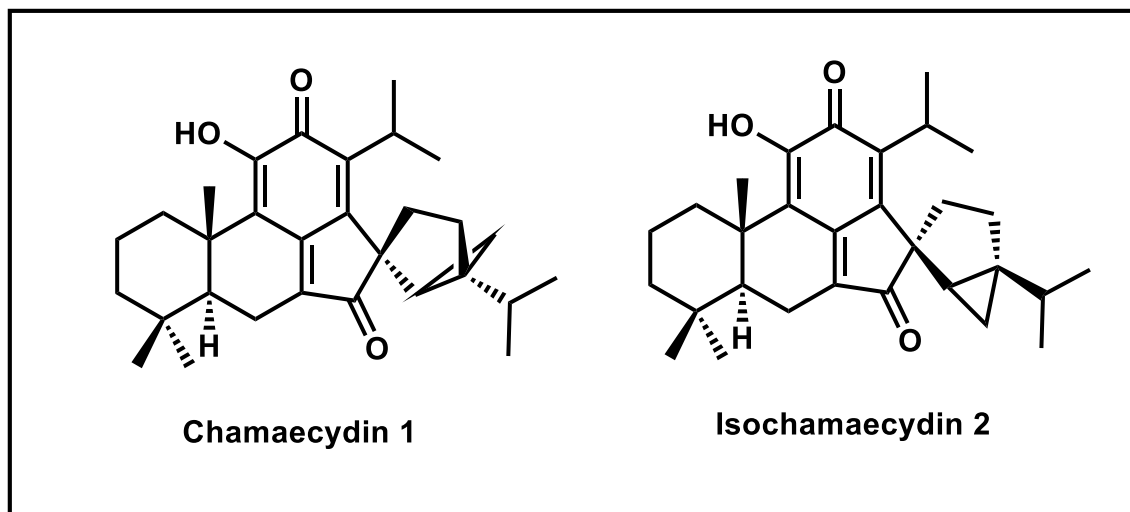


## RESEARCH ARTICLE

# Catalytic Asymmetric Total Synthesis of (+)-Chamaecydin and (+)-Isochamaecydin and their Stereoisomers

Yuan-He Zhang,<sup>[a,b]</sup> Le-Hua Deng,<sup>[a,b]</sup> Dong-Xing Tan,<sup>[a]\*</sup> and Fu-She Han<sup>[a,b]\*</sup>



Qi Lab. 2024 Annual Semiar  
Xiu HAN (D1)

# Cryptoquinonemethides (柳杉 *Cryptomeria*)



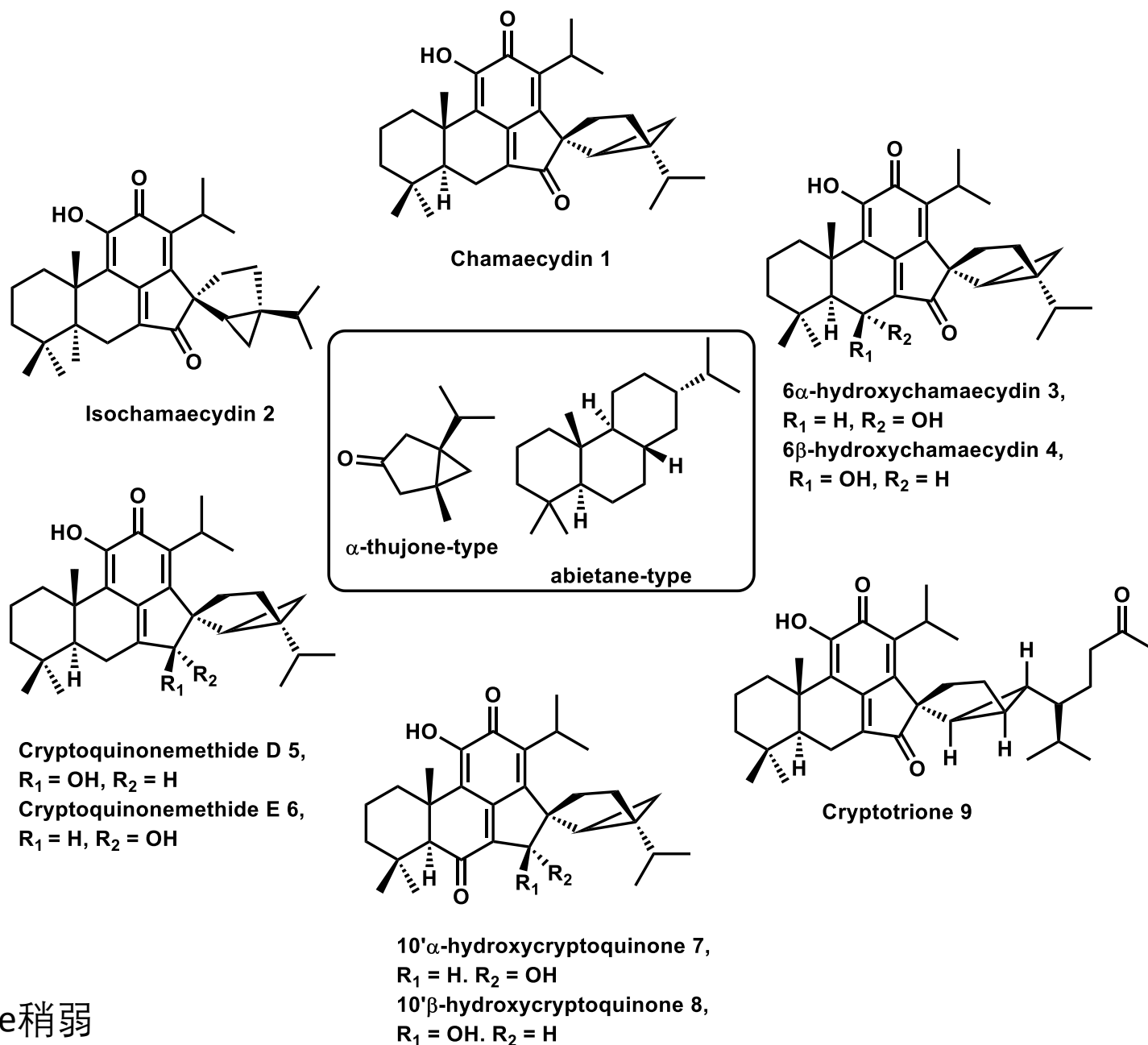
## 结构特性:

含亚甲基苯醌香松烷二萜骨架  
柏酮型双环[3,1,0]己烷结构

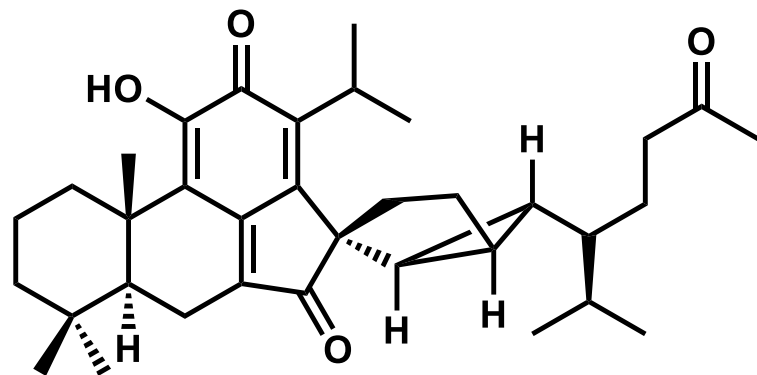
## 生物活性:

**Chamaecydin:** 对农业害虫 *Spodoptera litura* 表现出进食阻碍活性

**Cryptotrione:** 对人类口腔癌 KB 细胞的 IC<sub>50</sub> 值为  $6.44 \pm 2.23 \mu\text{M}$ , 仅比临床使用的抗癌药 etoposide 稍弱

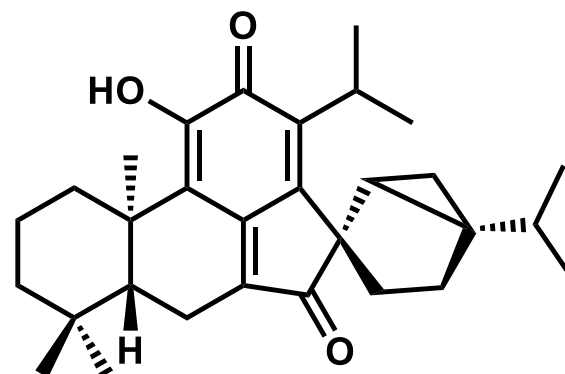


# Previous work : total synthesis of cryptotrione, (-)-chamaecydin/(-)-isochamaecydin

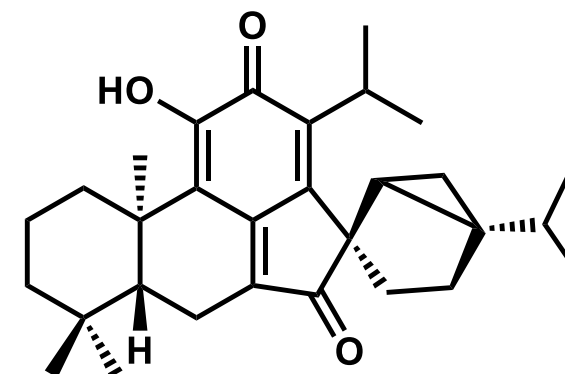


Cryptotrione

Xiaoshui Peng Lab.  
*Angew. Chem. Int. Ed.* 2020, 59, 19929  
27 LLSs



(-)-chamaecydin

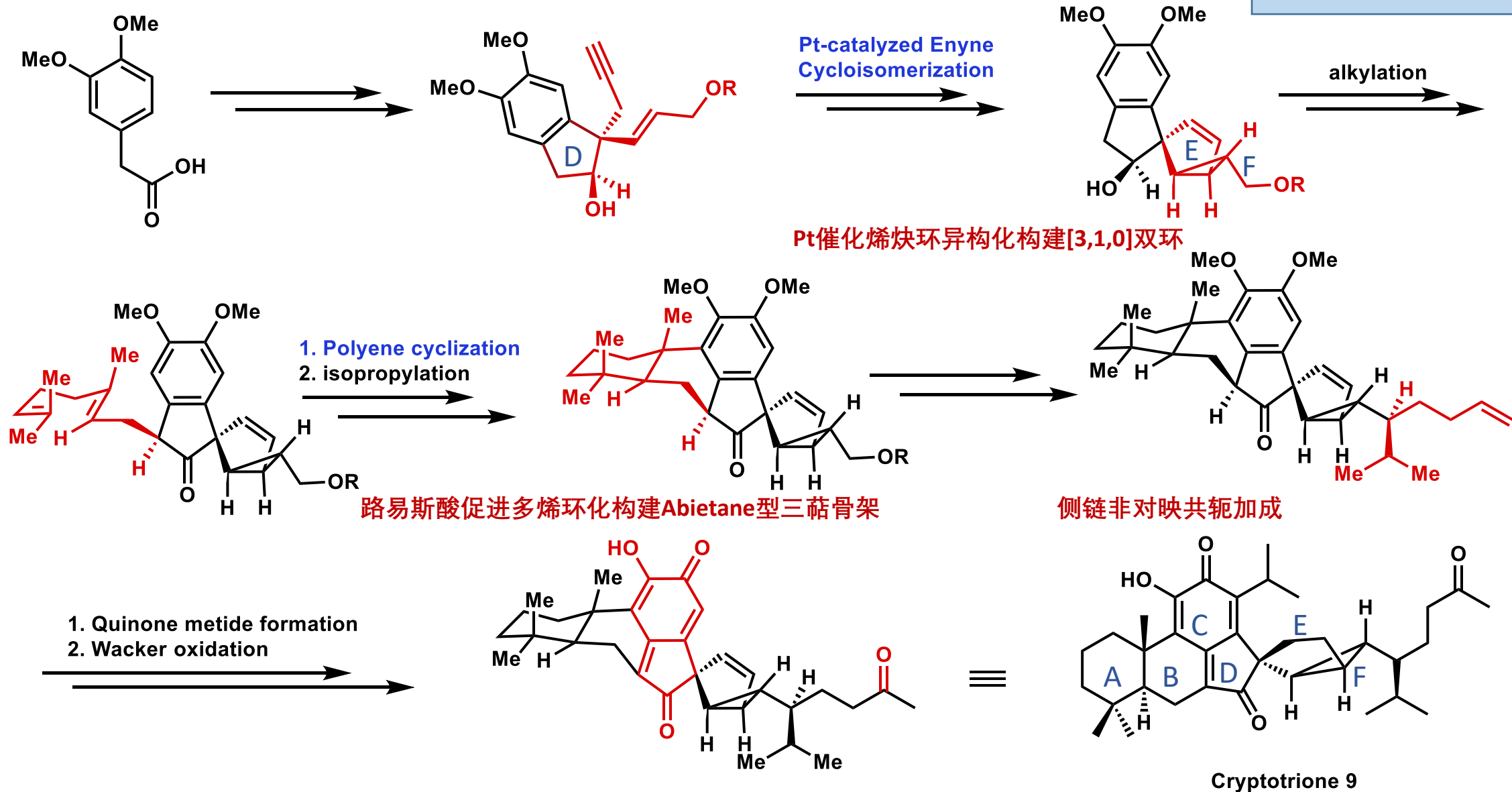


(-)-isochamaecydin

Zhixiang Xie Lab.  
*Org. Lett.* 2023, 259, 7769-7774  
18-20 LLSs

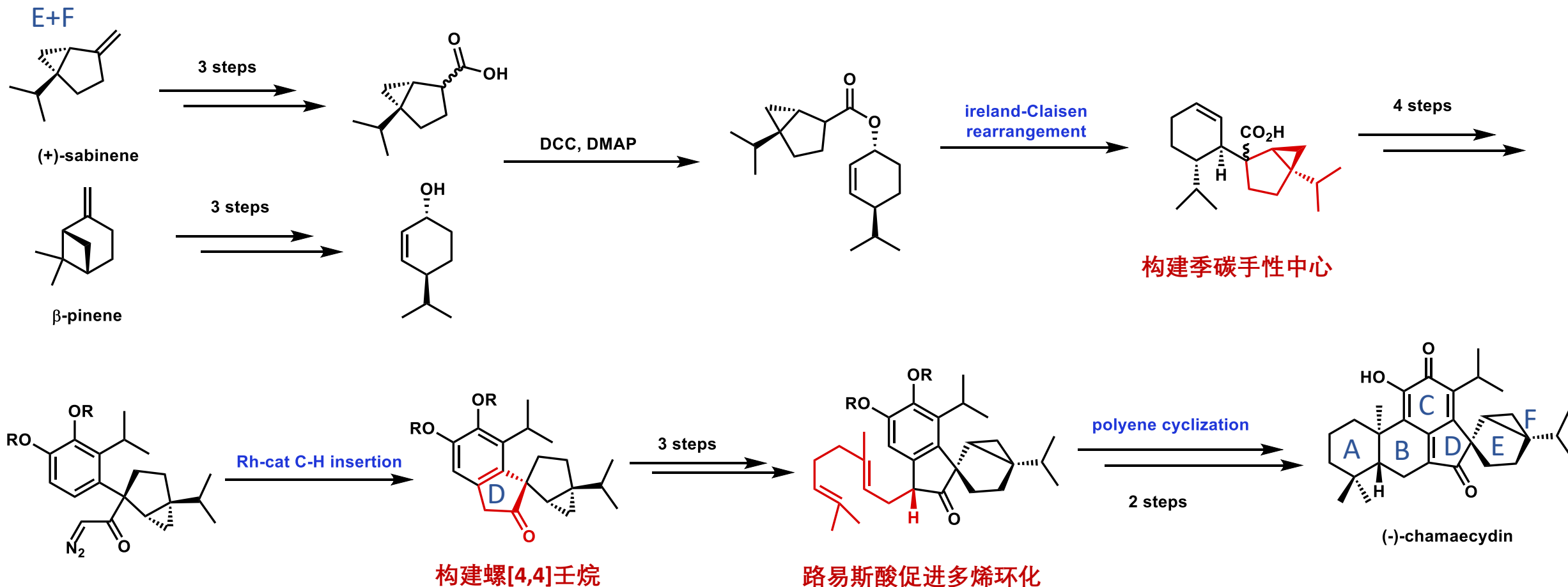
# Previous work : total synthesis of Cryptotrione (Peng Lab., 2020)

Synthetic design:  
C-D-(E+F)-(A+B)



# Previous work : total synthesis of (-)-Chamaecydin (Xie Lab., 2023)

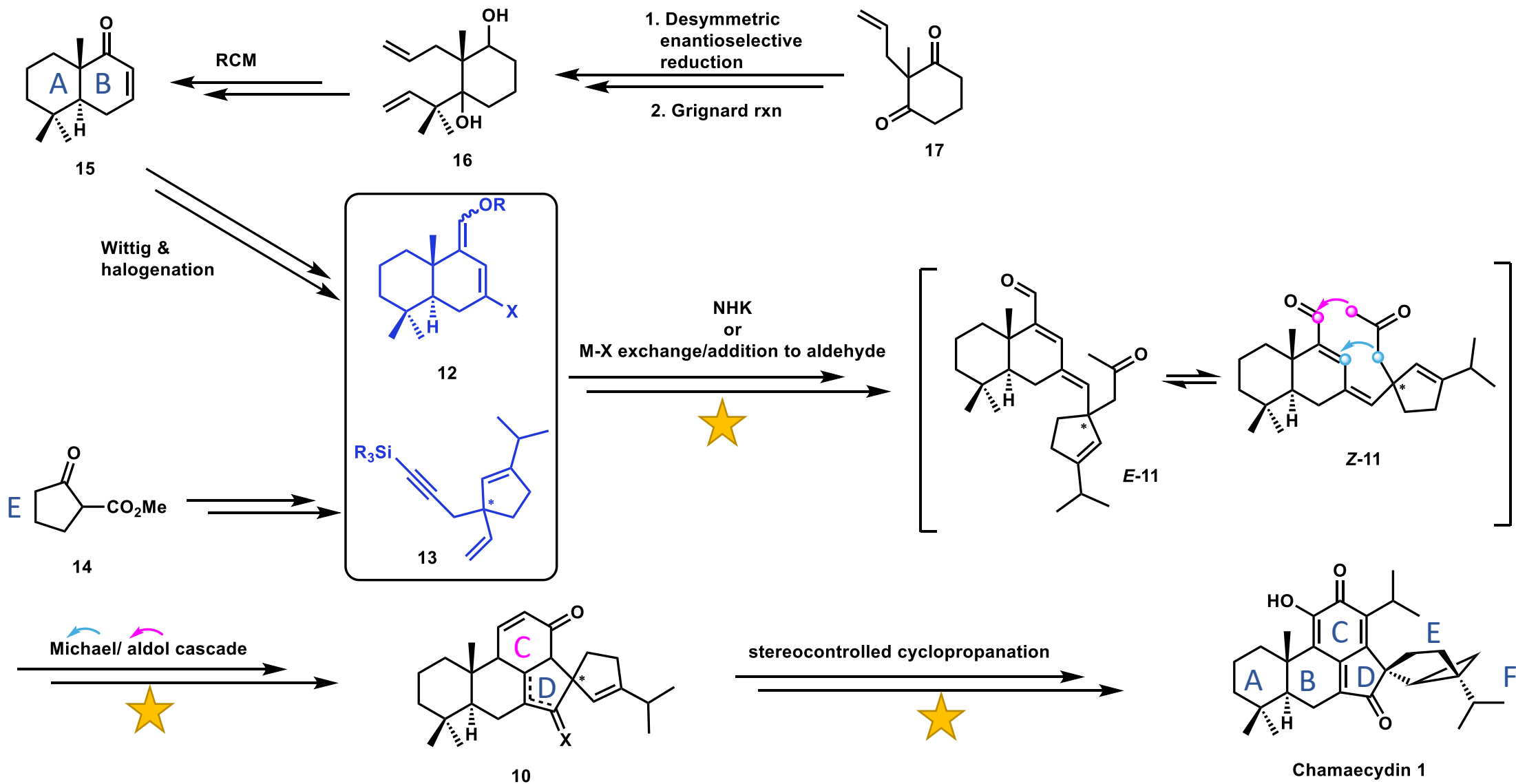
Synthetic design:  
C+(E+F)-D-(A+B)



