

Enantioselective Total Synthesis of (+)-Aberrarone

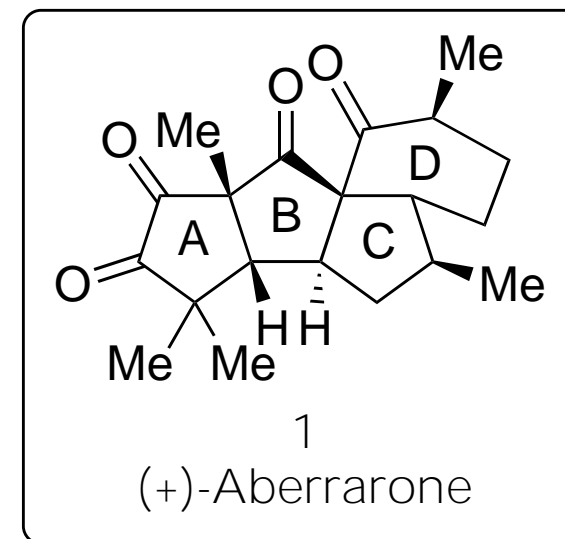
E. M. Carreira *et al.* *J. Am. Chem. Soc.*, **2022**, *144*, 15475.

(+)-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.

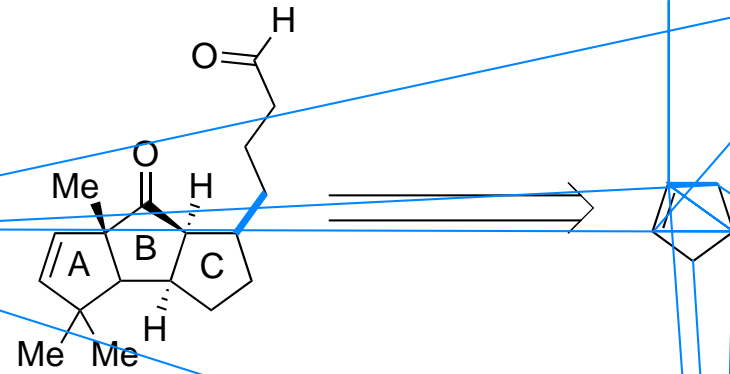
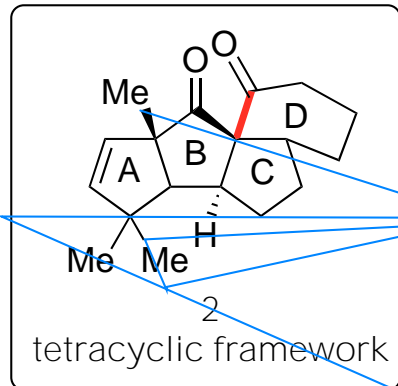
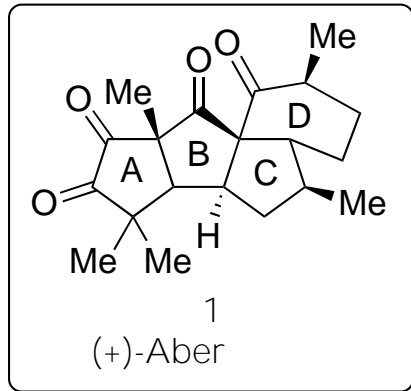
(+)-Aberrarone bears 5-5-5-6-fused tetracyclic framework, seven stereogenic centers including three quaternary carbons, and four ketones.

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.

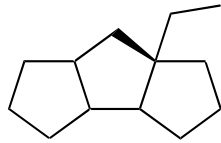
This is the first total synthesis of **(+)-Aberrarone**. A, B, D rings are constructed by a key cascade cyclization reaction in a single step.



Previous Study

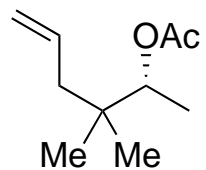


Retrosynthetic Analysis

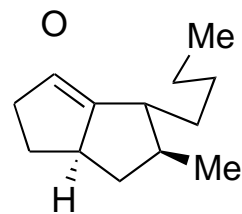
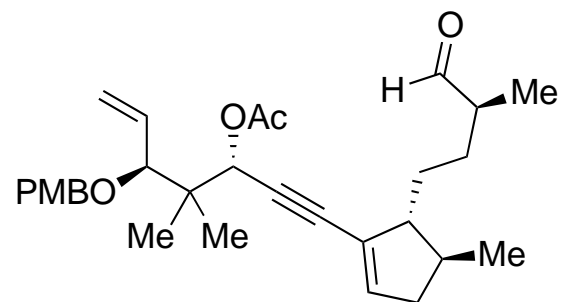
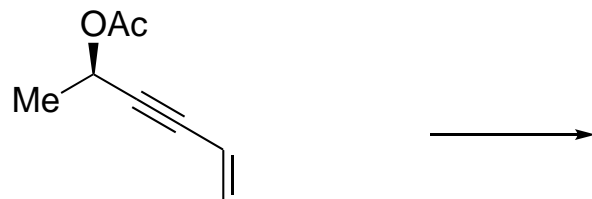


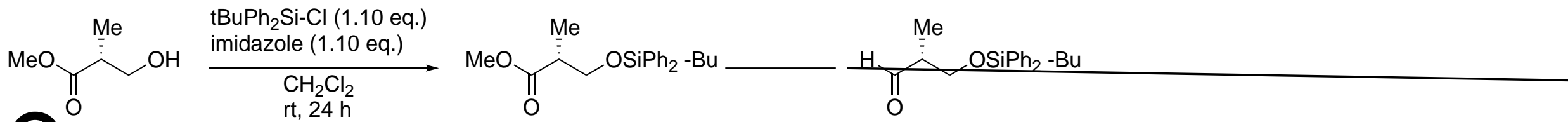
Overall
23 steps
16 steps (LLS)

Key Step: Inspired work



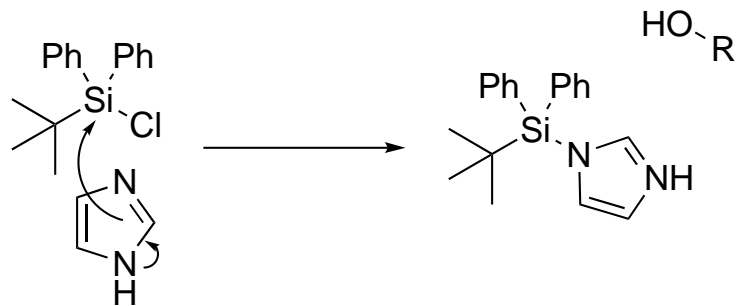
[]





