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学位論文題目 Zirconocene Mediated or Catalyzed Novel Carbon-Carbon Bond Forming Reactions of Alkynes

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Chapter 1

A General Introduction to Zirconocene Chemistry in Organic Synthesis

Application of transition metals in organic synthesis is the characteristics of modern organic chemistry. Intense current interest has been paid to the development of new methodology in which the selectivity (including chemo-, regio-, diastereo-, and enantio-) of carbon-carbon bond formation is controlled by a transition-metal template. Focusing on the reaction chemistry of low valent zirconocene compounds involving a unit of $[\text{Cp}_2\text{Zr}]$, this chapter is intended to briefly introduce new advances of zirconocene chemistry in organic synthesis.

Chapter 2

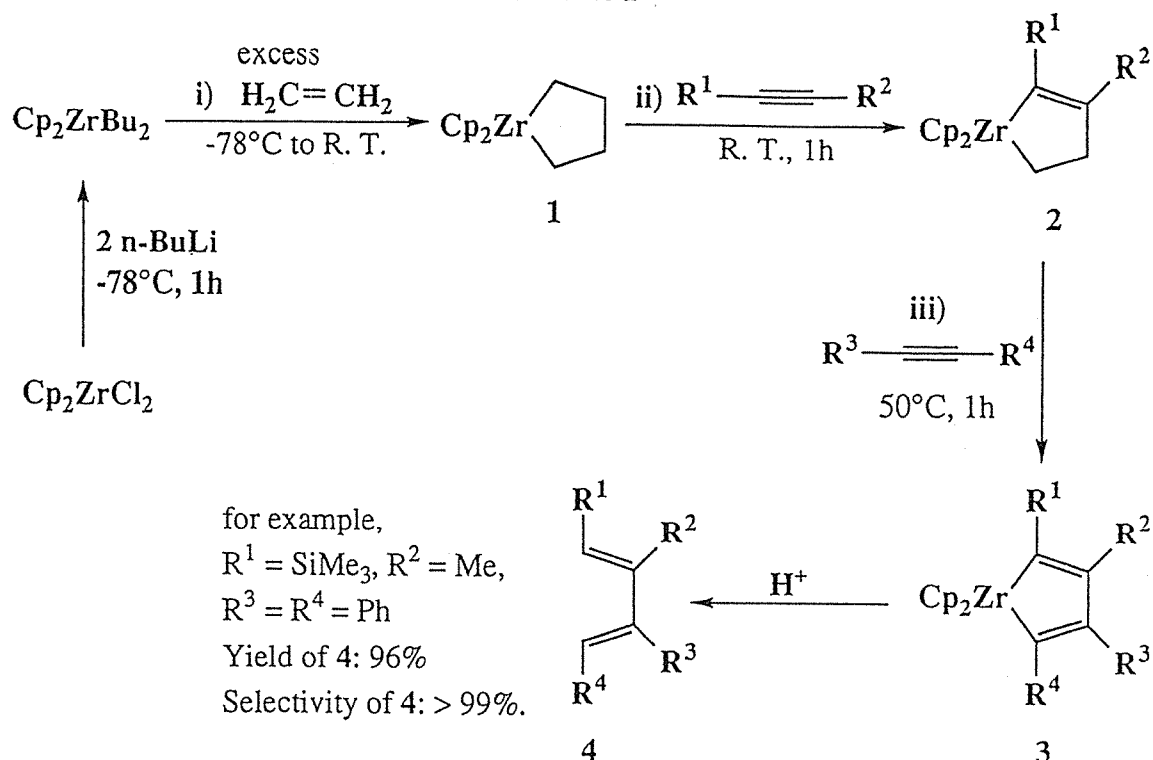
Highly Selective Formation of Zirconacyclopentadienes from Two Different Alkynes via Zirconacyclopentane. Reaction and Crystal Structure of Zirconacyclopentane

