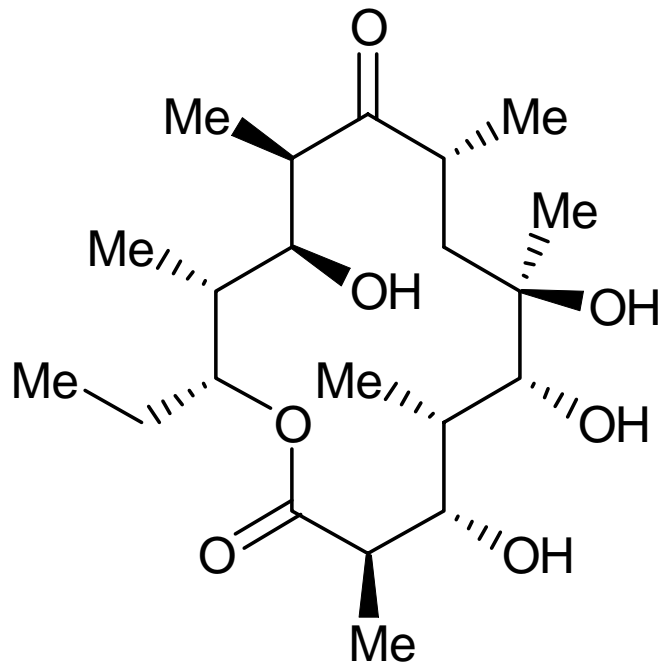


Total Synthesis of Erythronolide B

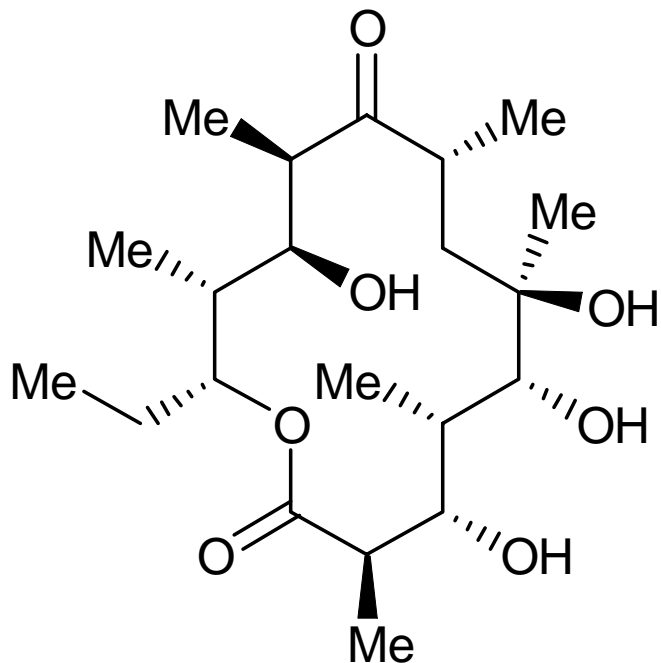


Guixing Wang

CEM 852

02/04/ 2005

Introduction

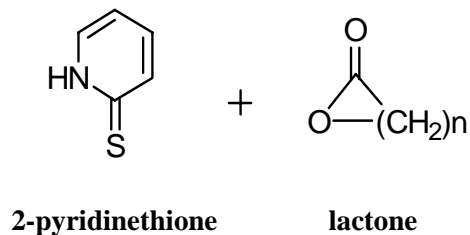
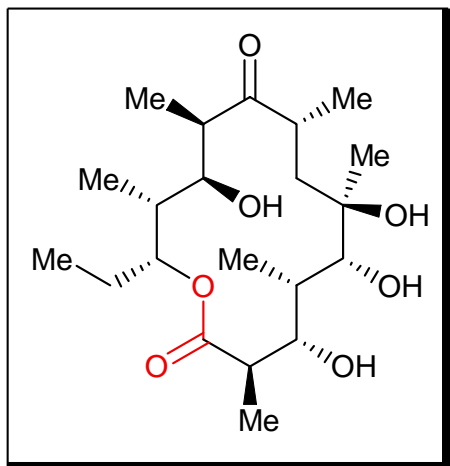
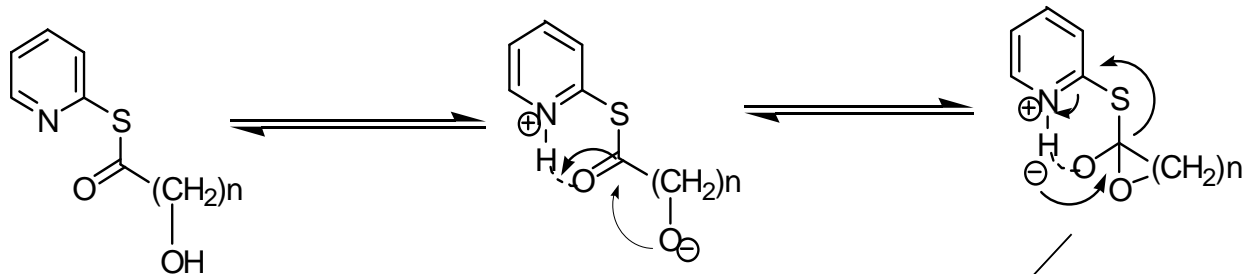


