

Chemoselective Carbon–Carbon Bond Formation Reactions of Zirconacyclopentenes

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The reaction of zirconacyclopentenes with allyl chloride in the presence of a copper salt and a lithium or magnesium salt proceeds at the alkenyl carbon on zirconium with high chemoselectivity; selective C–C bond formation at the alkyl carbon was also achieved by treatment of zirconacyclopentenes with a copper salt and a lithium or magnesium salt, methanol and allyl chloride.

Zirconacyclopentenes, which are prepared from alkynes and alkenes on zirconocene,¹ contain both alkenylzirconium and alkylzirconium moieties. Chemoselective transformation of these different Zr–C bonds is attractive, and several reactions of zirconacyclopentenes with various reagents have been reported.^{1a,1c,2} We have also reported chemoselective protonation and halogenation of zirconacyclopentenes in which both alkyl halides and alkenyl halides can be obtained selectively.³ Chemoselective C–C bond formation reactions of zirconacyclopentenes, however, have not been intensively investigated and only a few examples are known, e.g. reactions with carbonyl compounds⁴ or isonitriles.^{1a,1c,2,3c} These reactions proceeded at alkylzirconium of zirconacyclopentenes.† Herein, we describe chemoselective C–C bond formation in zirconacyclopentene **1** which provided both **2** and **3** *via* methods A and B, respectively (Scheme 1).

Recently we reported that allylation of alkenylzirconium compounds⁵ proceeds in the presence of copper and lithium or magnesium salts, also Lipshutz *et al.* reported a similar allylation of alkylzirconium compounds.⁶ We investigated which Zr–C bond of zirconacyclopentenes **1** reacts with allyl chloride, and whether the allylation reactions (R = allyl) of **1** proceed selectively to give either **2** or **3**. Surprisingly, the reaction of **1** gave only **2** as a product after hydrolysis (method A).

A typical procedure for chemoselective allylation of alkenyl carbon (method A, Scheme 2) is as follows. Zirconacyclopentenes were prepared as previously reported *in situ* from [(C₅H₅)₂ZrCl₂] (1.25 mmol), EtMgBr (2.5 mmol) and alkynes (1.0 mmol)^{1g} or [(C₅H₅)₂ZrCl₂] (1.2 mmol), BuLi (2.4 mmol) and alkynes (1.0 mmol) under an ethene atmosphere.^{1h} To a

solution of zirconacyclopentene **1a** (R¹ = R² = Et) (1 mmol) in THF (5 ml) were added copper(I) cyanide (8.9 mg, 0.1 mmol) and allyl chloride (95 mg, 1.25 mmol), and the mixture was stirred at 0 °C for 6 h. After quenching with 3 mol dm⁻³ HCl, workup gave 4,5-diethylhepta-1,4-diene **2a** in 95% yield (based on hex-3-yne by GC). When diphenylacetylene or 1-phenylhex-1-yne was employed as an alkyne, equimolar amounts of CuCN were required to obtain satisfactory results. Addition of lithium or magnesium salts was not necessary, since they were formed in the reaction of EtMgBr or BuLi with [(C₅H₅)₂ZrCl₂]. The results are shown in Table 1.

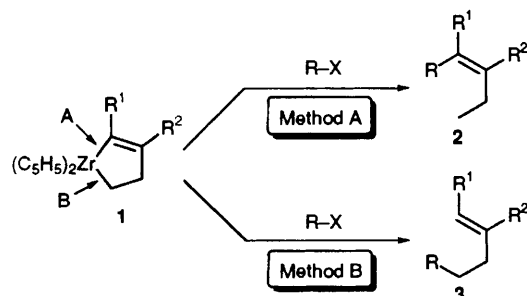
The allylation of **1** occurred exclusively at the alkenyl carbon to afford **2** in high yields and only a trace of alkyl-allylated product **3** and double allylated product **4** were detected. The stereochemistry of the double bonds in **1** was maintained throughout and the products showed *syn*-addition of alkynes. Even in the presence of 2.2 equiv. of allyl chloride and 20 mol% of CuCN the reaction of **1b** gave **2b** (79%) along with **3b** (5%) and **4b** (<1%) at 0 °C after 1 h.

Allylation of alkylzirconium was much slower than that of alkenylzirconium. Treatment of **6** with allyl chloride in the presence of 10 mol% of CuCN gave (*E*)-trideca-1,4-diene in 99% yield at room temp. after 3 h, while reaction of **7** gave only 2% of tridec-1-ene under the same conditions.

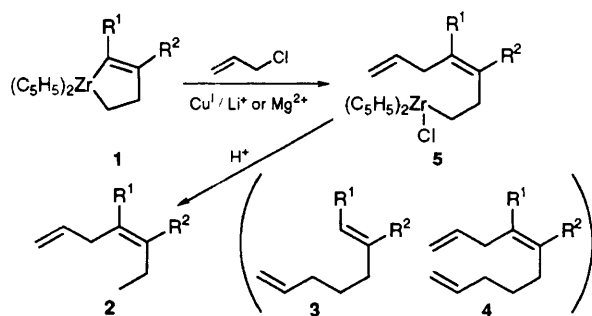
After treatment of **1a** (R¹ = R² = Et) with 1 equiv. of allyl chloride and 10 mol% of CuCN, zirconium species **5a** was observed by ¹H and ¹³C NMR (70% yield by ¹H NMR).‡ Treatment of **5b** (R¹ = R² = Bu) with 1 equiv. of methyl lithium at 50 °C for 3 h gave 1,2-dibutyl-3,4-dimethylcyclopent-1-ene **8** in 56% yield with 75:25 *trans*:*cis* ratio after hydrolysis. Showing that (*Z*)-3,4-dibutylhepta-1,3,6-triene was formed *via* β-hydrogen abstraction from dialkylzirconocene (Scheme 3).⁷ Cyclization of (*Z*)-3,4-dibutylhepta-1,3,6-triene with [(C₅H₅)₂ZrBu₂] (Negishi reagent) gave **8** as 84:16 mixture of *trans* and *cis* isomers.

