Literature Report

Ten-Step Asymmetric Total Synthesis of (+)-Pepluanol A

Reporter: Chang-Bin Yu

Checker: Li-Xia Liu

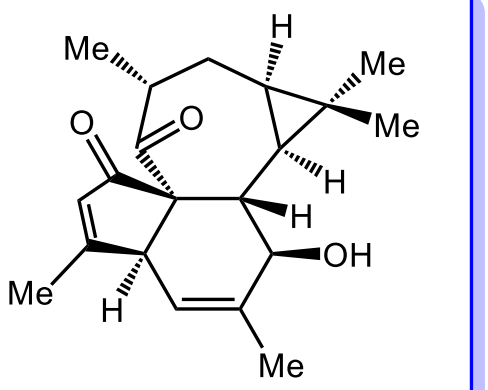
September 06, 2021

Dalian Institute of Chemical Physics

Yuan, P.; Gerlinger, C. K. G.; **Gaich. T.*** *et al. J. Am. Chem. Soc.* **2021,** *143,* 11934

Contents

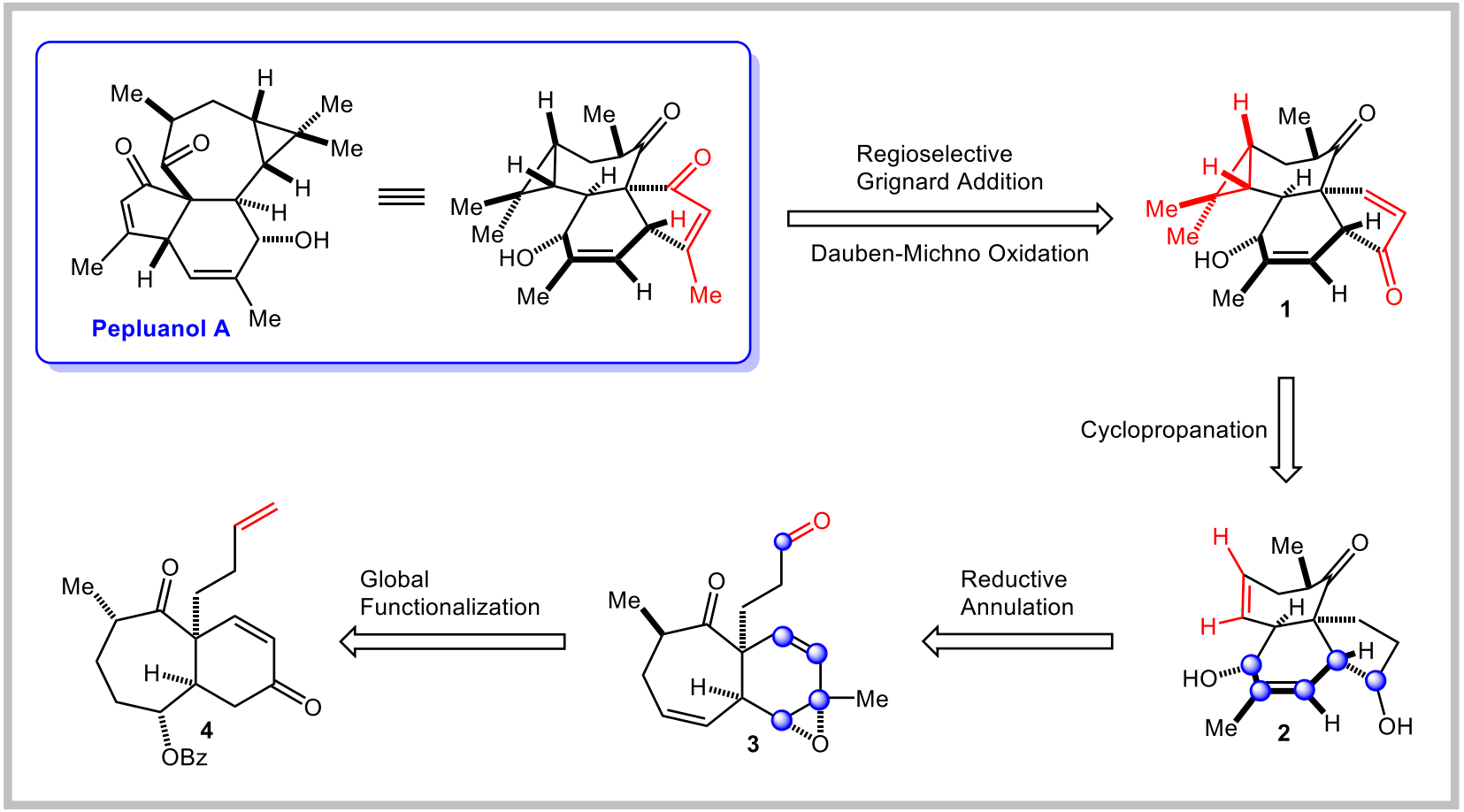
Introduction-Background



Pepluanol A

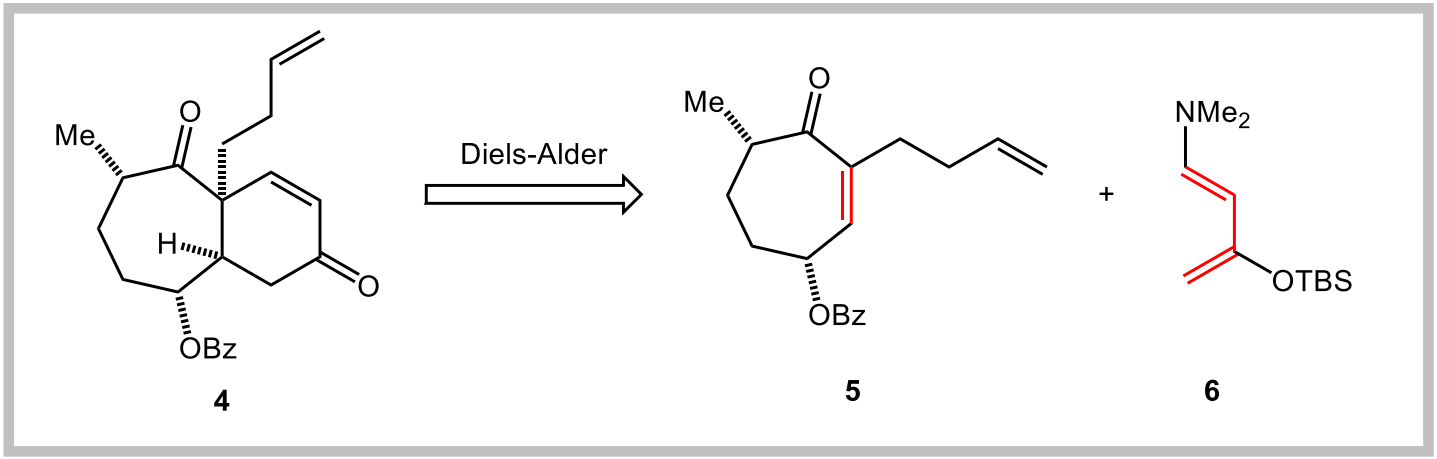
- Isolated from the plant of E. peplus in 2016
- Polycyclic structures
- A total of 7 contiguous stereocenters

