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学位授与の日付 平成 28 年 3 月 31 日

論 文 名 **Synthesis of the Phosphine- Olefin Ligands Based on the
Planar- Chiral Transition Metal Complexes and Application to the
Asymmetric Catalysis**
(面不斉遷移金属錯体を基盤とするホスフィン-オレフィン配位子の
合成および不斉触媒への応用)

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Synthesis of the Phosphine-Olefin Ligands Based on the Planar-Chiral Transition Metal Complexes and Application to the Asymmetric Catalysis

面不斉遷移金属錯体を基盤とするホスフィン-オレフィン配位子の合成および不斉触媒への応用

学位論文の要旨

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Introduction

Transition metal-catalyzed asymmetric reactions offer one of the most straightforward methods for the synthesis of optically active compounds from achiral starting materials.^{1,2} The steric and electronic factors of ligands have a profound influence upon the nature of the reactive metallic species and hence can affect the reactivity and selectivity of the metal complex formed. Therefore, the development of novel chiral ligands that can effectively induce the asymmetry in reactions is pivotal in organic synthesis and organometallic chemistry. In recent years, the phosphine-olefin ligands have received much attention as a new type of chiral ligand due to their interesting electron properties. Because they are topographically related to the tripod ligand, which is six electron donors, but the phosphine-olefin ligand can serve as four electron donors as a bidentate ligand.³ (Figure 1). Moreover, the phosphine-olefin ligands combined both of beneficial structure of a phosphine ligand and a diene ligand into a single framework, namely, the high coordination ability of phosphines and the good chiral environment created around the olefins (Figure 2).⁴

Figure 1. Topographical Complex A with $d^n + 4$ Electrons and a Tripod Complex B with $d^n + 6$ Electrons.

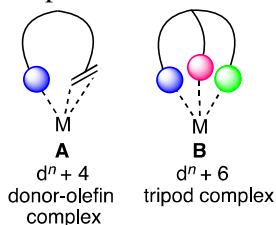
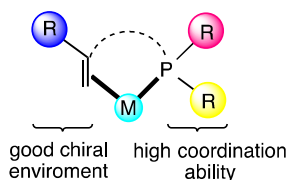


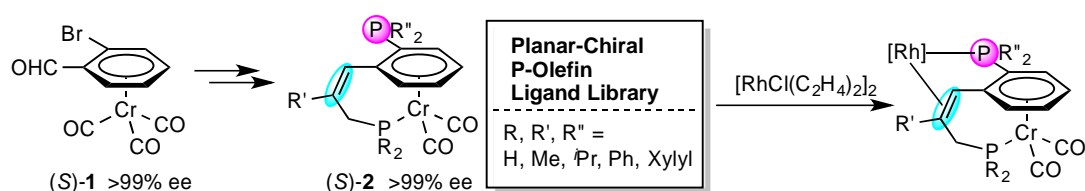
Figure 2. Design of Chiral Phosphine-Olefin Ligand.



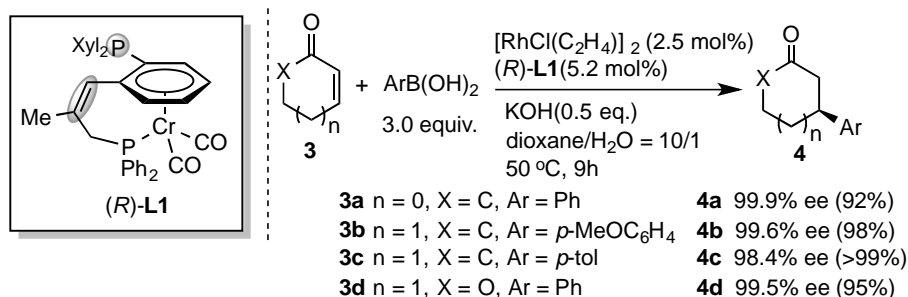
1. Phosphine-Olefin Ligands Based on a Planar-Chiral (p-Arene)chromium Scaffold: Design, Synthesis, and Application in Asymmetric Catalysis

It has been clarified that planar-chiral alkenylene-bridged (phosphino- π -arene)(phosphine)chromium species **2** are competent of coordinating to a rhodium(I) cation in the bidentate fashion not only at the phosphorus atom but also at the olefin moiety.⁵ The *P*-olefin chelate coordination of **2** constructs the efficient chiral environment at the rhodium(I) center, and thus some of their rhodium complexes show high enantioselectivity in the asymmetric 1,4- and 1,2-addition reactions of the arylboron nucleophiles. We have also succeeded in developing the common and more practical enantiospecific synthetic method of these phosphine-olefin ligands. The new synthetic method is fairly flexible with regard to the substituent variation, and a library of the planar-chiral (arene)chromium-based phosphine-olefin ligands can be constructed by the combinatorial method. Among the newly developed ligand library, (*R*)-**L1** which is with the bis(3,5-dimethylphenyl)phosphino group on the η^6 -arene ring was found to be the outstanding chiral ligand in the rhodium-catalyzed asymmetric reactions displaying excellent enantioselectivity of up to 99.9% ee.⁶

Scheme 1. Development of the Phosphine-Olefin Ligands Based on the Planar-Chiral (p-Arene)chromium Complexes.



