Total Synthesis of (+)-Alstonlarsine A

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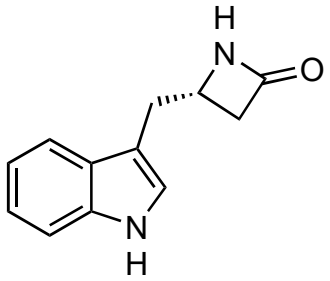
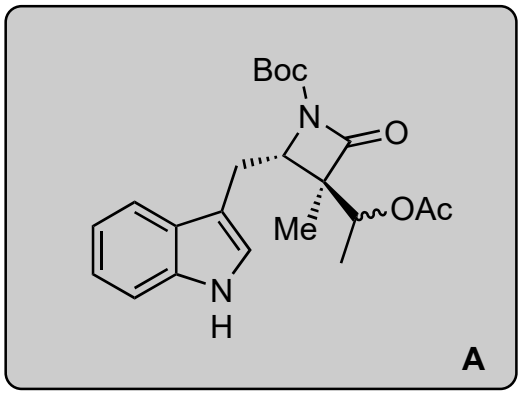


1-8

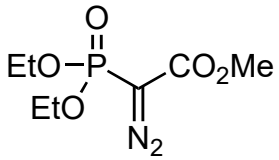
1) TBSCl, Et_3N, DMAP
2) NaH, *then* TBSCl
3) LDA, *then* MeI
4) Et_2NLi; *then* MeCHO, -100 °C
5) Ac_2O, Et_3N, DMAP
6) KF
7) Boc_2O, Et_3N, DMAP
8) HF

4) Mixture of diastereomers was carried forward



A

9) Provide a mechanism
(*Hint*: π-*deficient indoles do not react*)
see below

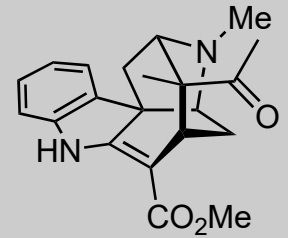


1

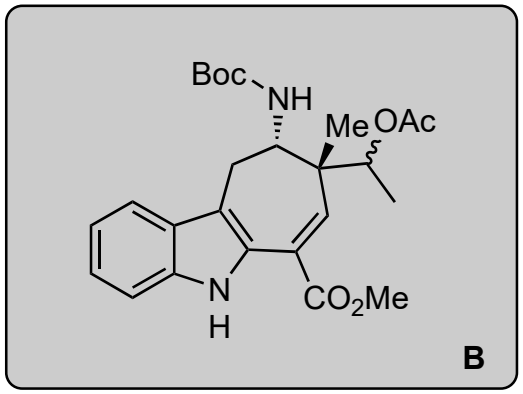
12) Named reaction
HWE reaction
(Masamune-Roush conditions)

9-12

9) **1**, $Cu(acac)_2$ (2 mol%), 120 °C
10) $NaBH_4$ (3 equiv.)
11) IBX
12) LiBr, Et_3N

