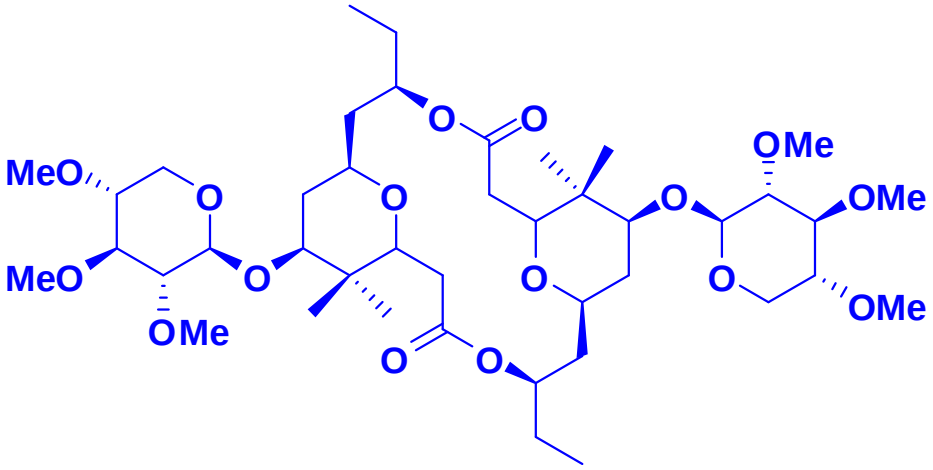
Total Synthesis of Cyanolide A in the Absence of Protecting groups, Chiral Auxiliaries, or Premetallated Carbon Nucleophiles



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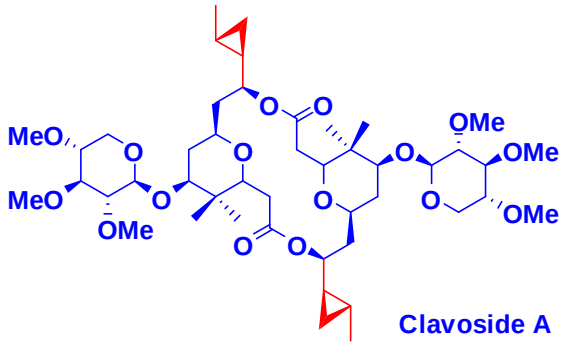
Introduction

It is a glycosidic 16- membered macrolide

Isolated from the Papua New Guinea cyanobacterium *Lyungbya boulillonii* by Gerwick and co-workers

This structure is closely related to the Clavoside family of natural products



It exhibits potent molluscicidal activity against the water snail *biomphalaria glabrata*

