaign), Louisville, and North Carolina (Chapel Hill).