

Literature Report (4)

Total Synthesis of Marinomycin A Based on a Direct Dimerization Strategy

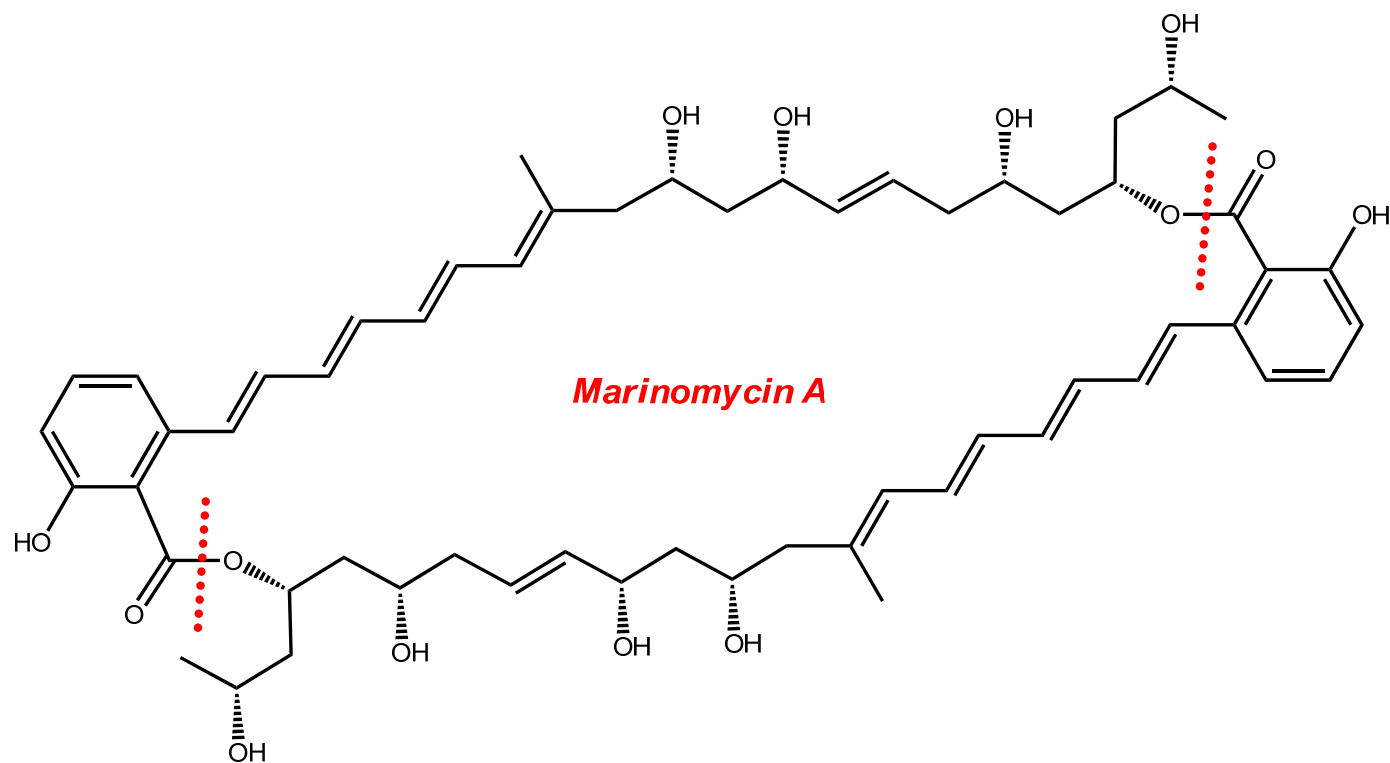
Reporter: Yue Ji
Checker: Zhang-Pei Chen
Date: 2014/09/09

Hatakeyama, S. *et al.*
Angew. Chem. Int. Ed. **2014**, 53, 8459.

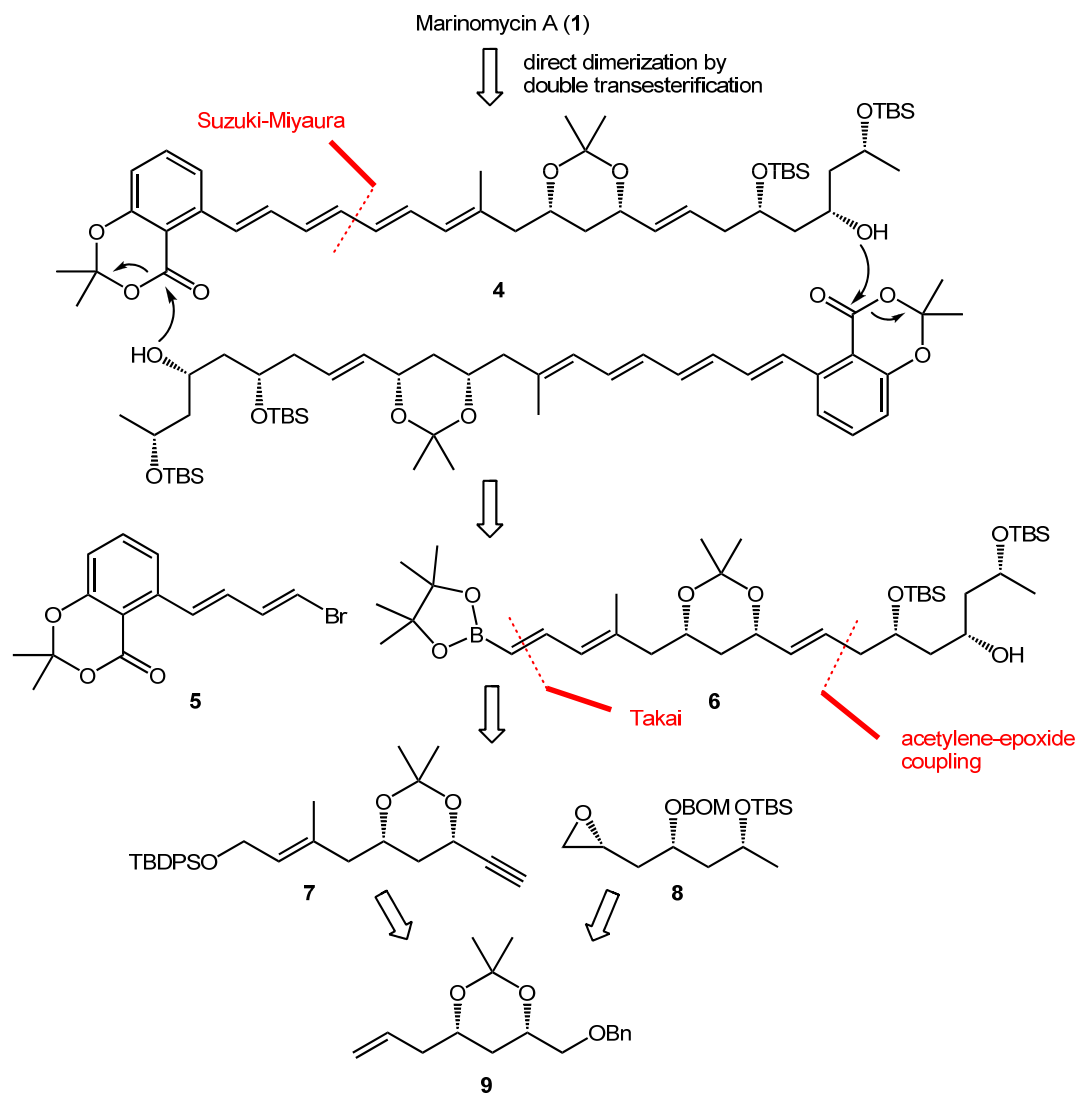
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Introduction

