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# Selective synthesis of α-methylenyl zirconacyclopentene via cross-coupling of alkyne and allene

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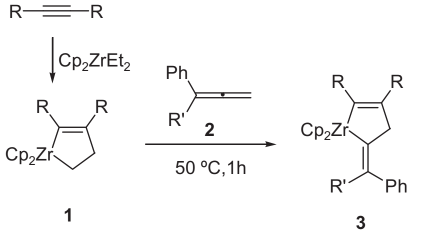
ABSTRACT

α-Methylenyl zirconacyclopentenes are synthesized regio- and stereoselectively via reductive intermolecular cross-coupling of alkynes and allenes promoted by zirconocene species ‘$Cp_2Zr$’. An interesting reductive intramolecular coupling of the α-methylenyl zirconacyclopentene has been observed in the presence of DMAD/CuCl, resulting in the generation of cyclobutene with an exocyclic double bond. Polysubstituted 1,4-dienes can be given with high selectivity and good yields.

Zirconacycle has emerged as a highly effective reagent in various organic synthetic protocols and its chemistry has been extensively explored.[1] Besides the common zirconacyclopentane, ziconacyclopentene and zirconacyclopentadiene, some functionalized zirconacycles have become more attractive in the last few decades. Xi and co-workers synthesized a series of zirconacyclo-silacyclo fused-ring intermediates which showed efficient activity in the formation of some ring skeletons.[2] Xie and co-workers developed the zirconacycles incorporating a carboranyl unit for the preparation of a range of functionalized carborane derivatives due to the rich chemistry of the zirconacycles.[3] Liu and co-workers Please check the edit of the word ‘conversion’ in the sentence ‘Liu and...formation’. and correct if necessary. reported on the preparation of α-alkynylzirconacyclopentenes[4a] and α-alkenyl zirconacyclopentenes[4b] giving the selectively chemical conversion to carbon–carbon bond formation. The functionalized zirconacycle exhibited various reactivities.

On the other hand, the exocylic carbon–carbon double bond is an important building block in synthetic chemistry,[6] which could be given by the transition metal-promoted cross-coupling of allene and another π-system.[7] Compared with acyclic polysubstituted alkenes, the regio- and stereochemistry of exocyclic double bonds are more controllable owing to the efficient contribution of the cyclic skeleton.[6a,8] Therefore, the synthesis of methylenyl substituted metallacycle with full control of both the regio- and stereochemistry should be a significant strategy. In this case, allene, which has attached much attention as a three-carbon unit and shown unique reactivity in numerous protocols,[2,5] has acted as an effective substrate to result in the generation of the exocylic double bond. Urabe and co-workers reported on the titanium alkoxide-mediated intermolecular coupling of functionalized allenes and alkynes affording 1,4-enynes.[9] Micalizio and co-workers investigated the titanium-mediated cross-coupling of allenic alcohols with alkynes which underwent divergent pathways to provide 1,4-dienes or cross conjugated trienes depending on the substitution of allenes.[10] However, although the structures of some zirconacyles involving allene had been studied, their synthetic applications are rare owing to the poor selectivity in the cyclization.[11] Herein, we would like to exhibit the selective formation of α-methylenyl zirconacyclopentenes via the cross-coupling of the alkyne[12] and allene mediated by the zirconocene (II) species. (Scheme 1).

A typical procedure is as follows. To a THF solution of zirconacyclopentene **1**, prepared in situ from Takahashi reagent and



**Scheme 1.** Synthesis of α-methylenyl zirconacyclopentene **3**.

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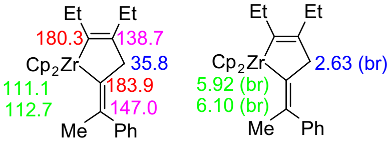
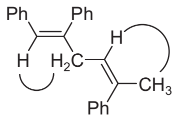


**3a**

**Figure 1.** In situ NMR data of **3a**.



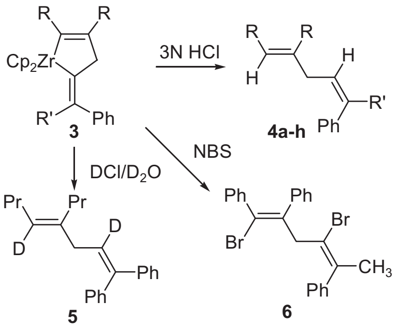
**4d**

**Figure 2.** NOE of **4d**.

alkyne,[1c–e] was added 1 equiv of allene **2** at 0 °C. The reaction mixture was then stirred for further 1 h at 50 °C to afford the α-methylenyl zirconacyclopentene **3** which was verified by in situ NMR of the reaction mixture of **3a** (R = Et, R′ = Me, 79% NMR yield using dibromomethane as the internal standard). In the case of $^{13}$C NMR (Fig. 1), there was a singlet at 111.12 and 112.73 ppm assignable to the two Cp rings. The two sp$^2$ carbon attached zirconium atom appeared characteristically at 180.32 and 183.87, respectively. The sp$^2$ carbon attached to the methyl group appeared at 147.02 ppm owing to the deshielding effect of the phenyl group as well as the coordination of the external carbon–carbon double bond to the zirconium center. The broad band of 2.63 in $^1$H NMR assigned a $CH_2$ involved in a metallacycle.

Hydrolysis of the reaction mixture with aqueous 3 N HCl afforded **4a–h** in excellent yield (Scheme 2, Table 1).

