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Abstract (Doctor)

Title of Thesis	Synthesis of Chiral Polymeric Organocatalysts of Cinchona Alkaloid Derivatives for their Application in Asymmetric Catalysis (シンコナルカロイド誘導体を用いるキラル高分子有機触媒の合成と不斉反応への応用)
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Approx. 800 words

The use of chiral polymer catalysts has become one of the essential techniques in organic synthesis. Due to the fact that, they can be easily separated from the reaction mixture and reused for many times. It is even possible to apply the polymeric catalysts to a continuous flow system. From the point of view of green chemistry, the chiral polymeric organocatalysis method provides a clean and safe alternative to conventional methods of asymmetric processes. Not only the practical aspect of the polymeric catalyst but also the particular micro environment they create in a polymer network, that make them attractive for utilization in organic reactions especially in stereoselective synthesis. Design of chiral polymers and their catalytic use is now extremely required in organic synthesis of fine chemicals.

Cinchona alkaloids are some of the most important sources of various kinds of efficient chiral organocatalysts. Each of the cinchona alkaloids, namely, quinine, cinchonidine, quinidine, and cinchonine, contain several functionalities such as secondary alcohol, quinuclidine, and quinoline rings in addition to the vinyl group. Cinchona alkaloids and their derivatives are classified as privileged organic chirality inducers, efficiently catalyzing many classes of organic reactions in a highly enantioselective fashion. As a unique class of bifunctional cinchona organocatalysts, cupreines and cupreidines have also been proved as powerful chiral catalysts for a wide array of asymmetric transformations. Compared to traditional cinchona catalysts, one of the most noticeable features of cupreines and cupreidines is that they bear a phenolic OH group at the C6' position and a free hydroxyl moiety at C9 position that could be utilized to tune the steric conformation by further functionalization to achieve higher efficiency in asymmetric reaction. However, low molecular weights chiral organocatalysts in asymmetric synthesis processes are hindered by mainly two factors; unable to be recycled and low catalyst loading.

With the advancement made in chiral polymeric organocatalysis, cinchona alkaloids as a privileged class of chirality inducers have found part in chiral polymeric organocatalysts design. Even though polymeric organocatalysts in asymmetric synthesis, sometimes exhibit poor reactivity by virtual of their heterogeneity, in some cases, a well-designed polymeric chiral organocatalyst may leads to higher selectivity with sufficient reactivity in asymmetric reactions. Therefore, chiral polymer design, synthesis and their catalytic use; has become an important tool for understanding the polymeric catalytic efficiency in asymmetric synthesis for fine chemicals production.

In this work, we focused on the design and synthesis of chiral polymeric organocatalysts derived from cinchona alkaloids and, evaluate their catalytic performance in asymmetric Michael addition reactions.

Chapter 1 shows the general idea of chiral organocatalysis based on literature review, it describes the generation, advantages and applicability of chiral organocatalysts. The whole idea is categorized into two concepts; low molecular weight chiral organocatalysts and polymeric chiral organocatalysts for their application in asymmetric synthesis. The importance of this research work is also explained.

Chapter 2 presents about the cinchona alkaloids and their derivatives as an important tool in asymmetric catalysis. In this chapter, the general structure of cinchona alkaloids and their catalytic sites have been presented and identified. The application of cinchona alkaloids derivatives in asymmetric synthesis have been summarized. Examples on cinchona alkaloids derivatives in monomeric, dimeric as well as polymeric form of chiral organocatalysts in different asymmetric reactions have been explained. In addition, general synthetic methodologies applied in this work have been briefly explained.

Chapter 3 and 4 describes the development of main-chain chiral polymeric organocatalysts of cinchona alkaloids. The repetitive Mizoroki-Heck coupling reaction as catalyzed by Palladium was employed as synthetic method. The C6'-OMe and C6'-OH free containing main-chain chiral polymeric catalysts were synthesized and evaluated in asymmetric Michael addition reactions. Higher enantioselectivities (up to 97% ee) and catalytic activities (up to 97% yield) were achieved.

In Chapter 5, synthesis of cross-linked chiral polysiloxanes of cinchona alkaloid derivative and their application to asymmetric catalysis is presented. The Platinum catalyzed hydrosilylation reaction was used for synthesis of cross-linked chiral polysiloxanes. The design, synthesis and catalytic performance evaluations in asymmetric Michael addition reactions have been summarized. Higher enantioselectivities (up to 99% ee) and sufficient catalytic activities were achieved.

Chapter 6 includes the general conclusion on the chiral polymers of cinchona alkaloids established in this work. Their catalytic performance evaluation based on the factors affecting their applicability in asymmetric synthesis are summarized. In addition, alternative synthetic approach of obtaining the comparable main-chain chiral polymers of cinchona alkaloid derivatives have been shortly explained.

List of publications and experimental results supporting informations of each chapter are included in the appendices.