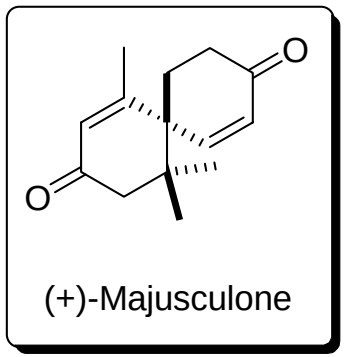
Enantioselective Synthesis of (+)-Majusculone

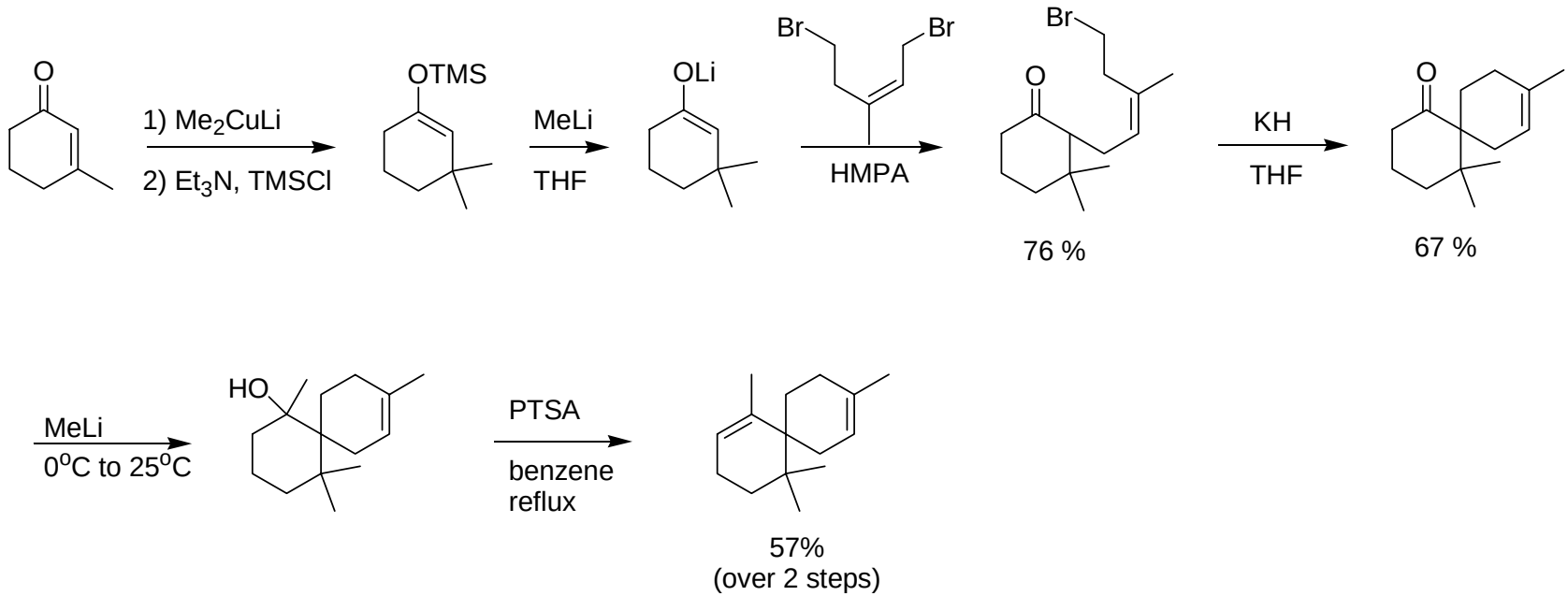
Taber, D. F.; Sikkander, M. I.; Storck, P. H. *J. Org. Chem.* **2007**, *ASAP*.

