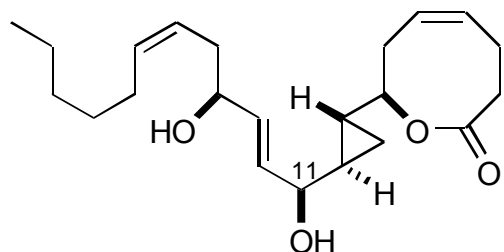
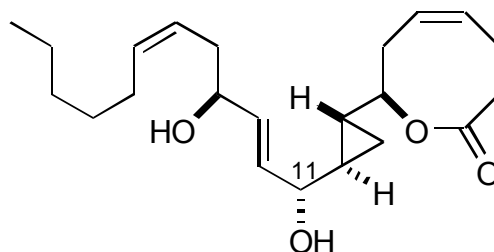


# Total Synthesis of Solandelactones E and F, Homoeicosanoids from the Hydroid *Solanderia Secunda*



**Solandelactone E**



**Solandelactone F**



-**Eicosanoids** are a class of oxygenated fatty acids derived from the 20-carbon atom fatty acid arachidonic acid.

-**Oxylipin** is a term collectively describe compounds derived from a fatty acid of any length (18, 20 or 22) by a series of reactions involving at least one mono- or dioxygenase dependant oxidation

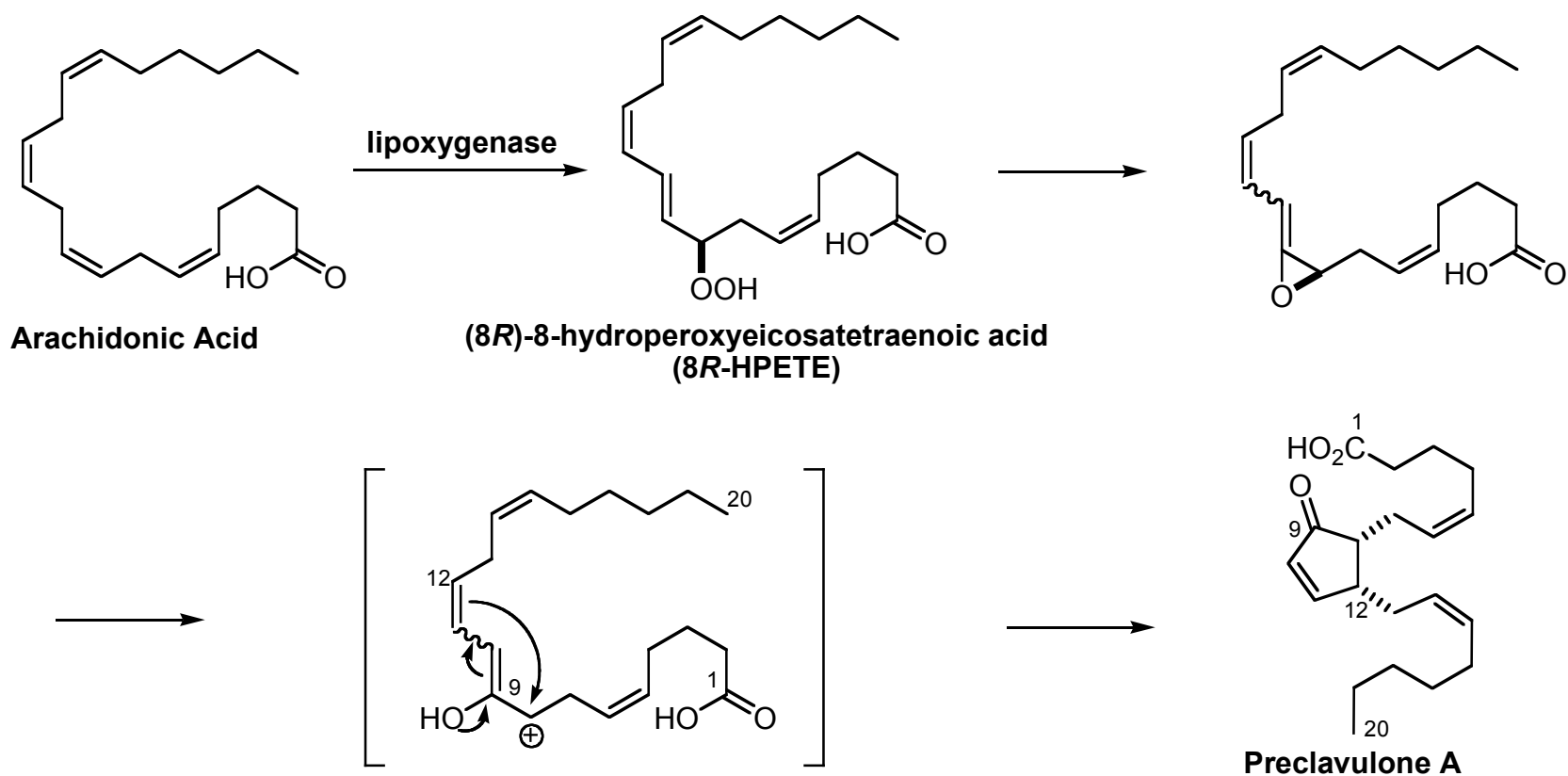
-**Hydroids** are animals without spines belonging to the order Hydroida

**Jennifer Davoren**

Current Literature: 8/18/07

White, James D.; Martin, William H. C.; Lincoln, Christopher; Yang, Jongtae. *Org. Lett.* **2007**, *9*, 3481-3483

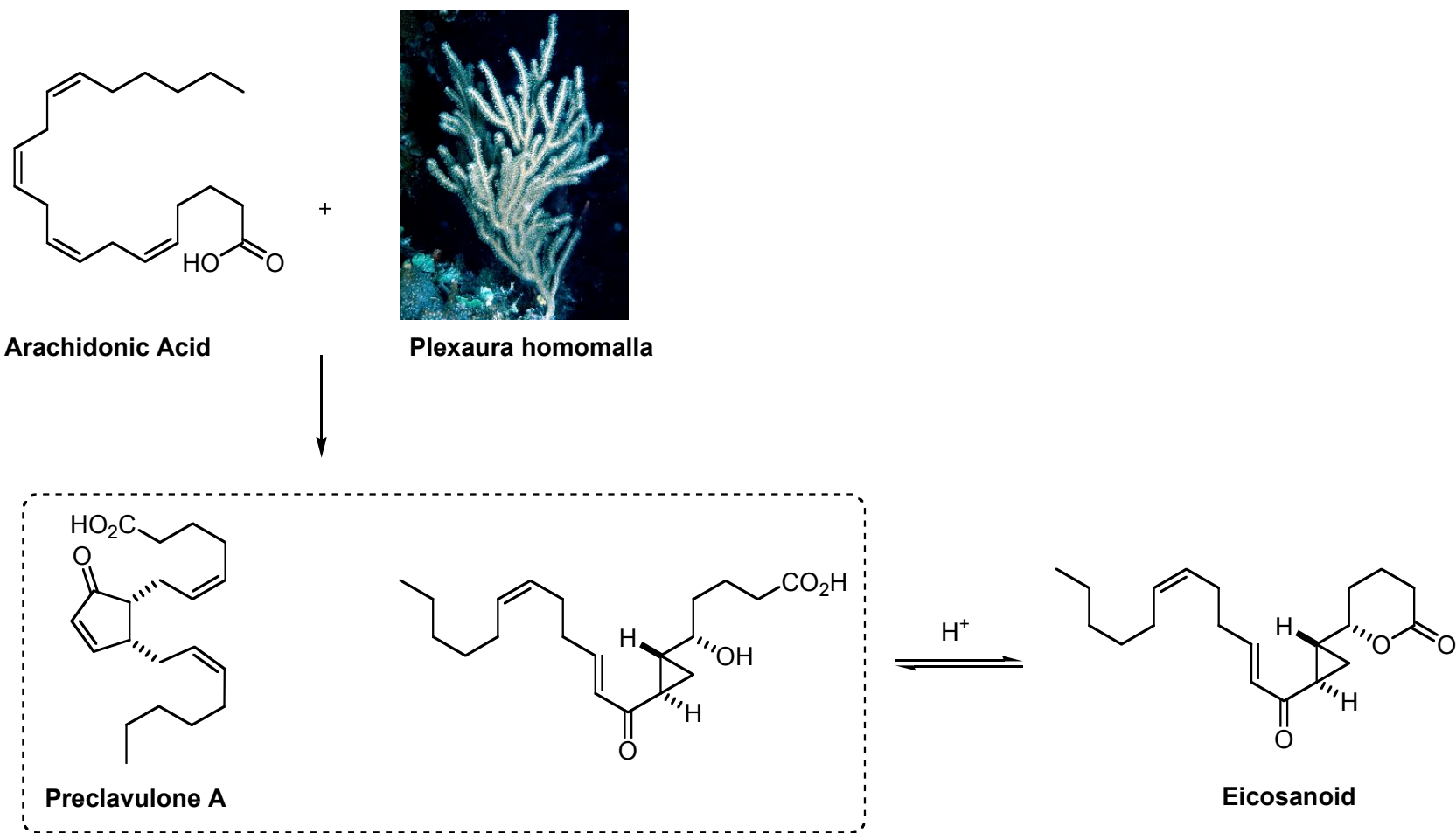
# Corey's Proposed Oxylin Biogenesis



• In an independent study, Harris incubated 8R-HPETE with an acetone powder of *Plexaura homomalla* and isolated Corey's proposed allene oxide.

