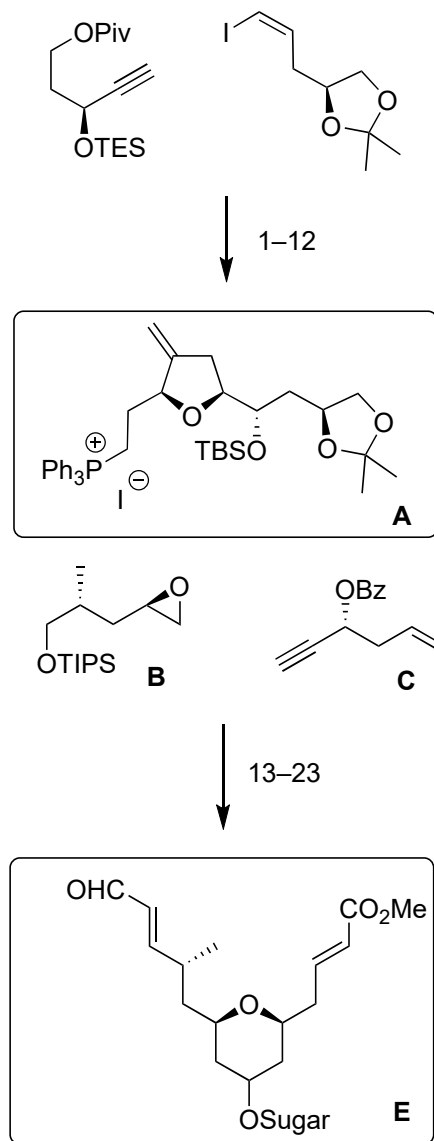


Enantioselective Total Synthesis of Mandelalide A and Isomandelalide A: Discovery of a Cytotoxic Ring-Expanded Isomer

N. Veerasamy, A. Ghosh, J. Li, K. Watanabe, J. D. Serrill, J. E. Ishmael, K. L. McPhail, R. G. Carter

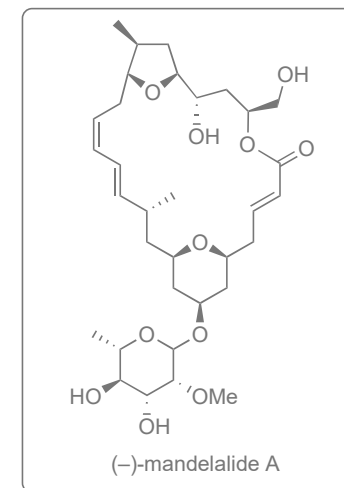
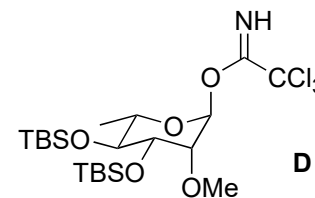
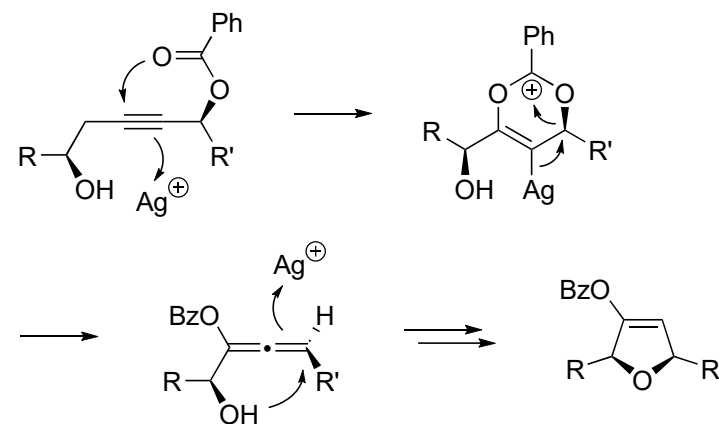
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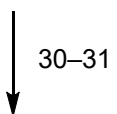
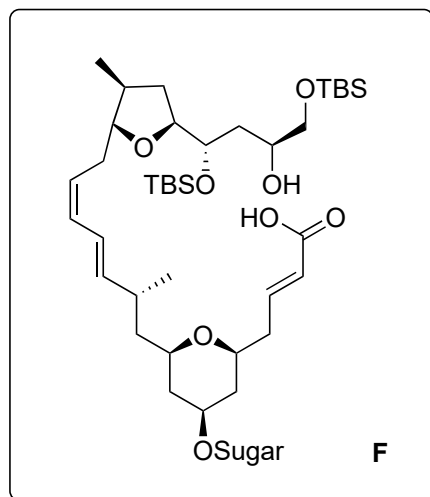
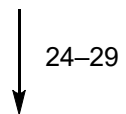
- 1) Pd(PPh₃)₄, CuI, *i*Pr₂NH
- 2) (DHQD)₂PHAL, K₂OsO₄•2H₂O
- 3) BzCl, Et₃N
- 4) HF•Py
- 5) AgBF₄, PhMe, reflux; then MeLi•LiBr, Et₂O
- 6) TBSOTf, 2,6-Lutidine
- 7) Cp₂TiMe₂, PhMe, 90 °C
- 8) Rh/Al₂O₃, H₂
- 9) DIBAL-H
- 10) Ms₂O, Et₃N
- 11) NaI, acetone
- 12) PPh₃, PhMe, heat

- 13) **C**, *n*BuLi, then **B**, BF₃•OEt₂
- 14) AgBF₄, PhMe, reflux
- 15) NaOMe, MeOH
- 16) TBAF
- 17) DMP, NaHCO₃
- 18) Ph₃P=CHCO₂Et
- 19) NaBH₄
- 20) **D**, TIPSOTf, MS 4Å
- 21) DIBAL-H
- 22) DMP, NaHCO₃
- 23) Grubbs-II, H₂C=CHCO₂Me

Mechanism of Step 5?



A



(-)-mandelalide **A**

- 24) NaHMDS; then **E**
25) TFA/DCM/H₂O
26) TBSOTf, 2,6-lutidine
27) DIBAL-H
28) MnO₂
29) NaClO₂

- 30) 2,4,6-trichlorobenzoyl chloride
DMAP, Et₃N
31) TAS-F

Structure of TAS-F?

