A Catalytic System Consisting of Vanadium, Chlorosilane, and Aluminum Metal in the Stereoselective Pinacol Coupling Reaction of Benzaldehyde Derivatives

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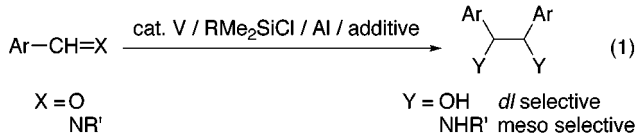
Introduction

Recently, the development of catalytic reactions for stoichiometric electron-transfer processes has attracted increasing attention because of the synthetic ease and efficiency of the process. This concept has been demonstrated in the pinacol coupling of ketones catalyzed by catalytic Cp_2TiCl_2/RMgBr[1] or electrochemical coupling using catalytic $SmCl_3$.[2] The silylation system is another catalytic method of reductive carbonyl coupling,[3] which was developed by Fürstner's group[4] and our group[5] independently to demonstrate the catalytic McMurry coupling and pinacol coupling reactions, respectively. Quite recently, high diastereoselectivity has been achieved in the pinacol coupling using a catalytic low-valent early transition metal system.[5c−e,6−9] Our system consisting of catalytic Cp_2VCl_2/R_3SiCl/Zn has been revealed to work in the diastereoselective pinacol coupling reaction of aliphatic aldehydes and aromatic aldimines, giving the corresponding vicinal diols and diamines with excellent *dl*- and *meso*-selectivity, respectively.[5c,e] However, this catalytic system does not exhibit enough stereoselectivity in the case of aromatic aldehydes. The stereoselectivity of the product depends on the individual components of the system and their cooperation. The stereochemical outcome of the coupling products is determined by the stereochemistry of the possible transition states. From these points of view, a vanadium (or titanium) catalyst and chlorosilane are considered to play a key role. It is also important how the catalyst is reduced with a co-reductant. The choice of co-reductants is expected to affect the reaction course, which prompted us to investigate the influence of the co-reductant on the stereoselectivity. We herein report a combination of a vanadium catalyst and an aluminum co-reductant in the presence of a chlorosilane that effects the selective reductive coupling of aromatic aldehydes and aldimines (eq 1).



(1)

Results and Discussion

To construct an efficient reduction system using a vanadium catalyst, we first examined the reduction of benzaldehyde (**1a**) with a vanadium catalyst (5 mol %) in the presence of Me_3SiCl and several metals. The results for the reductive coupling of **1a** by using several co-reductants such as Mg, Mn, Zn, and Al are summarized in Table 1.

The use of Mg as a co-reductant for the catalytic coupling of **1a** was not effective for the stereoselective coupling, because the reaction was accompanied by the formation of stilbene as a byproduct (ca. 10% yield, entry 1). However, Mn provided **2a** in improved yield and with similar diastereoselectivity (entry 2). The use of a VCl_3−Zn reagent, which is known to attain high stereoselectivity in the stoichiometric reductive coupling of aliphatic aldehydes,[10] improved the stereoselectivity (entry 3). Although the use of Al powder gave stilbene as a byproduct (ca. 10% yield), the highly *dl*-selective formation of the diol **2a** was observed in this system (entry 4). In the hope of improving the diastereoselectivity of the reaction, the influence of vanadium catalysts on this reductive coupling was studied. Cp_2VCl_2, which was an effective catalyst for the reductive coupling of secondary aliphatic aldehydes, indicated low yield and selectivity in the coupling of **1a** using Al powder and Me_3SiCl (entry 5). However, the oxovanadium $VOCl_3$, which is widely accepted as a one-electron oxidant, was found to catalyze a highly selective pinacol coupling of **1a** in the presence of Al powder and Me_3SiCl (entry 6). This result suggests that an active low-valent vanadium species may be generated in situ through reduction of the oxovanadium(V) with Al. The diastereoselectivity was improved under the optimized conditions, and this system was successfully applied to a variety of aromatic aldehydes to produce the corresponding 1,2-diols in good yields with excellent selectivity, as summarized in Table 2.

