

First isolated in 1950, however synthetic methods did not develop for another 20 years

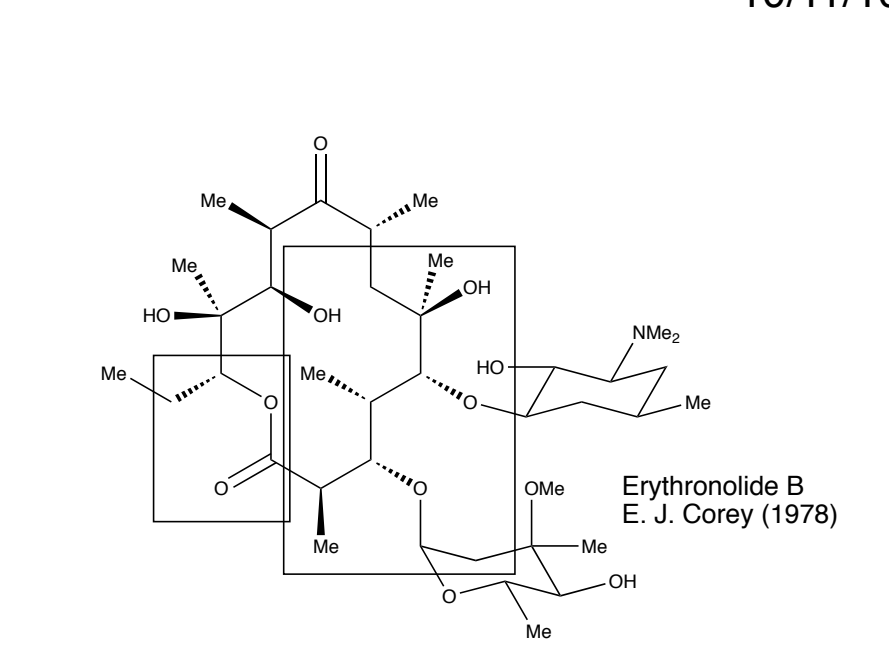
Polyketide class of natural products

Macrocyclic lactone sugars can be attached

Commonly found from marine sources.

Extremely limited in supply. 13 tons of sponge yielded 35 mg of natural product, and currently biosynthesis is the preferred method of production

Typically used for antibiotics but are also among the most potent cancer cell growth inhibitory agents tested to date



Antibacterial agent with wide use in therapy

Woodward was quoted in 1956 as saying, "Erythromycin, with all your advantages, looks at present quite hopelessly complex, particularly in view of its plethora of asymmetric centers."

