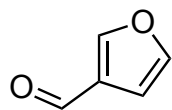
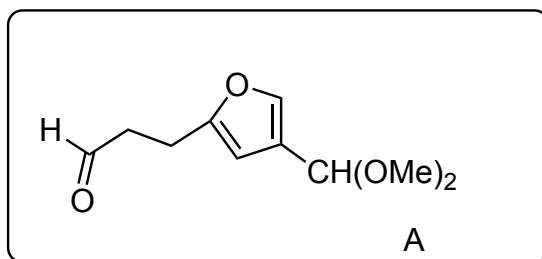


## Synthesis Challenge #5 AG Wegner

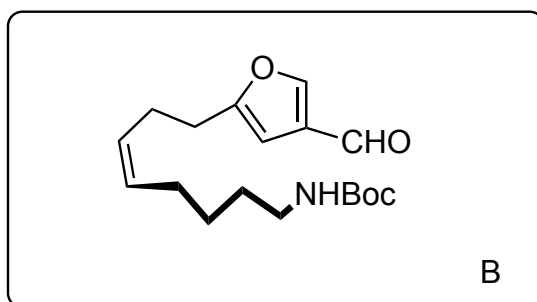
**Total Synthesis of (–)-Nakadomarin A**, S. Bonazzi, B. Cheng, J. S. Wzorek, D. A. Evans,  
*J. Am. Chem. Soc.*, **2013**, *135*, 9338–9341  
 7.11.2013



1,2,3



4



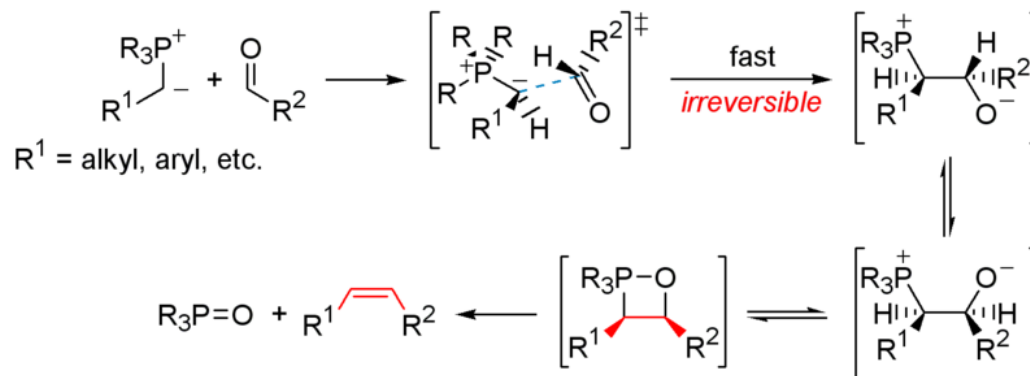
1) *n*-BuLi, morpholine, THF,  $-78\text{ }^{\circ}\text{C}$ ,  
 then *s*-BuLi, then  $\text{I}_2$   
 2)  $\text{CH}(\text{OMe})_3$ ,  $\text{TsOH}\cdot\text{H}_2\text{O}$ , 3 Å  
 molecular sieves (MS)  
 3)  $\text{Pd}(\text{OAc})_2$ , allyl alcohol,  $\text{NaHCO}_3$ ,  
 DMF,  $50\text{ }^{\circ}\text{C}$

4) KHMDS,  $\text{BocNH}(\text{CH}_2)_5\text{PPh}_3\text{I}$ ,  $-78$  to  $0\text{ }^{\circ}\text{C}$ , then HCl

What is the name of the reaction in step 3)?

Heck reaction

Please give a detailed mechanism of step 4)?

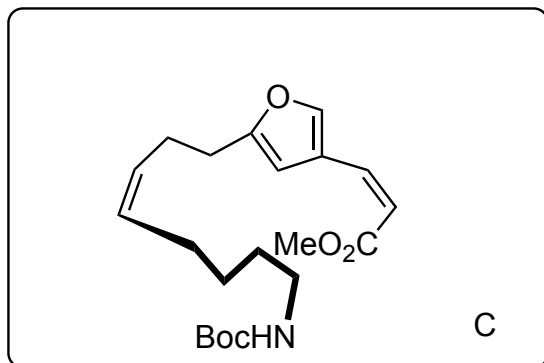


5

5)  $\text{CH}_3\text{O}_2\text{CCH}_2\text{P}(\text{O})(\text{OCH}_2\text{CF}_3)_2$ ,  
18-crown-6, KHMDS, THF,  $-78^\circ\text{C}$

What is name of the reaction in step 5)

