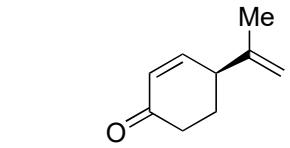
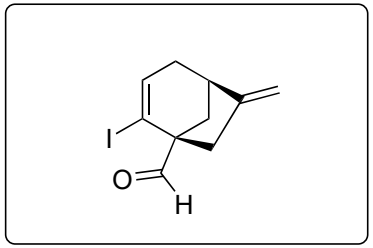
Total Synthesis of Isorosthin L and Isodenolin I

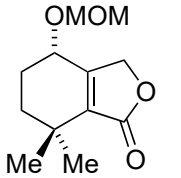
J. Ao, C. Sun, B. Chen, N. Yu, G. Liang, Angewandte Chemie (International ed. in English) **2022**, 61, e202114489.



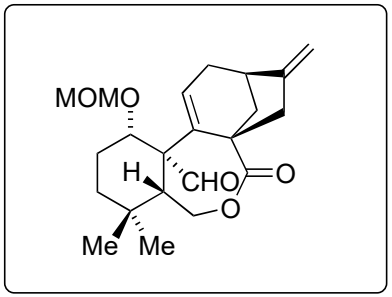
1 – 9



A



10 – 16



B

1. LiHMDS, Mander´s reagent, THF, –78 °C
2. Raney Nickel, THF, 0 °C
3. $NaBH_4$, EtOH, 0 °C
4. SO_2Cl_2, Na_2CO_3, CH_2Cl_2, 0 °C
5. IBX, EtOAc, 80 °C
6. K_2CO_3, NaI, acetone, 60 °C
7. KHMDS, DIBAL–H, Et_2O, –78 °C
8. $TrisNHNH_2$, THF, 0 to 25 °C
   then *n*-BuLi, I_2, Et_2O, –78 to –40 °C
9. IBX, DMSO, 25 °C

10. **A**, LDA, THF, –78 to –20 °C
11. AIBN, Bu_3SnH, toluene, 85 °C
    then NaOMe, MeOH, 0 to 25 °C
12. $LiAlH_4$, THF, 65 °C
13. TBSCl, imH, CH_2Cl_2, 0 to 25 °C
14. IBX, DMSO, THF, 25 °C
15. TBAF, THF, 0 °C to 25 °C
16. $Pb(OAc)_4$, CH_2Cl_2/benzene, 0 to 25 °C

Step 3: Explain why this step could be necessary.

Beta-ketoester is incompatible with the subsequent chlorination

Step 8: Reaction name?
Name of the reaction using NaH instead of *n*-BuLi and with which products can you eventually end up with?

Shapiro Reaction

Bamford-Stevens Reaction

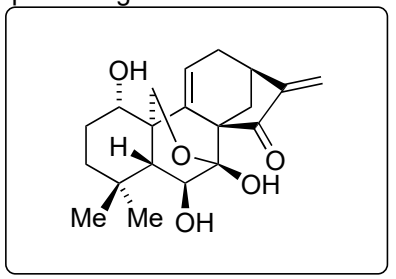
Products:
In protic solvent: Alkene
In aprotic solvent: Carbene

Step 10: Only 1 diastereomer is formed, Discuss the stereoselectivity of the two generated stereocenters

Alcohol: Felkhin Anh-Model
Tertiary Carbon: Control by OMOM-group

Hint step 11: Subsequent Epimerization

Hint step 14: Single oxidation

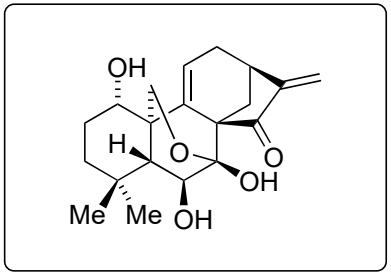


isorosthin L

B

17 – 23

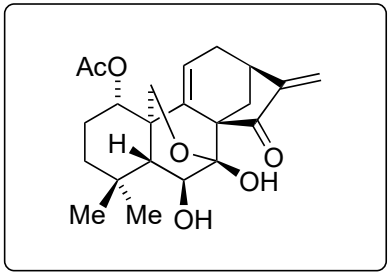
17. $LiBH_4$, THF, 0 to 25 °C
18. DMP, CH_2Cl_2, 0 to 25 °C
19. SmI_2, THF, 25 °C
20. MOMCl, DIPEA, NaI, DCE, 25 to 40 °C
21. *t*-BuOOH, SeO_2, CH_2Cl_2, 25 °C
22. DMP, NaHCO3, CH_2Cl_2, 0 to 25 °C
23. TFA, 25 °C



isorosthin L

24

24. Ac_2O, NEt_3, DMAP, CH_2Cl_2, 0 to 25 °C



isoadenolin I