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Highly Stereo-Controlled Pinacol Coupling Reaction of Benzaldehyde Derivatives by Use of Vanadium Catalytic System

2000

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Preface

The work presented in this thesis has been carried out under the guidance of Professor Toshikazu Hirao at Osaka University during 1997-1999.

This thesis deals with diastereoselective reductive coupling reaction using a catalytic amount of early transition metal in the present of co-reductant, chlorosilane, and additive. The results and findings obtained through this work gave important information on the control of stereoselectivity in the reductive coupling of aldehydes derivatives. This basic work is expected to contribute to the further development of the highly stereoselective catalytic synthesis of *vic*-bifunctionalized stretchers.

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Contents

General Introduction

The vicinally functionalized structures are often present in the natural products and biologically active molecules,[1] especially, the antitumor activity compounds such as the taxol,[2] attenol A,[3] and azinomycins,[4] which possess vicinal diol units (Figure 1).

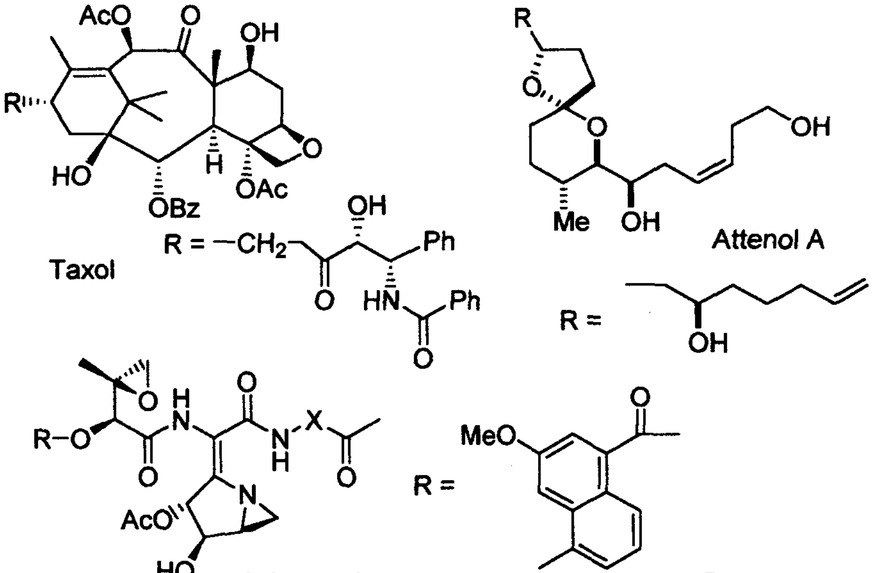


Figure 1

The optical active *vic*-diol and *vic*-diamine compounds are used as chiral ligands in a number of catalytic asymmetric synthesis.[5] For example, tartaric acid derivatives are employed for the enantioselective Sharpless epoxidation.[6] Also, Corey's group[7] reported that the chiral 1,2-diamines are excellent as chiral ligands in Lewis acid-catalyzed aldol condensation (Figure 2).

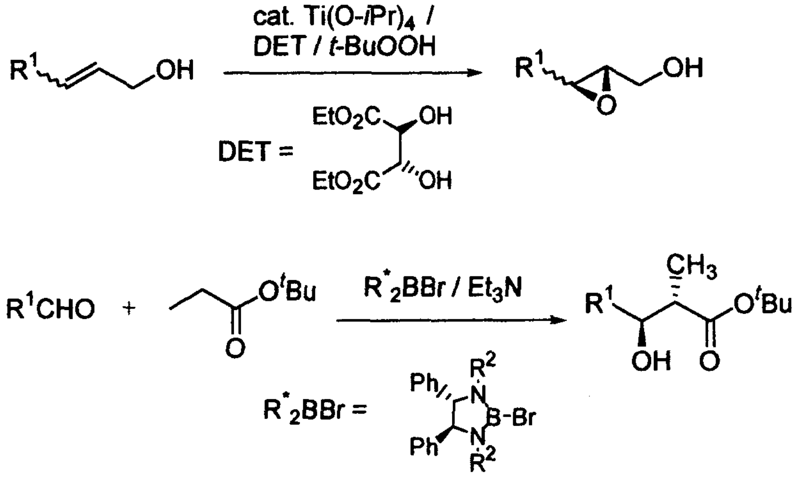
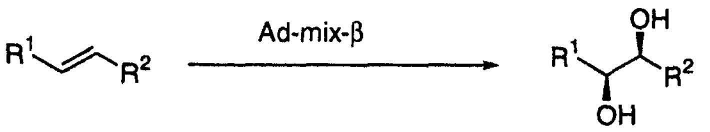


Figure 2

The *vic*-diol and *vic*-diamine compounds have been obtained from natural products such as sugars and amino acids, which were readily available and relatively cheap. However, since the *vic*-bifunctionalized compounds derived from sugars and amino acids are limited, a number of the synthetic methods of the *vic*-diol and *vic*-diamine units have been recently developed based on the organometallic procedures.[8] The presentative methods, which are widely utilized for the total synthesis of natural products and biologically active compounds, are shown in the following equations.

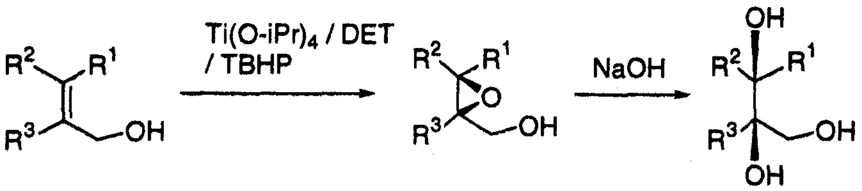
Asymmetric Osmium Oxidation[9] (Equation 1)



(1)

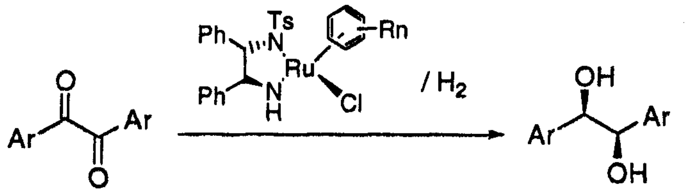
Ad-mix-β: $K_2OsO_2(OH)_4$,$(DHQD)_2$-PHAL, K_2CO_3, $K_3Fe(CN)_6$

Sharpless Asymmetric Epoxidation[10] (Equation 2)



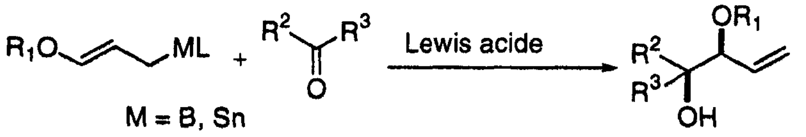
(2)

Reduction of 1,2-Diketone[11] (Equation 3)



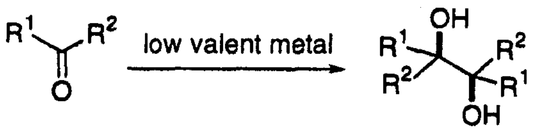
(3)

Addition to Carbonyl Compounds[12] (Equation 4)



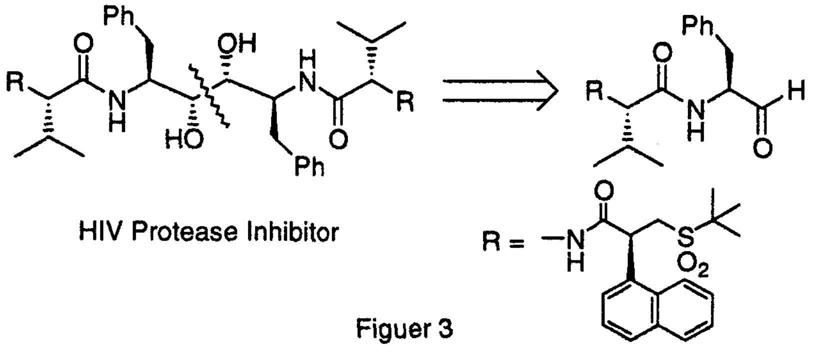
(4)

Pinacol Coupling Reaction[13] (Equation 5)



(5)

Among the procedures, the reductive coupling methods, *e.g.*, pinacol coupling reaction, are advantageous in terms of simplifying the synthetic route, because the required functional groups can be prepared before reductive coupling (Figure 3).



Figuer 3

The substrates for the coupling reaction, such as aldehydes and ketones, can be easily prepared by Swern oxidation[14] or Jones oxidation[14] of the corresponding alcohols.

The use of sodium or lithium as low-valent metals for pinacol coupling was difficult in the later stage of total synthesis, because they were too active to destroy other functional groups. According to the development of a new efficient low-valent metals for pinacol coupling reaction has been required. Mukaiyama's group[15] and Tyrlik's group[16] reported that the reagent consisted of titanium compound and Zn or Mg metal had been applied to pinacol coupling reaction and McMurry and co-workers[17] also revealed McMurry coupling reaction using $TiCl_3$-$LiAlH_4$ (Figure 4).

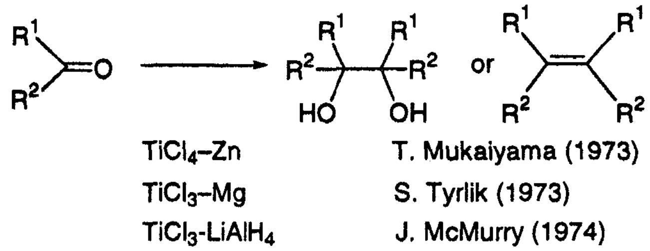
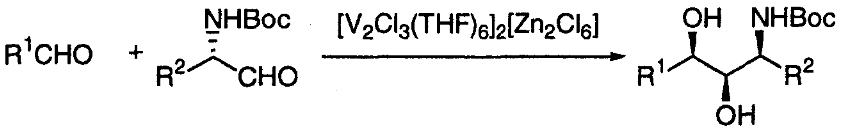


Figure 4

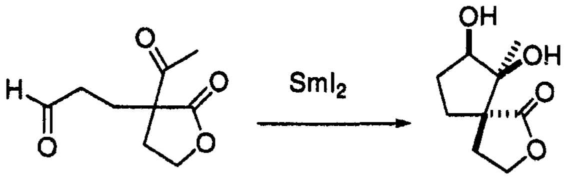
Recently, stereoselective pinacol coupling reactions have been developed using various low-valent transition metals[18, 19] (Equations 6 and 7). However, the dimerization reactions usually require stoichiometric or more excess amounts of low-valent metal complexes.



(6)

dl / meso = > 20 / 1

S. F. Pedersen (1994)

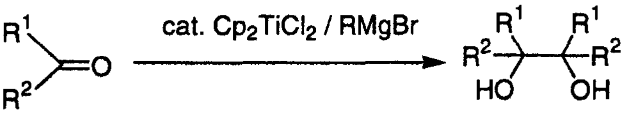


(7)

cis / *trans* = 200 / 1

G. A. Molander (1994)

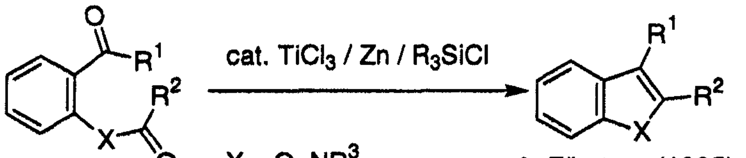
In contract, a catalytic pinacol coupling reaction of aldehyde can be disclosed for the first time by Zhang' group,[20, 21] using titanium compounds in presence of a Grignard reagent (Equation 8).



(8)

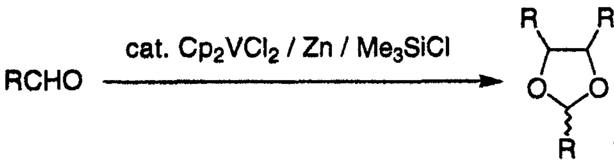
Y. Zhang (1988)

The method utilizing silyl chlorides as the additive for the catalytic reductive coupling, *i.e.,* McMurry and pinacol coupling, has been developed by Fürstner's group, [22] Hirao's groups, [23] and Endou's group[24] in 1995 and 1996 (Equations 9, 10, and 11).



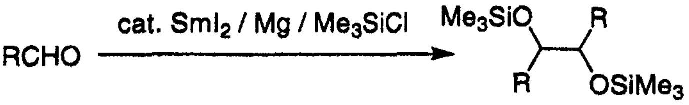
(9)

A. Fürstner (1995)



(10)

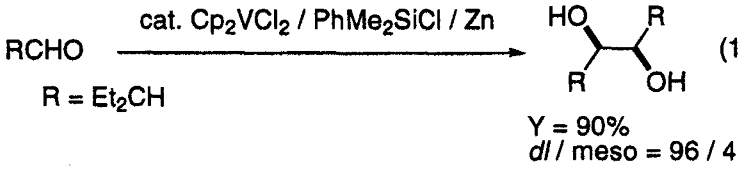
T. Hirao (1996)



(11)

T. Endo (1996)

However, these catalytic reactions consisting early transition metal, Me_3SiCl, and co-reductant did not indicate the high diastereoselectivity. Quite recently, high diastereoselectivities were observed in the several catalytic systems of pinacol coupling reaction.[25, 26] We also reported the catalytic system consisted of Cp_2VCl_2, $PhMe_2SiCl$, and Zn was effective for the diastereoselective pinacol coupling of secondary aldehydes.[27] (Equation 12).



(12)

This thesis deals with the catalytic pinacol coupling of aromatic aldehydes and aldimines with early transition metal catalyst, co-reductant, and additives. In chapter 1, it was clarified that the catalyst system consisting of $VOCl_3$ / Me_3SiCl / Al showed the excellent diastereoselectivity in pinacol coupling reaction of the benzaldehyde. In chapter 2, it was shown that Cp_2VCl_2 / $PhMe_2SiCl$ / Zn was the efficient catalytic system in diastereoselective reductive coupling reaction of benzaldimines, and in this case the excellent meso selectivity was observed. In addition, the pinacol coupling reaction was found to be promoted by the addition of imidazole in the Cp_2VCl_2 / $PhMe_2SiCl$ / Al catalyst system. Chapters 3 deals with the diastereoselective pinacol coupling reaction of the primary aliphatic aldehydes using the system consisted of cat. V / R'_3SiCl / M. The use of titanium catalyst instead of vanadium was formed to lead to the formation of 1,3-dioxsolane in the place of 1,2-diols in good yield with the *dl*-selectivity. Moreover, asymmetric catalytic pinacol coupling reaction of aldehydes was investigated.

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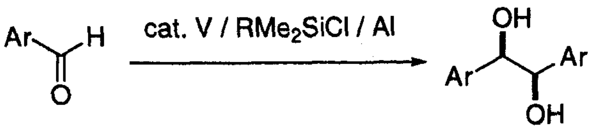
Chapter 1. High Diastereoselective Pinacol Coupling Reaction of Benzaldehydes by the Vanadium Catalyst

1-1. Introduction

The reductive dimerization of carbonyl compounds and their imine derivatives with low-valent metal complexes is an important method for vicinally bifunctonalized carbon-carbon bond formation.[1] However, the dimerization reactions usually require stoichiometric or more excess amounts of low-valent metal complexes. Recently, the development of catalytic reactions for stoichiometric electron transfer processes has attracted increasing attention because of the efficiency of the process. This concept has been demonstrated in pinacol coupling of ketones catalyzed by cat. Cp_2TiCl_2 / RMgBr[2] or electrochemical coupling using cat. $SmCl_3$.[3] The silylation system is another catalytic method of reductive carbonyl coupling, [4] which was developed by Fürstner's group[5] and our group[6] 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.[6c-e,7,8,9,10,11] Our system consisting of cat. Cp_2VCl_2 / R_3SiCl / Zn has been revealed to work in the diastereoselective pinacol coupling reaction of aliphatic aldehydes and aldimines, giving the corresponding vicinal diols and diamines with excellent *dl*- and *meso*-selectivity, respectively.[6c,6e] However, this catalytic system does not exhibit satisfactory diastereoselectivity in the case of aromatic aldehydes. The diastereoselectivity 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-reductant is expected to affect the reaction course, which prompted us to investigate the influence of the co-reductant on the stereoselectivity. In chapter 1, a combination of a vanadium catalyst and an aluminum co-reductant in the presence of a chlorosilane is reported to the selective reductive coupling of aromatic aldehydes. (Equation 1).

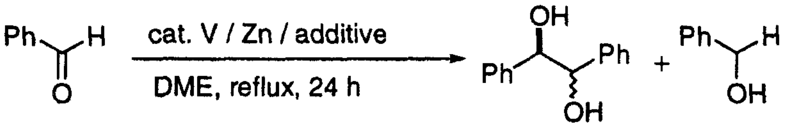


(1)

dl selective

1-2. Results and Discussion

At first, to construct the catalytic pinacol coupling reaction of the benzaldehyde (**1a**) using the vanadium catalyst, the influence of additives such as tin or silicon reagents on the diastereoselectivity was investigated (Equation 2 and Table 1).



