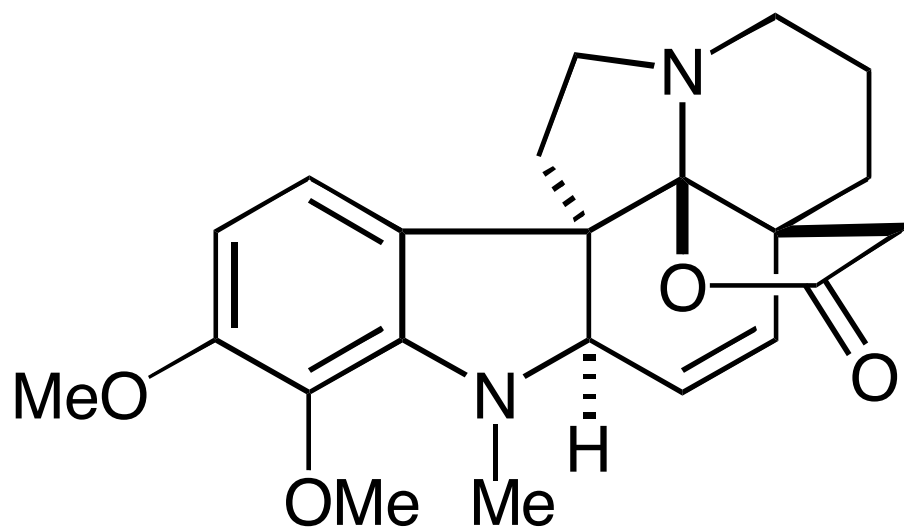


# Total Synthesis of Aspidophytine

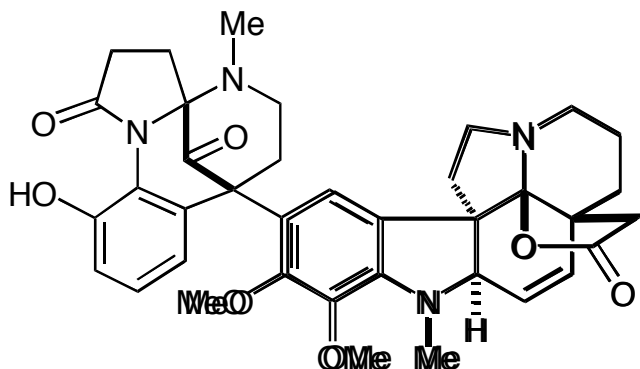
“La hierba de la cucaracha”



Jason M. Stevens

June 28<sup>th</sup> 2006

# Isolation and Structure Determination

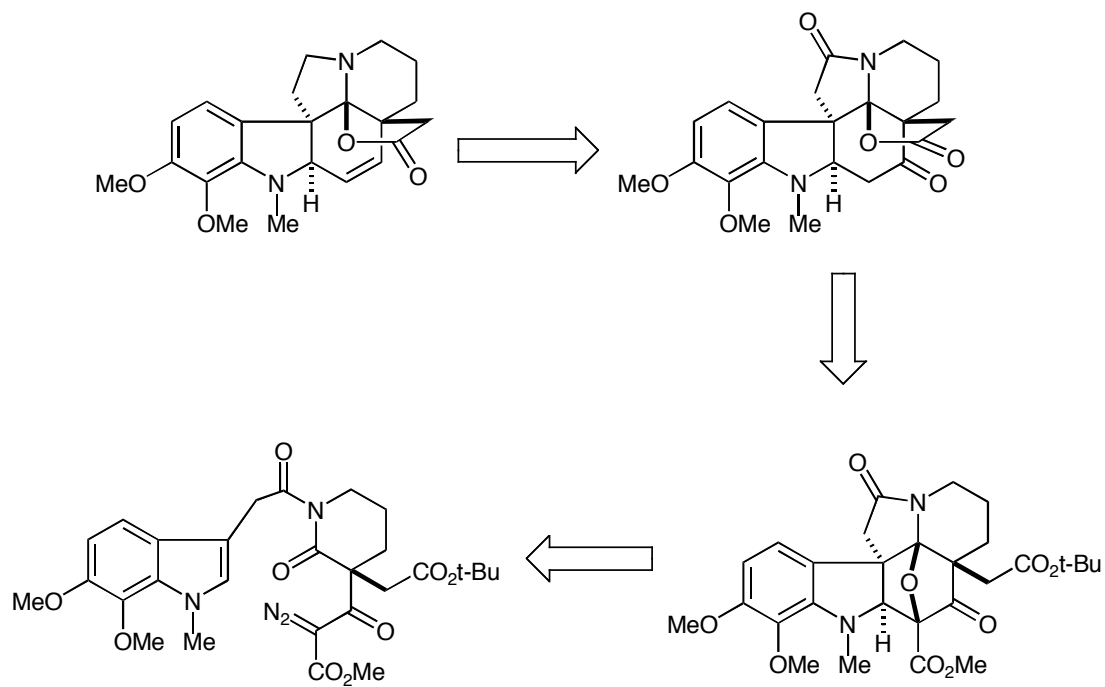


- In 1973 Cava and Yates isolated haplophytine from the plant *Haplophyton cimidum*, which is found in parts of Mexico and Central America
- The structure was determined by X-ray crystallography of haplophytine dibromide
- Haplophytine is believed to be one of the many alkaloids from this plant specimen that is responsible for its antickroach/insecticidal nature
- Aspidophytine was isolated by acidic cleavage of haplophytine
- Aspidophytine is believed to be a precursor in the biosynthesis as well as a potential synthetic intermediate to haplophytine

