Advanced Organic Chemistry: Synthesis Name:___Nancy Jackson_______

CHEM 311/511

Second Mid-term Exam

Tuesday November 24, 2009

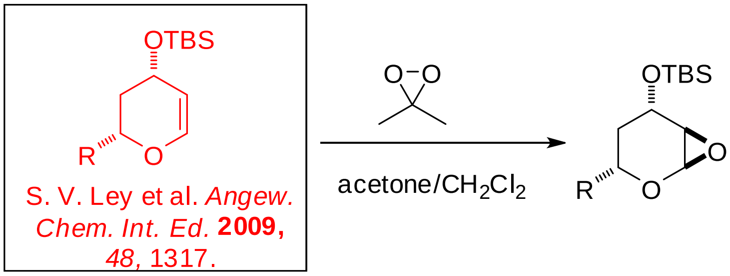
Review each question carefully before answering and be certain you understand everything the question is requesting. Do the easy questions first. If questions appear confusing or exceedingly complex, then you may need to rethink the question. Keep in mind the intended examination topics.

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. Maximum credit will be given for answers that correctly address stereochemical considerations in a particular reaction. Don't forget to include formal charges when appropriate.

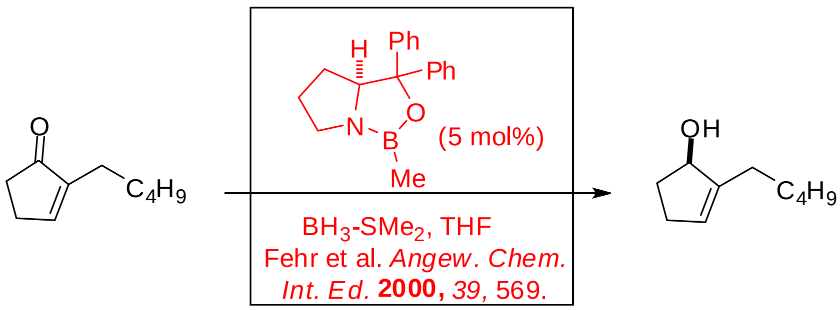
You may use models to assist in determining answers. You should use scrap paper to work out problems before entering your final answer on the exam sheets. In addition, feel free to use the back side of the exam sheets for scrap. If necessary, you may enter exam answers on the back side of the exam sheets, however you must clearly indicate which problems are located on the back of the exam pages.

1. <u>Box questions.</u> Provide the necessary information, products or reagents, to complete the following reactions. Undergraduates complete eight of the twelve boxes and graduate students complete ten of twelve. (34 pts.)

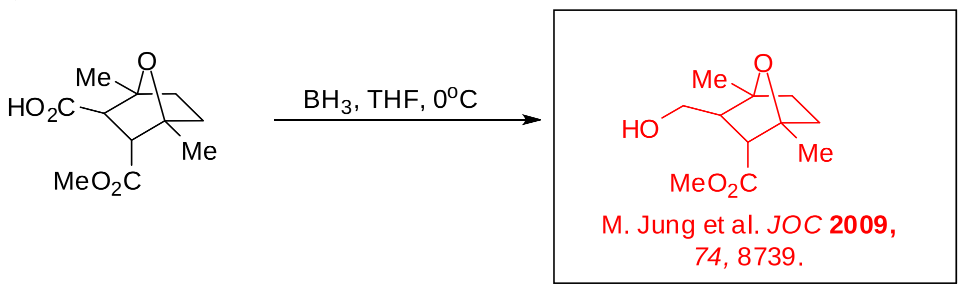
a)



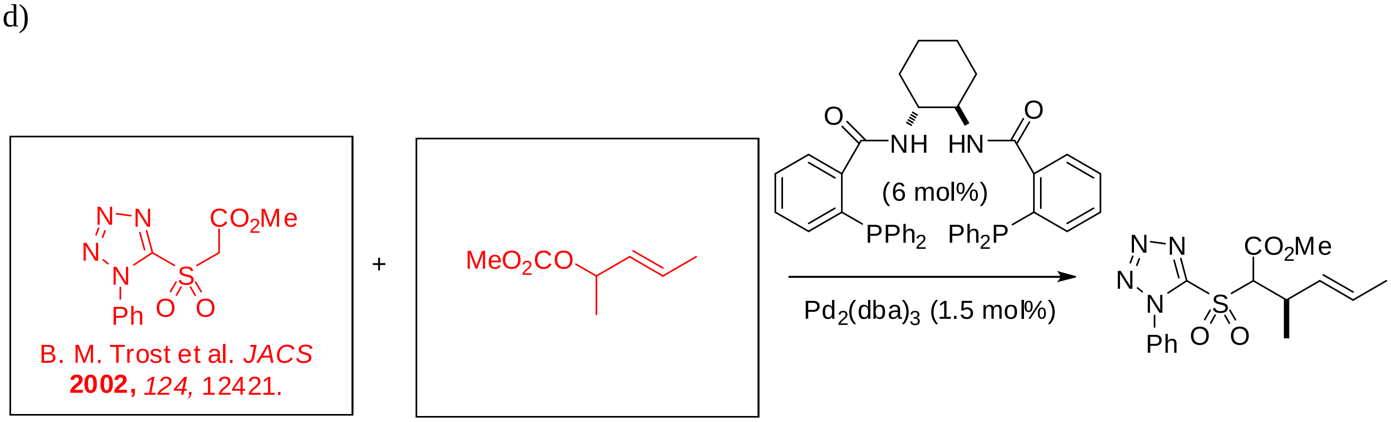
b)



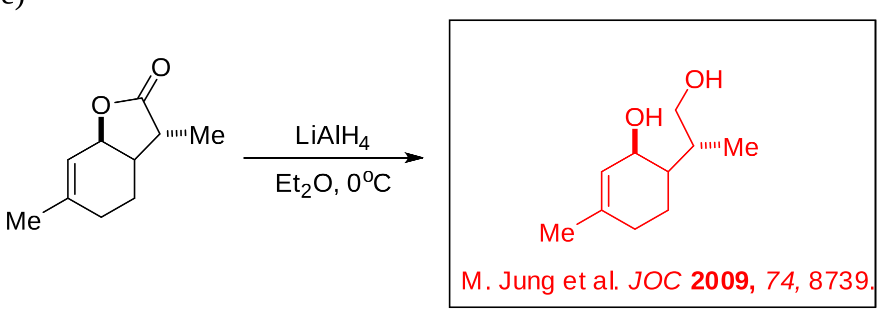
c)



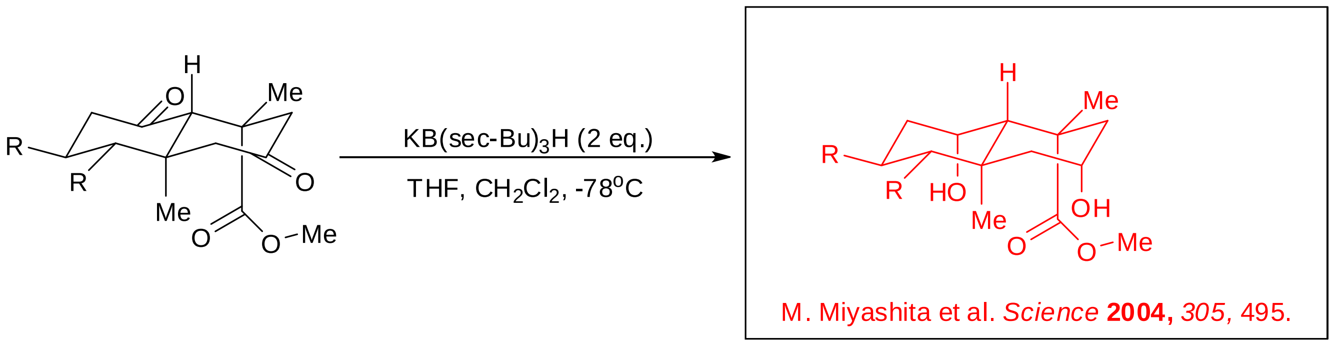
d)



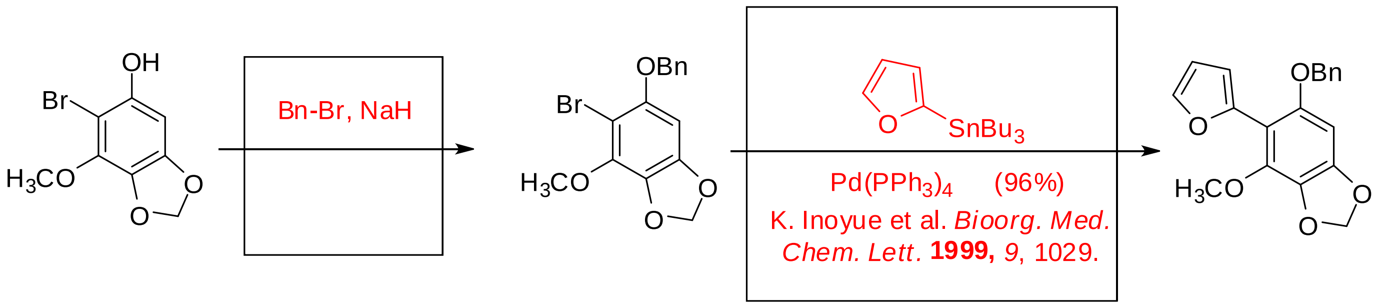
e)



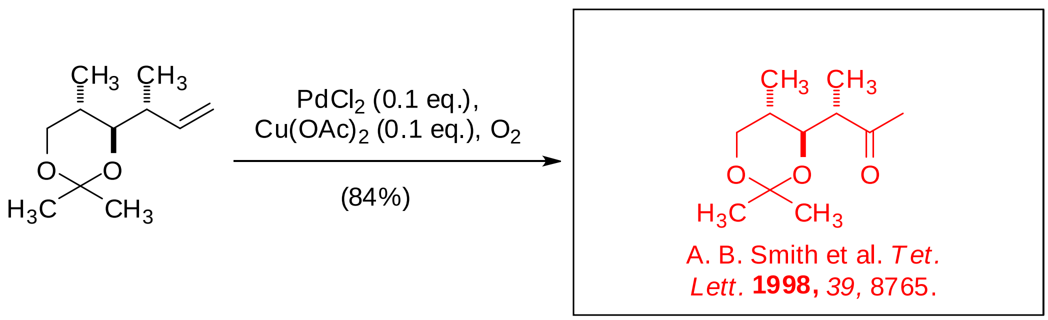
f)


R
R
H
O
Me
O
Me
O
O
Me
KB(sec-Bu)3H (2 eq.)
THF, CH2Cl2, -78oC
H
Me
R
R
HO
Me
OH
O
O
Me
M. Miyashita et al. Science 2004, 305, 495.

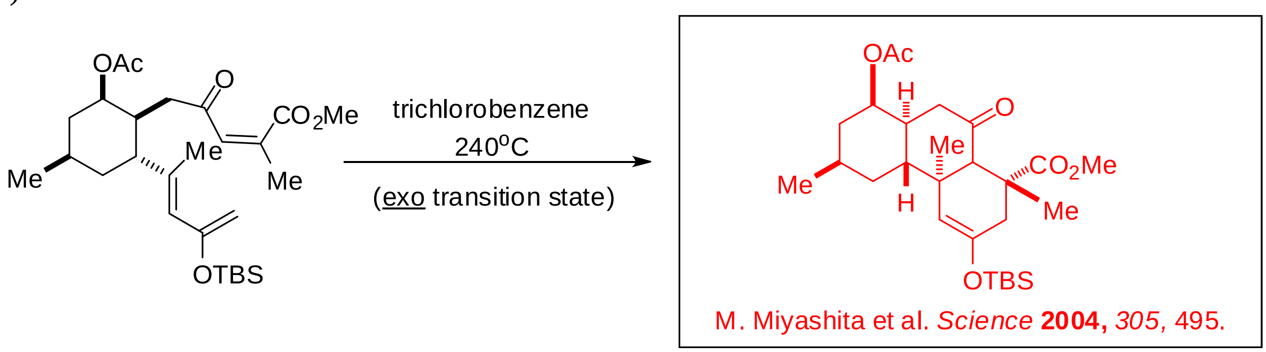
g)


OH
Br
H3CO
O
O
Bn-Br, NaH
OBn
Br
H3CO
O
O
O
SnBu3
Pd(PPh3)4 (96%)
K. Inoyue et al. Bioorg. Med. Chem. Lett. 1999, 9, 1029.
O
OBn
H3CO
O
O

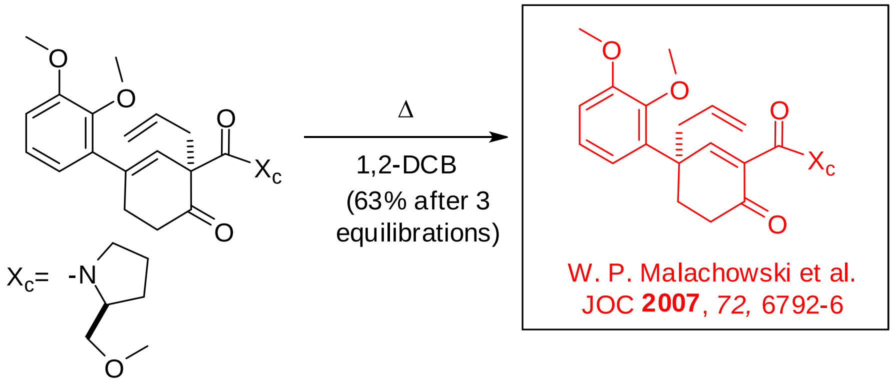
h)


