Synthesis of cobalt-containing monodentate phosphine ligand and application toward Suzuki cross-coupling reactions

Fung-E Hong *, Yi-Jung Ho, Yu-Chang Chang, Yi-Luen Huang

Department of Chemistry, National Chung-Hsing University, Taichung 40227, Taiwan

Abstract

A bulky, dicobalt complexed, mono-dentate phosphine, $[(\mu\text{-}PPh_2CH_2PPh_2)Co_2(CO)_4](\mu,\eta\text{-}PhC\equiv CPCy_2)$ (**4**), was prepared from the reactions of the bis(diphenylphosphino)methylene (dppm)-bridged dicobalt complex $Co_2(CO)_6(\mu\text{-}Ph_2PCH_2PPh_2)$ (**2**) with $PhC\equiv CPCy_2$ (**3**). Combination of **4** and $Pd(OAc)_2$ (1:1) gave an active catalyst for the palladium-catalyzed Suzuki coupling of aryl bromides with phenylboronic acid; the catalytic reactions can be performed even under low catalyst loadings (0.1–0.001 mol% **4**/$Pd(OAc)_2$). Compound **4** has been proved to be an authentic and effective mono-dentate phosphine ligand. Crucial factors such as **4**/$Pd(OAc)_2$ ratio, base being used, solvent volume, temperature, and electronic variation of the aryl bromides in reactions were also investigated and results are reported.
© 2004 Elsevier B.V. All rights reserved.

Keywords: Suzuki reaction; Palladium complex; Bulky phosphine ligand; Cobalt-containing complex; Alkyne-bridged dicobalt complex; Homogeneous catalysis

1. Introduction

Many phosphine ligands modified palladium catalysts were known for their notable capabilities in coupling aryl halides with unsaturated organic moieties in a variety of reactions such as Suzuki [1], Heck [2], Stille [3], Sonogashira [4], and etc. In recent years, Suzuki's palladium-catalyzed reaction has received wide acceptance in the field of cross-coupling reaction because of its exceptional capability in making C–C bond from a sp^2 or non-β-hydride-containing electrophile with a boronic acid derivative. Catalytic reaction employed by phosphine modified palladium complex is often benefited from its mild reaction conditions and selectivity in some cases. Consequently, numerous types of phosphines have been developed and their capacities as competent ligands have been demonstrated. It was established mechanistically that a well performed ligand constitutes species typically with either bulky and/or electron-rich character [1b,1e,1g,5]. Therefore, bulky monodentate phosphine ligands, such as tri-*tert*-butyl-phosphine [1a,1b,2a,2b,3a,3b,6], biphenyl-2-yl-di-*tert*-butyl-phosphine, biphenyl-2-yl-dicyclohexyl-phosphine [1c,1d,1e,1f,7], and more recently even a ferrocene derivative mono- or di-alkyl-phosphino-pentaphenyl-ferrocene [1g,2c,8], have been widely applied in Suzuki's palladium-catalyzed reaction. By its nature, the metal-containing phosphine ligand such as di-phenyl-phosphino-pentaphenyl-ferrocene, dppf, guarantees the bulkiness. In general, the catalytic performances are satisfactory while using these types of ligands. One of the most admired advantages of using dppf-like ligands is the flexibility of the biting angle which is caused by the free rotation of the two phosphino-containing Cp rings. By that way, it is possible for the ligand to adjust automatically to a proper biting position toward the targeted metal and make a firm chelation. However, there are

---

* Corresponding author. Tel./fax: +886 4 22862547.
  E-mail address: fehong@dragon.nchu.edu.tw (Fung-E Hong).

several annoying side effects accompanied with the advantages were reported as well. One of them is that dppf-like ligands might coordinate to more than one metal centers at the same time thereby causes the decaying of the ligand's reactivity. Therefore, we sought to develop a new type of metal-containing phosphine ligands that would be bulky and electron-rich in nature [1g,9].

Our previous works had demonstrated that several alkyne-bridged, dicobalt complexed, monodentate phosphines, $[(\mu\text{-}PPh_2CH_2PPh_2)Co_2(CO)_4][\mu,\eta\text{-}RC\equiv CPPh_2]$ (**1a**: R = Ph; **1b**: R = CMe₃; **1c**: R = SiMe₃), acted as potential bulky ligands in the palladium-catalyzed Suzuki coupling reaction [10].

1a: R=Ph
1b: R=CMe₃
1c: R=SiMe₃
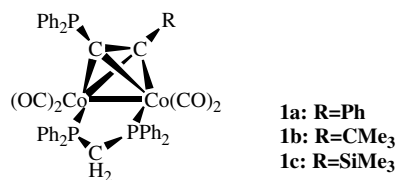
It is known that a palladium complex is more air-stable when it is coordinated by a phosphine with cyclohexyl substituent than that of *tert*-butyl one [1e]. The former complex is also allowed for higher turnover numbers in catalytic reaction, and run even at low catalyst loading [1e]. Therefore, a bulky, dicobalt complexed, phosphine with dicyclohexyl substituents on the phosphorous atom was designed and synthesized and employed as a monodentate phosphine ligand in the palladium-catalyzed Suzuki cross-coupling reactions. Herein some remarkable results are reported.

2. Results and discussion

2.1. Preparation of cobalt-containing monodentate phosphine ligands

Reaction of a dppm-bridged dicobalt compound $[Co_2(CO)_6(\mu\text{-}P,P\text{-}PPh_2CH_2PPh_2)]$ (**2**) [11] with one molar equivalent of alkynyl phosphine $PhC\equiv CPCy_2$ (**3**) [12] in toluene at 80 °C afforded alkyne-bridged dicobalt compound $[(\mu\text{-}PPh_2CH_2PPh_2)Co_2(CO)_4][\mu,\eta\text{-}PhC\equiv CPCy_2]$ (**4**). (Scheme 1). During the chromatographic processes, an oxidized complex, $[(\mu\text{-}PPh_2CH_2PPh_2)Co_2$

$(CO)_4](\mu,\eta\text{-}PhC\equiv CP(=O)Cy_2)$ (**5**), was obtained as well along with **4**. Both compounds **4** and **5** were characterized by spectroscopic means as well as by X-ray diffraction methods (Table 1).

