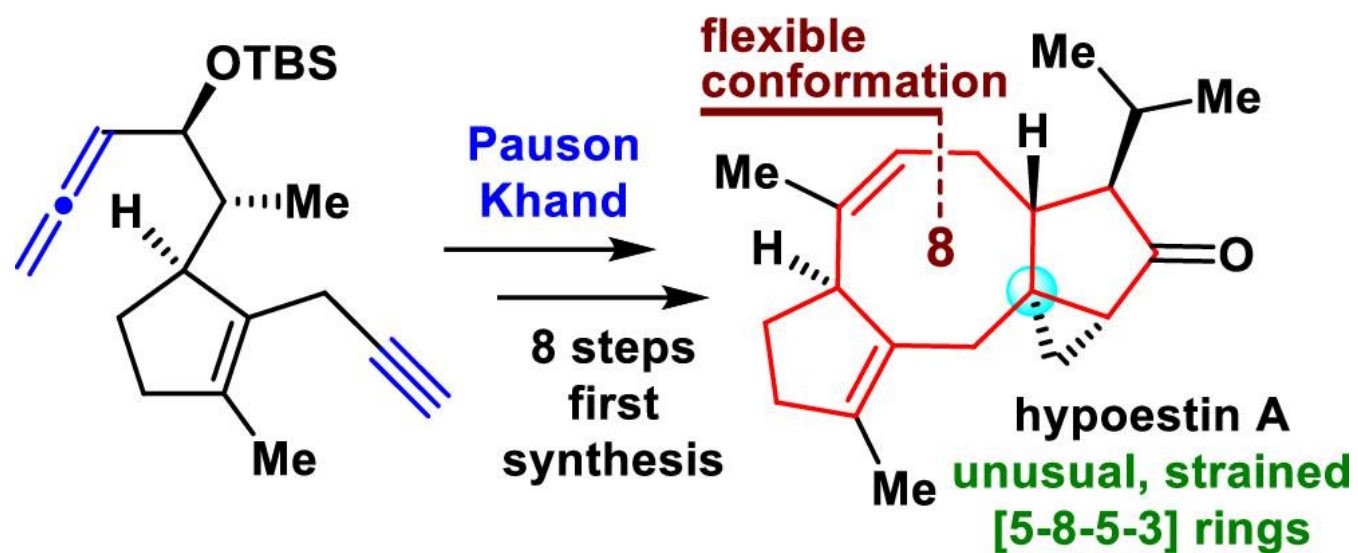


# Asymmetric Total Syntheses of Hypoestin A, Albolic Acid, and Ceroplastol II





ChuangChuang Li

■ **Education :**

1997-2001: B.S. in Chemistry (China Agricultural University)

Research advisor (2000-2001): Professor Dao-quan Wang

2001-2006: Ph.D. in Organic Chemistry (Peking University)

Research advisor: Professor Zhen Yang

2006-2008: Postdoctoral Associate (The Scripps Research Institute)

Research advisor: Professor Phil S. Baran

■ **Work Experience :**

2008-2013: Associate Professor

Shenzhen Graduate School, Peking University

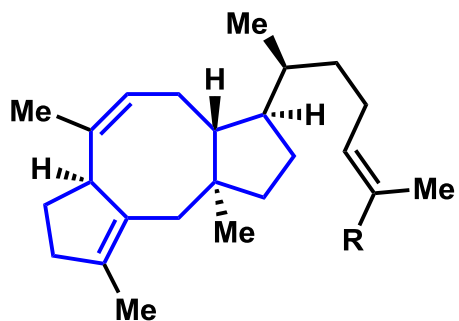
2014-now: Research Professor (tenure-track); Principal Investigator

Southern University of Science and Technology

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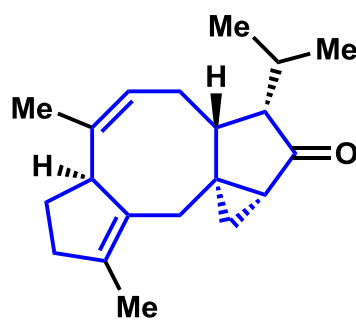
insect wax  
*Ceroplastes albolineatus*



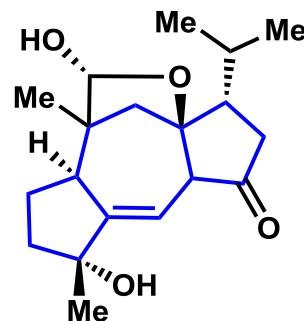
R=COOH, albolic acid (2)  
R=CH<sub>2</sub>OH, ceroplastol II (3)



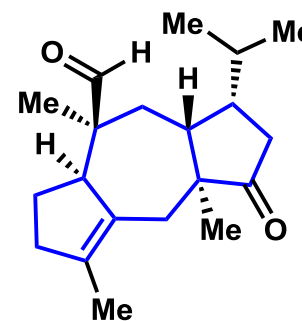
*Hypoestes purpurea*  
(Acanthaceae)



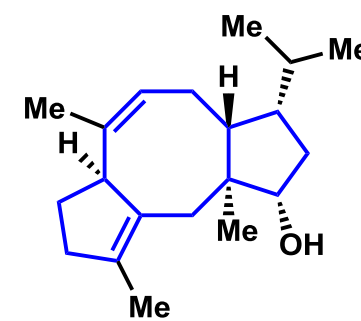
hypoestins B



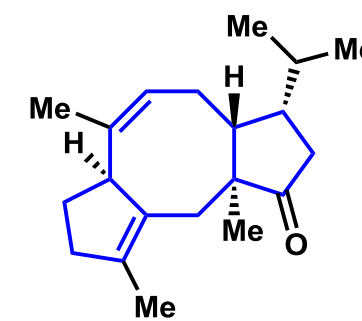
hypoestins C



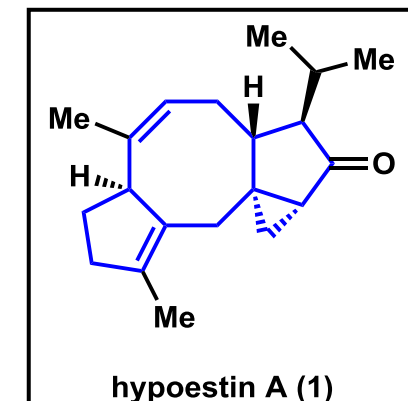
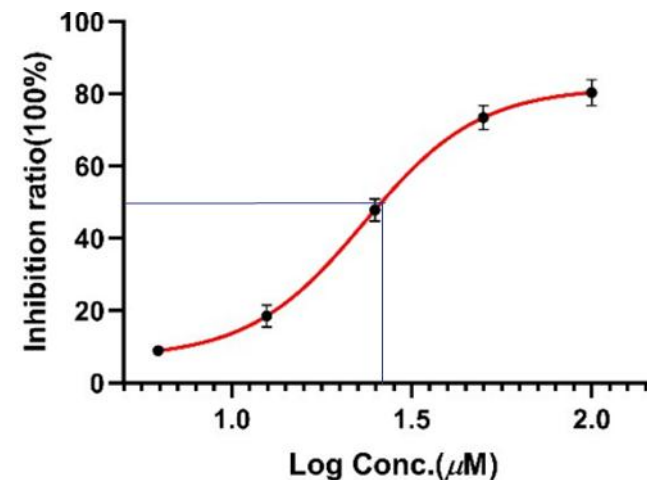
hypoestins D

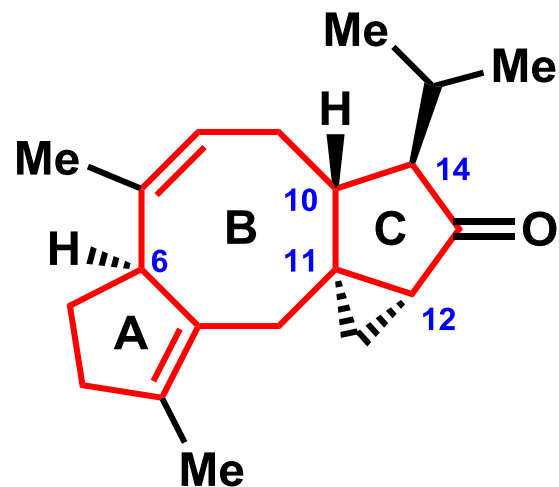


hypoestins E

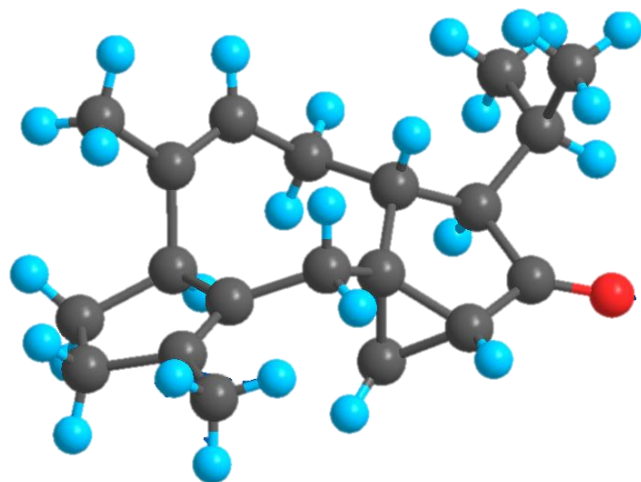


hypoestins F





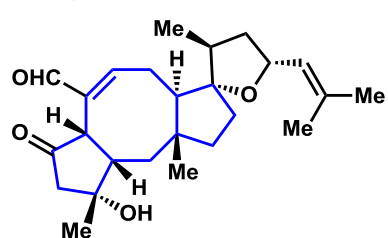
hypoestin A (1)



