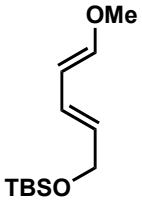
Total Synthesis of Cossonidine

01.08.18



1) **1**, 110 °C, PhMe
2) Pd/C, H_2

A

3) $LiAlH_4$ (4 eq.)
4) TPAP (5%), NMO (3.5 eq.)
5) $[Rh(PPh_3)_3]Cl$, PPh_3, $TMSCHN_2$, *i*PrOH

B

6) LiHMDS, then **2**, THF, -78 °C to 0 °C

C

7) **3**, CsF, MeCN, 70 °C

D

8) $Pd(PPh_3)_4$ (20 mol%), $PhSiH_3$ (2 eq.), DCM

E

9) DIH, *h*ν; DCE

F

10) TBAF
11) TEMPO (15 mol%), PIDA (3 eq.), NH_4OAc, $MeCN/H_2O$

G

12) LiHMDS, then MeI, -78 °C to rt

H

13) Co_2B, BH_3•*t*-$BuNH_2$, MeOH, Δ
14) $LiAlH_4$ (5 eq.), THF, Δ

hint: 3 transformations happen in step 14

I

15) *n*-BuLi, *h*ν; *i*-Pr_2NH, THF

J

16) Na, NH_3, *i*-PrOH, THF then HCl

K

17) pyrrolidine, MeOH, Δ

L

heptacycle

18) HBr/AcOH, Δ then K_2CO_3, MeOH

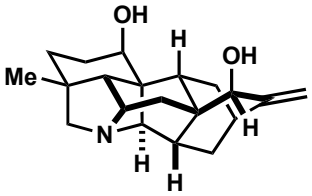
M + **N**

(desired) *(rearrangement product)*

19) Ph_3PCH_3Br, *n*-Buli, THF, Δ
20) $[Cu(CH_3CN)_4]OTf$ (20 mol%), MeObpy (20 %), ABNO (20%), NMI (40%), CH_3CN, air, 50 °C
21) $LiAlH_4$

O

22) SeO_2, 1,4-dioxane, 45 °C



cossonidine (39%)

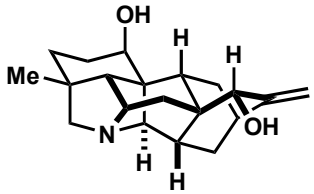
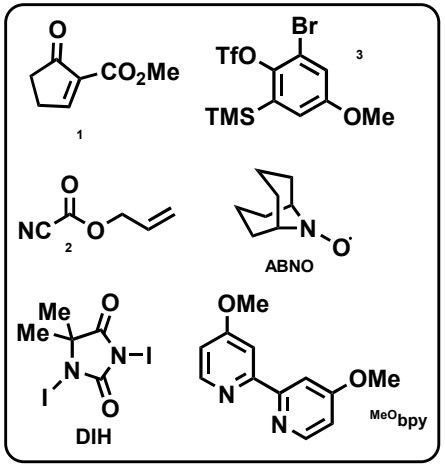
+

Q

(19%)

23) $NaBH_4$, $CeCl_3$, MeOH, 0 °C

(90%, dr=3:1)



15-*epi*-cossonidine