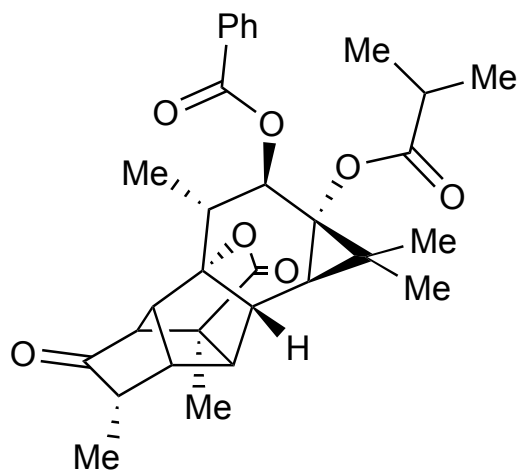


Asymmetric Total Synthesis of Pedrolide

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(+)-Pedrolide
 (>200 mg isolated)

- structural features:
 - unprecedented pedrolane skeleton
 - [5-5-5-6-6-3] hexacyclic core
 - includes a bicyclo[2.2.1]heptane motif
 - 12 contiguous stereocenters
 - 3 quaternary
 - highly oxygenated
- first synthesis by Carreira
 - 20 steps

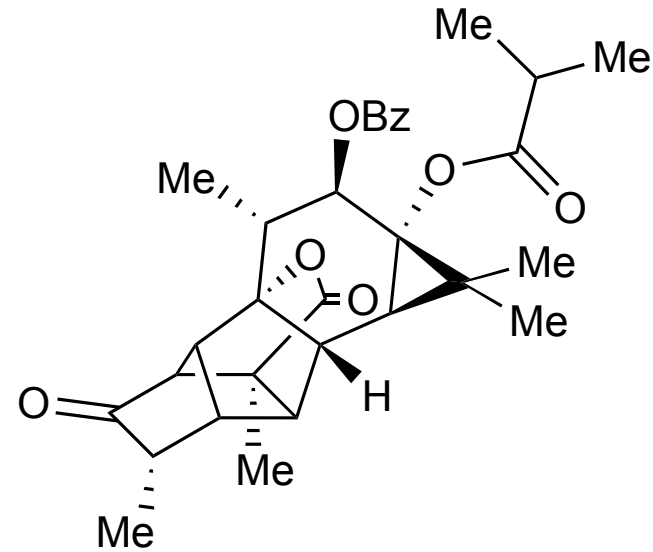
Nick Pugliano

Liu Group

07/03/2024

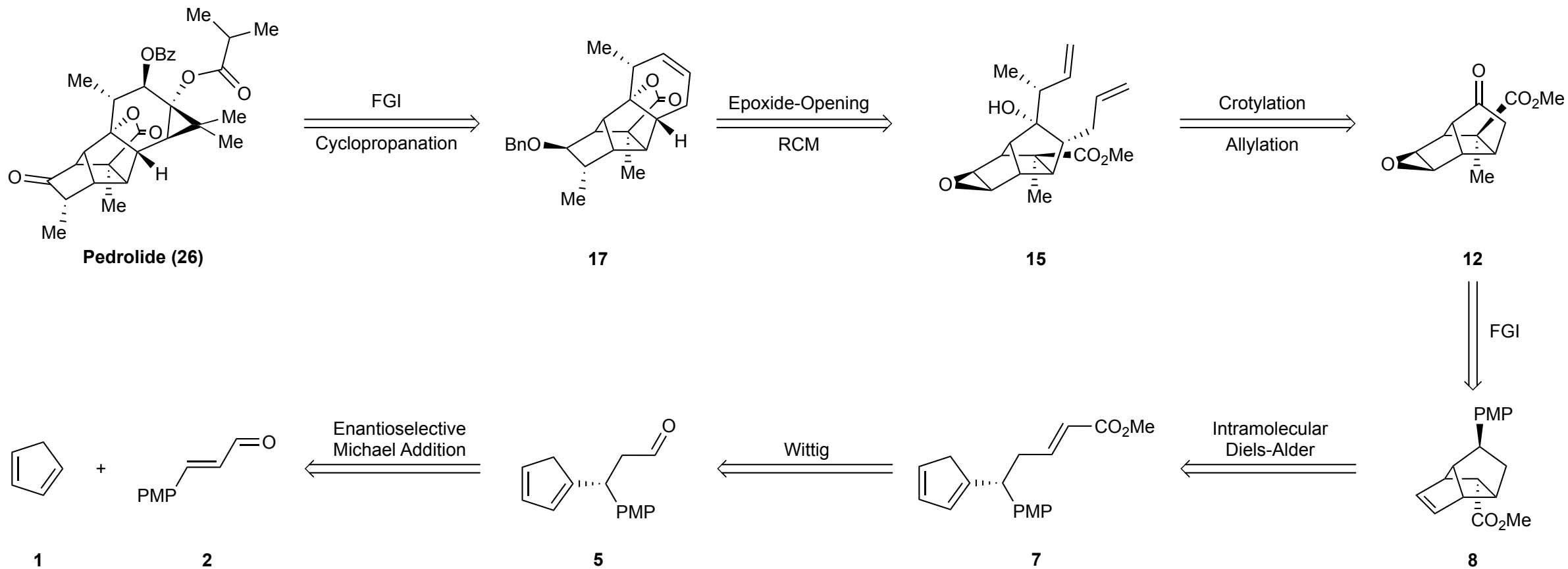
(+)-Pedrolide

- *Euphorbia* diterpenoid
 - Anti-HIV
 - Anti-inflammatory
 - Cytotoxic
 - Pro-inflammatory
- Led to:
 - Picato (ingenol mebutate) to treat actinic keratoses
 - Resiniferatoxin (phase III drug) to treat overactive bladder and chronic pain

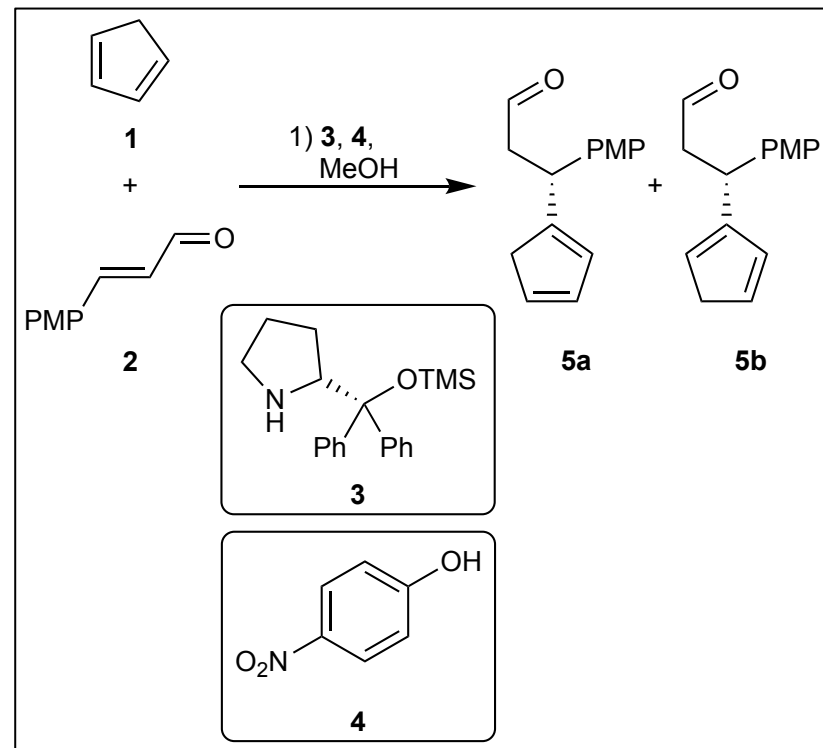
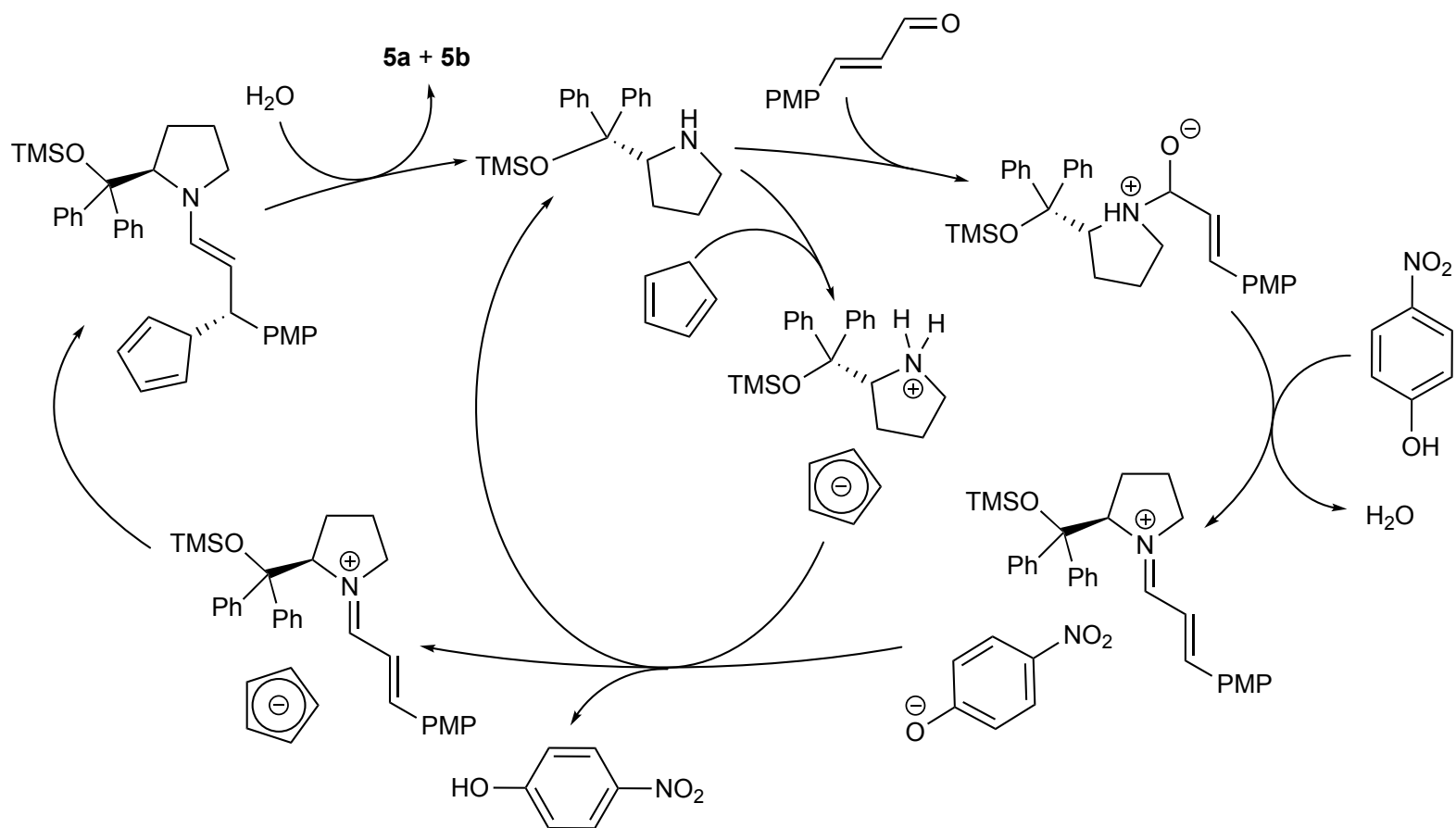


