Parallel Synthesis of Peptidic Dendrimers as Macromolecular Host for Enantioselective catalysis with the PSW1100

Josef Schroer*, Nhat Quang Nguyen-Trung*, Jérôme Giovannoni*, Anthony Clouet, Estelle Delort, Jean-Louis Reymond,
Chemspeed Technologies, Rheinstrasse 32, Augst, Switzerland*, Dept. of Chemistry & Biochemistry, Bern, Switzerland

Statement of Purpose: Peptide dendrimers are tree-like molecules that contain three different topological regions: the core, the branches and the surface (Figure 1). Each of these regions can exhibit functional properties, e.g. "enzyme like activity for hydrolysis of esters".

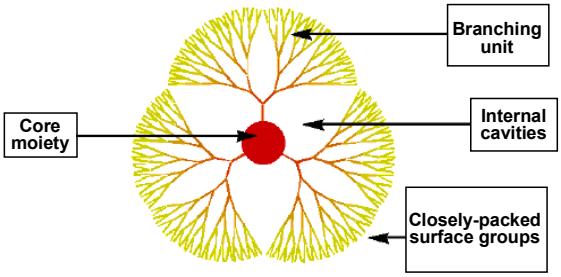

Fig 1. Structure of peptidic dendrimers

Recently Reymond and co-workers reported that peptide dendrimers displaying multiple histidine residues at the surface exhibit a strong positive dendritic effect in ester hydrolysis reactions[1] (Figure 2).

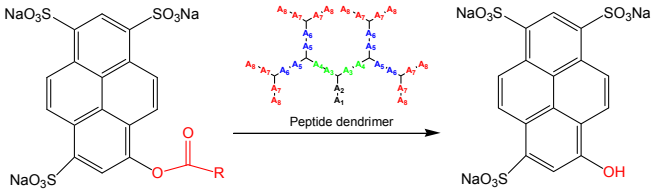

Fig 2. Esterhydrolysis catalyzed by peptidic dendrimers

Their investigations have shown that the catalytic activity is proportional to the number of histidine at the surface of the dendrimer. In order to investigate the contribution of each region in the catalysis, new peptide dendrimers have to be synthesized. Therefore an automated synthesis approach for the peptide dendrimers becomes crucial.

Methods: Herein, we report the parallel, automated synthesis of 16 peptide dendrimers with the Chemspeed Multiple Peptide Synthesiser PSW1100. During the synthesis of peptide dendrimers the loading is doubled after each coupling of the branching unit 2,3-diamino-propanoic acid.

One of the major challenges of this project was to adapt a variety of individual manual conditions to the requirement of automation suitable for a variety of different dendrimers.

As a result, all peptide dendrimers have been obtained in good purities and in yields comparable to manual synthesis. 16 peptide dendrimers have been synthesized in just 4 days, whereas manual synthesis allows for the synthesis of 2 dendrimers per week, only.

Results: This and other relevant examples, presented herein, impressively support the enormous value of a parallel and automated High Output Experimentation approach in new materials discovery.
Therefore, equipment which originally has been designed for the HTS approach in the pharmaceutical industry today also is established in the laboratories of (Bio) Material Scientists. This transition has caused increased technical demands on automated synthesis workstation capabilities. Only highly modular, flexible and scalable systems, those that can easily be configured to meet the needs of scientists, have a chance of covering the needs of the complex and demanding workflows of this industry.

References: Delort, E.; Nguyen-Trung, N.-Q.; Darbre, T.; Reymond, J.-L.; *The Journal of Organic Chemistry*, *2006*, **71** (12), p.4468-4480.