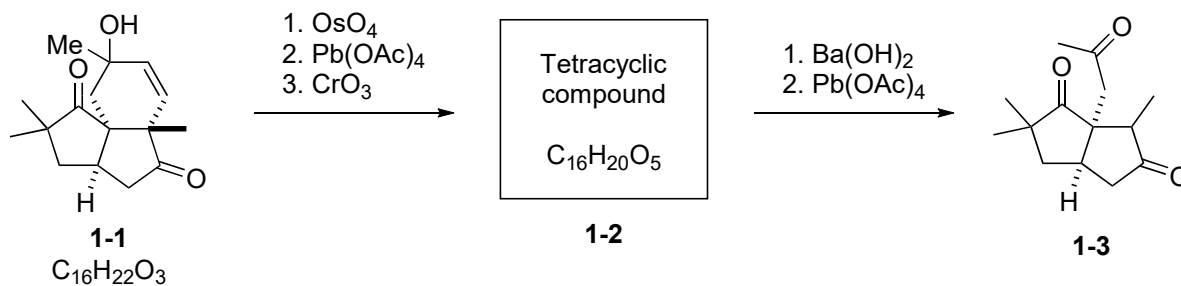
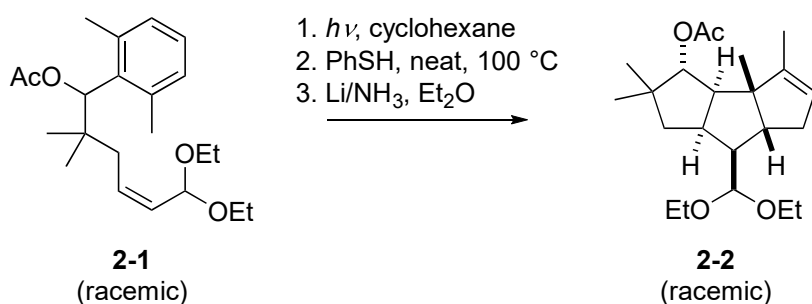


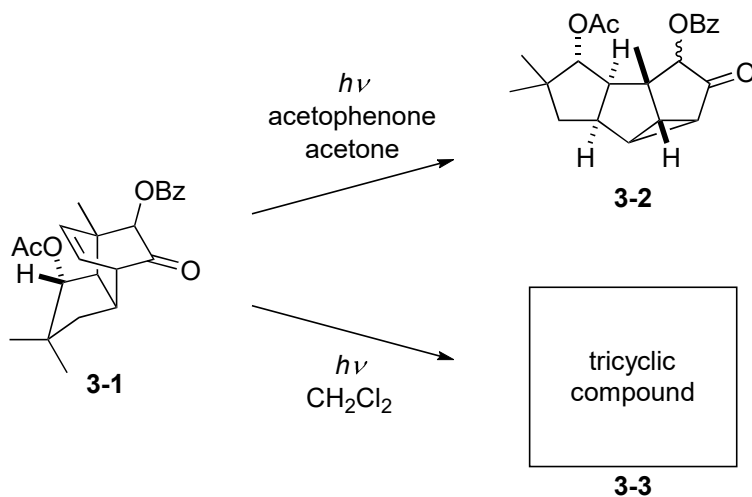
1. Please provide reasonable reaction mechanisms and fill in the blank.



2. Please provide reasonable reaction mechanism.

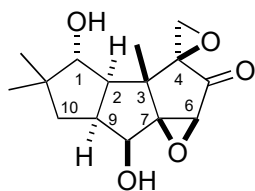


3. Photoreaction occurred using acetone and light and then compound **3-2** was obtained from **3-1**. However, if you use another condition like CH_2Cl_2 and light, you might not obtain compound **3-2**. Please guess the compound **3-3**.



Topic - Total synthesis of coriolin -

0. Introduction



coriolin (0-1)

- Isolated from *Coriolus consors*

Takeuchi, T.; Iinuma, H.; Iwanaga, J.; Takahashi, S.; Takita, T.; Umezawa, H. *J. Antibiotics* **1969**, 22, 215.

- Bioactivities

anti-bacterial and anti-tumor activity

Takeuchi, T.; Iinuma, H.; Iwanaga, J.; Takahashi, S.; Takita, T.; Umezawa, H. *J. Antibiotics* **1969**, 22, 215.

- Structure determination

Takahashi, S.; Iinuma, H.; Takita, T.; Maeda, K.; Umezawa, H. *Tetrahedron Lett.* **1969**, 53, 4663.

Takahashi, S.; Iinuma, H.; Takita, T.; Maeda, K.; Umezawa, H. *Tetrahedron Lett.* **1971**, 22, 1955.

Nakamura, H.; Takita, T.; Umezawa, H.; Kunishima, M.; Nakayama, Y. *J. Antibiotics* **1974**, 27, 301.

- Structural features

linear triquinane : Yokosaka san's PS_2011_10_14

eight continuous stereocenters

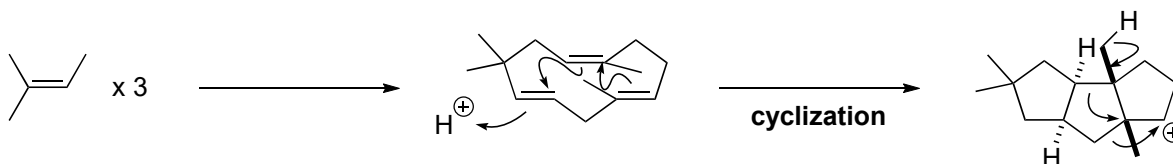
two quaternary carbons and two tetra-substituted carbons

- Biosynthesis

Feline, T. C.; Mellows, G.; Jones, R. B.; Phillips, L. *J. Chem. Soc. Chem. Commun* **1974**, 63.

Tanabe, M.; Suzuki, K. T. Jankowski, W. C. *Tetrahedron Lett.* **1974**, 26, 2271.

Nozoe, S. *Tetrahedron Lett.* **1976**, 3, 195.

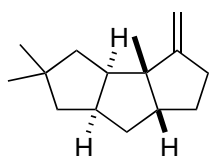


isoprene (0-2)

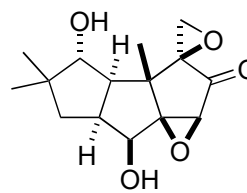
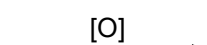
0-3

0-4

rearrangement



hirsutene (0-5)



coriolin (0-1)

- Total synthesis and formal total synthesis

(±)-coriolin

Tatsuta group (1980) : 25 steps (overall 0.3%)

Danishefsky group (1980) : 22 steps (overall 0.2%)

Ikegami group (1980) : 26 steps (overall 1.1%)

Trost group (1981) : 26 steps (overall 0.7%)

Mehta group (1982, 1986) : 19 steps (overall 0.8%)

Matsumoto group (1982) : 27 steps (overall 2.0%)

Wender group (1983) : **14 steps** (overall 0.4%)

Koreeda group (1983) : 18 steps (overall **5.8%**)

Mangus group (1983) : 19 steps (overall 0.7%)

Schuda group (1984) : 25 steps (overall 0.7%)

Funk group (1984) : 27 steps (overall 1.8%)

Little group (1985) : 26 steps (overall 0.3%)

Curran group (1988) : 22 steps (overall 1.7%)

Singh group (1999) : 19 steps (overall 0.1%)

Paquette group (2002) : 16 steps (overall 0.2%)

(-)-coriolin

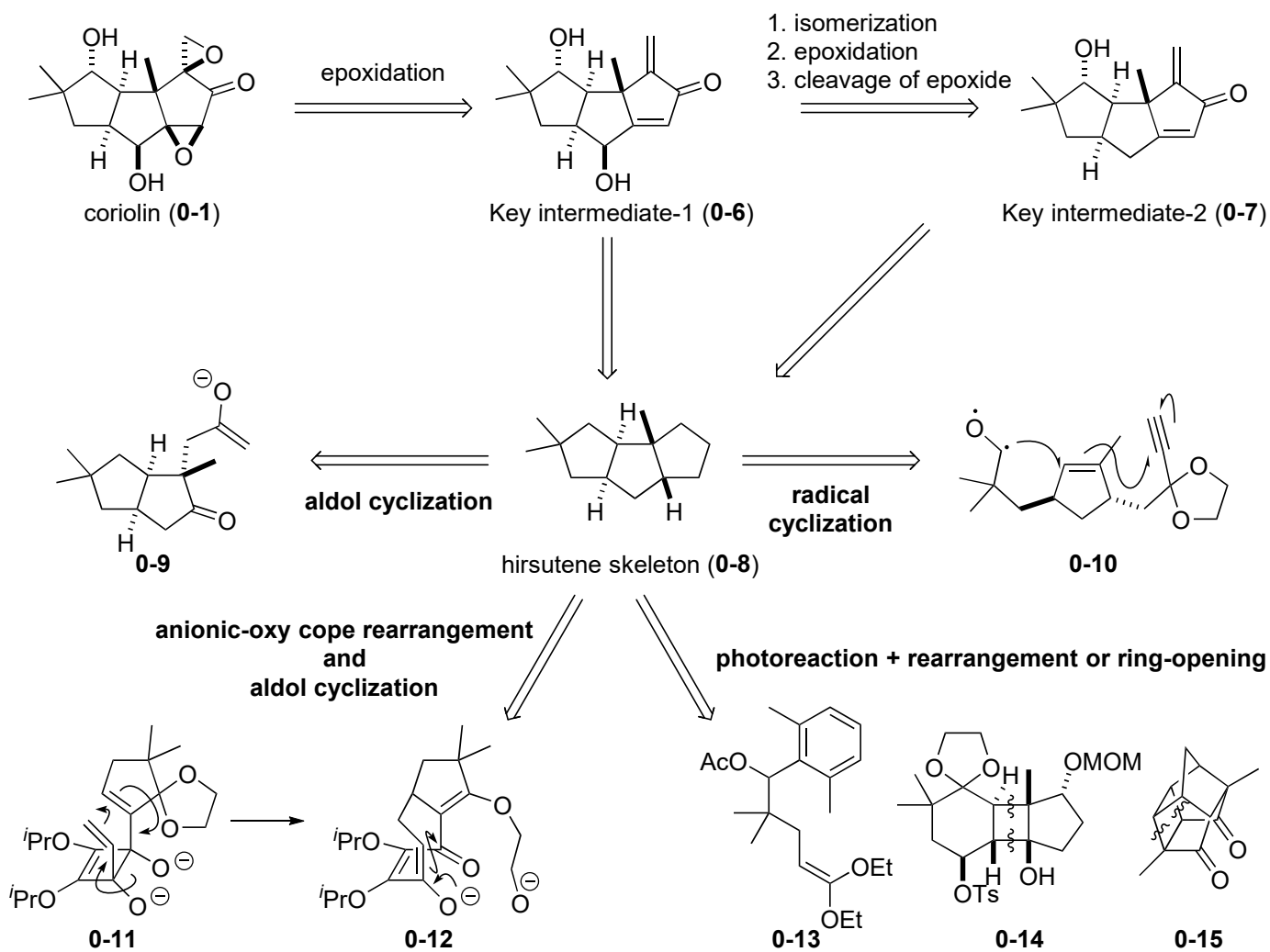
Demuth group (1986) : 16 steps (overall 0.2%)

Weings group (1993) : 21 steps (overall 0.2%)

