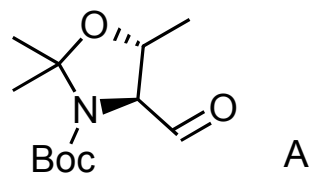


Synthesis Challenge # 51

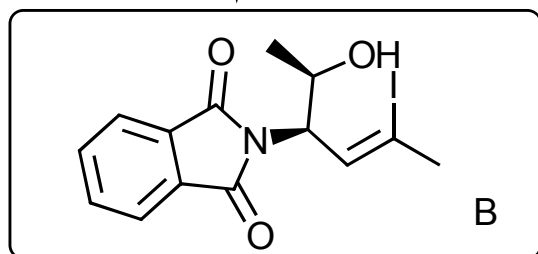
Total Synthesis of Thailanstatin A

K. C. Nicolaou, D. Rhoades, M. Lamani, M. R. Pattanayak, S. M. Kumar, *J. Am. Chem. Soc.* **2016**, *138*, 7532–7535

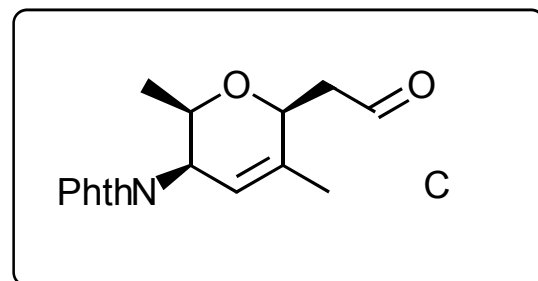
30.06.2016



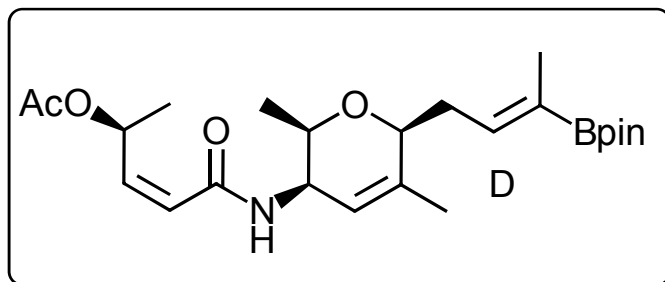
1-2



3-4



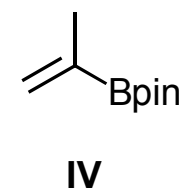
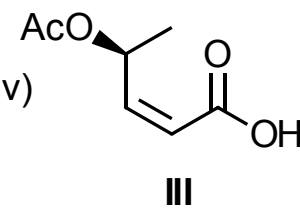
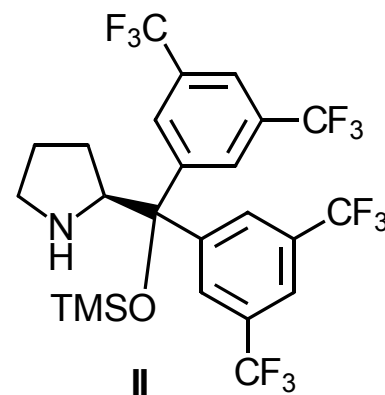
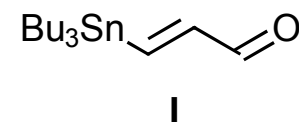
5-8

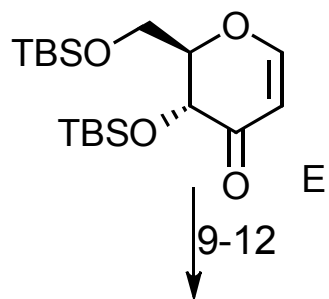


1) PPh_3EtI (2.0 equiv), *n*-BuLi (2.0 equiv), THF, 25 °C; then I_2 (1.9 equiv); then NaHMDS (1.9 equiv); then **A** (1.0 equiv), THF
2) formic acid (neat), 25 °C, then phthalic anhydride (1.1 equiv), Et_3N (20 equiv), DMAP (0.1 equiv)

