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Water-Soluble Palladium(II) Complexes with Sulfonated N-Heterocyclic Carbenes in Suzuki Cross-Coupling and Hydrodehalogenation Reactions

Roberto Garrido, Paulo S. Hernández-Montes, Álvaro Gordillo, Pilar Gómez-Sal, Carmen López-Mardomingo, and Ernesto de Jesús*

Departamento de Química Orgánica and Departamento de Química Inorgánica, Universidad de Alcalá, 28871 Alcalá de Henares, Madrid, Spain

S Supporting Information

ABSTRACT: Water-soluble Pd(II) complexes of general formula $Na_x[(NHC)PdCl_2L]$ (L = Cl⁻ (1), PPh₃ (2), PPh₂(C₆H₄-m-SO₃Na) (3), and 4-Mepy (4)), where NHC is a dianionic sulfonated and sterically hindered N-heterocyclic carbene, have been prepared. The new complexes are active catalysts for the Suzuki–Miyaura cross-coupling of aryl chlorides and boronic acids in mixtures of isopropyl alcohol/water or, in the case of water-soluble aryl chlorides, in pure water. The trichloride complex 1, the crystal structure of which is reported, catalyzes the coupling of inactivated and sterically hindered substrates under mild conditions (60 °C, 0.1 mol % Pd). The corresponding biphenyls are obtained in almost quantitative



yields, except in the case of some of the most hindered aryl chlorides, for which small amounts of arene are also formed by a competitive hydrodehalogenation process.

INTRODUCTION

Catalytic reactions in water involving metal complexes and organic substrates have been growing in importance over the past few decades.¹ In this area, some time ago we studied the synthetic potential of organosilanes for the Pd-catalyzed formation of C-C bonds in the aqueous phase and found that the high-yield coupling of aryl bromides with aryl- or vinylsilanes was possible under ligand-free conditions or in the presence of triarylphosphane ligands functionalized with hydrophilic groups.² These results highlighted the need to develop reaction conditions for efficient activation of the more readily available aryl chlorides. The Suzuki reaction between aryl halides and boron reagents was reported in water by Casalnuovo and Calabrese³ in 1990 and has concentrated a substantial part of the advances made in aqueous-phase crosscoupling reactions since then.⁴ As a consequence, a variety of catalysts that are able to assist the Suzuki coupling of aryl chlorides under mild conditions in pure water, or in combination with cosolvents, are currently known.⁵ Some of the best results have been obtained upon introducing hydrophilic substituents into sterically demanding and electron-rich phosphanes or in palladacyclic complexes similar to those that have furnished highly effective catalysts in conventional organic solvents.

The contribution of N-heterocyclic carbenes (NHCs) to significant advances in palladium-promoted cross-coupling⁶ and other transition-metal-catalyzed reactions⁷ has stimulated the

recent use of these ligands in aqueous-phase catalytic reactions.⁸ Early work by Özdemir and co-workers showed that mixtures of $Pd(OAc)_2$ and tetrahydrodiazepinium or imidazolinium salts catalyzed the Suzuki coupling of parasubstituted aryl chlorides under mild conditions in mixtures of DMF and H_2O .^{9,10} Subsequently, Huynh and co-workers reported the coupling of phenylboronic acid with the activated 4-chloroacetophenone in pure water in moderate yields using a preformed sterically bulky benzannulated NHC complex as catalytic precursor.^{11–13} Although these early studies used conventional hydrophobic NHC ligands, the design of watersoluble transition-metal complexes containing hydrophilic NHC ligands has attracted increasing attention over the past few years.¹⁴ Thus, Plenio and co-workers prepared a sulfonated analogue of the IPr ligand $(IPr-SO_3)^{15}$ and showed that the complex [(IPr-SO₃)PdCl(cinnamyl)] was able to couple inactivated and sterically hindered chloroarenes in water/nbutanol mixtures with high yields.¹⁶ In general terms, bis- and tris-ligated NHC complexes or mono-ligated complexes with less bulky ligands are less efficient for the activation of these challenging substrates,^{17–19} in accordance with design features found in PEPPSI (pyridine-enhanced precatalyst preparation stabilization and initiation)²⁰ and other highly active catalysts developed in nonaqueous media. Nevertheless, the only

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example of a catalyst that has been reported to catalyze the coupling of *para*-substituted chloroarenes in pure water at room temperature with good yields to date is a bis-ligated water-soluble NHC complex of a polymeric nature,²¹ although fragmentation probably occurs during the catalytic process.²² Several water-insoluble NHC precatalysts are among the most active systems in aqueous media.^{23–25} It should be noted, however, that the reactions are commonly performed in the presence of cosolvents or phase-transfer agents. In addition, this variety of reaction media makes a reliable comparison of the activity of the different catalysts more difficult.

In the past few years our group has investigated the synthesis, reactivity, and applications of water-soluble NHC Pt(II) complexes.²⁶ As such, we reasoned that related water-soluble Pd(II) complexes might be efficient activators of chloroarenes in aqueous-phase Hiyama reactions. In consequence, we prepared a series of mono(NHC) Pd(II) complexes containing the hydrophilic and sterically demanding IPr-SO₃ ligand previously reported by Plenio.¹⁵ Unfortunately, our efforts to couple chloroarenes and aryltri(alkoxo)silanes in water using these complexes as catalysts have been unsuccessful for the time being. In contrast, the activities observed in the Suzuki-Miyaura reaction were excellent, even with inactivated and sterically hindered chloroarenes, thus showing that the absence of reactivity in the Hiyama reaction was probably not related to oxidative addition of the haloarene. Herein we report the preparation and characterization of these new Pd complexes, together with their activity in the Suzuki-Miyaura coupling and in the hydrodehalogenation of chloroarenes. Although we failed to achieve our initial goals as regards the Hiyama reaction, the results obtained for the Suzuki-Miyaura reaction are illustrative of how optimal catalyst design is affected by the aqueous solvent.

RESULTS AND DISCUSSION

Synthesis and Characterization of the Water-Soluble NHC Palladium Complexes 1-4. The synthetic routes used to prepare complexes 1-4 are depicted in Scheme 1. The monosodium salt of the 1,3-(4-sulfonate-2,6diisopropylphenyl)imidazolium anion, H(IPr-SO₃), was prepared following the method reported by Plenio and coworkers.¹⁵ The trichloride mono-NHC complex Na₃[(IPr-SO₃)PdCl₃] (1; note that the IPr-SO₃ ligand is dianionic) was obtained in dimethyl sulfoxide (dmso) by reaction of palladium dichloride with the imidazolium salt H(IPr-SO₃) in the presence of sodium hydrogen carbonate as deprotonating agent and sodium chloride as a halide donor. Carbon dioxide and water were the only byproducts formed using this procedure. Monitoring of the reaction by ¹H NMR spectroscopy in dmso- d_6 showed that the imidazolium salt was entirely transformed into complex 1 under these reaction conditions. The isolated yield based on palladium dichloride was nevertheless moderate (54%) due to the formation of small amounts of metallic palladium during the reaction and the moderate efficiency of the purification step. Although related tribromide¹¹ and triiodide²⁷ NHC-Pd(II) complexes have been described in the literature, to the best of our knowledge this is the first example of an imidazol-2-ylidene complex of formula $[(NHC)PdCl_3]^-$.

Surprisingly, complex 1 was also the only or major NHCcontaining complex formed when attempts were made to prepare tetra-anionic dimer $Na_4[(IPr-SO_3)PdCl(\mu-Cl)]_2$ by deprotonation of the H(IPr-SO₃) salt with sodium *tert*-butoxide



in dmso followed by addition of palladium dichloride or $PdCl_2L_2$ complexes (L is a labile ligand; see Scheme 2). Similar procedures are used to synthesize NHC dimers such as the IPr derivative [(IPr)PdCl(μ -Cl)]₂,²⁸ which mediates the room-

Scheme 2. Attempts to Prepare Na₄[(IPr-SO₃)PdCl(µ-Cl)]₂



temperature Suzuki–Miyaura coupling of aryl chlorides in ethanol at very low catalyst loadings. 29 In the formation of ${\bf 1}$ under the above conditions, large amounts of the carbene ligand remained uncoordinated even after long reaction times. For instance, although reaction of the IPr-SO₃ ligand with a stoichiometric amount of [PdCl₂(PhCN)₂] at 90 °C was very fast at the beginning of the reaction and formed 40% of complex 1 in 10 min, the final conversion never exceeded 60-70%. Addition of a large excess of the palladium dichloride source increased the conversions, probably because the Pd compound serves as an additional source of chloride anions. Complex 1 was also the major product when the reaction depicted in Scheme 1 was performed in the absence of NaCl, although unreacted NHC and more extensive deposition of Pd black were observed under these conditions. It should be noted that the synthesis of $[(NHC)PdCl(\mu-Cl)]_2$ dimers is usually performed in solvents such as tetrahydrofuran, dichloromethane, or 1,4-dioxane, which have dielectric constants some 5 to 20 times smaller than that of dimethyl sulfoxide. The preferred formation of 1 even in the absence of an external Cl⁻ source is probably affected by the ability of dmso to stabilize ionic species and to coordinate to Pd, thereby facilitating the abstraction of chlorides from the PdCl₂ starting material.

Another reason that makes the preparation of [(NHC) $PdCl(\mu-Cl)]_2$ interesting is the versatility of these dimers as synthetic precursors for monomers of general formula [(NHC) ${\rm PdCl_2L}]^{.30,31}$ Nevertheless, complex 1 is also a useful starting material for the preparation of such monomers because the chloride ligand trans to the carbene is easily displaced by N- or P-donor ligands, as shown by preparation of the carbenephosphane or carbene-pyridine complexes 2-4 (Scheme 1). Phosphane complexes 2 and 3 were isolated as spectroscopically pure solids by partial evaporation of the dmso reaction solutions, followed by precipitation with acetone and subsequent recrystallization from methanol/diethyl ether. Complex 4 was isolated by direct precipitation from the dmso solution with diethyl ether, as the above procedure partially reversed the reaction (<10%) toward the formation of 1. Partial recoordination of the chloride ligand during evaporation of the dmso solvent is explained by the lower boiling point of the 4-picoline ligand (145 °C compared with 189 °C for dmso) and is a sign of the labile coordination of this ligand to the palladium(II) center. Interestingly, the addition of an excess of NaCl to solutions of 2-4 in dmso- d_6 does not displaces the neutral phosphane or pyridine ligands, thus suggesting that they are more strongly coordinated to the palladium(II) center than the chloride ligand in this solvent.

Complex 1 is insoluble in most organic solvents (including acetone, most alcohols, acetonitrile, THF, or dichloromethane) but soluble in water, methanol, and dmso. A solution in methanol or in ethanol–water mixtures decomposes slowly with formation of palladium black, probably due to reduction of the Pd(II) center by the primary alcohol, which is itself oxidized to the corresponding aldehyde.³¹ In contrast, alcoholic solutions of complexes 2-4 are stable, thereby denoting that coordination of the neutral ligand makes the Pd(II) complex more inert. C, H, N, and S elemental analyses obtained for 1-3 showed substantial variations depending on the crystallization procedure due to the presence of NaCl contaminating the samples and to the tendency of their sodium counterions to trap variable amounts of donor solvents (see X-ray structure of 1), which cannot be entirely removed by heating the solids

under high vacuum. A good accordance between experimental and calculated elemental analysis values was found for 1 when the solvent dmso molecules observed by ¹H NMR integration were taken into account (see Experimental Section for details).

The protons of the NHC ring appear in the ¹H NMR spectra of 1–4 at around 7.75 ppm in dmso- d_6 (7.45 ppm in D₂O) in the form of a singlet for 1 and 4 or a doublet for 2 and 3 (${}^{5}J_{H-P}$ = 1.0-1.3 Hz). The corresponding carbons resonate in the ${}^{13}C{}^{1}H$ NMR spectra at 125–126 ppm, with ${}^{4}J_{C-P} = 5.5$ Hz for 2 and 3, whereas the carbone C^2 carbons resonate at 167.7 ppm (2 and 3, ${}^4J_{C-P} \approx$ 198 Hz) and 152.7 ppm (4). These values are comparable to those found in related nonsulfonated IPr complexes, and, specifically, the ¹H and ${}^{13}C-{}^{31}P$ coupling constants in complexes 2 and 3 are in good agreement with those found in related complexes with a trans arrangement of the carbene and phosphane ligands.³² The carbene carbon was not visible in the case of 1 or in most other anionic complexes $[(NHC)PdX_3]^-$ reported to date (X = halogen).²⁷ The methyl protons of the isopropyl groups on the NHC ligand appear in all cases as two doublets in the range 1.0-1.3 ppm, in agreement with a $C_{2\nu}$ molecular symmetry and restricted rotation of the aryl-N bond. Coordination of the phosphane ligands to the Pd(II) center in 2 and 3 was also corroborated by the presence of a single resonance at ca. 20 ppm in their ${}^{31}P{}^{1}H$ spectra recorded in dmso- d_6 or D₂O.

The proposed structures were further supported by the ESI mass spectra, recorded in negative mode in methanol (1) or water (2–4), which showed peaks corresponding to the whole molecular fragment ionized by the loss of one or more Na⁺ cations. The notable intensity of the peaks corresponding to the additional loss of a chloride (1), phosphane (2 and 3), or 4-picoline (4) ligand is in agreement with the labilizing effect of the *trans* NHC ligand. Interestingly, the fragment [1 – Na]⁺ was observed in water only after addition of NaCl, thus suggesting that dissociation of the chloride ligand is especially favorable in this solvent.

Complexes 1–4 are rather stable in water at neutral pH and room temperature. The water stability of complex of 1 in neutral and alkaline solutions at room or higher temperatures is discussed in detail below. In the case of phosphane complexes 2 and 3, decomposition is accelerated when the solutions are left unprotected against air. In such cases, oxidation of the phosphane to the corresponding free oxide is extensive after 1 day and is partially accompanied by hydrolysis of the Pd-NHC bond and precipitation of palladium black.

X-ray Crystal Structure of Complex 1. Complex 1 crystallized with 11 molecules of dmso by slow diffusion of tertbutanol into a solution of the complex in dimethyl sulfoxide. The crystal structure is shown in Figure 1 together with a selection of the most important distances and angles. It consists of $[(IPr-SO_3)PdCl_3]^{3-}$ organometallic units (Figure 1a) organized into one-dimensional double chains due to interaction of both sulfonates and two of the three chloride ligands with triangular (Na⁺)₃ clusters (Figure 1b, mean Na… Na distance 3.33 Å). Seven dmso molecules are coordinated to the sodium cluster (mean Na-O distance 2.42 Å), and the structure is completed by four noncoordinated dmso molecules. As would be expected due to steric hindrance, the aryl rings are almost perpendicular to the imidazolium ring (87.6° and 88.4°), and this ring is almost perpendicular to the palladium coordination plane (88.7°). The Pd-C(1) distance of 1.957(5) Å is very similar to that reported for the dimer [(IPr)PdCl(μ -Cl)]₂ (1.9553(3) Å).²⁸ The Pd-Cl bond trans to the NHC



Figure 1. (a) ORTEP diagram of the $[(IPr-SO_3)PdCl_3]^{3-}$ organometallic moiety of 1·11dmso (50% probability ellipsoids; H atoms omitted for clarity). (b) View of the crystal structure highlighting the double chain of $[(IPr-SO_3)PdCl_3]^{3-}$ units and triangular $(Na^+)_3$ clusters. The dashed lines represent the O atoms of dmso molecules that are solvating the sodium clusters (other dmso atoms are omitted for clarity). Selected bond lengths (Å) and angles (deg): Pd-C(1), 1.957(5); Pd-Cl(1), 2.297(2); Pd-Cl(2), 2.393(1); Pd-Cl(3), 2.318(2); C(1)-Pd-Cl(1), 88.65(14); C(1)-Pd-Cl(3), 90.31(14); Cl(1)-Pd-Cl(2), 89.85(6); Cl(2)-Pd-Cl(3), 91.23(5); C(1)-Pd-Cl(2), 178.18(14); Cl(1)-Pd-Cl(3), 177.93(6); N(1)-C(1)-N(2), 104.6(4); Na(1)-Na(2), 3.322(3); Na(1)-Na(3), 3.286(3); Na(2)-Na(3), 3.386(3).

ligand is significantly elongated by the *trans* influence of the NHC [2.393(1) Å for trans and 2.297(2) and 2.318(2) Å for cis Cl ligands].

Stability of Complex 1 in Aqueous Media. The hydrolysis of metal–carbene bonds is difficult to reverse in a protic medium, thus making the stability of these bonds in aqueous media a key issue when dealing with water-soluble NHC catalysts. Metal–carbene bonds are usually fairly stable in water at low temperatures, and it is even possible to form such bonds in aqueous solutions.³³ However, the durability of the bonds over long time periods, at high temperatures, or under catalytic conditions has rarely been discussed for water-soluble NHC complexes. In this respect, it can be seen that solutions of complex 1 in deuterated water remained unaltered for at least 86 h under neutral conditions at temperatures up to 100 $^{\circ}$ C, as evidenced by ¹H NMR spectroscopy.

As cross-coupling reactions usually require the presence of a base as an activator, we also monitored the stability of solutions of complex 1 in deuterated water containing increasing amounts of NaOD (0.5, 1.0, and 1.6 M). Although the base reacted with the Pd–Cl bonds at room temperature, coordination of the carbene was not altered under these conditions. Thus, complex 1 evolved completely into a different NHC complex in 1.6 M NaOD, whereas two intermediates

were detected at the lower NaOD concentrations. The formation of a hydroxide of tentative formula $[(IPr-SO_3)]$ $Pd(OH)_n$ ⁿ⁻ can be proposed according to the peaks observed in the ESI-TOF mass spectrum obtained in negative mode for the 1.6 M NaOD solution.³⁴ At higher temperatures, hydrolysis of the Pd–NHC bond is still relatively slow although noticeably faster than in neutral solutions. Thus, decomposition was around 20% after 6 days at 80 $^{\circ}$ C and 40% after 63 h at 100 $^{\circ}$ C in 1 M NaOD (p-toluenesulfonic acid was used as an internal standard in these experiments). In addition to formation of the imidazolium salt IPr-SO₃, ring-opening products due to basic hydrolysis of this salt and deposition of palladium black were also observed. The Pd-NHC bond in complex 1 is therefore reasonably stable under conditions of temperature and alkalinity close to those employed in the cross-coupling reactions described below. It should be noted, however, that the hydrolytic stability of the active Pd(II)/Pd(0) species cannot be directly inferred from that of the catalytic precursor 1.

Suzuki–Miyaura Cross-Coupling Reactions. Crosscoupling of electronically inactivated 4-chloroanisol with phenylboronic acid was used during initial screening of conditions for the Suzuki–Miyaura reaction in aqueous media. A first set of experiments was conducted using a 0.1 mol % loading of complex 1 as catalyst and 3 equiv of NaOH as base (Table 1, entries 1 to 7). The performance of this catalyst was disappointing in pure water, giving undetectable conversions at 25 °C and reaching only 20% at 60 °C (entries 1 and 2). The reason for this poor behavior in water will be discussed later. Further experiments were performed in mixtures of water and isopropyl alcohol, with full conversions being attained in less than 6 h at 60 °C (entries 3 to 7).

