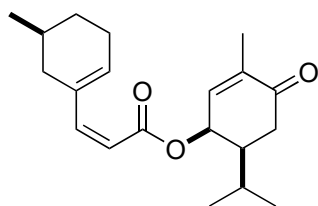


Problem Session (4) -revised-

2018/06/30 Akira Hirose

Please provide the reaction mechanisms.

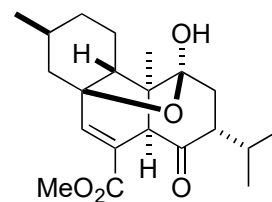
1



1-1

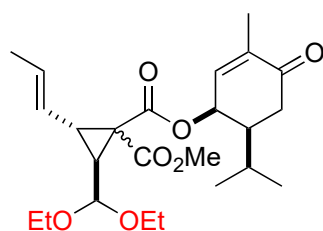
1. DMSO, 100 °C, 76%
2. *m*-CPBA, NaHCO₃, CH₂Cl₂
0 °C to rt (dr >10 : 1);
DBU, rt

3. RuCl₃·*n*H₂O, K₂S₂O₈, KOH
H₂O/THF (10/1), 60 °C
64% (2 steps)
4. TMS-diazomethane
benzene/MeOH (4/1), 0 °C to rt
75%



(+)-sarcophytin (1-2)

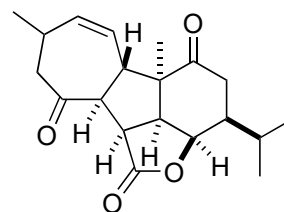
2



2-1
(dr 1.5 : 1)

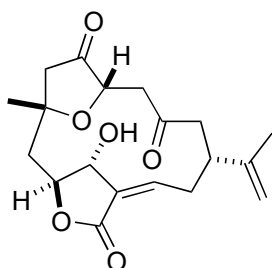
1. (Ir[dF(CF₃)ppy]₂(dtbpy))PF₆ (0.5 mol%)
PhSH, *p*-toluidine, blue LEDs
MeCN, 50%
2. Me₄NOH, *i*-PrOH/H₂O (10/1), rt;
work up and solvent was removed;
toluene, 120 °C, 4 h;
THF/2 M HCl aq (5/2), rt, 90%

3. Ni(acac)₂ (20 mol%), isoprene, Et₂Zn
THF, rt
4. Dess-Martin Periodinane, CH₂Cl₂, rt
94% (2 steps)
5. Grubbs II (20 mol%), CH₂Cl₂, reflux
85%



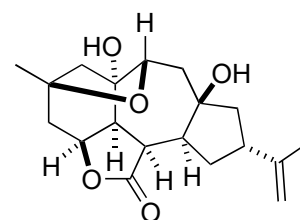
2-2

3

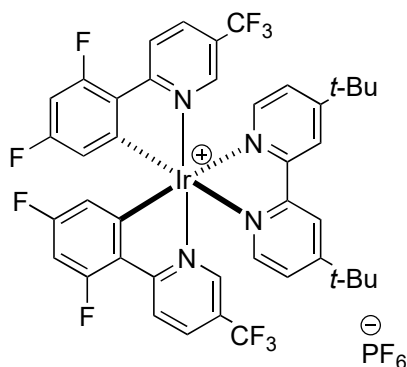


3-1

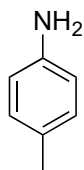
Sml₂ (10 eq), THF, rt
62%



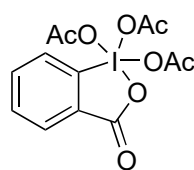
3-2



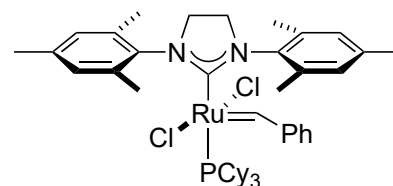
[Ir[dF(CF₃)ppy]₂(dtbpy)]PF₆



p-toluidine



Dess-Martin Periodinane



Grubbs II

Topic: construction of cembrene-based diterpenes core

Problem 1: Total synthesis of (+)-sarcophytin

isolation and bioactivity:

from the marine soft coral *Sarcophyton elegans* by Anjaneyulu in 1998

* *The absolute configuration in the original report was enantiomeric.*

(Anjaneyulu, A. S. R.; Venugopal, M. J. R. V.; Sarada, P.; Rao, G. V.; Clardy, J.; Lobkovsky, E. *Tetrahedron Lett.* **1998**, 39, 135.)

bioactivity:

not reported

cf. chatancin (**1-3**): a Platelet activating factor (PAF) antagonist

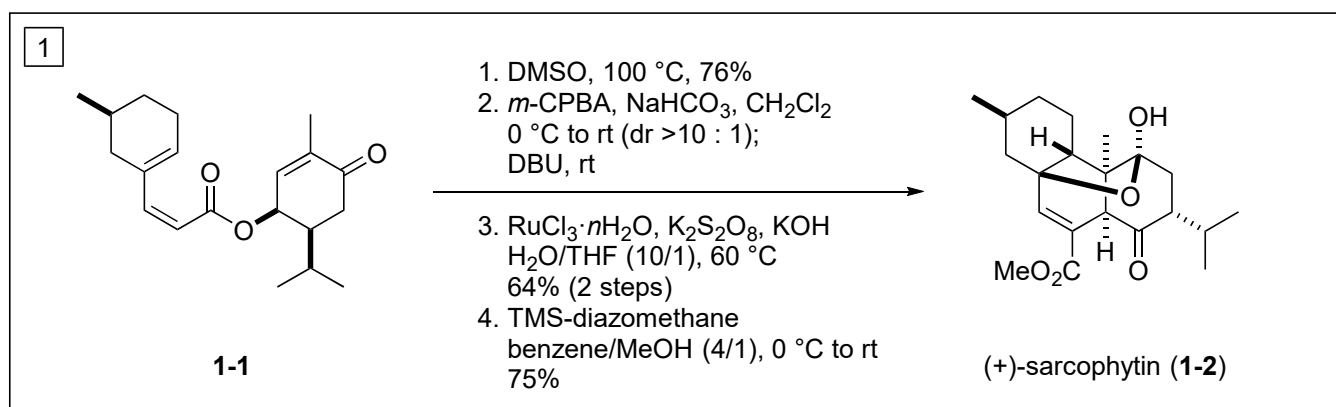
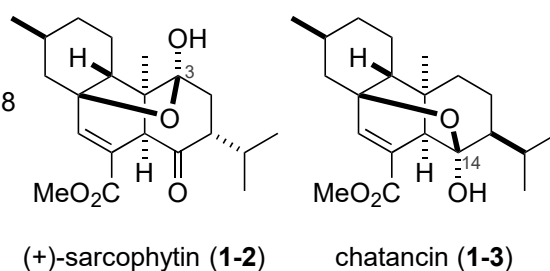
(Sugano, M.; Shindo, T.; Sato, A.; Iijima, Y.; Oshima, T.; Kuwano, H.; Hata, T. *J. Org. Chem.* **1990**, 55, 5803.)

total synthesis:

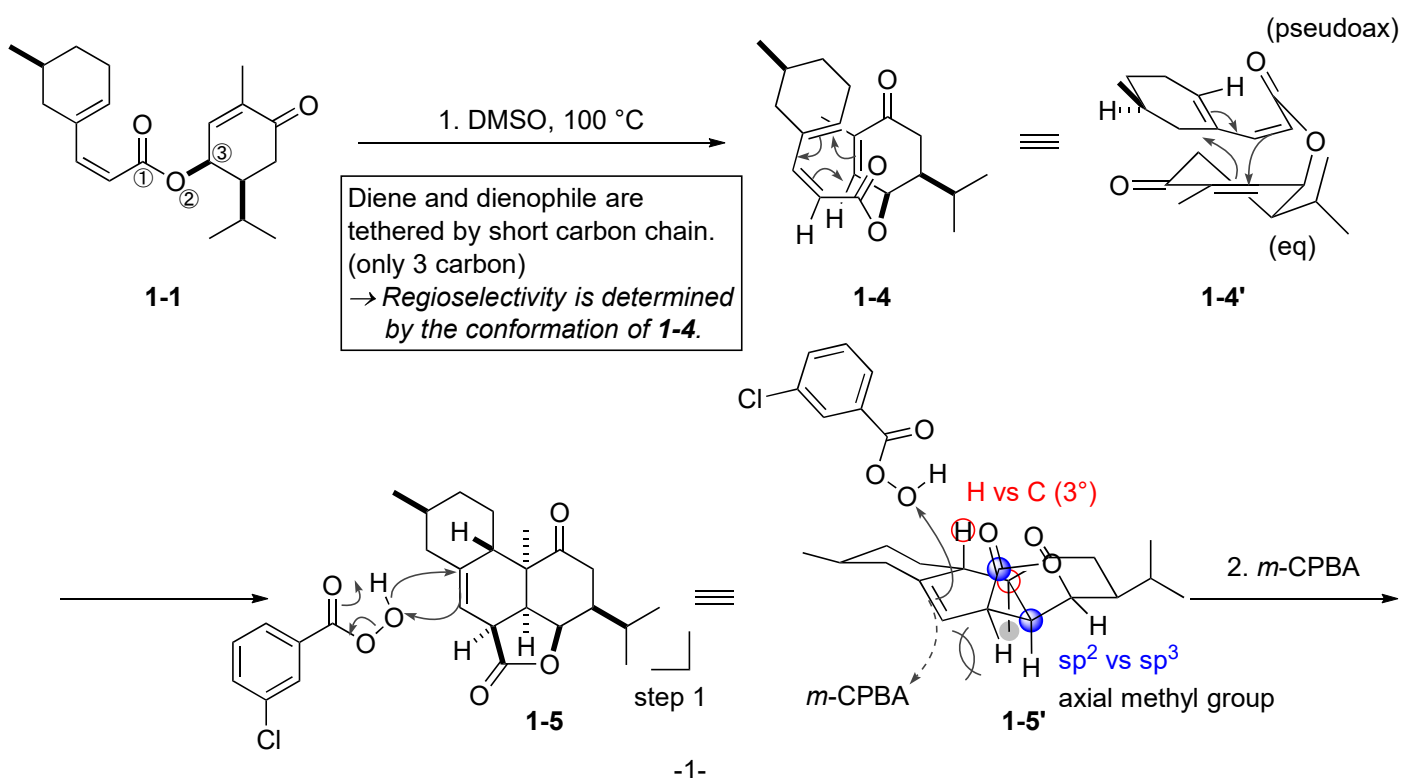
· Carreira, E. M. et al *Angew. Chem. Int. Ed.* **2018**, 57, 823.

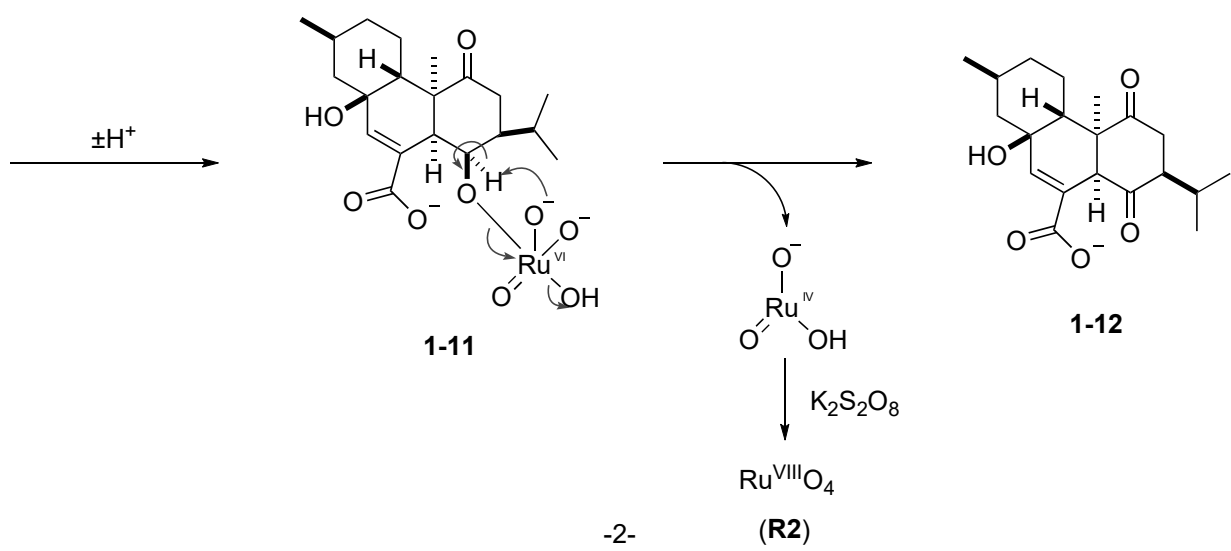
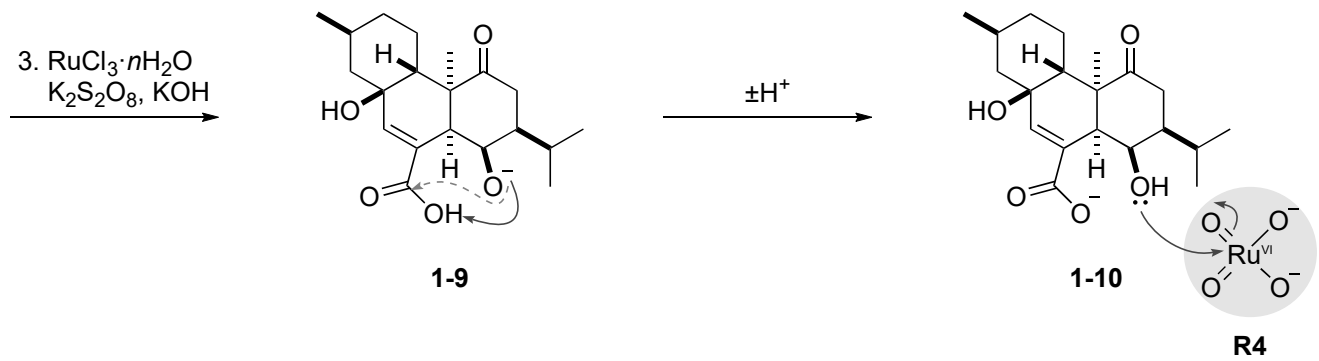
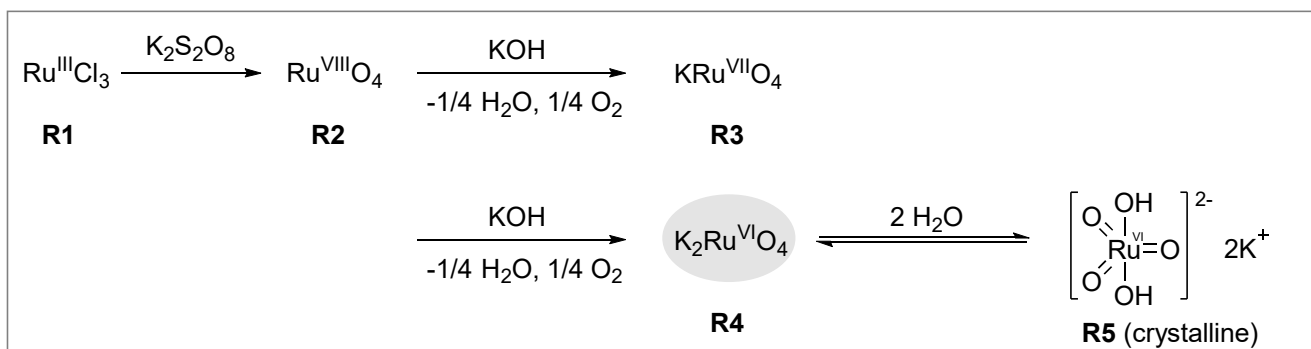
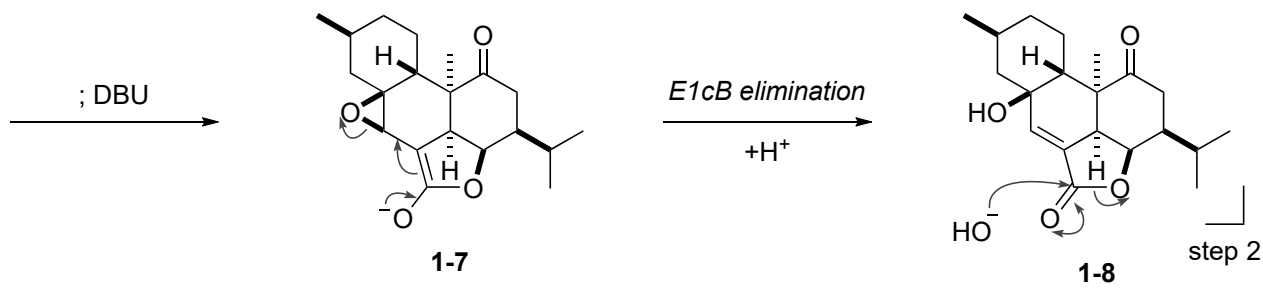
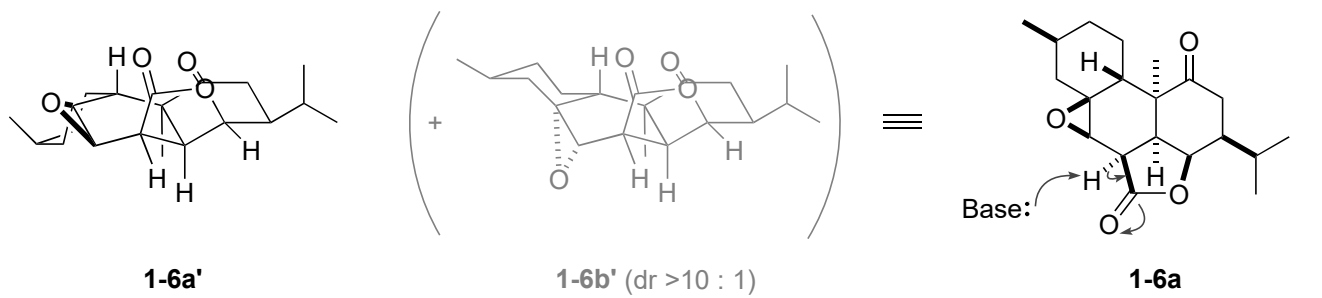
cf. chatancin (**1-3**):

