

# Enantioselective Total Synthesis of (+)-Aberrarone

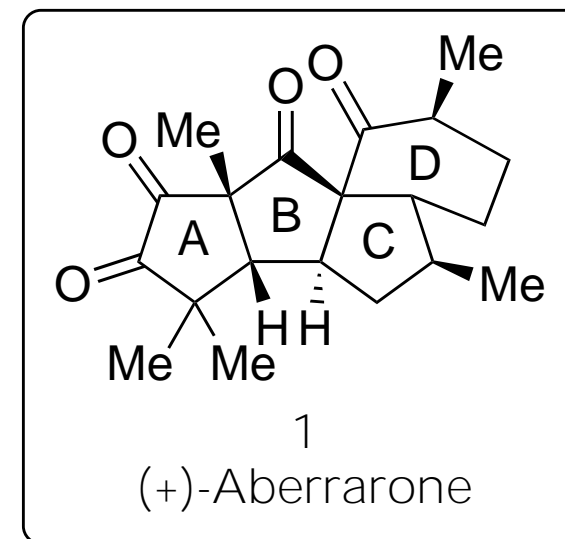
E. M. Carreira *et al.* *J. Am. Chem. Soc.*, **2022**, *144*, 15475.

**(+)-Aberrarone** was firstly isolated in 2009 from the Caribbean sea whip *Pseudopterogorgia elisabethae*, which exhibits anti-inflammatory effects and are present in various skin care products.

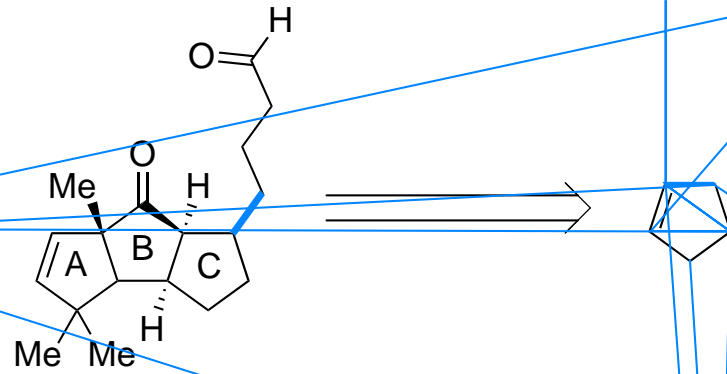
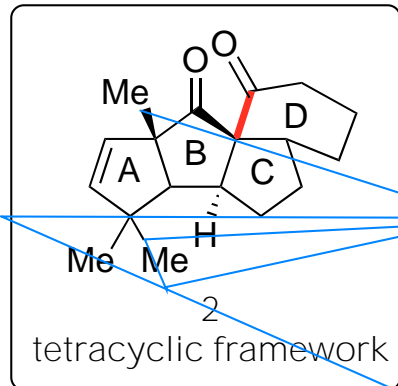
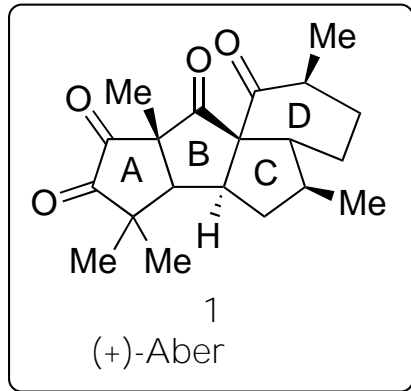
**(+)-Aberrarone** bears 5-5-5-6-fused tetracyclic framework, seven stereogenic centers including three quaternary carbons, and four ketones.

To date, there is only a single study toward the synthesis of a racemic analogue of Aberrarone. Also, the synthetic route was separate, iterative construction of the rings.

This is the first total synthesis of **(+)-Aberrarone**. A, B, D rings are constructed by a key cascade cyclization reaction in a single step.

