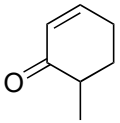
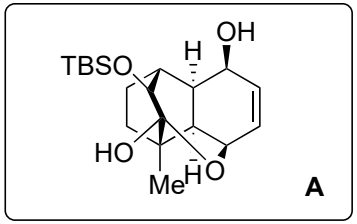
Total Synthesis of (±)-Myrocin C

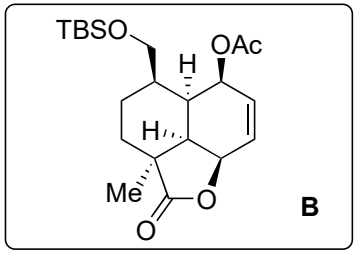
Chu-Moyer, M. Y., Danishefsky, S. J., Shulte, G. K.,
J. Am. Chem. Soc. **1994**, *116,* 11213–11228.



1-4



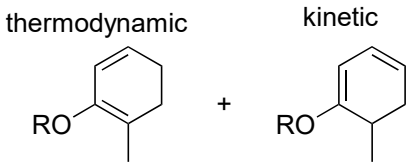
5-9



10-14

1) TBSOTf, Et_2NMe
2) *p*-benzoquinone, rt, 5 days
3) DMDO, -78 ºC to 0 ºC
4) $NaBH_4$, $CeCl_3 \bullet 7H_2O$

1: The thermodinamic product was separated and submitted to step 2

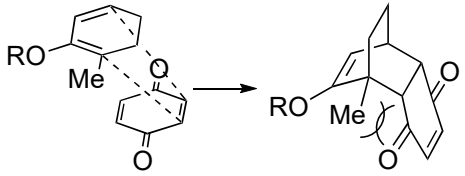


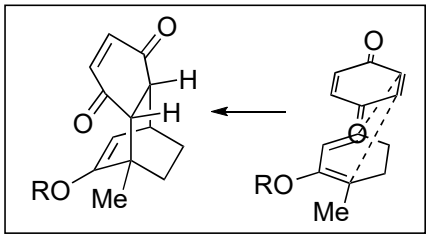
Name the reaction in step 4

Luche reduction

Explain the stereochemistry in step 2:

Endo product, π–orbital stabilization. 2 options:





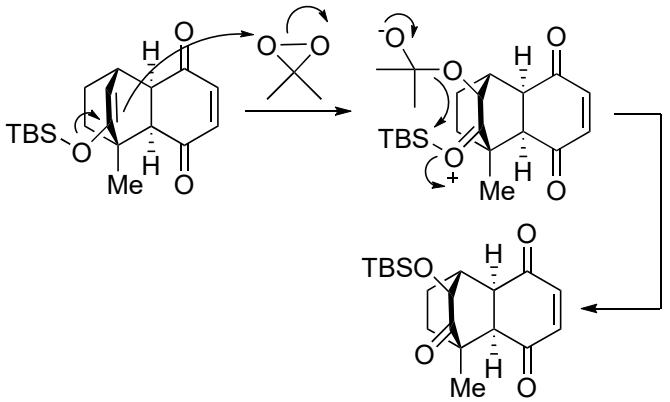
Only this product, lower energy transition state

5) Ac_2O, DMAP
6) TBAF
7) $NaIO_4$
8) $NaBH_4$
9) TBSOTf, Et_3N

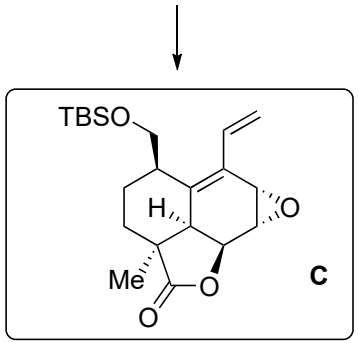
What is the role of LiCl in step 14?

Transmetallation step is faster when Cl and not OTf coordinates palladium. This works when solvent is not very polar.

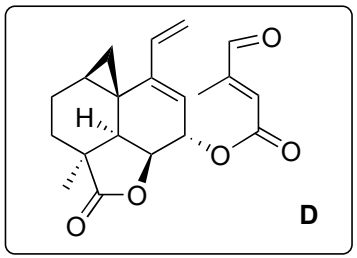
Explain the mechanism in step 3



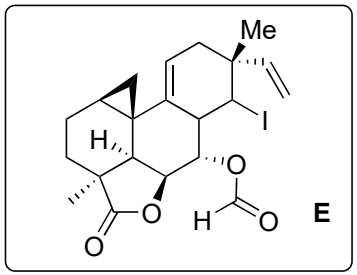
10) MeONa, MeOH, aq. workup
11) PDC
12) H_2O_2, NaOH, MeOH
13) NaHMDS, H–M reagent
14) LiCl, $Bu_3SnCHCH_2$, $Cl_2Pd(PPh_3)_2$



15-18



19-23



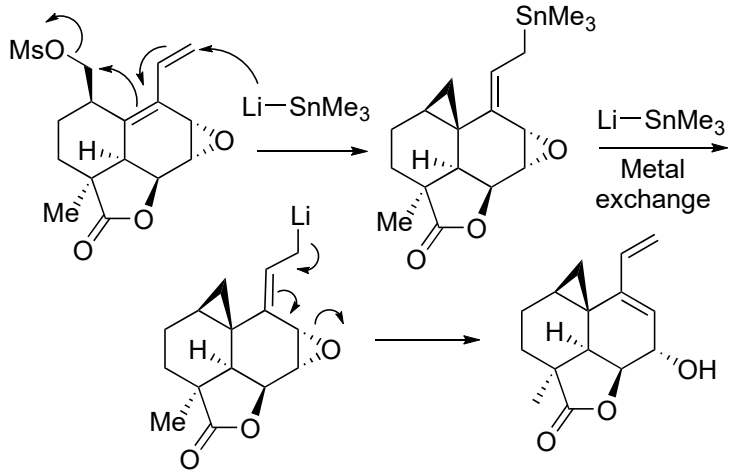
24-27

What is the role of AcOH in step 15?

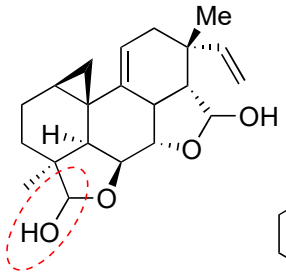
Neutralize the F^- anions to avoid epoxide opening and halohydrin formation

15) AcOH, TBAF
16) DMAP, Et_3N, MsCl
17) Me_3SnLi, 1.1 eq, 0 ºC, 5 min.
Then 1.1 more eq, 5 min
18) (*E*)-3-methyl-4-oxobut-2-enoic acid, DCC, DMAP

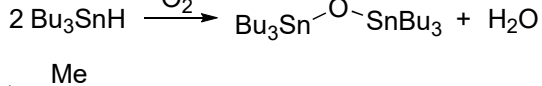
Explain the mechanism in step 17



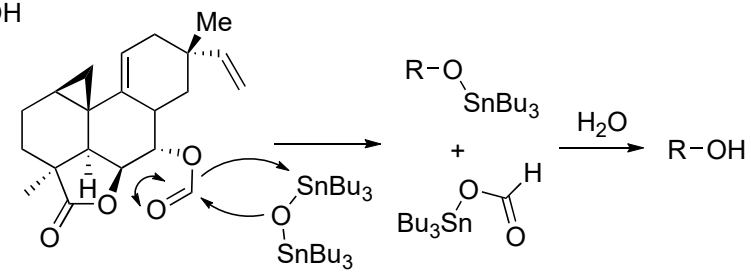
22: Regioselective reaction



24: Why aged $HSnBu_3$?

