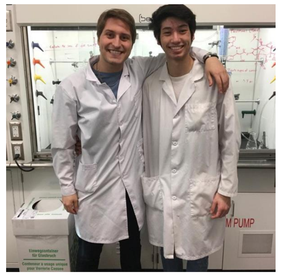
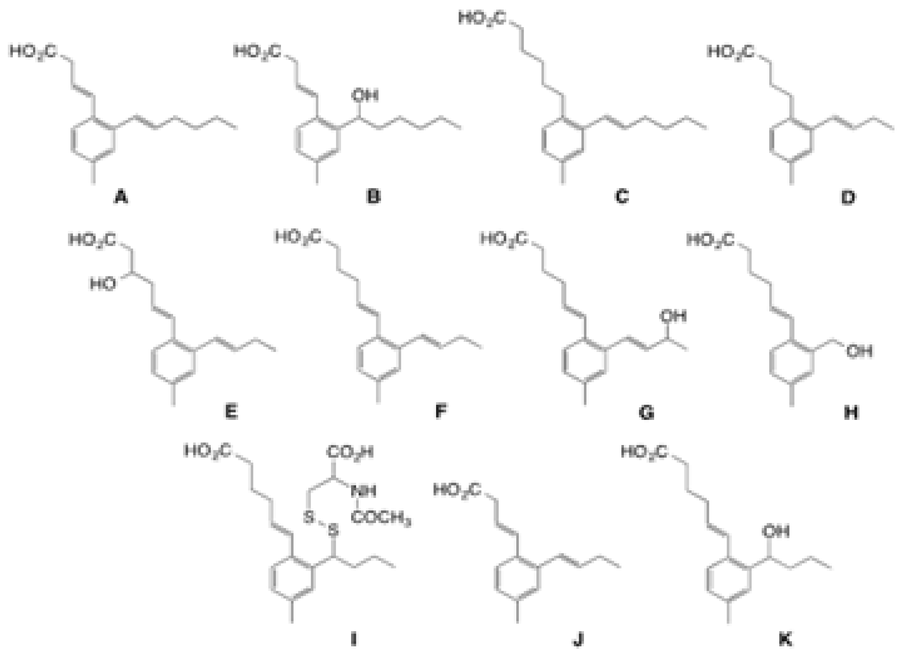
Total Synthesis of Lorneic Acid A

