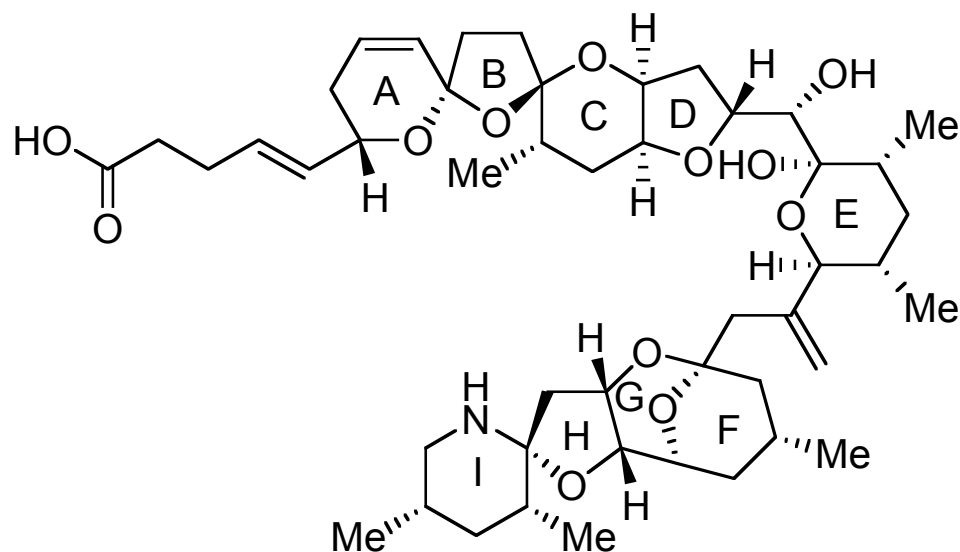


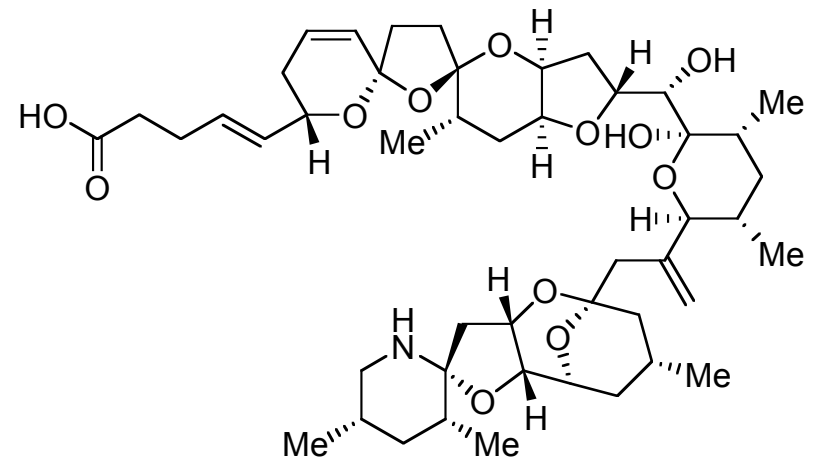
Azaspiracid



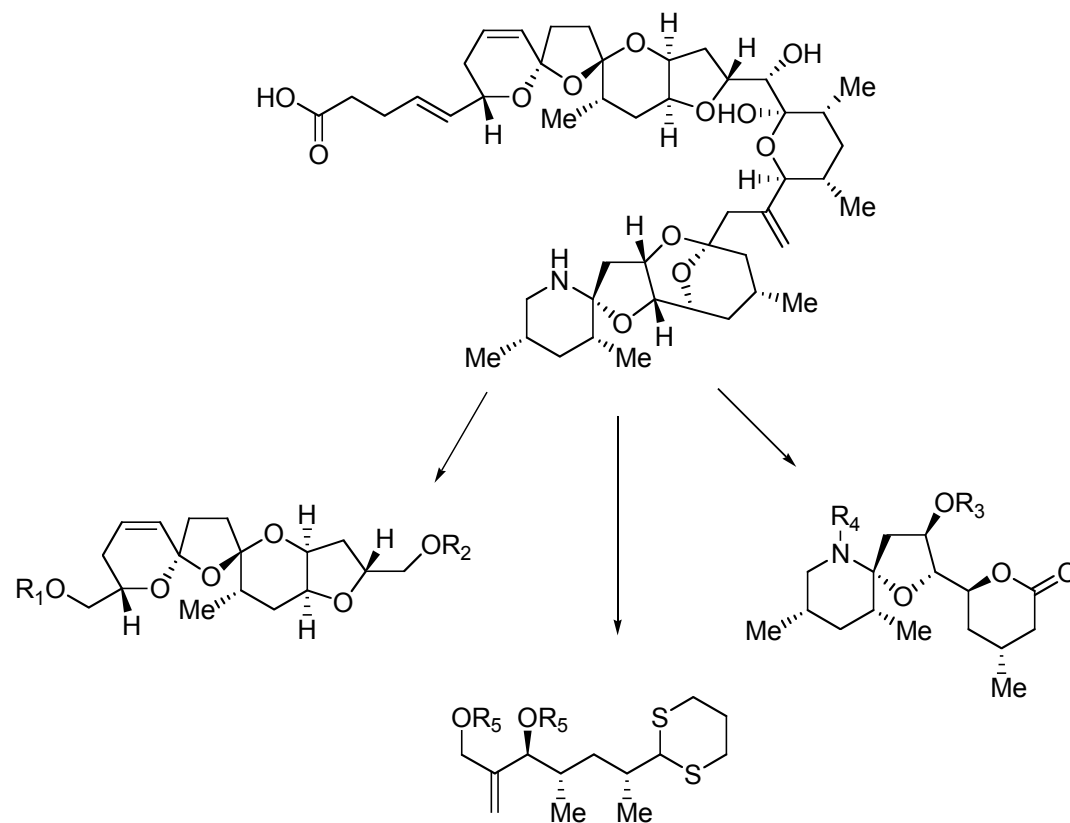
Yasumoto, T. *J. Am. Chem. Soc.* **1998**, *120*, 9967
Nicolaou et. al. *Angew. Chem. Int. Ed.* **2001**, *40*, 1262
Nicolaou et. al. *Angew. Chem. Int. Ed.* **2001**, *40*, 4068
Nicolaou et. al. *Angew. Chem. Int. Ed.* **2003**, *42*, 3643
Nicolaou et. al. *Angew. Chem. Int. Ed.* **2003**, *42*, 3649
Nicolaou et. al. *Angew. Chem. Int. Ed.* **2004**, *43*, 4312
Nicolaou et. al. *Angew. Chem. Int. Ed.* **2004**, *43*, 4318

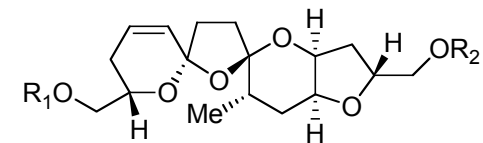
Azaspiracid

- Date: November, 1995
- Place: Kelly Harbor, Ireland
- Diarrheic shelfish poisoning (DSP)
- Seasonally occurring marine toxin
- Isolated from *Mytilus edulis*
- Structure elucidation Yasumoto et. al. in 1998
- Nine rings ABCD-E-FGHI
- *In vivo*: 0.2 mg/kg
- No mode of action known

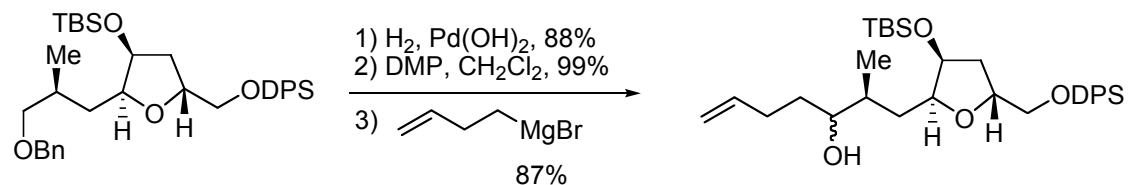
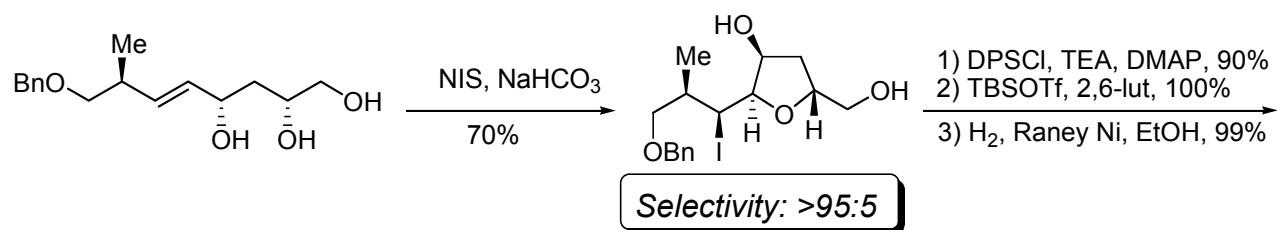
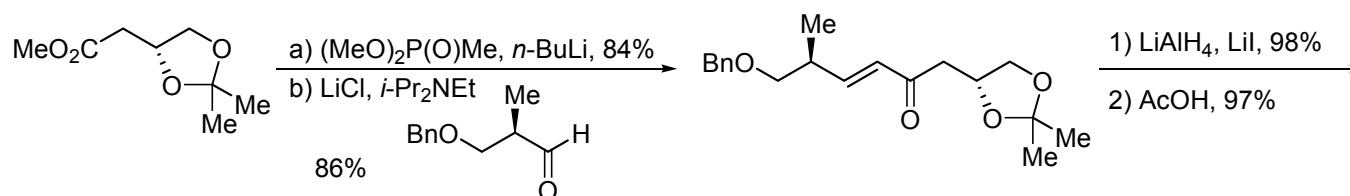


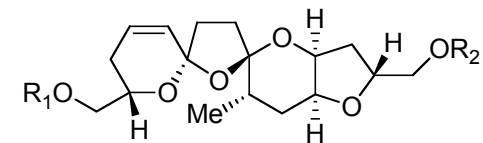
Retrosynthesis



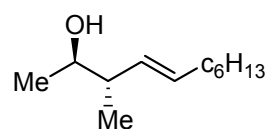


Opening Salvo...

