Enantioselective Total Synthesis of (−)-Alstoscholarisine A

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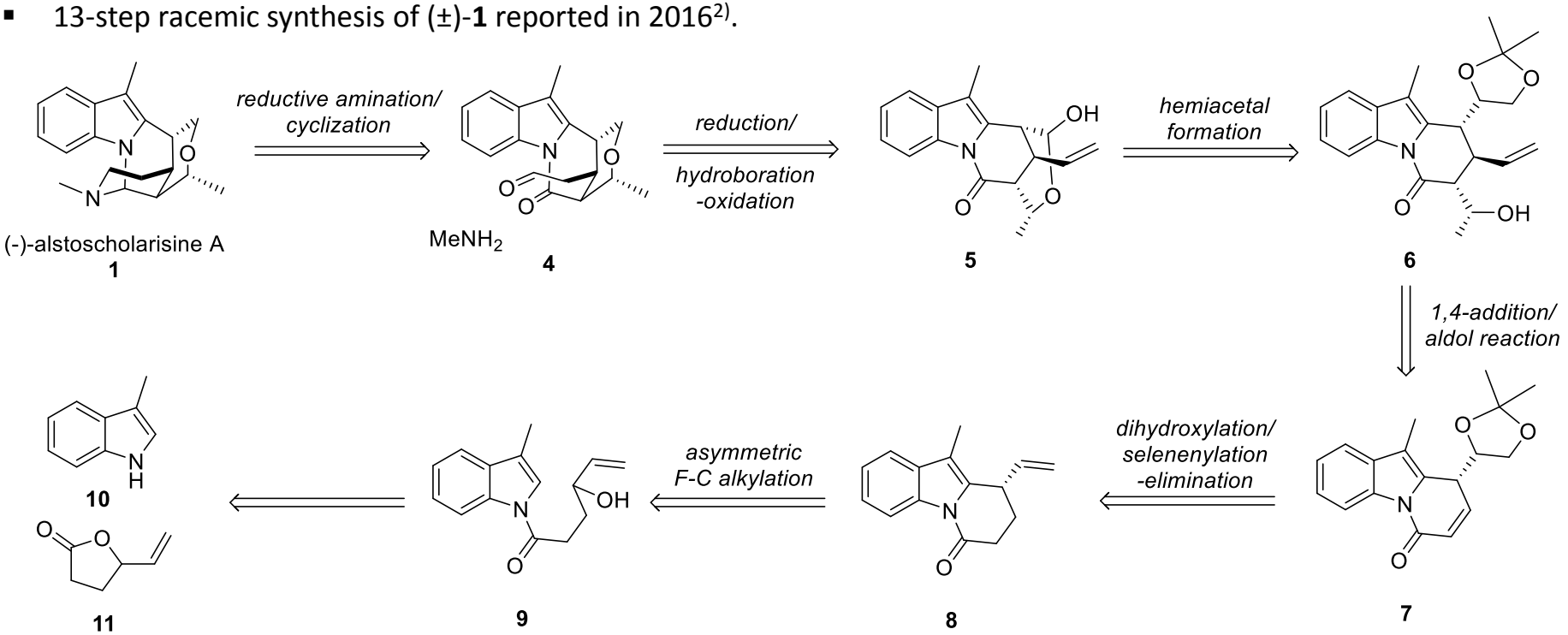
Presented by Hyelee Lee, Liu Research Group, Boston College

I. Introduction/retrosynthesis

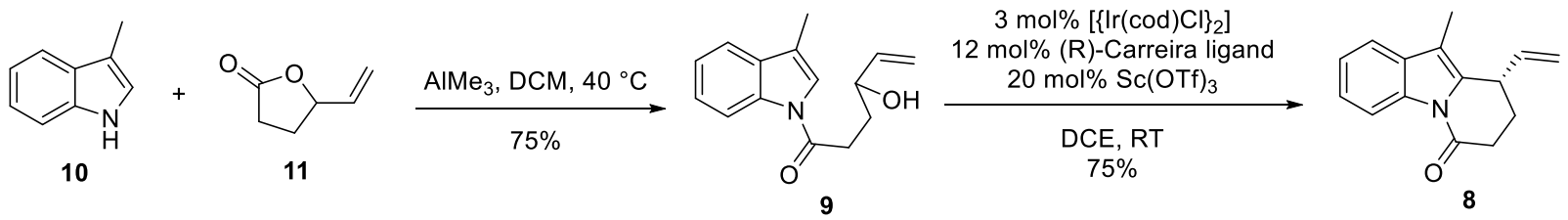
- Alstoscholarisines: monoterpenoid indole alkaloids with a complex pentacyclic structure.
- Recently discovered by Luo and co-workers from Alstonia scholaris[1)].
- Synthetically challenging pentacyclic core with five stereogenic centers.
- Bioactivity in promoting adult neuronal stem cells proliferation (0.1 ug/mL).
- 13-step racemic synthesis of (±)-**1** reported in 2016[2)].



1) Yang, X.-W.; Yang, C.-P.; Jiang, L.-P.; Qin, X.-J.; Liu, Y.-P.; Shen, Q.-S.; Chen, Y.-B.; Luo, X.-D. *Org. Lett*. **2014**, *16*, 5808.

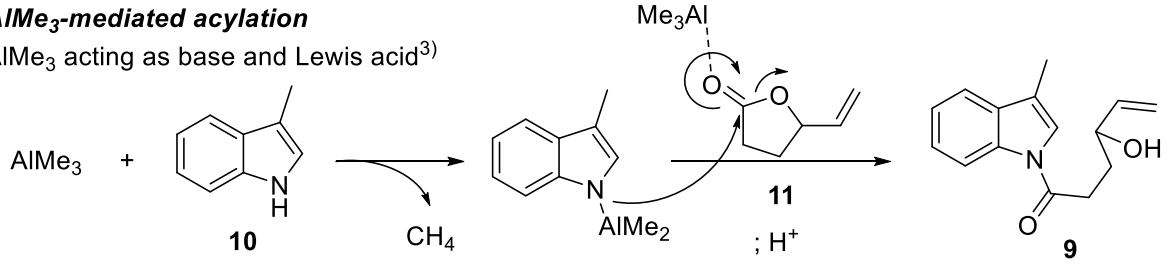
2) Bihelovic, F.; Ferjancic, Z. *Angew. Chem. Int. Ed*. **2016**, *55*, 2569.

