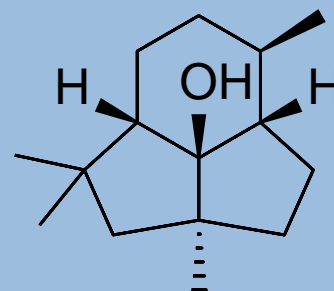


Enantiospecific Total Synthesis of the Highly Strained (-)-Persilphiperfolan-8-ol via Pd-Catalyzed Tandem Cyclozation

P. Hu and S. A. Snyder, *J. Am. Chem. Soc.* **2017**, *139*, 5007.

Daniel Meyer
University of Bern

05.07.2017, Journal Club



Scott A. Snyder

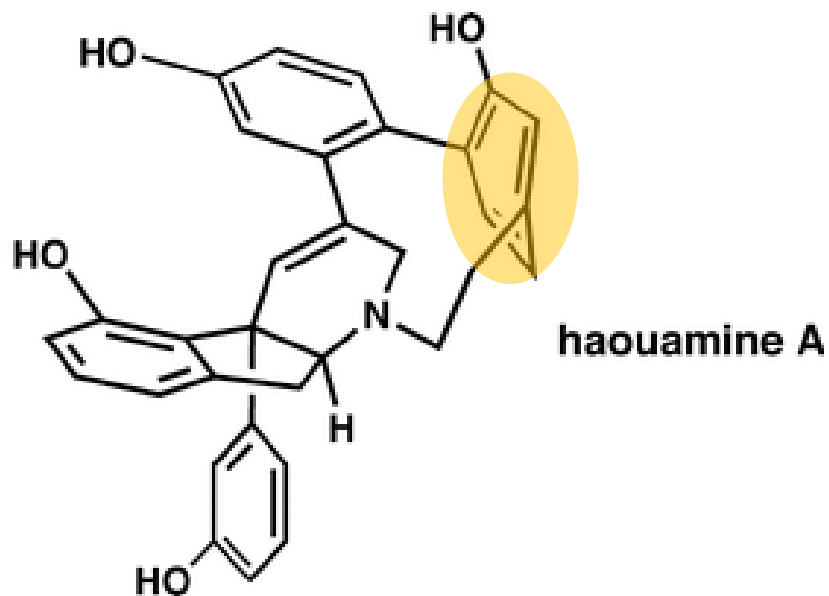
- > Undergraduate studies in Williamstown
- > PhD at K. C. Nicolaou (Scripps)
- > Postdoc E. J. Corey (Harvard University)
- > Independent career (Columbia University)
- > Associate Professor (Scripps)

- > Development of new reagents
- > Methods for rapid polycycle construction
- > Total synthesis

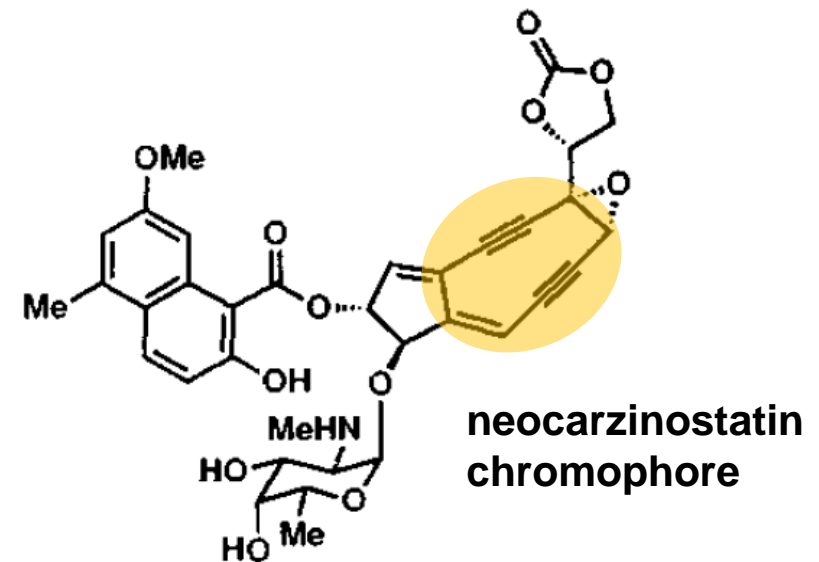


Strain in Natural Products

Bent arene rings



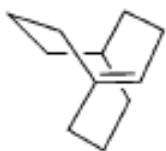
Medium sized rings with multiple sites of unsaturation