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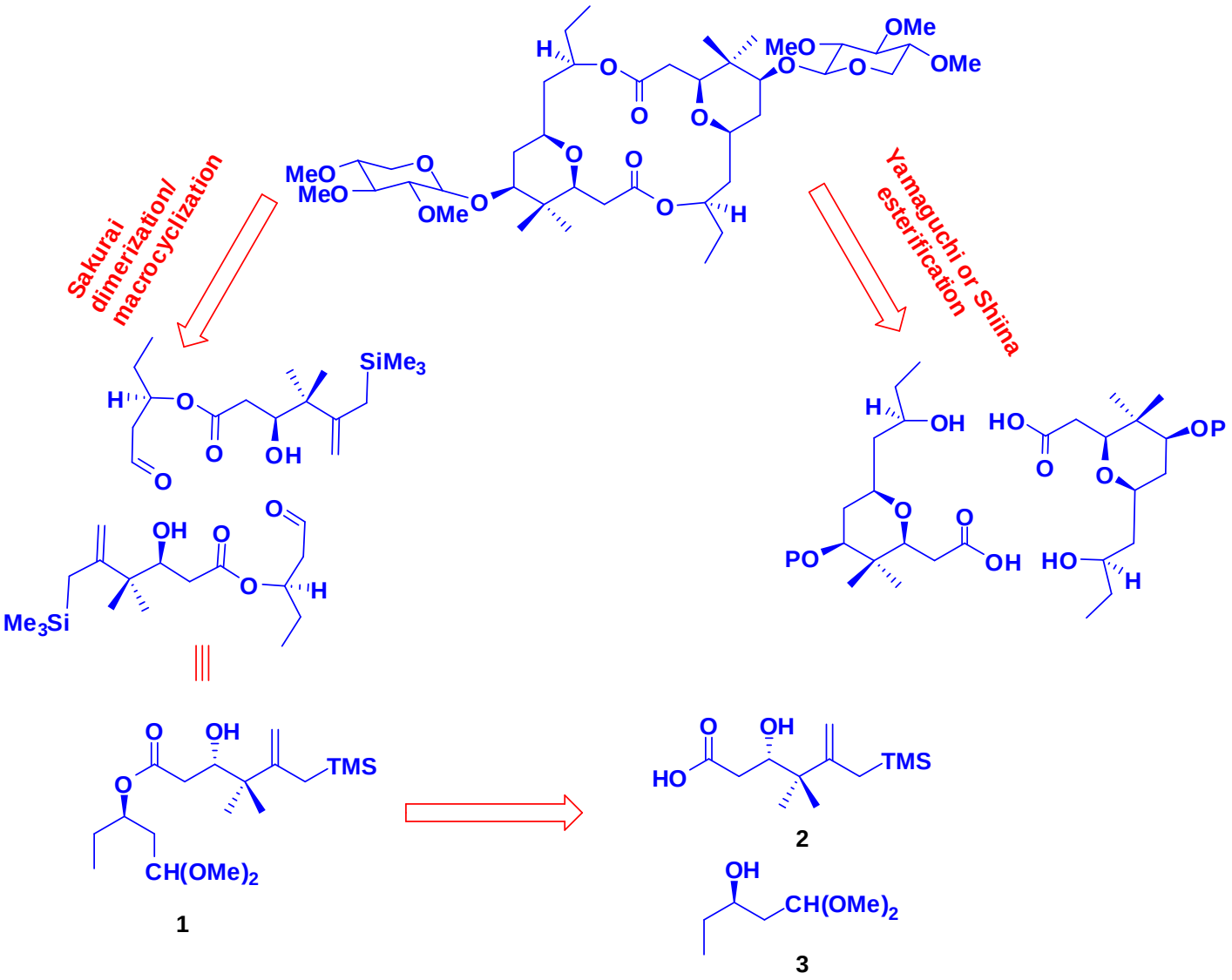
Rychnovsky's approach

Retrosynthetic analysis



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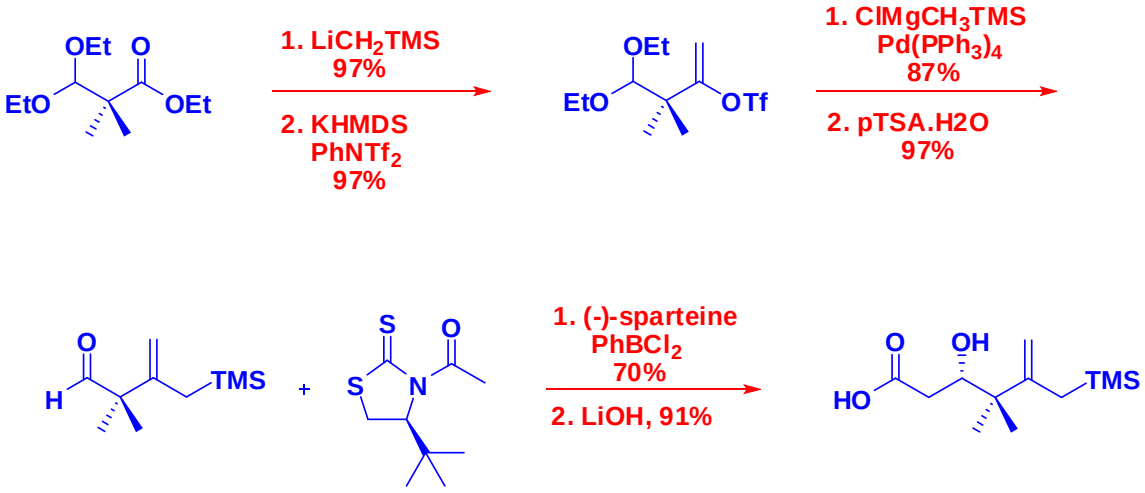
Synthesis of β- hydroxyacid 2