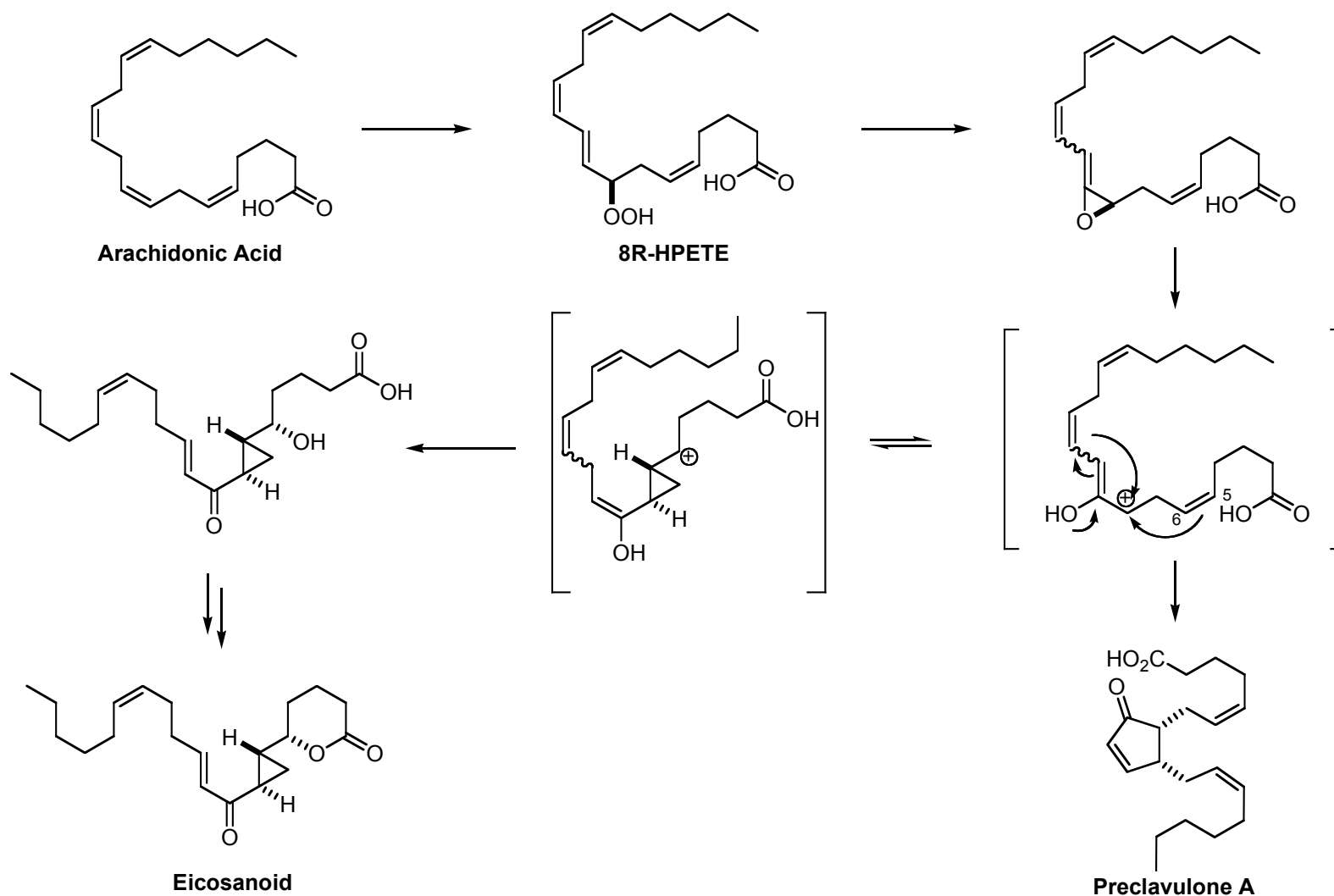
*J. Am. Chem. Soc.* **1987**, *109*, 289-290 & *J. Am. Chem. Soc.* **1989**, *111*, 1891-1892

