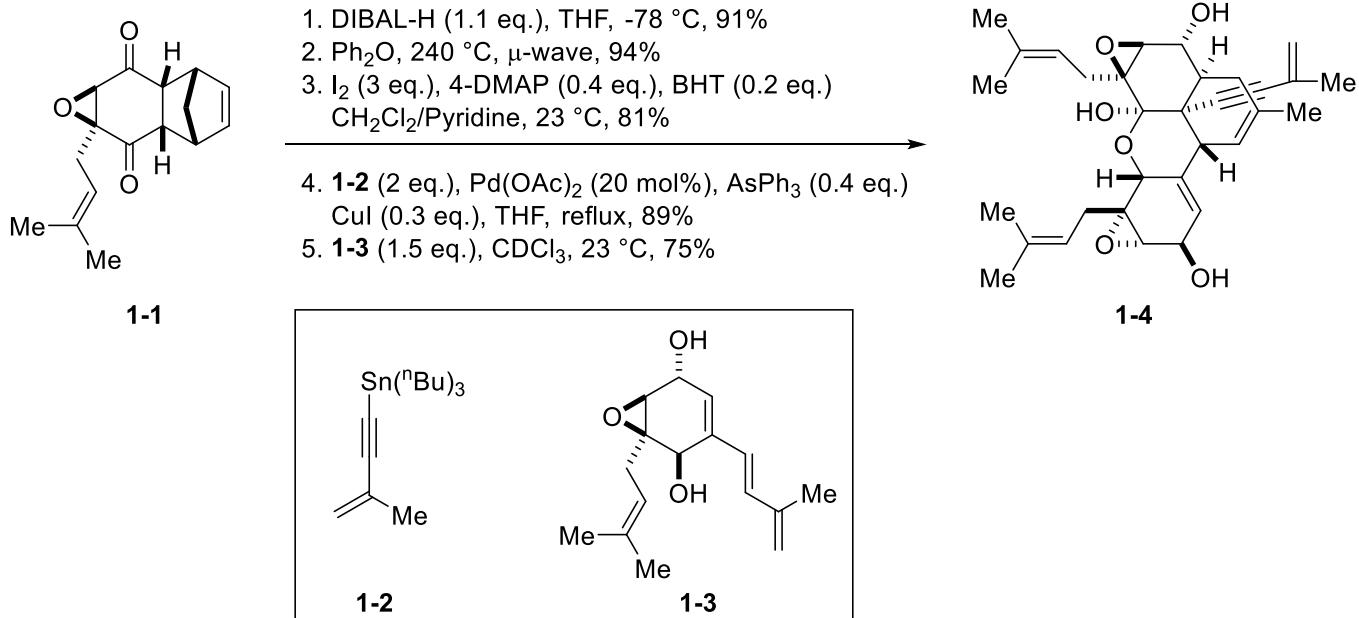


# Problem Session (1)

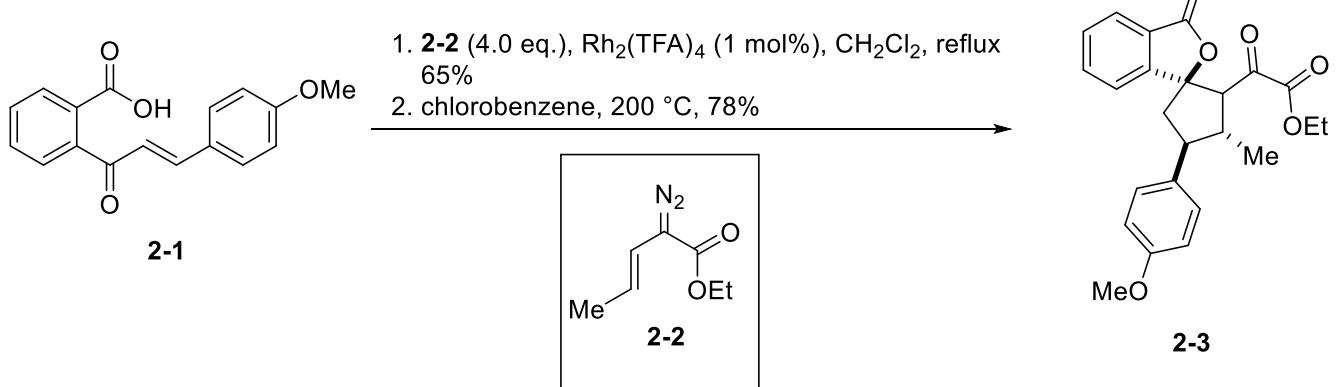
2019.5.18 Itsuki Watanabe

Please provide the reaction mechanisms.

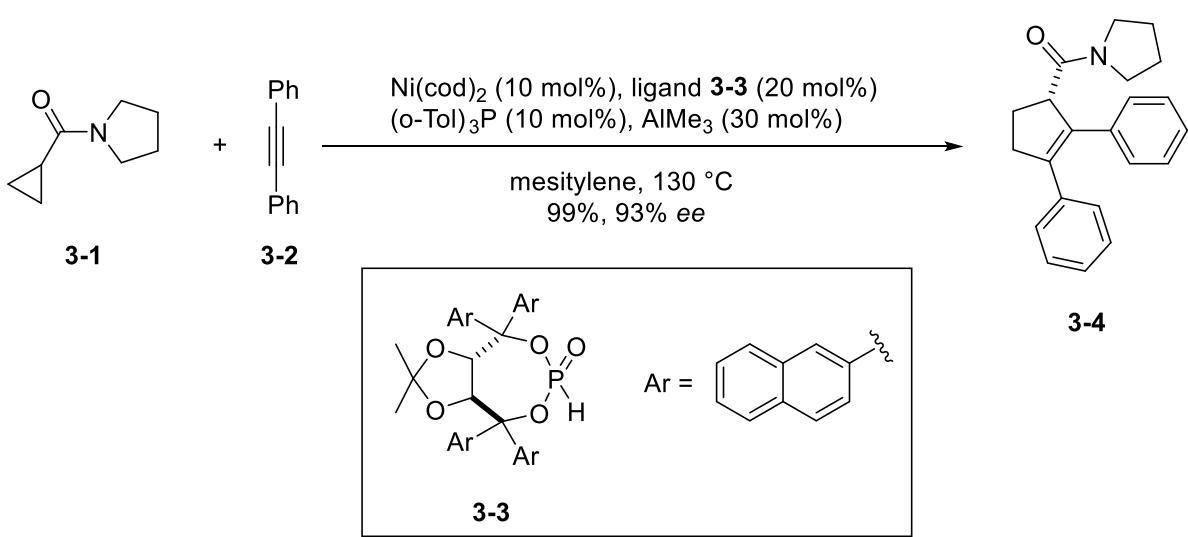
(1)



(2)



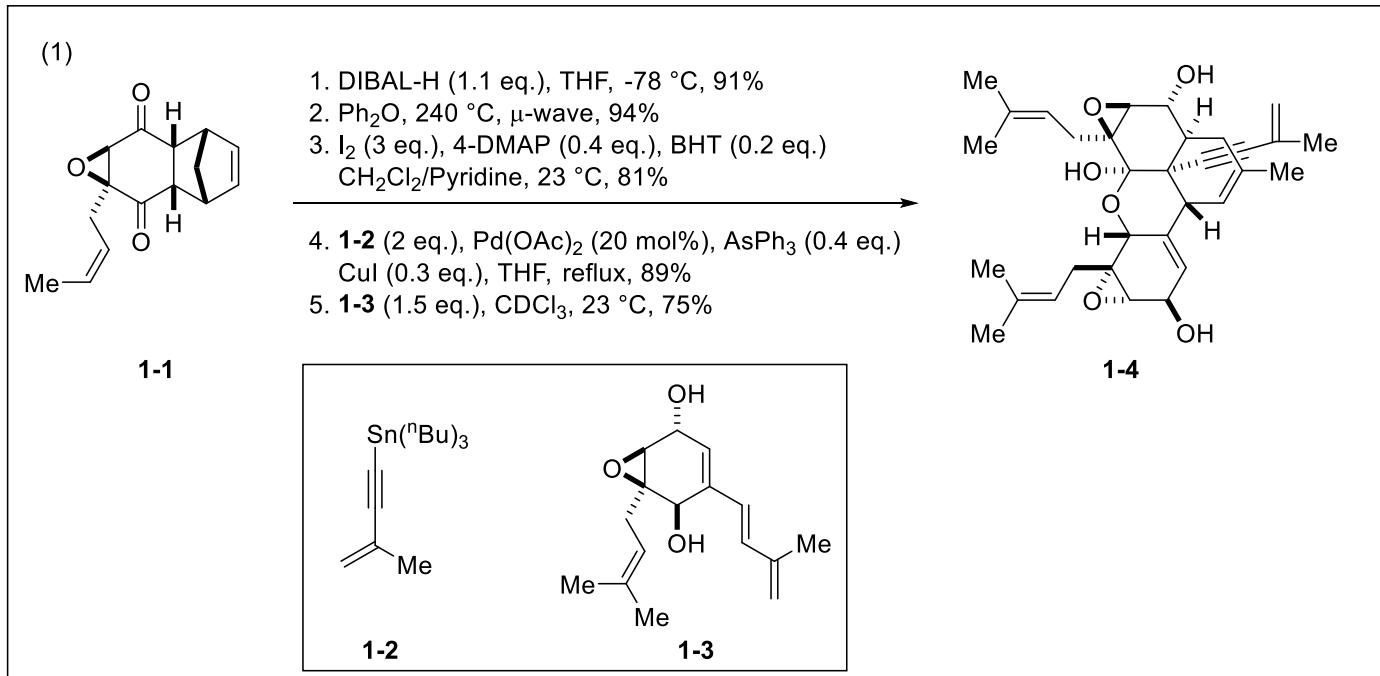
(3)



# Problem Session (1) - Answer

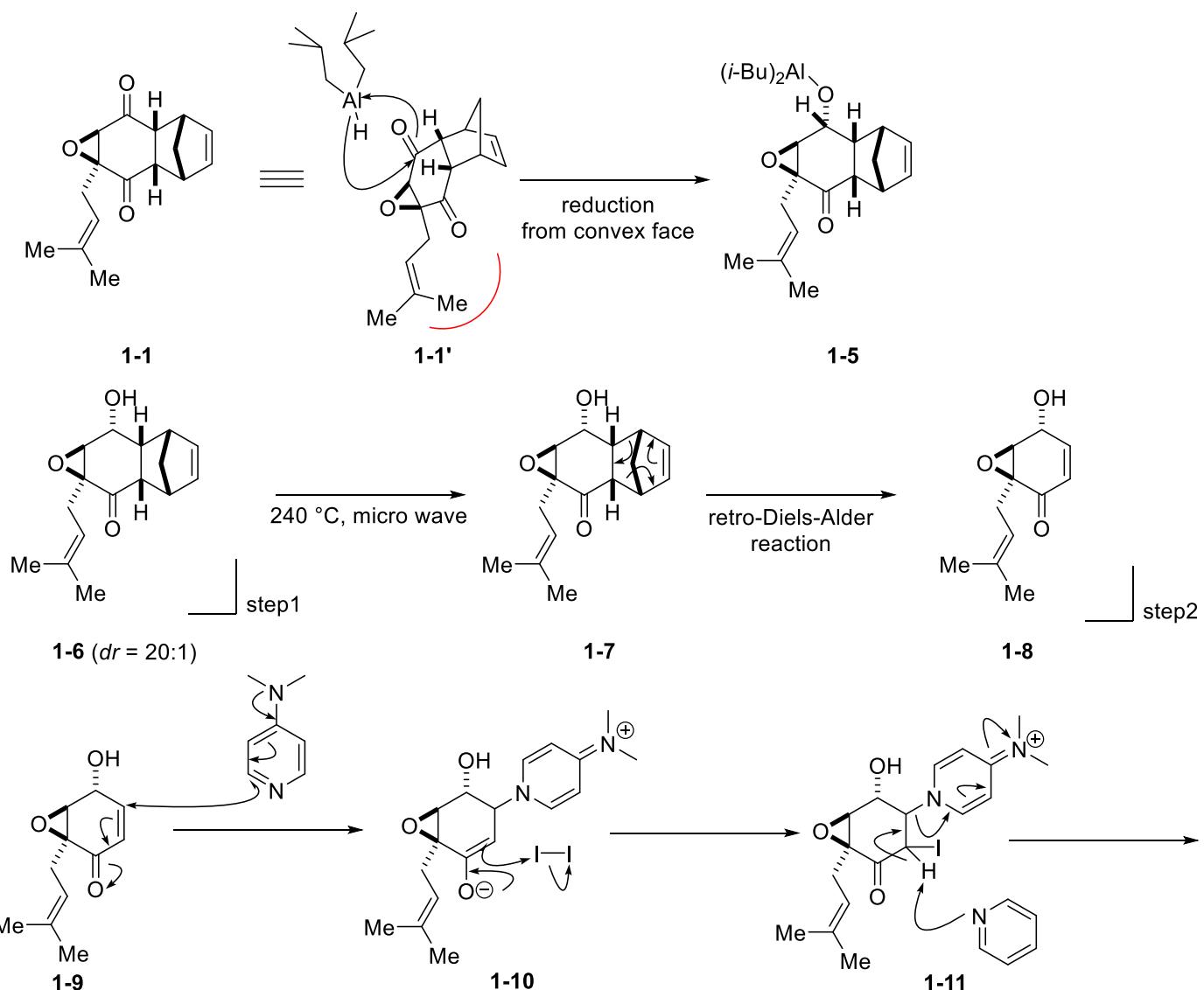
2019.5.18 Itsuki Watanabe

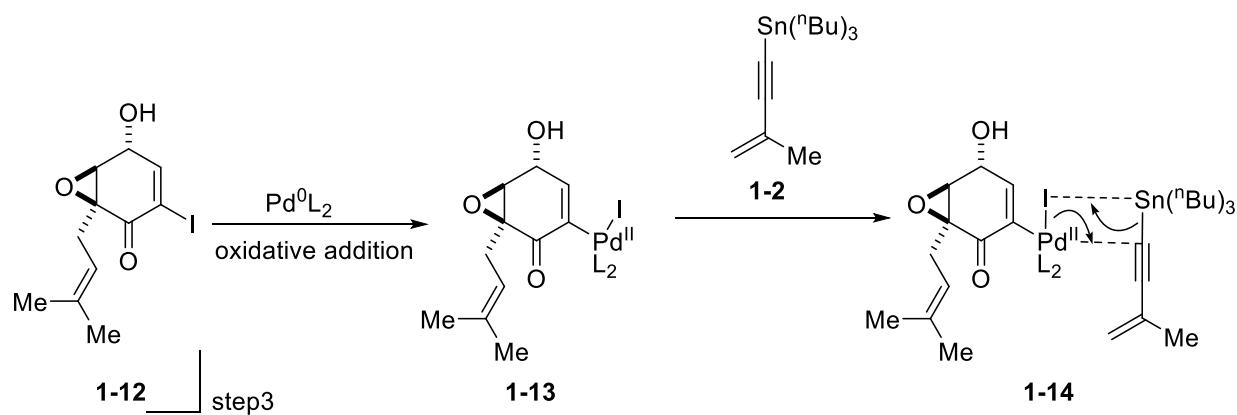
Topic: Cyclization



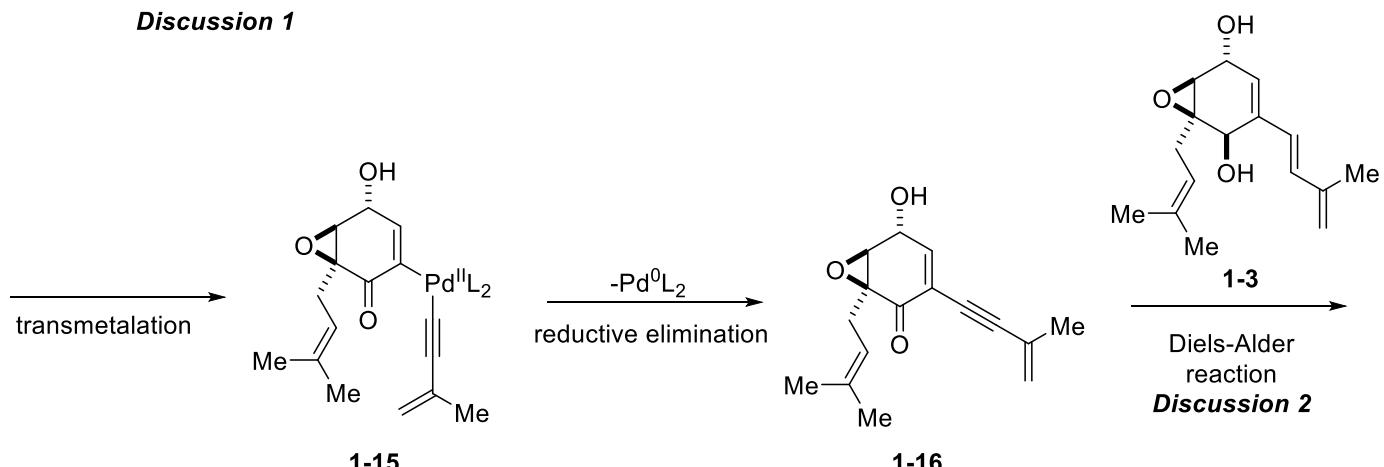
Kim, G.; Kim, J. M.; Chung, G.; Lee, H.; Han, S. *Org. Lett.* **2018**, *20*, 6886.