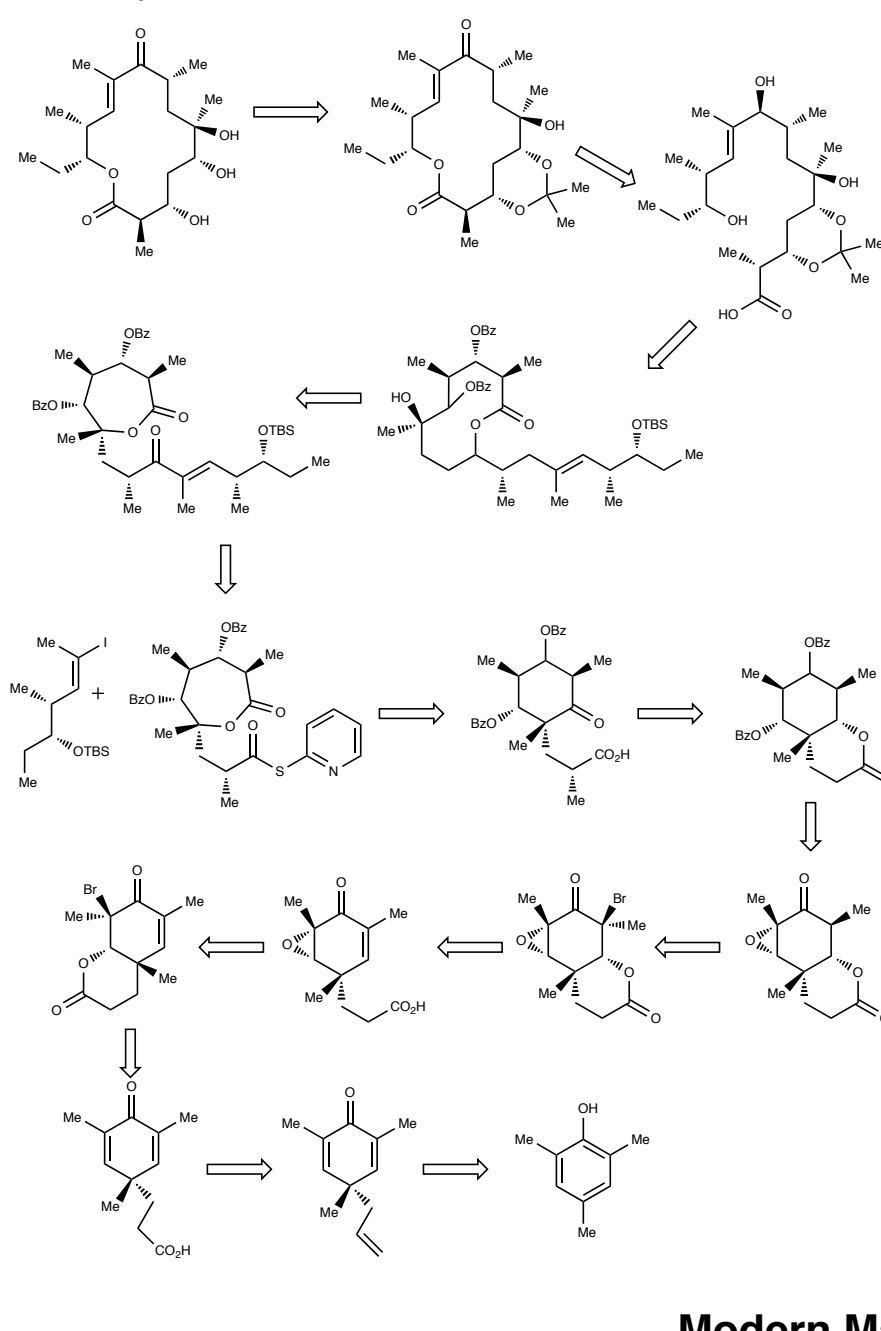
Possesses 10 asymmetric carbons

No way to successfully construct large-ring lactones had yet been discovered.

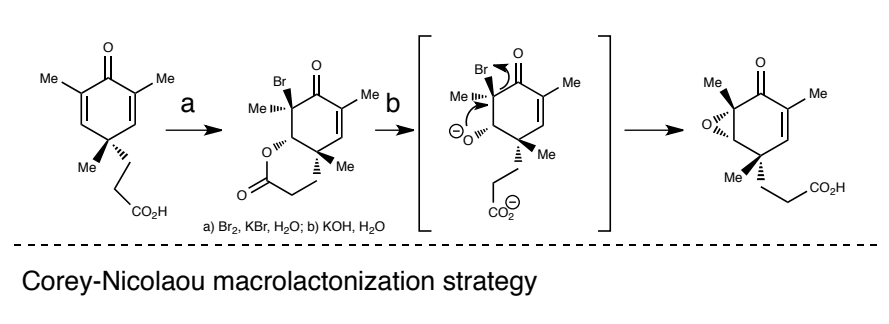
Gaul, C., J. T. Njardarson, et al. (2004). "The Migrastatin Family: Discovery of Potent Cell Migration Inhibitors by Chemical