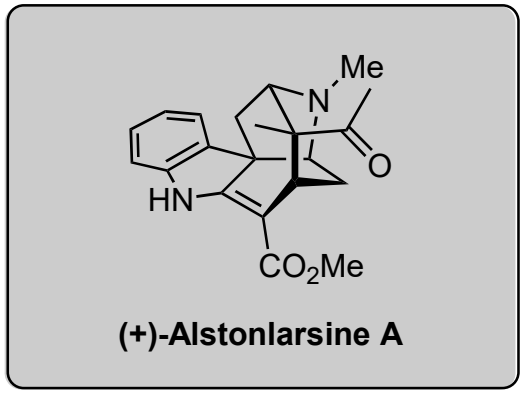


(+)-Alstonlarsine A



B

13-18



(+)-Alstonlarsine A

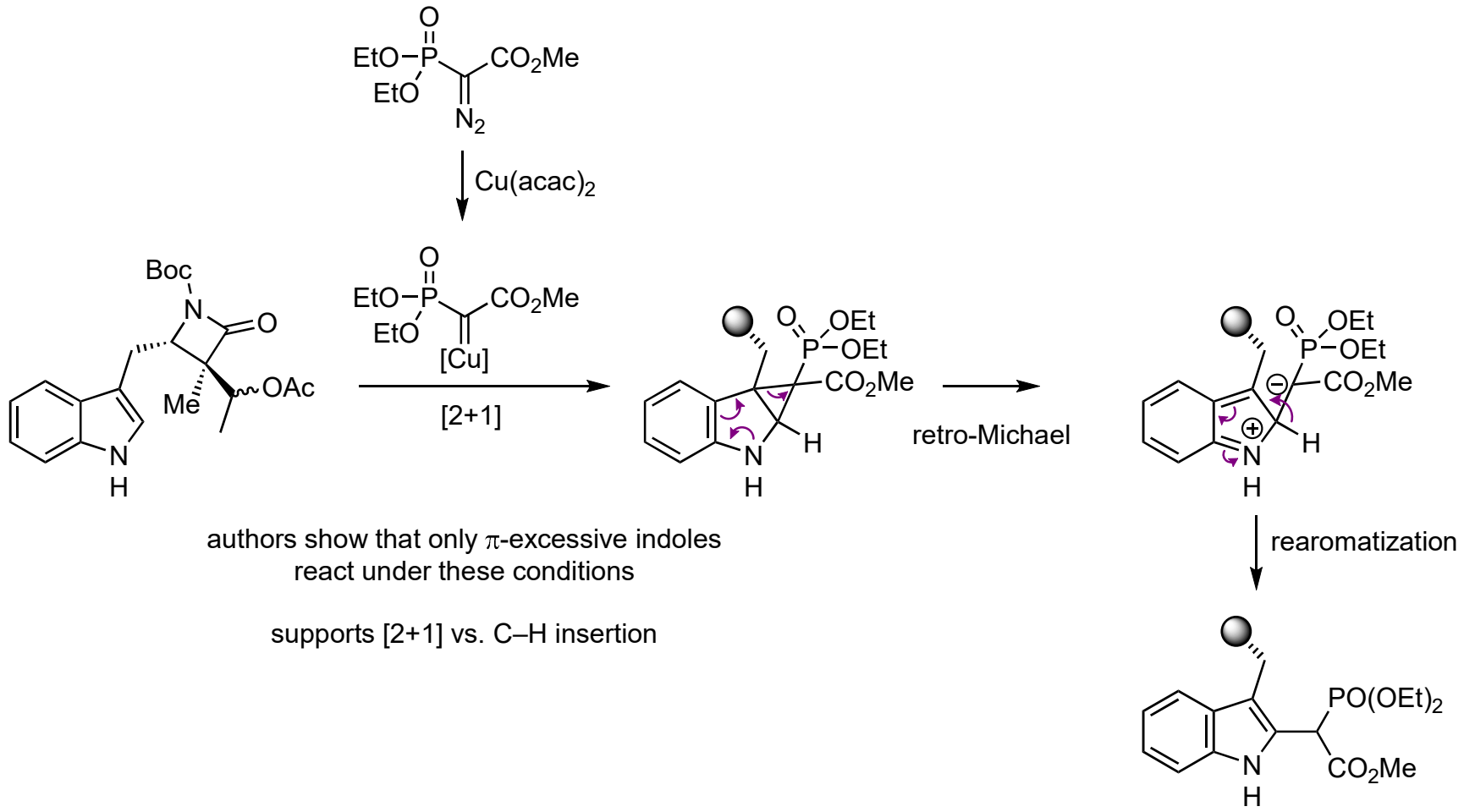
13) Boc_2O, Et_3N, DMAP
14) NaH, *then* MeI
15) TFA
16) MeCHO, 100 °C
17) NaH, $LiAlH_4$
18) NCS, Me_2S, Et_3N

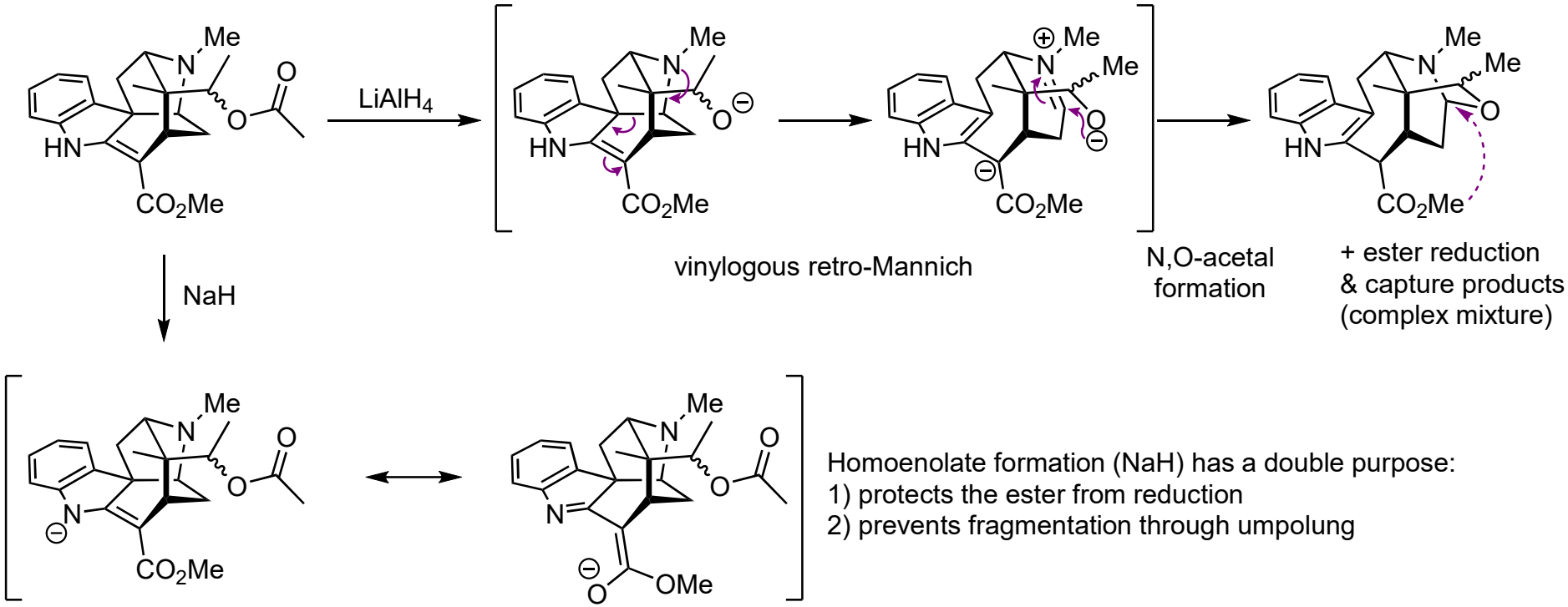
16) Two step cascade
Enamine formation / IEDDA

17) Provide reasoning for the role of NaH

see below

18) Named reaction
Corey-Kim oxidation


Cu(acac)2
[Cu]
[2+1]
retro-Michael
rearomatization
authors show that only π-excessive indoles
react under these conditions
supports [2+1] vs. C–H insertion


LiAlH4
NaH
vinylogous retro-Mannich
N,O-acetal formation
+ ester reduction & capture products (complex mixture)
Homoenolate formation (NaH) has a double purpose:
1) protects the ester from reduction
2) prevents fragmentation through umpolung