



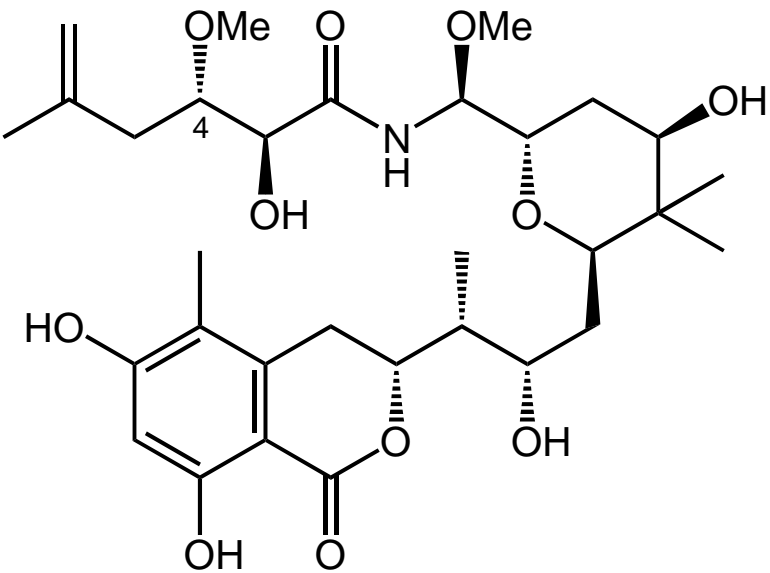
Literature Report 2010-01-12

Duan, Y. Checker: Wang, D.-S.

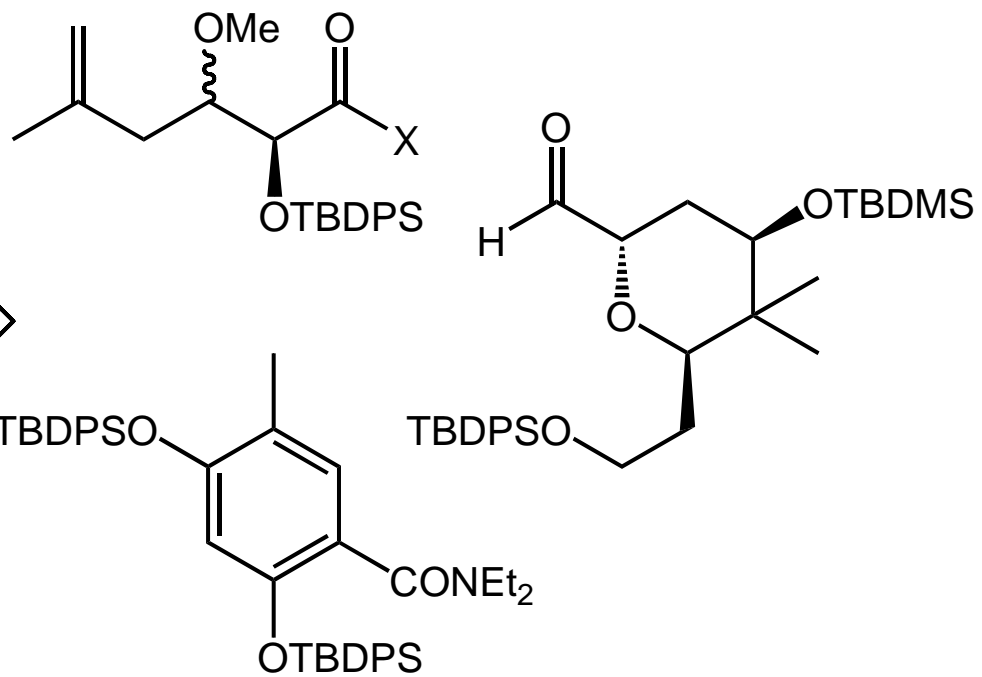
Progress toward the Total Synthesis of Psymberin/Irciniastatin A

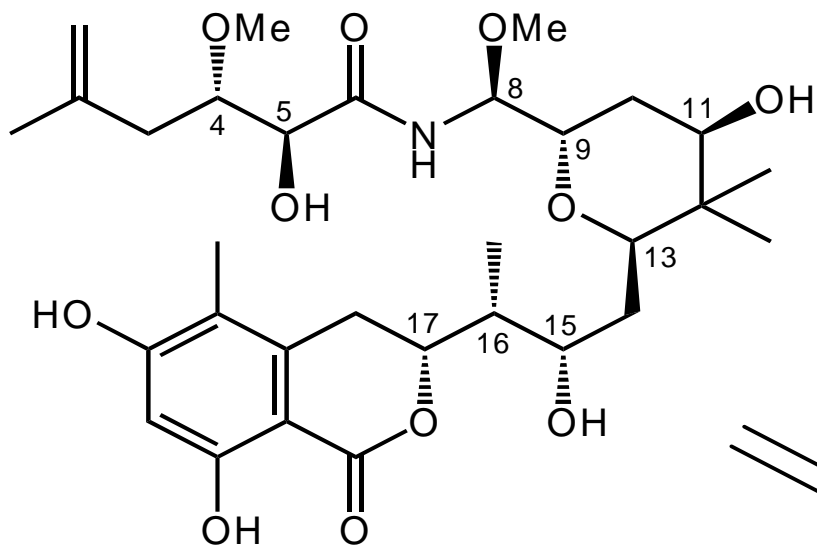
Konopelski, J.*, *et al*

J. Org. Chem. **2009**, 74, 5405-5410

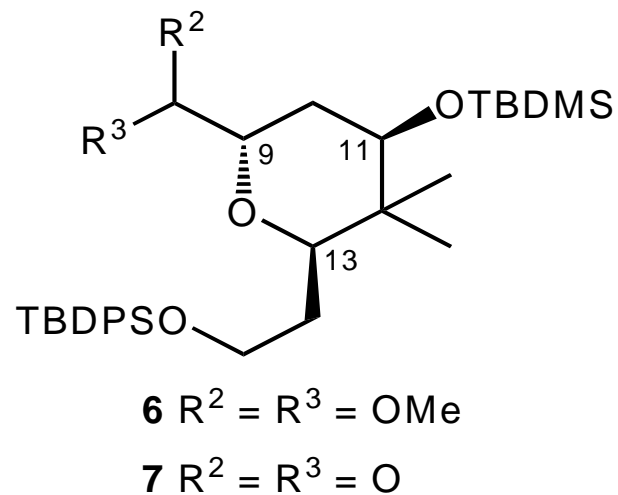
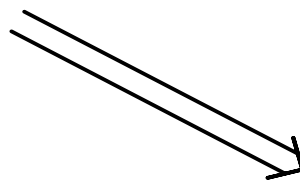
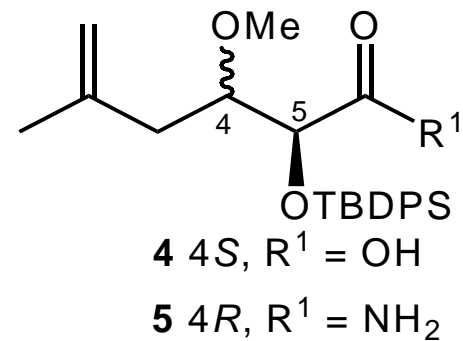
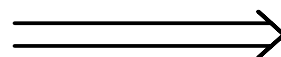
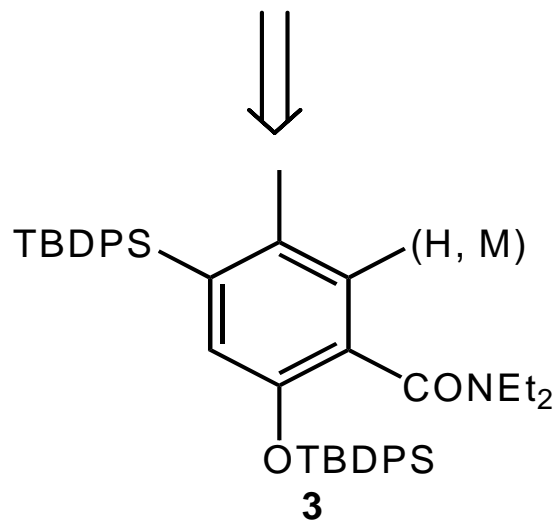


