N-alkyl 2-pyridones are a class of molecules that have very interesting biological and pharmaceutical applications, however, they happen to be very challenging to synthesize for a number of reasons. A few years ago our lab was interested in making these compounds using an oxygen to nitrogen alkyl-migration. One of these experiments involving an alkynyl side-chain migration produced a very interesting side-product. After a lot of optimization it was discovered that this side-product was the β-Iodo-N-alkenyl-2-pyridone shown in Figure 1. This compound is interesting because it has a number of synthetic handles with different levels of reactivity (As shown by the red arrows). These handles should allow us to run a reaction on one part of the molecule without affecting the others. My project this summer was to add a nitrogen to the alkynyl side-chain. And after doing the rearrangement, to use the synthetic handles to make unnatural β and γ amino-acids. The problem I have been tackling this summer comes from adding that nitrogen. Nitrogen is a very finicky and reactive element, and simply adding it the side-chain proved to be no small task. I have been trying to stop the nitrogen from doing any unwanted chemistry by testing two different systems for protecting the nitrogen.

My research methods come primarily in the form of organic synthesis. From commercially available products, it is a three-step series of reactions to make the β-Iodo-N-alkenyl-2-pyridone. So for each step I have to set-up the reaction. Then the next day I have to work-up reaction, and purify it to isolate the desired product. I then calculate a percent isolated yield for each reaction (which tells me how well the reaction works), and take an NMR spectra (which tells me if what I isolated is actually the product I was looking for). Since I am testing new systems, I am trying to optimize the percent yields for each of the steps of the process. This optimization can be done by changing the conditions of the reaction as well as changing parts of the work-up.

I have spent this summer exploring two different ways to protect the nitrogen when it is incorporated in to the side-chain of the β-Iodo-N-alkenyl-2-pyridone. The first way has been worked on a lot in past summers and the first two steps went in great yields, 74% and 65% respectively. The third step turned out to be very challenging and after many attempts to increase the yields the isolated yield never got above 24%. The other system I worked on this summer had never been tried before, and I spent much of the time figuring out the best ways to run each reaction, and the best ways to work up and purify the desired product of each step.

This summer spent doing research has benefited me in a number of ways. First and foremost, it has taught me many valuable skills, such as methods of organic synthesis, scientific writing and reading, along with presenting and talking about the research I did. These skills will surely prove invaluable when it comes time to apply for graduate school or for a job. Another skill that this summer has taught me is problem solving. A lot of times things don’t work out very well, and there are many problems that arise over the course of running a new reaction. This summer has helped to teach me how to confront those problems when they arise and then find creative solutions to them.