



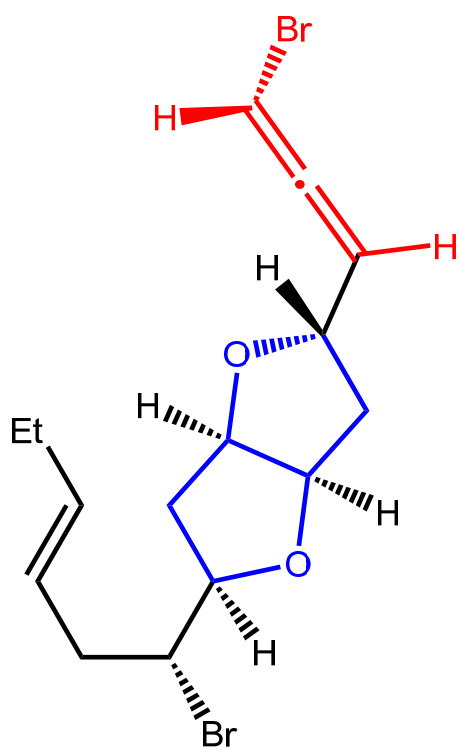
# Stereoselective Total Synthesis of (-)-Kumausallene

Kai Gao

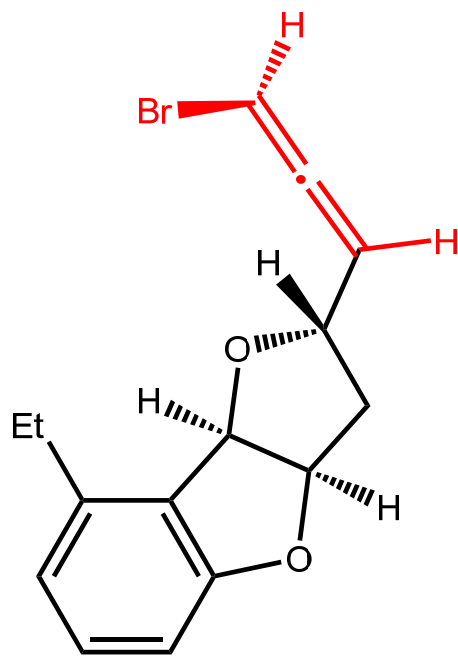
Checker: Chang-Bin Yu

Tang, W.\* *et al Org. Lett.* **2011**, *ASAP*

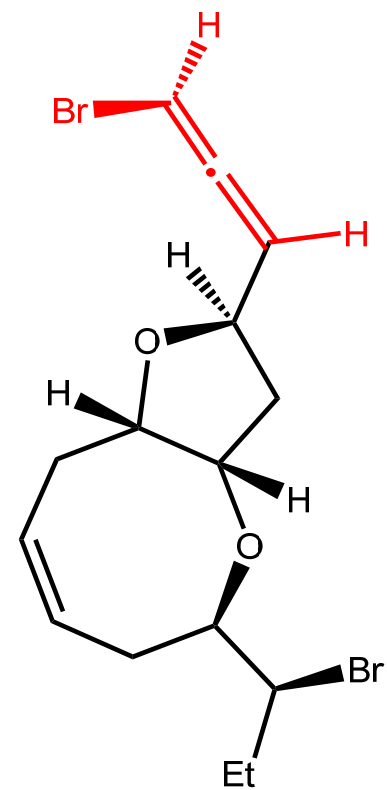
## Representative Natural Products with a Bromoallene Moiety