4S: Psymberin (1)
4R: 4-*epi*-Psymberin (2)

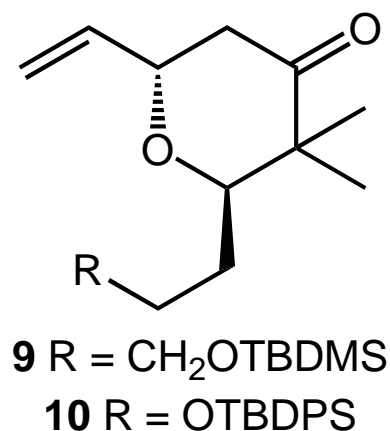
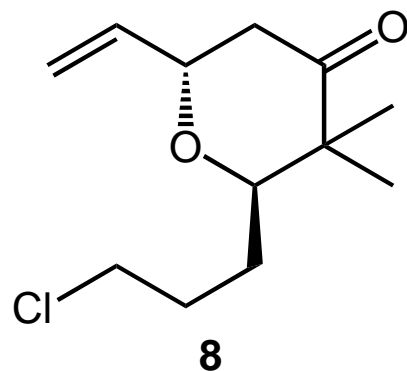




4S: Psymberin (1)
4R: 4-*epi*-Psymberin (2)

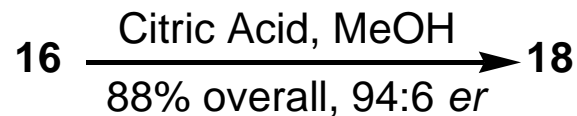
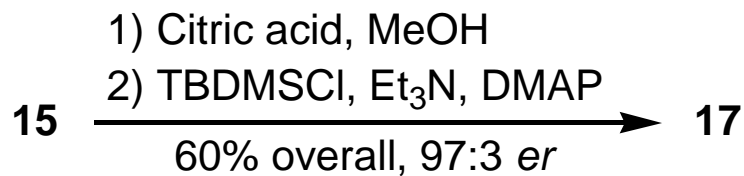
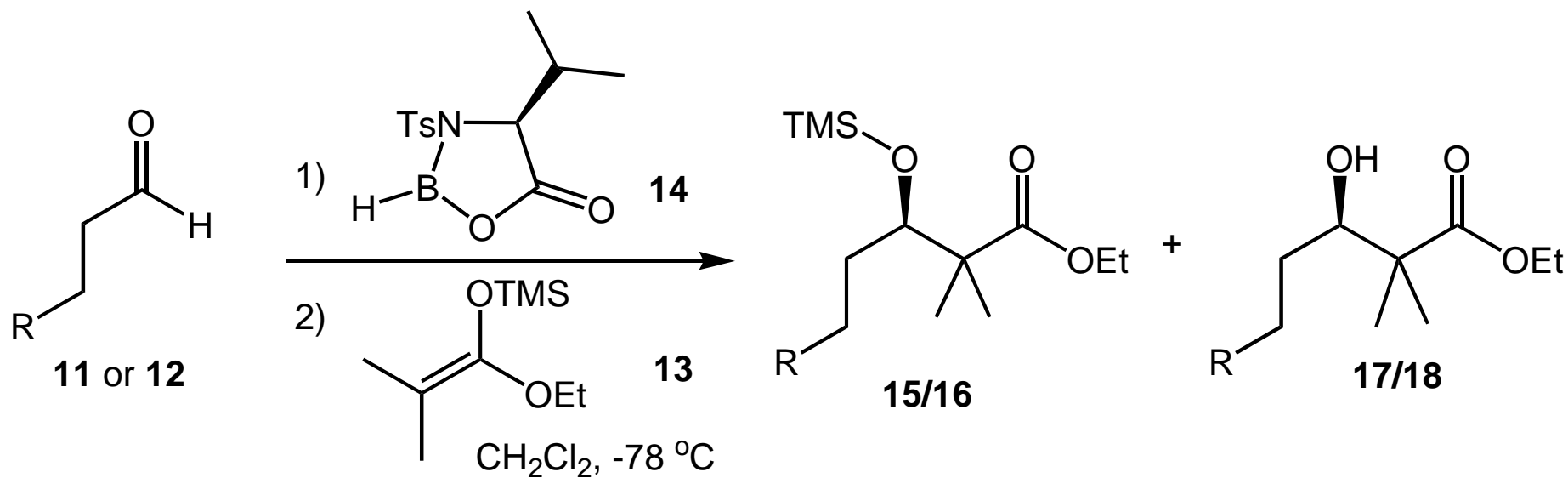


Kocienski's synthesis of compound **8** served as our template for rapid assembly of pyran core fragments **9** and **10**



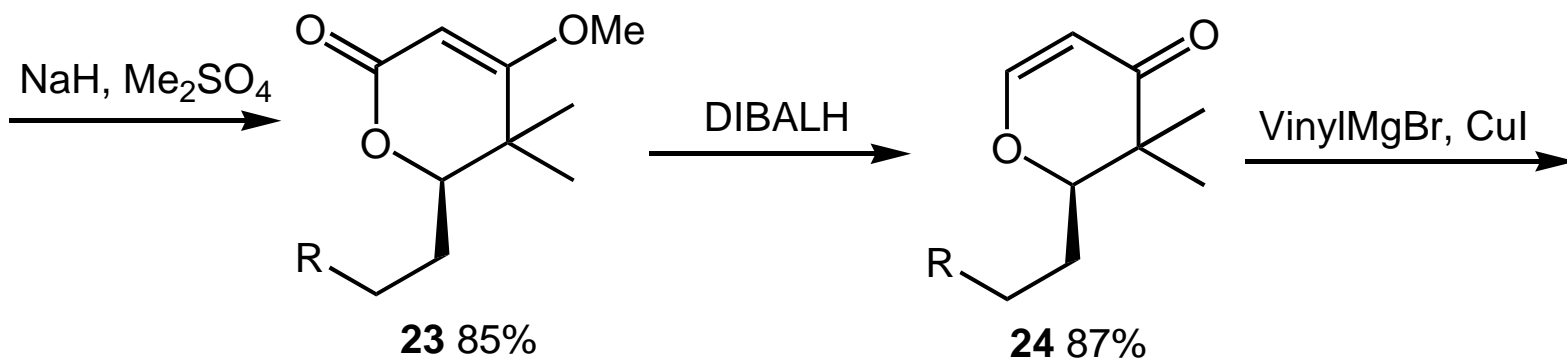
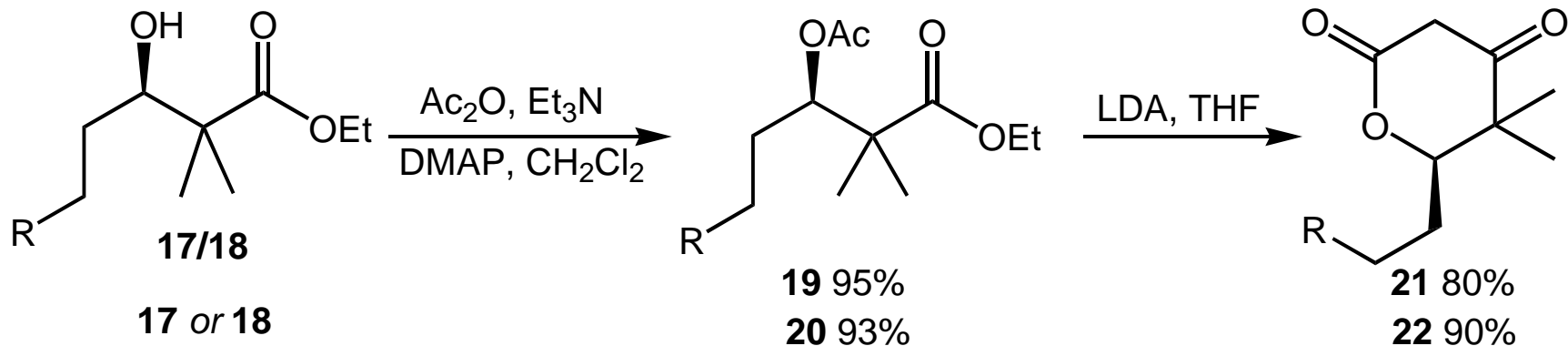
Kocienski, P. et al *Synlett* **1998**, 1432-1434