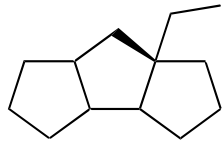


# Previous Study



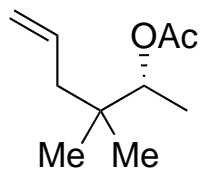
# Retrosynthetic Analysis

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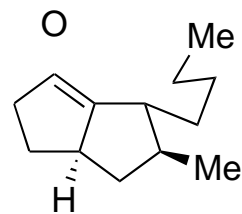
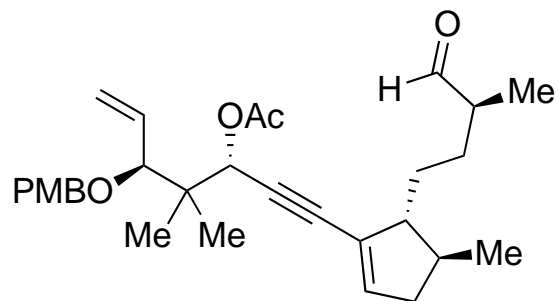
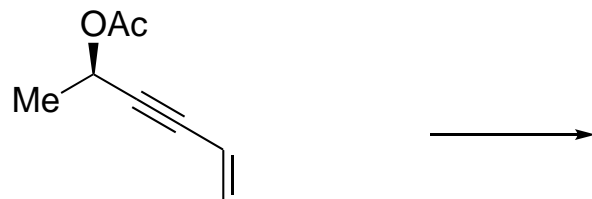


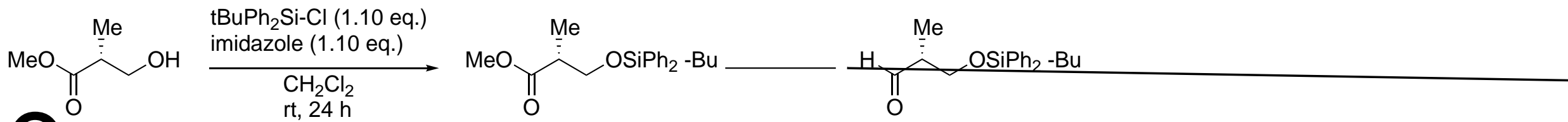
*Overall*  
*23 steps*  
*16 steps (LLS)*

# Key Step: Inspired work



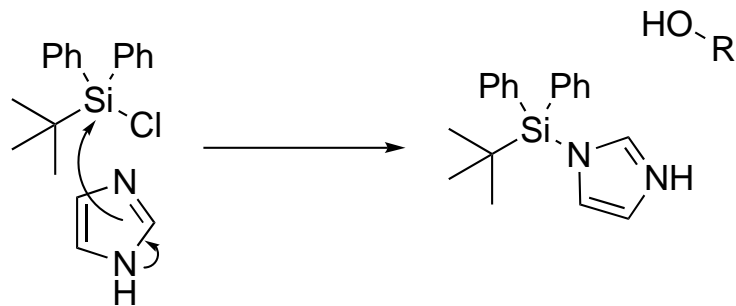
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(R)-Roche ester  
 25g \$558

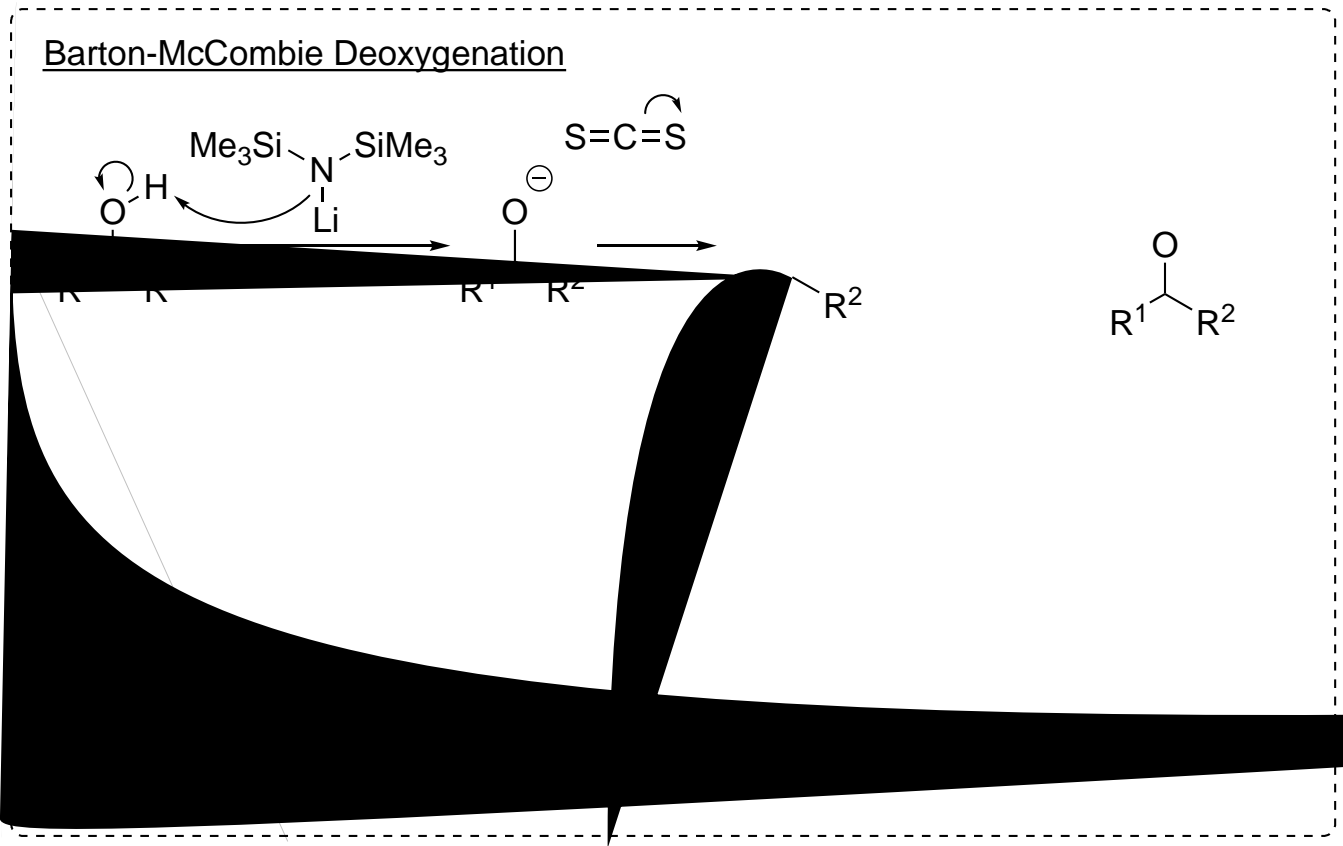
Silyl protection of alcohol

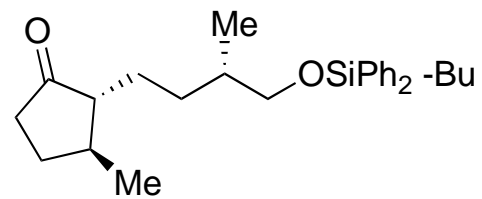


DIBAL reduction of ester to aldehyde

Carbon homologation by wittig reaction



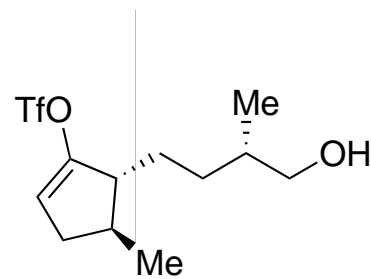




M

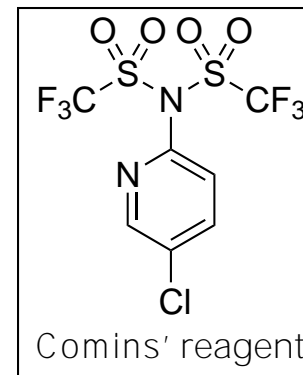
11

KHMDS (1.2 eq.)  
Comins reagent  
(1.1 eq.)  
THF, 78 C to rt



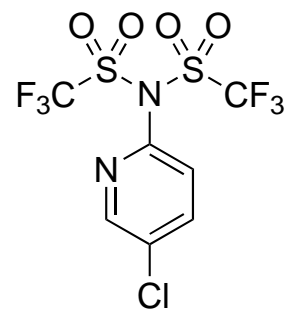
71%

12M

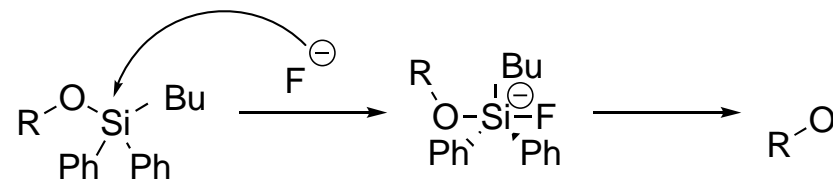


