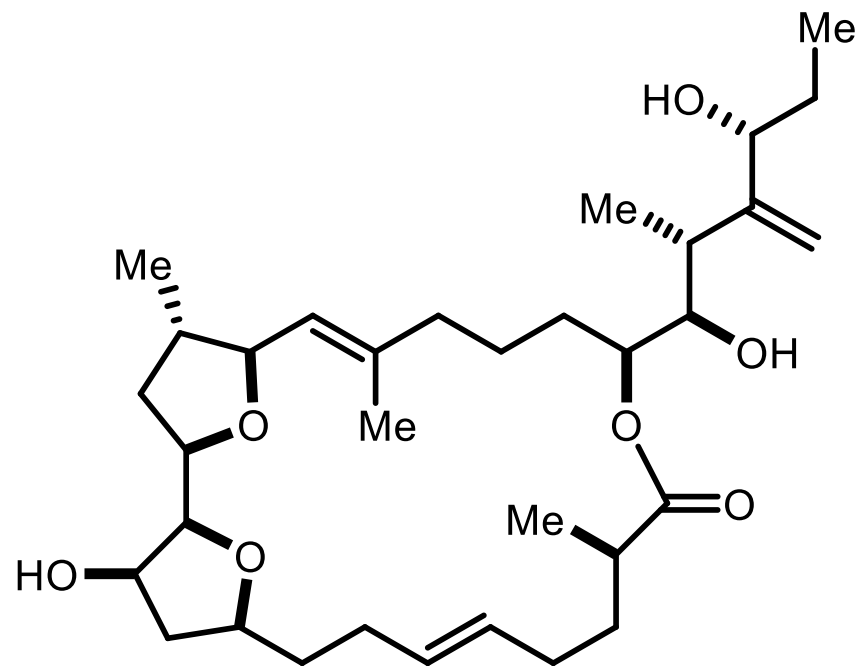


Total Synthesis and Stereochemical Revision of Iriomoteolide-2a

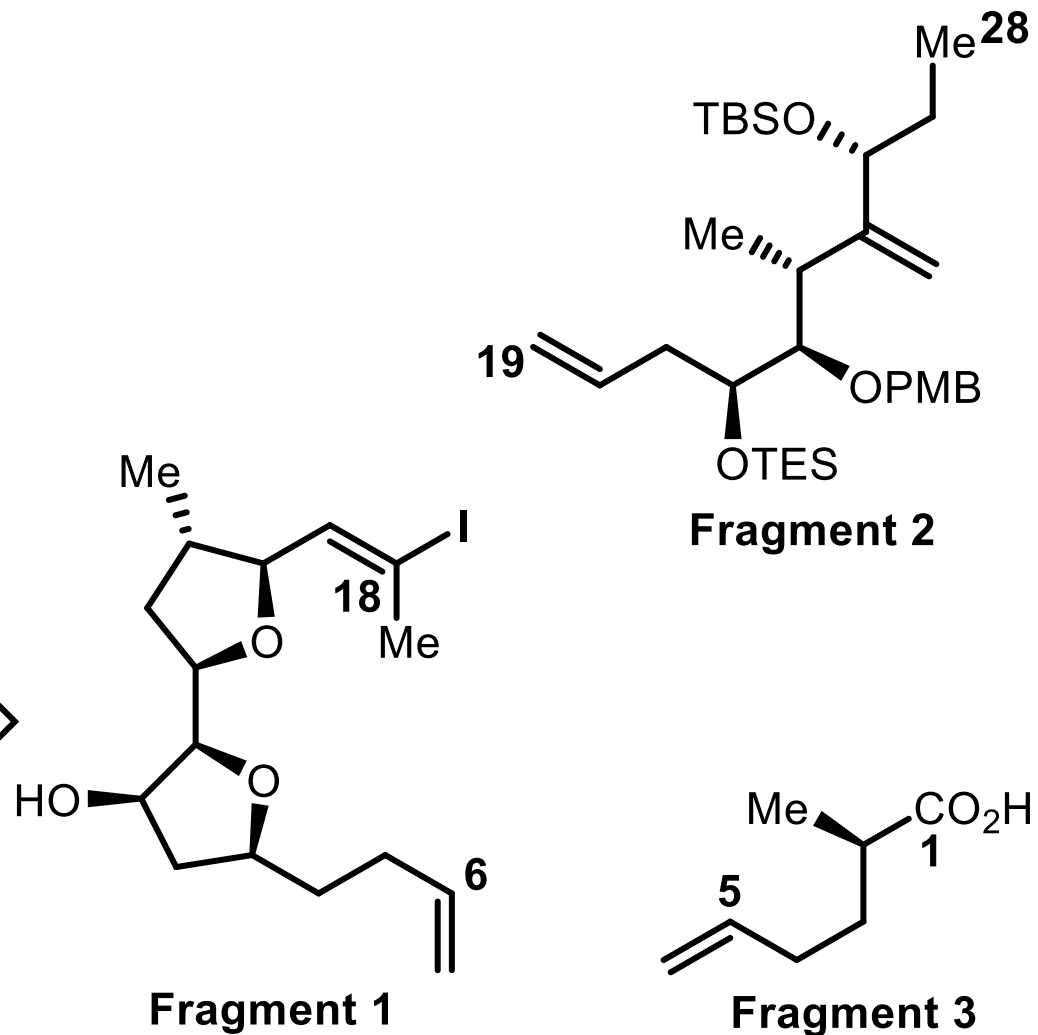
