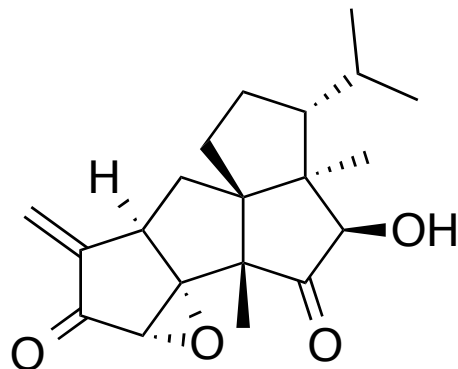


# Total Synthesis of (–)-Crinipellin A



Literature presentation, August 28<sup>th</sup> 2014

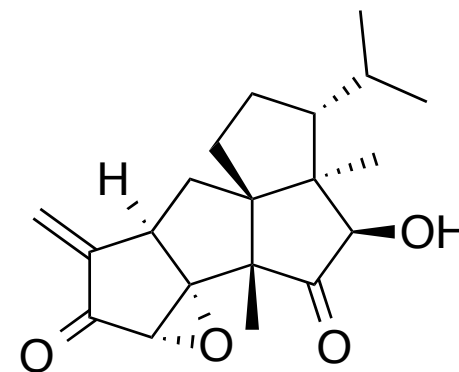
Kang, T.; Song, S. B.; Kim, W.-Y.; Kim, B. G.; Lee, H.-Y. *J. Am. Chem. Soc.* **2014**, *136*, 10274–10276.

(doi: 10.1021/ja5054412)

