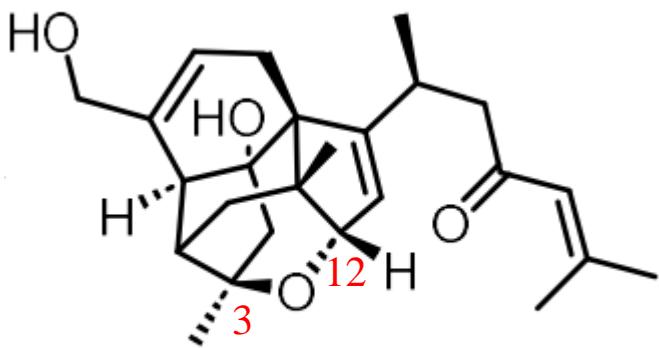
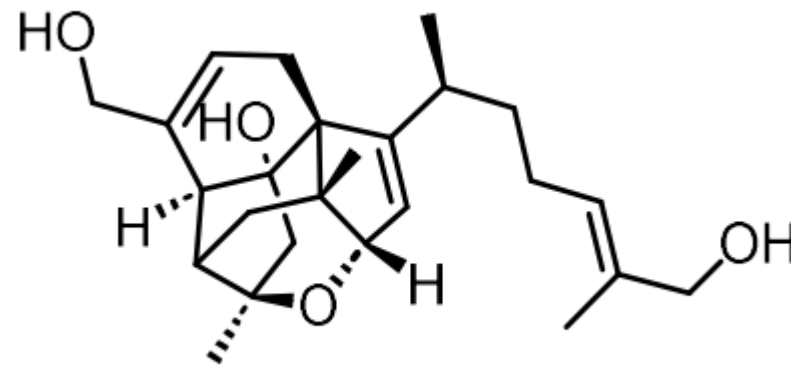


Bioinspired Total Synthesis of Bipolarolides A and B

Bo Li⁺, Chuanzhen Tan⁺, Tianhao Ma and Yanxing Jia*



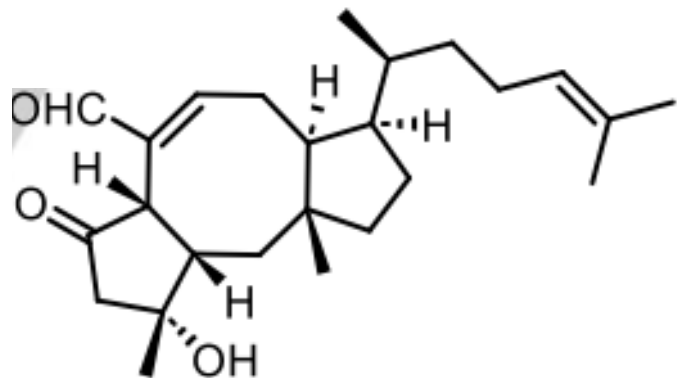
Bipolarolide A (1)



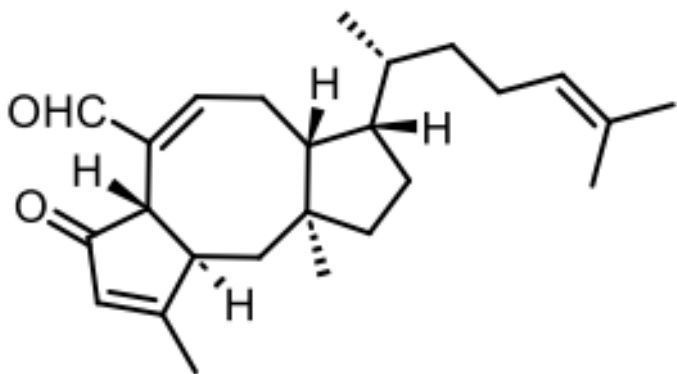
Bipolarolide B (2)

- *Unique 5/6/6/6/5 pentacyclic skeleton*
- *8 stereocenters: 7 contiguous, 2 all-carbon quaternary*
- *C3-C12 oxygen bridge*
- *First total synthesis*

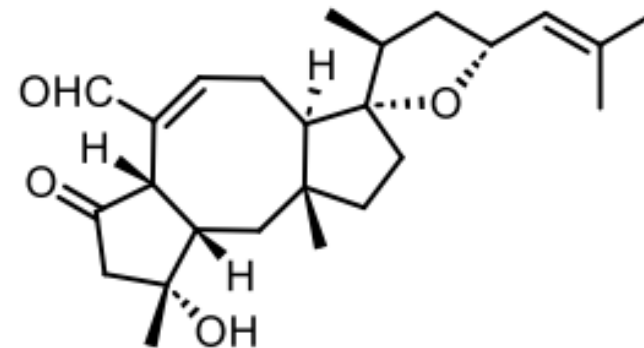
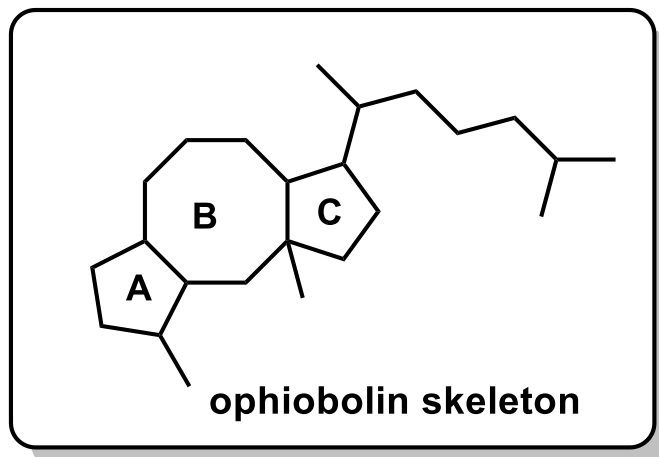
Reported total syntheses of ophiobolins