CH3 CH3
O O
H3C CH3
PdCl2 (0.1 eq.), Cu(OAc)2 (0.1 eq.), O2
(84%)
CH3 CH3
O O O
H3C CH3
A. B. Smith et al. Tet. Lett. 1998, 39, 8765.

i)

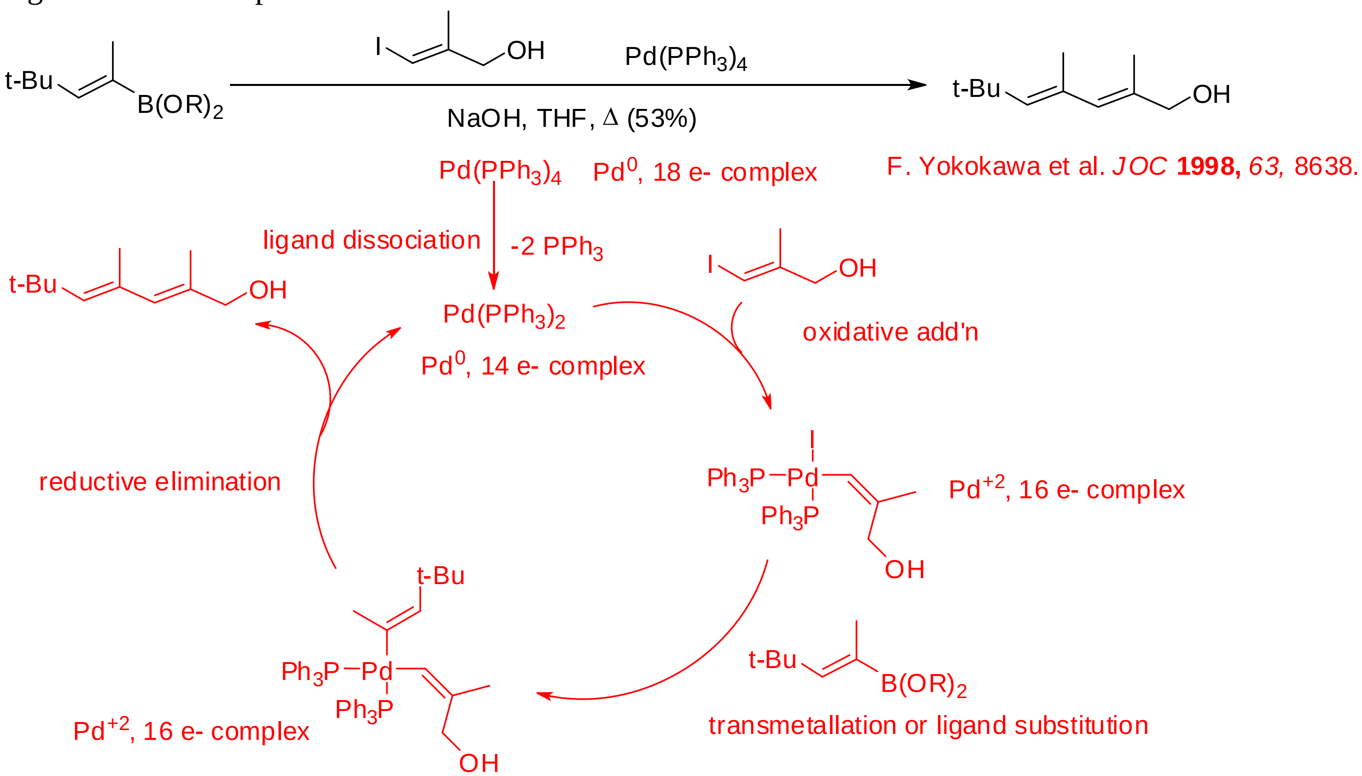

OAc
O
CO2Me
Me
Me
Me
OTBS
trichlorobenzene
240oC
(exo transition state)
OAc
H
O
Me
Me
CO2Me
H
Me
OTBS
M. Miyashita et al. Science 2004, 305, 495.

j)

