

other reagents and solvents used in solid-phase synthesis must have adequate purity, lest some of the impurities react with resin-bound peptide products.

Another concern during the repetitive steps is racemization. This is the partial loss of optical purity of the starting L-amino acid during its incorporation into the peptide chain. Experiments show that, during stepwise synthesis with any of the usual N-alpha-amino protecting groups, racemization does not occur within detection limits. Some of the older techniques to couple amino acids led to production of up to 10% racemic impurities. In a synthesis where racemization is known to be confined to one or two sites, it is sometimes possible to modify coupling conditions to minimize the problem.

In sum, solid-phase peptide synthesis has matured into a proven technology. It is used throughout the scientific world. However, the procedure requires a highly skilled workforce. This is especially true for large-scale production and purification.

The first biologically active peptide prepared by solid-phase synthesis was the smooth muscle hypotensive agent bradykinin. In the last 20 years, thousands of naturally occurring peptides or their analogues have been made by solid-phase peptide synthesis. With current methods any sequence of up to 50 residues can be reliably assembled.