- 14-membered lactone
- 10 asymmetric carbon atoms
- Structure determined in 1950's
- Total synthesis in 1970's
- Construction of large lactone

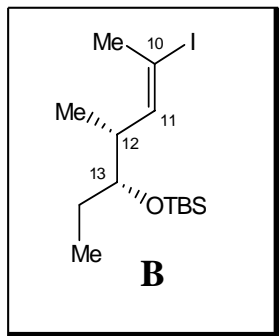
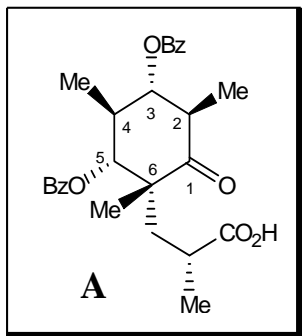
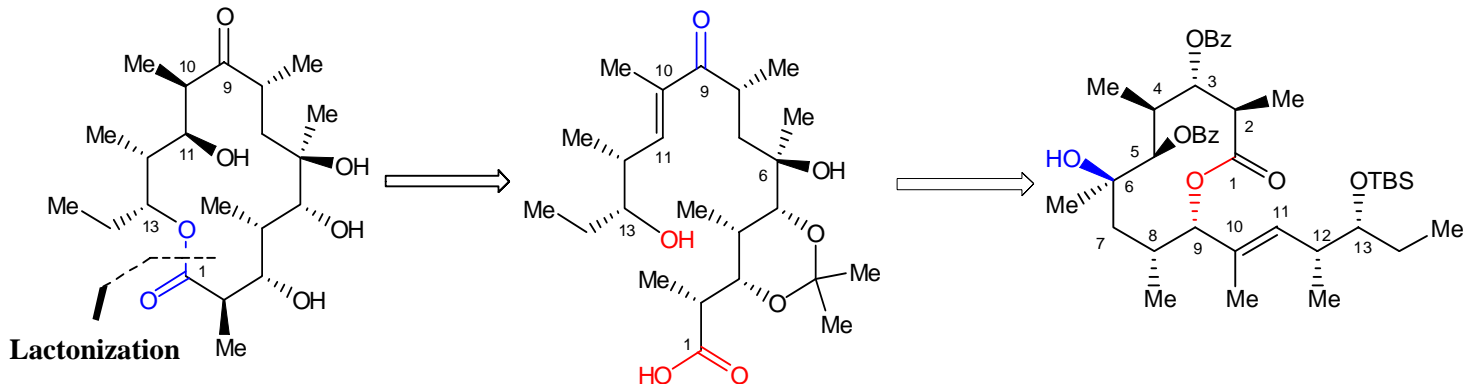
Flynn, E.H.; Sigal, M.V. Jr.; Wiley, P.F.; Gerzon, K. *J. Am. Chem. Soc.* **1954**, 76, 3121.

Corey, E.J.; Nicolaou, K.C. *J. Am. Chem. Soc.* **1974**, 96, 5614

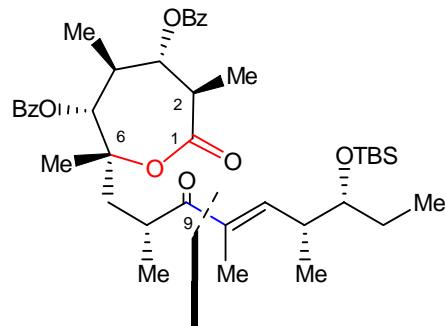
Corey-Nicolaou Macrolactonization Strategy



