RADOSLAV ŠUCHÁNEK

Abstract

The submitted doctoral dissertation addresses the design, synthesis, and application of synthetic *Cinchona* alkaloid analogues that could serve as new potential organocatalysts. The valuable properties of *Cinchona* alkaloids and their derivatives have proven crucial for efficient asymmetric catalysis. However, the total synthesis of these natural alkaloids and access to the entire pool of their stereoisomers are still not economically viable.

The first chapter of this work covers developing an efficient and inexpensive synthetic method for new, artificial 1,2-diamines whose chemical structures, although closely related to *Cinchona* alkaloids, have been simplified through modifications in both the bicyclic and the aromatic parts. Several derivatives differing in the size of the aromatic group and the structure of the bicyclic fragment were obtained using the developed method. Some of the synthesized 1,2-diamines were successfully resolved into enantiomerically pure forms and subsequently transformed into bifunctional derivatives (thioureas and squaramide derivatives). Both the 1,2-diamines themselves and their bifunctional derivatives were applied in several catalytic reactions, achieving efficiencies essentially equal to those of *Cinchona* alkaloids derivatives.

The second chapter focuses on the synthesis of compounds equipped with multiple multicentred hydrogen-bond donors. Their structures were based on mefloquine scaffold, a medicine and an analogue of *Cinchona* alkaloids. The 11-aminomefloquine molecule contains both primary and secondary amine groups, allowing their independent functionalization. These compounds were intended for use in anion-binding catalysis. However, during the study, it was found that their utility is limited, and the best catalytic performance was observed for reactions of unrelated mechanisms. During the synthetic study, a previously unreported rearrangement of squaramide derivatives was observed. This phenomenon was subsequently subjected to kinetic investigations in order to determine its mechanism and reaction parameters.

In the final chapter, a catalytic stereoselective synthesis of new bicyclo[2.2.1]heptanone derivatives was carried out using the reactivity of α,β-unsaturated *S*-thioesters in cycloaddition reactions with 2-cyclopentenone and its derivatives. The results showed that 13*N*-methyl-11-aminomefloquine proved to be an efficient and versatile catalyst. The selective reactivity of the *S*-thioester group in the new derivatives was further demonstrated in Fukuyama reduction and direct amide synthesis. The high stereoselectivity of the cycloaddition reaction was investigated using density functional theory (DFT) by calculating the energies of the proper transition states and analysing substrate–catalyst interactions present in the transition state.