Design and Synthesis of Ferrocenylmethylphosphines for Transition Metal Catalysis: From highly Active Cross-Coupling Catalysts to Highly Efficient Addition Reaction Catalysts

by

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A dissertation submitted to the Graduate Faculty in Chemistry in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York

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Abstract

DESIGN AND SYNTHESIS OF FERROCENYLMETHYLPHOSPHINES FOR TRANSITION METAL CATALYSIS: FROM HIGHLY ACTIVE CROSS-COUPLING CATALYSTS TO HIGHLY EFFICIENT ADDITION REACTION CATALYSTS

by

Yong Lu

Advisor: Professor Qiao-Sheng Hu

A series of phosphine-containing ligands have been developed and employed in palladium or nickel-catalyzed bond forming reactions. My research project spans from the design and synthesis of phosphine-containing macromolecule ligands and their application in palladium and nickel–catalyzed Suzuki cross-coupling reactions to the development of efficient palladacycle catalysts for addition reactions.

There are three aspects of my Ph. D. thesis research projects. Firstly, a family of ferrocenylmethylphosphine-containing dendrimers were synthesized and applied as ligands in palladium-catalyzed Suzuki cross-coupling of phenylboronic acids with aryl halides; Secondly, design and synthesis of bisphosphine-containing polymeric ligands and their application as ligands for nickel and palladium-catalyzed cross coupling reactions of arylboronic acids with aryl halides, arylboronic acids with arylboronic acids, and the reactions of activated tosylates with arylboronic acids; The last part involves a study on palladacycles as catalysts for addition reactions of arylboronic acids with α,β-unsaturated ketones and aromatic aldehydes.

Acknowledgements

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Chapter 1 Introduction

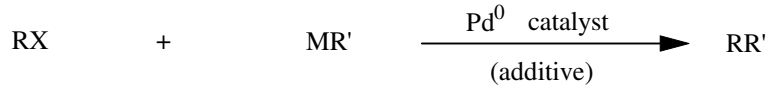
1.1 Overview of Transition Metal-Catalyzed Bond Forming Reactions

Transition metal-catalyzed carbon-carbon and carbon-heteroatom bond forming reactions are among the most powerful transformations in organic synthesis.[1, 2] They have been extensively used for the synthesis of a wide variety of organic compounds ranging from natural products, pharmaceuticals to other materials. Palladium catalysts have attracted much attention and are regarded as one type of the most powerful catalysts for those transformations.[3] Their popularity stems in part from their high tolerance of various functional groups, which allows them to be employed in the synthesis of highly complex molecules.[4]

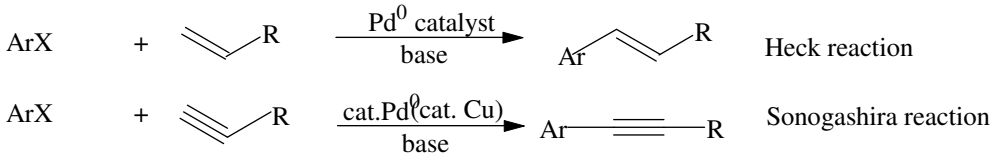
The palladium-catalyzed cross-coupling reactions of aryl and vinyl halides/triflates with organometallic reagents, e. g., the Kumada coupling, the Stille coupling, the Suzuki Coupling, etc., serve as a powerful tool for the construction of carbon-carbon bonds and carbon-heteroatom bonds (Scheme 1.1).[5] Organometallic reagents can be almost any type. For example, they can be alkyl, aryl, vinyl or alkynyl organometallic reagents. Most magnesium, tin and zinc reagents are reactive enough to directly serve as coupling partners without the need for an additive; while boron and silicon reagents, on the other hand, are usually much less reactive in the absence of an activator. So, the Suzuki and Hiyama cross-couplings are typically carried out in the presence of additives. The most common additives for the Suzuki cross-coupling are strong bases. And for Hiyama cross-coupling, TBAB(tetra-n-

butylammonium bromide) is the routine additive. The role of the additives is to form a higher valent, more reactive transmetalate complex.[3]

Scheme 1.1 Palladium-Catalyzed Cross-Coupling Reactions



R, R' = aryl	M = B	Suzuki
vinyl	Sn	Stille
X = Cl	Si	Hiyama
Br	Zn	Negishi
I	Mg	Kumada
OTf	etc.	
OTs		

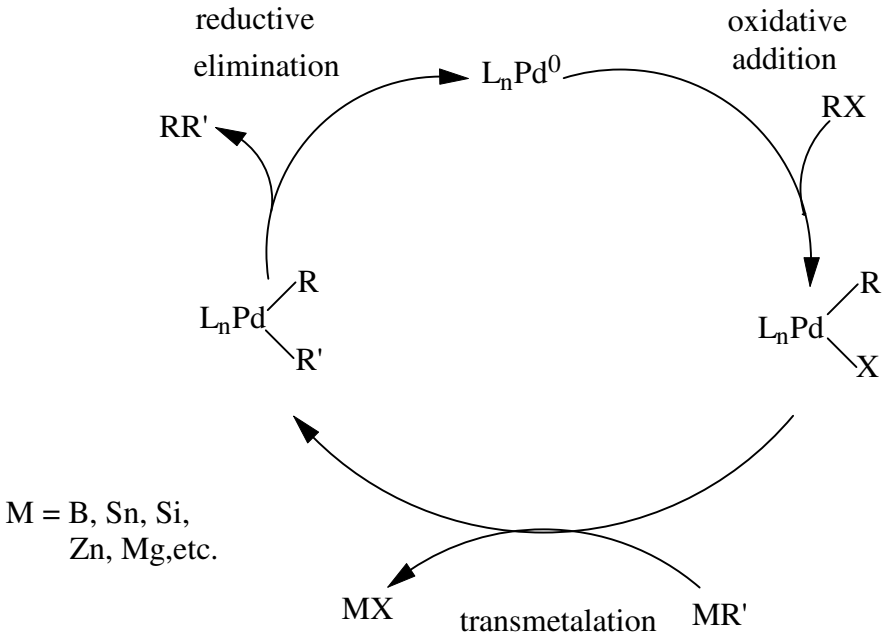


Among palladium-catalyzed cross-coupling reactions, the Suzuki cross-coupling reactions of aryl/vinyl halides/triflates with organoboronic acids have attracted a lot of attention. Their popularity is due to a variety of factors. First of all, a large number of organoboronic acids are commercially available; secondly, they are nontoxic and stable to heat, air and moisture; furthermore, the boron-containing byproducts of the Suzuki cross-coupling reactions can be readily separated from the desired compound.

The general catalytic cycle of palladium-catalyzed Suzuki cross-coupling reactions, which involves oxidative addition, transmetalation and reductive

elimination sequence, is shown in scheme 1.2. First, an organo halide undergoes oxidative addition with a palladium(0) catalyst to form a palladium (II) complex; secondly, transmetalation of an organoboronic acid with the palladium (II) complex to form a diorgano palladium (II) complex; finally, reductive elimination of the diorgano palladium (II) complex yields the coupling product and regenerates the palladium(0) catalyst.

Scheme 1.2 General Mechanism for Palladium-Catalyzed Cross-Coupling Reactions

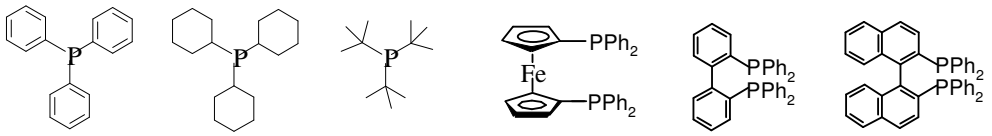


A very wide range of palladium(0) catalysts or precursors can be used for cross-coupling reactions. $Pd(PPh_3)_4$, $Pd_2(dba)_3$ and $Pd(dba)_2$ are most commonly used palladium (0) catalysts. The initial Pd^0 catalyst can also be generated *in situ* from a palladium (II) precursor to enter the catalytic cycle, since palladium (II) species such as $Pd(OAc)_2$, $PdCl_2(PPh_3)_2$ are stable in air and can be more easily handled. Oxidative addition is often the rate-determining step in the catalytic cycle. The relative

reactivity of aryl/alkenyl halides decreases in the order of I > OTf > Br » Cl. Before 1998, organic iodides, bromides and triflates are most common substrates in almost all of the palladium-catalyzed cross-coupling reactions. Although chlorides are the most useful substrates due to their lower cost and the wider diversity of available compounds, organic chlorides were rarely used as substrates in palladium-catalyzed cross-coupling reactions.[3] Chlorides were generally not reactive and could not oxidatively add to palladium (0) catalysts under the conditions employed to react with bromides, iodides, and triflates. The low reactivity of chlorides is usually due to the relative higher dissociation energy of C-Cl bond (bond dissociation energies for Ph-X: Cl: 96 kcal mol^{-1}; Br: 81 kcal mol^{-1}; I: 64 kcal mol^{-1}), which makes aryl chlorides reluctant to be oxidatively added to palladium (0) centers, which is the critical initial step in palladium-catalyzed coupling reactions.[6]

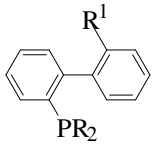
Generally, the transmetalation between organopalladium (II) halides and organoboron compound does not occur readily due to the low nucleophilicity of organic group on boron atom such as OH^-. However, the transmetalation step could take place in the presence of bases such as potassium phosphate, cesium carbonate, potassium fluoride and potassium carbonate. The general understanding is that the nucleophilicity of an organic group on the boron atom is enhanced by quaternization of the boron with negatively charged bases.[7a,7b] Although there is no direct evidence to show that the boronate anions, such as $RB(OH)_3^-$, can effect the transmetalation step, it is quite reasonable to assume a similar effect of bases for the transmetalation of organoboronic acids.[7c]

There are numerous ligands reported for transition metal-catalyzed cross-coupling reactions. According to the structure of the ligands, there are monodentate and bidentate ones; According to the elements coordinated with the transition metals, there are phosphine-containing ligands, carbon-based ligands and so on; according to the size of the ligands, there are monomeric ligands and polymeric ligands, which are also called macromolecule ligands. PPh_3, PCy_3, $P(t\text{-}Bu)_3$ are typical monodentate ligands; and DPPF, BIHEP, BINAP are typical bidentate ligands.



PPh_3 **PCy_3** **$P(t\text{-}Bu)_3$** **DPPF** **BIHEP** **BINAP**

Prior to 1998, there are no reports for effective palladium-catalyzed Suzuki reactions of electron-neutral or electron-rich aryl chlorides. Traditional palladium/triarylphosphine catalyst systems were only active for activated aryl chlorides. In 1998, the groups of Buchwald and Fu developed catalyst systems that could couple a wide range of aryl chlorides in good yield. Buchwald reported that aminophosphane **1** and biphenyl ligands **2** and **3** are very effective ligands for palladium-catalyzed Suzuki reactions of arylchlorides.[8,9]



R = Cy, R^1 = NMe_2 **1**

R = Cy, R^1 = H **2**

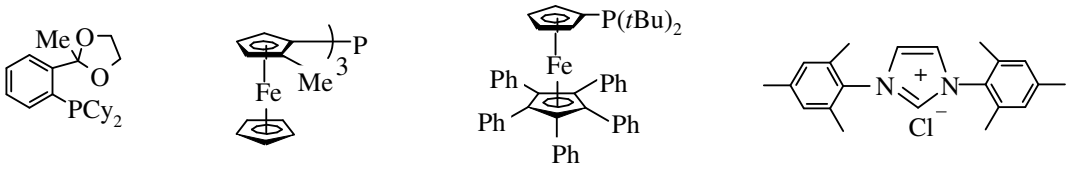
R = *t* Bu, R^1 = H **3**

Fu showed that $Pd/P(t\text{Bu})_3$ is a highly active catalyst for Suzuki cross couplings of activated aryl chloride at room temperature.[10a] Since the original report, $Pd/P(t\text{Bu})_3$ has been applied to Suzuki couplings of a wide range of activated and unactivated aryl and heteroaryl chlorides.[10] The use of 1:1 ratio of $P(t\text{Bu})_3$: Pd is important for obtaining high reactivity in room temperature Suzuki reactions of aryl chlorides. The

mechanism investigation showed that 12-electron Pd(*t*-Bu_3P) may play a key role in Pd/P(*t*Bu)$_3$-catalyzed couplings. Due to the electron-richness of P(*t*Bu)$_3$, aryl chloride can be rapidly oxidatively added to the (monophosphine)palladium(0) complex. And the steric demand of P(*t*Bu)$_3$ facilitates the reductive elimination to release the 12-electron (monophosphine)palladium(0) complex after the transmetalation step. The combination of the electron richness and steric hindrance make P(*t*Bu)$_3$ a particularly effective ligand for palladium-catalyzed cross-couplings of aryl chlorides, which were general inert toward other catalyst systems except Buchwald's biarylphosphines.

Later on, several groups have continuously employed bulky, electron-rich phosphines and *N*-heterocyclic carbenes as ligands for Suzuki cross-coupling reactions of deactivated aryl chlorides under mild conditions. Four widely used, highly active ligands **4-7** for the palladium-catalyzed cross-coupling reaction of aryl chlorides are listed in Scheme 1.3.

Scheme 1.3 More examples of electron rich, bulky ligands for cross-coupling reactions



4 **5** **6** **7**

Guram have determined that dialkylarylphosphanes **4** are effective for the cross-coupling of deactivated aryl chlorides with arylboronic acids at high temperature;[11] Pickett and Richards demonstrated that Pd/tris(2-methylferrocenyl)phosphane **5** can achieve Suzuki cross-couplings of unactivated aryl chlorides in modest to good yield.[12] Further, Hartwig realized the first room temperature C-O bond forming reactions of aryl chlorides with the combination of

$Pd(dba)_2$ and $Ph_5FcP(tBu)_2$ **6**.[13] Besides the phosphorus ligands, carbon-based ligands, specifically, *N*-heterocyclic carbenes, are also effective for the Suzuki coupling of unactivated aryl chlorides. Herrman et al. reported that palladium adducts of 1, 3-bis(2, 4, 6-trimethylphenyl)imidazol-2-ylidene (IMes) **7** can serve the purpose.[14]

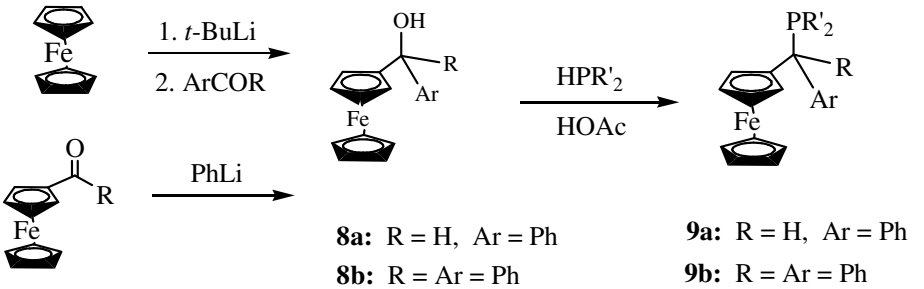
1.2 Development of Ferrocenylmethyl-Based Phosphines as Unique Ligands

In our group, we have been interested in developing highly efficient ligands for transition metal-catalyzed reactions. We are particularly interested in developing a system that will allow us to access a family of monophosphines including optically active ones.

Ferrocenylmethylphosphines have been selected for our study based on the following considerations: (a) ferrocenylmethyl alcohols including optically active forms are readily available, (b) the unique retentive S_N1 reaction at the α-position would allow the easy access of a family of ferrocenylmethylphosphines including optically active ones,[15] (c) the steric and electronic properties of ferrocenylmethylphosphines can be systematically tuned, and (d) their polymeric forms are expected to be readily accessible.

A protocol that directly converts ferrocenylmethyl alcohols to ferrocenylmethylphosphines has been developed in our group.[16,17] This protocol allowed us efficiently synthesize a family of ferrocenylmethylphosphines from readily available ferrocenylmethyl alcohols under mild conditions.[18,19] As a practicing project, I was involved in the synthesis of ferrocenylmethyl alcohol by the reaction of ferrocenecarboxaldehyde and ferrocenyl ketones with lithium reagents. This route gave excellent yields. For example, reaction of ferrocenecarboxaldehyde or benzoylferrocene with phenyllithium generated **8a** and **8b** in 91% and 92% yield (Scheme 1.5).

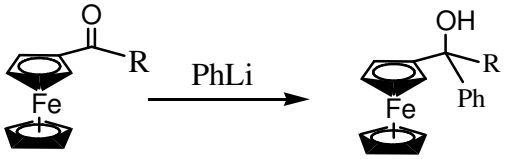
Scheme 1.4 Different Methods to Synthesize Ferrocenylmethylphosphines from Ferrocenylmethyl Alcohols



8a: R = H, Ar = Ph
8b: R = Ar = Ph
8c: R = H, Ar = 1-Naphthyl
8d: R = H, Ar = *o*-MeOPh

9a: R = H, Ar = Ph
9b: R = Ar = Ph
9c: R = H, Ar = 1-Naphthyl
9d: R = H, Ar = *o*-MeOPh
9e: R = H, Ar = Ph, R' = *t*-Bu

Scheme 1.5 Synthesis of Ferrocenylmethyl Alcohols from Ferrocenecarboxaldehyde and Ferrocenyl Ketones

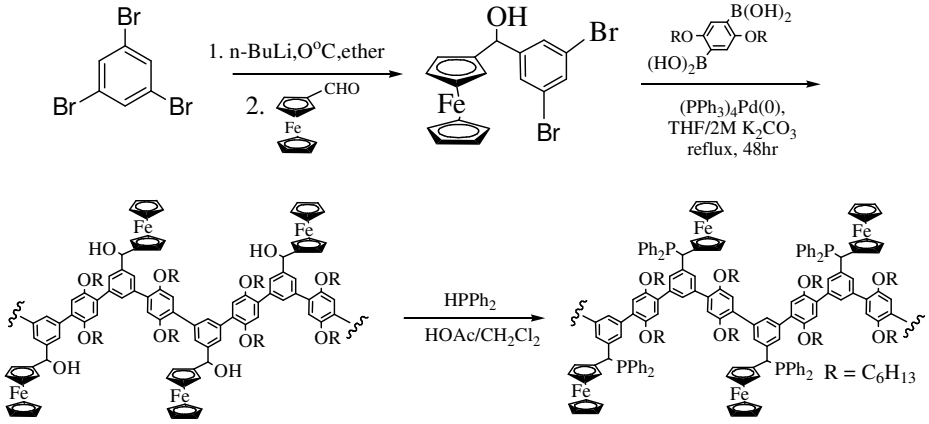


R= H or Ph

These readily available ferrocenylmethylphosphines have been employed to catalyze the room temperature Suzuki cross-coupling reactions of aryl halides with arylboronic acids.[21] It was found that these ferrocenylmethylphosphines can smoothly catalyze the coupling reaction between aryl bromides including electron-rich ones and arylboronic acid.

Based on the hypothesis that using rigid and sterically regular monophosphine-containing polymers as ligands could be a general approach to 12-electron monophosphine palladium(0) complexes which are difficult or impossible to be accessed by using monomeric monophosphines or flexible, sterically irregular monophosphine-containing polymers,[26] We designed and synthesized monophosphine-containing polymer **10** (Scheme 1.6).