Retrosynthetic Analysis and Strategy

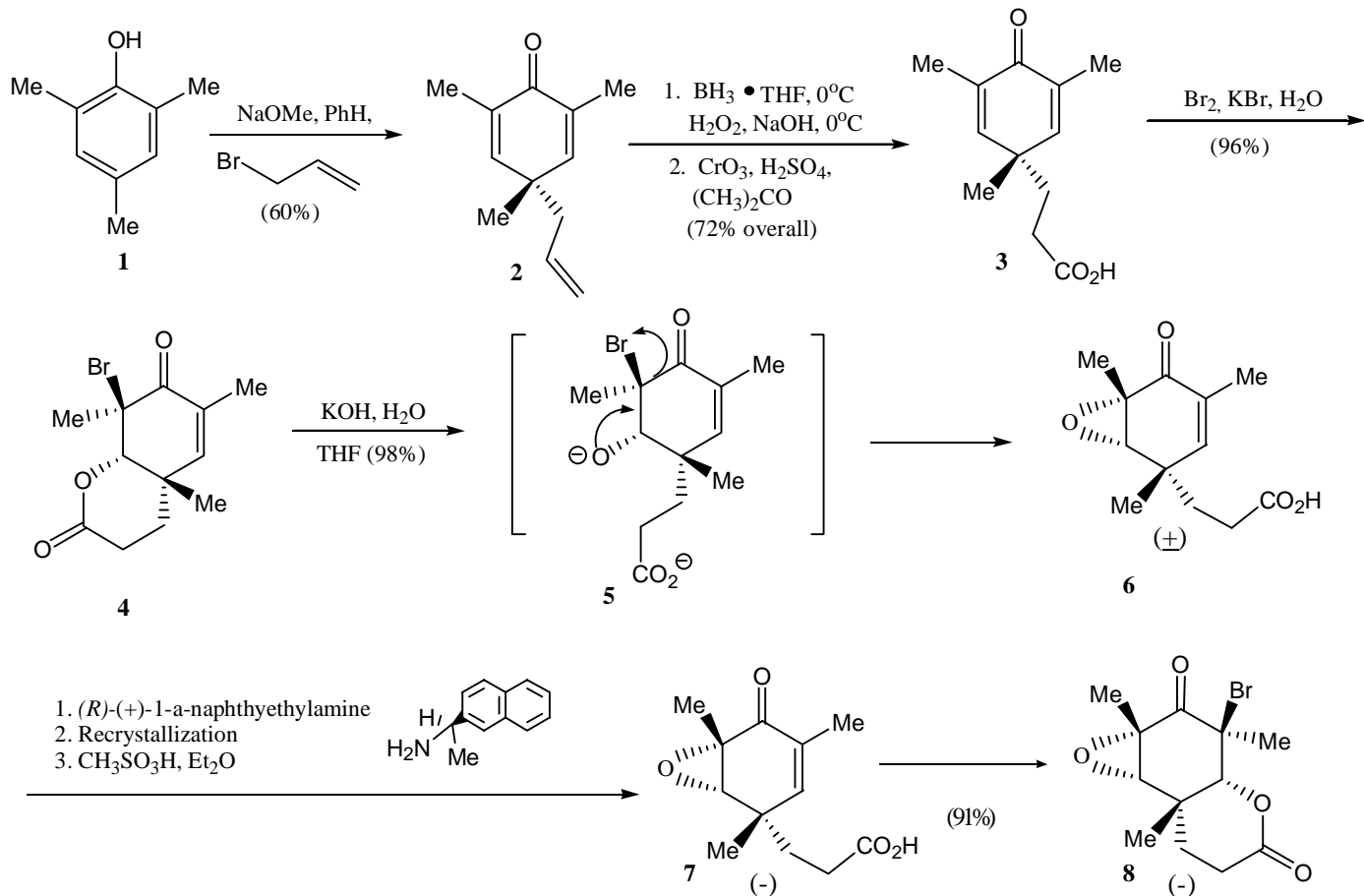


Bayer-Villiger



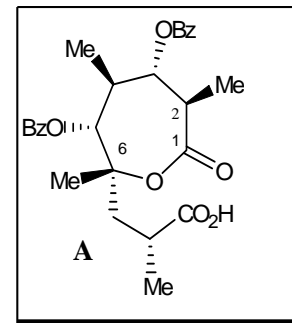
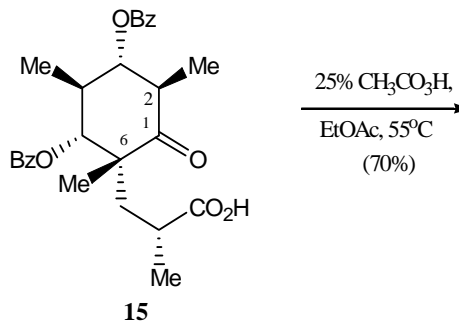
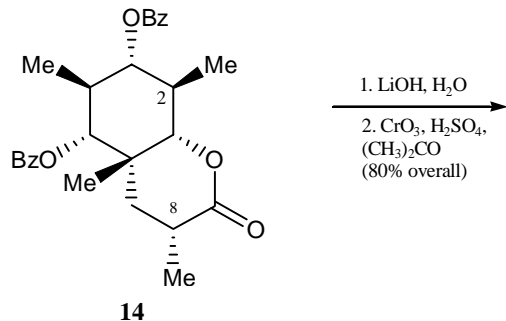
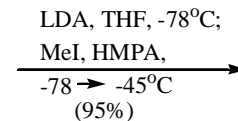
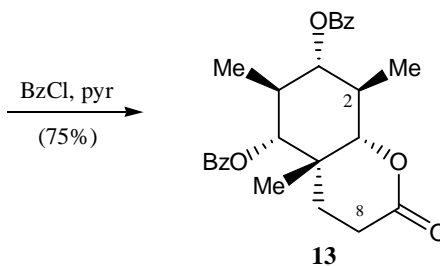
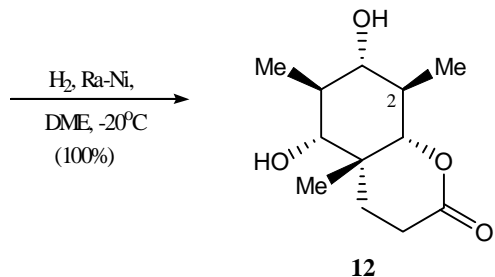
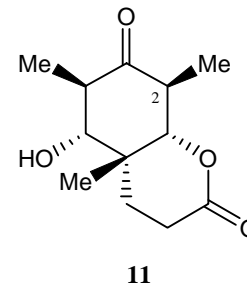
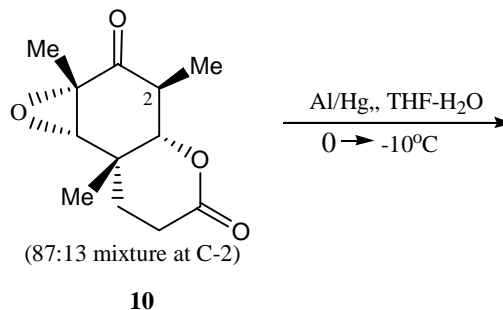
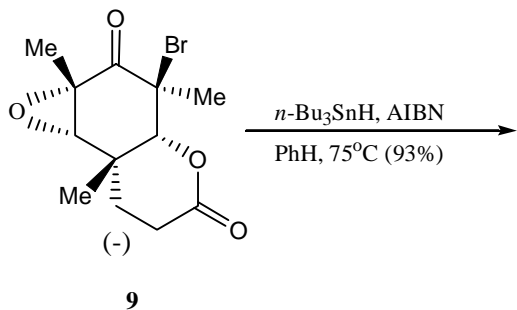
C-C bond formation

Synthesis of A

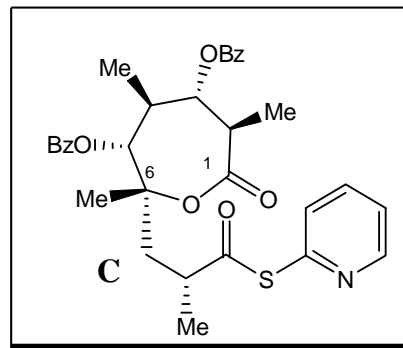
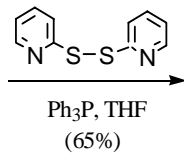
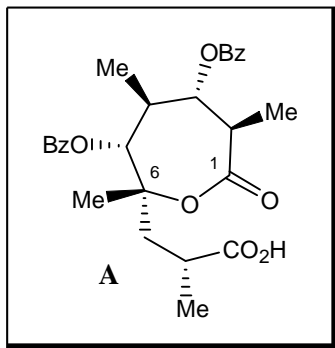


Absolute configuration confirmed by X-ray crystallography

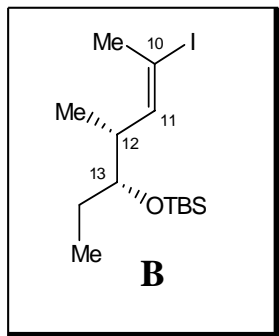
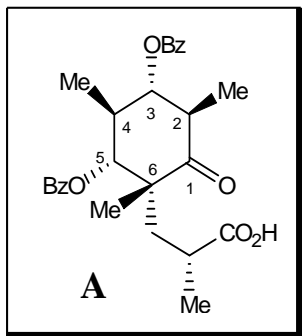
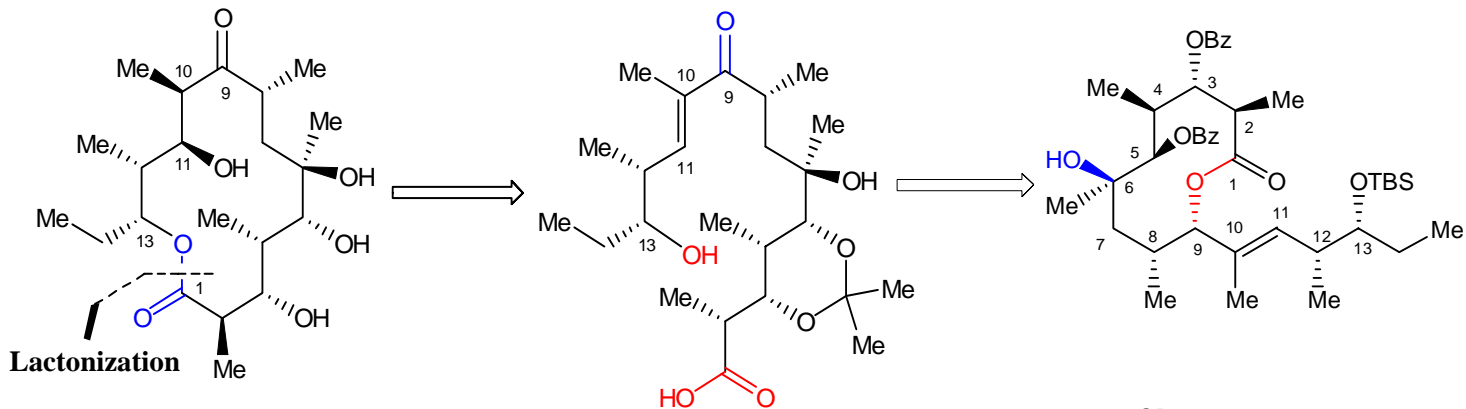
Synthesis of A (Continued)



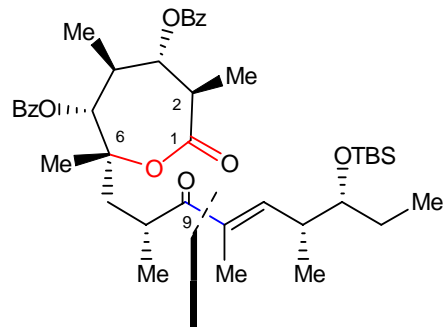
Synthesis of A (Continued)



Retrosynthetic Analysis and Strategy

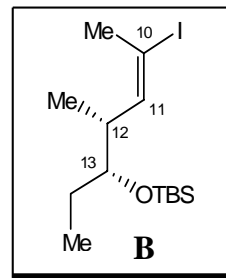
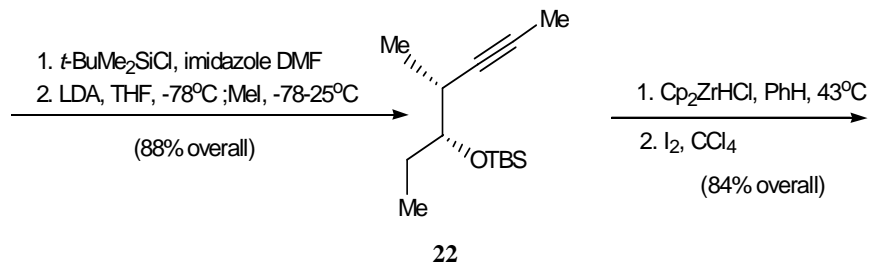
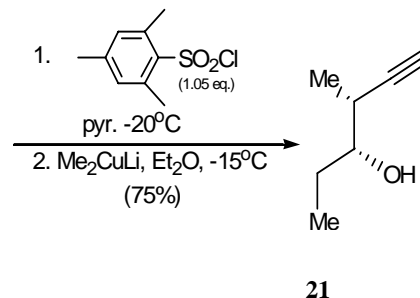
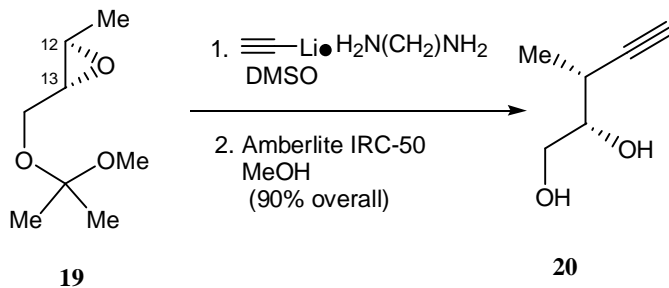
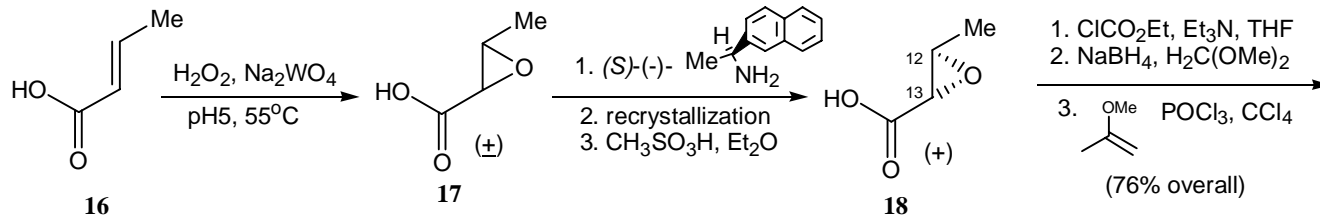