Pedrolide (26)

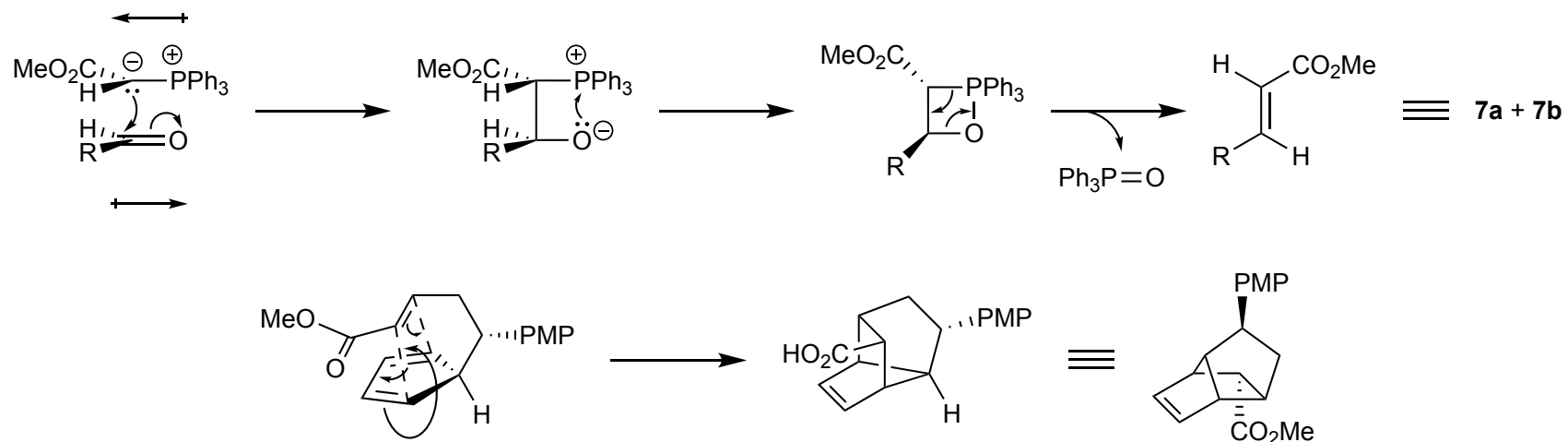
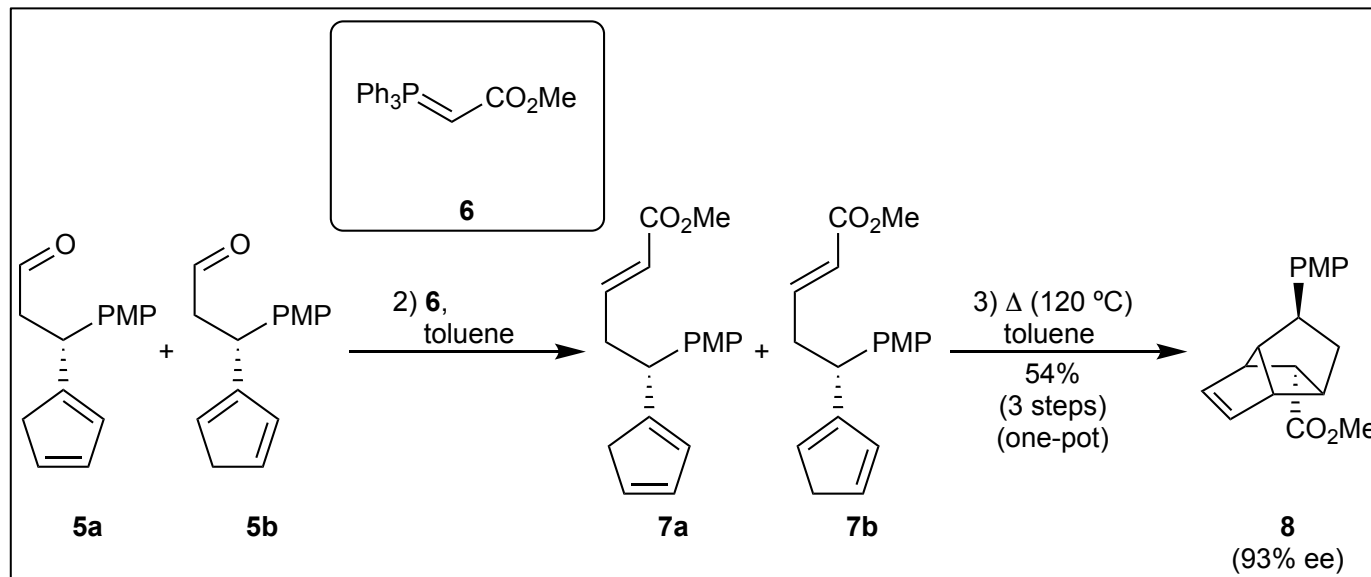
Retrosynthesis



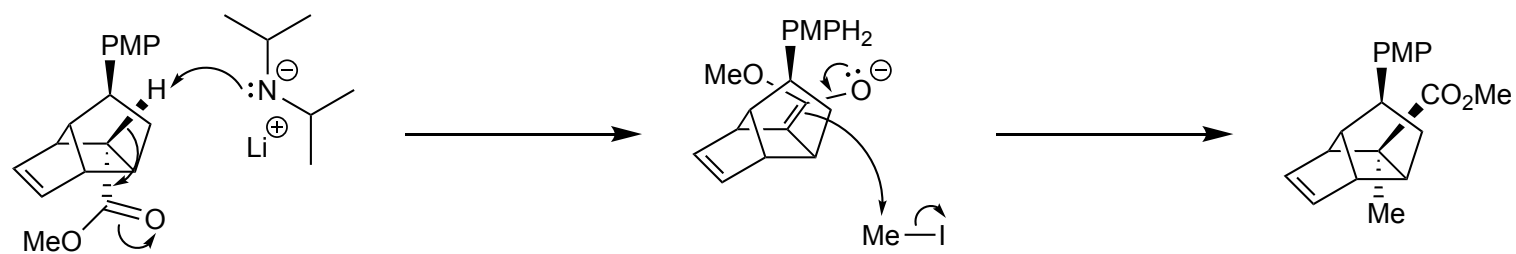
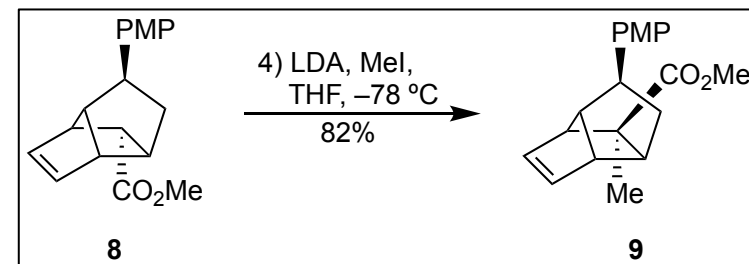
Enantioselective Michael Addition



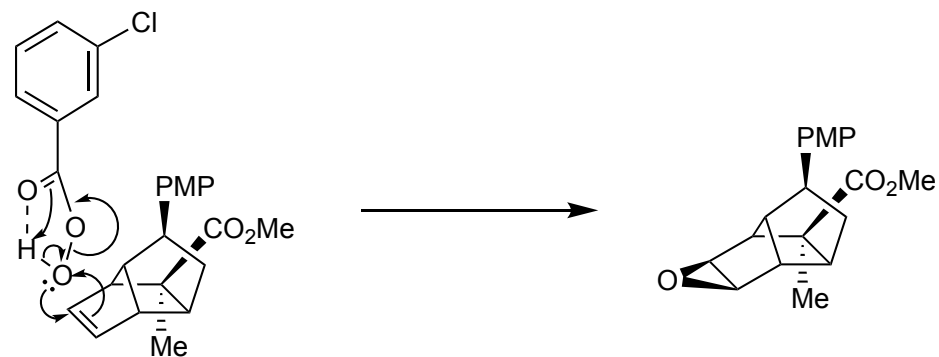
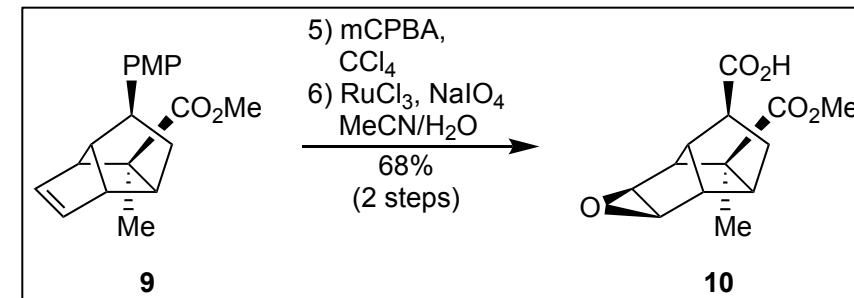
Wittig and Intramolecular Diels-Alder



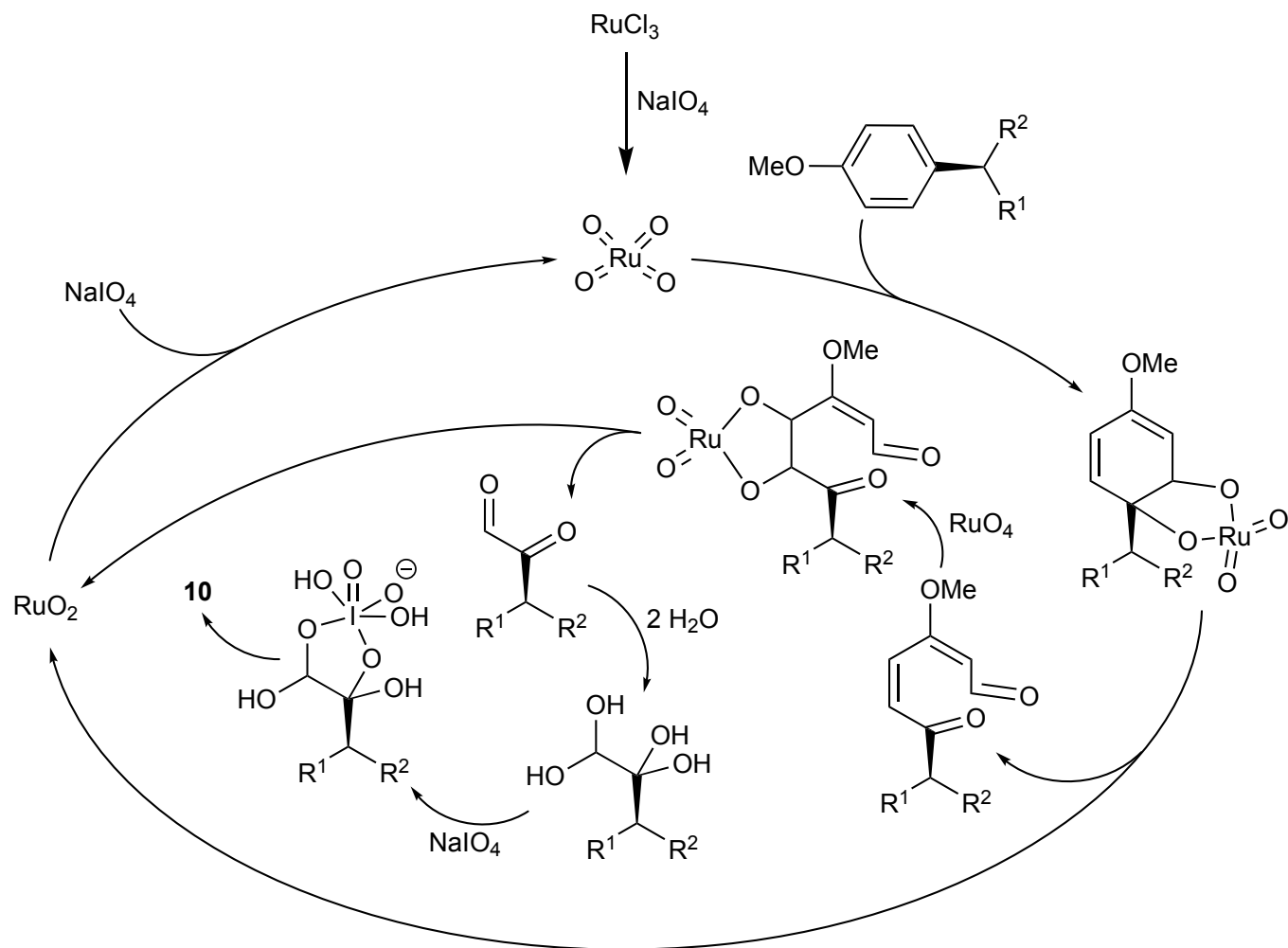
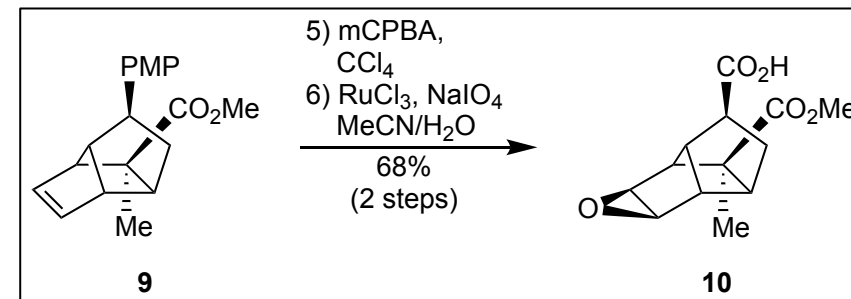
Methylation



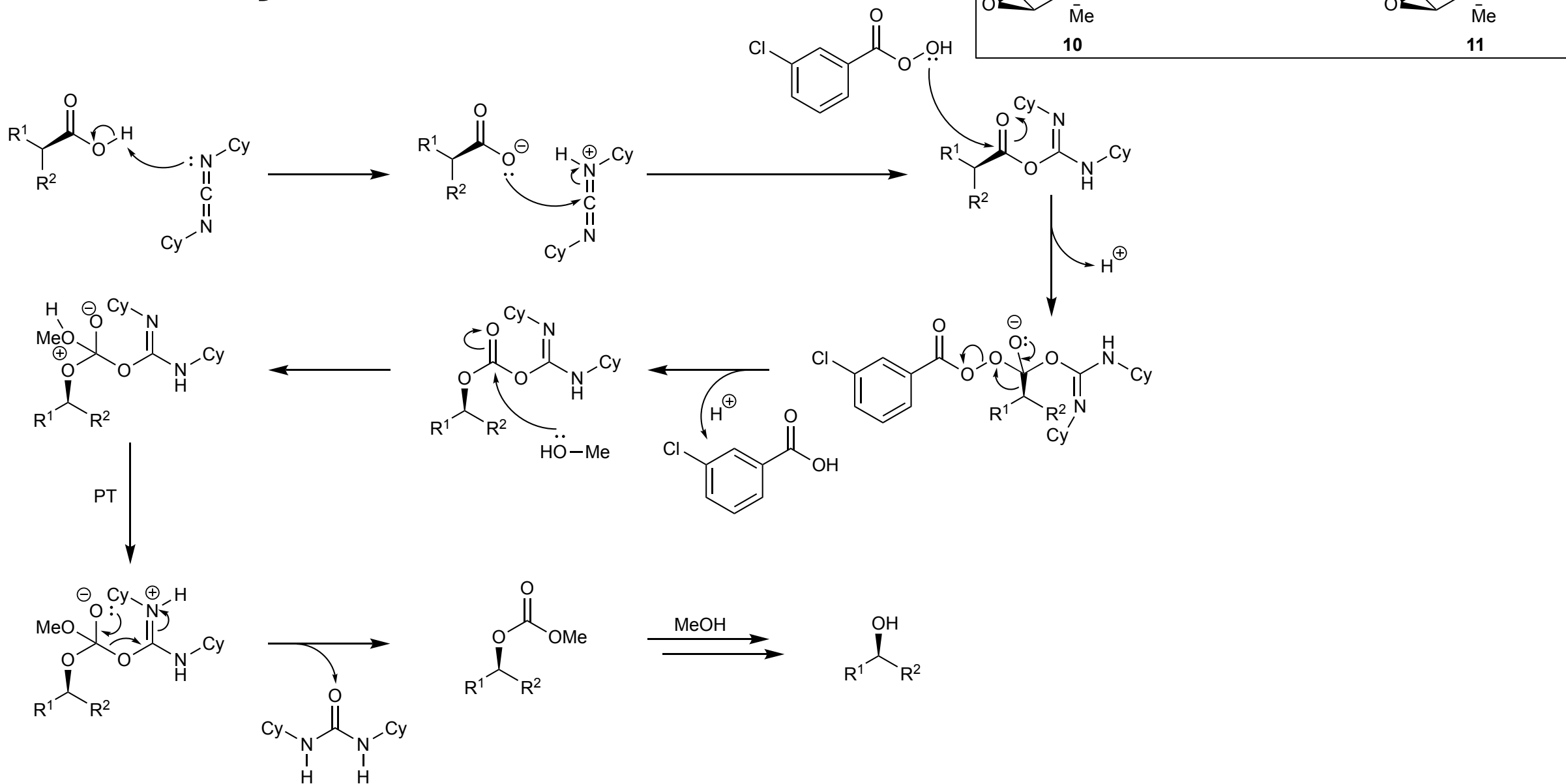
Epoxidation



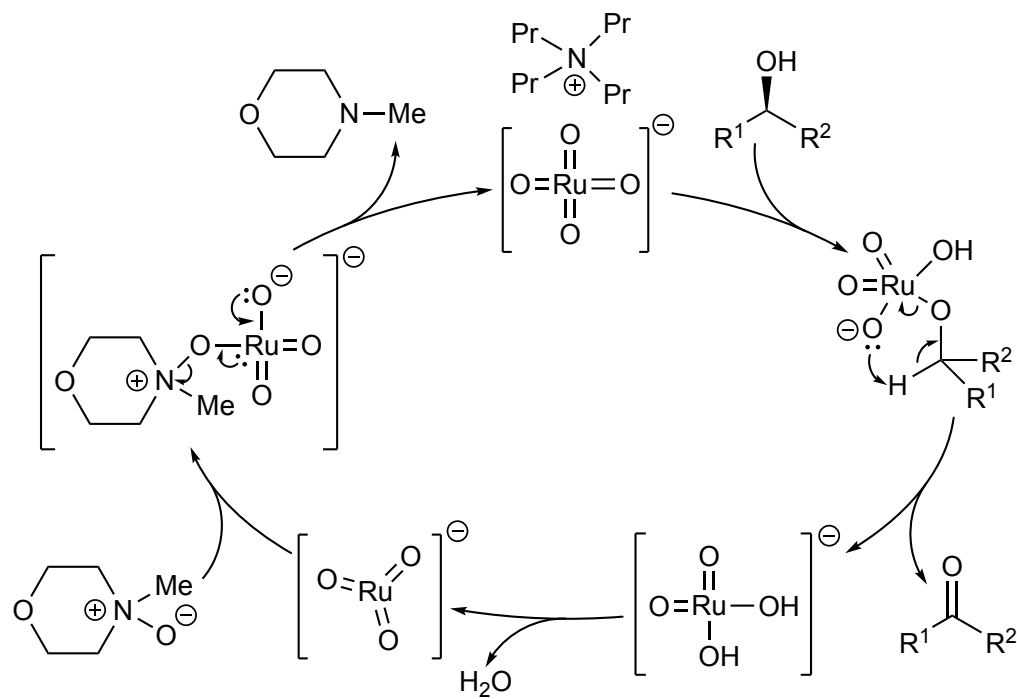
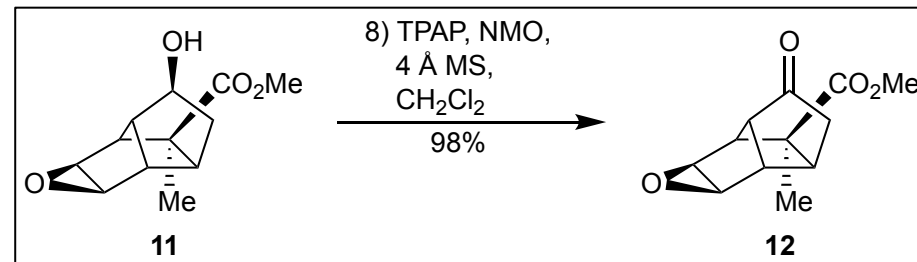
Oxidative Cleavage



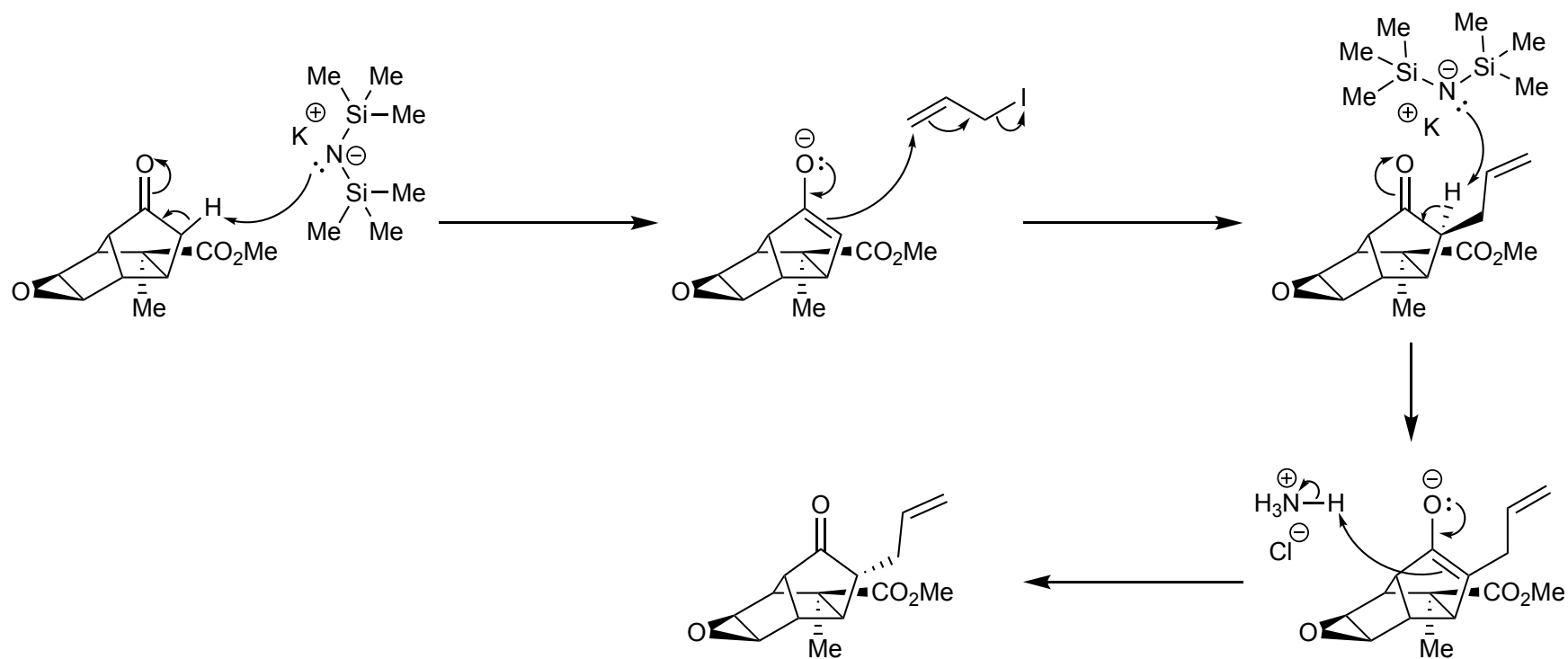
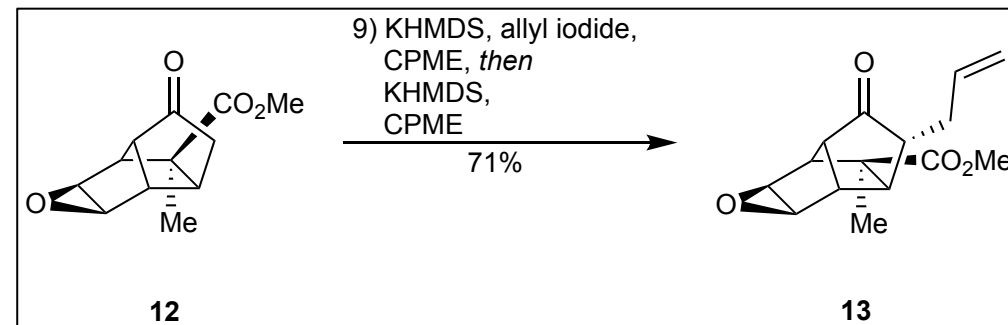
Carboxy-Inversion Reaction



