

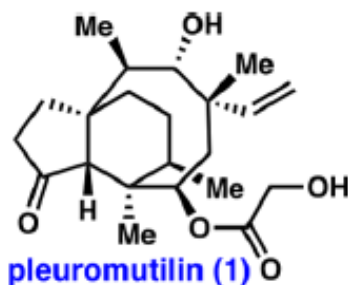
# Total Synthesis of (+)-Pleuromutilin

Elliot P. Farney, Sean S. Feng, Felix Schäfers, and Sarah E. Reisman

California Institute of Technology, *J. Am. Chem. Soc.*, **2018**, *140* (4), pp 1267–1270

(+)-Pleuromutilin is a diterpene natural product first isolated from the fungus *Clitopilus passeckerianus* in 1951 (+)-Pleuromutilin binds to the peptidyl transferase center of bacterial ribosomes, preventing protein synthesis.

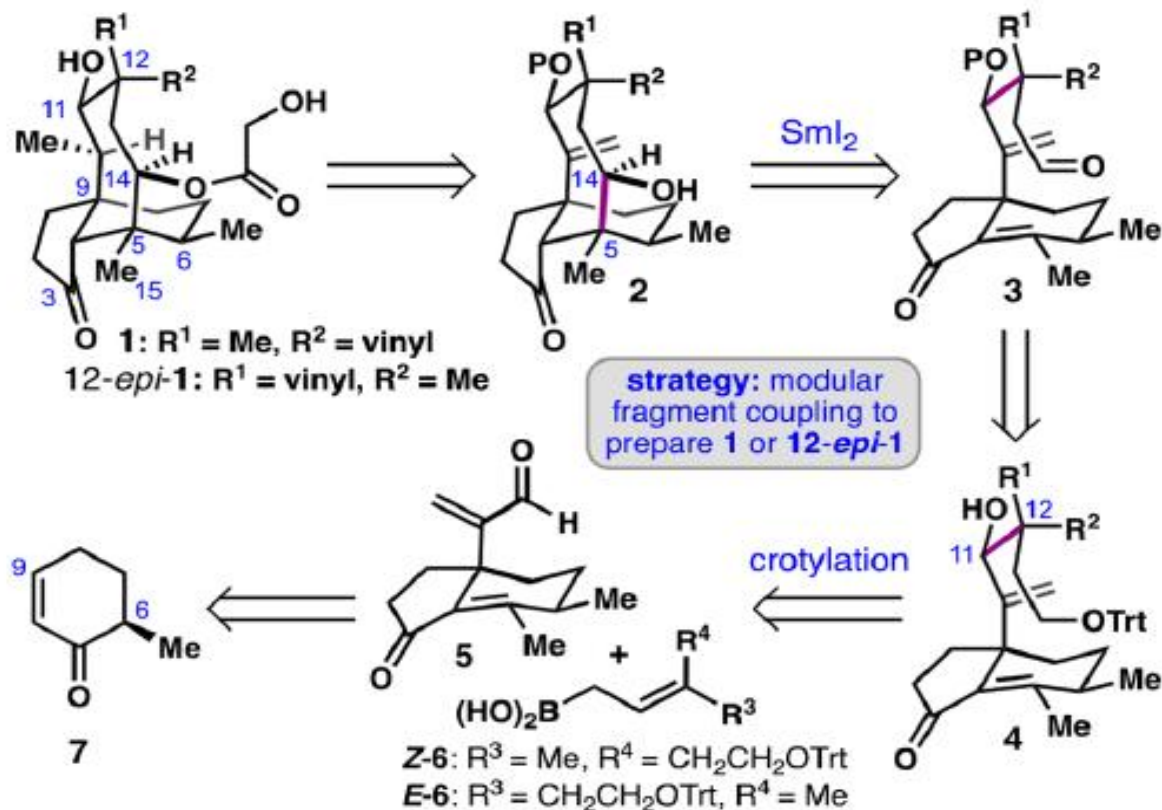
Recently, derivatives of 12-epi-mutilin have been developed as broad-spectrum antibiotics with efficacy against Gram-negative pathogens



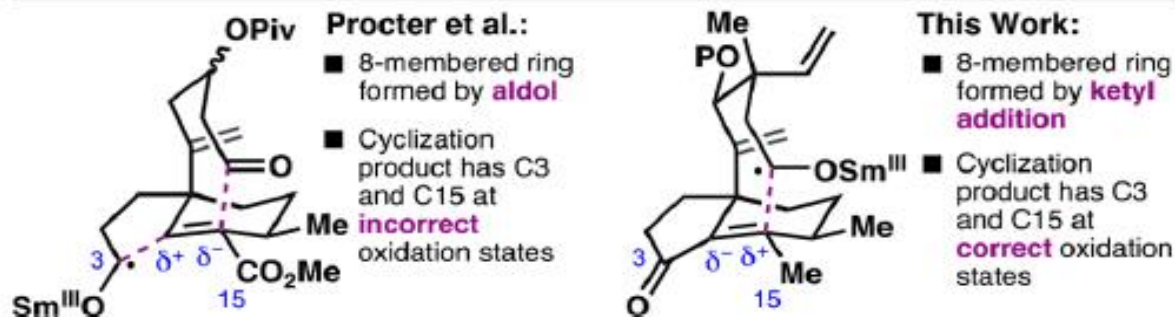
Four total syntheses of 1 have been reported to date, the most recent of which was disclosed by Herzon and co-workers in 2017.