Table 1. Screening of Cross-Coupling Reaction Conditions^a

		e			
MeO-	-CI	+ PhB(OH) ₂	1–4 (0.1 mol %) NaOH (3 equiv)	► MeO	
			H ₂ O : <i>i</i> -PrOH (1.2 : 0.8 v/v)		
entry	catalyst	temp (°C)	reaction time (h)	other conditions	$_{(\%)^b}^{\operatorname{conv}}$
1	1	25	12	in water only	0
2	1	60	12	in water only	20
3	1	25	12		60
4	1	60	12		100
5	1	60	6		100
6	1	60	3		93
7	1	60	1		80
8	1	25	12	base: K ₂ CO ₃	60
9	1	60	3	base: K ₂ CO ₃	70
10	1	60	15	under air	0
11	PdCl ₂	60	15	1 mol % Pd	0
12	2	60	6		100
13	3	60	6		85
14	4	60	6		74
15	2	60	1		63

^{*a*}In a typical experiment, a mixture of 0.5 mmol of aryl chloride, 1.2 equiv of arylboronic acid, 3.0 equiv of base, and 0.1 mol % of the corresponding Pd complex was stirred under an argon atmosphere in a previously degassed mixture of 1.2 mL of water and 0.8 mL of isopropyl alcohol. ^{*b*}Conversions were calculated by relative integration of the methyl signals of the chloroarene and biphenyl compounds. Each experiment was performed at least twice.

Replacement of NaOH with the weaker base K₂CO₃ did not improve the catalyst activity and made product purification more difficult, as the boron-containing byproducts were more soluble in the diethyl ether solutions used for extraction under these less basic conditions (entries 8 and 9). The above experiments were performed in degassed solvents under an inert atmosphere because the presence of air resulted in the loss of catalyst activity (entry 10). In this respect, the information available in the literature is contradictory. We can assume a deleterious effect of air in most cases taking into account that cross-coupling reactions with NHC Pd catalysts are routinely performed under an inert atmosphere.^{11,16,19,23} However, the fact that some NHC Pd complexes are active catalysts for the Suzuki-Miyaura reaction in aqueous media under aerobic conditions shows that inactivation by air does not occur under some circumstances.^{9,12,17,24,35} This dual behavior might suggest the involvement of active species of different nature depending on the specific catalytic system and reaction conditions.³⁶ In aqueous media, hydrolysis of the Pd-NHC bonds under catalytic conditions might be one of the conceivable origins for the observed disparities. For this reason, we performed a test using PdCl₂ as catalyst under ligand-free conditions and found that it was completely inactive after 15 h of reaction even when the catalyst loading was increased to 1 mol % (entry 11).³⁷

In a second set of experiments in which the catalytic performance of complexes 1-4 was compared (Table 1, entries 12 to 15), we found complex 1 to be the most active, followed by 2 (cf. conversions after 1 h in entries 7 and 15), whereas 3 and 4 are significantly less active (cf. conversions after 6 h in entries 5 and 12 to 14). The formation of active species during the catalytic cycle probably involves dissociation of the trans-NHC ligand (chloride, phosphane, or pyridine) from the Pd(II) precursor, before or after reduction, and from the Pd(0)resting states.⁶ It should be noted that dissociation energies in solution are affected by both the bonding energies involved and solvation effects. The superior performance observed for complex 1 under our catalytic conditions might be closely linked to the strong solvation of the anionic chloride ligand by water and, therefore, to the protic nature of the reaction medium.³⁸ The divergence found between the activities of the triphenylphosphane complex 2 and its sulfonated analogue 3 is intriguing in this respect.

The efficiency and versatility of Na₃[(IPr-SO₃)PdCl₃] (1) as catalyst was determined with a selection of chloroarenes and arylboronic acids (Scheme 3). The reactions were performed under the conditions optimized above for 4-chloroanisole and continued until complete conversion of the chloroarene. Yields of the biphenyl product were determined for the crude reaction mixture by ¹H NMR spectroscopy and verified by weighing the products isolated after purification (values in parentheses). para-Substituted chloroarenes reacted with phenylboronic or para-tolylboronic acids in less than 6 h at 60 °C to give the corresponding biphenyls (5a-5d) in yields of more than 96%, irrespective of the activating or deactivating nature of the substituent. Under the same conditions, 2-chloropyridine was almost quantitatively transformed into the corresponding heteroaromatic biphenyl 5e, whereas 3-chloropyridine required harsher conditions (24 h, 100 °C, 5f). Other authors have observed similar decreases in the reactivity of 3-halopyridines with respect to their homologues in position 2 in reactions performed in isopropyl alcohol with (NHC)Pd catalysts.³⁵ Sterically hindered biphenyls (5g-5k) were also obtained in

Scheme 3. Synthesis of Biphenyls by Suzuki–Miyaura Cross-Coupling Using Complex 1 as Catalyst^a



"Percentages were determined by ¹H NMR integration of the crude product using hexamethyldisiloxane as internal reference. Percentages in parentheses represent isolated yields after purification. See Supporting Information for details.

high yields at 60 °C when the reaction was continued for 24 h. The improvement in yields found when the electronically activated but sterically hindered ortho-tolylboronic acid was used instead of phenylboronic acid in the reaction with 2chloro-1,3-dimethylbenzene is noticeable (cf. 5i and 5i). The lower yields obtained for biphenyls 5h and 5i are due to the formation of small but significant amounts of toluene or 1,3dimethylbenzene, which were detected in the respective crude products by ¹H NMR spectroscopy. These compounds are formed by a competitive process involving hydrodehalogenation of the chloroarene, which is catalyzed by the Pd complex and uses isopropyl alcohol as the hydrogen source (see below).⁴⁰ The fact that only ortho-substituted chloroarenes gave detectable amounts of hydrodehalogenation products means that the cross-coupling reaction is slowed comparatively more by these hindered chloroarenes. An advantage of the aqueous environment is that some of the biphenyls crystallize as solids from the reaction mixture and can be isolated with a high level of purity by simple filtration at the end of the reaction.

