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Coupling Reaction of Alkenylzirconocenes with Aryl or Alkenyl Iodides in the Presence of CuCl/Pd(PPh$_3$)$_4$

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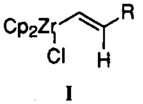
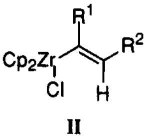
Abstract: Trisubstituted alkenylalkoxyzirconocenes which have been prepared from carbozirconation reactions of internal alkynes via zirconacyclopentenes reacted with aryl or alkenyl iodides in the presence of CuCl and a catalytic amount of Pd(PPh$_3$)$_4$ to give coupling products.

Alkenylzirconocenes have been useful intermediates for preparation of disubstituted or trisubstituted stereodefined alkenes,[1,2] since alkenylzirconocenes of type I and II are easily obtained by hydrozirconation reactions of alkynes,[3] or by oxidative addition of alkenyl halides to zirconocene.[4] Further coupling reactions of these alkenylzirconocenes with aryl iodides or alkenyl iodides have been developed by Negishi using Pd(PPh$_3$)$_4$ (for type I)[2a] and ZnCl$_2$/Pd(PPh$_3$)$_4$ (for type II)[5] as the catalyst systems. Recently, we have reported a novel preparative method of alkenylalkoxyzirconocenes (type III: **1a**-**1c**) and alkenylbromozirconocenes (**1d**) by various carbozirconation reactions of internal alkynes via zirconacyclopentenes. The reactions of zirconacyclopentenes with alcohols, allyl ethers, vinyl ethers and 4-bromo-1-butene gave ethylzirconation (**1a**),[6] allylzirconation (**1b**),[7] vinylzirconation (**1c**)[8] and cyclopropylmethylzirconation (**1d**)[9] products of alkynes, respectively. However, for type III, unfortunately neither Pd(PPh$_3$)$_4$ nor ZnCl$_2$/Pd(PPh$_3$)$_4$ gave positive results.



I



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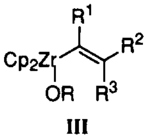
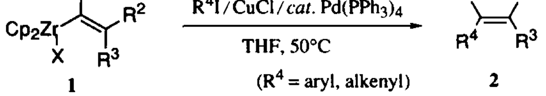


III

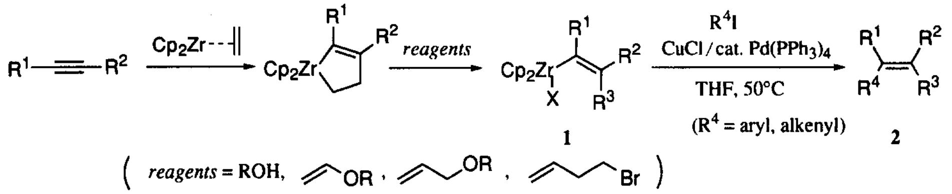
During the course of our study on the reactivity of type III,[10] we found that CuCl/Pd(PPh$_3$)$_4$ was a very useful combination for the coupling reaction of type III with aryl or alkenyl iodides to give stereodefined tetrasubstituted alkenes (eq 1).[11] In this paper we would like to report the coupling reaction of alkenylalkoxyzirconocenes of type III and alkenylbromozirconocenes with aryl or alkenyl iodides in the presence of CuCl and a catalytic amount of Pd(PPh$_3$)$_4$.



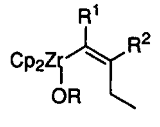
(1)

1 (R^4 = aryl, alkenyl) **2**

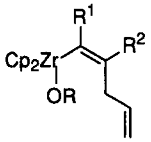
Typical procedure is as follows. A solution of zirconacyclopentene[12] prepared from 4-octyne (1 mmol) was treated with (a) t-butanol (1.1 mmol) at room temperature for 1h, (b) allyloxytrimethylsilane (2 mmol), at 50$_{o}$C for 1h, (c) butyl vinyl ether (2 mmol) at 50$_{o}$C for 6h, or (d) 4-bromo-1-butene (1.5 mmol) at 50^{c} C for 6h gave the corresponding carbozirconation products (**1a-d**). To the solution were added CuCl (1.3 mmol), iodobenzene (1 mmol) and Pd(PPh$_3$)$_4$ (0.05 mmol) in this order, and the mixture was stirred at 50°C for 3h. After the usual workup, compounds **2a**[13] (90%), **2k** (92%), **2o** (67%) and **2q** (77%) were obtained (eq 2). All were one-pot reactions.



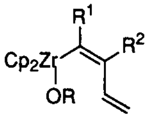
(2)



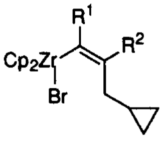
1a



1b



1c

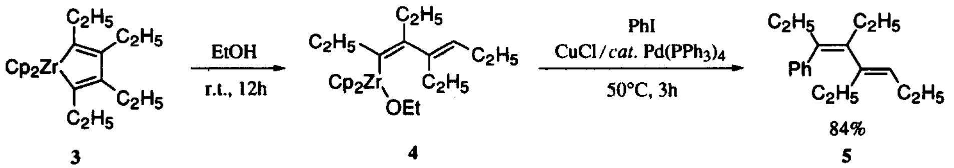


1d

The results are summarized in Table 1. To an alkyne were introduced two newly formed carbon–carbon bonds, one by the carbozirconation reaction and the other by a coupling reaction with aryl or alkenyl iodides. The final products, tetrasubstituted alkenes **2a-r**, were obtained in good to high yields. The carbozirconation reaction proceeded selectively in a *syn*-addition manner as reported[7], and the stereochemistry was retained during the coupling reaction. When allyloxytrimethylsilane was used, allylated compounds **2a-j** were obtained in good to high yields. Since the allylzirconation reaction was not regioselective when 1-phenyl-1-hexyne was employed, a mixture of two regioisomers **2h** was obtained in combined yield of 76% in a ratio of 3:1. In all cases, stereoisomerization of the alkene moiety or homo-coupling[14] of alkenylzirconium **1** was not observed.

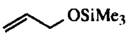
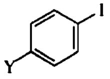
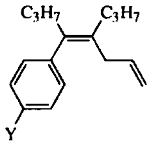
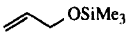
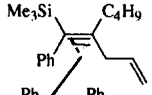
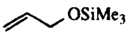
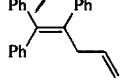
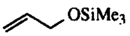
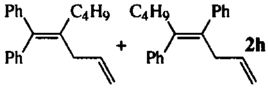
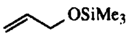
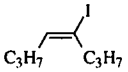
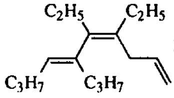
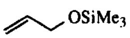
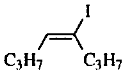
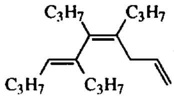
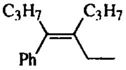
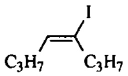
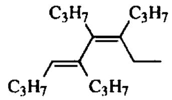
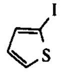
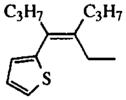
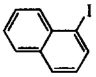
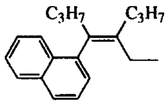
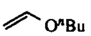
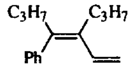
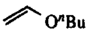
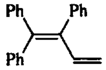
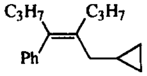
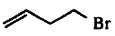
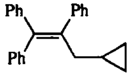
Various aryl iodides also successfully coupled with alkenylzirconium compounds of type III. *p*-Substituted phenyl iodides were examined (entry 2–5). The electron-donating or -withdrawing nature of *p*-substituents did not have significant influence on this reaction. 2-Iodothiophene and α-iodonaphthalene gave thienyl compound **2m** and naphthalene derivative **2n**, respectively. Instead of aryl iodides, alkenyl iodides were also employed to give pentasubstituted conjugated dienes **2i**, **2j** and **2l**.