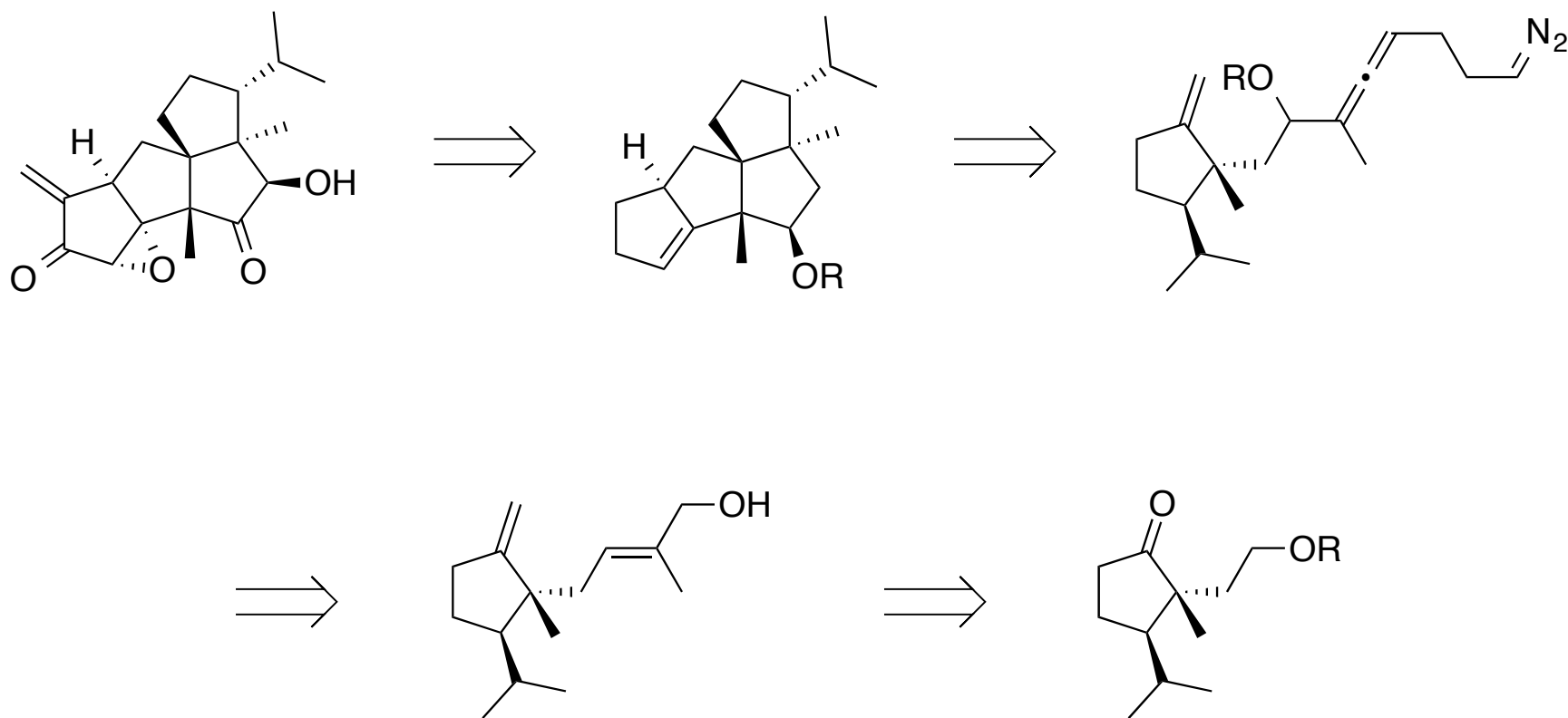
Julien Pomarole

# Introduction

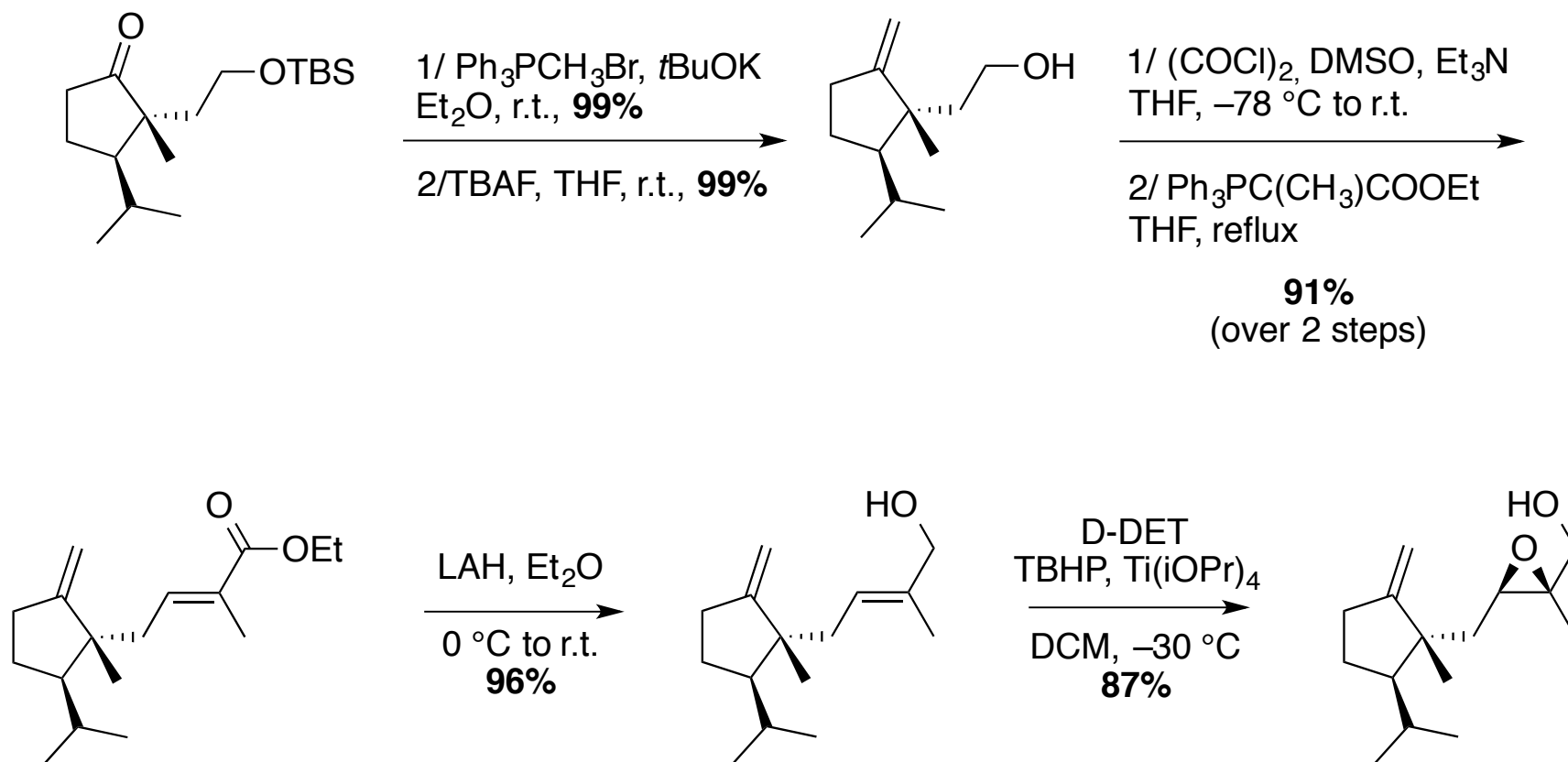
- > Isolated in 1979 from basidiomycete *Crinipellis stipitiaria*
- > Tetraquinane skeleton
- > 8 contiguous stereogenic centers



