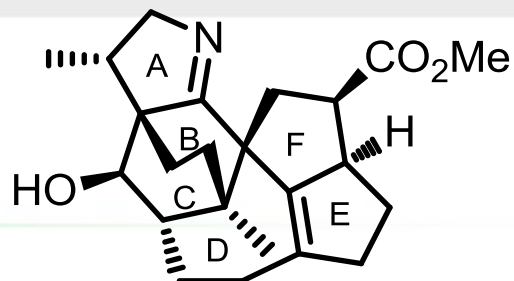
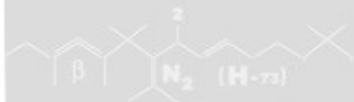
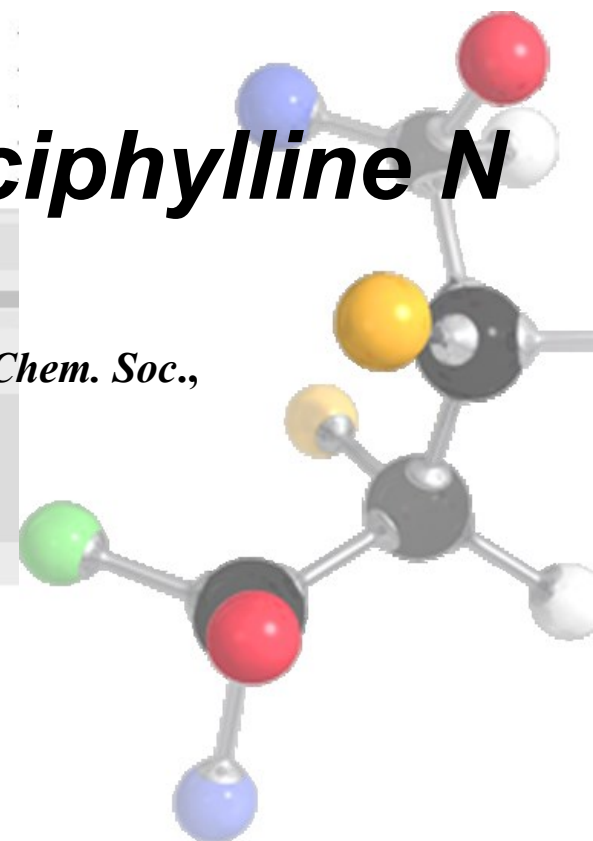


Total Synthesis of (-)-Calyciphylline N

Artem Shvartsbart and **Amos B. Smith, III** *J. Am. Chem. Soc.*,
DOI: 10.1021/ja411539w

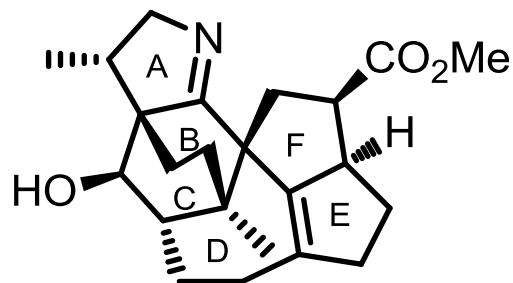


(-)-Calyciphylline N (1)



Current literature
Gong Xu
16.01.2014

About (-)-Calyciphylline N (1)

