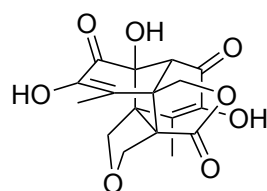
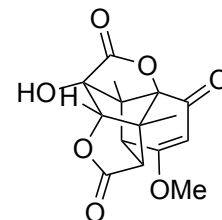


introduction:



epicolactone



preuisolactone A (2-3)

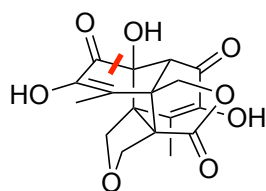
isolation: from *Epicoccum nigrum* (2012)<sup>1)</sup>

from *Preussia isomera* (2019)<sup>2)</sup>

structural features: highly oxygenated caged pentacyclic ring system

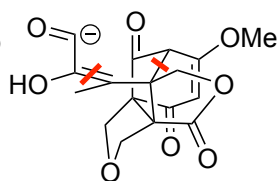
total synthesis: by Trauner's group (2015)<sup>3)</sup> (160903\_LS) by Trauner's group (2019)<sup>5)</sup> (**problem 2**)  
by Carreira's group (2018)<sup>4)</sup> (190206\_PS, **problem 1**)

retrosynthesis:

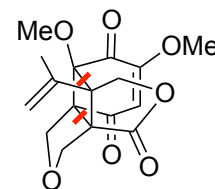


epicolactone

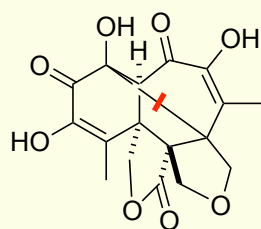
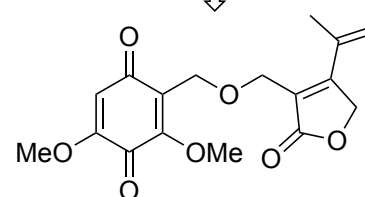
by Carreira's group  
acyl anion addition



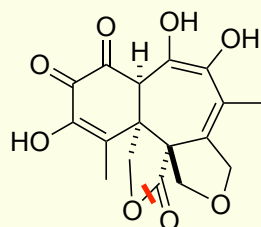
1,2-shift



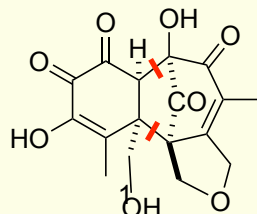
[2+2]



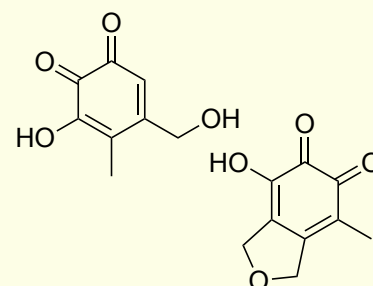
by Trauner's group  
vinylogous aldol reaction



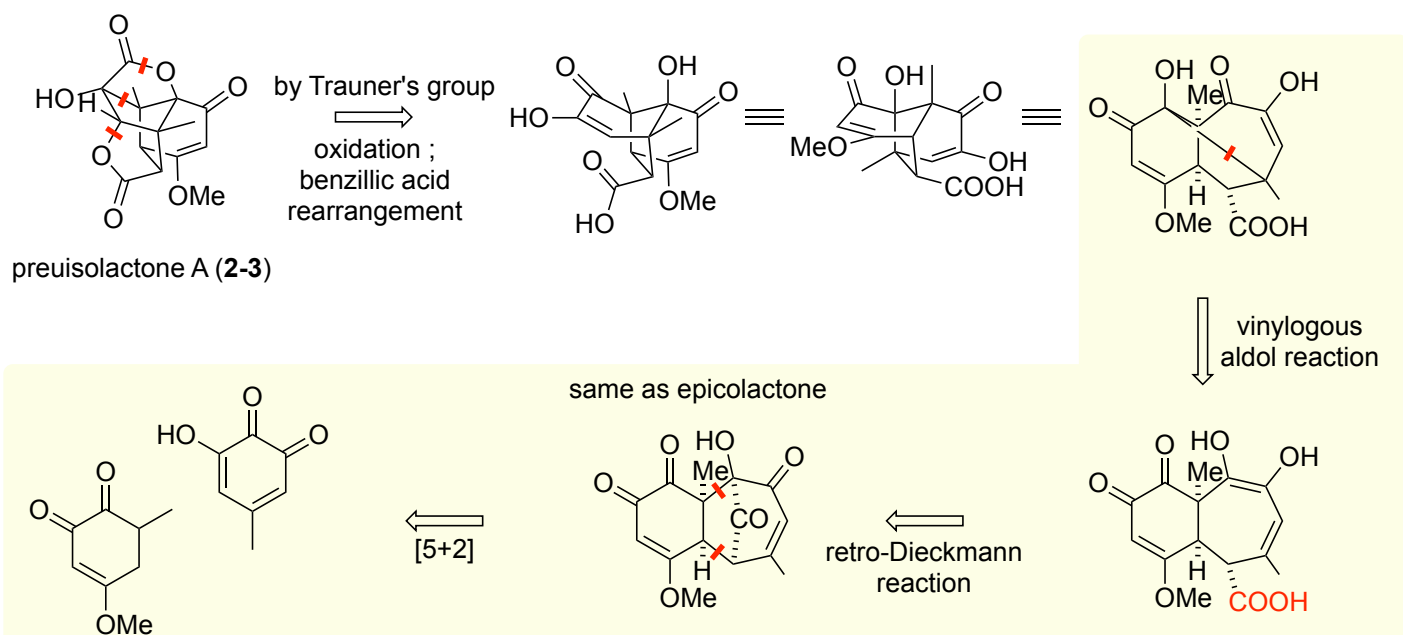
intramolecular nucleophilic attack



[5+2]

