Zirconocene-Mediated and/or Catalyzed Unprecedented Coupling Reactions of Alkoxymethyl-Substituted Styrene Derivatives

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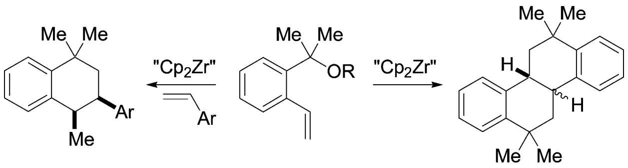
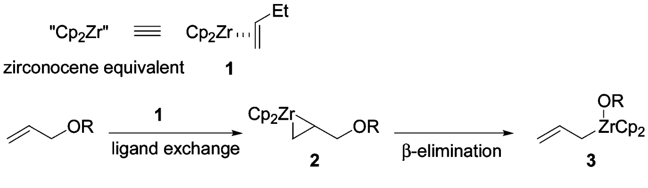
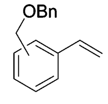


Reactions of *o*-(alkoxymethyl)styrene derivatives with a stoichiometric amount of zirconocene−butene complex (zirconocene equivalent, "Cp$_2$Zr") brought about an insertion of the zirconocene species into a benzylic carbon−oxygen bond. The oxidative insertion of Cp$_2$Zr to the benzylic carbon−oxygen bond is a result of sequential reactions: (i) formation of zirconacyclopropane by the ligand exchange with *o*-(alkoxymethyl)styrene, (ii) elimination of the alkoxy group through an aromatic conjugate system giving metalated *o*-quinodimethane species, and (iii) transfer of zirconium metal to the benzylic position. Through use of a catalytic amount of "Cp$_2$Zr", however, unprecedented homo-coupling reactions (dimerization) of *o*-(alkoxymethyl)styrene derivatives occurred to give a tetracyclic compound. On the other hand, reactions of *o*-(1-alkoxyisopropyl)styrene derivatives gave rise to the analogous tetracyclic compounds regardless of the amount of "Cp$_2$Zr" (stoichiometric or catalytic). Heterocoupling product between *o*-(1-alkoxyisopropyl)styrene and styrene congeners was obtained in high cis stereo- and regioselectivity by treating *o*-(1-alkoxyisopropyl)styrene derivatives with "Cp$_2$Zr" in the presence of an excess amount of styrene derivatives.

Introduction

Easy preparation and versatile reactivity of zirconocene−butene complex **1** ("Cp$_2$Zr", Cp = cyclopentadienyl)[1] attracted synthetic organic chemists to the use of "Cp$_2$Zr" as a zirconocene equivalent for the study of new carbon−carbon bond formation.[2] During the course of our studies of "Cp$_2$Zr"-mediated carbon−carbon bond formation reactions, we reported an efficient generation of allylic zirconocene **3** species from allylic ethers through β-alkoxy elimination of the zirconacyclopropane intermediate **2**.[3] On the basis of the formation of allylic zirconocene **3**, we were tempted to examine "Cp$_2$Zr"-catalyzed or -mediated reactions of alkoxymethyl-substituted styrene derivatives **4**, which possess a reactive olefin site to "Cp$_2$Zr" and a leaving alkoxy group through the aromatic π-conjugated system. Preliminary examination of the reactions of *o*-, *m*-, or *p*-alkoxymethyl-substituted styrene derivatives **4** toward "Cp$_2$Zr" showed a remarkable difference in reactivity.[4]





4 (*o*-, *m*- and *p*-isomers)

In this paper, we disclose a full account of the "Cp$_2$Zr"-mediated or -catalyzed reactions of *o*-, *m*-, and

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(1) Negishi, E.; Cederbaum, F. E.; Takahashi, T. *Tetrahedron Lett.* **1986**, *27*, 2829.

(2) For recent reviews, see: (a) Marek, I., Ed. *Titanium and Zirconium in Organic Synthesis*, Wiley-VCH: Weinheim, Germany, 2002. (b) Suzuki, K.; Wipf, P., Eds.; Recent advances in the chemistry of zirconocenes. In Symposium-in print *Tetrahedron* **2004**, *60*, 1267.

(3) For review, see: Hanzawa, Y.; Ito, H.; Taguchi, T. *Synlett* **1995**, 299.

(4) Hanzawa, Y.; Ikeuchi, Y.; Nakamura, T.; Taguchi, T. *Tetrahedron Lett.* **1995**, *36*, 6503.

