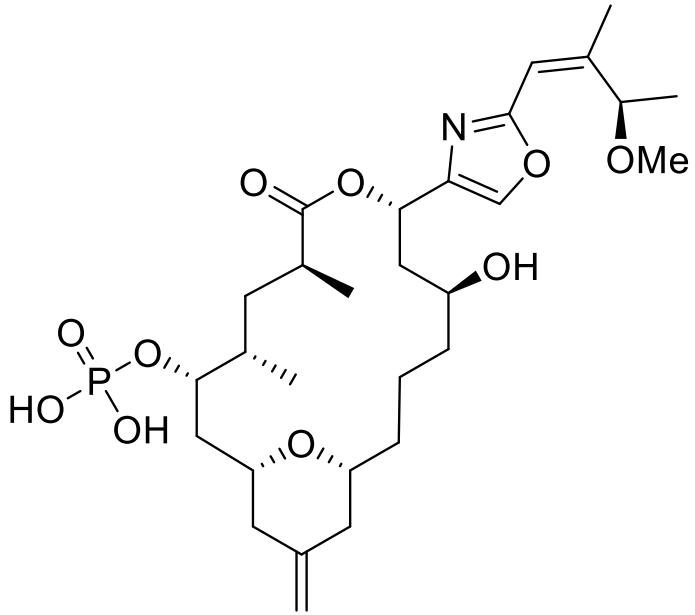
Total Synthesis of (–)-Enigmazole A[1]



(□)-Enigmazole A

Presented by: Grace Hubbell

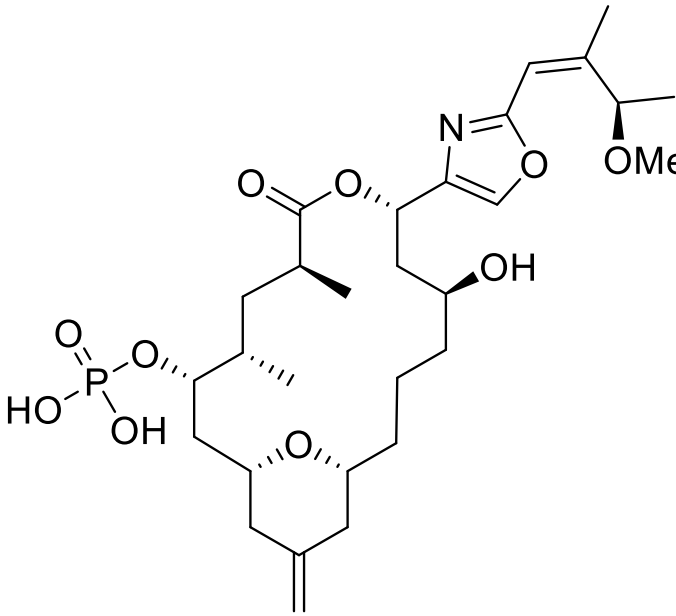
CEM 852

4/14/2018

1. *J. Am. Chem. Soc.* **2015**, *137*,

Background

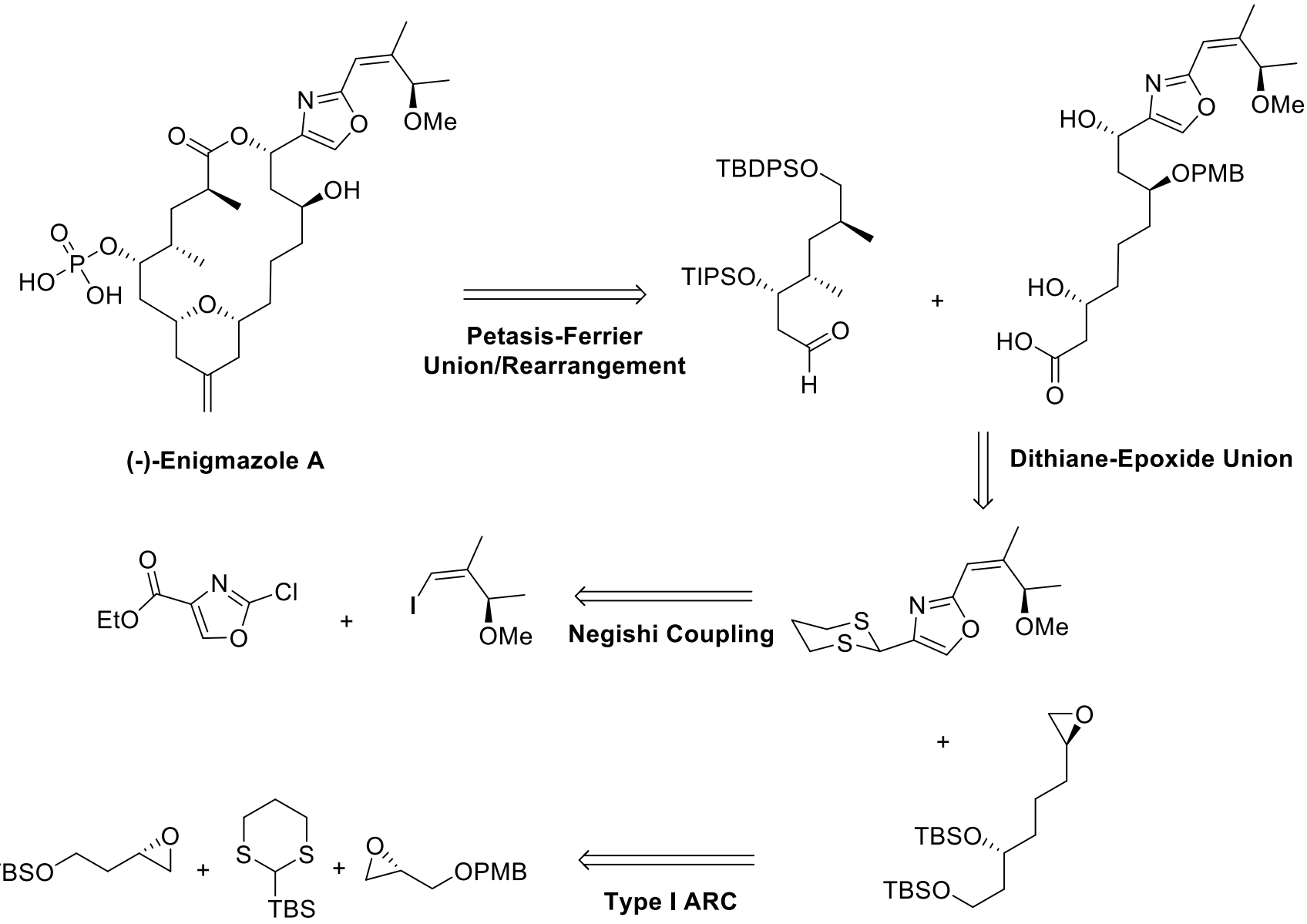
- Marine macrolide isolated from the marine sponge *Cinachyrella enigmatica* in 2006.[2]
- Cytotoxic towards NCI human tumor cell lines.[3]
- First total synthesis achieved in 2010 by Molinski.[4]