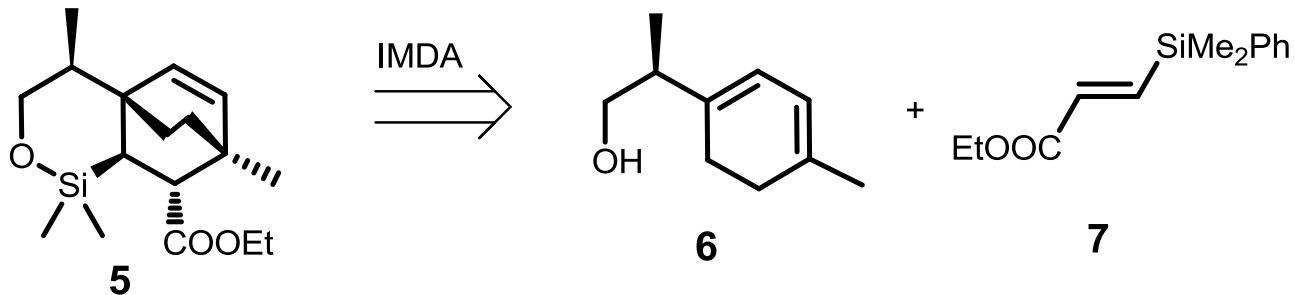
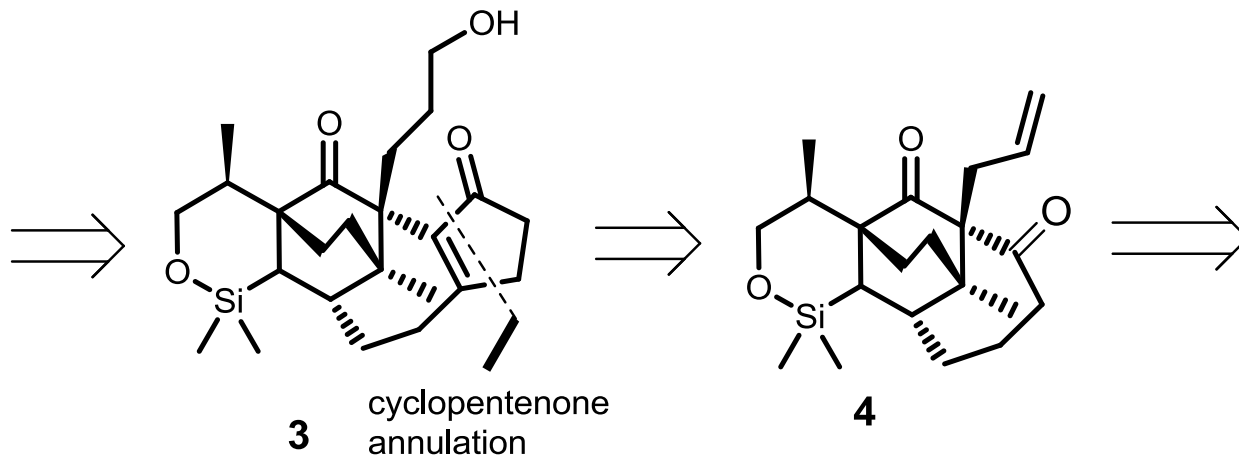
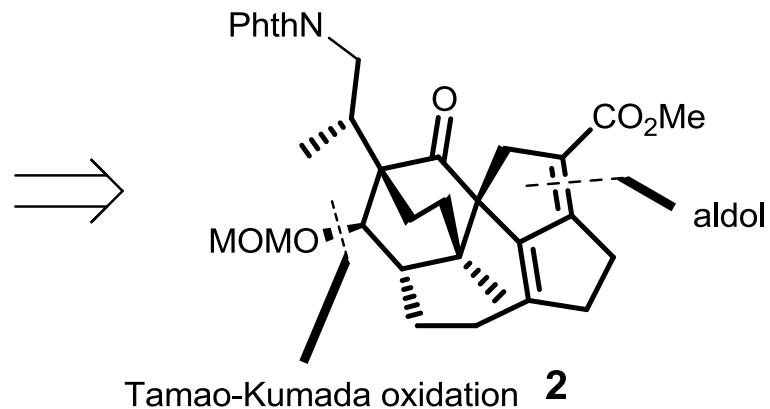
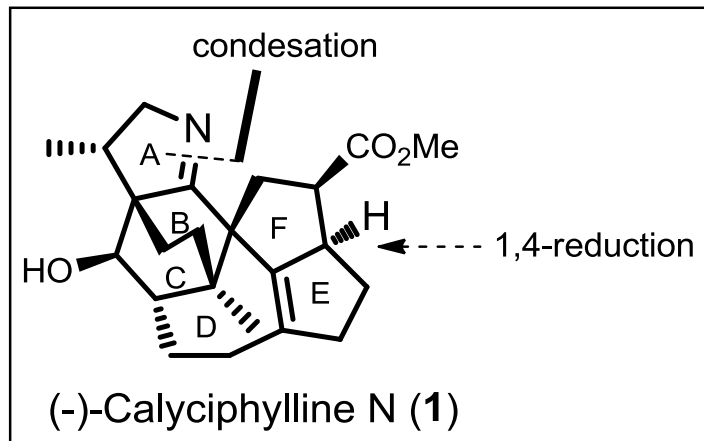