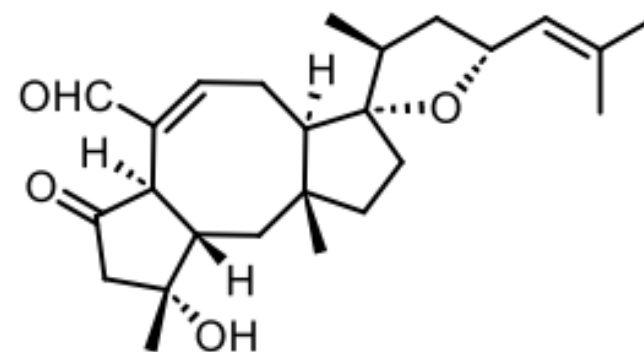
(+)-ophiobolin C (3)
1989, Kishi, 38 steps



(-)-6-*epi*-ophiobolin N (5)
2016, Maimone, 9 steps

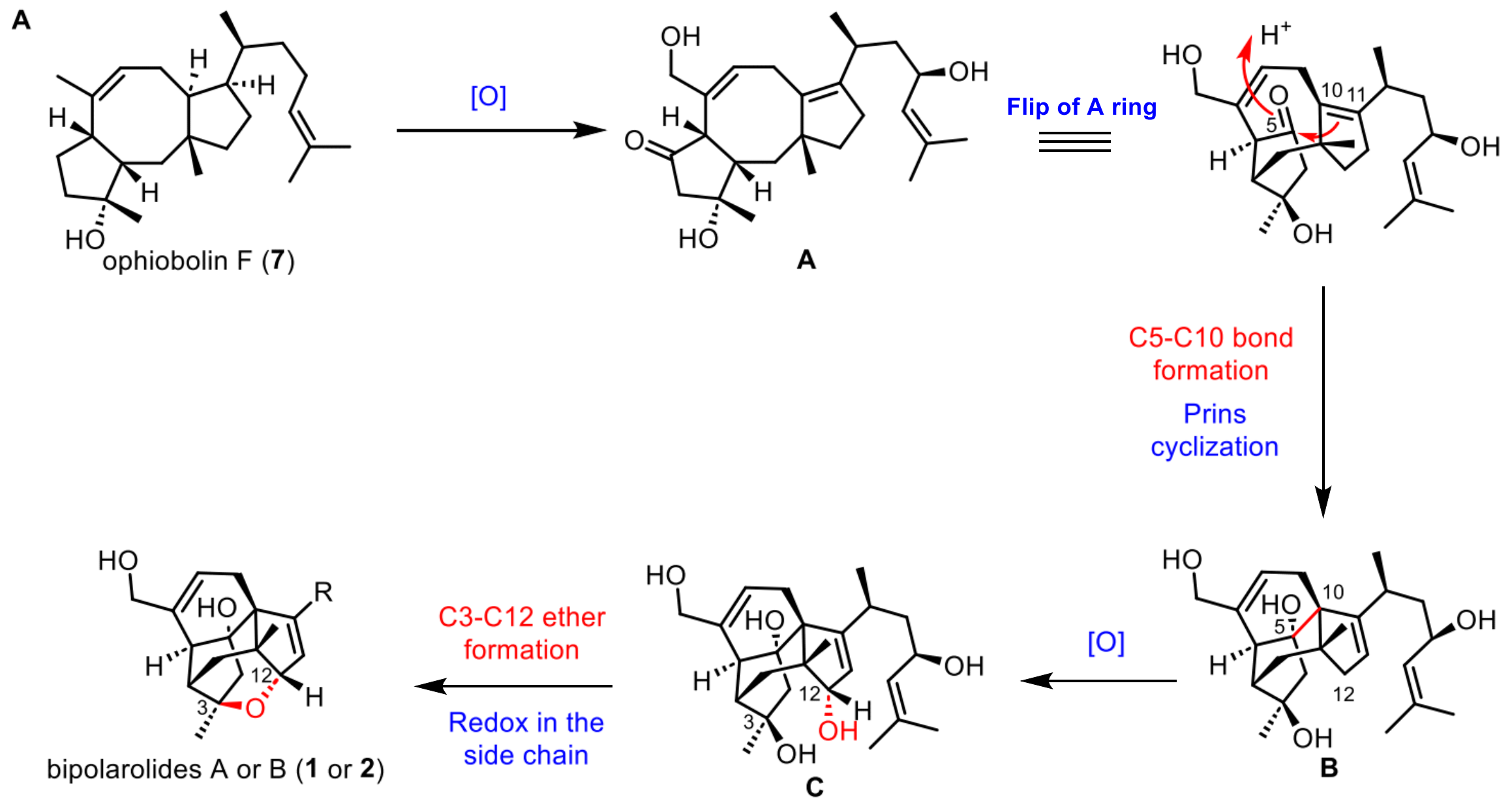


(+)-ophiobolin A (4)
2011, Nakada, 47 steps