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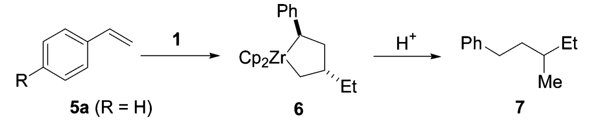


FIGURE 1. Regio- and stereoselective formation of **6**.[5]

p-alkoxymethyl-substituted styrene derivatives **4** and the unprecedented formation of homo- and heterocoupling products.

The reaction of styrene (**5a**) with “Cp$_2$Zr” has been reported to give regio- and stereoselectivily zirconacyclopentane intermediate **6**, which is converted to styrene−butene coupled product **7** in good yields by acid treatment (Figure 1).[5,6] In this coupling reaction, it is worth noting that the formation of the styrene−styrene homocoupling (dimerization) products has been reported to be less than 10% under thermodynamically equilibrated conditions.

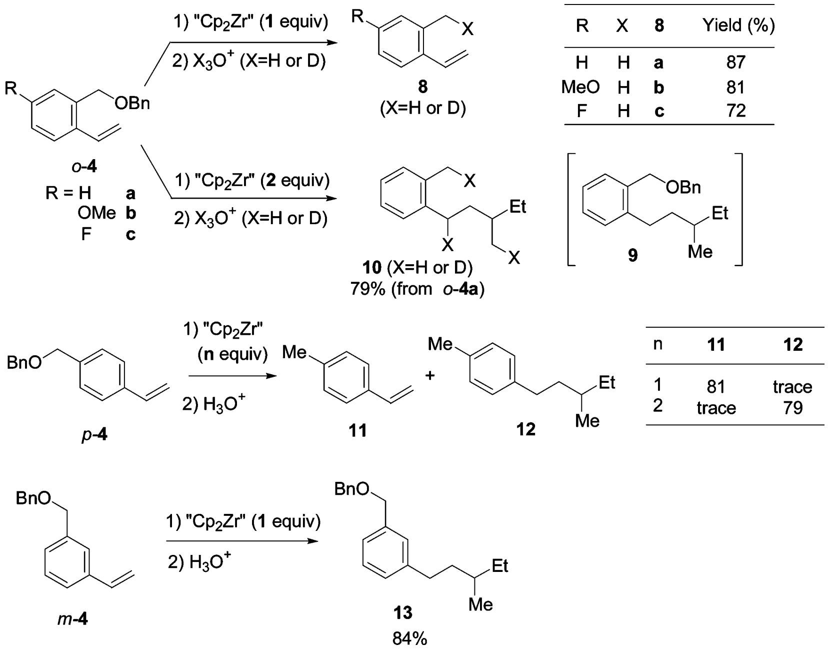
Results and Discussion

Generation of Benzylzirconocene Intermediates. The reactions of *o*-(benzyloxymethyl)styrene derivatives (*o*-**4a**−**c**) with a stoichiometric amount of “Cp$_2$Zr” in THF at room temperature gave *o*-methylstyrene compounds **8a**−**c** or the monodeuteriomethyl congener of **8a** after acidic workup (HCl−H$_2$O or DCl−D$_2$O) in good yields (Scheme 1). To our surprise, butene-coupling product **9** could not be detected in the reaction media. The double bond of *o*-**4a** is indispensable because the reaction of dibenzyl ether with “Cp$_2$Zr” under the same conditions did not afford any products except the recovered starting material. Through use of 2 equiv of “Cp$_2$Zr”, *o*-**4a** afforded butene-coupling compound **10a** (X = H) in a 79% yield, and three deuterium atoms were incorporated into **10a** (X = D) by DCl−D$_2$O workup. The reaction of *p*-(benzyloxymethyl)styrene (*p*-**4**) with “Cp$_2$Zr” indicated similar reactivity to that of *o*-**4a**. Thus, the formation of *p*-methylstyrene (**11**) or butene-coupling product **12** depended on the amount of “Cp$_2$Zr” employed. In the reaction of meta-substituted isomer *m*-**4** with an equivalent amount of “Cp$_2$Zr”, however, butene-coupling product **13** was obtained as the sole product as in the case of the styrene−“Cp$_2$Zr” reaction.

These results indicate that the insertion of zirconocene into the benzylic carbon−oxygen bond took place in the reactions of *o*- and *p*-**4** and not in the reaction of *m*-**4**, and thus, the importance of the π-conjugation is obvious. It is also obvious that benzylic zirconocene species is formed prior to the addition of the second “Cp$_2$Zr” in the reactions of *o*- and *p*-**4**. Thus, benzylzirconocene species **16**, for example, would be formed through (i) the ligand exchange of the first equivalent of “Cp$_2$Zr” with a double bond of *o*-**4a** giving a zirconacyclopropane derivative **14**, (ii) the elimination of the alkoxy group in **14** through the aromatic π-system to generate *o*-quinodimethane intermediate **15**,[7] and (iii) the transfer of the Cp$_2$Zr moiety to a benzylic position (Figure 2). The described processes (i−iii) explain the formation of **10** (X = H or D) in the reaction of *o*-**4a** with 2 equiv of “Cp$_2$Zr” or the formation of **13**.