Synthesis." *Journal of the American Chemical Society* 126(36): 11326-11337.

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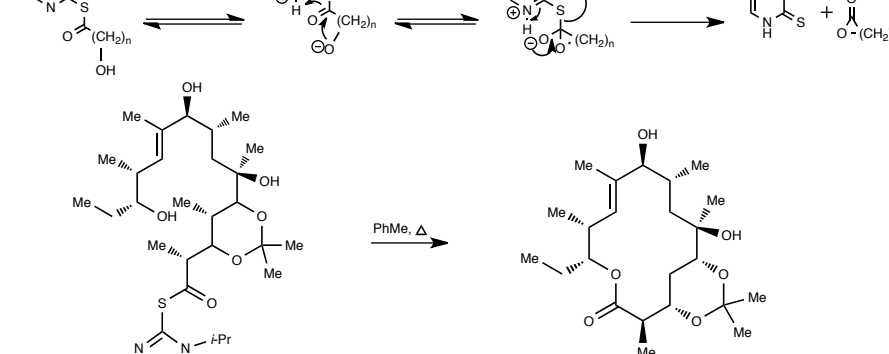
Retrosynthesis



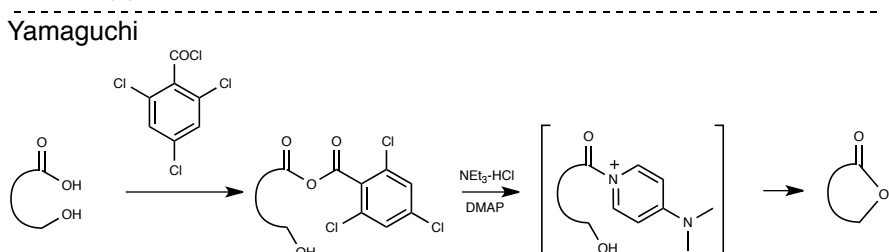
Bromolactonization



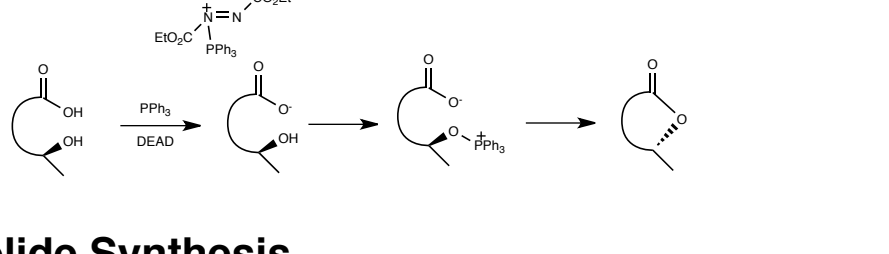
Corey-Nicolau macrolactonization strategy



