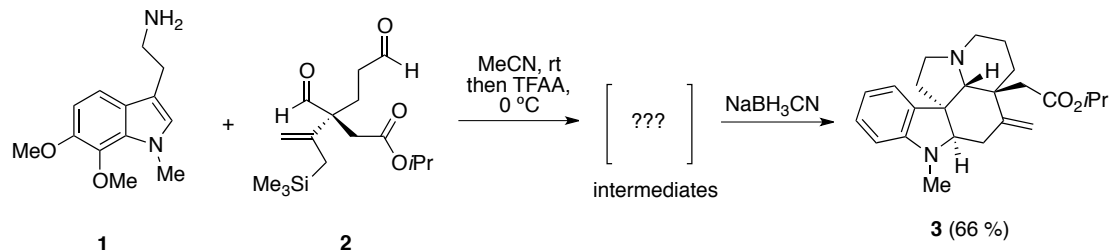


Enantioselective Total Synthesis of Aspidophytine

Problem:

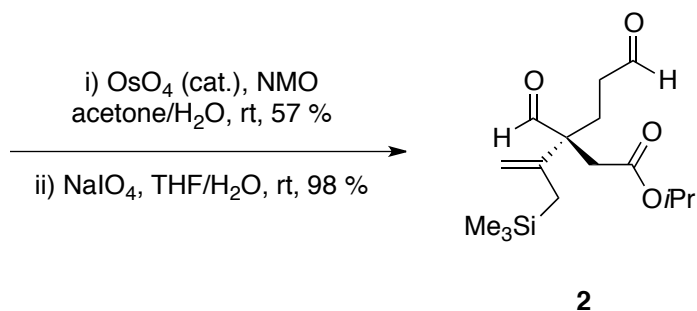
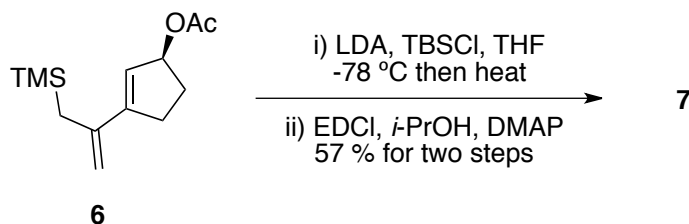
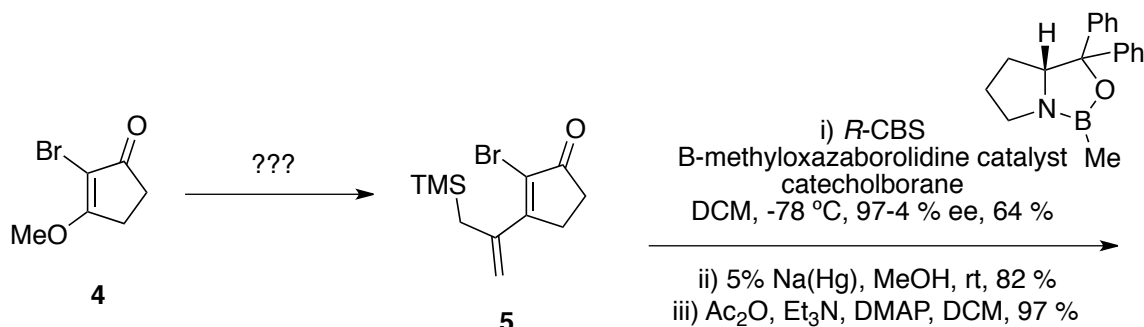


For 2nd year and higher students:

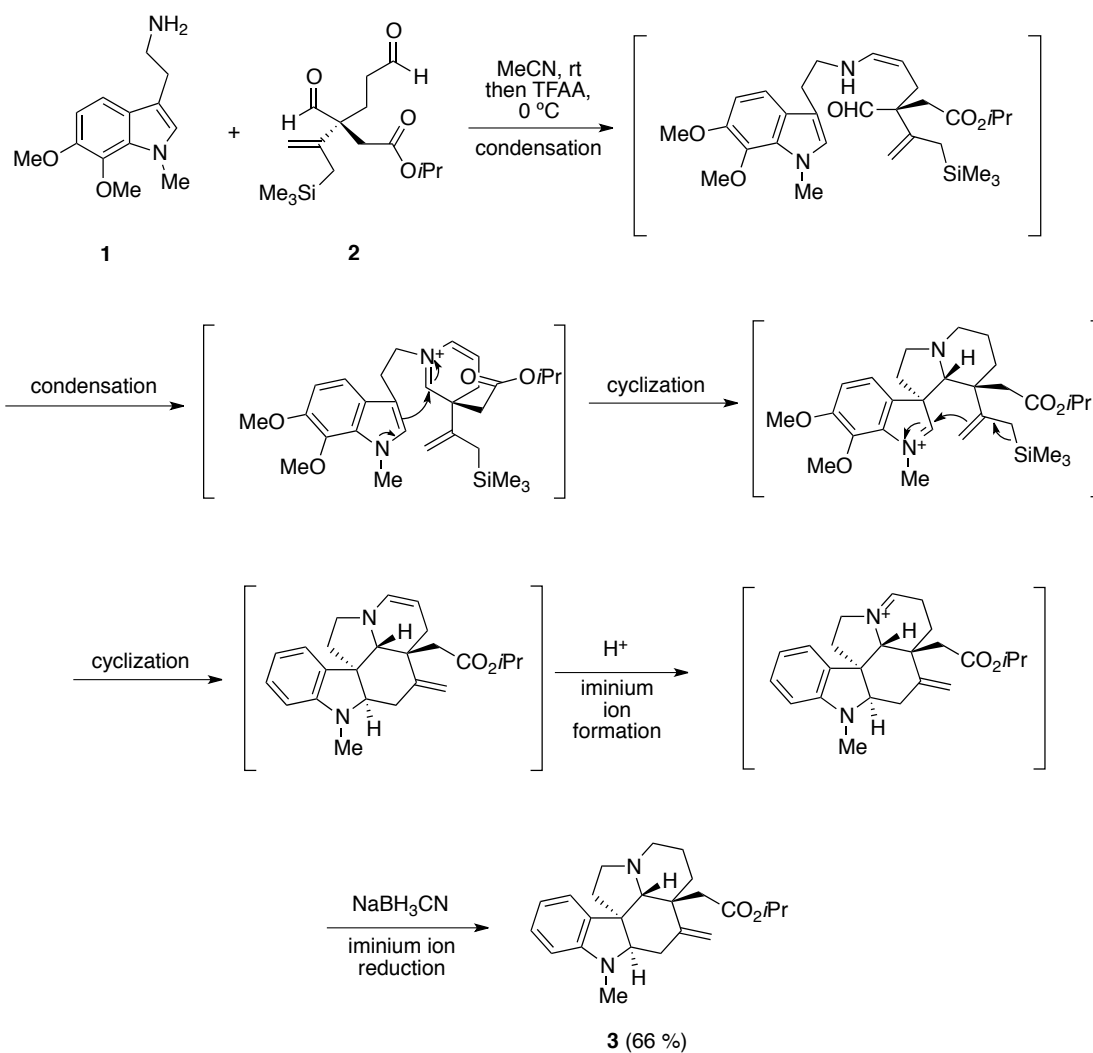
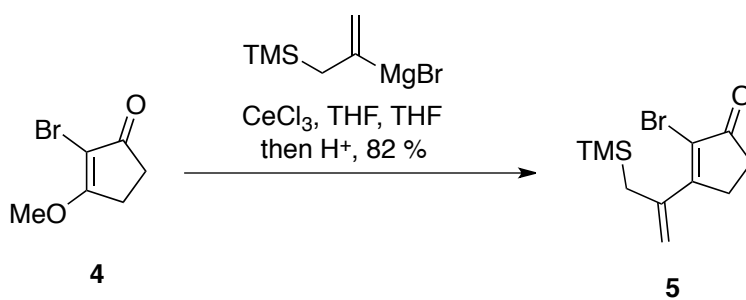
Give the mechanism of this reaction. (*Hints: i) Start with a condensation on the less hindered aldehyde. ii) The borohydride is used to reduce an imminium ion at the last step of the cascade.*)

For Masters and 1st year students:

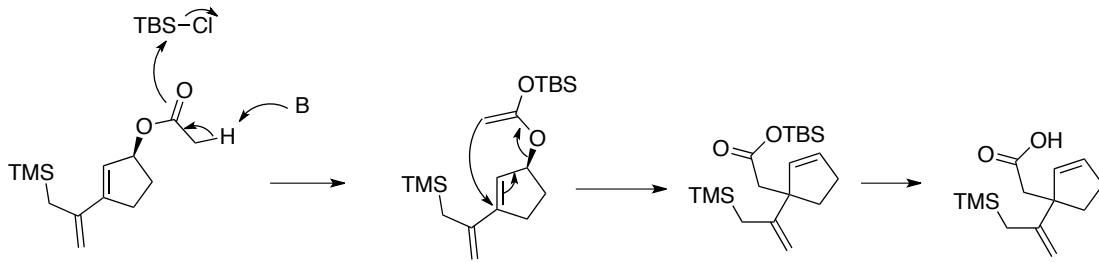
- Give the missing reagents for the transformation from 4 to 5.
- Give the structure of 7 and the mechanism for its formation. What is the name of the first reaction with LDA? (*Hint: In this transformation you form the quaternary carbon center.*) What is the role of DMAP in the second step (mechanism)?