## Answer

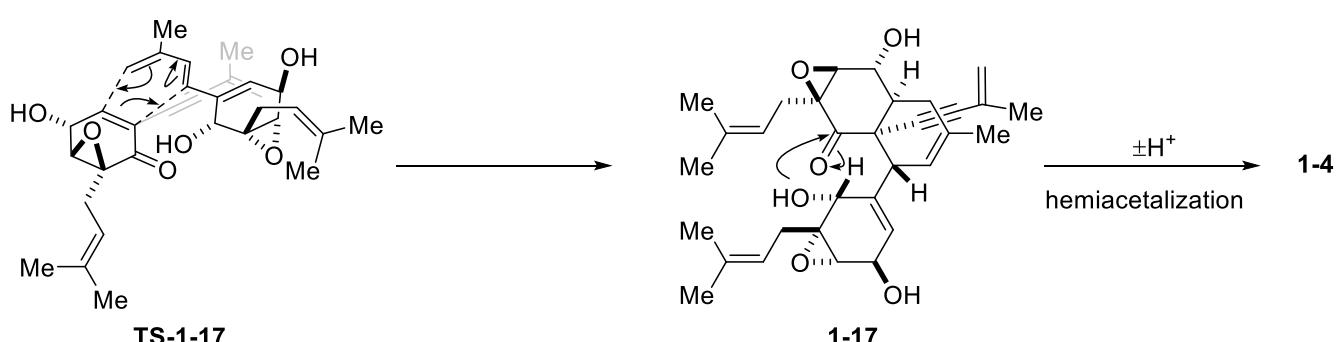




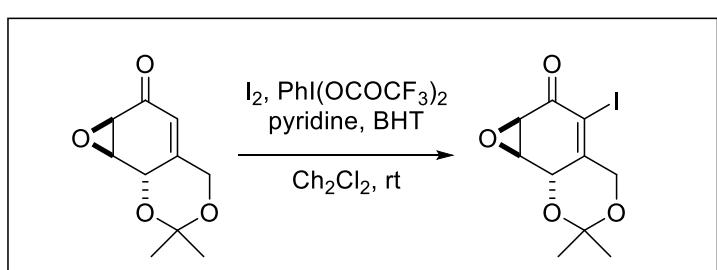
**Discussion 1**



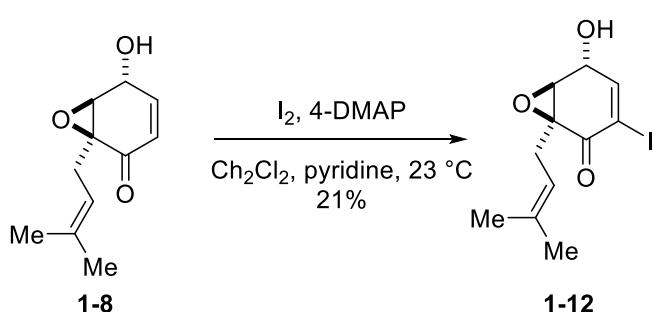
**Discussion 2**



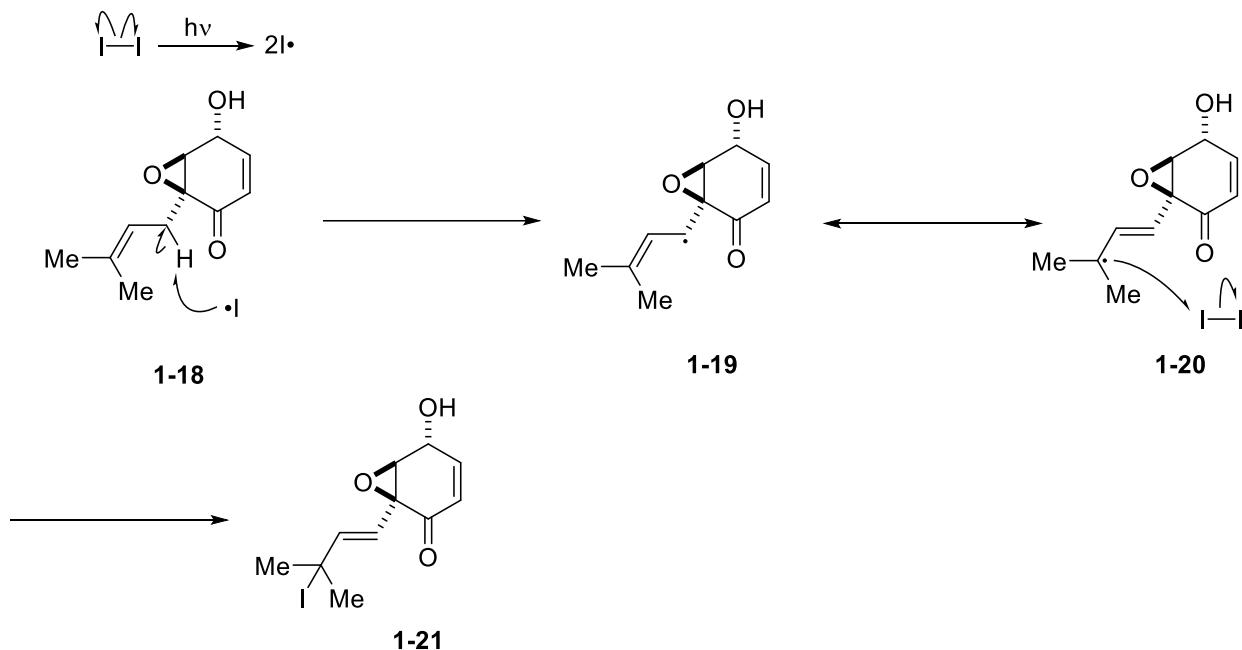
**Discussion 1 :** the side reaction of iodonation



Shoji, M.; Kishida, S.; Takeya, H.; Osada, H.; Hayashi Y. *Tetrahedron Lett.* **2002**, 43, 9155.



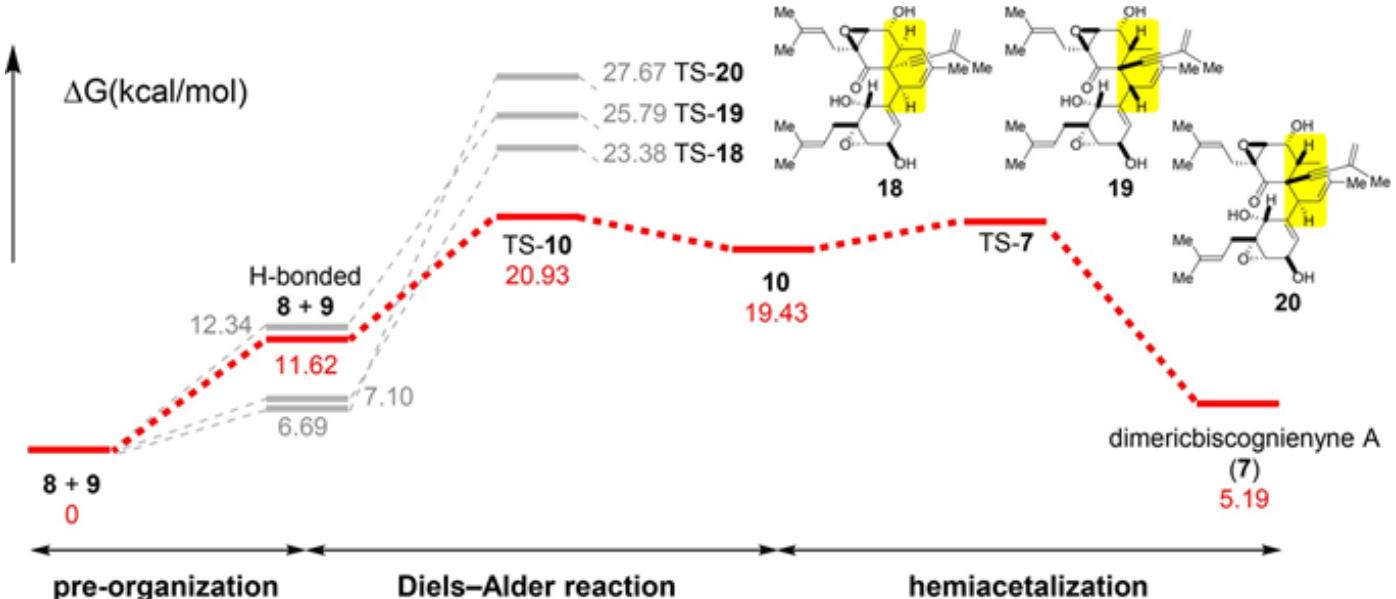
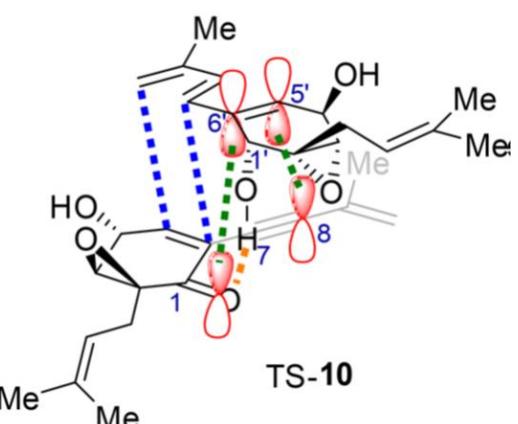
### Proposed side reaction

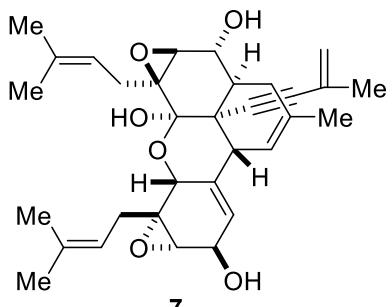
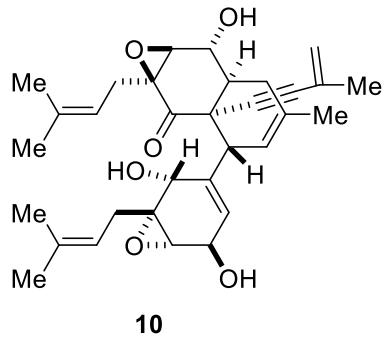


The author said that the side reaction occurred without addition of BHT or shading.