Yamaguchi

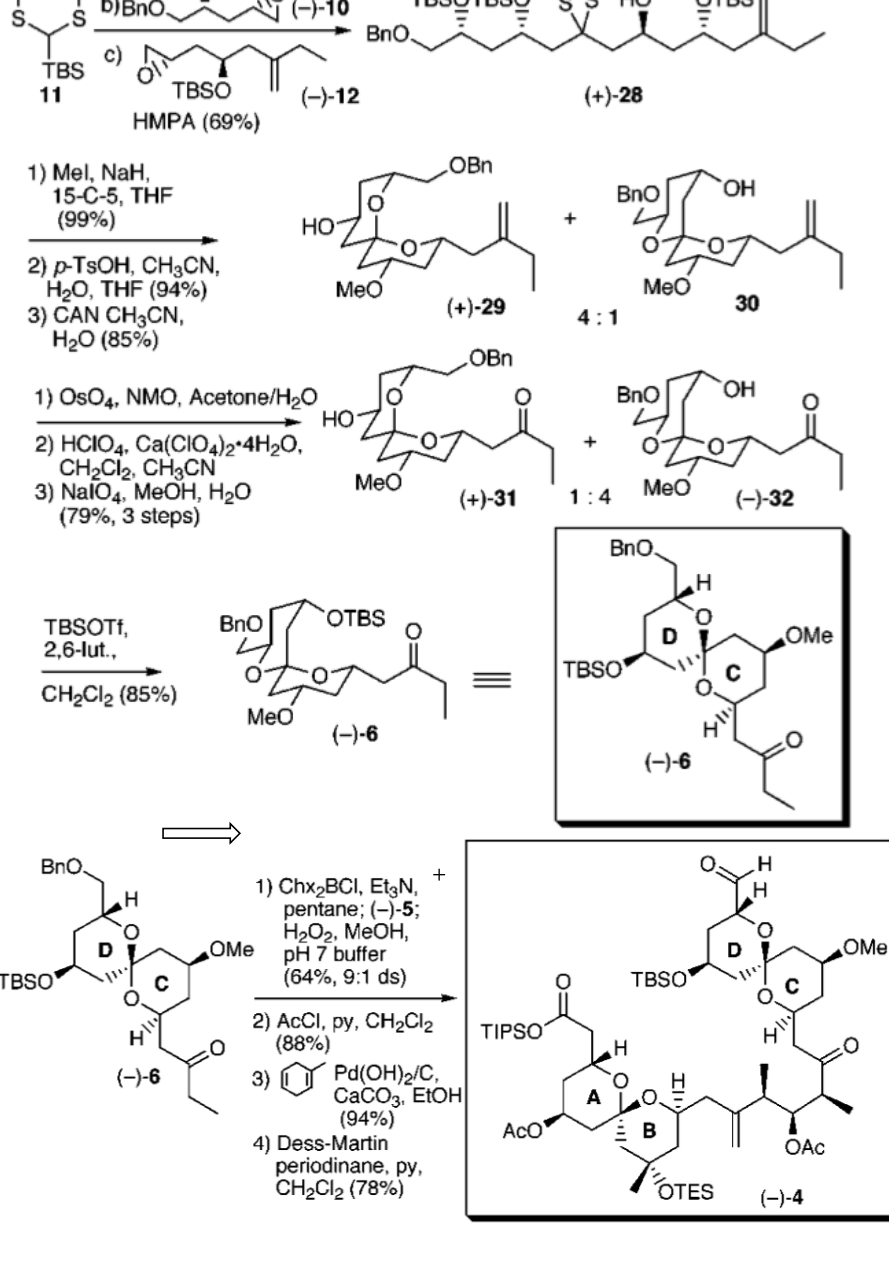
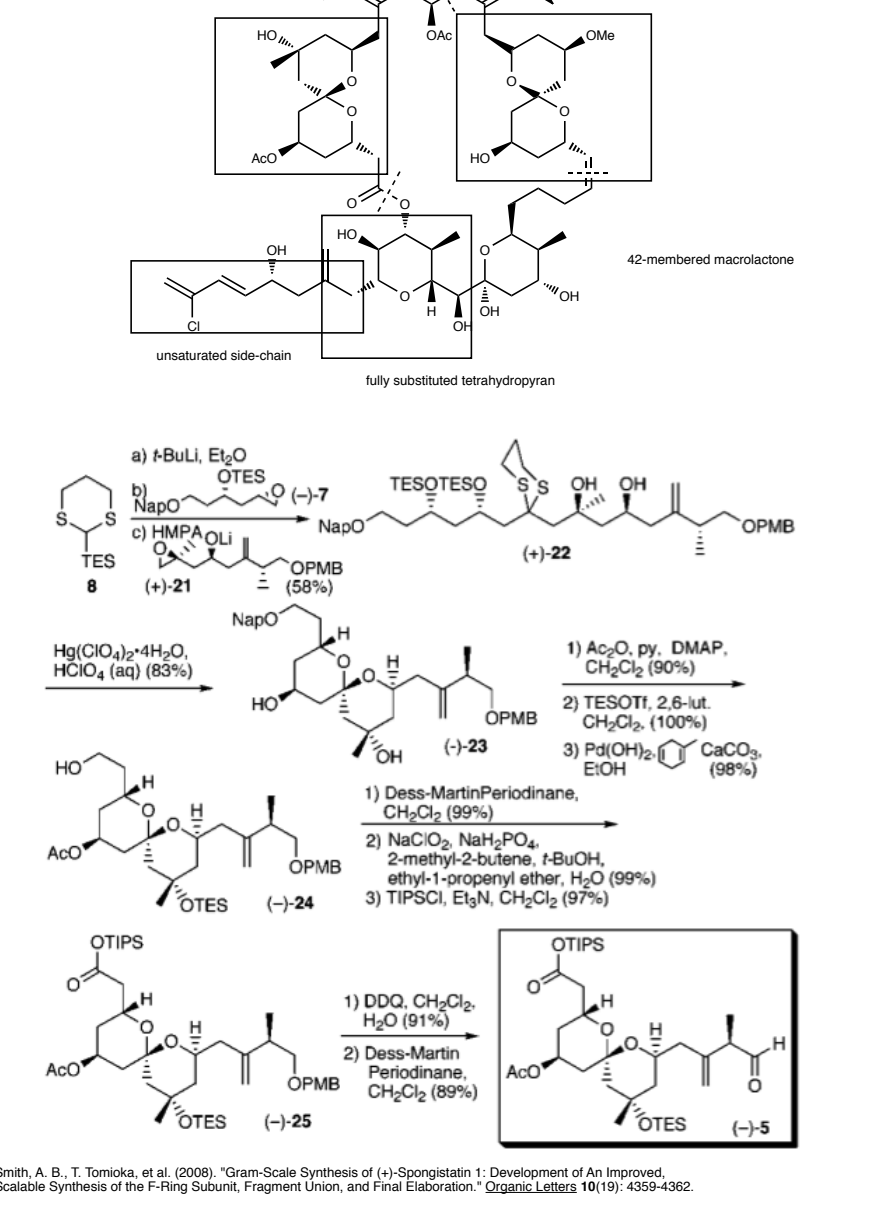


