

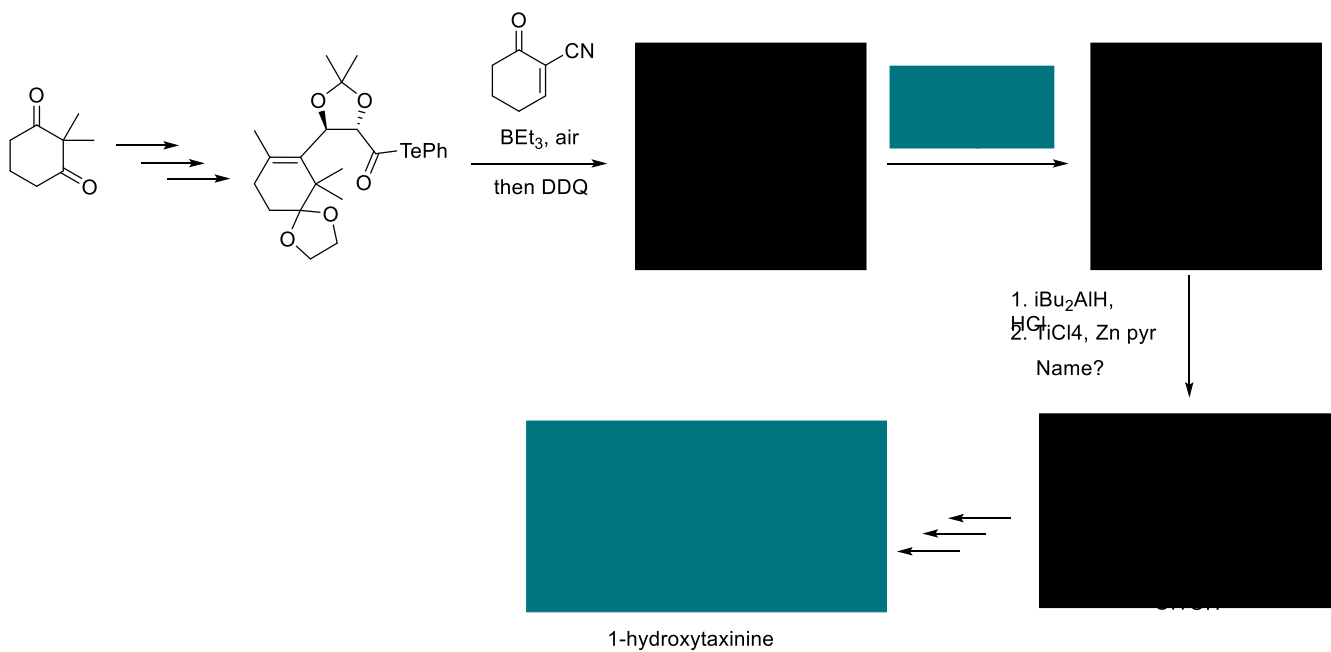
## Recent Advances in the Total Synthesis of Natural Products Containing Eight-Membered Carbocycles (2009-2019)

