Total Synthesis of (+)-Complanadine A Using an Iridium-Catalyzed Pyridine C-H Functionalization

Daniel F. Fischer and Richmond Sarpong

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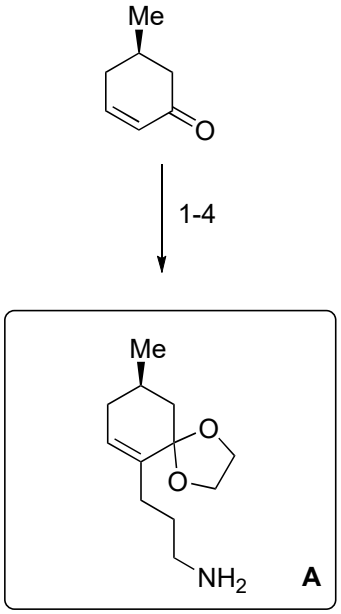
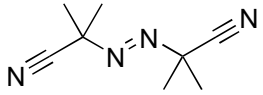


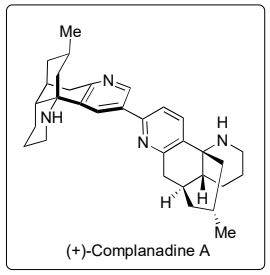
1) I_2, pyridine, DCM
2) acrylnitrile, AIBN, $HSnBu_3$,PhH
3) $HOCH_2CH_2OH$, $HC(OEt)_3$, TsOH, reflux
4) $LiAlH_4$, Et_2O, 0 °C

How would you make the starting material from (R)-pulgenone?

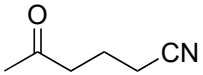
What is the structure of AIBN? Provide a mechanism.



AIBN



(+)-Complanadine A



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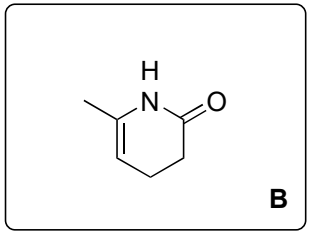
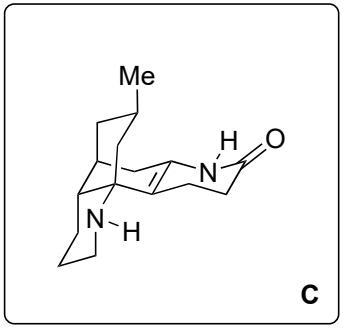


B

6

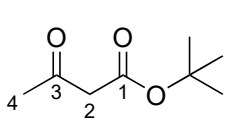


C

5) $Zn(NO_3)_2$, acetone oxime, H_2O 90 °C
then 120 °C, vacuum.

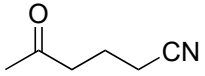
6) **A,** $HClO_4$, dioxane Δ

How would you prepare this starting material?

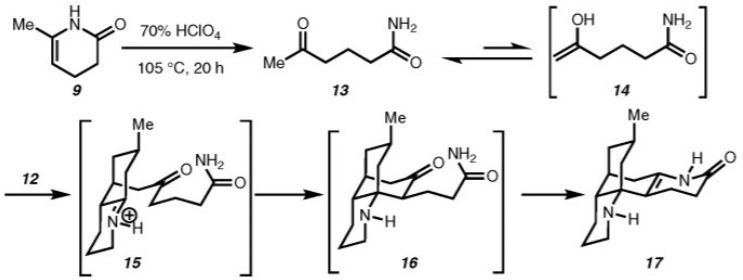


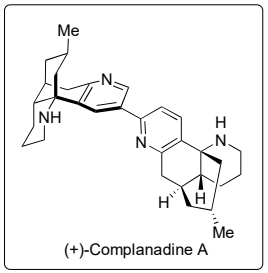
tert-butyl 3-oxobutanoate

1) acyrlonitrile, NaOEt, EtOH
2) TsOH, Δ



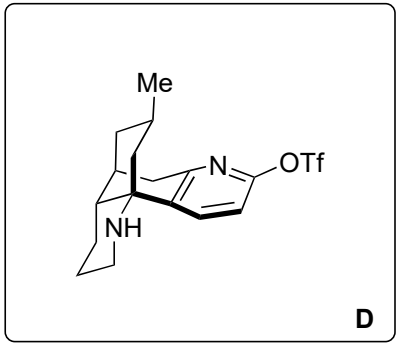
Provide a mechanism and rationalize the stereoselectivity for step 6.





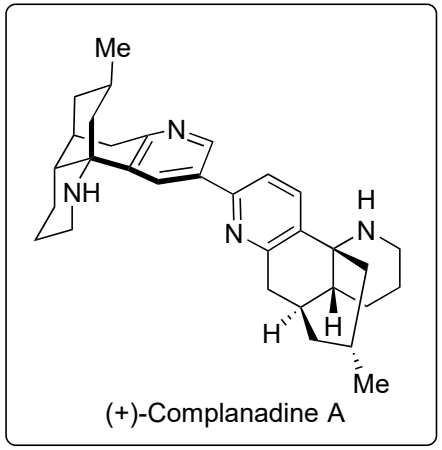
(+)-Complanadine A

7-9



D

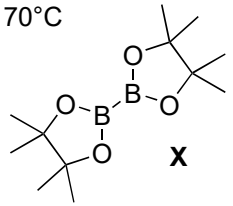
10-13



(+)-Complanadine A

7) Boc_2O, NEt_3, THF 60 °C
8) $Pb(OAc)_4$, $CHCl_3$, RT then K_2CO_3
9) Tf_2O, pyridine, -78 °C → RT

10) $Pd(OAc)_2$ dppf, NH_4O_2CH, NEt_3, DMF
11) **X**, $[Ir(COD)(OMe)]_2$, dtbu-bipy, THF, 80 °C
12) **D,** $PdCl_2(dppf)$, K_3PO_4, DMF
13) 6N HCl, 70°C



X

Provide a rationale for the regioselectivity in step 11
(a) J. Am. Chem. Soc. 2002, 124, 390. (b) Science 2002, 295, 305.

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What is the name of the reaction in step 12.