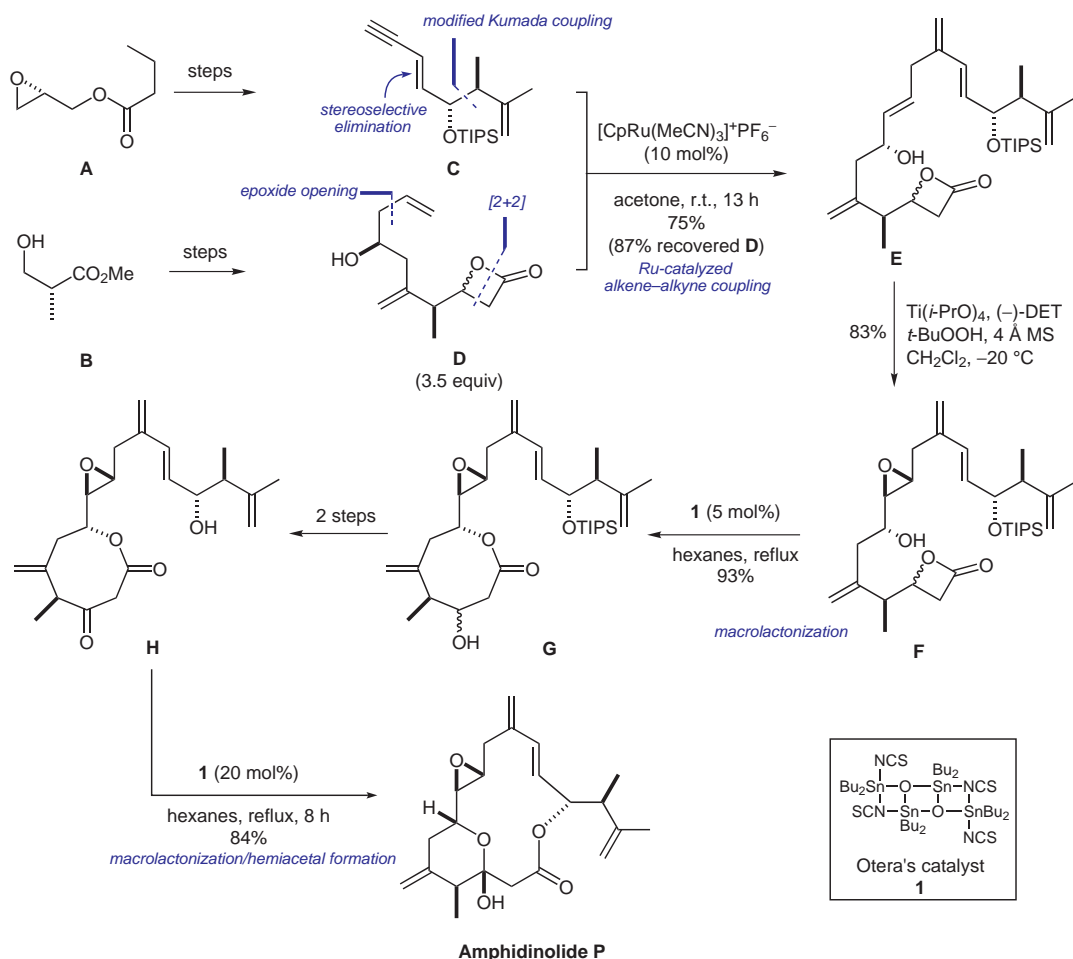


Synthesis of Amphidinolide P



Significance: Amphidinolide P is a cytotoxin isolated from the symbiotic dinoflagellates of the genus *Amphidinium sp.* found in the Okinawan flatworm *Amphiscolops sp.* Trost and co-workers use a highly chemo- and regioselective Ru-catalyzed alkene–alkyne coupling reaction to construct the backbone of the natural product and disclose the first example of the use of a β -lactone as a ‘thermodynamic spring’ in macrolactonization.

Comment: The readily available fragments **C** and **D** undergo Ru-catalyzed alkene–alkyne coupling to give the 1,4-diene **E** comprising of the entire backbone of the natural product. A Sharpless asymmetric epoxidation of **E** gave the epoxide **F** that underwent macrolactonization upon treatment with Otera's catalyst **1** to give the adduct **G**. Treating **H** with catalyst **1** effected a macrolactonization/hemiacetal forming reaction to give Amphidinolide P.