In ¹H NMR, there are two distinct chemical shifts 3.32 and 4.25 ppm were being observed for the methylene protons of **4**, whereas the ³¹P NMR spectrum displays two sets of singlet in the ratio of 2:1 at the chemical shifts of 38.5 and 16.8 ppm, respectively, for three phosphorous atoms. Similar observations of spectroscopic data are perceived in the case of **5**. In ¹H NMR, a large downfield shift for one of the methylene protons at 5.96 ppm is observed due to the weak intramolecular hydrogen bonding between the oxide and the adjacent methylene proton [10]. The ³¹P NMR spectrum of **5** shows two singlets in the ratio of 1:2 at 50.2 and 36.0 ppm for three phosphorous atoms and large downfield shifts are observed for the oxidized phosphorous atoms.

The ORTEP diagram for **4** is presented in Fig. 1. As shown, the phenyl rings of the bridged alkyne are pointed away from the center of the molecule to prevent severe steric hindrance. All of the coordinated carbonyl ligands are situated at the terminal positions. Interestingly, the coordinated dppm ligand and the substituent –PCy₂ are located on the opposite sides of molecule to minimize the steric effect among the bulky dicyclohexyl group. Similar structural pattern is observed for **5** as dipected in Fig. 2. The presumption of intramolecular hydrogen bonding between the oxygen atom (of the oxidized phosphorus) and the methylene proton (of the coordinated dppm) is not validated in this solid state structure. Nevertheless, a weak intramolecular interaction might be achieved through fluxional motion of the bridged dppm, which is evidenced by the observation of a large downfield shift in ¹H NMR at 5.96 ppm for **5**.

2.2. Suzuki reaction using cobalt-containing phosphine ligand 4 with Pd complex

Palladium-catalyzed Suzuki's coupling reactions using bromobenzene and phenylboronic acid as reaction substrates were carried out by employing the newly made cobalt-containing phosphine ligand **4**. First, the impact on the yield as a function of the amount of ligand employed was investigated. The catalytic process under investigation is consists of 1.0 mmol of aryl
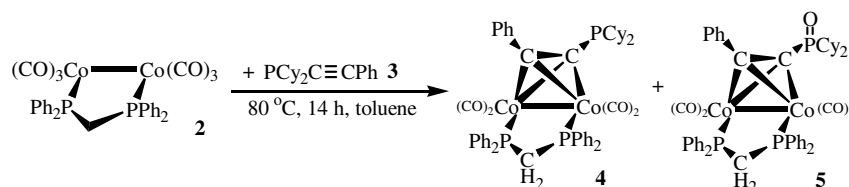
Scheme 1. Synthesis of cobalt-containing monodentate phosphine ligand.

Table 1
Crystal data of **4** and **5**

Formula	$C_{49}H_{49}Co_2O_4P_3 \cdot CH_2Cl_2$	$C_{49}H_{49}Co_2O_5P_3 \cdot CH_2Cl_2$
Formula weight	997.58	1013.58
Crystal systtem	Triclinic	Monoclinic
Space group	$P\bar{1}$	$P2(1)/c$
a (Å)	12.079(2)	13.092(2)
b (Å)	16.950(3)	20.633(4)
c (Å)	24.432(4)	19.234(3)
α (°)	82.501(4)	–
β (°)	83.149(4)	107.634(4)
γ (°)	79.855(4)	–
V (Å^3)	4858.2(14)	4951.5(14)
Z	4	4
D_{calc} (Mg/m^3)	1.364	1.360
λ(Mo Kα) (Å)	0.71073	0.71073
μ (mm^{-1})	0.934	0.919
θ Range (°)	1.84–26.14	1.49–26.01
Observed reflections ($F > 4\sigma(F)$)	3106	1773
Number of refined parameters	1084	559
[a]R_1 for significant reflections	0.0956	0.0580
[b]wR_2 for significant reflections	0.2406	0.1089
[c]Goodness-of-fit	0.972	0.902

[a] $R_1 = |\sum(|F_o| - |F_c|)/|\sum F_o||$.
[b] $wR_2 = \{\sum[w(F_o^2 - F_c^2)]^2 / \sum[w(F_o^2)^2]\}^{1/2}$; $w = 0.1315$ and 0.0500 for **4** and **5**.
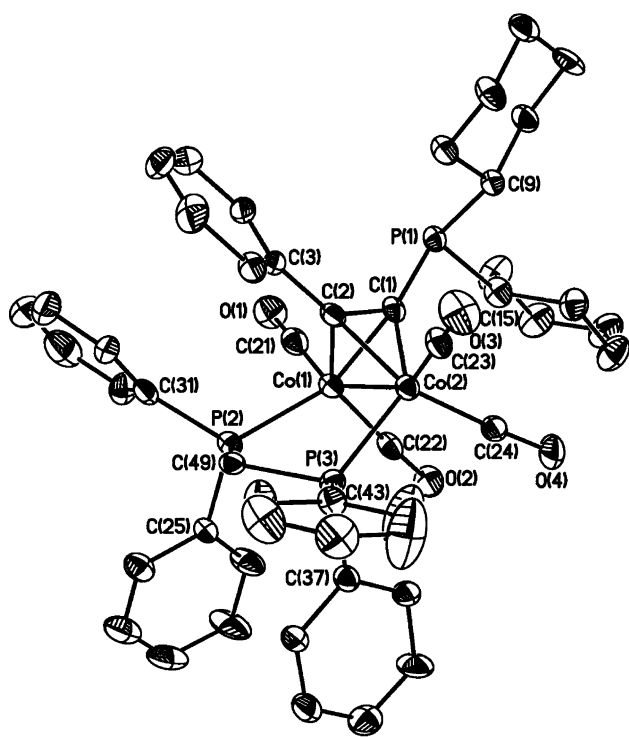[c] $GOF = [\sum w(F_o^2 - F_c^2)^2/(N_{rflns} - N_{params})]^{1/2}$.