Formation of Homocoupling Products (Dimerization). The reaction of *o*-(1-alkoxyisopropyl)styrene **17a**, which is a dimethyl-substituted analogue of *o*-**4a**, with an equivalent amount of “Cp$_2$Zr” afforded an unexpected homocoupling product **19a** as a mixture of trans/cis isomers[8] (ratio = 3.0/1). In addition, reduced product **18** was not detected (Scheme 2 and Table 1).[9] No deuterium was incorporated into **19a** by DCl−D$_2$O workup. The homocoupling reactions were affected by the substituent, and thus *p*-methoxy-substituted styrene derivative **17c** gave a complex mixture (entry 3). It is worth mentioning that the reaction of the fluorine-substituted isomer **17d** with “Cp$_2$Zr” (1 equiv) gave a corresponding homocoupling product **19c** in a 29% yield (trans/cis = 2.5) together with **20** (X = H) in a 50% yield as a single cis-stereoisomer (entry 4).[8] The incorporation of one deuterium atom into **20** (X = D) by DCl−D$_2$O workup indicates that the coupled product **20** is gener-

SCHEME 1



R	X	8	Yield (%)
H	H	a	87
MeO	H	b	81
F	H	c	72

n	11	12
1	81	trace
2	trace	79

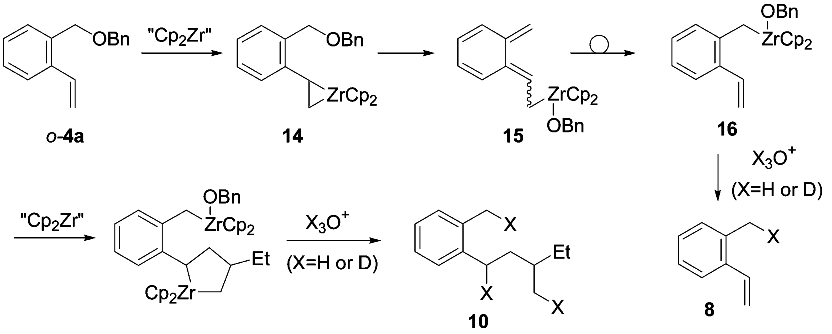


FIGURE 2. “Cp_2Zr”-mediated reaction pathway.

SCHEME 2

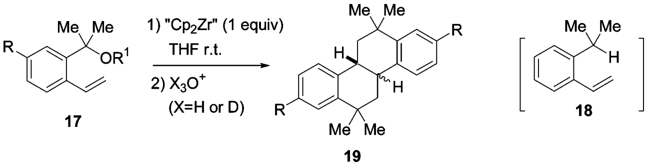
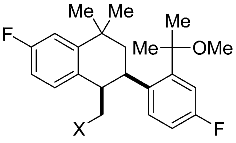


TABLE 1. Formation of 19[a]



20 (*cis only*)
X = H, D, or $ZrCp_2(OMe)$

entry	17	% yield[b] of **19** (trans/cis)	% yield[b] of **20**
1	**17a**: R = H;	**19a**: 83 (3.0)	–
2	**17b**: R = H; $R^1 = CH_3$	**19a**: 78	–
3	**17c**: R = CH_3O; $R^1 = CH_3$	complex mixture	
4[c]	**17d**: R = F; $R^1 = CH_3$	**19c**: 29 (2.5)	50
5[d]	**17d**: R = F; $R^1 = CH_3$	**19c**: 53	28

[a] Reaction conditions: **17** (0.5 mmol), “Cp_2Zr” (1.05 equiv), THF, rt. [b] Isolated yields. [c] 6.5 h of reaction time. [d] 97 h of reaction time.

SCHEME 3

$$\mathbf{17a} \xrightarrow[\text{room temp. THF}]{\text{"}Cp_2Zr\text{" (n equiv)}} \mathbf{19a} + \mathbf{17a}$$

n	Yield (%)[a] **19a**	Yield (%)[a] **17a**
1	83	-
1/2	84	-
1/3	62	31
1/3[b]	75	-

[a] Isolated yields. [b] *n*-BuLi (1/3 equiv) was added before hydrolytic workup.

ated as a zirconocene species in the reaction media. The prolonged reaction of **17d** (97 h) with an equivalent amount of “Cp_2Zr” increased the ratio of **19c** (53%) compared to **20** (28%) (entry 5), and thus the homocoupling reaction could be suggested to proceed with **20** (X = $ZrCp_2(OMe)$) as a key intermediate.

