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Preparation of Benzocycloheptene Derivatives from Zirconacyclopentadienes

Tamotsu Takahashi,* Wen-Hua Sun, Zheng Duan, and Baojian Shen

Catalysis Research Center and Graduate School of Pharmaceutical Sciences, Hokkaido University, and CREST, Science and Technology Corporation (JST), Sapporo 060-0811, Japan

tamotsu@cat.hokudai.ac.jp

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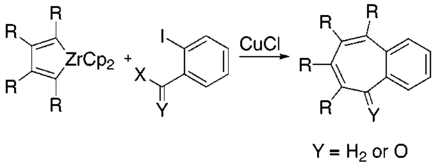
ABSTRACT

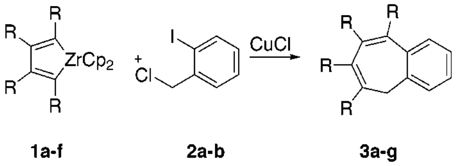


Reaction of zirconacyclopentadienes with 2-iodobenzyl halide and 2-iodobenzoyl halide afforded benzocycloheptene derivatives and benzocycloheptenone derivatives in good to high yields.

Benzocycloheptene derivatives are attractive in theoretical chemistry,[1] pharmaceutical sciences,[2] and coordination chemistry.[3] They have been prepared by several methods such as the enlargement of six-membered rings[4] and cyclization reactions.[5] However, preparation of benzocycloheptenes having substituted seven-membered rings has been very limited. In this paper we would like to report a novel type of [4 + 3] coupling reaction of zirconacyclopentadienes with 2-iodobenzyl or 2-iodobenzoyl halides.

Zirconacyclopentadienes are versatile intermediates that can be easily prepared symmetrically or unsymmetrically from alkynes or diynes. Recently we have reported the [4 + 4], [4 + 5], and [4 + 2] coupling reaction of zirconacyclopentadienes with bis(bromomethyl)arenes or a dihalobenzene derivative, giving eight-, nine-, or six-membered ring compounds.[6,7] During the course of our study, we found that 2-iodobenzyl or 2-iodobenzoyl halides can be a useful three-carbon unit for the [4 + 3] coupling of zirconacyclopentadienes as shown in Scheme 1.

Scheme 1



Typically, zirconacyclopentadienes were prepared by coupling of two alkynes with Cp_2ZrR_2 (R = Bu, Et, or Ph)

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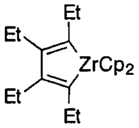
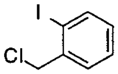
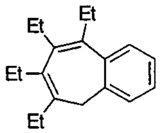
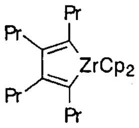
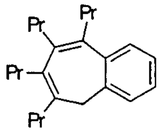
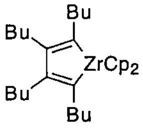
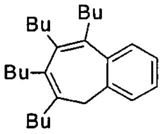
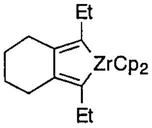
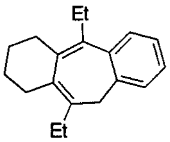
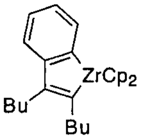
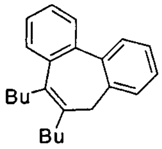
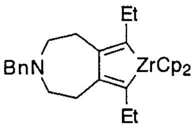
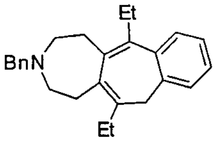
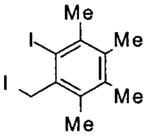
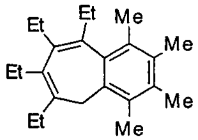
Table 1. Reaction of Zirconacyclopentadienes with 2-Iodobenzyl Halide

Zirconacyclopentadiene	2-Iodobenzyl halide	Product	Yield/%*
 **1a**	 **2a**	 **3a**	89 (70)
 **1b**	**2a**	 **3b**	92 (78)
 **1c**	**2a**	 **3c**	93 (74)
 **1d**	**2a**	 **3d**	93 (74)
 **1e**	**2a**	 **3e**	50 (41)
 **1f**	**2a**	 **3f**	54 (29)
1a	 **2b**	 **3g**	- (23)

* GC yield. Isolated yields are given in parentheses.

according to the literature.[8] To a solution of tetraethylzirconacyclopentadiene **1a** (1 mmol) prepared from Cp_2ZrBu_2 (1.2 mmol) and 3-hexyne (2 mmol) in THF was added 2-iodobenzyl halide **2a** (1 mmol). The reaction was carried out at 50 °C in the presence of a stoichiometric amount of CuCl (2 mmol) and dimethylpropyleneurea (DMPU, 2.5 mmol). After 1 h, the desired product, 1,2,3,4-tetraethylbenzoheptene, **3a**, was obtained in 70% yield after purification by column chromatography. Results are summarized in Table 1.