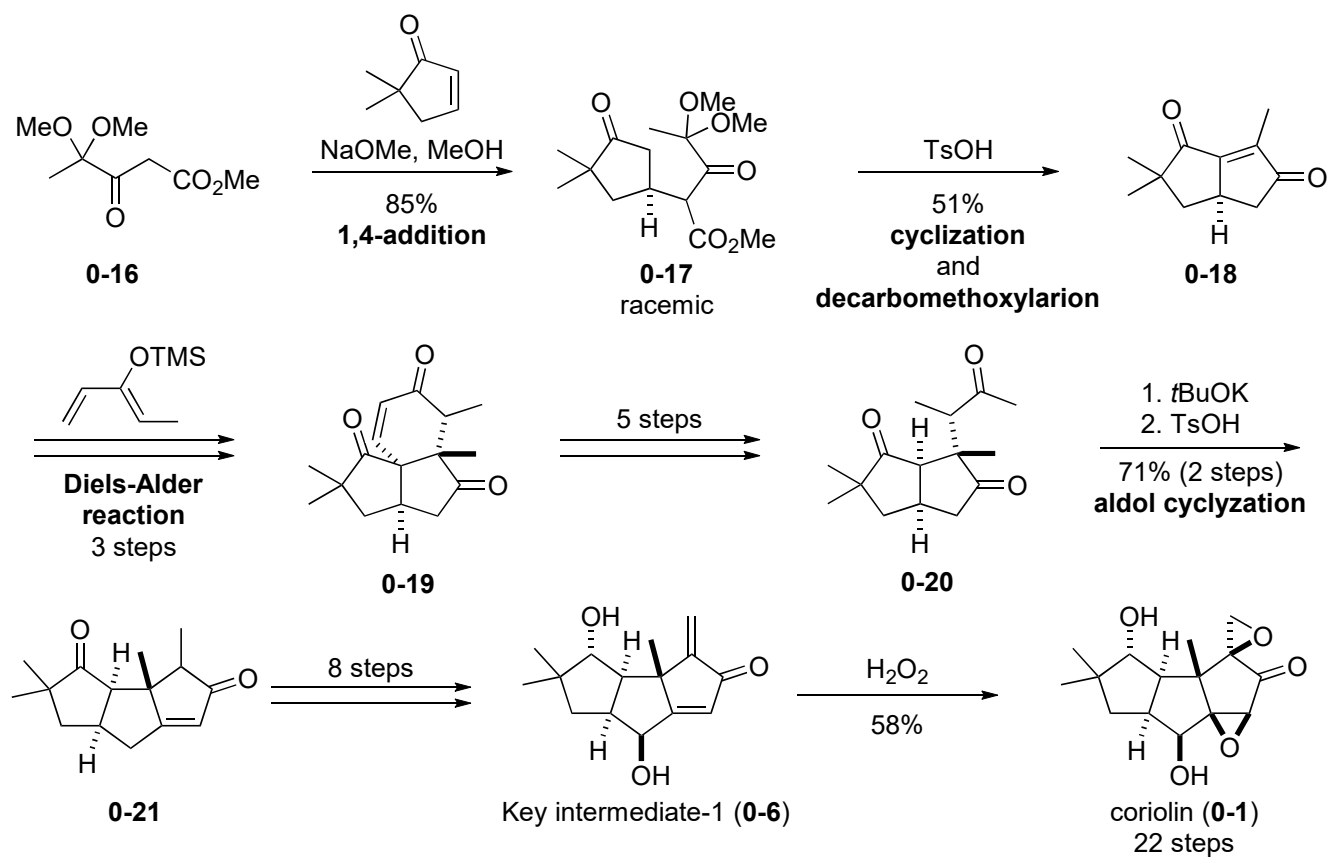
Kuwajima group (1997) : 31 steps (overall 4.4%)

Banwell group (2013) : 22 steps (overall 0.7%)

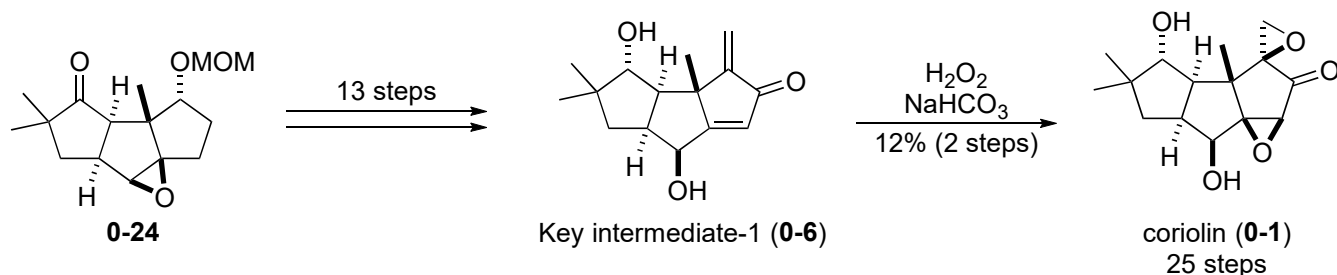
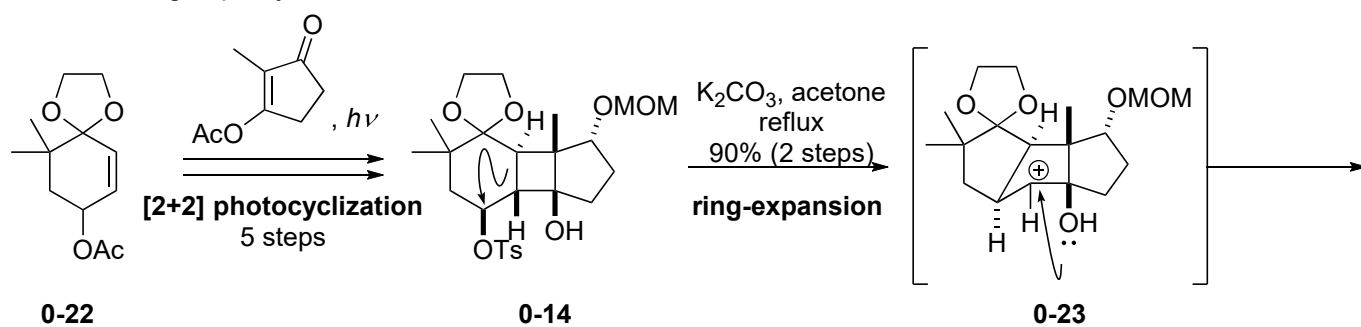
0-1. Retrosynthetic study



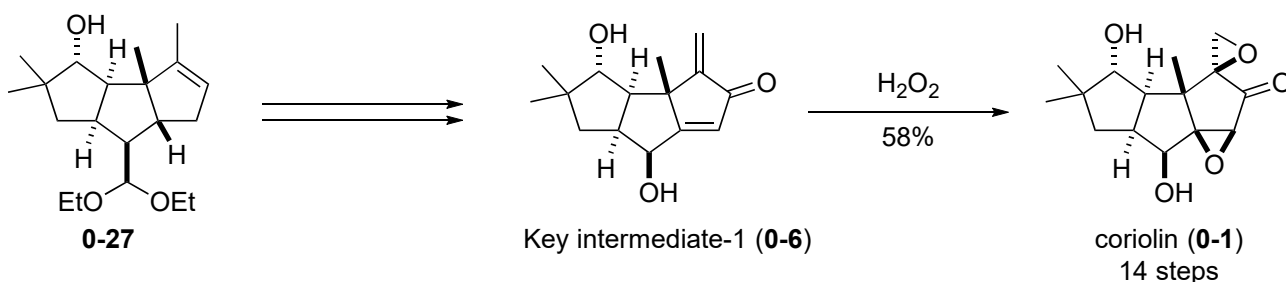
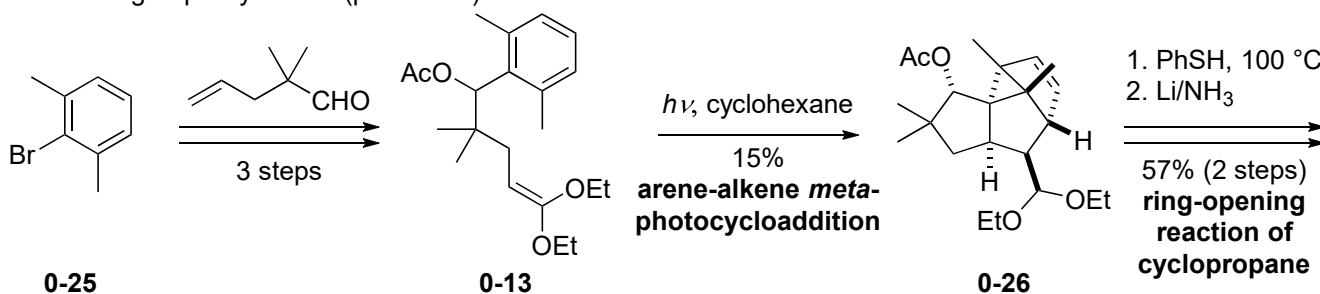
0-2. Danishefsky group's synthesis (problem 1)



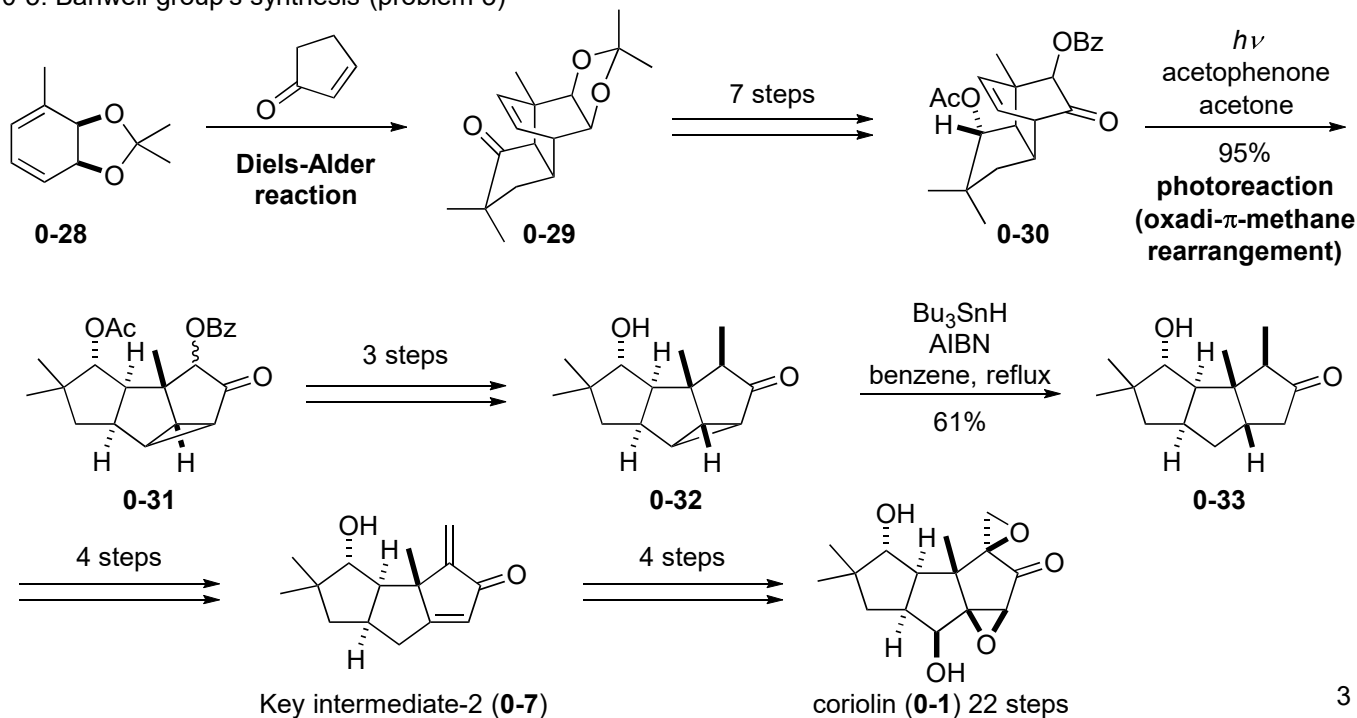
0-3. Tatsuta group's synthesis



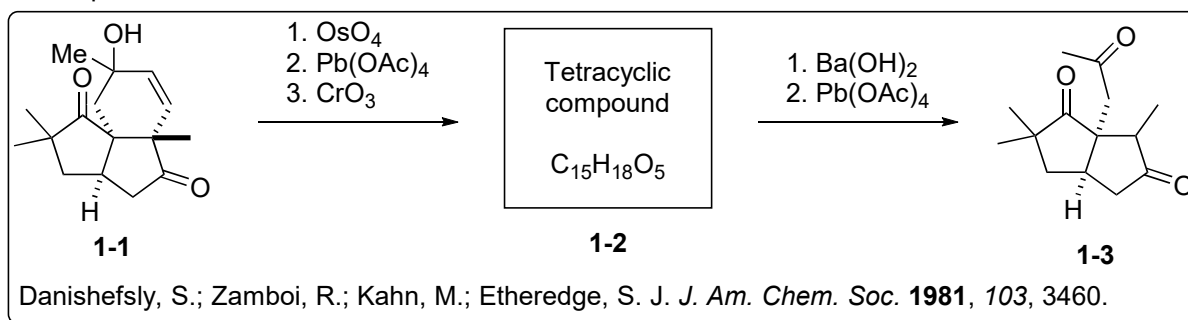
0-4. Wender group's synthesis (problem 2)