The lack of deuterium introduction into **19** by the acidic workup with DCl–D_2O suggests that dimeric product **19** was not generated as an organometallic compound in the reaction media. A half equivalent of “Cp_2Zr” to **17a** was sufficient (84% yield) for the formation of **19a** (Scheme 3). The use of 1/3 equiv of “Cp_2Zr”, however, indicated a formation of **19a** in a lower yield (62%) with considerable recovery of **17a** (31%), and the addition of *n*-BuLi (1/3 equiv) to the reaction mixture prior to the hydrolytic workup increased the yield of **19a** (75%). Thus, the homocoupling process is a catalytic process with respect to “Cp_2Zr”.

The reactions of *o*-(alkoxymethyl)styrene derivatives with a catalytic amount of Cp_2ZrCl_2 (10 mol %) in the presence of 3 equiv of *n*-BuMgCl in THF at refluxing temperature[10] are summarized in Table 2. Under the catalytic conditions, improved yields of dimers **19** were observed in comparison to those under the stoichiometric conditions (entries 4–7). It is interesting to note that the styrene derivatives *o*-**4**, which did not give dimerization products under the stoichiometric conditions, gave dimerization products **19** under the catalytic conditions (entries 1 and 3). In contrast to the result of the reaction of *o*-**4**, *p*-(benzyloxymethyl)styrene (*p*-**4**) resulted in polymerization under catalytic conditions.

The catalytic process for the formation of **19** consisted of the prior formation of zirconacyclopropane **14′** and the formation of dialkoxyzirconocene, which regenerated “Cp_2Zr” through the reaction with Grignard reagent, and the dimerization product **19** was expelled from the catalytic cycle as shown in Figure 3.

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[5] Swanson, D. R.; Rousset, C. J.; Negishi, E.; Takahashi, T.; Seki, T.; Saburi, M.; Uchida, Y. *J. Org. Chem.* **1989**, *54*, 3521.

[6] Besides the reactivity of styrene with a stoichiometric amount of **1**, the efficient alkylation reaction of the styrene double bond has been reported by treatment with a catalytic amount of Cp_2ZrCl_2 in the presence of Grignard reagent (3 equiv) and alkyl halides or tosylates. (a) Cesati, R. C., III; Armas, J.; Hoveyda, A. H. *Org. Lett.* **2002**, *4*, 395. (b) Armas, J.; Hoveyda, A. H. *Org. Lett.* **2001**, *3*, 2097. (c) Armas, J.; Kolis, S. P.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000**, *122*, 5977. (d) Terao, J.; Torii, K.; Saito, K.; Kambe, N.; Baba, A.; Sonoda, N. *Angew. Chem., Int. Ed.* **1998**, *37*, 2653. (e) Terao, J.; Watanabe, T.; Saito, K.; Kambe, N.; Sonoda, N. *Tetrahedron Lett.* **1998**, *39*, 9201. (f) Swanson, D. R.; Rousset, C. J.; Negishi, E.; Takahashi, T.; Seki, T.; Saburi, M.; Uchida, Y. *J. Org. Chem.* **1989**, *54*, 3521.

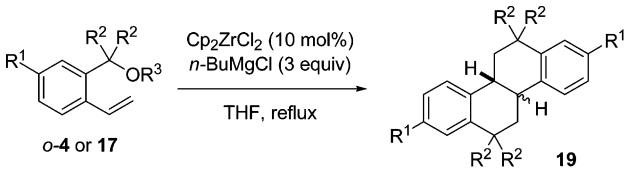
[7] The generation of *o*-quinodimethane intermediates from *o*-alkoxymethylstyrene and its related compounds through the elimination of an alkoxyl group has been reported. (a) Hirao, A.; Negishi, Y.; Hayashi, M.; Sako, K.; Ryu, W.; Loykulnant, S.; Matsuo, A.; Sugiyama, K. *Macromol. Chem. Phys.* **2001**, *202*, 3590. (b) Hirao, A.; Kitamura, K.; Takenaka, K.; Nakahama, S. *Macromolecules* **1993**, *26*, 4995. (c) Ishizone, T.; Kato, R.; Ishino, Y.; Hirao, A.; Nakahama, S. *Macromolecules* **1991**, *24*, 1449. See also: (d) Moss, R. J.; Rickborn, B. *J. Org. Chem.* **1986**, *51*, 1992. (e) Moss, R. J.; White, R.; Rickborn, B. *J. Org. Chem.* **1985**, *50*, 5132. (f) Moss, R. J.; Rickborn, B. *J. Org. Chem.* **1984**, *49*, 3694. (g) Tuschka, T.; Naito, K.; Rickborn, B. *J. Org. Chem.* **1983**, *48*, 70.

