

Total Synthesis of Longifolenes

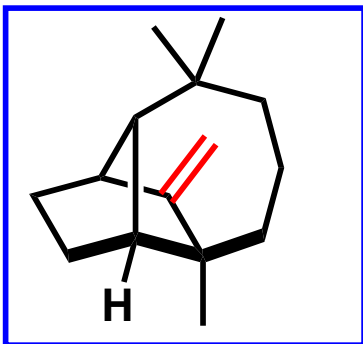


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CH-845 Course on Organic Synthesis

Longifolene

Longifolene



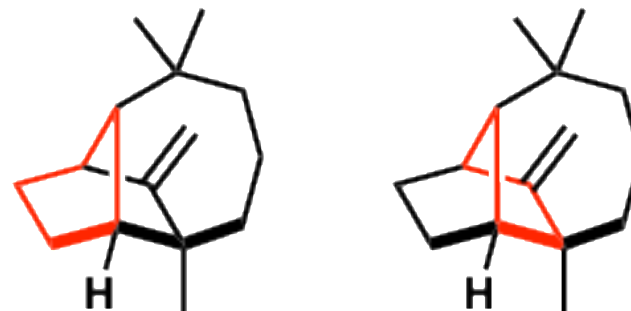
➤ **Longifolene** is the common (or trivial) chemical name of a naturally occurring, **oily liquid** hydrocarbon found primarily in the high-boiling fraction of certain **pine resins**

➤ The name is derived from that of a pine species from which the compound was isolated ***Pinus longifolia***

Naffa, P.; Ourisson, G. *Bulletin de la Société chimique de France*, **1954**, 1410

Simonsen, J. L., *J. Chem. Soc.* **1920**, 117, 570

No. of Rings in Longifolene

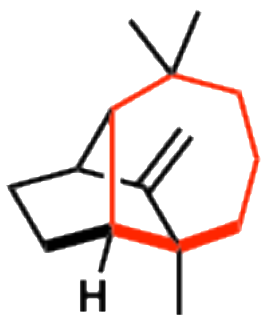


5-membered ring

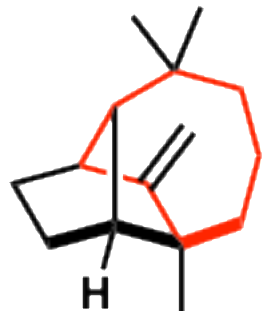


6-membered ring

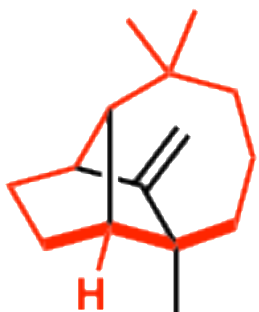
Corey's Total Synthesis of Longifolene



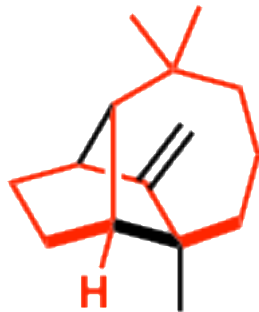
7-membered ring



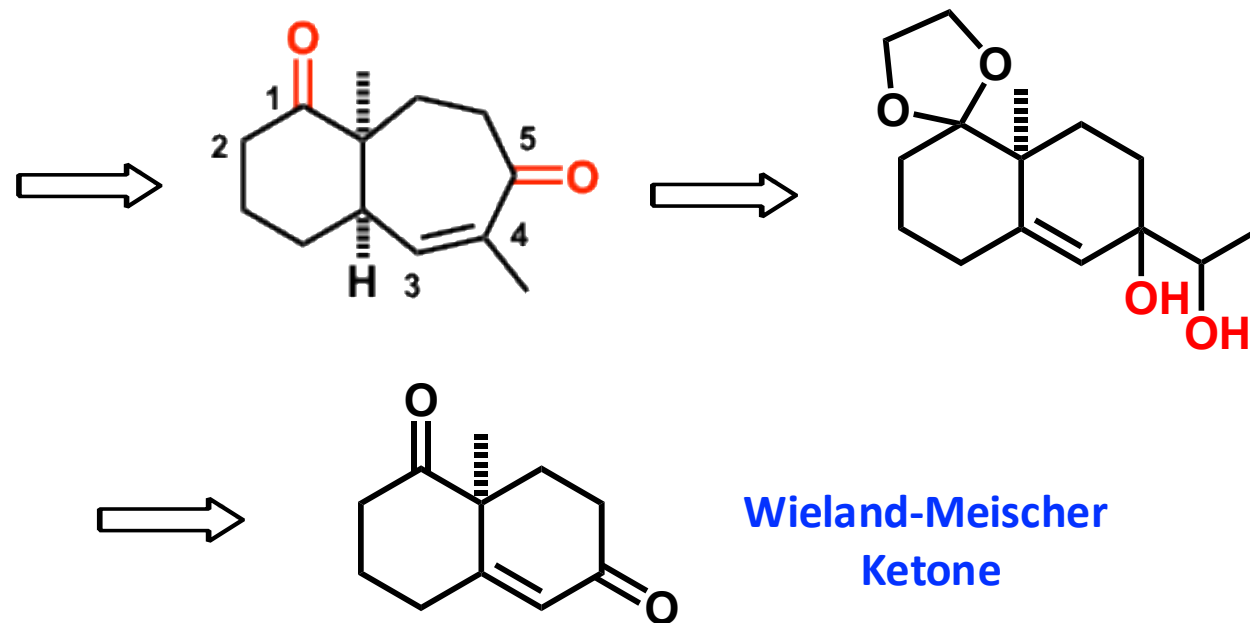
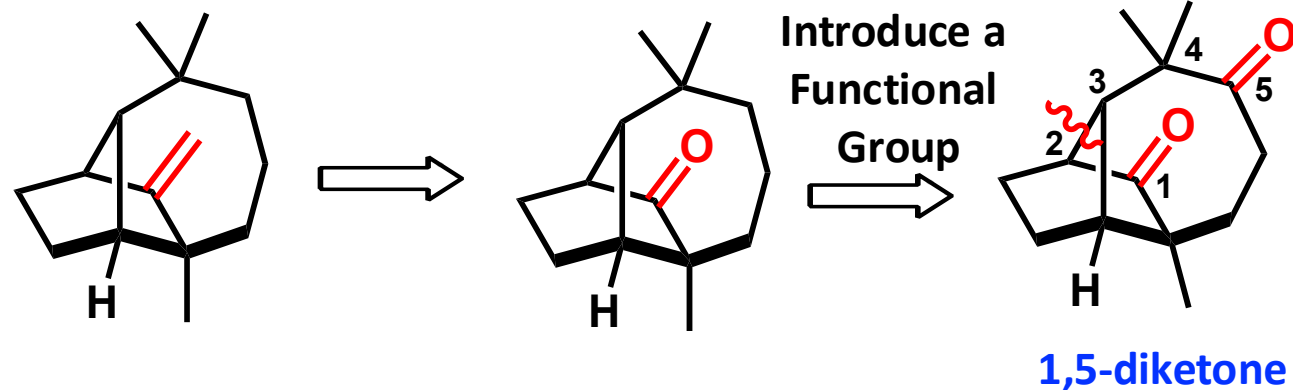
8-membered ring