Preparation and study of unsymmetrically substituted zirconacyclopentadienes **3** of two different alkynes are of great interest from the point of view of application as well as synthetic methodology. Selective cross-coupling and complete suppression of homo-coupling have been targeted. A practical procedure for the preparation of **3** has been developed via highly selective alkyne-alkyne cross coupling reactions using Cp_2ZrBu_2 and ethylene gas (Scheme 1). Firstly, alkynes were treated with 1.2 equiv. of Cp_2ZrBu_2 (Negishi reagent) under ethylene gas to give zirconacyclopentenes **2** with high selectivity. Subsequent addition of a second alkyne to the solution of zirconacyclopentenes **2** at 50°C gave **3** selectively. After hydrolysis substituted butadienes **4** were obtained in high yields. The intermediacy of zirconacyclopentane **1** plays a very important role in the selective and high-yield formation of **2** and **3**.

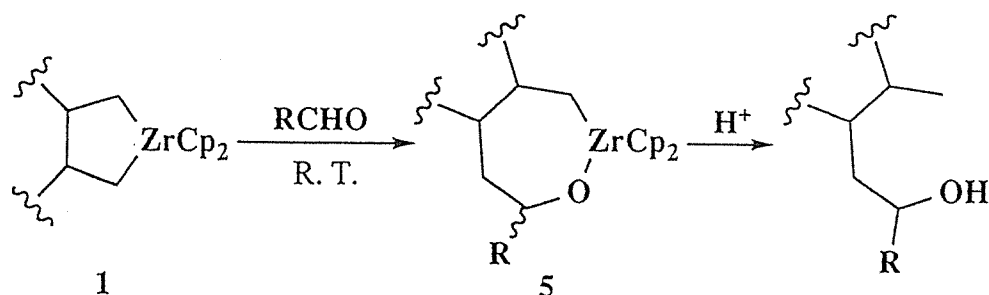
An insertion reaction of aldehydes into zirconacyclopentanes **1** under an atmosphere of ethylene forming 7-membered oxozirconacycloheptanes **5** is also reported in this chapter as the first example of this kind (Scheme 2). Bicyclic zirconacyclopentanes were also found undergoing the same addition reaction with aldehydes.

In addition, the structure of a zirconacyclopentane containing $\text{Zr}(\text{C}_4\text{H}_8)$ has been characterized by single crystal X-ray analysis. Results are described in the third section of this chapter.

Scheme 1



Scheme 2



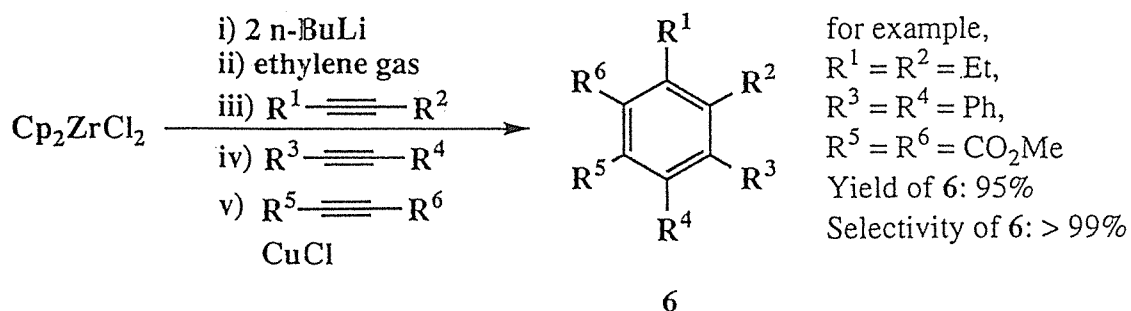
Chapter 3

Highly Selective Formation of Benzene Derivatives from Three Different Alkynes

Formation of benzene derivatives by cyclotrimerization of alkynes in the presence of transition metal complexes has been extensively and intensively studied. However, this chemistry is still of great current interest, since there is a crucial problem concerning regio- and chemo-selectivity of the cycloaddition reaction of different alkynes. In this chapter a selective one-pot aromatization reaction of three different alkynes is reported. Benzene derivatives 6 are formed selectively and with high yields by the cycloaddition reaction of zirconacyclopentadienes 3 with a third alkyne in the presence of CuCl (Scheme 3). Selective formation of 3 (as described previously in *Chapter 2*)

and then transmetalation of Zr-C bonds for Cu-C bonds are the key steps.

