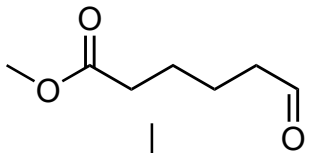
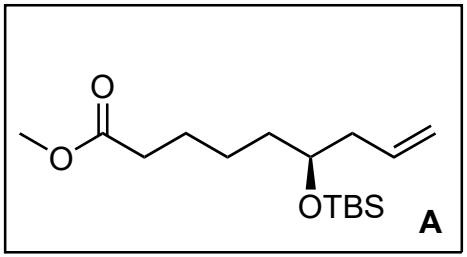
Total Synthesis of (-)-histrionicotoxin and (-)-histrionicotoxin 235A

Gilbert Stork and Kang Zhao

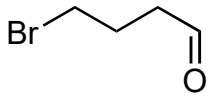
J. Am. Chem. Soc. **1990** *112*, 5875



1



A



2-6

B

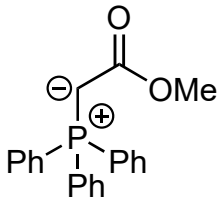
1) How? (2 steps)

2) **1**, THF
3) DIBAL
4) (R, R)-Diethyltartrat, (+)-DET, $Ti(O^iPr)_4$, ^tBuOOH
5) $(COCl)_2$, DMSO, NEt_3
6) $Me^+PPh_3I^-$, NaHMDS, THF

Using a boran reagent, how would you accomplish this transfromation?

What model would be used to predict the sterochemistry?

Name of step 1?



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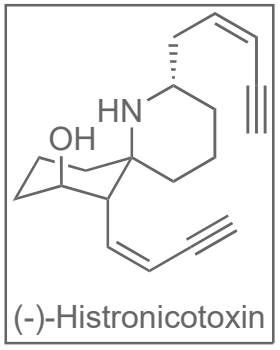
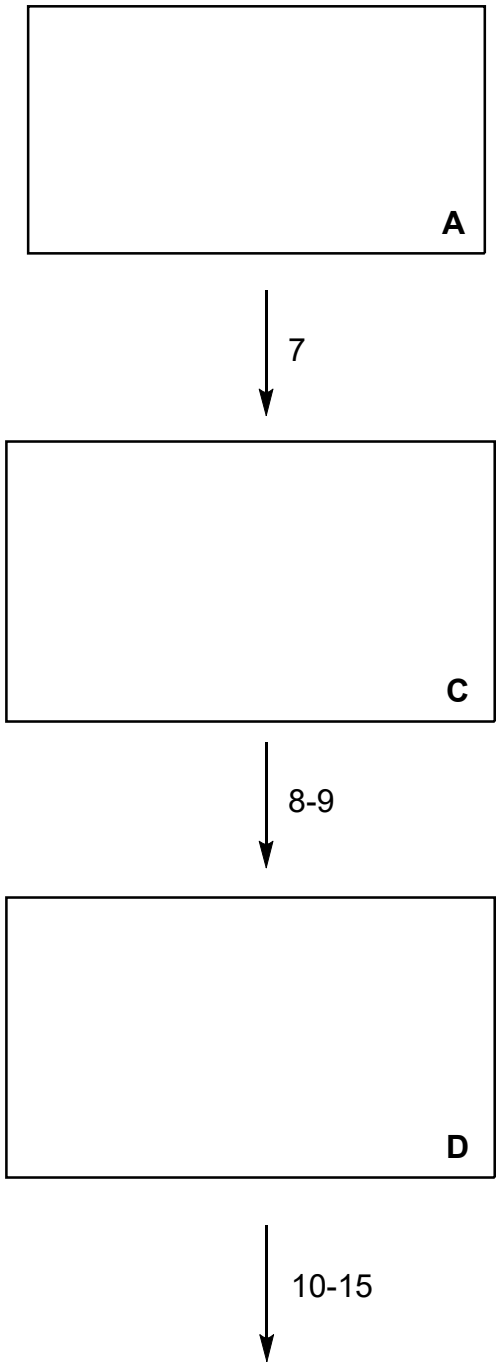


(-)-Histronicotoxin



7) LDA, -78 °C, HMPA/THF (6:11 v/v), **B**
then LDA, -78 °C, 2 h

8) O_3, *then* PPh_3
9) $(Ph_3P^+CH_2I)I^-$, $NaN(TMS)_2$

10) 5% HCl, THF
11) Ph_3P, CBr_4, ether
12) NH_4Cl, $AlMe_3$,PhH, 40 °C
13) AcO_2, Py, DMAP
14) $(CF_3CO_2)_2IPh$, MeCN, H_2O
15) Et_3N, DCE, 70 °C

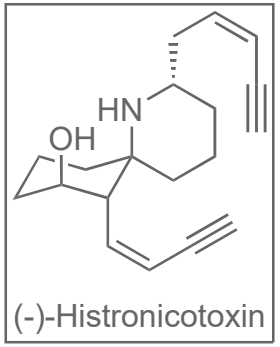
What is the mechanism of step 7?
Explain the selectivity.

What is the name of step 9 and its mechanism

hint: our collegue runs this reaction in complete darkness.

bigger hint: Look at the authors of this paper

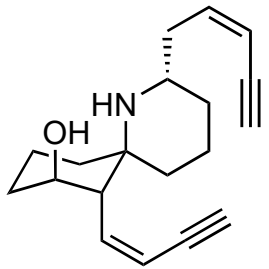
What is the name of $NaN(TMS)_2$



(-)-Histronicotoxin

E

16-18



(-)-Histronicotoxin

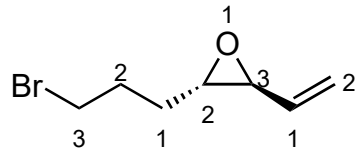
16) $Pd(PPh_3)_4$, CuI, PhH, TMS-acetylene
17) $Bu_4N^+F^-$
18) K_2CO_3, MeOH

C

19-25

(-)-Histronicotoxin 235A

19) 5% HCl, THF
20) Ph_3P, CBr_4, ether
21) NH_4Cl, $AlMe_3$,PhH, 40 °C
22) AcO_2, Py, DMAP
23) $(CF_3CO_2)_2IPh$, MeCN, H_2O
24) Et_3N, DCE, 70 °C
25) MeOH, Na_2CO_3 (aq)



trans-(2S,3S)-3-(3-bromopropyl)-2-ethenyl-oxirane