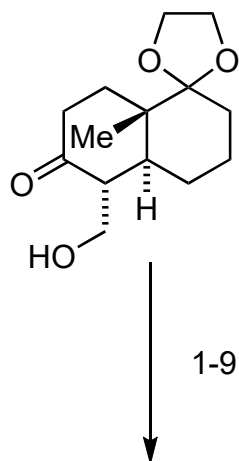
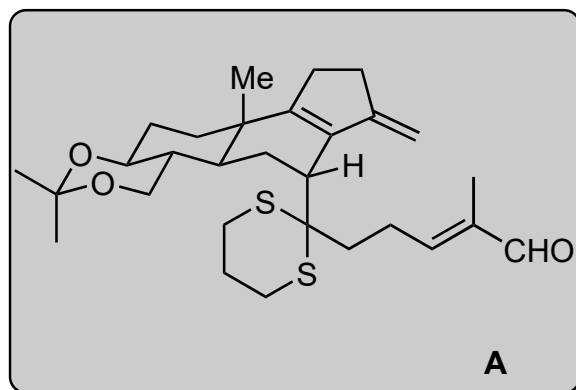


Divergent Total Syntheses of Rearranged Steroids Swinhoeisterols A-C

Huang, G.; Zhang, X.; Gu, Y.; Gui, J.
J. Am. Chem. Soc. **2025**, *147*, 20239-20245.

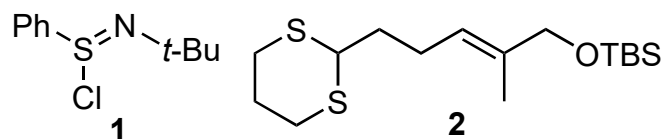


1-9

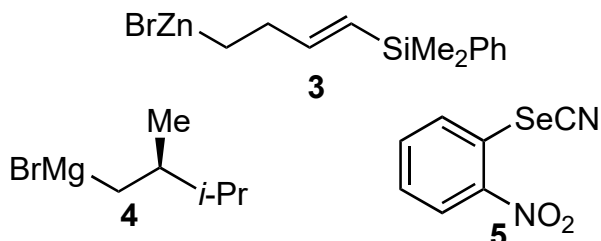


10-19

swinhoeisterol C

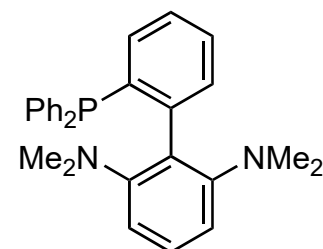


- 1) Li, *t*-BuOH, NH₃ (l)
- 2) *p*-TsOH, acetone
- 3) LiHMDS then **1**
- 4) Et₄NCl₃, NEt₃
- 5) **2**, *n*-BuLi, HMPA then substrate
- 6) KH, Comins' reagent
- 7) **3**, cat. Pd(OAc)₂, cat. PhCPhos, NMI, THF/DMA, 80 °C
- 8) TBAF·3H₂O, HMPA, 80 °C
- 9) TPAP, NMO, 4 Å MS

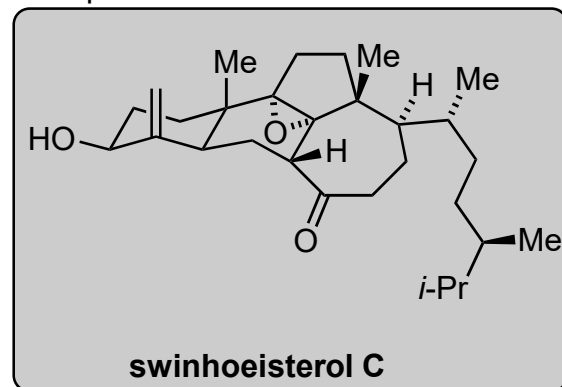


- 10) H₂N-DABCO, *t*-BuOK
- 11) Fe(dpm)₃, Ph(*i*-PrO)SiH₂
- 12) *t*BuOK
- 13) DIBAL-H, -40 °C then NH₄Cl (aq.)
- 14) DIBAL-H
- 15) TsCl, DMAP
- 16) **4**, CuBr·SMe₂
- 17) HgCl₂
- 18) O₃, pyr./DCM
- 19) **5**, *n*-Bu₃P then NaHCO₃, H₂O₂