# First Cyclopropane Containing Oxylinin

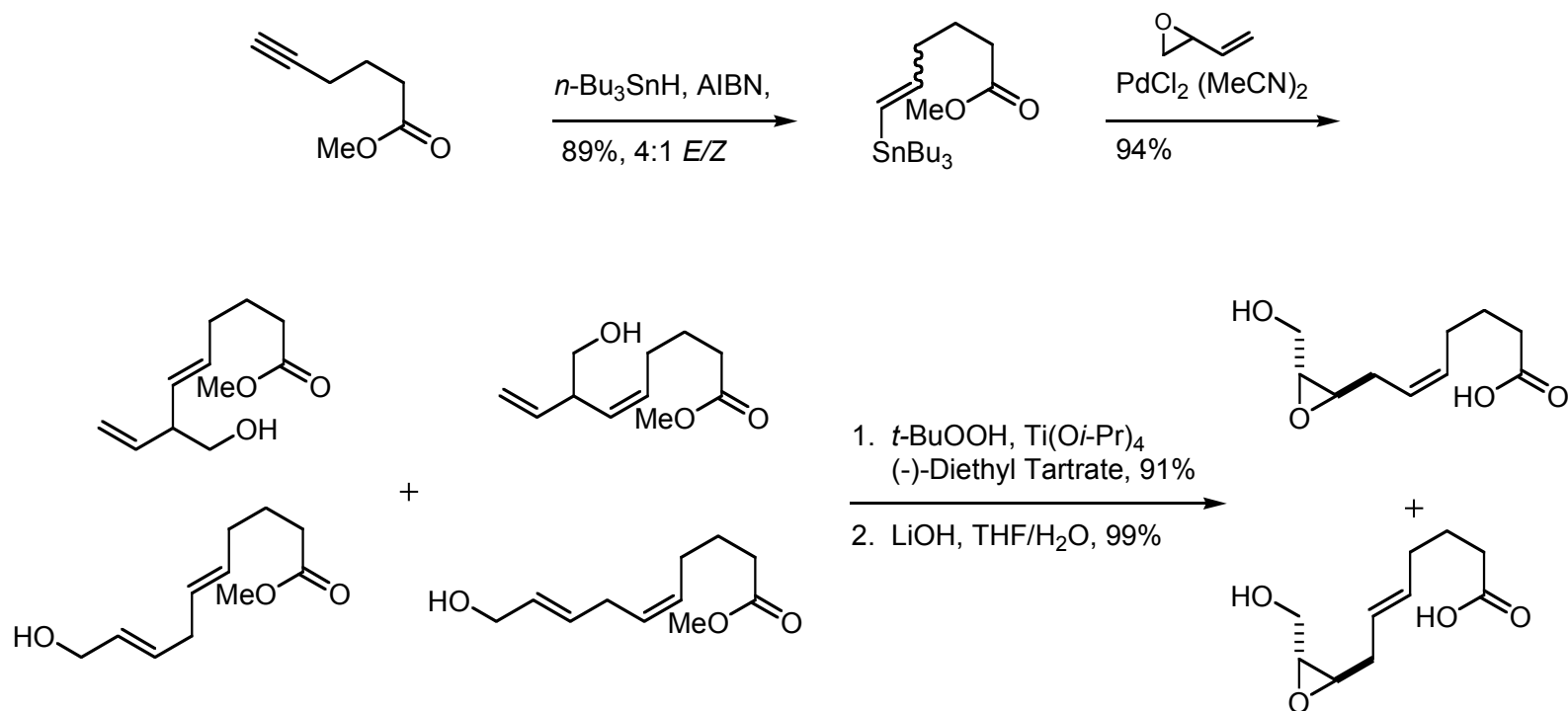


*J. Am. Chem. Soc.* **1989**, *111*, 5003-5005

# Extension of Corey's Proposed Oxylipin Biogenesis

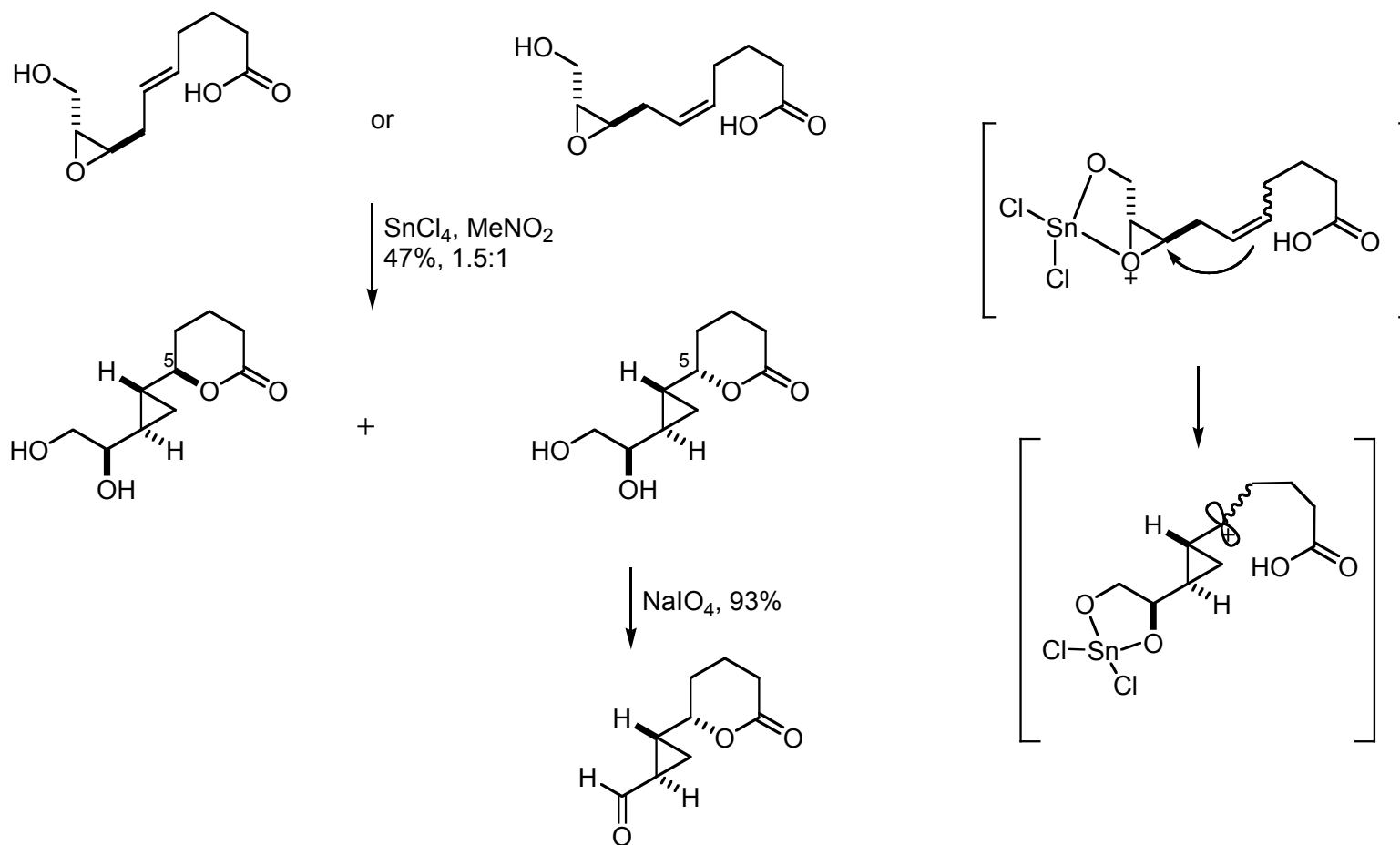


# White's Biosynthesis of Eicosanoid (1993)



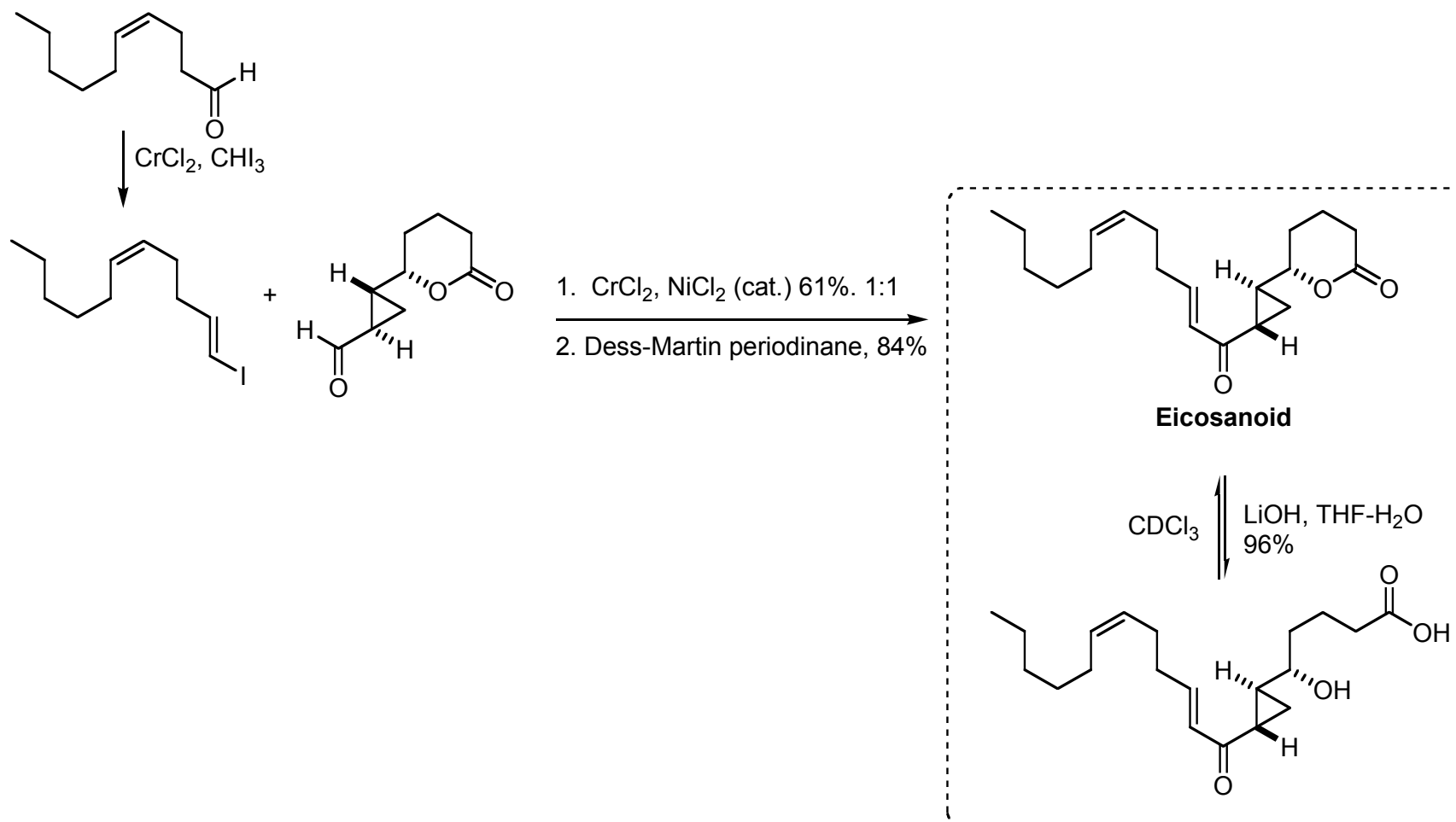
*J. Am. Chem. Soc.* **1993**, *115*, 2970-2971

# White's Biosynthesis of Eicosanoid (1993)



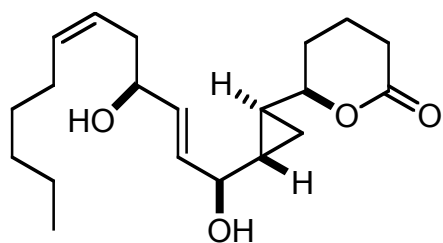
*J. Am. Chem. Soc.* **1993**, *115*, 2970-2971

# White's Biosynthesis of Eicosanoid (1993)

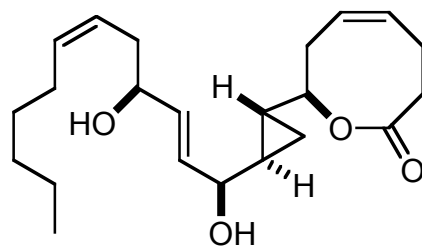


*J. Am. Chem. Soc.* **1993**, *115*, 2970-2971

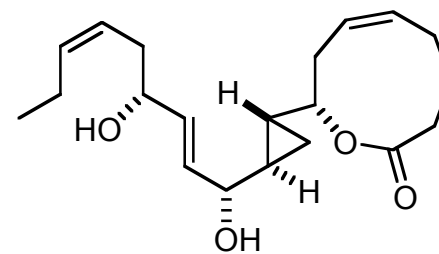
# Controlling the five stereocenters in the oxylipins



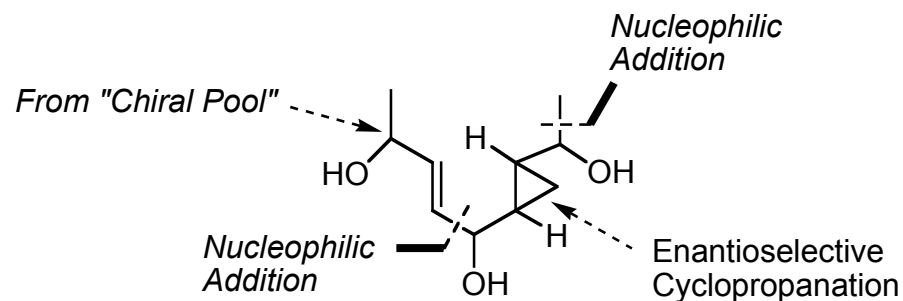
Constanolactone B



Solandelactone E



Neohalicholactone

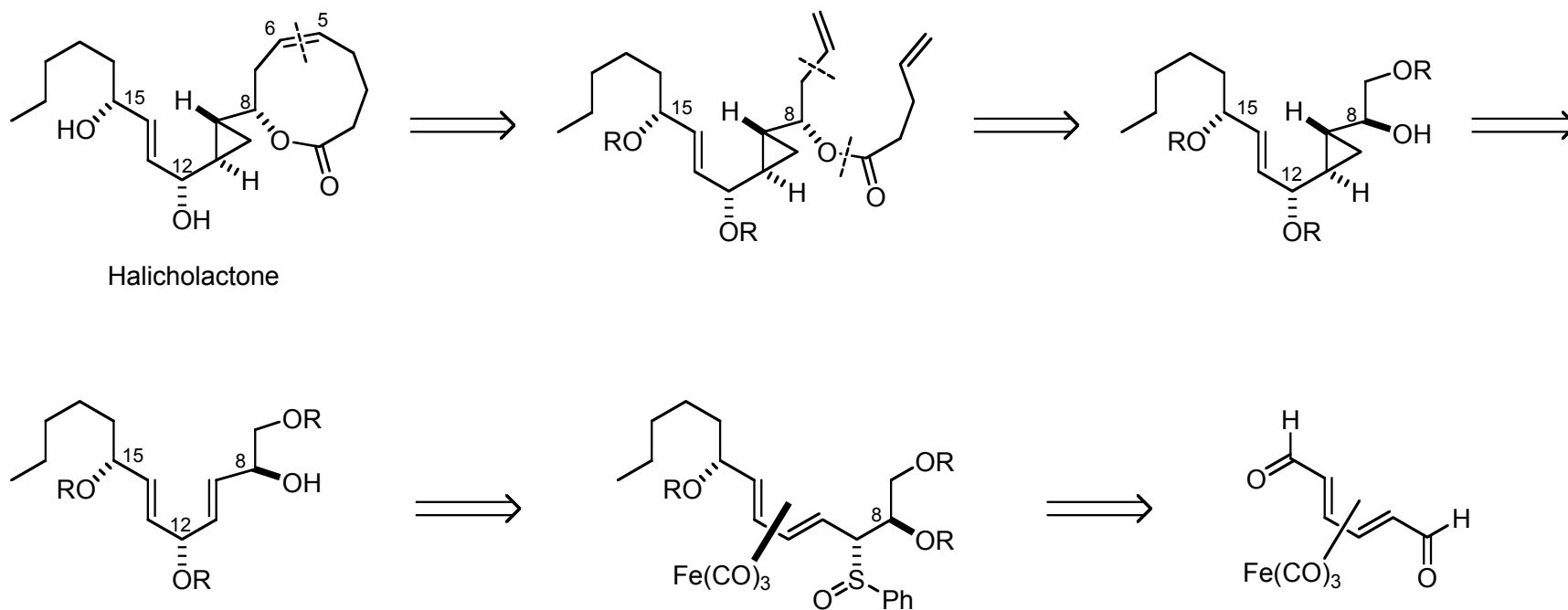


- Solandelactone oxylipins have 22 carbon atoms
- The constanolactones and halicholactones have 20 and therefore can be called eicosanoids or oxylipins

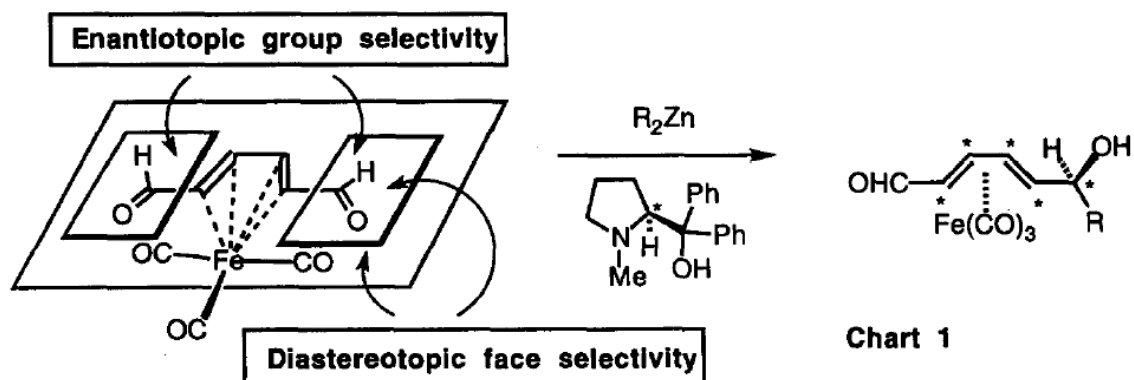
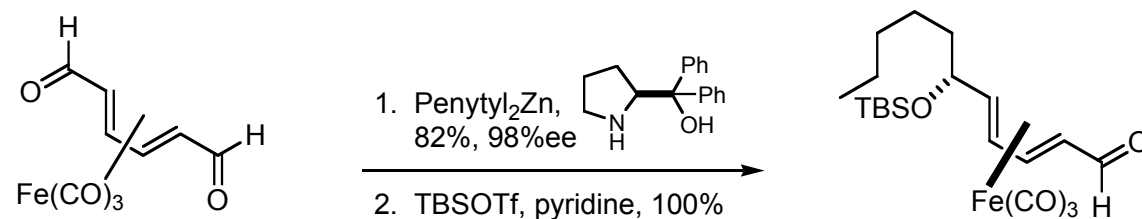


