

Articles

The Role of Ligand Transformations on the Performance of Phosphite- and Phosphinite-Based Palladium Catalysts in the Suzuki Reaction

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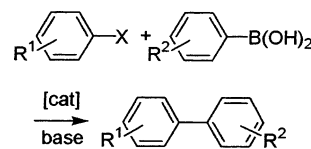
The orthometalated complex $\{[\text{Pd}(\mu\text{-Cl})\{\kappa^2\text{-}P,C\text{-}P(\text{OC}_6\text{H}_2\text{-}2,4\text{-}^t\text{Bu}_2)(\text{OC}_6\text{H}_3\text{-}2,4\text{-}^t\text{Bu}_2)_2\}]_2\}$ reacts with phenylboronic acid hydrate and K_2CO_3 in dimethylacetamide to give $[\text{Pd}\{\kappa^2\text{-}P,C\text{-}\mu^2\text{-}O\text{-}P(\text{O})(\text{C}_6\text{H}_2\text{-}2,4\text{-}^t\text{Bu}_2)(\text{C}_6\text{H}_3\text{-}2,4\text{-}^t\text{Bu}_2)(\text{DMAc})\}]$. When the reaction is repeated in dimethylformamide 3,3',5,5'-tetra-*tert*-butyl-2,2'-biphenol is isolated. Both compounds have been characterized crystallographically. The reaction of palladium dichloride with $\text{P}^i\text{Pr}_2\text{-}(\text{OC}_6\text{H}_4\text{-}4\text{-Et})$ in 2-methoxyethanol followed by recrystallization in the presence of ethanol leads to the formation of *trans*- $[\text{PdCl}_2\{\text{P}^i\text{Pr}_2(\text{OEt})_2\}]_2$, which was also characterized by crystallography. To determine whether related solvolytic processes have a bearing on catalytic activity, the performance of a range of catalysts with “hydrolyzed” and “nonhydrolyzed” ligands was assessed in the Suzuki coupling of aryl bromides. In some cases it was evident that hydrolysis plays a significant role on the catalytic activity; however, this depends not only on the ligand, but also on the combination of ligand and palladium precursor.

Introduction

The coupling of aryl halides with aryl boronic acids, the Suzuki reaction (Scheme 1), is one of the most powerful and versatile methods for the synthesis of biaryls.¹ There has recently been considerable interest in the development of a new, high-activity catalyst that can be used in low loadings in such reactions, and palladacyclic complexes have played a significant role in this regard.

The area was initiated by Beller, Herrmann and co-workers, who demonstrated that the palladacyclic complex **1** acts as a good catalyst in the coupling of aryl bromide substrates.² We demonstrated that the pincer complexes **2** and the orthopalladated triarylphosphite and phosphinite complexes **3** show good to excellent

Scheme 1. The Suzuki Biaryl Coupling Reaction



activity in such couplings,³ while Cole-Hamilton and co-workers demonstrated that the phosphine-based complexes **4** can also be used.⁴ High activity is not limited to phosphorus-based palladacycles but is also demonstrated by the *S*-donor complexes **5**,⁵ the imine-based catalyst **6**,⁶ and related oxime-containing species, **7**.⁷

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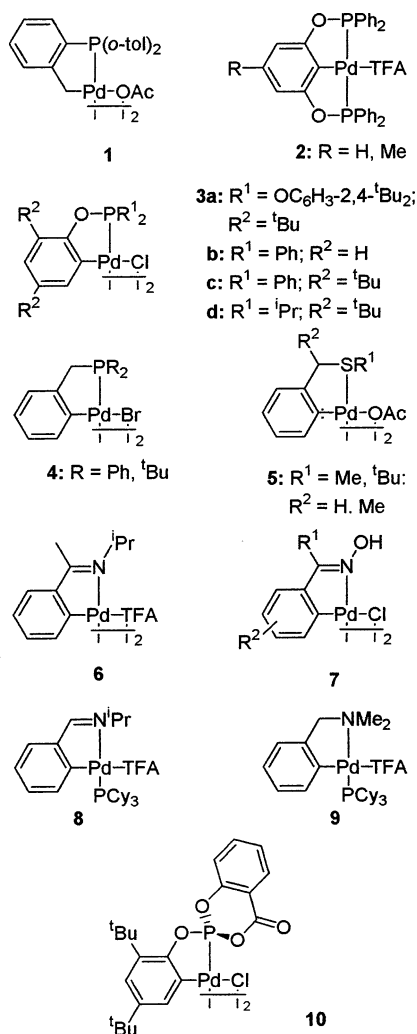
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Chart 1



Tricyclohexylphosphine adducts of both imine- and amine-based palladacycles, complexes **8** and **9**, show very good activity when aryl chlorides are used as substrates.⁸ Very recently we have found that similar adducts formed between complexes of the types **3** and **10** with tricyclohexylphosphine show among the highest activity yet reported in aryl chloride coupling reactions.⁹ Recently Li demonstrated that palladium–dialkylhydroxyphosphine complexes, Pd–PR₂(OH), formed on reaction of palladium precursors with secondary phosphine oxides via a tautomerization of the starting ligand, show good activity in a range of coupling reactions of aryl chlorides, including the Suzuki reaction.¹⁰ Once formed the Pd–PR₂(OH) complexes readily undergo base-promoted deprotonation of the hydroxyl group to give anionic species that are proposed to act as the true catalysts. It occurred to us that palladium phosphite and phosphinite complexes such as **3** may well undergo hydrolytic processes under catalytic conditions, which may in turn lead to the in situ generation of complexes related to those reported by Li with

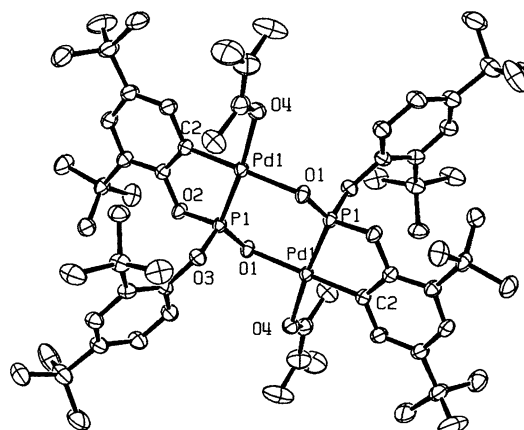


Figure 1. Molecular structure of [Pd{κ²-P,C-μ²-O-P(O)-(C₆H₂-2,4-^tBu₂)(C₆H₃-2,4-^tBu₂)(DMAc)}], **11**.

