A Ten-Step Total Synthesis of Speradine C

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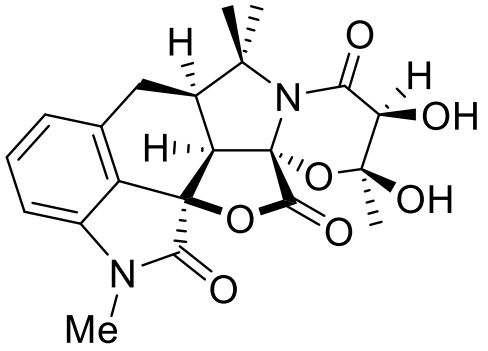
- Ergot-like alkaloid in the family of cyclopiazonic acids. It was firstly isolated from *Penicillium cyclopium* and is a mycotoxic metabolite.
- Also is a nanomolar inhibitor of sarco/endoplasmic reticulum Calcium ATPase (SERCA), which is essential for calcium reuptake in muscle contraction and relaxation cycles. SERCA is a promising target for development of new drugs against various diseases and insect pests.
- Speradine C contains an unprecedented 6/5/6/5/5/6 hexacyclic ring system with a 5,6-dihydroxy-4-oxo-1,3-oxazinane unit and six stereocenters including four oxygen-bearing carbon centers.
- A concise route to Speradine C was enabled by utilizing three different cyclizations to construct four different ring systems, one of which is inspired by the biosynthesis of cyclopiazonic acids.