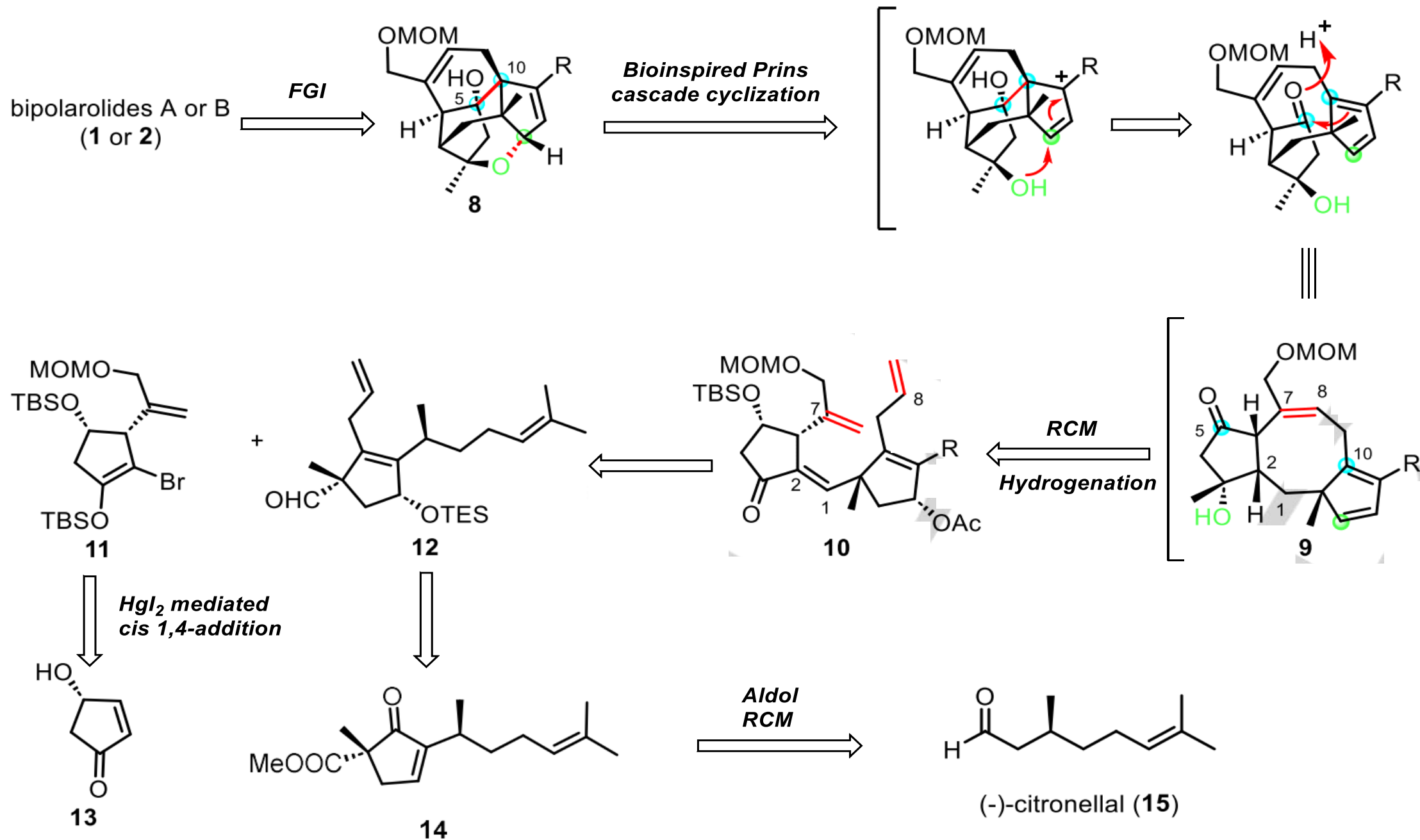


(+)-6-*epi*-ophiobolin A (6)
2019, Maimone, 14 steps

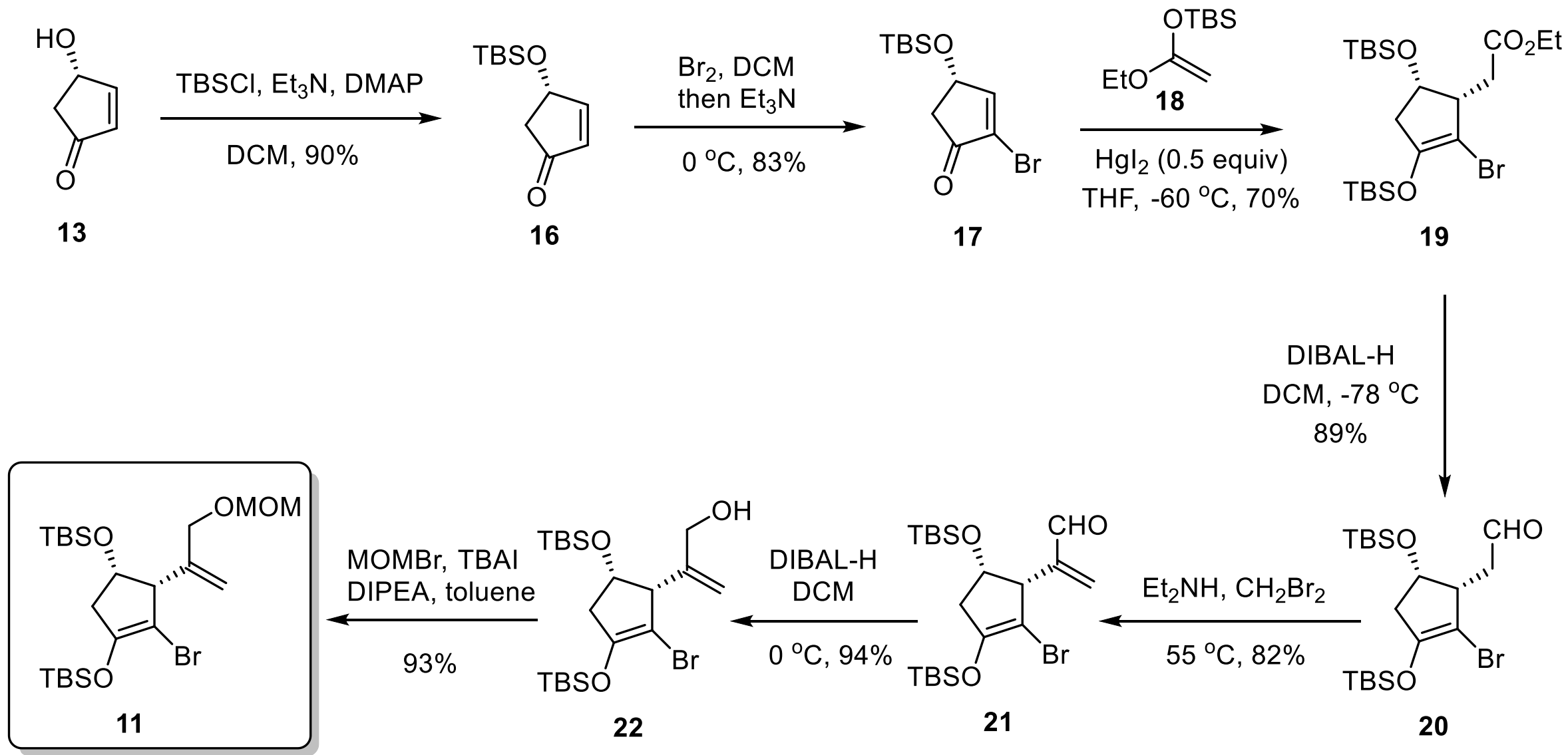
Putative biosynthetic pathway leading to bipolarolides A (1) and B (2) from ophiobolin F (7)



