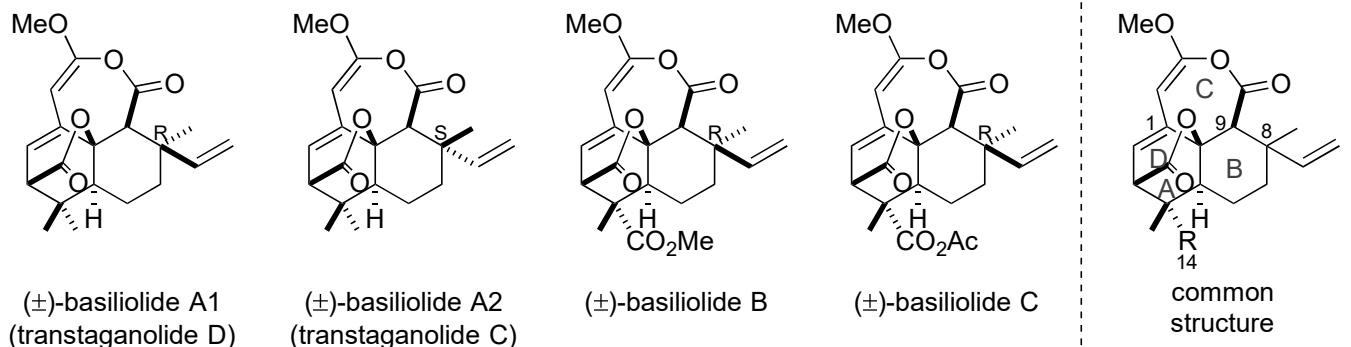


Topic : A Total Synthesis of (±)-Basilolide B by Lee *et al.*

Min, L. *et al.*, *Angew. Chem. Int. Ed.* **2014**, 53, 1294.

Introduction

1. About basilolide



Isolation : A plant *Thapsia garganica*

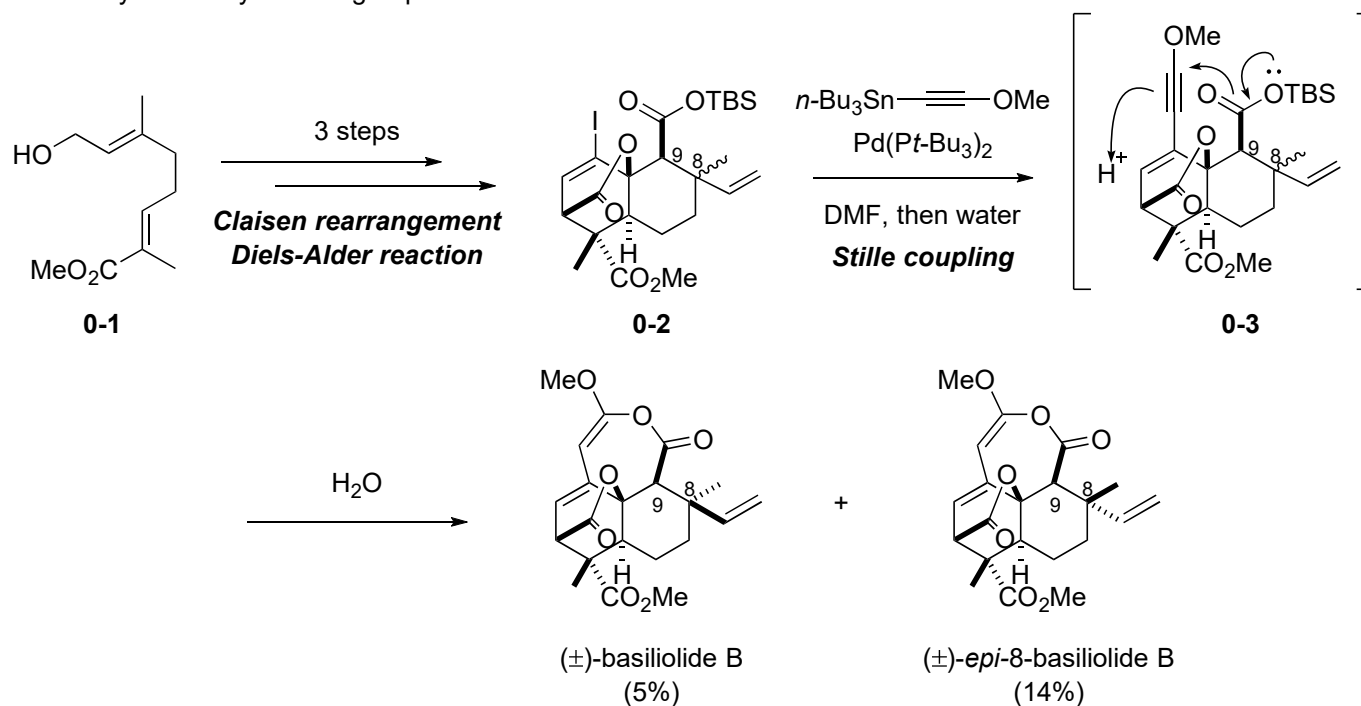
Appendino, G. *et al.*, *J. Nat. Prod.* **2005**, 68, 1213.

Bioactivity : Mobilization of intracellular  $Ca^{2+}$  and NFAT activation in the leukemia T-cell line Jurkat

Navarrete, C. *et al.*, *J. Pharmacol. Exp. Ther.* **2006**, 319, 422.

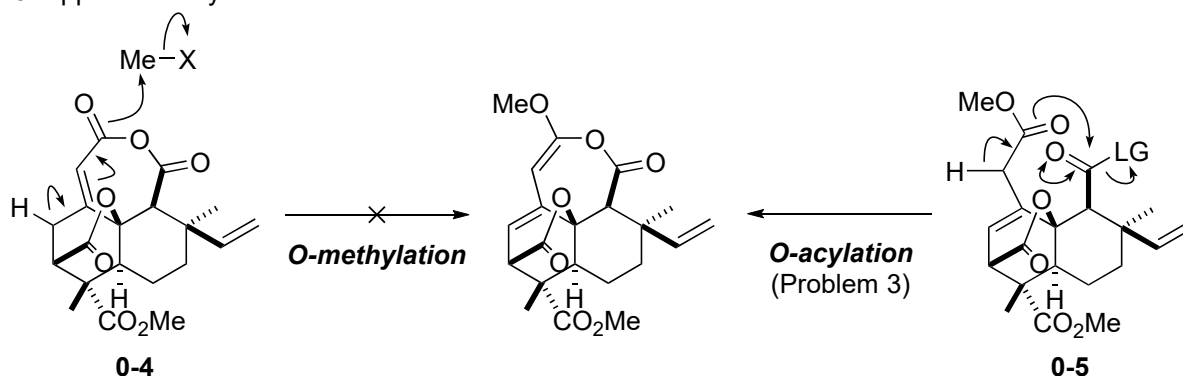
Features : Tetracyclic core including a seven-membered ring, a *trans*-decalin framework, a lactone bridge

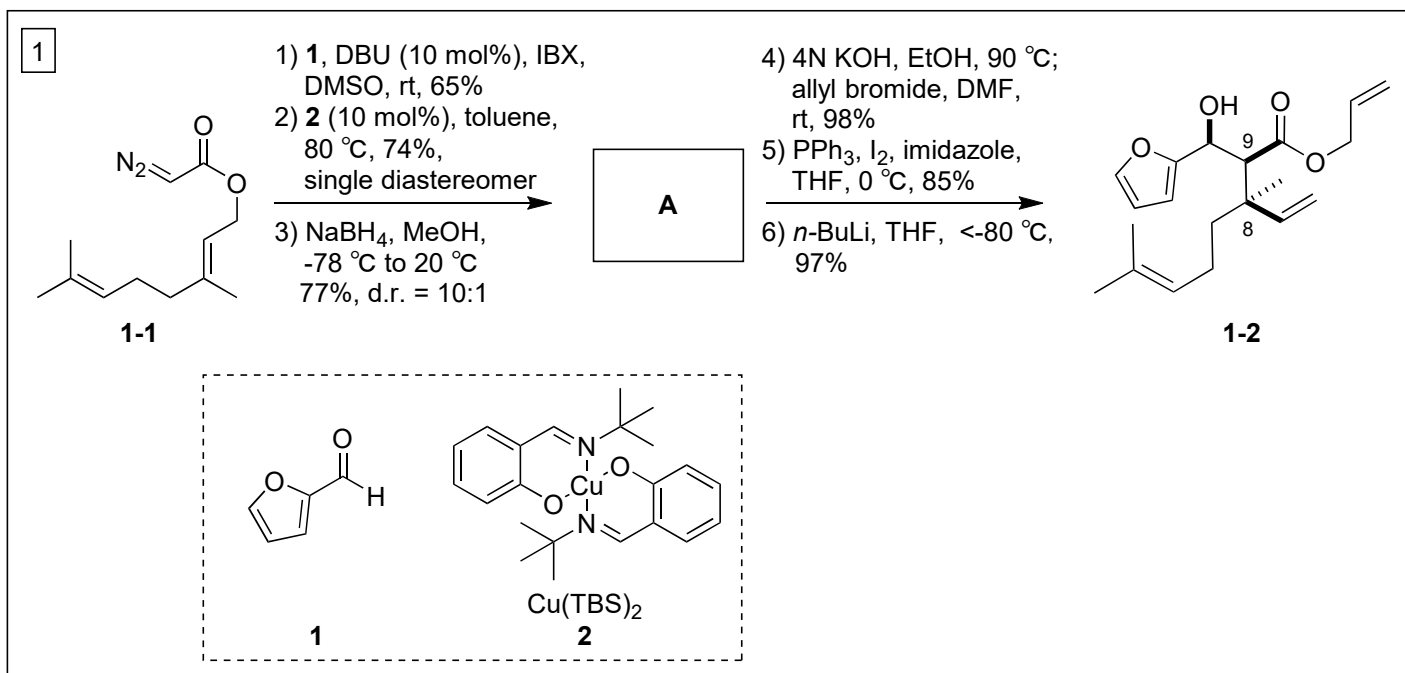
2. Total synthesis by Stoltz's group



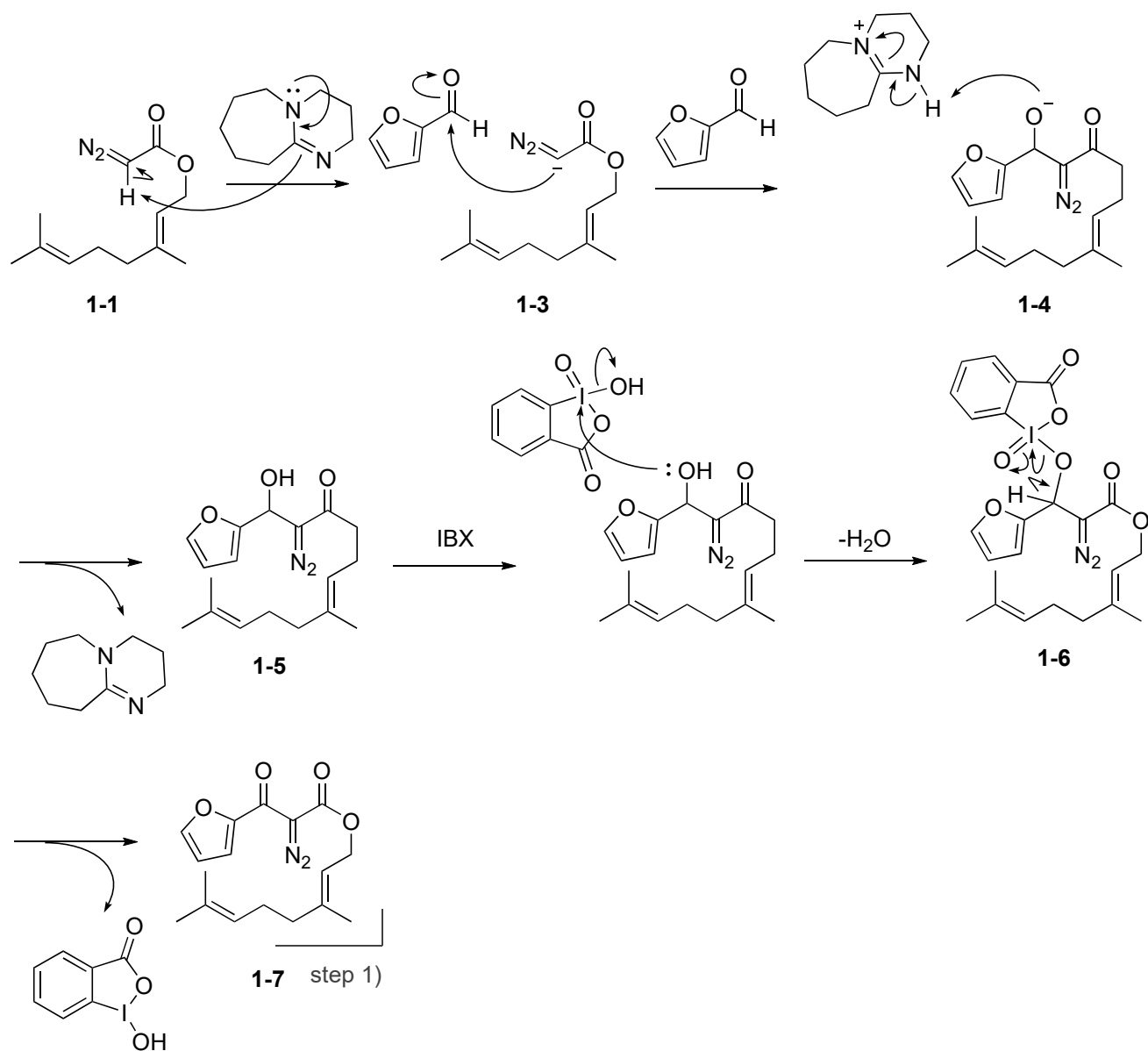
Nelson, H. M. *et al.*, *Angew. Chem. Int. Ed.* **2011**, 50, 3688.

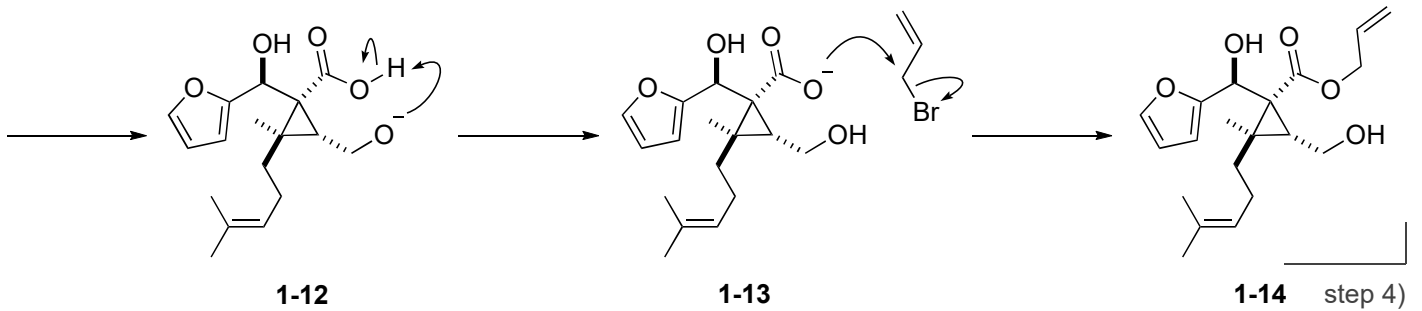
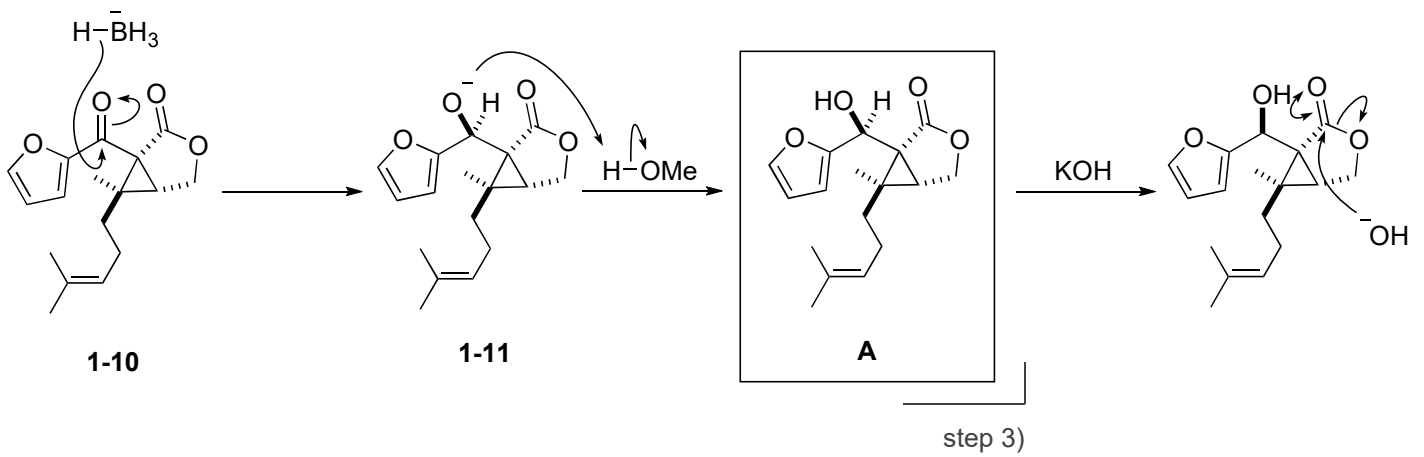
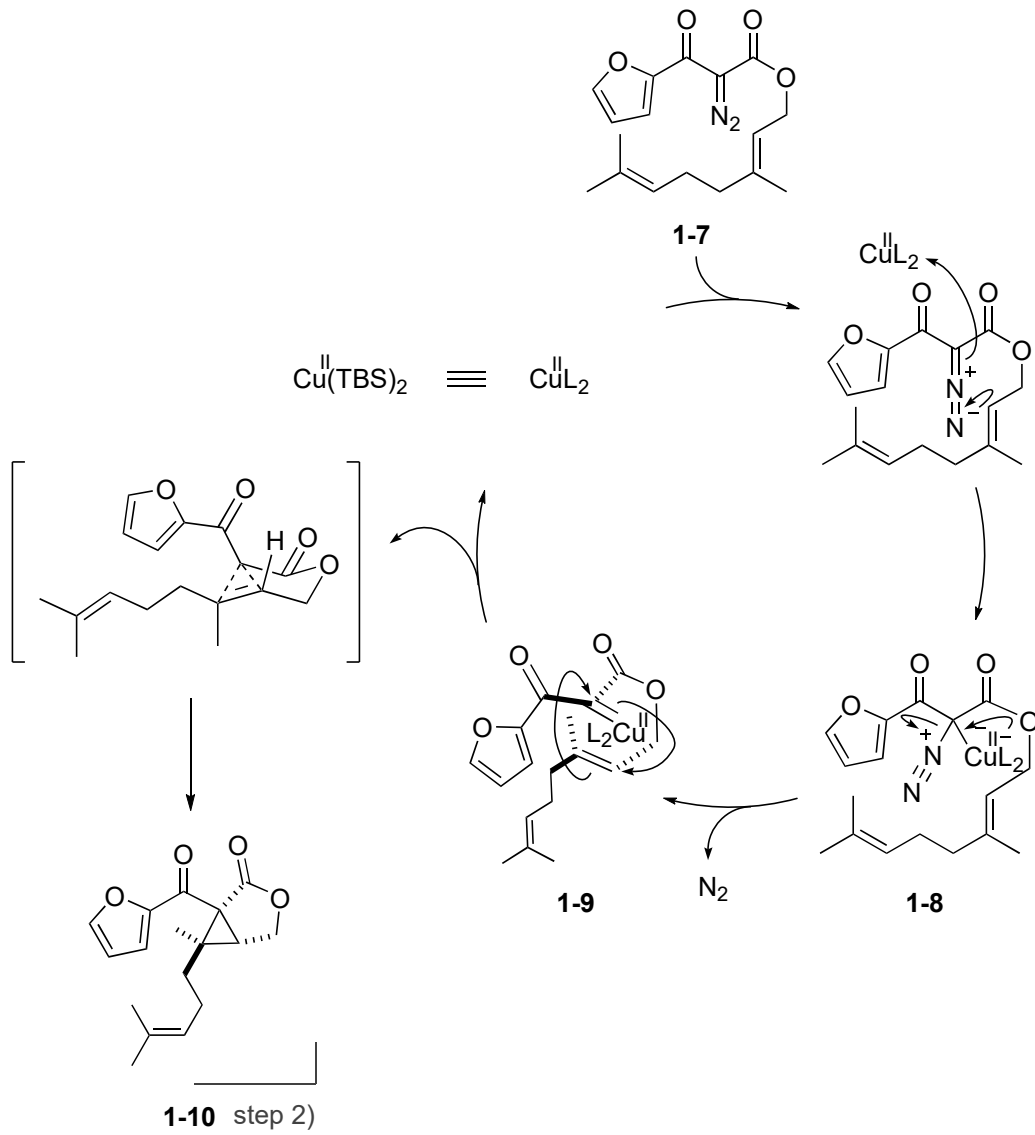
3. Approaches by authors

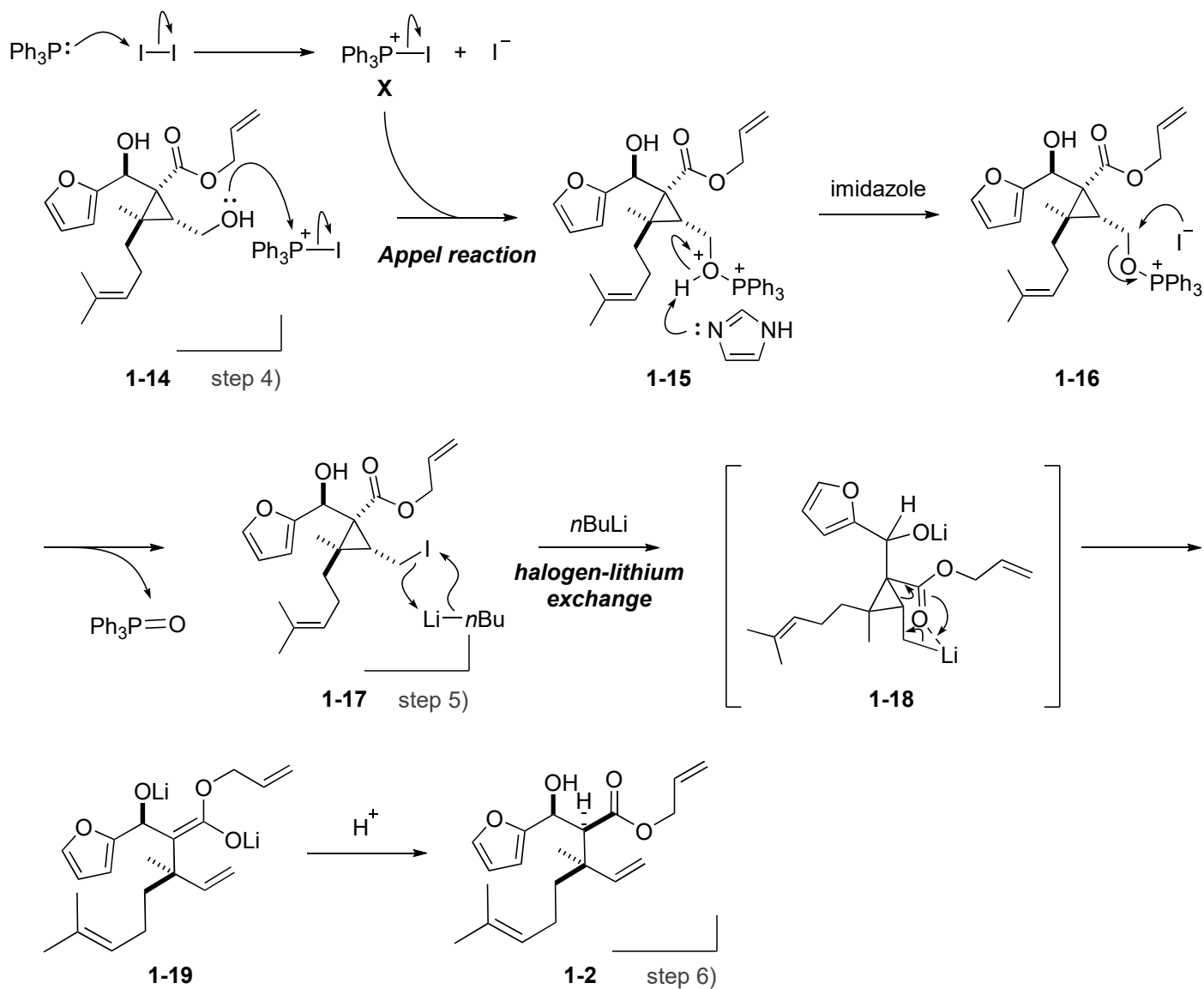




**Establishment of the stereogenic centers at C8 and C9**



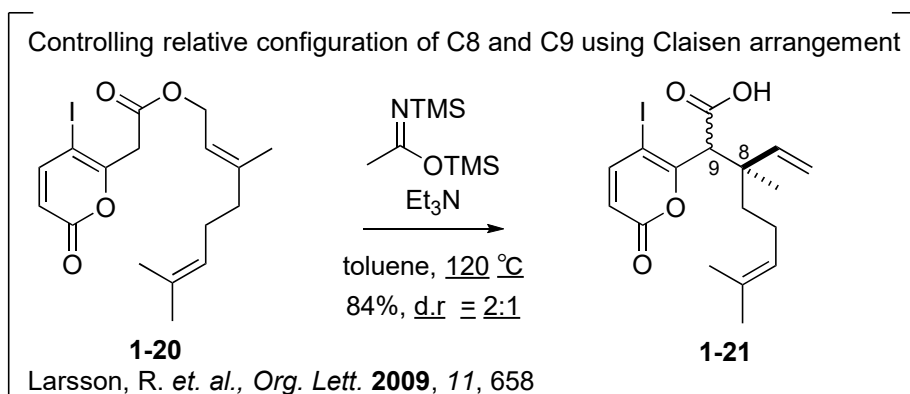




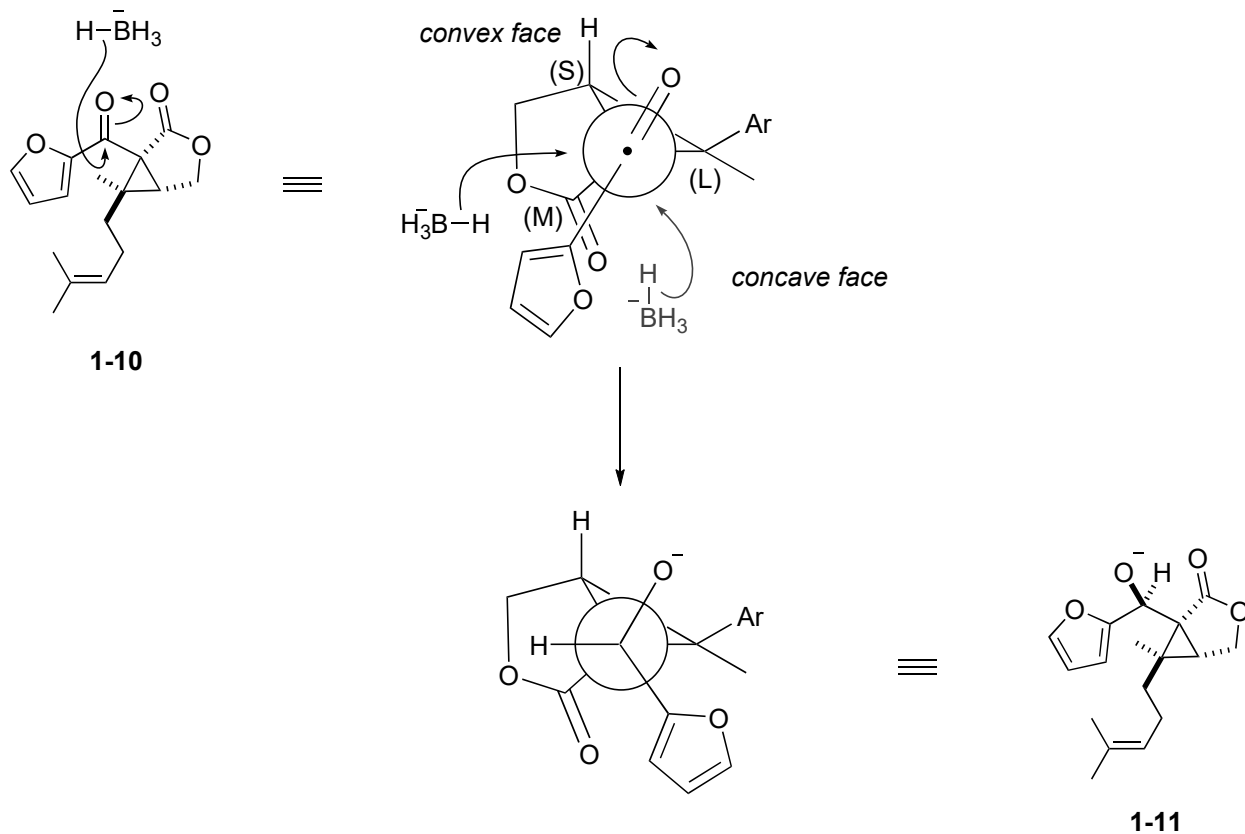
## Discussion

### 1. Cyclopropanation / ring opening vs. Claisen rearrangement

	Cyclopropanation / ring opening	Claisen rearrangement	
<input type="radio"/>	lower	temperature	higher
<input type="radio"/>	high	diastereoselectivity	low
	large	steric repulsion	small <input type="radio"/>
	at least 2 steps	steps	1 step <input type="radio"/>

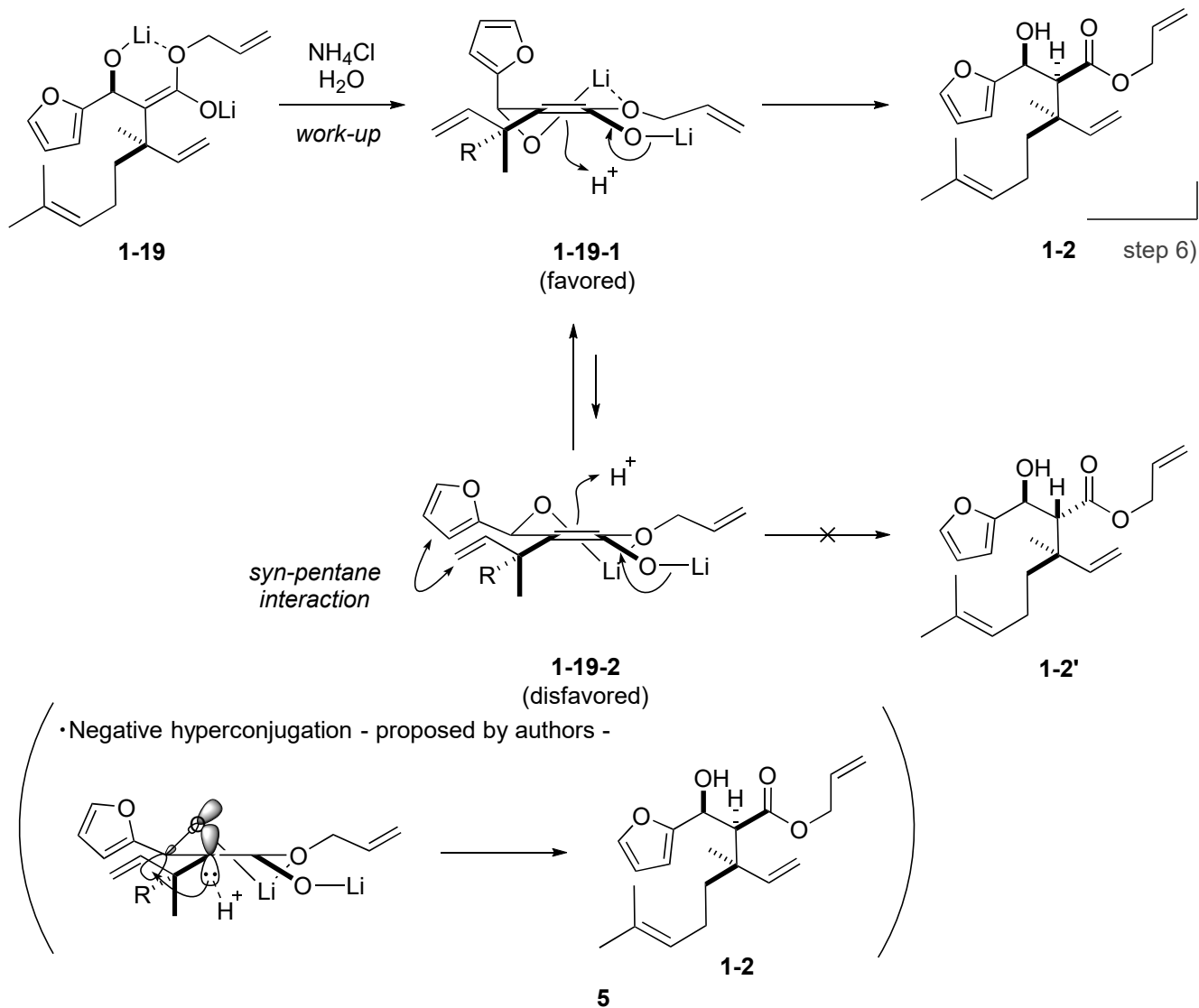


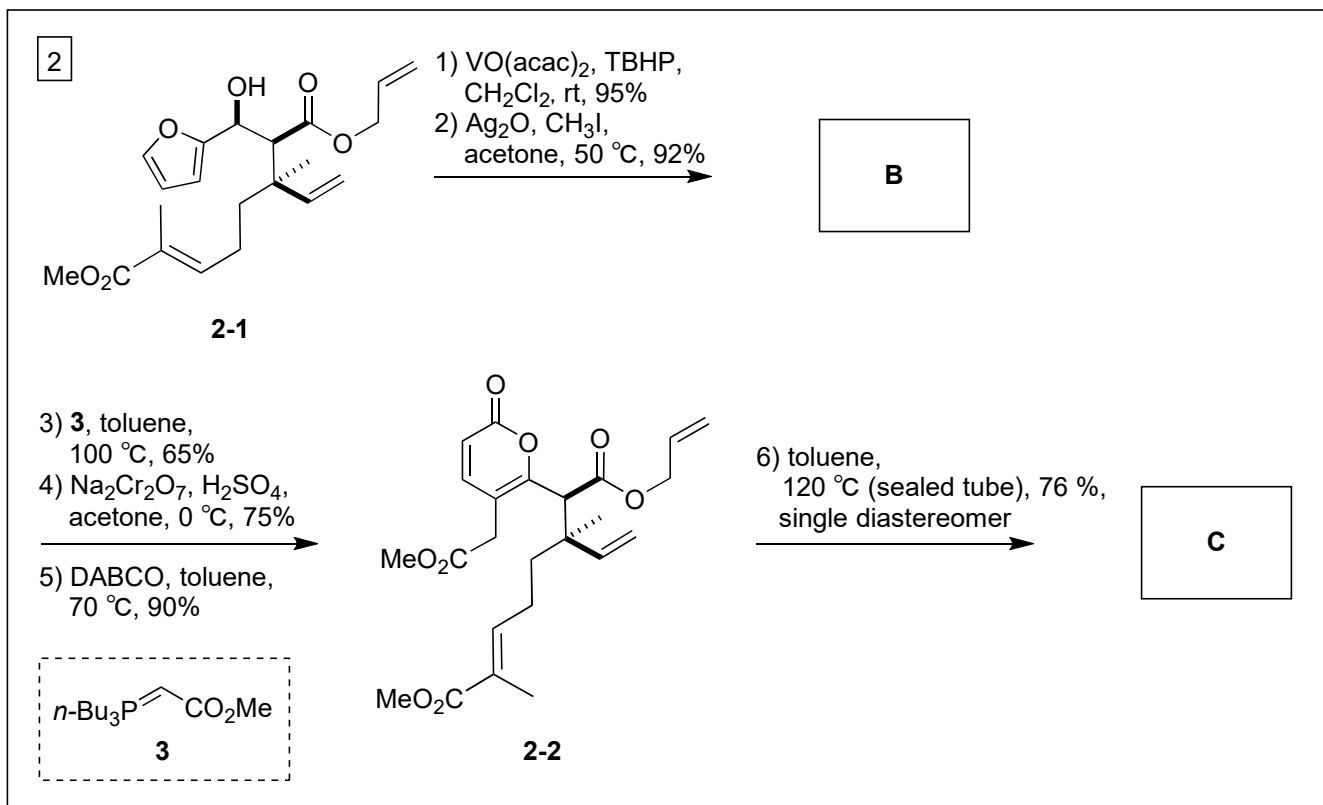
## 2. Diastereoselectivity in NaBH<sub>4</sub> reduction



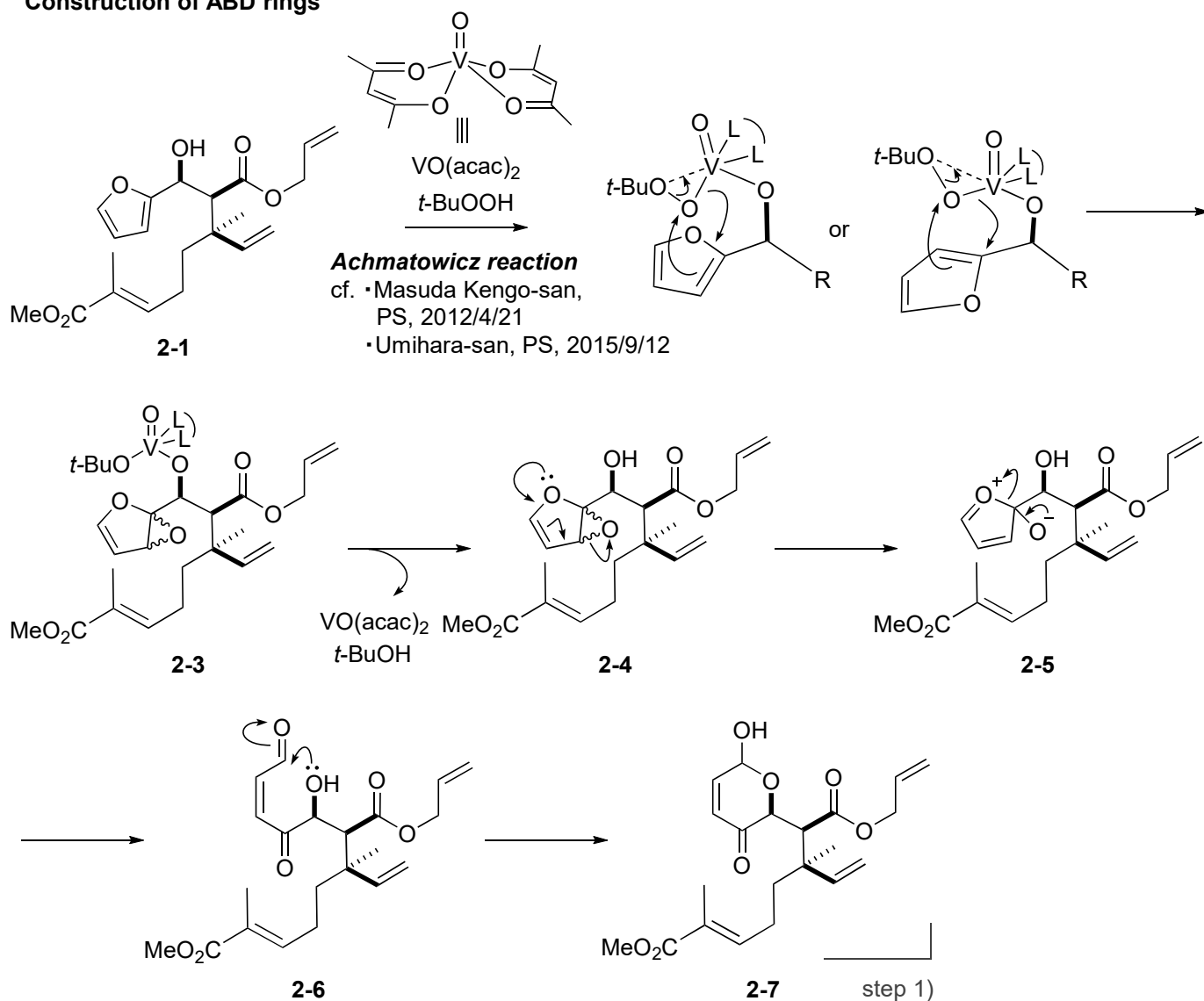
## 3. Diastereoselectivity at protonation

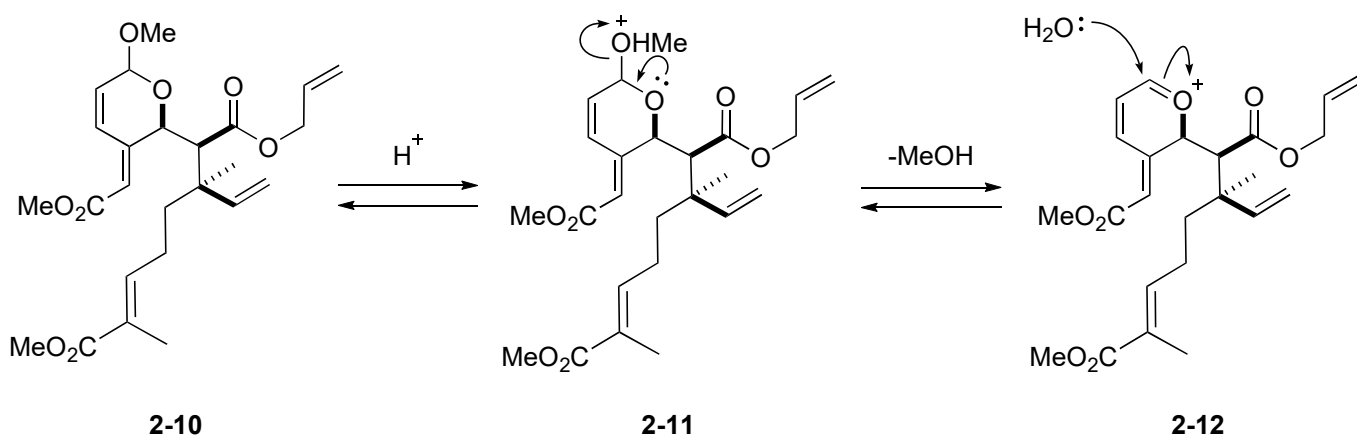
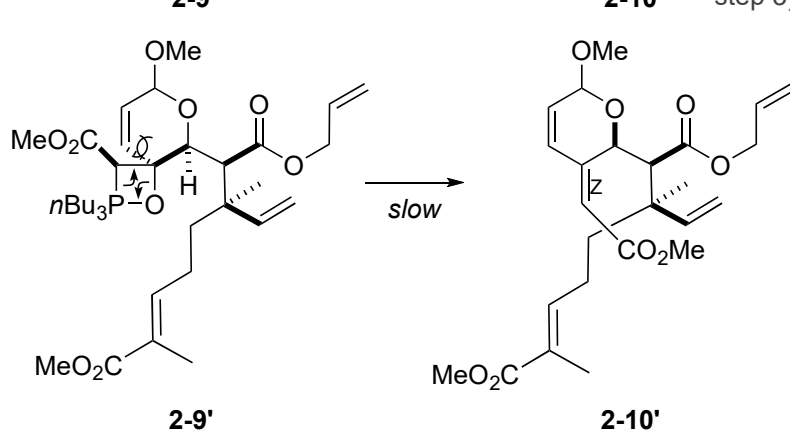
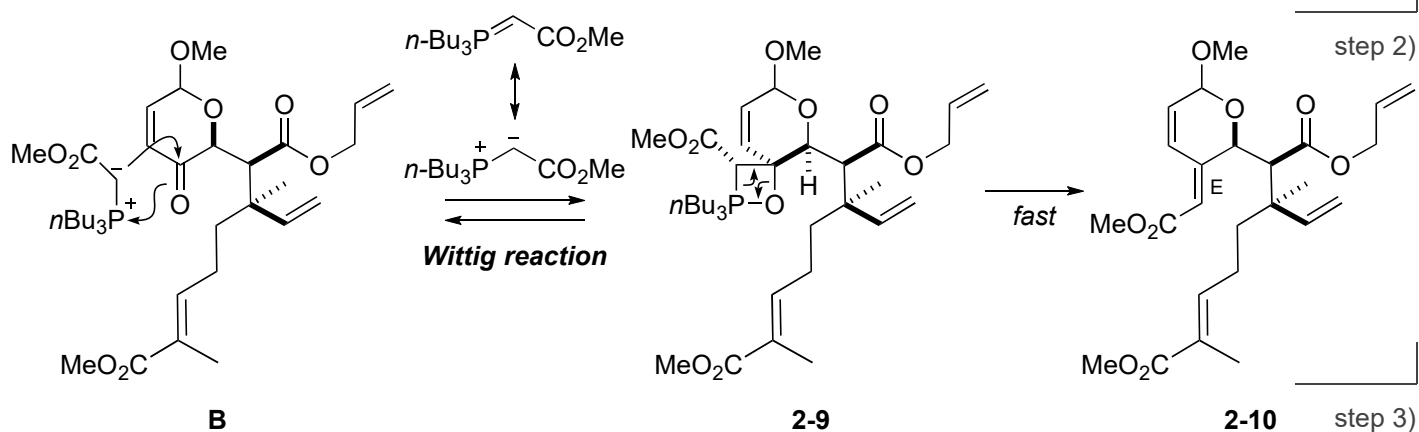
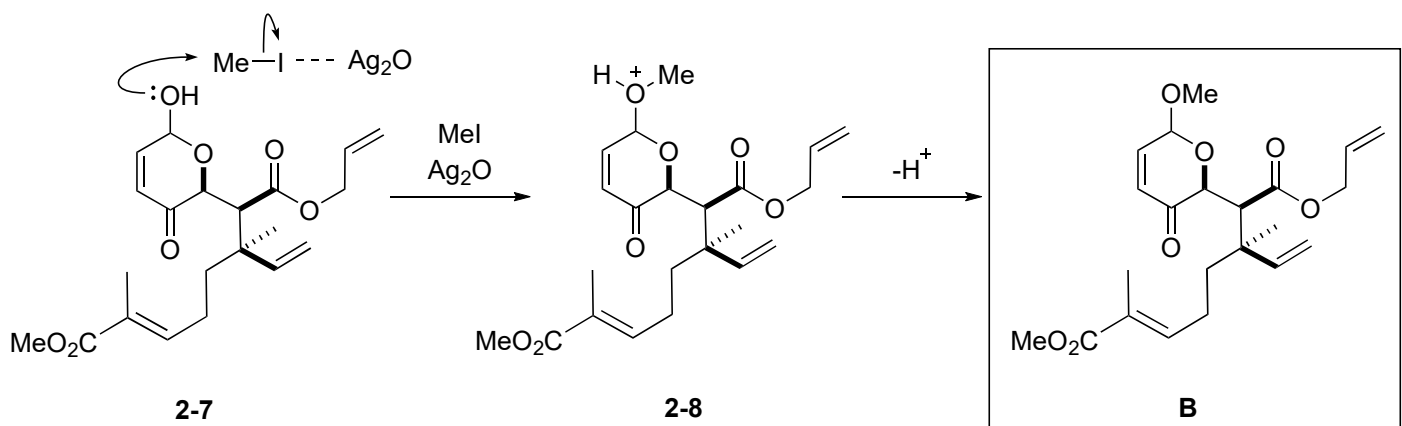
• Transition state half-chair conformation

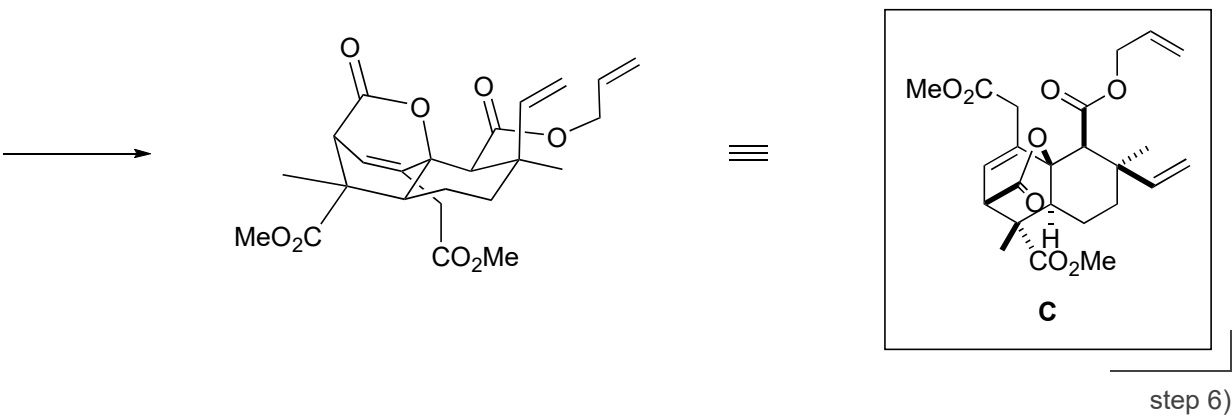
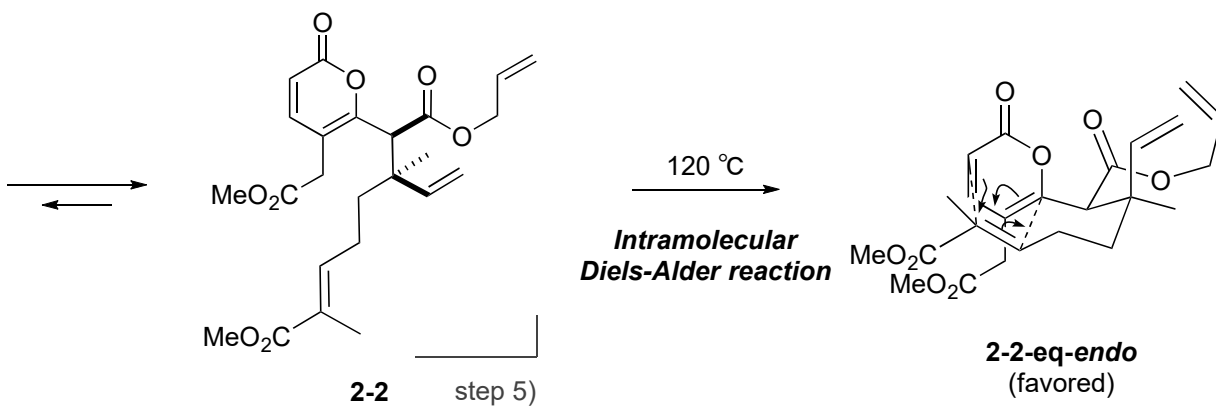
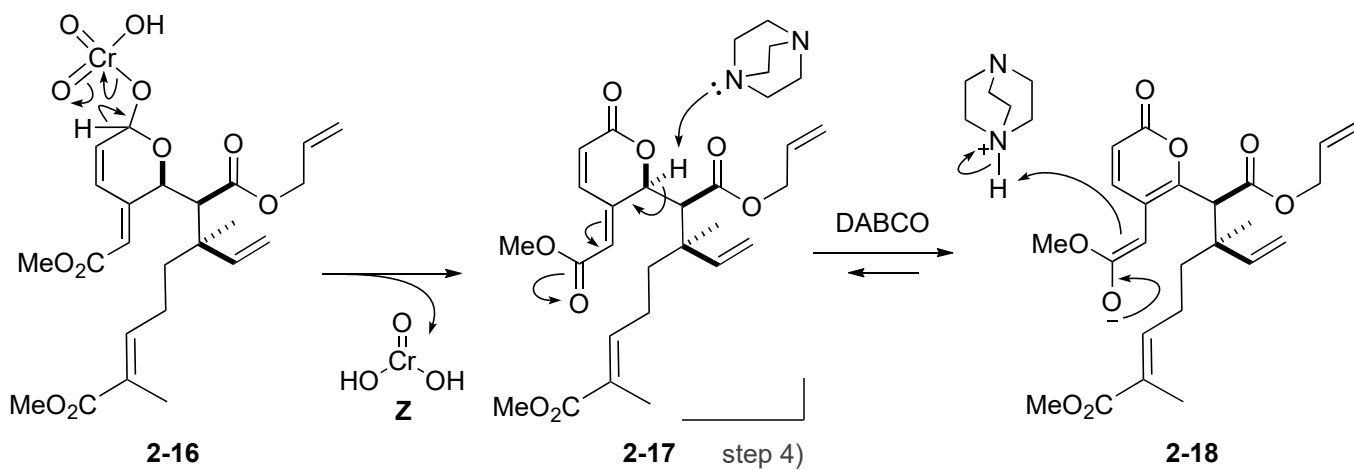
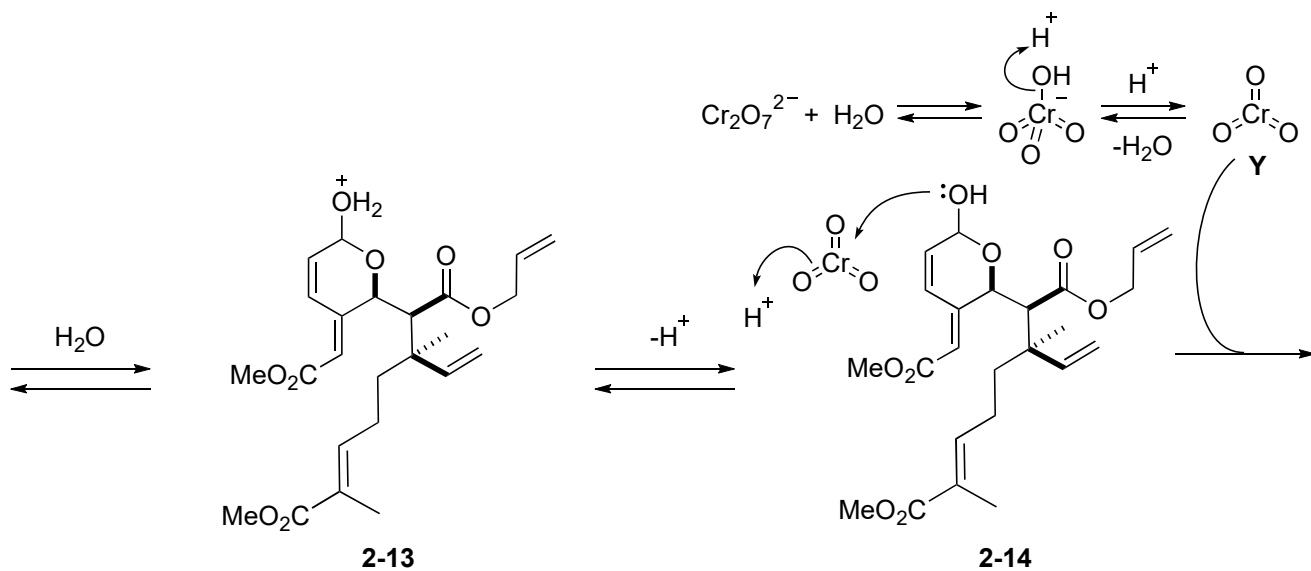




### Construction of ABD rings



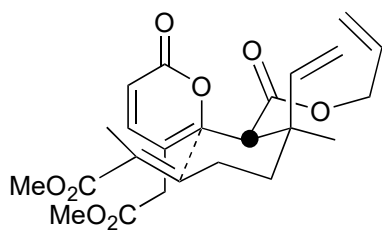




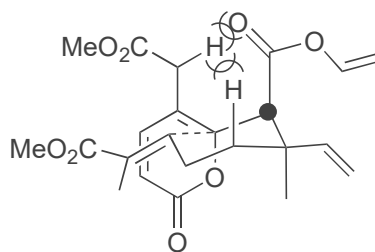


## Discussion

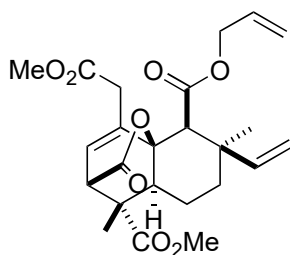
The diastereoselectivity of Diels-Alder reaction



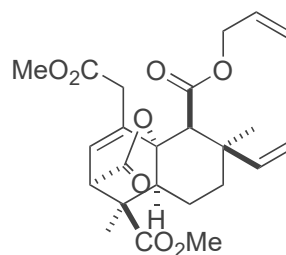
**2-2-eq-endo**



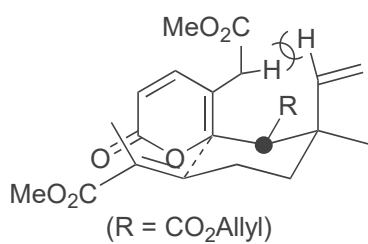
**2-2-ax-endo**



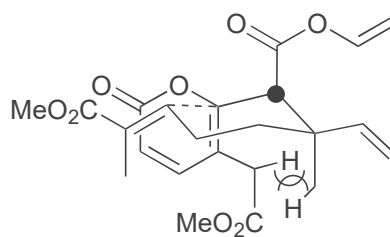
**C**



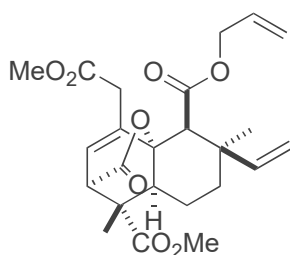
**C'-1**



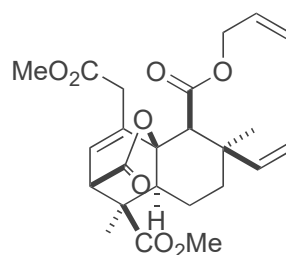
**2-2-eq-exo**  
(R = CO<sub>2</sub>Allyl)



**2-2-ax-exo**



**C'-2**

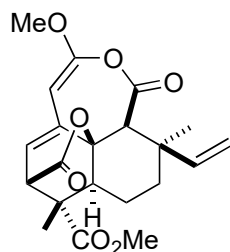


**C'-3**

3

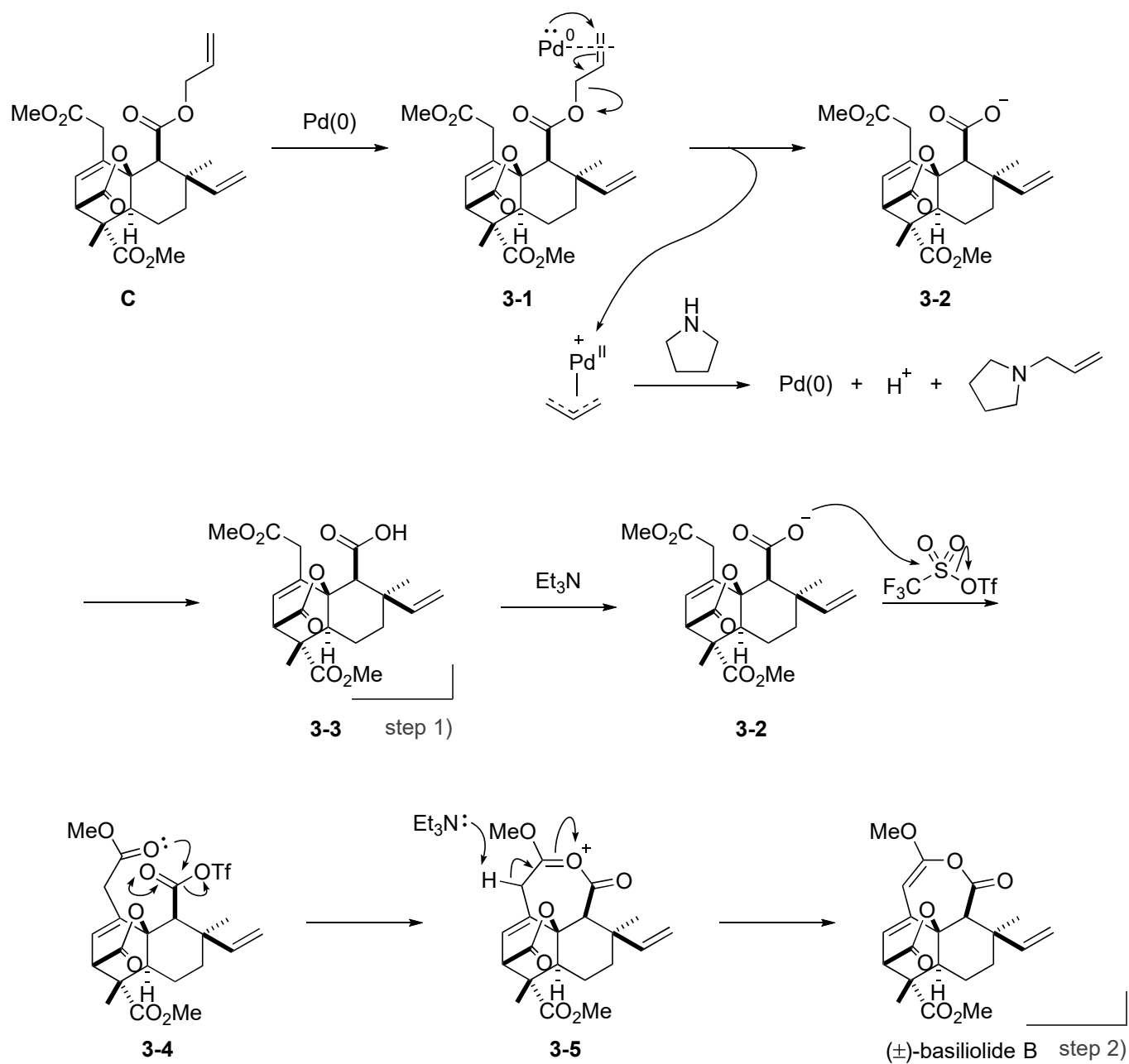
- 1) Pd(PPh<sub>3</sub>)<sub>4</sub>, PPh<sub>3</sub>,  
pyrrolidine, CH<sub>2</sub>Cl<sub>2</sub>,  
0 °C, 96%
- 2) Tf<sub>2</sub>O, Et<sub>3</sub>N, toluene,  
-78 °C for 10 min and  
0 °C for 5 min, 92%

C



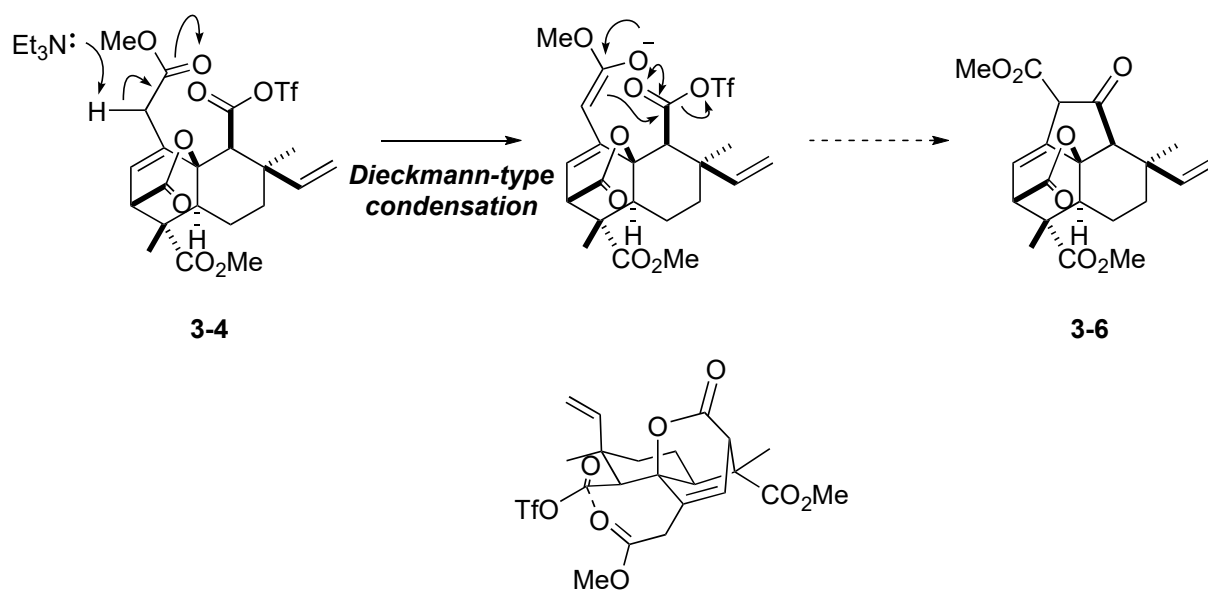
(±)-basiliolide B

## Construction of C ring



## Discussion

Why was C-ring constructed in good yield by O-acylation?



## Appendix

X-ray structure of Basililide B

