Total Synthesis of (–)-Histrionicotoxin through a Stereoselective Radical Translocation–Cyclization Reaction

Sato, M.; Azuma, H.; Daigaku, A.; Sato, S.; Takasu, K.; Okano, K.; Tokuyama, H.; *Angew. Chem. Int. Ed.* **2017, *56*,** 1087–1091.

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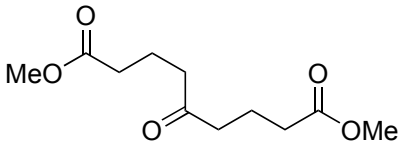

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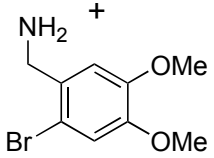


1–3

1) $NaBH(OAc)_3$, CH_2Cl_2, rt
2) K-Selectride, THF, 0 °C to rt
3) cat. TEMPO, NaOCl, KBr, $NaHCO_3$, CH_2Cl_2/H_2O, 0 °C

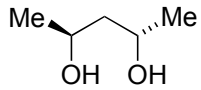
Mechanism of step 3?

C

4–6

4) vinylmagnesium bromide, THF, –78 °C to 0 °C
5) methyl acrylate, cat. Grubbs II, CH_2Cl_2, reflux
6) MnO_2, CH_2Cl_2, rt
7) diol **X**, cat. TMSOTf, TMSO*i*-Pr, CH_2Cl_2, 0 °C to rt

X =



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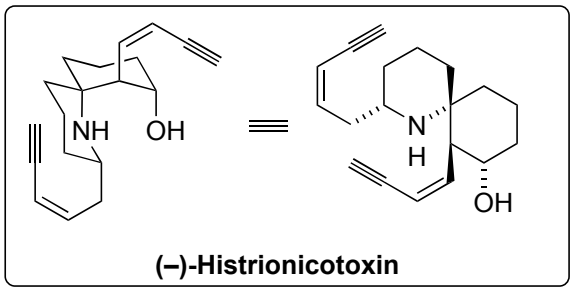
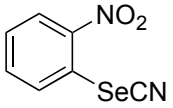


(–)-Histrionicotoxin

8–14

8) cat. AIBN, $(TMS)_3SiH$, benzene, reflux
9) cat. $FeCl_3$, SiO_2, acetone, rt.
10) Li, NH_3, *t*-BuOH/THF, –78 °C, 1 h
11) PBu_3, reagent **Y**, THF, 1 h

Y = 

12) *p*-TSA, toluene, reflux
13) TBDPSCl, imidazole, CH_2Cl_2, rt
14) *m*-CPBA, CH_2Cl_2, 0 °C to rt

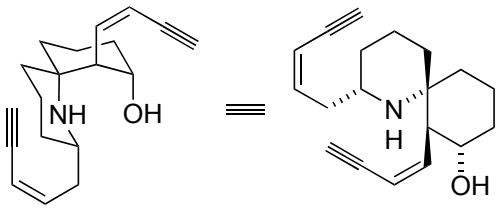
Mechanism of step 8?
What other reagents other than $(TMS)_3SiH$ could be used? Advantages/disadvantages?

E

15) $Ti(Oi\text{-}Pr)_4$, Et_2SiH_2, THF, reflux
then cool to –78 °C, allylMgCl, cat. $ZnCl_2$
17) TBAF, THF
18) $SOCl_2$, imidazole, CH_2Cl_2, 0 °C, 1 h
19) O_3, *then* Me_2S, CH_2Cl_2/MeOH, –78 °C to rt
20) PhP_3CH_2I, KHMDS, THF, –78 °C
21) TMS-acetylene, cat. $Pd(PPh_3)_4$, cat. CuI, Et_2NH
22) $LiAlH_4$, THF, 0 °C to rt

Name Reaction? Name 3 alternative methods for the formation of this functional group (also in other stereo- and regioselectivities)

15–22



(–)-Histrionicotoxin **F**