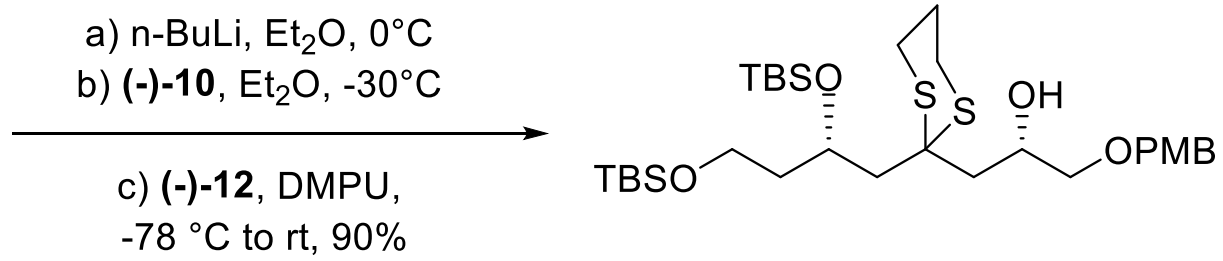
(±)-Enigmazole A

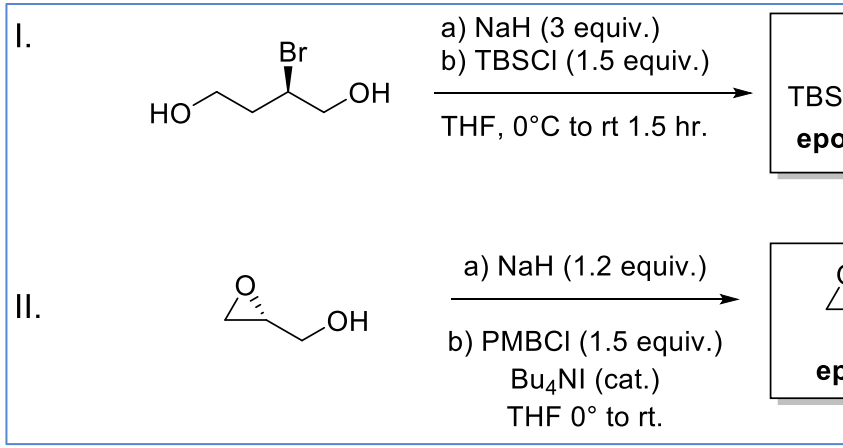
. Oku, N.; Gustafson, K.R.; Fuller, R.W.; Wilson, J.A.; Panell, L.K.; McMahon, J.B. *Symposium on the Chemistry of Natur*
roducts **2006,** 73.
. Oku, N.; Takada, K.; Fuller, R.W.; ;Wilson, J.A.; Peach, M.L.; Panell, L.K.; McMachon, J.B.; Gustafson, K.R. *J. Am. Chem*