Scheme 3

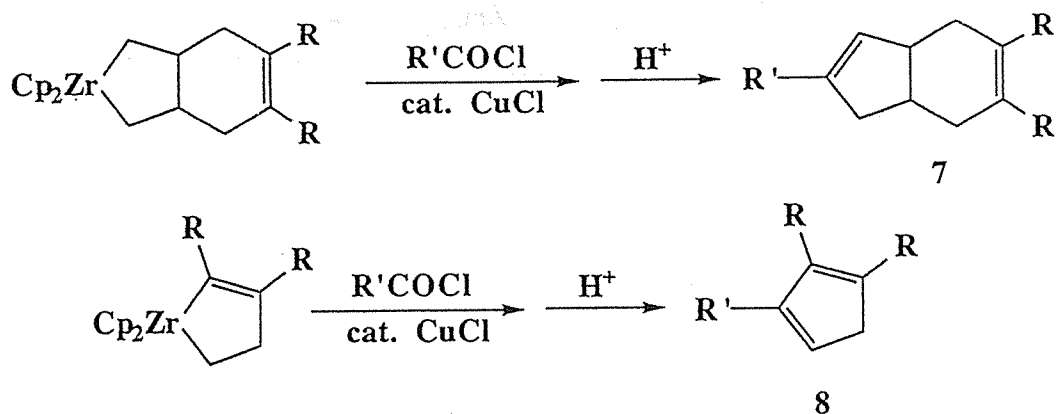


Chapter 4

Reaction of Zirconacyclopentane and Zirconacyclopentene with Acid Chloride in the Presence of CuCl: Formation of Five-membered Carbocyclic Rings

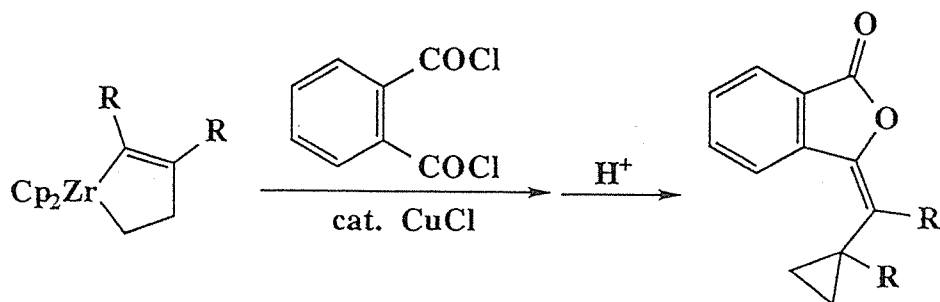
Zirconacyclopentanes reacted with RCOCl in the presence of a catalytic amount of CuCl to give cyclopentene derivatives 7 (Scheme 4). Similarly, zirconacyclopentenes reacted with RCOCl in the presence of a catalytic amount of CuCl to give cyclopentadiene derivatives 8 (Scheme 4). These reactions provide synthetic methods for the preparation of five-membered carbocyclic rings, which, especially cyclopentadiene derivatives, have been widely used for organometallic complexes as ligands.

Scheme 4



Reaction mechanisms, especially when the reaction of zirconacyclopentenes is concerned, are also discussed in this chapter. An intramolecular 1,4-addition is likely involved in the reaction of zirconacyclopentenes, as indicated by the formation of vinylcyclopropane derivatives (Scheme 5).