Fig. 1. ORTEP drawing of **4**. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (°): Co(1)–C(1) 1.935(9), Co(1)–C(2) 1.968(10), Co(1)–P(2) 2.216(3), Co(1)–Co(2) 2.477(2), Co(2)–C(2) 1.936(10), Co(2)–C(1) 1.971(10), Co(2)–P(3) 2.249(3), P(1)–C(1) 1.826(10), P(2)–C(49) 1.839(10), P(3)–C(49) 1.817(9), C(1)–C(2) 1.343(12), C(2)–C(3) 1.494(13), C(1)–Co(1)–C(2) 40.2(4), P(2)–Co(1)–Co(2) 100.31(9), C(2)–Co(2)–C(1) 40.2(4), P(3)–Co(2)–Co(1) 89.89(9), C(49)–P(2)–Co(1) 109.3(3), C(49)–P(3)–Co(2) 110.4(3), C(2)–C(1)–P(1) 135.5(8), Co(1)–C(1)–Co(2) 78.7(4), C(1)–C(2)–C(3) 137.5(9) Co(2)–C(2)–Co(1) 78.7(4), P(3)–C(49)–P(2) 107.7(5).
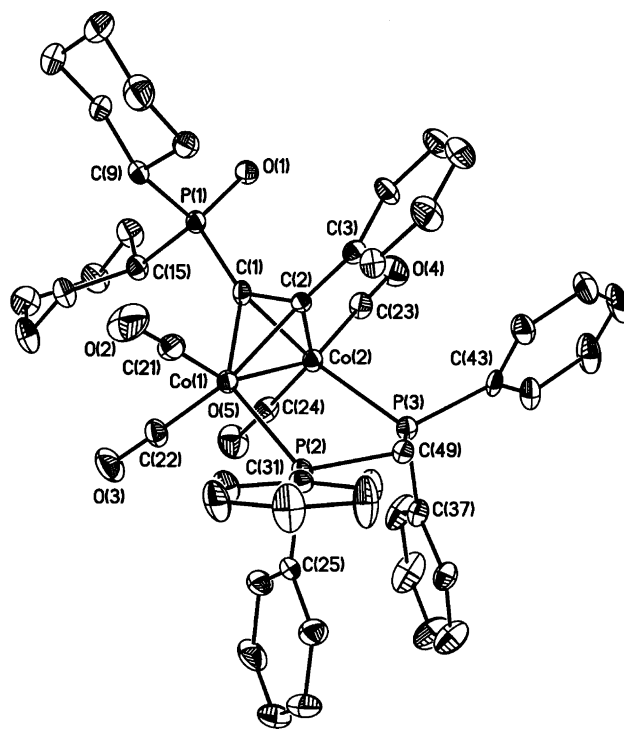

Fig. 2. ORTEP drawing of **5**. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and bond angles (°): Co(1)–C(1) 1.962(7), Co(1)–C(2) 1.948(7), Co(1)–P(2) 2.241(2), Co(1)–Co(2) 2.4759(14), Co(2)–C(2) 1.952(7), Co(2)–C(1) 1.970(7), Co(2)–P(3) 2.225(2), P(1)–O(1) 1.487(5), P(1)–C(1) 1.768(7), P(2)–C(49) 1.847(7), P(3)–C(49) 1.819(6), C(1)–C(2) 1.357(8), C(2)–C(3) 1.498(9), C(1)–Co(1)–C(2) 40.6(2), P(2)–Co(1)–Co(2) 93.80(6), C(2)–Co(2)–C(1) 40.5(2), P(3)–Co(2)–Co(1) 99.18(7), C(49)–P(2)–Co(1) 110.8(2), C(49)–P(3)–Co(2) 109.9(2), C(2)–C(1)–P(1) 138.9(6), Co(1)–C(1)–Co(2) 78.1(3), C(1)–C(2)–C(3) 136.3(7), Co(2)–C(2)–Co(1) 78.8(3), P(3)–C(49)–P(2) 109.3(3).

halide, 1.5 equivalent of phenylboronic acid, 1 mol% of $Pd(OAc)_2$ (based on aryl halide), 1–2 mol% of **4** (based on $Pd(OAc)_2$), 1 mL of toluene, and 3.0 equivalent of KF (based on aryl halide). The reaction mixture was stirred at 40 °C for a designated time period then work-up followed. The reactions were catalyzed smoothly by **4**/$Pd(OAc)_2$ complexes and in the absence of a phosphine complex, the reaction rates were much slower and only partial conversions are observed (Table 2). The conversion of bromobenzene against reaction time is depicted in Fig. 3.

The fact that by increasing the **4**/$Pd(OAc)_2$ ratio from 1:1 to 2:1 resulted in decreasing the yields of the biphenyl is noteworthy since it is generally believed that two molar equivalents of monodentate phosphine ligands are required for an effective catalytic Suzuki reaction [13]. This observation indicates that the optimum active catalyst, while **4** being used as ligand, is a low-coordinated palladium complex; an over-coordinated palladium complex in fact effectively diminishes its catalytic activity. Indeed, many experimental observations point to the same conclusion that the active catalysts are probably monophosphine complexes [14]. In addition, our previous works had demonstrated that a **4**-like ligand, [(μ-$Ph_2PCH_2PPh_2)Co_2(CO)_4(\mu,\eta-PPh_2C\equiv CP(=O)Ph_2)$], is able to act as chelating ligand through its phosphrous

site and one of the cobalt centers [15]. Preference for uni-phosphine ligand coordination is due to an extra, unusual cobalt–palladium direct bonding. Unfortunately, attempts to gain suitable crystallines of the **4**-chelated palladium complex for structural determination were unsuccessful. The crystal growing process always led the formation of the phosphine oxidized product **5**.

