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学 位 論 文 題 目 Preparation and Reactions of Titana-,  
Zircona- and Hafnacycles

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## Chapter 1

### General Introduction

Early transition metal-mediated and/or -catalyzed organic syntheses are a relatively new field. Particularly, the chemistry of group 4 metal complexes has been well studied due to their unique chemical and physical properties. They can play a role as catalysts for coupling reactions of unsaturated compounds via carbon-carbon bond formation. In addition, hydrometallation and carbometallation can be extended to the synthesis of general organic products and natural products. In addition, novel and/or synthetically useful reactions can be also expected from this area. The organometallic chemistry of the group 4 elements is well-developed and has given rise to a series of interesting new reaction patterns. The vast majority of this chemistry is associated with the  $Cp_2M$  fragment. In this chapter, the chemistry of group 4 metal organometallic complexes bearing a unit of  $[Cp_2M]$  ( $M=Ti, Zr, \text{ and } Hf$ ) and the variety of reactivities induced by low valent metallocene complexes will be briefly introduced.

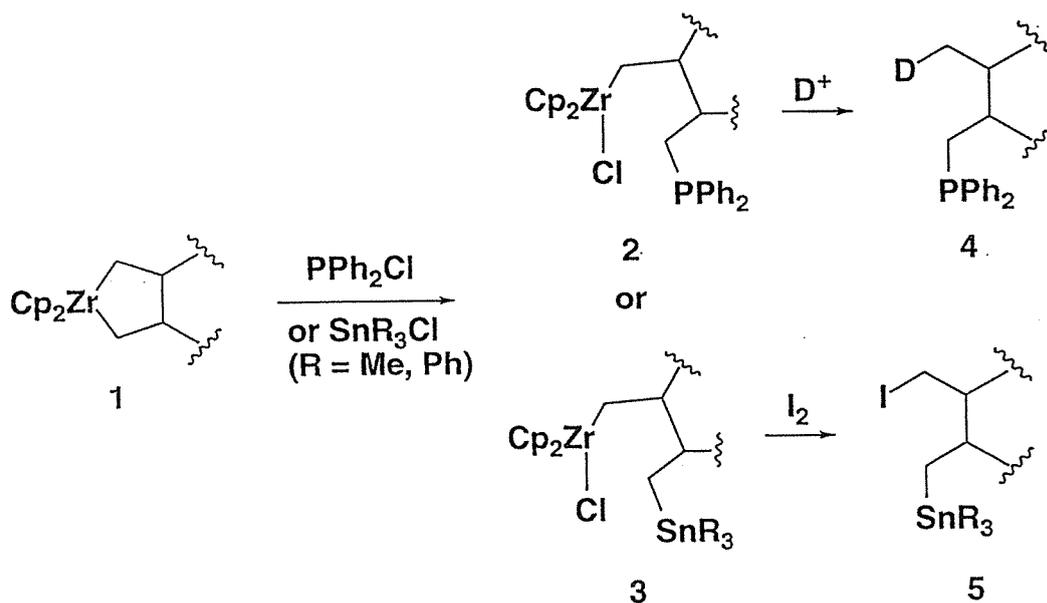
## Chapter 2

### Highly Selective Monofunctionalization of Zirconacyclopentanes and Dialkylzirconocene Complexes

Zirconacyclopentanes(1) have been readily prepared by intermolecular coupling or intramolecular cyclization of unsaturated compounds on  $Cp_2ZrBu_2$  (Negishi reagent). For the functionalization of zirconacyclopentanes, many reactions with various reagents have been reported. However, most of the final organic products were difunctionalized compounds or cyclized compounds. Consequently, only "symmetrical" compounds are formed from "symmetrical" zirconacyclopentanes. From the point of view of organic synthesis, formation of "unsymmetrical" compounds from "symmetrical" zirconacyclopentanes is very attractive.

In this chapter, a selective monofunctionalization reaction of zirconacyclopentanes using  $PPh_2Cl$  or  $SnR_3Cl$  ( $R=Me, Ph$ ) is reported. As shown in Scheme 1, reaction of zirconacyclopentanes with  $PPh_2Cl$  or  $SnR_3Cl$  ( $R=Me, Ph$ ) gave monofunctionalized products 4 or 5, respectively in good to high yields with high selectivities.

