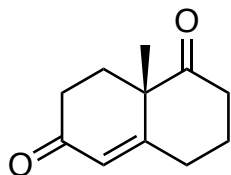


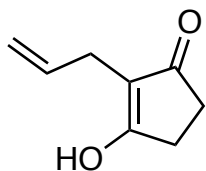
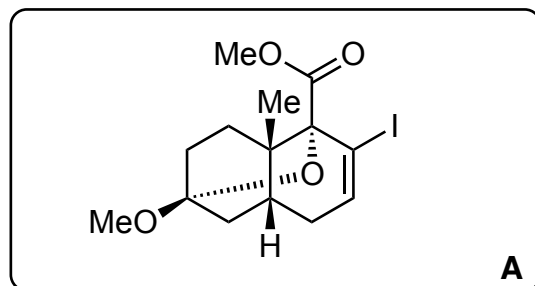
# Total Synthesis of (-)-Batrachotoxin Enabled by a Pd/Ag-Promoted Suzuki–Miyaura Coupling Reaction

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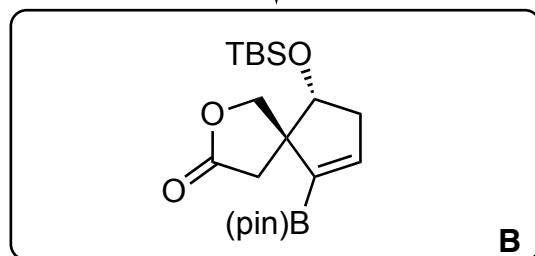
*Angew. Chem. Int. Ed.* **2023**, *62*, e202309688.



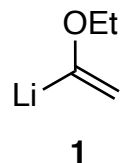
1-9



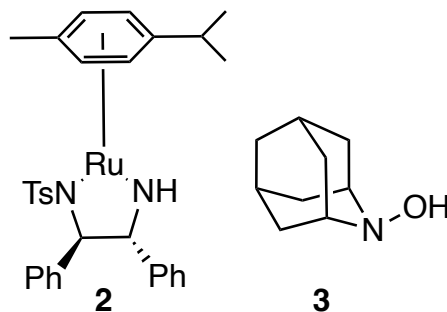
10-17



1. Pd/C, H<sub>2</sub>
2. (HOCH<sub>2</sub>)<sub>2</sub>, (+)-CSA
3. KH, PhS(O)OMe
4. Na<sub>2</sub>CO<sub>3</sub>, toluene, 110 °C
5. Br<sub>2</sub>, then pyridine
6. **1**, THF, -78 °C
7. (+)-CSA, CH(OMe)<sub>3</sub>, MeOH
8. *t*-BuLi, then I<sub>2</sub>
9. RuCl<sub>3</sub>, NaIO<sub>4</sub>



10. (HCHO)<sub>n</sub>, TsOH, AcOH
11. **2**, *i*-PrOH
12. TBSCl, imidazole
13. O<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub> then PPh<sub>3</sub>
14. K<sub>2</sub>CO<sub>3</sub>, MeOH
15. **3**, NaClO, NaHCO<sub>3</sub>
16. KN(TMS)<sub>2</sub>, then Comins' Reagent
17. Pd(PPh<sub>3</sub>)<sub>4</sub>, B<sub>2</sub>(pin)<sub>2</sub>, KF



Name the starting material

(+)-Wieland-Miescher ketone

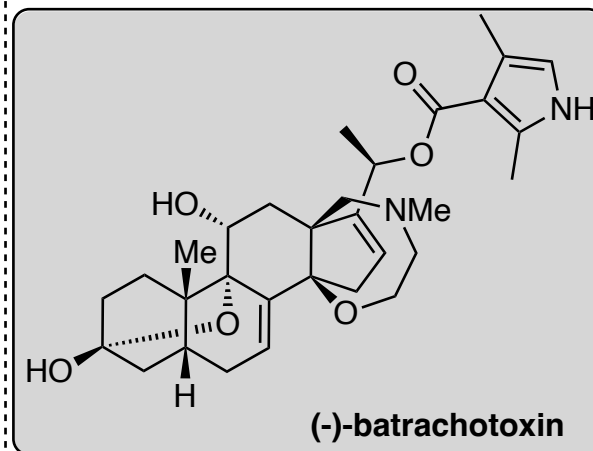
2. Hint: only 1 dioxolane ring is formed

