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This summer I worked on a chemical synthesis under my advisor Craig Streu. The main goal of my project was to make progress toward the completion of the synthesis of a novel PD-1/PDL-1 azolouge. This project was previously worked on by an Albion College student, Diana Kernenn, who took me under her wing my sophomore year, allowing me to have a successful transition into working on my own this summer. To better understand what I worked on this summer it is important to understand some background information. The title of my project might be long and confusing, but to sum it up, I was working on creating a drug to use as a treatment method for cancer. This specific cancer treatment is an immunotherapy. Immunotherapies are rather new to drug design, as they use the body's immune system to fight cancer. My drug specifically targets the PD-1 and PDL-1 interaction between the T-cells of the immune system and cancer cells. Within the body, cancer cells hide themselves from the immune system, as the PD-1/PDL-1 interaction occurs. This prevents the programmed cell death of the cancer cell from happening.

We designed this synthesis using steps to create an azolouge version of the molecule BMS-1166. (Figure 1) This molecule was created but failed to make it to market as it had many adverse side effects. An important aspect of the design of this drug is the azologue. An azologue is a nitrogen double bonded to another nitrogen. This allows the molecule to adopt two confirmations, Cis and Trans. Using UV light, the molecule can be switched between these two confirmations. Therefore you could take the drug in its inactive form, which has many benefits such as limiting the side effects of the drug throughout the body. The drug would bind to the PD-1 ligand where you would activate the drug using the UV light, preventing the PD-1/PDL-1 interaction between the T-cell and the cancer cell from occurring. Ultimately, allowing for the program destruction of the cancer cell, treating cancer.

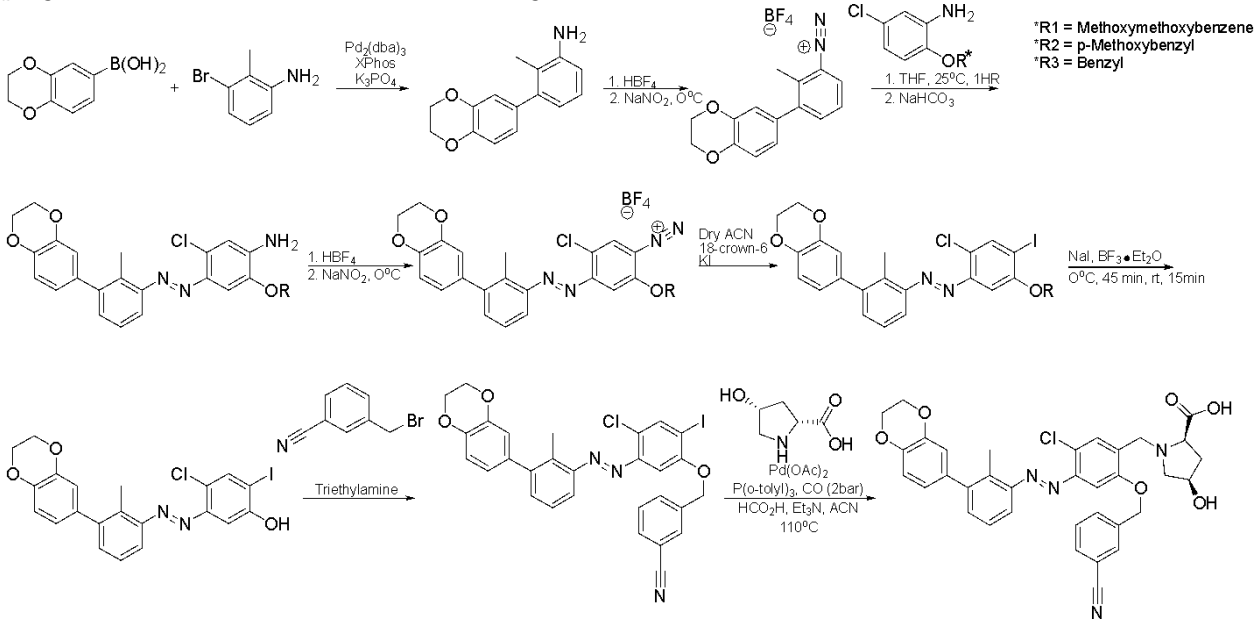

Figure 1: Synthesis of Azo-BMS-1166

Going into this project, four steps had been completed. Each arrow in Figure 1 represents a step. Each step represents a series of processes that have to be completed to go to the next step. This is very time-consuming, as many of the steps have to be done on a small scale to not put anyone in danger in the lab. Additionally, with each step, you get only a fraction of the starting material as the product. There is also a possibility you will not get the product you are looking for at all, meaning you will have to go back and

repeat the step with slight altercations. While I did not make any further progress within this synthesis, I was able to create enough starting materials and refine my skills to successfully keep working on completing this synthesis in the fall. Coming into the summer I spent a lot of time working on making the materials to do the next steps of the synthesis. However, I will not have to spend time in the fall doing this as it is already completed, which means I can hit the ground running.

In the future, I plan to present at Elkin Isaac in the spring of 2025, as well as, at the American Chemical Society convention for student research. Presenting my research will allow me to talk about the greater purpose of my undergrad research experience. Successfully finishing my synthesis could make great contributions not only to the college but to drug design as well. Publishing this work would allow for testing on large scales to be completed to determine if this drug is viable and able to make it to market. If it fails and does not make it to market, it still provides a basis for more research. Working on this project over the summer has allowed my love for research to grow. I love the independence and freedom that comes with research and learning to problem-solve when things do not go as planned. Overall, I can say this summer research experience has made me a better problem solver and more comfortable adapting to new situations. Lastly, I would like to thank the college and everyone involved in providing me with this opportunity and funding my research, especially the Anna and Carl Weiskittel Endowed Chemistry Fellowship!