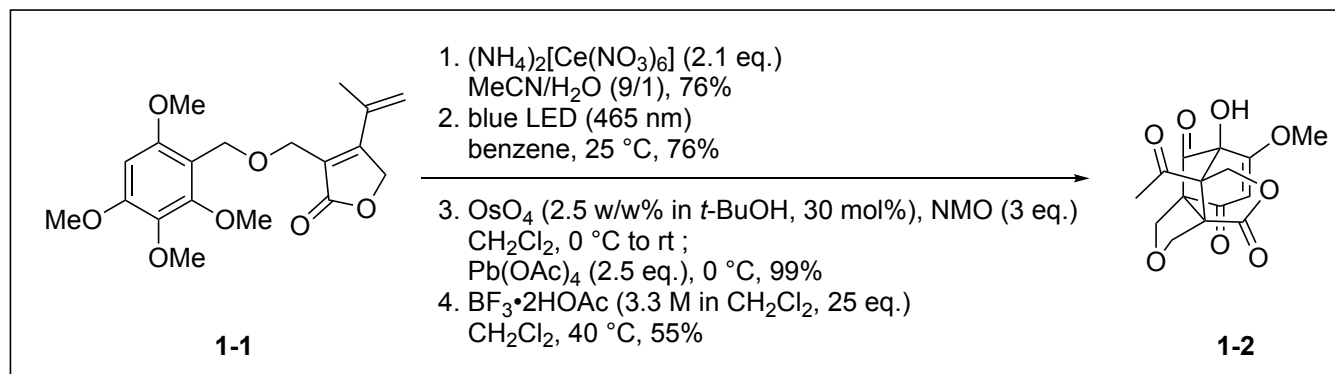


containing all oxygen atoms of epicolactone



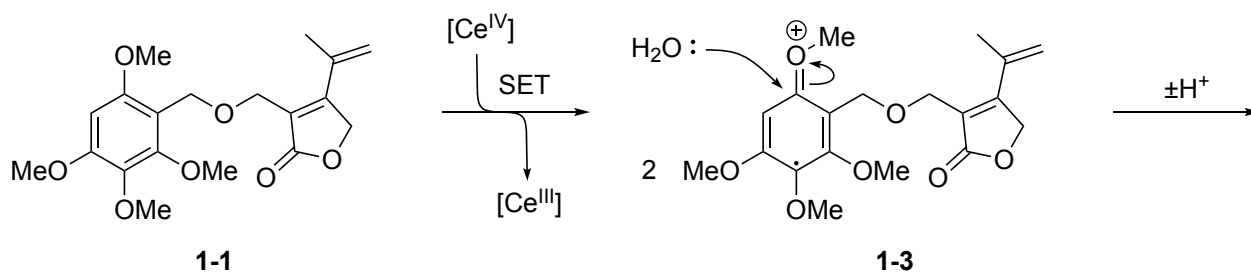
- 1) F. D. da Silva Araffljo, L. C. de Lima Fmvaro, W. L. Araffljo, F. L. de Oliveira, R. Aparicio, A. J. Marsaioli, *Eur. J. Org. Chem.* **2012**, 5225.
- 2) Xu, L.-L.; Chen, H.-L.; Hai, P.; Gao, Y.; Xie, C.-D.; Yang, X.-L.; Abe, I. *Org. Lett.* **2019**, 21 (4), 1078.
- 3) Ellerbrock, P.; Armanino, N.; Ilg, M. K.; Webster, R.; Trauner, D. *Nat. Chem.* **2015**, 7 (11), 879.
- 4) Kravina, A. G.; Carreira, E. M. *Angew. Chem., Int. Ed. Engl.* **2018**, 57, 13159.
- 5) Novak, A. J. E.; Grigglesstone, C. E.; Trauner, D. *J. Am. Chem. Soc.* **2019**, 141, 15515.

