

beginning of the twentieth century. Although quite powerful, they also require considerable labour, time, and skill because of the difficulty in successfully handling the intermediates.

In 1959 R. B. Merrifield of The Rockefeller University invented the solid-phase approach. He recognized the limitations of the earlier chemical procedures but retained their strengths. Early reports showed that both manual and automated peptide synthesis was possible. Subsequent efforts from numerous laboratories in the United States, UK, Europe, Canada and Japan improved the technique of peptide synthesis.

The remainder of this section goes on to describe the procedure of solid-phase peptide synthesis. The formation of peptide bonds starts with the reaction of a tert-butyloxycarbonyl (BOC)-amino acid with a chloromethyl group on the surface of styrene polymer. After the removal of the BOC protecting group with trifluoroacetic acid, a new BOC-amino acid is allowed to react to lengthen the peptide chain, and the process repeated with a stepwise strategy. Excess reagents and by-products are removed solely by filtration and washing. Finally, the desired peptide is freed of protecting groups and liberated from the resin by anhydrous hydrogen fluoride. However, it is very difficult to avoid the production of contaminating by-products. Furthermore, these by-products are not easily separated from the desired product due to their similarity in structure and properties. Efforts continue to improve this method.