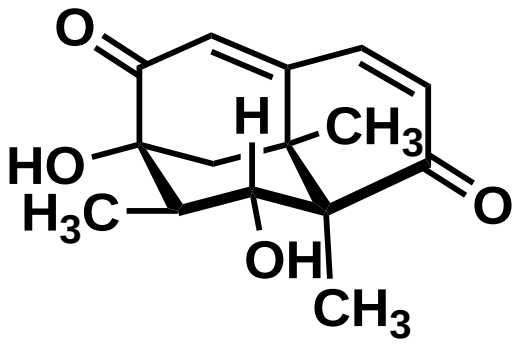
Total Synthesis of the Sesquiterpenoid Periconianone A Based on a Postulated Biogenesis



Liffert, R., Linden, A., Gademann, K.

J. Am. Chem. Soc. **2017**, *139*, 16096

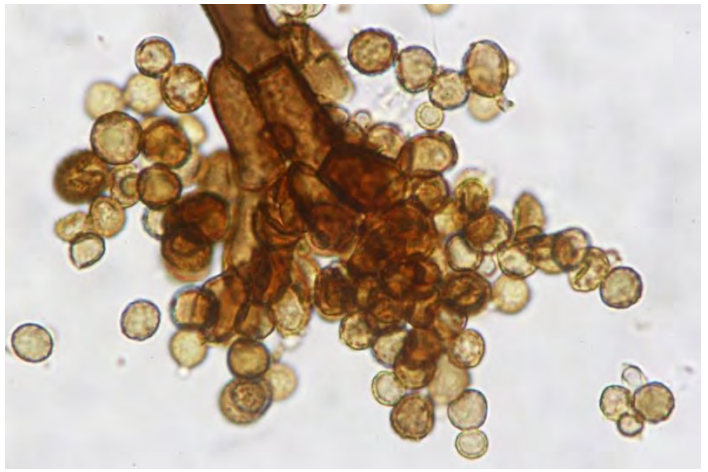
Presented by: Brendyn Smith

CEM 852

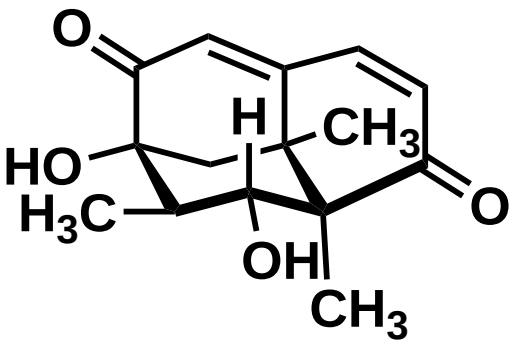
April 6th, 2019

Biological interest

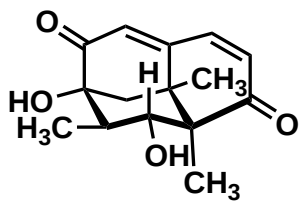
- Isolated from endophytic fungus *Periconia sp.*
- Neural anti-inflammatory activity
- Has potential for treating chronic heart failure
- Periconianone and simpler analogues demonstrated that they can reduce inflammatory biomarkers in inflamed cells



Periconia sp.

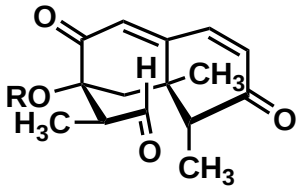


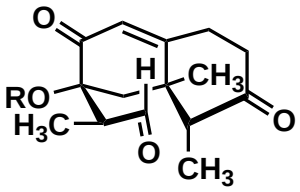
Biomimetic inspired retrosynthesis



biosynthetic hypothesis

aldol chemistry





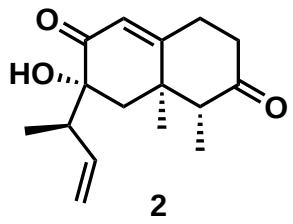
Key intermediate for biomimetic strategy

Key synthetic considerations:

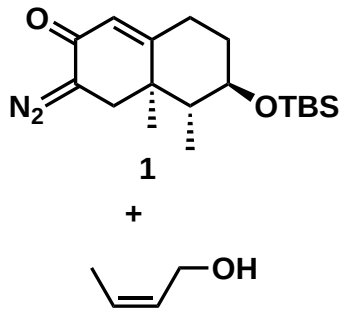
-late stage aldol (minimizing side-product(s); "quiz" at the end)

