Abstract of Doctoral Dissertation

Degree requested Doctor of Pharmaceutical Science　Applicant's name CHEN, Yen-Chou

Title of Doctoral Dissertation

Studies on Palladium-Catalyzed Reactions of Functionalized 2-Bromo-1,3-dienes
（官能基化2-ブロモ-1,3-ジエン類のパラジウム触媒反応に関する研究）

Allenes are a class of compounds characterized by two cumulated carbon−carbon double bonds. Because of their propadiene structures, they show distinctive steric and electronic properties and have emerged as highly interesting target molecules in organic synthesis. In the last few decades, we have developed a palladium-catalyzed reaction of preparing functionalized allenes starting with 2-halo-1,3-dienes and appropriate soft nucleophiles. This reaction is an ideal prototype for catalytic asymmetric synthesis of axially chiral allenes in the presence of a palladium species coordinated with a chiral bisphosphine ligand, and has showed the good to excellent enantioselectivities.

In this dissertation, I have been interested in examining the reactivities and further applications of functionalized 2-bromo-1,3-dienes in our Pd-catalyzed reaction, and the studies has been divided into four section. In the first section, Pd-catalyzed cyclizations of nucleophile-tethered 2-bromo-1,3-dienes was described. A palladium-catalyzed reaction for preparing various endocyclic allenes was developed, and the 2-bromo-1,3-dienyl substrates for the Pd-catalyzed reaction were readily prepared. As widely recognized, medium-membered carbocycles are difficult to construct and are provided in low yields in typical cyclization reactions. On the other hand, our method could provide medium- to large-membered carbocycle in relatively high yields (up to 67%). Additionally, our method of preparing endocyclic allenes was extended into an asymmetric counterpart by the use of a chiral Pd catalyst, and enantiomerically enriched axially chiral endocyclic allenes were obtained in up to 70% ee.

In the second section, Pd-catalyzed nucleophilic substitution on 3-bromopenta-2,4-dienyl esters is described. In 2012, our research group demonstrated that 3-bromopenta-2,4-dienyl acetate was an excellent precursor to prepare doubly functionalized allenes by the twofold Pd-catalyzed substitution reaction. We have investigated approaches to preparing various allenic derivatives via the Pd-catalyzed

nucleophilic substitution reaction between the newly prepared 3-bromopenta-2,4-dienyl esters (benzoate and phosphate) and soft nucleophiles. The reaction has been extended to the asymmetric counterparts using appropriate chiral Pd catalysts to give the axially chiral allenes in enantiomerically enriched forms.

In third section, the application of the palladium-catalyzed reaction in polymer chemistry is described. Since the Pd-catalyzed reaction between 3-bromopenta-2,4-dienyl acetate and 2 equivalents soft nucleophile provides the corresponding C_2-symmetic allenes with excellent regioselectivity, we have envisioned that the use of an appropriate bifunctional nucleophile in our palladium-catalyzed reaction might produce oligomeric/polymeric products, which possess allenic scaffolds as a repeating unit in their main chains. The Pd-catalyzed polymerization between 3-bromopenta-2,4-dienyl acetate and appropriate bifunctional nucleophiles provided allenic polymers in up to 82% yield and the M_n values reached up to 13700. Asymmetric synthesis of axially chiral allenic polymers was examined by the use of chiral palladium catalysts in the reaction. We have also developed a new method of determining the *R*/*S* distribution (enantio-regularity) of axially chiral allenic polymers.

In final section, bis(2-bromo-1,3-dienes) as a new bifunctional electrophile monomer in our Pd-catalyzed polymerization instead of using 3-bromopenta-2,4-dienyl acetate as a substrate was examined, and polymers were provided in up to 86% and the M_n values reached up to 22600. The asymmetric synthesis of corresponding axially chiral allenic polymers by the enantioselective Pd-catalyzed reaction will be described in detail.