



Title	Enantioselective Synthesis of Spiro Compounds and Their Applications to Asymmetric Catalysis
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## 論文内容の要旨

氏 名 ( 樊 璐 露 )

論文題名

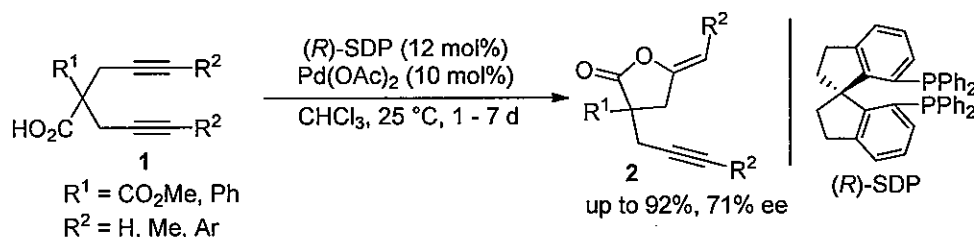
## Enantioselective Synthesis of Spiro Compounds and Their Applications to Asymmetric Catalysis

(エナンチオ選択的スピロ化合物の合成と不斉反応への展開)

## 論文内容の要旨

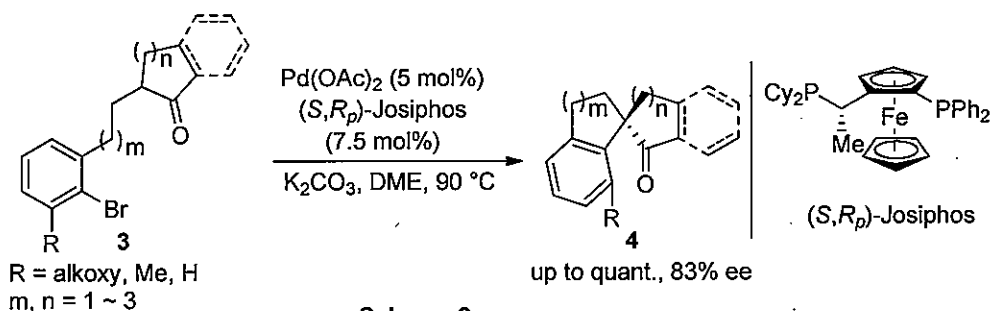
Chiral catalyst bearing spiro skeleton can provide efficient asymmetric environment because the structural feature of the two perpendicular rings connected through one carbon could afford a unique chirality and increase molecular rigidity. The reported spiro type catalysts could exhibit good asymmetric induction in catalytic reactions. Our group has also investigated chiral spiro compounds which can work as ligands, organocatalyst, and ionic liquids. However, the unavoidable optical resolution during preparation of spiro catalysts limits the development of them in asymmetric catalysis. This thesis describes two events: one is exploration of application of spiro ligand SDP in enantioselective synthesis of chiral heterocyclic compounds (see project 1); the other is exploration of catalytic enantioselective synthesis of spiro compounds with functionality that can go further transformation, aiming to develop various spiro type catalysts which could be used in asymmetric reactions (see project 2).

Project 1: we have applied chiral spiro ligand SDP to Pd-catalyzed enantioselective intramolecular cyclization of  $\alpha, \alpha$ -disubstituted- $\gamma$ -alkynoic acids **1**. This 5-*exo-dig* cyclization afforded dihydrofuran-2(3*H*)-ones **2** bearing a chiral quaternary carbon center in excellent yields with enantioselectivities up to 71% (Scheme 1).



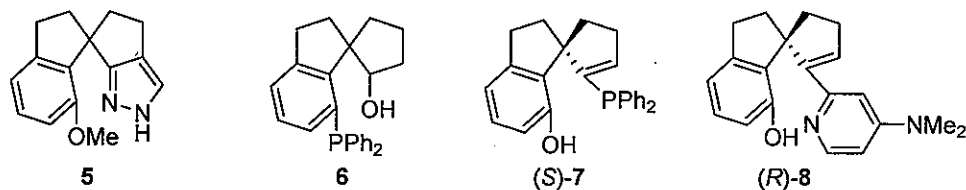
Scheme 1

Project 2: catalytic enantioselective synthesis of spiro cyclic ketones **4** as key intermediates were conducted by Pd-catalyzed intramolecular  $\alpha$ -arylation of  $\alpha$ -substituted cycloketones **3** (Scheme 2). Among our screening of various chiral ligands such as BINAP, MeO-MOP, DIOP, *i*-Pr-PHOX and BenzP\*, ferrocene type ligand Josiphos showed best asymmetric induction in this transformation. Under optimized reaction conditions, spiro cyclic ketones **4** were obtained up to quant. yield with 83% ee.