-ease of access to α–diazo intermediate 1

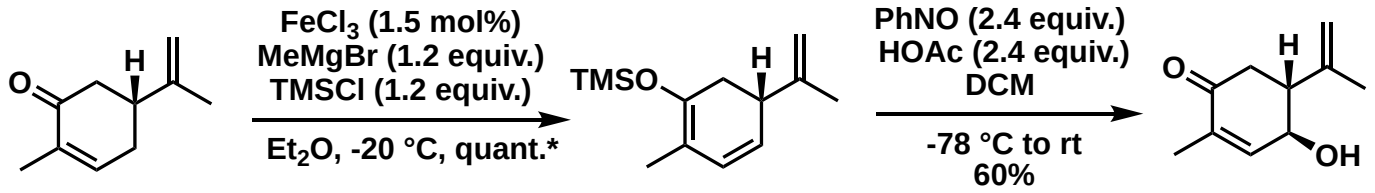
-how to access stereochemistry in compound 2 via Rh O-H insertion/ [3,3]-sigmatropic rearrangement strategy



2



Quick starting material prep from (R)-carvone



vinylogous Mukaiyama aldol

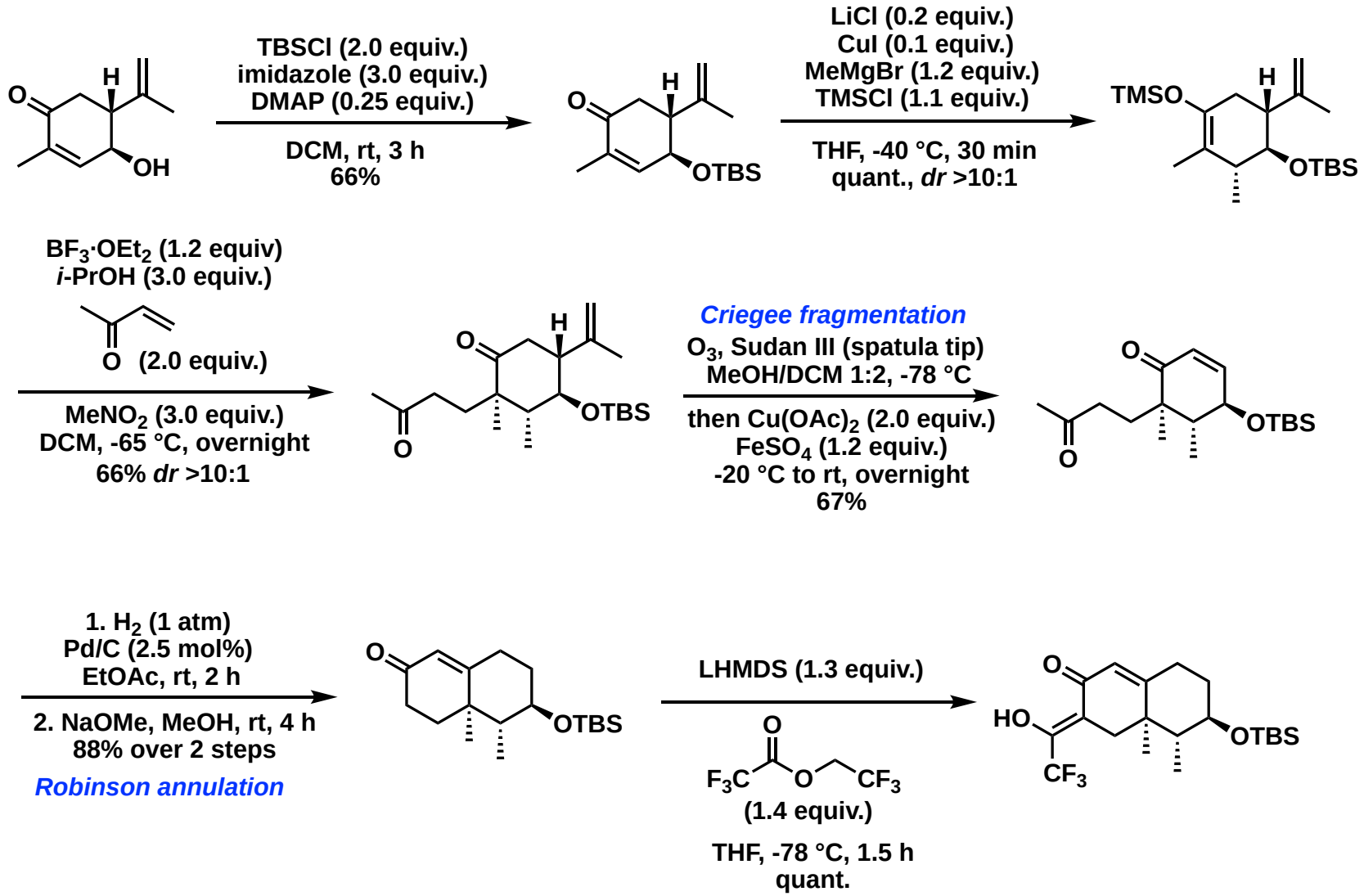
**This example used a carvone analogue with a reduced isoprenyl group:*