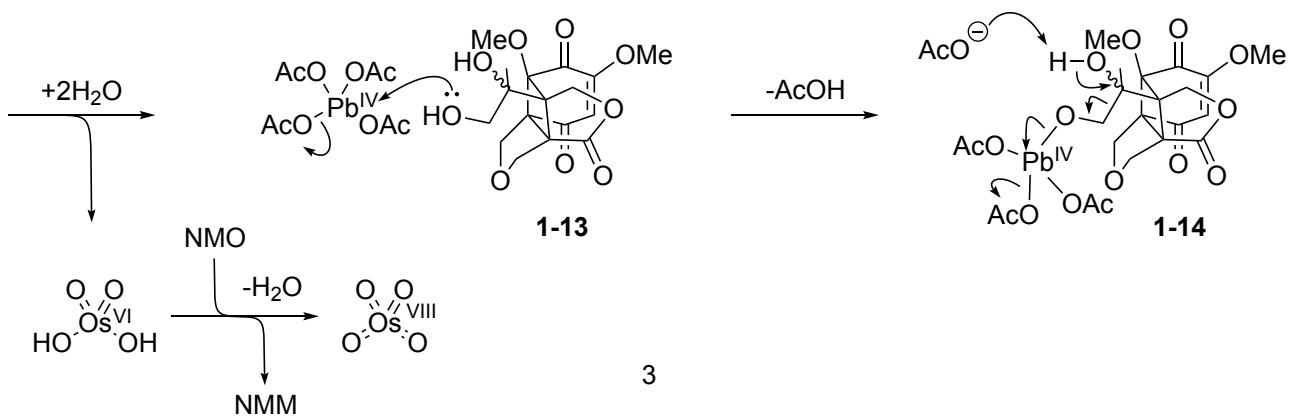
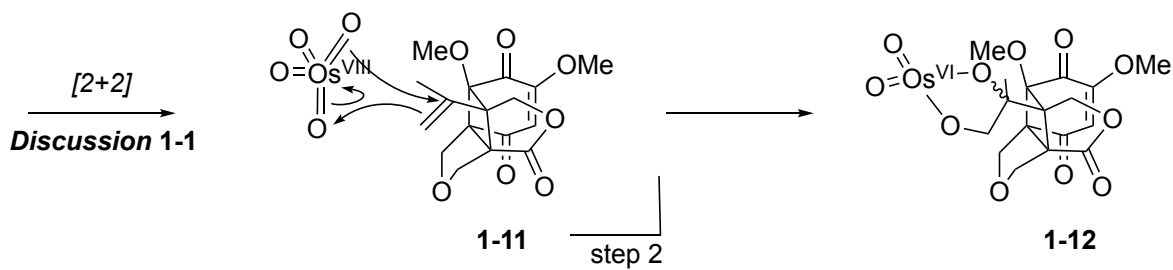
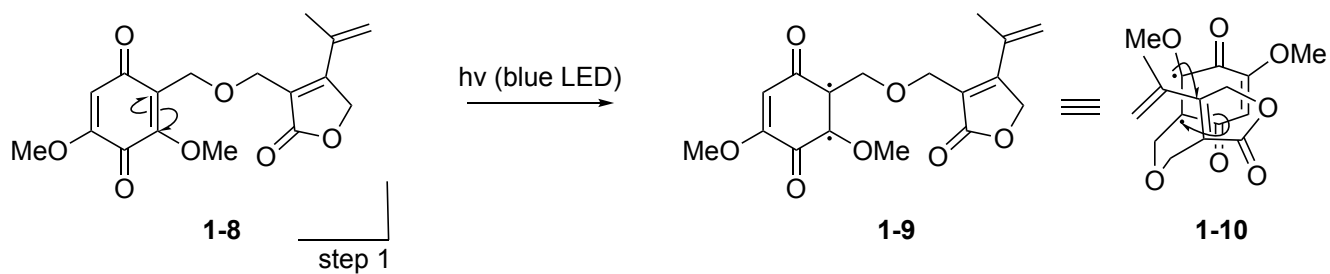
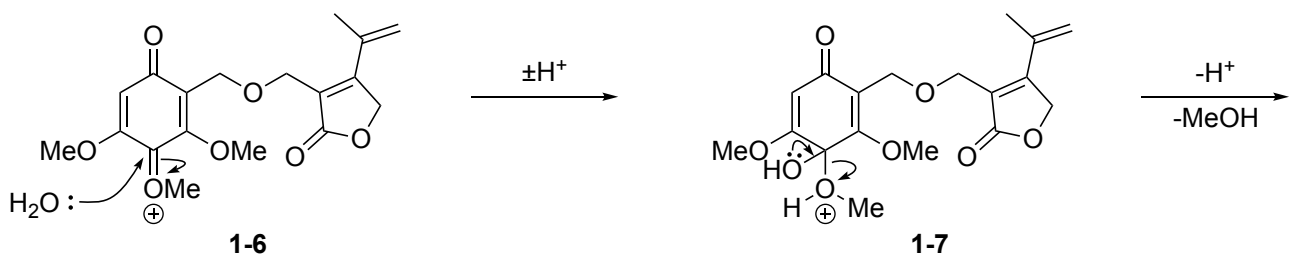
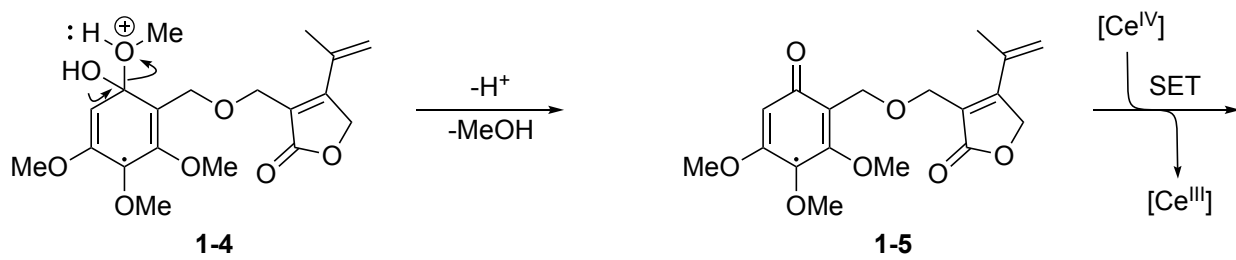
1