**1** (-)-kumausallene

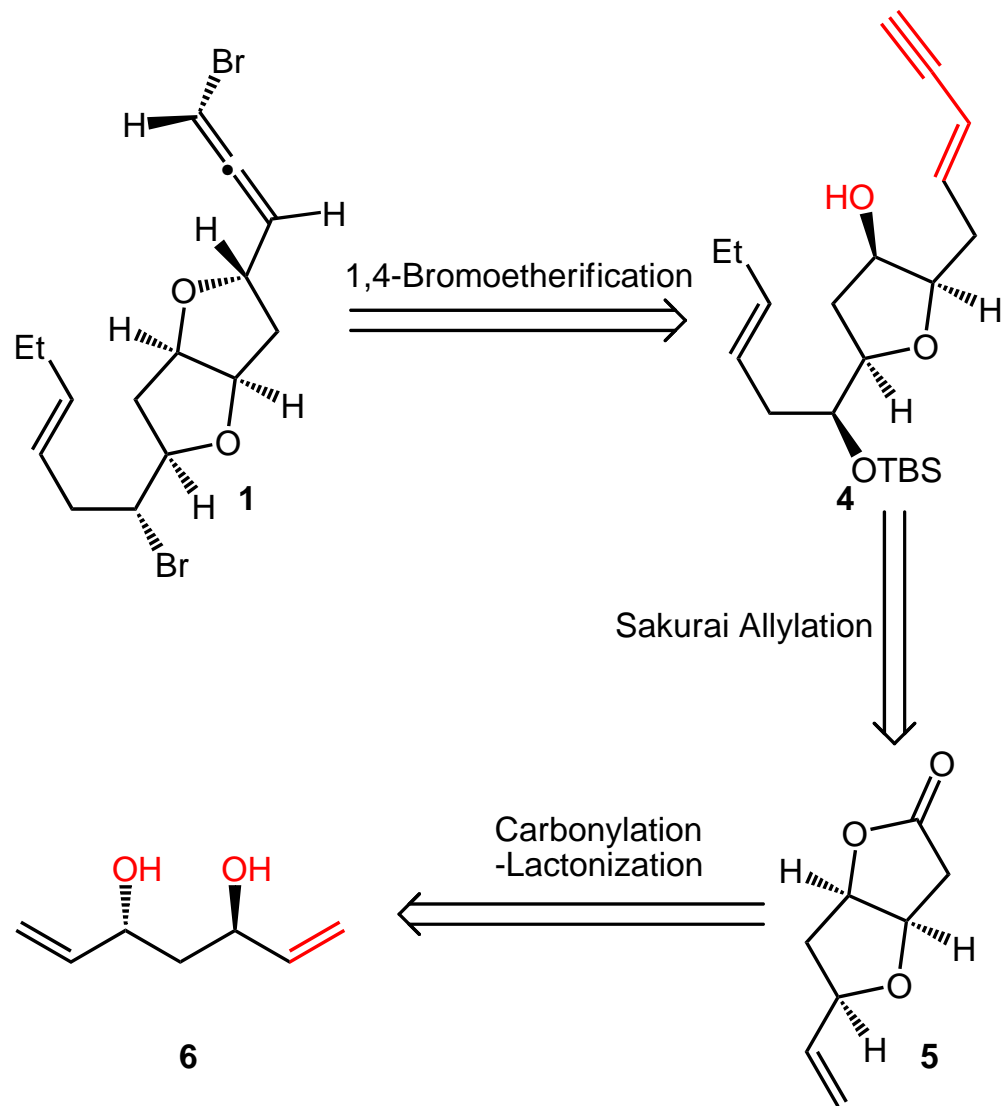


**2** (+)-panacene

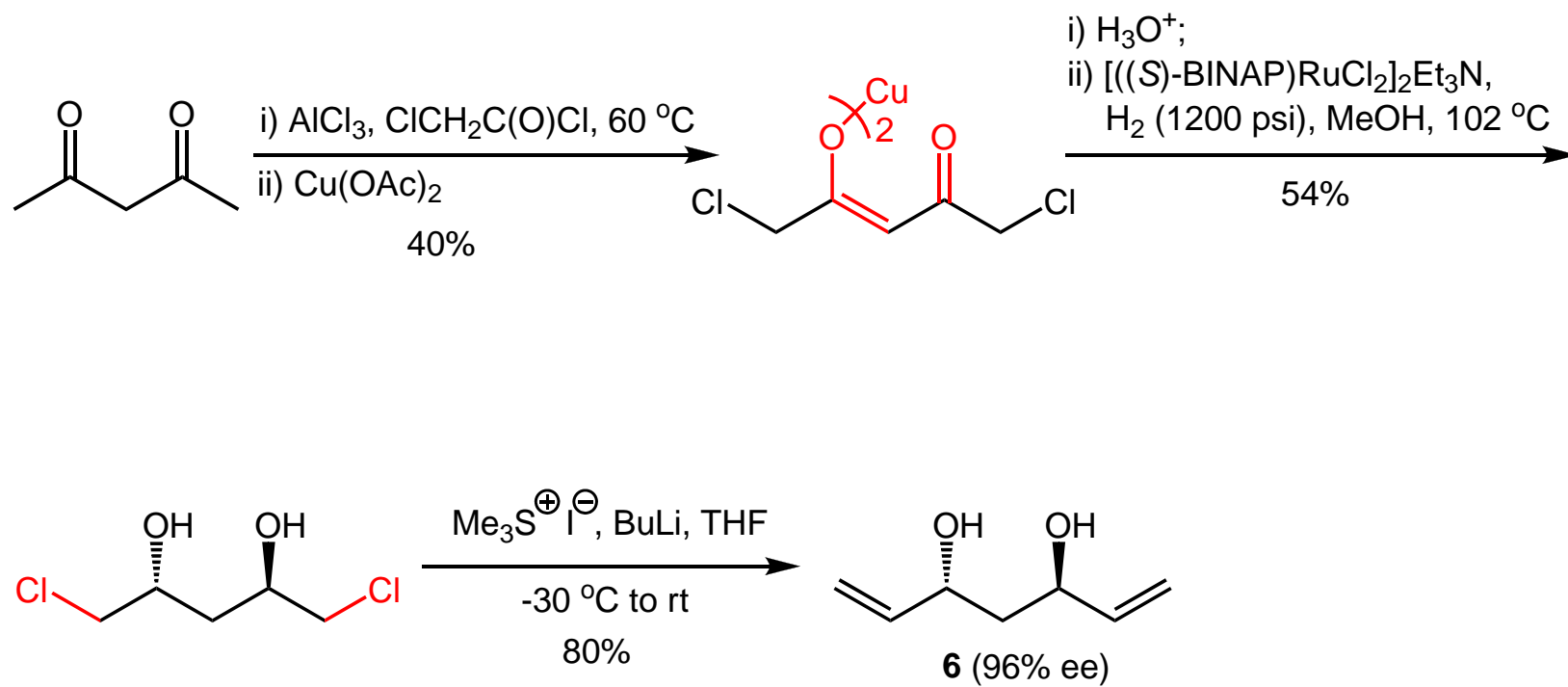


**3** (+)-laurallene

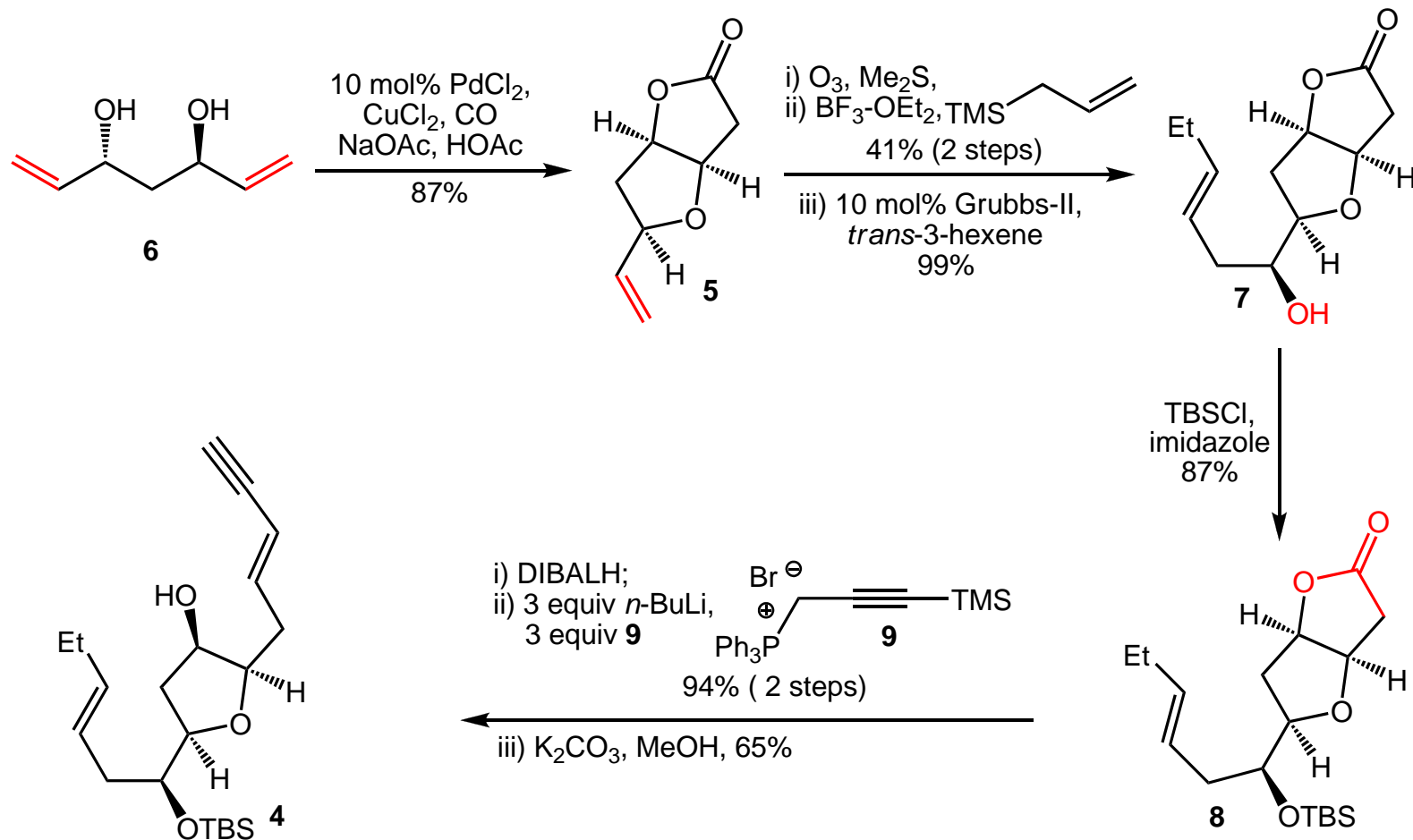
