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## Abstract

## 論文内容の要旨 (博士)

Title of Thesis 博士学位論文名	<b>Novel Catalytic Asymmetric Carbene Transfer Reactions of Functionalized Diazo Compounds with Olefins</b> (官能基化ジアゾ化合物とオレフィンとの新規触媒的不斉カルベン移動反応)
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(Approx. 800 words)

(要旨 1,200 字程度)

**Keywords:** asymmetric synthesis, cyclopropanation, heterogeneous catalysis, water-soluble catalysts.

Carbenes are very reactive species. The reactivity of a particular carbene depends on the substituent groups. Their reactivity can be affected by metals. Some of the reactions carbenes can do are insertions into C-H bonds, skeletal rearrangements, and additions to double bonds through cyclopropanation reactions. Chiral cyclopropane derivatives are valuable structural motifs found in numerous natural products with diverse biological activities. Thus, during the past two decades, the development of synthetic methodologies toward chiral cyclopropane compounds has attracted much attention and the transition-metal-catalyzed asymmetric cyclopropanation of olefins with diazoacetates is widely recognized as one of the more powerful methods in terms of highly stereoselective synthesis. In contrast to the excellent results obtained with diazoacetates, diazoacetamides are rarely used as a carbene source because of the low electrophilicity and steric hindrance of the resulting metal-carbene intermediate. This prompted us to explore the asymmetric cyclopropanation of olefins with various diazoacetamides, namely, diazo Weinreb amides, because the resulting cyclopropanes are potentially useful synthetic intermediates that can be easily converted to the corresponding aldehydes, ketones, and alcohols.

**Chapter 1** Describes the importance of the carbene transfer reactions, especially, the cyclopropanation reactions and the different strategies and types of catalysts have been also illustrated in this chapter. In addition, a brief summary of the most successful applications of the organometallic catalysts over the past ten years was provided.

**Chapter 2** We successfully developed of the first highly stereoselective cyclopropanation of diazo Wienreb amides with olefins using chiral Ru(II)-Pheox-type catalysts. Ru(II)-Amm-Pheox complex featuring an internal quaternary ammonium unit exhibited obviously higher activity and enantioselectivity as compared with previously described Ru(II)-Pheox complexes, to afford the corresponding chiral cyclopropyl Weinreb amides in high yields (up to 99%) with excellent diastereoselectivities (up to 99:1 dr) and enantioselectivities

(up to 96% ee). In addition, the use of acetoxy-functionalized diazoacetamide as a carbene source was found to be crucial for the high *trans*-selectivity of the cyclopropanation reaction. Moreover, the obtained chiral Weinreb amides were readily converted to various useful synthetic intermediates, such as alcohols, ketones, and aldehydes, in one step and without any loss of enantioselectivity.

**Chapter 3** In this chapter, We developed of the first highly stereoselective intramolecular cyclopropanation of *trans*-allylic diazo Wienreb amides. After the investigation of many chiral catalysts, Ru(II)-*Amm*-Pheox catalyst was proved to be the crucial catalyst for the high enantioselectivity for the cyclopropanation reaction. Moreover, the obtained chiral bicyclic compounds were readily converted to the corresponding ketone in one step and without any loss of enantioselectivity.

**Chapter 4** presents a water-soluble chiral Ru(II)-*Amm*-pheox complex as a reusable and highly enantioselective catalyst in intramolecular cyclopropanation of *trans*-allylic diazo Weinreb amides in a water/ether biphasic medium. We found that the Ru(II)-*Amm*-Pheox catalyst completely dissolved in water and completely undissolved in ether. The reaction occurred at the interface snice the products migrate to the ether-phase and the catalyst return back to react with another molecule of *trans*-allylic diazo Weinreb amide. A variety of Ru(II)-pheox catalysts with different functional groups were screened and found that the functionality of the ruthenium catalyst with ammonium group is important to furnish the cyclopropanation product in high yield. Different types of *trans*-allylic diazo Weinreb amide were investigated and afforded excellent reactivities up to 99% yield and enantioselectivities up to 99% ee. The easily separation of the ether-phase, which contains the cyclopropane product, allows the simple reuse of the catalyst in the water-phase at least six times with slightly decrease in reactivity or enantioselectivity.

**Chapter 5** provides the experimental and analytical data for chapters from 2 to 4.

In summary, we have successfully designed and synthesized novel Ru(II)-pheox type catalyst. Th catalyst showed excellent reactivities and selectivities in carbene transfer reactions. The catalyst had ability to be reused several times and stored after reused without loss of its catalytic activity or selectivity. In addition, no significant leaching of the catalysts was detected. The Ru(II)-*Amm*-pheox catalysts is expected to provide many further opportunities in asymmetric catalysis.