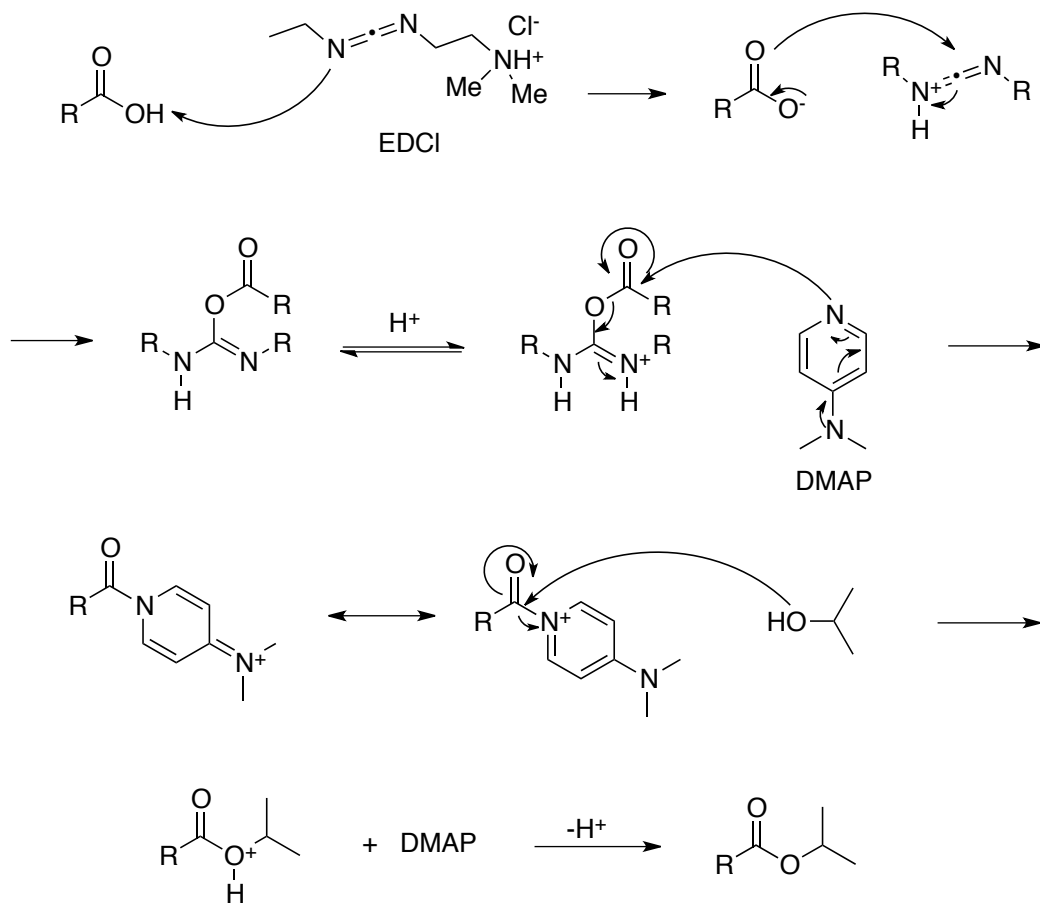
Solution:

Solution for Masters and 1st years:

- Ireland Claisen Rearrangement and esterification with EDCI and DMAP:



DMAP is used as catalysator to form a reactive amide and accelerate the esterification:



Comments:

A Pictet-Spengler cyclization generates the pyrrolidine ring and the new quaternary stereocenter. The stereocontrol obtained in this step is notable and may arise through interaction between the iminium ion carbon atom and the ester carbonyl oxygen atom, leading to preferential attack by the indole from the opposite face of the molecule. The stereochemistry of the resulting spirocyclic intermediate then governs the facial selectivity in the attack of the allylsilane substituent on the newly formed iminium ion to generate the pentacyclic system.

References:

F. He, Y. Bo, J. D. Altom, E. J. Corey, *J. Am. Chem. Soc.* **1999**, *121*, 6771.

Keywords:

Series of iminium ion cyclizations including a Pictet-Spengler reaction; Ireland Claisen rearrangement to install an all-carbon quaternary stereocenter; Esterification with EDCI and DMAP