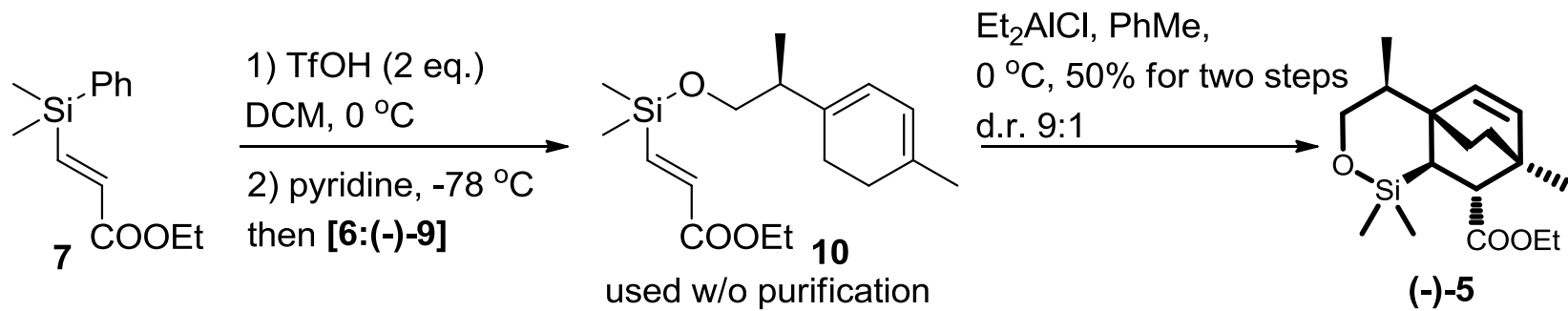
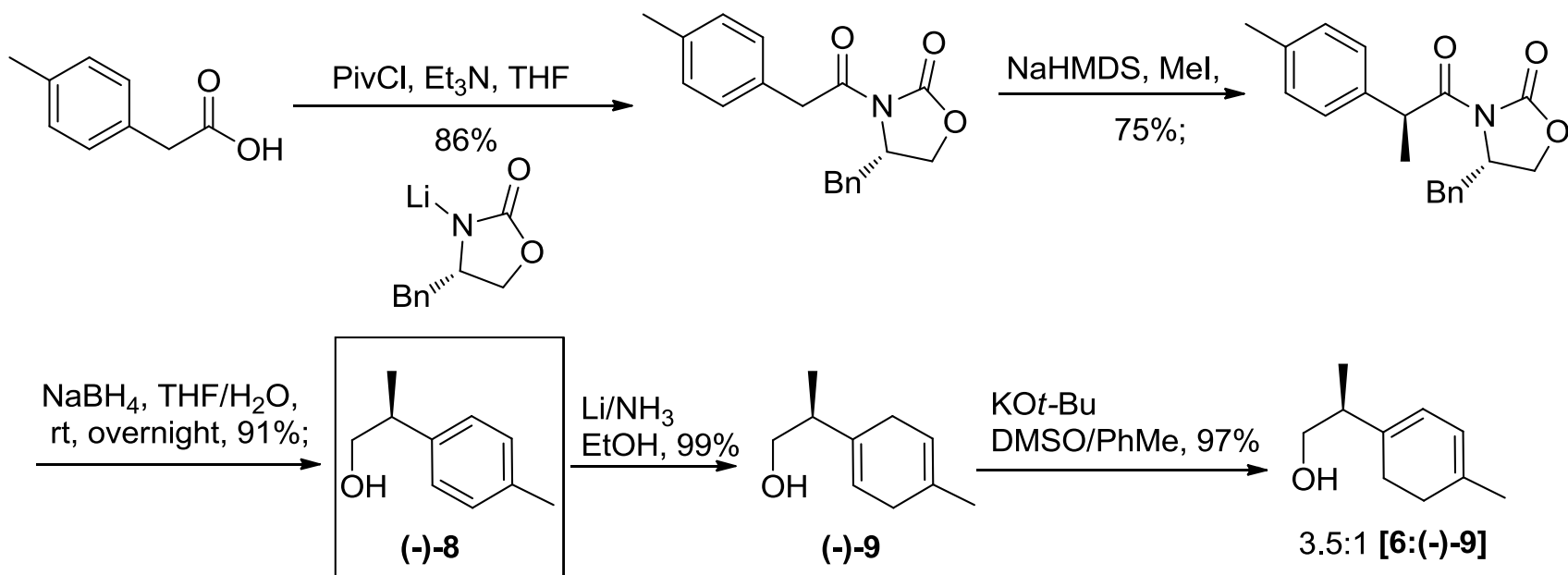
(-)-Calyciphylline N (1)