7. Hint: loss of (3H, triplet) and (2H, quartet), product shows 3 (3H, s) signals  
δ 3.31, 3.24, 1.95

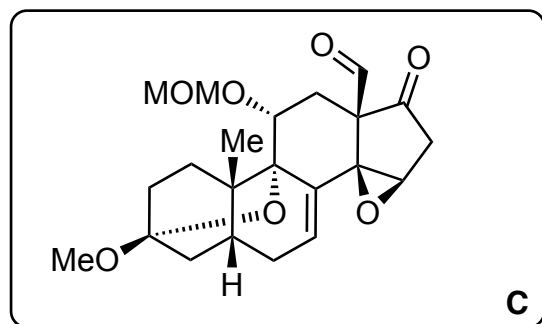
11. Hint: desymmetrization, single reduction, trans product

15. Name of 3?

AZADOL



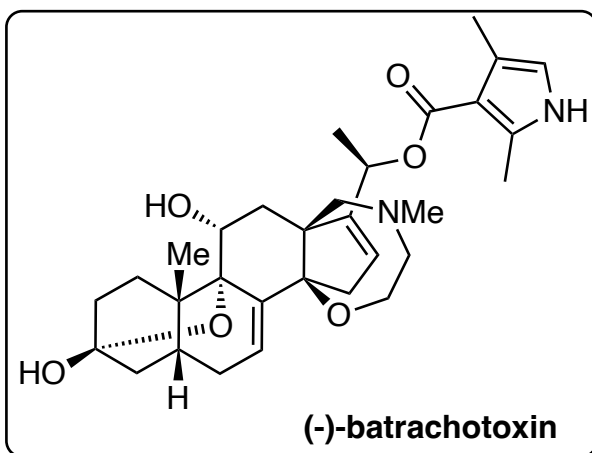
18-24



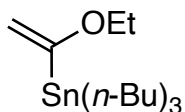
25-29

**(-)-batrachotoxinin A**

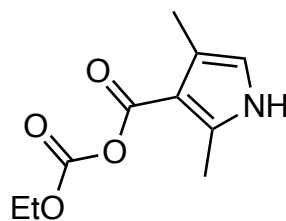
30



18. **A**, Pd(PPh<sub>3</sub>)<sub>4</sub>, Ag<sub>2</sub>O, THF
19. t-BuOK, THF, *then* n-Bu<sub>4</sub>NF
20. LiOH, THF/H<sub>2</sub>O, *then* HCl, 0 °C, *then* o-dichlorobenzene, 135 °C
21. NaBH(OAc)<sub>3</sub>, piperidine, DMF
22. TESCl, *i*-Pr<sub>2</sub>NEt *then* MOMBr, *then* (+)-CSA, MeOH
23. VO(Oi-Pr)<sub>3</sub>, MS 4A, PhC(CH<sub>3</sub>)<sub>2</sub>OOH
24. **3**, PhI(OAc)<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>
25. MeNH<sub>2</sub>, *then* NaBH(OCOCF<sub>3</sub>)<sub>3</sub>, *then* 2,6-lutidine, chloroacetyl chloride, *then* NaOEt
26. Pd/C, H<sub>2</sub>
27. KN(TMS)<sub>2</sub>, *then* PhNTf<sub>2</sub>
28. Pd(PPh<sub>3</sub>)<sub>4</sub>, **4**, LiCl, CuCl, *then* aq. oxalic acid
29. AlH<sub>3</sub>, THF, *then* aq. HCl
30. **5**, Et<sub>3</sub>N, benzene



**4**



**5**

**18. Name the reaction**  
Pd/Ag-catalyzed Suzuki-Miyaura

**20. Name the reaction**  
Dieckmann Condensation

*Hint: the hydroxyl handle formed in step 20 temporarily forms a hydroborate in 21 and a vanadium-oxidant complex in 23*

*25. Hint: lactamization*

**28. Name the reaction**  
Stille Coupling