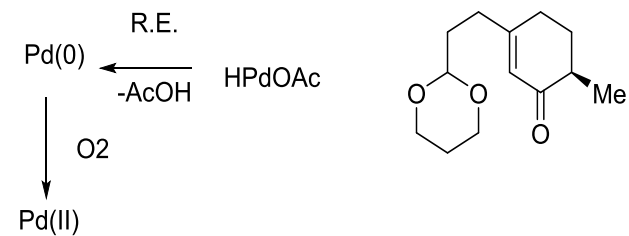
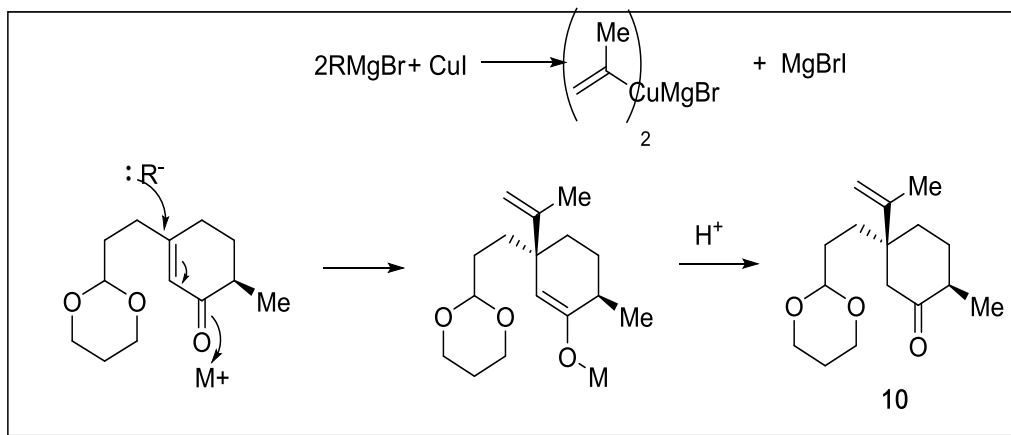
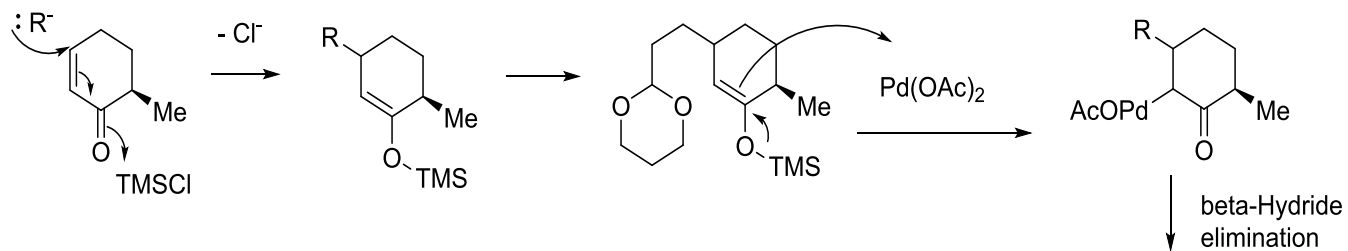
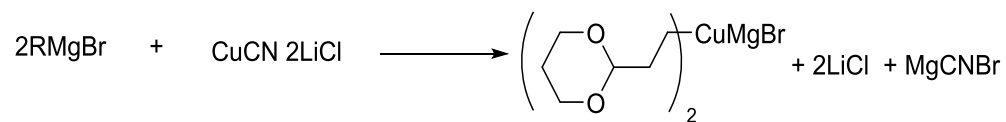
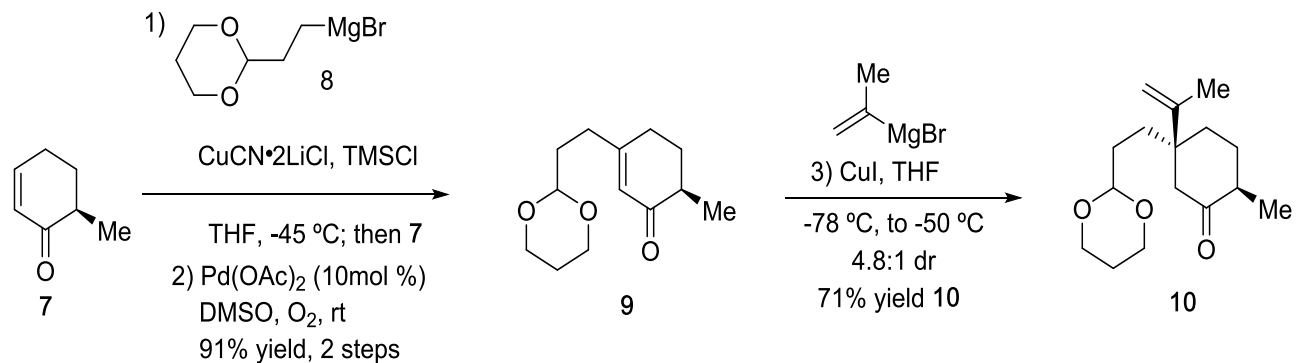
Here we report an approach that enables the preparation of (+)-pleuromutilin and (+)-12-epi-pleuromutilin in 18 steps from (+)-trans-dihydrocarvone.

