

Total Synthesis of (\pm)- Corymine

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PRESENTED BY: ALLISON VANECEK

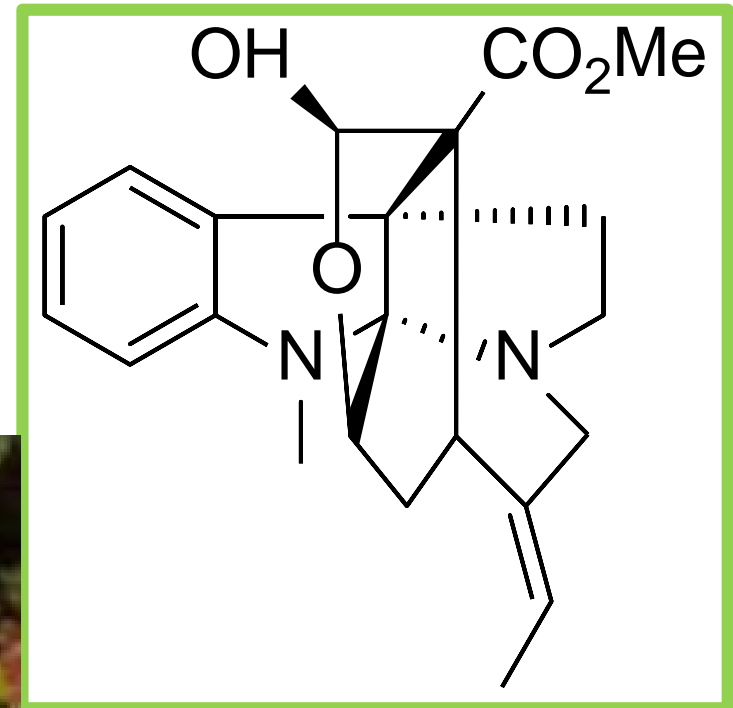
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Corymine

-Extracted from the leaves of *Hunteria zeylanica* (Thailand)

-Isolated in 1962

-Glycine receptor antagonist



Total Synthesis

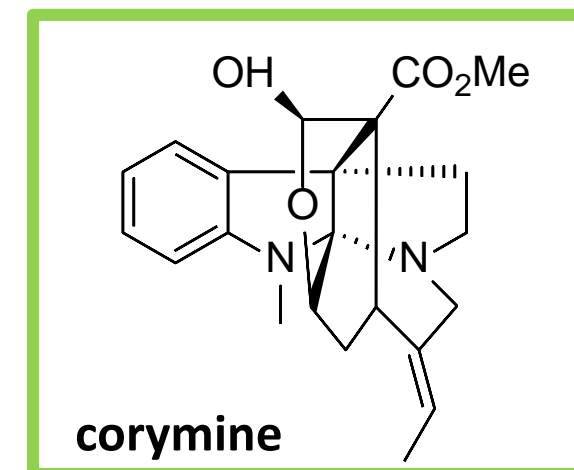
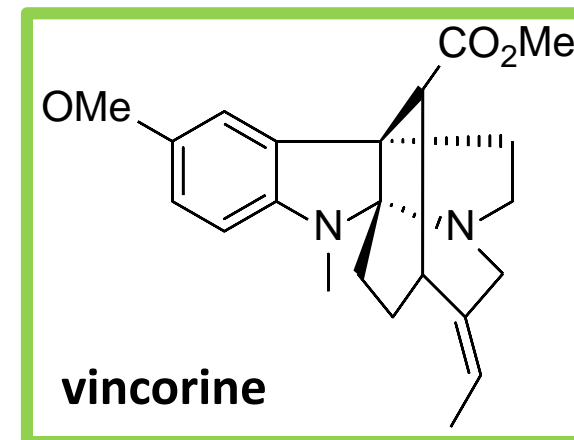
Belongs to a class of akuammiline indole alkaloids

Synthesis of (±)-Corymine was published in 2017

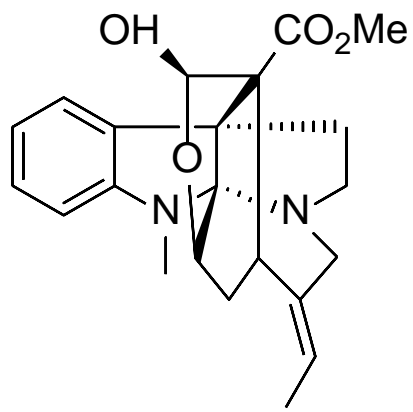
- Achieved in 21 steps
- 3.4% overall yield

Key Steps:

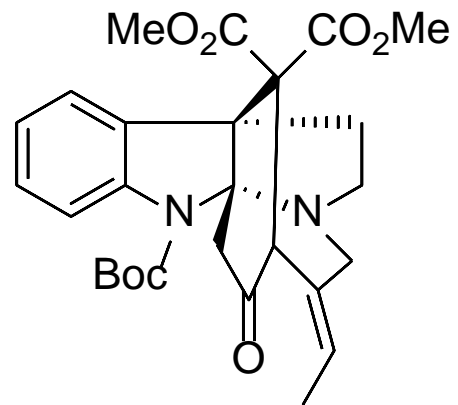
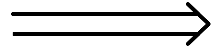
- Base-promoted addition of malonate to halo-oxindole
- Formation of a 12-membered cyclic enol ether by O-propargylation
- Propargyl Claisen rearrangement to give allenyl ketone
- Stereoselective Davis oxidation
- SmI_2 -mediated reductive C-O bond cleavage



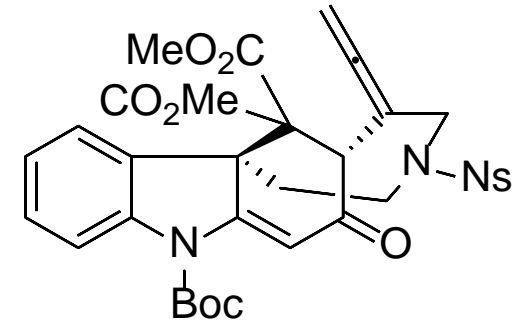
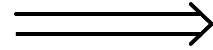
Retrosynthetic Design



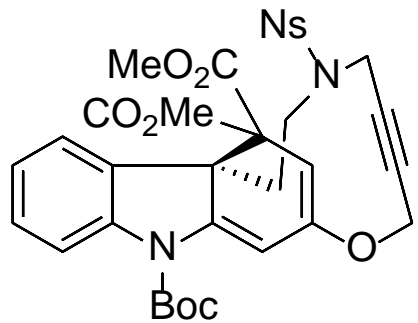
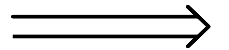
Davis oxidation



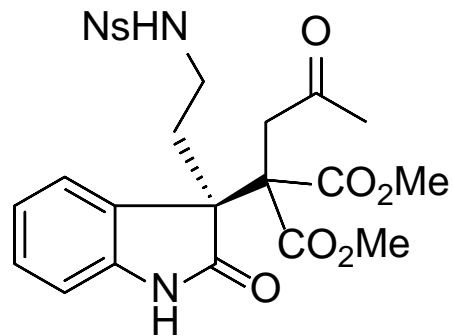
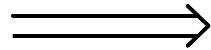
Michael addition
(A)



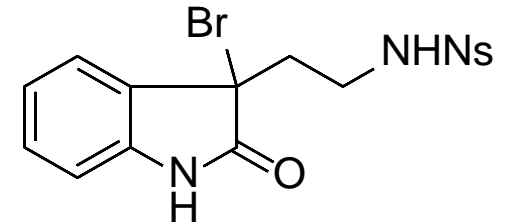
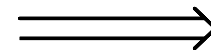
Claisen rearrangement
(B)



Condensation,
nucleophilic substitution
(C)



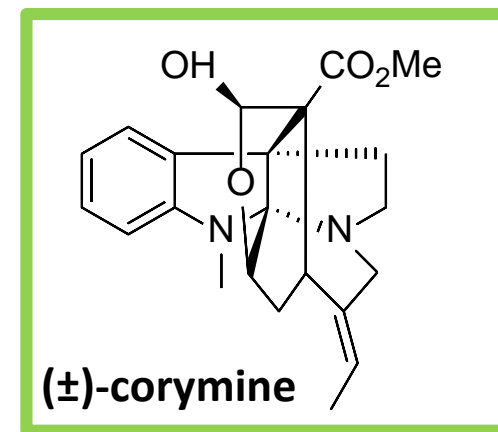
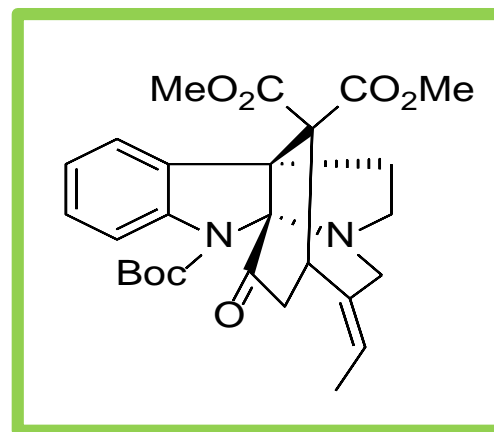
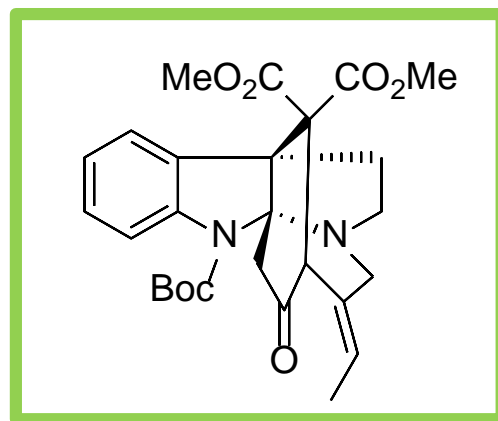
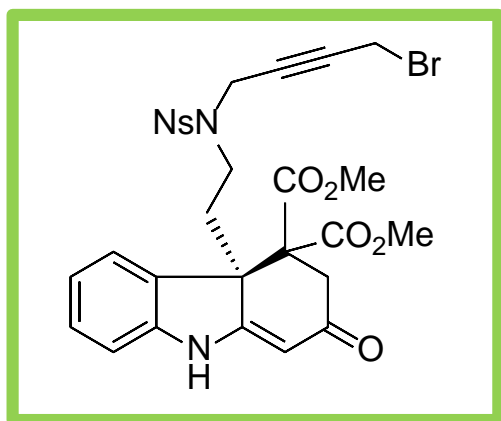
Nucleophilic addition
(D)