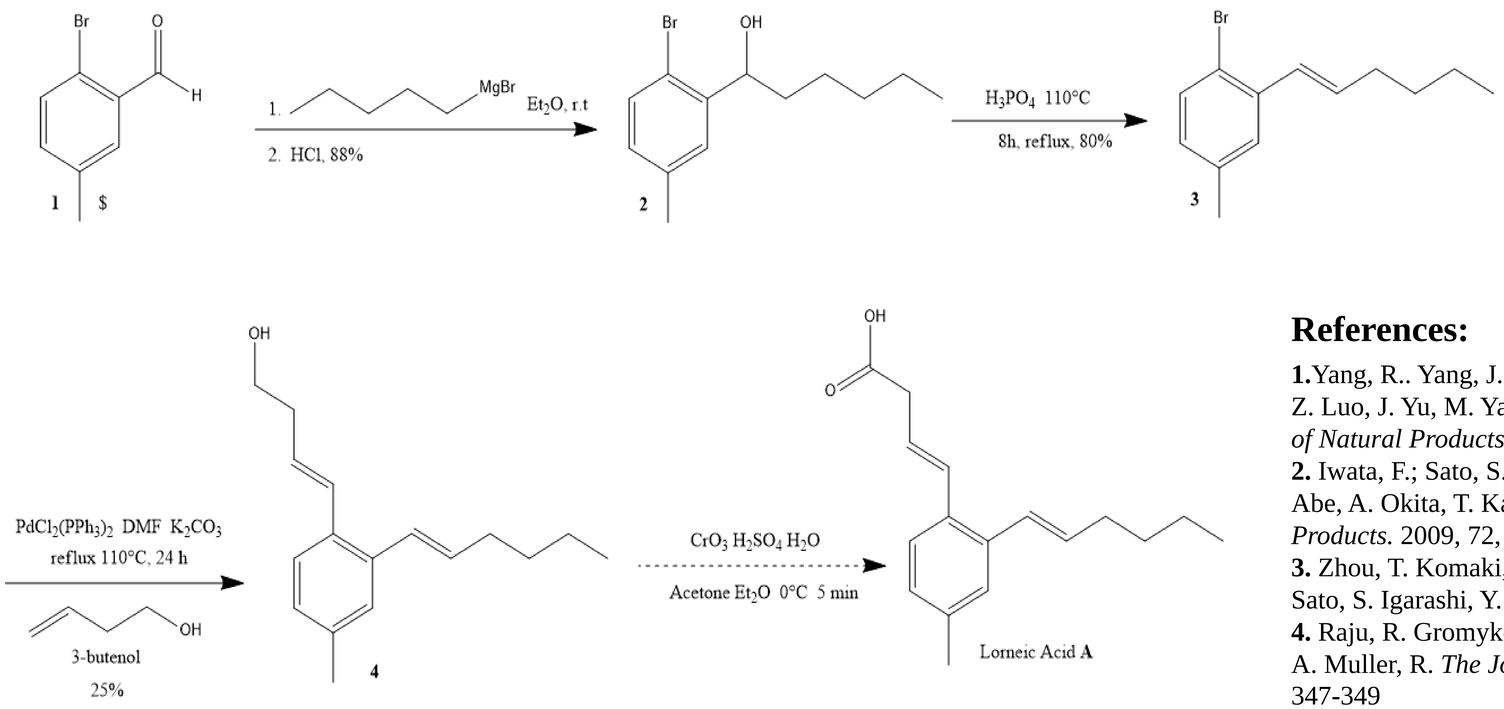
Brandon Sarrels and Dr. Claudia Lucero
Department of Chemistry
California State University, Sacramento



Abstract: The total synthesis of lorneic acid **A**, a trialkyl substituted aromatic obtained from an actinomyces strain, *Streptomyces* (NPS554), has been achieved in 4 steps from 2-bromo-5-metylbenzaldehyde. The key operation involved a Pd-catalyzed Heck reaction that attaches the necessary alcohol while concurrently forming a conjugated trans olefin. Lorneic acid **A** exhibits significant inhibition activity against phosphodiesterase (PDE), especially PDE5. As phosphodiesterase inhibitors, lorneic acid **A** has the potential to treat pulmonary hypertension, erectile dysfunction, heart failure, and other inflammatory diseases. The complex structure, phosphodiesterase inhibition, and natural scarcity all make lorneic acid **A** a significant synthetic target.

Introduction: In 2009, lorneic acids **A** and **B**, were extracted from an actinomyces strain (NPS554) isolated from a marine sediment in Miyazaki Harbor, Japan and were found to possess significant inhibition activity against phosphodiesterase (PDE). As phosphodiesterase inhibitors, these lorneic acids have the potential to treat arterial hypertension, dementia, depression, and schizophrenia by preventing the inactivation of secondary messengers. Although total syntheses of lorneic acids **A** and **B** have been previously accomplished from 4-methylbenzoic acid, these synthetic routes required 11-12 steps with overall yields of 20-26%. The goal of this project is to investigate a shorter and more efficient total synthesis of lorneic acid **A**, in 4 steps, as opposed to 11, and in higher overall yields.





Discussion: Currently, I am investigating the Jones Oxidation on trans cinnamyl alcohol before performing the reaction on my Heck Product. Also, I need to troubleshoot the Heck reaction by varying the base, reaction temperature, and equivalences. Finally, I need to characterize each step via ^{1}HNMR, ^{13}CNMR, IR, and HRMS for publication in our manuscript.

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