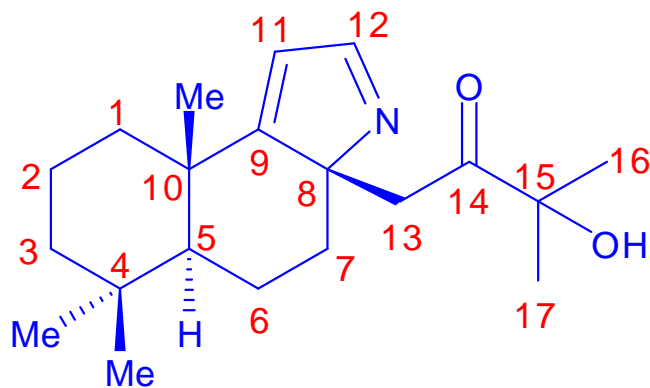


Total Synthesis of (-)- Chamobtusin A



Org. Lett. **2010**, *12*, 4709-4711

Introduction

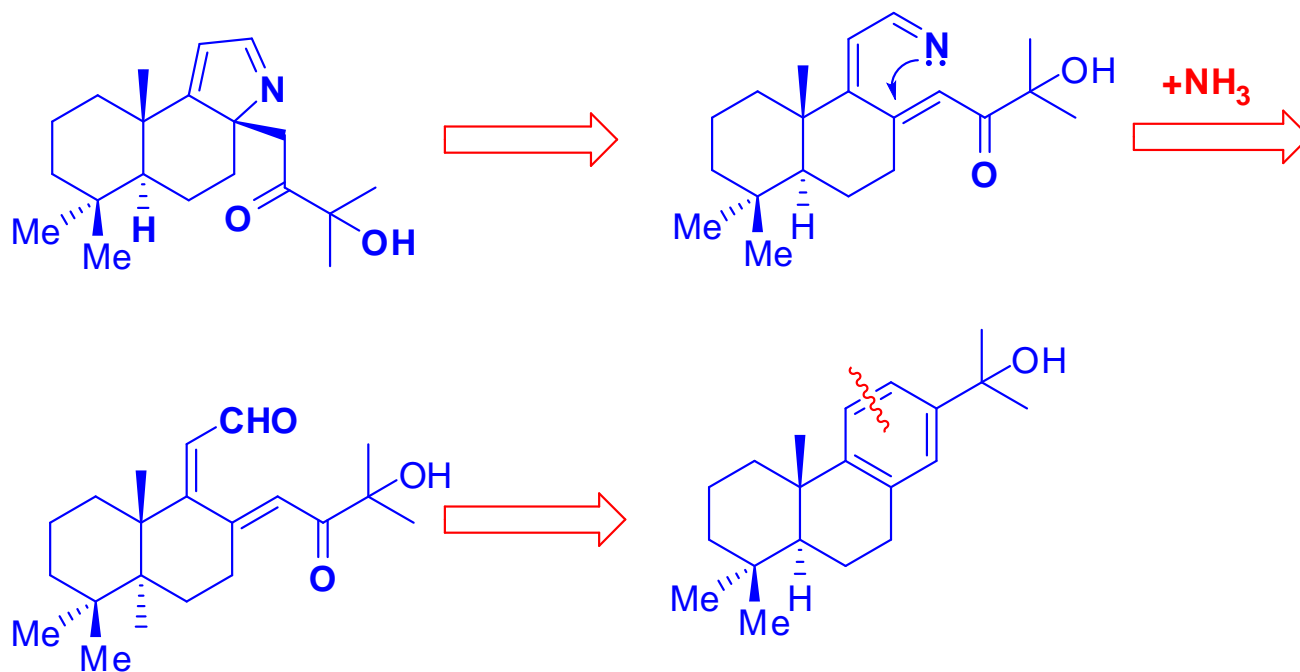
- Isolated from *Chamaecyparis obtusa cv. tetragon* in 2007 by Tan and co-workers.



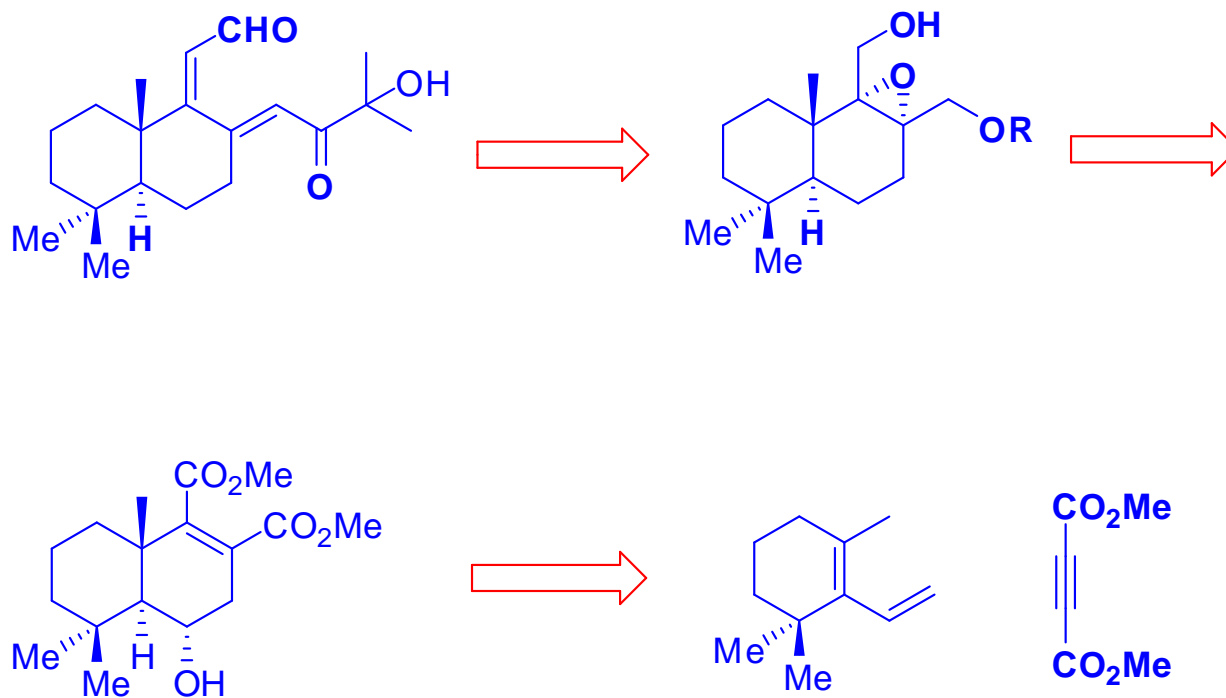
- It is a diterpene
- Structure was established mainly on the basis of 2D NMR
- Confirmed by single-crystal X-ray diffraction analysis