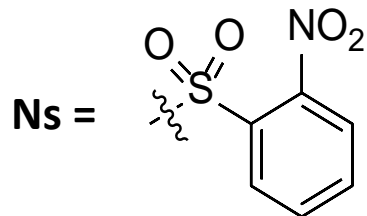
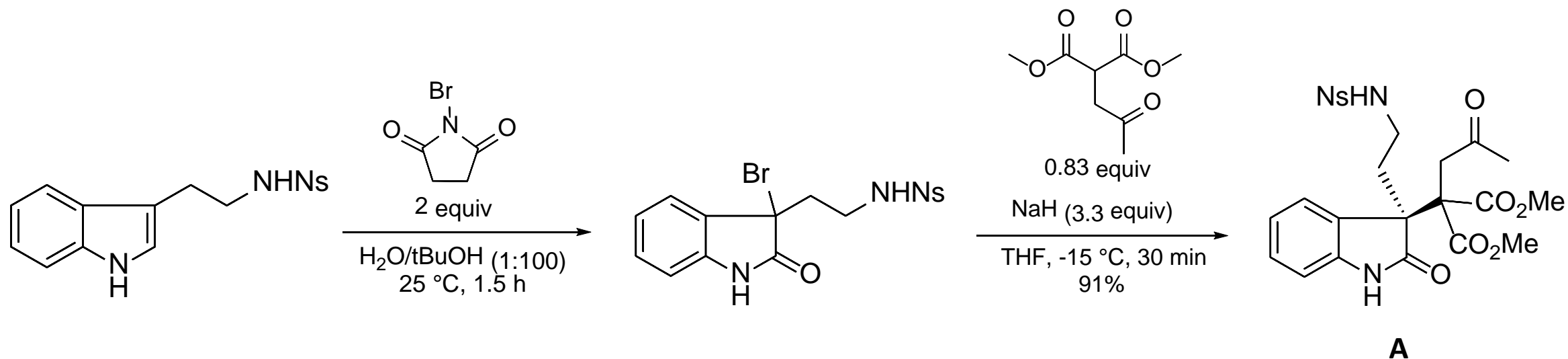
(E)

