A modular and enantioselective synthesis of the pleuromutilin antibiotics


1) Zn(CH\(_3\))\(_2\), 0.5% Cu(OTf)\(_2\), 1% X
   then CH\(_3\)Li, CH\(_3\)OC(O)CN
2) t-BuONa, CH\(_3\)I
3) KHMDS, PhNTf\(_2\)

4) 5% Pd(PPh\(_3\))\(_4\), CO, Sn(C\(_2\)H\(_3\))\(_4\)
5) 5% Cu(OTf)\(_2\)
6) Et\(_2\)AlCN, *then* DIBAL-H, *then* NaOH

**Hint:** The first stereocenter being formed has (R)-chirality.
(97:3 er, >20:1 dr over two steps)

Which named reaction is triggered in step 5?
Name reaction of step 6?

Please provide a mechanism for step 8.

(+)-pleuromutilin
How could you prepare D?

Please rationalize the diastereoselectivity of step 9 by providing a reasonable transition state.

Please explain the used stoichiometry by presenting a mechanism of step 12.
16) Ni(COD)$_2$, Y, Et$_3$SiH, then TBAF
17) DMP

18) SmI$_2$
19) Na, EtOH, then HCl

20) 1-(trifluoroacetyl)imidazole
21) O-tritylglycolic acid, EDC, DMAP then CH$_3$OH, NaHCO$_3$
22) Et$_2$Zn, then HCl

Please provide a mechanism for step 16. What is the role of Y?

Please explain step 22 with a mechanism.