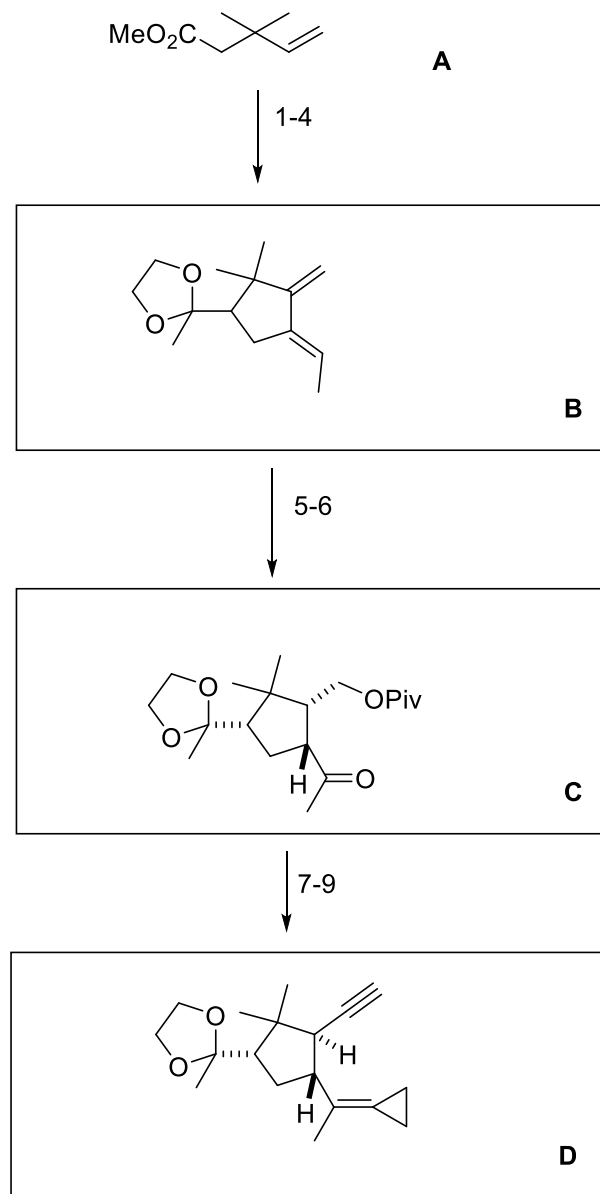


Synthesis Challenge 88

Total Synthesis and Structural Revision of a Harziane Diterpenoid,
M. Hçnig, E. M. Carreira, *Angew. Chem. Int. Ed.* **2020**, 59, 1192 –1196.

16.07.2020



- 1) LDA, 1-bromobut-2-yne THF, $-40\text{ }^{\circ}\text{C}$
- 2) $\text{Pd}(\text{OAc})_2$ (20 mol %), BBEDA (20 mol %), PhH, $65\text{ }^{\circ}\text{C}$
- 3) $\text{MeNHOMe} \cdot \text{HCl}$, MeMgBr , THF
- 4) Ethylene glycol, $(\text{EtO})_3\text{CH}$, PPTS (10 mol %)