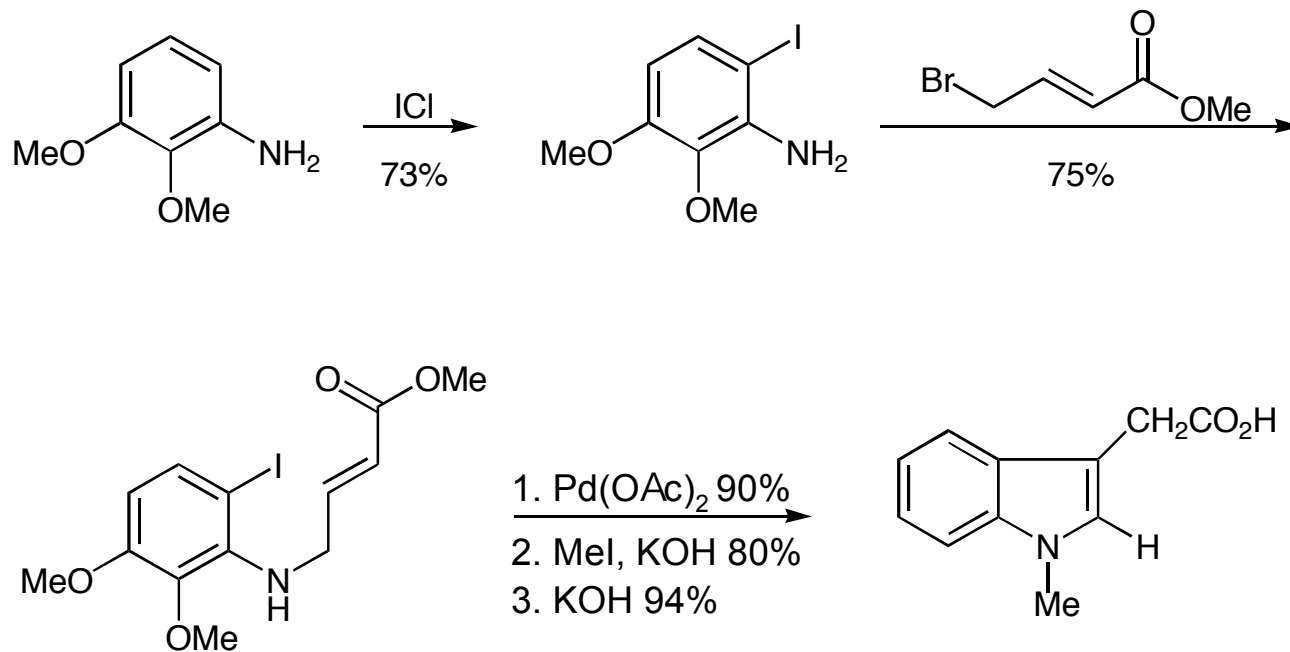
# Synthetic Efforts

- The first total synthesis was reported by Corey in 1999
  - He, F.; Bo, Y.; Altom, J. D.; Corey, E. J. *J. Am. Chem. Soc.* **1999**, *121*, 6771
- Two more total syntheses were later reported, Fukuyama in 2003, and Padwa in 2006
  - Sumi, S.; Matsumoto, S.; Tokuyama, H.; Fukuyama, T.; *Org. Lett.* **2003**, *5*, 1891
  - Sumi, S.; Matsumoto, S.; Tokuyama, H.; Fukuyama, T.; *Tetrahedron* **2003**, *59*, 8571
  - Mejía-Oneto, J. M.; Padwa, A.; *Org. Lett.* **2006**, *8*, ASAP

