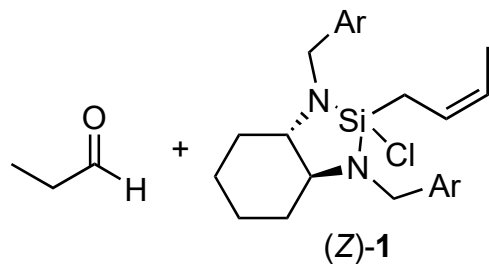
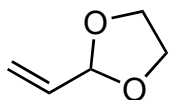
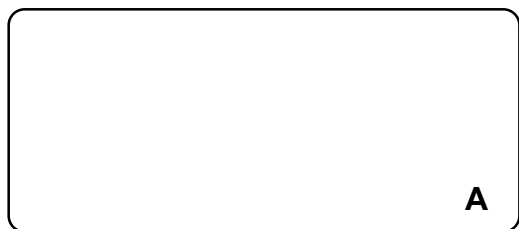


# Evolution of an Efficient and Scalable Nine-Step (Longest Linear Sequence) Synthesis of Zincophorin Methyl Ester

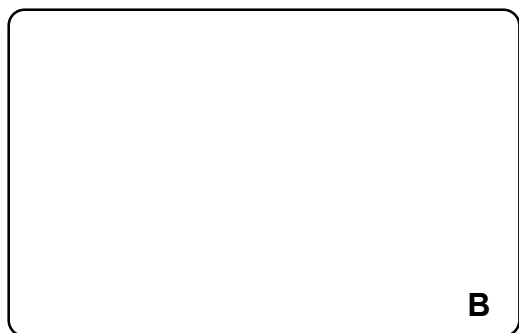
Chen, L.-A.; Ashley, M. A.; Leighton, J. L.  
*J. Am. Chem. Soc.* **2017**, *139*, 4568-4573.



1-6



7-13



Ar = 4-Br-Ph

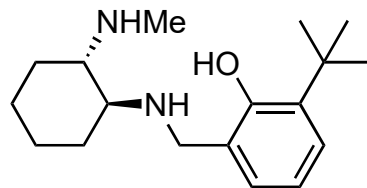
- 1) cat. Sc(OTf)<sub>3</sub>
- 2) Methacrolein, Hoveyda-Grubbs 2
- 3) TsCl, Et<sub>3</sub>N, cat. Me<sub>3</sub>N•HCl
- 4) (*E*)-1, cat. Sc(OTf)<sub>3</sub>
- 5) PMB-Br, Et<sub>3</sub>N, KHMDS, then LiBEt<sub>3</sub>H, Δ
- 6) Vinyl-BPin, Hoveyda-Grubbs 2

1) Product is (*S,S*)-configured

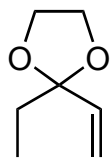
- 7) cat. Rh(acac)(CO)<sub>2</sub> / (*R,R*)-Ph-BPE, H<sub>2</sub>, CO, then CH<sub>2</sub>=CHCH<sub>2</sub>-SiCl<sub>3</sub>, DBU, **2**
- 8) PMB-Cl, Et<sub>3</sub>N, KHMDS, 18-crown-6
- 9) cat. OsO<sub>4</sub>, NaIO<sub>4</sub>, 2,6-lutidine
- 10) NaBH<sub>4</sub>
- 11) PPh<sub>3</sub>, CBr<sub>4</sub>, Et<sub>3</sub>N
- 12) **A**, cat. Pd(OAc)<sub>2</sub> / *Pt*-Bu<sub>2</sub>Me, NaOH
- 13) TMSOTf, 2,2'-bipy, then aq workup

7) Product is (*2S,3R*)-configured

13) Acetal hydrolysis



**2**



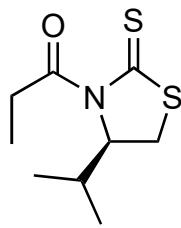
14-21



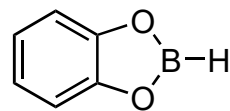
Zincophorin Methyl Ester

- 14) cat. Rh(acac)(CO)<sub>2</sub> / (S,S)-Ph-BPE, H<sub>2</sub>, CO
- 15) *trans*-crotyl-BPin; then 2 M aq HCl
- 16) cat. Rh(acac)(CO)<sub>2</sub> / PPh<sub>3</sub>, CO, H<sub>2</sub>
- 17) Ac<sub>2</sub>O, Pyridine, DMAP
- 18) **3**, TiCl<sub>4</sub>, DIPEA} added to previous, SnCl<sub>4</sub>
- 19) MeOH, DMAP
- 20) Cy<sub>2</sub>BCl, Et<sub>3</sub>N, then add **B**
- 21) **4**, then DDQ, H<sub>2</sub>O

- 14) Product is (*R*)-configured
- 15) Closed transition state
- 16) Product is a lactol



**3**



**4**