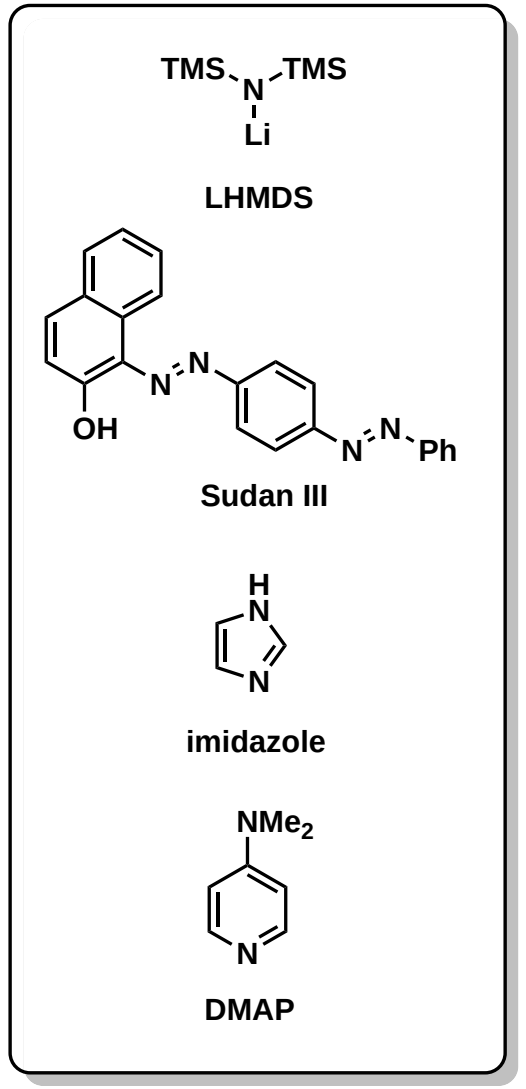
Ceccarelli, S. M., Piarulli, U., & Gennari, C., **2001**, *Tetrahedron*, *57*(40), 8531-8542.

Krafft, M. E., & Holton, R. A., *J. Am. Chem. Soc.* **1984**, *106*, 7619– 7621.

