2.4 Commercial Production of Peptides

The original methodology devised by B. Merrifield is unquestionably successful and has been employed in many laboratories. Problems identified at that level have led to improvements that have made large-scale synthesis commercially viable. One of the original motivations behind solid-phase synthesis was the possibility that the process could be automated. Equipment is now commercially available allowing the large-scale production of numerous peptides. However, it must be stressed that, even though automated systems perform all of the mechanical steps, the success of peptide synthesis is largely governed by the validity of the underlying chemistry. Also, the skill of the technicians is crucial.

Some of the most serious problems in peptide synthesis occur during removal of the peptide from the solid-phase resin (i.e. cleavage). Another problem results from impure starting amino acid derivatives. For example, amino acids are sometimes contaminated with 0.2-0.4% of the corresponding N-alpha-sec-butyloxycarbony-lamino acids. This contamination occurs as a result of the amino acid modification process. Most of the contaminants can be removed, but the remaining 0.3% is enough to decrease the efficiency of peptide synthesis. Fortunately, with proper care, most of the starting protected amino acids can now be obtained with adequate (greater than or equal to 99.7%) chemical and optical purity. All