


# Total Synthesis of Salimabromide: A Tetracyclic Polyketide from a Marine Myxobacterium

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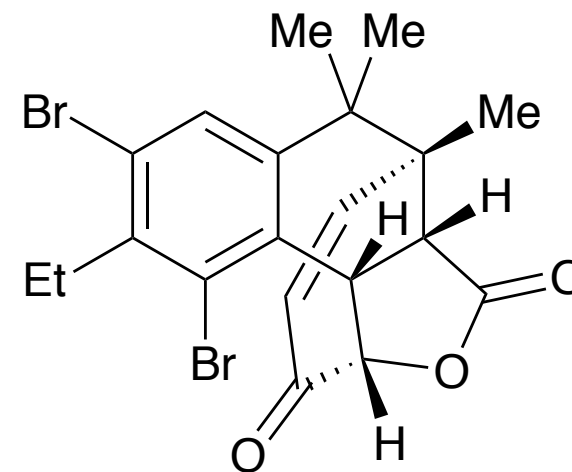
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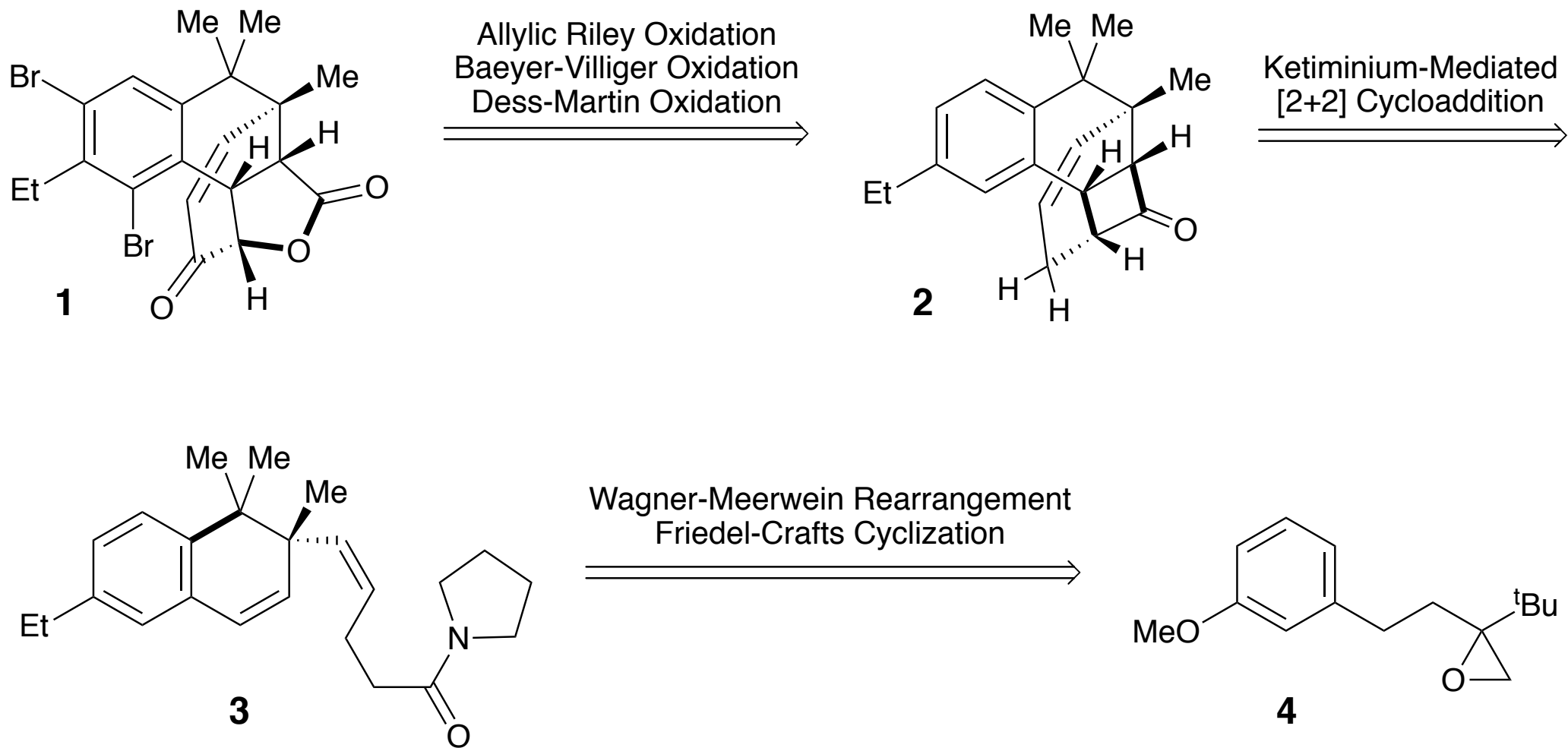
- Antibiotic polyketide previously isolated by König in 2013 from *Enhygromyxa salina*, which is a marine myxobacteria.
- Unprecedented tetracyclic ring-architecture:
  - Four consecutive stereocenters, one of which is a quaternary carbon center.
  - Highly-substituted seven-membered ring.
  - Conformational rigid due to five-membered lactone.