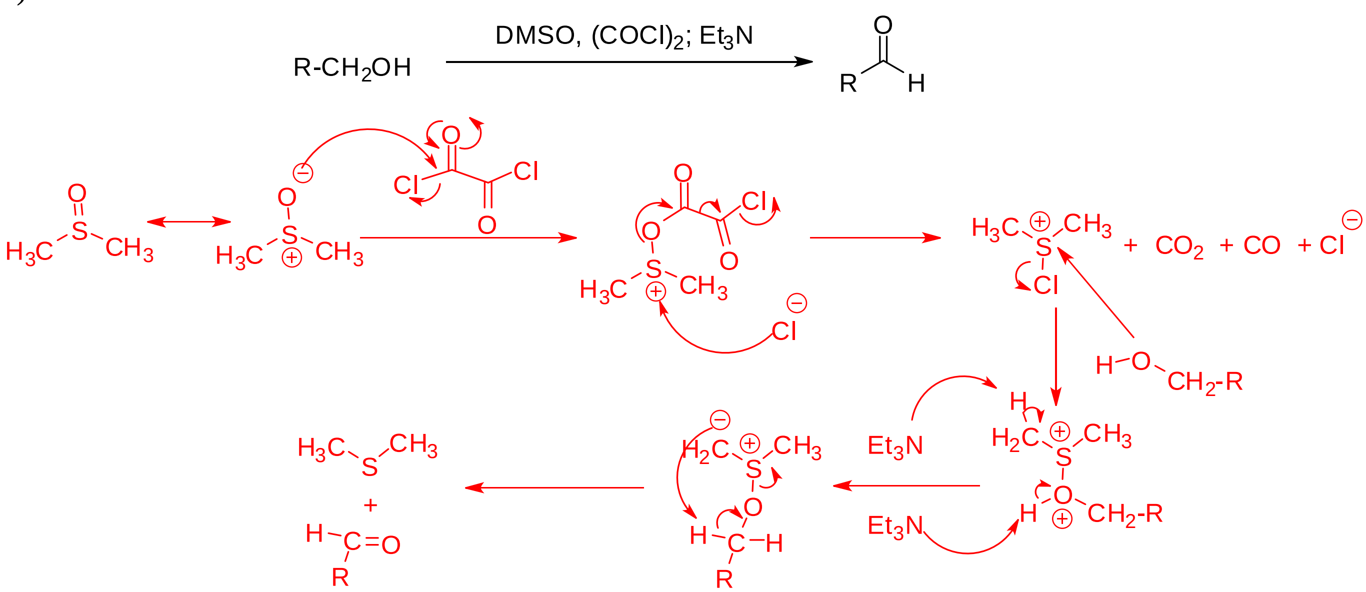

O
O
O
Xc
O
Xc= -N
O
Δ
1,2-DCB
(63% after 3 equilibrations)
O
O
O
Xc
O
W. P. Malachowski et al. JOC 2007, 72, 6792-6

2. <u>Mechanism questions.</u> Both undergraduates and graduate students complete two of the three mechanism questions. (30 pts.)

a) Provide the mechanism of the cross-coupling reaction shown below. Identify each step of the reaction by the type of step shown. Determine the oxidation state and electron count for the transition metal in all organometallic complexes.

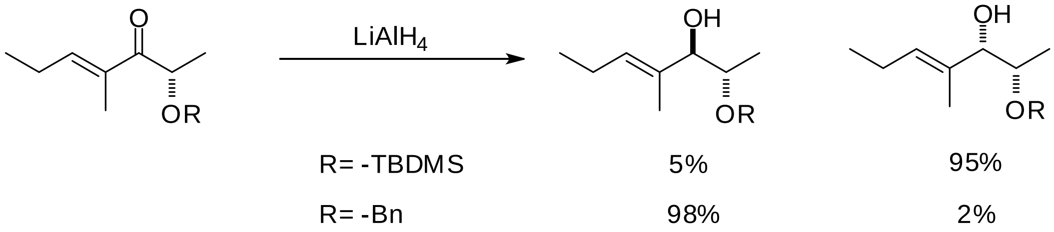


b) Provide a mechanism for the reaction shown below.