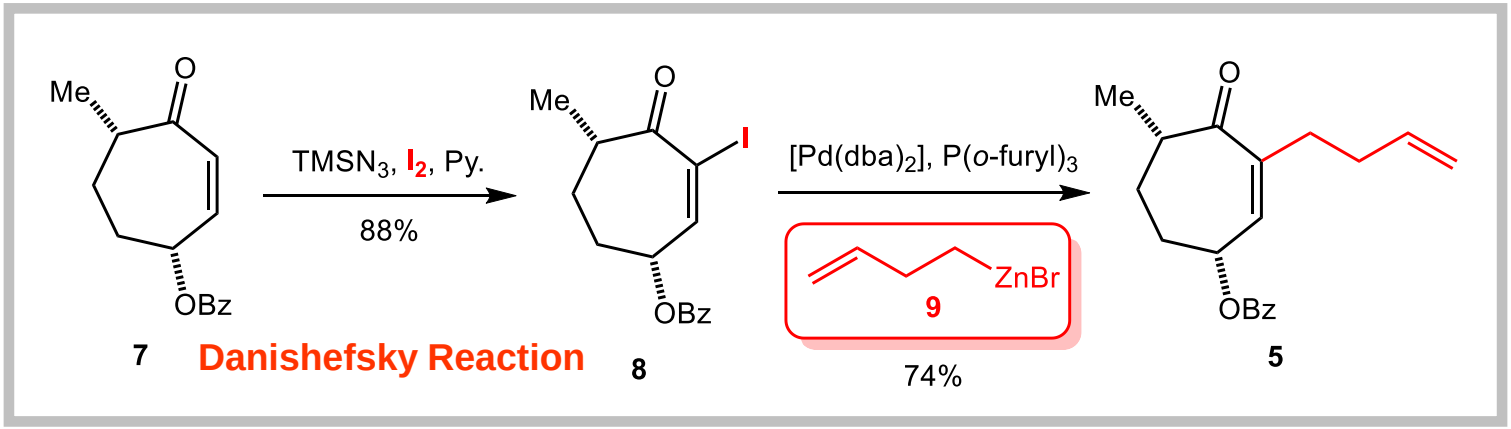
Retrosynthetic Analysis



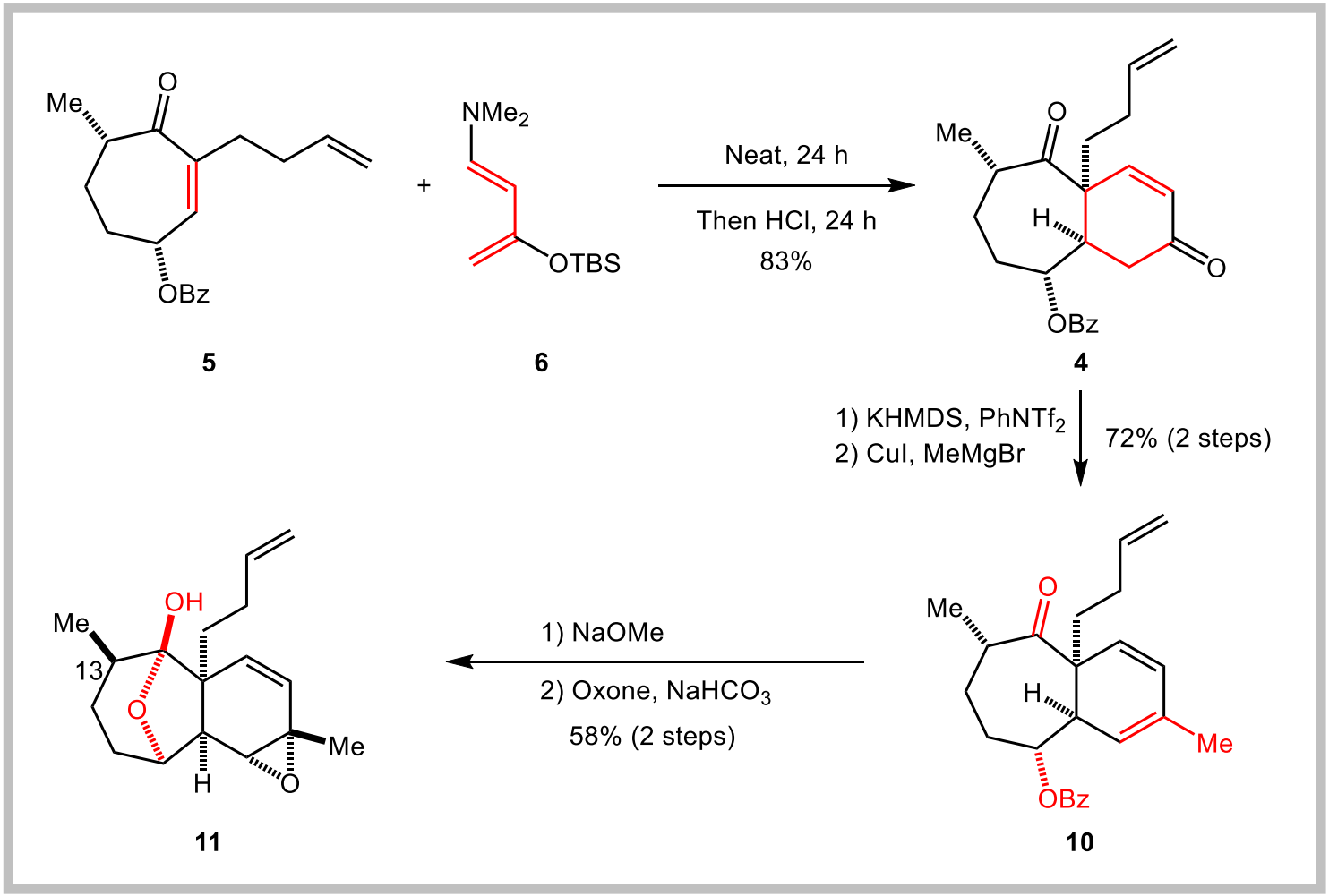
Xuan, J.; Liu, Z.; Zhu, A.; Rao, P.; Yu, L.; **Ding, H**.* *Angew. Chem. Int. Ed*. **2017**, *56*, 8898