Self-coupling of the aryl boronic acid is an unwanted side reaction encountered in palladium complexes, phosphines mediated, catalyzed coupling reactions [16]. When **4** was employed as the coordinating ligand, small amounts of biphenyl were observed (<5% by GC) as a result of aryl–aryl exchange followed by coupling with an aryl boronic acid even at 100 °C.

Subsequently, the impact of the base used on the reaction was examined. Among all the bases used, KF was found to be the most effective while the reaction was run in toluene (Table 3, entry 1) and the other bases such as K_3PO_4 and K_2CO_3 were substantially less effective than KF under the similar conditions (Table 3, entries 2 and 3). The bases Na_2CO_3, Cs_2CO_3, CsF and NEt_3 were failed to promote the reaction and gave very low conversions (Table 3, entries 4–7). Using KF or K_3PO_4 did not notably affect the reaction rates at 100 °C reaction temperature. However, the yields of the reactions carried out at room temperature were lowered when K_3PO_4 was used. In Suzuki's cross-coupling reactions, it is generally believed that Lewis-base facilitate the reaction process by binding it to the organoboron reagent and forming a more reactive four-coordinate "ate" complex, which then transfers the organic moiety to the palladium [1b,1h,1i,17]. For example, the treatment of arylboronic acid with excess KF produces $[Ar–BF_3]^-$, a reactive species which facilitates the aryl group transformation [18]. Interestingly, decreasing the amount of KF (2.0 molar equiv.) used in reaction resulted in increasing yield of the biphenyl (Table 2, entry 6 and Table 3, entry 1). This could be caused by the poor solubility of inorganic base in organic solvent [19].

Table 2
Suzuki coupling reactions employing phosphine **4**[a]

Entry	Pd (mol%)	Ligand (mol%)	Time (h)	Yield (%)
1	1.0	2.0	3	15
2	1.0	2.0	6	17
3	1.0	2.0	24	74
4	1.0	1.0	3	35
5	1.0	1.0	6	48
6	1.0	1.0	24	72
7	1.0	0	24	30

[a] Reaction conditions: 1.0 equiv. aryl bromide, 1.5 equiv. boronic acid, 3.0 equiv. KF, cat Pd(OAc)$_2$, cat ligand **4**, toluene (1 mL/mmol aryl bromide), 40 °C. Yields (average of two or more experiments) of products are determined by GC.
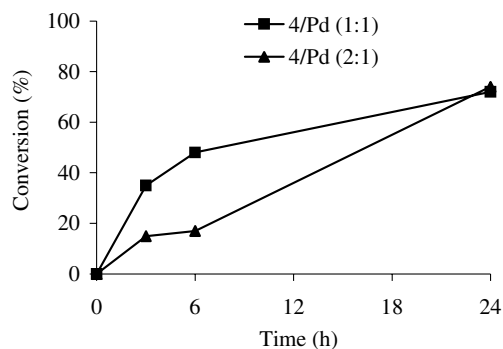

Fig. 3. Conversion of bromobenzene under the conditions listed in Table 2.

Table 3
Suzuki coupling reactions employing phosphine **4** at various bases[a]

Entry	Base	Yield (%)
1	KF	92
2	K_3PO_4	70
3	K_2CO_3	71
4	Na_2CO_3	5
5	Cs_2CO_3	8
6	CsF	10
7	$N(Et)_3$	5

[a] Reaction conditions: 1.0 equiv. aryl bromide, 1.5 equiv. boronic acid, 2.0 equiv. base, 1 mol% Pd(OAc)$_2$, 1 mol% cat ligand **4**, toluene (1 mL/mmol aryl bromide), 40 °C, 24 h. Yields (average of two or more experiments) of compounds are determined by GC.
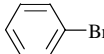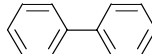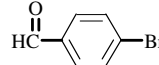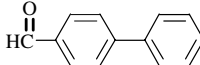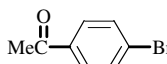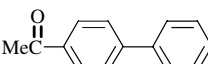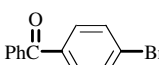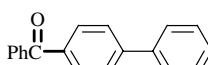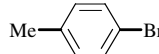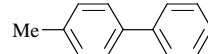
The reaction rate is also greatly affected by the amount of solvent used. For example, the coupling reactions were sluggish (<30% conversion) when 3 mL of toluene was used for the coupling of phenylboronic acid with bromobenzene. However, the yields of the biaryl were greatly improved (>90% conversion) by decreasing the amount of solvent to 1 mL provided that other factors are remained the same. With this small amount of solvent, the reactions are visibly heterogeneous. Using these optimized conditions, the efficiency of 4/Pd(OAc)₂ as catalyst in the reactions were investigated with various substituted arylhalides. As shown in Table 4, the cross-coupling reactions of arylboronic acids with diverse substituted bromobenzenes including electron poor derivatives (Table 4, entries 2–4) were performed efficiently and all completed at 40 °C. As expected, reactions involving electron-rich aryl bromides were considerably slower, nevertheless, heated to 60 °C allowed high conversions (Table 4, entries 5 and 6). While a variety of su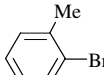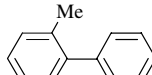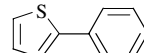bstrates were coupled with the catalyst system of 4/Pd(OAc)₂, reactions employing aryl bromide-containing heteroatom such as 2-bromothiophene did not proceed for completion (Table 4, entry 7). It is possible that the sulfur donor of the reagent or product might have displaced 4 in the coordination and resulted in the formation of a thiophene-containing palladium compound. Several closely related heteroatom-coordinated palla-

dium complexes have been reported with much less reactivities in coupling reactions [20].

