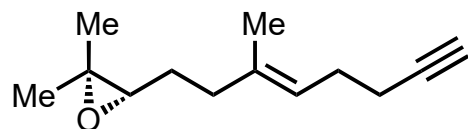
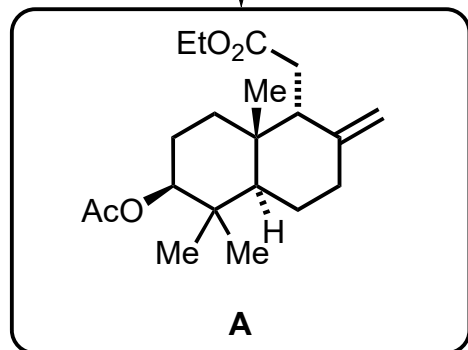


Total Synthesis of (+)-Cyclobutastellettolide B

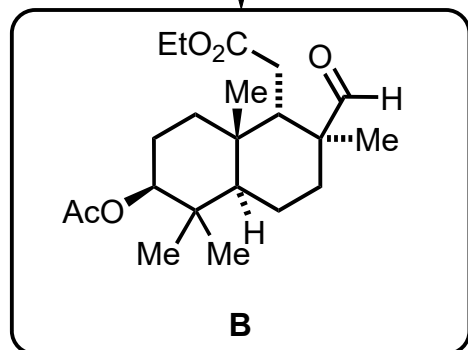
Zhongchao Zhang, Sijia Chen, Fu Tang, Kai Guo, Xin-Ting Liang, Jun Huang, Zhen Yang
J. Am. Chem. Soc. **2021**, *143*, 18287–18293.



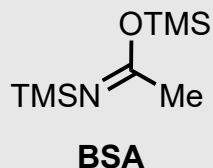
1–4



5–9



- 1) TiCl_4 , CH_2Br_2
- 2) $t\text{BuLi}$, DMF
- 3) NaBH_4
- 4) Pivalic acid (cat.),
 $\text{MeC}(\text{OEt})_3$, neat, reflux;
then AcOH , Ac_2O ;
then Et_3N , 4-DMAP



- 5) *m*CPBA
- 6) $\text{B}(\text{C}_6\text{F}_5)_3$
- 7) **BSA**, DBU
- 8) TFA, Et_2Zn , CH_2I_2
- 9) conc. HCl, acetone, reflux

Propose a route to the starting material.

see below

- 1) *Hint*: Product data:
 ^{13}C NMR (100 MHz, CDCl_3) δ 141.0, 120.9, 78.9, 49.1, 38.72,
 38.70, 37.2, 36.9, 28.0, 27.7, 21.2, 20.9, 15.4 ppm.

- 2) Name of the reaction?
 Bouveault aldehyde synthesis

- 4) Name the reaction.
 Johnson–Claisen rearrangement

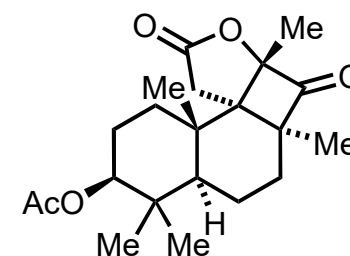
Hint: All functional groups competent of reacting with the ortho ester under these reaction conditions reacted. The telescoped steps constitute a protecting group manipulation.

- 6) Name the reaction.
 Meinwald rearrangement

Additional: Whose favorite Lewis acid is this? Which is your favorite one & why?

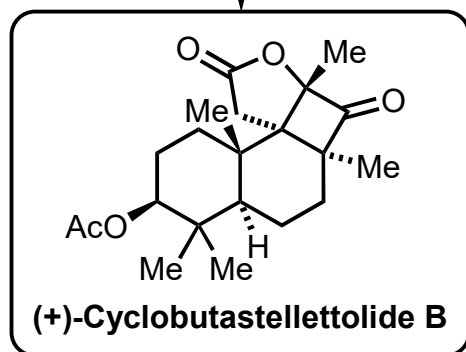
- 8) Name the reaction.
 Simmons–Smith cyclopropanation

- 9) *Hint*: The structural motif generated in step 8 is known to shapeshift to a different constitutional isomer. Think Kulinkovich reaction.