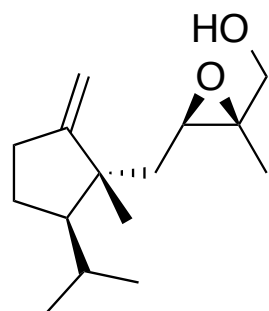
# Retrosynthesis



# Synthesis of the diazo-precursor

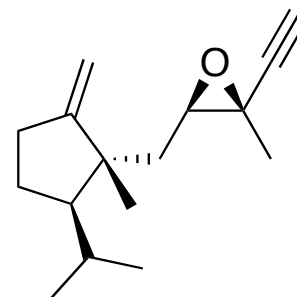


# Synthesis of the diazo-precursor



1/ (COCl)<sub>2</sub>, DMSO, Et<sub>3</sub>N  
THF, -78 °C to r.t.

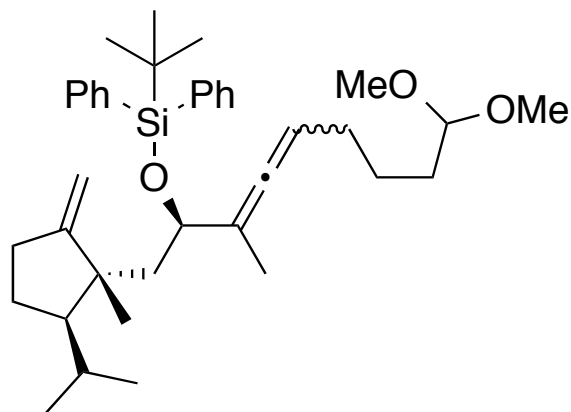
2/ Bestmann-Ohira reagent  
K<sub>2</sub>CO<sub>3</sub>, MeOH, r.t.



**87%**  
(over 2 steps)

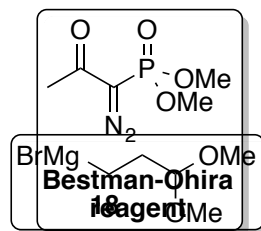
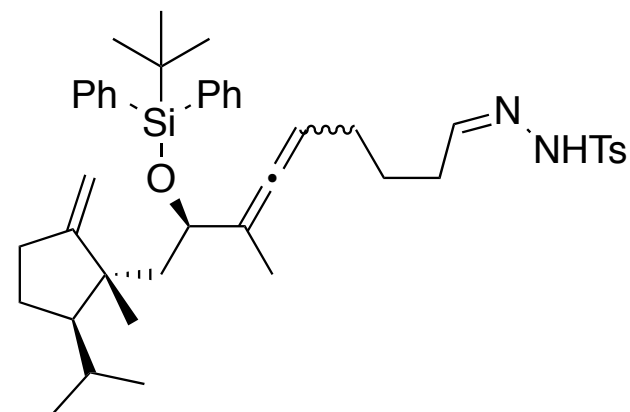
1/ Fe(acac)<sub>3</sub>, **18**  
THF, toluene  
-15 °C, **94%**

2/ TBDPSCI, imidazole  
DMAP, DCM, r.t., **96%**

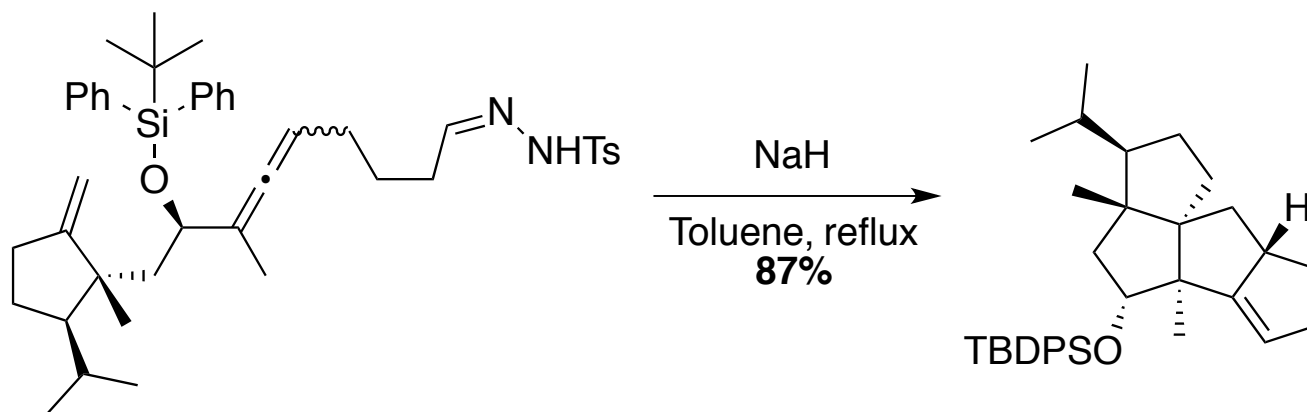


1/ *p*-TsOH·H<sub>2</sub>O, HCHO  
THF, H<sub>2</sub>O, r.t., **93%**

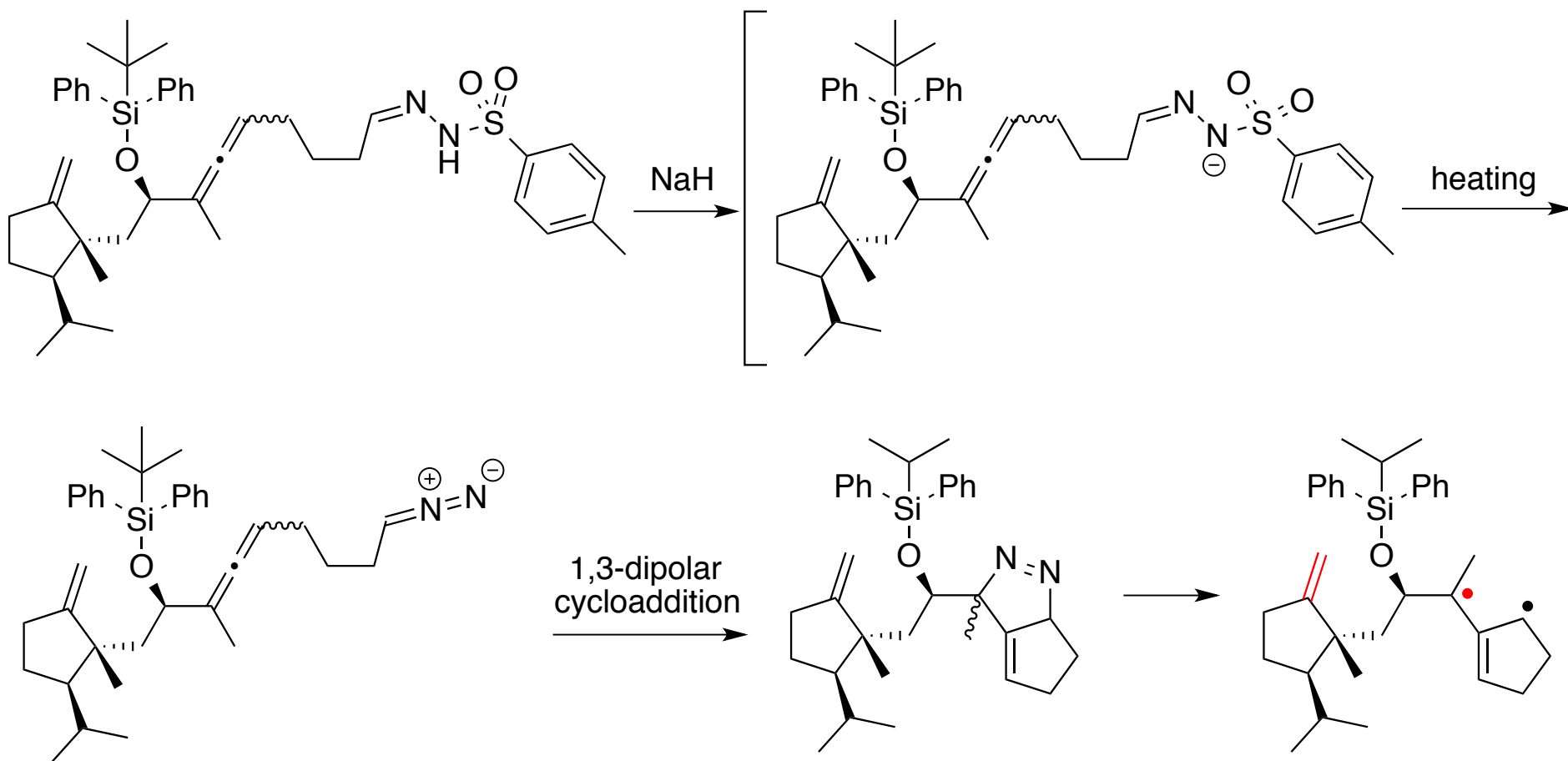
2/ H<sub>2</sub>NNHTs, MeOH  
r.t., **97%**



