Synthesis of Cossonidine (Davisine)

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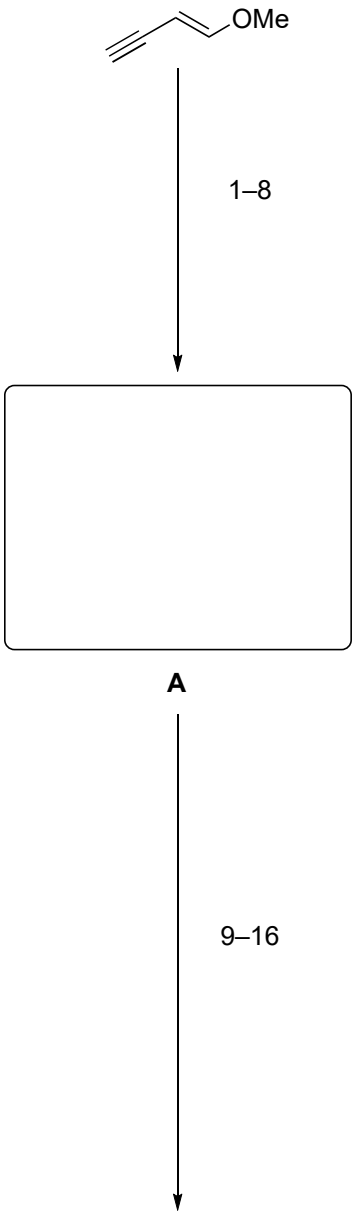
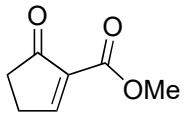


1) *n*-BuLi, then $(CH_2O)_n$, THF
2) $LiAlH_4$, Et_2O
3) TBSCl, ImH, CH_2Cl_2
4) **1**, toluene, 100 °C
5) $LiAlH_4$ excess, THF
6) TPAP, NMO, CH_2Cl_2
7) $[Rh(PPh_3)_3]Cl$, PPh_3, $TMSCHN_2$, *i*-PrOH
8) LiHMDS, *then* **2**, THF



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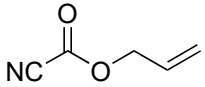

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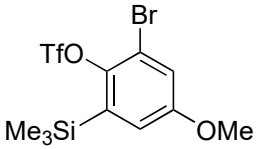

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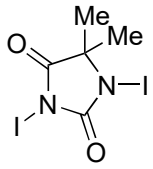


DIH

9) **3**, CsF, 70 °C, MeCN
10) $Pd(PPh_3)_4$, $PhSiH_3$, CH_2Cl_2
11) DIH, hν, DCE
12) TBAF, THF
13) TEMPO, PIDA, NH_4OAc, $MeCN/H_2O$
14) LiHMDS, *then* MeI, THF
15) CoB, BH_3•*t*-$BuNH_2$, MeOH
16) $LiAlH_4$, THF, 70 °C

4) What is the name of the reaction? Explain the regioselectivity.

7) What is the name of the reaction and the catalyst used?

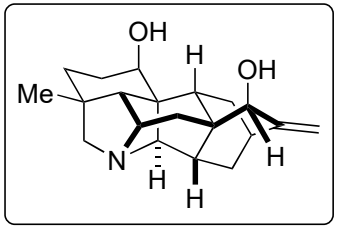
9) What is the reactive species formed? Show the mechanism.
Hint: A seven-membered ring is formed, reminiscent of the Dowd–Beckwith reaction.

10) **Hint:** The ArBr remains intact.

11) **Hint:** The vinyl group remains intact; after the reaction, an elimination occurs resulting in an alkene.

15) **Hint:** Chemoselective reduction of the nitrile group.

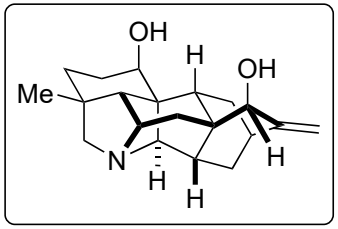
16) **Hint:** Debromination also occurs this is a good point to redraw the molecule



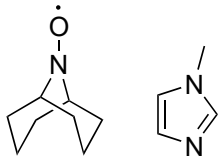
Cossonidine

B

17–24



Cossonidine



ABNO

NMI

17) *n*-BuLi, hν, *i*-Pr_2NH, THF
18) $Na_{(s)}$, $NH_{3(l)}$, *then* HCl
19) pyrrolidine, MW, 110 °C, MeOH
20) HBr/AcOH, *then* K_2CO_3, MeOH
21) Ph_3PCH_3Br, *n*-BuLi, THF
22) $[Cu(CH_3CN)_4]OTf$, ^{MeO}bpy, ABNO, NMI
23) $LiAlH_4$, THF
24) SeO_2, 1,4-dioxane

18) Please name the reaction and provide the mechanism.