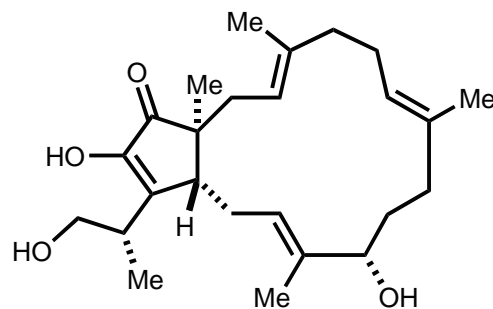


Total Syntheses of (-)-Terpestacin



Jason M. Stevens

05/02/2007

An Interesting History

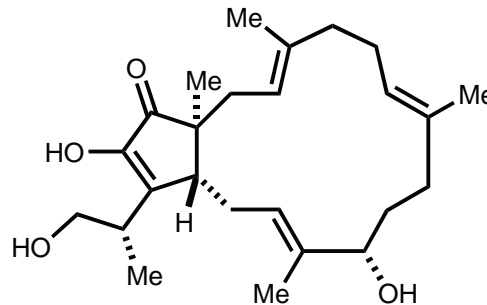
1993: Isolation of terpestacin (Oka) reported $[\alpha]_D = +26^\circ$ (CHCl_3) with the absolute configuration as shown.

1998: First asymmetric synthesis of shown absolute configuration of terpestacin by Tatsuda reports $[\alpha]_D = +27^\circ$ (CHCl_3).

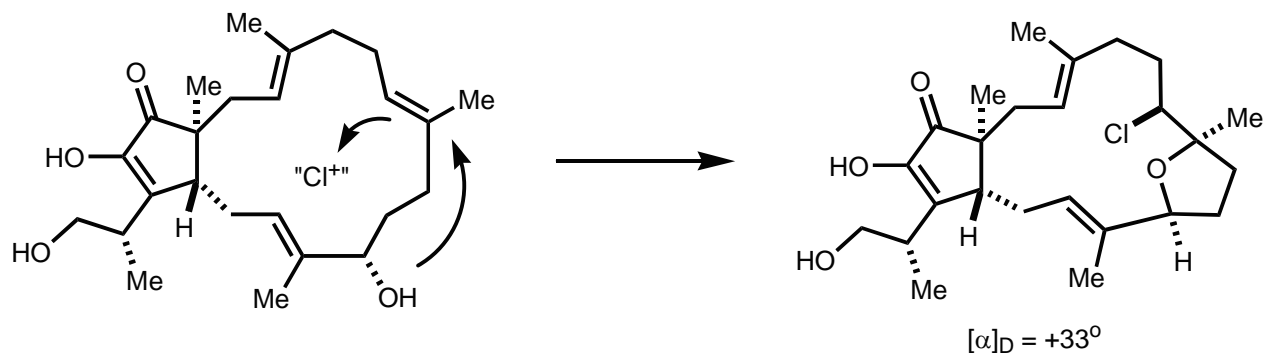
2001: Isolation of the enantiomer of terpestacin (Gräfe) reported $[\alpha]_D = -16^\circ$ (CDCl_3).

2002: Asymmetric synthesis of shown configuration of terpestacin by Myers reported $[\alpha]_D = -17^\circ$ (CHCl_3).

What's going on???



Chloroform is the Culprit



Solutions of the natural product had been stored in chloroform prior to the optical rotation measurements.

Note: CDCl_3 stored over K_2CO_3 test positive for chlorine, although identical lots of CDCl_3 stored over 4A mol. sieves did not.

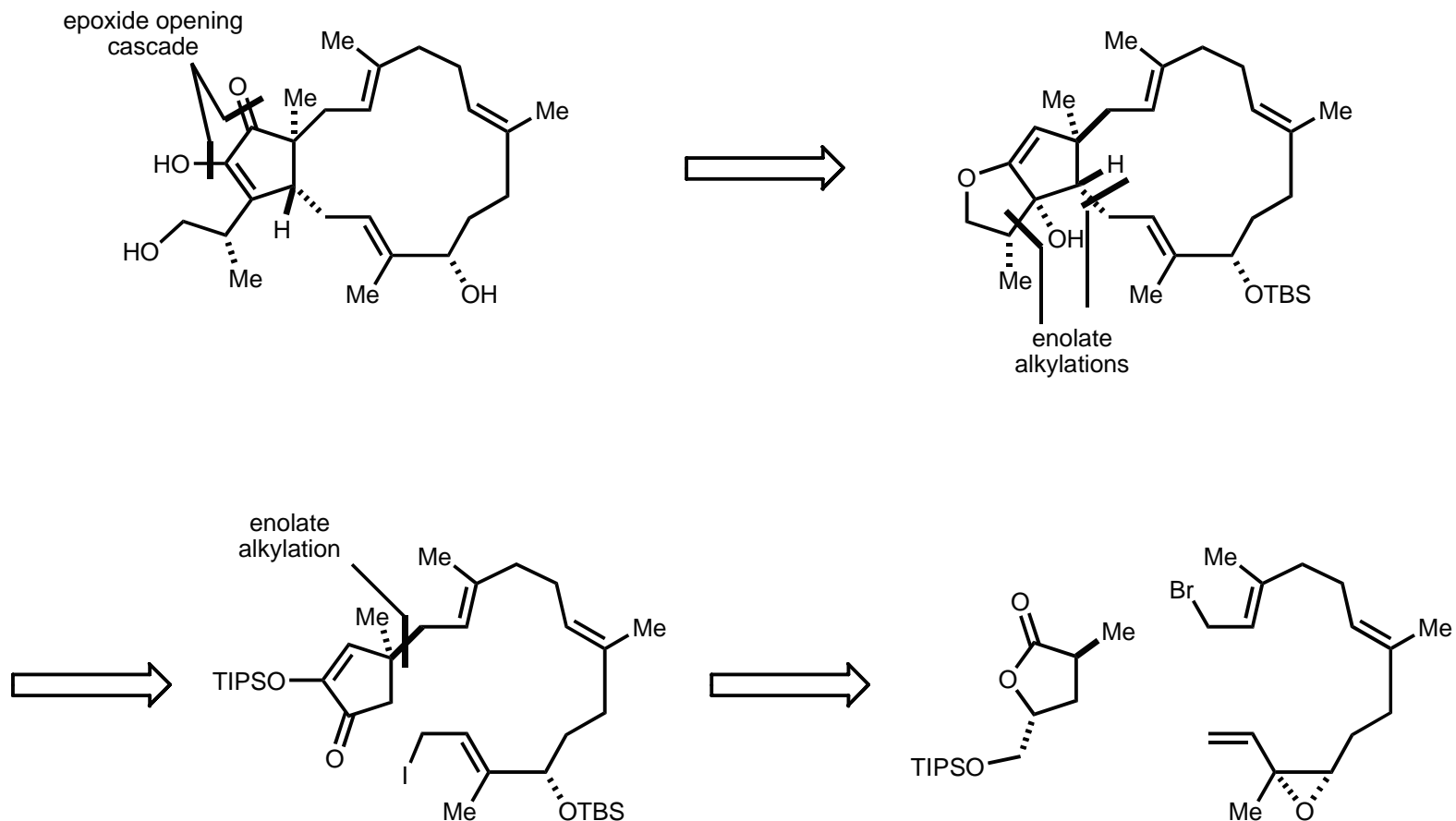
Now that we know what we're making...

Myer's total synthesis **2002**

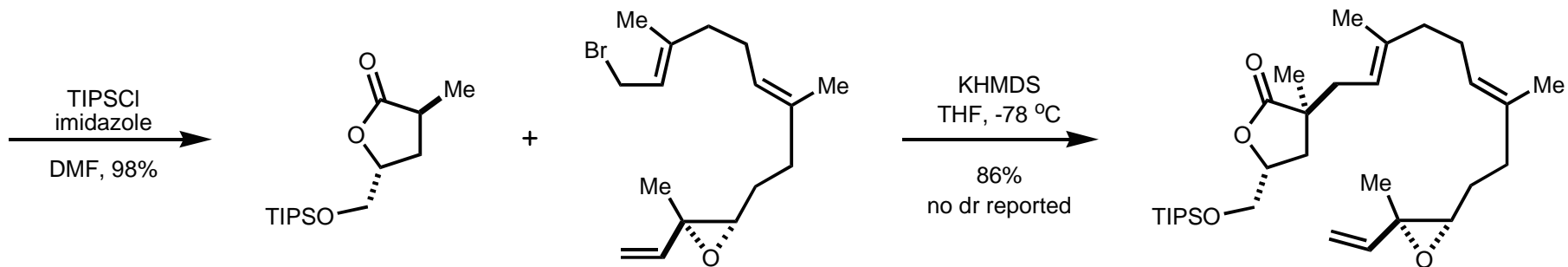
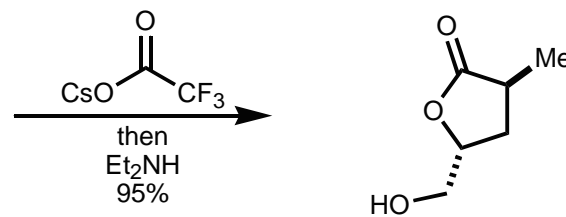
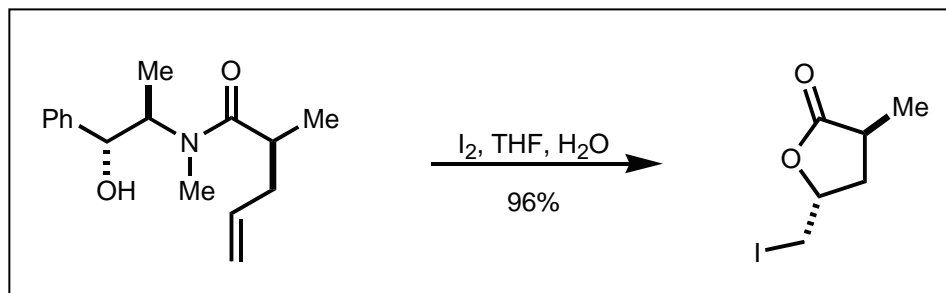
Jamison's total synthesis **2003, 2004**

Trost's total synthesis **2007**

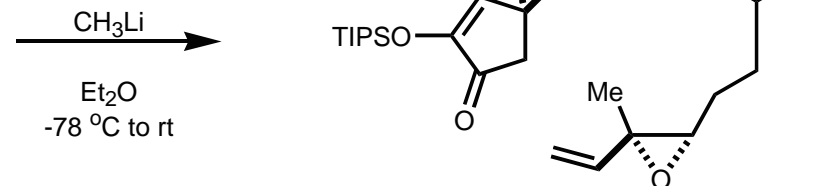
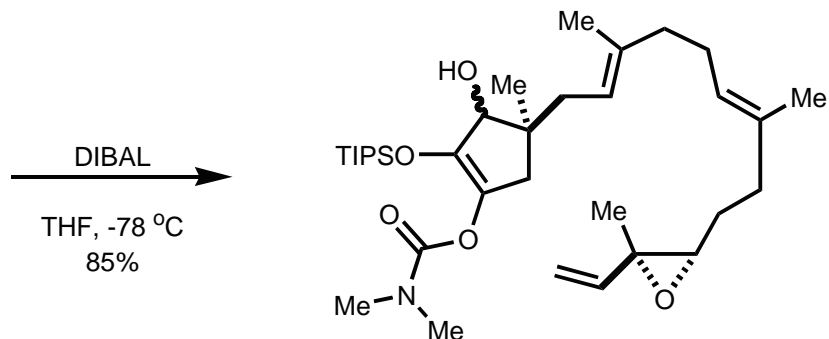
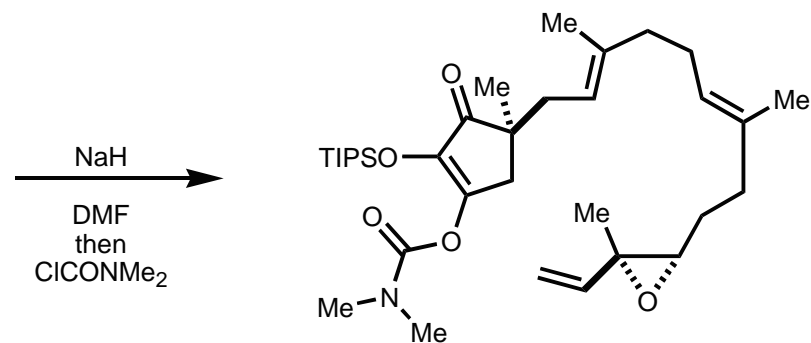
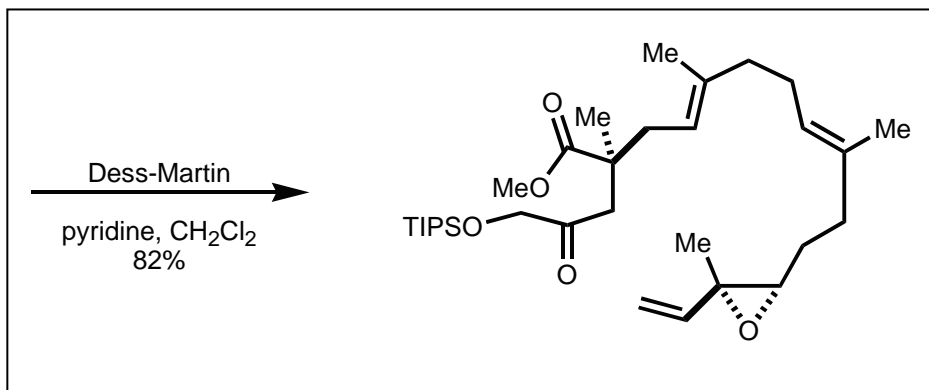
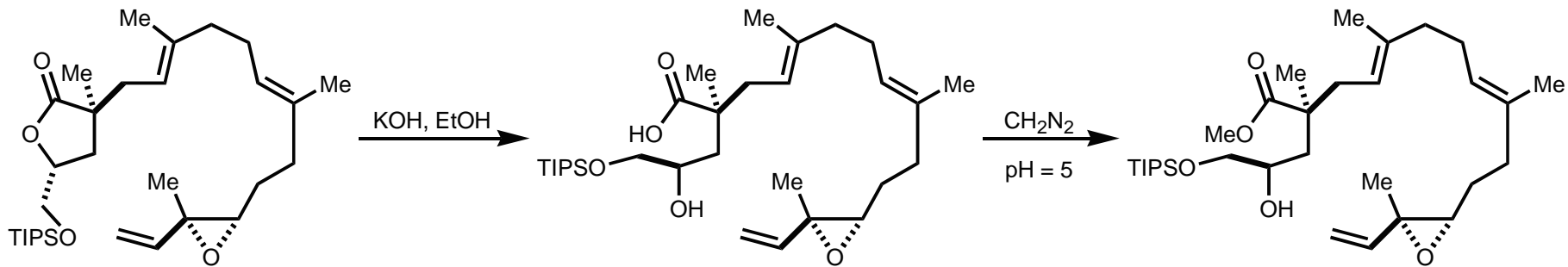
Myers Total Synthesis of (-)-Terpestacin



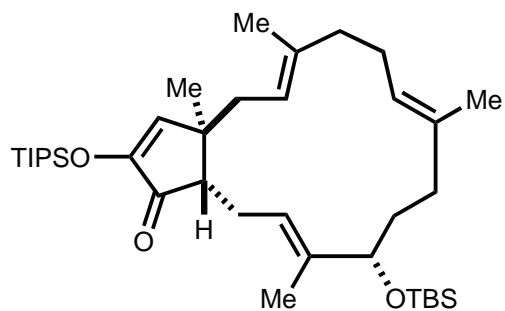
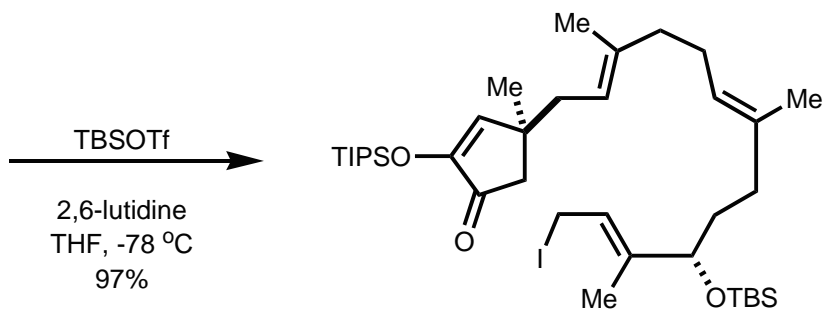
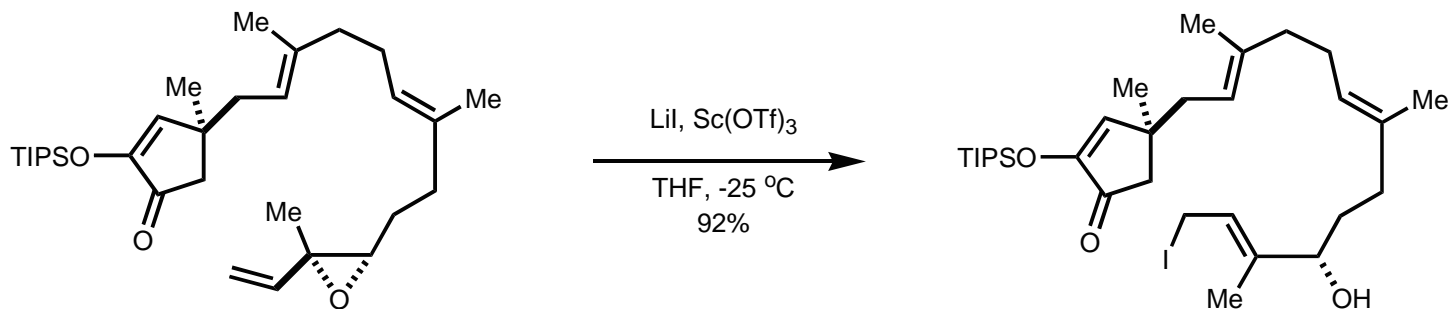
The First Enolate Alkylation



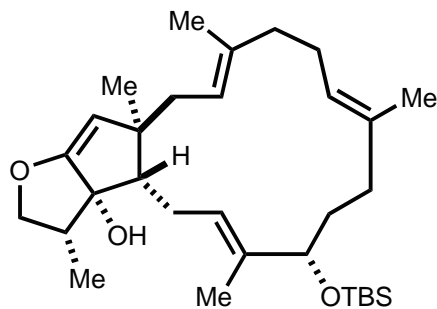
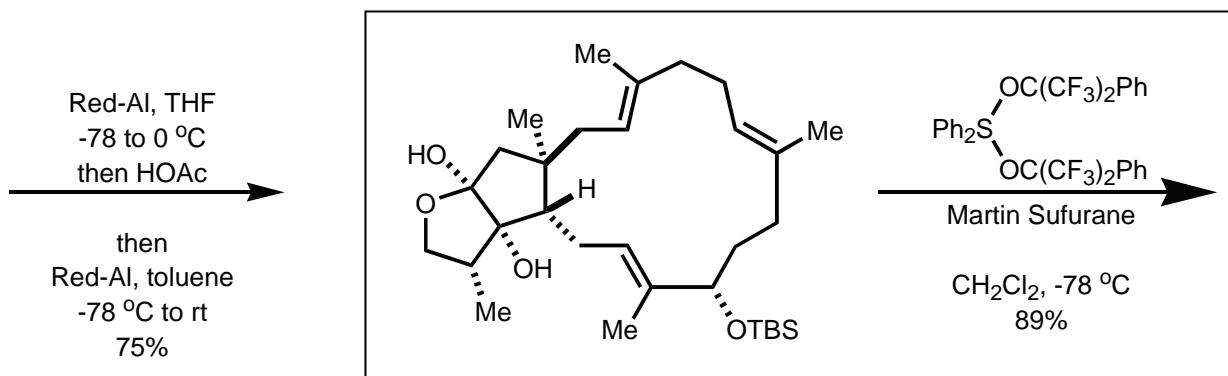
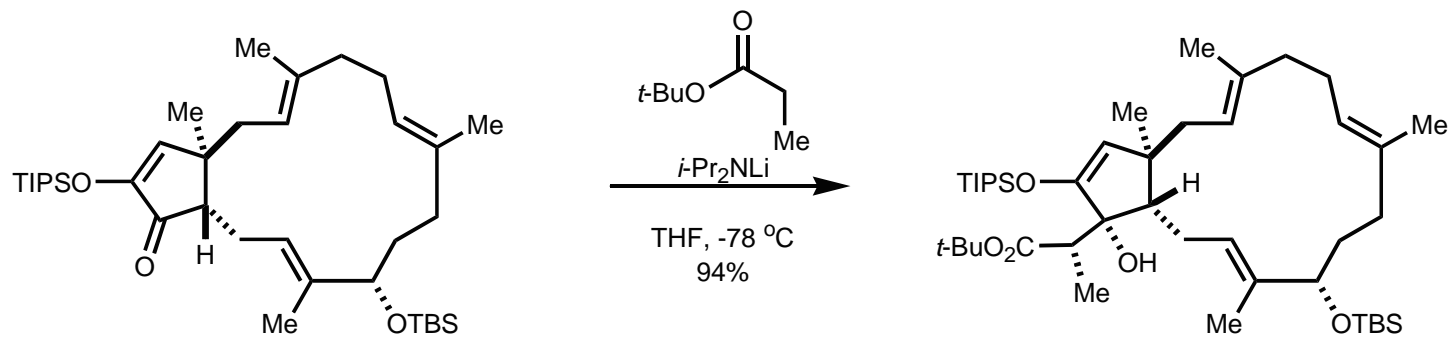
Preparing for the Second Enolate Alkylation



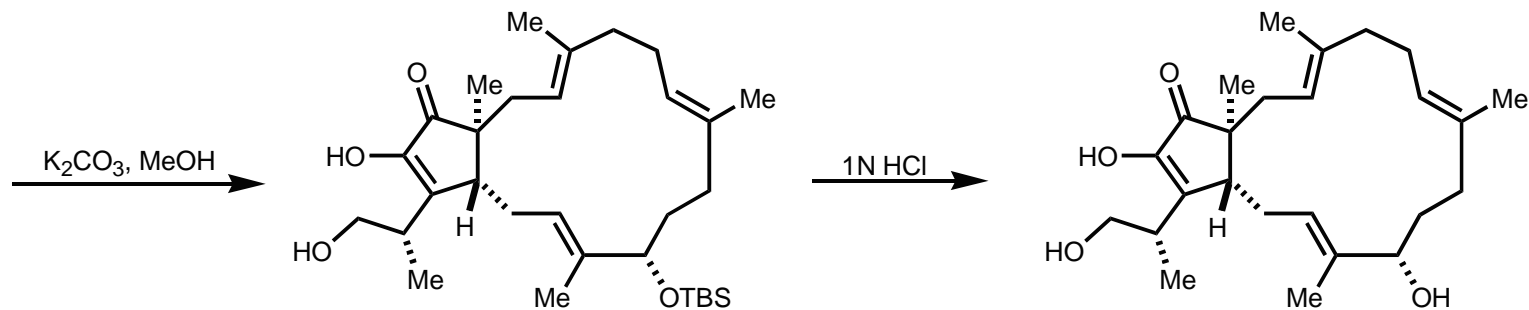
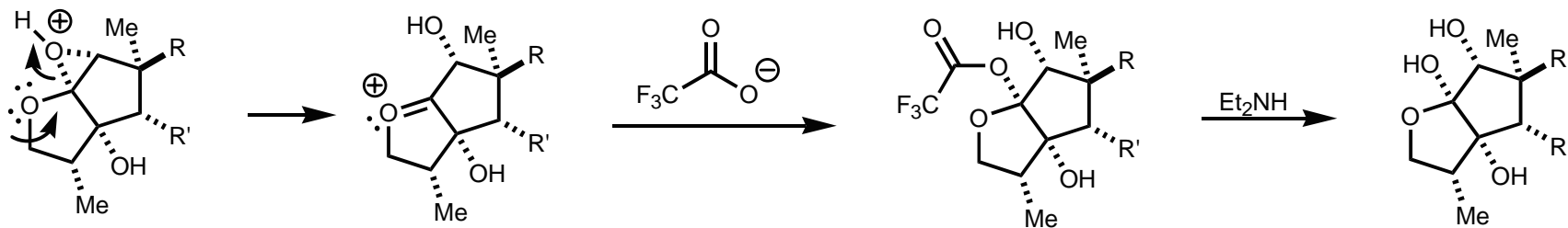
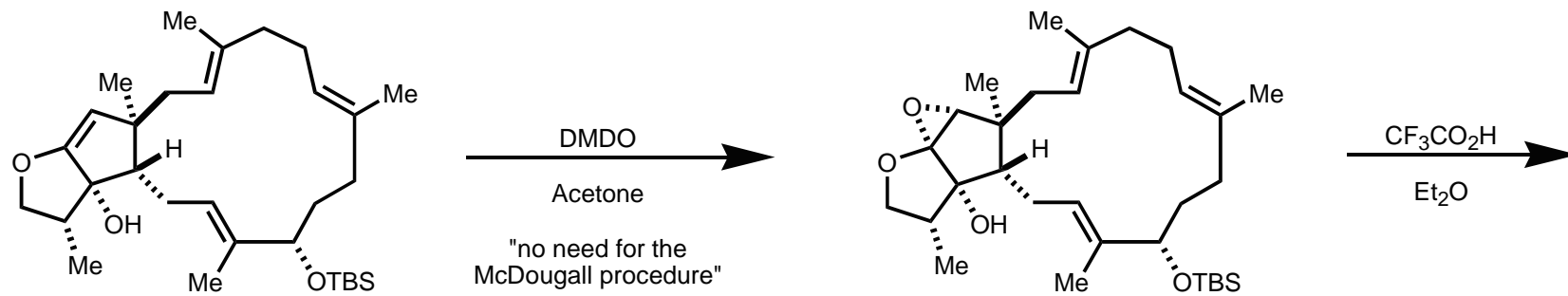
The Second Enolate Alkylation



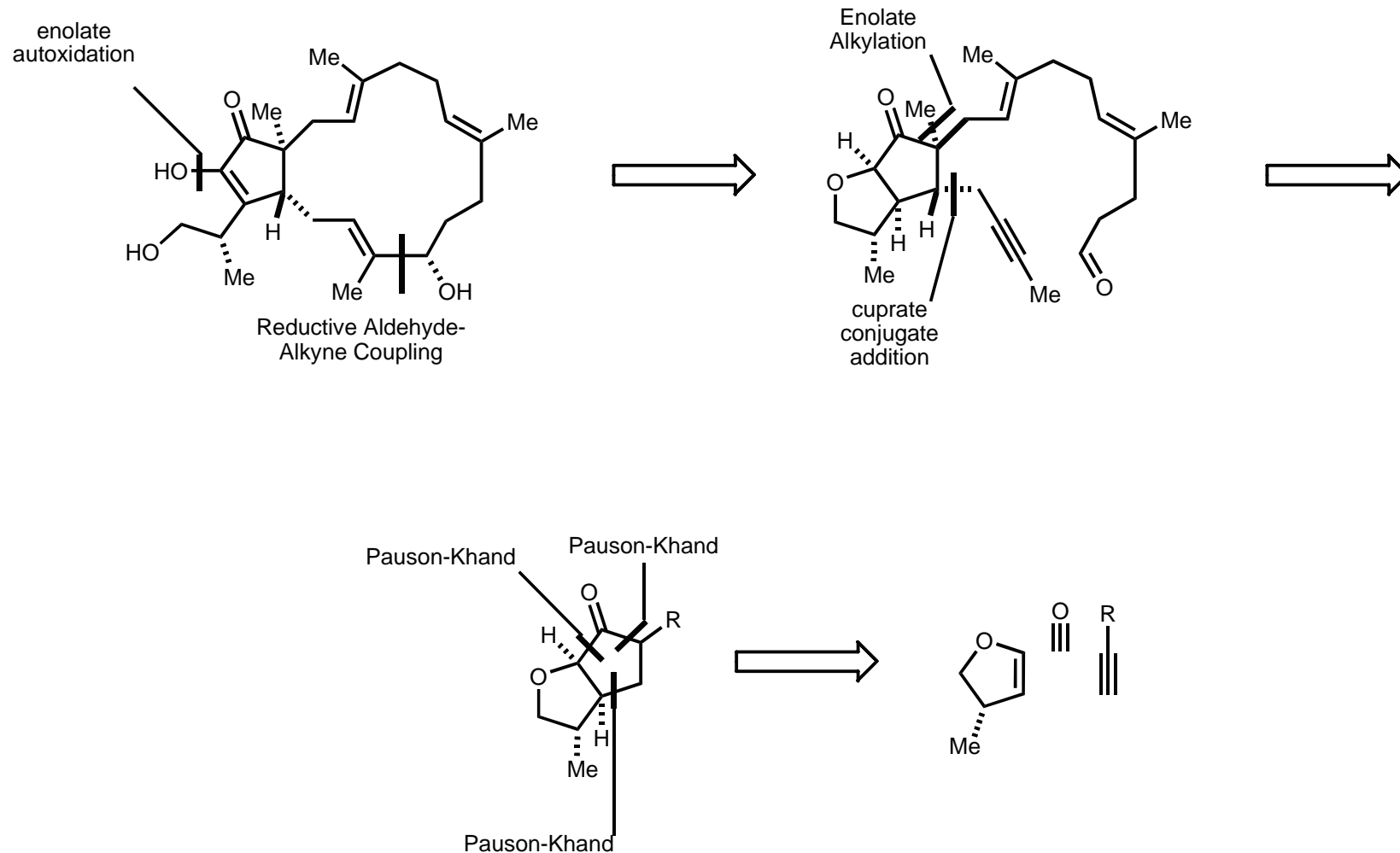
Installing the Side Chain



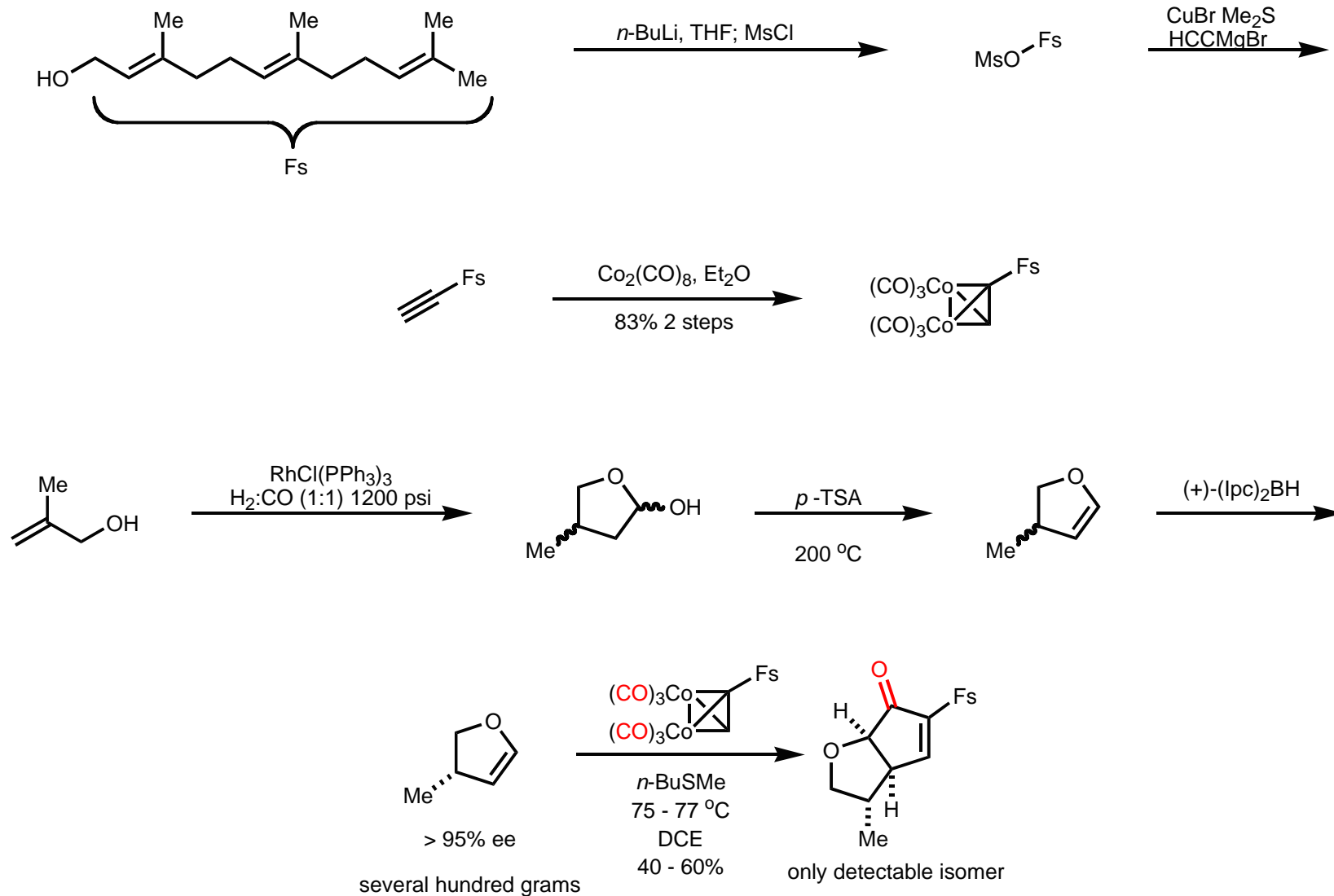
Completing the Total Synthesis



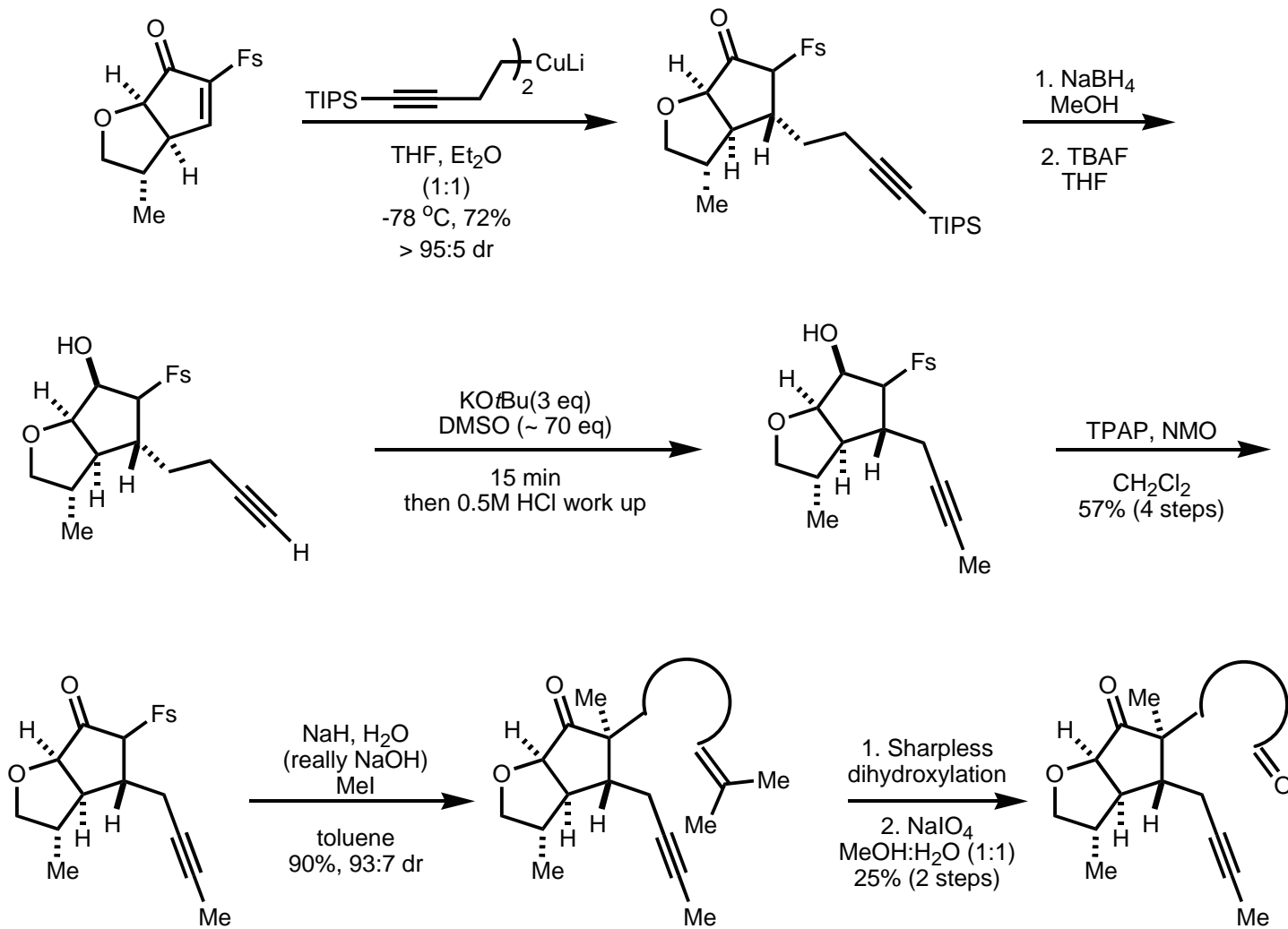
Jamison's Total Synthesis



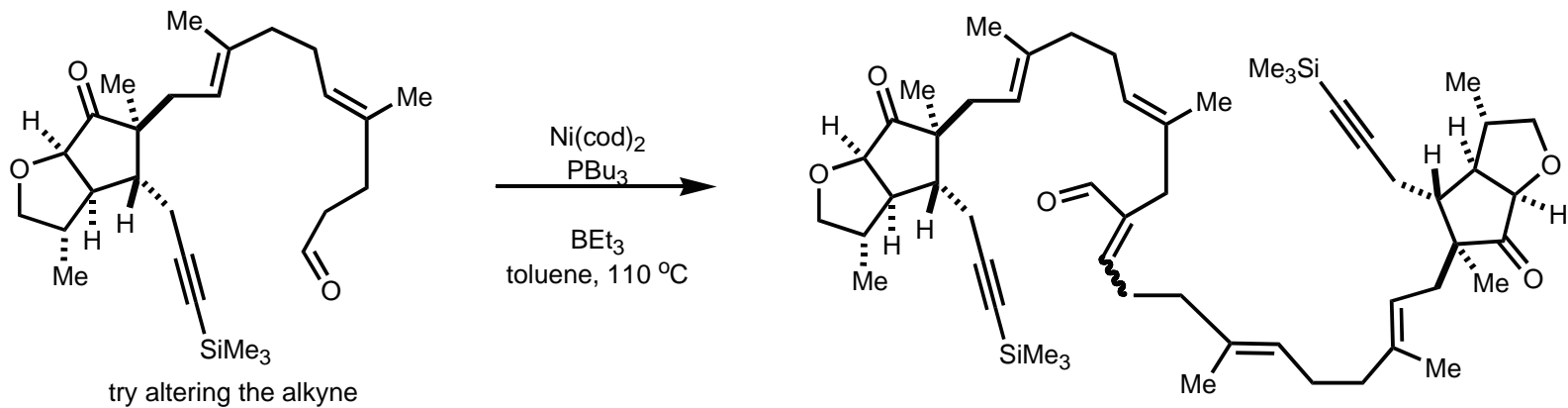
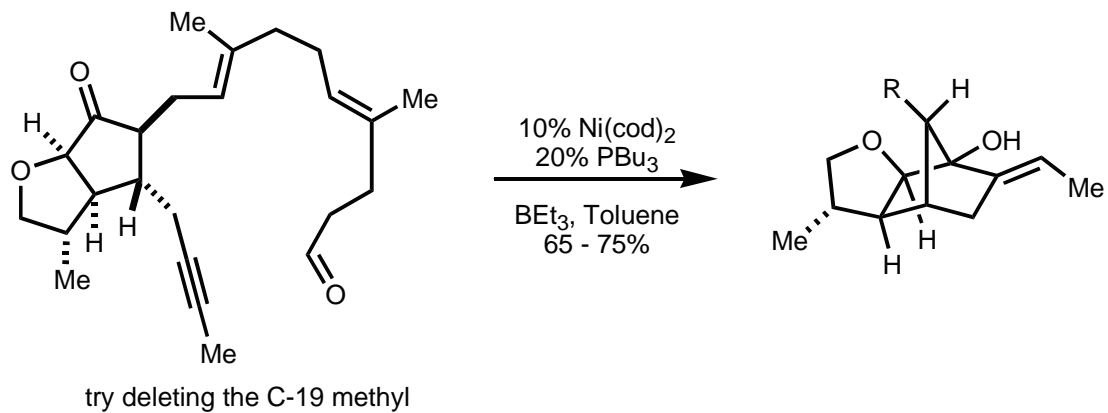
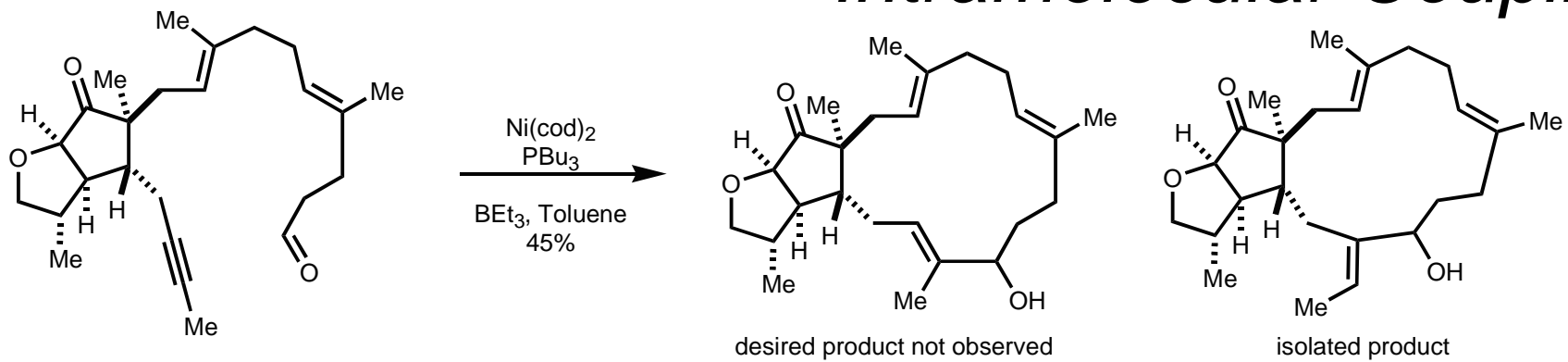
An Efficient preparation of the 5 Membered Ring



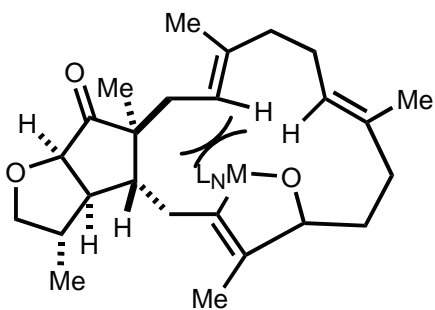
Preparing the Substrate for Macrocyclization



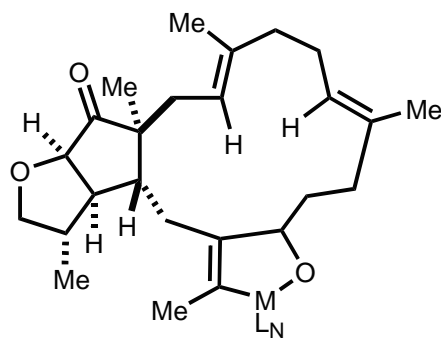
Intramolecular Coupling



Possible Explanation for Selective Formation of the 14-Membered Ring

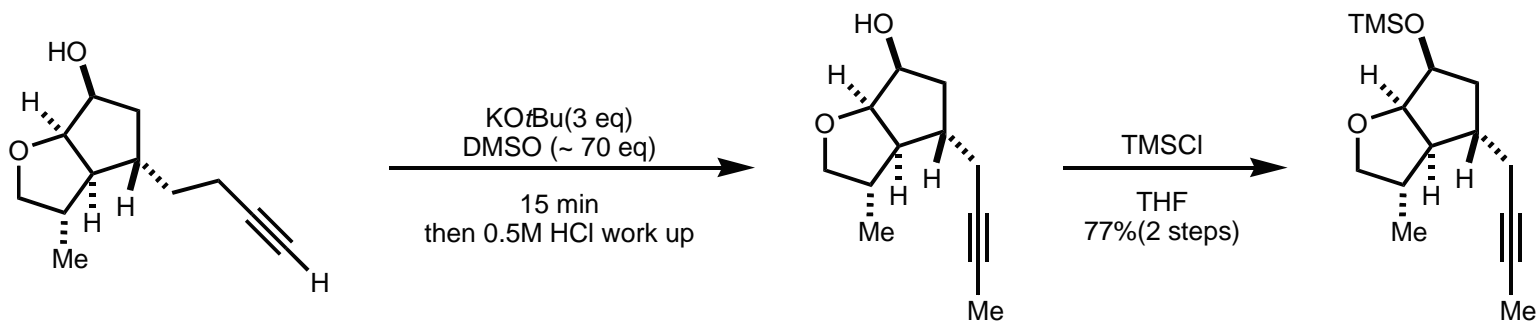
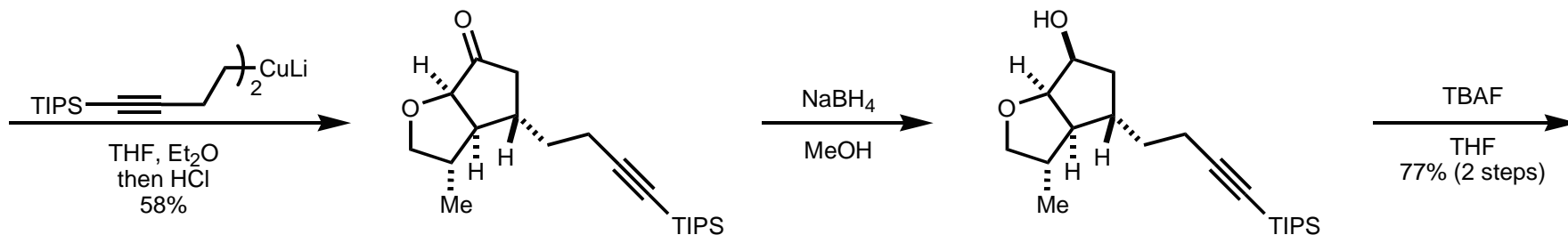
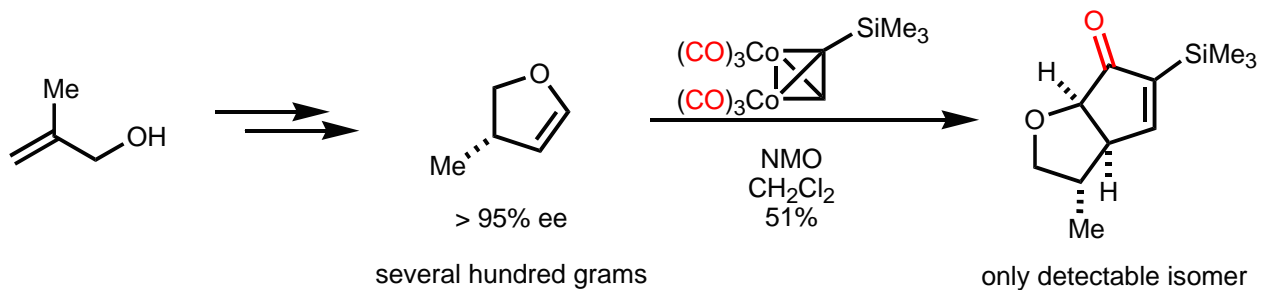


Leads to 15 membered ring

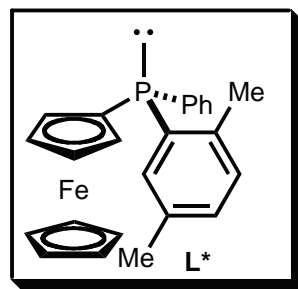
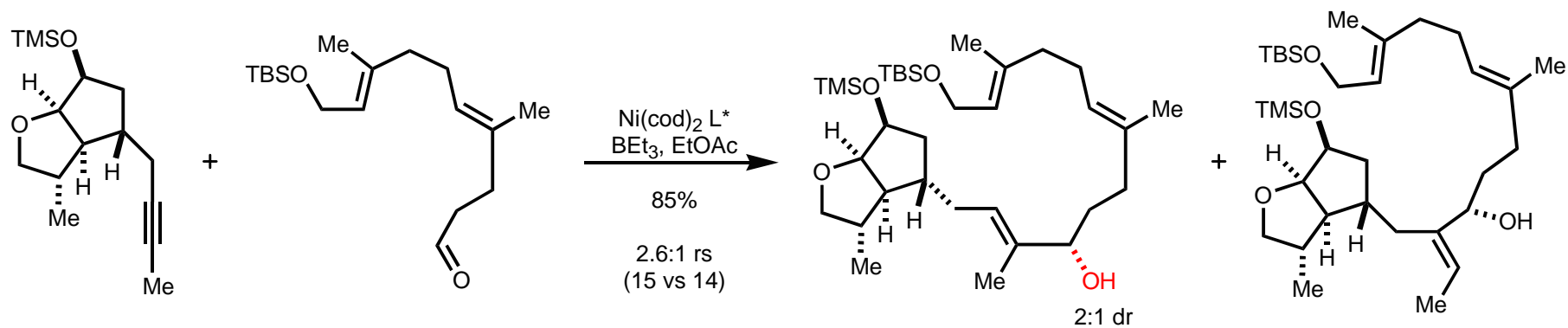


Leads to 14 membered ring

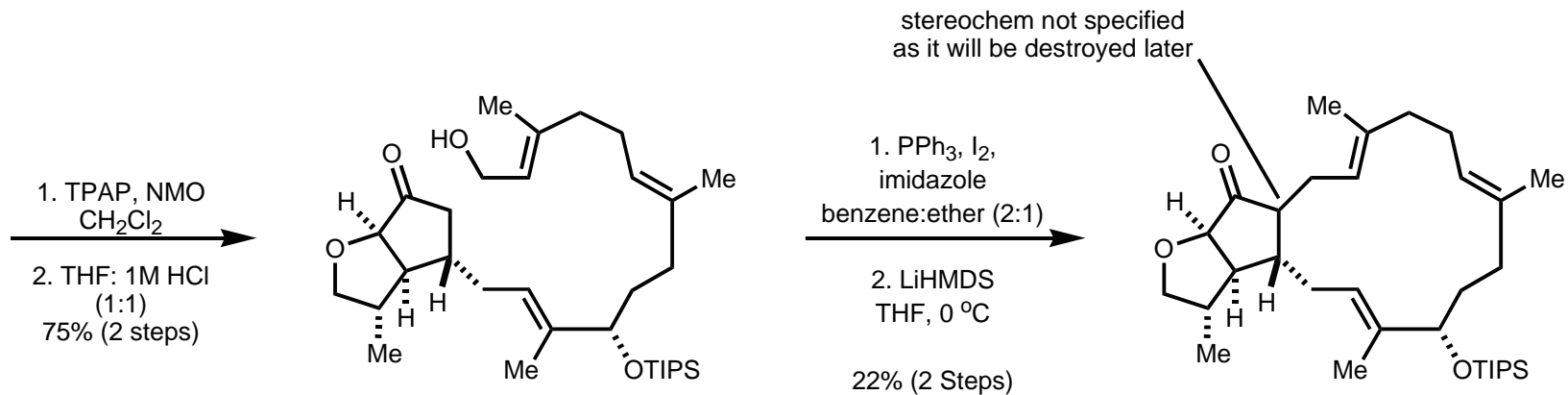
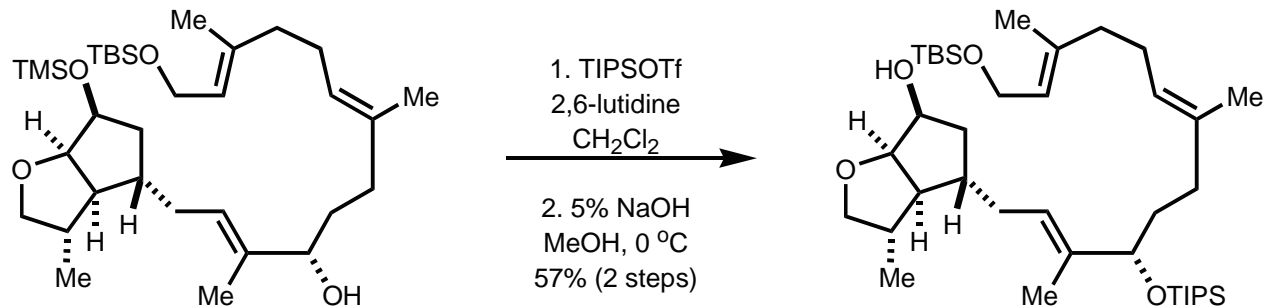
Try an Intermolecular Coupling



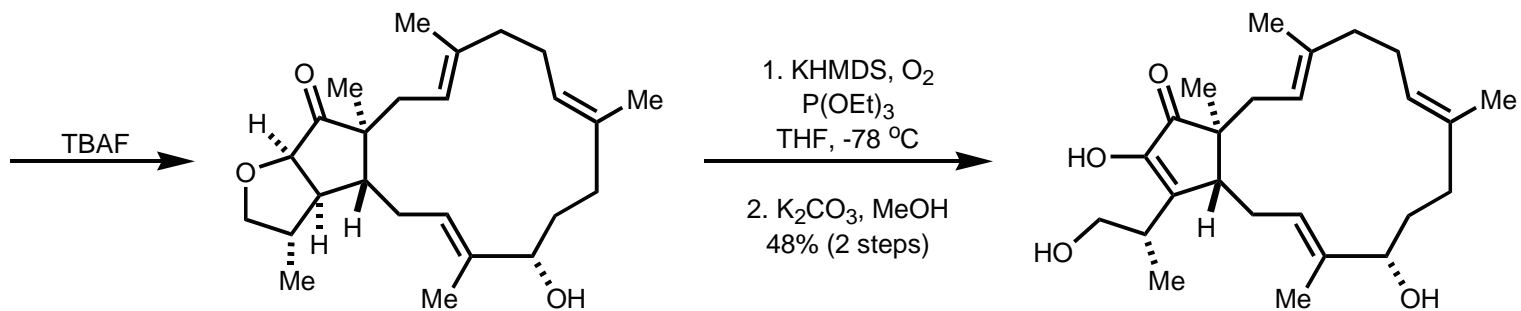
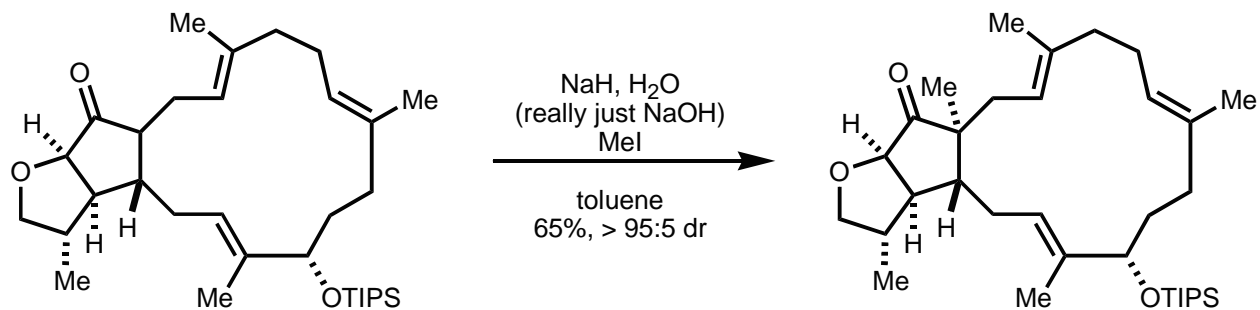
Intermolecular Coupling



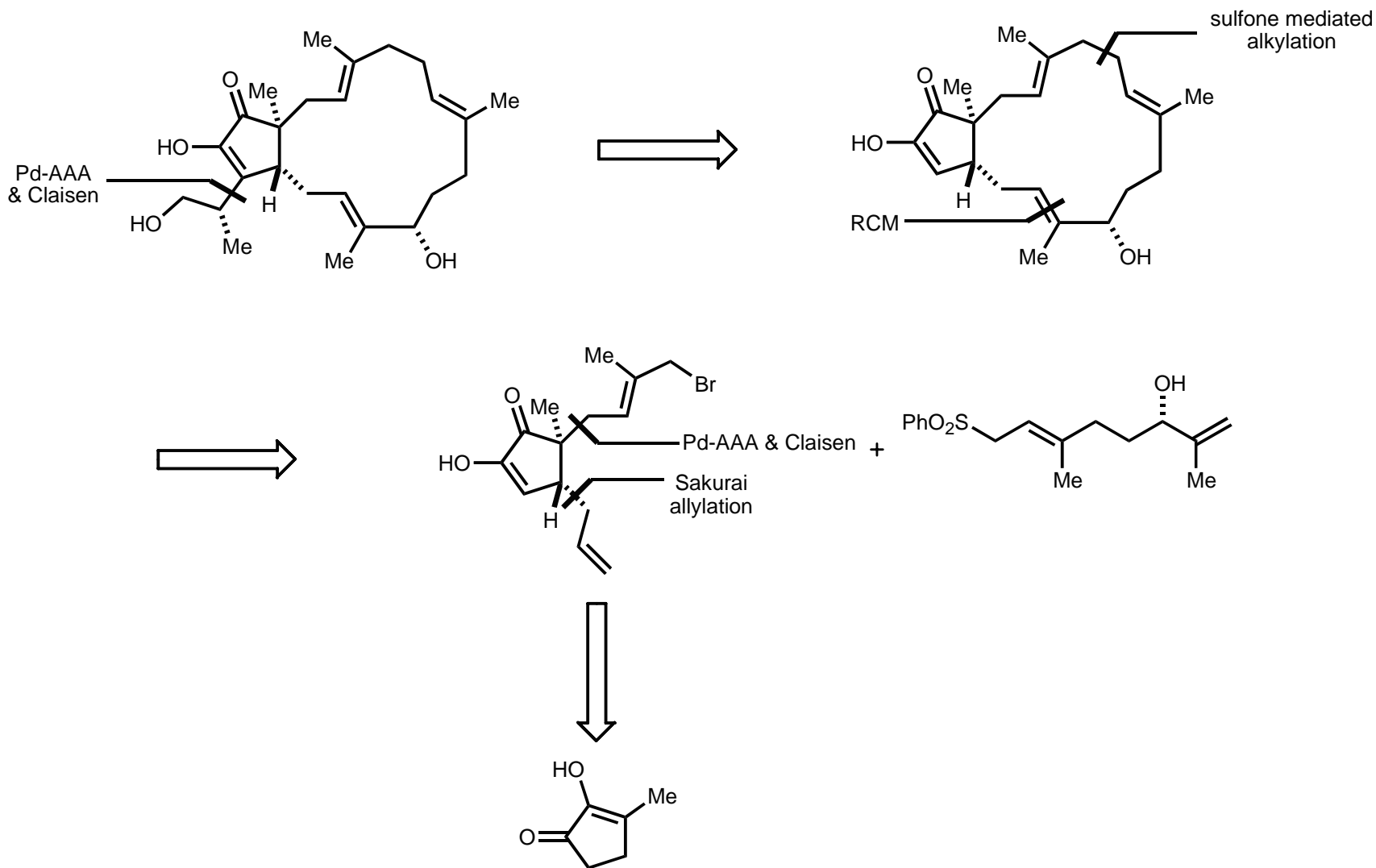
Assembling the Macrocycle



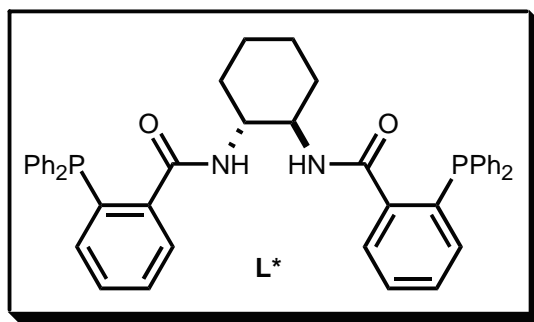
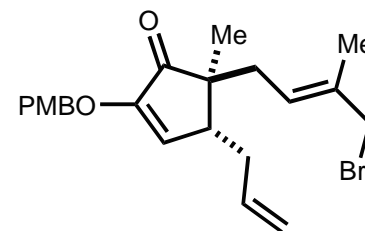
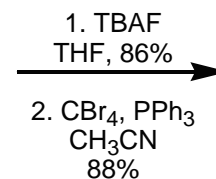
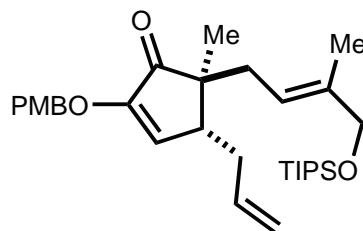
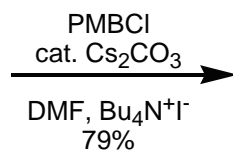
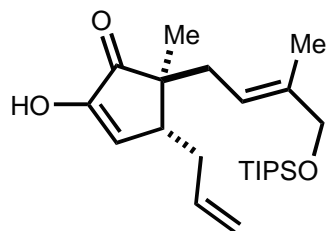
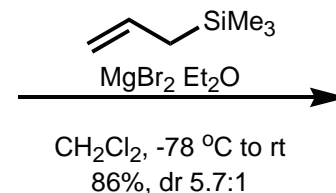
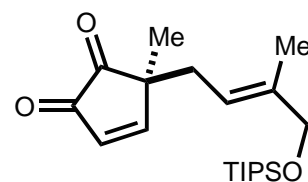
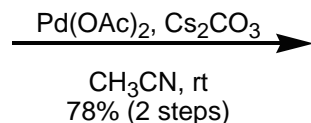
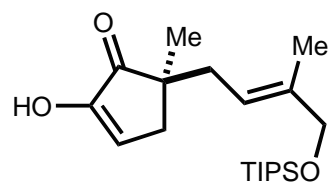
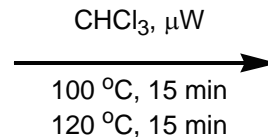
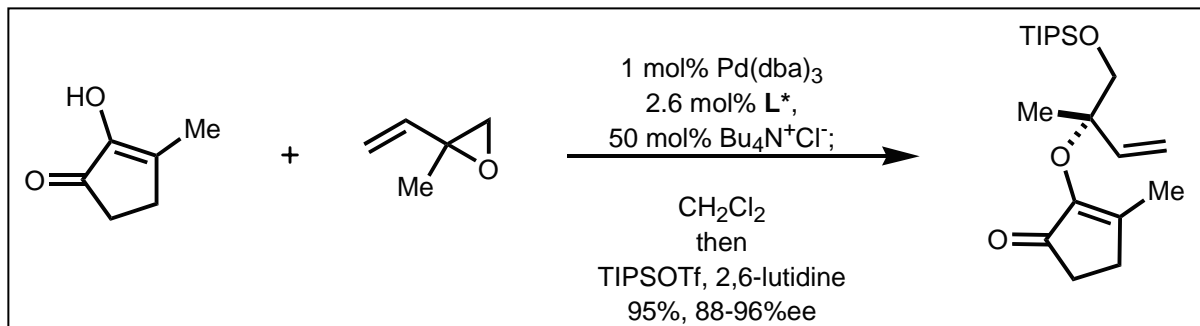
Completing the Total Synthesis



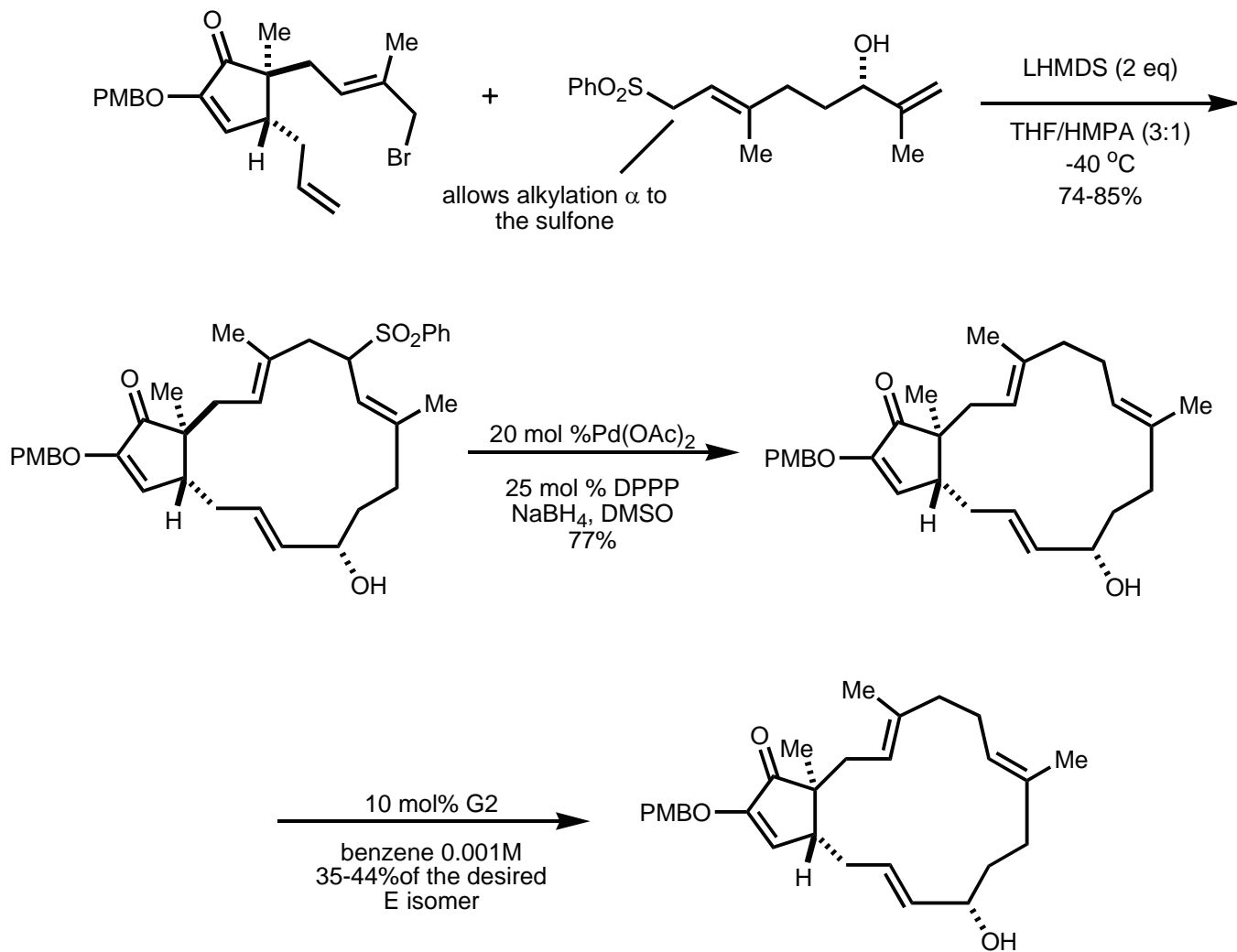
Trost's Total Synthesis of (-)-Terpestacin



Preparation of the Advanced Cyclopentenone



Sulfone Mediated Alkylation and RCM



Completing the Total Synthesis