Bayer-Villiger

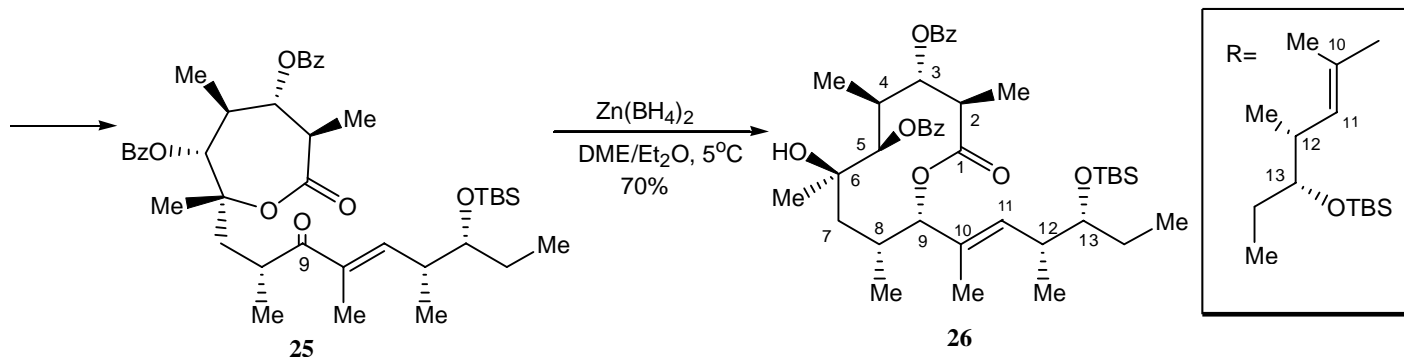
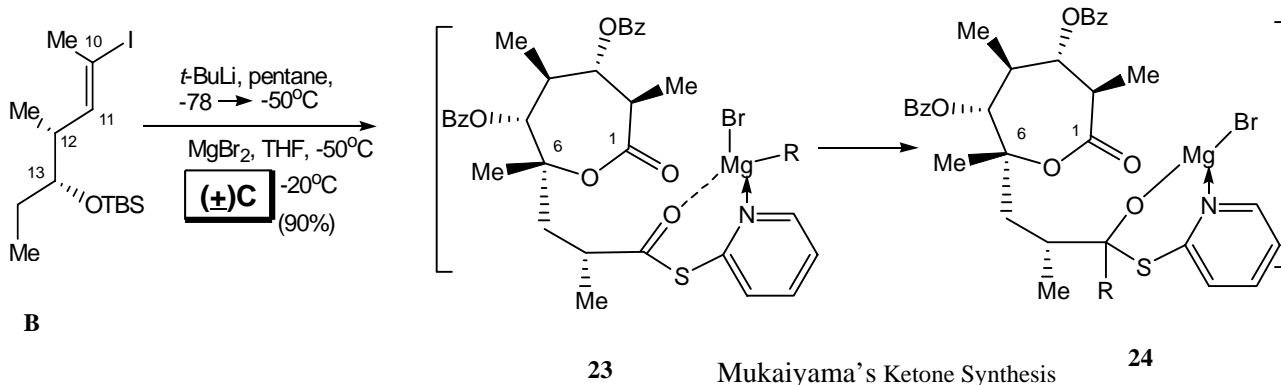


C-C bond formation

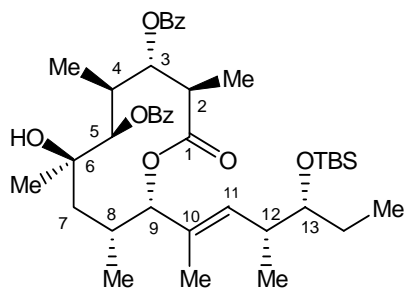
Synthesis of B



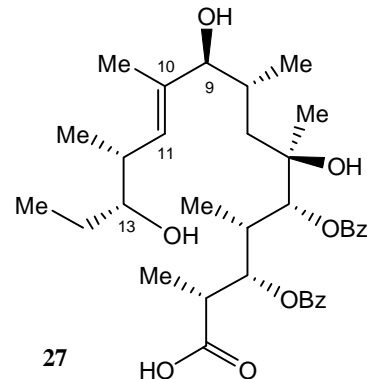
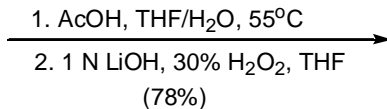
Synthesis of Erythronolide B (**B** + **C**)



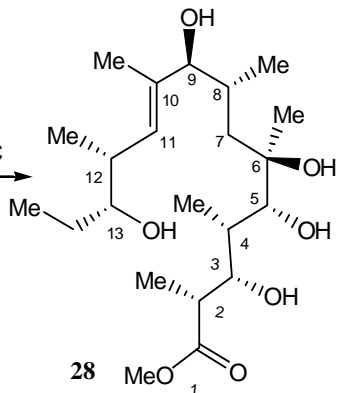
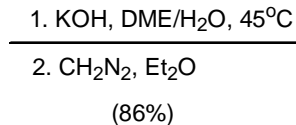
Synthesis of Erythronolide B (**B** + **C**) (Cont.)



