

Dissertation

Synthesis of bifunctional, chiral catalysts based on hydrogen bond donors and evaluation of their catalytic efficiency

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Abstract

Despite more than a century of research, enantioselective chemical transformations continue to present a formidable challenge in the field of organic synthesis. Presently, the emphasis is on developing methods that eliminate environmentally harmful or hazardous reagents. In this context, while modern chemical synthesis plays a significant role in enantioselective catalysis, there is a growing trend toward replacing heavy or precious metal compounds with organocatalysts.

In the first part, the results of designing, synthesizing, and applying chiral organocatalysts that feature a hydrogen bond donor unit are presented. These catalysts were rigorously tested in Michael additions, using derivatives of 5-substituted cyclohexanediones as nucleophiles, which are relatively unexplored yet possess immense synthetic potential. With the aid of a cinchona alkaloid squaramide-based catalyst, these substrates, when combined with benzylidenepyruvic acid esters, yielded products with high enantiomeric excess, reaching up to 99%. Subsequent transformations of the Michael adducts allowed us to obtain 1,4-dihydropyridine derivatives with exceptional optical and diastereomeric purity, exceeding 99% ee and displaying diastereomeric ratios above 20:1. Next, *S*-thioesters of acetylthioacetic acid as nucleophiles were explored, which, in conjunction with derivatives of β -nitrostyrene, produced products with optical purities ranging from 84% to 99% ee. Notably, the catalyst's distinctive feature was the structure of trans-1,2-diaminecyclohexane with a squaramide unit, where the second amino group's nature influenced selectivity, depending on whether β -nitrostyrene or β -bromonitrostyrene was the acceptor. Overall, sulfur-containing nucleophiles demonstrated higher reactivity compared to those with an oxygen atom in the examined Michael additions, as showcased in various catalytic trials.

The second part of research revolved around designing and synthesizing templates containing hydrogen bond donors, also with chiral properties. These templates were intended for use in regioselective C-H activation reactions. The catalytic activity of structures containing the squaramide unit, thiourea, or urea in the meta-olefination of aromatic compounds was compared. Additionally, asymmetric C-H activation through desymmetrization with chiral templates was examined as the concluding segment of research.

In the final part of this dissertation, investigations into photoinduced [2+2] olefin cyclization and the synthesis of hydrogen bond donor subunits for controlling the conformation of small oligopeptides as well are presented.

The extensive scope of research and the obtained results underscore the importance of catalysts featuring hydrogen bond donor units in various examined reactions, especially in asymmetric contexts. Despite their high effectiveness, the field of enantioselective organocatalysis warrants further exploration. Tailoring the catalyst's structure to match the transition state of the reaction, which is inherently dependent on its specific type, has been demonstrated as a crucial factor for achieving successful chemical transformations, as showcased in this dissertation.