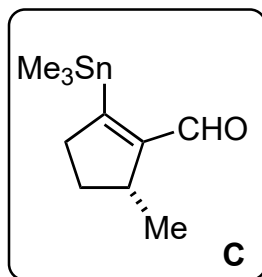
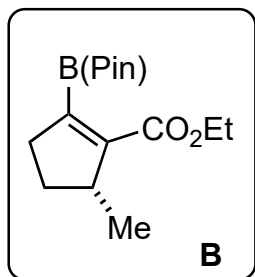
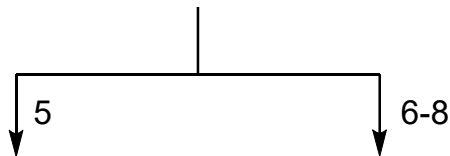
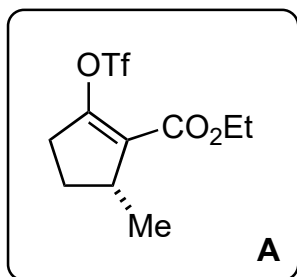
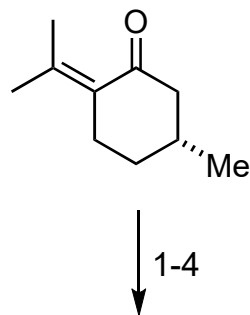


A Short Synthesis of Delavatine A Unveils New Insights into Site-Selective Cross-Coupling of 3,5-Dibromo-2-pyrone

Palani, V.; Hugelshofer, C. L.; Kevlishvili, L.; Liu, P.; Sarpong, R.

J. Am. Chem. Soc. **2019**, *141*, 2652–2660.



- 1) Br₂
- 2) EtONa
- 3) O₃
- 4) LDA, Tf₂O

- 5) Pd(dppf)Cl₂, B₂pin₂
- 6) (Me₃Sn)₂CuLi
- 7) Dibal-H
- 8) TPAP, NMO

2) Show the mechanism of step 2.
hint: A cyclopentane is formed

5) Which by-product must be avoided ?

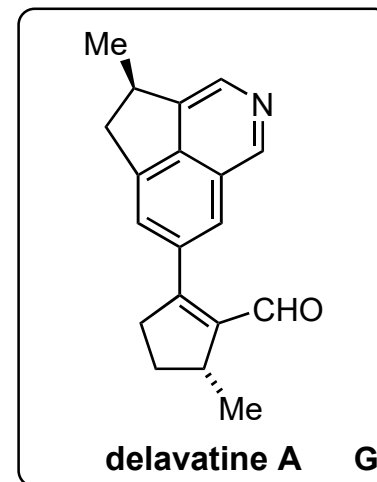
Suzuki-coupling between vinyl triflate and vinyl-boronate

6) Propose two mechanisms

Michael-retro-Michael or

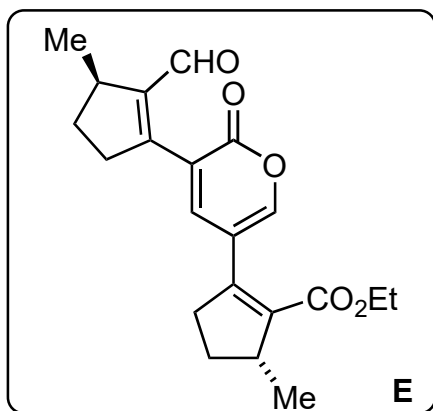
1,4-addition followed by an E1cB or

Oxidative addition-Reductive Elimination

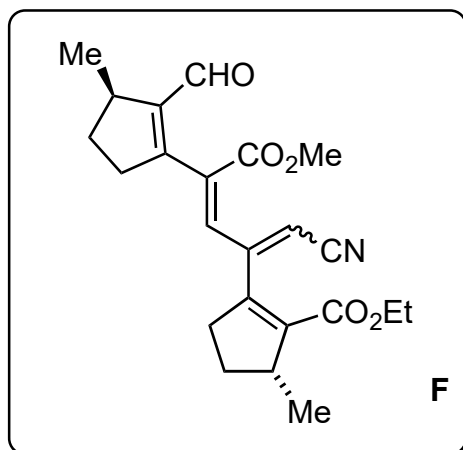


delavatine A G

D
↓ 9,10

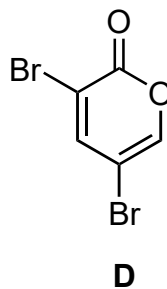


↓ 11



↓ 12-15
G

- 9) Pd(PPh₃)₄, CuI, **B**
10) Pd(PPh₃)₄, CuTC, **C**

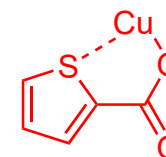


- 11) NaCN, *then* K₂CO₃, MeI

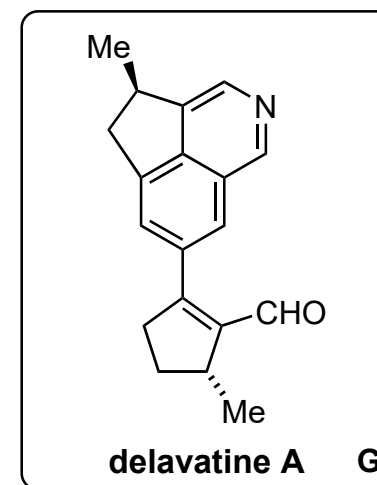
- 12) TBSOTf, Et₃N,
then DBU, PhMe, Δ
13) LiAlH₄
14) (COCl)₂, DMSO, Et₃N
15) NH₄OAc,

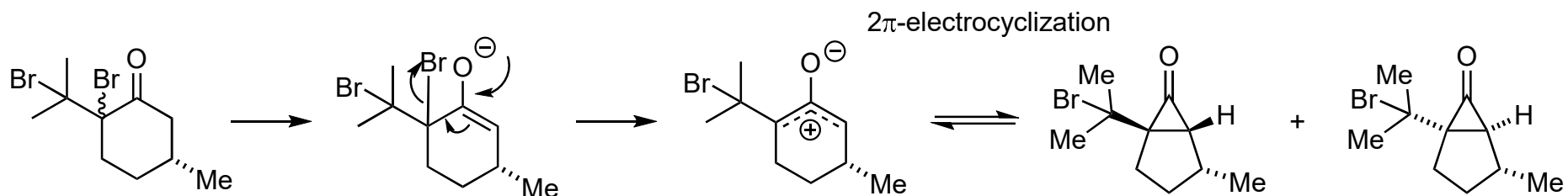
- 9) Give the name of steps 9 and 10
Suzuki-Cross-Coupling

- 10) Show the structure of CuTC



- 11) Show the mechanism of step 11
**1,6-addition followed by a
vinylogous retro-oxa-Michael**
12) Show the mechanism of step 12





Extra questions: Step 2

The relationship between oxyallyl cation and cyclopropanone is an equilibrium or a resonance? answer: **equilibrium**

It is an electrocyclization.

Conrotatory or disrotatory? **Disrotatory**

I want you to show me the mechanism of two reactions:

- an oxyallyl cation with a nucleophile;

Nucleophilic addition followed by enolate protonation

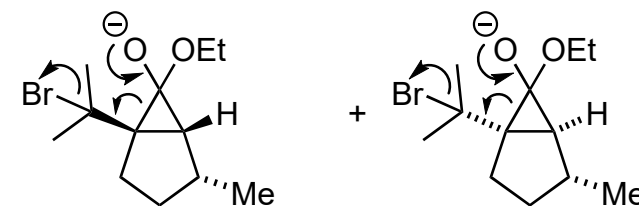
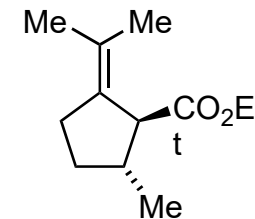
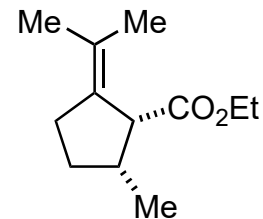
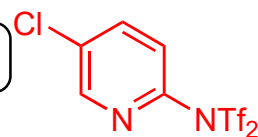
- with a diene: **4+3 cycloaddition**

Extra question: Step 4

Can you show two reagents to replace Tf_2O ? **PhNTf₂ and Comins**

Extra question: Step 5

How to avoid the Suzuki? **Avoid addition of base (double check)**



Extra questions: **Step 6**

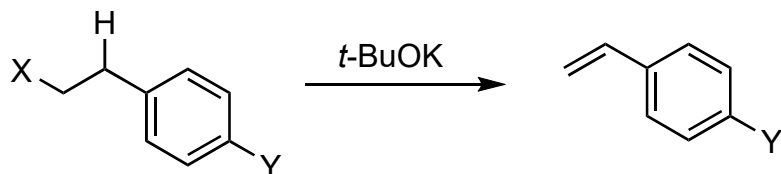
Why is there a typical 1,4 vs 1,2 selectivity for organocuprates?

Cu-coordinates to the double bond η -2 complex, migratory insertion then reductive elimination

Explain the mechanistical difference between E1cB and a E2 ?

E2 is concerted whereas E1cB is stepwise, in which initially there is a conjugated base formation prior to the elimination of the leaving group

Consider the elimination of a homobenzyl halide in the presence of a base



For Y = EDG or weak EWG: E2 Mechanism
(Me, MeO or Cl)

For Y = strong EWG: E1cB (CN or NO₂)

Mention that in a Hammett-Plot this is a classical example of shift in inclination typical of shift in reaction mechanism

Extra questions: **Step 9**

What kind of selectivity is operating in step 9? regioselectivity

Extra questions: **Step 10**

What is the synthetic advantage of preparing two building blocks from the same synthetic intermediate?

There is an overall reduction in the number of steps

Extra questions: **Step 12**

What is the role of DBU?

To eliminate the cyano after the electrocyclization

Extra questions: **Step 15**

Show the mechanism of step 15