3 total syntheses have been reported; by Gössinger (1998), Deslongchamps (2003), Maimone (2015)

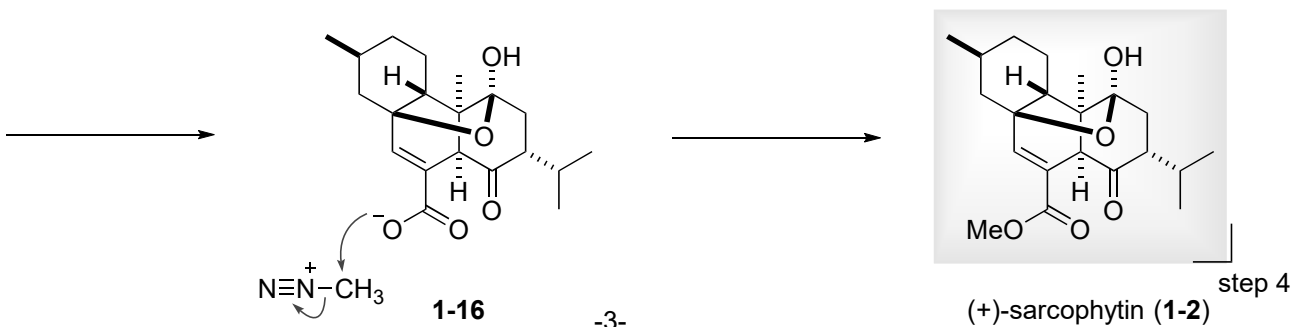
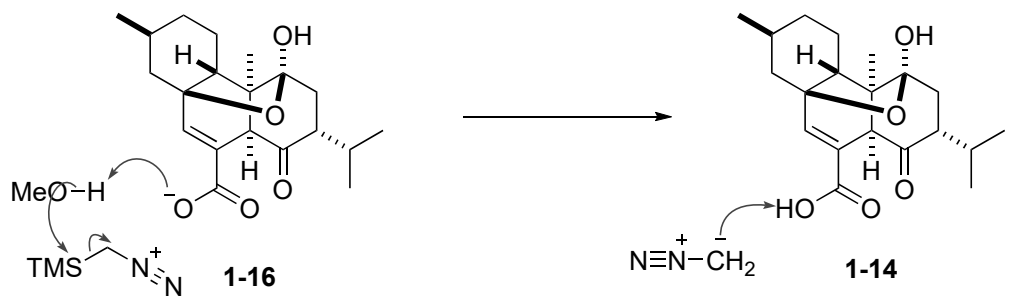
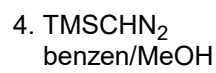
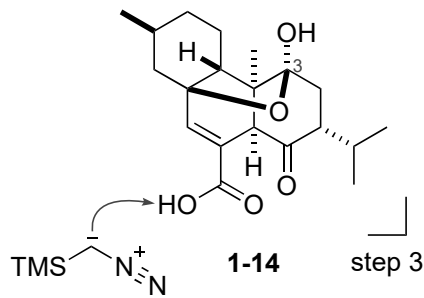
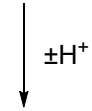
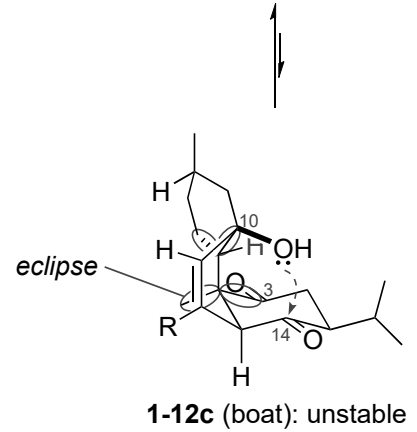
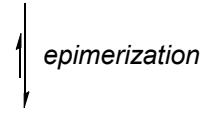
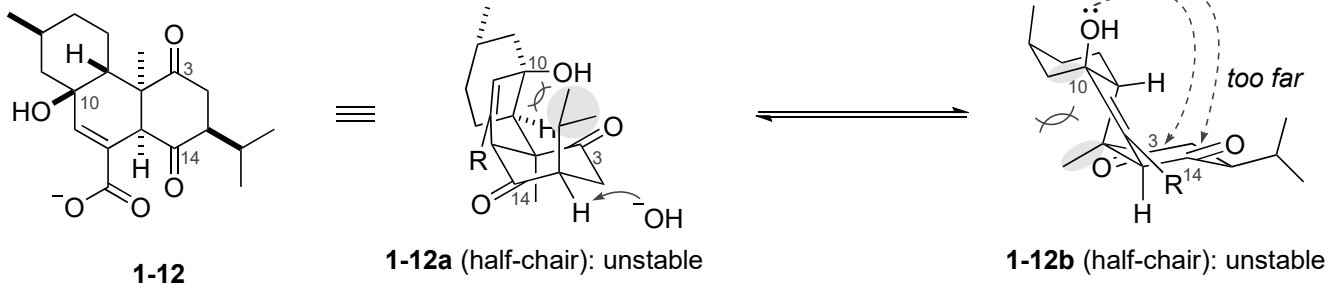


Nannini, L. J.; Nemat, S. J.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2018**, 57, 823.





