A Cascade Strategy Enables aTotal Synthesis of (±)-Morphine

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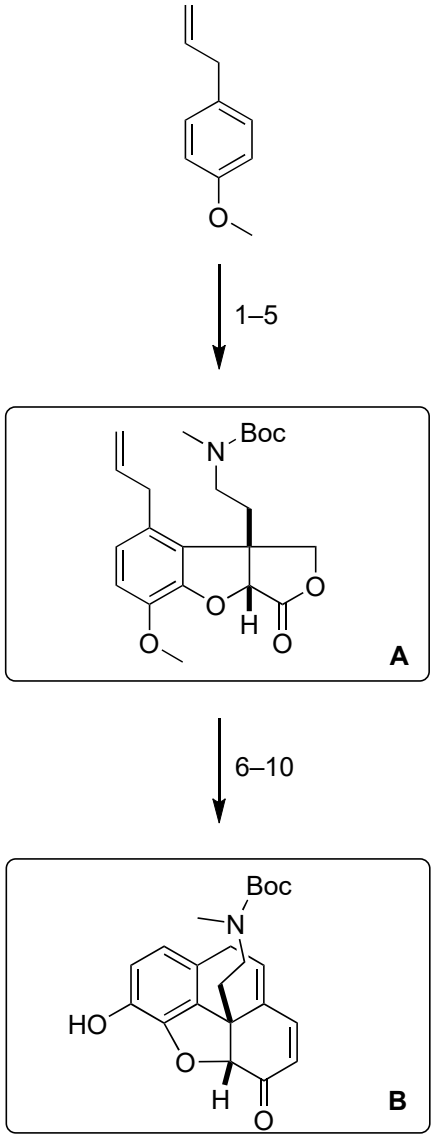
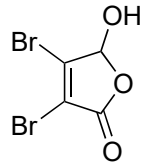


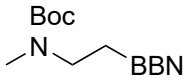
1) TMEDA, sec-BuLi,
then $B(OMe)_3$, NaOH, H_2O_2
2) **i**, aq. NaOH
3) $NaBH_4$ 0°C
then citric acid
4) **ii**, $Pd(dppf)Cl_2 \cdot CH_2Cl_2$
Cs_2CO_3, 40°C
5) (500 W Hg), DCE/HFIP, rt

6) KOH, t-BuOH/H_2O
then Na_2RuO_4, 50 °C
7) Ohira-Bestmann reagent,
K_2CO_3
8) Me(MeO)NH·HCl, NMM,
DMTMM
9) H_2C=CHMgBr, THF
10) HG-II, DCM

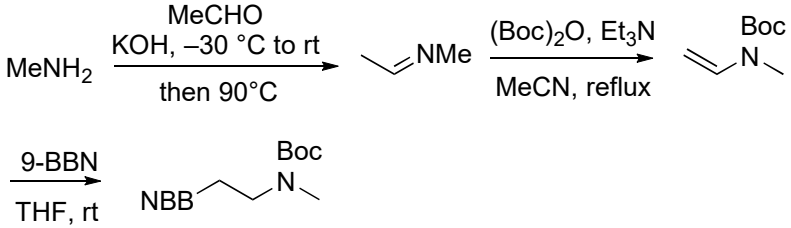
i:



ii:



How would you make **ii**?



Provide the mechanism for step 10 *(next page)*

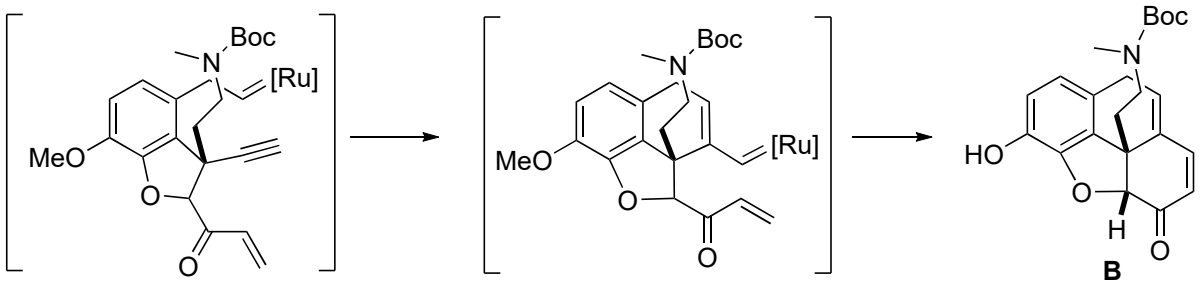
*Reaction of ruthenium alkylidene with the allyl component followed by intramolecular reaction with the alkyne to give a new ruthenium alkylidene intermediate which undergoes ring closing methatesis with the α,β-unsaturated ketone. The reaction afforded product **B** in 94 % isolated yield as a sole product.*

11-14

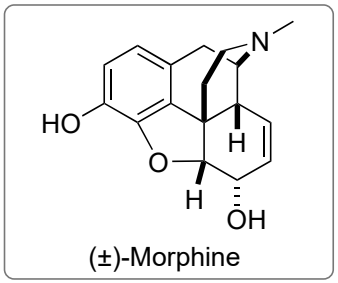
(±)-Morphine

11) TFA, rt, then aq. Na_2CO_3
12) HCl then aq. NaOH
13) $NaBH_4$
14) BBr_3

Mechanism for step 10



B



(±)-Morphine