1a **2a** **3a**

(2)

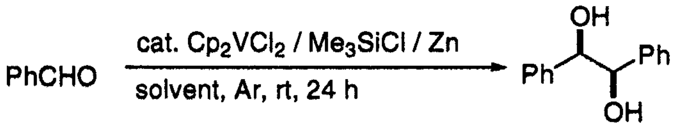
Table 1. **Influence of Additive on the Reductive of 1a** [a]

entry	additive	**1a** conversion [b]	**2a** yield, % [b]	**3a** yield, % [b]
1	HSnBu$_3$	100%	0	60 [c]
2 [d]	HSnBu$_3$	50%	0	30 [c]
3 [e]	HSnBu$_3$	10%	0	60 [c]
4	Allyl-SnBu$_3$	70%	0	trace [f]
5	imidazole	60%	mixture of **2a**, **3a**, and stilbene	
6	Me$_3$SiCl	100%	45 [g]	0
7	Allyl-SiMe$_3$	10%	0	trace [h]

[a] Reaction conditions: 2.0 mmol of **1a**, 10 mol% of Cp$_2$VCl$_2$, 1.2 eq. of addtive, 2.0 eq. of Zn, 10 mL of DME, reflux, 24 h. [b] Determined by ^{1}H NMR. [c] HSnBu$_3$ was recovered. [d] At room temperature. [e] Absence of Cp$_2$VCl$_2$. [f] Trace of allylation product was obtained. [g] *dl* / meso = 60 / 40. [h] Allylation product was not obtained.

When the reaction can be carried out with 10 mol% of Cp$_2$VCl$_2$[12], Zn (2.0 eq.), and tributyltin hydride (1.2 eq.), in the refluxing DME benzylalcohol (**3a**) was obtained in 60% yield, but tributyltin hydride was recovered quantitatively (entry 1). At room temperature the yield of **3a** was decreased (entry 2). In absence of vanadium catalyst, **1a** was recovered in 90% yield (entry 3). The use of allylstannane instead of tributyltin hydride gave the trace amounts of **3a** and the allylation product of **1a** and the unidentified mixture were obtained (entry 4). When the addition of imidazole to the system, vanadium catalyzed reduction of **1a** gave a mixture of **2a**, **3a**, and stilbene (entry 5). When Me_3SiCl was used as an additive,[13] **2a** was obtained in 45% yield with the low selectivity (*dl* / meso = 60 / 40) (entry 6). The reaction was very sluggish in the case of allylsilane (entry 7).

To construct the system permitting the excellent diastereoselectivity, the reduction of benzaldehyde (**1a**) with a Cp_2VCl_2 (5 mol%) in the presence of Me_3SiCl and zinc metal was examined. The results of the reductive coupling of **1a** by using several solvents such as DMF, CH_3CN, THF, DME, Et_2O, CH_2Cl_2, and toluene are summarized in Table 2.



(3)

1a **2a**

Table 2. Influence of Solvent on the Catalytic Pinacol Coupling Reaction [a]

entry	solvent	2a	
		yield, % [b]	*dl* / meso [b]
1	DMF	68	63 / 37
2	CH_3CN	59	55 / 45
3	THF	97	73 / 27
4	DME	62	60 / 40
5	Et_2O	60	60 / 40
6	CH_2Cl_2	trace	80 / 20
7	$PhCH_3$	no reaction	

[a] Reaction conditions: 3.3 mmol of **1a**, 5 mol% of Cp_2VCl_2, 2.0 eq. of Me_3SiCl, 2.0 eq. of Zn, 10 mL of solvent, rt, Ar, 24 h. [b] Determined by ^1H-NMR.

The use of DMF as a polar solvent was not effective for the diastereoselective coupling of **1a** (entry 1). Acetonitrile led to the decrease of the diastereoselectivity (entry 2). Tetrahydrofuran provided **2a** in improved yield with moderate diastereoselectivity (entry 3). Instead of THF, the use of Et_2O did not improve the diastereoselectivity (entry 4). Although CH_2Cl_2 was used as a solvent in the stoichiometric reductive coupling of aldehydes,[14] the catalytic reaction in CH_2Cl_2 resulted in the formation of the complex mixture (entry 5). The use of toluene resulted in the recovery of **1a** (entry 6).

To study the influence of temperature for the stereoselectivity, the reduction of **1a** was examined at several temperatures, and the results are summarized in Table 3.

Table 3. **Influence of Temperature on the Catalytic Pinacol Coupling** [a]

		2a	
entry	temp (°C)	yield, %[b]	*dl* / meso[b]
1	-25	26	73 / 27
2	rt	97	73 / 27
3	reflux	73	50 / 50

[a] Reaction conditions: 3.3 mmol of **1a**, 5 mol% of cat. Cp_2VCl_2, 6.6 mmol of Me_3SiCl, 6.6 mmol of Zn, 10 mL of THF, Ar, 24 h. [b] Determined by ^1H NMR.

In general, the reaction at the low temperature leads to the improvement of the selectivity, the present pinacol coupling at lower temperature (-25 °C) provided moderate selectivity (entry 1). The reaction at higher temperature decreased both the yield and the diastereoselectivity (entry 3).

Next, the influence of silyl agents on the diastereoselectivity of the catalytic Pinacol-coupling was investigated. In our previous paper, the bulkiness of the silyl agents was reported to improve the diastereoselectivity in the pinacol coupling of the secondary aldehydes.[6c] The results are summarized in Table 4.

The use of $PhMe_2SiCl$ improved the selectivity (entry 1). $(i\text{-}Pr)_3SiCl$ is more bulky silyl agent, and the complex mixture was provided (entry 3).

Table 4. Influence of Silyl Compound on the Pinacol Coupling Reaction [a]

entry	R_3SiCl	2a yield, %[b]	2a *dl* / meso[b]
1	$PhMe_2SiCl$	70	77 / 23
2	Me_3SiCl	97	73 / 27
3	$(i\text{-}Pr)_3SiCl$	mixture	

[a] Reaction conditions: 3.3 mmol of **1a**, 5 mol% of cat.Cp_2 VCl_2, 6.6 mmol of R_3SiCl, 6.6 mmol of Zn, 10 mL of THF, Ar, rt, 24 h. [b] Determined by ^1H NMR.

Next, the reduction of **1a** with vanadium catalysts in the presence of several metals was examined. Table 5 summarizes the results obtained from the reductive coupling of **1a** using several co-reductants such as Mg, Mn, Zn, and Al.

Table 5. Vanadium Catalyzed Pinacol Coupling of 1a [a]

entry	cat. V	M	2a yield, %[b]	2a *dl* / meso[b]
1	Cp_2VCl_2	Zn	97	73 / 27
2	$CpV(CO)_4$	Zn	82	72 / 28
3	Cp_2V	Zn	83	62 / 38
4	VCl_3	Zn	76	79 / 21
5	VCl_3	Mg	66	62 / 38[c]
6	VCl_3	Mn	83	68 / 32
7	VCl_3	Al	56	84 / 16[c]
8	Cp_2VCl_2	Al	50	60 / 40
9	$VOCl_3$	Al	70	90 / 10[d]

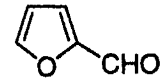
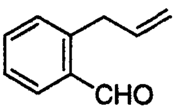
[a] Reaction conditions: 3.3 mmol of **1a**, 5 mol% of cat. V, 6.6 mmol of Me_3SiCl, 6.6 mmol of M, 10 mL of THF, rt, Ar, 24 h. [b] Determined by ^1H NMR. [c] Stilbene was obtained in ca. 10% yield. [d] Reaction temperture was 50 °C.

The use of $CpV(CO)_4$ as a vanadium catalyst for the catalytic coupling of **1a** provided **2a** in moderate yield with similar diastereoselectivity as the case of Cp_2VCl_2

(entry 2). Cp_2V was not effective for the stereoselective pinacol coupling (entry 3). The use of a VCl_3-Zn reagent, which is known to attain high stereoselectivity in the stoichiometric reductive coupling of aliphatic aldehydes,[14] improved the stereoselectivity (entry 4). 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 5). The use of Mn provided **2a** in improved yield with similar diastereoselectivity (entry 6). While the use of Al gave stilbene as a byproduct (ca. 10% yield), the highly *dl*-selective formation of the diol **2a** was observed in this system (entry 7). Furthermore, when the reductive coupling of **1a** was carried out in the absence of vanadium catalyst, the complex mixture was obtained. This result shows that the reaction active species consists of vanadium compound and aluminum.[15] To improve the diastereoselectivity of the catalytic pinacol reaction, the influence of vanadium catalysts on this reductive coupling was studied. Cp_2VCl_2 indicated both low yield and low selectivity in the coupling of **1a** using Al and Me_3SiCl (entry 8). On the other hand, the oxovanadium, $VOCl_3$, which was 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 9). This result suggests that an active low-valent vanadium species may be generated in situ from the reduction of the oxovanadium (V) with Al. Since the diastereoselectivity was improved under the optimized conditions, this system was then applied to a variety of aromatic aldehyde, which produces the corresponding 1,2-diols in good yields with excellent diastereoselectivity, as summarized in Table 6.

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, *p*-chloro, and *m*-chloro groups (**1b**, **1c**, and **1d**) were converted to the corresponding diol **2b**, **2c**, and **2d**, respectively, with excellent diastereoselectivity (entries 2, 3 and 4). In contrast, in the case of 4-cyanobenzaldehyde (**1e**) with an electron-withdrawing substituent, a complex mixture was obtained. On the other hand, **1f** with an electron-releasing substituent was reduced very slowly. Although 31% of **1f** was recovered after the reaction for 48 h, the diol **2f** was produced in a moderate yield with excellent selectivity (entry 6). The

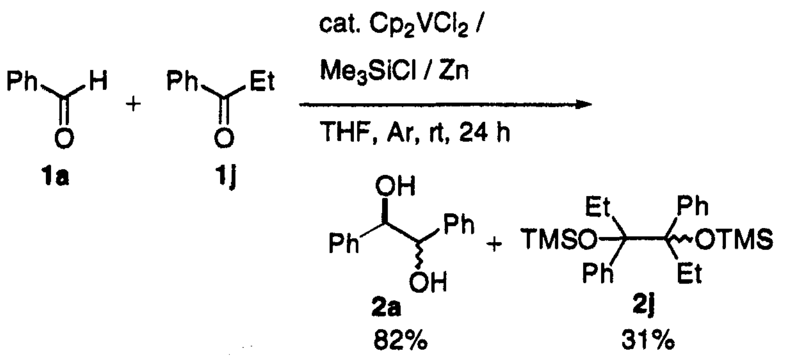
Table 6. Pinacol Coupling of **1** by Catalytic VOCl3 / Me_3SiCl / Al System [a]

entry	substrate		isolated yield, %	*dl* / meso [b]
1	PhCHO	**1a**	68	>95 / 5
2	*p*-ClC_6H_4CHO	**1b**	89	>95 / 5
3	*m*-ClC_6H_4CHO	**1c**	77	>95 / 5
4	*p*-MeC_6H_4CHO	**1d**	62	>95 / 5
5	*p*-CNC_6H_4CHO	**1e**	mixture	
6	*p*-$MeOC_6H_4CHO$	**1f**	49[c]	>95 / 5
7	*trans*-PhCH=CHCHO	**1g**	polymerization	
8		**1h**	polymerization	
9		**1i**	84	>95 / 5

[a] Reaction conditions: 3.3 mmol of **1**, 5 mol% of cat. $VOCl_3$, 6.6 mmol of Me_3SiCl, 6.6 mmol of Al, 10 mL of DME, 50 °C, Ar, 24 h. [b] Determined by ^1H NMR. [c] 48 h, recovery of **1f** 31%.

substituent of α,β-unsaturated aldehydes (**1g** and **1h**) gave a polymerization product (entries 7 and 8). The benzaldehyde **1i**[16] bearing an olefinic moiety also coupled diastereoselectively in a good yield, without formation of any cyclization product (entry 9).

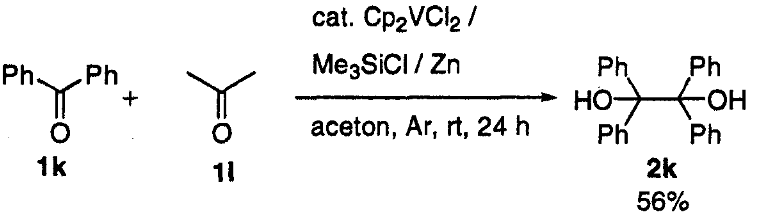
The cross pinacol coupling reaction by use of vanadium catalytic system was examined (Equations 4 and 5). Although **1a** was added to a THF solution of **1j** over 4



(4)

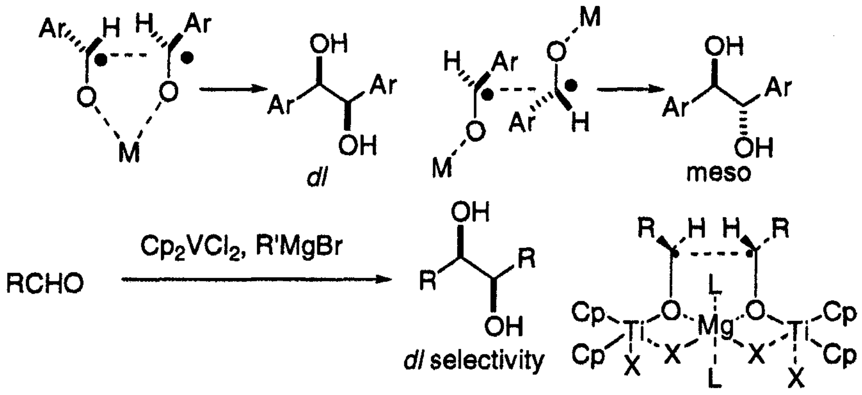
h, each homo-coupling product **2a** and **2j** was obtained and the cross-coupling product was not obtained at all (Equation. 4).

In the case of cross-coupling reaction with **1k** and **1l**, the cross-coupling product was not obtained, providing only **2k** in 56% yield (Equation 5).



(5)

Probably, these excellent *dl*-selectivities could be achieved by the formation of cyclic intermediate. Inanaga et al.[17] suggested that, in stoichiometric coupling of aldehydes by use of Cp_2TiCl_2, the cyclic intermediate has been proposed that two pair of lone pair on oxygen participate in coordination to both of low-valent metal complex (Ti) and reductant (Mg, Zn, Mn) and then R groups are arranged *anti* to each other to optimize the steric influence (Scheme 1), providing the 1,2-diol with the excellent *dl*-selectivity.



Scheme 1

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.

1-3. Experimental Section

General Methods

Melting points were determined on Yanagimoto micromelting point apparatus and are uncorrected. Infrared spectra were recorded on Perkin-Elmer 1605 infrared. ^1H

NMR or ^{13}C NMR spectra were recorded on Varian MERCURY300 spectrometer (300 MHz), JEOL JNM-GSX-400 spectrometer (400 MHz), and Bruker AM-600 spectrometer (600 MHz) in chloroform-*d* with tetramethylsilane or residual chloroform as an internal standard. Mass spectra were recorded on Varian Saturn 3 or JEOL JMS-DX-303. Elemental analyses were performed in the analytical section of our department. Thin-layer chromatography (TLC) was carried out on aluminum sheets precoated with silica gel 60 F_{254} (E. Merck). Column chromatography was performed on silica gel 60 (E. Merck). All reagents except Me_3SiCl are of commercial quality. Me_3SiCl is distilled under argon over K_2CO_3 and stores under argon. All dry solvents were freshly distilled under argon over an appropriate drying agent before use.

General Procedure for Reductive Coupling Reaction of Benzaldehyde (1a) (Table 1). To a mixture of Cp_2VCl_2 (50 mg, 10 mol%) and Zn (260 mg, 4.0 mmol) in DME (10 mL) was added the additive (2.4 mmol) at reflux temperature under argon. The reaction mixture was kept in reflux for 1 h. Then, the benzaldehyde derivative (**1a**), (2.0 mmol) was added to the mixture. The mixture was kept in reflux with magnetic stirring for 24 h. After cooling to room temperature, ether (10 mL) and HCl aq. (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 X 2), and brine (10 mL), dried over Na_2SO_4, and concentrated. The products were determined by ^1H NMR and ^{13}C NMR. Yield was shown in Table 1.

(*R, *R**)-1,2-Bisphenyl-1,2-ethanediol (2a):** *CAS* [579-43-1]; mp 138 °C; ^1H NMR (300 MHz, $CDCl_3$) 7.15 (m, 6H), 7.05 (m, 4H), 4.78 (s, 2H), 2.30 (br, 2H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 139.7, 128.1, 128.0, 127.0, 78.0; MS *m/z* 274 (M), 137 (base); Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.48; H, 6.59.

Benzyl alcohol (3a): *CAS* [100-51-6]; mp -15 °C; ^1H NMR (300 MHz, $CDCl_3$) 7.25 (m, 5H), 4.54 (d, 2H, $J = 7.0$ Hz), 2.85 (br, 1H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 141.1, 126.7, 127.7, 127,2, 65.3.

General Procedure for Reductive Coupling Reaction of Benzaldehyde Derivatives (1) (Table 6). To a mixture of Al (178 mg, 6.6 mmol) in DME (9.5 mL) was added the solution (0.5 mL) consisted 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 derivative (**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 and the color of the mixture turned to light blue with nebula. After cooling to room temperature, ether (10 mL) and HCl aq (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 X 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 X each 50 mL), giving **2**.

(*R, *R**)-1,2-Bisphenyl-1,2-ethanediol (2a):** *CAS* [579-43-1]; mp 138 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.15 (m, 6H), 7.05 (m, 4H), 4.78 (s, 2H), 2.30 (br, 2H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 139.7, 128.1, 128.0, 127.0, 78.0; MS *m/z* 274 (M), 137 (base); Anal. Calcd for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.48; H, 6.59.

(*R, *R**)-1,2-Bis(4'-chlorophenyl)-1,2-ethanediol (2b):** *CAS* [116262-76-1]; mp 82 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.24-6.92 (m, 8H), 4.64 (s, 2H), 2.82 (br, 2H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 139.2, 133.2, 128.6, 128.2, 78.3; Anal. Calcd for $C_{14}H_{12}Cl_2O_2$: C, 59.39; H, 4.27. Found: C, 59.31; H, 4.43.