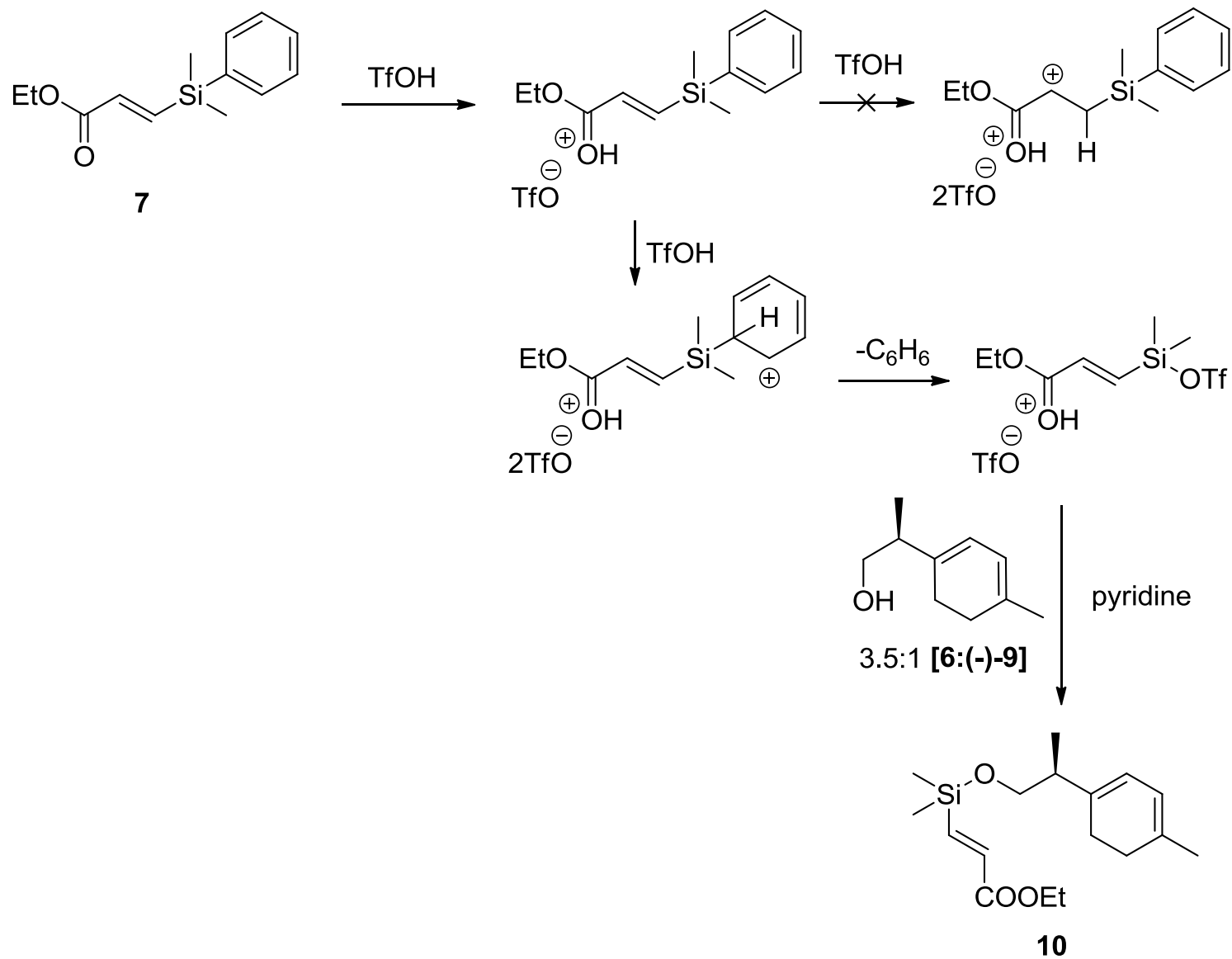
- Isolated from the leaves and stems of *Daphniphyllum calycinum* in 2008.
- The biological activity has not been investigated.
- **Structural features:**
six contiguous stereogenic centers, three of which are quaternary bridgehead, a