Li et al. *Chem. Rev.* **2020**, *120*, 5910-5953

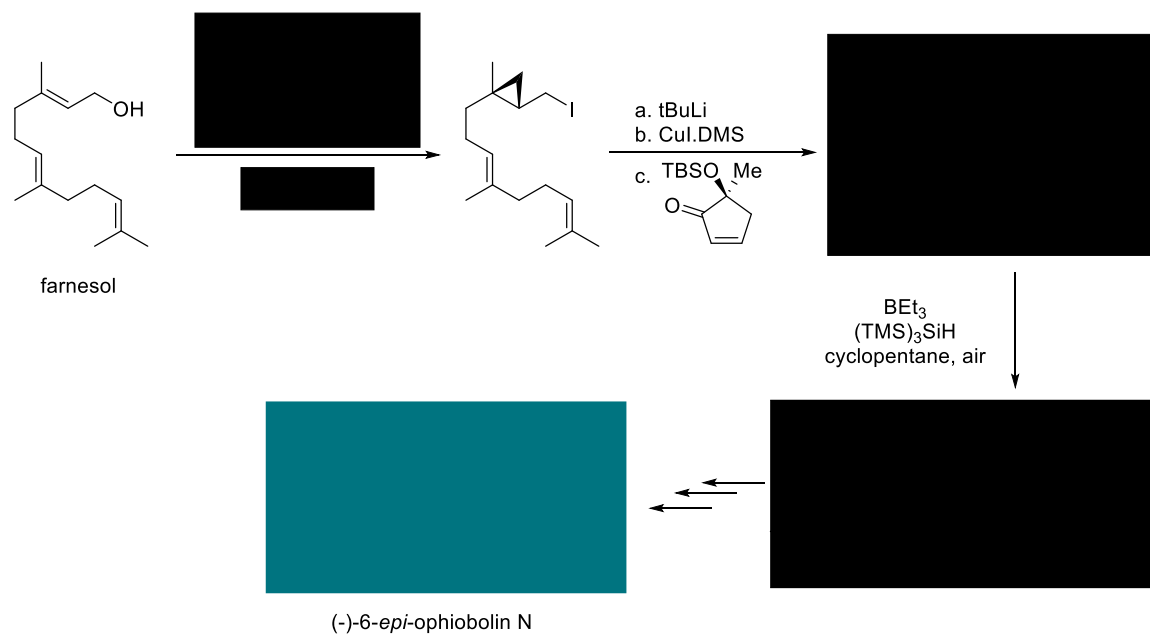
"The more there are methods to access a certain scaffold, more it is difficult to make that scaffold"  
-> 8-membered rings

Strain energy = 14 kcal/mol (cyclohexane: 1 kcal/mol)  
Multiple conformations because flexible -> stereoselectivity is challenging  
BC is generally favoured but depends on substitution pattern  
Challenge in TS: bridged, fused polycycles, FG tolerance

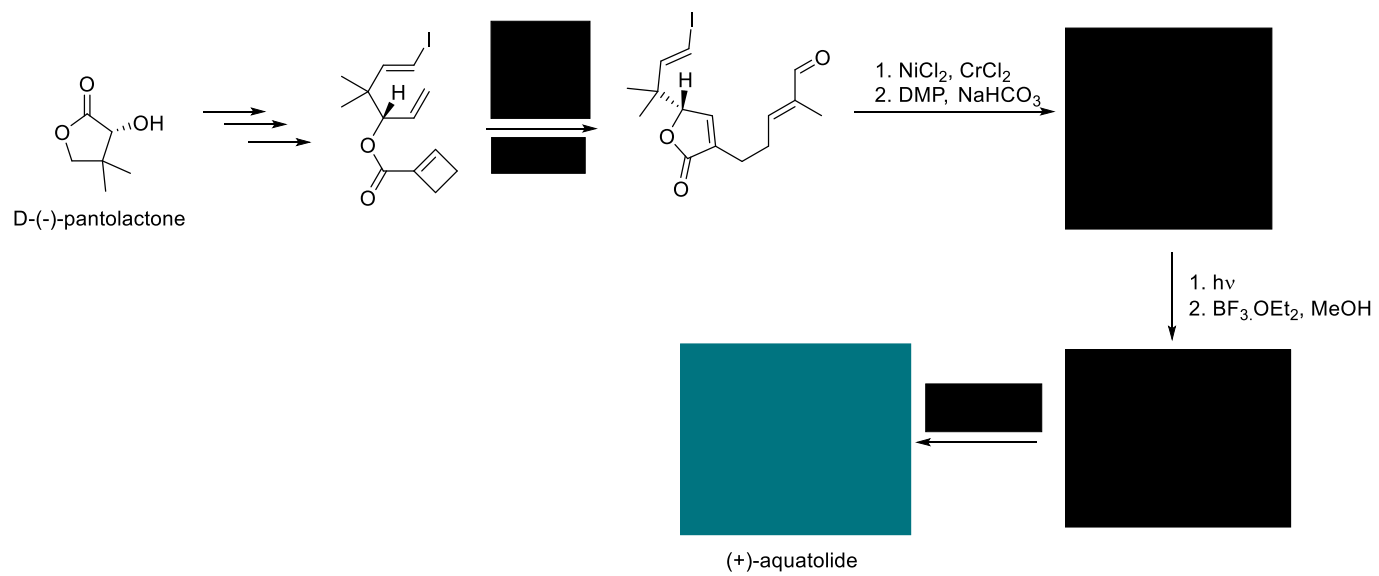
1-hydroxytaxinine (Inoue et al. *Angew. Chem. Int. Ed.* **2019**, *58*, 12159–12163)



