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Abstract (Doctor)

Title of Thesis	Synthesis of Functional Core-Corona Polymer Microsphere and Its Application to Asymmetric Organocatalysis
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Approx. 800 words

Chiral organocatalysts have been received considerable attention in asymmetric synthesis because of their advantages of being cost effective, readily available, non-toxic and environmental friendly. Among a variety of chiral organocatalysts, *Cinchona* alkaloids are one of the efficient organocatalysts in the asymmetric organocatalysis which are available in pseudoenantiomeric forms, due to their commercial availability at low prices, stability and easy handling in laboratory, as well as their convenient modifications by simple reactions. *Cinchona* derived quaternary ammonium salts are one of the most popular organocatalysts in the field of asymmetric catalysis especially for the synthesis of unnatural α -amino acids. Chiral imidazolidin-4-ones and their salts, originally developed by MacMillan and co-workers, are also one of the most important classes of chiral organocatalysts.

Immobilization of a chiral organocatalyst onto a heterogeneous support represents an attractive approach for catalytic asymmetric reactions from a viewpoint of its sustainability. Although there have been numerous reports on covalently bonded both polymer-immobilized chiral quaternary ammonium salt and MacMillan catalyst for asymmetric alkylation and the Diels-Alder reaction, respectively, these heterogeneous catalysts sometimes offer inherent disadvantages, such as low selectivity and low catalytic activity. These can be interpreted in terms of direct covalent-bonding of organocatalysts to the support material, decreasing the intrinsic properties of steric sensitivity of organocatalyst on asymmetric synthesis.

To solve the above problem, an alternative strategy involving the ionic immobilization of an organocatalyst on a support using an ion-exchange reaction has been reported. This method is a facile and general technique for the immobilization of ammonium onto sulfonated polymers regardless of kinds of ammonium and sulfonated polymer, which can be employed in mild conditions. In some cases, these ionically immobilized organocatalysts also showed low catalytic activity.

Nevertheless of the efficiency of polymer microsphere as polymer support, there is no report on the immobilization of chiral cinchonidinium salt or MacMillan catalyst onto polymer microsphere. Monodisperse sulfonated core-corona polymer microspheres seem to be suitable solid-supports for the ionic immobilization of chiral organocatalysts because of their high surface area, facile dispersibility, and high mechanical and thermal stability. In addition, an advantage of polymer microspheres is the ability to control their hydrophilic-hydrophobic balance, which offers suitable microenvironments for catalytic asymmetric reactions. Therefore, synthesis of well-defined core-corona polymer microsphere-supported

chiral organocatalyst is a new idea in asymmetric catalysis for obtaining optically active compounds. To investigate the effect of these polymeric organocatalysts in asymmetric catalysis, we have developed both core-corona polymer microsphere-supported chiral cinchonidinium salt and MacMillan catalyst and applied them as heterogeneous catalysts in the asymmetric alkylation and the Diels-Alder reaction, respectively.

Chapter I describes the generation introduction and background of this thesis work.

Chapter II describes the synthesis of narrowly disperse functional polymer microspheres having benzyl halide moiety by precipitation polymerization of various comonomers (styrene (St), methyl methacrylate (MMA), or 2-hydroxyethyl methacrylate (HEMA)), divinylbenzene (DVB) with 4-vinylbenzyl chloride (VBC). We have also successfully synthesized low cross-linked polymer microspheres using 10 mol% of crosslinker (DVB and a divinyl crosslinker) by precipitation polymerization and transformation reaction. The nature of comonomer and the molar ratio of monomers affected the yield and diameter of polymer particles.

Chapter III provides a novel strategy for the synthesis of well-defined hairy polymer or core corona polymer microspheres by precipitation polymerization and surface-initiated atom transfer radical polymerization (SI-ATRP). The M_n of grafted polymer can be controlled up to 15,000 g mol⁻¹ by changing the M/I, and the M_w/M_n was lower than 1.30 when $M/I \leq 150$. In this Chapter, monodisperse sulfonated core-corona polymer microsphere was also successfully synthesized from the graft copolymerization of an achiral monomer and phenyl *p*-styrenesulfonate with polymer microsphere having benzyl chloride moiety as a macroinitiator by SI-ATRP, followed by the treatment NaOH. The graft copolymerization of styrene and phenyl *p*-styrenesulfonate proceeded in a controlled manner, affording well-defined core-corona polymer microsphere when poly(DVB-HEMA-VBC) or poly(DVB-St-VBC) microsphere was used as a macroinitiator.

Chapter IV describes the synthesis of core-corona polymer microsphere-supported chiral cinchonidinium salt by the ion exchange reaction of sodium sulfonate moiety at the side chain of corona with chiral cinchonidinium salt, which was applied as chiral heterogeneous organocatalyst in the asymmetric alkylation of a glycine derivative to give high yields (up to 99%) and enantioselectivities (up to >99% ee). The effect of nature and size of core, nature and length of corona, grafting density, as well as the degree of crosslinking on the catalytic reactivity was investigated in detail in this chapter. The catalyst could be easily and quantitatively recovered from reaction mixture and reused several times without loss of the enantioselectivity. To our knowledge, this is the first report of core-corona polymer microsphere-supported cinchonidinium salt in the asymmetric alkylation.

Chapter V describes the synthesis of core-corona polymer microsphere-supported MacMillan catalyst by the neutralization reaction of sulfonic acid moiety at the side chain of corona with MacMillan catalyst precursor. We evaluated their catalytic efficiency in the asymmetric Diels-Alder reaction and obtained the desired adducts in good yield (up to 99%) with excellent ee value (up to 97% ee (*exo*) and >99% ee (*endo*)). The core and corona (kinds of monomer, diameter, and length of corona) significantly affected on the catalytic activity. The catalyst could be reused several times without loss of the enantioselectivity.

Chapter VI describes the general summary of this thesis work.