The reaction of **5c–d** with equimolar amounts of CuCN and allyl chloride at 50 °C for 1 h gave the double allylated products **4c** (R¹ = Ph, R² = Bu) and **4d** (R¹ = R² = Ph) in 70 and 91% yields, respectively.⁸

From the point of view of controlling a chemoselective reaction, development of a selective allylation of alkyl carbon in **1** (method B) to obtain **3** is very important. In the allylation



Scheme 1



Scheme 2 Method A

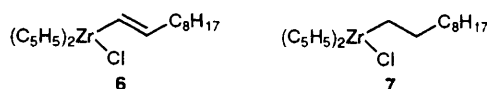
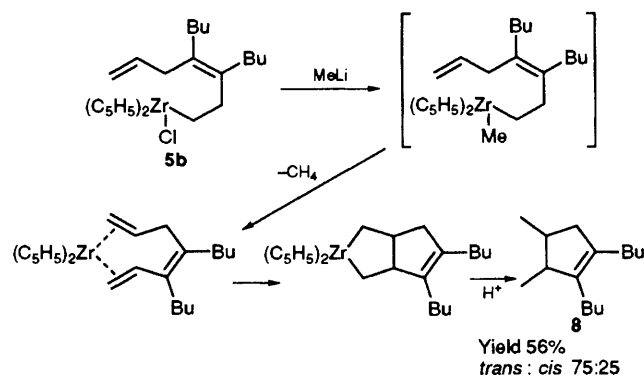
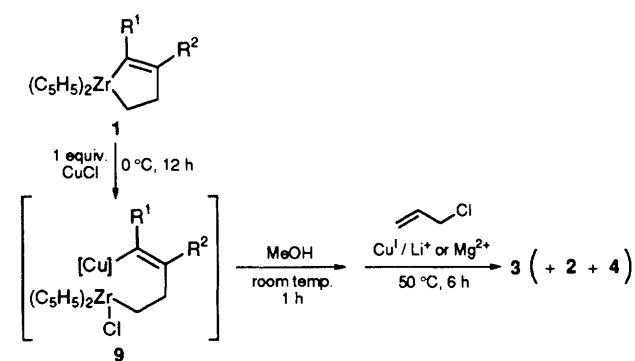


Table 1 Chemoselective allylation reactions of zirconacyclopentenes

Zirconacyclopentenes	R ¹	R ²	Equiv CuCN	T/°C	t/h	Yield (%)		
						2	3	4
1a	Et	Et	0.1	0	6	95	<1	<1
1b	Bu	Bu	0.1	0	6	81	—	—
1c	Ph	Bu	1.0	0	6	90	<1	<1
1d	Ph	Ph	1.0	-20	1	79	<1	<1

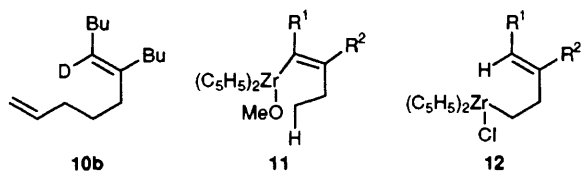


Scheme 3



		Yield (%)		
		3	2	4
a	R ¹ = R ² = Et	61	5	2
b	R ¹ = R ² = Bu	92	4	<1

Scheme 4 Method B



reaction described above, transmetalation of alkenyl carbon from zirconium to copper to form **9** is presumably the first step. After treatment of **1** with equimolar CuCl at 0 °C for 12 h, MeOH (1 equiv.) was added to the reaction mixture at room temp. Surprisingly, subsequent allylation of the reaction mixture with allyl chloride (2 equiv.) and additional CuCN (10 mol%) provided alkyl-allylated products **3** in good yields with good selectivity (Scheme 4).

The use of MeOD instead of MeOH gave **10b** with 94% deuterium incorporation. We previously reported that protonolysis of **1** with MeOH selectively occurred at alkyl carbon to afford **11**. The results obtained here support the formation of **9**. Presumably in the reaction of **9** with methanol, protonolysis occurred at the predominantly Cu–C bond rather than the Zr–C bond to afford **12**.

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture of Japan.

Received, 28th September 1994; Com. 4/05943C

Footnotes

† Insertion of isocyanide into Zr–alkenyl carbon was shown in a review (ref. 2).

‡ Selected data for **5a** (R¹ = R² = Et). ¹H NMR (C₆D₆, Me₄Si) δ 0.88–1.19 (m, 8H), 2.05–2.16 (m, 4H), 2.29–2.35 (m, 2H), 2.89–2.92 (m, 2H), 5.05–5.24 (m, 2H), 5.84 (s, 10H), 5.87–6.06 (m, 1H). ¹³C NMR (C₆D₆, Me₄Si) δ 13.94, 14.34, 24.51, 24.98, 35.60, 36.23, 56.71, 112.40, 114.57, 129.22, 138.09, 141.06.

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