Divergent Synthesis of Antiviral Diterpenes Wickerols A and B

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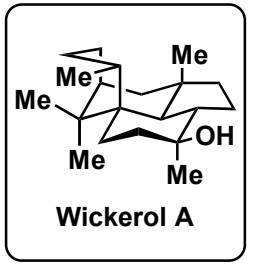
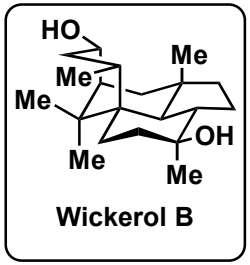
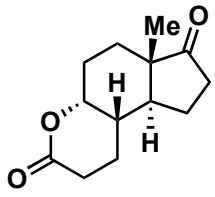


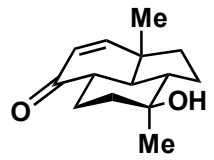
Wickerol A



Wickerol B

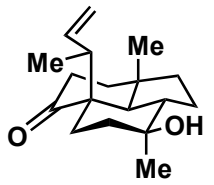


1–6



A

7–9



Intermediate B

1) TMSOTf, NEt_3, DCM *then* $Pd(OAc)_2$, O_2
2) $NaBH_4$, TFA, DCM
3) MeLi (3 equiv.), THF *then* Ac_2O, DMF, DIPEA, DMAP
4) SmI_2, HMPA/THF
5) Pd/C, H_2, MeOH *then* K_2CO_3
6) IBX, PTSA, DMSO

7) (*E*)-crotyl bromide, KO^tBu, DME
8) DIPEA, ethylene glycol, 165 °C
9) Li, NH_3, THF

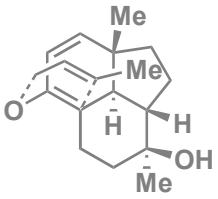
Step 1: What is the name of the reaction?

Larock-modified Saegusa-Ito Oxidation

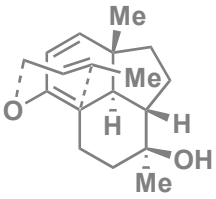
Step 6: Provide a mechanism for this reaction

Step 8: Classify the reaction and provide a rationale for the stereochemical outcome

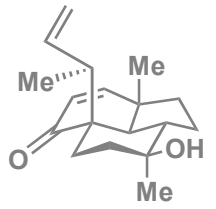
[3,3] sigmatropic Claisen rearrangement

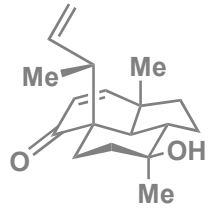


boat-like TS - disfavoured



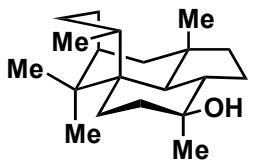
chair-like TS - favoured





Intermediate B

10–16

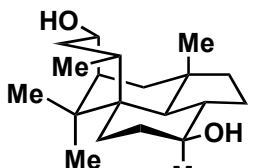


Wickerol A

10) $RhCl(PPh)_3$, HBCat, O_2, THF *then* NaOH, H_2O_2
11) PPh_3, NIS, imidazole, DCM
12) TMSI, HMDS, DCM
13) AgTFA, 2,6-lutidine, THF *then* PTSA
14) Zn, $ZrCl_4$, $PbCl_2$, CH_2I_2,THF
15) Et_2Zn, TFA, CH_2I_2, DCM
16) PtO_2, H_2, AcOH

Intermediate B

10'–15'



Wickerol B

10') $RhCl(PPh)_3$, HBCat, O_2, THF *then* NaOH, H_2O_2
11') DMP, DCM
12') 6N HCl, THF
13') Zn, $ZrCl_4$, $PbCl_2$, CH_2I_2,THF
14') Et_2Zn, TFA, CH_2I_2, DCM
15') PtO_2, H_2, AcOH

Proposed Mechanism for Step 6: