Literature Report

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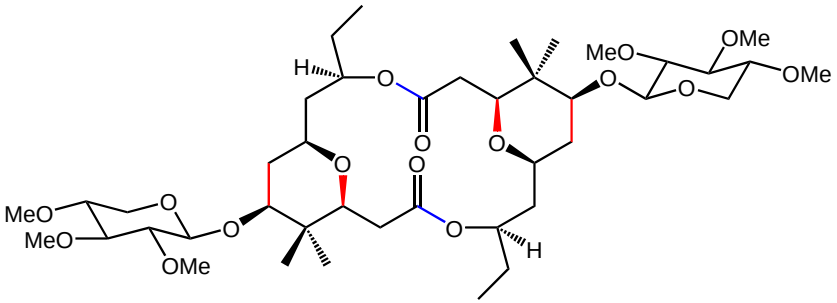
Checker: Zhi-Shi Ye

Total Synthesis of the Cyanolide A Aglycon

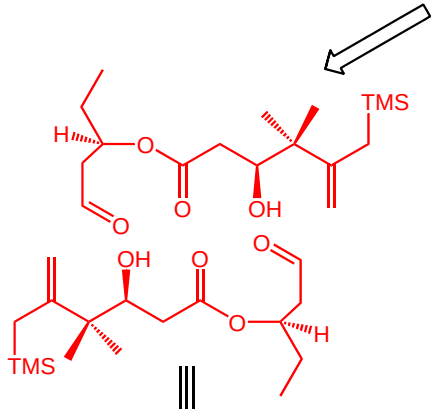
2011-06-28

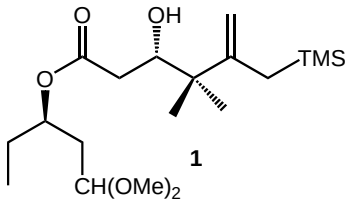
Rychnovsky, S. D. *et al J. Am. Chem. Soc*. **2011** ASAP

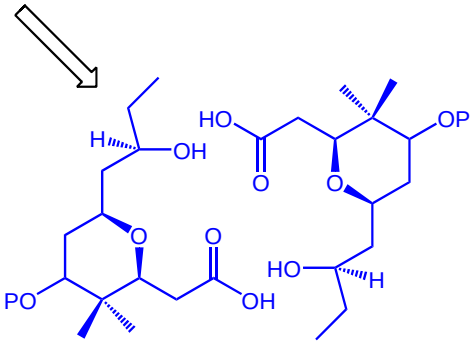
Retrosynthesis of cyanolide A

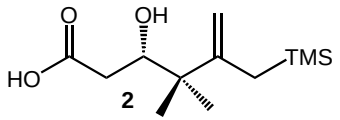


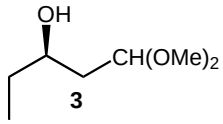
cyanolide A



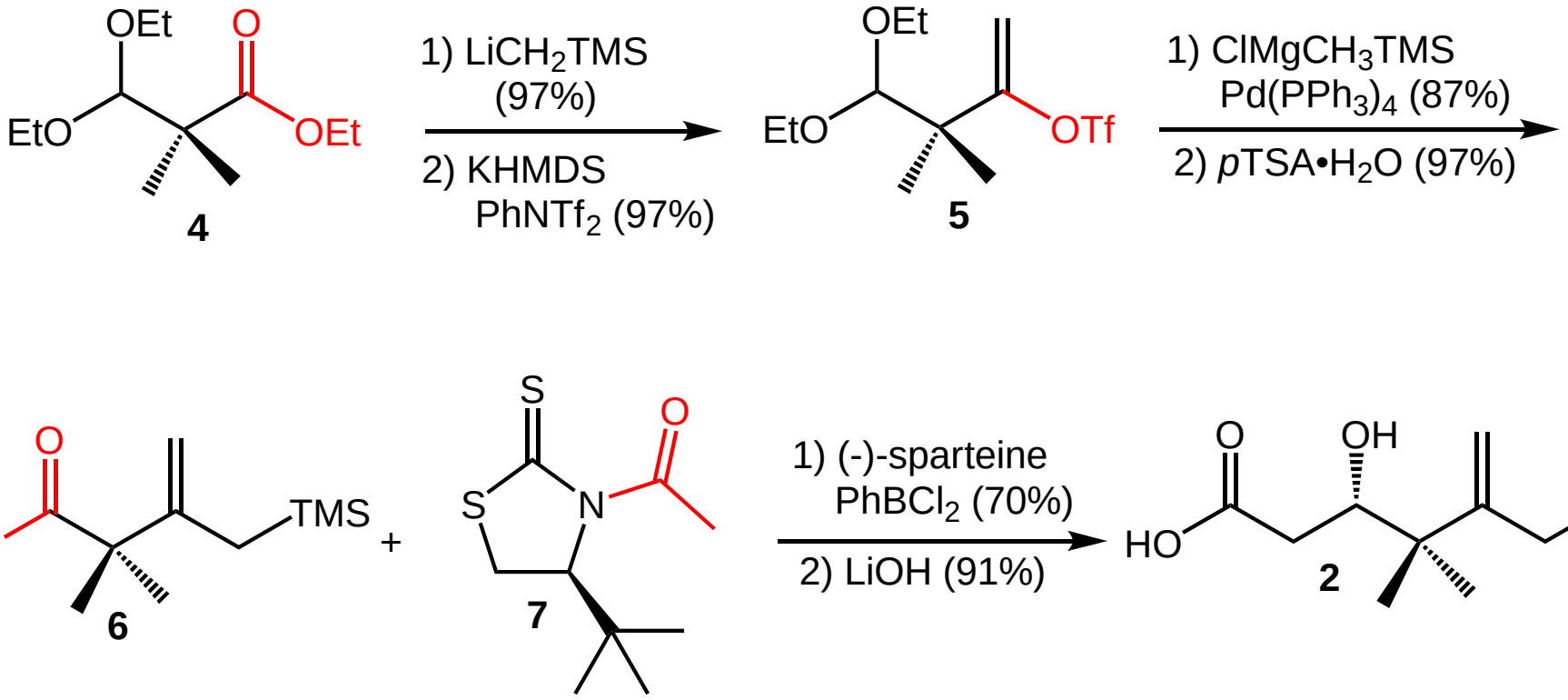




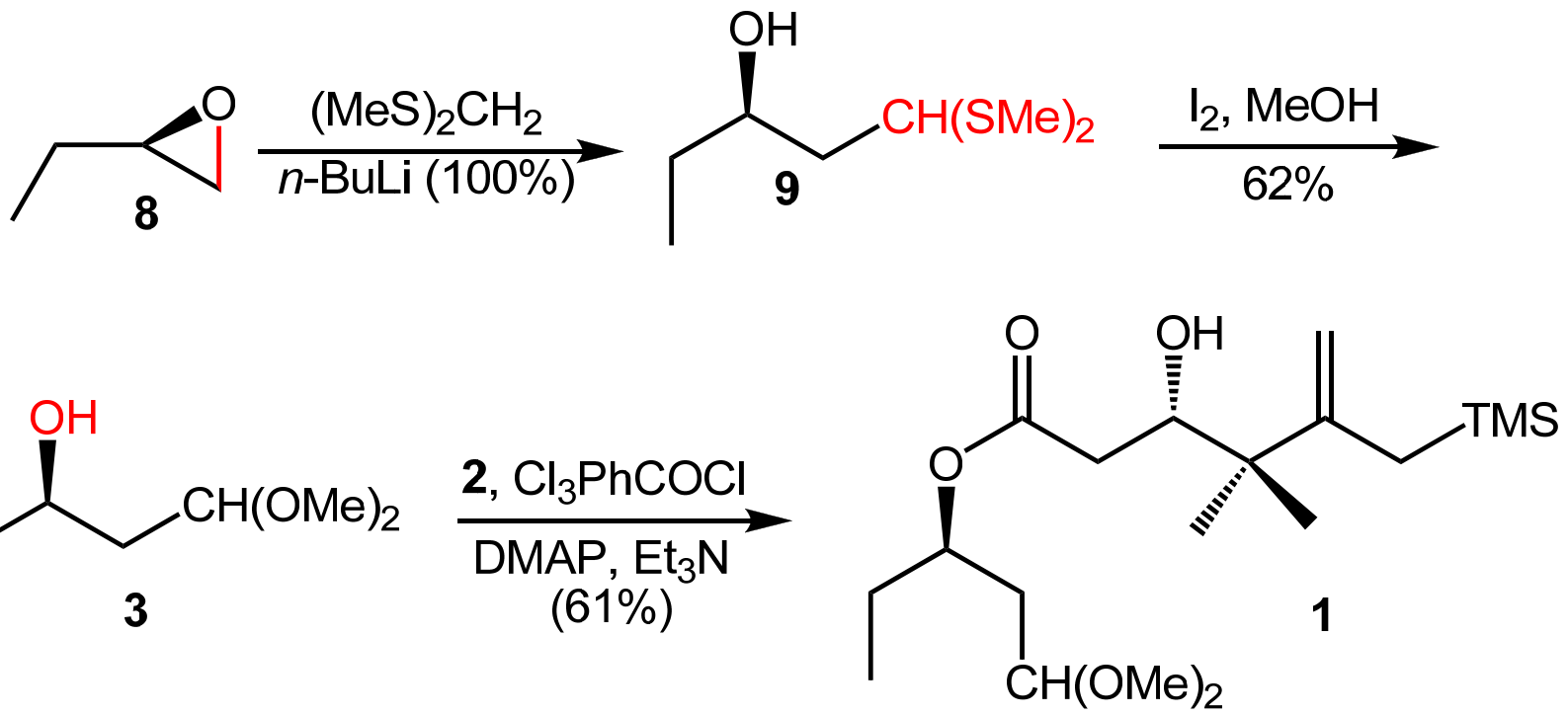




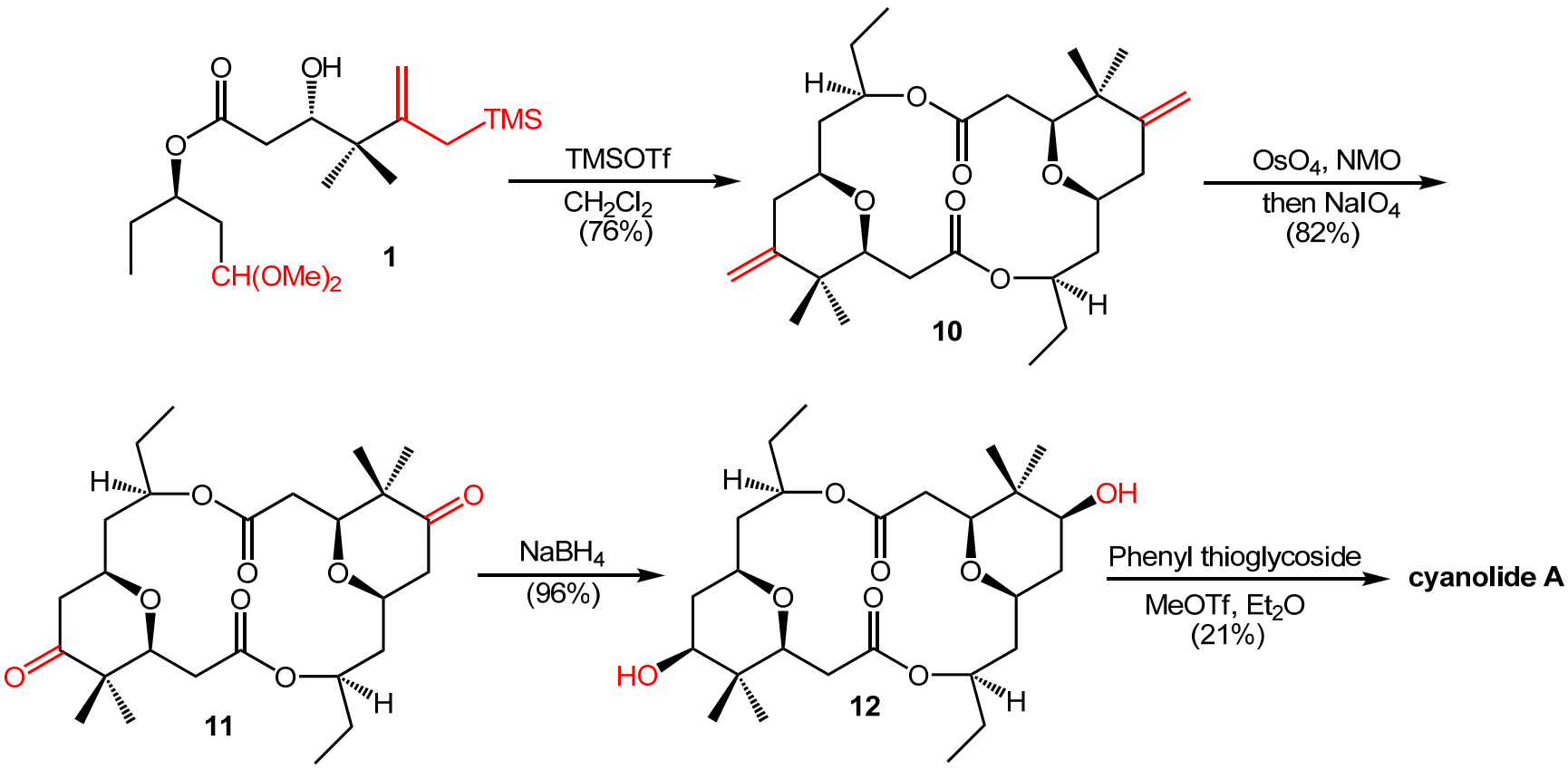
Synthesis of β-Hydroxyacid 2



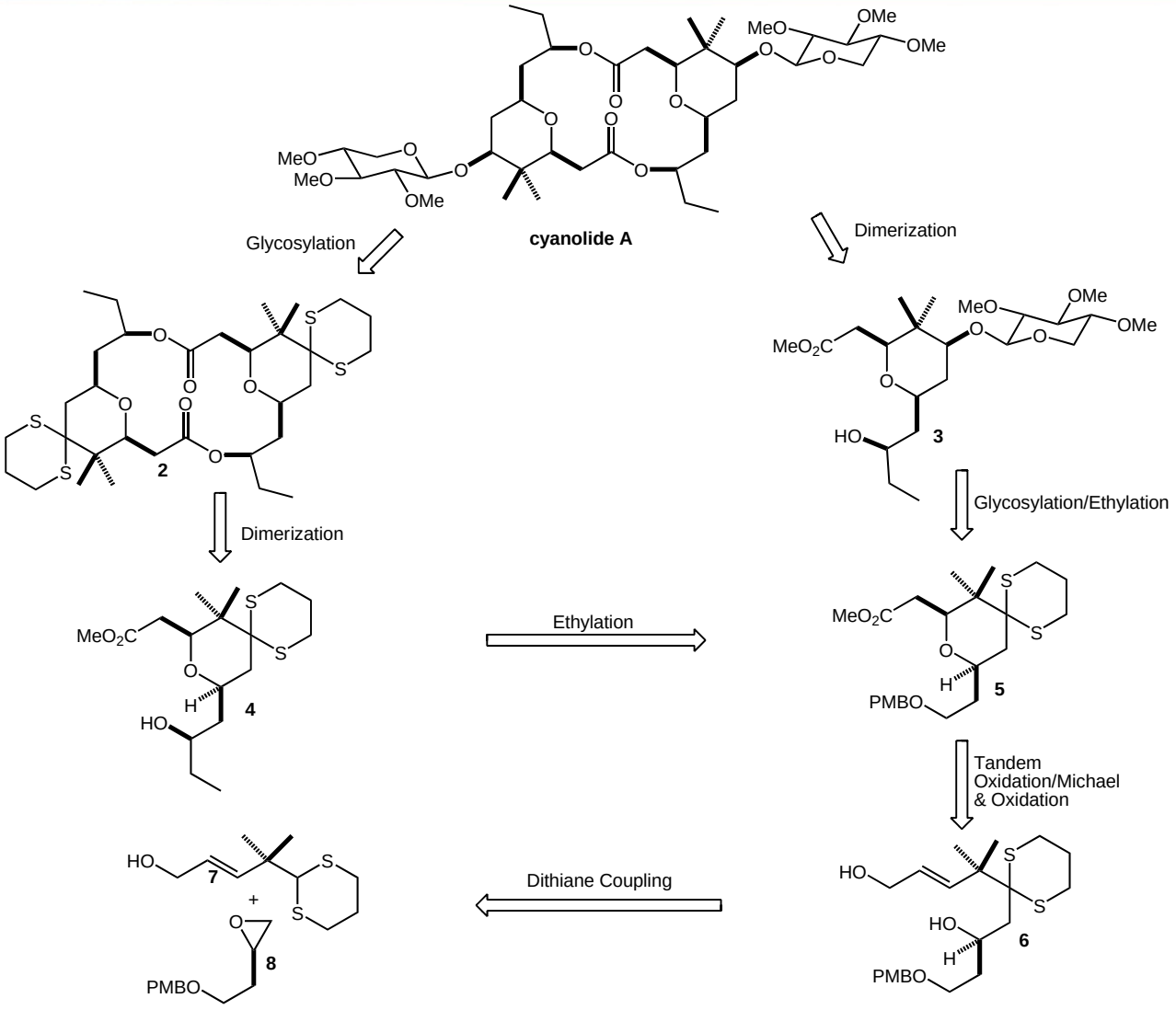
Synthesis of Monomer 1



Synthesis of Cyanolide A

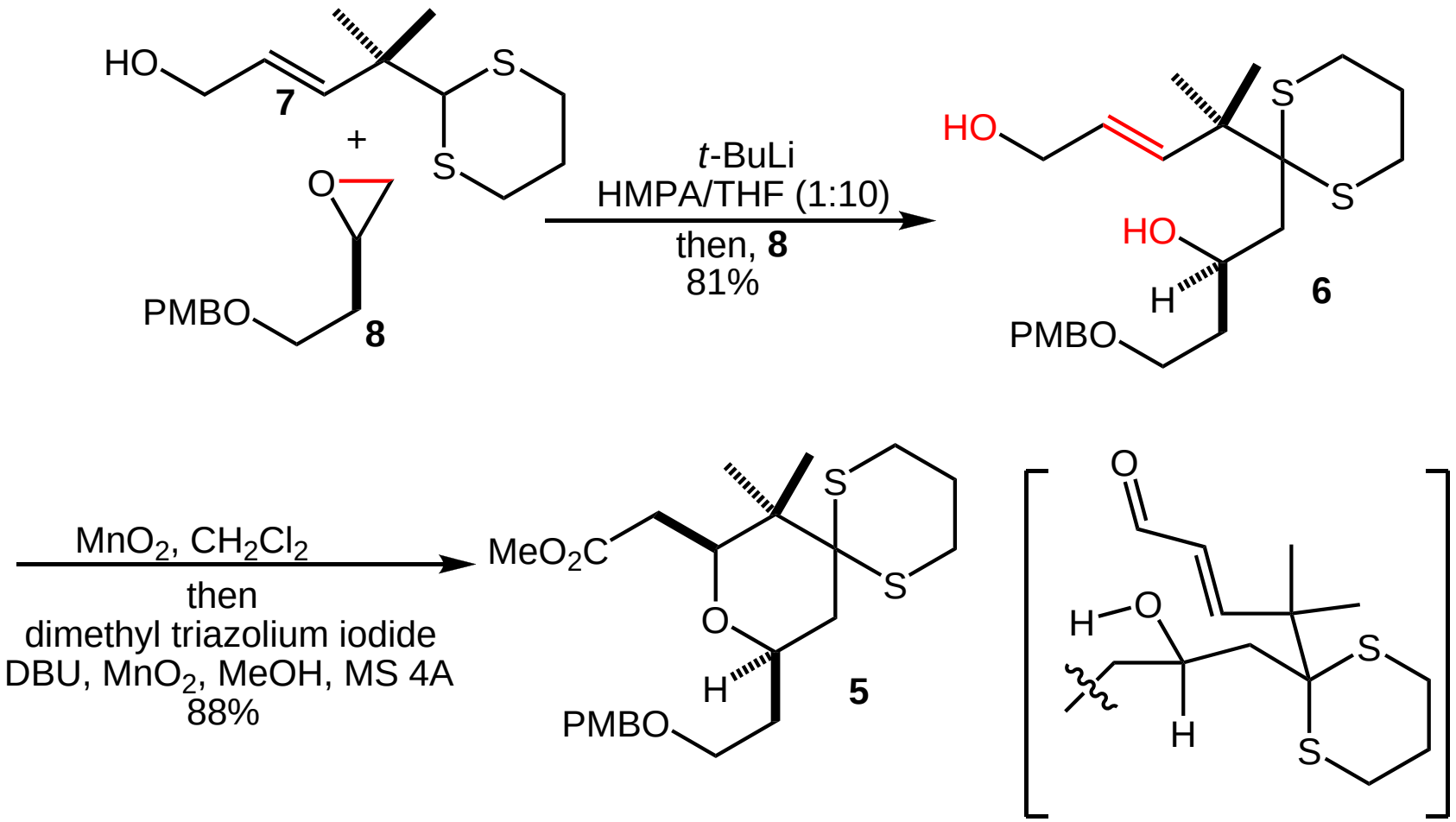


Hong's work

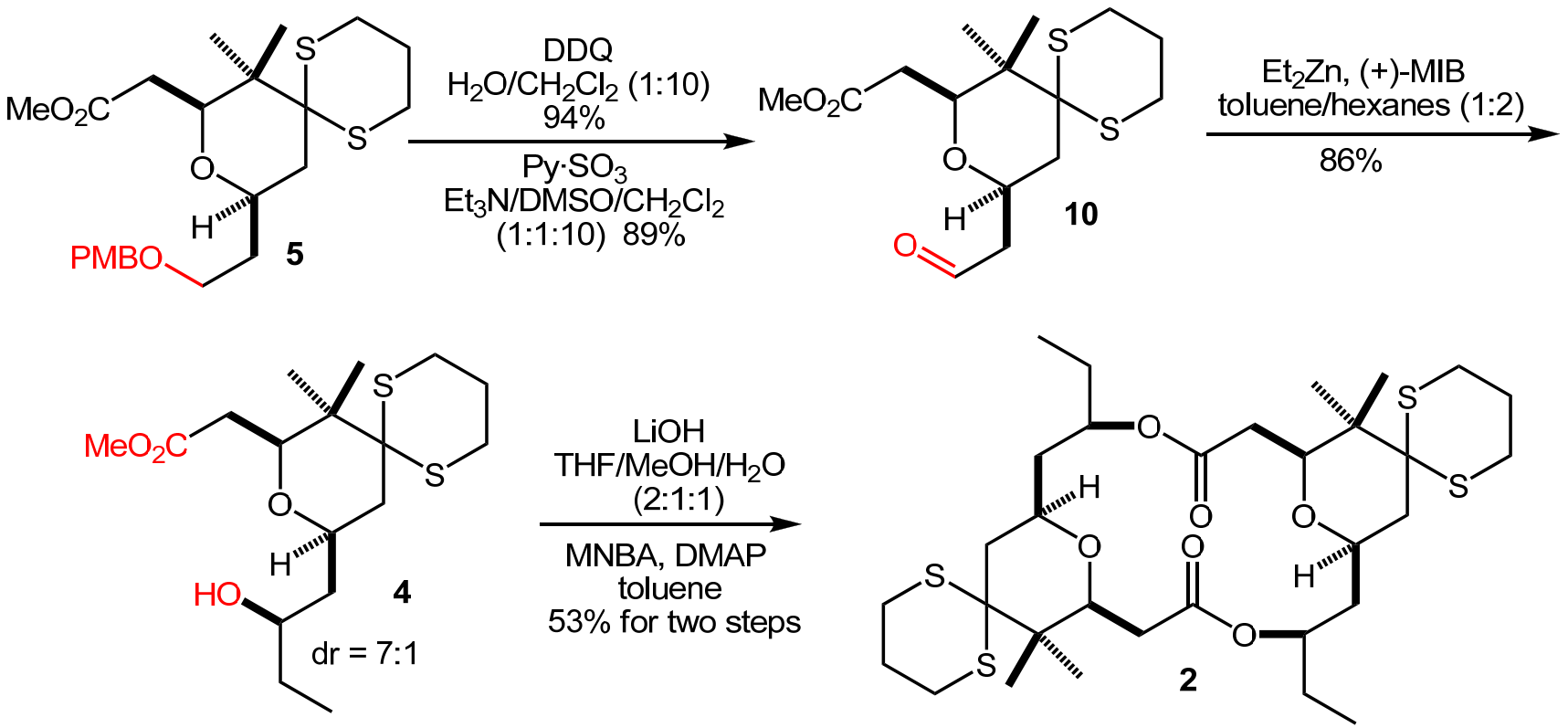


Hong, J. *et al Org. Lett.* **2010**, *12*, 2880

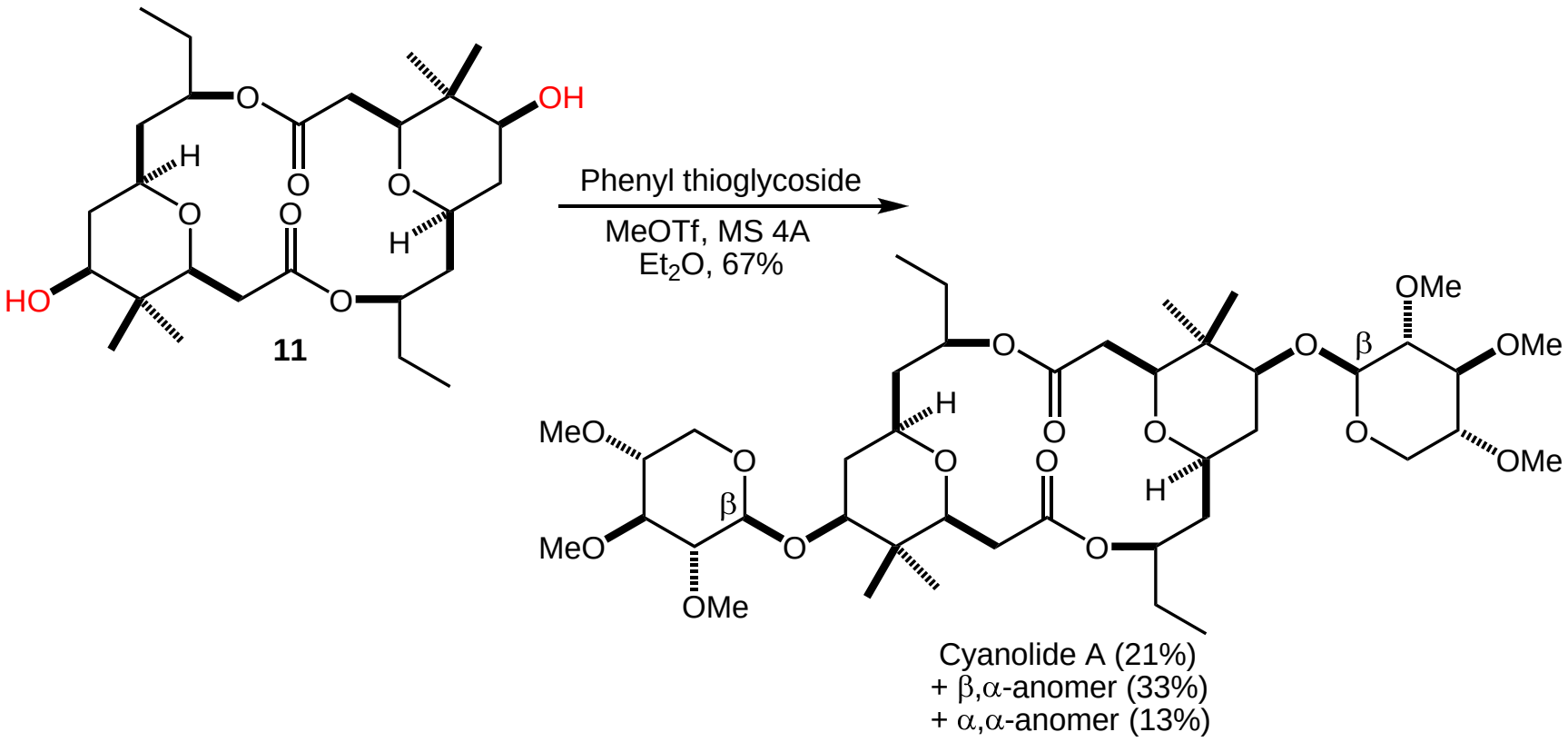
Synthesis of THP Ester 5



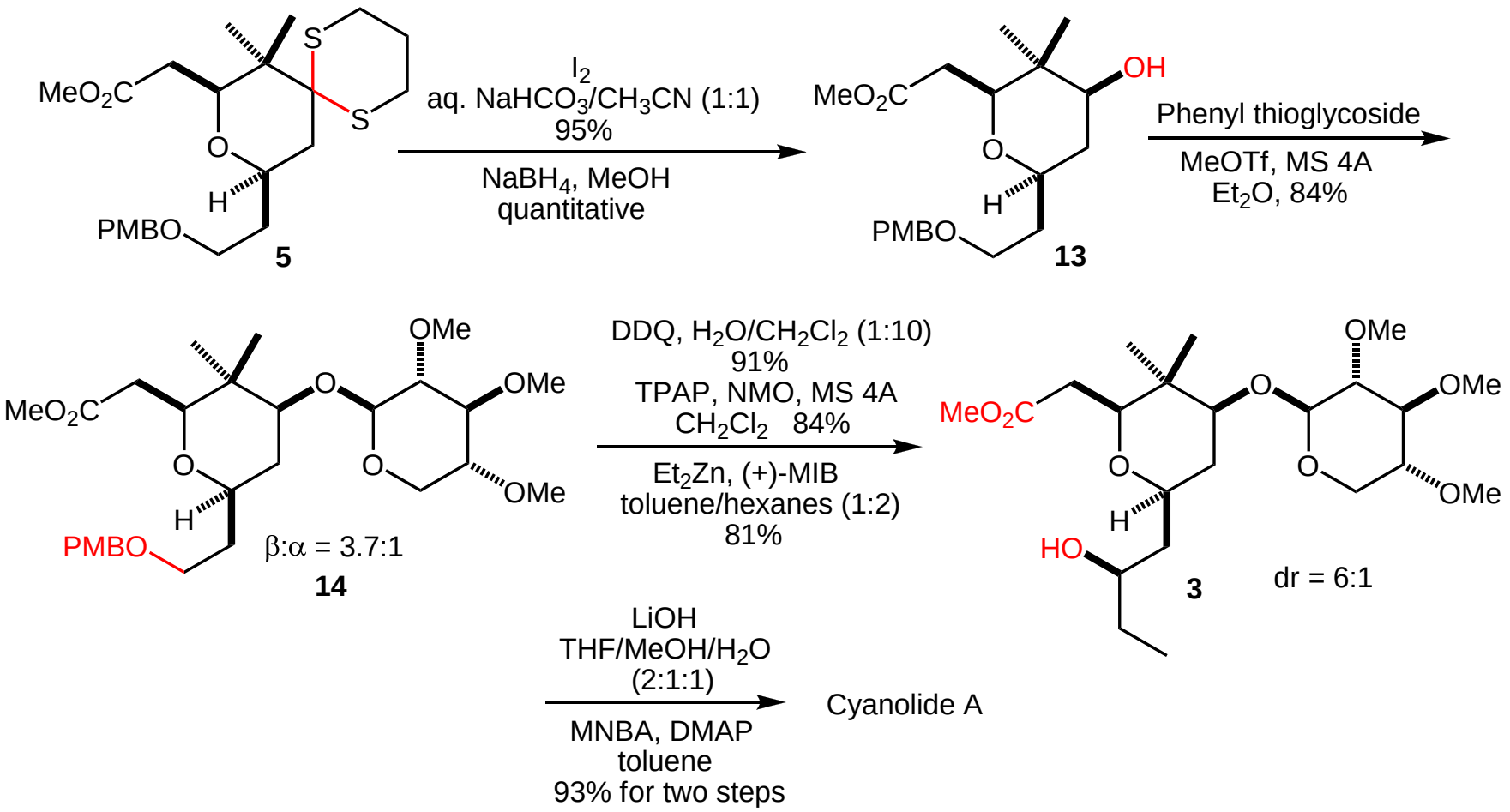
Dimerization-Glycosylation Strategy