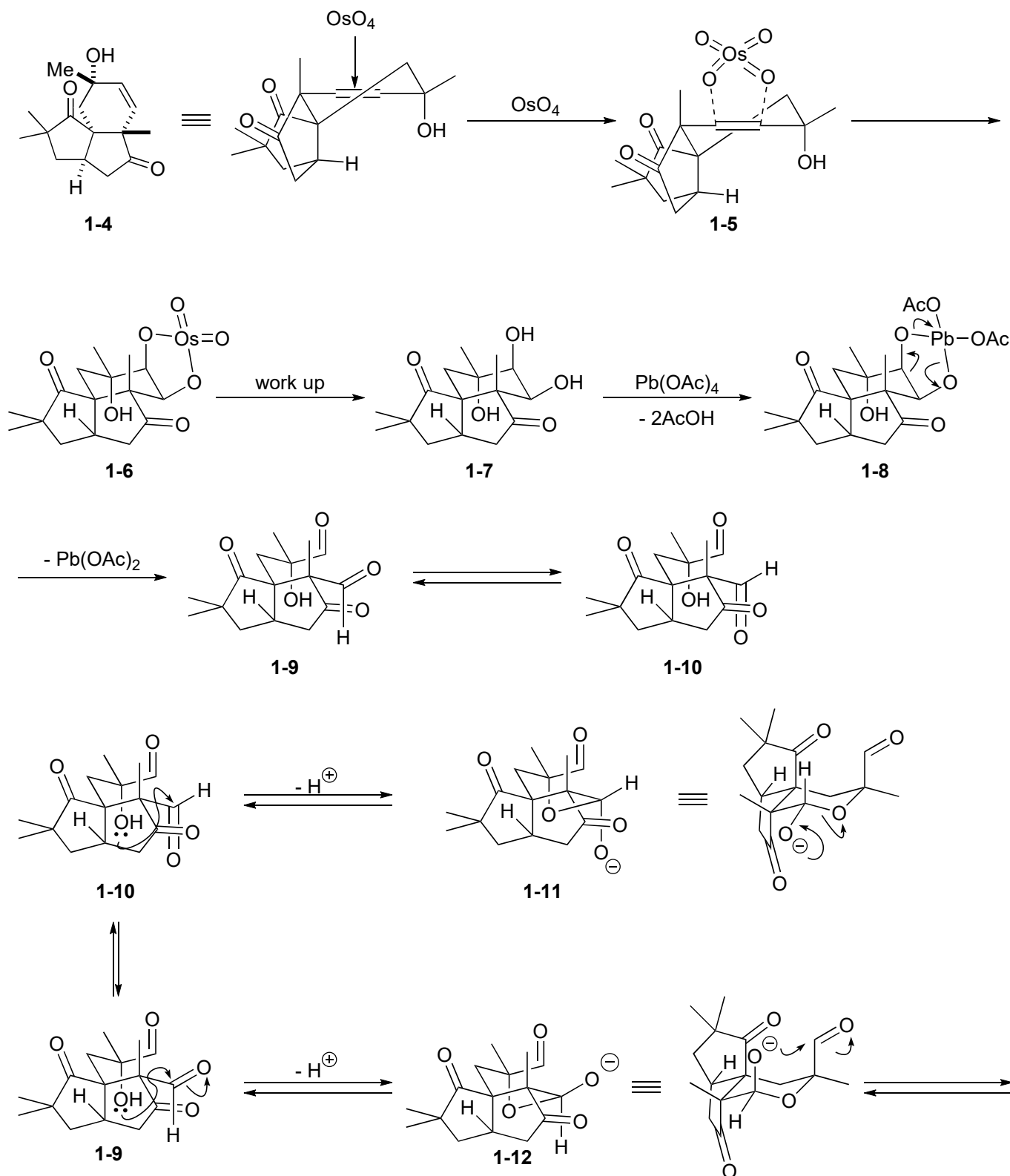
0-5. Banwell group's synthesis (problem 3)

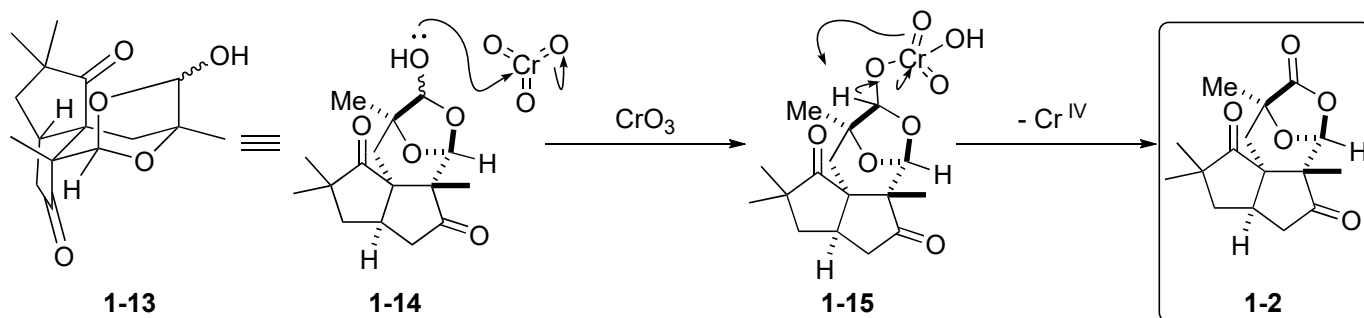


1. Please provide reasonable reaction mechanisms and fill in the blank.

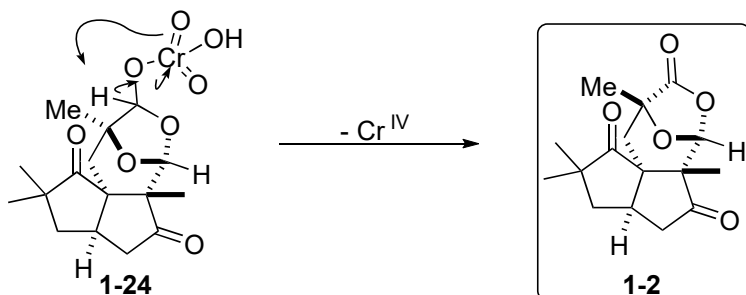
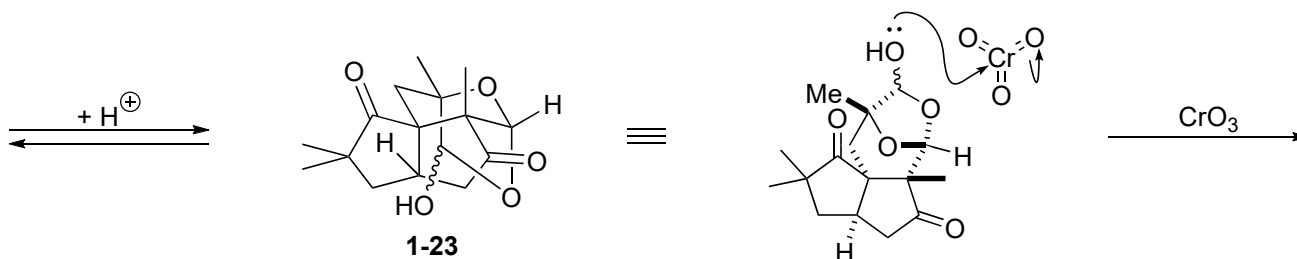
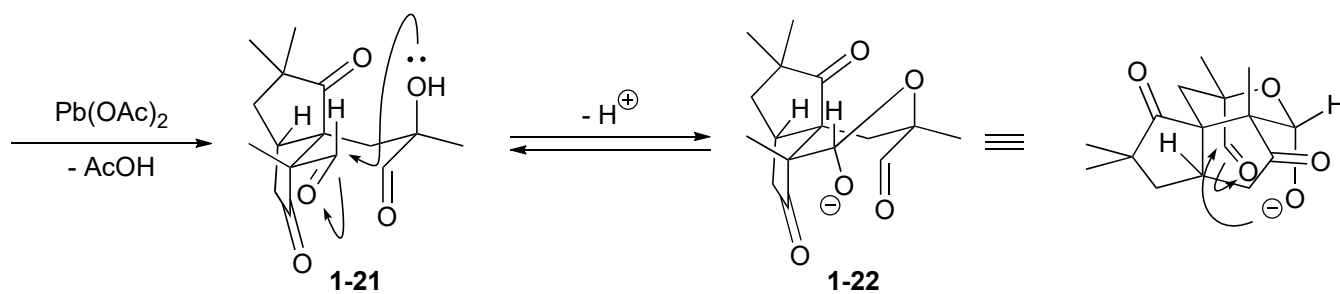
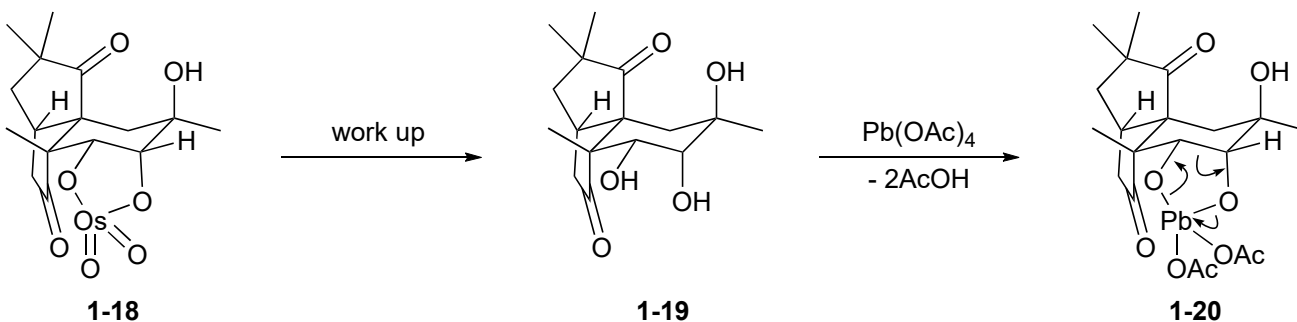
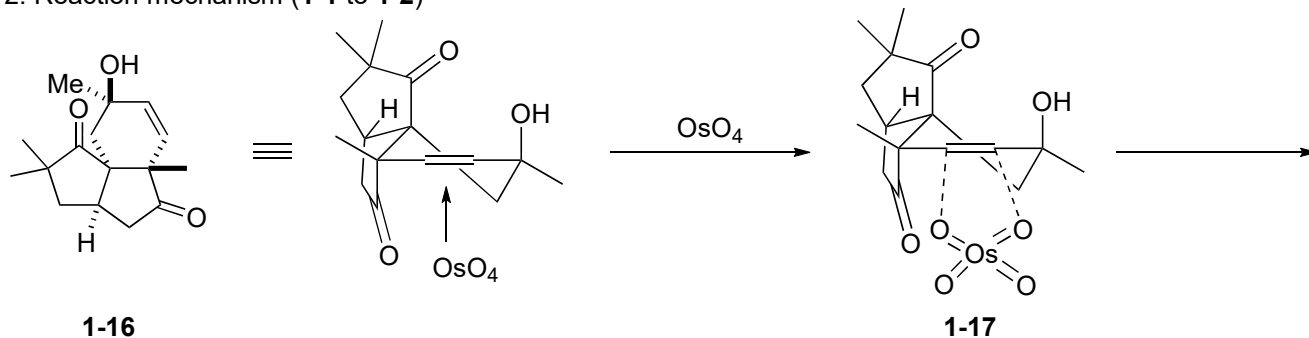


1-1. Reaction mechanism (1-1 to 1-2)