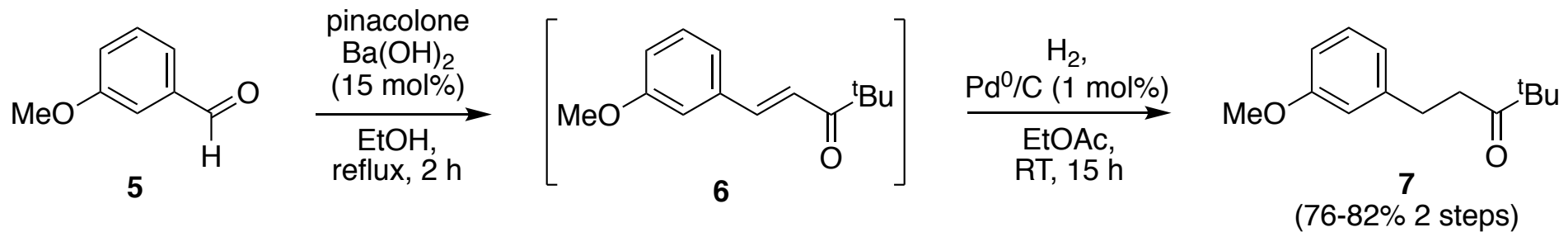
Kevin Byrne  
 Liu Research Group  
 March 26<sup>th</sup>, 2019



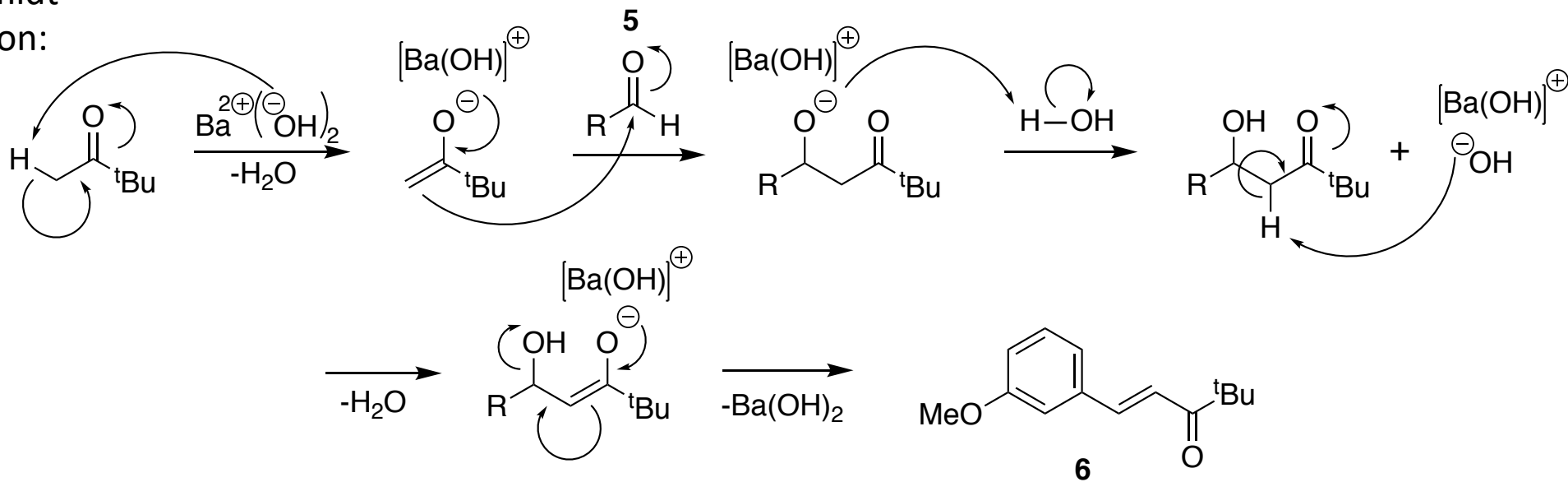
Salimabromide

# Retrosynthetic Analysis:

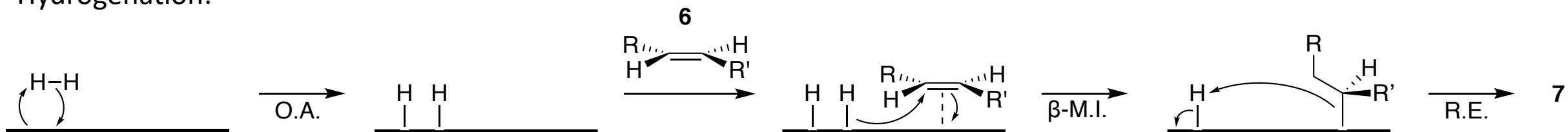


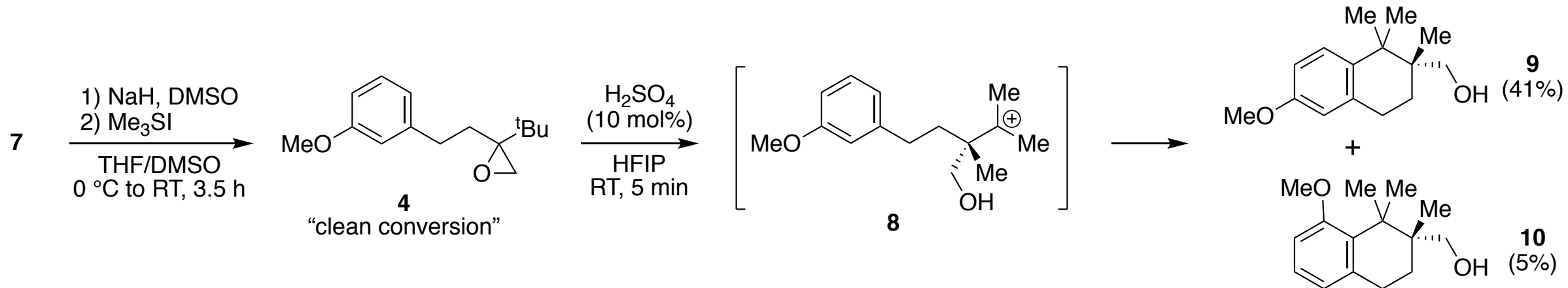


Claisen-Schmidt  
Condensation:

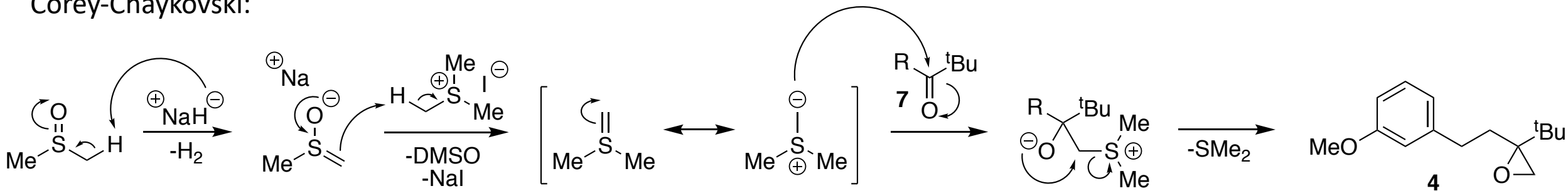


Hydrogenation:

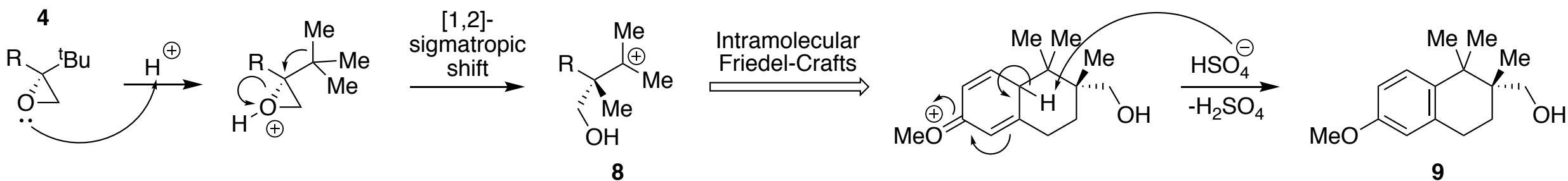


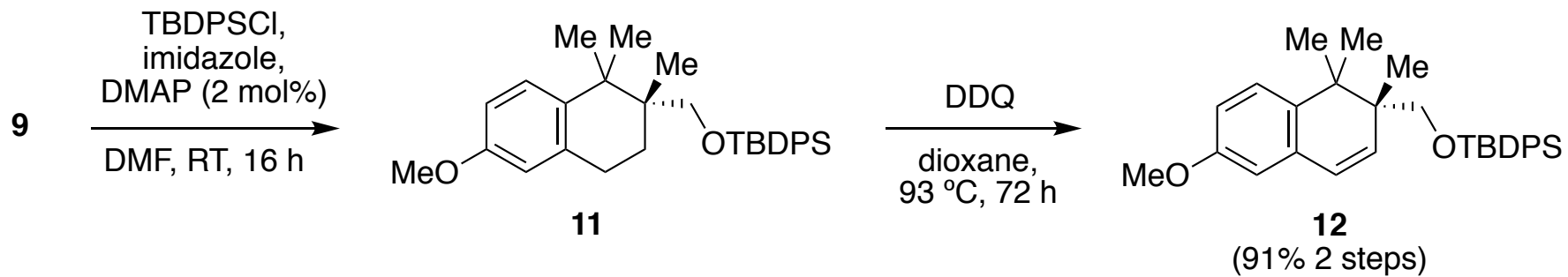


### Corey-Chaykovski:

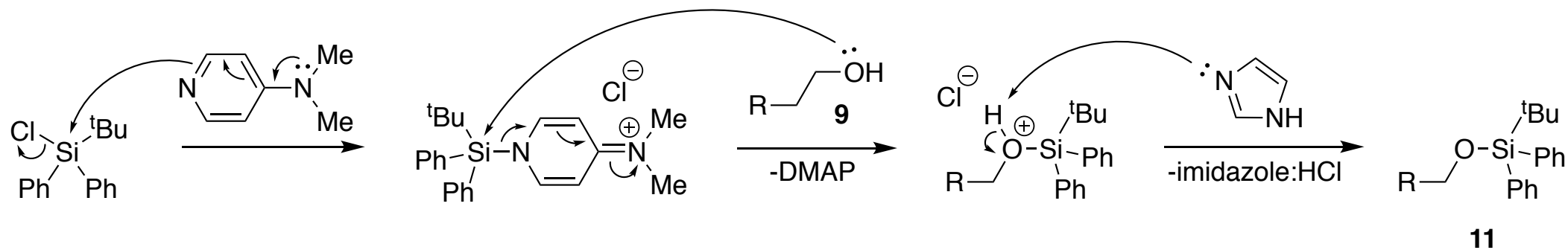


