Synthesis Challenge #7 AG Wegner

Total Synthesis of (–)-Ecklonialactone B

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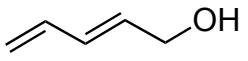
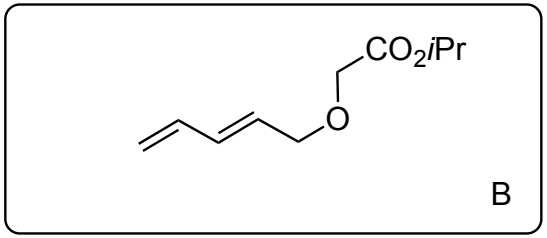


A

1-2

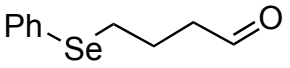
1) NaH, $BrCH_2CO_2H$, THF – 78ºC to rt
2) DCC, DMAP, *i*PrOH



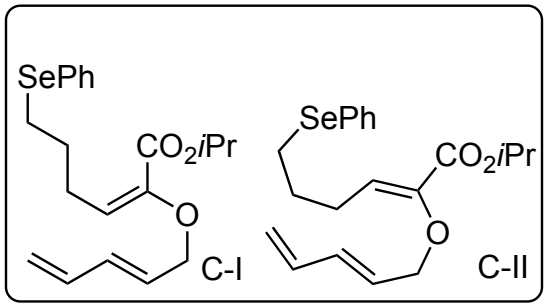
B

1-3

3) LDA, THF, –78ºC, 15 min; **I**
4) MsCl, Et_3N, CH_2Cl_2, rt
5) DBU, THF; pHPLC

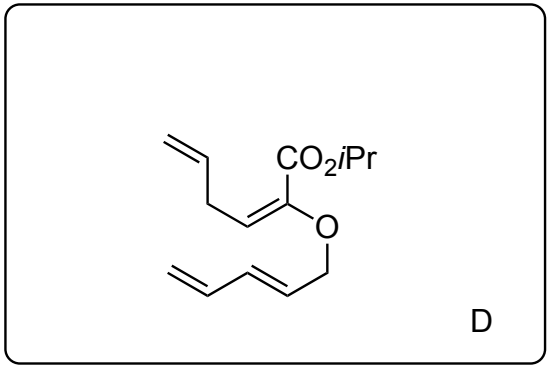


I

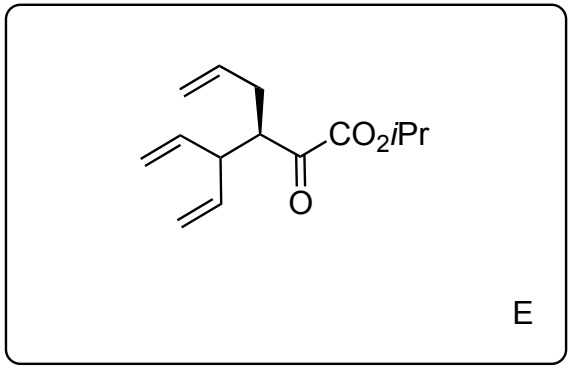


C-I was used in the next step

6

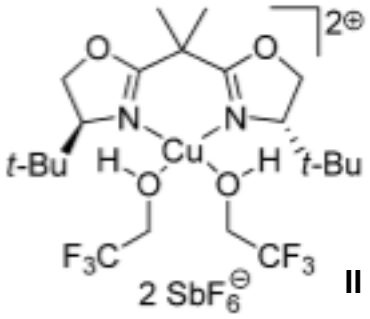


7

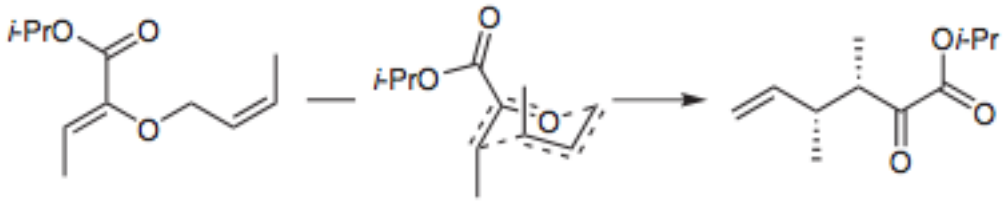


6) H_2O_2, $NaHCO_3$, THF, rt

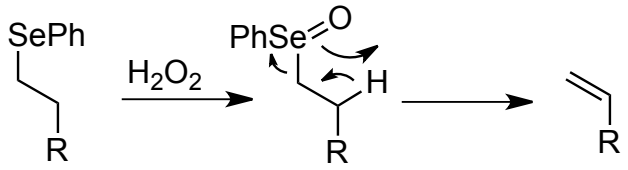
7) II (0.1 equiv.), rt



II



Please, provide mechanism for step 6)