Purification of Me_3SiCl is very important in these reductive coupling reactions. The use of undistilled Me_3SiCl lowered the diastereoselectivity of **2a** (*dl*/meso = 85/15). The benzaldehydes bearing *p*-methyl and

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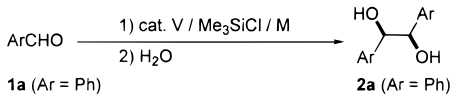
Table 1. Vanadium-Catalyzed Pinacol Coupling of 1a[a]



1a (Ar = Ph) **2a** (Ar = Ph)

			2a	
entry	cat. V	M	yield, %[b]	*dl*/meso[b]
1	VCl_3	Mg	66	62/38[c]
2	VCl_3	Mn	83	68/32
3	VCl_3	Zn	76	79/21
4	VCl_3	Al	56	84/16[c]
5	Cp_2VCl_2	Al	50	60/40
6	$VOCl_3$	Al	70	90/10[d]

[a] Reaction conditions: 3.3 mmol of **1a**, 5 mol % of cat. V, 6.6 mmol of Me_3SiCl, 6.6 mmol of M, 10 mL of THF, rt, Ar, 24 h. [b] Determined by ^1H NMR. [c] Stilbene was obtained in ca. 10% yield. [d] Reaction temperature was 50 °C.

Table 2. Pinacol Coupling of 1 by Catalytic $VOCl_3$/ Me_3SiCl/Al System[a]

			2	
entry	1		yield, %[b]	*dl*/meso[c]
1	C_6H_5	**1a**	68	> 95/5
2	*p*-MeC_6H_4	**1b**	62	> 95/5
3	*p*-ClC_6H_4	**1c**	89	> 95/5
4[d]	*p*-$MeOC_6H_4$	**1d**	49	90/10
5	*m*-ClC_6H_4	**1e**	77	> 95/5
6		**1f**	84	> 95/5

[a] Reaction conditions: 3.3 mmol of **1a**, 5 mol % of cat. V, 6.6 mmol of Me_3SiCl, 6.6 mmol of Al, 10 mL of DME, 50 °C, Ar, 24 h. [b] Isolated yield. [c] Determined by ^1H NMR. [d] Reaction time was 48 h.

p-chloro groups (**1b** and **1c**) were converted to the corresponding diols **2b** and **2c**, respectively, with excellent diastereoselectivity (entries 2 and 3), whereas **1d** with a strong electron-releasing substituent was reduced very slowly. Although 31% of **1d** was recovered after reaction for 48 h, the diol **2d** was produced in a moderate yield with excellent selectivity (entry 4). In contrast, the polymerization product was obtained in the case of *p*-cyanobenzaldehyde. The benzaldehyde **1f**[11] bearing an olefinic moiety also coupled diastereoselectively in a good yield, without formation of any cyclization product (entry 6).

Moreover, Al powder could successfully be employed as a co-reductant in the vanadium-catalyzed reductive coupling of benzaldimines (**3**), as illustrated in Table 3. Attempted reduction of **3a** under the reduction conditions mentioned above afforded a trace amount of products along with 50% of **1a**, which was formed by hydrolysis of the starting **3a** under the reaction conditions (entries 1 and 2). In comparison, Cp_2VCl_2 showed moderate catalytic activity in the presence of $PhMe_2SiCl$/Al in DMF (entry 3). It is noteworthy that the addition of imidazole to this system markedly improved the yield of **4a** (entry 4). Similarly, as observed in the reductive coupling of benzaldimines by use of a system of catalytic vanadium compound/chlorosilane/Zn,[5e,12] the present system of catalytic Cp_2VCl_2/$PhMe_2SiCl$/imidazole/Al also indicated *meso*-selectivity, and furthermore, the yields were improved successfully. Starting from *p*-methyl- and *p*-chlorobenzaldimines (**3b** and **3c**), the corresponding diamines were

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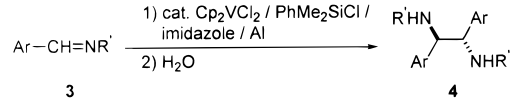
Table 3. Reductive Coupling of 3 by Catalytic Cp_2VCl_2/ $PhMe_2SiCl$/Al/Imidazole System[a]



3 **4**

					4	
entry	Ar	R′	**3**	cat. V	yield, %[b]	*dl*/meso[c]
1[d,e]	C_6H_5	allyl	**3a**	$VOCl_3$	trace[f]	
2[e]	C_6H_5	allyl	**3a**	$VOCl_3$	trace[f]	
3[e]	C_6H_5	allyl	**3a**	Cp_2VCl_2	30	13/87
4	C_6H_5	allyl	**3a**	Cp_2VCl_2	86	13/87
5	*p*-MeC_6H_4	allyl	**3b**	Cp_2VCl_2	62	11/89
6	*p*-ClC_6H_4	allyl	**3c**	Cp_2VCl_2	72	25/75
7	C_6H_5	isopropyl	**3d**	Cp_2VCl_2	quant	45/55
8	C_6H_5	*n*-hexyl	**3e**	Cp_2VCl_2	71	23/77

[a] Reaction conditions: 2.0 mmol. of **3**, 5 mol % of cat. V, 4.0 mmol of $PhMe_2SiCl$, 4.0 mmol of Al, 3.0 mmol of imidazole, 10 mL of DMF, rt, Ar, 24 h. [b] Isolated yield. [c] Determined by ^1H NMR. [d] Me_3SiCl was used instead of $PhMe_2SiCl$. [e] In the absence of imidazole. [f] **1a** was obtained in 50% yield.

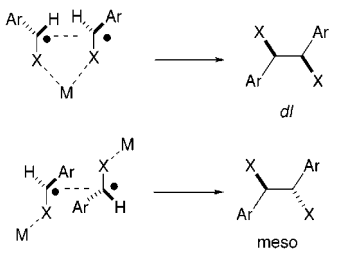
produced with moderate to good diastereoselectivity (entries 5 and 6). However, the selectivity was lowered by a change of the substituent on nitrogen from the allyl group to an isopropyl or *n*-hexyl group (entries 7 and 8). The diastereoselectivity strongly depends on the substituent on nitrogen.

In conclusion, it has been demonstrated that the reductive coupling of benzaldehydes could be catalyzed effectively by a vanadium complex in the presence of a chlorosilane and a co-reductant. The best result was obtained by use of Al as a co-reductant. An addition of imidazole to this system improved the yields of coupling of benzaldimines. The difference in the stereoselectivity might be explained by the difference in their intermediates.[12]

Experimental Section

General Procedure for Reductive Coupling Reaction of Benzaldehyde Derivatives (1). To a mixture of Al (178 mg, 6.6 mmol, Kanto Chemical Co., Inc.) in DME (9.5 mL) was added a solution (0.5 mL) of $VOCl_3$ (0.331 mL, 3.3 mmol) in DME (10 mL) at room temperature under argon. The reaction mixture was heated at 50 °C, and the color of the solution changed from brown to red purple. Distilled Me_3SiCl (0.838 mL, 6.6 mmol) was added to the reaction mixture, and the color changed from red purple to light blue. The benzaldehyde **1** (3.3 mmol) was added to the mixture, and the color again changed from light blue to brown. The mixture was kept at 50 °C with magnetic stirring for 24 h. After the mixture cooled to room temperature, ether (10 mL) and aqueous HCl (1.5 M, 10 mL) were added to the resulting mixture, and two liquid layers were separated. The organic layer was washed with saturated aqueous $NaHCO_3$ (10