Mitsunobo



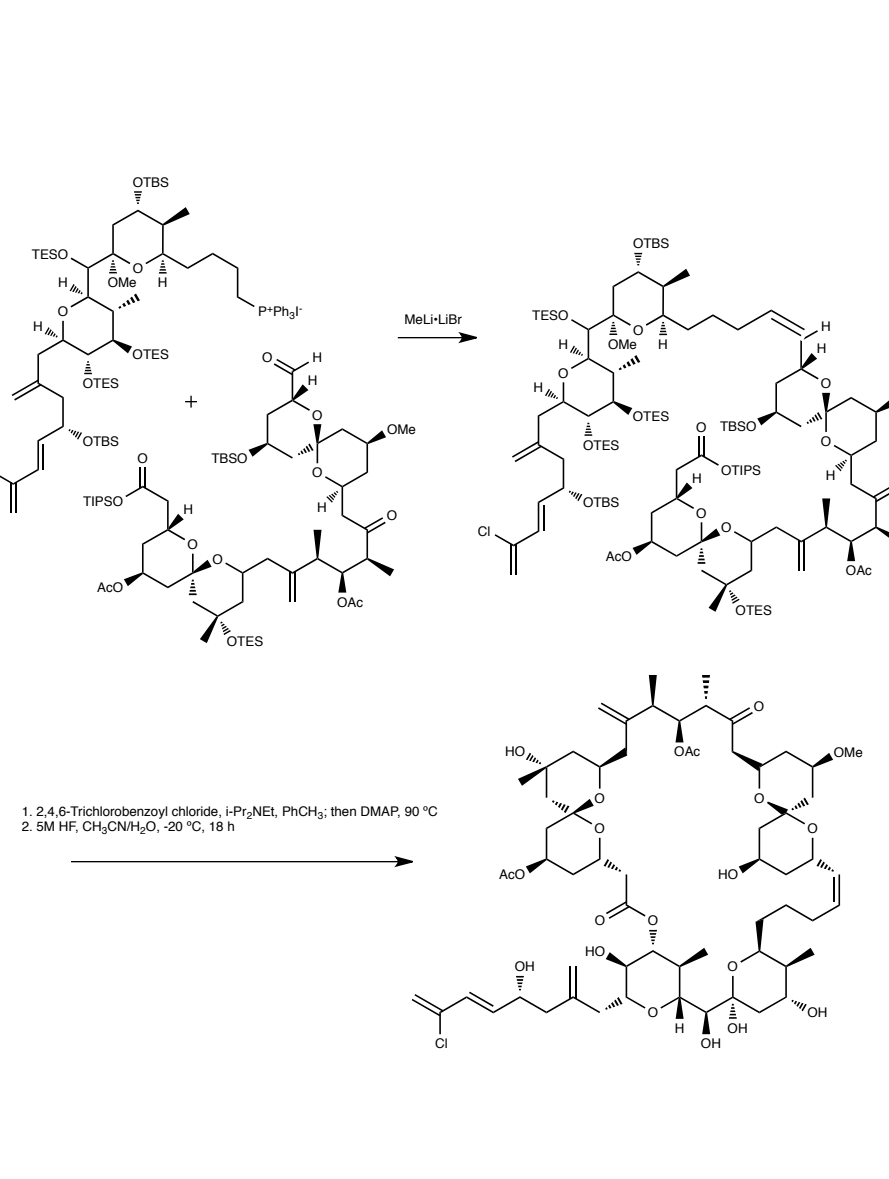
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Spongistatin 1