(-)-sabinene无法商业获得，无法实现(+)-chamaecydin全合成

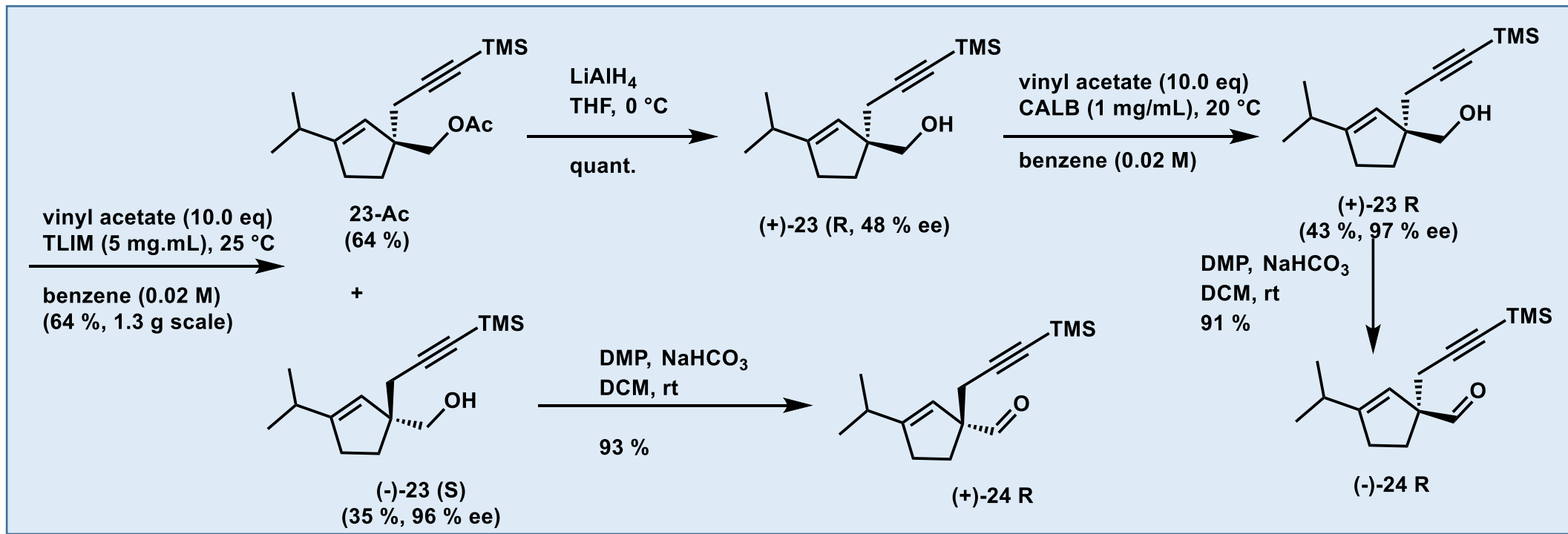
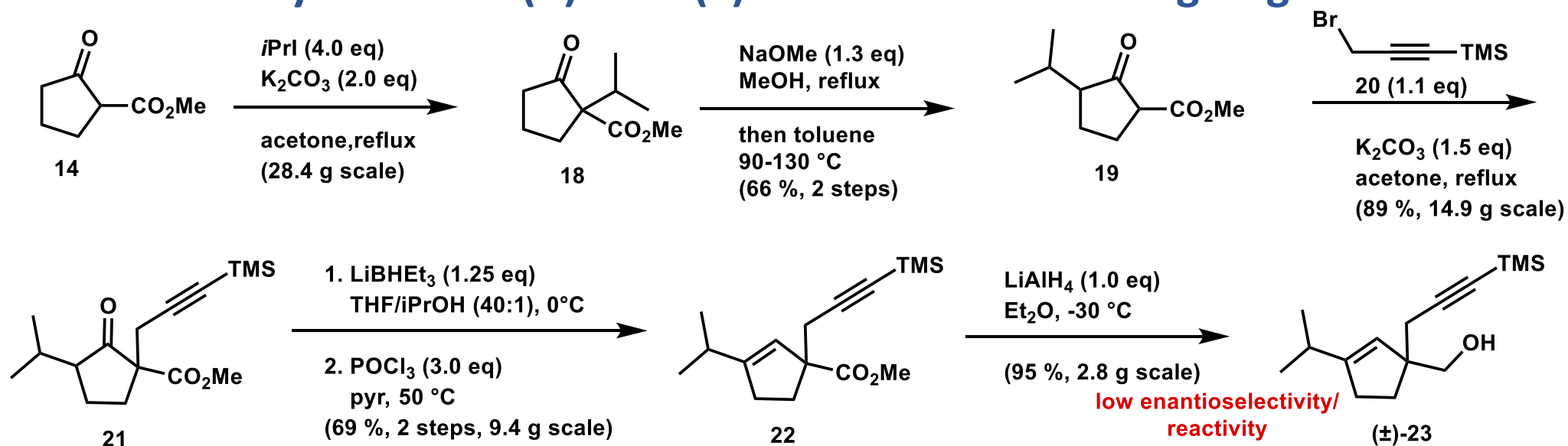
# This work: total synthesis of (+)-Chamaecydin, (+)-Isohamaecydin and their isomers (Han Lab., 2025)

Synthetic design:  
Convergent strategy  
(B+A)+E-(C+D)-F



16 LLSs from known compound, 17 LLSs from commercially available compound