The 4/Pd(OAc)₂ catalyst system allows for effective Suzuki coupling reactions at low catalyst loadings and with high turnover numbers (Table 5). Reactions with various ratios of substrate versus catalyst loadings were examined. As high as 99,000 turnover number was achieved when 0.001 mol% 4/Pd(OAc)₂ was employed as catalyst (Table 5, entry 5).

The palladium catalyst derived from phosphine ligand 4 with Cy substituent was noticeably more reactive than that derived from Ph substituent (less bulky and electron-rich ligand) reported earlier [10]. As shown above, both activated and unactivated aryl bromides can be coupled with arylboronic acids in the presence of 1% 4/Pd(OAc)₂ (1:1) complex. These results support the argument that the both electronic and steric factors are important to ligand activity. The reason for the highly active 4/Pd(OAc)₂ catalyst system in Suzuki reaction is not well understood for now. However, we believe that several structural features of this cobalt-containing phosphine ligand are of importance. First, the electron-richness of the phosphine, due to the electron-donating effect from coordinated dppm, facilitates the oxidative addition of the aryl bromide and binds tightly to the metal. Second and the most unique feature of the ligand is that the enhanced solubility of the

Table 4
Suzuki coupling of aryl bromides employing phosphine 4[a]

Entry	Halide	Product	Temp. (°C)	Time (h)	Yeild (%)
1			40	24	92
2			40	16	99
3			40	16	99
4			40	16	99
5			60	16	92
6			60	16	91
7			60	24	70

[a] Reaction conditions: 1.0 equiv. aryl bromide, 1.5 equiv. boronic acid, 2.0 equiv. KF, 1 mol% Pd(OAc)₂, 1 mol% cat ligand 4, toluene (1 mL/mmol aryl bromide); reaction times have not been minimized. Yields (average of two or more experiments) of compounds are determined by GC except entries 5–7 are presented in isolated yields.

Table 5
Suzuki coupling of aryl bromides employing phosphine **4** at various substrates/Pd ratios[a]
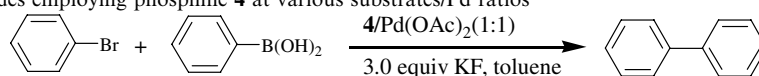
Entry	Pd (mol%)	Temp. (°C)	Time (h)	Yield (%)	TON
1	0.1	40	24	70	700
		60	24	96	960
2	0.05	80	16	85	4250
		80	24	99	4950
3	0.01	80	16	79	7900
		80	24	94	9400
4	0.005	80	24	80	40,000
		100	6	99	49,500
5	0.001	80	24	70	70,000
		100	16	99	99,000

[a] Reaction conditions: 1.0 equiv. aryl bromide, 1.5 equiv. boronic acid, 3.0 equiv. KF, cat Pd(OAc)$_2$, cat ligand **4** (1L/Pd), toluene (1 mL/mmol aryl bromide); reaction times have not been minimized. Yields (average of two or more experiments) of compounds are determined by GC.

cobalt-containing phosphine ligand in organic solvent, due to several attached organic moieties, which prevents the **4**-coordinated palladium intermediates from precipitation in the catalytic cycle. As known, ferrocenyl phosphine is not quite soluble in organic solvent because of its intrinsic ionic character. Third, the bulkiness of the ligand promotes the process of the reductive elimination [21].

2.3. Summary

We have developed a novel and efficient catalyst system of organometallic phosphine ligands for the palladium-catalyzed Suzuki coupling of aryl bromides with phenylboronic acid. The catalytic reactions were performed at ambient condition using low catalyst loadings. Indeed, results of Suzuki reactions employing **4** as the ligand were more efficient than that using **1a**–**c**; no matter what the reaction conditions or the loadings of catalyst employed. Further studies concerning the effectiveness of this class of phosphine ligands for other palladium-catalyzed reactions, as well as mechanistic studies to determine the factors responsible for the high activities of these catalysts are currently underway.

3. Experimental

3.1. General

All operations were performed in a nitrogen flushed glove box or in a vacuum system. Freshly distilled solvents were used. All processes of separations of the products were performed by Centrifugal Thin Layer Chromatography (CTLC, Chromatotron, Harrison model 8924) or column chromatography. GC analyses were performed on a HP-5890 FID GC with a QUA-DREX 007-CW fused silica 30 m column, and data were recorded on a HP ChemStation. ^{1}H NMR spectra were recorded on 300 MHz Varian VXR-300S spectrometer. The chemical shifts are reported in ppm relative to internal standard CHCl$_3$ or CH$_2$Cl$_2$. ^{31}P and ^{13}C NMR spectra were recorded at 121.44 and 75.46 MHz, respectively. Some other routine ^{1}H NMR spectra were recorded over Gemini-200 spectrometer at 200.00 MHz or Varian-400 spectrometer at 400.00 MHz. IR spectra of samples using KBr were recorded on a Hitachi 270-30 spectrometer. Mass spectra were recorded on JOEL JMS-SX/SX 102A GC/MS/MS spectrometer. Elemental analyses were recorded on Heraeus CHN-O-S-Rapid.

