Total Synthesis of (\pm) -Hippolachnin A

Stefan A. Ruider, Tobais Sandmeier, and Erick M. Carreira

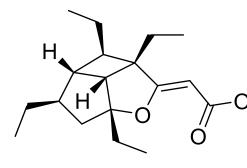
$$H$$
 O
 O
 O
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 O
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 O

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CEM 852 | Michigan State University | February 27 2018



Background

- Recently isolated marine polyketide
- Exhibits antifungal activity, and treatment for renal fibrosis, acute renal failure, and rhinitis
- Highly substituted cyclobutane ring and six stereocenters
- Its structure resembles other recently isolated polyketides



Retrosynthesis

- Unactivated cyclobutene is used for the generation of a quaternary stereocenter
- Entry into a scaffold that is common to multiple different marine natural products

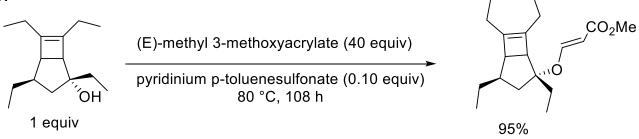
Step 2:

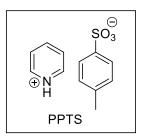
Step 3:

Angew. Chem. Int. Ed. 54. 2015, 54, 2378

Step 4:

Step 5:





Step 6:

$$\frac{\text{CO}_2\text{Me}}{\text{DCM, 0°C to RT, 20 h}}$$

Angew. Chem. Int. Ed. 2015, 54, 6037.

Step 7:

H CO₂Me
$$\frac{10\% \text{ Pd(OH)}_2/\text{C } (0.15 \text{ equiv})}{\text{H}_2 (10 \text{ bar}), \text{ MeOH, 20 h}}$$

1 equiv

exo product: 69% endo product: 13% overall: 90% (d.r. = 3:1)

Step 8:

Angew. Chem. Int. Ed. 2015, 54, 6037.