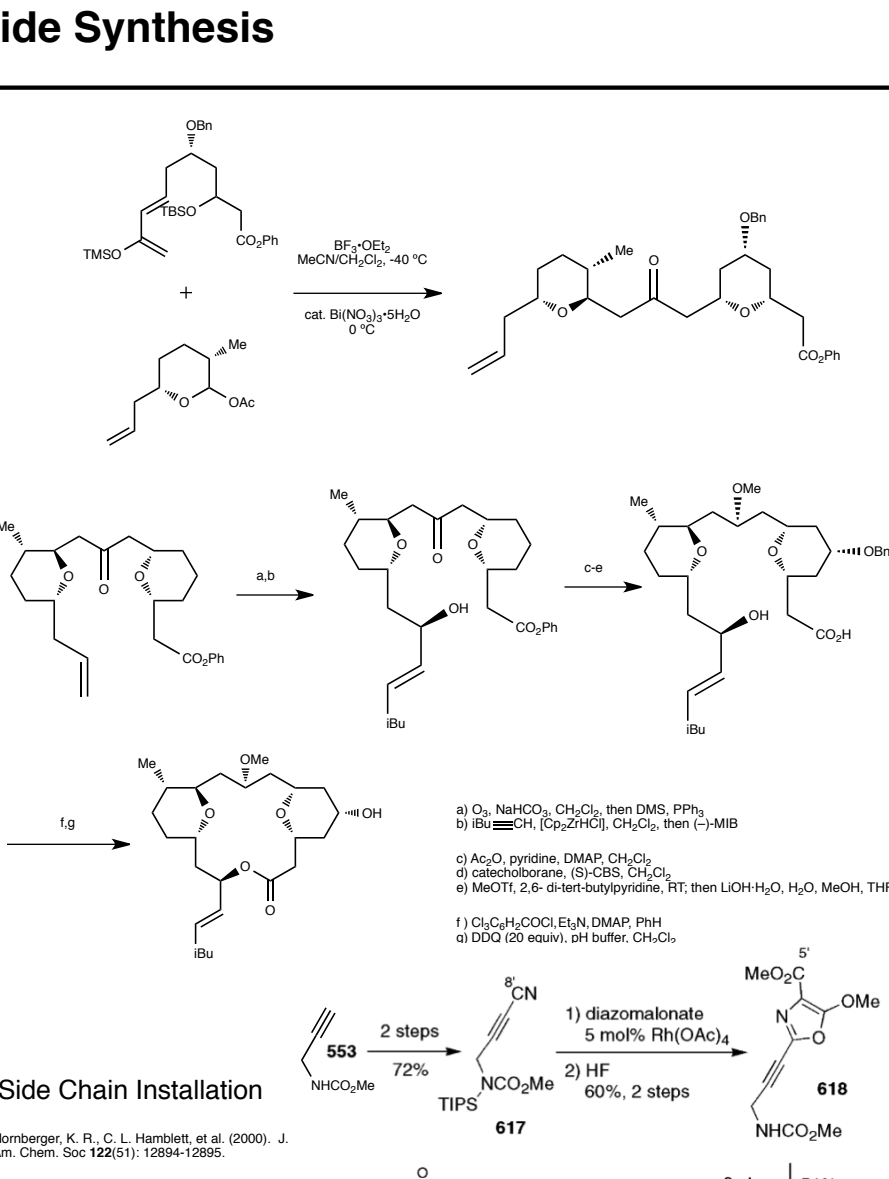
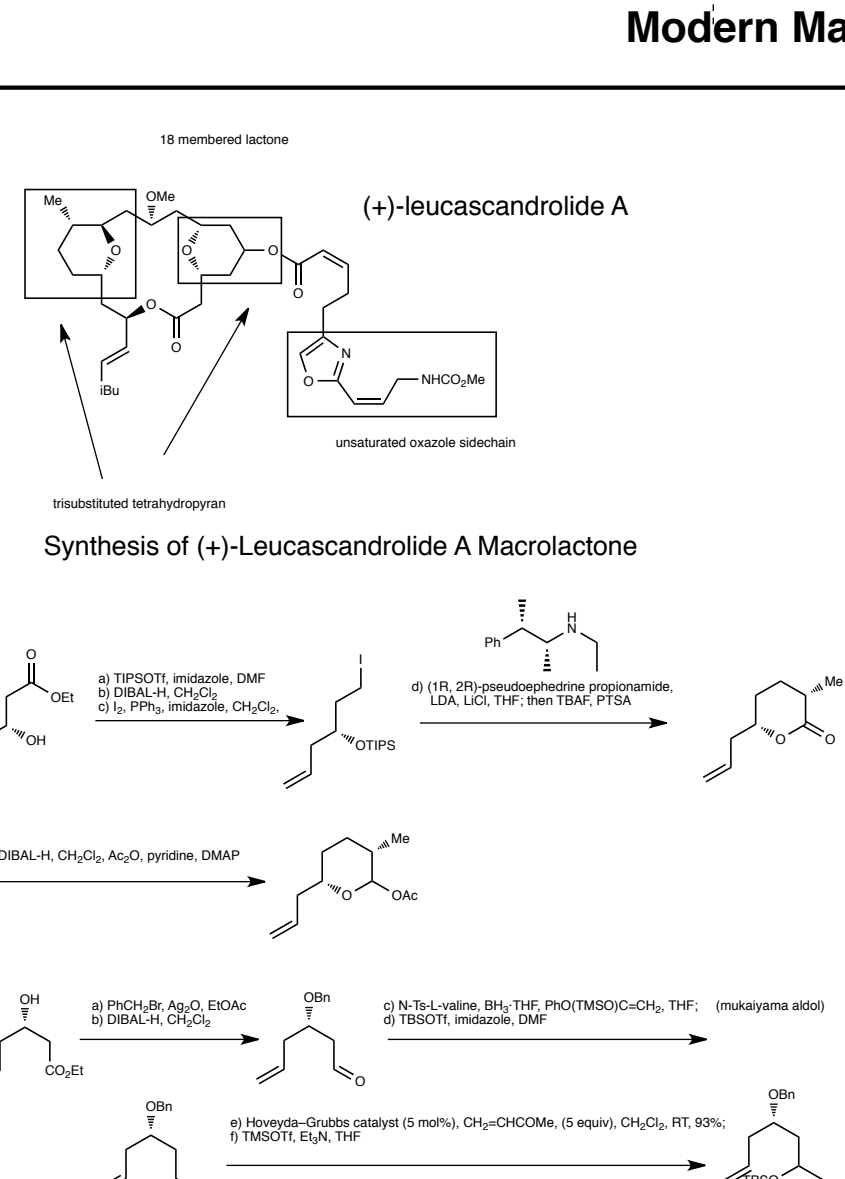
Smith, A. B., T. Tomoka, et al. (2006). "Oran-Scale Synthesis of (+)-Spongistatin 1: Development of An Improved Scalable Synthesis of the F-Ring Subunit, Fragment Union, and Final Elongation." *Organic Letters* 19(19): 4306-4307.