Scheme 5

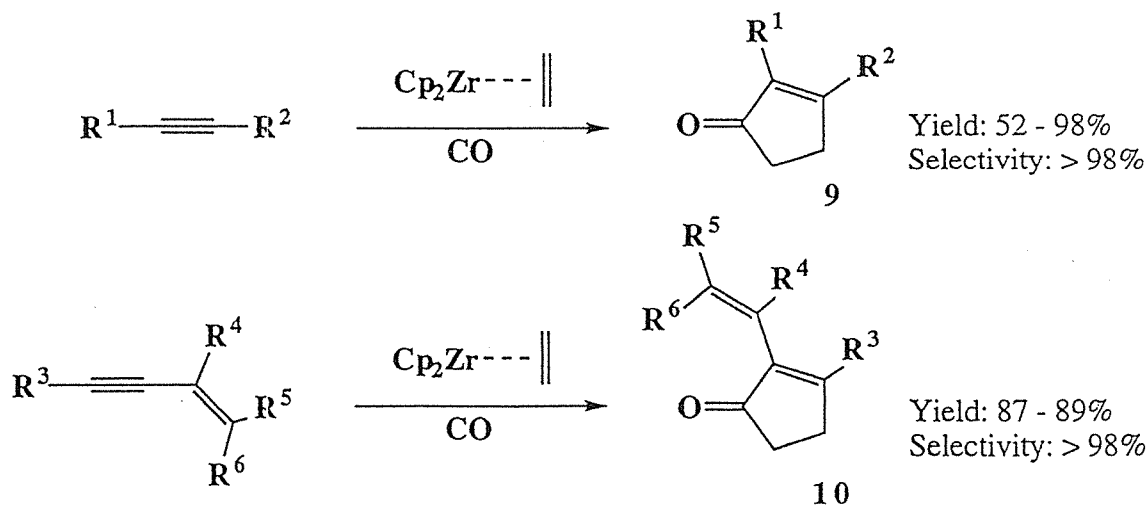


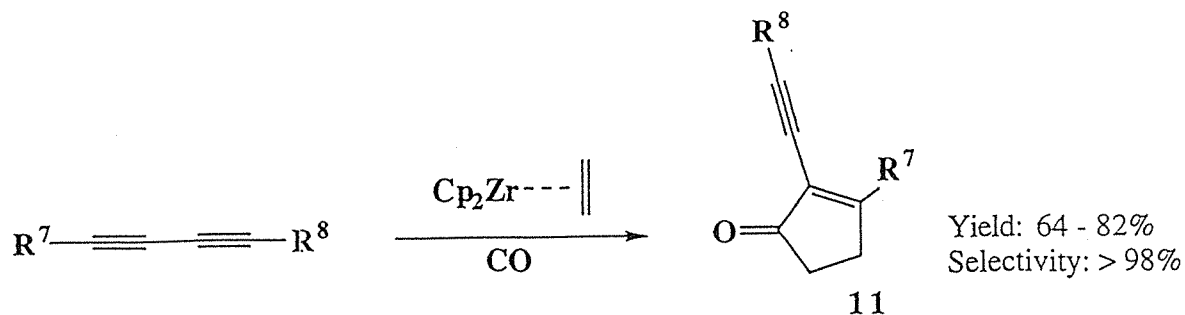
Chapter 5

Pauson-Khand Reaction: Zirconium Analogue. Preparation of α , β -Disubstituted Cyclopentenone by Intermolecular Coupling of an Alkyne, EtMgBr (or Ethylene) and CO

Cyclopentenone is one of the most important building blocks in organic synthesis. The Pauson-Khand reaction has been accepted as the most powerful method for cycloaddition of alkynes, alkenes, and carbon monoxide to form cyclopentenones using cobalt carbonyl complexes. However, when an intermolecular Pauson-Khand reaction using ethylene as one of the three components is carried out, high pressure and high temperature are normally required, furthermore, yield of cyclopentenone is usually very low. By taking advantage of the selective formation of zirconocyclopentenones **2**, functionalized α , β -substituted cyclopentenones of the type **9**, type **10**, and type **11** have been prepared in high yields and high selectivity by intermolecular cycloaddition of alkyne, ethylene, and CO, under a mild reaction condition (Scheme 6). In addition, bridged bicyclopentenones have been prepared by a similar procedure.

Scheme 6



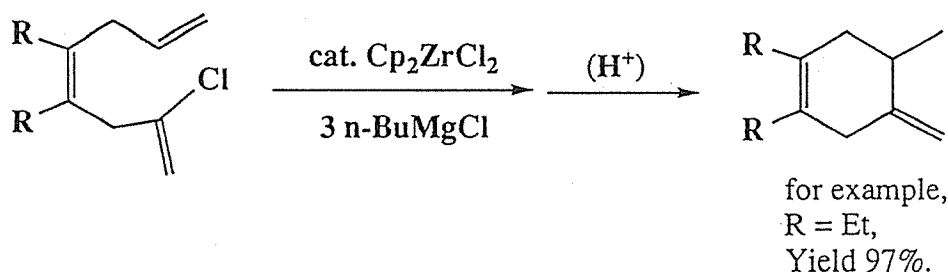


Chapter 6

Zirconocene Catalyzed or Mediated Vinylation-Cyclization Reaction

Intramolecular Heck reaction has been well known. This chapter describes the first example of an early transition metal catalyzed intramolecular cyclization reaction (Heck type). 2-Chloro-1,4,7-octatriene derivatives and 2-chloro-1,4,6-heptatriene derivatives cyclized in the presence of a catalytic amount of Cp_2ZrCl_2 and 3 equiv of $n\text{-BuMgCl}$ to give 4-methylene-5-methylcyclohexene derivatives and 4-methylene-3-methylcyclopentene derivatives, respectively, in good to high yields after treatment of the reaction mixture with HCl aq. (Scheme 7). Stoichiometric cyclization reaction of these compounds with Cp_2ZrBu_2 also gave the same products in high yields after hydrolysis. Mechanisms of this catalytic reaction are proposed.

Scheme 7



Chapter 7

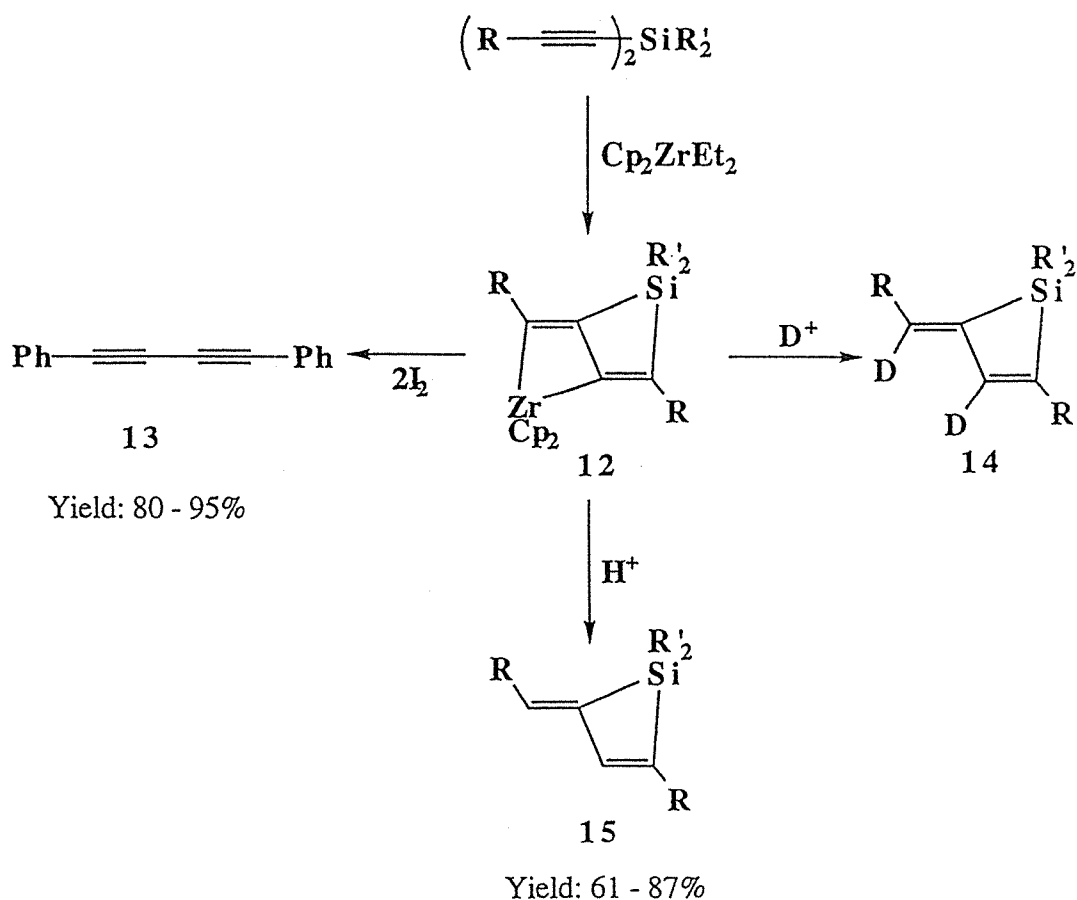
Zirconocene-Mediated Novel Rearrangement of Bis(alkynyl)silanes: Formation of *exo*-Alkylidene Silacyclobutene Derivatives

Carbon-carbon bond forming reactions from diorganometal compounds have been well known for transition metals, however, this type of reaction has been very rare for diorganosilicon compounds. Treatment of bis(phenylethynyl) diphenylsilane with zirconocene(II) species and iodine afforded 1,4-diphenyl-1,3-butadiyne 13 in 95% yield (Scheme 8). It has been made clear that an intermediate 12 of zirconacyclobutene moiety fused with a silacyclobutene ring

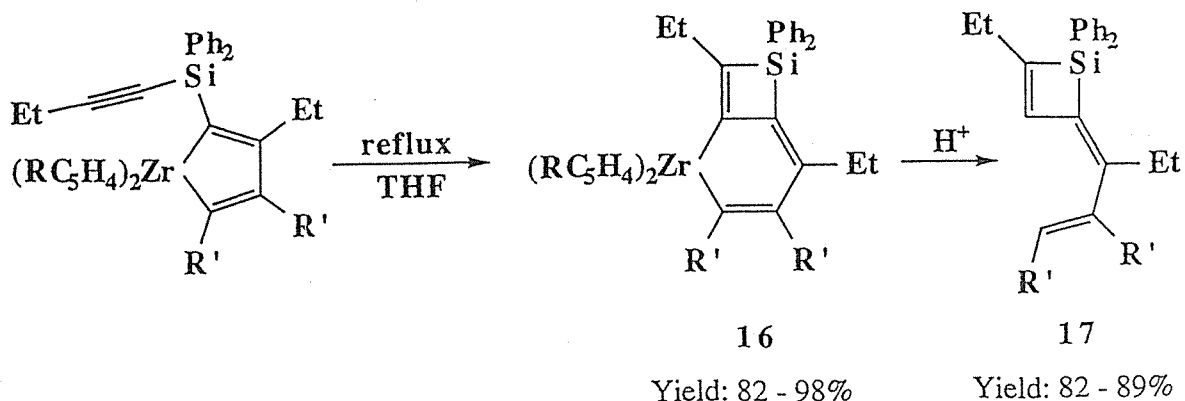
is formed. One of the four-four fused bicyclic intermediates 12 has been structurally confirmed by X-ray crystallography. Depending on substituents at the terminal of acetylenes of starting materials, *exo*-alkylidene silacyclobutenes with ethyl incorporation or without ethyl incorporation have been obtained in high yields after hydrolysis.

In the second section of this chapter, the author also reports the first example of an intramolecular C-C triple bond insertion into a zirconacyclopentadiene, then a novel rearrangement leading to the formation of the first example of a 1-zirconacyclohexa-2,4-diene compound fused with a moiety of silacyclobutene 16 (Scheme 9). Hydrolysis of 16 generated *exo*-alkylidene silacyclobutenes 17 in high yields. The structure of one of the intermediates 16 has been confirmed by X-ray crystallography.

Scheme 8



Scheme 9

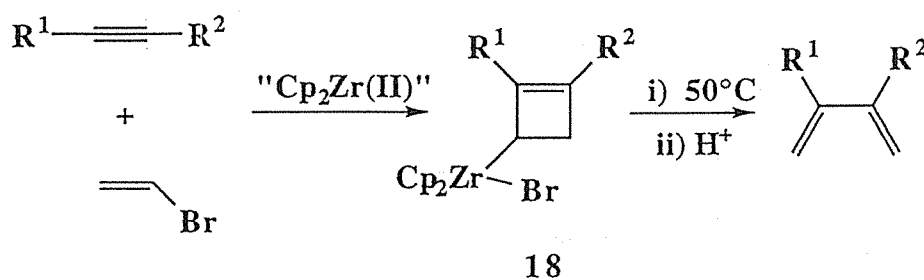


Chapter 8

Intermolecular Coupling of Alkyne with Vinyl Bromide *via* Carbon-Carbon Bond Cleavage and Skeletal Rearrangement

Modern organic chemistry is widely considered to have been born when formation of new carbon-carbon bonds was observed *via* carbon-carbon bond cleavage and rearrangement. Organometallic compounds or intermediates have been found to be very important for controlling selectivity of such rearrangement reactions. This chapter describes a novel intermolecular coupling reaction of alkynes with vinyl bromide *via* C-C bond activation and skeletal rearrangement (Scheme 10). The structure of the most important intermediate 18 has been confirmed by X-ray crystallography.

Scheme 10



審査結果の要旨

高選択的な炭素-炭素結合生成反応は実用的な有機合成反応を開発する上でもっとも重要な反応の一つである。本論文申請者の席振峰氏は低原子価ジルコノセン錯体を用いて二つの異なった不飽和結合を持つ基質を分子間で高選択的にカップリングさせ高収率で様々な非対称なジルコナサイクルを合成する手法を開発することに成功した。さらに、高選択的かつ高収率で得られたジルコナサイクルを出発物質として、いくつかの新しい高選択的な合成反応を開発した。また、2価ジルコノセン錯体を反応場として興味深い骨格変換反応も見出した。

例えば、3つのアセチレン類を遷移金属錯体によりカップリングさせベンゼン誘導体を合成する反応は広く知られているが、3つの異なるアセチレン類を分子間で選択的にカップリングさせ高収率でベンゼン誘導体を合成する実用的な方法は知られていなかった。その原因として2つの異なるアセチレン類を分子間で選択的にカップリングしてメタラシクロペンタジエンを合成することが難しいという事実が挙げられる。本研究では、 Cp_2ZrBu_2 およびエチレンガスを用いることによって、選択的なアセチレン-アセチレンクロスカップリング反応によるジルコナシクロペンタジエンの実用的な合成手法を開発することができた。この方法によって、加えたアセチレン類のホモカップリング生成物の副生を完璧に抑えることができた。そして、ジルコナシクロペンタジエンにCuClを添加することで3分子目のアセチレンを反応させ、選択的にベンゼン誘導体に導くことができた。この反応は高選択的、高収率でしかもone-potで3つの異なるアセチレン類を分子間でカップリングさせるのに成功した初めての例である。さらに本反応が95%以上の高い収率で進行している点は、今後の多様な合成反応への応用を行う上で非常に重要な成果であるといえる。また、カルボン酸の塩化物を用いると、五員環化合物が合成可能なことを示し、その高い合成反応への応用性を示している。ここで示された炭素-炭素結合の選択的な形成を一般化し、種々の合成反応に応用するためには、反応中間体の構造を解明することが必須となる。そこで、席振峰氏は、反応中間体の単離とその結晶構造の解明にまで研究範囲を広げ、種々の反応中間体の構造決定を行うことにも成功している。

こうした研究成果は、既に8報の論文(英文)としてまとめられており、本審査委員会では、席振峰氏の提出論文は学位を与えるに相応しいものとなっていると判定した。

面接による試験は、出願者に学位の論文の内容を約1時間で発表してもらい、その後、金属イオンの役割や反応機構を中心に1時間半にわたって質疑応答を行った。特に、本学位論文では高選択的な合成反応の開拓が主題となっており、研究戦略などについても活発な論議が展開された。

発表は論文の章立てに従って良く準備された資料を使って日本語で行われたが、質疑は英語と日本語の両者で行われ、研究内容や関連する分野についての質問にも適切に答えていた。細かな論議では、日本語よりは英語の方がやり易いようであったが、日本語・英語に関する語学力に何等問題はないと判定した。

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