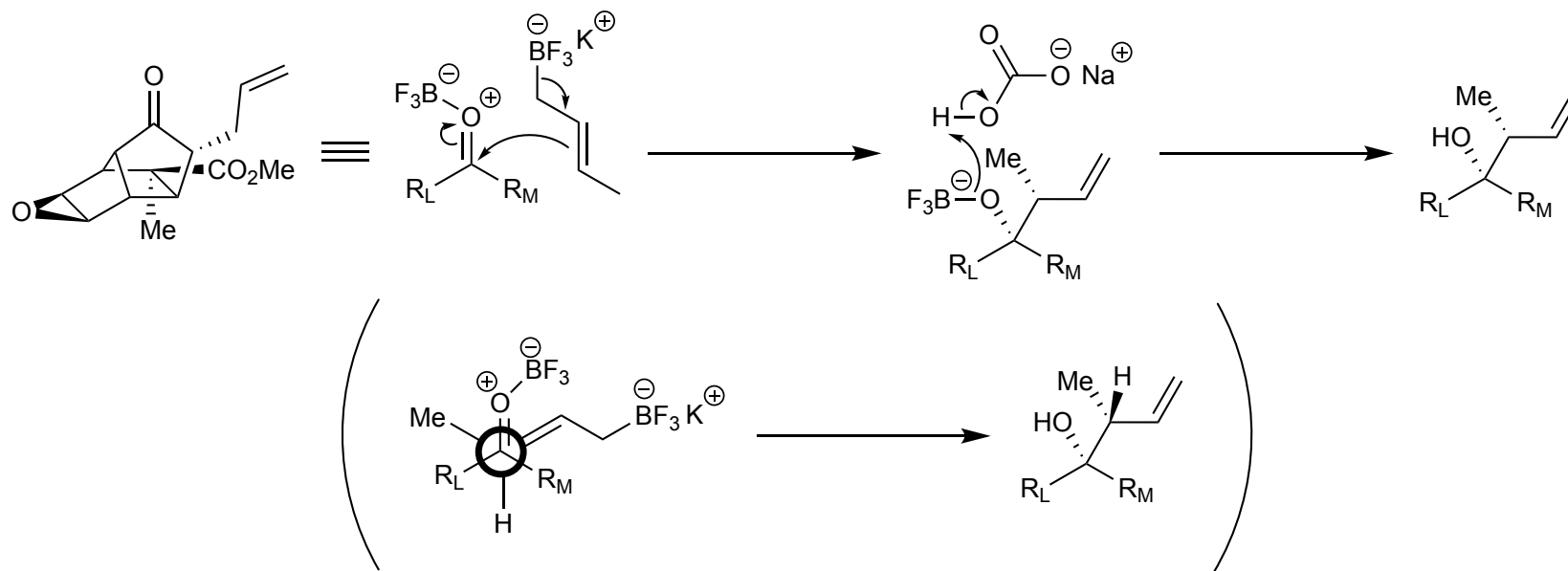
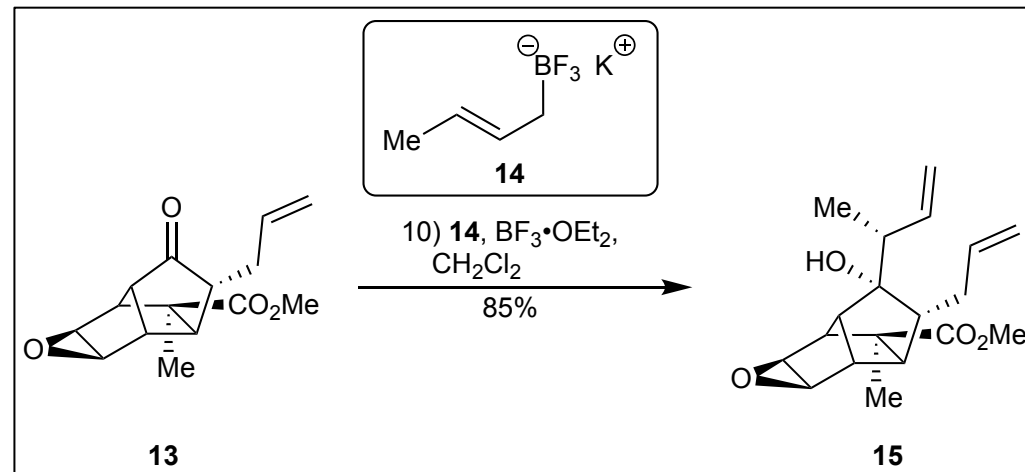
Ley Oxidation



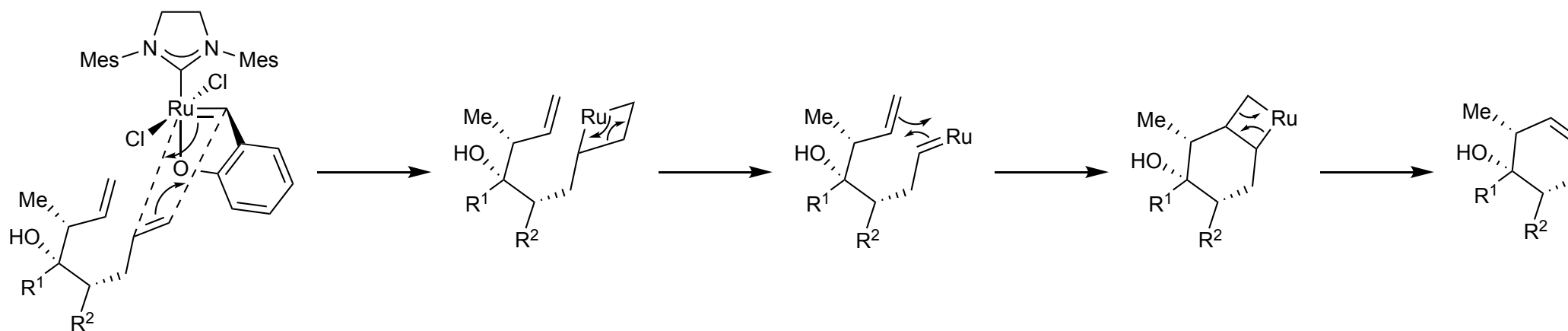
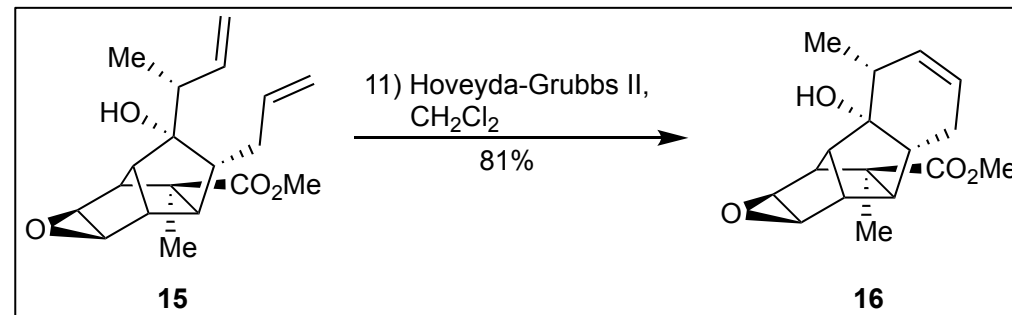
Allylation



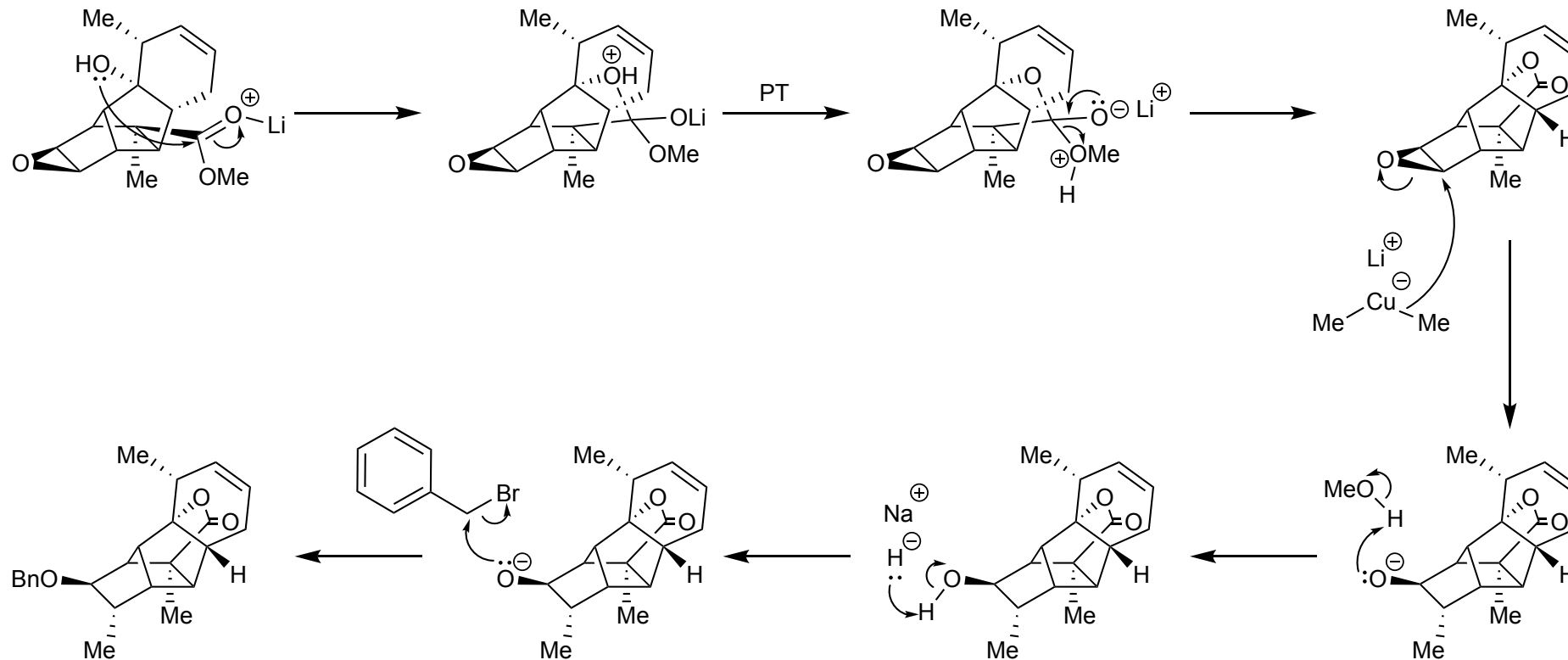
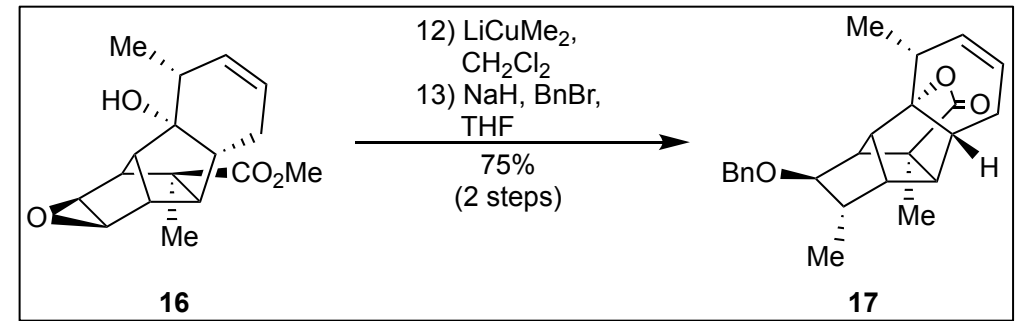
Crotylation



