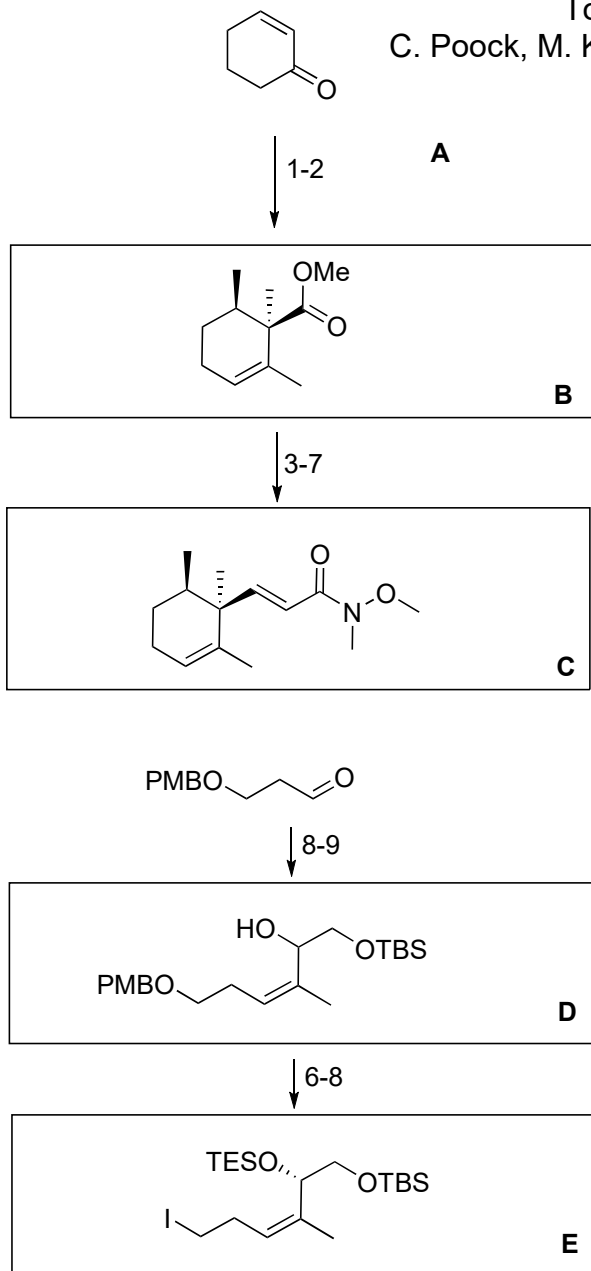


Synthesis Challenge 91

AG Wegner

Total Synthesis and Structure Revision of Halioxepine,
C. Poock, M. Kalesse, *Chem. Eur. J.*, **2020**, ASAP, doi: 10.1002/chem.202004847

10.12.2020

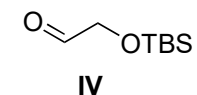
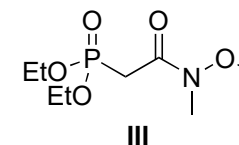
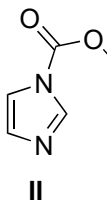
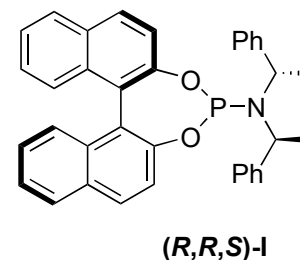


- 1) (I) Me₂Zn, Cu(OTf)₂, (**R,S,S**)-**I**
- (II) MeLi
- (III) **II**
- toluene, -78°C to 0°C
- 2) MeI, NaOtBu, MeOH, 0°C to rt

- 3) MeMgBr, THF, 0°C
- 4) pTsOH·H₂O, toluene, reflux
- 5) LiAlH₄, Et₂O, 0°C to rt
- 6) IBX, DMSO
- 7) nBuLi, **III**, THF, 0 to 60°C

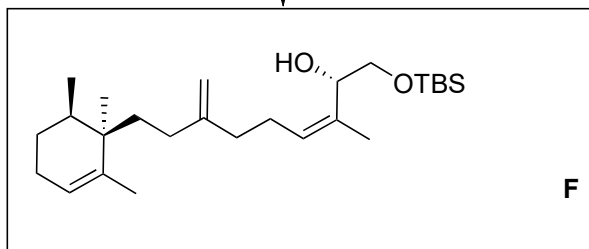
- 8) (I) EtPPh₃I, nBuLi
- (II) I₂
- (III) NaHMDS
- THF, -78°C to rt
- 9) tBuLi, **IV**, Et₂O, -78°C,

- 10) IBX, DMSO, rt
- 11) (+)-DIPCl, Et₂O, -30 to 18°C
- 12) TESOTf, 2,6-lutidine, CH₂Cl₂, -78°C
- 13) DDQ, CH₂Cl₂/pH₇-buffer, 0°C to rt
- 14) PPh₃, imidazole, I₂, CH₂Cl₂, 0°C

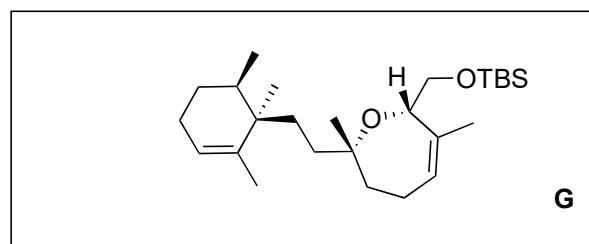


C + E

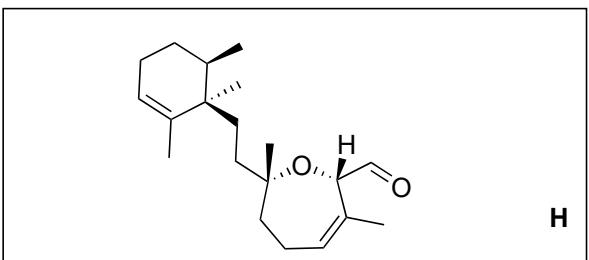
15-17



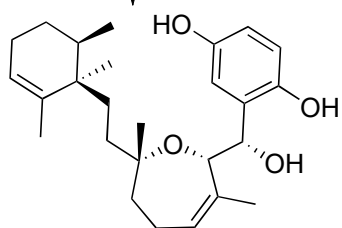
18-19



20-21



22-23



15) tBuLi, Et₂O, -78°C
16) Co(acac)₂, DiBAIH, THF, -78 to 0°C
17) PPTS, MeOH/THF, 0°C

18) (2,4,6-collidine)₂PF₆, CH₂Cl₂, 0°C
19) LiEt₃BH, THF, rt to 65°C

20) TBAF, THF, 0°C
21) IBX, DMSO, rt

22) (I) **V**, EtMgBr, Et₂O, 0°C to rt
(II) CH₂Cl₂,), 0 to 39°C
23) TBAF

Step 19) *dr*=1.2:1

Separation

