Saponification of N-Acylated L-Phenylalanine Wang and Merrifield Resins. Assessment of Cleavage Efficiency and Epimerization

Jon Carnahan\textsuperscript{1}, Martin J. O’Donnell\textsuperscript{1}, J. Geno Samaritoni\textsuperscript{1}, DeMarcus K. Crews\textsuperscript{2}, Brian M. Lawrence\textsuperscript{2} and William L. Scott\textsuperscript{1}

\textsuperscript{1}Department of Chemistry & Chemical Biology, Indiana University Purdue University Indianapolis; \textsuperscript{2}Department of Chemistry, Morehouse College, Atlanta, GA 30314

As part of a continuing effort to modify Distributed Drug Discovery (D3) synthetic procedures to enhance safety and accommodate the limited resources available to students in developing-world countries, we have recently begun to examine alternatives to trifluoroacetic acid (TFA)-cleavage of amino acid derivatives from polystyrene-based resins. Cleavage of a representative example, N-(4-chlorobenzoyl)-L-phenylalanine, from both Wang and Merrifield resins was accomplished in thirty minutes at room temperature using 0.5M sodium hydroxide in methanol/tetrahydrofuran. In a side-by-side comparison with cleavage using TFA, results indicated that saponification from Wang resin was incomplete after thirty minutes. Experiments designed to examine separately the effect of reaction time, temperature, and concentration were performed and results will be presented. Additionally, investigations were performed to assess the degree of epimerization which had occurred during cleavage of Merrifield-bound L-phenylalanine acylated with both (\textit{R})- and (\textit{S})-mandelic acid. Results revealed a small but significant amount of epimerization (15:1 to 31:1 diastereomeric ratios) after a thirty-minute cleavage time at room temperature.

Mentors: Martin J. O’Donnell; William L. Scott; J. Geno Samaritoni, Department of Chemistry & Chemical Biology, Indiana University Purdue University Indianapolis; Brian M. Lawrence, Department of Chemistry, Morehouse College, Atlanta, GA