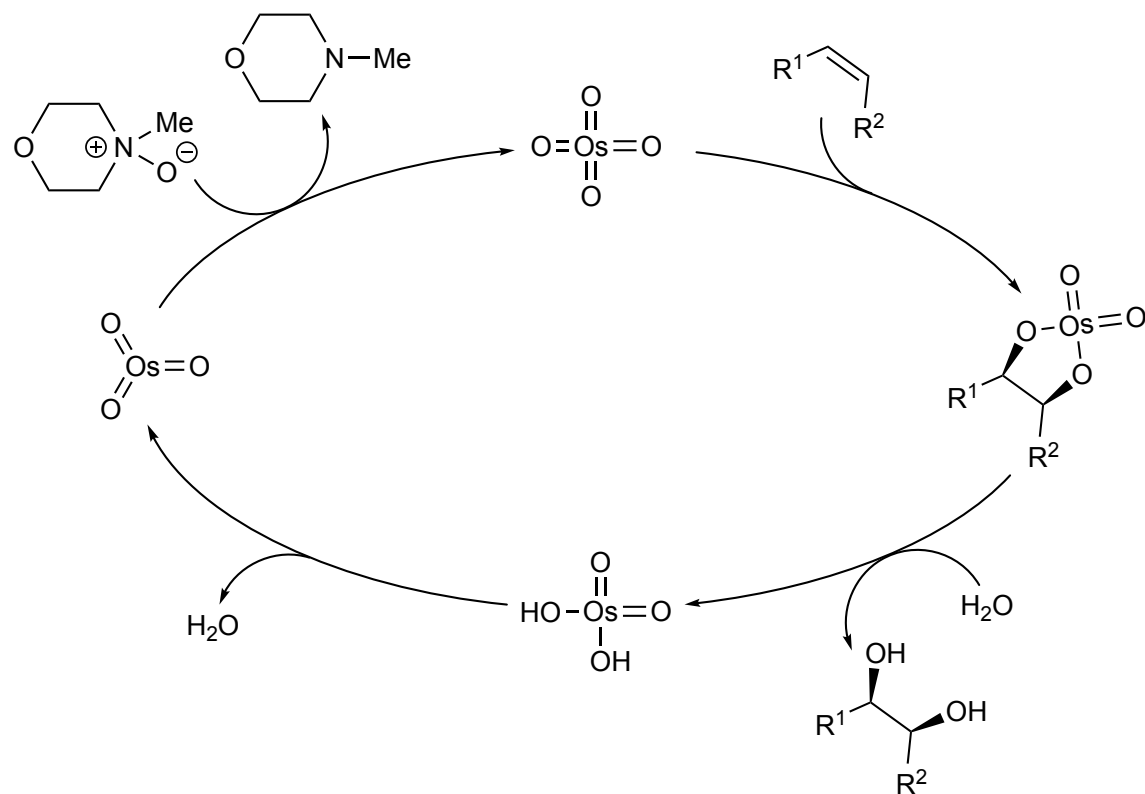
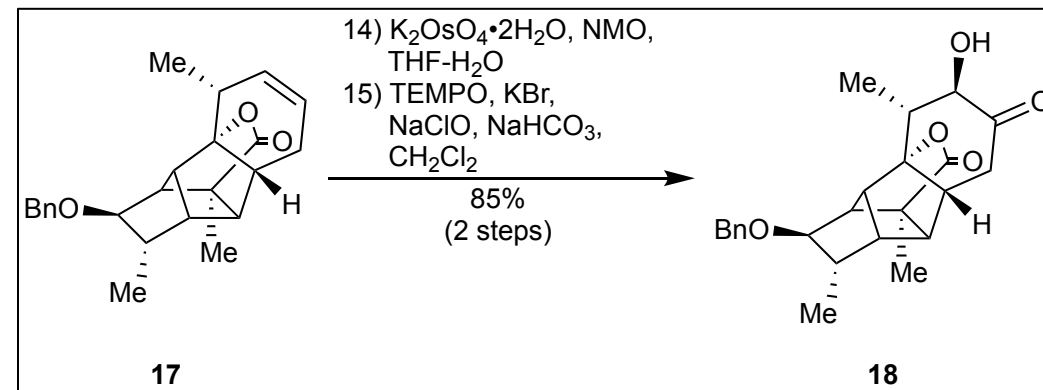
Ring-Closing Metathesis



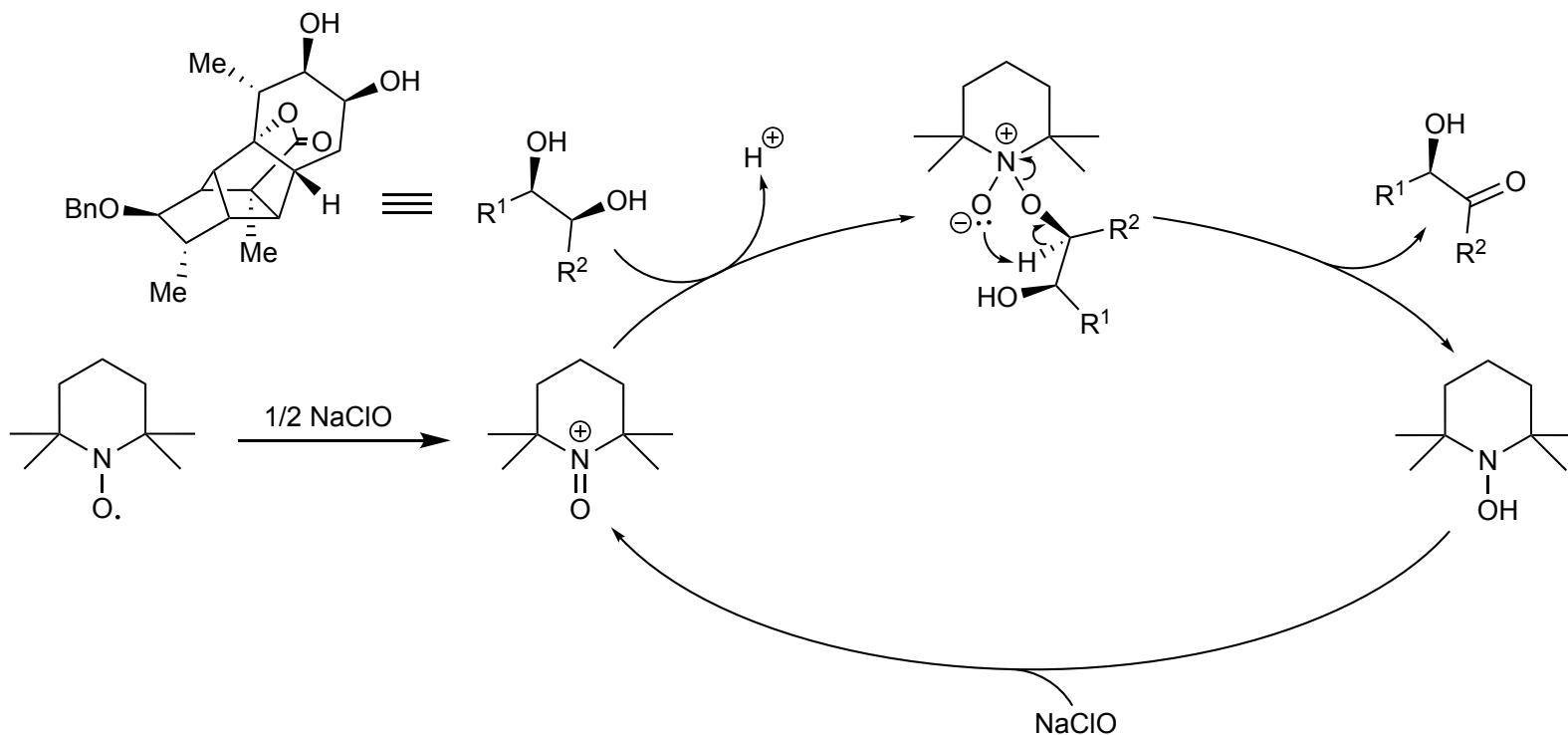
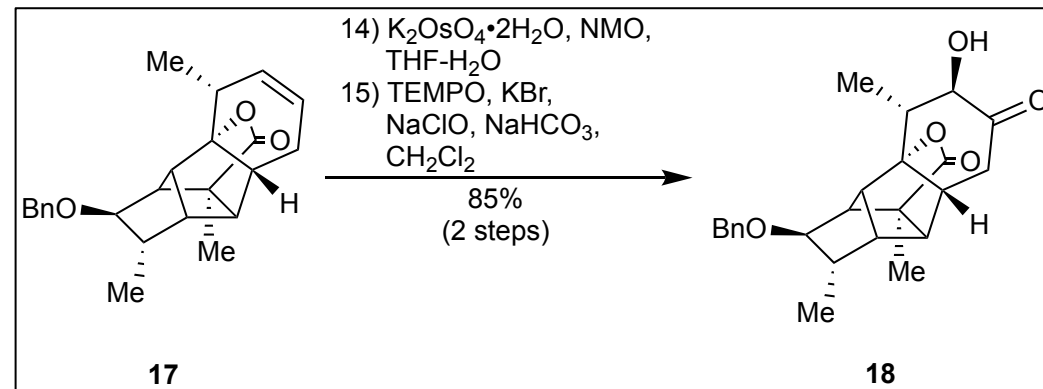
Lactonization, Epoxide Opening, and Benzyl Protection