Strain in Natural Products

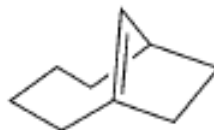
anti-Bredt double bonds

a) Isolable



$OS \leq 17 \text{ kcal mol}^{-1}$
Bicyclo[3.3.3]undec-1-ene

Observable



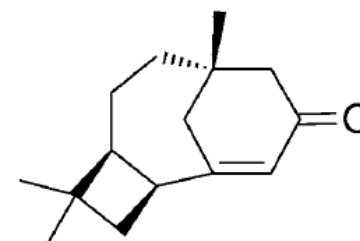
$17 \text{ kcal mol}^{-1} \leq OS \leq 21 \text{ kcal mol}^{-1}$
Bicyclo[4.2.1]non-1(9)-ene

Unstable

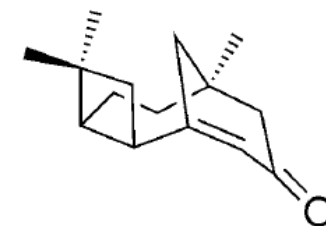


$OS \geq 21 \text{ kcal mol}^{-1}$
Bicyclo[2.2.2]oct-1-ene

bicyclo[4.3.1]decene



|||



Sesquiterpene was isolated from a New Zealand Eurypon sp. Sponge

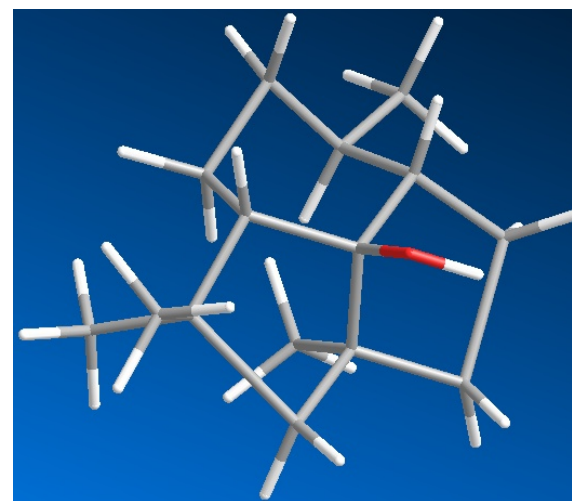
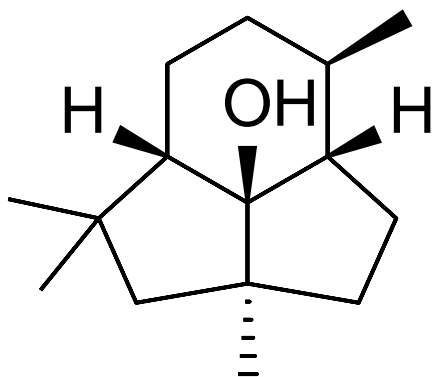
S-value: 9