Regioselectivity of hemiacetal formation; C3-keton vs C14-ketone



Problem 2: Total synthesis of (-)-pavidolide B

isolation:

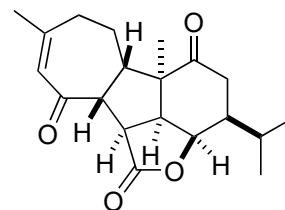
from the marine soft coral *Sinularia pavida* by Lin in 2012
(Shen, S.; Zhu, H.; Chen, D.; Liu, D.; van Ofwegen, L.; Proksch, P.; Lin, W.
Tetrahedron Lett. **2012**, 53, 5759.)

bioactivity:

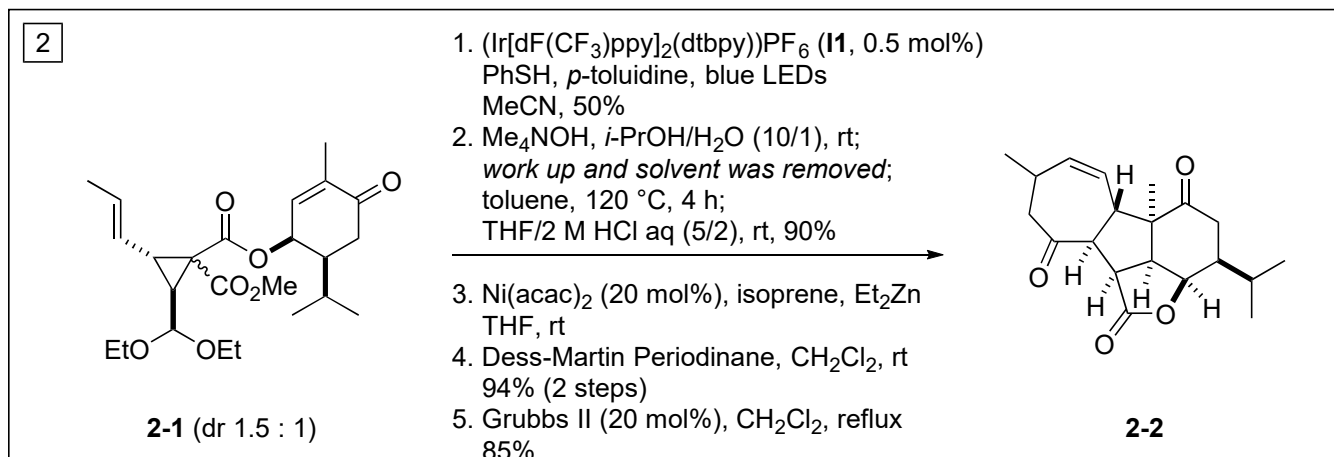
selective inhibition against human promyelocytic leukemia cell line HL-60

total synthesis:

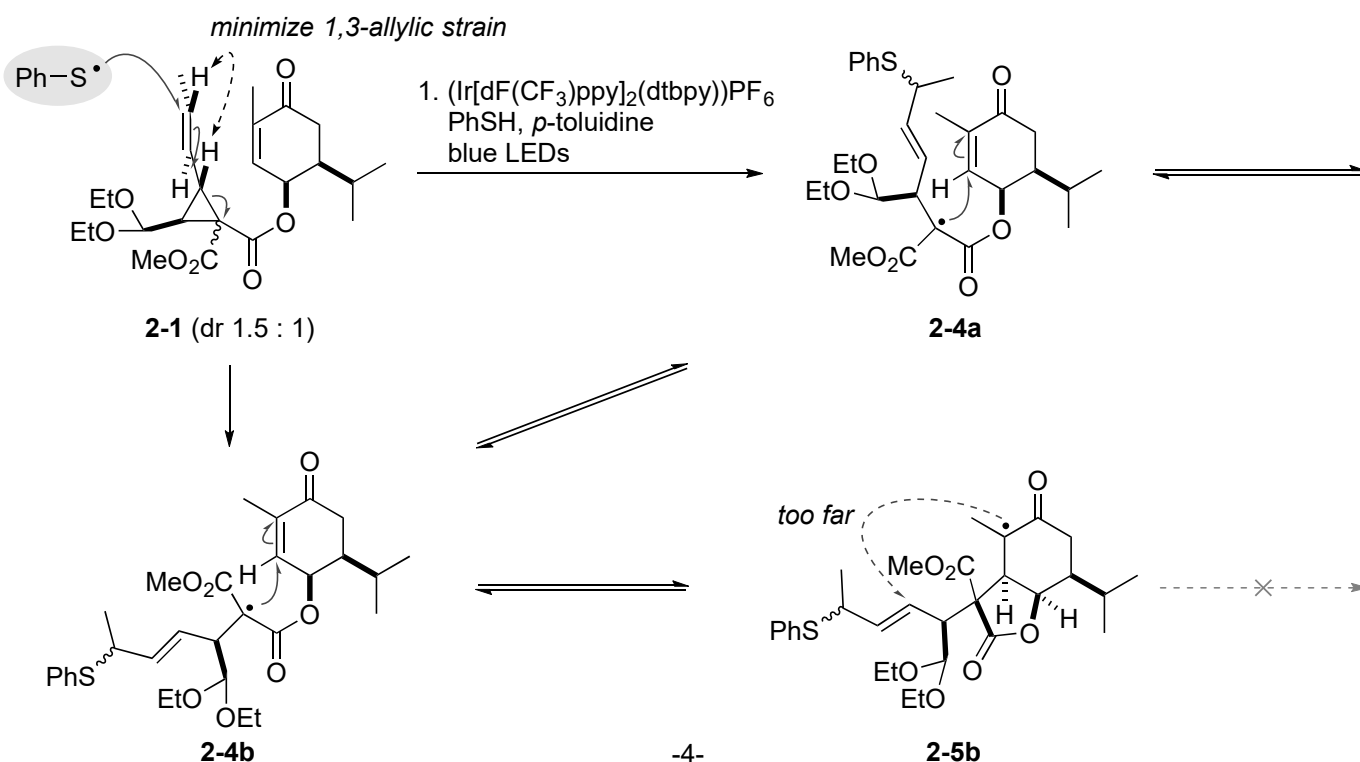
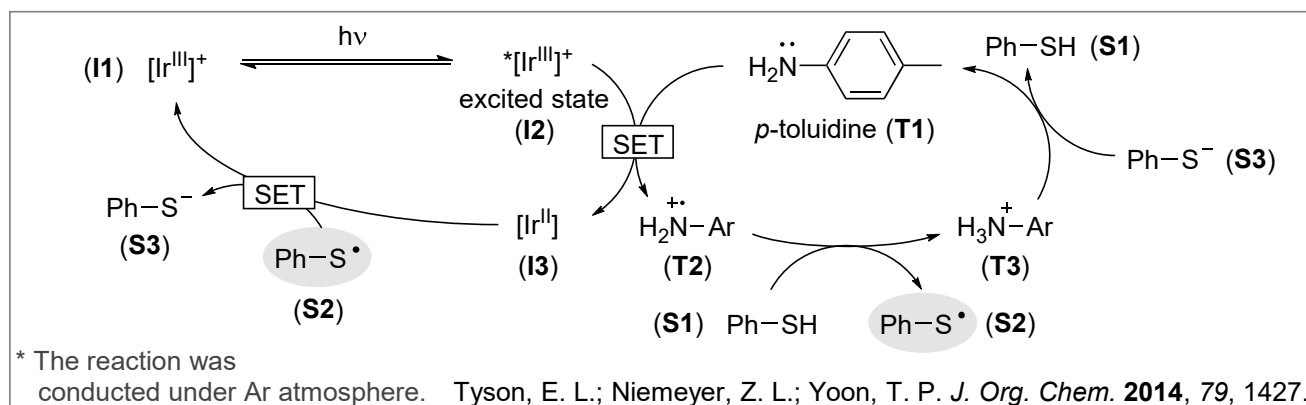
· Yang, Z. et al *J. Am. Chem. Soc.* **2017**, 139, 13989.