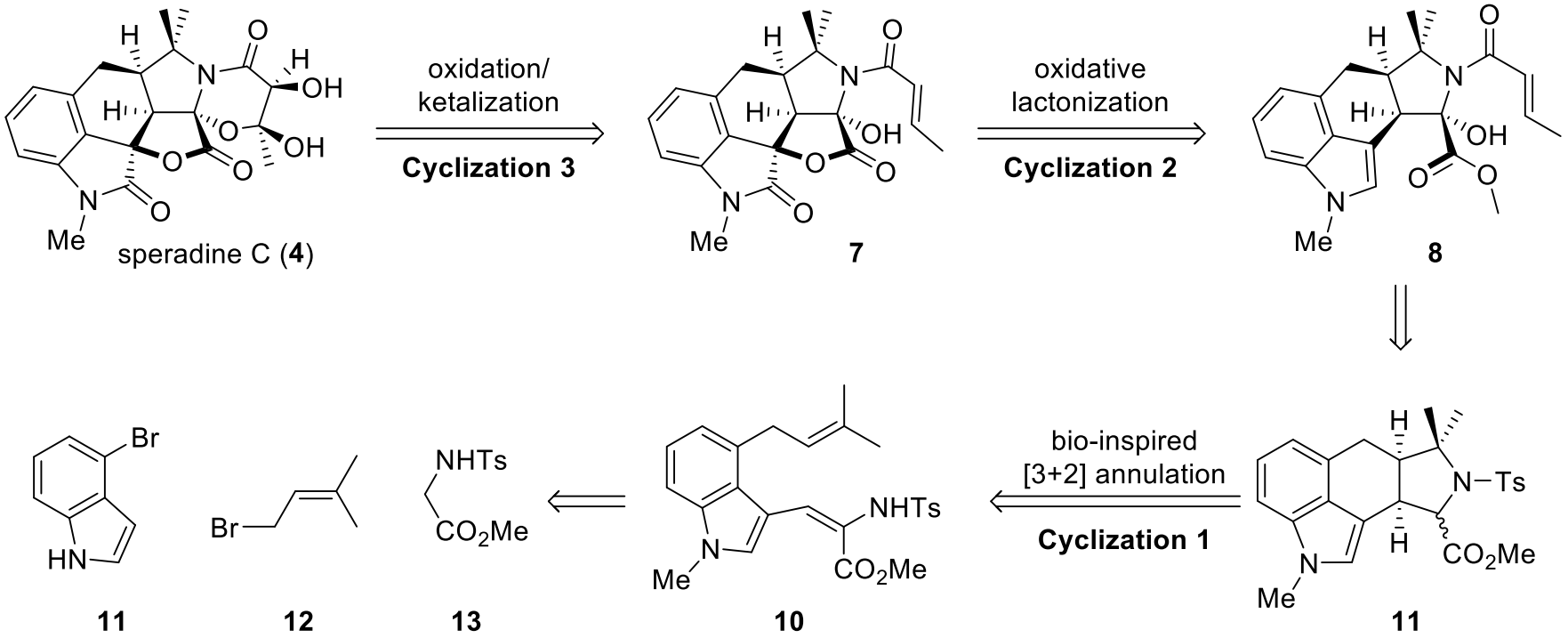


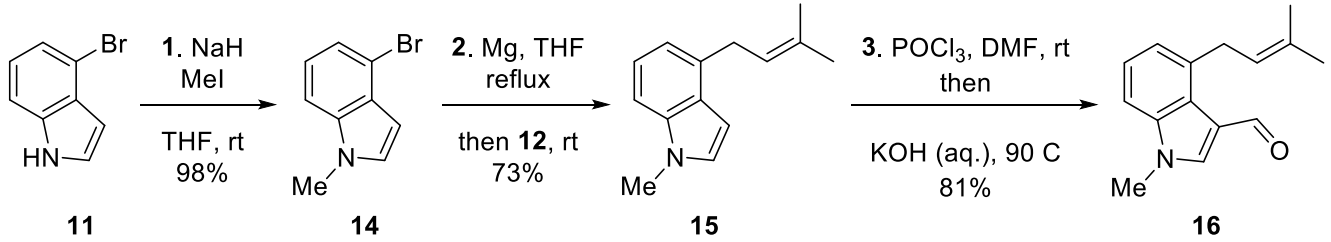
Speradine C (**4**)

