



Cp₂TiCl₂-Catalyzed Pinacol-Type Coupling of Aliphatic Aldehydes by Use of Zinc and Chlorosilane

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Abstract: Bis(cyclopentadienyl)titanium dichloride (Cp₂TiCl₂) exhibits excellent catalytic activity toward the pinacol-type coupling reaction of aliphatic aldehydes with the assistance of zinc powder and chlorosilane. © 1998 Elsevier Science Ltd. All rights reserved.

The reductive coupling reactions of carbonyl compounds with the aid of low-valent metals is an important method for the construction of a vicinally functionalized carbon-framework.¹ Although numerous reagents have been developed to accomplish the transformation, examples of the catalytic use of low-valent metals are limited to a few cases.² Recently, we have revealed a novel catalytic system consisting of a low-valent vanadium complex, zinc powder, and chlorosilane, which effects the catalytic pinacol-type coupling of aliphatic aldehydes.^{2h} During the course of our study on this catalytic system of vanadium, we found that bis(cyclopentadienyl)titanium dichloride (Cp₂TiCl₂) acts as a useful catalyst for the reductive coupling of aldehydes and ketones in the presence of zinc and chlorotrimethylsilane (eq 1).³⁻⁵



Table 1. Cp₂TiCl₂-Catalyzed Pinacol-Type Coupling of Et₂CHCHO^a

Run	Coreductant	Cat., mol%	Additive	Solvent	2, Yield, % ^b	dl / meso ^b
1	Zn	3.0	Me ₃ SiCl	DME	80	67 / 33
2	Zn	3.0	—	DME	0	
3	—	3.0	Me ₃ SiCl	DME	0	
4	Zn	1.0	Me ₃ SiCl	DME	75	65 / 35
5	Mg	3.0	Me ₃ SiCl	DME	0	
6	Mg	3.0	Me ₃ SiCl	THF	10	78 / 22
7	Zn	3.0	Me ₃ SiCl	THF	64	73 / 27
8	Zn	3.0	Me ₃ SiCl	Et ₂ O	27	35 / 65

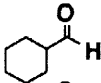

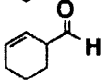

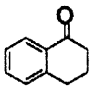
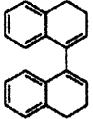
^a Reaction conditions: 1 (1.0 mmol), Zn (2.0 mmol), Me₃SiCl (2.0 mmol), solvent (7 mL), r.t., 13 h.

^b Determined by ¹H NMR.

As can be seen in Table 1, the catalytic pinacol-type coupling requires the presence of both zinc powder and chlorosilane⁶ (runs 1-3). The use of magnesium in place of zinc sharply decreased the yield of the coupling product 2 (runs 5-6). The amount of the catalyst could be reduced to 1.0 mol% (run 4). The reductive coupling proceeded efficiently by using DME or THF as a solvent, but not in Et₂O (runs 1, 7-8).

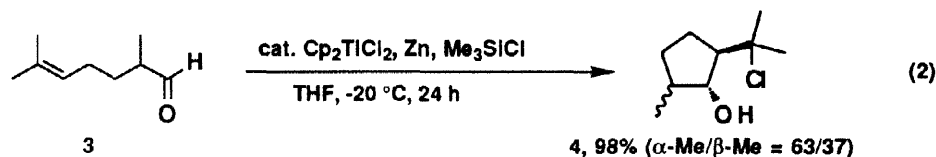
Table 2 represents the results of the Cp_2TiCl_2 -catalyzed reductive coupling of aldehydes and ketones. The procedure can be applied to primary and secondary aldehydes, providing the corresponding oxlanes **2** with moderate and excellent diastereoselectivities, respectively (runs 1-4). In the case of α -tetralone, the initial product, vicinal diol, underwent dehydration to give the corresponding conjugate diene (run 5).

Table 2. Cp_2TiCl_2 -Catalyzed Pinacol-Type Coupling^a

Run	Substrate	Product	Yield, % ^b	dl / meso ^b
1	${}^n\text{C}_5\text{H}_{11}\text{CHO}$	2 (R = ${}^n\text{C}_5\text{H}_{11}$)	60	63 / 37
2	$\text{PhCH}_2\text{CH}_2\text{CHO}$	2 (R = PhCH_2CH_2)	88	67 / 33
3 ^c		2 (R = )	87 (85) ^d	96 / 4
4 ^c		2 (R = )	66 (53) ^d	81 / 19
5			65 (60) ^d	

^a Reaction conditions: **1** (1.0 mmol), Zn (2.0 mmol; activated by the treatment with HCl (1.5 M) and washed with diethyl ether, purchased from Wako Pure Chemical Industries, Ltd.), Me_3SiCl (2.0 mmol), Cp_2TiCl_2 (3 mol%), DME (7 mL), r.t., 13 h unless otherwise stated. ^b Determined by ¹H NMR. ^c Reaction temperature, 0 °C. ^d Isolated yield.

Next, we demonstrated the intramolecular cyclization of aldehyde **3** bearing a carbon-carbon double bond at an appropriate position by using the cat. Cp_2TiCl_2 / Zn / Me_3SiCl system. The desired reaction proceeded successfully, affording the cyclopentanol derivative **4** in excellent yield, as indicated in eq 2. This cyclization also required the combination of the catalytic system. The absence of Cp_2TiCl_2 or Zn resulted in the complex mixture with the lower selectivity, suggesting that the present cyclization proceeds via a 5-*exo* cyclization of a ketyl-type intermediate and subsequent chlorine-atom transfer.



In conclusion, we have disclosed a novel catalytic system of Cp_2TiCl_2 , which is highly effective for the pinacol-type coupling of aliphatic aldehydes. Further investigation along this line is now in progress.

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- Conceivably, Me_3SiCl contributes to both activation of the catalyst and substrates and regeneration of the catalyst.