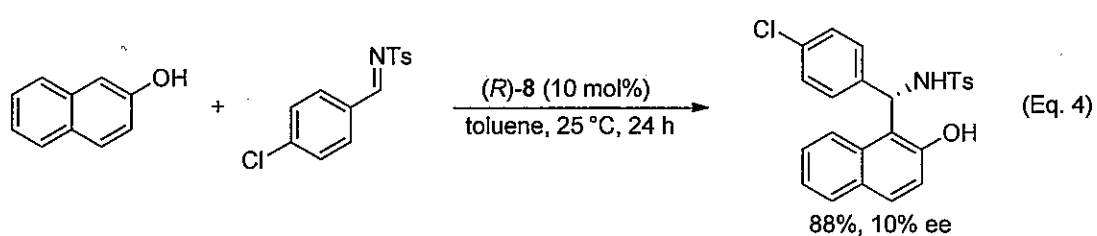
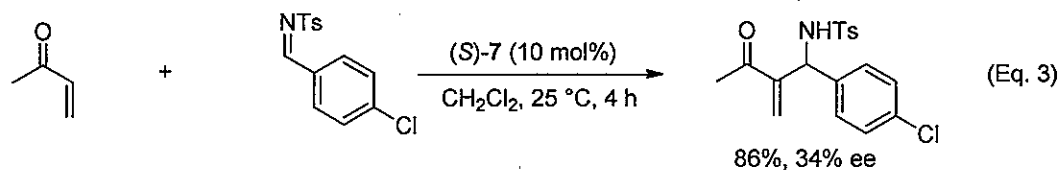
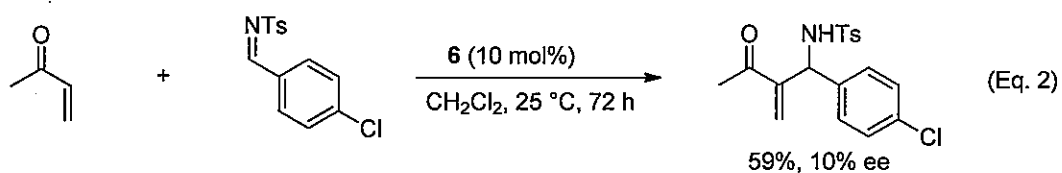
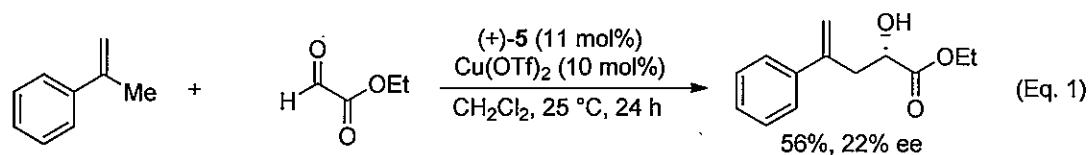


Scheme 2

The novel spiro ligand **5** and organocatalysts **6** – **8** were designed and synthesized from spiro cyclic ketones **4** ( $m = n = 1$ ,  $R = \text{OMe}$  or  $\text{OBn}$ ) (Fig. 1). Among them, pyrazole ligand **5** could be applied to copper-catalyzed ene reaction of glyoxylate to give desired product in 56% yield with 22% ee (Eq. 1). Organocatalyst **6** and **7** could catalyze aza-MBH reaction of methyl vinyl ketone with *p*-chlorophenyl *N*-tosyl imine to give corresponding products in 59% yield with 10% ee and 86% yield with 34% ee, respectively (Eq. 2 and 3). The spiro-DMAP catalyst **8** was able to catalyze Betti reaction of *p*-chlorophenyl *N*-tosyl imine with  $\beta$ -naphthanol to afford adduct in 88% yield with 10% ee (Eq. 4).



**Fig. 1**



## 論文審査の結果の要旨及び担当者

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論文審査の結果の要旨			
<p>学位申請者は、パラジウム触媒による環状ケトン類のエナント選択的分子内<math>\alpha</math>位アリール化反応を検討し、キラルな二座ホスフィン配位子である Josiphos を用いて比較的高い光学純度で目的のスピロ化合物を得ることに成功している。エナント選択的なスピロ骨格形成反応として新規性の高い反応である。キラルリガンドの置換基効果については、膨大な数のリガンドを検討し、ジシクロヘキシルホスフィンとジフェニルホスフィンを有する Josiphos が最も効果的であることを示している。得られたスピロ化合物を、酸-塩基型有機分子触媒やキラルリガンドへと変換し、エナント選択性に改善の余地があるものの、スピロ化合物のキラリティーを利用する触媒反応に応用できることも見いだしている。さらに、パラジウム触媒を用いて、プロキラルな<math>\gamma</math>-アルキン酸の 5-exo-dig 型環化反応によるテトラヒドロフラノンのエナント選択的合成も検討し、キラルなスピロ型ホスフィン配位子 SDP を用いて好結果を得ている。よって、本論文は博士（理学）の学位論文として十分価値あるものと認める。</p>			