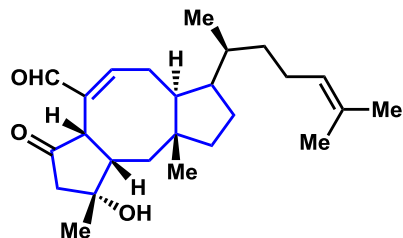
## Structural Features:

- Unusual [5-8-5-3] ring system
- Strained cyclopropane
- 5 Stereocenters: 4 contiguous
  - 1 all carbon quaternary
- No total synthesis reported

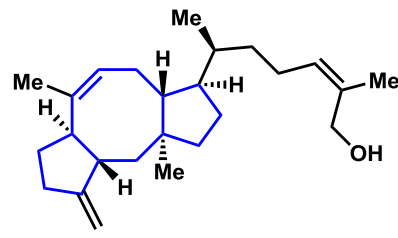
# Natural Products with [5-8-5] Skeleton



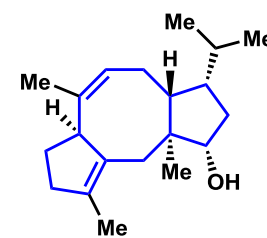
(+)-ophiobolin A



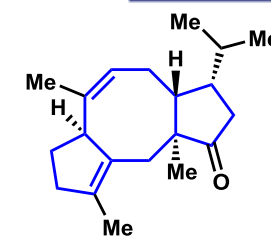
(+)-ophiobolin C



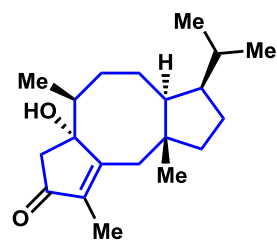
ceroplastol I



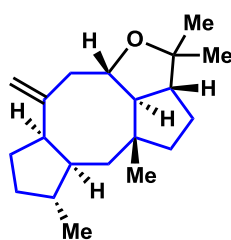
hypoestins E



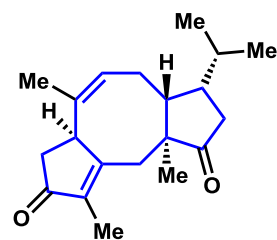
hypoestins F



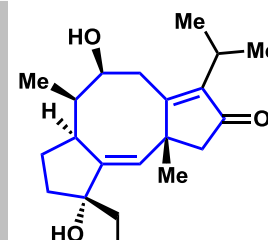
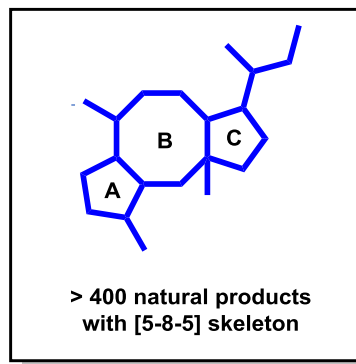
fusicoauritone



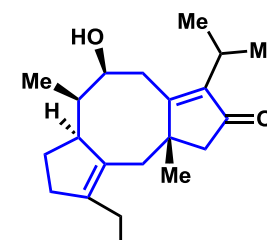
epoxydictymene



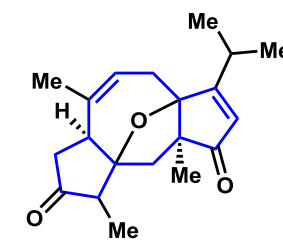
hypoestenone



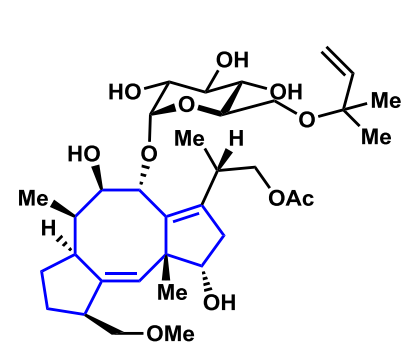
brassicene A



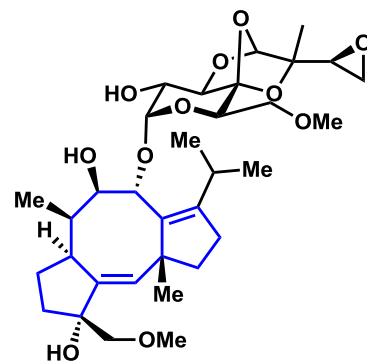
alterbrassicene D



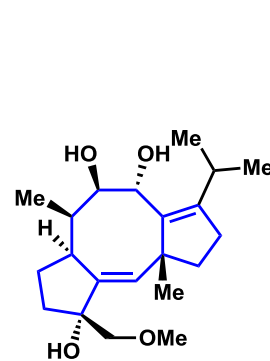
3(11)-epoxyhypoestenone



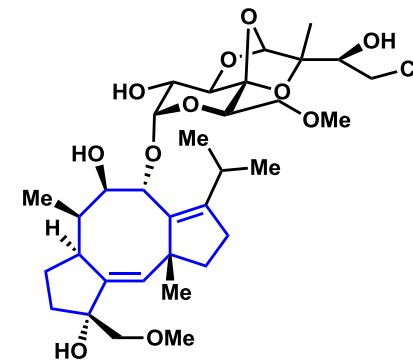
fusicoccin A



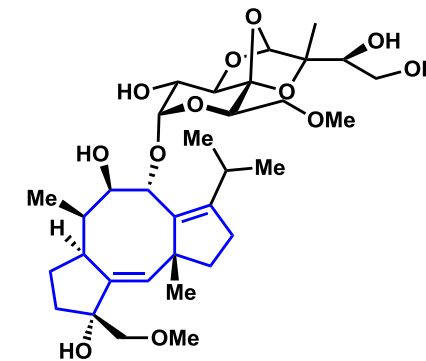
cotylenin A



cotylenol



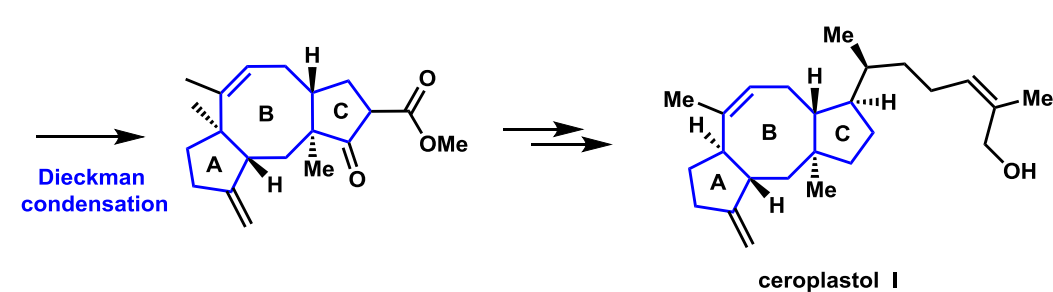
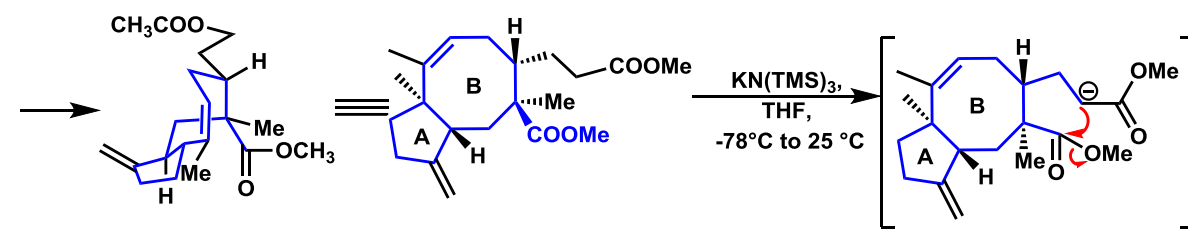
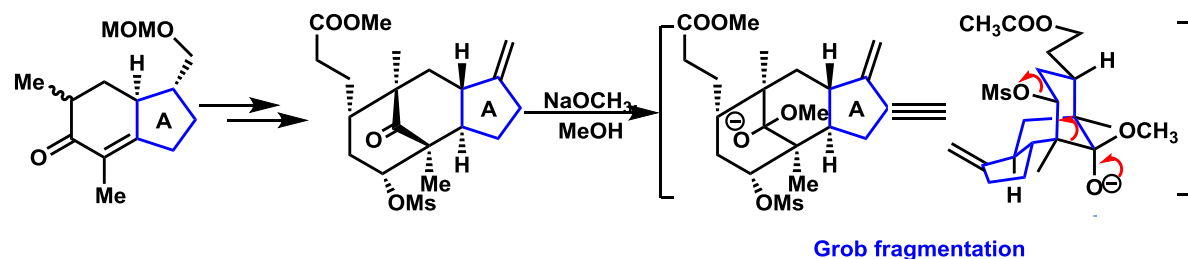
cotylenin B