# Tanaka's Total Synthesis of Halicholactone (2000)

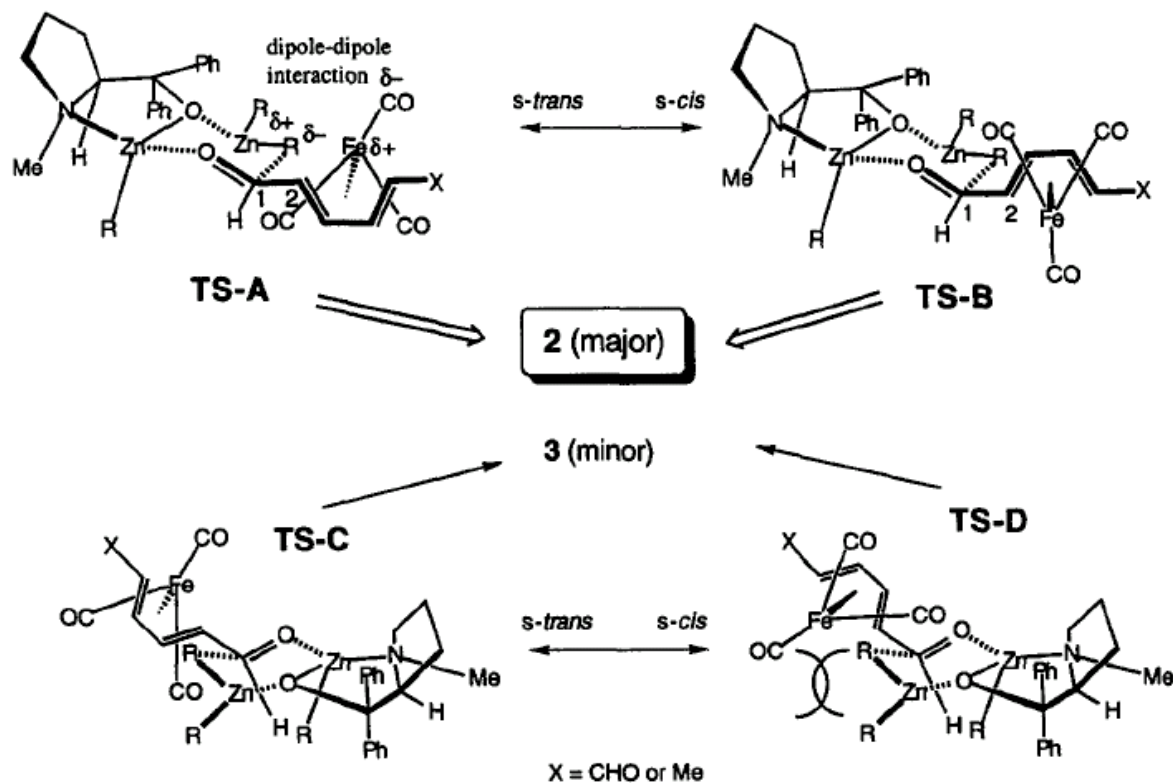
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# Tanaka's Total Synthesis of Halicholactone (2000)

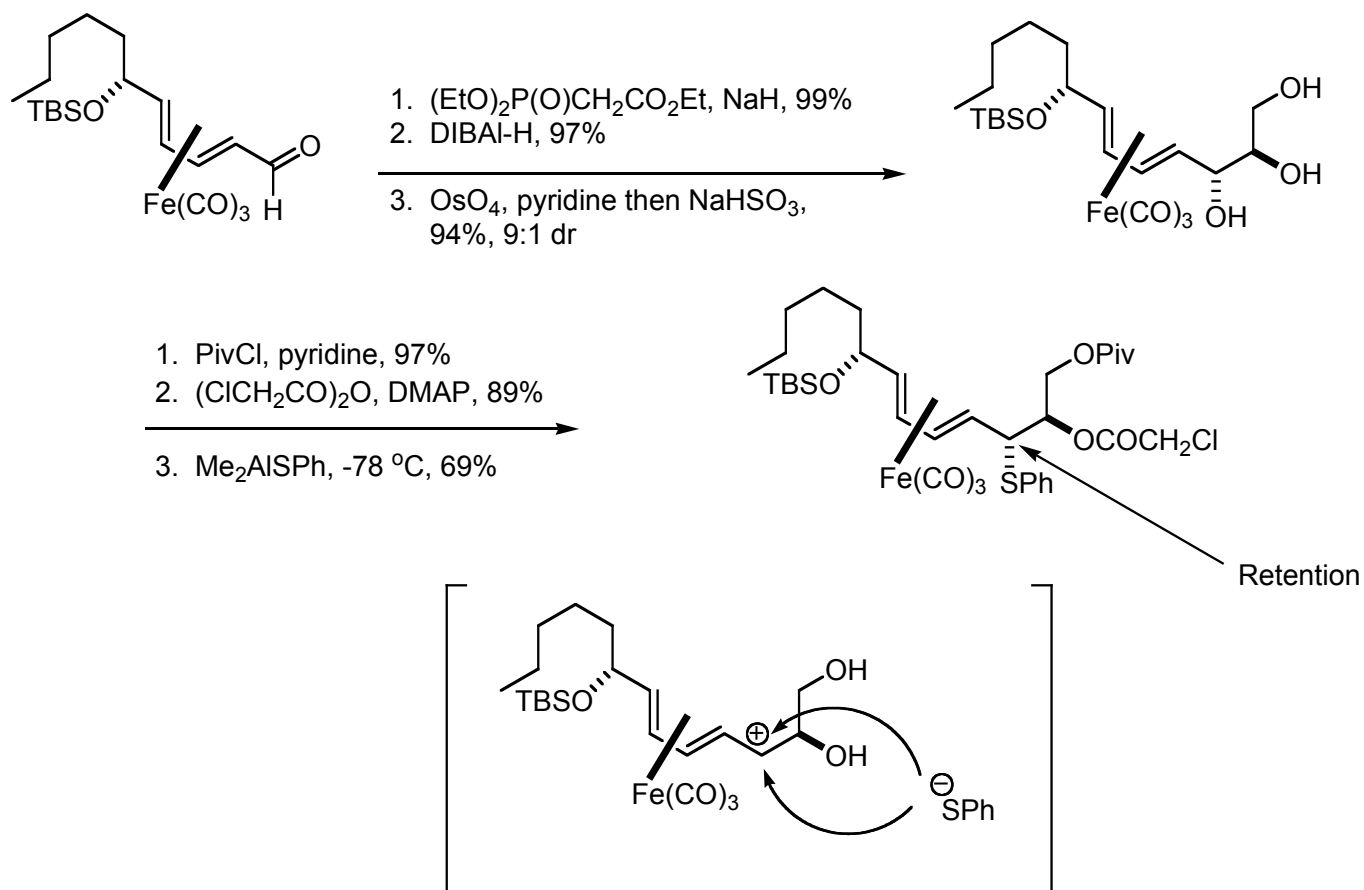


# Tanaka's Total Synthesis of Halicholactone (2000)

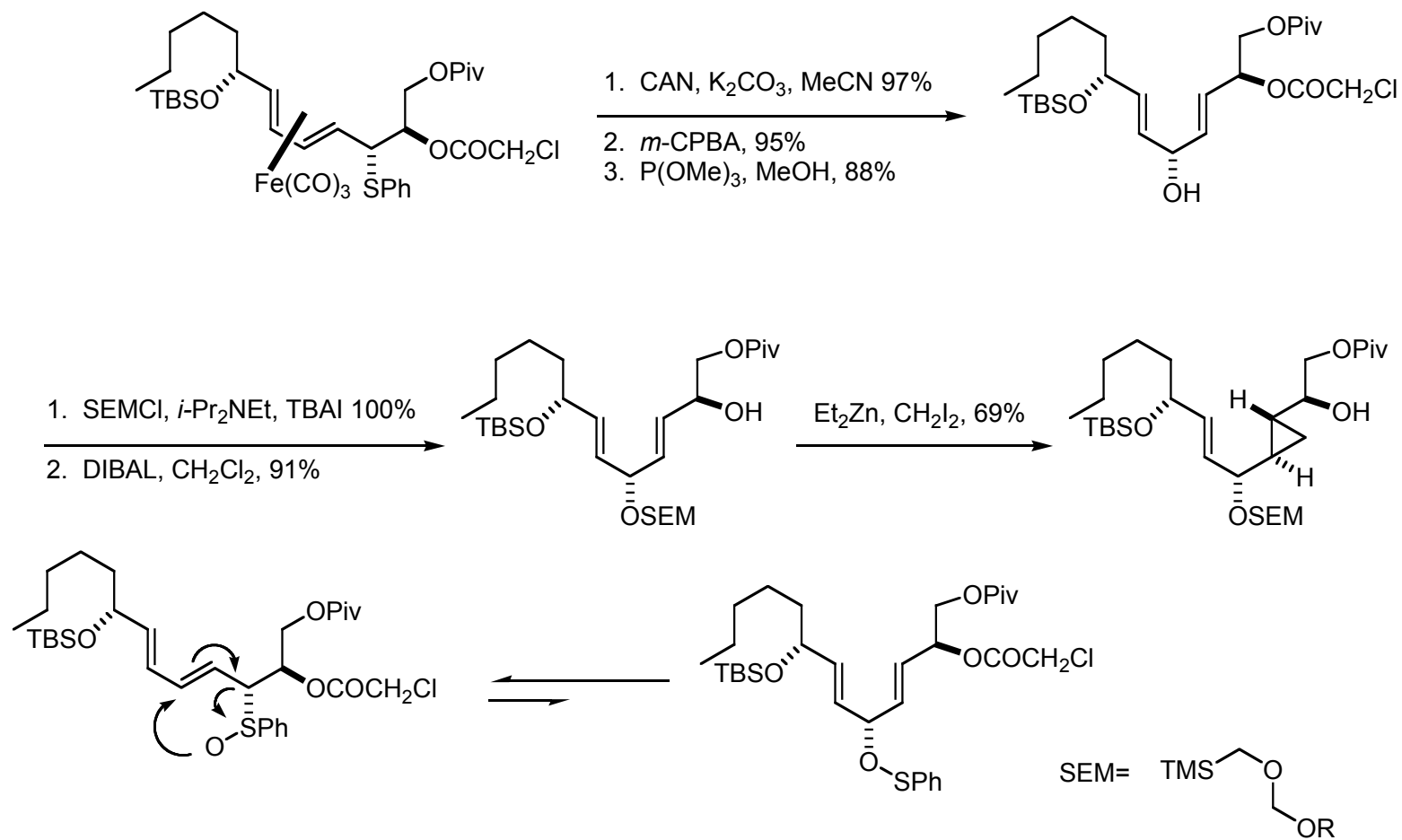


Although the TS-model A and B are interconvertible with each other via the rotation of the C1-C2 bond, the TS-model A seems to be more stable due to the dipole-dipole interaction of the Fe(CO)<sub>3</sub> moiety with dialkylzinc. This interaction can be observed in the TS-model A and D, but in the latter case, these two functional groups are located too close to interact each dipole moment ideally owing to the severe steric hindrance.