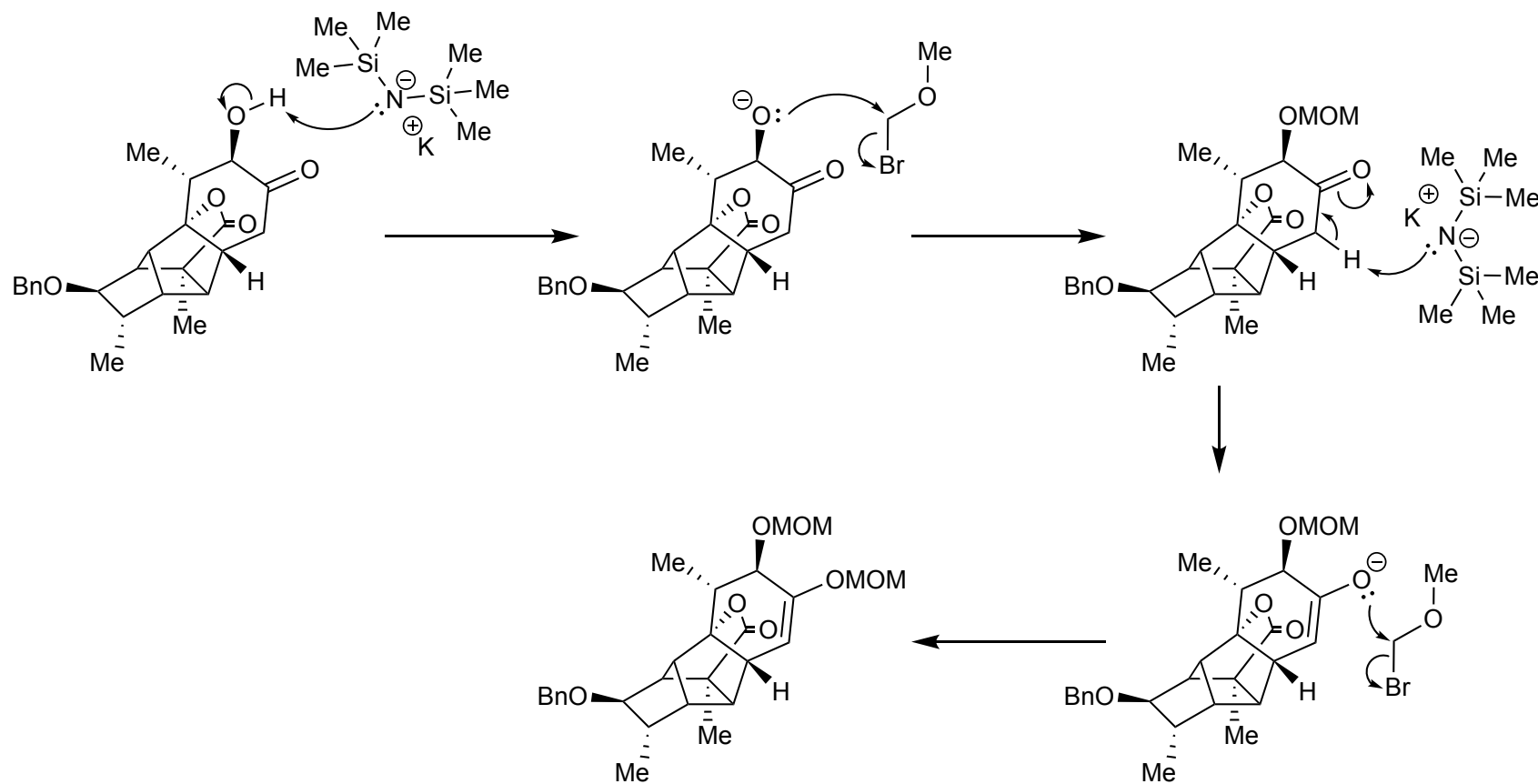
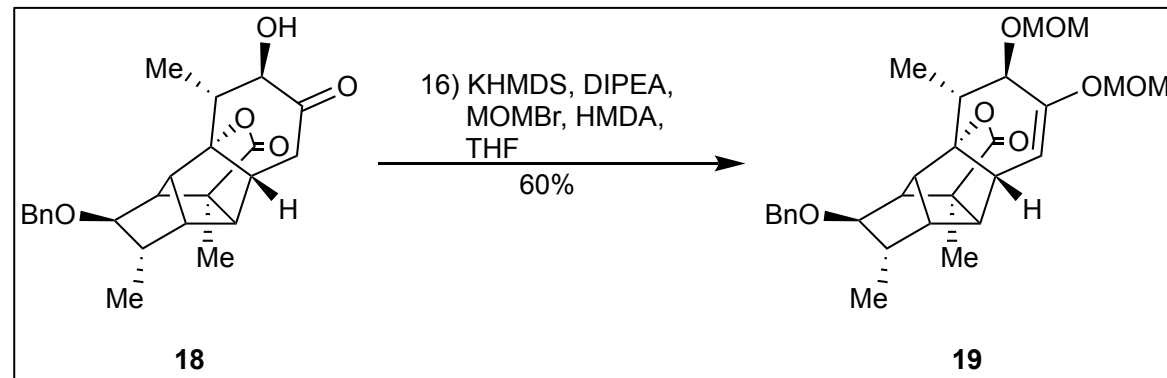
Diastereoselective Upjohn Dihydroxylation



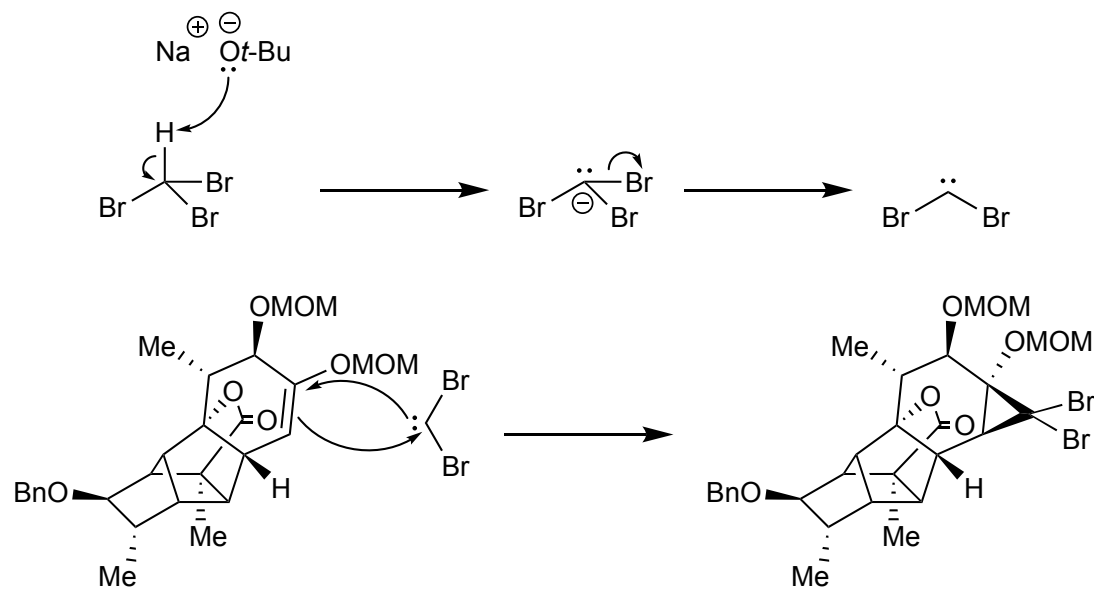
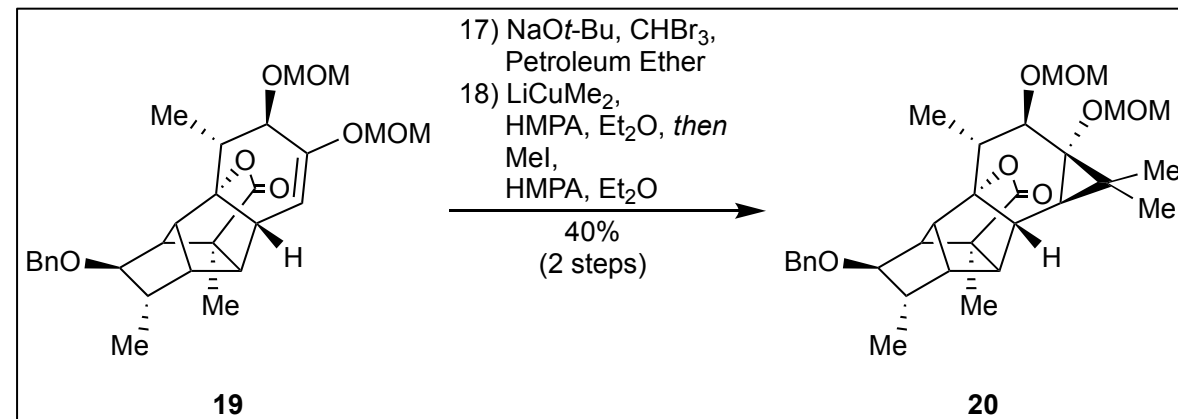
TEMPO Oxidation