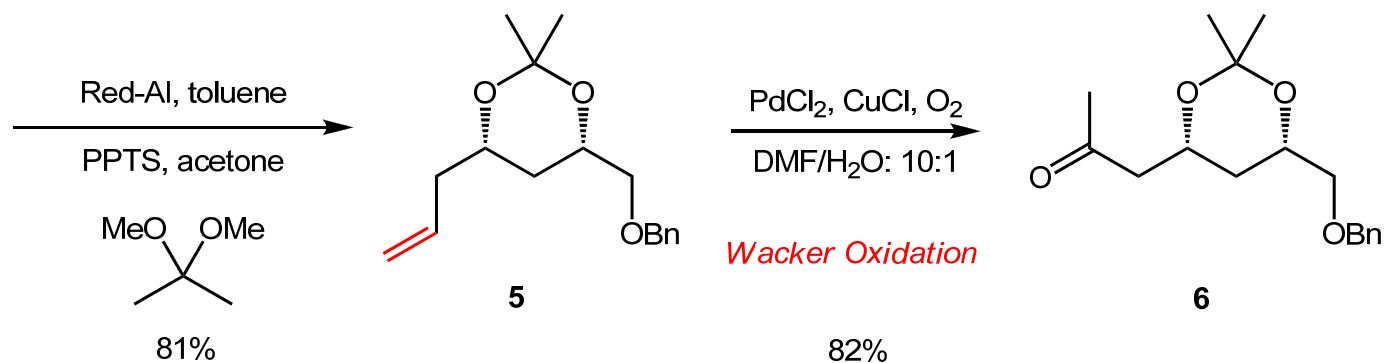
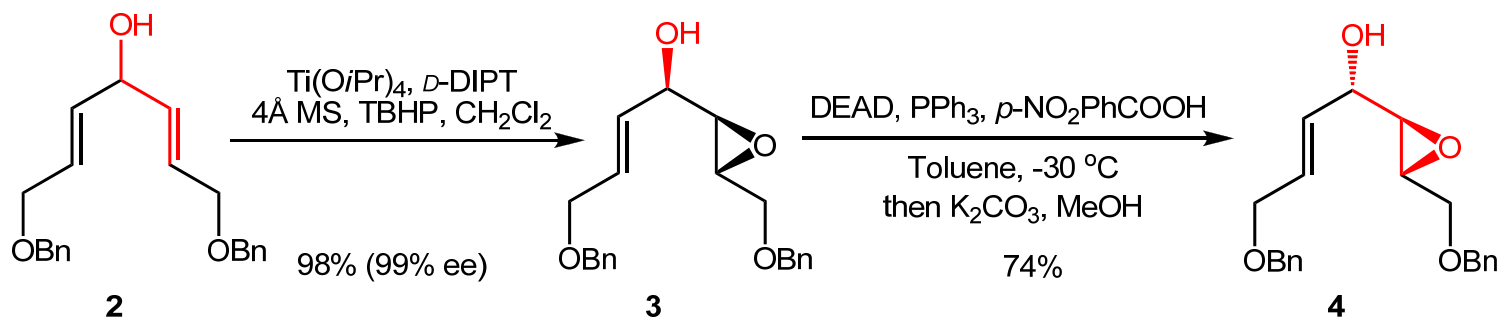


Retrosynthetic analysis of Marinomycin A

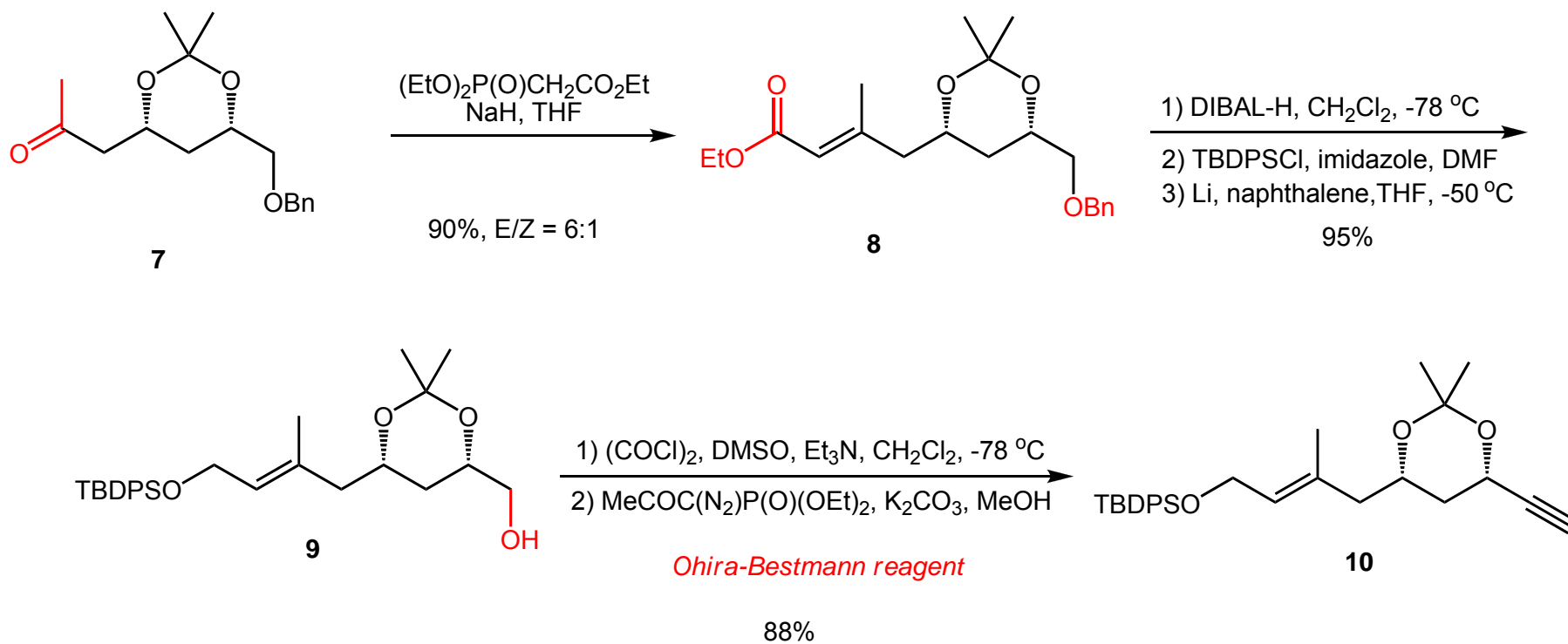


Hatakeyama, S. *et al.* *Angew. Chem. Int. Ed.* **2014**, *53*, 8459.

