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Attempts for the Synthesis of Indol-Ring Fluorinated Tryptophan Derivatives to Enhance the Activity of Antimicrobial Peptides

Authors : Anita K. Kovacs, Peter Hegyes, Zsolt Bozso, Gabor Toth

Abstract : Fluorination has been used extensively by the pharmaceutical industry as a strategy to improve the pharmacokinetics of drugs due to its effectiveness in increasing the potency of antimicrobial peptides (AMPs). Multiple-fluorinated indole-ring-containing tryptophan derivatives have the potential of having better antimicrobial activity than the widely used mono-fluorinated indole-ring containing tryptophan derivatives, but they are not available commercially. Therefore, our goal is to synthesize multiple-fluorinated indole-ring containing tryptophan derivatives to incorporate them into AMPs to enhance their antimicrobial activity. During our work, we are trying several methods (classical organic synthesis, enzymic synthesis, and solid phase peptide synthesis) for the synthesis of the said compounds, with mixed results. With classical organic synthesis (four different routes), we did not get the desired results. The reaction of serin with substituted indole in the presence of acetic anhydride led to racemic tryptophane; with the reaction of protected serin with indole in the presence of nickel complex was unsuccessful; the reaction of serin containing protected dipeptide with disuccinimidyl carbonate we achieved a tryptophane containing dipeptide, its chiral purity is being examined; the reaction of alcohol with substituted indole in the presence of copper complex was successful, but it was only a test reaction, we could not reproduce the same result with serine. The undergoing tryptophan-synthase method has shown some potential, but our work has not been finished yet. The successful synthesis of the desired multiple-fluorinated indole-ring-containing tryptophan will be followed by solid phase peptide synthesis in order to incorporate it into AMPs to enhance their antimicrobial activity. The successful completion of these phases will mean the possibility of manufacturing new, effective AMPs.

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