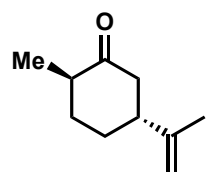


Total synthesis of (+)-Pleuromutilin



1) O₃, MeOH
2) Cu(OAc)₂·H₂O,
FeSO₄·7H₂O, MeOH

A

3) CuCN·2LiCl, **1**, THF, -78°C
then TMSCl
4) Pd(OAc)₂, O₂, DMSO

B

5) CuI, **2**, THF, -45°C, then **B**,
then **3**
6) Pd(OAc)₂, PPh₃,
CO, MeOH

C

7) BF₃·OEt₂,
Bu₄NSiPh₂F₂, **4**
8) PivCl,
py/DCM
9) HF, py
10) DMP

D

11) Sml₂, THF/^tBuOH

E

12) TBSOTf (>2eq), Et₃N
13) LAH
14) DMP
15) H₂, Pd/C, EtOH

F

16) ethylene glycol, HC(OMe)₃,
amberlyst
17) Sml₂, pyrrolidine/H₂O

G

18) LDA, *p*-MeBzCl, THF, -78°C
19) TCDI, reflux
20) *n*Bu₃SnH, AIBN
21) FeCl₃·SiO₂, acetone

H

22) TMSI, HMDS
23) *m*CPBA, NaHCO₃, DCM
24) TBAF, THF
25) HF(aq), MeCN
26) MOMCl, DIPEA, DCM

I

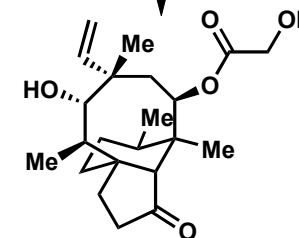
27) **5**, *n*BuLi, THF, -78°C,
then **I**
28) FeCl₃·SiO₂, acetone
29) NaBH₄, THF
30) NCS, DMS
31) CuCN, Me₂Zn, DMF, -20°C

J

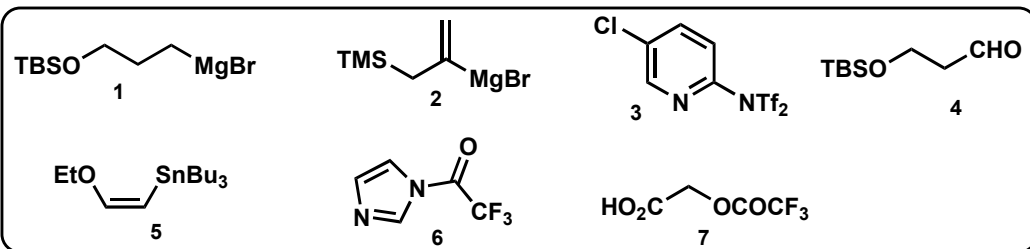
32) LAH
33) DMP
34) AcCl, EtOH

K

35) **6**, EtOAc,
36) **7**, EDCl,
DMAP, then
Et₃N, MeOH



(+)-Pleuromutilin



hint 1: intermediate **E** is a tricycle
hint 2: in step 13 only one
functional group is reduced