### Wagner-Meerwein Rearrangement:

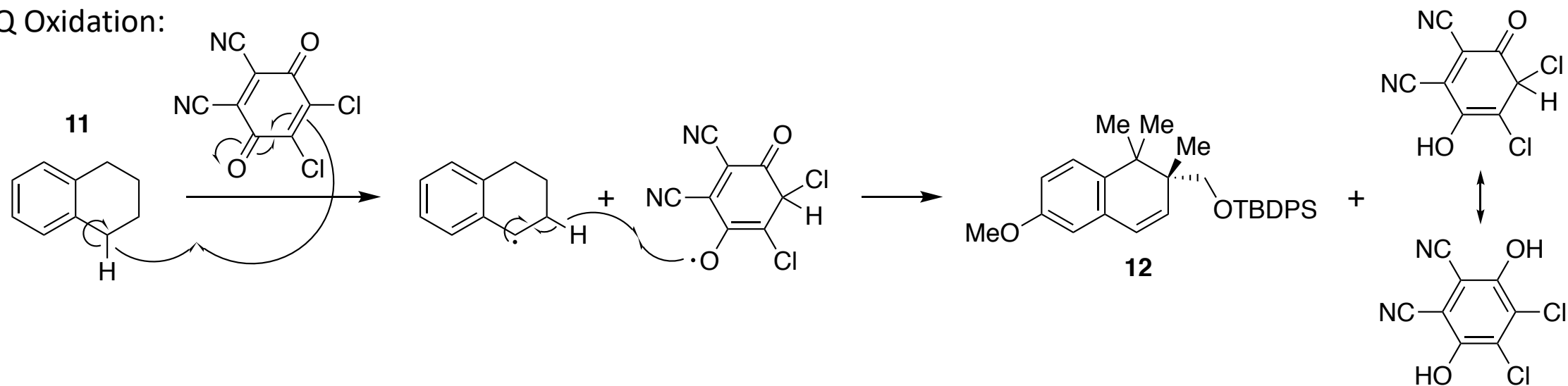


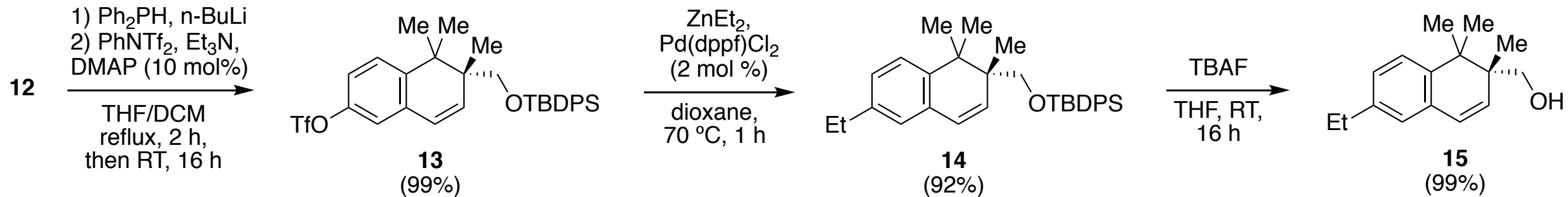


### TBDPS Protection:

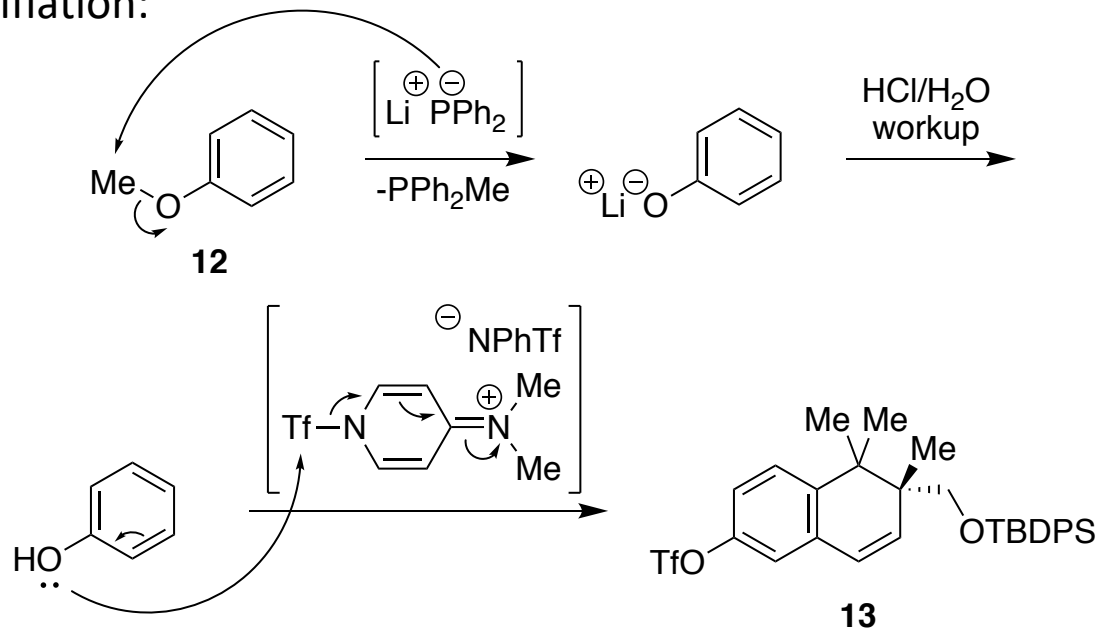


### DDQ Oxidation:

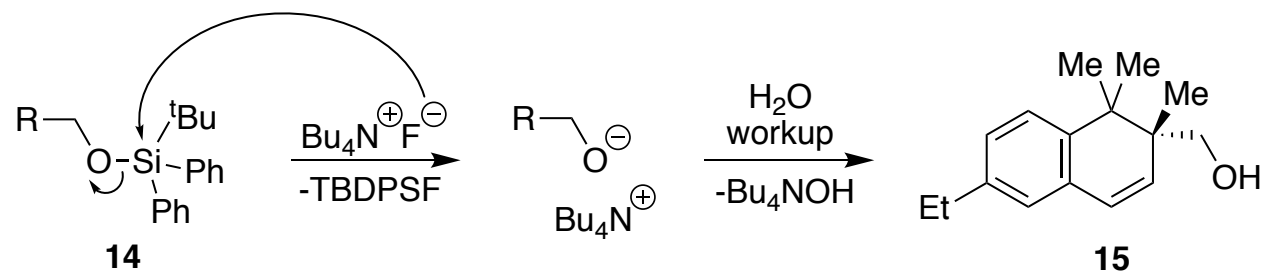