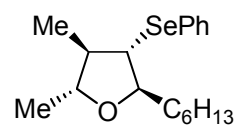




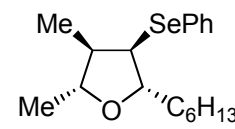
Mihelich and Hite



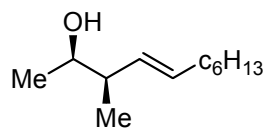
N-PSP 90%
PhSeCl 90%



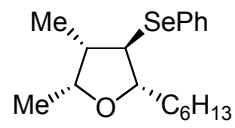
81
93



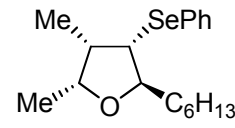
19
7



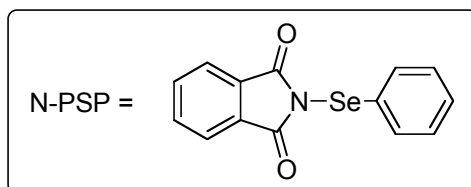
N-PSP 85%
PhSeCl 88%
I₂ 85%

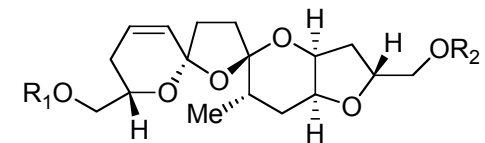


54
83