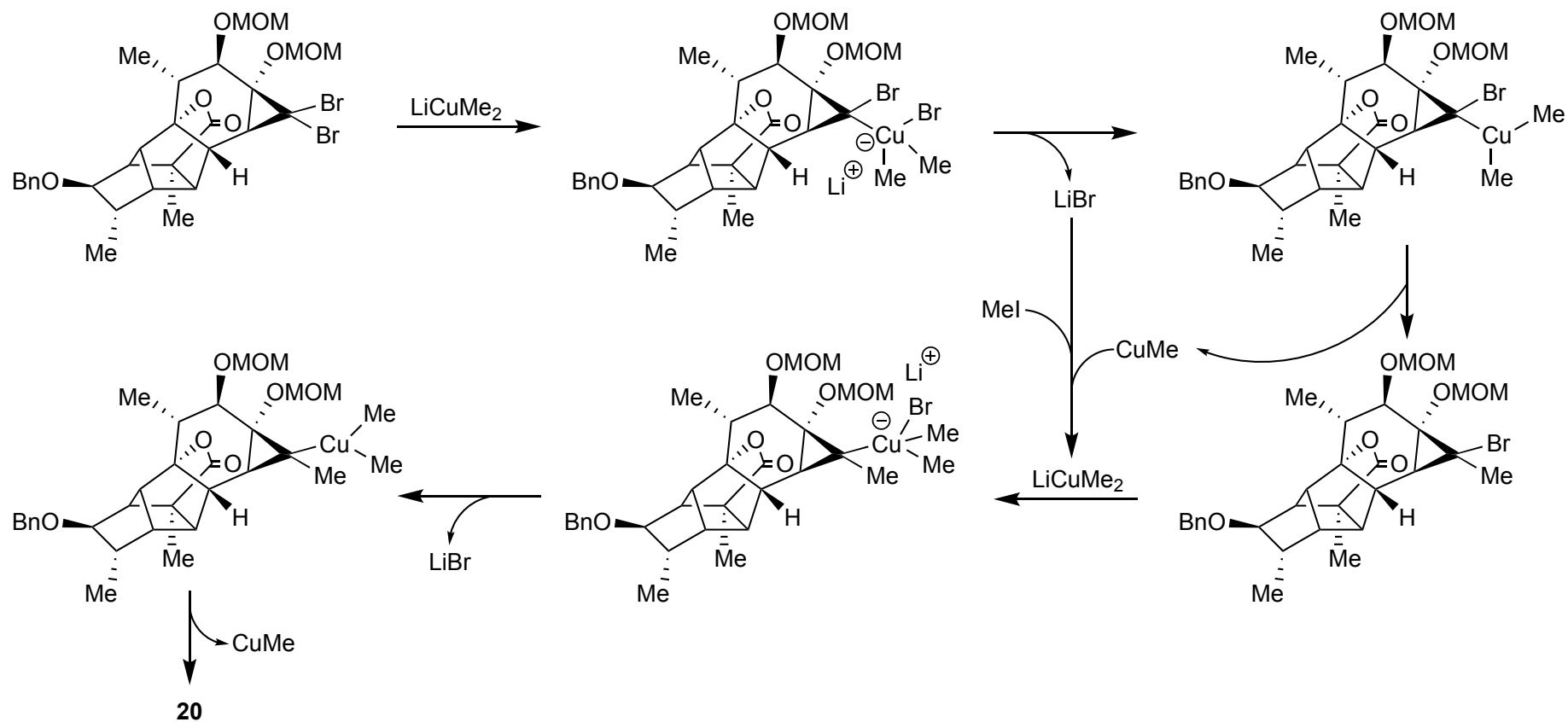
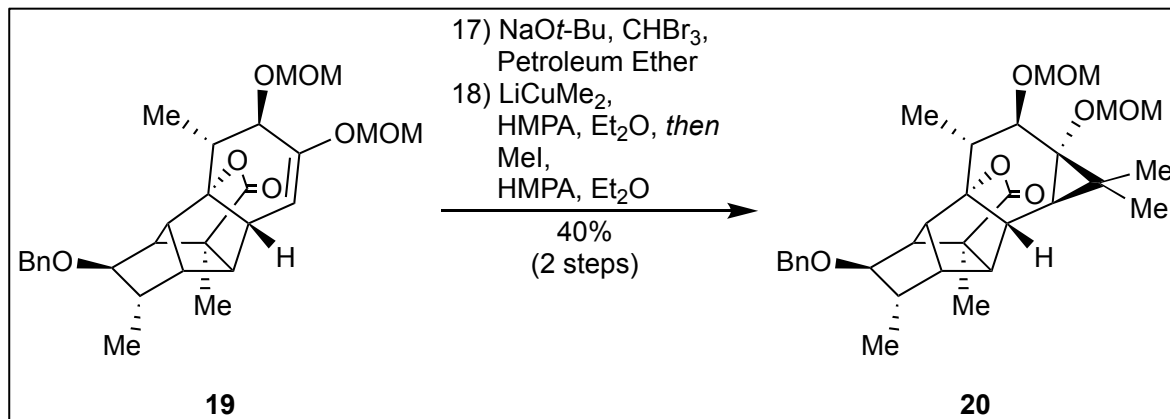
MOM Protection



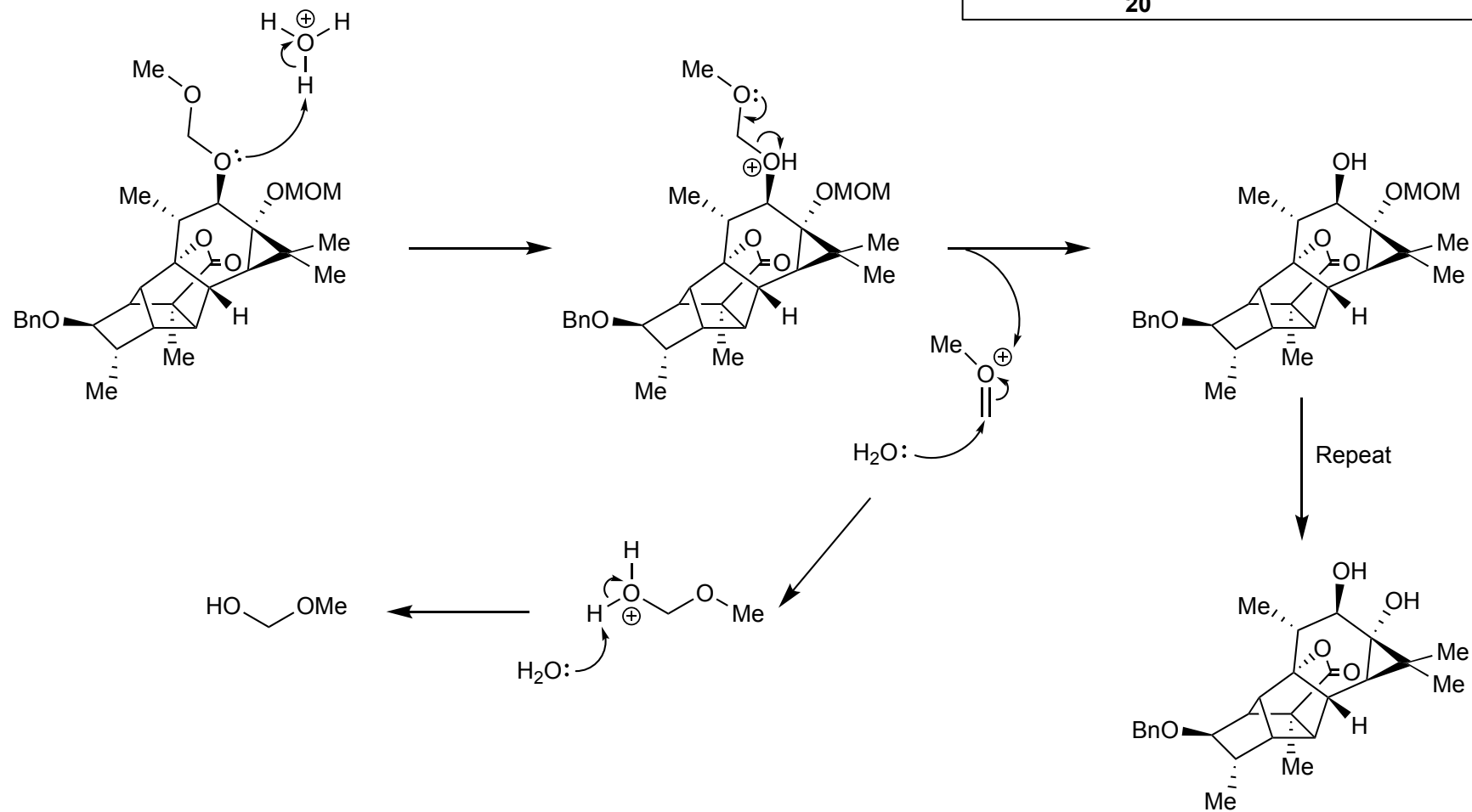
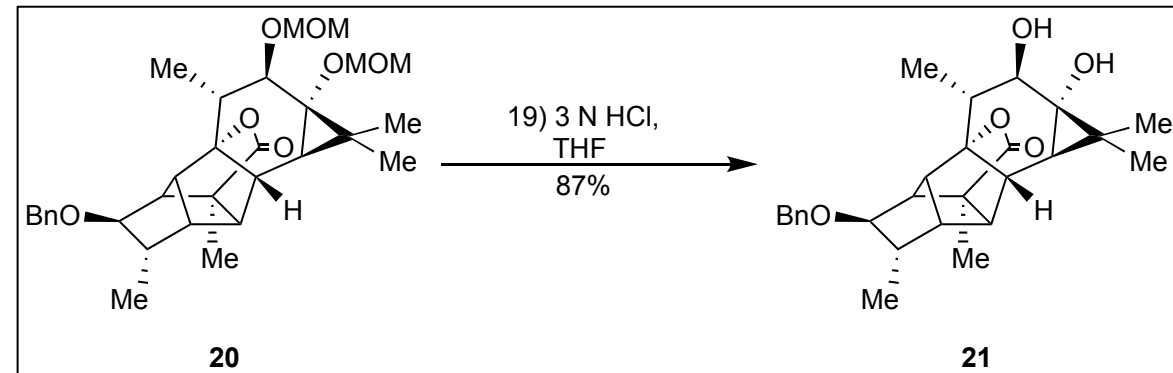
Cyclopropanation



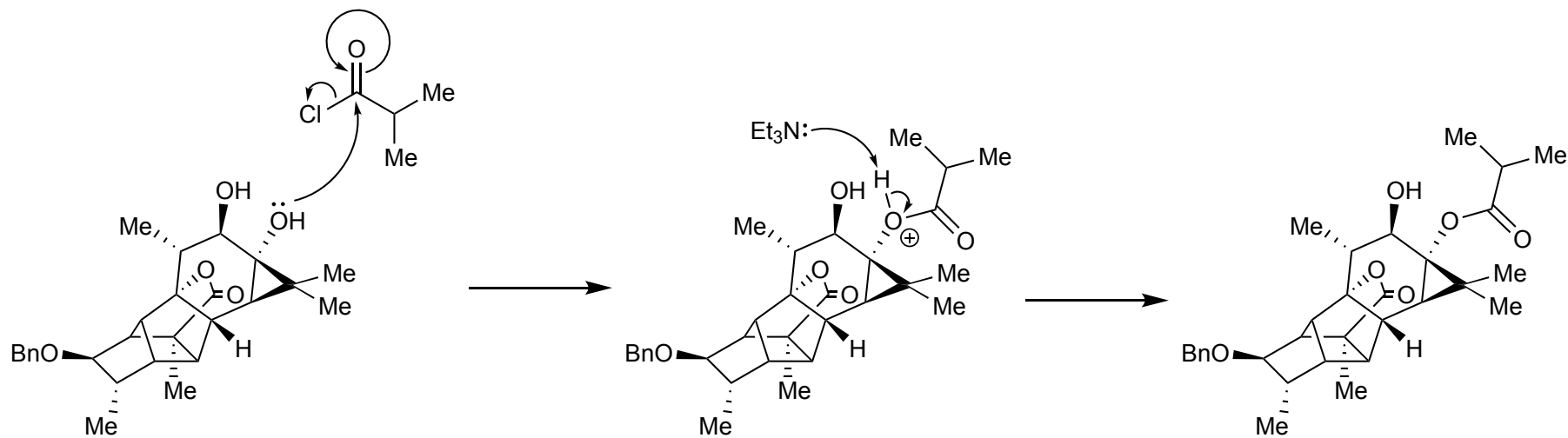
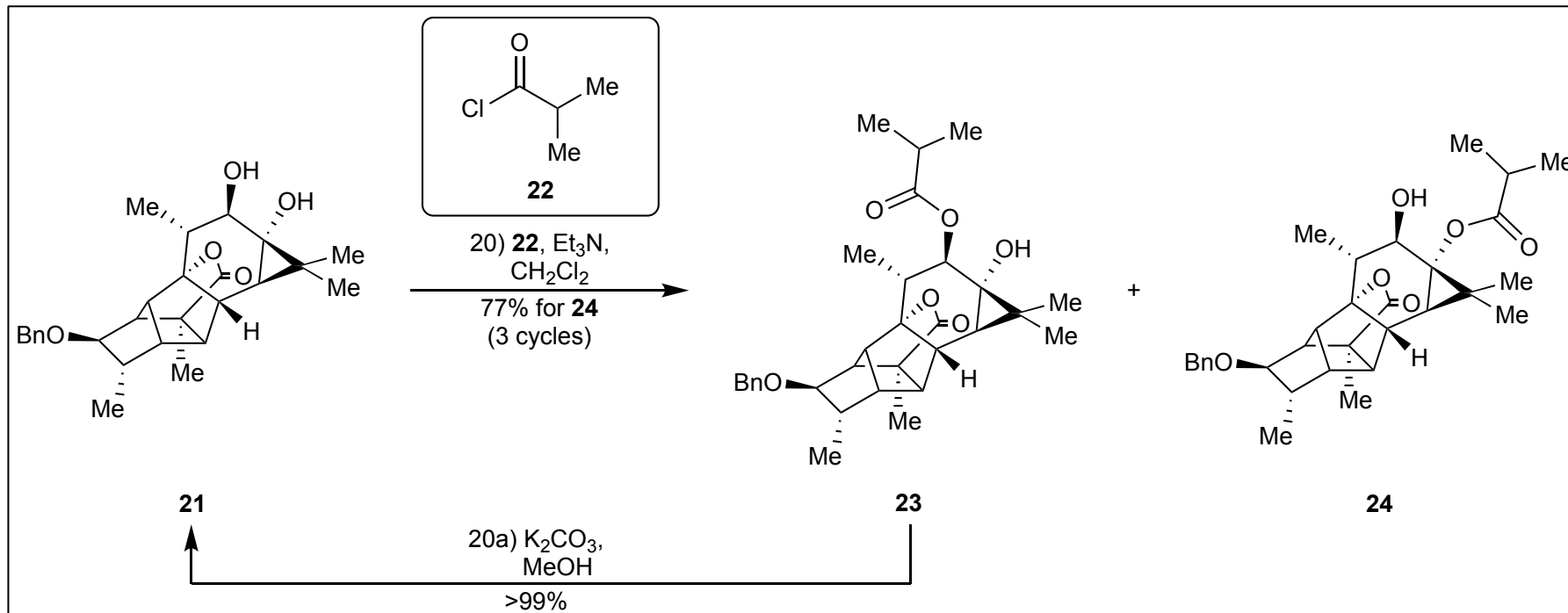
Cyclopropanation