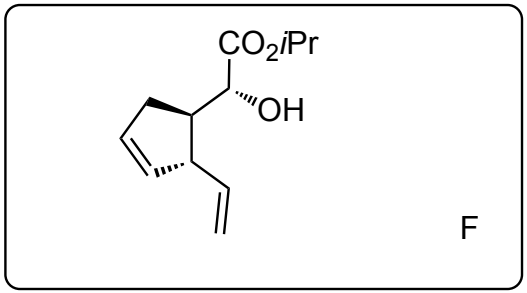
Grieco-Elimination

Please, provide mechanism for step 7)

Catalytic asymmetric Gosteli-Claisen-Rearrangement

8-9

8) K[(*s*Bu)$_3$BH], THF, –95ºC
9) Hoveyda-Grubbs

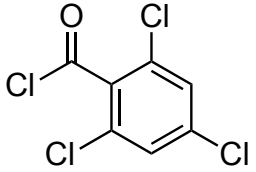


10-12

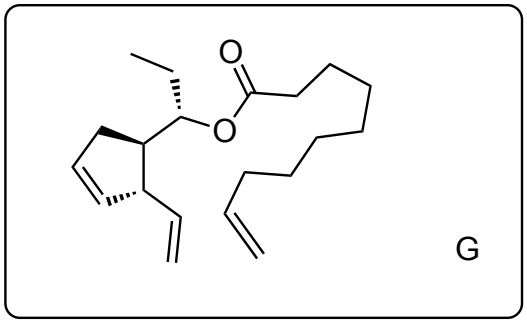
10) LAH, THF
11) NaH, THF, 0.5h; TsIm, rt 1h; CuI, MeMgBr, THF, –50ºC to 0ºC
12) H_2C=CH(CH_2)$_7$$CO_2$H, TCBC, Et_3N, DMAP

What is TCBC and what is the name of the reaction in Step 12?

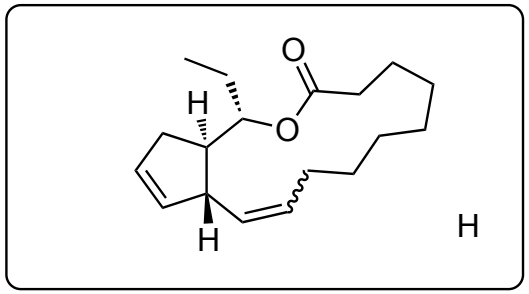
TCBC = 2,4,6-trichlorobenzoyl chloride



Yamaguchi-Esterfication

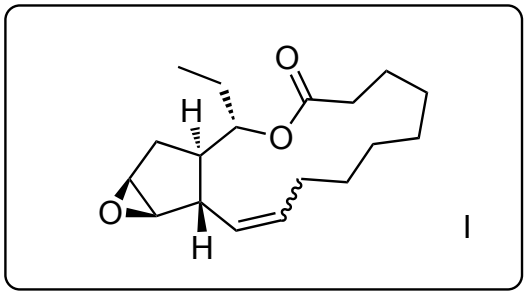


13



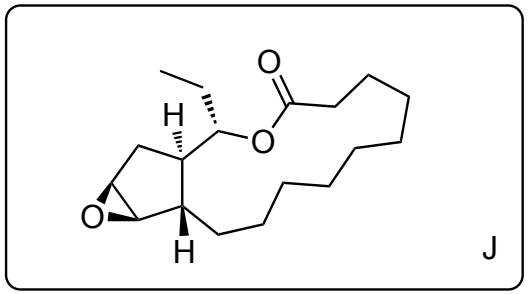
H

14-15



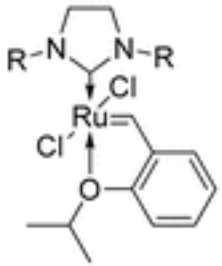
I

16



J

13) Steward-Grubbs

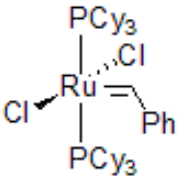


R = mesityl: Hoveydo-Grubbs
R = *o*-tolyl: Stewart-Grubbs

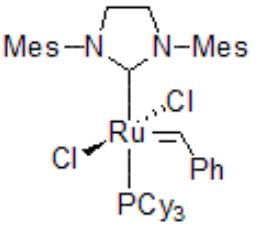
14) NBS, H_2O, acetone
15) Ag_2O, toluene

16) PtO_2, H_2, EtOAc

What is the difference between Steward and Hoveyda Grubbs (and Grubbs I and II)?

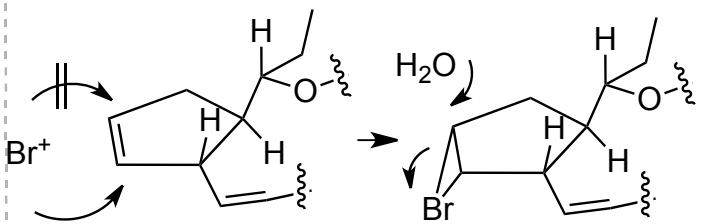


Grubbs I



Grubbs II

Please, rationalize the stereochemical outcome in step 14-15).



more accessible