60

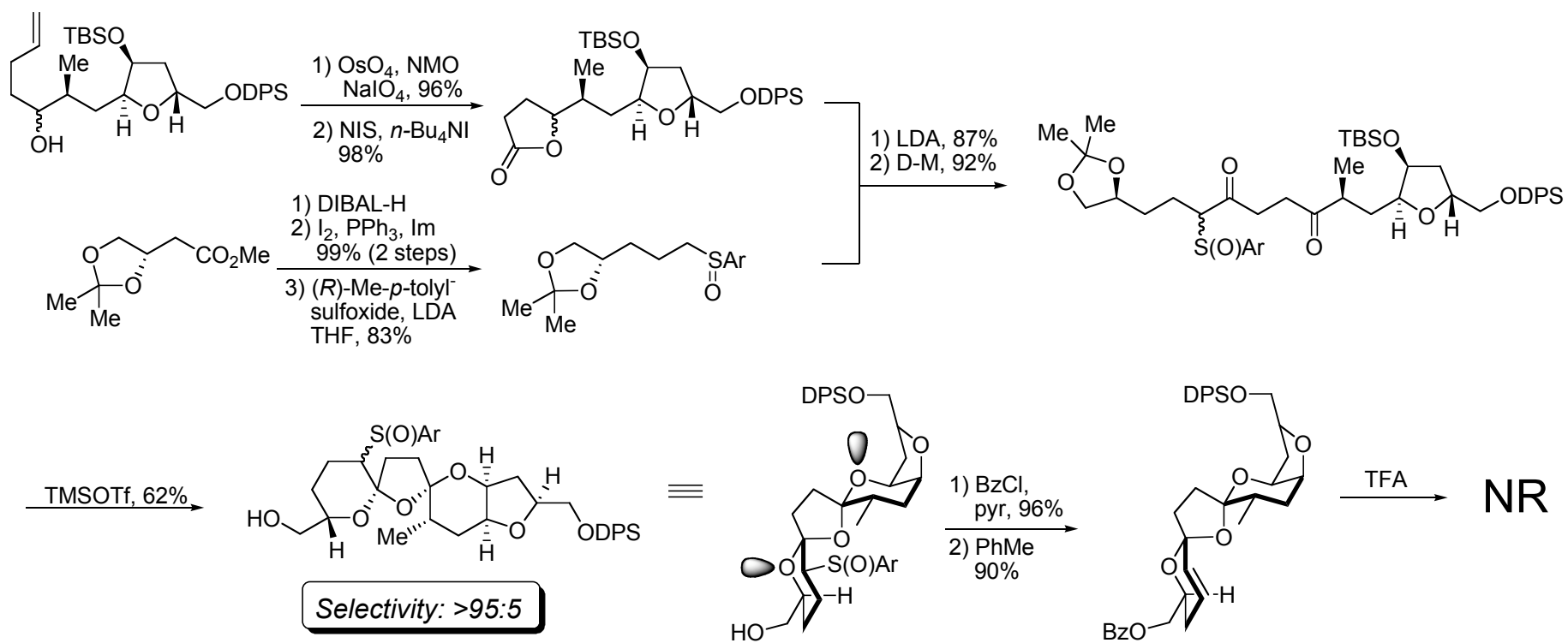


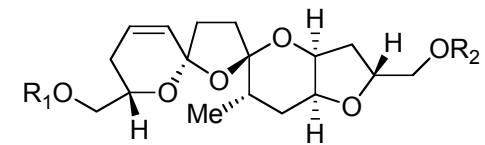
46
17
40



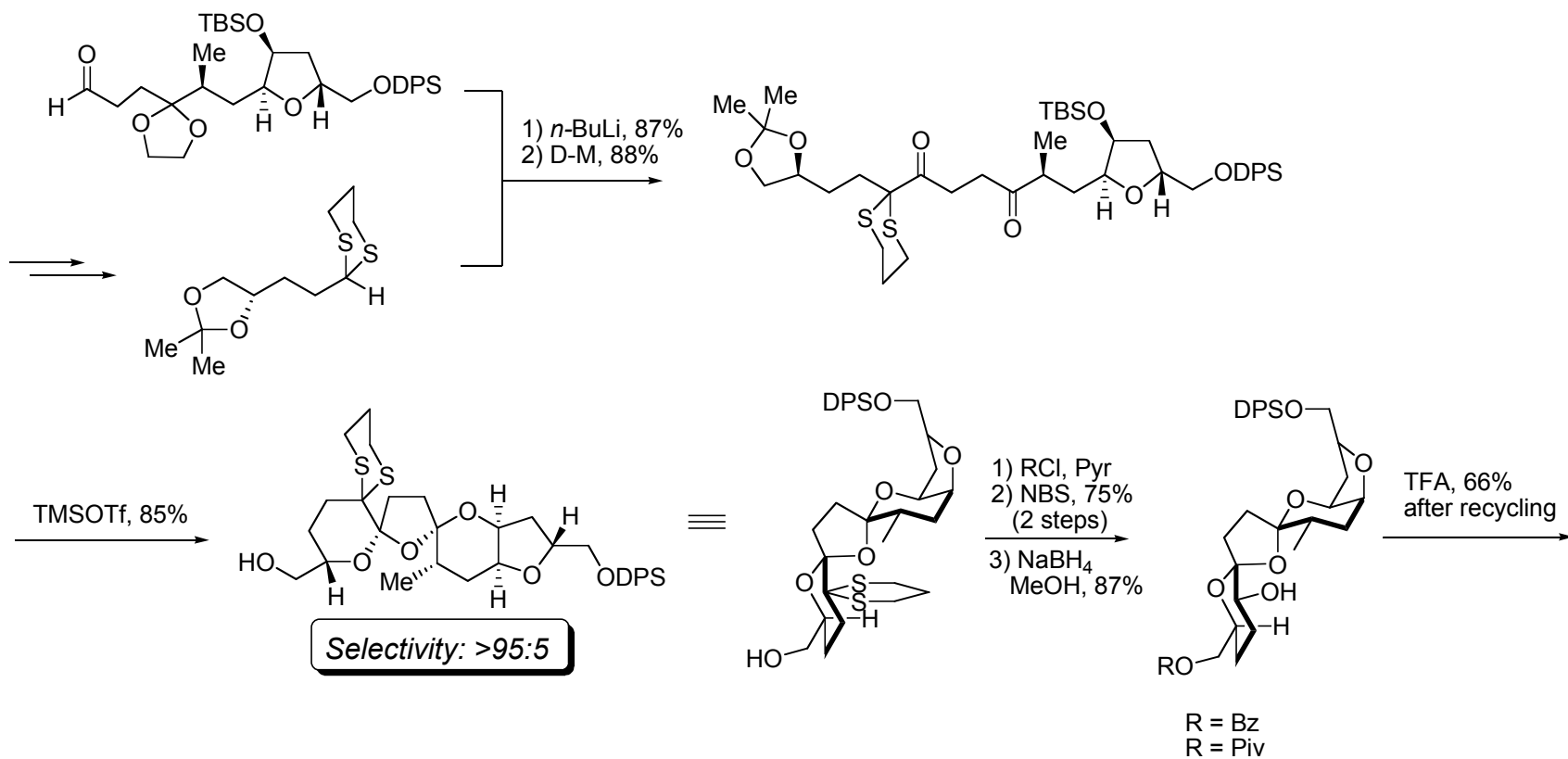


First Spiroketalization

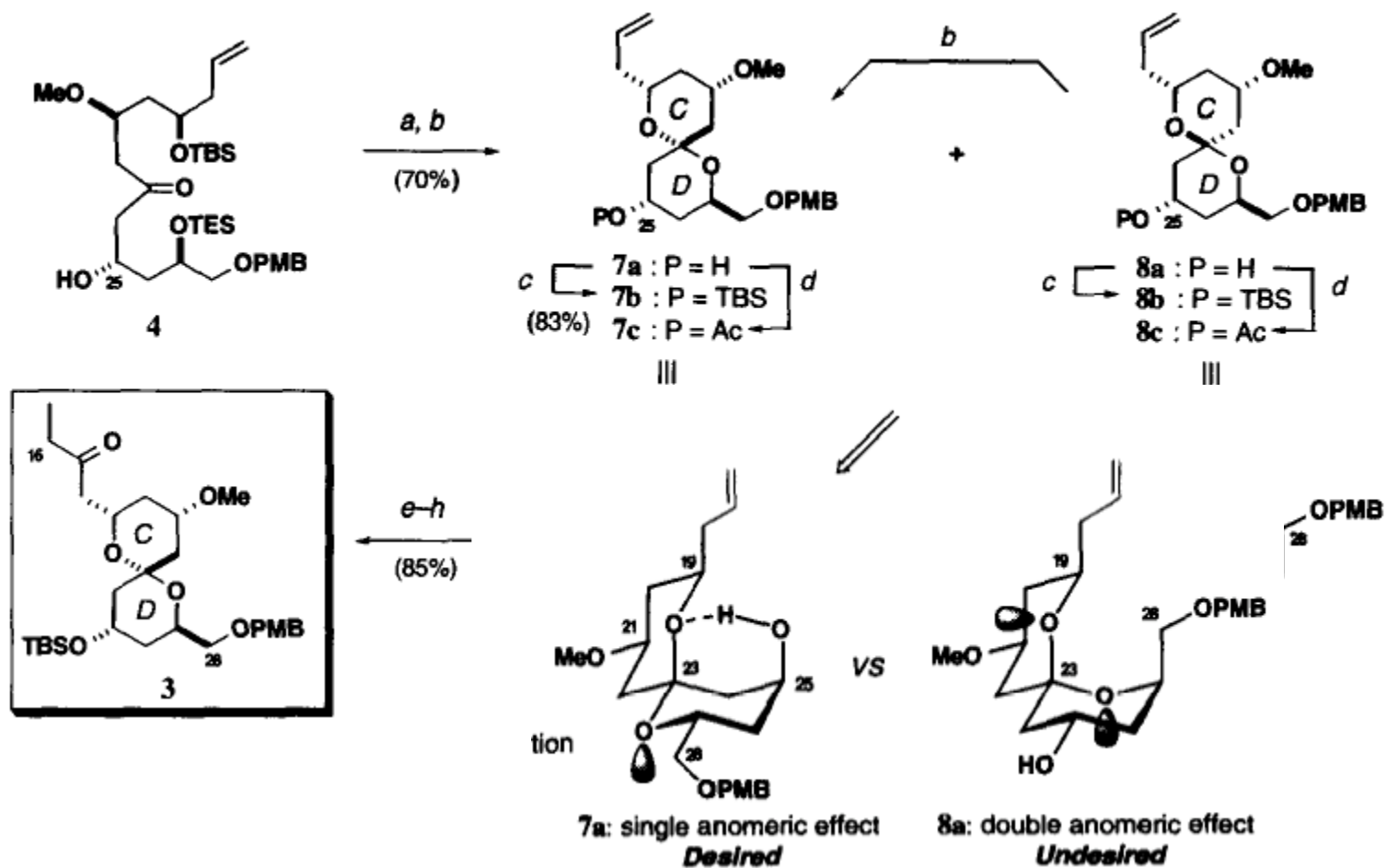




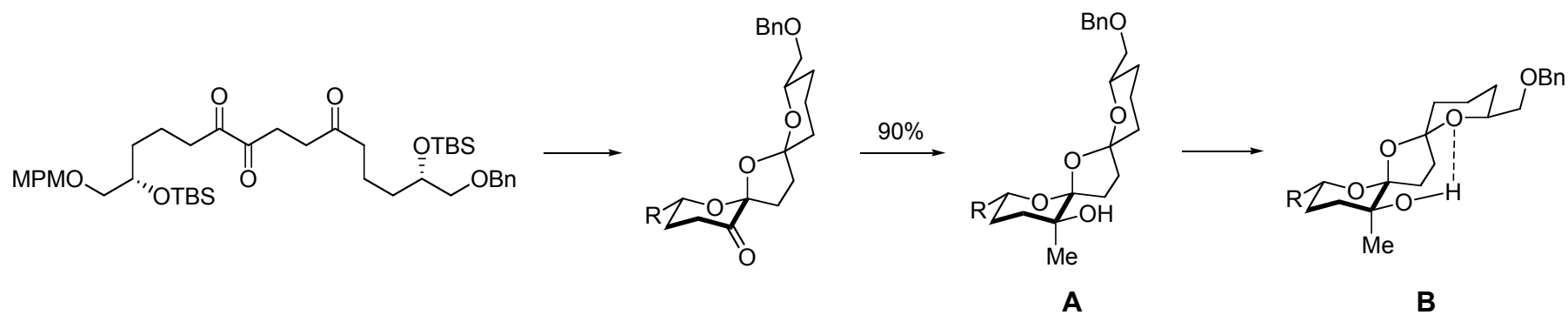
Second Spiroketalization



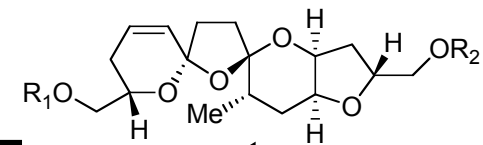
Patterson...



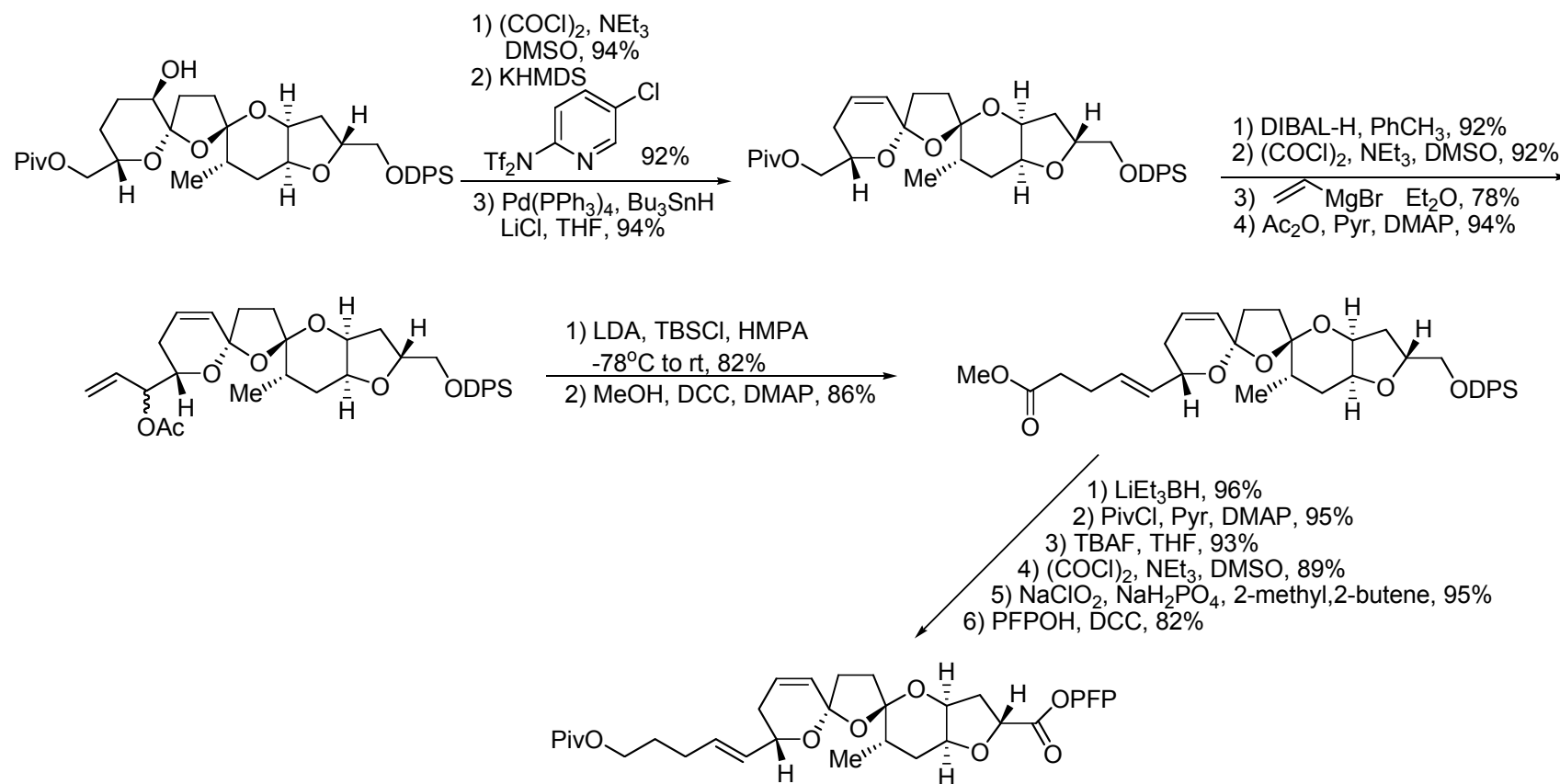
Murai...



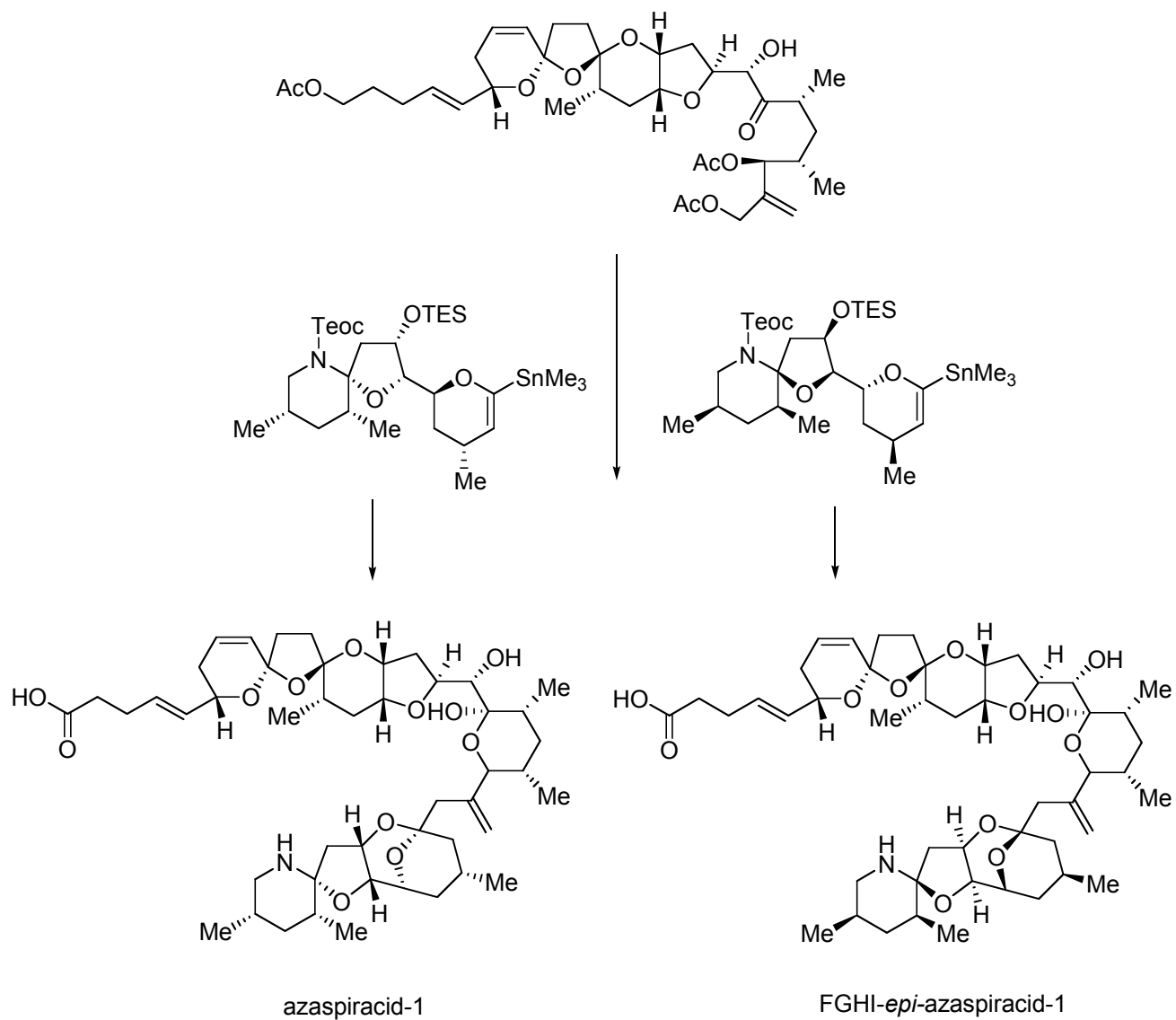
<i>Reagent</i>	<i>Conversion</i>
trace HCl-CDCl ₃ , 12 h	3:2
trace HCl-THF, 41.5 h	3:1
PPTS-THF, 24 h	NR
PTS-THF, 24 h	3:1



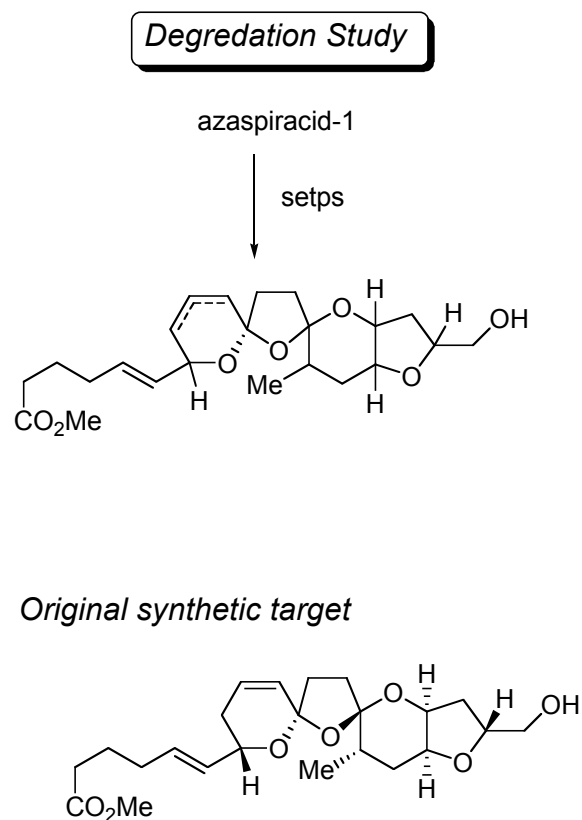
Completion of Proposed Target



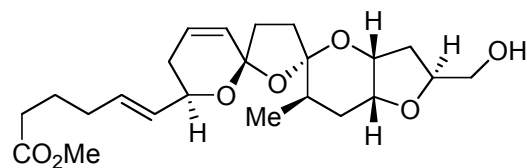
Skipping Ahead...



