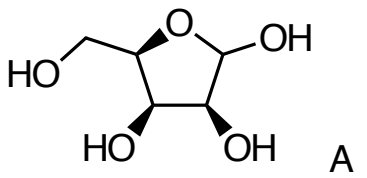
Synthesis Challenge # 35

"*A Carbohydrate Approach for the First Total Synthesis of Cochliomycin C: Stereoselective Total Synthesis of Paecilomycin E, Paecilomycin F and 6'-epi- Cochliomycin C*"

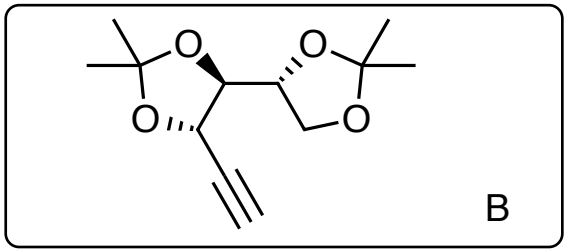
B. Mahankali, P. Srihari, *Eur. J. Org. Chem.* **2015**, *ASAP*, DOI: 10.1002/ejoc.201500395

28.05.2015



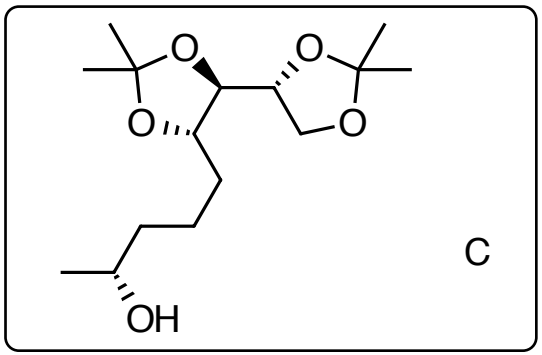
A

1-3



B

4-5



C

1) acetone H_2SO_4
2) Ohira-Bestmann reagent, K_2CO_3, MeOH
3) 2,2-DMP, PTSA, CH_2Cl_2

4) **I**, *n*BuLi, BF_3*OEt_2, THF –78°C
5) Raney-Ni, H_2, THF, rt

What is the name of compound A?
Is it D or L configured?

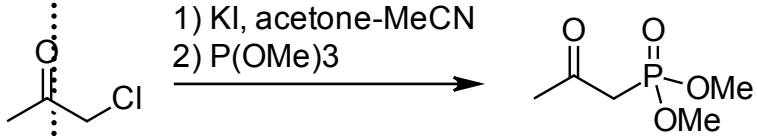
D-(–)-Lyxose

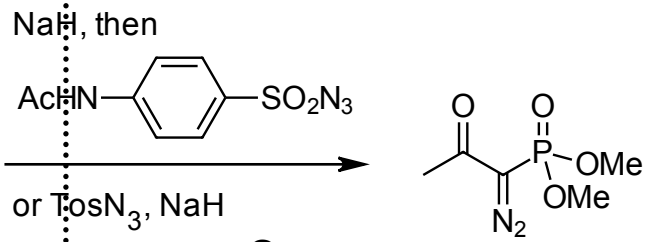
In step 1 only one regioisomer is formed. Why?

cis-diol prefered

Step 2 racemizes C2. The trans-isomer is taken further in the synthesis

How do you prepare the Ohira-Bestmann reagent?



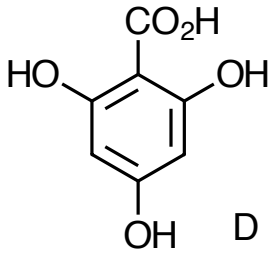


I

How do you prepare **I** enantioselective?

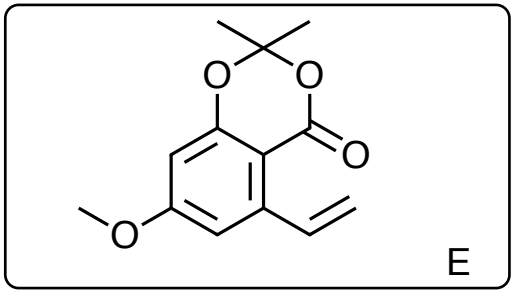
Here a "classic" chiral pool aproach from lactate:

Org. Synth. **1985**, *63*, 140
DOI: 10.15227/orgsyn.063.0140



D

12-16

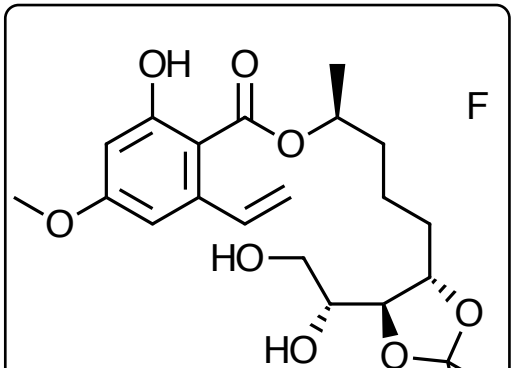


E

C + E

10-11

F



6) TFA, TFAA, acetone, rt
7) PPh_3, DIAD, MeOH, THF
8) Tf_2O, py, 0°C
9) **II**, $Pd(PPh_3)_4$, LiCl, PPh_3, DMF, rt

10) NaH, THF, 0°C to rt
11) dil. H_2SO_4, MeOH, 10°C

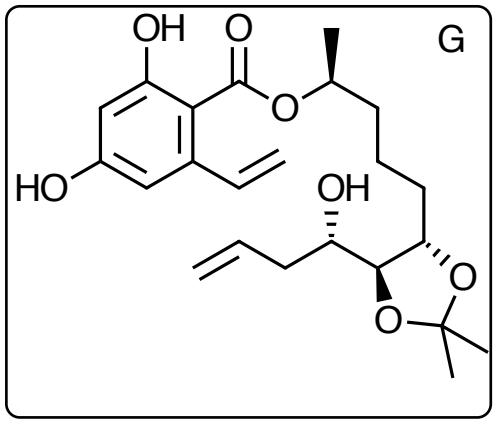
What is the name of the reaction in step 7)?
Mitsunobu-reaction
What is the role of LiCl in Step 9?

II

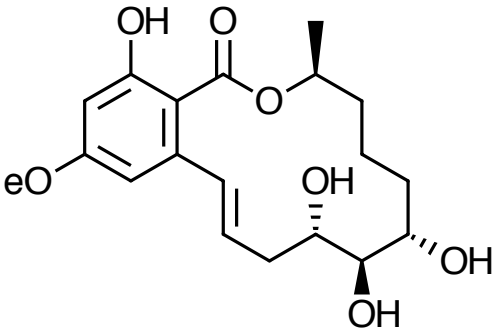
- Cl displaces OTf on Pd facilitating transmetallation
- accelerate oxidative addition by coordination to Pd
- enhances polarity of the solvent

Hint: In step 11) only one acetonide is cleaved selectively. Possible explanations?
Sterically less hindered

12-13



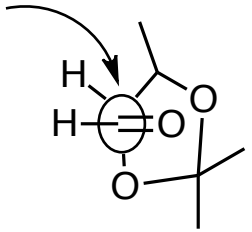
14-15



Paecilomycin F

12) $NaIO_4$, THF/water (3:1)
13) Zn, allyl bromide, THF/NH_4Cl

Please, explain the selectivety in step 13).
Felkin-Anh



14) Hoveyda-Grubbs II, toluene, 70ºC
15) MeOH*HCl, 0ºC to rt

What is the structure of Hoveyda-Grubbs II?