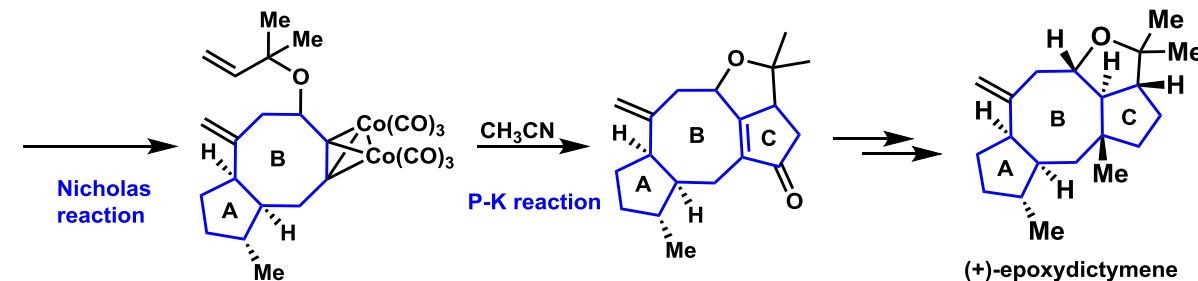
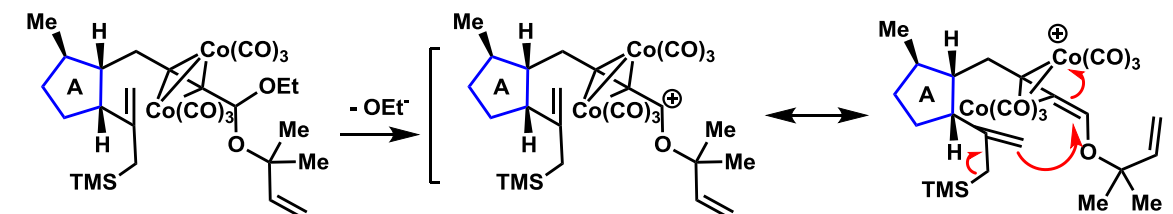
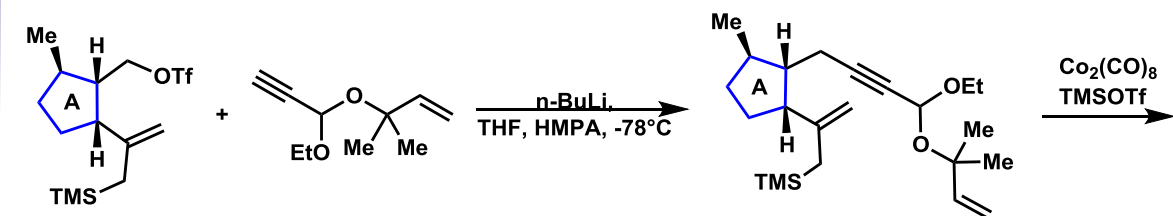
cotylenin D

■ **A → AB → ABC**

■ Grob fragmentation (Boeckman's work)

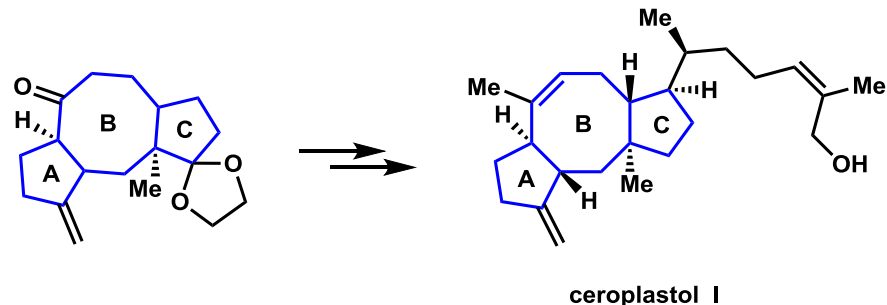
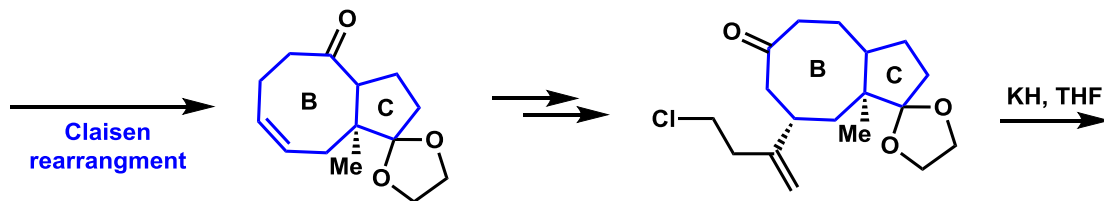
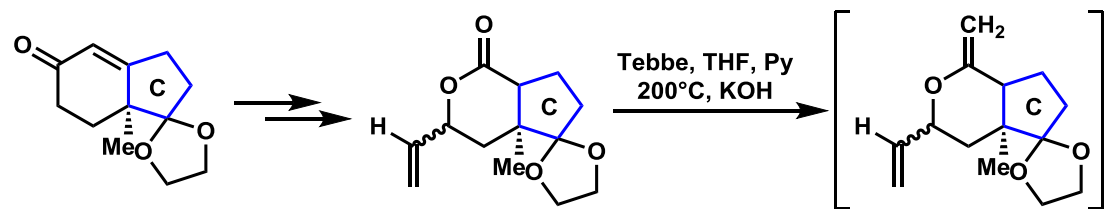


■ Nicholas reaction (Schreiber's work)



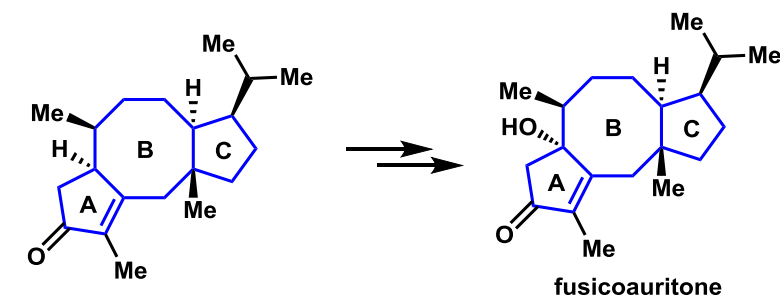
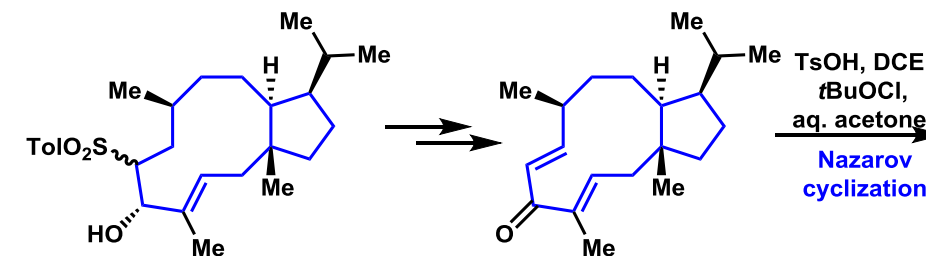
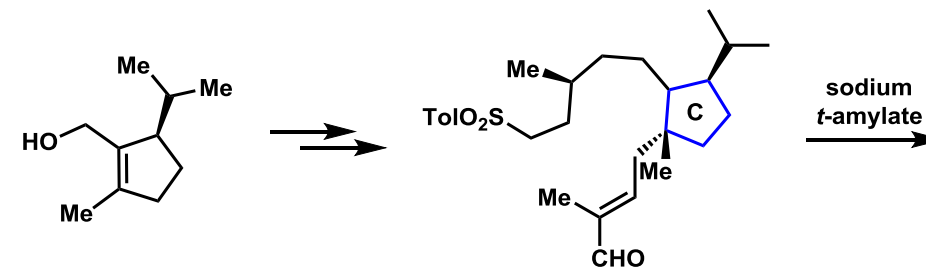
■ **C → CB → CBA**

■ Claisen rearrangement (Paquette's work)



