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Zirconium-Catalyzed Highly Regioselective Carbon-Carbon Bond Formation Reactions

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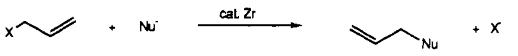
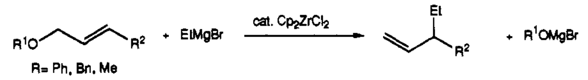
Recently Zr-catalyzed C-C bond formation reactions via Zr-alkene complexes have been reported.[2] For allylic compounds, catalytic C-C bond formation using the Cp_2ZrCl_2/EtMgBr system proceeded at the β-carbon of allylic compounds.[2a-c,e,i-j] To the best of our knowledge, however, the Zr-catalyzed allylation reaction (eq 1) has not been successful using this system.[3]



(1)

Herein we would like to describe highly selective zirconium-catalyzed allylation reactions at the γ-carbon of allylic ethers.

Treatment of allylic ethers with EtMgBr in the presence of catalytic amounts of Cp_2ZrCl_2 gave highly regioselective allylation products. These reactions proceeded exclusively at the γ-carbon of allylic ethers (eq 2).

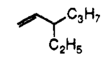
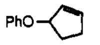
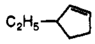
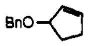
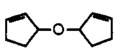
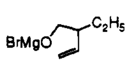
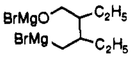
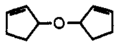


(2)

A typical procedure for this catalytic reaction is as follows. To a solution of zirconocene dichloride (29.2 mg; 0.1 mmol) in THF (5 mL) was added a THF solution of EtMgBr (0.93 M, 3.0 mmol) at −78 °C, and the mixture was stirred for 1 h. After *trans*-2-hexenyl phenyl ether (**1**) (176 mg; 1.0 mmol) was added, the reaction mixture was allowed to warm to room temperature and was stirred for 6 h. The reaction product 3-ethyl-1-hexene (**2**) was obtained in 70% yield with >99% regioselectivity. Carbon-carbon bond formation occurred only at the γ-carbon of allyl ether **1**. No formation of 4-octene, the α-attack product, was detected.

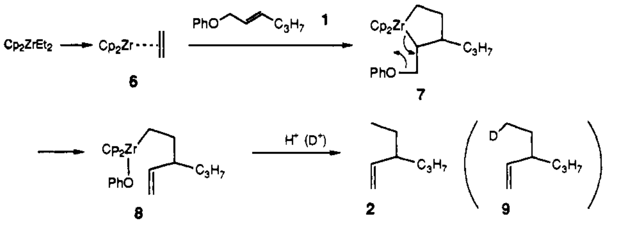
Results obtained here are shown in Table I, and the following are noteworthy. First, in the absence of Cp_2ZrCl_2, no desired product was obtained from the mixture of allylic ethers with EtMgBr under conditions used here. The use of MeMgBr instead of EtMgBr in the presence of Cp_2ZrCl_2 did not give the desired product as observed for the other catalytic reactions using zirconocene-alkene complexes. Second, Cp_2HfCl_2 could be used for this allylation reaction as a catalyst, although long reaction times were required. Third, carbon-carbon bond formation occurred exclusively at the γ-position of allylic ethers, and not even a trace of α-attack product could be detected. Fourth, the catalytic reactions of 2-hexenyl ethers or 2-cyclopentenyl ethers did not give organomagnesium compounds as products. Treatment of reaction mixtures with DCl/D_2O gave nondeuterated products (<1% deuterated product). In the case of the reaction of 2,5-dihydrofuran with 1.2 equiv of EtMgBr, 2-ethyl-3-buten-1-ol was cleanly formed in 65% yield after hydrolysis. However, when 5 equiv of EtMgBr was used, further C-C bond formation occurred to give double ethylation product **5**. The second ethylation is a Dzhemilev type of ethylation reaction of the terminal double bond of **4**.[2c]