Intelligence Gathering and Tentative Proposal

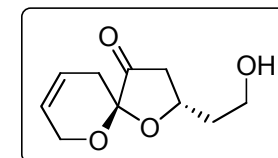
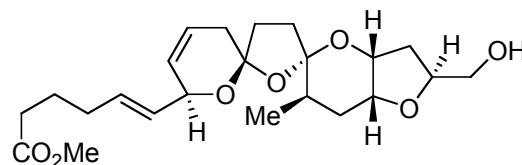


First revised structure:



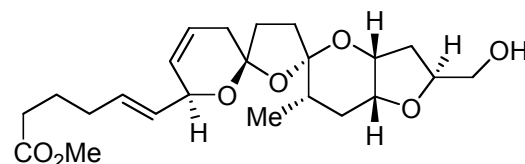
Enantiomer

Second revised structure:



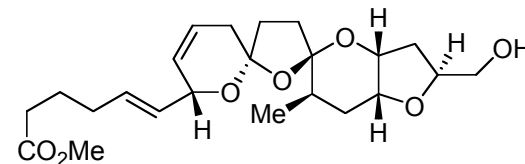
lissoketal

Third revised structure:

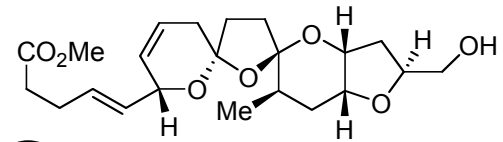


*Acid stability
NOE
Anomeric effect*

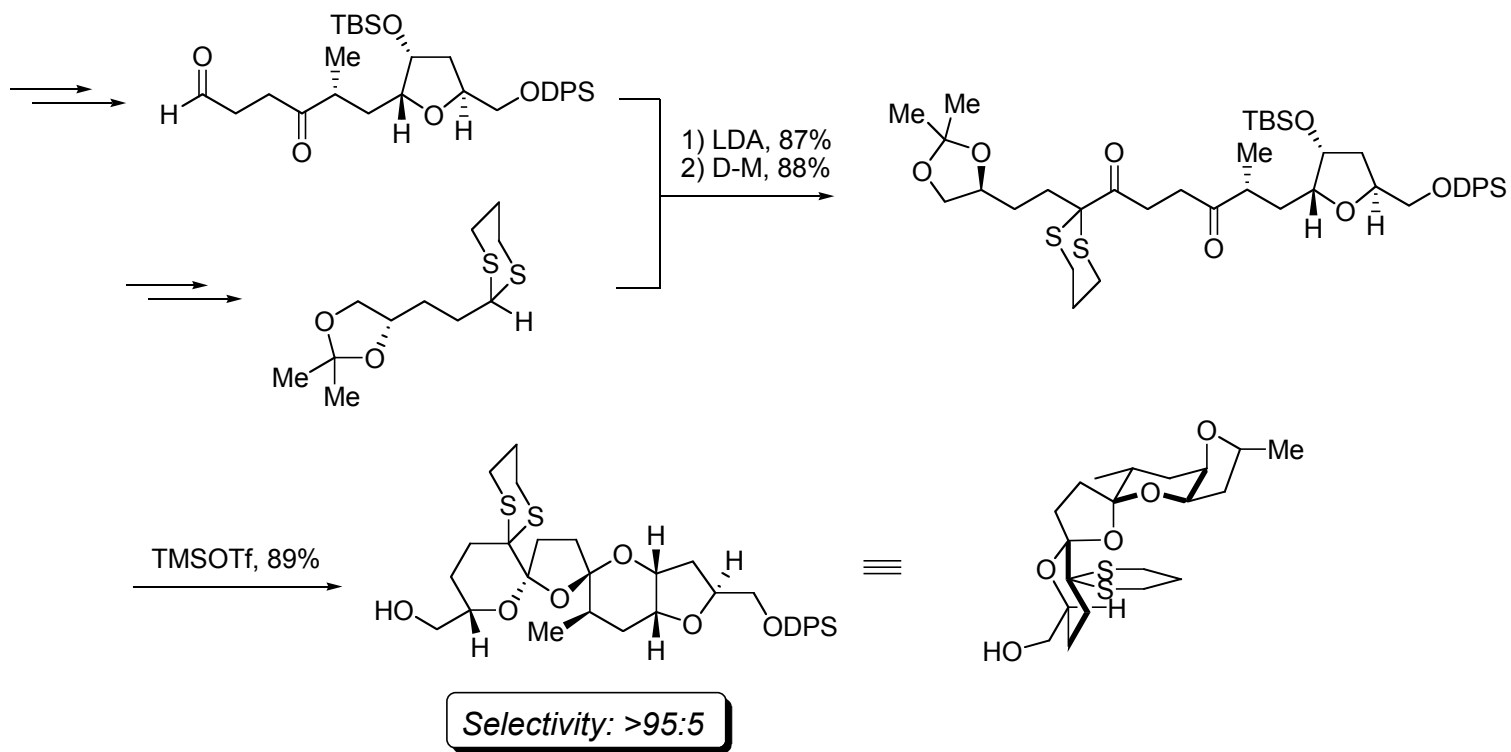
Fourth revised structure:



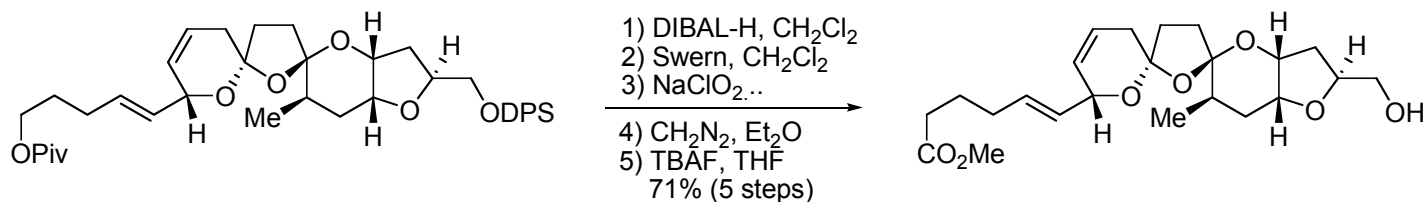
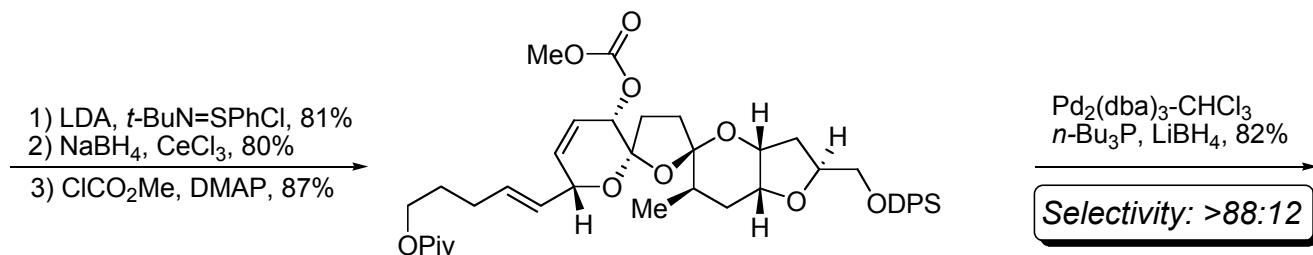
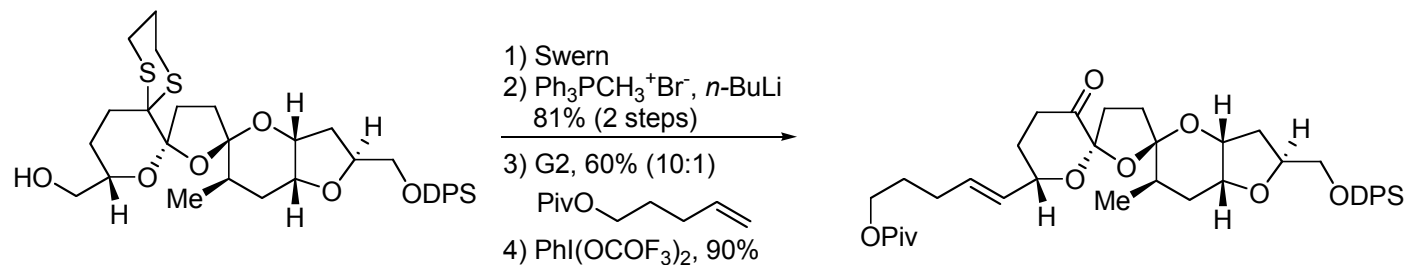
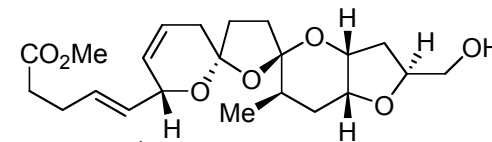
*Acid stability
NOE
Anomeric effect*

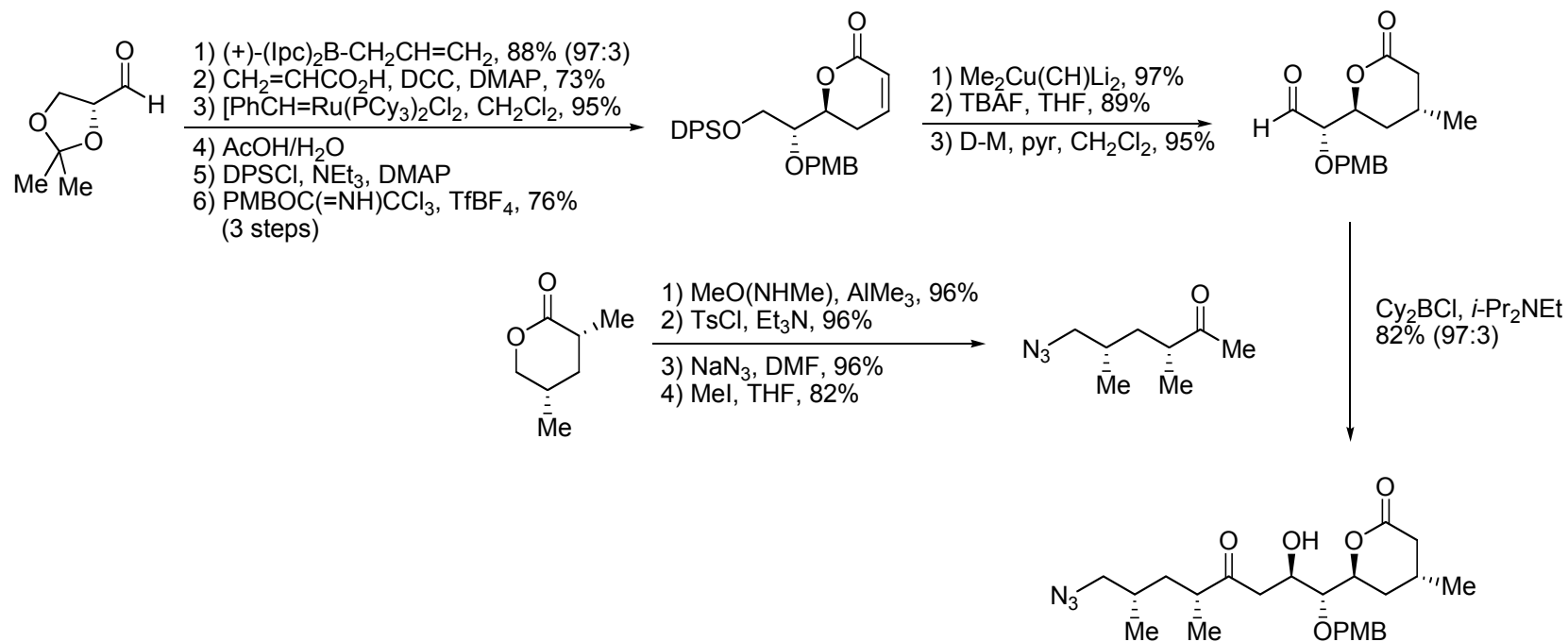
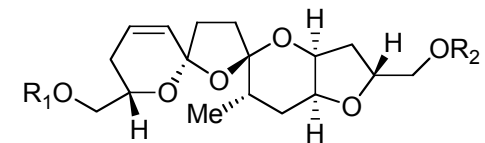


