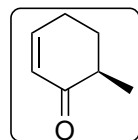
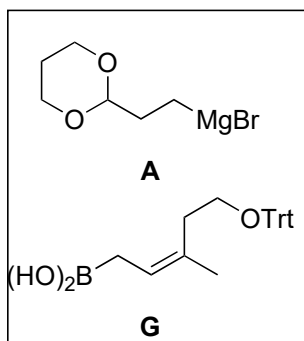


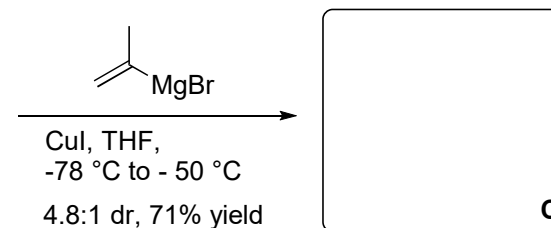
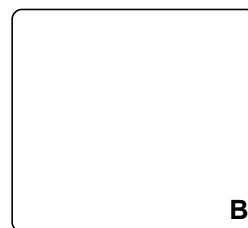


# Total synthesis of (+)-Pleuromutilin

*J. Am. Chem. Soc.* 2018, 140, 4, 1267–1270

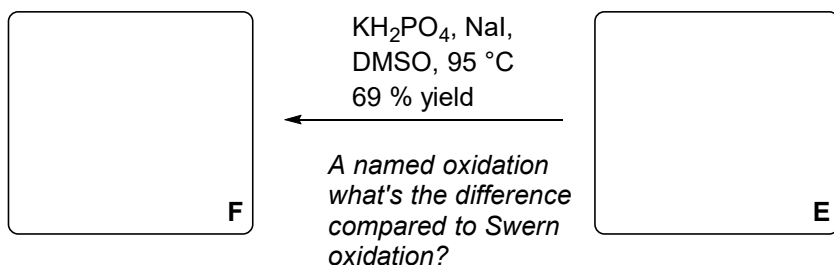
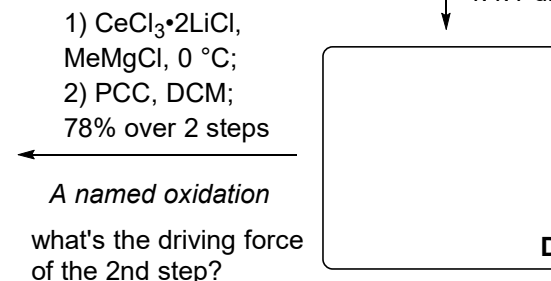


1) **A**, CuCN•2LiCl,  
TMSCl, THF, -45 °C  
2) 10 mol% Pd(OAc)<sub>2</sub>,  
DMSO, O<sub>2</sub>, r.t.  
91% yield, 2 steps

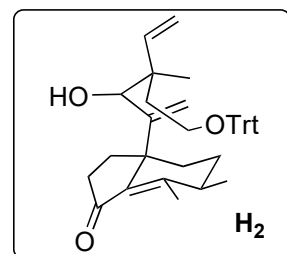


is TCCA aromatic?

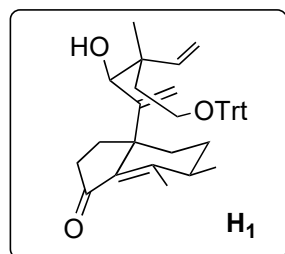
1) TCCA, EtOAc, 0 °C  
2) HCl(aq.), THF, 70 °C  
4.4:1 dr, 52% yield



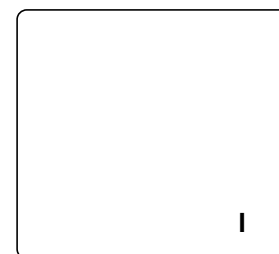
**G**, (*R*)-3,3'-Br<sub>2</sub>-BINOL (20 mol%), <sup>t</sup>BuOH,  
3Å MS, PhMe, 0 °C  
80% yield, 1.2:1 H<sub>1</sub>:H<sub>2</sub>



+

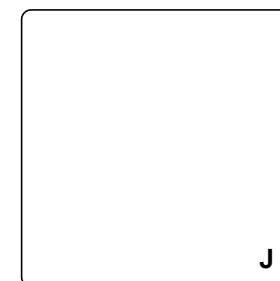


1) MOMCl, DIPEA;  
2) HCO<sub>2</sub>H, Et<sub>2</sub>O;  
3) [Cu(MeCN)<sub>4</sub>]OTf,  
4-OMebpy, ABNO,  
NMI, MeCN

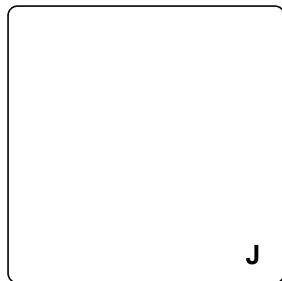


in Deoxygenated condition

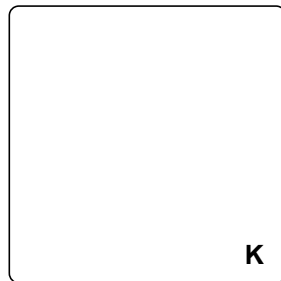
SmI<sub>2</sub> (3 eq.), H<sub>2</sub>O  
(6 eq.), THF, 0 °C,  
5 min  
then TMSCl (5 eq.)  
93% yield, 23:1 dr



What does TMSCl here do?



LiHMDS, TIPSOTf,  
THF, -78 °C to 0 °C

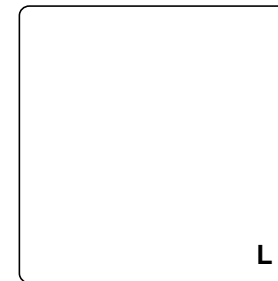


Degassed, anhydrous

Mn(dpm)<sub>3</sub> (13  
mol%), PhSiH<sub>3</sub>,  
TBHP, <sup>i</sup>PrOH, r.t.  
55% yield, single  
diastereomer

*transannular redox relay*

*What does TBHP  
usually do in HAT  
reaction catalysed by  
weak-field metal  
hydrides?*

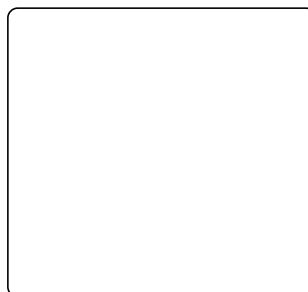


Li/NH<sub>3</sub>, EtOH,  
Et<sub>2</sub>O, -78 °C  
61% yield, 14:1 dr

TBHP: *tert*-butyl hydroperoxide

N: TFAO-CO<sub>2</sub>H

EDCI = EDC: 1-Ethyl-3-  
(3-dimethylaminopropyl)  
carbodiimide



N, EDCI, DMAP, DCM, r.t., 1 h

then MeOH, TEA;  
then HCl/THF, 50 °C