(+)-Majusculone



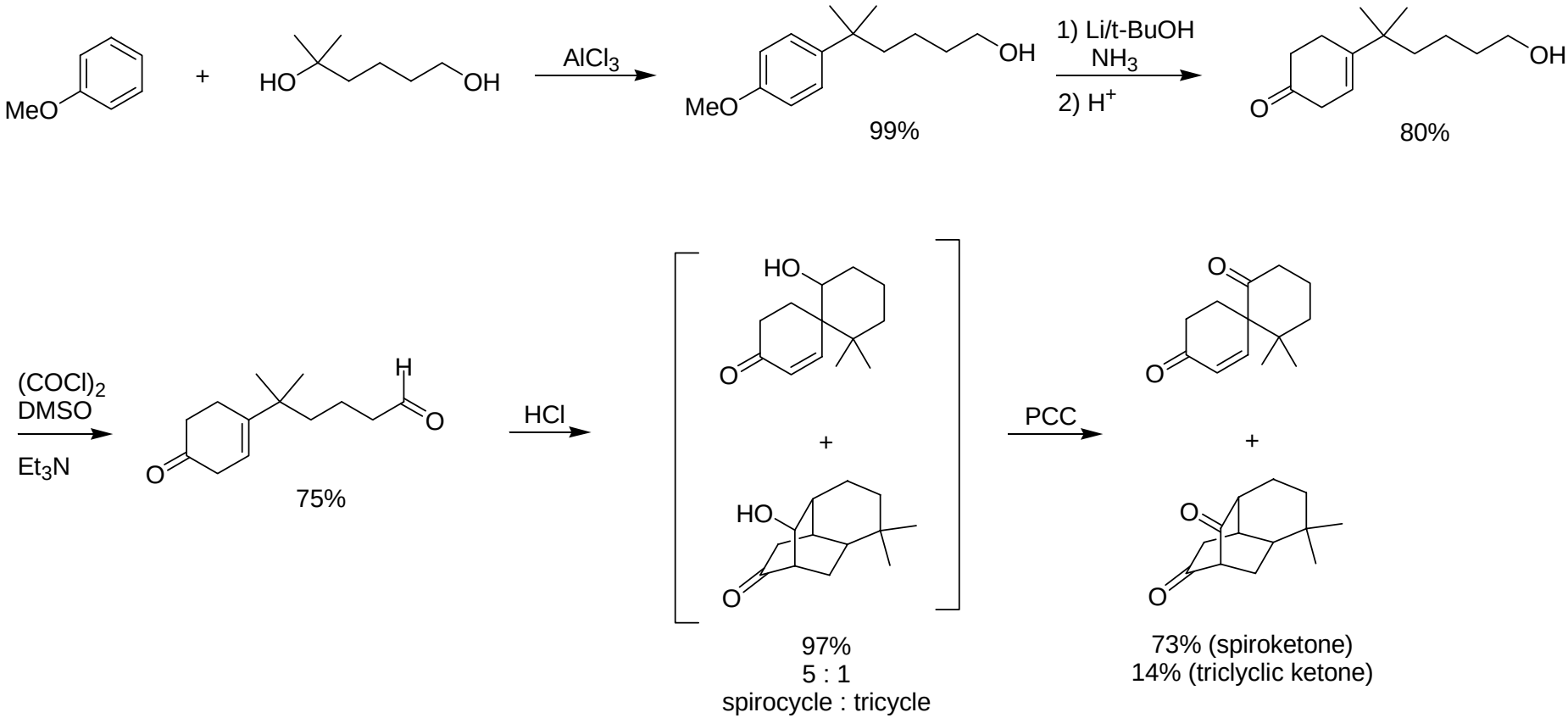
- Chamigrane sesquiterpene isolated from an extract of the red alga *Laurencia cartilaginea*
- Demonstrates moderate in vitro anthelmintic activity (<100 μM)
- Bromochamigrane analogs have exhibited selective and potent cytotoxicity in the NCI 60 cell antitumor screen, particularly the colon cancer subpanel
- No enantioselective synthesis of a chamigrane has been reported

