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Abstract (Doctor)

Title of Thesis	Synthesis of Cinchona Alkaloids-derived Chiral Squaramide Polymers and Their Application to Asymmetric Catalysis
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Approx. 800 words

Cinchona alkaloids-derived squaramide containing chiral main-chain polymers have been successfully synthesized and applied to asymmetric catalysis. Quinine, quinidine, cinchonidine and cinchonine are the common commercially available cinchona alkaloids. These are one of the popular sources for chirality inducers in the field of asymmetric catalysis. Cinchona alkaloids have various functionalities including a quinuclidine tertiary nitrogen, a secondary alcohol, a quinoline ring and a terminal olefin in their structure. The chemical modifications of the functionalities enable us to design new catalysts. Thus, several modifications have been already done by different research groups and synthesis of many monomeric and dimeric organocatalysts having cinchona squaramide moieties have also been reported. The acidic NH of the squaramide can act as a H-bond donor, whereas the tertiary nitrogen of the quinuclidine of cinchona alkaloids may acts as both a H-bond acceptor and a base. Thus the cinchona squaramide can act as a bifunctional H-bonding organocatalyst in the asymmetric transformations.

Cinchona derived squaramides can act as the efficient organocatalysts in different asymmetric transformations. Although several works have been reported with the low-molecular-weight squaramide catalysts derived from cinchona alkaloids, limited number of works have been carried out in the synthesis and application of chiral polymeric organocatalyst on the asymmetric transformation. Cinchona alkaloids containing polystyrene-supported side-chain type polymeric catalysts have been already synthesized and applied on asymmetric reactions. In case of polymer-supported catalysts, flexible and sterically irregular structures are used. On the other hand, the chiral main-chain polymeric organocatalysts contain the rigid and sterically regular structures in their backbone. This approach is more suitable to maintain the catalytic environment of the monomeric catalysts into the polymeric catalysts. The main-chain cinchona squaramide polymers can act as a good organocatalysts in asymmetric reactions due to the creation of a suitable microenvironment by the polymers which is very important for the stereoselectivity of the catalysts. The modification of a microenvironment of polymers is very important and it is possible to control the microenvironment precisely in the chiral main-chain polymeric catalysts. The enantioselectivity of low-molecular-weight monomeric catalysts can be maintained in the corresponding polymeric catalysts due to the formation of rigid and sterically regular backbone in the polymers structure. Cinchona squaramide polymeric catalysts can be prepared by the incorporation of low-molecular-weight dimeric squaramide, using suitable polymerization techniques under optimal reaction conditions.

Therefore, structural design and synthesis of main-chain chiral polymeric organocatalysts are very much attractive field of research in asymmetric synthesis to obtain enantiopure organic compounds. To understand the effect of main-chain chiral polymeric organocatalyst in asymmetric synthesis, we have synthesized several cinchona derived squaramide main-chain polymers using Mizoroki-Heck and ADMET polymerization methods and successfully applied in the enantioselective Michael addition reactions.

In this thesis, chapter 1 presents the general introduction which includes the structural features of cinchona alkaloids, chiral organocatalysts, polymeric organocatalysts and the background of this thesis work. This chapter also includes the general reviews about low-molecular-weight cinchona alkaloids squaramide catalyzed different asymmetric reactions, including Michael addition reaction, Friedel-Crafts reaction, Strecker reaction, and Mannich reaction.

Chapter 2 presents the synthesis of novel chiral squaramide polymers by the reaction of cinchona derived-squaramide and various aromatic diiodo compounds using Mizoroki-Heck polymerization. The Mizoroki-Heck reactions between the double bonds of the cinchona-based squaramide and aromatic diiodides proceeded smoothly to give cinchona squaramide chiral polymers. The asymmetric Michael addition of β -ketoesters to nitroolefins was successfully catalyzed by the squaramide polymers to give the corresponding Michael adducts in good yields and excellent enantioselectivities of up to 97% ee. As the polymeric catalysts were insoluble in commonly used organic solvents, these were recovered and reused without any loss of catalytic activity.

Chapter 3 describes the synthesis of novel chiral polymers of diamine connected cinchona squaramides using Mizoroki-Heck polymerization as highly efficient catalysts in the asymmetric Michael addition reaction. We designed novel cinchona squaramide dimers that contain two cinchona squaramide units connected by diamines. The olefinic double bonds in this dimer were used for Mizoroki-Heck polymerization with aromatic diiodides to give the corresponding chiral polymers in good yields. We have surveyed the effect of the chiral polymer structure on the catalytic activity and enantioselectivity of the asymmetric reaction. The novel squaramides and also polymers were applied in asymmetric Michael addition of β -ketoesters to nitroolefins to obtain the adducts in good yields with excellent stereoselectivities. In this case the polymeric catalysts were recovered and reused for several times.

Chapter 4 describes the synthesis of cinchona alkaloid-derived novel chiral squaramide polymers by acyclic diene metathesis (ADMET) polymerization and their application to asymmetric catalysis. The first synthesis of high molecular weight cinchona alkaloid-derived chiral squaramide polymers by ADMET polymerization is reported, using the Hoveyda-Grubbs 2nd generation catalysts (HG₂). We have synthesized novel chiral polymeric catalysts containing cinchona squaramide moieties in the main chain of the polymer by ADMET reaction. The ADMET polymerization reactions between the cinchona alkaloid-derived squaramide diene and HG₂ catalyst afforded the chiral polymers. The chiral polymers were also used as catalysts in asymmetric Michael addition reactions to give the products in good yields with excellent stereoselectivities. They were easily recovered from the reaction mixture and reused several times.

Chapter 5 presents the general summary of this whole thesis works.