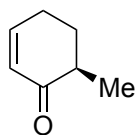
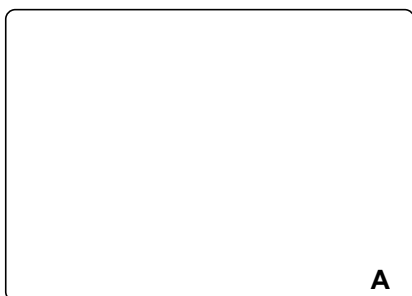


## Formal Total Synthesis of (+)-Pleuromutilin

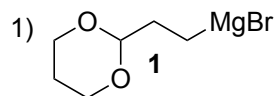
E. P. Farney, S. S. Feng, F. Schäfers, S. E. Reisman  
*JACS* **2018**, 140, 1267-1270.



1 – 3



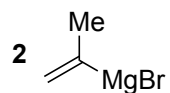
4 – 8



CuCN•2LiCl, TMSCl, THF, -45 °C, then **1**

2) Pd(OAc)<sub>2</sub>, DMSO, O<sub>2</sub>

3) **2**, CuI



4) TCCA, EtOAc

5) HCl (aq), THF, 70 °C

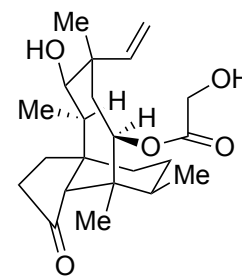
6) CeCl<sub>3</sub>•2LiCl, MeMgCl

7) PCC, CH<sub>2</sub>Cl<sub>2</sub>

8) KH<sub>2</sub>PO<sub>4</sub>, NaI, DMSO, 95 °C

2) Please name the reaction

7) Please name the reaction

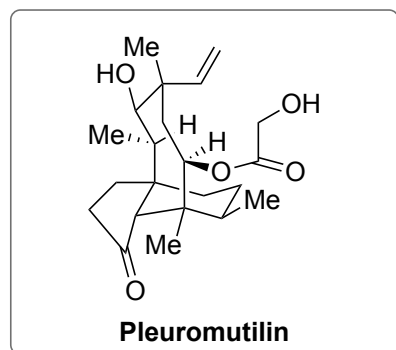


**Pleuromutilin**

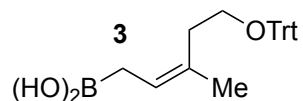
9 – 13



14 – 17



9) **3**, (*R*)-3,3'-Br<sub>2</sub>-BINOL, *t*-BuOH, 3 Å MS, PhMe



10) MOMCl, *i*-Pr<sub>2</sub>NEt

11) HCO<sub>2</sub>H, Et<sub>2</sub>O

12) [Cu(MeCN)<sub>4</sub>]OTf, 4-OMebpy, ABNO, 1-methylimidazole

13) Sml<sub>2</sub> (3 equiv.), H<sub>2</sub>O, THF, 0 °C, 5 min

then TMSCl (5 equiv)

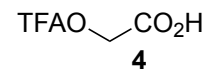
14) LiHMDS, TIPSOTf

15) Mn(dpm)<sub>3</sub>, PhSiH<sub>3</sub>, TBHP, *i*-PrOH

16) Li/NH<sub>3</sub>, EtOH, Et<sub>2</sub>O

17) **4**, EDCI, DMAP

then MeOH, NEt<sub>3</sub>; then HCl/THF, 50 °C



9) Please provide a general transition state

ABNO: 9-Azabicyclo[3.3.1]nonane N-Oxyl

15) Please conceptualize the reaction