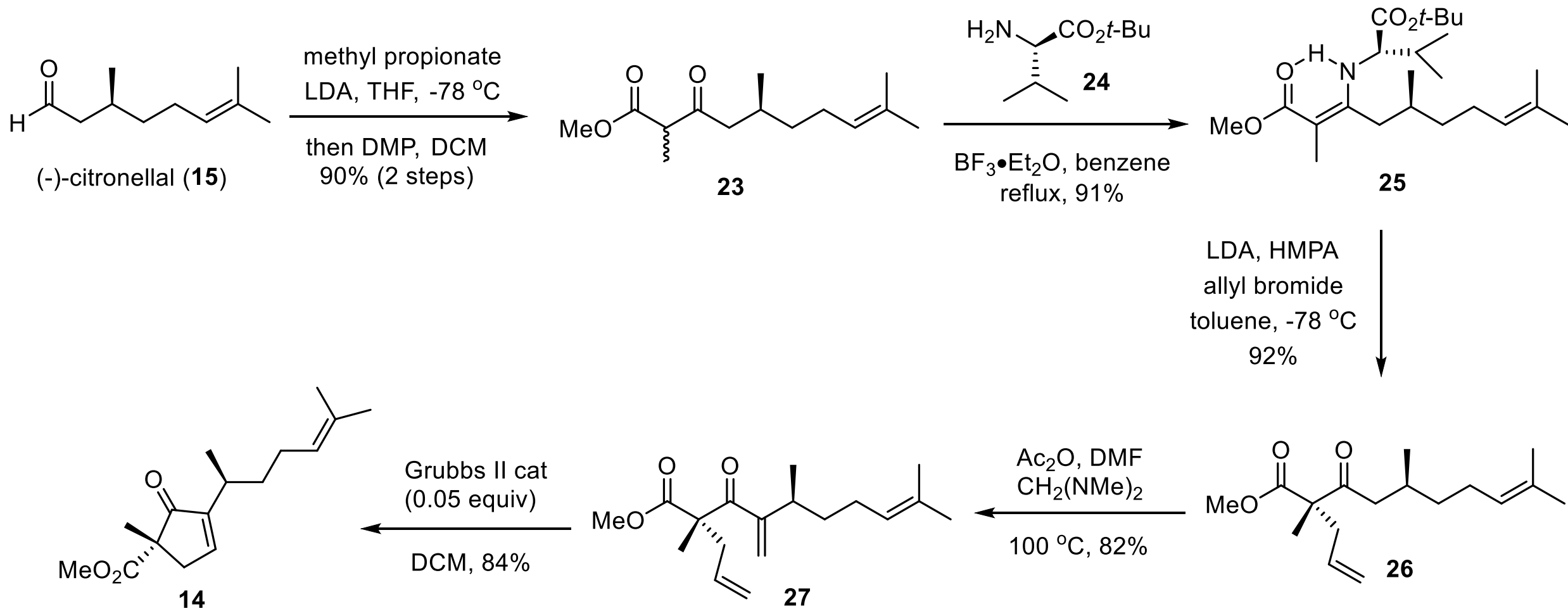
Retrosynthetic analysis



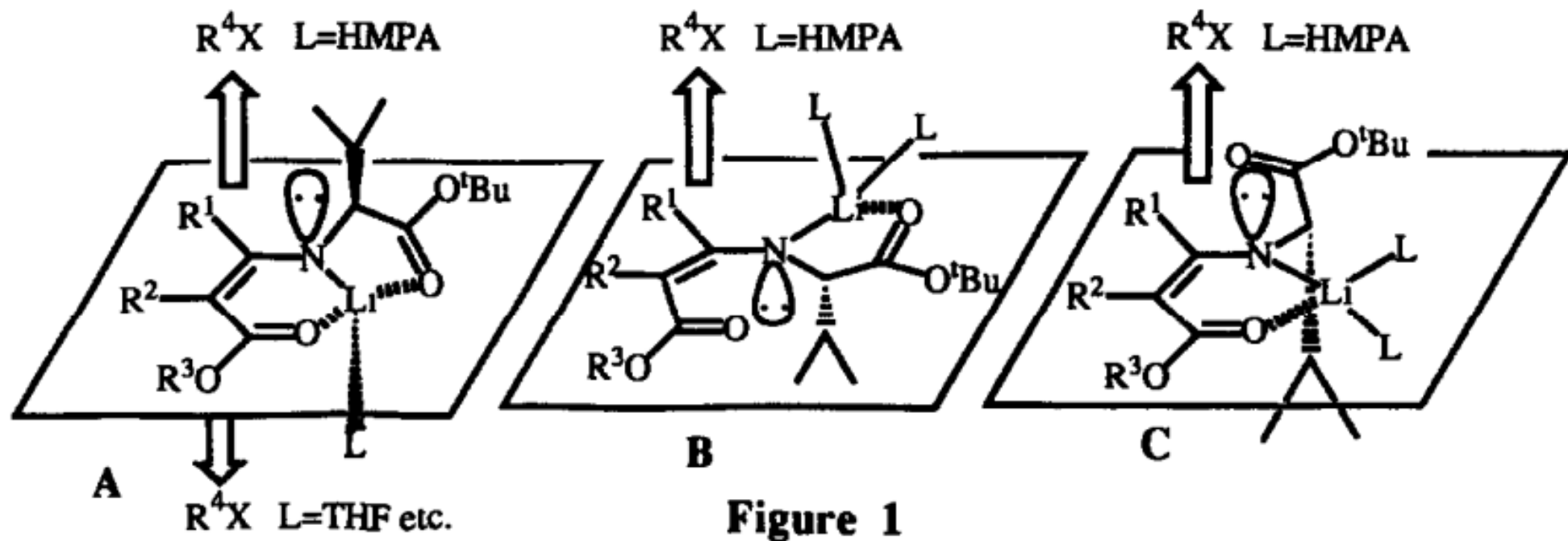
