Organometallic synthesis and asymmetric catalysis

Piperidine and pyrrolidine are common nitrogen ring structures in US FDA approved pharmaceuticals. Hydroamination, the formal addition of an N-H bond across a C=C unsaturated bond, is an attractive method for their synthesis as the reaction has 100% atom economy. Some of the most selective catalysts for these rings have been achieved using gold catalysts with highly engineered chiral phosphine ligands that must be prepared and resolved in multiple synthetic and purification steps. Our laboratory is developing titanium catalysts for asymmetric hydroamination using readily prepared ligands derived from naturally occurring amino acid starting materials. Success in this project will decrease the environmental impact relative to gold catalysis and improve the enantioselectivity of these reactions over that observed with previous titanium catalysis.

Catalysts consist of both the metal and a small molecule called a ligand which binds to the metal. Ligands are synthesized in a two- to three-step procedure and then they are attached to the metal precursor and used as a catalyst for the hydroamination reaction. You will gain experience on NMR spectroscopy, GC-MS, air-sensitive reaction chemistry and the use of a glove box. Current synthetic targets are shown below.

Titanium (and tantalum) complexes catalyze the intramolecular hydroamination of 1,3-aminoallenes as shown below. Our complexes form product 1 in high yield (100% when R’ = Me), and the enantiomeric excess is low (ca. 16%) for Ti, but much higher (ca. 75%) for Ta. We test all new complexes and substrates in the hydroamination reaction.