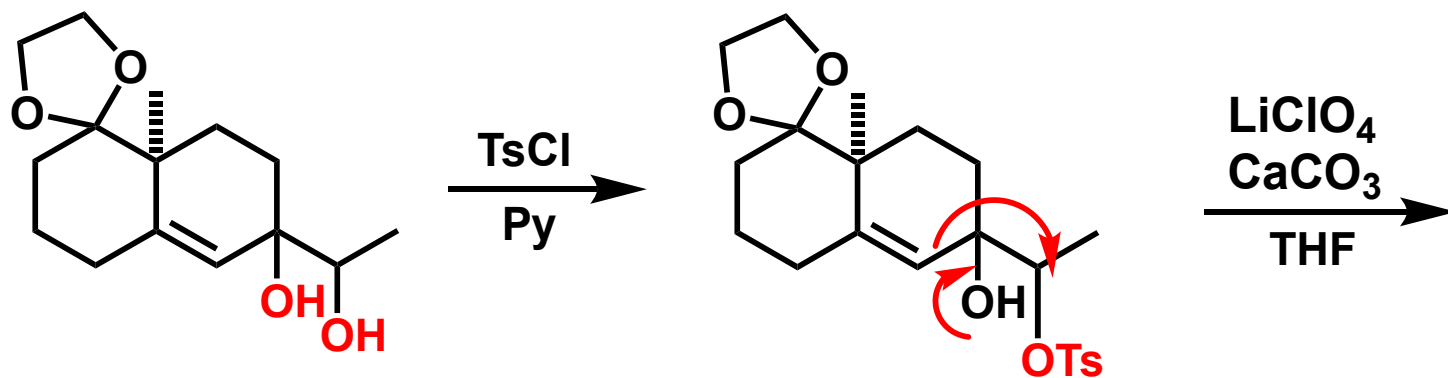
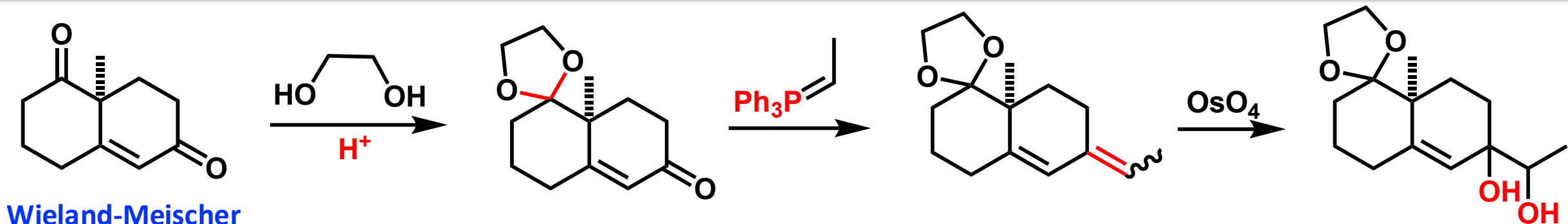
11-membered ring