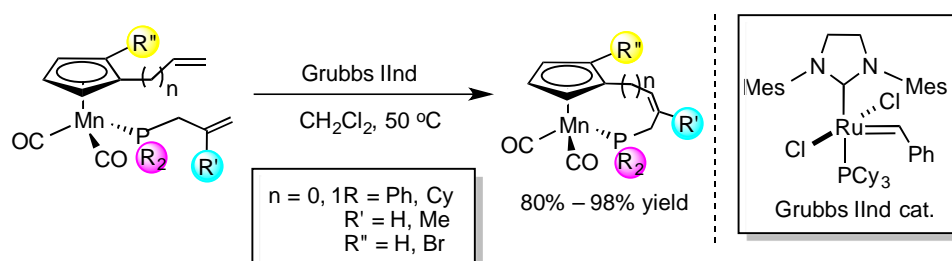
Scheme 2. Rhodium-Catalyzed Asymmetric 1,4-Addition of Arylboronic Acids to α,β -Unsaturated Carbonyl Compounds.



2. Ring-Closing Metathesis of (η^5 -Alkenylcyclopentadienyl)-(alkenylphosphine)manganese(I) Dicarbonyl Complexes

We previously reported that ring-closing metathesis (RCM) reactions of arene chromium complex⁷ and ferrocene⁸ by endo mode cyclization using the Grubbs catalyst, which leads to the formation of the chromium or ferrocene-containing ring systems with C₃ or C₄ bridge respectively. In this study, we investigated the reactivity of RCM reaction in (η^5 -cyclopentadienyl)-manganese(I) and examined the suitable ring size in this metal coordinating sphere. As the result, we have successfully achieved the RCM reaction in the coordination sphere of the (η^5 -cyclopentadienyl)manganese complexes by the Grubbs-II catalyst. A wide range of the substrates scope could be applied for the RCM reaction, and the various C₃- and C₄-bridged manganese complexes were synthesized. The X-ray analyses revealed their structural differences between the C₃- and the C₄-bridged complexes. The preferential formation of the C₄-bridged species over the C₄-bridged analogues was confirmed by the intramolecular competitive RCM experiment.⁹

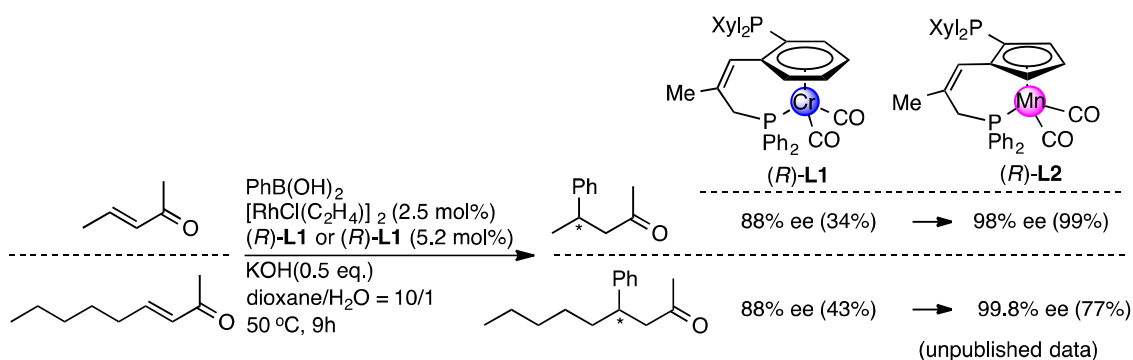
Scheme 3. Ring-Closing Metathesis Reaction of Manganese Complexes.



3. Development of the Highly Efficient and Robust Second Generation P-Olefin Ligands Based on Planar-Chiral Cyclopentadienyl Manganese Carbonyl Complexes

We have reported the phosphine-olefin ligand based on the planar chiral (π -arene) chromium platform.⁶ The planar-chiral Cr ligand (*R*)-**L1** was found to be an excellent ligand in Rh catalyzed 1,4 addition reaction of the cyclic enones. While **the reactions with acyclic enones were problematic in (*R*)-L1** which resulted in low reactivities and enantioselectivities. Thus, to expand the substrate scope in our phosphine-olefin ligand, we developed the second-generation planar-chiral P-olefin ligand based on a cyclopentadienyl manganese complex as a new platform with an isoelectronic structure. Among the series of second-generation P-olefin ligands, (*R*)-**L2** with xylyl group on phosphorous atom substituted in a cyclopentadienyl unit exhibited extremely high enantioselectivities and reactivities in rhodium catalyzed asymmetric 1,4-addition of arylboronic acids to cyclic and acyclic enones, which exceed the performance of the first generation chromium ligand (*R*)-**L1** over 99% ee in all cases. The single crystals of [RhCl(CH₂=CH₂)₂]/*rac*-**L1** and [RhCl(CH₂=CH₂)₂]/*rac*-**L2** complexes revealed their bite angles toward the rhodium atom as 91.58° and 90.70° respectively. This slight difference in their bite angle (0.88°) would induce the significant difference of enantioselectivity in rhodium catalyzed asymmetric reactions.^{10,11}

Scheme 4. Asymmetric 1,4-Addition Reactions of Acyclic Enones Using Planar-Chiral P-Olefin Ligands (*R*)-**L1** and (*R*)-**L2**.