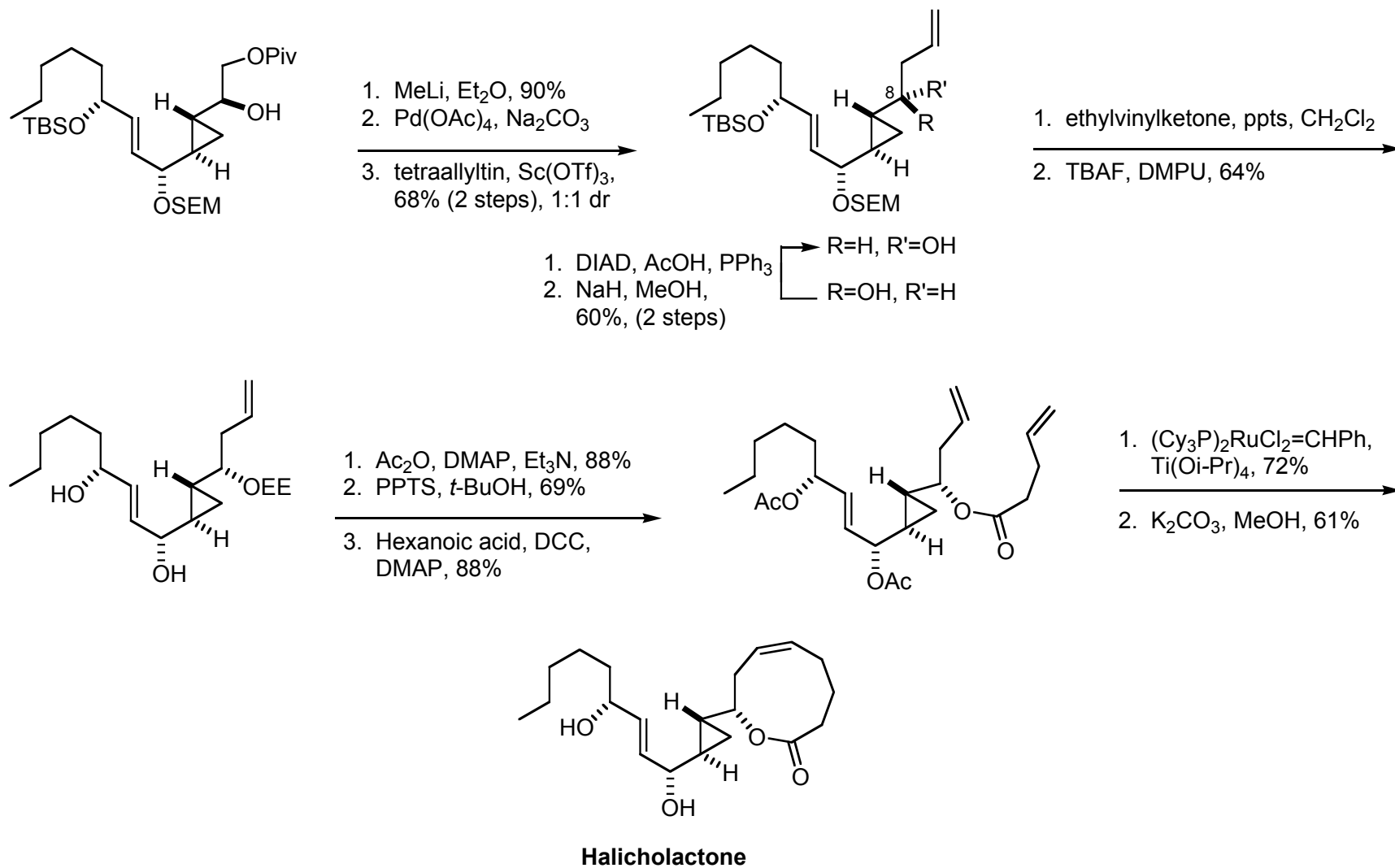
# Tanaka's Total Synthesis of Halicholactone (2000)



# Tanaka's Total Synthesis of Halicholactone (2000)

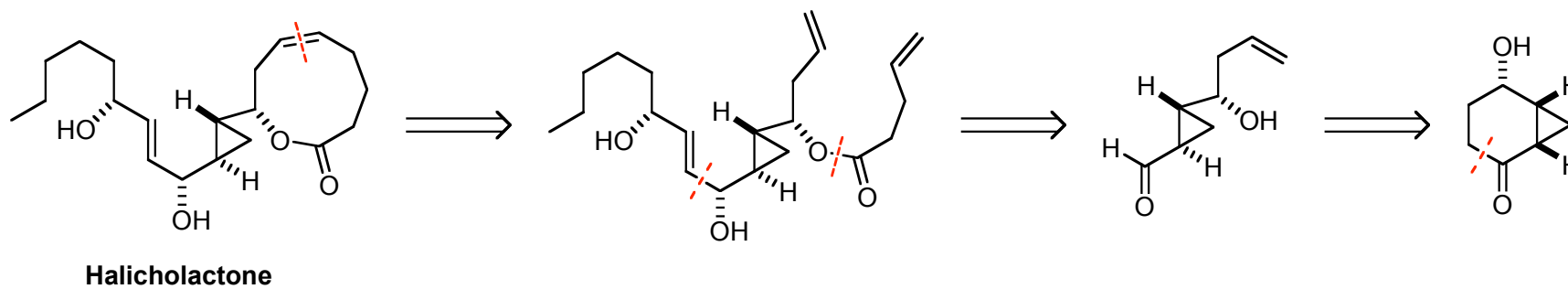


# Tanaka's Total Synthesis of Halicholactone (2000)



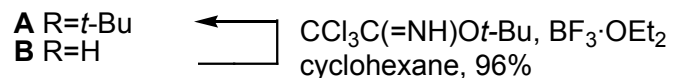
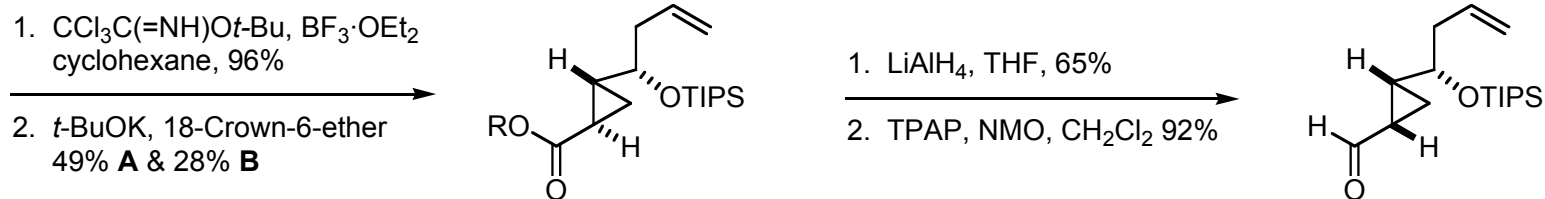
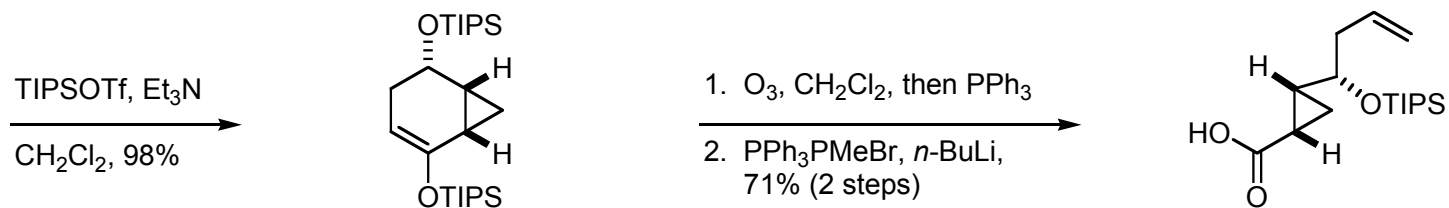
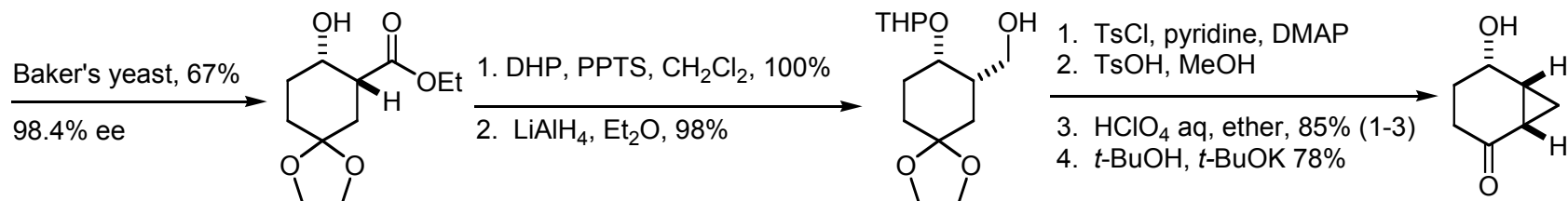
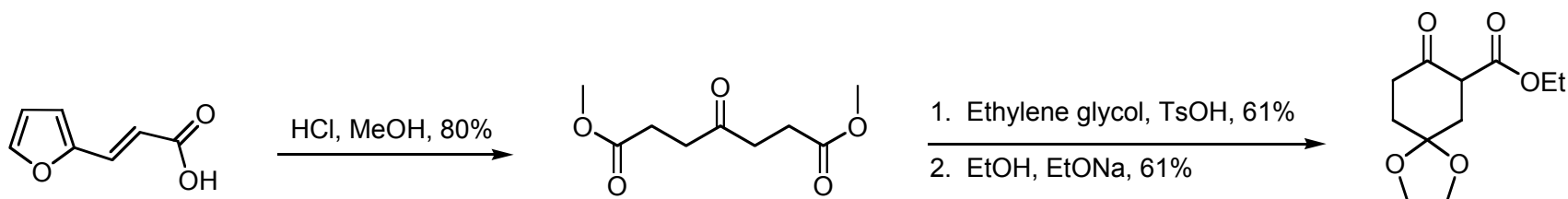
# Kitahara's Total Synthesis of Halicholactone (2002)