Retrosynthesis

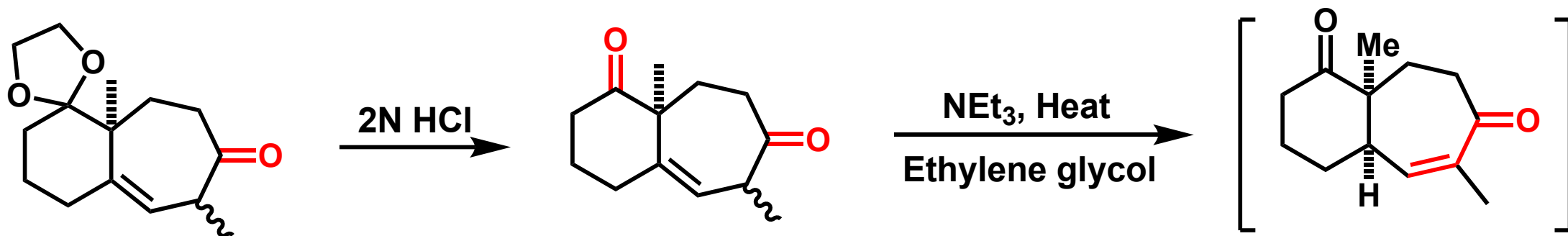


Corey's Total Synthesis of Longifolene

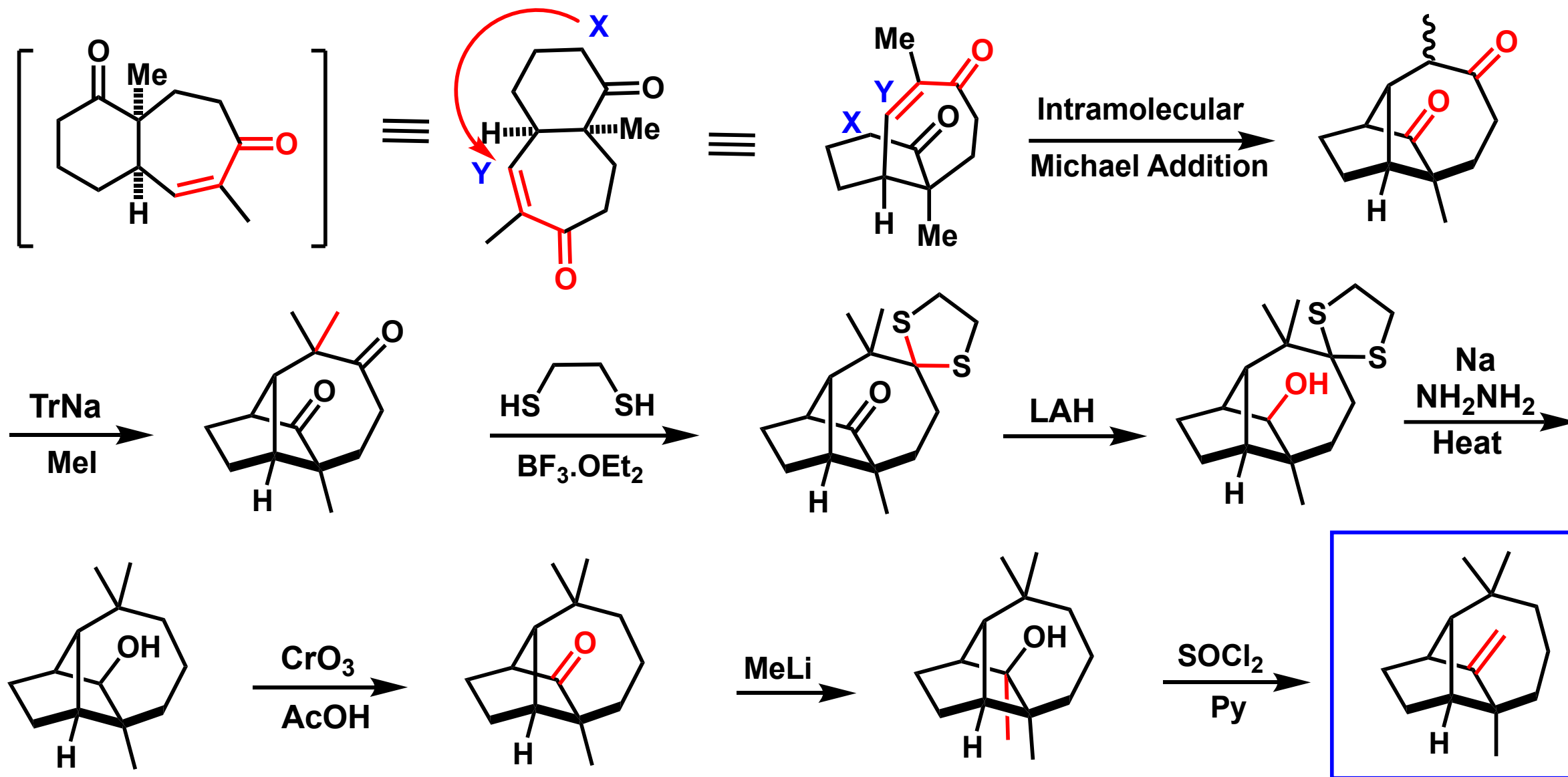


1. Protonation will happen at tertiary alcohol

2. How to make the secondary alcohol as a better leaving group

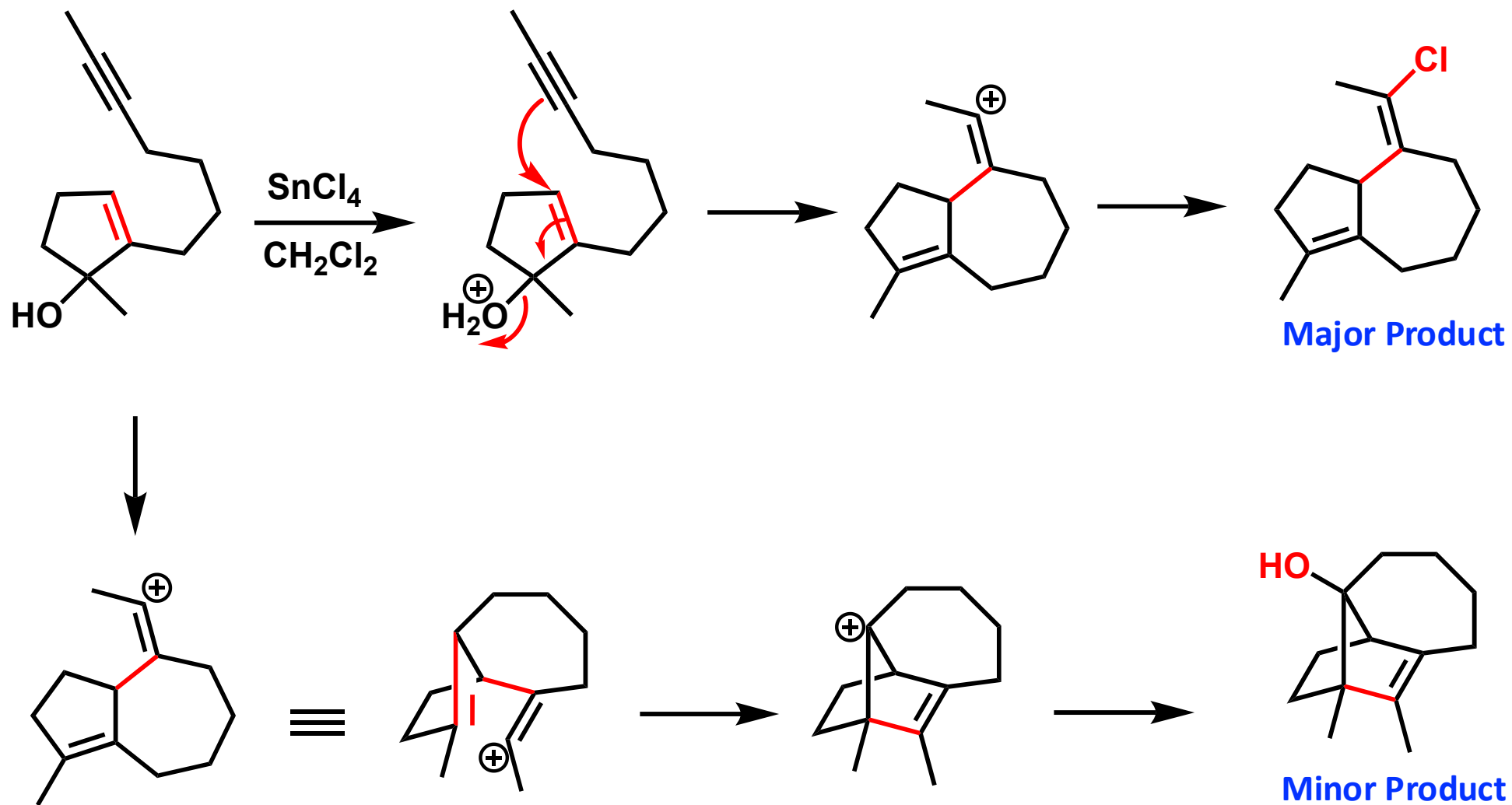


Corey's Total Synthesis of Longifolene



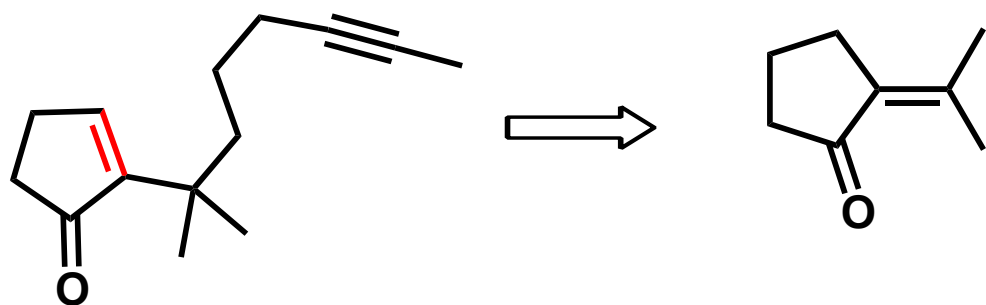
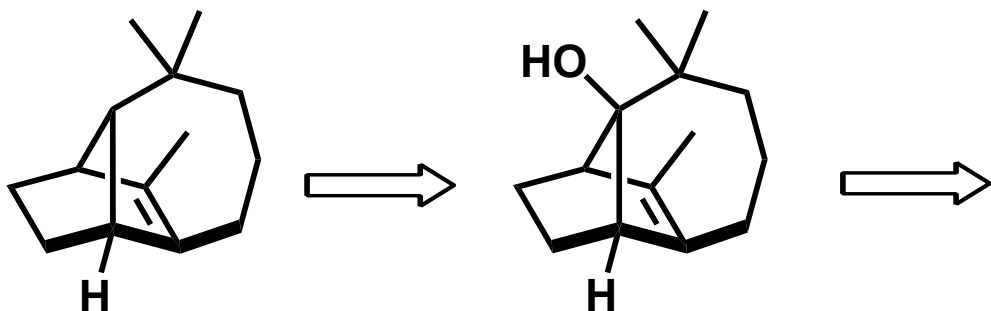