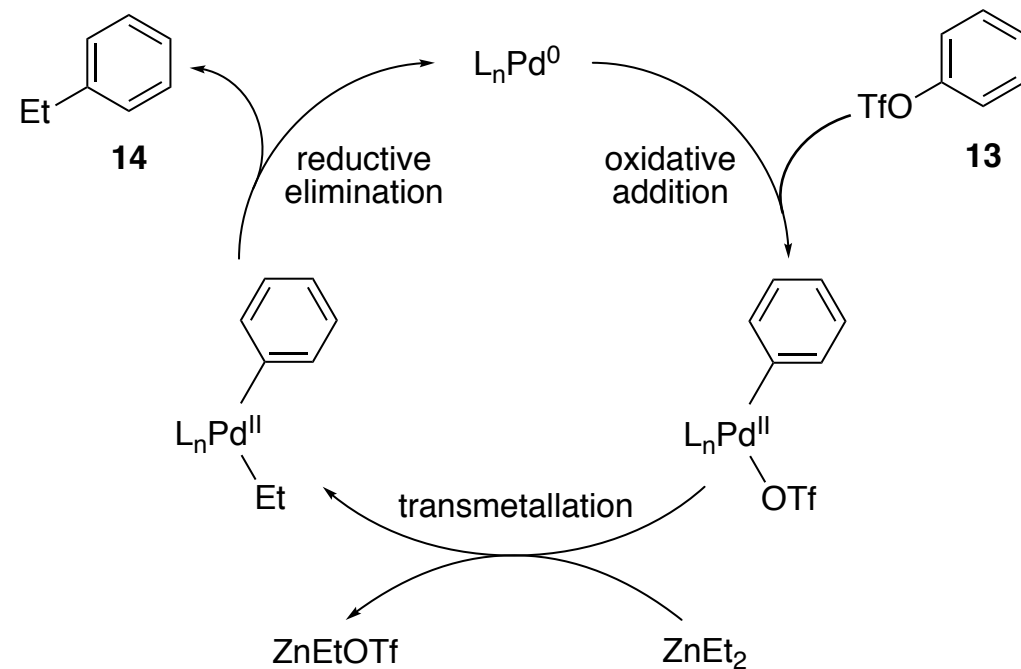
Triflation:

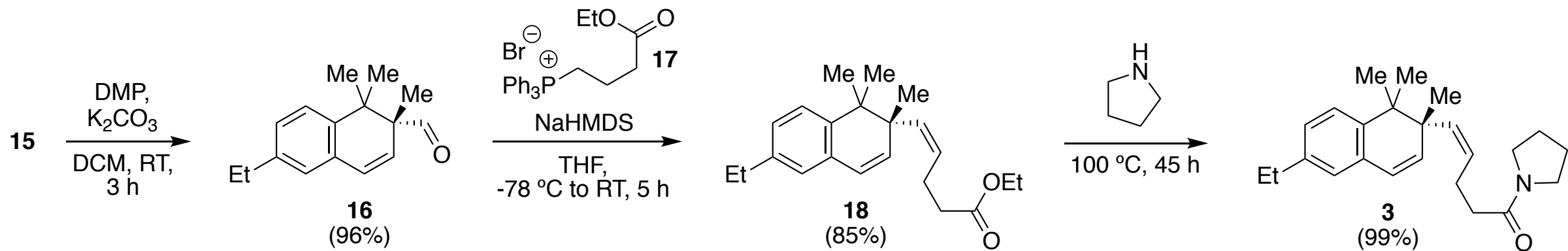


TBAF Deprotection:

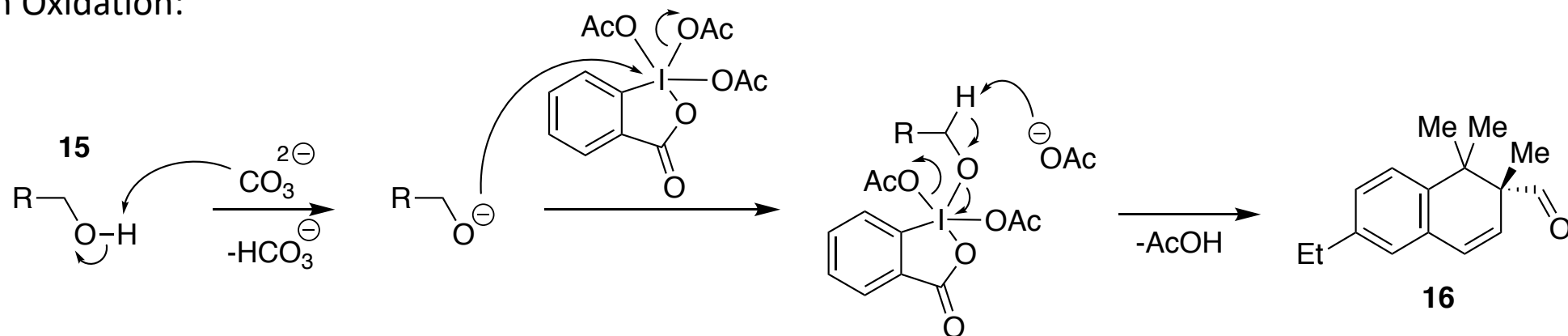


Negishi Cross-Coupling:

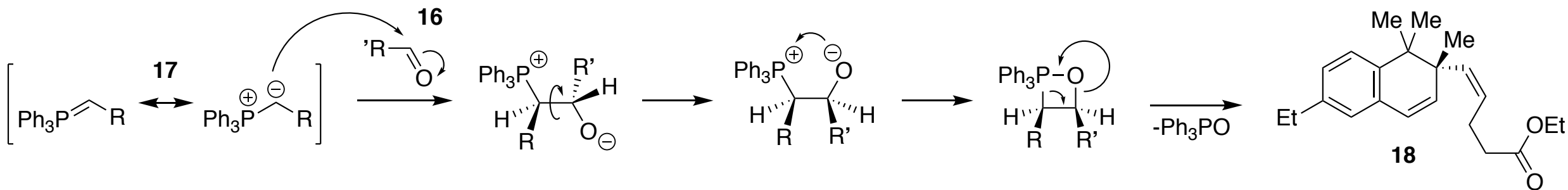




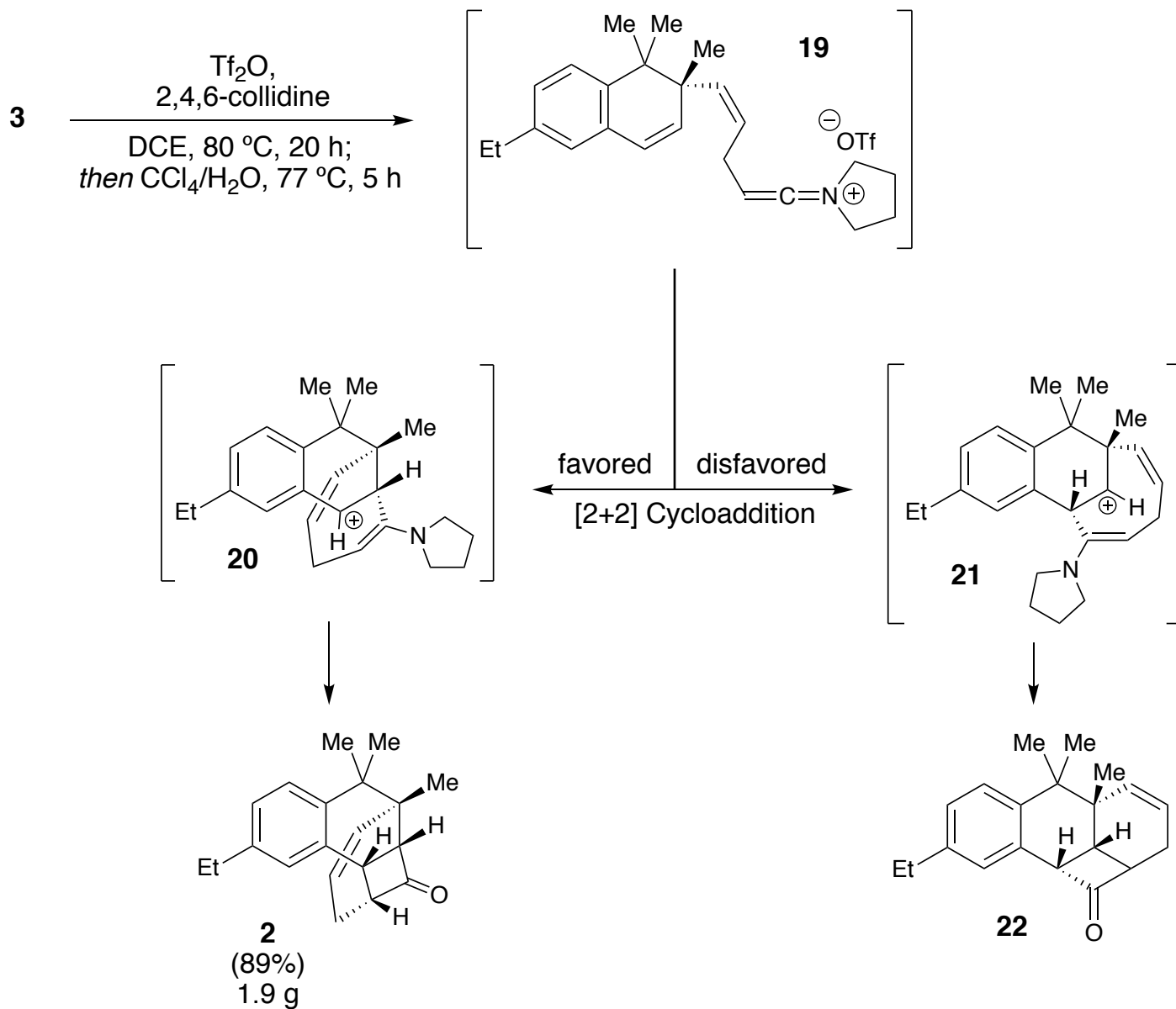
### Dess-Martin Oxidation:



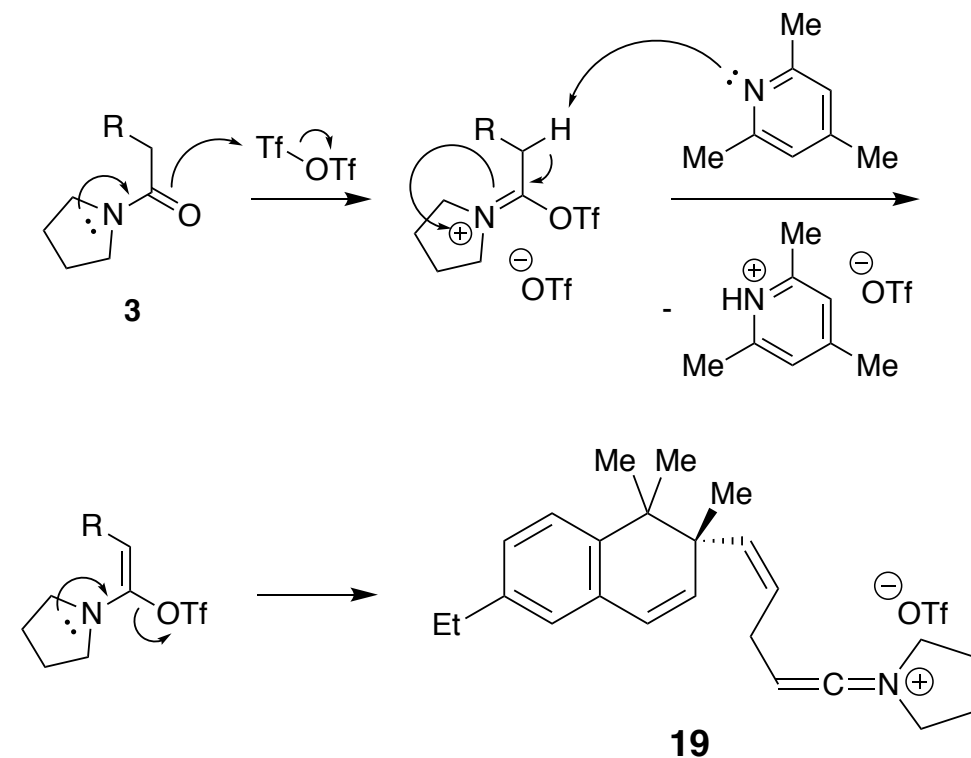
### Wittig Olefination:



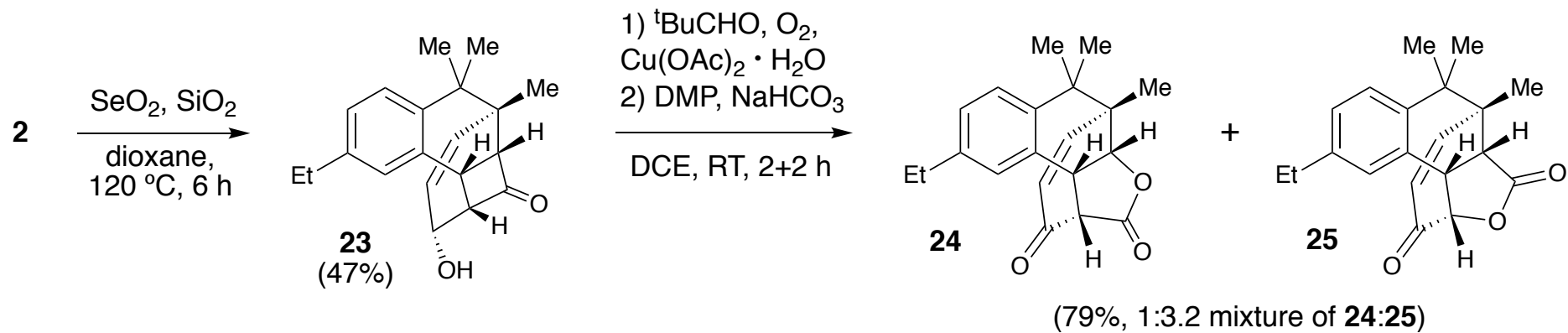
# Key Step:



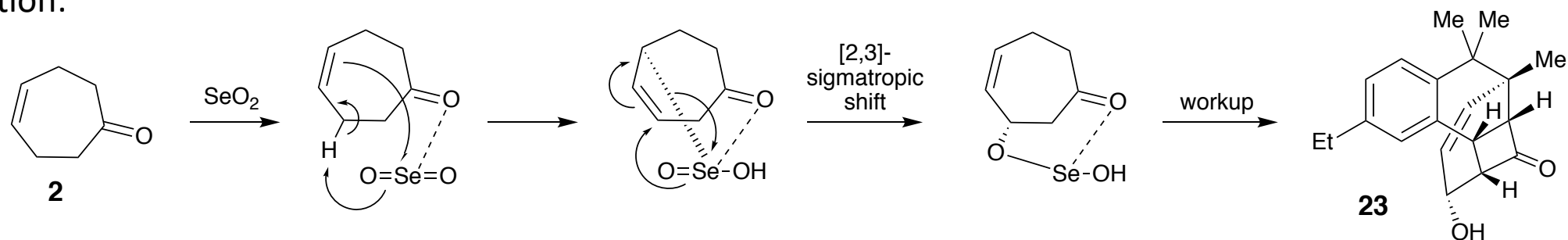
## Ketiminium Ion Formation:



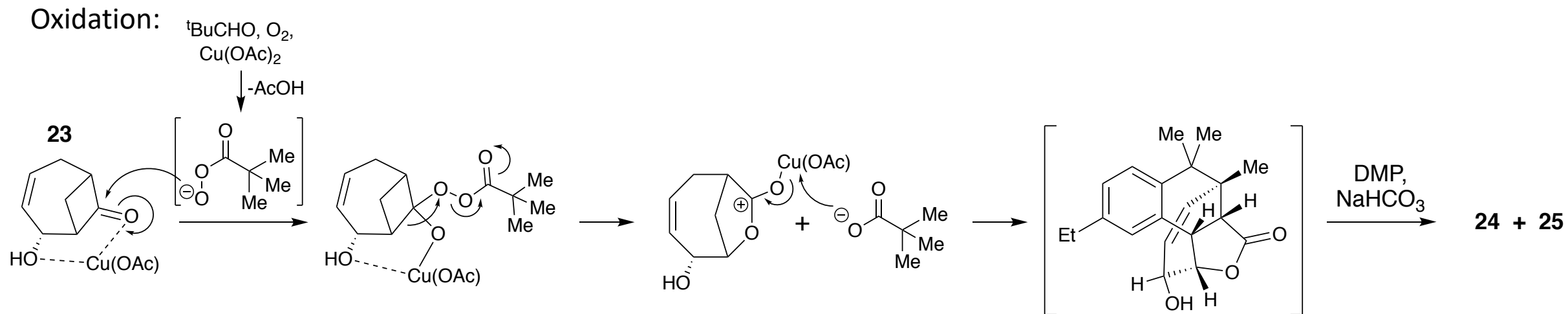


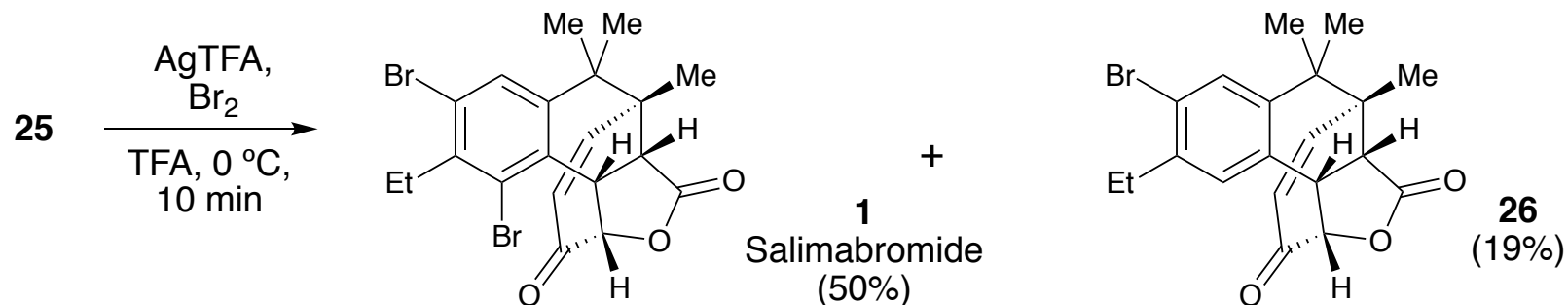


### Riley Oxidation:

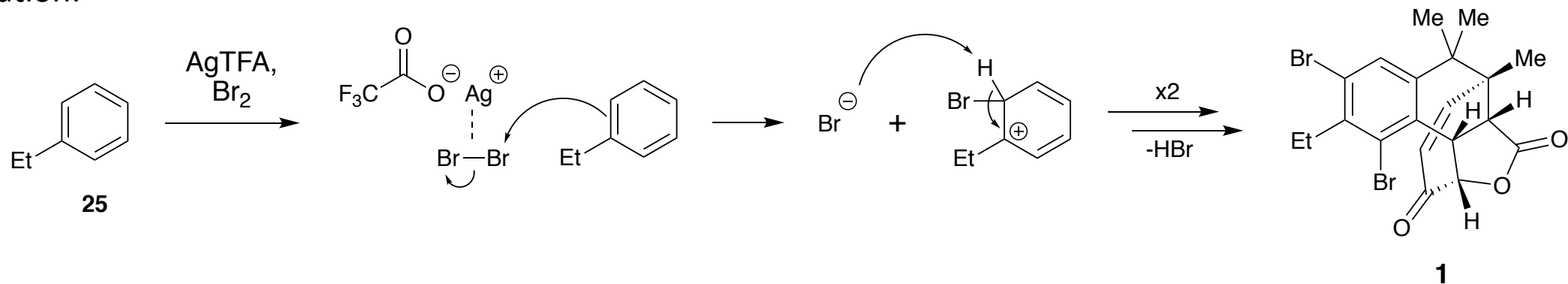


### Baeyer-Villiger Oxidation:





Bromination:



Conclusions:

- First total synthesis of salimabromide, a tetracyclic polyketide.
- 16 steps with an overall yield of 3.7%.
- Robust and practical transformations.
  - 1.9 g of the highly-advanced intermediate **2** was prepared from a single 10 g batch of 3-methoxybenzaldehyde.