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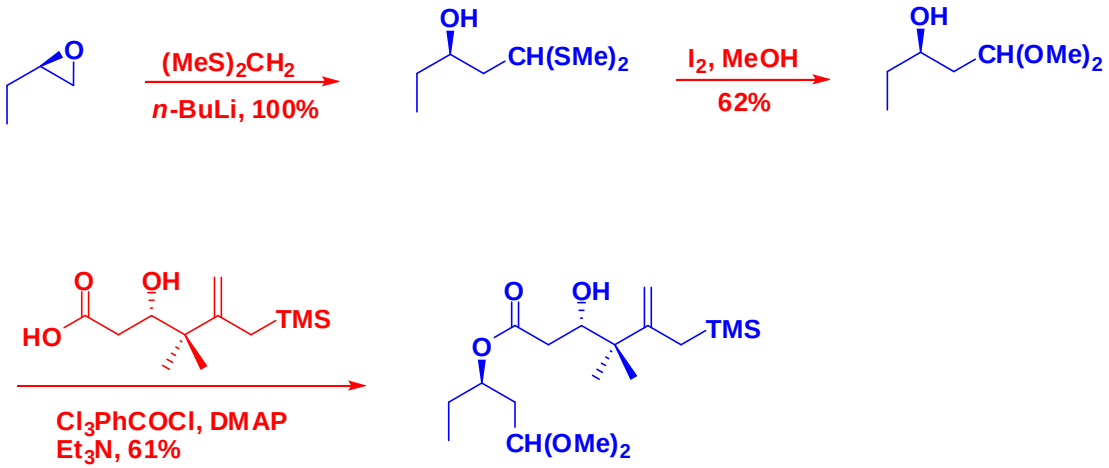
Synthesis of monomer 1



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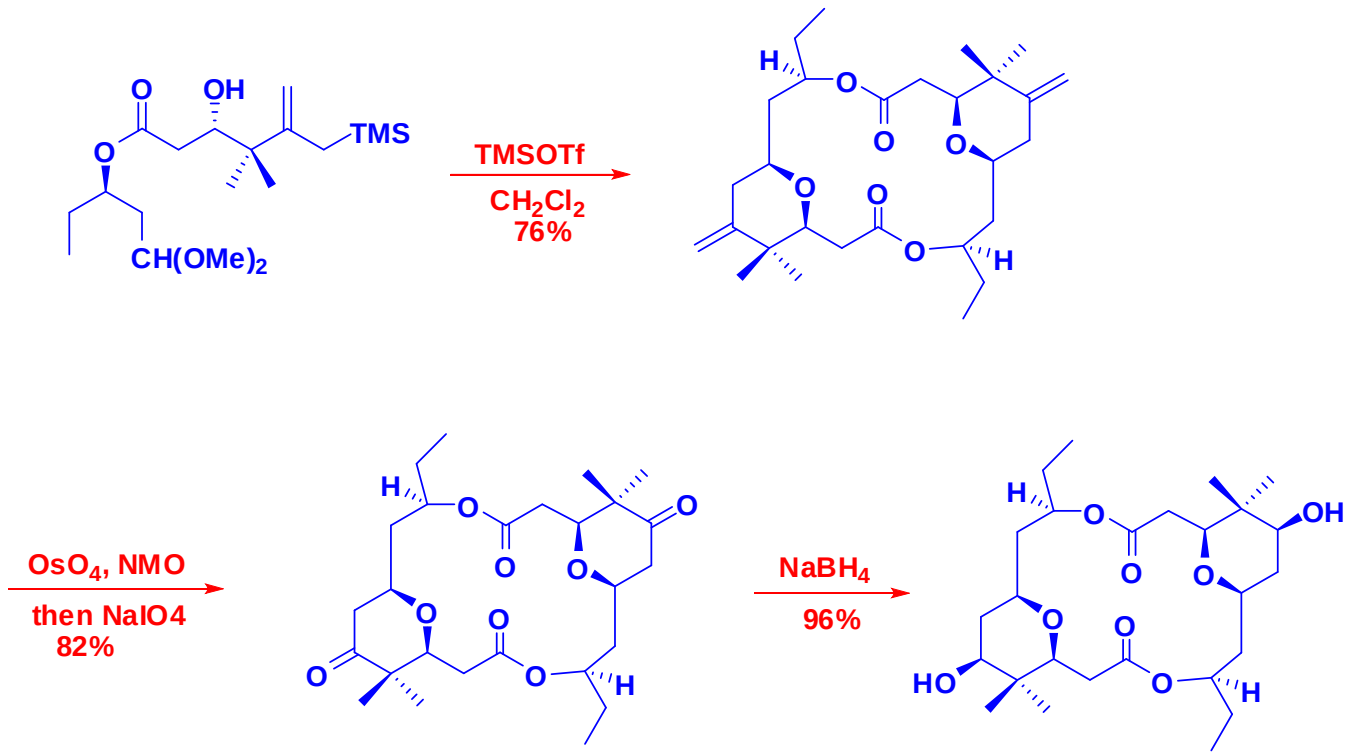
Synthesis of Cyanolide A by a Sakurai Dimerization