Scope of Total Synthesis

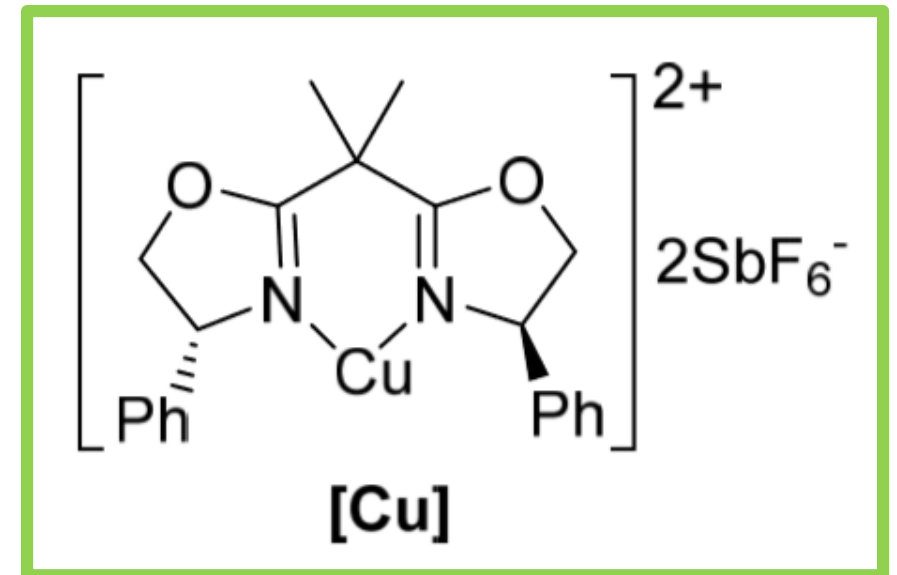
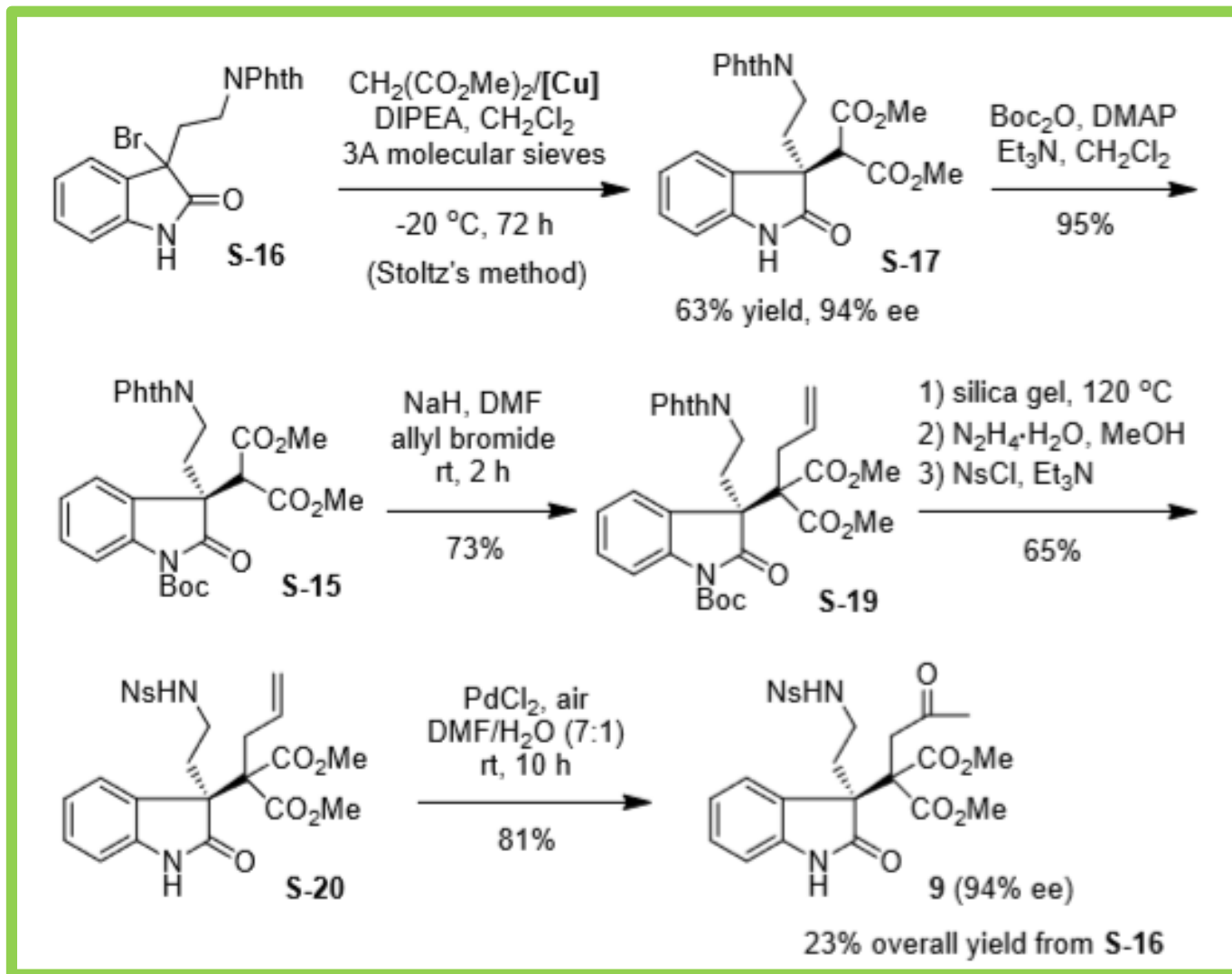
- 1) Generate carbazole skeletal structure
- 2) Generate key intermediate
- 3) 1,2-oxo-migration
- 4) Final Steps