Scheme 1.6 Synthesis of Ferrocenylmethylphosphine-Containing Polymer **10**



13 **10**

The application of **10** as ligands for room temperature Pd(0)-catalyzed Suzuki cross-coupling reaction of aryl chlorides with arylboronic acids showed rigid and sterically ferrocenylmethylphosphine-containing polymers indeed can serve as unique ligands to access 12-electron monophosphine palladium(0) complexes. However, high catalyst loading (5%) was still needed for the reaction. The ^{31}P NMR of **10**/Pd(0) complex study has been carried out, unfortunately, **10**/Pd(0) complexes are insoluble in THF-d_8. Such high catalyst loading was thus speculated to be due to several possible reasons: (a) formation of 14-electron $(R_3P)_2Pd(0)$ complexes, especially through interchain coordination of monophosphine moieties; (b) the formation of

insoluble **10/**Pd(0) complexes because it will limit the formation of (monophosphine)palladium(0) complexes and make it more difficult to access these catalytically active sites. (c) decomposition of 12-electron (R_3P)Pd(0) complexes, and (d) decomposition of the oxidative addition adduct (R_3P)ArPd(II)Cl complexes.

My dissertation work was initially aimed to address these reasons in the hope to develop cross-coupling catalyst systems that could be more efficient than Pd(0)**/10** catalyst system. The results are described in Chapters 2 and 3. Our interest in developing better catalysts for the addition reaction of arylboronic acids with carbonyl-containing compounds, and our understanding of the Pd(0)**/10** catalyst decomposition led us to the development and use of palladacycles as highly efficient addition catalysts. Our results of this part are summarized in Chapter 4.

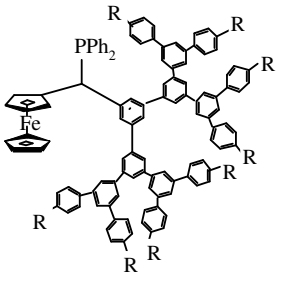
Chapter 2 Synthesis of Ferrocenylmethylphosphine-Containing Dendrimers

Dendrimers are well-defined, tree-like macromolecules. They generally emanate from a core and ramify outwards with each subsequent branching unit, also called each generation.[1] There are two fundamentally different construction concepts: the divergent method and the convergent method. With the divergent method, one branch unit after another will be successively attached to the core molecule; While in the convergent method, it is opposite to the divergent method, the skeleton is constructed stepwise starting from the end groups towards the inside and is finally react with a core molecule to produce the target dendrimer.

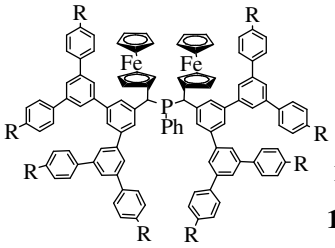
Dendrimer chemistry has become extremely popular in the past decades, and several potential applications of functionalized dendrimers, including catalysis have been explored.[2] They have been used to catalyze various reactions such as the Heck reaction, hydrogenation reaction, oxidation reaction, reduction reaction and so on. According to the position of the catalytic active sites, there are periphery-functionalized, core-functionalized and focal point-functionalized systems. The interest in developing dendrimer catalysts is related to the fact that functionalized dendrimers potentially can uniquely have the advantages of both homogeneous and heterogeneous catalytic systems. Basically, dendritic catalysts can have the activity and selectivity of a conventional homogeneous catalyst while they can be recovered from the reaction medium easily. Other advantages of dendritic catalysts include the ability to fine-tune the catalytic centers by ligand design.[3]

In our effort to develop highly active transition metal catalysts for carbon-carbon and carbon-heteroatom bond formations, we have designed and synthesized ferrocenylmethylphosphine-containing polymers as unique ligands to access 12-electron (R_3P)Pd(0) complexes. Despite polymer **10**/Pd(0) exhibited highly activity catalytic activity, 5% catalyst loading are needed.[4] We speculated such high catalyst loading requirement could be due to reasons including (a) interchain ligand coordination, (b) intrachain ligand coordination, (c) insolubility of the formed catalyst system, (d) instability of 12-electron (R_3P)Pd(0) complexes and (e) instability of initially formed Ar(R_3P)Pd(II)Cl complexes. We envisioned that if ferrocenylmethylphoshines were incorporated in the core of the dendrimers, the formed dendrimers such as **11** and **12** would have very large side arms, and they could be very soluble, and could avoid interchain/intrachain crosslinking. The tree-like monodendron arms might provide the steric shielding effects as exhibited by the reported bulky monophosphines and N-heterocyclic carbenes. Thus the bulky monodendron arms will prevent two monophosphine moieties to coordinate to a same transition metal species such as palladium, therefore leading to the formation of highly active, coordinatively unsaturated 12 electron monophosphine palladium(0) complexes. Furthermore, the dendrimer structure could efficiently avoid the crosslinking problem since it is more bulky than our previous monophosphine containing polymer ligand **10**. Therefore, if the high catalyst loading for polymer **10**/Pd(0) complexes were due to these reasons, dendrimer/Pd(0) complexes should be more active catalyst system than polymer **10**/Pd(0) complexes. In addition, the macromolecular nature of dendrimers might also allow the easy recovery and reuse of

the ligands. We thus decided to prepare ferrocenylmethylphosphine-containing dendrimers such as **11** and **12** and study their catalytic behavior in the hope to gain better understanding of polymer**10**/Pd(0) catalyst system and to develop more efficient access to highly active 12-electron-complexes.



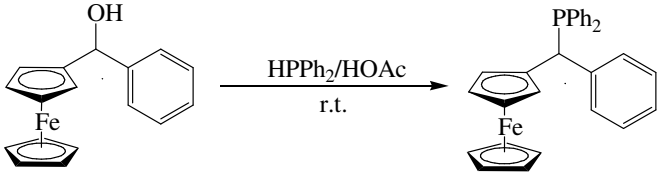
11



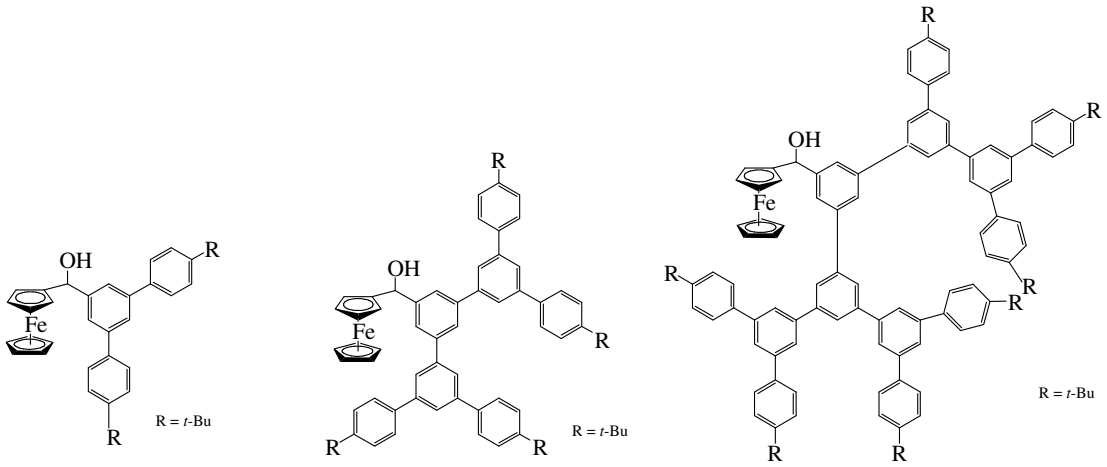
12

Previously, we reported the direct conversion of ferrocenylmethyl alcohols to ferrocenylmethylphosphines under mild conditions (Scheme 2.1).[5] The process has been successfully applied for the synthesis of a ferrocenylmethyl phosphine-containing polymer **10** from ferrocenylmethyl alcohol-containing polymer **13** (Scheme 1.6)[4]. We envisioned that ferrocenylmethyl alcohol-containing dendrimers such as **14-16** should also undergo similar conversions to give corresponding ferrocenylmethylphosphine -containing dendrimers.

Scheme 2.1 Direct Conversion of Ferrocenylmethyl Alcohol to Monophosphine



8a **9a**

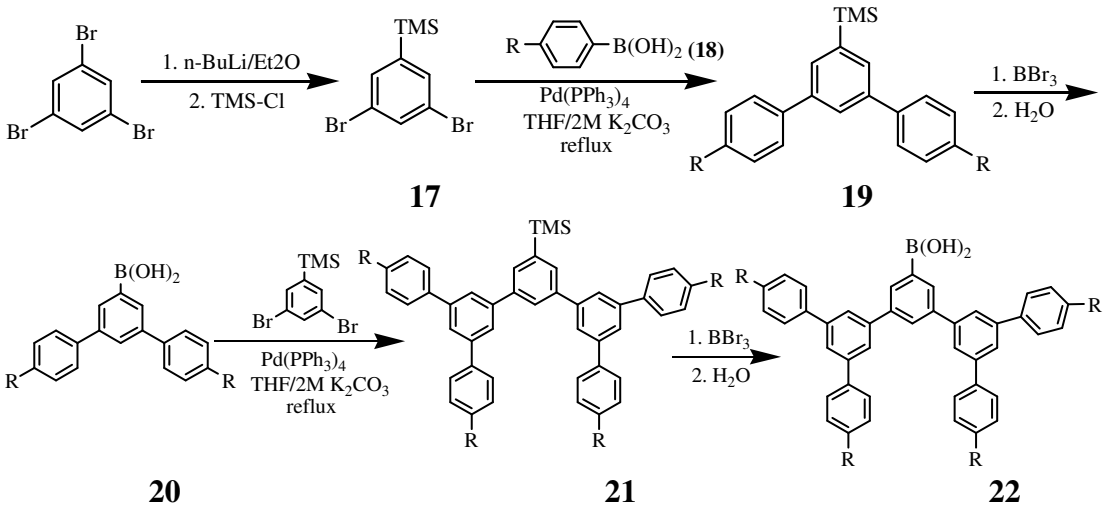


14 **15** **16**

The convergent method was used to synthesize ferrocenylmethyl alcohol-containing dendrimers **14-16**.[33] The required monodendron boronic acids were prepared by following a reported method.[6] As shown in Scheme 2.2, reaction of 1, 3, 5-tribromobenzene with *n*-BuLi followed by treatment with TMSCl yielded dibromide **17**. THF was initially used as solvent. After two trials, we found that THF was not a good solvent for this reaction because no desired product was obtained. We then used diethyl ether (Et_2O) as solvent as reported by Miller.[16] When 1:1 ratio of 1,3,5-tribromo-benzene and *n*-BuLi was used, the desired product was obtained in 60% yield along with unreacted starting material and significant amounts of debrominated product 1, 3-dibromobenzene. The formation of debrominated 1,3-dibromobenzene indicates that 1, 3-dibromophenyl Lithium reacted with a proton (H^+) source, either moisture or HCl from chlorotrimethylsilane (Me_3SiCl). We reasoned that increased amount of *n*-BuLi may help to increase the yield of our desired product. We hence tried the reaction with different ratio of 1, 3, 5-tribromobenzene to *n*-BuLi. We found that 1:1.4 ratio of 1, 3, 5-tribromobenzene to *n*-BuLi gave acceptable result.

The desired product was observed in >90% yield from ^{1}H NMR. Purification of the product by vacuum distillation gave **14** in 90% yield.

Scheme 2.2 Preparation of Dendronized Boronic Acids

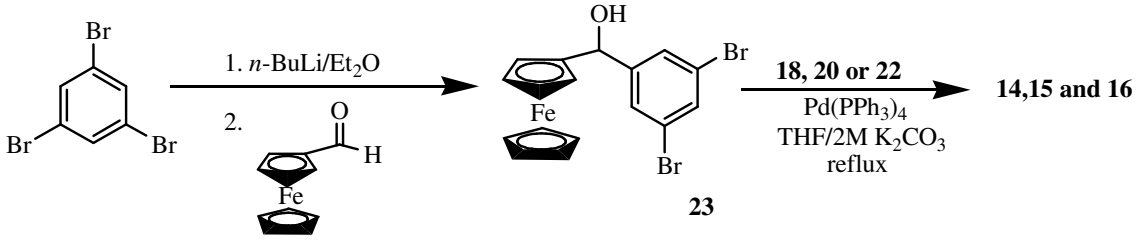


In the presence of a catalytic amount of $Pd(PPh_3)_4$, **17** was cross-coupled with *p-tert*-butylphenylboronic acid **18** in THF/2M K_2CO_3 to give **19**. Conversion of **19** to **20** was carried out by reaction of **19** with BBr_3 in CH_2Cl_2 followed by hydrolysis (KOH aqueous solution) at 0^oC[15]. **20** was obtained as a white solid in 72% yield after purification by flash chromatography.

Palladium(0)-catalyzed cross-coupling reaction of **20** with **17** generated **21**. **21** was converted to the second generation boronic acid **22** by the procedure similar to the conversion of **19** to **20**. By using the standard Suzuki cross coupling condition, ferrocenylmethyl alcohol containing dendrimers **14**-**16** were synthesized by coupling dibromoferrocenyl alcohol **23**, which was prepared from 1,3,5-tribromobenzene and ferrocenecarboaldehyde,[4] with monodendron boronic acids **18**, **20** and **22**, respectively (Scheme 2.3). The yield for **14**, **15** and **16** were 98%, 63% and 50% respectively. The decreasing yields from the zero-generation **14** to the second-

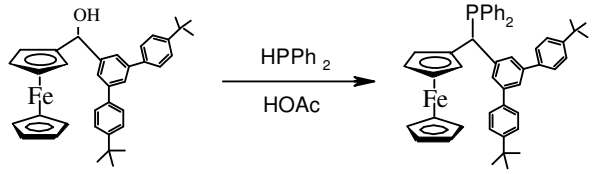
generation **16** suggested that higher generation dendronized boronic acids coupled much less efficiently with dibromide **23** than the zero-generation boronic acid **18**. Dendrimers **14**-**16** are yellow solids and soluble in common organic solvents such as CH_2Cl_2, THF and toluene.

Scheme 2.3 Synthesis of Monophosphine-Containing Dendrimers

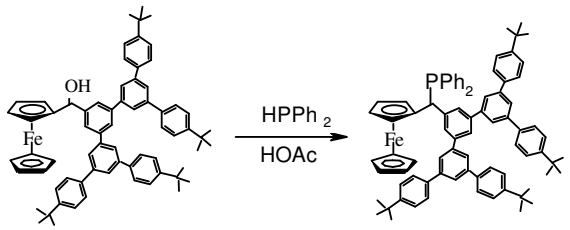


We then synthesized monophosphine-containing dendrimers (**24, 25, and 11**). Conversion of 0 and first generation ferrocenylmethyl alcohol dendrimers **14** and **15** to their diphenylphosphine-containing dendrimers **24** and **25** were carried out in HOAc (Scheme 2.4). **24** and **25** are soluble in common organic solvents such as CH_2Cl_2, THF, toluene and $CHCl_3$. The yields of this reaction were 43%, 58% respectively.

Scheme 2.4 Synthesis of 0 and 1st Generation Monophosphine-Containing Dendrimers



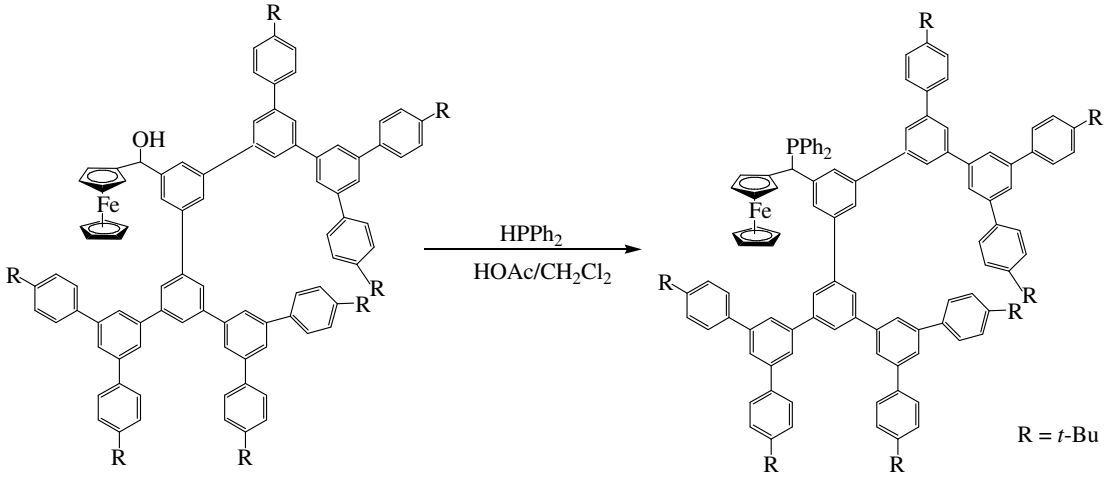
24



25

The second generation dendrimer **16** has been converted to its monophosphine analog **11** by reaction with $HPPh_2$ in acetic acid (Scheme 2.5). Excess $HPPh_2$ was added to a solution of **16** in HOAc at room temperature. The reaction mixture was stirred at room temperature overnight. Evaporation of solvents yielded a yellow solid. The solid was purified by washing with degassed methanol. **11** is a yellow solid and soluble in CH_2Cl_2, THF, and toluene. ^1H NMR spectrum showed that the conversion of –OH to $–PPh_2$ was almost complete since it only has very small amount of the peak of the methylene group that connects to the OH group at 5.66 ppm and the OH peaks at 2.58 ppm. ^{31}P NMR in $CDCl_3$ (H_3PO_4 as standard) shows one peak at 5.88 ppm and also one minor peak at 23.48 ppm was observed, which is corresponding to oxidized phosphine.

Scheme 2.5 Synthesis of Second Generation Ferrocenylmethyl-Containing Dendrimer **11**



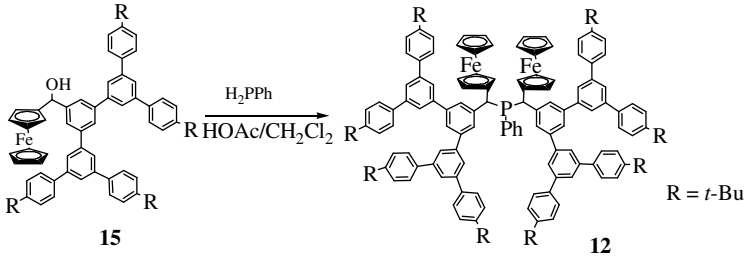
11

The low yields of this type of reaction were probably due to the fact that the products could be somewhat dissolved in methanol and lost during methanol wash. And for the three generation monophosphine containing dendrimers, it is difficult to get pure compounds since they are easily to be oxidized during solution and part of the products was oxidized during workup. Furthermore, pure spectra were not obtained maybe because the samples were partially oxidized in NMR tubes during NMR collecting.

The synthesis of more electron-rich monophosphine containing dendrimer **12** was carried out by reaction of ferrocenylmethyl alcohol **15** with H_2PPh in HOAc at room temperature (Scheme 2.6). H_2PPh was added to a solution of **15** in HOAc under N_2 and the mixture was stirred overnight at room temperature. Yellow solid was precipitated out from the reaction mixture. The mixture was filtered and the product was purified by washing with degassed methanol. ^1H NMR spectrum showed that the conversion of –OH to $–PPh_2$ was almost complete since it only has very small amount of the peak of the methylene group that connects to the OH group at 5.62 ppm and the

OH peaks at 2.60 ppm. ^{31}P NMR in $CDCl_3$ (H_3PO_4 as standard) shows one major peak at 15.43 ppm and one minor peak at 18.99 ppm.

