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Continuous flow solid phase synthesis of various peptides and foldamers with exceptionally low amino acid consumption

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Abstract

The importance of synthesis of peptides and foldamers is warranted by the need for peptide-based medicines, the roles of peptides and foldamers in drug discovery, etc. Since its introduction by Merrifield, peptide synthesis was performed almost exclusively on solid supports. It has been applied for the synthesis of foldamers as well. The solid-phase peptide synthesis (SPPS) technique has subsequently been progressively developed. However, still a general property of these methodologies are the high number of amino acid equivalents required for total coupling.1

Continuous-flow (CF) approaches have recently gained in significance among synthetic techniques.2 We show here that the number of amino acid equivalents used for SPPS can be lowered drastically to around 1.5 equivalents through the application of a CF technique and by complete reaction parameter optimization.

Under the optimized conditions the couplings of all 20 proteinogenic amino acids with 1.5 amino acid equivalents proceeded with excellent conversions. To demonstrate the efficiency of the CF-SPPS methodology, known difficult sequences were synthetized in automated way. As further evidence of the effectiveness, β-peptide foldamers with alicyclic side-chains.

Biography

István M. Mándity is head of Institute of Organic Chemistry, Faculty of Pharmacy at the Semmelweis University (SU Budapest), Hungary. He is the head of the Artificial Transporter Momentum Research Group, Institute of Materials and Environmental Chemistry, Research Center for Natural Sciences, Budapest Hungary. The main focus of his research is the investigation of novel continuous flow synthesis techniques and foldamer chemistry. He is active in the utilization of green solvents and reagents for the synthesis of various useful building blocks. He is working on peptide and foldamer based artificial chloride ion transporters for the potential treatment of cystic fibrosis. His results are under exploitation. He is presently author of 45 scientific manuscripts in peer reviewed journals and books with 671 independent citation and has an H-index of 17. He is the inventor of 2 patents.

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