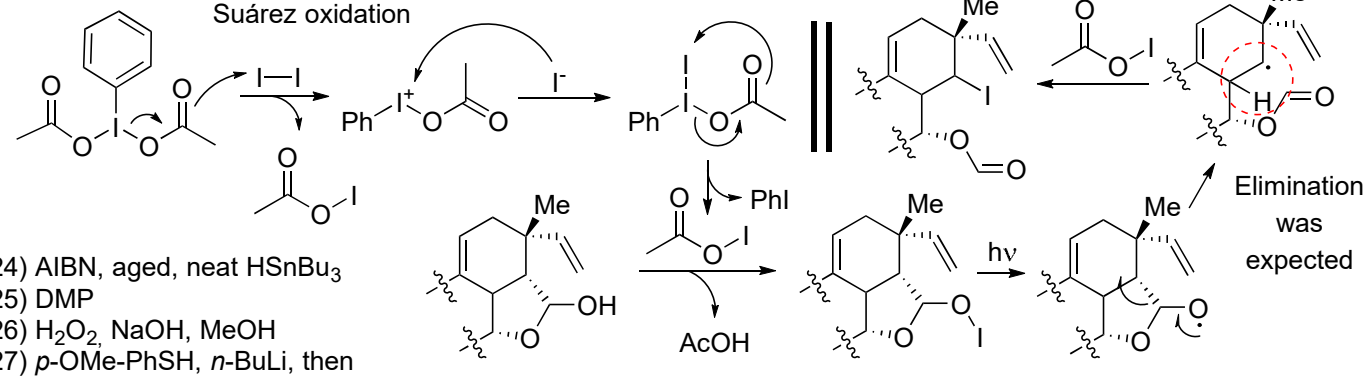


19) PhH, reflux
20) Ph_3PCH_3Br, NaHMDS
21) DIBALH
22) PDC
23) DIB, I_2, hν

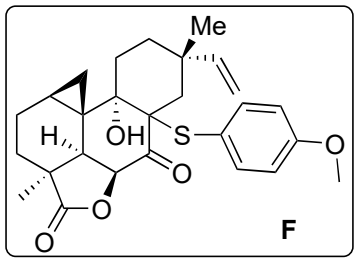


Explain the mechanism and name the reaction in step 23.

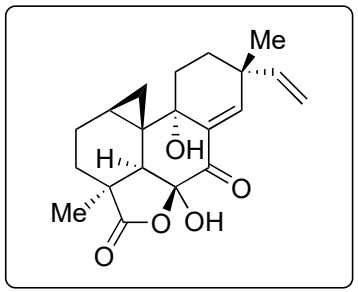
Suárez oxidation



24) AIBN, aged, neat $HSnBu_3$
25) DMP
26) H_2O_2, NaOH, MeOH
27) *p*-OMe-PhSH, *n*-BuLi, then Me_3Al, then **25**



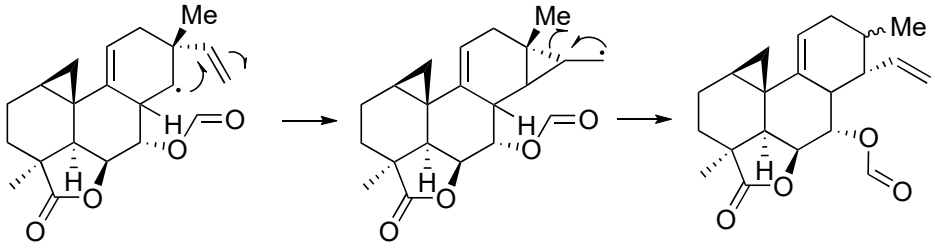
28-30



(±)-Myrocin C

24: Why neat $HSnBu_3$?

To minimize the following rearrangement:



28) DMDO
29) *t*-BuOK, *t*-BuOH, O_2
30) $P(OEt)_3$