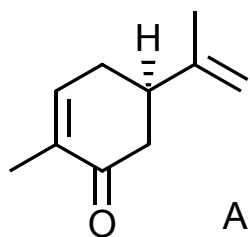


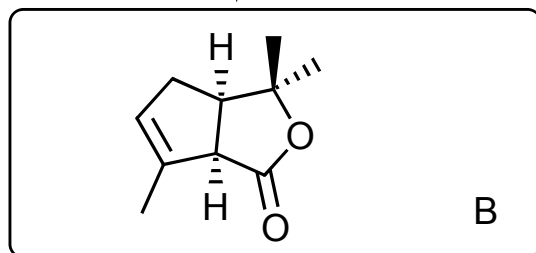
## Synthesis Challenge # 47

Synthesis of Eupalinilide E, a Promoter of Human Hematopoietic Stem and Progenitor Cell Expansion

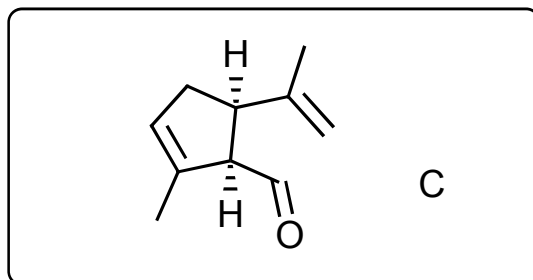
T. C. Johnson, M. R. Chin, T. Han, J. P. Shen, T. Rana, D. Siegel, *J. Am. Chem. Soc.*, **2016**, DOI: 10.1021/jacs.6b03055



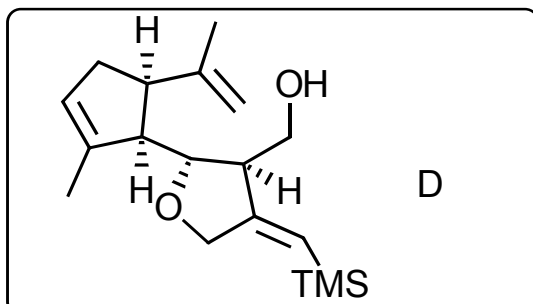
1-4



5-8



9-11



- 1) HBr, AcOH, 0 °C, 1 h
- 2) Br<sub>2</sub>, AcOH, 23 °C, 2.5 h
- 3) *i*-PrNH<sub>2</sub>, Et<sub>2</sub>O, 0 °C, 12 h
- 4) 10% aq. AcOH, THF, 50 °C, 3 h

*Hint: The synthesis has been designed to proceed on a multi gramm scale. The smallest scale on this page was 21 g.*

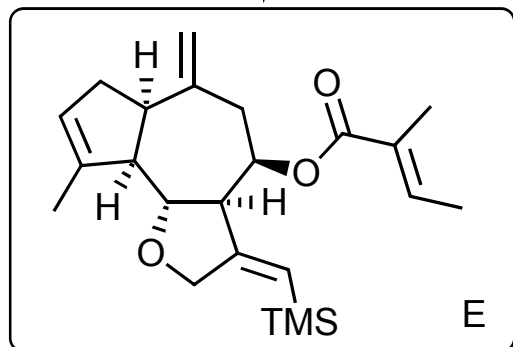
Favorskii-rearrangement

- 5) LiAlH<sub>4</sub>, Et<sub>2</sub>O, 0 °C, 1 h
- 6) Ac<sub>2</sub>O, 150 °C
- 7) LiAlH<sub>4</sub>, Et<sub>2</sub>O, 0 °C, 1 h
- 8) DMP, NaHCO<sub>3</sub>, H<sub>2</sub>O, CH<sub>2</sub>Cl<sub>2</sub>

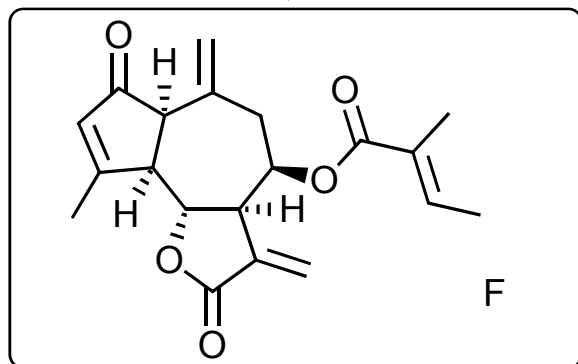
- 9) tetravinyltin, *n*-butyllithium, -78 to 23 °C, 15 min, then 10, -78 °C, 15 min, then HMPA, propargyl bromide, -78 to 23 °C, 3 h
- 10) *n*-butyllithium, -78 °C, 20 min, then: TMSCl, -78 to 23 °C
- 11) Pd(OAc)<sub>2</sub> (5 mol %), B<sub>2</sub>pin<sub>2</sub>, PhMe, MeOH, 50 °C, 15 h, then H<sub>2</sub>O<sub>2</sub>, NaOH, THF, 0 °C, 1 h

Borylative en-yne cyclization

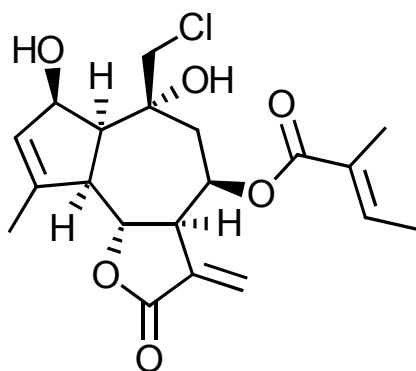
12-14



15-16



17-18



12)  $(\text{COCl})_2$ , DMSO, triethylamine,  
 $\text{CH}_2\text{Cl}_2$ ,  $-78\text{ }^\circ\text{C}$ , 2.5 h  
13)  $\text{Et}_2\text{AlCl}$ ,  $\text{CH}_2\text{Cl}_2$ ,  $-78\text{ }^\circ\text{C}$   
14) tiglic acid, 2,4,6-TCBC, triethyl-  
amine, DMAP, PhMe,  $80\text{ }^\circ\text{C}$ , 2 h

Swern oxidation

Yamaguchi esterification

15) TFA,  $\text{CH}_2\text{Cl}_2$ ,  $23\text{ }^\circ\text{C}$ , 2 h  
16)  $\text{CrO}_3$ , 3,5-DMP,  $\text{CH}_2\text{Cl}_2$ ,  $0\text{ }^\circ\text{C}$

3,5-DMP = 3,5-dimethylpyrazole

17)  $\text{Yb}(\text{OTf})_3$ ,  $\text{NaBH}_4$ , MeOH/THF,  
 $-78\text{ }^\circ\text{C}$ , 2 h  
18)  $\text{Al}(\text{O}^i\text{sec-Bu})_3$ , TBHP,  $\text{CH}_2\text{Cl}_2$ ,  
 $0$  to  $23\text{ }^\circ\text{C}$ , 40 min,  
then LiCl, HCl, THF,  $23\text{ }^\circ\text{C}$ , 5 min