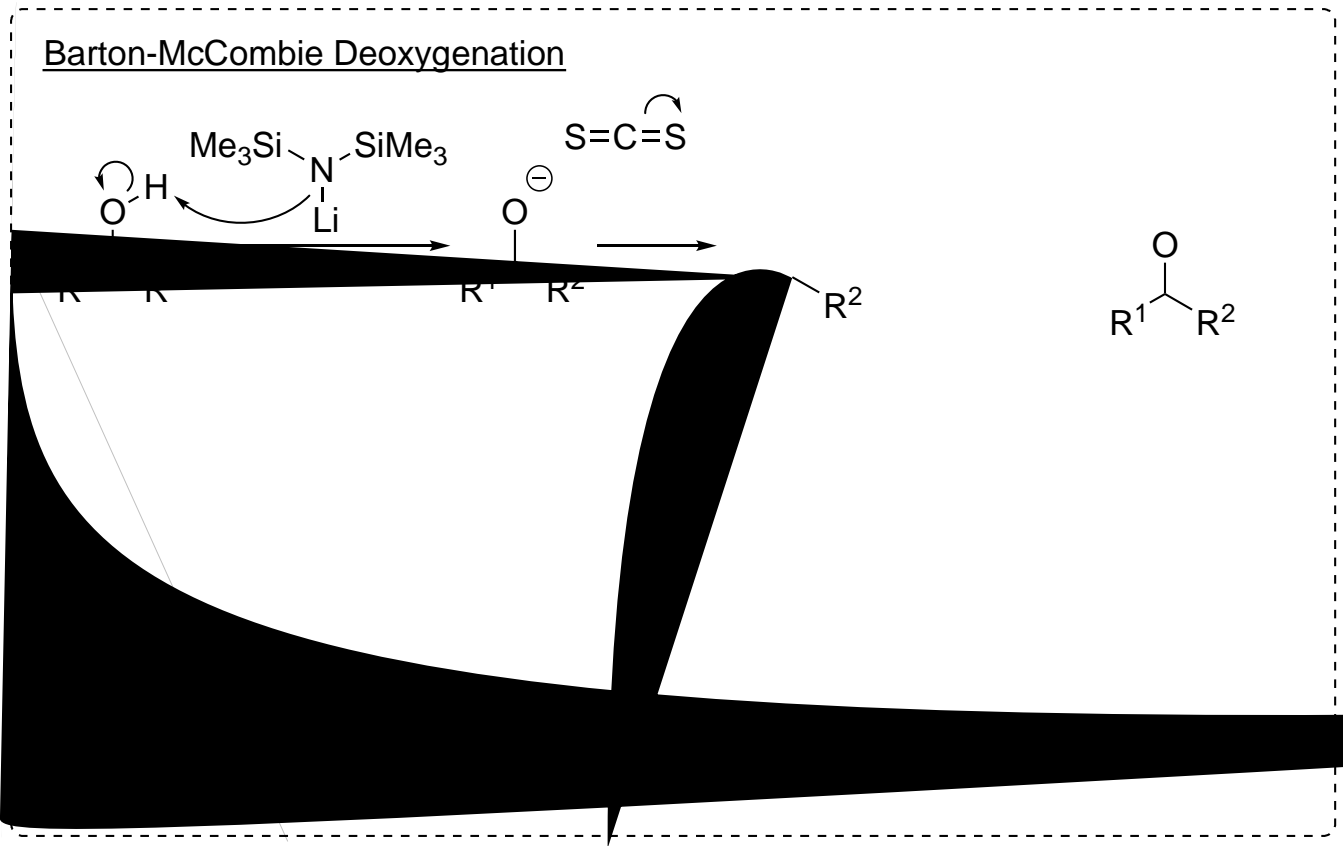
(R)-Roche ester
25g \$558

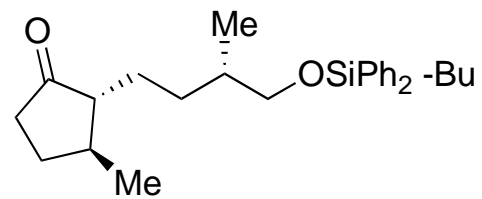
Silyl protection of alcohol



DIBAL reduction of ester to aldehyde

Carbon homologation by wittig reaction

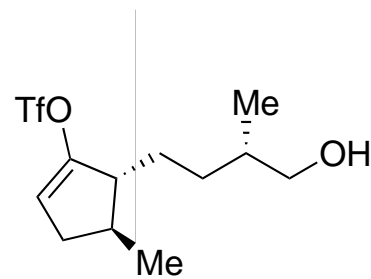




M

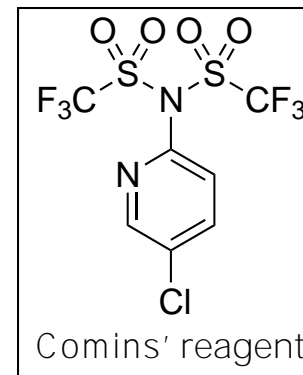
11

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