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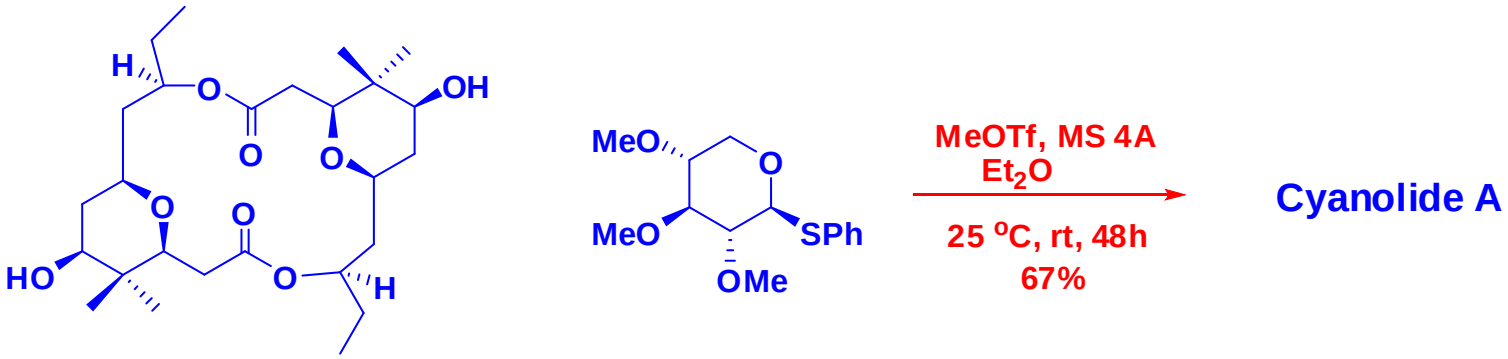

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