Table 1. Selected Bond Lengths (Å) and Angles (deg) for [Pd{κ²-P,C-μ²-O-P(O)(C₆H₂-2,4-^tBu₂)(C₆H₃-2,4-^tBu₂)(DMAc)}], **11**

Pd(1)–O(1)	2.1349(18)	Pd(1)–C(2)	1.997(3)
Pd(1)–P(1)	2.1638(7)	Pd(1)–O(4)	2.1549(19)
P(1)–O(1)	1.5065(18)	P(1)–O(2)	1.6198(18)
P(1)–O(3)	1.6216(19)	O(2)–C(1)	1.406(3)
O(3)–C(7)	1.403(3)	C(1)–C(2)	1.393(4)
P(1)–Pd(1)–C(2)	80.06(8)	P(1)–Pd(1)–O(1)	99.95(5)
O(4)–Pd(1)–C(2)	95.69(9)	O(1)–Pd(1)–O(4)	85.18(7)
P(1)–Pd(1)–O(4)	173.55(6)	O(1)–Pd(1)–C(2)	179.12(9)
Pd(1)–P(1)–O(1)	123.88(8)	Pd(1)–P(1)–O(2)	108.32(7)
Pd(1)–P(1)–O(3)	104.74(7)	Pd(1)–O(1)–P(1)	118.4(1)
P(1)–O(2)–C(1)	112.45(15)	P(1)–O(3)–C(7)	124.57(16)
O(2)–C(1)–C(2)	117.0(2)	Pd(1)–C(2)–C(1)	120.63(19)

PR₂(OH) ligands (R = alkyl, aryl, aryloxy). We now present evidence that these complexes can indeed engage in hydrolytic and solvolytic chemistry and address whether such processes have a role in the observed high activity of phosphite- and phosphinite-based catalysts in Suzuki coupling reactions.

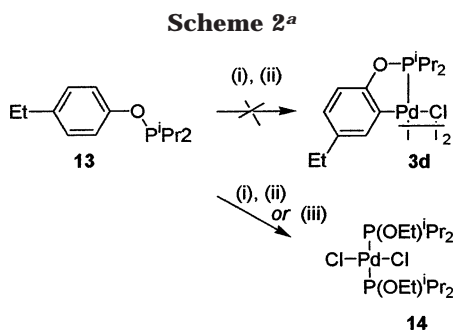
Results and Discussion

We were initially alerted to the potential of palladacyclic complexes of the type **3** to undergo hydrolytic reactions during studies on the activation of the catalyst **3a**. An NMR scale reaction of the palladacycle (10 mg) with 1.5 equiv of phenylboronic acid and 2 equiv of potassium carbonate in dimethylacetamide was heated at 100 °C for 5 h. The ¹H, ¹³C, and ³¹P NMR spectra of the reaction mixture were all broad and proved not to be useful in the characterization of the products. However, when the sample was left to stand at room temperature for several days a small amount of crystals was obtained and characterized by X-ray crystallography. The compound proved to be a new dimeric palladium complex, [Pd{κ²-P,C-μ²-O-P(O)(C₆H₂-2,4-^tBu₂)-(C₆H₃-2,4-^tBu₂)(DMAc)}], **11**, the molecular structure of which is shown in Figure 1, while selected data are given in Table 1. Complex **11** is, we believe, a unique example of an orthometalated diarylphosphito complex. While the orthometalation observed in the starting complex **3a** is maintained in the complex **11**, one of the nonorthometalated aryloxy residues in the starting material has been lost by hydrolysis, possibly with adventitious water arising from the boronic acid, present as a hydrate, in the presence of the base. The six-

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^a Conditions: (i) PdCl₂, 2-MeOC₂H₄OH, Δ, 18 h. (ii) Recrystallize, CH₂Cl₂/EtOH, 1–2 weeks. (iii) 0.5 equiv of PdCl₂, EtOH, Δ, 18 h.

membered ring containing the two palladium atoms adopts a chair conformation. The P–O bond length in this ring is significantly shorter than those of both the orthometalated and nonorthometalated aryloxy residues which are essentially the same length. Most of the bond lengths of the five-membered metallacycle are the same as those of complex **3a**,^{3c} except the P–O bond length which is slightly longer and the O–C bond length which is slightly shorter. All of the angles in the five-membered ring are comparable with those of complex **3a** except the Pd–C2–C1 angle, which is slightly more acute. The asymmetric unit contains a molecule of benzene, presumably derived from the phenylboronic acid.¹¹

When the reaction was repeated in DMF, again the the ¹H, ¹³C, and ³¹P NMR spectra proved to be uninformative. Leaving the solution to stand resulted in the formation of a small amount of crystals. This second compound was characterized by X-ray crystallography and was shown to be the known biphenol 3,3',5,5'-tetra-*tert*-butyl-2,2'-biphenol, **12**.¹² While it is evident that the biphenol **12** is formed by the oxidative coupling of two 2,4-di-*tert*-butylphenoxy residues,¹³ it is not clear at this stage whether the residues are coupled as free phenols lost during the hydrolytic formation of **11** from **3a** or whether the coupling occurs between two aryloxy residues still incorporated in phosphite ligands. The former process could arise from a metal-promoted pathway, the latter by internal reorganization and reductive elimination.

Evidence that phosphinite complexes are also able to undergo solvolytic processes was obtained when we attempted the synthesis of the orthopalladated complex **3d** from palladium dichloride and the ligand **13** in 2-methoxyethanol at reflux temperature. Slow recrystallization of the product mixture from dichloromethane/ethanol did not yield the expected product **3d**, but rather gave the new complex *trans*-[PdCl₂{PⁱPr₂(OEt)}₂], **14** (Scheme 2).