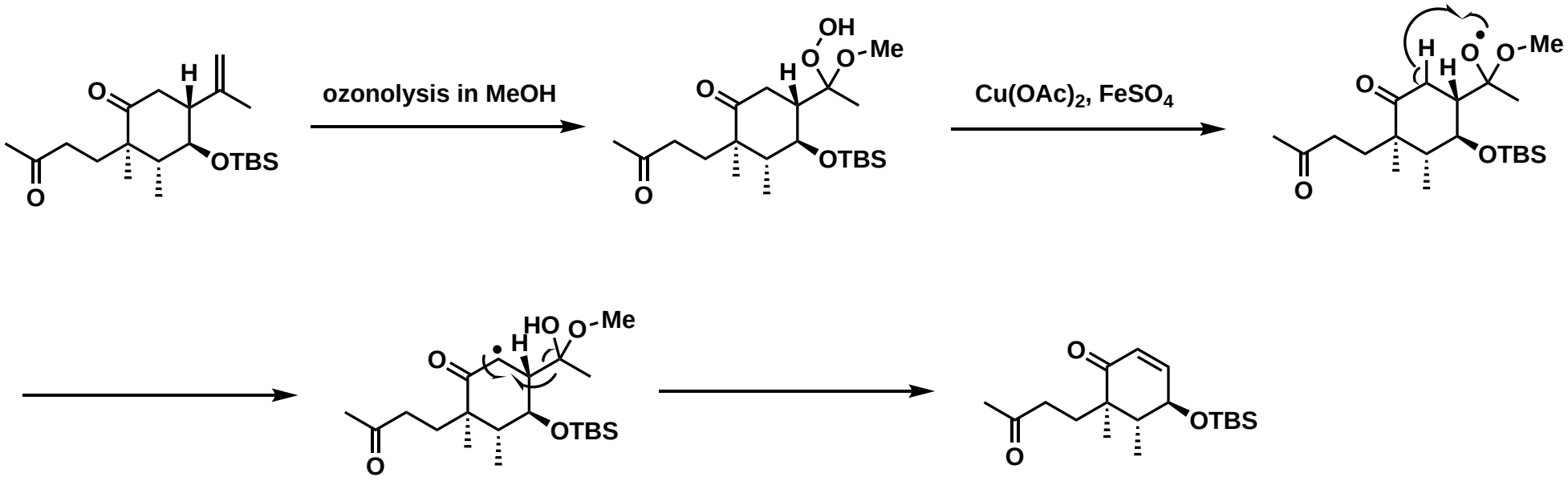
Tian, G. Q., Yang, J., & Rosa-Perez, K., *Org. Lett.*, **2010**, *12* (21), pp 5072–5074

