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Zirconium Mediated Regioselective Carbon-Carbon Bond Formation Reactions

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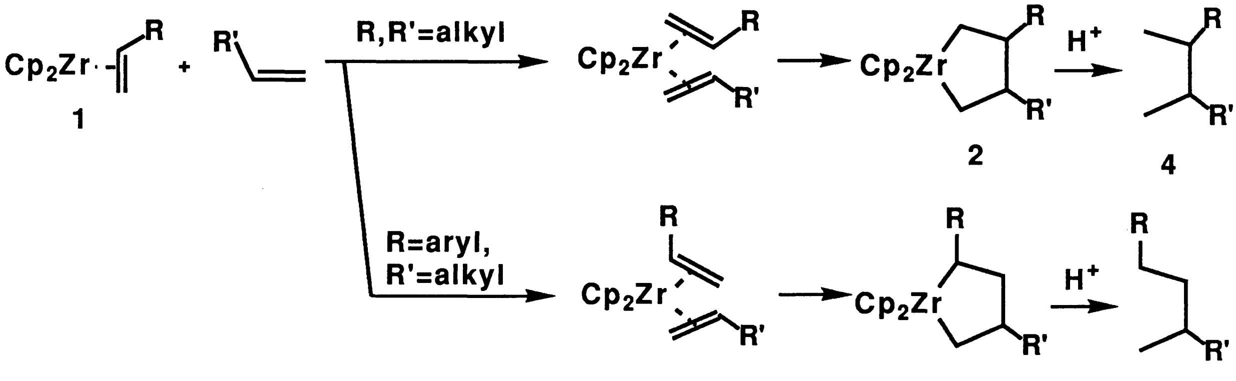
Reactions of zirconocene-alkene complexes with aldehydes gave alcohols as coupling products after hydrolysis. The carbon-carbon bond formation proceeded at C1 carbon of alkenes, in sharp contrast to the reactions of alkene-alkene coupling on zirconium. A similar alcohol was also obtained by the reaction of zirconacyclopentane with aldehyde after hydrolysis. Treatment of $(C_5Me_5)_2ZrEt_2$ with styrene gave 2-phenylbutane after hydrolysis contrary to the case of Cp_2ZrEt_2 which afforded 1-phenylbutane.

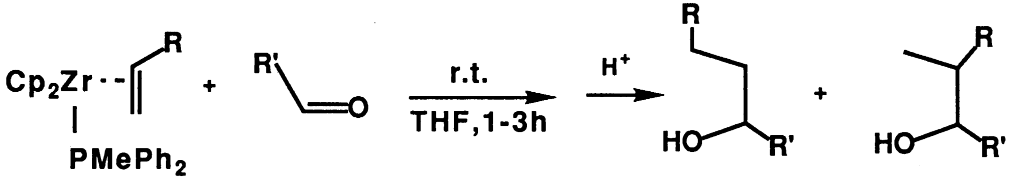
The first zirconocene-alkene complex, zirconocene-stilbene complex, was prepared[1) and its structure was determined by our group and Negishi's group.[2) Since then this area has attracted much attentions and zirconocene-alkene complexes have been prepared by several groups.[3-7) Recently we have found regio- and stereoselective carbon-carbon bond formation reactions of zirconocene-alkene complexes as shown below (Scheme 1).[8) Zirconocene-alkene species **1**, which could be quantitatively generated in situ by β-hydrogen abstraction and elimination of an alkane from dialkylzirconocenes, reacted with alkenes with high regioselectivities (>99%) to give zirconacyclopentanes **2** or **3**, and after hydrolysis the substituted butanes **4** or **5** were obtained. In these reactions the alkyl group R and/or R' comes to β-position of zirconacyclopentanes **2** with >99% regioselectivities, whereas aryl group R comes to α-position with >99% selectivities.



Scheme 1.

In the course of further investigations of reactions of these zirconocene-alkene complexes, we found regioselective carbon-carbon bond formation reactions of **1** with aldehydes, which led to the formation of alcohols after hydrolysis. Interestingly, the reaction with aldehydes gave the coupling products with an opposite orientation to the reaction with alkenes. Furthermore, we would like to describe here that phenyl group came to β-position of zirconacyclopentane in the reaction of styrene-ethylene coupling on zirconium when C_5Me_5 ligand was used instead of Cp ligand.