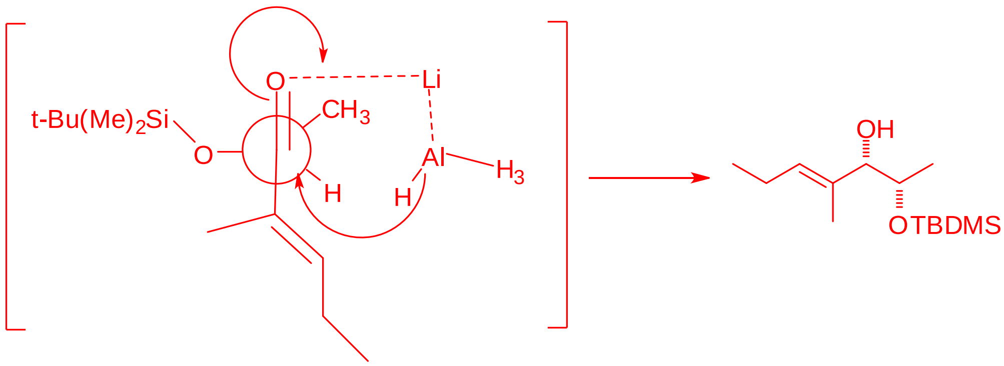


c) The reaction shown below was described by Larry Overman and a co-worker in **1982** (*Tet. Lett. 23*, 2355). They found remarkable ketone reduction stereoselectivity resulted from careful selection of a protecting group on the adjacent alpha-hydroxy group. Determine which of the protecting groups, tert-butyldimethylsilyl

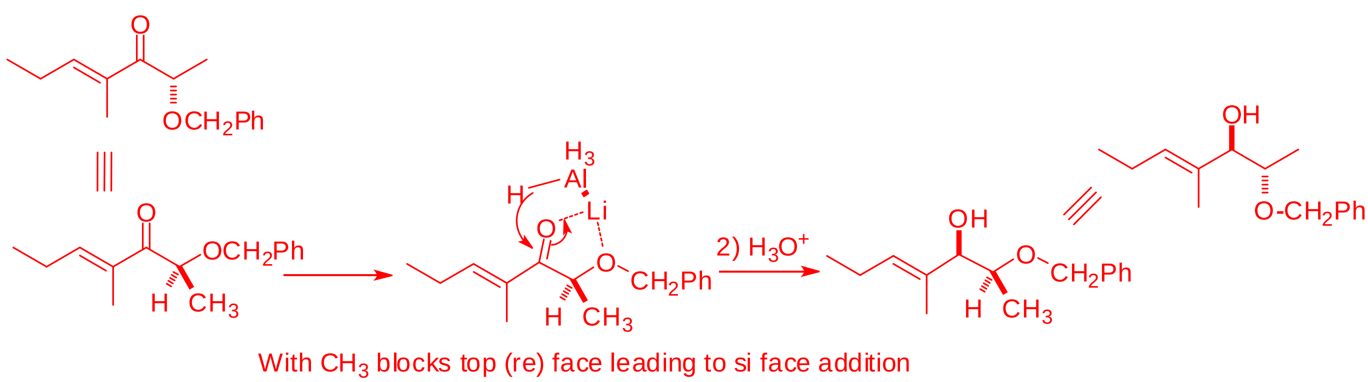
(TBDMS) or benzyl (Bn), affords the Felkin-Anh product and which affords the chelation control product by drawing <u>one</u> of the transition states. Suggest a reason why the ether group that adheres to Felkin-Anh predictions does not get involved in chelation control.



Felkin-Anh transition state with R=TBDMS:



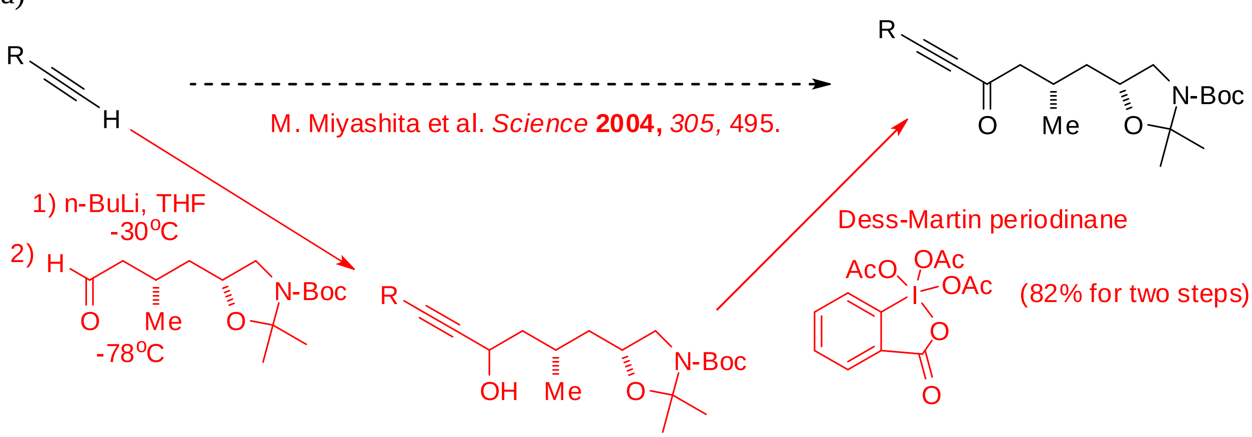
Chelation control transition state with R=Bn:



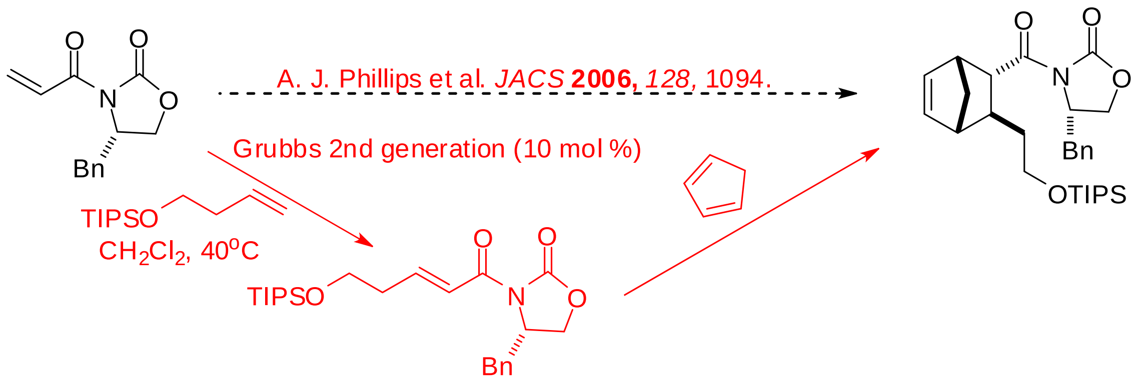
The TBDMS group is too bulky to permit efficient chelation between the ether O and the lithium cation.

3. <u>Synthesis questions.</u> Provide a series of synthetic reactions to transform the starting material to the product shown. Graduate students must do four of five syntheses; undergraduates need to do three of five. (36 pts.)

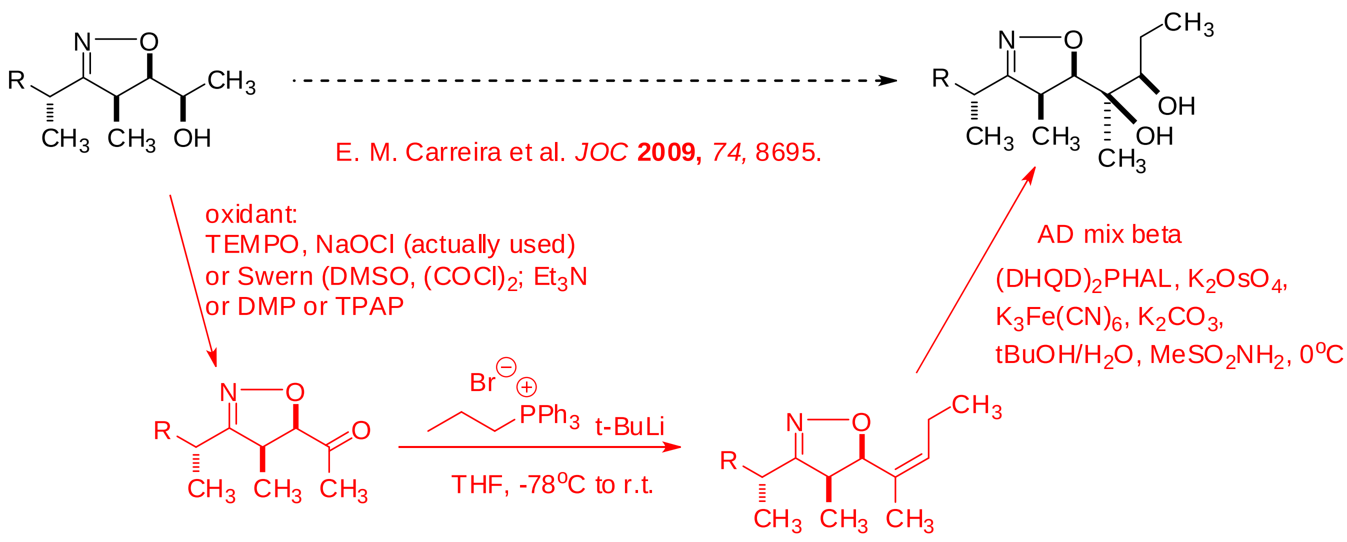
a)



