Studies on the Self-Assembly of Dipeptides

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Introduction

Understanding the structure of amino acids and peptides is a major part of biochemistry courses. The research project discussed here will focus on the development of an experiment showcasing the construction of dipeptides. The peptide bond is a fundamental bond in biochemistry. Peptide bonds are formed through the covalent bonding between the carboxylic acid end of one amino acid and with amino group of another amino acid. This research will focus on creating the following dipeptides: phenylalanine-phenylalanine (abbreviated Phe-Phe), tyrosine-tyrosine (Tyr-Tyr), phenylalanine-tyrosine (Phe-Tyr), and tyrosine-phenylalanine (Tyr-Phe).

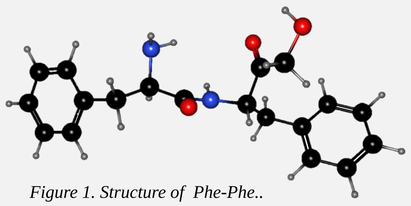


Figure 1. Structure of Phe-Phe..

Research has shown that the dipeptide, Phe-Phe, self assembles into alpha-helical structures.[1] Alpha helices are secondary cork-screw shaped protein structures. Non-covalent interactions drive this supramolecular self-assembly.

This experiment provides hands on training in nanomaterial analysis with dynamic light scattering (DLS). DLS is used to determine the size of small particles/polymers in suspension or solution. It will help to visualize the dipeptides. The remaining three dipeptides: Tyr-Tyr, Phe-Tyr, and Tyr-Phe, will be compared to Phe-Phe to see if they also form alpha helices.[1]

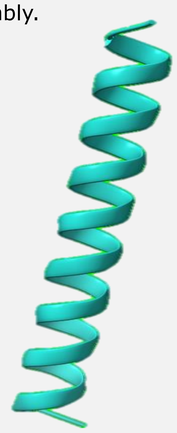
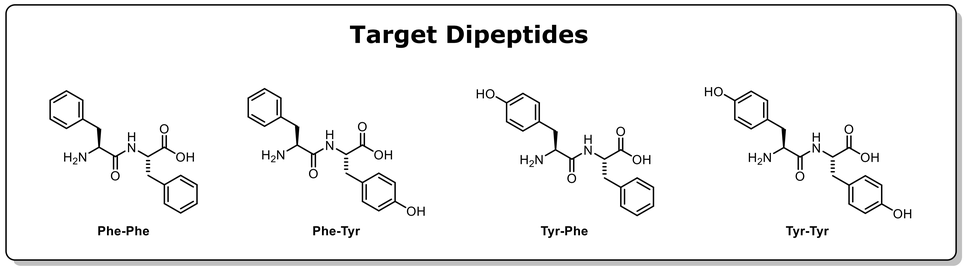


Figure 2. General alpha-helical structure.

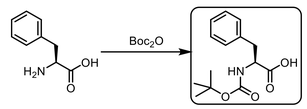
Aims and Comparison of Experimental Methods

Project Aims: Develop a simple, accessible laboratory experiment that showcases the construction of dipeptides allowing biochemistry students to synthesize, characterize, and analyze dipeptides.

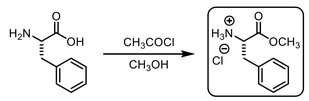


Batch-Style Peptide Synthesis

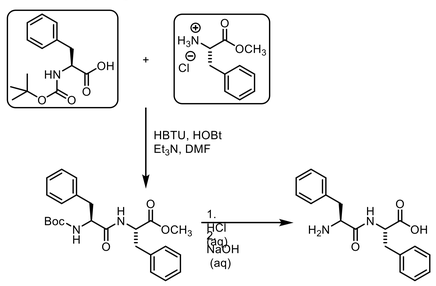
Preparation of Boc-Phe-OH



Preparation of H_2N-Phe-OCH_3

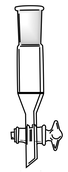


Coupling of Formation of Phe-Phe



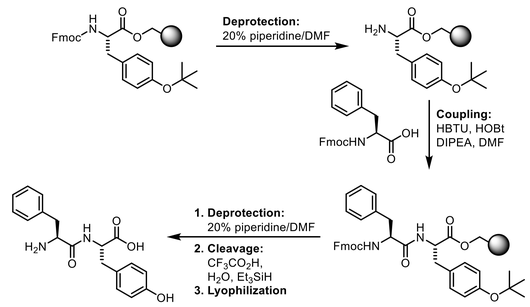
Scheme 1. Synthetic steps for the formation of the dipeptide Phe-Phe.

Traditional Solid-Phase Peptide Synthesis (SPPS)



Peptide Synthesizer

Figure 3. Traditional SPPS vessel and Biotage® Initiator+ Alstra™ peptide synthesizer.



Traditional SPPS vs. Using a Peptide Synthesizer

Using traditional SPPS to synthesis dipeptides is a long process that involves doing repetitive steps and wait periods that are hours long. Using a peptide synthesizer shortens this process by reducing experimental steps.

Results and Analysis

Figure 4. Malvern Panalytical™ Zetasizer Nano ZS DLS measurement system.

The dipeptides: Tyr-Tyr (62%) and Phe-Tyr (<50%) were successfully synthesized using the peptide synthesizer. Dynamic light scattering (DLS) will be used to determine the length and size of the alpha-helical structures.

Dynamic light scattering (DLS) is a technique that uses photons to measure the distance between small particles.

Future Work

The research will continue to synthesize the other two dipeptides: Phe-Phe and Tyr-Tyr. These peptides will be characterized and analyzed via dynamic light scattering (DLS). The other three dipeptides will be compared to Phe-Phe to see if they also self-assemble into alpha-helical structures.[1]

References

1. Fraczyk, J. *et. al*. Search for Fibrous Aggregates Potentially Useful in Regenerative Medicine Formed under Physiological Conditions by Self-Assembling Short Peptides Containing Two Identical Aromatic Amino Acid Residues. *Molecules* **2018**, *23*, 568.

Acknowledgements

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