[8] Structure was determined by X-ray analysis.

[9] Although dimer **19a** was obtained in a lower yield, using methyl ether **17b**, than benzyl ether **17a**, for easy preparation of substrates, methyl ether derivatives were prepared for the other substrates. See the Supporting Information.

[10] It was essential to heat the reaction mixture to reflux to bring about an efficient formation of **19**.

TABLE 2. Formation of 19 from *o*-4 or 17 under Catalytic Conditions[a]



entry	*o*-4 or 17	% yield[b] of **19** (trans/cis)
1	***o*-4a**	**19d**: 57 (1.3)
2	***o*-4b**	**19e**: nd
3	***o*-4c**	**19f**: 52 (2.1)
4	**17a**	**19a**: 89 (2.8)
5	**17b**	**19a**: 81 (3.0)
6	**17c**	**19b**: 55 (2.4)
7	**17d**	**19c**: 44[c] (1.4)

[a] Reaction conditions: *o*-4 or **17** (0.5 mmol), Cp_2ZrCl_2 (10 mol %), *n*-BuMgCl (3 equiv), THF, reflux. [b] Isolated yields. [c] Coupled product **20** was also obtained in a 34% yield.

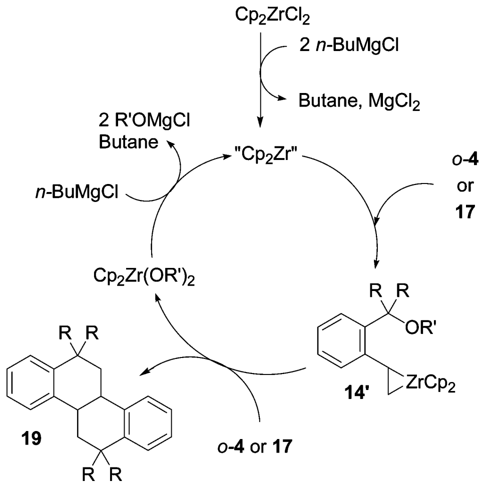
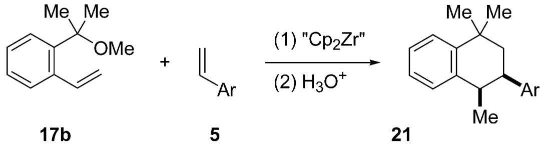
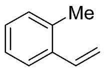


FIGURE 3. Catalytic cycle for the formation of **19**.

TABLE 3. Heterocoupling Reactions of 17b with Styrene Derivatives[a]



entry	**5** Ar		**21** yield (%)[b]	
1	C_6H_5-	**5a**	56 (21)	**21a**
2[c]	C_6H_5-	**5a**	85 (5)	**21a**
3[d]	C_6H_5-	**5a**	85 (5)	**21a**
4	4-F-C_6H_4-	**5b**	81 (5)	**21b**
5	3,5-$(CF_3)_2$-C_6H_3-	**5c**	11 (-)	**21c**
6	4-CH_3O-C_6H_4-	**5d**	35 (60)	**21d**
7	2-CH_3O-C_6H_4-	**5e**	59 (29)	**21e**
8	***o*-4a + 5a**		 Me **8a**	

[a] Reaction conditions: **17b** (0.5 mmol), **5** (3 equiv), “Cp_2Zr” (1.2 equiv), THF, rt. [b] Isolated yields. The yields of **19** are shown in parentheses. [c] 1 equiv of **5a** was used. [d] Reaction conditions: Cp_2ZrCl_2 (10 mol %), *n*-BuMgCl (3 equiv), THF, reflux.

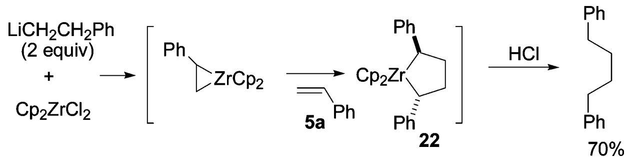
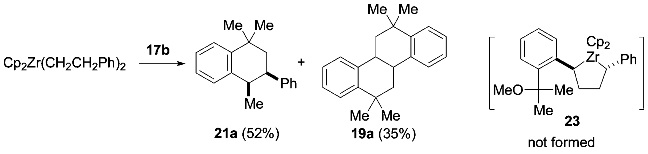


FIGURE 4. Regio- and stereoselective formation of **22** by Negishi et al.