Setting the stage with some familiar (and unfamiliar) transformations



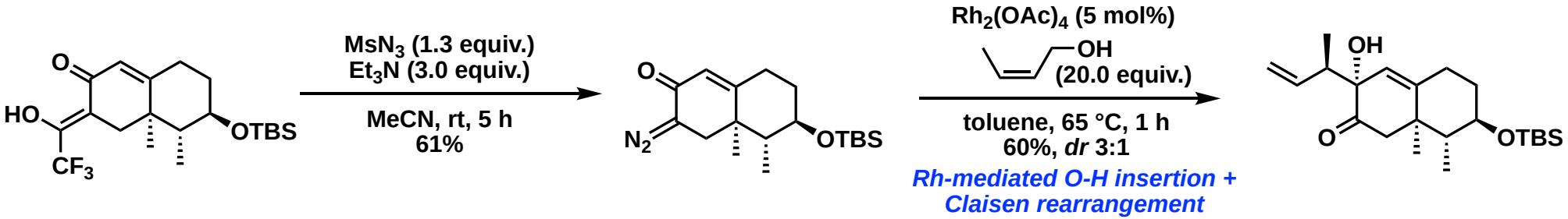


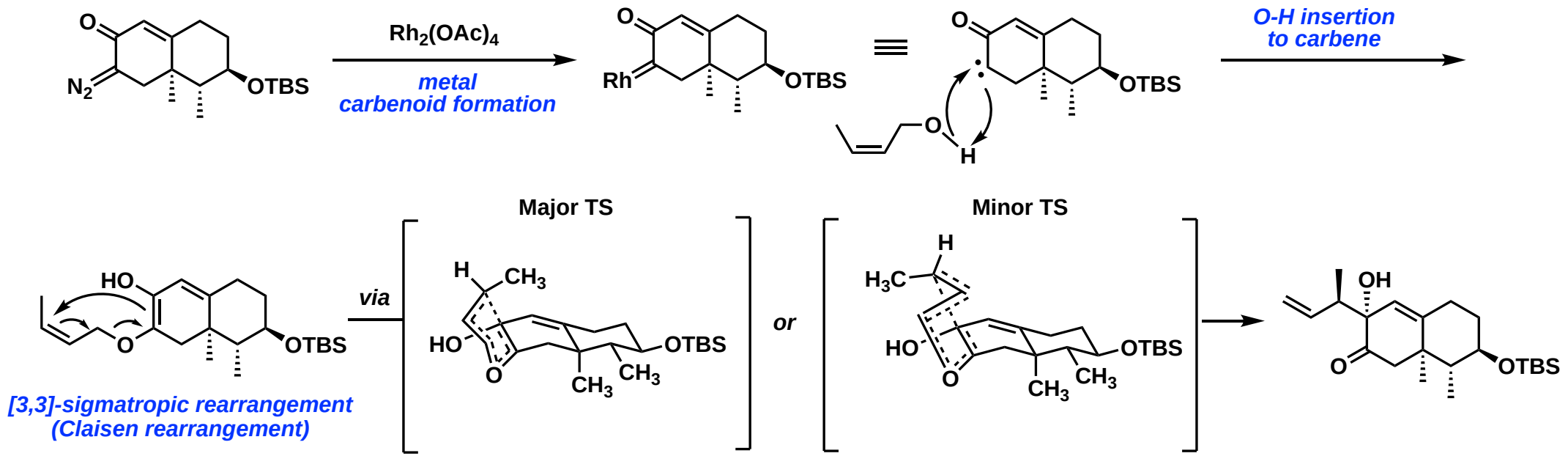
Criegee fragmentation mechanism



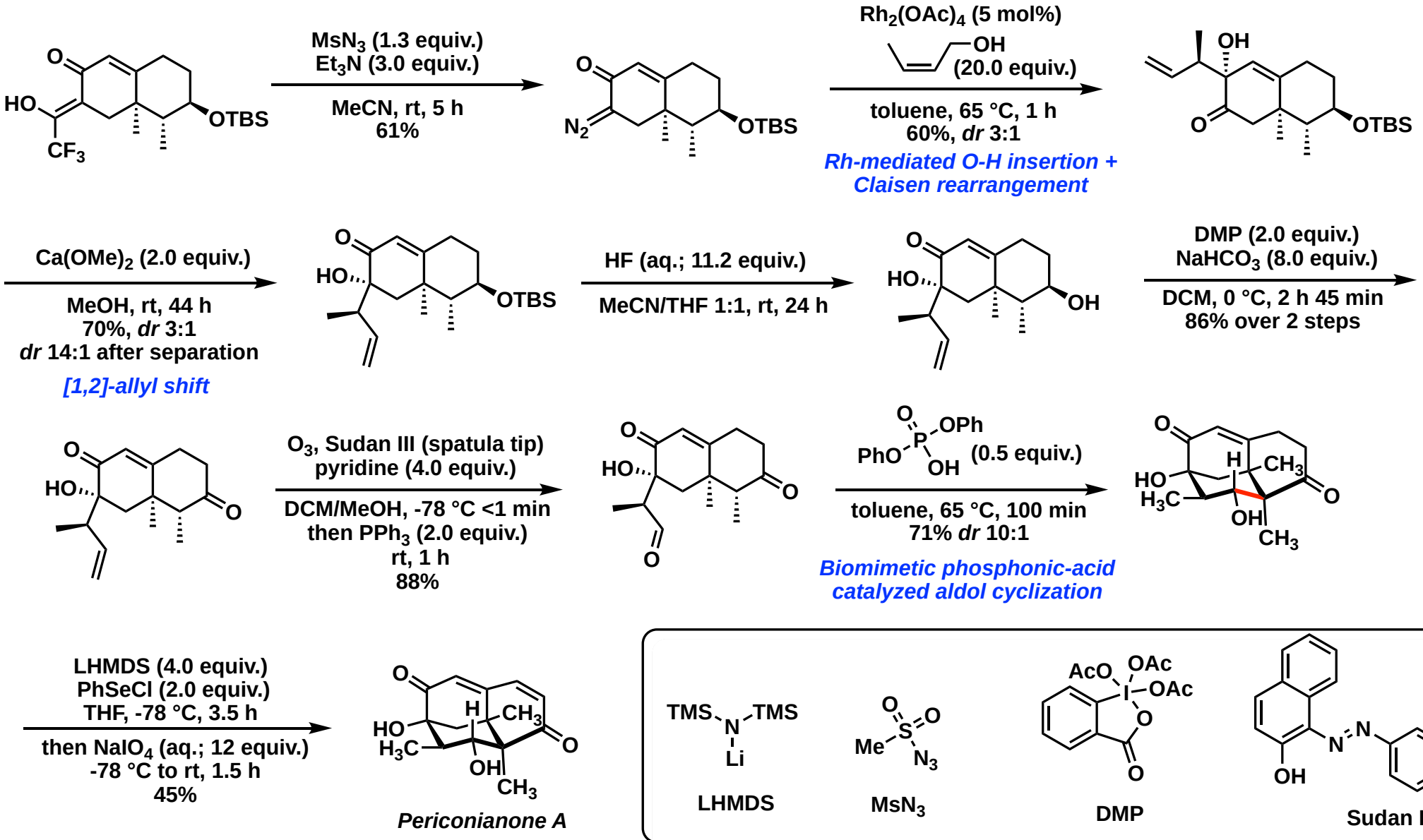
Schreiber, S. L., *J. Am. Chem. Soc.*, **1980**, *102* (19), pp 6163–6165

