Studies on Catalytic Asymmetric Hydrogenation of Fused Carbocyclic Arenes

金, 玉樹

氏　　名　：　金　玉樹　（Yushu Jin）

論 文 名　：　Studies on Catalytic Asymmetric Hydrogenation of Fused Carbocyclic Arenes
(多環式芳香族炭素環の触媒的不斉水素化に関する研究)

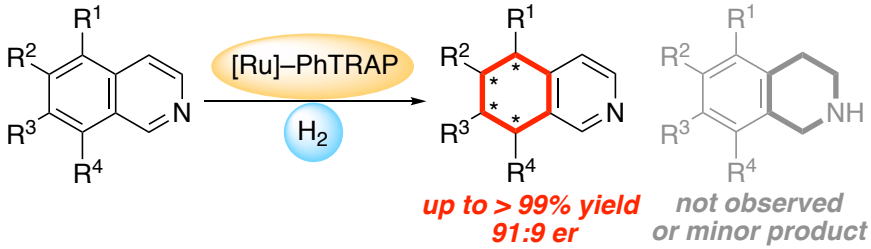
区　　分　：　甲

論　文　要　約

The asymmetric hydrogenation of aromatic compounds is one of the most straightforward ways to construct saturated enantio-enriched 5- or 6-membered rings. The method provides the possibility to create multiple chiral centers in a single process. The asymmetric hydrogenation of heteroarenes has been frequently reported since the 21st century. As compare to heteroarenes, asymmetric hydrogenation of carbocyclic arenes is less explored because the substrates are highly stabilized with their own aromaticity. Nevertheless, Glorius group firstly reported the asymmetric hydrogenation of carbocycles in quinoxalines with a chiral carbene–ruthenium catalyst. In the following years, our group reported the hydrogenation of naphthalenes, as well as quinoline carbocycles, with high enantioselectivities by using PhTRAP–ruthenium catalyst.

The first topic of this thesis described my study on catalytic asymmetric chemoselective hydrogenation of isoquinoline carbocycles. Hydrogenation of isoquinolines generally affords pyridine-ring reductive products. However, the asymmetric hydrogenation of isoquinoline carbocycles may be unexpected for many chemists. Until now, only the asymmetric hydrogenation of the isoquinoline pyridine rings has been reported by Zhou, Mashima, and Zhang. In this research, it was found that the hydrogenation of isoquinolines selectively took place on their carbocycles by using the chiral *trans*-chelation bisphosphine PhTRAP–ruthenium complex. The heterocyclic moiety of the isoquinoline remained intact during the reduction of the carbocycle, although the pyridine ring is commonly more reactive than the dearomatization of benzene moiety. The bite angle of the chelate bisphosphine ligand PhTRAP is vital to achieve this unique chemoselectivity. The PhTRAP–ruthenium catalyst allowed the selective formation of 5,6,7,8-tetrahydroisoquinolines as the major products. Various 5- and 8-substituted isoquinoline carbocycles were exclusively reduced to give the corresponding 5,6,7,8-tetrahydroisoquinolines in high yields, while the hydrogenations of 6- and 7-substituted isoquinolines proceed with moderate to high chemoselectivities. Furthermore, the above hydrogenations proceeded through enantioselective fashion, yielding the desired 5,6,7,8-tetrahydroisoquinolines with moderate to good enantiomer ratio. The mechanism of this hydrogenation was investigated through some deuteration experiments. As a result, the deuteration indicated that the

stereogenic center was created during the initial addition of H_2 to the aromatic ring in the hydrogenation of 5-substituted isoquinolines.



The second topic of this thesis described a kinetic resolution of 1-aryl-2-methoxynaphthalenes through the asymmetric hydrogenation. Kinetic resolution represents one of the most classical and efficient methodologies to obtain enantio-pure compounds. Recently, Zhou reported a highly efficient kinetic resolution of axially chiral 5- and 8-substituted quinolines via asymmetric transfer hydrogenation of the heteroarene. Inspired by our recent achievements on the asymmetric hydrogenation of carbocyclic arenes, in this research, we found that the hydrogenation of axially chiral 1-(biphenyl-2-yl)-2-methoxynaphthalene was accompanied by a kinetic resolution with high efficiency (s = 20) through the asymmetric catalysis, PhTRAP–ruthenium. The starting material was recovered from the reaction mixture with 98% ee in 30% isolated yield when the substrate was treated with 5.0 MPa of H_2 in toluene at 80 ˚C for 14 h in the presence of [RuCl(*p*-cymene)-{(*S*,*S*)-(*R*,*R*)-PhTRAP}]Cl catalyst. The reaction exclusively provided the chiral 5,6,7,8-tetrahydronaphthalene with 65% ee in 45% isolated yield. The kinetic resolution through the hydrogenation is applicable to some axially chiral naphthalenes with high efficiency.