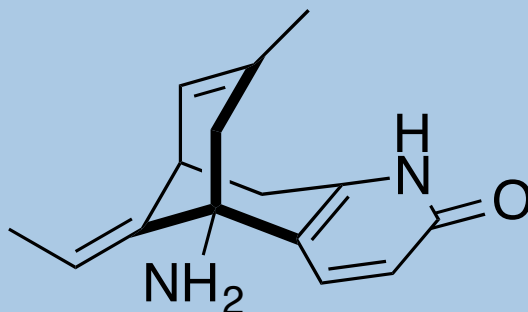


# Cyclobutane Synthesis and Fragmentation. A Cascade Route to the Lycopodium Alkaloid (–)-Huperzine A

White, J. D \*.; Li, Y.; Kim, J.; Terinek, M. *J. Org. Chem.* **2015**, ASAP

DOI : 10.1021/acs.joc.5b01619



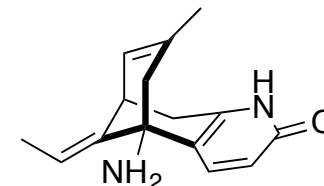
# James D. White

- > Ph.D. at the MIT with G. Büchi in 1965
- > Assistant Professor, Harvard University, 1967-1971
- > Associate Professor, Oregon State University, 1971-1976
- > Professor, Oregon State University, 1976-1992
- > Distinguished Professor, Oregon State University, 1992-2003
- > Distinguished Professor Emeritus, Oregon State University, 2003-present
- > Research interest : Total synthesis of complex natural products

