A chemical subunit called a β-lactam is the main subunit of numerous antibiotics, although bacterial resistance has rendered many of these ineffective. We are developing a new synthesis for an analog, called γ-lactam, which involves the modification of a precursor chemical into an alkene (with C-C double bonds). Our modification protocol is a significant simplification of existing methods, and thus provides an exciting alternative to them. A primary goal for this research project involves the rearrangement of a β to γ-lactam (in which an expansion from a four- to five-membered ring occurs). The hypothesis that, since this new reaction works on simple model compounds, it will similarly function on a variety of substrates, including precursors to new antibiotics. γ-Lactams are involved in many biologically active molecules in addition to antibiotics, so it will be of great scientific utility to perfect the β-lactam-to-γ-lactam conversion.

My research will be broken down into three steps, of which the first will consist of creating C=C from C=O bonds. A special, air-sensitive reagent will be made, to which will be added the C=O compound; this will then form the desired C=C bond (an alkene). If necessary, purification of the products will be carried out by a common technique known as column chromatography. The second step will be in forming a β-lactam ring, which will be carried out as the result of a [2+2] cycloaddition between the alkene and a chemical called chlorosulfonyl isocyanate (CSI). The resulting β-lactam will be allowed to stir for an extended period of time whereupon the ring should expand to form the γ-lactam. The third step will be examining the rearrangement of the β to γ-lactam. Developing the desired alkenes will require five weeks. Creating the β-lactams will also require five weeks. Finally, examining the rearrangements will require five weeks as well. Altogether, my research project should be completed within a semester’s time.

This is my junior year as a Chemistry minor, for which I have nearly completed all my required classes. These requirements include two semesters of Organic lab work and lecture. In addition, this semester I am taking the departmental “Introduction to Chemical Research” class (CHM 3500). I have learned a great amount of information and lab techniques, including analyzing compounds using specific instruments, in these classes. In addition, I have gained countless skills working with Dr. Black and his research group for over 20 weeks, which has definitely given me the skills to complete this project successfully.

It is very important in the medical world today to develop new medicines to fight the increasing number of antibiotic-resistant bacteria. The beta lactam moiety is the medicinally functional part (the “pharmacophore”) of a great many antibiotics, including cephalosporins and third-generation analogs. It would be of great value to develop synthetic methods for making γ-lactams, which are involved in many biologically active molecules, but whose exploitation in antibiotic research is just beginning. This research will contribute to existing knowledge in two ways. First, a novel, rapid synthesis of C-C double bonds from C-O double bonds will be developed. Secondly, a new, efficient route to γ-lactams will be optimized.

There are two tasks carried out in any organic chemical research, following a reaction: product purification and analysis. By analyzing an infrared (IR) spectrum, the alkene will be confirmed as to whether it is pure or whether there is starting material still in the solution, whereupon a column chromatographic separation must be carried out. Also, proton NMR spectra (which enable various proton groups in a molecule to be seen) will be run, and gas chromatography will be used to separate and quantify the mixtures. Additionally, by determining percent yields of the products, I will determine if I have a synthesis that is viable. These are standard procedures with which I am familiar, due to both coursework and training in the research group here at Eastern Illinois University.

The results of this project can be disseminated in a few ways. First, I am a member of the American Chemical Society, which holds a number of meetings throughout the semester where I will be able to discuss the results of this synthesis and research. We also hope to submit scientific papers describing this research project to the Journal of Organic Chemistry, or another peer-reviewed publication, by the end of next semester.