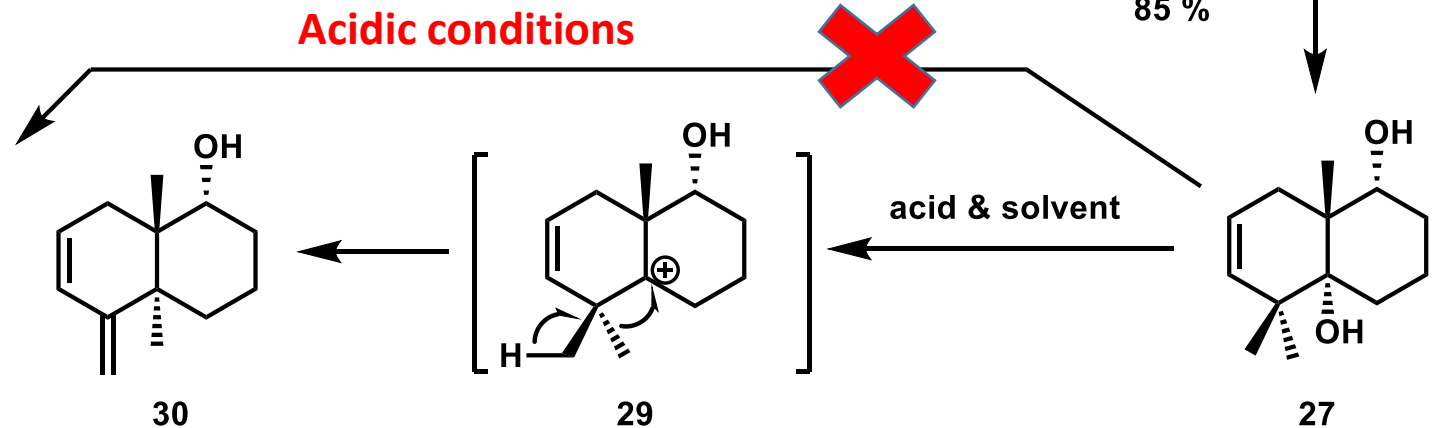
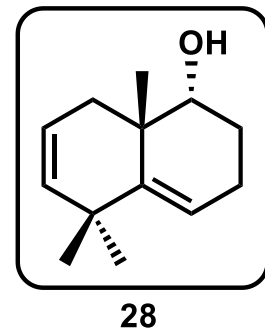
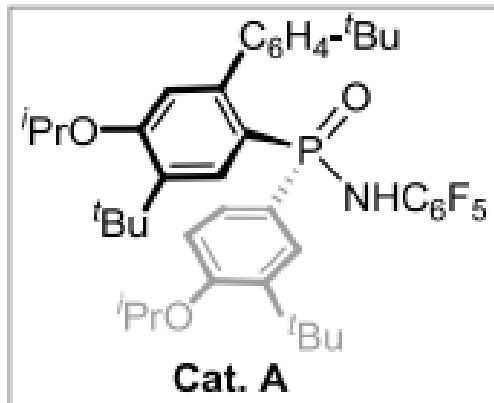
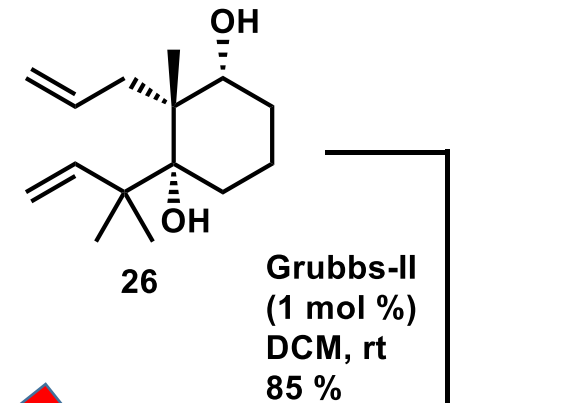
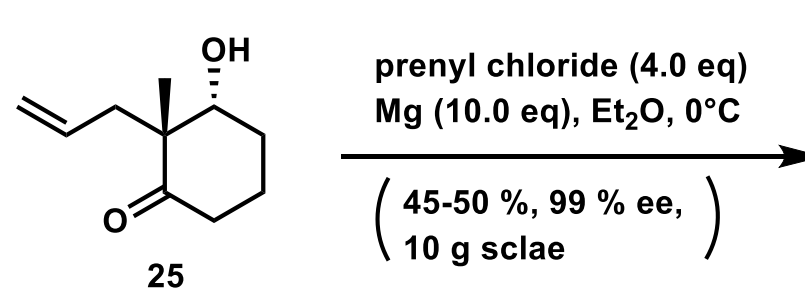
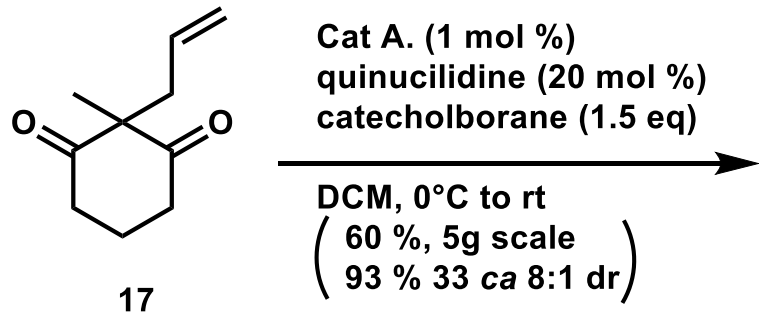
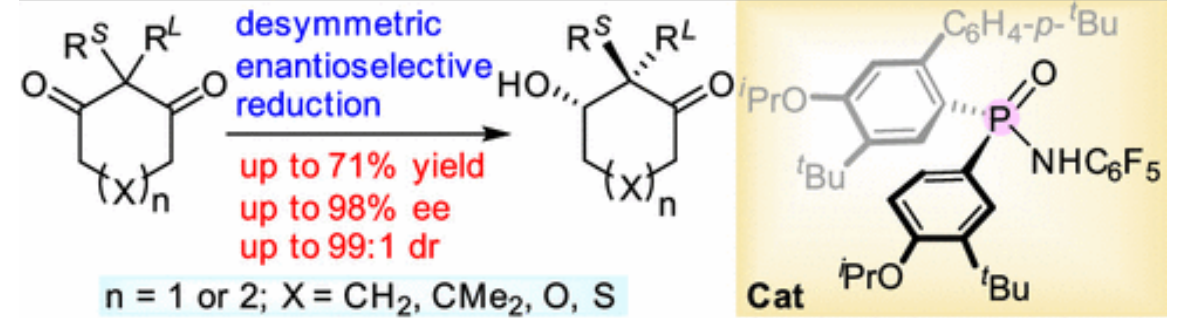
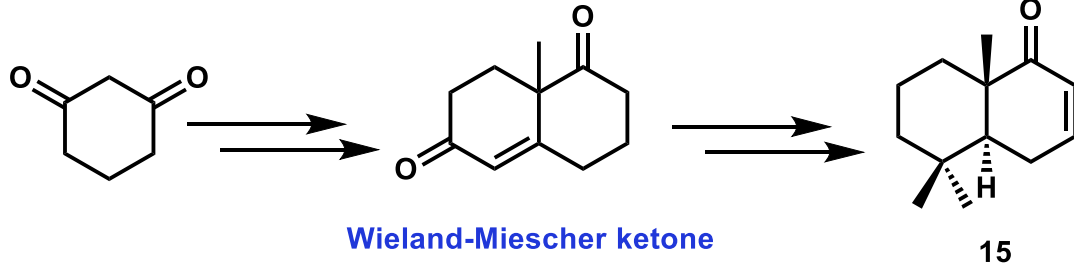
# Part 1. Synthesis of (R)- and (S)-five-membered E ring fragment



