

ABSTRACT

2,5-Diketopiperazines (DKPs) are widely distributed in nature and exhibit various biological activities e.g. antibiotic or antifungal and cytotoxic effects. They are defined as a privileged structure i.e. they have been selected over time by nature to be part of many biologically active compounds. They are therefore interesting compounds for medicinal chemists.

This thesis describes the development of general, efficient and high yielding methods for the synthesis of DKPs using both solution and solid phase protocols. The use of water as solvent in combination with microwave heating afforded high yields of DKPs. Using the solid phase method for synthesis the polar PEGA resin in water also afforded high yields of products using microwave heating. To obtain chemically diverse diketopiperazines a method for the synthesis of unnatural amino acids was developed using the Schöllkopf's procedure for amino acid synthesis. Spiro-amino acids containing five-, six- and seven-membered rings were synthesized in good yields and short reaction times, and have also been incorporated into DKPs.

Furthermore the development of a general method for the synthesis of 1,3,4,6-tetrasubstituted DKPs has been developed by which the substituents could be introduced regioselectively. Its use as a scaffold has been shown by the regiospecific derivatizations of the substituents.

The use of DKPs as scaffolds for peptidomimetics has also been explored. Computer based molecular modelling showed that 1,3,4-trisubstituted DKP derivatives could have applicability as β -turn peptidomimetics. To test this hypothesis two potential DKP-based somatostatin mimetics containing the side chain moieties of Trp, Lys and Phe in the 1-, 3- and 4-positions, respectively, have been synthesized.

ISBN 978-91-628-7018-8