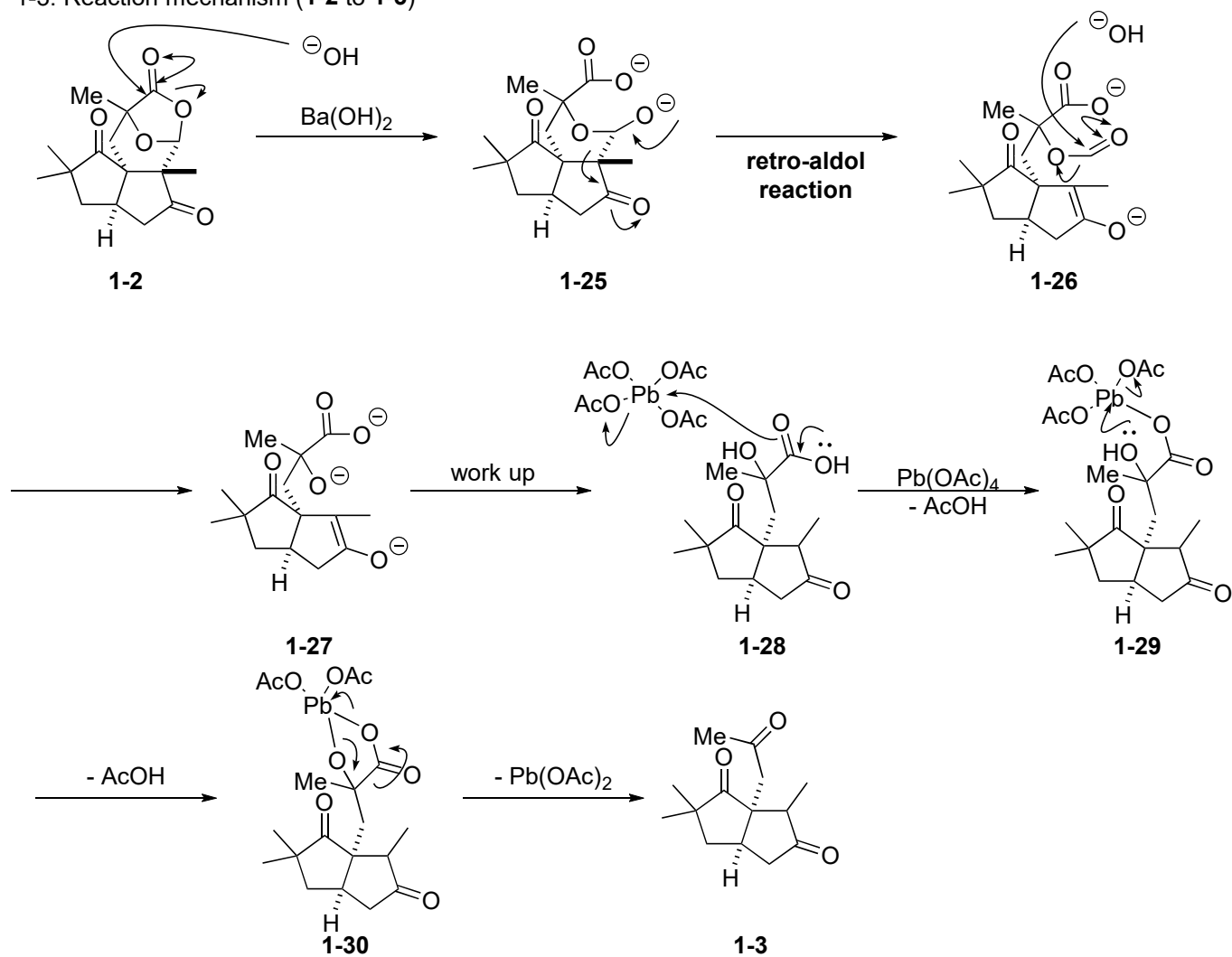




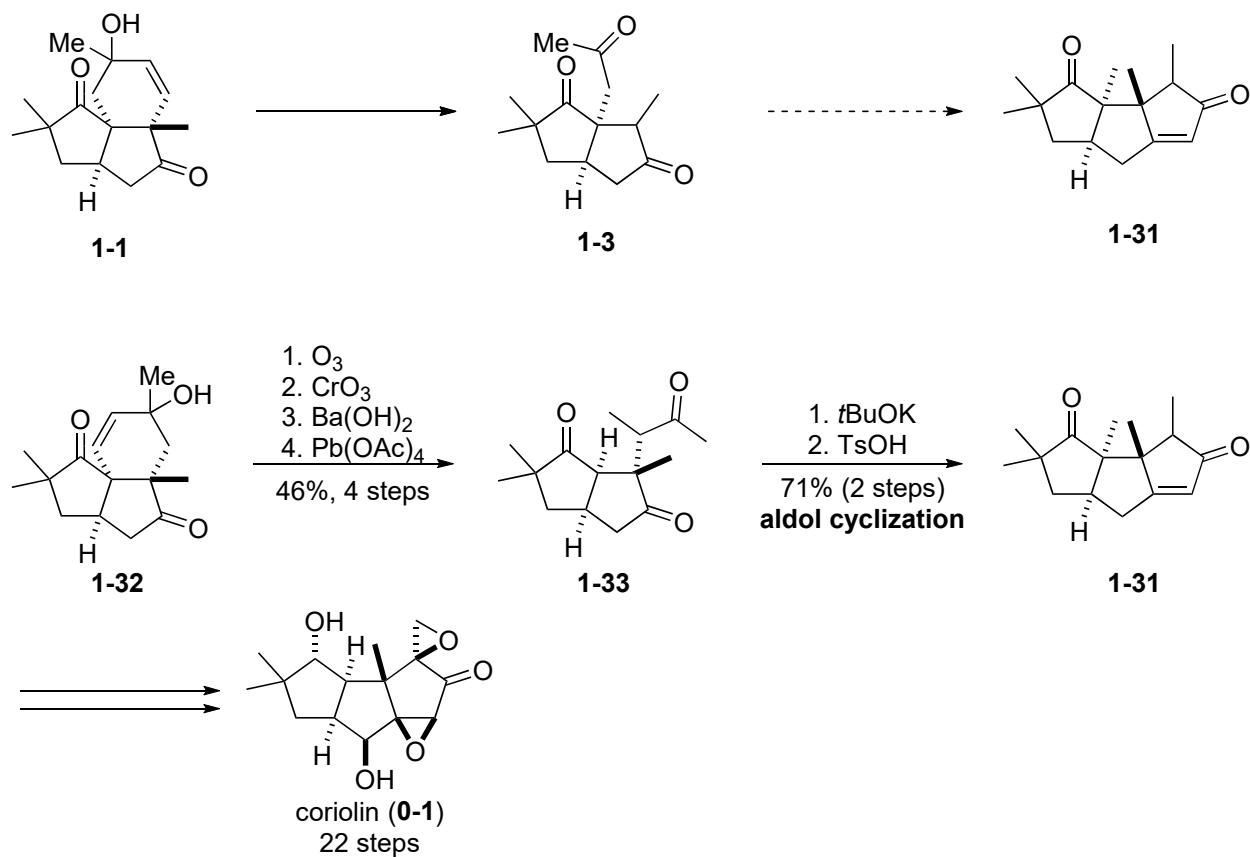
1-2. Reaction mechanism (1-1 to 1-2)



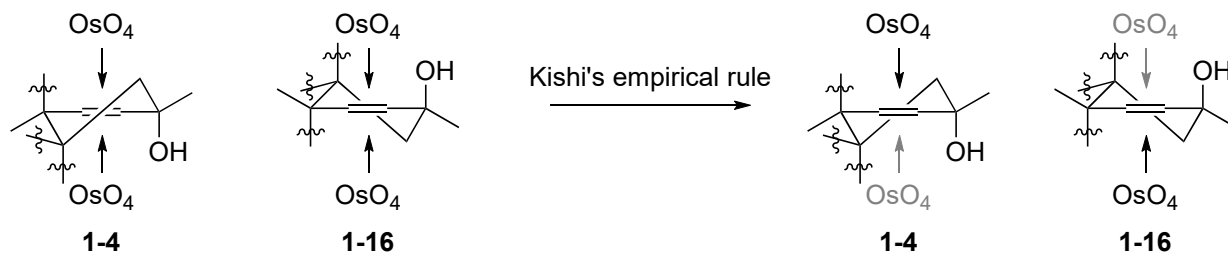
1-3. Reaction mechanism (1-2 to 1-3)



1-4. Total synthesis of coriolin



1-5. Selectivity of dihydroxylation



No steric repulsion between olefin and osmium

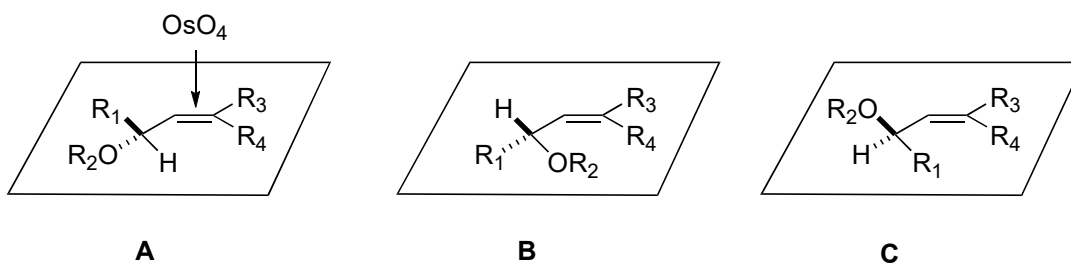
Osmium tetroxide reacted against hydroxyl group

Kishi's empirical rule

- The relative stereochemistry between the preexisting hydroxyl or alkoxy group and the adjacent newly introduced hydroxyl group of the major product in all cases erythro.

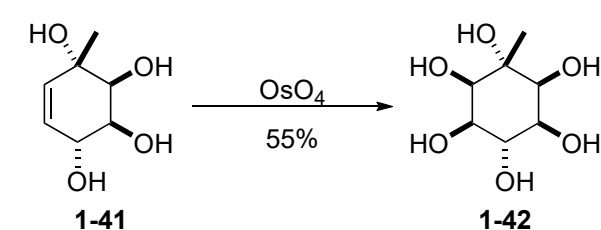
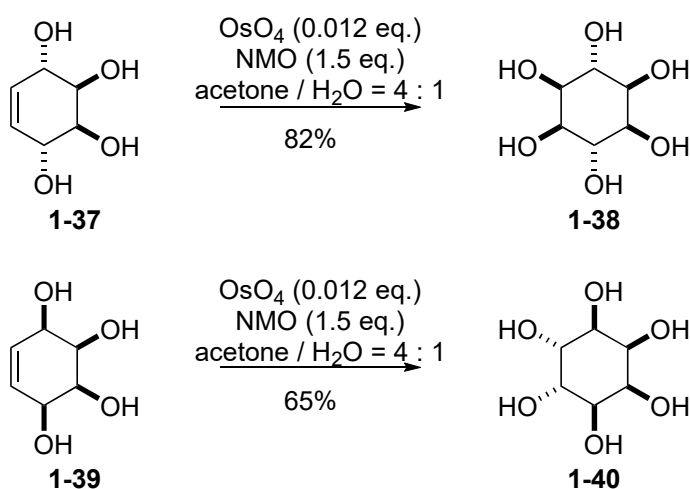
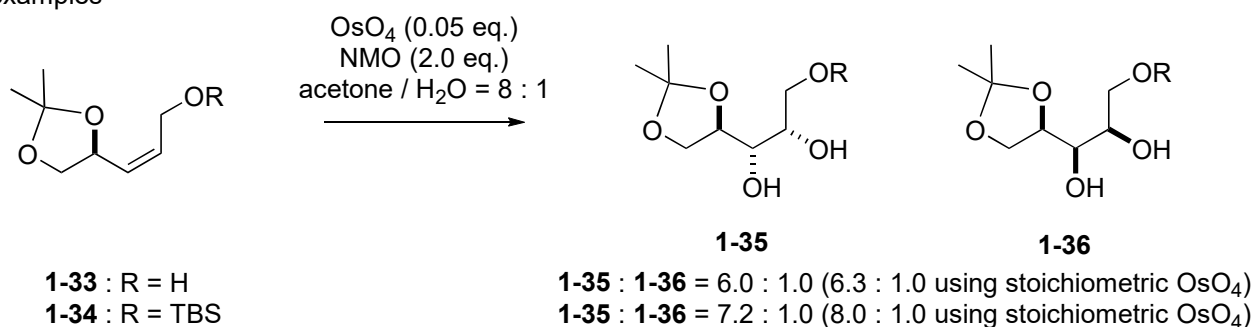
Cha. J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron Lett* **1983**, 24, 3943.

Cha. J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron* **1984**, 40, 2247.



Sterically least compressed conformation (minimum energy)