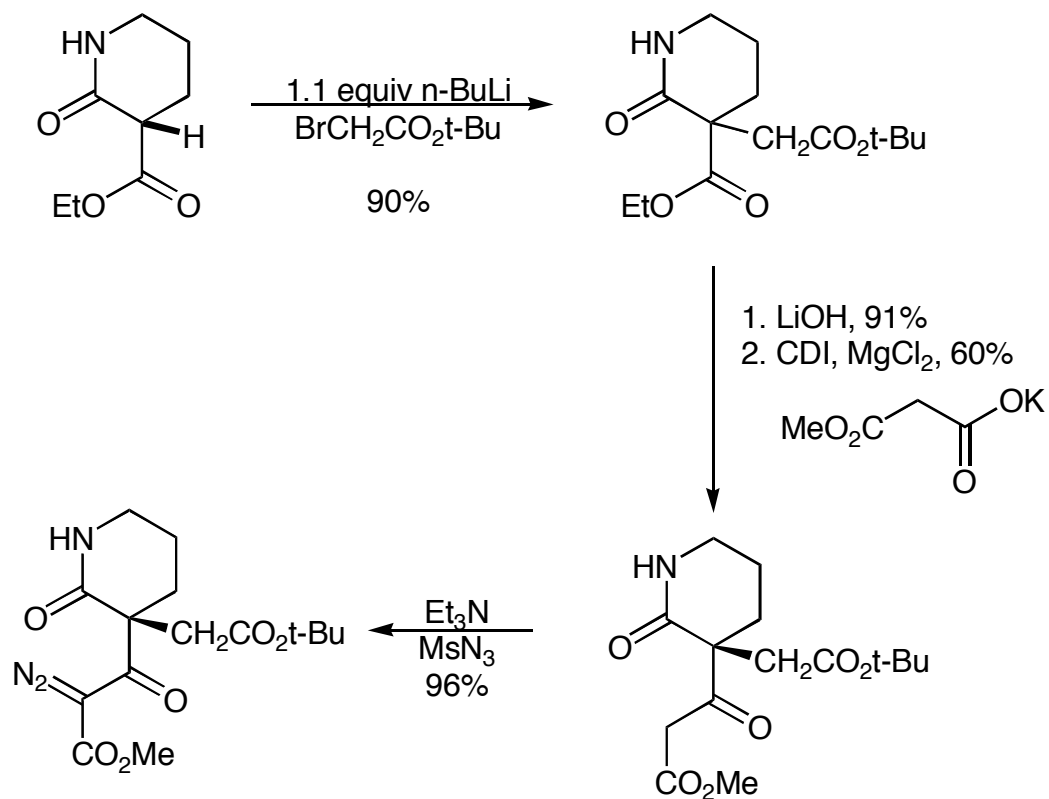
# Padwa's Strategy



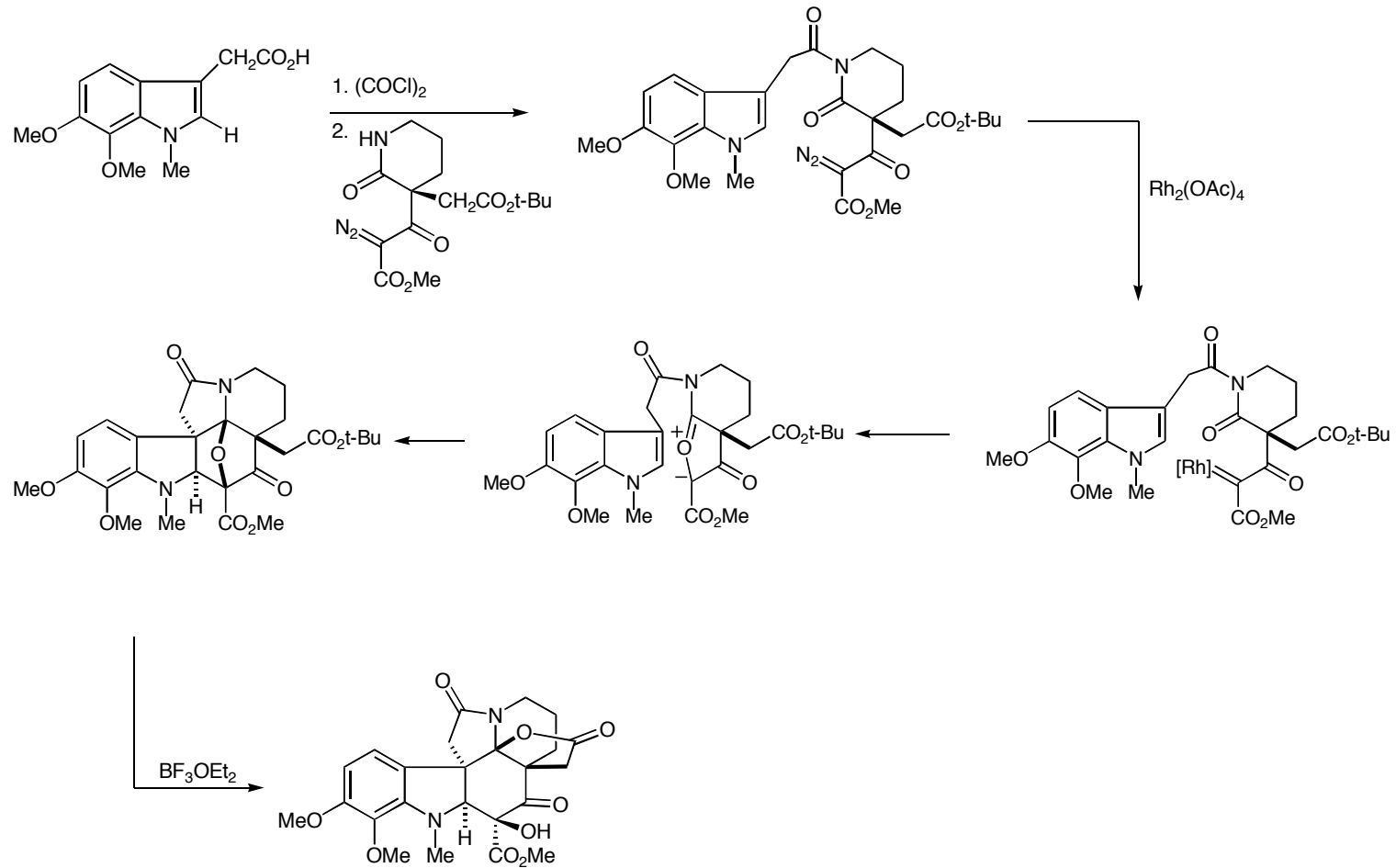
# Construction of the Indole



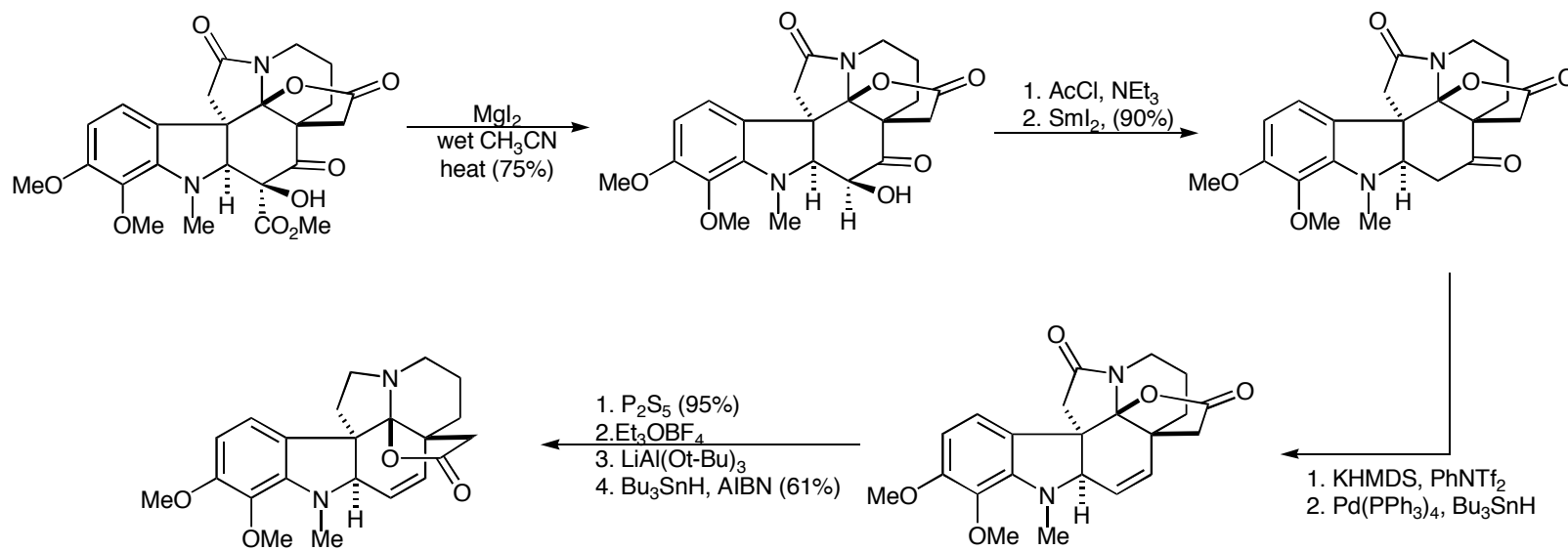
# Construction of the $\alpha$ -Diazo Imide Cycloadduct Precursor