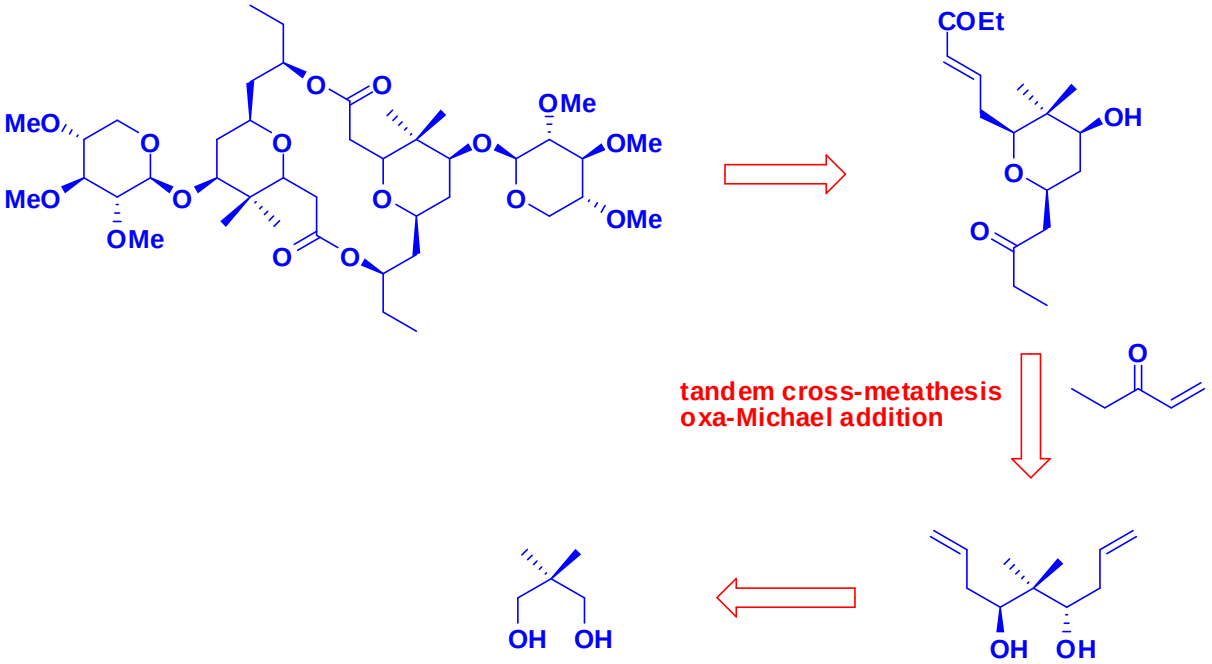
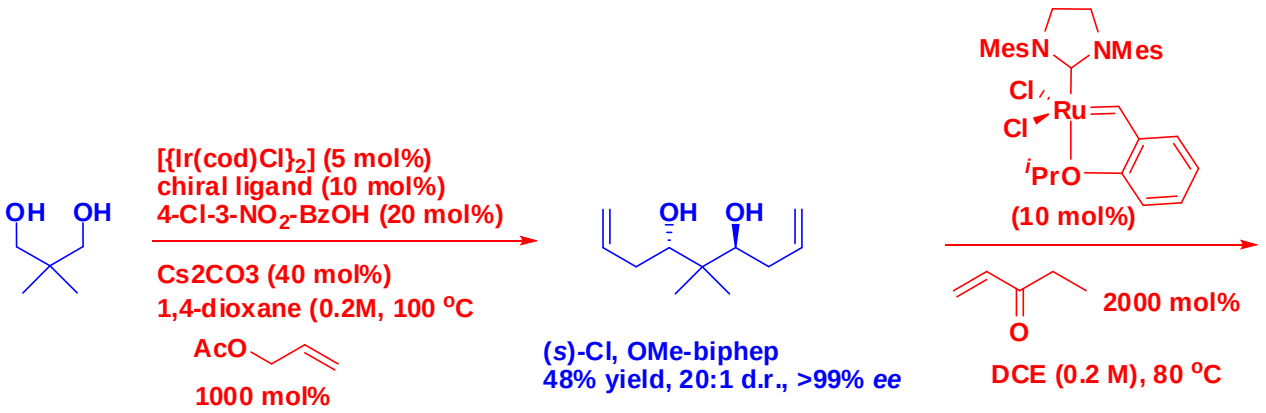
Krische's approach