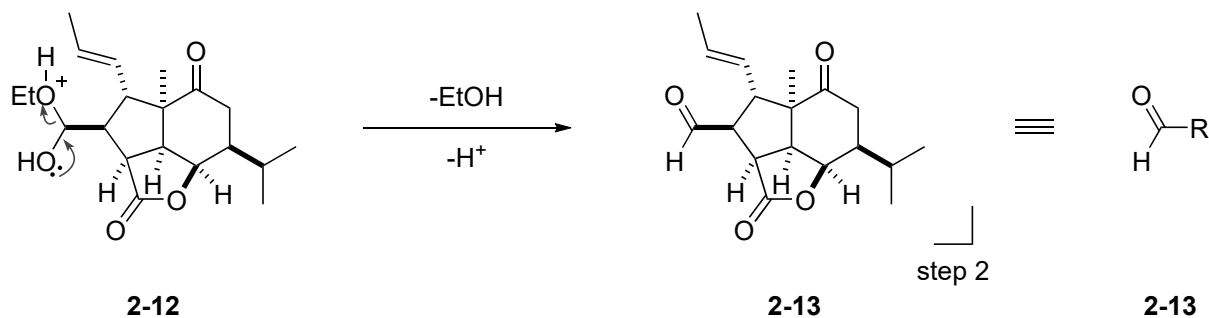
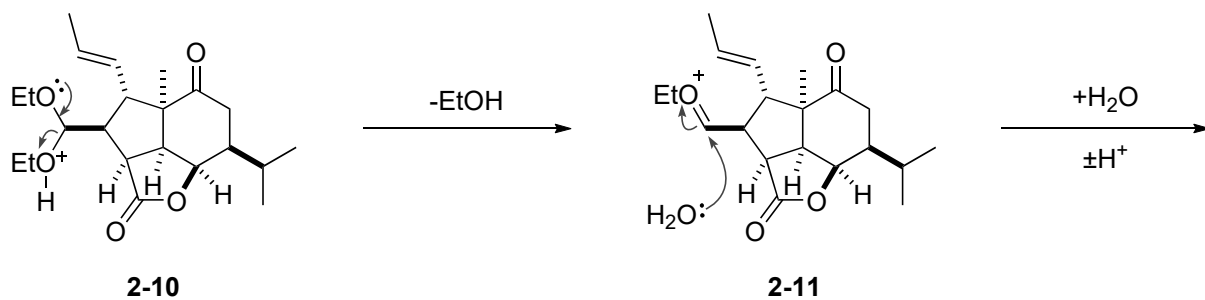
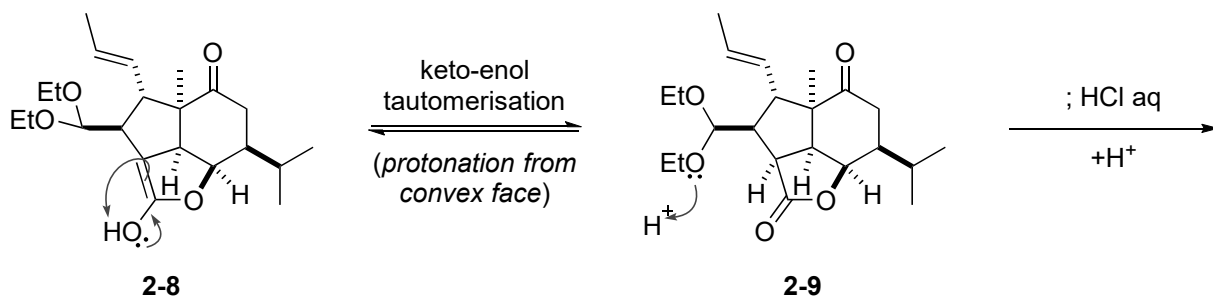
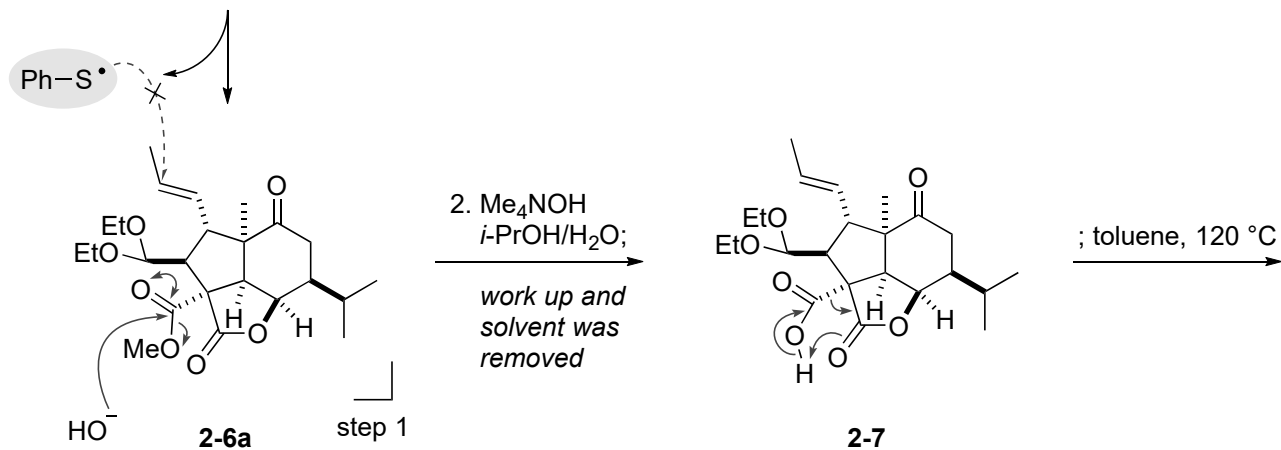
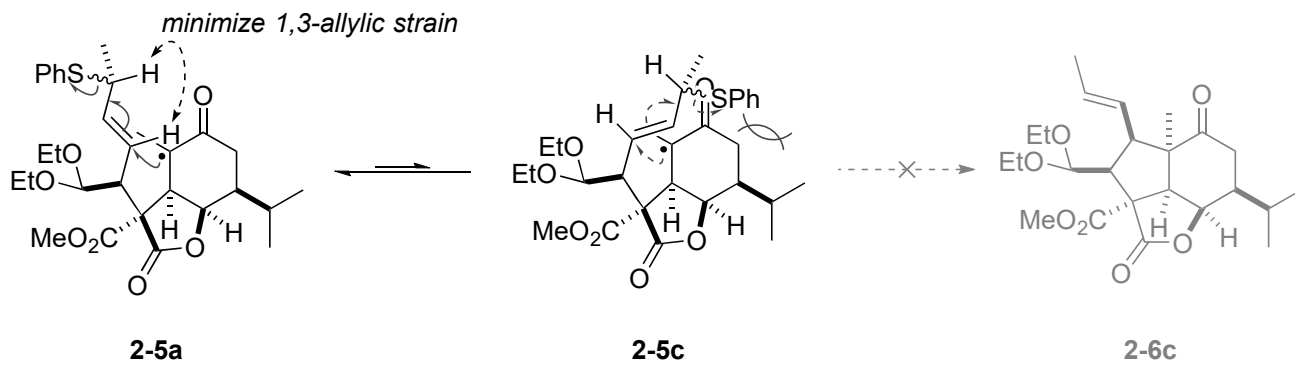