The structure of **14** was confirmed unequivocally by X-ray crystal analysis and the molecule is shown in Figure 2, while selected data are given in Table 2. As

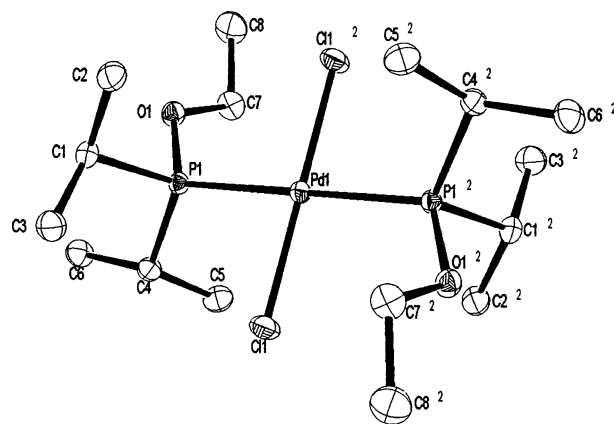


Figure 2. Molecular structure of [PdCl₂{PⁱPr₂(OEt)}₂], **14**.

Table 2. Selected Bond Lengths (Å) and Angles (deg) for [PdCl₂{PⁱPr₂(OEt)}₂], **14**

Pd(1)–P(1)	2.3265(10)	Pd(1)–Cl(1)	2.2975(7)
P(1)–O(1)	1.6156(14)	P(1)–C(1)	1.830(2)
P(1)–C(4)	1.8332(19)	O(1)–C(7)	1.450(2)
Cl(1)–Pd(1)–P(1)	88.24(2)	C(1)–P(1)–Pd(1)	110.23(7)
C(4)–P(1)–Pd(1)	116.50(6)	O(1)–P(1)–Pd(1)	117.64(5)
O(1)–P(1)–C(1)	97.60(8)	O(1)–P(1)–C(4)	105.68(8)
C(1)–P(1)–C(4)	107.18(9)		

can be seen the phosphinite ligands adopt a *trans*-configuration presumably as a consequence of their high steric profile, since the *cis*-configuration in which the π-donor chlorides would be *trans* to the π-acidic phosphinite ligands would be preferred electronically. Complex **14** is more conveniently prepared in 73% yield by heating 2 equiv of ligand **13** with palladium dichloride in ethanol at reflux temperature (Scheme 2).

Interestingly the “transesterification” reaction of the aryldialkylphosphinite **13** is not seen with palladium complexes of triarylphosphinites, PAr₂(OAr), or triarylphosphites, P(OAr)₃. We have previously found that such ligands readily undergo orthopalladation reactions when heated in 2-methoxyethanol at reflux temperature and that these and their nonorthometalated palladium(II) counterparts can be recrystallized from alcohols.^{3b,c} Both of these observations indicate that the coordinated ligands are stable with respect to transesterification.

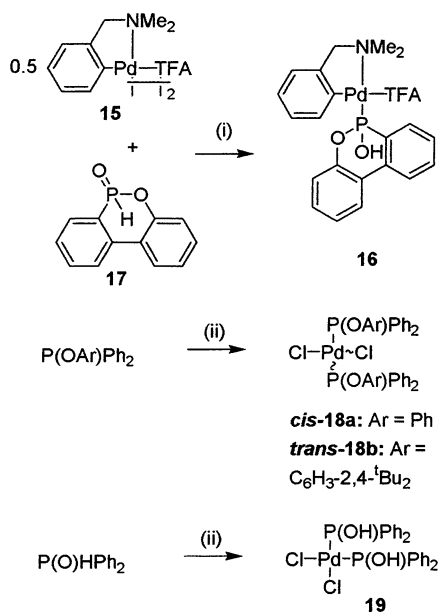
Evidently solvolytic processes can occur with both phosphite and phosphinite complexes of palladium. To assess whether in situ hydrolysis of such systems could help account for the high activity observed when complexes of the type **3** are used in Suzuki coupling reactions with aryl bromide substrates,^{3b,c} we decided to compare the activity of palladium catalysts with representative phosphite and phosphinite ligands with those containing comparable “hydrolyzed” PR₂(OH) ligands. The preformed catalysts synthesized were complex **16**, formed by reaction of the commercially available compound **17** with dimer **15**, which has previously been found to act as an excellent catalyst precursor⁸ (Scheme 3); the complexes **18a,b**, formed by reaction of the appropriate triarylphosphinite ligands with palladium [PdCl₂(NCMe)₂]; and complex **19**, formed by reaction of diphenylphosphine oxide with [PdCl₂(NCMe)₂].

The ³¹P NMR spectrum of **16** shows a singlet at δ 95.2 ppm, whereas that of the starting material **17** shows a

(11) For recent examples of this process see: Goosse, L. *J. Chem. Commun.* **2001**, 669 and references therein.

(12) See Supporting Information for the crystal structure of **12**.

(13) For recent examples of the production of **12** by oxidative coupling see: (a) Gupta, R.; Mukherjee, R. *Tetrahedron Lett.* **2000**, *41*, 7763. (b) Nishino, H.; Satoh, H.; Yamashita, M.; Kurosawa, K. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1919. (c) Lockwood, M. A.; Blubaugh, T. J.; Collier, A. M.; Lovell, S.; Mayer, J. M. *Angew. Chem., Int. Ed.* **1999**, *38*, 225 and references therein.

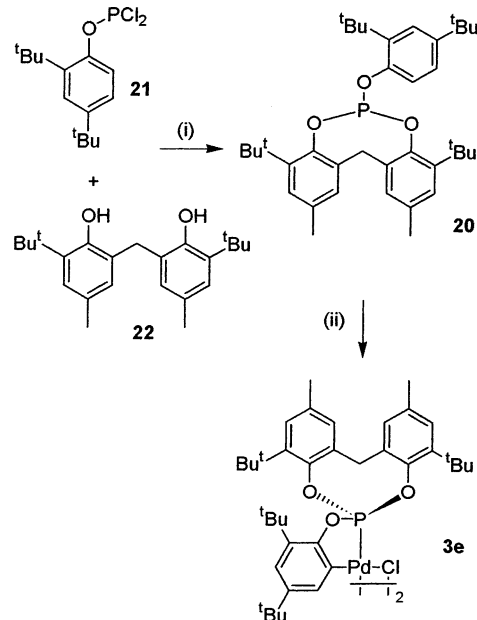
Scheme 3. Synthesis of Preformed Catalysts^a

^a Conditions: (i) CH₂Cl₂, rt, 1 h. (ii) 0.5 equiv of [PdCl₂(NCMe)₂], CH₂Cl₂, rt, 1 h.

doublet with a large (592 Hz) ¹J_(PH) coupling at δ 95 ppm. The ¹H NMR of complex **16** shows a broad singlet at 5.04 ppm for the O–H proton whereas that of the ligand **17** shows a doublet at 8.07 ppm for the P–H, with a phosphorus coupling of 592 Hz. This indicates that it is the P–OH tautomer that coordinates to the palladium center. The resonances associated with the orthometalated *N,N*-dimethylbenzylamine are closely similar to those found for other phosphine adducts,^{14,8} supporting the formulation of **16** as a simple phosphine adduct. The presence of the trifluoroacetate ligand was confirmed by IR spectroscopy, which showed a peak at 1545 cm⁻¹ corresponding to the C=O stretch.

