Abstract

Asymmetric organocatalysis represents the third pillar of asymmetric catalysis, alongside transition metal catalysis and enzyme catalysis. Organocatalysts activate the starting substrates by either covalent or non-covalent interactions. Non-covalent organocatalysts work on the principle of weak intermolecular interactions such as hydrogen bonds. In this PhD thesis we have been working on the synthesis and application of non-covalent bifunctional organocatalysts, studying their mechanisms of action in selected organocatalysed reactions and testing potential heterocyclic substrates in new organocatalysed transformations.

In the first part, new bifunctional non-covalent organocatalysts based on enamines and dienamines (benzenediamines) as hydrogen bond donors with (*S*)-quinine chiral framework were prepared (24 catalysts synthesised). The prepared catalysts were tested on a model reaction of Michael addition of acetylacetone to *trans*-β-nitrostyrene. The prepared new organocatalysts showed inferior catalytic properties (up to 72 % *ee*) compared to the already established related organocatalysts of squaramide or urea type. In the following, attempts were made to synthesise five-membered analogues of squaramide organocatalysts based on maleimides as double hydrogen bond donors. We were not successful in preparing complete analogues, but we successfully prepared maleimide organocatalysts with a single hydrogen bond donor and protected maleimide organocatalysts. During the preparation of the maleimide organocatalysts, the chemical reactivity of the maleimides was further investigated.

In the second part, we studied the performance of established bifunctional non-covalent asymmetric squaramide-based organocatalysts in two enantioselective conversions. The first reaction studied was the Michael addition of malononitrile to arylidene pyrrolin-4-ones, which resulted in heteroannulation to dihydropyrano[3,2-*b*]pyrrole. The second reaction was the organocatalysed Michael addition of tetramic and tetronic acids to *trans*-β-nitrostyrene. The mechanism of the organocatalysed reactions was postulated using experimental data and DFT calculations and the origin of the enantioselectivity was elucidated. In the case of the addition of malononitrile to arylidenepyrroline-4-one, the influence of the solvent and the configuration of the arylidenepyrroline-4-one on the enantioselectivity of the reactions was further investigated. It turns out that the enantioselectivity of the reaction can be controlled both by the configuration of the Michael acceptor and by the choice of the solvent. Thus, using a single organocatalyst, we were able to reverse the enantioselectivity of the reaction by changing the

solvent from methanol to dichloromethane. The change in the enantioselectivity of the reaction was explained by a change in the reactive conformation of the organocatalyst in the chosen solvent.

In the third part, new bifunctional phase transfer organocatalysts were prepared from (+)-10-camphorsulfonic acid. The chiral framework of camphor was used to replace the well-established chiral frameworks based on derivatives of quinuclidine, *trans*-1,2-cyclohexanediamine and α-amino acids. Various bifunctional camphor-based phase transfer organocatalysts with thiosuccinic and squaramidic hydrogen bond donors and iodide and trifluoroacetate counterions were prepared (10 catalysts). The prepared phase transfer organocatalysts were tested in various model reactions such as electrophilic functionalisations of cyclic β-keto ester and alkylation of an imine derivative of glycine with methyl acrylate. The prepared phase transfer organocatalysts did not provide high enantioselectivities (up to 29 % *ee*), but the reactions proceeded in most cases with complete conversion.

In the last part of the work, different heterocyclic systems were prepared and tested as substrates in (asymmetric) organocatalysed reactions. Brominated pyridone and quinolone heterocycles were prepared. The prepared heterocycles were tested in a cascade organocatalysed cyclopropanation reaction with pyrrolon and pyrazolone Michael acceptors. This afforded 3D-rich bispyrocyclic systems. The diastereoselectivity of the reactions depended on the catalyst and base used, respectively. We were not able to determine the enantioselectivity due to the complex mixtures of diastereomers.