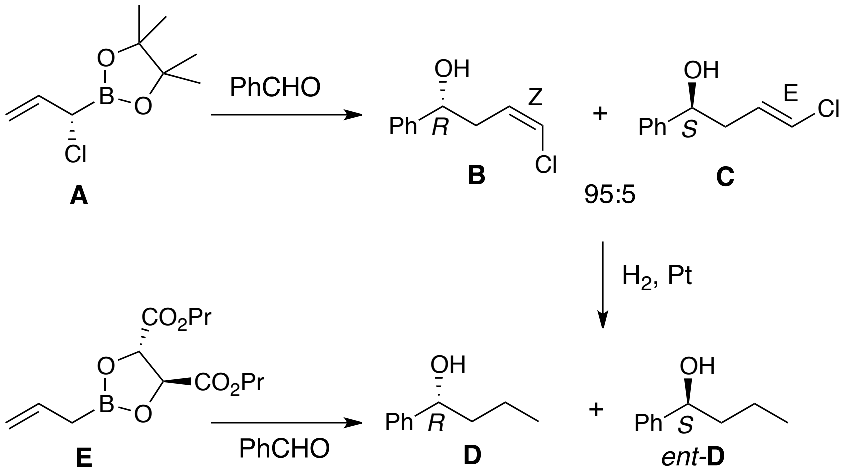
CEM 852 Exam-2

April 2, 2016

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.

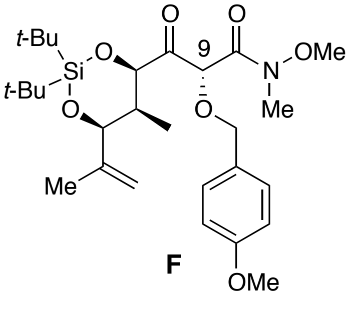
I. Given the time we recently spent enough on crotylations, I have to start here. The reaction shown below of optically active **A** with benzaldehyde affords (*R*)-**B** and (*S*)-**C** in a ratio of 93:7. Draw the two Zimmerman-Traxler transition structures that will afford (*R*)-**B** and (*S*)-**C** with their observed respective olefin geometries. (6 pts)



Hydrogenation of **B** affords **D**, while hydrogenation of **C** affords its enantiomer. Allylation of benzaldehyde with optically active **E** directly affords **D** and ent-**D** with **D** being the major enantiomer formed. *Both allylations proceed with the same level of enantioselectivity*, yet the two-step process (starting with **A**) can afford **D** in greater enantiomeric excess than the one-step process (starting with **E**). Explain (3 pts).

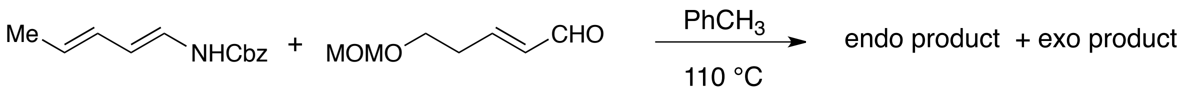
II. Illustrate **four** of the following **six** "name" reactions: Brook rearrangement, Danishefsky's diene, Nef reaction, Negishi coupling, Peterson olefination, 2,3-Wittig rearrangement. (8 pts)

III. 1,3-Dicarbonyls normally undergo rapid epimerization at the α-position. Yet in his cytovaricin synthesis Evans was able to form and then react compound **F** without loss of the C-9 stereochemistry. Evans suggests that attenuation of C-H acidity by allylic 1,3-strain is responsible for this fact. Illustrate this explanation using Newman projections. (3 pts)



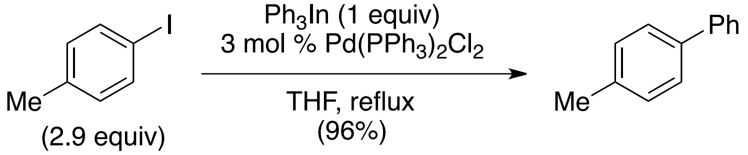
F

IV. Draw the endo and exo products that would result from the [4+2]-cycloaddition shown below (4 pts)



Is the reaction above a normal or inverse electron demand Diels-Alder? (2 pts)

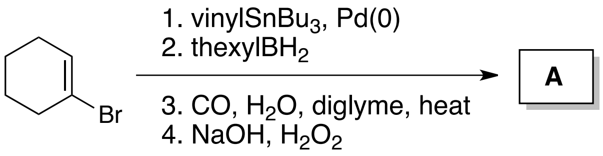
V. Organoindium reagents can undergo Pd(0) catalyzed cross-coupling reactions with a variety of sp^2 and sp halides. The catalytic cycle for these indium couplings is similar to the generalized catalytic cycle shown in class. However, to account for the stoichiometry of indium couplings one should partially modify that generalized catalytic cycle.