As pointed out in the Introduction, the use of phase-transfer agents or cosolvents is common in cross-coupling reactions performed in aqueous media due to the low solubility of many haloarenes in pure water, especially under low-temperature conditions similar to those employed in this work. However, the positive effect of isopropyl alcohol in the reactions reported herein may also be ascribed to the involvement of this alcohol in preactivation of the catalyst by reducing the Pd(II) precursor

to the active Pd(0) species. Recently, Diebolt et al. observed that the presence of an alcohol was necessary to ensure the catalytic activity of [(NHC)PdCl₂{P(OR)₃}] complexes in Suzuki-Miyaura couplings performed in dioxane and gave evidence to support the participation of the alcohol in the reduction of Pd(II) to Pd(0).³¹ We performed a final experiment using only water as solvent and a cholorarene soluble in this solvent under alkaline conditions. Thus, the reaction of 4-chlorobenzoic acid with phenylboronic acid in water afforded the corresponding biphenyl derivative 51 in 6 h at 60 °C almost quantitatively (or 20 h at room temperature and 1 mol % of 1), thus showing that activation of 1 under these conditions is efficient even in the absence of isopropyl alcohol and supporting the proposal that the main role of the cosolvent is to increase the solubility of common chloroarenes in the reaction media.

The relatively low Pd loading (0.1 mol %) and moderate temperature (60 °C) required by complex 1 to couple inactivated and sterically hindered chloroarenes in very high yields can be compared with the conditions reported for the coupling of similar substrates with related Pd complexes. Plenio and co-workers¹⁶ used higher temperatures (100 °C) and identical Pd loadings of the closely related catalyst [(IPr- SO_3 PdCl(cinnamyl)] in water/*n*-butanol mixtures, although 1naphthylboronic acid was used as coupling agent. During the preparation of this article, Herrmann and co-workers reported PEPPSI-Pd-NHC catalysts [(NHC-SO₃)PdBr₂(py)] with less sterically hindered sulfonated NHC ligands for the coupling of bromoarenes in pure water at room temperature, although these catalysts were less efficient with chloroarenes.¹⁷ Another useful comparison can be established with the nonsulfonated derivative [(IPr)PdCl₂(XPhos)], which has recently been reported by Cazin and co-workers to be a very efficient catalyst in water/isopropyl alcohol at 100 °C at Pd loadings of 0.03 mol %.²³ Nevertheless, these performances are not as good as those obtained with Pd-NHC complexes in conventional organic solvents, including in pure or technical grade alcohols.^{29,39,41}

Hydrodehalogenation of Chloroarenes.⁴²⁻⁴⁴ The hydrodehalogenation of 1-chloronaphthalene (6a in Scheme 4) was used for initial screening of conditions from which the following observations can be drawn. First, the reaction is inhibited in the presence of oxygen and has to be performed under an inert atmosphere, as was also the case for the Suzuki-Miyaura coupling. Second, hydrodehalogenation requires higher Pd loadings (0.5 mol %) than the Suzuki-Miyaura reaction, in accordance with the relative kinetics observed above for both processes. Third, $Pd(OAc)_2$ is inactive under similar conditions, as shown by the fact that no dehalogenation was observed with this catalyst after 20 h of reaction under the conditions specified in Scheme 4. Finally, the reaction kinetics is highly dependent on the basicity of the aqueous solution. Thus, the conversions improved when the concentration or the Brönsted strength of the base was increased (NaOH, KOH > $K_3PO_4 > Na_2CO_3 > NaHCO_3$, NEt₃). The classical mechanism for Pd-catalyzed hydrodehalogenation consists of oxidative addition of the chloroarene to the Pd(0) catalyst, coordination of an isopropoxide anion to the palladium(II)-aryl complex followed by β -H elimination to form acetone and a hydride, and finally reductive elimination of ArH from the PdHAr species.⁴³ The low concentration of isopropoxide ion in an aqueous medium probably limits the kinetics of the overall reaction and explains the beneficial effect of the increasing alkalinity of the solution. Navarro et al. noticed an inhibiting





 a Conversions determined by GC-MS. See Supporting Information for details.

effect of the addition of more of 1.05 equiv of *t*BuOK in the microwave-assisted hydrodehalogenation of chloroarenes catalyzed by [(IPr)Pd(allyl)Cl] in isopropyl alcohol.⁴⁴ Under such conditions, the deprotonation equilibrium *t*BuO⁻ + *i*PrOH \Leftrightarrow *t*BuOH + *i*PrO⁻ is displaced to the isopropoxide side and the excess of base probably decreases the yields by competitive coordination to the metal center.⁴⁵ Other electronically deactivated or sterically hindered chloroarenes were also tested (Scheme 4). Dehalogenation was complete after 16 h at 60 °C in 3 M NaOH in all cases, although it is possible to reduce the reaction time to 4 h and the concentration of base to 0.5 M with substrates such as 1-chloronaphthalene.

CONCLUSIONS

In summary, we have prepared new water-soluble Pd(II) complexes of general formula $Na_{v}[(NHC)PdCl_{2}L]$ (L = Cl⁻, PR₃, or 4-Mepy). These complexes contain the sulfonated and sterically hindered 1,3-(4-sulfonate-2,6-diisopropylphenyl)imidazol-2-ylidene NHC ligand and are active catalysts for the Suzuki-Miyaura cross-coupling of aryl chlorides and boronic acids in aqueous media. The trichloride complex is the most active catalyst, probably reflecting the weaker coordination and stronger solvation of the chloride ligand in protic solvents. This outlines the importance of considering strategies specific to water in order to enhance catalytic performance by modifying the ligands surrounding the palladium center. The mild conditions employed to couple inactivated and sterically hindered substrates (60 °C, 0.1 mol % Pd) compare well with those reported for aqueous media with some of the most active NHC-based catalysts. Although isopropyl alcohol has been used as cosolvent to activate water-insoluble aryl chlorides, the reaction can be performed in pure water with soluble substrates. This use of isopropyl alcohol is associated with the formation of small amounts of arene by hydrodehalogenation for some of the most hindered chloroarenes. Further work is under way in our laboratory on the use of these catalysts in other reactions involving the activation of aryl chlorides in water. In addition, the contradictory effect of the presence of air on the activity of NHC catalysts in the Suzuki–Miyaura reaction requires further attention.