SCHEME 4



Formation of Heterocoupling Products. Although the mechanism for the Cp_2ZrCl_2-catalyzed or “Cp_2Zr”-mediated homocoupling formation of **19**, which will be discussed later, is still unclear, it may be of interest to investigate the possibility for the heterocoupling reaction of **17** with other olefins. Attempts to obtain such heterocoupling products would contribute to the understanding of the reaction mechanisms for the formation of **19**. The results of the reaction of **17** with styrene (**5a**) as a heterocoupling partner are shown in Table 3. Thus, in the “Cp_2Zr”-mediated reaction of **17b** with 1 equiv of styrene (**5a**), heterointermolecular coupling product **21a** was obtained in a 56% yield as a single cis-stereoisomer[8] along with homodimer **19a** (21% yield), and neither styrene (**5a**)−butene nor styrene−styrene coupling product (see, Figure 1) was obtained. Use of 3 equiv of styrene (**5a**) increased the yield of **21a** to 85% (entry 2). Treatment of the reaction mixture with DCl/D_2O afforded the monodeuteriomethyl compound of **21a** in an excellent deuterium content (>95% D, 79% yield). The intermolecular heterocoupling reaction of **17** was restricted to a styrene double bond, without a substituent on the double bond, as a coupling partner (Table 3). All other examined unsaturated compounds, such as maleic anhydride, 3,4-dihydrofuran, phenylacetylene, diphenylacetylene, *cis*- or *trans*-stilbene, and α- or *β*-methylstyrene, did not give a heterocoupling product but gave the homocoupling product **19**. It should be noted that the “Cp_2Zr”-mediated reaction of *o*-benzyloxymethystyrene (***o*-4a**) with styrene (**5a**) gave a reduced product **8a** as the sole product (entry 8). The heterointermolecular coupling reaction of **17b** with styrene (**5a**) was also carried out under the same catalytic conditions with a similar efficiency to the stoichiometric conditions (entry 3).

Mechanistic Consideration of Coupling Reactions. Concerning the “Cp_2Zr”-mediated styrene−styrene homocoupling reaction, the reaction of $Cp_2Zr(CH_2CH_2Ph)_2$ with styrene has been reported to give *trans*-2,5-diphenylzirconacyclopenatane intermediate **22**.[5] The stereo- and regioselective formation of **22** was ex-

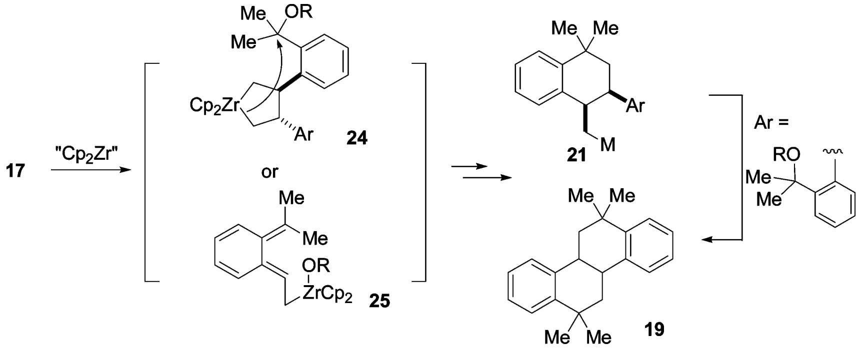
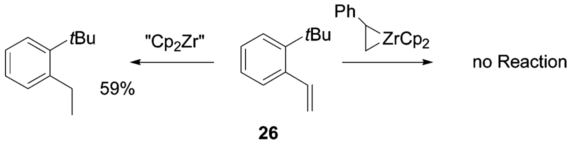


FIGURE 5. Supposed intermediates.