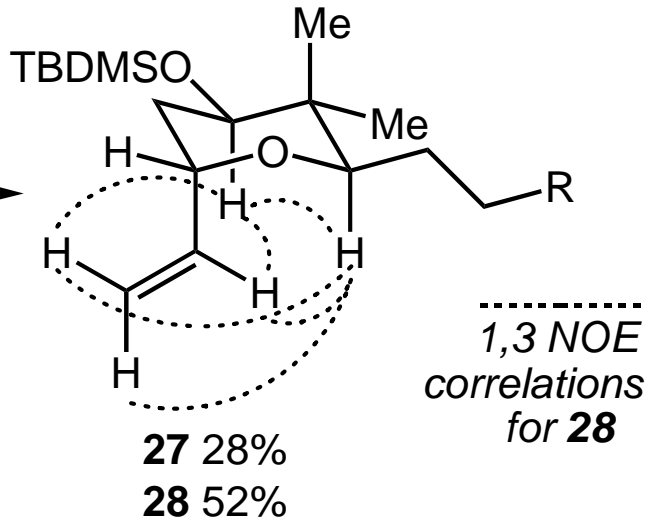
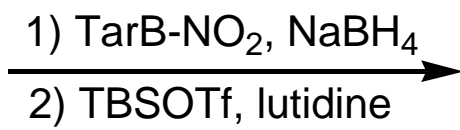
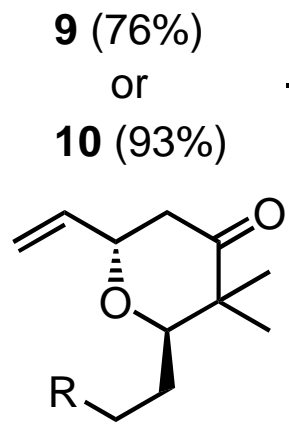
Kocienski, P. et al *J. Chem. Soc., Perkin Trans. I* **2000**, 2357-2384



