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Synthesis of the Tetracyclic Scaffolds of the Endiandric Acids Through Iterative Cross- Coupling

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Reflective Essay

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My senior thesis project in chemistry describes the synthesis of two distinct tetracyclic structural motifs that are present in a number of bioactive natural products. Chemical synthesis involves running a sequence of reactions to convert a simple, commercially-available starting material into a more complex molecule, one step at a time, ultimately arriving at the final desired product. My research process consisted of the following three tasks: 1) devising a potential synthetic strategy for my target tetracycles, 2) executing the synthesis in the lab, and 3) modifying the strategy as needed based on the outcomes my experiments.

I embarked on the journey toward the tetracycles in the fall semester of my sophomore year, when I joined the laboratory of Professor David Vosburg. This was my first time encountering chemical research, both in the lab and via the literature. Working alongside a senior student who was working on his thesis research at the time, I became acquainted with the laboratory equipment and techniques of a synthetic chemist. I also learned about the SciFinder Scholar database and chemistry journals to which the Claremont Colleges Library subscribes. Once I was exposed to the research problems pursued by the Vosburg lab, as well as the resources that were available to assist in solving them, I became excited about exploring new synthetic routes to the tetracycles. I was particularly interested in strategies that would allow us to synthesize various analogs of these tetracyclic compounds in a highly efficient and flexible manner.

In order for me to propose my own synthesis, I first had to understand the previous approaches that have been taken by the lab. For this reason, I spent my junior year reading up on the theses written by numerous Vosburg lab alumni, making note of the strengths and weaknesses of each approach. I also found it equally important to familiarize myself with the work that was being done in other chemistry labs to solve similar problems. The combination of past student theses and a grant proposal from the Vosburg lab pointed me to Martin Burke at the University of Illinois, Urbana-Champaign, who had recently published on an iterative cross-coupling (ICC) method for synthesizing polyene natural products. I realized that ICC could be an attractive and promising way to prepare my targets – the tetracyclic structures were believed to arise in nature from polyene precursor molecules, after all. Having read about the merits and the

applications of Burke's ICC in natural product synthesis, I came up with an original research proposal that incorporated points of strength from the chemistry by both the Vosburg lab and the Burke group. The remainder of my junior year was spent revising the proposal and coming up with back-up plans, with guidance from Professor Vosburg.

Come senior year, my newly-proposed synthesis of the tetracycles was ready to be tested in the lab. This is the project that I am currently pursuing for my senior thesis. As it was my first time running any of the reactions included in the strategy, I initially encountered problems in preparing and purifying many of the intermediate molecules. Overcoming these unforeseen obstacles required that I return to SciFinder and chemistry journal articles to carefully re-read the procedures that other scholars have used to access and handle molecules with similar chemical properties. I have modified my original proposal several times based on experiments that did not pan out as expected, and SciFinder proved particularly useful in these situations. Although most of the relevant chemical literature was published online, I also relied on printed resources for instructions on reagent purification and summaries of notable chemical reactions.

Crucial to the successful execution of my thesis research were my relationships with each and every one of my mentors and collaborators. In addition to Professor Vosburg, who has been a fantastic advisor to work with, I am also indebted to the mentorship I received from Derek Tan and Inder Sharma at the Memorial Sloan Kettering Cancer Center during Summer 2014. Derek and Inder introduced to me a whole new palette of chemistry and laboratory techniques that strengthened my foundations in organic synthesis, which were highly applicable to my research at Harvey Mudd. I am also grateful to Martin Burke for sharing with us a gram of the key synthetic building block that thwarted my initial efforts.

My senior thesis would not have been possible without access to SciFinder and various chemical journals provided by the Claremont Colleges Library. SciFinder was indispensable for looking up and studying specific examples of reactions related to those used in my own synthesis, guiding me whenever I was searching for a new route to take. I found it especially helpful that SciFinder indicated not just the way, but also the advantages and the risks associated with each option. The access to chemistry journals was essential for getting my hands on papers that provided relevant background for my thesis, and for managing them, I was fortunate to have learned about Zotero through the library website. It amazes me whenever I reflect on the myriad

ways in which various faculty and the Claremont Colleges Library have supported me in my research. Looking back at my research journey over the three years, I can say with certainty that it has been an exhilarating and rewarding experience.

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**Eun Bin Go
Harvey Mudd College**

Senior Thesis

**“Synthesis of the Tetracyclic Scaffolds of the
Endiandric Acids through Iterative Cross-
Coupling”**

This thesis is currently available only to The Claremont Colleges.
URL: http://scholarship.claremont.edu/hmc_theses/68