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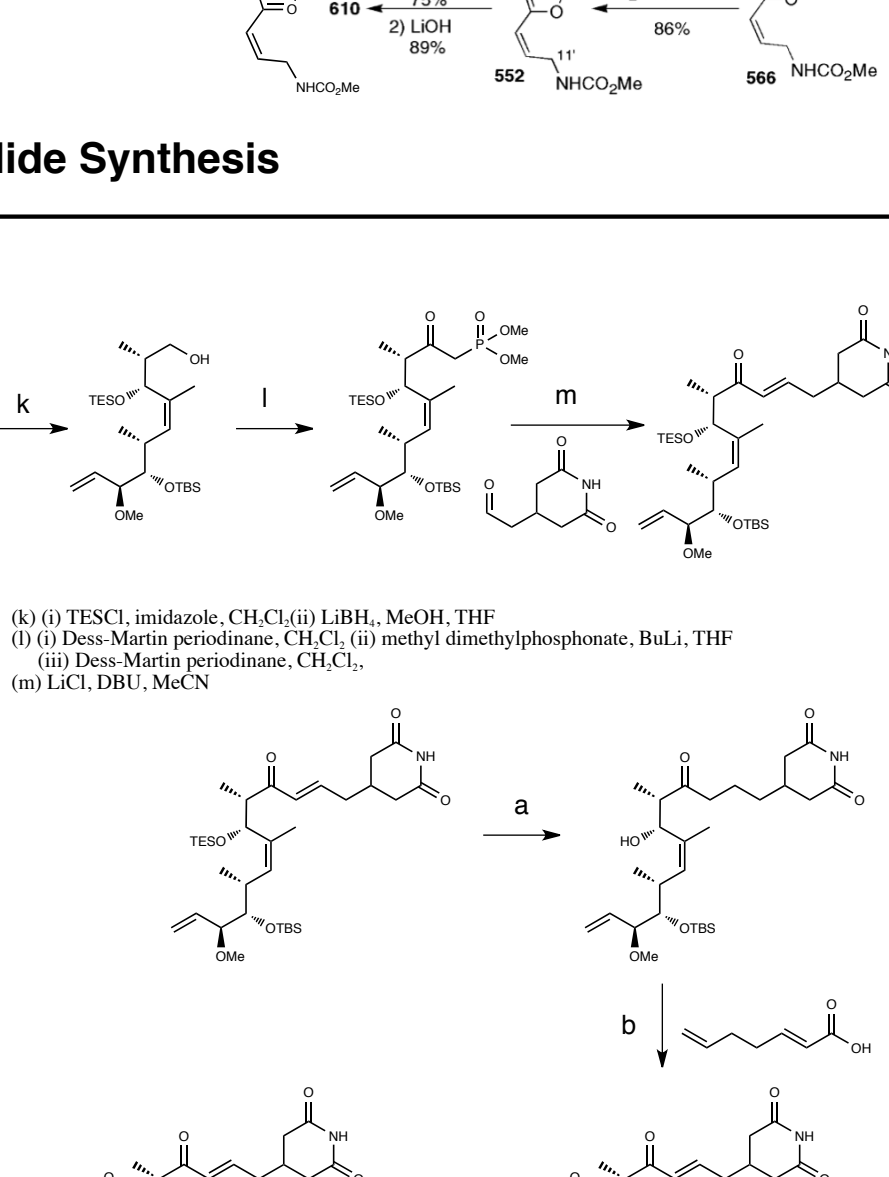
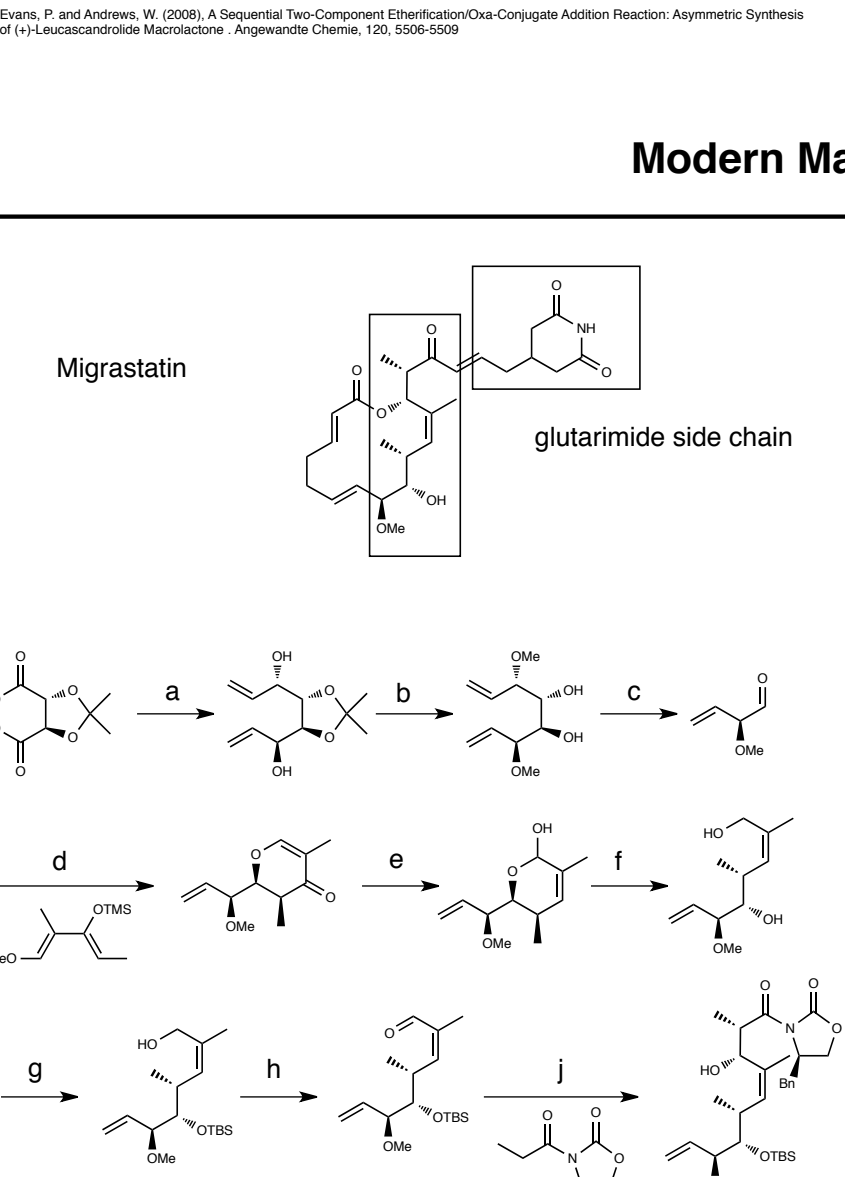
Evans, P. and Andrews, W. (2006). A Sequential Two-Component Etherification/Oxa-Conjugate Addition Reaction: Asymmetric Synthesis of (+)-Leucascandrolide Macrolactone. *Angewandte Chemie*, 118, 5056-5059