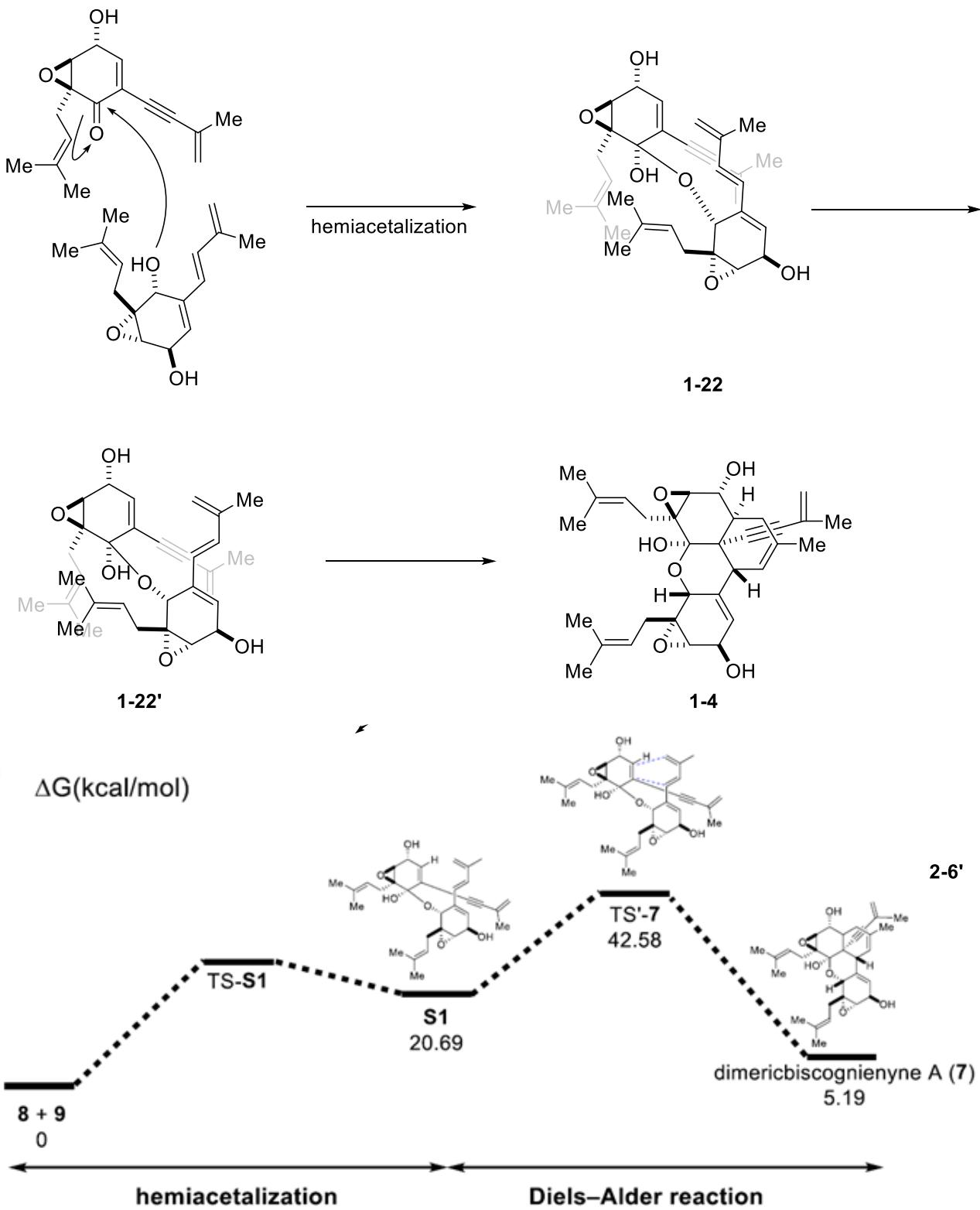
### Discussion 2-1 : stereoselectivity of Diels-Alder reaction

- $\pi-\pi$  Interactions shown in the right figure stabilize the transition state.
- C1' Hydroxyl group of diene is involved in the hydrogen bonding with the C1 carbonyl moiety of dienophile.

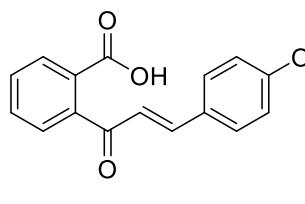




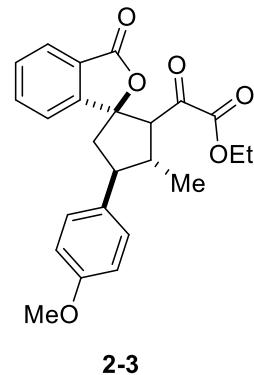
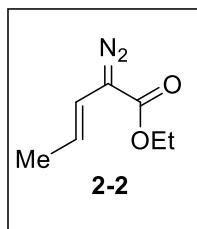
**Discussion 2-2 :** Reaction pathway of hemiacetalization followed by Diels-Alder reaction



(2)

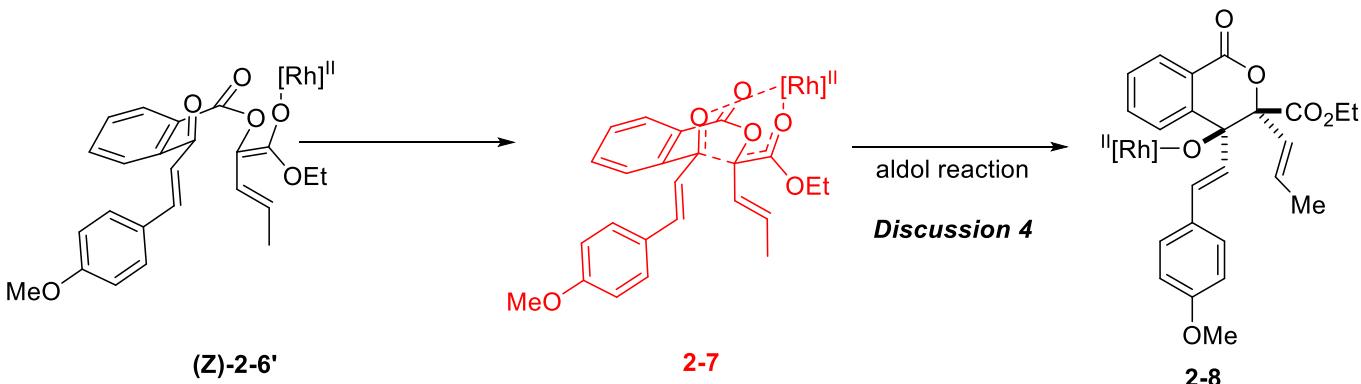
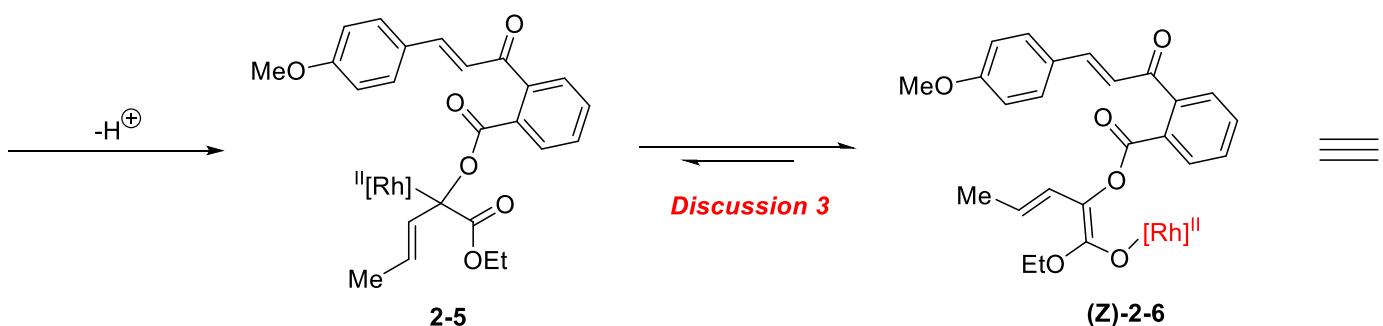
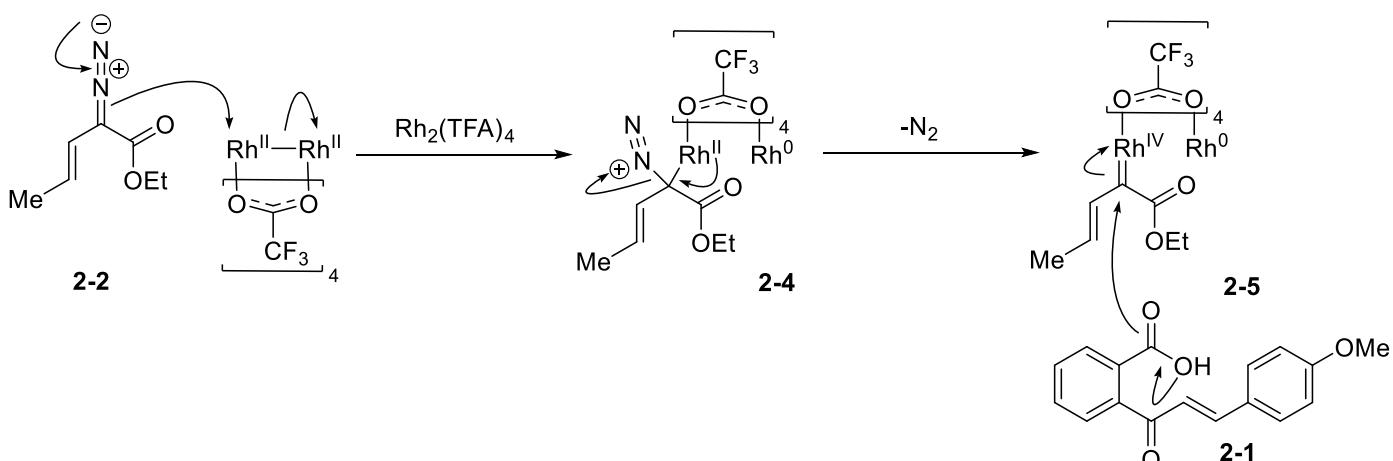