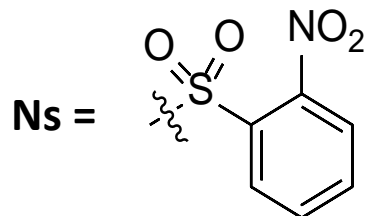
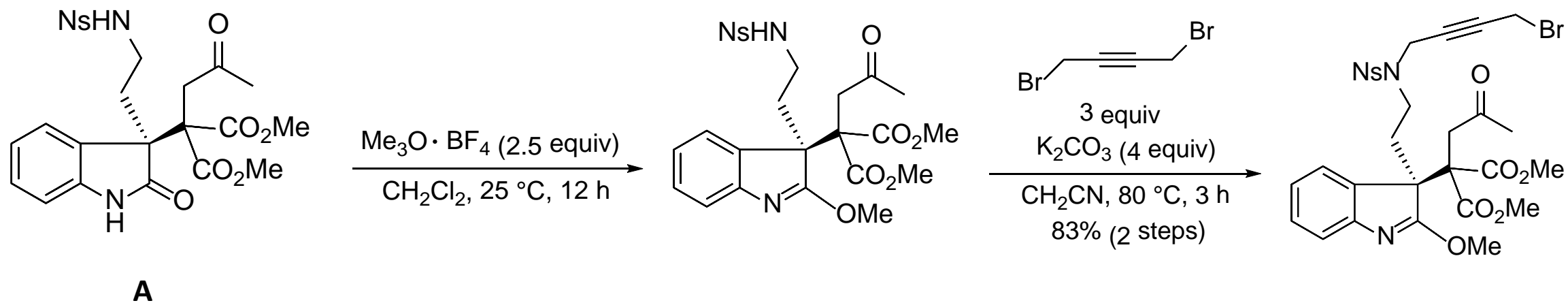
1) Synthesis of the Carbazole



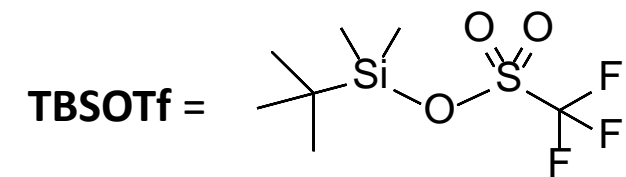
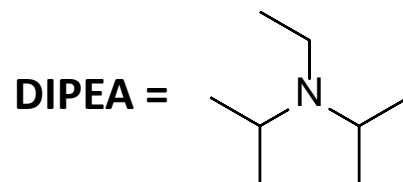
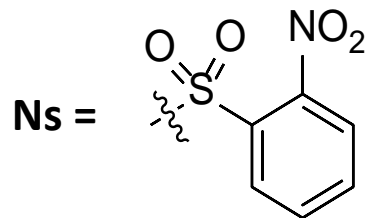
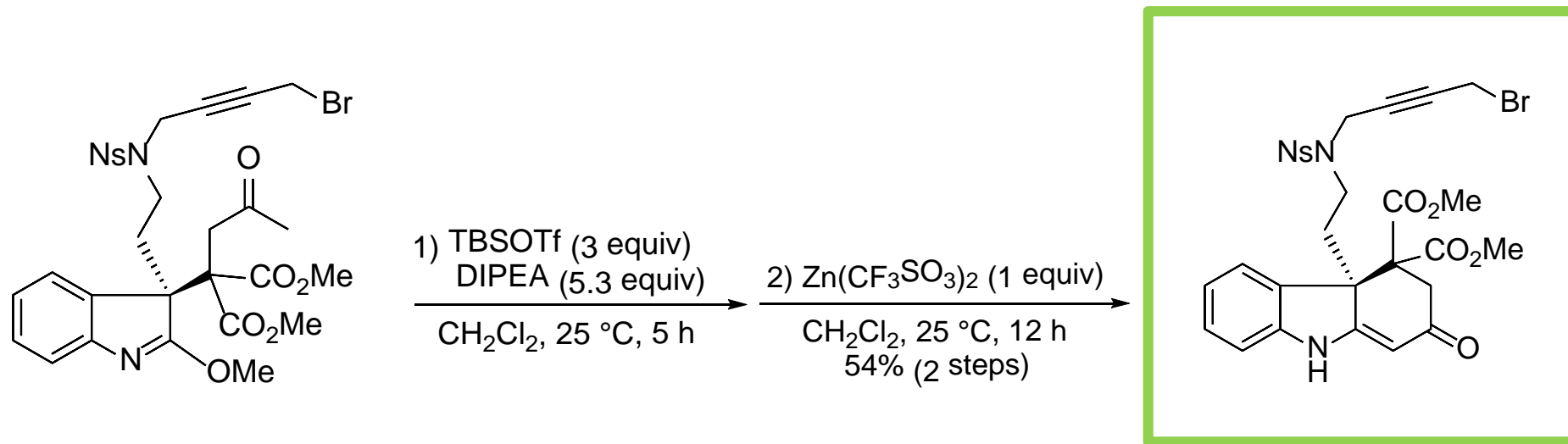
Enantioselective Synthesis of Compound A