The ³¹P NMR spectra of the complexes **18a,b** show singlets at δ 101.1 and 102.8 ppm, respectively, ca. 52–55 ppm upfield of their analogous orthopalladated complexes **3b,c** and consistent with nonorthometalated phosphinite ligands on a palladium(II) center.^{3c} The ¹H NMR spectra indicated that all the ortho-protons are indeed present. The IR spectra of complex **18a** shows two Pd–Cl stretches at 305 and 335 cm⁻¹, indicative of a cis disposition about the palladium center, whereas a single Pd–Cl stretch at 370 cm⁻¹ is seen for **18b** indicating a trans geometry. The IR data are very similar to those reported previously for analogous triarylphosphite complexes.¹⁵ The cis geometry of **16a** is preferred electronically as this renders the π-acidic phosphinite ligands trans to the π-basic chlorides; the bulk of the phosphinite ligands in **18b** overrides this electronic preference.

The ³¹P spectrum of complex **19** shows a singlet at δ 79.6 ppm compared with a doublet at δ 45.0 for diphenylphosphine oxide, indicating that the ligand has coordinated as the hydroxyphosphine tautomer. The ¹H NMR spectrum shows a broad singlet at δ 5.30 corresponding to the hydroxyl proton. The IR spectrum shows

Scheme 4. Synthesis and Orthometalation of a Bulky Triarylphosphite^a

^a Conditions: (i) NEt₃, toluene, Δ, 18 h. (ii) PdCl₂, toluene, Δ, 18 h.

two Pd–Cl stretches at 312 and 345 cm⁻¹, indicating a cis geometry about the palladium.

The phosphite ligand **20** was prepared by heating the dichlorophosphite **21** with the diol **22** in toluene in the presence of triethylamine (Scheme 4). Ligand **20** was then used to generate the palladacyclic catalyst **3e** by heating it with palladium dichloride in toluene.

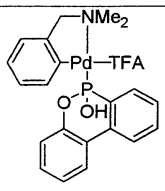
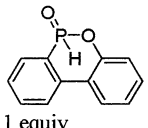
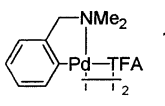
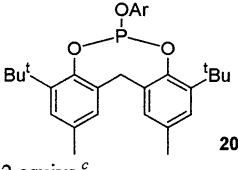
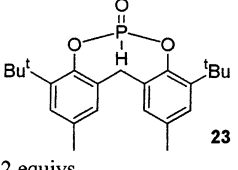
The application of complexes **3e**, **16**, **18a,b**, and **19** and related complexes formed in situ as catalysts in the Suzuki coupling reaction was then investigated. In all cases the initial coupling studied was that of phenylboronic acid with 4-bromoanisole as this is an electronically challenging bromide, thus results from this reaction are a useful indicator of catalyst performance. The results of this study are summarized in Table 3.

As can be seen, the preformed catalyst **16** showed slightly lower activity than catalysts formed in situ from complex **15** and either 1 or 2 equiv of the ligand **17** (entries 1–4). This demonstrates that complexes with P–OH tautomers of comparatively π-acidic ligands can give good activity in coupling reactions. Next we compared the performance of the catalysts formed in situ from complex **15** and 2 equiv per palladium of the phosphinite ligands PR₂(OC₆H₃-2,4-^tBu₂) (R = Ph, ⁱPr) with the analogous systems containing the ligands PR₂(OH) (entries 5–8). As can be seen, the hydroxyphosphine systems show good activity, but only about half that of the analogous phosphinites. This demonstrates that in this case hydrolysis cannot account for all the activity seen with the phosphinite ligands. However, when a similar comparison is made between the triarylphosphite **20** and its hydrolyzed analogue **23** (entries 9 and 10), it can be seen that there is essentially no difference in performance. Therefore it seems, at first sight at least, as if hydrolysis may be playing a role in this case. As well as being dependent on the ligand, the extent to which hydrolysis may play a role also seems to be dependent on the palladium source. Comparing

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Table 3. The Suzuki Coupling of 4-Bromoanisole with Phenylboronic Acid^a

Entry	Palladium source (mol% Pd)	Added ligand	Conv. (%) ^b	TON
1	 16 (0.001)	-	30	30,000
2	"	 17 1 equiv.	28	28,000
3	 15 (0.001)	" 1 equiv.	40	40,000
4	"	" 2 equivs.	42	42,000
5	"	2 PPh ₂ (OAr) ^c	60	60,000
6	"	2 P ⁱ Pr ₂ (OAr) ^c	79	79,000
7	"	Ph ₂ P(O)H, 2 equivs.	35	35,000
8	"	ⁱ Pr ₂ P(O)H, 2 equivs.	30	30,000
9	" (0.001)	 20 2 equivs. ^c	74	74,000
10	"	 23 2 equivs.	75	75,000
11	[Pd ₂ (dba) ₃] (0.0001)	2 PPh ₂ (OAr) ^c	36	360,000
12	[Pd ₂ (dba) ₃] (0.0001)	2 P ⁱ Pr ₂ (OAr) ^c	590	590,000
13	[Pd ₂ (dba) ₃] (0.0001)	2 PPh ₂ (O)H	17	170,000
14	[Pd ₂ (dba) ₃] (0.0001)	2 P ⁱ Pr ₂ (O)H	10	100,000
15	[PdCl ₂ {PPh ₂ (O)H} ₂] (0.001)	(18a) -	70	70,000
16	[PdCl ₂ {PPh ₂ (OAr)} ₂] ^c (0.001)	(18b) -	77	77,000
17	[PdCl ₂ {PPh ₂ (OH)} ₂] (19) (0.001)	-	69	69,000

