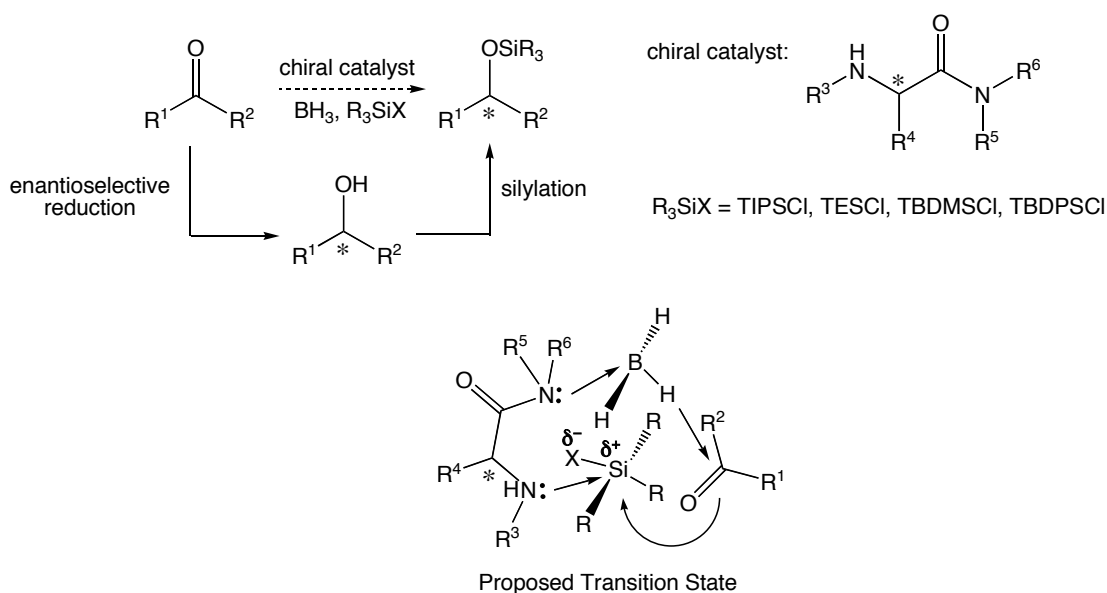


Research in my group focuses on the development of novel strategies that provide access to valuable building blocks used in the synthesis of biologically active compounds in an expeditious and stereocontrolled manner.

Tandem Enantioselective Reduction of Ketones-Silyl Protection to Form Silyl Ethers

The ultimate goal of this project is to develop a method that allows for the enantioselective reduction of ketones and subsequent silylation of the alkoxides to form silyl ethers in one step. The “one step” strategy would provide an excellent alternative to the reduction of a ketone followed by isolation of the alcohol, silylation, and second purification of the desired enantiomerically pure silyl ethers. The synthesis of silyl ethers in one step employs the rationale that the desired silyl ethers will result from the simultaneous activation of BH_3 , the hydride source, and electrophile (R_3SiX) by an amino-acid-based catalyst. Activation of the ketone will be as a result of the pentavalent silane acting as a Lewis acid. The result will be the bringing of all the key reagents in close proximity to one another to form an organized transition state that allows for the enantioselective reduction/silylation to occur.



1,4-Conjugate Addition of Dienolates to α,β -Unsaturated Aldehydes and the Synthesis of Kavain

The addition of nucleophiles to α,β -unsaturated aldehydes has garnered plenty of attention because of the susceptibility of nucleophiles to add in a 1,2-fashion rather than achieving 1,4-addition. Recent advances include the formation of iminium ions with chiral imidazolidinones that allow for the LUMO-lowering activation of α,β -unsaturated aldehydes (David MacMillan). In an effort to further expand on the scope of nucleophilic additions to a variety of α,β -unsaturated aldehydes, it is our goal to investigate the 1,4-

addition of methyl 4-bromo-3-methoxycrotonate or methyl 3-methoxycrotonate. We will focus our work on developing conditions that allow for the dienolate to add from the C2 site rather than the C4 site. In addition, we will apply the methodology to the synthesis of the biologically active natural product, kavain. Kavain is isolated from the Polynesian shrub kava found in the western Pacific. Traditionally, the extract of the roots of kava is used in beverages to promote relaxation. The active principal ingredients are 15 kavalactones, but the most prevalent is kavain. Investigations have reported that kava possesses anxiolytic, anesthetic, antifungal, antithrombic, anticonvulsive, and analgesic properties. Recently, it has also been reported that kava may treat ovarian cancer and leukemia. We would also pursue the syntheses of other kavalactones found in kava such as methysticin and yangorin. It is expected that all three syntheses can be accomplished in 3-4 steps from 4-bromo-3-methoxycrotonate.