Chemistry
BOSTON COLLEGE

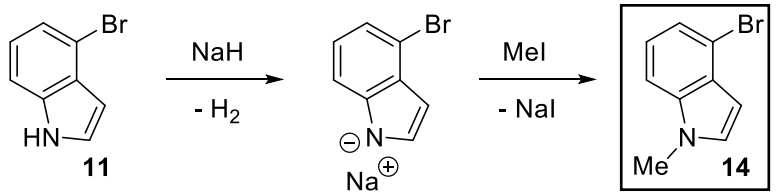
Ricky Alvarado
May 9th, 2019
Liu Group

Retrosynthesis

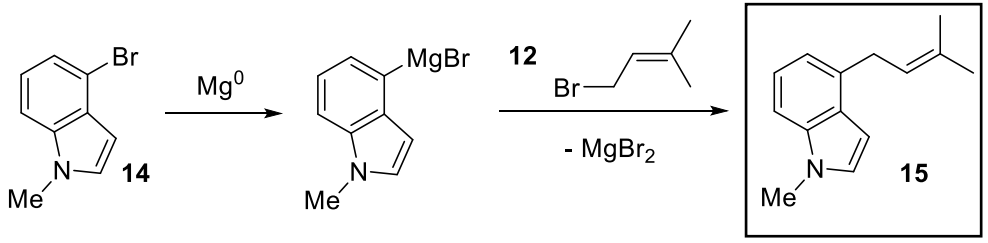




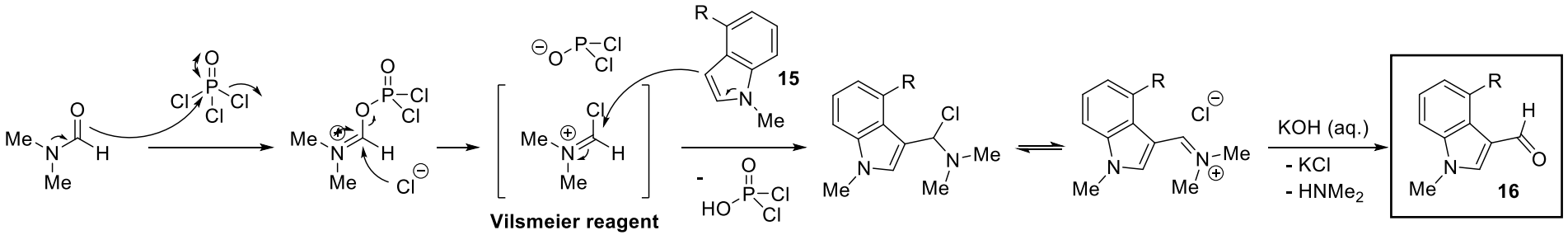