^a Reaction conditions: phenylboronic acid (15 mmol), 4-bromoanisole (10 mmol), K₂CO₃ (20 mmol), toluene (30 mL), 110 °C, 18 h.
^b Based on conversion of 4-bromoanisole to 4-methoxybiphenyl, determined by GC (hexadecane standard). ^c Ar = C₆H₃-2,4-^tBu₂.

the performance of the catalysts formed in situ from palladium bis(dibenzylideneacetone) and either the phosphinite ligands PR₂(OC₆H₃-2,4-^tBu₂) (R = Ph, ⁱPr) or their hydrolyzed counterparts, it can be seen that hydrolysis cannot account fully for the activity observed with the phosphinites. It is also interesting to note that here palladium bis(dibenzylideneacetone) appears to be a better palladium source than complex **15**, in contrast to the findings obtained in the Suzuki coupling of aryl chlorides catalyzed by analogous tricyclohexylphosphine complexes.^{8,16}


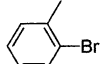
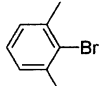
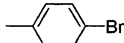
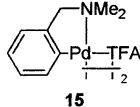
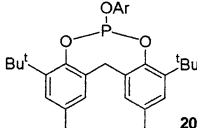
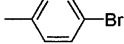
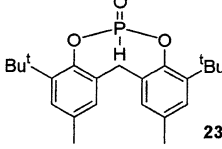
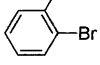
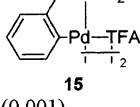
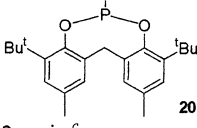
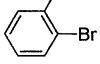
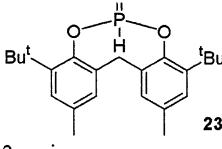
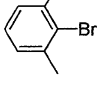
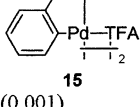
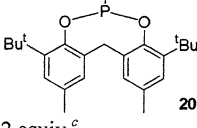
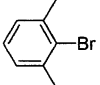
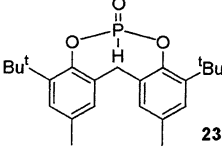
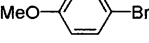
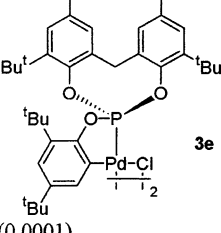
By contrast when the preformed aryldiphenylphosphinite complexes **18a,b** are compared with the hydroxydiphenylphosphine complex **19** (entries 15–17) very similar activity results, again indicating that, at least with triarylphosphinites, hydrolysis is important.

It is not possible to perform analogous studies with the PⁱPr₂(OAr) and PⁱPr₂(OH) ligands at this stage as we were unable to cleanly synthesize the appropriate palladium dichloride adducts of the latter ligands.

To establish whether the observed similarity in performance of some of the catalysts and their hydrolyzed counterparts is indeed significant, rather than just a coincidence for this particular coupling, we investigated their performance in the coupling of three further bromides, namely 4-bromotoluene, 2-bromotoluene, and 2-bromo-*m*-xylene (Table 4).

Comparing the activities of the preformed phosphinite complex **18a** with the analogous hydroxyphosphine complex **19** in the coupling of all three aryl bromide substrates (entries 1–6) it can be seen that, as in the case with 4-bromoanisole, they are essentially identical. The performances of the catalysts formed in situ from complex **15** and either ligand **20** or ligand **23** are again

Table 4. Suzuki Coupling of Aryl Bromides with Phenylboronic Acid^a

Entry	Aryl bromide	Palladium source (mol% Pd)	Added ligand	Conv. (%) ^b	TON
1		[PdCl ₂ {PPh ₂ (OPh)} ₂] (18a) (0.001)	-	31	31,000
2	“	[PdCl ₂ {PPh ₂ (OH)} ₂] (19) (0.001)	-	27	27,000
3		[PdCl ₂ {PPh ₂ (OPh)} ₂] (18a) (0.001)	-	91	91,000
4	“	[PdCl ₂ {PPh ₂ (OH)} ₂] (19) (0.001)	-	85	85,000
5		[PdCl ₂ {PPh ₂ (OPh)} ₂] (18a) (0.001)	-	45	45,000
6	“	[PdCl ₂ {PPh ₂ (OH)} ₂] (19) (0.001)	-	42	42,000
7		 15 (0.001)	 20 2 equiv. ^c	21	21,000
8		“	 23 2 equivs.	21	21,000
9		 15 (0.001)	 20 2 equiv. ^c	78	78,000
10		“	 23 2 equivs.	60	60,000
11		 15 (0.001)	 20 2 equiv. ^c	30	30,000
12		“	 23 2 equivs.	28	28,000
13		 3e (0.0001)	-	43	430,000

^a Reaction conditions: phenylboronic acid (15 mmol), 4-bromoanisole (10 mmol), K₂CO₃ (20 mmol), toluene (30 mL), 110 °C, 18 h.^b Based on conversion of aryl bromide to Suzuki coupled biphenyl, determined by GC (hexadecane standard). ^c Ar = C₆H₃-2,4-^tBu₂.

essentially identical except in the coupling of 2-bromotoluene where the hydrolyzed system shows slightly lower activity. Therefore it may be concluded that for both preformed catalyst systems of the type $[\text{PdCl}_2\text{-}\{\text{PPh}_2(\text{OAr})\}_2]$ or catalysts formed in situ from complex **15** and the triarylphosphite **20**, hydrolysis occurs during the activation of the pre-catalysts and that the true active catalysts contain hydrolyzed forms of the ligands.

It is difficult to extrapolate these data to all systems with triarylphosphinite and triarylphosphite ligands since both catalytic activity and the influence of hydrolysis are not only dependent on the ligand type but also on the nature of the palladium precursor. In all cases the activity observed is substantially lower than when palladacycles with orthometalated triarylphosphite or phosphinites ligands are used under the same conditions. For instance, the palladacycle formed from ligand **20**, complex **3e**, shows a maximum TON of 430 000 in the coupling of phenylboronic acid with 4-bromoanisole (Table 4, entry 13), while complex **3c** shows TONs of up to 2.6 million in the same reaction.^{3c} Therefore it is not possible at this stage to determine what extent the hydrolysis of the ligands has on the performance of these very high activity catalysts. Regardless, the data obtained here certainly point to the fact that hydrolysis does play a role. From this study it is apparent that potential hydrolytic processes should be taken into account during both the rational design of new precatalysts and studies into their in situ activation.