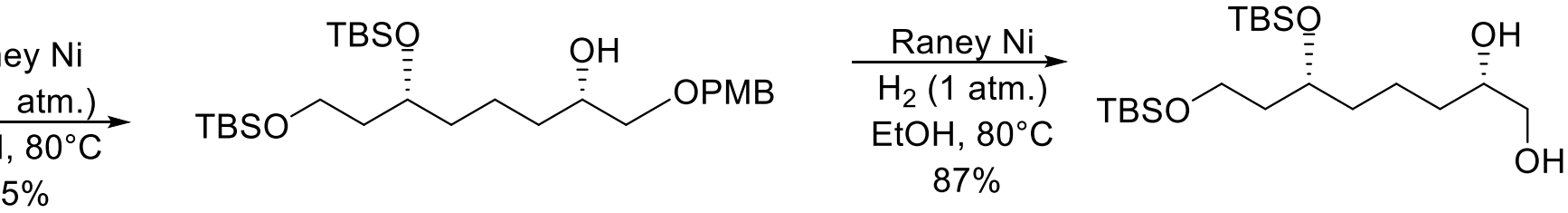
Retrosynthetic Approach & Key Reactions

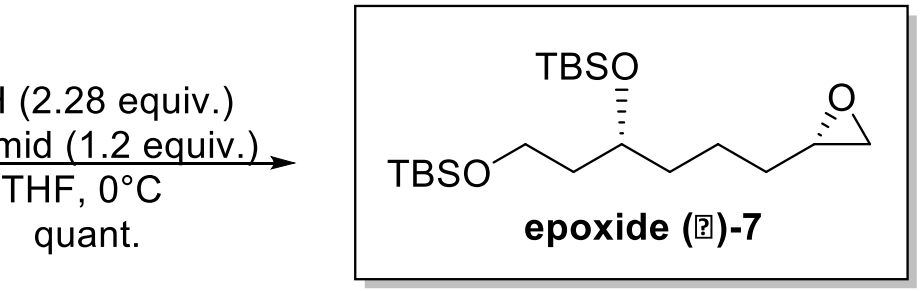


paration of **Epoxide (–)- 7**