3.2. Synthesis of PhCCPCy$_2$ (**3**)

Phenylacetylene (1.021 g, 10.000 mmol) and dimethylether (10 mL) were placed in a 100 ml round-bottomed flask charged with magnetic stirrer. In a separate round-bottomed flask, one molar equivalent of *n*-butyllithium (2.0 M in cyclohexane) dissolved in dimethylether (5 mL) was taken. The latter solution was slowly added to the above mixture at −78 °C and remained to stir at that temperature for more than one hour. Then, one molar equivalent of chlorodicyclohexylphosphine (2.327 g, 10.0 mmol) dissolved in 5 ml dimethylether (5 mL) was slowly added to it. The reaction mixture was allowed to warm up to room temperature and contiued to stir for another 14 h. The solvent was then removed under reduced pressure and toluene was added to precipitate the lithium

chloride. After filtration, the resulted solution was further purified by chromatography. The white solid obtained in needle form was identified as **3**. The isolated yield obtained in the reaction is 75.0% (2.238 g, 7.500 mmol).

Complex 3: ^{1}H NMR (CDCl$_3$, δ/ppm): 7.47–7.26 (5H, arene), 2.00–1.23 (22H, PCy$_2$). ^{31}P NMR (CDCl$_3$, δ/ppm): −19.8 (s, 1P, PCy$_2$).

3.3. Synthesis of [(μ-PPh$_2$CH$_2$PPh$_2$)Co$_2$(CO)$_4$](μ,η-PhCCPCy$_2$) (4), [(μ-PPh$_2$CH$_2$PPh$_2$)Co$_2$(CO)$_4$](μ,η-PhCCP(=O)Cy$_2$) (5)

1.000 mmol of dicobalt octacarbonyl, Co$_2$(CO)$_8$ (0.342 g), 1.000 mmol of dppm (0.385 g) and 10 mL of toluene were taken in a 100 mL round-bottomed flask charged with magnetic stirrer. The solution was stirred at 65 °C for 6 h, a yellow-colored compound, Co$_2$(CO)$_6$(μ-P,P-PPh$_2$CH$_2$PPh$_2$), was yielded. Without separation, the reaction flask was further charged with one molar equivalent of **3** (0.298 g) in 5 mL of toluene and then the solution was allowed to stir at 80 °C for 14 h. Then the solvent was removed under reduced pressure and the resulted dark red-colored residue was separated by CTLC. A purple band was eluted out by mixed solvent system (CH$_2$Cl$_2$: hexane = 1:1) and the compound was identified as **4** with the yield of 77.0% (0.703 g, 0.770 mmol). A small red band, followed by **4** during the chromatographic process, was eluted out and the red-colored compound was identified as **5** with the yield of 9.8% (0.091 g, 0.098 mmol).

Complex 4: ^{1}H NMR (CDCl$_3$, ppm): 7.77–7.00 (m, 25H, arene), 3.30–3.16 (m, 2H, CH$_2$), 2.12–0.92 (m, 22H, PCy$_2$). ^{13}C NMR (CDCl$_3$, ppm): 132.4–128.1 (30C, arene), 26.2–25.8 (12C, PCy$_2$). ^{31}P NMR (CDCl$_3$, ppm): 38.5 (s, 2P, dppm), 16.8 (s, 1P, PCy$_2$). IR (KBr, cm^{-1}): 2015(s), 1989(s), 1964(s) (C=O). MS (FAB): m/z 913 (M$^+$). Anal. Calc. for C$_{49}$H$_{49}$Co$_2$O$_4$P$_3$: C, 64.48; H, 5.41. Found: C, 63.73; H, 5.86%.

Complex 5: ^{1}H NMR (CDCl$_3$, δ/ppm): 7.77–7.26 (m, 25H, arene), 5.96, 3.27 (s, s, 2H, CH$_2$), 2.06–1.11 (m, 22H, PCy$_2$). ^{13}C NMR (CDCl$_3$, δ/ppm): 132.4–128.1 (30C, arene), 26.5–25.7 (12C, PCy$_2$). ^{31}P NMR (CDCl$_3$, δ/ppm): 50.2 (s, 1P, PCy$_2$), 36.0 (s, 2P, dppm). IR (KBr, cm^{-1}): 2024(s), 2000(s), 1970(s) (C=O). MS (FAB): m/z 929 (M$^+$). Anal. Calc. for C$_{49}$H$_{49}$Co$_2$O$_5$P$_3$: C, 62.69; H, 5.62. Found: C, 63.37; H, 5.32%.

3.4. General procedure for the Suzuki coupling reactions

The four reactants, Pd(OAc)$_2$ (2.200 mg, 0.010 mmol), phosphine ligand **4** (9.127 mg, 0.010 mmol), the boronic acid (0.183 g, 1.500 mmol) and KF (0.116 g, 2.000 mmol), were taken into a suitable oven-dried Schlenk flask. The flask was evacuated and backfilled with nitrogen before adding toluene (1 mL) and the aryl

halide (1.000 mmol) through a rubber septum. The aryl halides being solids at room temperature were added prior to the evacuation/backfill cycle. The flask was sealed with Teflon screw cap and the solution was stirred at the required temperature for designated hours. Then, HCl(aq) (2.3 M, 10 mL) was added to quench the reaction. For entries 2–4 in Table 4, only H$_2$O rather than HCl(aq) was added. The aqueous layer was extrated with CH$_2$Cl$_2$ (30 mL). The organic extracts were dried over anhydrous magnesium sulfate and the solution was filtered through silica gel. The solvent was removed on a rotary evaporator. The residue was dissolved in toluene (9 mL), naphthalene (internal standard, 1 M in toluene, 1 mL) was added, and the mixture was analyzed by GC. Isolation and purification of the coupled products from the representative reactions was done by column chromatography (silica gel, CH$_2$Cl$_2$/hexane).

