Solid-Phase Synthesis of Peptides

Ahmed Hashim Harb[1], Lili Arabuli[2]

The University of Georgia, School of Health Sciences and Public Health
[1]BA Student of pharmacy program in English; [2]Supervisor, PhD, Associated Professor

Solid-phase synthesis is an advanced synthetic route for preparation of peptides. In the early 1960s, Merrifield proposed the use of a polystyrene-based solid support for peptide synthesis. Peptides could be assembled stepwise from the C to N terminus using N^{α}-protected amino acids. SPPS of a tetrapeptide was achieved by using Cbz as an α-amino-protecting group, coupling with *N,N'*-dicyclohexylcarbodiimide (DCC), and liberating the peptide from the support by saponification or by use of HBr[1]. The general process for synthesizing peptides on a resin starts by attaching the first amino acid, the C-terminal residue, to the resin. To prevent the polymerization of the amino acid, the alpha amino group and the reactive side chains are protected with a temporary protecting group. Once the amino acid is attached to the resin, the resin is filtered and washed to remove byproducts and excess reagents. Next, the N-alpha protecting group is removed in a deprotection process and the resin is again washed to remove byproducts and excess reagents. Then the next amino acid is coupled to the attached amino acid. This is followed by another washing procedure, which leaves the resin-peptide ready for the next coupling cycle. The cycle is repeated until the peptide sequence is complete. Then typically, all the protecting groups are removed and the peptide resin is washed, and the peptide is cleaved from the resin.

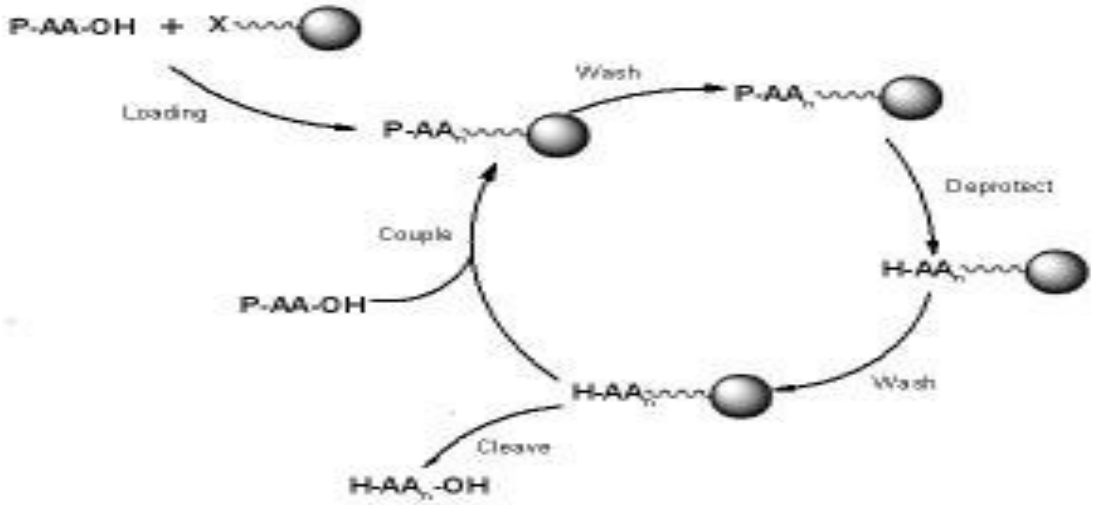

Fig. General Solid Phase Peptide Synthesis Cycle

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