Abstract

This work deals with the stereoselective synthesis of α-aminocyclobutanecarboxylic acids and in particular, two cyclobutane derivatives of natural amino acids: ornithine and serine. These cyclobutane amino acids could potentially have interesting biological properties. In the new pathway the key-step is based on a stereoselective one-pot asymmetric Strecker-reaction from racemic or optically active α-substituted cyclobutanones.

In the first part, we report two new synthetic methods for optically active α-substituted cyclobutanones. The first one is based on enzymatic transesterification of 2-hydroxycyclobutanone or methyl acetal derivatives to give corresponding enantiopure alcohol and acetate with good yields and excellent enantiomeric excesses. Both compounds are transformed in few steps into both enantiomers of 2-benzyloxycyclobutanone. The second method describes an asymmetric alkylation of chiral imines or hydrazones prepared from cyclobutanones. Thus optically active α-substituted cyclobutanones, some of which are detected in irradiated foodstuffs, are obtained with good yields and good enantiomeric excesses.

In the second part, we describe the synthesis of cyclobutane amino acid analogues of serine and ornithine. The key-step for amino nitrile formation is an asymmetric Strecker reaction from chiral or racemic cyclobutanones, in which the diastereoselectivity under various conditions is specified and absolute configurations of amino nitriles are determined by X-ray crystallographic analysis. These amino nitriles give for the first time in three steps serine and ornithine derivatives. In this part we also report a one-pot asymmetric alkylation-Strecker reaction to obtain optically active β-alkylated amino nitriles, which are potentially precursors of optically active β-alkylated aminocyclobutanecarboxylic acids.