Retrosynthetic Analysis

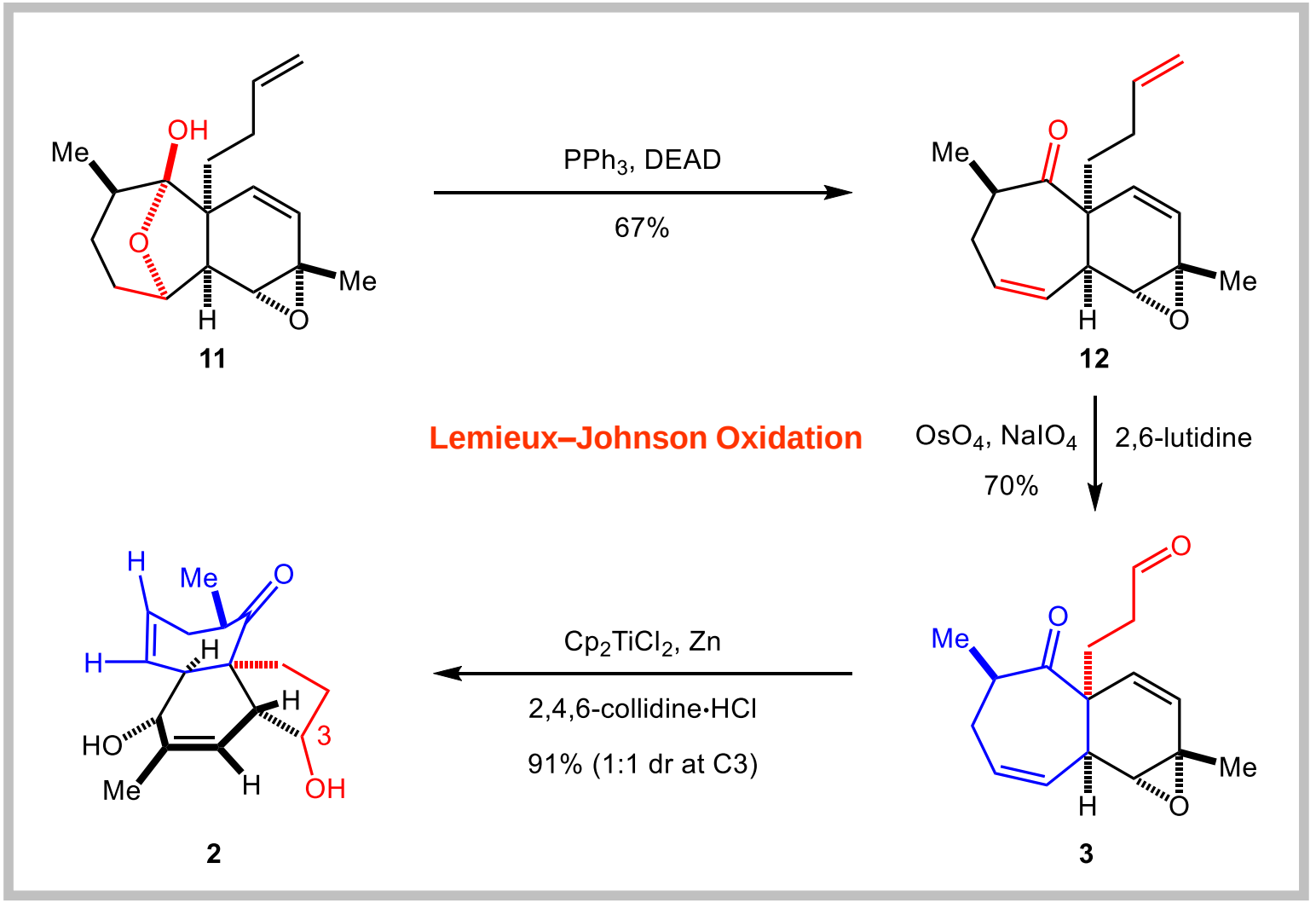




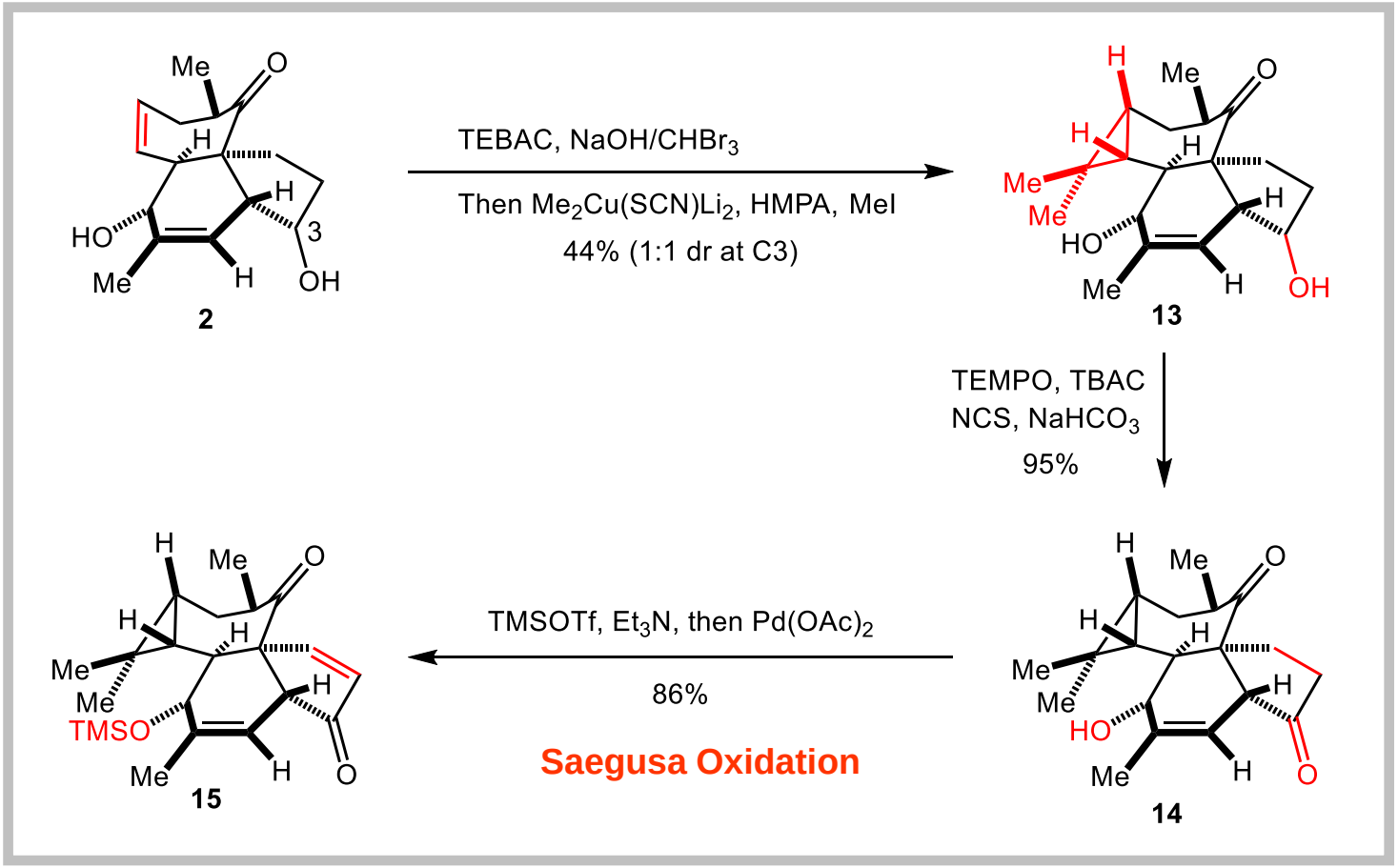
Retrosynthetic Analysis



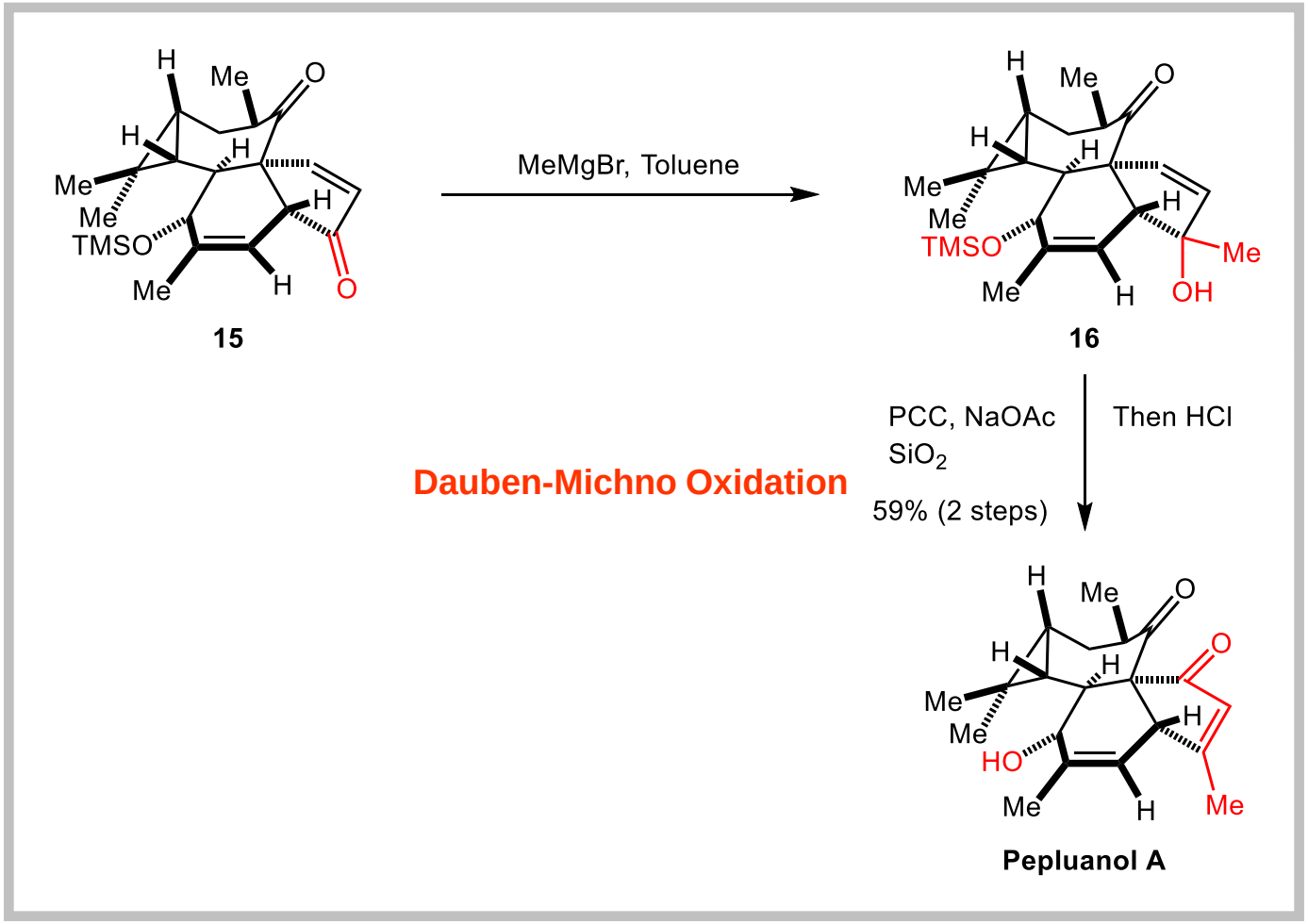
