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## Rh(I)-catalyzed addition of alkenylzirconocene chlorides to aldimine derivatives

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**Abstract**— $[RhCl(COD)]_2$  (2 mol%) catalyzed reactions of alkenylzirconocene chloride complexes to *N*-Ts, -PO(OEt)<sub>2</sub> and COOR aldimine derivatives were efficiently carried out in dioxane at room temperature to give allylic amine derivatives in excellent yields. This is the first example of the catalytic addition reactions of alkenylzirconocene chloride complexes to aldimine derivatives. © 2003 Elsevier Science Ltd. All rights reserved.

Organozirconium compounds are gaining an increasing importance in organic synthesis.<sup>1</sup> Alkyl- or alkenylzirconocene chlorides, which are stable complexes at ambient temperature and readily accessible through hydrozirconation of alkenes or alkynes with Schwartz reagent ( $Cp_2ZrHCl$ ),<sup>2</sup> are considered convenient organometallic reagents as donors of alkyl or alkenyl anions. However, the inherently low reactivity of the organozirconocene chloride to the electrophilic reagents (e.g. aldehyde, aldimine, etc.) restrained its use as a synthetic reagent. Thus, the use of a catalyst or a stoichiometric mediator for the reaction of organozirconocene chlorides is essential to bringing about the carbon–carbon bond formation (Scheme 1).

It has been reported that  $Ag(I)^3$  or  $ZnBr_2^4$  is an efficient catalyst for the addition of alkyl- and alkenylzirconocene chloride to aldehydes. It has also been reported that the Me<sub>2</sub>Zn-mediated addition of alkenylzirconocene chloride to aldehydes<sup>5</sup> or aldimines<sup>5,6</sup> yields allylic alcohols or amines, respectively. To our knowledge, however, an efficient catalyst for the addition of organozirconocene chlorides to aldimine is unknown. Recently, Rh-catalyzed additions of organometallic reagents, such as tin (Sn),<sup>7</sup> bismuth (Bi),<sup>8</sup> titanium (Ti),<sup>9</sup> silicon (Si),<sup>10</sup> lead (Pb),<sup>11</sup> and boron (B),<sup>12</sup> to aldehydes, imines or  $\alpha$ , $\beta$ -unsaturated carbonyl compounds are being extensively studied by many research groups, and the validity is well recognized. Particularly, an efficient enantioselective version of the Rh-catalyzed addition of the organometallic reagents to  $\alpha,\beta$ -enone, aldehyde, and imine derivatives in the presence of a chiral phosphine ligand highlights the significance of Rh-catalyzed reaction in modern organic synthesis. In this report, we present Rh(I)-catalyzed addition reactions of alkenylzirconocene chloride complexes 1 to aldimine derivatives 2. It is the first example of the catalytic process for the addition of alkenylzirconocene chloride complexes 1 to aldimine derivatives 2 (Scheme 2).

At the outset, we examined the Rh(I)-catalyzed reactions of (E)-3,3-dimethyl-1-butenyl zirconocene chloride (1a), which is obtained by the hydrozirconation of *t*-butyl acetylene, with imine compounds derived from benzaldehyde and amines, and the results are shown in Table 1.



Scheme 1. Additions of organozirconocene derivatives to carbon-heteroatom double bonds.



Scheme 2.

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<sup>a</sup> Reactions were carried out at ambient temperature and monitored by TLC. Ratio of 1a:phenylaldimines=2:1.<sup>16</sup>

<sup>b</sup> Yields were isolated and calculated from phenlaldimines.

The reaction of **1a** with *N*-benzylidene aniline (**2a**) by using a [RhCl(cod)]<sub>2</sub> (2 mol%) catalyst yielded no trace of the addition product (entry 1). The lack of the reactivity of 2a would be a result of the low electrophilicity of the imine 2a. The same observation has been reported in the Rh(I)-catalyzed reaction of arylstannane compound with 2a.<sup>7h</sup> The reaction of 1a with *N*-benzylidene *p*-toluenesulfonamide (**2b**), which is activated by the electron-withdrawing sulforyl group, thus, indicated an excellent reactivity to give product 3a in 99% yield (entry 2). In the [RhCl(cod)]<sub>2</sub>-catalyzed reactions of 1a with 2b, dioxane turned out to be an excellent solvent compared to THF, toluene, or CH<sub>2</sub>Cl<sub>2</sub> (entries 2-5). Instead of using *N*-*p*-toluenesulfonyl group (N-Ts) of **2b**, N-substituents, such as N-PO(OEt)<sub>2</sub> and N-COOMe, also indicated a high reactivity under identical conditions, albeit the reactions were less efficient (entries 6 and 8). It should be mentioned that the bulky N-COt-Bu group retarded the reaction (entry 7). As for the examined catalysts, a cationic Rh(I) complex, [Rh(cod)<sub>2</sub>]BF<sub>4</sub>, exhibited excellent catalytic activity (entry 9). It is interesting to note that [Rh(OH)(cod)]<sub>2</sub> showed a high efficiency as well (entry 10). The neutral Rh catalyst, such as Rh(PPh)<sub>3</sub>Cl, or Rh(acac)(C<sub>2</sub>H<sub>4</sub>)<sub>2</sub>, was an inefficient catalyst (entries 11 and 12). Since the Rh(I)-catalyzed reaction of alkenylstannane with N-Ts aldimine 2b has been reported to proceed under heating conditions (60°C, 20 h),<sup>7</sup> the mildness of the present Rh-catalyzed additions of alkenylzirconocene chlorides 1 to N-Ts aldimine **2b** (ambient temperature, 0.5–3 h) is notable. Next, we investigated the effect of phosphine ligand as an additive and the results are listed in Table 2.