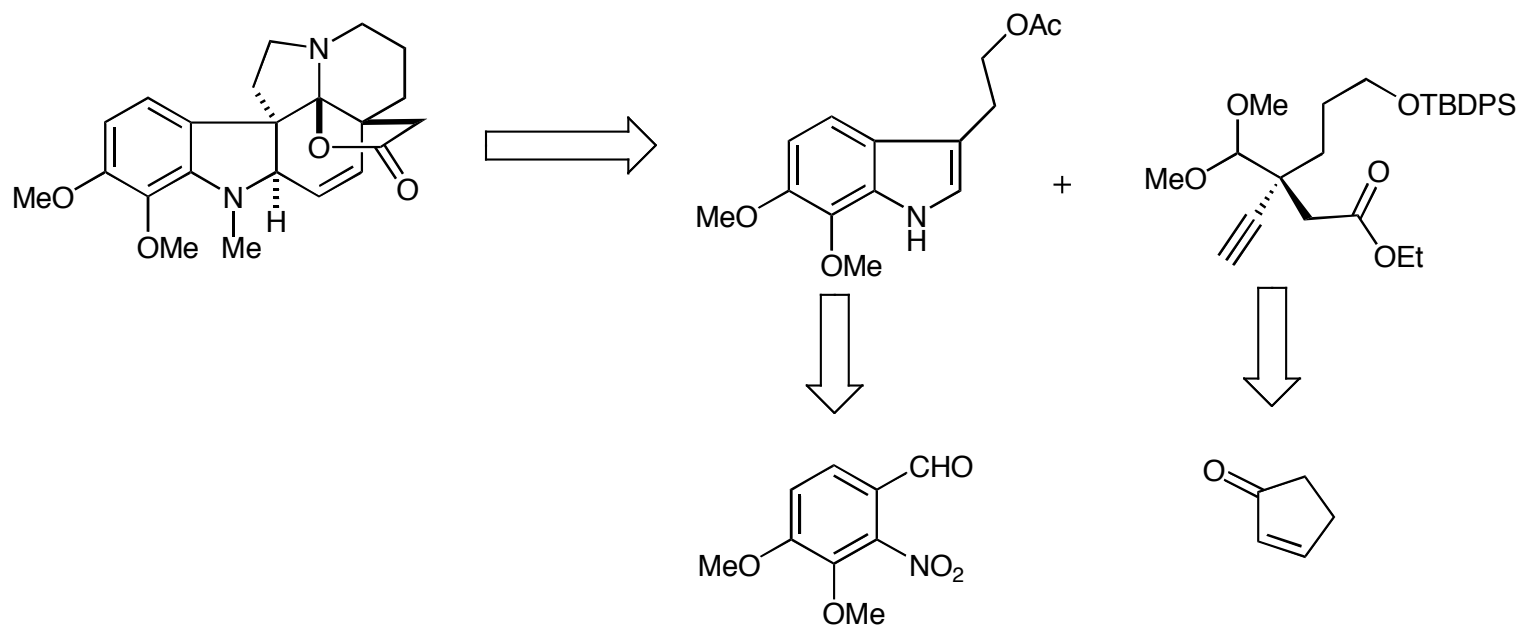
# Dipolar Cycloaddition



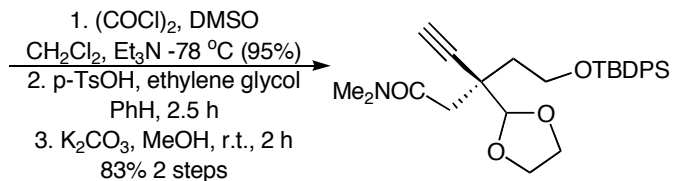
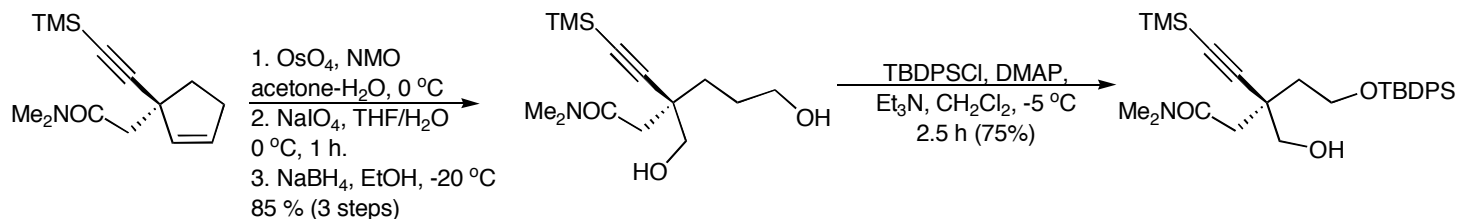
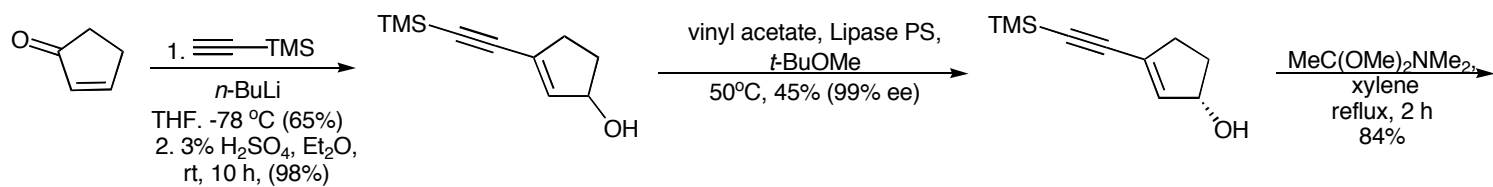
# Completion of Aspidophytine



