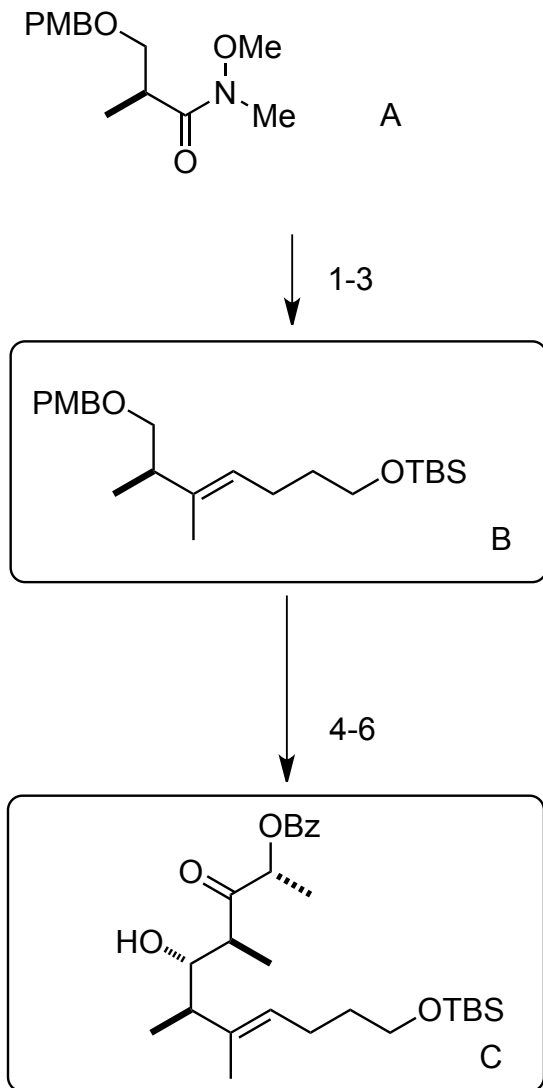


Synthesis Challenge #12 AG Wegner

Total Synthesis of the Antimitotic Marine Macrolide (–)-Leiodermatolide, I. Paterson, K.K.-H. Ng, S. Williams, D. C. Millican, S. M. Dalby, *Angew. Chem. Int. Ed.* **2014**, 53, ASAP, DOI: 10.1002/anie.201310164

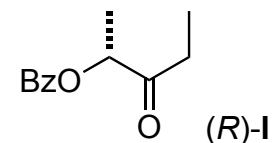
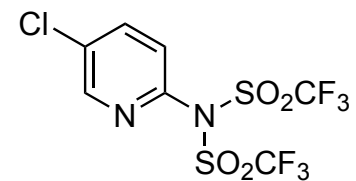
06.02.2014



1) TBSO(CH₂)₄MgBr, THF, –78 °C,
 2) LiHMDS, THF ; Comins reagent, –78 - 20 °C,
 3) (MeBO)₃, [Pd(PPh₃)₄] (10 mol %), K₂CO₃, dioxane, 50°C

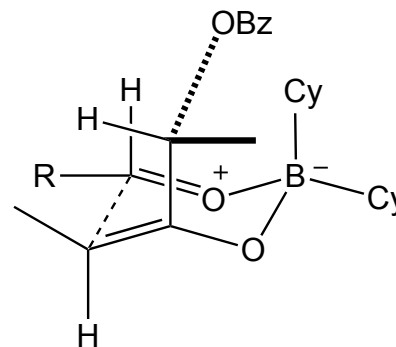
4) DDQ, pH 7 buffer, CH₂Cl₂
 5) DMP, NaHCO₃, CH₂Cl₂
 6) (R)-I, *c*-Hex₂BCl, Et₃N, Et₂O, –78 - 20°C

What is Comin's reagent?

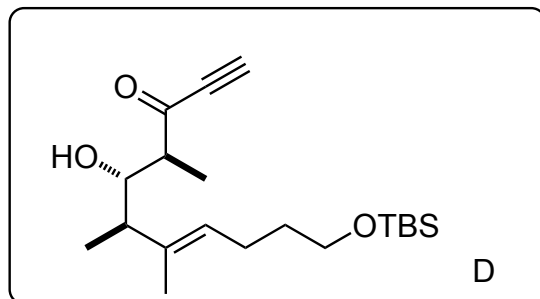


Please, provide a detailed mechanism for step 6).

via Zimmermann-Traxler-TS, anti-selective Aldol addition:

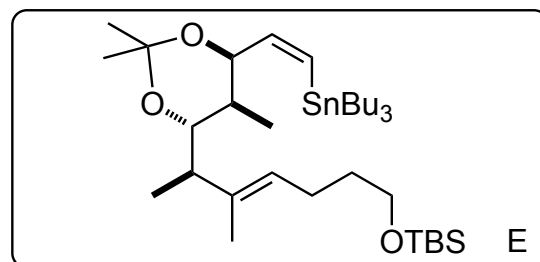


↓
7-10



- 7) TMSCl, imid, CH₂Cl₂
- 8) LiCCTMS, THF, -78 °C
- 9) K₂CO₃, MeOH
- 10) NaIO₄/SiO₂, CH₂Cl₂