(+)-Cyclobutastellettolide B

10–13



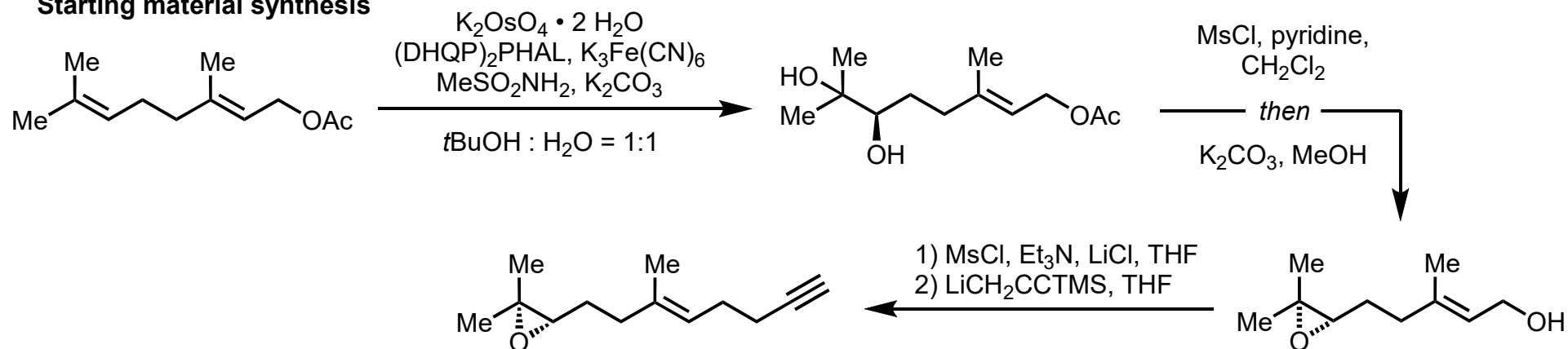
- 10) EtPPh_3Br , $n\text{BuLi}$
- 11) K_2OsO_4 , NMO
- 12) $(\text{COCl})_2$, DMSO, Et_3N
- 13) Compact fluorescent lamp (CFL), CHCl_3

10–13) Name the reactions.

Wittig olefination, Upjohn dihydroxylation, Swern oxidation, Norrish–Yang cyclization.

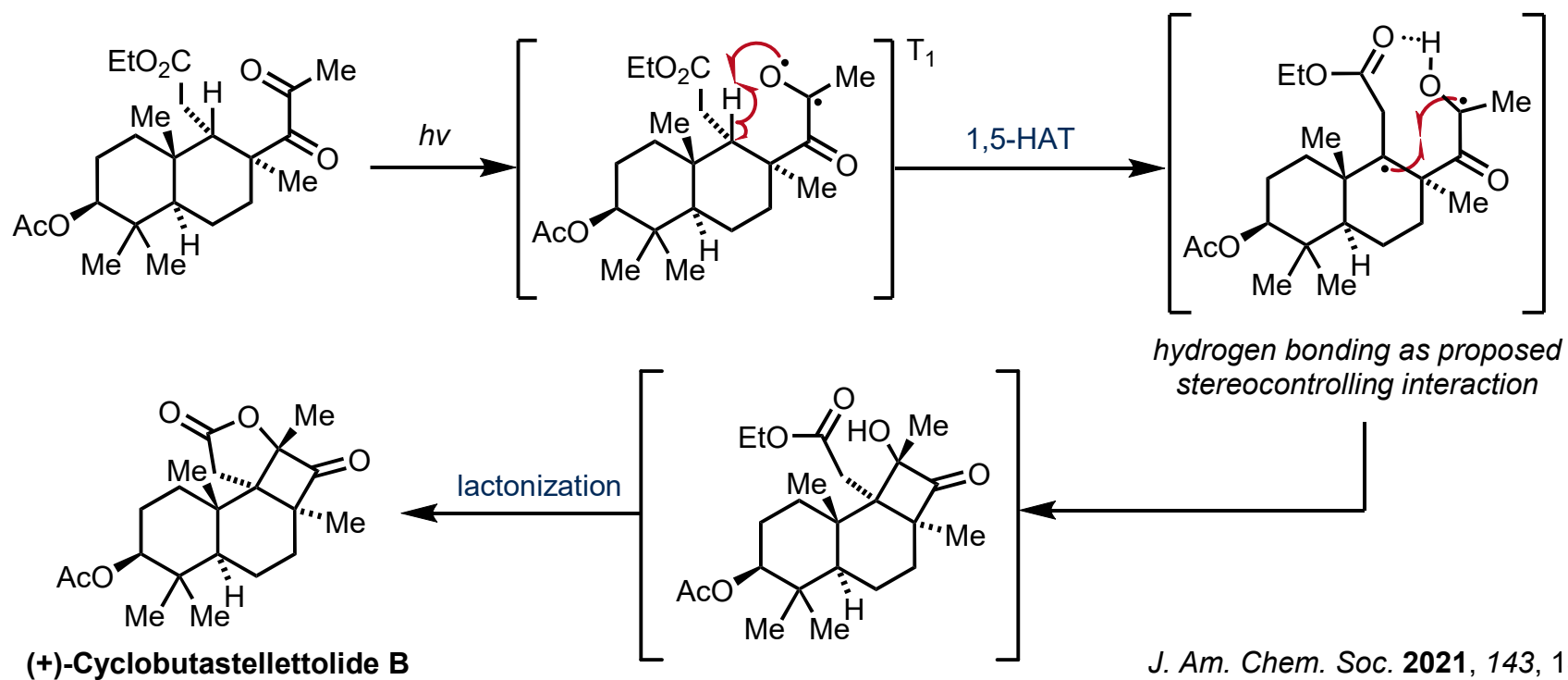
For 13: Also consider writing the detailed reaction mechanism.
see below

Starting material synthesis



Tetrahedron Lett. **1993**, 34, 5995–5998.
J. Am. Chem. Soc. **2020**, 142, 8116–8121.

Proposed mechanism for the Norrish–Yang cyclization



J. Am. Chem. Soc. **2021**, 143, 18287–18293.