-amino Thioamide Sidechains in PPII Mimetic Peptoids

Jack Sharland, 2018

Cell signaling protein-protein interactions govern the way cells behave in living organisms. Specifically the Gorske lab is interested in designing a mimic for the polyproline type 2 (PPII) helix. The lab is interested in studying this motif due its association with a protein binding site, the WW domain. The interaction between these two motifs has been linked with the progression of diseases like cancer and Alzheimer's. If a biological probe could be designed to mimic the PPII helix we could begin to better understand its functions within the cell and how it contributes to unregulated cell growth. In searching for viable biological probe it is important to design a probe that is both biostable and biomimetic. Peptoids are an

discourage backbone-backbone n to π* interactions at the C-terminus by using an ester cap. After the peptoid was synthesized, I capped the product with a trifluoroacetyl group to make it easier to isolate and discourage backbone-backbone n to π* interactions at the *N*-terminus. I was able to synthesize some product with my first two attempts however the yield was low. This was likely due to difficulties with the addition of the β sidechain to the backbone. I retried the synthesis, this time freebasing the amine and increasing the quantity of base at each amine addition to make the amines more nucleophilic. The modified synthesis gave excellent yield and I ended up with about 0.5g of pure product which was quickly and easily isolated in one step on a Biotage. Product purity was assessed by HPLC and the identity of the product was confirmed by LCMS and NMR. I had enough of this material to run two thionation reactions and a structural study on the unthionated product which is currently in progress. The thionation trial in which the reaction vessel was heated for several days displayed product formation based on analytical HPLC data. In the future I will isolate thionated product by prep-HPLC and finish the structural study and compare the overall secondary structures of both the thionated and un-thionated β-amino amide containing peptoids. Then I will explore the incorporation of different β sidechains and assess the viability of thionation prior to peptoid sidechain addition.

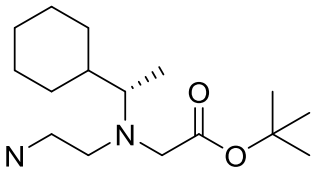

Figure 1: Unthionated version of successfully synt -amino amide containing peptoid.

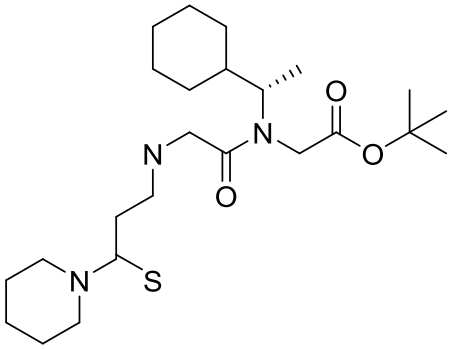

Figure -amino amide containing peptoid.

Faculty Mentor: Benjamin Gorske

Funded by the Kufe Family Research Fellowship

References: 1. Boit, Tim "Study of Amide and Thioamide Side Chain Influence on cis/trans Isomerism of Peptoid Backbone Amides", Bowdoin College 2016.