■ **C → C(B+A) → CBA**

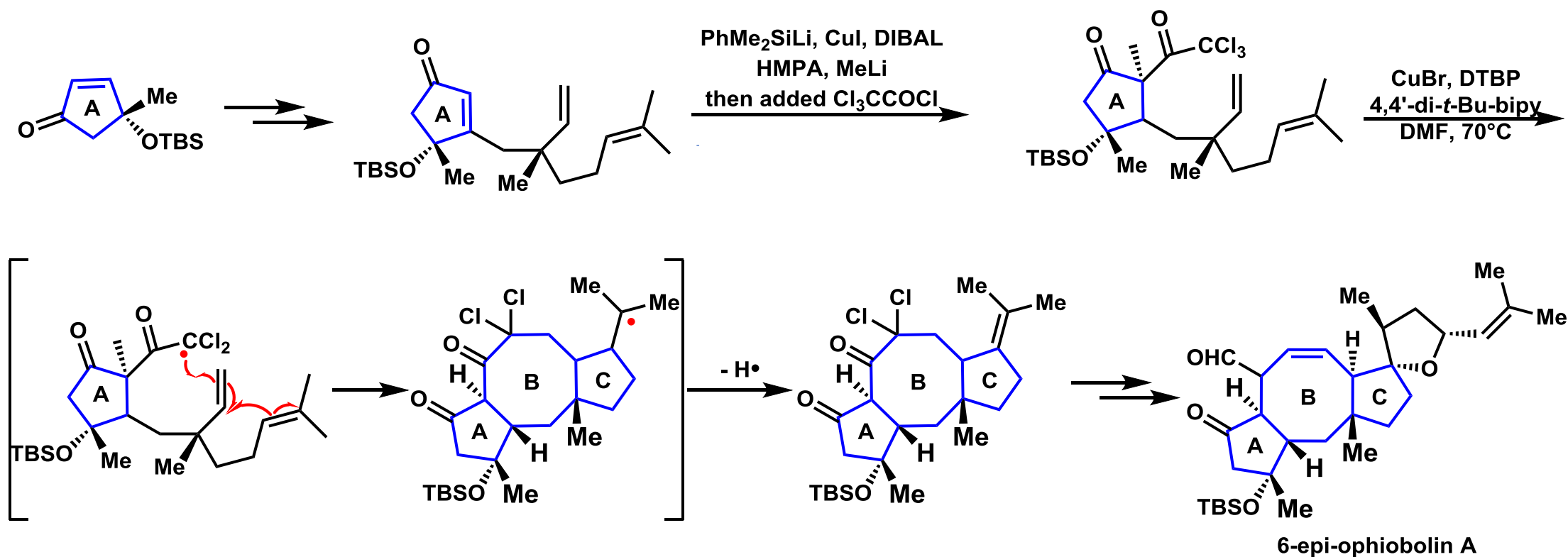
■ Nazarov cyclization (Williams' work)





# Synthetic Strategies

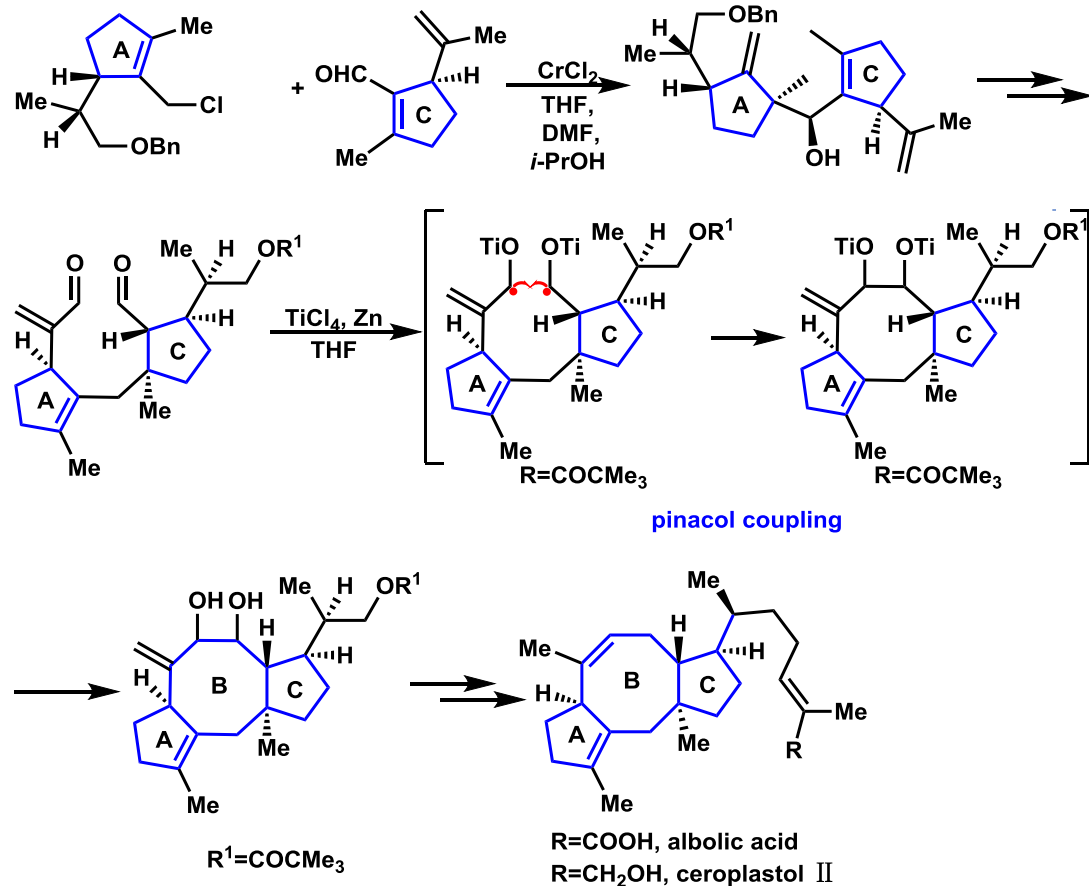
- **A** → **ABC**
- Radical cyclization (Maimone's work)



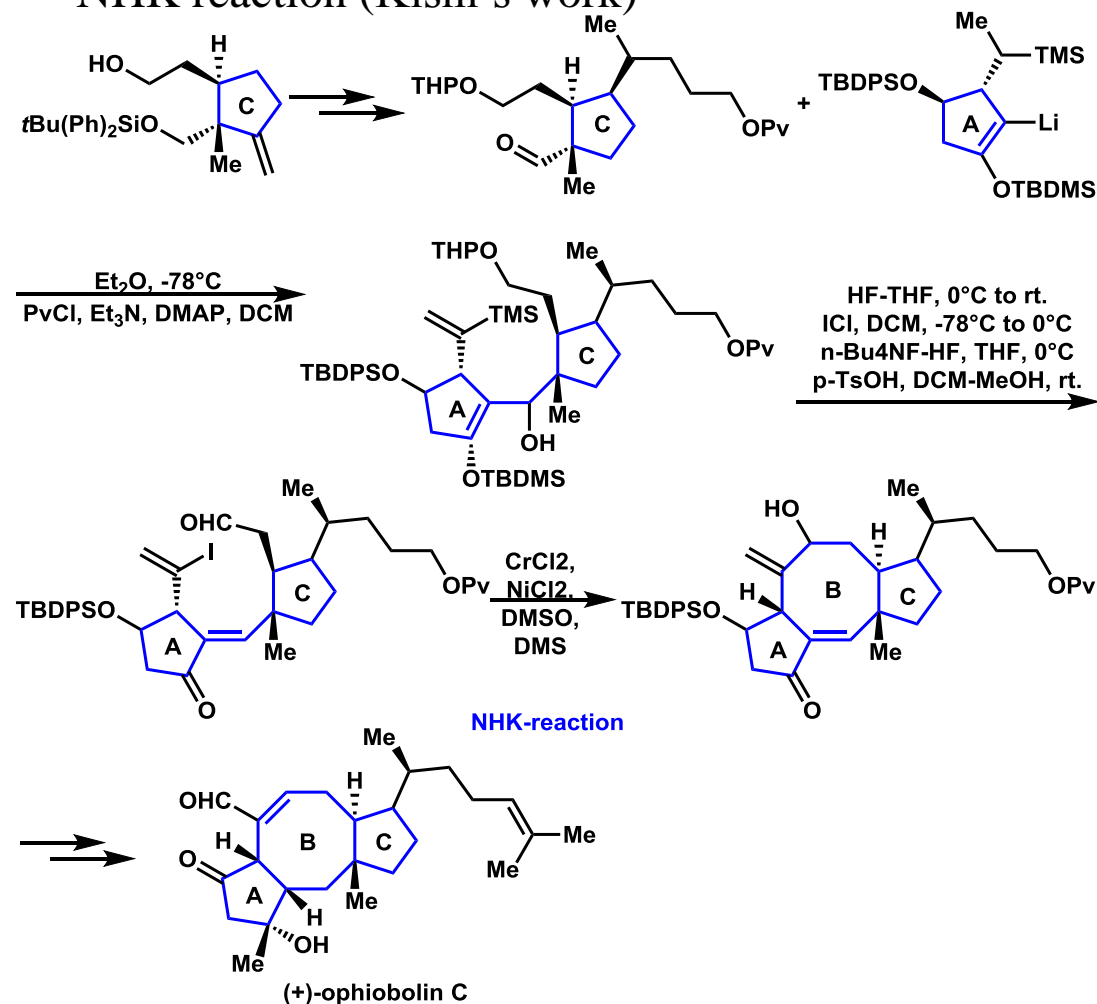


■ **A+C → AC → ABC**

■ Pinacol coupling (Kato's work)