Canonne Synthesis



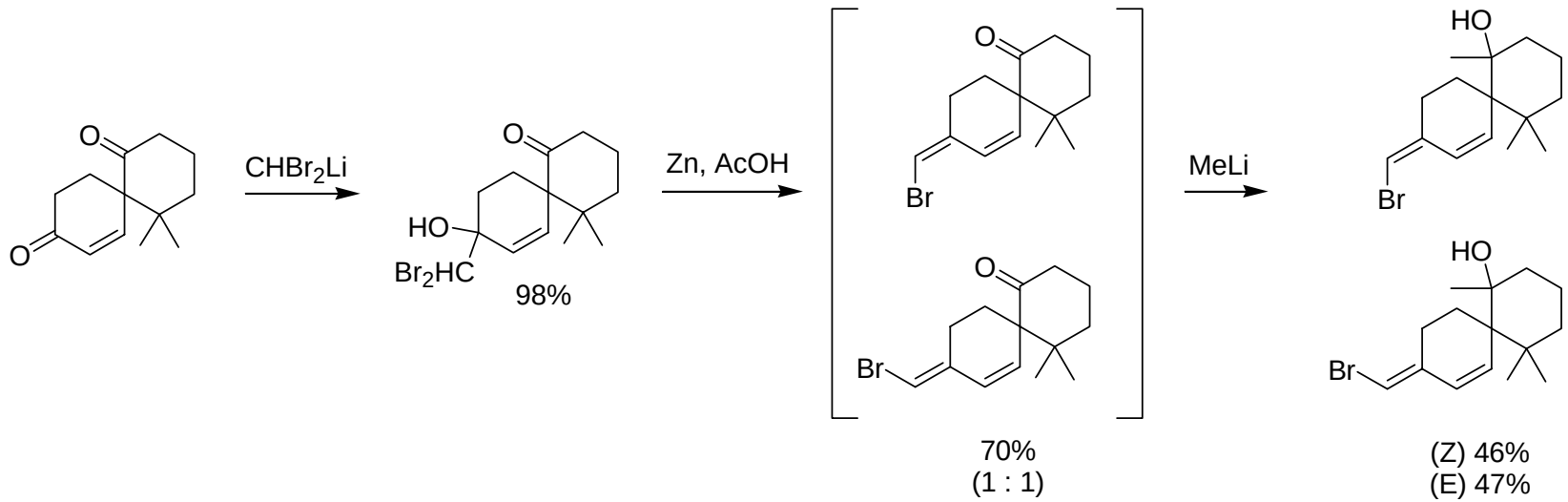
Plamondon, J.; Canonne, P. *Tetrahedron Lett.* **1991**, *32*, 589-592.