## Retrosynthetic Analysis of (-)-Kumausallene



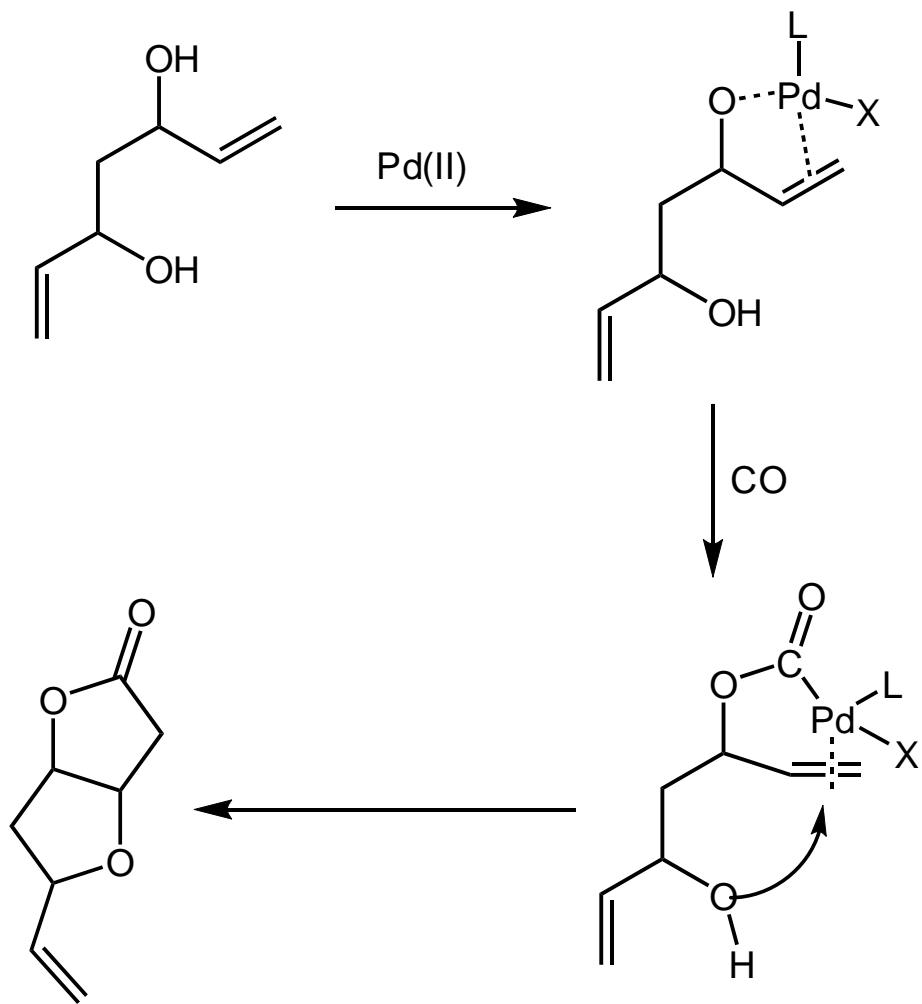
## Preparation of C<sub>2</sub>- Symmetric Diol **6**



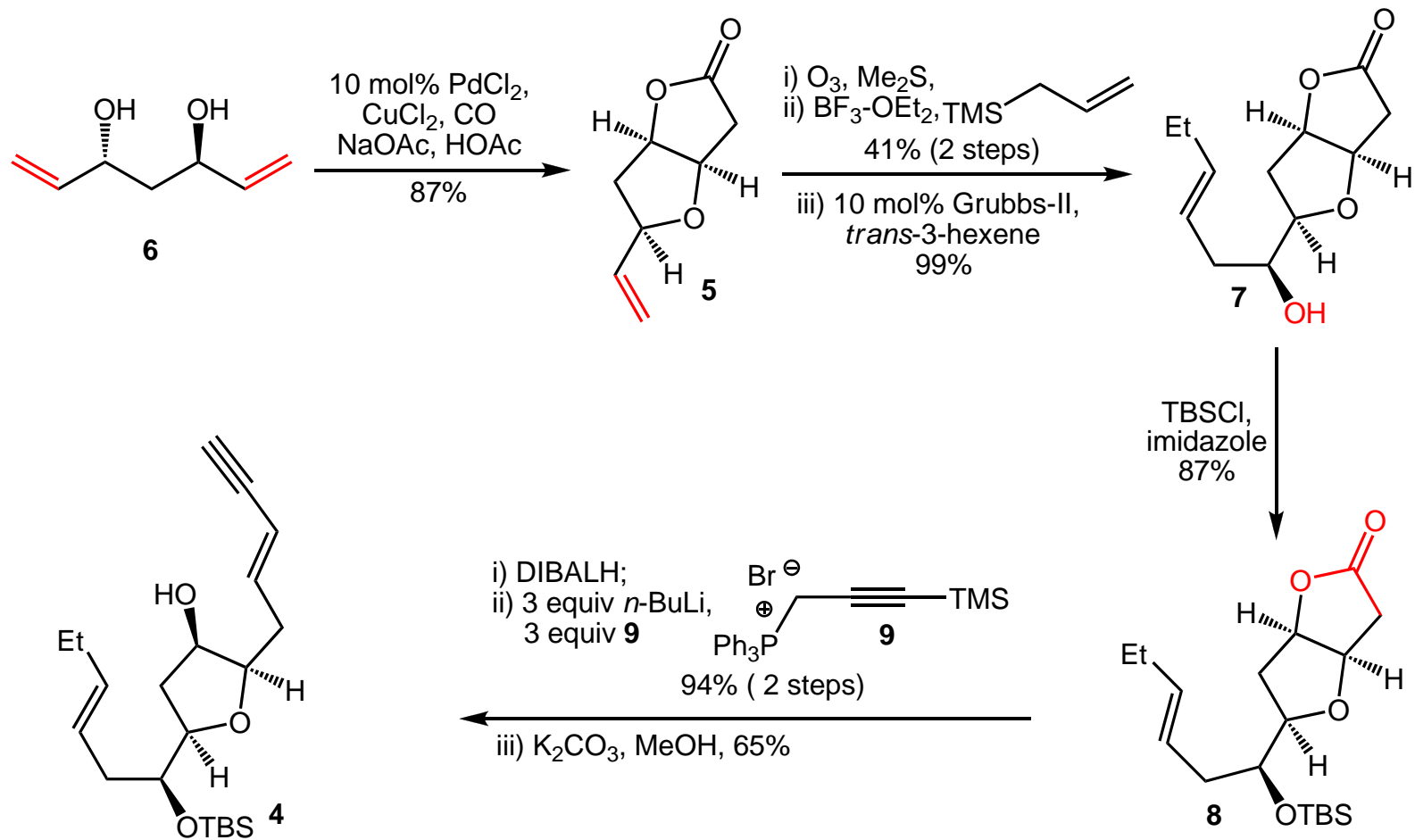
# Synthesis of Trisubstituted THF Ring



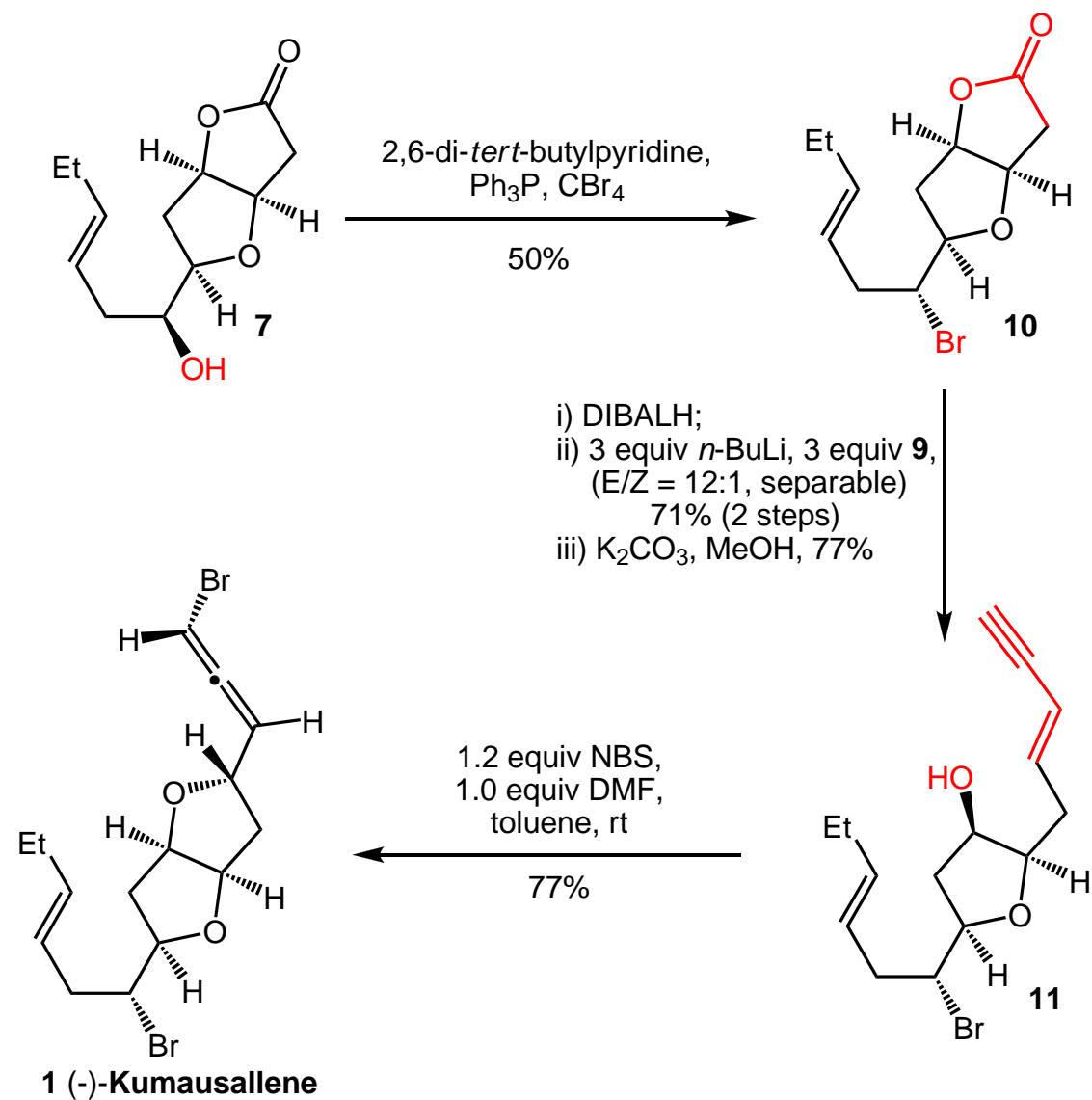
## Palladium-catalyzed Oxocarbonylation Reaction