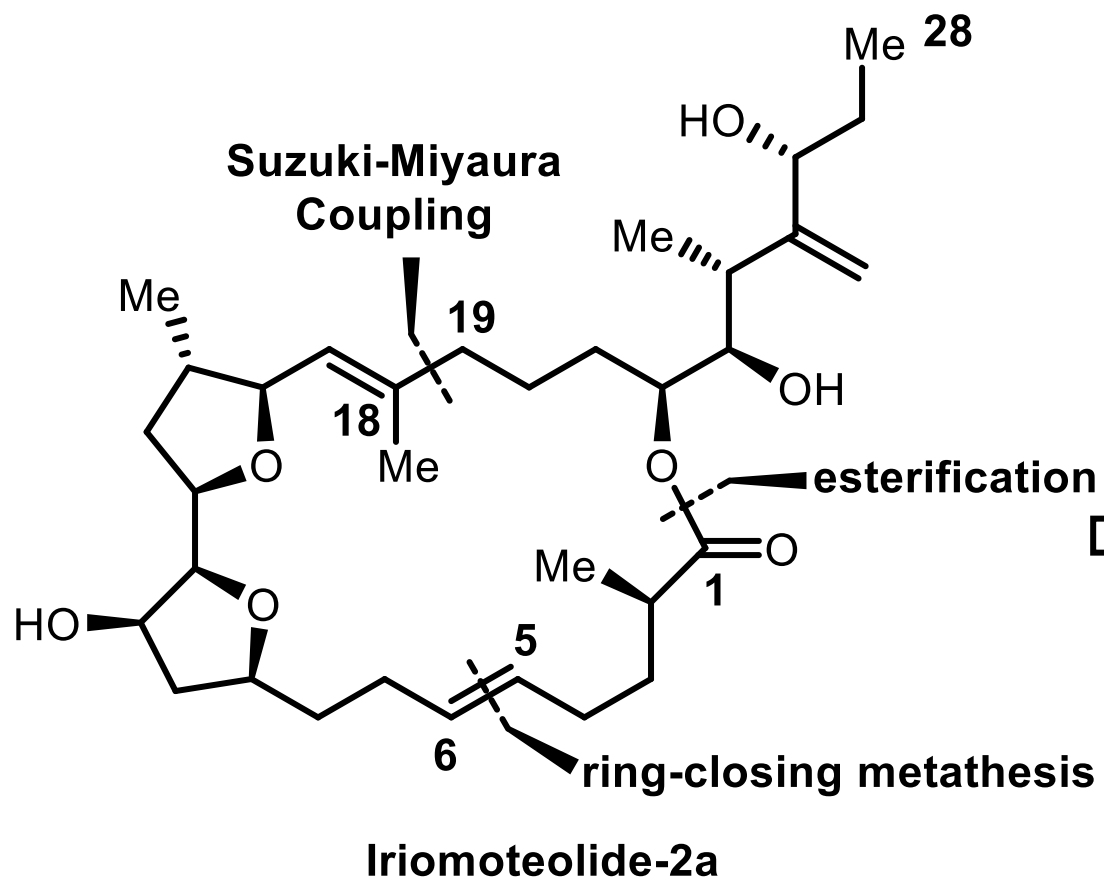
*Keita Sakamoto, Akihiro Hakamata, Masashi Tsuda, and Haruhiko Fuwa**