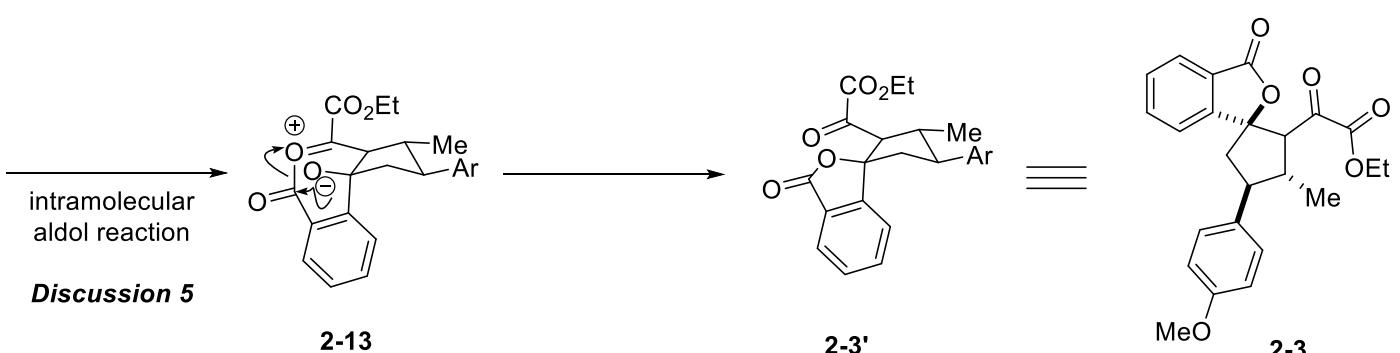
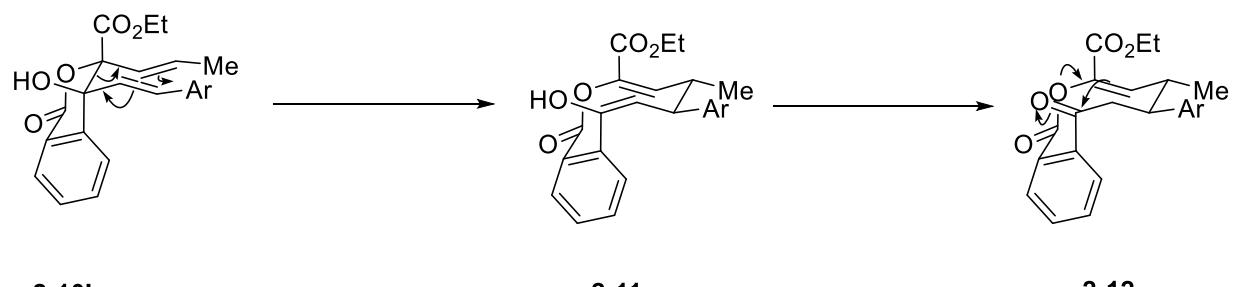
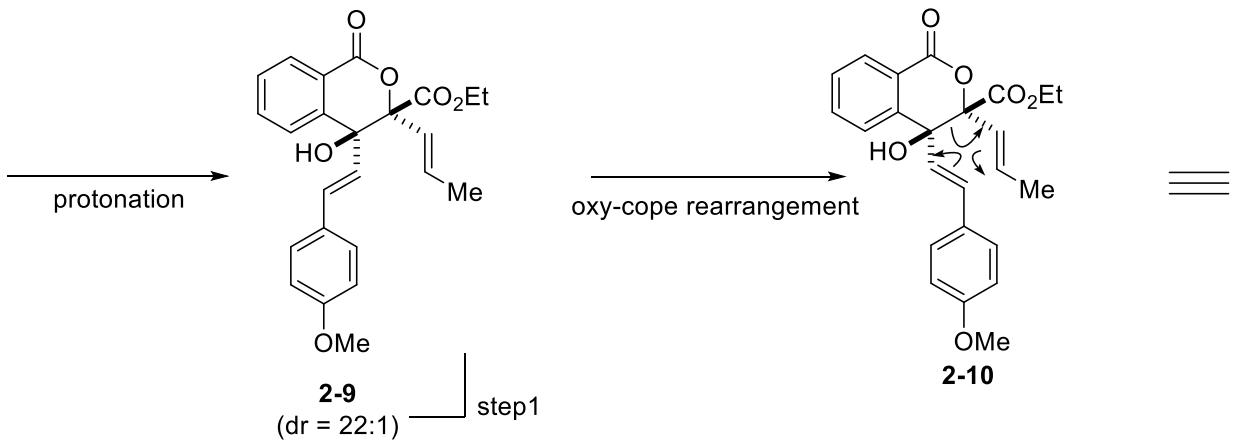
1. **2-2** (4.0 eq.),  $\text{Rh}_2(\text{TFA})_4$  (1 mol%),  $\text{CH}_2\text{Cl}_2$ , reflux  
65%  
2. chlorobenzene,  $200^\circ\text{C}$ , 78%



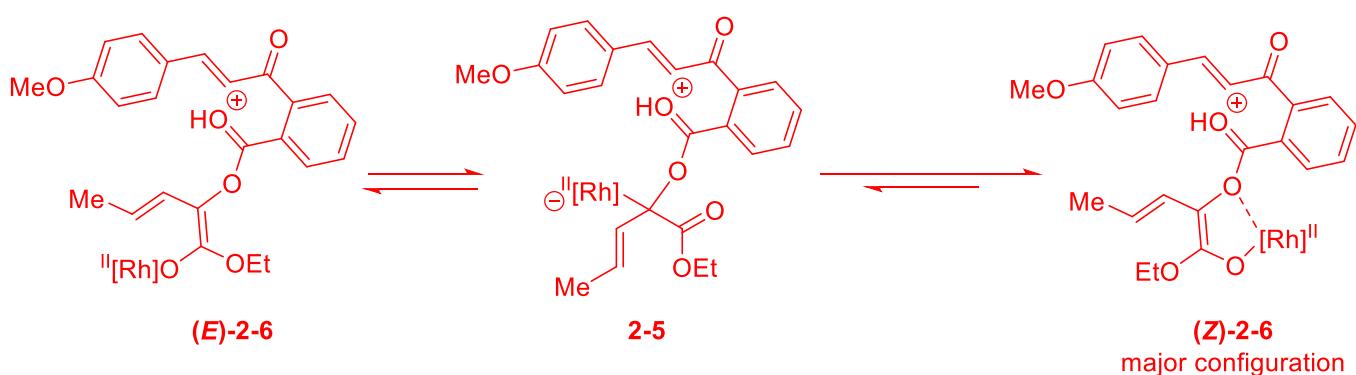
Nicholas, P. M.; Joseph, C. S.; Ayushi, C.; Indrajeet, S., *Org. Lett.*, **2018**, *20*, 7585-7589.