Comins' reagent

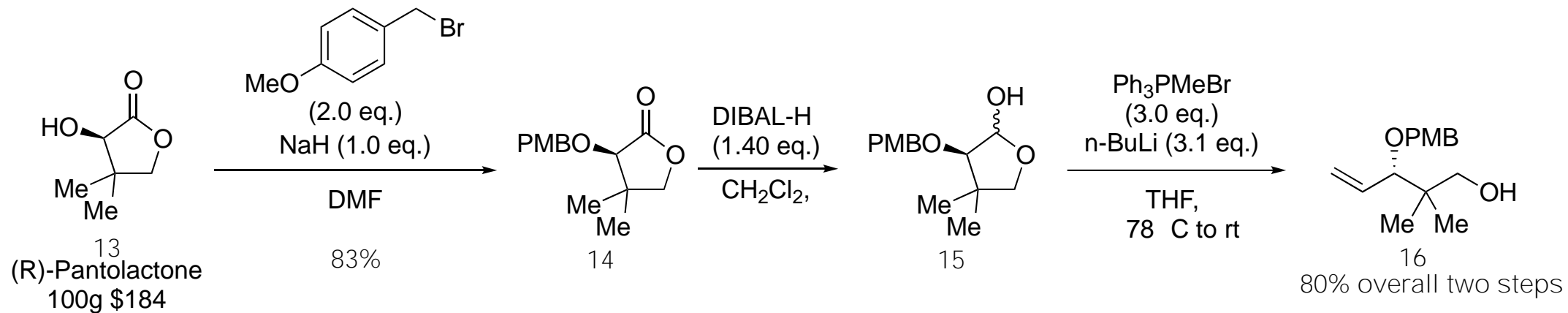
e



Deprotection of silyl protecting groups

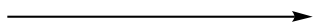




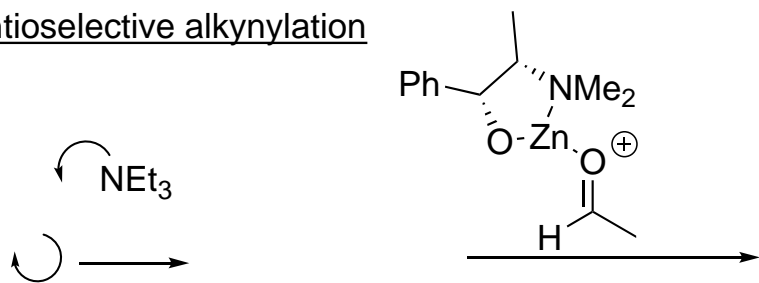


DIBAL reduction of ester to aldehyde

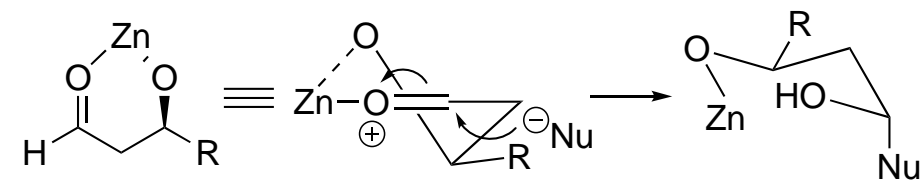
DMSO (30 eq.)

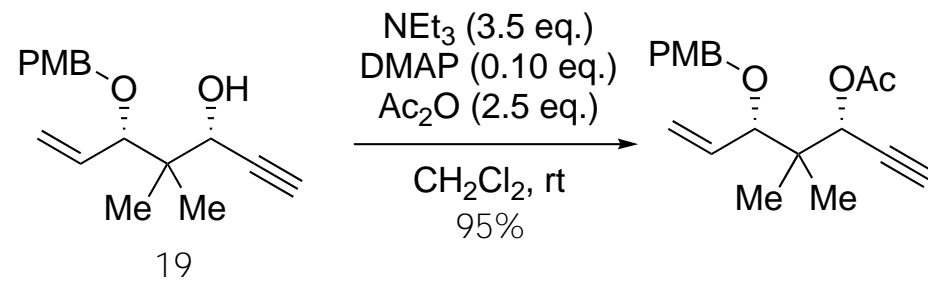


Enantioselective alkylation



Diastereoselective alkylation (without chiral ligand)

