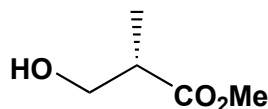
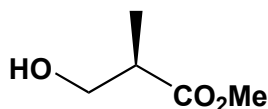


Massachusetts Institute of Technology
Organic Chemistry 5.512

May 4, 2005
Prof. Rick L. Danheiser

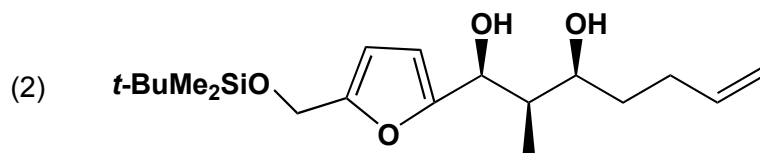
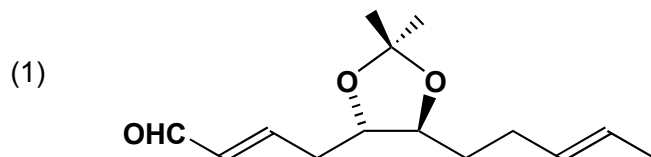
Problem Set 7
Stereocontrolled Synthesis of Acyclic Molecules
Review Problems for Second Exam

Design a highly stereoselective synthesis of the following target molecules beginning with commercially available materials. Be sure to explicitly identify all reagents necessary for each transformation. Enantiomerically enriched reagents may be used if they are commercially available; however, with the exception of the two compounds shown below, each stereogenic center in the target molecule must be generated in your synthetic route. In other words, the stereogenic carbons in the chiral reagents you employ cannot be directly incorporated in the final product. The exceptions are (S) and (R) methyl 3-hydroxy-2-methylpropionate, which are commercially available and have been widely employed in total synthesis.

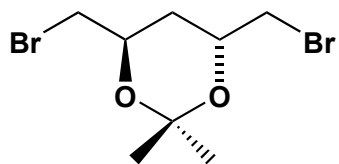


A stereoselective synthesis of each of these target molecules has been reported in the literature and a reference for each synthesis is provided at the end as an appendix. In addition, an outline of these literature syntheses will be posted on the 5.512 website later this week for your reference. Note, however, that the original route to each molecule may not be the optimal approach, especially in view of new methods that have been reported since the literature route was developed!

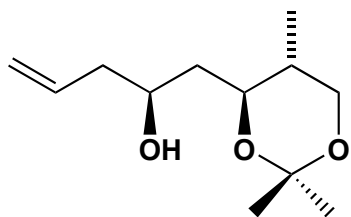
To derive maximum benefit from these problems, I recommend that for each target you consider all possible synthetic routes that can be envisioned based on the methods and strategies studied in 5.512, and then critically compare your viable approaches and decide which would be most practical and efficient.



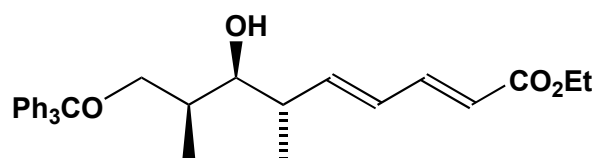
(3)



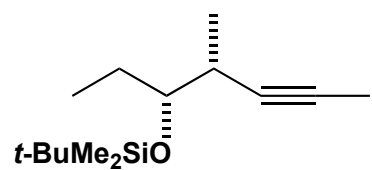
(4)



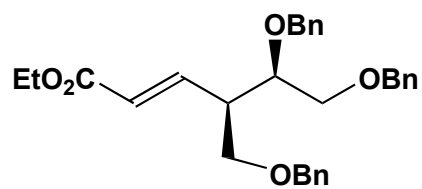
(5)



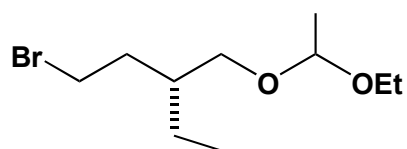
(6)