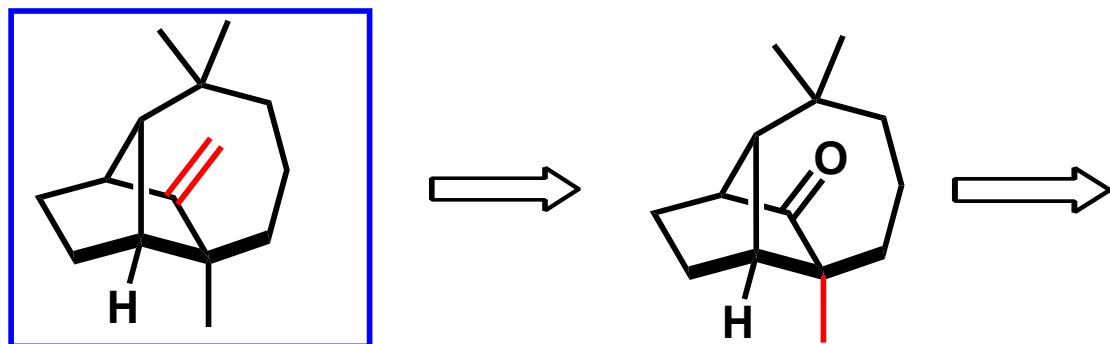
- The total synthesis of **Longifolene** was reported by **Corey** and co-workers in **1964**
- The synthesis was started from **Wieland Miescher ketone**
- The key reactions were intramolecular **Michael addition** and **1,2-diol rearrangement**
- Their total synthesis was completed in **15 linear steps** with a **2.8 % overall yield**