### Scheme 1



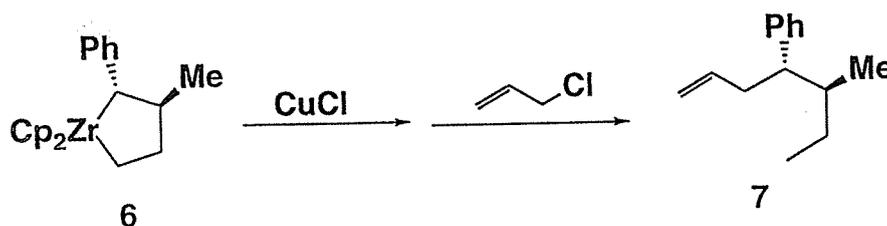
### Chapter 3

#### Highly Regio- and Diastereoselective Carbon-Carbon Bond Formation Reaction of Zirconacyclopentanes Using Copper Salt.

Regioselective and stereoselective reactions are very attractive and useful for organic synthesis. A large number of copper-catalyzed carbon-carbon bond formation reactions have been reported, e.g., allylation reaction of alkenylzirconocenes, alkenylzirconocene, zirconacyclopentenes and zirconacyclopentadienes. However, not only a further carbon-carbon bond formation reaction of unsymmetrical zirconacyclopentanes but also a carbon-carbon bond formation method which gives diastereomerically pure products from zirconacyclopentanes remains to be investigated.

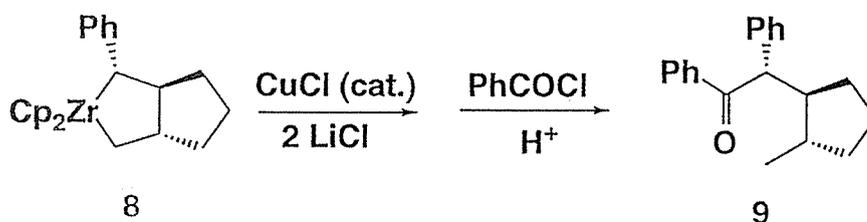
Reaction of unsymmetrical zirconacyclopentanes (**6**) bearing substituents in  $\alpha$ -position with allyl chloride in the presence of a stoichiometric or a catalytic amount of copper chloride gave allylated products (**7**) with high regioselectivity and diastereomeric purities (Scheme 2).

### Scheme 2



The reaction of zirconacyclopentane(8) with benzoyl chloride in a same condition above leads to the isolation of crystals of compound(9) in 58% yield as shown in Scheme 3. The X-ray structure analysis of 9 indicates that stereochemistry is retained from zirconacyclopentanes to benzoylated compound during transmetalation from zirconium to copper. This high stereoselectivity is due to the effect of added copper chloride. In place of unsymmetrical zirconacyclopentanes, allylation of symmetrical zirconacyclopentanes were investigated as a fundamental study. Finally, as an application of this reaction, tricyclic compound was synthesized from obtained allylated compounds.

Scheme 3

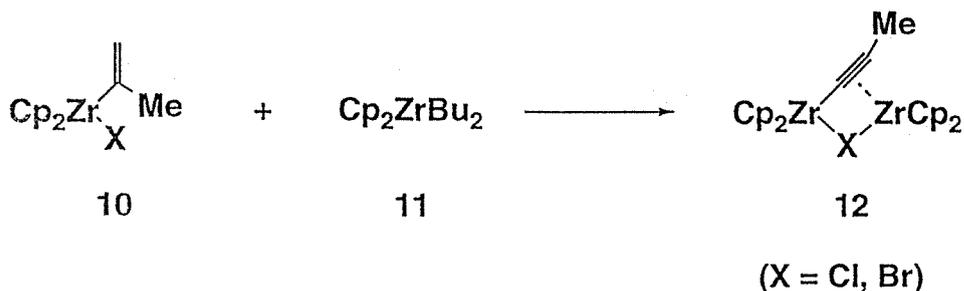


#### Chapter 4

#### Reaction of Alkenylzirconocene with Dialkylzirconocene: Unexpected Formation of Bimetallic ( $\mu$ -Alkynyl)zirconocene Complexes