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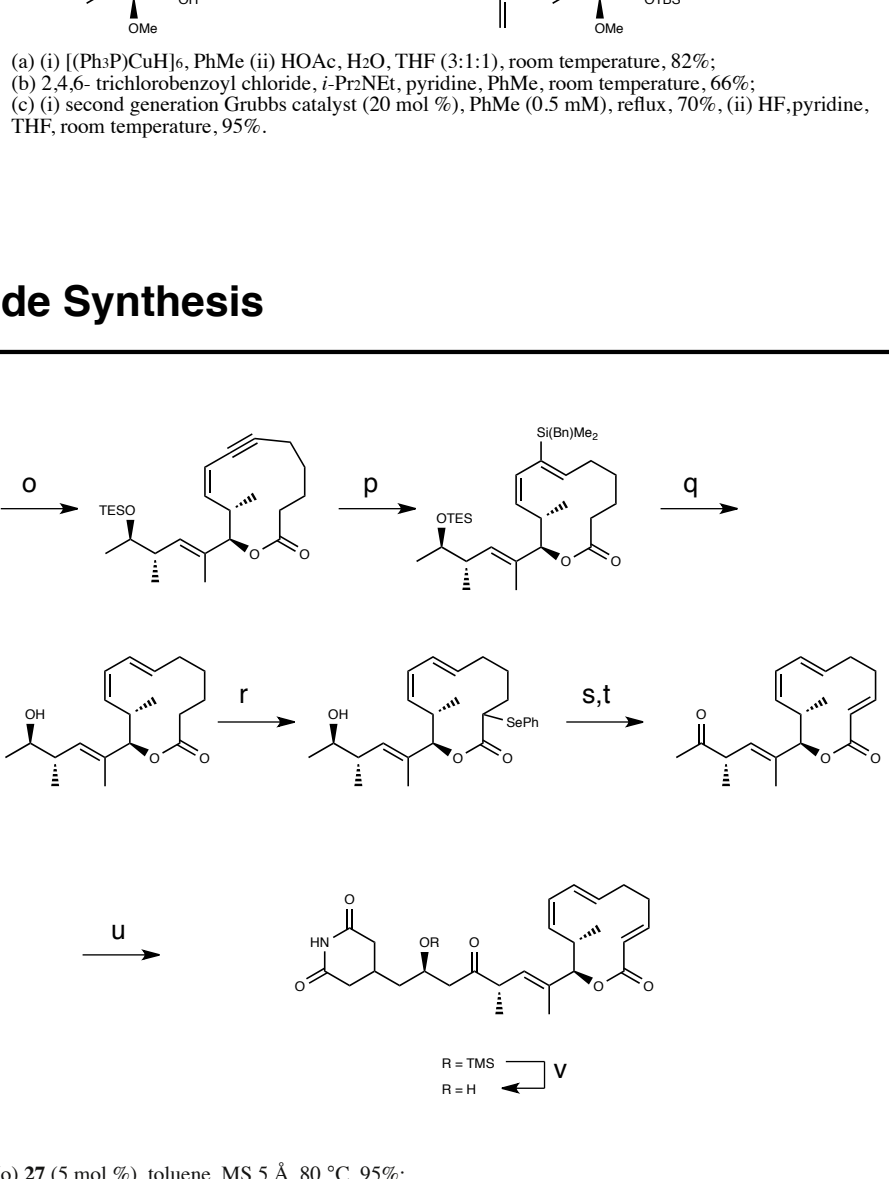
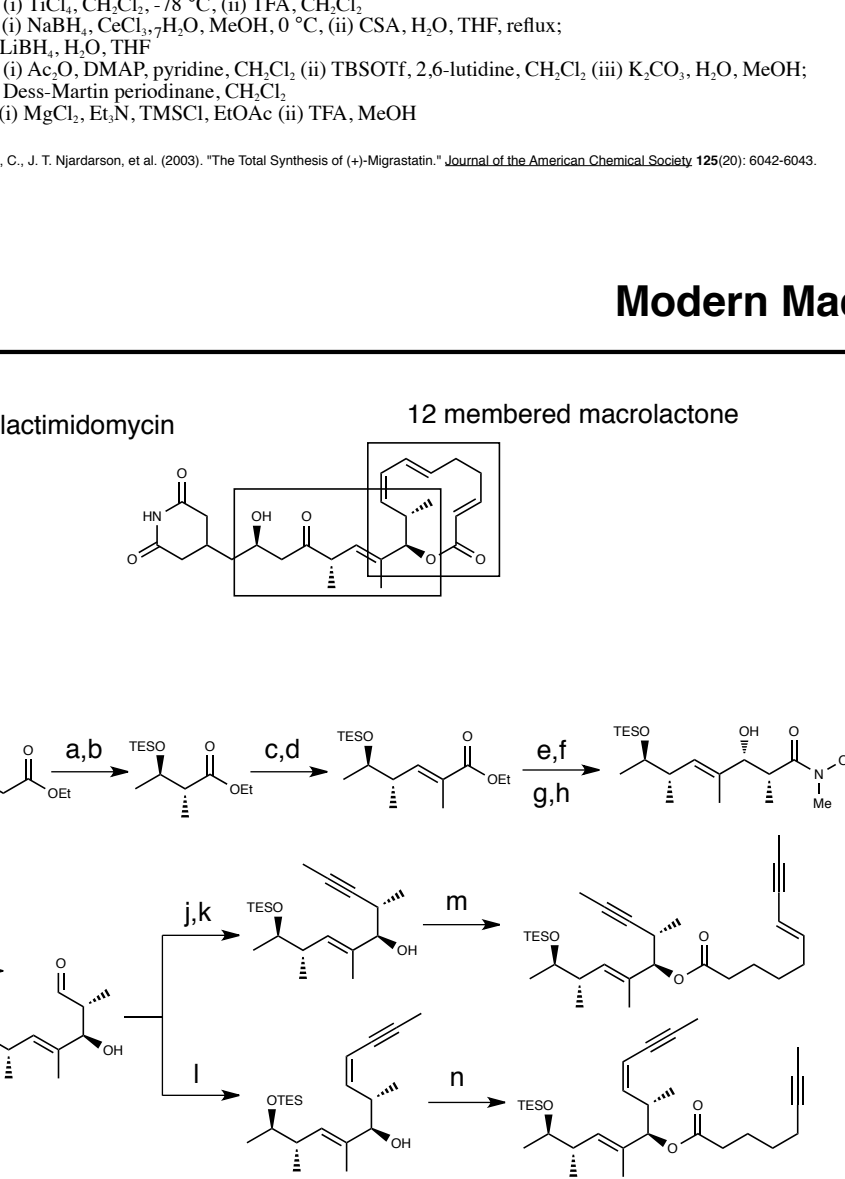
Gaul, C., J. T. Njardarson, et al. (2003). "The Total Synthesis of (+)-Migrastatin." *Journal of the American Chemical Society* 125(20): 6042-6043.

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Moine, K. and A. Furstner (2010). "Concise Total Synthesis of the Potent Translation and Cell Migration Inhibitor Lactimidomycin." *Journal of the American Chemical Society* 132(10): 4056-4065.

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