fused A ring **dihydropyrrole**, and a DEF **decahydrocyclopentazulene** ring system surrounding a central bicyclo[2.2.2]octane BC core.

Retrosynthesis

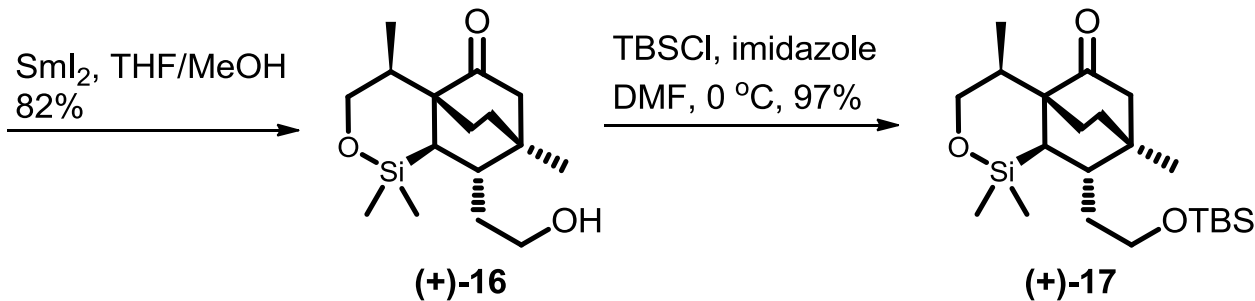
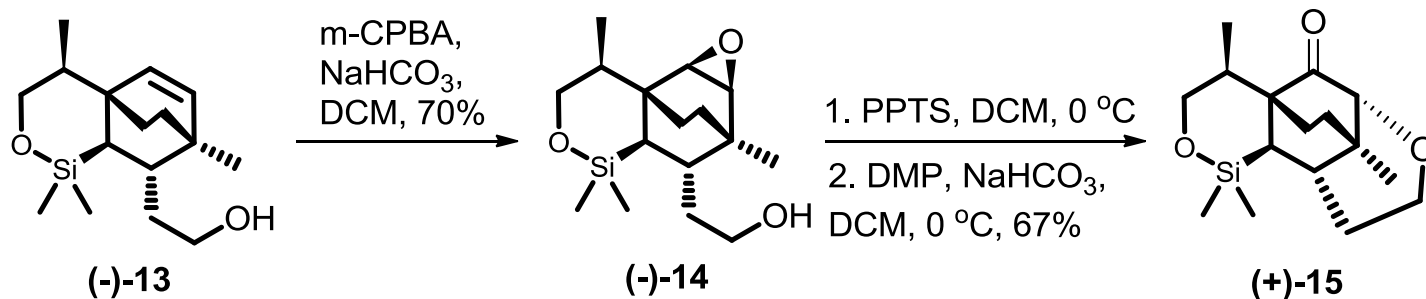
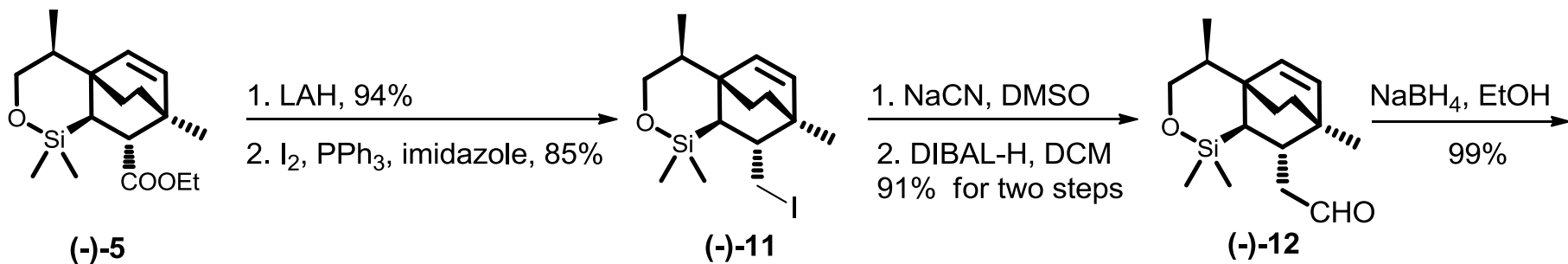




