Convergent and Efficient Total Synthesis of (+)-Heilonine enabled by C-H Functionalizations

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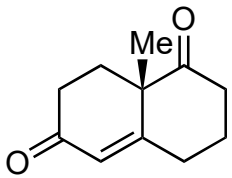

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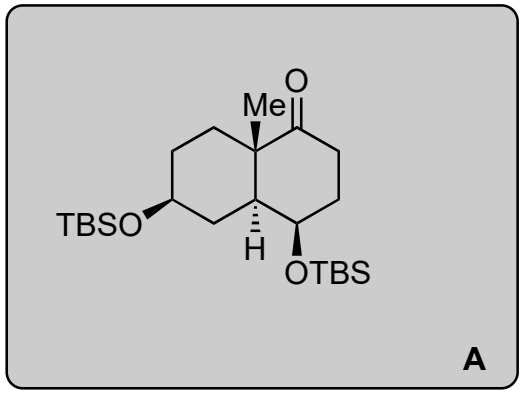

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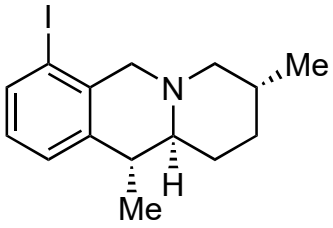
6-8

1) *p*-TsOH•H_2O, $HOCH_2CH_2OH$
2) Na_2-Eosin Y, 456 nm LED, O_2, CH_3CN, Thiourea, MeOH
3) KOH
4) $LiAl(O\textit{t}\text{-}Bu)_3H$, -78 °C to 23 °C, *then* 1 N HCl
5)TBSOTf, 2,6-lutidine



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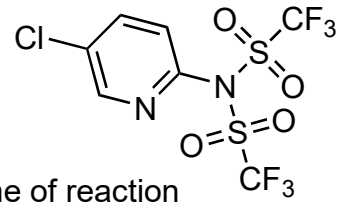
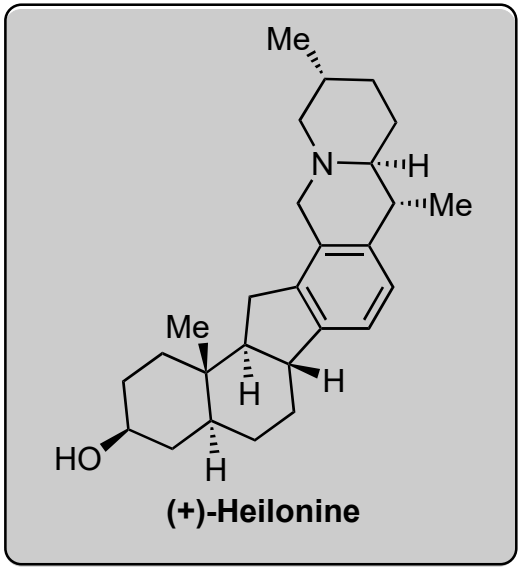
6) NaHMDS, Comins' reagent
7) $Pd(PPh_3)_4$, LiCl, $(Me_3Sn)_2$
8) $Pd(PPh_3)_4$, LiCl, CuCl, CO (1 atm), 1,4-dioxane

1) Name the starting molecule
Wieland-Miescher ketone

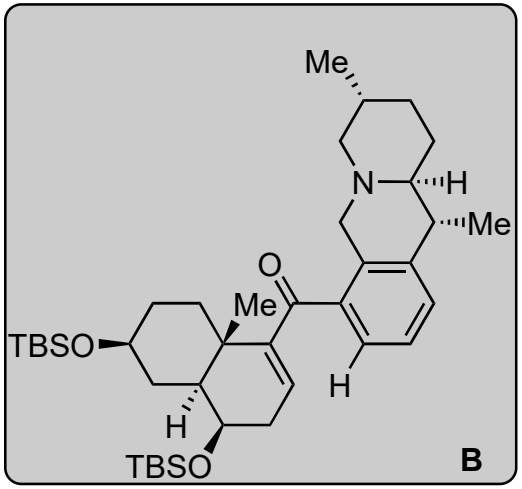
6) Structure of Comins' reagent



8) Name of reaction
Stille Coupling



(+)-Heilonine



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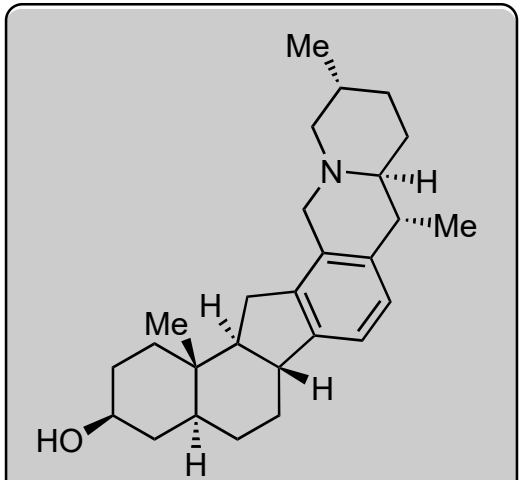

9) hν (370 nm), AcOH, *then* KOH, MeOH/THF
10) $NaBH_4$, 0 °C to 23 °C
11) NaHMDS, CS_2, MeI, THF -78 °C to -50 °C
12) Et_3B, *n*-Bu_3SnH, air
13) TfOH, -78 °C to -40 °C

9) Name of reaction
Nazarov Cyclization

Note: Minor product epimerized to major product with i-*P*r_2NH, MeOH

11) Name of reaction
Barton-McCombie Deoxygenation
Note/hint: Alternative to 10-12: Zn, conc. HCl, EtOH