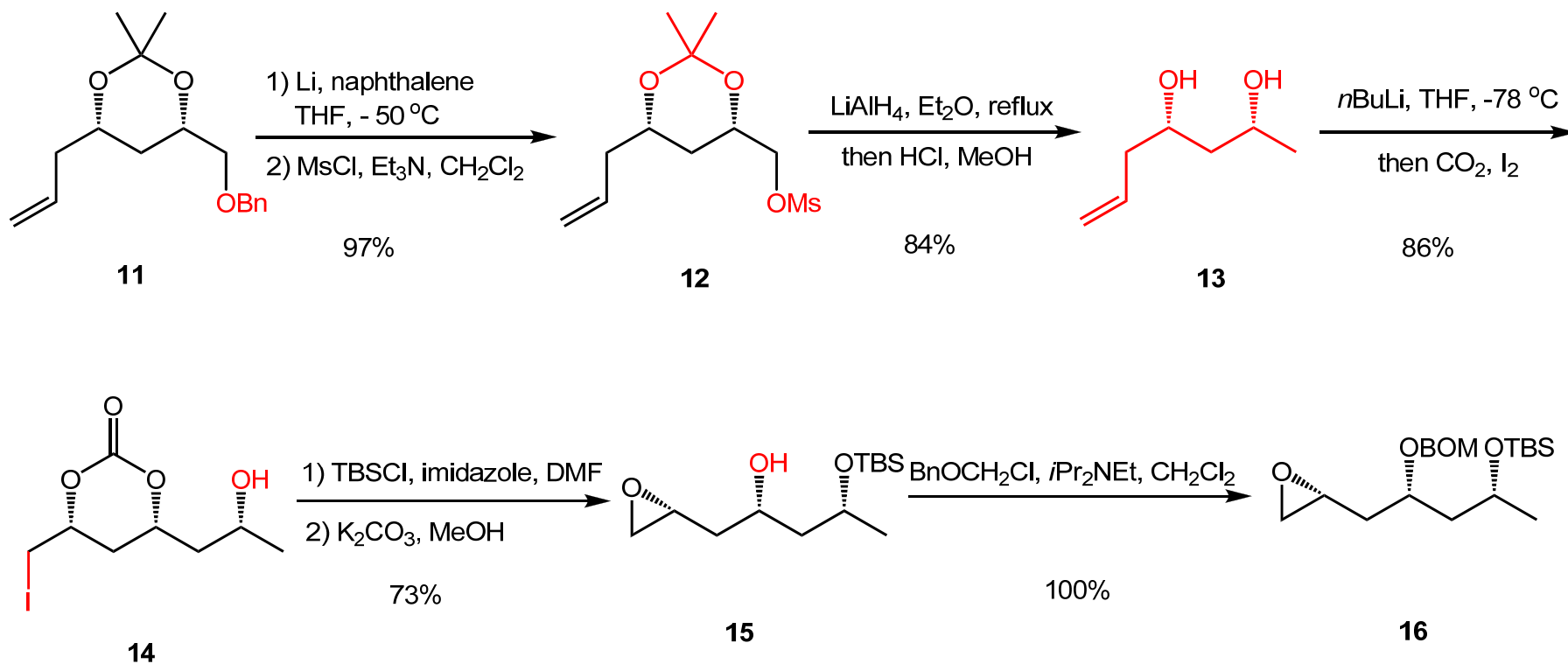
Total Synthesis by the Hatakeyama Group



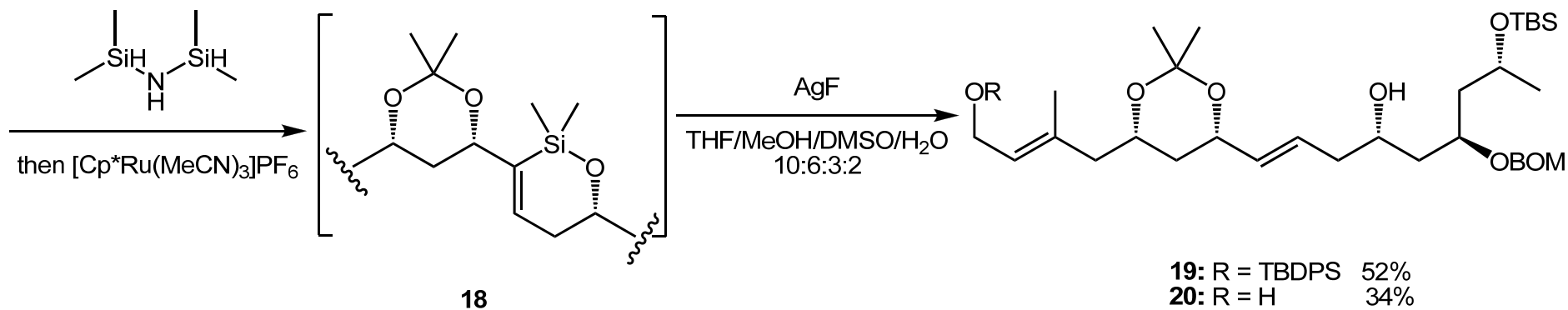
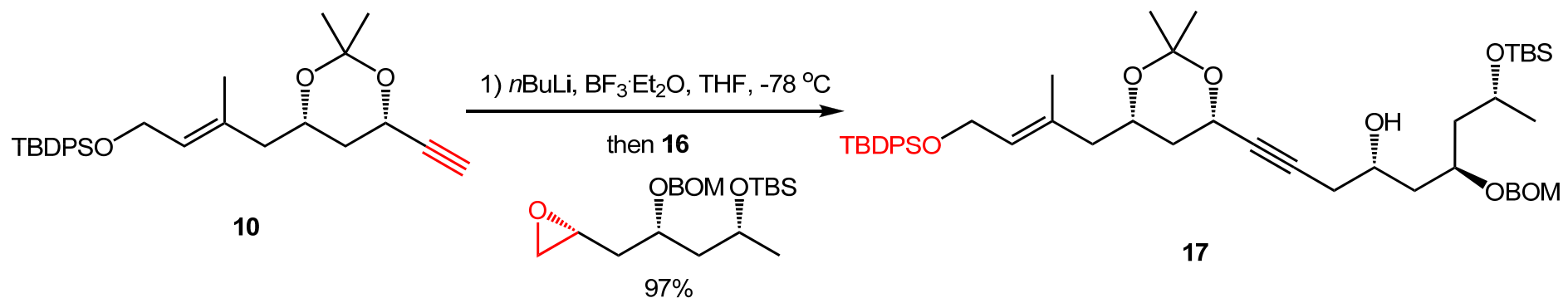
Total Synthesis by the Hatakeyama Group