Johnson's Serendipitous Observation

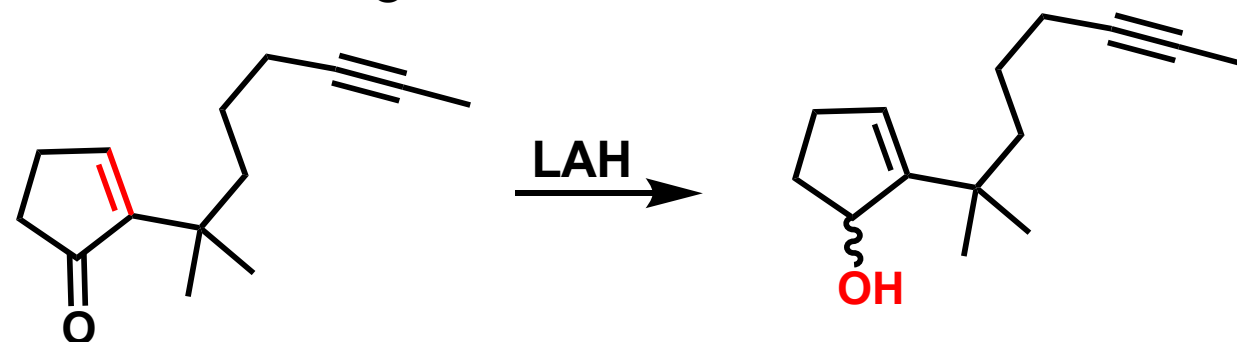
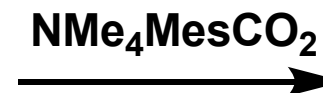
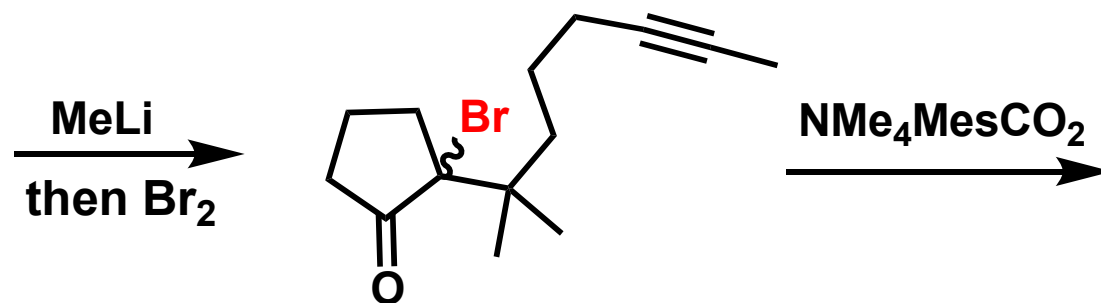
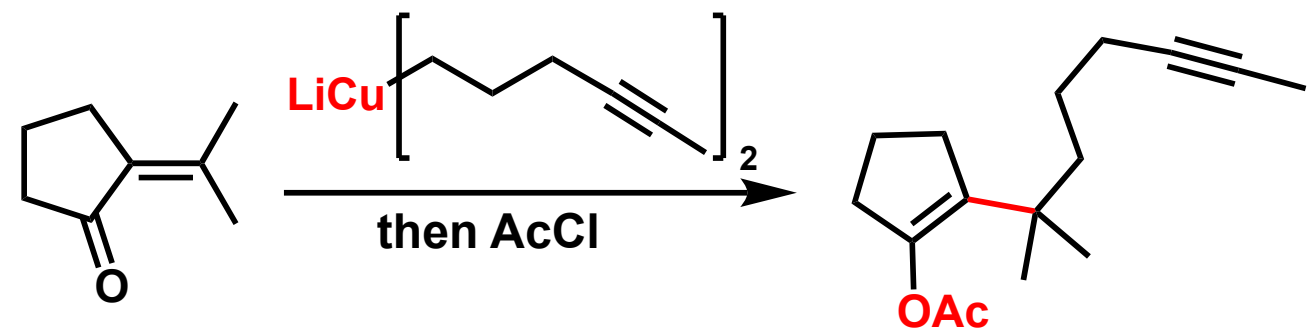