### Answer



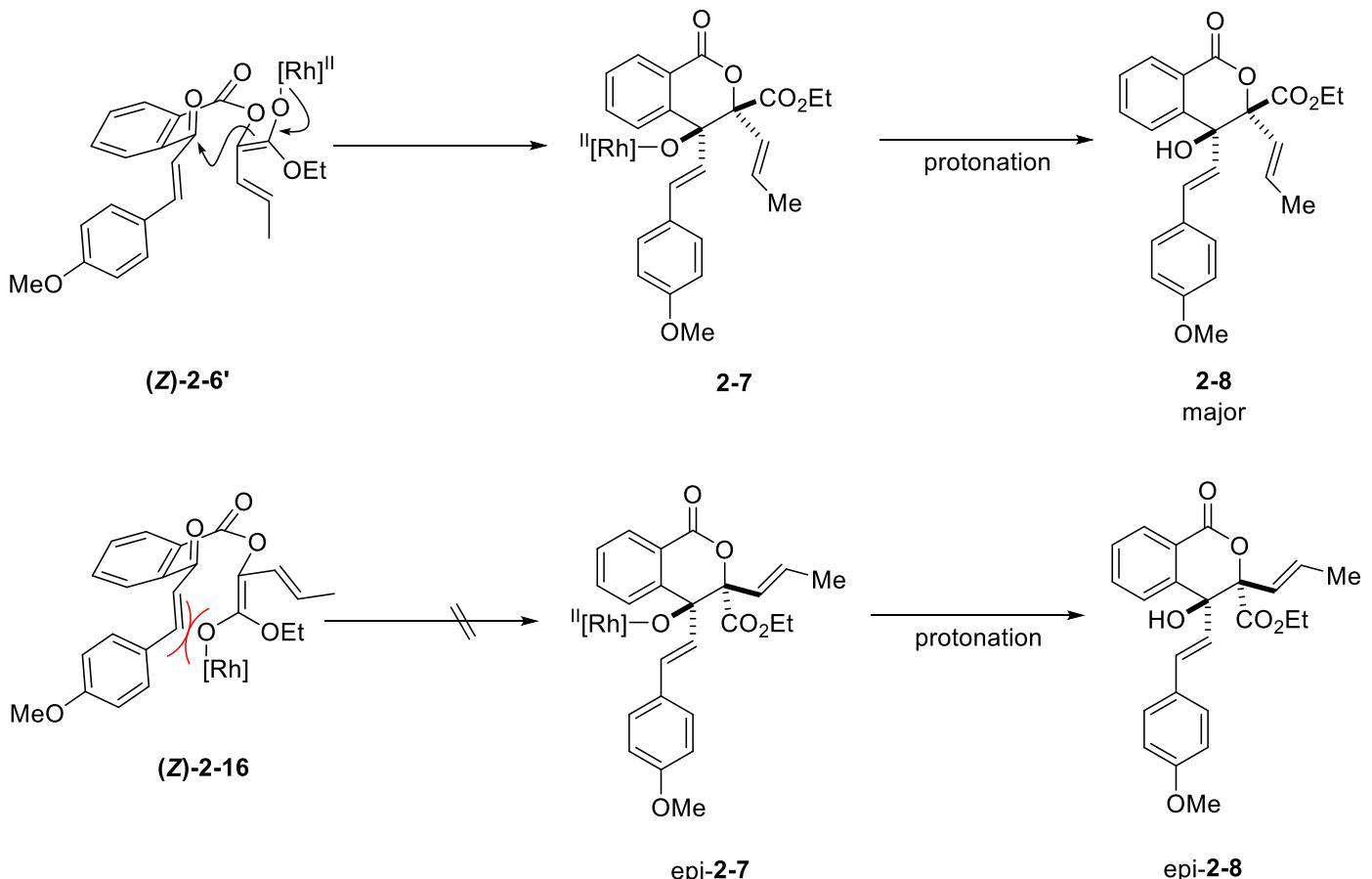


### Discussion 3 : configuration of 2-6



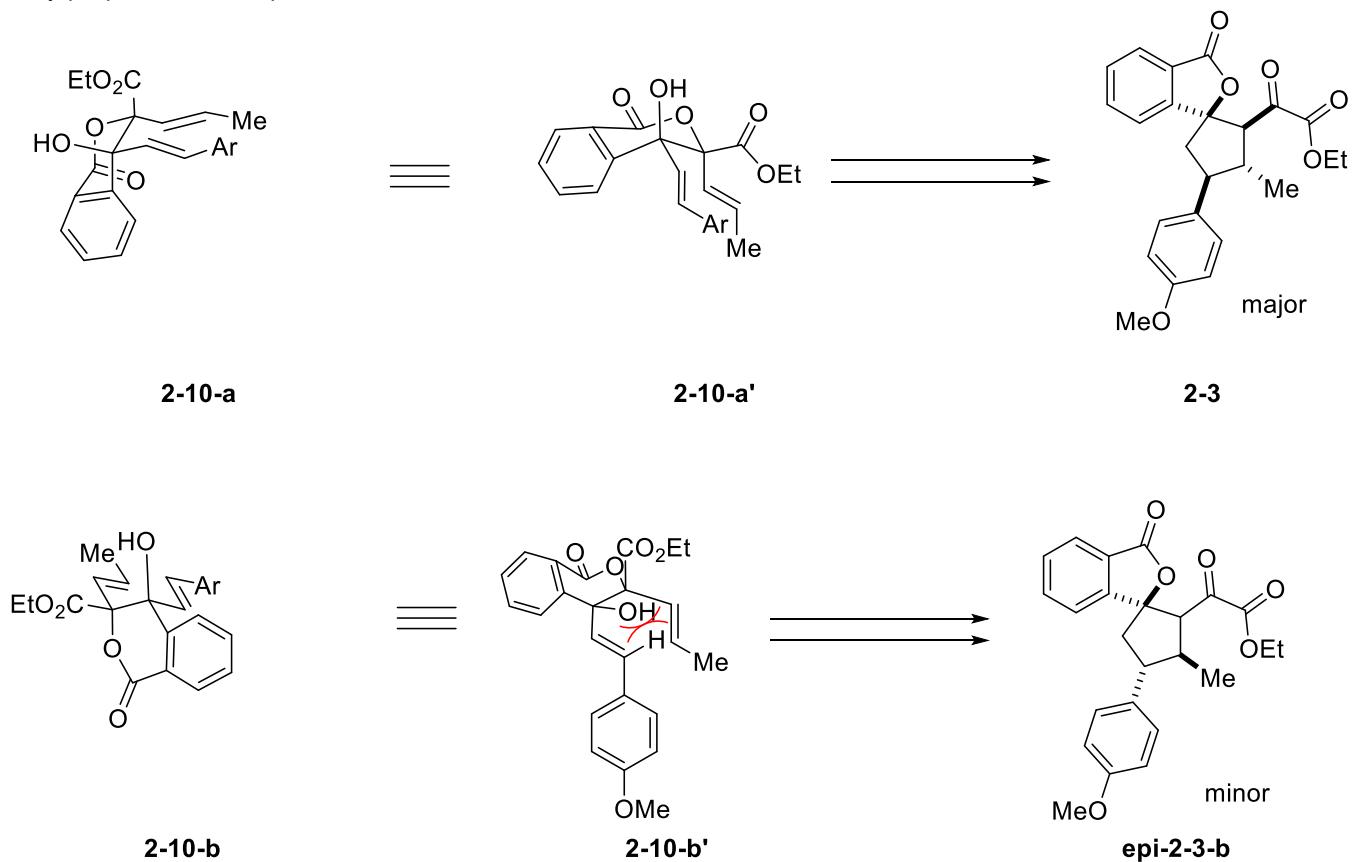
(Z)-2-6 would be a major configuration, due to the chelate formation between Rh and oxygen.

**Discussion 4 : stereoselectivity of aldol reaction**



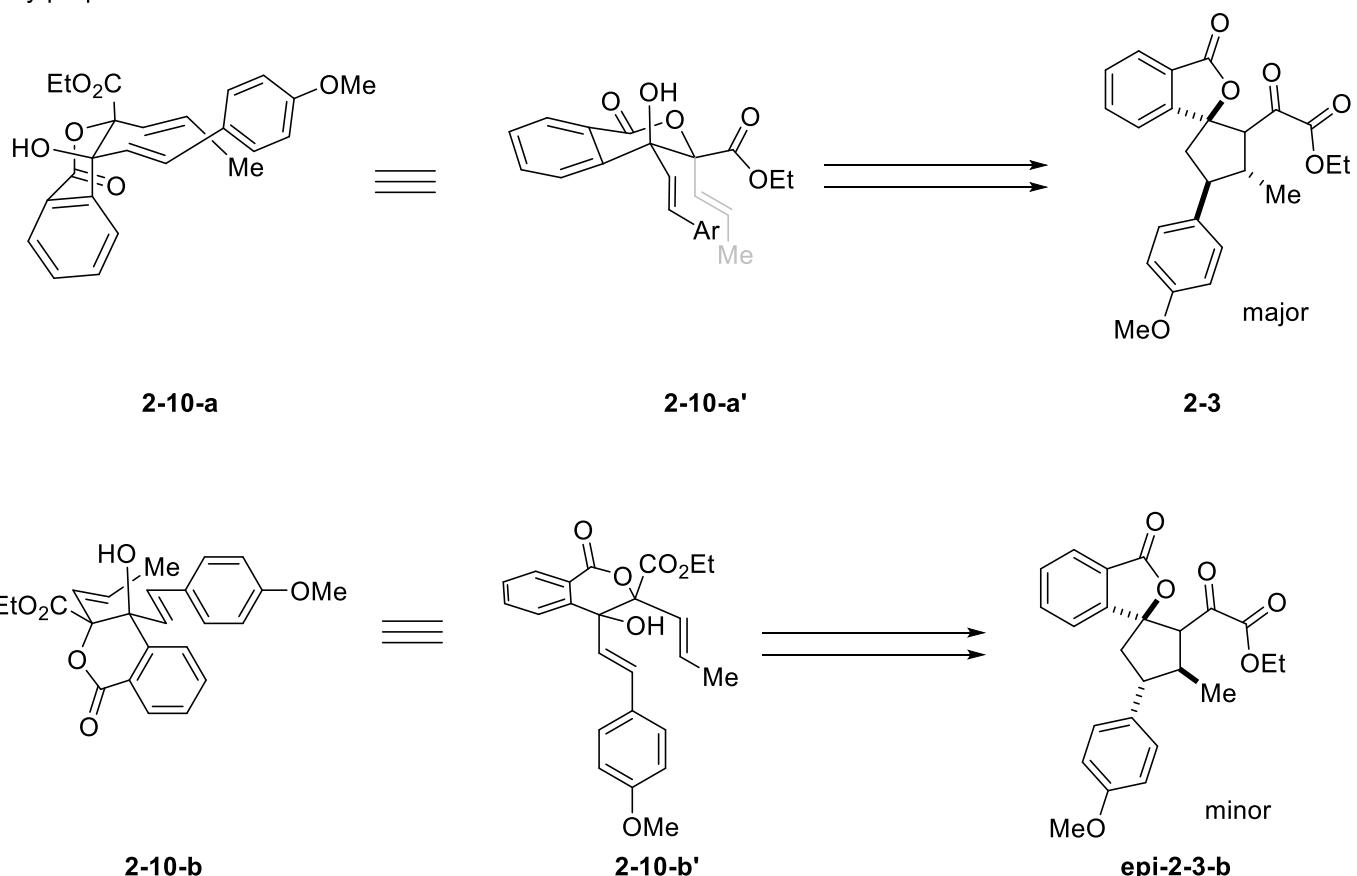
**Discussion 5 : stereoselectivity of oxy-cope rearrangement intramolecular aldol reaction**

