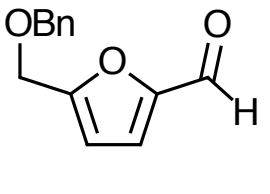
Synthesis Challange # 31

AG Wegner

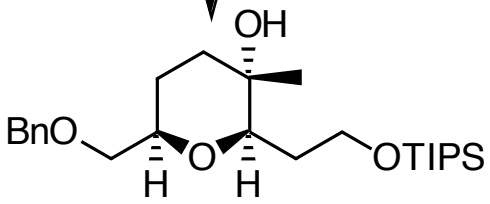
Structural Revision of (+)-Uprolide F Diacetate Confirmed by Asymmetric Total Synthesis

L. Zhu, R. Tong, *Org. Lett.* **2015**, ASAP, DOI: 10.1021/acs.orglett.5b00700



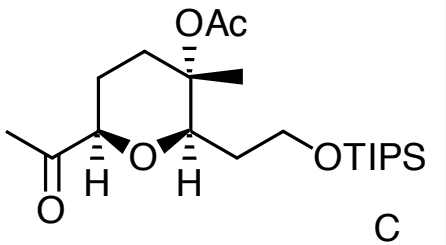
A

?



B

1-5



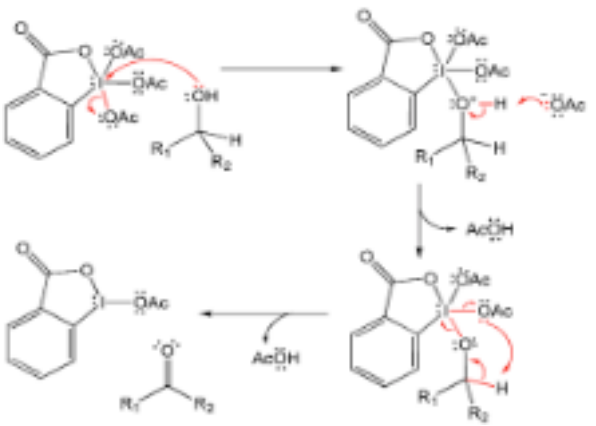
C

1) Ac_2O, iPr_2NEt, DMAP
2) $Pd(OH)_2/C$ (10 mol %), H_2 (1.0 atm)
3) DMP, $NaHCO_3$
4) $CeCl_3$, MeLi, THF, –78 °C
5) DMP, $NaHCO_3$, CH_2Cl_2,

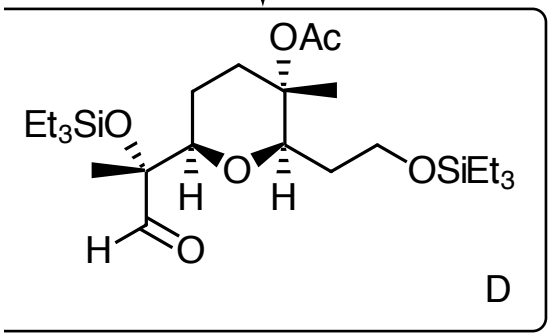
Please design an asymmetric synthesis of B starting from A.

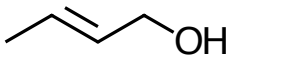
See: Zhu, L.; Liu, Y.; Ma, R.; Tong, R. *Angew. Chem., Int. Ed.* **2015**, *54*, 627.

Please, provide a detailed mechanism for step 3and 5).



