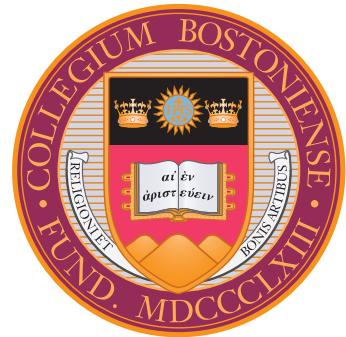


# Total synthesis presentation

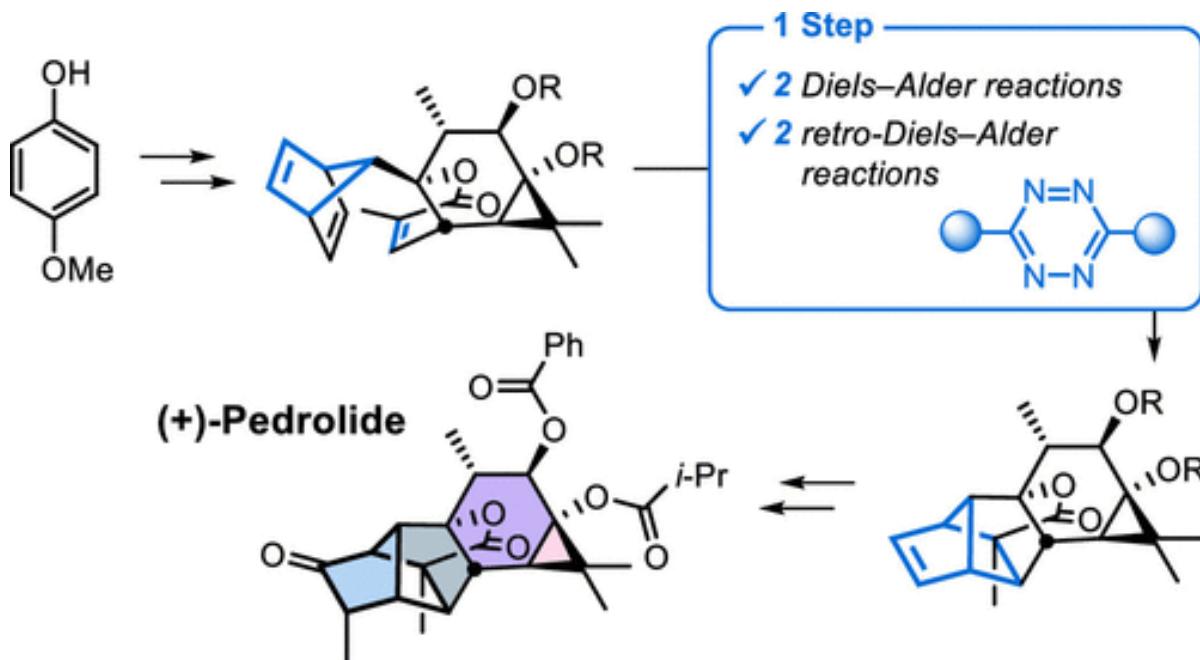


**Changhang Dai**  
Liu Group Meeting  
Jun 21st, 2023

# Enantioselective Total Synthesis of (+)-Pedrolide

Marlene Fadel and Erick M. Carreira\*

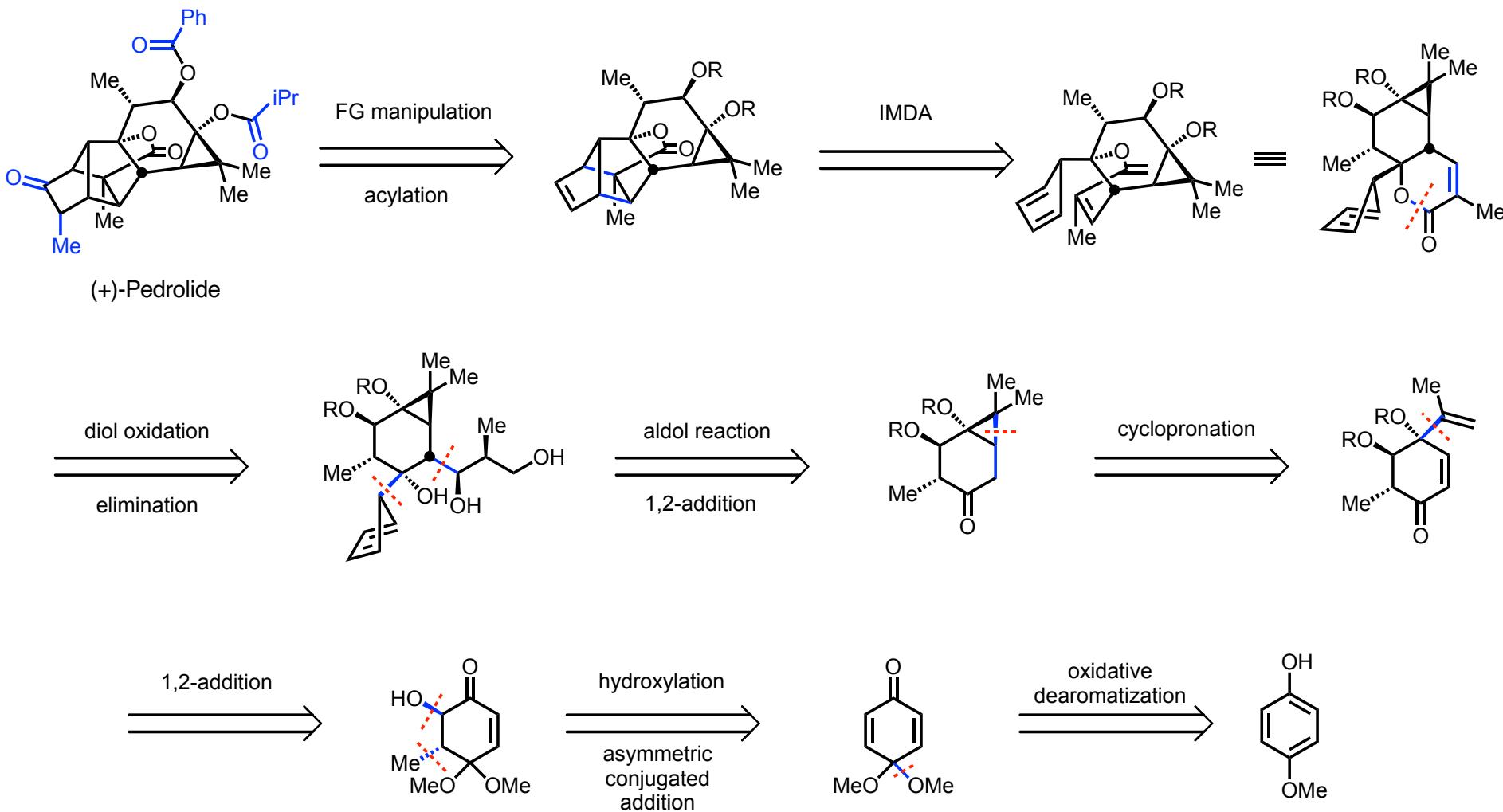
J|A|C|S  
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

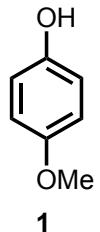


- Isolated in 2021 from *Euphorbia pedroi* by Ferreira and co-workers
- Biosynthetically derive from a tigliane precursor by proposal

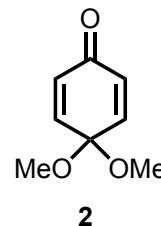
- New scaffold: pedrolane
- 5–5–6–6–3-fused skeleton
- bicyclo[2.2.1]heptane
- 12 stereogenic centers

