Thionation of Peptoid !-Aminoamide Side Chains for Polyproline Type II Helix Mimicry Sophia Conwell, Class of 2018

A greater understanding of cell signaling pathways is becoming increasingly important as age-related diseases like Alzheimer's Disease increase in prevalence.¹ These pathways can be better understood using biological probes to understand the interactions between proteins in the body. Cell signaling pathways allow for cellular communication within the body. When these communications run awry, it can cause disease.^{2,3} A cell signaling domain of particular interest is the WW Domain. This domain is known to act in pathways that have been linked to Alzheimer's Disease and cancer.^{4,5} This domain preferentially binds to the polyproline type II (PPII) conformation of proteins.⁶ Thus, a molecule that could form and maintain this PPII shape could interact with this domain as proteins do.⁷ Polypeptides have the ability to adopt this shape, but they are rapidly broken down in the body by the enzymes that break down proteins because they have the similar primary structure made of amino acids as proteins do. Peptoids, however, are *N*-substituted glycine oligomers, so that the R-group is found on the shape is favored by

trans amide bonds, while its counterpart, the PPI helix, is favored by *cis* amide bonds.⁹ The *cis* and *trans* conformations of a peptoid are in equilibrium with each other, as the molecule can rotate freely around the amide bonds. To maintain and stabilize a PPII helix, therefore, the *trans* conformation must be stabilized, which can be done using n /* interactions, whereby lone pair electrons on a carbonyl oxygen donate into the ?

References

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