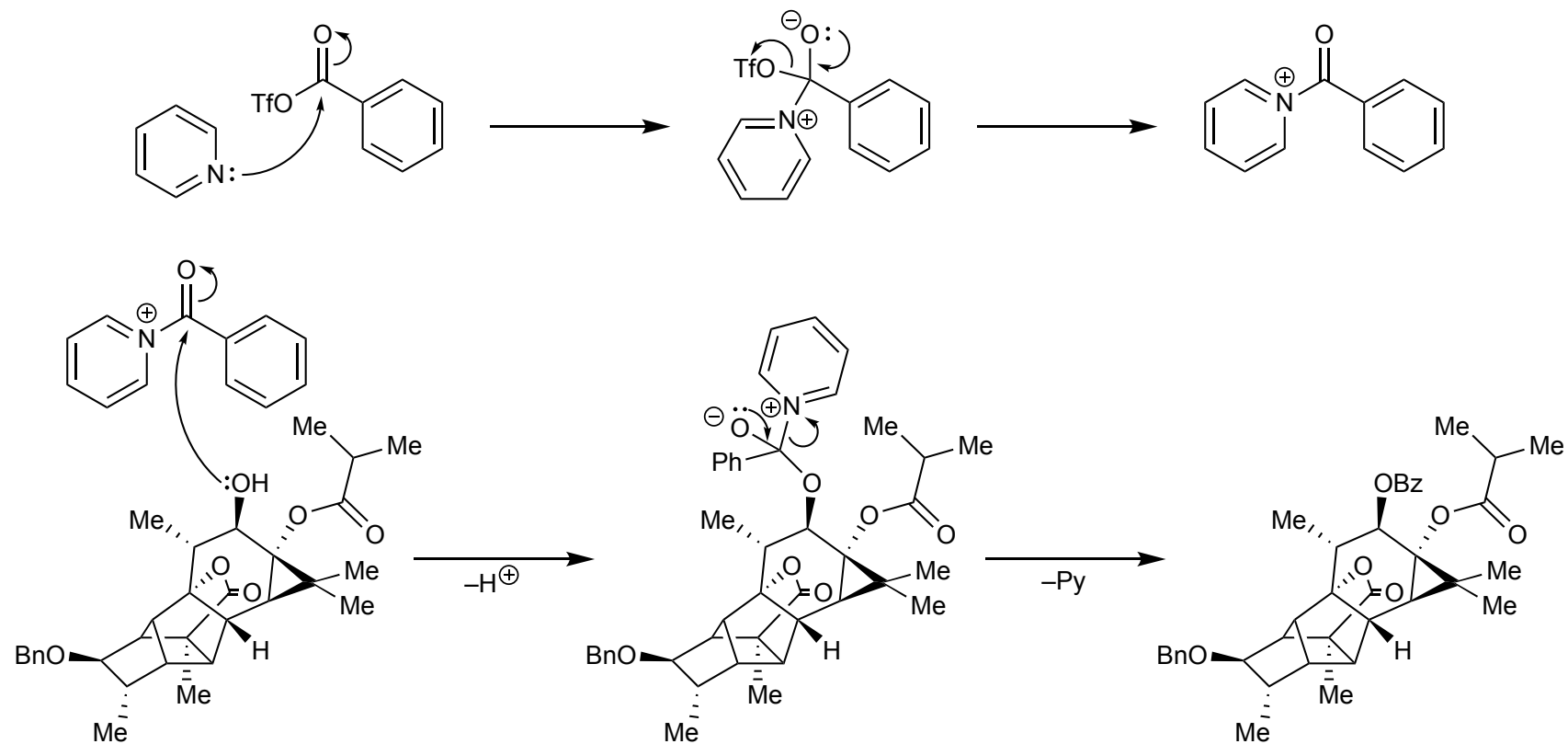
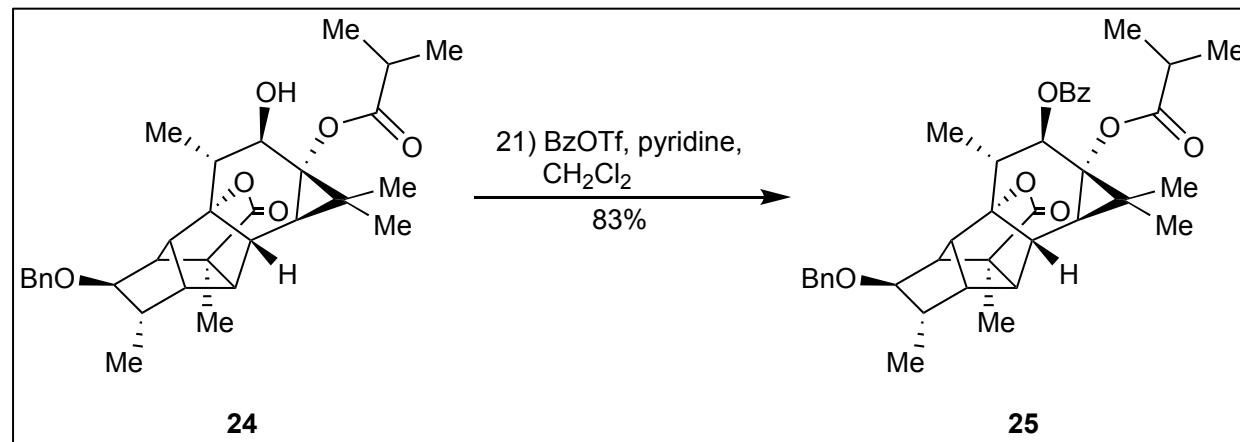
MOM Deprotection



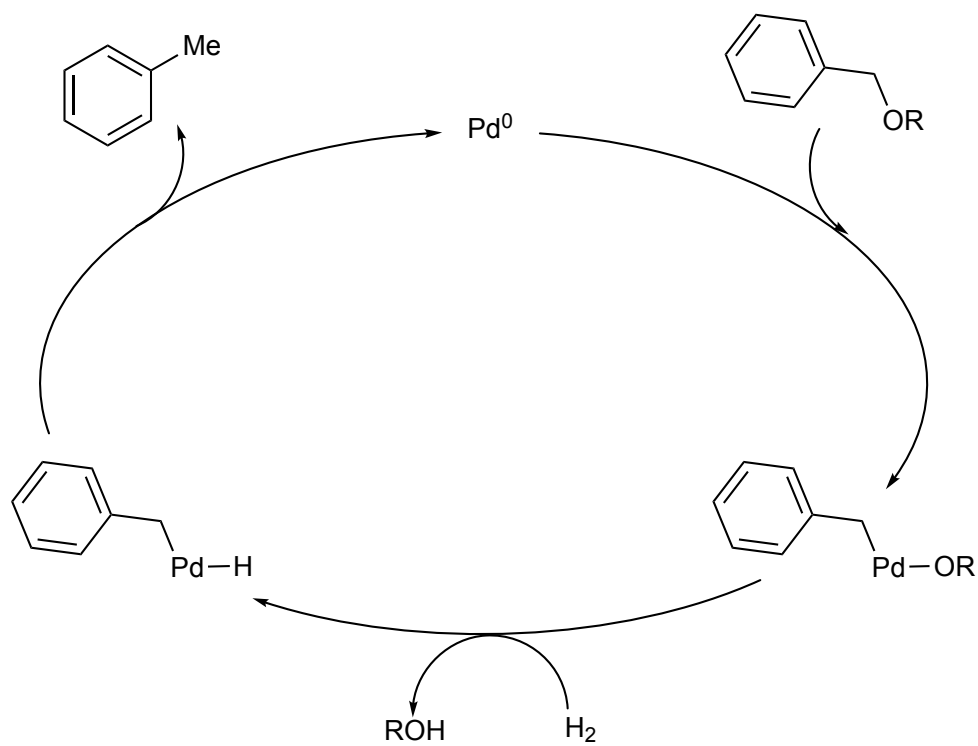
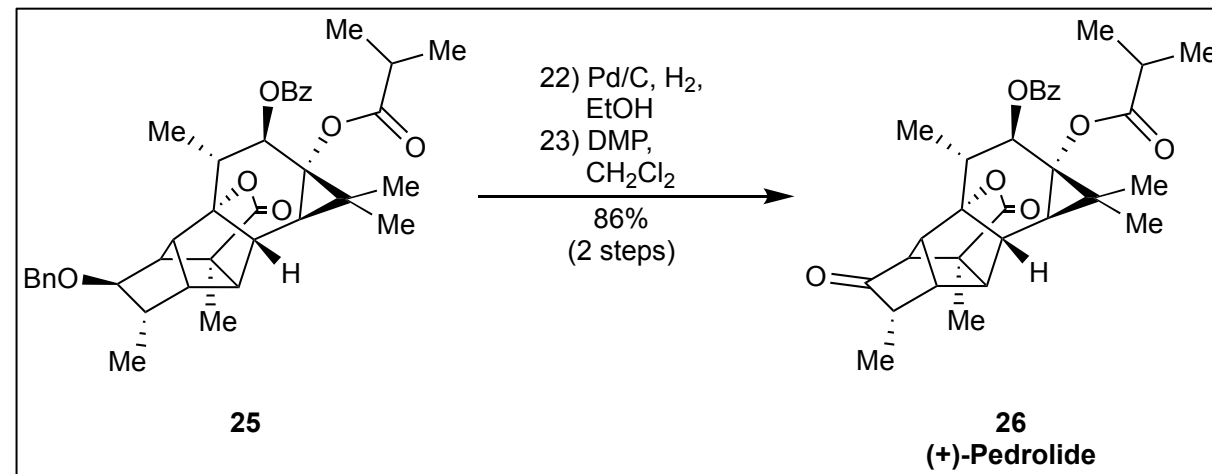
Isobutyration



Benzoylation



Benzyl Deprotection



Dess-Martin Oxidation