Synthesis of Intermediate 2



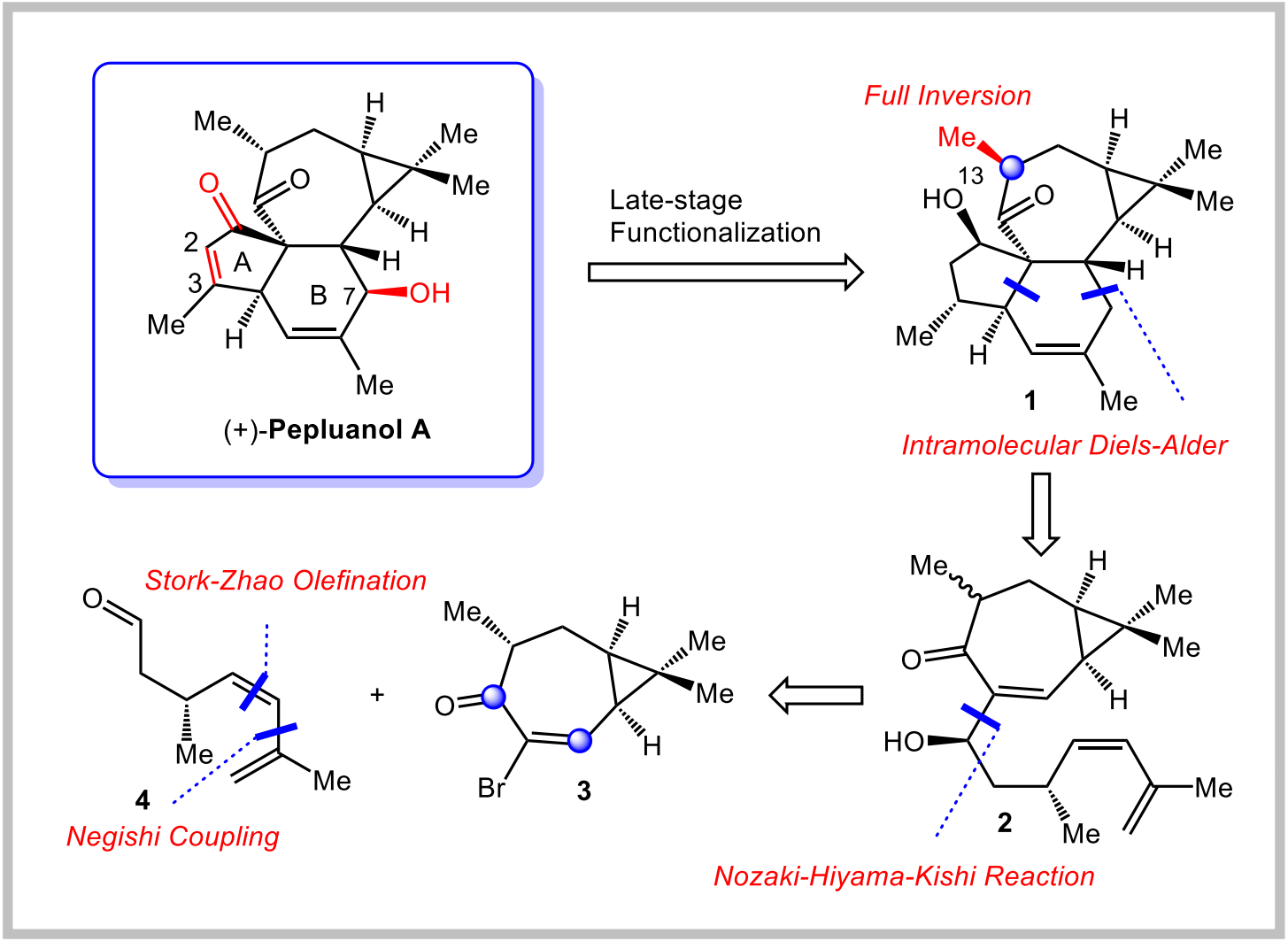
Synthesis of Intermediate 15



Synthesis of (+/-)-Pepluanol A

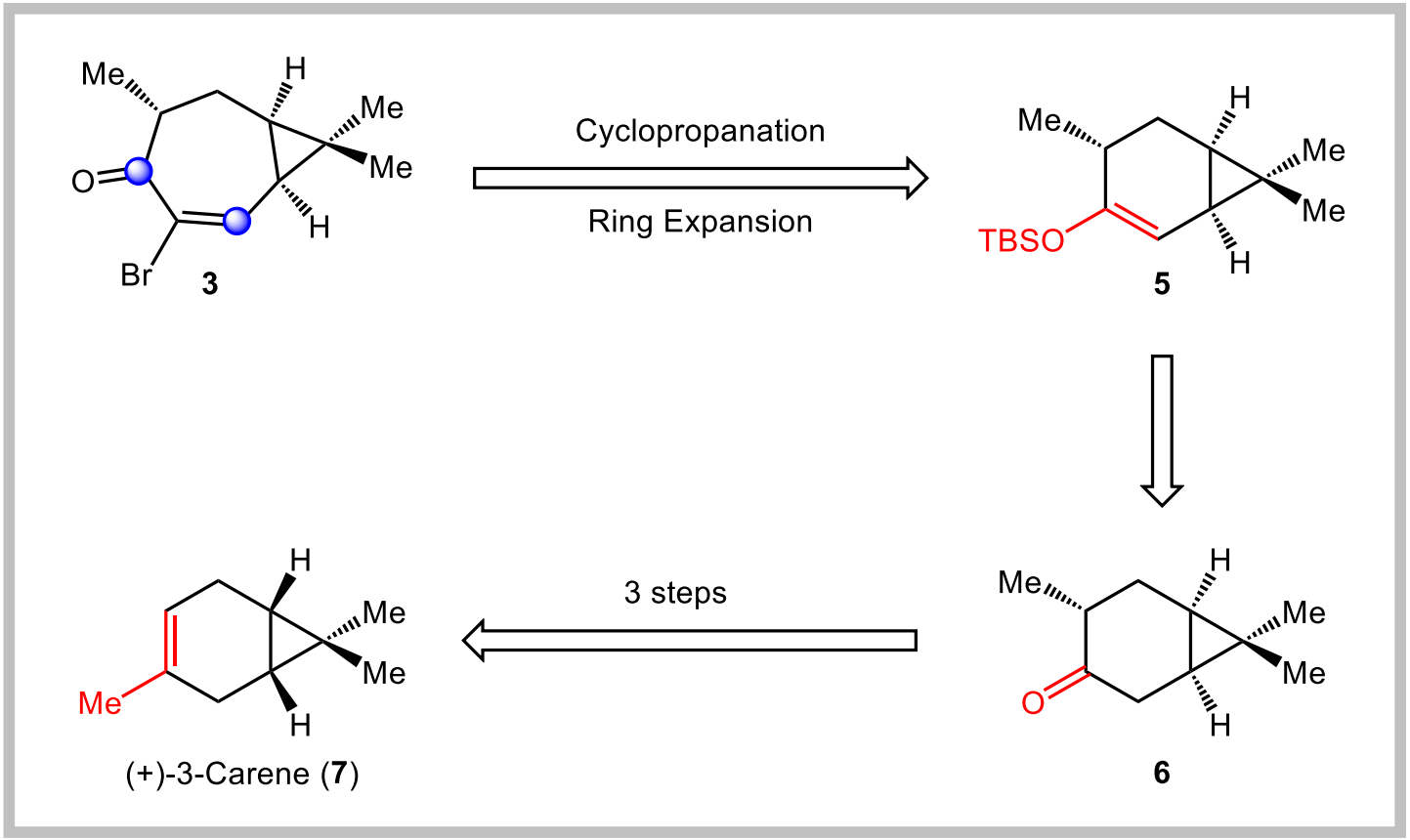