7

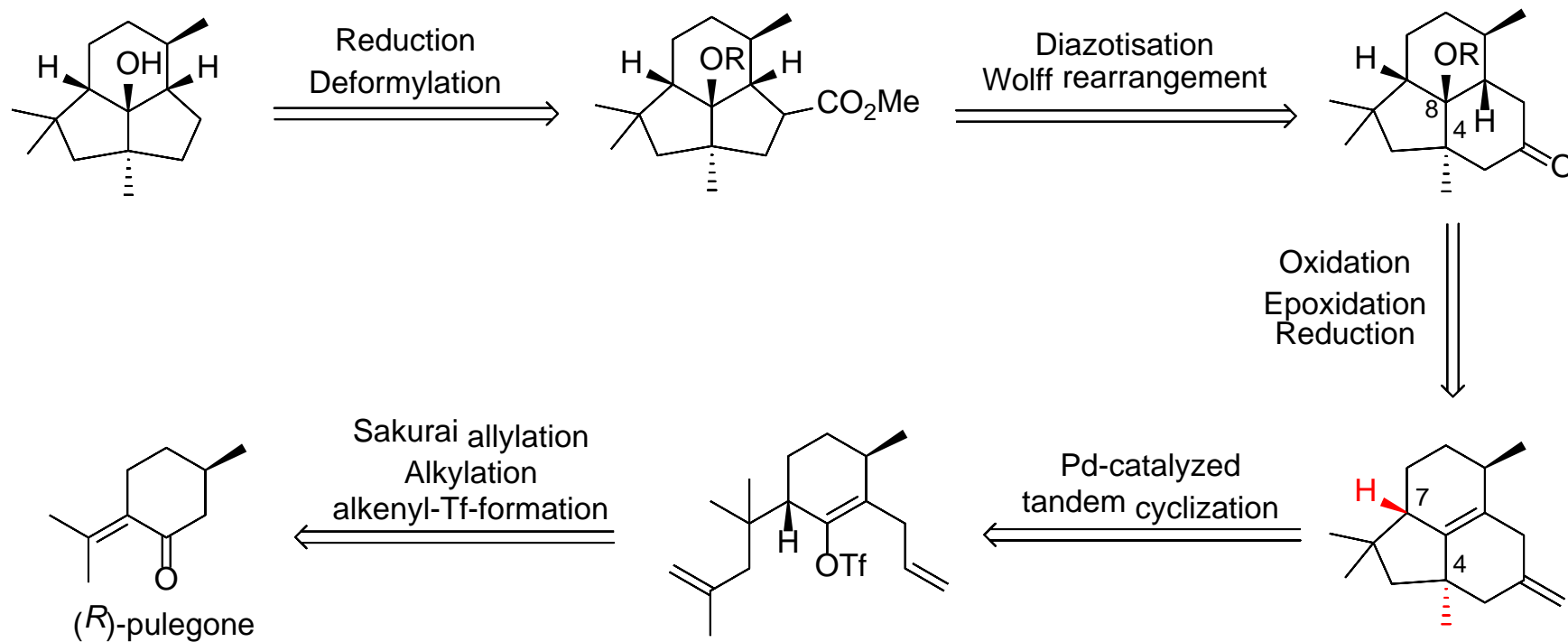
6

Strain in Natural Products

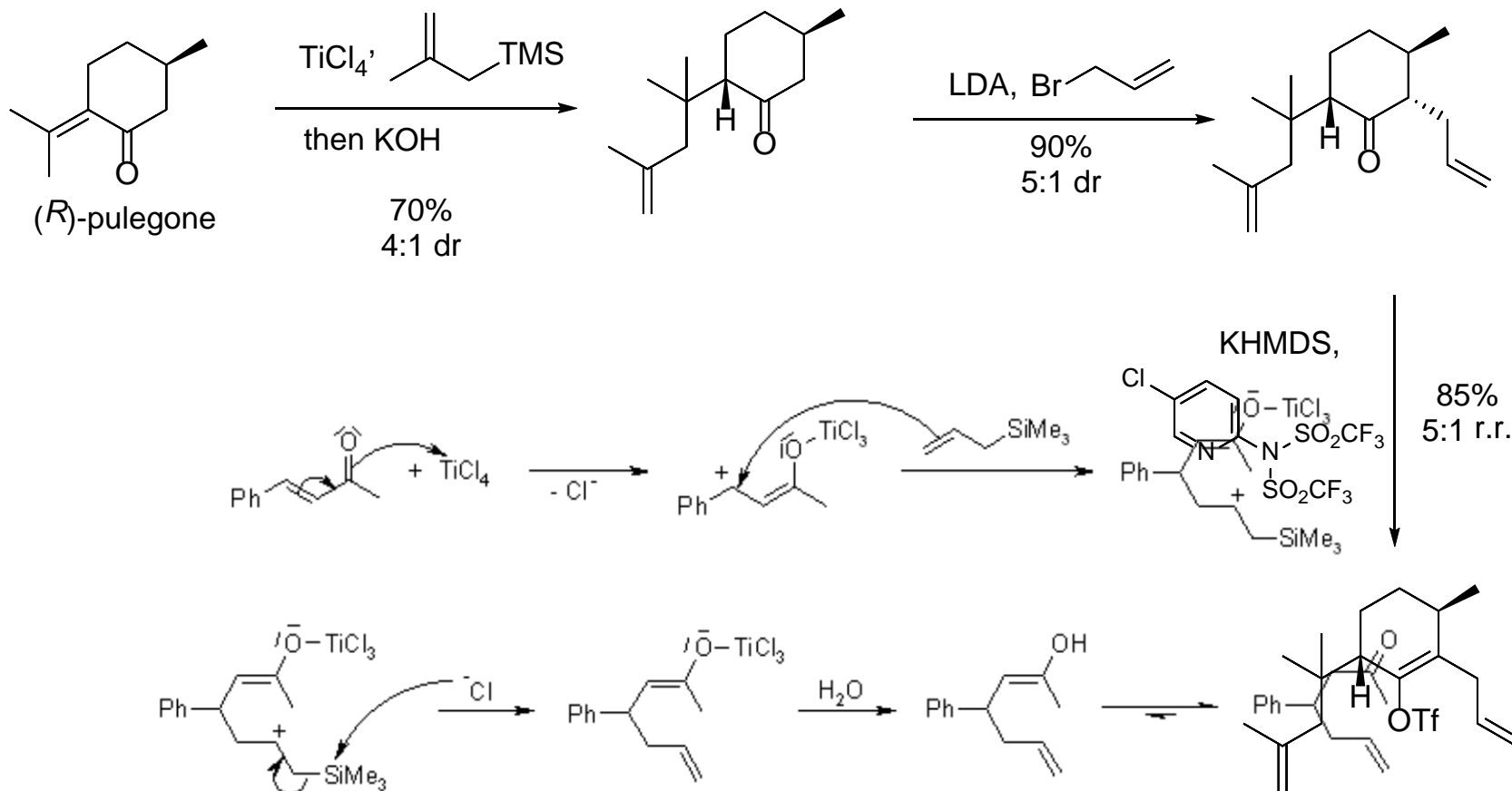
- > trans-bicyclo[3.3.0]octanes
 - Strain energy of *trans* 6-13 kcal/mol higher than *cis*
- > Only 10 out of 2000 bicyclo[3.3.0]octanes are *trans*
- > To date 4 natural product synthesized with this structure