(*R, *R**)-1,2-Bis(3'-chlorophenyl)-1,2-ethanediol (2c):** *CAS* [188839-74-9]; mp 80 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.24-7.21 (m, 4H), 7.17 (m, 2H), 6.92 (m, 2H), 4.66 (s, 2H), 2.82 (br, 2H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 141.5, 134.2, 129.4, 128.3, 126.9, 125.2, 78.2; Anal. Calcd for $C_{14}H_{12}Cl_2O_2$: C, 59.39; H, 4.27. Found: C, 59.31; H, 4.43.

(*R, *R**)-1,2-Bis(4'-methylphenyl)-1,2-ethanediol (2d):** *CAS* [66749-58-4]; mp 105-107 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.20-7.10 (m, 8H), 4.70 (s, 2H), 2.95 (br, 2H), 2.35 (s, 6H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 137.4, 137.3, 128.8, 128.1, 127.1, 78.9, 21.3; MS *m/z* 247 (M), 121 (base); Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.30; H, 7.49. Found: C, 79.05; H, 7.59.

(*R, *R**)-1,2-Bis(4'-methoxyphenyl)-1,2-ethanediol (2f):** *CAS* [39090-28-3]; mp 132-134 °C; ^{1}H NMR (300 MHz, $CDCl_3$) 7.10 (m, 4H), 6.80 (m, 4H), 4.65 (s, 2H), 3.80 (s, 6H), 2.90 (br, 2H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 159.3, 132.4, 128.4, 113.9, 78.9, 55.4; MS *m/z* 274 (M), 137 (base); Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found:

C, 69.76; H, 6.91.

(R^*, R^*)-1,2-Bis(2'-allylphenyl)-1,2-ethanediol (2i): mp: 57 °C; IR (neat) 3304, 1032, 1002, 761 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) 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 (75.0 MHz, CDCl$_3$) 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.

Reductive Cross-Coupling Reaction with Benzaldehyde (1a) and Propiophenone (1j) (Equation 4). To a mixture of Cp$_2$VCl$_2$ (50 mg, 10 mol%) and Zn (260 mg, 4.0 mmol) in THF (10 mL) was added trimethylchlorosilane (0.540 mL, 5 mmol) at room temperature under argon. The reaction mixture was kept at room temperature for 1 h. Propiophenone (**1j**) (268 mg, 2.0 mmol) was added to the mixture and stirred for 10 minutes. Then, **1a** (214 mg, 2.0 mmol) was added to the mixture. The mixture was kept in room temperature with magnetic stirring for 24 h. Ether (10 mL) and HCl aq (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 X 2), and brine (10 mL), dried over Na$_2$SO$_4$, and concentrated. The products determined by ^{1}H NMR and ^{13}C NMR. Yield was shown in Equation 4.

3,4-Diphenyl-3,4-bis(trimethylsilyloxy)hexane (2j): Colorless solid (obtained as a stereo isomeric mixture (44/56)); [*dl*-isomer]: ^{1}H NMR (300 MHz, CDCl$_3$) 7.45 (d, 4H, J = 8.0 Hz), 7.33 (t, 4H, J = 8.0 Hz), 7.25 (t, 2H, J = 8.0 Hz), 2.44 (q, 2H, J = 7.6 Hz), 1.11 (q, 2H, J = 7.6 Hz), 0.59 (t, 6H, J = 7.6 Hz), 0.00 (s, 18 H); ^{13}C NMR (100 MHz, CDC13) 141.8, 128.8, 125.8, 87.9, 25.8, 9.7, 2.9. [*meso*-isomer]: 7.06 (t, 2H, J = 8.0 Hz), 7.00 (t, 4H, J = 8.0 Hz), 6.78 (d, 4H, J = 8.0 Hz), 2.36 (q, 8H, J = 7.2 Hz), 2.13 (q, 2H, J = 7.2 Hz), 0.76 (t, 6H, J = 7.2 Hz), 0.20 (s, 18 H); ^{13}C NMR (100 MHz, CDC13) 142.4, 126.5, 126.1, 87.0, 26.6, 9.3, 2.5; MS (CI) *m/z* = 413 (M$^+$-1), MS (EI) *m/z* = 399 (M$^+$-Me).

Reductive Cross Coupling Reaction of Benzophenone (1k) with Acetone (1l) (Equation 5). To a mixture of Cp$_2$VCl$_2$ (50 mg, 10 mol%) and Zn (260 mg, 4.0 mmol, Aldrich Chemical Co., Inc.) in acetone (10 mL) was added trimethylchlorosilane (0.540

mL, 5 mmol) at room temperature under argon. The reaction mixture was kept in at room temperature for 1 h. Benzophenone (**1k**) (376 mg, 2.0 mmol) was added to the mixture, which was kept at room temperature with magnetic stirring for 24 h. Ether (10 mL) and HCl aq (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 X 2), and brine (10 mL), dried over Na_2SO_4, and concentrated. The products were determined by ^1H NMR and ^{13}C NMR. Yield was shown in Equation 5.

Benzopinacole (2k): *CAS* [464-72-2]; mp 185 °C; ^1H NMR (300 MHz, $CDCl_3$) 7.27 (m, 8H), 7.14 (m, 12H), 3.03 (br, 2H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 145.0, 129.4, 128.1, 127.8, 83.9.

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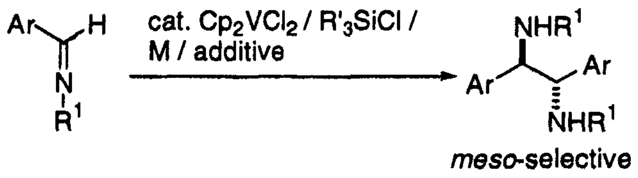
Chapter 2. High *Meso*-Selective Reductive Coupling Reaction of Benzaldimines by the Vanadium Catalyst

2-1. Introduction

The reductive dimerization of carbonyl compounds and their imine derivatives with low-valent metal complexes is an important method for vicinally bifunctonalized carbon-carbon bond formation.[1] Although the dimerization reactions usually require stoichiometric or more excess amounts of low-valent metal complexes, a catalytic reductive coupling procedure has been disclosed recently by the combination of an early transition metal catalyst, a chlorosilane, and a zero-valent metal as a co-reductant. For example, Fürstner and his coworkers reported the catalytic McMurry coupling of aldehydes promoted by cat. $TiCl_3$ / R_3SiCl / Zn,[2] and, independently, we achieved the catalytic pinacol coupling of aldehydes induced by cat. Cp_2VCl_2 / Me_3SiCl / Zn, which provides 1,3-dioxolanes as a mixture of diastereoisomers (*dl* / meso = 63 / 37). [3, 4] Furthermore, the catalytic pinacol coupling of aldehydes was reported to proceed with high diastereoselectivity using the catalytic systems of low-valent titanium complexes.[5]

As for the catalytic dimerization of aldimines, there are only few reports, describing that the Cp_2TiCl_2-catalyzed reduction of aldimines with Sm metal exhibits high *dl*-selectivity of the product, the vicinal diamines, (up to 80%de).[6, 7] 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. During the course of our studies on the catalytic pinacol coupling, a catalytic dimerization of aldimines using the cat. Cp_2VCl_2 / $PhMe_2SiCl$ / Zn or cat. Cp_2VCl_2 / $PhMe_2SiCl$ / Al / additive was examined, which successfully provides the corresponding 1,2-diamines in high yields, and more surprisingly, unprecedented high *meso*-selectivity was observed (Equation 1).



(1)

2-2. Results and Discussion

At first, the reductive dimerization of *N*-benzylidenebenzylamine (**1a**) with Cp_2VCl_2 in the presence or absence of additives such as zinc metal and Me_3SiCl was examined (Equation 2 and Table 1).

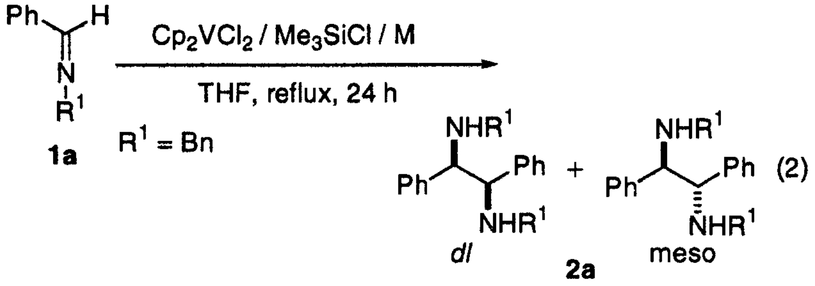


Table 1. **Reaction of 1a with Cp_2VCl_2 in the Presence of Additive** [a]

entry	Cp_2VCl_2	M	Me_3SiCl	2a yield, % [b]	 *dl* / meso [b]
1	+		-	0	
2	+		+	0	
3	+	Zn	-	40	42 / 58
4	-	Zn	-	0	
5	+	Zn	+	73	34 / 66
6	-	Zn	+	trace	54 / 46
7	+ [c]	Zn	+	37	34 / 66
8	+ [c]	Zn	+ [d]	45	48 / 52
9	+ [c]	Mg	+	20	20 / 80
10	+ [c]	Sm	+	mixture	

[a] Reaction conditions: 2.0 mmol of **1a**, 1 eq. of Cp_2VCl_2, 2 eq. of M, 2.5 eq. of Me_3SiCl, 5 mL of THF, reflux, 24 h, Ar. [b] Isolated yield. Determined by ^1H NMR. [c] 10 mol% of Cp_2VCl_2 was used.

When the reaction of **1a** with 2 eq. of Cp_2VCl_2 in refluxing THF was conducted for 24 h, the desired reductive coupling product was not obtained at all (entry 1). While the absence of zinc metal in the Cp_2VCl_2-catalyzed reduction system did not cause the reduction of **1a** even in the presence of Me_3SiCl (entry 2), the combination of Cp_2VCl_2 and zinc metal led to the coupling product **1a** in 40% yield (entry 3). Since no reduction took place with zinc metal alone (entry 4), the active reducing species is likely to be a low-valent vanadium complex formed in situ by the reduction of Cp_2VCl_2 with zinc metal. Furthermore, the addition of Me_3SiCl to this system successfully improved the yield of **2a** (entry 5). The fact that the attempted reduction of **1a** using a Me_3SiCl / Zn system[8] gave only trace amounts of **2a** (entry 6), clearly indicates that the efficient pinacol-type coupling of aldimines requires a reduction system composed of Cp_2VCl_2, Zn, and Me_3SiCl. Next, the reductive coupling in the presence of a catalytic amount of Cp_2VCl_2 (i.e., cat. Cp_2VCl_2 / Me_3SiCl / Zn) was examined, which successfully provided the reductive coupling product **2a** in low yield (entry 7). When $PhMe_2SiCl$ was used as a silylating agent, the yield of **2a** was improved (entry 8). The use of Mg as a co-reductant led to **2a** in poor yield with moderate selectivity (entry 9). Moreover, the attempted reduction of **1a** using cat. Cp_2VCl_2 / Me_3SiCl / Sm[9] gave rise to only complex mixture (entry 10).

Since the best combination has been revealed to be cat. Cp_2VCl_2 / $PhMe_2SiCl$ / Zn, the influence of solvent on the reductive coupling of **1a** was studied by using cat. Cp_2VCl_2 / $PhMe_2SiCl$ / Zn. The results are summarized in Table 2.

Table 2. **The Influence of Solvent on the Reductive Coupling of 1a** [a]

entry	solvent	2a yield, % [b]	 *dl* / meso [b]
1	CH_2Cl_2	48	50 / 50
2	THF	45	48 / 52
3	DME	36	35 / 65
4	DMF	88	27 / 73
5	NMP	90	35 / 65
6	HMPA	quant	39 / 61

[a] Reaction conditions: 2.0 mmol of **1a**, 10 mol% of Cp_2VCl_2, 2.0 eq. of Zn, 2.0 eq. of $PhMe_2SiCl$, 5 mL of solvent, rt, 24 h, Ar. [b] Isolated yield. Determined by ^1H NMR.

In place of THF, the reductive coupling of **1a** in CH_2Cl_2 yielded 48% of **2a** without any diastereoselection (entry 1). Although the catalytic reductive coupling of imines was generally shown the *dl*-selectivity, the use of DME as a solvent surprisingly, provided **2a** with the *meso*-selectivity in the low yield (entry 3). When the polar solvents such as HMPA, NMP and DMF were used, the yield increased dramatically as shown in entries 4, 5, and 6. In particular, the use of DMF improved both the yield and the diastereoselectivity, giving the *meso*-1,2-diamine **2a** preferentially.

To study the influence of temperature on the diastereoselectivity, we next examined the reduction of **1a** at several temperatures. The results are summarized Table 3.

Table 3. **Influence of Temperature on the Redactive Coupling of 1a** [a]

entry	temp, °C	2a yield, % [b]	2a *dl* / meso [b]
1	-25	79	17 / 83
2	rt	88	27 / 73
3	75	69	36 / 64

[a] Reaction conditions: 2.0 mmol of **1a**, 10 mol% of Cp_2VCl_2, 2.0 eq. of Zn, 2.0 eq. of $PhMe_2SiCl$, 5 mL of DMF, 24 h, Ar.
[b] Isolated yield. Determined by ^1H NMR.

When the reductive coupling was performed at -25 °C, the diastereoselectivity was improved up to 83 / 17 (entry 1). On the other hand, heating at 75 °C led to decrease in both the yield and selectivity (entry 3).

Next, the influence of silylating agents on the diastereoselectivity was studied. We reported in the previous paper that the bulkiness of the silylating agent improved the diastereoselectivity in the pinacol coupling of the secondary aldehydes.[5e] The results are summarized Table 4 .

The use of Me_3SiCl resulted in the low yield of **2a** (entry 1). The sterically hindered *t*-$BuMe_2SiCl$ may be expected to induce higher diastereoselectivity, but **2a** was obtained in moderate yield with low selectivity (entry 3). In the case of 1-(trimethylsilyl)imidazole or *N,O*-bis(trimethylsilyl)acetamide, no reduction took place at all (entries 4 and 5). These results suggest that the electronic and steric effects of the silyl substituents play an important role in this reductive coupling of the aldimine **1a**. Interestingly, the desired reaction could proceed using benzyl bromide (entry 6).

Table 4. **Influence of Silyl Compound on the Reductive Coupling of 1a** [a]

entry	R'$_3$SiX	**2a** yield, % [b]	**2a** *dl* / meso [b]
1	Me_3SiCl	52	25 / 75
2	$PhMe_2SiCl$	88	27 / 73
3	$^tBuMe_2SiCl$	48	35 / 65
4	Me_3Si-Im [c]	trace	
5	BSA [d]	no reaction	
6	benzyl bromide	61 [e]	40 / 60

[a] Reaction conditions: 2.0 mmol of **1a**, 10 mol% of Cp_2VCl_2, 2.0 eq. of Zn, 2.0 eq. of $PhMe_2SiCl$, 5 mL of DMF, rt, 24 h, Ar. [b] Isolated yield. Determined by ^{1}H NMR. [c] Me_3Si-Im = trimethylsilylimidazole. [d] BSA = *N,O*-bis(trimethylsilyl)- acetamide. [e] A trace of the *N*-benzylation product was obtained.

Table 5 represents the reduction of **1a** catalyzed by several vanadium compounds. The reductive coupling by use of $CpV(CO)_4$ or VCl_3[10] gave the *meso*-1,2-diamine in moderate yield (entries 2 and 3). With Cp_2TiCl_2,[11] the reduction gave **2a** with moderate selectivity, but the yield was lowered (entry 4). These results show that the more efficient catalyst formed in situ from Cp_2VCl_2 and Zn.

Table 5. **Optimization of Catalyst for Reductive Coupling of 1a** [a]

entry	cat. V	**2a** yield, % [b]	**2a** *dl* / meso [c]
1	Cp_2VCl_2	88	27 / 73
2	$CpV(CO)_4$	52	25 / 75
3	VCl_3	45	18 / 82
4	Cp_2TiCl_2	35	26 / 74

[a] Reaction conditions: 2.0 mmol of **1a**, 10 mol% of cat. V, 2.0 eq. of Zn, 2.0 eq. of $PhMe_2SiCl$, 5 mL of DMF, rt, 24 h, Ar. [b] Isolated yield. [c] Determined by ^{1}H NMR.

To study the influence of the substitution on nitrogen for the diastereoselectivity, the catalytic reductive coupling of several aldimine derivatives was examined. The results are summarized in Table 6.

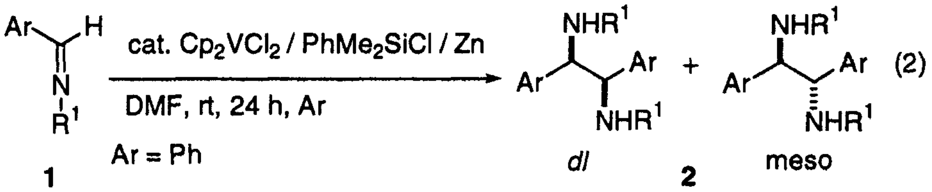


Table 6. Cp_2VCl_2 / $PhMe_2SiCl$ / Zn Catalyzed Reductive Coupling of **1** [a]

entry	R^1	1	2 yield, % [b]	 dl / meso [c]
1	$PhCH_2$	**1a**	88	27 / 73
2	*n*-Hexyl	**1b**	quant	33 / 67
3	*i*-Propyl	**1c**	quant	50 / 50
4	Allyl	**1d**	56	8 / 92
5	Phenethyl	**1e**	64	17 / 83
6	Phenyl	**1f**	90	25 / 75

[a] Reaction conditions: 2.0 mmol of **1**, 10 mol% of Cp_2VCl_2, 2.0 eq. of Zn, 2.5 eq. of $PhMe_2SiCl$, 5 mL of THF, rt, 24 h, Ar. [b] Isolated yield. [c] Determined by ^1H NMR.

Starting from *N*-hexylaldimine **1b**, the 1,2-diamine **2b** was obtained in good yield with moderate diastereoselectivity (entry 2). In the case of **1c** bearing *N*-isopropyl group, the diastereoselectivity was not observed (entry 3). In particular, the excellent *meso*-selectivity was realized with *N*-allyl substituted imines (entry 4). The use of *N*-phenethyl gave **2e** with the high diastereoselectivity (entry 5). Phenyl substituents on the nitrogen afforded the corresponding 1,2-diamine **2f** in good yield with the moderate *meso*-selectivity (entry 6). These results suggest that the diastereoselectivity strongly depends on the substituent on the nitrogen of **1**.

Equation 3 and Table 7 represent the results of the Cp_2VCl_2-catalyzed reductive coupling of *N*-allyl aldimine derivatives. Both *p*-methyl- and *p*-chloro-substituted aldimines (**1h** and **1i**) underwent reductive coupling similarly as the case of the aldimine **1a** itself (entries 2 and 4). On the other hand, the use of the derivatives bearing electron-releasing or electron-withdrawing substitution (*p*-methoxy (**1g**) or *p*-cyano (**1j**)) provided **2** with low or moderate selectivity (entries 1 and 5).

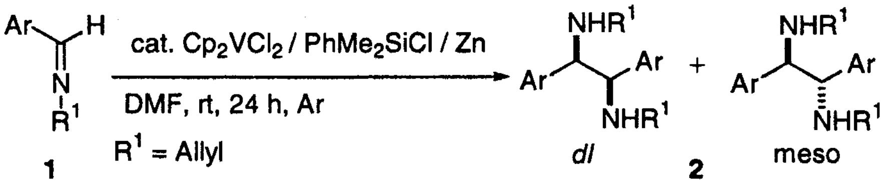


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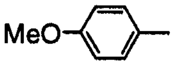
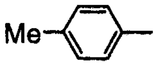
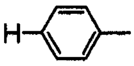
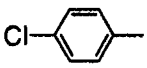
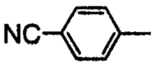
Table 7. **Influence of Phenyl Substitution on the Reductive Coupling of 1** [a]

entry	Ar	1	2 yield, % [b]	 *dl* / meso [c]
1		**1g**	73	38 / 62
2		**1h**	51	10 / 90
3		**1d**	56	8 / 92
4		**1i**	46	16 / 84
5		**1j**	82	45 / 55

[a] Reaction conditions: 2.0 mmol of **1**, 10 mol% of Cp_2VCl_2, 2.0 eq. of Zn, 2.5 eq. of $PhMe_2SiCl$, 5 mL of THF, rt, 24 h, Ar. [b] Isolated yield. [c] Determined by ^1H NMR.

We next examined the reductive dimerization of *N*-benzylideneallylamine (**1d**) with Al as a co-reductant in the presence or absence of the additive. The results are summarized Table 8.

(4)

When the reaction of **1d** with Al as a co-reductant instead of Zn in DMF was conducted for 24 h, the desired reductive coupling product was obtained in 30% yield (entry 1). The addition of imidazole, which is widely used as a base for the silylation of alcohols, improved the yield, providing **2d** in 86% yield with *meso*-selectivity (*dl* / meso = 13 / 87) (entry 2). Although the use of *N*-methylimidazole or 2-methylimidazole instead of imidazole improved the selectivity, the reactions were very sluggish (entries 2 and 3). In the case of 4-methylimidazole, **2d** was obtained in the low yield with the low selectivity (entry 4). When the reductive coupling of **1d** can be carried out in THF, the reaction did not occur (entry 6). The absence of cat. Cp_2VCl_2 provided **2d** in 17% yield with the low selectivity (entry 7). As observed in the reductive coupling of aldimines by use of the system of cat. V / chlorosilane / Zn, the present system of cat. Cp_2VCl_2 / $PhMe_2SiCl$ / Al / imidazole also indicated a similar *meso*-selectivity.

Table 8. **Reductive Coupling Reaction of 3a by Use of Al** [a]

entry	solvent	additive	yield, % [b]	**2d** *dl* / meso [c]
1	DMF	——	30	13 / 87
2	DMF	imidazole	86	13 / 87
3	DMF	*N*-methylimidazole	23	9 / 91
4	DMF	2-methylimidazole	41	8 / 92
5	DMF	4-methylimidazole	37 [d]	44 / 56
6	THF	imidazole	no reaction	
7 [e]	DMF	imidazole	17	35 / 65

[a] Reaction conditions : 2 mmol of **1d**, 2.0 eq. of Al, 2.0 eq. of $PhMe_2SiCl$, 5 mol% of Cp_2VCl_2, 1.5 eq. of additive, 10 mL of solvent, Ar, 24 h. [b] Isolated yield. [c] Determined by ^1H NMR. [d] Benzaldehyde was recovered 15% yield. [e] In the absence of cat. Cp_2VCl_2.

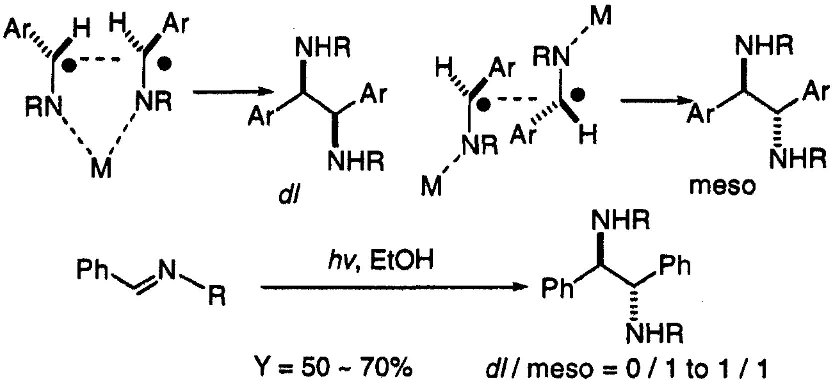
Table 9 shows the reductive coupling of the various imines **1** using cat. Cp_2VCl_2 / $PhMe_2SiCl$ / Al / imidazole. Starting from *p*-methyl- and *p*-chloro benzaldimines (**1h** and **1j**), the corresponding diamines were produced with good diastereoselectivity (entries 2 and 3). In contract, the selectivity was lowered by the change of the *N*-substituent from the allyl group to the *i*-propyl, *n*-hexyl or phenyl one (entries 4, 5 and 6). The diastereoselectivity strongly depends on the substituent on nitrogen possibly due to the steric effect. In the case of the aliphatic aldimine **1l** or the benzaldimines derived from amino acids (**1m** and **1n**) respectably, the reductive coupling can not be carried out by this catalytic system (entries 7 and 8).

Table 9. **Reductive Coupling Reaction of 1 by cat. Cp_2VCl_2 / $PhMe_2SiCl$ / Al / Imidadole** [a]

entry	R^1	R^2		2 yield, % [b]	2 *dl* / meso [c]
1	C_6H_5	Allyl	**1d**	86	13 / 87
2	*p*-MeC_6H_4	Allyl	**1h**	62	11 / 89
3	*p*-ClC_6H_4	Allyl	**1j**	72	25 / 75
4	C_6H_5	*i*-Propyl	**1c**	quant	45 / 55
5	C_6H_5	*n*-Hexyl	**1b**	71	23 / 77
6	C_6H_5	Ph	**1k**	quant	29 / 71
7	*i*-Pr	Bn	**1l**	trace	
8	C_6H_5	$(CH_2)_2CO_2Et$	**1m**	9 [d]	10 / 90
9	C_6H_5	CH_2CO_2Et	**1n**	mixture	

[a] Reaction conditions : 2.0 mmol of **1**, 2.0 eq. of Al, 2.0 eq. of $PhMe_2SiCl$, 5 mol% of Cp_2VCl_2, 1.5 eq. of imidazole, 10 mL of solvent, Ar, 24 h. [b] isolated yield. [c] Determined by ^1H NMR. [d] Cyclobutylamine drivative was obtained in 20% yield.

Probably, these excellent *meso*-selectivities could be achieved by the formation of acyclic intermediate. Padwa's group[12] and Beak's group[13] suggested that the photo-reductive coupling of aldimines gives 1,2-diamines with the high *meso*-selectivity (Scheme 1).



Scheme 1

In general, in stereoselective coupling of carbonyl compounds using the early transition metal and the stoichiometric reductant, the cyclic intermediate, which has been proposed that two pairs of lone pair on oxygen participate in coordination to both of low-valent metal complex (Ti) and reductant (Mg, Zn, Mn) and then R groups are arranged *anti* to each other to optimize the steric influence, leading to the excellent *dl*-selectivity[3, 5, 6, 14] (Figure 1).

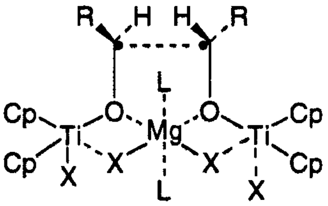
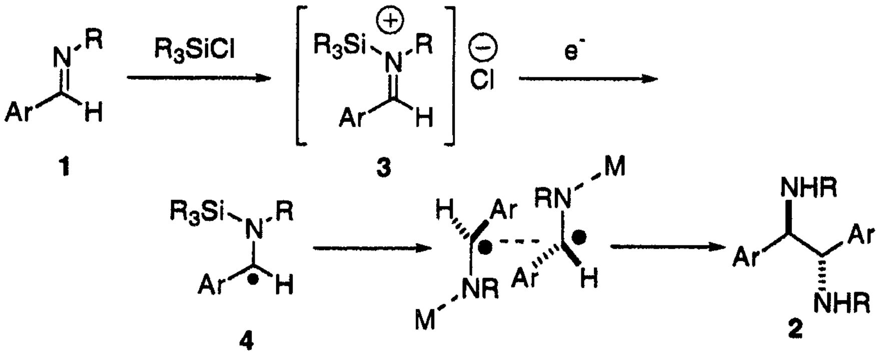


Figure 1

However, these similar models can not explain the stereochemistry of the present reductive coupling of aldimines and another intermediate models may be operative. Although the real mechanism for this reductive coupling requires further detailed mechanistic experiments, a possible pathway for the preferential formation of *meso*-1,2-diamines may be accounted for in Scheme 2.



Scheme 2

To begin with, the silylation of **1** with a silyl chloride gives the iminium salt **3**. Subsequently, the α-amino radical intermediate (**4**) formed in situ by the reduction of the aldimine with a low-valent vanadium complex provides the 1,2-diamine (**2**). In the dimerization of **4**, the repulsion of the lone pair on nitrogen and steric hindrance between the aryl groups seem to contribute to the *meso*-selection (Scheme 2).

It has been demonstrated that the reductive coupling of aldimines can be catalyzed effectively by Cp_2VCl_2 in the presence of chlorophenyldimethylsilane and zinc metal. The high *meso*-selectivity has been attained for the first time in the pinacol-type coupling reaction.

2-3. Experimental Section

Melting points were determined on Yanagimoto micromelting point apparatus. Infrared spectra were recorded on Perkin-Elmer 1600. ^{1}H NMR or ^{13}C NMR spectra were recorded on Varian MERCURY300 spectrometer in chloroform-d with tetramethylsilane or residual chloroform as an internal standard. Mass spectra were recorded on Varian Saturn 3 or JEOL JMS-DX-303. Elemental analyses were performed in the analytical section of our department. Thin-layer chromatography (TLC) was carried out on aluminum sheets precoated with silica gel 60 F254 (E. Merck). Column chromatography was performed on silica gel 60 (E. Merck). All reagents are of commercial quality. All dry solvents were freshly distilled under argon over an appropriate drying agent before use.

Preparation of Aldimine Derivative 1.[15] The carbonyl compound (50 mmol) was stirred with chromatographic alumina (25.0 g; about 200 mesh) under argon. The amine (50 mmol) was slowly added to the carbonyl compound dispersed on alumina. Then, the mixture was stirred at room temperature for 2 h. The aldimine derivative **1** was extracted with $CHCl_3$ (30 mL X 2) and the extract was evaporated under reduced pressure. The residue was purified with a bulb-to-bulb apparatus to give **1**.

***N*-Benzylidenebenzylamine (1a):** (7.15 g, 37 mmol, 53%): bp 127 °C / 0.25 mmHg; IR (neat) 1640 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) 8.32 (s, 1H), 7.77-7.22 (m, 10H, aromatic protons), 4.77 (d, 2H, $J = 1.4$ Hz); ^{13}C NMR (75.0 MHz, $CDCl_3$) 161.8 (CH), 139.2 (C), 136.1 (C), 130.6 (CH), 128.4 (CH), 128.3, (CH), 128.1 (CH), 127.8 (CH), 126.8 (CH), 61.9 (CH_2).

***N*-Benzylidene-*n*-hexylamine (1b):** (7.15 g, 37 mmol, 53%): ^{1}H NMR (300 MHz, $CDCl_3$) 8.32 (s, 1H), 7.77-7.22 (m, 5H, aromatic protons), 4.65 (t, 2H, $J = 6.8$ Hz) 1.71 (m, 2H), 1.44 (m, 6H), 0.85 (t, 3H, J = 7.0 Hz); ^{13}C NMR (75.0 MHz, $CDCl_3$) 160.7, 136.4, 130.4, 128.6, 128.0, 61.8, 31.7, 27.0, 22.6, 14.1.

***N*-Benzylidene-*i*-propylamine (1c):** (4.5 g, 34 mmol, 67%): ^{1}H NMR (300 MHz, $CDCl_3$) 8.18 (s, 1H), 7.61-7.27 (m, 5H, aromatic protons), 3.41 (m, 1H) 1.51 (d, 6H, $J = 7.2$ Hz); ^{13}C NMR (75.0 MHz, $CDCl_3$) 158.3, 136.4, 130.3, 128.5, 128.4, 128.0, 61.6, 24.1.

***N*-Benzylideneallylamine (1d):** (4.4 g, 28 mmol, 58%): bp 130 °C / 0.10 mmHg; ^{1}H

NMR (300 MHz, $CDCl_3$) 8.30 (s, 1H), 7.76-7.23 (m, 5H, aromatic protons), 6.07 (m, 1H), 5.15 (m, 2H) 4.26 (m, 2H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 162.0, 136.1, 135.9, 130.7, 128.6, 128.1, 116.1, 63.5.

***N*-Benzylideneaniline (1f):** (6.7 g, 37 mmol, 74%): ^1H NMR (300 MHz, $CDCl_3$) 8.43 (s, 1H), 7.80-7.23 (m, 10H, aromatic protons); ^{13}C NMR (75.0 MHz, $CDCl_3$) 160.3 (CH), 152.1 (C), 136.2 (C), 131.3 (CH), 129.1 (CH), 128.8 (CH), 125.9 (CH), 120.8 (CH).

***N*-(4-Methoxybenzylidene)allylamine (1g):** (5.7 g, 31 mmol, 65%): bp 140 °C / 0.07 mmHg; ^1H NMR (300 MHz, $CDCl_3$) 8.26 (s, 1H), 7.72-7.18 (m, 4H, aromatic protons), 6.03 (m, 1H), 5.20 (m, 2H), 4.24 (d, 2H, J = 5.6 Hz), 3.82 (s, 3H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 161.8, 140.8, 135.9, 133.4, 129.2, 128.0 115.9, 63.5, 56.3.

***N*-(4-Methylbenzylidene)allylamine (1h):** (7.0 g, 33 mmol, 67%): bp 123 °C / 0.10 mmHg; ^1H NMR (300 MHz, $CDCl_3$) 8.34 (s, 1H), 7.68-7.19 (m, 4H, aromatic protons), 6.05 (m, 1H), 5.23 (m, 2H), 4.18 (d, 2H, J = 5.6 Hz), 2.37 (s, 3H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 161.8, 139.4, 135.9, 133.4, 129.2, 128.0 115.9, 63.5, 24.1.

***N*-(4-Chlorobenzylidene)allylamine (1i):** (7.0 g, 30 mmol, 61%): bp 120 °C / 0.07 mmHg; ^1H NMR (300 MHz, $CDCl_3$) 8.33 (s, 1H), 7.72-7.33 (m, 4H, aromatic protons), 6.05 (m, 1H), 5.23 (m, 2H), 4.20 (d, 2H, J = 5.6 Hz); ^{13}C NMR (75.0 MHz, $CDCl_3$) 160.5 (C), 134.6 (C), 129.4 (CH), 128.4 (CH), 128.0 (CH), 127.0 (CH), 115.7 (CH), 63.5 (CH_2).

***N*-(4-Cyanobenzylidene)allylamine (1j):** (7.6 g, 34 mmol, 67%): ^1H NMR (300 MHz, $CDCl_3$) 8.41 (s, 1H), 7.90-7.28 (m, 4H, aromatic protons), 6.05 (m, 1H), 5.23 (m, 2H), 4.18 (d, 2H, J = 5.6 Hz); ^{13}C NMR (75.0 MHz, $CDCl_3$) 159.8 (C), 139.9 (C), 138.5 (C),, 128.6 (CH), 127.2 (CH), 118.5 (CH), 115.8 (CH), 114.0 (CH), 63.1 (CH_2).