Table I. Zirconium-Catalyzed C-C Bond-Forming Reaction of Allylic Ethers[a]

substrate	EtMgBr (equiv)	time (h)	product	yield (%)
 **1**	3	6	 **2**	70
	3	6	**2**	50
	3	6	**2**	60
	2	6[b]	**2**	51
	2	6	 **3**	75
	3	6	**3**	76
	2	6	**3**	77
	1.2	1	 **4**	65
	5	48	 **5**	53
 [c]	2	65	**3**	65

[a] Reaction conditions: Cp_2ZrCl_2:allylic ether = 0.1:1; room temperature in THF. [b] 50 °C for 6 h after being stirred at room temperature for 6 h. [c] Cp_2HfCl_2 was used as a catalyst.

To elucidate the mechanism of this catalytic reaction, we carried out the following stoichiometric reactions of allylic ethers with Cp_2ZrEt_2 or Cp_2ZrBu_2. Reaction of *trans*-2-hexenyl phenyl ether (**1**) with 1 equiv of Cp_2ZrEt_2 gave product **2** in 74% yield at room temperature after hydrolysis and deuterolysis gave deuterated product **9** (>98% D incorporated). Formation of intermediate species **8** was detected by ^1H and ^{13}C NMR (65% yield by ^1H NMR).[4] This species **8** could be also prepared by addition of 1 equiv of phenol to bis(3-propyl-4-pentenyl)zirconocene.[5]



Treatment of **8** with 2 equiv of EtMgBr at room temperature for 1 h liberated the desired product **2** in 71% yield after 1 h along

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[1] JPSP Fellowship 1992 (IMS).

[2] (a) Dzhemilev, U. M.; Vostrikova, O. S.; Sultanov, R. M. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1983**, 218-220. (b) Dzhemilev, U. M.; Vostrikova, O. S. *J. Organomet. Chem.* **1985**, *285*, 43-57. (c) Dzhemilev, U. M.; Vostrikova, O. S.; Tolstikov, G. A. *J. Organomet. Chem.* **1986**, *304*, 17-39. (d) Takahashi, T.; Seki, T.; Saburi, M.; Negishi, E. XIVth International Conference on Organometallic Chemistry, Detroit, MI, 1990, B17. (e) Hoveyda, A. H.; Xu, Z. *J. Am. Chem. Soc.* **1991**, *113*, 5079-5080. (f) Takahashi, T.; Seki, T.; Nitto, Y.; Saburi, M.; Rousset, C. I.; Negishi, E. *J. Am. Chem. Soc.* **1991**, *113*, 6266-6268. (g) Knight, K. S.; Waymouth, R. M. *J. Am. Chem. Soc.* **1991**, *113*, 6268-6270. (h) Hoveyda, A. H.; Xu, Z.; Morken, J. M.; Houri, A. F. *J. Am. Chem. Soc.* **1991**, *113*, 8950-8952. (i) Lewis, D. P.; Muller, P. M.; Whitby, R. J. *Tetrahedron Lett.* **1991**, *32*, 6797-6800. (j) Hoveyda, A. H.; Morken, J. M.; Houri, A. F.; Xu, Z. *J. Am. Chem. Soc.* **1992**, *114*, 6692-6697. (k) Wischmeyer, U.; Knight, K. S.; Waymouth, R. M. *Tetrahedron Lett.* **1992**, *33*, 7735-7738.

[3] Reaction of $(C_5H_7)_2Mg$ with allyl bromide has been reported: Yasuda, H.; Yamauchi, M.; Nakamura, A., Sei, T.; Kai, Y.; Yasuoka, N.; Kasai, N. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1089-1100.