SCHEME 5



plained to be a result of the favorable thermodynamic effect of benzylic and/or agostic interaction of the α-phenyl group to Zr (Figure 4). Treatment of **17b** with $Cp_2Zr(CH_2CH_2Ph)_2$ under identical conditions afforded **19a** and **21a**, and a product derived from 2-[2-(methoxyisopropyl)phenyl]-5-phenylzirconacyclopentane **23**, which corresponds to **22** could not be obtained (Scheme 4). At this point in time, either one of the intermediates, zirconacyclopentane **24** or *o*-quinodimethane intermediate **25**, could be involved as a key intermediate for the formation of **19** or **21** (Figure 5). It is interesting to note that the reaction of *o-tert*-butylstyrene (**26**) with an equivalent amount of "Cp$_2$Zr" gave *o-tert*-butylethylbenzene (59%) along with the recovered **26** (35%) (Scheme 5). Furthermore, the reaction of $Cp_2Zr(CH_2CH_2Ph)_2$ with *o-tert*-butylstyrene (**26**) ended with a recovery of **26**. These observations imply that a ligand exchange would be possible in the reaction of *o-tert*-butylstyrene (**26**) with "Cp$_2$Zr" giving **26**−zirconocene complex, which did not react with butene. It is also obvious that **26** did not couple with styrene−zirconocene complex, and thus, the participation of the alkoxy group in *o*-**4** or **17** plays a significant role in the reaction with "Cp$_2$Zr". It should also be noted that the stereochemistry of heterocoupling products **21** or the supposed intermediate **20d** (R = F) for homocoupling (see, Scheme 2) is cis while the stereochemistry of homodimer **19** itself is a mixture of cis and trans isomers. Thus, the stereochemical outcome of homodimer **19** would suggest that once formed cis stereochemistry in **20** does not last through the reaction.[11]

Conclusions

In conclusion, we found unexpected and unprecedented reactions of "Cp$_2$Zr" with (alkoxymethyl)styrene derivatives. Reactions of *o*- or *p*-(alkoxymethyl)styrene derivatives with a stoichiometric amount of "Cp$_2$Zr" resulted in the insertion of zirconocene into a benzylic carbon−oxygen bond. Reactions of *o*-(1-alkoxyisopropyl)styrene derivatives with a stiochiometric and/or a catalytic amount of "Cp$_2$Zr" (Cp_2ZrCl_2 (10 mol %)) in the presence of 3 equiv of *n*-BuMgBr cause dimerization reactions as a major product. The catalytic process turned out to be efficient also for the dimerization of *o*-(alkoxymethyl)styrene, which yields benzylzirconocene species under the stoichiometric conditions. Heterocoupling reactions of *o*-(1-alkoxyisopropyl)styrene derivatives with styrene have been brought about in high cis-stereoselectivity. Although the precise reaction mechanism for the described formation of homo- and heterocoupling products has yet to be elucidated, the intramolecular Diels−Alder reaction is supposed to be involved at this point in time.

Experimental Section

Typical Procedure for Generation and Butene-Coupling Reactions of Benzylzirconocene Intermediates. To a solution of Cp_2ZrCl_2 (153 mg, 0.53 mmol) in THF (5 mL) was added *n*-BuLi (1.6 M solution in *n*-hexane, 0.66 mL, 1.05 mmol) at −78 °C and the mixture was stirred for 1 h at the same temperature. To this solution was added a solution of *o*-**4a** (112 mg, 0.50 mmol) in THF (2 mL) with gradual warming to room temperature, and the solution was stirred for 3 h. To this reaction mixture was added 1 M HCl (aq), extracting with ether. The organic layer was washed with brine and dried over anhydrous $MgSO_4$, and the filtrate was concentrated to dryness. The residue was purified by flash chromatography (*n*-hexane) to give **8a** (52 mg, 88%).

1-Methy-2-vinylbenzene (8a): The structure was confirmed by comparison of spectral data from a commercially available sample.

1-Methyl-2-(3-methylpentyl)benzene (10): This product was prepared from *o*-**4a** (112 mg, 0.50 mmol), Cp_2ZrCl_2 (307 mg, 1.05 mmol), and *n*-BuLi (1.6 M, 1.31 mL, 2.10 mmol) according to the typical procedure. Colorless oil. IR (neat) 2961, 2928, 2873, 1906, 1605, 1493, 739 cm^{-1}. ^{1}H NMR (CDCl$_3$, 300 MHz) δ 7.25−7.13 (4H, m), 2.78−2.56 (2H, m), 2.37 (3H, s), 1.66−1.25 (5H, m), 1.02 (3H, d, $J = 6.1$ Hz), 0.96 (3H, t, $J = 7.2$ Hz). ^{13}C NMR (CDCl$_3$, 75.5 MHz) δ 141.4, 135.7, 130.1, 128.7, 125.9, 125.7, 37.3, 34.7, 30.9, 29.4, 19.23, 19.19, 11.4. EI-MS (*m*/*z*) 176 (M$^+$).