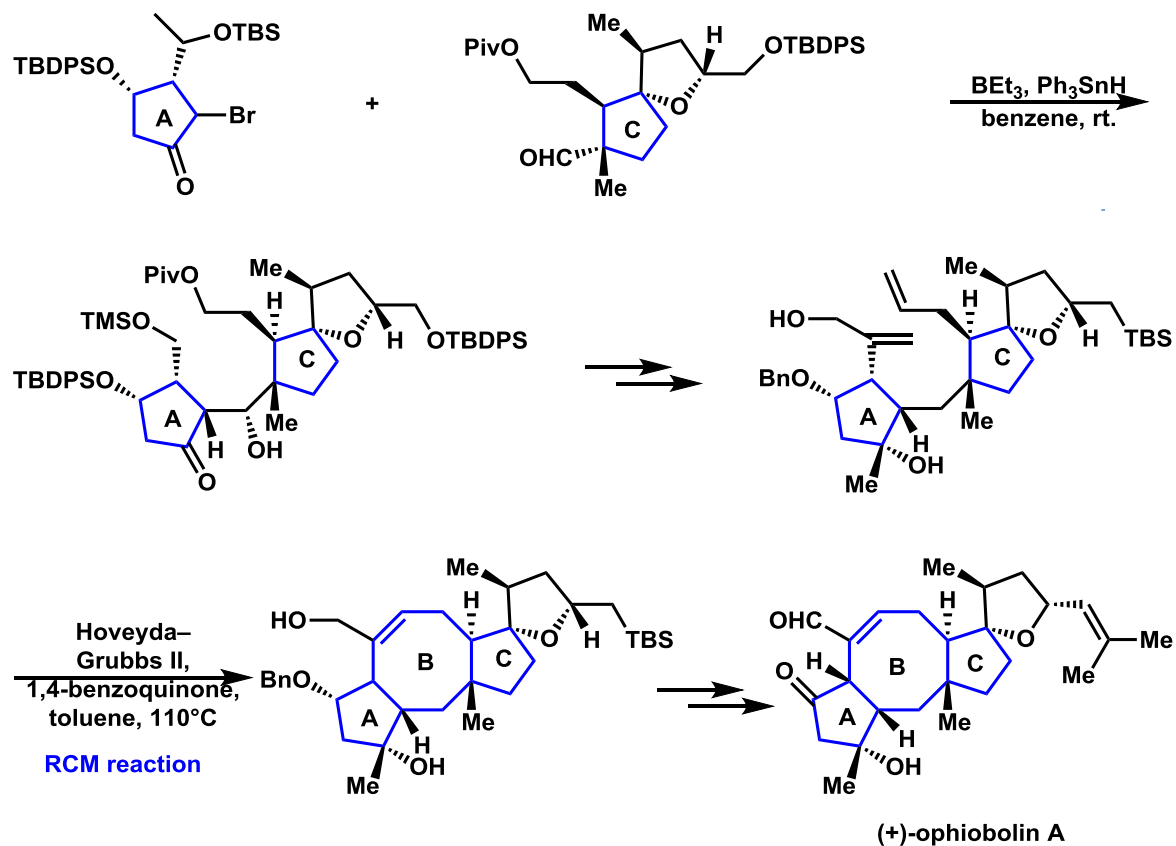
■ NHK reaction (Kishi's work)