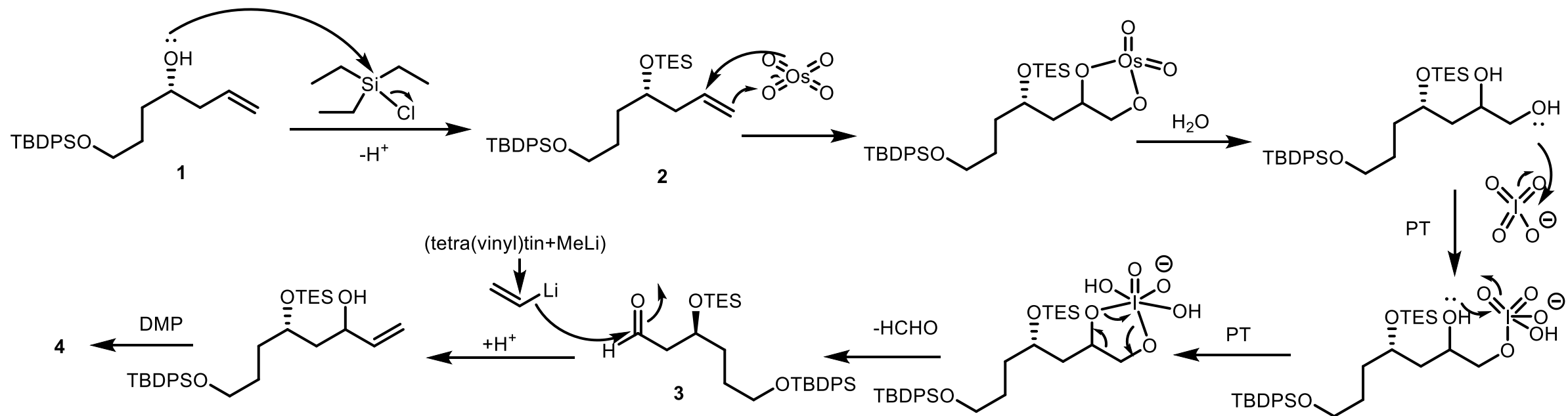
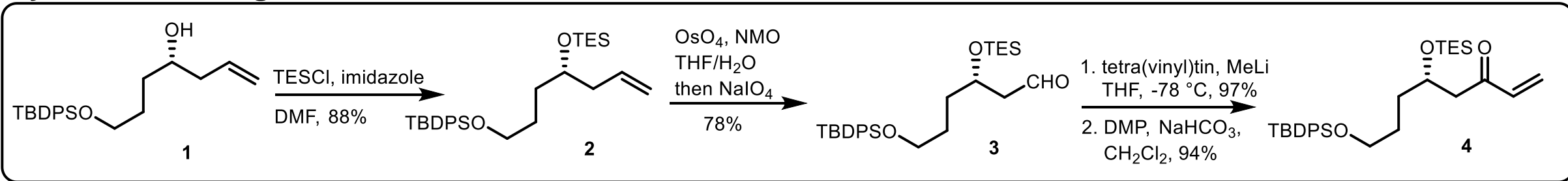
Iriomoteolide-2a

- Isolated from a cultured broth of the benthic dinoflagellate *Amphidinium* sp. (HYA024 strain).
- 23-membered macrocyclic backbone with a bis(tetrahydrofuran) substructure and a side chain containing four stereogenic centers.
- Remarkable in vitro cytotoxicity against human B lymphoma DG75 cells and human cervix adenocarcinoma HeLa cells.
- In vivo antitumor activity against murine leukemia P388 cells.

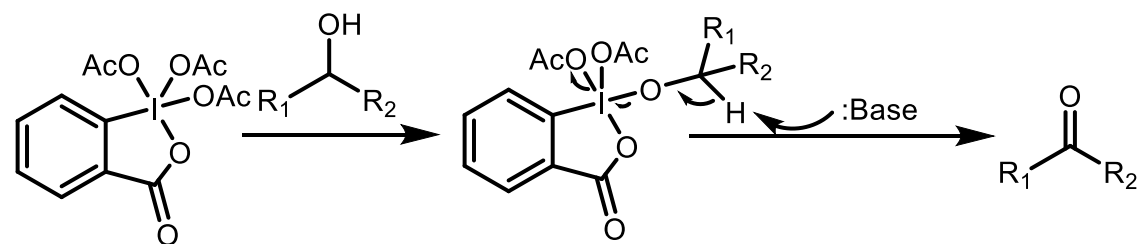
Retrosynthetic Analysis



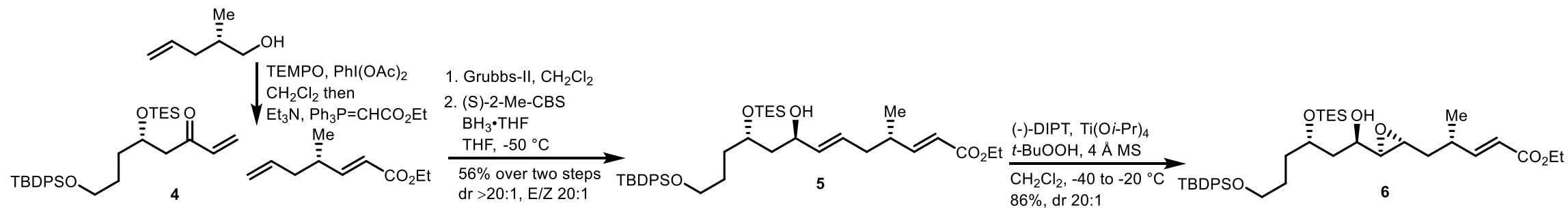
Synthesis of Fragment 1



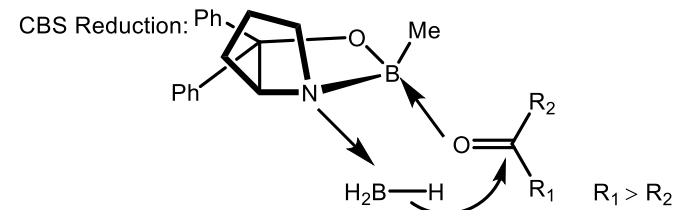
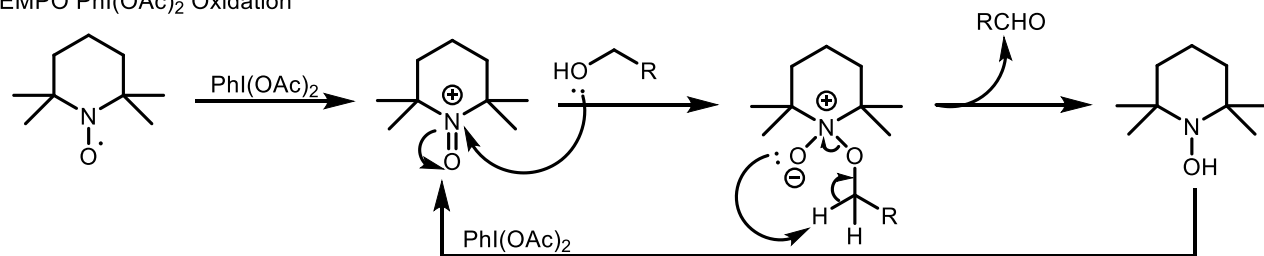
DMP Oxidation Mechanism:



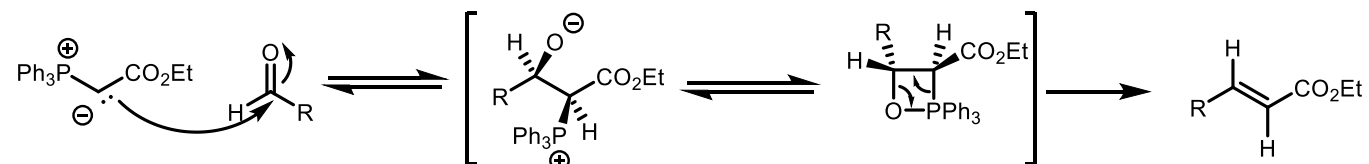
Synthesis of Fragment 1



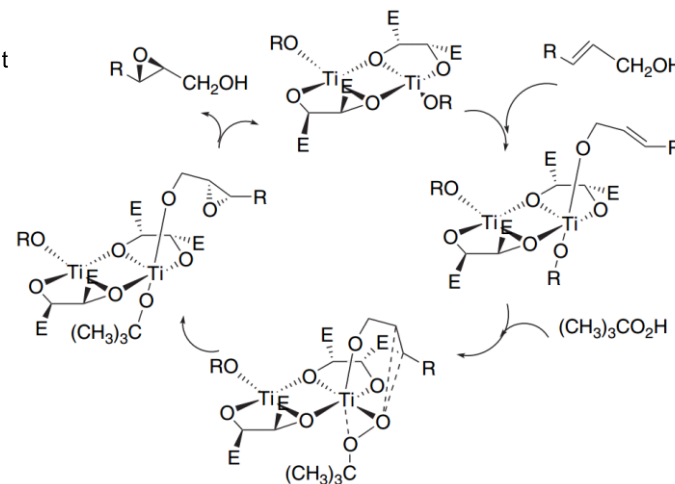
TEMPO PhI(OAc)₂ Oxidation



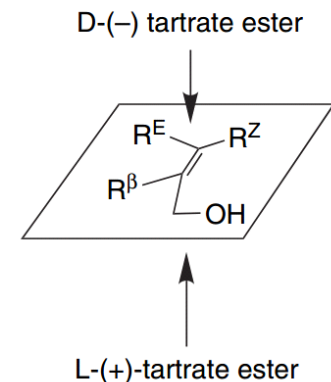
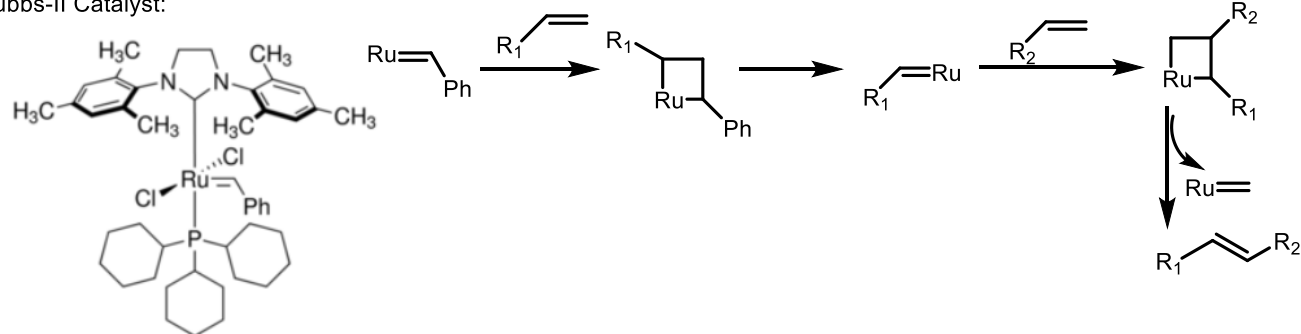
Horner-Wadsworth-Emmons Olefination