Although the 2 mol% [RhCl(cod)]<sub>2</sub>-catalyzed reaction of **1a** with **2b** efficiently proceeds to give **3a** without adding phosphine ligand (1 h, 99% yield) (entry 2, Table 1), an addition of a monodentate or bidentate phosphine ligand (P/Rh=2/1) to the mixture retarded

the reaction at ambient temperature (entries 1, 3, 5 and 7, Table 2). Heating of the reaction mixture at 80°C, however, gave **3a** in excellent yields in a short period of time (0.5 h, entries 4 and 6). A similar observation about the addition of phosphine ligand has been made Rh(I)-catalyzed reactions of arylstannanes to in aldimines.7f It should be mentioned that the addition of phosphine ligands, such as PPh<sub>3</sub>, dppe, and dppb, to the Rh(acac)( $C_2H_4$ )<sub>2</sub> catalyst, which is known to be an efficient catalyst for the conjugate addition reactions of organometallics, did not improve the yield of 3. The present [RhCl(cod)]<sub>2</sub>-catalyzed alkenylation procedure of N-Ts aldimine through the use of alkenylzirconocene chloride 1 was extended to a variety of N-Ts aldimine derivatives and alkenylzirconocene chloride complexes, and the results are shown in Table 3.

*N*-Ts aldimines derived from aromatic or aliphatic aldehydes reacted with  $\mathbf{1}$  to give allylic amine products in good to excellent yields (entries 1–6). The electron-

**Table 2.**  $[RhCl(cod)]_2$ -catalyzed reactions of **1a** with **2b** in dioxane in the presence of phosphine ligand<sup>a</sup>

Entry	P-ligand	Temp. (°C)	Time (h) <sup>b</sup>	3a Yield (%) <sup>c</sup>
1	PPh <sub>3</sub>	Ambient	12	48
2	PPh <sub>3</sub>	80	0.5	40
3	Dpped	Ambient	12	90
4	Dppe	80	0.5	95
5	Dppb <sup>e</sup>	Ambient	12	39
6	Dppb	80	0.5	87
7	Dppf <sup>f</sup>	Ambient	12	74
8	Dppf	80	12	80

<sup>a</sup> The ratio of P/Rh is 2/1.

<sup>b</sup> Reactions were monitored by TLC.

<sup>c</sup> Isolated yields.

<sup>d</sup> 1,2-Bis(diphenylphosphino)ethane.

<sup>e</sup> 1,4-Bis(diphenylphosphino)butane.

<sup>f</sup> 1,1'-Bis(diphenylphosphino)ferrocene.