Scheme 2.6 Synthesis of More Electron-Rich Ferrocenylmethyl-Containing Dendrimer **12**



After obtaining dendrimers **11**, **12**, **24** and **25,** we have employed them as ligands for palladium-catalyzed Suzuki coupling reactions of aryl halides with phenylboronic acid was examined. Our results are shown in Table 2.1

Table 2.1 Palladium-Catalyzed Cross-Couplings of Aryl Halides with Phenylboronic Acids

Ar-X + $(HO)_2$B-Ar' —(ligand/Pd(II), KF, THF,r.t.)→ Ar-Ar'

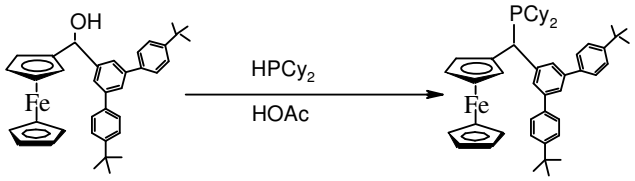
Entry	Ar-X	Ar'-B$(OH)_2$	Ligands/Pd(II)	time(hrs)	Conversion(%)
1			3mol%**11** /$Pd_2(dba)_3$ (2:1)	24	53
2			2mol%**11** /$Pd_2(dba)_3$ (2:1)	24	45
3			2mol%**12** /$Pd(OAc)_2$ (1:1)	24	0
4	MeO- 		2mol%**24** /$Pd_2(dba)_3$ (2:1)	24	77
5	MeO- 		2mol%**25** /$Pd_2(dba)_3$ (2:1)	24	0
6	MeO- 		2mol%**24** /$Pd(OAc)_2$ (1:1)	24	78
7	MeO- 		2mol%**25** /$Pd(OAc)_2$ (1:1)	24	39
8	MeO- 		2mol%**11** /$Pd(OAc)_2$ (1:1)	24	0
9	MeO- 		2mol%**12** /$Pd(OAc)_2$ (1:1)	24	0
10	MeO- 		2mol%**24** /$Pd(OAc)_2$ (1:1)	24	0
11	MeO-		2mol%**25** /$Pd(OAc)_2$ (1:1)	24	0

As shown in Table 2.1, our study revealed that **11** is an active ligand for Pd(0)-catalyzed cross-coupling reactions of aryl bromides, but not an active one for less reactive aryl chloride. Catalyst derived from Pd(II) and **12**, which is more bulkier and more electron rich than **11**, failed to catalyze the cross-coupling reactions of both aryl bromides and chlorides, suggesting the high catalyst loading in polymer**10**/Pd(0) systems was likely due to the instability of 12-electron $(R_3P)Pd(0)$ complexes or $Ar(R_3P)Pd(II)X$ complexes, rather than due to the inter/intra chain ligand coordination to form 14-electron complexes or the insolubility of the catalysts.

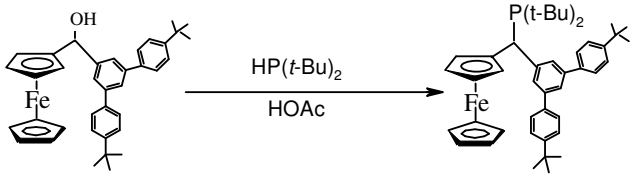
To confirm that 12-electron $(R_3P)Pd(0)$ complexes could indeed be formed from this dendrimer system, we synthesized monophosphine-containing dendrimers **26** and **27** which contain more electron rich dicyclohexylphosphine moiety(dendrimer **26**) and di-*tert*- butylphosphine moiety(dendrimer **27**).

Ferrocenylmethyl alcohol dendrimer **14** was converted to dicylohexylphosphine-containing dendrimer **26** by reacting **14** with dicyclohexyl phosphine in acetic acid at room temperature (Scheme 2.7). This reaction was much faster than the one with diphenylphosphine and was completed in 3 hours based on TLC. But problems of purification were also met during workup.

Scheme 2.7 Synthesis of More Electron-Rich Ferrocenylmethyl-Containing Dendrimers **26** and **27**



26

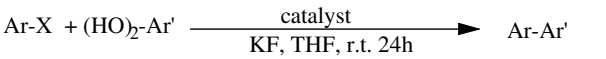


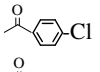
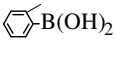
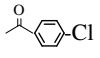
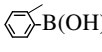
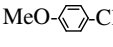
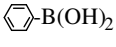
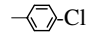
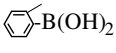
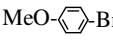
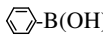
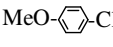
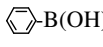
27

With the similar method as synthesis of **26**, ferrocenylmethyl alcohol dendrimer **14** was converted to its corresponding di-*tert*-butylphosphine containing dendrimer **27** by reacting of **14** with di-*tert*-butylphosphine in acetic acid at room temperature. This reaction gave yellow solid after purification by methanol and the yield was 43.7%.

The catalytic activity of dendrimers **26** and **27** as palladium (0) catalysts were checked in Suzuki coupling reaction of aryl halides with phenylboronic acid. The results of these coupling reactions are shown in Table 2.2.

Table 2.2 Palladium-Catalyzed Cross-Couplings of Aryl Halides with Arylboronic Acids

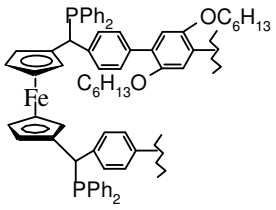


Entry	Ar-X	Ar'-B(OH)$_2$	Catalyst	Yield(%)
1			2mol%**27** /$Pd_2(dba)_3$ (2:1)	60
2			3mol%**27** /$Pd_2(dba)_3$ (2:1)	55
3			2mol%**27** /$Pd_2(dba)_3$ (2:1)	8
4			2mol%**27** /$Pd_2(dba)_3$ (2:1)	0
5			2mol%**27** /$Pd(OAc)_2$ (1:1)	0
6			2mol%**26** /$Pd_2(dba)_3$ (2:1)	0

As shown in Table 2.2, Pd(0)/**27** complex could catalyze the cross-coupling of aryl chlorides with arylboronic acids. The catalytic activity of di(*tert*-butyl)phosphine containing 0 generation dendrimer **27** is better than that of the dicyclohexyl one **26**. These observations suggested that the 12-electron Pd(0) complexes should exist in these dendrimer catalyst system. For the cross-coupling reaction of aryl bromides with arylboronic acids listed in the Table 2.1 and Table 2.2, diphenylphosphine-containing dendrimers are better than the di(*tert*-butyl) one **27**. 1st generation diphenylphosphine containing dendrimer **25** is better than the 2nd generation **11**. These results could be explained that with lower generation dendrimers, more stable 14-electron $(R_3P)_2Pd(0)$ complexes could be more readily formed, and 14-electron $(R_3P)_2Pd(0)$ complexes have been demonstrated to catalyze the cross-coupling reactions of aryl bromides with arylboronic acids. Higher generation dendrimers and dendrimer **27** might tend to form 12-electron $(R_3R)Pd(0)$ complexes. However, because of the instability of either of 12-electron $(R_3R)Pd(0)$ complexes or $Ar(R_3P)Pd(II)X$, formed by the oxidative addition of 12-electron $(R_3P)Pd(0)$ complexes with ArX, low or no catalytic activity was observed for these dendrimers.

The above results showed that with the increase of the generation of the dendrimers, that is, with the increase of the bulky groups, the catalytic activity of the ligands decreased, suggesting the high catalyst loading requirement in polymer**10**/Pd(0) catalyst systems was likely due to the decomposition of either $(R_3P)Pd(0)$ or $Ar(R_3P)Pd(II)X$ complexes. This conclusion was supported by the results from the study of monophosphine-containing polymers by other people in our group. Although it is conceivable for us to design dendrimer ligand systems that can

differentiate these two possibilities, the synthesis of such dendrimers will be more steps than those described. We therefore decided to work on bisphosphine-containing polymer ligand **29** which has two phosphines in each repeating unit (see the next chapter).

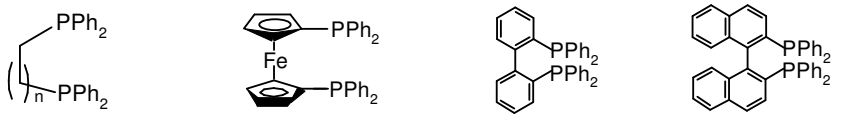


29

Chapter 3 Synthesis of Ferrocenylmethyl-Based Bisphosphine-Containing Polymers for Transition Metal Catalysis

3.1 Introduction

Bisphosphines such as 1,n-diphenylphosphinoalkanes (DPPA) and derivatives, 2,2'–bis(diphenylphosphino)-1,1'-binaphthyl(BINAP), 1,1'-bis(diphenylphosphino) ferrocene(DPPF), and 2,2'-bis(diphenylphosphino)-1,1'-biphenyl (BIPHEP) represent a large group of bidentate ligands in transition metal catalysis.[1,2] They have been proven as very useful ligands in transition metal-catalyzed bond forming reactions including catalytic hydrogenations and transition metal-catalyzed cross-coupling reactions.[1,2] For example, DPPF and BINAP are powerful ligands for a number of organic transformations.[3] Hartwig showed that BINAP-ligated palladium complexes BINAP/$Pd(OAc)_2$ could catalyze the α-arylation of nitriles in toluene at 100°C. He also showed that the combination of $Ni(COD)_2$ and DPPF with the acid cocatalyst (TFA) in THF could lead to almost complete consumption of morpholine with cyclohexadiene at room temperature after 48 hours.



DPPA **DPPF** **BIPHEP** **BINAP**

Optically active bisphosphines including BINAP have been reported as efficient ligands in asymmetric catalysis.[4] Fujihara reported the asymmetric hydrosilylation of styrene with trichlorosilane under mild conditions using novel chiral BINAP-Pd catalysts. Noyori, R.'s group reported the synthesis of a RuH(η'-

BH_4)(BINAP)(1,2-diamine) complex. The complex showed an excellent catalytic efficiency in asymmetric hydrogenation reaction without addition of any bases. Taguchi has employed tol-BINAP-Pd to catalyze the asymmetric *N*-allylation reaction of ortho-*tert*-butylanilide derivatives with diallyl carbonate. It gave moderate enantioselectivity.

Development of recoverable and reusable bisphosphines for this purpose has been intensively studied in the past years. Since 1970s, studies have been carried out to immobilize bidentate bisphosphines in polymer networks.[5] For instance, Bayston incorporated the BINAP framework onto an insoluble polymer (polystyrene). The resulting polymer-bound BINAP, after treatment with $[Ru(cod)(2\text{-methylallyl})_2]_2$ and HBr, provides high ee's in hydrogenation of β-keto esters and acrylic acids. The polymer can be recycled as the catalyst for several times while high ee's are maintained. Noyori used the same polymer-bound BINAP to make a polymer-bound BINAP/diamine ruthenium catalyst, which has shown high ee's and turnover numbers for hydrogenation of simple ketones. Chan has developed a highly effective polyester-supported BINAP ligand through copolymerization of chiral 5, 5'-diaminoBINAP, chiral pentanediol, and terephthaloyl chloride. The ligand has been successfully applied in Ru-catalyzed asymmetric hydrogenation of 2-(6'-methoxy-2-naphthyl)acrylic acid. A dendrimer-supported BINAP ligand has also been reported. Pu has developed several polymer-based chiral ligands such as poly(BINAP) and BINOL-BINAP. These ligands have successfully been applied in Rh-catalyzed hydrogenation of (*Z*)-methyl α-(benzamido)cinnamate and Ru-catalyzed hydrogenation of simple ketones. Lemaire et al. have reported a poly-NAP Ru

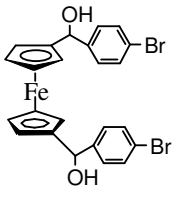
complex, which provides 99% ee in hydrogenation of methyl acetoacetate even after four recycles of the catalyst.

However, despite polymer-supported bisphosphines possess advantages such as easy recovery and reuse, and sometimes higher catalytic activities for derived catalysts compared to their monomeric counterparts, limited number of polymer-supported bisphosphines have been developed and their applications as ligands in transition metal catalysis have not reached the level that parallels to that of their monomeric counterparts.

Careful examination suggested that the unbalanced advantage-application phenomena for reported bisphosphine-containing polymers likely resulted from deficiencies associated with their synthesis and/or catalysis. The synthesis of previously reported bisphosphine-containing polymers is often characterized by long synthetic steps and/or from not readily available starting materials. In addition, the performance of many of the reported bisphosphine-containing polymers is not as good as its monomeric counterparts for chosen transformations. It is thus of great interest to develop new types of bisphosphine-containing polymers that meet the following criteria: (a) starting materials are readily available , (b) the synthetic elaboration is short, (c) their electronic and steric properties are tunable, and (d) they should perform equally well compared to or better than its monomeric counterparts for chosen transformations.

As described in previous chapters, we have developed a protocol to synthesize ferrocenylmethyl-containing ligands **9a** and **10** directly from corresponding ferrocenylmethyl alcohols (scheme 2.1).[6,7] Since 1, 1'-bis(hydroxymethyl)ferrocenes

such as **28** are readily available via one-step reaction from ferrocene and aldehydes and the hydroxyl groups of **28** are structurally similar to that of ferrocenylmethyl alcohol, we reasoned that the hydroxyl groups in **28** should behave similarly to that of **8a** and should also be able to be directly converted to diphenylphosphino moieties. We envisioned that a new family of ferrocene-based bisphosphine-containing polymers from readily available starting materials in very short synthetic steps could be possible. In this chapter, the synthesis of two examples of this new type of ferrocenylmethyl-based bisphosphine-containing polymers, **29** and **30**, and their application as ligands for transition metal catalysis was described.



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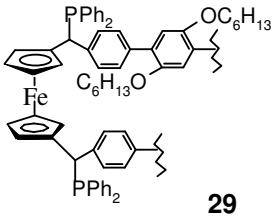

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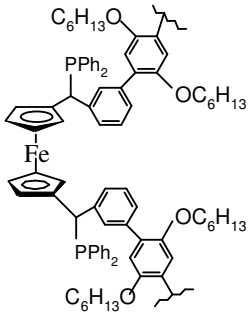

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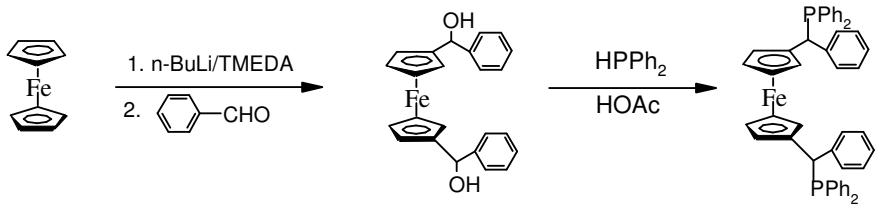
3.2 Preparation of Ferrocenylmethyl-Based Bisphosphine-Containing Polymers

We began our study by testing the reaction of $HPPh_2$ with diol **31**, which was readily prepared from ferrocene and benzaldehyde.[8,9,10] We were pleased to find that bisphosphine **32** was indeed formed directly from **31** under the conditions that are similar to the preparation of **9a**. The reaction of **31** with diphenylphosphine in acetic acid at room temperature yielded **32** smoothly (47%, Scheme 3.1)

Scheme 3.1 Synthesis of Ferrocenylmethyl Bisphosphine-Containing Monomeric Counterpart **32**

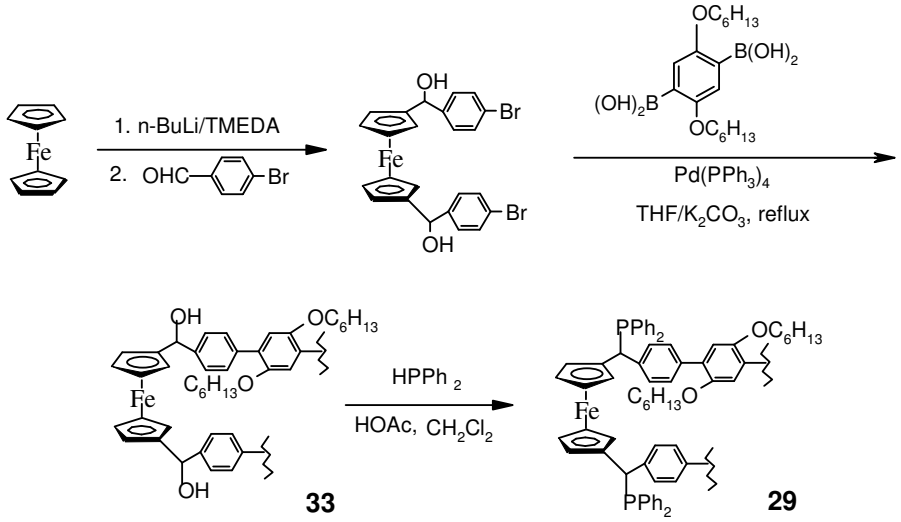


31 **32**

Having established the feasibility to directly convert 1, 1'-bis(hydroxymethyl) ferrocenes to 1,1'-bis(diphenylphosphinomethyl)ferrocenes, we then extended this protocol to the preparation of ferrocene-based bisphosphine-containing polymers. As shown in scheme 3.2, starting from the low cost ferrocene, reaction with *n*-BuLi and N,N,N',N'-tetramethylethylenediamine (TMEDA) followed by treatment with 4-bromobenzaldehyde generated dibromide **28** in 75% yield.[9] Suzuki cross-coupling of **28** with diboronic acid in THF/2M K_2CO_3 give ferrocenylmethyl bishydroxyl-containing polymer **33**. By following the same procedure as the synthesis of **32** from **31**, we were pleased to find that treatment of polymer **33** with $HPPh_2$ smoothly generated polymer **29**. Polymer **29** is soluble in common organic solvent such as THF, toluene, methylene chloride and can be precipitated out from methanol. GPC

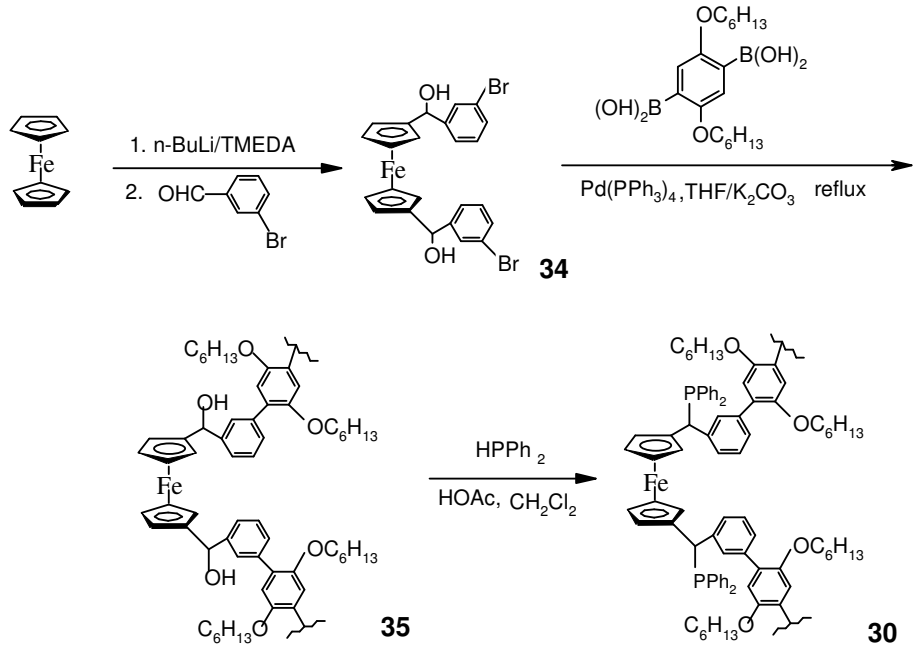
(polystyrene standards, THF) analysis shows that its molecular weight is M_W= 4 300, M_n=3 100 (PDI =1.41). The complete conversion of –OH to –PPh_2 was confirmed by ^{1}H NMR.