A typical coupling reaction was carried out as follows. Diethylzirconocene was prepared in situ by adding ethylmagnesium bromide in THF (2 mmol, 1.0 M, 2 cm^3) to a solution of Cp_2ZrCl_2 (1 mmol) in THF (5 cm^3) at -78 °C. The mixture was stirred for 1 h at the same temperature. After addition of $PMePh_2$ (1 mmol, 0.186 cm^3), the mixture was warmed to room temperature and stirred for 1 h. To this reaction mixture containing the zirconocene-ethylene complex thus prepared in high yield was added octanal (1 mmol, 0.156 cm^3). After stirring it for 2h, the resulting mixture was treated with dilute HCl_{aq} and extracted with hexane. Evaporation and distillation gave 3-decanol. Results are shown in Table 1. Products were analyzed by GC and NMR spectroscopy. Yields were determined by GC using internal standards.



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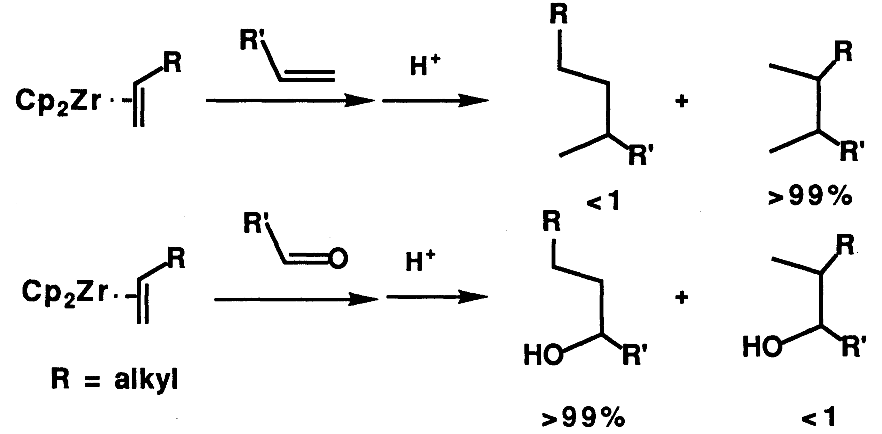
Scheme 2.

Table 1. Regioselective carbon-carbon bond formation reaction of zirconocene-alkene complex $Cp_2Zr(RCH=CH_2)(PMePh_2)$ with aldehydes R'CHO

R	R'	Time/h	Yield/% a)	Regioselectivity/% b)	
				6	7
H	$n\text{-}C_7H_{15}$	2	97	-	-
H	$n\text{-}C_4H_9(C_2H_5)CH$	2	97	-	-
H	$Ph(CH_3)CH$	1	90	-	-
H	Ph	2	95	-	-
CH_3	$n\text{-}C_7H_{15}$	2	71	>99	<1
CH_3	$n\text{-}C_4H_9(C_2H_5)CH$	2	46	>99	<1
CH_3	$Ph(CH_3)CH$	3	48	>99	<1
CH_3	Ph	2	67	>99	<1
C_2H_5	$n\text{-}C_7H_{15}$	2	29	>99	<1
C_2H_5	$n\text{-}C_4H_9(C_2H_5)CH$	2	64	>99	<1
C_2H_5	$Ph(CH_3)CH$	3	35	>99	<1

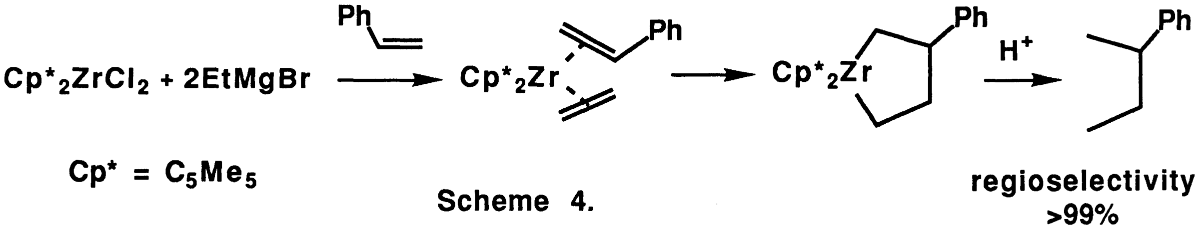
a), b) Determined by GC and NMR spectroscopy.