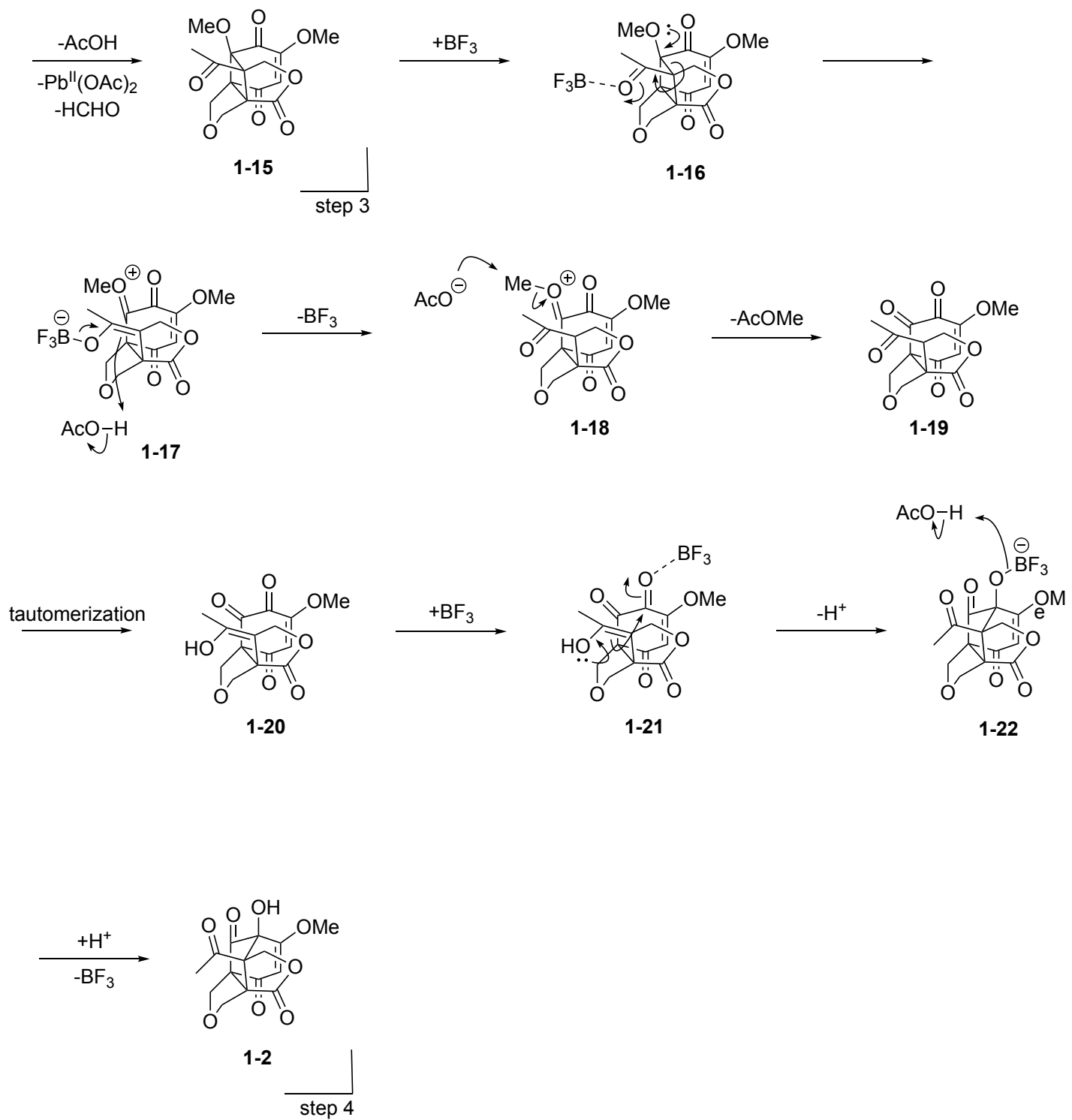


Answer:

Kravina, A. G.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2018**, 57, 13159.



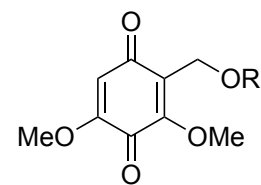
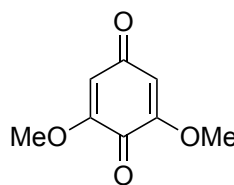
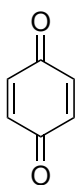




\* For more information of this retroaldol-aldol sequence, please also see 190209\_PS.

## Discussion 1-1: [2+2] photocycloaddition

### 1. UV and visible absorption



**1-8**

UV and visible absorption  
(in dioxane/H<sub>2</sub>O = 7/3)

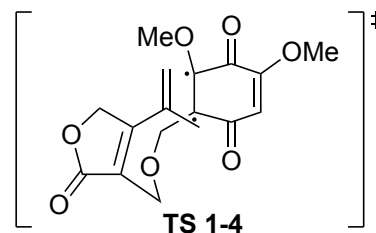
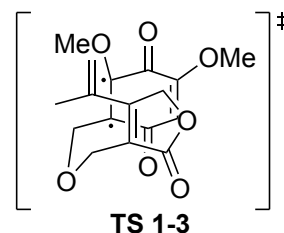
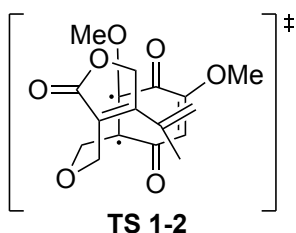
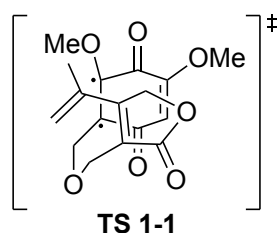
244, 302, 434, 453 nm

280, 379, 466 nm

→Methoxy groups raise HOMO level and decrease the excitation energy of quinone.

Villemin, D.; Hammadi, M.; Hachemi, M. *Synth. Commun.* **2002**, 32 (10), 1501.

### 2. Selectivity

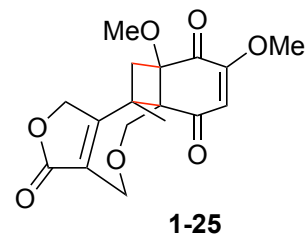
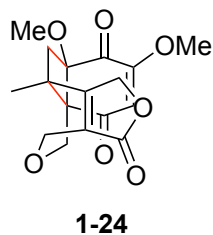
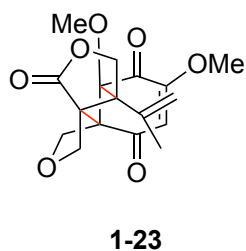
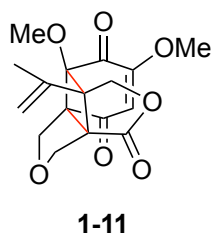