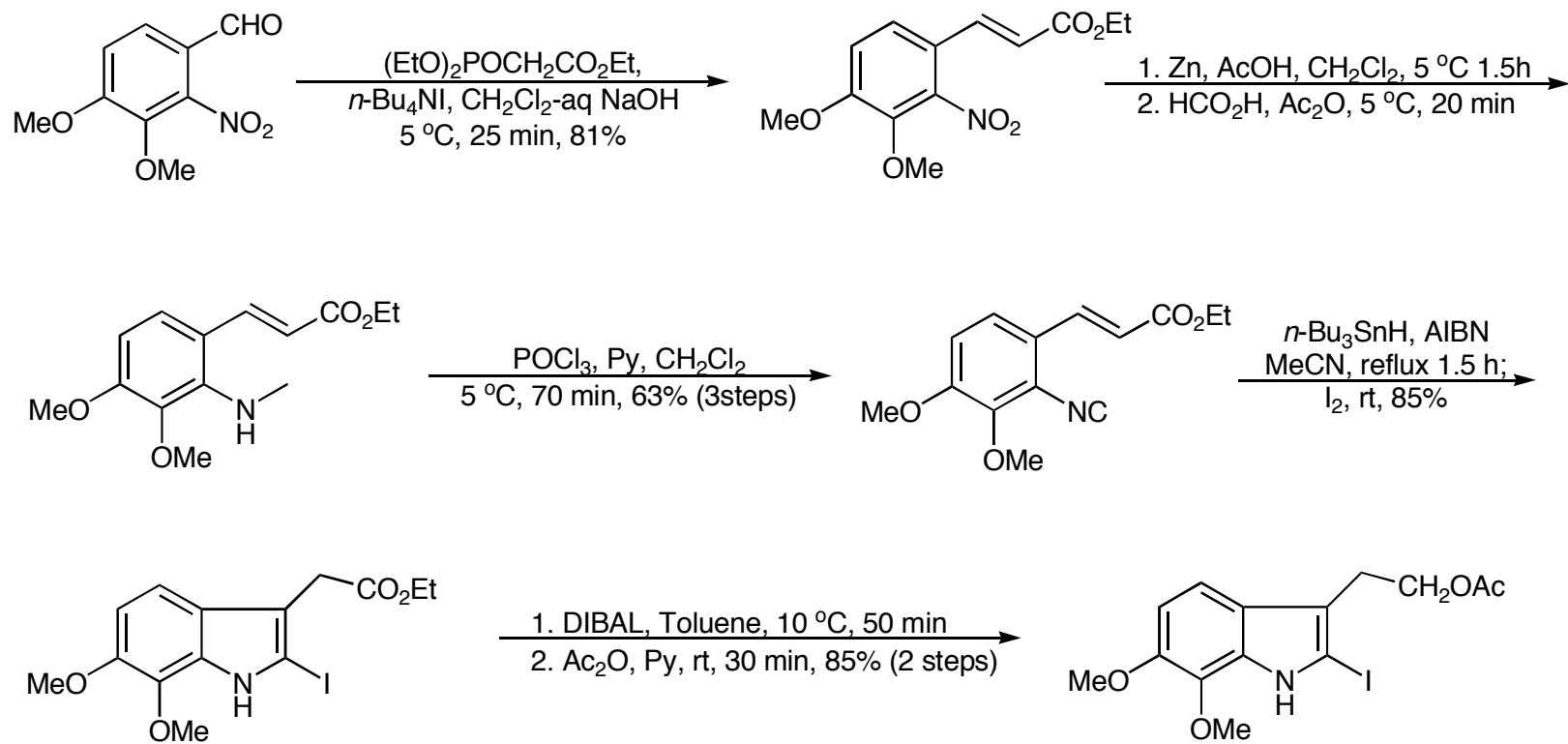
# Fukuyama's Strategy



# Fukuyama's First Generation Synthesis

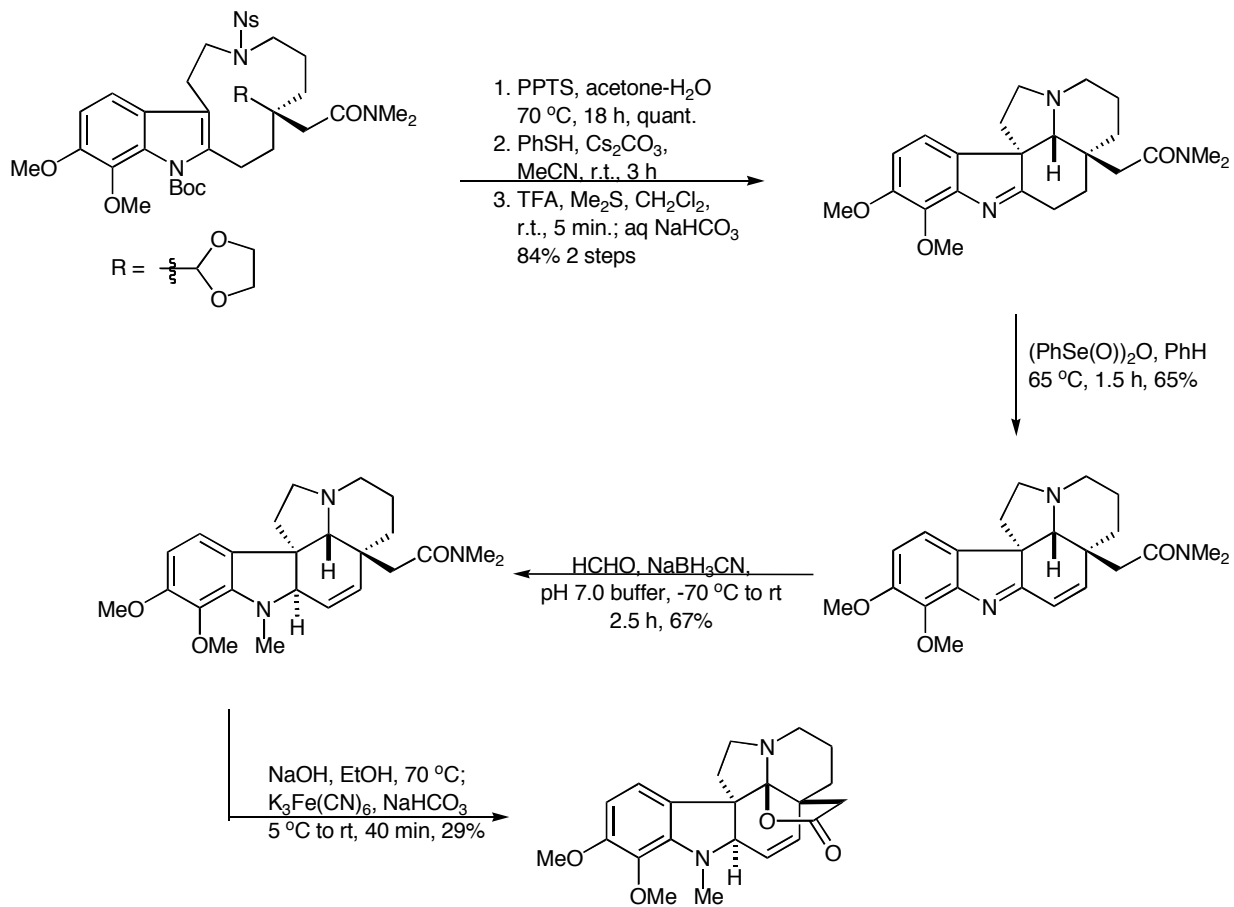


# Construction of the Indole Coupling Partner

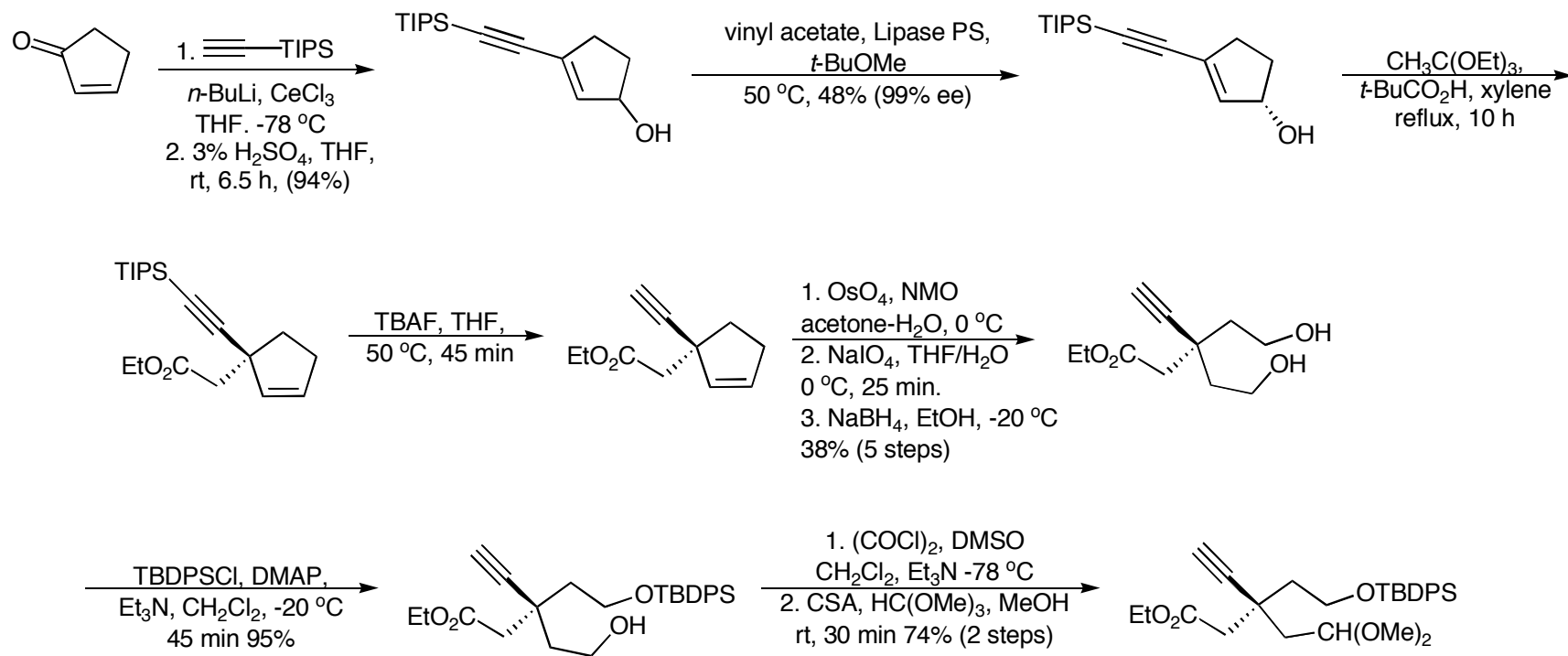