my proposal-steric repulsion

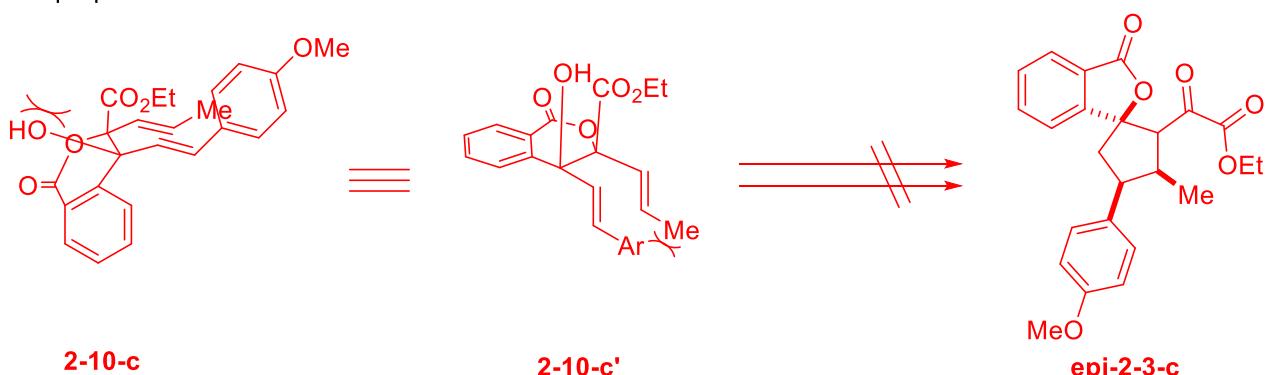


**Discussion 5 :** stereoselectivity of oxy -cope rearrangement intramolecular aldol reaction

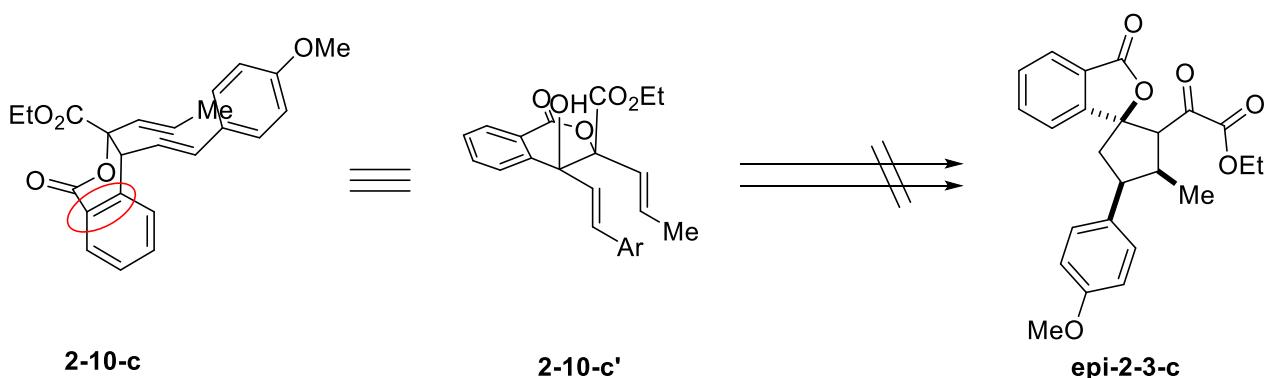
my proposal



other proposal

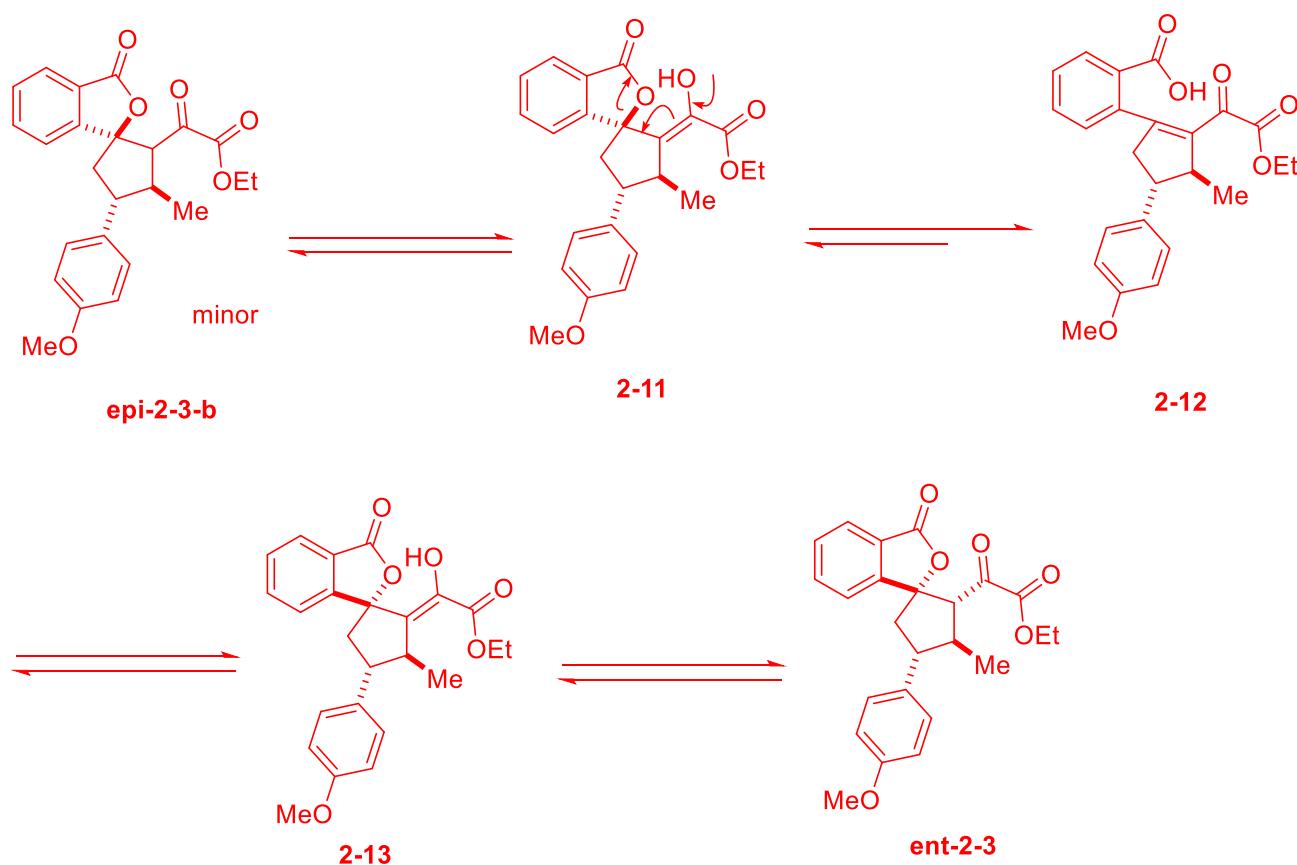


Compound epi-2-3-c was not synthesized because of steric interaction

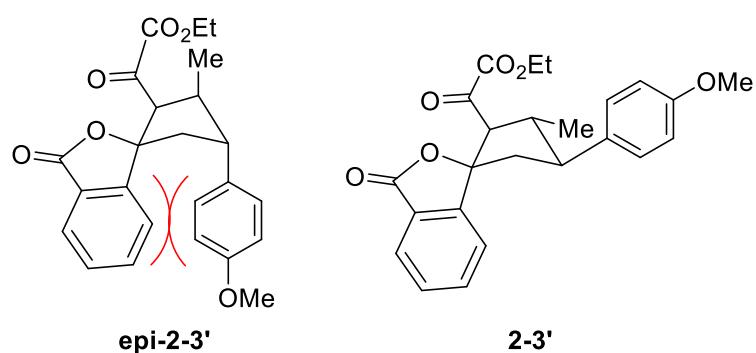


Compound **epi-2-3-c** was not synthesized because of rigid configuration.

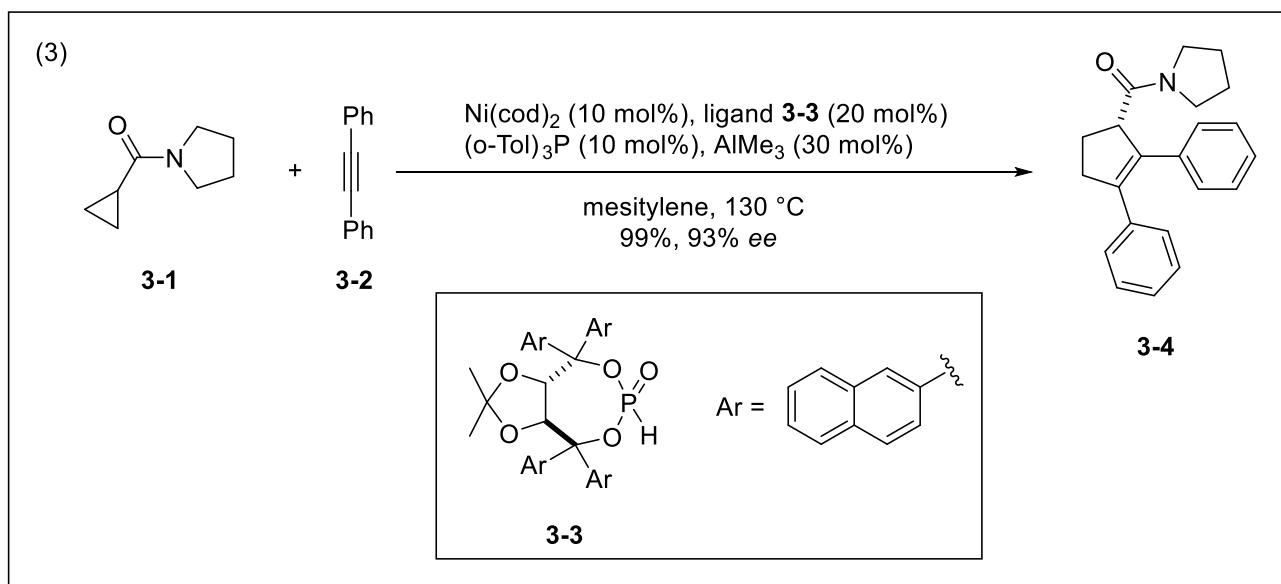
other proposal-isomerization



Isomerization of **epi-2-3-b** may have occurred to give the most stable **ent-2-3**.

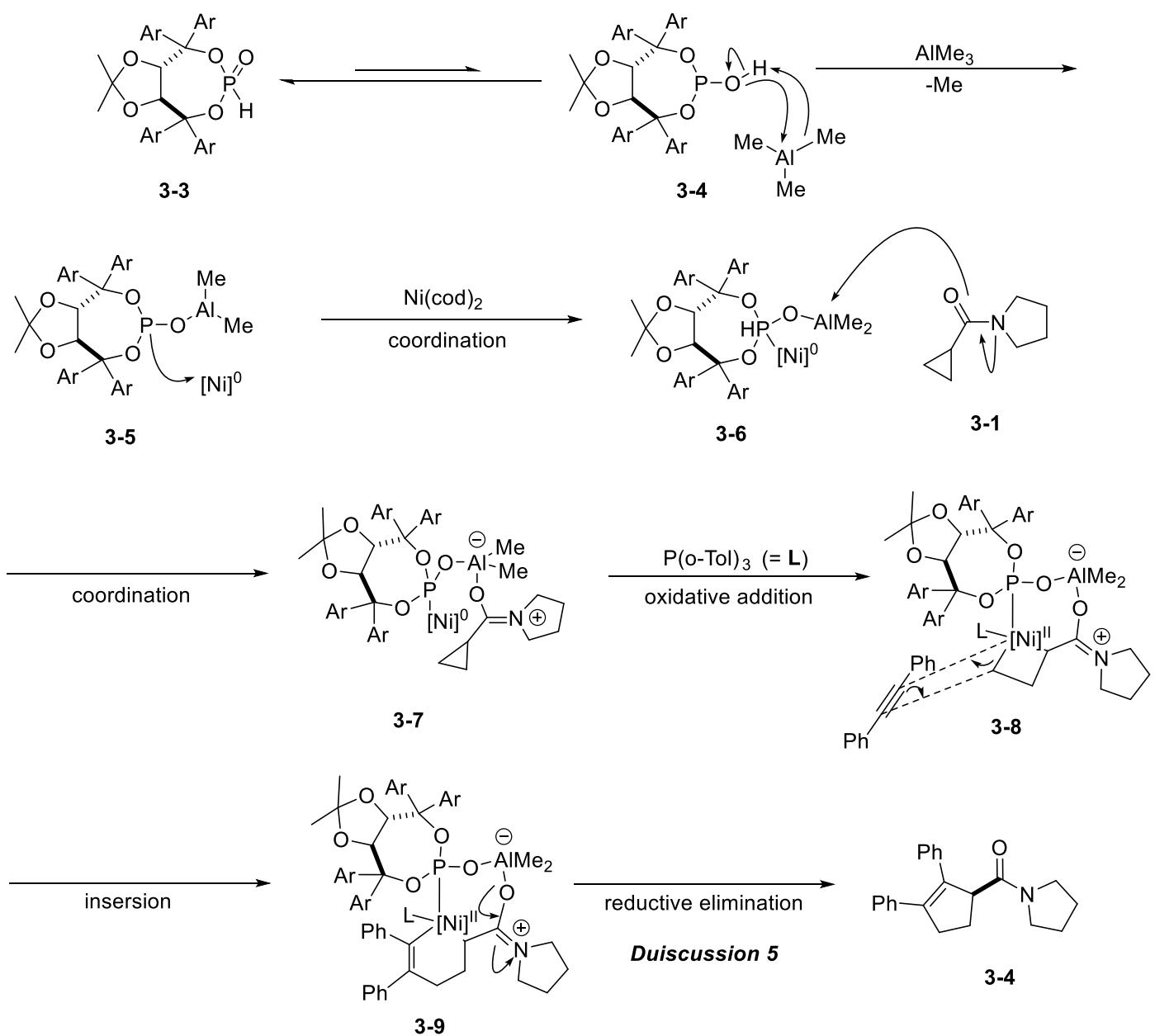


The compound **epi-2-3'** was unstable because of steric interaction between aryl.

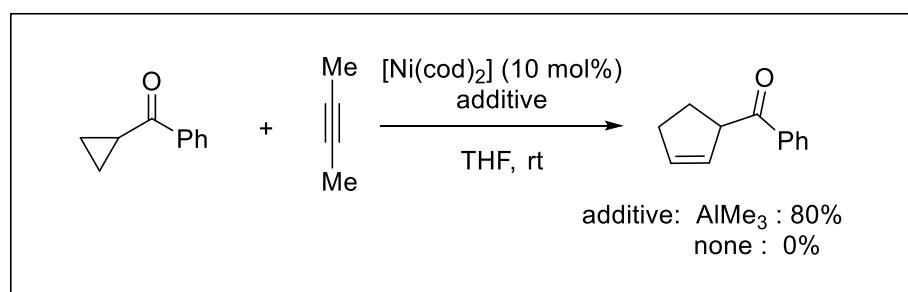


Lue, Q.; Wang, D.; Tang, Z.; Luan, Y.; Li, J.; Pu, Y.; Ye, M., *J. Am. Chem. Soc.*, **2017**, 139, 18150-18153.

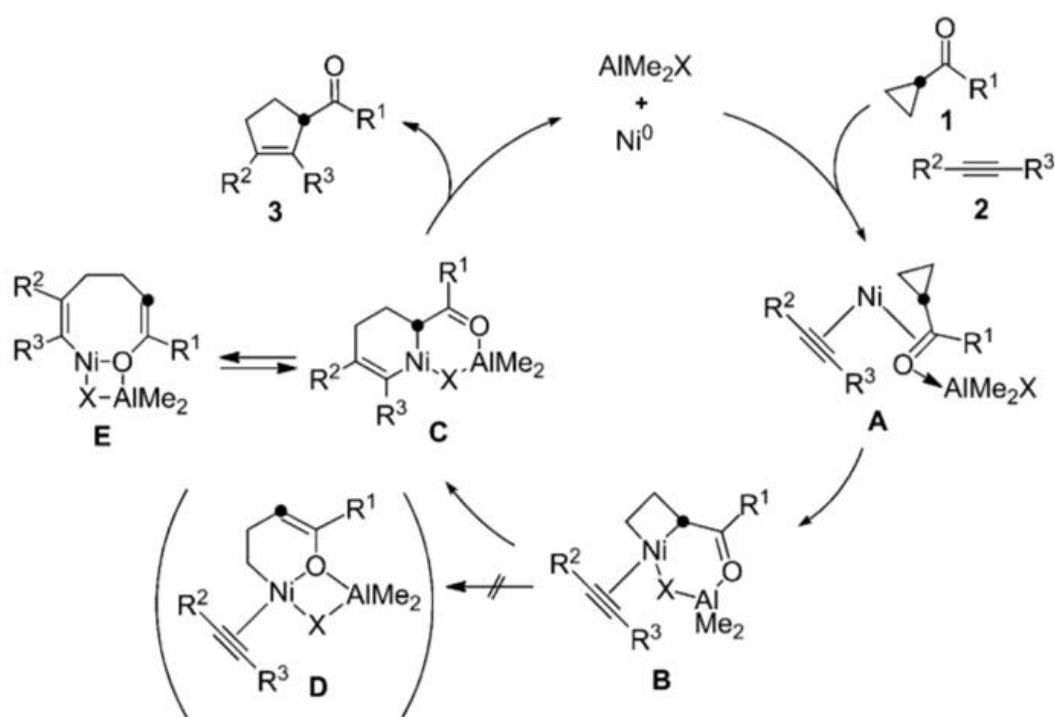
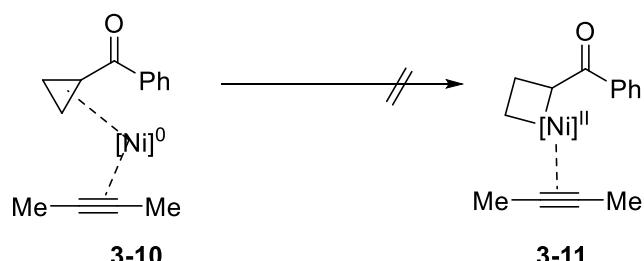
### Answer



**Discussion 5 : the roles of bimetallic catalyst**



Tamaki, T.; Ohashi, M.; Ogoshi, S., *Angew. Chem. Int. Ed.* **2011**, 50, 12067-12070



The ring opening reaction of cyclopropyl phenyl ketone with  $\text{AlMe}_3$  to give butyl ketone is promoted by nickel catalyst without ligand.