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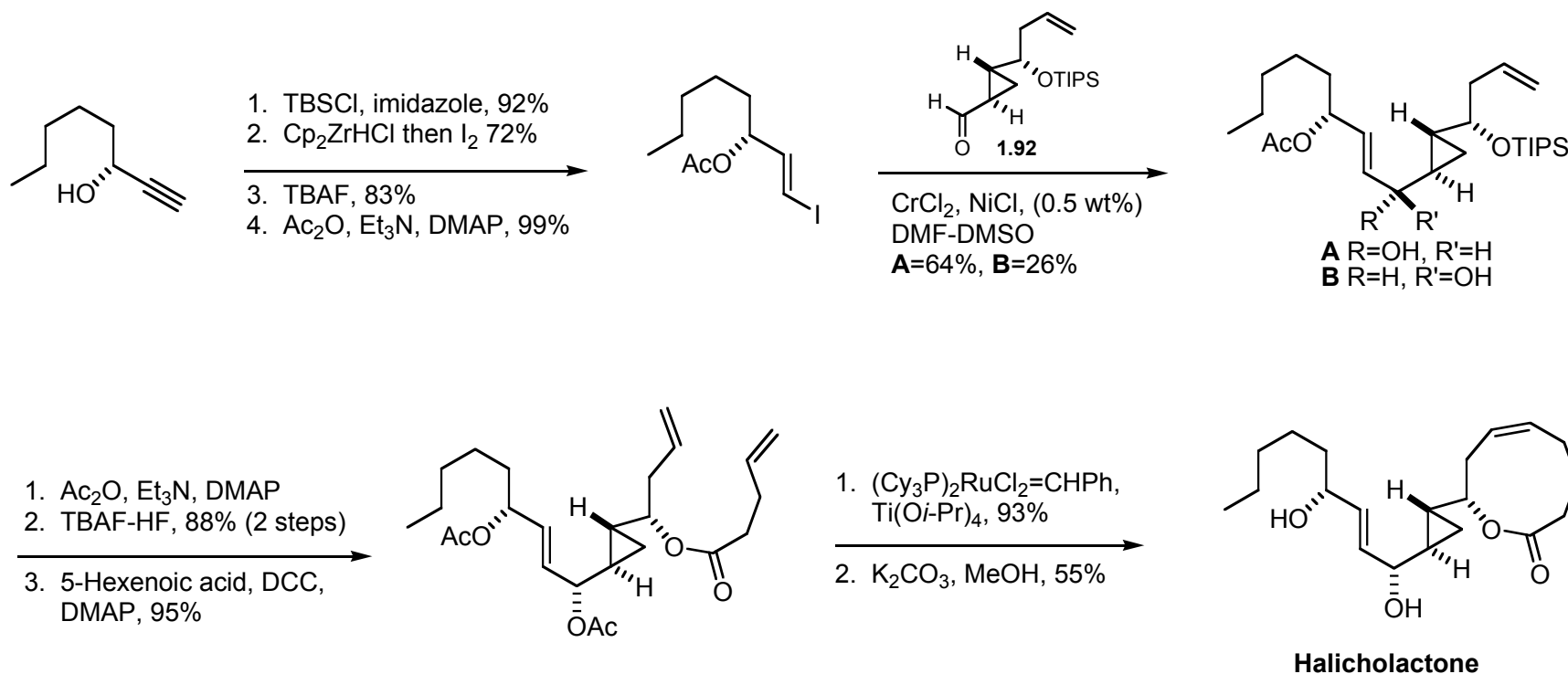
*Heterocycles* **2002**, 58, 99-104

# Kitahara's Total Synthesis of Halicholactone (2002)



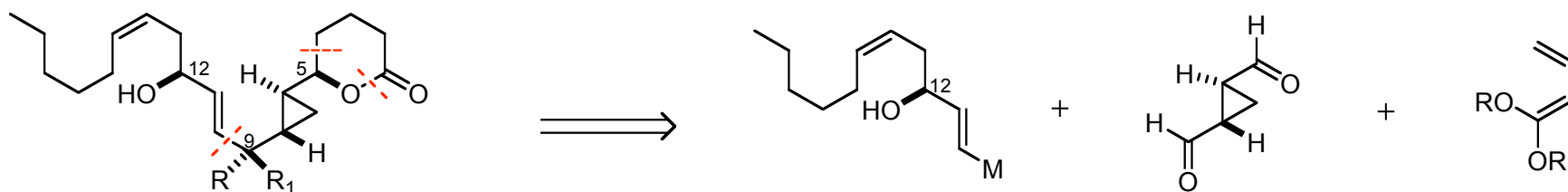


# Kitahara's Total Synthesis of Halicholactone (2002)



# Pale's Total Synthesis of Constanolactones A and B (2000)

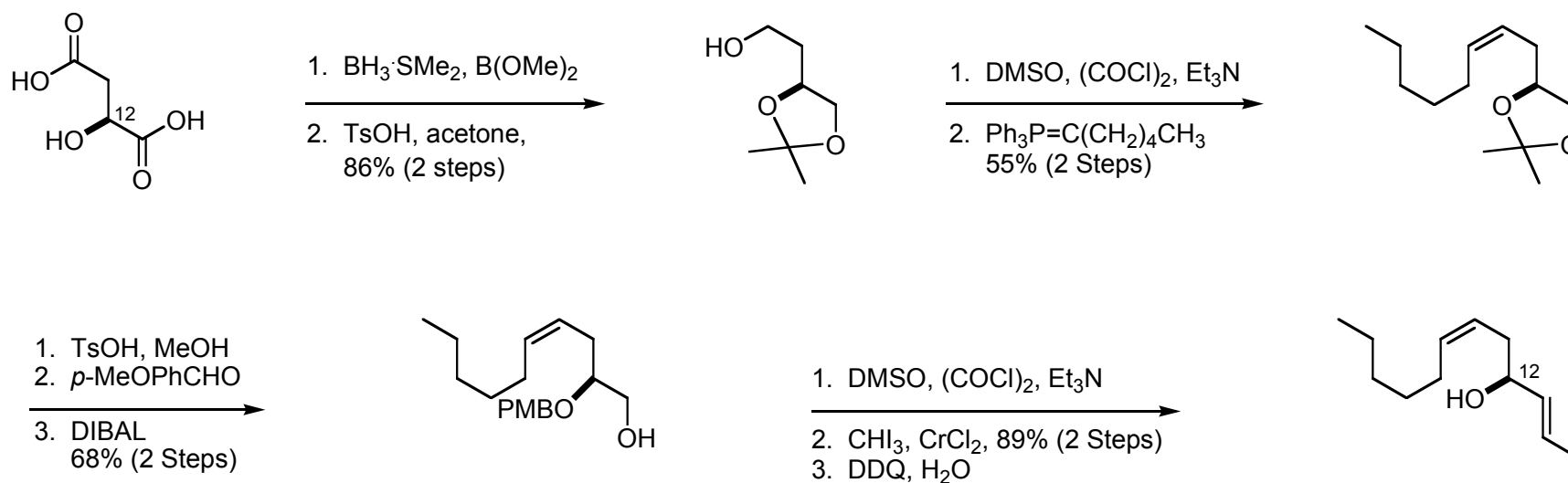
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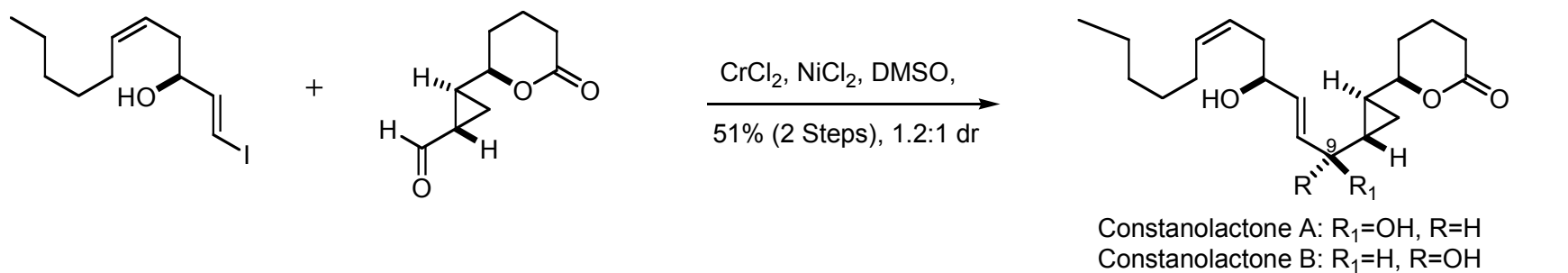
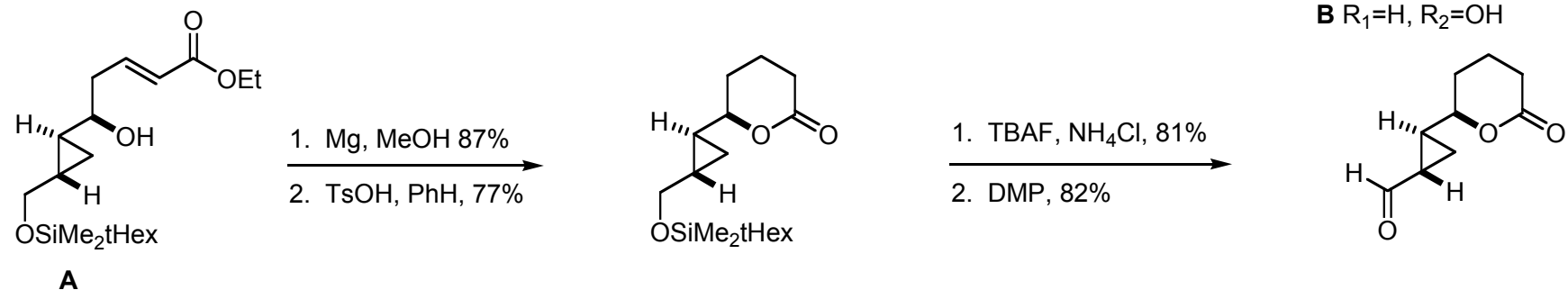
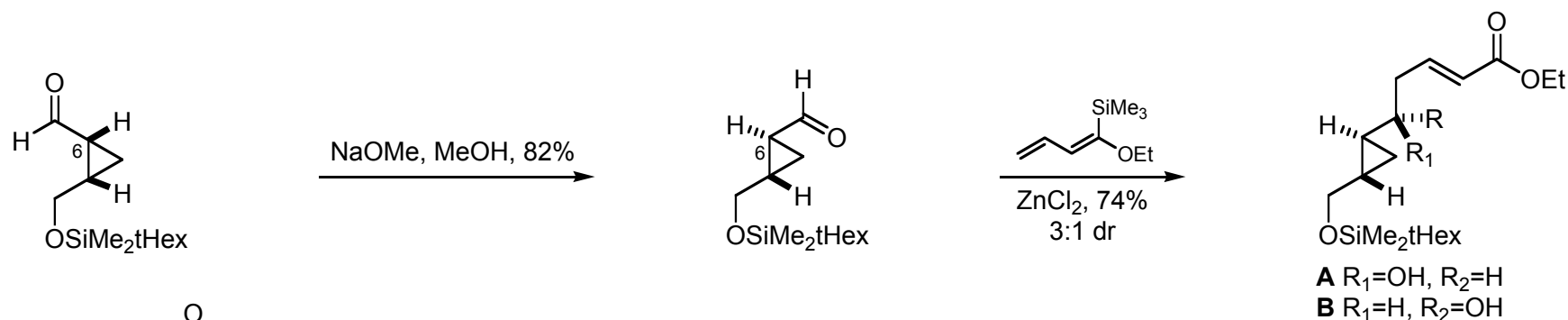
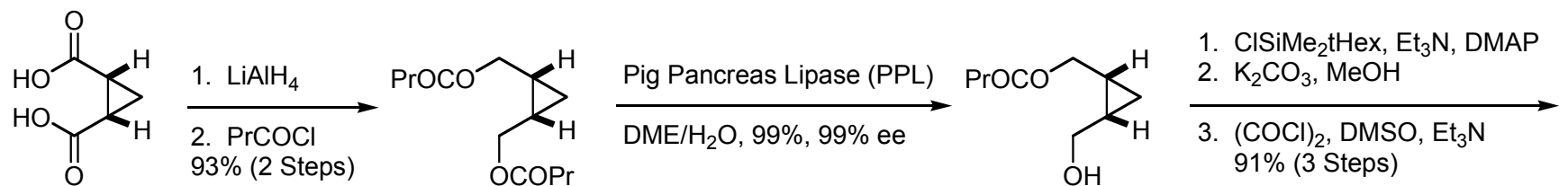
Constanolactone A:  $R_1=OH$ ,  $R=H$   
Constanolactone B:  $R_1=H$ ,  $R=OH$

