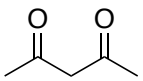
Synthesis Challenge 106

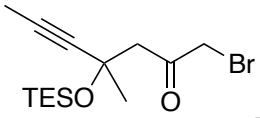
Total Synthesis of the Guangnanmycin A Alcohol

K. Yahata, A. Fürstner, Angew. Chem. Int. Ed. **2024**, e202319070

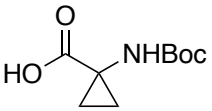
08.02.2024



??? **A**



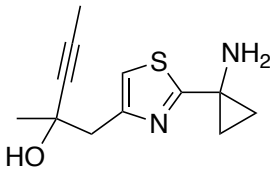
B



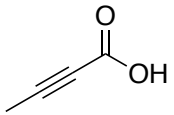
C

1-4

1) Boc_2O, pyridine, NH_4OH, MeCN
2) Lawesson's reagent, THF
3) **B**, EtOH, 70°C
4) HCl, 1,4-dioxane



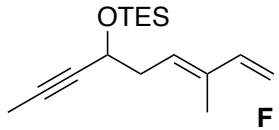
D



E

5-8

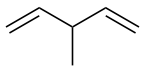
5) MeNH(OMe)·HCl, EDCI, Et_3N, DMAP (5 mol%), CH_2Cl_2, 0°C to RT
6) **I**, *sec*-BuLi, THF,
7) Dibal-H, CH_2Cl_2
8) TESCl, imidazole, CH_2Cl_2,



F

Please draft a synthesis of **B**

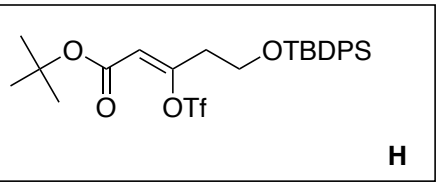
a) *i*PrMgCl, then MeC CMgBr, THF, 50 °C b) TESCl, imidazole, CH_2Cl_2
c) TBSOTf, Et_3N, CH_2Cl_2, 0 °C
d) NBS, $NaHCO_3$, THF, -78 °C to 0 °C,



I

G

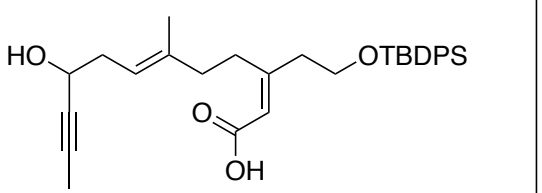
9-11



H

9) TBDPSCl, imidazole, CH_2Cl_2
10) *t*BuOOCCH$_2$Br, Zn, THF, 60 °C
11) Tf_2O, LiOH, toluene/H_2O, 0 °C

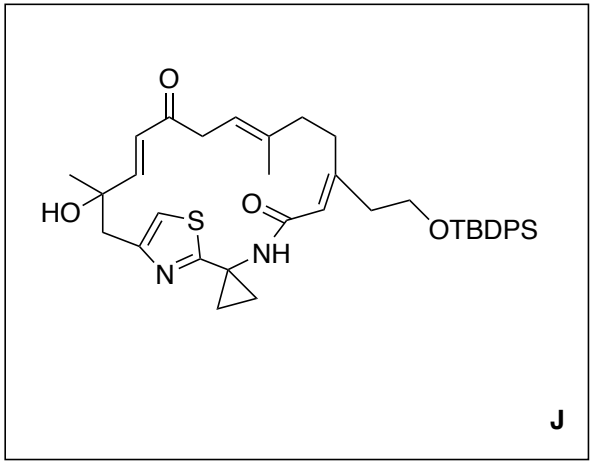
12-14



i

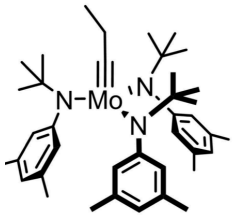
12) **F**, 9-H-9-BBN, THF; then **H**, $[(PPh_3)_2PdCl_2]$ (5 mol %), Cs_2CO_3, THF/H_2O
13) TMSOTf, 2,6- lutidine, CH_2Cl_2, 0 °C,
14) Amberlyst 15, MeOH

15-16

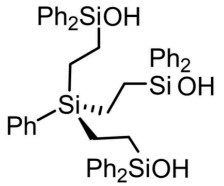


J

15) **i**, **D**, HATU, *i*Pr$_2$NEt, DMF
16) **II** (40 mol %), **III** (40 mol %), MS 5 Å, toluene, reflux
17) $[CpRu\text{-}(MeCN)_3]PF_6$ (20 mol %), PCy_3 (20 mol %), NH_4PF_6 (20 mol %), THF, reflux

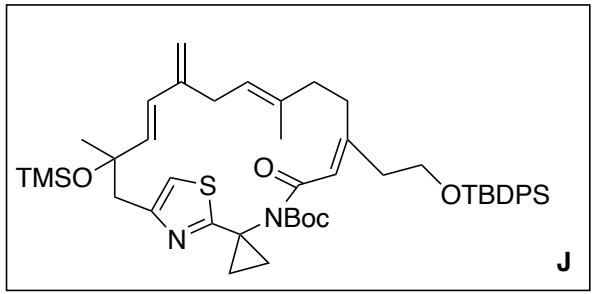


II



III

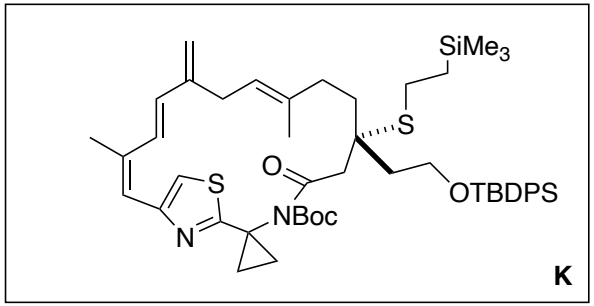
18-21



J

18) $TMSCH_2Li$, $CeCl_3$, THF, -78 °C
19) KHMDS, THF, 0°C
20) TMSCl, imidazole, CH_2Cl_2, 0 °C
21) Boc_2O, DMAP, THF

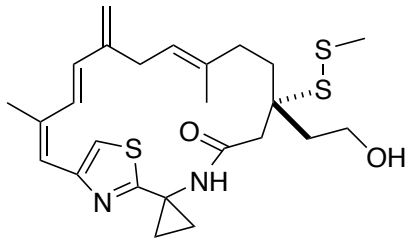
22-24



K

22) $TMSCH_2CH_2SH$, DBU, THF
23) PPTS (5 mol %), CH_2Cl_2, MeOH
24) methanesulfonyl chloride, Et_3N

25-27



25) TMSOTf, 2,6-lutidine, CH_2Cl_2
26) $[MeSSMe_2]BF_4$, MeSSMe, MeCN, THF, 0 °C
27) HF·pyridine, pyridine, MeCN, THF,