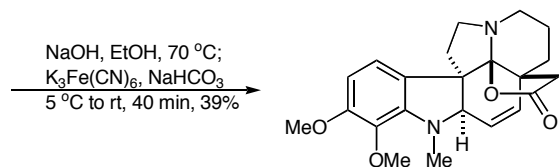
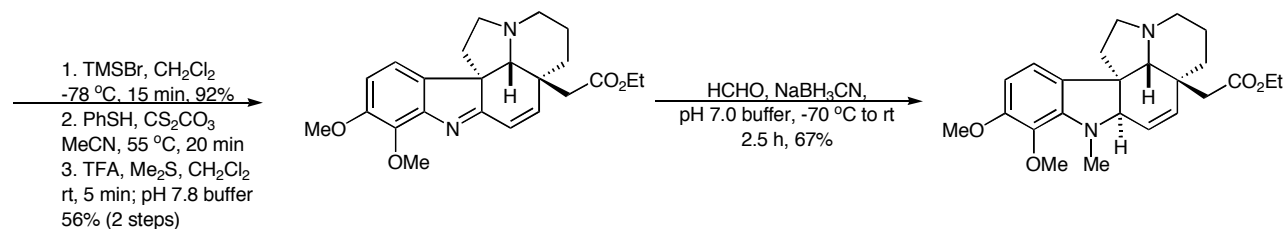
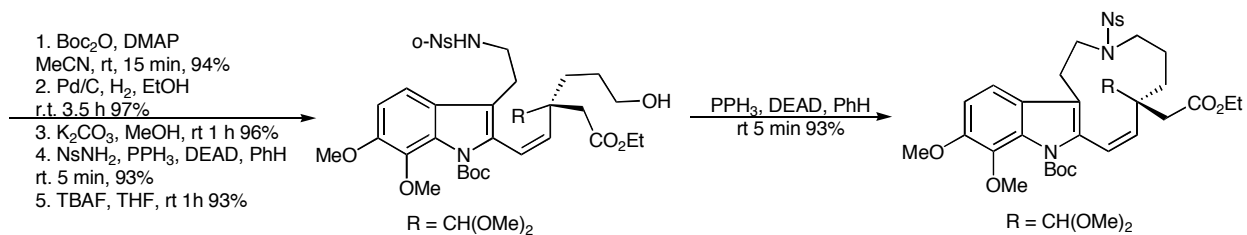
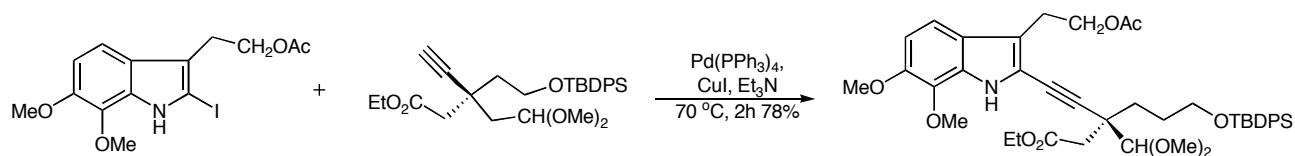
# Finishing the Synthesis