EXPERIMENTAL SECTION

Reagents and General Techniques. All reactions were carried out under an argon atmosphere using sealed ampules or standard Schlenk techniques. Unless otherwise stated, reagents and solvents were used as received from commercial sources. Solvents (synthesis grade) were deoxygenated before use. Dimethyl sulfoxide (dmso) was stirred over calcium hydride for 24 h and distilled under vacuum under an argon atmosphere. Deionized water (type II quality) was obtained using a Millipore Elix 10 UV water purification system. The monosodium salt of 1,3-(4-sulfonate-2,6-diisopropylphenyl)imidazolium (HIPr-SO₃⁻) was prepared as described in the literature.¹⁵ 1 H, 13 C, and 31 P NMR spectra were recorded with a Varian Mercury 300, Unity 300, or Unity 500 Plus spectrometer. Chemical shifts (δ , ppm) are quoted relative to SiMe₄ (¹H, ¹³C) or 85% H_3PO_4 (³¹P) and were measured by internal referencing to the ¹³C or residual ¹H resonances of the deuterated solvent or by the substitution method in the case of ³¹P. Coupling constants (J) are given in hertz. When required, two-dimensional ¹H-¹³C HSQC and HMBC experiments were carried out for the unequivocal assignment of ¹H and ¹³C resonances. The Analytical Services of the Universidad de Alcalá performed the C, H, N, and S analyses using a LECO CHNSO-932 microanalyzer and the ESI mass spectra using an Agilent G3250AA LC/MSD TOF Multi mass spectrometer. Some ESI mass spectra were recorded by the SIDI Service of the Universidad Autónoma de Madrid using an Applied Biosystems QSTAR mass spectrometer. GC-MS analyses were performed using an Agilent 7820/5975C system.

Na₃[(IPr-SO₃)PdCl₃] (1). The monosodium salt of 1,3-(4-sulfonate-2,6-diisopropylphenyl)imidazolium (0.4109 g, 0.720 mmol), palladium dichloride (0.1550 g, 0.874 mmol), sodium hydrogen carbonate (0.0890 g, 1.06 mmol), and sodium chloride (0.0600 g, 1.03 mmol) were introduced into a 100 mL Schlenk. Dry dmso (15 mL) was then added using a syringe, and the mixture was stirred vigorously for 2 days at 90 °C. The dmso solution was subsequently concentrated to 8-10 mL, and tert-butanol was slowly added to form a double layer. Slow crystallization from the double layer (1 day) afforded yellowish crystals, which were separated by filtration and dissolved again in dry dmso. The solution was filtered through diatomaceous earth to remove any traces of metallic palladium. Complex 1 precipitated from this solution as a yellow solid by addition of tert-butanol and was dried under vacuum overnight at 160 °C (0.390 g, 54% based on Pd). A reasonable agreement between the number of solvent molecules detected by ¹H NMR spectroscopy and the elemental analysis results was obtained as follows. The solid was dissolved in dmso and crystallized by slow diffusion of tert-butanol. The crystals were crushed and dried for 12 h at 160 °C under high vacuum. Anal. Calcd (%) for C35H58Cl3N2Na3O10PdS6 (1.4dmso, 1140.98): C, 36.84; H, 5.12; N, 2.46; S, 16.86. Found: C, 36.55; H, 5.19; N, 2.55; S, 15.02. ¹H NMR (500 MHz, D₂O): δ 7.65 (s, 2H, Ar), 7.47 (s, 1H, Imz), 2.74 (sept, J = 6.6, 2H, CHMe₂), 1.26 (d, ${}^{3}J$ = 6.6, 6H, CHMe₂), 0.93 (d, ${}^{3}J$ = 6.9, 6H, CHMe₂). ¹H NMR (300 MHz, dmso-d₆): δ 7.78 (s, 1H, Imz), 7.57 (s, 2H, Ar), 2.96 (sept J = 6.9, 2H, CHMe₂), 1.31 (d, ³J = 6.6, 6H, CHMe₂), 1.03 (d, ³J = 6.9, 6H, CHMe₂). ¹³C{¹H} NMR (125 MHz, D_2O): δ 148.3 (s, Ar C²), 144.6 (s, Ar C⁴), 136.9 (s, Ar C¹), 127.2 (s, Imz C^{4,5}), 121.6 (s, Ar C³), 29.3 (s, CHMe₂), 25,2 (s, CHMe₂), 22.5 (s, CHMe₂). ¹³C{¹H} NMR (75 MHz, dmso- d_6): δ 148.8 (s, Ar C⁴), 145.3 (s, Ar C²), 134.3 (s, Ar C¹), 126.2 (s, Imz C^{4,5}), 120.4 (s, Ar C³), 27.7 (s, CHMe₂), 25.4 (s, CHMe₂), 22.4 (s, CHMe₂). ESI-MS (negative ion, MeOH) m/z: 802.9760 [M - Na]⁻ (calcd 802.9760) 10%; 389.9942 [M - 2Na]²⁻ (calcd 389.9934) 3%; 723.0361 [M - $3Na - Cl + H^{-}$ (calcd 723.0354) 5%; 745.0197 $[M - 2Na - Cl^{-}]$ (7%) (calcd 745.0173).

 $Na_2[(IPr-SO_3)PdCl_2(PPh_3)]$ (2). A solution of compound 1 (47.2 mg, 57.0 μ mol) and PPh₃ (15.0 mg, 57.0 μ mol) in dmso (1 mL) was stirred for 5 min at room temperature. The solvent was then evaporated under vacuum at 80 °C to almost dryness. The addition of