# Synthesis of Trisubstituted THF Ring

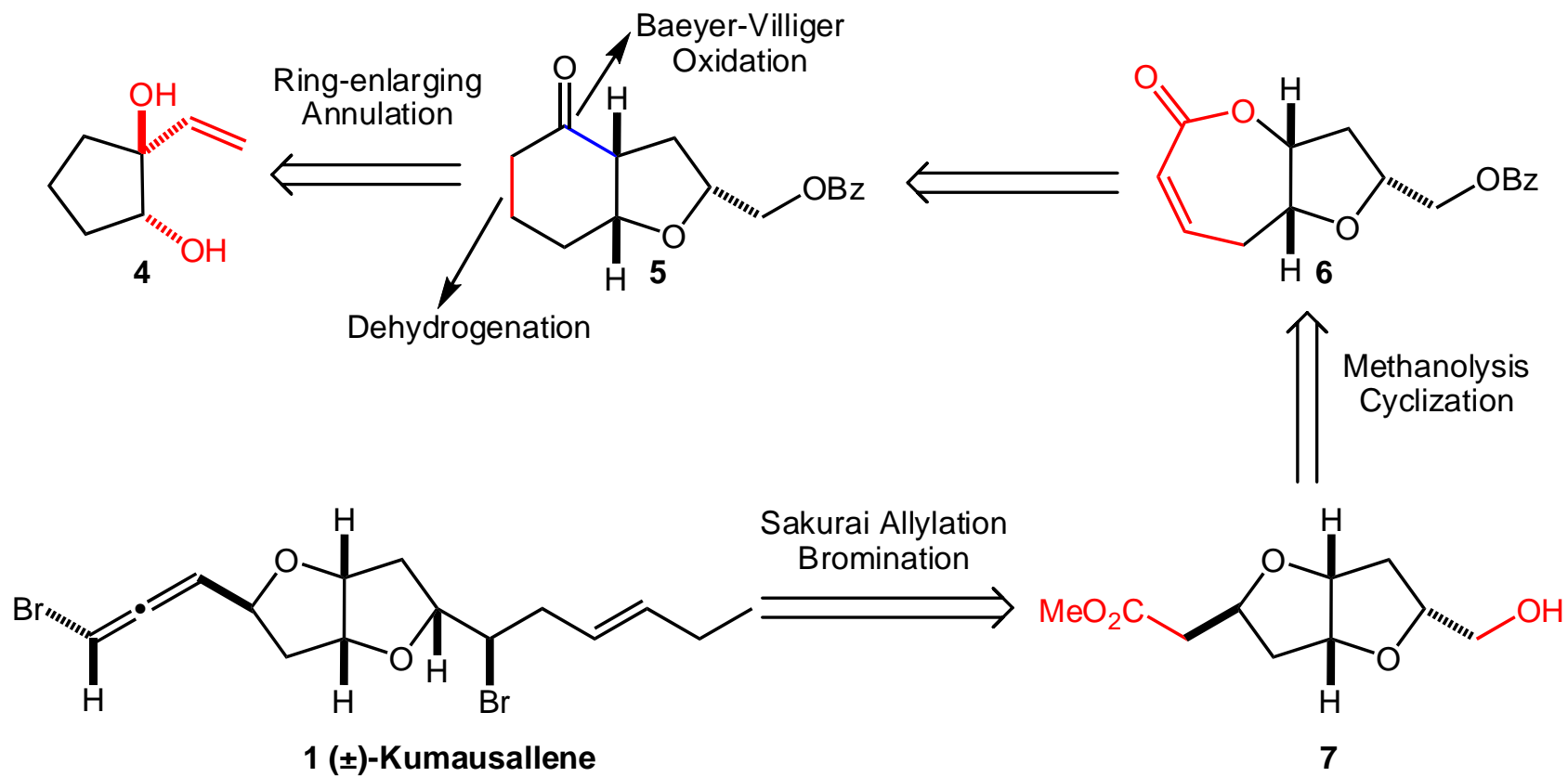


## Completion of (-)-Kumausallene



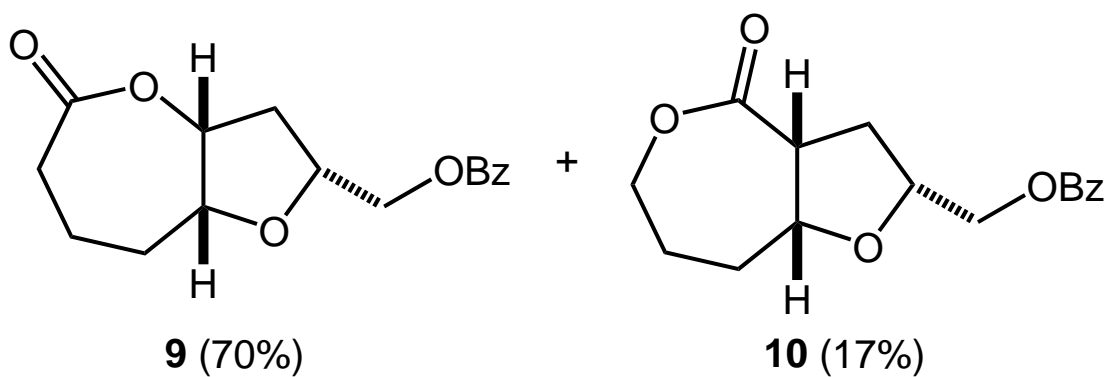
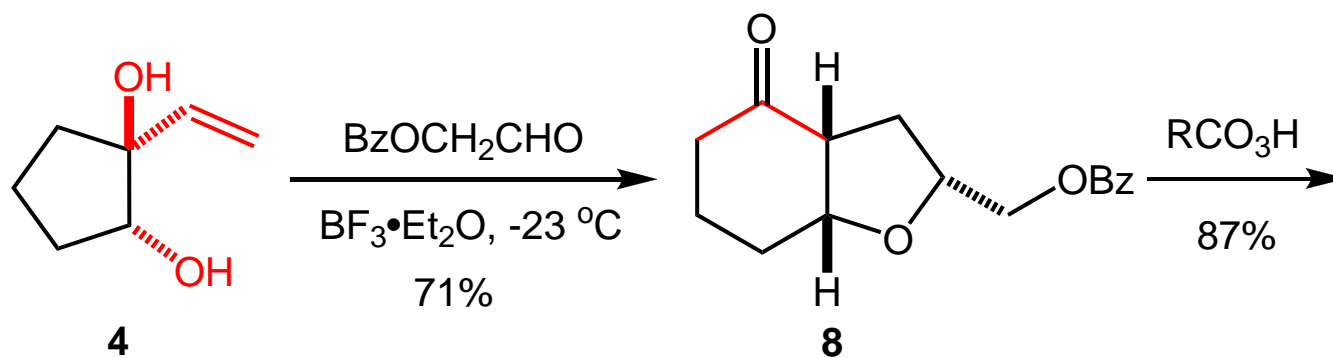


## Overman's Work

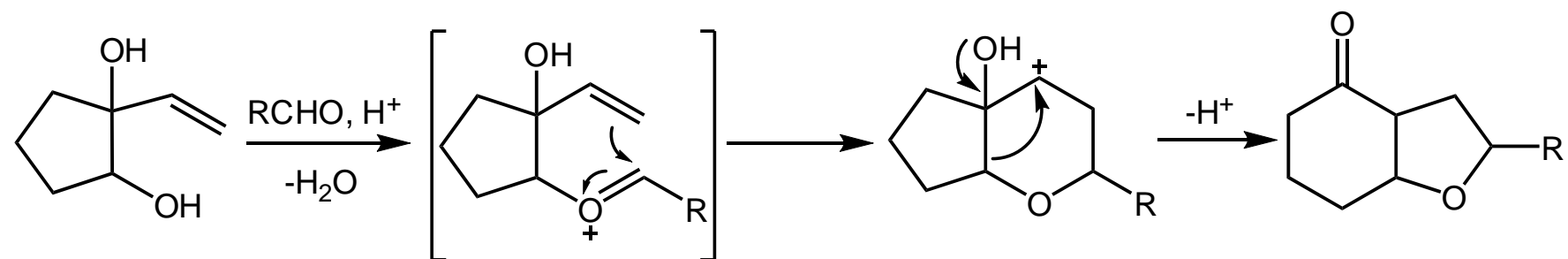


Overman, L. E.\* *et al* *J. Org. Chem.* **1993**, *58*, 2468.

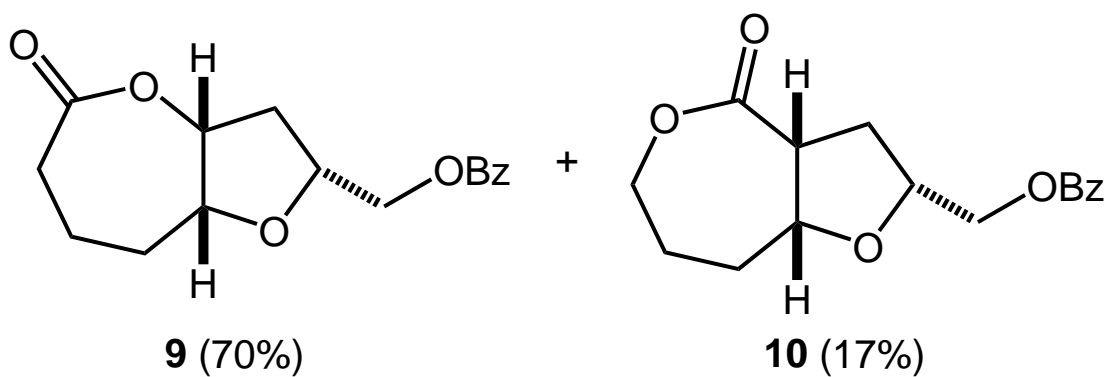
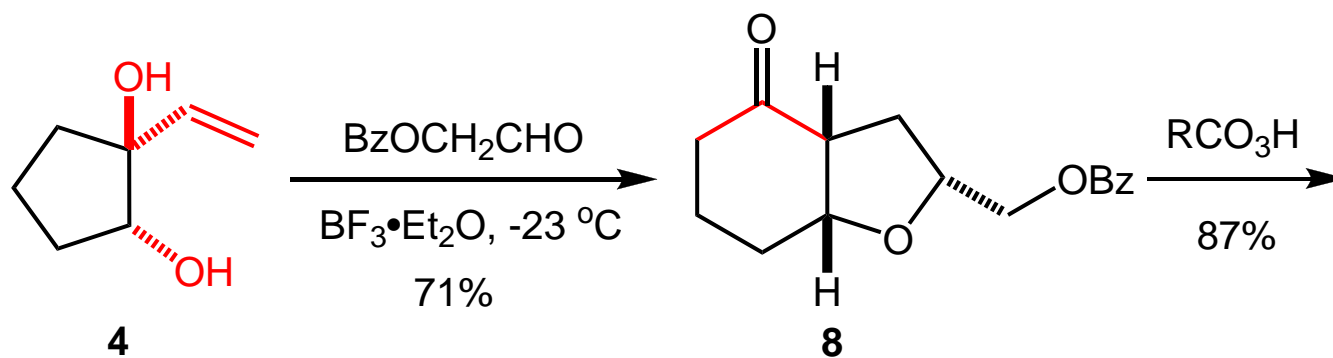
## Synthesis of 13