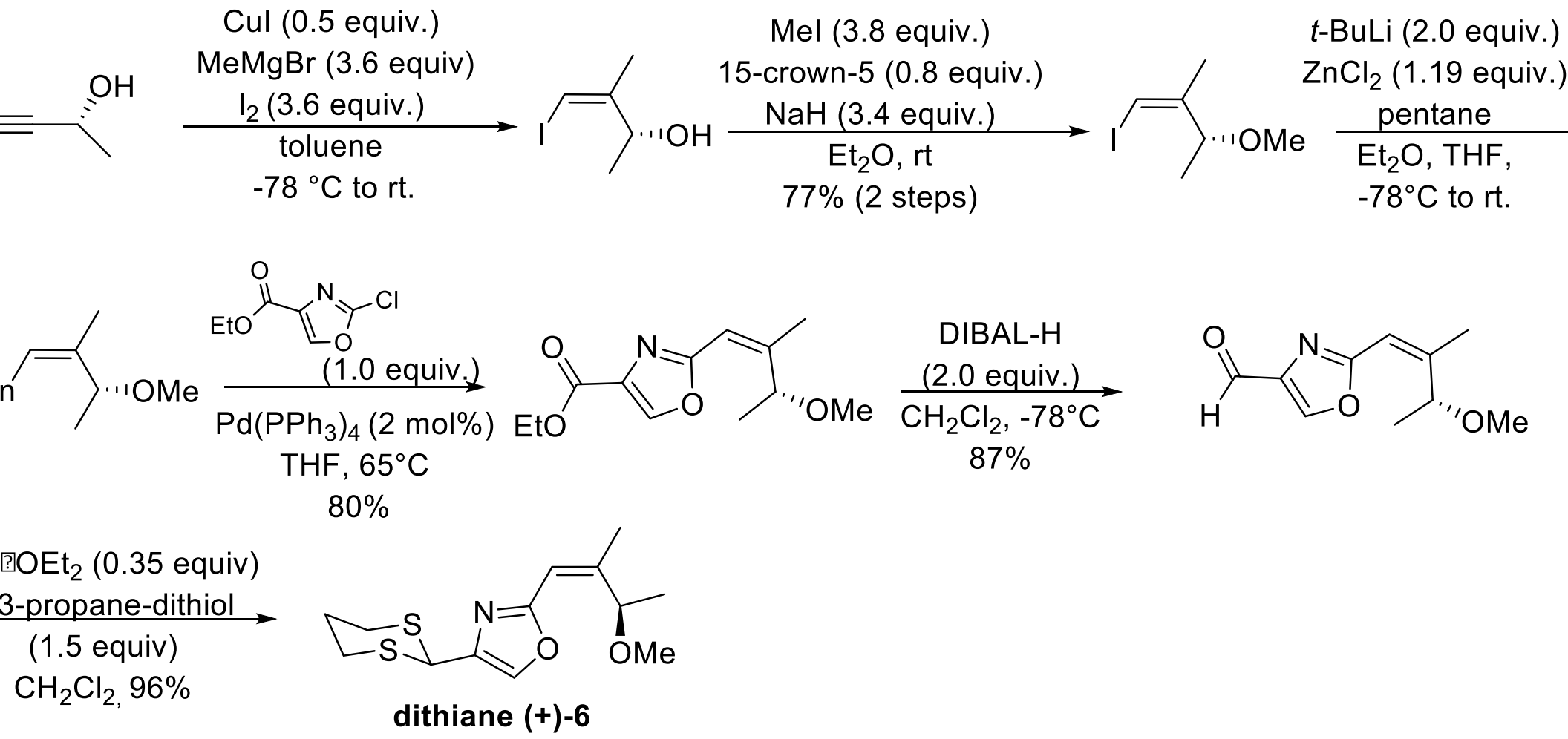






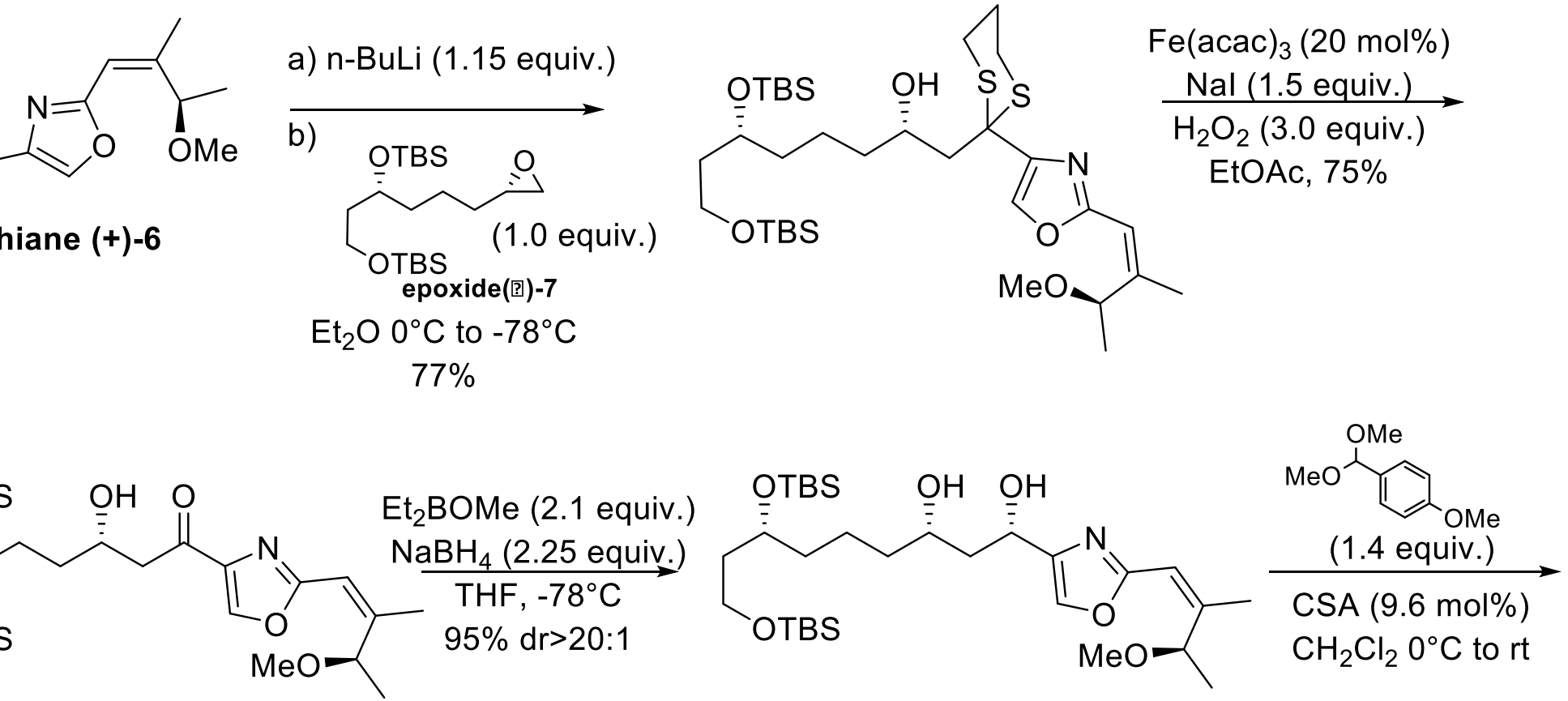
m. Eur. J. **2014,** *20*(30) 9336.
em. Eur. J. **2012**, *18*(52) 16868.