It was found that zirconacyclopentadienes **1a**−**d**, either monocyclic or bicyclic, underwent the reaction well and gave the corresponding products in high yields. Heterobicyclic zirconacyclopentadiene **1f**[9] gave the product **3f**. However, the reaction did not proceed for the zirconacyclopentadienes with aryl or silyl substituents in the α-position.

It is noteworthy that in the case of a zirconaindene **1e**, which has a benzene moiety in the zirconacycle, the reaction

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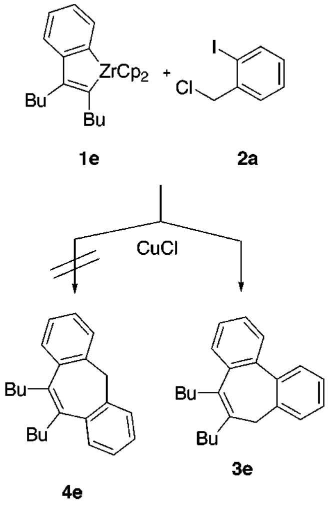
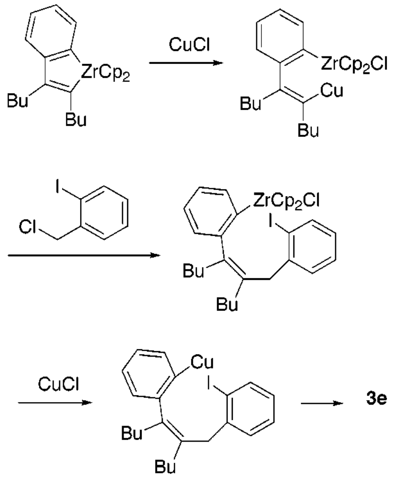
[9] Buchwald, D. L.; Watson, B. T.; Huffman, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 7411−7413 and references therein.

Scheme 2



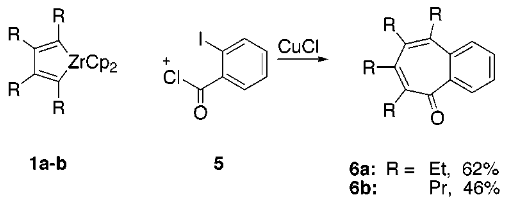
proceeded, and it is in contrast to the case with phenyl-substituted zirconacyclopentadienes. Reaction of the unsymmetrical zirconaindene with **2a** might afford a mixture of two isomers, **3e** and **4e**. As a matter of fact, only **3e** was obtained as shown in Scheme 2. A plausible mechanism of the reaction of **1e** with **2a** is shown in Scheme 3. We have reported the transmetalation of zirconacyclopentadienes or zirconaindenes to copper.[10] An alkyl-substituted sp^2 carbon attached to zirconium reacts with CuCl faster than the aryl carbon attached to zirconium. The more reactive carbon attached to copper reacts with the benzyl carbon of **2a** first. Then, intramolecular coupling of the arylzirconium moiety with the aryl iodide moiety of **2a** proceeds in the presence of CuCl. This mechanism rationalizes the selective formation of **3e**. As shown in Table 1, 2-iodo-3,4,5,6-tetramethylbenzyliodide can be used for the formation of benzocycloheptenes, although the isolated yield was only 23%.

Scheme 3



Similar [4 + 3] coupling reaction of zirconacyclopentadiene was observed in the reaction with 2-iodobenzoyl chloride **5**. Under the same conditions the benzocycloheptenone derivatives **6a,b** were obtained as shown in Scheme 4.

Scheme 4



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Supporting Information Available: Characterization and ^{1}H and ^{13}C NMR spectra for **3a−g** and **6a,b**. This material is available free of charge via the Internet at http://pubs.acs.org.

OL005533R

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