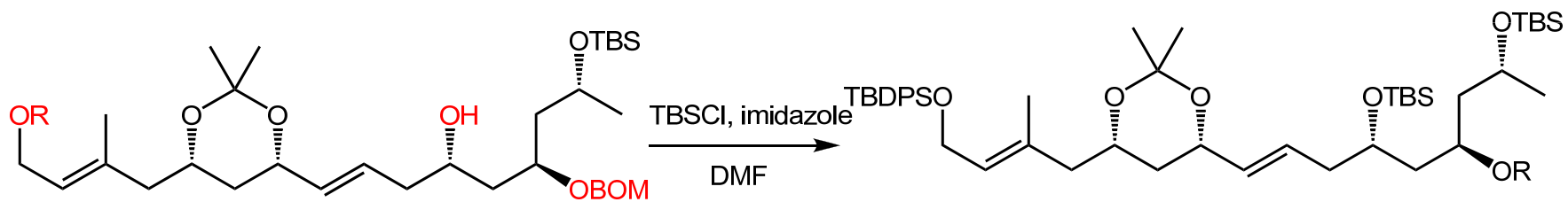
Total Synthesis by the Hatakeyama Group



Total Synthesis by the Hatakeyama Group



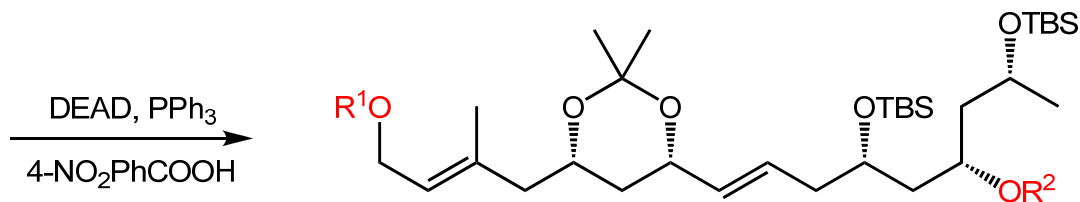
Total Synthesis by the Hatakeyama Group



19: R = TBDPS

97%

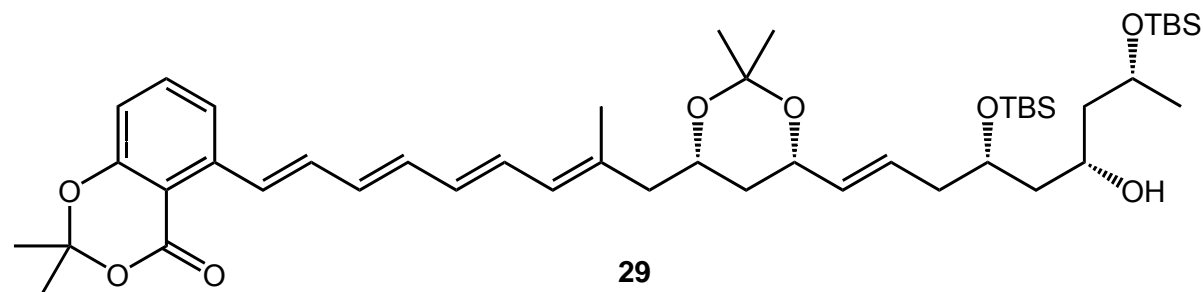
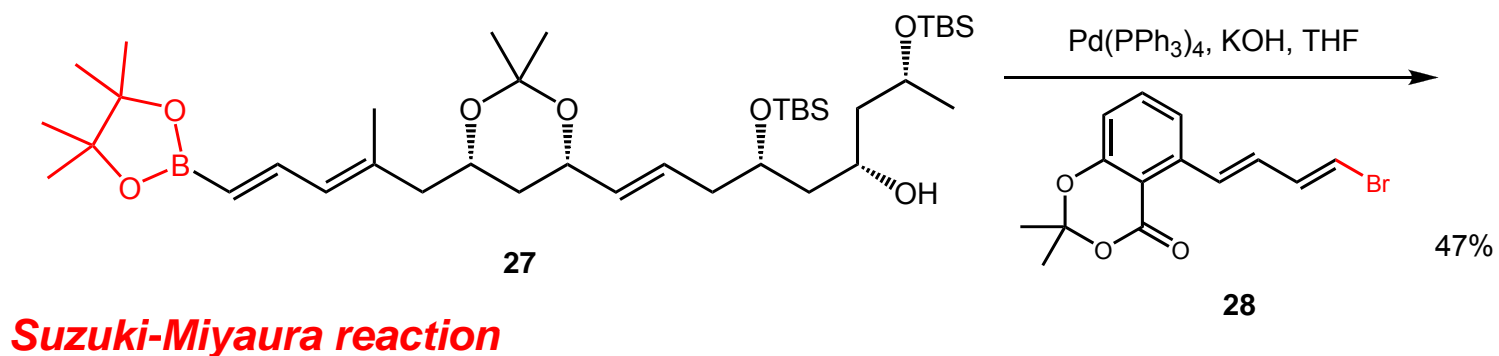
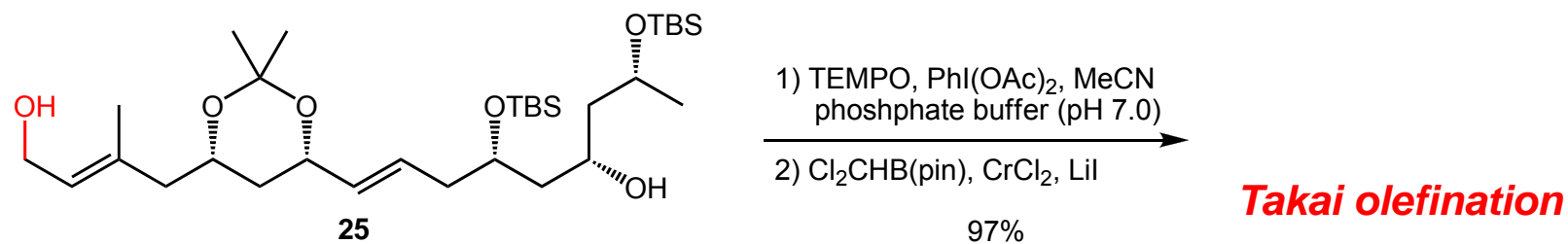
Li, naphthalene
THF, -60 °C $\left\{ \begin{array}{l} \text{21: R = BOM} \\ \text{22: R = H} \end{array} \right.$
100%



