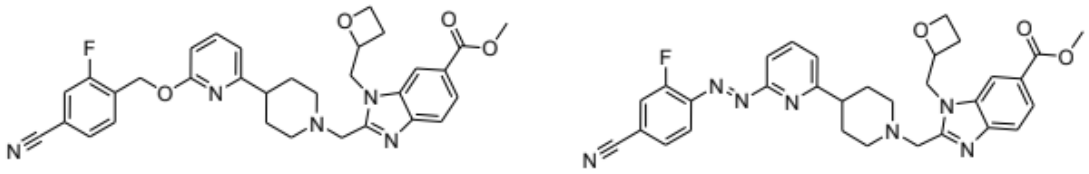
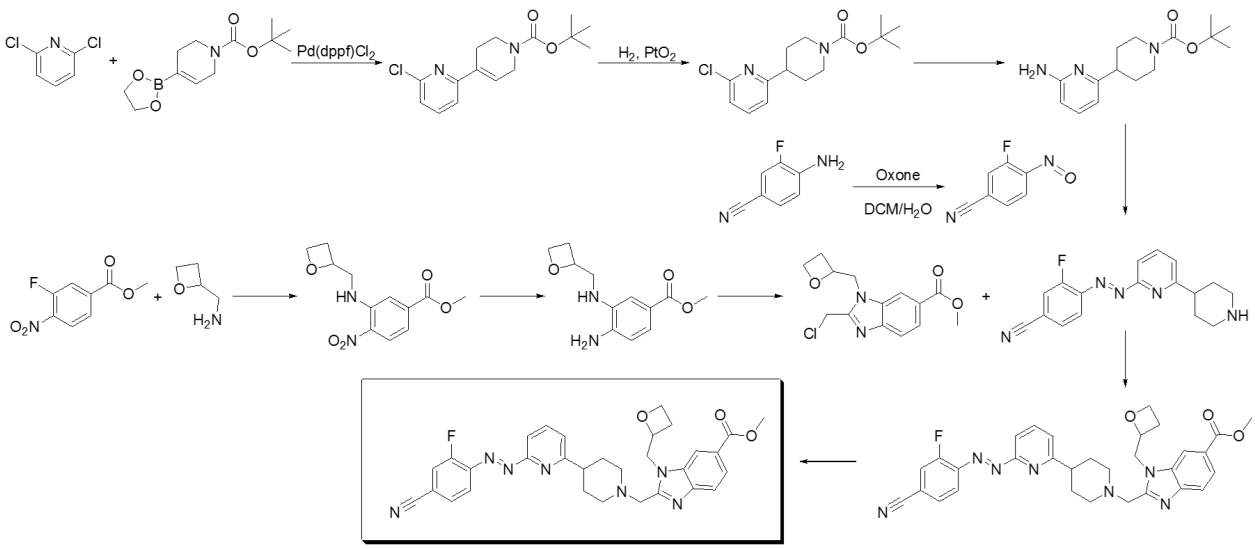
End of Summer FURSCA Report 2023

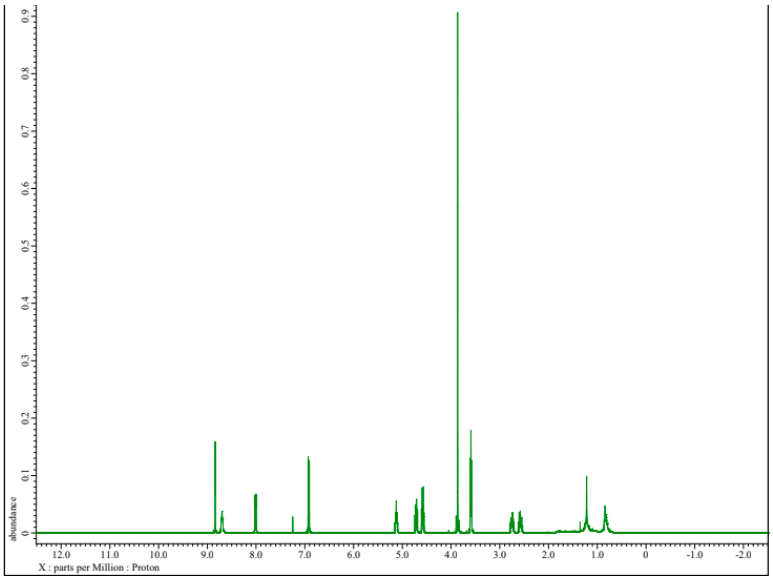
Diabetes mellitus, more commonly known as diabetes, is a disorder in which the human body cannot regulate the intake of sugars properly. This can happen due to prolonged periods of high blood sugar. Type 1 diabetes is also known as juvenile diabetes since it occurs in children. Type 1 diabetes occurs when the pancreas is unable to provide or produce insulin to help with the intake of sugar. This is generally because of the loss of a type of cell called beta cells. Type 2 diabetes is when the cells are no longer able to recognize insulin and therefore do not respond to it properly. Just because your body stops responding to insulin it doesn't mean that your body doesn't stop making it. So there is a buildup of insulin which leads to an increase in fat storage which really can only be undone by exercise and diet which is difficult for a lot of people. Type 2 diabetes is what the drug I'm working on targets. The drug I am working on is related to the blockbuster therapeutic Rhybelsus®, a diabetic drug that only works if injected. Recently, danuglipron, an orally available drug with a similar mode of action, has been developed. We aim to switch this drug from its current form to an azo form, making it photoswitchable from its thermostable *trans* form to its *cis* form and vice versa. The ultimate goal is to determine if the azo compound has suitable photokinetic and biological properties for further development.



The proposed compound, along with its parent compound, danigulipron, are shown in **Figure 1** above. We aim to switch this drug from its current non-azo form to an azo form by replacing the oxygen-carbon bond with a nitrogen-nitrogen double bond. As a result, we could switch the compound from *trans* to *cis* form with UV-light.



The proposed synthesis of my drug is shown in **Figure 2** above, shows the synthetic steps we will take to create the azo form. Each arrow in the synthesis represents a chemical reaction. There are ten steps in total, but fortunately, this is a convergent synthesis, so the longest linear sequence is six steps, which substantially facilitates its feasibility. Our proposed synthesis is a slight modification of the reported synthesis for the parent compound. A key step is the acid-catalyzed formation of the azo bond via Mills coupling. Each step will be monitored by TLC and purified using polarity differences by flash silica gel chromatography.[5] Purified products will be analyzed by NMR. So far I have successfully synthesized all the steps in red shown in the figure above.



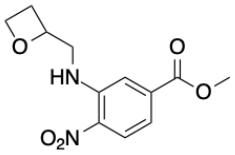


Figure 3 and 4: The product shown here is the product of 2a which I have successfully synthesized. This graph shows that I have created a pure and stable compound that I can use to continue onto the next steps of my synthesis. This is just one of the 5 I have successfully synthesized thus far.

I plan to present all my research at Elkin Isaac and the American Chemistry Society. I also plan to write my senior thesis on this project. This project has helped me learn what research is and grow as a researcher. It has also given me another prospective option for a future career during my gap year or just to pursue a career in this field. This project made a difference in my life as it has taught me many skills needed to work most research fields at major chemical or pharmaceutical companies. If my research is successful, I hope to be able to provide a photoswitchable diabetes drug that can be taken orally and reduce the use of needles and other major side-effects. I hope that this drug can provide a somewhat stable and regular life for those with diabetes. I would like to thank FURSCA for all their help and assistance in making my project happen.