A Nonsymmetric Pincer-Type Palladium Catalyst In Suzuki, Sonogashira, and Hiyama Couplings in Neat Water

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A new PCN palladium pincer complex containing a phosphinoamino group has been synthesized, fully characterized, and applied to Hiyama, copper-free Sonogashira, and Suzuki cross-coupling reactions performed in water. The use of the latter catalyst provides competitive yields, catalyst loadings, and reaction media.

Introduction

Among the plethora of palladium catalysts employed for a good number of modern organic transformations, pincer-type palladium complexes constitute an appealing niche due to their suitable balance between stability and reactivity.[1] In the context of cross-coupling reactions, the latter complexes allow for the use of minimal amounts of such homogeneous catalysts.[2] In addition to an improved catalytic efficiency, much effort has been devoted to the development of more sustainable conditions, such as the recovery of the catalyst or the use of environmentally more friendly reaction media.[3,4] Water is a nonflammable, safe, and cheap solvent with a great potential, since organic products can be readily separated from the aqueous layer and many reactions proceed with better selectivity in aqueous environments. Moreover, in some cases, mostly depending on the stability of the catalyst, reuse of the aqueous layer containing the catalyst has been reported.[5]

Following our research on the development of new catalytic systems to perform cross-coupling reactions,[6] we envisaged the construction of the new nonsymmetric PCN pincer-type palladium complex **1** according to the retrosynthetic Scheme 1.

Unlike the vast majority of the existing pincers, the nonsymmetry of **1** could provide a better tuning of its catalytic properties, but at the cost of a more challenging synthetic route, as the scarcity of the existing palladium PCN pincers strongly suggests (Figure 1).[7–10] Dupont and Monteiro described the synthesis of complex **3**,[7] which was subsequently applied to Suzuki coupling,[8] and the group of Motoyama prepared palladacycle **4** in order to use it as a catalyst in stereoselective transformations.[9] Recently, Song et al. prepared and characterized complexes **5** and **6**.[10]

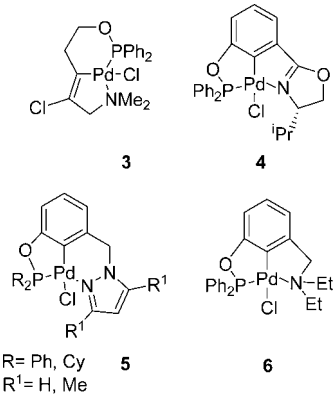
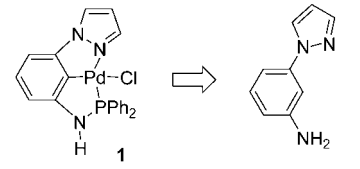


Figure 1. Existing PCN palladium complexes.

Scheme 1. Retrosynthetic Analysis of 1



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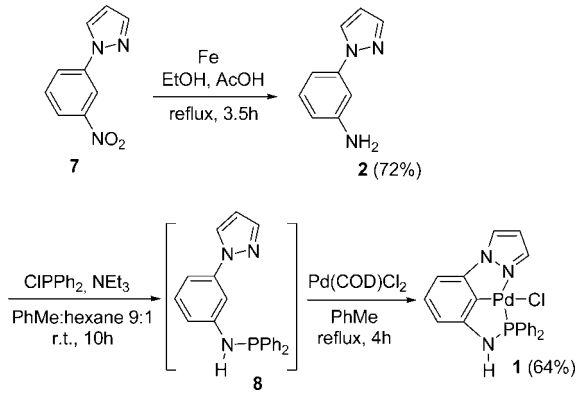
Scheme 2. Synthesis of Palladium Complex 1



Herein we report the synthesis and the most relevant catalytic properties of new complex **1** in Suzuki, Sonogashira, and Hiyama cross-coupling reactions, mainly performed in aqueous media.

Results and Discussion

After reduction of the readily available[11] 1-(3-nitrophenyl)pyrazole **7** to amine **2**, treatment with $ClPPh_2$ provided the air-sensitive, unstable ligand **8**, which was reacted without further purification with $Pd(COD)Cl_2$ in toluene to provide the target pincer **1** (Scheme 2). In this key step, a ^{31}P NMR monitoring of the transformation to phosphinamine **8** (δ_P 28 ppm), the suitable proportion of hexane and toluene solvents (1:9) and a quick filtering of the crude product onto a suspension of $Pd(COD)Cl_2$ in degassed toluene under argon became especially crucial. The so-obtained complex **1** was found to be air and thermally stable.

Several techniques were employed in order to confirm the structure of palladacycle **1**. The shift from 28 ppm (intermediate **8**) to a singlet at 91 ppm in the ^{31}P NMR spectrum of **1** suggested coordination to palladium. In addition, loss of hydrogen at the central aromatic proton due to palladation was confirmed by ^1H NMR, DEPT, and HSQC experiments. Finally, a simple recrystallization of palladacycle **1** in acetone provided monocrystals suitable for X-ray diffractometry analysis. Figure 2 and Table 1 show the main structural features of **1**. In addition to other spectroscopic evidence, the short C9−Pd distance (1.957(8) Å), comparable to that of other PCP and PCN pincers,[8c,10,12] ensures an effective palladation of this aromatic carbon, an a priori difficult task if the already reported failures at the formation of pincer complexes by C−H activation of nonhalogenated aromatic positions are considered.[13] It can therefore be suggested, in comparison with other reported pincers,[13] that this difficult reaction is driven by the additional stability gained by this PCN system, in a fashion similar to that for the reported complexes **5** and **6**.[10] The strongly distorted square planar geometry around the palladium atom is also remarkable, as shown by the Cl−Pd−C9 and P−Pd−N1 bond angles. The small (160.6°) P−Pd−N1 bond angle is in accordance with a pincer consisting of two five-membered-ring

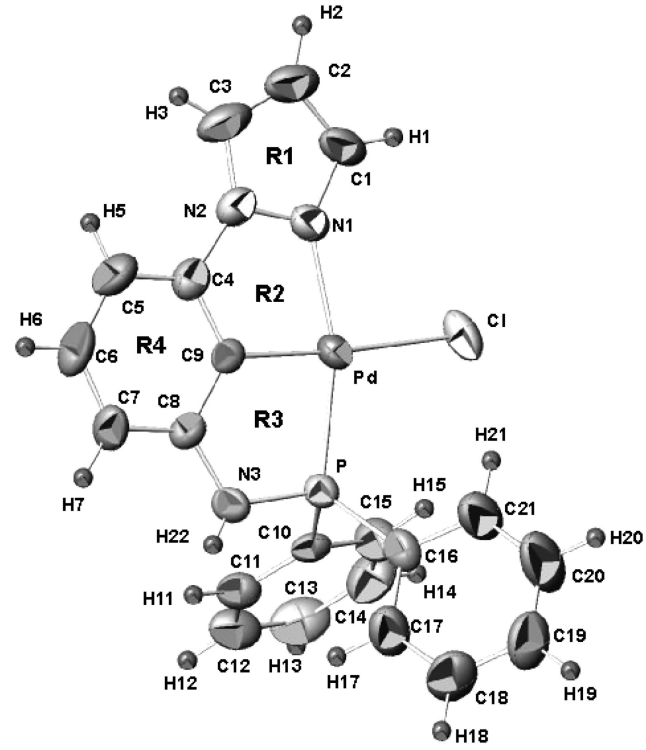


Figure 2. Molecular structure of the PCN pincer complex **1**. Ellipsoids are given at the 50% probability level.

Table 1. Selected Bond Lengths (Å) and Angles (deg) of PCN Complex 1

Bond Lengths (Å)			
Pd−C(9)	1.957(8)	Pd−Cl	2.386(2)
Pd−N(1)	2.080(7)	P−N(3)	1.654(7)
Pd−P	2.208(2)	N(3)−C(8)	1.396(10)
Bond Angles (deg)			
N(3)−P−C(16)	108.0(4)	N(3)−P−Pd	104.4(2)
N(3)−P−C(10)	106.3(4)	Cl−Pd−C(9)	175.6(2)
C(16)−P−C(10)	103.1(4)	N(1)−Pd−-P	160.6(2)
Dihedral Angles (deg)			
P−N(3)−C(8)−C(7)		−179.8(7)	
N(1)−N(2)−C(4)−C(5)		−179.9(8)	
Pd−N(1)−N(2)−C(4)		−0.4(9)	
Pd−P−N(3)−C(8)		−0.6(7)	

palladacycles[14] and reflects a relative steric strain of the almost planar (see torsion angles of Table 1) tetracyclic core, which probably influences its catalytic activity. Figure 3 shows the unit cell featuring a central inversion center (i) in the intermolecular packing, which is further stabilized by a weak intermolecular $\pi-\pi$ type interaction between the bicyclic R1−R2 pyrazolopalladacycle moieties[15] (see Figure 4) and a linear N3−H22···Cl hydrogen bonding defined by N3−H22 = 0.73 Å, H22···Cl = 2.56 Å, and N3−Cl = 3.25 Å (Figure 5).

Having fully characterized palladacycle **1**, its catalytic activity was preliminarily evaluated with Hiyama cross-coupling. Al-

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(15) The nature and extent of the $\pi-\pi$ interactions were evaluated by the program CONTACTOS. See: Albert, A.; Cano, F. H. In *Cristalografía*; Hernández-Cano, F., Foces-Foces, C., Martínez-Ripoll, M., Eds.; Publicaciones CSIC: Madrid, 1995; p 183

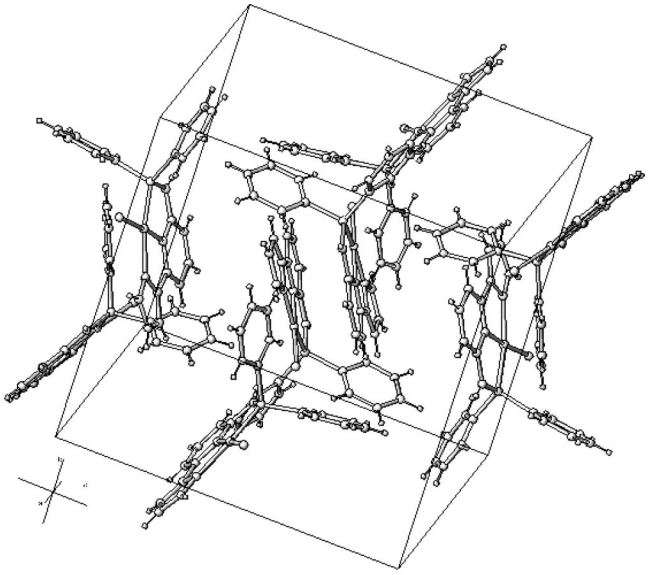


Figure 3. Perspective view of the unit cell of **1**.

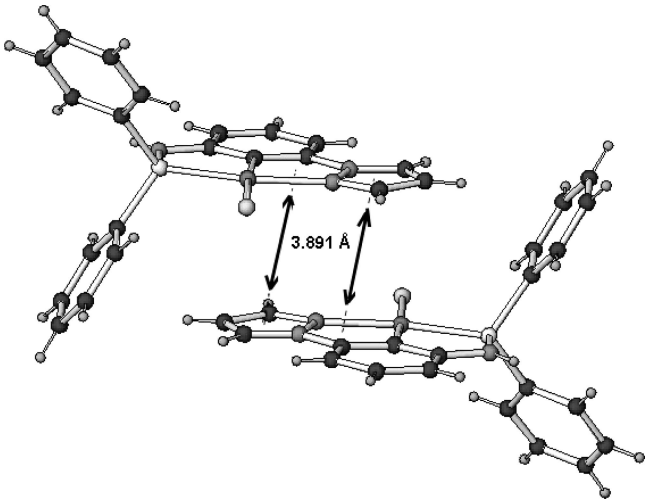


Figure 4. Intermolecular $\pi-\pi$ interactions.

though the pioneering work by Hiyama et al. claimed the need of fluoride ions in order to facilitate the transmetalation step,[16] it has been shown that the latter process can be similarly promoted by sodium hydroxide.[17] Accordingly, the two procedures displayed in Table 2 were assayed in order to arylate (trimethoxysilyl)benzene, one of them in aqueous media, as imposed by one of our main aims in this research. Moderate yields were obtained by both protocols, and relatively high loadings were required. Nevertheless, it should be pointed out that, as far as we know, this is the first example of a Hiyama coupling or arylation with an arylsilane derivative performed by a palladium complex of a tridentate ligand.

Copper-free Sonogashira coupling was the next process in which the activity of catalyst **1** was examined. Three different reaction conditions, in which complex **1** replaced palladium

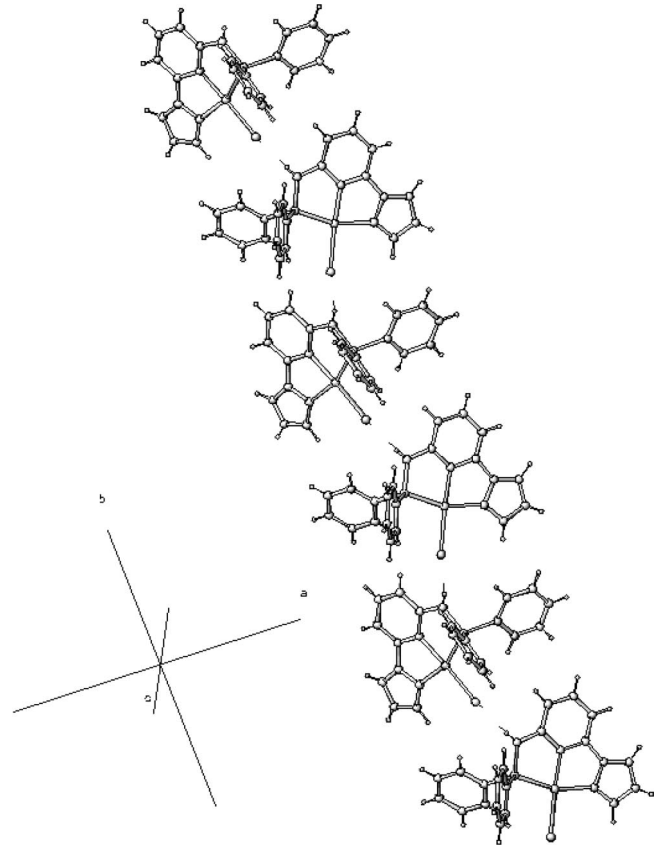
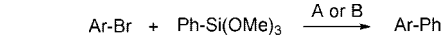


Figure 5. One-dimensional chain structure of complex **1** formed by C−H···Cl hydrogen bonds.

Table 2. Preliminary Hiyama Coupling Assays Performed with Catalyst 1



Method A: **1** (2 mol%), NaOH, H_2O, 140 °C, 3h
Method B: **1** (4 mol%), $^nBu_4NF$, *o*-xylene, 80 °C, 4h

entry	Ar	method A (%)[a]	method B (%)[a]
1	4-AcC_6H_4	82 (80)[b]	61 (57)[b]
2	4-MeOC_6H_4	28	40
3	4-$NO_2C_6H_4$	13[c]	51

[a] Determined by ^{1}H NMR spectroscopy on the basis of the amount of starting aryl halide. Diethylene glycol dimethyl ether was used as internal standard. [b] Isolated yields (flash column chromatography). [c] 4 mol % of **1** was required.

sources and ligands of bibliographic procedures,[18] were applied to arylation of phenylacetylene with a series of aryl iodides, providing moderate to good yields in most cases. Although thermal activation provides generally better results (method C), there is no clear trend on whether the electronic properties of the iodides influence the reaction outcome. Again, aqueous conditions employing complex **1** resulted in comparative efficiency (Table 3). Our previous work on NCN pincer complexes had provided an exceedingly effective catalyst (TON values up to 8×10^5),[6a] but the versatility of the presented PCN complex **1** for working under different reaction conditions, including aqueous mixtures, cannot be overlooked.

Finally, the catalytic activity of palladacycle **1** was thoroughly tested in Suzuki cross-coupling, a more adequate reaction for

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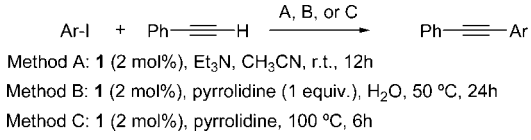
Table 3. Copper-Free Sonogashira Alkynylation Assays Performed with Catalyst 1



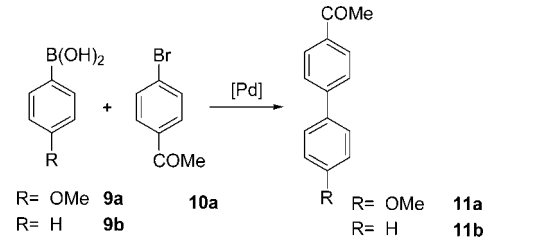
entry	Ar	A (%)[a]	B (%)[a]	C (%)[a]
1	Ph	84 (80)[b]	83 (78)[b]	>99 (96)[b]
2	1-Naph[c]	77	44	93
3	4-$MeOC_6H_4$	52	50	89
4	2-MeC_6H_4	33	62	84
5	3-MeC_6H_4	71	73	<5
6	4-$NH_2C_6H_4$	36	16	75
7	4-$NO_2C_6H_4$	97 (92)[b]	60 (57)[b]	60 (55)[b]
8	4-ClC_6H_4	<5	<5	>99

[a] Determined by ^{1}H NMR spectroscopy on the basis of the amount of starting aryl halide. Diethylene glycol dimethyl ether was used as internal standard. [b] Isolated yields (flash column chromatography). [c] 1-Naph = 1-naphthyl.

use of an aqueous environment.[19] Taking into account our experience in this process,[6a,c] a brief optimization of experimental conditions was performed using phenylboronic and 4-methoxyphenylboronic acids (**9a**,**b**) and 4-bromoacetophenone (**10a**) as model substrates (Table 4). Although coupling in MeOH or EtOH was effected with excellent results at room temperature (Table 4, entries 1 and 2), a reduction in catalyst loading or change in the boronic acid employed provoked a decrease in reaction yields (entries 3−5), a problem that was not sorted out by the use of aqueous mixtures of these alcohols or higher temperatures (entries 6−10). Next, a set of different assays were performed employing water as the only solvent (entries 11−23), providing the conditions displayed in entry 21 (0.01 mol % of **1**, 2.0 equiv of K_2CO_3, 1 mL of H_2O per mmol of aryl halide, 100 °C, 2 h) as the most convenient for the synthesis of both biaryls **11a**,**b**. It should be pointed out that, in contrast with other catalytic systems that require specific bases/additives or relative amounts of starting materials,[20] the use of pincer **1** in water proved to be quite insensible to such variables/variations, a clear advantage from a practical point of view. The latter optimized conditions were applied to an array of arylboronic acids and aryl halides, providing the results displayed in Table 5. Good to excellent yields were obtained in all cases, regardless of the electronic or steric nature of the coupling partners.

Due to the excellent results achieved, most of the biaryls **11** were prepared from aryl bromides, although iodides proved to be useful coupling partners (Table 5, entries 15 and 16) and even 4-chloroacetophenone coupled with phenylboronic acid with an acceptable yield (entry 5), but higher temperature and catalyst loading and longer reaction times were required. Taking the generation of biaryl **11a** as a model reaction, the amount of catalyst was gradually decreased to 10^{-4} mol %, still resulting in quantitative yield (>99%). When 10^{-5} mol % of catalyst **1** was employed, an 82% yield was observed, thus achieving a TON value of 8 200 000, the highest reported so far for a Suzuki coupling catalyzed by a PCN pincer complex.[21] The same protocol was applied to the coupling between 1-naphthyl bromide and 1-naphthylboronic acid leading to 1,1′-binaphthyl (**11p**), reaching in this case a TON value of 3 700 000.

Table 4. Selected Suzuki Coupling Assays Catalyzed by 1



entry	reacn conditions[a]	**11** (amt (%))[b]
1	**9a**, **1** (2 mol %), K_2CO_3, MeOH, 25 °C	**11a** (>99)
2	**9a**, **1** (2 mol %), K_2CO_3, EtOH, 25 °C	**11a** (>99)
3	**9a**, **1** (10^{-2} mol %), K_2CO_3, MeOH, 25 °C	**11a** (<5)
4	**9a**, **1** (10^{-2} mol %), K_2CO_3, EtOH, 25 °C	**11a** (72)
5	**9b**, **1** (10^{-2} mol %), K_2CO_3, EtOH, 25 °C	**11b** (41)
6	**9a**, **1** (10^{-2} mol %), K_2CO_3, MeOH:H_2O (3:1), 25 °C	
7	**9a**, **1** (10^{-2} mol %), K_2CO_3, EtOH:H_2O (3:1), 25 °C	**11a** (10)
8	**9a**, **1** (10^{-2} mol %), K_2CO_3, MeOH:H_2O (3:1), 60 °C	**11a** (80)
9	**9a**, **1** (10^{-2} mol %), K_2CO_3, EtOH:H_2O (3:1), 60 °C	**11a** (51)
10	**9a**, **1** (10^{-2} mol %), K_2CO_3, EtOH, 60 °C	**11a** (34)
11	**9a**, **1** (2 mol %), K_2CO_3, H_2O, 25 °C	**11a** (>99)
12	**9a**, **1** (2 mol %), K_2CO_3, H_2O, 50 °C	**11a** (>99)
13	**9a**, **1** (10^{-2} mol %), K_2CO_3, H_2O, 25 °C	**11a** (62)
14	**9a**, **1** (10^{-2} mol %), K_2CO_3, H_2O, 50 °C	**11a** (>99)
15	**9b**, **1** (10^{-2} mol %), K_2CO_3, H_2O, 50 °C	**11b** (80)
16	**9a**, **1** (10^{-2} mol %), K_3PO_4, H_2O, 100 °C	**11a** (>99)
17	**9a**, **1** (10^{-2} mol %), Na_2CO_3, H_2O, 100 °C	**11a** (>99)
18	**9a**, **1** (10^{-2} mol %), NaOH, H_2O, 100 °C	**11a** (74)
19	**9a**, **1** (10^{-2} mol %), KOH, H_2O, 100 °C	**11a** (>99)
20	**9a**, **1** (10^{-2} mol %), K_2CO_3, H_2O, 100 °C	**11a** (>99)
21	**9b**, **1** (10^{-2} mol %), K_2CO_3, H_2O, 100 °C	**11b** (>99)
22[c]	**9a**, **1** (10^{-2} mol %), K_2CO_3, H_2O, 100 °C	**11a** (95)
23[d]	**9a**, **1** (10^{-2} mol %), K_2CO_3, H_2O, 100 °C	**11a** (96)

[a] 1.5 equiv of **9**, 1.0 equiv of **10a**, and 2.0 equiv of base were employed for a reaction time of 2 h. [b] Determined by ^{1}H NMR on the basis of the amount of starting aryl halide. Diethylene glycol dimethyl ether was used as internal standard. [c] 1.0 equiv of **9** was used. [d] 1.2 equiv of **9** was used.

At this point, a comparison in terms of catalytic efficiency and scope of application can be established between our complex **1** and other structurally related phosphinite-type PCN pincer catalysts. Dupont et al. employed palladium complex **3** to catalyze Mizoroki−Heck reactions in DMA, obtaining excellent yields and TONs (up to 1 000 000).[8d] The same group also assayed Suzuki coupling in 1,4-dioxane of 4,7-dibromo-2,1,3-benzothiadiazoles,[8a] 5,8-dibromoquinoxalines,[8b] and a range of aryl bromides and chlorides[8c] with good yields but using high catalyst loadings.[21] The group of Motoyama prepared the asymmetric "Phemox-OP" derived complex **4**, but its application to catalysis is still under investigation.[9] Recently, Song et al. prepared phosphinite complexes **5** and **6** and studied their catalytic properties in the Suzuki cross-coupling of phenylboronic acid in DMF. They concluded that the best results (moderate to good yields employing two aryl chlorides and several aryl bromides) were obtained by means of complexes **5** having the dicyclohexylphosphinoxy group (R = Cy; R^1 = H, Me), again with relatively high catalyst loading.[10,21] Our complex **1**, bearing the key (diphenylphosphino)amino moiety, has proven to be an excellent, much more efficient, and general catalyst in Suzuki coupling and shows a satisfactory activity in Sonogashira and pioneering Hiyama coupling reactions, with

(19) See for example: (a) Genet, J. P.; Savignac, M. *J. Organomet. Chem.* **1999**, *576*, 305. (b) Zhao, Y.; Zhou, Y.; Ma, D.; Liu, J.; Li, L.; Zhang, T. Y.; Zhang, H *Org. Biomol. Chem.* **2003**, *1*, 1643. (c) Andrade, C. K. Z.; Alves, L. M. *Curr. Org. Chem.* **2005**, *9*, 195.

(20) See for example: Hahn, F. E.; Jahnke, M. C.; Pape, T. *Organometallics* **2007**, *26*, 150. (b) Vicente, J.; Abad, J.-A.; López-Serrano, J.; Jones, P. G.; Nájera, C.; Botella-Segura, L. *Organometallics* **2005**, *24*, 5044.

(21) Dupont, Monteiro et al. and Song et al. reported TONs up to 480 and 1400 with their PCN pincers in Suzuki coupling, respectively.[8c,10]

Table 5. Biaryls Prepared by Suzuki Coupling Employing Catalyst 1

Ar^1-X + Ar^2-B(OH)$_2$ $\xrightarrow[H_2O,\ 100,\ 2h]{\mathbf{1}\ (0.01\ mol\%),\ K_2CO_3}$ Ar^1-Ar^2

9 **10** **11**

entry	X	Ar^1	Ar^2	**11** (%)[a]
1	Br	4-AcC_6H_4	4-$MeOC_6H_4$	**11a** (>99) (97)[b]
2	Br	4-AcC_6H_4	Ph	**11b** (>99)
3	Br	4-AcC_6H_4	4-FC_6H_4	**11c** (92)
4[c]	Br	4-AcC_6H_4	1-Naph	**11d** (>99)
5[d]	Cl	4-AcC_6H_4	Ph	**11b** (72)
6	Br	3-$MeOC_6H_4$	4-$MeOC_6H_4$	**11e** (>99)
7	Br	3-$MeOC_6H_4$	Ph	**11f** (87)
8	Br	4-$MeOC_6H_4$	4-$MeOC_6H_4$	**11g** (87) (83)[b]
9	Br	4-$NO_2C_6H_4$	Ph	**11h** (>99) (96)[b]
10	Br	4-$NO_2C_6H_4$	4-$MeOC_6H_4$	**11i** (>99)
11	Br	4-CNC_6H_4	Ph	**11j** (>99)
12	Br	4-CNC_6H_4	4-$MeOC_6H_4$	**11k** (>99)
13[c]	Br	4-CNC_6H_4	1-Naph	**11l** (>99)
14[c]	Br	1-Naph	4-$MeOC_6H_4$	**11m** (78) (75)[b]
15	I	Ph	4-$MeOC_6H_4$	**11n** (96)
16	I	3,5-$Me_2C_6H_3$	4-$MeOC_6H_4$	**11o** (80)
17[c]	Br	1-Naph	1-Naph	**11p** (>99)
18[c]	Br	2-PhC_6H_4	Ph	**11q** (>99)

[a] Determined by NMR on the basis of the amount of starting aryl halide. Diethylene glycol dimethyl ether was used as internal standard. [b] Yields in italics are isolated yields (flash column chromatography). [c] 1-Naph: 1-Naphthyl; 2-PhPh: 2-Biphenyl. [d] 1.0 equiv. of 4-chloroacetophenone, 1.5 equiv. of phenylboronic acid, 1.0 equiv. of *n*-Bu_4NI and 2 mol% of **1** were used at 150 °C for a reaction time of 4 h

the crucial advantage of the use of aqueous environments. It can be tentatively proposed that both the relatively distorted square planar geometry due to a higher ring strain (a pincer consisting of two different five-membered-ring palladacycles) and the phosphinoamino function have a beneficial effect not only in the activity of pincer **1** but also in its solubility in aqueous media and stability under the reaction conditions.

Recycling of catalyst **1** in the Suzuki coupling reaction leading to **11a** (1.5 equiv of **9a**, 1.0 equiv of **10a**, 0.01 mol % of **1**, 2.0 equiv of K_2CO_3, H_2O, 100 °C, 2 h) was finally assayed. Taking into account the simple workup required to obtain the formed biaryl **11a** (extraction of the aqueous reaction mixture with diethyl ether or dichloromethane), further runs with the same aqueous layer containing the catalyst were performed after adding starting materials **9a** and **10a** and K_2CO_3. Although the first and second runs provided the same results (>99% yield), a dramatic decrease was observed in the third run (9% yield), probably due to a gradual decomposition of catalyst **1** under the reaction conditions.[22]

To summarize, a new PCN-type palladium pincer complex containing a phosphinoamino group has been readily prepared by a one-pot phosphorylation/palladation of 3-(pyrazol-1-yl)benzenamine. This hydrophilic complex not only surpasses all the existing PCN pincer complexes in catalytic activity but also allows the reaction to be conducted in aqueous media, with all the advantages that it implies. Moreover, comparisons between aqueous and nonaqueous protocols have been performed, providing promising results in Hiyama and Sonogashira couplings, reactions which have been catalyzed for the first time by a PCN catalyst. The reported examples in arylation of organosilicon compounds (Hiyama) are pioneering in the field of pincer palladium catalysts. Finally, a general, highly efficient aqueous protocol for the Suzuki coupling of aryl halides catalyzed by our PCN pincer complex is presented. This procedure can be accomplished with notably high TON numbers, and in addition to the simplicity of the catalyst separation/product isolation method, effective reuse of the aqueous layer containing the catalyst is also featured.

The catalytic activity of the presented PCN pincer complex in other palladium-catalyzed reactions is currently being investigated in our laboratories.

Experimental Section

General Procedures. All reagents were purchased and used as received except when indicated. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-300 instrument (300 MHz for ^1H and 75.4 MHz for ^{13}C) at 20 °C. Chemical shifts (δ) are given in ppm downfield from Me_4Si and are referenced as internal standard to the residual solvent (unless indicated) $CDCl_3$ (δ 7.26 for ^1H and δ 77.00 for ^{13}C). ^{31}P NMR spectra were recorded on a Bruker AV-500 (500 MHz for ^1H and 202.4 MHz for ^{31}P). Chemical shifts (δ) were measured in ppm relative to H_3PO_4 (δ 0.00 for ^{31}P) as external standard. Coupling constants, *J*, are reported in hertz (Hz). Melting points were determined in a capillary tube and are uncorrected. TLC was carried out on SiO_2 (silica gel 60 F254, Merck), and the spots were located with UV light. Flash chromatography was carried out on SiO_2 (silica gel 60, Merck, 230−400 mesh ASTM). IR spectra were recorded on a Perkin-Elmer 1600 FT infrared spectrophotometer as KBr plates or as thin films, and only noteworthy absorptions are reported in cm^{-1}. Drying of organic extracts during workup of reactions was performed over anhydrous Na_2SO_4. Evaporation of solvents was accomplished with a Büchi rotatory evaporator. LRMS and HRMS were measured using a Waters GCT mass spectrometer. A prismatic single crystal was selected under a polarizing microscope and mounted on a glass fiber. Single-crystal X-ray diffraction data were collected at room temperature on an Oxford Diffraction XCALIBUR2 automatic diffractometer (Mo Kα radiation) equipped with a CCD detector. Lattice constants were obtained by using a standard program belonging to the software of the diffractometer, confirming at the same time the good quality of the single crystal. The Lorentz−polarization and absorption corrections were made with the diffractometer software, taking into account the size and shape of the crystal. The structures were solved by direct methods (SHELXS97[23]) and subsequent difference Fourier calculations. Details of the crystal structure determination of **1** are given in Table 6.

Synthesis of Amine 2. A solution of the nitro derivate **7** (100 mg, 0.5 mmol) in EtOH (0.63 mL) was added to a solution of AcOH in H_2O (20%, 0.26 mL). Iron dust (236.4 mg, 4.2 mmol) was added, and the mixture was refluxed for 3.5 h under vigorous agitation. After it was cooled, the mixture was diluted with EtOAc (4 mL) and filtered through a plug of Celite, the filter cake being further washed with EtOAc (6 mL). The resulting solution was washed with a 5% aqueous $NaHCO_3$ solution (1 × 4 mL) and H_2O (2 × 3 mL) and dried over anhydrous sodium sulfate. The solvent was removed in vacuo, and the residue was purified by flash chromatography (40% hexane/EtOAc) to provide 60.7 mg (72% yield) of 3-pyrazol-1-ylphenylamine (**2**) as greenish prisms. Mp: 37−39 °C (40% hexane/EtOAc). ^1H NMR (300 MHz, $CDCl_3$): δ 3.82 (2H,

(22) For a review on the role of active species in Suzuki couplings, see: (a) Phan, N. T. S.; van der Sluys, M.; Jones, C. W. *Adv. Synth. Catal.* **2006**, *348*, 609. The decomposition of several palladacycles to form active Pd(0) clusters or colloids has been reported. See, for example: (b) Gaikwad, A. V.; Gadi Rothenberg, G. *Phys. Chem. Chem. Phys.* **2006**, *8*, 3669. (c) Bergbreiter, D. A.; Osburn, P. L.; Frels, J. D. *Adv. Synth. Catal.* **2005**, *347*, 172. Interestingly, although ^{31}P NMR of the aqueous layer after the first run (concentrated in vacuo and redissolved in acetone-d_6) showed as the main signal that at 91.3 ppm corresponding to complex **1**, after the second run the intensity of the latter signal had significantly diminished in favor of other unidentified ones.

(23) Sheldrick, G. M. SHELXS97: Program for the Refinement of Crystal Structures; University of Göttingen, Göttingen, Germany, 1997.

Table 6. Summary of Crystal Structure Determination for PCN Complex 1

formula	$C_{21}H_{17}ClN_3PPd$
mol wt	484.20
cryst syst, space group	orthorhombic, *Pbca*
unit cell dimens *a, b, c* (Å)	15.4670(7), 15.8451(7), 15.8451(7)
α, β, γ (deg)	90, 90, 90
V (Å^3), Z	3883.3(3), 8
ρ_{calcd} (g cm^{-3})	1.656
$F(000)$	1936
θ range (deg)	2.87−23.82
μ (mm^{-1})	1.186
no. of collected/unique rflns	22 903/2974 (R(int) = 0.0856)
goodness of fit on F^2	1.532
final R indices ($I > 2\sigma(I)$)	R1 = 0.0951, wR2 = 0.1241
R indices (all data)	R1 = 0.0988, wR2 = 0.1254
largest diff peak and hole (e Å^{-3})	+0.443 and −0.483

NH_2), 6.43 (s, 1H, H_{pyr}-4), 6.58 (d, J = 7.92 Hz, 1H, H_{arom}-6), 6.99 (d, J = 7.96 Hz, 1H, H_{arom}-4), 7.08 (s, 1H, H_{arom}-2), 7.19 (t, J = 7.98 Hz, 1H, H_{arom}-5), 7.69 (s, 1H, H_{pyr}-3), 7.87 (d, J = 2.28 Hz, 1H, H_{pyr}-5). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 105.3 (C_{arom}-2), 106.9 (C_{pyr}-4), 108.1 (C_{arom}-4), 112.6 (C_{arom}-6), 126.5 (C_{pyr}-5), 129.7 (C_{arom}-5), 140.3 (C_{pyr}-3), 140.5 (C_{arom}-3), 147.5 (C_{arom}-1). Anal. Calcd for $C_9H_9N_3$: C, 67.90; H, 5.70; N, 26.40. Found: C, 67.87; H, 5.71; N, 26.42. HRMS (EI): m/z calcd for $C_9H_9N_3$ 159.0796, found 159.0799.

Synthesis of [2-(1*H*-Pyrazolyl-κ*N2*)-6-((diphenylphosphino)amine-κ*P*)phenyl-κ*C1*]palladium(II) Chloride (1). A solution of $ClPPh_2$ (0.56 mL, 3.1 mmol) in dry, degassed toluene (9.6 mL) was added dropwise to a solution of amine **2** (500 mg, 3.1 mmol) and NEt_3 (0.43 mL, 3.14 mmol) in a degassed mixture of anhydrous toluene and hexane (9:1; 37.3 mL) under argon at room temperature in a Schlenk tube. The mixture was stirred at the same temperature for 10 h. After verification by ^{31}P NMR that the main signal appeared at 28.5 ppm, the crude mixture was filtered under argon and, without further purification, added to a suspension of Pd(COD)Cl_2 (897.9 mg, 3.14 mmol) in dry, degassed toluene (39 mL) at room temperature. The mixture was heated to reflux with stirring for 4 h. After it was cooled, the crude reaction mixture was filtered, the filtrand was washed with acetone (400 mL), and the filtrate was concentrated in vacuo. The residue was redissolved in acetone (2 mL) and cooled to −20 °C to provide a suspension, which was filtered to yield 979.9 mg (64%) of complex **1** as a green powder. Mp: 210−212 °C dec. ^{31}P NMR (202.4 MHz, acetone-d_6): δ 91.3. ^{1}H NMR (300 MHz, acetone-d_6): δ 6.67−6.69 (m, 1H, H-2), 6.70−6.72 (m, 1H, H-6), 7.03−7.08 (m, 2H, H-5, H-7), 7.51−7.57 (m, 6H, H-12, H-13, H-14, H-18, H-19, H-20), 7.95 (s, 1H, H-1), 8.05−8.09 (m, 4H, H-11, H-15, H-17, H-21), 8.53 (d, J = 2.25 Hz, 1H, H-3). ^{13}C NMR ^{1}H (75.5 MHz, acetone-d_6): δ 103.5 (C-5), 106.8 (d, J = 4.13 Hz, C-2), 108.2 (d, J = 19.09 Hz, C-7), 126.9 (C-6), 127.4 (C-3), 128.6 (d, J = 11.64 Hz, C-12, C-14, C-18, C-20), 131.3 (d, J = 2.73 Hz, C-13, C-19), 131.8 (d, J = 13.73 Hz, C-11, C-15, C-17, C-21), 133.32 (C-4), 133.7 (C-8), 134.6 (d, J = 13.38 Hz, C-10, C-16), 139.5 (d, J = 2.93 Hz, C-1), 143.4 (C-9). Anal. Calcd for $C_{21}H_{17}ClN_3PPd$: C, 52.09; H, 3.54; N, 8.68; Found: C, 52.12; H, 3.53; N, 8.65; HRMS (EI): m/z calcd for $C_{21}H_{17}ClN_3PPd$ 482.9883, found 482.9889.

General Procedure for Hiyama Cross-Coupling Reactions. Method A. Pincer complex **1** (2 mol %) was added to a mixture of trimethoxyphenylsilane (1.2 mmol), NaOH (2.5 mmol), and water (5 mL) in a 10 mL round-bottom flask open to the atmosphere. The mixture was stirred for 10 min at room temperature, and the aryl bromide was added (1 mmol). After it was stirred at 140 °C for 1.5 h, the reaction mixture was cooled and H_2O (5 mL) was added. The aqueous layer was extracted with Et_2O (3 × 6 mL). The combined organic extracts were dried over sodium sulfate and concentrated in vacuo. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR using diethylene glycol dimethyl ether as internal standard.

Method B. Pincer complex **1** (4 mol %) was added to a mixture of trimethoxyphenylsilane (1.2 mmol), Bu_4NF (2 mmol), and *o*-xylene (1 mL) in a 5 mL round-bottom flask under an argon atmosphere. The mixture was stirred for 10 min at room temperature, and the aryl bromide was added (1 mmol). After it was stirred at 80 °C for 4 h, the reaction mixture was cooled and H_2O (5 mL) was added. The aqueous layer was extracted with Et_2O (3 × 6 mL). The combined organic extracts were dried over sodium sulfate and concentrated in vacuo. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR using diethylene glycol dimethyl ether as an internal standard.

General Procedure for Sonogashira Cross-Coupling Reactions. Method A. Pincer complex **1** (2 mol %) was added to a mixture of aryl iodide (1 mmol), phenylacetylene (1.5 mmol), NEt_3 (3 mmol), and CH_3CN (5 mL) in a 10 mL round-bottom flask open to the atmosphere. After it was stirred for 12 h at room temperature, the reaction mixture was cooled and H_2O (5 mL) was added. The aqueous layer was extracted with EtOAc (3 × 6 mL). The combined organic extracts were dried over sodium sulfate and concentrated in vacuo. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR using diethylene glycol dimethyl ether as an internal standard.

Method B. Pincer complex **1** (2 mol %) was added to a mixture of aryl iodide (1 mmol), phenylacetylene (1.5 mmol), pyrrolidine (1 mmol), and H_2O (1.5 mL) in a 5 mL round-bottom flask open to the atmosphere. After it was stirred for 12 h at 50 °C, the reaction mixture was cooled and H_2O (5 mL) was added. The aqueous layer was extracted with EtAcO (3 × 6 mL). The combined organic extracts were dried over sodium sulfate and concentrated in vacuo. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR using diethylene glycol dimethyl ether as an internal standard.

Method C. Pincer complex **1** (2 mol %) was added to a mixture of aryl iodide (1 mmol), phenylacetylene (1.5 mmol), and pyrrolidine (2 mL) in a 5 mL round-bottom flask open to the atmosphere. After it was stirred at 100 °C for 6 h, the reaction mixture was cooled and the solvent was removed under reduced pressure. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR using diethylene glycol dimethyl ether as an internal standard.

Suzuki Cross-Coupling Reactions. General Procedure. Pincer complex **1** (0.01 mol %) was added to a mixture of aryl halide (1 mmol), arylboronic acid (1.5 mmol), K_2CO_3 (2 mmol), and water (1 mL) in a 5 mL round-bottom flask open to the atmosphere. After it was stirred at 100 °C for 2 h, the reaction mixture was cooled and Na_2CO_3 (5 mL of a 10% solution in water) was added. The aqueous layer was extracted with CH_2Cl_2 (3 × 6 mL). The combined organic extracts were dried over sodium sulfate and concentrated in vacuo. The residue was dissolved in $CDCl_3$ and analyzed by ^{1}H NMR using diethylene glycol dimethyl ether as an internal standard.

Reuse of Catalyst 1 in Suzuki Couplings. A 5 mL round-bottom flask was charged with ArBr (1 mmol), $ArB(OH)_2$ (1.5 mmol), catalyst **1** (0.01 mol %), K_2CO_3 (2 mmol), and water (1 mL). The mixture was stirred at 100 °C for 2 h in air. After the mixture was cooled, the aqueous layer was extracted with dichloromethane (3 × 3 mL), and the flask was charged again with aryl bromide (1 mmol), arylboronic acid (1.5 mmol) and K_2CO_3 (2 mmol). Every time, after cooling and extraction with CH_2Cl_2 (3 × 3 mL), the reagents and base were added and the reaction was repeated. As previously explained in the General Procedure, the combined organic extracts were dried over sodium sulfate and evacuated in vacuo and the residue was analyzed by ^{1}H NMR using diethylene glycol dimethyl ether as an internal standard.

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Supporting Information Available: A CIF file giving full crystallographic data for complex **1** and text giving ^{1}H and ^{13}C NMR data of all coupling products. This material is available free of charge via the Internet at http://pubs.acs.org.

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