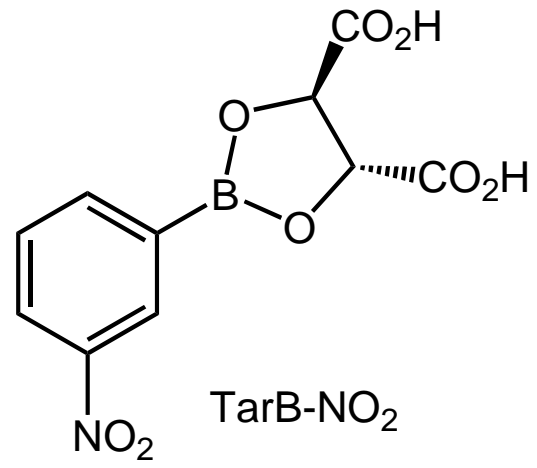
11, 15, 17 R = CH₂OTBDMS

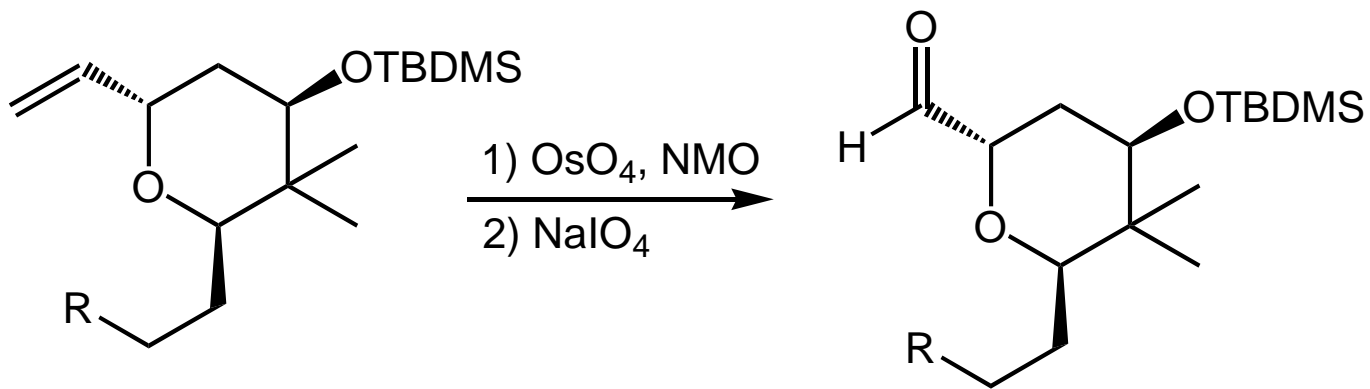
12, 16, 18 R = OTBDPS





19, 21, 23, 25, 27: R = CH₂OTBDMS
20, 22, 24, 26, 28: R = OTBDPS



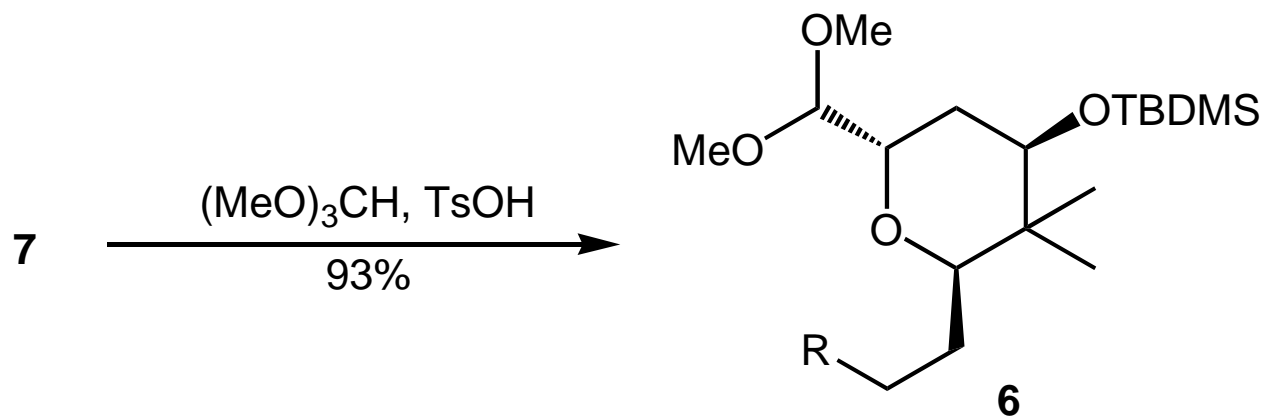


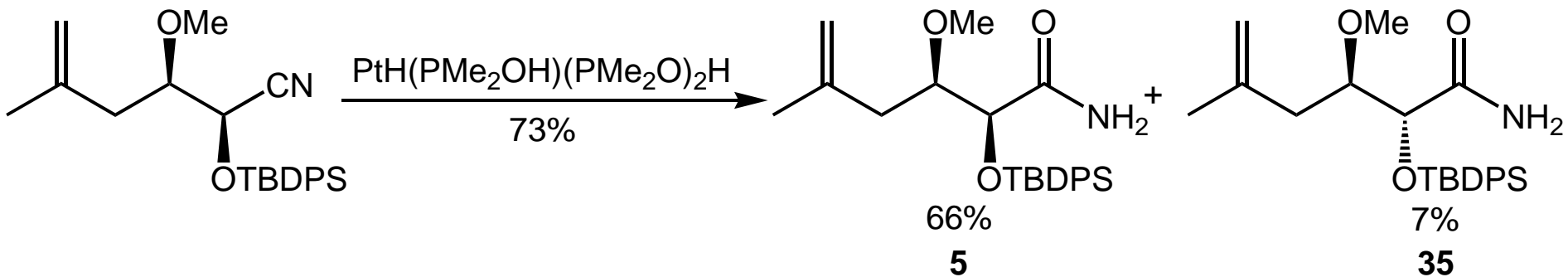
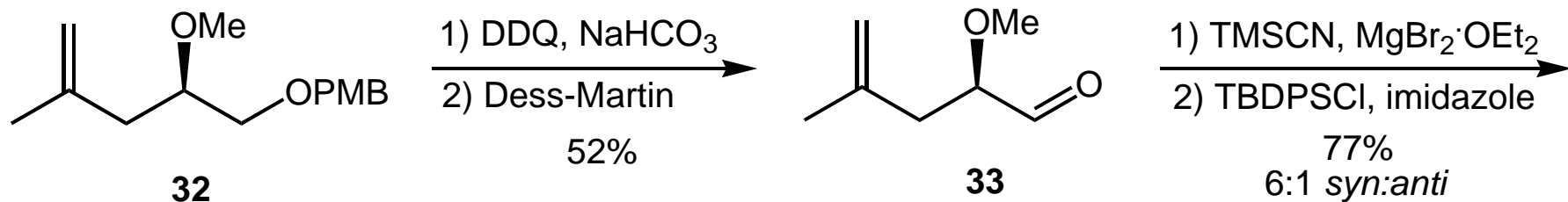
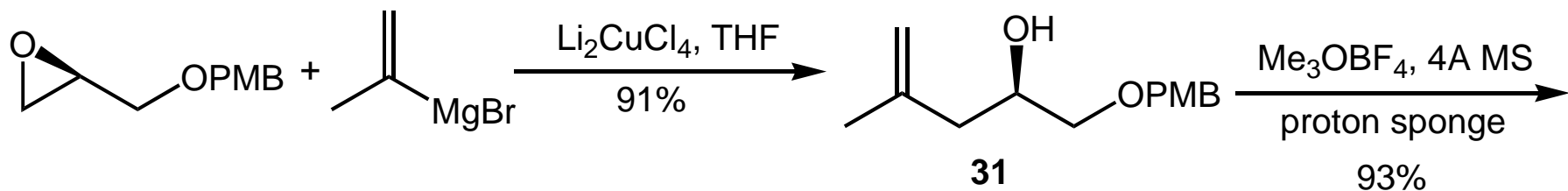
27 R = CH_2OTBDMS

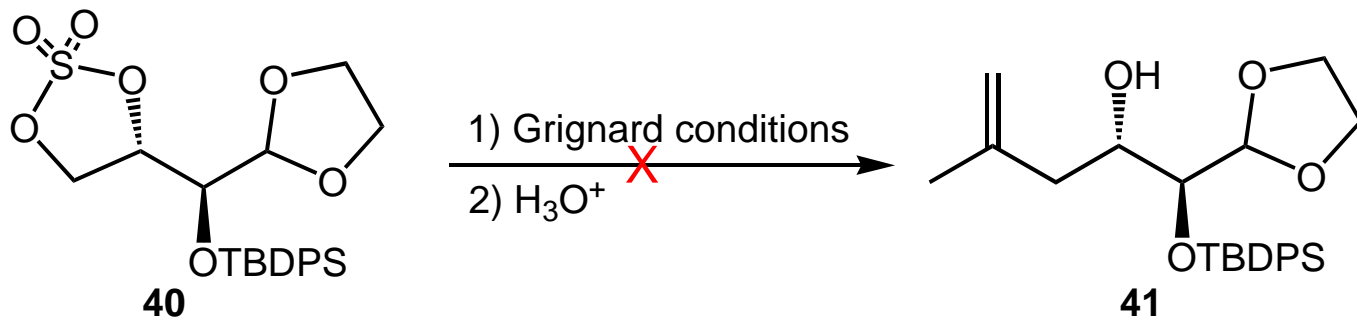
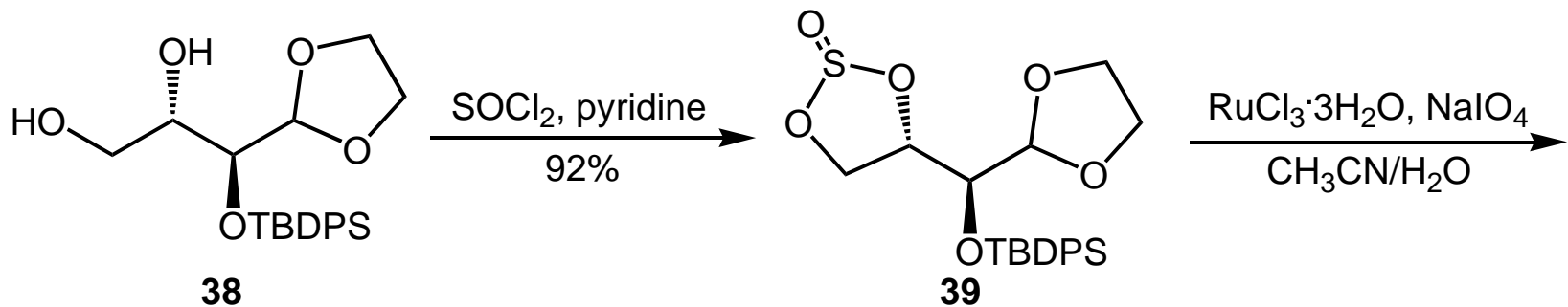
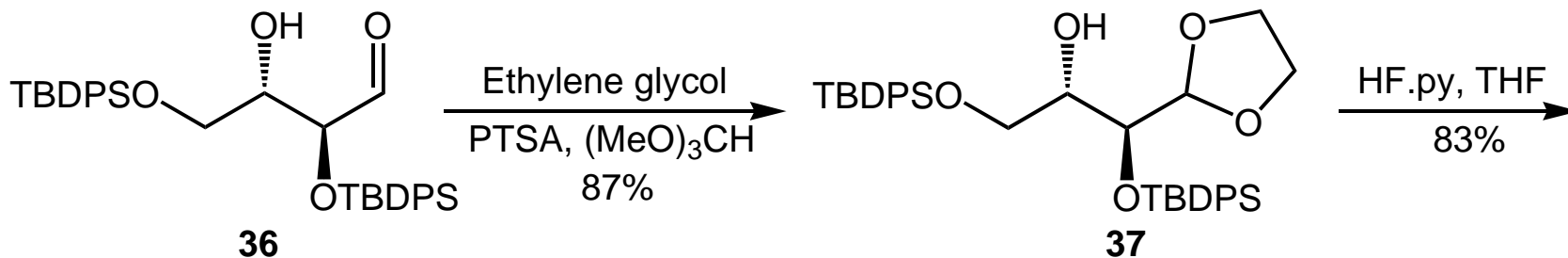
28 R = OTBDPS