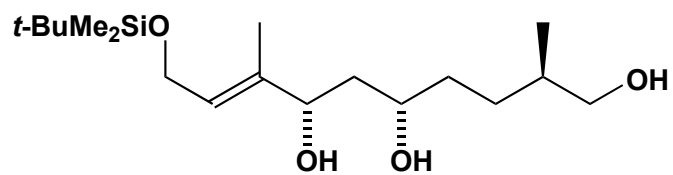
(7)



(8)

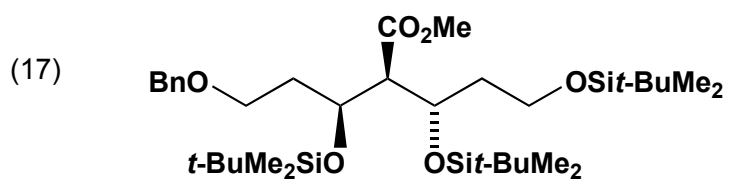
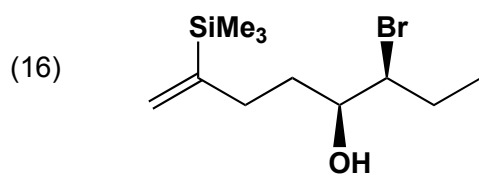
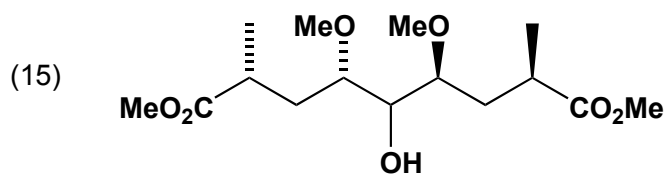
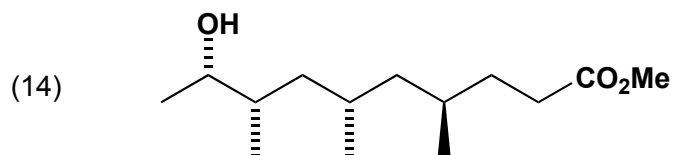
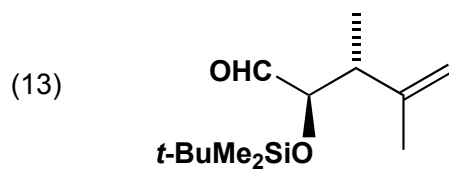
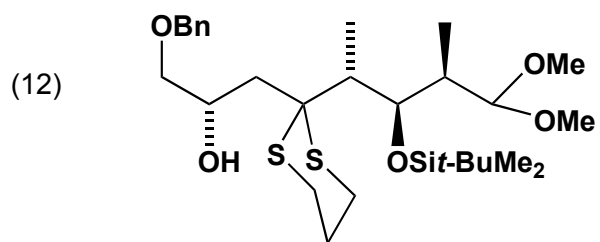
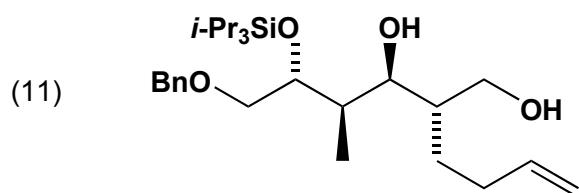


(9)



(10)





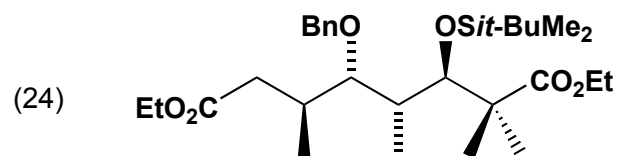




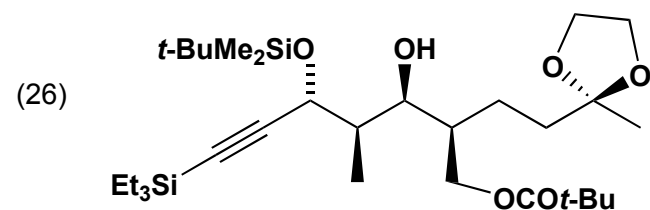
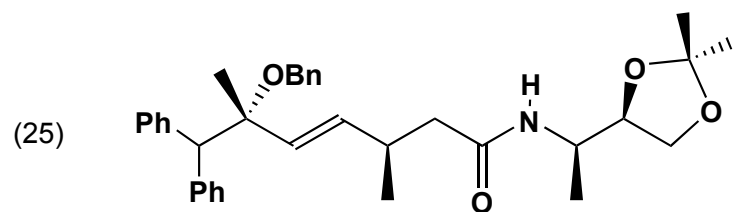
See total synthesis of roflamycoin,
S. Rychnovsky *J. Am. Chem. Soc.*
1994, *116*, 175