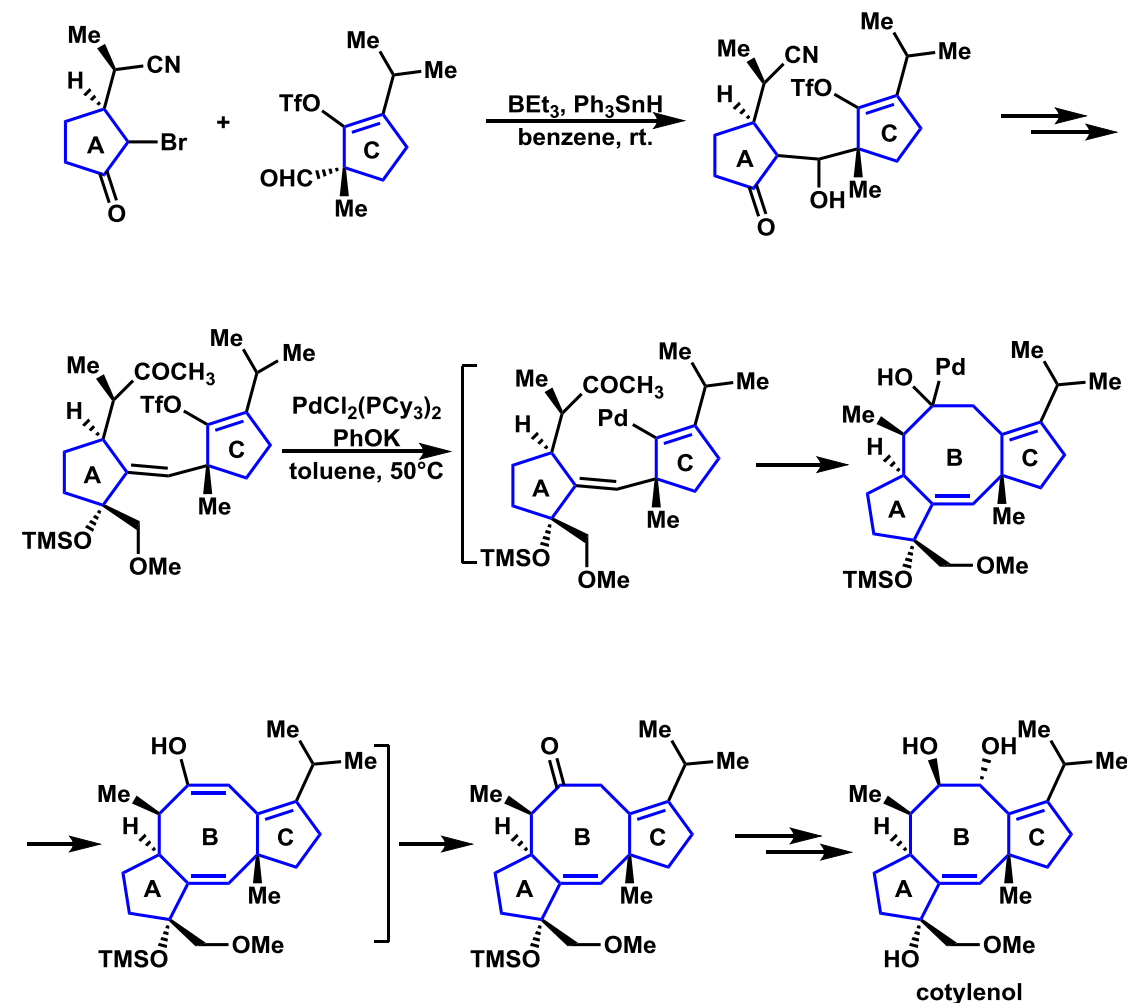
# Synthetic Strategies

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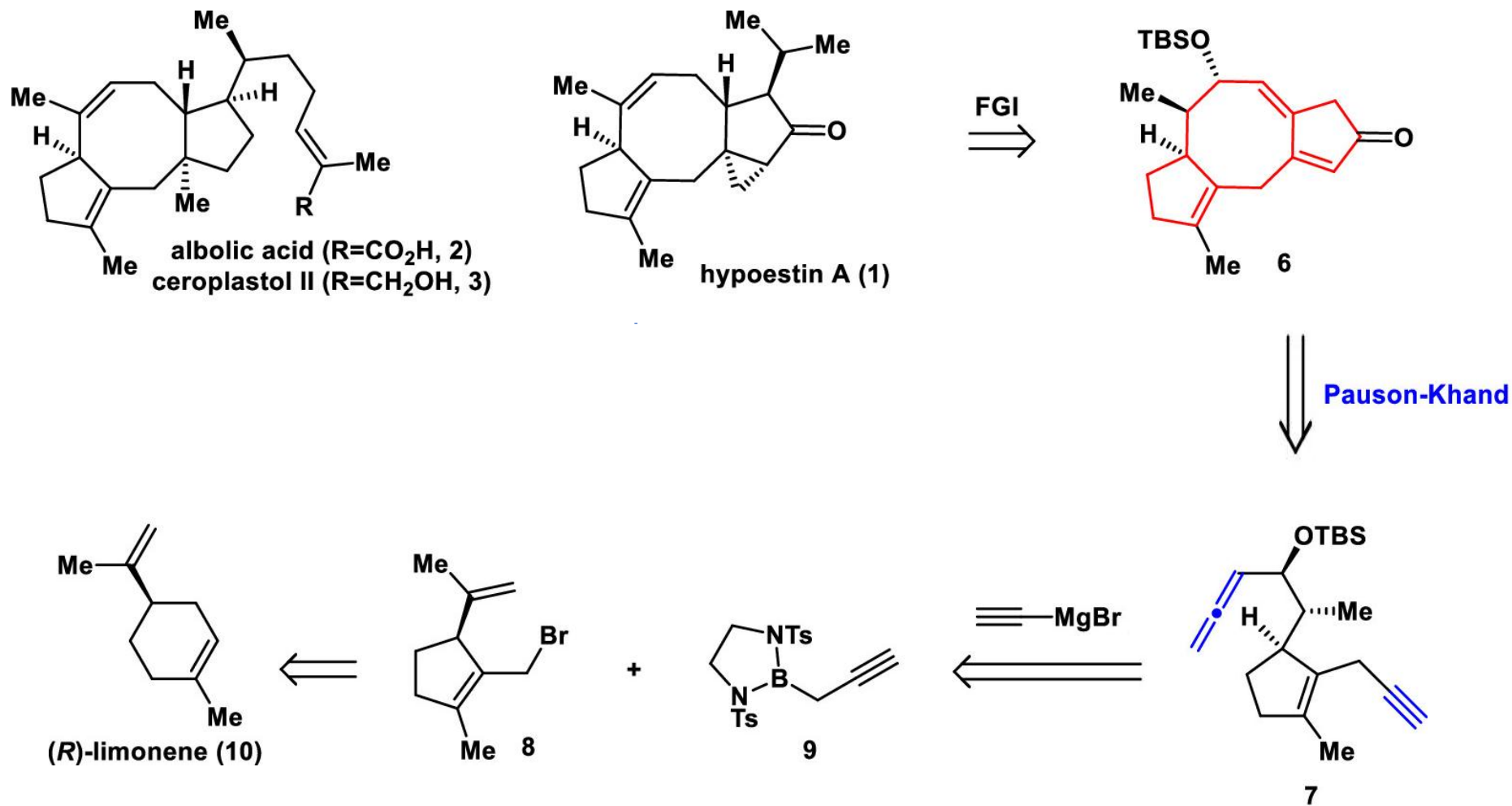
- $A+C \rightarrow AC \rightarrow ABC$
- RCM (Nakada's work)



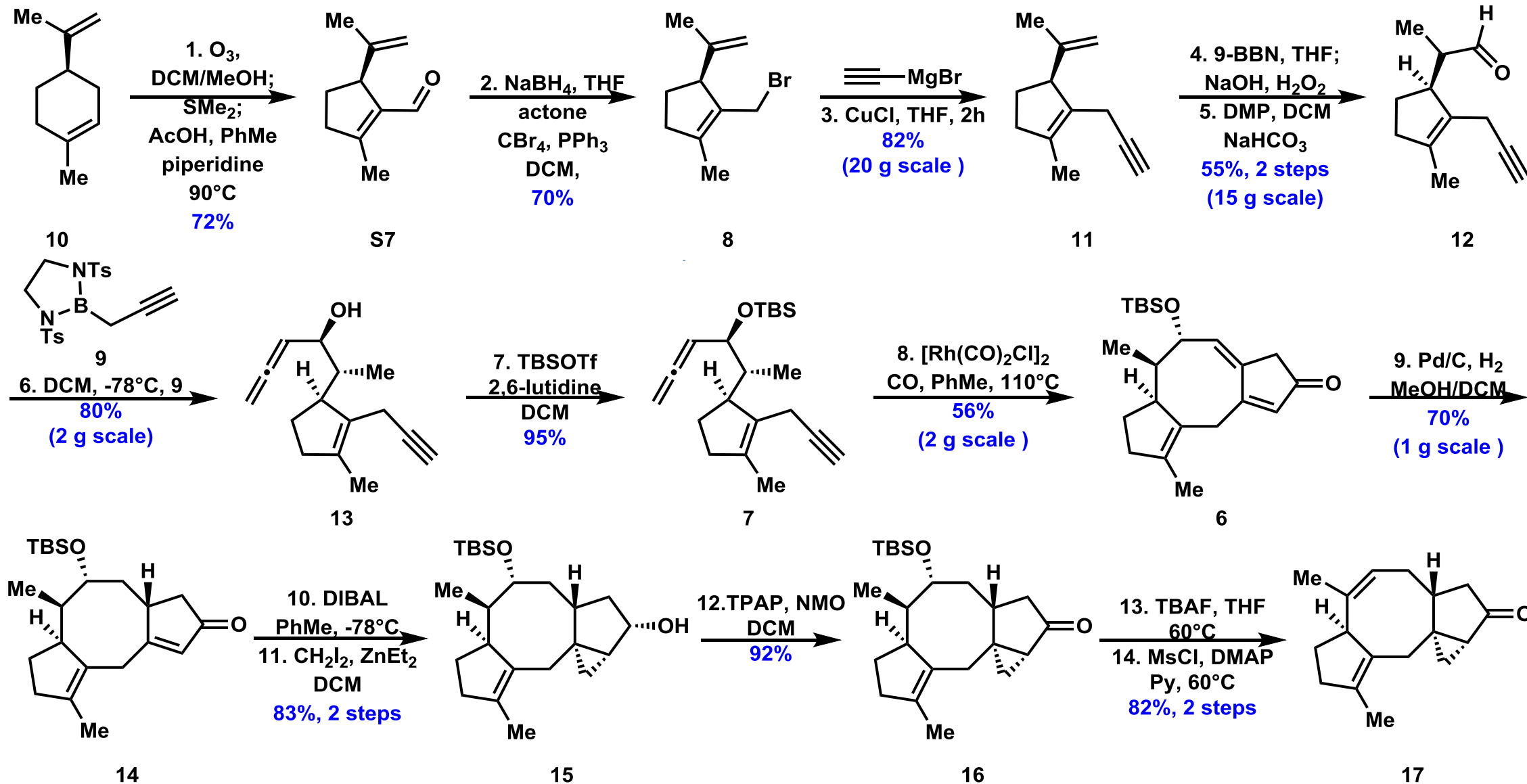
## Palladium mediated cyclization (Nakada's work)