Bimetallic transition metal complexes are attractive because both metal center have the potential to interact simultaneously with an organic molecule. Reaction of alkenylzirconocenes  $\text{Cp}_2\text{ZrX}(\text{MeC}=\text{CH}_2)$  ( $\text{X}=\text{Cl}$  or  $\text{Br}$ ) (10) with dialkylzirconocenes,  $\text{Cp}_2\text{ZrBu}_2$  (11) yielded unexpected bimetallic zirconocene complexes,  $\text{Cp}_2\text{Zr}(\mu\text{-X})(\mu\text{-C}\equiv\text{CCH}_3)\text{ZrCp}_2$  ( $\text{X}=\text{Cl}$  or  $\text{Br}$ ) (12) (Scheme 4). Its structure ( $\text{X}=\text{Cl}$ ) was determined by X-ray crystallography. The monitoring of the reaction of  $\text{Cp}_2\text{ZrBu}_2$  with  $\text{Cp}_2\text{ZrBr}(\text{MeC}=\text{CH}_2)$  revealed that the first step of this reaction was an exchange reaction of the Bu group of  $\text{Cp}_2\text{ZrBu}_2$  and the Br group of the alkenylzirconocene.

Scheme 4



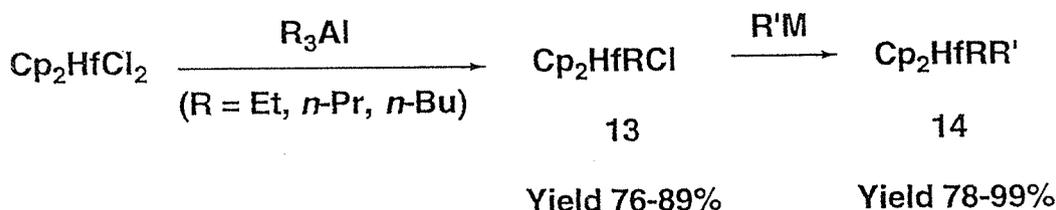
## Chapter 5

### Preparation and Reactions of $\text{Cp}_2\text{HfCl}$ , $\text{Cp}_2\text{HfRR}'$ and Hafnacyclopentenes

In comparison with the chemistry of zirconocene derivatives which has been extensively studied over the past two decades, the corresponding hafnocene chemistry has remained undeveloped. Dialkylzirconocene compounds play an important role in the zirconium(II) chemistry but they are not stable at room temperature when alkyl groups have a  $\beta$ -hydrogen. In order to investigate the reaction mechanism of such zirconium chemistry, there are some difficulties due to the unstability of dialkylzirconocenes. Therefore, the synthesis of more stable dialkylhafnocene complexes was investigated.

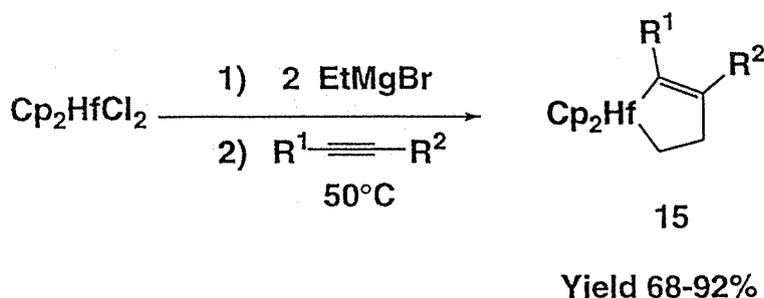
Reaction of  $\text{Cp}_2\text{HfCl}_2$  with  $\text{R}_3\text{Al}$  ( $\text{R}=\text{Et}$ ,  $n\text{-Pr}$  or  $n\text{-Bu}$ ) selectively produced monoalkylhafnocene complexes  $\text{Cp}_2\text{HfRCl}$  (13) in high yields. The treatment of 13 with alkylation reagents such as  $\text{R}'\text{Li}$  or  $\text{EtMgBr}$  afforded unsymmetrical dialkylhafnocene complexes  $\text{Cp}_2\text{HfRR}'$  (14) in good to excellent yields (Scheme 5).

#### Scheme 5



It is found that  $\text{Cp}_2\text{Hf}(\text{sec-Bu})_2$  can be used as a good precursor of  $\text{Cp}_2\text{Hf}(\text{II})$  species. Hafnacyclopentenes (15) were prepared in good yields by the reaction of  $\text{Cp}_2\text{HfEt}_2$  with alkynes (Scheme 6).