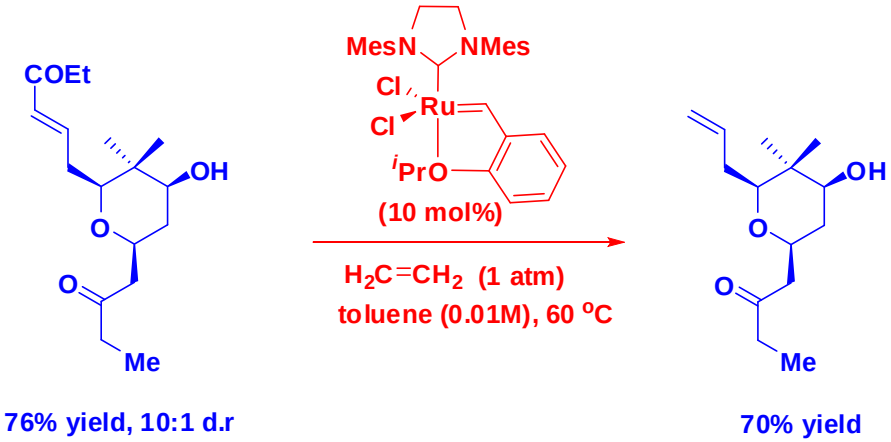
Retrosynthetic analysis



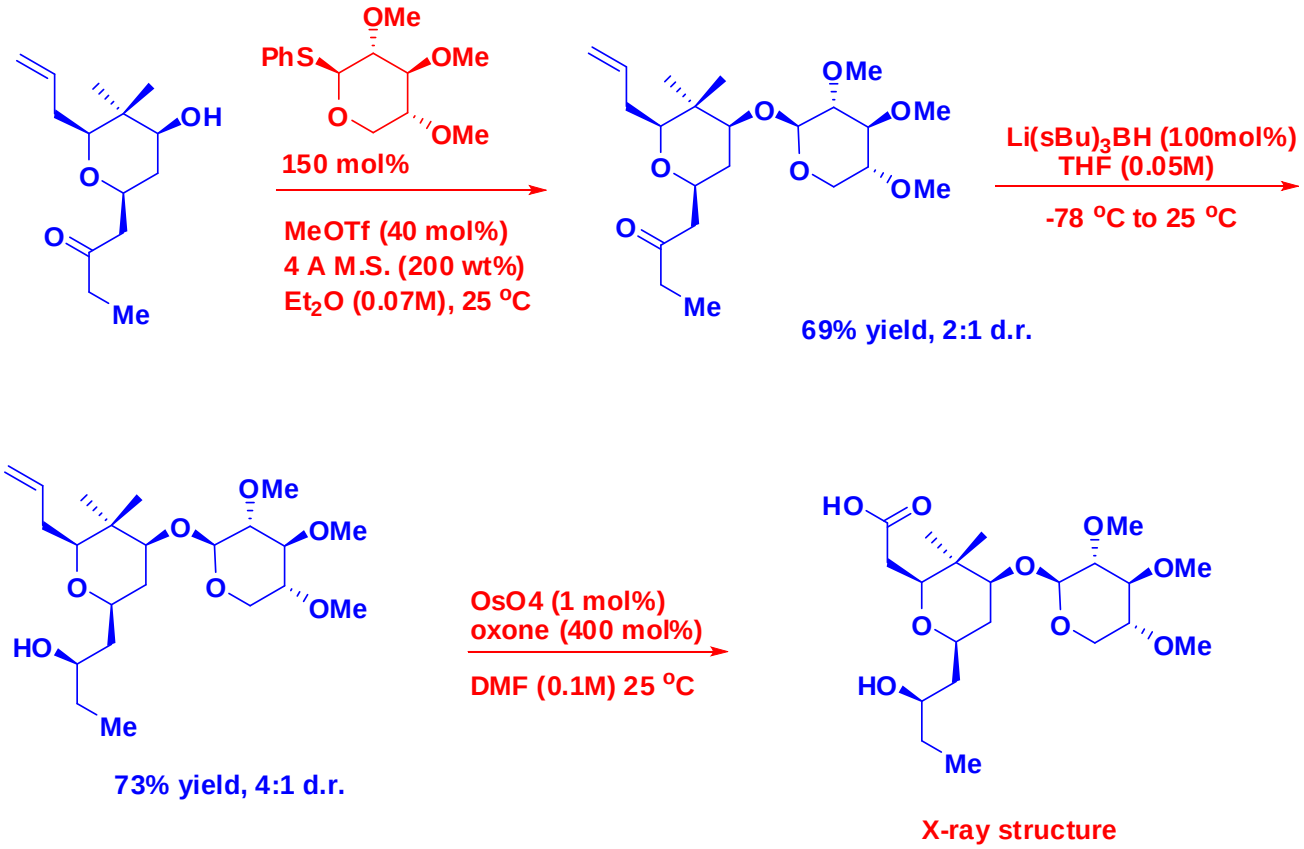
J. Am. Chem. Soc. **2011**, 33, 9727-9729