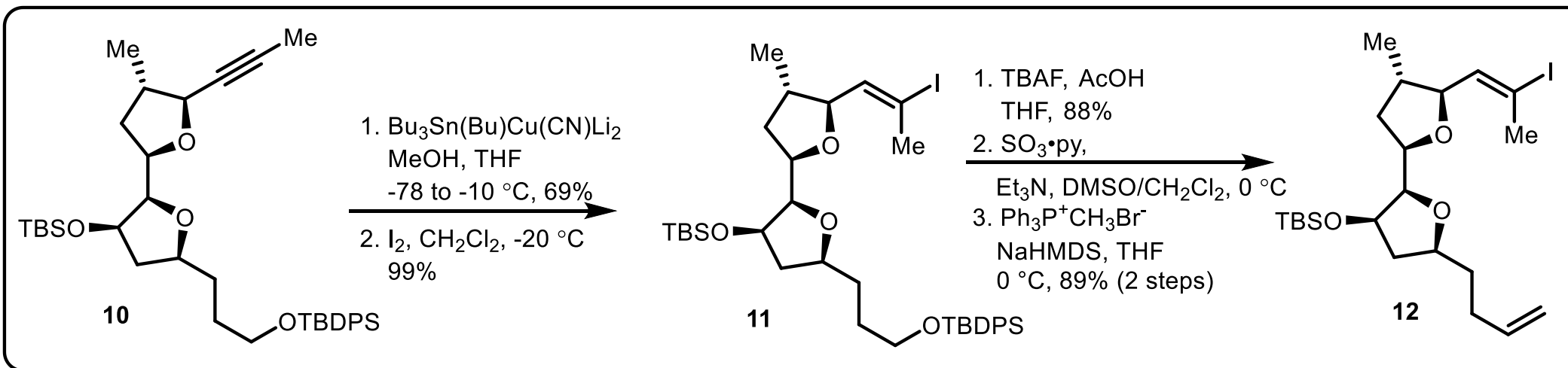
Sharpless Asymmetric Epoxidation



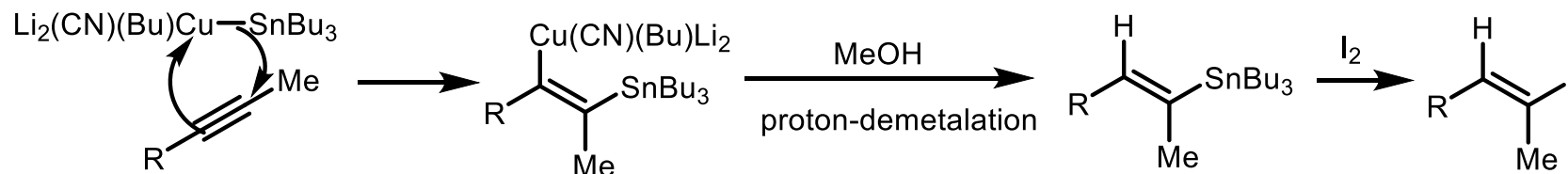
Grubbs-II Catalyst:



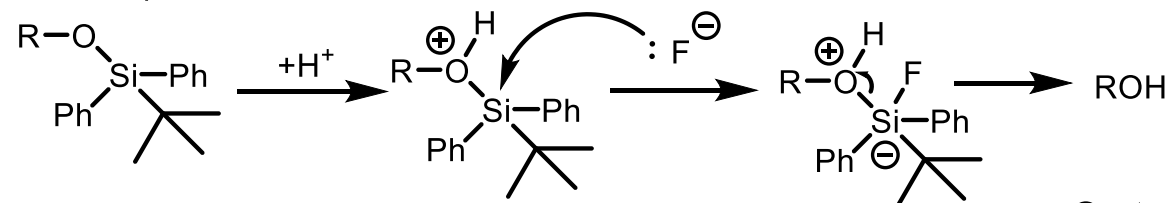
Synthesis of Fragment 1



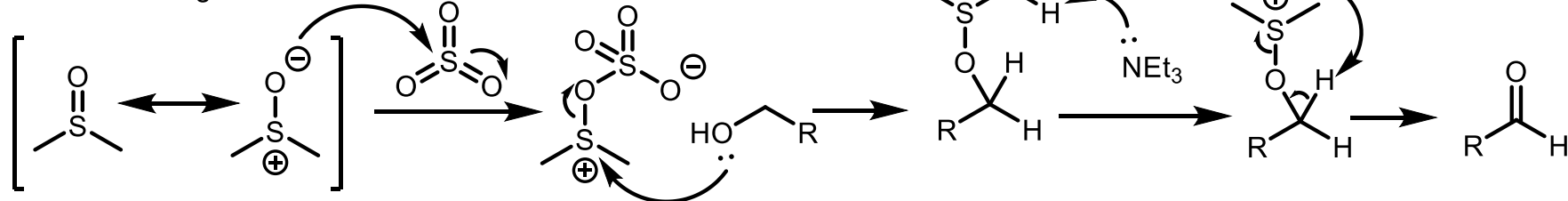
Stannylation/iodination Mechanism:



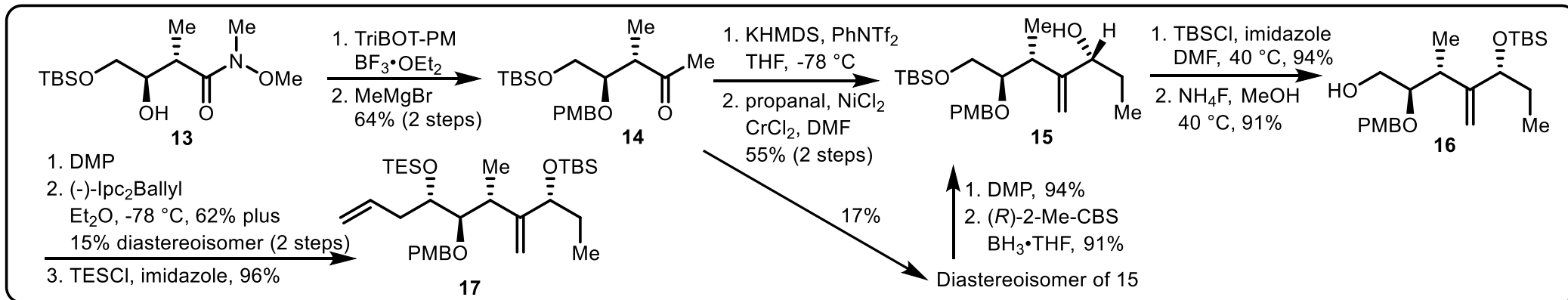
TBAF Deprotection:



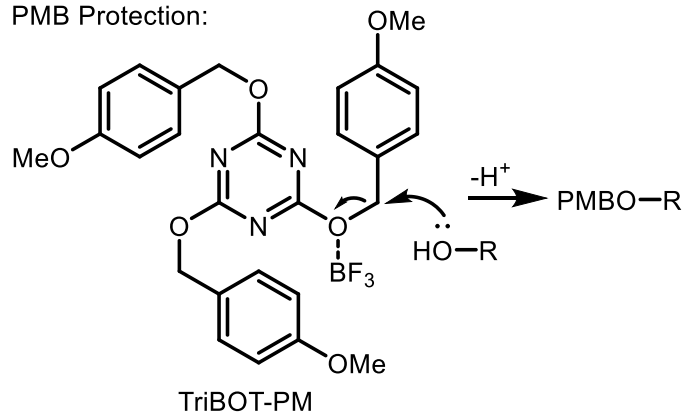
Parikh–Doering Oxidation:



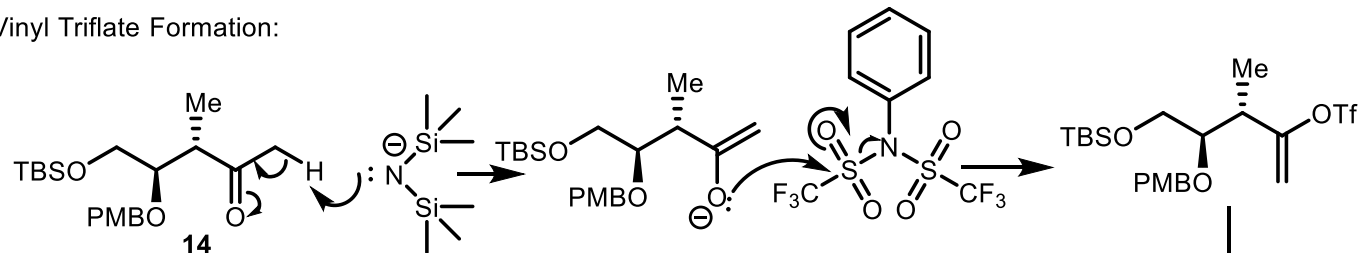
Synthesis of Fragment 2



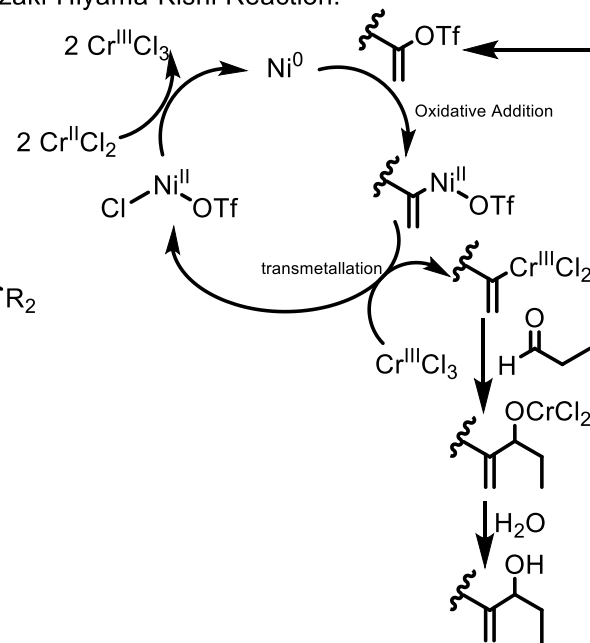
PMB Protection:



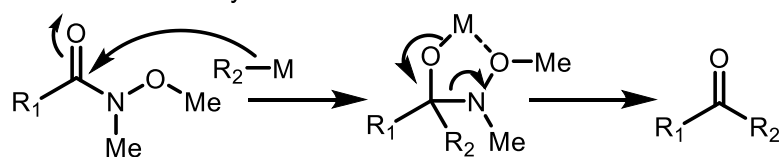
Vinyl Triflate Formation:



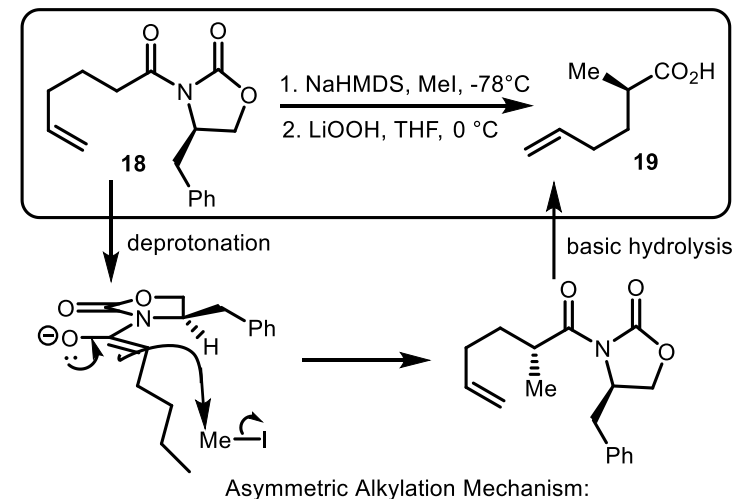
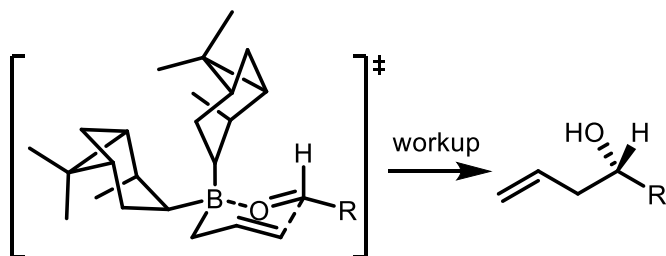
Nozaki-Hiyama-Kishi Reaction:



Weinreb Ketone Synthesis:



(-)-Ipc₂Ballyl Crotylation:



Synthesis of Fragment 3

End Game