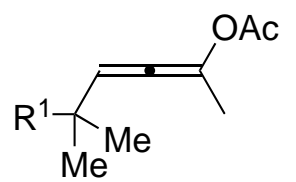
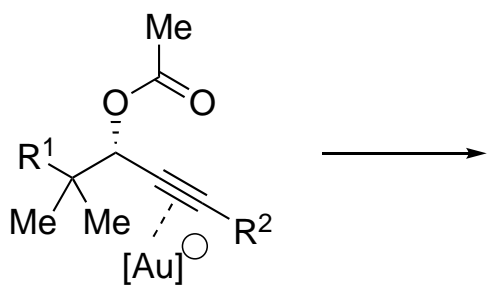
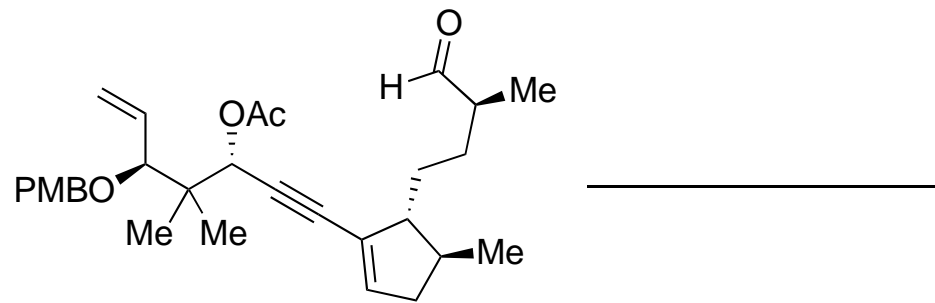


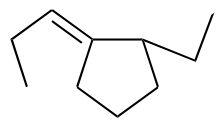
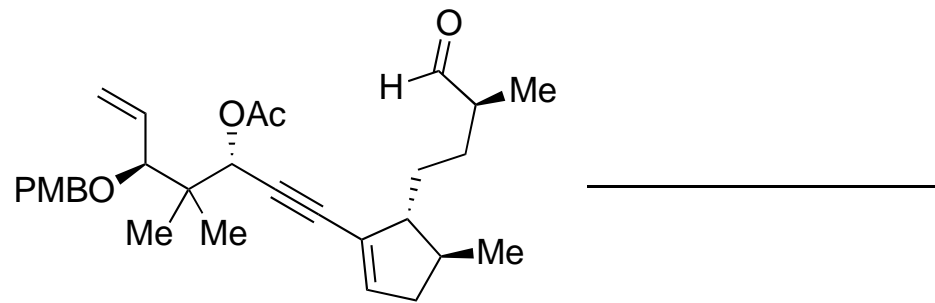


Acetyl protection of alcohol

d





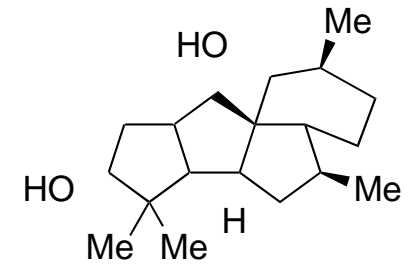


Intramolecular aldol reacti

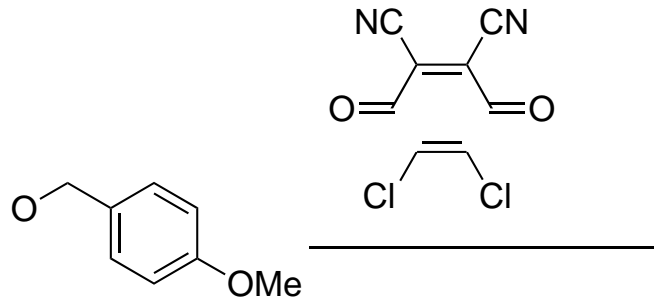
LiAlH<sub>4</sub>  
(1.0 eq.)

THF,

3.7 : 1 dr



Deprotection of PMB group by DDQ



LAH reduction of ketone to alcohol