Scheme 3.2 Synthesis of Bisphosphine-Containing Polymer **29**



Polymer **30** was prepared in a similar manner by starting from ferrocene and 3-bromobenzaldehyde (Scheme 3.3). Polymer **30** is also soluble in common organic solvents such as THF, toluene, methylene chloride. The complete conversion of –OH to –PPh_2 was also conformed by ^{1}H NMR.

Scheme 3.3 Synthesis of Bisphosphine-Containing Polymer **30**



3.3 Application of Ferrocenylmethyl-Based Bisphosphine-Containing Polymers as Ligands for Transition Metal Catalysis

3.3.1 Ferrocenylmethyl-Based Bisphosphine-Containing Polymers as Ligand for Pd-catalyzed Suzuki Coupling of Aryl Chlorides with Arylboronic Acids

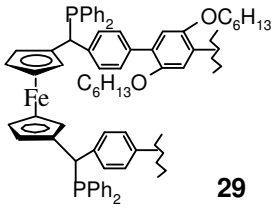
Transition metal-catalyzed Suzuki cross-coupling of deactivated aryl chlorides with arylboronic acids has been realized recently and represents a notable advance in transition metal-catalyzed chemistry.[11-13] Although a number of ligands can now achieve this objective, truly recoverable and reusable ligands are rare.[14] Bisphosphine-containing polymer **29** was applied as such a ligand in the palladium-catalyzed Suzuki cross-coupling reactions of aryl chlorides with arylboronic acids (Eq. 3.1). Unfortunately no reaction was observed based on ^{1}H NMR spectroscopy. And the ligand **29** could not be recovered after reaction.

$$\mathrm{ArCl} + \mathrm{Ar'B(OH)_2} \xrightarrow{\textbf{29}/\mathrm{Pd}} \mathrm{Ar\text{-}Ar'} \qquad (\textbf{Eq}.3.1)$$

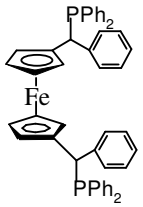
Later study of the **29**-catalyzed addition reaction of arylboronic acids with aryl aldehydes gave us a hint about why no reaction took place in above reaction. Palladacycle could be formed very easily by mixing **29** with Pd sources. We believe that palladacycle was formed during the **29**-catalyzed Suzuki cross-coupling of arylboronic acid with aryl chloride. No reaction was observed because the produced palladacycle was not active toward the cross-coupling of arylboronic acids with aryl chlorides since palladacyles are known as active species toward the Suzuki cross-coupling only at high temperature. In order to confirm our explanation and explore more active catalyst systems, nickel-catalyzed cross coupling reaction was chosen to be studied because nickel is more active and it is very difficult to form metallacycle.

3.3.2 Ferrocenylmethyl-Based Bisphosphine-Containing Polymers as Ligand for Ni-catalyzed Suzuki Coupling of Aryl Chlorides with Arylboronic Acids

We have employed **29** as ligands for Ni(0)-catalyzed Suzuki coupling reactions of aryl chlorides with arylboronic acids. As shown in Table 3.1, $Ni(COD)_2$/**29** complexes (9 mol %/3 mol %) smoothly catalyzed the coupling reaction between aryl chlorides including electron-rich ones and arylboronic acids. The corresponding monomeric ligand **32** was also applied in the same reaction for the comparative purpose. The polymer ligands exhibited similar catalytic efficiency as bisphosphine **32** (Table 3.1, entries 12, 13) and can be readily recovered and reused (Table 3.1, entries 2, 5, 8).

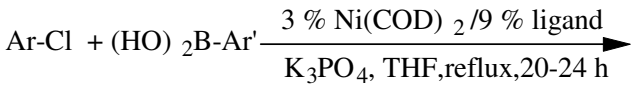


29



32

Table 3.1 Ni(0)-Catalyzed Cross-Couplings of Aryl Chlorides with Arylboronic Acids

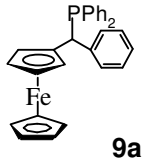


Entry	Ar-Cl	Ar'-B(OH) 2	Ligand	Yield(%)[b]
1	MeO-C6H4-Cl	C6H5-B(OH)2	**29**	84
2	MeO-C6H4-Cl	C6H5-B(OH)2	**29**	82[c]
3	C6H5-Cl	C6H5-B(OH)2	**29**	60
4	MeO-C6H4-Cl	3-Me-C6H4-B(OH)2	**29**	60
5	MeO-C6H4-Cl	3-Me-C6H4-B(OH)2	**29**	69[c]
6	C6H5-Cl	3-Me-C6H4-B(OH)2	**29**	67
7	MeO-C6H4-Cl	C6H5-C6H4-B(OH)2	**29**	78
8	MeO-C6H4-Cl	C6H5-C6H4-B(OH)2	**29**	84[c]
9	C6H5-Cl	C6H5-C6H4-B(OH)2	**29**	99
10	MeO-C6H4-Cl	C6H5-B(OH)2	**30**	89
11	C6H5-Cl	C6H5-C6H4-B(OH)2	**30**	93
12	C6H5-Cl	C6H5-C6H4-B(OH)2	**32**	95[d]
13	MeO-C6H4-Cl	C6H5-B(OH)2	**32**	82[d]

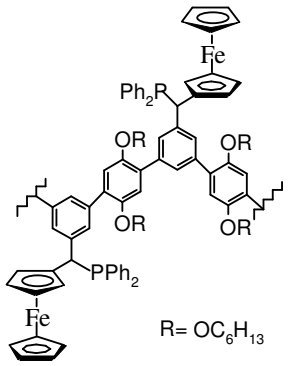
a. Reaction conditions (not optimized): aryl chlorides (1.0 mmol.), arylboronic acids (1.5 equiv.), K_3PO_4 (3 equiv.), 3 mol% $Ni(COD)_2$, ligand (9 mol % based on repeat unit), THF (2 ml).
b. Isolated yields. c. Recovered polymer was used. d. Conversion based on ^1H NMR.

To gain insight into the coordination nature of the new type of bisphosphine-containing polymers in Ni(0)-catalyzed cross-coupling of aryl chlorides with arylboronic acids, we have compared the catalytic behavior of different ligands using the cross-coupling reaction of *p*-chloroanisole with phenylboronic acid as the model

reaction. We found that monodentate ferrocenylmethylphosphine **9a** as well as its polymeric form **10** was efficient ligand for room temperature Ni(0)-catalyzed cross-coupling of aryl chlorides with arylboronic acids (Table 3.2, entries 1, 2). On the other hand, the same reactions only take place at elevated temperature when bidentate DPPF and 1, 2 bis(diphenylphosphino)ethane (DPPE) are used as ligands (Table 3.2, entries 3-5).[13] We found that the catalytic property of polymer **29** was very similar to that of DPPF and DPPE (Table 2, entries 6-9). These results suggested that the phosphine moieties in polymer **29** and **32** most likely functioned as bidentate ligands rather than monodentate ones.

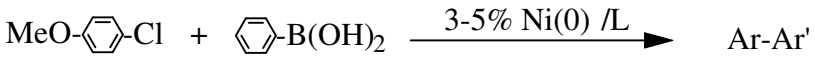


9a



10

Table 3.2 Ni(0)-Catalyzed Cross-Couplings of *p*-Chloroanisole with Phenylboronic Acid[a]



Entry	Ligand	Temperautre	Yield(%)[b]
1	**9a**	Room Temp.	89
2	**10**	Room Temp.	33
3	DPPF or DPPE	Room Temp.	less than 10
4	DPPF	80°C	86[c]
5	DPPE	80°C	84[d]
6	**29**	Room Temp.	0
7	**32**	Room Temp.	0
8	**29**	70°C	84
9	**32**	70°C	82

a. Reaction conditions: p-chloroanisole (1.0 equiv.), phenylboronic acid (1.5 equiv.), K_3PO_4 (3 equiv.), THF (2 ml). b. Isolated yield. c. Ref. 12a d. Ref. 12c.

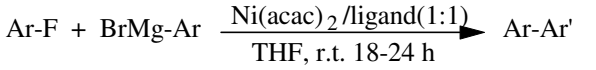
3.3.3 Bisphosphine-containing polymer 29 as ligands for Ni(0)-catalyzed cross-coupling reaction of Grignard reagents with aryl fluorides

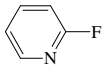
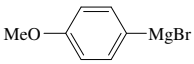
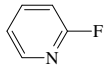
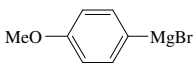
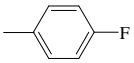
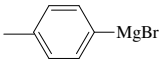
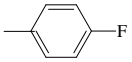
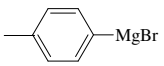
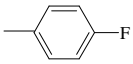
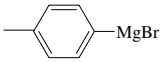
Carbon-fluorine bonds are the strongest single bonds in organic compounds and are inert to many reagents[15]. Therefore, developing reactions that replace fluorine atoms in organic molecules with other atoms or functional groups is a challenging theme in organic chemistry. As for metal-mediated transformations, the cross-coupling reactions of alkyl and aryl fluorides with Grignard reagents were studied.

Several reactions using fluoroarenes have already been developed involving cleavage of sp^2 C-F bonds. Herrmann reported cross coupling reaction of aryl fluorides and aryl Grignard reagents at room temperature catalyzed by the complex bis[1,3-di-(2',6'-diisopropylphenyl)imidazolin-2-ylidene]nickel(0).[16] Yu reported first $Pd(PPh_3)_4$-catalyzed amination, stille coupling and Suzuki coupling of electron-deficient aryl fluorides.[17] Mongin reported the first cross-coupling reactions of fluoroazines and –diazines with aryl Grignard reagents at room temperature using commercially available ligands such as DPPE, DPPF and DPPP.[18]

When the bisphosphine-containing polymer **29** was applied as a ligand in the nickel-catalyzed cross-coupling reaction of aryl Grignard and aryl fluorides, it showed similar catalytic reactivity as DPPE and its corresponding monomeric counterpart **32**. Further, it can be recovered and reused. Table 3.3 shows the results of Ni(0)-catalyzed cross-coupling of aryl Grignard with aryl fluorides. Polymer **29** has been demonstrated recoverable and reusable (Table 3.3, entry 5).

Table 3.3 Ni(0)-Catalyzed Cross-Coupling Reactions of Aryl Fluorides with Grignard Reagents



Entry	Ar-F	BrMg-Ar	$Ni(acac)_2$	ligand	Yield(%)[b]
1			5 %	**29**	53
2			5 %	**32**	68
3			5 %	**29**	76[c]
4			5 %	**32**	77[c]
5			10 %	**29**	78[c,d]

a. Reaction conditions (not optimized): fluoride (1.0 mmol.), Grignard reagent (1.5 -2.0 equiv.), 1:1 ratio of $Ni(acac)_2$ /ligand (based on repeat unit), THF (2 ml). b. Isolated yield c. Based on ^1H NMR. d. Recovered polymer was used.

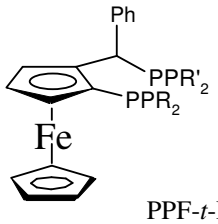
3.3.4 Bisphosphine-Containing Polymer 29 as Ligands for Cross-Couplings of Aryl/Alkenyl Tosylates

Aryl/alkenyl tosylates are a large family of unique, attractive synthetic feedstock for organic synthesis. They can be easily prepared from phenols/enols and *p*-toluenesulfonyl chlorides. Further, tosylates are more stable and less expensive compared to aryl triflates. But the main disadvantage is that tosylates are generally much less reactive.

Previous reported cross-couplings of aryl tosylates with nickel,[19-21] iron,[22,23] copper[24] or palladium catalysts generally required high temperatures, activated tosylates or high catalyst loading.[20,25-28] Recently, we reported the Ni(0)/PCy_3 as a general catalyst system for the room temperature Suzuki cross-coupling reactions of aryl arenesulfonates with arylboronic acids.[29] Despite its high reactivity, the $Ni(COD)_2$/PCy_3 (COD = cyclooctadiene) catalyst system suffers from the following disadvantages: (a) both $Ni(COD)_2$ and PCy_3 are oxygen-sensitive, and (b) a large amount of expensive PCy_3 (12 mol%), which can not be recovered and reused, is required for the catalysis. We reason it will be practically more useful if the catalyst systems are derived from more air-stable ligands, especially recoverable and reusable ones.

Bisphosphines have been employed for the cross-couplings of aryl tosylates. Percec reported the $NiCl_2$(dppe)-, $NiCl_2$(dppf)-, $NiCl_2$(dppp)-catalyzed cross-coupling reactions of aryl tosylates with aryl boronic acids.[30] Hartwig reported a bisphosphine ligand, PPF-*t*-Bu which can oxidatively adds aryl tosylates at room temperature to form isolable aryl palladium (II) tosylate complexes.[31] This mild activation created

palladium-catalyzed couplings of aryl tosylates with aryl Grignard reagents and amines at room temperature.

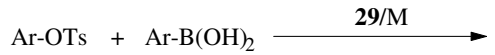


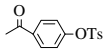
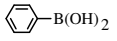
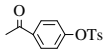
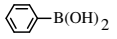
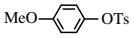
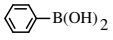
PPF-*t*-Bu R = Ph, R' = *t*-Bu

As polymer **29** has been established as bidentate, and recoverable and reusable bisphosphines for Ni(0)-catalyzed Suzuki cross-couplings, the application of **29** as ligands for the cross-couplings of aryl tosylates with arylboronic acids were studied. The results are shown in Table 3.4. We started the study with the reaction of 4-acetyl toluene tosylate with phenylboronic acid first (Table 4, Entry 1), 50% conversion was observed. When the solvent changed from THF to dioxane, 89% isolated yield was obtained (Table 3.4, Entry 2). The possible reason that led to the huge difference is the reaction temperature. The real reaction temperature is 80^{o}C when dioxane is used as a solvent. But for THF, the real reaction temperature is only around 67^{o}C even the reaction temperature is heated to 80^{o}C because the boiling point of THF is 67^{o}C. The success in the activated aryl tosylates encouraged us to study the reaction of deactivated aryl tosylates. The reaction of 4-methoxylphenyltosylate with phenylboronic acid gave around 30% conversion in dioxane at 80^{o}C (Table 3.4, Entry 3). While at room temperature, no product was observed when 4-methylphenyltosylate reacted with phenylboronic acid. When Ni(II) was used instead of Ni(0), the reaction of 4-methoxylphenyl tosylate with phenylboronic acid did not take place. We also tested the palladium system with ligand **29**. Unfortunately, both

Pd(0) and Pd(II) did not work. This might be due to the fact that the intrinsic property of the Pd is not as reactive as Ni.

Table 3.4 Cross-coupling Reactions of Aryl Tosylates with Arylboronic Acids



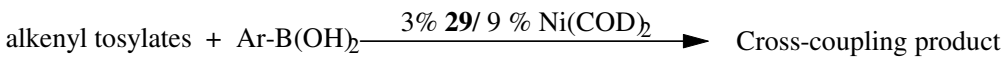
Entry	Ar-X	Ar-B(OH)2	**29**/M	Solvent	temp.(°C)	Yield(%)b
1			4 %/2 %Ni(COD)2	THF	80	50c
2			4 %/2 %Ni(COD)2	dioxane	80	89
3			6 %/3 % Ni(COD)2	dioxane	80	30c

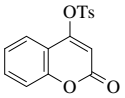
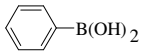
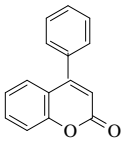
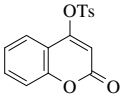
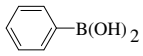
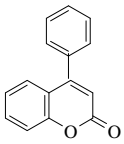
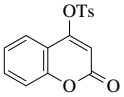
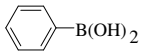
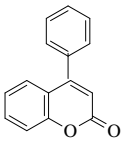
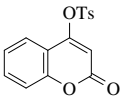
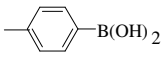
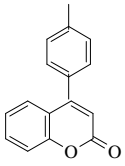
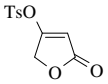
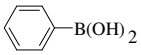
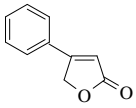
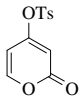
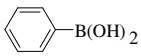
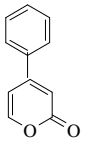
a. Reaction conditions: aryl tosylate (1.0 mmol.), phenylboronic acid (1.5 equiv.), K_3PO_4 (3 equiv.), solvent (1.5 ml), Reaction time: 24 hrsb. Isolated yield. c. Conversion

The success of cross-couplings of activated aryltosylates with arylboronic acids encouraged us to test the Ni(0)/**29**-catalyzed cross-coupling reactions of readily accessible 4-toluenesulfonyloxy-coumarin and 4-toluenesulfonyloxy-2(*5H*)-furanone with arylboronic acids. The results are listed in Table 3.5. Starting with the cross-coupling of 4-*p*-toluenesulfonyloxy-coumarin with phenylboronic acid, we found that under the conditions that (9% of bis(1,5- cyclooctadiene) nickel(0) [$Ni(COD)_2$]/3% **29**, 3 equivalent of potassium phosphate (K_3PO_4) as base, dioxane as solvent), the reaction went to completion in 21 hrs and the desired product was isolated in 93% yield(Table 3.5, Entry 2). Further, the bispolymer ligand **29** could be recovered and reused (Table 3.5, Entry 3). When the 4-methylphenylboronic acid was used as the substrate, 97% isolated yield was achieved. This result implied that 4-toluenesulfonyloxycoumarin was more reactive than aryl tosylates (Table 3.4). We thus carried out Ni(0)/**29**-catalyzed cross-coupling reactions of 4-*p*-toluenesulfonyloxy-2(*5H*)-furanone with arylboronic acids (Table 3.5, Entry 5). It

was found that the reaction was complete in 42 hrs, but the isolated yield is only 48%. This means that most probably the 4-*p*-toluenesulfonyloxy-2(*5H*)-furanone was decomposed during the reaction under the reaction condition. When the reaction temperature was lowered to 50^{o}C, the reaction was not complete in 22 hrs. The cross-couplings of another activated alkenyl tolsylate, 4-*p*-toluenesulfonyloxy-2-hexanone with phenylboronic acid (Table 3.5, Entry 6) was also tested. 35% Isolated yield was achieved after 18 hrs.