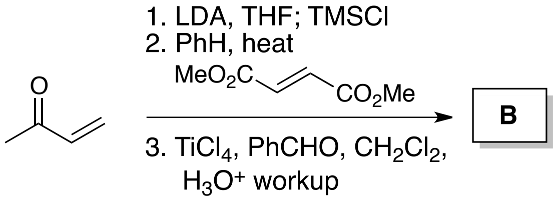
Given the information proved above illustrate a catalytic cycle for the organoindium cross-coupling shown above, *being sure to account for stoichiometry* and the oxidation state of palladium. (6 pts)

VI. 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)

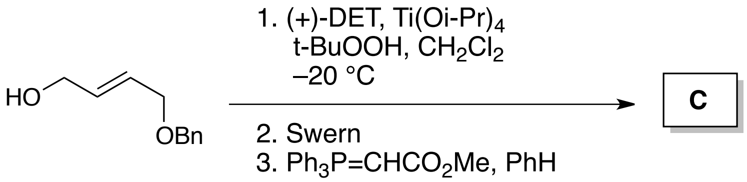
1.



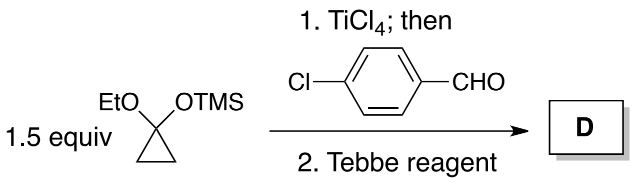
2.



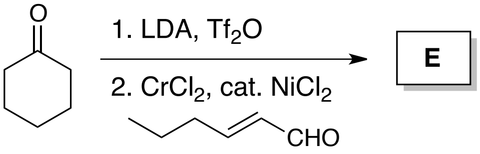
3.



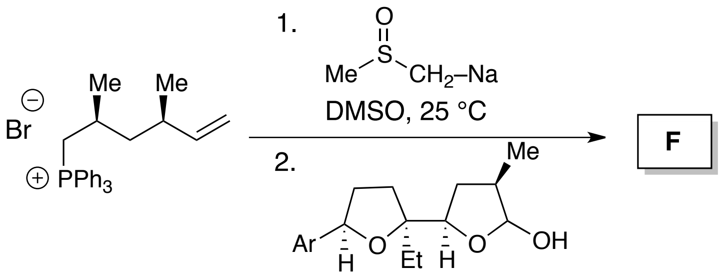
4.


1.5 equiv
EtO
OTMS
1. $TiCl_4$; then
Cl
CHO
2. Tebbe reagent
D

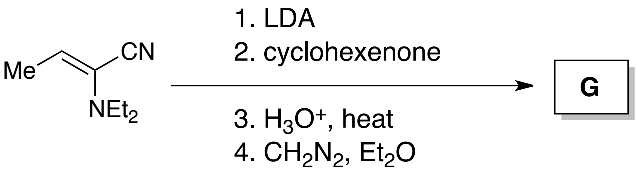
5.


O
1. LDA, Tf_2O
2. $CrCl_2$, cat. $NiCl_2$
CHO
E

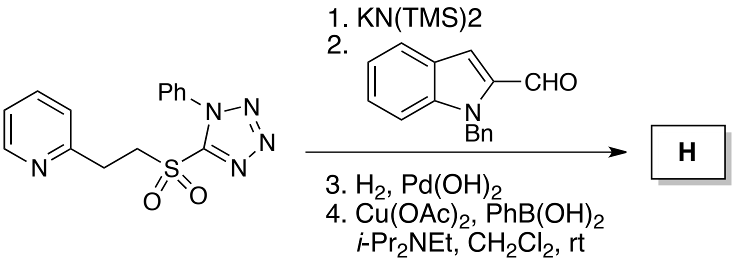
6.


Br
Me
Me
PPh$_3$
1.
O
Me
S
CH$_2$–Na
DMSO, 25 °C
2.
Me
Ar
H
O
Et
H
O
OH
F

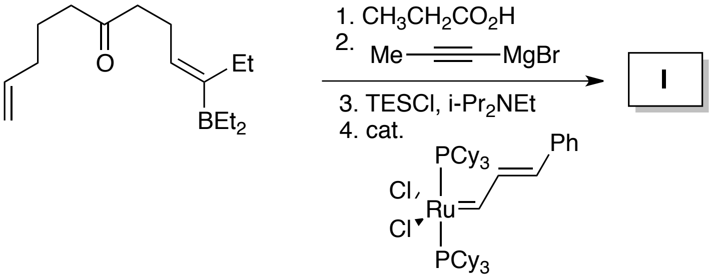
7.