Synthesis of alkenyl bromide 11



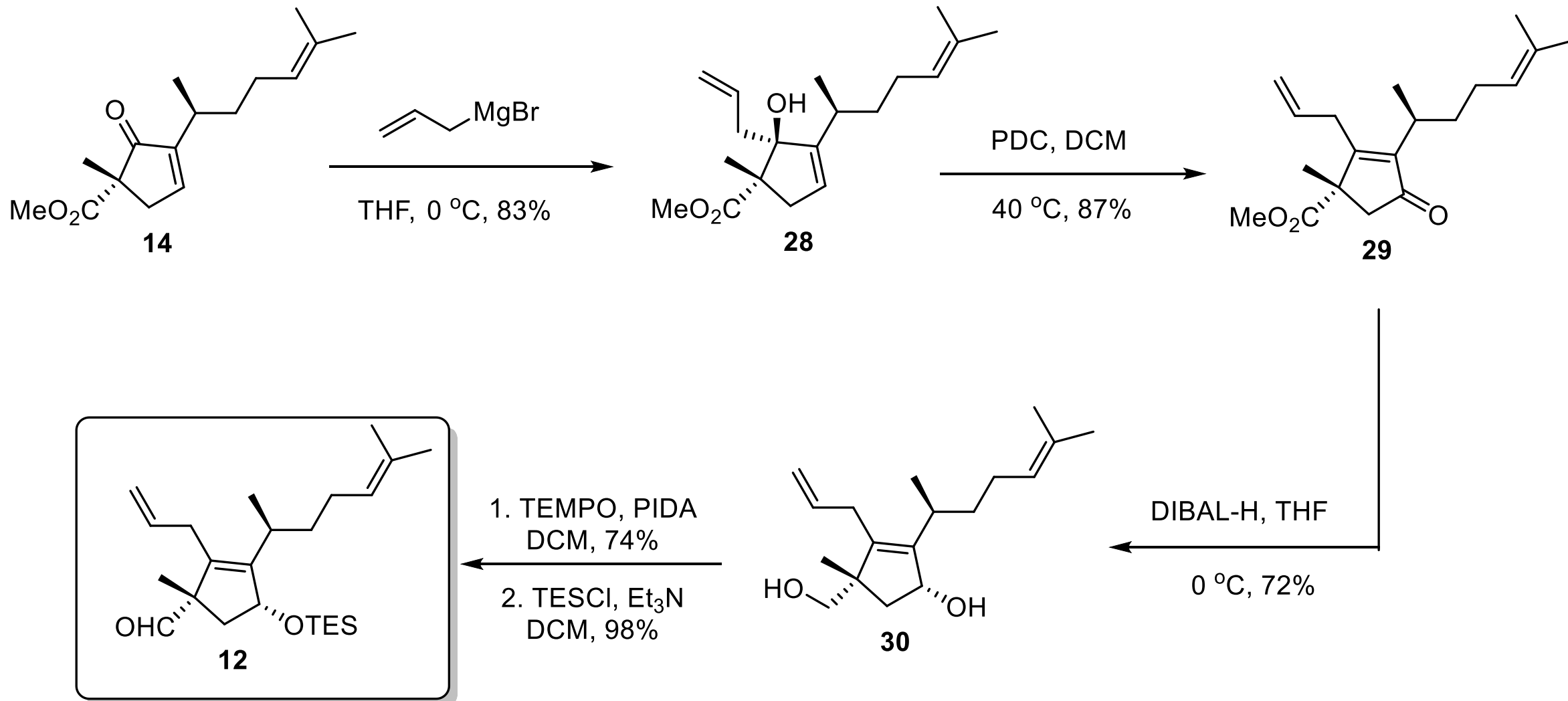
Synthesis of aldehyde 12