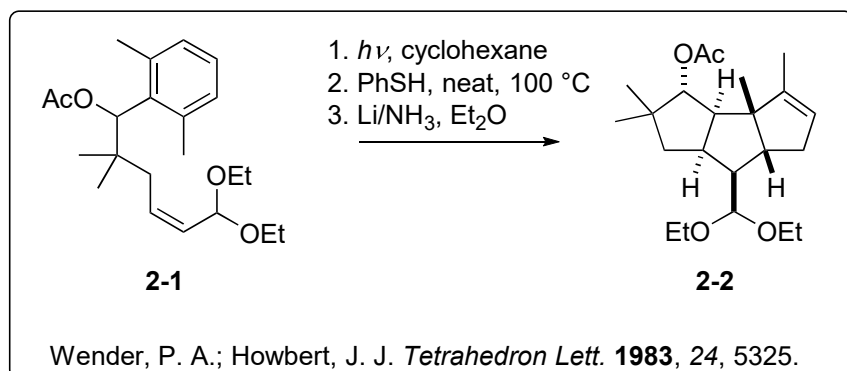
Some examples



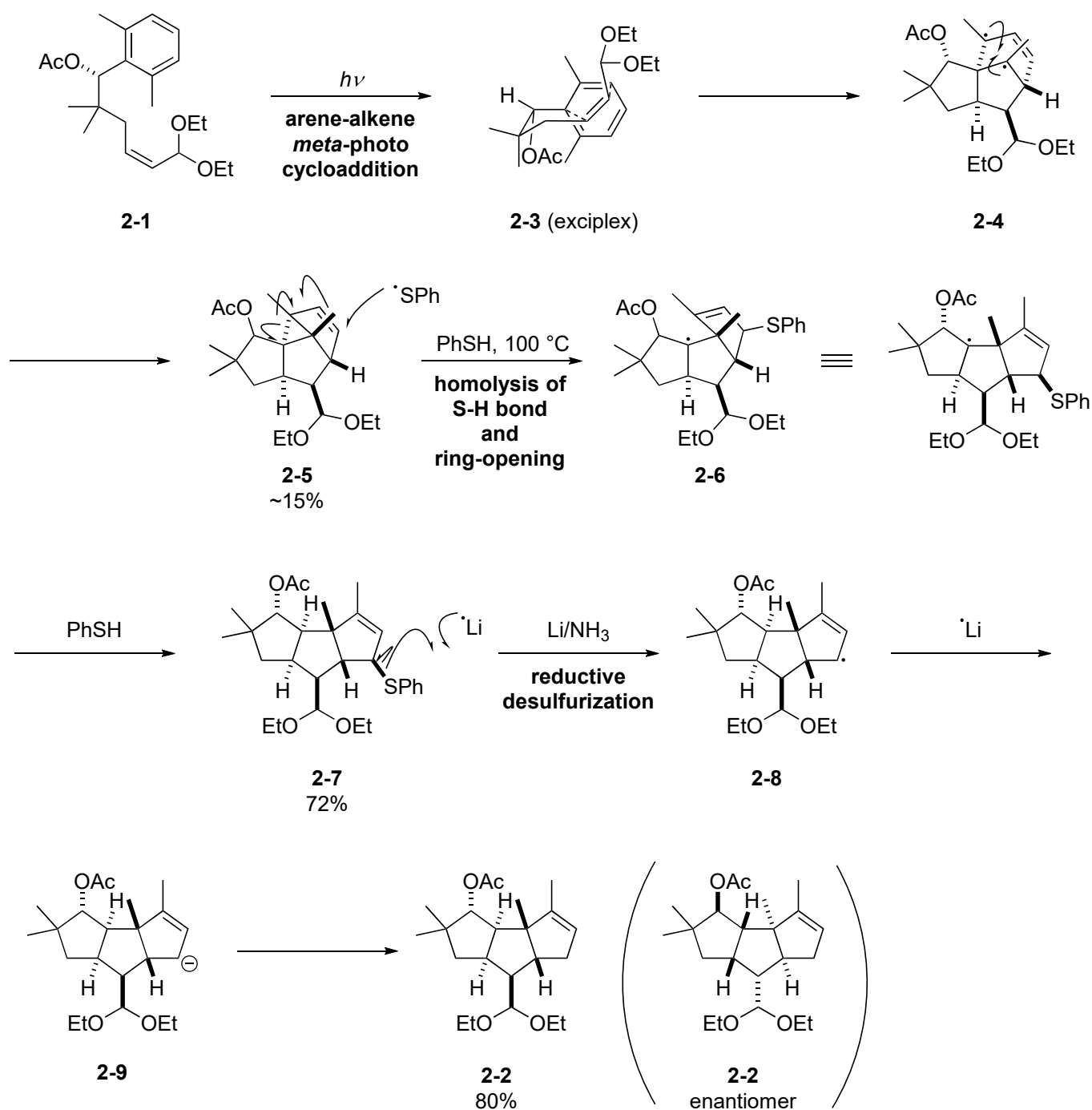
Carless, H. A. J.; Oak, B. Z. *Tetrahedron Lett.* **1991**, 32, 1671.

Carless, H. A. J.; Busia, K.; Oak, B. Z. *Synlett* **1993**, 672.

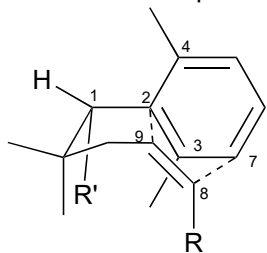
2. Please provide reasonable reaction mechanism.



2-1. Reaction mechanism

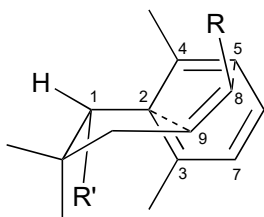


2-2. *meta* addition possibilities



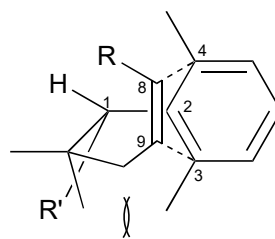
2-10

R = CH(OEt)₂, R' = OAc
C2-C9, C7-C8



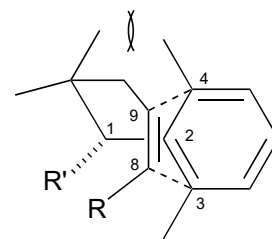
2-11

R = CH(OEt)₂, R' = OAc
C2-C9, C5-C8



2-12

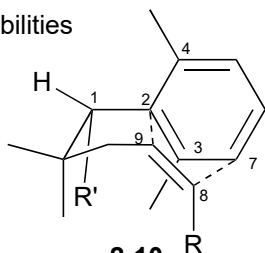
R = CH(OEt)₂, R' = OAc
C3-C9, C4-C8



2-13

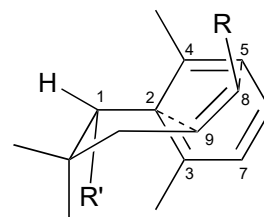
R = CH(OEt)₂, R' = OAc
C3-C8, C4-C9

2-3. *exo/endo* possibilities



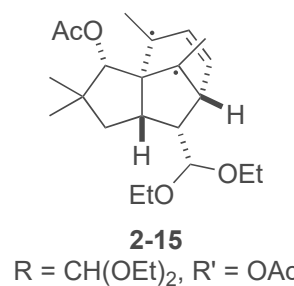
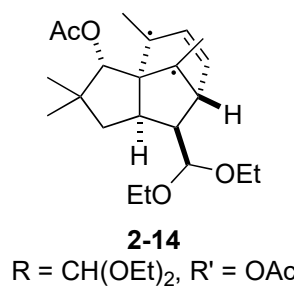
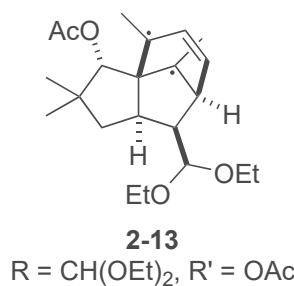
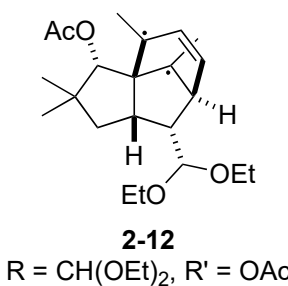
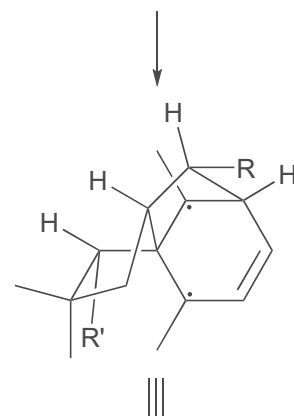
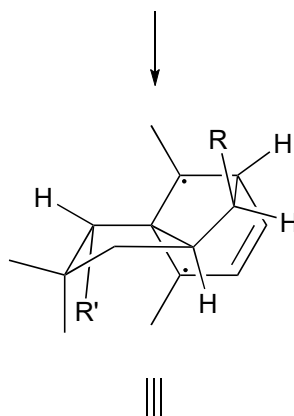
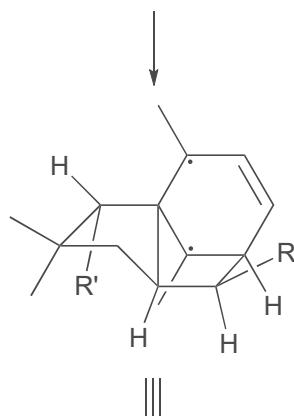
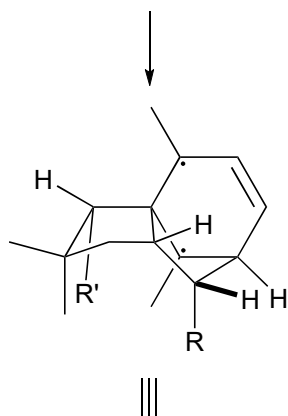
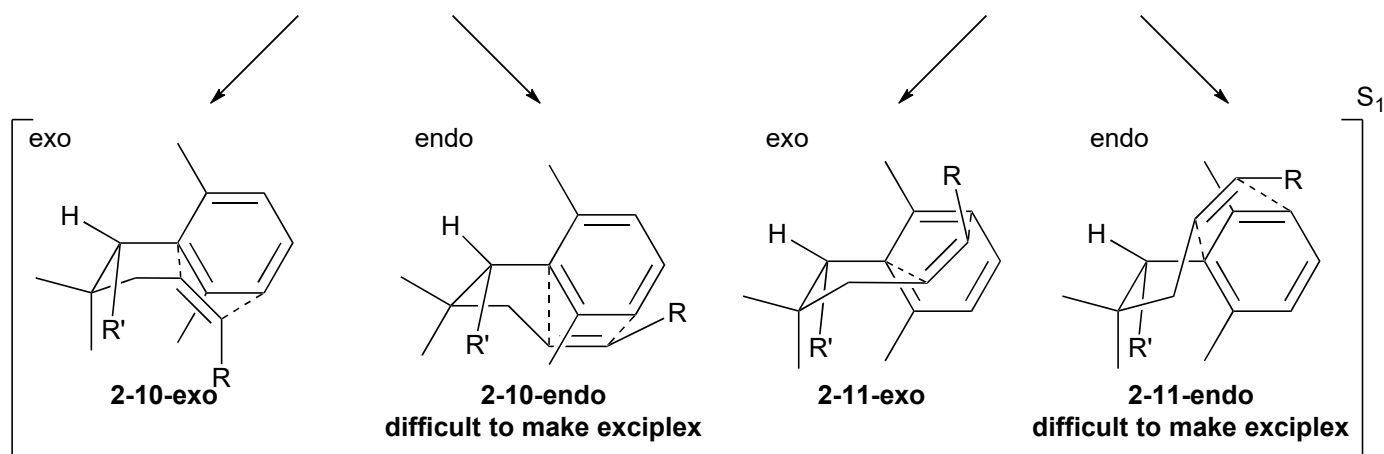
2-10

