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Efficient Suzuki Coupling of Aryl Chlorides Catalyzed by Palladium(0) with a P,N Heteroligand and Isolation of Unsaturated Intermediates

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Summary: A mixture of $Pd_2(dba)_3/[\eta\text{-}C_5H_4CH{=}N(C_6H_5)]Fe[\eta\text{-}C_5H_4P(t\text{-}Bu)_2]$ (**1**) *efficiently catalyzes the Suzuki cross-couplings of a range of arylboronic acids and aryl chlorides, affording the desired biaryl products in high isolated yields. Two catalytically active Pd(0) intermediates, viz. 16-electron* $[\eta\text{-}C_5H_4CH{=}N(C_6H_5)]Fe[\eta\text{-}C_5H_4P(t\text{-}Bu)_2]Pd(dba)$ (**2**) *and 14-electron linear* $Pd\{[\eta\text{-}C_5H_4CH{=}N(C_6H_5)]Fe[\eta\text{-}C_5H_4P(t\text{-}Bu)_2]\}_2$ (**3**) *together with an oxidative addition product are isolated and crystallographically established.*

Suzuki coupling of aryl halides with arylboronic acids presents an attractive scientific and technological incentive in organometallic catalysis today.[1−3] The challenges are illustrated by the possible use of coordinatively and electronically unsaturated Pd(0) in tackling the energetically demanding C−Cl activation.[1,2] Some of the best supporting ligands are bulky phosphines,[4] N-heterocyclic carbenes (NHC),[5] etc. Our continual interest in 1,1′-bis(diphenylphosphino)ferrocene[6,7] chemistry and phosphineless catalysis[8] provides an impetus to develop a ligand system that does not overexpose or overprotect the metal, thus achieving a delicate balance between stability and activity. This can be achieved through the use of a ferrocenyl moiety as a spatial support in conjunction with a potentially bidentate hemilabile[9] ligand that is sensitive to the metal needs. In this communication, we report such a new heterodifunctional P,N ligand, $[\eta\text{-}C_5H_4CH{=}N(C_6H_5)]Fe[\eta\text{-}C_5H_4P(t\text{-}Bu)_2]$ (**1**), which promotes effective and efficient Suzuki coupling and C−Cl activation and supports the formation of isolable low-coordinated Pd(0) species.

A $Pd_2(dba)_3$/**1** mixture (dba = dibenzylideneacetone) catalyzes the Suzuki cross-coupling reactions of a variety of arylboronic acids and aryl chlorides, affording the desired biaryls in remarkably high isolated yields. (Table 1) For example, 4-chloroacetophenone couples with phenylboronic acid in the presence of 1 mol % of Pd to give a quantitative yield of 4-acetylbiphenyl at 70 °C in THF (entry 1), whereas the reaction of 4-chlorobenzonitrile with phenylboronic acid occurs at a low catalyst load (0.01 mol % Pd) to give a good TON of 10 000 (entry 2), which is comparable to the values for many other efficient systems, although exceedingly high TONs are known.[4a,e]

To gain a better insight into the structure−activity relationship, we examined the spectroscopic and crystallographic characteristics of the active key intermediate(s). ^{31}P and ^{1}H NMR analyses of the catalyst mixture of **1** and $Pd_2(dba)_3$ (1:1 ratio of **1** to Pd) in C_6D_6 revealed two main products, $[\eta\text{-}C_5H_4CH{=}N(C_6H_5)]Fe[\eta\text{-}C_5H_4P(t\text{-}Bu)_2]Pd(dba)$ (**2**) and $Pd\{[\eta\text{-}C_5H_4CH{=}N(C_6H_5)]Fe[\eta\text{-}C_5H_4P(t\text{-}Bu)_2]\}_2$ (**3**), in a ratio of ∼4:1 (Scheme 1). There are no hydride signals or unusual resonances that could indicate agostic Pd···H interactions with the ferrocenyl or butyl groups. When the ligand concentration is doubled to 2-fold, **3** becomes the sole species. A C_6D_6 solution of pure **2** converts to **3** upon addition of 1 molar equiv of **1**. Complex **3** can be synthesized (94%) from **1** and $(C_5H_5)Pd(C_3H_5)$ (1:1).[10a,b] Both **2** (Figure 1) and **3** (Figure 2) were isolated and structurally characterized.[11] Complex **2** is a 16-electron Pd(0) species with a heterodifunctional chelate supplemented by an olefin

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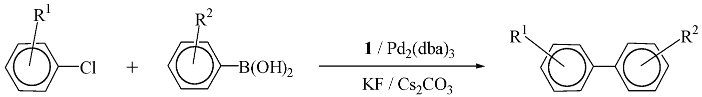
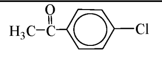
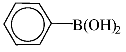
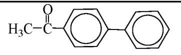
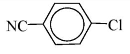
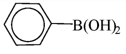
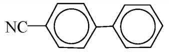
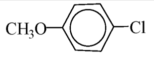
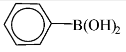
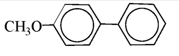
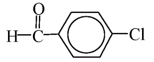
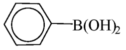
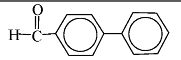
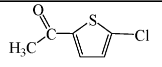
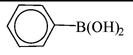
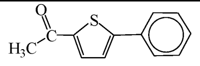
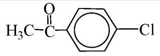
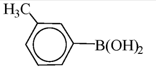
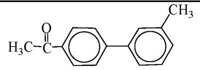
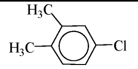
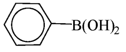
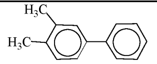
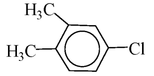
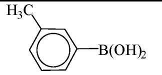
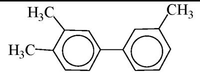
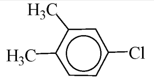
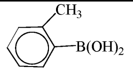
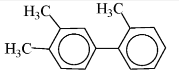
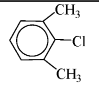
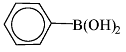
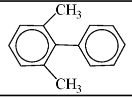
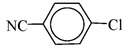
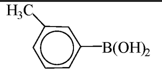
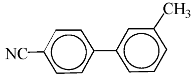
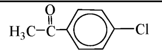
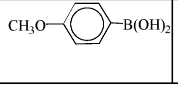
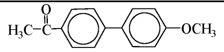
10.1021/om0494770 CCC: $27.50

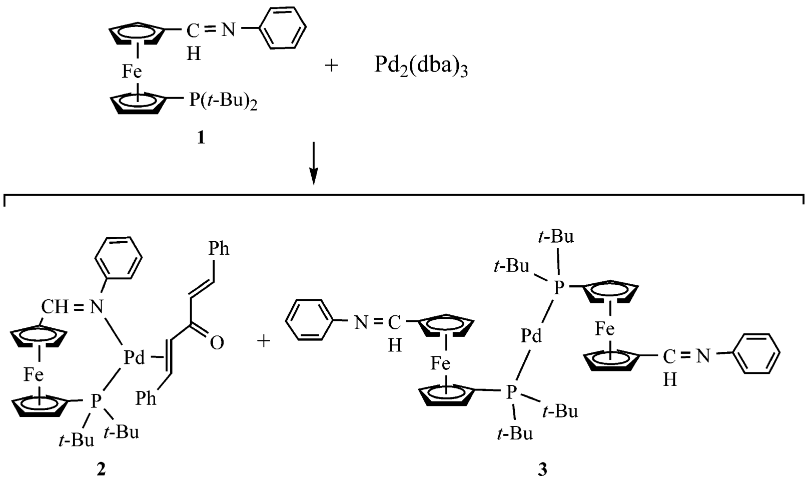
Table 1. Suzuki Cross-Coupling of Aryl Chlorides with Boronic Acids Catalyzed by Pd(0) with Ligand 1[a]



Entry	Aryl chlorides	Boronic acid	Product	Conditions[b]	Yield [%][c]
1				1 mol % of Pd, THF, 70 °C, 16 h	100
2				0.01 mol %, dioxane, 100 °C, 16 h	52 (100)[d]
3				2 mol %, dioxane, 110 °C, 15 h	99
4				2 mol %, dioxane, 110 °C, 15 h	99
5				2 mol %, dioxane, 90 °C, 5 h	96
6				0.1 mol %, dioxane, 100 °C, 3 h	100
7				1 mol %, dioxane, 100 °C, 4 h	96
8				1 mol %, dioxane, 100 °C, 14 h	99
9				1 mol %, dioxane, 100 °C, 14 h	96
10				1 mol %, dioxane, 100 °C, 14 h	91[d]
11				0.5 mol %, dioxane, 100 °C, 14 h	100
12				2 mol %, dioxane, 110 °C, 4 h	98

[a] Pd:**1** = 1:1; ArCl:Ar′B(OH)$_2$:KF:Cs$_2$CO$_3$ = 1:1.2:3:3. [b] The reaction duration was generally not optimized. [c] Yields of isolated products. [d] Pd:**1** = 1:2.

Scheme 1



(dba) coordination, whereas **3** is a 14-electron linear Pd(0) compound supported by a unidentate metalloligand with dangling imine. These compounds indicate that **1** is potentially hemilabile and difunctional and uses its bidentate potential to adapt electronically and geometrically to stabilize different forms of unsaturated Pd(0). In its deficiency, the dba olefin can lend additional support.

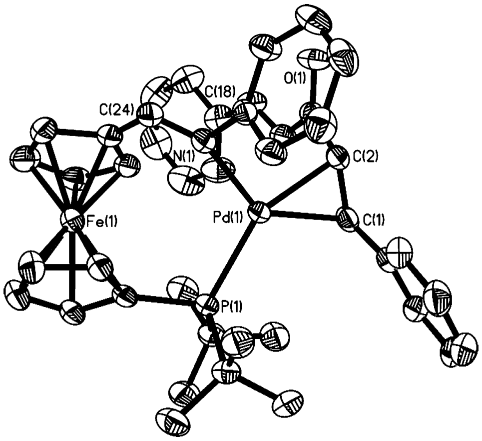


Figure 1. ORTEP representation of the X-ray structures of **2**. Hydrogen atoms are omitted for clarity. Thermal ellipsoids are drawn at the 40% probability level. Selected bond lengths (Å) and angles (deg): Pd(1)–C(1) = 2.108(4), Pd(1)–C(2) = 2.150(3), Pd(1)–N(1) = 2.218(3), Pd(1)–P(1) = 2.3385(10), N(1)–C(24) = 1.281(4); N(1)–Pd(1)–P(1) = 110.94(8), C(1)–Pd(1)–C(2) = 38.97(13).

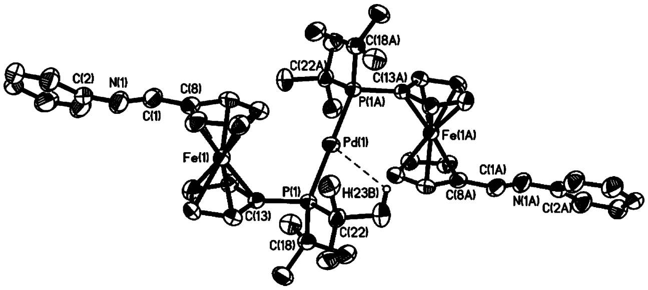
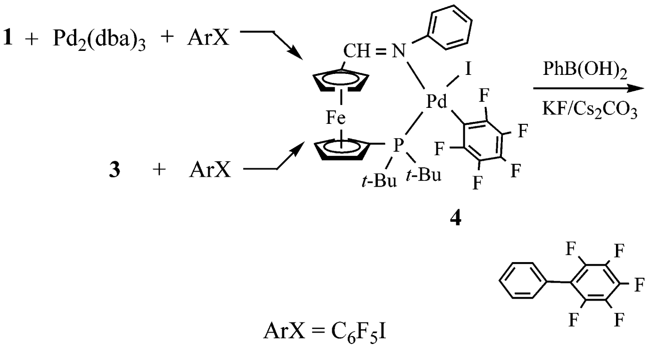


Figure 2. ORTEP representation of the X-ray structures of **3**. Hydrogen atoms are omitted for clarity. Thermal ellipsoids are drawn at the 40% probability level. Selected bond lengths (Å) and angles (deg): Pd(1)···H(23B) = 2.931, Pd(1)–P(1) = 2.2828(16), N(1)–C(1) = 1.258(7); P(1)–Pd(1)–P(1A) = 180.0.

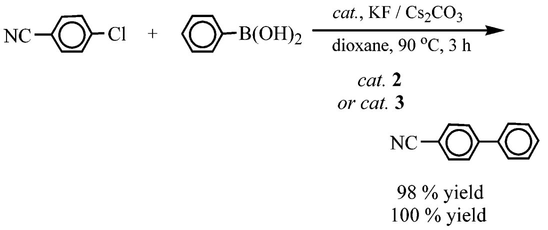
The Pd–N bond (2.218(3) Å) of **2** is significantly longer, and presumably weaker, than its counterpart in $PdCl_2Fe[\eta\text{-}C_5H_4NC(H)Ph\text{-}N]_2$ (2.056(10) and 2.023(11) Å),[8a] $Pd_2Cl_4\{Fe[\eta\text{-}C_5H_4(CH_2)_2N(CH_3)_2]\}_2$ (2.128(4) and 2.128(5) Å),[8b] and other weak Pd–N bonds.[12a,b] Its fragility highlights the value of imine in protecting and, if needed, exposing the catalytic center.

Scheme 2



The Pd–C(dba) bond (mean 2.129 Å) is between that in a (P,O)Pd(dba) complex (2.102 Å)[4g] and (dppf)Pt(dba) (2.134 Å).[7a] Complex **3**, being a rare example of two-coordinated linear Pd(0) phosphines,[10] to our knowledge, also offers the first crystallographic proof of a difunctional ligand that switches to a monodentate mode to support a low-coordinate and highly unsaturated Pd(0). Although the complex could in principle take up the usual four-coordinate form through P,N chelation for both ligands, it opts to adopt the sterically less but electronically more demanding low-coordinate form. Negligible contacts between the metal and *t*Bu protons (Pd···H(23B) = 2.931 Å, which is significantly longer than those in $Pd[(o\text{-}Tol)_3P]_2$ and $Pd[PPh(t\text{-}Bu)_2]_2$ (2.508, and 2.73 Å, respectively))[10] indicate an authentic two-coordinate Pd(0) with the ferrocenyl moieties providing “spatial protection” in the vicinity. Its isolation suggests that low-coordinate Pd(0) may also be stabilized by ligands other than the documented monophosphines PR_3. The facile torsional twist of the C_5 ring has moved the dangling imine N atom to an anti position, thus minimizing intramolecular Pd···N contacts. There is no evidence of a Pd–P,N–Pd bridge or intermolecular Pd···N contacts in the solid state.

To illustrate the activity of the isolated **2** and **3**, they catalyze (0.25 mol % Pd) the formation of biphenyl-4-carbonitrile in near-quantitative yields at 90 °C (eq 1).



(1)

Complexes **3** and **2** can be conveniently prepared in situ by stoichiometric mixing of **1** with $Pd_2(dba)_3$. The catalytic efficiency is comparable to that of other highly active Pd systems, e.g. $P(t\text{-}Bu)_3$,[4c] ferrocene-derived triarylphosphine,[13a] or (pentaphenylferrocenyl)di-*tert*-butylphosphine.[13b] When the catalyst load is lowered to 0.01 mol % (Pd), the activity of **3** is superior to that of **2** (100 and 52%, respectively; see Table 1, entry 2).

If **2** and **3** are active intermediates, they should undergo oxidative addition with organohalides readily.[14]

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[11] Crystal data for **2** ($\mathbf{2}\cdot CH_2Cl_2$): $M_r = 1717.89$, monoclinic, space group $C2/c$, $a = 19.8738(19)$ Å, $b = 19.5297(19)$ Å, $c = 20.4146(18)$ Å, $\alpha = 90°$, $\beta = 92.943(2)°$, $\gamma = 90°$, $V = 7913.1(13)$ Å^3, $Z = 4$, $\rho = 1.442$ Mg m^{-3}, $F(000) = 3536$, λ(Mo Kα) = 0.710 73 Å, $\mu = 1.030$ mm^{-1}, $T = 223(2)$ K, crystal dimensions 0.36 × 0.06 × 0.06 mm. Of 27 623 reflections measured, 9068 unique reflections were used in refinement. Final $R = 0.0471$ ($R_w = 0.1051$). Crystal data for **3**: $M_r = 973.07$, triclinic, space group $P\bar{1}$, $a = 8.304(5)$ Å, $b = 11.806(7)$ Å, $c = 12.260(7)$ Å, $\alpha = 107.168(11)°$, $\beta = 93.342(12)°$, $\gamma = 91.761(12)°$, $V = 1145.0(12)$ Å^3, $Z = 1$, $\rho = 1.411$ Mg m^{-3}, $F(000) = 506$, λ(Mo Kα) = 0.710 73 Å, $\mu = 1.030$ mm^{-1}, $T = 295(2)$ K, crystal dimensions 0.24 × 0.04 × 0.02 mm. Of 12 318 reflections measured, 5120 unique reflections were used in refinement. Final $R = 0.0471$ ($R_w = 0.1223$). Crystal data for $\mathbf{4}\cdot 0.25C_6H_{14}\cdot 0.5THF$: $M_r = 897.70$, monoclinic, space group $P2_1/c$, $a = 16.600(2)$ Å, $b = 11.3938(16)$ Å, $c = 18.179(3)$ Å, $\alpha = 90°$, $\beta = 102.386(3)°$, $\gamma = 90°$, $V = 3358.3(8)$ Å^3, $Z = 4$, $\rho = 1.775$ Mg m^{-3}, $F(000) = 1774$, λ(Mo Kα) = 0.710 73 Å, $\mu = 2.066$ mm^{-1}, $T = 223(2)$ K, crystal dimensions 0.36 × 0.08 × 0.02 mm. Of 23 200 reflections measured, 7697 unique reflections were used in refinement. Final $R = 0.0524$ ($R_w = 0.0965$).

[12] (a) Crociani, L.; Bandoli, G.; Dolmella, A.; Basato, M.; Corain, B. *Eur. J. Inorg. Chem.* **1998**, 1811. (b) Reddy, K. R.; Surekha, K.; Lee, G.-H.; Peng, S.-M.; Liu, S.-T. *Organometallics* **2000**, *19*, 2637. (c) Jalil, M. A.; Fujinami, S.; Nishikawa, H. *Dalton* **2001**, 1091.

[13] (a) Liu, S.-Y.; Choi, M. J.; Fu, G. C. *Chem. Commun.* **2001**, 2408. (b) Kataoka, N.; Shelby, Q.; Stambuli, J. P.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 5553.

[14] Grushin, V. V.; Alper, H. *Chem. Rev.* **1994**, *94*, 1047.

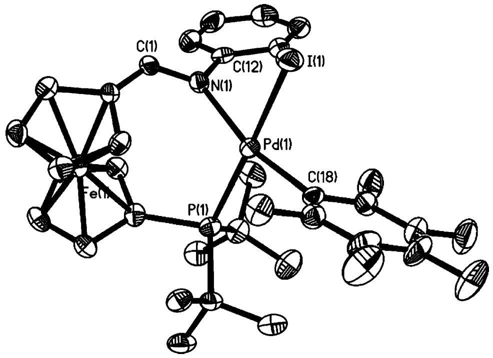

Figure 3. ORTEP representation of the X-ray structures of **4**. Hydrogen atoms are omitted for clarity. Thermal ellipsoids are drawn at the 40% probability level. Selected bond lengths (Å) and angles (deg): Pd(1)−C(18) = 2.005(5), Pd(1)−N(1) = 2.146(5), Pd(1)−P(1) = 2.4003(16), Pd(1)−I(1) = 2.6632(7), N(1)−C(1) = 1.286(6); C(18)−Pd(1)−I(1) = 82.81(16), N(1)−Pd(1)−P(1) = 98.41(13), C(18)−Pd(1)−P(1) = 94.73(16), N(1)−Pd(1)−I(1) = 84.92(13), P(1)−Pd(1)−I(1) = 171.02(4), C(18)−Pd(1)−N(1) = 166.0(2).

Indeed, a mixture of **1** and $Pd_2(dba)_3$ (giving mainly **2** in situ) reacts with C_6F_5I (**1**:Pd:ArX = 1:1:3.6) at room temperature for 1 h to give $[\eta\text{-}C_5H_4CH{=}N(C_6H_5)]Fe[\eta\text{-}C_5H_4P(t\text{-}Bu)_2]Pd(I)(C_6F_5)$ (**4**; 41%) as the only identifiable product. The latter can also be prepared (31%) from **3** and C_6F_5I (Scheme 2).

Single-crystal crystallographic analysis of **4** revealed the oxidative addition Pd(II) product, in which **1** is cis chelating (Figure 3). The imine faces the more *trans*-labilizing aryl. The large P(1)−Pd(1)−N(1) chelate angle (98.41(13)°) squeezes the I(1)−Pd(1)−C(18) angle to 82.81(16)°, perhaps promoting iodo−aryl contact and hence the reductive elimination step. Preliminary experiments on **4** suggested that it reacts with phenylboronic acid in the presence of KF/Cs_2CO_3 in dioxane to give 2,3,4,5,6-pentafluorobiphenyl in ca. 75% yield, which is consistent with **4** being an intermediate in the Suzuki coupling.

Our ferrocene-functionalized difunctional P,N ligand is highly efficient and effective in promoting Suzuki couplings. Through its stereogeometrical mobility and coordination flexibility, it stabilizes yet activates low-coordinate Pd(0) species, to the extent that they can be isolated and used under moderate thermal conditions in catalytic reactions. These are somewhat unexpected but valuable features that could immensely benefit other Pd(II/0) catalysts and catalysis. This work further suggested that low-coordinate and low-valent palladium could benefit from the structural and dynamic (hemi)-lability of the difunctional ligands in promoting challenging cross-couplings. This would complement the current use of monodentate phosphines in highly unsaturated metal catalysts.

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Supporting Information Available: Text describing the synthesis and characterization of complexes **2**−**4** and the catalytic experiments, together with complete listings of bond lengths and angles, ORTEP diagrams, tables of atomic coordinates and equivalent isotropic displacement parameters, anisotropic displacement parameters, and hydrogen coordinates and isotropic displacement parameters of complexes **2**−**4**; crystallographic data for **2**−**4** are also available as CIF files. This material is available free of charge via the Internet at http://pubs.acs.org.

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