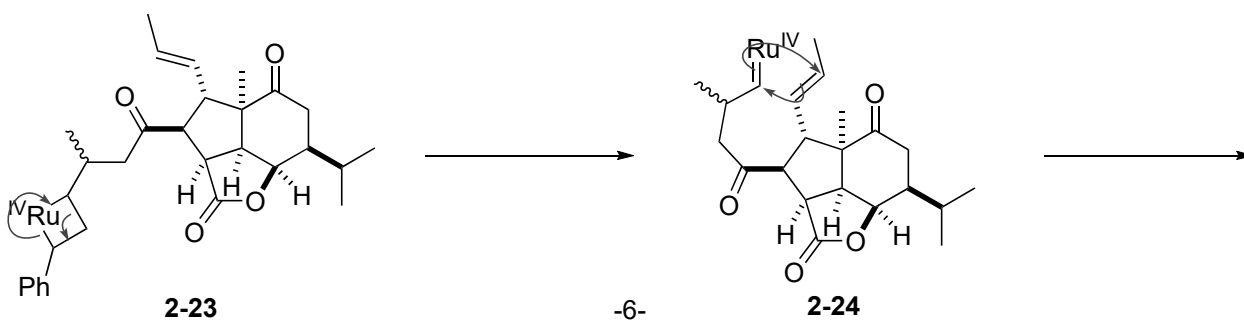
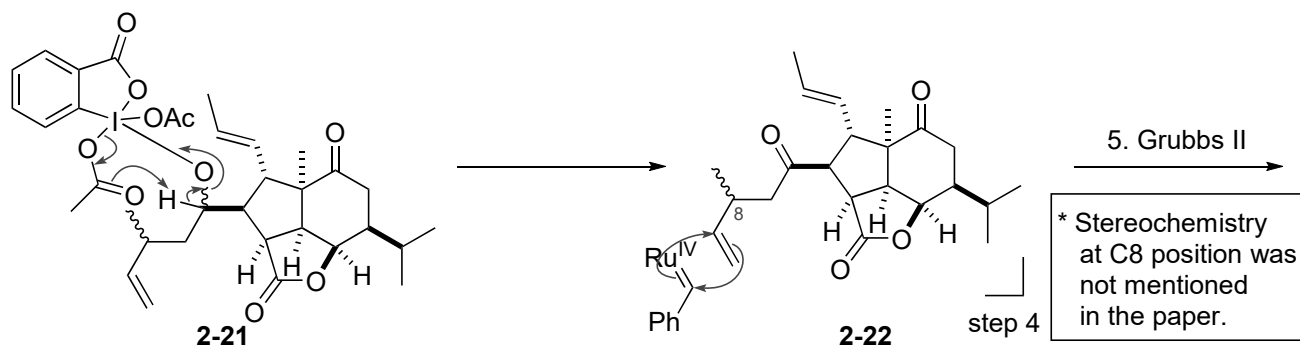
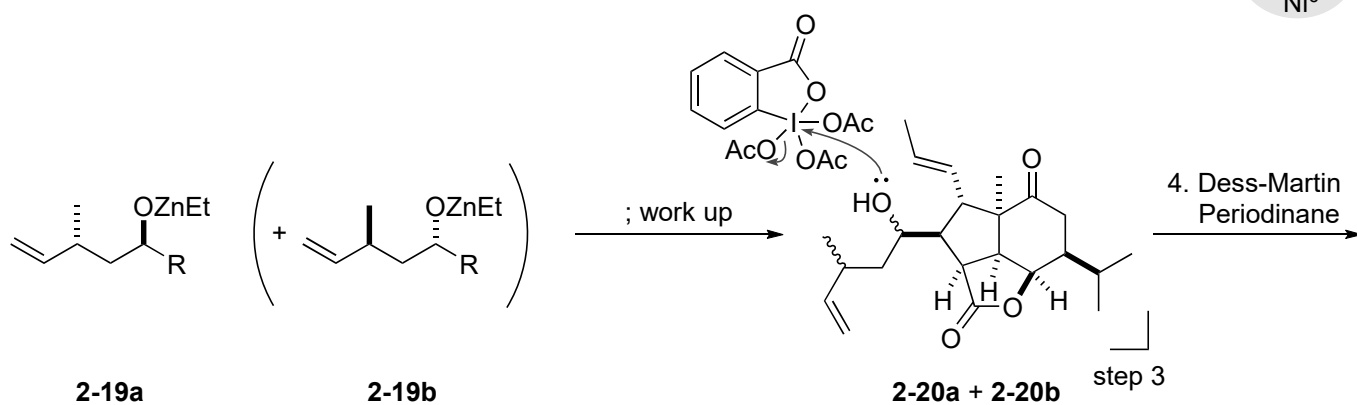
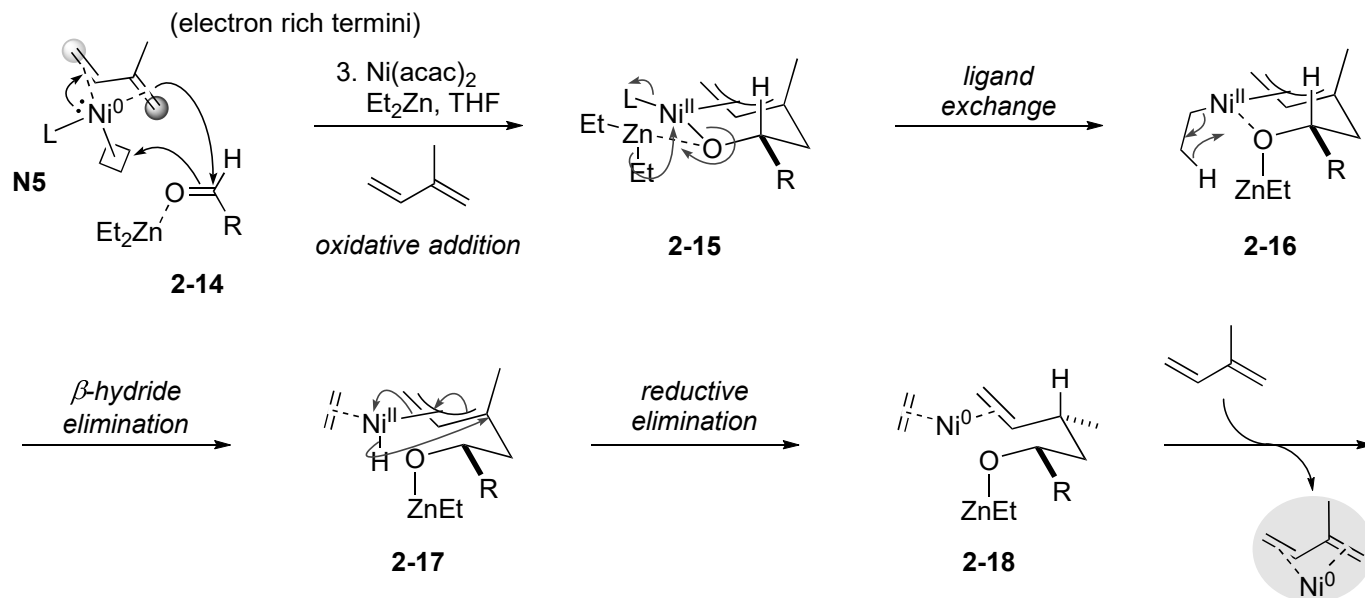
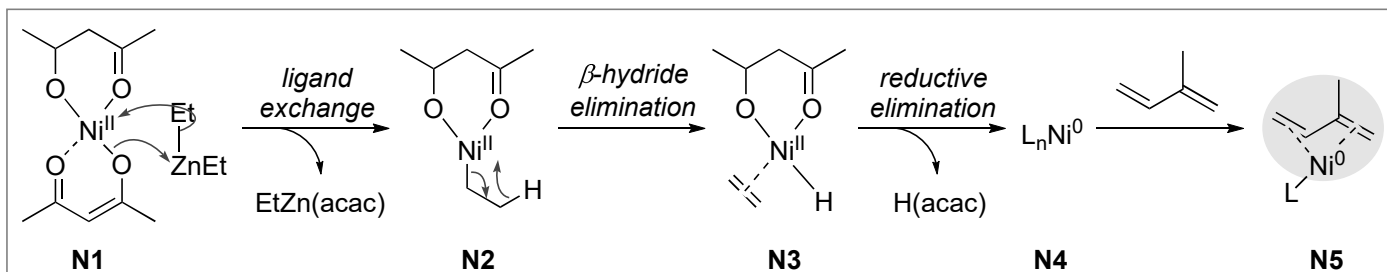
pavidolide B (**2-3**)

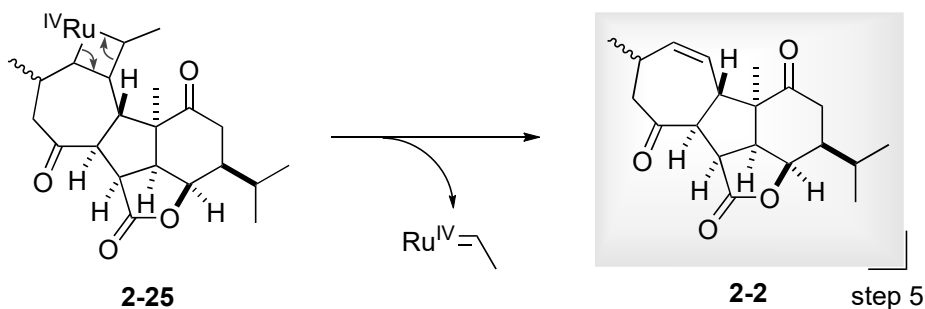


Zhang, P.-P.; Yan, Z.-M.; Li, Y.-H.; Gong, J.-X.; Yang, Z. *J. Am. Chem. Soc.* **2017**, 139, 13989.

