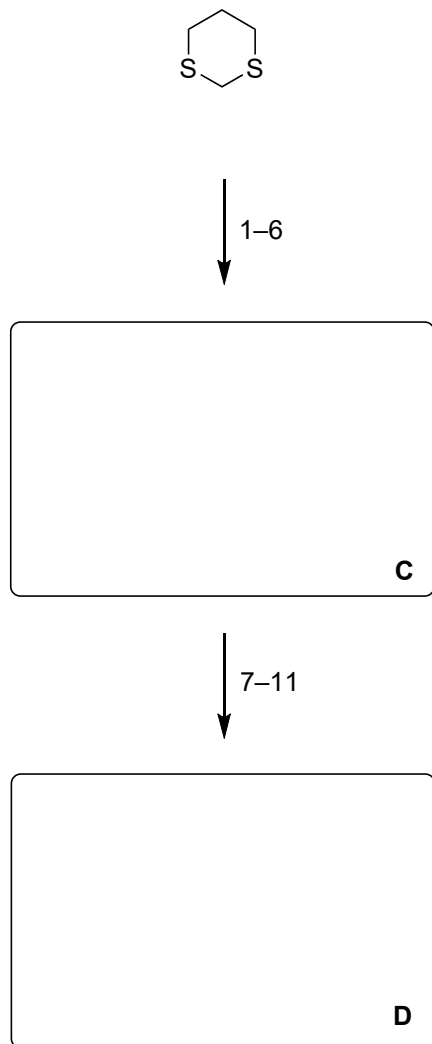


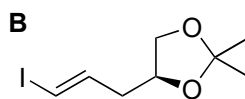
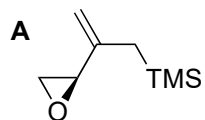
# Total Synthesis of (-)-Mandelalide A Exploiting Anion Relay Chemistry (ARC): Identification of a Type II ARC/CuCN Cross-Coupling Protocol

Minh H. Nguyen, Masashi Imanishi, Taichi Kurogi, and Amos B. Smith, III

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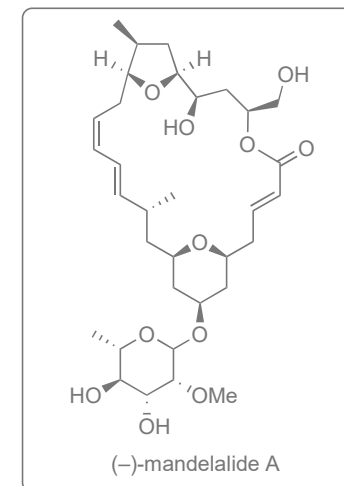
- 1) *n*BuLi,  
then **A**,  
then **B**, CuCN (0.75 eq.)  
then TBAF
- 2) MeI, CaCO<sub>3</sub>, 65 °C
- 3) NaBH<sub>4</sub>
- 4) K<sub>2</sub>OsO<sub>4</sub>•2H<sub>2</sub>O, pyridine-N-oxide  
Cu(OTf)<sub>2</sub>, citric acid  
pH = 6.5 phosphate buffer/MeCN
- 5) TBSOTf, 2,6-Lutidine
- 6) (PPh<sub>3</sub>)<sub>3</sub>RhCl, H<sub>2</sub>

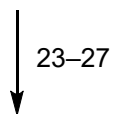
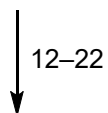
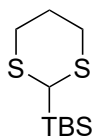


- 7) HF, pyridine
- 8) DMP
- 9) Ph<sub>3</sub>PCH<sub>2</sub>I<sub>2</sub>, NaHMDS
- 10) CeCl<sub>3</sub>•7H<sub>2</sub>O, (COOH)<sub>2</sub>
- 11) TBSCl, imidazole

Hint: Only one position  
reacts in step 7 and also  
in step 11.

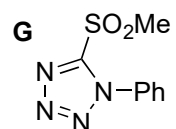
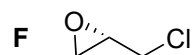
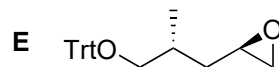
Mechanism of reaction 4?



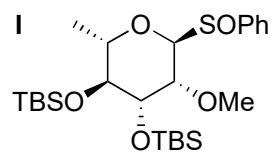


(-)-mandelalide A

- 12) *n*BuLi  
then **E**,  
then HMPA  
then **F**  
then CH<sub>2</sub>=CH-MgBr, CuI
- 13) MsCl, Et<sub>3</sub>N
- 14) TBAF, reflux
- 15) MeI, CaCO<sub>3</sub>
- 16) NaBH<sub>4</sub>
- 17) PMBBBr
- 18) PPTS
- 19) H<sub>2</sub>C=CH-COOMe, Grubbs I
- 20) DMP
- 21) **G**, NaHMDS
- 22) LiOH



- 23) 2,4,6-trichlorobenzoyl chloride  
DMAP, Et<sub>3</sub>N, **D**
- 24) DDQ
- 25) **I**, Tf<sub>2</sub>O, MS 4Å  
2,6-di-*t*Bu-4-Me-pyridine
- 26) Pd(OAc)<sub>2</sub>, Cs<sub>2</sub>CO<sub>3</sub>, Et<sub>3</sub>N, DMF
- 27) HF, pyridine



Compare and classify step 1 and step 12

Name of reaction 25?