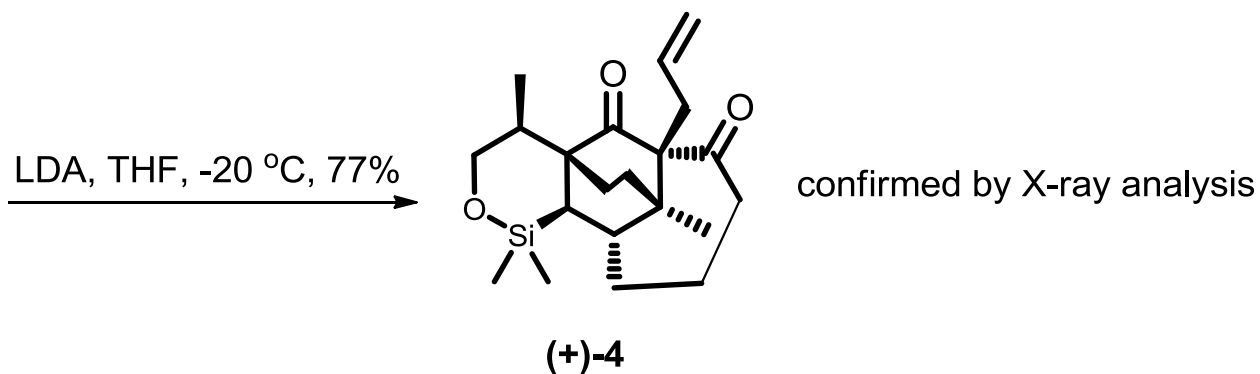
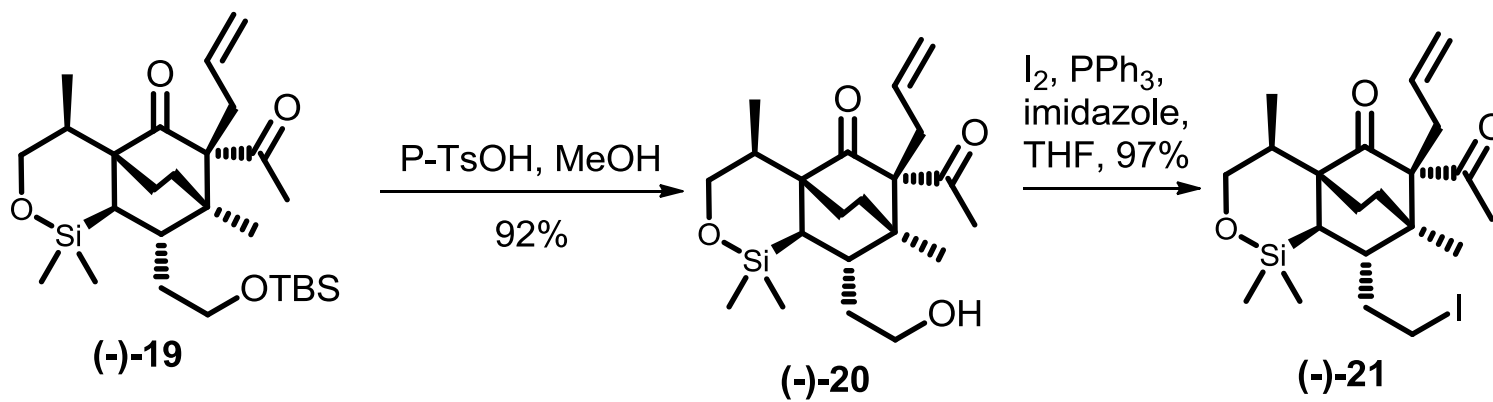
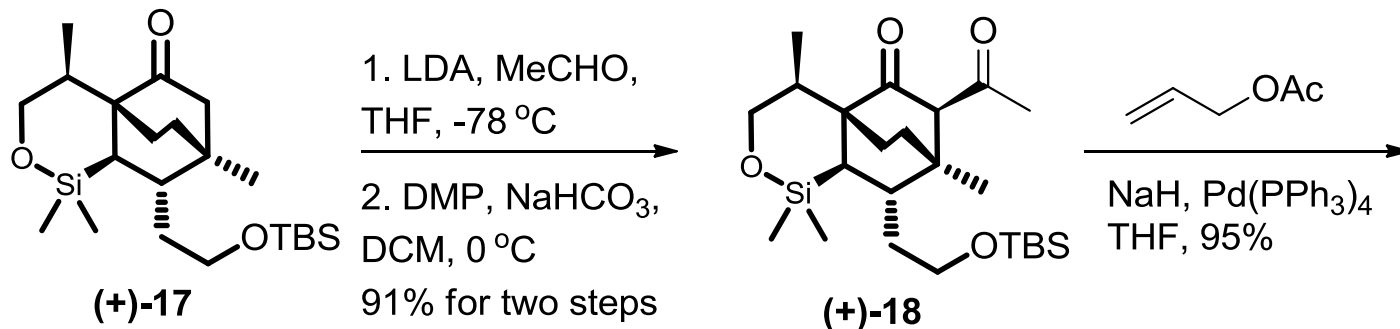
Synthesis of silyl ether **10** from silyl acrylate **7**

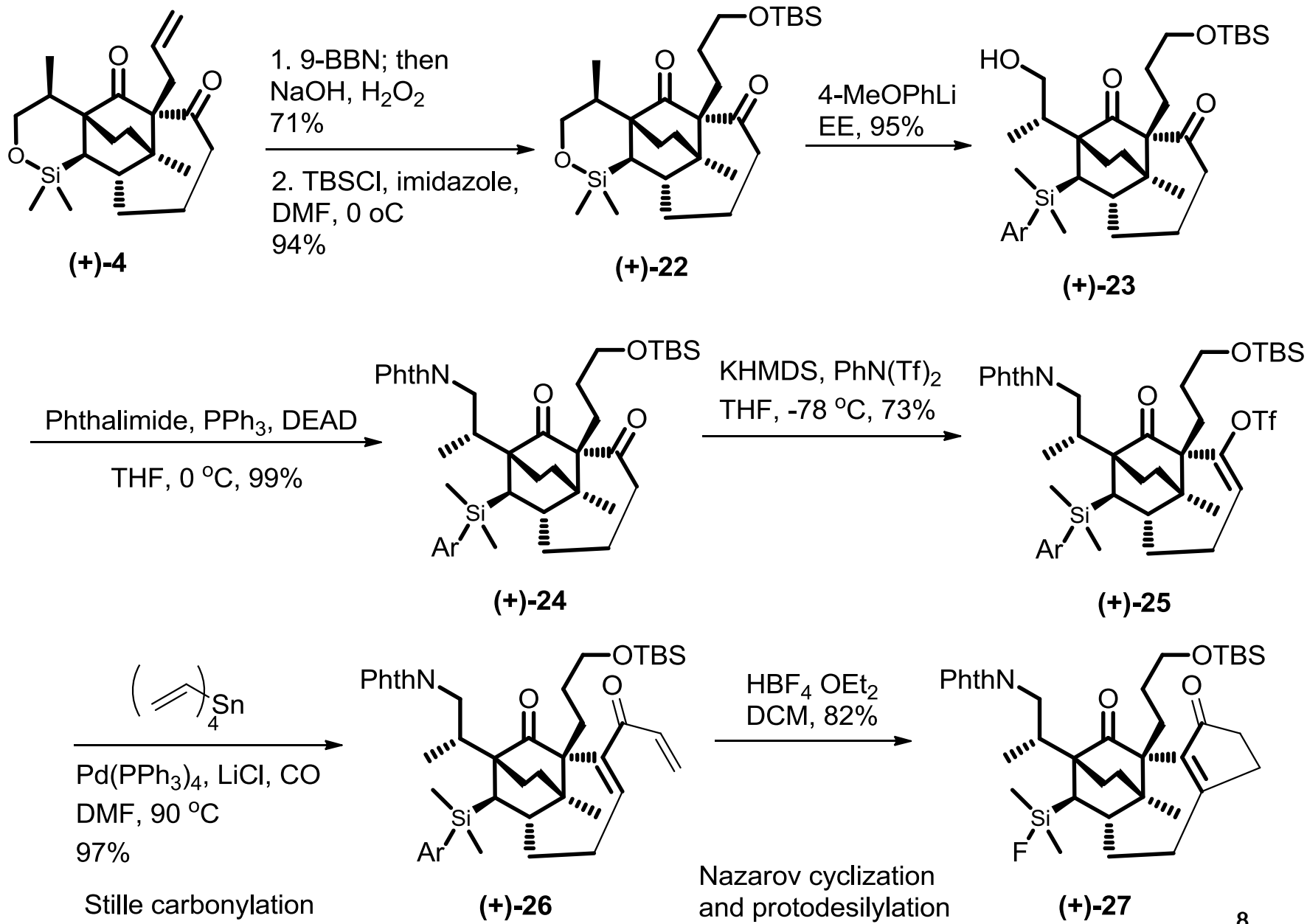


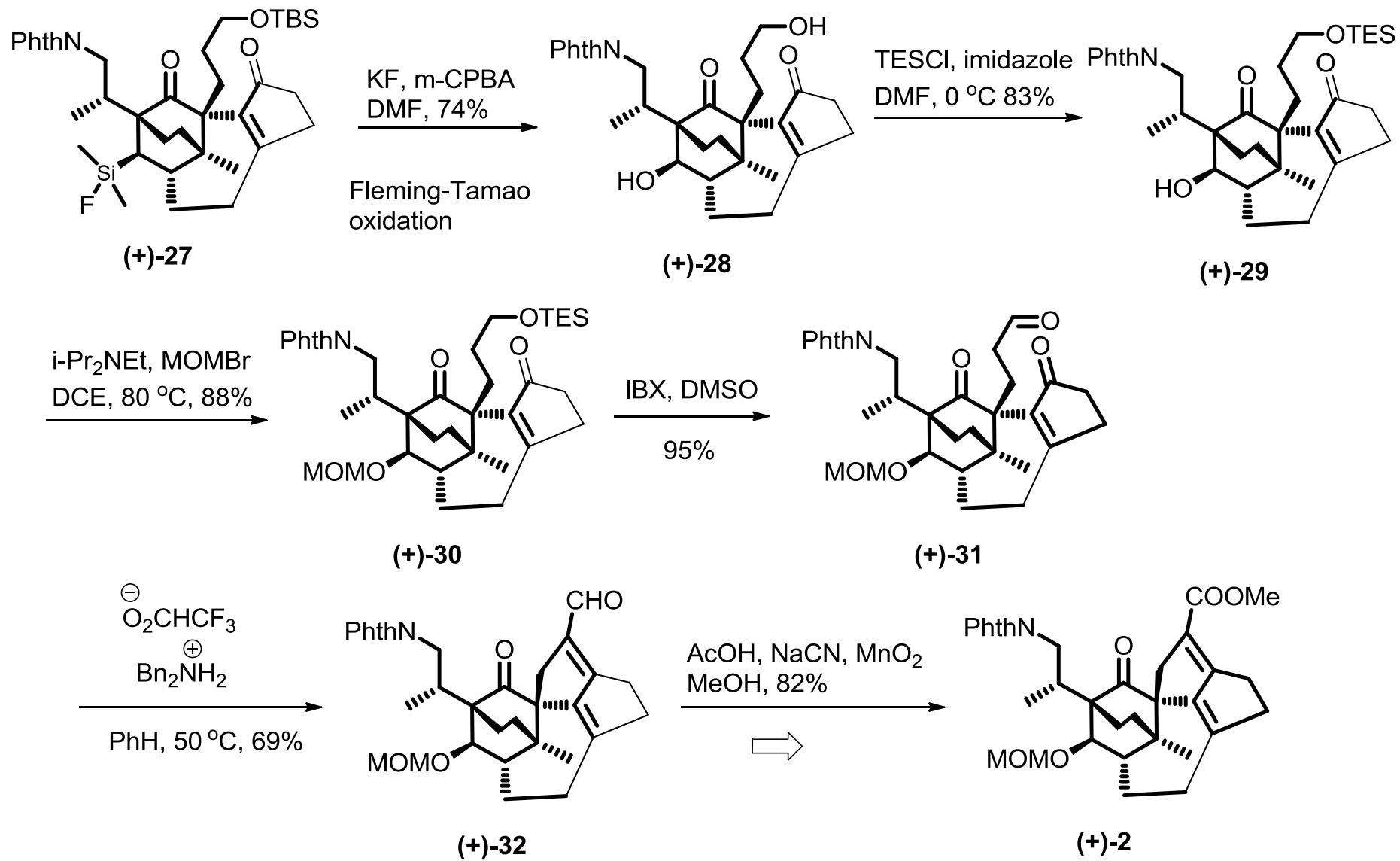
Installation of the C1 ketone

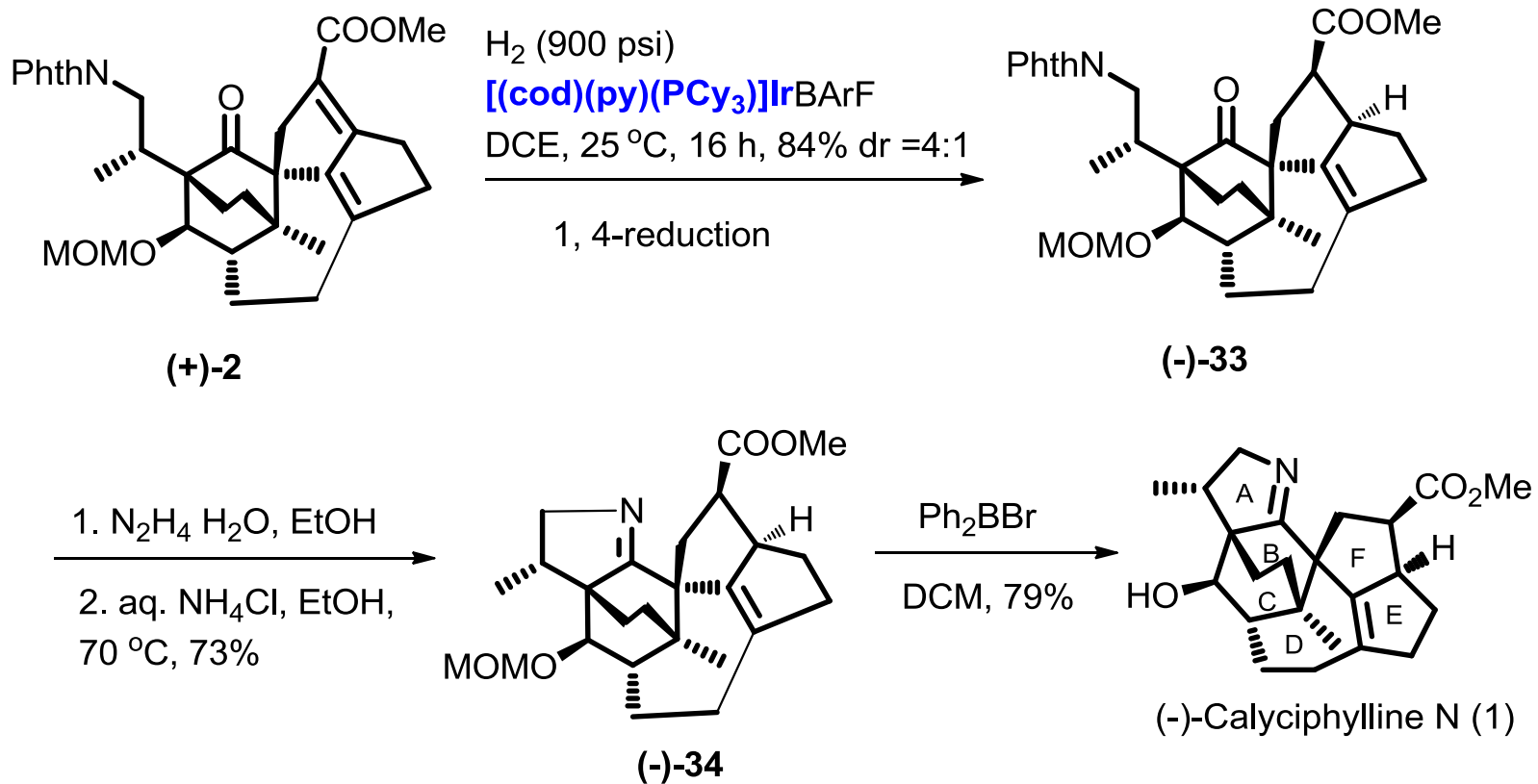


Construction of ring D

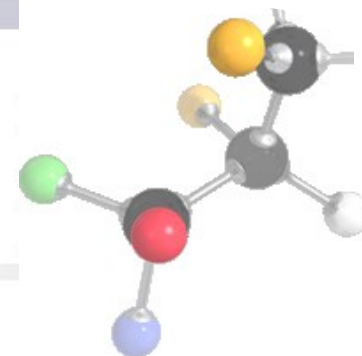








Summary



- The first total synthesis of a member of the calyciphylline alkaloids, (–)-calyciphylline N (1), has been achieved with a longest **linear sequence** of 37 steps from known alcohol (–)-8.
- **Highlights of the synthesis include:**
- a Et_2AlCl -promoted, highly stereoselective, substrate-controlled intramolecular **Diels–Alder reaction**;
- a transannular enolate alkylation;
- an effective **Stille carbonylation/Nazarov cyclization sequence**;
- a high-risk **diastereoselective hydrogenation** of a fully substituted conjugated diene ester.