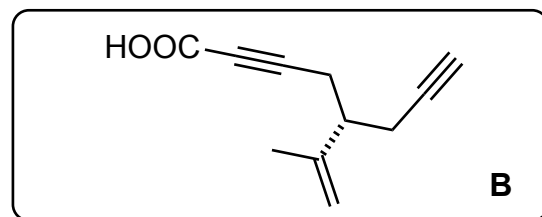
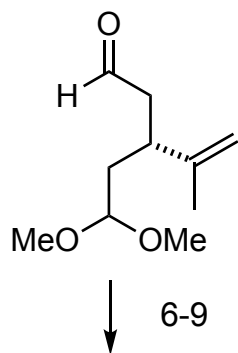
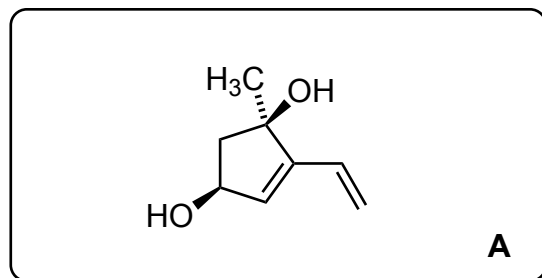
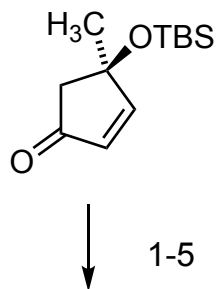


The Total Synthesis of (-)-Scabrolide A

Hafeman, N. J.; Loskot, S. A.; Reimann, C. E.; Pritchett, B. P.; Virgil, S. C.; Stoltz, B. M.
J. Am. Chem. Soc. **2020**, *142*, 8585–8590.



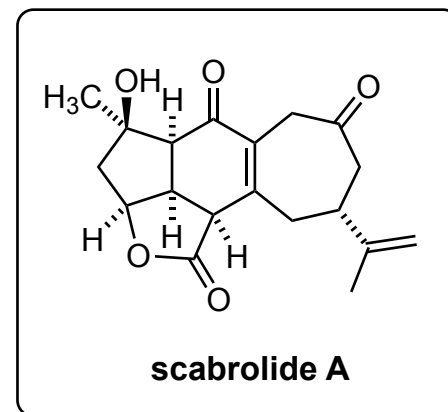
- 1) vinylMgBr, CuBr•DMS, TMSCl, HMPA/THF, $-78\text{ }^{\circ}\text{C}$
- 2) LiTMP, TESCl, THF, $-78\text{ }^{\circ}\text{C}$
- 3) DDQ, HMDS, PhMe, $23\text{ }^{\circ}\text{C}$
- 4) NaBH₄, CeCl₃•7H₂O, MeOH, $-78\text{ }^{\circ}\text{C}$
- 5) TBAF, THF, $60\text{ }^{\circ}\text{C}$

- 6) Br₂CHPPh₃Br, *t*-BuOK, THF, 0 to $23\text{ }^{\circ}\text{C}$
- 7) *n*-BuLi, THF, $-78\text{ }^{\circ}\text{C}$ then TMSCl then HCl, H₂O/THF/dioxane, $23\text{ }^{\circ}\text{C}$
- 8) CBr₄, PPh₃, CH₂Cl₂, $0\text{ }^{\circ}\text{C}$
- 9) *n*-BuLi, THF, $-78\text{ }^{\circ}\text{C}$ then CO₂, $-78\text{ }^{\circ}\text{C}$ to $23\text{ }^{\circ}\text{C}$ then TBAF, $23\text{ }^{\circ}\text{C}$

- 1) How would you prepare the starting material in two steps?
from (*R*)-linalool (see below)
see: *Science* **2016**, *352*, 1078.

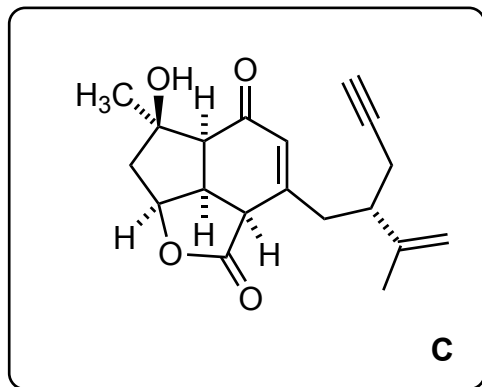
- 4) Name reaction
Lucho reduction

- 6) Name reaction of sequence 6-7
Corey-Fuchs homologation

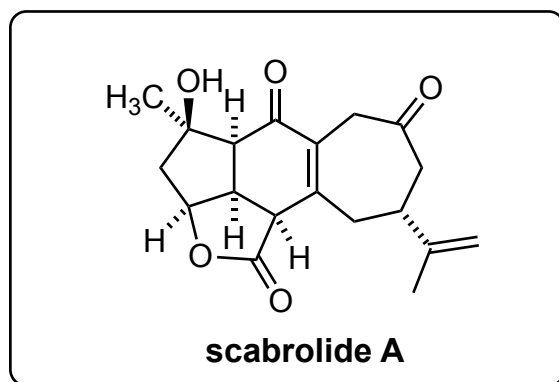


A + B

10-14



15-21



- 10) DIC, DMAP, CH₂Cl₂, 0 °C
- 11) xylenes, 140 °C
- 12) VO(acac)₂, TBHP, CH₂Cl₂/PhMe, 23 °C
- 13) Cp₂TiCl₂, Mn, collidine•HCl, THF, 23 °C
- 14) IBX, MeCN, 50 °C

- 15) *m*-CPBA, CH₂Cl₂, 0 to 23 °C
- 16) Ph(CH₃)₂SiH, [RuCp*(MeCN)₃]PF₆, CH₂Cl₂, 0 °C
- 17) *hν* (350nm), PhH, 23 °C
- 18) Cp₂TiCl₂, Mn, collidine•HCl, THF, 23 °C
- 19) Hg(OAc)₂, AcOOH/AcOH, 23 °C
- 20) *o*-NO₂PhSeCN, *n*-Bu₃P, THF, 23 °C then H₂O₂, 0 to 23 °C
- 21) CuI, NIS, PhMe, 90 °C

11) Name reaction
Diels-Alder cycloaddition

14) *hint: accompanied olefin migration*

16) *hint: α-selective*

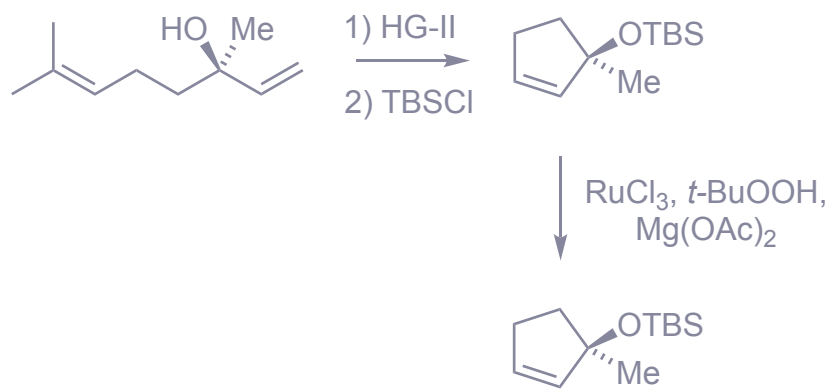
17) *hint: two rings are formed*

19) Name reaction
Hg-mediated Tamao-Fleming ox.

20) Name reaction
Grieco dehydration

21) Propose a mechanism
see below

Synthesis of SM:



Mechanism from step 21:

