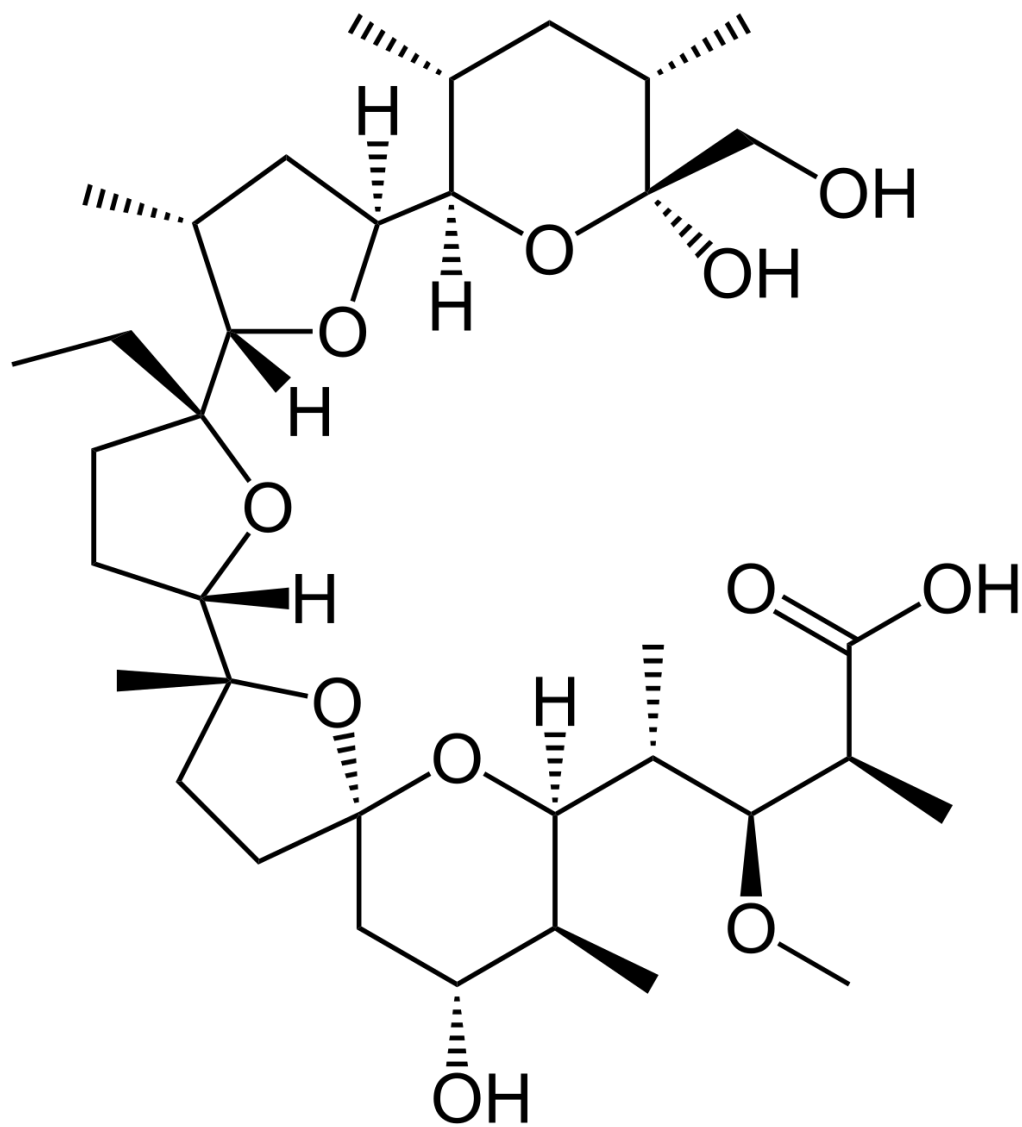


Total Synthesis of Monensin

CEM 852 – Spring 2022
Methods of Organic Synthesis
1/21/2022

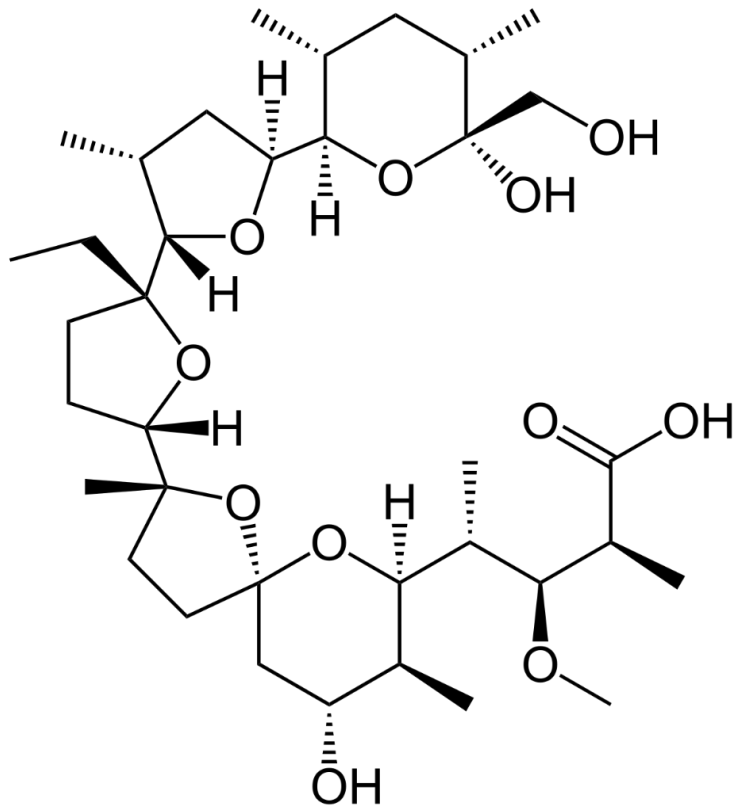


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Monensin



- ✓ A polyether antibiotic isolated from *Streptomyces cinnamomensis*.
- ✓ The structure was first elucidated by Agtarap *et al.* in 1967.¹
- ✓ The first total synthesis of monensin was reported by Yoshito Kishi in 1979.²
- ✓ The second total synthesis was reported by W. C. Still in 1980.³

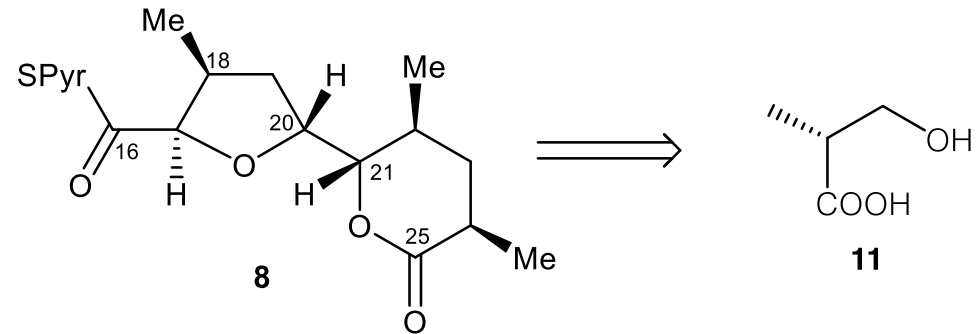
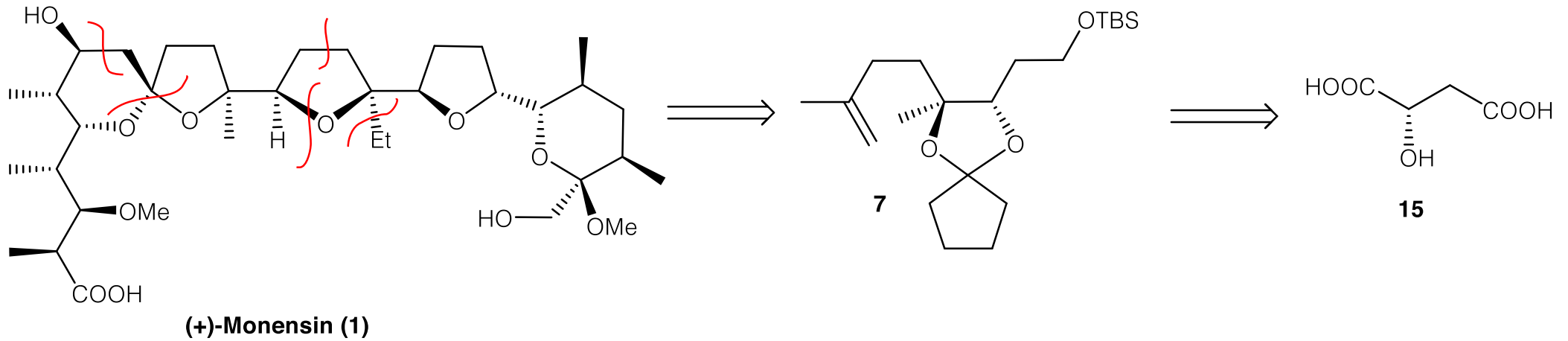
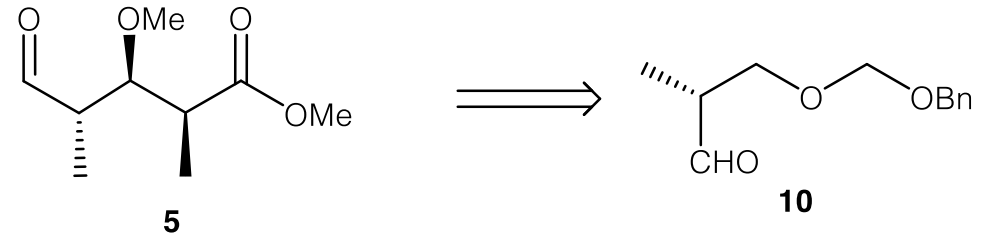
¹ A. Agtarap, J. W. Chamberlain, M. Pinkerton, and L. Steinrauf, *J. Am. Chem. Soc.* **1976**, 89, 5737.

² Fukuyama, T.; Wang, C. L. J.; Kishi, Y. Synthetic Studies on Polyether Antibiotics. 5. Total Synthesis of Monensin. 2. Stereocontrolled Synthesis of the Right Half of Monensin. *J. Am. Chem. Soc.* **1979**, 101, 260–262.

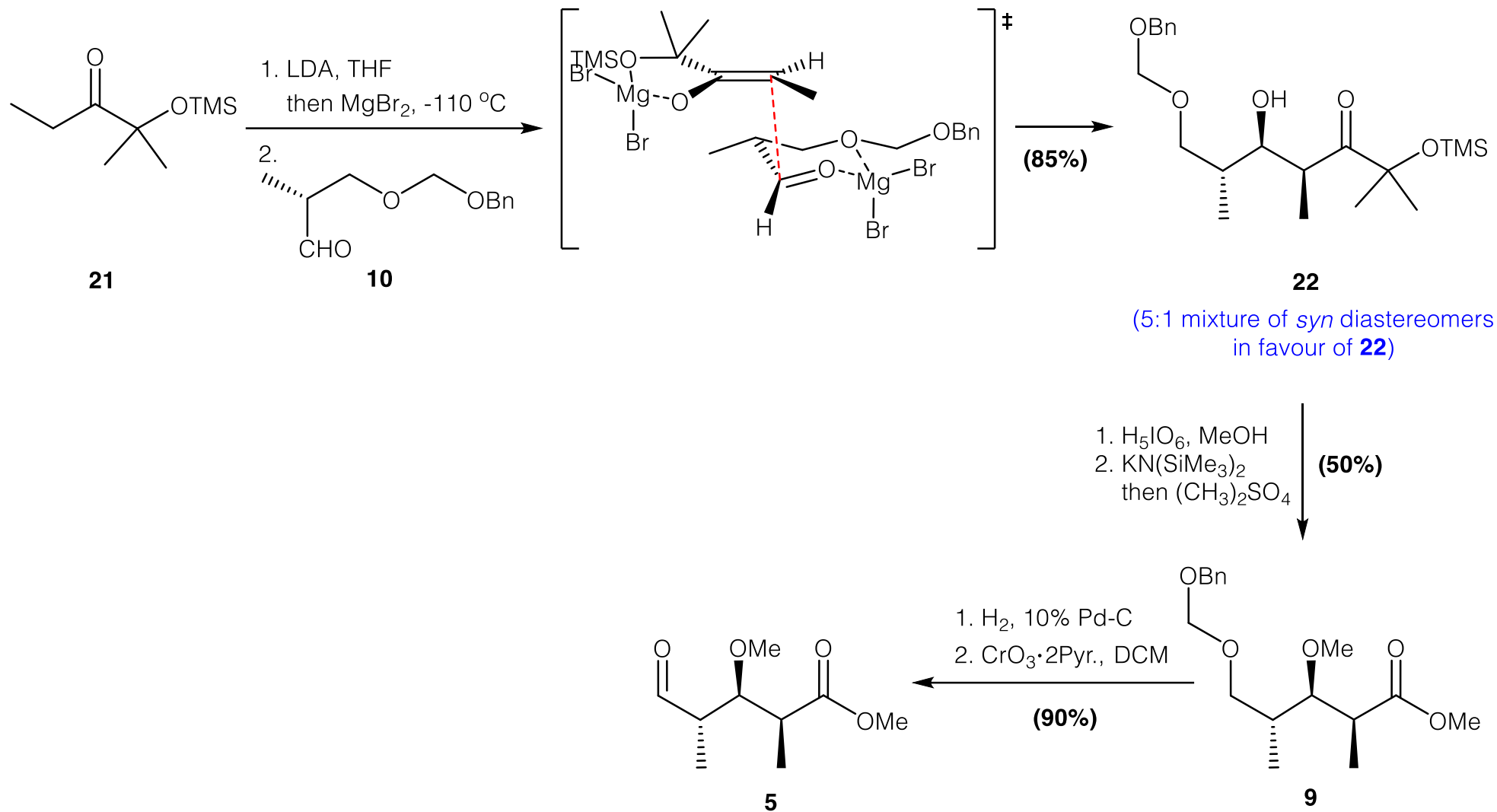
³ Collum, D. B.; McDonald, J. H.; Still, W. C. Synthesis of the Polyether Antibiotic Monensin. *J. Am. Chem. Soc.* **1980**, 102, 2117–2122



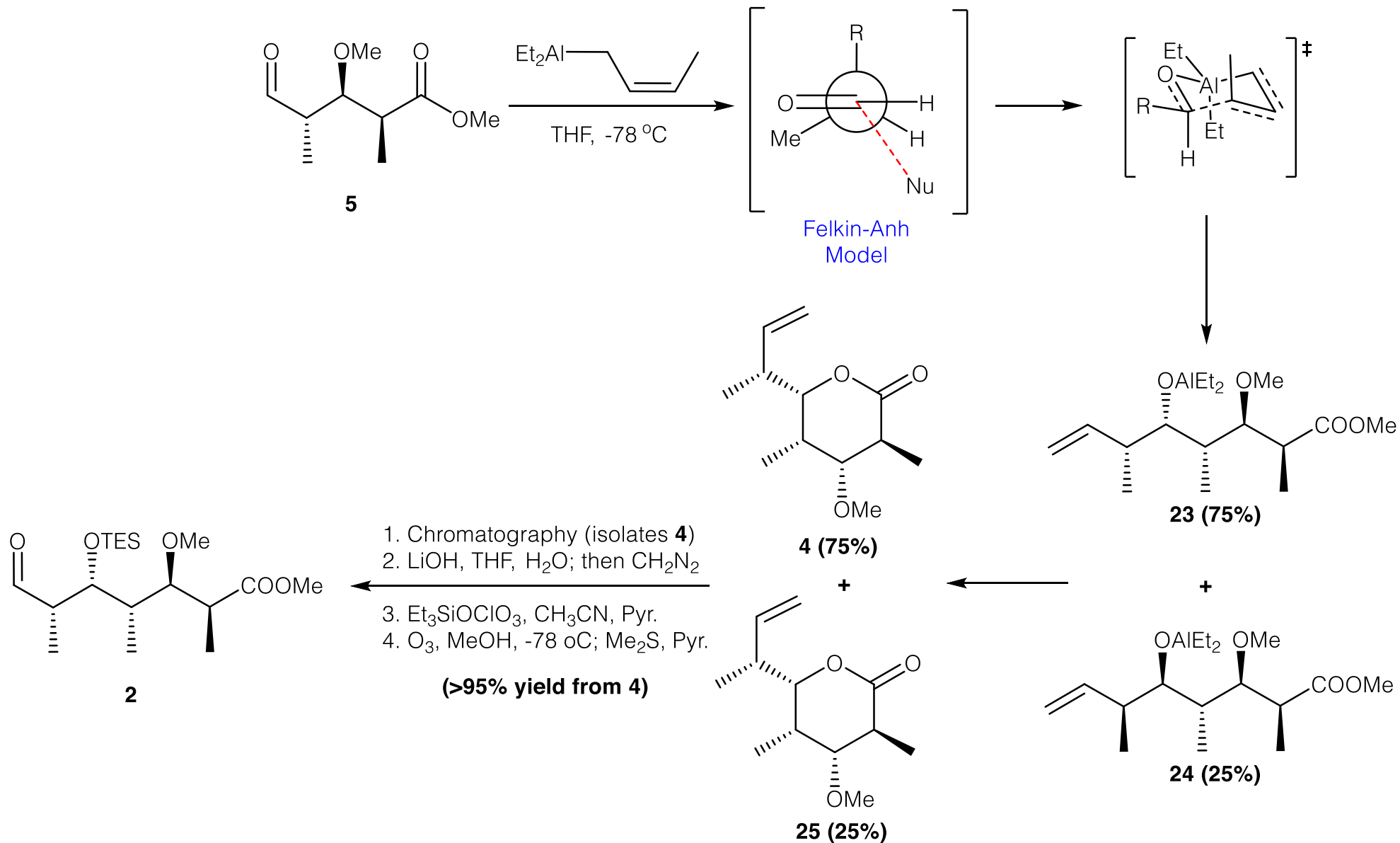
Retro-Synthetic Analysis



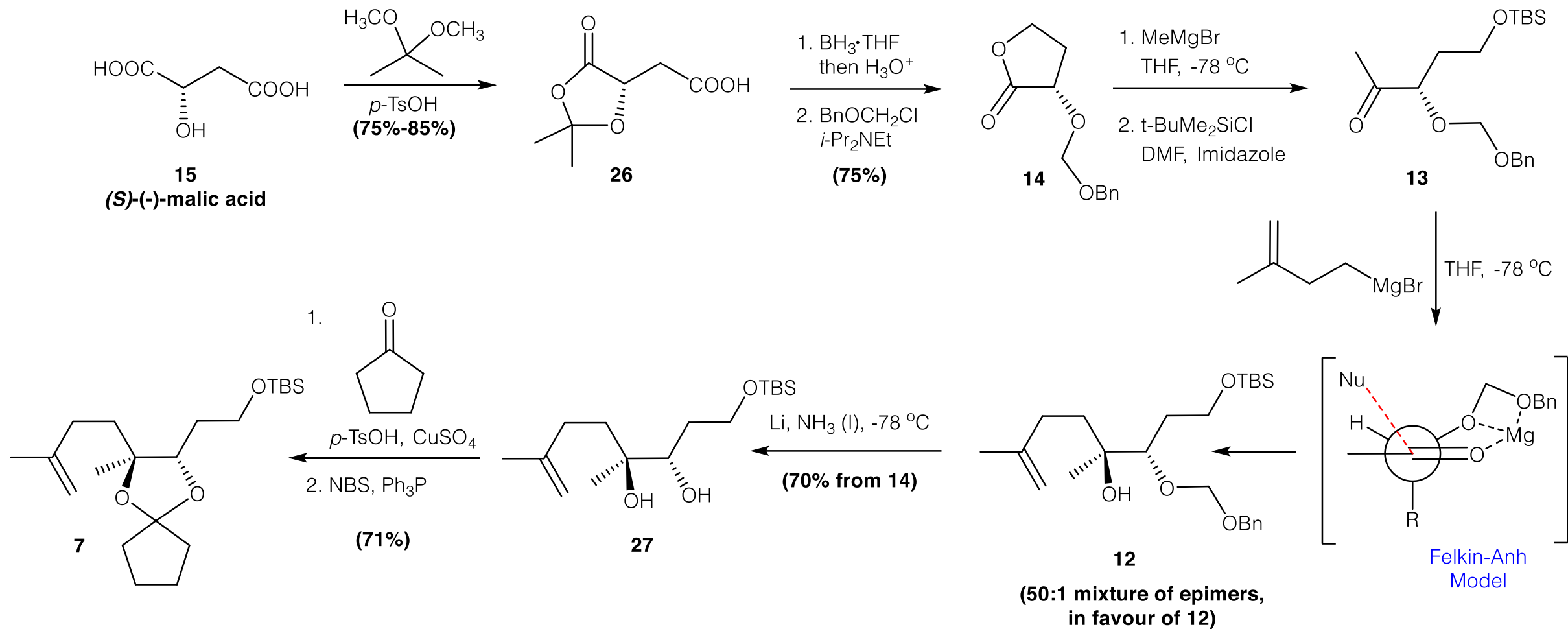
Synthesis of Monensin