***N*-(*i*-Propylidene)benzylamine (1k):** ^1H NMR (300 MHz, $CDCl_3$) 7.65 (s, 1H), 7.90-7.28 (m, 5H, aromatic protons), 4.56 (m, 2H), 2.49 (m, 1H) 1.19 (m, 6H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 170.1 (C), 139.4 (C), 128.4 (CH), 127.7 (CH), 126.8 (CH), 64.8 (CH_2), 34.1 (CH), 19.3 (CH_3), 19.2 (CH_3).

Preparation of Aldimine Derivative 1l and 1m.[16] To a solution of ethyl ester of amino acid hydrochloride (50 mol) in THF (50 mL) at 0 °C was added anhydrous $MgSO_4$ (10 g), the benzaldehyde (5.4 g, 50 mmol), and trimethylamine (6.0 mL, 50 mmol), and the mixture was stirred with a magnetic bar for 3 h. The solid phase was filtered off and the organic solvent was evaporated under reduced pressure. Anhydrous pentane (10 ml) was added to the residue, and the eventually formed precipitate was filtered off. The filtrate was concentrated on reduced pressure and the residue was distilled to give **1**.

Ethyl 3-(1-phenylmethylidene)aminopropanoate (1l): (6.1 g, 32 mmol, 64%), ^{1}H NMR (300 MHz, $CDCl_3$) 8.34 (s, 1H), 7.73-7.40 (m, 5H), 3.87 (q, 2H, J = 6.6 Hz), 3.68 (s, 3H), 2.75 (t, 2H, J = 6.6 Hz); ^{13}C NMR (75.0 MHz, $CDCl_3$) 172.3, 162.2, 135.8, 130.6, 128.9, 128.5, 128.0, 77.4, 56.6, 51.7, 35.3.

Ethyl 2(-1-phenylmethylidene)aminoacetate (1m): (5.4 g, 25 mmol, 50%), ^{1}H NMR (300 MHz, $CDCl_3$) 8.29 (s, 1H), 7.80-7.38 (m, 5H), 4.40 (d, 2H, J = 0.9 Hz), 4.24 (q, 2H, J = 7.2 Hz), 1.30 (t, 3H, J = 7.2 Hz); ^{13}C NMR (75.0 MHz, $CDCl_3$) 169.9, 165.2, 135.4, 131.0, 128.8, 128.4, 128.3, 62.1, 61.1, 14.3.

Representative Procedure for Reductive Coupling Reaction of Aldimine Derivative 1 by Use of the System Consisted of cat. Cp_2VCl_2, $PhMe_2SiCl$, and Zn. To a mixture of Cp_2VCl_2 (25 mg, 0.1 mmol) and zinc (262 mg, 4.0 mmol) in DMF (5 mL) was added $PhMe_2SiCl$ (683 mg, 4.0 mmol) at room temperature under argon. After stirring for 1 h, aldimine derivative (**1**) (2.0 mmol) was added to the mixture. The mixture was kept at room temperature with magnetic stirring for 24 h. $CHCl_3$ (10 mL) and HCl aq (1.5 M, 10 mL) were added to the resulting mixture and two liquid layers were separated. The organic layer was washed with NaOH aq (3.0 M, 10 mL), saturated aqueous $NaHCO_3$ (10 mL), water (10 mL X 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, X each 50 mL), giving **2**.

General Procedure for Reductive Coupling Reaction of Aldimine Derivatives 1 by Use of the System Consisted of cat. Cp_2VCl_2, $PhMe_2SiCl$, Al, and Imidazole. 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 (5 mL) was added $PhMe_2SiCl$ (683 mg, 4.0 mmol) at room temperature under argon. After stirring for 1 h, aldimine derivative (**1**) (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 HCl aq (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 X 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 X each 50 mL), giving **2**.

The Structure Determination of 1,2-Diamines 2. The structures of **2g**, **2h**, **2i** and **2j** were determined on the analogy of other compounds such as **2a**. The structures of 1,2-diamines were determined by comparison of the spectral data with those of the authentic samples reported or prepared shown below (**2a, 2b, 2c, 2e, 2f, 2k, 2l, 2m,** and **2m**).

Synthesis of *(R*, R*)-N,N'*-Diallyl-1,2-diphenyl-1,2-ethylenediamine (2d). To a solution of tetrakis(triphenylphoshine)palladium (116 mg, 0.10 mmol) in THF (5 mL) was added allyl acetate (110 mg, 1.1 mmol) at reflux under argon. After the reaction mixture was stirred for 0.5 h, *dl*-1,2-diphenyl-1,2-ethylenediamine (106 mg, 0.5 mmol) was added to the mixture. The solution was kept at reflux with magnetic stirring for 24 h. $CHCl_3$ (10 mL) and HCl aq. (1.5 M, 10 mL) were added to the resulting mixture and two liquid layers were separated. The organic layer was washed with NaOH aq. (3.0 M, 10 mL), saturated aqueous $NaHCO_3$ (10 mL), water (10 mL X 2), and brine (10 mL), dried over Na_2SO_4, and concentrated to give **2d** (*dl*-isomer).

Synthesis of *N,N'*-Dibenzyl-1,2-diphenyl-1,2-ethylenediamine (2a) or *N,N'*-Diphenyl-1,2-diphenyl-1,2-ethylenediamine (2f): To a mixture of Cp_2TiCl_2 (25 mg, 0.1 mmol) and samarium (150 mg, 1.0 mmol) in THF (5 mL) was added **1** (2.0 mmol) at reflux under argon. The reaction mixture was stirred for 24 h. $CHCl_3$ (10 mL) and HCl aq. (1.5 M, 10 mL) were added and the two liquid layers were separated. The organic layer was washed with NaOH aq. (3.0 M, 10 mL), saturated aqueous $NaHCO_3$ (10 mL), water (10 mL X 2), and brine (10 mL), dried over Na_2SO_4, and concentrated to give **2** (*dl*-isomer as a major product). 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, X each 50 mL).

***(R, S)-N,N'*-Dibenzyl-1,2-diphenyl-1,2-ethylenediamine(2a):** *CAS* [27549-76-4]; ^1H

NMR (300 MHz, $CDCl_3$) 7.28-7.15 (m, 20H), 3.86 (s, 4H), 3.74 (d, 2H, *J* = 6.6 Hz), 3.37 (d, 2H, *J* = 6.6 Hz), 1.96 (m, 2H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 140.9 (C), 140.6 (C), 136.4 (C), 136.0 (C), 128.5 (CH), 128.2 (CH), 127.5 (C), 127.4 (CH), 67.2 (CH), 50.9 (CH_2)

(*R*, *S*)-*N*,*N'*-Dihexyl-1,2-diphenyl-1,2-ethylenediamine (2b): *CAS* [60509-69-5]; ^1H NMR (300 MHz, $CDCl_3$) 7.28-7.15 (m, 10H), 3.79 (s, 2H), 2.23 (m, 4H), 1.31-1.07 (m, 16H), 0.75 (m, 6H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 140.6 (C), 136.4 (C), 128.5 (CH), 127.5 (C), 68.5 (CH), 47.3 (CH_2), 31.5 (CH_2), 29.5 (CH_2), 26.5 (CH_2), 22.5 (CH_2), 13.9 (CH_3).

(*R*, *S*)-*N*,*N'*-Di(1-methylethyl)-1,2-diphenyl-1,2-ethylenediamine (2c): *CAS* [55079-98-6]; ^1H NMR (300 MHz, $CDCl_3$) 7.28-7.00 (m, 10H), 3.91 (s, 2H), 2.53 (m, 2H), 0.87 (d, 6H, *J* = 4.8 Hz), 0.84 (d, 6H, *J* = 4.8 Hz); ^{13}C NMR (75.0 MHz, $CDCl_3$) 140.6 (C), 136.4 (C), 128.5 (CH), 127.5 (C), 65.4 (CH), 45.3 (CH_2), 24.2 (CH_3), 21.8 (CH_3).

(*R*, *S*)-*N*,*N'*-Diallyl-1,2-diphenyl-1,2-ethylenediamine (2d): A pale yellow solid (obtained as a stereoisomeric mixture (*dl* / meso = 8 / 92)); mp 55-56 °C (uncorrected); IR (neat) 3053, 1453, 740 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.28-7.15 (m, 10H), 5.64-5.51 (m, 2H), 4.89-4.80 (m, 4H), 3.75 (s, 2H), 2.94-2.92 (m, 2H), 2.78-2.70 (m, 2H), 1.51 (br, 2H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 140.6 (C), 136.4 (C), 128.2 (CH), 128.2 (CH), 127.4 (CH), 115.5 (CH_2), 67.3 (CH), 49.4 (CH_2); MS (EI) MS (EI) *m/z* 293 ($[M+H]^+$, 91), 236 (11), 146 (100), 104 (16), 91 (18), 77 (5); Anal. Calcd for $C_{20}H_{24}N_2$: C, 82.15; H, 8.27; N, 9.58. Found: C, 81.82; H, 8.35; N, 9.48.

(*R, *R**)-*N*,*N'*-Diallyl-1,2-diphenyl-1,2-ethylenediamine (2d):** (*dl* product); IR (neat) 3431, 1454, 760, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) 7.17-7.00 (m, 10H), 5.92-5.79 (m, 2H), 5.11-5.02 (m, 4H), 3.70 (s, 2H), 3.16-2.98 (m, 2H), 2.96-2.93 (m, 2H), 2.06 (br, 2H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 141.0 (C), 136.9 (C), 127.8 (CH), 127.7 (CH), 126.7 (CH), 115.5 (CH_2), 68.2 (CH), 50.0 (CH_2); Anal. Calcd for $C_{20}H_{24}N_2$: C, 82.15; H, 8.27; N, 9.58. Found: C, 82.42; H, 8.26; N, 9.31.

(*R*, *S*)-*N*,*N'*-Diphenethyl-1,2-diphenyl-1,2-ethylenediamine (2e): *CAS* [103276-50-2]; ^1H NMR (300 MHz, $CDCl_3$) 7.56- 7.00 (m, 20H), 3.18 (s, 2H), 3.70 (s, 2H), 2.23 (m, 8H), 1.32 (br, 2H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 141.0 (C), 140.4 (C), 136.9 (C), 135.7 (C), 128.3 (C), 127.8 (CH), 127.7 (CH), 127.4 (C), 68.3 (CH), 48.5 (CH_2), 35.9 (CH_2).

(*R*, *S*)-*N*,*N*'-Diphenyl-1,2-diphenyl-1,2-ethylenediamine (2f): *CAS* [35583-26-7]; ^{1}H NMR (300 MHz, CDCl$_3$) 7.56-7.00 (m, 20H), 3.86 (s, 2H); ^{13}C NMR (75.0 MHz, CDCl$_3$) 142.0 (C), 141.7 (C), 136.7 (C), 136.3 (C), 128.0 (C), 127.8 (CH), 127.7 (CH), 127.4 (C), 68.3 (CH).

(*R*, *S*)-*N*,*N*'-Diallyl-1,2-di(4-methoxyphenyl)-1,2-ethylenediamine (2g): ^{1}H NMR (300 MHz, CDCl$_3$) 7.30-6.98 (m, 8H), 5.59-5.33 (m, 2H), 4.83-4.57 (m, 4H), 3.86 (s, 2H), 2.99-2.74 (m, 4H), 1.72 (br, 2H); ^{13}C NMR (75.0 MHz, CDCl$_3$) 137.8 (C), 136.9 (C), 128.9 (CH), 128.5 (CH), 127.7 (CH), 115.4 (CH$_2$), 67.4 (CH$_2$), 49.7 (CH$_2$), 49.5 (CH$_3$).

(*R*, *S*)-*N*,*N*'-Diallyl-1,2-di(4-methylphenyl)-1,2-ethylenediamine (2h): A pale yellow oil (obtained as a stereoisomeric mixture (*dl* / meso = 10 / 90)); IR (neat) 2921, 1454, 824, 735 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) 7.08-7.07 (m, 4H), 7.00-6.98 (m, 4H), 5.59-5.43 (m, 2H), 4.83-4.76 (m, 4H), 3.65 (s, 2H), 2.89-2.82 (m, 2H), 2.74-2.67 (m, 2H), 2.22 (s, 6H), 1.72 (br, 2H); ^{13}C NMR (75.0 MHz, CDCl$_3$) 137.8 (C), 136.9 (C), 128.9 (CH), 128.5 (CH), 127.7 (CH), 115.4 (CH$_2$), 67.4 (CH$_2$), 49.7 (CH$_2$), 21.1 (CH$_3$); MS (EI) *m/z* 321 ([M-H]$^+$, 7), 264 (8), 160 (100), 105 (12), 91 (9), 77 (2); Anal. Calcd for $C_{22}H_{28}N_2$: C, 82.45; H, 8.81; N, 8.74. Found: C, 82.37; H, 8.79; N, 8.59.

(*R*, *S*)-*N*,*N*'-Diallyl-1,2-di(4-chlorophenyl)-1,2-ethylenediamine (2i): A pale yellow solid (obtained as a stereoisomeric mixture (*dl* / meso = 16 / 84)); mp 57-58 °C; IR (neat) 3434, 1456, 1091, 739 cm^{-1}; ^{1}H NMR (300 MHz, CDCl$_3$) 7.16-6.95 (m, 8H), 5.53-5.40 (m, 2H), 4.76 (m, 4H), 3.61 (s, 2H), 2.78 (dd, 2H, J = 7.1, 2.6 Hz), 2.61 (dd, 2H, J = 14.4, 6.6 Hz), 2.11 (br, 2H); ^{13}C NMR (75.0 MHz, CDCl$_3$) 139.2 (C), 132.9 (C), 129.6 (CH), 128.4 (CH), 127.7 (CH), 116.0 (CH$_2$), 66.5 (CH$_2$), 49.6 (CH$_2$); MS (EI) *m/z* 180 ([M/2]$^+$, 100), 178 (58), 144 (5), 115 (4), 89 (7); Anal. Calcd for $C_{20}H_{22}N_2Cl_2$: C, 66.49; H, 6.14; N, 7.75. Found: C, 66.27; H, 6.11; N; 7.72.

(*R*, *S*)-*N*,*N*'-Diallyl-1,2-di(4-cyanophenyl)-1,2-ethylenediamine (2j): ^{1}H NMR (300 MHz, CDCl$_3$) 7.56-7.12 (m, 8H), 5.77-5.63 (m, 2H), 5.13-4.76 (m, 4H), 3.94 (s, 2H), 3.13-2.99 (m, 4H), 1.67 (br, 2H); ^{13}C NMR (75.0 MHz, CDCl$_3$) 146.1 (C), 136.8 (C), 132.8 (CH), 128.0 (CH), 127.7 (CH), 116.0 (CH$_2$), 111.2 (C), 66.7 (CH$_2$), 49.6 (CH$_2$).

(*R*, *S*)- Ethyl 3-[(2-[2-(ethyloxycarbonyl)ethyl]amino-1,2-diphenylethyl)amino]-propanoate (1m): ^{1}H NMR (300 MHz, CDCl$_3$) 7.43-7.21 (m, 10H), 3.82 (s, 2H), 3.72 (s, 6H), 2.72-2.54 (m, 4H), 2.38-2.24 (m, 4H); ^{13}C NMR (75.0 MHz, CDCl$_3$) 172.3, 135.8, 130.6, 128.9, 128.5, 128.0, 93.2, 77.4, 56.6, 51.7, 35.3.

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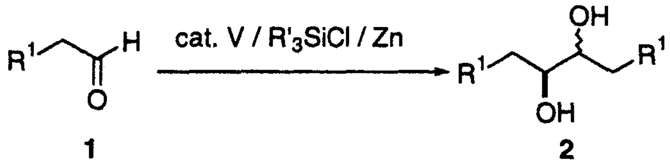
Chapter 3. The Control of the Stereoselectivity in the Catalytic Pinacol Coupling Reaction

3-1. Introduction

In chapters 1 and 2, the highly diastereoselectivity reductive coupling reactions of benzaldehydes and benzaldimines are achieved by catalytic low-valent vanadium complex, giving 1,2-diols and 1,2-diamines, respectively. The catalytic enantioselective pinacol coupling reaction of aliphatic aldehydes is not enough to be investigated.[1,2] This chapter deals with the diastereoselective pinacol coupling reaction of the primary aliphatic aldehydes using the system consisted of cat. V / R'_3SiCl / co-reductant (Equation 1). In addition, the use of titanium catalyst instead of vanadium one was found to lead to the formation of 1,3-dioxsolanes in the place of 1,2-diols in good yield with the *dl*-selectivity (Equation 2). Moreover, in asymmetric catalytic pinacol coupling reaction was investigated and the use of valine derivative as a chiral ligand caused the enantioselectivity (10%*ee*) (Equation 3).



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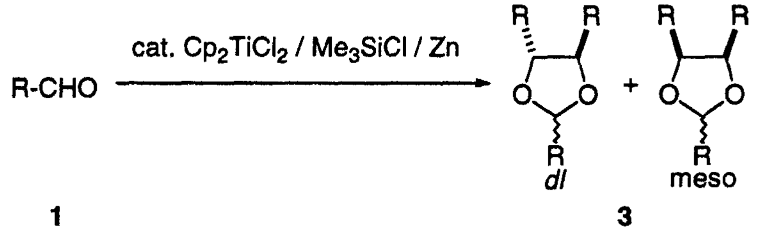

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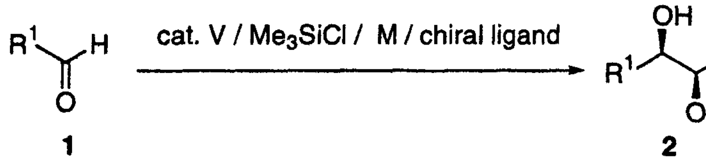
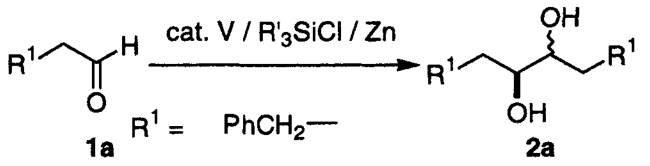


(3)

3-2. Results and Discussion

The influence of vanadium catalyst (5 mol%) in the pinacol coupling of 3-phenylpropionaldehyde (**1a**) was examined as summarized in Table 1.



(4)

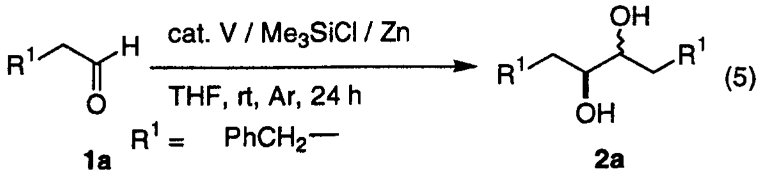
When the reaction of **1a** with Cp_2VCl_2 in presence of $PhMe_3SiCl$ and Zn^3 was conducted for 24 h, the desired reductive coupling product was obtained with the low selectivity (entry 1). The use of $CpVOCl_2$ led to the moderate yield of **2a** with the similar selectivity (entry 3). When $CpVCl_3$ was used as a catalyst, the selectivity and yield were improved slightly (entry 5). The pinacol coupling of **1a** at a low temperature in the presence of vanadium catalyst was examined. The pinacol coupling reaction at −78 °C using Cp_2VCl_2, gave **2a** in the low yield with the similar selectivity (entry 2). On the other hand, **2a** was not obtained by use of $CpVOCl_3$ at a low temperature (−78 °C and −30 °C) (entry 4). The use of $CpVCl_3$ at −78 °C led to decrease of the yield (entry 6).

Table 1. Influence of cat. V and Temprature for the Pinacol Coupling Reaction of 1a [a]

entry	cat. V	temp °C	**2a** yield, % [b]	*dl* / meso [c]
1	Cp_2VCl_2	rt	74	56 / 44
2	Cp_2VCl_2	-78	63	57 / 43
3	$CpVOCl_2$	rt	63	57 / 43
4	$CpVOCl_2$	-78	no reaction [d]	
5	$CpVCl_3$	rt	82	60 / 40
6	$CpVCl_3$	-78	54	58 / 42

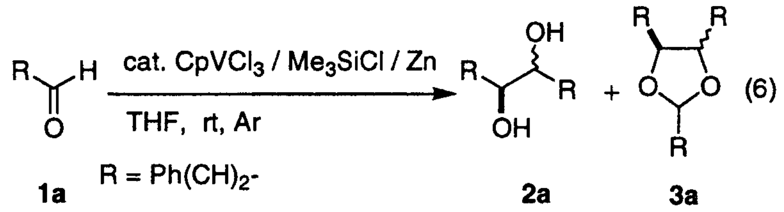
[a] Reaction conditions: 3.3 mmol of **1a**, 5 mol% of cat. V, 6.6 mmol of $PhMe_2SiCl$, 6.6 mmol of Zn, 10 mL of THF, Ar, 24 h. [b] Isolated yield. [c] Determined by ^1H NMR. [d] The reaction did not occured at -30 °C.

To optimize the conditions getting the excellent diastereoselectivity, the pinacol coupling of **1a** in variety of conditions was demonstrated. The results are summarized in Equations 5, 6, and 7. Although in our previous paper, the better selectivity of 1,2-diols for aliphatic secondary aldehydes[4] was obtained in the case of $PhMe_2SiCl$ rather than Me_3SiCl, the distinct difference of Me_3SiCl and $PhMe_2SiCl$ was not observed here. In the presence of Me_3SiCl, the use of Cp_2VCl_2 gave the similar diastereoselectivity as obtained with $CpVCl_3$ (Equation 5).



cat. V	
Cp_2VCl_2	62% yield, *dl* / meso = 63 / 37
$CpVCl_3$	62% yield, dl / meso = 64 / 36

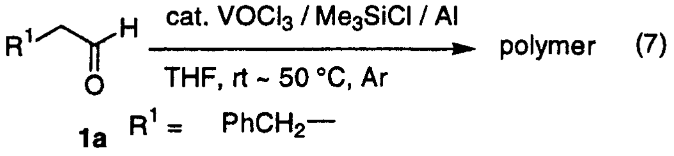
Next, the influence of concentration was examined in the presence of cat. $CpVCl_3$ / Me_3SiCl / Zn. The results were shown in the Equation 6.



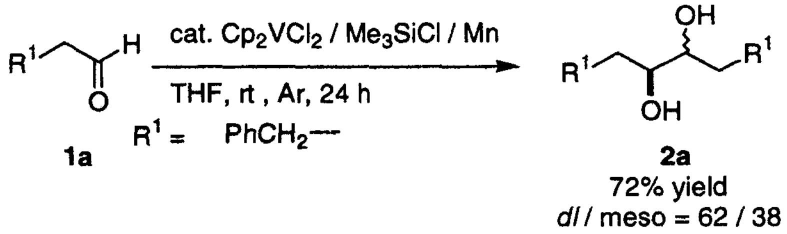
	2a	3a
1a was dropwised for 4 h.	40% yield, 71 / 28 (*dl* / meso)	45% yield, 58 / 42 (*dl* / meso)
1000 mL of THF was used.	no reaction	

When the THF solution (10 mL) of **1** (335 mg, 2.5 mmol) was added dropwise over 4 h, the selectivity of **2** was improved upto 71 / 29 (*dl* / meso) and **5** was obtained as the major product (45% yield, *dl* / meso = 58 / 42). In the case of the high dilution conditions (1000 mL), the pinacol coupling reaction of **1** did not take place at all for 48 h.

In chapter 1, the catalytic system consisted of $VOCl_3$, Me_3SiCl, and Al gave the good results in the pinacol coupling reaction of benzaldehyde derivatives[5]. The reaction of **1a** did not proceed with this catalytic system at room temperature[6] and the polymerization product was obtained at 50 °C (Equation 7).

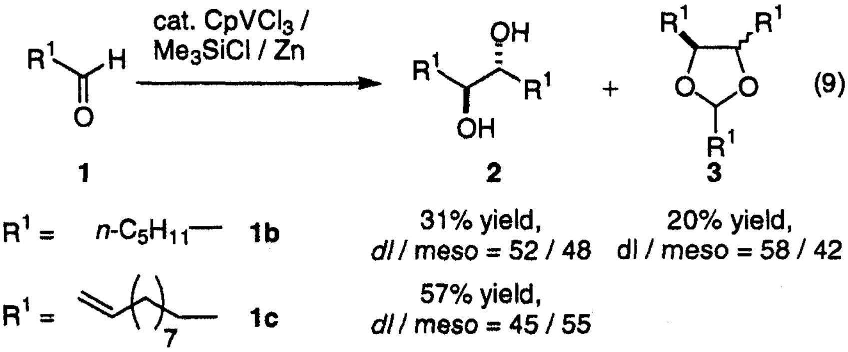


When Mn[7] as a co-reductant instead of Zn was used in the coupling of **1**, the selectivity did not change drastically, giving **2** in the moderate yield (Equation 8).



(8)

The pinacol coupling of several primary aldehydes (**1**) was examined and the results are summarized in Equation 9.



(9)

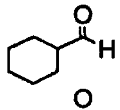
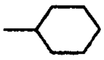
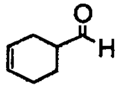
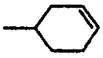
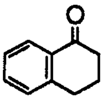
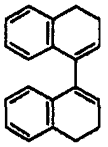
In the case of **1b**, the diastereoselectivity was not observed, giving **2b** in the low yield and, additionally, 1,3-dioxolane **3b** was obtained as a byproduct (20% yield, *dl* / meso = 58 / 42). When **1c** underwent the pinacol coupling by use of $CpVCl_3$, **2c** was provided in 57% yield with no selectivity. In this reaction of **1c**, 1,10-undecadiene was obtained as a byproduct[8] (32% yield).

The pinacol coupling reaction by use of titanium catalyst instead of vanadium was then investigated. The results are summarized in Equation 10 and Table 2.

(10)

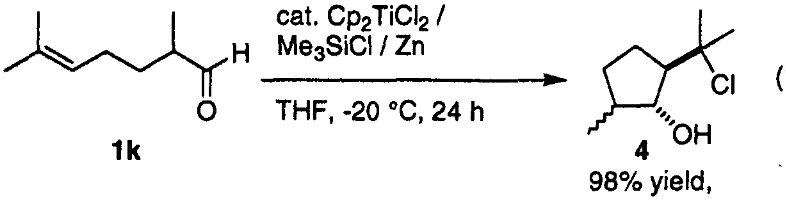
The procedure could be applied to primary and secondary aldehydes, providing the corresponding 1,3-dioxolanes **3** in good yields with moderate diastereoselectivity (entries 1, 2, 3, and 4). Furthermore, the excellent diastereoselectivity was observed by use of the aldehydes bearing the 6-membered ring at the α-position (**1g** and **1h**). In the case of α-tetralone, the initial product, vicinal diol, seemed to undergo dehydration to give the corresponding conjugate diene (entry 6).

Table 2. Cp_2TiCl_2-Catalyzed Pinacol-type Coupling Reaction [a]

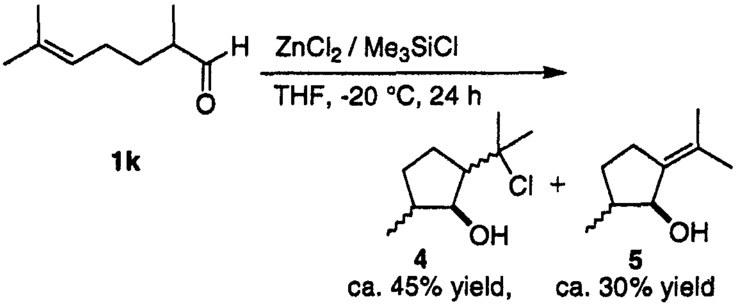
entry	substrate	1	product	5 yield, % [b]	dl / meso [c]
1	$PhCH_2CH_2CHO$	**1a**	R = $PhCH_2CH_2$	88	67 / 33
2	n-$C_5H_{11}CHO$	**1b**	R = n-C_5H_{11}	60	63 / 37
3	Et_2CHCHO	**1d**	R = Et_2CH	80	67 / 33
4 [d]		**1e**	R = 	87	96 / 4
5 [d]		**1f**	R = 	66	81 / 19
6		**1g**		65	

[a] Reaction conditions: **1** (1.0 mmol), Zn (2.0 mmol), Me_3SiCl (2.0 mmol), Cp_2TiCl_2 (3 mol%), DME (7 mL), rt, 13 h. [b] Isolated yield. [c] Determined by ^1H NMR. [d] Reaction temperature, at 0 °C.

Next, the intramolecular cyclization of aldehyde **1k** bearing a carbon-carbon double bond at an appropriate position by using the cat. Cp_2TiCl_2 / Me_3SiCl / Zn system was demonstrated (Equations 11 and 12). The desired reduction proceeded successfully, affording the cyclopentanol derivative **6** in the excellent yield (Equation 11).



(11)

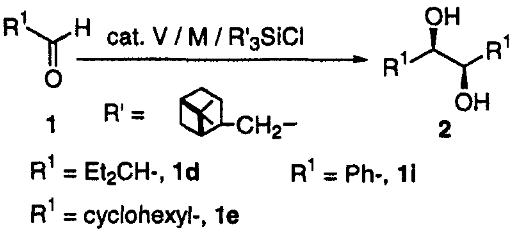


(12)

Although this reaction may proceed via the ene-carbonyl reaction,[9] the use of zinc

(II) chloride in the absence of Cp_2TiCl_2 or Zn resulted in the complex mixture, as indicated in Equation 12. In addition, it is shown that the vanadium catalyst has been to shown induce this cyclization reaction in our previous paper.[4] The present cyclization is considered to proceed by the catalytic system consisted of Cp_2TiCl_2, Me_3SiCl, and Zn and did not proceed via the ene-carbonyl reaction.

Asymmetric catalytic pinacol coupling reaction of aldehydes by a chiral silyl compounds was examined as shown in Equation 13 and Table 3.



(13)

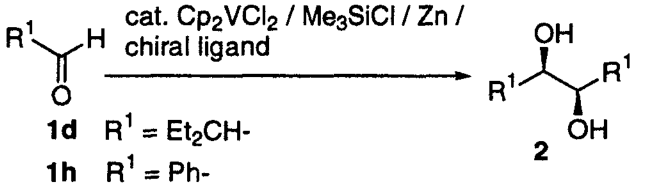
Table 3. **Asymmetric Pinacol Coupling Reaction by the Use of Chiral Silyl Compound [a]**

entry	R^1	cat. V	M	temp, °C	**2** yield, % [b]	dl / meso [c]	%ee [d]
1	**1d**	Cp_2VCl_2	Zn	rt	60	>95 / 5	5
2	**1d**	Cp_2VCl_2	Zn	-78	no reaction		
3	**1d**	Cp_2VCl_2	Mg	rt	15	84 / 16	5
4	**1d**	Cp_2VCl_2	Mn	rt	12	78 / 22	8
5	**1d**	Cp_2VCl_2	Al	rt	trace		
6	**1d**	VCl_3	Zn	rt	no reaction		
7	**1d**	$CpV(CO)_4$	Zn	rt	27	86 / 14	10
8	**1e**	Cp_2VCl_2	Zn	rt	mixture		
9	**1h**	$VOCl_3$	Al	50	78	92 / 8	5
10	**1h**	$VOCl_3$	Al	rt	26	92 / 8	3

[a] Reaction condition:**1** (2.0 mmol), cat. V (5 mol%), $R'Me_2SiCl$ (2 eq.), M (2 eq.), Solvent (10 mL), Ar, 24 h. [b] Isolated yield. [c] Determined in ^1H NMR. [d] Determined by ^{19}F NMR of MTPA ester of **2**.

Although the chiral silyl compound was demonstrated to be efficient in the pinacol coupling of **1d**, the enantioselectivity was low despite of the moderate yield with the high diastereoselectivity (entries 1). At low temperature the reaction did not take place at all (entry 2). The use of the co-reductant (Mg, Mn, and Al) instead of Zn led to only decreas in the yield (entries 3, 4, and 5). The use of a VCl_3-Zn reagent[1] did not cause the reduction of **1d**. The use of CpV(CO)$_4$ also gave **2d** in the low yield and the enantioselectivity of **2d** was again low (entry 6). When the reaction of **1e** can be carried out instead of **1d**, the complex mixture was obtained (entry 7). Although the chiral silyl compound was applied to the coupling of benzaldehyde (**1h**), the similar results were obtained (entries 9 and 10).

Next, the asymmetric pinacol coupling by use of chiral ligands was examined. The results are summarized in Equation 14 and Tables 4 and 5.

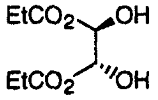
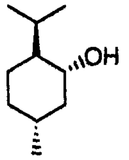
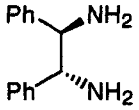
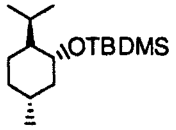
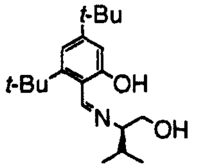
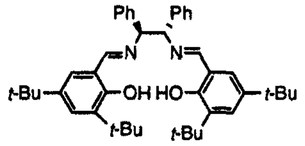
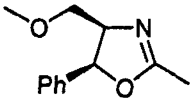


(14)

The asymmetric pinacol coupling reaction of the secondary aldehyde (**1d**) with a chiral ligand (15 mol%) in the presence of Cp$_2$VCl$_2$, Me$_3$SiCl, and Zn was examined (Table 4).

Although diethyl tartaric acetate as a chiral ligand has been demonstrated to be effective in Sharpless enantioselective epoxidation,[10] such an enantioselectivity was not observed in the pinacol coupling reaction by use of vanadium catalytic system (entry 1). The *l*-menthol and it's derivatives were ineffective for the enantioselective pinacol coupling reaction of **1d** (entries 2 and 5). Addition of dihydrocholesterol, a similar result was obtained (entry 3). Though 1,2-diamine has been applied to many asymmetric catalytic reactions as a chelating ligand,[11] the enantioselectivity could not be observed (entry 4). Although Schiff base gives the complex with the vanadium,[12] the enantioselectivity was not observed (entries 6 and 7). The use of the oxazoline resulted in the similar selectivity (entry 8).

Table 4. **Pinacol Coupling Reaction of 1d by Use of Chiral Ligands** [a]

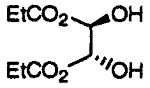
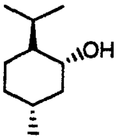
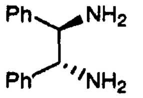
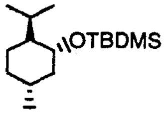
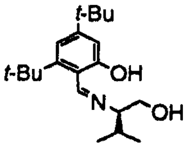
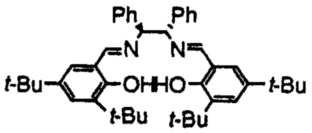
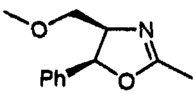
entry	chiral ligand	yield, % [b]	**2d** *de*, % [c]	*ee*, % [d]
1		85	60	4
2		90	70	3
3	dihydrocholesterol	93	70	6
4		93	86	3
5		70	90	2
6		quant	78	8
7		84	80	5
8		84	78	6

[a] Reaction condition; **1d** (2.5 mmol), Cp_2VCl_2 (5 mol%), Me_3SiCl (2 eq.), Zn (2 eq.), chiral ligand (15 mol%), THF (10 mL), Ar, rt, 24 h. [b] Isolated yield. [c] Determined by ^1H NMR. [d] Determined by ^{19}F NMR of the MTPA diester of **2d**.

Next, the asymmetric pinacol coupling reaction of benzaldehyde (**1h**) with a chiral ligand (15 mol%) in the presence of $VOCl_3$, Me_3SiCl, and Al was examined. Although various chiral ligands were examined as tried above, the remarkable results on the enantioselectivity were not obtained (Table 5). However, the enantioselectivity was observed slightly, when the ligand derived from valine was used (entry 6).

In summary, we have disclosed a novel catalytic system of Cp_2TiCl_2, which is also effective for the pinacol-type coupling of aliphatic aldehydes, providing 1,3-dioxolane exclusively with the moderate yield. In addition, the enantioselectivity was observed slightly in the asymmetric pinacol coupling reaction of benzaldehyde, when the ligand derived from valine was used.

Table 4. **Pinacol Coupling Reaction of 1h by Use of Chiral Ligands** [a]

entry	chiral ligand	yield, % [b]	**2h** *de*, % [c]	*ee*, % [d]
1		80	50	5
2		80	56	4
3	dihydrocholesterol	70	60	3
4		60	64	5
5		70	90	2
6		86	86	10
7		70	70	7
8		73	72	5

[a] Reaction condition; **1h** (2.5 mmol), $VOCl_3$ (5 mol%), Me_3SiCl (2 eq.), Al (2 eq.), chiral ligand (15 mol%), DME (10 mL), Ar, 50 °C, 24 h. [b] Isolated yield. [c] Determined by 1H NMR. [d] Determined by ^{19}F NMR of the MTPA diester of **2h** or ^1H NMR of the diacetate with $Eu(hfc)_3$.

3-3. Experimental Section

General Methods

Melting points were determined on Yanagimoto micromelting point apparatus and are uncorrected. Infrared spectra were recorded on Perkin-Elmer 1605 infrared. ^1H NMR or ^{13}C NMR spectra were recorded on Varian MERCURY300 spectrometer (300

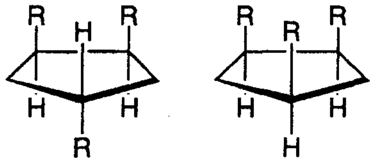
MHz), JEOL JNM-GSX-400 spectrometer (400 MHz), and Bruker AM-600 spectrometer (600 MHz) in chloroform-*d* with tetramethylsilane or residual chloroform as an internal standard. Mass spectra were recorded on Varian Saturn 3 or JEOL JMS-DX-303. Elemental analyses were performed in the analytical section of our department. Thin-layer chromatography (TLC) was carried out on aluminum sheets precoated with silica gel 60 F_{254} (E. Merck). Column chromatography was performed on silica gel 60 (E. Merck). All reagents except TMSCl are of commercial quality. TMSCl is distilled under argon over K_2CO_3 and stores under argon. All dry solvents were freshly distilled under argon over an appropriate drying agent before use.

General Procedure for Pinacol Coupling Reaction of the Primary Aldehydes 1 (Table 1 and Equations 5, 6, 8, and 9). To a mixture of vanadium complex (0.165 mmol, 5 mol%) and co-reductant metal (6.6 mmol) in solvent (10 mL) was added silyl reagent (6.6 mmol) at each temperature under argon. The reaction mixture was kept at the temperature employed in the tables for 1 h. Aldehyde **1** (3.3 mmol) was added to the mixture. The mixture was kept at the same temperature with magnetic stirring for 24 h. Ether (10 mL) and HCl aq (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 X 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 X each 50 mL), giving **2** or **3** as the mixture of *dl* and meso isomers. The products and stereoselectivity were determined by ^{1}H NMR and ^{13}C NMR. Yields were shown in Table 1 and Equations 5, 6, 8, and 9.

1,6-Diphenyl-3,4-hexanediol (2a): [*dl* isomer] ^{1}H NMR (300 MHz, $CDCl_3$, 57 °C) 7.26-7.11 (m, 10H, aromatic proton), 3.42 (m, 2H), 2.81-2.70 (m, 2H), 2.67-2.58 (m, 2H), 2.30 (br, 2H), 1.81-1.71 (m, 2H); ^{13}C NMR (75.0 MHz, $CDCl_3$, 57 °C) 141.7, 128.3, 127.4, 125.7, 73.8, 35.4, 32.0. [meso isomer] ^{1}H NMR (300 MHz, $CDCl_3$, 57 °C) 7.26-7.11 (m, 10H, aromatic proton), 3.56 (m, 2H), 2.81-2.70 (m, 2H), 2.67-2.58 (m, 2H), 2.14 (br, 2H), 1.81-1.71 (m, 2H); ^{13}C NMR (75.0 MHz, $CDCl_3$, 57 °C) 141.7, 128.3, 127.4, 125.8, 74.1, 33.2, 32.3.

2,4,5-Triphenethyl-1,3-dioxolane (3a): [*dl* isomer] ^{1}H NMR (300 MHz, $CDCl_3$, 57 °C)

7.50-7.08 (m, 15H, aromatic proton), 5.12 (t, 1H, J = 5.0 Hz), 3.76-3.67 (m, 2H), 2.97-2.60 (m, 6H), 2.14-1.62 (m, 6H); ^{13}C NMR (75.0 MHz, $CDCl_3$, 57 °C) 141,6, 141.5, 128.4, 128.3, 128.2, 127.4, 125.8, 125.7, 102.7, 80.3, 36.1, 34.8, 32.0, 30.3. [meso isomer **a**] ^{1}H NMR (300 MHz, $CDCl_3$, 57 °C) 7.50-7.08 (m, 15H, aromatic proton), 5.28 (t, 1H, J = 5.0 Hz), 4.14-4.10 (m, 2H), 2.97-2.60 (m, 6H), 2.14-1.62 (m, 6H); ^{13}C NMR (75.0 MHz, $CDCl_3$, 57 °C) 141,6, 141.5, 128.4, 128.3, 128.2, 127.4, 125.8, 125.7, 102.9, 81.4, 36.4, 34.9, 32.6, 30.3. [meso isomer **b**] ^{1}H NMR (300 MHz, $CDCl_3$, 57 °C) 7.50-7.08 (m, 15H, aromatic proton), 5.03 (t, 1H, J = 5.0 Hz), 4.02-3.98 (m, 2H), 2.97-2.60 (m, 6H), 2.14-1.62 (m, 6H).



isomer **a** isomer **b**

6,7-Dodecanediol (2b): [*dl* isomer] ^{1}H NMR (300 MHz, $CDCl_3$, 57 °C) 3.44 (m, 2H), 1.97 (br, 2H), 1.70-1.15 (m, 16H), 0.89-0.78 (m, 6H); ^{13}C NMR (75.0 MHz, $CDCl_3$, 57 °C) 74.9, 31.5, 32.0, 25.4, 22.6, 14.0; [meso isomer] ^{1}H NMR (300 MHz, $CDCl_3$, 57 °C) 3.62 (m, 2H), 1.97 (br, 2H), 1.70-1.15 (m, 16H), 0.89-0.78 (m, 6H); ^{13}C NMR (75.0 MHz, $CDCl_3$, 57 °C) 74.6, 33.8, 32.0, 25.8, 22.6, 14.0.

11,12-docosanediol (2c): [*dl* isomer] ^{1}H NMR (300 MHz, $CDCl_3$, 57 °C) 3.44 (m, 2H), 1.97 (br, 2H), 1.70-1.15 (m, 16H), 0.89-0.78 (m, 6H); ^{13}C NMR (75.0 MHz, $CDCl_3$, 57 °C) 74.9, 31.5, 32.0, 25.4, 22.6, 14.0; [meso isomer] ^{1}H NMR (300 MHz, $CDCl_3$, 57 °C) 3.62 (m, 2H), 1.97 (br, 2H), 1.70-1.15 (m, 16H), 0.89-0.78 (m, 6H); ^{13}C NMR (75.0 MHz, $CDCl_3$, 57 °C) 74.6, 33.8, 32.0, 25.8, 22.6, 14.0.

Reductive Coupling Reaction of 1a by Use of cat. $VOCl_3$ / Me_3SiCl / Al (Equation 7). To a mixture of Al (178 mg, 6.6 mmol, Kanto Chemical Co., Inc.) in THF (9.5 mL) was added the solution (0.5 mL) consisted of $VOCl_3$ (0.331 mL, 3.3 mmol) in THF (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. **1a** (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 and the color of the mixture turned to light blue with nebula. After cooling to room temperature, ether (10 mL) and HCl aq (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 X 2), and brine (10 mL), dried over Na_2SO_4, and concentrated. The polymerization product was obtained. The result was summarized in Equation 7.

General Procedure for Pinacol Coupling Reaction of the Primary Aldehydes 1 (Table 2): To a mixture of Cp_2TiCl_2 (25 mg, 0.10 mmol, 3 mol%) and zinc metal (432 mg, 6.6 mmol) in DME (7 mL) was added Me_3SiCl (0.838 mL, 6.6 mmol) at the temperature employed in Table 2 under argon. The reaction mixture was kept at the same temperature for 1 h. Aldehyde (3.3 mmol) was added to the mixture. The mixture was kept at the same temperature with magnetic stirring for 24 h. Ether (10 mL) and HCl aq (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 X 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 X each 50 mL), giving **3** with the mixture of *dl* and meso isomers. The products and stereoselectivity were determined by ^{1}H NMR and ^{13}C NMR. Yields were shown in Table 2.

2,4,5-Triphenethyl-1,3-dioxolane (3a): [*dl* isomer] ^{1}H NMR (300 MHz, $CDCl_3$, 57 °C) 7.50-7.08 (m, 15H, aromatic proton), 5.12 (t, 1H, *J* = 5.0 Hz), 3.76-3.67 (m, 2H), 2.97-2.60 (m, 6H), 2.14-1.62 (m, 6H); ^{13}C NMR (75.0 MHz, $CDCl_3$, 57 °C) 141,6, 141.5, 128.4, 128.3, 128.2, 127.4, 125.8, 125.7, 102.7, 80.3, 36.1, 34.8, 32.0, 30.3. [meso isomer **a**] ^{1}H NMR (300 MHz, $CDCl_3$, 57 °C) 7.50-7.08 (m, 15H, aromatic proton), 5.28 (t, 1H, *J* = 5.0 Hz), 4.14-4.10 (m, 2H), 2.97-2.60 (m, 6H), 2.14-1.62 (m, 6H); ^{13}C NMR (75.0 MHz, $CDCl_3$, 57 °C) 141,6, 141.5, 128.4, 128.3, 128.2, 127.4, 125.8, 125.7, 102.9, 81.4, 36.4, 34.9, 32.6, 30.3. [meso isomer **b**] ^{1}H NMR (300 MHz, $CDCl_3$, 57 °C) 7.50-7.08 (m, 15H, aromatic proton), 5.03 (t, 1H, *J* = 5.0 Hz), 4.02-3.98 (m, 2H), 2.97-2.60 (m, 6H), 2.14-1.62 (m, 6H).

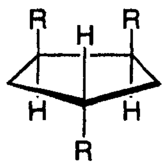
2,4,5-Tri-*n*-pentyl-1,3-dioxolane (3b): [*dl* isomer] ^{1}H NMR (300 MHz, $CDCl_3$, 57 °C)

4.97 (t, 1H, *J* = 5.6 Hz), 3.59-3.54 (m, 2H), 1.73-1.17 (m, 18H), 0.93-0.86 (m, 9H); ^{13}C NMR (75.0 MHz, CDCl$_3$, 57 °C).
[meso isomer **a**] ^{1}H NMR (300 MHz, CDCl$_3$, 57 °C) 4.89 (t, 1H, *J* = 5.6 Hz), 3.93-3.88 (m, 2H), 1.73-1.17 (m, 18H), 0.93-0.86 (m, 9H); ^{13}C NMR (75.0 MHz, CDCl$_3$, 57 °C).
[meso isomer **b**] ^{1}H NMR (300 MHz, CDCl$_3$, 57 °C) 5.12 (t, 1H, *J* = 5.6 Hz), 4.04-4.00 (m, 2H), 1.73-1.17 (m, 18H), 0.93-0.86 (m, 9H).

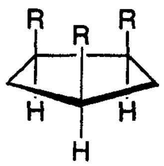
2,4,5-Tri-2-ethylpropyl-1,3-dioxolane (3d): [*dl* isomer] ^{1}H NMR (300 MHz, CDCl$_3$, 57 °C) 4.82 (d, 1H, *J* = 4.3 Hz), 3.69 (t, 1H, *J* = 6.3 Hz), 1.71-1.19 (m, 12H), 0.96-0.87 (m, 9H); ^{13}C NMR (75.0 MHz, CDCl$_3$, 57 °C).
[meso isomer **a**] ^{1}H NMR (300 MHz, CDCl$_3$, 57 °C) 4.89 (t, 1H, *J* = 5.6 Hz), 3.93-3.88 (m, 2H), 1.73-1.17 (m, 12H), 0.93-0.86 (m, 9H); ^{13}C NMR (75.0 MHz, CDCl$_3$, 57 °C).
[meso isomer **b**] ^{1}H NMR (300 MHz, CDCl$_3$, 57 °C) 5.12 (t, 1H, *J* = 5.6 Hz), 4.04-4.00 (m, 2H), 1.73-1.17 (m, 12H), 0.93-0.86 (m, 9H).

2,4,5-Tri-cyclohexyl-1,3-dioxolane (3e): [*dl* isomer] ^{1}H NMR (300 MHz, CDCl$_3$) 4.45 (m, 1H), 3.18 (m, 2H), 1.89-0.82 (m, 30H); ^{13}C NMR (75.0 MHz, CDCl$_3$) 104.3, 41.9, 41.8, 27.1, 26.6, 26.3, 26.1, 25.8, 25.7. [meso isomer **a**] ^{1}H NMR (300 MHz, CDCl$_3$) 4.62 (m, 1H), 3.18 (m, 2H), 1.89-0.82 (m, 30H). [meso isomer **b**] ^{1}H NMR (300 MHz, CDCl$_3$) 4.40 (m, 1H), 3.18 (m, 2H), 1.89-0.82 (m, 30H).

2,4,5-Tri-3-cyclohexenyl-1,3-dioxolane (3f): [*dl* isomer] ^{1}H NMR (300 MHz, CDCl$_3$) 7.52 (m, 1H), 5.59 (m, 1H), 4.62 (m, 1H), 3.12 (m, 2H), 1.89-0.82 (m, 30H); ^{13}C NMR (75.0 MHz, CDCl$_3$) 104.3, 41.9, 41.8, 27.1, 26.6, 26.3, 26.1, 25.8, 25.7. [meso isomer **a**] ^{1}H NMR (300 MHz, CDCl$_3$) 4.62 (m, 1H), 3.18 (m, 2H), 1.89-0.82 (m, 30H). [meso isomer **b**] ^{1}H NMR (300 MHz, CDCl$_3$) 4.40 (m, 1H), 3.18 (m, 2H), 1.89-0.82 (m, 30H).



isomer **a**



isomer **b**

1,1'-Di-3,4-dihydronaphtalene (3g): ^{1}H NMR (300 MHz, CDCl$_3$) 7.19-6.95 (m, 8H, aromatic proton), 6.11 (t, 2H, *J* = 4.5 Hz), 291 (t, 4H, *J* = 7.9 Hz), 2.43 (dt, 4H, *J* = 7.9, 4.5 Hz); ^{13}C NMR (75.0 MHz, $CDCl_3$) 138.3, 135.8, 134.7, 128.0, 127.3, 126.7, 125.3, 28.2, 23.3.

Intramolecular Pinacol Coupling Reaction (Equations 11 and 12): To a mixture of Cp_2TiCl_2 (25 mg, 0.10 mmol, 3 mol%) and zinc metal (432 mg, 6.6 mmol) in DME (7 mL) was added Me_3SiCl (0.838 mL, 6.6 mmol) at the temperature employed in the Equations 11 and 12 under argon. The reaction mixture was kept at the same temperature for 1 h. Aldehydes **1** (3.3 mmol) was added to the mixture. The mixture was kept at the same temperature with magnetic stirring for 24 h. Ether (10 mL) and HCl aq (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 X 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 X each 50 mL), giving **3** with the mixture of *dl* and meso isomers. The products and stereoselectivity were determined by ^{1}H NMR and ^{13}C NMR. Yields were shown in Equations 11 and 12.