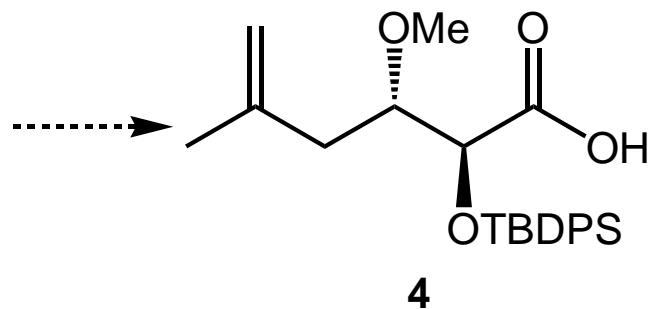
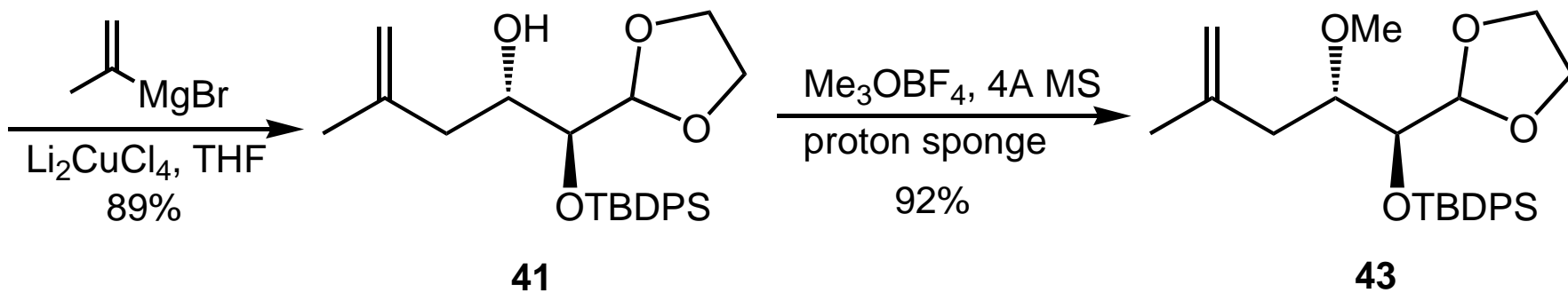
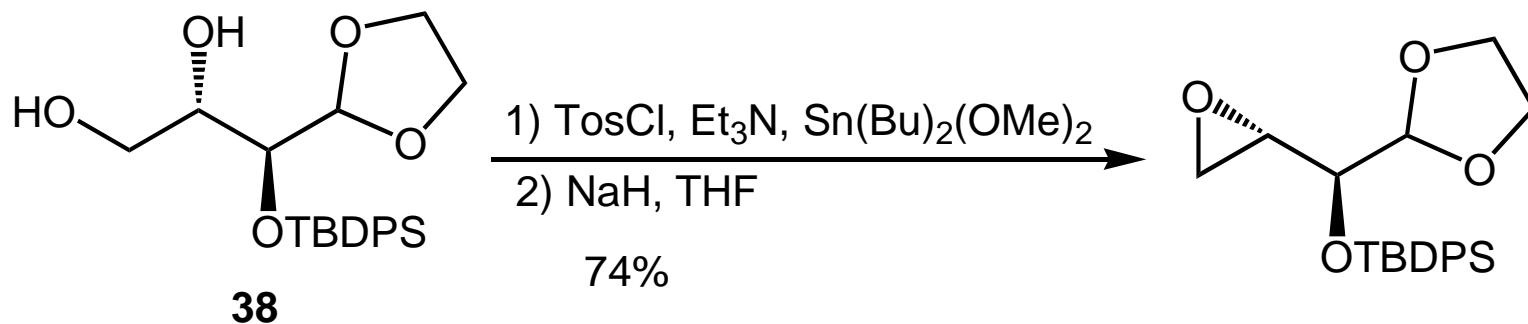
29 R = CH_2OTBDMS 50%

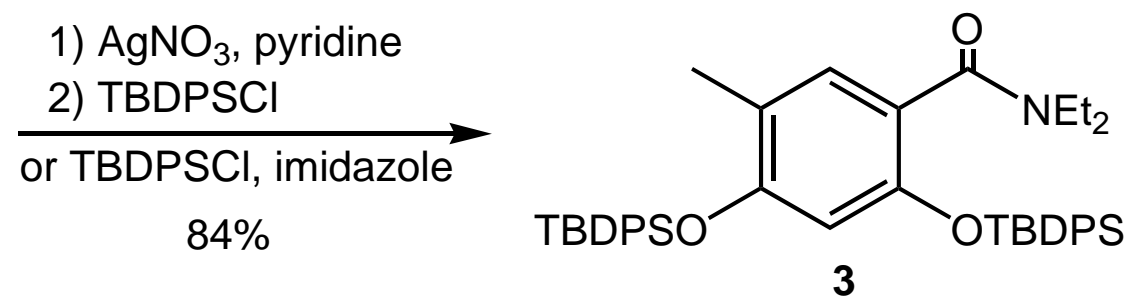
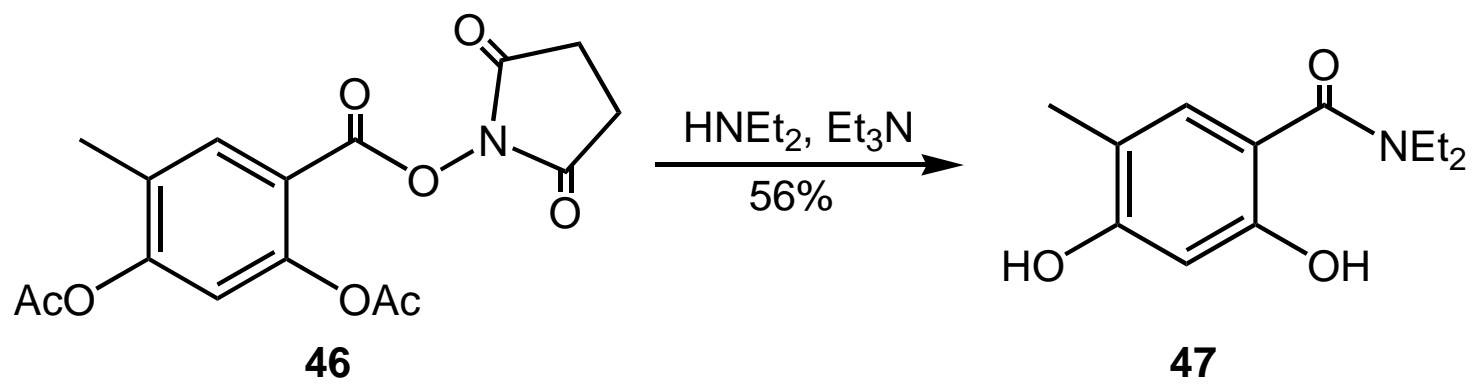
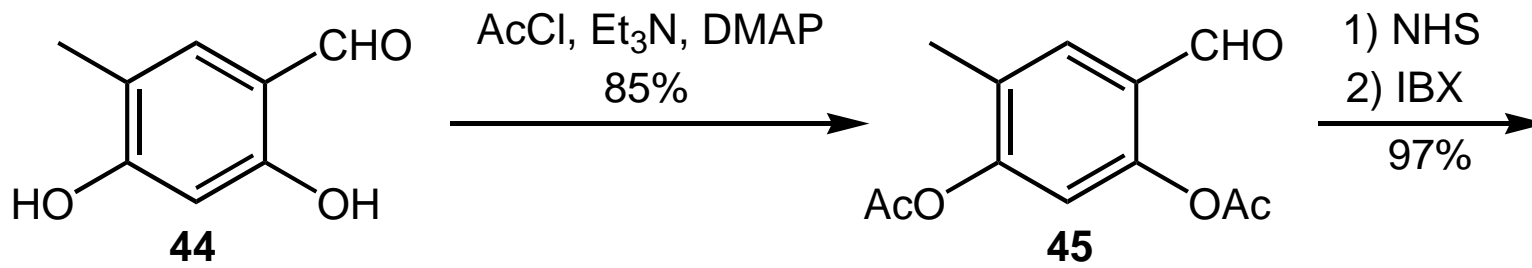
7 R = OTBDPS 95%