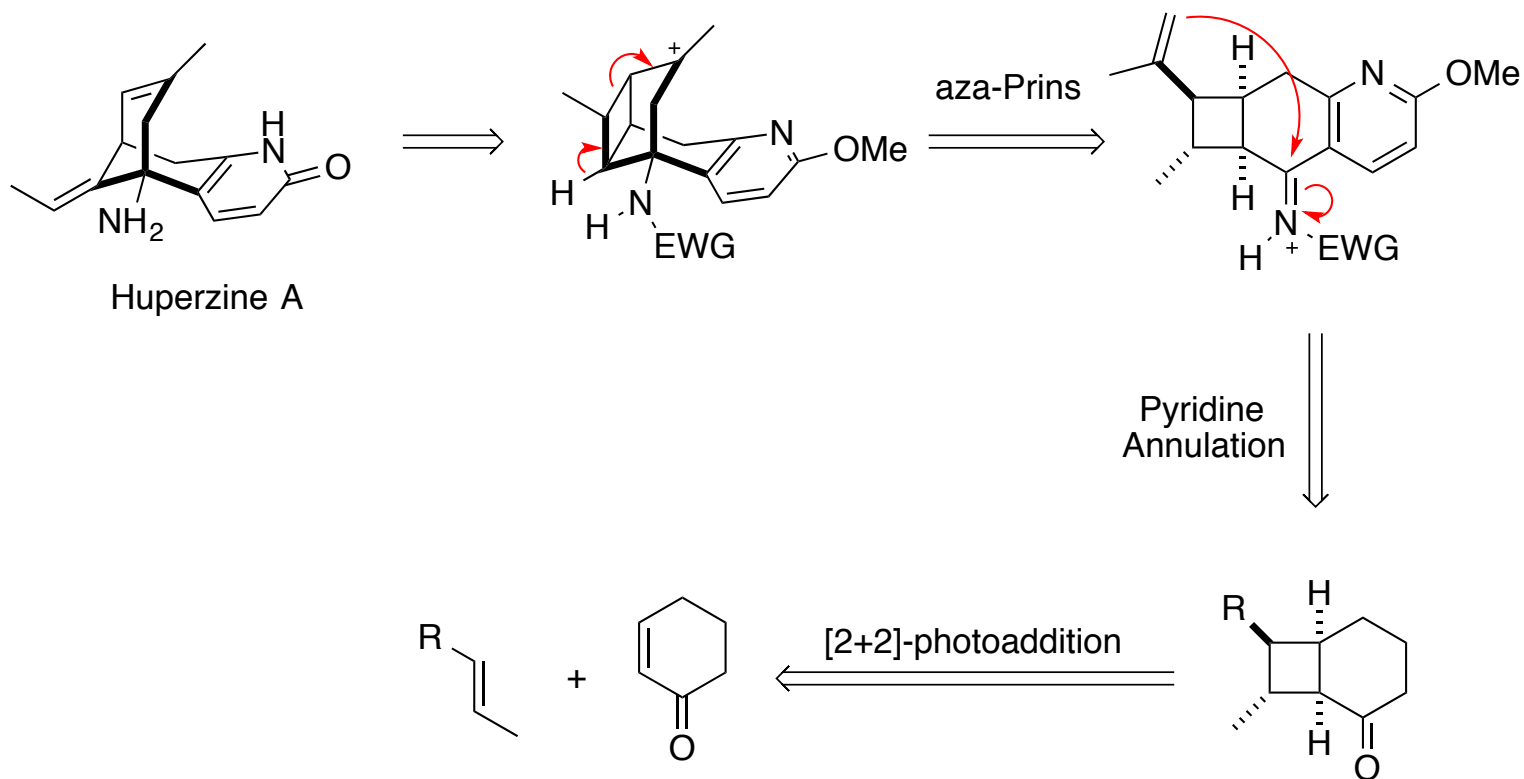


# Introduction

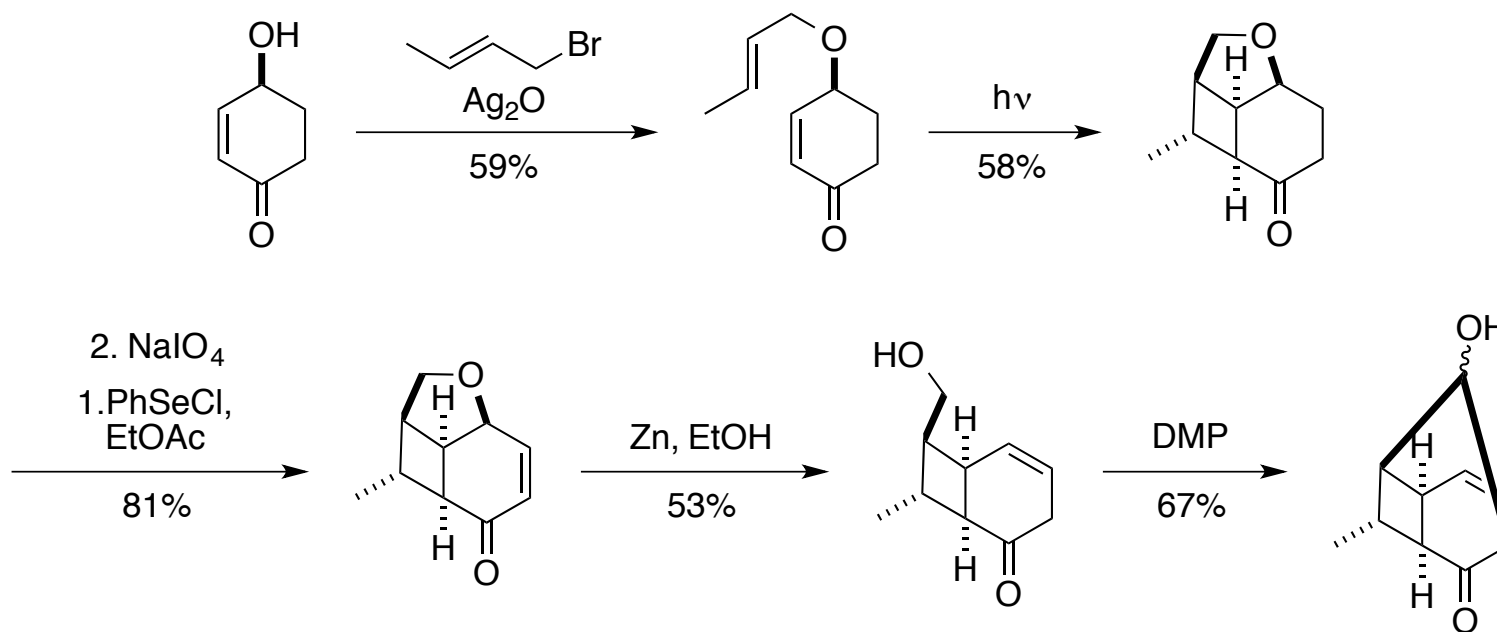
- > Lycopodium alkaloid family
- > Found in the chinese club moss *Huperzia serrata* and in the New Zealand club moss *Lycopodium varium*
- > First enantioselective synthesis by Kozikowski et al. in 1991
- > Most efficient synthesis by G.Q.Lin and co. in 2012
  - 10 Steps 17% overall yield
- > Interesting activity against Alzheimer's disease