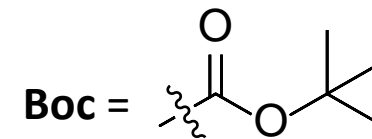
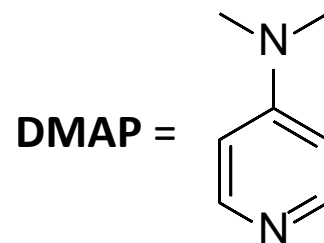
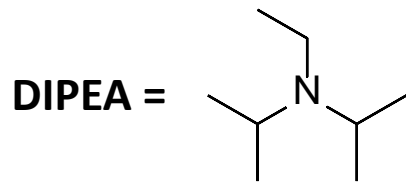
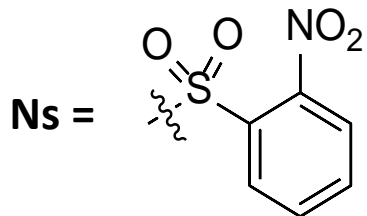
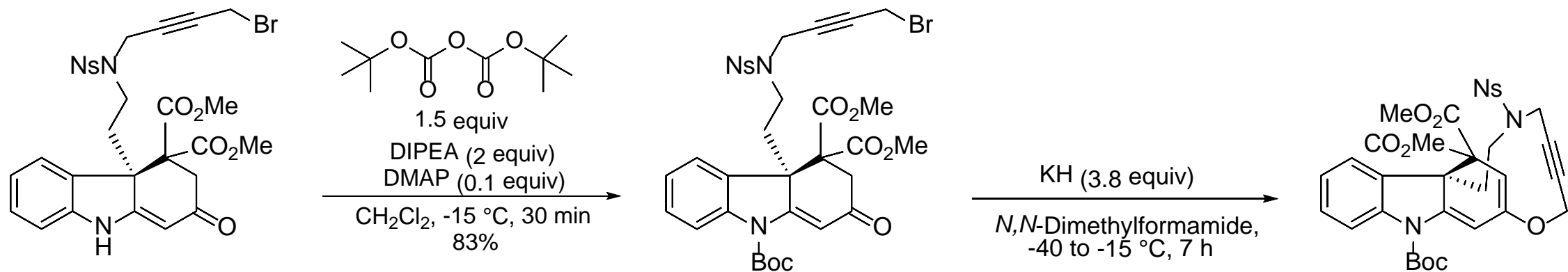
Synthesis of the Carbazole



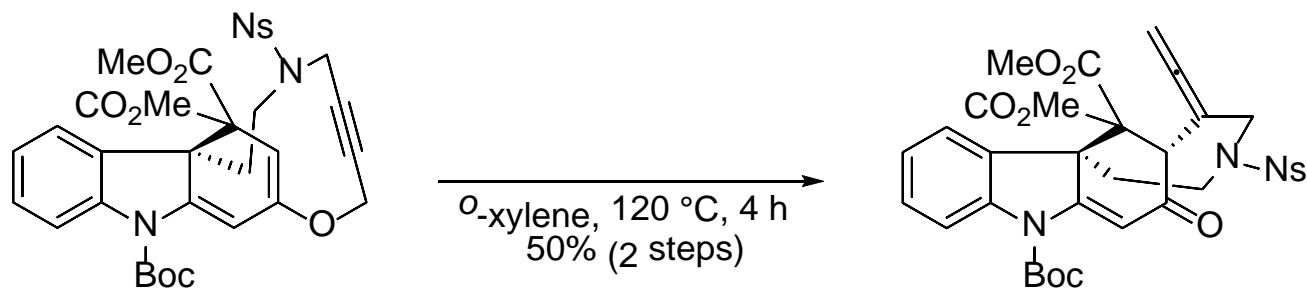
Synthesis of the Carbazole



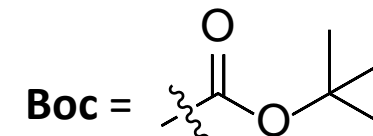
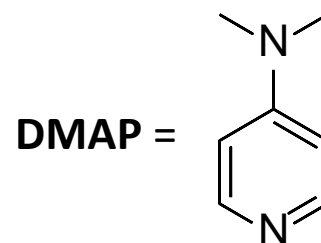
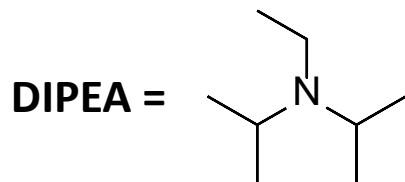
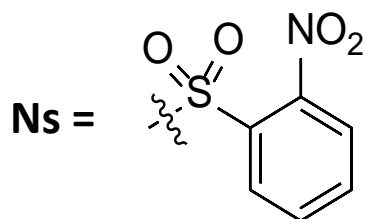
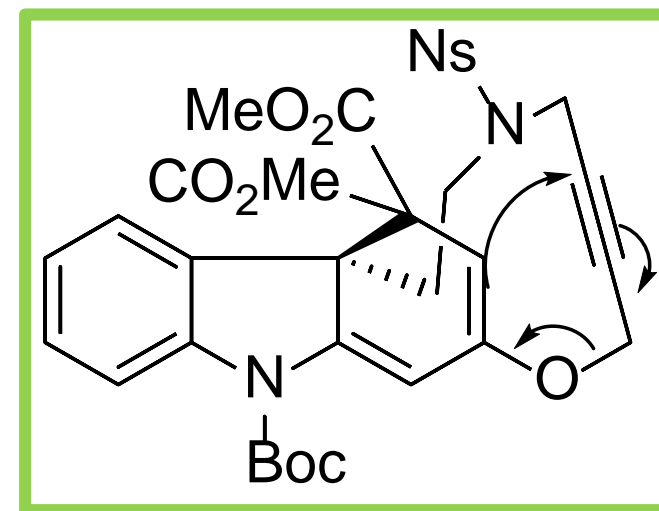
Synthesis of the Key Intermediate