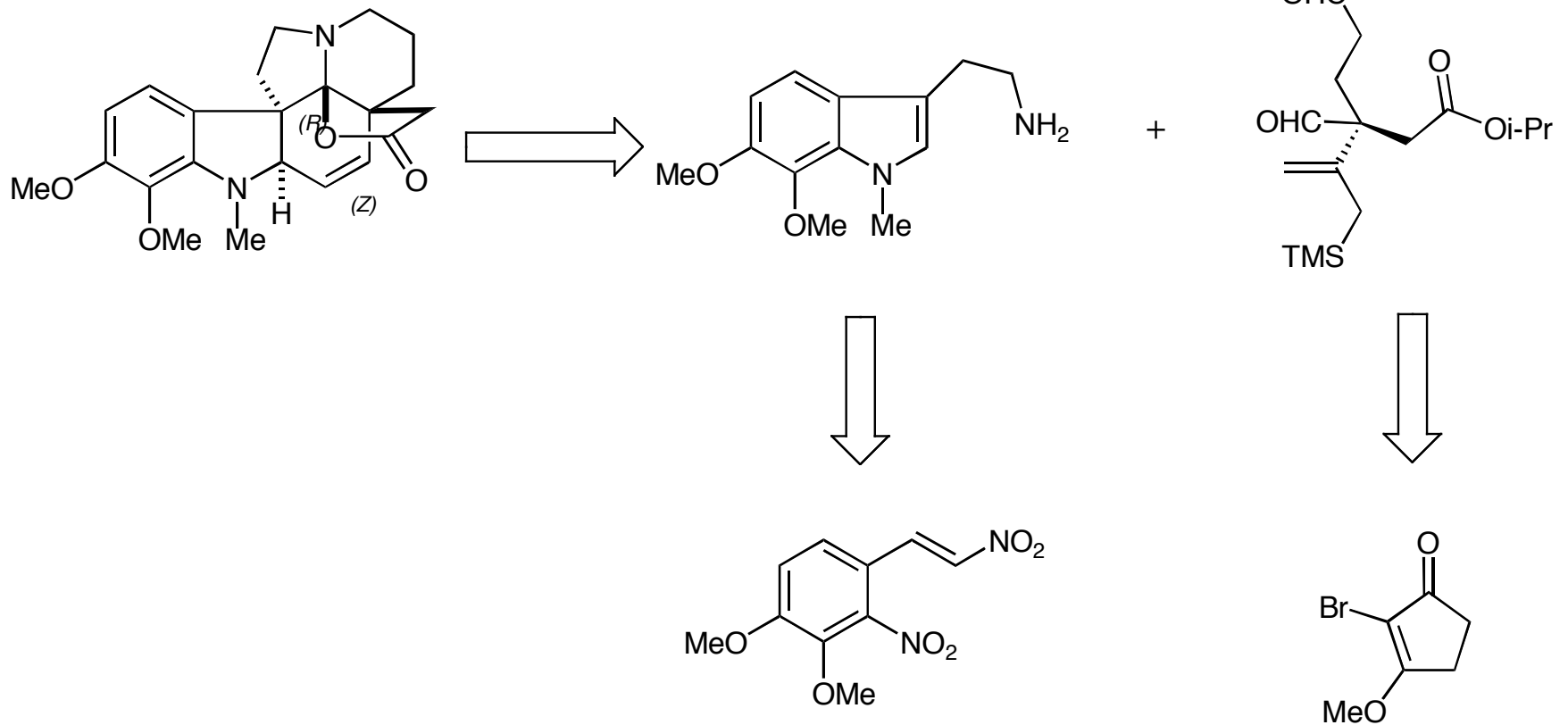
# Fukuyama's Second Generation Synthesis