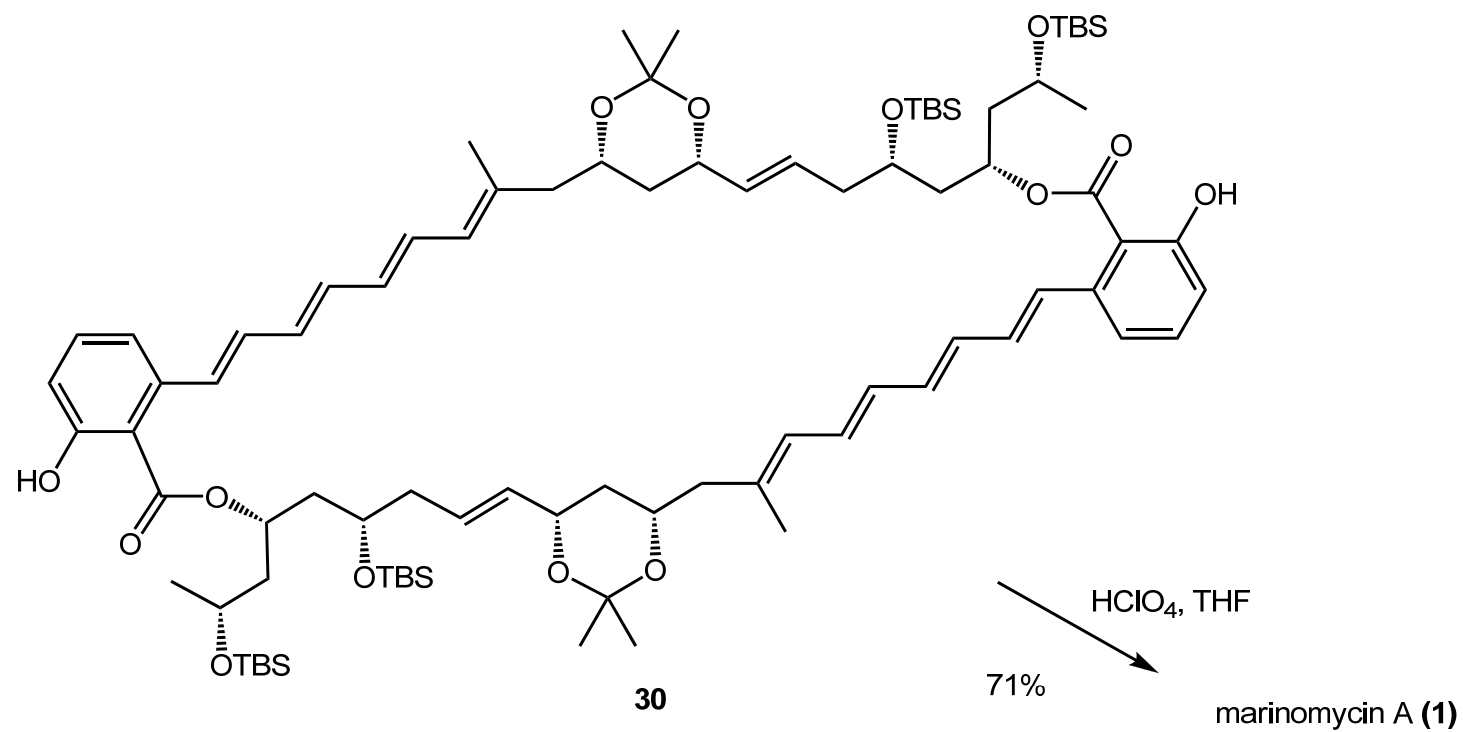
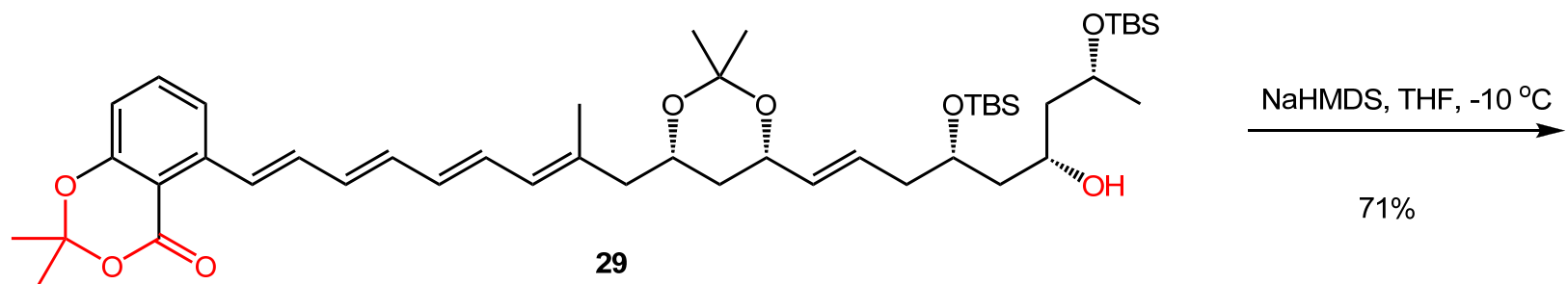
76%

89% TBAF, AcOH, DMF $\left\{ \begin{array}{l} \text{23: R}^1 = \text{TBDPS, R}^2 = \text{4-NO}_2\text{PhCO} \\ \text{24: R}^1 = \text{H, R}^2 = \text{4-NO}_2\text{PhCO} \\ \text{25: R}^1 = \text{R}^2 = \text{H} \end{array} \right.$
100% NaOMe