Table 3.5 Ni(0)-Catalyzed Cross-Coupling Reactions of Activated Alkenyl Tosylates with arylboronic acids[a]



Entry	Alkenyl tosylates	Ar-B(OH)$_2$	Solvent	Product	Yield(%)[b]
1			THF		61
2					90
3					88[c]
4					97
5					48
6					35

a. Reaction conditions: tosylate (1.0 mmol), phenylboronic acid (1.5 equiv.), 3 mol %Ni(COD)$_2$ 9 mol% of **29** (based on repeating unit), solvent (1.5 ml). b. Isolated yield

c. Recoverd **29** was used as the ligand.

In summary, the synthesis of two examples of a new type of ferrocene-based bisphosphine-containing polymers and their application as bidentate ligands for

Ni(0)-catalyzed cross-coupling reactions are described. Our study showed that (a) this new family of ferrocene-based bisphosphine-containing polymers could be readily accessible in very short steps from readily available starting materials, (b) the catalytic property of the new ferrocene-based bisphosphine containing polymers exhibited in Ni(0)-catalyzed cross-coupling reactions of aryl chlorides with arylboronic acids, and aryl fluorides with Grignard reagents, and aryl tosylates with arylboronic acids was comparable to that of its monomeric counterpart, and (c) the polymer ligands could be recovered and reused.

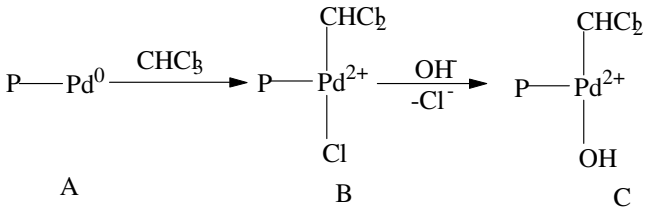
Chapter 4 Palladium(II)-Catalyzed Addition Reactions of Arylboronic Acids with α, β-Unsaturated Ketones and Aromatic Aldehydes

4.1 Introduction

The addition of organometallic reagents to carbonyl group-containing compounds is a powerful tool for the construction of carbon-carbon bonds.[1,2] It has been widely used in organic synthesis. Among various organometallic reagents, organoboron reagents are nontoxic and practically useful for carbon-carbon bond formations with various electrophiles in the presence of a transition metal catalyst and have attracted much attention.[3] Rhodium(I)-catalyzed carbon-carbon bond forming reactions with organoboron reagents have been remarkably developed.[2] For example, Miyaura et al. found that rhodium(I) complexes not only can catalyze the 1, 2-addition of aryl/alkenylboronic acids to aldehydes and *N*-arylsulfonyl aldimines,[4,5] but also can effectively catalyze the 1, 4-addition with α, β-unsaturated carbonyl compounds.[6] Recently, palladium-catalyzed conjugate additions have attracted much attention and the corresponding reports on them have showed up. Several groups have reported palladium-catalyzed addition reactions of organoboron reagents. For example, Uemura demonstrated that palladium(0)-$SbCl_3$ catalyzed the conjugate addition of arylborons to α, β-unsaturated carbonyl compounds.[7] A cationic palladium(II) complex is also reported as an active catalyst for the 1, 4-addition reactions.[8] More recently, Ohta reported that in the presence of a base and catalytic amount of palladium(0) complex with chloroform, the addition reaction of

arylboronic acids with aldehydes gave the corresponding secondary alcohols in good yields.[9] Ohta also proposed a possible mechanism for this addition reaction,[9] which is shown in Scheme 4.1. First, phosphine and dichloromethyl-coordinating palladium(II) intermediate B is generated by oxidative addition of chloroform to phosphine-coordinated palladium(0) complex A, and dichloromethylpalladium(II) intermediate B produces a hydroxyl palladium(II) species C by counteranion exchange. Then, transmetalation between arylboronic acid and the hydroxyl palladium(II) species C occurs to generate an arylpalladium(II) intermediate, and the insertion of the aldehyde into the carbon-palladium bond affords the palladium alkoxide. The palladium alkoxide complex is hydrolyzed to give the corresponding alcohol, and the hydroxyl palladium(II) species C is reproduced. It is unclear whether mononuclear and or multinuclear palladium complexes are the catalytically active species.

Scheme 4.1 Possible Intermediates



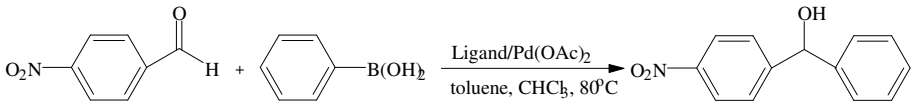
In addition, the substrate scope for this very attractive catalyst system is very limited. Considering that the high enantioselective addition of arylboronic acids with aldehydes has not been achieved, we believed it would be important to develop highly active/enantioselective palladium catalysts for this addition reaction. Our study started with the intention to clear the mechanism for the $Pd(OAc)_2/PPh_3/CHCl_3$ catalyst system: mononuclear Pd(II) complex might be the catalytically active catalyst.

By understanding the reaction mechanism, we hope to develop more efficient Pd catalysts for the addition of arylboronic acids with carbonyl group-containing compounds.

4.2 Initial Study of $Pd(OAc)_2$/Phosphine/$CHCl_3$-Catalyzed Addition Reaction of Arylboronic Acids with Aromatic Aldehydes

We have demonstrated in our previous studies that ferrocenylmethylphosphine -containing polymers could function as unique monodentate or bidentate ligands, suggesting it might be possible to employ these polymeric ligands for the mechanism study. We began our study with our bisphosphines-containing polymer **29** and ferrocenylmethylphosphine polymer **10** as ligands for the addition reaction of phenylboronic acids with 4-nitrobenzaldehyde at the same condition as that of the Ohta's. We found that both polymers were excellent ligands for the reaction. For comparison purpose, monomeric ferrocenylphosphines **9a** and **32**, and several other phosphines were also employed as the catalyst. The results are listed in Table 4.1.

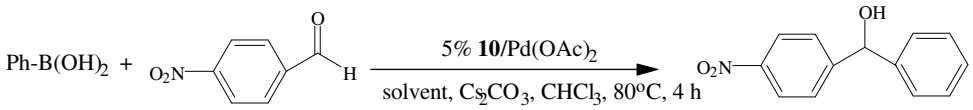
Table 4.1 Ligand Screening



Entry	Ligand	Reaction Time	Yield (%)
1	PPh_3	6 h	5
2	DPPF	21 h	<5
3	(*o*-toluene)$_3$P	21 h	<5
4	*t*-Bu_3P	6 h	10
5	**9a**	2 h	68
6	**10**	3 h	95
7	**10**	2 h	50
8	**29**	6 h	80
9	**32**	6 h	64
10	**29**	3 h	35

From Table 4.1, we can see that PPh_3 was not an effective ligand for the reaction of phenylboronic acid with 4-nitrobenzaldehyde. Catalysts derived from DPPF, (*o*-toluene)$_3$P, and *t*-Bu$_3$P also only showed very limited catalytic reactivity (Entry 1, 2, 3 and 4). Among the ligands screen, we found monodentate ligands **10** and **9a** have better catalytic activity than the bidentate ones **29** and **32** (Entry 5, 6 and 7 verse entry 8, 9, 10). The optimization of the reaction conditions for the reaction of phenylboronic acid with 4-nitrobenzaldehyde was studied by using **10** and **9a** as ligands. The solvents were screened and the results for the use of ligand **10** were listed in Table 4.2.

Table 4.2 Reaction Optimization[a]

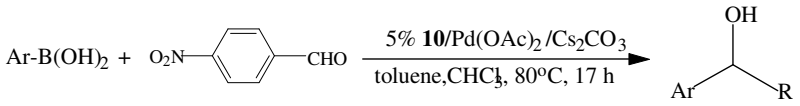


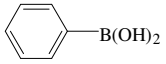
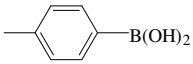
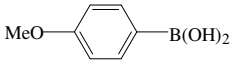
entry	solvent	Yield (%)[b]
1	toluene	86
2	CH_2Cl_2	86
3	THF	65
4	dioxane	67

a. Reaction conditions: 4-nitrobenzaldehyde (0.5 mmol), phenylboronic acid (2.0 equiv.), solvent (1.2 mL),Cs_2CO_3 (1.0 equiv.),**10** (5%), $Pd(OAc)_2$ (5%), reaction temperature: 80°C, reaction time: 4 h. b Based on ^{1}H NMR.

From Table 4.2, we can see that among the solvents we screened, toluene and dichloromethane are good solvents, while THF and dioxane are bad solvents for the reaction of phenylboronic acids with 4-nitrobenzaldehyde. With the toluene as the solvent, several arylboronic acids were reacted with 4-nitrobenzaldehyde, the results were shown in Table 4.3.

Table 4.3 10-Catalyzed Addition of Arylboronic Acids with Aldehydes[a]

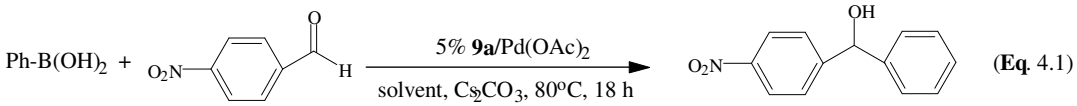


Entry	Ar-B(OH)$_2$	Yield (%) [b]
1		93
2		92
3		90

[a] Reaction conditions (not optimized): aldehyde (0.5 mmol, 1.0 equiv.), arylboronic acid (2.0 equiv.), **10** (5%), $Pd(OAc)_2$ (5%), Cs_2CO_3(1.0 equiv.) toluene (1.2 mL). [b] isolated yields.

From Table 4.3, we can see that **10** is an excellent ligand for the reaction of arylboronic acids with 4-nitrobenzaldehyde. Like other palladium catalyzed reactions, it is hard to recover and reuse the polymeric ligand **10**. The endeavor of the recovery and reuse of **10** for this reaction failed. The possible reason of the fail may be the decomposition of the palladium-based catalyst complex.

The effect of $CHCl_3$ was studied next. To our surprise, the reaction of phenylboronic acid with 4-nitrobenzaldehyde was complete after 18 hours without adding $CHCl_3$ when toluene was used as the solvent. When the solvent was switched to dichloromethane, the reaction was also complete in 18 h. This further conformed that the additive $CHCl_3$ is not necessary. Since the $CHCl_3$ is not necessary for the reaction of phenylboronic acid with 4-nitrobenzaldehye, obviously, the reaction might be catalyzed by palladium species other than the one proposed by Ohta.

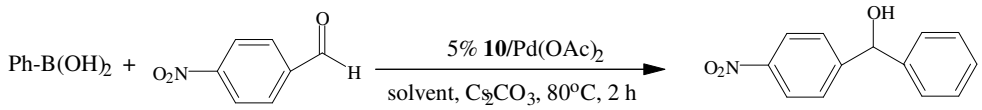


(**Eq**. 4.1)

4.3 $Pd(OAc)_2$/Ferrocenylmethylphosphine-Catalyzed Addition Reactions of Arylboronic Acids with Aromatic Aldehydes

The optimization of the new condition (without $CHCl_3$ additive) was then studied. The solvents were screened. And the results are shown in Table 4.4. At 80°C, toluene and dichloromethane are good solvents. They gave similar yield (Table 4.4, Entry 1, 2). When the reaction temperature was lowered to 40-45°C, the reaction could not be complete in 17 h no matter toluene or dichloromethane was used as the solvent. Considering that the reaction needs 80°C to be complete, toluene is chosen as the right solvent since the boiling point of dichloromethane is only 39.8°C and is not easy to handle at high temperature.

Table 4.4 Reaction Optimization[a]

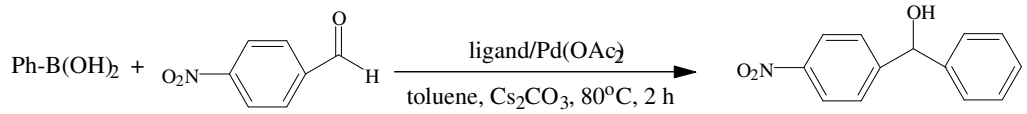


Entry	Solvent	Reaction temperature	Reaction Time	Yield (%)[b]
1	toluene	80	2 h	68
2	CH_2Cl_2	80	2 h	70
3	$ClCH_2CH_2Cl$	80	2 h	39
4	THF	80	2 h	22
5	dioxane	80	2 h	15
6	DMF	80	2 h	16
7	toluene	40	17 h	69
8	CH_2Cl_2	40	17 h	73

a. Reaction conditions: 4-nitrobenzaldehyde (0.5 mmol), phenylboronic acid (2.0 equiv.), solvent (1.2 mL), Cs_2CO_3(1.0 equiv.),**10** (5%), $Pd(OAc)_2$ (5%). b Based on ^1H NMR.

With toluene as the solvent, the catalytic reactivity of monomeric ligand **9a** and polymeric ligand **10** were compared. The results were shown in Table 4.5.

Table 4.5 Comparison Between Monomeric Ligand **9a** and Polymeric Ligand **10**[a]

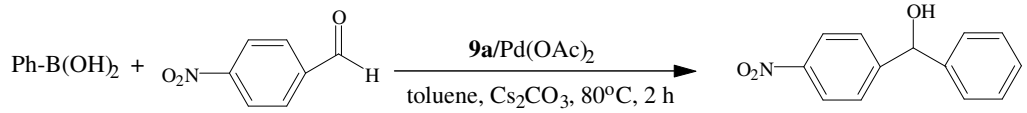


Entry	Ligand	Yield (%)[b]
1	**10**	50
2	**9a**	68

a. Reaction conditions: 4-nitrobenzaldehyde (0.5 mmol), phenylboronic acid (2.0 equiv.), solvent (1.2 mL), CS_2CO_3 (1.0 equiv.), ligand (5%), $Pd(OAc)_2$ (5%). b Based on ^1H NMR.

From Table 4.5, monomeric ligand **9a** exhibited higher efficiency than its corresponding polymeric one **10**. So we turned our attention to **9a**. With toluene as the solvent, the ratio of monophosphine-containing ligand **9a** to $Pd(OAc)_2$ was examined. The results were listed in Table 4.6. From Table 4.6, we can see that 1:1 ratio of **9a** to $Pd(OAc)_2$ gave the best yield.

Table 4.6 Effect of Ratio **9a** to $Pd(OAc)_2$ on the Yield of the Reaction[a]

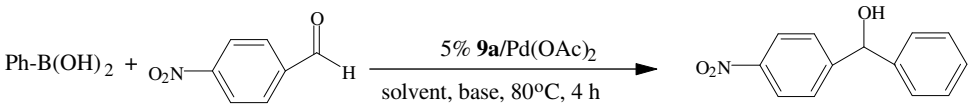


Entry	**9a** : $Pd(OAc)_2$	Yield (%)[b]
1	1 : 1	83
2	2 : 1	50
3	3 : 1	75

a. Reaction conditions: 4-nitrobenzaldehyde (0.5 mmol), phenylboronic acid (2.0 equiv.), solvent (1.2 mL), CS_2CO_3 (1.0 equiv.), **9a** (5%), $Pd(OAc)_2$ (5%). b Based on ^1H NMR.

Keep the 1:1 ratio of **9a** to $Pd(OAc)_2$, the effect of solvents and bases were screened. The results are listed in the Table 4.7.

Table 4.7 Solvents and Based Screen

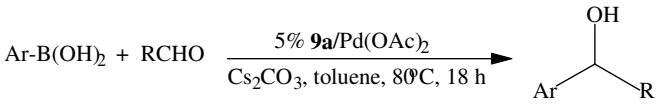


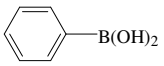
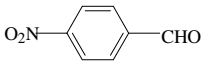
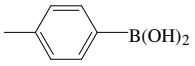
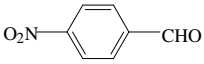
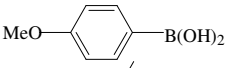
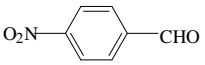
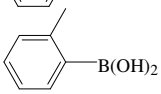
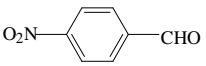
Entry	Solvent	Base	Yield (%)[b]
1	toluene	Cs_2CO_3	91
2	CH_2Cl_2	Cs_2CO_3	50
3	$ClCH_2CH_2Cl$	Cs_2CO_3	54
4	THF	Cs_2CO_3	50
5	toluene	K_3PO_4	48
6	toluene	KF	32
7	toluene	K_2CO_3	31
8	toluene	Na_2CO_3	21
9	toluene	Ag_2CO_3	18

a. Reaction conditions: 4-nitrobenzaldehyde (0.5 mmol), phenylboronic acid (2.0 equiv.), solvent (1.2 mL), base (1.0 equiv.), **9 a** (5%), $Pd(OAc)_2$ (5%). b Based on ^1H NMR.

From Table 4.7, it is clear that under this condition, toluene is also the best solvent and Cs_2CO_3 is the best base for the **9a**/$Pd(OAc)_2$ catalyzed addition reaction of phenylboronic acid with 4-nitrobenzaldehyde. With the 1:1 ratio of **9a** to $Pd(OAc)_2$, toluene as the solvent, Cs_2CO_3 as the base, the addition reaction of several arylboronic acids with nitrobenzaldehydes were studied. The results are listed in Table 4.8.

Table 4.8 Addition of Arylboronic Acids with Nitrobenzaldehydes[a]



entry	Ar-B(OH)$_2$	RCHO	yield (%) [b]
1			90
2			94
3			97
4			91

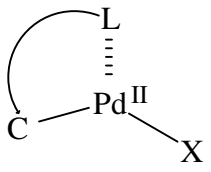
[a] Reaction conditions (not optimized): aldehyde (0.5 mmol, 1.0 equiv.), arylboronic acid (2.0 equiv.), Cs_2CO_3 (1.0 equiv.), toluene (1.2 mL), 80°C. [b] isolated yields.

The results in above table showed that all the substrates gave excellent yields. **9a** is a highly efficient ligand for palladium-catalyzed addition reaction of arylboronic acids with activated aromatic aldehydes.

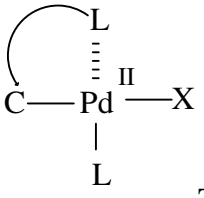
4.4 Palladacycle 36-Catalyzed Addition Reaction of Arylboronic acids with Aldehydes and α, β-Unsaturated Ketones

During our previous study of ferrocenylmethylphosphine-containing polymer **10** as a ligand for palladium-catalyzed Suzuki cross-coupling reactions of arylboronic acid with aryl chlorides, we noticed that some insoluble **10**/palladium(0) complexes are formed during the reactions.[10] But the real catalytic active monophosphine palladium(0) complex should be homogenous and soluble in THF. Considering above phenomena and the fact that palladacycles can be formed when mixing palladium(0) with monophosphine, we reasoned that the insoluble complex we observed during the **10**/palladium(0)-catalyzed Suzuki cross-coupling reactions might be palladacycles.

Palladacycles, which are palladium compounds containing at least one metal-carbon bond intramolecularly stabilized by at least one donor atom, are one of the most popular class of organopalladium derivatives. Palladacycles can be divided into two types: anionic four-electron donor (Type I) and six-electron donor (Type II).