Indole methylation

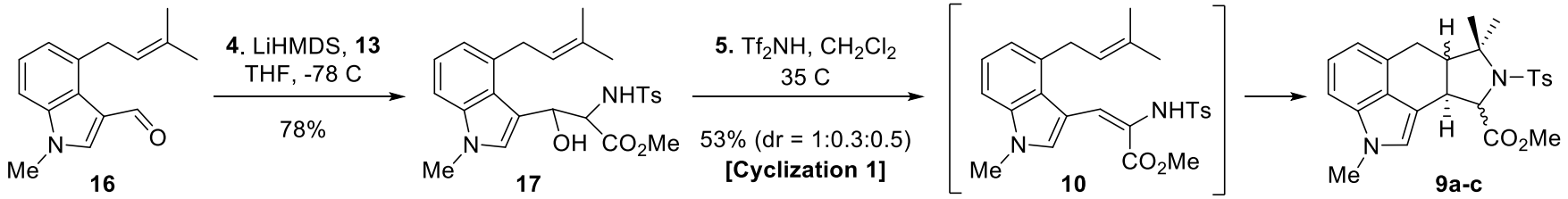


Grignard Reaction and alkylation

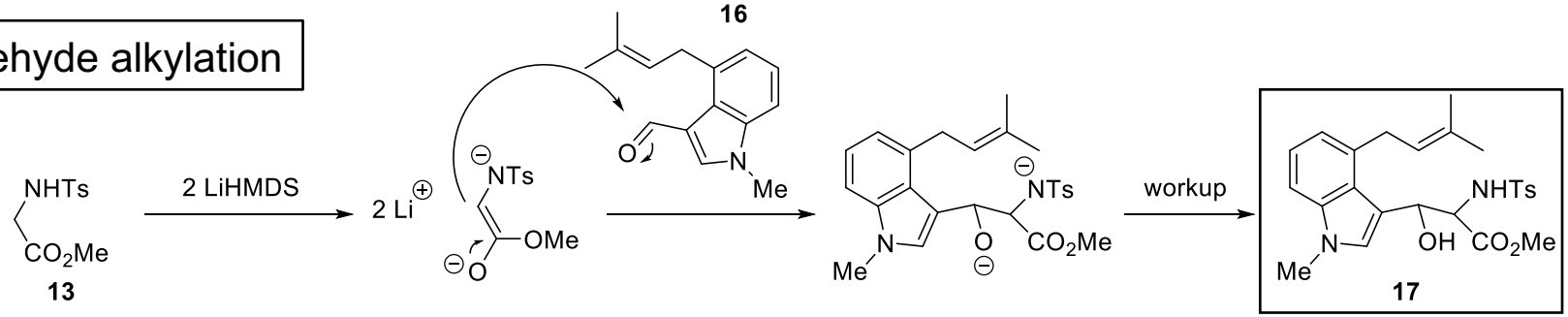


Vilsmeier-Haack Reaction

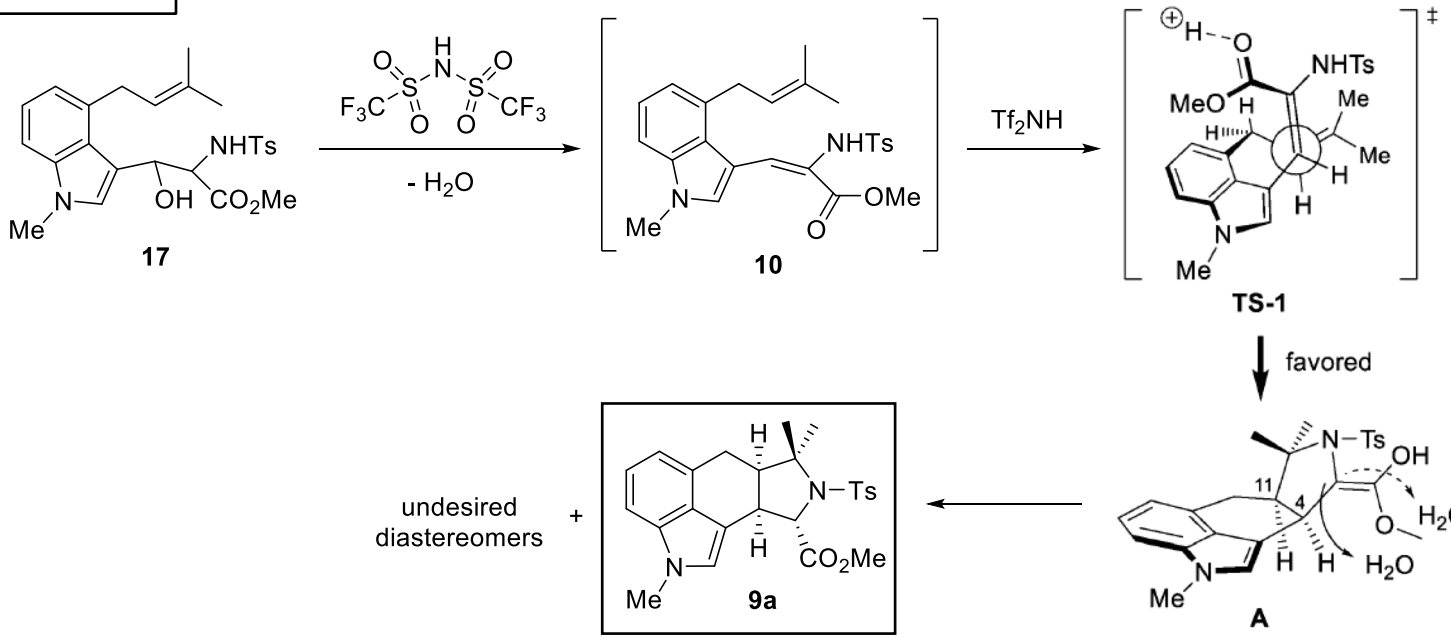


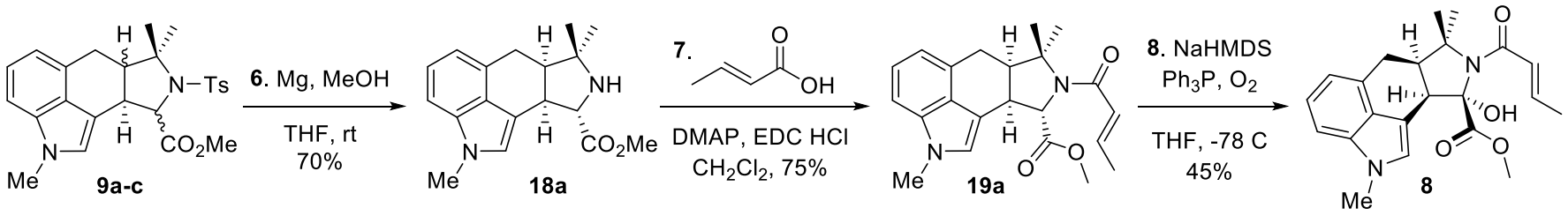


Aldehyde alkylation

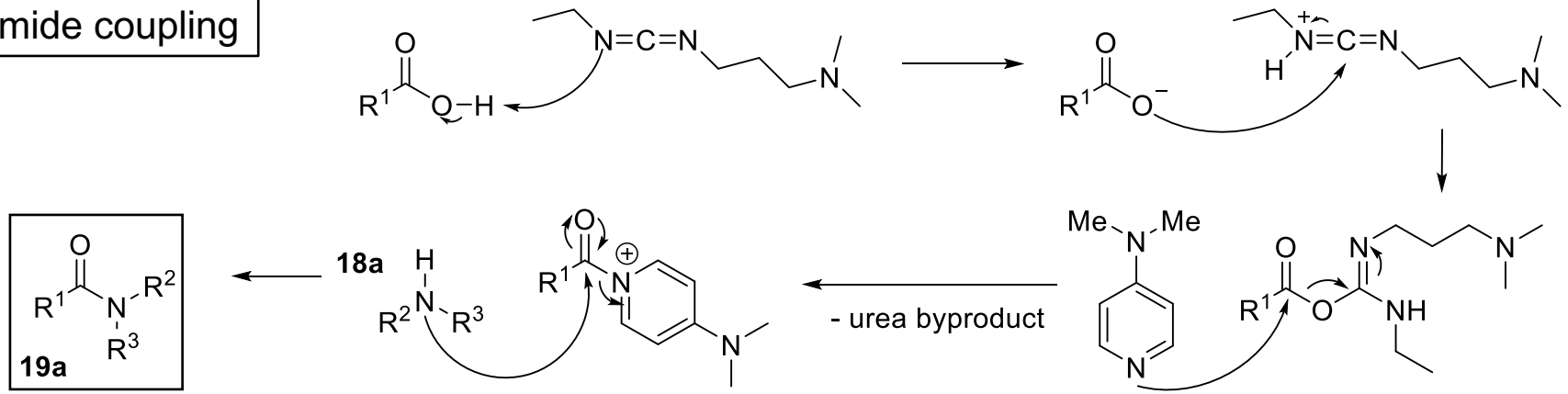


Cyclization 1

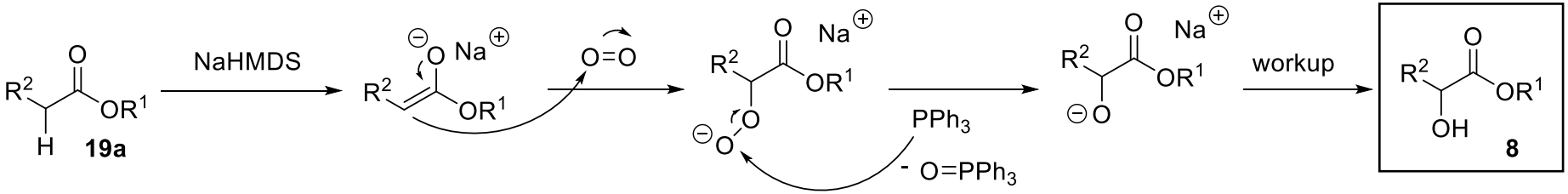


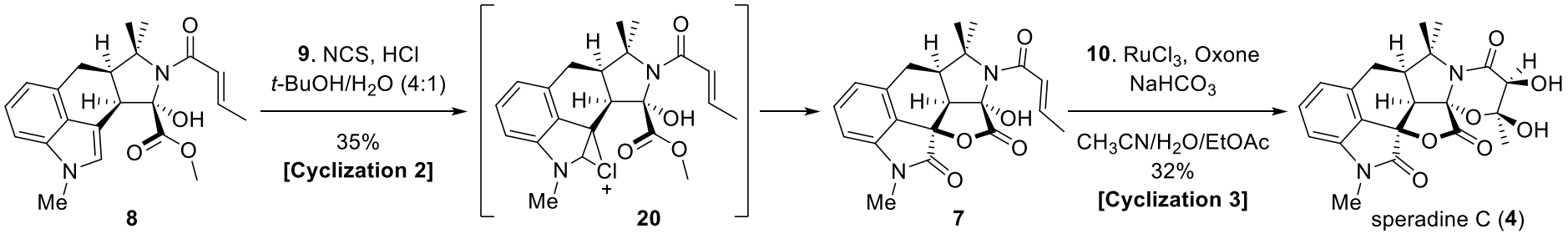


Amide coupling

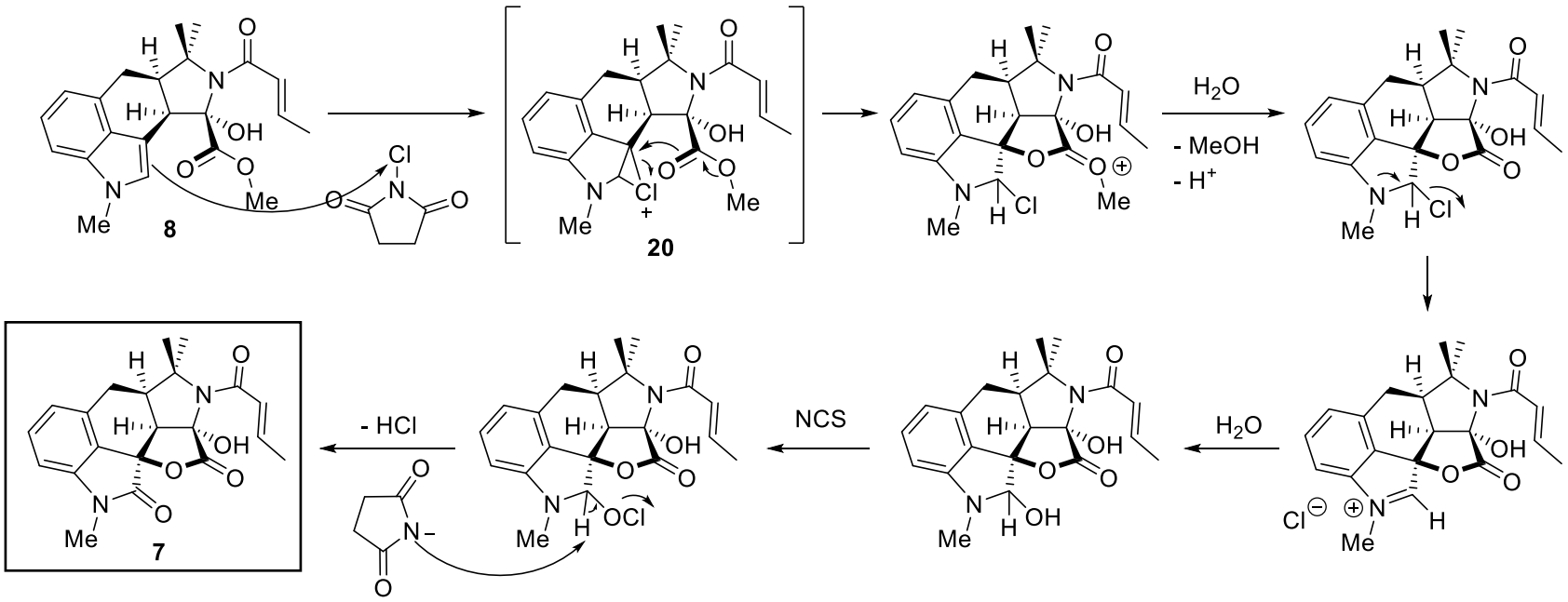


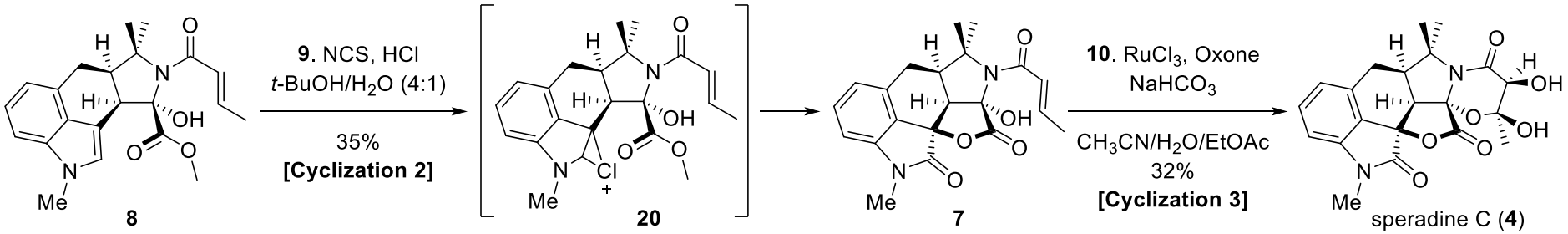
α-Hydroxylation of ester





Cyclization 2: NCS Oxidation





Cyclization 3: Ru-catalyzed Ketohydroxylation of Olefin, then hemiacetal formation