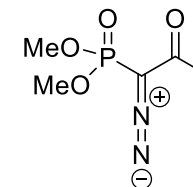
BBEDA=bis-benzylidene ethylenediamine

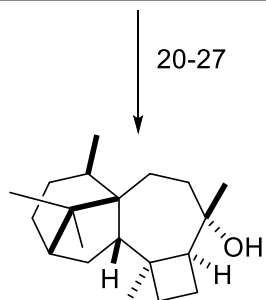
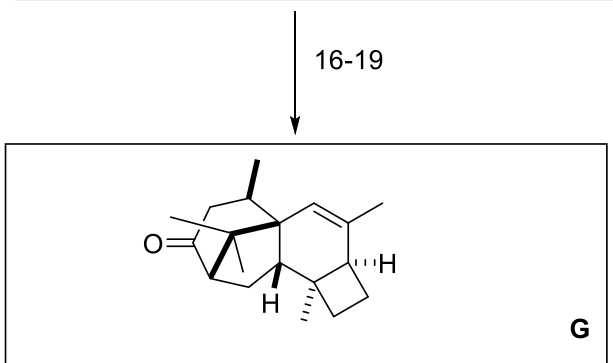
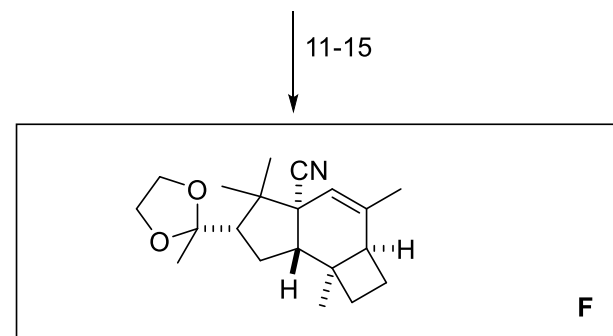
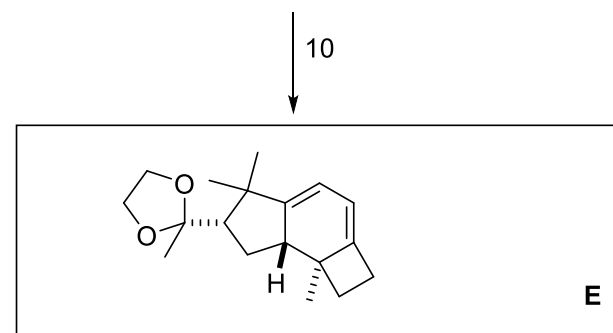
- 5) $\text{BH}_3 \cdot \text{THF}$, THF, $0\text{ }^{\circ}\text{C}$, then NaOH , H_2O_2 ,
- 6) Piv-Cl , pyridine, CH_2Cl_2 , $-78\text{ }^{\circ}\text{C}$, then MeOH , DMP , NaHCO_3 , CH_2Cl_2

- 7) $\text{Cp}_2\text{Ti}(\text{C}_3\text{H}_5)_2$, NaHCO_3 , PhMe, $55\text{ }^{\circ}\text{C}$, then LiAlH_4 , PhMe, $0\text{ }^{\circ}\text{C}$
- 8) NMO , TPAP (5 mol %), 4 Å MS, CH_2Cl_2
- 9) K_2CO_3 , MeOH , then Ohira-Bestmann reagent

Step 7) Petasis reagent, similar to Tebbe

Step 9)





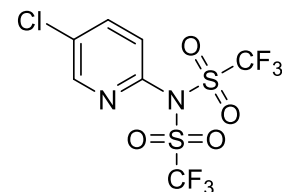
10) $\text{Ph}_3\text{PAuNTf}_2$ (3 mol %), CH_2Cl_2 , $-10\text{ }^\circ\text{C}$ to $0\text{ }^\circ\text{C}$

11) *thexylborane*, THF, $-10\text{ }^\circ\text{C}$,
then NaOH, H_2O_2
12) TPAP (5 mol %), NMO, 4 Å MS, CH_2Cl_2
13) Et_2AlCN , PhMe, $0\text{ }^\circ\text{C}$ to $10\text{ }^\circ\text{C}$
14) NaHMDS, THF, $-78\text{ }^\circ\text{C}$
then Comins' reagent, THF, $-78\text{ }^\circ\text{C}$ to $0\text{ }^\circ\text{C}$
15) $\text{Pd}(\text{PPh}_3)_4$ (5 mol %), ZnMe_2 , THF, $0\text{ }^\circ\text{C}$

16) PPTS, H_2O -acetone (1:9), $40\text{ }^\circ\text{C}$
17) TBSOTf, 2,6-lutidine, CH_2Cl_2 , $0\text{ }^\circ\text{C}$
18) DIBAL-H, CH_2Cl_2 , $0\text{ }^\circ\text{C}$ to r.t.,
then aq. NaOH, silica gel, $0\text{ }^\circ\text{C}$ to r.t.,
19) CuI, MeLi, $\text{BF}_3 \cdot \text{OEt}_2$, Et_2O , $-78\text{ }^\circ\text{C}$ to $10\text{ }^\circ\text{C}$

20) $\text{RuCl}_3 \cdot x\text{ H}_2\text{O}$ (20 mol %), NaIO_4 , DCE- H_2O
21) LHMDS, THF, $-78\text{ }^\circ\text{C}$ to $0\text{ }^\circ\text{C}$
22) $\text{Ph}_3\text{PCH}_3\text{Br}$, KO^tBu , THF, $0\text{ }^\circ\text{C}$ to r.t.
24) DIBAL-H, CH_2Cl_2 , $0\text{ }^\circ\text{C}$
25) KHMDS, CS_2 , THF, $-78\text{ }^\circ\text{C}$ to r.t.,
then MeI
26) AIBN (38 mol %), Bu_3SnH , PhH, $80\text{ }^\circ\text{C}$
27) $\text{Co}(\text{acac})_2$ (18 mol %), O_2 (1 atm), PhSiH_3 , THF

Ley-Griffin Oxidation



Step 18) Reduction to aldimine

Step 25/26) Barton–McCombie