Johnson's Synthesis of Longifolene

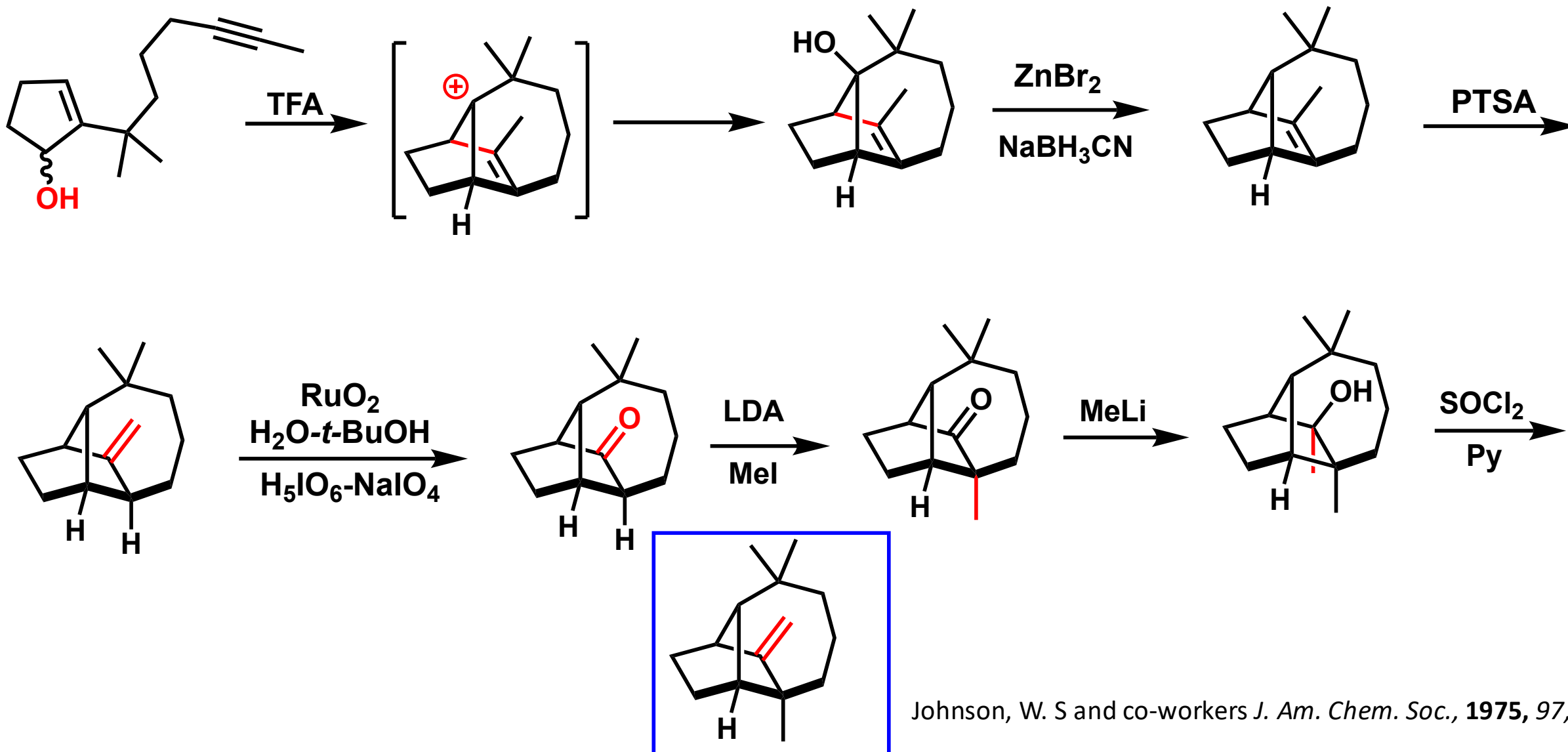
Retrosynthesis



Forward Synthesis



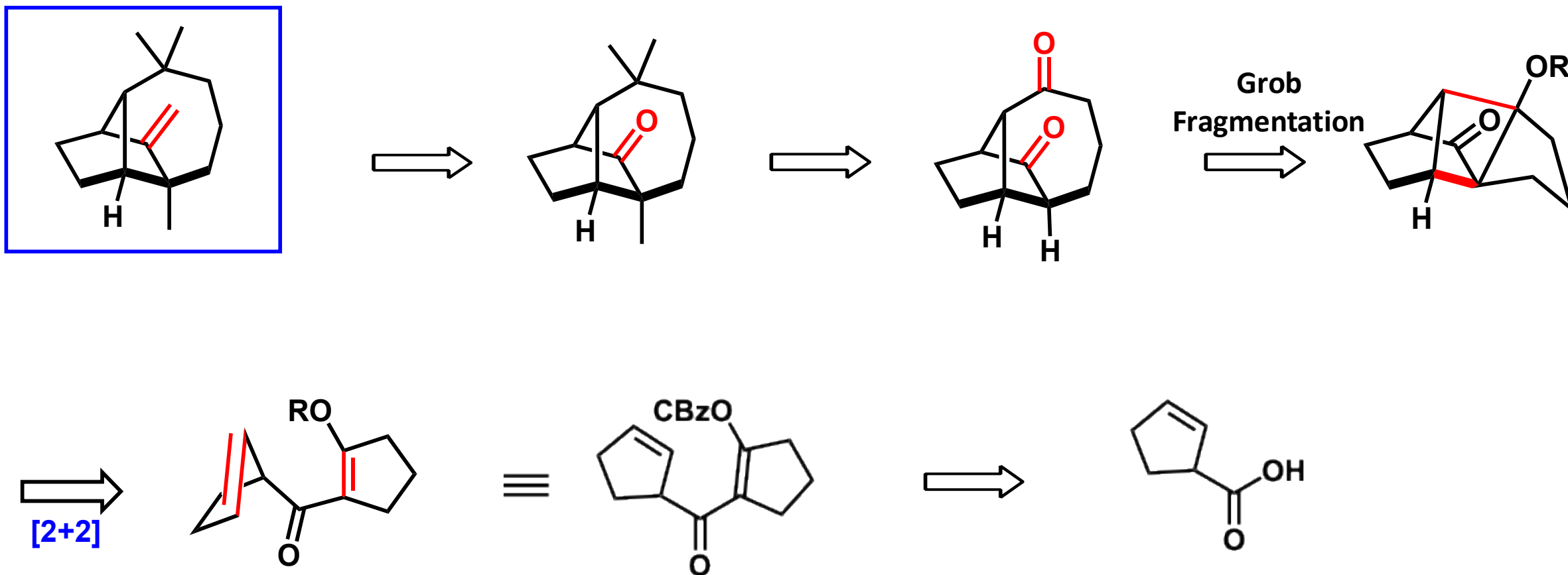