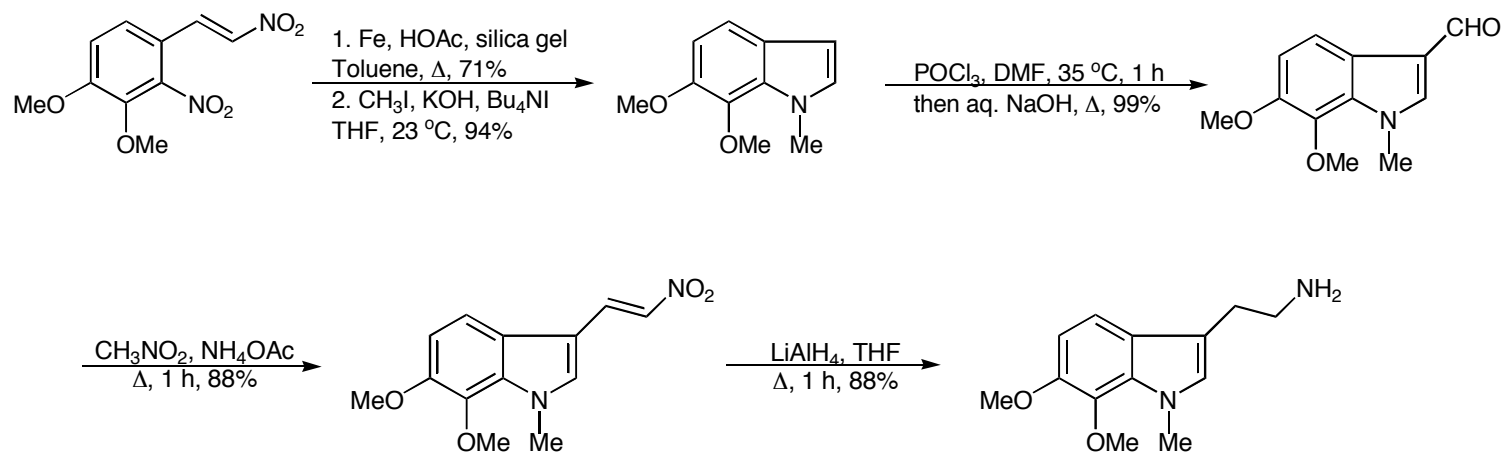
# Completion of Aspidophytine



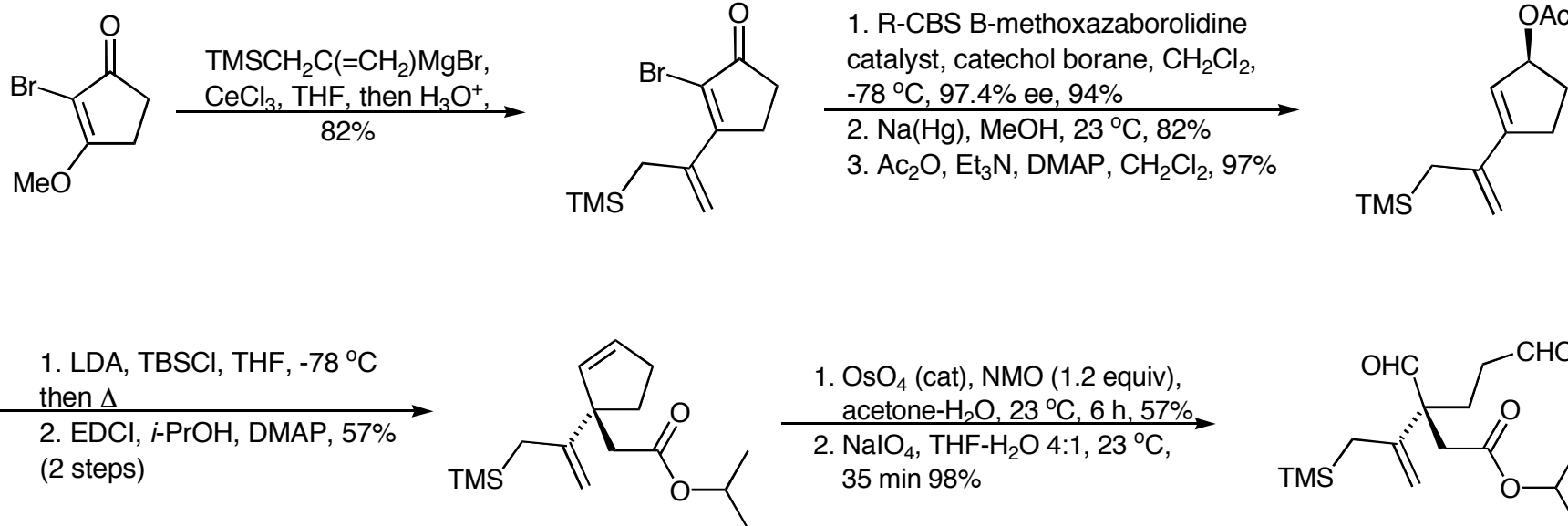
# Corey's Strategy



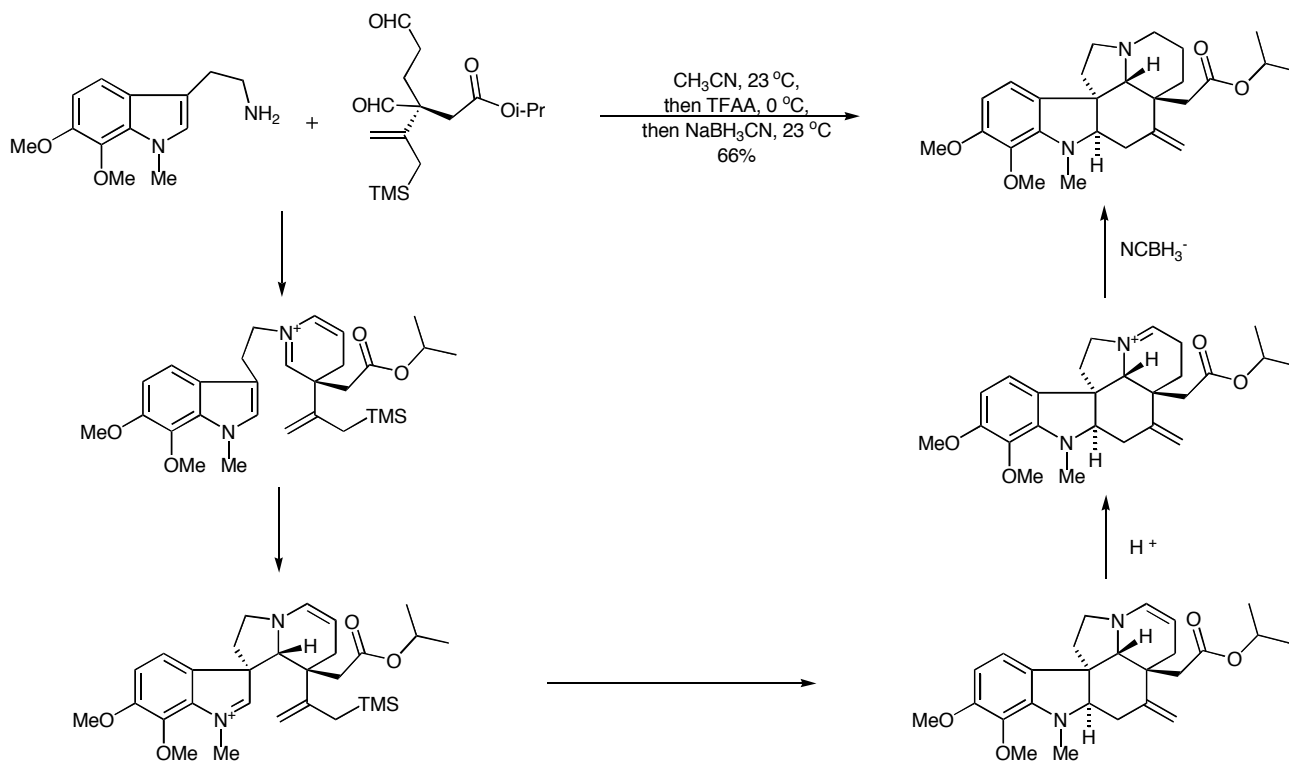
# Synthesis of the Indole System



# Synthesis of Dialdehyde



# Assembly of the Aspidophytine Skeleton



# Completion of Aspidophytine