II. Forward synthesis

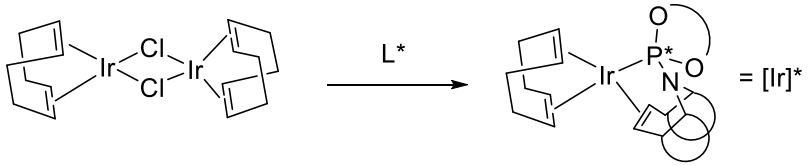


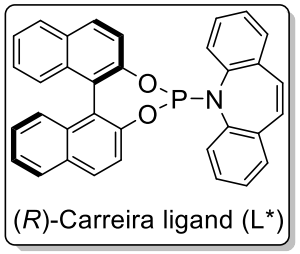
$AlMe_3$-mediated acylation

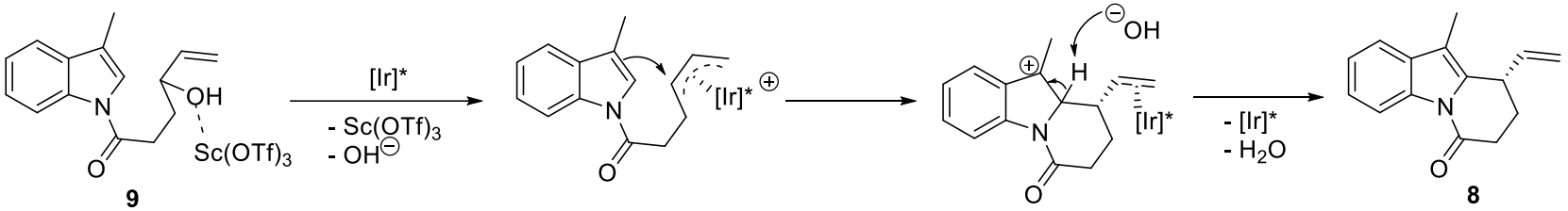
$AlMe_3$ acting as base and Lewis acid[3)]



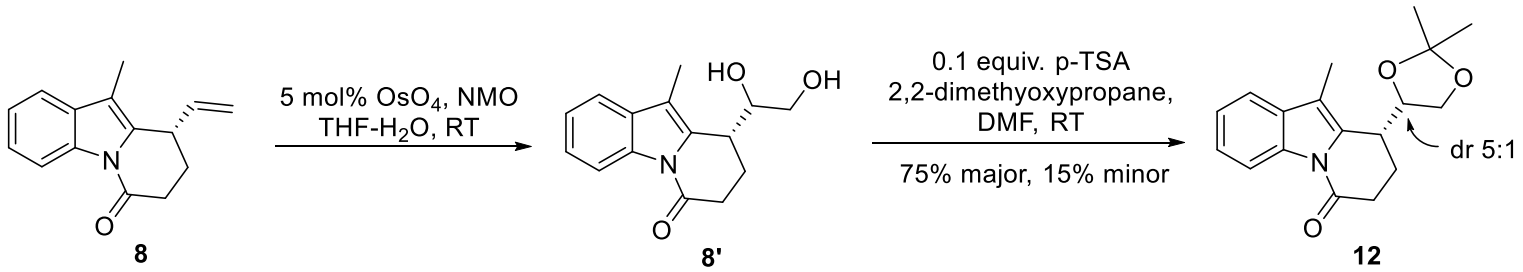
Ir-catalyzed enantioselective cyclization



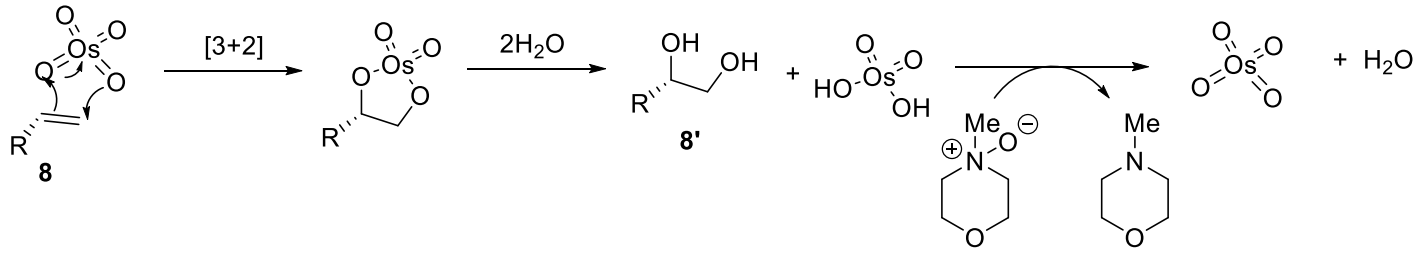




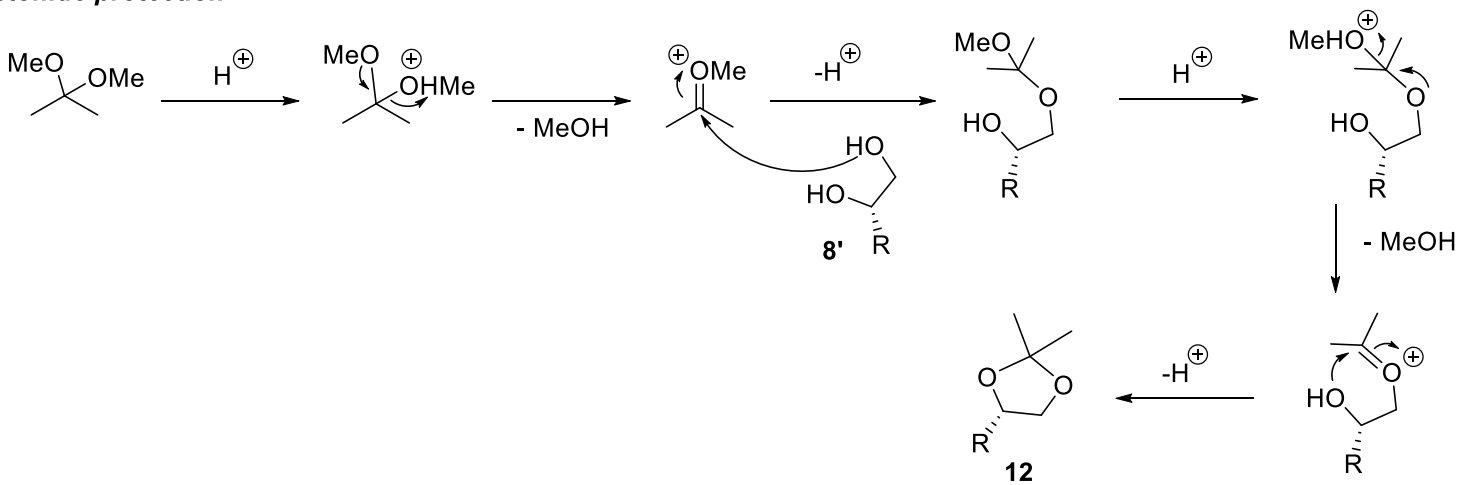
3) Basha, A.; Lipton, M.; Weinreb, S. M. *Tetrahedron Lett.* **1977**, *18*, 4171.

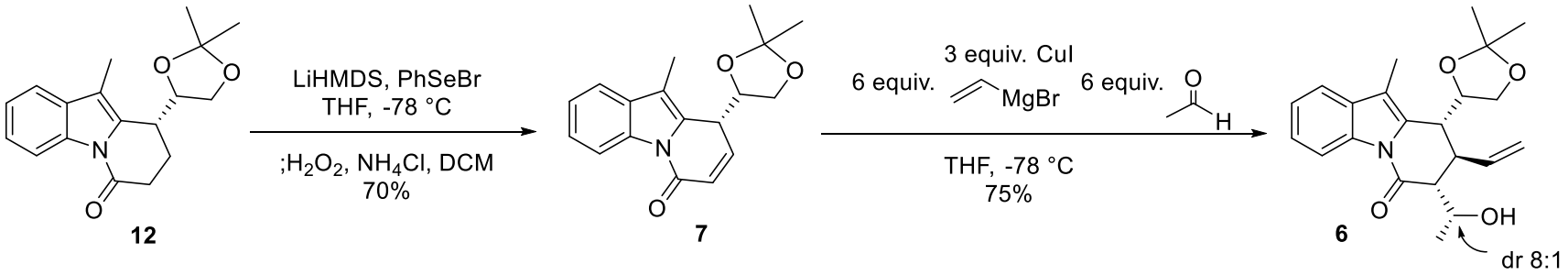


Dihydroxylation

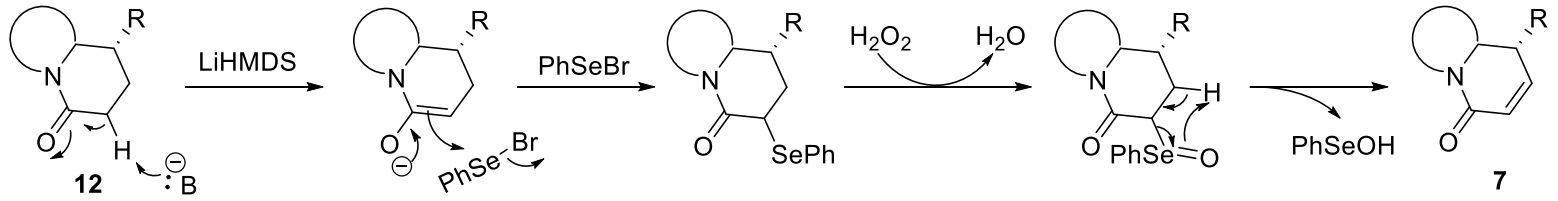


Acetonide protection

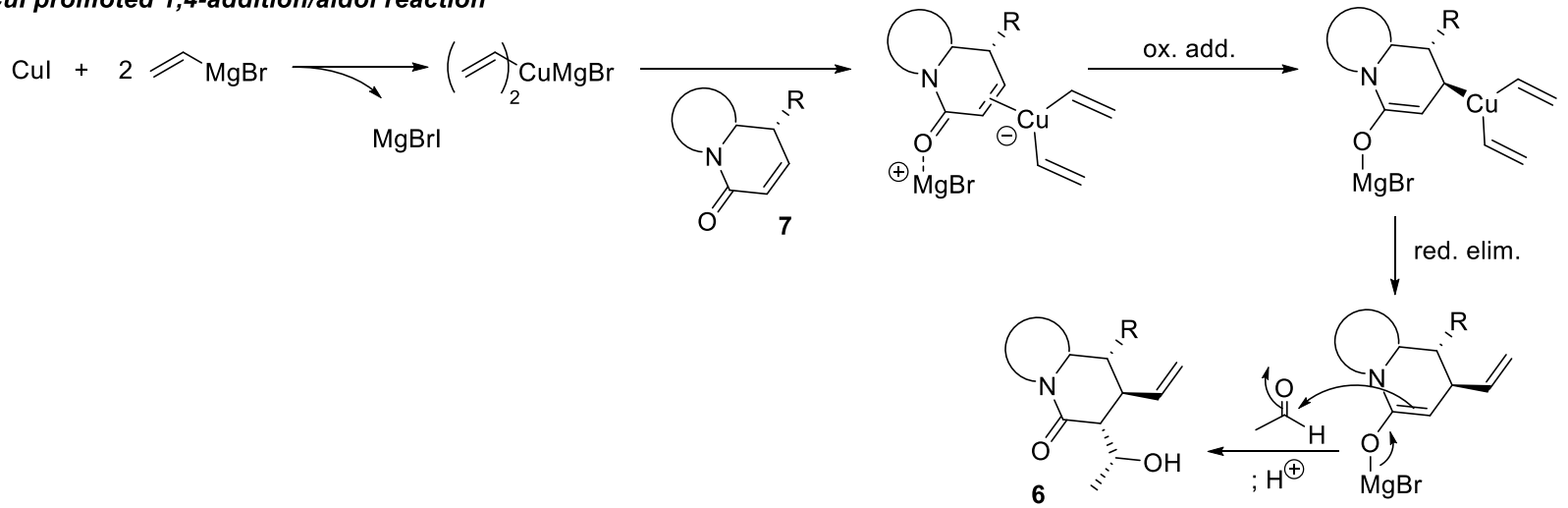


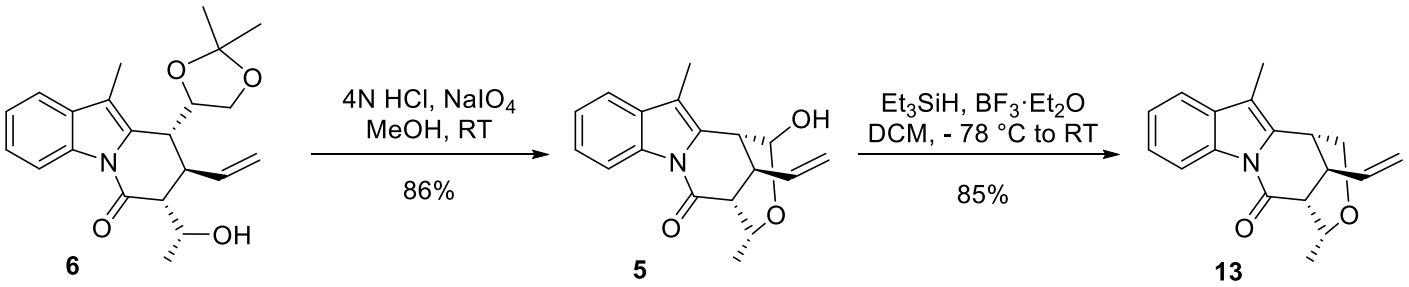


Selenenylation-elimination

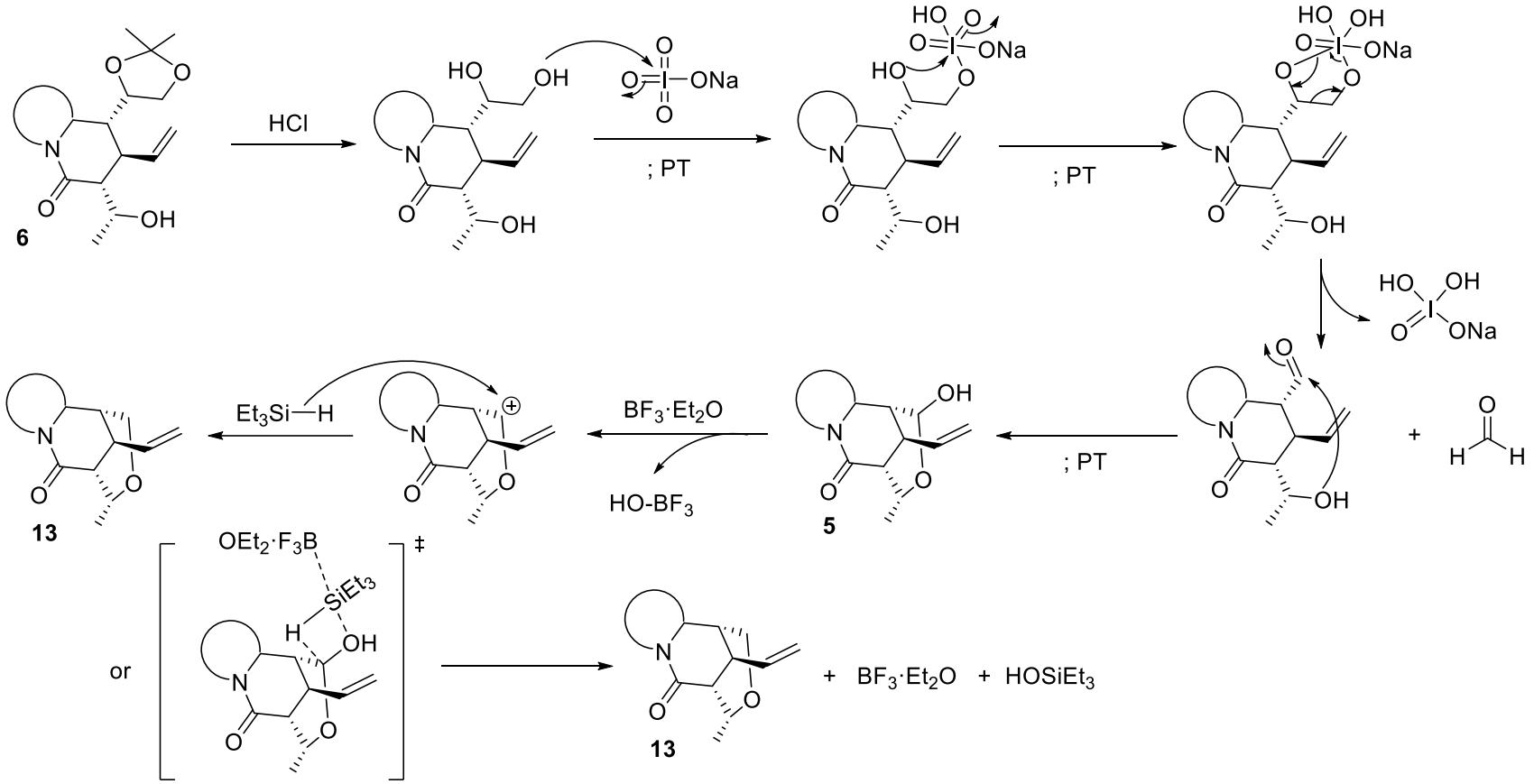


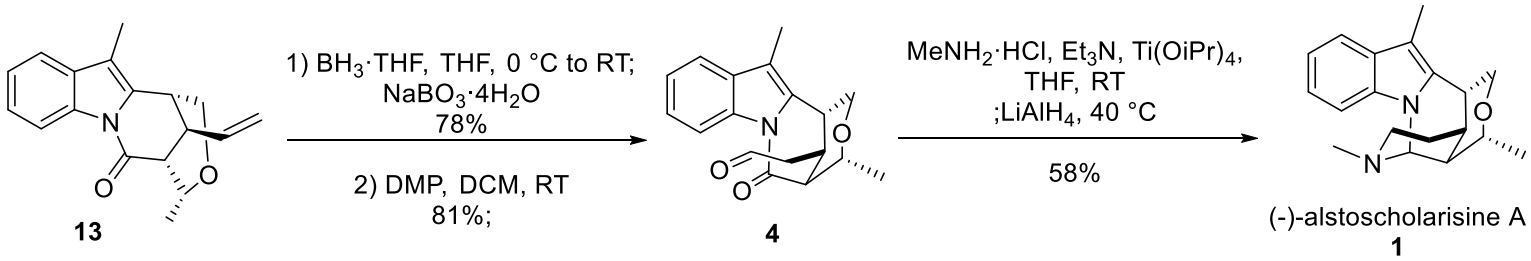
CuI promoted 1,4-addition/aldol reaction



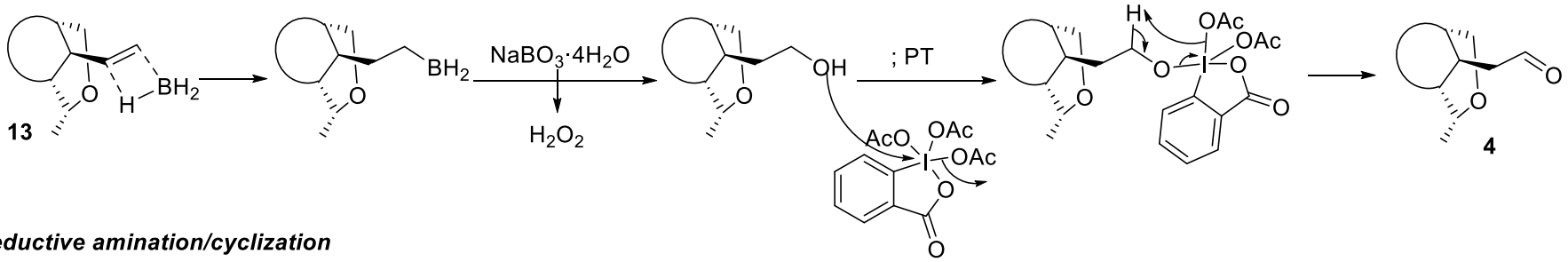


Hemiacetal formation/reduction





Hydroboration-oxidation/DMP oxidation



Reductive amination/cyclization