*Tetrahedron: Asymmetry* **1998**, *9*, 3951-3954  
*Tetrahedron Lett.* **2000**, *41*, 3077-3081

# Pale's Total Synthesis of Constanolactones A and B (2000)

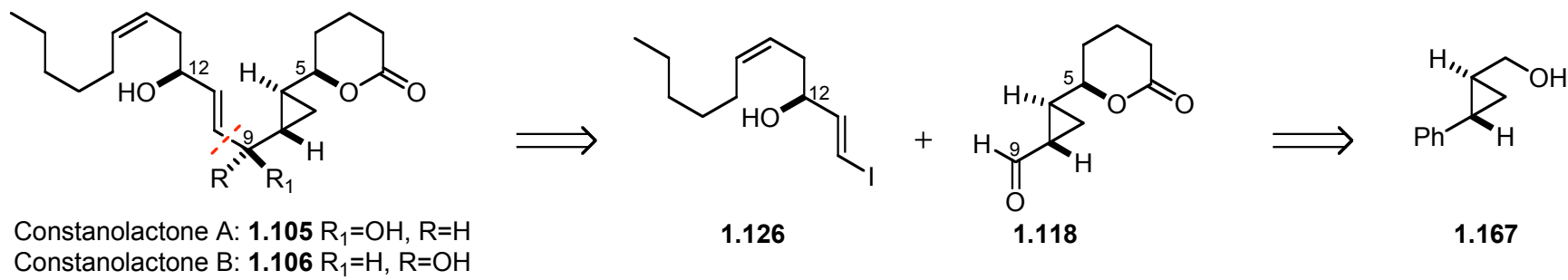


# Pale's Total Synthesis of Constanolactones A and B (2000)

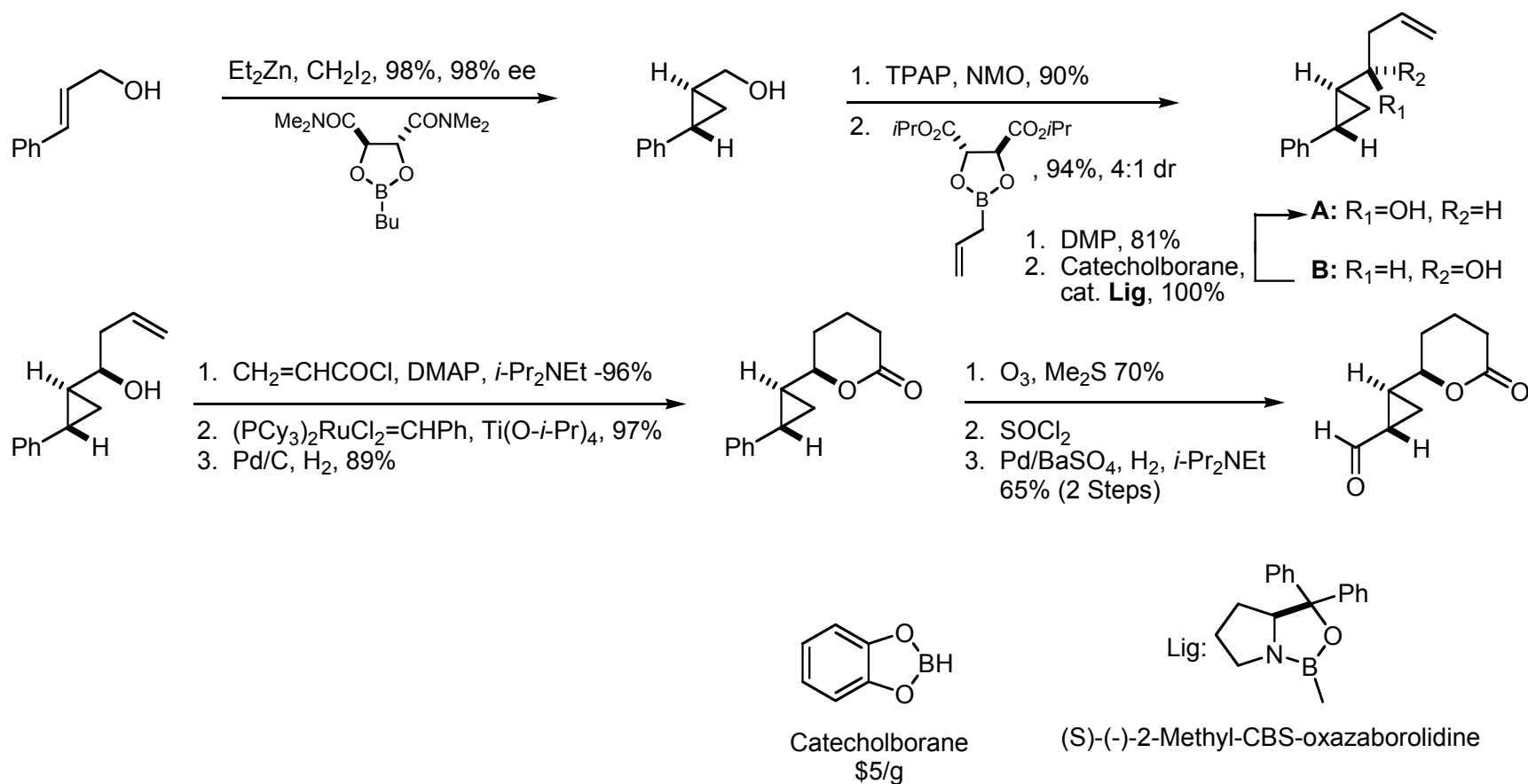


## Pietruszka's Total Synthesis of Constanolactones A and B (2003)

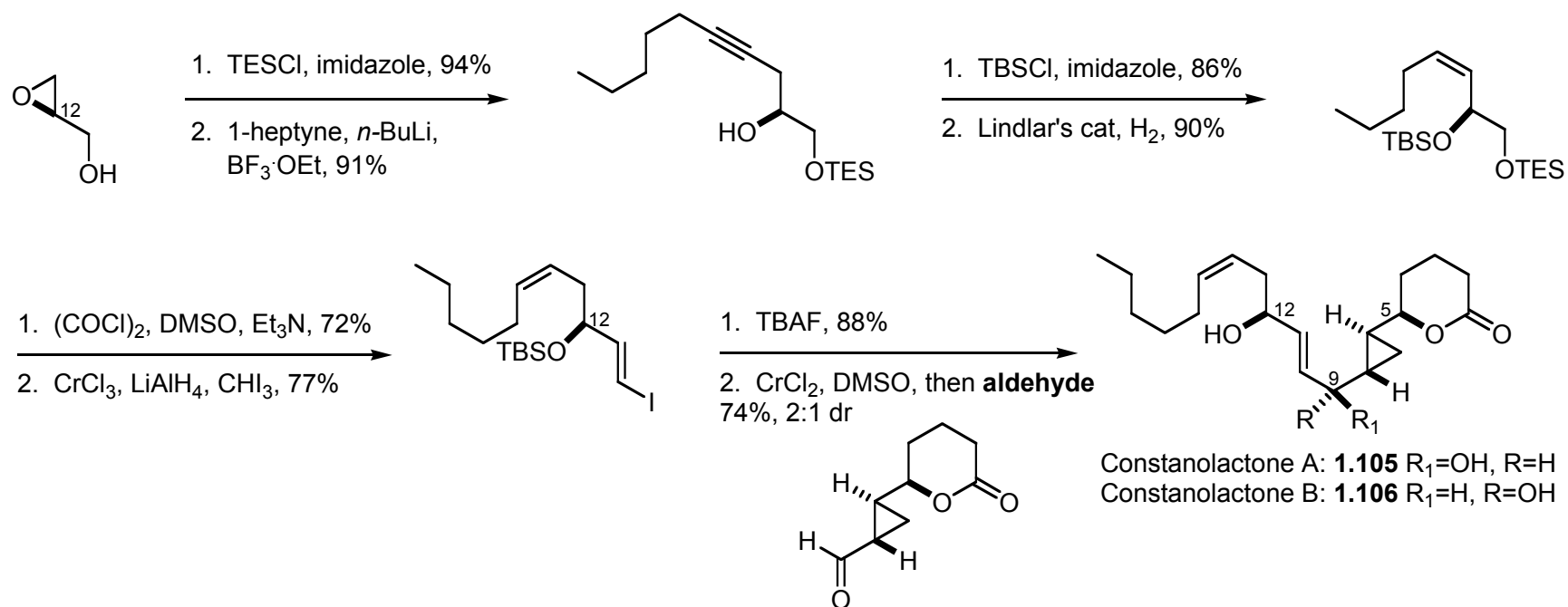
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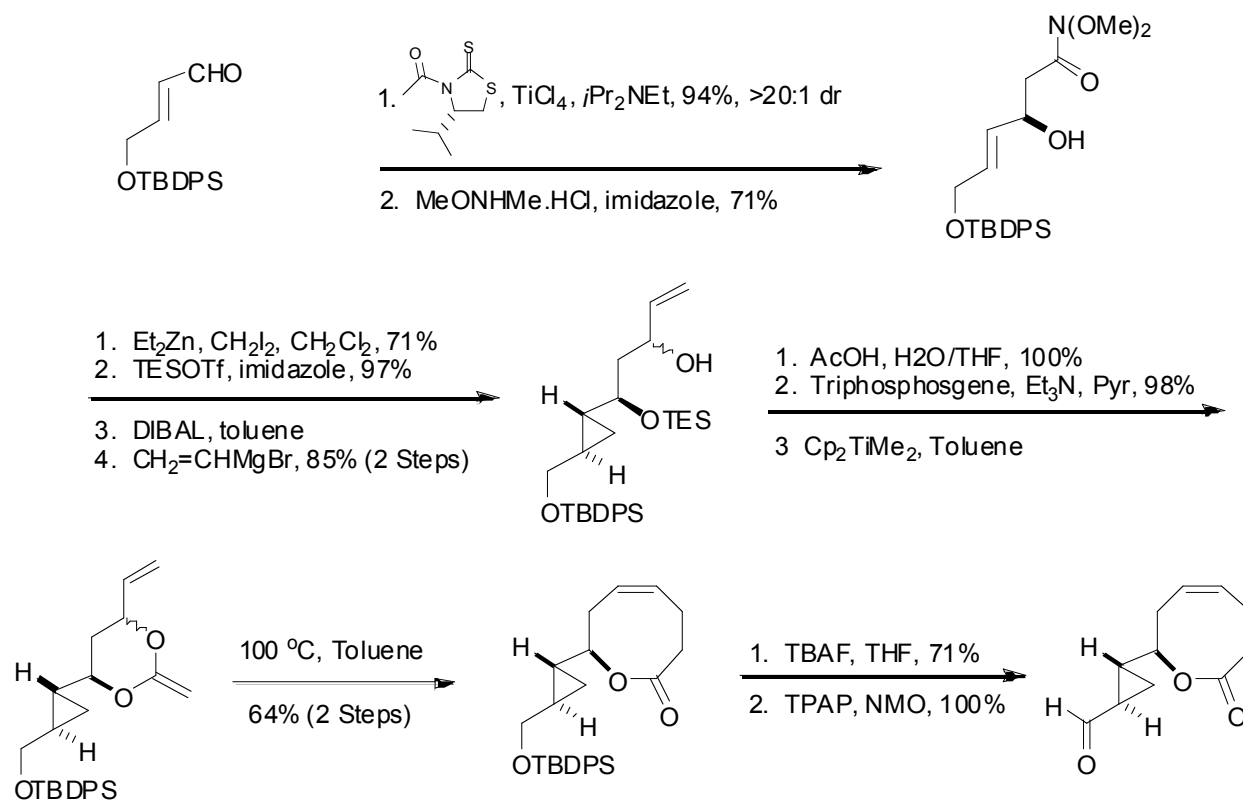
# Pietruszka's Total Synthesis of Constanolactones A and B (2003)