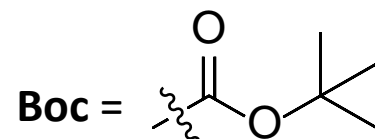
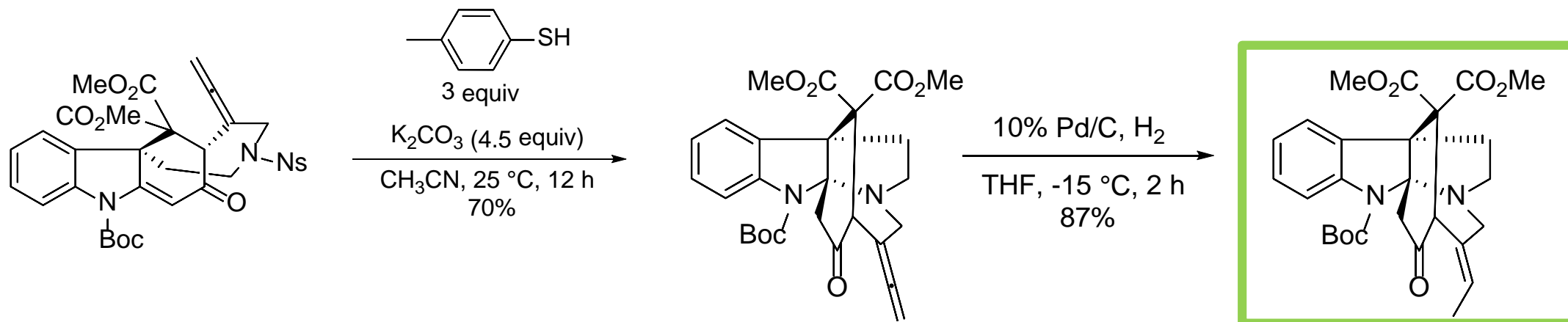
Synthesis of the Key Intermediate



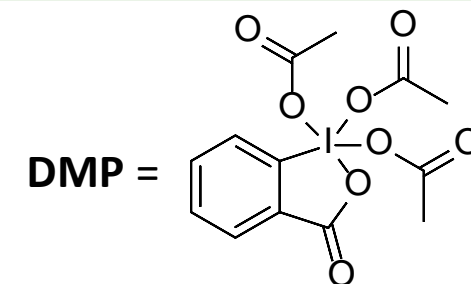
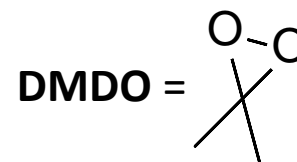
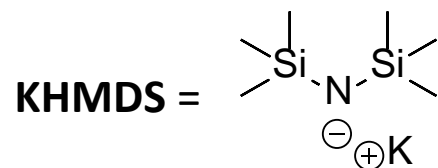
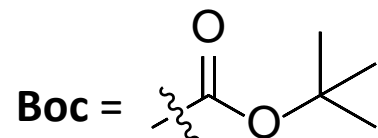
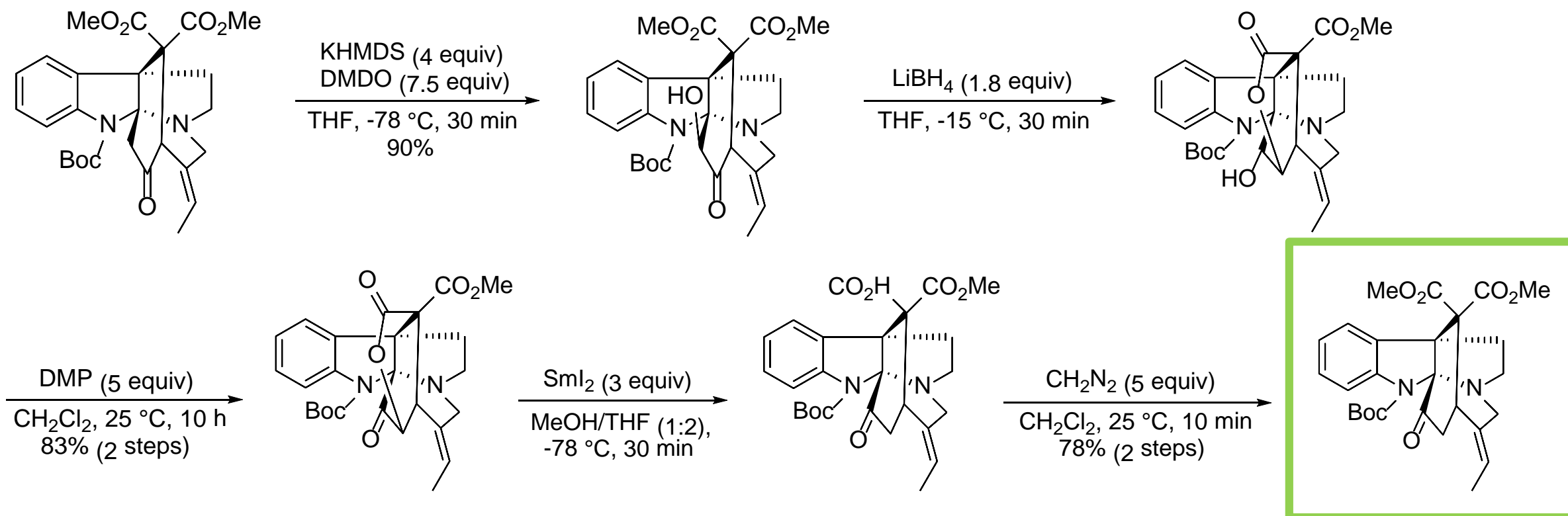
Claisen Rearrangement