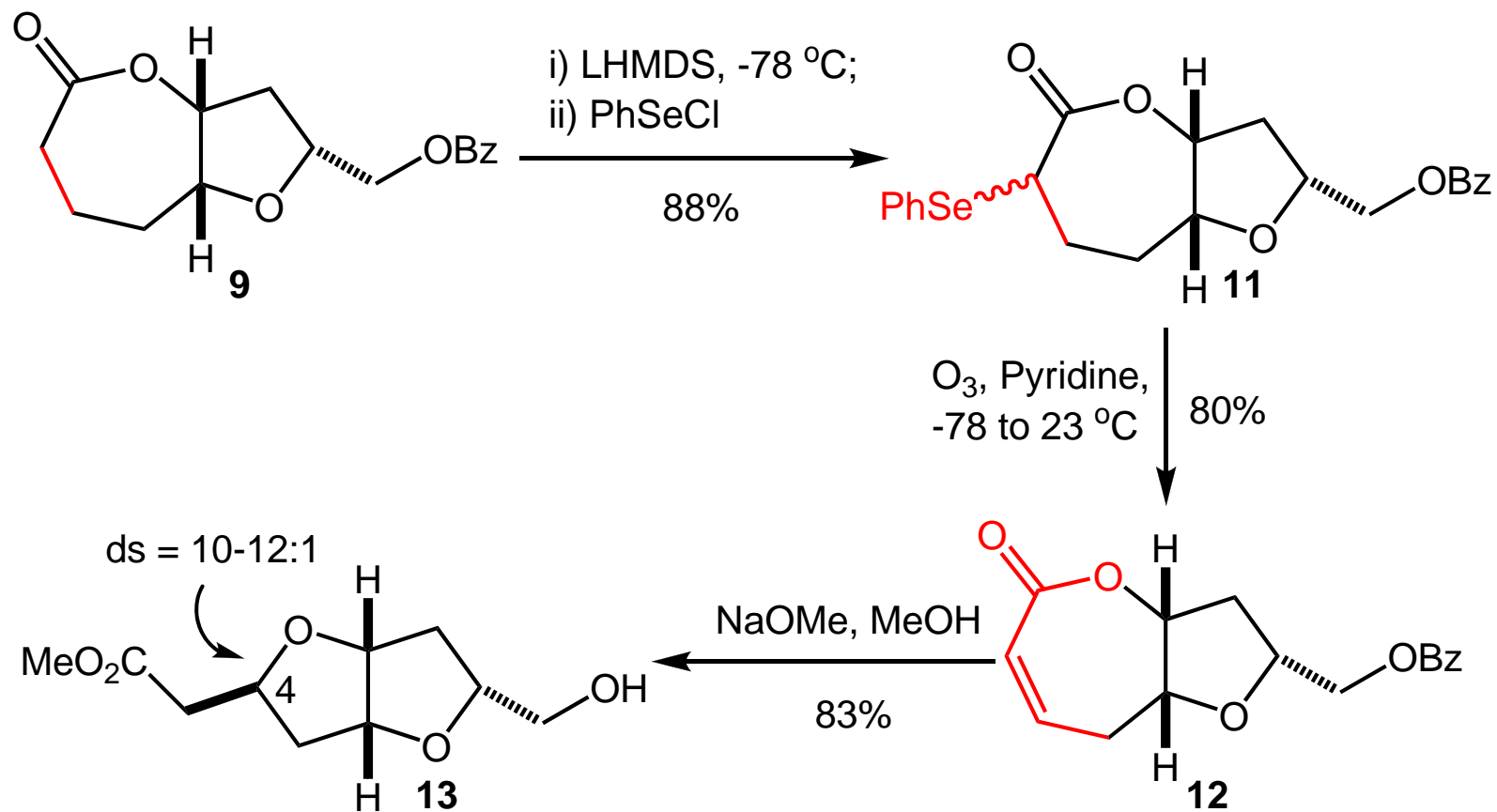
## Ring-Enlarging Annulation



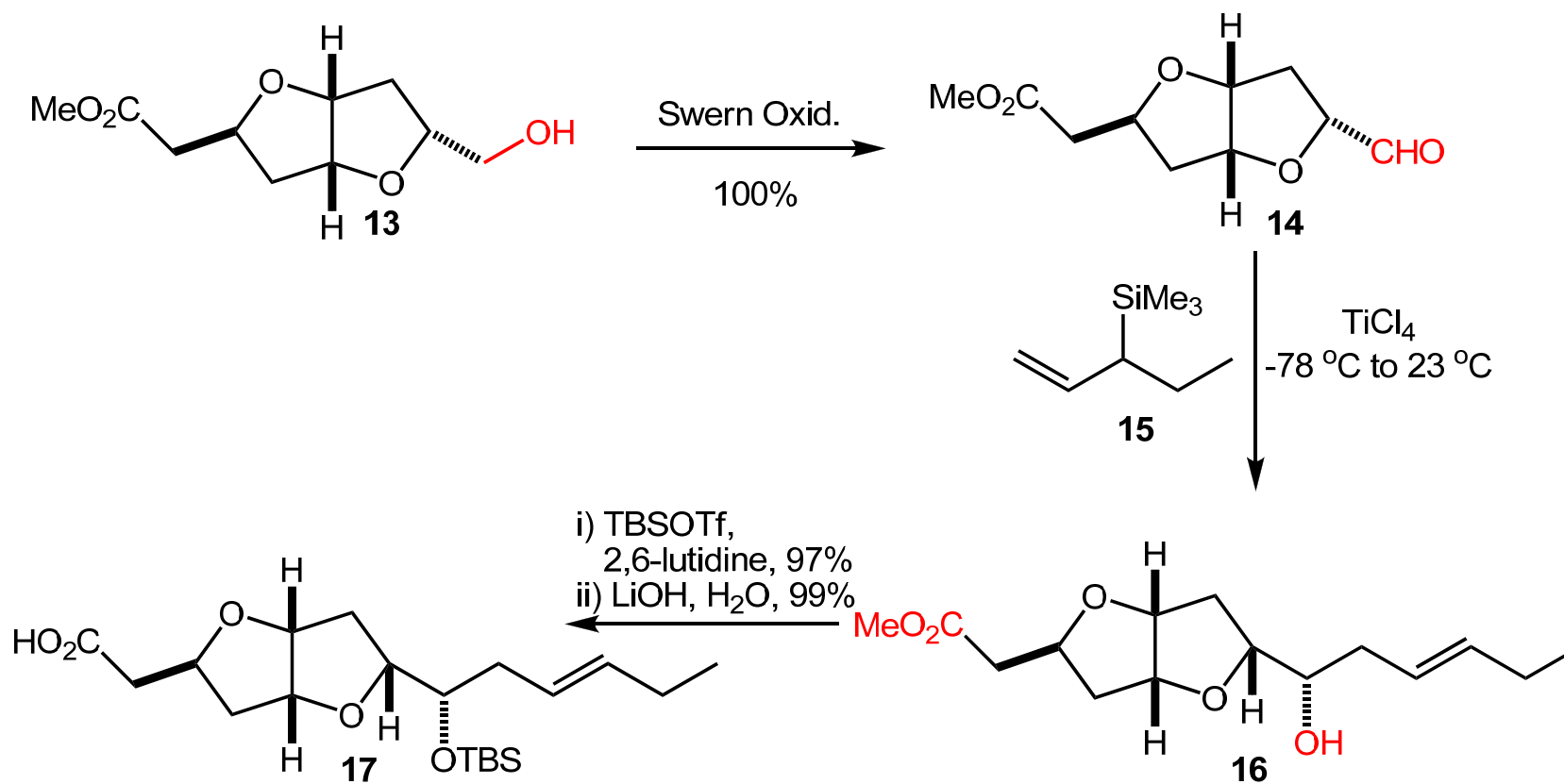
## Synthesis of 13



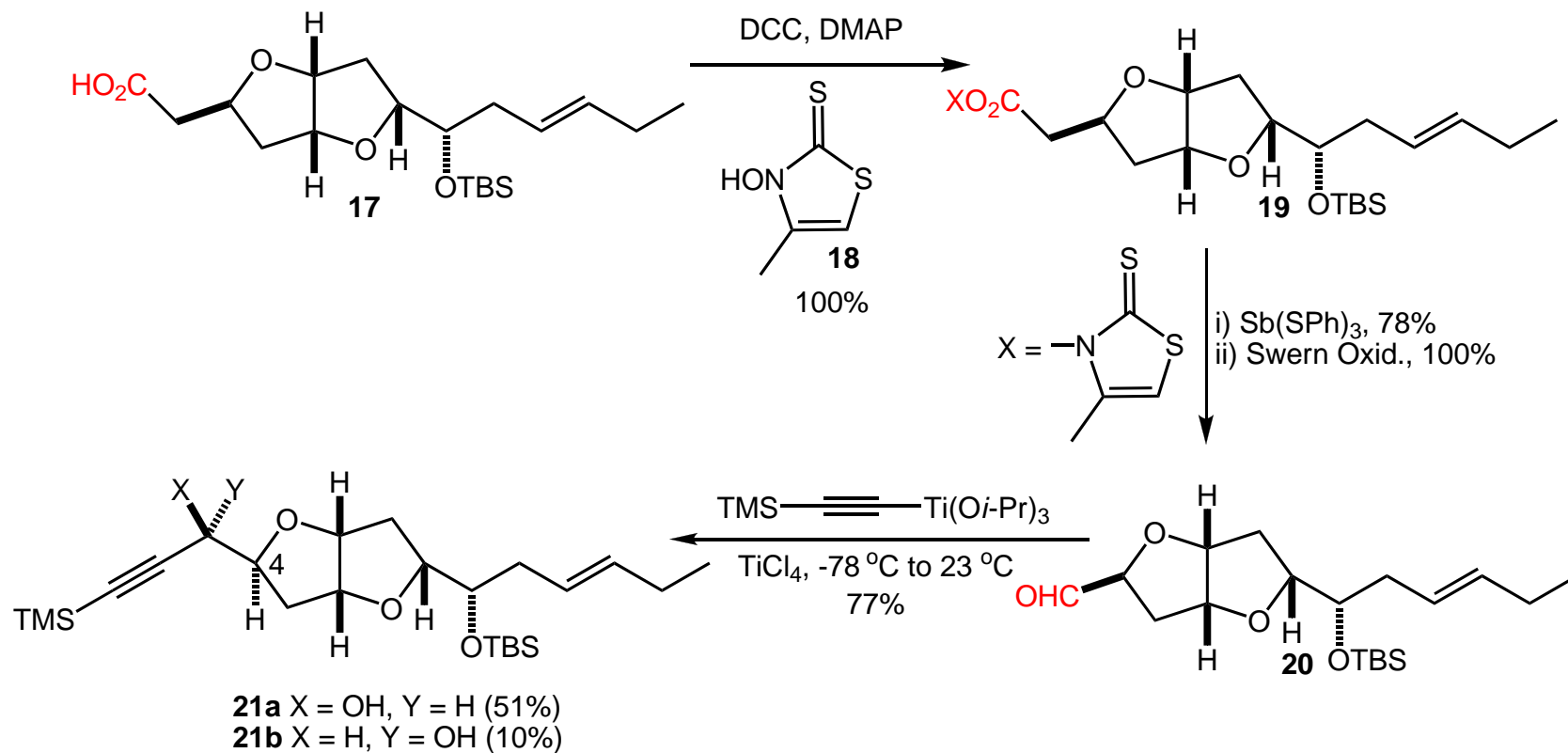
## Synthesis of 13



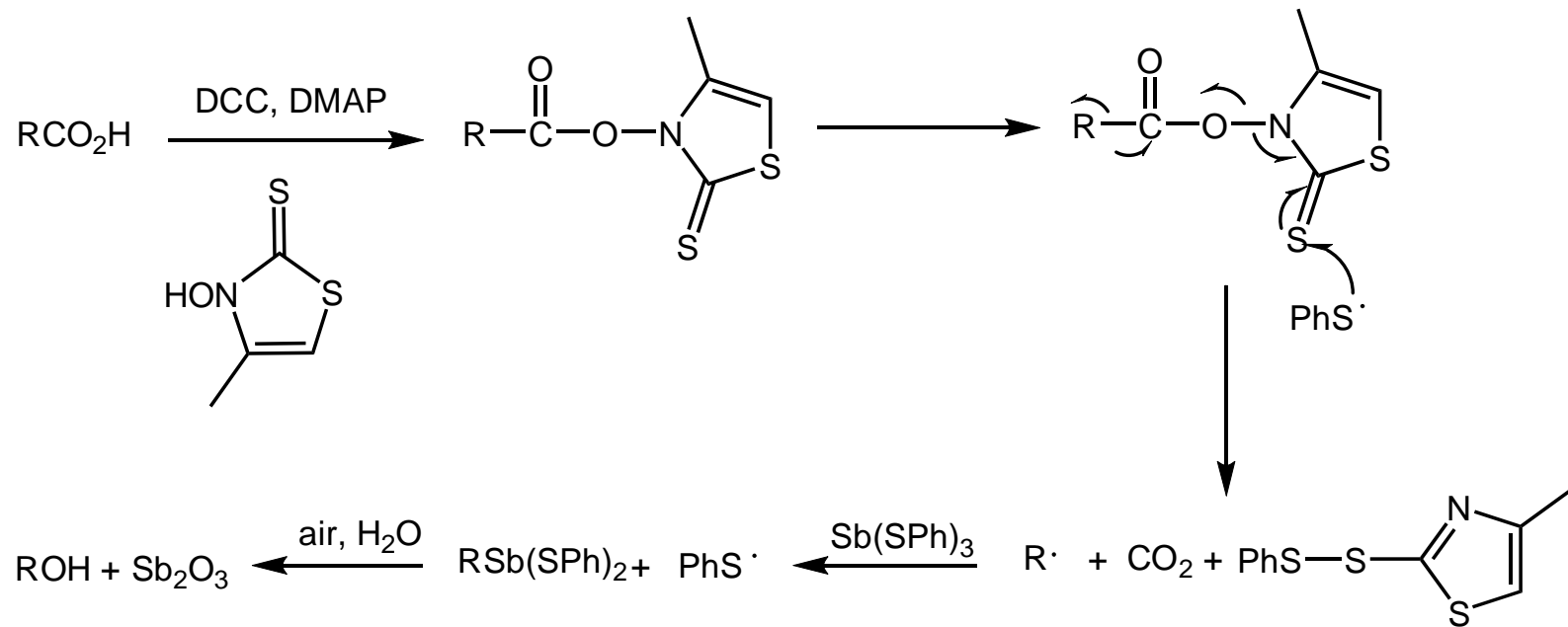