Me
CN
NEt$_2$
1. LDA
2. cyclohexenone
3. H_3O^+, heat
4. CH_2N_2, Et_2O
G

8.

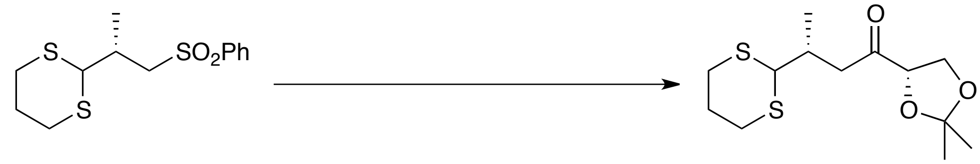

1. KN(TMS)2
2.
CHO
N
Bn
Ph
N
N
N
N
N
S
O
O
3. H_2, $Pd(OH)_2$
4. $Cu(OAc)_2$, $PhB(OH)_2$
i-Pr_2NEt, CH_2Cl_2, rt
H

9.

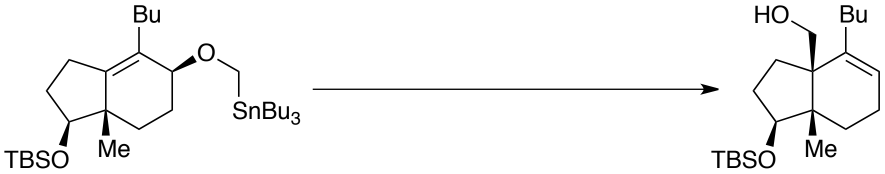

O
Et
BEt$_2$
1. $CH_3CH_2CO_2H$
2. Me
MgBr
3. TESCl, i-Pr_2NEt
4. cat.
PCy$_3$
Ph
Cl
Ru
Cl
PCy$_3$
I

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. (15 pts)

1.

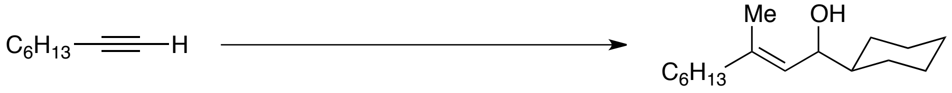


2.

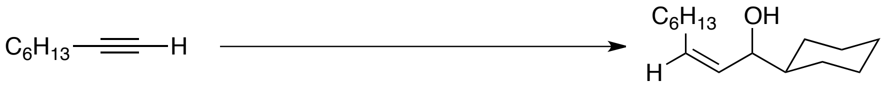


3.

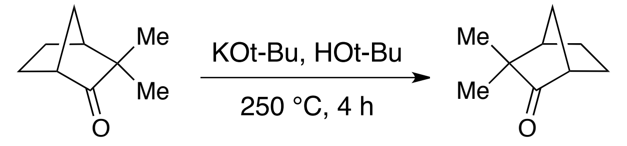
4.



5.

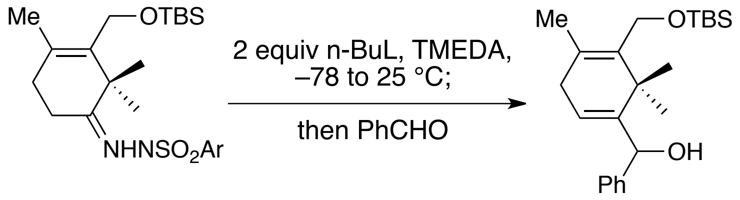


VII. Upon heating with a base (+)-camphenilone will completely racemize in 4 hours. This racimization process is reported to proceed through the homoenolate. Provide a detailed arrow (electron) pushing mechanism for this reaction. (Note: in absence of a base (+)-camphenilone remains enatiomerically pure after 4 days at 250 °C). (5 pts)