As shown in Table 1, alkene-complexes prepared in situ reacted with various aldehydes to give the corresponding alcohols in moderate yields after hydrolysis. It is known that the reaction of zirconocene-stilbene complex with acetaldehyde or acetone gave alcohol after hydrolysis. However, two regioisomers **6** and **7** are the possible products for the reactions of propene ($R=CH_3$) and 1-butene ($R=C_2H_5$) complexes. It is noteworthy that the regioisomers **6** were predominantly obtained with ≥99% selectivities. Interestingly, the selectivity observed here is opposite to that for the reactions of **1** with alkenes. Scheme 3 presents the difference in regioselectivities for the reactions of zirconium-alkene complexes with alkenes and aldehydes.



Scheme 3.

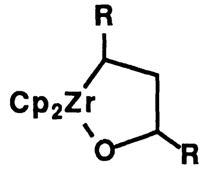
High regioselectivities of alkene-alkene coupling reactions can be explained by the presence of the equilibrium and the steric repulsion between Cp ligand and alkyl R group. β,β'-Dialkylzirconacyclopentane is the most thermodynamically stable compound among its isomeric products. In the case of aryl group, electronic factor is , in turn, the major one in determining orientation of R group. The presence of aryl group at α-carbon stabilize the negative charge of the carbon adjacent to zirconium. However, the steric effect can be expected even in the case of aryl group by the use of sterically hindered ligand. Indeed, the use of pentamethylcyclopenetadienyl ligand instead of Cp group led the formation of 2-phenylbutane after hydrolysis with >99% regioselectivity (Scheme 4, yield 38%).



Scheme 4.

For the reactions of zirconocene-alkene complexes with aldehydes, the factors which control the regioselectivities are not elucidated yet, but probably aldehydes attack the sterically less-hindered site of alkenes on zirconium.

Reactions of titanocene-ethylene complex with aldehydes have been reported.[9)] The products, 1-oxa-5-titanacyclopentanes were fully characterized by X-ray analysis very recently.[10)] The structure of zirconium analogue, 1-oxa-5-zirconacyclopentane, have been also determined by X-ray.[11)] Therefore, a possible reaction pathway of C-C bond formations of alkenes with aldehydes on zirconium involves the formation of oxazirconacyclopentane compounds **8**.[12,13)] Indeed, deuterolysis of the reaction mixture gave **9** (R = H, R' = Ph) and **10** (R = CH_3, R' = Ph) with 85% and 94% D incorporations, respectively. Unfortunately, monitoring the reaction of **1** (R = H) with benzaldehyde or 2-phenylpropanal in THF at room temperature by NMR spectroscopy did not show the clean formation of one species such as oxazirconacyclopentanes.



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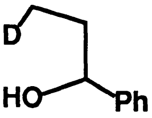

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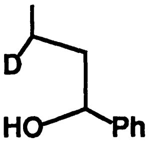

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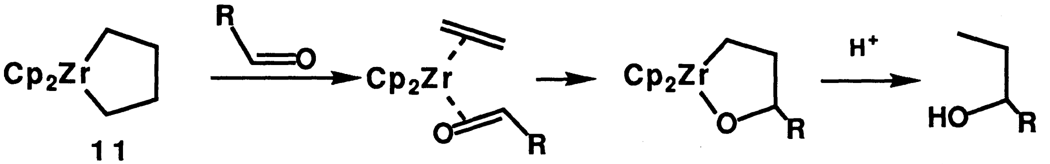
It was found, further, that the treatment of zirconacyclopentane **11** with 2-phenylpropanal gave the same alcohol, 2-phenyl-3-pentanol, in 53% yield after hydrolysis (50 °C, 1 h) as in the reaction of **1** with 2-phenylpropanal. This reaction can be explained by the β,β'-carbon-carbon bond activation, followed by the formation of oxazirconacyclopentanes as shown in Scheme 5.[14]



Yield 53%
$R=Ph(CH_3)CH$-

Scheme 5.

Further investigations are now in progress to make clear the factors which control the regioselectivities in the reactions of zirconocene-alkene complexes.

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