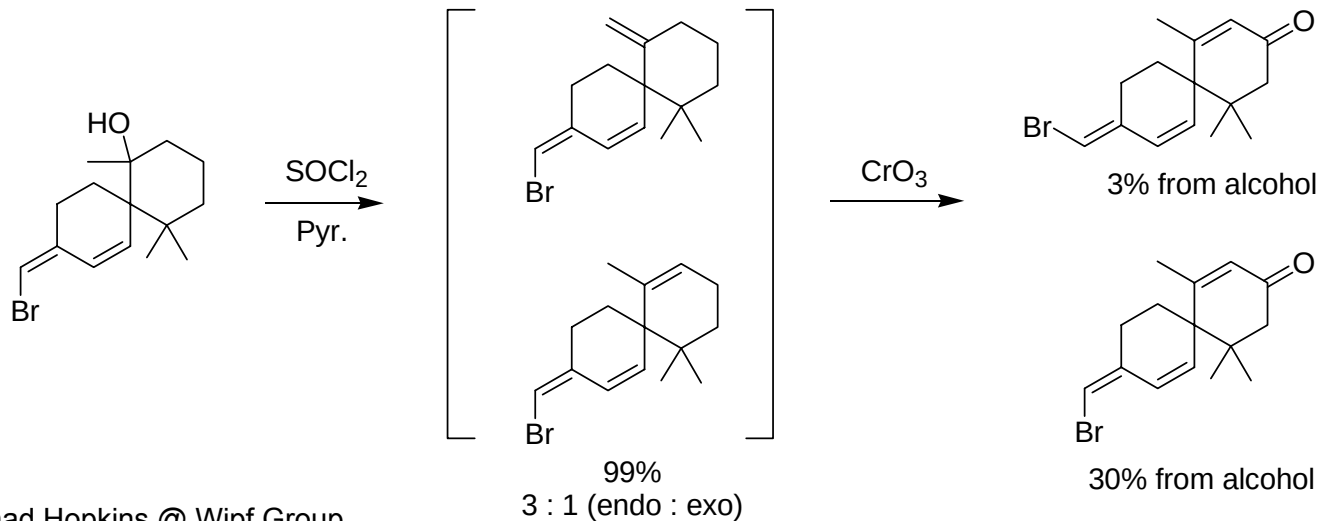
Yamada Synthesis



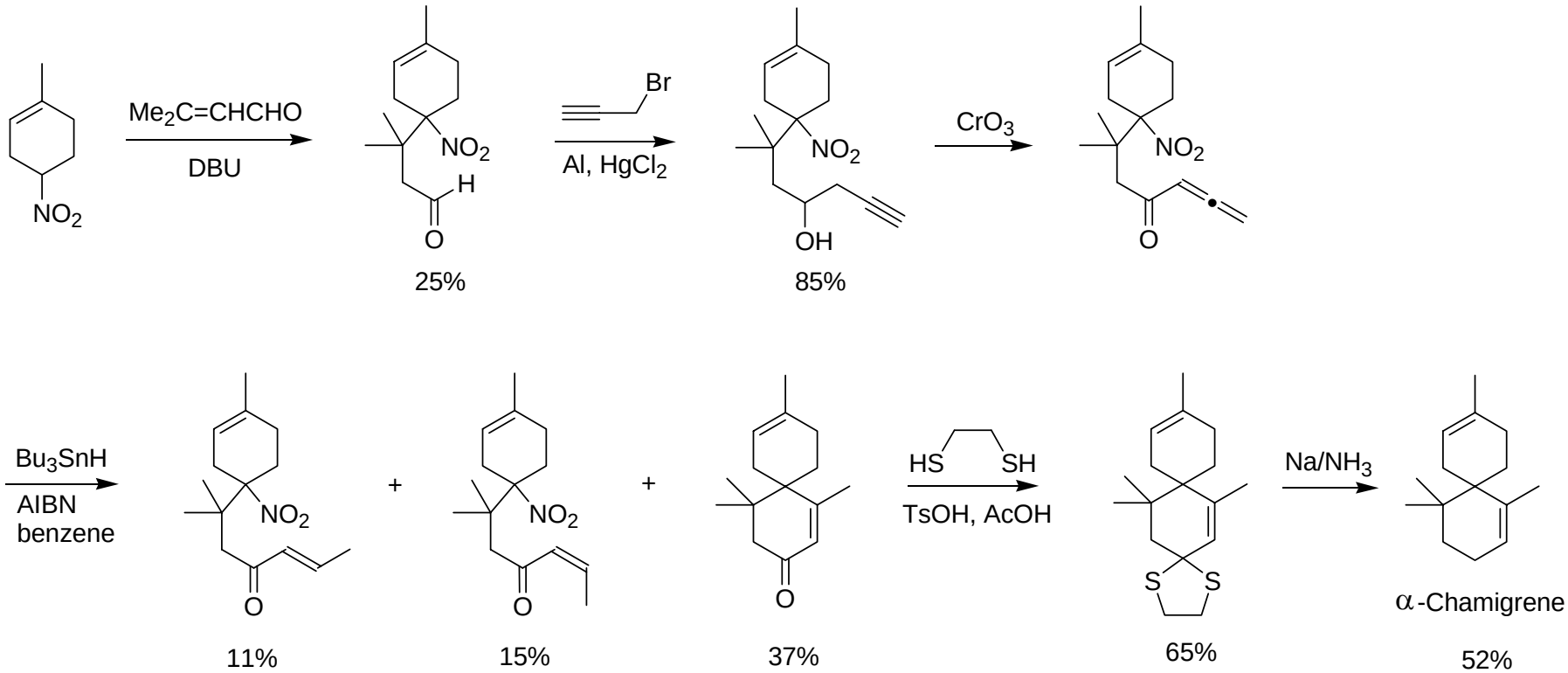
Niwa, H.; Yoshida, Y.; Hasegawa, T.; Yamada, K. *Tetrahedron* **1991**, *47*, 2155-2162.

Yamada Synthesis (contd.)



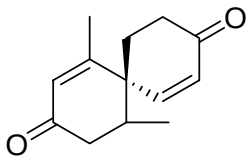


Chen Synthesis

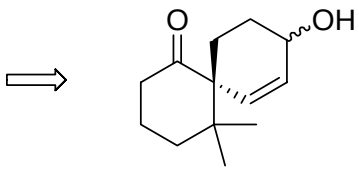


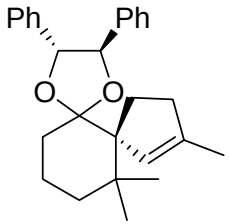
Chen, Y.-J.; Wang, C.-Y.; Lin, W.-Y. *Tetrahedron* **1996**, *52*, 13181-13188.

Retrosynthetic Analysis

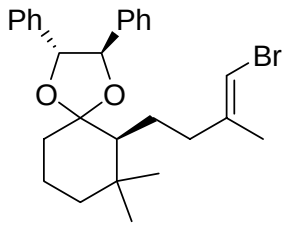


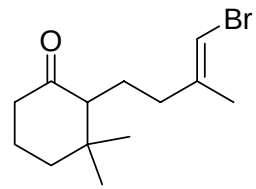
(+)-majusculone

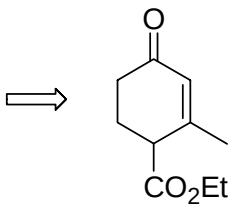




intramolecular
C-H insertion

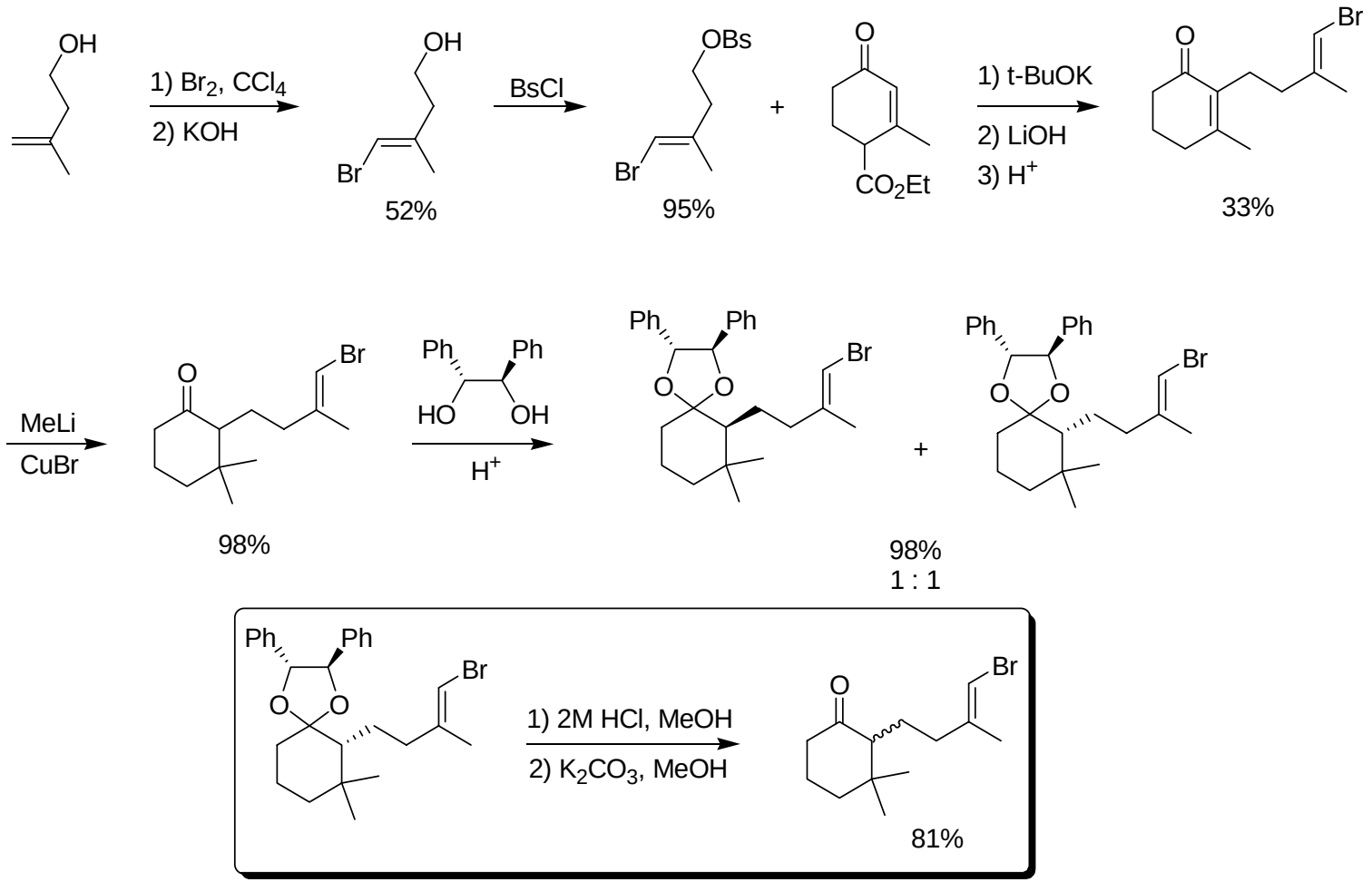




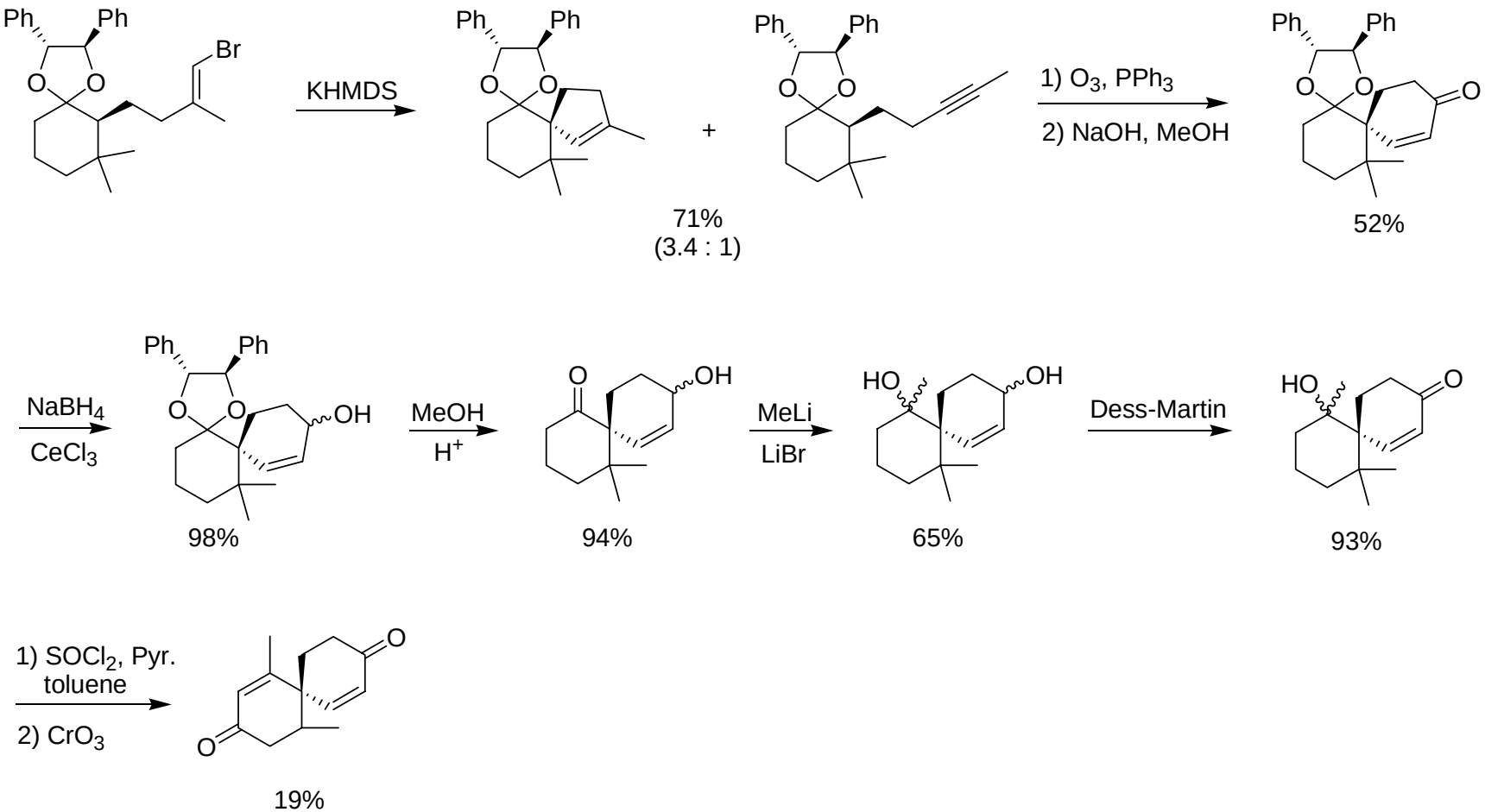


Hagemann's ester

Synthesis of (+)-Majusculone



Completion of (+)-Majusculone



Key Points

- First enantioselective synthesis of a chamigrane sesquiterpene
- Synthetic linchpin lies in an intramolecular alkylidene C-H insertion
- Spirocyclization with retention of absolute configuration makes this a valuable tool for natural product synthesis