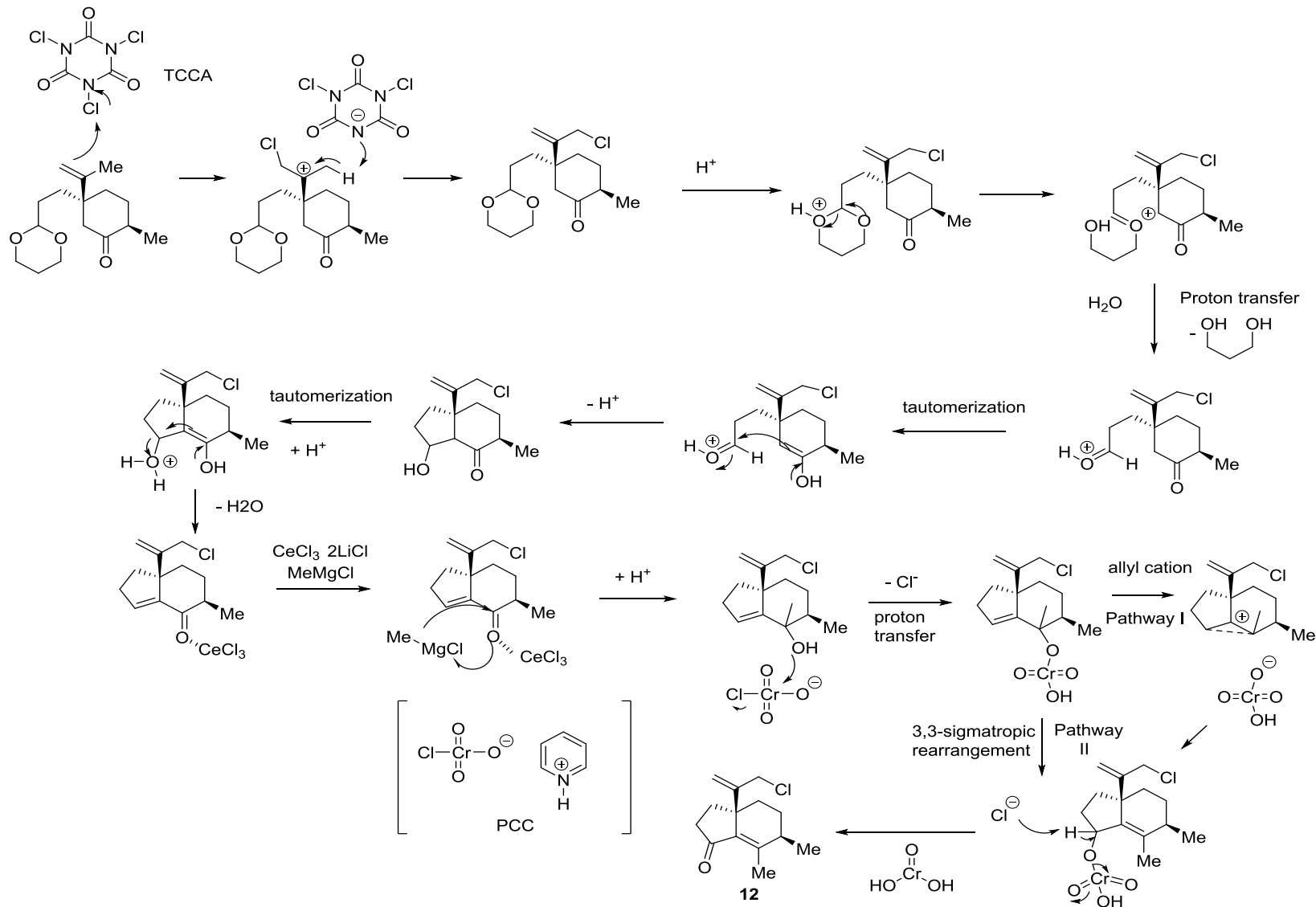
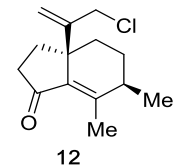
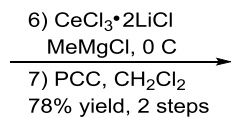
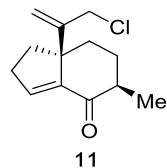
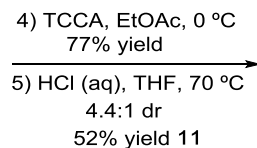
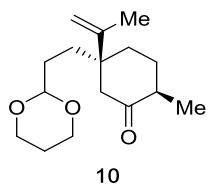
# Retrosynthetic Route

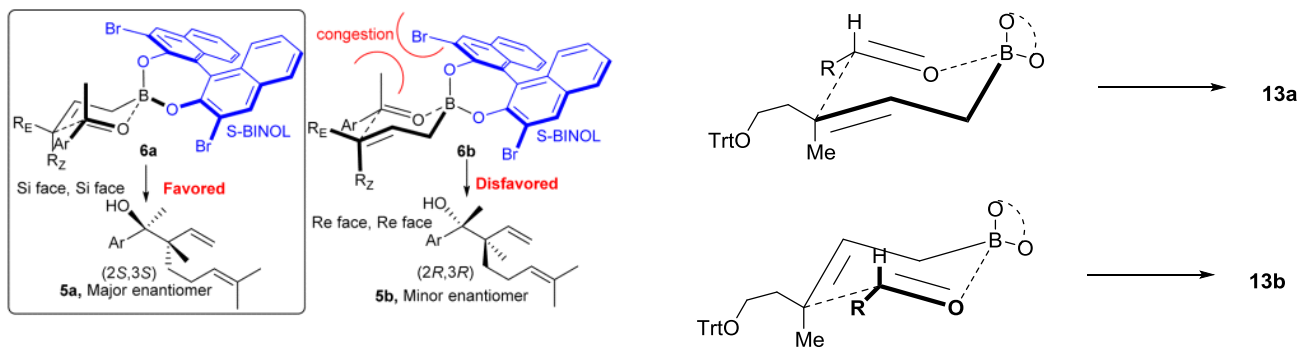
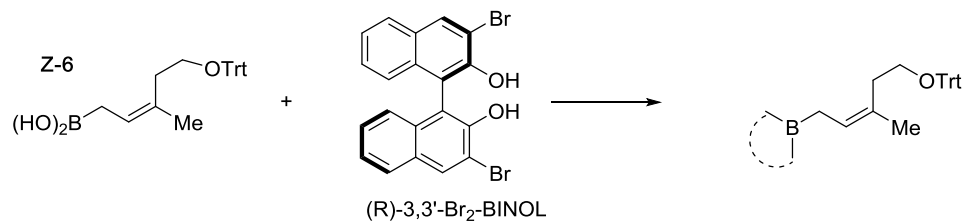
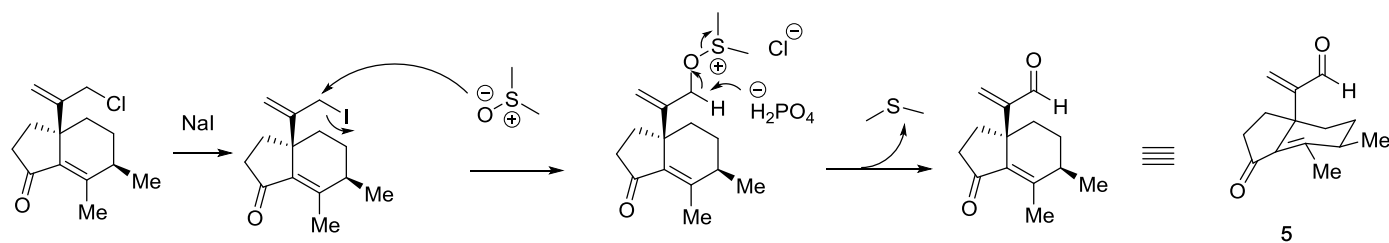
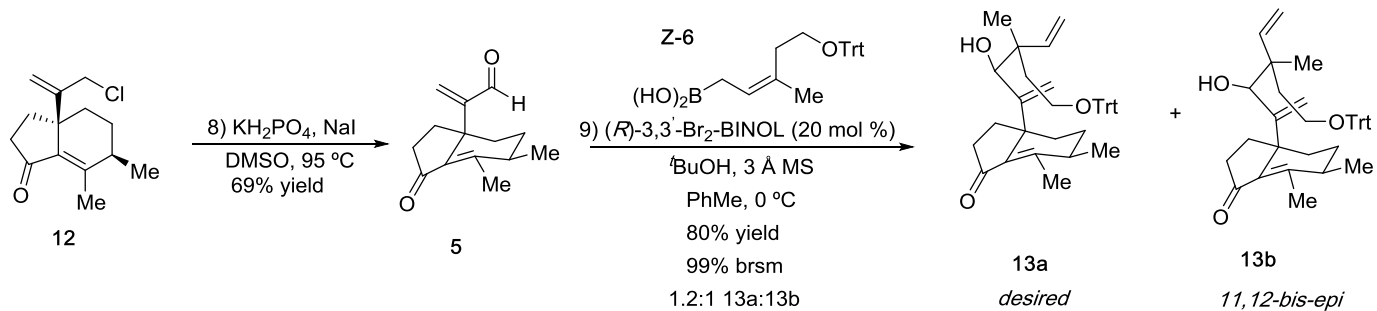


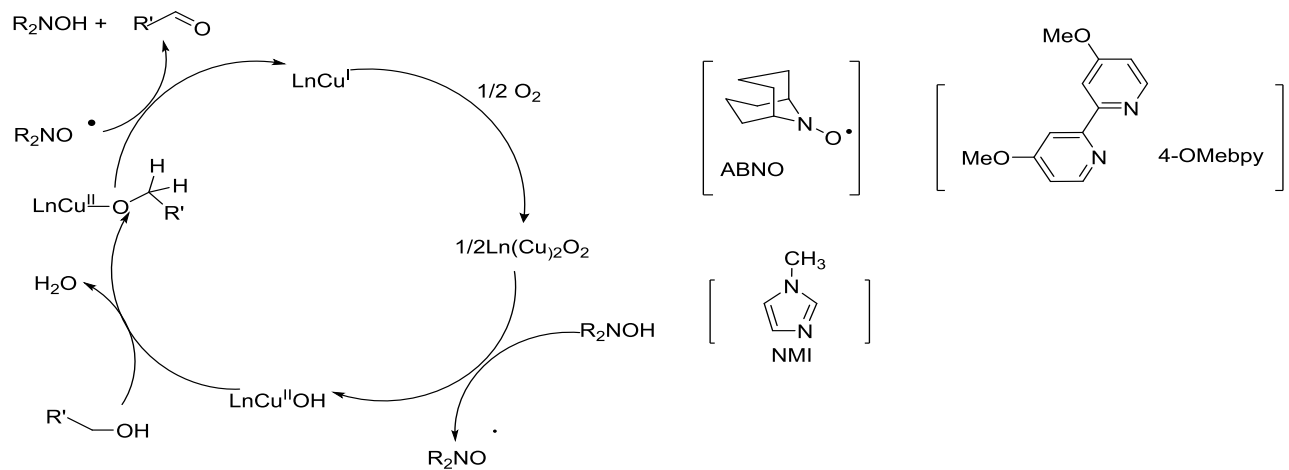
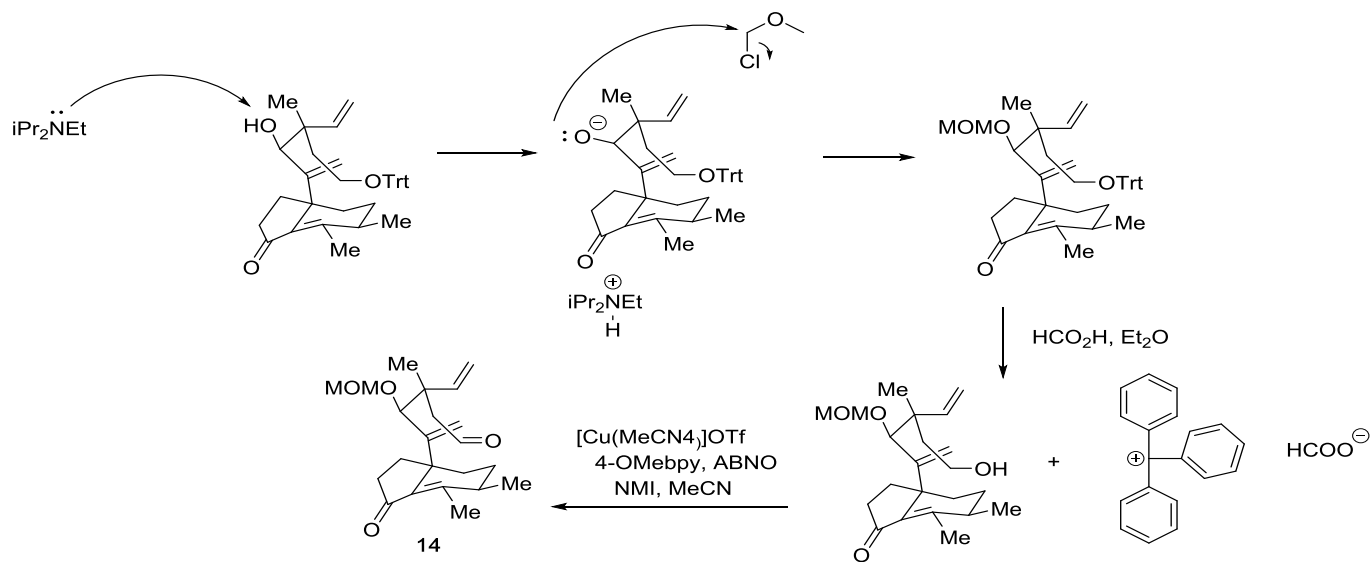
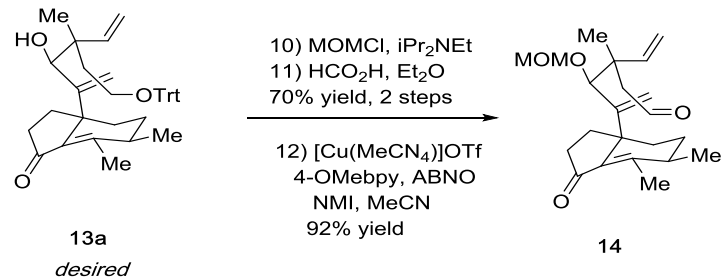
## Comparison of $\text{SmI}_2$ Approaches to Pleuromutilin Framework

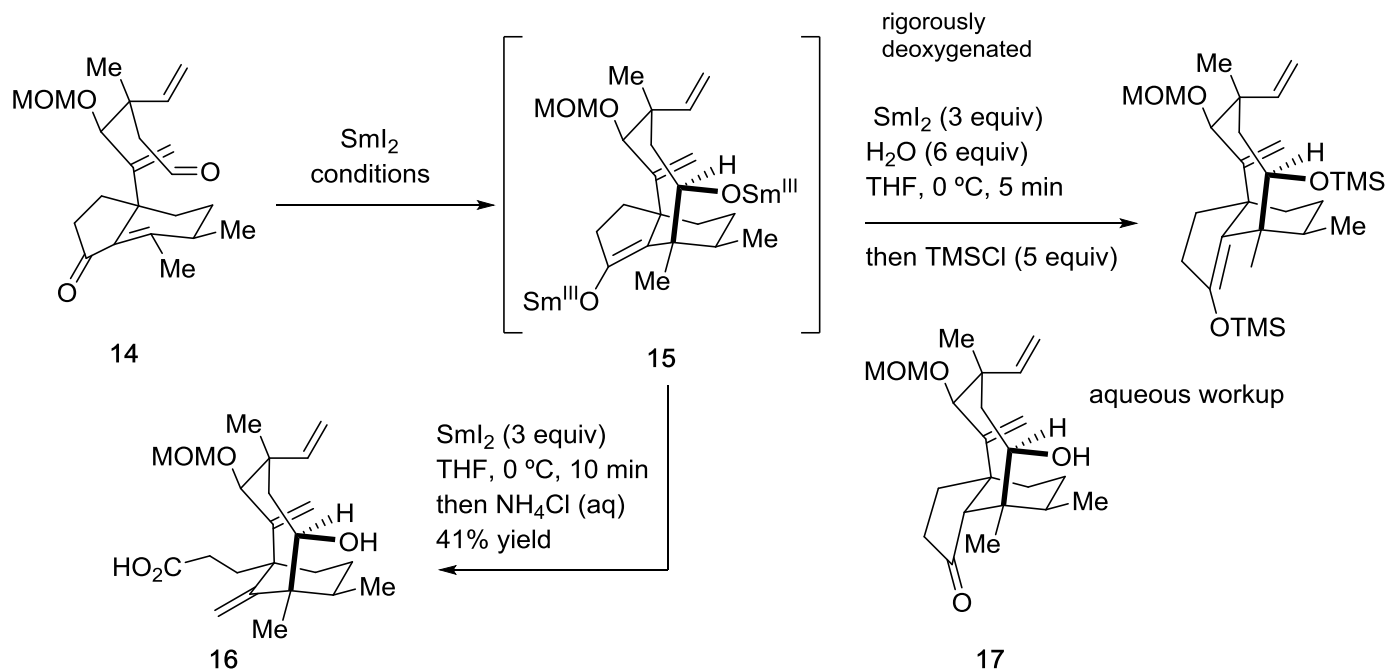
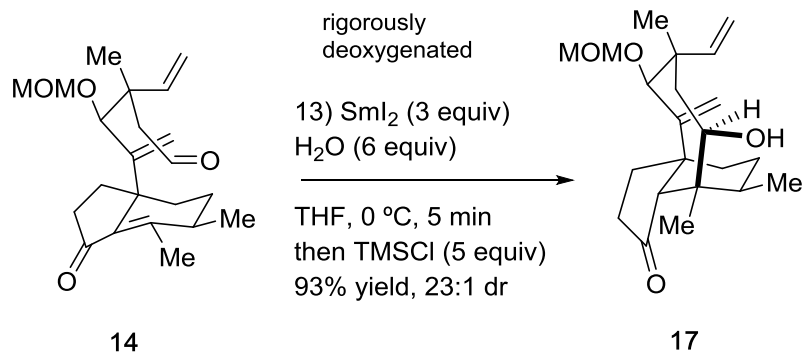