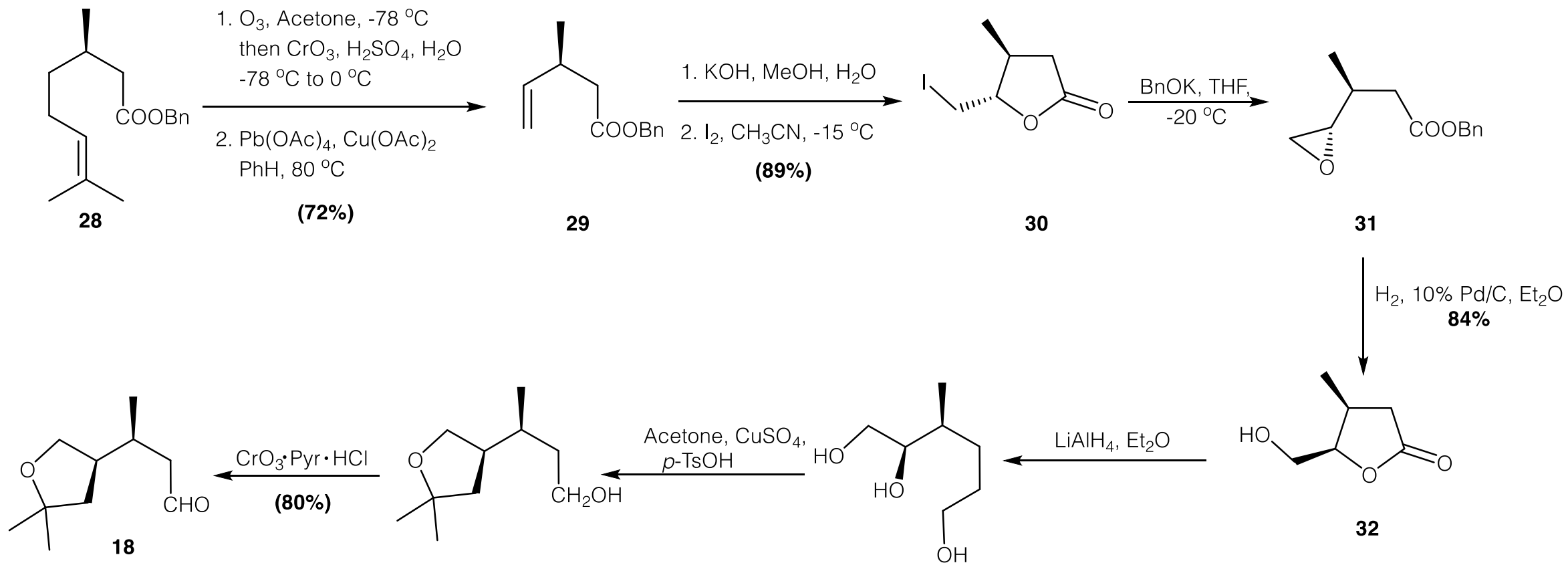
Synthesis of Monensin



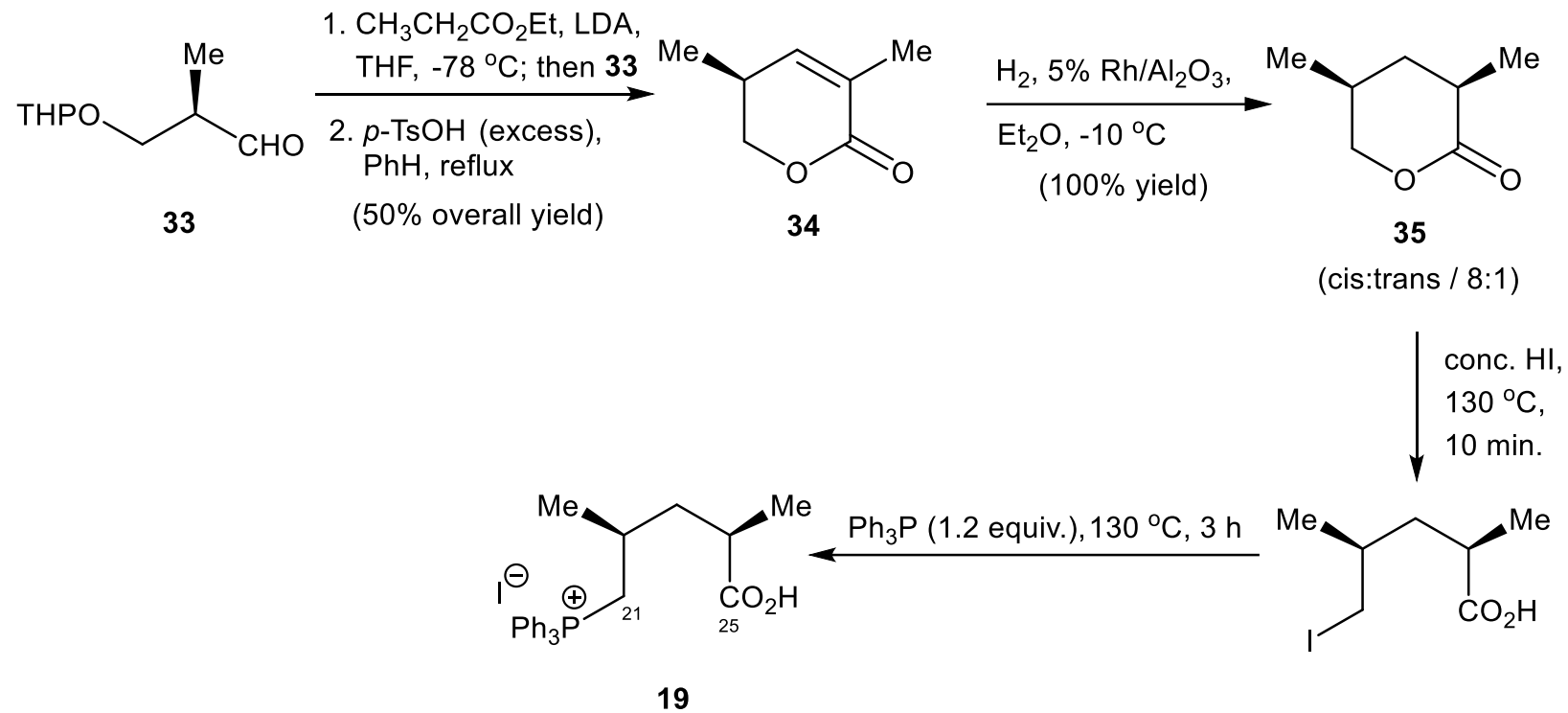
Synthesis of Monensin (*contd...*)



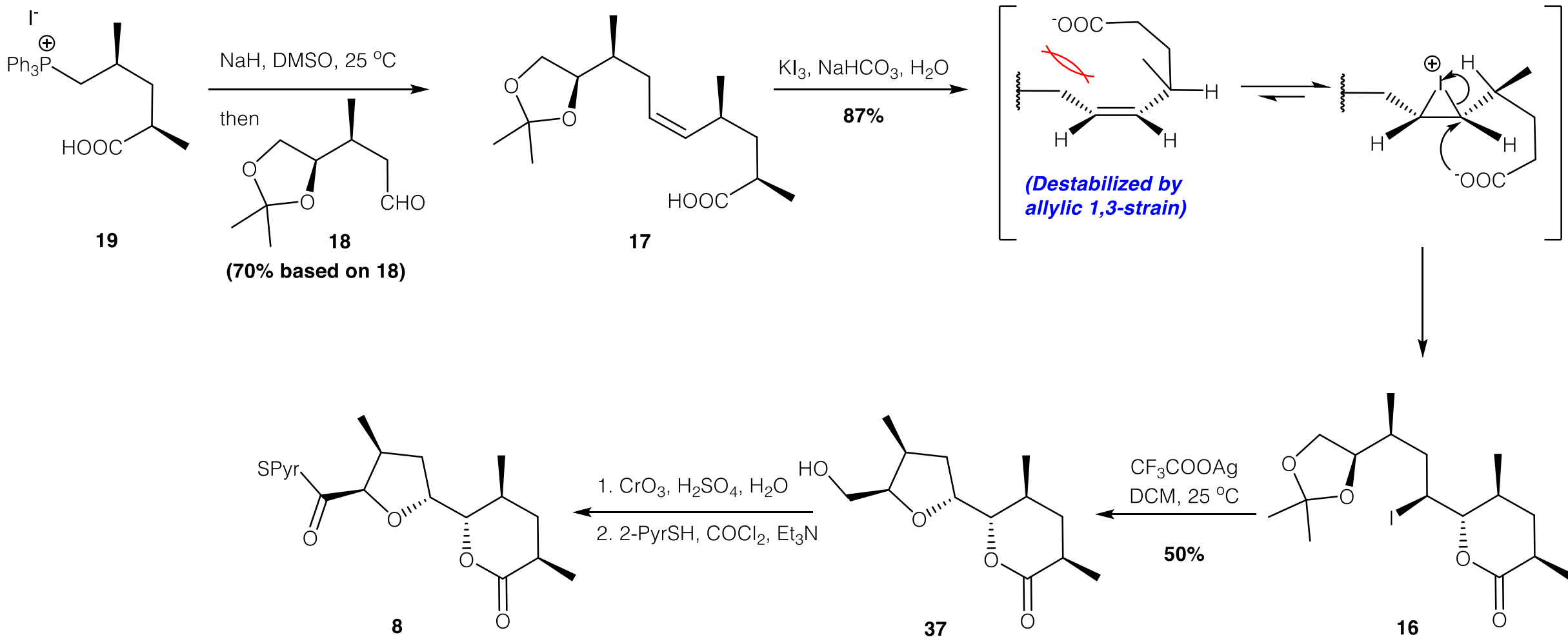
Synthesis of Monensin (*contd...*)



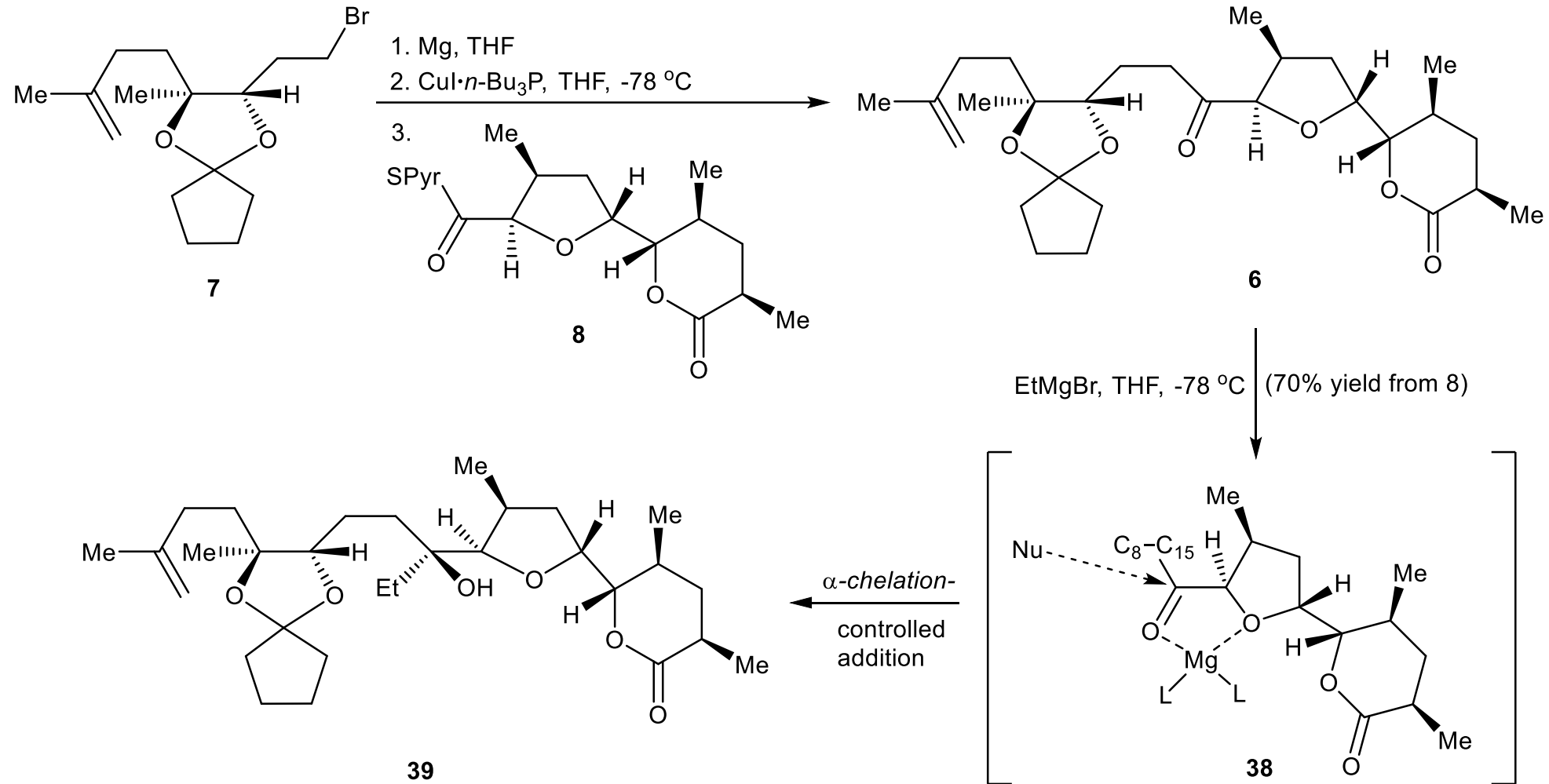
Synthesis of Monensin (*contd...*)



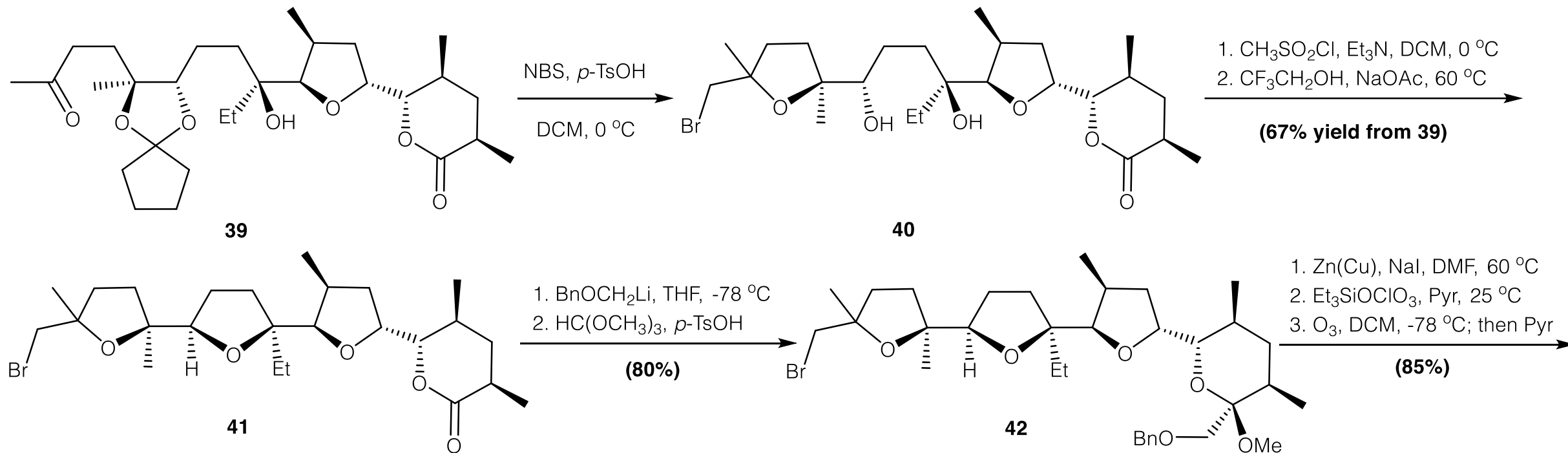
Synthesis of Monensin (*contd...*)



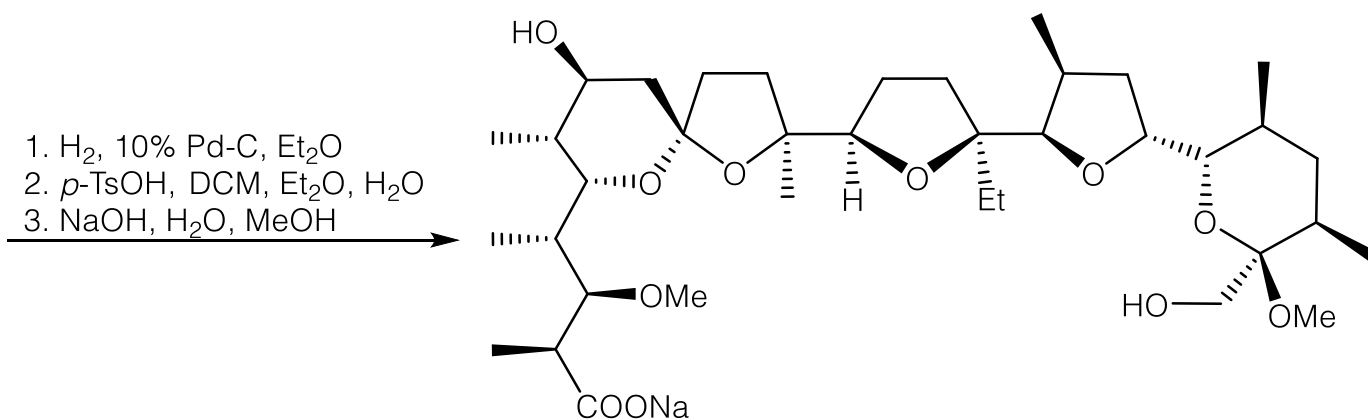
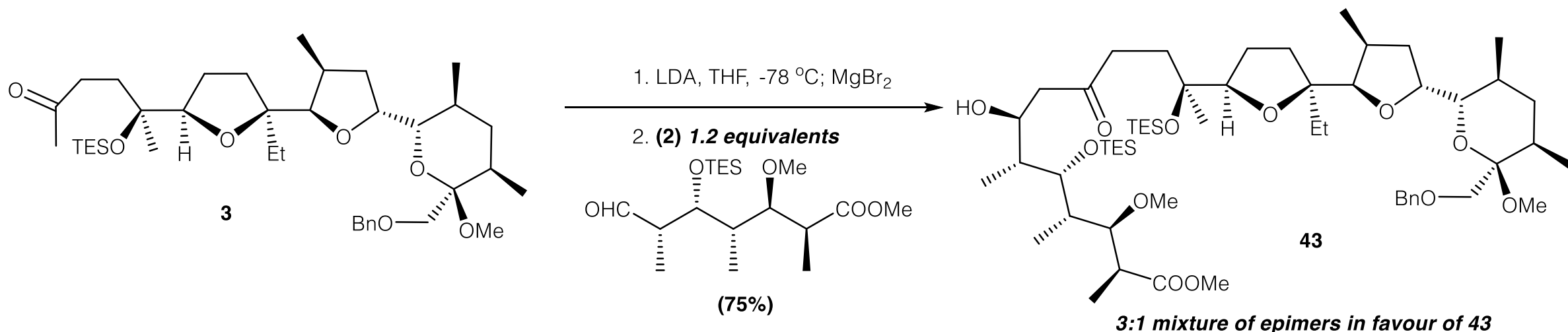
Synthesis of Monensin (*contd...*)



