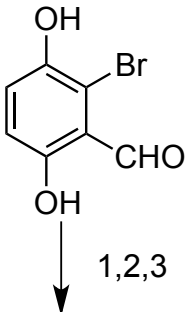
Synthesis Challenge #4 AG Wegner

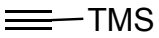
Total Synthesis of (+)-Clavilactone A and (–)-Clavilactone B by Ring-Opening/Ring-Closing Metathesis, K. Takao, R. Nanamiya , Y. Fukushima , A. Namba , K. Yoshida, K. Tadano, *Org. Lett.*, **2013**, *15*, pp 5582–5585

31.10.2013



1,2,3

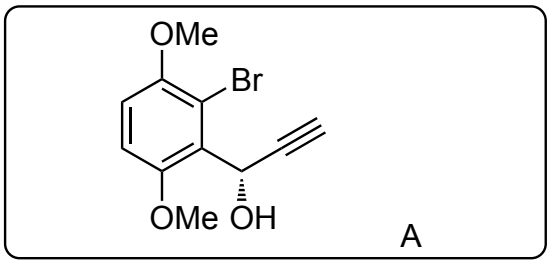
1) K_2CO_3, Me_2SO_4, DMF, rt
2) **I**, (*S*)-Binol, Et_2Zn, *N*-methylimidazole, $Ti(OiPr)_4$
3) K_2CO_3, MeOH, rt



I

please provide a detailed mechanism for step 2)

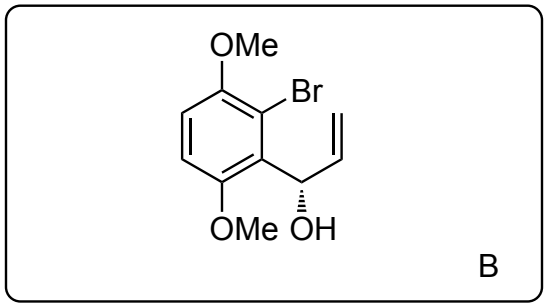
Enantiselective Addition with trimethylsilylacetylene under You's condition (*J. Org. Chem.* **2007**, *72*, 5457.)



A

4

4) H_2, Lindlar cat. Pyridine, EtOAc, rt

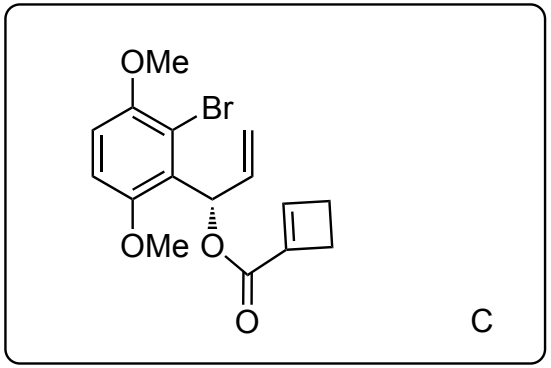


B

How can you determine the absolut configuration of B?

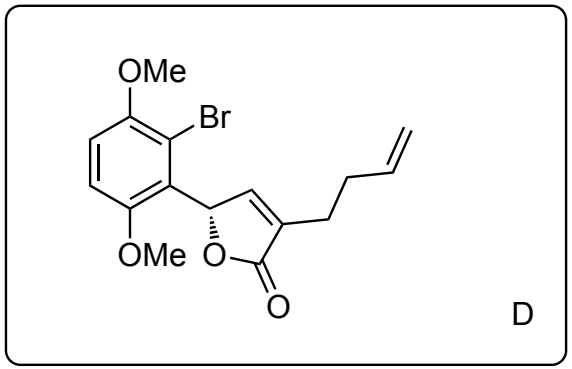
The absolute configuration was determined from the $\Delta\delta$ values of the α-methoxy-α-(trifluoromethyl)phenylacetic acid (MTPA) ester derived from B in their 1H NMR spectra.