Johnson's Synthesis of Longifolene



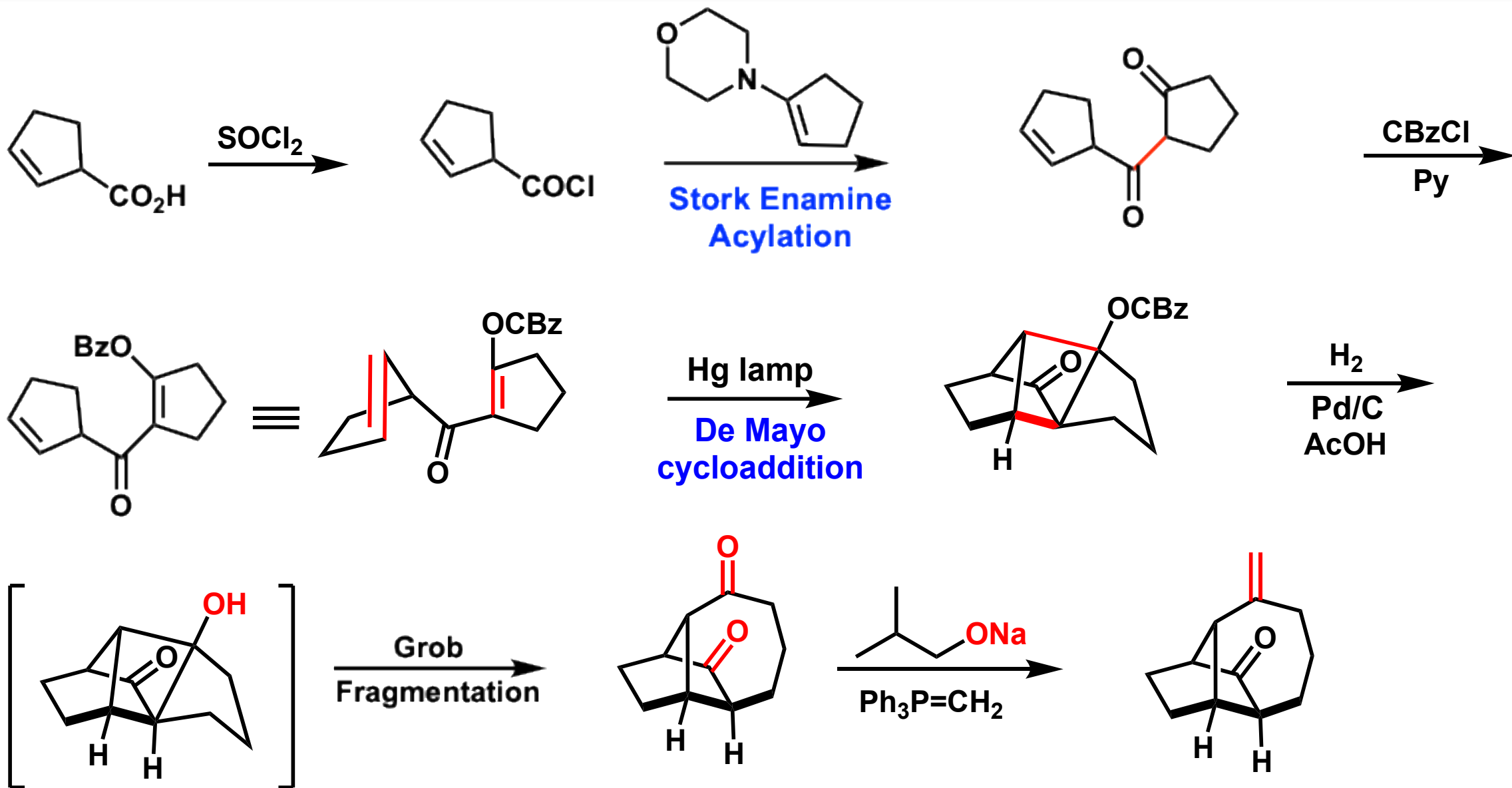
Johnson, W. S and co-workers *J. Am. Chem. Soc.*, **1975**, 97, 4777