3.5. General procedure for the Suzuki coupling reactions at low catalyst loadings (<0.1 mol% Pd)

An oven-dried sealable Schlenk flask was evacuated and backfilled with argon and charged with the boronic acid (0.183 g, 1.500 mmol) and KF (0.174 g, 3.000 mmol). The flask was evacuated and backfilled with argon, and toluene (1 mL) and the aryl halide (1.000 mmol) were added through a rubber septum. A separate flask was charged with Pd(OAc)$_2$ (2.200 mg, 0.010 mmol) and **4** (9.127 mg, 0.010 mmol) and purged with argon. Toluene (10 mL) was added, the mixture was stirred for 1 min at room temperature, and then 100 μL of this solution (0.01 mol% Pd, 0.01 mol% **4**) was added to the Schlenk flask. The flask was sealed with Teflon screw cap and the solution was stirred at the required temperature for designated hours. Then, HCl(aq) (2.3 M, 10 mL) was added to quench the reaction. The aqueous layer was extracted with CH$_2$Cl$_2$ (30 mL). The organic extracts were dried over anhydrous magnesium sulfate and the solution was filtered through silica gel. The solvent was removed on a rotary evaporator. The residue was dissolved in toluene (9 mL), naphthalene (internal standard, 1 M in toluene, 1 mL) was added, and the mixture was analyzed by GC.

3.6. X-ray crystallographic studies

Suitable crystals of **4** and **5** were sealed in thin-walled glass capillaries under nitrogen atmosphere and mounted on a Bruker AXS SMART 1000 diffractometer. Intensity data were collected in 1350 frames with increasing ω (width of 0.3° per frame). The absorption correction was based on the symmetry equivalent reflections using SADABS program. The space group determination was based on a check of the Laue symmetry and systematic absences, and was confirmed using the structure solution. The structure was solved by direct

methods using a SHELXTL package [22]. All non-H atoms were located from successive Fourier maps and the hydrogen atoms were refined using a riding model. Anisotropic thermal parameters were used for all non-H atoms and fixed isotropic parameters were used for H atoms [23]. Crystallographic data of **4** and **5** are summarized in Table 1.

Acknowledgment

Appendix A. Supplementary data

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Center, CCDC Nos. 230925 and 232204 for compounds **4** and **5**, respectively. Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk). Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2004.11.030.

References

[1] (a) N. Miyura, A. Suzuki, Chem. Rev. 95 (1995) 2457;
(b) A.F. Littke, G.C. Fu, Angew. Chem., Int. Ed. 37 (1998) 3387;
(c) D.W. Old, J.P. Wolfe, S.L. Buchwald, J. Am. Chem. Soc. 120 (1998) 9722;
(d) J.P. Wolfe, S.L. Buchwald, Angew. Chem., Int. Ed. 38 (1999) 2413;
(e) J.P. Wolfe, R.A. Singer, B.H. Yang, S.L. Buchwald, J. Am. Chem. Soc. 121 (1999) 9550;
(f) A. Suzuki, J. Organomet. Chem. 576 (1999) 147;
(g) A.F. Littke, C. Dai, G.C. Fu, J. Am. Chem. Soc. 122 (2000) 4020;
(h) M.R. Netherton, C. Dai, K. Neuschutz, G.C. Fu, J. Am. Chem. Soc. 123 (2001) 10099;
(i) J. McNulty, A. Capretta, J. Wilson, J. Dyck, G. Adjabeng, A. Robertson, Chem. Commun. (2002) 1986;
(j) J. Hassan, M. Sevignon, C. Gozzi, E. Schulz, M. Lemaire, Chem. Rev. 102 (2002) 1359;
(k) J.J. Yin, M.P. Rainka, X.-X. Zhang, S.L. Buchwald, J. Am. Chem. Soc. 124 (2002) 1162;
(l) N. Kataoka, Q. Shelby, J.P. Stambuli, J.F. Hartwig, J. Org. Chem. 67 (2002) 5553.
[2] (a) A.F. Littke, G.C. Fu, J. Org. Chem. 64 (1999) 10;
(b) A.F. Littke, G.C. Fu, J. Am. Chem. Soc. 123 (2001) 6989;
(c) J.P. Stambuli, S.R. Stauffer, K.H. Shaughnessy, J.F. Hartwig, J. Am. Chem. Soc. 123 (2001) 2677.
[3] (a) A.F. Littke, G.C. Fu, Angew. Chem., Int. Ed. 38 (1999) 2411;
(b) A.F. Littke, L. Schwarz, G.C. Fu, J. Am. Chem. Soc. 124 (2002) 6343.