Retrosynthetic Analysis

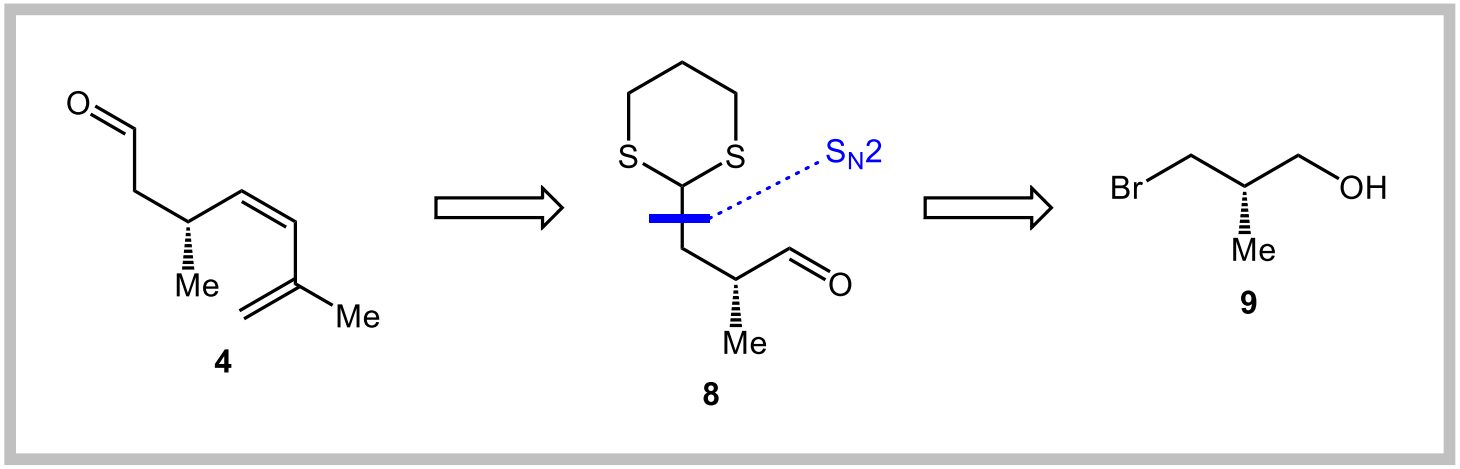


Yuan, P.; Gerlinger, C. K. G.; **Gaich. T.*** *et al. J. Am. Chem. Soc.* **2021,** *143,* 11934