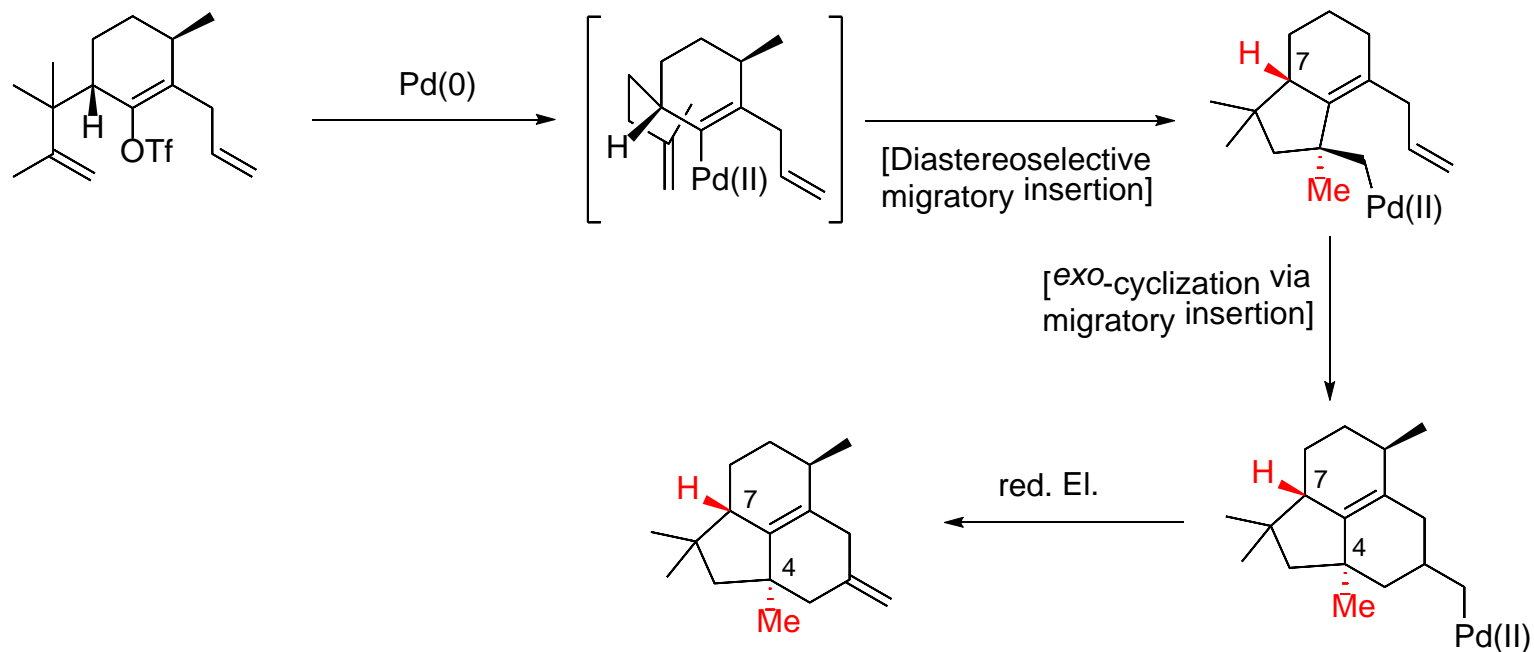
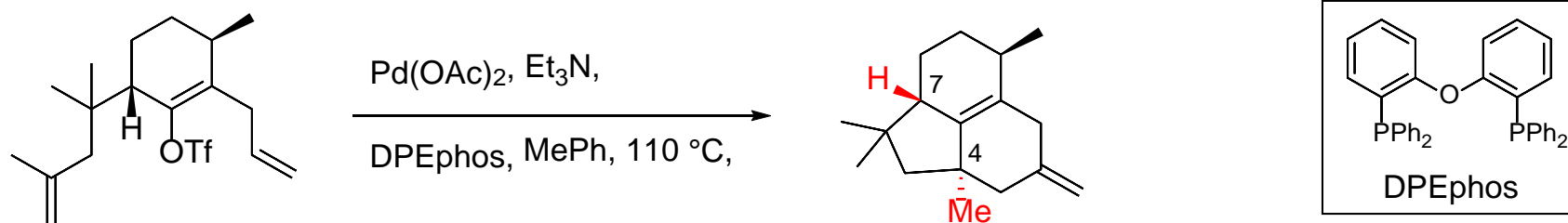
Retrosynthetic Analysis