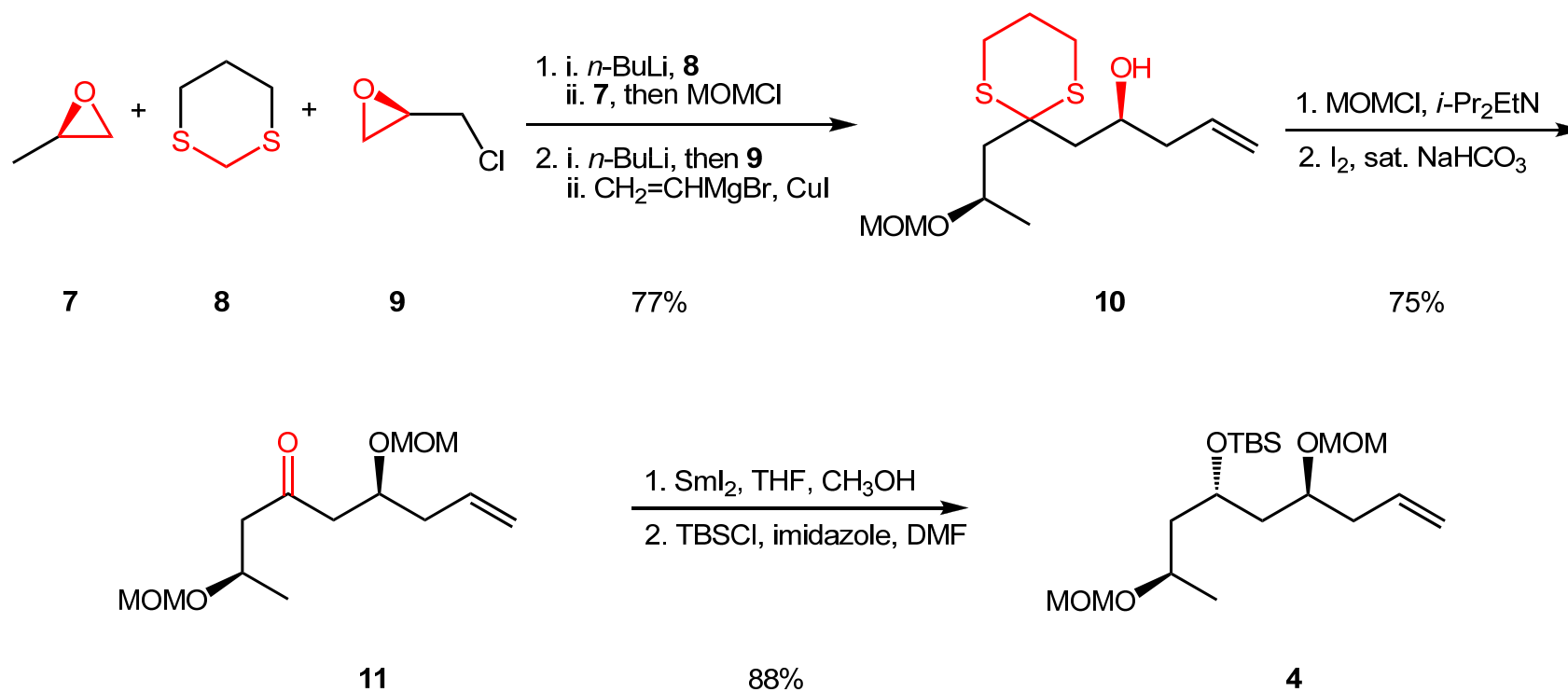
Total Synthesis by the Hatakeyama Group



Total Synthesis by the Hatakeyama Group

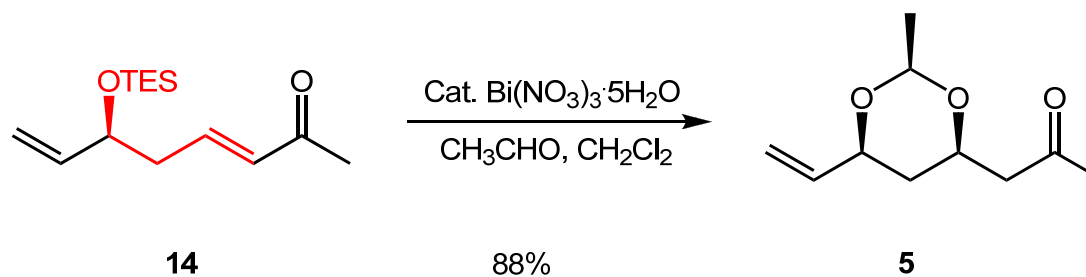
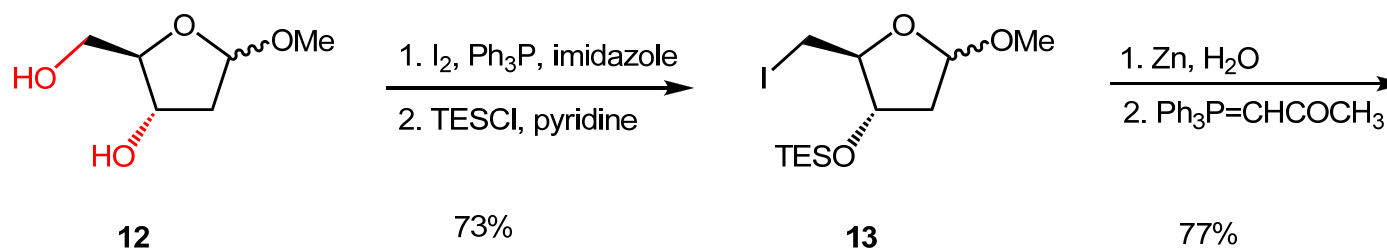