[4] T. Hundertmark, A.F. Littke, S.L. Buchwald, G.C. Fu, Org. Lett. 2 (2000) 1729.
[5] (a) A. Zapf, A. Ehrentraut, M. Beller, Angew. Chem., Int. Ed. 39 (2000) 4153;
(b) M.L. Clarke, D.J. Cole-Hamilton, J.D. Woolins, Dalton Trans. (2001) 2721;
(c) G.Y. Li, J. Org. Chem. 67 (2002) 3643.
[6] (a) M. Nishiyama, T. Yamamoto, Y. Koie, Tetrahedron Lett. 39 (1998) 617;
(b) T. Yamamoto, M. Nishiyama, Y. Koie, Tetrahedron Lett. 39 (1998) 2367;
(c) M. Kawatsura, J.F. Hartwig, J. Am. Chem. Soc. 121 (1999) 1473;
(d) G. Mann, C. Incarvito, A.L. Rheingold, J.F. Hartwig, J. Am. Chem. Soc. 121 (1999) 3224;
(e) J.F. Hartwig, M. Kawatsura, S.I. Hauck, K.H. Shaughnessy, L.M. Alcazar-Roman, J. Org. Chem. 64 (1999) 5575;
(f) X. Bei, T. Crevier, A.S. Guram, B. Jandeleit, T.S. Powers, H.W. Turner, T. Uno, W.H. Weinberg, Tetrahedron Lett. 40 (1999) 3855;
(g) M. Watanabe, M. Nishiyama, Y. Koie, Tetrahedron Lett. 40 (1999) 8837;
(h) S.R. Chemler, D. Trauner, S.J. Danishefsky, Angew. Chem., Int. Ed. 40 (2001) 4544;
(i) C. Dai, G.C. Fu, J. Am. Chem. Soc. 123 (2001) 2719.
[7] (a) A. Aranyos, D.W. Old, A. Kiyomori, J.P. Wolfe, J.P. Sadighi, S.L. Buchwald, J. Am. Chem. Soc. 121 (1999) 4369;
(b) J.M. Fox, X. Huang, A. Chieffi, S.L. Buchwald, J. Am. Chem. Soc. 122 (2000) 1360;
(c) J.P. Wolfe, H. Tomori, J.P. Sadighi, J. Yin, S.L. Buchwald, J. Org. Chem. 65 (2000) 1158;
(d) H. Tomori, J.M. Fox, S.L. Buchwald, J. Org. Chem. 65 (2000) 5334;
(e) W.A. Moradi, S.L. Buchwald, J. Am. Chem. Soc. 123 (2001) 7996;
(f) S. Kuwabe, K.E. Torraca, S.L. Buchwald, J. Am. Chem. Soc. 123 (2001) 12202;
(g) T. Hamada, A. Chieffi, J. Ahman, S.L. Buchwald, J. Am. Chem. Soc. 124 (2002) 1261;
(h) E.M. Vogl, S.L. Buchwald, J. Org. Chem. 67 (2002) 106.
[8] (a) Q. Shelby, N. Kataoka, G. Mann, J.F. Hartwig, J. Am. Chem. Soc. 122 (2000) 10718;
(b) S.R. Stauffer, N.A. Beare, J.P. Stambuli, J.F. Hartwig, J. Am. Chem. Soc. 123 (2001) 4641;
(c) N.A. Beare, J.F. Hartwig, J. Org. Chem. 67 (2002) 541;
(d) T.J. Colacot, H.A. Shea, Org. Lett. 6 (2004) 3723;
(e) F.Y. Kwong, K.S. Chan, C.H. Yeung, A.S.C. Chan, Chem. Commun. (2004) 2336;
(f) Z. Weng, S. Teo, L.L. Koh, T.S.A. Hor, Organometallics 23 (2004) 4342.
[9] (a) G. Mann, J.F. Hartwig, J. Am. Chem. Soc. 118 (1996) 13109;
(b) N. Kataoka, Q. Shelby, J.P. Stambuli, J.F. Hartwig, J. Org. Chem. 67 (2002) 5553;
(c) A. Salzer, Coord. Chem. Rev. 242 (2003) 59;
(d) O. Delacroix, J.A. Gladysz, Chem. Commun. (2003) 665;
(e) J.G. Planas, J.A. Gladysz, Inorg. Chem. 41 (2002) 6947;
(f) Q.-S. Hu, Y. Lu, Z.-Y. Tang, H.-B. Yu, J. Am. Chem. Soc. 125 (2003) 2856;
(g) T.E. Pickett, F.X. Roca, C.J. Richards, J. Org. Chem. 68 (2003) 2592;
(h) Z.-Y. Tang, Y. Lu, Q.-S. Hu, Org. Lett. 5 (2003) 297.
[10] F.-E. Hong, Y.-J. Ho, Y.-C. Chang, Y.-C. Lai, Tetrahedron 60 (2004) 2639.
[11] F.-E. Hong, Y.-C. Chang, R.-E. Chang, S.-C. Chen, B.-T. Ko, Organometallics 21 (2002) 961.
[12] T.J. O'Connor, H.A. Patel, Can. J. Chem. 49 (1971) 2706.

[13] J.-I. Uenishi, J.-M. Beau, R.W. Armstrong, Y. Kishi, J. Am. Chem. Soc. 109 (1987) 4756.

[14] (a) J.P. Stambuli, M. Buhl, J.F. Hartwig, J. Am. Chem. Soc. 124 (2002) 9346;
(b) B.B. Robin, S.J.C. Catherine, Organometallics 22 (2003) 987.

[15] F.-E. Hong, C.-P. Chang, Y.-C. Chang, Dalton Trans. (2003) 3892.

[16] (a) K.C. Kong, C.H. Cheng, J. Am. Chem. Soc. 113 (1991) 6313;
(b) M.M. Marcial, M. Perez, R.J. Pleixats, Org. Chem. 61 (1996) 2346.

[17] (a) S.P. Stanforth, Tetrahedron 54 (1998) 263;
(b) N. Miyaura, in: L.S. Liebeskind (Ed.), Advances in Metal-Organic Chemistry, vol. 6, London, 1998, JAI Press, pp. 187–243;
(c) A. Suzuki, in: F. Diederich, P.J. Stang (Eds.), Metal-Catalyzed Cross-Coupling Reactions, Wiley-VCH, New York, 1998 (Chapter 2).

[18] S.W. Wright, D.L. Hageman, L.D. McClure, J. Org. Chem. 59 (1994) 6095.

[19] (a) C.R. LeBlond, A.T. Andrews, Y. Sun, J.R. Sowa Jr., Org. Lett. 3 (2001) 1555;
(b) J.C. Thomas, S.G. Ernest, K. Amanda, Organometallics 21 (2002) 3301.

[20] G.A. Grasa, A.C. Hillier, S.P. Nolan, Org. Lett. 3 (2001) 1077.

[21] (a) V.V. Grushin, H. Alper, Chem. Rev. 94 (1994) 1047;
(b) A.H. Roy, J.F. Hartwig, J. Am. Chem. Soc. 123 (2001) 1232.

[22] G.M. Sheldrick, SHELXTL PLUS User's Manual. Revision 4.1, Nicolet XRD Corporation, Madison, WI, USA, 1991.

[23] The hydrogen atoms were ride on carbons or oxygens in their idealized positions and held fixed with the C–H distances of 0.96 Å.