## Part 2. Synthesis of A-B ring fragment 39 and 40

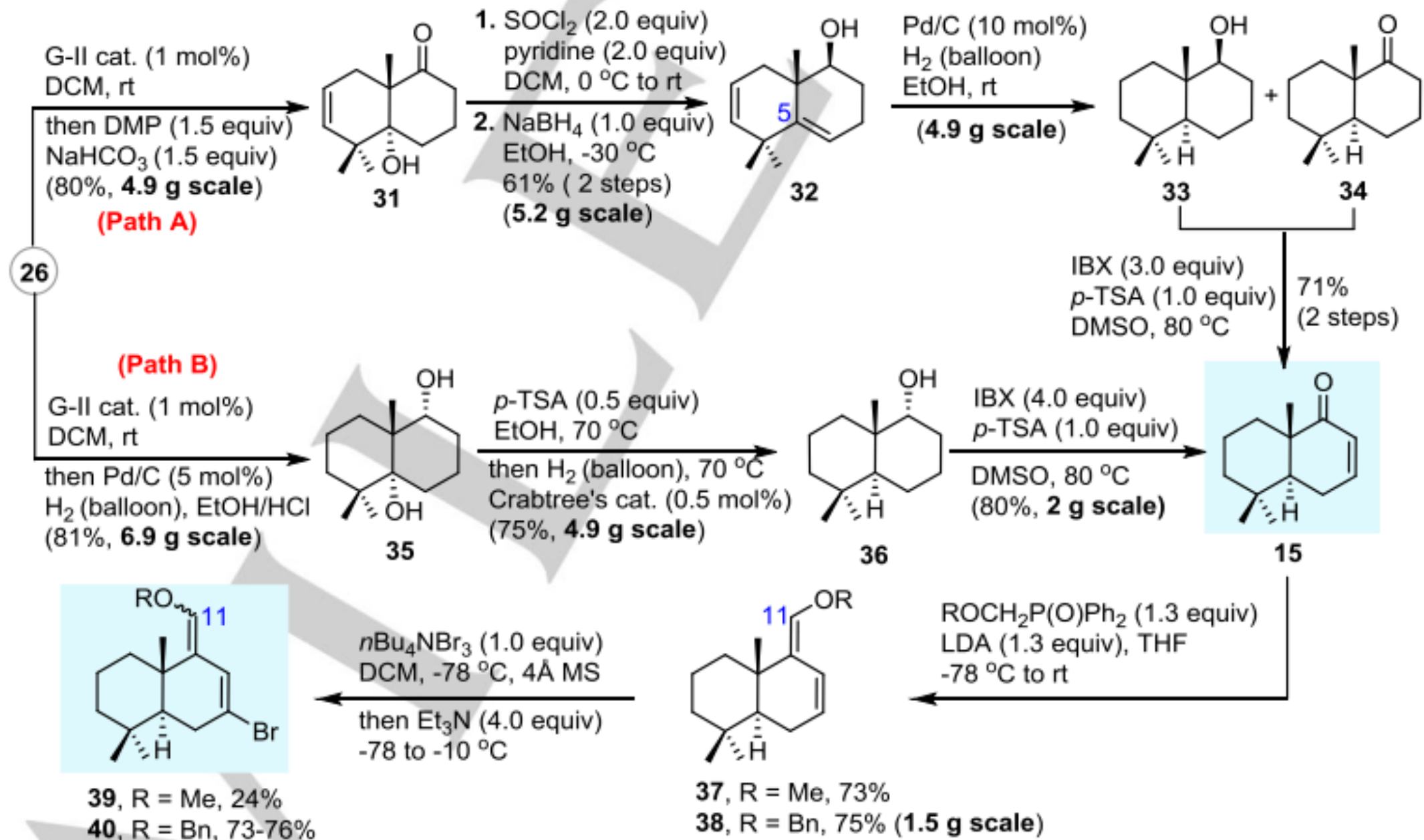
*J. Am. Chem. Soc.* **2021**, 143, 2994

11 linear steps

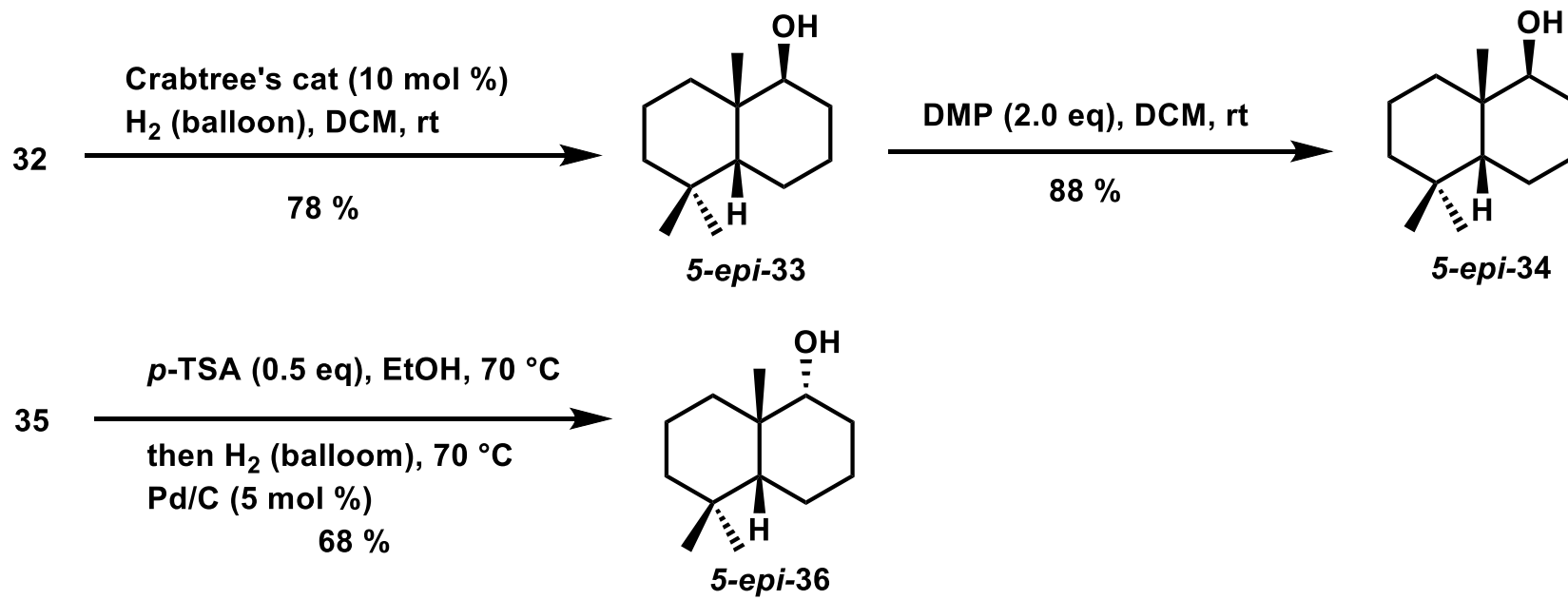




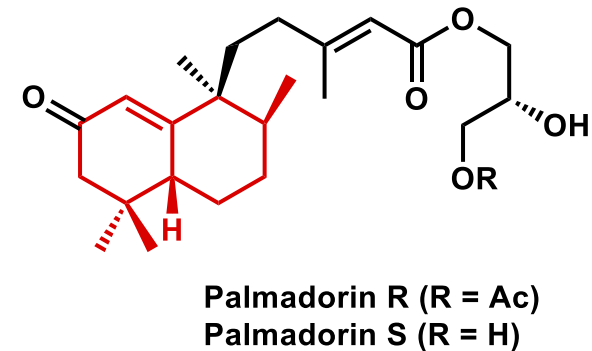