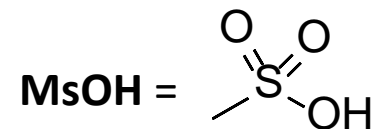
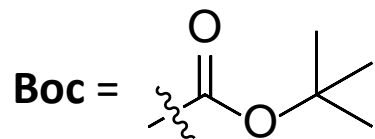
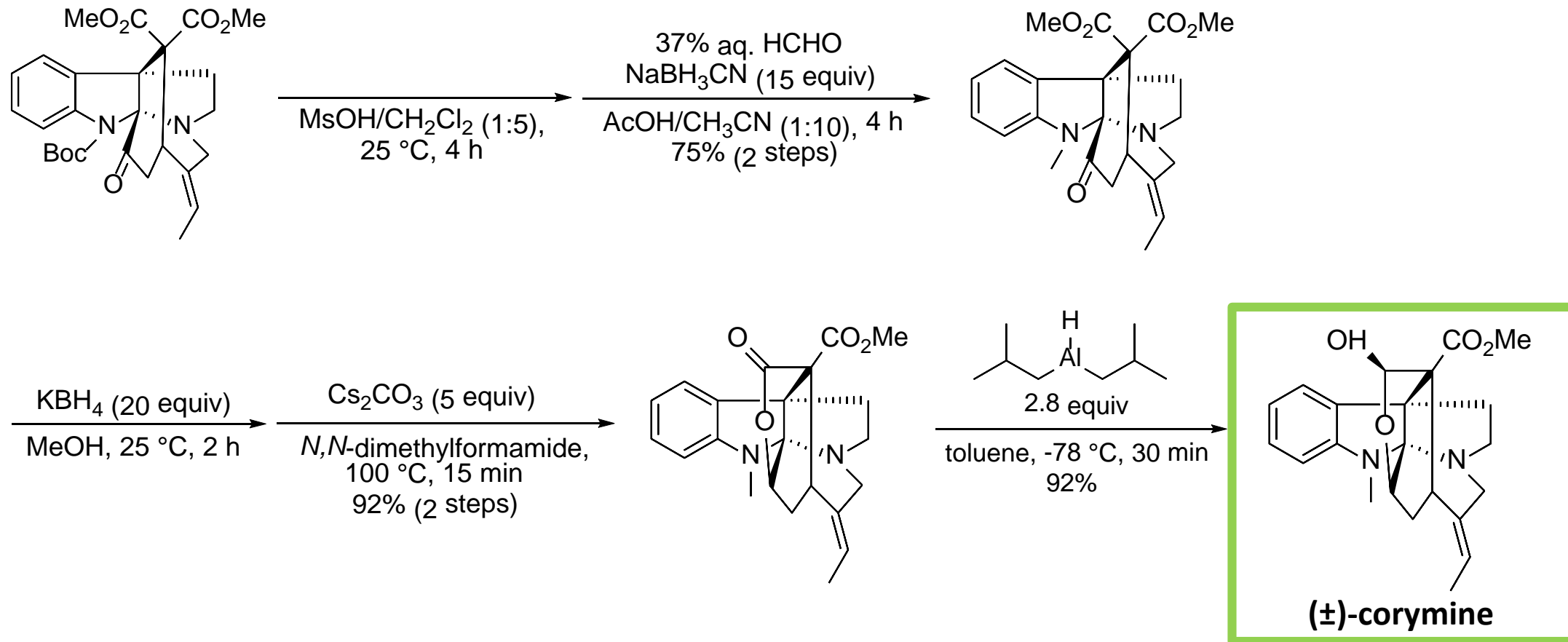
Synthesis of the Key Intermediate



1,2-oxo-migration



Final Steps



Thank You
Questions?