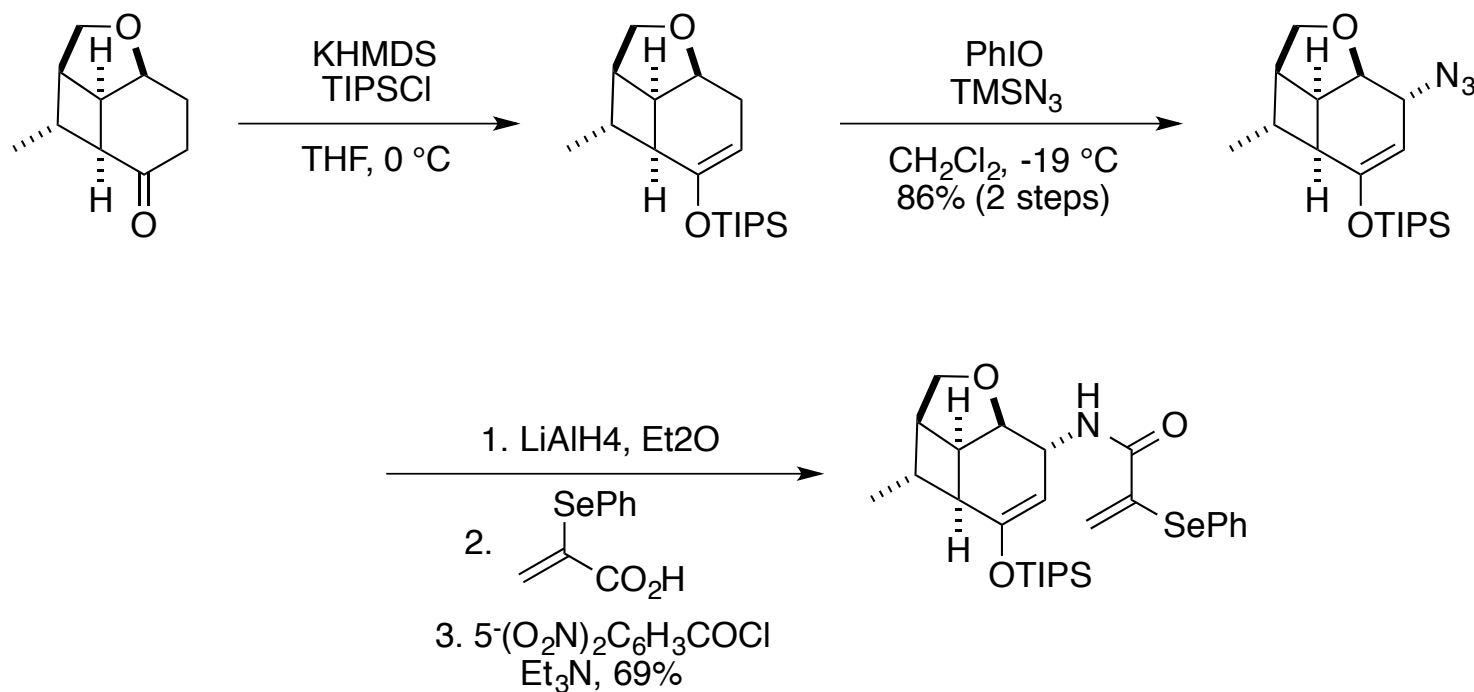
# Retrosynthetic Approach



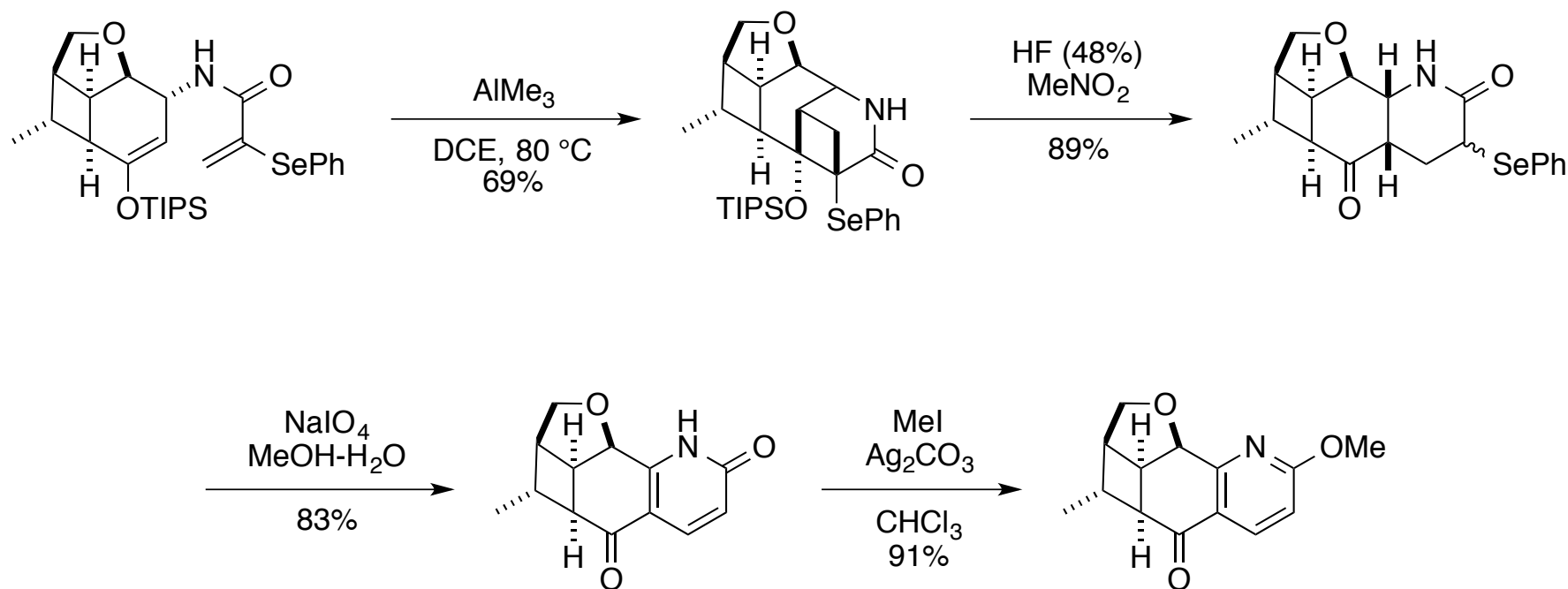
# Intramolecular Photocycloaddition



