Exploring the Impact of Beta-turn Peptoid Catalysts on Enantioselective Trifluoromethylation Reactions

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My work focuses on synthesizing a library of peptoids which will be used as catalysts for a reaction called trifluoromethylation, which adds a CF_3 group (a carbon, hydrogen, and three connected fluorines) to a molecule. Being able to perform this reaction quickly, consistently, and on a large variety of molecules is of growing interest in the pharmaceutical industry due to properties of fluorine that slow the degradation of medications within the body and improve a compound's ability to permeate cell membranes, positioning it as a solution to the challenges that currently limit between eighty and 90 percent of drugs from obtaining FDA approval. The benefits of adding fluorine to a medication are additive, hence why it is appealing to add three.

To do this, we use what is called the Rupert-Prakash Reagent to add our trifluoromethyl group to our compound. Alone, the reaction moves incredibly slowly, if at all, therefore requiring the need of a catalyst to actually proceed. However, not any catalyst can do the job. Compounds are three dimensional structures whose function can change rather significantly depending on the orientation of the components that make them up. A major example of this is Thalidomide, which was prescribed in the 50's and 60's to treat morning sickness. While one version had sedative effects, the other was eventually shown to cause birth defects. Therefore, it is of utmost importance to be able to make uniform medications with only molecules of the same orientation, which includes how we add our trifluoromethyl groups. This is called enantioselectivity and is the second component of my project aim.

The catalysts that I am working on synthesizing are peptoids, which are modeled off the naturally occurring peptides that build the proteins in our bodies. The distinction between them is that peptoids are structured slightly differently, making them able to withstand the conditions necessary for trifluoromethylation. Their other benefit is that they are easy to build and manipulate, enabling us to experiment with large varieties of sidechains and structures without making them too bulky to be effective.

My peptoid library is made up of beta-turn structures, almost like C-shaped folds, as opposed to the helix structures that most of my other lab mates are working with. So far, I have synthesized peptoids with the same components as each other in different orders to gain more insight into how the beta-turn reacts and what is most effective at producing enantioselective products. I have yet to test the peptoids that have been synthesized, and will be continuing my work in the fall to get results that I will then use to synthesize a new library.

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