**Table 3.** [RhCl(cod)]<sub>2</sub>-catalyzed reactions of 1 with *N*-Ts aldimine derivatives<sup>a</sup>

R <sup>1</sup>	$\overset{\text{CI}}{\swarrow} \overset{\text{rs}}{\overset{\text{ZrCp}_2}{\twoheadrightarrow}} \overset{\text{R}^{\text{Ts}}}{\overset{\text{R}^2}{\overset{\text{H}}{\longrightarrow}}} H$	2 mol% [RhCl(cod)] <sub>2</sub> dioxane, rt R	H 1 ~~~~	IN <sup>∠Ts</sup> 人 <sub>R<sup>2</sup></sub>
Entry	R <sup>1</sup>	R <sup>2</sup>	Time (h)	Yield (%) <sup>b</sup>
1	<i>t</i> -Bu 1a	Ph <b>2b</b>	1	<b>3a</b> 99
2	1a	p-CF <sub>3</sub> C <sub>6</sub> H <sub>5</sub>	1	83
3	1a	p-CH <sub>3</sub> OC <sub>6</sub> H <sub>5</sub>	1	96
4	1a	$n - C_8 H_{17}$	3	75
5	1a	$cy-C_6H_{11}$	1	97
6	1a	t-Bu	2	91
7	1a	PhCH=CH	12	<10
8	OEt	2b	6	70
9	Ph	2b	12	58
10	$n-C_4H_9$	2b	3.5	98
11	BnOC <sub>2</sub> H <sub>4</sub>	2b	12	83°
12	BnOCH <sub>2</sub>	2b	12	72°
13	$(E)-n-C_{3}H_{7}CH=C(n-C_{3}H_{7})-ZrCp_{2}Cl$	2b	24	80°
14	$Ph(CH_2)_4ZrCp_2Cl$	2b	24	-

<sup>a</sup> Ratio of 1:N-Ts aldimines = 2:1. Reactions were monitored by TLC.

<sup>b</sup> Yields were isolated and calculated from N-Ts aldimines.

<sup>c</sup> Ratio of 1:N-Ts aldimines = 3:1.

withdrawing or -donating substituent had little effect on the reaction rate (monitored by TLC) and product yields (entries 1-3). N-Ts imine derived from cinnamaldehyde proceeded to give product in a low yield (<10%) under identical conditions (entry 7). Alkenylzirconocene chloride complexes other than 1a indicated a comparable reactivity under the same conditions (entries 8-13). Although alkenylzirconocene chloride generated from internal alkyne, 4-octyne, reacted with *N*-Ts aldimine **2b** to give a product in good yield, it took a longer time (24 h) for the completion of the reaction (entry 13). Alkylzirconocene chloride complex did not react with N-Ts aldimine even by the use of Rh(I) catalysts listed in Table 1 (entry 14). Thus, the present Rh(I)-catalyzed addition of zirconocene complex to N-Ts aldimine is restricted to the alkenylzirconocene complex. It is known that the transfer of alkyl ligand from zirconocene to other metals (transmetalation) is more difficult than that of alkenyl ligands.<sup>13</sup> This could explain the nonreactivity of the *alkylzir*conocene chloride complex under the described reaction conditions. These results suggest that the present reaction involves the transfer of an alkenyl group from zirconium to rhodium metal (transmetalation) giving an alkenylrhodium species 4 and the following insertion of the carbon-nitrogen double bond of aldimine 2 into the Rh-carbon bond (Scheme 3).

In conclusion, we have presented the first catalytic addition of alkenylzirconocene chlorides 1 to *N*-Ts addimines through the use of Rh(I) catalyst. The ready



Scheme 3. Supposed catalytic cycle for the formation of 3.

access of alkenylzirconocene chlorides 1 and the present efficient reaction with aldimine compounds 2 could increase the significance of alkenylzirconocene chloride complex 1 as an alkenyl organometallic reagent. Further work on the Rh(I)-catalyzed addition of 1 to aldehydes and  $\alpha$ , $\beta$ -unsaturated carbonyl compounds (enone, ester, and amide) is now in progress and detailed results will be published in due course.

## Typical experimental procedure

Preparation of a solution of alkenylzirconocene chloride **1a** in dioxane. A suspension of  $Cp_2ZrHCl^{14}$  (258 mg, 1.0 mmol)<sup>15</sup> in dry  $CH_2Cl_2$  (4 mL) was treated at room temperature with 3,3-dimethyl-1-butyne (0.13 mL, 1.07 mmol), and the mixture was allowed to stir for 15 min. After the removal of all volatiles in vacuum, the resulting white solid **1a** was then dissolved in dry dioxane (4 mL), and the solution was directly used with the next reaction.

[*RhCl(cod)*]<sub>2</sub>-catalyzed reaction of **1a** with **2b**. A solution of *N*-benzylidene-4-methyl-benzenesulfonamide (**2b**)<sup>16</sup> (130 mg, 0.5 mmol) in dry dioxane (1 mL) and [RhCl(cod)]<sub>2</sub> (4.9 mg, 0.01 mmol) were added to a solution of **1a**, prepared as described, at room temperature. The reaction mixture was stirred for 1 h before being quenched with saturated aq. NaHCO<sub>3</sub>. The solution was extracted (3×) with EtOAc, and washed with brine before drying (MgSO<sub>4</sub>). After the usual workup, the crude product was purified by a silica gel column chromatography (hexane:EtOAc = 10:1) to give *N*-(4,4dimethyl-1-phenyl-pent-2-eny)-4-methyl-benzenesulfon amide (**3a**) in 99% yield.

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