Experimental Section

General Methods. All reactions were carried out under nitrogen following standard Schlenk techniques. Solvents were dried and freshly distilled prior to use. All other chemicals were used as received. Complex **15**, compound **23**, and $\text{PPh}_2(\text{OPh})$ were prepared according to literature methods.^{8,17,18} GC analyses were performed on a Varian 3800 GC fitted with a 25 m CP Sil 5CB column and data were recorded on a Star workstation.

General Method for the Preparation of Aryl Diisopropylphosphinite Ligands. A mixture of the appropriate predried (toluene azeotrope) phenol (31.4 mmol), chlorodiisopropylphosphine (5.0 mL, 31.4 mmol), and triethylamine (5.0 mL, 35.9 mol) in toluene (80 mL) was heated at reflux temperature for 17 h. Petroleum ether 60–80 (50 mL) was added to the cooled reaction mixture, which was then filtered through Celite to remove $[\text{Et}_3\text{NH}]\text{Cl}$. The precipitate was washed with petrol (3×10 mL) and the solvents removed from the combined organic fractions under reduced pressure to yield the diisopropylphosphinite ligands as pale yellow oils which were not purified further.

$\text{P}^i\text{Pr}_2(\text{OC}_6\text{H}_4\text{-4-Et})$, **13.** Yellow oil. Yield: 7.26 g (97%). ^1H NMR (300 MHz, CDCl_3): δ 1.32 (dd, 6H, $^3J_{\text{HH}} = 7.2$ Hz, $^3J_{\text{PH}} = 15.8$ Hz, $\text{CH}(\text{CH}_3)_2$), 1.40 (t, 3H, $^3J_{\text{HH}} = 7.0$ Hz, CH_2CH_3), 1.42 (dd, 6H, $^3J_{\text{HH}} = 7.2$ Hz, $^3J_{\text{PH}} = 11.0$ Hz, $\text{CH}(\text{CH}_3)_2$), 2.18 (apparent d of heptets, 2H, $^2J_{\text{PH}} = 2.34$ Hz, $^3J_{\text{HH}} = 7.2$ Hz, $\text{CH}(\text{CH}_3)_2$), 2.75 (q, 2H, $^3J_{\text{HH}} = 7.0$ Hz, CH_2CH_3), 7.18 (d, 2H, $^3J_{\text{HH}} = 7.9$ Hz), 7.22 (d, 2H, $^3J_{\text{HH}} = 8.0$ Hz, aromatic). ^{31}P NMR (121.5 MHz, CDCl_3): δ 149.4 (s). Anal. Calcd for $\text{C}_{14}\text{H}_{23}\text{OP}$: C, 70.56; H, 9.73. Found: C, 70.15; H, 9.2.

$\text{P}^i\text{Pr}_2(\text{OC}_6\text{H}_3\text{-2,4-Bu}_2)$. Pale yellow oil. Yield: 9.72 g (96%). ^1H NMR (300 MHz, CDCl_3): δ 1.13 (dd, 6H, $^3J_{\text{HH}} = 7.0$ Hz,

$^3J_{\text{PH}} = 15.2$ Hz, $\text{CH}(\text{CH}_3)_2$), 1.19 (dd, 6H, $^3J_{\text{HH}} = 7.1$ Hz, $^3J_{\text{PH}} = 11.0$ Hz, $\text{CH}(\text{CH}_3)_2$), 1.30 (s, 9H, 'Bu), 1.41 (s, 9H, 'Bu), 2.04 (apparent d of heptets, 2H, $^2J_{\text{PH}} = 2.3$ Hz, $^3J_{\text{HH}} = 7.2$ Hz, $\text{CH}(\text{CH}_3)_2$), 7.11 (dd, 1H, $^3J_{\text{HH}} = 8.5$ Hz, $^4J_{\text{HH}} = 2.6$ Hz, H5), 7.29 (d, 1H, $^4J_{\text{HH}} = 2.6$ Hz, H3), 7.50 (dd, 1H, $^3J_{\text{HH}} = 8.5$ Hz, $^4J_{\text{HP}} = 6.2$ Hz, H6). ^{31}P NMR (121.5 MHz, CDCl_3): δ 138.4 (s). Anal. Calcd for $\text{C}_{20}\text{H}_{35}\text{OP}$: C, 74.49; H, 10.94. Found: C, 74.0; H, 10.6.

Preparation of 2,4-Di-*tert*-butylphenyl Diphenylphosphinite, $\text{PPh}_2(\text{OC}_6\text{H}_3\text{-2,4-Bu}_2)$. A mixture of predried (toluene azeotrope) 2,4-di-*tert*-butylphenol (6.89 g, 33.4 mmol), chlorodiphenylphosphine (6.0 mL, 33.4 mmol), and triethylamine (7.0 mL, 50.0 mmol) in toluene (50 mL) was heated at reflux temperature for 17 h. The mixture was filtered through Celite to remove $[\text{Et}_3\text{NH}]\text{Cl}$, the precipitate was washed with toluene (2×10 mL), and the volatiles were removed from the combined organic fractions under reduced pressure to yield the title compound as a white solid that was not purified further. Yield: 12.78 g (98%). ^1H NMR (300 MHz, CDCl_3): δ 1.32 (s, 9H, 'Bu), 1.39 (s, 9H, 'Bu), 7.05 (dd, 1H, $^3J_{\text{HH}} = 8.5$ Hz, $^4J_{\text{HP}} = 3.0$ Hz, H6), 7.12 (dd, 1H, $^3J_{\text{HH}} = 8.5$ Hz, $^4J_{\text{HH}} = 2.5$ Hz, H5), 7.36 (d, 1H, $^4J_{\text{HH}} = 2.5$ Hz, H3), 7.40 (m, 6H, Ph), 7.63 (m, 4H, Ph). ^{31}P NMR (121.5 MHz, CDCl_3): δ 108.5 (s). Anal. Calcd for $\text{C}_{26}\text{H}_{31}\text{OP}$: C, 80.0; H, 8.0. Found: C, 80.1; H, 7.95.