# Retrosynthetic Analysis



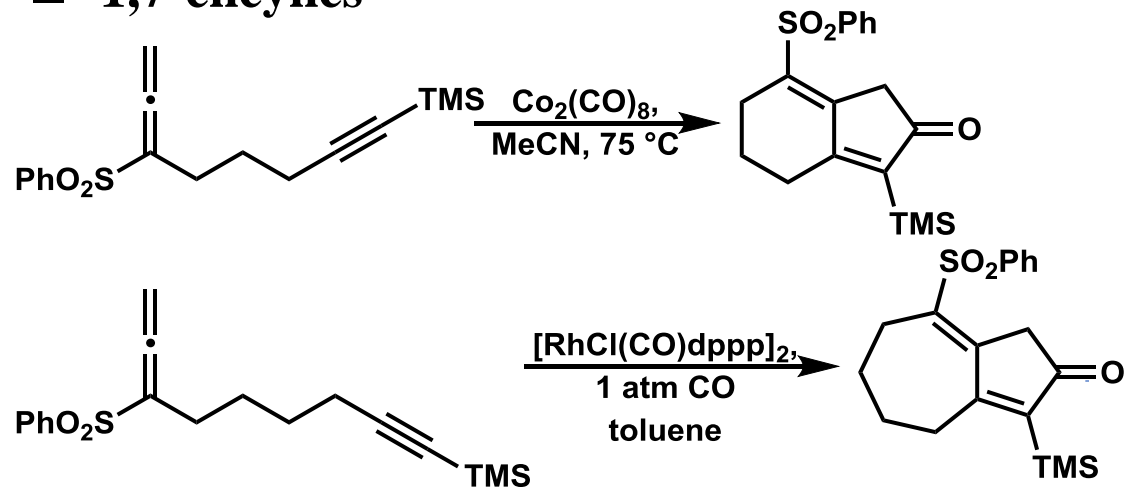
# Experimental procedures



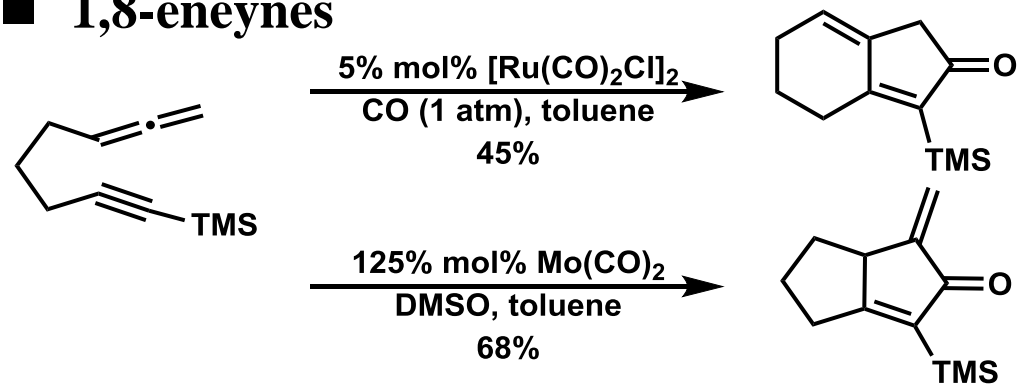
# P-K Reaction

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## 1,7-eneynes

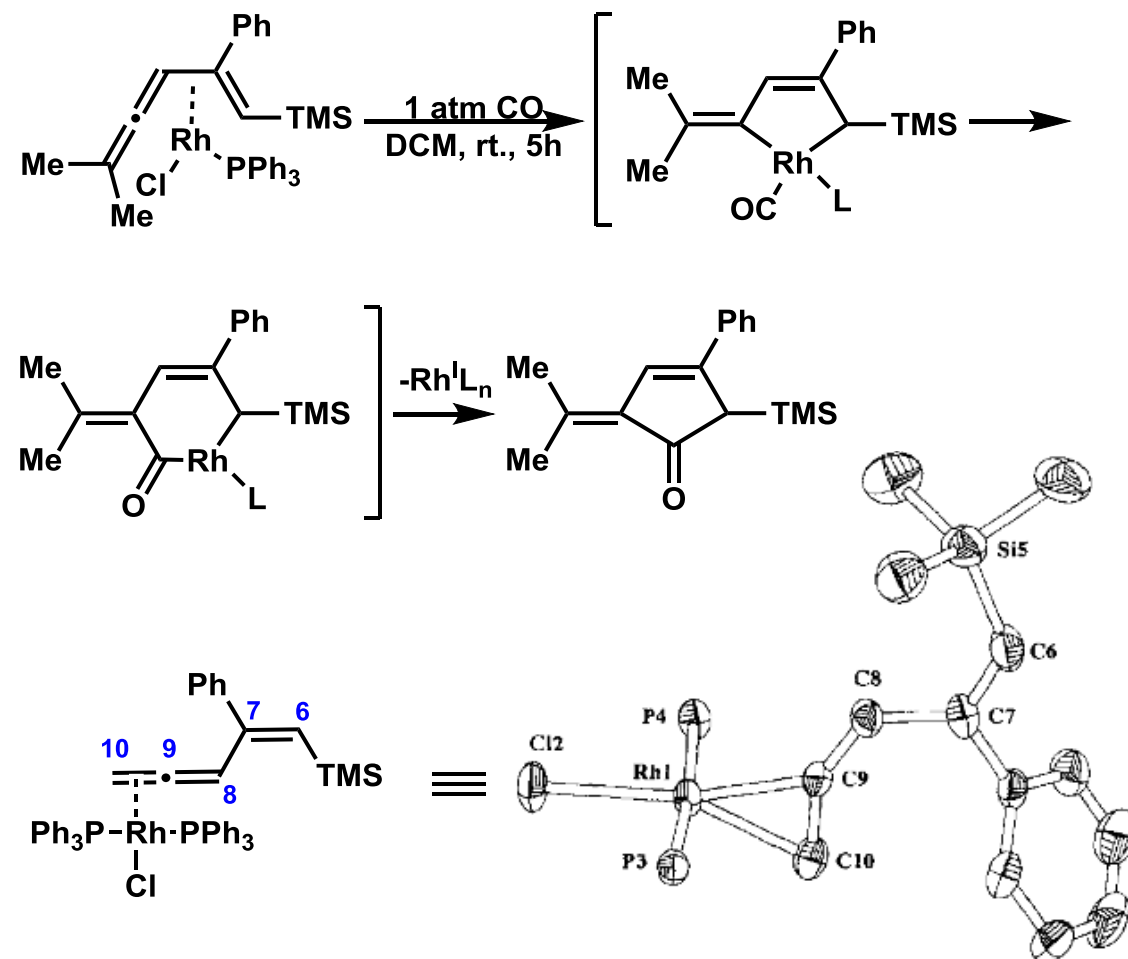


## 1,8-eneynes

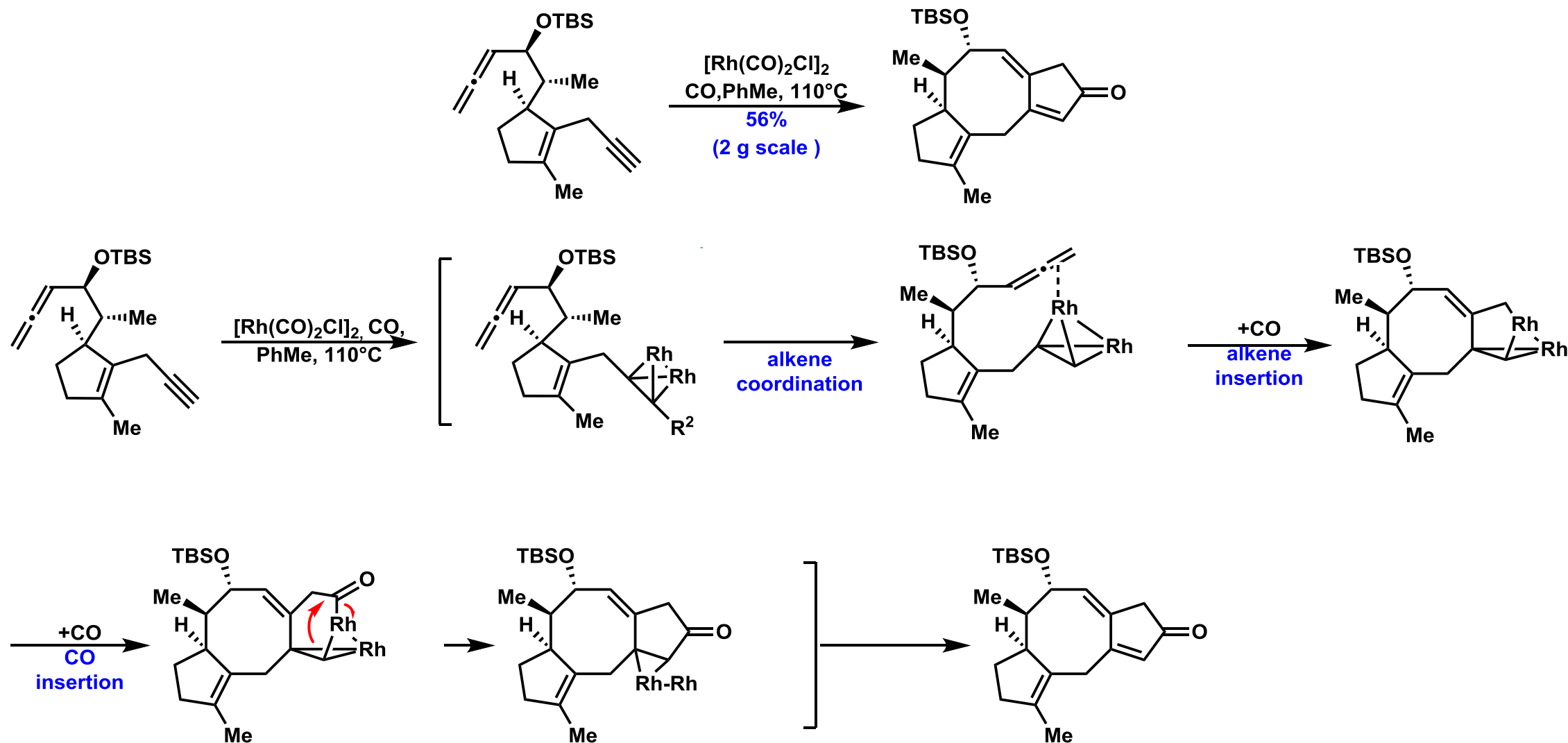


*Org. Lett.*, **2002**, 4, 11, 1931–1934;  
*Angew. Chem., Int. Ed. Engl.*, **1995**, 34, 2691;  
*J. Org. Chem.*, **2003**, 68, 1376–1385;  
*Org. Lett.*, **2002**, 4, 10, 1755–1758

