Abstract

The development of novel methodologies and synthetic strategies for the preparation of complex 3D heterocyclic compounds with the well-defined spatial arrangement of functional groups represents one of the most studied research problems in current synthetic chemistry. Nowadays, organocatalysis (beside transition-metal catalysis and biocatalysis) became the most popular tool, because of usage small chiral organic compound for asymmetric induction and acceleration of reaction.

In this thesis, the development of novel organocatalytic methodologies for the preparation of various heterocyclic compounds is described. The utility of novel methodologies is demonstrated by easy access to chiral building block molecules or products with valuable physical or biological properties.

In the first part, a novel [4+2] cycloaddition reaction of sulfur-containing heterocyclic electron-deficient alkenes with allenic compounds catalyzed by chiral tertiary amine is described. Organocatalytic cycloaddition reaction of 3-benzylidene benzo[*b*]thiophenones with allenoates was investigated and optimized. Dihydro-2*H*-pyranes were obtained in high isolated yields (up to 92%) and optical purities (up to 99% *ee*). The robustness and synthetic utility of the developed methodology was demonstrated by a simple work-up of organocatalytic reaction using filtration.

In the second part, novel Michael/alkylation organocascade reactions catalyzed by chiral secondary amines for the preparation of heterocyclic (spiro)compounds are introduced. Organocatalytic method for preparation of spirooxindole-fused cyclopentanes in the reaction of readily available 3-(2-bromoethyl)-oxindoles and α,β-unsaturated aldehydes was found and optimized. Corresponding spirooxindoles were obtained as two diastereomers in excellent combined yields of two diastereomers (up to 98%) and excellent enantiopurities (up to 99% *ee*). Late-stage transformations of enantioenriched products led to derivatives, which showed interesting biological activities. The same organocascade concept was used for asymmetric cyclopropanation reactions leading to 1,2,3-substituted cyclopropanes, using α,β-unsaturated aldehydes with chloromethyl-4-nitroisoxazoles and *meso*-chloromethyl BODIPY derivatives, respectively. After optimization of reaction conditions for cyclopropanation of 4-nitroisoxazole (typically 1,5/1/1 dr) derivatives, corresponding cyclopropanes were isolated as a mixture of three diastereomers with excellent combined yields of three diastereomers (up to 98%) and excellent optical purities (up to 99% *ee*). Synthetic utility of enantioenriched products was demonstrated by the preparation of enantioenriched intermediate valuable for the total synthesis

of a natural product. To our delight, only one diastereomer was isolated in asymmetric cyclopropanation of BODIPY derivatives. Corresponding 1,2,3-substituted cyclopropanes were isolated in excellent yields (up to 98%) and stereocontrol (up to 99% *ee*, >20/1 dr) under optimized reaction conditions. In addition, a study explaining the reaction mechanism (DFT computations) was accomplished.