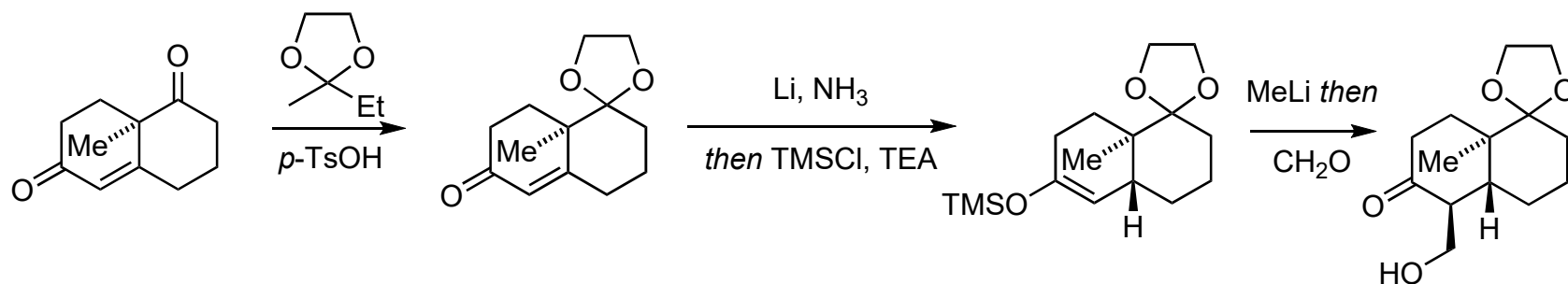
1) From what famous ketone is the starting material made? Propose a reasonable route from this molecule to the starting material. Propose a stereochemical rationale for the major product of step 1. See solution below.
 7) Propose a reasonable mechanism. Structure of PhCPhos:



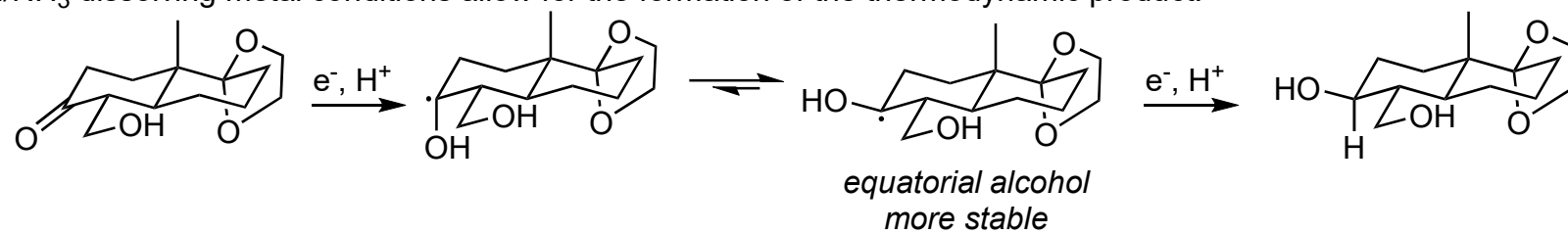
- 11) Who developed this type of reductive olefin coupling? Phil Baran.
- 12) Epimerization
- 17) Swinhoeisterol A was also made in 1 step from this intermediate.
- 19) Swinhoeisterol B was also made in 1 step from swinhoeisterol C.



Solution to step 1: The starting material is made from (+)-Wieland-Mischer ketone (the (+)-enantiomer is known from *ACIE* **2021**, 61, e202112838) and the synthesis is shown below for the (–)-enantiomer (*JACS* **1988**, 110, 8483-8487)



Li/NH₃ dissolving metal conditions allow for the formation of the thermodynamic product:



Solution to step 7: This is a Negishi/Heck cascade. Strategically, the use of the vinyl silane (rather than the terminal alkene) served to limit formation of isomeric cyclopentadienes via Pd-H insertion/deinsertion and subsequent 1,5-H shifts. The stereochemistry of the vinyl silane was confirmed by an NOE observed with the adjacent pseudo-equatorial hydrogen.

