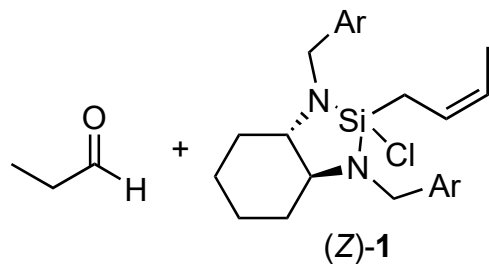
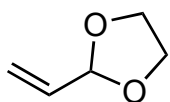
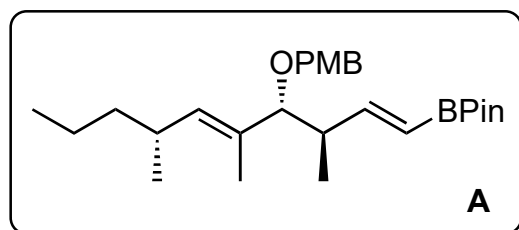


Evolution of an Efficient and Scalable Nine-Step (Longest Linear Sequence) Synthesis of Zincophorin Methyl Ester

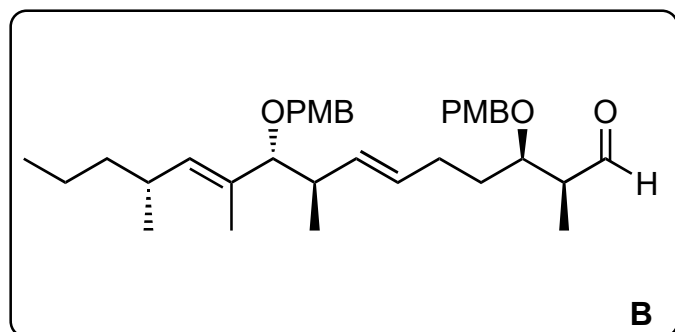
Chen, L.-A.; Ashley, M. A.; Leighton, J. L.
J. Am. Chem. Soc. **2017**, *139*, 4568-4573.



1-6



7-13



Ar = 4-Br-Ph

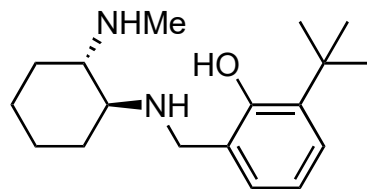
- 1) cat. Sc(OTf)₃
- 2) Methacrolein, Hoveyda-Grubbs 2
- 3) TsCl, Et₃N, cat. Me₃N•HCl
- 4) (*E*)-1, cat. Sc(OTf)₃
- 5) PMB-Br, Et₃N, KHMDS; then LiBEt₃H, Δ
- 6) Vinyl-BPin, Hoveyda-Grubbs 2

- 7) cat. Rh(acac)(CO)₂ / (*R,R*)-Ph-BPE, H₂, CO; then CH₂=CHCH₂-SiCl₃, DBU, **2**
- 8) PMB-Cl, Et₃N, KHMDS, 18-crown-6
- 9) cat. OsO₄, NaIO₄, 2,6-lutidine
- 10) NaBH₄
- 11) PPh₃, CBr₄, Et₃N
- 12) **A**, cat. Pd(OAc)₂ / *Pt*-Bu₂Me, NaOH
- 13) TMSOTf, 2,2'-bipy

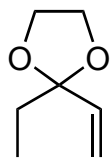
1) Product is (*S,S*)-configured

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

13) Acetal hydrolysis



2



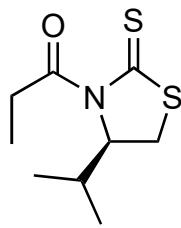
14-21



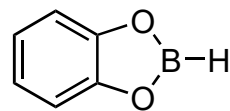
Zincophorin Methyl Ester

- 14) cat. Rh(acac)(CO)₂ / (S,S)-Ph-BPE, H₂, CO
 15) *trans*-crotyl-BPin; then 2 M aq HCl
 16) cat. Rh(acac)(CO)₂ / PPh₃, CO, H₂
 17) Ac₂O, Pyridine, DMAP
 18) **3**, TiCl₄, DIPEA} added to previous, SnCl₄
 19) MeOH, DMAP
 20) Cy₂BCl, Et₃N, then add **B**
 21) **4**, then DDQ, H₂O

- 14) Product is (*R*)-configured
 16) Product is a lactol



3



4