#### Scheme 6

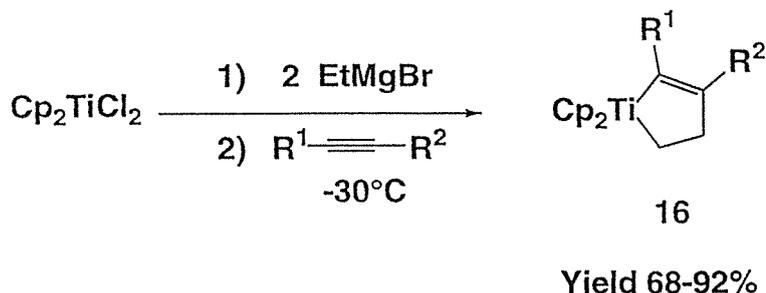


## Chapter 6

### Reaction of $\text{Cp}_2\text{TiCl}_2$ with $\text{EtMgBr}$ and Alkynes

The combination of  $\text{Cp}_2\text{ZrCl}_2/\text{EtMgBr}$  led to further catalytic intermolecular carbon-carbon bond formation reactions. However, surprisingly, the similar type of intermolecular coupling reactions using  $\text{Cp}_2\text{TiCl}_2/\text{EtMgBr}$  to give titanacycles have not been reported. In this chapter, the first example of titanacyclopentene(16) formation by an intermolecular coupling of  $\text{Cp}_2\text{TiCl}_2$ ,  $\text{EtMgBr}$  and an alkyne is reported(Scheme 7).

Scheme 7



Reaction of  $\text{Cp}_2\text{TiCl}_2$  with 2 equiv of  $\text{EtMgBr}$  followed by the addition of various of internal alkynes at  $-30^\circ\text{C}$  gave the corresponding titanacyclopentenes(16) in high yields with high selectivities. This reaction is very similar to that of  $\text{Cp}_2\text{ZrCl}_2/\text{EtMgBr}$  system. In a sharp contrast to zirconium, the formed titanacyclopentenes are thermally unstable to decompose. After hydrolysis of titanacyclopentenes, trisubstituted olefins were obtained in good to excellent yields.

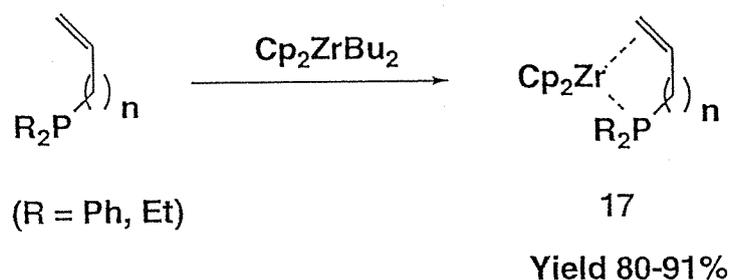
## Chapter 7

### Preparation and Reactivity of Zirconocene(II) Complexes Stabilized by Olefinic Phosphine Ligands

The preparation of zirconocene-alkene complexes and their reactivity was recently reported. Most preparative method for  $\text{Cp}_2\text{Zr(II)}$  species is the reaction of  $\text{Cp}_2\text{ZrCl}_2$  with 2 equiv of alkyl metals such as *n*-BuLi or  $\text{EtMgBr}$ , which produced zirconium-alkene complexes such as  $\text{Cp}_2\text{Zr}(\text{CH}_2=\text{CHEt})$  or  $\text{Cp}_2\text{Zr}(\text{CH}_2=\text{CH}_2)$ . However, zirconium-alkene complex is sometimes rather thermally unstable and decompose under exposure to moisture and air in solution. There is no report of fairly stable zirconium-alkene complexes.

Reaction of  $\text{Cp}_2\text{ZrBu}_2$  (Negishi reagent) generated from  $\text{Cp}_2\text{ZrCl}_2$  with two molar equivalents of *n*-butyllithium, with bidentate olefinic phosphine ligand yielded a stabilized  $\text{Cp}_2\text{Zr(II)}$  complexes(17) (Scheme 8).

Scheme 8



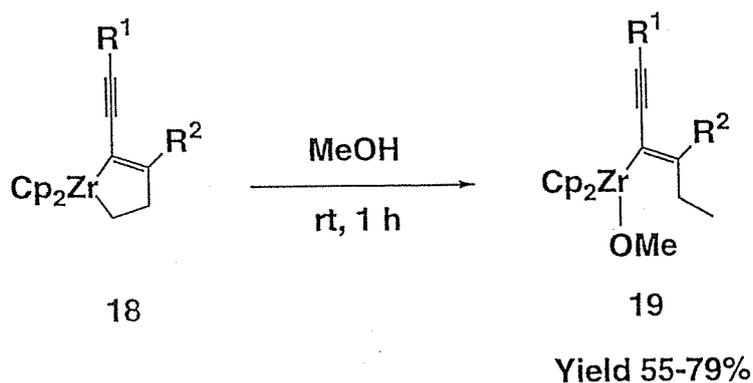
## Chapter 8

Properties of Zirconacyclopentenes with Alkynyl Substituents at  $\alpha$ -Position

Recently, it has been reported that zirconocene-ethylene complex catalyzed highly regioselective carbon-carbon bond formation reaction of 1,3-conjugated diynes. In these reactions zirconacyclopentenes (**18**) with the alkynyl substituent at  $\alpha$ -position were observed.