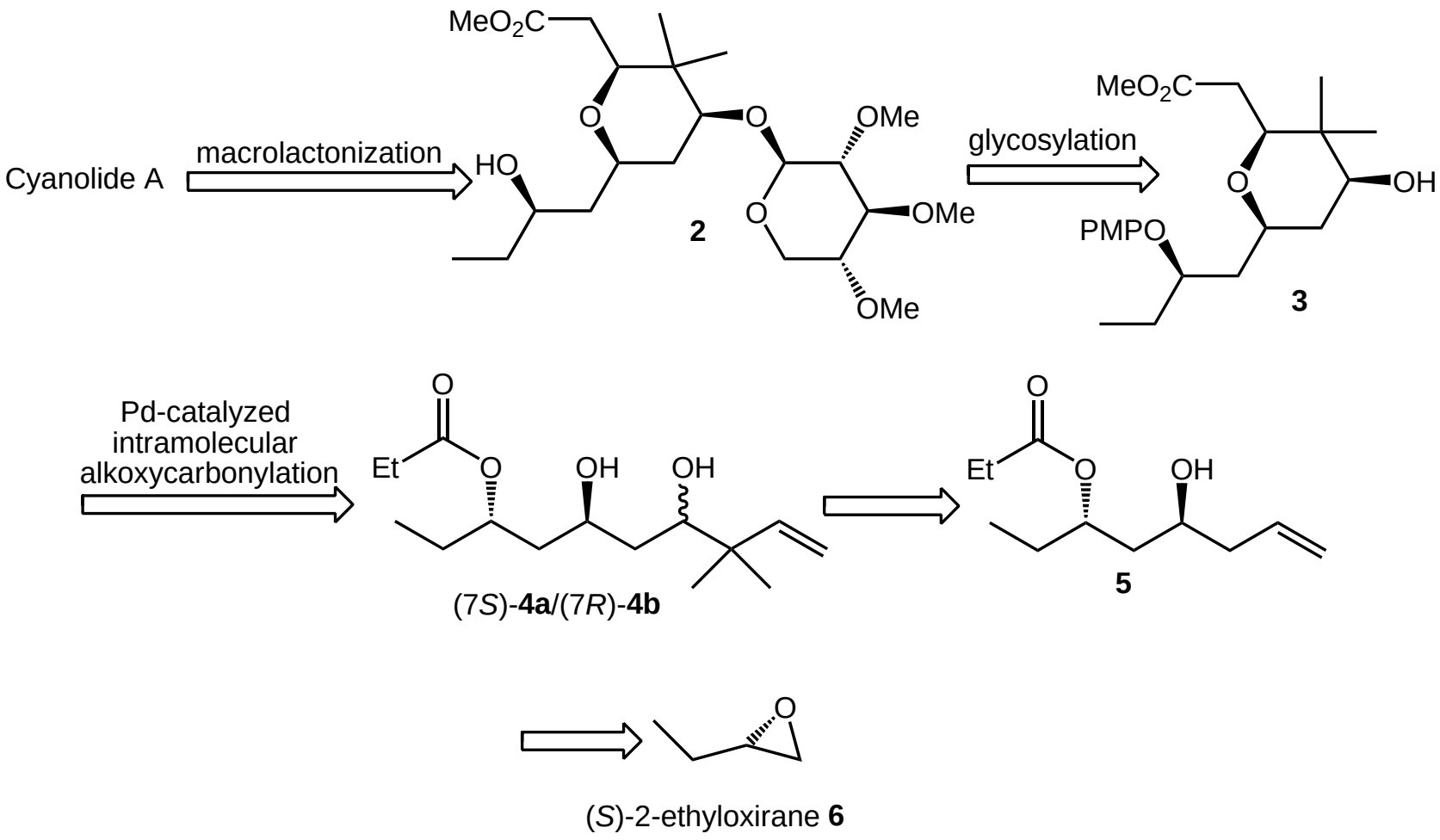
Dimerization-Glycosylation Strategy



Glycosylation-Dimerization Strategy

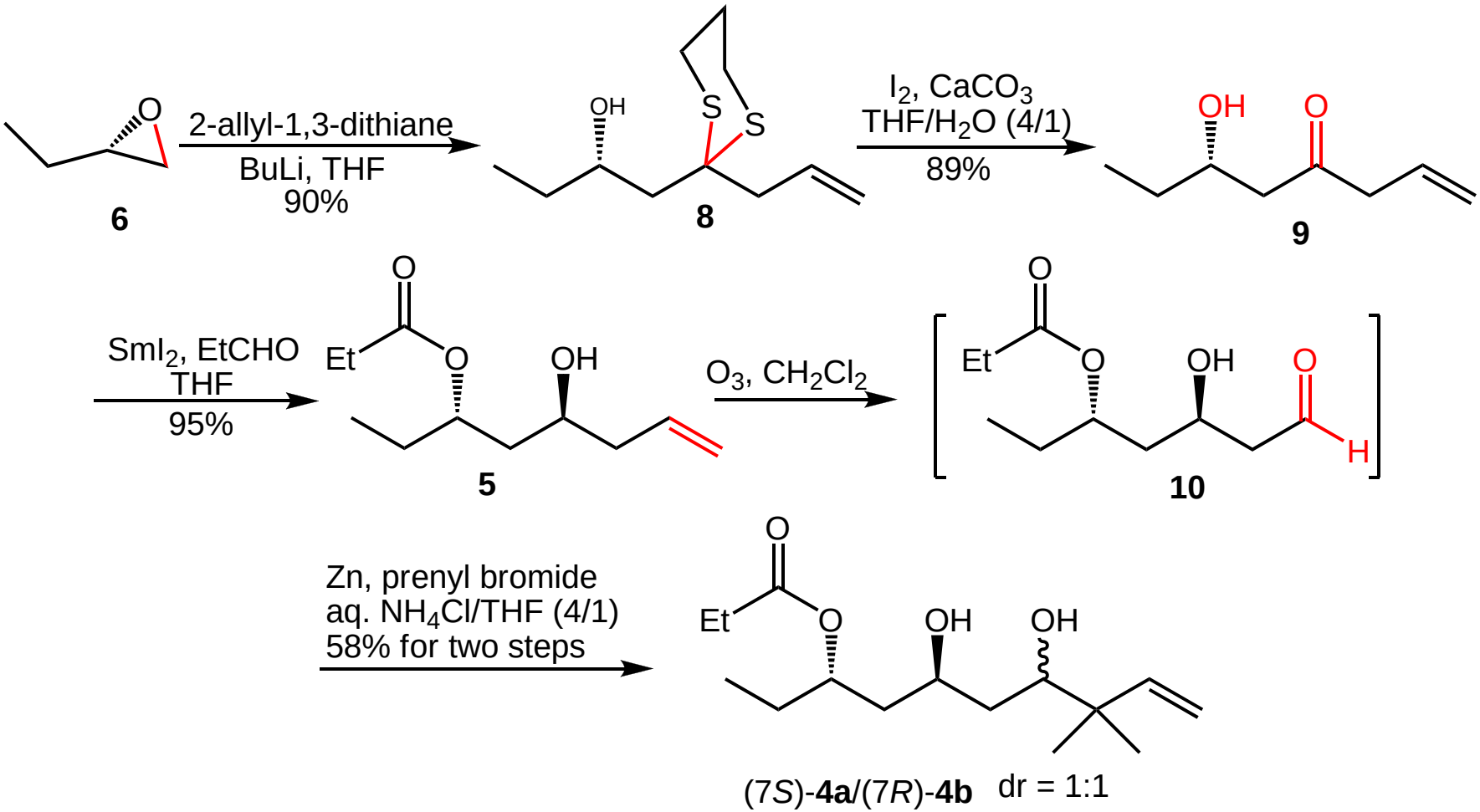


She's work

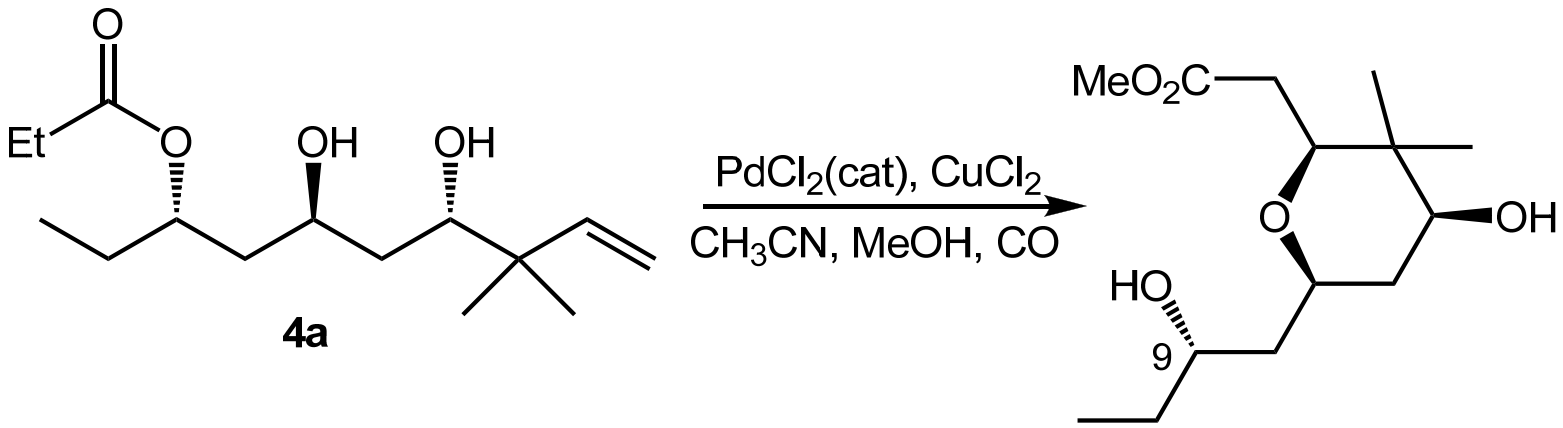


She, X. *et al Org. Biomol. Chem.* **2011**, *9*, 984

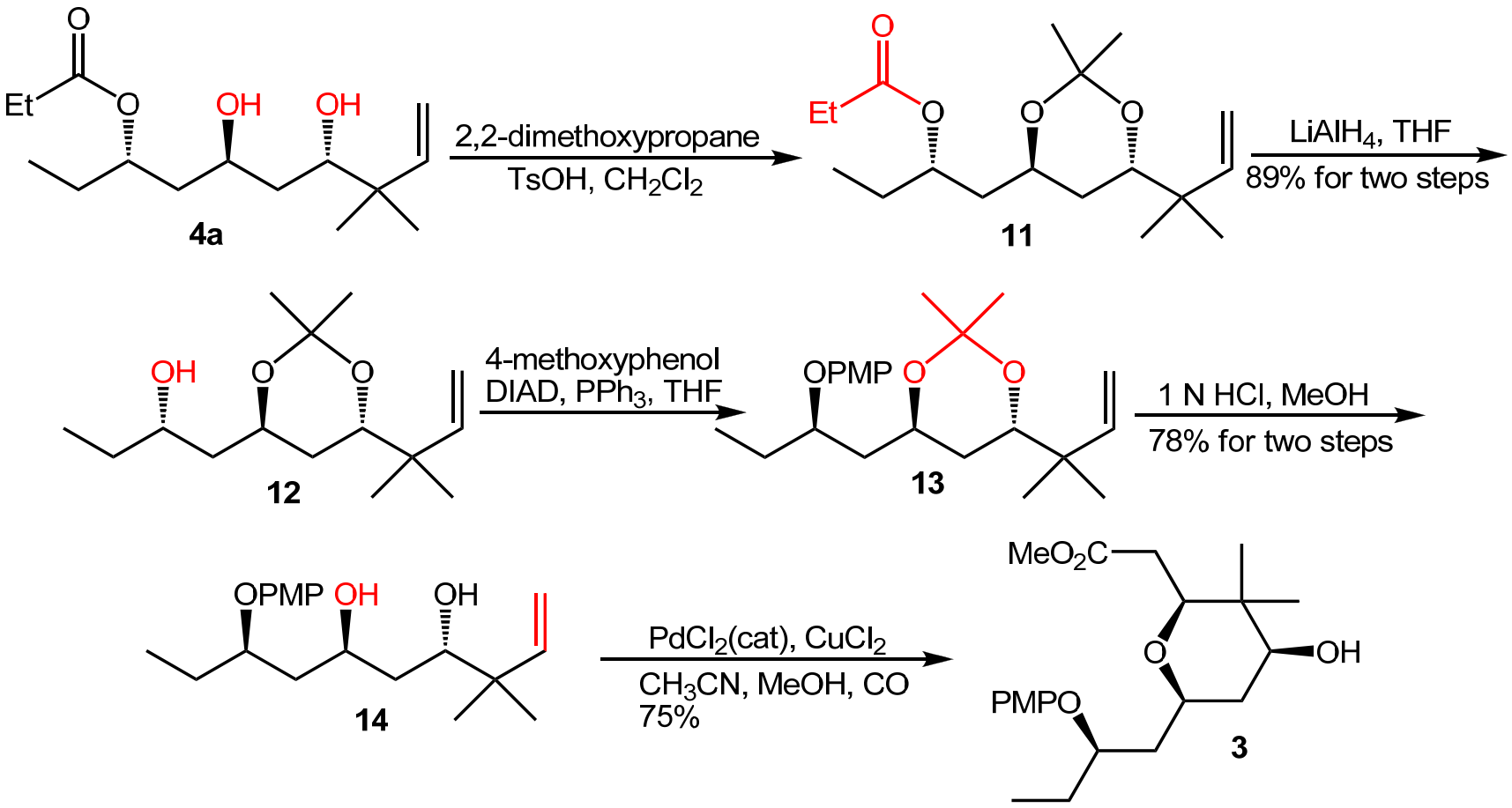
Synthesis of Diols 4a and 4b



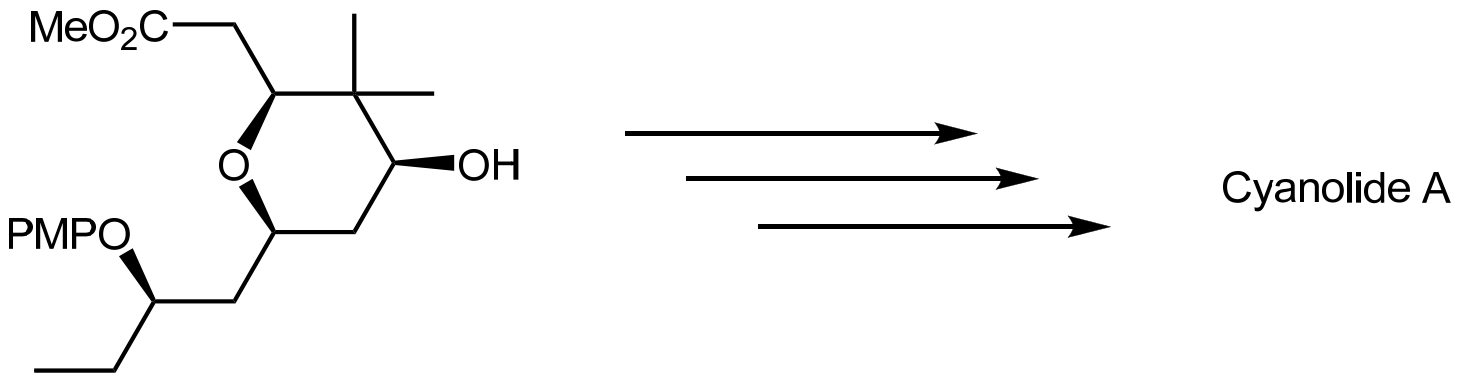
Pd-catalyzed Intramolecular Alkoxycarbonylation with 4a



Synthesis of Alcohol 3



Synthesis of Cyanolide A



The C_2-symmetric macrodiolide cyanolide A was isolated by Gerwick and co-workers from the cyanobacteria *Lyngbya bouillonii* collected near Pigeon Island, Papua New Guinea. The dimer exhibits significant molluscicidal activity against *Biomphalaria glabrata* (LC50 = 1.2 μ M). This unique biological activity of cyanolide A and its interesting structure have inspired four total syntheses. All of the completed syntheses have relied on either Yamaguchi's or Shiina's lactonization protocol to form the macrocylic dimer from complex monomers. Here we report an alternative synthesis of the cyanolide A aglycon in a concise process that avoids the use of protecting groups.

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In summary, the total synthesis of the aglycon of cyanolide A has been completed with a longest linear sequence of 10 steps and 18% overall yield without the use of protecting groups. This marks the shortest synthesis reported to date. A key Sakurai dimerization/macrocyclization reaction was exploited to develop a significant amount of the molecular complexity in a single step. This strategy allowed facile formation of 3,3-disubstituted tetrahydropyrans, which has proved challenging in other approaches. Further applications of the dimerization/macrocyclization strategy are under development.

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