Preparation of **Dithiane (+)-6**

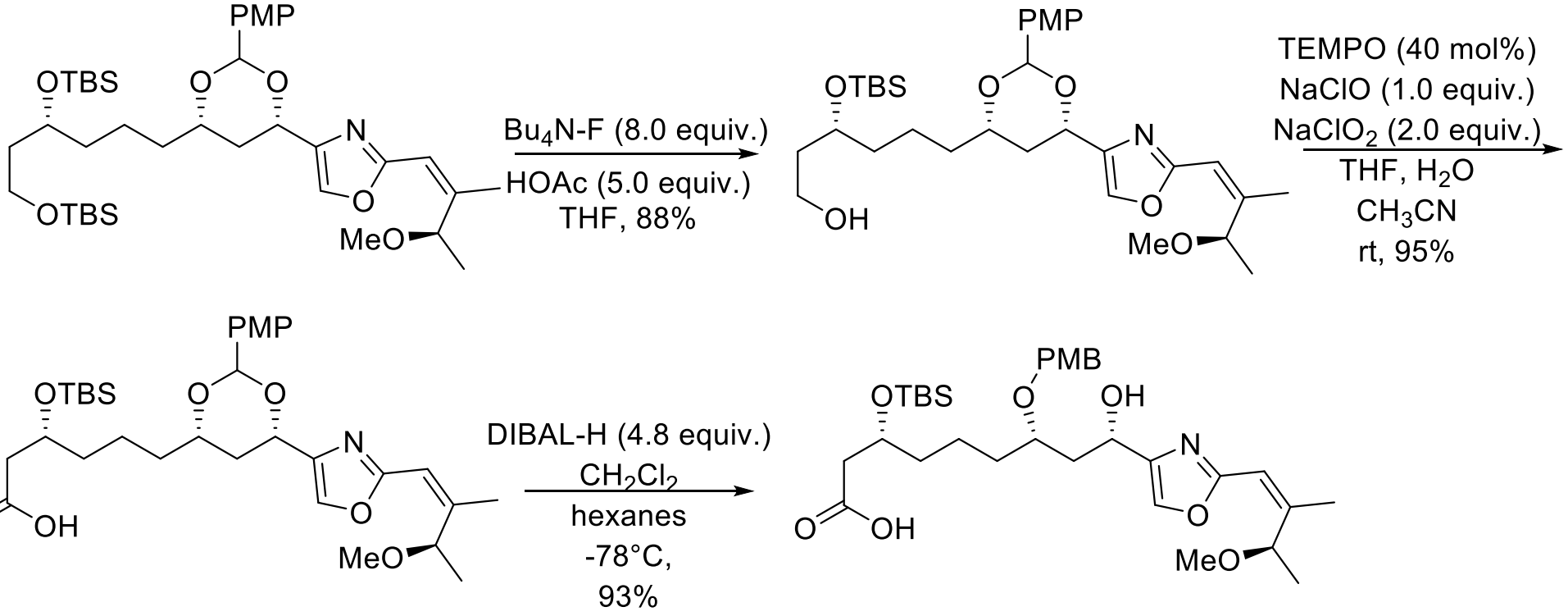


dithiane (+)-6

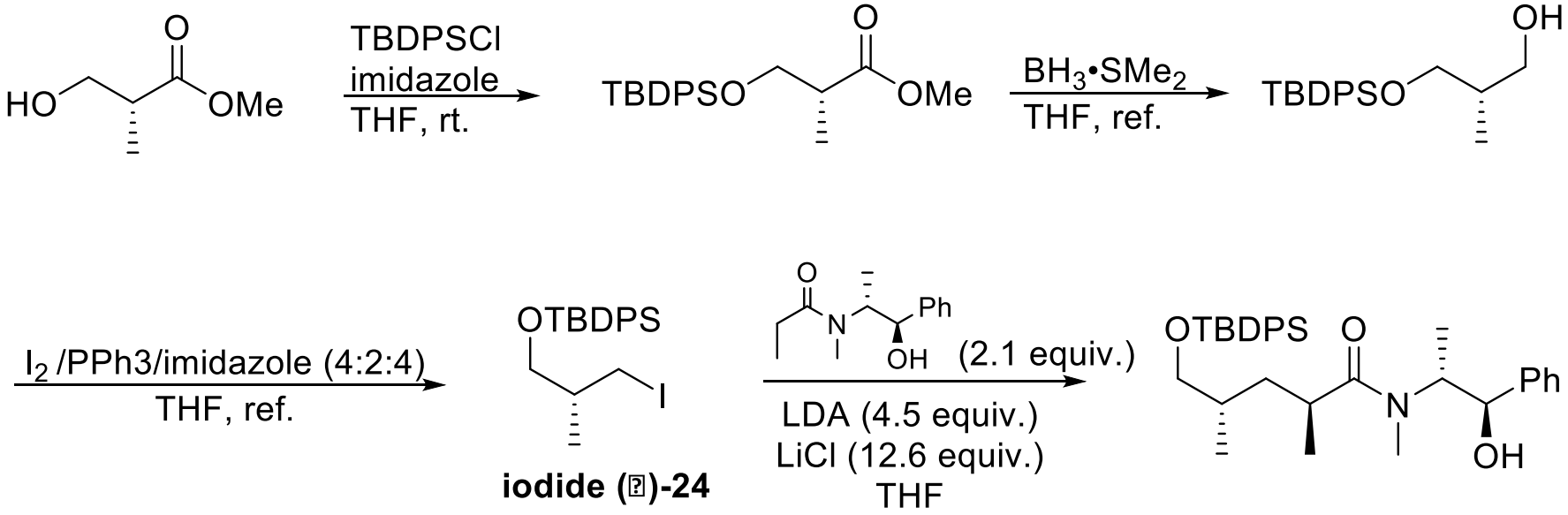
Construction of **Eastern Hemisphere (+)-5**



