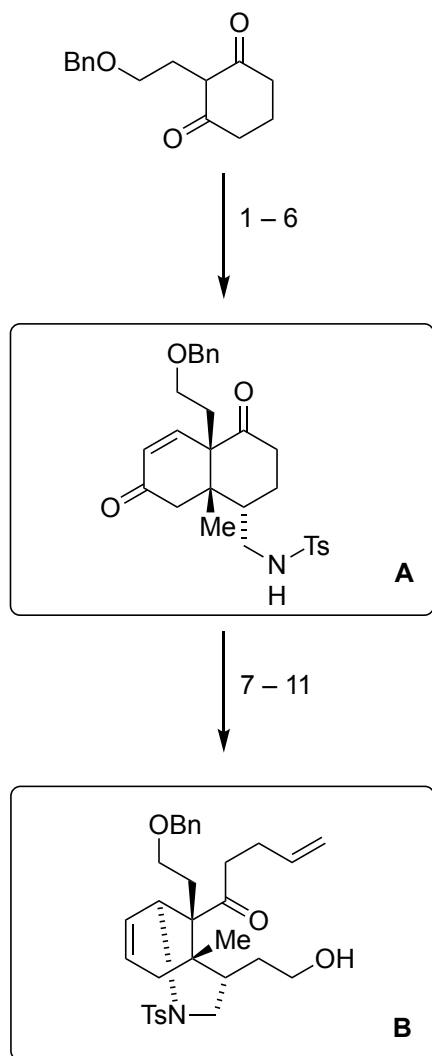


# Enantioselective Total Synthesis of (-)-Caldaphnidine O via a Radical Cyclization Cascade

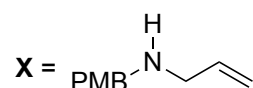
Lian-Dong Guo, Jingping Hu, Yan Zhang, Wentong Tu, Yue Zhang, Fan Pu, and Jing Xu  
*J. Am. Chem. Soc.* **2019**, *141*, 13043–13048.



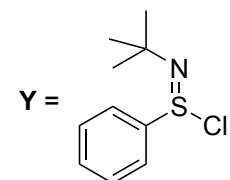
- 1) MVK,  $\text{NEt}_3$ ,  
*then* L-Prolinamide, HOAc
- 2)  $\text{CH}(\text{OMe})_3$ , PTSA,  
*then* HCHO, **X**
- 3) 1,3-Dimethylbarbituric acid,  $\text{Pd}(\text{Ph}_3)_4$   
*then*  $\text{NAHCO}_3$ , TsCl
- 4)  $\text{ZnMe}_2$ , LiBr,  $\text{Ni}(\text{acac})_2$
- 5) LiHMDS, **Y**
- 6) CAN

- 7) KHMDS,  $\text{PhNTf}_2$ ,  
*then* KHMDS, Davis' oxaziridine
- 8)  $\text{Pd}(\text{OAc})_2$ ,  $\text{PPh}_3$ , HCOOH, DIPEA
- 9) 3-butenylmagnesium bromide,  $\text{CeCl}_3$
- 10)  $\text{Pb}(\text{OAc})_4$
- 11)  $\text{NaBH}_4$

Hint: The (*R*)-enantiomer is formed in step 1.

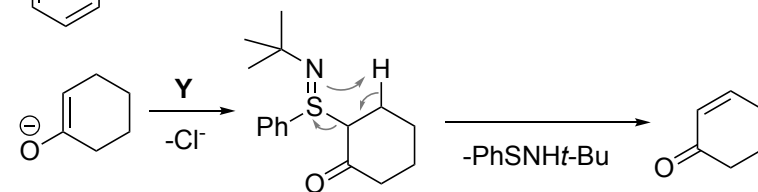


Step 2: Methyl enol ether formation,  
*then* vinylogous Mannich

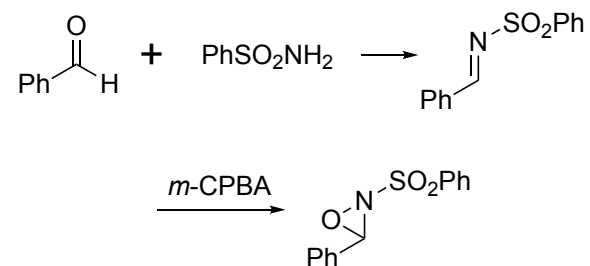


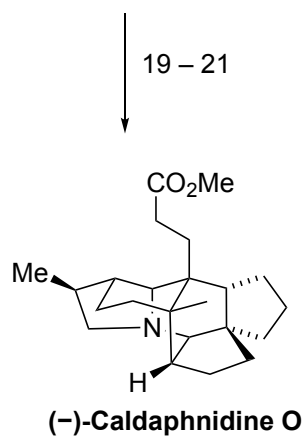
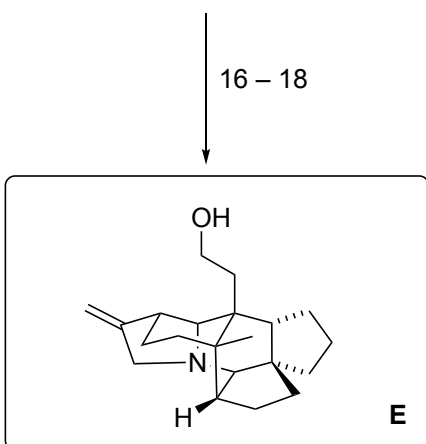
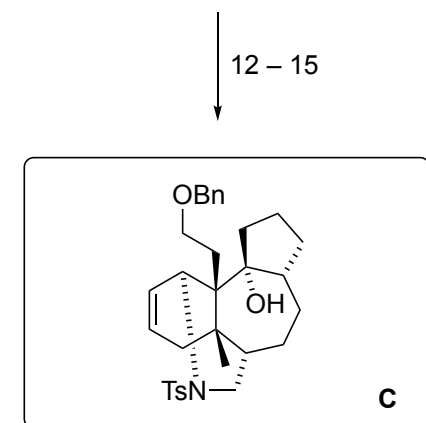
Step 4: conjugate addition under Luche's  
 conditions

Step 5: Name and mechanism?  
 Mukaiyama dehydrogenation



Step 7: How do you prepare Davis' oxaziridine?





- 12) I<sub>2</sub>, PPh<sub>3</sub>, imidazole  
 13) LDA  
 14) 9-BBN, NaOMe, I<sub>2</sub>  
 15) SmI<sub>2</sub>, Fe(dbm)<sub>3</sub>

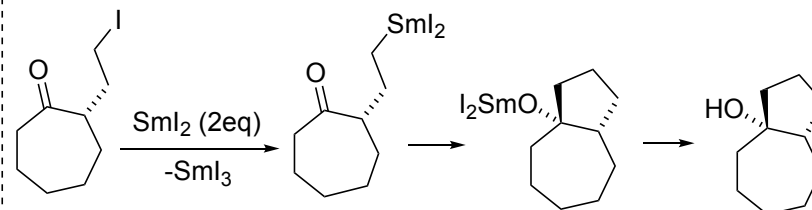
- 16) SOCl<sub>2</sub>, pyridine  
 17) Na-naph  
*then* propargyl bromide  
 18) *n*-Bu<sub>3</sub>SnH, AIBN  
*then* *p*-TsOH

- 19) (COCl)<sub>2</sub>, DMSO, TEA  
 20) *n*-BuLi, **Z**  
*then* *p*-TsOH  
*then* NaOMe  
 21) H<sub>2</sub>, Pt/C

Hint for step 13: A 2:1 mixture of diastereomers is formed. It ultimately (step 16) converges back into the same intermediate.

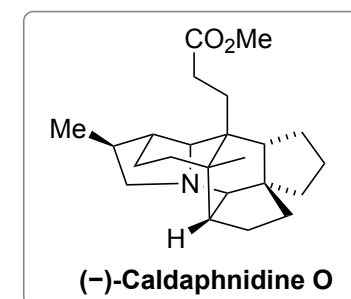
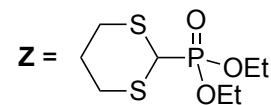
Step 15: What are the names associated with and the mechanism of this reaction?

*Kagan Molander coupling*



Step 18 - KEY STEP: Please provide a mechanism and classify each of the three steps happening in this cyclization cascade.

*5-exo-trig, 1,5-HAT, 5-exo-trig, mechanism below*



Mechanism of step18