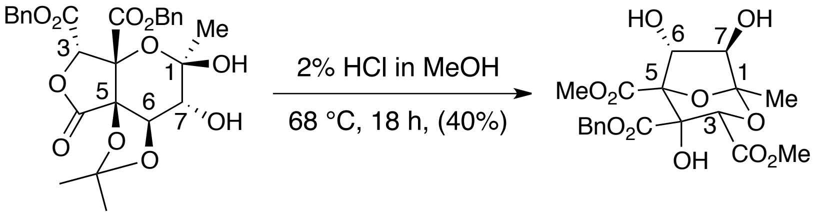


(+)-camphenilone (±)-camphenilone

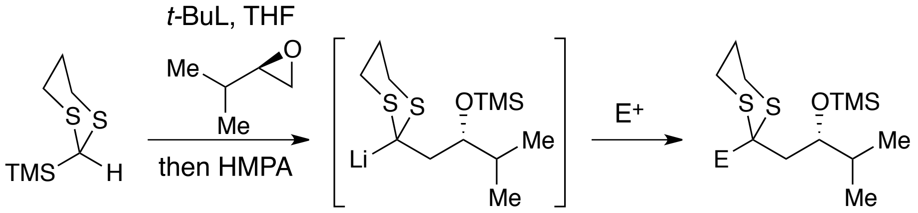
VIII. Provide a detailed arrow (electron) pushing mechanism for the reaction below. (5 pts)



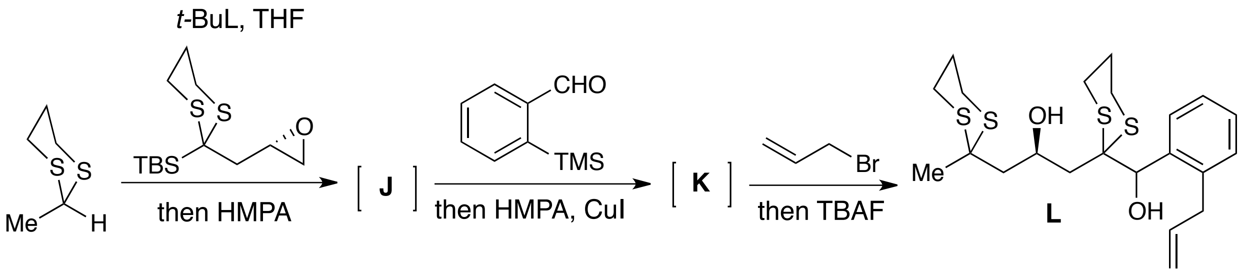
IX. Provide a detailed arrow (electron) pushing mechanism for the reaction below. (5 pts)



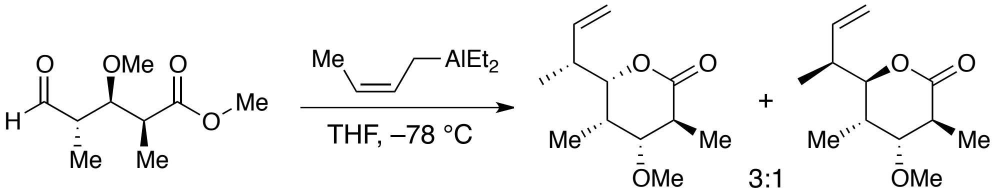
X. In class, we saw examples of anion relay chemistry such that shown below. In this sequence, the dithiane anion reacts with an epoxide, opening the epoxide and generating an alkoxide intermediate. Treating that intemediate with HMPA triggers a Brook rearrangement, which regenerates a new dithiane anion that can react with another electrophile.



A variation of this chemistry is shown below. Provide the structures for intermediates **J** and **K** (6 pts)



XI. Explain the stereochemical outcome of the reaction below. (5 pts)



Bonus Question: As discussed in class, Professor Peter Wagner (MSU) was well knownfor his thorough study of the Norrish type II reaction and for creative use of this reaction to establish fundamental aspects of excited state reactivity. These studies began during his post-doctoral stint with George Hammond, where they demonstrated that the Norrish type II cleavage of aliphatic ketones occurs from both excited singlet and triplet states. Peter's other accomplishments included demonstrating that the quantum efficiencies of most triplet ketone reactions do not reflect relative reactivities of the excited states but rather the partitioning of biradical intermediates between product formation and reversion to ketone; showing that the reactivity of excited ketones and structural effects thereon mimic those of alkoxy radicals; demonstrating that thermal interconversion of excited triplets can allow efficient photochemistry to occur from upper excited states; producing a thorough analysis of how hydrogen abstraction by triplet ketones is affected by varying degrees of charge transfer; and development of a clear understanding of how rates and product distributions for intramolecular bifunctional reactions depend on the competition among reaction, bond rotations, and excited state decay. On what holiday was Peter born? (2 pts)

(a) New Year's Day

(b) Independence Day

(c) Thanksgiving Day

(d) Christmas Day

(e) Arbor Day