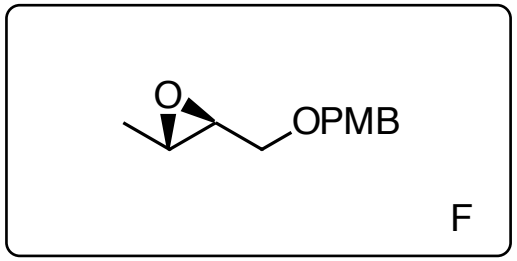
6-9



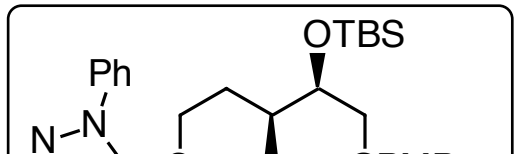


E

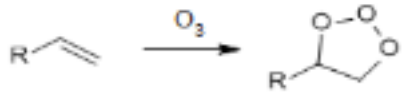
10-12



13-17



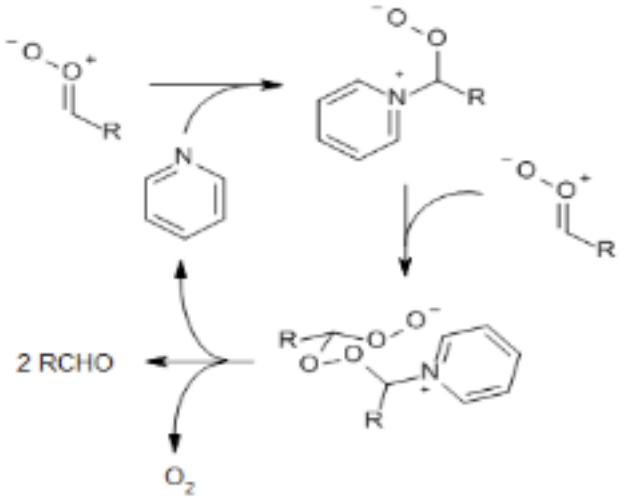
6) $CeCl_3$, vinylMgBr
7) Bu_4NF
8) TESOTf, 2,6-lutidine
9) O_3, pyridine



10) $Ti(OiPr)_4$ (cat), (+)-diisopropyl L-tartrate (cat), tBuOOH
11) TsCl, Et_3N, DMAP (cat)
12) NaH, PMBOH, DMF,

13) CuI, vinylMgBr
14) TBSCl, imidazole, DMF
15) 9-BBN, THF,
then 3 N NaOH, 30 wt % H_2O_2
16) PPh_3, PTSH, DIAD
17) Ammonium molybdate tetrahydrate (cat), 30 wt % H_2O_2

Please, provide a detailed mechanism for step 9).

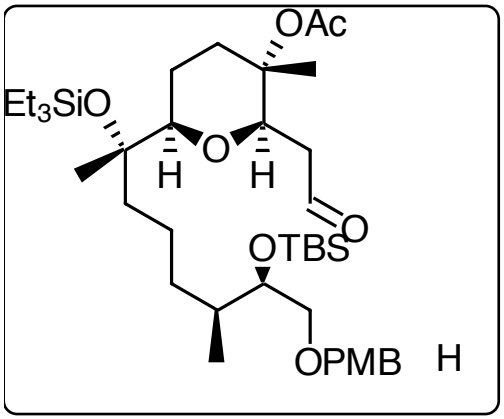


Please, provide a detailed mechanism for step 15). What is the name of the reaction in 16)?

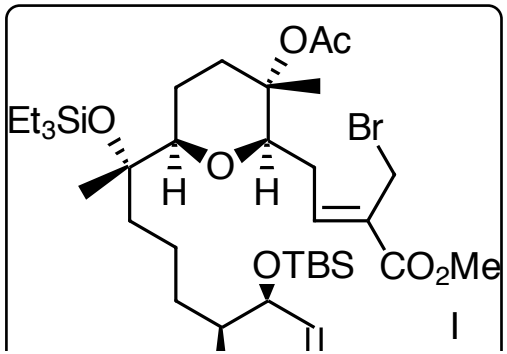
Step 15) Hydroboration
Step 16) Mitsunobu reaction