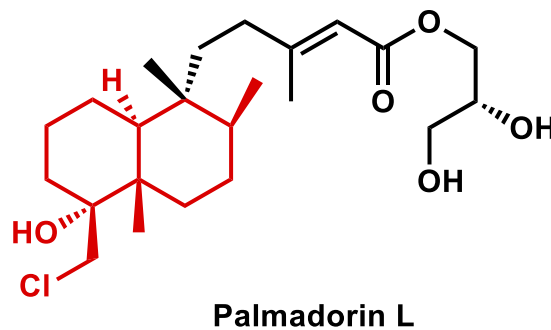
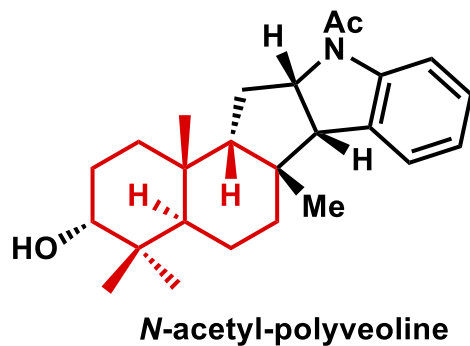
## Part 2. Synthesis of A-B ring fragment 39 and 40



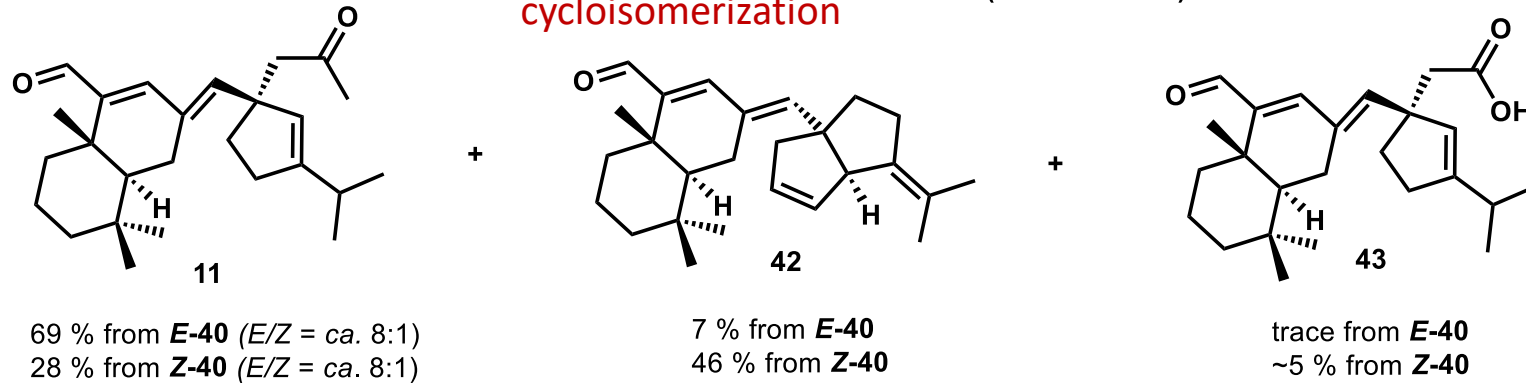
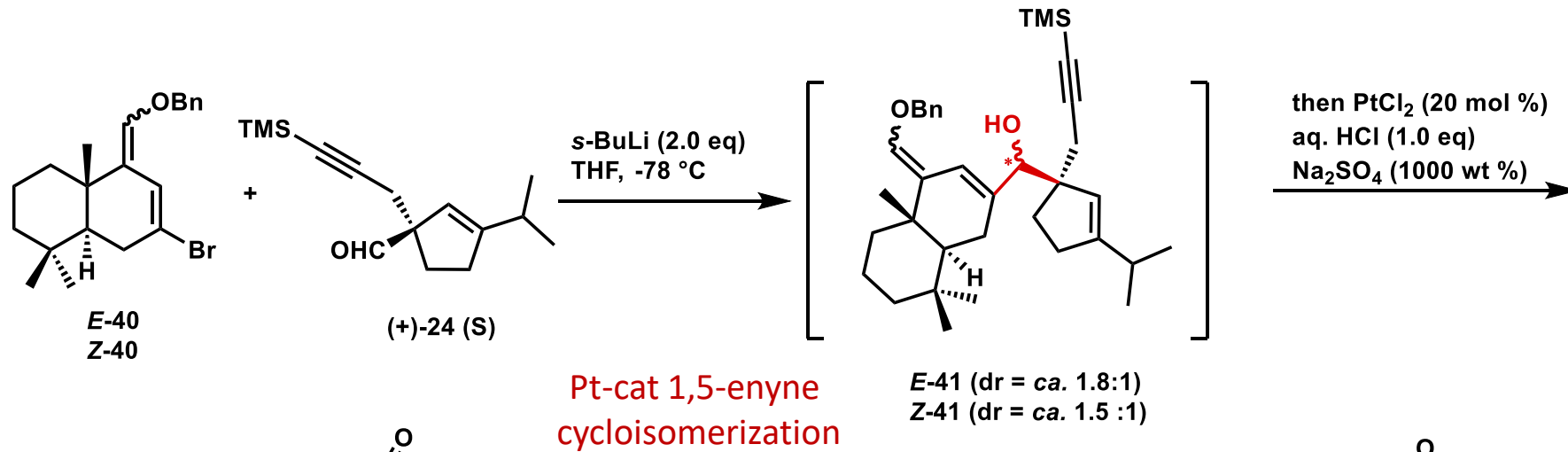
## Part 2. Synthesis of A-B ring fragment 39 and 40



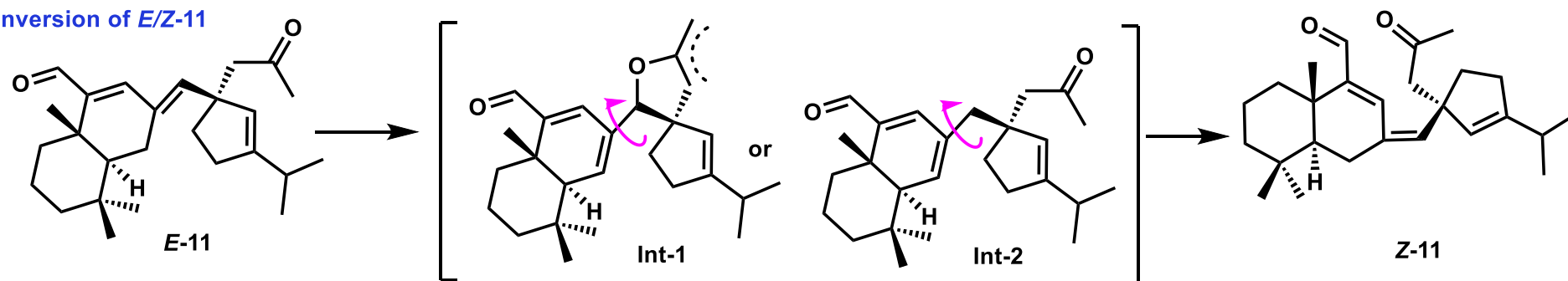
Potential chiral building blocks for:



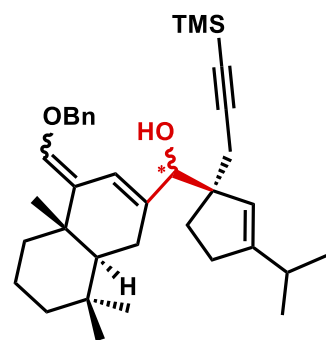
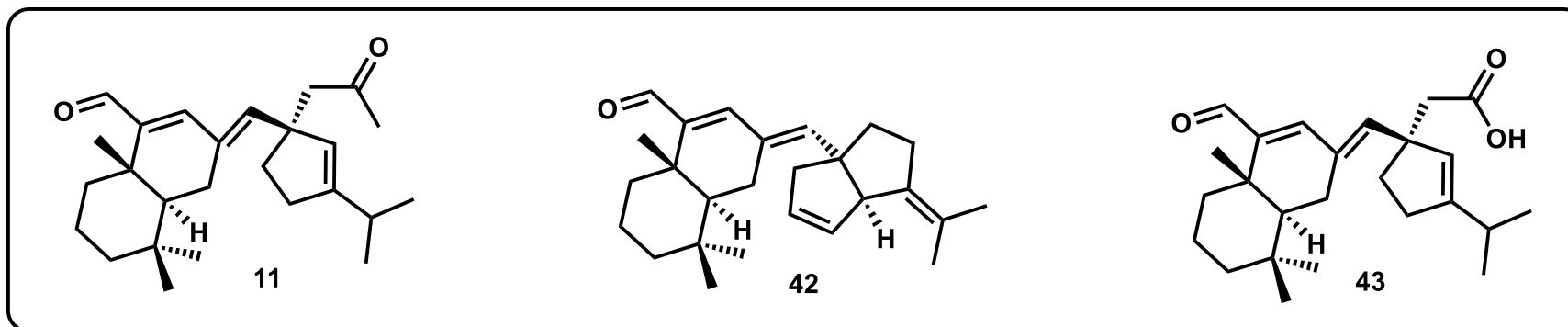
# Part 3. Synthesis of 11