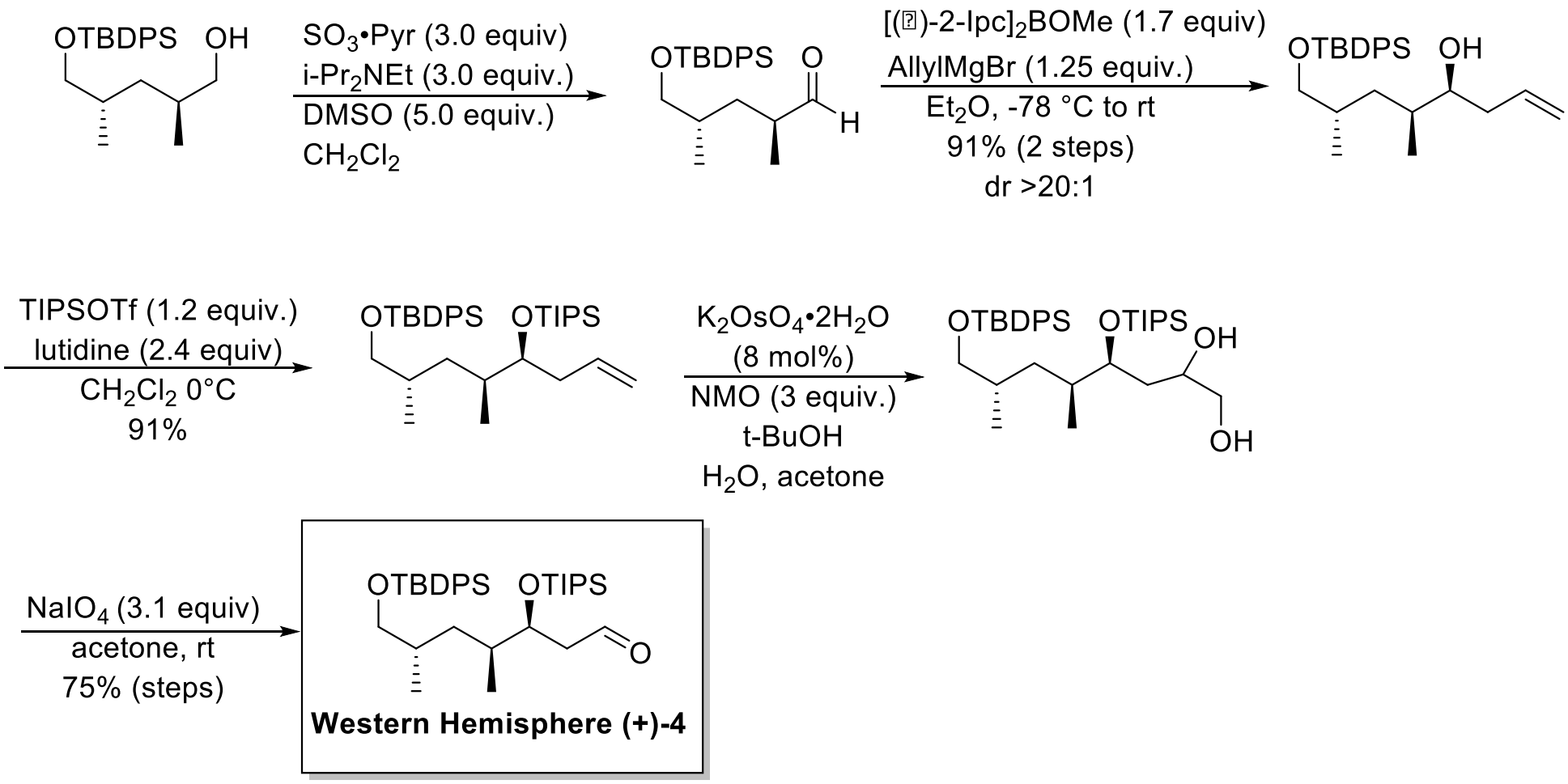
Construction of **Eastern Hemisphere (+)-5**