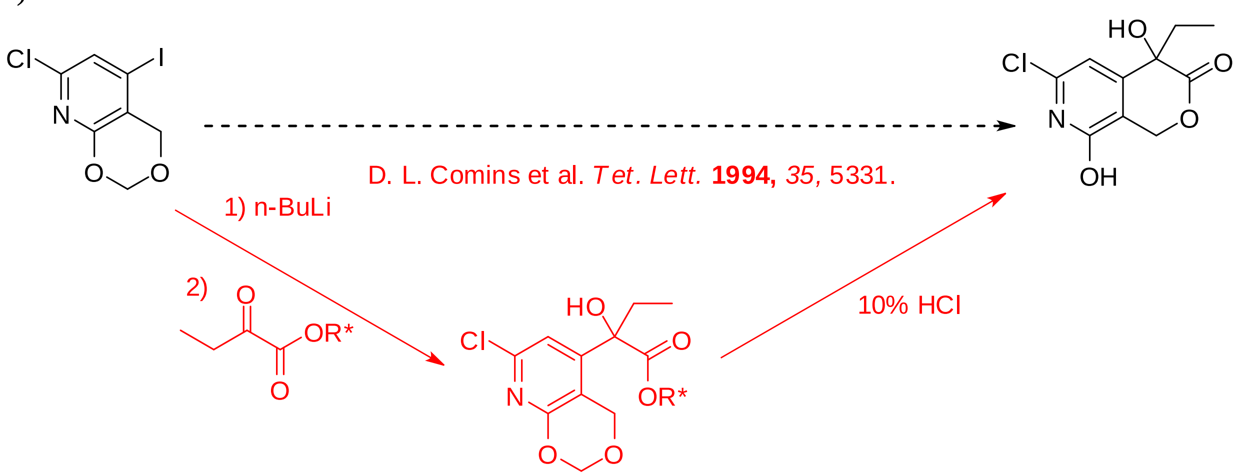
b)


A. J. Phillips et al. JACS 2006, 128, 1094.
Grubbs 2nd generation (10 mol %)
TIPSO
CH2Cl2, 40oC
TIPSO
N
O
O
O
Bn
OTIPS

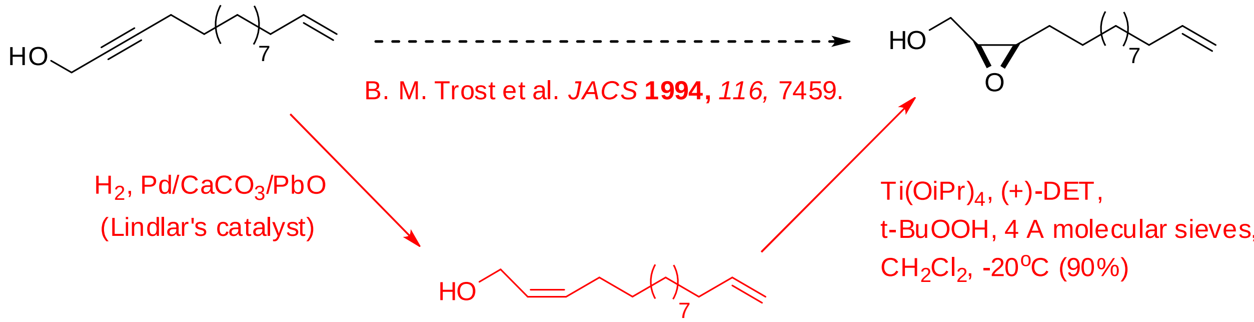
c)


N—O
R
CH3
CH3 CH3 OH
E. M. Carreira et al. JOC 2009, 74, 8695.
oxidant:
TEMPO, NaOCl (actually used)
or Swern (DMSO, (COCl)2; Et3N
or DMP or TPAP
Br
PPh3 t-BuLi
THF, -78oC to r.t.
AD mix beta
(DHQD)2PHAL, K2OsO4,
K3Fe(CN)6, K2CO3,
tBuOH/H2O, MeSO2NH2, 0oC
OH
OH

d)


Cl
I
N
O
O
D. L. Comins et al. Tet. Lett. 1994, 35, 5331.
1) n-BuLi
2)
OR*
10% HCl
HO
OH

e)


HO
7
B. M. Trost et al. JACS 1994, 116, 7459.
HO
7
O
H2, Pd/CaCO3/PbO
(Lindlar's catalyst)
HO
7
Ti(OiPr)4, (+)-DET,
t-BuOOH, 4 A molecular sieves,
CH2Cl2, -20oC (90%)