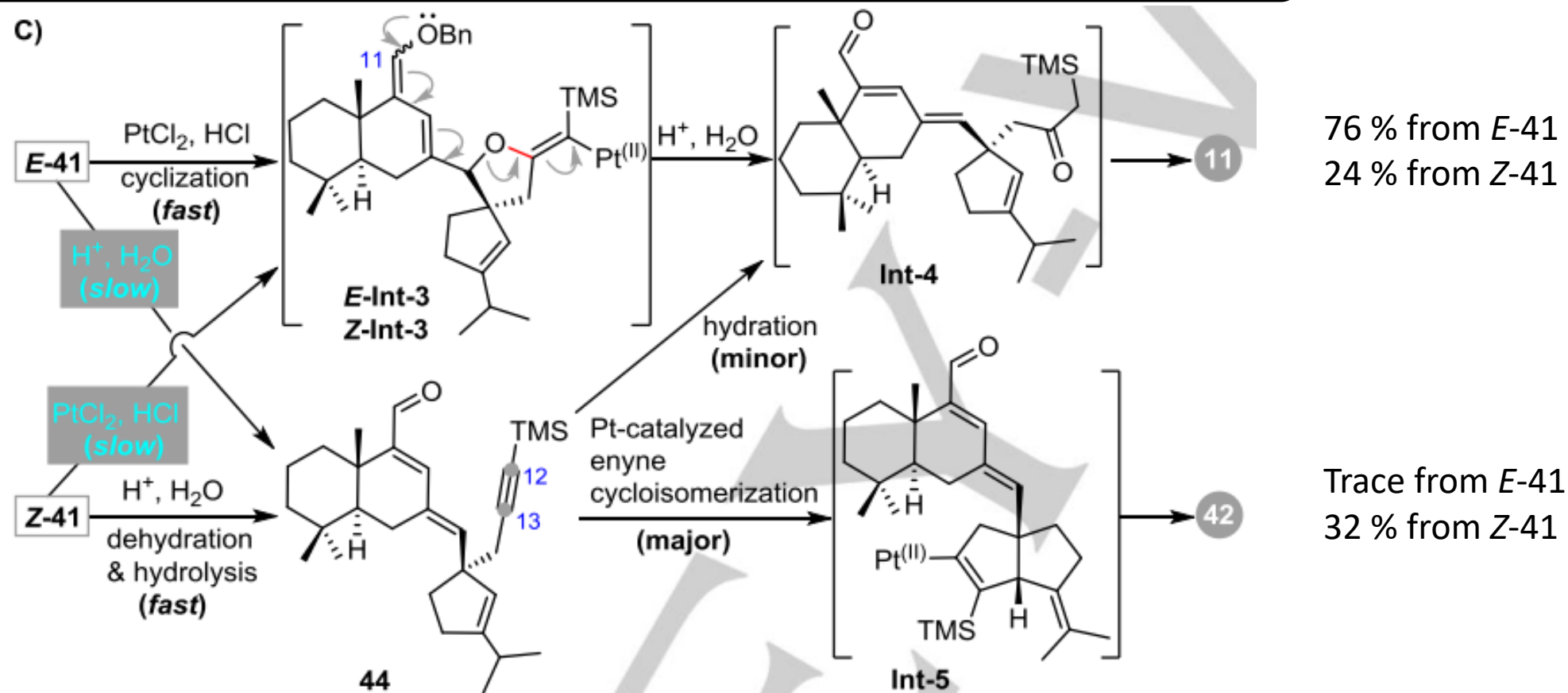
inversion of **E/Z-11**



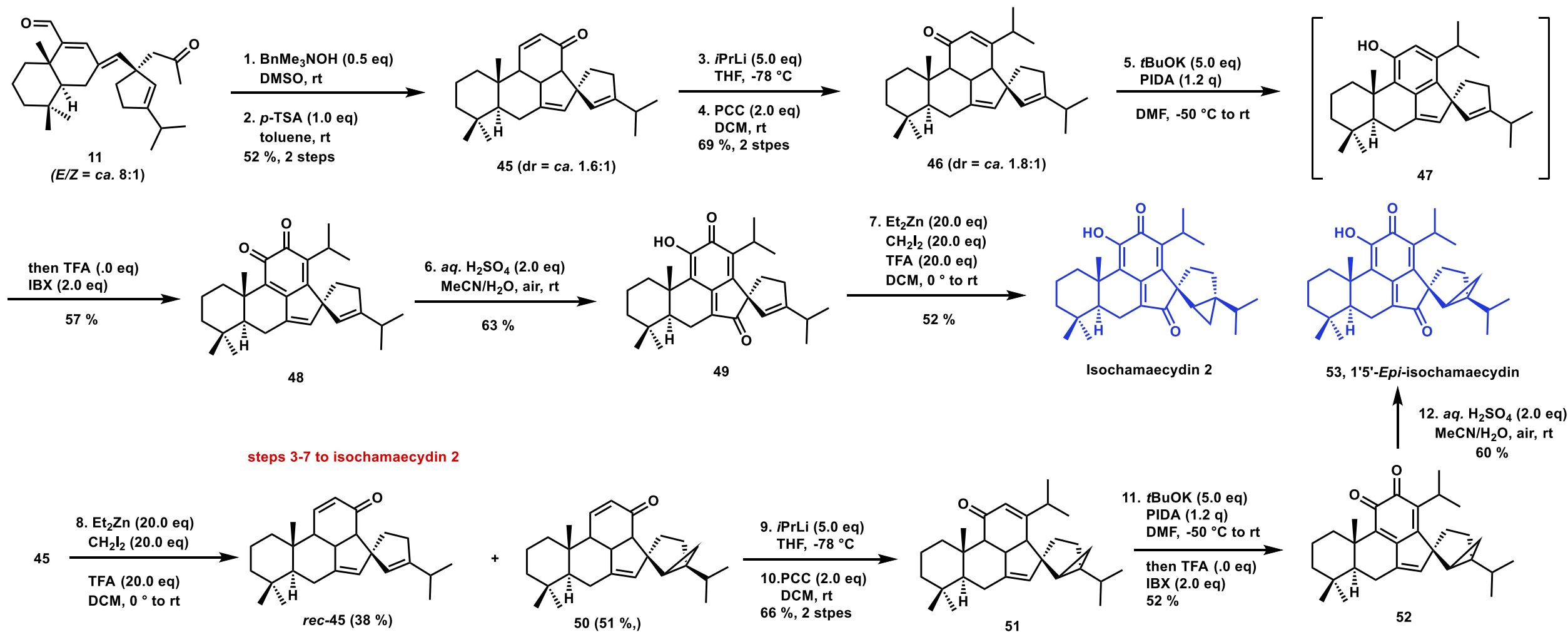
## Part 3. Synthesis of 11: reaction mechanism



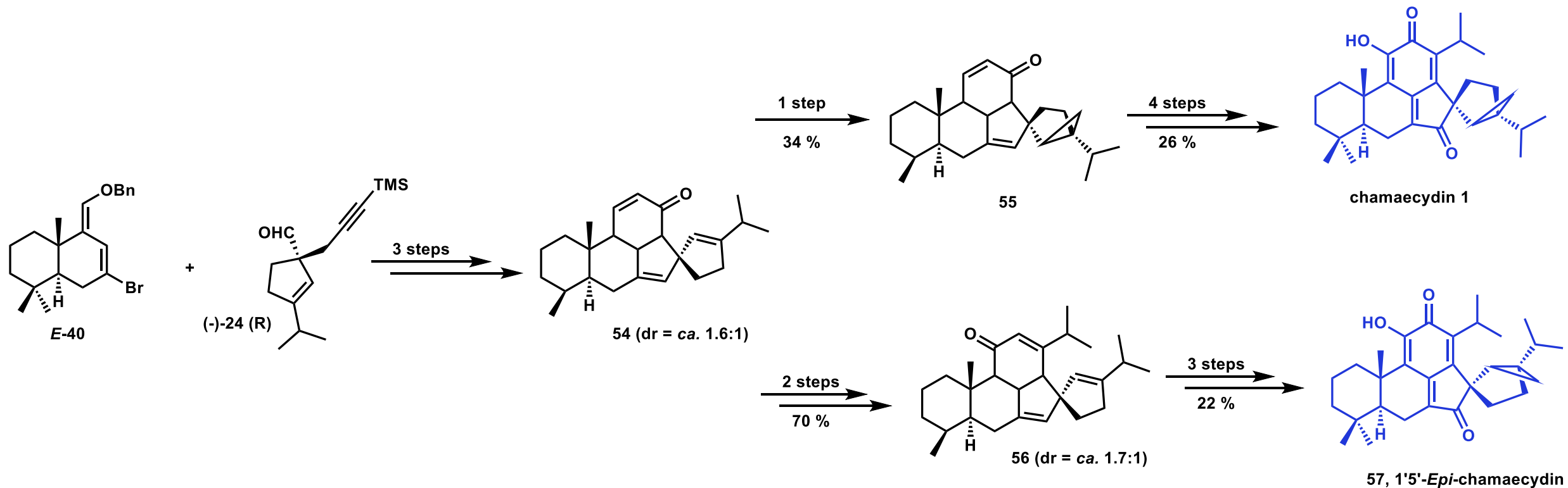
*E*-41 (dr = ca. 1.8:1)  
*Z*-41 (dr = ca. 1.5:1)



# Part 4. Completion of the total synthesis of (+)-isochamaecydin and 1',5'-Epi-isochamaecydin



## Part 5. Completion of the total synthesis of (+)-chamaecydin and 1',5'-Epi-chamaecydin



Thanks for listening!