## Synthesis of 21a



# Synthesis of 21a

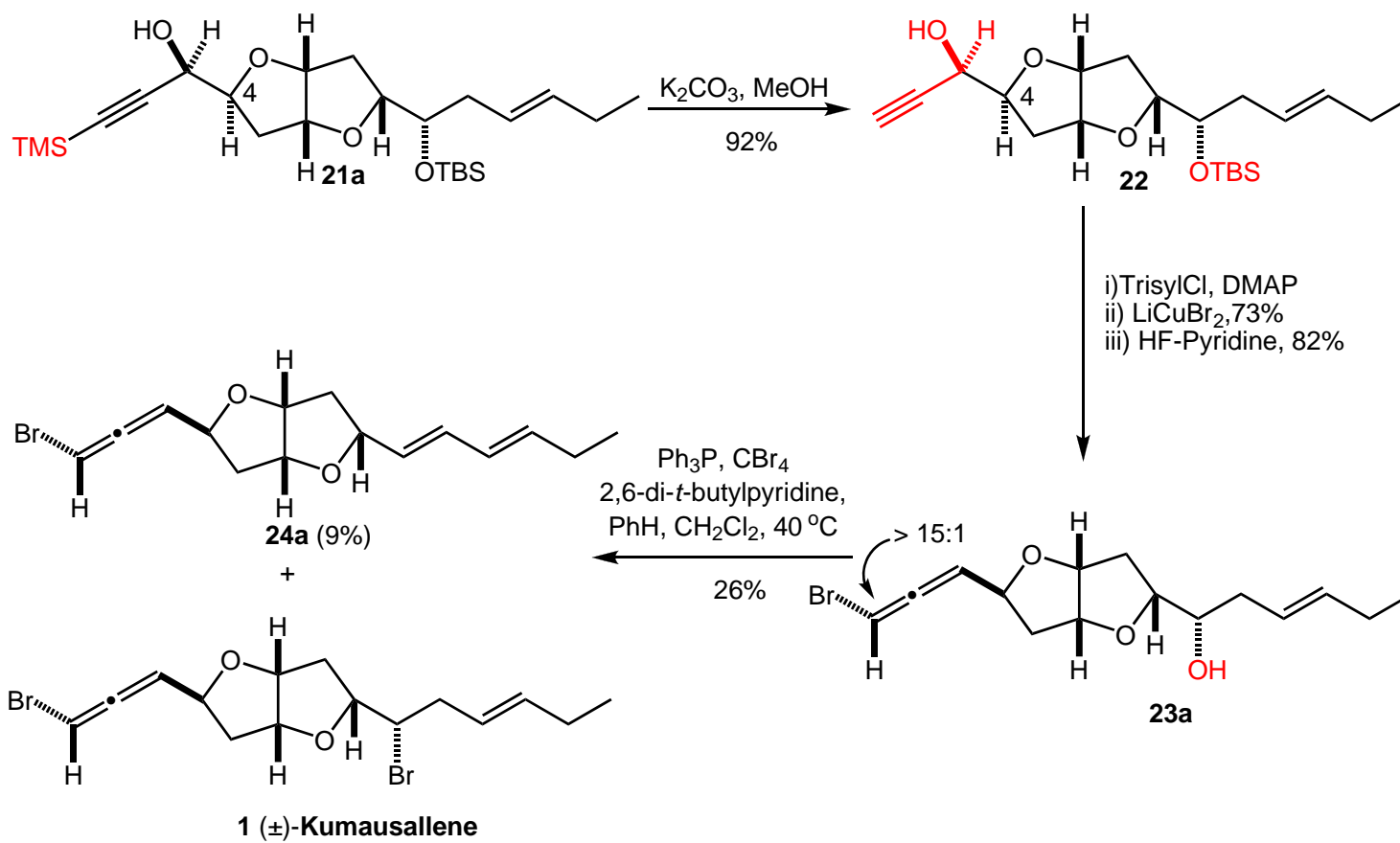


# 脱羰基反应

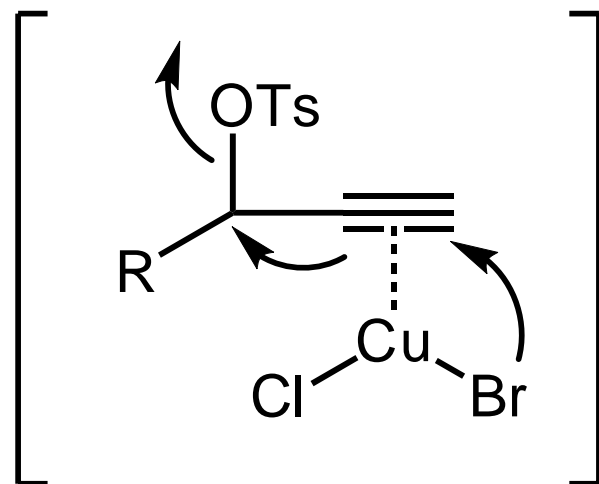
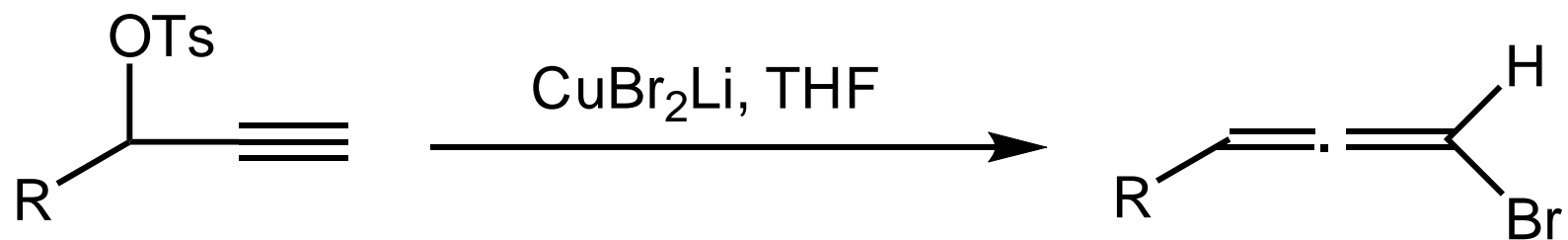