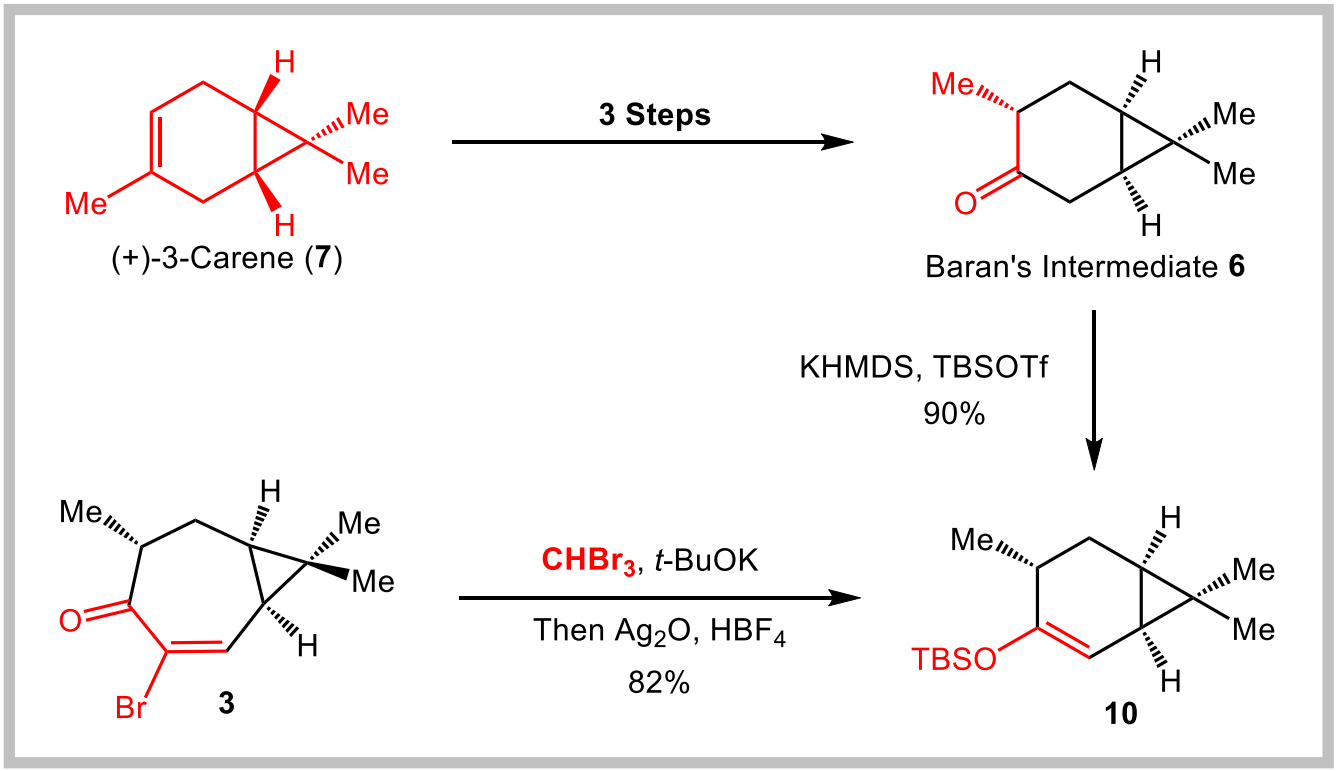
Retrosynthetic Analysis



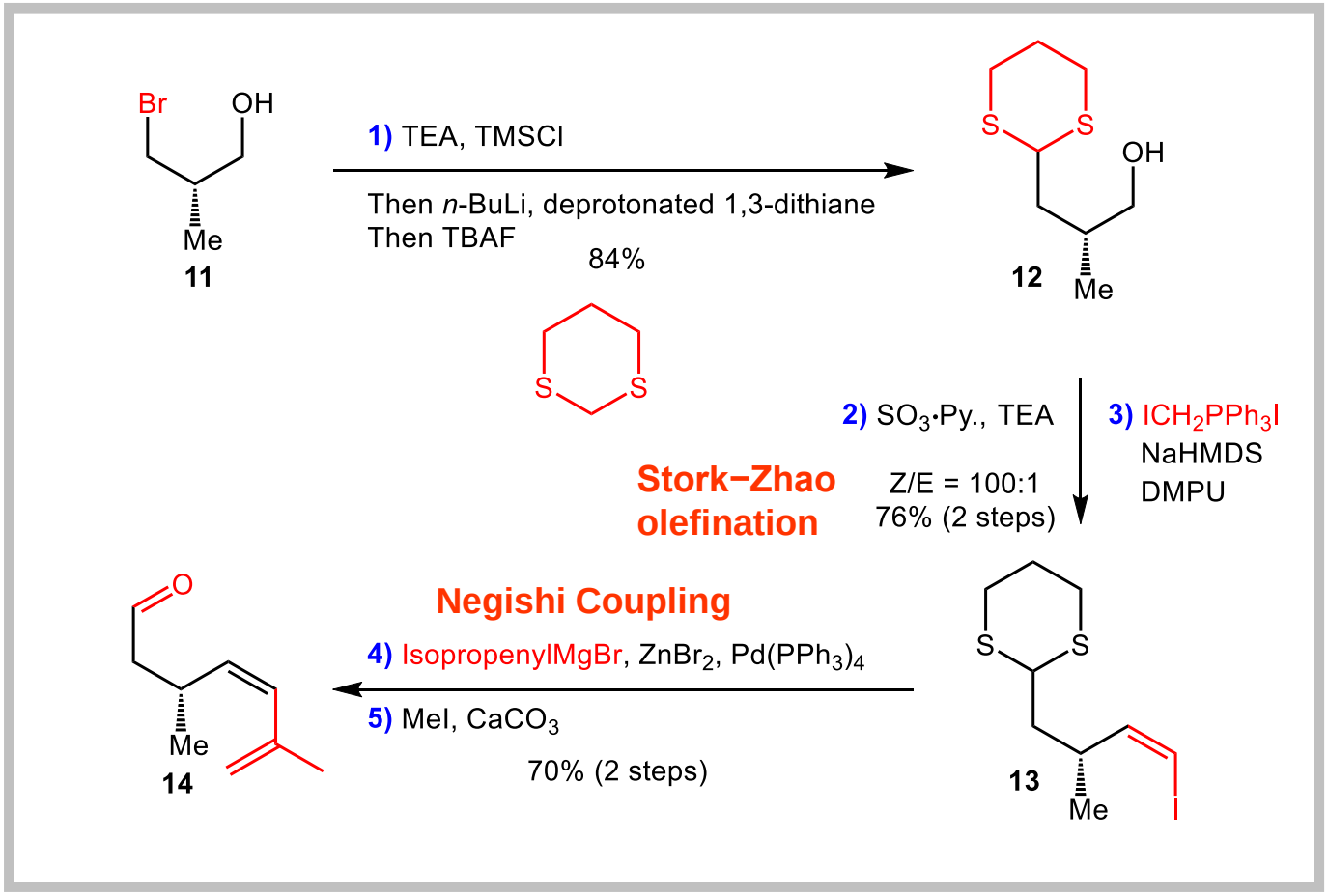
Retrosynthetic Analysis



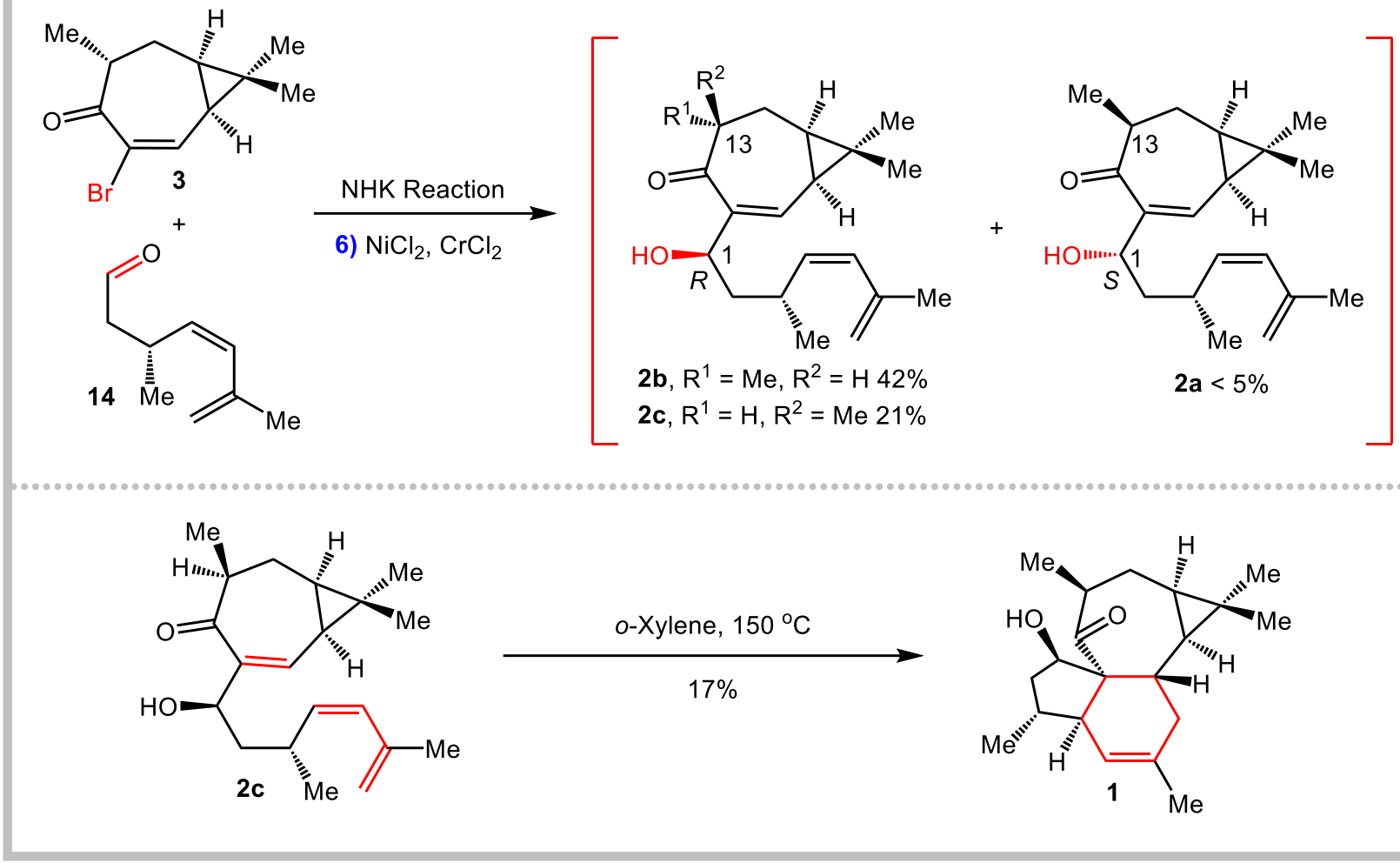
Synthesis of Intermediate 3



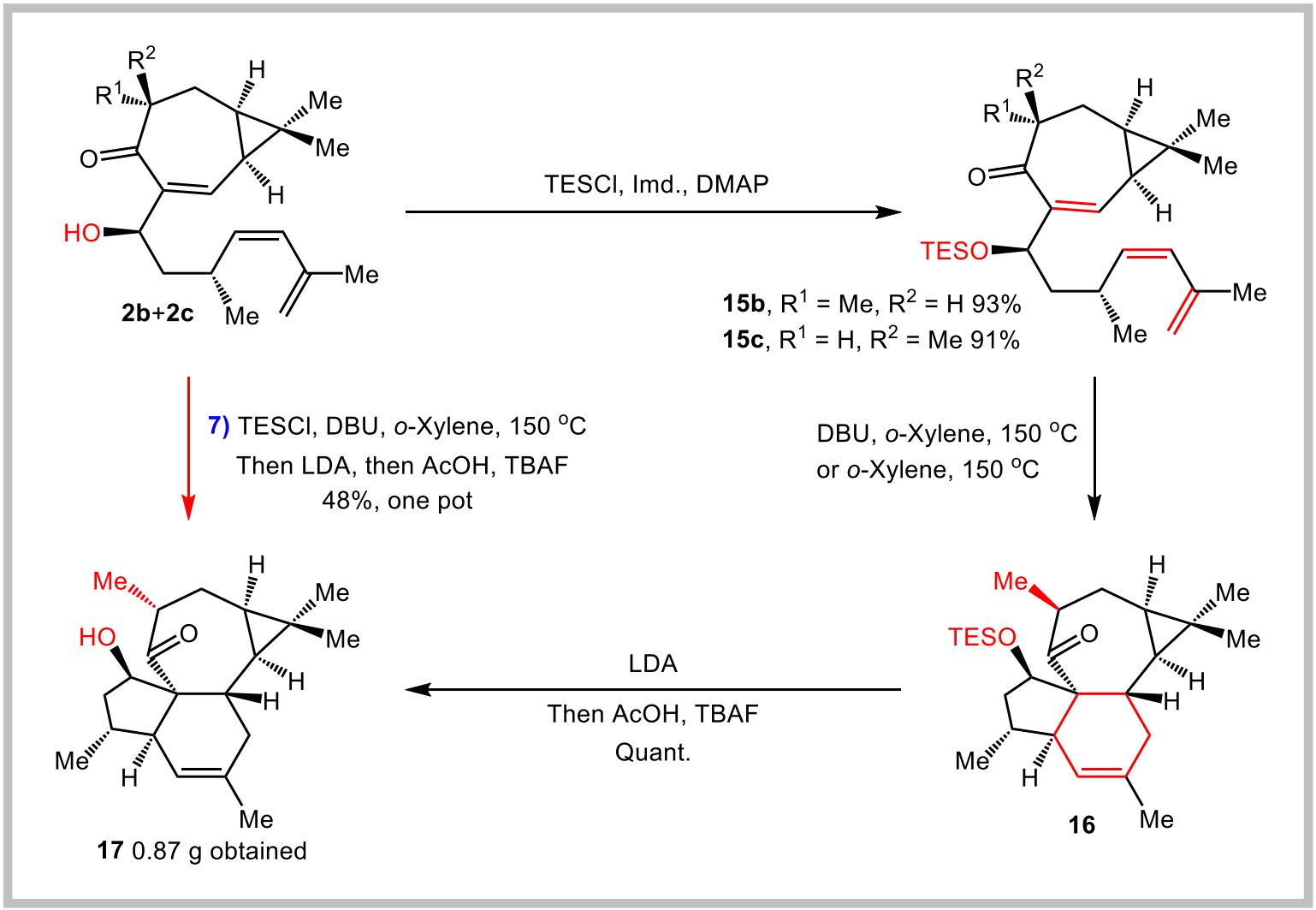
Synthesis of Intermediate 14



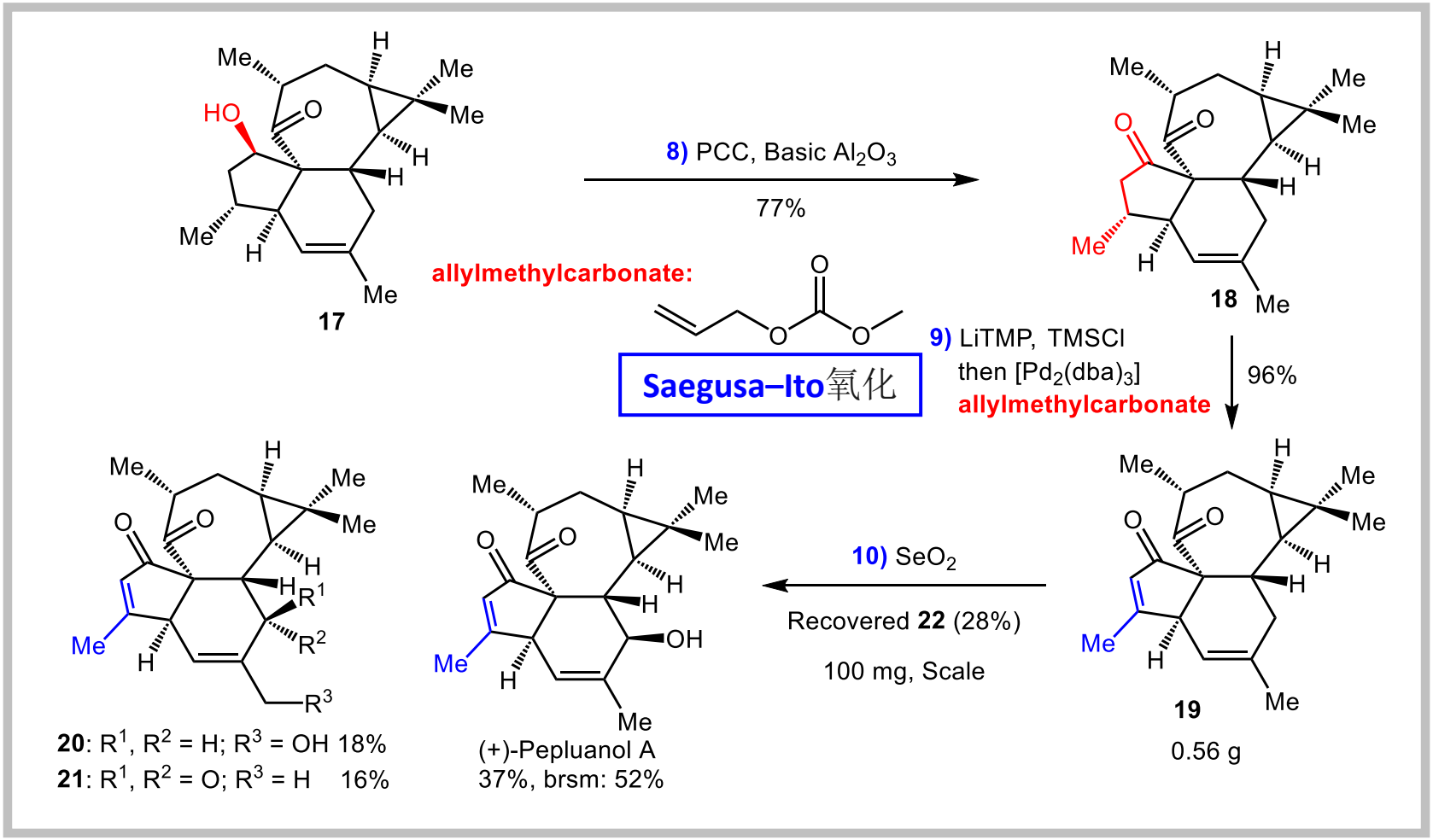
Synthesis of Intermediate 1



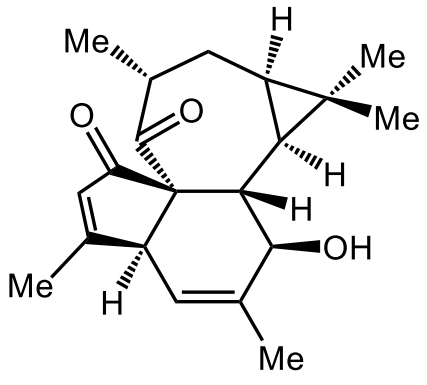
Synthesis of Intermediate 13



Synthesis of (+)-Pepluanol A



Summary



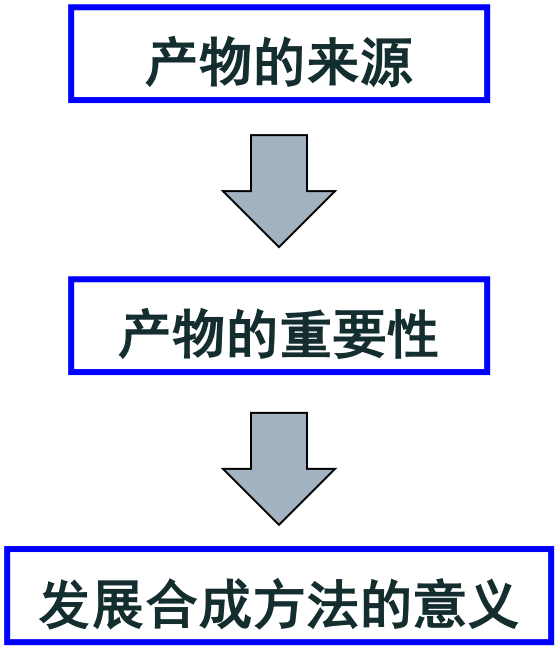
Pepluanol A

- **Ding's Work:**
  - **22** steps and **0.85%** yields
- **Gaich's Work:**
  - **10** steps and **2.4%** yields

- **Curtin−Hammett-driven Stereoconvergent Intramolecular Diels−Alder Reaction**
- **Nozaki−Hiyama−Kishi Reaction**
- **Negishi coupling**

The First Paragraph

写作思路：

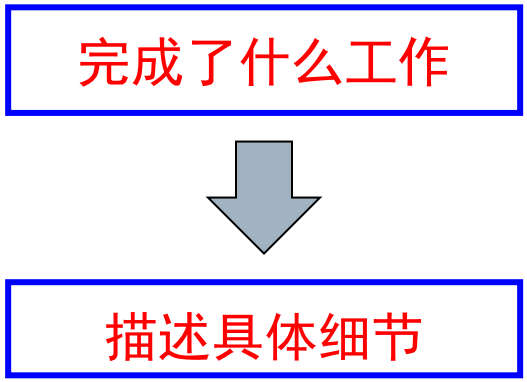


The First Paragraph