Typical Procedure for Homocoupling Reactions under Catalytic Conditions. To a solution of **17b** (88 mg, 0.50 mmol) and Cp_2ZrCl_2 (14.6 mg, 0.05 mmol) in THF (5.2 mL) was added *n*-BuMgCl (0.84 M solution in THF, 1.79 mL, 1.50 mmol) at room temperature and the mixture was refluxed for 5 h. To this reaction mixture was added by 1 M HCl (aq) at 0 °C, extracting with ether. The organic layer was washed with brine and dried over anhydrous $MgSO_4$, and the filtrate was concentrated to dryness. The residue was purified by flash chromatography (*n*-hexane) to give **19a** (59 mg, 81%) as a

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[11] It is known that the formation of **19d** by intramolecular Diels−Alder reaction of *o*-quinodimethane intermediate is generated from a sulfone derivative. Thus, the formation of **19** from **21** might have occurred via a similar pathway. See: Levy, L. A.; Sashikumar, V. P. *J. Org. Chem.* **1985**, *50*, 1760.

mixture of trans/cis = 3.0. Recrystallization from EtOH gave *trans*-**19a** as a single isomer.

***trans*-6,6,12,12-Tetramethyl-4b,5,6,10b,11,12-hexahydrochrysene (*trans*-19a):** Colorless crystalline solid. Mp (EtOH) 169.5−172.0 °C. IR (KBr) 2955, 2905, 2854, 1485, 1344, 755, 743 cm^{-1}. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.46−7.18 (8H, m), 2.88 (2H, dd, J = 11.0, 1.0 Hz), 2.44 (2H, dd, J = 12.5, 1.0 Hz), 1.71 (2H, dd, J = 12.5, 11.1 Hz), 1.44 (12H, s). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 145.8, 138.9, 127.0, 126.1, 125.6, 125.4, 44.0, 38.6, 35.3, 33.1, 32.6. EI-MS (*m/z*) 290 (M$^+$). Anal. Calcd for $C_{22}H_{26}$: C, 90.73; H, 9.27. Found: C, 91.03; H, 9.23.

***cis*-6,6,12,12-Tetramethyl-4b,5,6,10b,11,12-hexahydrochrysene (*cis*-19a)**: Colorless crystalline solid. Mp (ether) 161.4−163.4 °C. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.43−7.15 (8H, m), 3.25 (2H, dd, J = 13.1, 4.2 Hz), 1.99 (2H, br t, J = 13.1 Hz), 1.69 (2H, dd, J = 14.2, 4.2 Hz), 1.40 (6H, s), 1.35 (6H, s). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 145.0, 140.0, 129.5, 126.4, 125.7, 125.3, 43.4, 35.3, 34.8, 31.3, 30.3.

Typical Procedure for Heterocoupling Reactions. To a solution of Cp_2ZrCl_2 (175 mg, 0.60 mmol) in THF (5 mL) was added *n*-BuLi (1.6 M solution in *n*-hexane, 0.75 mL, 1.20 mmol) at −78 °C with 1 h of stirring at the same temperature. To this solution was added a solution of **17b** (112 mg, 0.50 mmol) and **5a** (156 mg, 1.50 mmol) in THF (2 mL), which was gradually warmed to room temperature and stirred for 3 h. To this reaction mixture was added 1 M HCl (aq), extracting with ether. The organic layer was washed with brine and dried over anhydrous $MgSO_4$, and the filtrate was concentrated to dryness. The residue was purified by flash chromatography (*n*-hexane), and further purification was carried out by MPLC (*n*-hexane) to give **21a** (106 mg, 85%).

1,1,4-Trimethyl-3-phenyl-1,2,3,4-tetrahydronaphthalene (21a): Colorless crystalline solid. Mp (ether) 75.4−76.4 °C. IR (KBr) 2962, 2931, 1487, 1452, 1040, 763, 751, 699 cm^{-1}. ^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.37−7.31 (3H, m), 7.26−6.97 (6H, m), 3.38 (1H, ddd, J = 13.6, 4.8, 1.9 Hz), 3.09 (1H, dq, J = 7.2, 4.8 Hz), 2.25 (1H, dd, 13.6, 13.0 Hz), 1.73 (1H, dd, J = 13.0, 1.9 Hz), 1.44 (3H, s), 1.31 (3H, s), 0.87 (3H, d, J = 7.2 Hz). ^{13}C NMR (CDCl$_3$, 100 MHz) δ 144.8, 144.4, 142.1, 129.2, 128.2, 127.8, 126.9, 126.2, 126.0, 125.6, 40.4, 39.4, 37.2, 35.2, 32.7, 32.3, 18.1. EI-MS (*m/z*) 250 (M$^+$). Anal. Calcd for $C_{19}H_{22}$: C, 91.14; H, 8.86. Found: C, 91.25; H, 8.46.

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Supporting Information Available: Experimental procedures and characterization data for products and starting materials, and X-ray data of **19a**−**c**,**f**, **20**, and **21a** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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