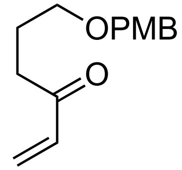
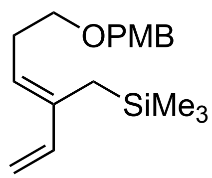
Synthesis Challenge AG Wegner

Total Synthesis of (+)-Asperolide C by Iridium-Catalyzed Enantioselective Polyene Cyclization

Oliver F. Jeker, Alberto G. Kravina, and Erick M. Carreira, *Angew. Chem. Int. Ed.* **2013**, *52, ASAP,* DOI: 10.1002/anie.201307187
24.10.2013

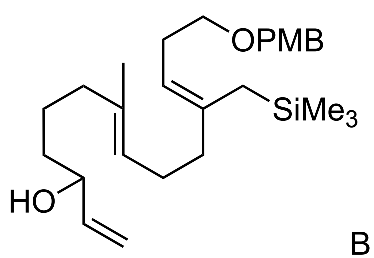


1,2,3



A

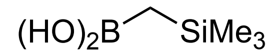
4,5



B

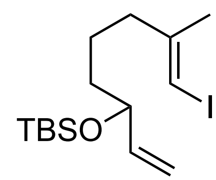
1) LiHMDS (1.25 equiv), *t*Bu-Me_2SiCl (1.25 equiv), –78 ºC
2) $PhNTf_2$ (1.5 equiv), CsF (2.5 equiv), $(MeOCH_2)_2$,
3) **I** (1.5 equiv), [Pd(dppf)Cl_2]·CH_2Cl_2 (10 mol%), Ph_3As (10 mol%), Cs_2CO_3

4) 9-BBN (1.1 equiv), THF, 0 8C to RT; then **II** (1.0 equiv), [Pd-(dppf)Cl_2]·CH_2Cl_2 (2.7 mol %), NaOH
5) PPTS (10 mol %), MeOH



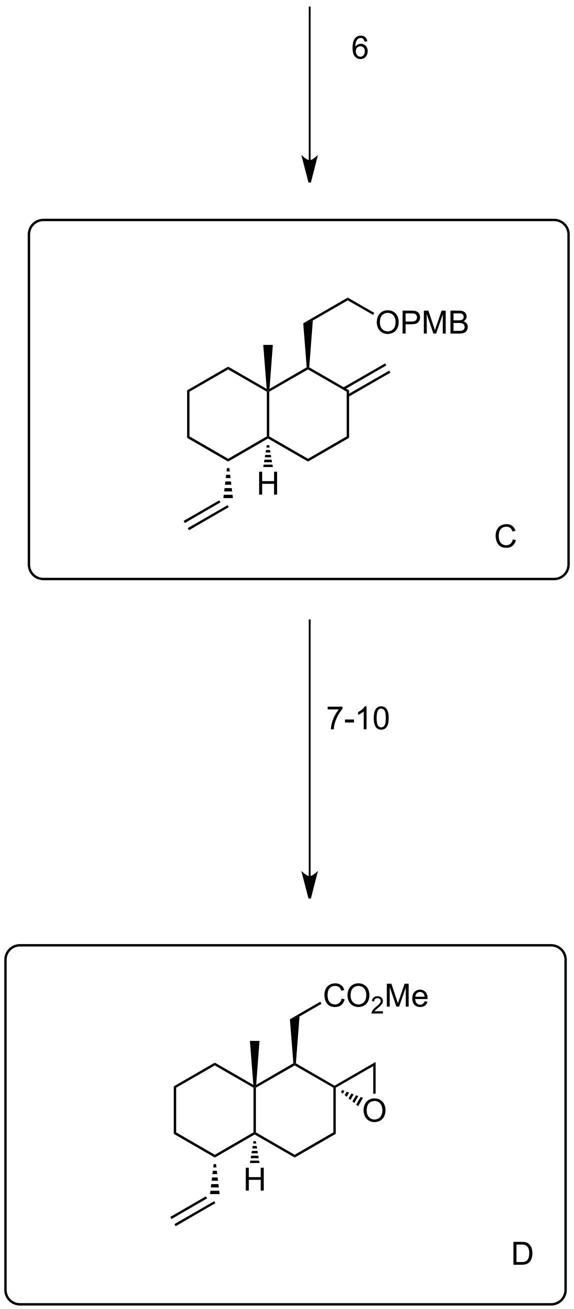
I

please provide a detailed mechanism for step 4)



II

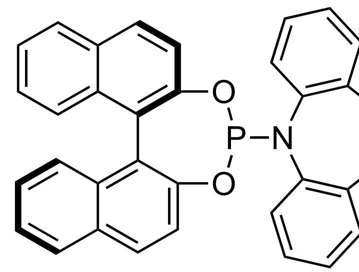
1. Step: Hydroboration
2. Suzuki-cross-coupling



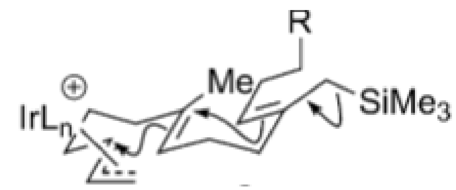
6) [{Ir(cod)Cl}$_2$] (3.2 mol%)
Zn(OTf)$_2$ (16 mol%), (*R*)-**III**
(12.8 mol%)

