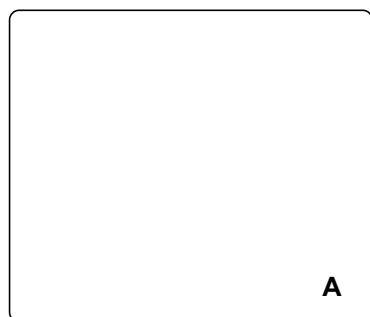
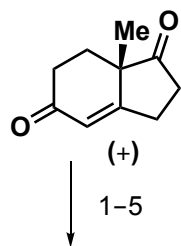
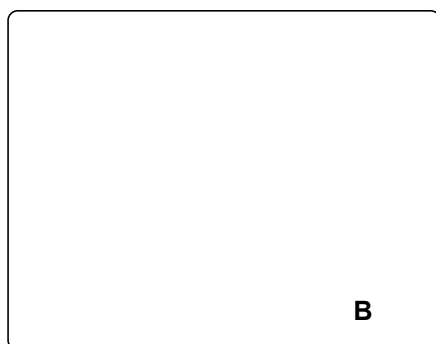


# Asymmetric synthesis of batrachotoxin: Enantiomeric toxins show functional divergence against Na<sub>v</sub>

Logan, M. M., Toma, T., Thomas-Tran, R., Du Bois, J.  
*Science*, 2016, 354, 865–869.

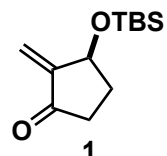


6-9



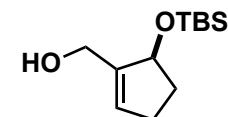
- 1) H<sub>2</sub>, Pd/C, HCl, ethylene glycol
- 2) TESOTf, Et<sub>3</sub>N
- 3) CHBr<sub>3</sub>, KO<sup>t</sup>-Bu
- 4) TMSC≡CLi, THF
- 5) camphor sulfonic acid, MeOH

- 6) *t*-BuLi, THF, -90 °C, then **1**
- 7) K<sub>2</sub>CO<sub>3</sub>, MeOH
- 8) TMSC≡CSiEt<sub>2</sub>Cl, imidazole
- 9) *n*-Bu<sub>3</sub>SnH, O<sub>2</sub>, Et<sub>3</sub>B, Ph<sub>2</sub>O, 150 °C



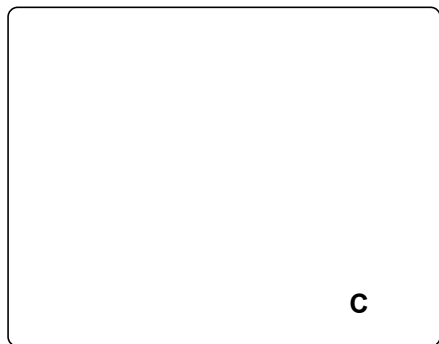
Please name the starting material.  
How would you make it?

How would you make intermediate **1** from:

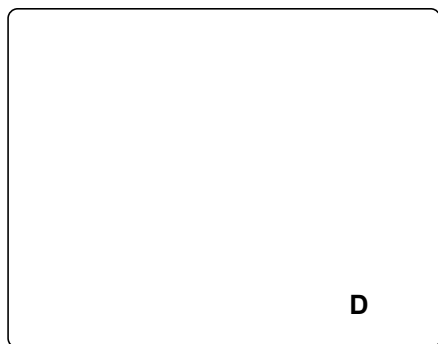


Step 9: Please provide the mechanism.

10-14



15-20



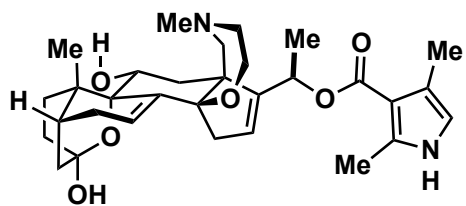
- 10) TBAF, THF, 60 °C
- 11) IBX, OsO<sub>4</sub>, NaIO<sub>4</sub>
- 12) MeNH<sub>2</sub>, NaB(O<sub>2</sub>CCF<sub>3</sub>)<sub>3</sub>H
- 13) ClCH<sub>2</sub>COCl, 2,6-lutidine
- 14) NaOEt/EtOH

- 15) KHMDS, PhNTf<sub>2</sub>
- 16) CuCl<sub>2</sub>, O<sub>2</sub>
- 17) NaClO<sub>2</sub>, NaH<sub>2</sub>PO<sub>4</sub>, DMSO/H<sub>2</sub>O
- 18) SOCl<sub>2</sub>, pyridine
- 19) NaN<sub>3</sub>, acetone/H<sub>2</sub>O
- 20) AcOH/H<sub>2</sub>O, 90 °C

Step 20: Please name the reaction.

D

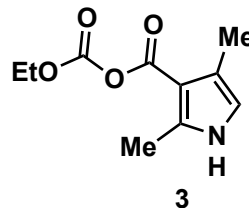
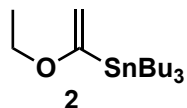
↓  
21-25



(-)-Batrachotoxin (BTX)

LD<sub>50</sub> = 2 μg/kg

- 21) *p*-TsOH, 4Å MS, PMBCH<sub>2</sub>OH
- 22) **2**, Pd(PPh<sub>3</sub>)<sub>4</sub>, LiCl, CuCl, then 1 M oxalic acid
- 23) AlH<sub>3</sub>
- 24) *p*-TsOH, acetone/H<sub>2</sub>O
- 25) Et<sub>3</sub>N, **3**



Step 23: How would you make AlH<sub>3</sub>?