# Pietruszka's Total Synthesis of Constanolactones A and B (2003)



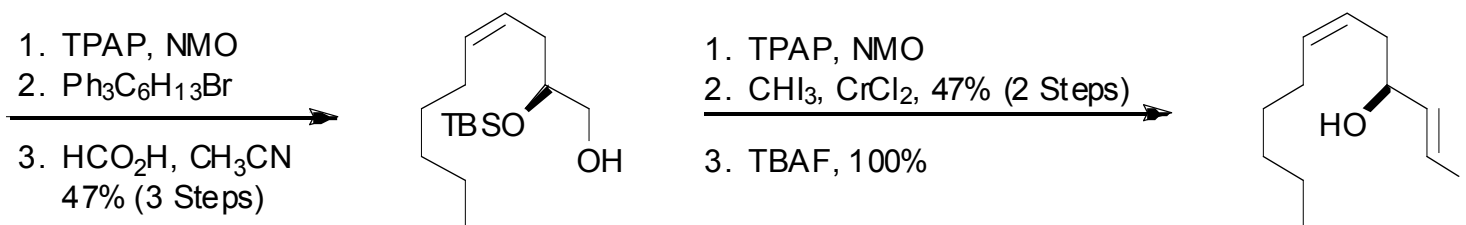
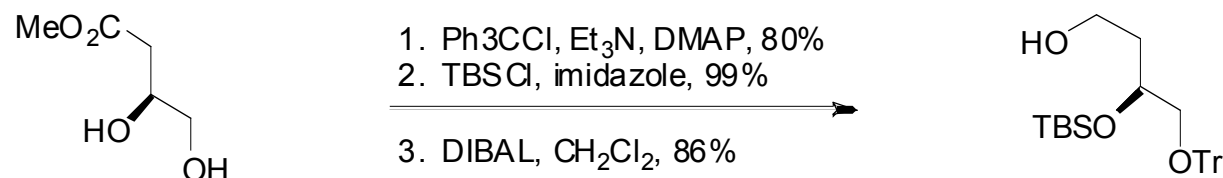
# White's Total Synthesis of Solandelactone E and F (C1-C11)



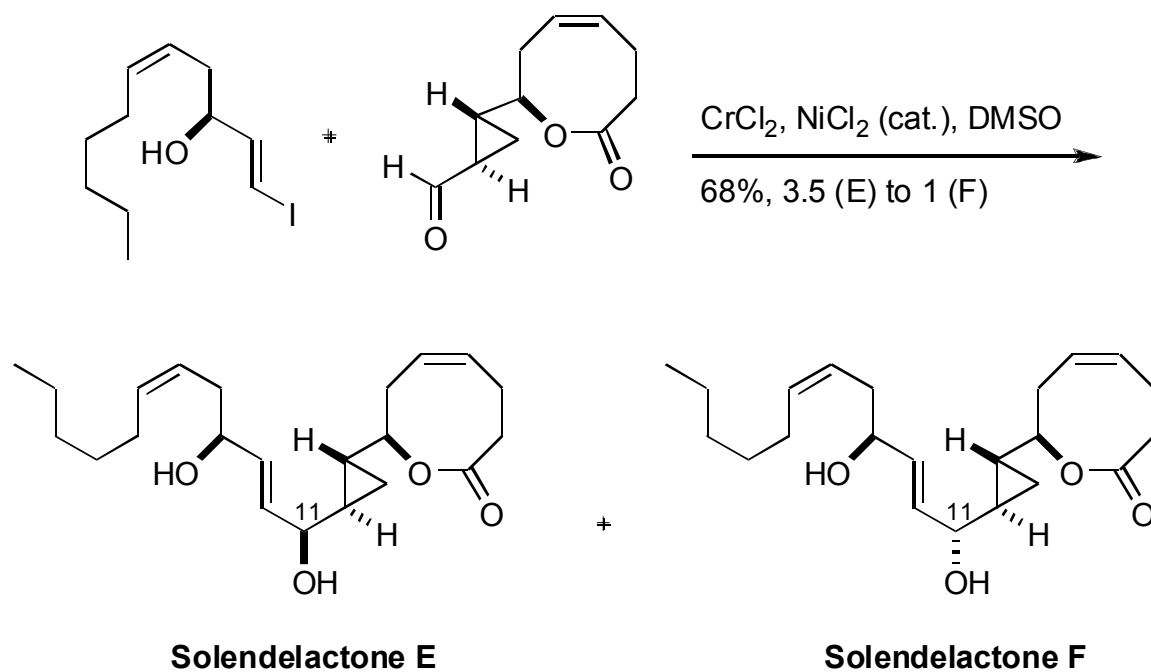


# White's Total Synthesis of Solandelactone E and F (C12-C22)

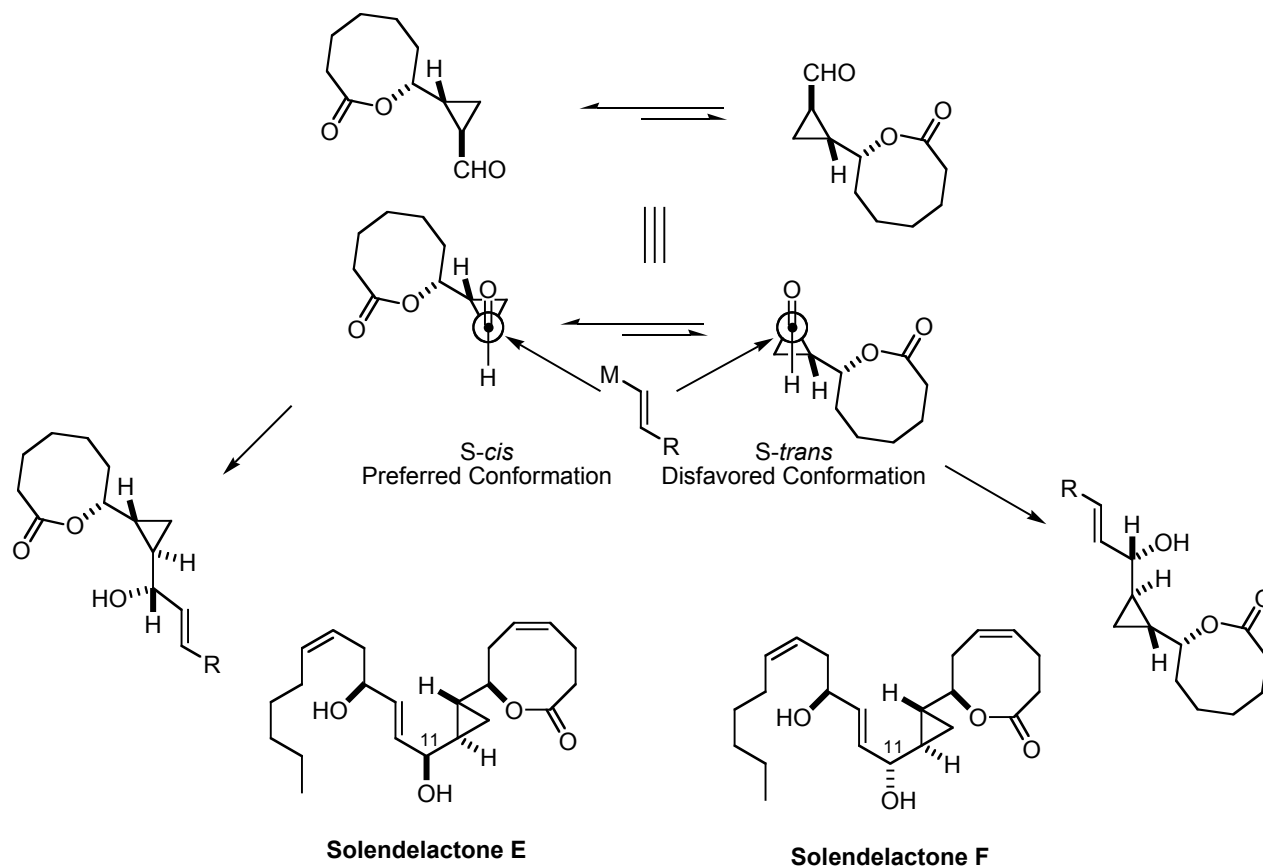
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# White's Total Synthesis of Solandelactone E and F



# Solandelactone E and F Stereochemical Assignments



Computational studies indicate that the *S*-(*cis*)-conformation is favored by 1.6-3.0 kcal over the *S*-(*trans*)-conformation depending on the substitution pattern of the cyclopropane. If the conformation of the transition state of addition is similar to that of the substrate, then the ability of the cyclopropyl group to conjugate with the carbonyl - system would explain the experimentally observed selectivity.

*Tocanne, J. F. Tetrahedron 1972, 28, 389-416.*

# Conclusions

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- White has completed the first total synthesis of solandelactone F and the second total synthesis of solandelactone E
- The structural revision of solandelactones E and F was confirmed
- The C(1)-C(11) was completed in 14 linear steps, and C(12)-C(22) was completed in 10 linear steps making the synthesis a total of 25 steps from commercially available starting materials
- Synthesis features a Nagao asymmetric aldol reaction, a diastereoselective cyclopropanation, a Claisen rearrangement to form the saturated 8-membered lactone, and a Nozaki-Hiyama-Kishi coupling for linking the two major fragments at C(11) and C(12)
- Synthesis can very quickly be adapted to synthesis the other 6 solandelactones by reducing the olefin in either the lactone or the C(11)-C(22) fragment