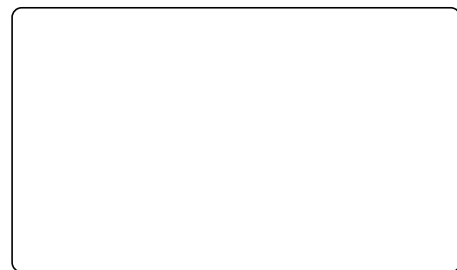
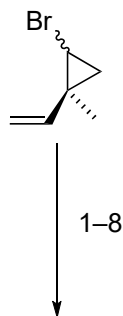


Synthesis of Scopadulic Acid A

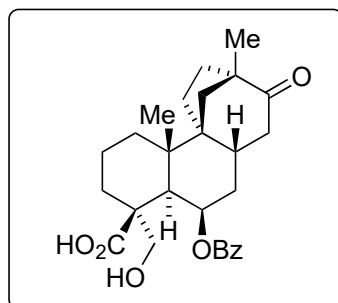
David J. Kucera, Stephen J. O'Connor and Larry E. Overman

J. Org. Chem. **1993**, 58, 5304–5306.



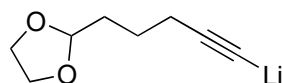
A

9–24



Scopadulic Acid A

- 1) *t*-BuLi, $-78\text{ }^{\circ}\text{C}$ then TBSO(CH₂)₃CHO
- 2) (COCl)₂, DMSO, NEt₃
- 3) TMSOTf, NEt₃
- 4) PhH, $110\text{ }^{\circ}\text{C}$ then, PPTS, *i*-PrOH/H₂O, $23\text{ }^{\circ}\text{C}$
- 5) Ph₃PMeBr, base
- 6) (COCl)₂, DMSO, NEt₃
- 7) **1**, $-78\text{ }^{\circ}\text{C}$ to $0\text{ }^{\circ}\text{C}$
- 8) RedAl, $23\text{ }^{\circ}\text{C}$ then NIS, $-78\text{ }^{\circ}\text{C}$ to $23\text{ }^{\circ}\text{C}$ then TBDMSCl, ImH, DMF



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- 9) Pd(OAc)₂, PPh₃, Ag₂CO₃, $90\text{ }^{\circ}\text{C}$ then TBAF
- 10) TPAP, NMO
- 11) Me₂Zn, LiBr, Ni(acac)₂
- 12) (CH₂OH)₂, Amberlyst 15
- 13) *m*-CPBA, NaHCO₃ then LiAlH₄
- 14) 20% aq. HCl, MeOH, $65\text{ }^{\circ}\text{C}$
- 15) MOMCl, (*i*-Pr)₂NEt
- 16) Et₂AlCN, TMSCl, NEt₃ then HCl
- 17) LiAlH₄ then TMSCl, DMAP, py
- 18) LDA, BnOCH₂Br, $-78\text{ }^{\circ}\text{C}$ to $0\text{ }^{\circ}\text{C}$
- 19) KOH, K₂CO₃, $140\text{ }^{\circ}\text{C}$ then CH₂N₂
- 20) BzCl, DMAP, py, $100\text{ }^{\circ}\text{C}$
- 21) HCl, MeOH, $70\text{ }^{\circ}\text{C}$
- 22) PCC, CH₂Cl₂, $23\text{ }^{\circ}\text{C}$
- 23) *n*-PrSLi, DMPU, $23\text{ }^{\circ}\text{C}$
- 24) Pd/C, H₂, MeOH

4) What is the name of the reaction? Only one of the TMS enol ethers reacts as desired; the other is recovered as the hydrolyzed product. The desired product has (R) stereochemistry.

5) Name two alternative methods to perform this reaction.

7) The product is a mixture of diastereoisomers. How can the undesired isomer be converted into the desired one? What is the approximate pK_a of the shown anion, and why is it less basic than *n*-BuLi?

8) Hint: A hydroxy group is required in this reaction — it results in formation of the Z-isomer.

9) Draw the full mechanism.

14) Hint: This step involves more than just deprotection.

16) What is the name of the reagent used here?

17) The nitrile group remains after this step.

19) How can CH₂N₂ be generated in situ?

22) What is the name of the reagent?