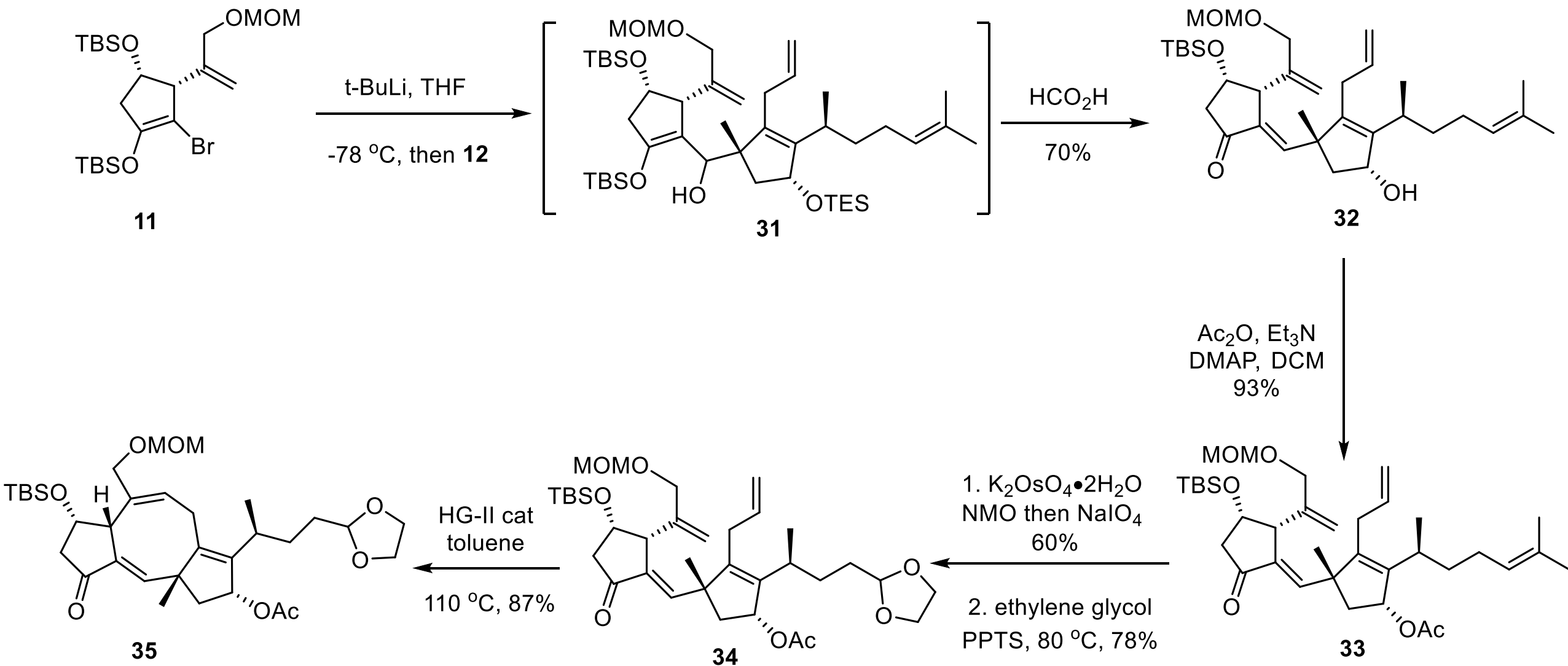
Asymmetric alkylation of α -alkyl β -keto esters