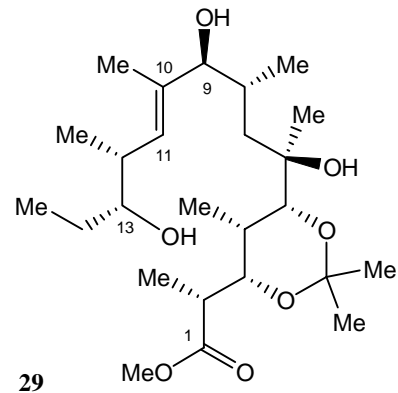
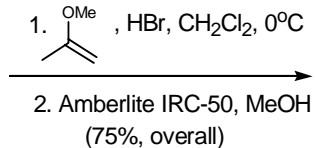
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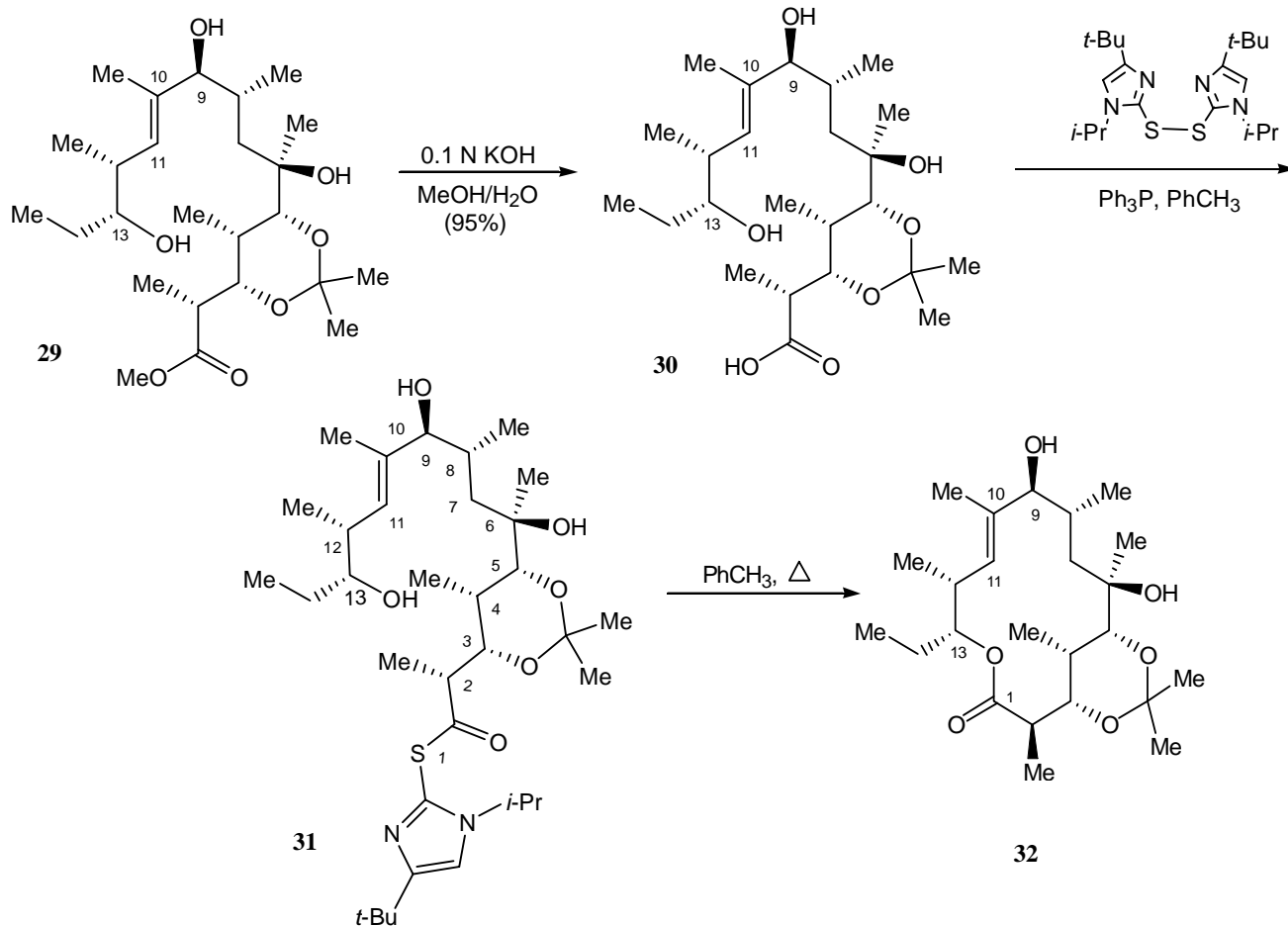