Type I
Palladacycles

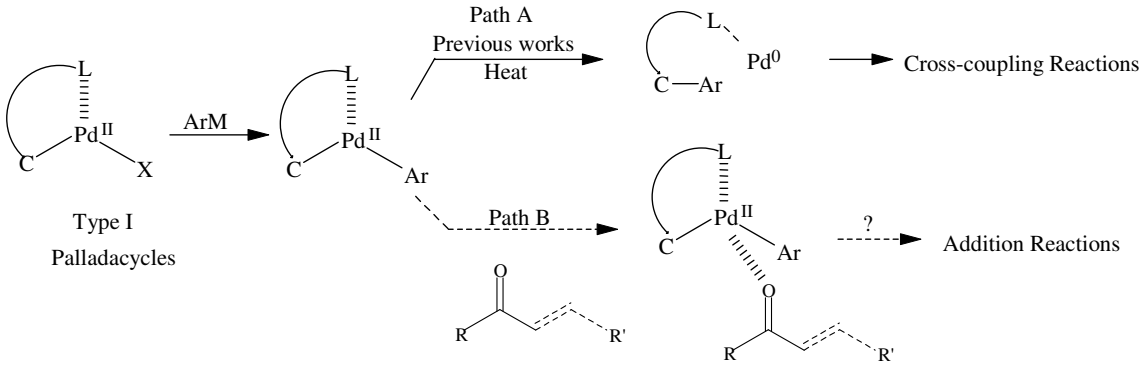


Type II
Palladacycles

Type I palladacycles usually exist as halogen or acetate bridged dimmers. They are readily accessible and air/moisture stable.[12] They have been demonstrated as efficient catalyst systems for a series of bond forming reactions including cross-coupling reactions.[11] Mechanistic studies suggested that in cross-coupling reactions such as the Suzuki couplings, palladacycles served as the sources of catalytically active species

by undergoing transmetalation with organometallic reagents to form transmetalated intermediates such as A followed by reductive elimination (Scheme 4.2). As it has been established that the Pd(II) center in palladacycles could act as a Lewis acid,[12] we reasoned that when carbonyl moieties were present in the reaction system, in addition to undergoing reductive elimination to form Pd(0) species(Path A), A might coordinate with a carbonyl moiety to form complexes B (Path B). On the basis that elevated temperature, typically higher than 100 ^{o}C, was required for palladacycles to generate catalytically active species for cross-coupling reactions, we surmised that the reductive elimination of A should be slow, especially at lower temperature, such as room temperature. B might undergo aryl transfer to form addition products much faster than reductive elimination to form cross-coupling products, and type I palladacycle could thus catalyze addition reaction

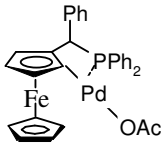
Scheme 4.2 General Routes of Palladacycle-Catalyzed Coupling and Addition Reactions



of arylboronic acids to carbonyl group containing compounds.[13] This hypothesis could explain the reason why the reaction of phenylboronic acid with 4-nitrobenzaldehyde could be complete in 18 hours with **10**/palladium catalyst complex without the use of $CHCl_3$. As palladacycles are moisture and air-stable and haven't been explored as addition catalysts for the addition of arylboronic acids with

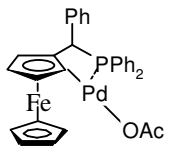
carbonyl-containing compounds, we envisioned that the exploration of such palladacycle-catalyzed addition reaction would create a new paradigm for palladacycle catalysis chemistry and may provide powerful catalysis systems for organic synthesis.

As we have demonstrated that **9a**/$Pd(OAc)_2$ was an efficient catalyst system for the addition reactions of arylboronic acids with aldehydes. We tried to prepare the expected palladacycle **9b** from the reaction of **9a** with $Pd(OAc)_2$. When the **9b** was applied as catalyst in the addition reaction of arylboronic acids with aldehydes, it showed similar catalytic activity as the active species which was produced in situ by mixing **9a** with $Pd(OAc)_2$. Results are shown in Table 4.9. From Table 4.9, we can see that **9b** is a highly efficient catalyst for the reaction of arylboronic acids with 3-nitrobenzaldehyde. Further, it also showed high catalytic activity in the addition reaction of phenylboronic acids with chalcone (Eq. 4.2). The reaction of arylboronic acids with chalcone was complete within two and a half hours at room temperature based on ^{1}HNMR spectroscopy.

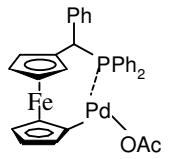


9b

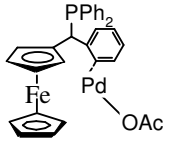
Unfortunately we met with numerous difficulties when we tried to purify the expected palladacycle **9b**. The difficulty may come from the phenyl ring on **9a.** On ^{31}P NMR spectroscopy, there are always two small peaks. Although we tried very hard, the small peak could not be removed. So **9b** could not pass the elemental analysis. The reasons for the observed phenomena may as



9b



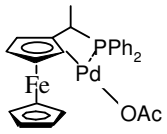
9b+



9b++

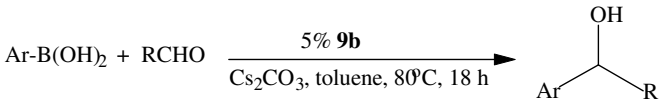
follows. There are other isomers for **9b** such as **9b+, 9b++**.

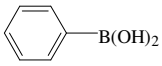
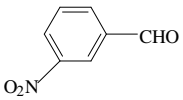
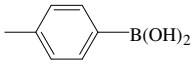
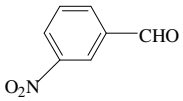
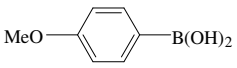
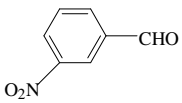
We ended in turning our attention to other palladacycles. Palladacycle **36** was selected based on the following reasons: a) it has similar electron-richness of the Pd-bonded aromatic part as **9a**; b) it has similar size of the ligand part as **9a**; c) it is readily available. So the ferrocenyl-containing palladacycle **36** was prepared and employed as a ligand in the reaction of phenylboronic acid and chalcone. We were pleased to find that **36** was indeed an excellent catalyst for the addition reaction, 95% conversion was achieved after one hour reaction (Table 4.10, Entry 1). We have further employed **36** for the optimization of the reaction conditions and our results were also listed in Table 4.10. We found that among the solvents we screened, toluene was the best solvent, and K_3PO_4 and KF were the best bases among the bases we tested.



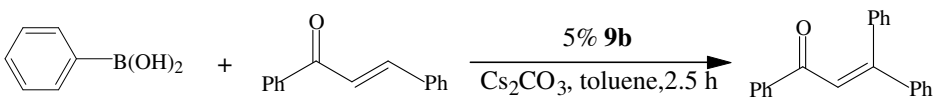
36

Table 4.9 9b-Catalyzed Addition of Arylboronic Acids with 3-Nitrobenzaldehyde[a]



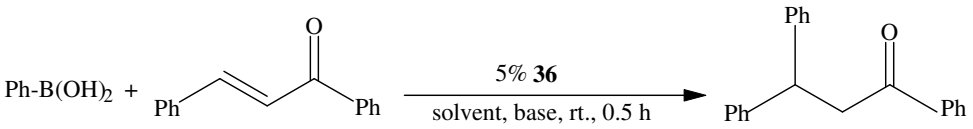
entry	Ar-B(OH)$_2$	RCHO	yield (%) [b]
1			98
2			95
3			90

[a] Reaction conditions (not optimized): aldehyde (0.5 mmol, 1.0 equiv.), arylboronic acid (2.0 equiv.), Cs_2CO_3 (1.0 equiv.), toluene (1.2 mL), 80 °C. [b] isolated yields.



(**Eq.** 4.2)

Table 4.10 Reaction Optimization[a]



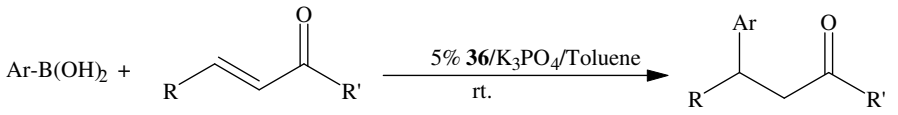
Entry	Solvent	Base	Conversion (%)[b]
1	toluene	Cs_2CO_3	95[c]
2	$ClCH_2CH_2Cl$	K_3PO_4	57
3	CH_2Cl_2	K_3PO_4	56
4	THF	K_3PO_4	54
5	dioxane	K_3PO_4	72
6	toluene	K_3PO_4	99
7	toluene	Cs_2CO_3	79
8	toluene	KF	99
9	toluene	K_2CO_3	68
10	toluene	Ag_2CO_3	36

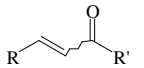
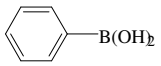
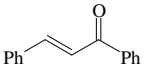
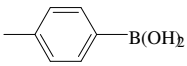
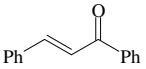
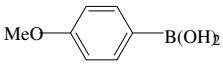
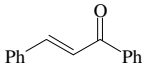
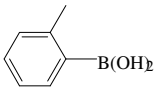
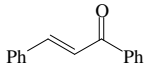
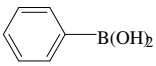
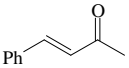
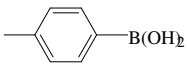
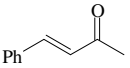
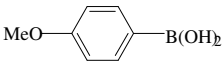
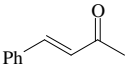
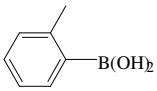
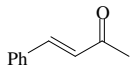
a. Reaction conditions: chalcone (1.0 equiv.), phenylboronic acid (2.0 equiv.), solvent (1.2 mL), base (1.0 equiv.), 5% **36**, room temperature, 0.5 h. b Based on ^{1}H NMR. c Reaction time: 1h.

With palladacycle **36** as the catalyst, toluene as the solvent, and K_3PO_4 as the base, the reaction of a number of arylboronic acids and α, β-unsaturated ketones were examined, and the results are listed in table 4.11. From table 4.11, we can see that all the substrates gave excellent yield under our conditions and **36** was a highly active, general catalyst for the room temperature 1, 4-addition of arylboronic acids with α, β-unsaturated ketones. The reaction, like other Pd(II)-catalyzed 1, 4-addition of arylboronic acids with α, β-unsaturated ketones, probably involved Pd(II)-enolates as the intermediates, which could undergo reductive elimination to form Heck type cross-coupling products or protonation to generate the 1, 4-addition products. The fact that the Heck coupling product, which are sometimes seen in other Pd(II) catalyst systems, were not detected during reaction based on ^{1}H NMR spectrum. This

suggested that the reaction was conducted with a different mechanism. The reductive elimination process of the Pd(II)-enolate intermediates in this reaction occurred much slower than that of their protonation process.[14]

Table 4.11 Palladacycle 36-Catalyzed Michael Addition of Arylboronic Acids with α, β-Unsaturated Ketones[a]



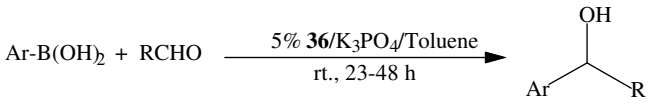
entry	Ar-B(OH)2		yield (%) [b]
1			95[c]
2			93[c]
3			91[c]
4			94[c]
5			81[d]
6			93[d]
7			93[d]
8			89[d]

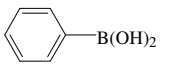
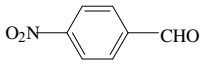
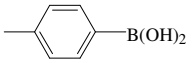
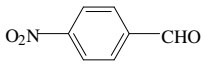
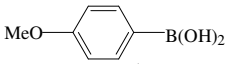
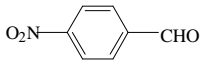
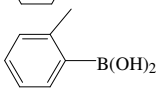
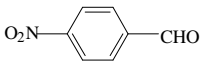
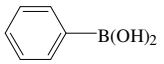
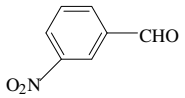
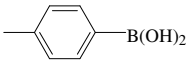
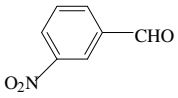
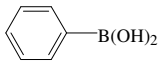
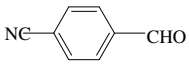
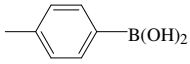
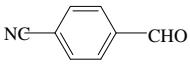
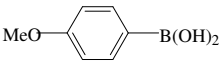
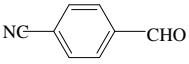
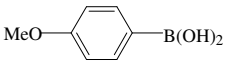
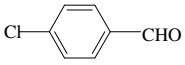
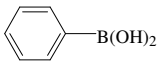
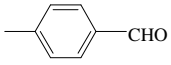
[a] Reaction conditions (not optimized): ketone (1.0 equiv.), arylboronic acid (2.0 equiv.), **36** (5%), K_3PO_4 (1.0 equiv.), toluene (1.5 mL), room termperature. [b] isolated yields. [c] Reaction time: 3h. [d] Reaction time: 22 h.

36 was also employed as the catalyst for the addition reaction of arylboronic acids with aldehydes (Table 4.12). We were pleased to find that the catalytic activity of **36** is much higher than that of the previous palladacycle **9b** which was generated from **9a** and $Pd(OAc)_2$. **36** could efficiently catalyze addition reaction of arylboronic acids with nitroaldehydes at room temperature overnight. We further studied the

reaction of arylboronic acids with other aromatic aldehydes. Complete conversions and high yields were obtained, although the reaction of arylboronic acids with these aldehydes needed longer time to be complete (48 h).

Table 4.12 Palladacycle **36**-Catalyzed Addition of Arylboronic Acids with Aldehydes[a]



entry	Ar-B(OH)$_2$	RCHO	yield (%) [b]
1			98
2			99
3			94
4			91
5			80
6			95
7			86
8			95
9			98
10			80
12			91

[a] Reaction conditions (not optimized): aldehyde (0..25 mmol, 1.0 equiv.), arylboronic acid (1.2-2.0 equiv.),**36**(5%), K_3PO_4(1.0 equiv.) toluene (1 mL), room temperature. [b] isolated yields.

In summary, through the study of $Pd(OAc)_2$/phosphine/$CHCl_3$ and $Pd(OAc)_2$/ferrocenylmethylphosphine catalyst systems for the addition reaction of arylboronic acids with aldehydes, we discovered a new family of highly efficient

palladium catalysts, Type I palladacycles, for the addition of arylboronic acids with carbonyl-containing compounds. Our study suggested that other readily available and air/moisture stable metalacycles including palladacycles might also be highly efficient, practical catalysts for addition reactions. Our study may also lead to the development of asymmetric version of these addition reactions.

Experimental Section:

Chapter Two

General procedure of the synthesis of 14-16: Under N_2, to a mixture of dibromide **10** (1.0 equiv.), 4-tert-butylphenylboronic acid **11**(or **13**, or **15**) (2.2 equiv.), and $Pd(PPh_3)_4$ (0.02 equiv.), and degassed K_2CO_3 solution (1:1 in volume, 10 ml/mmol **10**). The mixture was refluxed overnight. After cooling to room temperature, the reaction mixture was extracted with diethyl ether. The organic layer was washed with water. The solvent was removed by rota-evaporation. Chromatography on silica gel and vacuum drying yielded the products as yellow solids.

14: ^{1}H NMR ($CDCl_3$, 200 MHZ) δ 7.69 (t, J = 1.6 Hz, 2H, 1H), 7.59(d, J = 1.6 Hz, 2H), 7.58 (d, J = 8.6 Hz, 4H), 7.47 (d, J = 8.6 Hz, 4H), 5.58 (d, J = 3.2 Hz, 1H), 4.3 ~ 4.2 (M, 9h), 2.54 (d, J = 3.2 Hz, 1H), 1.37 (s, 18H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 150.8, 142.9, 142.5, 142.2, 38.5, 127.3, 126.0, 125.3, 94.5, 72.3, 68.8, 68.6, 67.8, 66.5, 34.8, 31.6

15: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.88(br.s 1H), 7.82(br.s, 6H), 7.75(br.s, 2H), 7.66(d, J = 8.2 Hz, 8H), 7.52(d, J = 8.2 Hz, 8H), 5.63(d, J=2.6, 1H), 4.34(m, 2H), 4.29(s, 5H), 4.22(m, 2H), 2.62(d, J=2.6, 1H),1.39(s, 36H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 150.8, 144.8, 142.4, 142.3, 142.2, 138.5, 127.3, 126.0, 125.5, 125.2, 124.6, 94.7, 72.4, 68.8, 68.6, 67.9, 66.0, 34.8, 31.6

16: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.98(m, 8H), 7.88(m, 5H), 7.82(br.s, 8H), 7.65(d, J=8.4, 16H), 7.49(d, J=8.2, 16H), 5.70 (d, J=3.2, 1H), 4.35 (m, 2H), 4.31(s, 6H), 4.22 (m, 2H), 2.61(d, J=3.2, 1H), 1.38(s, 72H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 150.8, 144.8, 142.9, 142.5, 142.2, 138.5, 131.1, 129.1, 127.3, 126.0, 125.6, 125.3, 94.5, 72.3, 68.8, 68.6, 67.8, 66.5, 34.8, 31.6

Synthesis 24, 25, 11: Diphenylphosphine (2.0 equiv., 10 wt% in hexane) was added in a solution of **14** (or **15**, or **16**, 0.5 mmol) in 5 ml degassed HOAc under N_2. The mixture was stirred at room temperature overnight. The solvents were removed by vacuum. The residue was dissolved in small amount of CH_2Cl_2, and precipitated from

methanol. This process was repeated three times. **24** (or **25**, or **11**) was obtained as a yellow solid.

24: ^{1}H NMR ($CDCl_3$, 200MHz) δ 7.80~7.77 (m, 3H), 7.67(d, J = 8.4, 4H), 7.53(d, J= 8.2, 4H), 7.32~7.26(m, 8H), 7.24~7.17(m, 2H), 4.42(d, J = 7.2Hz, 1H), 4.24(s, 1H), 4.06(s, 1H), 3.88(s, 1H), 3.81(s, 5H), 3.58(s, 1H), 1.39(s, 18H)

^{13}C NMR ($CDCl_3$, 50 MHz) δ 150.6, 143.3(d, J = 10.2 Hz), 141.2, 138.6, 137.8, 137.6, 137.5, 137.2, 134.7(d, J = 20.1 Hz), 133.6 (d, J = 18.6Hz), 132.8, 131.1, 130.8, 129.3, 129.1, 129.0, 128.6, 128.2, 128.1, 127.3, 127.1,125.9, 124.2, 90.4(d, J = 19 Hz), 70.1, 68.7, 68.4,68.2, 68.0, 67.9, 66.7, 34.8, 31.6
^{31}P NMR ($CDCl_3$, 81 MHz, H_3PO_4 as standard) δ 5.49

25: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.82~7.78 (m, 9H), δ 7.70~7.66(m, 8H), δ 7.56~7.52 (m, 8H), δ 7.36~7.17(m, 10H), δ 3.89(s, 9H), δ 1.40(s, 36H)

^{13}C NMR ($CDCl_3$, 50 MHz) δ 150.8, 142.4, 141.7, 138.6, 134.8, 134.4, 134.0, 133.6, 128.4, 128.2, 127.3, 126.1, 125.1, 68.8, 34.8, 31.6

^{31}P NMR ($CDCl_3$, 81 MHz, H_3PO_4 as standard) δ 25.8, 23.6, 22.6, 5.74

11: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.82~7.78(m, 45H), δ 7.68(d, J=8.4, 16H), δ 7.54 (d, J=8.4, 16H), δ 3.89 (s, 9H), δ 2.08(s, 2H) δ 1.40(s, 72H)

^{13}C NMR ($CDCl_3$, 50 MHz) δ 150.8, 142.5, 141.8, 138.6, 137.6, 137.3, 134.8, 134.4, 134.0, 133.6, 131.2, 129.3, 129.1, 128.8, 128.4, 128.2, 128.0, 127.4, 127.1, 126.1, 125.4, 125.2, 124.7, 69.2, 68.8, 69.4, 68.3, 68.2, 66.9, 34.9, 31.7

^{31}P NMR ($CDCl_3$, 81 MHz, H_3PO_4 as standard) δ 5.68

General Procedure for the room temperature Pd(0)/dendrimer ligands-catalyzed Suzuki cross-coupling reaction of aryl bromides or aryl chlorides: To a vial containing ligand (0.03 mmol), $Pd(OAc)_2$ (0.03 mmol), or $Pd_2(dba)_3$ (0.015 mmol), arylboronic acid (1.5 mmol, 1.5 equiv.), KF(3 mmol, 3.0 equiv) was added THF (2.0 ml). After the mixture was stirred at room temperature for ca. 5 min, aryl halide (1.0 mmol) was added by a syringe. The reaction mixture was allowed to stir for 24 h. The reaction was quenched by water and extracted with diethyl ether. The organic layer was washed with brine. Evaporation of solvents and purification of the remaining

mixture by column chromatography on silica gel with ethyl acetate/hexane afforded the biphenyl products.

