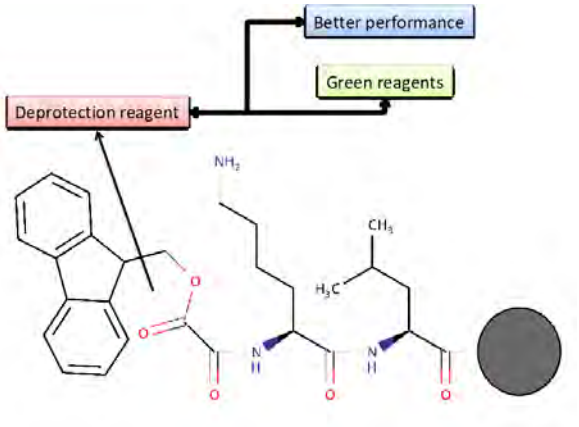
Deprotection in simultaneous peptide synthesis

Constanza Cardenas C
Curauma Biotechnology Nucleus. Pontificia Universidad Católica de Valparaíso, Chile

Statement of the Problem: deprotection in Fmoc solid phase peptide synthesis is a crucial step that influences the yield and purity of the product. One of the reagent commonly used is piperidine, a secondary amine that, in addition to being a toxic reagent and having a pungent odor, has a DEA-controlled substance status, therefore, it needs to be replaced. Our group explores the use of other reagents, as a replacement for piperidine, not only by their restriction but also looking for a greener chemistry in peptide synthesis. Methodology: four peptides with different sequences and characteristics were selected to be synthesized with two different methodologies, first by microwave-automated synthesis and second by tea-bag manual synthesis. Three deprotection reagents were used: Piperidine, piperazine, and 4-methyl piperidine. Findings: Although the three deprotection reagents showed similar performance in the microwave assisted synthesis, we found that 4-Methylpiperidine has better performance in the tea-bag simultaneous synthesis. Additionally, it has a lower toxicity than piperidine and it is not a controlled substance, which is why it is a good alternative as a removal reagent in the synthesis of peptides..



Recent Publications

1. Houghten RA (1985) General method for the rapid solid-phase synthesis of large numbers of peptides: specificity of antigen-antibody interaction at the level of individual amino acids. Proc Natl Acad Sci USA 82:5131–5135. https://doi.org/10.1073/pnas.82.15.5131

2. Carpino LA, Han GY (1970) 9-Fluorenylmethoxycarbonyl function, a new base-sensitive amino-protecting group. J Am Chem Soc 92:5748–5749. https://doi.org/10.1021/ja00722a043

3. Kimmerlin, T., & Seebach, D. (2005). '100 years of peptide synthesis': ligation methods for peptide and protein synthesis with applications to beta-peptide assemblies. The journal of peptide research : official journal of the American Peptide Society, 65(2), 229–260. https://doi.org/10.1111/j.1399-3011.2005.00214.x

4. Luna, O. F., Gomez, J., Cárdenas, C., Albericio, F., Marshall, S. H., & Guzmán, F. (2016). Deprotection Reagents in Fmoc Solid Phase Peptide Synthesis: Moving Away from Piperidine?. Molecules (Basel, Switzerland), 21(11), 1542. https://doi.org/10.3390/molecules21111542