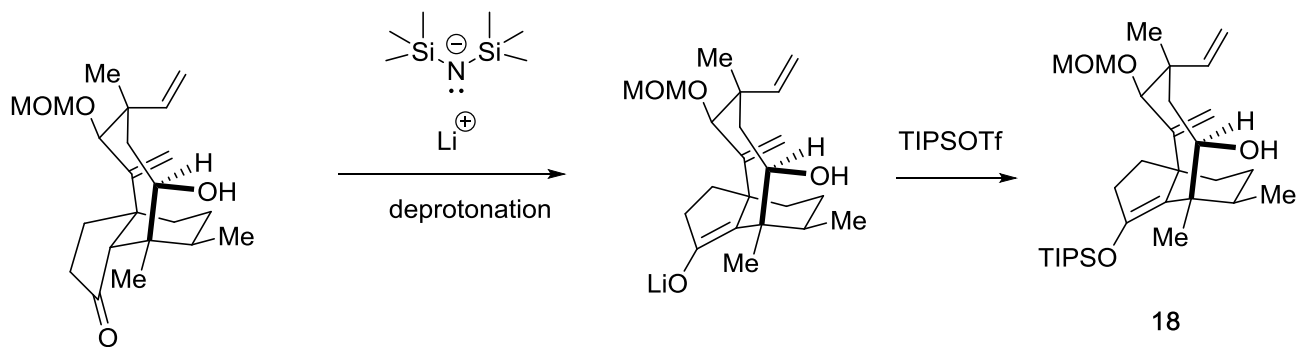
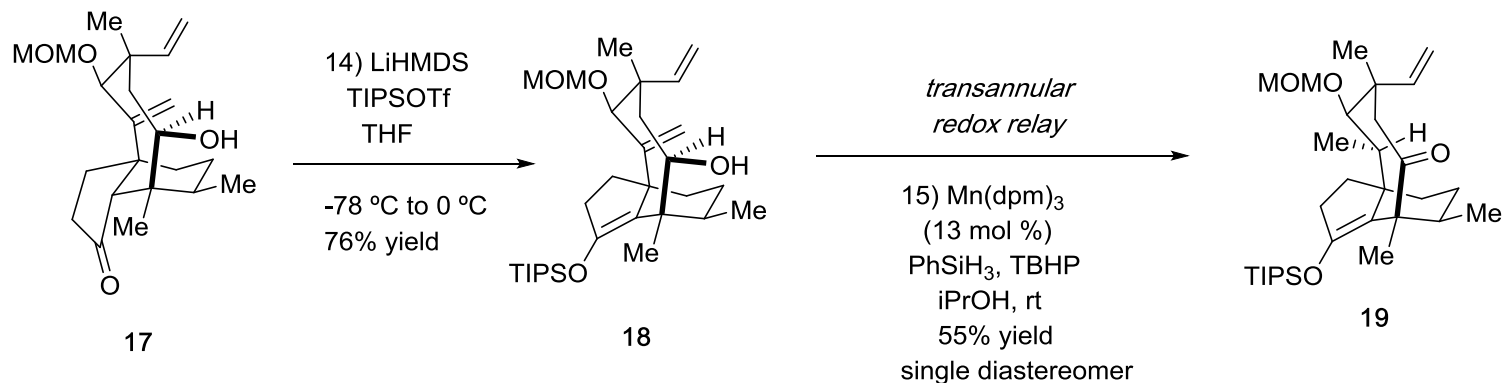