The stereochemical assignment of **3** is based on the NOESY spectrum of **4d** (entry 4). The NOE of 1H-$CH_2$ and 4H-$CH_3$ points to a 1*Z*,4*Z* framework characteristic, respectively (Fig. 2), which indicate the *E*-configuration of the exocyclic double bond in the intermediate **3d**. Besides the configuration of the double bond inside it zirconacyclopentene **3** has been restricted by the ring skeleton, the exocyclic double bonds of **3a–d** have been generated highly stereoselectively in this reductive cross-coupling. All the ratios of the stereoisomers of **4a–d** is above 99% based on the $^1$H NMR of the mixture of the reaction.



**Scheme 2.** Reaction of **3** with electrophiles.

**Table 1**
Quenching of α-methylenyl zirconacyclopentene **3** with electrophiles

| Entry | 3 | | El | Yield of **4–6**[a] (%) |
|---|---|---|---|---|
| | R | R′ | | |
| 1 | Et | $CH_3$ (**3a**) | $H^+$ | 90 (44) (**4a**) |
| 2 | *n*-Pr | $CH_3$ (**3b**) | $H^+$ | 92 (85) (**4b**) |
| 3 | *n*-Bu | $CH_3$ (**3c**) | $H^+$ | 77 (69) (**4c**) |
| 4 | Ph | $CH_3$ (**3d**) | $H^+$ | 84[b] (45) (**4d**) |
| 5 | Et | Ph (**3e**) | $H^+$ | 96 (95) (**4e**) |
| 6 | *n*-Pr | Ph (**3f**) | $H^+$ | 95 (92) (**4f**) |
| 7 | *n*-Bu | Ph (**3g**) | $H^+$ | 74 (64) (**4g**) |
| 8 | Ph | Ph (**3h**) | $H^+$ | 91[b] (83) (**4h**) |
| 9 | *n*-Pr | Ph (**3f**) | $D^+$ | 87 (71) (**5**) |
| 10 | Ph | $CH_3$ (**3d**) | $Br^+$ | 70 (65) (**6**) |

[a] GC yields. Isolated yields are given in the parentheses.
[b] NMR yields using dibromomethane as internal standard.

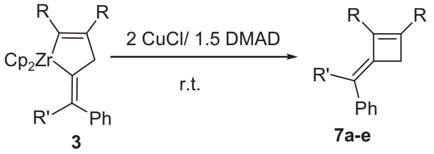
Interestingly, when the in situ prepared α-methylenyl zirconacyclopentene **3** was treated with 1.5 equiv of DMAD in the presence of 2 equiv of CuCl at 0 °C in THF, 3-methylenylcyclobuta-1-ene derivatives **7** were afforded during which the copper mirror could be observed (Table 2).[13] No NOE was observed between the methyl and $CH_2$ in the cyclobuta-1-ene **7a**, which indicated the *E*-configuration of the exocylic double bond (entry 1). Polymerization during the reaction and purification by column chromatography resulted in lower isolated yields (entries 1 and 5, Table 2).

Transmetallation of Zr–C to Cu–C bond has been proven to be effective for activating the Zr–C bond.[14] The dicopper-transmetallation product **8** of the zirconacycle **3** is reasonably stable and can not undergo the common intramolecular coupling even when heated at 50 °C in THF for 3 h (Scheme 3). The addition of the DMAD resulted in the formation of the cyclobutene species **7** and the DMAD skeleton was not detected in any of the cases, which indicated that the DMAD acted as an oxidant in this conversion.[15] Therefore the cooperation of the DMAD and CuCl worked in this reaction.

It was reported that the zirconacyclopentadiene, containing tow conjugative $C^{sp2}$-Zr bonds, underwent a cycloaddition with DMAD in the presence of CuCl to produce benzene derivatives.[16] In the case of α-methylenyl zirconacyclopentene **3**, the exocyclic double bond leads to an unconjugative zirconacyclopentene, based on which the chemistry of **3** absolutely differ from that of the zirconacyclopentadiene.

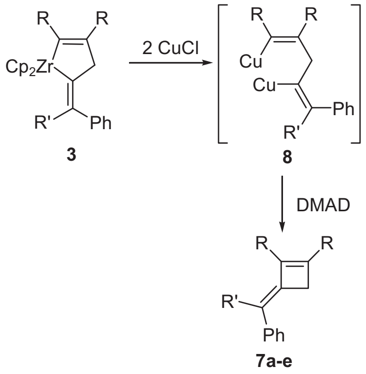
In conclusion, we have demonstrated the efficient generation of α-methylenyl zirconacyclopentene species via an intermolecular reductive cross-coupling regio- and stereoselectively, which can readily give the polysubstituted 1,4-diene derivatives in high yield. Also, the methylenyl cyclobutene can be obtained from the intramolecular reductive cyclization of the active zirconocene species. In addition, the internal and external carbon–carbon double bond in the α-methylenyl zirconacyclopentene will provide the poten-

**Table 2**
Formation of methylenyl cyclobutene **7**



| Entry | 3 | | Product **7** | Yield[a] (%) |
|---|---|---|---|---|
| | R | R′ | | |
| 1 | Ph | $CH_3$ (**3d**) | **7a**[b] | 71[c] (43) |
| 2 | Et | Ph (**3e**) | **7b** | 91 (63) |
| 3 | *n*-Pr | Ph (**3f**) | **7c** | 89 (64) |
| 4 | *n*-Bu | Ph (**3g**) | **7d** | 80 (73) |
| 5 | Ph | Ph (**3h**) | **7e** | 69[c] (45) |

[a] GC yields. Isolated yields are given in the parentheses.
[b] Ratio of *E*/*Z* of exocyclic double bond is 95:5.
[c] NMR yields using dibromomethane as internal standard.



**Scheme 3.** Formation of methylenylcyclobutene **7**.

tial selectivity in further conversion. Further investigation into the reactivity of α-methylenyl zirconacyclopentene is in progress.

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## Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.06.134.

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