Total Synthesis by the Evans Group

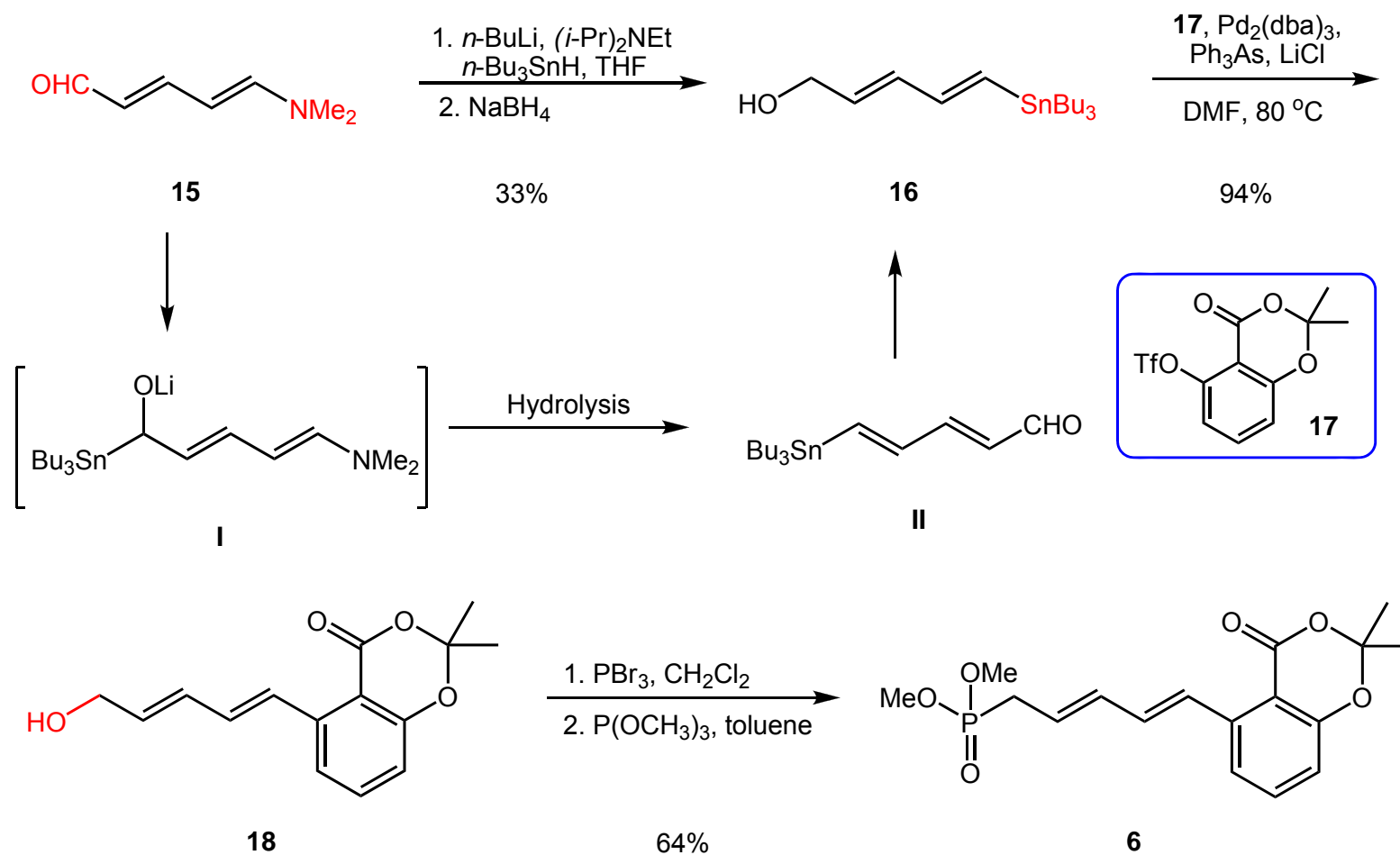


Evans, P. A. *et al.* *Nat. Chem.* **2012**, *4*, 680.