Still-Gennari variation of the Horner  
Wadsworth-Emmons reaction

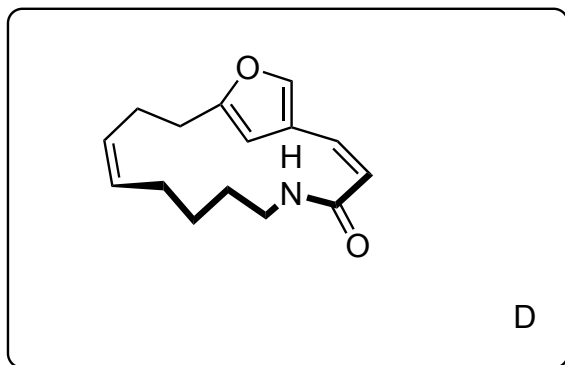


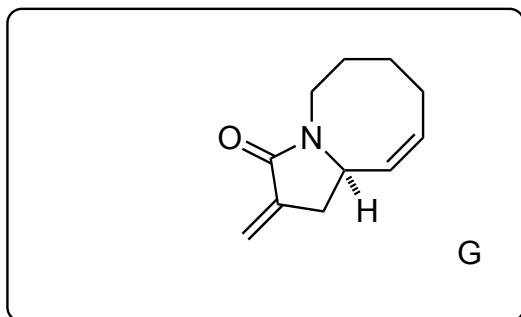
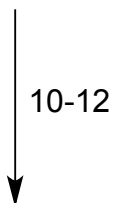
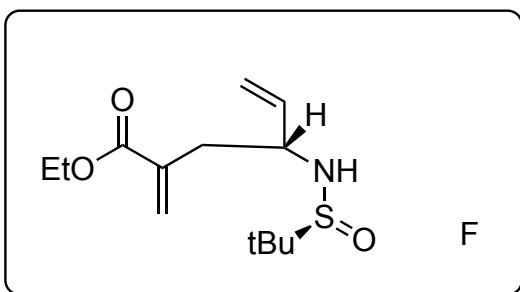
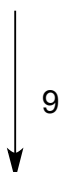
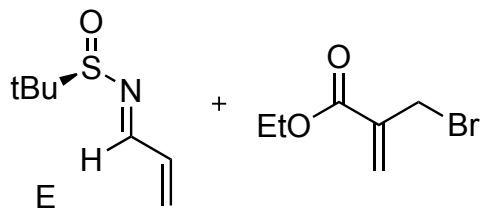
6-8

6) NaOH, MeOH, H<sub>2</sub>O, rt  
7) TFA, DCM, 0 °C to rt  
8) HBTU, NEt<sub>3</sub>, CH<sub>3</sub>CN, 50 °C

What is HBTU?

*N,N,N',N'*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate



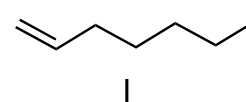


9) Zn, LiCl, DMF, H<sub>2</sub>O (1 equiv)

10) HCl, MeOH, then NaOH  
 11) NaH, I, DMF  
 12) 1st Grubbs

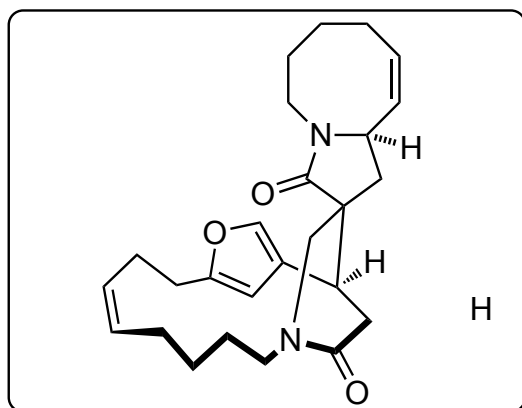
Please, determine the absolute configuration of E.

(R)

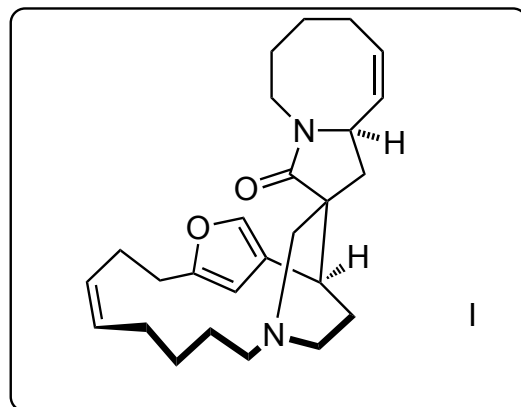


D + G

13

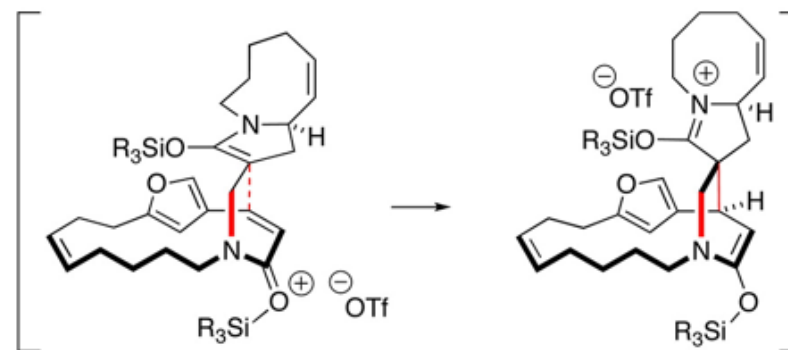


14



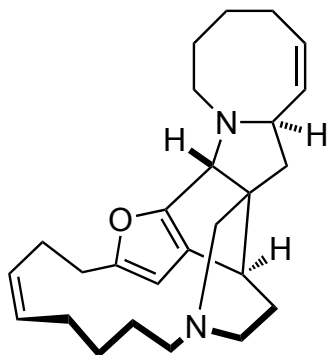
13) **D**, TBSOTf, *i*Pr<sub>2</sub>NEt, DCE, rt, then **G**, DCE, 14 h;

Please give a detailed mechanism of step 13)?



14) Me<sub>3</sub>OBF<sub>4</sub>, 4 Å MS, DCM, rt, 2 h, then NaBH<sub>4</sub>, MeOH, 0 °C to r

15



(-)-Nakadomarin A

15)  $\text{Tf}_2\text{O}$ , 2,6-di-*tert*-butyl-4-methylpyridine, DCM, rt, 30 min, then  $\text{NaBH}_3\text{CN}$ , MeOH, rt;