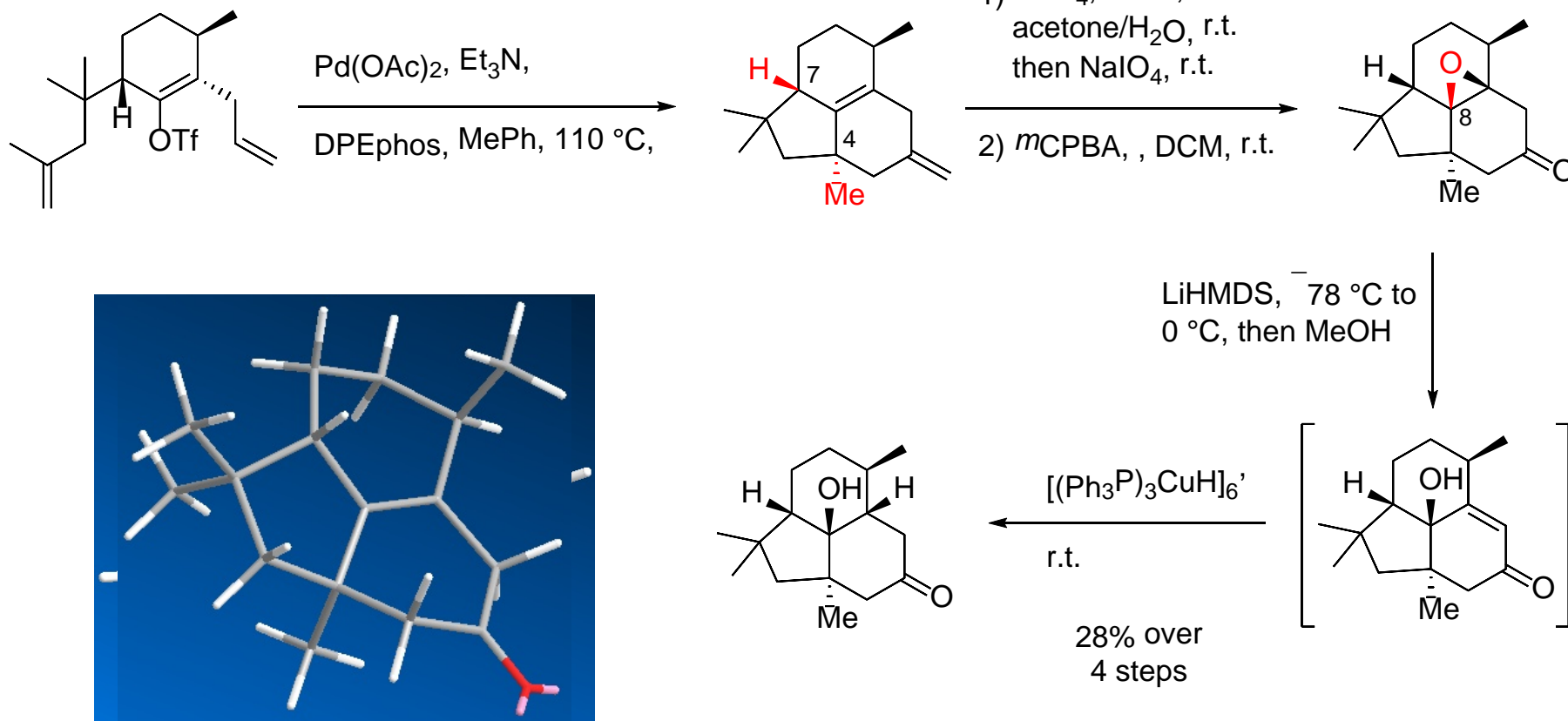
Forward Synthesis



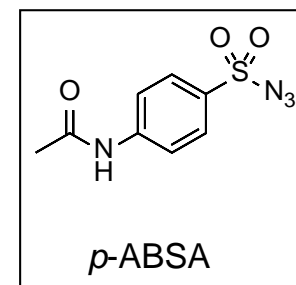
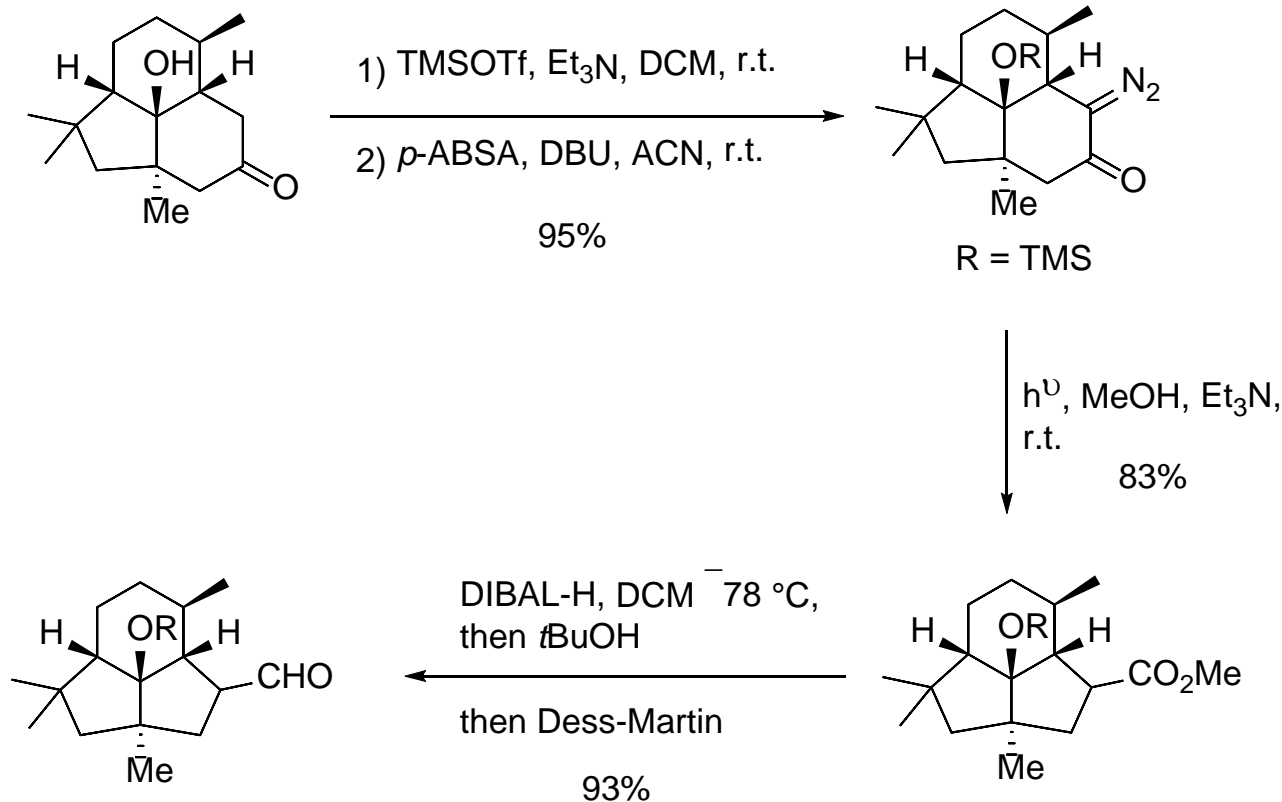
Forward Synthesis