acetone (40 mL) resulted in precipitation of a pale yellow solid, which was separated by filtration and dried under vacuum for 1 h. The solid was recrystallized by dissolution in methanol and precipitated by slow diffusion of diethyl ether into the methanol solution (1 day). The yellow powder thus obtained was filtered and dried overnight under vacuum at 60 °C (36.5 mg, 62%). ¹H NMR (300 MHz, dmso- d_6): δ 7.75 (d, 2H, ${}^{5}J_{P-H} = 1$, Imz), 7.61 (s, 4H, Ar), 7.26–7.36 (m, 9H, Ph), 7.21–7.18 (m, 6H, Ph), 3.10 (sept, ${}^{3}J$ = 6.7, 4H, CHMe₂), 1.19 (d, ${}^{3}J$ = 6.6, 12H, CHMe₂), 1.0 (d, ${}^{3}J = 6.9$, 12H, CHMe₂). ${}^{1}H$ NMR (300 MHz, D₂O): δ 7.66 (s, 4H, Ar), 7.45 (d, 2H, ${}^{5}J_{P-H} = 1.4$, Imz), 7.24 (m, 3H, Ph), 7.15–7.06 (m, 12H, Ph), 2.85 (sept, ${}^{3}J = 6.7, 4H$, CHMe₂), 1.09 (d, ${}^{3}J = 6.7$, 12H, CHMe₂), 0.90 (d, ${}^{3}J = 6.7$, 12H, CHMe₂). ¹³C{¹H} NMR (75 MHz, dmso- d_6): δ 167.8 (d, ² J_{C-P} = 198.6, Imz C²), 148.6 (s, Ar C⁴), 145.1 (s, Ar C²), 134.9 (s, Ar C¹), 134.0 (d, ${}^{2}J_{C-P} = 10.7$, Ph C²), 129.5 (s, Ph C⁴), 129.3 (d, ${}^{1}J_{C-P} = 44$, Ph C¹), 127.3 (d, ${}^{3}J_{C-P} = 9.7$, Ph C³), 125.1 (d, ${}^{4}J = 5.5$, Imz C⁴⁻⁵), 120.3 (s, Ar C³), 27.7 (s, CHMe₂), 25.4 (s, CHMe₂), 22.2 (s, CHMe₂). ³¹P{¹H} NMR (121 MHz, dmso- d_6): δ 20.2 (s). ³¹P{¹H} NMR (121 MHz, D₂O): δ 20.9 (s). ESI-MS (negative ion, H₂O) m/z: 1007.1100 $[M - Na]^{-}$ (calcd 1007.1085) 3%; 985.1268 $[M - 2Na + H]^{-}$ (calcd 985.1265) 76%; [M - 2Na - PPh₃ + H]⁻ 723.0352 (calcd 723.0354) 100%

 $Na_{3}[(IPr-SO_{3})PdCl_{2}\{P(C_{6}H_{5})_{2}(C_{6}H_{4}-m-SO_{3})\}]$ (3). This compound was prepared starting from 1 (10.3 mg, 12.4 μ mol) and PPh₂(C₆H₄*m*-SO₃Na) (4.5 mg, 12.4 μ mol) by a similar method to that described above for 2. The yellow crystals thus obtained were filtered and dried overnight under vacuum at 60 $^{\circ}\mathrm{C}$ (4.90 mg, 35%). $^{1}\mathrm{H}$ NMR (300 MHz, dmso- d_6): δ 7.75 (d, 2H, ${}^{5}J_{P-H}$ = 1.3, Imz), 7.62 (s, 4H, Ar H³), 7.56 (ddd, ${}^{3}J_{H-H} = 7.7$, ${}^{4}J_{H-H} = 1.6$, 1H, C₆H₃SO₃⁻ H⁴), 7.47 (dt, ${}^{3}J_{P-H}$ = 12.5, ${}^{3}_{J_{H-H}}$ = 7.8, ${}^{4}_{J_{H-H}}$ = 1.6, 1H, $C_{6}H_{3}SO_{3}^{-}$ H⁶), 7.37 (td, ${}^{4}_{J_{P-H}}$ = 2.5, ${}^{3}_{J_{H-H}}$ = 7.5, 1H, $C_{6}H_{3}SO_{3}^{-}$ H⁶), 7.37 (td, ${}^{4}_{J_{P-H}}$ = 2.5, ${}^{3}_{J_{H-H}}$ = 7.5, 1H, $C_{6}H_{3}SO_{3}^{-}$ H⁵), 7.33–7.27 (m, 6H, Ph), 7.25 (dt, ${}^{3}_{J_{P-H}}$ = 8.8, ${}^{4}_{J_{H-H}}$ = 1.7, 1H, $C_{6}H_{3}SO_{3}^{-}$ H²), 7.16–7.10 (m, 4H, Ph), 3.10 (sept, ${}^{3}J_{H-H} = 6.6$, 4H, CHMe₂), 1.20 (d, ${}^{3}J_{H-H} = 6.6$, 12H, $CHMe_2$), 1.04 (d, ${}^{3}J_{H-H}$ = 6.9, 12H, $CHMe_2$). ¹H NMR (300 MHz, D_2O): δ 7.67 (s, 4H, Ar H³), 7.47 (d, 2H, ${}^{5}J_{P-H}$ = 1.4, Imz), 7.31–7.12 (m, 14H, Ph + $C_6H_3SO_3^-$), 2.86 (sept, ³J = 6.7, 4H, CHMe₂), 1.11 (d, ${}^{3}J = 6.7, 12H, CHMe_{2}), 0.91 (d, {}^{3}J = 6.7, 12H, CHMe_{2}). {}^{13}C{}^{1}H$ NMR (75 MHz, dmso- d_6): δ 167.7 (d, ${}^2J_{C-P}$ = 198, Imz C²), 148.5 (s, Ar C⁴), 147,0 (d, J = 6.2, C₆H₃SO₃⁻ C³), 145.1 (s, Ar C²), 136.5 (d, J = 20.3, C₆H₃SO₃⁻ C⁶), 134.9 (s, Ar C¹), 133.9 (d, ${}^2J_{C-P}$ = 10.5, Ph C^2), 129.5 (s), 129.1 (d, ${}^{1}J_{C-P}$ = 42.5, Ph C^1), 128.9 (s, Ph C^4), 128.4 (s), 127.3 (d, ${}^{3}J_{C-P} = 9.8$ Hz, Ph C³), 127.0 (s), 126.9 (s, C₆H₃SO₃⁻ C⁴), 125.2 (d, ${}^{4}J = 5.5$, Imz C⁴⁻⁵), 120.3 (s, Ar C³), 27.7 (s, CHMe₂), 25.4 (s, CHMe₂), 22.2 (s, CHMe₂). ³¹P{¹H} NMR (121 MHz, dmso d_6): δ 20.7 (s). ³¹P{¹H} NMR (121 MHz, D₂O): δ 21.2 (s). ESI-MS (negative ion, H₂O) m/z: 1109.0474 [M - Na]⁻ (calcd 1109.0472) 8%; 1087.0652 [M - 2Na + H]⁻ (calcd 1087.0653) 4%; 1065.0838 [M - 3Na + 2H]⁻ (calcd 1065.0833) 5%; 723.0355 [M - TPPMS - $2Na + H^{-}$ (calcd 723.0354) 100%; $[M - TPPMS - Na^{-} 745.0191]$ (calcd 745.0173) 56%.

