



## Highly Substituted Enyne Formation by Coupling Reaction of Alkenylzirconium Compounds with Alkynyl Halides

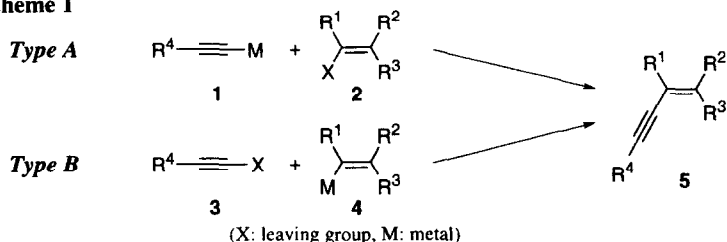
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**Abstract:** Alkenylzirconium compounds, which were prepared by carbozirconation or hydrozirconation of alkynes, reacted with alkynyl halides in the presence of CuCl to give highly substituted 1,3-enynes in good yields. This reaction was done conveniently in one-pot from alkynes. © 1997 Elsevier Science Ltd.

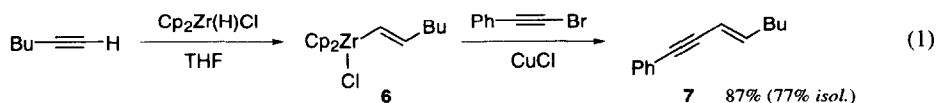
Conjugated enynes are of great interest in organic synthesis.<sup>1,2</sup> Recent organometallic chemistry has demonstrated stereoselective formation of 1,3-enynes.<sup>3</sup> Two major coupling patterns are shown in Scheme 1 which involves i) a coupling of an alkynyl metal **1** with an alkenyl halide **2** (*Type A*) and, conversely, ii) a coupling of an alkynyl halide **3** with an alkenyl metal **4** (*Type B*) to give 1,3-enynes **5**. However, the crucial problem lies in the limitation of general stereoselective synthetic methods of *highly* substituted alkenyl compounds **2** or **4**.

Scheme 1

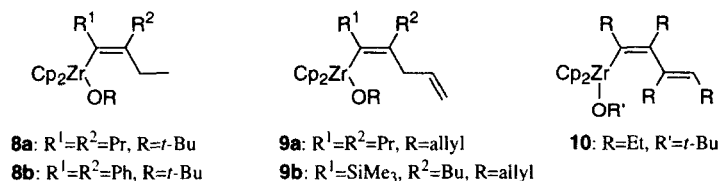


We have recently reported the formation of alkenylzirconium compounds (**4** where M=Zr, R<sup>3</sup>≠H) by carbozirconation reactions,<sup>4,5</sup> and also the coupling reaction between the *sp*<sup>2</sup> carbon centers of **4** and aryl or alkenyl iodides mediated by CuCl with a catalytic amount of Pd(PPh<sub>3</sub>)<sub>4</sub>.<sup>6</sup> We would like to report herein the coupling reaction of alkenylzirconium compounds with alkynyl halides which gives *highly* substituted enynes **5** according to the *Type B* pattern.

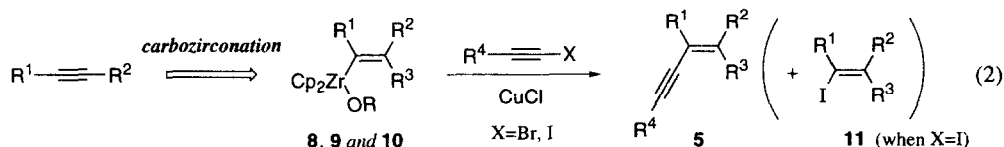
Phenylethynyl bromide reacted with alkenylzirconium compound **6**, prepared by hydrozirconation of 1-hexyne, in the presence of CuCl to give *disubstituted* enyne **7** in 87% yield (eq. 1).



For preparation of *trisubstituted* enynes where  $R^1=H$ , carbocupration<sup>7</sup> or carboalumination<sup>8</sup> of terminal alkynes gave alkenylmetal species **4**, and the subsequent coupling reaction with alkynyl halides was successful. However, because of the limited examples of carbometallation of internal alkynes,<sup>1b</sup> the preparation of *tetrasubstituted* enynes by coupling between *sp*<sup>2</sup>- and *sp*-carbons has not been systematically studied, to the best of our knowledge.