# Completion of ( $\pm$ )-Kumausallene

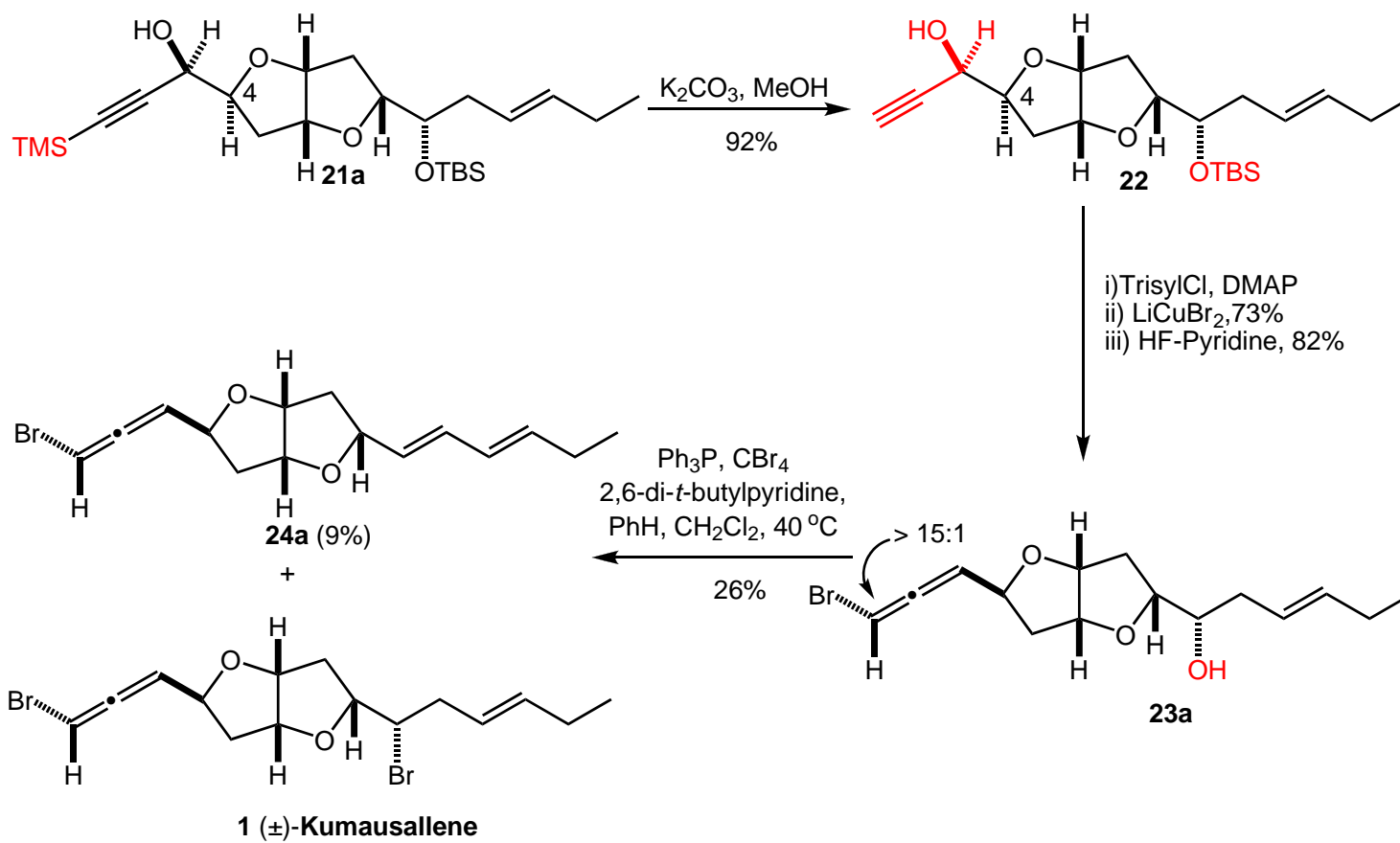


## 溴代丙二烯片断的合成

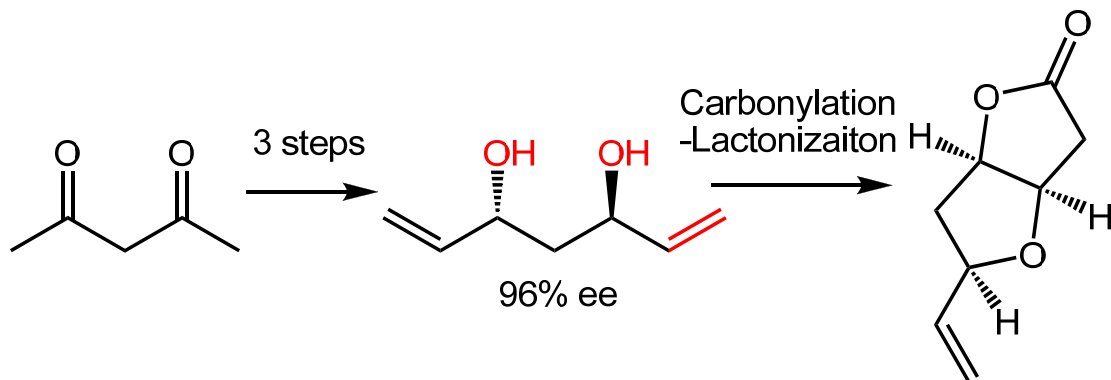


$\text{S}_{\text{N}}2'$  Displacement

# Completion of ( $\pm$ )-Kumausallene

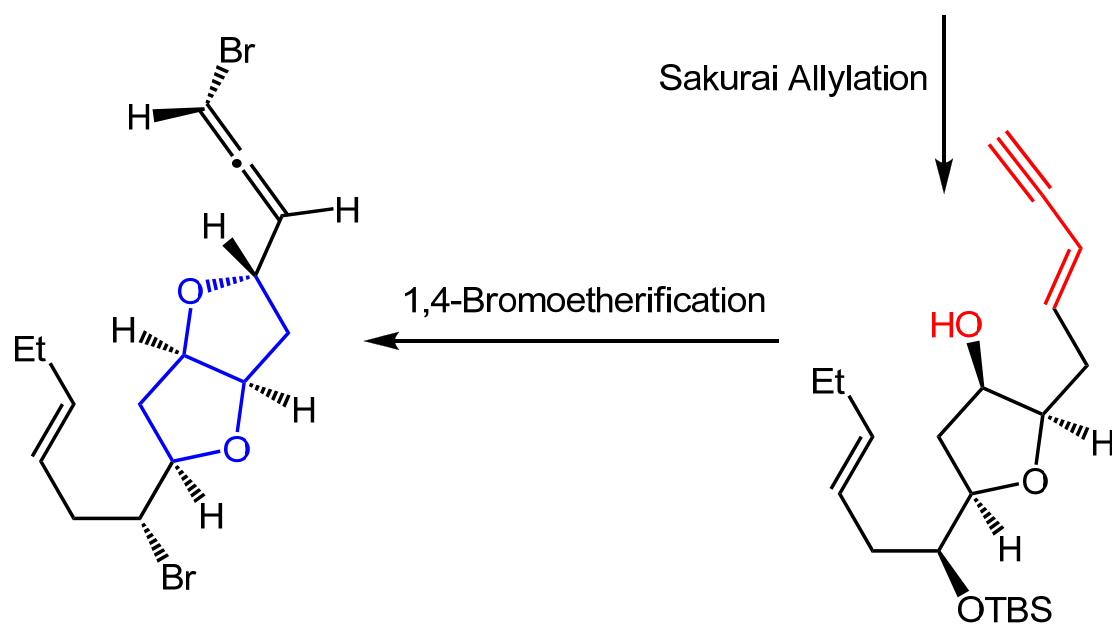


# Summary

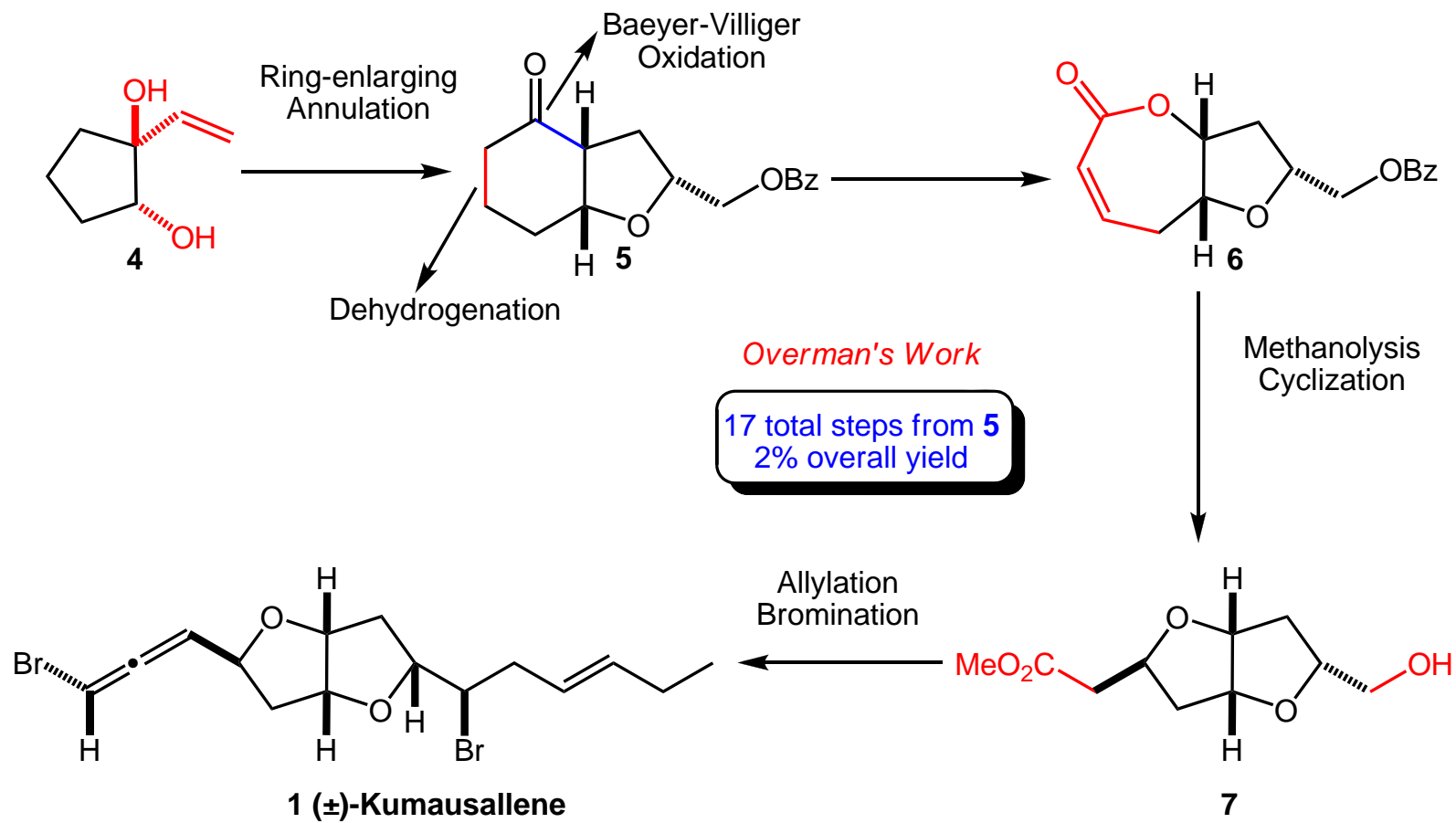



*This Work*

12 total steps  
from acetylacetone




# Summary





(-)-Kumausallene **1** belongs to a family of nonisoprenoid sesquiterpenes with a unique bromoallene moiety. The first total synthesis of ( $\pm$ )-kumausallene was accomplished by Overman. In this synthesis, the complex dioxabicyclo[3.3.0]octane core was constructed by an elegant ring-expansion annulation strategy and the bromoallene moiety was introduced by stereoselective  $S_N2'$  displacement of propargylic sulfonate. In the first enantioselective synthesis of (-)-kumausallene by Evans, the 2,5-*cis*-substituted tetrahydrofuran (THF) ring was prepared by an acyl radical cyclization and a very efficient biomimetic strategy was undertaken to forge the bromoallene and the adjacent THF ring simultaneously. We herein describe the first diastereo- and enantioselective total synthesis of (-)-kumausallene employing a desymmetrization strategy for the construction of the 2,5-*cis* substituted THF ring, which is distinctly different from two previous syntheses.



In summary, we have completed the first diastereo- and enantioselective synthesis of (-)-kumausallene in 12 steps from acetylacetone. We recognized the hidden symmetry of the target and prepared the 2,5-*cis*-substituted THF ring by desymmetrizing a  $C_2$ -symmetric diol using a palladium catalyzed cascade reaction. A stereoselective biomimetic cyclization was realized when the 1,4-bromoetherification was conducted on the proposed enyne precursor in biosynthesis.