Preparation of $\text{P}(\text{OC}_6\text{H}_3\text{-2,4-Bu}_2)\{\text{OC}_6\text{H}_2\text{-2-Bu-4-Me-6-CH}_2\}$, **20.** A mixture of 2,2'-methylenebis(6-*tert*-butyl-4-methylphenol) (1.00 g, 2.94 mmol), dichloro-2,4-di-*tert*-butylphenyl phosphite (1.00 g, 3.23 mmol), and triethylamine (1.0 mL, 7.2 mmol) in toluene (100 mL) was heated at reflux temperature for 18 h. The suspension was allowed to cool to room temperature and then filtered through Celite. The clear solution is evaporated to dryness in vacuo, yielding the crude product as a gum that is washed repeatedly with *n*-pentane to give a colorless solid. Yield: 1.39 g (82%). ^1H NMR (300 MHz, CDCl_3): δ 1.32 (s, 18H, 'Bu), 1.53 (s, 9H, 'Bu), 1.34 (s, 9H, 'Bu), 2.32 (s, 6H, CH_3), 3.48 (d, 1H, $^2J_{\text{HH}} = 12.8$ Hz, CH_2), 4.50 (dd, 1H, $^2J_{\text{HH}} = 12.8$ Hz, $^5J_{\text{HP}} = 2.8$ Hz, CH_2), 7.05 (d, 2H, $^4J_{\text{HH}} = 2.2$ Hz, H3'), 7.15 (d, 2H, $^4J_{\text{HH}} = 2.2$ Hz, H5'), 7.16 (dd, 1H, $^3J_{\text{HH}} = 8.5$ Hz, $^4J_{\text{HH}} = 2.5$ Hz, H5), 7.42 (d, 1H, $^4J_{\text{HH}} = 2.5$ Hz, H3), 7.59 (dd, 1H, $^3J_{\text{HH}} = 8.5$ Hz, $^4J_{\text{HP}} = 2.7$ Hz, H6). $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 121.5 MHz): δ 133 (s). Anal. Calcd for $\text{C}_{37}\text{H}_{51}\text{O}_3\text{P}$: C, 77.32; H, 8.94. Found: C, 76.8; H, 9.4.

Preparation of $[\{\text{Pd}(\mu\text{-Cl})\{\kappa^2\text{-P,C-P}(\text{OC}_6\text{H}_2\text{-2,4-Bu-4-Me-6-CH}_2)\}_2\}]_2$, **3e.** A mixture of PdCl_2 (0.150 g, 0.85 mmol) and the ligand **20** (0.500 g, 0.91 mmol) in toluene (15 mL) was heated at reflux temperature for 18 h. The solution was allowed to cool to room temperature and then the solvent was removed in vacuo. The crude product was dissolved in dichloromethane (25 mL), filtered through Celite, and concentrated to ca. 5 mL. Addition of methanol (15 mL) gave a bright yellow precipitate of the product, which was collected by filtration and dried in vacuo. Yield: 0.325 g (53%). ^1H NMR (CDCl_3 , 300 MHz): δ 0.91, 1.10, 1.14, 1.20 (s, br, 36H, 'Bu), 2.14 (s, 6 H, CH_3), 3.65 (m, br, 1H, CH_2), 4.47 (m, br, 1H, CH_2), 6.91, 6.95, 7.18, 7.35 (m, 6H, br). $^{31}\text{P}\{^1\text{H}\}$ NMR (CDCl_3 , 121 MHz): δ 119.0 (s, br, major isomer), 117.0 (s, minor isomer). Anal. Calcd for $\text{C}_{31}\text{H}_{39}\text{O}_3\text{P}_2$: C, 62.10, H, 7.04. Found: C, 61.9; H, 7.1.

Preparation of *trans*- $[\text{PdCl}_2\{\text{P}^i\text{Pr}_2(\text{OEt})\}_2]$, **14.** A mixture of PdCl_2 (0.500 g, 2.82 mmol) and ligand **13** (1.344 g, 5.64 mmol) in ethanol (50 mL) was heated at reflux temperature overnight and the resulting orange solution was cooled and a yellow-orange solid precipitated. The crude solid was recrystallized from CH_2Cl_2 /pentane to give the title complex as a yellow solid. Yield: 1.347 g (73%). ^1H NMR (300 MHz, CDCl_3): δ 1.30 (t, 6H, br, $^3J_{\text{HH}} \approx 7$ Hz, CH_2CH_3), 1.45 (dd, 6H, $^3J_{\text{HH}} = 7.4$ Hz, $^3J_{\text{PH}} = 10.7$ Hz, $\text{CH}(\text{CH}_3)_2$), 1.51 (dd, 6H, $^3J_{\text{HH}} = 7.4$ Hz, $^3J_{\text{PH}} = 10.5$ Hz, $\text{CH}(\text{CH}_3)_2$), 2.50 (apparent d of heptets, 4H, $^3J_{\text{HH}} = 7.1$ Hz, $^2J_{\text{PH}} \approx 2$ Hz, $\text{CH}(\text{CH}_3)_2$), 4.20 (q, 4H, $^3J_{\text{HH}} \approx 7$ Hz, CH_2CH_3). ^{31}P NMR (121.5 MHz, CDCl_3): δ

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140.9. IR (KBr) $\nu(\text{Pd}-\text{Cl})$: 315, 347 cm^{-1} . Anal. Calcd for $\text{C}_{16}\text{H}_{38}\text{Cl}_2\text{O}_2\text{P}_2\text{Pd}$: C, 51.43; H, 7.09. Found: C, 51.0; H, 7.4. ^1H NMR (300 MHz, CDCl_3): δ 1.30 (t, 6H, br, $^3J_{\text{HH}} \approx 7$ Hz, CH_2CH_3), 1.45 (dd, 6H, $^3J_{\text{HH}} = 7.4$ Hz, $^3J_{\text{PH}} = 10.7$ Hz, $\text{CH}(\text{CH}_3)_2$), 1.51 (dd, 6H, $^3J_{\text{HH}} = 7.4$ Hz, $^2J_{\text{PH}} = 10.5$ Hz, $\text{CH}(\text{CH}_3)_2$), 2.50 (apparent d of heptets, 4H, $^3J_{\text{HH}} \approx 2$ Hz, $^2J_{\text{PH}} = 7.1$ Hz, $\text{CH}(\text{CH}_3)_2$), 4.20 (q, 4H, $^3J_{\text{HH}} \approx 7$ Hz, CH_2CH_3). ^{31}P NMR (121.5 MHz, CDCl_3): δ 140.9.