# Retrosynthetic analysis

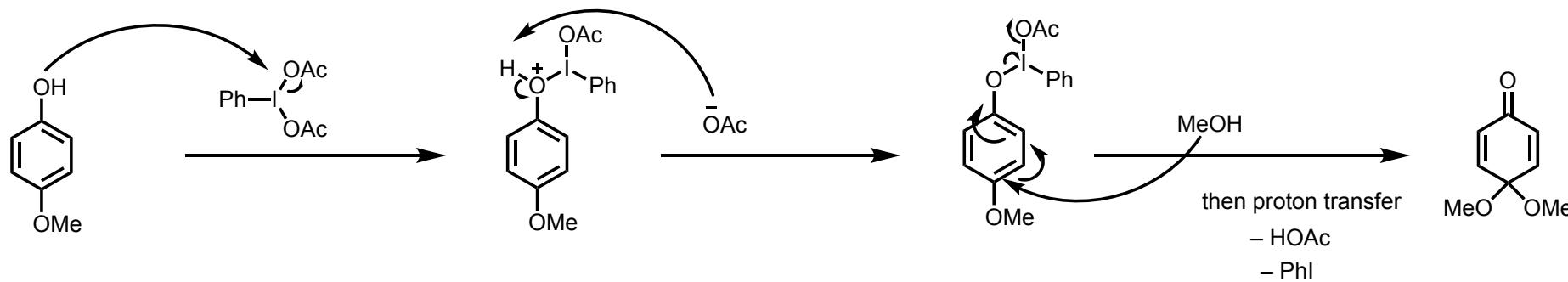
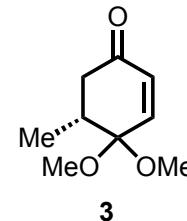


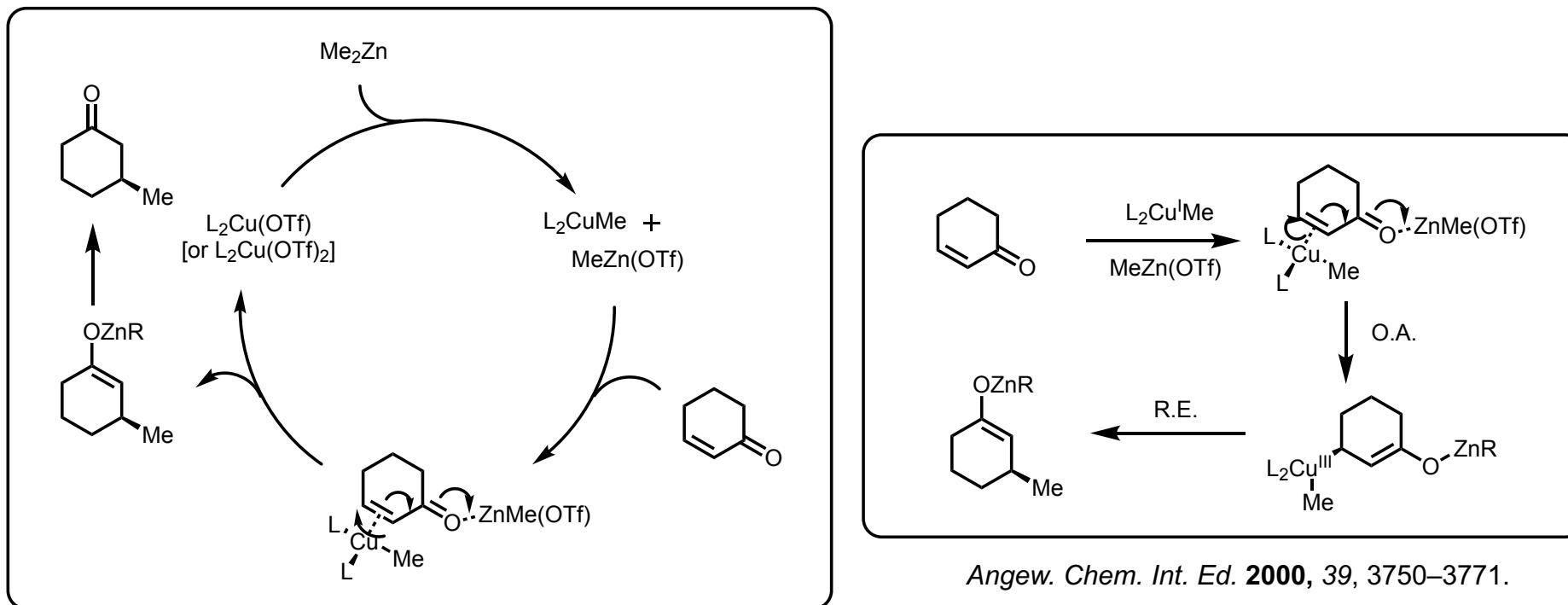
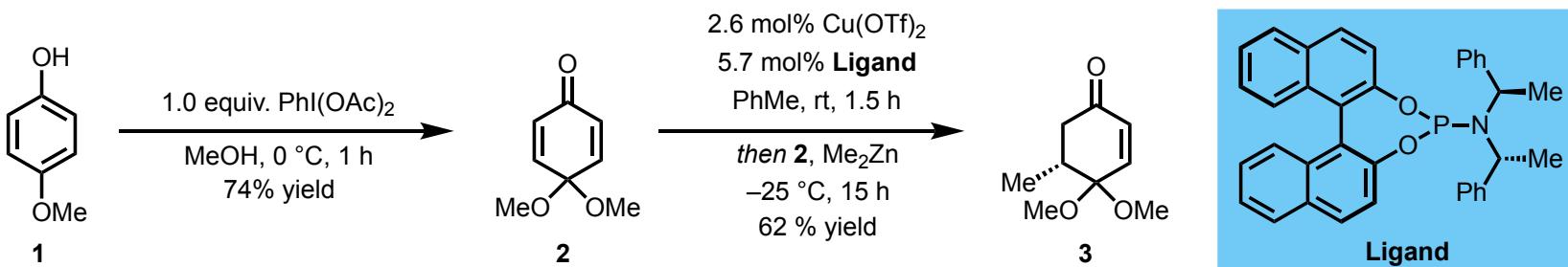


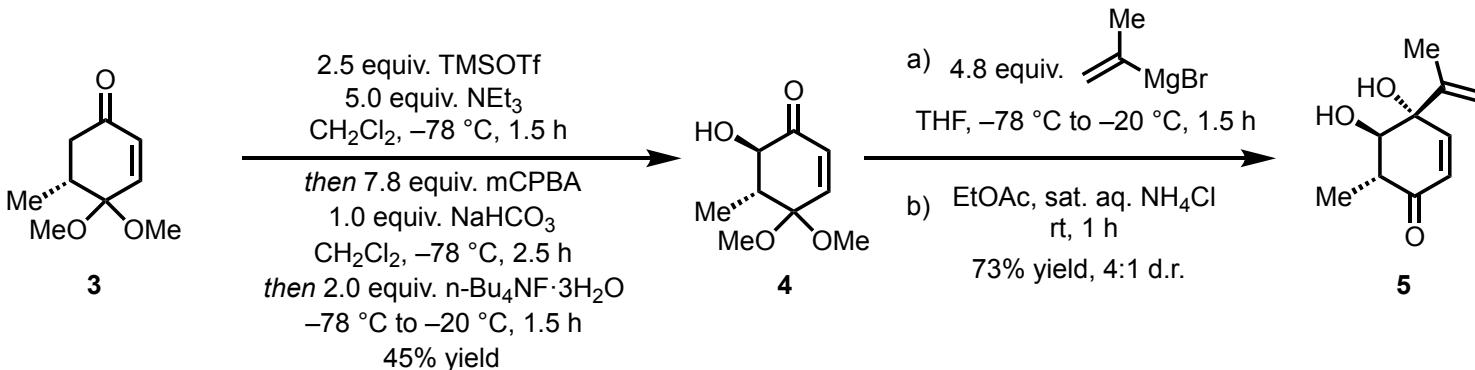
1.0 equiv.  $\text{PhI(OAc)}_2$   
MeOH, 0 °C, 1 h  
74% yield



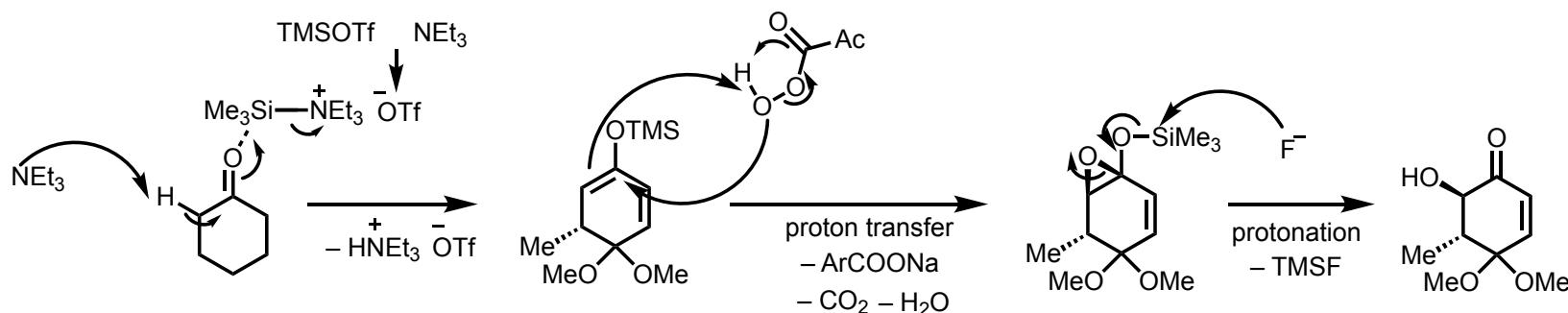
2.6 mol%  $\text{Cu(OTf)}_2$   
5.7 mol% **Ligand**  
PhMe, rt, 1.5 h  
then **2**,  $\text{Me}_2\text{Zn}$   
–25 °C, 15 h  
62 % yield



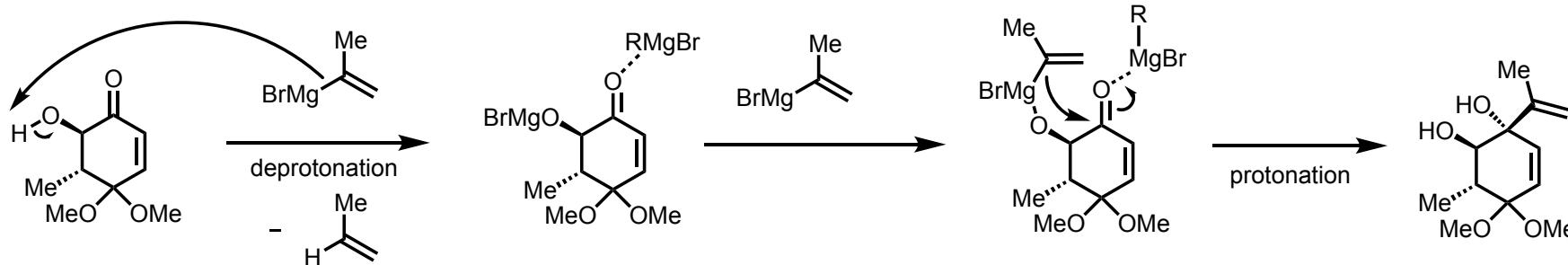


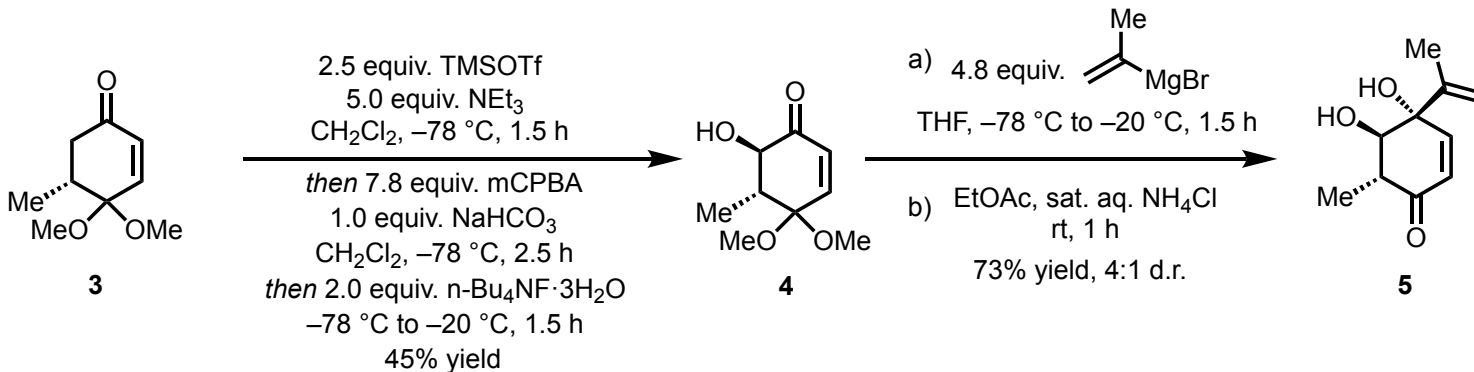


Rubottom reaction:

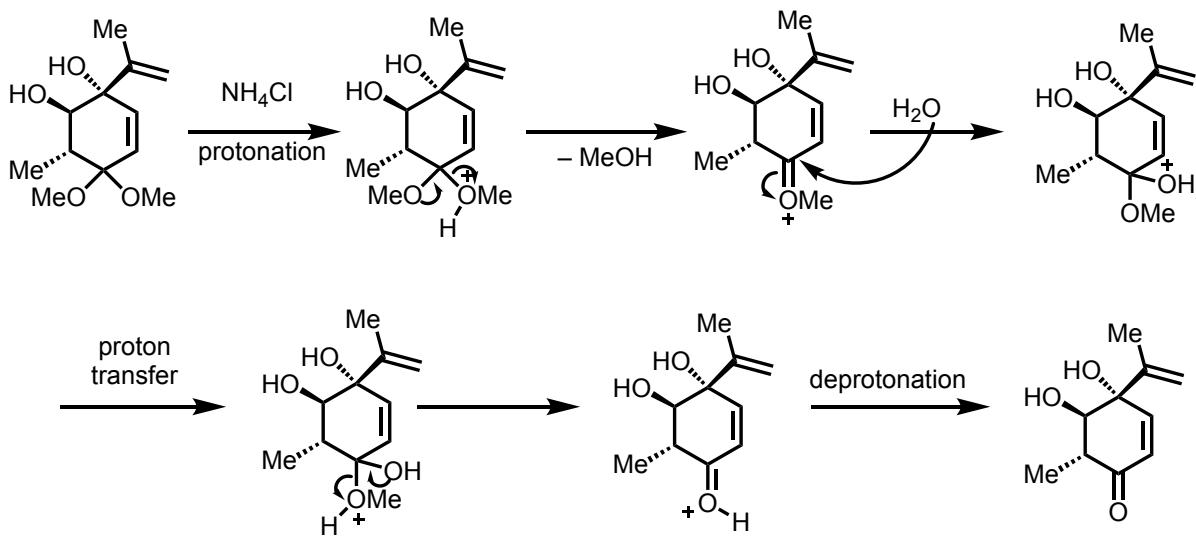


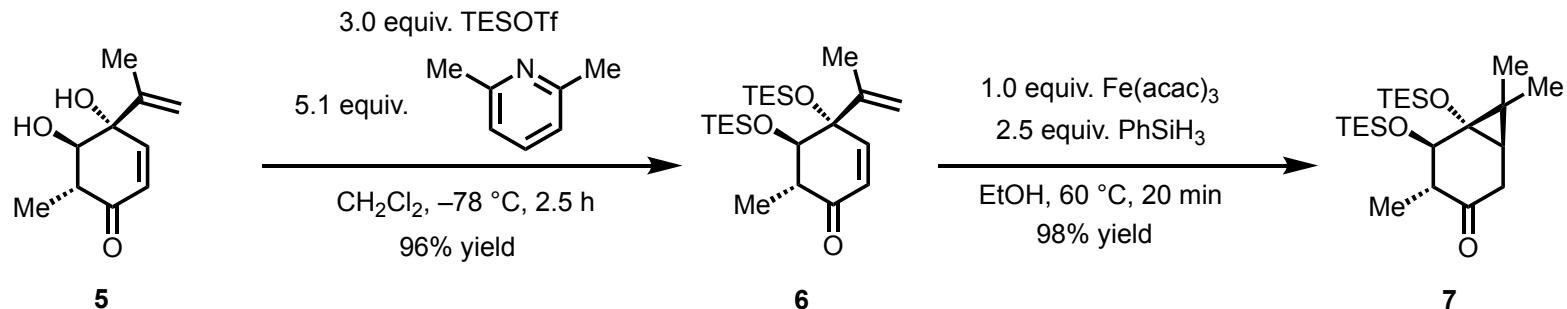
Grignard addition:



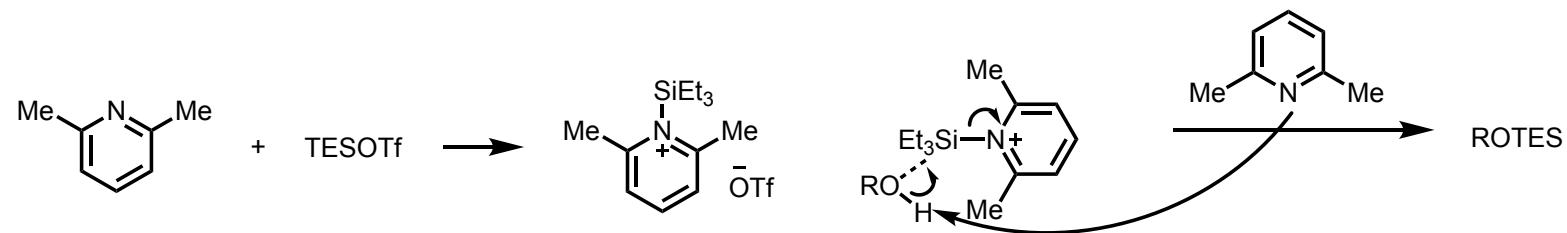


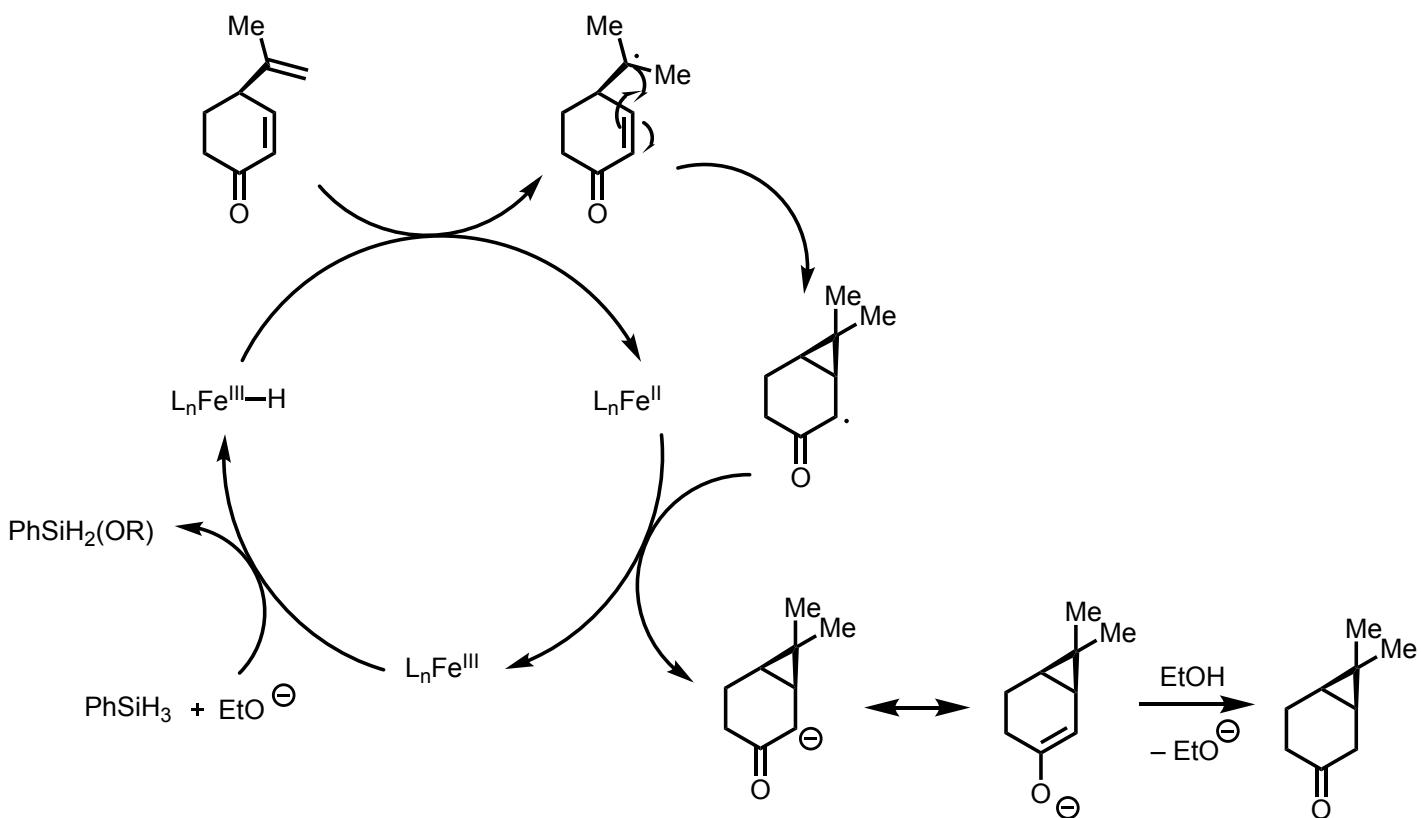
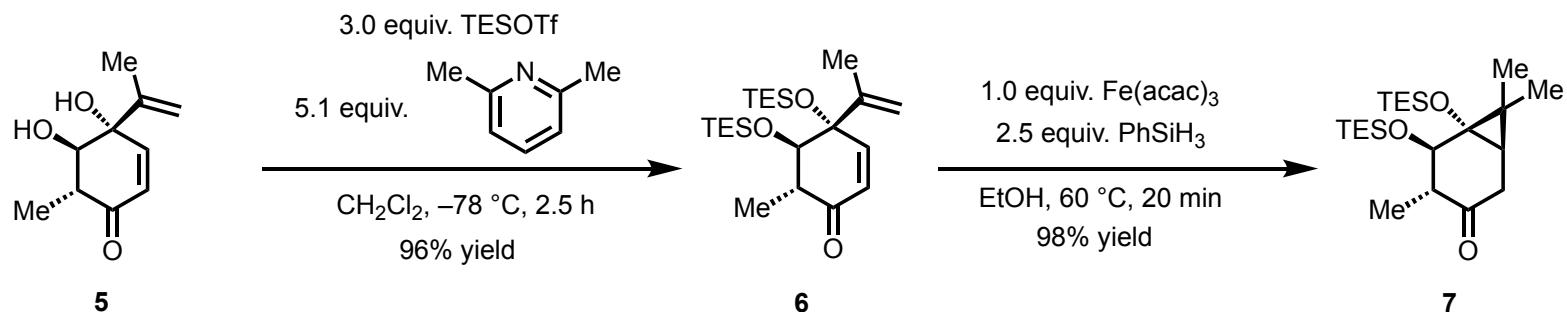
Acetal hydrolysis:

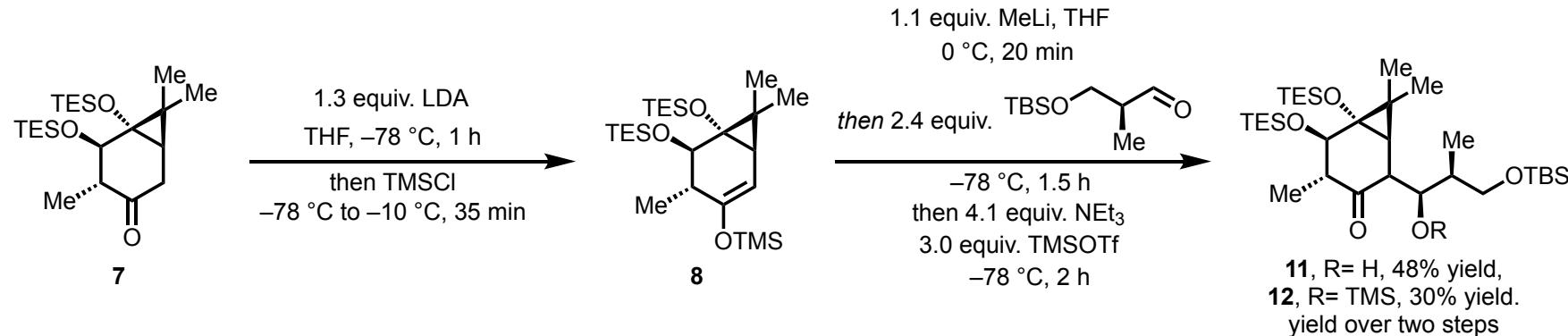




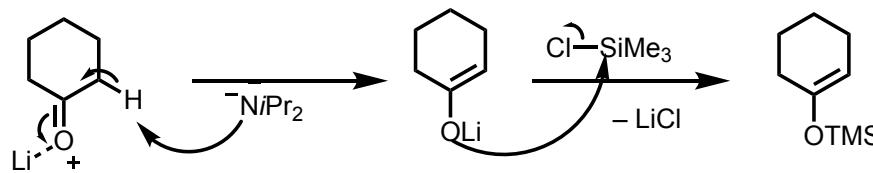
TES protection:



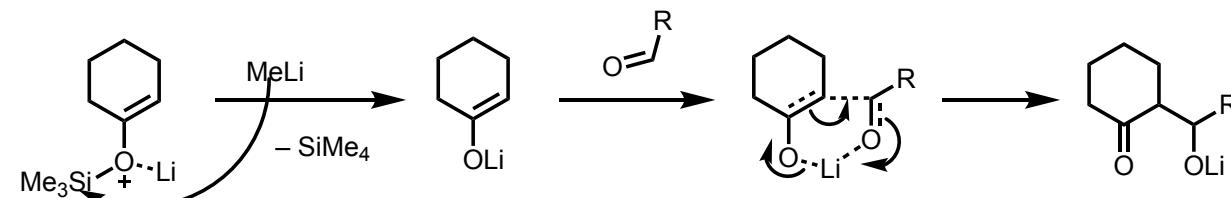


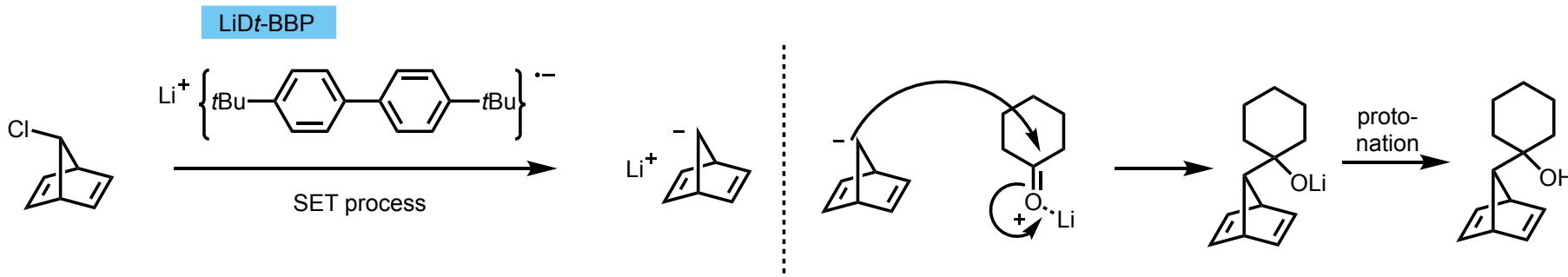
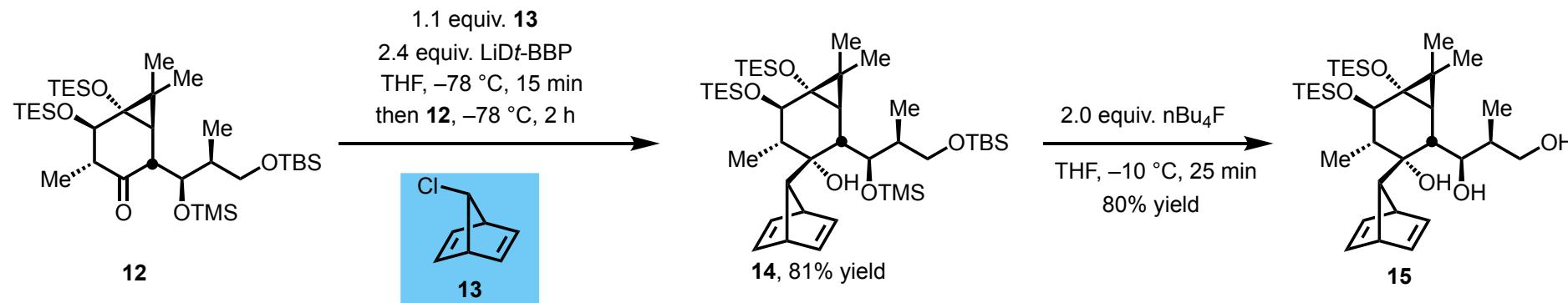


TMS protection:

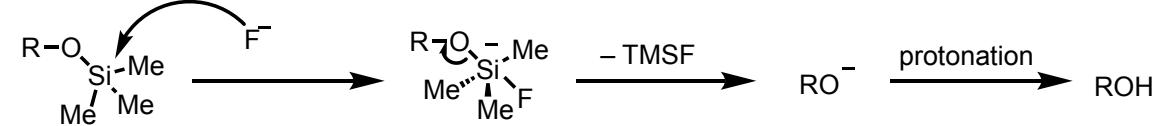


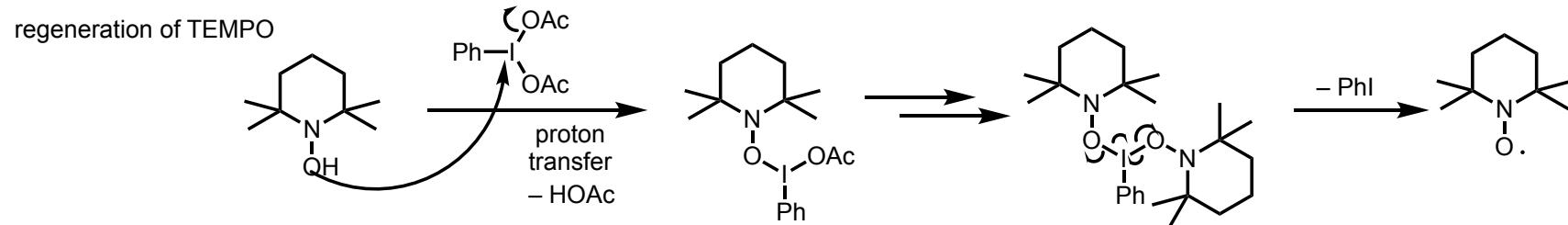
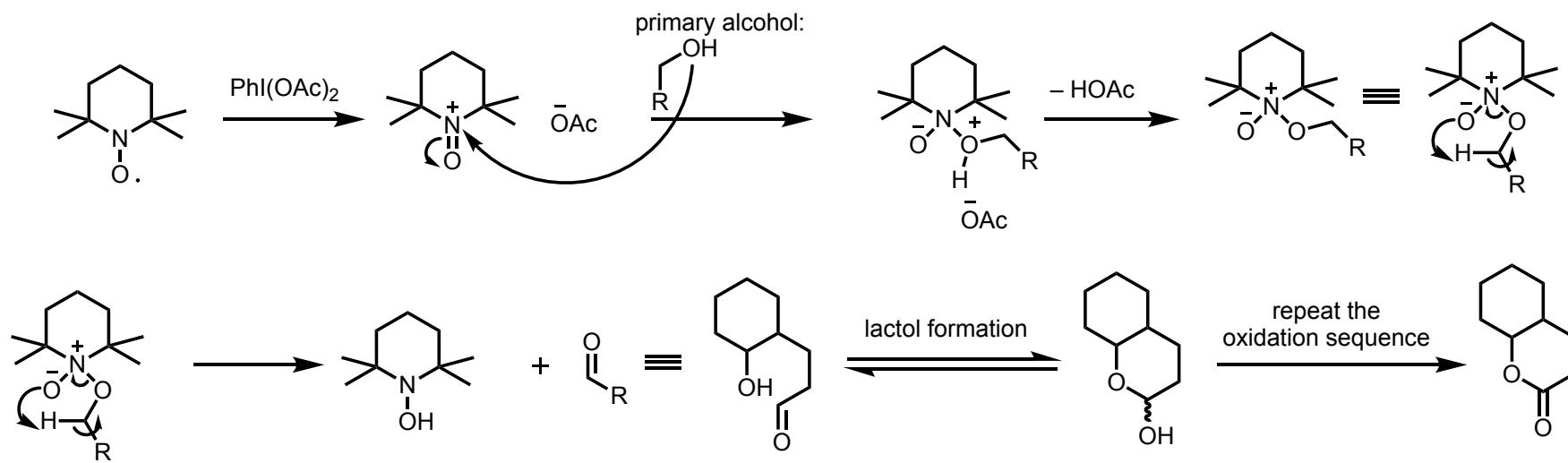
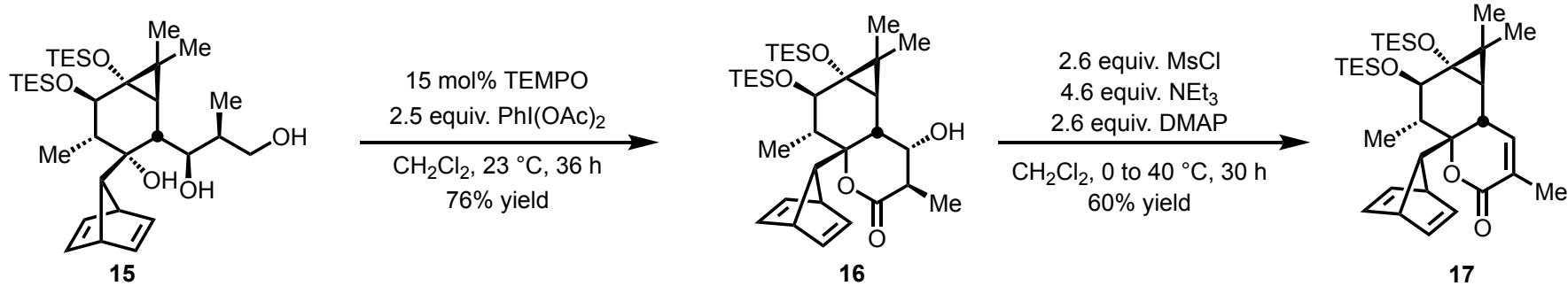
Aldol reaction:

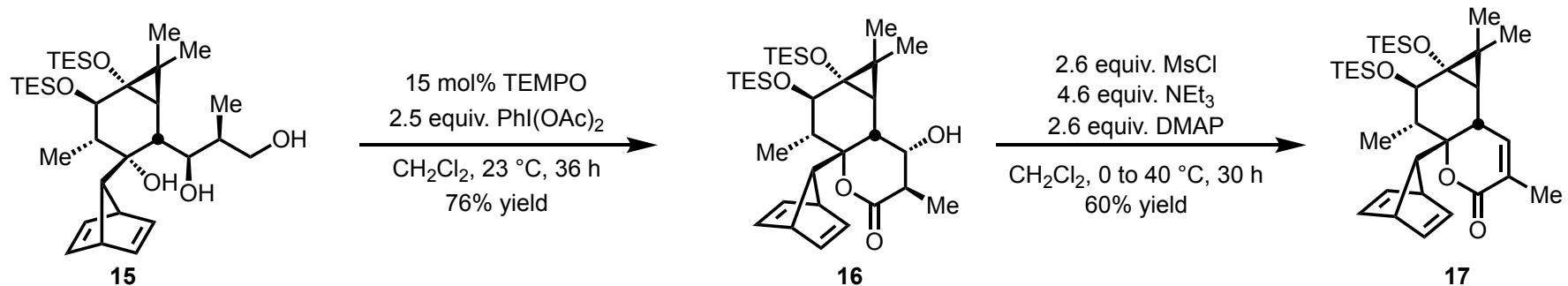




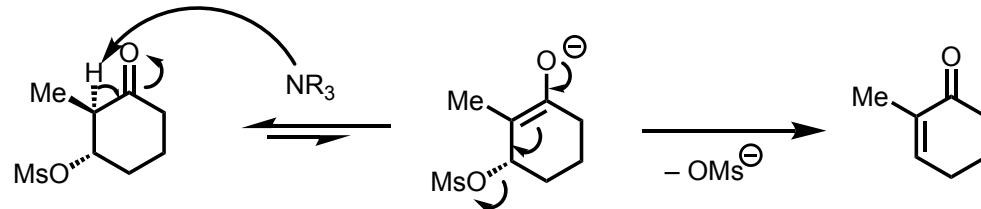
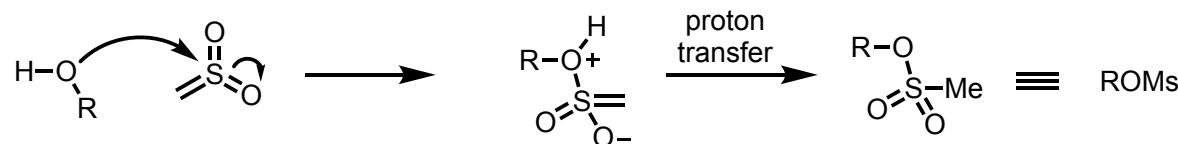
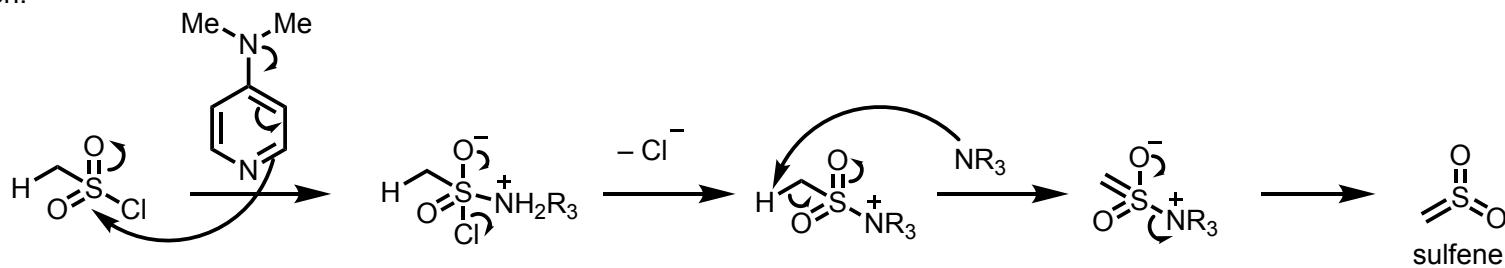
silyl group deprotection:

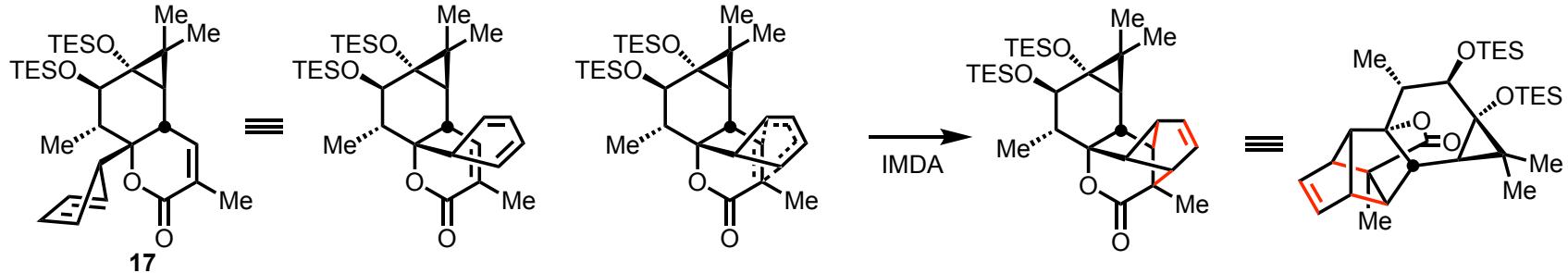
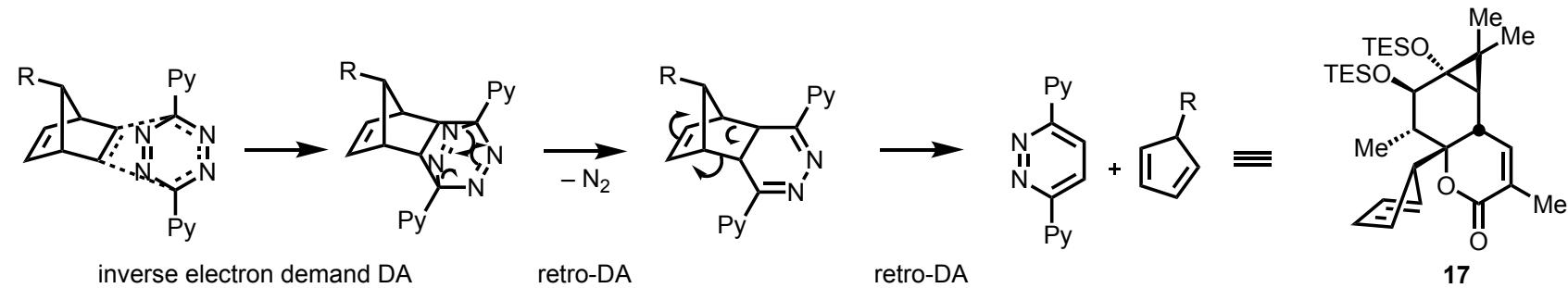
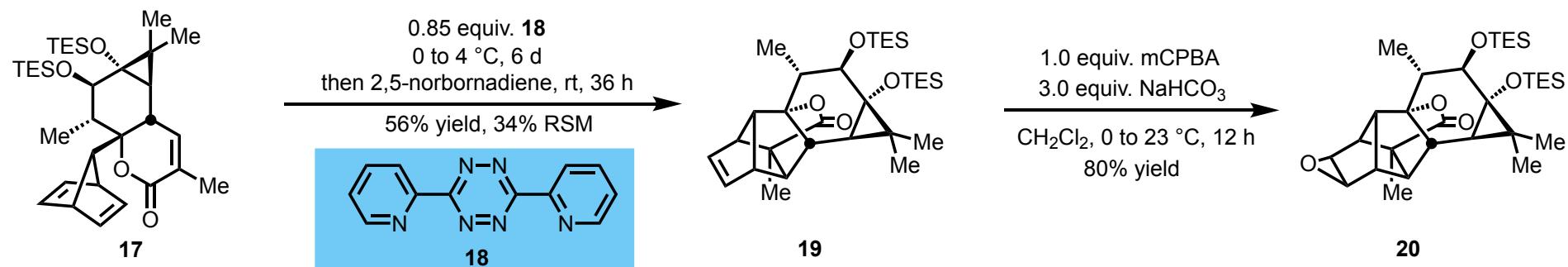




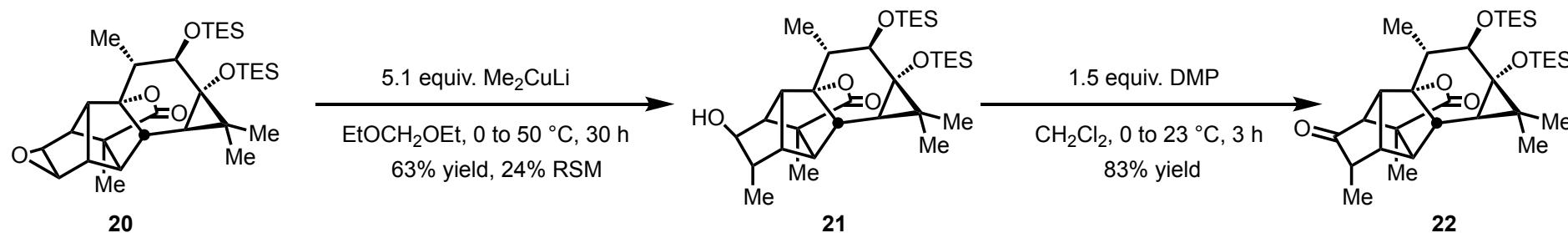


mesylation:

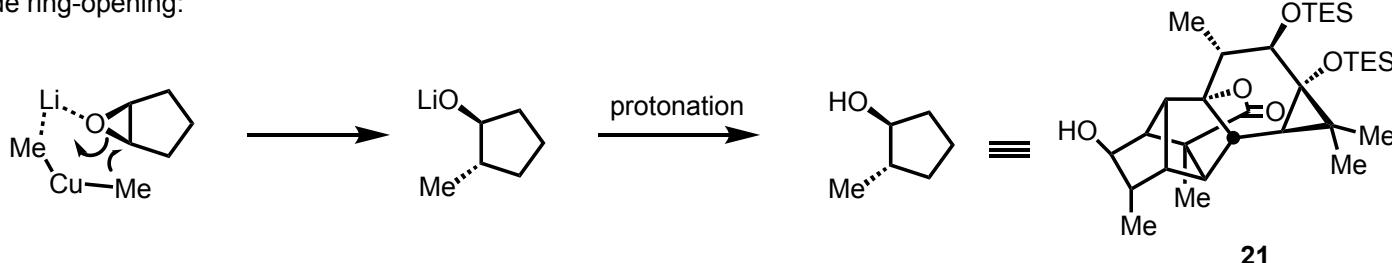




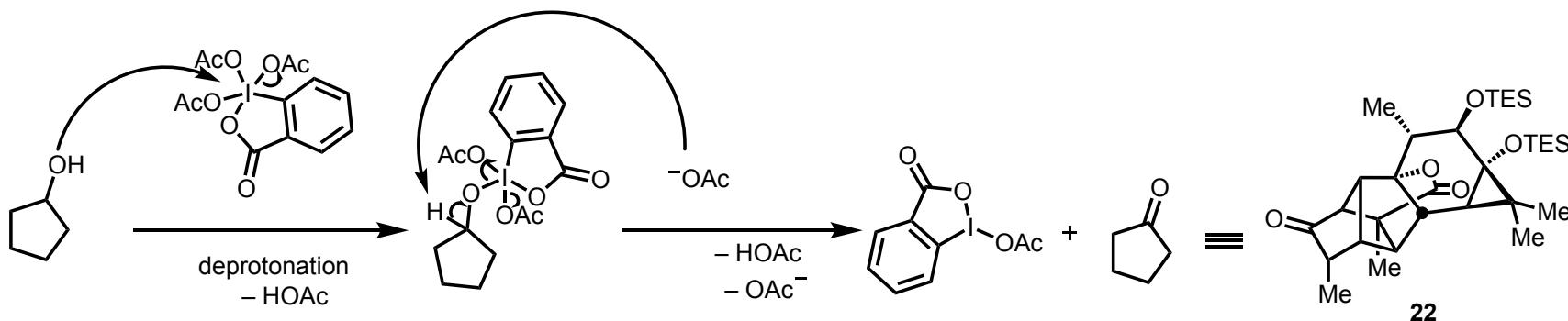
epoxidation see rubottom reaction mechanism

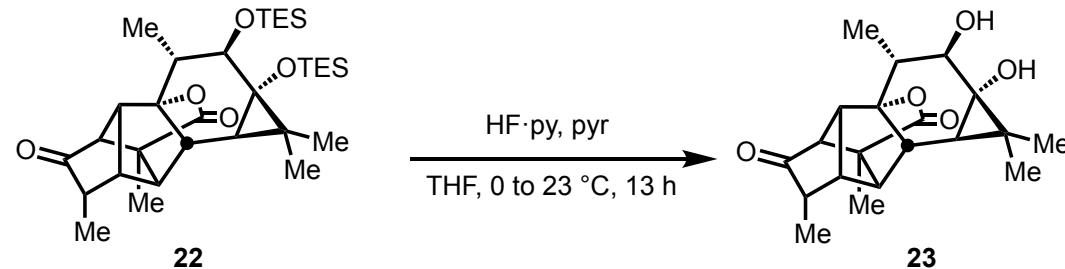


epoxide ring-opening:

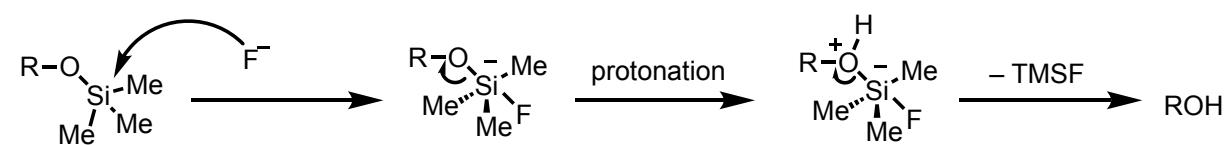


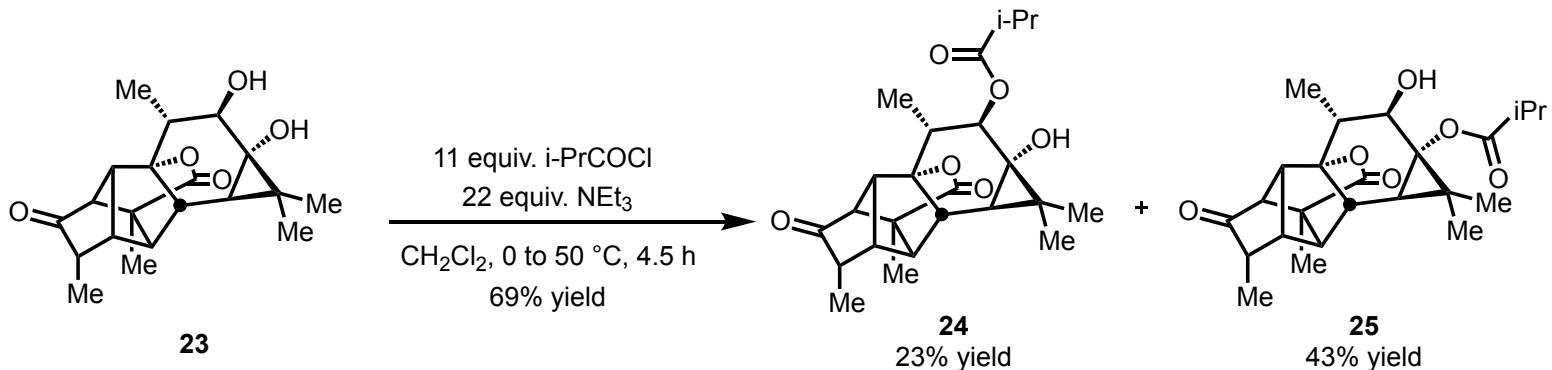
DMP oxidation:



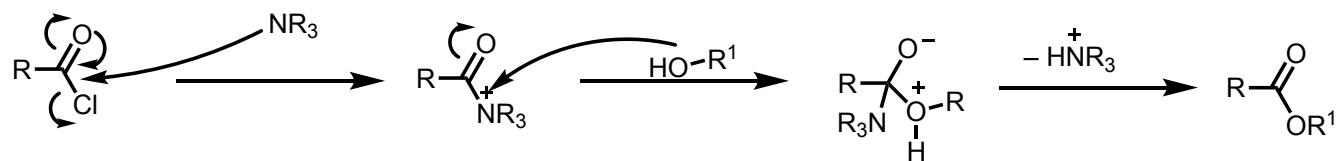


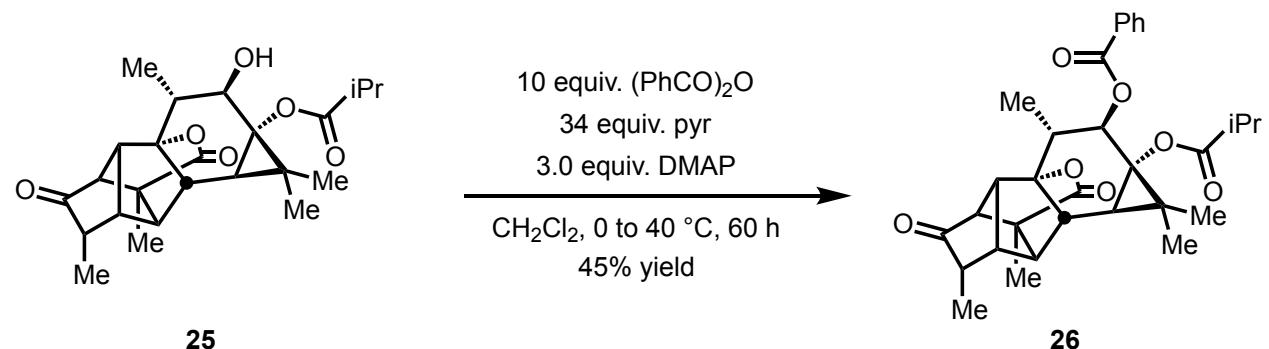
silyl group deprotection: see previous slide





acylation:





acylation:

