

学 位 論 文 題 名

Reaction of Zirconacycles with Bi-functional
Compounds *via* Transmetalation to Cu, Zn and Li

(ジルコナサイクロの Cu, Zn, Li へのトランスメタル化を利用した
2つの反応サイトをもつ化合物との反応)

学位論文内容の要旨

Ph.D. thesis described by Mr. Duan Zheng consists of 5 chapters, which focused on the development of novel synthetic method using transmetalation of zirconacycles to Cu, Zn and Li. The contents of 5 chapters are the following: (i) A brief review of transmetalation reactions of zirconacycles (Chapter 1). (ii) Transmetalation of zirconacyclopentadienes to Zn (Chapter 2). (iii) Reaction of zirconacyclopentadienes with bi-functional compounds (Chapter 3). (iv) Stepwise activation of the two zirconium-carbon bonds by combination of transmetalation to Li and Cu (Chapter 4). (v) Summary of this thesis (Chapter 5). The details about chapter 2 to 4 are shown below.

Chapter 2. Transmetalation of zirconacycles to zinc

It is known that zirconacyclopentadienes or zirconaindenes reacted with allyl halides in the presence of CuCl to give the double allylation products. However, in the presence 2 equiv. of ZnCl₂ and a catalytic amount of Pd(PPh₃)₄, zirconacyclopentadienes reacted with allyl halides to give the monoallylation products. The formation of the double allylation product was not observed. Interestingly, when an unsymmetrical zirconacyclopentadiene that was prepared from diphenylacetylene and 3-hexyne, was employed, the monoallylation selectively took place at the carbon with a phenyl substituent. In the case of zirconaindenes, however, the reactions with allyl halides gave ring-closing products such as naphthalene derivatives regioselectively. This is in sharp contrast to the double allylation reaction in the presence of CuCl. By transmetalation to Zn, zirconacyclopentadienes also reacted with highly activated alkenes, such as benzalmalononitrile, to afford the mono-addition products.

Chapter 3. Reaction of zirconacyclopentadienes with bi-functional compounds

Transmetalation to Cu is one efficient way for activation of zirconacyclopentadiene. It can easily transform zirconacyclopentadiene to a dicopper compound, which has higher reactivity. This dimetallic intermediate can react with a bi-functional compound to form a cyclic compound.

Cyclopentadienes or fulvenes are important intermediates in organic synthesis and useful ligands in catalysis. Zirconacyclopentadienes reacted with benzal halides in

the presence of CuCl and dimethylpropyleneurea (DMPU) to give penta-substituted cyclopentadienes in moderate to good yields. Treatment of zirconacyclopentadienes with 1,1-dibromo-1-alken-3-yne and 1,1-dibromo-1, 3-alkadiene afforded the fulvene derivatives in good yields.

During the course of the study, 2-iodobenzyl chlorides or 2-iodobenzoyl chlorides were chosen as bi-functional compounds. They were useful three carbon building blocks for the [4+3] coupling with zirconacyclopentadienes. These reactions gave the benzocycloheptene and benzocycloheptenone derivatives in moderate to high yields, respectively.

The reactions described in previous are the combination of coupling reactions. It is interesting to investigate the combination of coupling with carbometalation reactions. Since the Cu mediated cycloaddition of zirconacyclopentadienes to activated alkynes has been realized, intramolecular reaction of zirconacyclopentadienes with unactivated alkynes was investigated. The *o*-iodoalkynylbenzene was chosen for this purpose. The reaction of zirconacyclopentadienes with *o*-iodoalkynylbenzene afforded benzocycloheptene derivatives in good yields. In order to verify the structure of the carbometalation intermediate and the configuration of the final product, further reaction of the vinyl copper intermediate with allyl chloride or benzoyl chloride was investigated. The corresponding allylated or acylated product was obtained. The acylated compound was characterized by X-ray analysis and it clearly shows the benzoyl group is in the same side of an Et group, which suggested the carbocupration proceeded in a *syn* manner.

Chapter 4. Mixed transmetalation of zirconacyclopentadiene to lithium and copper

It is known that, in the presence of CuCl, zirconacyclopentadienes reacted with propargyl halides by S_N2' reaction to afford benzene derivatives. In the case of zirconacyclopentanes, reactions with propargyl halides proceeded similarly to afford the diallenes. No propargylation reaction was found in any cases. It is interesting to note that the propargylation reaction was performed by transmetalation to Li. Addition of 1.1 equiv of MeLi to a zirconacyclopentadiene solution at -78°C , followed by the reaction with propargyl bromide at the same temperature, gave the monopropargylation product after hydrolysis. Deuterolysis of the reaction mixture gave a monodeuterated propargylation compound.

Zirconacyclopentadiene has two Zr-C bonds. Selective activation of these bonds is attractive and has synthetic potential. During the course of the study on monopropargylation of zirconacyclopentadienes by transmetalation to Li, deuterolysis of the intermediate afforded the mono-deuterated product. This result suggests one Zr-C bond still remained. Based on this result, activation of this Zr-C bond was carried out for the carbometalation reaction by transmetalation to Cu. Interestingly, the isolated products were penta-substituted benzene derivatives. This is because the cyclic exo-olefin products easily isomerized into benzene derivatives.

学位論文審査の要旨

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段 征君の学位論文は5章からなり、ジルコナサイクルのトランスメタル化とそれを利用した合成手法の開発がまとめられている。

第1章はイントロダクションでこれまでの既知のジルコナサイクルの化学が述べられている。第2章はジルコナサイクルを Zn にトランスメタル化させ、パラジウム触媒存在下アリルハライドと反応させるとモノアリレーションが進行することを見い出している。またジルコナサイクルとしてジルコナインデンを用いるとナフタレン誘導体が選択的に生成することを報告している。これらモノアリレーション反応とインデン生成の違いについて検討を行っている。

第3章ではジルコナシクロペンタジエンを塩化銅を用いて銅金属上へトランスメタル化させ、1、1-ジハロアルケン類との反応によるフルベン合成反応を開発すると共に、2-ヨードベンジルハライドや2-ヨードベンゾイルハライドなどとの4+3カップリング反応を利用して、7員環化合物の新規合成手法の開発に成功している。さらに炭素-炭素3重結合へのカルボメタレーション反応を組み合わせるため、2-ヨードアルキニルベンゼンとの反応を行い、ベンゾシクロヘプタジエン誘導体へ導いている。

第4章ではジルコナシクロペンタジエンのリチウム試薬との反応で、リチウムへトランスメタル化することにより、プロパルギルハライドの炭素

ーハライド結合への反応を実現した。従来のジルコナシクロペンタジエンとプロパルギルハライドとの反応では銅へのトランスメタル化反応が用いられていたため、プロパルギルハライドの炭素－炭素3重結合への反応が選択的に進行してアレン類を与えていたが、リチウム試薬を用いることで反応部位を選択的にかえ、選択的なプロパルギル化に成功している。これは有機金属試薬の硬さ、柔らかさで説明することができる。段氏はさらにリチウムを使ってプロパルギル化した反応生成物がまだ1つの炭素－金属結合を持つことに目をつけ、銅塩を加えることにより、ベンゼン誘導体に導いている。

第5章は全体のまとめが書かれている。

このように段氏の博士論文はジルコナサイクルの新しいトランスメタル化を開発すると共にそれを利用した有機合成手法を展開したもので、その新規性、質、量とも博士の学位として十分であると判断された。