7) DDQ (1.1 equiv), pH 7 buffer,
8) DMP (1.5 equiv),
9) $NaClO_2$ (4.0 equiv), NaH_2PO_4 (6.0 equiv), 2-methyl-2-butene (70 equiv), tBuOH/H_2O,RT; thenMe$_3$SiCHN$_2$
10) DMDO (1.1 equiv), acetone,

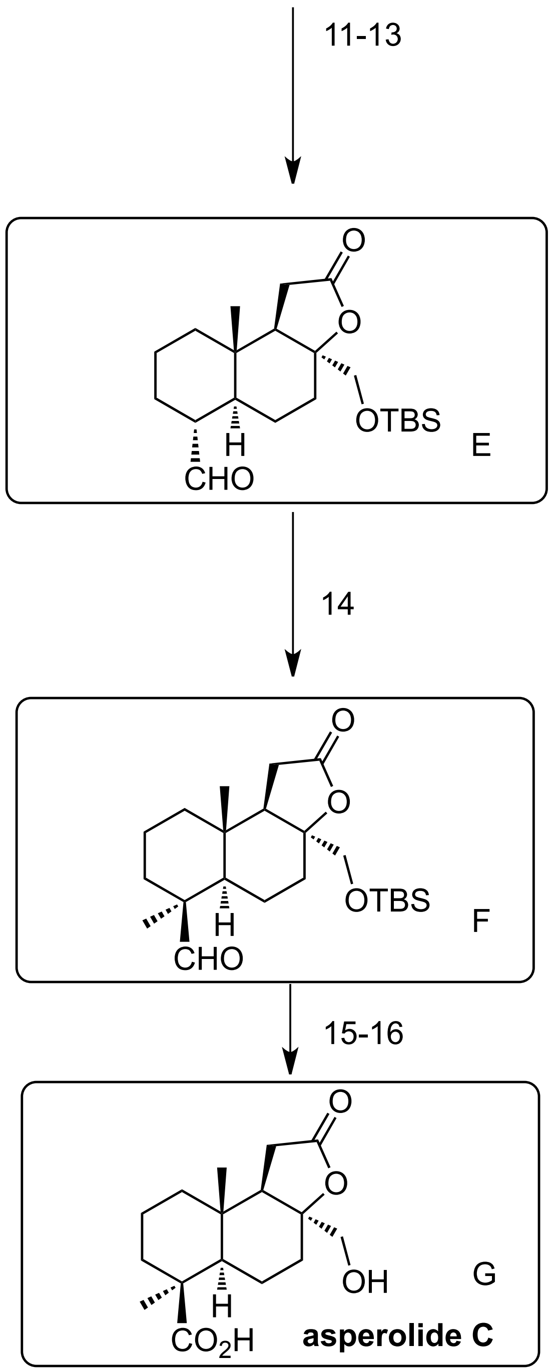
Please give a detailed mechanism of step 6. Illustrate the stereochemical outcome by a 3D drawing of the transitionstate.



(*R*)-**III**



DMDO = dimethyldioxirane

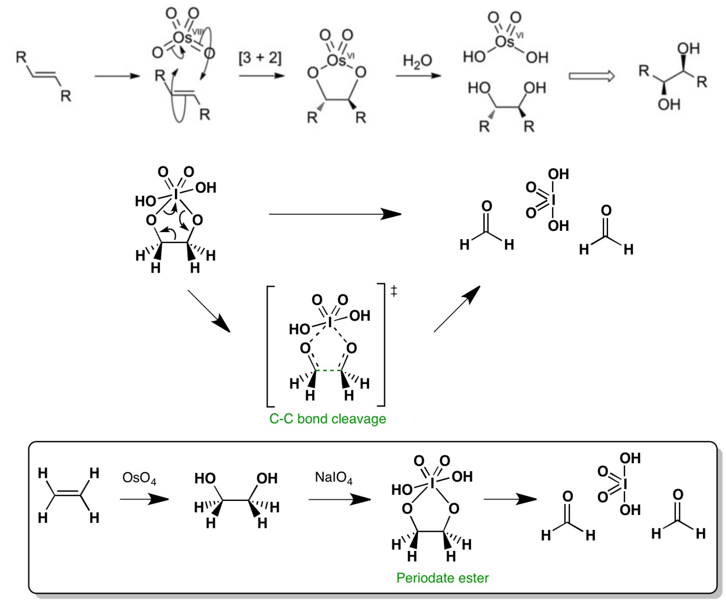


11) CF_3CO_2H (1.2 equiv), CH_2Cl_2,
12) tBu-Me_2SiCl (3.0 equiv), imidazole (6.0 equiv), DMAP (10 mol %)
13) OsO_4 (20 mol %), $NaIO_4$ (5.0 equiv), 2,6-lutidine

14) tBuOK, MeI (1.25 equiv), –20 ºC to 0 ºC

15) $NaClO_2$ (6.0 equiv), NaH_2PO_4 (6.0 equiv), 2-methyl-2-butene (30 equiv), tBuOH/H_2O
16) TBAF (1.5 equiv), THF, 0 ºC

please provide a detailed mechanism for step 13)



Please, rationalize the selectivity in step 14).