(R = CH(OEt)₂, R' = OAc)
C2-C9, C7-C8

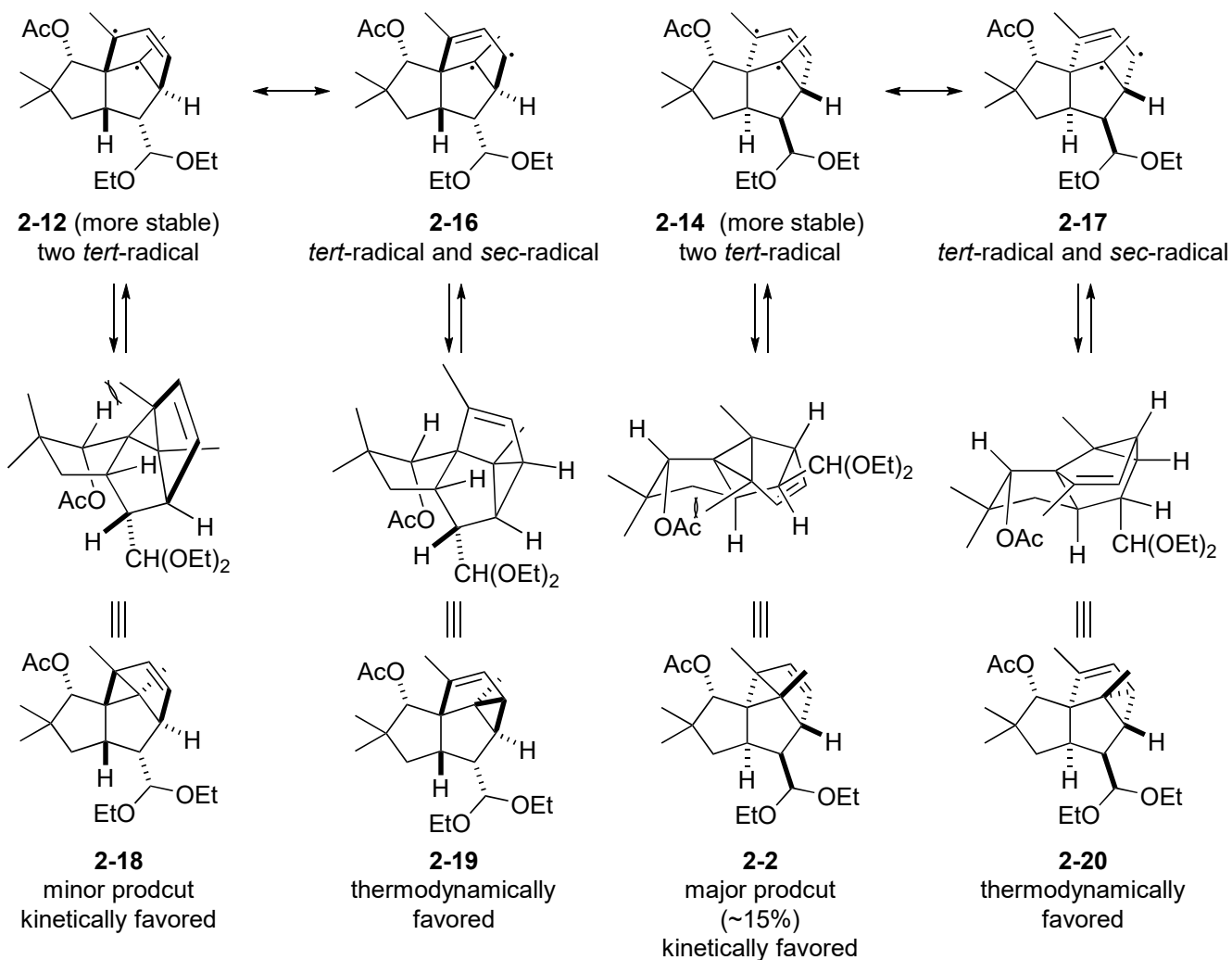


2-11

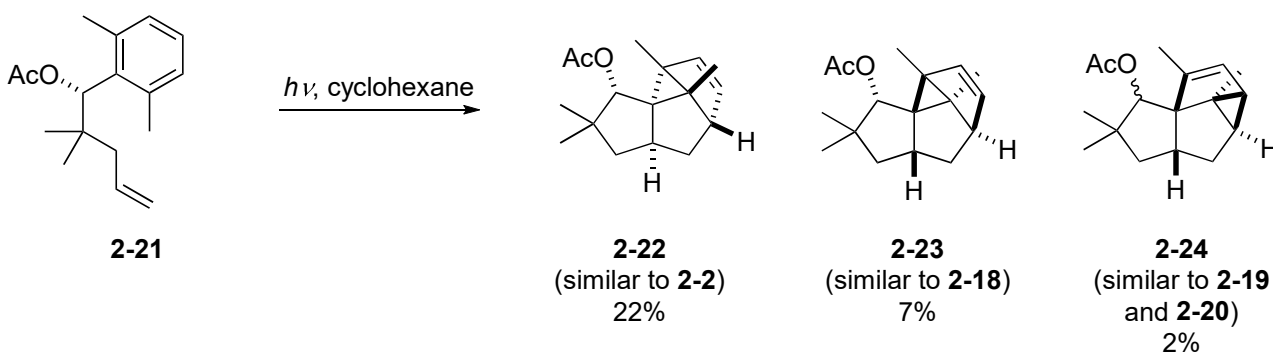
R = CH(OEt)₂, R' = OAc
C2-C9, C5-C8



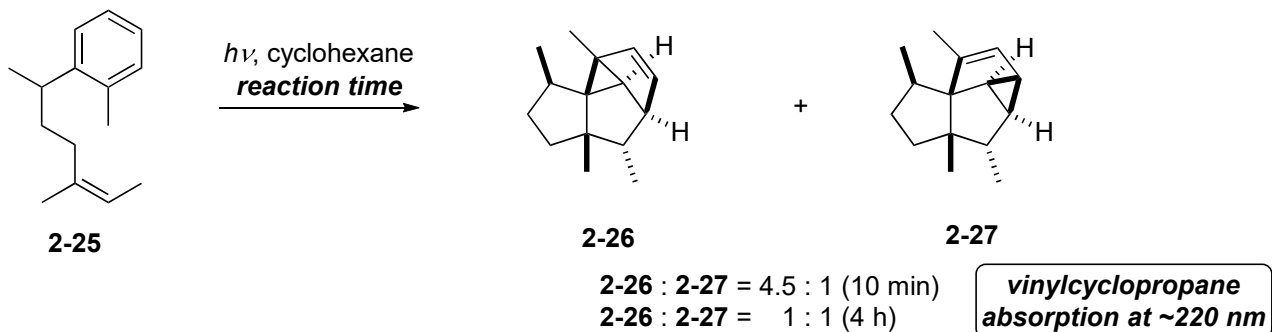
2-4. Formation of cyclopropane

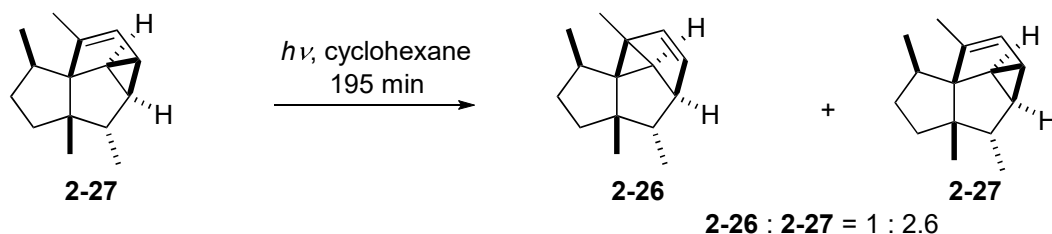
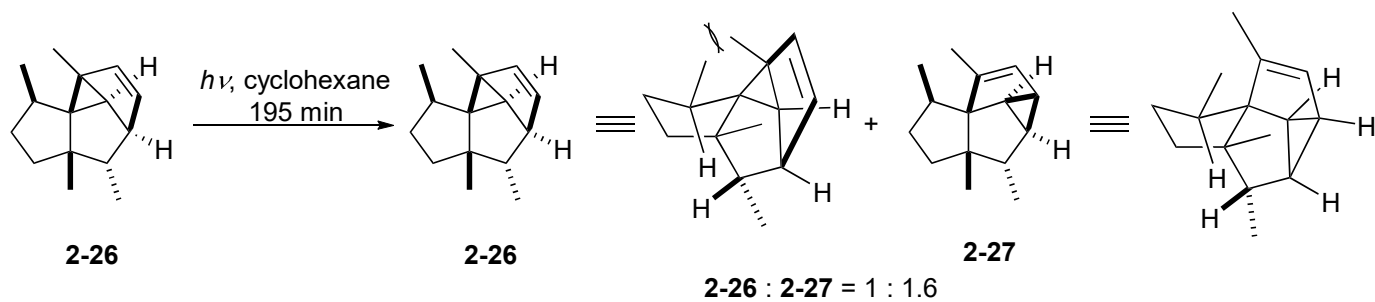


Result of another substrate (Wender, P. A.; Howbert, J. J. *Tetrahedron Lett.* **1982**, 23, 3983.)

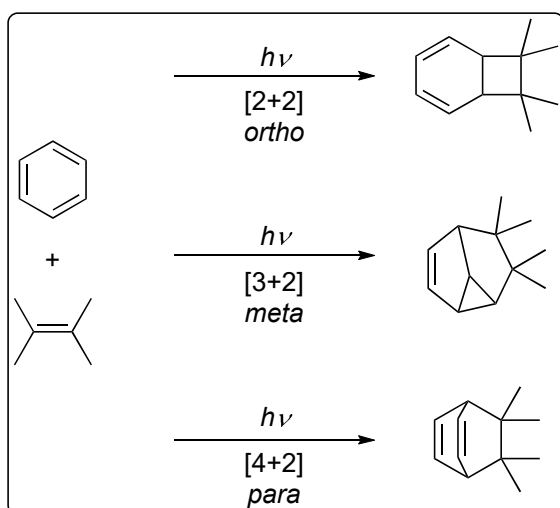


Ring-opening of vinylcyclopropane (Wender, P. A; Dreyer, G. B. *Tetrahedron* **1981**, 37, 4445.)





2-5. *ortho*, *meta*, *para* selectivity



In general, [4+2] does not occur under light condition.

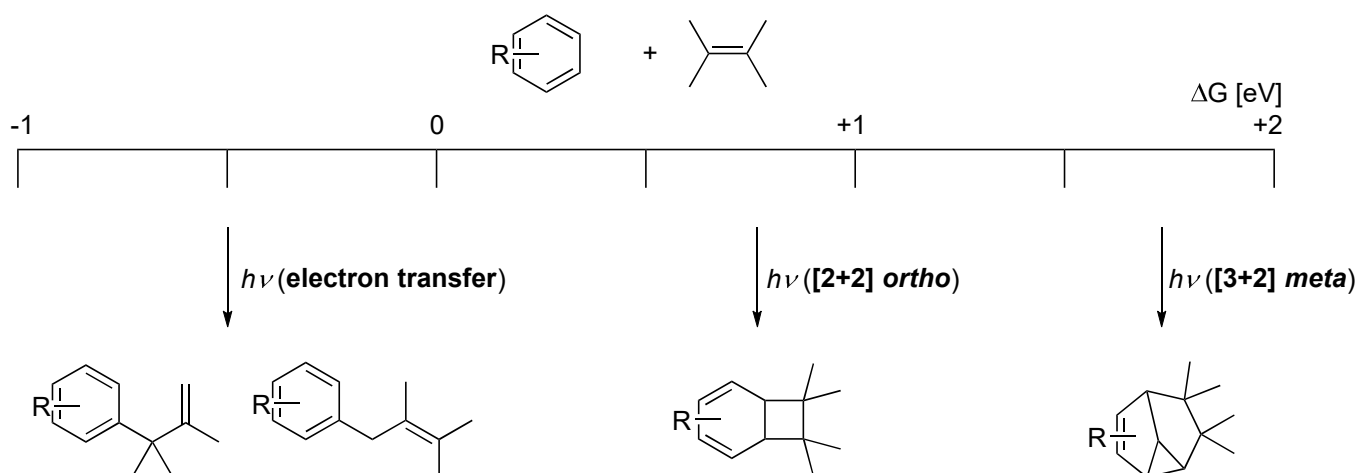
The mode selectivity predicted by the two reaction partners involved.

The Weller equation determines whether or not electron transfer will occur from an excited-state. (Eq. 1)

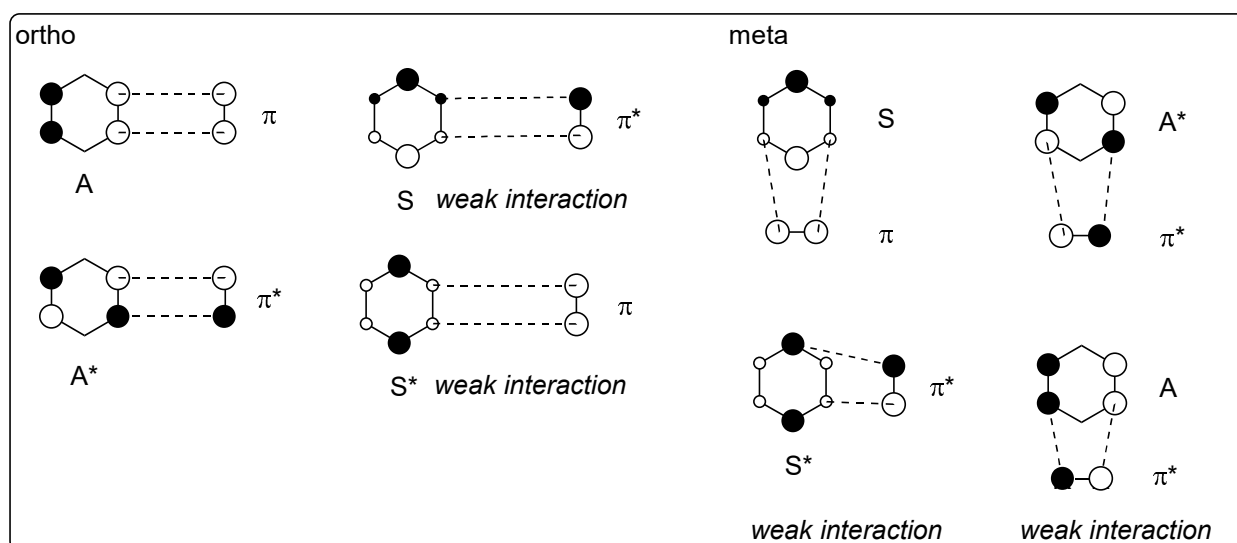
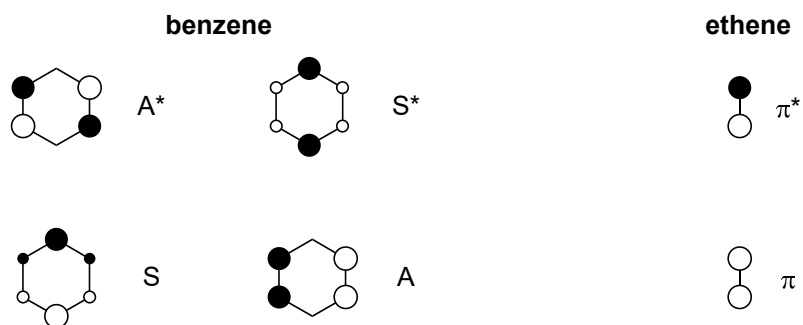
$$\Delta G^{\text{ET}} = E_{\frac{1}{2}}^{\text{ox}}(\text{D}) - E_{\frac{1}{2}}^{\text{red}}(\text{A}) - \Delta E_{\text{excit}} + \Delta E_{\text{coul}} \quad (1)$$

with ΔG^{ET} = free enthalpy of the radical ion pair formation, ΔE_{excit} = excitation energy of the chromophore, ΔE_{coul} = coulomb interaction energy of the radical ions and $E_{\frac{1}{2}}^{\text{ox or red}}$ = half wave potential of donor and acceptor.