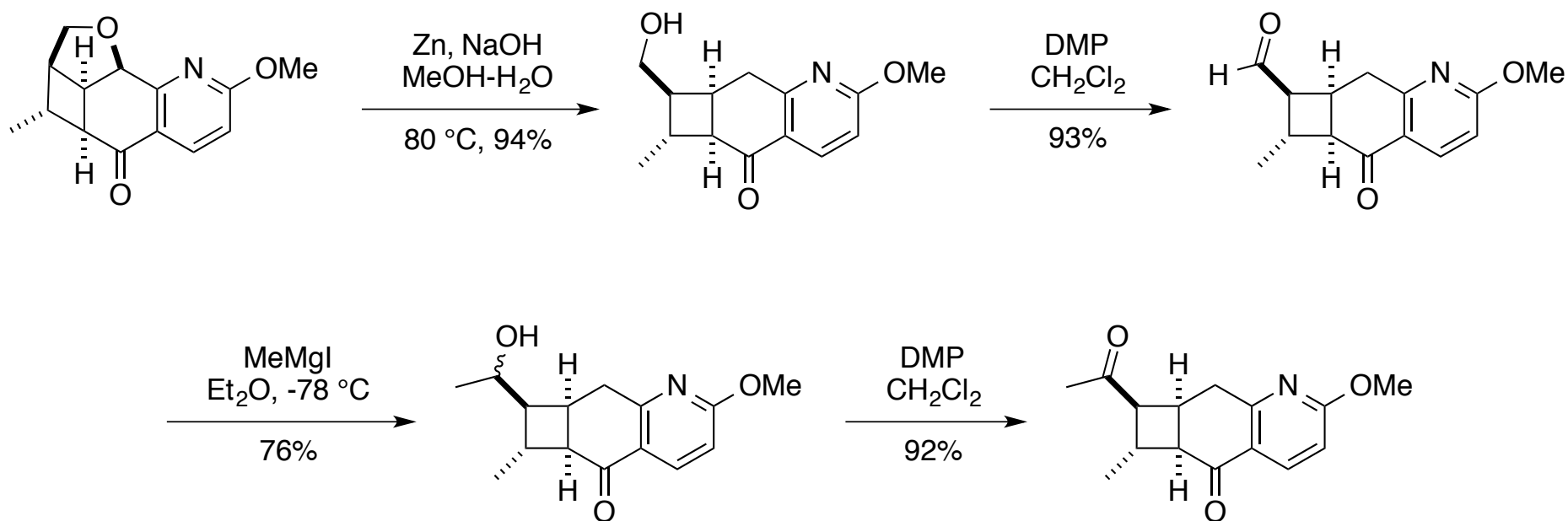
# Acrylamide Formation



# Pyridine Formation

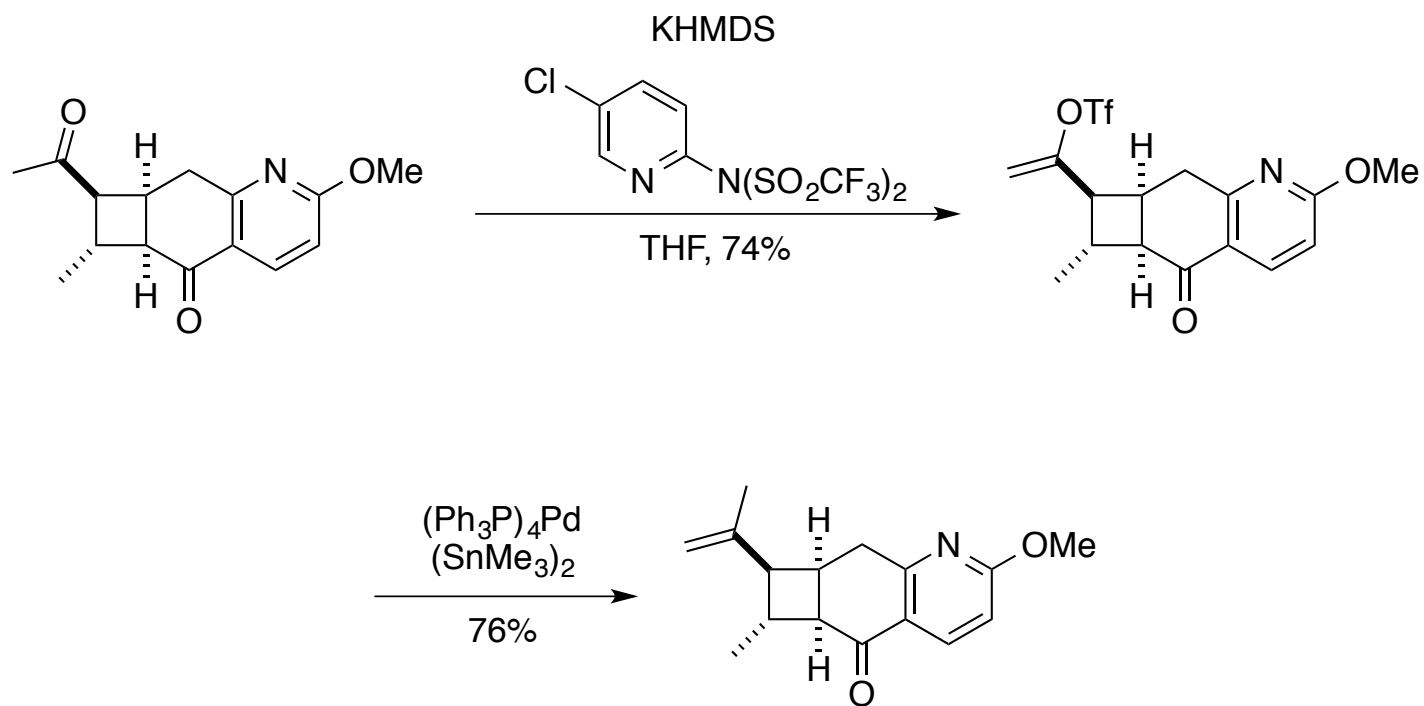


# Opening of the THF Ring and Oxidation