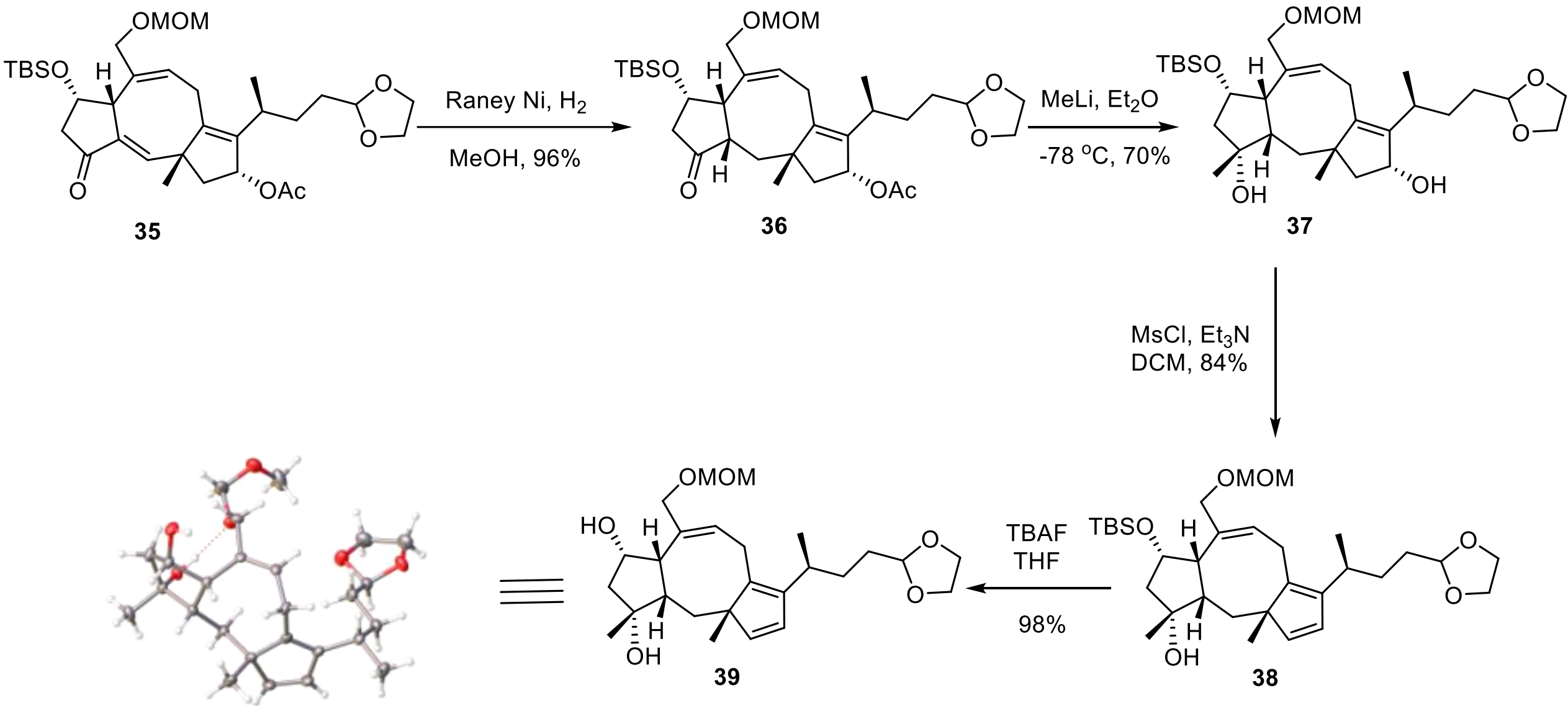
Synthesis of aldehyde 12



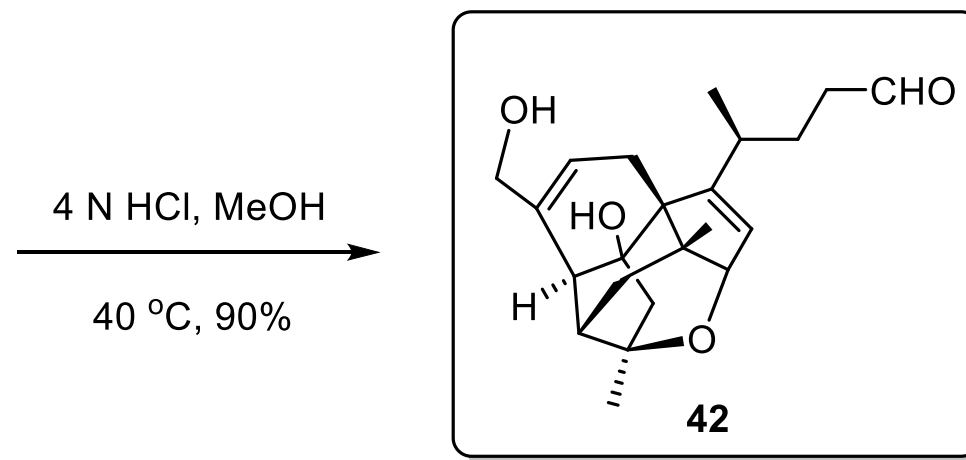
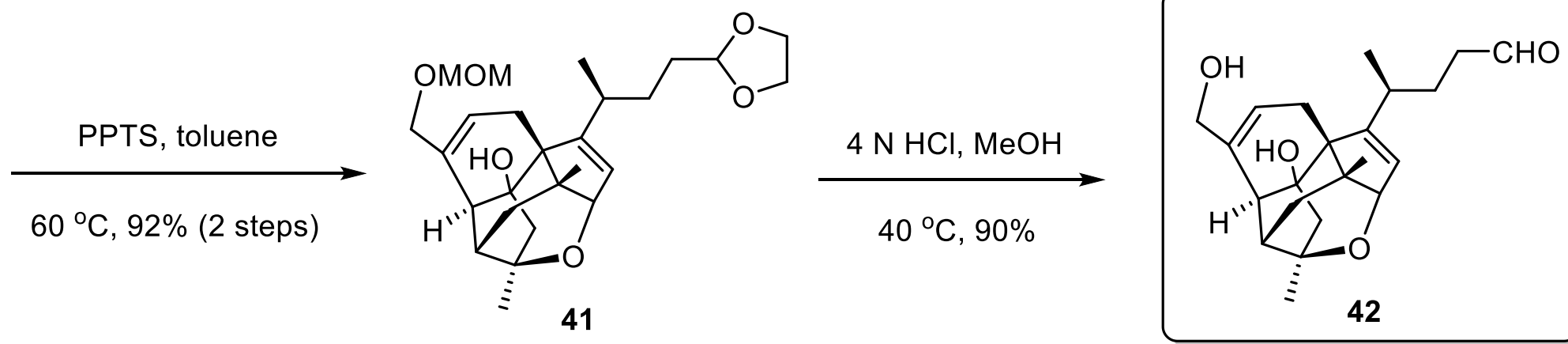