ΔG^{ET} rises above 1.5 eV, *meta* photocyclization additions prevail.



2-6. Frontier Molecular Orbitals of benzene and ethene

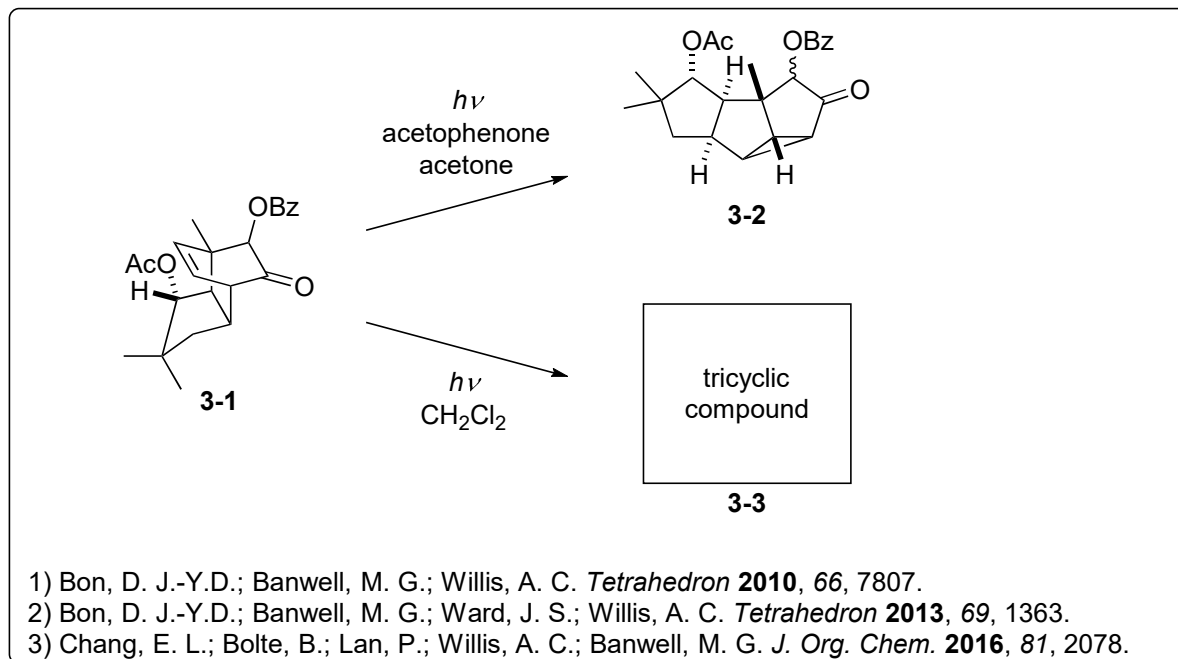


The S \rightarrow A* configuration stabilizes the meta complex more than the ortho.

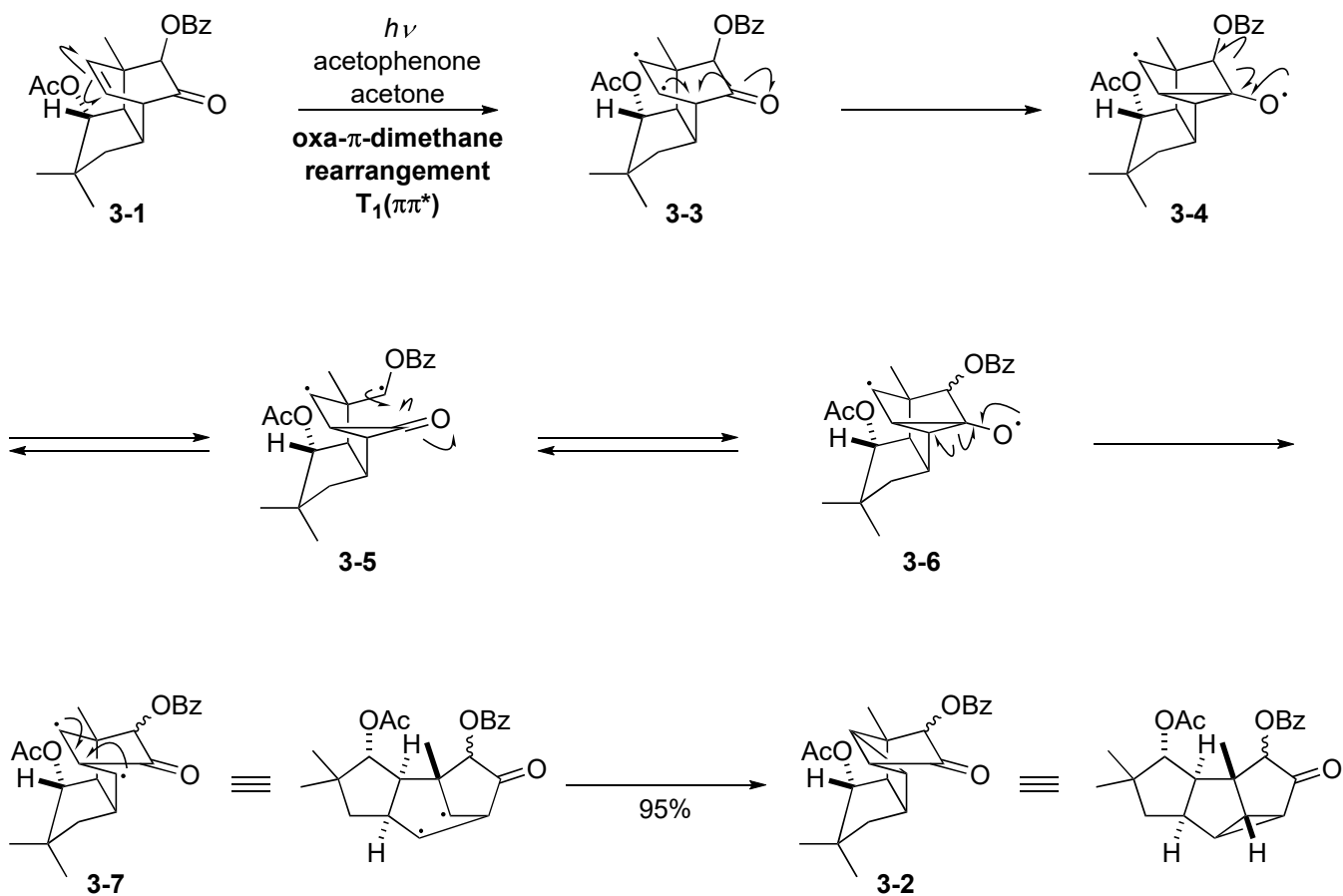
- In the meta mode, the S \rightarrow A* configuration is highly stabilized and although the overlap is less than in the ortho mode, the S orbital and the simultaneous lowering of A* causes more stabilization than ortho.

Cornelisse, J. *Chem. Rev.* **1993**, 93, 615.

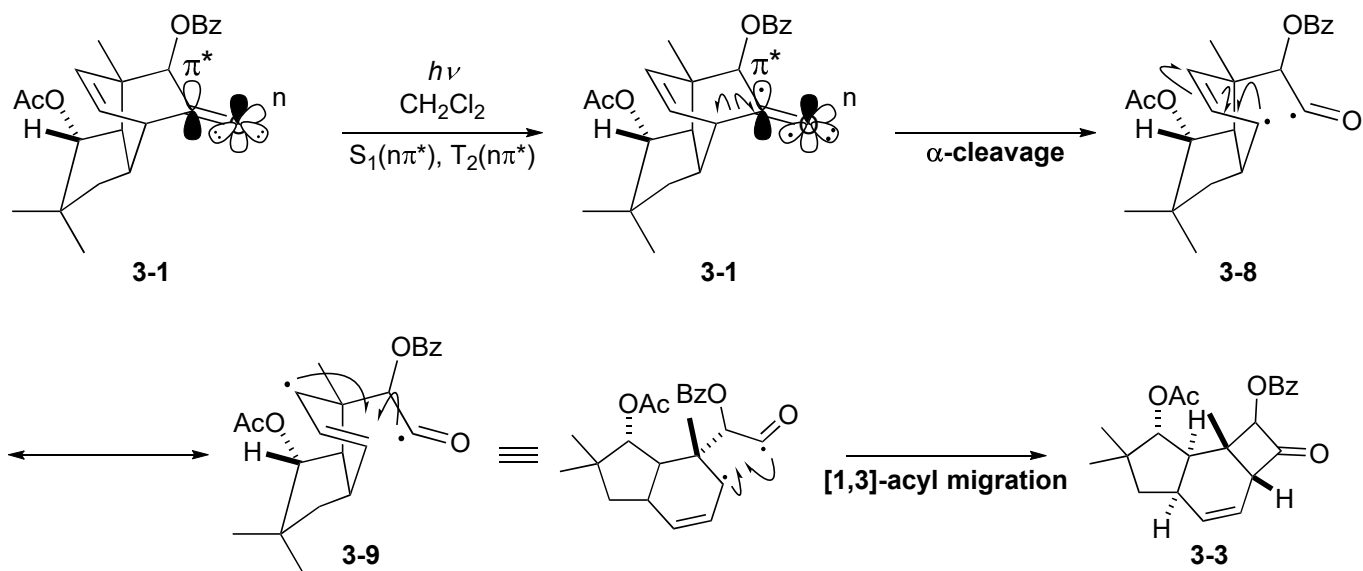
3. Photoreaction occurred using acetone and light and then compound **3-2** was obtained from **3-1**. However, if you use another condition like CH_2Cl_2 and light, you might not obtain compound **3-2**. Please guess the compound **3-3**.



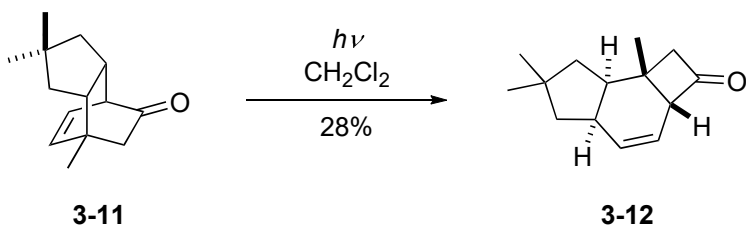
3-1. Reaction mechanism from **3-1** to **3-2**



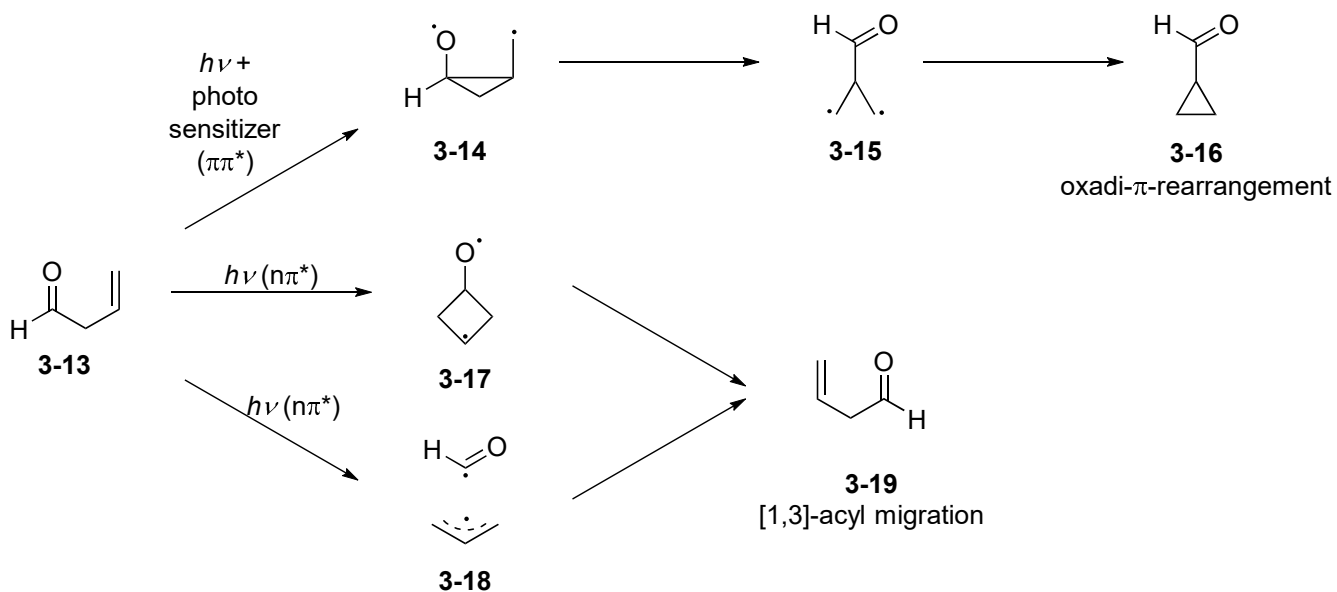
3-2. Possible reaction mechanism from 3-1 to 3-3