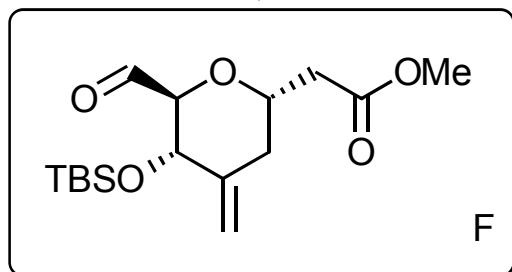
3) **I** (1.2 equiv), $\text{Pd}_2(\text{dba})_3$ (10mol%), NMP, 25 °C, 16 h
4) **II** (0.2 equiv), PhCO_2H (0.2 equiv), CH_2Cl_2 , 0 °C, 6.5 h

5) 10% Pd/C (50% w/w), H_2 (80 bar), HFIP, 25 °C, 24 h, 93% (dr 7:3)
6) Tebbe reagent (1.0 equiv), THF,
7) MeNHNH_2 (10 equiv), PhH, 25 °C, 2 h; then EDCI (3.0 equiv), NMM (3.0 equiv), **III** (2.0 equiv), CH_2Cl_2 ,
8) **IV** (5.0 equiv), Grubbs II cat. (0.1 equiv)

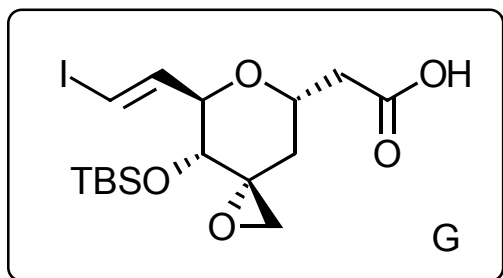




9-12

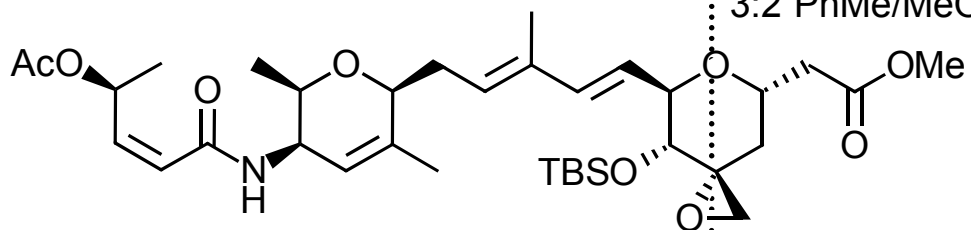


13-16



D + **G**

17-18



9) **V** (2.0 equiv), I₂ (0.1 equiv), MeCN, then K₂CO₃ (0.1 equiv), MeOH, 25 °C
 10) Ph₃PCH₃Br (2.5 equiv), *t*-BuOK (2.0 equiv), THF, 0 °C, 1 h
 11) PPTS (1.0 equiv), MeOH, 25 °C
 12) (COCl)₂ (1.5 equiv), DMSO (3.0 equiv), then Et₃N (5.0 equiv)

13) CrCl₂ (6.0 equiv), CHI₃ (3.0 equiv), THF, 25 °C
 14) TBAF (2.0 equiv), THF
 15) VO(acac)₂ (0.1 equiv), *t*-BuOOH (2.1 equiv), CH₂Cl₂, 0 → 25 °C
 16) LiOH (1.5 equiv), 10:1 THF/H₂O

17) Pd(dppf)Cl₂·CH₂Cl₂ (0.02 equiv), K₃PO₄ (1.0 equiv), **D** (1.1 equiv), **G** (1.0 equiv), 1,4-dioxane/MeCN/H₂O (3:1:1), 25 °C, 10 min
 18) TMSCHN₂ (3.0 equiv), 3:2 PhMe/MeOH, 0 → 25 °C, 3 h