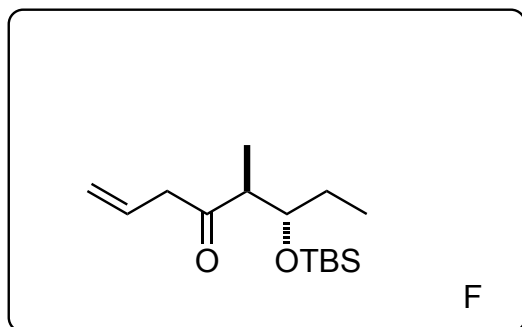
↓
11-14



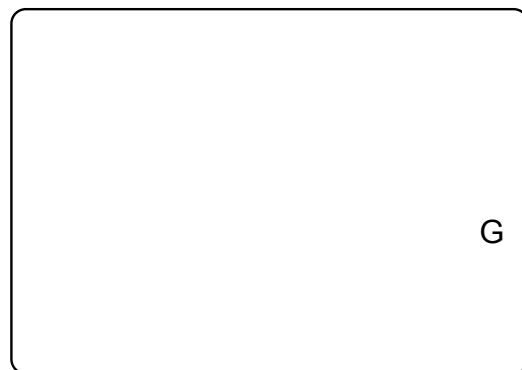
- 11) NaI, AcOH, THF
- 12) NBH(OAc)₃, MeCN, AcOH (3:1), -30°C,
- 13) Me₂C(OMe)₂, PPTS, CH₂Cl₂,
- 14) *t*BuLi, Bu₃SnCl, Et₂O, -78°C

(R)-I

↓ 15-18

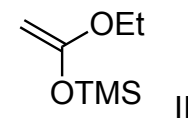


↓ 19-20



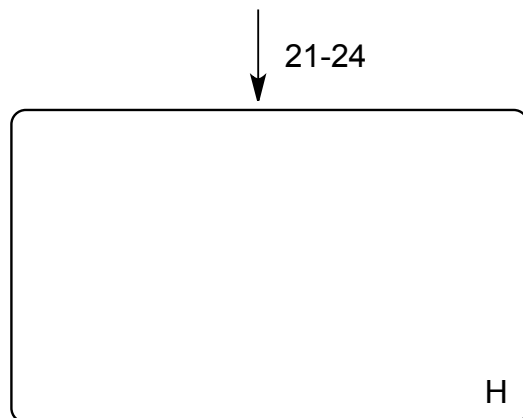
15) *c*-Hex₂BCl, Et₃N, Et₂O; EtCHO, -78 - 20°C,
16) TBSOTf, 2,6-lutidine, CH₂Cl₂, -78°C
17) H₂C=CHCH₂MgBr, THF, -78°C
18) NaIO₄, MeOH, pH 7 buffer

19) II, BF₃·OEt₂, CH₂Cl₂, -78°C
20) 3M HCl, THF, H₂O

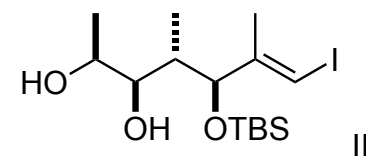


Please, provide a detailed Mechanism for step 19).

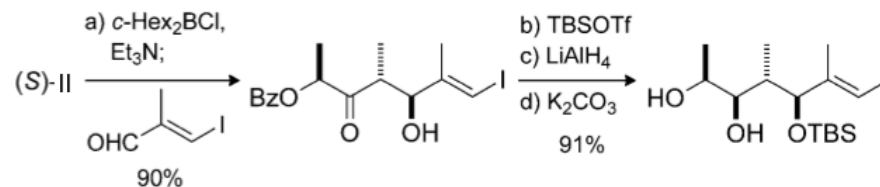
Mukaiyama Aldol controlled by 1,2-induction by Felkin-Anh and 1,3-induction based on the Evans polar model



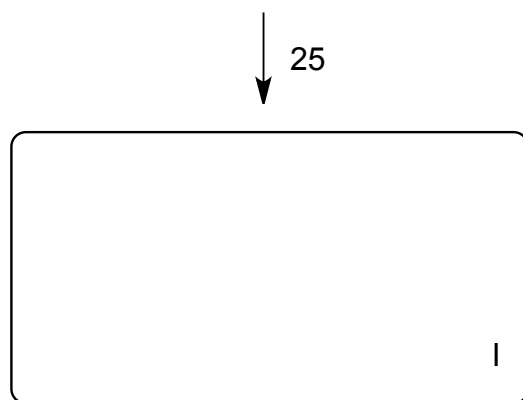
21) TMSCl, imid, CH₂Cl₂
 22) **III**, Pd(OAc)₂ (10 mol %), Ag₂CO₃, DMF, 80 °C
 23) NaIO₄/ SiO₂, CH₂Cl₂
 24) [ICH₂PPh₃]I, NaHMDS, THF, -78 °C



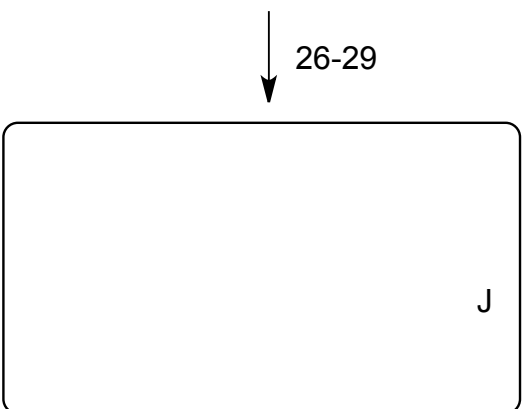
Please, provide a synthesis of **III**.



E + H



25) [Pd(PPh₃)₄](10 mol %), CuTC, Bu₄NPh₂PO₂, DMF



26) HF·py, pyridine, THF
 27) TEMPO, PhI(OAc)₂, CH₂Cl₂
 28) NaClO₂, NaH₂PO₄, 2-methyl-2-butene, tBuOH, H₂O, THF
 29) TBAF, THF, 50 °C

What is the name of the reaction in step 28)?

Pinnick-Oxidation

