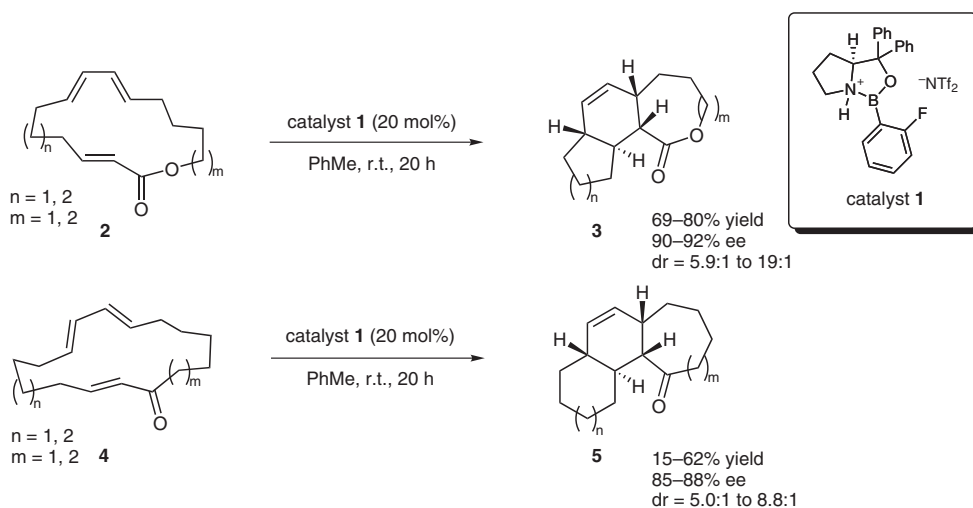
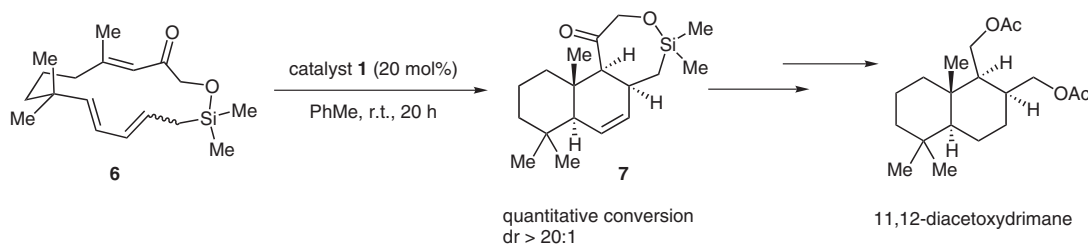


Transannular Diels–Alder Reaction Catalyzed by Chiral Oxazaborolidine



Application of asymmetric TDA in natural product synthesis:



Significance: While catalytic, asymmetric intermolecular and intramolecular Diels–Alder reactions are well established, the present paper provides the first report of the corresponding transannular Diels–Alder (TADA) reaction. A survey of various Lewis and Brønsted acid catalysts revealed that oxazaborolidine **1** was the only catalyst able to promote cyclization of macrolactone **2** ($n, m = 1$). Subsequently, various-sized macrocycles containing α, β -unsaturated lactone or ketone dienophilic moieties were cyclized to furnish tricyclic *endo* products containing medium-to-large-sized rings in good to excellent diastereo- and enantioselectivities.

Comment: This is a creative application of Corey's proline-derived oxazaborolidine system into a hitherto unexplored area of asymmetric catalysis. While catalyst **1** is often seen with an *o*-tolyl boron substituent, it was found that substitution with 2-FC₆H₄ provided TADA products in significantly higher ee values (10% vs. 90%). Also, chiral macrocyclic substrates could undergo cycloaddition to give products with significantly higher diastereomeric ratios than those obtained under thermal or conventional Lewis acid catalysis. To illustrate the utility of this process in natural product synthesis, **2** was cyclized to give **3**, which was eventually transformed into 11,12-diacetoxydrimane.