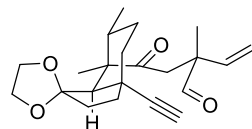
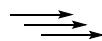
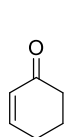
(-)-6-*epi*-ophiobolin N (Maimone et al. *Science*, **2016**, 352, 1078-1082)



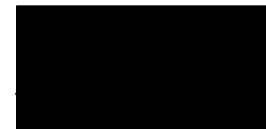
(+)-aquatolide (Takao et al. *Angew. Chem. Int. Ed*, **2019**, *58*, 9851-9855)



(+)-Pleuromutilin (Herzon et al. *Science*, **2017**, 356, 956-959)



Ni(cod), IPr  
Et<sub>3</sub>SiH, TBAF

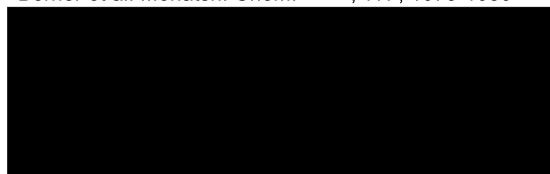


1. DMP  
2. SmI<sub>2</sub>  
3. Na, EtOH



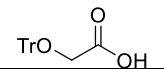
(+)-12-*epi*-mutilin

Berner et al. *Monatsh. Chem.* **1986**, 117, 1073-1080



(+)-pleuromutilin

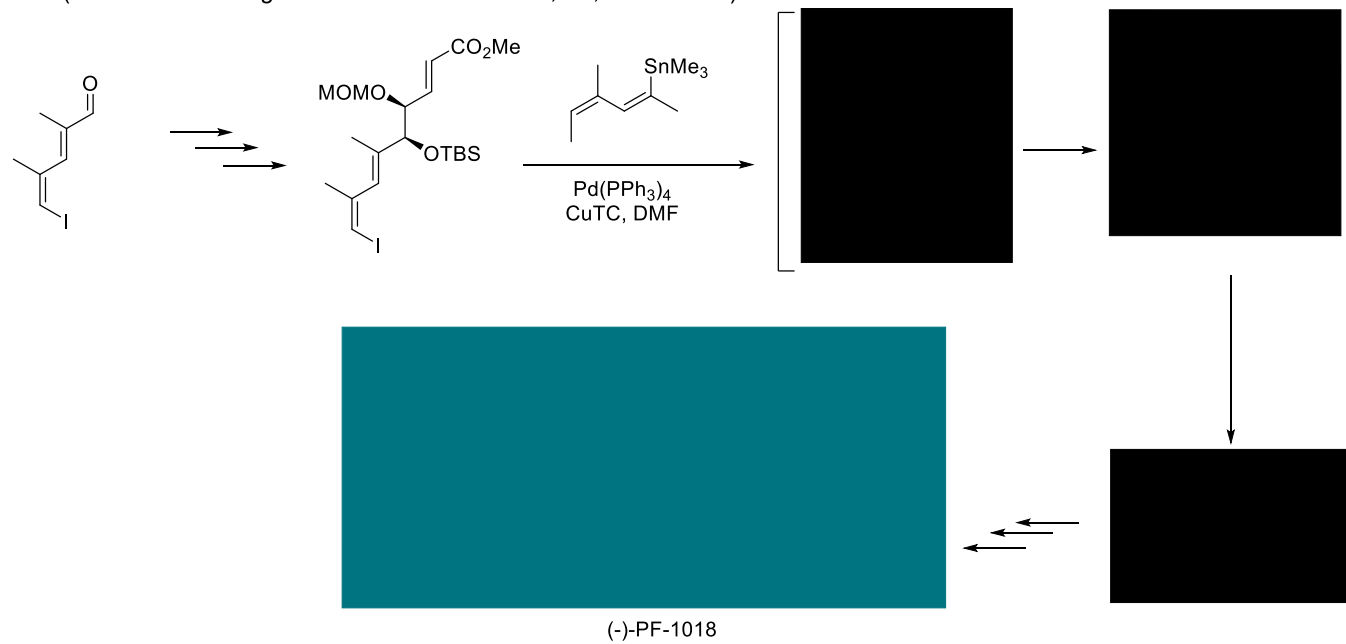
1. TFA-imidazole  
2. EDC, DMAP



3. Et<sub>2</sub>Zn  
then HCl

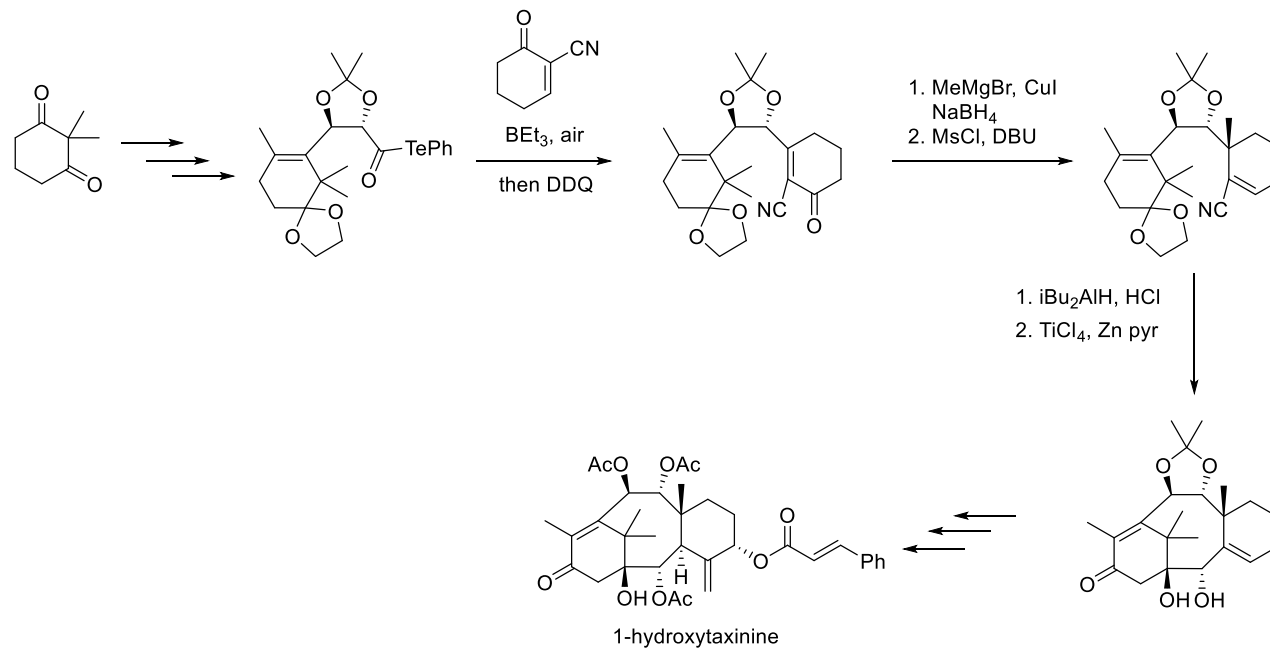


PF-1018 (Trauner et al. *Angew. Chem. Int. Ed.* **2020**, *59*, 9263-9267)