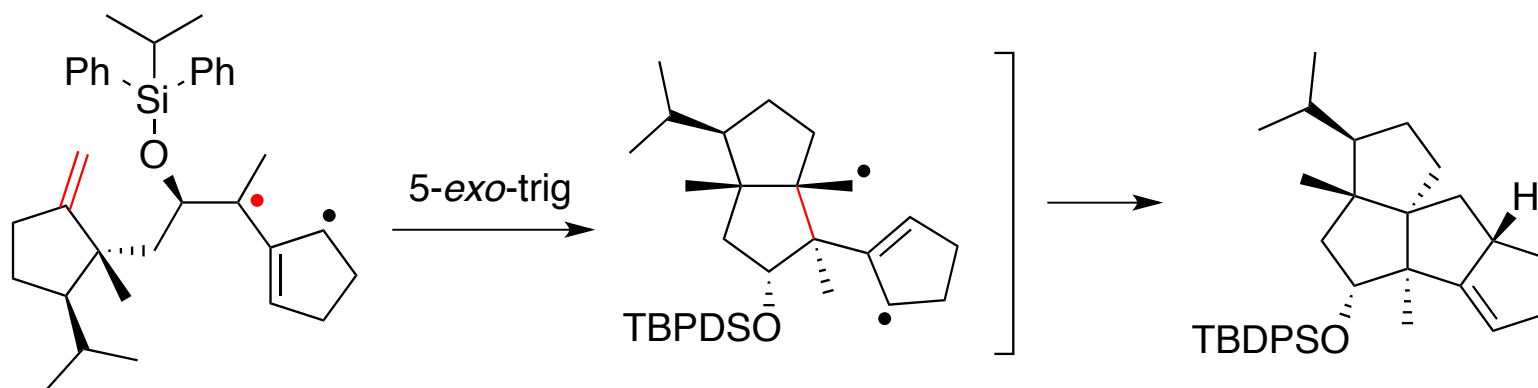
# Synthesis of tetracyclic skeleton



# Mechanism proposed by the authors

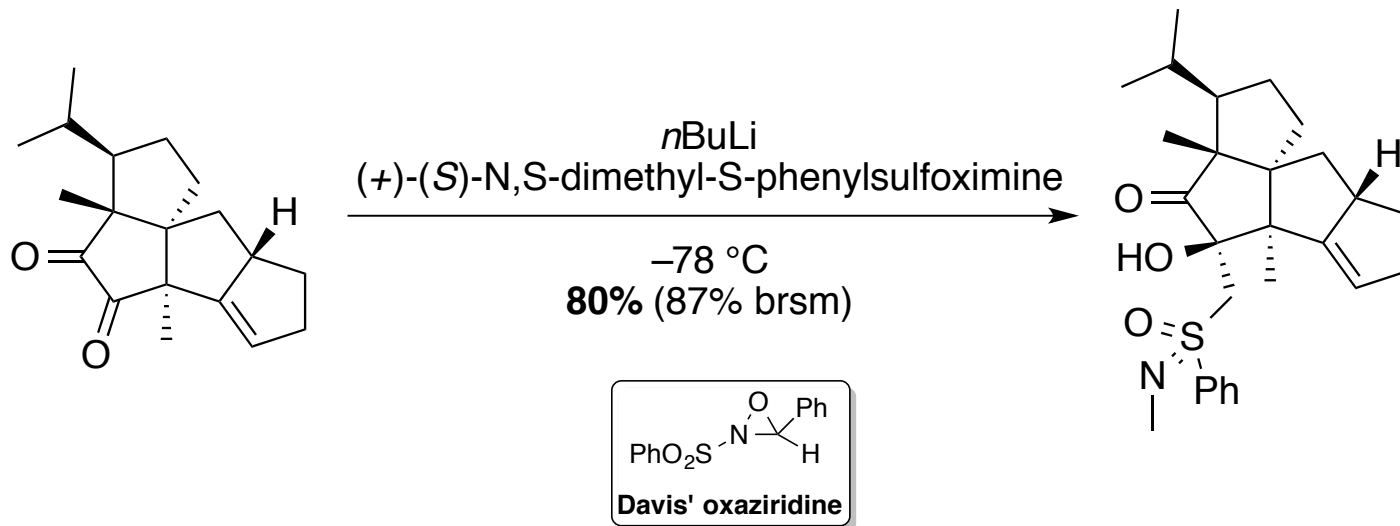
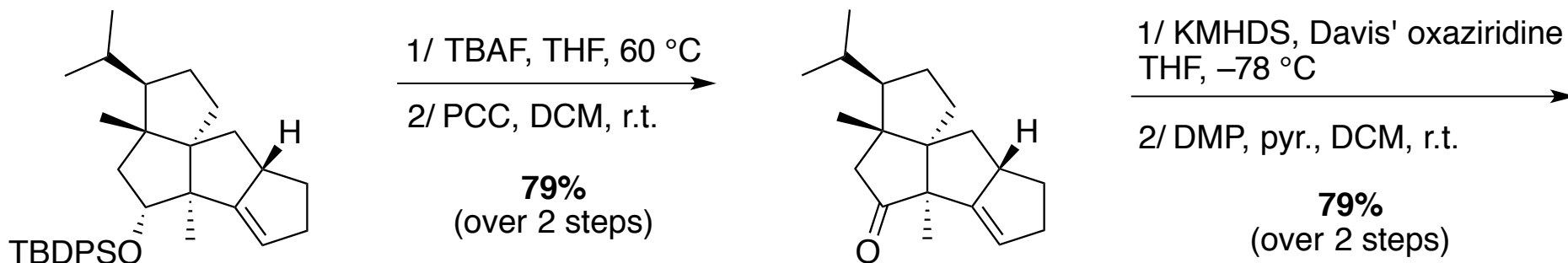