During the course of search of further reactivities of zirconacyclopentenes (**18**), selective zirconium-carbon bond cleavage were observed as found in zirconacycles before. In this chapter, it is reported that treatment of zirconacyclopentenes (**18**) with 1 equiv or excess of methanol generated monoprotonated compounds, i.e., alkenylzirconium methoxide complexes (**19**) by highly selective zirconium- $sp^3$  carbon bond cleavage. The correlation of the alkynyl substituent with zirconium atom in prepared complexes above was considered by the  $^{13}\text{C}$  NMR spectroscopy (Scheme 9).

Scheme 9



## 論文の審査結果の要旨

本論文は、 $Cp_2M$ 骨格 ( $Cp$ =シクロペンタジエン: $M=Ti, Zr, Hf$ )を有する第IV族前周期遷移金属錯体の新たな合成法と反応性を明らかにしており、8章からなっている。

序文では、ジルコノセン、ハフノセンおよびチタノセンの一般的合成法と反応例を示している。第2章では、有機リンおよび有機スズ化合物とジルコナシクロペンタンとの反応により、一つの官能基を選択的にシクロペンタン環に導入させる反応を見いだしている。第3章では、塩化銅存在下、塩化アリールあるいは塩化ベンゾイルと非対称ジルコナシクロペンタンとの反応で立体構造を保持させながら、位置選択的に炭葉一炭繋結合を生成させる増炭反応に成功している。第4章では、アルケニルジルコナセンとジアルキルジルコナセンとの反応で、アルキニル基が架橋した新しいタイプの2核ジルコナ金属錯体の合成に成功し、その結晶構造をX線解析により明らかにしている。第5章では、 $Cp_2HfCl_2$ とトリアルキルアルミニウムとの反応による選択的なモノアルキルハフノセン錯体の合成法の確立、またモノアルキルハフノセン錯体とアルキルリチウムまたはグリニヤ試薬との反応による非対称ジアルキルハフノセン錯体の合成法を見い出している。第6章では、ジクロロチタノセンに2等量のエチルグリニヤ試薬を反応させた後、各種の内部アルキンを反応させて、一連のチタナシクロペンテン錯体を得る一般的な合成法を確立している。第7章では、湿気、空気に対して極めて不安定で、取り扱いが困難であったアルケニルジルコナセンを有機リンにオレフィンを結合させた二座配位子を用いて、付加体を形成させて、その安定性を飛躍的に向上させている。第8章では、ジルコナシクロペンテン化合物は、大きな置換基は圧倒的に $\alpha$ 位に入り易いことに注目して、 $\alpha$ 位にアセチレン骨格を導入して、新たな炭素一炭素結合生成反応を見いだしている。

以上の通り、本研究はジルコナシクロペンタン化合物を利用して、位置選択的な置換基導入反応と立体特異的な炭素一炭素結合生成反応を数多く見い出しており、有機合成化学への大きな貢献を行っている。また、ジルコナセンに比べて、研究が遅れていたチタノセンおよびハフノセンのモノアルキルおよびジアルキル錯体の簡易な合成法を見だし、将来、これらの化合物群の出発原料になることが期待される。

本研究に関する論文は、既に権威のある英文雑誌に既に3報報告しており、その内容に関しても博士論文として十分であると判断される。

西原康師君の博士論文に対する口述試験に関しては、60分の研究発表と90分の一般常識を含めた論文内容の質疑応答を行った。前周期有機金属錯体に関する一般的な質問および有機Ti, Zr, Hf錯体の合成と反応性に関する詳細な質問に対しても、質疑内容を十分把握した上でよどみなく答えており、論文博士としての学力および知識は十分であると判断された。

公開発表会においても、ジルコナセン、ハフノセンおよびチタノセンに関する質問が数多くなされたが、いずれも問題なく答えており、学力的には十二分であると判断された。博士論文は英語で書かれており、また同君は大学院在学中にアメリカで3ヶ月の研究活動を行っており、英語の能力に関しても十分であると判断された。以上の理由で、審査委員全員一致で合格と判定した。