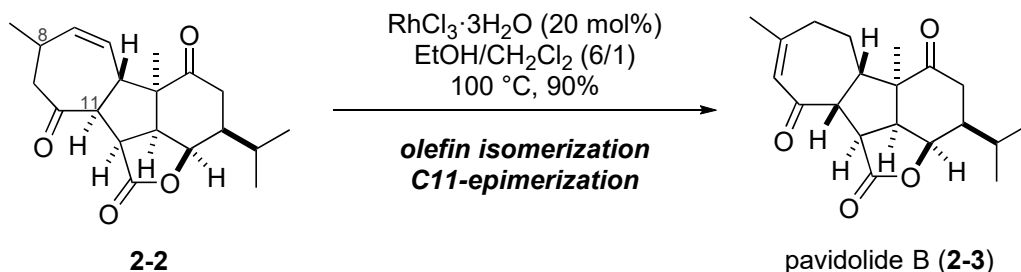








Note: Completion of total synthesis



Problem 3: Construction of polycyclic structure -biosynthetic study of *sinulanocembranolide A*-

isolation:

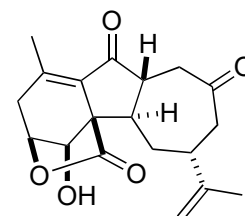
from the marine soft coral *Sinularia gaweli* by Yen in 2013
(Yen, W.-H.; Su, Y.-D.; Chang, Y.-C.; Chen, Y.-H.; Chen, Y.-H.; Dai, C.-F.; Wen, Z.-H.; Su, J.-H.; Sung, P.-J. *Tetrahedron Lett.* **2013**, *54*, 2267.)

bioactivity:

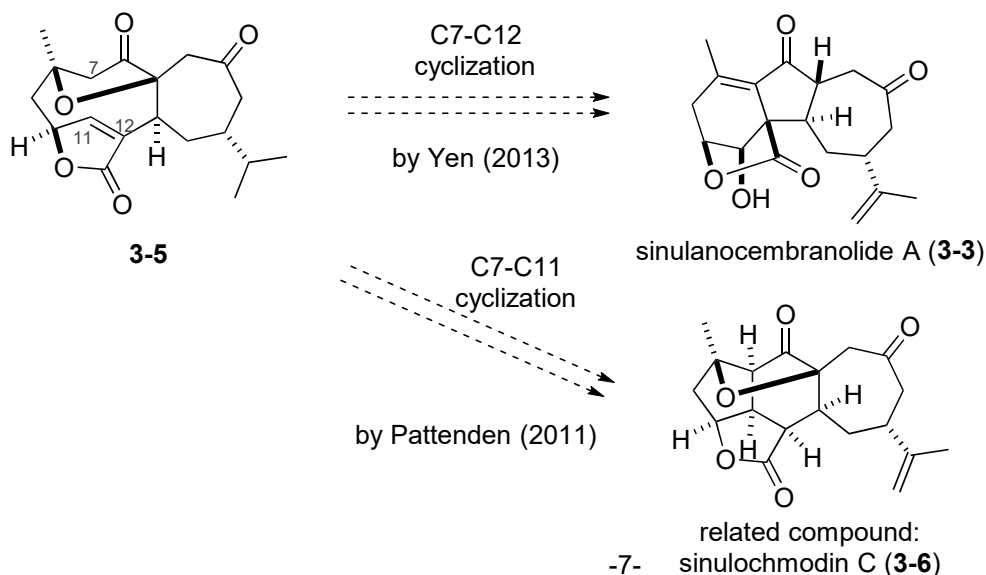
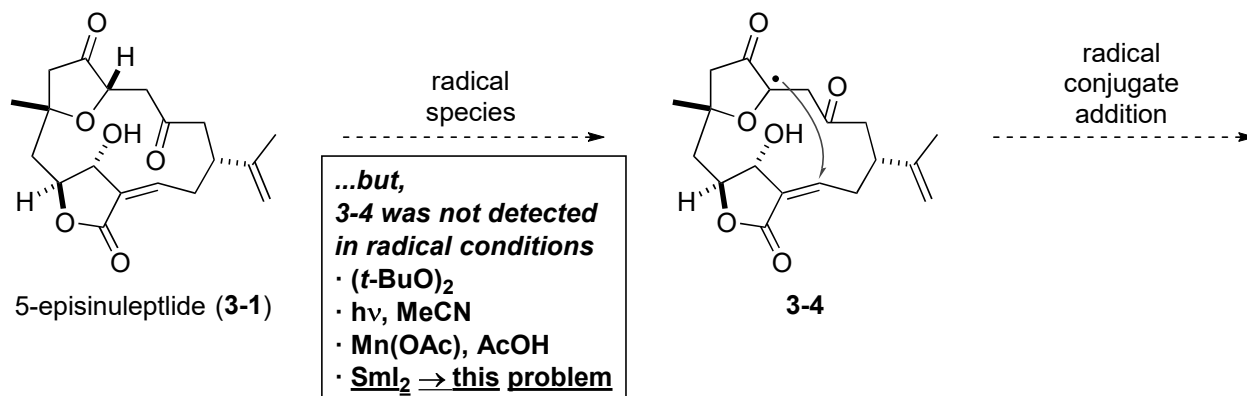
not reported

biosynthetic studies:

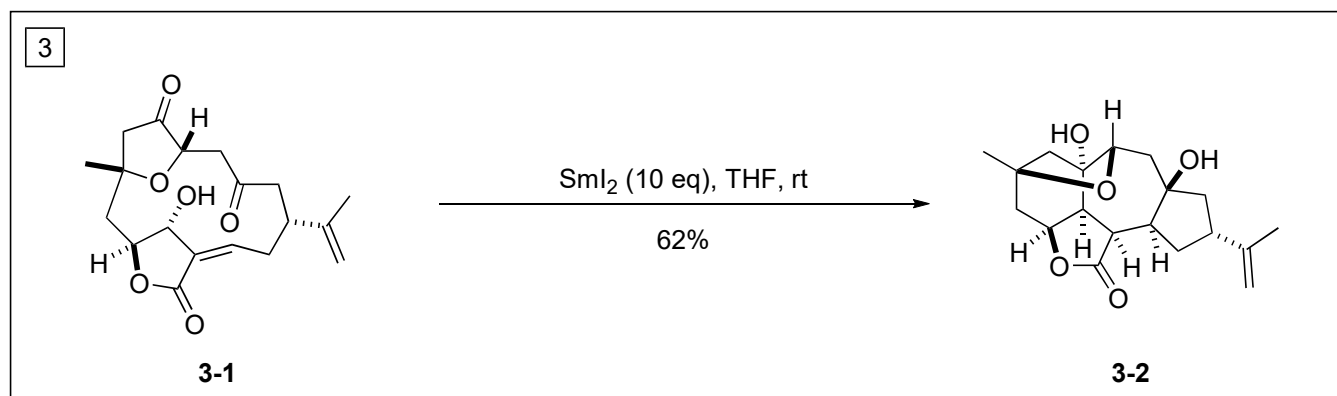
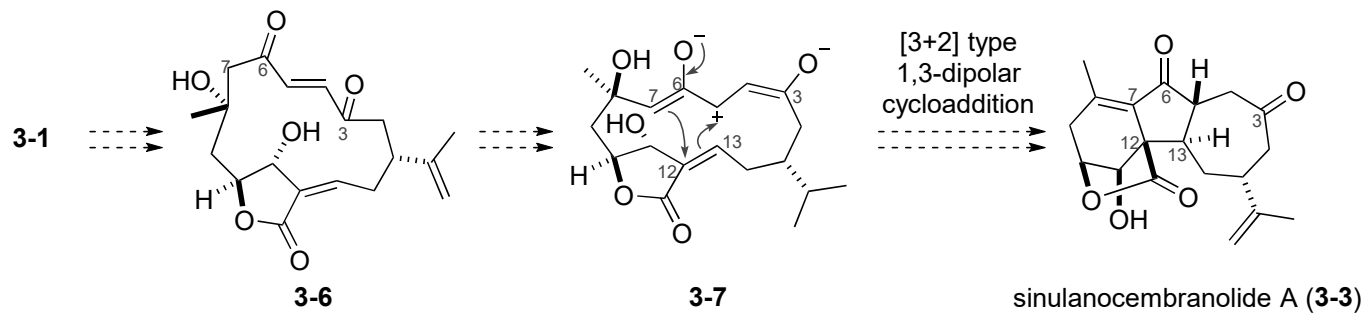
1. Proposed biosynthetic pathway by Pattenden (2011) and Yen (2013)



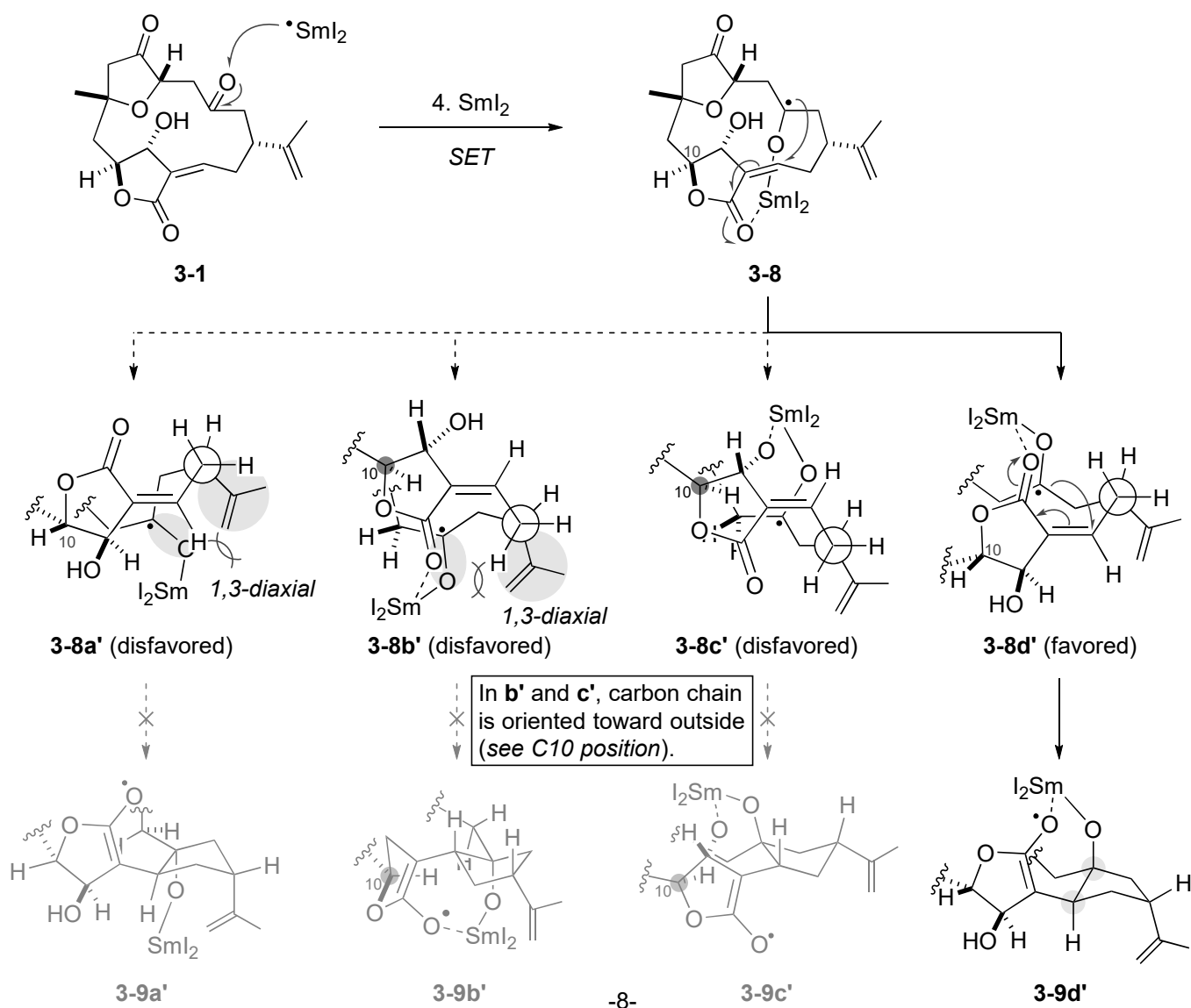
sinulanocembranolide A (**3-3**)

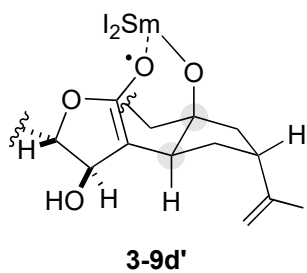


2. New proposal by Pattenden (2013): non-radical pathway

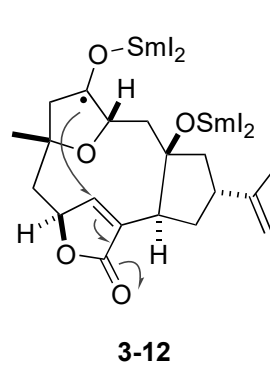
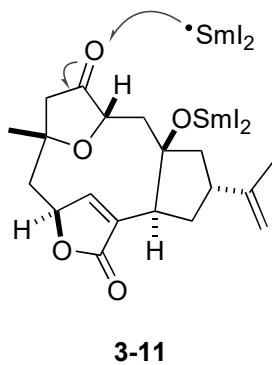
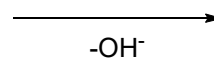
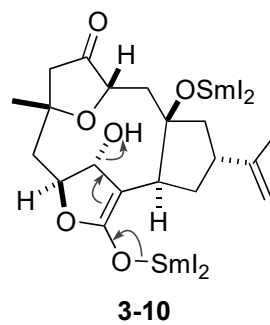
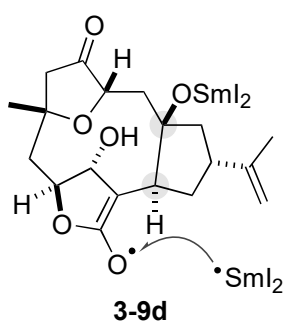


Palframen, M. J.; Pattenden, G. *Tetrahedron Lett.* **2013**, *54*, 6822.

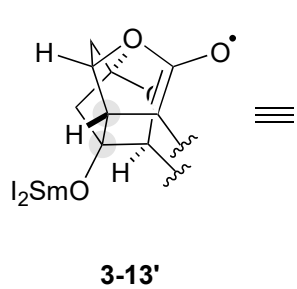
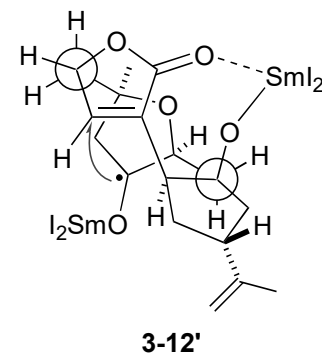




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