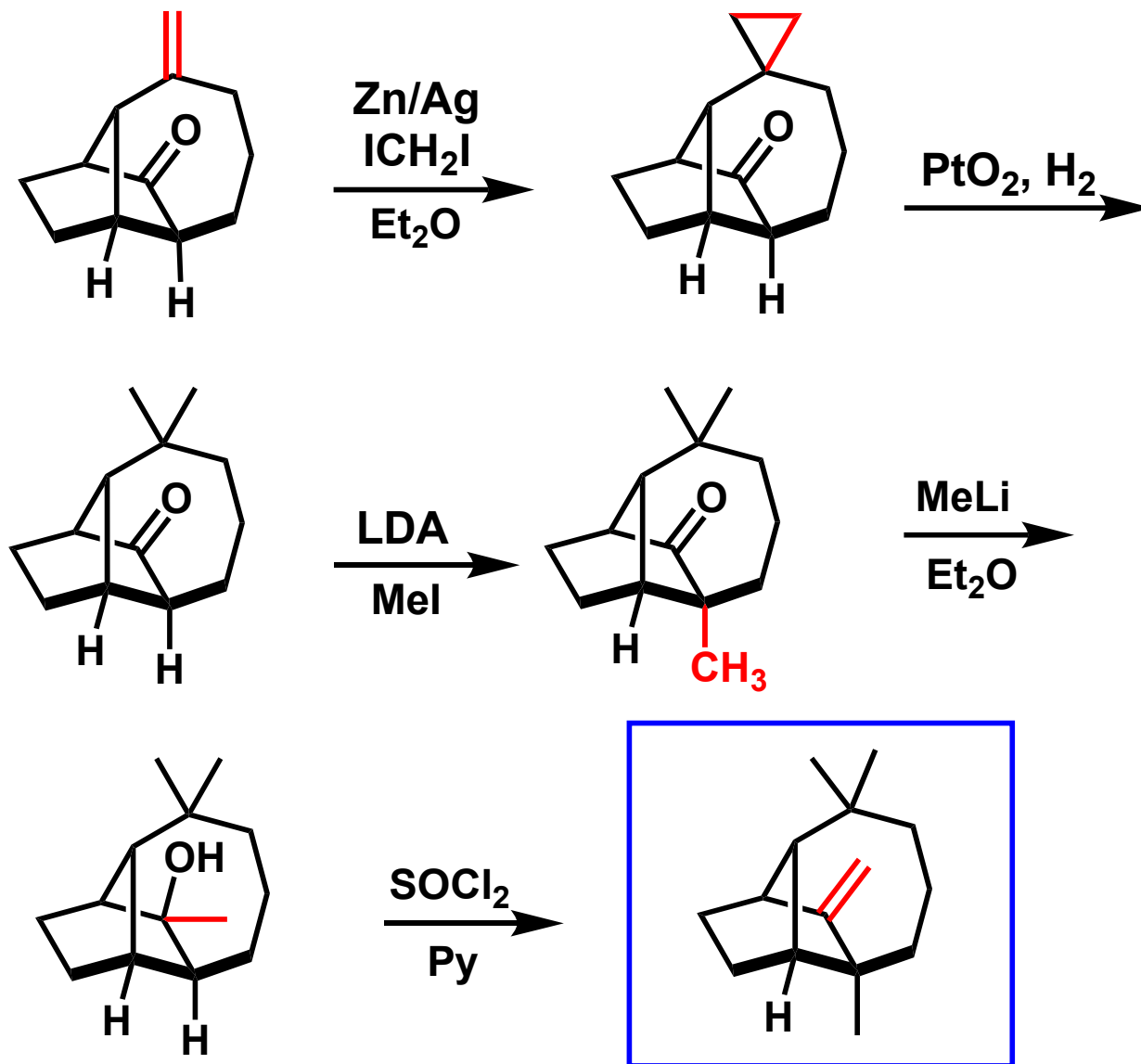
- The total synthesis of **longifolene** was reported by **Johnson** and co-workers in **1975**
- The synthesis was started from, **2-isopropylidenecyclopentanone**
- The synthesis involved a **polyene type cyclization** as the key step
- Their total synthesis was completed in **11 linear steps** with a **26.6 % overall yield**

Oppolzer's Synthesis of Longifolene



Oppolzer's Synthesis of Longifolene





Summary

- The total synthesis of longifolene was reported by Oppolzer and co-workers in 1978
- The synthesis was started from, a commercially available 2,4 cyclopentadiene-1-carboxylic acid
- The key chemical transformations in this synthesis include, De Mayo [2+2] cycloaddition reaction and Grob Fragmentation
- Their total synthesis was completed in 11 linear steps with a 23% overall yield

- Corey's total synthesis was completed in **15 linear steps with a 2.8 % overall yield**
- Johnson total synthesis was completed in **11 linear steps with a 26.6 % overall yield**
- Oppolzer's total synthesis was completed in **11 linear steps with a 23% overall yield**