# Mechanism proposed by the authors

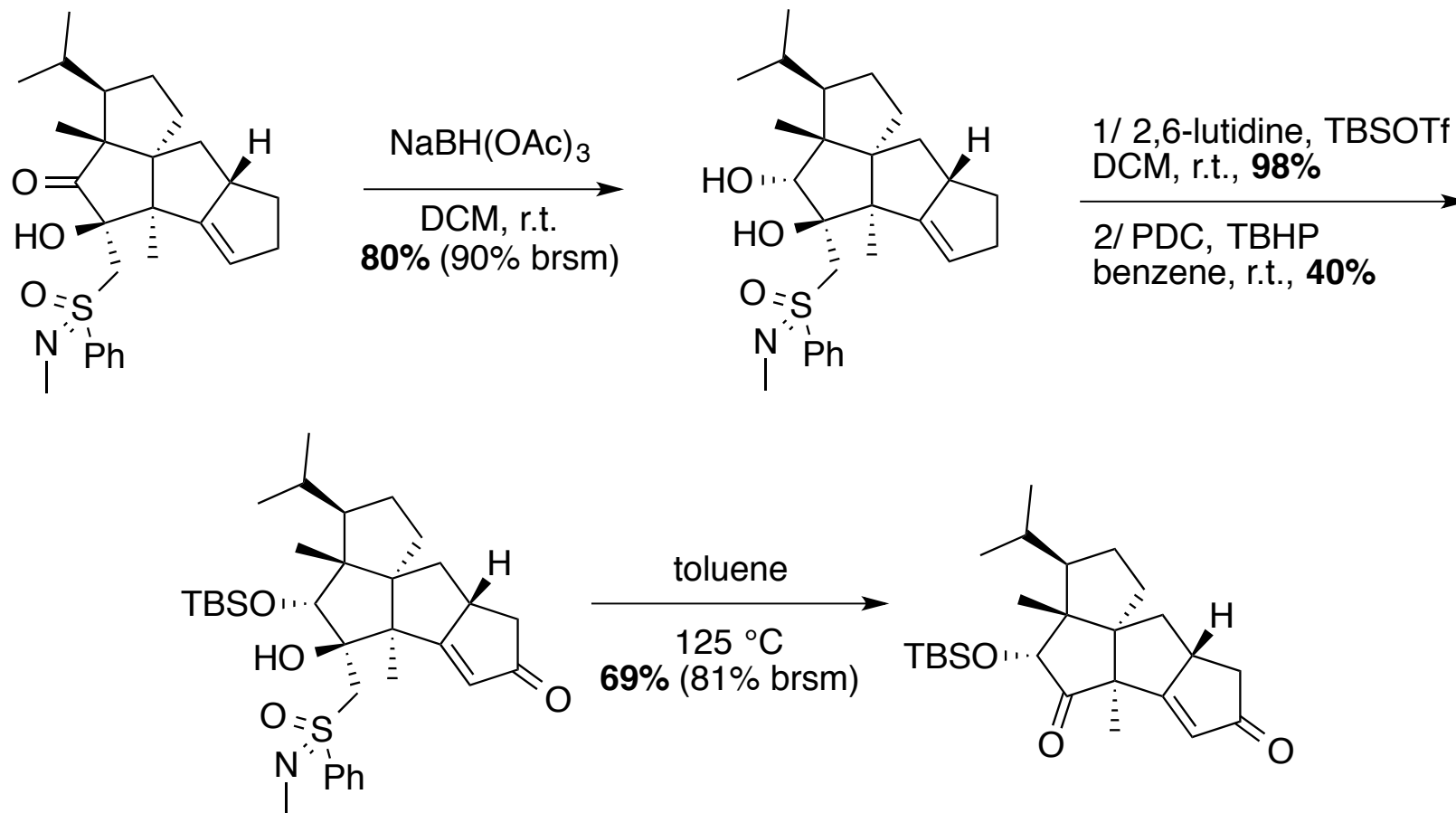




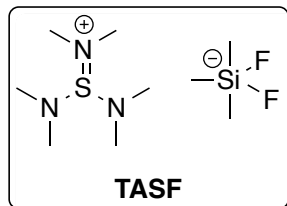
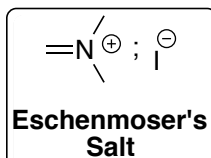
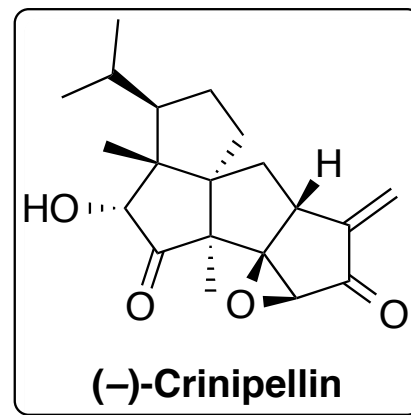
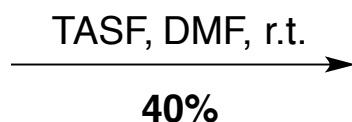
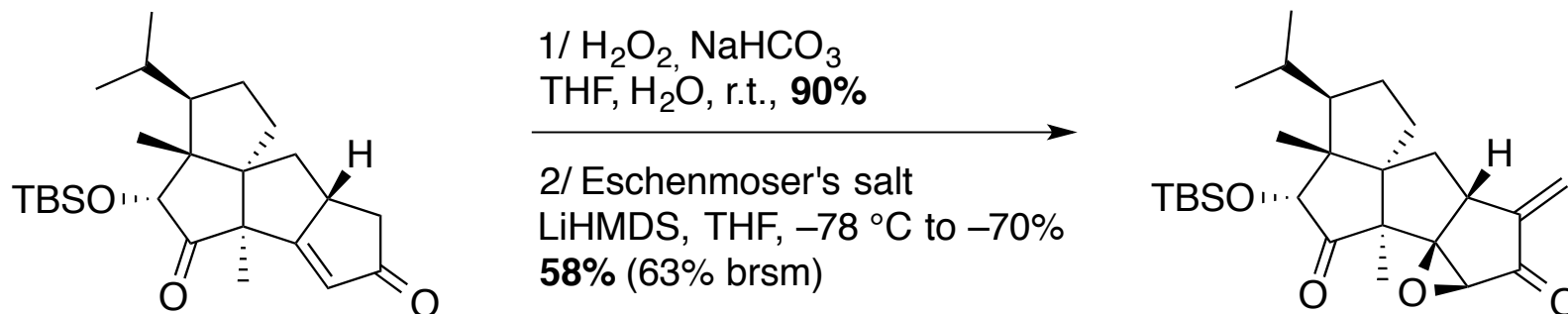
# End of the synthesis