With more than 750 congeners, Euphorbia diterpenes are one of the largest families of diterpene natural products known. They are isolated from plants of the Euphorbia which, due to their constituents, have a long-standing tradition as medicinal plants in herbal folk medicine. Euphorbia plants are used to treat a variety of diseases, and over the past decades, intensive investigations on the bioactivity of these diterpenes have revealed cytotoxic, antiviral, multidrugresistance-reversing (MDR), and antitumor properties. Euphorbia diterpenes are structurally diverse including the lathyrane, tigliane, daphnane, jatrophane, and the ingenane backbones. Each member of this diterpene subfamily exhibits a complex molecular scaffold, thus attracting great attention from the synthetic community.

The Last Paragraph

写作思路：



The Last Paragraph

In conclusion, we have developed an asymmetric synthesis to (+)-pepluanol A (**1**) requiring only **10 isolated steps**. The individual steps are robust and work on a gram scale, including the Curtin-Hammett-driven stereoconvergent Diels-Alder reaction. A key feature of our synthesis relies on the fully convertible configuration of the methyl group at C-13. The desired configuration at position C-13 in the natural product is opposite to the required configuration for successful conversion in the Diels-Alder reaction but can be fully inverted afterward. The overall yield for (+)-pepluanol A (**1**) is **8.6%** from known intermediate **11** and 2.4% from commercially available (+)-3-carene **12**.

Representative examples

In conclusion, we have developed an asymmetric synthesis to (+)-pepluanol A requiring only 10 isolated steps.

A key feature of our synthesis relies on the fully convertible configuration of the methyl group at C-13.

Encouraged by these outcomes, the total synthesis of Euphorbia diterpenoid (+/-)-pepluanol A was then executed.

Thanks

for your kind attention !