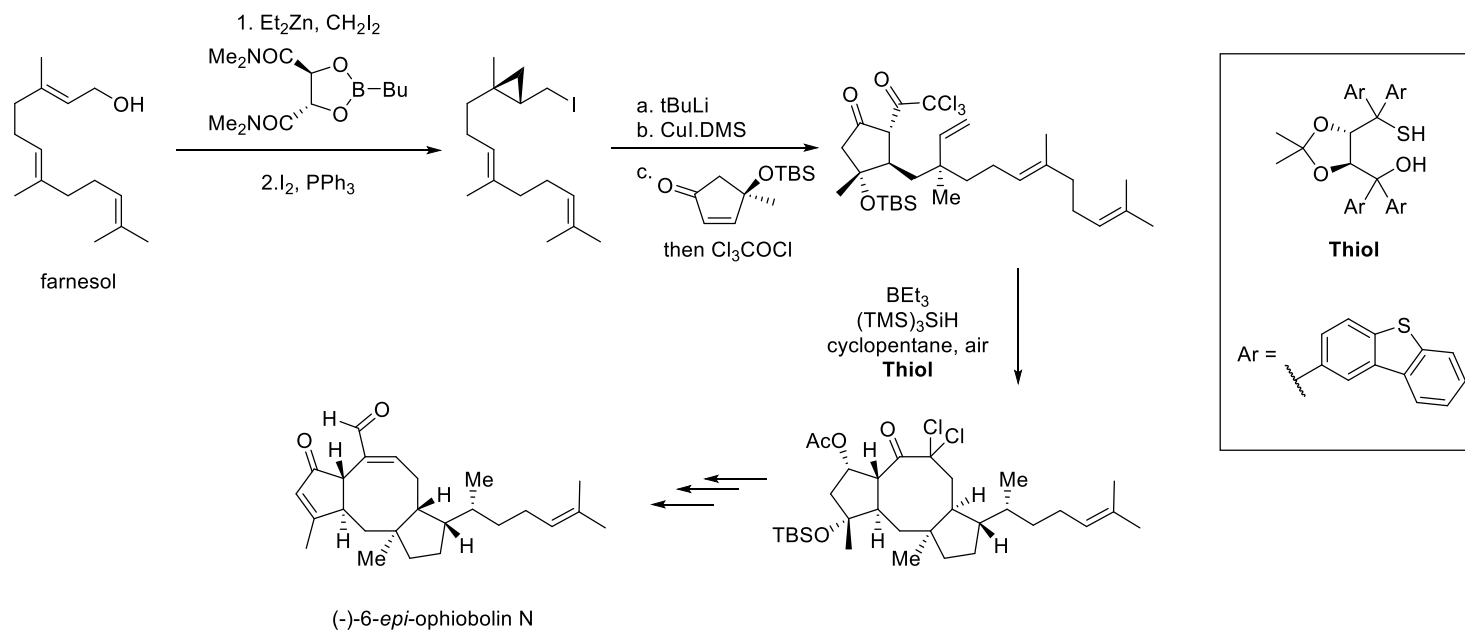


**SOLUTIONS**

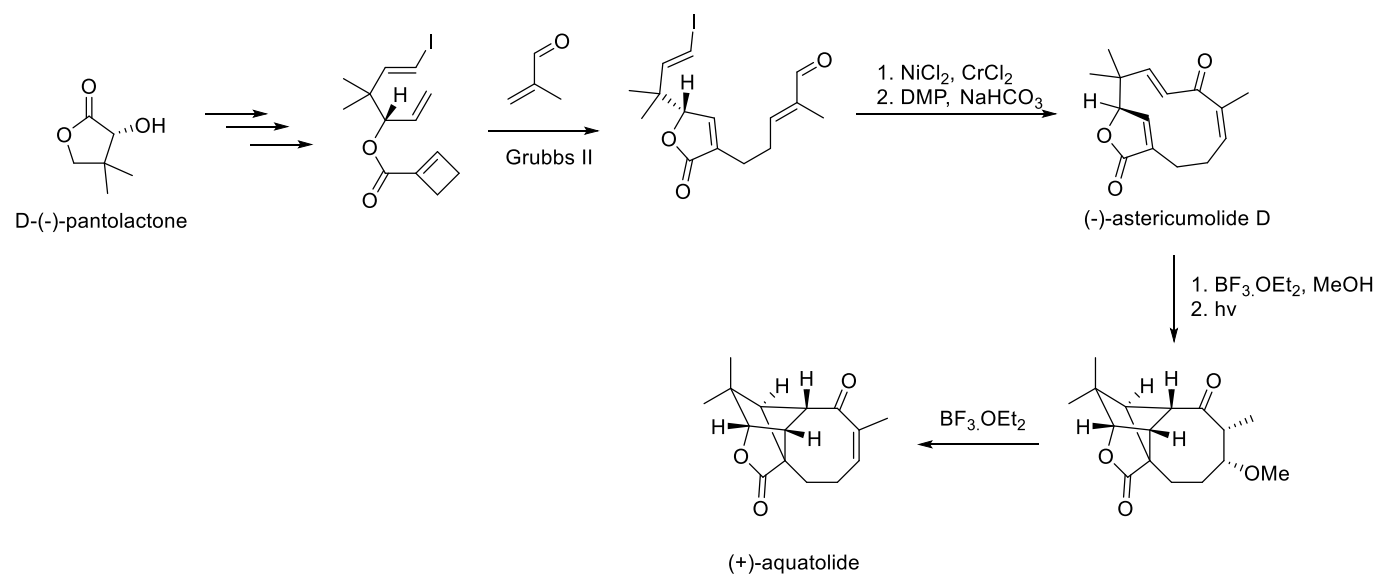
1-hydroxytaxinine (Inoue et al. *Angew. Chem. Int. Ed.* **2019**, 58, 12159–12163)



(-)-6-*epi*-ophiobolin N (Maimone et al. *Science*, **2016**, 352, 1078-1082)