5



C

6

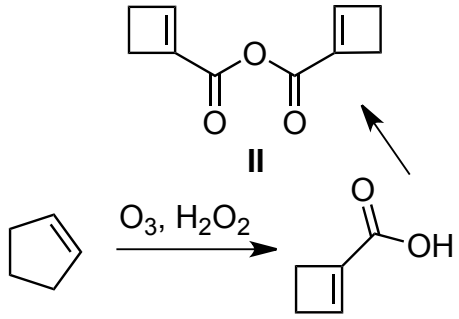


D

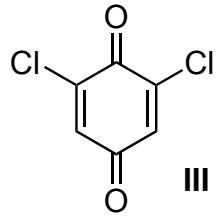
5) LDA, **II**, THF, –78ºC to 0ºC

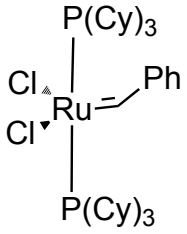
6) 1st Grubbs cat (10 mol%), **III** (50 mol%), toluene, then Ethylene (1 atm), 2nd Grubbs cat (5 mol%), 80ºC

Please sugest a synthesis for **II**.

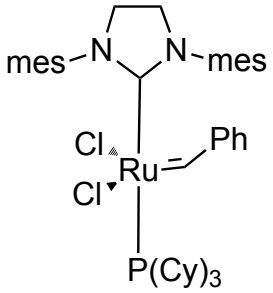


What is the difference beween 1st Grubbs and 2nd Grubbs?
Please, give a detailed mechanism of step 6).





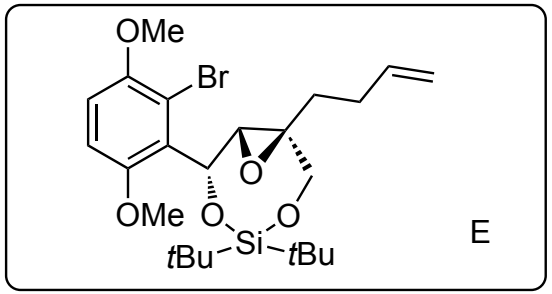
Grubbs I



Grubbs II

7-9

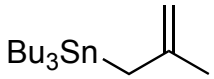
7) DIBALH, THF, –78ºC
8) tBu$_2$Si(OTf)$_2$, Pyridine, CH_2Cl_2, –78ºC to rt
9) *m*-CPBA, CH_2Cl_2



E

10

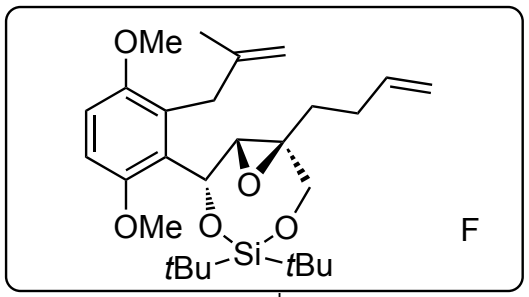
10) **IV**, Pd(PPH$_3$)$_4$, CuCl, 1,4-dioxane, 100ºC



IV

What is the name of the reaction in step 10)?

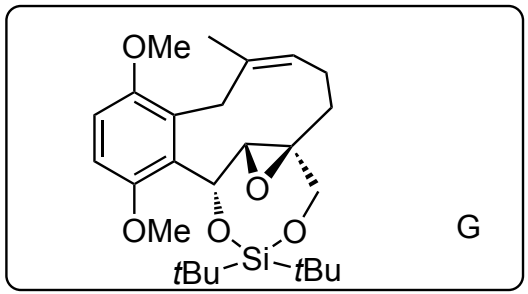
Stille reaction



F

11

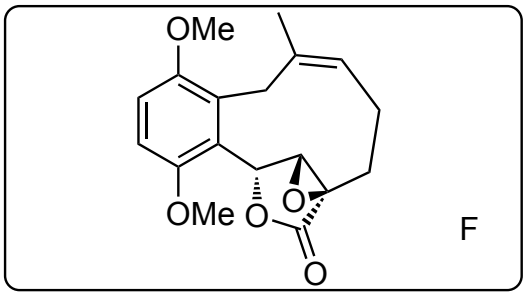
11) 2nd Grubbs, **III**, toluene



G

12-13

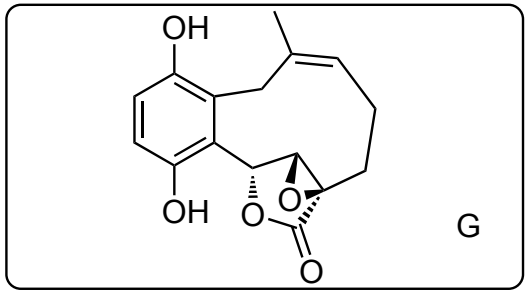
12) TBAF, THF, rt
13) TPAP, NMO, MS 4Å, MeCN



F

14-15

14) CAN, MeCN-H_2O, rt
15) NBH_4, MeOH-H_2O, rt



G