Watanabe's approach for the total synthesis of chamobtusin A

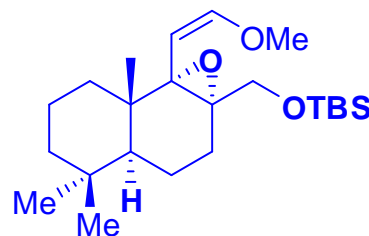
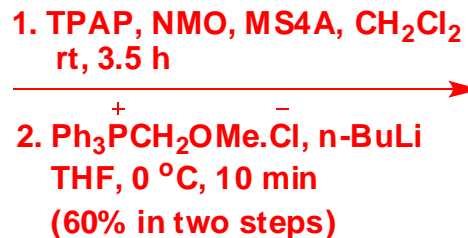
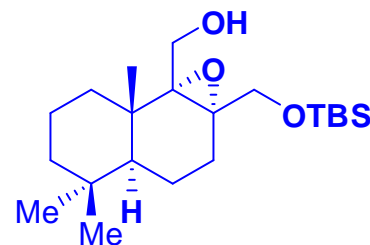
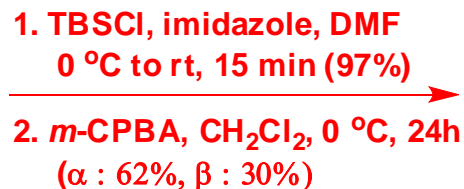
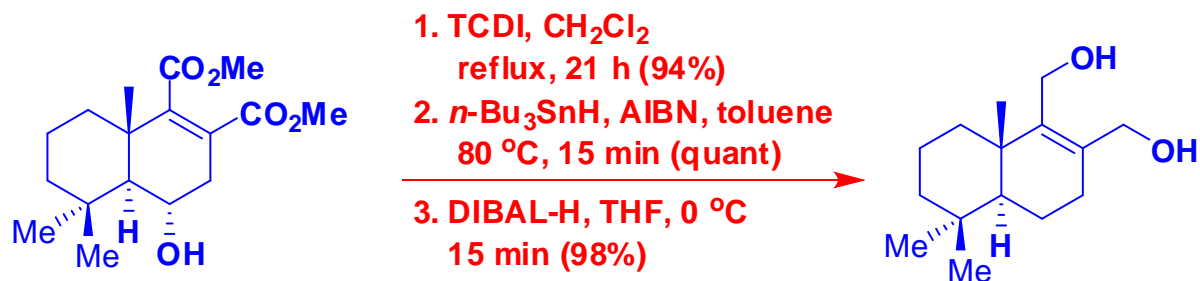
Presumed biosynthesis:



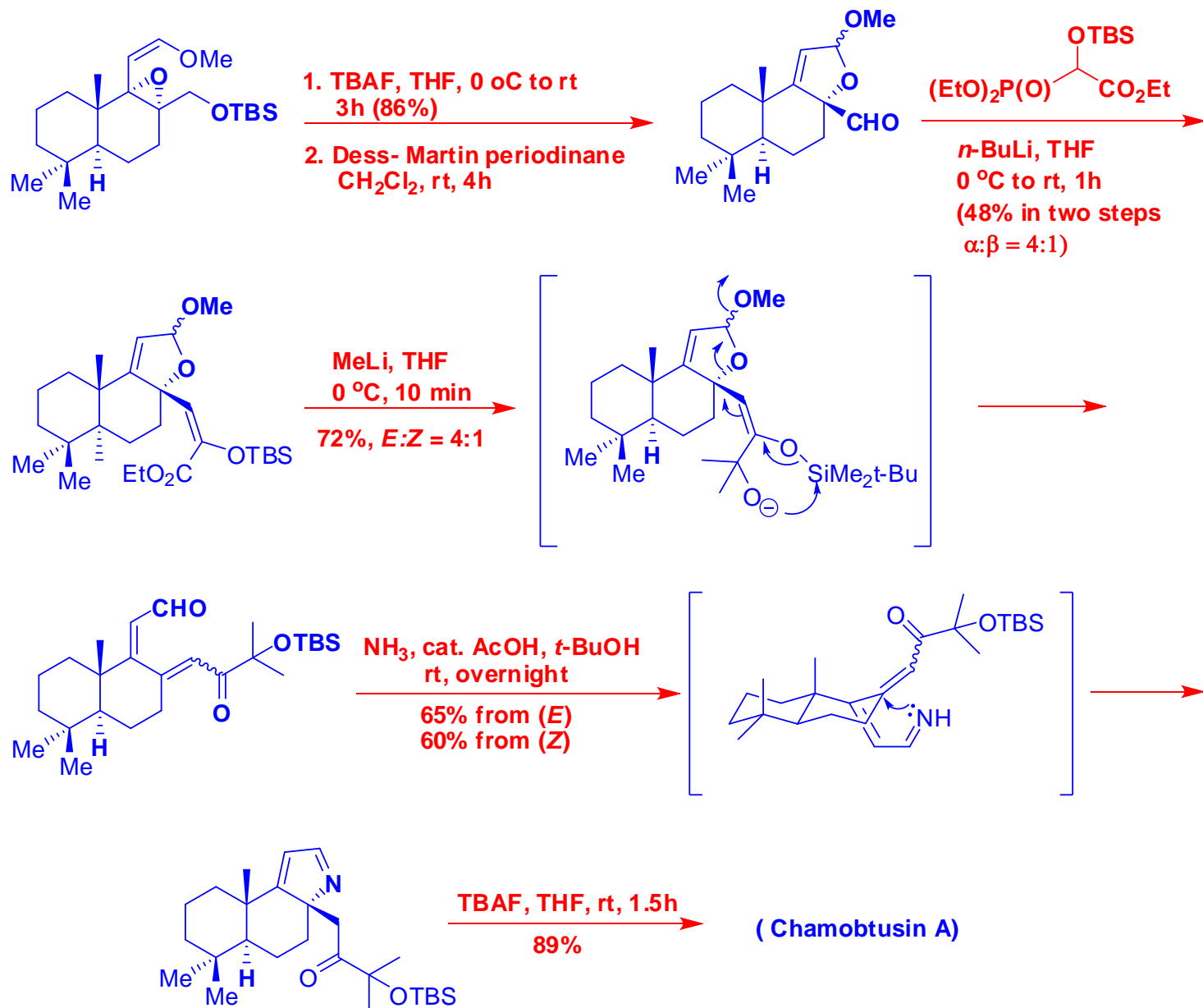
Retrosynthetic analysis:



First stage of the synthesis:

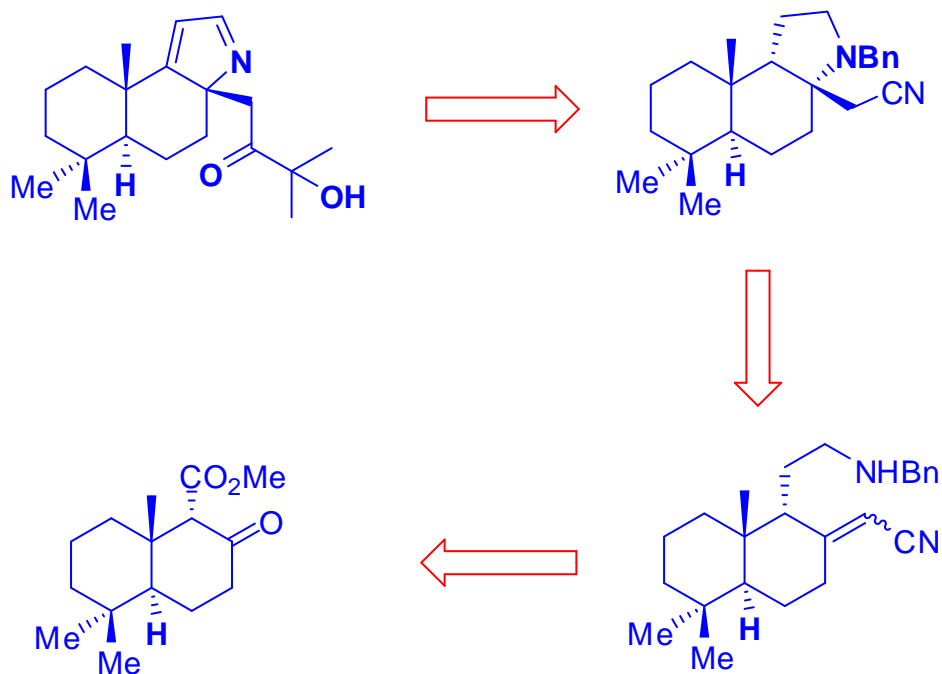


Completion of the synthesis:

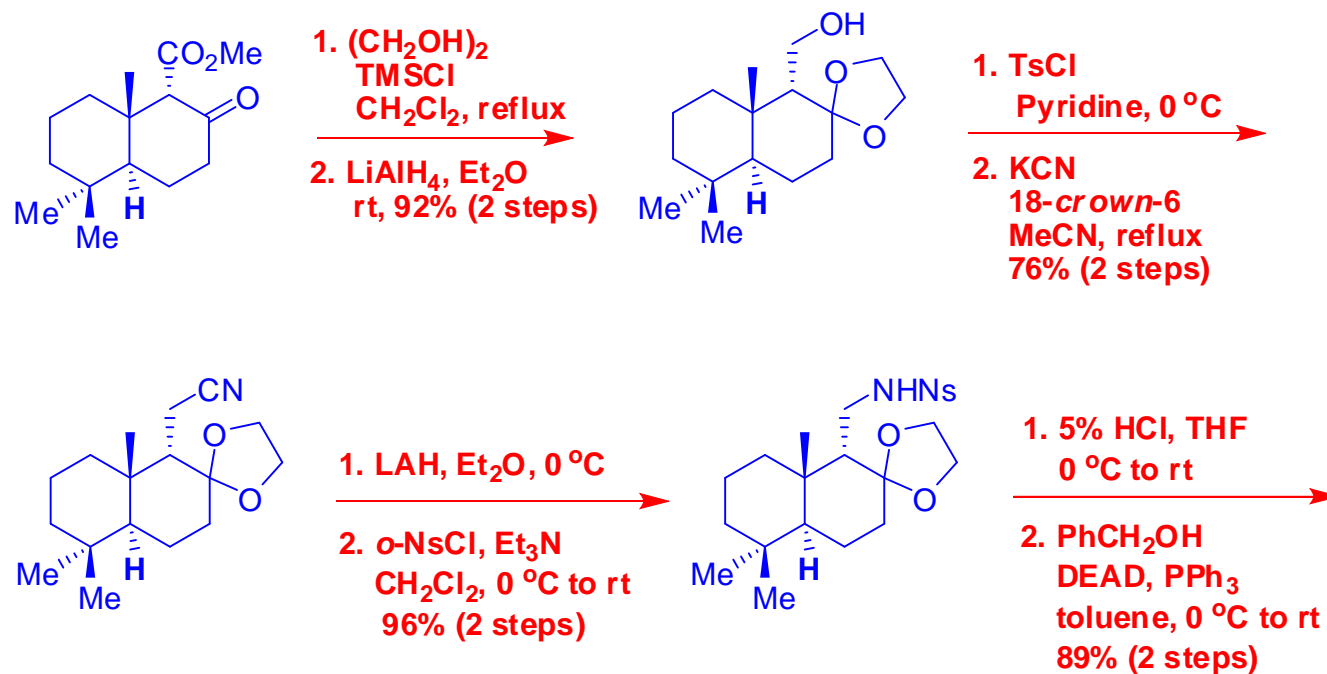


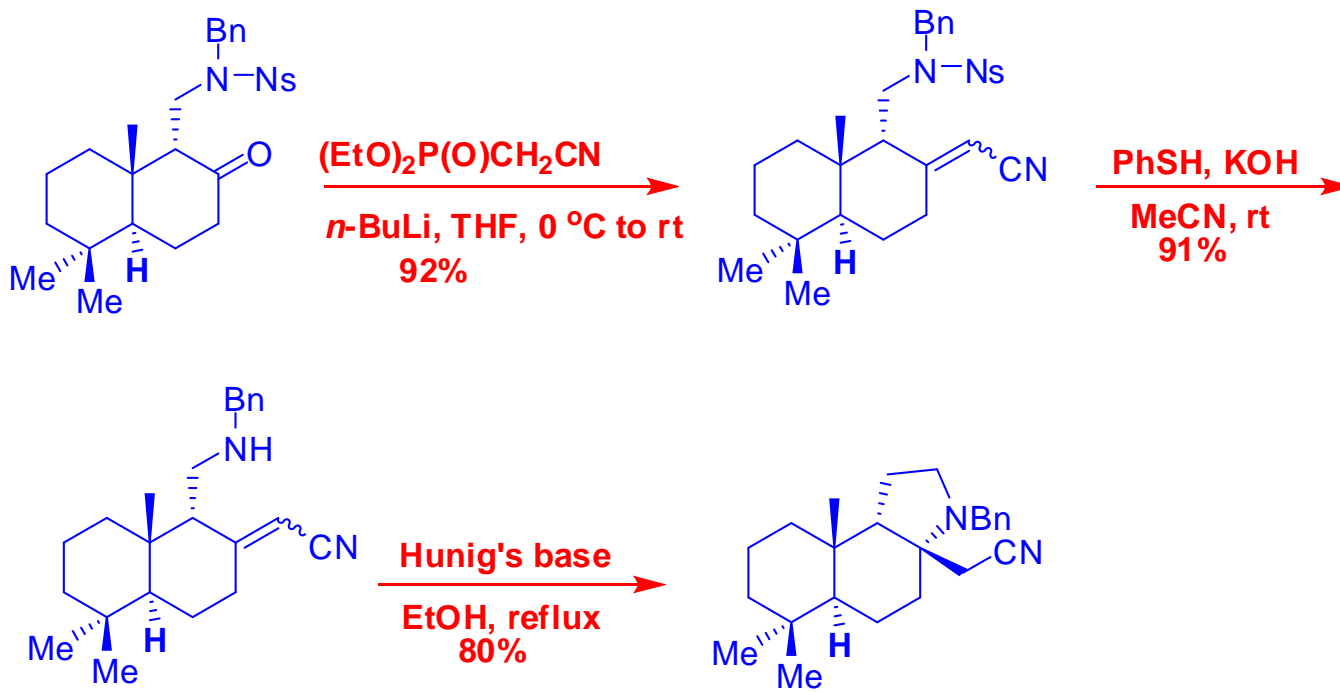
Aoyagi's strategy for the total synthesis of chamobtusin A

Retrosynthetic Analysis:

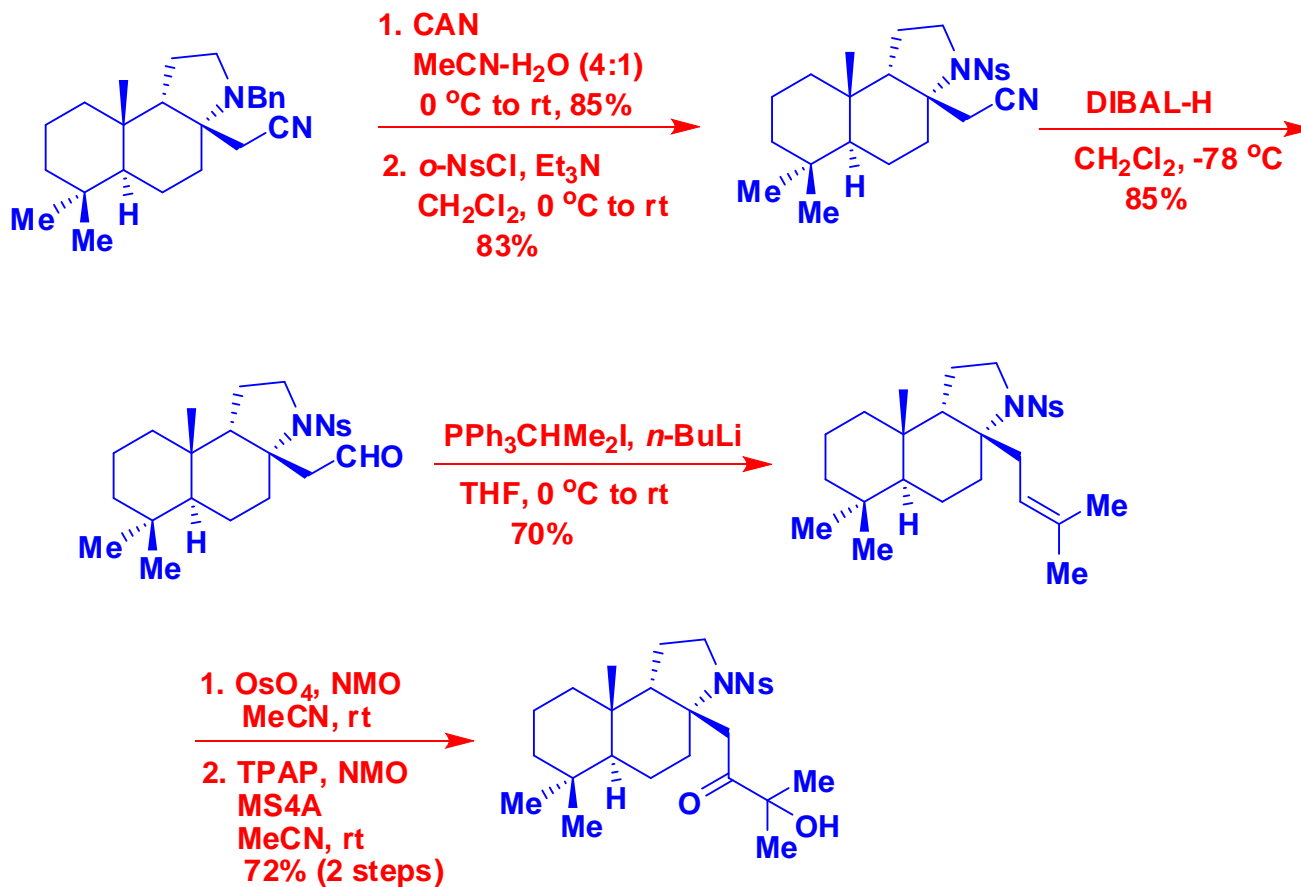


Synthesis of perhydrobenzoindole:

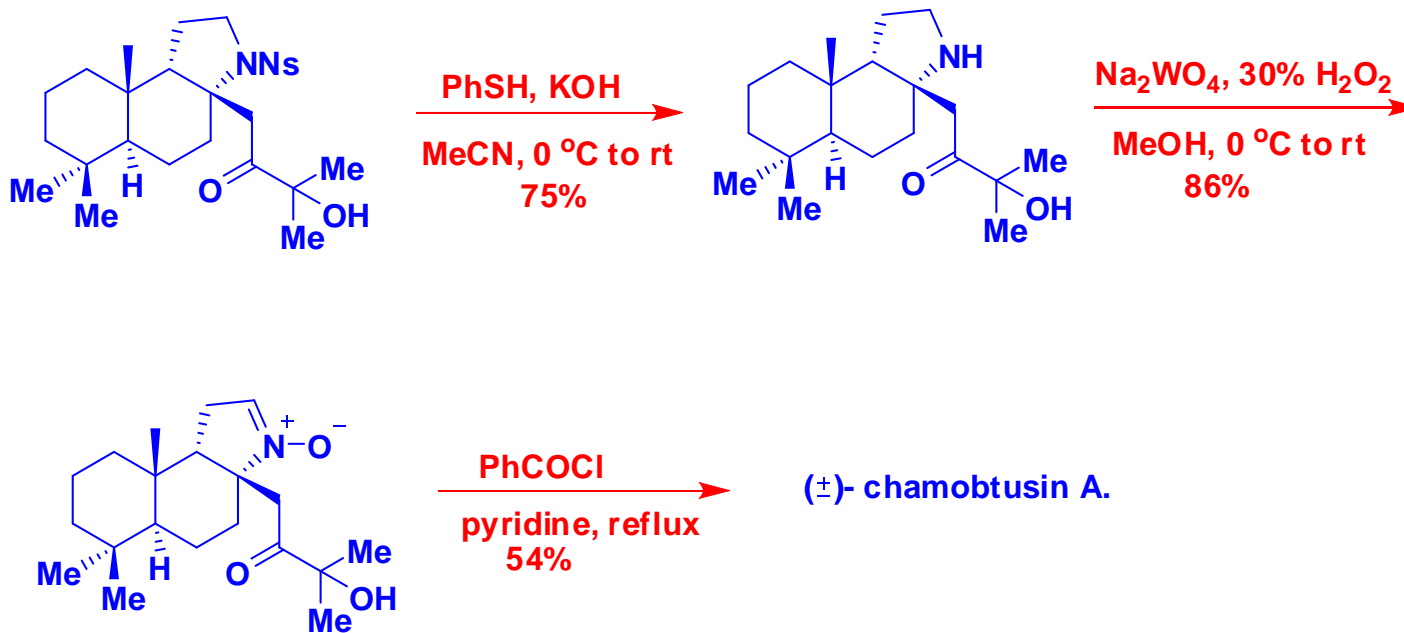




Construction of the C-8 side chain:

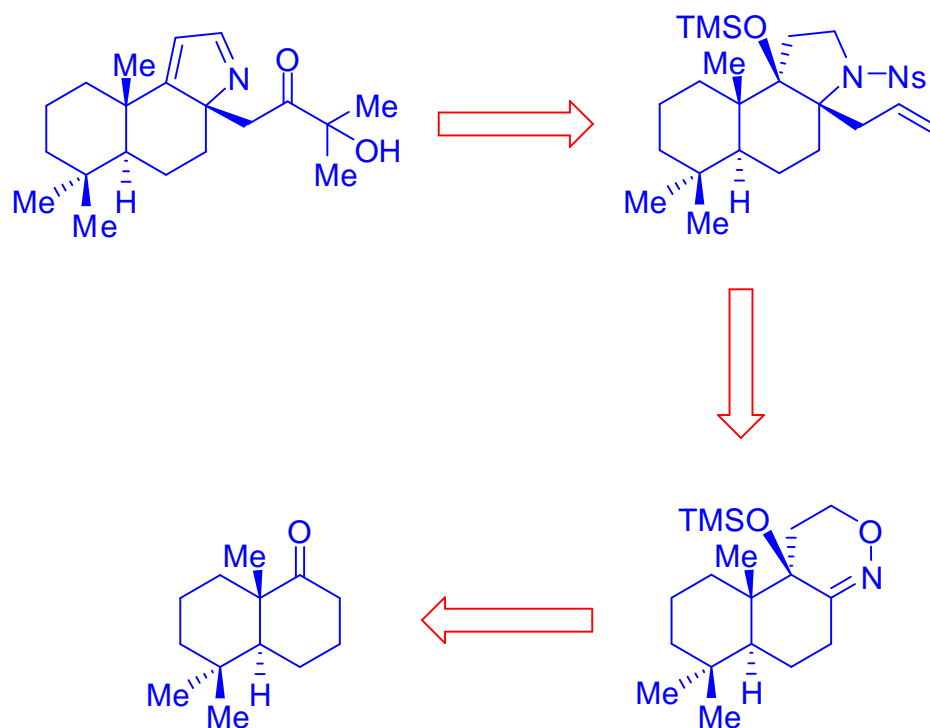


Synthesis of chamobtusin

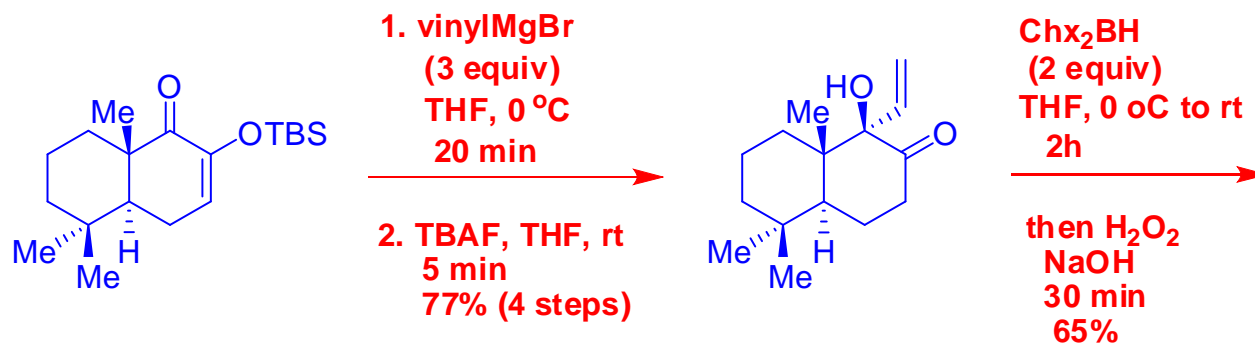
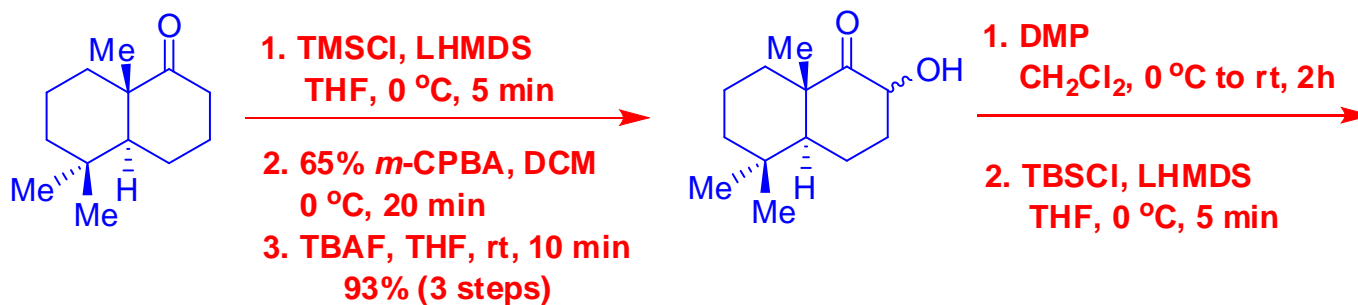


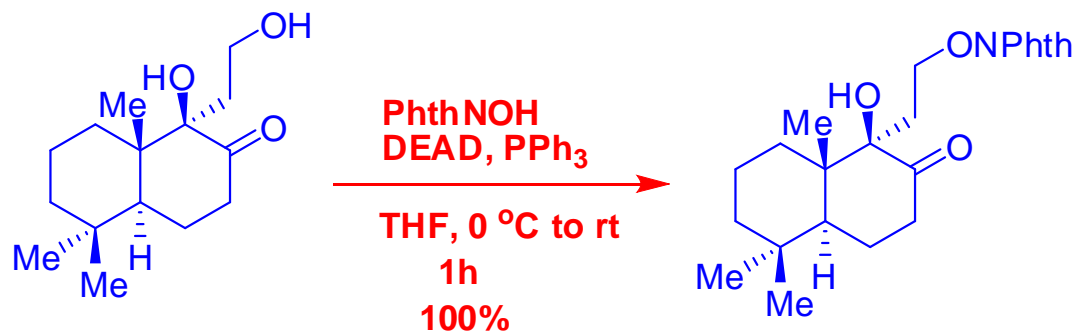
Aoyagi's strategy for the total synthesis of (-)- chamobtusin A