[4] **8**: ^1H NMR (C_6D_6/THF, Me_4Si) δ 0.8-1.0 (m, 5H), 1.2-1.9 (m, 7H), 4.9-5.1 (m, 2H), 5.6-5.8 (m, 1H), 6.04 (s, 10H), 6.47 (d, J = 8.2 Hz, 2H), 6.7-6.8 (m, 1H), 7.09 (t, J = 7.8 Hz, 2H); ^{13}C NMR (C_6D_6/THF, Me_4Si) δ 14.66, 21.28, 37.23, 39.51, 40.70, 50.58, 111.70, 113.78, 118.40, 119.37, 129.58, 145.01, 165.69. This intermediate **8** was in equilibrium with some species like a dimer or oligomer which could not be identified. In a 1:1 mixture of THF/C_6D_6, its ^1H NMR showed that the yield of **8** was 56%. When THF was added to this mixture, the yield gradually increased to 65%; intensities of other small peaks decreased. GC yields of hydrolysis product **2** were constant. NMR yields were obtained using a peak at 6.04 ppm assigned to Cp ligand.

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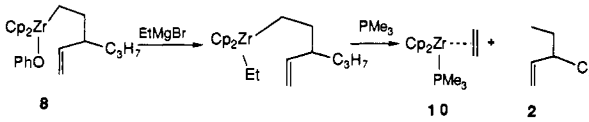
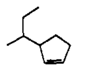
with the zirconocene–ethylene complex (or zirconacyclopropane) $Cp_2Zr(CH_2{=}CH_2)(PMe_3)$ (**10**).[6] Deuterated product was not obtained after deuterolysis of the reaction mixture. On the other hand, addition of **1** to Cp_2ZrBu_2 instead of Cp_2ZrEt_2 did not give any butylated products. Only less-bulky substrates such as cyclopentenyl ether afforded butylated product **11** (yield 65%), which was obviously not from the nucleophilic attack by *n*-butyl group but via zirconocene–butene complex. In fact, deuterolysis of the reaction mixture gave **12** (>98% D). Stoichiometric reaction of cyclopentenyl ethers with Cp_2ZrEt_2 gave **13** (>97% D) after deuterolysis, as expected.





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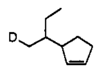

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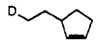

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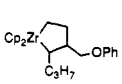
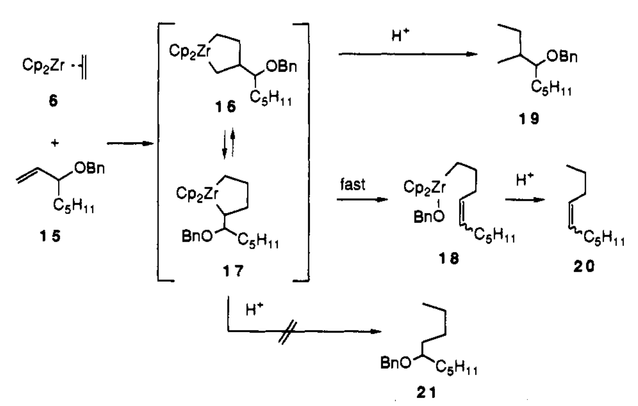


14

It is known that Cp_2ZrEt_2 is converted into zirconocene-ethylene complex.[6b] The zirconocene–ethylene complex stabilized with PMe_3 **10** reacted with *trans*-2-hexenyl phenyl ether to give intermediate **8** at 60 °C after 23 h, and hydrolysis of the reaction mixture gave **2** in 57% yield. Cyclopentenyl ether reacted with **10** to give 3-ethylcyclopentene (**3**) in 71% yield at room temperature after hydrolysis. In addition treatment of this reaction mixture with 1 equiv of EtMgBr regenerated **10** in 80% yield in the presence of PMe_3 and released product **3** in 78% yield.