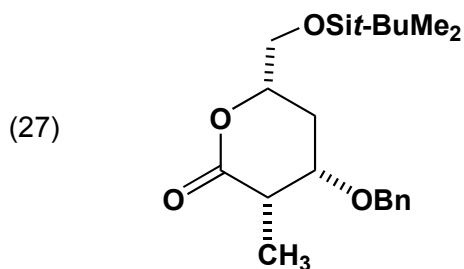
See synthesis of C(1)-C(14) fragment
of callipeltoside A, T. R. Hoyer
Org. Lett. **1999**, *1*, 169



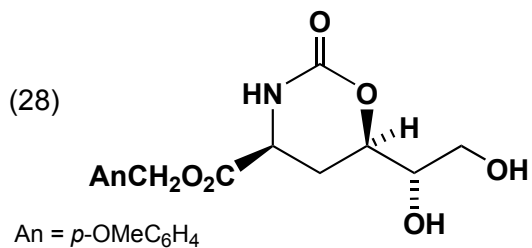
Intermediate for synthesis of epothilone A; see,
for example J. S. Panek *Org. Lett.* **2000**, 2, 2575



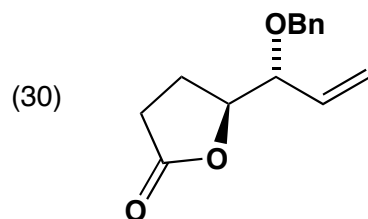
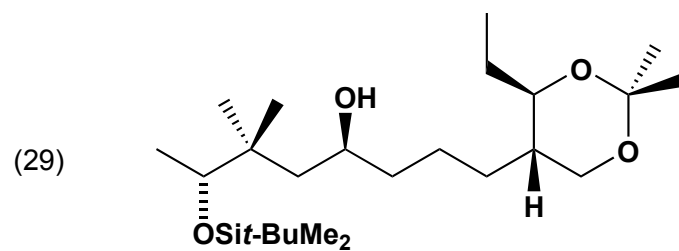
See total synthesis of sanglifehrin A,
K. C. Nicolaou et al.
J. Am. Chem. Soc. **2000**, 122, 3830



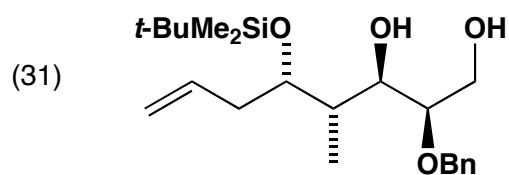
See synthetic studies on miyakolide,
S. Masamune et al.
J. Org. Chem. **1997**, 62, 8978



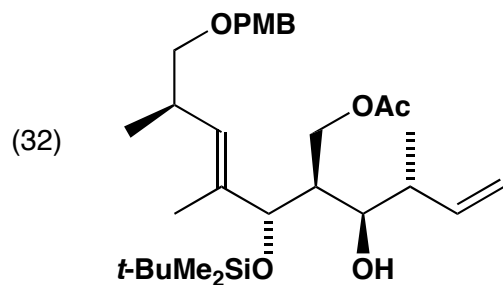
See J. E. Baldwin et al.
Tetrahedron Lett. **1987**, 28, 3605



See total synthesis of resiniferatoxin,
P. A. Wender et al.
J. Am. Chem. Soc. **1997**, *119*, 12976



See synthetic studies on spongistatin 1,
M. T. Crimmins et al.
Org. Lett. **2001**, *3*, 949



See total synthesis of (+)-13-deoxytedanolide,
A. B. Smith et al.
J. Am. Chem. Soc. **2003**, *125*, 350

