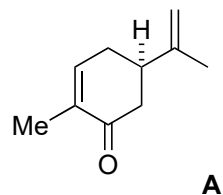


A Concise, Efficient and Scalable Total Synthesis of Thapsigargin and Nortilobide

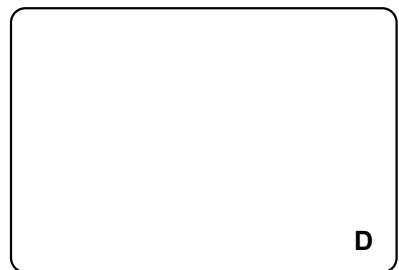
Dezhi Chen and P. Andrew Evans, *J. Am. Chem. Soc.* **2017**, *139*, 6046 - 6049



1-3



4-5



6-8

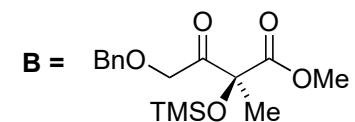
- 1) *t*BuOCl
- 2) DIBAL-H *then* TBSCl
- 3) Pd₂(dba)₃•CHCl₃, (*S*)-BINAP, LiCl, *then* **B**, LiHMDS

- 4) O₃, PPh₃, *then* piperidinium acetate
- 5) VCl₃(THF)₃, Zn, HMPA

- 6) Co(acac)₂, PhSiH₃, O₂
- 7) Ac₂O, DMAP
- 8) Pd(OH)₂/C, H₂, *then* IBX, *then* NaBH₄

Name of **A**?

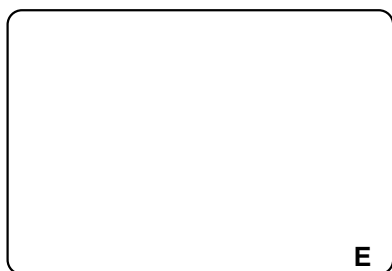
Mechanism of **step 3**?



How would you synthesize this ketoester?

Mechanism of **step 5**? How do you explain the stereoselectivity?

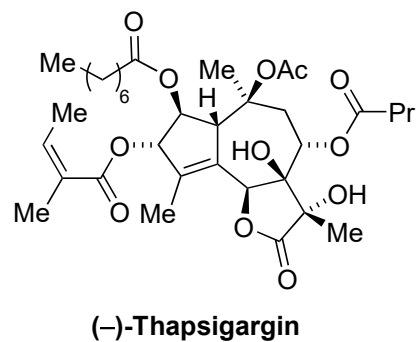
Mechanism of **step 6**?



9-10



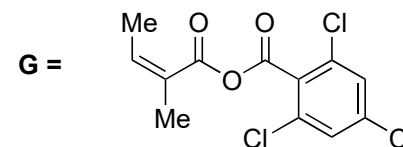
11-12



9) $(\text{PrCO})_2\text{O}$, DMAP, then CrO_3
 10) $\text{Mn}(\text{OAc})_3$, $\text{C}_7\text{H}_{15}\text{CO}_2\text{H}$

11) $\text{Zn}(\text{BH}_4)_2$
 12) **G**, NaHCO_3

Mechanism of **step 10**?
 What other conditions could accomplish the same transformation?



Bonus question - 'Thapsigargin Wars' Edition:

Some great chemistry from Baran and Massanet is featured in a competing short, scalable synthesis of (-)-thapsigargin (*ACS Cent. Sci.* **2017**, 3, 47-51). What are the conditions and mechanism?