*Na*₂[(*IPr-SO*₃)*PdCl*₂(*NC*₆*H*₄-4-*CH*₃)] (4). A mixture of compound 1 (50.5 mg, 61.0 μmol) and 4-picoline (5.7 mg, 61 μmol) was stirred for 5 min in dmso (0.5 mL) at room temperature under an argon atmosphere. Addition of cold diethyl ether (20 mL, −15 °C) resulted in precipitation of an orange solid, which was separated by filtration and dried for 1 h under vacuum at 40 °C (40 mg, 76%). ¹H NMR (300 MHz, dmso-*d*₆): δ 8.21 (d, ³*J* = 6.6, 2H, *py*-4-Me H²), 7.76 (s, 2H, Imz), 7.57 (s, 4H, Ar H³), 7.16 (d, ³*J* = 6.3, 2H, *py*-4-Me H³), 3.06 (sept, ³*J* = 6.3, 4H, *CHMe*₂), 2.23 (s, 3H, *py*-4-Me), 1.33 (d, ³*J* = 6.3, 12H, *CHMe*₂), 1.05 (d, ³*J* = 6.6, 12H, *CHMe*₂). ¹³C{¹H} NMR (50 MHz, dmso-*d*₆): δ 152.7 (s, Imz C²), 149.5 (s, *py*-4-Me C²), 149.3 (s, *py*-4-Me C⁴), 148.6 (s, Ar C⁴), 145.2 (s, Ar C²), 134.6 (s, Ar C¹), 125.2 (s, Imz C⁴⁻⁵), 124.6 (s, *py*-4-Me C³), 120.4 (s, Ar C³), 27.7 (s, CHMe₂), 25.4 (s, *CHMe*₂), 22.5 (s, *CHMe*₂), 19.9 (s, *py*-4-Me Me). ESI-MS (negative ion, H₂O) *m/z*: 816.0933 [M – 2Na + H][−] (calcd 816.0932) 29%; 780.1178 [M – 2Na – CI][−] (calcd 780.1166) 13%; 723.0360 [M – C₆H₇N – 2Na + H][−] (calcd 723.0354) 100%.

General Procedure for the Suzuki–Miyaura Cross-Coupling Reactions. All operations were performed under an argon atmosphere using deoxygenated solvents. The catalyst was added in the form of a freshly prepared 1.2 mM solution in deoxygenated water. The reaction of 4-chloroanisole and phenylboronic acid is given as a typical example. A mixture of phenylboronic acid (0.077 g, 0.60 mmol), sodium hydroxide (0.0612 g, 1.5 mmol), and 4-chloroanisole (0.061 mL, 0.50 mmol) was stirred in water (or water/isopropyl alcohol) for 2 min at room temperature. After addition of the selected Pd catalyst (0.42 mL of the 1.2 mM solution, 0.5 μ mol, 0.1 mol %), the reaction mixture was vigorously stirred at the temperature and for the time specified in Table 1 or Scheme 3 (see also Supporting Information). After cooling to room temperature, the reaction mixture was treated as specified below.

For determination of conversions and yields, the reaction mixture was extracted with diethyl ether $(3 \times 15 \text{ mL})$ and the combined ethereal layers were dried over MgSO₄ and concentrated to approximately 1 mL in a rotary evaporator at room temperature. Conversions and yields were measured by ¹H NMR integration of the crude product in CDCl₃ using an internal standard (hexamethyldisiloxane, 0.107 mL, 0.5 mmol) and the relative integrals of the 4-chloroanisole reagent for conversions or 4-phenylanisole product for yields.

To obtain pure samples of the biphenyl **5c**, the reaction mixture was filtered and the white solid washed twice with a basic water solution and dried under vacuum (78.3 mg, 85%). The same procedure was used for other biphenyls that precipitated as solids from the reaction mixture. In other cases, the product was extracted with diethyl ether and purified by flash chromatography on silica gel 60 (0.04–0.063 mm) with hexane or a mixture of hexane and ethyl acetate (95:5) as eluent (see Supporting Information for details).

General Procedure for the Hydrodehalogenation of Aryl Chlorides. The reactions were carried out under an argon atmosphere. Water and isopropyl alcohol were deoxygenated with argon before use. Complex 1 (2.1 mg, 0.5 mol %) and sodium hydroxide (0.1225 g, 3.000 mmol) were dissolved in a 1:1 mixture of water and isopropyl alcohol (1 mL), and then the corresponding aryl chloride (0.5 mmol) was added. The reaction mixture was heated to 60 °C in a silicone bath and vigorously stirred for 16 h, then allowed to cool to room temperature, and hexadecane (0.5 mmol) was added. The mixture was extracted with ethyl acetate (3×10 mL), and the combined organic layers were dried over MgSO₄. After filtration, conversions were determined by gas chromatography using the added hexadecane as internal standard.

X-ray Crystallographic Studies. Suitable single crystals of 1 were obtained by slow diffusion of *tert*-butanol into a solution of the complex in dmso. A summary of crystal data, data collection, and refinement parameters for the structural analysis is given in Table S1. Crystals were glued to a glass fiber using an inert polyfluorinated oil and mounted in the low-temperature N₂ stream of a Bruker-Nonius Kappa-CCD diffractometer equipped with an area detector and an Oxford Cryostream 700 unit.

Intensities were collected using graphite-monochromated Mo K α radiation ($\lambda = 0.71073$ Å). Data were measured with exposure times of 190 s per frame (5 sets; 347 frames; phi/omega scans; 1.9° scan width). Raw data were corrected for Lorenz and polarization effects. The structure was solved by direct methods, completed by subsequent difference Fourier techniques, and refined by full-matrix least-squares on F^2 (SHELXL-97).⁴⁶ Anisotropic thermal parameters were used in the last cycles of refinement for the non-hydrogen atoms. Absorption correction procedures were carried out using the multiscan SORTAV (semiempirical from equivalent) program. Hydrogen atoms were included in the last cycle of refinement from geometrical calculations and refined using a riding model. All calculations were performed using the WINGX system.⁴⁷

ASSOCIATED CONTENT

S Supporting Information

¹H, ¹³C{¹H}, and ³¹P NMR data for compounds 1–4, crystallographic data for compound 1 in CIF format, synthetic and purification procedures, and spectroscopic characterization of the cross-coupling products. The Supporting Information is

available free of charge on the ACS Publications website at DOI: 10.1021/om501295b.

AUTHOR INFORMATION

Corresponding Author

*E-mail: ernesto.dejesus@uah.es.

Notes

The authors declare no competing financial interest.

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