Retrosynthetic Analysis for Chamobtusin A

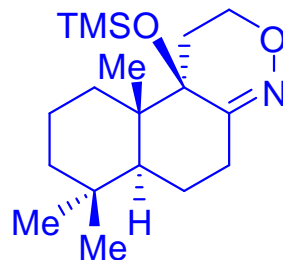


Preparation of 1,2-Oxazine

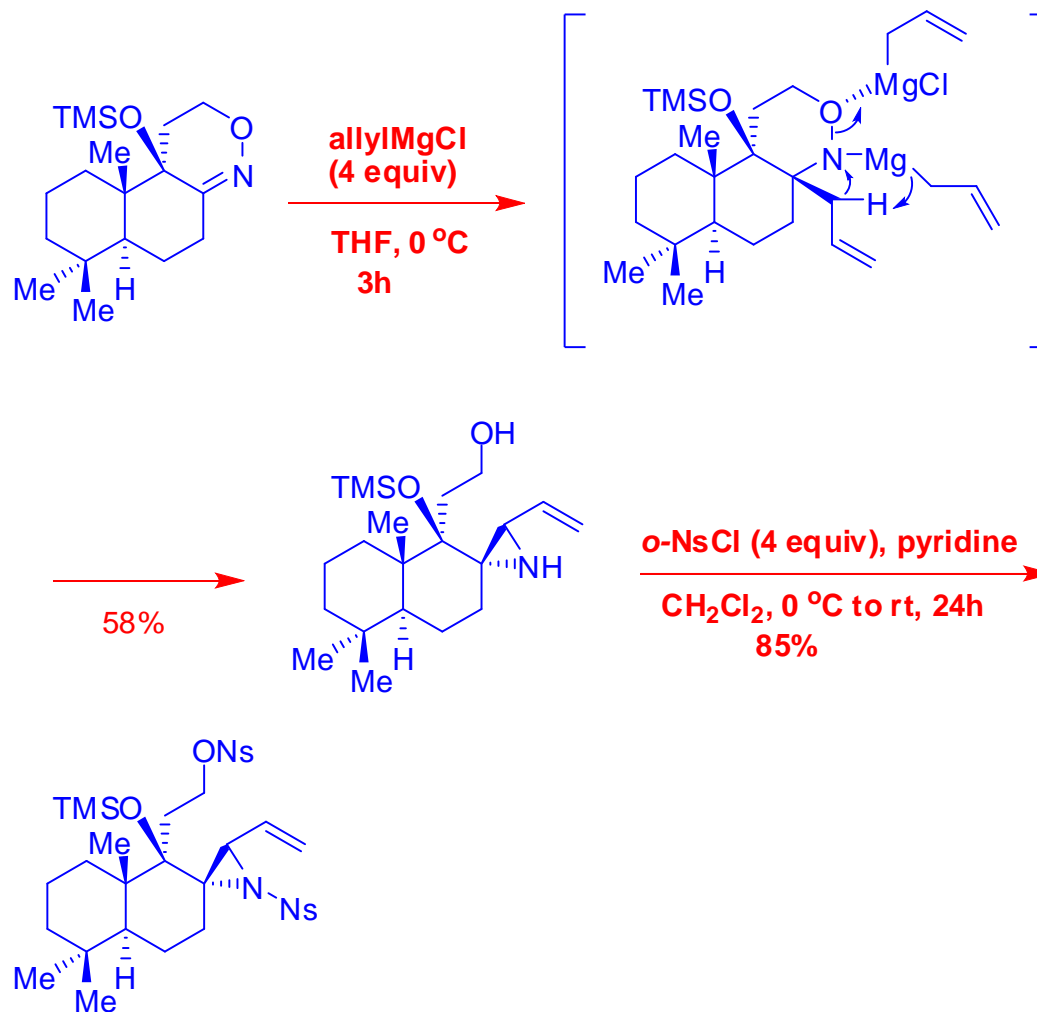




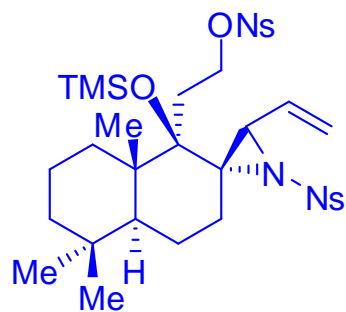
1. NH₂NH₂·H₂O
CHCl₃, rt, 20 min
2. CH₃CO₂H, EtOH
reflux, 12 h
3. TMSOTf, 2, 6-lutidine
CH₂Cl₂, 0 °C, 5 min
84%



Formation of Vinylaziridine Derivative

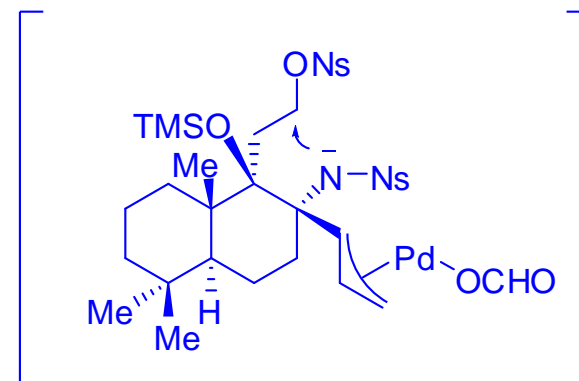


Synthesis of Perhydrobenzoindeole

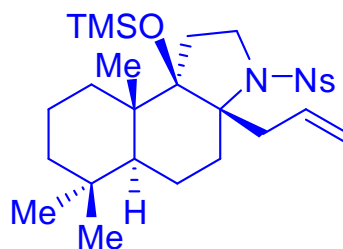


$\text{Pd}_2(\text{dba})_3\text{CHCl}_3$ (0.04 equiv)
 PPh_3 (0.1 equiv), HCO_2H (4 equiv)

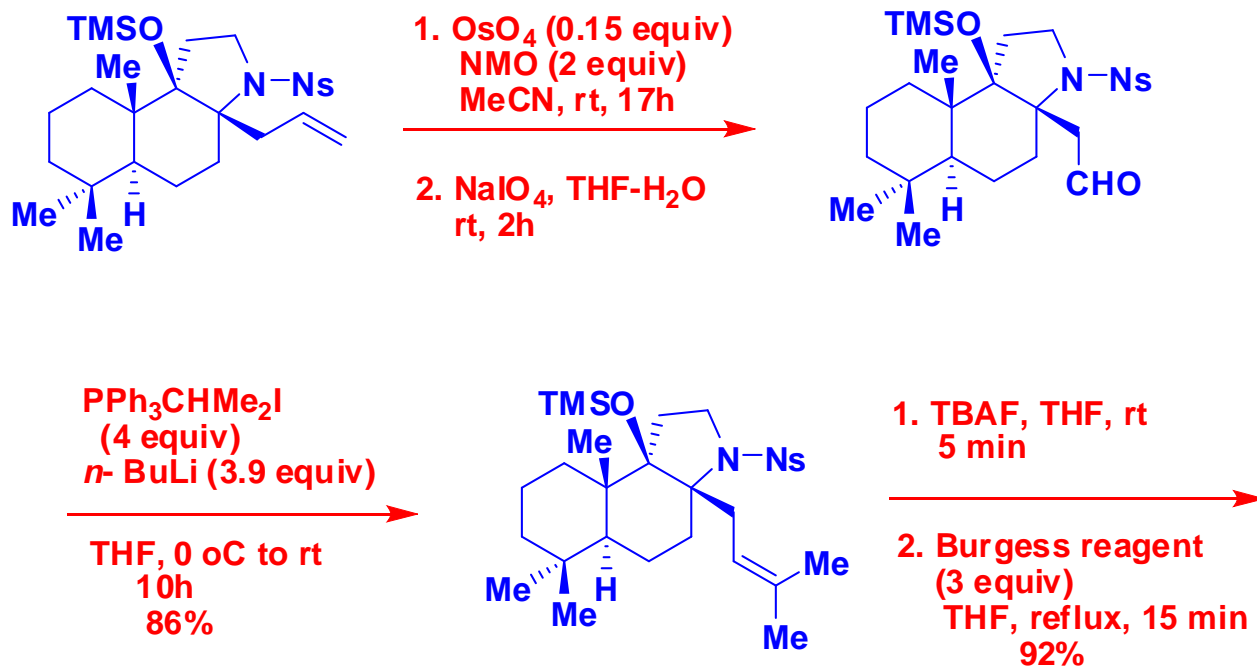
Et_3N , THF, rt, 20 h

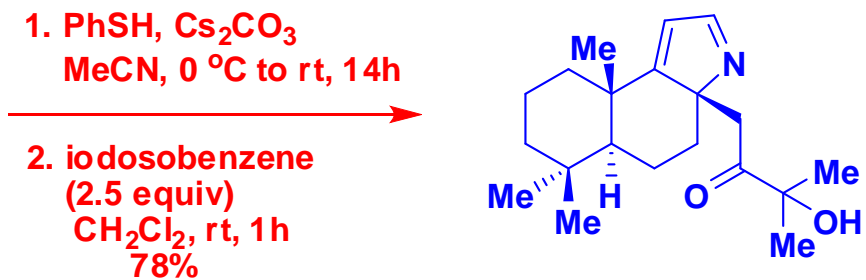
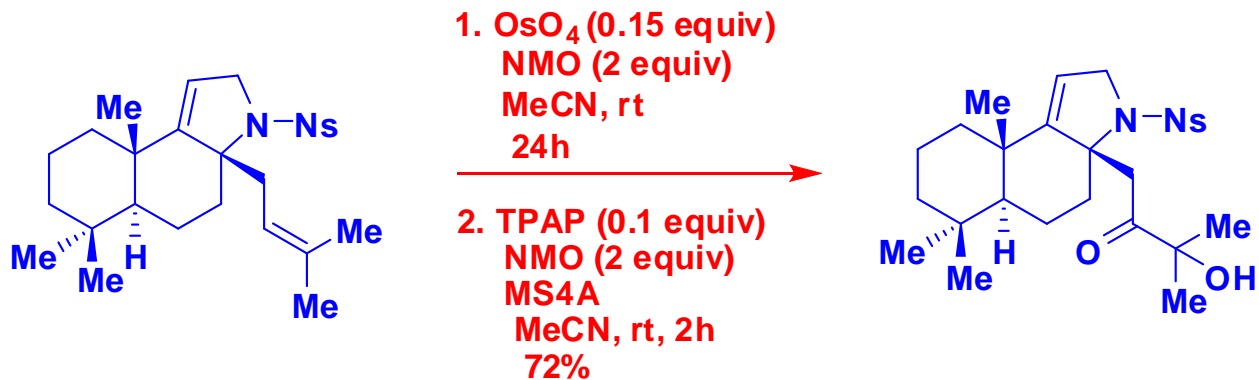


92%



Synthesis of (-)-Chamobtusin A





(-)- Chamobtusin A

Key features:

1. Novel aziridine formation from the corresponding 1,2-oxazine derivative
2. Palladium-mediated annulations of the vinylaziridine derivative

Conclusion:

1. Watanabe synthesized chamobtusin A in 13 steps with 5.3% overall yield
2. Aoyagi synthesized this molecule both optically active and racemic forms