(12) The stereoselectivity for the formation of diols and diamines is described in ref 5d; a cyclic intermediate is suggested to favor the formation of the *dl*-isomer. On the other hand, an acyclic intermediate is proposed to give *meso*-selectivity. Although the role of a co-reductant requires further detailed mechanistic experiment, it may affect the transition state.



mL), water (10 mL × 2), and brine (10 mL), dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (25 g; eluent, hexane/ethyl acetate = 50:0, 48:2, 46:4, 44:6, 42:8, 40:10, 35:15, 30:20, 25:25, each × 50 mL), giving **2**.

The registry numbers are as follows. *(R*,R*)*-1,2-Bisphenyl-1,2-ethanediol (**2a**): 655-48-1; *(R*,R*)*-1,2-bis(4′-methylphenyl)-1,2-ethanediol (**2b**): 66749-58-4; *(R*,R*)*-1,2-bis(4′-chlorophenyl)-1,2-ethanediol (**2c**): 116262-76-1; *(R*,R*)*-1,2-bis(4′-methoxyphenyl)-1,2-ethanediol (**2d**): 39090-28-3; *(R*,R*)*-1,2-bis(3′-chlorophenyl)-1,2-ethanediol (**2e**): 188839-74-9.

***(R*,R*)*-1,2-Bis(2′-allylphenyl)-1,2-ethanediol (2f).** Mp 57 °C; IR (neat) 3304, 1032, 1002, 761 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51−6.86 (m, 10 H), 5.64−5.44 (m, 2 H), 4.91−4.69 (m, 4 H), 2.94 (m, 2 H), 2.83 (dd, 2 H, J = 16.2, 6.6 Hz), 2.61 (dd, 2 H, J = 16.2, 6.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.1 (C), 137.7 (C), 137.0 (CH), 129.4 (CH), 127.8 (CH), 127.5 (CH), 126.4 (CH), 115.6 (CH_2), 74.5 (CH), 36.1 (CH_2); MS (EI) m/z 296 (M^+), 148. Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81,50; H, 7.43.

General Procedure for Reductive Coupling Reaction of Aldimine Derivatives (3). To a mixture of Cp_2VCl_2 (25 mg, 0.1 mmol), Al (108 mg, 4.0 mmol), and imidazole (204 mg, 3.0 mmol) in DMF (10 mL) was added $PhMe_2SiCl$ (683 mg, 4.0 mmol) at room temperature under argon. After the mixture stirred for 1 h, **3** (2.0 mmol) was added to the mixture. The mixture was kept at room temperature with magnetic stirring for 24 h. Chloroform (10 mL) and aqueous HCl (1.5 M, 10 mL) were added to the resulting mixture, and two liquid layers were separated. The organic layer was washed with saturated aqueous $NaHCO_3$ (10 mL), water (10 mL × 2), and brine (10 mL), dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (25 g; eluent, hexane/ethyl acetate = 50:0, 48:2, 46:4, 44:6, 42:8, 40:10, 35:15, 30:20, 25:25, each × 50 mL), giving **4**.

The registry numbers are as follows. *(R,S)-N,N′*-Diallyl-1,2-diphenyl-1,2-ethanediamine (**4a**): 219517-92-7; *(R,S)-N,N′*-diallyl-1,2-di(4-methylphenyl)-1,2-ethanediamine (**4b**): 219517-93-8; *(R,S)-N,N′*-diallyl-1,2-di(4-chlorophenyl)-1,2-ethanediamine (**4c**): 219517-94-9; *(R,S)-N,N′*-di(1-methylethyl)-1,2-diphenyl-1,2-ethanediamine (**4d**): 55079-98-6; *(R,S)-N,N′*-dihexyl-1,2-diphenyl-1,2-ethanediamine (**4e**): 60509-69-5.

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