In addition to type III compounds, this catalyst system of CuCl/Pd(PPh$_3$)$_4$ could be used for dienylzirconium compound **4**. Zirconacyclopentadiene **3** was monoprotonated by alcoholysis to give dienylzirconium complex **4**, and further treatment with iodobenzene under similar reaction conditions gave the coupling product **5** in 84% yield (eq 3).



(3)

Table 1. Coupling Products of Alkenylzirconocenes with Aryl or Alkenyl Iodides

Entry	R^1—≡—R^2	Reagents	R^4I		Products		Yields (%)[a]
1	C_3H_7—≡—C_3H_7			Y=H		**2a**	90
2				Y=CH_3		**2b**	66
3				Y=CO_2Et		**2c**	74
4				Y=OMe		**2d**	82
5				Y=NO_2		**2e**	74
6	Me_3Si—≡—C_4H_9		PhI			**2f**	68
7	Ph—≡—Ph		PhI			**2g**	51
8	Ph—≡—C_4H_9		PhI			**2h**	76 (75:25)[b]
9	C_2H_5—≡—C_2H_5					**2i**	64
10	C_3H_7—≡—C_3H_7					**2j**	81
11	C_3H_7—≡—C_3H_7	^{t}BuOH	PhI			**2k**	92
12	C_3H_7—≡—C_3H_7	^{t}BuOH				**2l**	90
13	C_3H_7—≡—C_3H_7	^{t}BuOH				**2m**	76
14	C_3H_7—≡—C_3H_7	^{t}BuOH				**2n**	76
15	C_3H_7—≡—C_3H_7		PhI			**2o**	67
16	Ph—≡—Ph		PhI			**2p**	66
17	C_3H_7—≡—C_3H_7		PhI			**2q**	77
18	Ph—≡—Ph		PhI			**2r**	84

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[a] Yields were determined by GC. [b] Ratio of regioisomers.

When the CuCl/Pd(PPh_3)$_4$ system was applied to alkenylzirconium compounds of type I and II, the desired coupling compounds were the major product. However, a considerable amount of homo-coupling products was observed even in the presence of Pd(PPh_3)$_4$.

We conclude that, when an alkenylzirconocene has an OR ligand (**1a-c**, **4**), Pd(PPh_3)$_4$ or $ZnCl_2$/Pd(PPh_3)$_4$ was not useful for the coupling reactions of alkenylzirconocenes with aryl or alkenyl iodides. Use of a stoichiometric or catalytic amount of CuCl did not give satisfactory results. However, a combination of CuCl and a catalytic amount of Pd(PPh_3)$_4$ was very effective.

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13. Compound **2a**: ^{1}H-NMR ($CDCl_3$, Me_4Si) δ 0.84 (t, 3H, J=7.3Hz), 0.96 (t, 3H, J=7.4Hz), 1.19-1.33 (m, 2H), 1.41-1.55 (m, 2H), 2.14 (t, 2H, J=7.8Hz), 2.32 (t, 2H, J=7.6Hz), 2.57 (d, 2H, J=6.3Hz), 4.87-4.94 (m, 2H), 5.61-5.76 (m, 1H), 7.06-7.30 (m, 5H); ^{13}C-NMR ($CDCl_3$, Me_4Si) δ 14.00 (CH_3), 14.32 (CH_3), 21.47 (CH_2), 22.01 (CH_2), 32.88 (CH_2), 36.21 (CH_2), 37.57 (CH_2), 114.91 (CH_2), 125.93 (CH), 127.81 (CH), 128.73 (CH), 133.35 (q), 137.72 (CH), 143.74 (q); HRMS calcd for $C_{17}H_{24}$, 228.1877, found 228.1870.
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