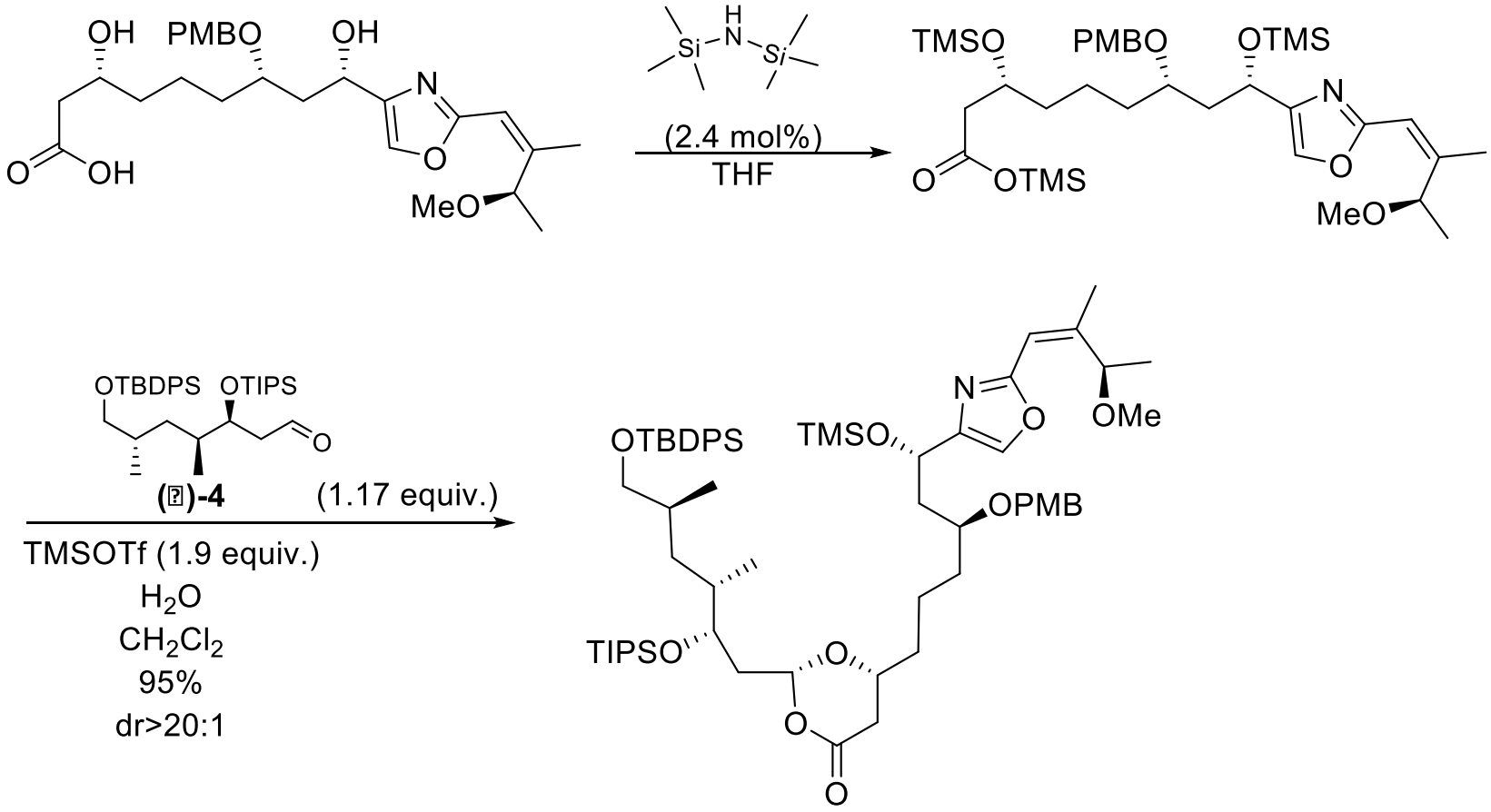
Construction of **Western Hemisphere (–)-4**



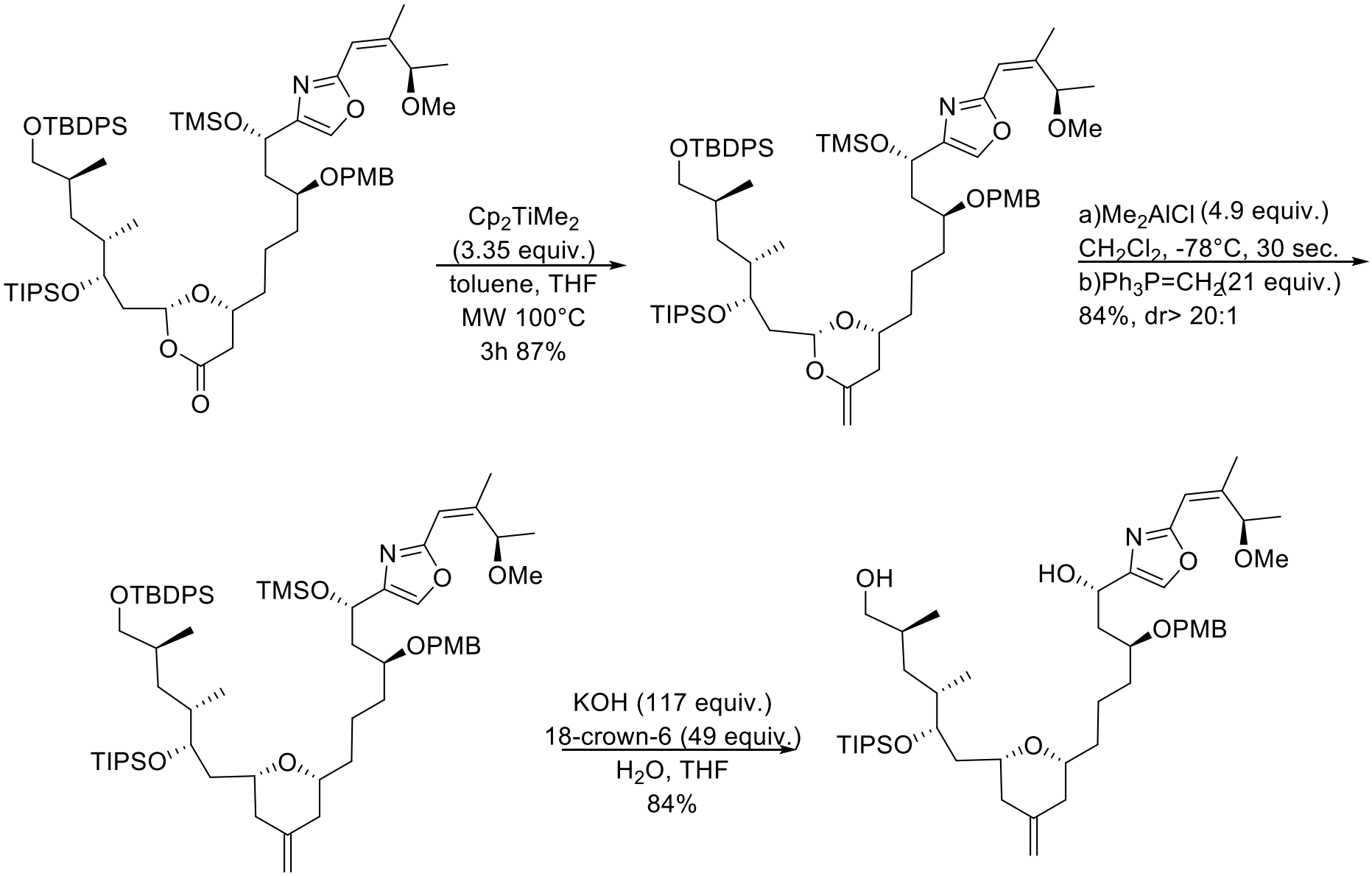
Construction of **Western Hemisphere (–)-4**



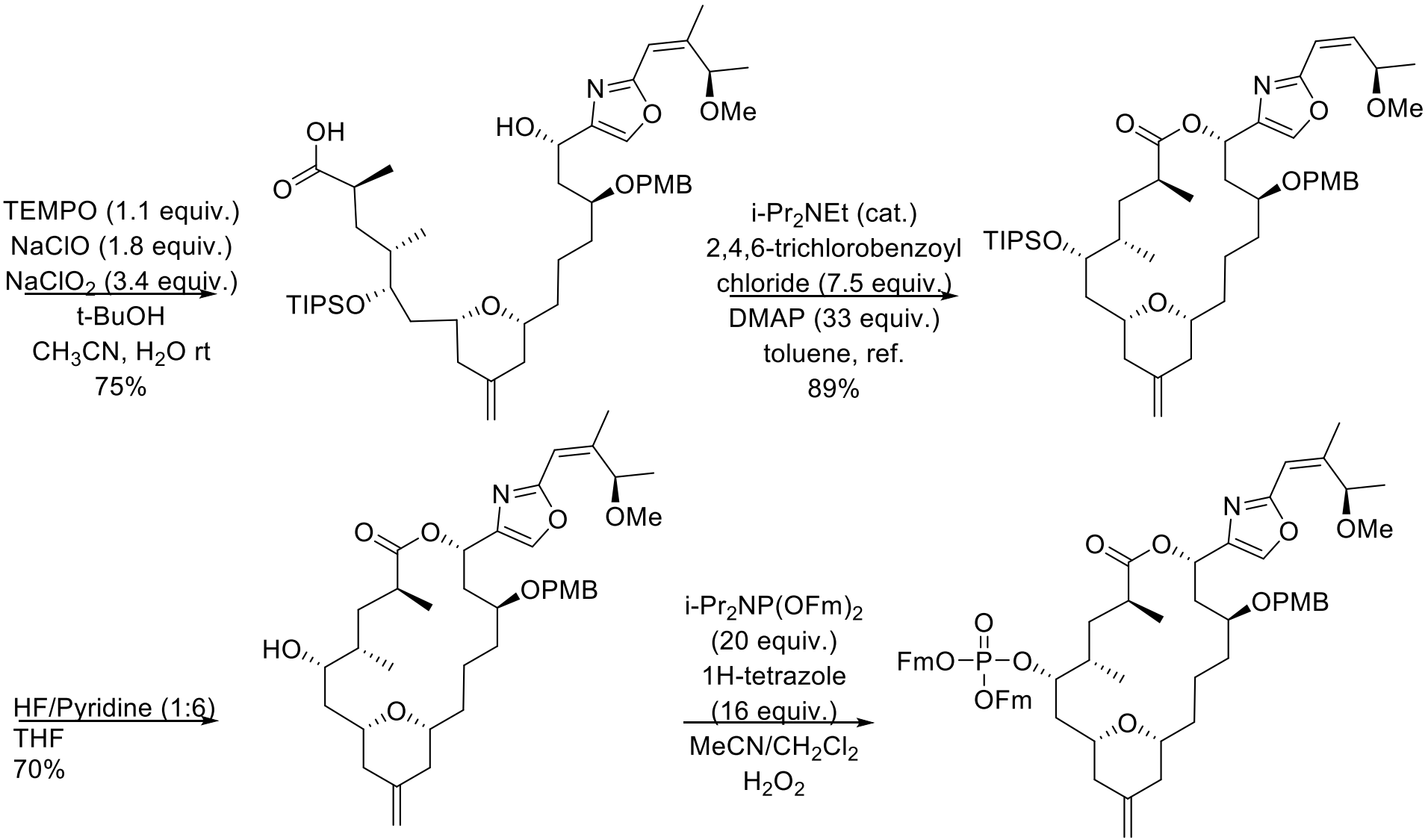
Petasis-Ferrier Union/Rearrangement



Petassis-Ferrier Union/Rearrangement



Macrolactone **(+)-33** Formation



Phosphoric Acid Formation