One of the key steps + stereochemical explanation





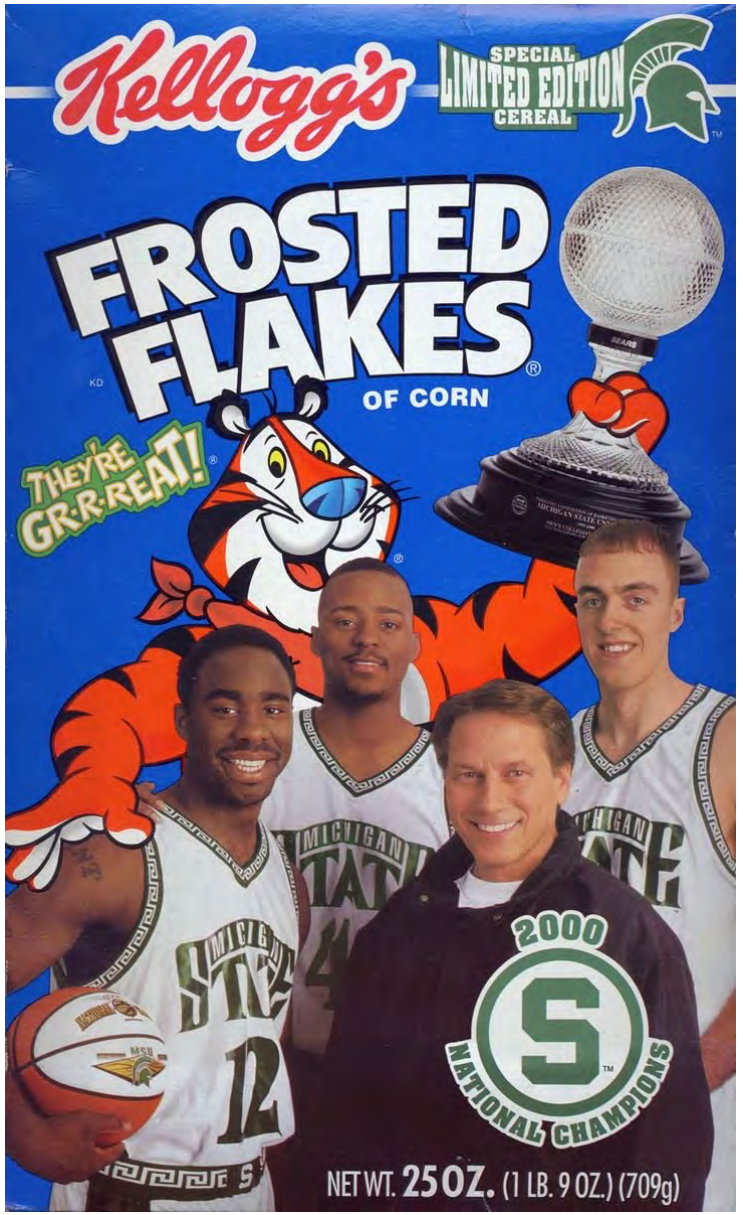
Synthesis completion enabled by biomimetic aldol



Congrats to the Gademann group at U. of Zurich

Go Green!


BIG TEN CHAMPIONS 2018
BIG TEN CHAMPIONS 2019


Kellogg's
SPECIAL LIMITED EDITION CEREAL
FROSTED FLAKES
OF CORN
THEY'RE GR-R-REAT!
2000
NATIONAL CHAMPIONS
NET WT. 25 OZ. (1 LB. 9 OZ.) (709g)