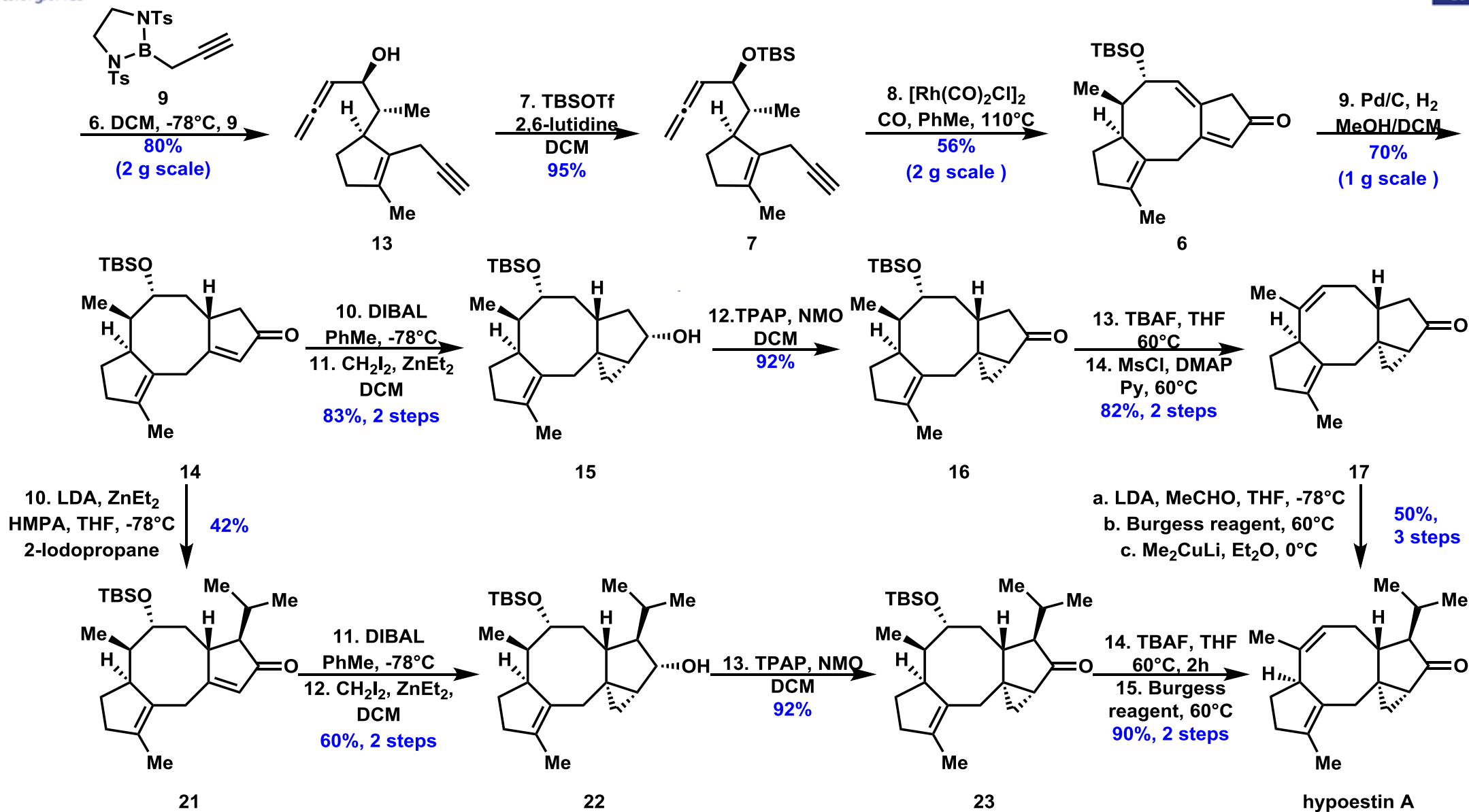
## [4+1]



# ■ 1,9-eneynes

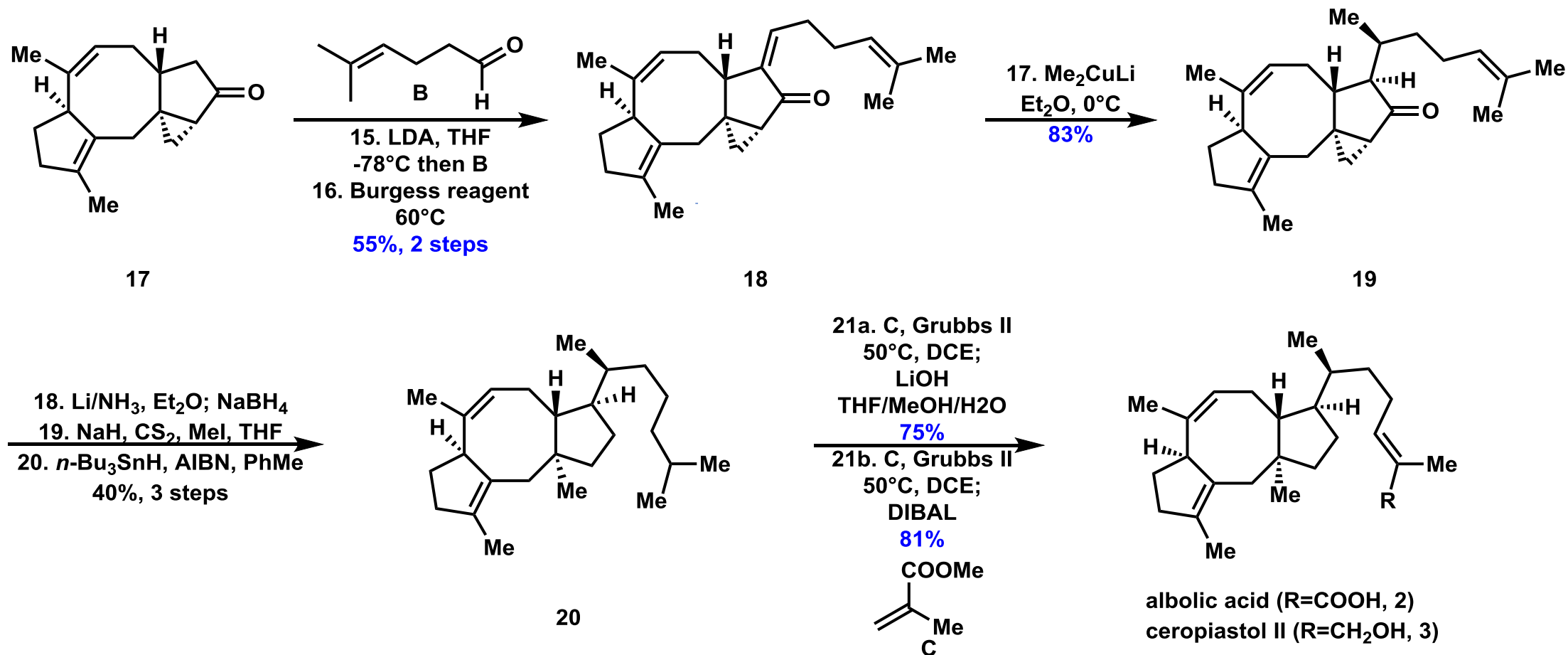


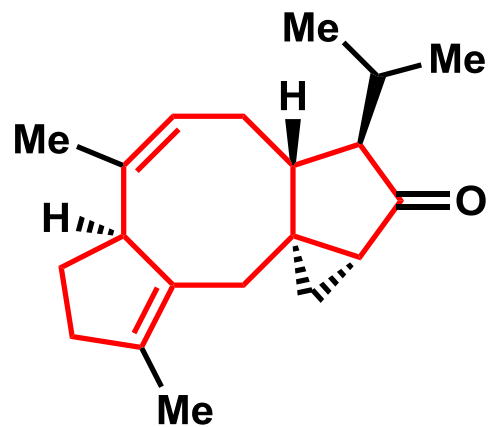
# Experimental procedures





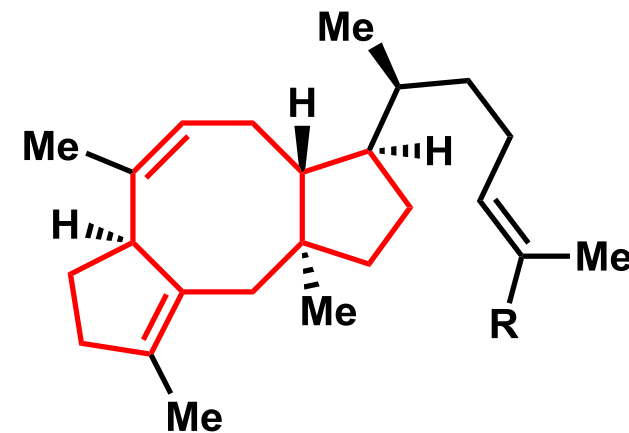
# Experimental procedures





**hypoestin A**

- First asymmetric total synthesis of hypoestin A
- 17 steps (0.021% overall yield)
- from commercially available (R)-limonene



**R=COOH, albolic acid**

**R=CH<sub>2</sub>OH, ceroplastol II**

- second asymmetric total syntheses of albolic acid and ceroplastol II
- 21 steps 0.0058% for albolic acid
- 21 steps 0.0063% for ceroplastol

**Thanks for Your Attention!**