Chapter Three

Preparation of 1, 1'-bis(1-hydroxy-1-phenylmethyl)ferrocene 31: Ferrocene (5.0g, 27.2mmol) was dissolved in 30ml diethyl ether in 100ml long-necked flask at room temperature. *N,N,N'N'*-tetramethylenediamine (TMEDA) (13ml, 81.6 mmol) was added into the mixture and stirred for 5 minutes followed by adding *n*-Buli (33ml, 1.6 M in hexane, 52.8 mmol). The mixture was stirred for 5 hours before it was cooled to -78 ^{o}C. Under -78 ^{o}C, benzaldehyde (5.5 ml, 54.4 mmol) was added. The mixture was allowed to warm to room temperature and stirred overnight. The reaction was quenched by distilled water, extracted by diethyl ether, washed with brine. Rotate evaporation followed by flash chromatograph by a mixture of hexane and ethyl acetate gave **31** as a yellow solid (6.5 g, 70% yield). m.p.: 119.0~ 120.5^{o}C.

^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.29 ~ 7.16 (m, 10H), 5.49 (s, 1H), 5.42 (s, 1H), 5.04 (br.s, 1H), 5.01 (br.s, 1H), 4.39 ~ 4.00 (m, 8H)

^{13}C NMR ($CDCl_3$, 50 MHz) δ 144.19, 143.71, 128.23, 128.12, 127.33, 127.28, 126.15, 126.13, 93.92, 93.42, 72.62, 71.68, 68.20, 68.06, 67.83, 67.57, 67.09, 66.64, 66.60, 66.35

UV (diethyl ether): 225.0, 254.2 nm.

Anal. Calcd for $C_{24}H_{22}FeO_2$: C, 72.38%; H, 5.53%. Found: C, 72.24%; H, 5.66%.

Preparation of bisphosphine 32: To a solution of **31** (0.394 g, 1 mmol) in CH_2Cl_2 (5 ml), HOAc (2 ml) was added under N_2. $HPPh_2$ (9.3 ml, 10 wt% in hexanes,) was syringed into the flask. The mixture was stirred overnight at room temperature. The solvents were evaporated under vacuum. The residue was dissolved in a small amount of degassed CH_2Cl_2, excessive amount of MeOH was added. The mixture was separated by centrifuge. The precipitate was obtained by syringing out the solvent.

The process was repeated three times. After drying under vacuum, **32** was obtained as a yellow powder (0.331 g, 47% yield).

^{1}H NMR (CD_2Cl_2, 150 MHz) δ 7.38 ~ 7.13 (m, 30H), 4.17 (d, J=1.5, 0.7H), 3.97 (d, J=1.5, 1.4H), 3.85 (s, 1.4H), 3.50 (s, 0.9H), 3.47 (s, 1.8H), 3.40 (s, 1.3H), 3.37 (s, 0.7H), 3.13 (s, 0.8H), 2.88 (s, 1.4H).

^{13}C NMR ($CDCl_3$, 50 MHz): δ 142.11, 141.90, 134.59, 134.19, 133.27, 132.91, 129.50, 129.31, 128.74, 128.22, 128.03, 127.92, 127.80, 127.66, 126.27, 70.22, 67.00, 67.71, 67.15, 47.26, 46.93.

^{31}P NMR ($CDCl_3$, 81 MHz, H_3PO_4 as standard) δ 5.182, 4.677

UV (CH_2Cl_2): 221.7, 252.2 nm.

Anal. Calcd. for $C_{48}H_{40}FeP_2$: C, 78.48%; H, 5.45%. Found: C, 78.04%; H, 5.47%.

Preparation of dibromide 28: *n*-Buli (9.2 ml, 1.6M in hexanes, 15 mmol) was added to a solution of TMEDA (2.3 ml, 15 mmol, 2.3 ml) in diethyl ether (5 ml) at room temperature, and the resulting solution was allowed to stir for 5 min. This solution was then added to a solution of ferrocene (0.920g, 5 mmol) in diethyl ether (10 ml) at room temperature. The reaction mixture was allowed to stir for 12 h, orange suspension was observed. The reaction mixture was then cooled to -78℃, and a solution of 4-Bromobenzaldehyde (1.85 g, 10 mmol) in THF (5 ml) was added by a syringe. The reaction mixture was allowed to warm to room temperature. The reaction was quenched by water after stirring overnight. The organic phase was extracted by diethyl ether, washed with brine and the solvent was removed by rota-evaporator. Purification by flash chromatography provided **28** as a yellow solid (1.8g, 65% yield). m.p.: 152.5~ 154.5^{o}C.

^{1}H NMR ($CDCl_3$, 150 MHz): δ 7.48 (d, J=2.1, 2H), 7.47 (d, J= 2.1, 2H), 7.32 (d, J= 2.1, 2H), 7.30 (d, J= 2.1, 2H), 5.91 (d, J=0.9, 1.6H), 5.86 (d, J=1.0, 2.4H), 5.45 (d, J=

1.0, 2.4H), 5.43 (d, J=0.9, 1.6H), 4.26 (s, 0.8H), 4.19 (s, 1.2H), 4.13 (s, 1H) 4.06 ~ 4.05 (m, 5H).

^{13}C NMR ($CDCl_3$, 50 MHz) δ 145.05, 144.94, 130.74, 128.36, 119.36, 119.69, 93.84, 93.61, 70.42, 69.99, 68.10, 67.97, 67.89, 67.77, 67.08, 66.95, 66.78, 66.59, 66.43, 66.30, 66.15

UV (diethyl ether): 235.0, 260.0 nm, 441.7nm.

Anal. Calcd for $C_{24}H_{20}Br_2FeO_2$: C, 51.84%; H, 3.61%; Br, 28.50%. Found: C, 52.24%; H, 3.63%; Br, 28.16%.

Preparation of polymer 33: To a mixture of dibromide **28** (0.552g, 1.0mmol) and diboronic acid (0.374g, 1.02mmol) in THF/K_2CO_3 (8ml/8ml) was added $Pd(PPh_3)_4$(23mg, 0.002mmol) under N_2, the mixture was refluxed for 24 hours and bromobenzene was added to cap the end group. After another 12 hours refluxing, the reaction mixture was cooled to room temperature and extracted by methylene chloride. The organic layer was washed by brine, and solvent was evaporated by using a rota-evaporator. The residue was redissolved in methylene chloride and precipitated from MeOH. The solvent was removed by a syringe. The dissolution-precipitation-syringe procedure was repeated three more times. After drying under vacuum, **33** was obtained as a yellow solid in 96% yield.

GPC (polystyrene standards), MW=8,100, Mn=3,900 (PDI=2.08).

^{1}H NMR ($CDCl_3$, 200 MHz) δ7.25 (br.s, 8H), 6.60 (br.s, 2H), 5.67 (br.d, J=9.6, 2H), 4.53 (br.s, 2H), 4.17 (br. s, 6H), 3.65 (br.s, 4H), 1.60 (br.s, 4H), 1.25 (br.s, 12H), 0.88 (br.s, 6H).

^{13}C NMR ($CDCl_3$, 50 MHz) δ149.60, 142.19, 137.27, 131.55, 129.45, 127.85, 125.32, 115.68, 94.71, 93.86, 73.0, 72.07, 68.60 ~65.30 (m), 31.54, 29.34, 25.77, 22.59, 14.09

UV (CH_2Cl_2): 240.8, 275.8, 327.5 nm.

Anal. Calcd for $(C_{42}H_{48}FeO_4)_n$: C, 74.99%; H, 7.19%. Found: C, 74.34%; H, 7.09%. The relative large difference between the theoretical value and the experimental one is believed to be caused by the end groups.

Preparation of polymer 29: To a solution of polymer **33** (0.67 g, 1 mmol based on repeating unit) in CH_2Cl_2 (5 ml), HOAc (2 ml) was added under N_2. $HPPh_2$ (1.64 ml, 10 wt% in hexanes) was syringed into the flask. The mixture was stirred overnight at room temperature. The solvents were evaporated under vacuum. The residue was dissolved in a small amount of degassed CH_2Cl_2 and precipitated from degassed MeOH. The process was repeated four more times. The precipitate was obtained by syringing out the solvent. After drying under vacuum, **29** was obtained as a yellow solid (0.534 g, 53% yield).

GPC (polystyrene standards), MW=4,300, Mn=3,100 (PDI=1.41).

^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.90 ~ 6.61 (br.m, 30H), 4.40 ~ 3.00 (br.m, 12H), 1.58 (br.s, 4H), 1.23 (br.s, 12H), 0.84 (br.s, 6H)

^{13}C NMR ($CDCl_3$, 50 MHz) δ 150.34, 140.38, 137.25, 136.30, 134.70, 134.29, 133.25, 132.88, 131.46, 130.24, 129.10, 129.41, 128.39, 127.81, 125.92, 116.29, 89.83, 88.45, 72.24, 71.43, 70.43, 69.52, 68.89, 68.40, 67.82, 66.00, 46.70, 31.49, 29.42, 25.78, 22.62, 14.14.

^{31}P NMR ($CDCl_3$, 81 MHz, H_3PO_4 as standard) δ 5.228, 4.723

UV (CH_2Cl_2): 235.2, 274.7, 326.5 nm.

Anal. Calcd for $(C_{66}H_{66}FeO_2P_2)_n$: C, 78.56%, H, 6.59%. Found: C, 77.08%; H, 6.61%. The relative large difference between the theoretical value and the experimental one is believed to be caused by the end groups.

Preparation of dibromide 34: *n*-Buli (18.75 ml, 1.6M in hexane, 30 mmol) was added to a solution of TMEDA (4.6 ml, 30 mmol) in diethyl ether (8 ml) at room

temperature and the resulting solution was allowed to stir for 5 minutes. The solution was then added to a suspension of ferrocene (1.84 g, 10 mmol) in diethyl ether (30 ml) at room temperature. The reaction mixture was allowed to stir for 12 h. Orange suspension was observed. The reaction mixture was then cooled to -78 ^{o}C and 3-bromobenzaldehyde (2.33 ml, 20 mmol) was added. The reaction mixture was warmed to room temperature and stirred for 12 hours. The reaction was quenched with distilled water and the mixture was extracted with ethyl acetate, washed with brine. Rotate evaporation followed by flash chromatography by a mixture of hexane and ethyl acetate provided **34** as a yellow solid (3.3 g, 60 %).

^{1}H NMR ($CDCl_3$, 150 MHZ) δ 7.46, 7.38 (s, s, 2H), 7.32, 7.27 (d, J=2.0, d, J=2.0, 2H), 7.18, 7.10 (d, J=1.8, d, J=1.8, 2H), 7.09, 7.02 (t, J=2.0, t, J=2.0, 2H), 5.42, 5.37(s, s, 2H), 5.46, 5.27 (s, s, 2H), 4.37~ 4.09 (m, 8H).

^{13}C NMR ($CDCl_3$, 50 HZ) δ146.28, 145.80, 130.48, 129.89, 129.81, 129.16, 129.04, 124.70, 124.67, 122.34, 122.27, 93.39, 92.84, 72.08, 71.18, 68.50, 68.38, 68.20, 67.90, 67.16, 66.71, 66.43, 66.30.

Preparation of polymer 35: To a mixture of dibromide (0.828 g, 1.5 mmol) and diboronic acid (0.56 g, 1.53 mmol) in THF/K_2CO_3 (7 ml/7 ml) was added $Pd(PPh_3)_4$ (46 mg, 0.003 mmol, 2mol%) under N_2, the mixture was refluxed for 27 hours and bromobenzene was added to cap the end group. after another one hour refluxing, the reaction mixture was cooled to room temperature and extracted with methylene chloride. After washing by brine, solvent was evaporated by using a rota-evaporator. The residue was redissolved in methylene chloride and precipitated from MeOH. The solvent was removed by a syringe. The redissolvation-precipitation procedure was repeated three times. After drying under vacuum, **35** was obtained as a yellow solid (0.50 g, 50% yield).

GPC (polystyrene standards): M_W=2,100, M_n=1,300 (PDI=1.58).

^{1}H NMR ($CDCl_3$, 200 MHZ) δ 7.58 ~ 6.85 (m, 10H), 5.63 ~ 5.39 (m, 4H), 4.48 ~ 4.05 (m, 8H), 3.82 (br.s, 4H), 1.61 (br.s, 4H), 1.37 ~ 1.15 (m, 12H), 0.85 (br.s, 6H)

^{13}C NMR ($CDCl_3$, 50 HZ) δ 153.28, 150.14, 146.62, 146.42, 146.20, 145.94, 143.82, 143.69, 143.37, 143.15, 138.27, 132.07, 132.00, 131.90, 130.56, 130.40, 130.28, 129.82, 129.74, 129.23, 129.12, 128.78, 128.66, 128.03, 127.92, 127.53, 127.49, 126.16, 124.74, 122.30, 122.22, 116.20, 93.95, 93.72, 93.63, 93.51, 93.43, 93.27, 93.14, 92.91, 73.06, 72.95, 72.13, 71.92, 71.10, 69.59, 68.32, 68.24,68.18, 68.08, 67.95, 67.86, 67.70, 67.15, 66.80, 66.68, 66.63, 66.48, 66.29, 66.20, 31.46, 29.65, 29.28, 25.71, 22.58, 14.04.

Preparation of polymer 30: To a solution of polymer **8** (0.4 g, 0.6 mmol) in CH_2Cl_2 (5 ml), HOAc (2 ml) was added under N_2. $HPPh_2$ (5.56 ml, 10 wt % in hexanes,) was syringed into the flask. The mixture was stirred overnight at room temperature. The solvents were evaporated under vacuum. The residue was dissolved in a small amount of degassed CH_2Cl_2 and precipitated from degassed MeOH. The process was repeated four more times. The precipitate was obtained by syringing out the solvent. After drying under vacuum, **30** was obtained as a yellow solid (0.26 g, 43% yield).

GPC (polystyrene standards): M_W=2,100, M_n=900 (PDI=2.35).

^{1}H NMR ($CDCl_3$, 200 MHZ): δ 7.56 ~ 6.72 (m, 30H), 4.46 ~ 2.82 (m, 12H), 1.65 (br.s, 4H), 1.25 (br.s, 12H), 0.85 (br.s, 6H)

^{13}C NMR ($CDCl_3$, 50 HZ): δ 152.17, 143.79, 140.20, 139.42, 138.69, 137.05, 136.30, 136.17, 135.50, 135.17, 135.05, 134.30, 133.28, 133.03, 132.47, 132.39, 131.57, 131.16, 130.81, 130.73, 130.52, 130.40, 130.26, 129.96, 129.81, 129.53, 126.66, 123.81, 123.60, 118.30, 91.85, 91.31. 72.41, 71.64, 70.71, 70.46, 70.05, 69.65, 69.30, 68.75, 68.60, 48.46, 48.11, 33.51, 31.34, 27.72, 24.57, 15.79

^{31}P NMR ($CDCl_3$, 81 MHz, H_3PO_4 as standard): δ 5.89, 5.14, 4.69.

General procedure for $Ni(COD)_2$/ligand-catalyzed Suzuki Cross-coupling reactions of aryl chloride with arylboronic acids: To a vial containing **29** or **30** (45mg, 0.0045mmol), $Ni(COD)_2$ (4.12mg, 0.0015mmol), arylboronic acid (91 mg,

0.75mmol), K_3PO_4 (318 mg, 1.5 mmol) was added THF (2.0ml). After the mixture was stirred at room temperature for ca. 5 min, aryl chloride (0.0613ml, 0.5mmol) was added by a syringe. The reaction mixture was allowed to reflux for 24 h. the reaction was quenched by water and extracted with diethyl ether. The organic layer was washed with brine. Evaporation of solvents and purification of the residue by column chromatography on silica gel with ethyl acetate/hexane afforded the biphenyl products.

4-Methylbiphenyl: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.57 (d, J=7.2Hz, 2H), 7.49 (d, J=7.8 Hz, 2H), 7.41 (t, J=7.8 Hz, 2H), 7.31 (t, J=7.8, 1H), 7.24 (d, J=7.8 Hz, 2H), 2.384 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 141.12, 138.32, 136.98, 129.45, 128.68, 127.14, 126.96, 21.08

4-Methoxybiphenyl: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.55~7.52 (m, 4H), 7.41 (t, J=7.8 Hz, 2H), 7.30 (t, J=7.8, 1H), 6.97 (d, J=9.0 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 159.08, 140.77, 133.72, 128.69, 128.12, 126.70, 126.66, 114.15, 55.30

4-Acetylbiphenyl: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.01 (d, J=8.7 Hz, 2H), 7.66 (d, J=8.7 Hz, 2H), 7.60 (d, J=7.2 Hz, 2H), 7.45 (t, J=7.2 Hz, 2H), 7.38 (t, J=7.2 Hz, 1H), 2.61 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 197.64, 145.64, 139.73, 135.72, 128.87, 128.83, 128.15, 127.17, 127.11, 26.58

4-Methoxy-4'-methylbiphenyl: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.50 (d, J=8.4 Hz, 2H), 7.44 (d, J=8.4 Hz, 2H), 7.22 (d, J=8.4 Hz, 2H), δ 6.96(d, J=8.4 Hz, 2H), δ 3.84 (s, 3H), 2.38 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 158.89, 137.93, 136.32, 133.71, 129.41, 127.93, 126.56, 114.12, 55.31, 21.03

4, 4'-dimethylbiphenyl: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.46 (d, J=7.8 Hz, 4H), 7.22 (d, J=7.8 Hz, 4H), 2.397 (s, 6H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 138.26, 136.67, 129.41, 126.78, 21.06

4-Methoxy-2'-methylbiphenyl: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.25 ~7.21 (m, 6H), 6.94 (d, J=9.0, 2H), 3.83 (s, 3H), 2.27 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 158.46, 141.50, 135.43, 134.32, 130.26, 130.21, 129.86, 126.93, 125.72, 113.44, 55.21, 20.51

4-Methyl-2'-methylbiphenyl: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.23~ 7.21 (m, 8H), 2.39 (s, 3H), 2.27 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 141.91, 139.06, 136.40, 135.42, 130.32, 129.89, 129.11, 128.82, 127.11, 125.79, 21.22, 20.56

General procedure for 29/Ni(acac)$_2$-catalyzed cross-coupling reactions of aryl fluorides with Grignard reagents: In dry box, to a schlenk flask containing a magnetic stir bar was added Ni(acac)$_2$ (12.8 mg, 0.05 mmol), bispolymer ligand **29** (50 mg, 0,05 mmol based on repeating unit) and aryl fluorides(0.106 ml, 1.0 mmol). After the flask was taken out of the dry box, it was vacuumed by oil pump and filled with N_2. The vacuum/filling procedure was repeated 3 times before the aryl Grignard reagent (1.5 ml, 1M in THF, 1.5 mmol.) and dry THF (1.5ml) was added. The mixture was stirred under N_2 at room temperature for 22-24 hours. The reaction was quenched by distilled water, extracted by diethyl ether. After removing the solvent by rota-evaporator, the crude materials obtained was checked by ^{1}H NMR. The product was isolated by column chromatography on silica gel with ethyl acetate/hexane as eluent.

2-(4-methoxyphenyl)pyridine ^{1}H NMR ($CDCl_3$, 600 MHZ) δ 8.65 (d, J=5.4, 1H), 7.95 (d, J=8.4, 2H), 7.71 (t, J=5.4, 1H), 7.66 (d, J=7.0, 1H), 7.16 (t, J=7.0, 1H), 7.00 (d, J=8.4, 2H), 3.86 (s, 3H). ^{13}C NMR (CDCl3, 150 MHZ) δ 160.44, 157.11, 149.54, 136.61, 132.04, 128.13, 121.37, 119.76, 114.10, 55.33

General procedure for Ni(COD)$_2$/ligand-catalyzed Cross-coupling reactions of alkenyl tosylates with arylboronic acids: To a vial containing **29** (45mg, 0.0045mmol), Ni(COD)$_2$ (4.12mg, 0.0015mmol), alkenyl tosylates (0.5 mmol), arylboronic acid (0.75mmol), K_3PO_4 (318 mg, 1.5 mmol) was added THF (2.0ml). After the mixture was stirred at room temperature for ca. 5 min, aryl chloride (0.0613ml, 0.5mmol) was added by a syringe. The reaction mixture was allowed to reflux for 24 h. the reaction was quenched by water and extracted with diethyl ether. The organic layer was washed with brine. Evaporation of solvents and purification of

the residue by column chromatography on silica gel with ethyl acetate/hexane afforded the biphenyl products.

4-phenylcoumarin: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.560 ~ 7.498 (m, 5H), 7.470~7.454 (m, 2H), 7.422 (d, J=8.4 Hz, 1H), 7.253~7.227 (m, 1H), 6.391 (s, 1H). ^{13}C NMR ($CDCl_3$, 150.868 MHz) δ 160.982, 155.891, 154.399, 135.410, 132.156, 129.916, 129.098, 128.660, 127.234, 124.398, 119.195, 117.542, 115.400

4-(4-methylphenyl)coumarin ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.563 ~ 7.531 (m, 2H), 7.411 (d, J=8.4 Hz, 1 H), 7.369 ~ 7.331 (m, 4 H), 7.231 (t, J=7.5 Hz 1H), 6.370 (s, 1H), 2.459 (s, 3H). ^{13}C NMR ($CDCl_3$, 150.868 MHz) δ 161.101, 155.958, 154.420, 140.132, 132.521, 132.058, 129.776, 128.628, 127.280, 124.324, 119.300, 117.528, 115.112, 21.597

4-phenyl-2(5H)-furanone ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.519 ~ 7.463 (m, 5H), 6.382 (s, 1H), .5.233 (s, 2H). ^{13}C NMR ($CDCl_3$, 150.868 MHz) δ 174.111, 164.152, 132.030, 129.864, 129.541, 126.680, 113.269, 71.254

Chapter Four

Preparation of Palladacycle 9b from 9a and $Pd(OAc)_2$: A mixture of the ferrocenylphenyldiphenylphosphine (342 mg, 0.86 mmol) and palladium acetate (193 mg, 0.86 mmol) was dissolved in 4 ml toluene at room temperature. The mixture was stirred at room temperature. After 10 min, a brown suspension was observed. The solid was collected by vacuum filtration. The crude product was washed with toluene and CH_2Cl_2. After drying under vacuum, **9b** was obtained as a yellow solid (260 mg, 50% yield).

^{31}P NMR: 77.4 (major), 61.1(minor) 60.4(minor).

Preparation of Palladacycle 36: 1-Ferrocenylethyl acetate, prepared from acetic anhydride (1.62 ml, 17.2 mmol), 1-ferrocenylethanol (1.58 g, 6.86 mmol) and 5 ml pyridine at room temperature, was dissolved in 15 ml acetic acid, and diphenylphosphine (27 ml, 10% in hexanes, 11.6 mmol) was added. After the mixture was heated at 110^{o}C for 48 hrs, the volatile stuff including solvent and excess diphenylphosphine was removed by vacuum distillation. The crude 1-ferrocenylethyldiphenylphosphine was directly used for the next step. A mixture of the crude 1-ferrocenylethyldiphenylphosphine (342 mg, 0.86 mmol) and palladium acetate (193 mg, 0.86 mmol) was dissolved in 4 ml toluene at room temperature. The mixture was stirred at room temperature. After 10 min, a brown suspension was observed. The solid was collected by vacuum filtration. The crude product was washed with toluene and CH_2Cl_2. After drying under vacuum, **36** was obtained as a yellow solid (260 mg, 50% yield).

^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.58 (t, J = 9.3 Hz, 2H), 7.94 (t, J = 9.3 Hz, 2H), 7.59 -7.54 (m, 3H), 7.09 (t, J = 7.2 Hz, 1H), 6.77 (t, J = 7.2 Hz, 2H), 4.15-3.99 (m, 4H), 3.78 (br, 4H), 3.70 (m, 1H), 2.22 (s, 3H), 0.69 (dd, J = 7.2 Hz, 16.8Hz, 3H).

^{13}C NMR ($CDCl_3$, 150 MHz) δ 180.63, 134.61(d, J = 12 Hz), 133.55 (d, J = 10.5 Hz), 133.32 (d, J = 45.3 Hz), 130.98, 130.02, 129.25 (d, J = 41.1 Hz), 128.68 (d, J = 10.5Hz), 128.54 (d, J = 10.1 Hz), 100.88 (d, J = 28.5 Hz), 96.08, 70.52, 68.98, 66.27, 62.94 (d, J = 22.1 Hz), 34.64 (d, J = 38.0 Hz), 25.70, 22.06.

^{31}P NMR ($CDCl_3$, 81 MHz, H_3PO_4 as standard): δ 65.20 ppm

Anal. Calcd. for $C_{26}H_{25}O_2FePPd$: C, 55.47%; H, 4.44%; Found: C, 55.52%; H, 4.67%.

General procedure for palladacycle 36-catalyzed Michael addition reactions of arylboronic acids with α, β-unsaturated ketones: To a vial containing α , β - unsaturated ketone (0.5 mmol), arylboronic acid (0.75 - 1.0 mmol), K_3PO_4 (0.5 mmol) and palladacyle **36** (14.5 mg, 0.025 mmol) was added toluene (1.5 ml). After the mixture was stirred at room temperature for 2-4 hrs, the reaction was quenched by adding small amount of water. Column chromatography on silica gel with ethyl acetate/hexane afforded the Michael addition product.

General procedure for palladacycle 36-catalyzed 1, 2-addition reactions of arylboronic acids with aldehydes: To a vial containing aldehyde (0.5 mmol), arylboronic acid (0.75 - 1.0mmol), K_3PO_4 (0.5 mmol) and palladacycle **30** (14.5 mg, 0.025 mmol) was added toluene (2.0 ml). After the mixture was stirred at room temperature for 24-48 hrs, the reaction was quenched by adding small amount of water. Column chromatography on silica gel with ethyl acetate/hexane afforded the 1, 2-addition products.

1,3,3-Triphenyl-1-propanone: 2 ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.93 (d, J = 7.8 Hz, 2H), 7.54 (t, J = 7.8 Hz, 1H), 7.43 (t, J = 7.8 Hz, 2H), 7.27 ~ 7.24 (m, 8H), 7.17 (m, 2H), 4.83 (t, J = 7.2 Hz, 1H), 3.74 (d, J = 7.2 Hz, 2H). ^{13}C NMR (CDCl3, 150 MHz): δ 197.96, 144.12, 137.05, 133.05, 128.57, 128.54, 128.03, 127.82, 126.35, 45.91, 44.71

1,3-Diphenyl-3-(4-methylphenyl)-1-propanone:3 ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.94(d, J = 7.8 Hz, 2H), 7.55 (t, J = 7.8 Hz, 1H), 7.44 (t, J = 7.8 Hz, 2H), 7.26 (m, 4H), 7.15 (d, J = 7.8 Hz, 3H), 7.08 (d, J = 7.8 Hz, 2H), 4.79 (t, J = 7.2 Hz, 1H), 3.72 (d, J = 7.2 Hz, 2H), 2.28 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 198.01, 144.35, 141.10, 137.05, 135.81, 132.98, 129.20, 128.53, 128.49, 128.01, 127.73, 127.63, 126.24, 45.52, 44.75, 20.93.

3-(4-methoxyphenyl)-1, 3-Diphenyl-1-propanone:4 ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.92 (d, J = 7.8 Hz, 2H), 7.54 (t, J = 7.2 Hz, 1H), 7.43 (t, J = 7.2 Hz, 2H), 7.25 (m, 4H), 7.18 ~ 7.16 (m, 3H), 6.8 (d, J = 8.4 Hz, 2H), 4.77 (t, J = 7.2 Hz, 1H), 3.75 (s, 3H), 3.70 (d, J =7.2 Hz, 2H). 13C NMR (CDCl3, 150 MHz): δ 198.11, 157.99, 144.49, 137.05, 136.23, 133.03, 128.74, 128.56, 128.51, 128.03, 127.70, 126.27, 113.90, 55.18, 45.11, 44.89

1, 3-Diphenyl-3-(2-methylphenyl)-1-propanone: ^{1}H NMR (CDCl3, 600 MHz): δ 7.92 (d, J = 7.8 Hz, 2H), 7.53 (t, J = 7.2 Hz, 1H), 7.42 (t, J = 7.8 Hz, 2H), 7.26 ~ 7.2 (m, 5H), 7.12 ~ 7.09 (m, 4H), 5.02 (t, J = 7.2 Hz, 1H), 3.73 (dd, J =16.8, 7.2 Hz, 1H), 3.68 (dd, J =16.8, 7.2 Hz, 1H), 2.32(s, 3H). 13C NMR (CDCl3, 150 MHz): δ 198.04, 143.75, 141.78, 137.07, 136.42, 133.02, 130.76, 128.56, 128.44, 128.04, 128.00, 126.33, 126.19, 125.99, 45.00, 41.85, 19.88

4, 4-Diphenyl-2-butanone: ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.28 ~ 7.25 (m, 4H), 7.22 (d, J = 7.2 Hz, 4H), 7.17 (t, J = 7.2 Hz, 2H), 4.58 (t, J = 7.8 Hz, 1H), 3.18 (d, J = 7.8 Hz, 2H), 2.07 (s, 3H) ^{13}C NMR (CDCl3, 150 MHz): δ 206.80, 143.82, 128.56, 127.68, 126.42, 49.66, 46.02, 30.62

4-(4-Methylphenyl)-4-phenyl-2-butanone: ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.26 (dd, J= 7.8, 7.2 Hz, 2H), 7.21 (d, J = 7.2 Hz, 2H), 7.16 (t, J = 7.2 Hz, 1H), 7.11 (d, J = 7.2 Hz, 2H), 7.07 (d, J = 7.8 Hz, 2H), 4.54 (t, J = 7.8 Hz, 1H), 3.15 (d, J = 7.8 Hz, 2H), 2.28 (s, 3H), 2.06 (s, 3H). 13C NMR (CDCl3, 150 MHz): δ 206.94, 144.06, 140.80, 135.94, 129.24, 128.53, 127.60, 127.52, 126.33, 49.74, 45.67, 30.60, 20.92

4-(4-Methoxyphenyl)-4-phenyl-2-butanone: ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.26 (t, J= 7.2 Hz, 2H), 7.20 (d, J = 7.2 Hz, 2H), 7.16 (t, J = 7.2 Hz, 1H), 7.13 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.4 Hz, 2H), 4.53 (t, J = 7.8 Hz, 1H), 3.75 (s, 3H), 3.14 (d, J = 7.8 Hz, 2H), 2.06 (s, 3H). 13C NMR (CDCl3, 150 MHz): δ 206.97, 158.06, 144.82, 135.92, 128.61, 128.52, 127.55, 126.32, 113.92, 55.16, 49.86, 45.25, 30.62

4-(2-Methylphenyl)-4-phenyl-2-butanone: ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.24 ~ 7.20 (m, 3H), 7.20 ~ 7.13 (m, 4H), 7.13 ~ 7.09 (m, 2H), 4.78 (t, J = 7.2 Hz, 1H), 3.15 (d, J = 7.2 Hz, 2H), 2.30 (s, 3H), 2.07 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 206.89, 143.47, 141.51, 136.36, 130.78, 128.46, 127.94, 126.43, 126.26, 126.25, 126.04, 49.98, 41.94, 30.65, 19.83.

4-Nitrophenyl(phenyl)methanol: ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.19 (d, J = 8.4 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H), 7.36-7.32 (m, 5H), 5.93 (d, J = 3.0 Hz, 1H), 2.41(d, J = 3.0Hz, 1H) ^{13}C NMR ($CDCl_3$, 150 MHz): δ 150.76, 147.04, 142.63, 128.84, 128.29, 126.99, 126.63, 123.58, 75.39

4-Methylphenyl(4-nitrophenyl)methanol: ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.18 (d, J= 8.4 Hz, 2H), 7.57 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 7.8 Hz, 2H), 7.17 (d, J = 7.8 Hz, 2H), 5.89 (s, 1H), 2.34 (s, 3H), 2.28 (br.s, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 150.91, 147.11, 139.85, 138.30, 129.61, 126.97, 126.67, 123.62, 75.36, 21.11

4-Methoxyphenyl(4-nitrophenyl)methanol: ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.16 (d, J= 8.4 Hz, 2H), 7.55 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 7.8 Hz, 2H), 6.87 (d, J = 7.8 Hz, 2H),5.86(s, 1H), 3.79 (s, 3H), 2.37 (s, 1H) ^{13}C NMR ($CDCl_3$, 150 MHz): δ 159.51, 151.06, 146.99, 134.96, 128.06, 126.90, 123.54, 114.21, 74.99, 55.26

2-Methylphenyl(4-nitrophenyl)methanol: ^{1}H NMR ($CDCl_3$, 600 MHz): δ 8.13 (d, J =8.4 Hz, 2H), 7.48 (d, J = 8.4 Hz, 2H), 7.30 (d, J = 6.6 Hz, 1H), 7.212 (m, 2H), 7.16 (d, J =6.6 Hz, 1H) 6.05 (s,1H), 2.63 (s, 1H), 2.28 (s, 3H) ^{13}C NMR ($CDCl_3$, 150 MHz): δ 150.21, 147.00, 140.33, 135.54, 130.95, 128.26, 127.46, 126.90, 126.43, 123.49, 72.56, 19.29

3-Nitrophenyl(phenyl)methanol: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.26 (s, 1H), 8.08 (d, J = 7.8 Hz, 1H), 7.68 (d, J = 7.8 Hz, 1H), 7.46 (t, J = 7.8 Hz, 1H), 7.36 ~ 7.33 (m, 4H), 7.31 ~ 7.27 (m, 1H), 5.88 (s, 1H), 2.51 (s, 1H) ^{13}C NMR ($CDCl_3$, 150 MHz): δ 148.30, 145.74, 142.72, 132.42, 129.32, 128.90, 128.33, 126.60, 122.38, 121.26, 75.34

4-Methylphenyl(3-nitrophenyl)methanol: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.27 (s, 1H), 8.09 (d, J = 7.8 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.48 (t, J = 7.8 Hz, 1H), 7.23 (d, J = 7.8 Hz, 2H), 7.16 (d, J = 7.8, 2H), 5.87 (s, 1H), 2.43 (s, 1H), 2.33 (s, 3H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 148.30, 145.94, 139.90, 138.20, 132.36, 129.58, 129.26, 126.59, 122.28, 121.21, 75.18, 21.09

4-Cyanophenyl(phenyl)methanol: ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.63 (d, J = 7.5 Hz, 2H), 7.52 (d, J = 7.5 Hz, 2H), 7.38- 7.26 (m, 5H), 5.88 (d, J = 3.0 Hz, 1H), 2.36 (d, J = 3.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 150 MHz): δ 148.81, 142.77, 132.22, 128.83, 128.25,126.96, 126.64, 118.77, 111.08, 75.58

4-Cyanophenyl(4-methylphenyl)methanol: ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.58 (d, J = 8.4 Hz, 2H), 7.48 (d, J = 7.8 Hz, 2H), 7.19 (d, J = 7.8 Hz, 2H), 7.14 (d, J = 8.4 Hz, 2H), 5.79 (s, 1H), 2.54 (s, 1H), 2.32 (s, 3H) ^{13}C NMR ($CDCl_3$, 150 MHz): δ 149.04, 139.91, 138.06, 132.14, 129.47, 126.88, 126.60, 118.80, 110.89, 75.37, 21.06

4-Cyanophenyl(4-methoxyphenyl)methanol: ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.58 (d, J = 8.2 Hz, 2H), 7.47 (d, J = 8.2 Hz, 2H), 7.21 (d, J = 8.6 Hz, 2H), 6.85 (d, J = 8.6 Hz, H), 5.78 (d, J = 3.0 Hz, 1H), 3.77 (s, 3H), 2.71 (d, J = 3.0 Hz, 1H). ^{13}C NMR

($CDCl_3$, 150 MHz): δ 159.38, 149.17, 135.06, 132.10, 128.01, 126.83, 118.80, 114.11, 110.78, 75.02, 55.22

4-Chlorophenyl(4-methoxyphenyl)methanol: ^1H NMR ($CDCl_3$, 600 MHz): δ 7.30 (br. S, 4H), 7.25 (d, J = 8.4 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 5.77 (d, J = 3.0 Hz, 1H), 3.77(s, 3H), 2.19 (d, J = 3.0 Hz, 1H). 13C NMR (CDCl3, 150 MHz): δ 159.18, 142.42, 135.74, 133.04, 128.47, 127.87, 127.71, 113.96, 75.10, 55.25

4-Methylphenyl(phenyl)methanol: ^1H NMR ($CDCl_3$, 200 MHz): δ 7.35 - 7.24 (m, 7H), 7.14 (d, J = 7.6 Hz, 2H), 5.81 (d, J = 3.2 Hz, 1H), 2.32 (s, 3H), 2.21 (d, J = 3.2 Hz, 1H). 13C NMR (CDCl3, 150 MHz): δ 143.91, 140.91, 137.25, 129.15, 128.42, 127.42, 126.48, 126.40, 76.05, 21.09

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