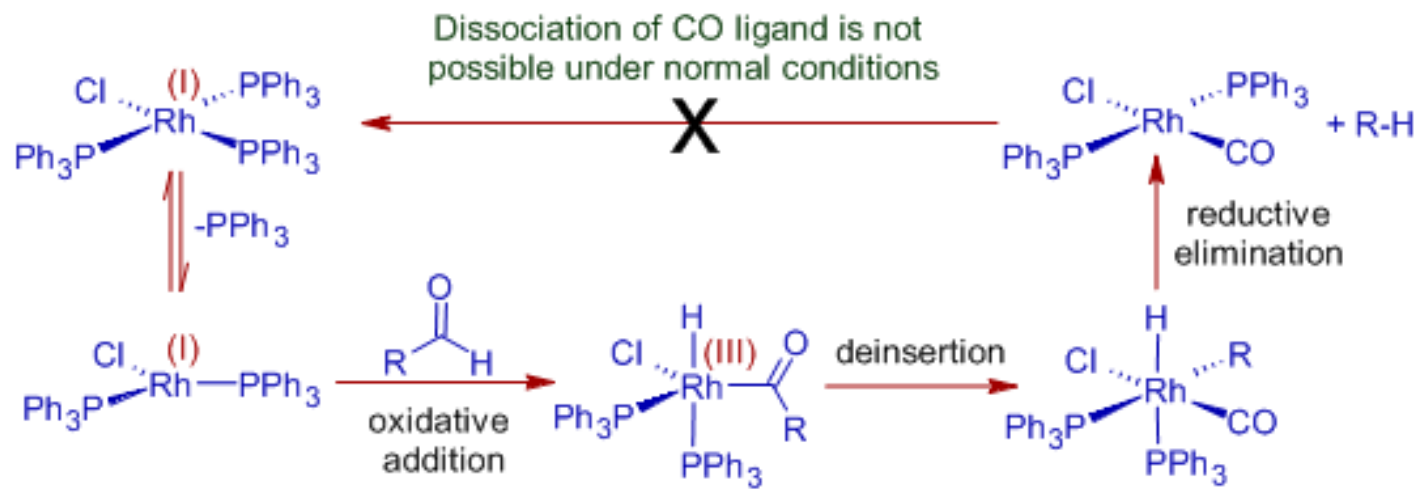
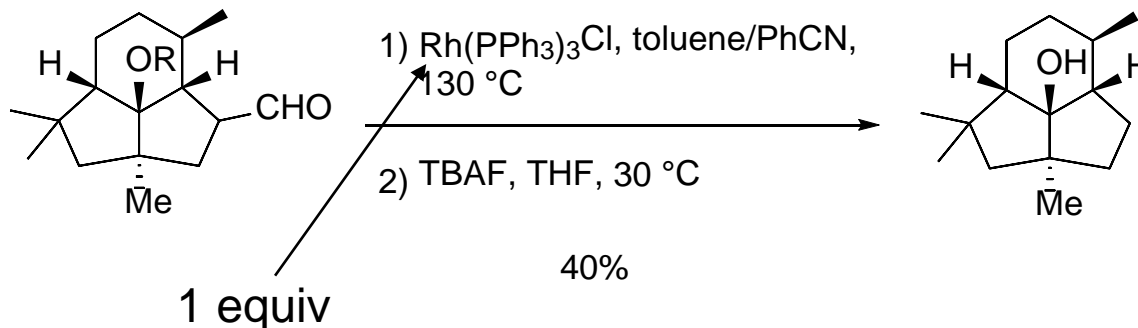
Forward Synthesis