Synthesis of Monensin (*contd...*)



Synthesis of Monensin (*contd...*)



Sodium salt of (+)-monensin (1)



Conclusion

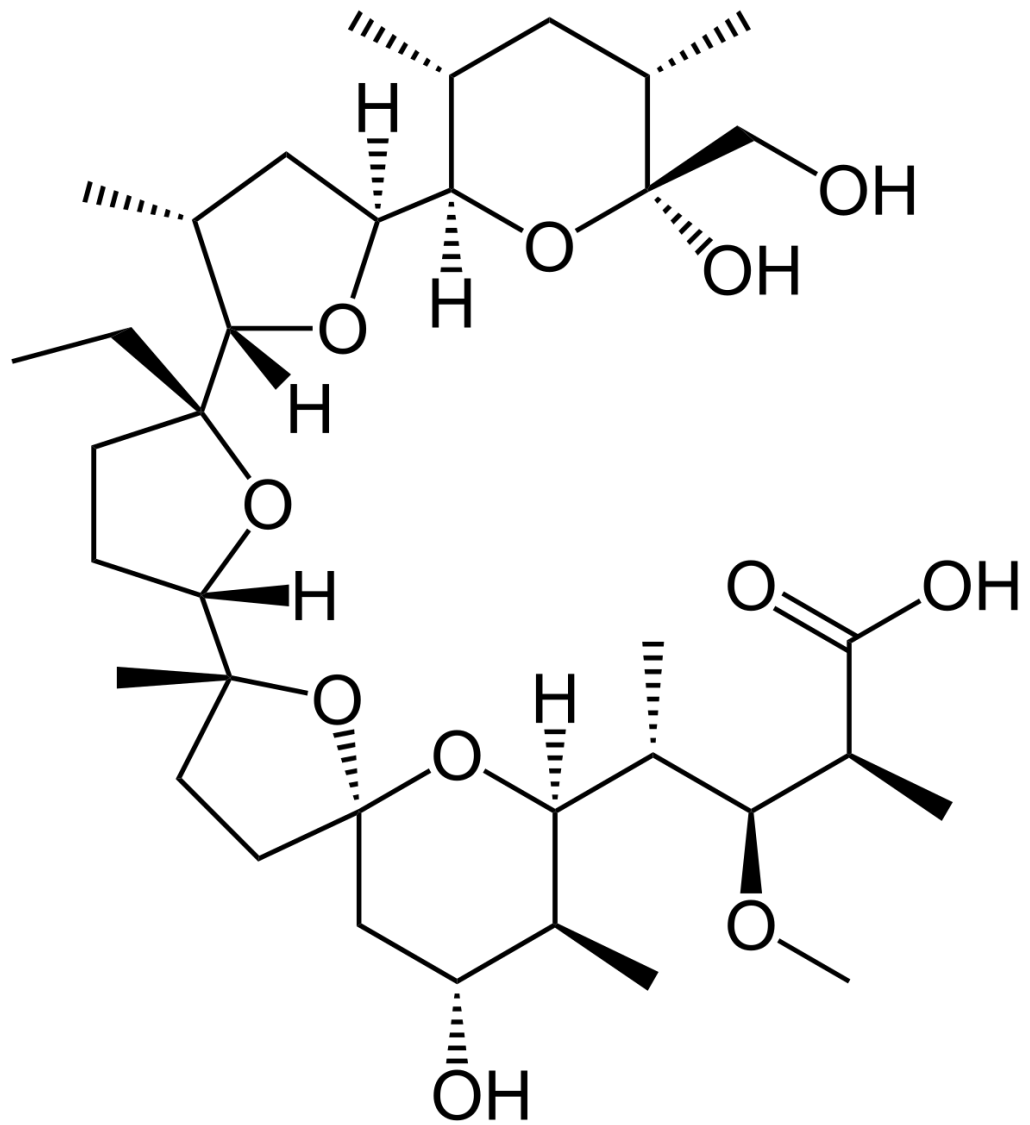
✓ Monensin was synthesized in a convergent synthetic pathway consisting of 34 steps.

Convergent synthetic pathway had been helpful improving the overall yield.

✓ Interesting stereo-controlled reactions were used. Out of the 17 stereocenters, only 3 were derived from the starting materials. Other 14 were generated by the stereo-controlled reaction.

✓ A stereo-controlled reaction type used multiple times in this pathway is controlling the stereochemistry of carbonyl C by *chelation of organometallic agents*.





Thank You !!!