4. Summary

We have successfully developed new type of planar chiral phosphine olefin ligands based on transition metal platform. Initially, in the first-generation (π -arene)chromium ligand, the combination of substituents was optimized by making a ligand library. Furthermore, a planar chiral transition metal scaffold was optimized to cyclopentadienyl manganese complex. As the result, reactivities, enantioselectivities and substrate scope greatly improved in the second-generation ligand over the first-generation ligand in Rh catalyzed asymmetric reactions.

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Publication List

- (1) “Phosphine-Olefin Ligands Based on a Planar-Chiral (η^5 -Arene)chromium Scaffold: Design, Synthesis, and Application in Asymmetric Catalysis”, Ogasawara, M.; Tseng, Y.-Y.; Arae, S.; Morita, T.; Nakaya, T.; Wu, W.-Y.; Takahashi, T.; Kamikawa, K. *J. Am. Chem. Soc.* **2014**, *136*, 9377.
- (2) “Ring-Closing Metathesis of (η^5 -Alkenylcyclopentadienyl)-(alkenylphosphine)manganese(I) Dicarbonyl Complexes”, Tseng, Y.-Y.; Kamikawa, K.; Wu, Q.; Takahashi, T.; Ogasawara, M. *Adv. Synth. Catal.* **2015**, *357*, 2255.
- (3) “Development of the Highly Efficient and Robust Second Generation P-Olefin Ligands Based on Planar-Chiral Cyclopentadienyl Manganese Carbonyl Complexes”, Tseng, Y.-Y.; Kamikawa, K.; Takahashi, T.; Ogasawara, M., *manuscript in preparation*.

学位論文審査結果の要旨

遷移金属触媒を用いる触媒的不斉合成の開発において、高い反応性と立体選択性を示す不斉配位子の設計および合成は、極めて重要な課題である。本論文では、面不斉遷移金属錯体を基盤とした新規なホスフィン-オレフィン配位子の開発ならびに、不斉触媒反応への応用について検討した結果について述べられている。論文の内容については、以下の通りである。

(1) 面不斉アレーンクロム錯体を母核にもつ新規ホスフィン-オレフィン不斉配位子の開発を行った。この配位子は、アレーン上のホスフィノ基とオレフィン部位とがロジウムに対して、二座配位することを X 線結晶解析より明らかにした。さらに、配位子の 3 箇所を様々な置換基で置き換えた不斉配位子ライブラリーを作成し、それぞれの配位子を用いてロジウム触媒不斉 1,4-付加反応を行い、配位子構造と反応性、立体選択性との活性相関について精査した。その結果、最も高い立体選択性、反応性を示すホスフィン-オレフィン不斉配位子を開発することに成功したことが示された。この不斉配位子を用いたロジウム触媒不斉 1,4-付加反応では、最高で **99.9% ee (99% 収率)** で対応する付加体を合成できることを見出している。

(2) 遷移金属配位空間内における閉環メタセシス反応についてさらなる知見を得ることを目的とし、シクロペンタジエニルマンガン錯体を用いたエンド型閉環メタセシス反応について検討を行った結果について述べた。シクロペンタジエニル基上にビニルあるいはアリル基を有し、アリルジフェニルホスフィンが配位したマンガン錯体を合成し、炭素架橋部位が三炭素からなる環化体と四炭素からなる環化体の合成を行った結果、どちらの環化生成物も良好な収率で得られることを見出している。

(3) 上述の面不斉アレーンクロム錯体を母核にもつホスフィン-オレフィン不斉配位子における欠点を克服した第二世代型面不斉シクロペンタジエニルマンガン錯体を母核にもつ新規ホスフィン-オレフィン不斉配位子の開発を行った。クロム配位子が溶液中で徐々に分解するのに対して、マンガン配位子は溶液中において安定であり、さらにクロム配位子では良い結果を与えなかった非環状エノンに対する不斉 1,4-付加反応においても非常に高い立体選択性 (**最大 99.8% ee**) および反応性 (**最大 99%**) で対応する付加体を与えることを見出した。

本研究成果は、これまでに開発されたホスフィン-オレフィン配位子の性能を大きく上回るものであり、触媒的不斉合成のさらなる発展に大いに寄与するものである。したがって、本学位審査委員会は、本論文が学位論文として十分な内容を有しているものと判断した。

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