

Article

The Suzuki Reaction in Aqueous Media Promoted by P, N Ligands

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Abstract: The synthesis and structure of palladium complexes of trisubstituted PTA derivatives, PTA_{R_3} , are described. Water-soluble phosphine ligands 1,3,5-triaza-7-phosphaadamantane (PTA), tris(aminomethyl)phosphine trihydrobromide, tri(aminomethyl)phosphine, 3,7-dimethyl-1,5,7-triaza-3-phosphabicyclo[3,3,1]nonane (RO-PTA), 3,7-diacetyl-1,3,7-triaza-5-phosphabicyclo[3.3.1]nonane (DAPTA), lithium 1,3,5-triaza-7-phosphaadamantane-6-carboxylate ($\text{PTA-CO}_2\text{Li}$), 2,4,6-triphenyl-1,3,5-triaza-7-phosphatrimethyl[3.3.1.1]decane, and 2,4,6-triphenyl-1,3,5-triaza-7-phosphatrimethyl[3.3.1.1]decane were used as ligands for palladium catalyzed Suzuki reactions in aqueous media. RO-PTA in combination with palladium acetate or palladium chloride was the most active catalyst for Suzuki cross coupling of aryl bromides and phenylboronic acid at 80 °C in 1:1 water:acetonitrile. The activity of Pd(II) complexes of RO-PTA is comparable to $\text{PPh}_2(m\text{-C}_6\text{H}_4\text{SO}_3\text{Na})$ (TPPMS) and $\text{P}(m\text{-C}_6\text{H}_4\text{SO}_3\text{Na})_3$ (TPPTS) and less active than tri(4,6-dimethyl-3-sulfonatophenyl)phosphine trisodium salt (TXPTS). Activated, deactivated, and sterically hindered aryl bromides were examined, with yields ranging from 50% to 90% in 6 h with 5% palladium precatalyst loading. X-ray crystal structures of (RO-PTA) PdCl_2 , $(\text{PTA}_{\text{R}_3})_2\text{PdCl}_2$ (R = Ph, *p*-*tert*-butyl C_6H_5), and PTA_{R_3} (R = *p*-*tert*-butyl C_6H_5) are reported.

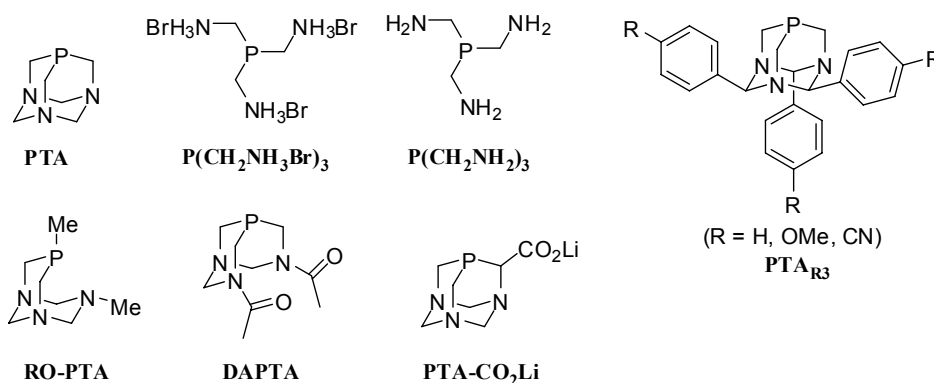
Keywords: C–C coupling; aqueous phase Suzuki reaction; 1,3,5-triaza-7-phosphaadamantane (PTA); water-soluble phosphine ligands

1. Introduction

Transition metal catalyzed C–C bond formations are one of the most important transformations in organic synthesis [1]. Pd-catalyzed coupling reactions are among the most efficient methods to construct carbon-carbon and carbon-heteroatom bonds [2-10]. Heck [2,3], Suzuki [2,4], Stille [5,6], Sonogashira [7,8], and Buchwald-Hartwig [9,10] couplings are widely used to synthesize natural products, materials, and polymers. Since Casalnuovo's initial report of palladium-catalyzed cross-coupling reactions in aqueous solvents using TPPMS/Pd(OAc)₂ [11], a variety of catalytic systems in aqueous media have been developed and used for cross-coupling reactions [12-27]. Some recent examples of aqueous phase Suzuki reactions involve sterically demanding ligands [12,22-23], ligand free palladium catalysts [14,24], palladium nanoparticles on ionic liquids co-polymerized with styrene [15], and ZrO₂ impregnated with palladium nanoparticles [17].

We have been interested in the chemistry of the neutral, air-stable and water soluble 1,3,5-triaza-7-phosphaadamantane (PTA) [28-34]. Several PTA derivatives have been published in the literature including ring-opened PTA (RO-PTA) [35,36], DAPTA [28,36,37], PTA-CO₂Li [33], P(CH₂NH₃Br)₃ [38], P(CH₂NH₂)₃ [30], and PTA_{R3} (R = Ph, *p*-PhOCH₃, *p*-PhCN) [30] (Figure 1). Due to the excellent donating properties and water solubility of PTA Joó, Darensbourg, and others introduced PTA to aqueous phase catalysis [39-45]. PTA and complexes of PTA have been utilized as catalysts for other reactions including but not limited to aqueous or aqueous biphasic hydrogenation of alkenes and aldehydes [41-43], hydroamination [46], the Baylis-Hillman reaction [47,48], Sonagashira coupling [49], Huisgen cycloadditions of azides and terminal alkynes [50], and allylation of acetylacetone by allylic carbonates [51]. PTA has also been used as a ligand in regioselective Suzuki reactions of dihaloimidazoles and dihalooxazoles [52].

Figure 1. PTA and derivatives of PTA.



2. Results and Discussion

Palladium complex **1** was obtained as a yellow solid in 78% yield by reacting RO-PTA and PdCl₂(COD) in methylene chloride at room temperature for one hour (Scheme 1). Compound **1** is slightly soluble in organic solvents and soluble in water; however, aqueous solutions of **1** form black precipitates over several hours indicating decomposition. The square planar palladium center of **1**, Figure 2, contains similar bond lengths and bond angles as the analogous palladium acetate derivative

synthesized by Peruzzini and coworkers [53]. The ^{31}P -NMR spectrum of **1** contains a singlet at -26.6 ppm in D_2O , downfield from the *cis*-palladium acetate derivative (-46.6 ppm) in CD_2Cl_2 [53]. Peruzzini and coworkers obtained the ^{31}P -NMR spectrum of *trans*- $\text{PdCl}_2\{\kappa^1\text{-P}(\text{RO-PTA})\}_2$ which exhibits a singlet at -49.0 ppm in CD_2Cl_2 and -31.2 ppm in D_2O showing that the NMR resonances can shift significantly downfield upon changing the solvent from CD_2Cl_2 to D_2O [53].

Scheme 1. Synthesis of (RO-PTA) PdCl_2 (**1**).

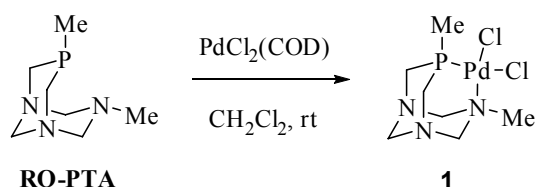
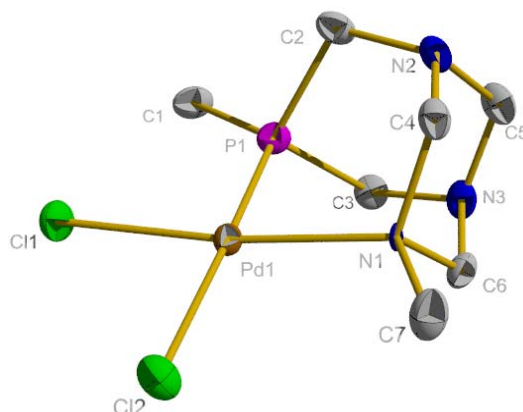


Figure 2. Thermal ellipsoid plot (50% probability) of **1**. Hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg.): Pd1-N1 = 2.131(3), Pd1-P1 = 2.1884(12), Pd1-Cl1 = 2.3007(11), Pd1-Cl2 = 2.4074(11), N1-Pd1-P1 = 85.42(8), N1-Pd1-Cl1 = 173.12(9), P1-Pd1-Cl2 = 177.82(4), P1-Pd1-Cl1 = 89.94(4).



The PTA_{R_3} ligands were synthesized by the reaction of $\text{P}(\text{CH}_2\text{NH}_2)_3$ and either benzaldehyde or *p*-*tert*butylbenzylaldehyde under acidic conditions (Scheme 2). X-ray quality crystals of **2** were grown by slow diffusion of diethyl ether into a methylene chloride solution of **2**, Figure 3. Palladium complexes of the PTA_{R_3} ligands were prepared by stirring two equivalents of PTA_{R_3} and $\text{PdCl}_2(\text{COD})$ in chloroform at room temperature overnight (Scheme 2). The products were obtained as yellow powders in 78% yield for **3** and 83% yield for **4**. The ^{31}P -NMR spectrum of **4** contained the expected singlet resonance at -51.4 ppm in CDCl_3 . Compound **3** was obtained as a mixture of *cis* and *trans* isomers as seen by ^{31}P -NMR spectroscopy which contained a resonance at -51.5 for the *trans* isomer and one at -34.0 ppm for the *cis* isomer in CDCl_3 . X-ray quality crystals of the *trans* isomers of **3** and **4** were obtained and the structures (Figures 4 and 5) are similar to the previously reported *trans*- $\text{PdCl}_2(\text{PTA}_{\text{PhOMe}_3})_2$ [30].

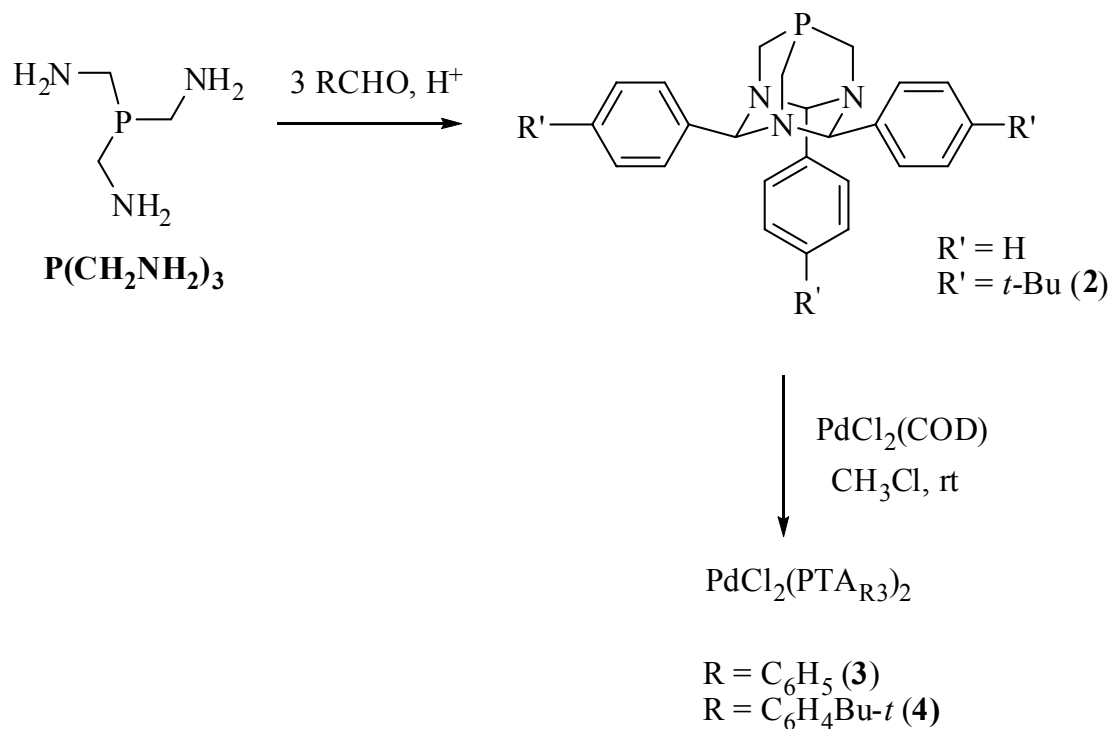
Scheme 2. Synthesis of PTA_{R3} and palladium complexes.

Figure 3. Thermal ellipsoid plot (50% probability) of **2**. Hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg.): P1-C_{ave} = 1.858(4), N-C_{ave} = 1.481(4), C4-C7 = 1.516(5), C5-C17 = 1.520(5), C6-C27 = 1.515(5), C-P1-C_{ave} = 95.65(18).

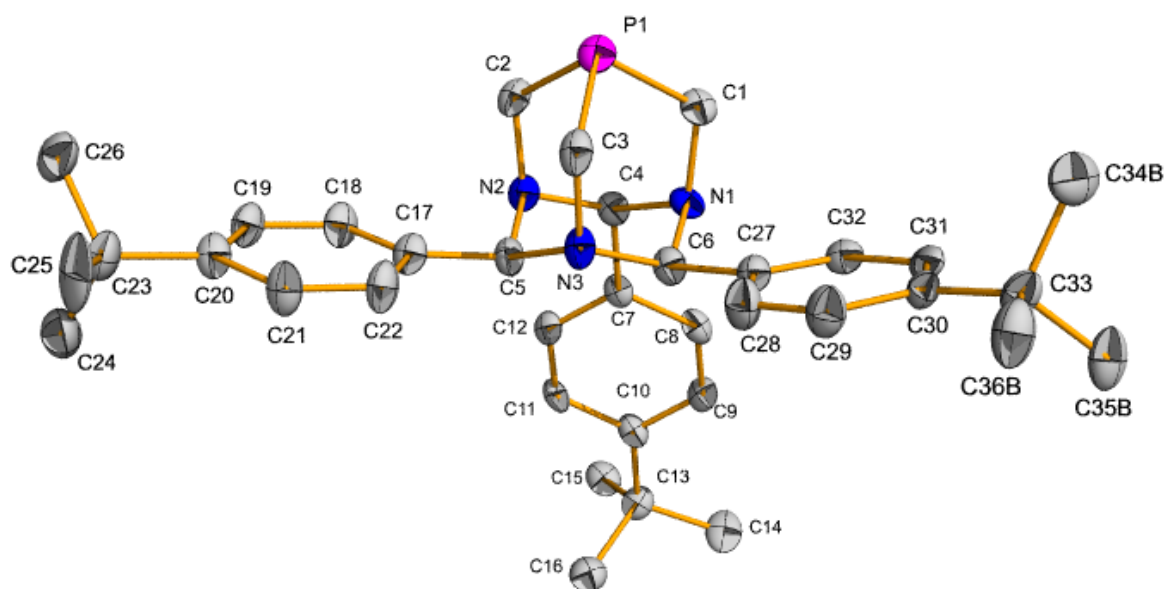


Figure 4. Thermal ellipsoid plot (50% probability) of **3**. Hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg.): Pd1-Cl1 = 2.2930(7), Pd1-P1 = 2.2895(7), P-Pd-P1 = 180.00(6), Cl-Pd-Cl1 = 180.00(5), Cl1-Pd1-P1 = 87.78(3).

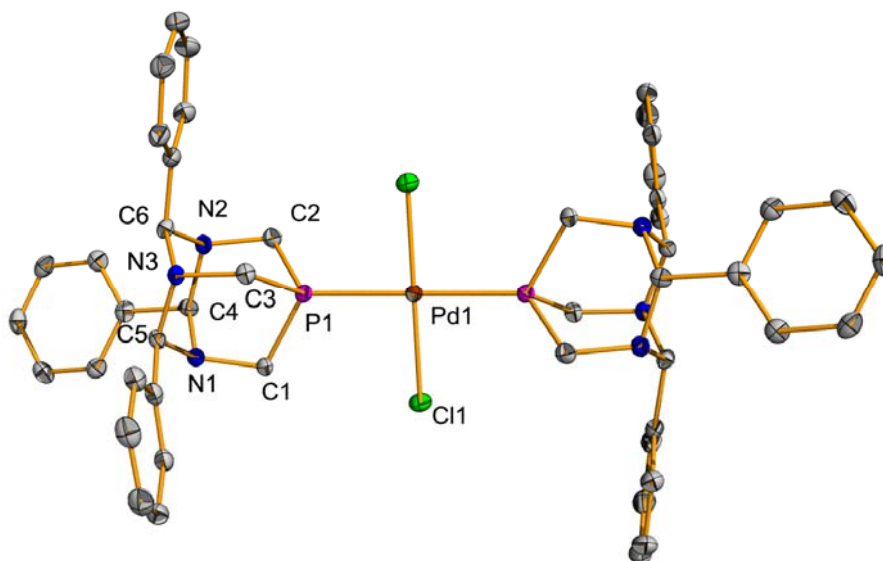
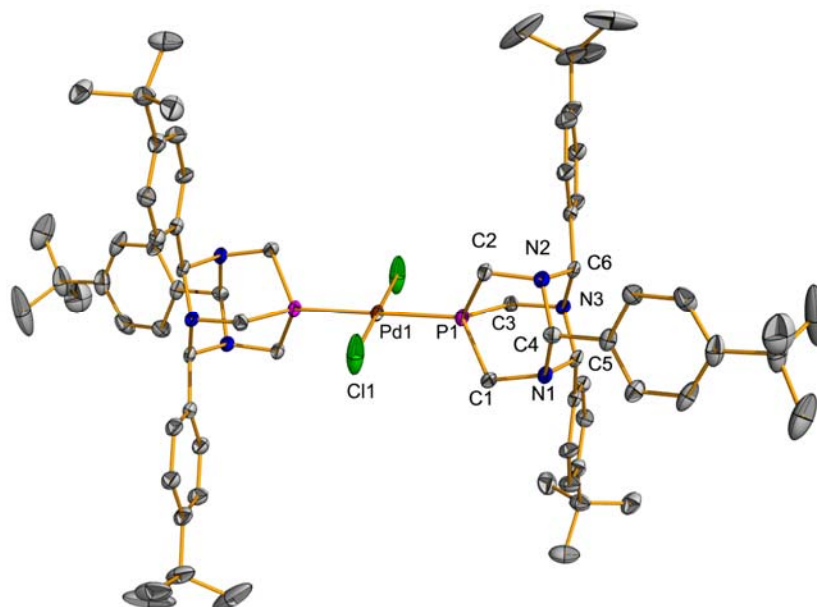


Figure 5. Thermal ellipsoid plot (50% probability) of **4**. Hydrogen atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg.): Pd1-Cl1 = 2.2911(17), Pd1-P1 = 2.2959(13), P-Pd-P1 = 180.0, Cl-Pd1-Cl1 = 180.0, Cl1-Pd1-P1 = 91.87(5).



2.1. Suzuki-Miyaura Coupling

Initial studies on the catalytic activity of Pd(II) complexes of the water soluble ligands described were performed using phenylboronic acid and bromobenzene in 1:1 H₂O:CH₃CN with sodium carbonate as a base and 5% Pd(OAc)₂ loading. The combination of PTA and Pd(OAc)₂ produced a modestly active catalyst at 80 °C over 72 h (66%, Table 1, entry 3). No product was observed at room temperature or at 50 °C. The catalyst decomposed quickly to a black precipitate. Formation of black

precipitate is not surprising because PTA, with a cone angle of 103° , is not large enough to support the coordinatively unsaturated active catalyst. The addition of mercury to the reactions essentially shut down catalysis (Table 1, entries 4, 5, 7), indicating that colloidal palladium likely was involved.

Table 1. Suzuki Coupling catalyzed by Pd(II) and PTA with and without Hg.

Entry	Catalyst	Time (h)	% Yield ^a
1	Pd(OAc) ₂ PTA ₂	24	36.3
2	Pd(OAc) ₂ PTA ₂	48	63.3
3	Pd(OAc) ₂ PTA ₂	72	66
4 ^b	Pd(OAc) ₂ PTA ₂	24	3.0
5 ^b	Pd(OAc) ₂ PTA ₂	48	4.9
6	PdCl ₂ PTA ₂	48	51.5
7 ^b	PdCl ₂ PTA ₂	48	5.0

^a Isolated yield after column chromatography; ^b ~0.5 mL Hg added.

PTA derivatives were then employed as ligands in the palladium catalyzed Suzuki coupling (Table 2). All the PTA derivatives explored here resulted in higher yields, 40%–91% than PTA in less time.

Table 2. Palladium catalyzed Suzuki coupling reactions in aqueous media utilizing water-soluble PTA derivatives.

Entry	Precatalyst	Ligand	Pd:L	Yield (%) ^a
1	Pd(OAc) ₂	DAPTA	1:2	40
2	Pd(OAc) ₂	DAPTA	1:3	42
3	Pd(OAc) ₂	PTA _{Ph3}	1:2	65
4	Pd(OAc) ₂	2	1:2	56
5	3	-	1:2	58
6	4	-	1:2	60
7	Pd(OAc) ₂	PTA-CO ₂ Li	1:1	60
8	Pd(OAc) ₂	PTA-CO ₂ Li	1:2	76
9	Pd(OAc) ₂	PTA-CO ₂ Li	1:3	75
10	Pd(OAc) ₂	P(CH ₂ NH ₃ Br) ₃	1:1	74
11	Pd(OAc) ₂	P(CH ₂ NH ₃ Br) ₃	1:2	77
12	Pd(OAc) ₂	P(CH ₂ NH ₃ Br) ₃	1:3	78
13	Pd(OAc) ₂	P(CH ₂ NH ₂) ₃	1:1	77
14	Pd(OAc) ₂	P(CH ₂ NH ₂) ₃	1:2	80
15	Pd(OAc) ₂	RO-PTA	1:2	86

Table 2. Cont.

16	Pd(OAc) ₂	RO-PTA	1:3	82
17 ^b	Pd(OAc) ₂	RO-PTA	1:2	52
18	PdCl ₂	RO-PTA	1:2	89
19	PdCl ₂	RO-PTA	1:3	85
20	1	-	1:1	91
21	Pd(OAc) ₂	-	-	88
22	PdCl ₂	-	-	80

^a Isolated yield after column chromatography; ^b ~0.5 mL Hg added.

The DAPTA/Pd(OAc)₂ system provided only slightly better yields, 40%–42%, than PTA (Table 2, entries 1 and 2). Catalysts generated from PTA_{R3}/Pd(OAc)₂ provided the product in moderate yields, 56%–65% (Table 2, entries 3–6). The potentially chelating ligand PTA-CO₂Li with Pd(OAc)₂ was slightly more effective with 60%–76% yields depending on the number of equivalents of ligand added (Table 2, entries 7–9). Catalysts derived from P(CH₂NH₃Br)₃ or P(CH₂NH₂)₃ and Pd(OAc)₂ were more active with yields ranging from 74%–80% (Table 2, entries 10–14). The most active system studied was RO-PTA with Pd(II) salts. The *in situ* catalyst (RO-PTA/Pd(II)) showed very good activity with yields between 82% to 89% depending on ration of ligand to Pd(II) (Table 2, entry 15,16,18,19). The preformed catalyst (**1**) was the most active with yields of 91% obtained for the Suzuki coupling of bromobenzene and phenylboronic acid (Table 2, entry 20).

The ratio of ligand to palladium also affected the amount of product produced. The largest change in yield was observed with PTA-CO₂Li, as the L:Pd ratio increased from 1:1 to 2:1 the yield increased from 60 to 76%. Increasing the ratio to 3:1 ligand to palladium had little effect on catalysis (Table 2, entry 7–9). Increasing the L:Pd ratio for P(CH₂NH₃Br)₃ (Table 2, entry 10–12) and P(CH₂NH₂)₃ (Table 2, entry 13,14) from 1:1 to 2:1 resulted in only a small increased yield. Increasing the ratio of RO-PTA:Pd(II) from 1:2 to 1:3 resulted in a slight decrease in the coupling product (Table 2, entry 15,16,18,19). Changing the palladium source from Pd(OAc)₂ to PdCl₂ with RO-PTA resulted in a small difference in yield with PdCl₂ being slightly more active (Table 2, entry 15,16,18,19). It is important to note that the reaction remained clear during catalysis for entries 7–16 and 18–19; unlike the PTA/Pd(OAc)₂ system where palladium black was clearly visible. Addition of Hg to the reaction catalyzed by RO-PTA and Pd(OAc)₂ resulted in a decrease in yield from 86 to 52% (Table 2, entry 17) indicating that the reaction is mainly homogeneous. RO-PTA and P(CH₂NH₂)₃ ligand are potential (P, N) bidentate ligands and due to the hemilabile functionality [54] the catalyst can be stabilized, reducing the amount of palladium black formed. Ligand free coupling reactions with Pd(OAc)₂ and PdCl₂ were explored under the above conditions as a control (Table 2, entry 21–22). Not surprisingly under aqueous conditions Pd(OAc)₂ and PdCl₂ are very good catalysts with biphenyl yields of 88 and 80% respectively. This was not unexpected as palladium catalysts have been reported to be excellent heterogenous Suzuki coupling catalysts in aqueous media [4,24,55].

2.2 Catalyst Scope

Pd(OAc)₂, RO-PTA, and sodium carbonate were used to study the catalyst scope under optimized reaction conditions. It is well-established that electron-deficient aryl bromides are good substrates in

palladium catalyzed cross coupling reactions. With optimal reaction conditions in hand, the scope of the catalyst system was explored with a range of aryl bromides. Suzuki coupling yields were affected by the steric and electronic parameters of the aryl halides (Table 3). Electron neutral aryl bromides such as 4-bromotoluene (Table 3, entry 1) and electron deficient aryl bromides such as 4-bromo-benzonitrile (Table 3, entry 5) coupled well under the conditions described above. Electron donating aryl bromides such as 1-bromo-4-methoxybenzene (Table 3, entry 4) and sterically demanding aryl bromides such as 2-bromotoluene (Table 3, entry 2) resulted in decreased coupling. No catalytic turnover was observed with the sterically demanding 2-bromo-*m*-xylene (Table 3, entry 3). The sterically demanding electron donating 2-bromoanisole resulted in a modest yield (Table 3, entry 6) comparable with electron donating aryl bromide 1-bromo-4-methoxybenzene (Table 3, entry 4). The sterically demanding electron withdrawing 1-bromo-2-nitrobenzene resulted in good but lower yield (Table 3, entry 7) than the electron withdrawing sterically unhindered 4-bromobenzonitrile (Table 3, entry 5). The catalytic activity of RO-PTA/Pd(OAc)₂ is comparable to Suzuki coupling utilizing water soluble phosphines such as TPPMS and TPPTS [19-21]. When compared to water soluble TXPTS and palladacycles developed by Shaughnessy *et al.* [22-23,27] or water soluble diamine ligands [25,26] catalysis by RO-PTA was much less effective.

Table 3. Coupling of aryl halides with phenylboronic acid catalyzed by RO-PTA/Pd(OAc)₂.

Entry ^b	Bromide	Precatalyst	Yield (%) ^a
1		Pd(OAc) ₂	84
2		Pd(OAc) ₂	65
3		Pd(OAc) ₂	<5
4		Pd(OAc) ₂	50
5		Pd(OAc) ₂	90
6		Pd(OAc) ₂	55
7		Pd(OAc) ₂	77

^a Isolated yield after purification by column chromatography; ^b Reactions were run in 1:1 water: acetonitrile at 80 °C for 6 h

3. Experimental

3.1. General

Standard Schlenk and drybox techniques were used for all reactions unless noted. Prior to use, solvents were distilled under nitrogen from the appropriate drying agent (sodium/benzophenone for tetrahydrofuran, calcium hydride for hexanes; magnesium/iodine for methanol). Water (deionized) and acetonitrile were deoxygenated by sparging with nitrogen. Deuterated NMR solvents were purchased from commercial sources and used as received. All NMR spectra were recorded on either a Varian NMR System 400 or Varian Unity Plus 500 FT-NMR spectrometer. ^1H - and ^{13}C -NMR spectra were referenced to a residual solvent relative to tetramethylsilane. Phosphorus chemical shifts are relative to an external reference of 85% phosphoric acid in D_2O with positive values downfield of the reference. Tetrakis(hydroxymethyl)phosphonium chloride was obtained from Cytec and used without further purification. PTA [44,56], PTA_{Ph_3} [30], $\text{P}(\text{CH}_2\text{NH}_3\text{Br})_3$ [38], $\text{P}(\text{CH}_2\text{NH}_2)_3$ [30], $[\text{Me-PTA}]^+\text{T}^-$ [35], DAPTA [36,37], $\text{PTA-CO}_2\text{Li}$ [33], and $\text{PdCl}_2(\text{COD})$ [57] were synthesized according to previously reported methods. The synthesis of ROPTA was performed by a modification of a method reported by Schmidbaur [35]. Palladium chloride and palladium acetate were purchased from Strem and stored in a drybox. Aryl bromides and phenylboronic acids were purchased from Acros Organics and used without further purification.

3,7-Dimethyl-1,5,7-triaza-3-phosphabicyclo[3.3.1]nonane (RO-PTA): Prepared by a modification of a method reported by Schmidbaur [35]. To a mixture of condensed liquid ammonia (80 mL) and $[\text{Me-PTA}]^+\text{T}^-$ (9.00 g, 30.2 mmol) was added sodium metal (878 mg, 38.2 mmol) at $-78\text{ }^\circ\text{C}$ until the color turned dark blue. Stirring was continued for 20 min at $-78\text{ }^\circ\text{C}$. The ammonia was slowly evaporated at room temperature. To the residue was added hexanes (200 mL) and the resulting mixture vigorously stirred for several minutes before filtering under nitrogen. The hexane was removed under reduced pressure resulting in a white, crystalline solid (1.50 g, 29%). Spectral data were identical to previously reported data [35].

cis-(3,7-Dimethyl-1,5,7-triaza-3-phosphabicyclo[3.3.1]nonane)dichloro palladium (II) (1): To a solution of $\text{PdCl}_2(\text{COD})$ (142.8 mg, 0.5 mmol) in methylene chloride (15 mL) was added RO-PTA (86.5 mg, 0.5 mmol). Precipitation was observed after 10 min, but the reaction was stirred for another hour. The precipitate was filtered off, washed with methylene chloride ($2 \times 10\text{ mL}$), collected and dried *in vacuo* to give the product as a yellow solid (136 mg, 78%). $^1\text{H-NMR}$ (D_2O , 400 MHz): δ 4.71 (d, $J = 12.0\text{ Hz}$, 2H), 4.18–4.13 (m, 4H), 4.02 (d, $J = 12.8\text{ Hz}$, 2H), 3.86 (d, $J = 6.8\text{ Hz}$, 1H), 3.83 (d, $J = 6.4\text{ Hz}$, 1H), 2.52 (s, 3H), 1.67 (d, $J = 14.4\text{ Hz}$); $^{31}\text{P-NMR}$ (D_2O , 161.9 MHz): δ -26.6 . X-ray quality crystals were obtained by slow evaporation of the dilute solution of chloroform and ether.

2,4,6-tri(p-tert-Butylphenyl)-1,3,5-phosphatricyclo[3.3.1.1]decane (2): Tris(aminomethyl)phosphine trihydrobromide (1.091 g, 3.0 mmol) and sodium hydroxide (360 mg, 9 mmol) were added to a 100 mL Schlenk flask in a drybox. Fresh distilled methanol (40 mL) was added via syringe resulting in a clear solution. Hydrogen chloride (30 μL 2.0 M in Et_2O , 0.06 mmol) and 4-*tert*-butylbenzaldehyde (2.60 mL, 15 mmol) were added to the resulting solution via syringe. The resulting solution was stirred overnight

at room temperature. Methanol was removed under reduced pressure. The resultant white residue was dissolved in methylene chloride (100 mL) and sodium bromide was extracted by water (2×50 mL). The organic layer was dried over anhydrous potassium carbonate, filtered, and the methylene chloride removed under reduced pressure. The residue was dissolved in methylene chloride (5 mL), absolute ethanol (120 mL) was added, and the flask was set in the freezer overnight. The precipitate was filtered off, washed with ethanol (2×15 mL) and dried *in vacuo* to give the product as a white, crystalline solid (1.063, 64%). $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ 7.66–7.40 (m, 6H), 7.51–7.48 (m, 4H), 7.31 (d, $J = 8.40$ Hz, 2H), 5.95 (s, 1H), 5.49 (s, 2H), 4.48 (d, $J_{\text{PH}} = 9.20$ Hz, 1H), 4.44 (d, $J_{\text{PH}} = 9.20$ Hz, 1H), 3.87 ($J_{\text{PH}} = 9.60$ Hz, 1H), 3.84 (d, $J_{\text{PH}} = 10.00$ Hz, 1H), 3.73 (d, $J_{\text{PH}} = 9.20$ Hz, 2H), 1.37 (s, 18 H), 1.28 (s, 9H). $^{13}\text{C-NMR}$ (100.5 MHz, CDCl_3): δ 150.4, 150.2, 137.3, 136.1, 126.8, 126.1, 125.8, 125.7, 82.9 (d, $^3J_{\text{PC}} = 2.90$ Hz), 75.1 (d, $^3J_{\text{PC}} = 2.70$ Hz), 46.4 (d, $J = 19.50$ Hz), 35.71 (d, $J = 18.69$ Hz), 34.76, 34.6, 31.7, 31.6; $^{31}\text{P-NMR}$ (161.7 MHz, CDCl_3): $-\text{111.9}$. X-ray-quality crystals were obtained by slow diffusion of ether into a methylene chloride solution of ligand **2**, resulting in the formation of clear and colorless blocks over the course of ten days.

bis(2,4,6-Triphenyl-1,3,5-triaza-7-phosphatricyclo[3.3.1.1]decane)dichloro palladium (II) (3): To a solution of $\text{PdCl}_2(\text{COD})$ (57.1 mg, 0.2 mmol) in chloroform (15 mL), 2,4,6-triphenyl-1,3,5-triaza-7-phosphatricyclo[3.3.1.1]decane (155.2 mg, 0.4 mmol) in chloroform (5 mL) was added via syringe. The resulting solution was stirred overnight at room temperature and the solvent removed under vacuum. The residue was taken up into a minimum amount of methylene chloride (2 mL), hexanes (20 mL) was added, and the flask was set in the freezer overnight. The precipitate was filtered off, washed with hexanes (2×5 mL), and dried under vacuum to give the product as a yellow solid (148 mg, 78%). ^1H and $^{31}\text{P-NMR}$ spectra showed both *cis* and *trans* isomers in CDCl_3 in a ratio of approximately 1:1. $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ 7.66–7.26 (m, 30 H), 5.99 (s, 2H), 5.95 (s, 2H), 5.45 (s, 1H), 5.43 (s, 1H), 4.52 (s, 2H), 4.48 (s, 2H), 4.16 (s, 2H), 4.12 (s, 2H), 4.02 (s, 2H), 2.94 (s, 2H); $^{31}\text{P-NMR}$ (161.7 MHz, CDCl_3): δ $-\text{34.0}$, $-\text{51.5}$. X-ray-quality crystals were obtained by slow diffusion of ether into a methylene chloride solution of compound **3**.

trans-bis(2,4,6-tri(p-tert-butylphenyl)-1,3,5-phosphatricyclo[3.3.1.1]decane)dichloro palladium (II) (4): To a solution of $\text{PdCl}_2(\text{COD})$ (65.6 mg, 0.23 mmol) in chloroform (15 mL) ligand **2** (255.8 mg, 0.46 mmol) in chloroform (5 mL) was added via syringe. The resulting solution was stirred overnight at room temperature, and the solvent removed under vacuum. The residue was taken up into a minimum amount of methylene chloride (2 mL), hexanes (20 mL) was added, and the flask was set in the freezer overnight. The precipitate was filtered off, washed with hexanes (2×5 mL), and dried under vacuum to give the product as a yellow solid (256 mg, 83%). $^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ 7.54–7.49 (m, 20 H), 7.31–7.31 (m, 4H), 5.97 (s, 2H), 5.40 (s, 4H), 4.52 (s, 2H), 4.48 (s, 2H), 4.22 (s, 2H), 4.18 (s, 2H), 3.97 (s, 4H), 1.37 (s, 36 H), 1.24 (18H) (161.7 MHz, CDCl_3): δ $-\text{51.4}$. X-ray-quality crystals were obtained by slow diffusion of ether into a methylene chloride solution of compound **4**.

3.2. General Procedure for the Suzuki Coupling Reaction Aryl Halides and Arylboronic Acids

A round bottom flask equipped with stir bar in the drybox was charged with palladium chloride or palladium acetate (11.2 mg, 0.05 mmol), an appropriate amount of ligand, sodium carbonate (212 mg,

2.0 mmol) and phenylboronic acid (183 mg, 1.5 mmol). Deoxygenated 1:1 H₂O:CH₃CN (5 mL) and aryl halide (1.0 mmol) were added and the reaction was stirred at 80 °C for 6 h unless noted. The reaction was cooled to room temperature, saturated sodium bicarbonate (20 mL) was added, and the organics were extracted with ethyl acetate (3 × 30 mL). The combined ethyl acetate extracts were dried (MgSO₄) and the solvent was removed under reduced pressure. The crude material was flash chromatographed on a short silica gel column.

3.3. Mercury Experiment

A Schlenk flask with stir bar was charged with palladium chloride or palladium acetate (8.8 mg or 11.2 mg respectively, 0.05 mmol), PTA (17.3 mg, 0.10 mmol), and sodium carbonate (212.0 mg, 2.0 mmol) under N₂ atmosphere. Five mL of deoxygenated H₂O was then added via syringe and the catalyst solution was stirred for 1.5 h. A 25 mL round bottom was charged with phenylboronic acid (183 mg, 1.5 mmol) and bromobenzene (105 µL, 1.00 mmol), equipped with a condenser under N₂ atmosphere. Deoxygenated CH₃CN (5 mL) and catalyst solution (5 mL) were added via syringe. The reaction mixture was stirred for 15 min followed by the addition of a few drops of mercury before heating to 80 °C. After 24 or 48 h the reaction was allowed to cool to room temperature. The mixture was then extracted with dichloromethane (3 × 5 mL). The combined organic extracts were dried over Na₂SO₄ and the solvent removed under reduced pressure. The crude product was purified on a short column of silica gel.

Biphenyl (Tables 2 and 3). Bromobenzene (105 µL, 1.00 mmol) and phenylboronic acid (183 mg, 1.5 mmol) were coupled by the above procedure. The product was isolated by column chromatography on silica gel with hexanes as the elution solvent. A white solid was obtained (132 mg, 86%) with spectral data identical to previously reported [58].

4-Methyl-1,1'-biphenyl (Table 4, entry 1). 4-Bromotoluene (123 µL, 1.00 mmol) and phenylboronic acid (183 mg, 1.5 mmol) were coupled by the above procedure. The product was isolated by column chromatography on silica gel with hexanes as the elution solvent. A white solid was obtained (133 mg, 84%) with spectral data identical to previously reported [58].

2-Methyl-1,1'-biphenyl (Table 4, entry 2). 2-Bromotoluene (120 µL, 1.0 mmol) and phenylboronic acid (183 mg, 1.5 mmol) were coupled by the above procedure. The product was isolated by column chromatography on silica gel with hexanes as the elution solvent. A white solid was obtained (109 mg, 65%) with spectral data identical to previously reported [59].

4-Methoxy-1,1'-biphenyl (Table 4, entry 4). 4-Bromoanisole (125 µL, 1.00 mmol) and phenylboronic acid (183 mg, 1.50 mmol) were coupled by the above procedure. The product was isolated by column chromatography on silica gel with 5% ethyl acetate-hexanes as the elution solvent. A colorless oil was obtained (92 mg, 50%) with spectral data identical to previously reported [58].

4-Cyano-1,1'-biphenyl (Table 4, entry 5). 4-Bromobenzonitrile (182.0 mg, 1.00 mmol) and phenylboronic acid (183 mg, 1.50 mmol) were coupled by the above procedure. The product was isolated by column chromatography on silica gel with 75:25:5 hexanes-CH₂Cl₂-ethyl acetate as the

elution solvent. A pale yellow solid was obtained (160.9 mg, 90%) with spectral data identical to previously reported [58].

2-Methoxy-1,1'-biphenyl (Table 4, entry 6). 2-Bromoanisole (123.7 μL , 1.00 mmol) and phenylboronic acid (183 mg, 1.50 mmol) were coupled by the above procedure. The product was isolated by column chromatography on silica gel with hexanes as the eluting solvent. A pale yellow oil was obtained (101.3 mg, 55%) with spectral data identical to previously reported [60].

2-Nitro-1,1'-biphenyl (Table 4, entry 7). 1-Bromo-2-nitrobenzene (202 mg, 1.00 mmol) and phenylboronic acid (183 mg, 1.50 mmol) were coupled by the above procedure. The product was isolated by column chromatography on silica gel with hexanes and 5% ethyl acetate/hexanes as the elution solvent. A light yellow oil was obtained (153.7 mg, 77%) with spectral data identical to previously reported [61].

3.4. X-ray Crystallography

X-ray crystallographic data were obtained on a Bruker APEX CCD diffractometer. The structures were solved by direct methods and refined using SHELXTL, version 6.10 [62,63]. Crystallographic data and data collection parameters may be found in Table 4. CCDC 827744–827747 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html.

Table 4. Crystallographic data for compounds 1–4.

	1	2	3	4
Empirical Formula	$\text{C}_7\text{H}_{16}\text{Cl}_2\text{N}_3\text{PPd}$	$\text{C}_{36}\text{H}_{48}\text{N}_3\text{P}$	$\text{C}_{52}\text{H}_{58}\text{C}_{12}\text{N}_6\text{OP}_2\text{Pd}$	$\text{C}_{74}\text{H}_{98}\text{C}_{18}\text{N}_6\text{P}_2\text{Pd}$
Fw	350.50	553.74	1022.28	1523.52
T(K)	100(2)	100(2)	100(2)	100(2)
$\lambda(\text{\AA})$	0.71073	0.71073	0.71073	0.71073
cryst syst	Monoclinic	Triclinic	Triclinic	Triclinic
space group	P21/c	P-1	P-1	P-1
a(\AA)	8.60830(10)	8.2876(8)	11.10810(10)	12.0121(3)
b(\AA)	11.5593(2)	11.8367(12)	14.6003(2)	12.7019(3)
c(\AA)	12.0933(2)	17.4678(19)	16.9813(2)	13.9564(3)
$\alpha(\text{deg})$	90	97.424(7)	113.3050(10)	116.1830(10)
$\beta(\text{deg})$	107.1980(10)	100.306(7)	102.5090(10)	94.1170(10)
$\gamma(\text{deg})$	90	104.442(8)	100.2660(10)	99.6960(10)
V(\AA^3)	1149.55(3)	1605.2(3)	2359.92(5)	1857.75(8)
Z	4	2	2	1
Dcalc (Mg/m ³)	2.025	1.146	1.439	1.362
abs coeff (mm ⁻¹)	2.184	0.114	0.620	0.626
cryst size (mm ³)	0.07 \times 0.06 \times 0.03	0.56 \times 0.56 \times 0.04	0.12 \times 0.08 \times 0.07	0.31 \times 0.09 \times 0.05
θ data collect (deg)	2.48 to 26.37 -10 \leq h \leq 9	1.81 to 22.50 -8 \leq h \leq 8	1.38 to 27.43 -14 \leq h \leq 14	1.65 to 27.55 -15 \leq h \leq 15
Index ranges	-14 \leq k \leq 13 -14 \leq l \leq 15	-12 \leq k \leq 12 -18 \leq l \leq 18	-18 \leq k \leq 18 -21 \leq l \leq 21	-16 \leq k \leq 16 -18 \leq l \leq 18

Table 4. Cont.

	1	2	3	4
reflns collected	21262	10984	59870	30379
indep reflns	2351	4121	10747	8530
	R _{int} = 0.0452	R _{int} = 0.0822	R _{int} = 0.0622	R _{int} = 0.0674
abs correction	SADABS	SADABS	SADABS	SADABS
data/restraints/param	2351/0/127	4121/0/418	10747/0/582	8530/0/421
GOF F ²	1.088	0.930	1.033	1.051
final R indices	R1 = 0.0343	R1 = 0.0643,	R1 = 0.0424	R1 = 0.0810
[I \square 2 σ (I)]	wR2 = 0.0761	wR2 = 0.1190	wR2 = 0.0898	wR2 = 0.2168
R indices	R1 = 0.0462	R1 = 0.1289	R1 = 0.0755	R1 = 0.1200
(all data)	wR2 = 0.0791	wR2 = 0.1363	wR2 = 0.1046	wR2 = 0.2426
CCDC no.	827747	827746	827745	827744

4. Conclusions

We have reported here the synthesis and structure of palladium(II) complexes of RO-PTA (**1**) and PTA_{R3} (**3–4**). The air stable, water-soluble, and potentially hemilabile P,N ligand RO-PTA was successfully used for the Suzuki reaction in aqueous media. The combination of RO-PTA and palladium acetate generated an effective catalyst for the Suzuki coupling reaction. Electron neutral and electron deficient aryl bromide substrates coupled well with phenylboronic acid in good yields. The catalytic system was modestly effective in the Suzuki coupling reaction for electron-rich and sterically bulky aryl bromides. Catalytic activity of RO-PTA is comparable to TPPMS and TPPTS and less active than water-soluble diamines and phosphines like TXPTS.

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References and Notes

- Jana, R.; Pathak, T.P.; Sigman, M.S. Advances in transition metal (Pd, Ni, Fe)-catalyzed cross-coupling reactions using alkyl-organometallics as reaction partners. *Chem. Rev.* **2011**, *111*, 1417-1492.
- Liu, S.; Xiao, J. Toward green catalytic synthesis-Transition metal-catalyzed reactions in non-conventional media. *J. Mol. Catal. A: Chem.* **2007**, *270*, 1-43.
- Beletskaya, I.P.; Cheprakov, A.V. The Heck reaction as a sharpening stone of palladium catalysis. *Chem. Rev.* **2000**, *100*, 3009-3066.
- Alonso, F.; Beletskaya, I.P.; Yus, M. Non-conventional methodologies for transition-metal catalysed carbon-carbon coupling: a critical review. Part 2: The Suzuki reaction. *Tetrahedron* **2008**, *64*, 3047-3101.

5. De Souza, M.V.N. Stille reaction: An important tool in the synthesis of complex natural products. *Curr. Org. Syn.* **2006**, *3*, 313-326.
6. Espinet, P.; Echavarren, A.M. The mechanisms of the Stille reaction. *Angew. Chem. Int. Ed. Engl.* **2004**, *43*, 4704-4734.
7. Doucet, H.; Hierso, J.-C. Palladium-based catalytic systems for the synthesis of conjugated enynes by Sonogashira reactions and related alkynylations. *Angew. Chem. Int. Ed. Engl.* **2007**, *46*, 834-871.
8. Chinchilla, R.; Najera, C. The Sonogashira reaction: A booming methodology in synthetic organic chemistry. *Chem. Rev.* **2007**, *107*, 874-922.
9. Schlummer, B.; Scholz, U. Palladium-catalyzed C–N and C–O coupling—A practical guide from an industrial vantage point. *Adv. Synth. Catal.* **2004**, *346*, 1599-1626.
10. Hartwig, J.F. Carbon-heteroatom bond-forming reductive eliminations of amines, ethers, and sulfides. *Acc. Chem. Res.* **1998**, *31*, 852-860.
11. Casalnuovo, A.L.; Calabrese, J.C. Palladium-catalyzed alkylations in aqueous media. *J. Am. Chem. Soc.* **1990**, *112*, 4324-4330.
12. Shaughnessy, K.H. Beyond TPPTS: New approaches to the development of efficient palladium-catalyzed aqueous-phase cross-coupling reactions. *Eur. J. Org. Chem.* **2006**, 1827-1835.
13. Zhou, J.; Li, X.; Sun, H. An efficient and recyclable water-soluble cyclopalladated complex for aqueous Suzuki reactions under aerial conditions. *J. Organomet. Chem.* **2010**, *695*, 297-303.
14. Liu, C.; Ni, Q.; Hu, P.; Qiu, J. Oxygen-promoted PdCl₂-catalyzed ligand-free Suzuki reaction in aqueous media. *Org. Biomol. Chem.* **2011**, *9*, 1054-1060.
15. Wang, J.; Song, G.; Peng, Y. Reusable Pd nanoparticles immobilized on functional ionic liquid co-polymerized with styrene for Suzuki reactions in water-ethanol solution. *Tetrahedron Lett.* **2011**, *52*, 1477-1480.
16. Mejías, N.; Pleixats, R.; Shafir, A.; Medio-Simón, M.; Asensio, G. Water-soluble palladium nanoparticles: Click synthesis and applications as a recyclable catalyst in Suzuki cross-couplings in aqueous media. *Eur. J. Org. Chem.* **2010**, *2010*, 5090-5099.
17. Monopoli, A.; Nacci, A.; Calò, V.; Ciminale, F.; Cotugno, P.; Mangone, A.; Giannossa, L.C.; Azzone, P.; Cioffi, N. Palladium/zirconium oxide nanocomposite as a highly recyclable catalyst for C–C coupling reactions in water. *Molecules* **2010**, *15*, 4511-4525.
18. Shaughnessy, K.H. Hydrophilic ligands and their application in aqueous-phase metal-catalyzed reactions. *Chem. Rev.* **2009**, *109*, 643-710.
19. Casalnuovo, A.L.; Calabrese, J.C. Palladium-catalyzed alkylations in aqueous media. *J. Am. Chem. Soc.* **1990**, *112*, 4324-4330.
20. Genet, J.P.; Blart, E.; Savignac, M. Palladium-catalyzed cross-coupling reactions in a homogeneous aqueous medium. *Synlett* **1992**, 715-717.
21. Ueda, M.; Nishimura, M.; Miyaura, N. A palladium-catalyzed biaryl coupling of arylboronic acids in aqueous media using a gluconamide-substituted triphenylphosphine (GLCAphos) ligand. *Synlett* **2000**, *6*, 856-858.
22. Moore, L.R.; Shaughnessy, K.H. Efficient aqueous-phase Heck and Suzuki couplings of aryl bromides using tri(4,6-dimethyl-3-sulfonatophenyl)phosphine trisodium salt (TXPTS). *Org. Lett.* **2004**, *2*, 225-228.

23. Moore, L.R.; Western, E.C.; Craciun, R.; Spruell, J.M.; Dixon, D.A.; O'Halloran, K.P.; Shaughnessy, K.H. Sterically demanding, sulfonated, triarylphosphines: Application to palladium-catalyzed cross-coupling, steric and electronic properties, and coordination chemistry. *Organometallics* **2008**, *27*, 576-593.
24. Wallow, T.I.; Novak, B.M. Highly efficient and accelerated Suzuki aryl couplings mediated by phosphine-free palladium sources. *J. Org. Chem.* **1994**, *59*, 5034-5037.
25. Wu, W.-Y.; Chen, S.-N.; Tsai, F.-Y. Recyclable and highly active cationic 2,2'-bipyridyl palladium(II) catalyst for Suzuki cross-coupling reaction in water. *Tetrahedron Lett.* **2006**, *47*, 9267-9270.
26. Pawar, S.S.; Uppalla, L.S.; Shingare, M.S.; Thore, S.N. Sodium 2-(2-pyridin-3-ylethylamino)ethyl sulfonate: an efficient ligand and base for palladium-catalyzed Suzuki reaction in aqueous media. *Tetrahedron Lett.* **2008**, *49*, 5858-5862.
27. Huang, R.; Shaughnessy, K.H. Water-soluble palladacycles as precursors to highly recyclable catalysts for the Suzuki coupling of aryl bromides in aqueous solvents. *Organometallics* **2006**, *25*, 4105-4112.
28. Frost, B.J.; Mebi, C.A. Aqueous organometallic chemistry: Synthesis, structure, and reactivity of the water-soluble metal hydride CpRu(PTA)₂H. *Organometallics* **2004**, *23*, 5317-5323.
29. Wong, G.W.; Harkreader, J.L.; Mebi, C.A.; Frost, B.J. Synthesis and coordination chemistry of a novel bidentate phosphine: 6-(Diphenylphosphino)-1,3,5-triaza-7-phosphaadamantane (PTA-PPh₂). *Inorg. Chem.* **2006**, *45*, 6748-6755.
30. Huang, R.; Frost, B.J. Development of a series of P(CH₂NCHR)₃ and trisubstituted 1,3,5-triaza-7-phosphaadamantane ligands. *Inorg. Chem.* **2007**, *46*, 10962-10964.
31. Mebi, C.A.; Frost, B.J. Isomerization of *trans*-[Ru(PTA)₄Cl₂] to *cis*-[Ru(PTA)₄Cl₂] in water and organic solvent: Revisiting the chemistry of [Ru(PTA)₄Cl₂]. *Inorg. Chem.* **2007**, *46*, 7115-7120.
32. Frost, B.J.; Harkreader, J.L.; Bautista, C.M. Synthesis and solid state structure of Co(II) complexes of O=PTA. *Inorg. Chem. Comm.* **2008**, *11*, 580-583.
33. Wong, G.W.; Lee, W.-C.; Frost, B.J. Insertion of CO₂, ketones, and aldehydes into the C-Li bond of 1,3,5-triaza-7-phosphaadamantan-6-ylolithium. *Inorg. Chem.* **2008**, *47*, 612-620.
34. Frost, B.J.; Lee, W.-C.; Pal, K.; Kim, T.H.; VanDerveer, D.; Rabinovich, D. Synthesis, structure, and coordination chemistry of O=PTA and S=PTA with group 12 metals (PTA = 1,3,5-triaza-7-phosphaadamantane). *Polyhedron* **2010**, *29*, 2373-2380.
35. Assmann, B.; Angermaier, K.; Paul, M.; Riede, J.; Schmidbaur, H. Synthesis of 7-alkyl/aryl-1,3,5-triaza-7-phosphoniaadamantane cations and their reductive cleavage to novel N-methyl-P-alkyl/aryl[3.3.1]bicyclononane ligands. *Chem. Ber.* **1995**, *128*, 891-900.
36. Siele, V.I. Some reactions of 1,3,5-Triaza-7-phosphaadamantane and its 7-oxide. *J. Heterocycl. Chem.* **1977**, *14*, 337-339.
37. Darensbourg, D.J.; Ortiz, C.G.; Kamplain, J.W. A new water-soluble phosphine derived from 1,3,5-triaza-7-phosphaadamantane (PTA), 3,7-diacetyl-1,3,7-triaza-5-phosphabicyclo[3.3.1]nonane. Structural, bonding, and solubility properties. *Organometallics* **2004**, *23*, 1747-1754.
38. Frank, A.W.; Daigle, D.J. Triacidic salts of tris(aminomethyl)phosphines and their oxides. *Phosphorus Sulfur Relat. Elem.* **1981**, *10*, 255-259.

39. Darensbourg, D.J.; Stafford, N.W.; Joo, F.; Reibenspies, J.H. Water-soluble organometallic compounds. 5. The regio-selective catalytic hydrogenation of unsaturated aldehydes to saturated aldehydes in an aqueous two-phase solvent system using 1,3,5-triaza-7-phosphaadamantane complexes of rhodium. *J. Organomet. Chem.* **1995**, *488*, 99-108.
40. Darensbourg, D.J.; Joo, F.; Katho, A.; Stafford, J.N.W.; Benyei, A.; Reibenspies, J.H. Nucleophilic addition of a water-soluble phosphine to aldehydes. Isolation of (1-hydroxyalkyl)phosphonium salts and the crystal structure of the (1-methoxy-1-benzyl)(m-sulfonatophenyl)diphenyl phosphonium salt. *Inorg. Chem.* **1994**, *33*, 175-177.
41. Darensbourg, D.J.; Joo, F.; Kannisto, M.; Katho, A.; Reibenspies, J.H.; Daigle, D.J. Water-soluble organometallic compounds. 4. Catalytic hydrogenation of aldehydes in an aqueous two-phase solvent system using a 1,3,5-triaza-7-phosphaadamantane complex of ruthenium. *Inorg. Chem.* **1994**, *33*, 200-208.
42. Darensbourg, D.J.; Joo, F.; Kannisto, M.; Katho, A.; Reibenspies, J.H. Water-soluble organometallic compounds. 2. Catalytic hydrogenation of aldehydes and olefins by new water-soluble 1,3,5-triaza-7-phosphaadamantane complexes of ruthenium and rhodium. *Organometallics* **1992**, *11*, 1990-1993.
43. Kovacs, J.; Todd, T.D.; Reibenspies, J.H.; Joo, F.; Darensbourg, D.J. Water-soluble organometallic compounds. 9. Catalytic hydrogenation and selective isomerization of olefins by water-soluble analogues of Vaska's complex. *Organometallics* **2000**, *19*, 3963-3969.
44. Phillips, A.D.; Gonsalvi, L.; Romerosa, A.; Vizza, F.; Peruzzini, M. Coordination chemistry of 1,3,5-triaza-7-phosphaadamantane (PTA): Transition metal complexes and related catalytic, medicinal, and photoluminescent applications. *Coord. Chem. Rev.* **2004**, *248*, 955-993.
45. Bravo, J.; Bolano, S.; Gonsalvi, L.; Peruzzini, M. Coordination chemistry of 1,3,5-triaza-7-phosphaadamantane (PTA) and derivatives, Part II. The quest for tailoring ligands, complexes and related applications. *Coord. Chem. Rev.* **2010**, *254*, 555-607.
46. Krogstad, D.A.; Cho, J.; DeBoer, A.J.; Klitzke, J.A.; Sanow, W.R.; Williams, H.A.; Halfen, J.A. Platinum (II) and Palladium(II) 1,3,5-triaza-7-phosphaadamantane (PTA) complexes as intramolecular hydroamination catalysts in aqueous and organic media. *Inorg. Chim. Acta* **2006**, *359*, 136-148.
47. Tang, X.; Zhang, B.; He, Z.; Gao, R.; He, Z. 1,3,5-Triaza-7-phosphadamantane (PTA): A practical and versatile nucleophilic phosphine organocatalyst. *Adv. Synth. Catal.* **2007**, *349*, 2007-2017.
48. He, Z.; Tang, X.; Chen, Y.; He, Z. The First air-stable and efficient nucleophilic trialkylphosphine organocatalyst for the Baylis-Hillman reaction. *Adv. Synth. Catal.* **2006**, *348*, 413-417.
49. Ruiz, J.; Cutillas, N.; Lopez, F.; Lopez, G.; Bautista, D. A Copper and amine-free Sonogashira reaction of aryl halides catalyzed by 1,3,5-triaza-7-phosphaadamantane palladium systems. *Organometallics* **2006**, *25*, 5768-5773.
50. García-Álvarez, J.; Díez, J.; Gimeno, J. A highly efficient copper(I) catalyst for the 1,3-dipolar cycloaddition of azides with terminal and 1-iodoalkynes in water: Regioselective synthesis of 1,4-disubstituted and 1,4,5-trisubstituted 1,2,3-triazoles. *Green Chem.* **2010**, *12*, 2127-2130.
51. Komine, N.; Ishiguro, K.; Kanai, S.; Hirano, M.; Komiya, S. Branch selective allylation of acetylacetone catalyzed by Water-soluble rhodium complex catalyst. *J. Organomet. Chem.* **2011**, *696*, 1927-1930.

52. Strotman, N.A.; Chobanian, H.R.; He, J.; Guo, Y.; Dormer, P.G.; Jones, C.M.; Steves, J.E. Catalyst-controlled regioselective Suzuki coupling at both positions of dihaloimidazoles, dihalooxazoles, and dihalothiazoles. *J. Org. Chem.* **2010**, *75*, 1733-1739.
53. Caporali, M.; Bianchini, C.; Bolaño, S.; Bosquain, S.S.; Gonsalvi, L.; Oberhauser, W.; Rossin, A.; Peruzzini, M. Synthesis and characterization of κ^1 -P and κ^2 -P,N palladium (II) complexes of the open cage water soluble aminophosphine PTN. *Inorg. Chim. Acta* **2008**, *361*, 3017-3023.
54. Weng, Z.; Teo, S.; Hor, T.S. A metal unsaturated and ligand hemilability in Suzuki coupling. *Acc. Chem. Res.* **2007**, *40*, 676-684.
55. Liu, C.; Ni, Q.; Bao, F.; Qiu, J. A simple and efficient protocol for a palladium-catalyzed ligand-free Suzuki reaction at room temperature in aqueous DMF. *Green Chem.* **2011**, *13*, 1260-1266.
56. Daigle, D.J.; Pepperman, A.B., Jr.; Vail, S.L. Synthesis of a monophosphorus analog of hexamethylenetetramine. *J. Heterocycl. Chem.* **1974**, *11*, 407-408.
57. Drew, D.; Doyle, J.R. Cyclic diolefin complexes of platinum and palladium. *Inorg. Synth.* **1990**, *28*, 346-349.
58. Arvela, R.K.; Leadbeater, N.E. Suzuki coupling of aryl chlorides with phenylboronic acid in water, using microwave heating with simultaneous cooling. *Org. Lett.* **2005**, *7*, 2101-2104.
59. Huang, R.; Shaughnessy, K.H. Water-soluble palladacycles as precursors to highly recyclable catalysts for the Suzuki coupling of aryl bromides in aqueous solvents. *Organometallics* **2006**, *25*, 4105-4112.
60. Wolfe, J.P.; Singer, R.A.; Yang, B.H.; Buchwald, S.L. Highly active palladium catalysts for Suzuki coupling reactions. *J. Am. Chem. Soc.* **1999**, *121*, 9550-9561.
61. Hiyama, J.-H.; Li, C.-C.; Deng, C.-L.; Liu, W.-J.; Xie, Y.-X. Pd(OAc)₂/DABCO as an inexpensive and efficient catalytic system for Hiyama cross-coupling reactions of aryl halides with aryltrimethoxysilanes. *Synthesis* **2005**, *18*, 3039-3044.
62. Sheldrick, G.M. SHELXTL: *Structure Determination Software Suite*, version 6.10; Bruker AXS: Madison, WI, USA, 2001.
63. Sheldrick, G.M. A short history of SHELX. *Acta Crystallogr. Sect. A* **2008**, *64*, 112-122.

Sample Availability: Samples of most compounds are available from the authors.

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