Doctoral Dissertation

Cross-Pinacol Coupling Reaction Catalyzed by Dinuclear Complexes

（二核金属錯体による触媒的クロスピナコールカップリング反応）

Akihiro Miyasaka

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Department of Applied Chemistry

Graduate School of Engineering,

Osaka University

Preface

The studies presented in this thesis were performed under the guidance of Professor Toshikazu Hirao, Department of Applied Chemistry, Graduate School of Engineering, Osaka University during 2008-2014.

The objects of this thesis are studies on the catalytic system using dinuclear complex for cross-pinacol coupling reaction.

The author hopes that this basic work described in this thesis contributes to the further development of cross-pinacol coupling, dinuclear catalyst, and so on.

Akihiro Miyasaka

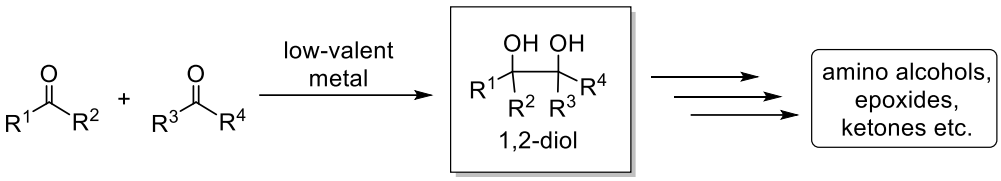
Department of Applied Chemistry
Graduate School of Engineering
Osaka University
Suita, Osaka
Japan

January, 2014

Contents

General Introduction

The reductive coupling reactions of carbonyl compounds with the aid of low-valent early transition metals provide an important method for the construction of a vicinally functionalized carbon-framework (Scheme 1).[1] The popularity of this reaction stems from its intrinsic ability to furnish 1,2-diols, which are a very important class of compounds. These can be converted into a number of compounds such as amino alcohols, epoxides, ketones etc.



Scheme 1.

These diols can serve as the structural motif in total synthesis, and as chiral auxiliaries or chiral ligands. In fact, the pinacol coupling reaction has been used as key steps in the synthesis of taxol[2] and HIV protease inhibitors (Figure 1).[3]

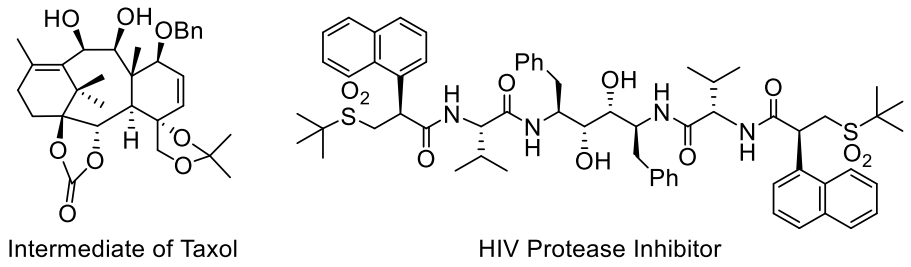
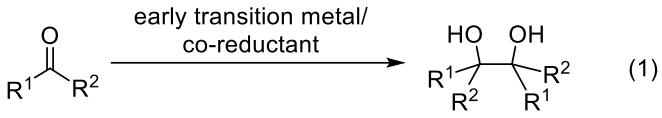


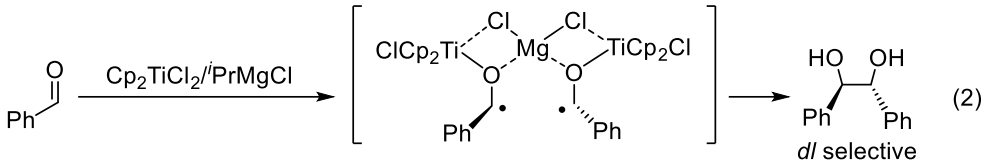
Figure 1. The structure of intermediate of Taxol and HIV protease inhibitor.

Sodium or lithium is used as low-valent metals for pinacol coupling. However, their application range is limited due to the low tolerance for some functional groups. A combination of early transition metal salts with metallic reductants such as Mg and Zn is effective to make the reaction conditions milder. Tyrik's group[4a] and Mukaiyama's group[4b] reported the reaction system consisted of $TiCl_3$/Mg and $TiCl_4$/Zn, respectively (Equation 1). McMurry and co-workers also revealed the pinacol coupling reaction using $TiCl_3/LiAlH_4$.[4c]

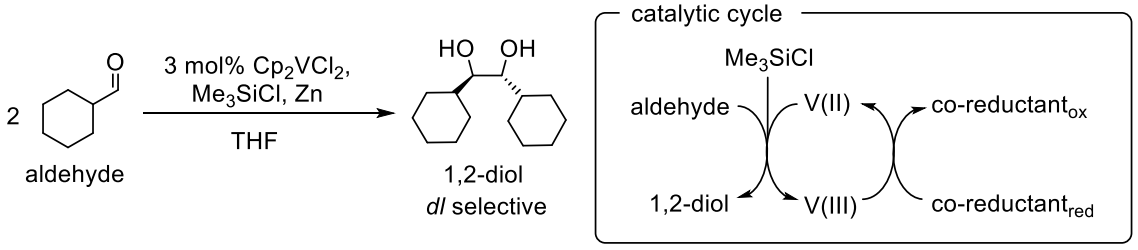


$TiCl_3$/Mg: S. Tyrlik, et al. (1973)
$TiCl_4$/Zn: T. Mukaiyama, et al. (1973)
$TiCl_3$/$LiAlH_4$: J. McMurry, et al. (1974)

Stereoselective pinacol coupling reactions have been developed. For example, Inanaga's group reported *dl* selective coupling reaction using Cp_2TiCl_2/^{i}PrMgCl through the magnesium bridged intermediate (Equation 2).[5]



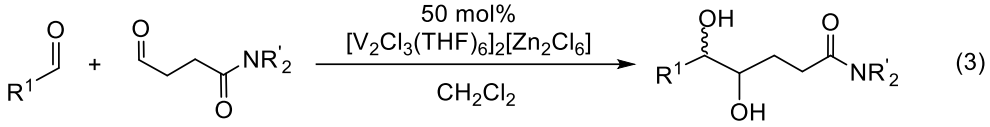
In our group, a catalytic system for the pinacol coupling reaction, consisting of a catalytic amount of vanadium or titanium compound with a chlorosilane and a co-reductant such as Zn was revealed (Scheme 2).[6] *dl*-Selective pinacol coupling reactions using Cp_2VCl_2 catalyst was also reported.[6g]



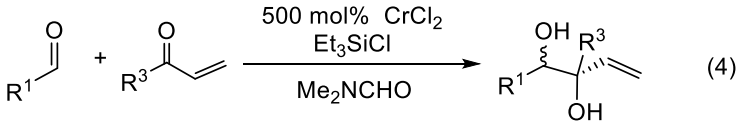
Scheme 2.

In contrast, the intermolecular cross-pinacol coupling reaction is still a challenging issue due to the difficulty in the discrimination of two aldehydes in the reaction, which is apparently more important than the homo-coupling reactions as a tool for the convergent synthetic strategies. So far, there are only a few examples for the cross-pinacol-type coupling, which strongly depend on the combination of substrates.[7]

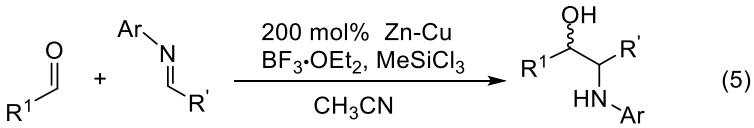
For example, Pedersen's group reported the cross-pinacol coupling reactions using stoichiometric dimeric vanadium complex between aldehydes containing an appropriately placed chelating group and aliphatic aldehydes (Equation 3).[7b-f]



Takai and co-workers showed that the reaction of *α,β*-unsaturated ketone treated with an excess of chromium compound produces the corresponding allylic Cr^{III} intermediate. The organometallic chromium species attacks to aliphatic aldehyde to give the corresponding 1,2-diol (Equation 4).[7j] Groth and co-workers developed the chromium-mediated cross-coupling reaction of *α,β*-unsaturated carbonyl compounds and aldehydes using a catalytic amount of chromium chloride with a chlorosilane and a co-reductant.[7k,l]



Shimizu's group reported cross-coupling reaction between aldehyde and aldimine using *in situ* generated borane-silicon complex (Equation 5).[7i]



As mentioned above, cross-coupling reactions strongly depend on substrate control. Therefore, the developments of more versatile methods for cross-pinacol coupling are required. For that reason, a reductant control strategy is extremely important for this catalytic reaction.

In this context, the author envisioned that the controlled arrangement of two metals on the rigid scaffold can provide spatially regulated reaction sites for the cross-pinacol coupling reaction (Figure 2). Therefore, the bimetallic complex, in which two discriminated active sites (M^1, M^2) and two different substituents (R^5 and R^6) are three-dimensionally regulated through a rigid scaffold, would lead to multifunctional catalysts depending on the individual activated sites. The substituents around each metal are expected to interact with substrates based on steric repulsion, π-π interaction, or hydrophobic interaction. By using these effect, cross-pinacol coupling compound would be preferentially produced based on the selective activation of two different aldehydes in the discriminated active sites.

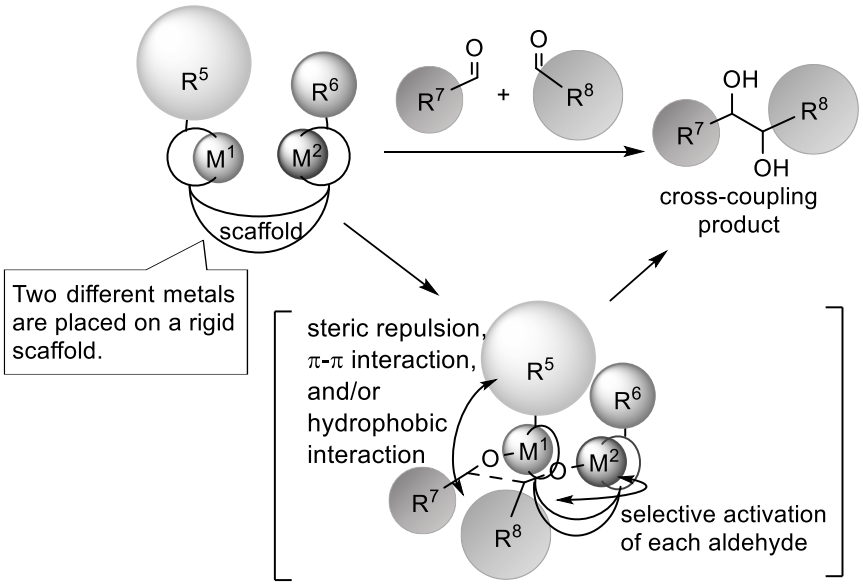


Figure 2. Concept for cross-pinacol coupling reaction with ligand controlled dual activation.

This thesis deals with design and synthesis of the dinuclear complexes for the intermolecular cross-pinacol coupling reaction. In chapter 1, the rigid bis-biphenol ligand on a hexaaryl scaffold for a dinuclear complex was synthesized. Its application for the titanium-induced cross-pinacol coupling reaction was performed based on step-by-step activation of two different aldehydes. In chapter 2, the dinuclear vanadium(V)-dihemisalen complexes on the hexaaryl scaffold were designed and synthesized. By using the dinuclear vanadium catalyst, the cross-pinacol coupling reaction between two different aromatic aldehydes was investigated. In chapter 3, The hetero dinuclear complexes with vanadium(V) and titanium(IV) were synthesized from the corresponding disalicylaldehyde compound. Using the hetero dinuclear catalysts, the selective intermolecular cross-pinacol coupling reactions between aliphatic and aromatic aldehydes were demonstrated.

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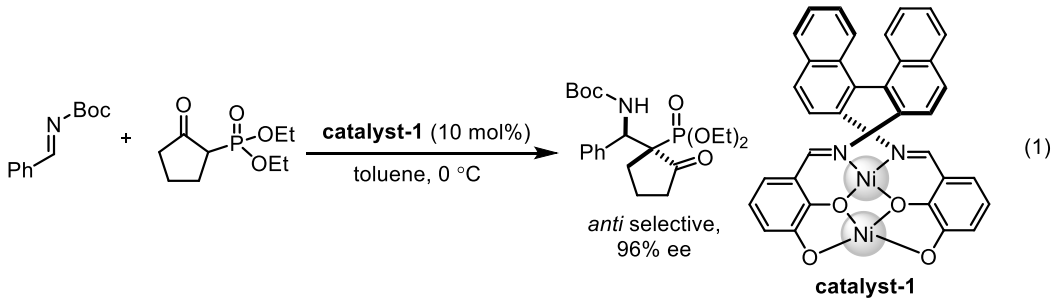
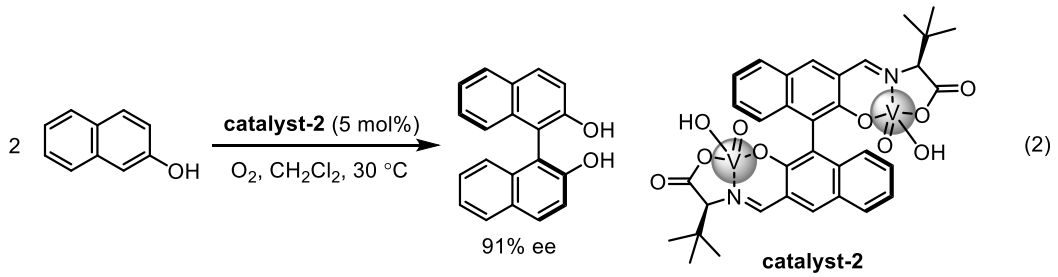
Chapter 1. Synthesis of Three-dimensionally Arranged Bis-biphenol Ligand and Its Application for Cross-Pinacol Coupling Reaction

1-1. Introduction

Dinuclear transition metal complex catalysts have attracted much attention,[1] which are also found sometimes in the active sites of enzymes to catalyze the reactions.[2] Some advantages are considered for dinuclear transition metal catalysts as follows: 1) dual activation of two substrates, 2) positioning two substrates appropriately for the reaction, and 3) electrically cooperating effect. So far, many dinuclear catalysts have been developed and applied to organic reactions.[3] For example, Shibasaki *et al.* reported the asymmetric Mannich reaction with dinuclear nickel catalysts, where the dual activation of each substrate is suggested (Equation 1).[3d] Sasai *et al.* reported the asymmetric oxdative coupling reaction of naphthols using divanadium catalyst (Equation 2).[3e]



(1)



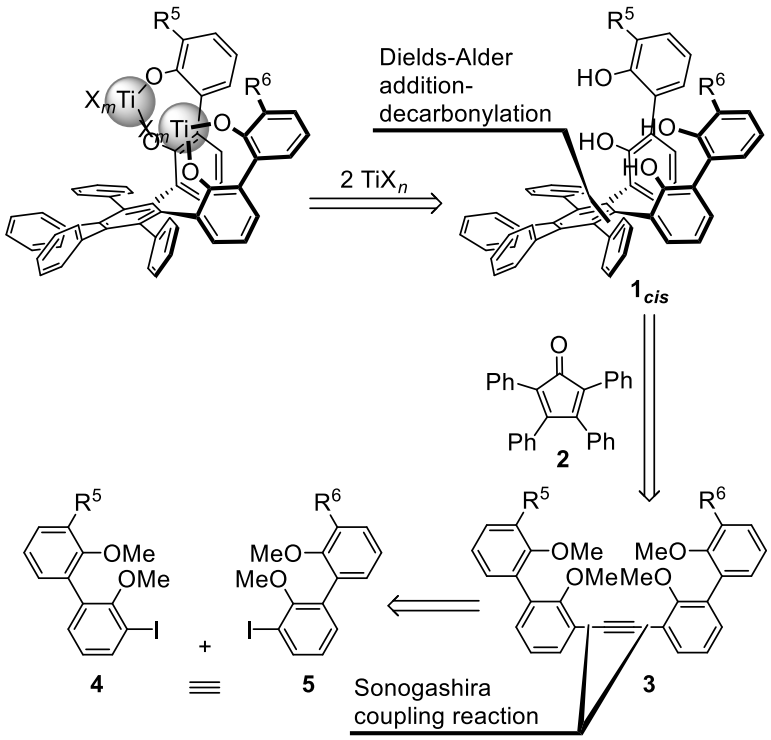
(2)

On the other hand, biphenol structures are widely utilized as the functional ligands.[4] For example, Mukaiyama *et al.* reported the asymmetric aldol reactions with the titanium-naphthol catalysts.[4a] Inanaga reported the asymmetric homo-pinacol coupling reaction with a stoichiometric amount of low-valent titanium complex with bis-binaphtol ligand.[4b]

In this context, the rigid bis-biphenol ligand **1**$_{cis}$ on the hexaphenylbenzene scaffold was designed based on my concept of dinuclear complexes for intermolecular cross-pinacol coupling reaction (Scheme 1). The utility of the bis-biphenol ligand depends on such conformationally regulated structure although there are various reports of ligands possessing two biphenol moieties.[3d,4] Here, chapter 1 deals with the synthesis of the bis-biphenol ligand **1**$_{cis}$ and its preliminary studies on the ligand controlled cross-pinacol coupling reaction based on step-by-step activation of two different aldehydes.

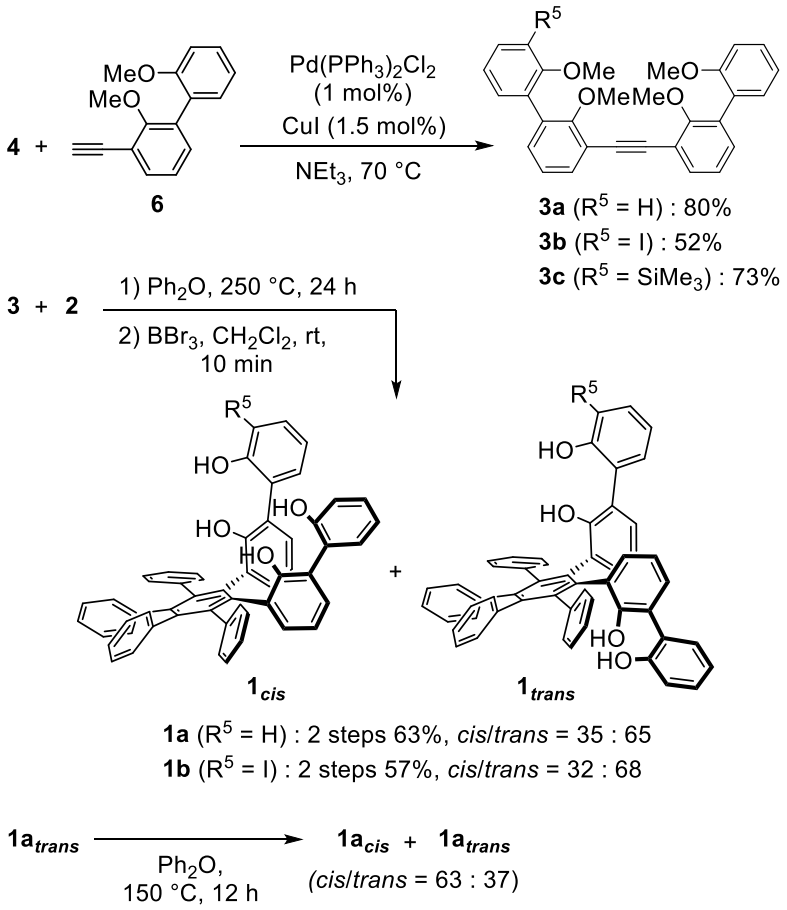
1-2. Result and Discussion

The present synthetic strategy for ligand **1**$_{cis}$ is outlined retrosynthetically in Scheme 1. The author envisaged that **1**$_{cis}$ is constructed via the Diels-Alder addition-decarbonylation reaction[5] of tetraphenylcyclopentadienone (**2**) with the tolan **3** possessing two bis-biphenol moieties. Such the tolan **3** would arise from the two biphenol derivatives **4**, **5**, and acetylene spacer through the repetitive Sonogashira coupling reaction.



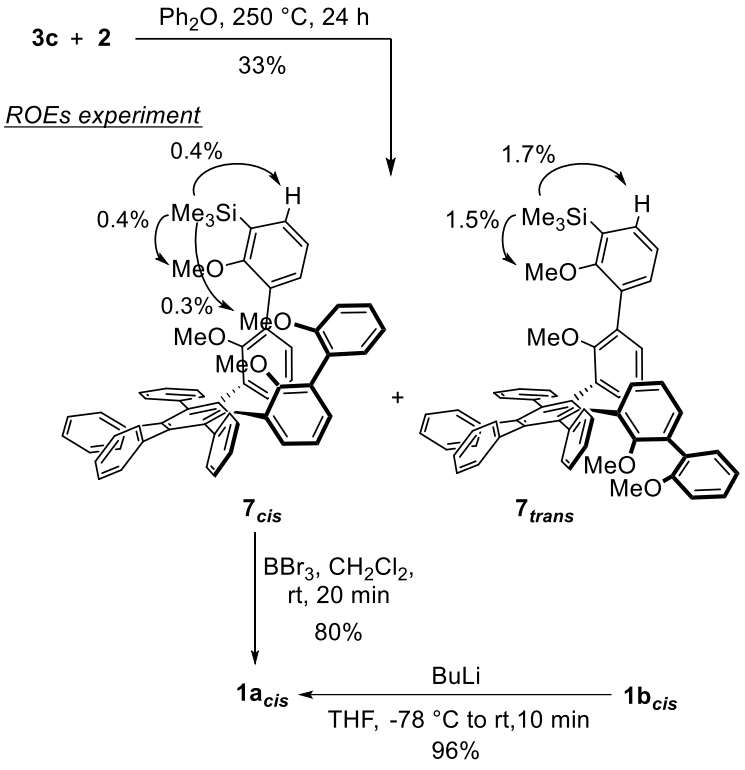
Scheme 1.

Scheme 2 shows the synthesis of **1**$_{cis}$. Iodide **4** and ethynyl compound **6**[6] were coupled by the Sonogashira reaction to give the bis(biphenyl) compounds **3a**, **3b** and **3c** in moderate yields. The thus-obtained **3a** and **3b** were treated with **2** in diphenyl ether at 250 °C, followed by deprotection of the methoxy group by BBr_3 to give the bis-biphenol ligand **1a** and **1b** as the diastereomixtures (2 steps 57% for **1a** and 63% for **1b**, Scheme 2). The *cis*/*trans* ratios for **1a** and **1b** are 35/65 and 32/68, respectively (structural assignment is described in the next paragraph). Diastereomers were able to be separated by silica-gel chromatography. The gram scale synthesis was possible.



Scheme 2.

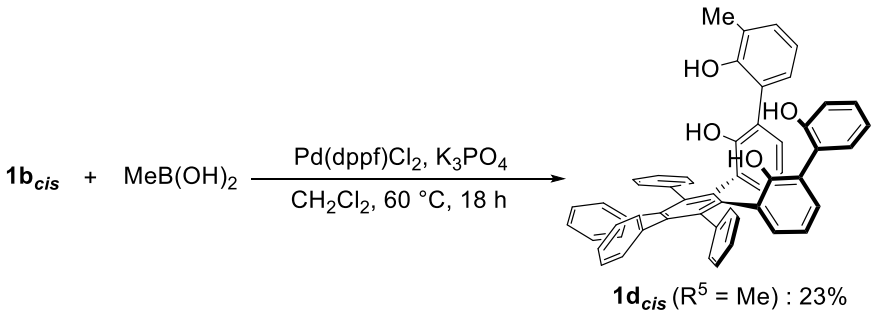
The structural assignment was determined by 1D ROESY experiments of trimethylsilyl derivative **7*cis***, which was prepared by the reaction of **3c** with **2**, followed by the separation of the *cis*/*trans* diastereomers by preparative thin-layer chromatography (Scheme 3). The isomer, in which ROEs were observed between the trimethylsilyl and methoxy groups, was assigned as a *cis*-isomer. Trimethylsilyl derivative **7*cis*** was transformed to **1a*cis*** by treatment with BBr_3 for the deprotection of the methoxy and trimethylsilyl groups. In this way, the structure of **1a*cis*** was determined. Similarly, the *cis*/*trans* determination of **1b*cis*** was carried out by the transformation to **1a*cis*** by deiodination.



Scheme 3.

The desired *cis*-isomer is a minor product in the Diels-Alder addition-decarbonylation reaction, which made us investigate the isomerization equilibrium. The treatment of the demethylated compound **1a*trans*** in diphenyl ether at 150 °C for 12 h resulted in the *trans*- and *cis*-isomers in 37 : 63 (Scheme 2). This finding permits the better conversion to **1a*cis***. In contrast, this isomerization did not occur in THF at reflux temperature even after 24 h to indicate the conformational rigidity.

Furthermore, the derivatization is possible by using the iodo-substituent of **1b*cis***. For example, the *B*-alkyl Suzuki-Miyaura cross-coupling reaction with $MeB(OH)_2$ allowed the introduction of the methyl group with the formation of **1d*cis*** (Scheme 4).



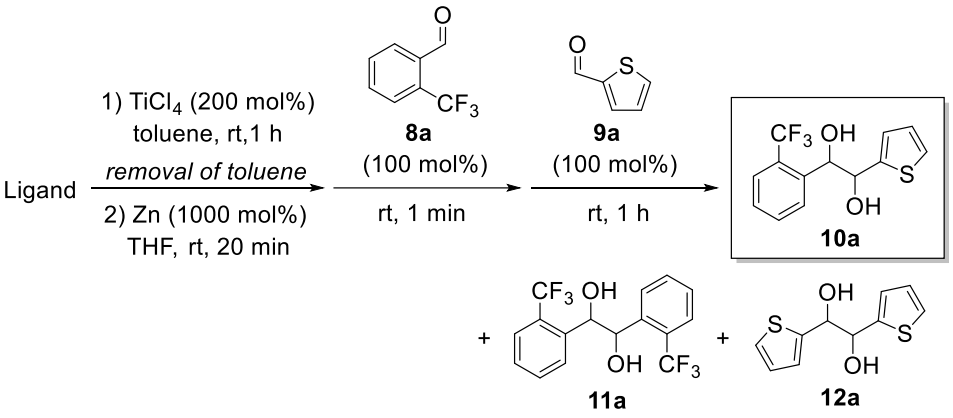
Scheme 4.

Complexation of **1a*cis*** with $TiCl_4$ was followed by ^1H NMR. The integral ratio for the OH protons in the phenoxy group decreased by half by addition of 1 equivalent $TiCl_4$. The peaks disappeared after further addition of one equivalent of $TiCl_4$, suggesting the formation of the corresponding dinuclear complex.

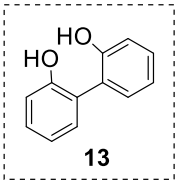
Step-by-step activation of two-different aldehydes was studied for the cross-pinacol coupling reaction using the stoichiometric amount of **1a*cis*** (Table 1). First, the ligand (100 mol%) was mixed with 200 mol% of $TiCl_4$ for complexation in toluene under argon at room temperature. After 1 h, the solvent was replaced to THF. Then, activated Zn (1000 mol%) was added to the mixture to generate the reduced Ti complex.[7] *o*-Trifluoromethyl benzaldehyde (**8a**) was added to the reaction mixture at room temperature. One minute later, 2-thienylaldehyde (**9a**) was added to the reaction mixture at the same temperature.

Cross-coupling product **10a** was obtained in 56% yield, where homo-coupling products **11a** and **12a** were also formed in 36 and 43% yields, respectively (Entry 1).[8,9] In contrast, the same reaction using 2,2'-biphenol (**13**) instead of **1a*cis*** gave only homo-coupling products **11a** and **12a** in 77 and 71% yields, respectively, without formation of **10a** (Entry 2).[8-10] Similarly, the same reaction without **1a*cis*** led to only homo-coupling products **11a** and **12a** in 69 and 49% yields, respectively (Entry 3).[9,10]

Table 1. Cross-pinacol coupling reaction based on step-by-step activation using the ligand **1a**$_{cis}$.[a]



Entry	Ligand	Yield [%][b,c]		
		10a (*syn*/*anti*)	**11a**	**12a**
1	**1a**$_{cis}$	56 (51/49)	36	43
2	**13**[d]	0	77	71
3	none	0	69	49



[a] All reactions were performed using **8a** (0.456 mmol), **9a** (0.456 mmol), ligand (0.456 mmol), and $TiCl_4$ (0.912 mmol). [b] Yield of **10a** = (mole of **10a)** / 0.456 mmol x 100; yield of **11a** = [(mole of **11a**) x 2] / 0.456 mmol x 100; yield of **12a** = [(mole of **12a**) x 2] / 0.456 mmol x 100. [c] Determined by ^{1}H NMR of the crude mixture. [d] The reaction was performed using **13** (0.912 mmol).

The increase of cross-selectivity may be accounted for as follows (Figure 1). In the reaction with bis-biphenol ligand **1**$_{cis}$, *o*-trifluoromethyl benzaldehyde (**8a**) is first activated with one side of the titanium (Figure 1a, intermediate **A**). On this occasion, the production of the homo-diol **11a** through the dimerization of **A** could be suppressed due to the steric hinderance of the bulky ligand. Then, the reaction with **A** and 2-thienylaldehyde (**9a**) would afford the 1,2-diol **10a** through the intermediate **B**. The mono-titanium reagent with biphenol **13** as a ligand also activate the aldehyde **8a** (Figure 1b). Then, the dimerization of the thus-generated radical species should immediately occur to give homo-diol **11a**. After the addition of the aldehyde **9a**, the unreacted mono-titanium reagent is likely to react with thiophenylaldehyde to give homo-couplng product **12a.** Therefore, the conditions with bis-biphenol ligand **1**$_{cis}$ are considered to afford the

cross-coupling product **10a** as a major product. In contrast, the same reaction with the mono-titanium reagent with **13** as a ligand gave only homo-coupling products **11a** and **12a**. These results indicate a clear steric effect of bis-biphenol ligand $\mathbf{1}_{cis}$ for the cross-pinacol reaction.

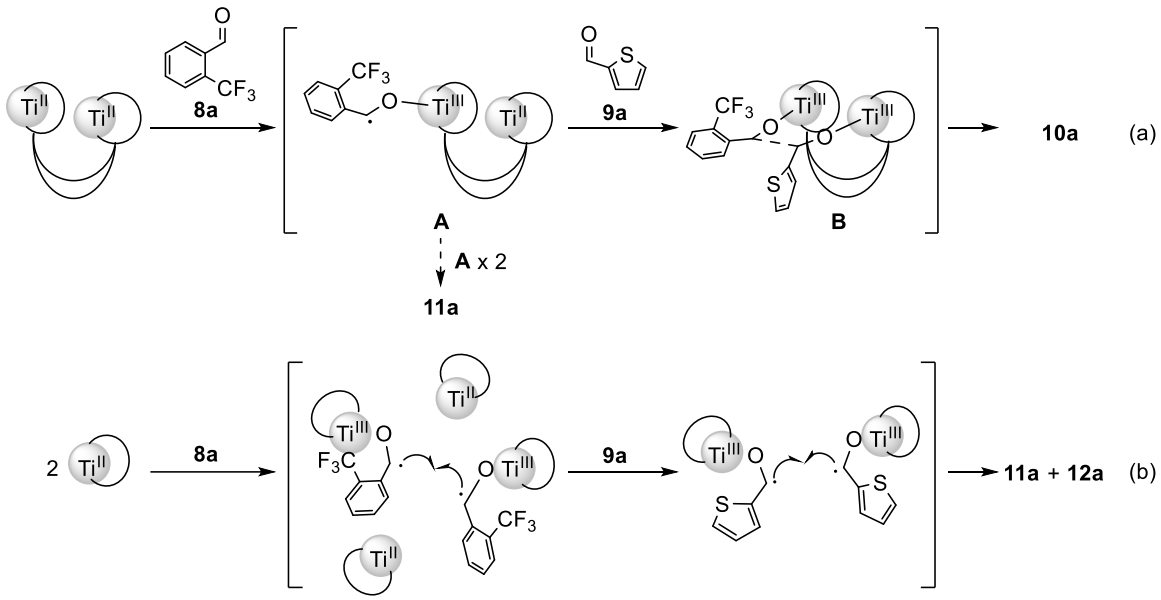


Figure 1. A possible mechanism for the cross-pinacol coupling reaction with titanium reagent: (a) the reaction with bis-biphenol ligand $\mathbf{1}_{cis}$. (b) the reaction with biphenol ligand **13**.

In conclusion, the three-dimensionally arranged bis-biphenol ligand on the hexaaryl scaffold for the dinuclear complex was synthesized to show conformational stability. The formation of dinuclear titanium complex permitted preliminary investigation on the cross-pinacol coupling reaction utilizing step-by-step activation of two different aldehydes by three-dimensionally arranged two metals. Further increase of cross-selectivity is expected by the left-right asymmetric ligand.

1-3. Experimental Section

General Method

^{1}H and ^{13}C NMR spectra were measured on JEOL ECS-400 or Varian INOVA 600 spectrometer. $CDCl_3$ was used as a solvent and the residual solvent peak (^{1}H, δ 7.26; ^{13}C, 77.16 ppm) was used as a reference. Infrared spectra were recorded on JASCO FT/IR-480plus. Mass spectra were measured on JEOL JMS-DX-303 spectrometer using fast atom bombardment (FAB) mode, and electron impact (EI) mode. Column chromatography was conducted on silica gel (Wakogel C-200). All reagents and solvents were purchased from commercial sources.

Synthesis

Tolan 3a

To a Et_3N (80 mL) solution of 3-iodo-2,2'-dimethoxybiphenyl (5.54 g, 16.3 mmol), $PdCl_2(PPh_3)_2$ (114 mg, 0.163 mmol), and CuI (47 mg, 0.245 mmol) was added 3-ethynyl-2,2'-dimethoxybiphenyl (**6**, 4.27 g, 17.9 mmol) at room temperature under argon. The reaction mixture was stirred at 70 ℃ for 3 h. Then, Et_3N was removed from the reaction mixture by distillation under vacuum. Ether and 1 M HCl were added. The aqueous layer was extracted twice with ether. The combined organic layer was washed with saturated aqueous $NaHCO_3$, water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/dichloromethane = 1/0 to 1/1) to give the product **3a** (5.85 g, 13.0 mmol, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, J = 7.2, 1.6 Hz, 2H), 7.35 (dd, J = 7.2, 1.6 Hz, 2H), 7.27-7.22 (m, 4H), 7.11 (dd, J = 7.2, 7.2 Hz, 2H), 7.01 (ddd, J = 6.4, 6.4, 0.6 Hz, 2H), 6.98 (d, J = 7.2 Hz, 2H), 3.789 (s, 6H), 3.786 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 159.11, 156.94, 133.05, 132.53, 132.18, 131.41, 129.05, 127.37, 123.27, 120.49, 117.41, 110.96, 90.53, 61.20, 55.73 ppm; IR (KBr, cm^{-1}) 3014, 2962, 2833, 1579, 1496, 1461, 1414, 1236, 1002; HRMS (FAB, *m*/*z*) calculated for $C_{30}H_{26}O_4$ [M^+]: 450.1831, found: 450.1813.

Tolan 3b

To a Et_3N (20 mL) solution of 3,3'-diiodo-2,2'-dimethoxybiphenyl (1.24 g, 2.67 mmol), $PdCl_2(PPh_3)_2$ (28.1 mg, 0.040mmol), and CuI (12.8g, 0.067 mmol) was added 3-ethynyl-2,2'-dimethoxybiphenyl (**6**, 0.70 g, 2.93 mmol) at room temperature under argon. The reaction mixture was stirred at 70 ℃ for 16 h. Then, Et_3N was removed from the reaction mixture by distillation under vacuum. Ether and 1 M HCl were added. The aqueous layer was extracted twice with ether. The combined organic layer was washed with saturated aqueous $NaHCO_3$, water and brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/dichloromethane = 1/0 to 1/1) to give the product **3b** (0.80 g, 1.39 mmol, 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.56 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.53 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.36 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H), 7.31 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.30 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.28-7.24 (m, 2H), 7.13 (dd, *J* = 7.6, 7.6 Hz, 2H), 7.02 (ddd, *J* = 7.6, 7.6, 0.6 Hz, 1H), 6.99 (d, *J* = 7.6 Hz, 1H), 6.91 (dd, *J* = 7.6, 7.6 Hz, 1H), 3.87 (s, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 3.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 159.13, 158.62, 157.37, 156.92, 139.06, 133.76, 133.00, 132.56, 132.44, 132.39, 132.16, 131.81, 131.69, 131.39, 129.10, 127.26, 125,.68, 123.42, 123.35, 120.50, 117.64, 117.22, 110.98, 92.56, 91.11, 90.03, 61.34, 61.22, 60.72, 55.74 ppm; IR (KBr, cm^{-1}) 2932, 1578, 1496, 1463, 1412, 1237, 1124, 1075, 1005; HRMS (FAB, *m*/*z*) calculated for $C_{30}H_{25}IO_4[M^+]$: 576.0798, found: 576.0813.

Tolan 3c

To a THF (20 mL) solution of **3b** (302 mg, 0.524 mmol) was added 2.64 M BuLi (0.24 mL, 0.63 mmol) at -78 ℃ under argon. The reaction mixture was stirred for 30 min. In the meantime, the temperature was raised from -78 ℃ to -40 ℃ over 30 min. The reaction mixture was cooled to -78 ℃ again. Trimethylsilyl chloride (0.10 mL, 0.786 mmol) was added to the mixture at the same temperature. Then, the cooling bath was removed. The mixture was stirred for 2 h at room temperature. Ice water and dichloromethane were added to the mixture. The aqueous layer was extracted twice with dichloromethane. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography

(hexane/dichloromethane = 1/0 to 3/2) to give the product **3c** (111.5 mg, 0.213 mmol, 41%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, J = 7.6, 1.6 Hz, 1H), 7.54 (dd , J = 7.6, 1.6 Hz, 1H), 7.43 (dd, J = 7.6, 1.6 Hz, 1H), 7.40-7.33 (m, 3H), 7.29-7.24 (m, 2H), 7.18-7.10 (m, 3H), 7.02 (dd, J = 7.6 Hz, 2H), 7.00 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 163.18, 159.13, 158.59, 156.93, 134.78, 133.71, 133.31, 133.00, 132.92, 132.55, 132.32, 131.88, 131.40, 129.69, 129.09, 127.31, 123.53, 123.32, 123.20, 120.50, 117.63, 117.32, 110.98, 90.94, 90.35, 61.21, 61.09, 60.67, 55.74, -0.23 ppm; IR (KBr, cm^{-1}) 2937, 2345, 1496, 1459, 1415, 1390, 1227, 1073, 1008; HRMS (FAB, *m*/*z*) calculated for $C_{33}H_{34}O_4Si[M^+]$: 522.2226, found: 522.2234.

Bis(biphenol) 1a

To Ph_2O (60 mL) were added tolan **3a** (6.39 g, 14.2 mmol) and tetraphenyl-cyclopentadienone (5.46 g, 14.2 mmol) at room temperature under argon. The reaction mixture was stirred at 250 ^{o}C for 24 h. The mixture was poured into silica-gel column to purify (hexane/dichloromethane = 1/0 to 2/1). The thus-obtained product was dissolved in dichloromethane, then BBr_3 (1 M in dichloromethane, 200 mL) was added to the mixture at room temperature, which was stirred for 10 min. Ice water was added to the mixture. The aqueous layer was extracted with dichloromethane twice. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 1/0 to 2/1) to give the products **1a** (*cis*/*trans* = 35/65, 6.7 g, 8.92 mmol, 63%).

1a$_{cis}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (ddd, J = 7.6, 7.6, 0.8 Hz, 2H), 6.97 (d, J = 7.6 Hz, 2H), 6.82-6.95 (m, 26H), 6.79 (d, J = 7.6 Hz, 2H), 6.69 (dd, J = 7.6, 7.6 Hz, 2H), 5.46 (s 2H), 5.30 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 157.22, 149.77, 142.13, 141.85, 140.17, 140.10, 135.62, 132.66, 131.47, 131.41, 131.13, 130.98, 130.80, 130.60, 129.85, 128.10, 126.98, 126.89, 126.81, 126.59, 125.90, 125.61, 123.82, 123.29, 121.20, 120.31, 117.19 ppm; IR (KBr, cm^{-1}) 3424, 2962, 1719, 1603, 1490, 1442, 1397, 1260, 1220, 1073, 1029; HRMS (FAB, *m*/*z*) calculated for $C_{54}H_{38}O_4[M^+]$: 750.2770, found: 750.2764.

1a$_{trans}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (ddd, J = 8.0, 8.0, 2.4 Hz, 2H), 7.05 (d, J = 8.0, 1.2 Hz, 2H), 7.02-6.84 (m, 28H), 6.71 (dd, J = 8.0, 8.0 Hz, 2H), 5.13 (s, 2H), 4.63 (s, 2H) ; ^{13}C NMR (100 MHz, $CDCl_3$) 153.27, 148.98, 141.93, 141.80, 139.96, 139.76,

136.36, 131.43, 131.36, 131.13, 131.08, 130.98, 130.11, 129.89, 128.41, 127.15, 126.90, 126.81, 126.20, 125.71, 123.89, 122.64, 121.17, 120.64, 116.77 ppm; IR (KBr, cm^{-1}) 3532, 3403, 3056, 3026, 1601, 1491, 1457, 1440, 1399, 1286, 1216, 1176, 1153, 1072, 753, 700; HRMS (FAB, *m*/*z*) calculated for $C_{54}H_{38}O_4[M^+]$: 750.2770, found: 750.2781.

Bis(biphenol) 1b

To Ph_2O (15 mL) were added tolan **3b** (731 mg, 1.27 mmol) and tetraphenylcyclopentadienone (488 mg, 1.27 mmol) at room temperature under argon. The reaction mixture was stirred at 250 °C for 24 h. The mixture was poured into silica-gel column to purify (hexane/dichloromethane = 1/0 to 2/1). The thus-obtained product was dissolved in dichloromethane, then BBr_3 (1 M in dichloromethane, 15 mL) was added to the mixture at room temperature. The mixture was stirred for 10 min. Ice water was added to the mixture. The aqueous layer was extracted twice with dichloromethane. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 1/0 to 2/1) to give the products **1b** (*cis*/*trans* = 32/68, 634 mg, 0.723 mmol, 57%).

1b*cis* : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, *J* = 7.2, 2.4 Hz, 1H), 7.26 (ddd, *J* = 7.2, 7.2, 1.2 Hz, 1H), 7.17 (d, *J* = 7.2 Hz, 1H), 7.02-6.82 (m, 27H), 6.74-6.59 (m, 3H), 5.57 (s, 3H), 4.67 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 152.80, 152.45, 149.88, 149.49, 142.05, 142.02, 141.88, 141.78, 140.13, 140.05, 139.98, 139.36, 135.91, 135.52, 132.86, 132.74, 131.47, 131.38, 131.08, 130.95, 130.74, 130.61, 130.33, 129.82, 128.52, 128.18, 127.21, 126.89, 126.82, 126.69, 126.53, 126.02, 125.89, 125.63, 124.30, 124.16, 123.66, 122.94, 122.55, 121.71, 120.67, 120.18, 116.80, 86.20 ppm; IR (KBr, cm^{-1}) 3521, 3054, 1601, 1495, 1441, 1398, 1227, 1071; HRMS (FAB, *m*/*z*) calculated for for $C_{54}H_{37}IO_4[M^+]$: 876.1737, found: 876.1735.

1b*trans* : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.27 (ddd, *J* = 7.6, 7.6, 1.6 Hz, 1H), 7.09-6.84 (m, 28H), 6.75-6.65 (m, 3H), 5.39 (s, 1H), 5.21 (s, 1H), 5.16 (s, 1H), 4.65 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 153.22, 152.25, 149.00, 148.97, 141.95, 141.85, 141.81, 139.92, 139.72, 139.62, 139.12, 136.43, 136.11, 131.63, 131.46, 131.39, 131.31, 131.13, 131.02, 130.95, 130.69, 130.04, 129.99, 129.88, 128.71, 128.32, 127.18, 127.13, 126.89, 126.82, 126.22, 126.20, 125.71, 124.63, 123.80, 122.89, 122.71,

122.57, 121.15, 120.67, 120.56, 116.69, 85.49 ppm; IR (KBr, cm^{-1}) 3536, 3051, 1601, 1492, 1440, 1318, 1230, 1169, 1070, 1029; HRMS (FAB, *m*/z) calculated for $C_{54}H_{37}IO_4[M^+]$: 876.1737, found: 876.1746.

Bis(dimethoxybiphenyl) compound 7

To Ph_2O (3 mL) were added tolan **3c** (34 mg, 0.067 mmol) and tetraphenylcyclopentadienone (26 mg, 0.067 mmol) at room temperature under argon. The reaction mixture was stirred at 250 ºC for 12 h. After cooling to room temperature, the mixture was poured into silica-gel column to purify (hexane/dichloromethane = 1/0 to 2/1), which gave the products **7** (*cis*/*trans* = 33/67, 19.2 mg, 0.022 mmol, 33%). *Cis*/*trans* diastereomers were separated by preparative thin-layer silica-gel chromatography (hexane/dichloromethane = 2/3). The structure was determined based on 1D ROESY experiments.

7*cis* : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 1H), 7.21 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.10-6.96 (m, 30H), 6.65 (d, *J* = 7.2 Hz, 1H), 3.66 (s, 3H), 3.30 (s, 3H), 3.12 (s, 3H), 2.85 (s, 3H), 0.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 156.46, 155.90, 141.12, 141.04, 140.22, 137.78, 133.95, 133.87, 133.54, 133.41, 133.14, 132.78, 131.93, 131.87, 131.59, 131.51, 131.04, 130.79, 130.28, 129.97, 128.95, 128.25, 126.60, 126.54, 126.30, 125.28, 125.13, 122.54, 120.81, 120.27, 120.10, 111.09, 59.62x2, 59.47, 55.63, -0.39 ppm; IR (KBr, cm^{-1}) 2945, 1700, 1600, 1496, 1462, 1386, 1242, 1074, 1014; HRMS (FAB, *m*/z) calculated for $C_{61}H_{54}O_4Si[M^+]$: 878.3791, found: 878.3772.

7*trans* : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31-7.21 (m, 2H), 7.18 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.04-6.72 (m, 30H), 3.71 (s, 3H), 3.21 (s, 3H), 2.98 (s, 3H), 2.92 (s, 3H), 0.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 156.72, 153.95, 141.15, 140.78, 140.65, 140.56, 140.07, 140.02, 138.12, 134.01, 133.68, 133.42, 132.43, 131.93, 131.73, 131.66, 131.41, 131.12, 130.64, 129.32, 129.14, 128.49, 126.59, 126.27, 126.15, 125.29, 125.24, 125.13, 122.82, 121.01, 120.45, 111.13, 60.12, 59.61x2, 55.68, -0.35 ppm; IR (KBr, cm^{-1}) 2944, 1600, 1496, 1463, 1385, 1225, 1075, 1015; HRMS (FAB, *m*/z) calculated for $C_{61}H_{54}O_4Si[M^+]$: 878.3793, found: 878.3772.

Desilyration of 7_{cis}

To dichloromethane (0.5 mL) were added bis(dimethoxybiphenyl) compound **7_{cis}** (6.5 mg, 0.0074 mmol) and BBr_3 (1 M in dichloromethane, 0.44 mL) at room temperature. The mixture was stirred for 20 min. Ice water was added to the mixture. The aqueous layer was extracted twice with dichloromethane. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue were filtered with ethyl acetate through a short pad of silicagel, to give the products **$1a_{cis}$** (4.4 mg, 0.0059 mmol, 80%).

Deiodination $1b_{cis}$

To a THF (1.5 mL) solution of **$1b_{cis}$** (23 mg, 0.0264 mmol) was added 2.64 M BuLi (0.10 mL, 0.264 mmol) at -78 ℃ under argon. Then, the cooling bath was removed. The mixture was stirred for 10 min at room temperature. Ice water and dichloromethane were added to the mixture. The aqueous layer was extracted twice with dichloromethane. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated, to give the product **$1a_{cis}$** (19.0 mg, 0.025 mmol, 96%).

Bis(biphenol) $1d_{cis}$

To a THF (1 mL) and dichloromethane (1 mL) solution were added **$1b_{cis}$** (100 mg, 0.114 mmol) and $MeB(OH)_2$ (10.3 mg, 0.172 mmol), $PdCl_2$(dppf) (9.3 mg, 0.017 mmol), and K_3PO_4 (145 mg, 0.684 mmol) at room temperature under argon. The reaction mixture was stirred at 60 ^oC for 18 h. Water was added to the mixture. The aqueous layer was extracted twice with dichloromethane. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by preparative thin-layer silica-gel chromatography (hexane/ethyl acetate = 4/1) to give the product **$1d_{cis}$** (19.8 mg, 0.026 mmol, 23%). ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (ddd, J = 7.2, 7.2, 1.2 Hz, 1H), 7.10 (d, J = 7.2.Hz, 1H), 7.01 (d, J = 7.2 Hz, 1H), 6.97-6.82 (m, 27H), 6.78 (dd, J = 7.2, 7.2 Hz, 1H), 6.70 (dd, J = 7.2, 7.2 Hz, 1H), 6.67 (dd, J = 7.2, 7.2 Hz, 1H), 6.54 (s, 1H), 5.62 (s, 1H), 5.39 (s, 1H), 5.03 (s, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 152.81, 151.77, 149.97, 149.60, 142.10, 142.05, 141.80, 141.77, 140.19, 140.12, 140.08, 136.18, 135.34, 132.77, 132.51, 131.49, 131.42, 131.27, 131.14, 131.07, 130.97, 130.90,

130.78, 130.69, 130.50, 129.66, 128.38, 128.21, 128.10, 127.11, 126.88, 126.81, 126.64, 126.52, 126.38, 125.96, 125.87, 125.60, 124.60, 123.57, 123.22, 122.86, 121.30, 120.63, 120.44, 120.16, 116.95, 16.58 ppm; IR (KBr, cm^{-1}) 3522, 3443, 3052, 3024, 2921, 1700, 1653, 1496, 1491, 1457, 1441, 1437, 1216, 755, 733, 699; HRMS (FAB, *m*/*z*) calculated for $C_{55}H_{40}O_4[M^+]$: 764.2927, found: 764.2949.

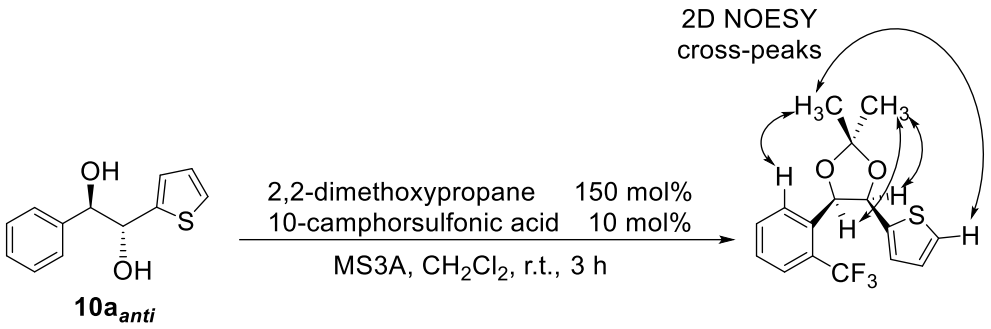
Pinacol coupling reaction

To a toluene (10 mL) solution of **1a*cis*** (342 mg, 0.456 mmol) was added 0.912 M toluene solution of $TiCl_4$ (1.0 mL, 0.912 mmol) at room temperature under argon. The reaction mixture was stirred for 1 h. Then, toluene was removed from the reaction mixture by distillation under vacuum. THF (10 mL) and activated Zn dust (298 mg, 4.56 mmol) were added to the mixture at room temperature. The reaction mixture was stirred for 20 min. Then, *o*-(trifluoromethyl)benzaldehyde (60 µL, 0.456 mmol) was added to the mixture at room temperature. After 1 min, 2-thiophenealdehyde (43 µL, 0.456 mmol) was added to the mixture, which was stirred for 1 h. 1 M HCl was added to the mixture. The aqueous layer was extracted twice with ethyl acetate. The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and evaporated. The resulting crude products were filtered with ethyl acetate through a short pad of silicagel. The yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene (25.6 mg, 0.152 mmol) as an internal standard. *Syn*/*anti* of **10a** was determined by 2D NOESY experiment of **10a*anti*** after acetonide formation as described below.

10a*syn* : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.63 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.43 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.24 (dd, *J* = 4.8, 1.2 Hz, 1H), 6.94 (dd, *J* = 4.8, 1.2 Hz, 1H), 6.87 (d, *J* = 4.8 Hz, 1H), 5.29 (br, 1H), 5.13 (dd, *J* = 4.8, 4.8 Hz, 1H), 2.91 (d, *J* = 5.6 Hz, 1H), 2.84 (d, *J* = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 144.08, 139.25, 132.18, 128.78, 128.29, 127.81 (q, *J* = 29.5 Hz), 126.92, 126.01 (q, *J* = 5.7 Hz), 125.20, 124.61, 124.38 (q, *J* = 272.7 Hz), 73.74, 73.23 ppm; IR (KBr, cm^{-1}) 3406, 3285, 2925, 1653, 1457, 1320, 1312, 1178, 1109, 1085, 1062, 1048, 1035, 1027, 771, 763, 726, 710, 702, 668, 664; HRMS (FAB, *m*/*z*) calculated for $C_{13}H_{11}F_3NaO_2S[(M\text{-}Na)^+]$: 311.0330, found: 311.0328.

10a$_{anti}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ7.65 (d, J = 7.6 Hz, 1H), 7.46-7.40 (m, 2H), 7.36 (ddd, J = 7.6, 7.6, 2.4 Hz, 1H), 7.29 (d, J = 5.2 Hz, 1H), 6.92 (dd, J = 5.2, 3.6 Hz, 1H), 6.81 (d, J = 3.6 Hz, 1H), 5.44 (d, 3.6 Hz, 1H), 5.17 (d, J = 3.6 Hz, 1H), 2.71 (s, 1H), 2.43 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 141.90, 138.25, 131.87, 128.72, 128.02, 127.88 (q, J = 30.5 Hz), 126.61, 126.31, 126.02, 125.56 (q, J = 5.7 Hz), 124.48 (q, J = 272.7 Hz), 73.98, 72.56 ppm; IR (KBr, cm^{-1}) 3415, 2925, 2853, 1635, 1310, 1166, 1155, 1114, 1069, 1056, 1046, 1035, 768, 704; HRMS (FAB, m/z) calculated for $C_{13}H_{11}F_3NaO_2S[(M\text{-}Na)^+]$: 311.0330, found: 311.0328.

Acetonide formation of 10a$_{anti}$



To a dichloromethane (1.5 mL) solution were added **10a$_{anti}$** (53.7 mg, 0.186 mmol), 10-camphorsulfonic acid (4.3 mg, 0.0185 mmol), MS3A (310 mg), and 2,2-dimethoxypropane (34 μL, 0.277 mmol) at room temperature under argon. The reaction mixture was stirred for 3 h. Saturated aqueous $NaHCO_3$ was added to the mixture. Then, MS3A was removed from the reaction mixture by filtration. The aqueous layer was extracted twice with dichloromethane. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/dichloromethane = 1/0 to 2/3) to give the product (24.6 mg, 0.0749 mmol, 40%). ^{1}H NMR (400 MHz, $CDCl_3$) δ7.54 (d, J = 7.6 Hz, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.30 (dd, J = 7.6, 7.6 Hz, 1H), 7.23 (dd, J = 7.6, 7.6 Hz, 1H), 6.99 (dd, J = 4.8, 0.8 Hz, 1H), 6.64 (dd, J = 4.8, 3.6 Hz, 1H), 6.46 (d, J = 3.6 Hz, 1H), 5.86 (d, J = 6.8 Hz, 1H), 5.77 (d, J = 6.8 Hz, 1H), 1.84 (s, 3H), 1.60 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$); 142.45, 135.10, 131.43, 128.74, 127.77, 127.22 (q, J = 30.5 Hz), 126.47, 125.15 (q, J = 5.7 Hz), 124.71, 124.63, 124.43 (q, J = 272.7 Hz), 109.24, 78.51, 26.91, 24.50 ppm; IR (neat, cm^{-1}) 3075, 2991, 2939, 1609, 1587, 1495, 1458, 1440, 1383, 1314, 1284, 1265,

1248, 1214, 1162, 1121, 1055, 1035, 961, 882, 862, 840, 815, 796, 768, 738, 701, 661, 598, 571, 513; HRMS (EI, *m*/*z*) calculated for $C_{16}H_{15}F_3O_2S$ [M^+]: 328.0745, found: 328.0743.

1-4. Reference and Notes

1. For selected recent reviews and a highlight in a few years: a) R. S. Brown, Z.-L. Lu, C. T. Liu, W. Y. Tsang, D. R. Edwards, A. A. Neverov, *J. Phys. Org. Chem.* **2010**, *23*, 1-15; b) R. M. Haak, S. J. Wezenberg, A. W. Kleij, *Chem. Commun.* **2010**, 2713-2723; c) S. Kuwata, T. Ikariya, *Dalton Trans.* **2010**, *39*, 2984-2992; d) M. North, *Angew. Chem. Int. Ed.* **2010**, *49*, 8079-8081.
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3. For selected reviews: a) E. K. van den Beuken, B. L. Feringa, *Tetrahedron* **1998**, *54*, 12985-13011; b) P. Molenveld, J. F. J. Engbersen, D. N. Reinhoudt, *Chem. Soc. Rev.* **2000**, *29*, 75-86; c) J.-A. Ma, D. Cahard, *Angew. Chem. Int. Ed.* **2004**, *43*, 4566-4583; d) S. Matsunaga, M. Shibasaki, *Bull. Chem. Soc. Jpn.* **2008**, *81*, 60-75; e) S. Takizawa, T. Katayama, H. Sasai, *Chem. Commun.* **2008**, 4113-4122.
4. a) T. Mukaiyama, A. Inubushi, S. Suda, R. Hara, S. Kobayashi, *Chem. Lett.* **1990**, 1015-1018; b) J. Inanaga, *Organometallic News* **2008**, *1*, 20-25; c) Y. Ihori, Y. Yamashita, H. Ishitani, S. Kobayashi, *J. Am. Chem. Soc.* **2005**, *127*, 15528-15535.
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7. a) T. Mukaiyama, T. Sato, J. Hanna, *Chem. Lett.* **1973**, 1041-1044; b) J. Inanaga, Y. Handa, *Tetrahedron Lett.* **1987**, *28*, 5717-5718.
8. *Syn* and *anti* ratio for **10a** is 51:49. *Syn* and *anti* were determined by the 2D NOESY experiments after acetonide formation of **10a**$_{anti}$, see experimental section for details. The *dl* and *meso* ratios for **11a** and **12a** are 71:29 and 76:24, respectively, which were

determined based on the literatures: a) Y.-G. Li, Q.-S. Tian, J. Zhao, Y. Feng, M.-J. Li, T.-P. You, *Tetrahedron: Asymmetry* **2004**, *15*, 1707-1710; b) J. Broeker, M. Knollmueller, P. Gaertner, *Tetrahedron: Asymmetry* **2006**, *17*, 2413-2429; c) V. Rauniyar, H. Zhai, D. G. Hall, *J. Am. Chem. Soc.* **2008**, *130*, 8481-8490.

9. Yield was calculated as follows: (mol of product)/(maximal mol of producible product)x100.
10. Dominant formation of homo-coupling products may be accounted for by the completion of the coupling reaction of *o*-trifluoromethyl benzaldehyde before addition of thienylaldehyde due to the higher reactivity of the former one.

Chapter 2. Design and Synthesis of Dinuclear Hemisalen Complex on Hexaarylbenzene Scaffold and Its Application for Cross-Pinacol Coupling Reaction

2-1. Introduction

Dual reactive sites allow to position two substrates appropriately for the reaction, activate them, and induce electrically cooperating effect. Well-organized dinuclear transition metal complexes are considered to permit such a system, which is also found sometimes in active sites of enzymes to catalyze the reactions.

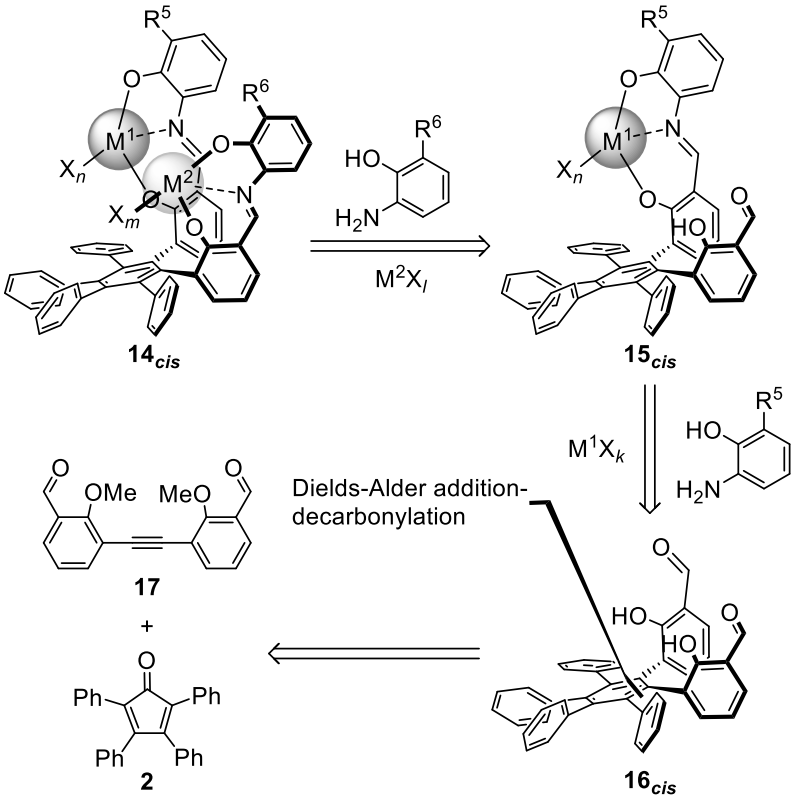
In chapter 1, bis-biphenol ligand is shown to be effective for the intermolecular cross-pinacol coupling reaction. However, preparation of the bis-biphenol ligands with a variety of R^5 and R^6 substituents is not easy because the introduction of these substituents are required in the early stage of the ligand synthesis, which limits the investigation with various combinations of substituents around each metal center.

Hemisalen structures often form the stable metal complexes by the reaction with the metal salt, which are easy to construct from salicylaldehyde and amino alcohol. The hemisalens are widely utilized as the functional ligands. For example, vanadium(V) hemisalen complexes are known to catalyze oxidation reactions,[1,2] such as oxidative coupling of naphthols,[1,2b,c,d] asymmetric oxidative kinetic resolution of α-hydroxy esters,[2e] and oxidation of sulfides.[2a]

In this context, the sterically controlled dinuclear complex **14**$_{cis}$ bearing the hemisalen coordination moieties were designed (Scheme 1). Here, chapter 2 deals with the synthesis of hemisalen vanadium(V) complexes on the hexaaryl scaffold and their application for cross-pinacol coupling reaction between two defferent aromatic aldehydes.

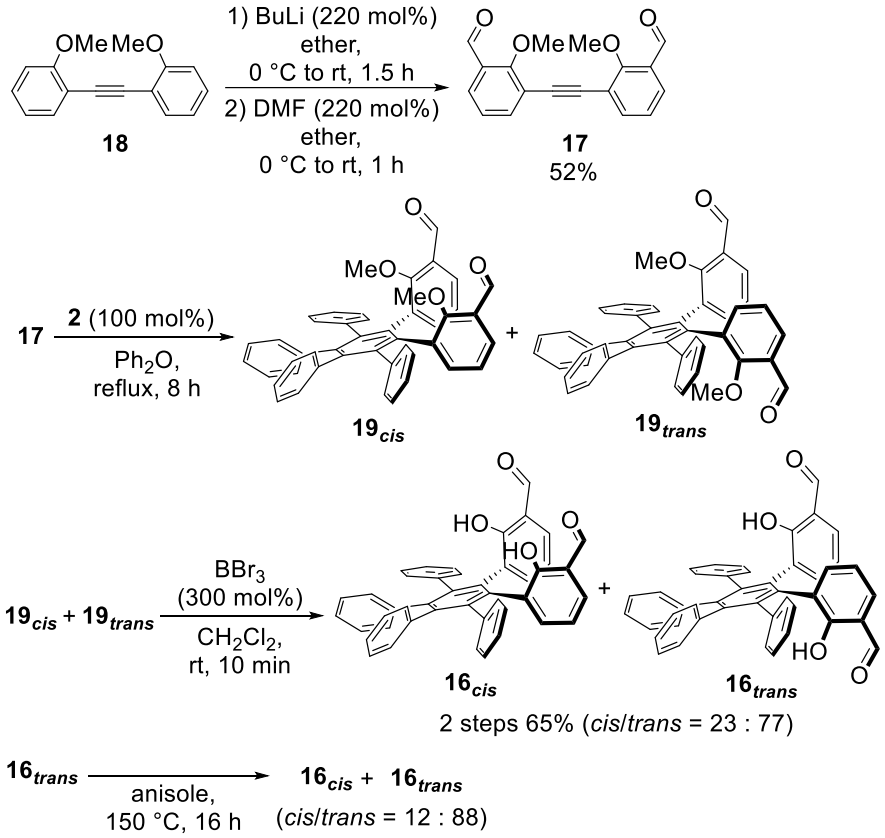
2-2. Results and Discussion

The present synthetic strategy is outlined in Scheme 1. The dinuclear complex **14**$_{cis}$ is envisaged to be constructed via condensation of the monoaldehyde **15**$_{cis}$ with various aminophenols, followed by complexation with a transition metal, such as a vanadium(V) compound. The monoaldehyde **15**$_{cis}$ is similarly prepared from the dialdehyde **16**$_{cis}$.[3] The dialdehyde **16**$_{cis}$ would arise from the Diels-Alder addition-decarbonylation reaction[4] of the tolan **17** with tetraphenylcyclopentadienone (**2**).



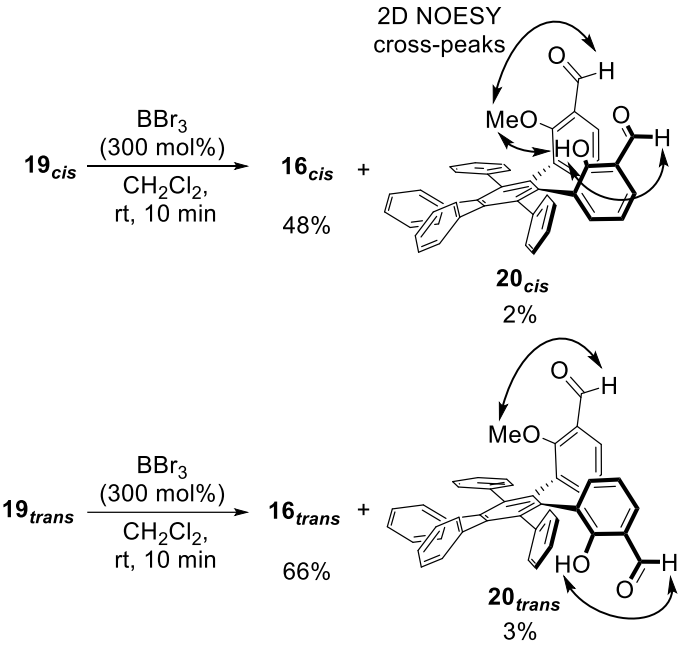
Scheme 1.

Synthesis of **16**$_{cis}$ is shown in Scheme 2. 1,2-Bis(2-methoxyphenyl)ethyne (**18**)[5] was treated with BuLi, followed by trapping of DMF to give the dialdehyde **17** in 52% yield. The Diels-Alder addition-decarbonylation of **17** with the cyclopentadienone **2** in Ph_2O at reflux led to the dimethoxyhexaarylbenzene **19** (a mixture of *cis* and *trans* isomers). The thus-obtained mixture of **19**$_{cis}$ and **19**$_{trans}$ was treated with BBr_3 to give the hexaarylbenzene **16** (2 steps 65%, *cis*/*trans* = 23 : 77). The diastereomers were able to be separated by silica-gel chromatography. The gram scale synthesis was possible.



Scheme 2.

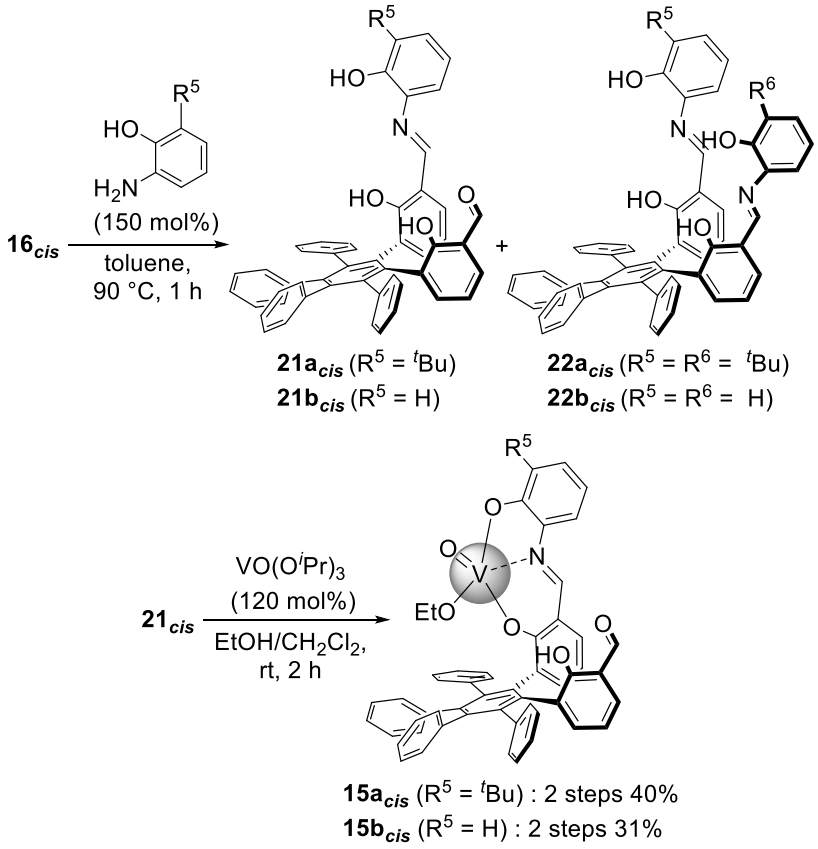
The structural assignment of the *cis*/*trans* isomers was determined by 2D NOESY experiments of the desymmetrized monomethoxy derivative **20** shown in Scheme 3. Dimethoxyhexaarylbenzenes $\mathbf{19}_{cis}$ and $\mathbf{19}_{trans}$ were separately treated with three equivalents of BBr_3 to give the disalicylaldehyde **16** and small amounts of the monomethoxy salicylaldehydes $\mathbf{20}_{cis}$ and $\mathbf{20}_{trans}$ (2% and 3% yields, respectively). The isomer $\mathbf{20}_{cis}$, in which cross-peaks were observed between the methoxy group and the hydroxyl one of another side in a 2D NOESY spectrum, was assigned as a *cis* isomer. The *cis*/*trans* determination of the disalicylaldehyde **16** was carried out by the transformation from each isomer of the monomethoxy derivative **20** by deprotection.



Scheme 3.

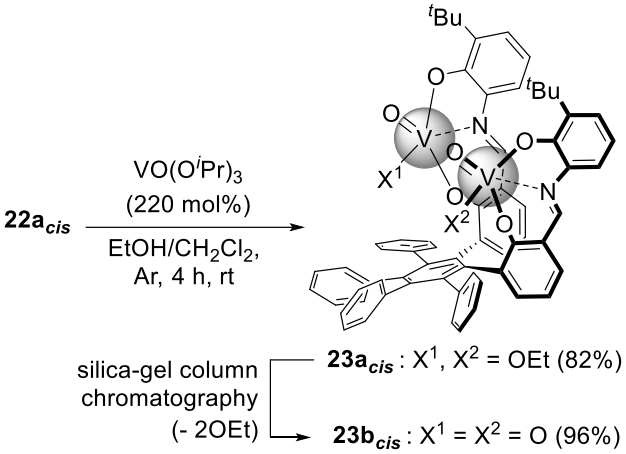
The *cis* isomer $\mathbf{16}_{cis}$ was a minor product in the Diels-Alder addition-decarbonylation reaction, however the treatment of $\mathbf{16}_{trans}$ in anisole at 150 °C for 16 h led to *cis* and *trans* isomers (Scheme 2, *cis*/*trans* = 12 : 88). This isomerization did not occur at 90 °C even after 24 h, indicating the conformational rigidity.

Condensation of the disalicylaldehyde **16**$_{cis}$ with 2-amino-6-*tert*-butylphenol led to the mono- and dihemisalen ligands **21a**$_{cis}$ and **22a**$_{cis}$ (Scheme 4). Complexation of the monohemisalen ligand **21a**$_{cis}$ with VO(O^iPr)$_3$ in the ethanol/dichloromethane solution gave mononuclear vanadium(V) complex **15a**$_{cis}$ (R^5 = ^{t}Bu) in 40% yield (2 steps). Electrospray ionization (ESI) mass (positive mode) of **15a**$_{cis}$ in ethanol mainly detected the peak corresponding to the monoethoxide complex ([**15a**$_{cis}$+Na]$^+$ 902.3). Thermogravimetry (TG) analysis showed the mass loss corresponding to one equivalent of ethanol at 250-350 °C. In addition, ^{1}H NMR spectrum in $CDCl_3$/CD_3OD also supports the coordination of one ethanol. [6,7] In the ^{1}H NMR spectrum, two sharp signals assigned to CHO protons (δ 9.46 and 9.41) were observed. Two distinct resonances (-520 and -526 ppm) were also observed in the ^{51}V NMR spectrum. These results may suggest the formation of the *endo* and *exo* diastereomers as reported by Chakravorty.[8] Mononuclear vanadium(V) complex **15b**$_{cis}$ (R^5 = H) were also synthesized (31% yield, 2 steps).



Scheme 4.

The dihemisalen ligand **22a*cis*** was complexed with $VO(O^iPr)_3$ to give the dinuclear vanadium(V) complex **23a*cis*** in 82% yield (Scheme 5). Elemental analysis supports the formula of the diethoxide complexes **23a*cis*** (Anal. Calcd. for $C_{68}H_{62}N_2O_8V_2$: C, 71.82; H, 5.50; N, 2.46. Found: C, 71.58; H, 5.32; N, 2.47). TG analysis of **23a*cis*** showed the mass loss corresponding to two equivalents of ethanol. ^1H NMR spectrum in $CDCl_3/CD_3OD$ also indicated two equivalents of ethoxides. ^1H and ^{51}V NMR spectra in $CDCl_3/CD_3OD$ suggested a mixture of the diastereomers or the V-O-V linked complex. In the ESI mass (positive mode) spectra of **23a*cis*** in ethanol, both the diethoxide complexes ($[M+Na]^+$ 1159.3) and the V-O-V linked complex ($[M-2EtO+O+Na]^+$ 1085.2) were observed. One of the plausible structures for **23a*cis*** is shown in Scheme 5.[9] The coordinated ethoxides in **23a*cis*** were lost by the silica-gel column chromatography to give the complex **23b*cis***. Matrix-assisted laser desorption ionization time-of-flight (MALDI TOF) mass (negative mode) spectra were consistent with the expected value for the V-O-V linked dinuclear complex ($[\mathbf{23b}_{cis}]^-$ 1062.0, see experimental section). The peaks of hydroxide were not observed in the IR spectrum of **23b*cis***. The obtained compound is likely to have the V-O-V linked structure, as reported in the ref. 2d.[10]



Scheme 5.

Complexation of the dihemisalen ligand **22a**$_{cis}$ with VO(O^iPr)$_3$ was also followed by ^{1}H NMR (Figure 1). The singlet peak for CHN protons (▲) in the aldimine moiety was decreased by the addition of a half equivalent of VO(O^iPr)$_3$ with the concomitant appearance of the new signals (■) assignable to the monometallic complexes (Figure 1b). Then, an equimolar mixture of **22a**$_{cis}$ and VO(O^iPr)$_3$ almost induced the convergence to these peaks (■) (Figure 1c). When one and a half equivalents of VO(O^iPr)$_3$ were added, the peaks corresponding to the dinuclear hemisalen complexes appeared (●) (Figure 1d). These three singlets and two broad peaks (●) grew with two equivalents of VO(O^iPr)$_3$ (Figure 1e), where the vanadium(V) dihemisalen complexes may exist as a mixture of the three diastereomers (*endo-endo*, *exo-exo* and *endo-exo*) and the V-O-V linked structure. Use of more than two equivalents of VO(O^iPr)$_3$ did not induce the new peaks (Figure 1f).

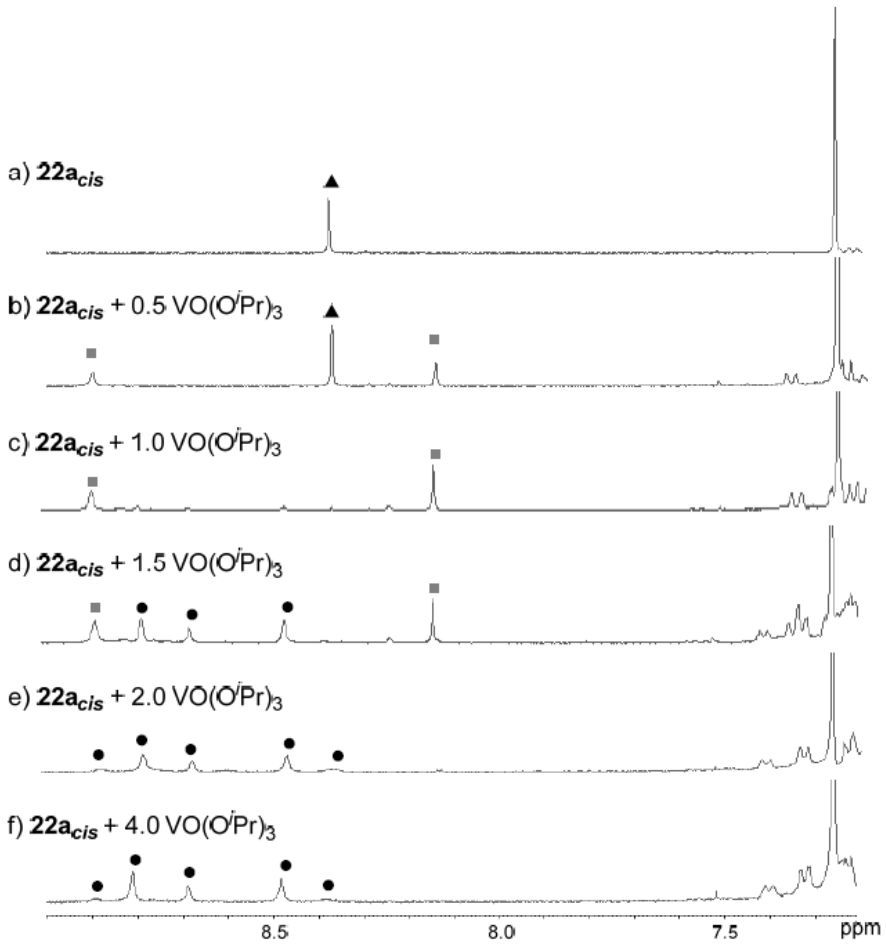
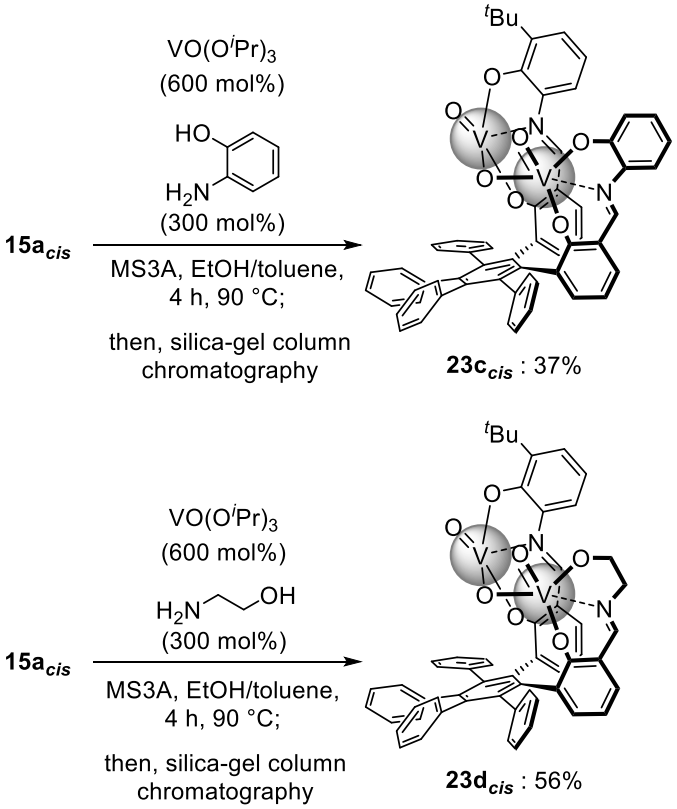


Figure 1. ^{1}H NMR spectra for the complexation of **22a**$_{cis}$ with VO(O^{i}Pr)$_3$. Each reaction was carried out in ethanol/dichloromethane at room temperature for 1 h under argon. Then, the solvent was replaced by $CDCl_3/CD_3OD$ (20 : 1) for the ^{1}H NMR study.

Based on the synthetic plan shown in Scheme 1, the desymmetrized dinuclear complex **23c*cis*** was synthesized by the treatment of the monoaldehyde **15a*cis*** with 2-aminophenol and $VO(O^iPr)_3$ (Scheme 6). After the reaction, the reaction mixture was purified by silica-gel column chromatography. ^1H NMR spectrum of **23c*cis*** showed the absence of ethoxide. IR spectrum of **23c*cis*** did not show the peaks assignable to hydroxide. MALDI TOF mass (negative mode) spectra also supported the expected value for the V-O-V linked desymmetrized dinuclear complex **23c*cis*** ([**23c*cis***]$^-$ 1006.1, see experimental section).[10] ^1H and ^{51}V NMR spectra in $CDCl_3$ are not simple, which might be dependent on the diastereomers. Use of monoethanolamine instead of aminophenol gave **23d*cis*** in 56% yield.

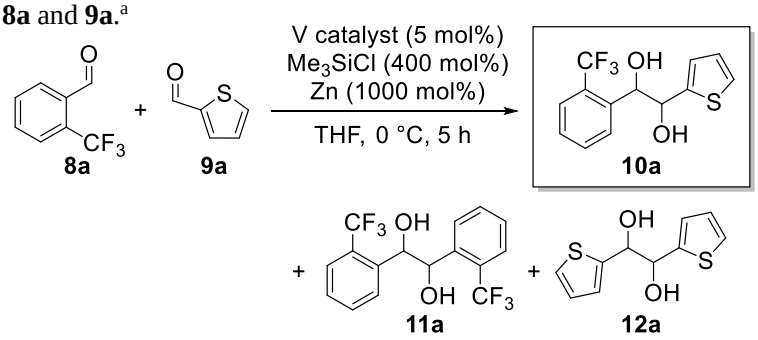


Scheme 6.

With such complexes in hand, the intermolecular cross-pinacol coupling reaction was examined. The vanadium catalysts were first activated to a divalent species by using a chlorosilane and a co-reductant. Then, two different aromatic aldehydes were added to the reaction mixture at the same time. The author initially utilized *o*-(trifluoromethyl)-benzaldehyde (**8a**) and thiophene-2-carbaldehyde (**9a**) as the substrates. The reaction was carried out in THF with 5 mol% vanadium catalyst, two equivalents of Me_3SiCl, and an excess amount of activated Zn powder at 0 °C. After that, the mixture was treated with aqueous HCl, and the subsequent desilylation with tetrabutylammonium fluoride afforded the corresponding hetero- and homo-coupling products.

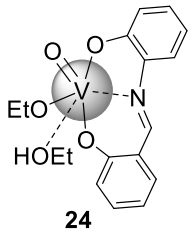
The results of catalytic intermolecular cross-pinacol coupling reaction are shown in Table 1. In the conditions with the di-*tert*-butyl substituted dinuclear complex **23b**$_{cis}$ (Entry 1), the 1,2-diol **10a** was obtained in 48% yield (*syn*/*anti* = 52 : 48). Next, the coupling reaction with the desymmetrized dinuclear complexes **23c**$_{cis}$ and **23d**$_{cis}$ were investigated. In the use of the catalyst **23c**$_{cis}$, the cross-coupling product **10a** was obtained in 48% yield, where the ratio of *syn*-diol formation was preferred up to *syn*/*anti* = 78 : 22 (Entry 2). Interestingly, the use of **23d**$_{cis}$ formed the 1,2-diol **10a** in the highest yield and selectivity (55%, *syn*/*anti* = 84 : 16) in this reaction (Entry 3). These results show the steric effect of the ligand could improve both cross- and diastereo-selectivity. For comparison, the same reaction with the *trans* catalyst **23d**$_{trans}$ gave **10a** in only 30% yield (Entry 4). Then, the use of condition with the simple mononuclear vanadium(V) hemisalen complex **24**[6] was performed to give the cross-coupling product **10a** as a minor product in 26% yield (Entry 5).[11] In the brank reaction without the vanadium reagents, only Zn as a reductant did not yield the pinacol coupling products (Entry 6). Therefore, the vanadium catalyst was found to be essential.

Table 1. Vanadium-catalyzed cross-pinacol coupling reaction with **8a** and **9a**.[a]



Entry	V catalyst	Yield [%][b,c]			**10a** : **11a** : **12a** (molar ratio)
		10a (*syn*/*anti*)	**11a**	**12a**	
1	**23b**$_{cis}$	48 (52/48)	38	42	2.5 : 1 : 1.1
2	**23c**$_{cis}$	48 (78/22)	30	51	3.2 : 1 : 1.7
3	**23d**$_{cis}$	55 (84/16)	33	43	3.3 : 1 : 1.3
4	**23d**$_{trans}$	30 (54/46)	55	44	1.1 : 1 : 0.8
5	**24**[d]	26 (57/43)	65	33	0.8 : 1 : 0.5
6	none	<1	-	-	-

[a] All reactions were performed using **8a** (0.4 mmol), **9a** (0.4 mmol), and the catalyst (0.02 mmol). [b] Yield of **10a** = (mole of **10a)** / 0.4 mmol x 100; yield of **11a** = [(mole of **11a**) x 2] / 0.4 mmol x 100; yield of **12a** = [(mole of **12a**) x 2] / 0.4 mmol x 100. [c] Determined by ^{1}H NMR of the crude mixture. [d] The reaction was performed using **24** (0.04 mmol).



24

The increase of cross-selectivity may be accounted for as follows (Figure 2). The higher reactive aldehyde **8a** is first activated with one side of the vanadium due to the steric repulsion between **8a** and R^5 (Figure 2, intermediate **A**). Then, the smaller aldehyde **9a** is preferentially reduced by another side of the active site. The thus-generated two ketyl radical species from **8a** and **9a** would result in the corresponding C-C bond formation to give 1,2-diol **10a** through the intermediate **B**.

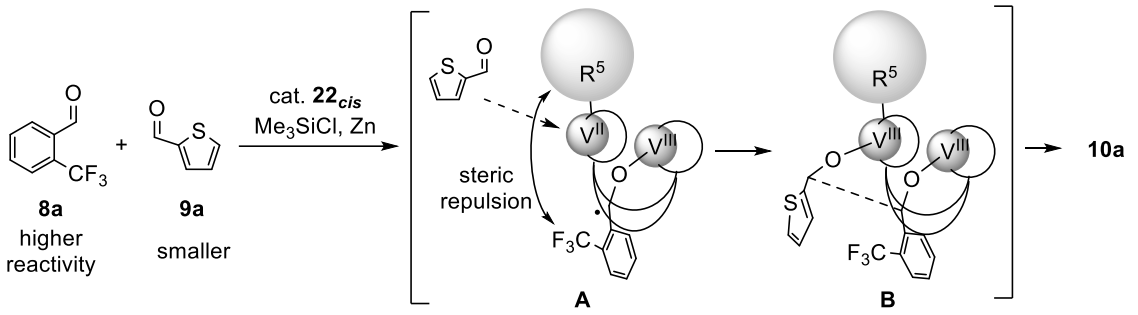
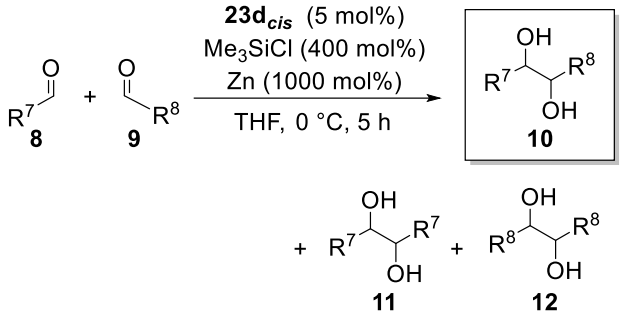


Figure 2. A possible mechanism for the cross-pinacol coupling reaction with the dinuclear vanadium catalyst **22*cis***.

Under the above-mentioned conditions using **23d*cis***, the author next investigated the cross-coupling reaction of a variety of two different aromatic aldehydes **8** and **9** to examine the effects of the substituted group. The results are summarized in Table 2. The *ortho*-trifluoromethyl and fluoro substituted benzaldehyde with benzaldehyde (Entries 2, 3) showed moderate yields (45% and 48%, respectively).[11] The reaction between benzaldehyde and thiophenealdehyde gave the cross-coupling product **10d** in 35% yield (Entry 4).

Table 2. Catalytic cross-pinacol coupling reaction of the two different aromatic aldehydes using **23d**$_{cis}$.[a]



Entry	R^7	R^8	Yield [%][b,c]			**10** : **11** : **12** (molar ratio)
			10 (*syn*/*anti*)	**11**	**12**	
1	*p*-$CF_3C_6H_4$	thiophen	**10a** - 55 (84/16)	**11a** - 33	**12a** - 43	3.3 : 1 : 1.3
2	*p*-$CF_3C_6H_4$	C_6H_5	**10b** - 45 (63/37)	**11a** - 43	**12b** - 43	2.1 : 1 : 1.0
3	*p*-FC_6H_4	C_6H_5	**10c** - 48 (66/34)	**11b** - 52	**12b** - 52	1.8 : 1 : 1.0
4	C_6H_5	thiophen	**10d** - 35 (75/25)	**11c** - 47	**12a** - 37	1.5 : 1 : 0.8

[a] All reactions were performed using **8** (0.4 mmol), **9** (0.4 mmol), and **23d**$_{cis}$ (0.02 mmol). [b] Yield of **10** = (mole of **10)** / 0.4 mmol x 100; yield of **11** = [(mole of **11**) x 2] / 0.4 mmol x 100; yield of **12** = [(mole of **12**) x 2] / 0.4 mmol x 100. [c] Determined by ^{1}H NMR of the crude mixture.

In conclusion, the dinuclear vanadium(V) dihemisalen complexes on the hexaaryl scaffold were designed and synthesized. Furthermore, intermolecular cross-pinacol coupling reactions using dinuclear hemisalen complexes have been developed. The desymmetrized vanadium catalyst was effective for the both cross- and diastereo-selectivity in the coupling reaction. Further increase of cross-selectivity is expected by introduction of the heterobimetalls to the ligand.

2-3. Experimental Section

General Method

^{1}H, ^{13}C, and ^{51}V NMR spectra were measured on JEOL ECS-400 spectrometer. $CDCl_3$ was used as a solvent and the residual solvent peak (^{1}H, δ 7.26; ^{13}C, 77.16 ppm) was used as a reference. ^{51}V NMR spectra were referenced to $VOCl_3$, (0 ppm) as an external reference. Infrared spectra were recorded on JASCO FT/IR-480plus. Mass spectra were measured on JEOL JMS-DX-303 spectrometer using fast atom bombardment (FAB) mode and Bruker autoflex III mass spectrometer using matrix-assisted laser desorption ionization time-of-flight (MALDI TOF) mode. Electrospray ionization (ESI) mass analyses were performed on an Applied Biosystems Mariner API-TOF Workstation. Column chromatography was conducted on silica-gel (Wakogel C-200). $VO(O^{i}Pr)_3$ was distilled under argon before use. *N*,*N*,*N'*,*N'*-Tetramethylethane-1,2-diamine, Ph_2O, and ethanol were distilled under argon over an appropriate drying agent before use. Other reagents and solvents were purchased from commercial sources.

Synthesis

Tolan 17

To an ether (320 mL) solution of 1,2-bis(2-methoxyphenyl)ethyne (**18**, 13.5 g, 56.7 mmol) and *N*,*N*,*N'*,*N'*-tetramethylethane-1,2-diamine (18.5 mL, 125 mmol) was dropwise added a 2.50 M hexane solution of BuLi (50 mL, 125 mmol) at 0 °C under argon. The reaction mixture was stirred for 30 min at the same temperature. Then, the ice water bath was removed. The mixture was stirred for 1 h. The reaction mixture was cooled to 0 °C again. DMF (9.6 mL, 125 mmol) was added to the mixture at the same temperature. Then, the cooling bath was removed. The mixture was stirred for 1 h. Saturated aqueous NH_4Cl was added to the mixture. The aqueous layer was extracted twice with dichloromethane. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 1/0 to 13/1) to give the product **17** (8.63 g, 29.3 mmol, 52%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.42 (d, J = 0.8 Hz, 2H), 7.84 (dd , J = 8.0, 2.0 Hz, 2H), 7.76 (dd, J = 8.0, 2.0 Hz, 2H), 7.21 (ddd, J = 8.0, 8.0, 0.8 Hz, 2H), 4.19 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 189.40, 164.13, 139.66, 129.45, 129.01, 124.16, 117.67, 90.30, 63.19 ppm;

IR (KBr, cm^{-1}) 3358, 2992, 2952, 2862, 2834, 2753, 1955, 1688, 1577, 1481, 1456, 1423, 1390, 1328, 1278, 1250, 1075, 986, 819, 793, 771, 756, 631, 553, 480; HRMS (FAB, *m*/*z*) calculated for $C_{18}H_{14}O_4$ [M^+]: 294.0892, found: 294.0900.

Dimethoxysalicylaldehyde 19_{cis} and 19_{trans}

To Ph_2O (35 mL) were added tolan **17** (3.10 g, 10.5 mmol) and tetraphenyl-cyclopentadienone **2** (4.05 g, 10.5 mmol) at room temperature under argon. The reaction mixture was stirred at reflux for 8 h. The mixture was poured into silica-gel column to purify (hexane/dichloromethane = 10/1 to hexane/ethyl acetate = 7/1) to give the products **19** (2.81 g, 4.32 mmol, 41%, *cis*/*trans* = 30 : 70).

19_{cis} : ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.99 (s, 2H), 7.43 (dd, *J* = 8.0, 2.0 Hz, 2H), 7.14 (dd, *J* = 8.0, 2.0 Hz, 2H), 7.01 (d, *J* = 7.6 Hz, 2H), 6.96 (d, *J* = 7.6 Hz, 2H), 6.79-6.94 (m, 16H), 6.70-6.78 (m, 4H), 3.76 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 190.05, 160.64, 141.44, 141.05, 140.37, 139.99, 139.89, 136.29, 133.75, 131.63, 131.42, 131.23, 128.66, 127.92, 126.79, 126.70, 126.60, 125.84, 125.48, 121.65, 63.37 ppm; IR (KBr, cm^{-1}) 3079, 3055, 3024, 3002, 2995, 2950, 2858, 1742, 1690, 1580, 1496, 1473, 1442, 1422, 1388, 1246, 1180, 1074, 1002, 759, 699, 561; HRMS (FAB, *m*/*z*) calculated for $C_{46}H_{34}O_4$ [M^+]: 650.2457, found: 650.2470.

19_{trans} : ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.00 (s, 2H), 7.43 (dd, *J* = 7.6, 2.0 Hz, 2H), 7.39 (dd, *J* = 7.6, 2.0 Hz, 2H), 7.04 (d, *J* = 7.6 Hz, 2H), 6.95 (dd, *J* = 7.6 Hz, 2H), 6.79-6.94 (m, 18H), 6.80 (dd, *J* = 7.6, 7.6 Hz, 2H), 3.71 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) 190.07, 159.93, 141.57, 140.71, 140.35, 139.75, 139.48, 136.05, 134.26, 131.93, 131.59, 131.38, 131.02, 128.71, 127.91, 126.86, 126.79, 126.72, 126.01, 125.55, 122.16, 63.09 ppm; IR (KBr, cm^{-1}) 3079, 3056, 3024, 2996, 2946, 1863, 2724, 1687, 1601, 1679, 1496, 1469, 1455, 1442, 1384, 1247, 1075, 1002, 830, 759, 698, 561, 509, 427, 408; HRMS (FAB, *m*/*z*) calculated for $C_{46}H_{34}O_4$ [M^+]: 650.2457, found: 650.2477.

Disalicylaldehyde 16_{cis} and monosalicylaldehyde 20_{cis}

To a dichloromethane (3 mL) solution of **19_{cis}** (110 mg, 0.169 mmol) was dropwise added a 1 M dichloromethane solution of BBr_3 (0.51 mL, 0.510 mmol) at room temperature under argon. The reaction mixture was stirred for 10 min. Ice water was

added to the mixture. The aqueous layer was extracted twice with dichloromethane. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/dichloromethane = 1/0 to 1/5) to give diol **16**$_{cis}$ (50.3 mg, 0.081 mmol, 48%) and monool **20**$_{cis}$ (2.5 mg, 0.0039 mmol, 2%).

16$_{cis}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.92 (s, 2H), 9.61 (s, 2H), 7.06-7.15 (m, 6H), 6.76-6.88 (m, 18H), 6.60 (dd, J = 7.6, 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 196.31, 159.17, 141.42, 141.17, 140.38, 140.26, 139.91, 135.30, 132.58, 131.62, 131.35, 131.17, 130.94, 129.87, 126.97, 126.88, 126.59, 126.20, 125.69, 125.42, 119.76, 118.18 ppm; IR (KBr, cm^{-1}) 3647, 3055, 3030, 2861, 1658, 1617, 1496, 1441, 1388, 1346, 1302, 1219, 1148, 1079, 1054, 1027, 940, 909, 864, 827, 767, 754, 698, 668, 563, 537, 471; HRMS (FAB, *m*/*z*) calculated for $C_{44}H_{30}O_4$[M^+]: 622.2144, found: 622.2148.

20$_{cis}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.01 (s, 1H), 10.02 (s, 1H), 9.61 (s, 1H), 7.42 (dd, J = 7.6, 2.0 Hz, 1H), 7.17 (dd, J = 7.6, 2.0 Hz, 1H), 7.14 (dd, J = 7.6, 2.0 Hz, 1H), 7.05-7.11 (m, 2H), 6.99 (dd, J = 7.6, 2.0 Hz, 1H), 6.71-6.95 (m, 19H), 3.77 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 196.59, 190.56, 161.12, 159.22, 141.81, 141.54, 141.21, 140.81, 140.47, 140.30, 140.26, 140.18, 140.11, 136.03, 135.44, 133.51, 132.85, 131.73, 131.65, 131.57, 131.29, 131.21, 130.89, 129.89, 128.33, 127.49, 126.89, 126.79, 126.69, 126.57, 126.18, 125.83, 125.73, 125.49, 121.67, 119.82, 118.22, 63.15 ppm; IR (KBr, cm^{-1}) 3056, 3024, 2950, 2859, 2742, 1689, 1656, 1615, 1579, 1472, 1441, 1386, 1218, 1150, 1076, 1002, 755, 698, 667, 542; HRMS (FAB, *m*/*z*) calculated for $C_{45}H_{32}O_4$[M^+]: 636.2301, found: 636.2322.

Disalicylaldehyde 16$_{trans}$ **and monosalicylaldehyde 20**$_{trans}$

To a dichloromethane (3 mL) solution of **19**$_{trans}$ (110 mg, 0.169 mmol) was dropwise added a 1 M dichloromethane solution of BBr_3 (0.51 mL, 0.510 mmol) at room temperature under argon. The reaction mixture was stirred for 10 min. Ice water was added to the mixture. The aqueous layer was extracted twice with dichloromethane. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/dichloromethane =

1/0 to 1/4) to give diol **16**$_{trans}$ (69.5 mg, 0.1121 mmol, 66%) and monool **20**$_{trans}$ (3.6 mg, 0.0057 mmol, 3%).

16$_{trans}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.09 (s, 2H), 9.60 (s, 2H), 7.29 (dd, *J* = 7.6, 2.0 Hz, 2H) , 7.09 (dd, *J* = 7.6, 2.0 Hz, 4H), 6.79-6.92 (m, 18H), 6.59 (dd, *J* = 7.6, 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) 196.65, 158.46, 141.08, 140.99, 140.34, 140.29, 139.34, 135.55, 132.87, 131.57, 131.46, 130.80, 130.10, 130.05, 126.98, 126.70, 125.79, 125.43, 119.32, 118.71 ppm; IR (KBr, cm^{-1}) 3645, 3055, 3022, 2855, 1656, 1620, 1496, 1441, 1389, 1353, 1333, 1300, 1271, 1218, 1149, 1055, 1027, 942, 910, 864, 766, 752, 699, 68, 563, 547, 471, 412; HRMS (FAB, *m*/*z*) calculated for $C_{44}H_{30}O_4$ [M^+]: 622.2144, found: 622.2149.

20$_{trans}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.06 (s, 1H), 10.02 (s, 1H), 9.58 (s, 1H), 7.44 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.39 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.26 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.10 (dd, *J* = 7.6, 2.0 Hz, 1H), 6.75-7.01 (m, 21H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 196.64, 190.27, 159.99, 158.44, 141.43, 141.34, 141.27, 140.43, 140.29, 140.19, 139.87, 139.65, 139.35, 136.24, 135.39, 134.38, 133.01, 131.79, 131.69, 131.46, 131.39, 130.95, 130.20, 129.94, 128.49, 127.83, 127.07, 126.86, 126.77, 126.65, 126.62, 126.48, 125.94, 125.83, 125.51, 122.37, 119.43, 118.47, 63.17 ppm; IR (KBr, cm^{-1}) 3056, 3022, 2933, 2854, 2743, 1689, 1578, 1440, 1387, 1217, 754, 698, 543; HRMS (FAB, *m*/z) calculated for $C_{45}H_{32}O_4$[M^+]: 636.2301, found: 636.2297.

Monohemisalen 21a$_{cis}$ and dihemisalen 22a$_{cis}$

To a toluene solution (140 mL) of disalicylaldehyde **16**$_{cis}$ (458 mg, 0.736 mmol) was added 2-amino-6-(*tert*-butyl)phenol (182 mg, 1.10 mmol) at room temperature under argon. The reaction mixture was stirred at 90 °C for 1 h. Then, the reaction mixture was cooled to room temperature, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/dichloromethane = 1/0 to 1/3) to give mono imine **21a**$_{cis}$ (231 mg, 0.299 mmol, 41%) and diimine **22a**$_{cis}$ (228 mg, 0.249 mmol, 34%).

21a$_{cis}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.03 (s, 1H), 11.00 (s, 1H), 9.60 (s, 1H), 8.39 (s, 1H), 6.80-7.22 (m, 27H), 6.63 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.58 (dd, *J* = 7.6, 7.6 Hz, 1H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 196.31, 163.20, 159.17, 157.89, 148.88,

141.44, 141.40, 141.13, 140.97, 140.50, 140.46, 140.37, 139.96, 136.84, 136.75, 136.07, 135.75, 135.27, 132.51, 131.64, 131.39, 131.35, 131.15, 130.98, 130.93, 130.10, 129.28, 126.92, 126.85, 126.72, 126.58, 126.19, 125.66, 125.39, 119.85, 119.71, 118.50, 118.24, 118.06, 115.61, 34.97, 29.48 ppm; IR (KBr, cm^{-1}) 3080, 3057, 3024, 2955, 2913, 2869, 1654, 1615, 1440, 752, 699; HRMS (FAB, *m*/*z*) calculated for $C_{54}H_{44}NO_4$ [(*M*-H)$^+$]: 770.3270, found:770.3286.

22a*cis* : ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.99 (s, 2H), 8.41 (s, 2H), 7.18 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.14 (dd, *J* = 7.6, 1.6 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 4H), 6.80-6.92 (m, 20H), 6.78 (dd, *J* = 8.0, 8.0 Hz, 2H), 6.58 (dd, *J* = 8.0, 8.0 Hz, 2H), 6.00 (s, 2H), 1.33 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) 163.10, 157.96, 148.86, 141.41, 140.89, 140.65, 136.68, 136.61, 136.11, 135.83, 131.71, 131.46, 131.41, 131.26, 131.04, 129.57, 126.83, 126.68, 126.57, 126.13, 126.00, 125.60, 125.33, 119.75, 118.53, 118.00, 115.49, 34.87, 2945 ppm; IR (KBr, cm^{-1}) 3503, 3397, 3080, 3055, 3026, 2997, 2955, 2912, 2871, 1611, 1678, 1496, 1441, 1392, 1364, 1340, 1299, 1269, 1236, 1200, 1177, 1152, 1140, 1082, 1057, 1028; HRMS (FAB, *m*/*z*) calculated for $C_{64}H_{56}N_2O_4$ [(*M*-H)$^+$]: 917.4318, found: 917.4290.

Monohemisalen vanadium complexes 15a*cis*

To a dichloromethane/ethanol (2.5 and 0.5 mL, respectively) solution of **21a*cis*** (74.8 mg, 0.097 mmol) was added $VO(O^iPr)_3$ (28 μL, 0.117 mmol) at room temperature under argon. The reaction mixture was stirred for 2 h. Then, dichloromethane and ethanol were removed from the reaction mixture by distillation under vacuum until a precipitation appeared. The reaction mixture was filtered through a membrane filter. The residue was washed with hexane to give the product **15a*cis*** (83.7 mg, 0.095 mmol, 98%). ^{1}H NMR (400 MHz, $CDCl_3$/CD_3OD = 20 : 1) δ 9.49 (s, 0.36H), 9.45 (s, 0.64H), 8.86 (s, 0.36H), 9.85 (s, 0.64H), 6.50-7.40 (m, 29H), 3.69 (q, *J* = 7.2 Hz, 2H), 1.47 (s, 9H), 1.22 (t, *J* = 7.2 Hz, 3H); ^{51}V NMR (105.1 MHz, $CDCl_3$/CD_3OD= 20 : 1) -520, -526 ppm; IR (KBr, cm^{-1}) 3052, 3025, 2956, 2928, 2909, 2861, 1655, 1607, 1437, 1297, 1254, 996, 752, 698, 668; MS (ESI, ethanol, *m*/*z*) calculated for $C_{56}H_{46}NNaO_6V$ [(*M*+Na)$^+$]: 902.3, found: 902.3.

Monohemisalen vanadium complexes 15b*cis*

To toluene (240 mL) were added **16*cis*** (800 mg, 1.28 mmol) and 2-amino-phenol (209 mg, 1.92 mmol) at room temperature under argon. The reaction mixture was stirred at 90 ^{o}C for 1 h. Then, the reaction mixture was cooled to room temperature, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/dichloromethane = 1/0 to 0/1) to give the mixture of mono imine compound and **16*cis*** (750.7 mg). To dichloromethane (56 mL) and ethanol (5 mL) solution of this mixture (750.7 mg) was added $VO(O^iPr)_3$ (293 μL, 1.24 mmol) at room temperature under argon. The reaction mixture was stirred for 2 h. Brine was added to the mixture. The aqueous layer was extracted twice with dichloromethane. The combined organic layer was dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (dichloromethane/ethanol = 1/0 to 1/1) to give the product **15b*cis*** (326 mg, 0.396 mmol, 31%). ^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$ = 20 :1) δ 9.44 (s, 0.31H), 9.41 (s, 0.69H), 8.83 (s, 0.69H), 8.81 (s, 0.31H), 6.50-7.60 (m, 29H), 3.61 (q, *J* = 7.2 Hz, 2H), 1.16 (t, *J* = 7.2 Hz, 3H); ^{51}V NMR (105.1 MHz, $CDCl_3/CD_3OD$ = 20 : 1) -521, -527 ppm; IR (KBr, cm^{-1}) 3052, 3025, 2960, 2933, 2853, 1654, 1607, 1557, 1439, 1301, 751, 699, 545; HRMS (FAB, *m*/*z*) calculated for $C_{50}H_{33}NO_5V$ [(*M*-OEt)$^+$]: 778.1798, found: 778.1790.

Dihemisalen vanadium complexes 23a*cis*

To a dichloromethane/ethanol (5 and 0.8 mL, respectively) solution of **22a*cis*** (82.9 mg, 0.090 mmol) was added $VO(O^iPr)_3$ (47 μL, 0.199 mmol) at room temperature under argon. The reaction mixture was stirred for 4 h. The reaction mixture was filtered through a membrane filter. The residue was washed with hexane to give the product **23a*cis*** (92.4 mg, 0.081 mmol, 82%). ^{1}H NMR (400 MHz, $CDCl_3/CD_3OD$ = 20 : 1) δ 8.86 (br, 0.21H), 8.81 (s, 0.63 H), 8.69 (s, 0.32H), 8.48 (s, 0.63H), 8.40 (br, 0.21H), 6.50-7.33 (m, 32H), 3.67 (q, *J* = 7.2 Hz, 4H), 1.20-1.50 (m, 18H), 1.21 (t, *J* = 7.2 Hz, 6H); ^{51}V NMR (105.1 MHz, $CDCl_3/CD_3OD$ = 20 : 1) -483.58, -504.19, -509.11, -523.85, -533.87 ppm; IR (KBr, cm^{-1}); 3056, 3025, 2955, 2907, 2865, 1606, 1571, 1553, 1434, 1370, 1254, 1147, 1056, 994, 861, 740, 699, 668, 637, 594, 567, 473, 447, 434, 414; MS (ESI, ethanol, *m*/*z*) calculated

for $C_{68}H_{62}N_2NaO_8V_2$ [(*M*+Na)$^+$]: 1159.3, found: 1159.3; Anal. Calcd. for $C_{68}H_{62}N_2O_8V_2$: C, 71.82; H, 5.50; N, 2.46. Found: C, 71.58; H, 5.32; N, 2.47.

Dihemisalen vanadium complexes 23b*cis*

23a*cis* (53.8 mg, 0.047 mmol) was treated by silica-gel column chromatography (hexane/dichloromethane = 1/0 to 0/1) to give the product **23b*cis*** (48.3 mg, 0.045 mmol, 96%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (s, 0.93 H), 8.68 (s, 0.18H), 8.48 (s, 0.89H), 6.60-7.50 (m, 32H), 1.52 (s, 8.37H), 1.43 (s, 8.01H), 1.36 (s, 1.62H); ^{51}V NMR (105.1 MHz, $CDCl_3$) -497.55, -501.24 ppm; IR (KBr, cm^{-1}); 3054, 3024, 2953, 2906, 2867, 1604, 1588, 1570, 1552, 1496, 1477, 1431, 1369, 1301, 1250, 1146, 1080, 1027, 994, 909, 885, 861, 822, 752, 699, 668, 638, 617, 593, 568, 477, 433, 418, 404; HRMS (MALDI TOF, *m*/*z*) calculated for $C_{64}H_{52}N_2O_7V_2$ [M^-]: 1062.2648, found: 106.2701.

Dihemisalen vanadium complexes 23c*cis*

To a toluene/ethanol (10 and 1 mL, respectively) solution of **15a*cis*** (99.0 mg, 0.113 mmol), 2-aminophenol (36.8 mg, 0.338 mmol) and MS4A (1.98 g) was added $VO(O^iPr)_3$ (159 μL, 0.675 mmol) at room temperature under argon. The reaction mixture was stirred at 90 °C for 4 h. Then, the reaction mixture was cooled to room temperature, and then brine was added to the mixture. The aqueous layer was extracted twice with dichloromethane. The combined organic layer was dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/dichloromethane = 1/0 to 1/9) to give the product **23c*cis*** (42.0 mg, 0.0417 mmol, 37%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (s, 0.94H), 8.63 (s, 0.16H), 8.32 (s, 0.47H), 8.31 (s, 0.43H), 6.60-7.60 (m, 33H), 1.50-1.55 (m, 9H); ^{51}V NMR (105.1 MHz, $CDCl_3$) -488.91, -491.03, -529.88, -535.79 ppm; IR (KBr, cm^{-1}); 3053, 3023, 2953, 2907, 2865, 1604, 1586, 1555, 1477, 1432, 1371, 1279, 1257, 1147, 1080, 1026, 995, 861, 750, 699, 669, 646, 592, 543, 475, 432; HRMS (MALDI TOF, *m*/*z*) calculated for $C_{60}H_{44}N_2O_7V_2$ [M^-]: 1006.2022, found: 1006.2048.

Cross-Pinacol coupling reaction

To a THF (2.4 mL) solution of **23d**$_{cis}$ (21.5 mg, 0.020 mmol) and activated Zn dust (298 mg, 4.0 mmol) was added Me_3SCl (206 μL, 1.6 mmol) at room temperature under argon. The reaction mixture was stirred for 20 min. Then, the reaction mixture was cooled to 0 °C with ice water bath. The 0.080 M THF solution (1 mL) of *o*-(trifluoromethyl)-benzaldehyde (53 μL, 0.40 mmol) and 2-thiophenealdehyde (38 μL, 0.40 mmol) was added to the mixture, which was stirred for 5 h at 0 °C. 6 M HCl was added to the mixture. The aqueous layer was extracted twice with ethyl acetate. Tetrabutylammonium fluoride (252 mg, 0.80 mmol) was added to the combined organic layer. Then, the mixture was washed with 1 M HCl and brine, dried over $MgSO_4$, and evaporated. The yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene (22.0 mg, 0.133 mmol) as an internal standard.

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1-Phenyl-2-(2-(trifluoromethyl)phenyl)ethane-1,2-diol (10b$_{syn}$ **and 10b**$_{anti}$**)**

10b$_{syn}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 7.6 Hz, 1H), 7.60 (dd, J = 7.6, 7.6 Hz, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.38 (dd, J = 7.6, 7.6 Hz, 1H), 7.20-7.28 (m, 5H), 5.21 (dd, J = 4.4, 4.4 Hz, 1H), 4.89 (dd, J = 4.4, 4.4 Hz, 1H), 2.71 (d, J = 4.4 Hz, 1H), 2.70 (d, J = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 140.23, 139.56, 132.03, 129.00, 128.43, 128.43, 128.04, 127.72 (q, J = 29.6 Hz), 126.41, 125.88 (q, J = 5.7 Hz), 124.30 (q, J = 272.6 Hz), 77.48, 73.34 ppm; IR (KBr, cm^{-1}) 3427, 3264, 3065, 3034, 2944, 1451, 1311, 1167, 1116, 1060, 1043, 770, 714, 696, 667; HRMS (FAB, *m*/*z*) calculated for $C_{15}H_{13}F_3NaO_2$ [(*M*-Na)$^+$]: 305.0765, found: 305.0766.

10b$_{anti}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.2 Hz, 1H), 7.35-7.44 (m, 3H), 7.29-7.31 (m, 3H), 7.21-7.43 (m, 2H), 5.40 (dd, J = 3.6, 2.8 Hz, 1H), 4.91 (dd, J = 3.6, 2.8 Hz, 1H), 2.45 (d, J = 2.8 Hz, 1H), 2.22 (d, J = 3.6Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 141.90, 138.25, 131.87, 128.72, 128.02, 127.88 (q, J = 30.5 Hz), 126.61, 126.31, 126.02, 125.56 (q, J = 5.7 Hz), 124.48 (q, J = 272.7 Hz), 73.98, 72.56 ppm; IR (neat, cm^{-1}) 3409, 3066, 3033, 2925, 1455, 1312, 1162, 1121, 1059, 769, 707; HRMS (FAB, *m*/*z*) calculated for $C_{15}H_{13}F_3NaO_2$ [(*M*-Na)$^+$]: 305.0765, found: 305.0766.

1-(2-Fluorophenyl)-2-phenylethane-1,2-diol (10c$_{syn}$ and 10c$_{anti}$)

10c$_{syn}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (dd, J = 7.2, 1.2 Hz, 1H), 7.20-7.28 (m, 6H), 7.13 (dd, J = 7.2, 1.2 Hz, 1H), 6.91 (ddd, J = 10.4, 8.4, 1.2 Hz, 1H), 5.07 (dd, J = 5.6, 4.0 Hz, 1H), 4.86 (dd, J = 5.6, 3.2 Hz, 1H), 2.75 (d, J = 4.0 Hz, 1H), 2.74 (d, J = 3.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 160.12 (d, J = 245.1 Hz), 139.88, 129.61 (d, J = 8.6 Hz), 128.54 (d, J = 3.8 Hz), 128.37, 128.160, 127.46 (d, J = 13.4 Hz), 126.71, 124.29 (d, J = 3.9 Hz), 115.38 (d, J = 21.9 Hz), 77.87, 73.13 ppm; IR (KBr, cm^{-1}) 3586, 3335, 2913, 2876, 1587, 1491, 1454, 1339, 1227, 1195, 1104, 1084, 1054, 849, 804, 764, 703, 643, 571, 529; HRMS (FAB, *m*/*z*) calculated for $C_{14}H_{13}FNaO_2$ [(*M*-Na)$^+$]: 255.0797, found: 255.0799.

10c$_{anti}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18-7.28 (m, 7H), 7.06 (ddd, J = 7.6, 7.6, 0.8 Hz, 1H), 6.99 (ddd, J = 10.4, 10.4, 1.6 Hz, 1H), 5.29 (dd, J = 4.0, 4.0 Hz, 1H), 4.98 (dd, J = 4.0, 4.0 Hz, 1H), 2.39 (d, J = 4.0 Hz, 1H), 2.32 (d, J = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 160.21 (d, J = 245 Hz), 139.88, 129.61(d, J = 8.6 Hz), 128.54 (d, J = 3.8 Hz), 128.37, 128.16, 127.46 (d, J = 13.4 Hz), 126.71, 124.29 (d, J = 3.9 Hz), 115.38 (d, J = 21.9 Hz), 77.87, 73.13 ppm; IR (KBr, cm^{-1}) 3365, 3061, 332, 2924, 2883, 1588 1492, 1456, 1228, 1038, 833, 751, 698, 553, 498; HRMS (FAB, *m*/*z*) calculated for $C_{14}H_{13}FNaO_2$ [(*M*-Na)$^+$]: 255.0797, found: 255.0800.

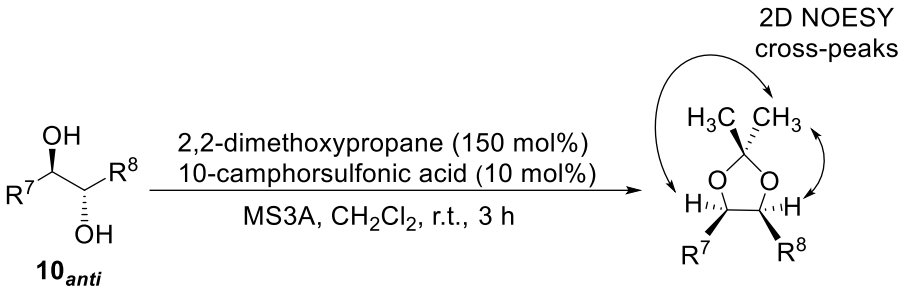
1-Phenyl-2-(thiophen-2-yl)ethane-1,2-diol (10d$_{syn}$ and 10d$_{anti}$)

10d$_{syn}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22-7.29 (m, 6H), 6.86 (dd, J = 5.2, 3.6 Hz, 1H), 6.69 (dd, J = 4.8, 0.8 Hz, 1H), 5.01 (dd, J = 7.6, 2.4 Hz, 1H), 4.80 (dd, J = 7.6, 2.4 Hz, 1H), 2.94 (d, J = 7.6 Hz, 1H), 2.83 (d, J = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 143.35, 139.86, 128.34, 128.22, 127.05, 126.63, 125.52, 125.22, 79.07, 75.10 ppm; IR (KBr, cm^{-1}) 3348, 3062, 2920, 1454, 1408, 1236, 1200, 1057, 1003, 849, 808, 762, 697, 626, 602, 549, 515, 490; HRMS (FAB, *m*/*z*) calculated for $C_{12}H_{12}NaO_2S$ [(*M*-Na)$^+$]: 243.0456, found: 243.0452.

10d$_{anti}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.35 (m, 6H), 6.94-6.97 (m, 2H), 5.09 (dd, J = 5.6, 4.0 Hz, 1H), 4.89 (dd, J = 5.6, 3.2 Hz, 1H), 2.34 (d, J = 3.2 Hz, 1H), 2.31 (d, J = 4.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 142.97, 139.63, 128.50, 128.34, 127.01, 126.62, 126.03, 125.80, 77.92, 74.81 ppm; IR (KBr, cm^{-1}) 3376, 3033, 2900, 1495, 1453,

1436, 1347, 1278, 1238, 1195, 1173, 1023, 846, 826, 768, 753, 697, 621, 520; HRMS (FAB, *m*/*z*) calculated for $C_{12}H_{12}NaO_2S$ [(*M*-Na)$^+$]: 243.0456, found: 243.0459.

Acetonide formation of 10*anti*



To a dichloromethane (1.5 mL) solution of **10*anti*** (0.186 mmol), 10-camphorsulfonic acid (4.3 mg, 0.0185 mmol) and MS3A (310 mg) was added 2,2-dimethoxypropane (34 μL, 0.277 mmol) at room temperature under argon. The reaction mixture was stirred for 3 h. Saturated aqueous $NaHCO_3$ was added to the mixture. Then, MS3A was removed from the reaction mixture by filtration. The aqueous layer was extracted twice with dichloromethane. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/ dichloromethane = 1/0 to 2/3) to give the acetonide.

Acetonide formation of 10b*anti*

Yield: 52%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.0 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.21 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.13 (dd, *J* = 8.0, 8.0 Hz, 1H), 6.99-7.03 (m, 5H), 5.92 (d, *J* = 3.2 Hz, 1H), 5.54 (dd, *J* = 3.2 Hz, 1H), 1.86 (s, 3H), 1.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 137.98, 135.94, 131.21, 129.34, 127.61, 127.49, 127.33, 127.32 (q, *J* = 30.5 Hz), 127.02, 125.06 (q, *J* = 5.7 Hz), 124.40 (q, *J* = 272.7 Hz), 108.99, 81.46, 77.16, 26.67, 24.32 ppm; IR (neat, cm^{-1}) 3068, 3036, 2991, 2940, 1457, 1383, 1324, 1287, 1264, 1215, 1160, 1120, 1051, 1034, 887, 768, 899; HRMS (EI, *m*/*z*) calculated for $C_{18}H_{17}F_3O_2$ [M^+]: 322.1181, found: 322.1183.

Acetonide formation of 10c*anti*

Yield: 73%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.99-7.06 (m, 6H), 6.91 (dd, *J* = 7.6, 7.6 Hz, 1H), 6.68 (dd, *J* = 8.8, 8.8 Hz, 1H), 5.83 (d, *J* = 7.2 Hz,

1H), 5.57 (d, *J* = 7.2 Hz, 1H), 1.83 (s, 3H), 1.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 159.29 (d, *J* = 243.2 Hz), 137.75, 128.78 (d, *J* = 8.5 Hz), 127.69 (d, *J* = 3.8 Hz), 127.58, 127.52, 127.08, 125.74 (d, *J* = 13.3 Hz), 123.60 (d, *J* = 2.8 Hz), 114.31 (d, *J* = 21 Hz), 108.97, 81.05, 75.53 (d, *J* = 2.9 Hz), 26.72, 24.38 ppm; IR (neat, cm^{-1}) 3067, 3033, 2990, 2935, 1491, 1457, 1382, 1261, 1230, 1215, 1162, 1104, 1081, 1053, 889, 756, 698; HRMS (EI, *m*/z) calculated for $C_{17}H_{17}FO_2$ [M^+]: 272.1213, found: 272.1211.

Acetonide formation of 10d*anti*

Yield: 68%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13-7.18 (m, 5H), 7.03 (dd, *J* = 5.2, 1.2 Hz, 1H), 6.70 (dd, *J* = 5.2, 3.6 Hz, 1H), 6.53 (dd, *J* = 2.0, 1.2 Hz, 1H), 5.72 (d, *J* = 7.2 Hz, 1H), 5.51 (d, *J* = 7.2Hz, 1H), 1.82 (s, 3H), 1.59 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 142.05, 136.85, 127.84, 127.67, 126.80, 12.12, 125.21, 125.13, 109.26, 81.25, 78.47, 27.09, 24.88 ppm; IR (neat, cm^{-1}) 3067, 3032, 2988, 2936, 2893, 1455, 1382, 1248, 1217, 1157, 1082, 1053, 879, 863, 812, 740, 698; HRMS (EI, *m*/z) calculated for $C_{15}H_{16}O_2S$ [M^+]: 260.0871, found: 260.0875.

2-4. Reference and Notes

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7. Either hydroxyl group or aldehyde moiety on the other side of the salicylaldehyde moiety may chelate to vanadium center to form the octahedral hexa-coordinate structure.
8. S. Mondal, S. P. Rath, K. K. Rajak, A. Chakravorty, *Inorg. Chem.* **1998**, *37*, 1713-1719.
9. The coordination geometry is not clear at this stage. According to the ref. 1, the octahedral coordination might be possible.
10. ^{1}H and ^{51}V NMR spectra in $CDCl_3$ are not simple, which might be dependent on the diastereomers.
11. *Syn* and *anti* were determined by the 2D-NOESY experiments after acetonide formation of **10**, see experimental section for details.

Chapter 3. Synthesis of Hetero Dinuclear Hemisalen Complex on Hexaarylbenzene Scaffold and its Application for Cross-Pinacol Coupling Reaction

3-1. Introduction

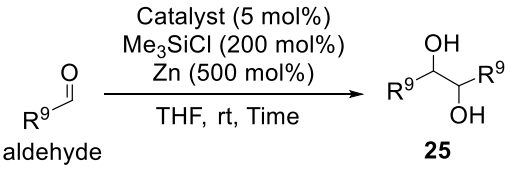
Further increase of cross-selectivity is expected by introduction of the hetero bimetals to the ligand because the reactivity of substrates strongly depends on the metal in the pinacol coupling reaction. For example, low valent vanadium on Schiff base complexes activates aromatic aldehydes,[1a] but does not activate aliphatic aldehydes (as shown in the results and discussion in this chapter). In contrast, low valent titanium activates both aliphatic and aromatic aldehydes.[1b-d]

Therefore, the hetero bimetallic complex with vanadium and titanium would be effective for controlling the cross-pinacol coupling reaction between aliphatic and aromatic aldehydes. Here, chapter 3 deals with the synthesis of hetero dihemisalen complexes **14**$_{cis}$, and their application for the cross-pinacol coupling reaction between aliphatic and aromatic aldehydes.

3-2. Results and Discussion

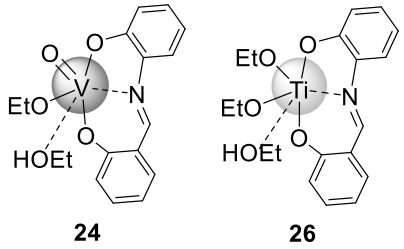
The author first investigated homo-pinacol coupling reactions using mononuclear vanadium hemisalen catalyst **24** were studied (Table 1). The vanadium catalyst **24** activated benzaldehyde in the presence of Me_3SiCl and Zn to give the corresponding homo-coupling product **25** in 97% yield (Entry 1). In contrast, the homo-coupled 1,2-diols were not obtained under the similar conditions when aliphatic aldehydes were used as substrates (Entries 2-4). In contrast, the titanium catalyst **26** activated aliphatic aldehyde to give the corresponding homo-coupling product **25** in 52% yield (Entry 5).

Table 1. Homo-pinacol coupling reaction of aromatic or aliphatic aldehyde using metal-hemisalen catalyst.[a]

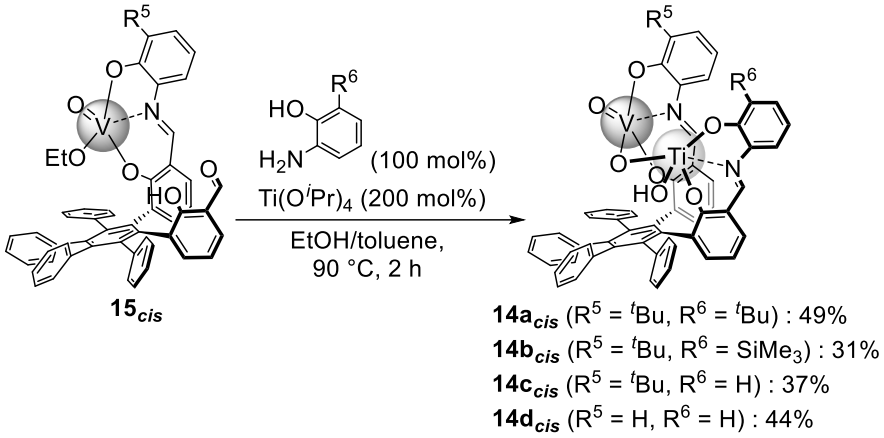


Entry	Catalyst	R^9	Time [h]	Yield of **25**[b] [%]	*dl*/*meso*
1	**24**	Ph	1	97	86/14
2	**24**	C_2H_4Ph	6	0	-
3	**24**	CH_2Ph	6	0	-
4	**24**	C_2H_5	6	0	-
5	**26**	C_2H_4Ph	1	52	68/32

[a] All reactions were performed using aldehyde (0.4 mmol) and **24** or **26**(0.02 mmol). [b] Determined by ^{1}H NMR of the crude mixture.



The hetero dinuclear complexes **14**$_{cis}$ were synthesized (Scheme 1). Vanadium(V) complex **15a**$_{cis}$ was treated with 2-amino-6-*tert*-butylphenol and Ti(O^iPr)$_4$ in the ethanol/toluene under reflux to give hetero bimetallic complex **14a**$_{cis}$ (R^5 = ^{t}Bu, R^6 = ^{t}Bu) in 49% yield. In the MALDI-TOF mass (negative mode) spectrum of **14a**$_{cis}$, the mainly observed mass was 1059.19, which corresponds to the V-O-Ti linked hetero dinuclear complex ([**14a**$_{cis}$-H]$^-$).[2] ^{1}H NMR spectrum of **14a**$_{cis}$ showed the absence of alkoxide. IR spectrum of **14a**$_{cis}$ supports the presence of hydroxide. Furthermore, other substituted hetero bimetallic complexes **14b**$_{cis}$ (R^5 = ^{t}Bu, R^6 = $SiMe_3$), **14c**$_{cis}$ (R^5 = ^{t}Bu, R^6 = H) and **14d**$_{cis}$ (R^5 = H, R^6 = H) were synthesized as well. The formation of these complexes was determined by the MALDI-TOF mass (negative mode) spectra.[3]



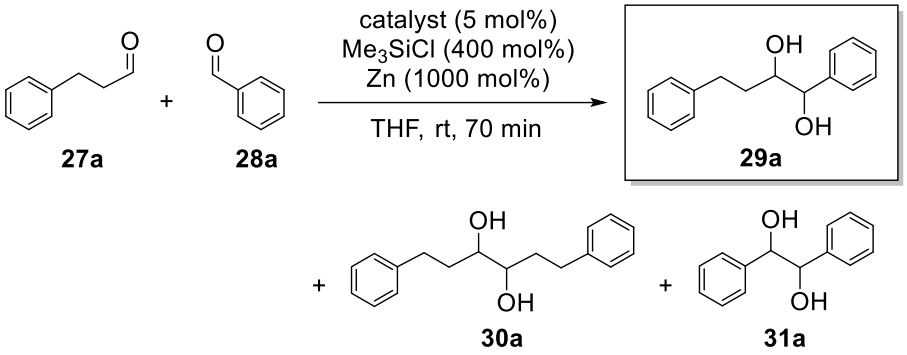
Scheme 1.

With such complexes in hand, the intermolecular cross-pinacol coupling reaction between aliphatic and aromatic aldehydes was examined (Table 2). The hetero dinuclear catalyst **14*cis*** (5 mol%) was first activated to a low-valent species by using Me_3SiCl and excess amount of activated Zn powder at room temperature. Two equivalents of aliphatic aldehyde **27** were added to the reaction mixture, then aromatic aldehyde **28** was dropwise added over 1 hour. The author initially chose 3-phenylpropanal (**27a**) and benzaldehyde (**28a**) as the substrates.

The results of catalytic intermolecular cross-pinacol coupling reaction are shown in Table 2. First, the conditions with the hetero dinuclear complex **14a*cis*** were used to give the desired 1,2-diol **29a** as a minor product (17% yield, Entry 1).[4] Similarly, the same reaction with Me_3Si-substituted complex **14b*cis*** led to the hetero-coupling product in 15% yield (Entry 2). By switching the substituent on the titanium side of hetero dinuclear catalyst from ^{t}Bu to H, the selectivity for the cross-coupling dramatically increased, providing 1,2-diol **29a** in 69% yield (Entry 3). In the case of dinuclear catalyst **14d*cis*,** the desired cross-coupling product was obtained in 73% yield (*syn*/*anti* = 59 : 41), where the molar ratio of **29a**/**30a**/**31a** is enhanced up to 7.1 : 1 : 1.1 (Entry 4). On the other hand, diastereoselectivity of cross-coupling reaction was not controlled. For comparison, the same reaction with the mixture of mononuclear vanadium complex **24**[5] and mononuclear titanium complex **26**[6] decreased the cross-selectivity of **29a** (**29a**/**30a**/**31a** = 2.4 : 1 : 0.1,

Entry 5). In the absence of the vanadium and titanium catalysts, no cross-coupling product was obtained (Entry 6).

Table 2. Screening of catalysts for cross-pinacol coupling reaction of **27a** and **28a**.[a,b]



Entry	catalyst	Yield [%][c,d]			**29a** : **30a** : **31a** (molar ratio)
		29a (*syn*/*anti*)	**30a**	**31a**	
1	**14a**$_{cis}$	17 (63/37)	0	17	1.0 : - : 1
2	**14b**$_{cis}$	15 (68/32)	0	21	1.4 : - : 1
3	**14c**$_{cis}$	69 (64/36)	12	29	5.9 : 1 : 1.2
4	**14d**$_{cis}$	73 (59/41)	10	23	7.1 : 1 : 1.1
5	**24** + **26**[e]	88 (63/37)	37	7	2.4 : 1 : 0.1
6	none	0	-	-	-

[a] All reactions were performed using **27a** (0.4 mmol), **28a** (0.2 mmol), and the catalyst (0.01 mmol). [b] 1 hour addition of **28a** using syringe pump. [c] Yield of **29a** = (mole of **29a)** / 0.2 mmol x 100; yield of **30a** = [(mole of **30a**) x 2] / 0.4 mmol x 100; yield of **31a** = [(mole of **31a**) x 2] / 0.2 mmol x 100. [d] Determined by ^{1}H NMR of the crude mixture. [e] The reaction was performed using **24** (0.01 mmol) and **26** (0.01 mmol).

The increase of cross-selectivity may be accounted for as follows (Figure 1). The titanium-centered active site of the hetero dinuclear catalyst first activates aliphatic aldehyde **27a** because of its higher reducing ability (Figure 1, intermediate **A**). On this occasion, the formation of the homo-diol **30a** through the dimerization of **A** should be suppressed due to the steric hinderance of the bulky ligand. Next, slowly added aromatic aldehyde **28a** is activated with the vacant vanadium center, then the thus-generated two ketyl radical species of **27a** and **28a** would form the corresponding C-C bond to give 1,2-diol **29a** through the intermediate **B**. Bulky trimethylsilyl- or *tert*-butyl group of titanium side would interrupt the reaction with aliphatic aldehyde **27a**. Therefore, the conditions with dinuclear catalyst **14d**$_{cis}$ are considered to preferentially afford the cross-coupling product. Thus, the involvement of the hetero dinuclear catalyst was suggested to be essential to work the reaction efficiently.

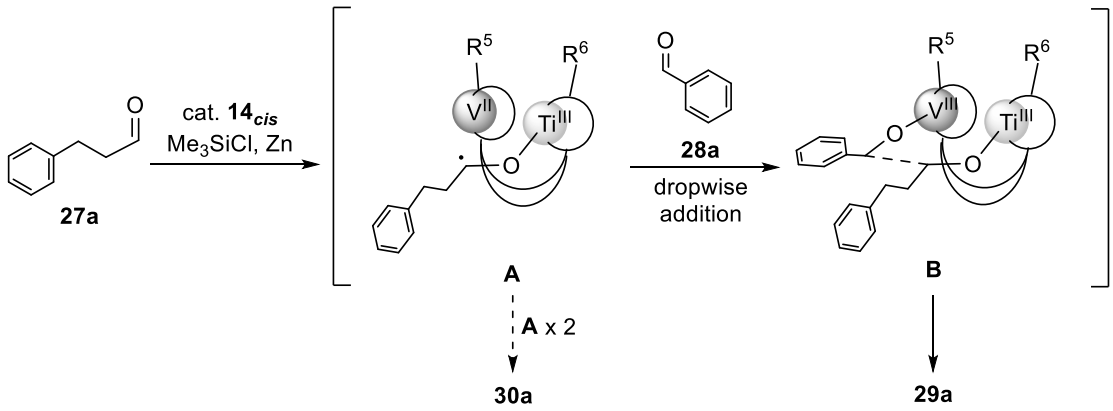
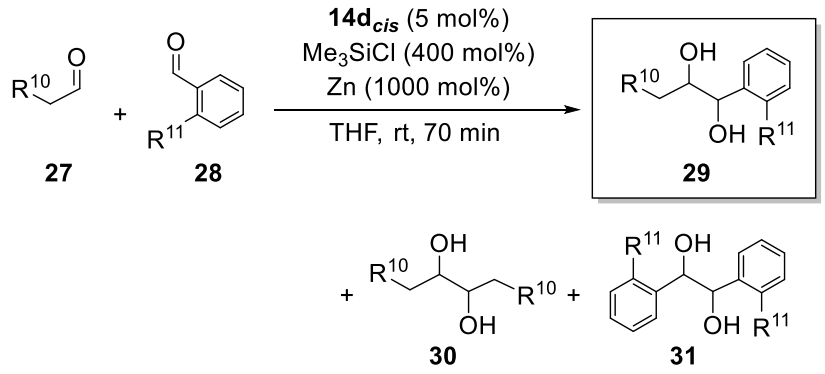


Figure 1. A possible mechanism for the cross-pinacol coupling reaction with the hetero dinuclear catalysts **14**$_{cis}$.

Under the above optimized conditions using **14d*cis***, the author next investigated the cross-coupling reaction of a variety of aliphatic aldehydes **27** and aromatic aldehydes **28**. The results are summarized in Table 3. The reaction between 3-phenylpropanal and *o*-fluoro substituted benzaldehyde showed high yields (81%, Entry 2). The reaction with 2-(trifluoromethyl)benzaldehyde gave 1,2-diol **29c** in 70% yield (Entry 3). When 2-phenylacetaldehyde was employed as an aliphatic aldehyde, cross-coupling product **29d** was obtained in a moderate yield (88%, Entry 4).[7a] The use of pentanal led to **29e** in 69% yield (Entry 5).[7b,c]

Table 3. Cross-pinacol coupling reaction using hetero dinuclear catalyst **14d*cis***.[a,b]



Entry	R^{10}	R^{11}	Yield [%][c,d]			**29** : **30** : **31** (molar ratio)
			29 (*syn*/*anti*)	**30**	**31**	
1	CH_2Ph	H	**29a** - 73 (59/41)	**30a**- 10	**31a** - 23	7.1 : 1 : 1.1
2	CH_2Ph	F	**29b** - 81 (51/49)	**30a**- 19	**31b** - 14	4.2 : 1 : 0.3
3	CH_2Ph	CF_3	**29c** - 70 (46/54)	**30a** - 7	**31c** - 17	9.5 : 1 : 1.1
4	Ph	H	**29d** - 88 (62/38)	**30b**- 36	**31a** - 11	2.4 : 1 : 0.2
5	C_3H_7	H	**29e** - 69 (64/36)	**30c** - 5	**31a** - 24	13.2 : 1 : 2.3

[a] All reactions were performed using **27** (0.4 mmol), **28** (0.2 mmol), and **14d*cis*** (0.01 mmol). [b] 1 hour addition of **28** by syringe pump. [c] Yield of **29** = (mole of **29)** / 0.2 mmol x 100; yield of **30** = [(mole of **30**) x 2] / 0.4 mmol x 100; yield of **31** = [(mole of **31**) x 2] / 0.2 mmol x 100. [d] Determined by ^{1}H NMR of the crude mixture.

In conclusion, the dihemisalen ligand on the hexaarylbenzene scaffold was designed, where hetero dinuclear complexes **14**$_{cis}$ with vanadium(V) and titanium(IV) were synthesized from the key intermediate **16**$_{cis}$ for the cross-pinacol coupling reaction. Using such novel hetero dinuclear catalyst, the intermolecular cross-pinacol coupling reactions between aliphatic and aromatic aldehydes have been demonstrated. The hetero dinuclear catalyst was shown to be effective for the cross-selectivity in the coupling reaction.

3-3. Experimental Section

General Method

^{1}H, ^{13}C, and ^{51}V NMR spectra were measured on JEOL ECS-400 spectrometer. $CDCl_3$ was used as a solvent and the residual solvent peak (^{1}H, δ7.26; ^{13}C, 77.16 ppm) was used as a reference. ^{51}V NMR spectra were referenced to $VOCl_3$ (0 ppm) as an external reference. Infrared spectra were recorded on JASCO FT/IR-480plus. Mass spectra were measured on JEOL JMS-DX-303 spectrometer using fast atom bombardment (FAB) mode or Bruker autoflex III mass spectrometer using matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) mode. Column chromatography was conducted on silica-gel (Wakogel C-200). $VO(O^iPr)_3$ and $Ti(O^iPr)_4$ were distilled under argon before use. Ethanol were distilled under argon over an appropriate drying agent before use. Other reagents and solvents were purchased from commercial sources.

Synthesis

Hetero dihemisalen complex 14a$_{cis}$

To a toluene/ethanol (4 mL/2 mL, respectively) solution of **15a**$_{cis}$ (60.0 mg, 0.0682 mmol) and 2-amino-6-(*tert*-butyl)phenol (11.3 mg, 0.0682 mmol) was added $Ti(O^iPr)_4$ (40.0 μL, 0.136 mmol) at room temperature under argon. The reaction mixture was stirred at 90 °C for 2 h. Then, the reaction mixture was cooled to room temperature, and evaporated. The mixture was purified by silica-gel column chromatography (hexane/ethyl acetate = 1/0 to 1/2) to give the product **14a**$_{cis}$ (35.1 mg, 0.0331 mmol, 49%). ^{1}H NMR (400 MHz, $CDCl_3$) δ8.86 (s, 1H), 8.31 (s, 1H), 6.70-7.30 (m, 30H), 6.60 (dd, J = 8.0, 8.0

Hz, 1H), 6.42 (dd, *J* = 7.2, 7.2 Hz, 1H), 1.48 (s, 9H), 1.16 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 163.99, 163.24, 161.16, 161.04, 155.28, 153.96, 141.55, 140.97, 140.87, 140.70, 140.64, 140.58, 140.34, 139.26, 139.10, 138.45, 138.13, 137.53, 137.01, 136.39, 132.51, 132.38, 132.27, 131.87, 131.67, 131.55, 131.46, 130.68, 129.75, 128.85, 127.35, 126.88, 126.69, 126.64, 126.60, 126.44, 126.15, 125.69, 125.51, 125.35, 122.61, 120.37, 119.71, 119.66, 119.51, 118.18, 112.41, 112.24, 34.79, 34.71, 29.55, 29.21, 22.90, 18.63 ppm; ^{51}V NMR (105.1 MHz, $CDCl_3$) -573 ppm; IR (KBr, cm^{-1}) 3626, 3054, 2953, 2907, 2865, 1607, 1435, 1372, 1255, 752; HRMS (FAB, *m*/*z*) calculated for $C_{64}H_{52}N_2O_6TiV[(M\text{-}OH)^+]$: 1043.2744, found: 1043.2752; MS (MALDI, *m*/*z*) calculated for $C_{64}H_{52}N_2O_7TiV[(M\text{-}H)^-]$: 1059.27, found: 1059.19.

2-Amino-6-(trimethylsilyl)phenol

To $HN(SiMe_3)_2$ (3.0 mL, 14.1 mmol) was added 2-bromo-6-nitrophenol (1.0 g, 4.59 mmol) at room temperature under argon. The reaction mixture was heated to reflux, and stirred for 3 h. Then, $HN(SiMe_3)_2$ was removed from the reaction mixture by distillation under vacuum. THF (15 mL) and a 1.13 M ether solution of PhLi (8.1 mL, 9.17 mmol) were added to the mixture at -84 °C. The reaction mixture was stirred for 1 h. Then, the ice chloroform bath was removed. The mixture was stirred for 1 h at room temperature. Saturated aqueous NH_4Cl was added to the mixture. The aqueous layer was extracted twice with ether. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/dichloromethane = 1/0 to 5/1) to give 2-nitro-6-(trimethylsilyl)phenol as a mixture of trimethyl(phenyl)silane (139.2 mg, 2-nitro-6-(trimethylsilyl)phenol/ trimethyl(phenyl)silane = 73 : 27). Ethanol (15 mL) and 10 wt% Pd on charcoal (33.1 mg, 0.0310 mmol) were added to the mixture, and hydrogenated with H_2 for 3 h at room temperature. The reaction mixture was filtered, and evaporated. The residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 1/0 to 2/1) to give 2-amino-6-(trimethylsilyl)phenol (57.9 mg, 0.319 mmol, 7%). ^{1}H NMR (400 MHz, $CDCl_3$) δ6.92 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.87 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.81 (dd, *J* = 7.6, 7.6 Hz, 1H), 0.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) 151.32, 132.79, 127.26, 125.89, 121.21, 120.92, -0.61 ppm; IR (KBr, cm^{-1}) 3387, 3299, 3065, 2953, 2698, 2638, 1591, 1449, 1406,

1368, 1293, 1249, 1219, 1205, 1157, 1112, 915, 897, 838, 787, 757, 693, 642, 605; HRMS (FAB, *m*/*z*) calculated for $C_9H_{15}NOSi$ [M^+]: 181.0923, found: 181.0922.

Hetero dihemisalen complex 14b*cis*

To a toluene/ethanol (6 mL/3 mL, respectively) solution of **15a*cis*** (80.0 mg, 0.0909 mmol) and 2-amino-6-(trimethylsilyl)phenol (16.5 mg, 0.0909 mmol) was added $Ti(O^iPr)_4$ (53.3 μL, 0.182 mmol) at room temperature under argon. The reaction mixture was stirred at 90 °C for 2 h. Then, the reaction mixture was cooled to room temperature, the mixture was purified by silica-gel column chromatography (hexane/ethyl acetate = 1/0 to 1/1) to give the product **14b*cis*** (30.3 mg, 0.0281 mmol, 31%). MS (MALDI, *m*/*z*) calculated for $C_{63}H_{52}N_2O_7SiTiV$[(*M*-H)$^-$]: 1075.25, found: 1074.81.

Hetero dihemisalen complex 14c*cis*

To a toluene/ethanol (20 mL/2 mL, respectively) solution of **15a*cis*** (120 mg, 0.136 mmol) and 2-aminophenol (14.9 mg, 0.136 mmol) was added $Ti(O^iPr)_4$ (80 μL, 0.272 mmol) at room temperature under argon. The reaction mixture was stirred at 90 °C for 2 h. Then, the reaction mixture was cooled to room temperature, the mixture was purified by silica-gel column chromatography (dichloromethane/ethanol = 1/0 to 4/1) to give the product **14c*cis*** (50.6 mg, 0.0457 mmol, 37%). In the MALDI-TOF mass (negative mode) spectrum of **14c*cis***, the dehydrated dimer species (2[**14c*cis***]-H_2O) was also observed MS (MALDI, *m*/*z*) calculated for $C_{60}H_{44}N_2O_7TiV$[(*M*-H)$^-$]: 1003.21, found: 1003.07, calculated for $C_{120}H_{88}N_4O_{13}Ti_2V_2$[(2*M*-$H_2O$)$^-$]: 1990.42, found: 1990.34.

Hetero dihemisalen complex 14d*cis*

To a toluene/ethanol (20 mL/2 mL, respectively) solution of **15b*cis*** (120 mg, 0.146 mmol) and 2-aminophenol (15.9 mg, 0.146 mmol) was added $Ti(O^iPr)_4$ (85.6 μL, 0.292 mmol) at room temperature under argon. The reaction mixture was stirred at 90 °C for 2 h. Then, the reaction mixture was cooled to room temperature, the mixture was purified by silica-gel column chromatography (dichloromethane/ethanol = 1/0 to 4/1) to give the product **14d*cis*** (61.0 mg, 0.0643 mmol, 44%). In the MALDI-TOF mass (negative mode) spectrum of **14d*cis***, the dehydrated dimer species (2[**14d*cis***]-H_2O) was also observed. MS

(MALDI, *m*/*z*) calculated for $C_{56}H_{36}N_2O_7TiV[(M\text{-}H)^-]$: 947.14, found: 946.99, calculated for $C_{112}H_{72}N_4O_{13}Ti_2V_2[(2M\text{-}H_2O)^-]$: 1878.29, found: 1878.12.

General procedure for the intermolecular cross-pinacol coupling reaction

To a THF (2 mL) solution of **14d*cis*** (9.5 mg, 0.010 mmol) and activated Zn dust (129 mg, 2.0 mmol) was added Me_3SiCl (103 μL 0.80 mmol) at room temperature under argon. The reaction mixture was stirred for 10 min. Then, aliphatic aldehyde **27** (0.40 mmol) was added to the mixture. The 0.05 M THF solution (4 mL) of aromatic aldehyde **28** (0.20 mmol) was dropwise added over 1 h to the mixture, which was stirred for 10 min at room temperature. 1 M HCl was added to the mixture. The aqueous layer was extracted twice with ethyl acetate. The combined organic layer was washed with 6 M HCl and saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and evaporated. The yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene (11.2 mg, 0.0667 mmol) as an internal standard. *Syn*/*anti* of 1,2-diol **29** was determined by 2D NOESY experiment of **29*anti*** after acetonide formation as described below.

1,4-Diphenylbutane-1,2-diol (29a)

According to general procedure for the intermolecular cross-pinacol coupling reaction, 3-phenylpropanal and benzaldehyde were reductively coupled into 1,4-diphenylbutane-1,2-diol **29a** (73%).

29a*syn* : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20-7.40 (m, 7H), 7.10-7.20 (m, 3H), 4.51 (br, 1H), 3.75 (br, 1H), 2.82 (m, 1H), 2.61 (m, 1H), 1.70 (m, 1H), 1.59 (m, 1H).

29a*anti* : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20-7.40 (m, 7H), 7.10-7.20 (m, 3H), 4.69 (dd, *J* = 3.2, 3.2 Hz, 1H), 3.86 (m, 1H), 2.83 (m, 1H), 2.64 (m, 1H), 2.28 (d, *J* = 3.2 Hz, 1H), 1.87 (d, *J* = 5.2 Hz, 1H), 1.77 (m, 1H), 1.61 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 142.02, 140.38, 128.60x2, 128.51, 128.12, 126.94, 125.98, 77.27, 74.57, 33.48, 32.22 ppm; IR (KBr, cm^{-1}) 3343, 3251, 2934, 1452, 699; HRMS (FAB, *m*/*z*) calculated for $C_{16}H_{17}O_2[(M\text{-}H)^-]$: 241.1234, found: 241.1232.

1-(2-Fluorophenyl)-4-phenylbutane-1,2-diol (29b)

According to general procedure for the intermolecular cross-pinacol coupling reaction, 3-phenylpropanal and 2-fluorobenzaldehyde were reductively coupled into 1-(2-fluorophenyl)-4-phenylbutane-1,2-diol **29b** (81%).

29b$_{syn}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (dd, J = 7.6, 7.6 Hz, 1H), 7.20-7.30 (m, 3H), 7.10-7.20 (m, 4H), 7.03 (m, 1H), 4.87 (dd, J = 4.8, 4.8 Hz, 1H), 3.79 (m, 1H), 2.81 (m, 1H), 2.64 (m, 1H), 2.57 (d, J = 4.8 Hz, 1H), 2.33 (d, J = 4.8 Hz, 1H), 1.60-1.80 (m, 2H).

29b$_{anti}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (ddd, J = 7.6, 7.6, 2.0 Hz, 1H), 7.20-7.30 (m, 3H), 7.10-7.20 (m, 4H), 7.02 (ddd, J = 9.2, 7.6, 1.2 Hz, 1H), 5.09 (dd, J = 4.4, 4.4 Hz, 1H), 3.97 (m, 1H), 2.81 (m, 1H), 2.64 (m, 1H), 2.38 (d, J = 4.4 Hz, 1H), 1.92 (d, J = 5.6 Hz, 1H), 1.74 (m, 1H), 1.58 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 160.03 (d, J = 244.1 Hz), 141.92, 129.40 (d, J = 8.6 Hz), 128.58, 128.55 (d, J = 5.7 Hz), 128.52, 127.30 (d, J = 13.3 Hz), 126.02, 124.44 (d, J = 2.9 Hz), 115.34 (d, J = 21.9 Hz), 73.79, 70.91, 33.06, 32.20 ppm; IR (KBr, cm^{-1}) 3369, 3253, 2936, 1454, 1101, 1064; HRMS (FAB, m/z) calculated for $C_{16}H_{16}FO_2[(M\text{-}H)^-]$: 259.1140, found: 259.1135.

4-Phenyl-1-(2-(trifluoromethyl)phenyl)butane-1,2-diol (29c)

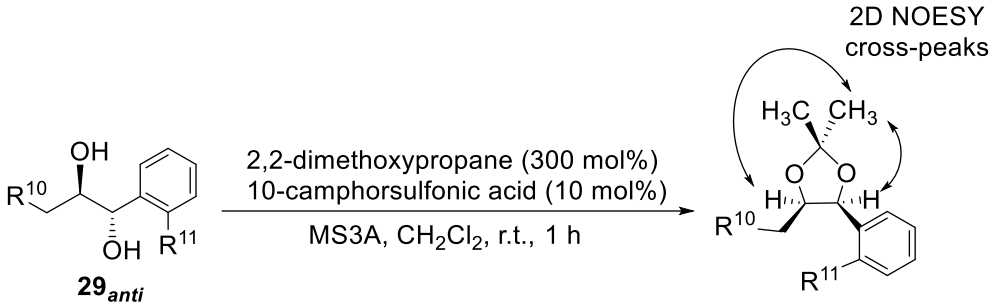
According to general procedure for the intermolecular cross-pinacol coupling reaction, 3-phenylpropanal and 2-(trifluoromethyl)-benzaldehyde were reductively coupled into 4-phenyl-1-(2-(trifluoromethyl)- phenyl)butane-1,2-diol **29c** (70%).

29c$_{syn}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 7.6 Hz, 1H), 7.62 (d, J = 7.6 Hz, 1H), 7.56 (dd, J = 7.6, 7.6 Hz, 1H), 7.40 (dd, J = 7.6, 7.6 Hz, 1H), 7.25 (dd, J = 7.2 Hz, 7.2 Hz, 2H), 7.16 (t, J = 7.2 Hz, 1H), 7.11 (d, J = 7.2 Hz, 2H), 4.96 (dd, J = 4.4, 4.4 Hz, 1H), 3.78 (m, 1H), 2.84 (m, 1H), 2.69 (d, J = 4.4 Hz, 1H), 2.63 (m, 1H), 2.37 (d, J = 4.4 Hz, 1H), 1.84 (m, 1H), 1.60 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 141.63, 140.32, 132.33, 128.49x2, 128.44, 128.10, 127.93 (q, J = 29.5 Hz), 126.02, 125.91 (q, J = 5.7 Hz), 124.38 (q, J = 272.7 Hz), 74.86, 72.39, 34.58, 32.11 ppm; IR (KBr, cm^{-1}) 3245, 2949, 1310, 1167, 1121; HRMS (FAB, m/z) calculated for $C_{17}H_{16}F_3O_2[(M\text{-}H)^-]$: 309.1108, found: 309.1105.

29c$_{anti}$: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 7.6 Hz, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.58 (dd, J = 7.6, 7.6 Hz, 1H), 7.41 (dd, J = 7.6, 7.6 Hz, 1H), 7.26 (dd, J = 7.2, 7.2

Hz, 2H), 7.17 (t, *J* = 7.2 Hz, 1H), 7.15 (d, *J* = 7.2 Hz, 2H), 5.14 (s, 1H), 3.96 (m, 1H), 2.86 (m, 1H), 2.60 (m, 1H), 2.41 (d, *J* = 3.2 Hz, 1H), 1.95 (d, *J* = 5.6 Hz, 1H), 1.80 (m, 1H), 1.74 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 141.97, 139.54, 132.26, 129.09, 128.55, 128.52, 128.15 (q, *J* = 29.6 Hz), 128.06, 126.01, 125.91 (q, *J* = 5.7 Hz), 124.46 (q, *J* = 272.7 Hz), 74.18, 72.34, 32.82, 32.21 ppm; IR (KBr, cm^{-1}) 3323, 2957, 1312, 1162, 1117; HRMS (FAB, *m*/*z*) calculated for $C_{17}H_{16}F_3O_2$[(*M*-H)$^-$]: 309.1108, found: 309.1101.

General procedure for the formation of the acetonide of 1,2-diol



To a dichloromethane (15 mL) solution were added **29*anti***, 10-camphorsulfonic acid (10 mol%), MS3A (23 g), and 2,2-dimethoxypropane (300 mol%) at room temperature under argon. The reaction mixture was stirred for 1 h. Saturated aqueous $NaHCO_3$ was added to the mixture. Then, MS3A was removed from the reaction mixture by filtration. The aqueous layer was extracted twice with dichloromethane. The combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica-gel column chromatography (hexane/ethyl acetate = 1/0 to 8/1) to give the acetonide product.

2,2-Dimethyl-4-phenethyl-5-phenyl-1,3-dioxolane

According to general procedure for the formation of the acetonide of 1,2-diol, **29a*anti*** (77.2 mg, 0.319 mmol) was converted into 2,2-dimethyl-4-phenethyl-5-phenyl-1,3-dioxolane (64.5 mg, 0.228 mmol, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ7.20-7.40 (m, 7H), 7.14 (dd, *J* = 7.2, 7.2 Hz, 1H), 7.02 (d, *J* = 7.2 Hz, 2H), 5.19 (d, *J* = 6.8 Hz, 1H), 4.35 (m, 1H), 2.64 (m, 1H), 2.44 (m, 1H), 1.66 (s, 3H), 1.46 (s, 3H), 1.45 (m, 1H), 1.23 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 141.92, 137.97, 128.61, 128.41, 128.34, 127.90, 127.09, 125.90, 108.35, 80.10, 78.26, 33.53, 32.43, 27.79, 25.36 ppm; IR (KBr, cm^{-1}) 3066, 3031,

1700, 1288, 702; HRMS (EI, *m*/*z*) calculated for $C_{19}H_{23}O_2[(M+H)^+]$: 283.1693, found: 283.1696.

4-(2-Fluorophenyl)-2,2-dimethyl-5-phenethyl-1,3-dioxolane

According to general procedure for the formation of the acetonide of 1,2-diol, **29b*anti*** (16.3 mg, 0.0626 mmol) was converted into 4-(2-fluorophenyl)-2,2-dimethyl-5-phenethyl-1,3-dioxolane (10.2 mg, 0.0340 mmol, 54%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (dd, *J* = 7.2, 7.2, 1H), 7.20-7.30 (m, 3H), 7.10-7.20 (m, 2H), 7.04 (d, *J* = 7.2 Hz, 2H), 7.00 (m, 1H), 5.50 (d, *J* = 6.8 Hz, 1H), 4.46 (m, 1H), 2.68 (m, 1H), 2.49 (m, 1H), 1.66 (s, 3H), 1.49 (s, 3H), 1.42 (m, 1H), 1.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 159.86 (d, *J* = 244.0 Hz), 141.92, 129.18 (d, *J* = 7.6 Hz), 128.58, 128.29, 128.28 (d, *J* = 3.8 Hz), 125.90, 125.44 (d, *J* = 13.4 Hz), 124.23 (d, *J* = 2.9 Hz), 114.97 (d, *J* = 21.0 Hz), 108.33, 77.58, 73.94 (d, *J* = 3.8 Hz), 33.39, 32.37, 27.81, 25.38 ppm; IR (KBr, cm^{-1}) 2958, 2930, 1728, 1261, 1057; HRMS (EI, *m*/*z*) calculated for $C_{19}H_{22}FO_2[(M+H)^+]$: 301.1598, found: 301.1607.

2,2-Dimethyl-4-phenethyl-5-(2-(trifluoromethyl)phenyl)-1,3-dioxolane

According to general procedure for the formation of the acetonide of 1,2-diol, **29c*anti*** (21.7 mg, 0.070 mmol) was converted into 2,2-dimethyl-4-phenethyl-5-(2(trifluoromethyl)phenyl)-1,3-dioxolane (4.4 mg, 0.0126 mmol, 18%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.55 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.38 (dd, *J* = 7.6, 7.6 Hz, 1H), 7.21 (dd, *J* = 7.2, 7.2 Hz, 2H), 7.13 (t, *J* = 7.2 Hz, 1H), 7.02 (d, *J* = 7.2 Hz, 2H), 5.57 (s, 1H), 4.41 (m, 1H), 2.72 (m, 1H), 2.44 (m, 1H), 1.68 (s, 3H), 1.49 (s, 3H), 1.34 (m, 1H), 1.12 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 141.81, 136.57, 131.93, 128.93, 128.52, 128.41, 127.89, 127.54 (q, *J* = 30.5 Hz), 125.92, 125.76 (q, *J* = 5.7 Hz), 124.38 (q, *J* = 272.7 Hz), 108.37, 78.42, 75.67, 33.82, 32.71, 27.63, 25.05 ppm; IR (KBr, cm^{-1}) 2931, 1314, 1162, 1123; HRMS (EI, *m*/*z*) calculated for $C_{20}H_{22}F_3O_2[(M+H)^+]$: 351.1566, found: 351.1569.

3-4. Reference and Notes

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2. The coodination geometry is not clear at this stage. Ti(IV)-O-V(V) linked hetero complex and/or Ti(IV)-OH complex are described below: a) R. Z. Khaliullin, A. T. Bell, *J. Phys. Chem. B* **2002**, *106*, 7832-7838; b) F. Caruso, L. Massa, A. Gindulyte, C. Pettinari, F. Marchetti, R. Pettinari, M. Ricciutelli, J. Costamagna, J. C. Canales, J. Tanski, M. Rossi, *Eur. J. Inorg. Chem.* **2003**, *17*, 3221-3232.
3. In the MALDI-TOF mass (negative mode) spectrum of the hetero dinuclear complexes without bulky substituent on titanium side such as **14c**$_{cis}$ and **14d**$_{cis}$, the corresponding dimer species were also observed, see experimental section for details.
4. *Syn* and *anti* were determined by the 2D-NOESY experiments after acetonide formation of **29**$_{anti}$, see experimental section for details.
5. Preparation of mononuclear vanadium(V) hemisalen complex is described below: M. J. Clague, N. L. Keder, A. Butler, *Inorg. Chem.* **1993**, *32*, 4754-4761.
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7. The chemical sifts of ^{1}H NMR spectra for the cross-coupling products **29d** and **29e** were identical with the reported ones: a) T. Kawakami, I. Shibata, A. Baba, *J. Org. Chem.* **1996**, *61*, 82-87; b) G. Bellucci, C. Chiappe, A. Cordoni, *Tetrahedron: Asymmetry* **1996**, *7*, 197-202; c) P. Jiao, M. Kawasaki, H. Yamamoto, *Angew. Chem. Int. Ed.* **2009**, *48*, 3333-3336.

Conclusion

In this dissertation, the catalytic system using dinuclear complex for cross-pinacol coupling reaction was investigated. The reductive coupling reactions of carbonyl compounds provide an important method to synthesize 1,2-diols directly. Although catalytic and/or diastereoselective methods for homo-coupling have been developed, the intermolecular cross-pinacol coupling reaction has not been mature yet. The reported methods so far strongly depends on the substrate control. Therefore, a reductant control strategy is desired and a challenging issue for the cross-pinacol coupling reaction.

In this work, the author envisioned that the dinuclear complex, in which two discriminated active sites are three-dimensionally regulated through a rigid scaffold, would lead to multifunctional catalysts based on the selective activation of two different aldehydes.

In chapter 1, the bis-biphenyl ligand on the hexaaryl scaffold for the dinuclear complex was designed and synthesized. The formation of dinuclear titanium complex permitted preliminary investigation on the cross-pinacol coupling reaction utilizing step-by-step activation of two different aromatic aldehydes.

In chapter 2, the dinuclear vanadium(V) dihemisalen complexes were designed and synthesized. The desymmetrized vanadium catalyst was effective for the both cross- and diastereo-selectivity in the coupling reaction.

In chapter 3, the hetero dihemisalen complexes with vanadium and titanium were synthesized. Using such a novel hetero dinuclear catalyst, the intermolecular cross-pinacol coupling reactios between aliphatic and aromatic aldehydes have been demonstrated. The hetero dinuclear catalyst was shown to be effective for the cross-selective coupling reaction.

The reductive cross-coupled method offers a direct approach to synthesize hetero-diols Furthermore, such a dinuclear complexes is envisioned to be applied to other reactions needed dual activation by metals.

List of Publications

1. Synthesis of Three-dimensionally Arranged Bis-biphenol Ligand on Hexaaryl Benzene Scaffold and Its Application for Cross-Pinacol Coupling Reaction
   Toru Amaya, Akihiro Miyasaka, and Toshikazu Hirao
   Tetrahedron Lett. **2011**, *52*, 4567-4569.

2. Design and Synthesis of Dinuclear Hemisalen Complex on Hexaarylbenzene Scaffold
   Akihiro Miyasaka, Toru Amaya, and Toshikazu Hirao
   Tetrahedron Lett. **2012**, *53*, 5589-5592.

3. Synthesis of Hetero Dinuclear Hemisalen Complex on Hexaarylbenzene Scaffold and its Application for Cross-Pinacol Coupling Reaction
   Akihiro Miyasaka, Toru Amaya, and Toshikazu Hirao
   Chem. Eur. J. in press.

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