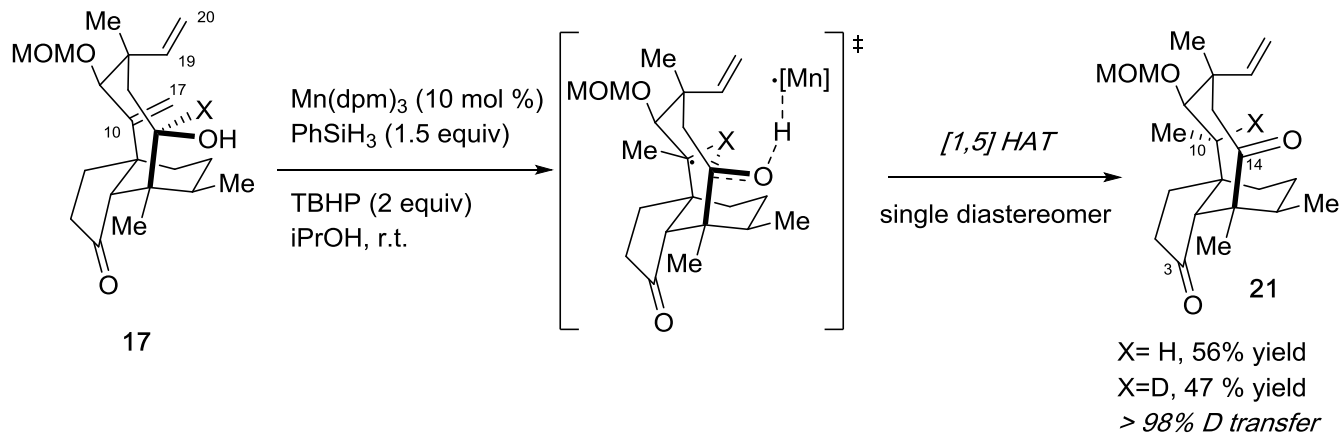




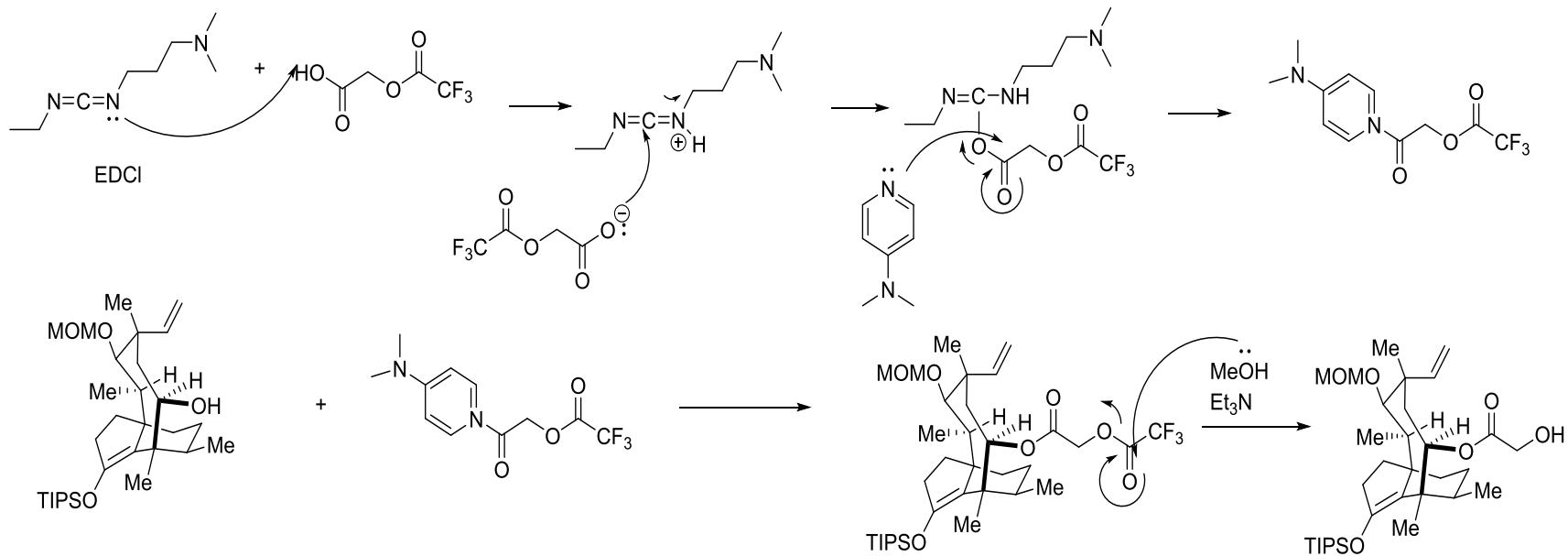
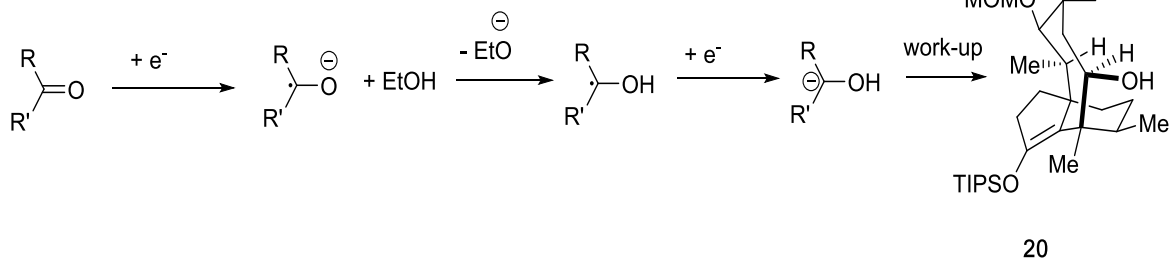
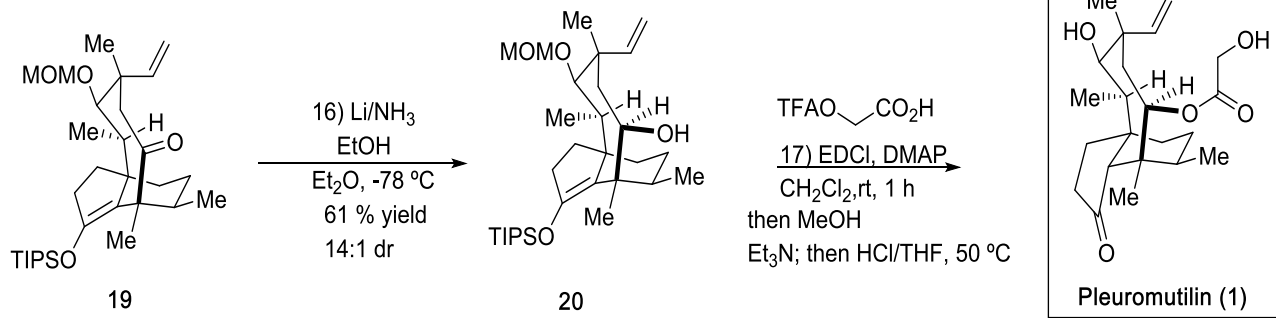




### Redox Relay by Transannular [1,5]-HAT







synthesis of *12-epi-1*