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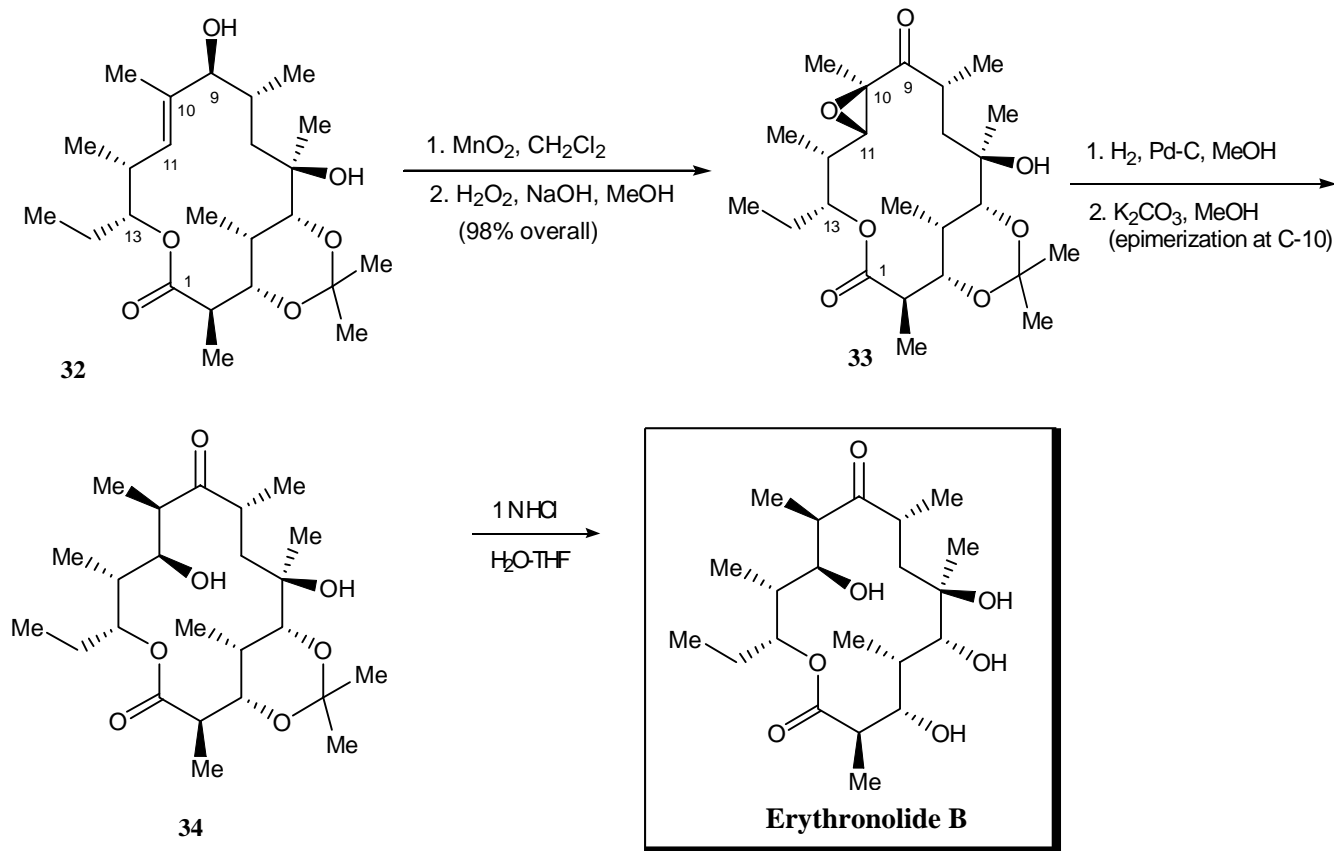


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Synthesis of Erythronolide B (**B** + **C**) (Cont.)



Synthesis of Erythronolide B (**B** + **C**) (Cont.)



Conclusion

- Bromolactonization: create asymmetric carbons
- Bayer-Villiger oxidation: regioselective & stereospecific
- Mukaiyama's ketone synthesis: coordinated tetrahedral intermediate
- Corey-Nicolaou double activation method: form large-ring lactone