D + G

18-21



22-25

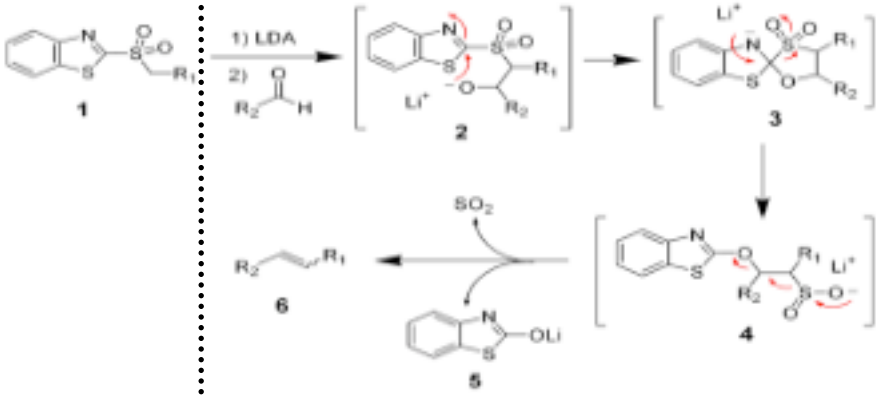


18) LiHMDS
19) AcOH/THF/H_2O = 1/4/1
20) Pd/C (10 mol %), H_2
21) DMP (1.2 equiv), $NaHCO_3$

22) methyl acrylate, PBu_3 (cat)
23) CBr_4, PPh_3, iPr_2NEt
24) DDQ, pH = 7.0 buffer
25) DMP, $NaHCO_3$

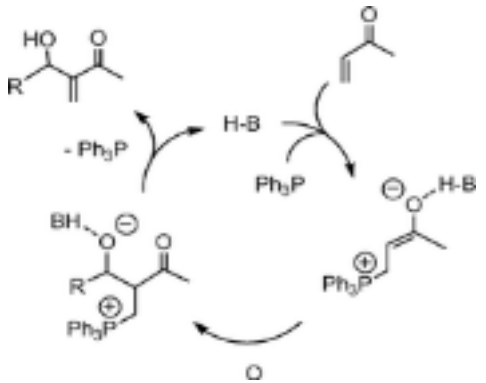
Please, provide a detailed mechanism for step 18)?

Julia-Kocienski-olifination, mechanism here shown with another solfone.

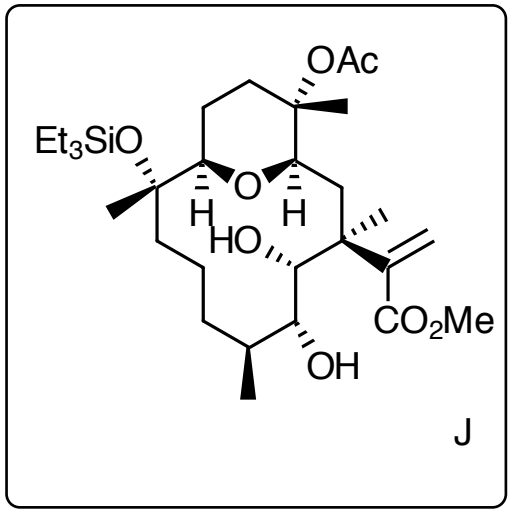


Please, provide a detailed mechanism for sequence 22).

Morita-Baylis-Hillman reaction

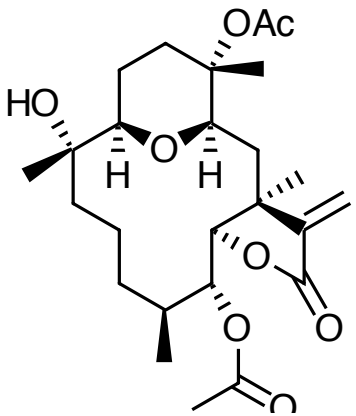


26



J

27-30



26) $CrCl_2$, 4 Å molecular sieves

27) MeOH, CF_3COOH/CH_2Cl_2 = 1/4
28) Bu_4NF
29) NaH
30) Ac_2O, iPr_2NEt, DMAP

Please provide a mechanism for step 26.
Nazaki-Hiyama-Kishi reaction via