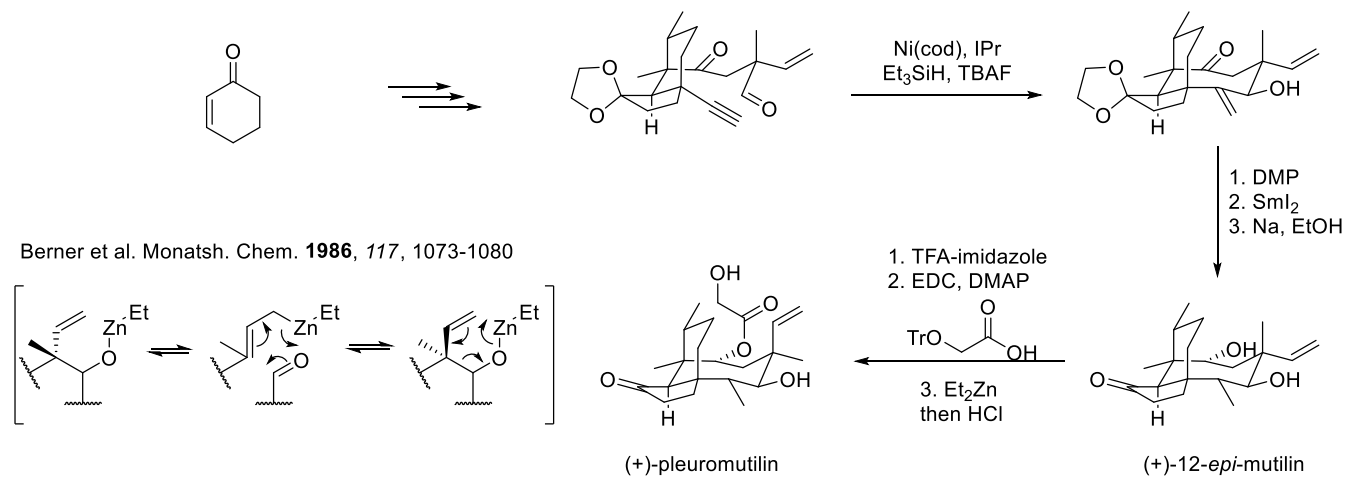


(+)-aquatolide (Takao et al. *Angew. Chem. Int. Ed.*, **2019**, *58*, 9851-9855)





(+)-Pleuromutilin (Herzon et al. *Science*, **2017**, 356, 956-959)



PF-1018 (Trauner et al. *Angew. Chem. Int. Ed.* **2020**, 59, 9263-9267)