2-(1-Chloro-1-methylethyl)-5-methyl-1-cyclopentanol (4). Pale yellow oil (obtained as a stereoisomeric mixture (α-Me/ β-Me = 67/23)); ^{1}H NMR (300.0 MHz, $CDCl_3$) [α-Me isomer] 3.60 (t, 1H, J = 7.7 Hz), 2.17 (br, 1H), 2.08-2.02 (m, 1H), 1.88-1.73 (m, 3H), 1.63 (s, 3H), 1.55 (s, 3H), 1.41-1.09 (m, 2H), 1.04 (d, 3H, J = 6.3 Hz); ^{13}C NMR (75.0 MHz, $CDCl_3$) 81.5, 74.7, 58.8, 42.9, 31.8, 30.7, 30.4, 25.6, 17.4. [β-Me isomer] 3.72 (t, 1H, J = 7.7 Hz), 2.17 (br, 1H), 2.08-2.02 (m, 1H), 1.88-1.73 (m, 3H), 1.65 (s, 3H), 1.52 (s, 3H), 1.41-1.09 (m, 2H), 1.00 (d, 3H, J = 6.9 Hz); ^{13}C NMR (75.0 MHz, $CDCl_3$) 76.8, 73.7, 61.1, 45.8, 39.7, 32.0, 30.8, 27.2, 13.3. IR (KBr) 3487, 2946, 1458, 1377, 1104, 911, 738 cm^{-1}; MS (EI) *m/z* =140 (M^+); Anal. Calcd for $C_9H_{17}OCl$: C, 61.18; H, 9.70. Found: C, 61.47; H, 9.87.

2-Isopropenyl-5-methyl-1-cyclopentanol (5). Colorless oil (obtained as a stereoisomeric mixture); ^{1}H NMR (300.0 MHz, $CDCl_3$) 4.98-4.80 (m, 2H), 3.55-3.47 (m, 1H), 2.07-1.85 (m, 1H), 1.80 (s, 3H) 1.78-1.00 (m, 6H), 0.96-0.89 (m, 3H); ^{13}C NMR (75.0 MHz, $CDCl_3$) 147.5, 146.6, 112.8, 111.9, 71.2, 70.4, 54.1, 53.9, 42.7, 42.3, 34.3, 33.3, 31.5, 31.0, 29.7, 28.0 19.2, 18.5.

General Procedure for Pinacol Coupling Reaction of 1 by Use of Dimethychlorosilyl Methyl-7,7-dimethylnorpinene (Equation 13 and Table 3). To a mixture of vanadium complex (0.165 mmol, 5 mol%) and co-reductant metal (6.6 mmol) in solvent (10 mL) was added dimethychlorosilyl methyl-7,7-dimethylnorpinene (1523 mg, 6.6 mmol) at the temperature employed in Table 3 under argon. The reaction mixture was kept in the same temperature for 1 h. Aldehyde (3.3 mmol) was added to the mixture. The mixture was kept at the same temperature with magnetic stirring for 24 h. Ether (10 mL) and HCl aq (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 X 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 X each 50 mL), giving **2** with the mixture of stereoisomeric isomers. Diastereoselectivity was determined by ^{1}H NMR and ^{13}C NMR. Enantioselectivity was determined by ^{19}F NMR of MTPA diester of **2**. Yields, and diastereoselective excess, and enantioselective excess are shown in Table 3.

General Procedure for Asymmetric Pinacol Coupling Reaction of 2-Ethylbutanal (1d) (Table 4): To a solution of Cp_2VCl_2 (25 mg, 0.10 mmol, 5 mol%) in THF (10 mL) was added chiral ligand (0.30 mmol, 15 mol%) under argon and stirred for 1 h. Then, zinc metal (262 mg, 4.0 mmol) and Me_3SiCl (0.508 mL, 4.0 mmol) was added to the mixture and the reaction mixture was kept at each temperature for 1 h. 2-Ethylbutanal (202 mg, 2.0 mmol) was added to the mixture and the mixture was kept at room temperature with magnetic stirring for 24 h. Ether (10 mL) and HCl aq (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 X 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 X each 50 mL), giving **2d** with the mixture of *dl* and meso isomers. Diastereoselectivity of **2d** was determined by ^{1}H NMR and ^{13}C NMR. Enantioselectivity was determined by ^{19}F NMR of MTPA di-ester of **2d**. Yields, and diastereoselective excess, and enantioselective excess are shown in Table 4.

General Procedure for Asymmetric Pinacol Coupling Reaction of Benzaldehyde 1h (Table 5). To a solution of a chiral ligand (3.0 mmol, 15 mol%) in DMF (9.5 mL) the solution (0.5 mL) consisted of $VOCl_3$ (0.200 mL, 2.0 mmol) in DME (10 mL) was added and the mixture was stirred for 1 h. Then, Al (108 mg, 4.0 mmol) was added 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 (0.508 mL, 4.0 mmol) was added to the reaction mixture and the color changed from red purple to light blue. Benzaldehyde (1h) (214 mg, 2.0 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 and the color of the mixture turned to light blue with nebula. After cooling to room temperature, ether (10 mL) and HCl aq (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 X 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 X each 50 mL), giving **2h** with the mixture of *dl* and meso isomers. Diastereoselectivity of **2h** was determined by ^{1}H NMR and ^{13}C NMR. Enantioselectivity was determined by acetyl diester of **2h**. Yields, and diastereoselective excess, and enantioselective excess are shown in Table 4.

3,6-Diethyl-4,5-octanediol (2d). Colorless solid; mp 88-89 C; ^{1}H NMR (400 MHz, $CDCl_3$) 3.78 (d, 2H, J = 1.8 Hz), 2.68 (br, 2H), 1.70-1.45 (m, 10H), 1.08 (t, 12H, J = 7.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) 72.9, 43.2, 22.3, 20.8, 11.6, 11.5; IR (KBr) 3294, 2953, 1028 cm^{-1}; MS (EI) m/z = 202 (M+); Anal. Calcd for $C_{12}H_{26}O_2$: C, 71.23; H, 12.95. Found: C, 70.81; H, 12.74.

1,2-Di(3-cyclohexyl)-1,2-ethanediol (2e). Colorless solid (obtained as a stereoisomeric mixture); ^{1}H NMR (400 MHz, $CDCl_3$) [stereoisomeric mixture] 3.39-3.54 (m, 2 H), 1.31-2.20 (m, 18 H); ^{13}C NMR (100 MHz, $CDCl_3$) 74.53; 74.39, 36.48, 36.34, 28.36, 28.20, 25.85, 25.51, 25.15, 25.07, 25.03, 24.95, 24.68, 24.20; IR (KBr) 3307, 3022, 2912, 1419, 1067 cm^{-1}.

1,2-Bisphenyl-1,2-ethanediol (2h). *CAS* {579-43-1}; mp 138 °C; ^{1}H NMR (300 MHz,

$CDCl_3$) 7.15 (m, 6H), 7.05 (m, 4H), 4.78 (s, 2H), 2.30 (br, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) 139.7, 128.1, 128.0, 127.0, 78.0.

Synthesis of α-Methyl-α-(trifloromethy)phenyl ester of 3,6-Diethyl-4,5-octanediol (2d). To a solution of **2d** (20 mg, 0.1 mmol) in CH_2Cl_2 (1.0 mL) was added α-methyl-α-(trifloromethy)phenyl (0.056 mL, 0.2 mmol) at room temperature under argon. Then, *N,N*-dimethyl-4-aminopyridine (49 mg, 0.4 mmol) was added to the reaction mixture and the reaction mixture was kept with magnetic stirring for 5 h. Ether (10 mL) and HCl aq (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 X 2), and brine (10 mL), dried over Na_2SO_4, and concentrated. Diester was obtained as a mixture of stereoisomeric isomers without purification.

3-Ethyl-1-(1-ethylpropyl)-2-[(2,2,2-trifluoro-1-methoxy-1-phenylethyl)carbonyloxy]pentyl 3,3,3-trifluoro-2-methoxy-2-phenylpropanoate. ^1H NMR (300.0 MHz, $CDCl_3$) 7.64-7.28 (m, 20H), 5.34-5.28 (s, 4H), 3.56 (m, 3H), 3.54 (m, 3H), 1.58-1.25 (m, 16H), 0.95-0.87 (m, 24H); ^{19}F NMR (300.0 MHz, $CDCl_3$) -71.55, -71.59; ^{13}C NMR (75 MHz, $CDCl_3$) 171.3, 170.9, 131.1, 130.4, 128.7, 128.6, 127.5, 127.3, 125.0, 124.9, 121.1, 120.9, 79.4, 79.3, 72.4, 72.1, 43.1, 42.4, 42.4, 42.2, 22.4, 22.3, 22.2, 21.5, 21.2, 20.4, 11.8, 11.6.

Synthesis of 2-(Methylcarbonyloxy)-1,2-diphenylethy acetate. To a solution of **2h** (20 mg, 0.1 mmol) in CH_2Cl_2 (5.0 mL) was added acetyl chloride (0.25 mL) at room temperature under argon. Then, triethylamine (1 mL, 9.1 mmol) and *N,N*-dimethyl-4-aminopyridine (49 mg, 0.4 mmol) were added to the reaction mixture and the reaction mixture was kept for with magnetic stirring for 5 h. Ether (10 mL) and HCl aq (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 X 2), and brine (10 mL), dried over Na_2SO_4, and concentrated. Diester was obtained as a single product without purification.

2-(Methylcarbonyloxy)-1,2-diphenylethy acetate. ^1H NMR (300.0 MHz, $CDCl_3$) 7.12-7.04 (m, 10H), 5.98 (s, 2H), 1.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) 169.9, 136.4, 128.6, 128.4, 128.3, 127.8, 127.7, 77.5, 21.4.

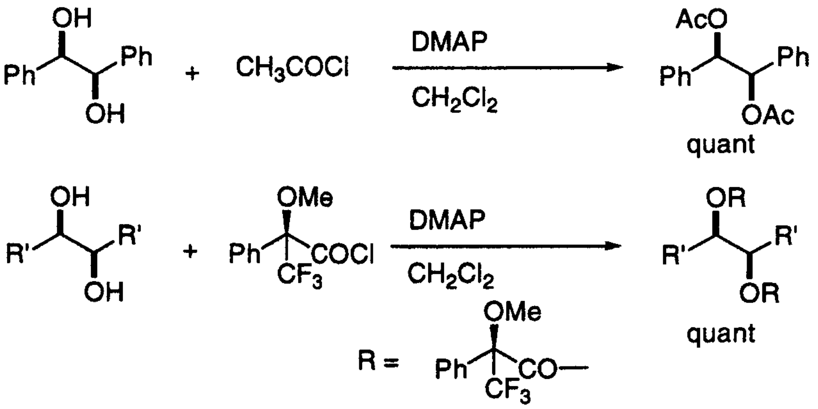


Figure 1

3-4. References and Notes

1 Pedersen's group and Cinquini's group reported the high diastereoselectivity and enantioselectivity for the stoichiometric reductive coupling of aldehydes. References see: (a) Kang, M.; Park, J.; Pedersen, S. F. *Synlett.* **1997**, 41. (b) Konradi, A.; Kemp, S.; Pedersen, S. F. *J. Am. Chem. Soc.* **1994,** *116,* 1316. (c) Konradi, A. W.; Pedersen, S. F. *J. Org. Chem.* **1992,** *57,* 28. (d) Raw, A. S.; Pedersen, S. F. *J. Org. Chem.* **1991,** *56,* 830. (e) Freudenberger, J. H.; Konradi, A. W.; Pedersen, S. F. *J. Am. Chem. Soc.* **1989,** *111,* 8014. (f) Annunziata, R.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Giaroni, P. **1991,** *57,* 782.

2 The high diastereoselectivity was achieved in the catalytic pinacol coupling reaction of the secondary aliphatic aldehydes. Reference see: Hirao, T.; Asahara, M.; Muguruma, Y.; Ogawa, A. *J. Org. Chem.* **1998,** *63,* 2812.

3 The use of catalytic system consisted of cat. Cp_2VCl_2 / $PhMe_2SiCl$ / Zn provided 1,2-diol in good yield with high selectivity for the pinacol coupling reaction of the secondary aldehydes; see reference 2.

4 Hirao, T.; Asahara, M.; Muguruma, Y.; Ogawa, A. *J. Org. Chem.* **1998,** *63,* 2812.

5 Hirao, T.; Hatano, B.; Imamoto, Y.; Ogawa, A. *J. Org. Chem.* **1999,** *64,* 7665-7667.

6 1,2-Diol was observed on thin-layer chromatography (TLC).

7 Gansäuer's group reported that the catalytic system consisted of cat. Cp_2TiCl_2 / 2,4,6-collidine hydrochloride / Mn gives the high selectivity of pinacol coupling of benzaldehydes. References see: Gansäuer, A.; Bauer, D. *J. Org. Chem.* **1998,** *63,* 2070.

8 In the case of **1c**, the initial product, 1-undecen-11-ol, underwent dehydration to give the corresponding 1,10-undecadiene.

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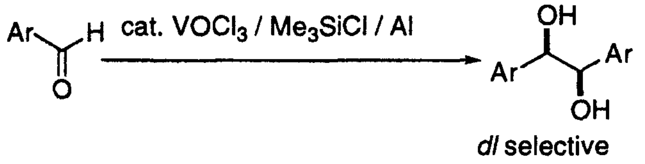
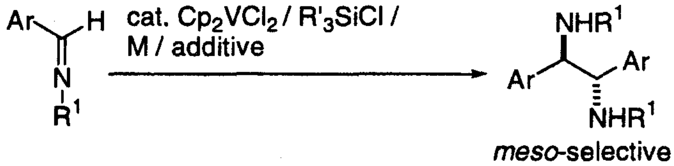
Conclusion

This thesis deals with diastereoselective reductive coupling reactions using the catalytic amount of early transition metal in the present of co-reductant, chlorosilane, and additive. The results and findings obtained through this work gave important information on the control of stereoselectivity in the reductive coupling of aldehydes derivatives. This basic work is expected to contribute to the further development of the highly stereoselective catalytic synthesis of *vic*-bifunctionalized stretchers.

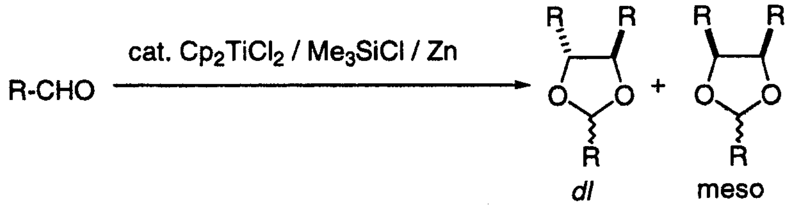
In chapter 1, $VOCl_3$ in the presence of Me_3SiCl and Al worked as an efficient catalyst in the catalytic pinacol coupling of benzaldehyde derivatives. This reductive coupling reaction proceeded through the cyclic intermediate, which has been proposed that two pair of lone pair on oxygen of aldehydes participate in coordination to both of low-valent metal complex and reductant and then R groups are arranged *anti* to each other to optimize the steric influence, and provided 1,2-diols with high *dl*-selectivity.



In chapters 2, it was shown that Cp_2VCl_2 / $PhMe_2SiCl$ / Zn was the efficient catalyst system in diastereoselective reductive coupling reaction of benzaldimines. In the case of the aldimines, *meso*-selectivity is in contract to the *dl*-selectivity observed in the catalytic pinacol coupling of aldehydes. In addition, it was found that the reaction was promoted by the addition of imidazole to the Cp_2VCl_2 / $PhMe_2SiCl$ / Al catalyst system.



Chapters 3 deals with the diastereoselective pinacol coupling reactions for the primary aliphatic aldehydes using the system consisted of cat. V / R'_3SiCl / M. In addition, the use of titanium catalyst instead of vanadium was fomed to lead to the formation of 1,3-dioxsolanes in the place of 1,2-diols in good yield with the *dl*-selectivity. Moreover, in asymmetric catalytic pinacol coupling reaction was investigated and the use of valine derivative as the chiral ligand caused the enantioselectivity (10%*ee*).



The early transition metals such as vanadium and titanium complex were demonstrated in the catalytic pinacol coupling reaction in the presence of Me_3SiCl and co-reductant. This catalytic system gave 1,2-diols, 1,2-diamines, and 1,3-dioxolanes with high diastereoselectivity.

List of Publications

1) Cp_2TiCl_2-Catalyzed Pinacol-Type Coupling of Aliphatic Aldehydes by Use of Zinc and Chlorosilane

Toshikazu Hirao, Bunpei Hatano, Motoki Asahara, Yasuaki Muguruma, and Akiya Ogawa

Tetrahedron Letters, **1998**, *39,* 5247-5248.

2) Cp_2VCl_2-Catalyzed *Meso*-Selective Pinacol Coupling Reaction of Aldimines in the Presence of Chlorosilane and Zinc Metal

Bunpei Hatano, Akiya Ogawa, and Toshikazu Hirao

The Journal of Organic Chemistry, **1998**, *63,* 9421-9424.

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

Toshikazu Hirao, Bunpei Hatano, Yuka Imamoto, and Akiya Ogawa

The Journal of Organic Chemistry, **1999**, *64,* 7665-7667.

List of Supplementary Publications

1) A Novel Redox System for the Palladium(II)-Catalyzed Oxidation Based on Redox of Polyanilines

Toshikazu Hirao, Masayoshi Higuchi, Bunpei Hatano and Isao Ikeda

Tetrahedron Letters. **1995**, *36*, 5925-5928.

2) High 1,3-Asymmetric Induction in Addition of Allylic Tin Reagents to Chiral 3-Substituted 3,4-Dihydroisoquinolines Activated by Acyl Chlorides

Bunpei Hatano, Yoshikazu Haraguchi, Sinpei Kozima, and Ryohei Yamaguchi

Chemistry Letters. **1995**, 1003-1004.

3) Triflate Ion-Promoted Addition Reactions of Allylsilane to Quinolines and

Isoquinolines Acylated by Chloroformate Esters

Ryohei Yamaguchi, Bunpei Hatano, Tatsuya Nakayasu, and Sinpei Kozima

Tetrahedron Letters. **1997,** *38,* 403-406.

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