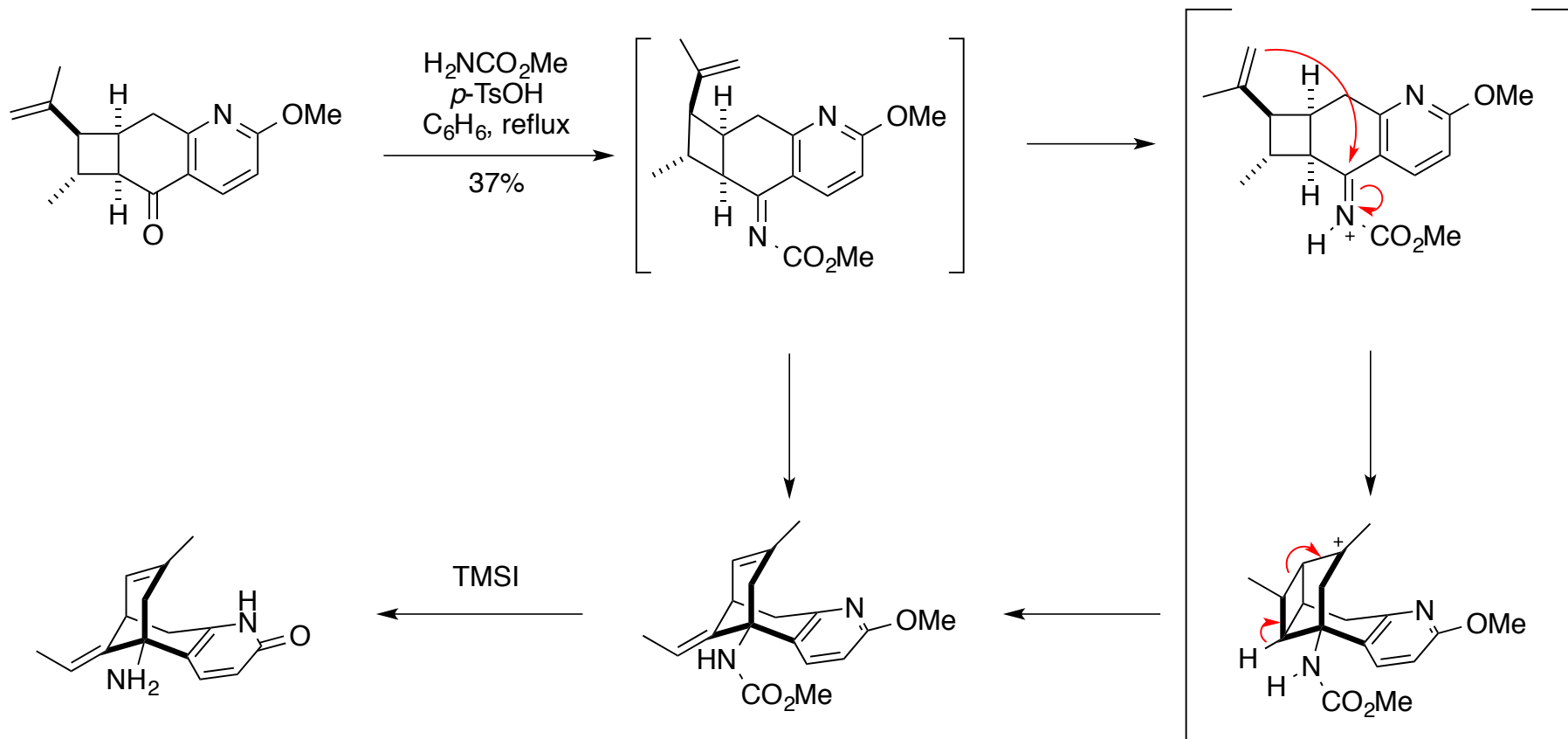




# Selective Methylenation



# Aza-Prins Cyclisation



# Conclusion

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- > Key Step : Aza-Prins Cyclisation
- > 17 Steps overall yield of 1%
  - Not the most efficient (–)-Huperzine A synthesis

**Thank you for your attention**

# β-Azidation

