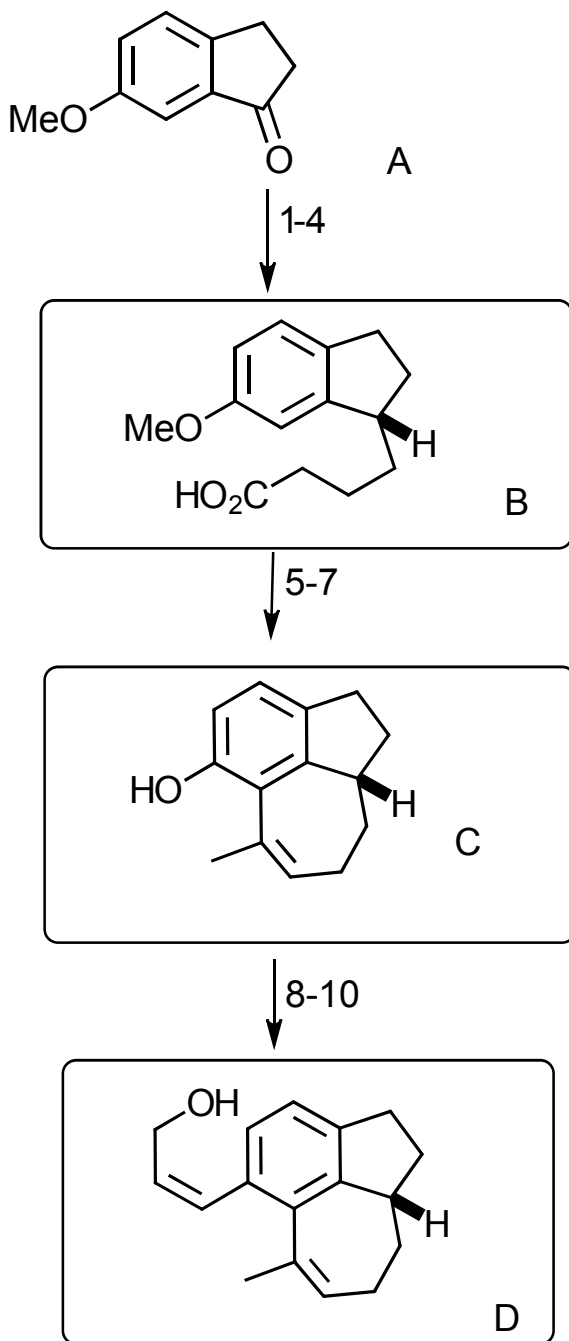


Synthesis Challenge # 45

Total Synthesis of (-)-Daphenylline

R. Yamada, Y. Adachi, S. Yokoshima, T. Fukuyama, *Angew. Chem. Int. Ed.* **2016**, ASAP, DOI: 10.1002/anie.201601958

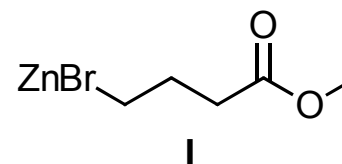
14.04.2016



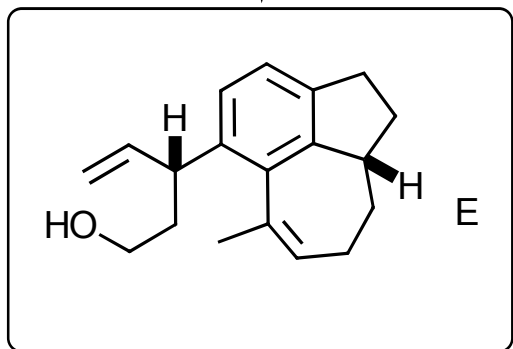
- 1) NaBH₄, CH₂Cl₂, MeOH
- 2) PCl₃, pyridine, CH₂Cl₂, -10°C
- 3) I, NiBr₂·diglyme, (S)-*i*Pr-Pybox, DMA
- 4) aq. NaOH, EtOH

- 5) TFAA, TFA, CH₂Cl₂, RT;
aq. Na₂CO₃, MeOH, RT
- 6) BBr₃, CH₂Cl₂, 0°C
- 7) MeMgBr, THF, 0°C;
MgBr₂, TsOH·H₂O, THF, 50°C