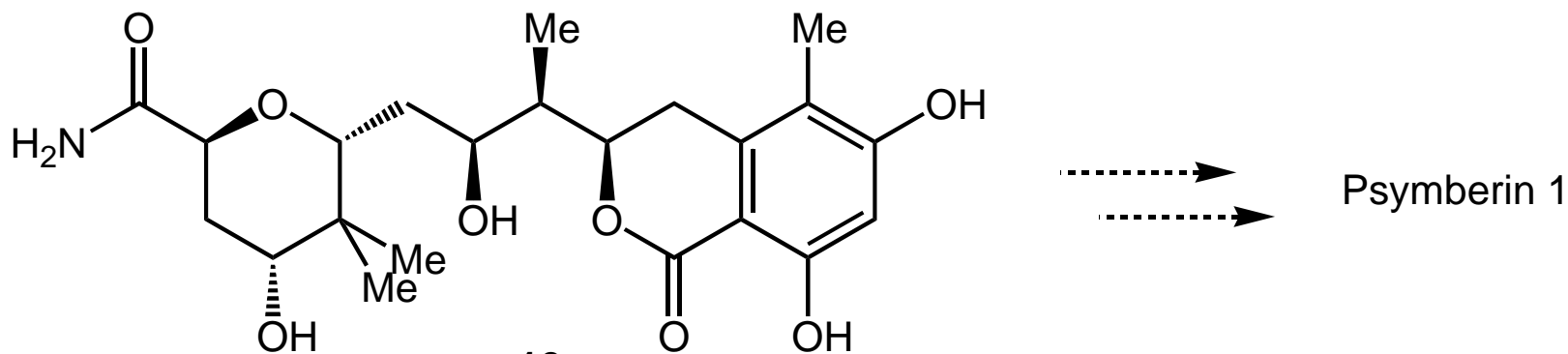
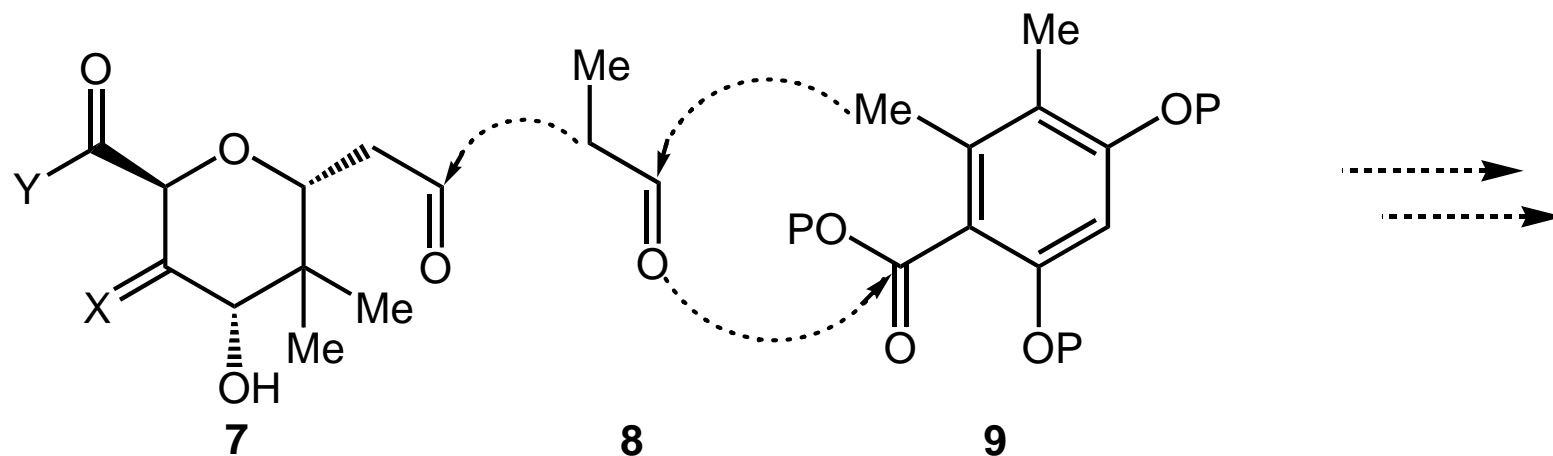
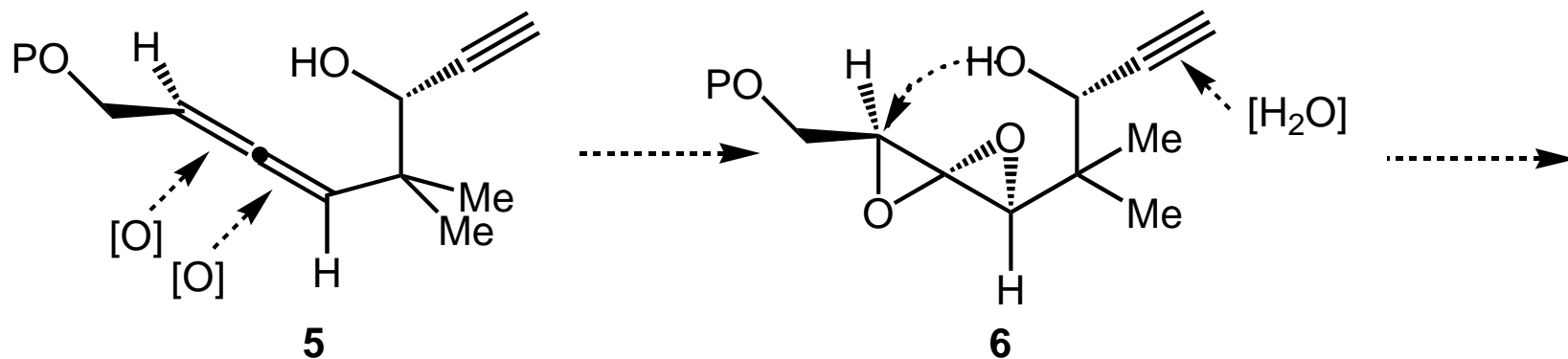


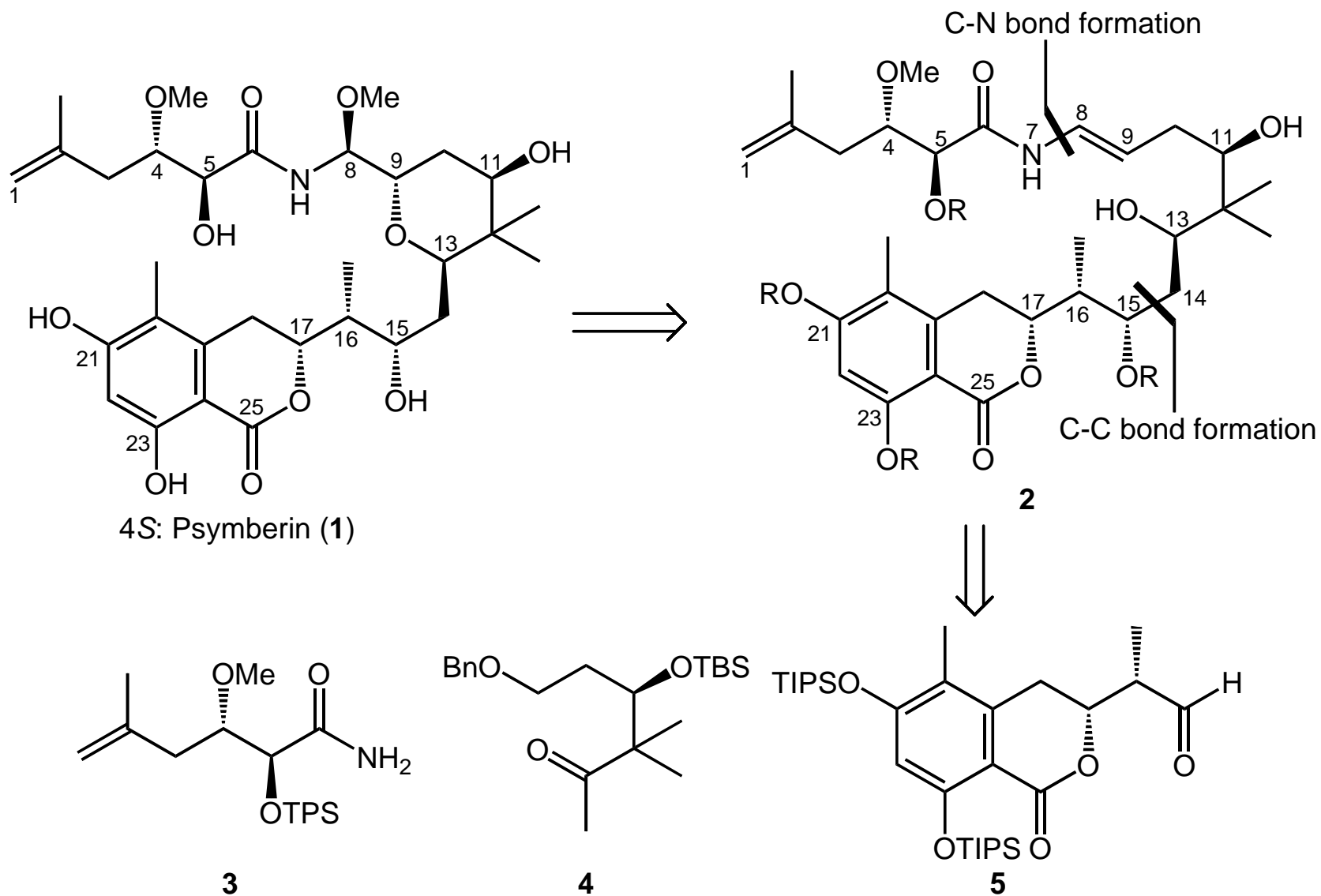


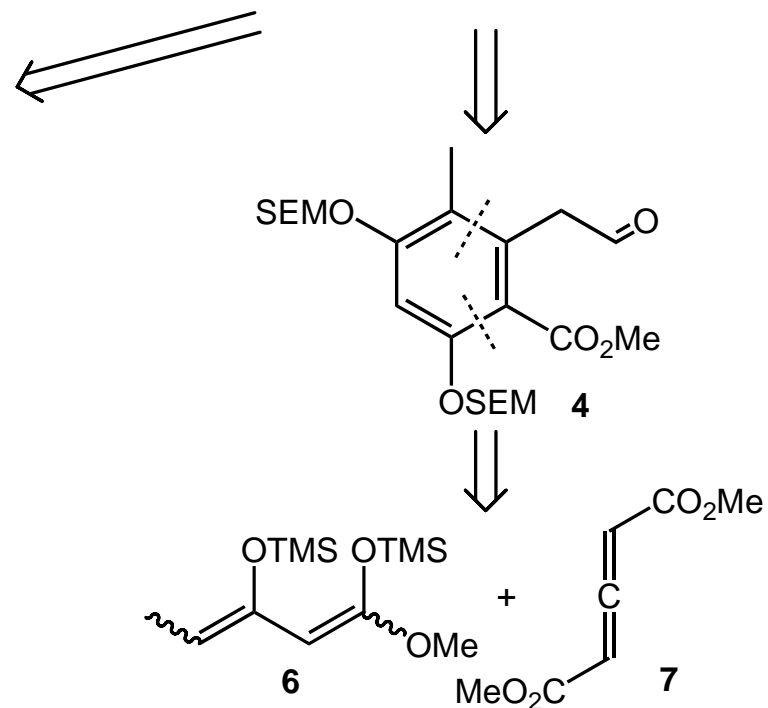
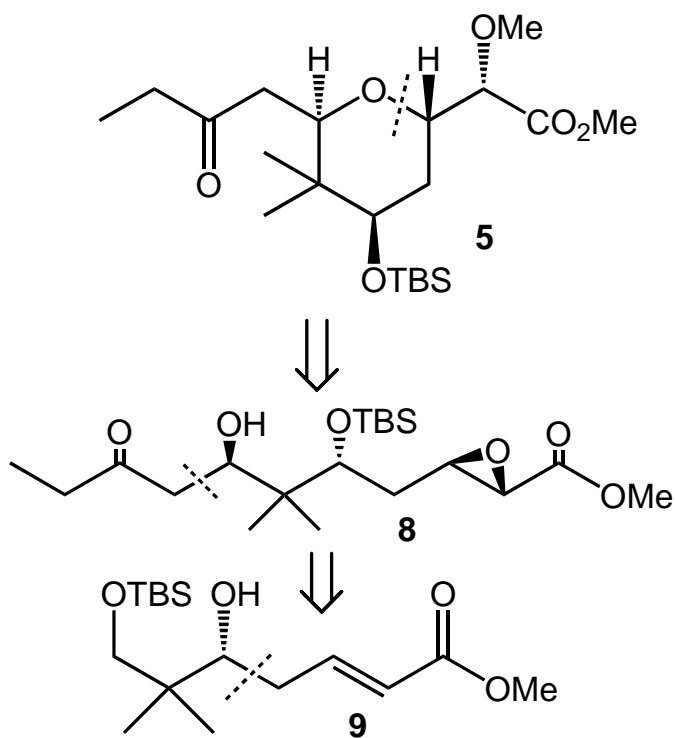
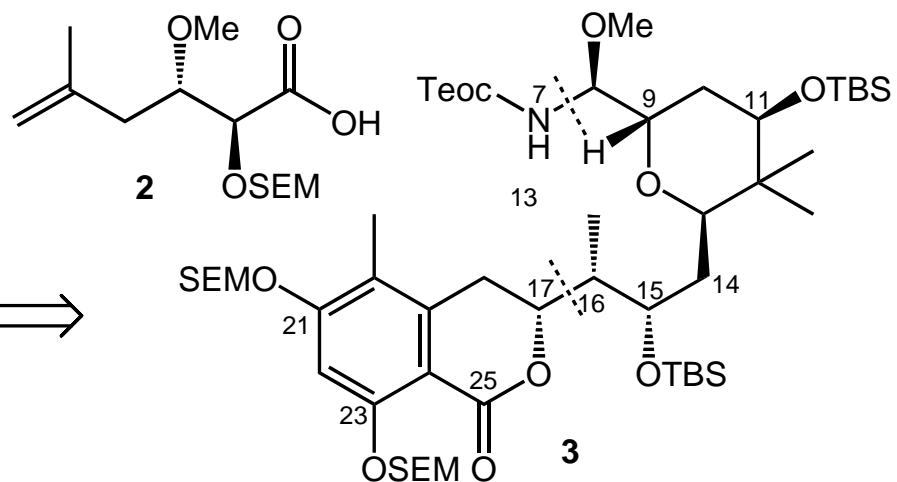
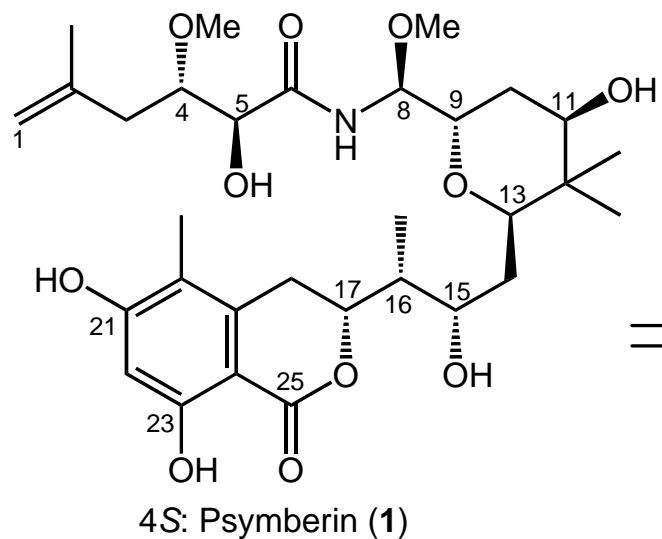


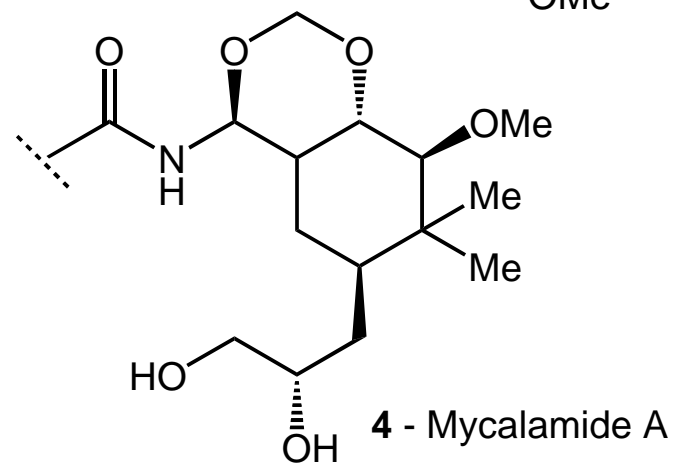
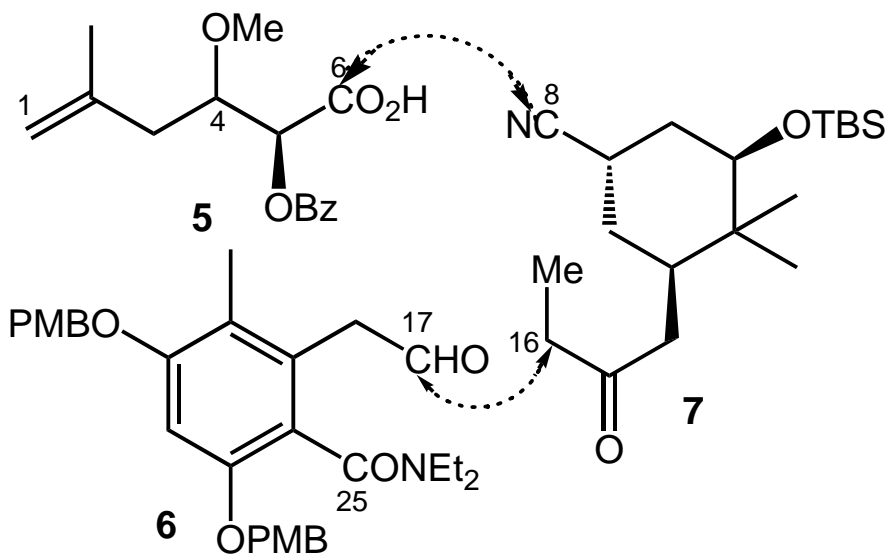
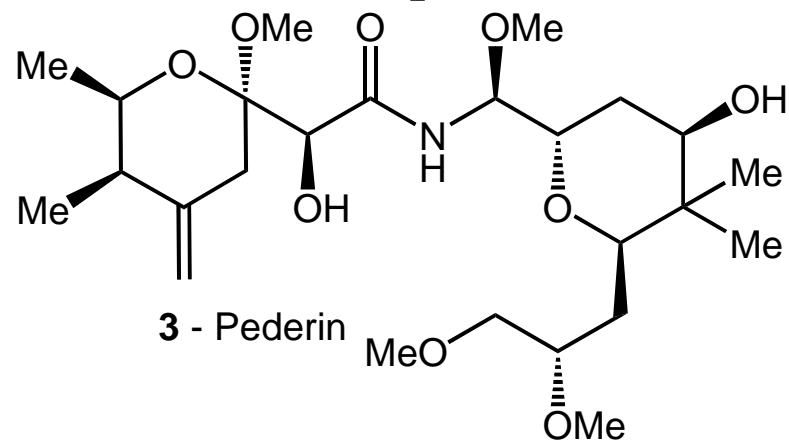
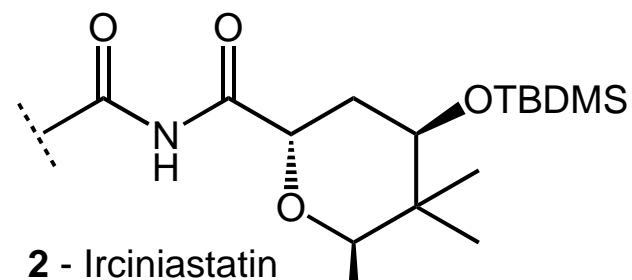
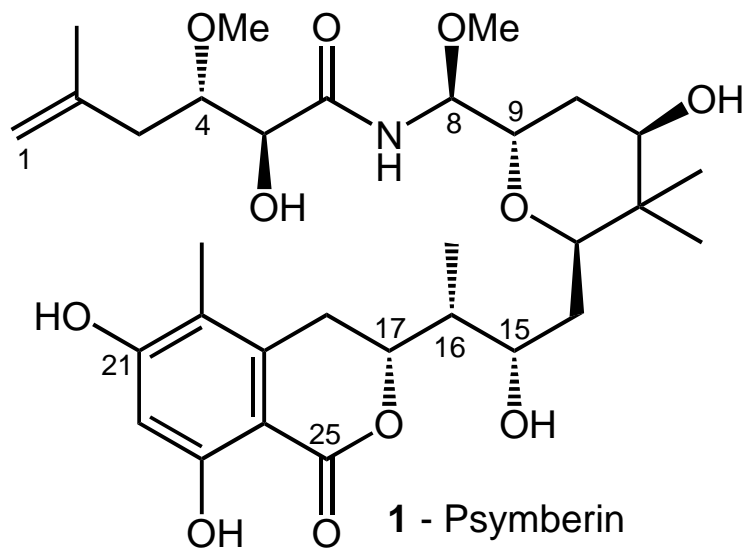













- In late 2003, our colleagues in the research group of Professor Philip Crews isolated a highly potent cytotoxic marine natural product from “an undescribed and inconspicuous sponge, *Psammocinia* sp.” The molecule, psymberin (assigned by Crews et al. as either **1** or **2**), was later determined to be identical to iriciniastatin A, a compound isolated and reported by Pettit and co-workers from extracts of *Ircinia* *ramose*. The dual isolation of this compound from different sponges combined with the reported difficulty in isolating the compound from many sponge extracts adds evidence to the speculation that this molecule, along with structurally similar compounds, may in fact take origin from symbiotic bacteria. Over the past 6 years, a number of publications relating to the synthesis and semisynthesis of psymberin and analogues have been developed. To embark on the total synthesis of this remarkably active molecule, we endeavored to develop a rapid and convergent approach to both **1** and **2** as well as libraries of stereoisomer and structural analogues. Our successful efforts to produce several key building blocks are disclosed herein.

- 
- Our initial unpublished results as well as personal communication with Professor De Brabander indicate the envisioned disconnection of this aryl fragment may suffer from the hydrolytic stability of the diethylamide, which has thus far been entirely resistant to lactone closure outside of highly acidic refluxing conditions. Thus, some retooling of our dihydroisocoumarin synthesis is apparently necessary. This chemistry, as well as further elaboration of the pyran core and the preliminary results for our envisioned N7-C8 coupling scenarios, are currently under investigation in our laboratory. These findings, combined with the eventual completion of the total synthesis of **1**, will be reported in due course.