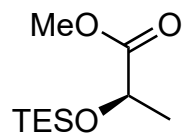


Total Synthesis of (+)-Mutilin

Han Chen, Zesheng Li, Peng Shao, Haosen Yuan, Si-Cong Chen, Tuoping Luo
J. Am. Chem. Soc. **2022**, *144*, 15462-15467.

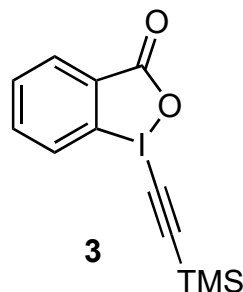
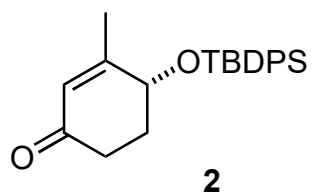
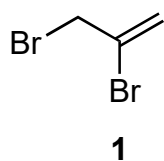


1-7



8-11

- 1) CeCl_3 , $\text{TMSCH}_2\text{MgCl}$ (excess)
- 2) H_2SO_4
- 3) *n*-BuLi then **1**
- 4) TBSCl, imH
- 5) *t*-BuLi, (2-Th)Cu(CN)Li then **2**, TMSCl
- 6) TBAF, **3** then silica gel
- 7) $\text{Et}_3\text{N}\cdot\text{HF}$



- 8) *t*-BuOK, *t*-BuOH
- 9) LiHMDS then MeOC(O)CN
- 10) toluene, reflux then NaOH, $\text{MeOD}/\text{D}_2\text{O}$
- 11) TBSOTf, 2,6-lutidine

3) Name the rearrangement.

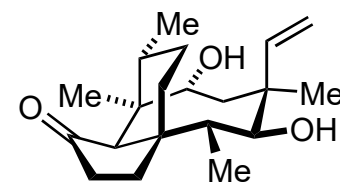
6) Draw a mechanism for this transformation.
Hint: an allene forms.

7) TBDPS remains.

9) Hint: a tricycle is formed.

10) Name the reaction.

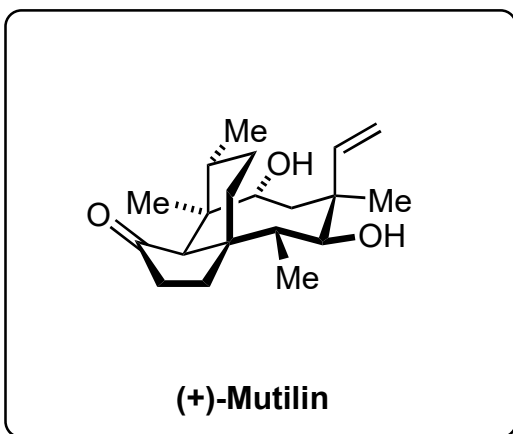
Hint: 4 deuterium atoms are incorporated during basic hydrolysis, .



(+)-Mutilin



↓ 12-18



- 12) 365 nm *then* HF·py
- 13) PtO₂, H₂
- 14) LiHMDS *then* TIPSOTf *then* MeI
- 15) LDA *then* MeCHO
- 16) Martin's sulfurane
- 17) TBAF, reflux
- 18) Na, EtOH

12) Name the reaction.

Hint: the 5-6-8 skeleton is formed.

Rationalise why deuterium was incorporated in the previous step.

14) Hint: 2 equiv. base, 1 equiv. electrophile each

16) Draw the structure of the reagent.

How does it work?

17) Hint: No deuterium present in the molecule after this step.

