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Abstract (Doctor)

Title of Thesis	Design and synthesis of chiral hyperbranched polymers of cinchona squaramides and their application to asymmetric catalysis
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Approx. 800 words

The main objective of this research is to study the influence of synthetic chiral polymers in asymmetric reaction processes. Chiral hyperbranched polymers (HBPs) of cinchona squaramides was synthesized for evaluating their catalytic performance in asymmetric synthesis. For obtaining chiral hyperbranched polymers and linear polymers, the use of cinchona alkaloids derivatives involves with the design stage. Then, Mizoroki-Heck (MH) coupling reaction and Yamamoto coupling reaction were used as synthetic methodology to obtain the chiral hyperbranched polymers and chiral linear polymers respectively and finally, the catalytic activity of chiral polymeric catalysts was assessed in asymmetric Michael addition reactions. Cinchona alkaloids and their derivatives have been widely employed as chiral organocatalysts in diverse asymmetric synthesis, because of their outstanding catalytic activity for several asymmetric reactions. Quinine, quinidine, cinchonidine and cinchonine are the major cinchona alkaloids which are commonly commercially available. Cinchona alkaloids are useful for suitable modifications to versatile catalysts in asymmetric reactions due to their several functionalities such as secondary alcohol, quinoline ring, quinuclidine and vinyl group. Although numbers of cinchona alkaloid derivatives have been found in chiral organocatalysts, their polymers have not been synthesized. The polymeric catalyst design is an essential tool to understand the efficient catalytic process in asymmetric transformations. 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. So, cinchona squaramide can act as a bifunctional H-bonding organocatalyst in the asymmetric synthesis. Thus, cinchona derived squaramides were used for the design of chiral polymeric organocatalysts in this work.

Cinchona derived squaramides have been proven as 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 squaramide polymeric catalysts can be prepared by the incorporation of low molecular weight dimeric squaramide, using suitable polymerization techniques under optimal reaction conditions. In our previous reports, we have established MH polymerization reaction which was a reliable C-C bond forming reaction to synthesize chiral linear polymers from cinchona alkaloid derivatives. In this work, we chose to synthesize chiral HBPs. We noticed that this (MH) methodology is applicable toward the synthesis of chiral HBPs from cinchona alkaloid derivatives. Chiral HBPs are highly branched tree-like three-dimensional structures which have drawn a lot of attention in various applications. Chiral HBPs containing chiral catalytic moieties are potential polymer catalysts in asymmetric catalysis. Cinchona-based chiral HBPs have not been reported to date. In this work, we designed and synthesized cinchona-based chiral HBPs containing squaramide moiety by MH polymerization and another new coupling reaction which is called Yamamoto coupling and obtained polymers were successfully applied in the enantioselective Michael addition reactions.

The novel chiral cinchona squaramide HBPs were synthesized first by the reaction of cinchona squaramide dimer and tri or tetrasubstituted aromatic iodide via a MH polycondensation reaction. The MH reactions occurred smoothly between the double bonds of the cinchona squaramide and aromatic tri- or tetraiodides to give chiral hyperbranched polymers. Chiral HBPs were then applied in the asymmetric Michael addition reaction and excellent enantioselectivity (>99% ee) was observed with good yield in the Michael addition reaction of β -ketoesters to *trans*- β -nitrostyrene. Because of insolubility of polymeric catalysts in common organic solvents, the HBPs can be easily separated and reused up to six times without losing their catalytic activity and enantioselectivity. This is the first example of chiral HBP organocatalyst successfully applied to the asymmetric Michael addition reaction.

Then the novel chiral HBPs from cinchona squaramide containing both vinyl (A) and iodophenyl (B) groups in AB₂ and A₂B type monomers was designed and synthesized. These were successfully polymerized by the MH coupling reaction between the vinyl and iodophenyl functionalities to give chiral HBPs. The chiral HBPs prepared by one step MH polymerization were used as catalysts in asymmetric Michael reactions. In case of the reaction between methyl 2-oxocyclopentanecarboxylate and *trans*- β -nitrostyrene, the HBP catalysts showed high catalytic activity with excellent diastereoselectivity and enantioselectivity. Reactions between some other substrate combinations also occurred smoothly with the HBP catalysts. Interestingly, the HBP catalysts gave higher diastereoselectivity compared to that obtained with the low molecular weight catalyst. Somewhat higher catalytic activity was also observed with HBP catalyst. Precise control

of the catalyst conformation may be possible in case of polymer catalyst. These results show that the design of chiral HBP catalyst may lead the development of high-performance polymeric catalyst. The HBP catalysts were easily recovered from the reaction mixture and reused several times without any decrease in catalytic activity and stereoselectivity.

After that the synthesis of cinchona squaramide-based chiral polymers via the Yamamoto coupling reaction was described. Yamamoto coupling reaction occurs between aromatic halides. This coupling reaction is nickel-catalyzed reaction of organic halides in the presence of neutral ligands. Yamamoto coupling reaction is advantageous because only a single, halogen-functionalized monomer can be used to form polymer. With homopolymers, three copolymers were also synthesized from low molecular weight cinchona squaramide with achiral diiodo or dibromo aromatic compounds. Chiral polymers were applied to the asymmetric Michael addition reactions and afforded good to excellent enantioselectivities. The polymeric catalysts were recovered from the reaction mixture and reused several times without any decrease in catalytic activity.