Total Synthesis of Indole Alkaloid (+)-Alstonlarsine A

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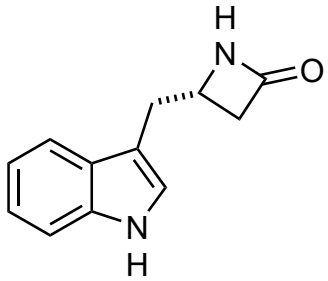
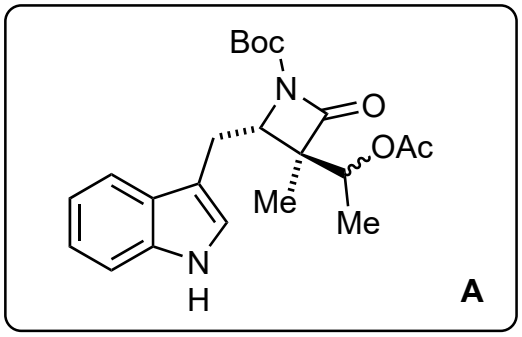


1-8

1) DMAP (cat.), TBSCl, Et_3N
2) NaH, TBSCl, 0 °C to r.t.
3. LDA, THF, –78 °C then MeI
4) Et_2NLi, THF, –78 °C
then MeCHO, –100 °C
5) DMAP (cat.), Ac_2O, Et_3N
6) KF, MeOH, 0 °C
7) DMAP (cat.), $(Boc)_2O$, Et_3N
8) 50% aq HF

1) The starting material is a non-natural structural derivative of which amino acid? Name the 3- and 1-letter codes.
tryptophan (derived from β-homotryptophan).
Trp, W.
4) Name the reaction. Aldol reaction.
6) *Hint:* monodeprotection of the β-lactam.

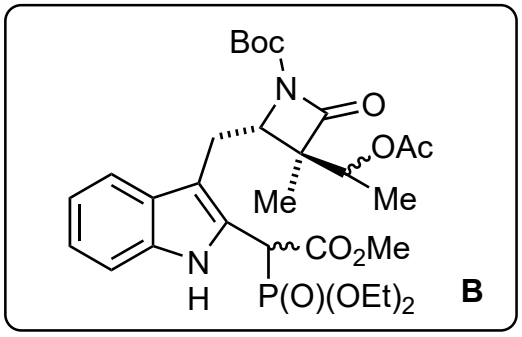


A

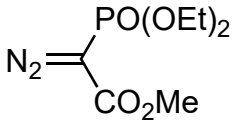
9

9) $Cu(acac)_2$ (2 mol%), **1**, 120 °C

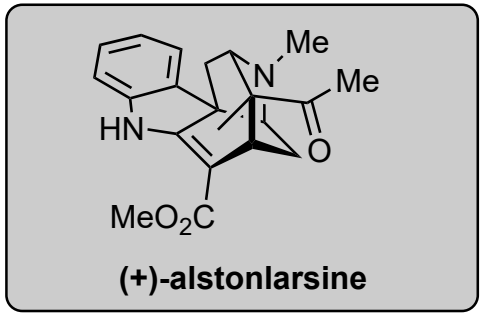
9) *Hint*: a formal C-H insertion occurs.



B



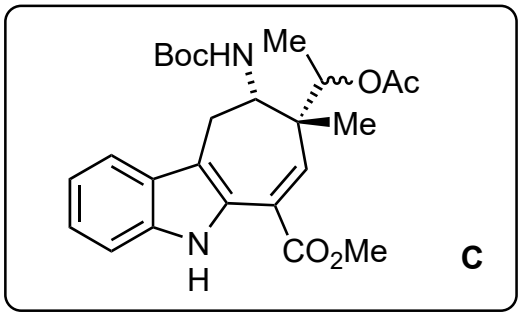
1



(+)-alstonlarsine

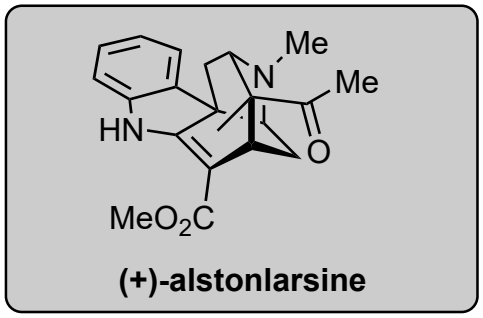
B

10-15



C

16-18



(+)-alstonlarsine

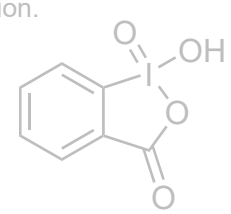
10) $NaBH_4$, MeOH/H_2O, 0 °C
11) IBX, 75 °C
12) LiBr, Et_3N
13) $(Boc)_2O$, Et_3N, DMAP (10 mol%)
14) NaH, 0 °C
then MeI, 0 °C to r.t.
15) TFA

16) MeCHO, PhMe, 100 °C
17) NaH, $LiAlH_4$, THF, 0 °C
18) Me_2S, NCS, 0 °C
then **substrate**, –78 to –50 °C,
then Et_3N, –50 °C

10) *Hint:* acetate is unreacted.

11) Draw the structure of IBX.

12) Name the reaction. Horner-Wadsworth-Emmons olefination.



16) Name the reaction. (inverse-electron-demand intramolecular dearomative) Diels-Alder cycloaddition.

17) The acetate, resistant to acidic or basic hydrolysis, was selectively removed under reductive conditions with $LiAlH_4$. Reason the inclusion of NaH. "the purpose of NaH was to deprotonate indole N-H, thus temporarily protecting CO_2Me group from reduction and increasing selectivity."

18) Name the reaction. Corey-Kim oxidation.