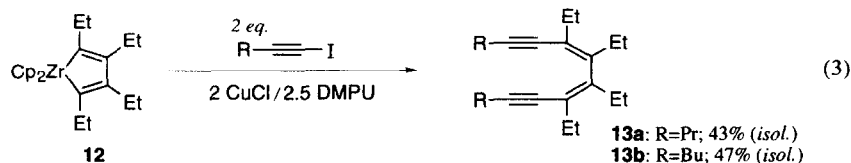


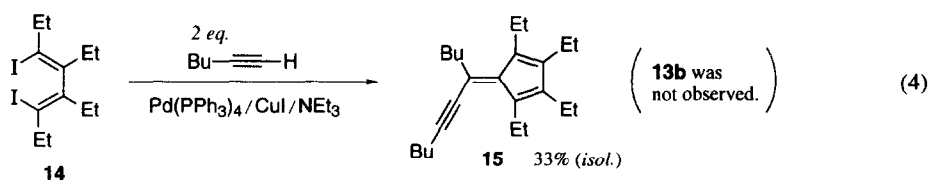
Alkenylzirconium compounds **8a** and **8b** were prepared from alcoholysis of zirconacyclopentenes by *t*-BuOH,<sup>4</sup> and **9a** and **9b** were prepared by the reaction of zirconacyclopentenes with diallyl ether.<sup>5a,b</sup> Dienylzirconium compound **10** was prepared from a zirconacyclopentadiene by the treatment of *t*-BuOH for 12 h at room temperature. We found that alkenylzirconium complexes of types **8**, **9** and **10** efficiently reacted with alkynyl halides in the presence of CuCl to give fully substituted 1,3-enynes **5** ( $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4 \neq H$ ) in a well-stereodefined manner (eq. 2). The reaction proceeded in the absence of a palladium catalyst in contrast to the arylation reaction.<sup>6,7</sup> When alkynyl iodides were employed, the products were contaminated typically with 10–20% of alkenyl iodides **11**, which were not readily separable. On the other hand, the use of alkynyl bromide afforded enynes in high yields. Formation of alkenyl bromides was not observed.



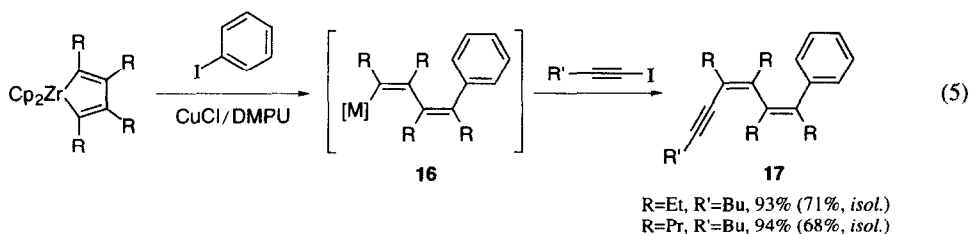
As shown in Table 1, the yields were good to high. In all cases, alkenylalkoxyzirconium compounds were treated by an equimolar amount of CuCl and alkynyl bromide at room temperature for 3 h. The reactions were carried out under an inert gas atmosphere, and the reaction mixtures were analyzed by GC. All the products were purified by flash column chromatography on silica gel.

This coupling method was also applied to zirconacyclopentadiene **12**. When **12** was treated with CuCl (2.0 equiv.) and DMPU (2.5 equiv.),<sup>9</sup> it reacted with two equivalents of alkynyl iodide to give diene-diyne compounds **13** (eq. 3). However, when the frequently used CuI/Pd/amine condition<sup>10,11</sup> was applied to diiododiene **14** and 1-hexyne, not **13b** but a fulvene derivative **15**<sup>12</sup> was obtained in a low yield (eq. 4).





Furthermore, a combination of two successive coupling reactions gave unsymmetrically substituted diene derivatives from symmetrical zirconacyclopentadienes. The first coupling reaction proceeded with aryl iodide in the presence of CuCl and DMPU, under the same conditions as we reported,<sup>9</sup> to give monoarylated compound **16** as an intermediate. Interestingly, no diarylation products were obtained at this stage even when an excess amount of iodobenzene was used. Since one metal-carbon bond remained on the intermediate **16**, the second coupling was successful with an alkynyl iodide to afford 3,5-dien-1-yne compound **17** in one-pot in excellent yields (eq. 5). The use of alkynyl iodide did not give iodination products of **16**.



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**Table 1.** Formation of 1,3-Enynes<sup>a</sup>

Alkenylzirconium	R <sup>4</sup> —C≡C—X	Products	Yields, % GC (Isolated)
<b>8a</b>	Bu—C≡C—Br		83 (76)
<b>8a</b>	Bu—C≡C—I		68 <sup>b</sup>
<b>8a</b>	Ph—C≡C—Br		81 (50)
<b>8b</b>	Ph—C≡C—Br		64 (49)
<b>9a</b>	Bu—C≡C—Br		91 (67)
<b>9a</b>	Ph—C≡C—Br		87 (65)
<b>9b</b>	Bu—C≡C—Br		88 (74)
<b>10</b>	Bu—C≡C—Br		66 (54)

<sup>a</sup> Conditions: **8**, **9** or **10** (1.0 eq.), CuCl (1.0 eq.) and alkynyl halide (1.0 eq.), room temp., 3 h.

<sup>b</sup> (*E*)-5-Ethyl-4-iodo-4-octene was formed in 11% yield as a by-product and was not separable from the desired product by silica gel column chromatography.

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