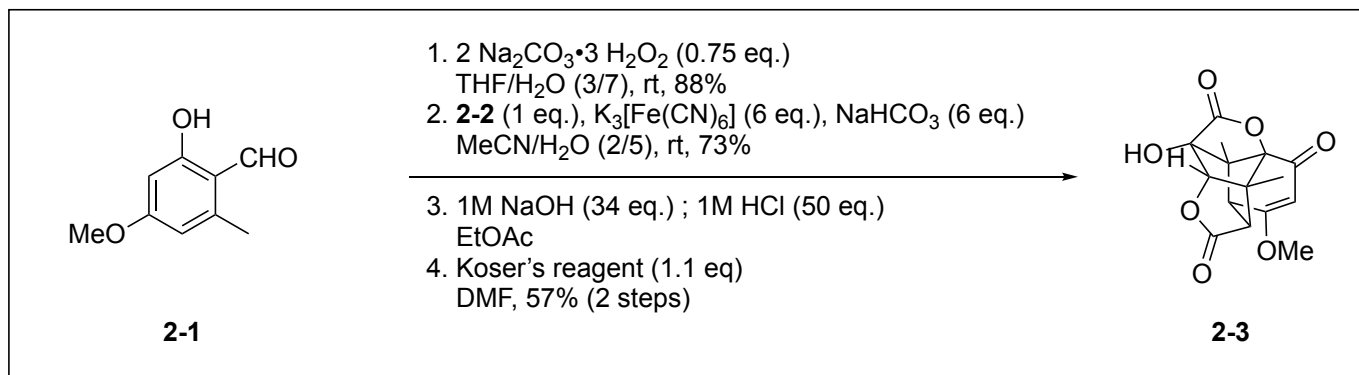
cis 4,5 ring  
formation ↓ favored

trans 4,5 ring  
formation ↓ unfavored

trans 4,7 ring  
formation ↓ unfavored

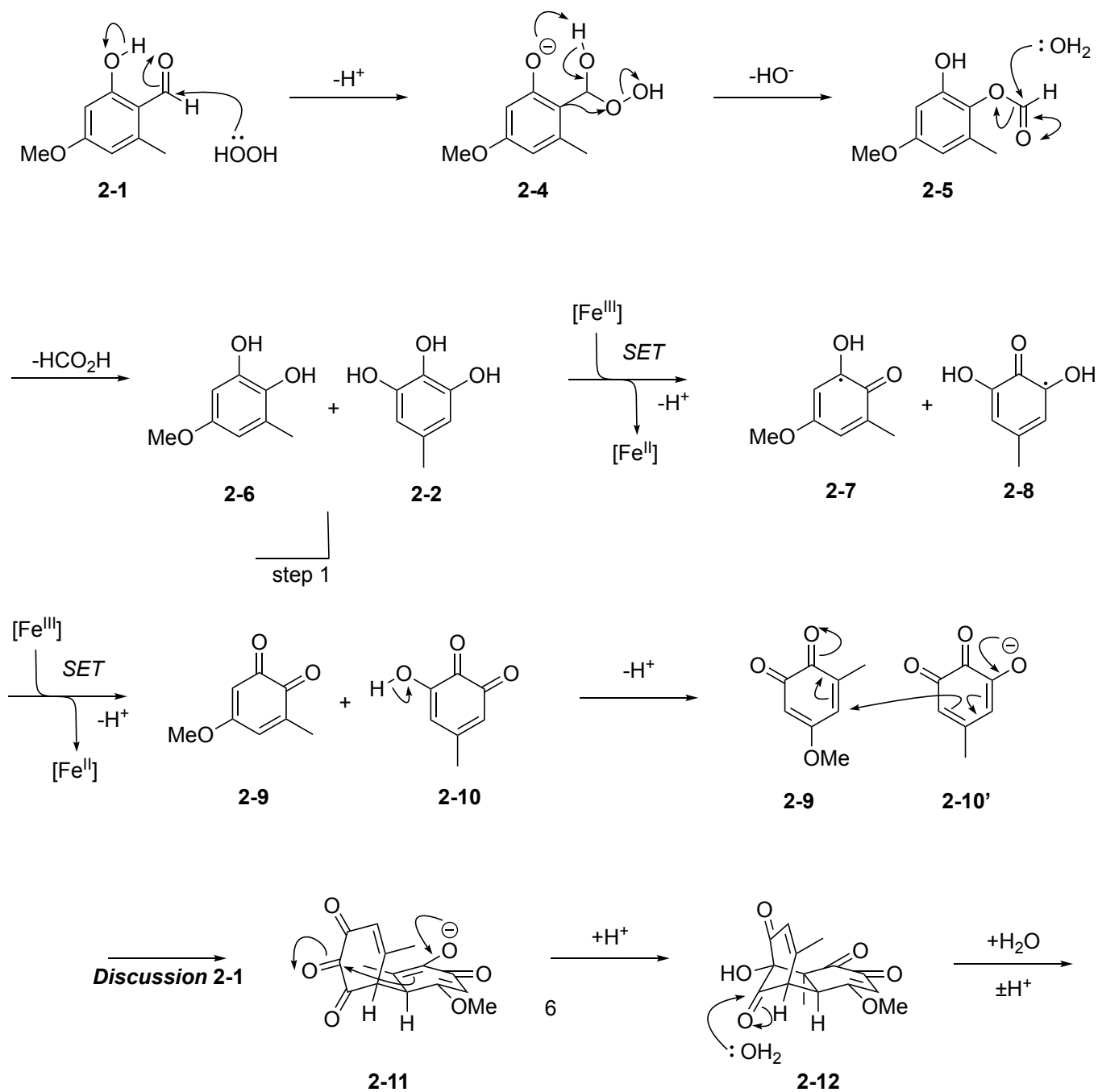
cis 4,7 ring  
formation ↓ less favored

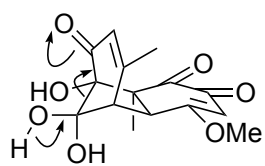




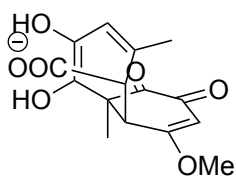
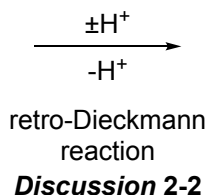
**Answer:**

Novak, A. J. E.; Grigglesstone, C. E.; Trauner, D. J. *Am. Chem. Soc.* **2019**, *141*, 15515.

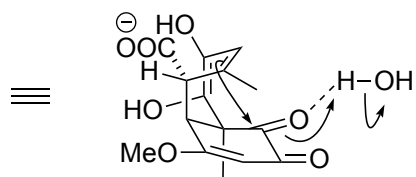




**2-13**

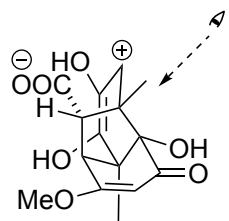


**2-14**

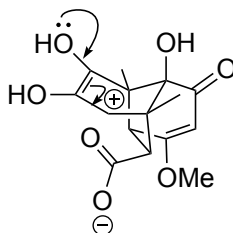


**2-15**

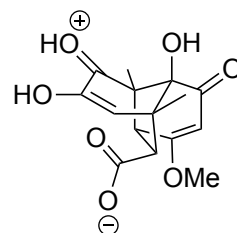
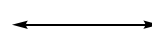
**Discussion 2-3**



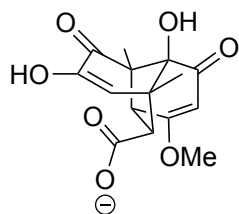
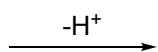
**2-16**



**2-17**

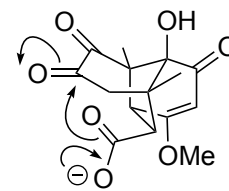


**2-18**



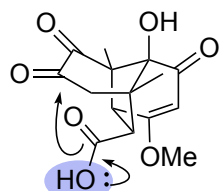
**2-19**

tautomerization



**2-21**

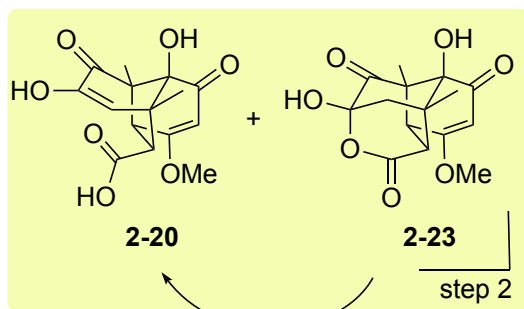
+acid



**2-24**

less nucleophilic

tautomerization

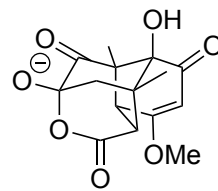


**2-20**

**2-23**

step 2

mild basic  
 condition  
 ↔  
 strong basic  
 condition

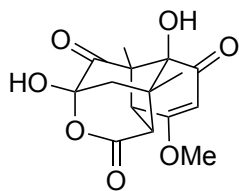


**2-22**

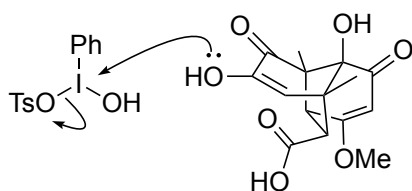
step 3

The mixture of **2-20** and **2-23** was obtained after 2nd and 3rd step. After 2nd step, **2-23** was major. Whereas after 3rd step, **2-20** was major.

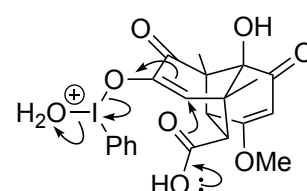
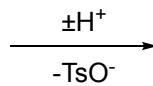
+PhI(O)OTs



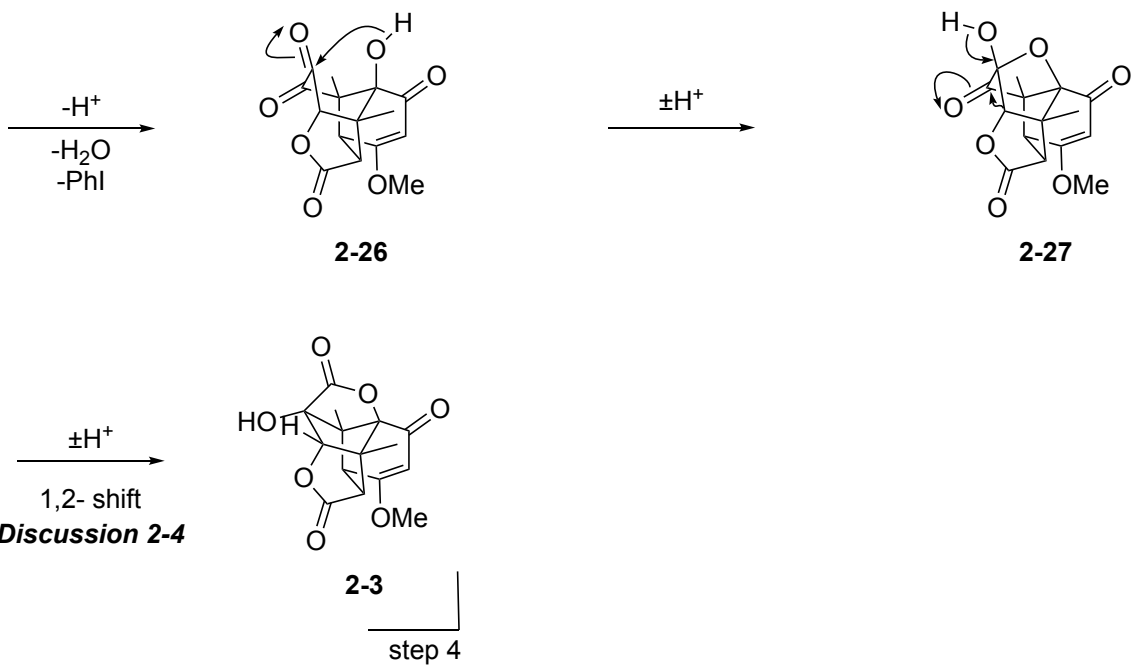
**2-23**



**2-20<sub>7</sub>**

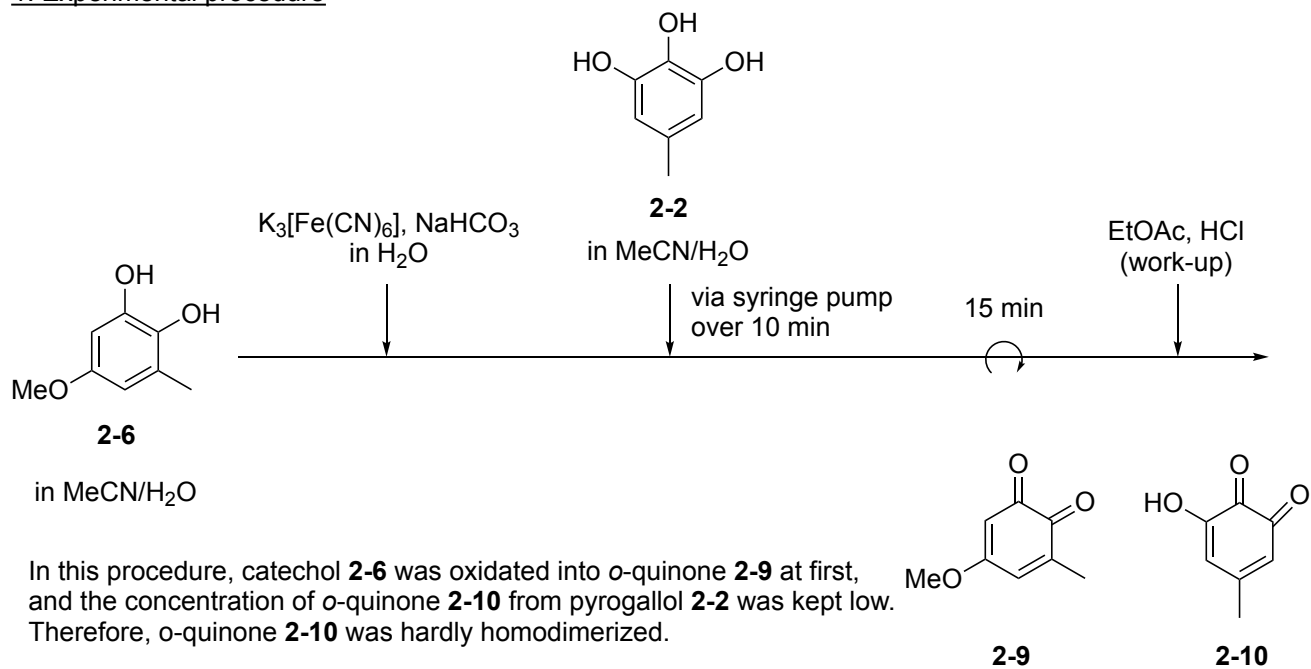


**2-25**



### Discussion 2-1: [5+2] cycloaddition

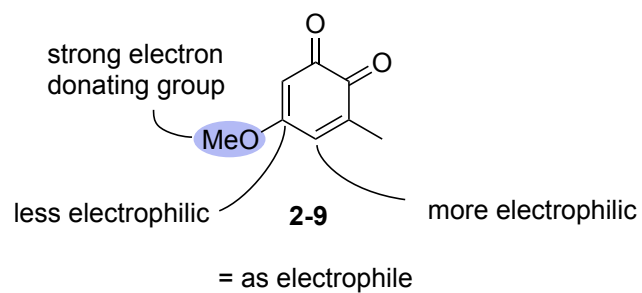
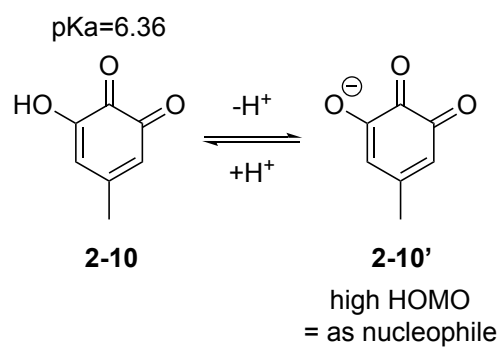
#### 1. Experimental procedure



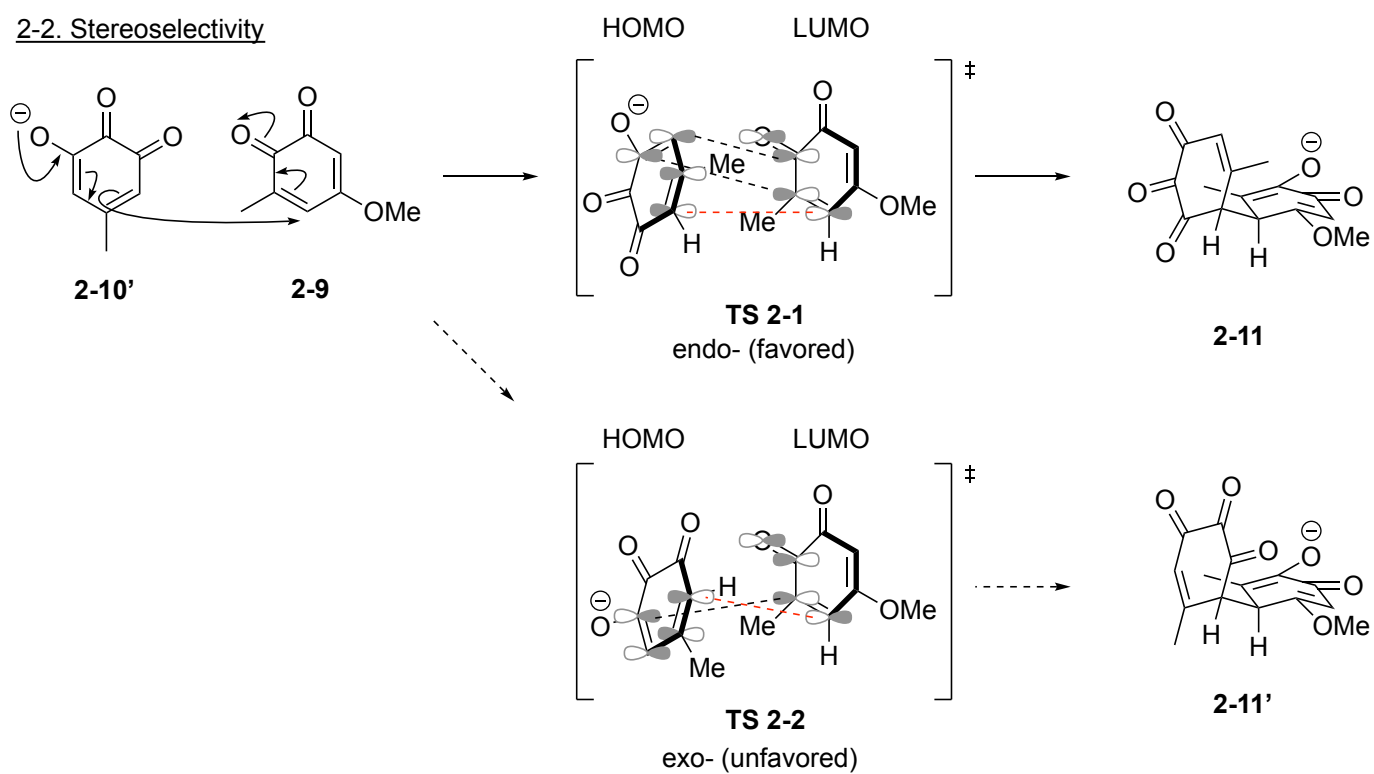


## 2. Selectivity

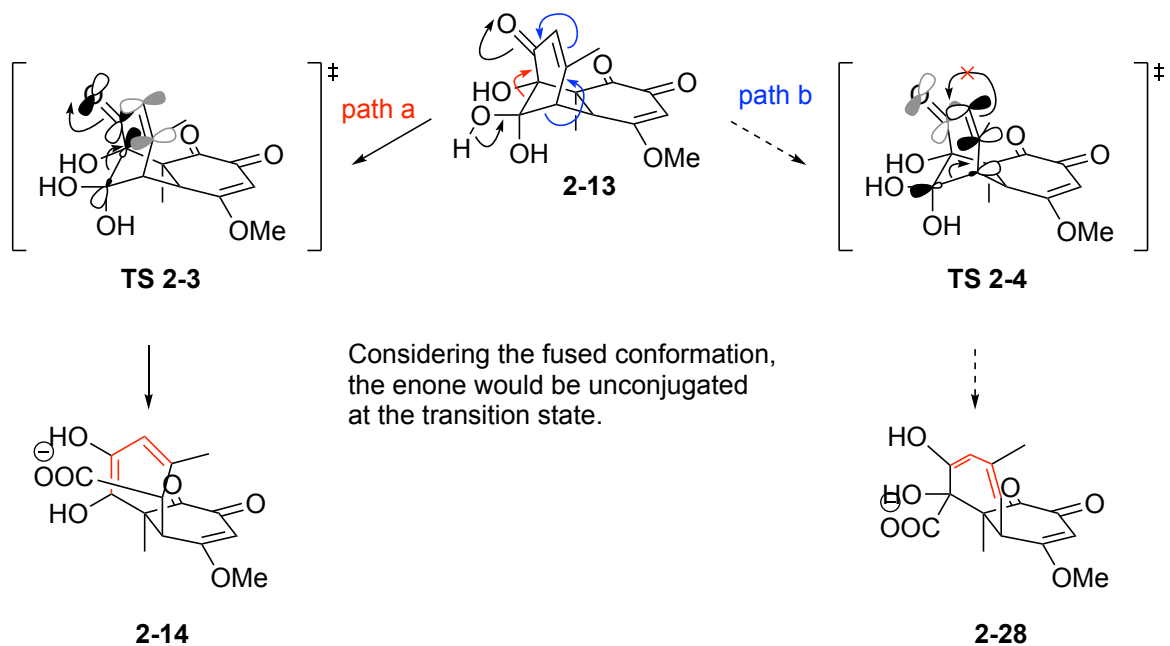
### 2-1. Chemoselectivity



### 2-2. Stereoselectivity

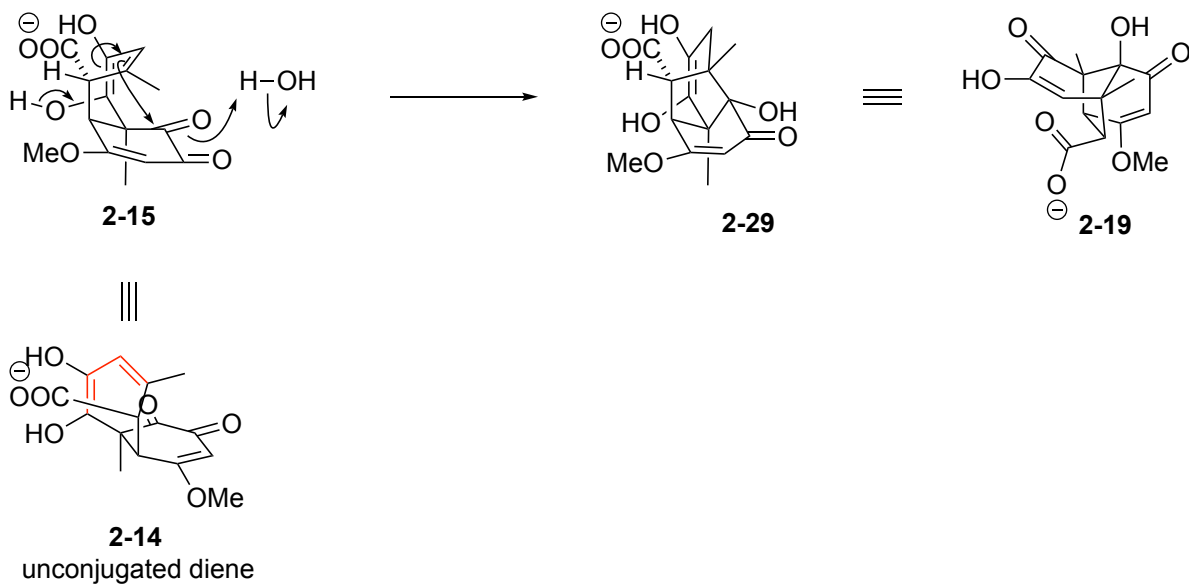


## Discussion 2-2: Selectivity of retro-Dieckmann reaction



## Discussion 2-3: Construction of 5 membered ring

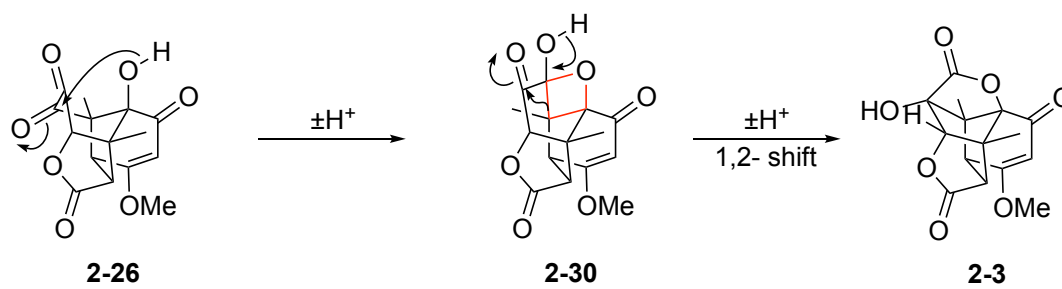
The reaction mechanism proposed by Trauner's group (vinylogous aldol reaction)



However, this vinylogous aldol reaction seems to be impossible since the diene couldn't be conjugated.

### Discussion 2-4: 1,2-shift

The reaction mechanism proposed by Trauner's group



This oxetane formation seems to be unfavored.