5 Conclusions and Future Work

The original project aimed at developing a method to synthesise cyclic depsipeptides has been diverted to synthesise a cyclic peptide natural product due to unforeseen difficulties when studying on zygosporamide. The major problem involved inherent difficulties in protecting the terminal residue, which is a leucic acid (hydroxyl acid), prior to coupling it onto the rest of the peptide chain anchored onto solid-supported safety-catch linker **5**. The project was, therefore, directed towards developing a new method to synthesise small cyclic peptides instead. However, the work was performed to synthesise integerrimide A, a cyclic heptapeptide natural product.

An efficient solid-phase total synthesis of constrained cyclic peptide integerrimide A (**40**) has been accomplished in 16 steps and 19% overall yield, based on the manufacturer's stated resin substitution from commercially available materials. This work is, to the best of our knowledge, the first example where the final Fmoc removal from the *N*-terminus of a linear peptide precursor (**52**) and subsequent macrocyclisation were performed directly and in a tandem manner when the 4-sulfamylbutyryl safety-catch linker was employed. Further efforts to investigate and optimise the anti-cancer activity of the compound and its mechanism of action may be carried out. Such works can include application of the method developed to synthesise, for example, point-mutation analogues of integerrimide A to improve bioactivity of the molecule, namely in structure-activity relationship studies. Additional synthesis of other selected cyclic peptide natural products of different ring sizes may also be carried out.