Forward Synthesis



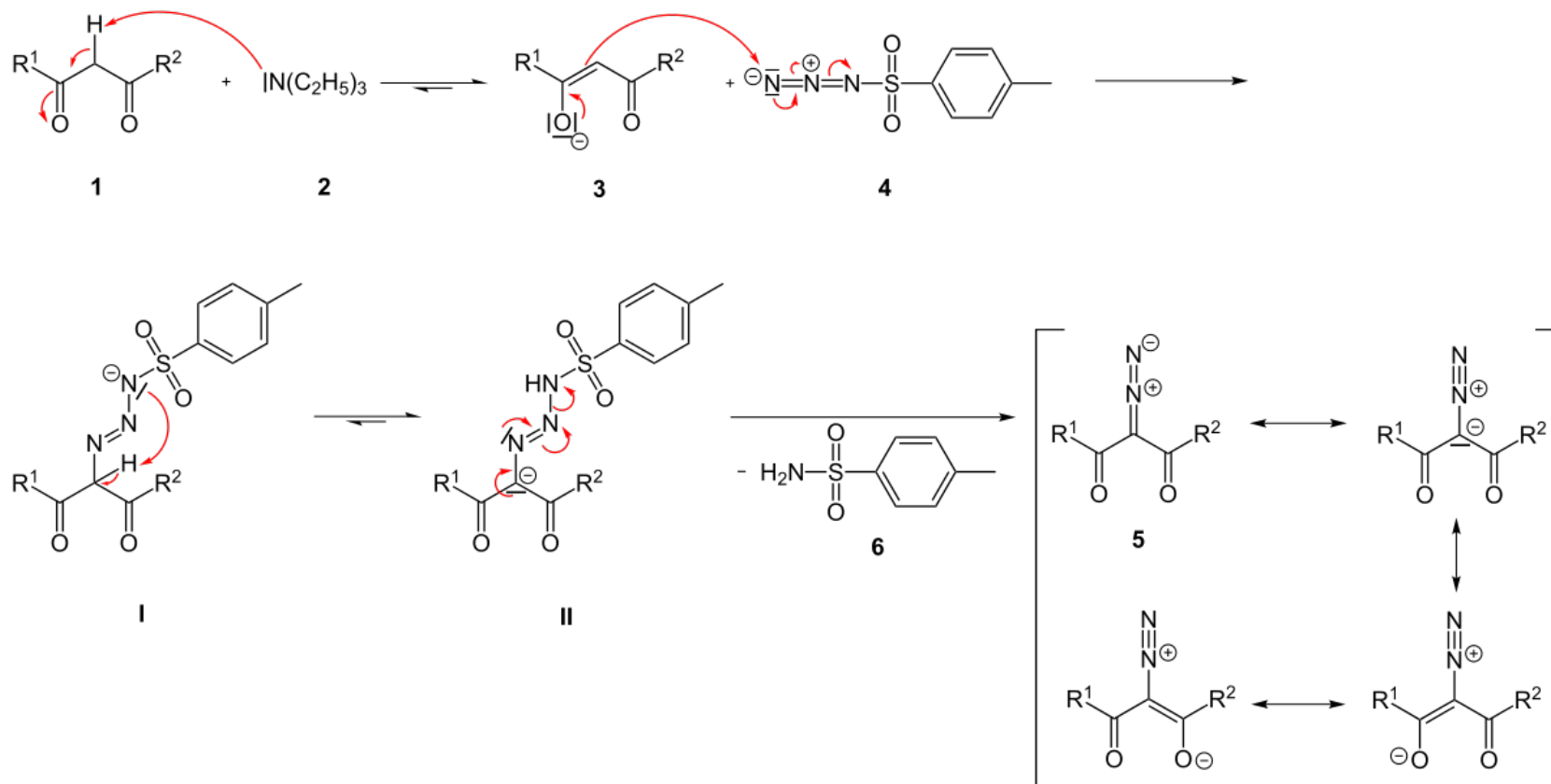
Forward Synthesis



Conclusion

- > First total synthesis of (–)-persilphiperfolan-8-ol
- > 4.4% yield over 13 steps
- > Key step is the Pd-catalysed tandem cyclization

Diazo transfer



Wolff rearrangement