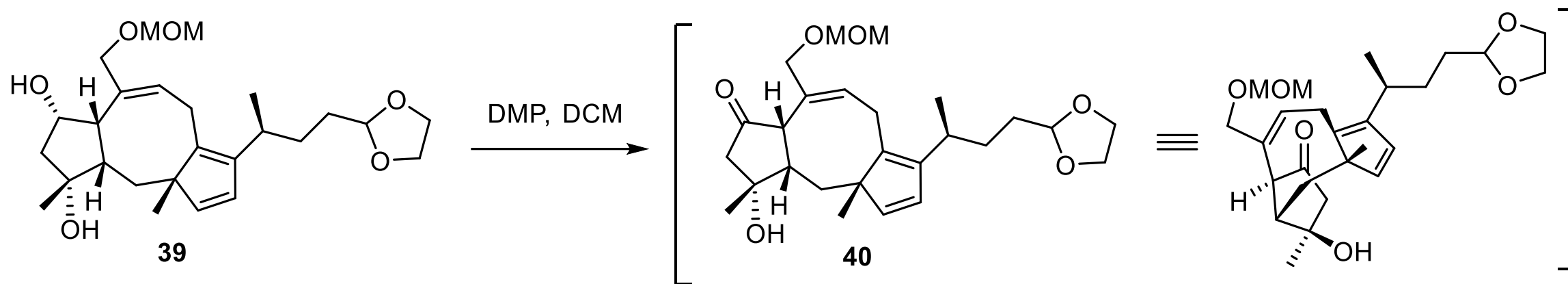
Synthesis of aldehyde 42



Synthesis of aldehyde 42



Synthesis of aldehyde 42



Total synthesis of bipolarolides A (1) and B (2)