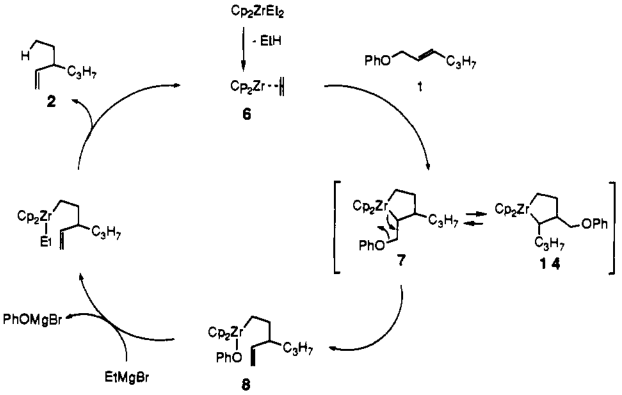
Two zirconacyclopentanes, **7** and **14**, are possible zirconacyclopentane intermediates formed by the reaction of **6** with **1**. Unfortunately, these zirconacyclopentanes **7** and **14** were not detected. However, a reaction of Cp_2ZrEt_2 with **15** at −15 °C for 2 h gave a mixture of **19** and **20** in 66% and 17% yields, respectively, after hydrolysis. When this reaction mixture was gradually warmed to 0 °C and stirred for 2 h, the yields of **19** and **20** became 31% and 45%, respectively. At room temperature, only **20** was obtained in 66% yield after hydrolysis. The product **19** completely disappeared. Cooling the mixture to −15 °C again did not give **19** after hydrolysis. During this reaction, the product **21** was not detected.

This result suggests that an equilibrium between regioisomers **16** and **17** exists and that zirconacyclopentane **17** is converted into **18** rapidly by abstraction of OBn group by Zr, since hydrolysis of the mixture did not give **21** but only **20**. Only **18** was formed at room temperature, even though regioisomers **16** and **17** were formed as intermediates. This result clearly explains the highly selective C–C bond formation at the γ-position of allylic ethers.



The results obtained here strongly suggest the following catalytic reaction mechanism, as shown in Scheme I. Allylic ether **1** reacts with zirconocene–ethylene complex **6** to produce zirconacyclopentane **7** and its isomer **14**. Sequential C–Zr and C–O bond cleavages of **7** afford **8**. Since **7** and its isomer **14** are in equilibrium, the isomer **14** is also converted into **8** via **7**. An alternative route involving the attack of ethylene at the γ-carbon of the allylic ether and simultaneous C–O bond cleavage without forming zirconacyclopentane intermediate **7** cannot be ruled out. This mechanism explains why catalytic allylations proceeded exclusively at the γ-position of allylic compounds. Intermediate **8** easily reacts with EtMgBr to liberate the desired product **2** and regenerates the zirconocene–ethylene complex **6** as described above. The product of oxidative addition of allylic ether to the zirconium(II) species[7] is unlikely to be an intermediate. Stoichiometric reaction of allylic ether **1** with Cp_2ZrBu_2[8] did not give the desired product **2** after treatment with EtMgBr.

Scheme I



Further investigations on zirconium-catalyzed selective reactions using the zirconocene–alkene complex system are now in progress.

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Supplementary Material Available: Experimental procedures and analytical data (3 pages). Ordering information is given on any current masthead page.

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(5) Takahashi, T.; Aoyagi, K.; Hara, R.; Suzuki, N. *Chem. Lett.* **1992**, 1693–1696.

(6) (a) Alt, H. G.; Denner, C. E.; Thewalt, U.; Rausch, M. D. *J. Organomet. Chem.* **1988**, *356*, C83–C85. (b) Takahashi, T.; Murakami, M.; Kunishige, M.; Saburi, M.; Uchida, Y.; Kozawa, K.; Uchida, T.; Swanson, D. R.; Negishi, E. *Chem. Lett.* **1989**, 761–764.

(7) (a) Rousset, C. J.; Swanson, D. R.; Lamaty, F.; Negishi, E. *Tetrahedron Lett.* **1989**, *30*, 5105–5108. (b) Ito, H.; Taguchi, T.; Hanzawa, Y. *Tetrahedron Lett.* **1992**, *33*, 1295–1298. (c) Ito, H.; Nakamura, T.; Taguchi, T.; Hanzawa, Y. *Tetrahedron Lett.* **1992**, *33*, 3769–3772.

(8) Negishi and co-workers demonstrated that Cp_2ZrBu_2 could be used as a Cp_2Zr equivalent. Negishi, E.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829–2832.