EASTERN MICHIGAN UNIVERSITY

Chemistry Department

M. S. Thesis Seminar

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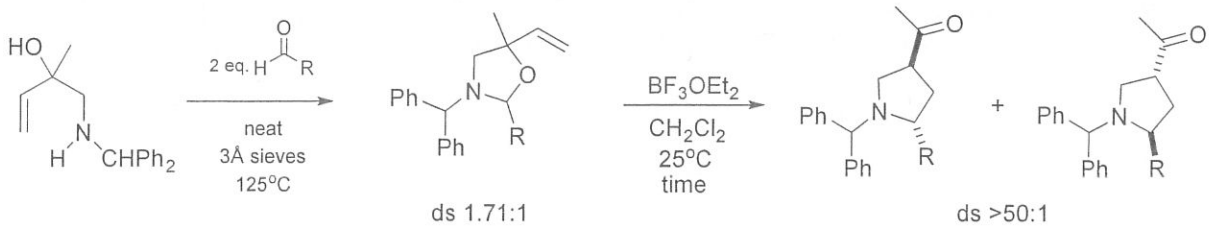
(Harriet Lindsay, advisor)

Monday, Nov. 10th, 4:00 pm, Sci Complex Rm 145

Advancments in the diastereoselective synthesis of acyl pyrrolidines via the tandem aza-Cope-Mannich-cyclization pathway

We have developed a Lewis-acid catalyzed, diastereoselective aza-Cope rearrangement—Mannich cyclization to form acyl pyrrolidines from conformationally mobile substrates. In earlier studies from the Lindsay lab, Brønsted acid-catalyzed reactions to form the same acyl pyrrolidines resulted in diastereoselectivities of 8:1 *trans* to *cis* at elevated temperatures (60°C) over the course of 150 minutes. We have demonstrated an improvement in our method yielding exclusively the trans isomers at ambient temperature with substoichiometric amounts of BF3OEt2 within 3 minutes. Catalyst loadings as low as 0.5 mol% of BF_3OEt_2 initiate this transformation. Our synthetic method employs the oxazolidine starting material as a mixture of diastereomers to produce one pyrrolidine diastereomer. Both ethyl and substituted phenyl oxazolidines were successfully rearranged. This work is the first example of a truly catalytic aza-Cope—Mannich reaction as provides the first examples of diastereoselective syntheses of 2-phenyl-3-acyl-pyrrolidines via this reaction.



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