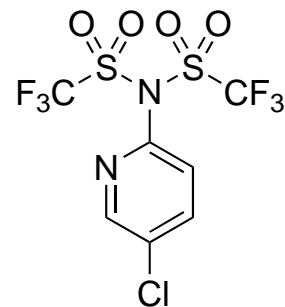
71%

12

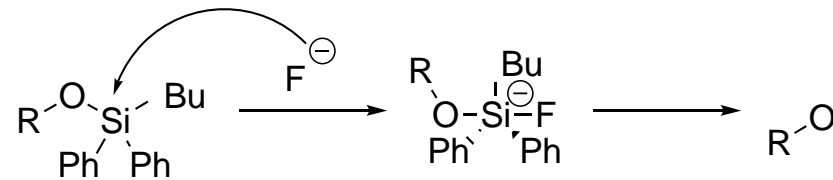


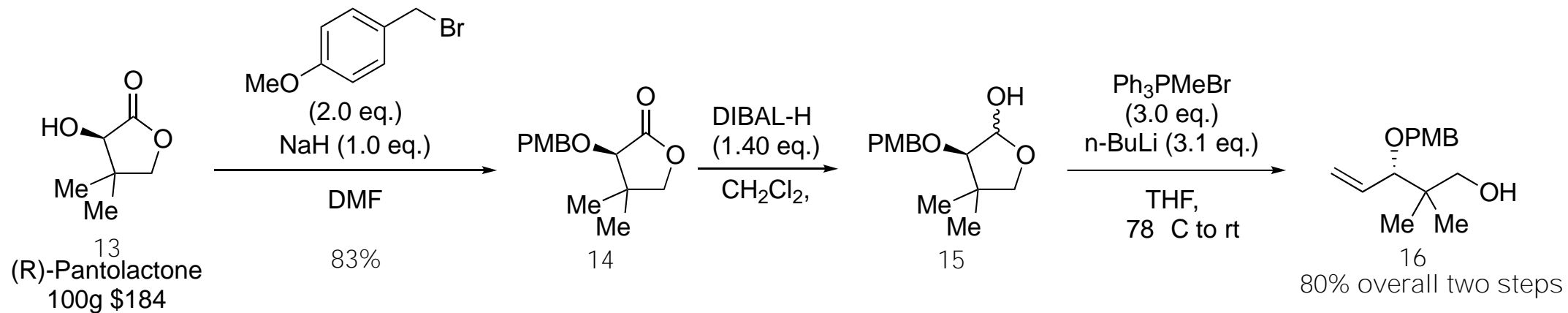
Comins' reagent

e



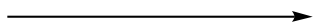
Deprotection of silyl protecting groups



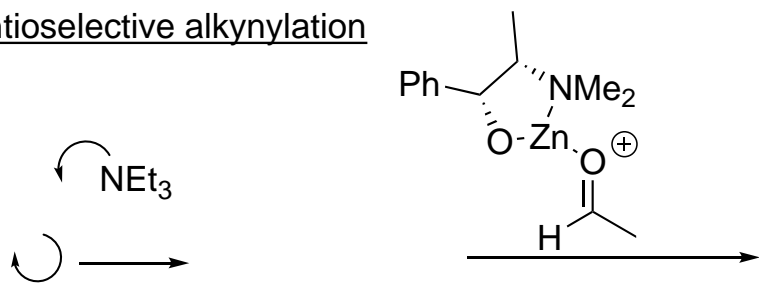


DIBAL reduction of ester to aldehyde

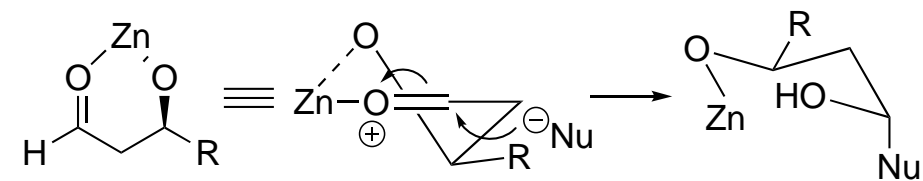
DMSO (30 eq.)

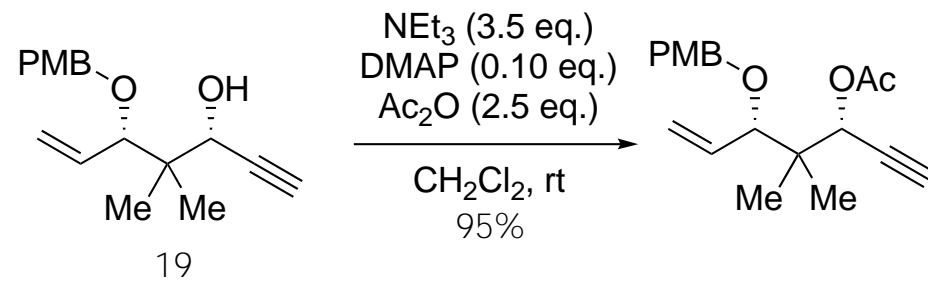


Enantioselective alkylation



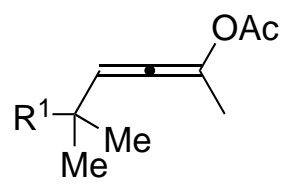
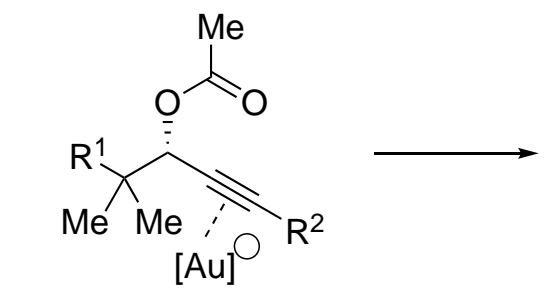
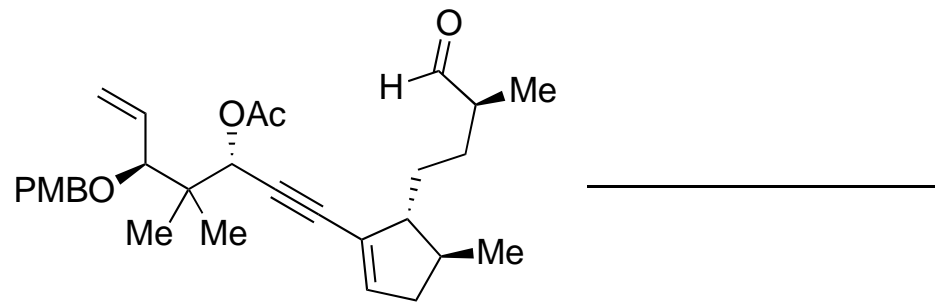
Diastereoselective alkylation (without chiral ligand)

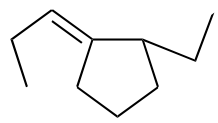
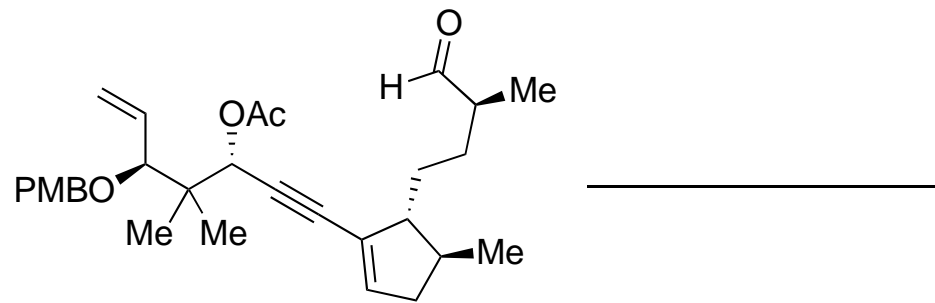




Acetyl protection of alcohol

d



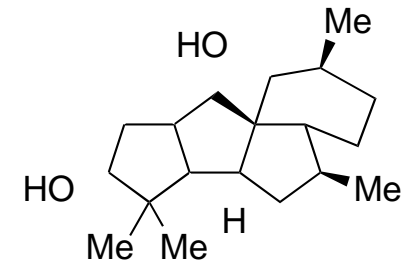


Intramolecular aldol reacti

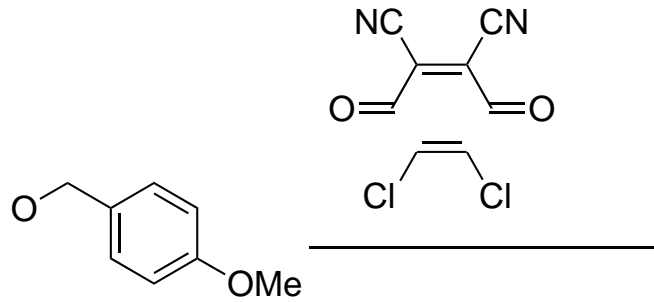
LiAlH₄
(1.0 eq.)

THF,

3.7 : 1 dr



Deprotection of PMB group by DDQ



LAH reduction of ketone to alcohol