Preparation of $[\text{Pd}(\kappa^2\text{-}N,C\text{-NMe}_2\text{CH}_2\text{C}_6\text{H}_4)(\text{TFA})\{\text{P}(\text{OH})\text{-}(\text{cyclo-OC}_6\text{H}_4\text{-}2\text{-C}_6\text{H}_4)\}_2]$, **16.** A solution of $\{[\text{Pd}(\mu\text{-TFA})(\kappa^2\text{-}N,C\text{-C}_6\text{H}_4\text{CH}_2\text{NMe}_2)\}_2\}$ (1.00 g, 1.41 mmol) and 6*H*-dibenz[*c,e*][1,2]-oxaphosphorin-6-oxide (0.61 g, 2.83 mmol) in CH_2Cl_2 (10 mL) was stirred at room temperature for 1 h during which time a precipitate formed. The resulting white solid was collected by filtration and recrystallized from $\text{CH}_2\text{Cl}_2/\text{MeOH}$ to yield the title complex as a white solid. Yield: 0.51 g (63%). ^1H NMR (300 MHz, CDCl_3): δ 2.21 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 3.28 (d, 1H, $^2J_{\text{HH}} = 12$ Hz, CH_2N), 3.32 (d, 1H, $^2J_{\text{HH}} = 12$ Hz, CH_2N), 5.04 (1H, s, br, OH), 7.19 (m, br, 4H, orthometalated ring), 7.86 (complex overlapping multiplets, 8H, aromatic). ^{31}P NMR (121.5 MHz, CDCl_3): δ 95.2 (s). IR (KBr) $\nu(\text{C}=\text{O})$: 1545 cm^{-1} . Anal. Calcd for $\text{C}_{23}\text{H}_{21}\text{F}_3\text{NO}_4\text{PPd}$: C, 48.48; H, 3.71; N, 2.46. Found: C, 48.75; H, 3.3; N, 2.6.

General Method for the Preparation of the Complexes $[\text{PdCl}_2(\text{L})_2]$. A solution of $[\text{PdCl}_2(\text{NCMe})_2]$ (0.50 g, 1.93 mmol) and appropriate ligand (3.85 mmol) in CH_2Cl_2 (20 mL) was stirred for 1 h at room temperature. Hexane (15 mL) was added to precipitate the product, which was then recrystallized from $\text{CH}_2\text{Cl}_2/\text{hexane}$ and dried in vacuo.

***cis*- $[\text{PdCl}_2\{\text{PPh}_2(\text{OPh})\}_2]$, **18a**.** Pale orange solid. Yield: 0.62 g (44%). ^1H NMR (300 MHz, CDCl_3): δ 7.07 (m, 2H, H4 of OPh), 7.20 (m, 4H, OPh), 7.28 (m, 4H, OPh), 7.46 (m, 12H, PPh), 7.67 (m, 8H, PPh). ^{31}P NMR (121.5 MHz, CDCl_3): δ 101.1 (s). IR (KBr) $\nu(\text{Pd}-\text{Cl})$: 305, 335 cm^{-1} . Anal. Calcd for $\text{C}_{36}\text{H}_{30}\text{-Cl}_2\text{O}_2\text{P}_2\text{Pd}$: C, 58.92; H, 4.12. Found: C, 59.6; H, 4.6.

***trans*- $[\text{PdCl}_2\{\text{PPh}_2(\text{OC}_6\text{H}_3\text{-}2,4\text{-Bu}_2)\}_2]$, **18b**.** Yellow solid. Yield: 0.44 g (88%). ^1H NMR (300 MHz, CDCl_3): δ 1.36 (s,

18H, Bu), 1.39 (s, 18H, Bu), 7.30 (dd, 2H, $^3J_{\text{HH}} = 7.5$ Hz, $^4J_{\text{HH}} = 2.5$ Hz, H5 OAr), 7.36 (d, 2H, 2.5 Hz, H3 OAr), 7.41 (m, 12H, Ph), 7.78 (m, 8H, Ph), 7.90 (d, 2H, $^3J_{\text{HH}} = 7.5$ Hz, H6 OAr). ^{31}P NMR (121.5 MHz, CDCl_3): δ 102.8 (s). IR (KBr) $\nu(\text{Pd}-\text{Cl})$: 370 cm^{-1} . Anal. Calcd for $\text{C}_{52}\text{H}_{62}\text{Cl}_2\text{O}_2\text{P}_2\text{Pd}$: C, 65.17; H, 6.52. Found: C, 64.7; H, 6.4.

***cis*- $[\text{PdCl}_2\{\text{PPh}_2(\text{OH})\}_2]$, **19**.** Yellow solid. Yield: 0.78 g (69.8%). ^1H NMR (300 MHz, CDCl_3): δ 5.30 (s, br, 2H, POH), 7.23 (m, 8H, H2, Ph), 7.38 (m, 4H, $^3J_{\text{HH}} = 6.0$ Hz, H4), 7.56 (m, 8H, Ph). ^{31}P NMR (121.5 MHz, CDCl_3): δ 79.6 (s). IR (KBr) $\nu(\text{Pd}-\text{Cl})$: 312, 345 cm^{-1} . Anal. Calcd for $\text{C}_{24}\text{H}_{22}\text{Cl}_2\text{O}_2\text{P}_2\text{Pd}$: C, 49.55; H, 3.81. Found: C, 49.85; H, 3.64.

Catalysis. In a three-necked flask under an atmosphere of nitrogen were placed the appropriate aryl bromide (10.0 mmol), phenyl boronic acid (1.83 g, 15.0 mmol), K_2CO_3 (2.76 g, 20.0 mmol), and toluene (30 mL total, including catalysis solution). The correct amount of catalyst was added as a toluene solution made up by multiple volumetric dilutions of stock solutions and the mixture was heated at reflux temperature for 18 h. The mixture was cooled in an ice bath, quenched with aqueous HCl (2 M, 100 mL), extracted with dichloromethane (3×100 mL), dried over MgSO_4 , and evaporated to dryness. Hexadecane (0.068 M in CH_2Cl_2 , 3.0 mL) and dichloromethane (5–7 mL, to ensure complete dissolution) were added. The conversion to coupled product was then determined by GC analysis.

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Supporting Information Available: Complete crystal structure data for compounds **11**, **12**, and **14**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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