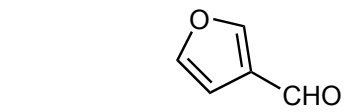
Total Synthesis of (−)-Nakadomarin A

Simone Bonazzi, Bichu Cheng, Joseph S. Wzorek, David A. Evans, *J. Am. Chem. Soc.,* **2013**, *135* (25), 9338–9341.



1-3

1) *n*-BuLi, morpholine *then s*-BuLi, I_2
2) $CH(OCH_3)_3$, TsOH
3) $Pd(OAc)_2$, 2-propenol, $NaHCO_3$, NH_4Cl

Please provide a mechanism for step1 and 3.

A

4, 5

4) KHMDS, $BocNH(CH_2)_5PPh_3I$, - 78°C to 0 °C *then* 1M HCl
5) $CH_3O_2CCH_2P(O)(OCH_2CF_3)_2$, 18-crown-6, KHMDS, - 78°C

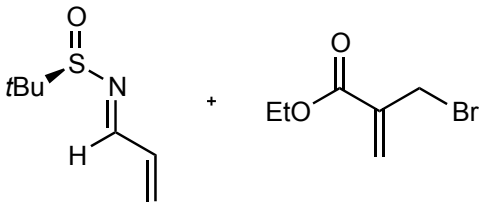
Name of reaction in step 4 and 5.

B

6-8

6) NaOH, MeOH/H_2O
7) TFA
8) HBTU, NEt_3

C



+

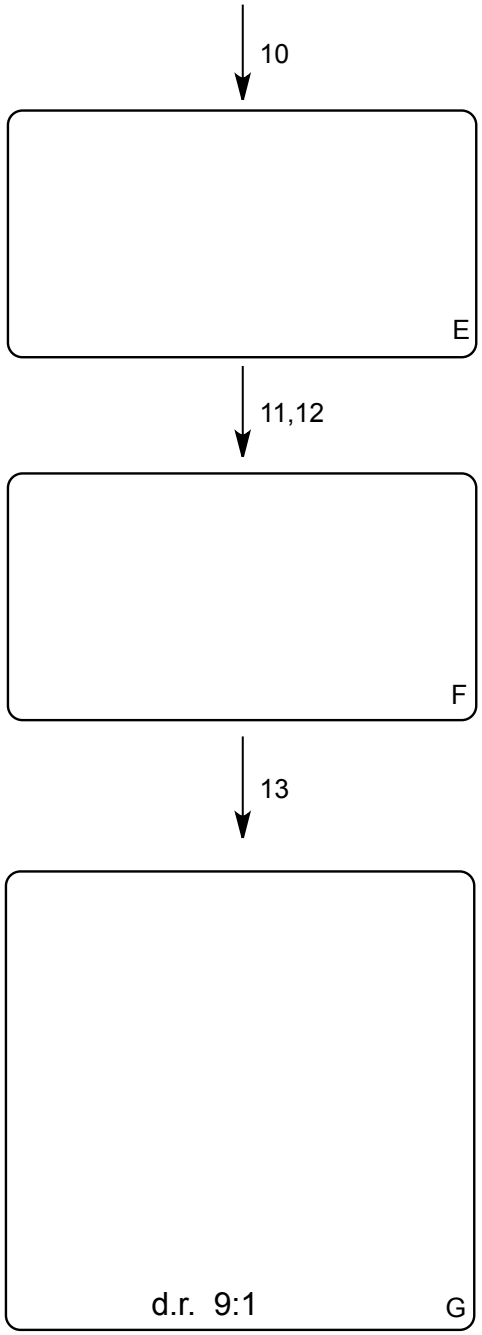
9

9) Zn, LiCl, H_2O (1 equiv.)

d.r. 95 : 5

D

Please determine the absolute configuration of the starting material according to CIP nomenclature.
How would you synthesise the allylic bromide?



10) HCl, MeOH *then* NaOH

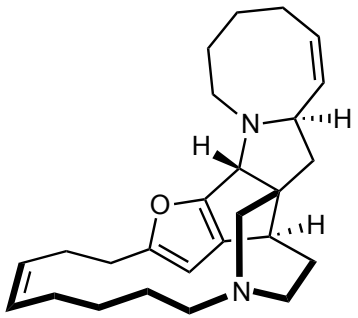
11) NaH, $I(CH_2)_4CH=CH_2$, DMF
12) Grubbs I, CH_2Cl_2

Please provide a structure of Grubbs I.

13) **C**, TBSOTf (2 equiv.),
iPr_2NEt, r.t.

Please provide a mechanism for step 13.

14



(–)-Nakadomarin A

14) Tf_2O (3 equiv.),
2,6-di-*tert*-butyl-4-methylpyridine
then Red-Al (excess)

Please provide a mechanism for step 14.
Structure of Red-Al?