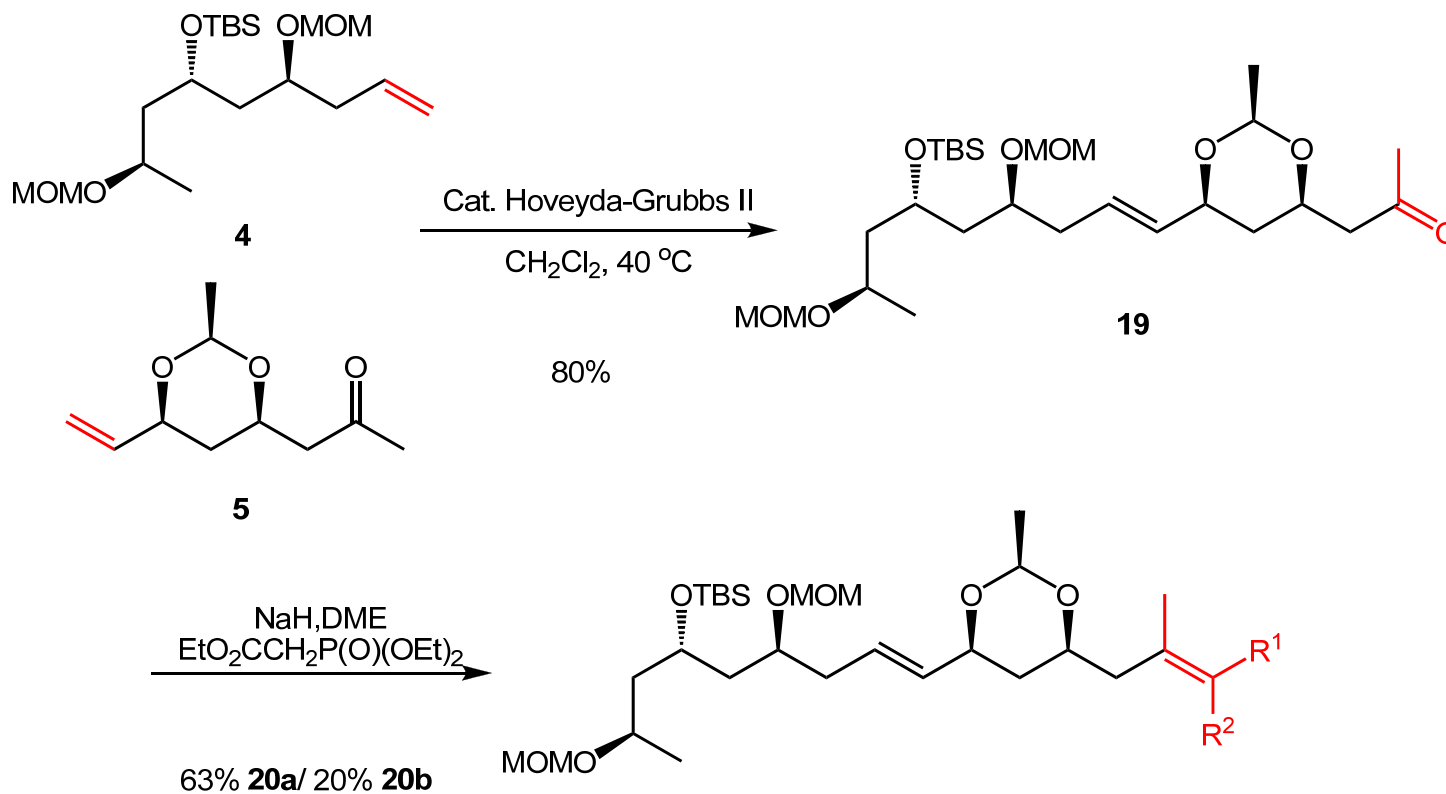
Total Synthesis by the Evans Group



Total Synthesis by the Evans Group



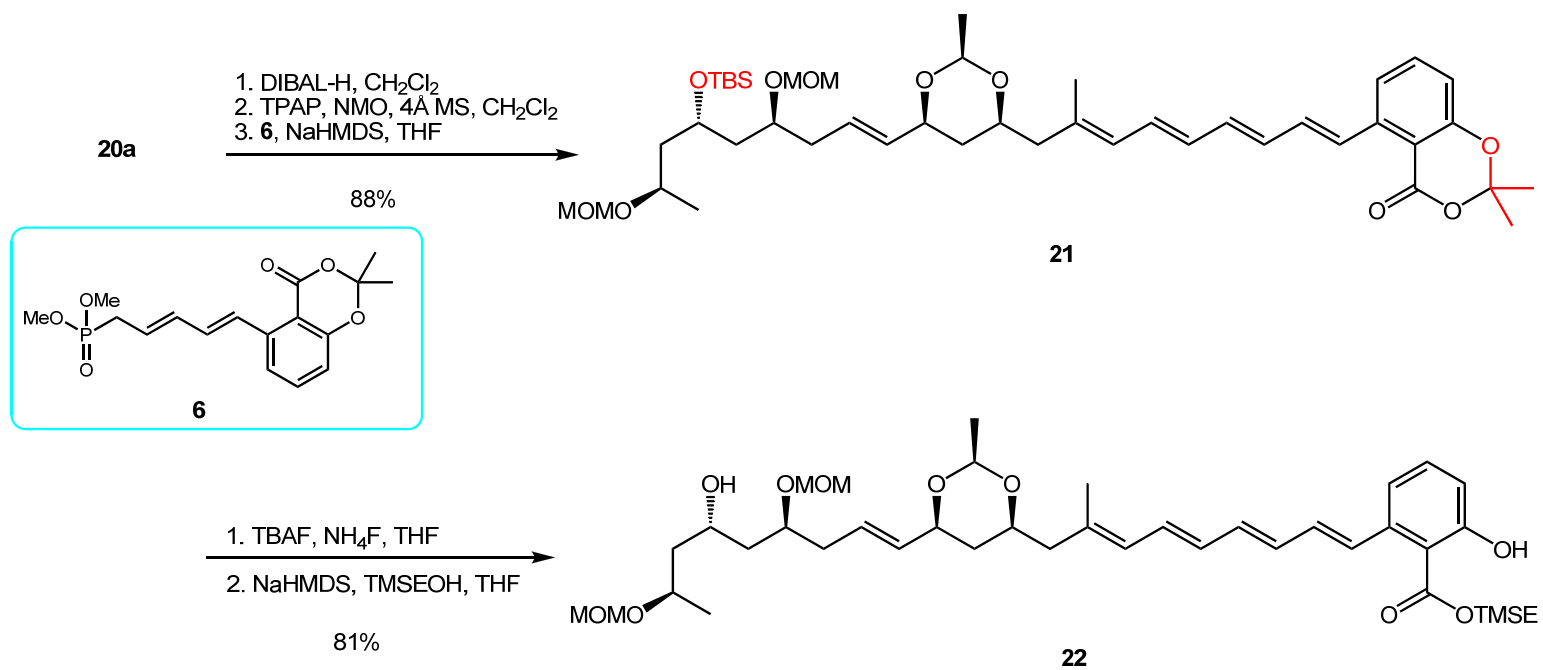
Total Synthesis by the Evans Group



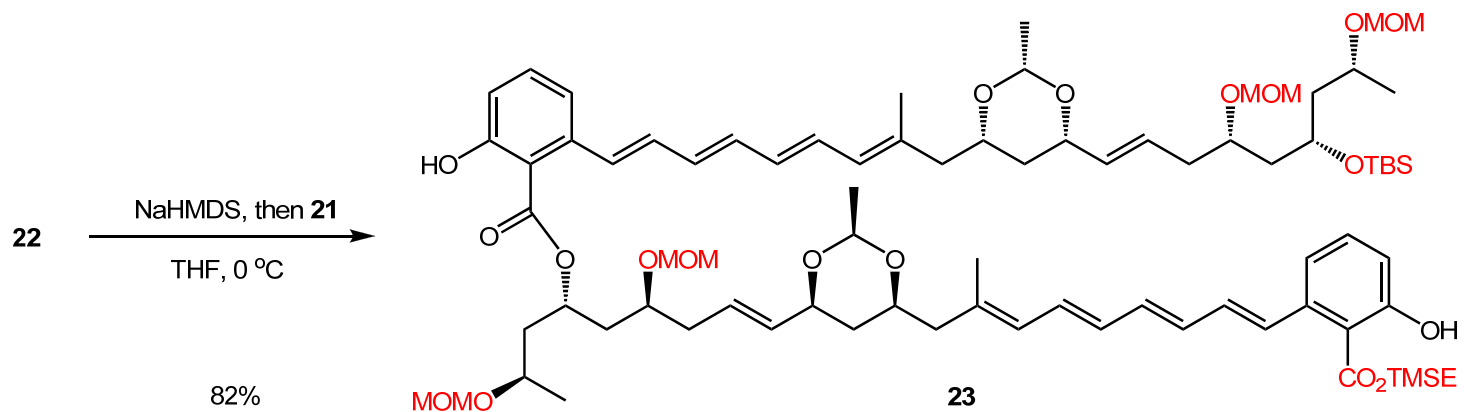
1. *n*-BuLi, *p*-MeOC₆H₄SH, **20a** R¹ = CO₂Et, R² = H
2. *m*-CPBA, -78°C to RT **20b** R¹ = H, R² = CO₂Et

50% **20a** / 38% **20b**

Total Synthesis by the Evans Group



Total Synthesis by the Evans Group



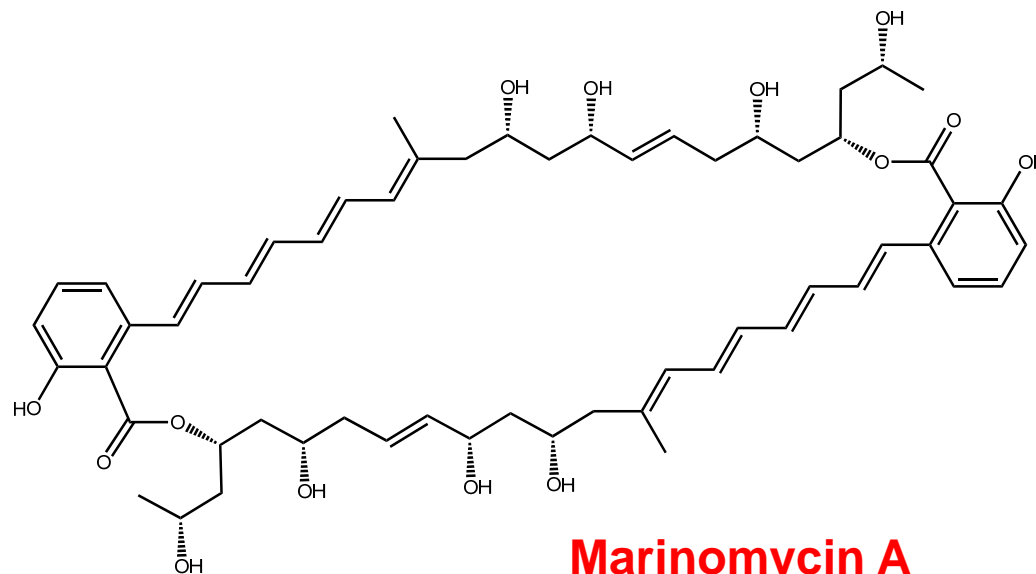
1. MOMCl, *i*Pr₂NEt
2. TBAF, NH₄F, THF

3. 2-Bromo-1-ethylpyridinium tetrafluoroborate, NaHCO₃
4. MgBr₂, *n*BuSH, CH₃NO₂

Marinomycin A

19%

Summary



The Evans Group in 2012

18-step sequence, 3.5% overall yield

The Hatakeyama Group in 2014

24-step sequence, 4.0% overall yield

The Nicolaou Group in 2007

In 2006, Fenical et al. disclosed the isolation of marinomycins A–C (**1–3**), structurally novel 44-membered C₂-symmetrical dimeric polyene-polyol macrolides, from the saline culture broth of a marine actinomycete, *Marinispora* strain CNQ-140, which was cultured from a sediment sample collected deep off the coast of La Jolla in California.

In conclusion, we have accomplished the convergent total synthesis of (+)-marinomycin A (**1**) in 24 steps (the longest linear sequence) in 4.0% overall yield starting from asymmetric epoxidation of σ -symmetrical dialkenyl carbinol **10**. The synthesis is practical and enables us to obtain hundred mg quantities of marinomycin A (**1**). The present work presents the first successful example of a direct dimerization approach to marinomycin A (**1**).