Synthesis

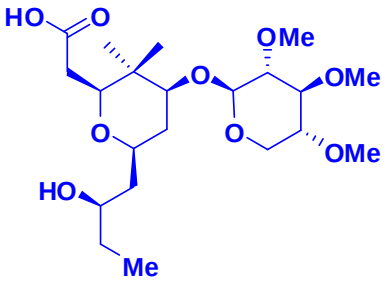




J. Am. Chem. Soc. **2011**, 33, 9727-9729



J. Am. Chem. Soc. **2011**, 33, 9727-9729



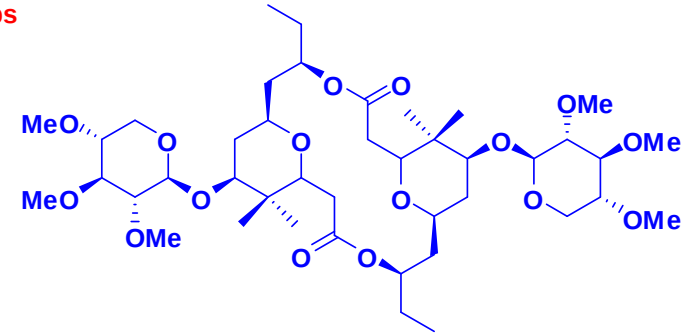
X-ray structure

MNBA (300 mol%
DMAP (2000 mol%

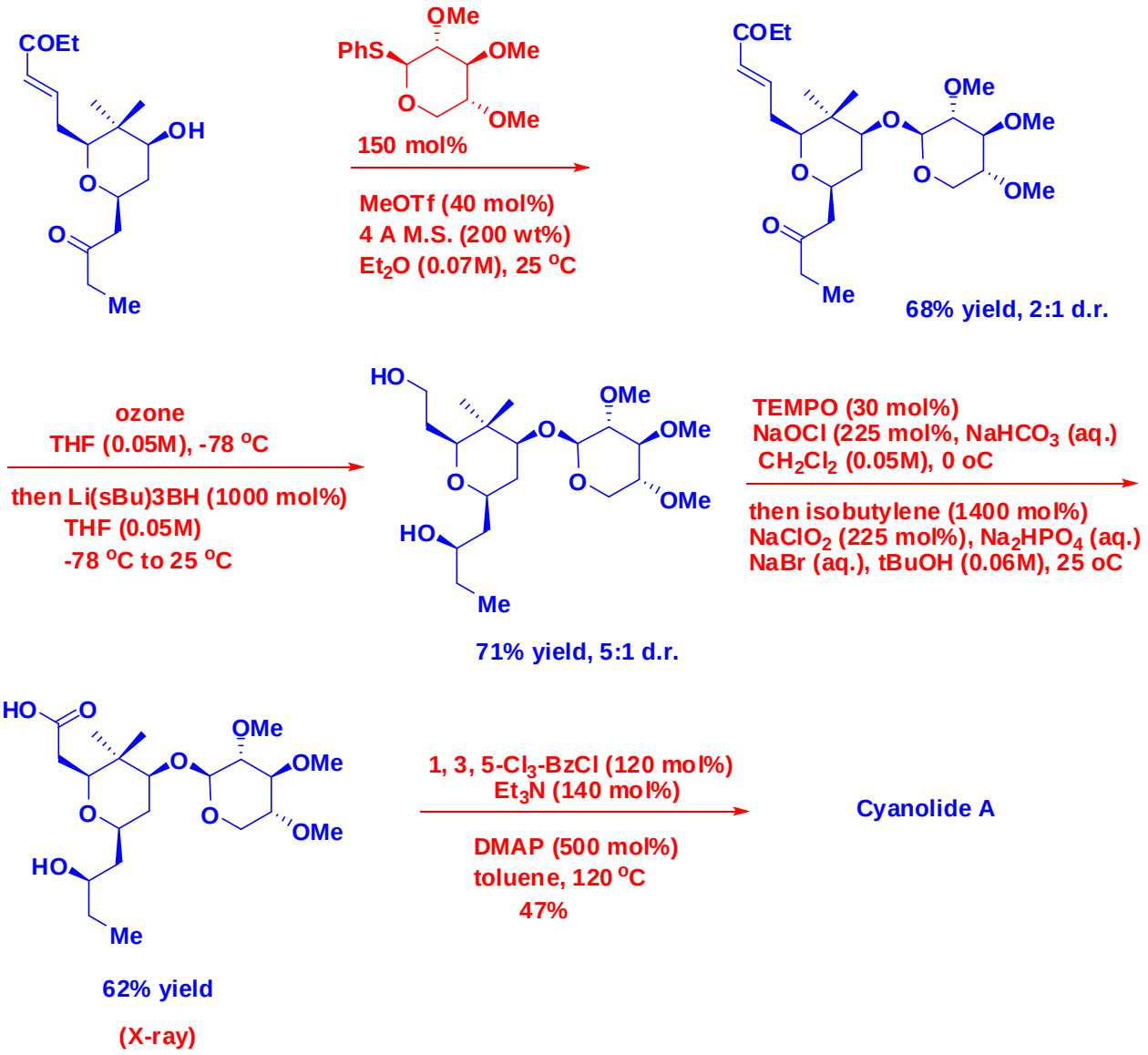
toluene (0.004M), 90 °C

18% over two steps

Cyanolide A



J. Am. Chem. Soc. **2011**, 33, 9727-9729



J. Am. Chem. Soc. **2011**, 33, 9727-9729

Key features

1. Double allylation of 1,3 glycols
2. Cascading cross-metathesis/ oxa-Michael cyclization

Conclusion

Rychnovsky synthesized Cyanolide A in 10 longest linear steps (18 total steps)

Shortest route to the total synthesis of Cyanolide A was accomplished by Krische

1. Kirche's first generation total synthesis- 7 longest linear steps (11 total steps)
2. Second generation total synthesis -6 longest linear steps (10 total steps)