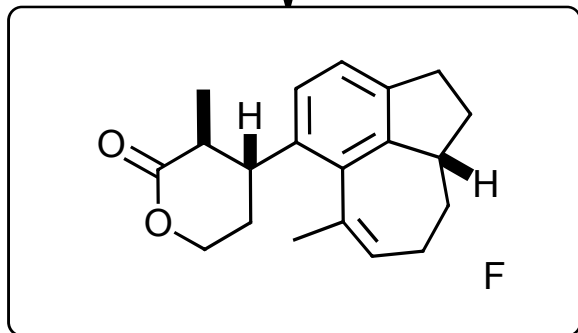
- 8) Tf₂O, pyridine, CH₂Cl₂, 0°C
- 9) propargyl alcohol, PdCl₂(dppf)·CH₂Cl₂,
pyrrolidine, TBAI, DMF, 60°C
- 10) H₂, Lindlar catalyst, quinoline,
EtOAc, RT



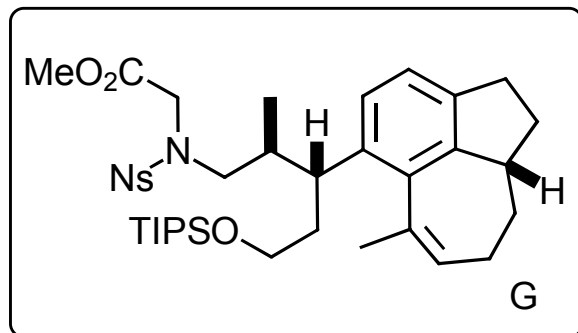
11-12



13-17



18-20

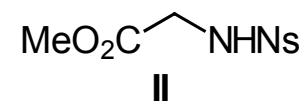


11) *n*-butyl vinyl ether, Hg(OAc)₂, 60°C
12) *i*Bu₃Al, hexane, 10°C

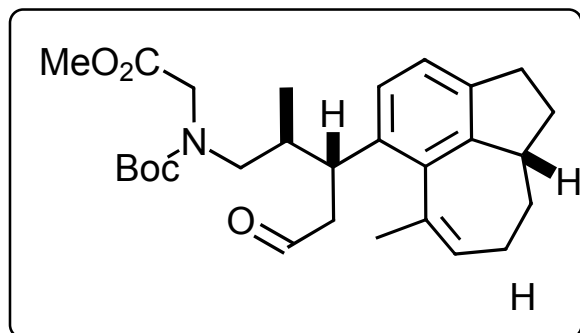
13) TBSCl, imidazole, DMF, RT
14) 9-BBN, THF, 0°C; aq. H₂O₂,
aq. NaOH, 0°C to RT
15) AZADOL, PhI(OAc)₂, phosphate
buffer (pH 6.8), MeCN, RT
16) TFA, CH₂Cl₂, RT
17) LDA, THF, -78°C; MeI, HMPA

AZADOL = 2-hydroxy-2-azaadamantane

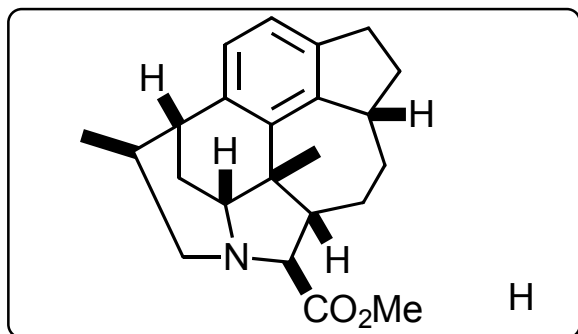
18) LiAlH₄, THF, 0°C
19) TIPSCl, imidazole, DMF, RT
20) II, DEAD, Ph₃P, toluene, 70°C



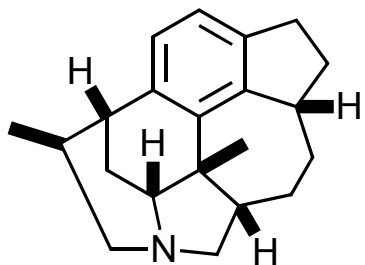
21-23



24



25-27



21) PhSH, K₂CO₃, DMF, 50°C
22) TBAF, THF, RT; Boc₂O, aq.
NaHCO₃, CH₂Cl₂, RT
23) Dess-Martin periodinane, CH₂Cl₂

24) NaOAc, BHT, MS4Å, toluene,
microwave, 200°C

BHT = 3,5-di-*tert*-butyl-4-hydroxytoluene

25) NH₃, MeOH, 70°C
26) Burgess reagent, CH₂Cl₂, RT
27) NaBH₄, MeOH, reflux