Example of actual synthesis

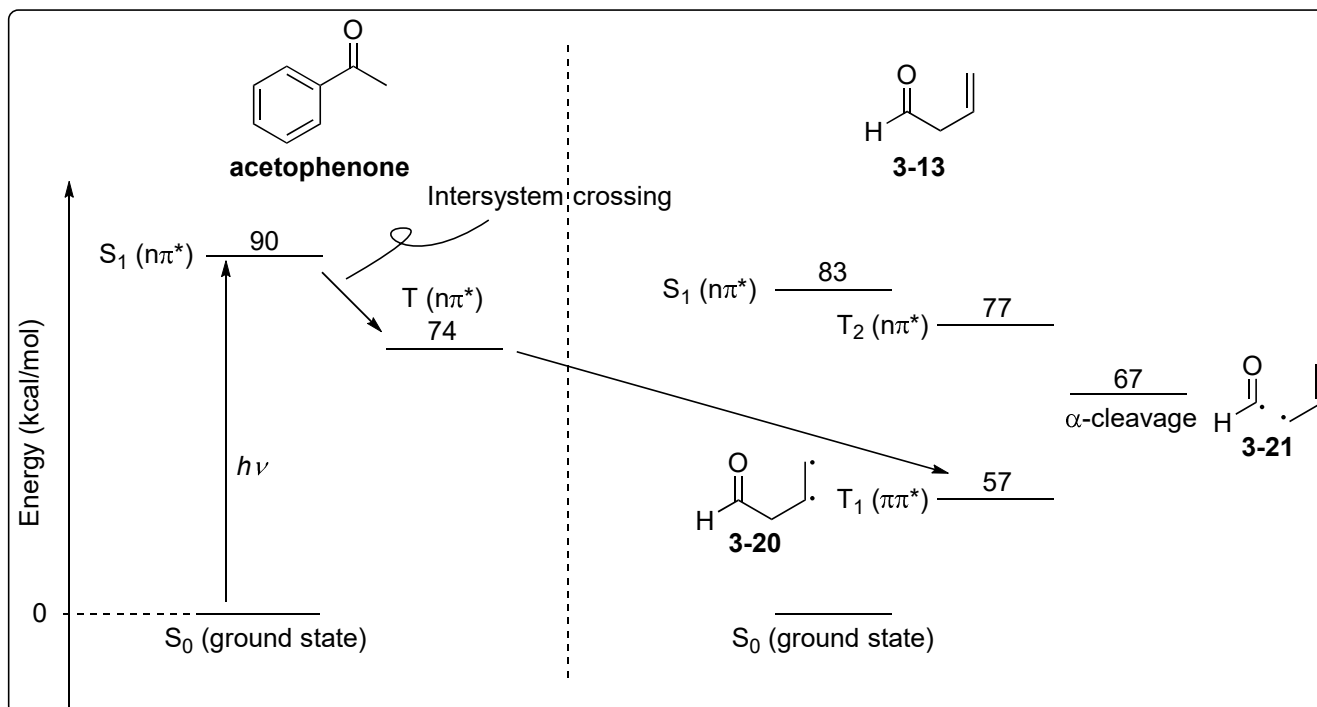
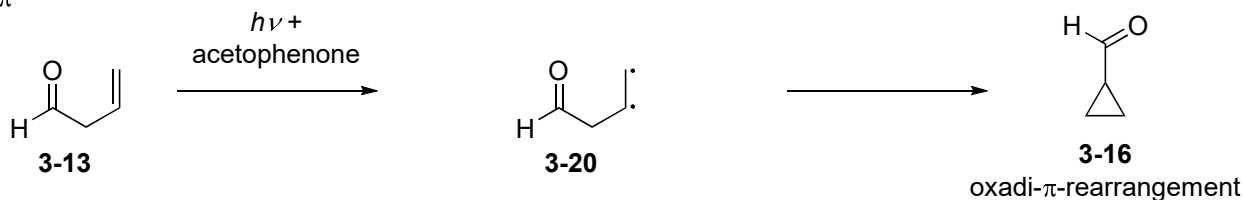


3-3. Oxadi- π -methane rearrangement and [1,3]-acyl migration (Givens rearrangement)

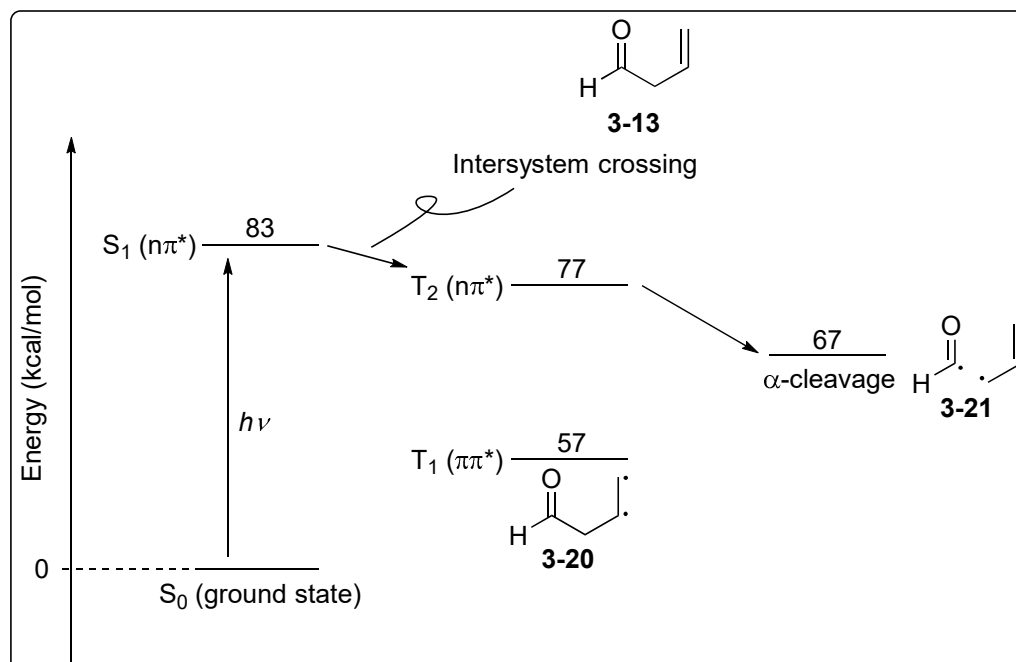
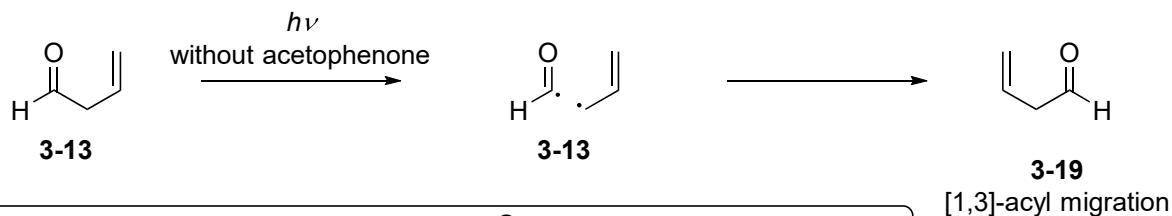


3-3-1. Energy diagram ($\pi\pi^*$ vs. $n\pi^*$)

$\pi\pi^*$



$n\pi^*$



Houk, K. N. *Chem. Rev.* **1976**, *76*, 1.

Dietlin, C.; Allonas, X.; Defoin, A.; Fouassier, J.-P. *Photochem. Photobiol. Sci.* **2008**, *7*, 558.

3-3-2. Energy of transition state
 MC-SCF/6-31G(d) : E (kcal/mol)

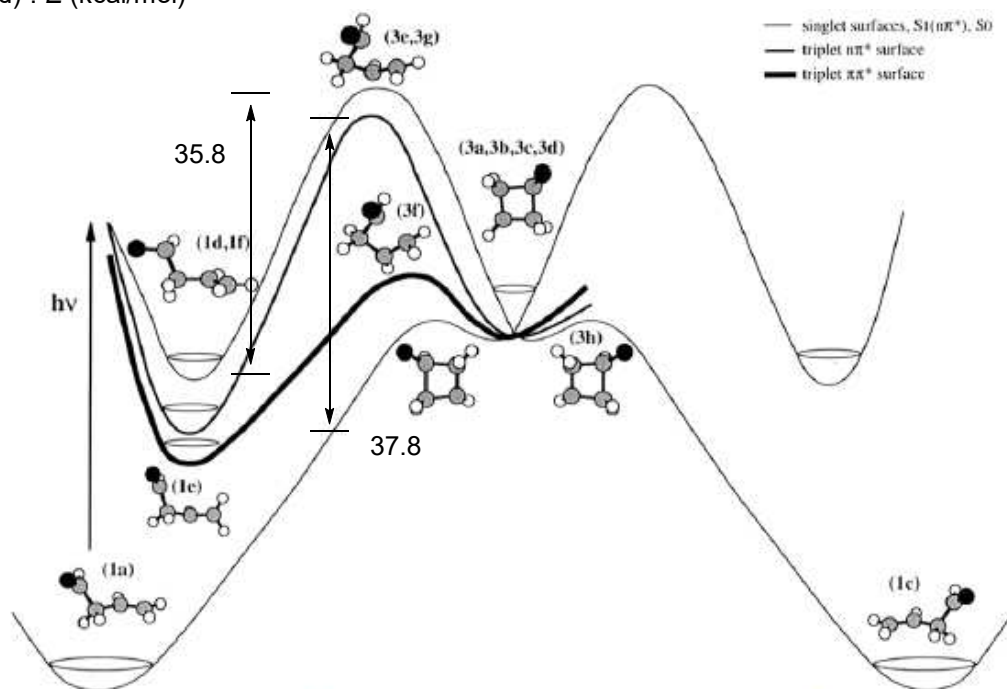


Figure 6. A schematic representation of the potential energy surface for the quasi-concerted [1,3]-shift reaction.

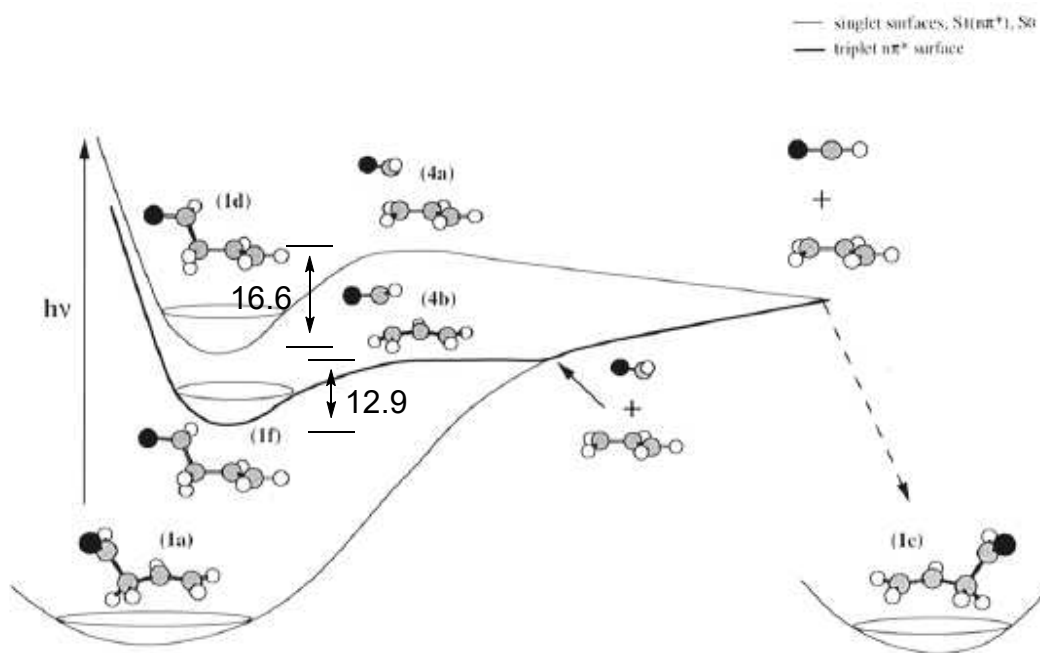


Figure 7. A schematic representation of the potential energy surface for fragmentation.

Wilsey, S.; Bearpark, M. J.; Bernardi, F.; Olivucci, M.; Robb, M. A. *J. Am. Chem. Soc.* **1996**, *118*, 176.