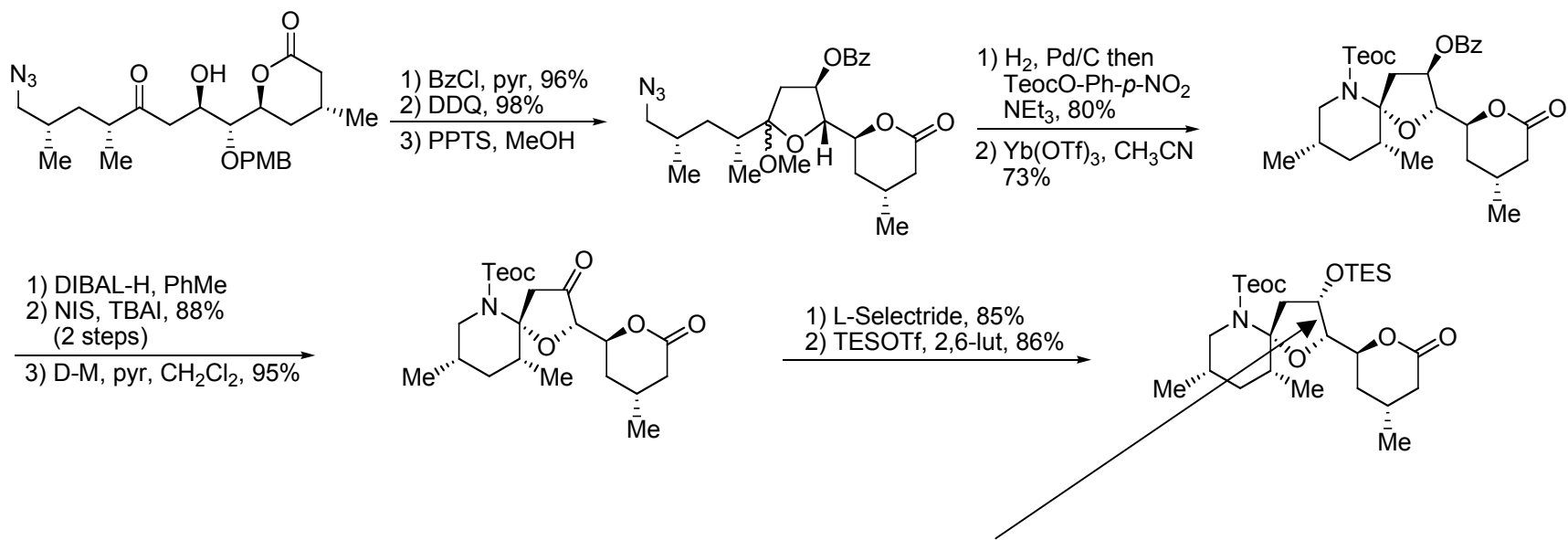
Synthesis of Fourth Revised Structure



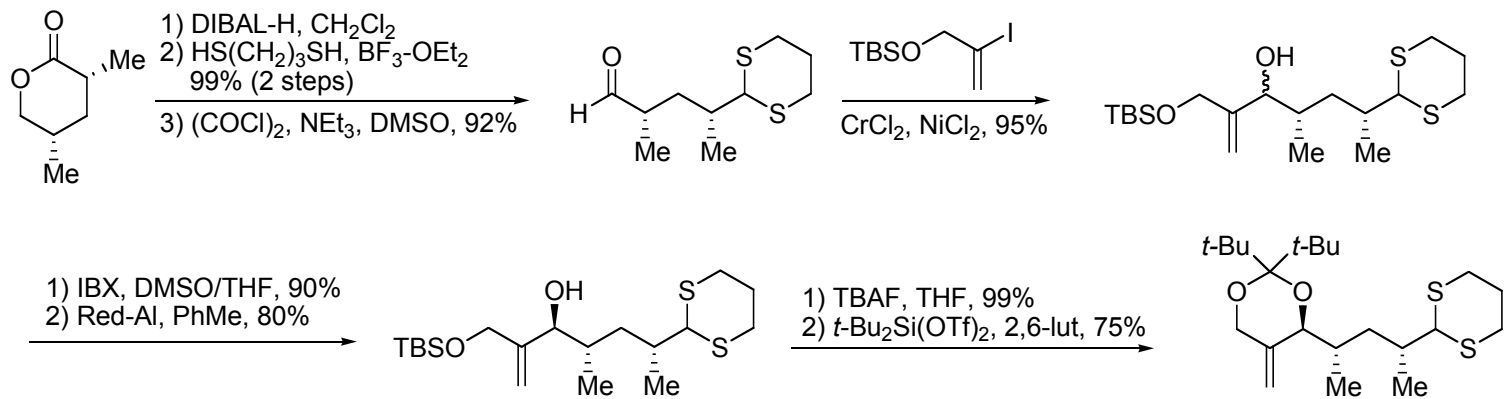
Completion of Fragment

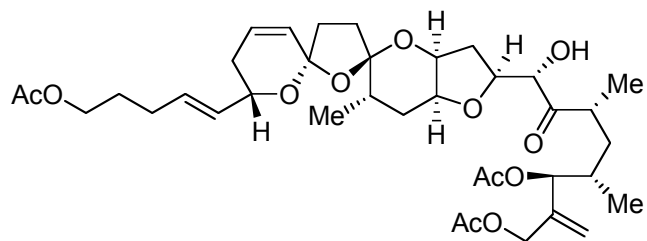
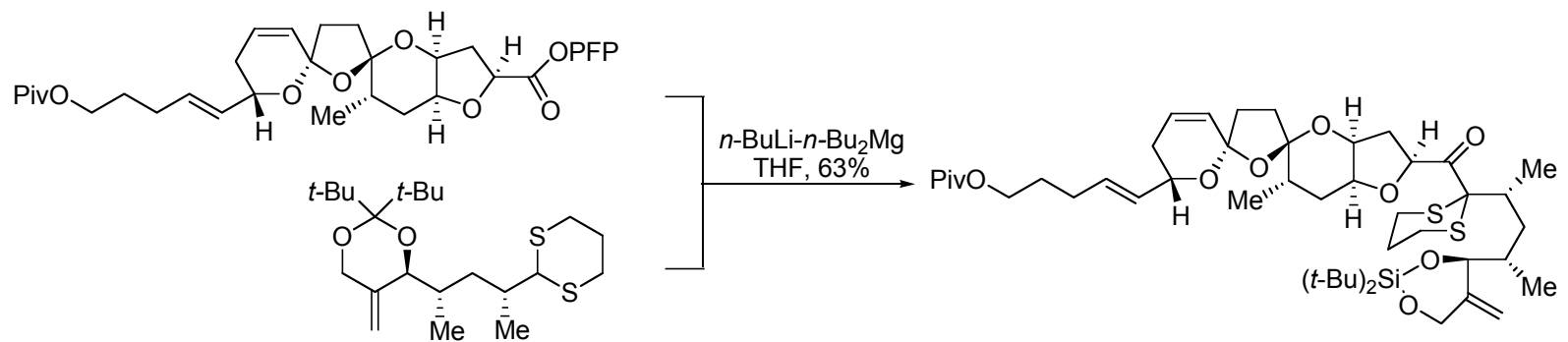






Stereocenter inverted?





- 1) DIBAL-H, CH_2Cl_2 , 55%
 2) TBAF, THF, 78%
 3) Ac_2O , py, 84%
 4) $\text{PhI}(\text{OCOCF}_3)_2$, 78%