# End of the Synthesis



# End of the synthesis



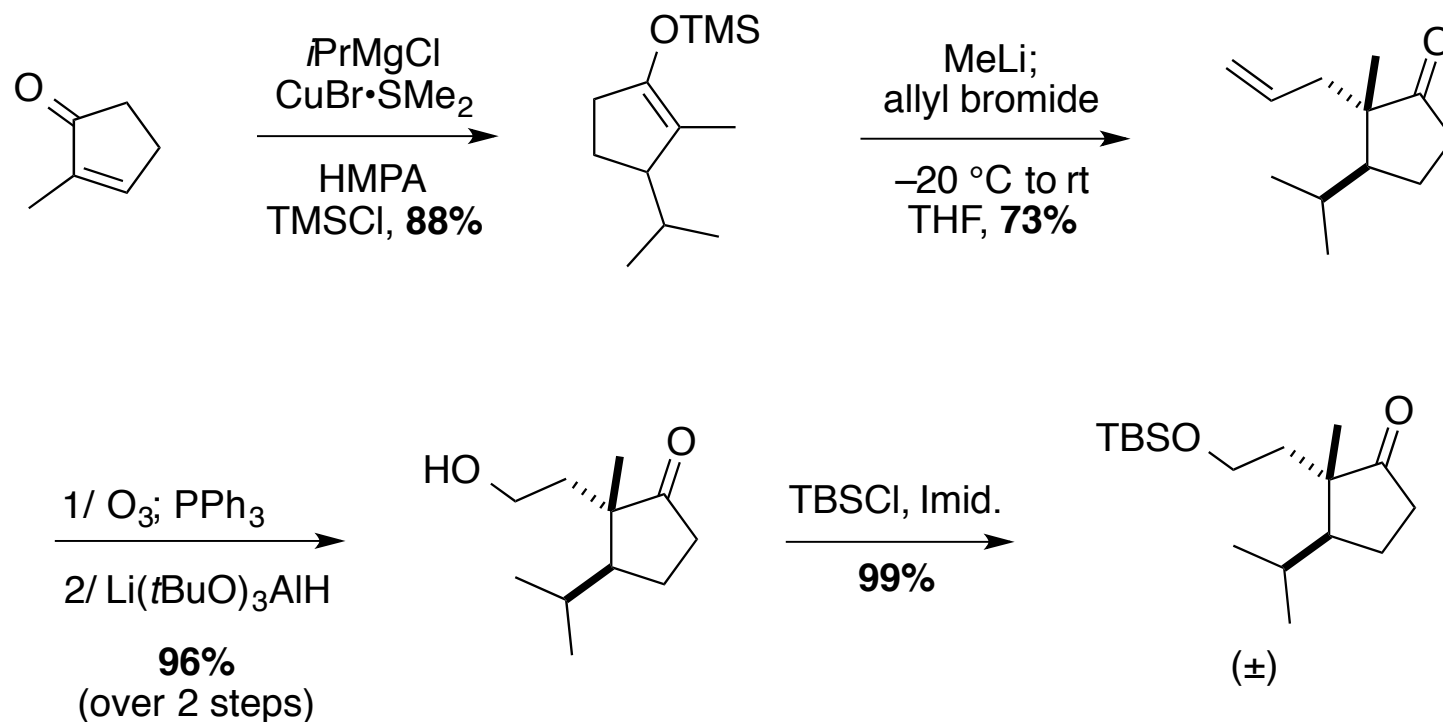
# Conclusion

- > First asymmetric total synthesis
- > Key step : TMM diyl mediated tandem cycloaddition reaction
- > 25 linear steps : Overall Yield = 1%

Thank you for your attention

!!!

# Synthesis of starting material



# Synthesis of starting material

