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Guanidine/Pd(OAc)$_2$-Catalyzed Room Temperature Suzuki Cross-Coupling Reaction in Aqueous Media under Aerobic Conditions

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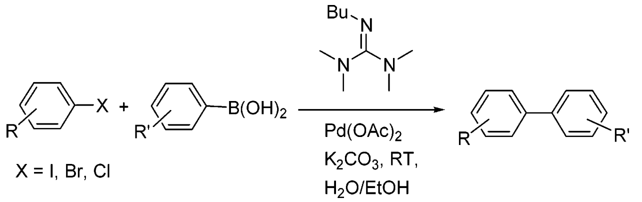
Received December 21, 2006



A highly efficient Pd(OAc)$_2$/guanidine aqueous system for the room temperature Suzuki cross-coupling reaction has been developed. The new water-soluble and air-stable catalyst Pd(OAc)$_2$·(**1f**)$_2$ from Pd(OAc)$_2$ and 1,1,3,3-tetramethyl-2-*n*-butylguanidine (**1f**) was synthesized and characterized by X-ray crystallography. In the presence of Pd(OAc)$_2$·(**1f**)$_2$, coupling of arylboronic acids with a wide range of aryl halides, including aryl iodides, aryl bromides, even activated aryl chlorides, was carried out smoothly in aqueous solvent to afford the cross-coupling products in good to excellent yields and high turnover numbers (TONs) (TONs up to 850 000 for the reaction of 1-iodo-4-nitrobenzene and phenylboronic acid). Furthermore, this mild protocol could tolerate a broad range of functional groups.

Introduction

The palladium-catalyzed Suzuki cross-coupling reaction is a very favorable and versatile method for forming carbon−carbon bonds between aryls and has found widespread use in organic synthesis.[1] Many research groups have focused their interest on the development of efficient and active catalytic systems in the past years. Generally, phosphine ligands[2] are required to stabilize the active palladium species in the palladium-catalyzed Suzuki cross-coupling reaction. However, many of the phosphine ligands are sensitive to air, and they are also expensive, toxic, and unrecoverable, which results in significant limitations on their synthetic application. Therefore, the development of a phosphine-free Pd catalyst is a topic of enormous interest. A few phosphine-free *N*-based ligands, such as *N*-heterocyclic carbenes,[3] *N*,*O*- or *N*,*N*-bidentate ligands,[4] aryloximes,[5] arylimines,[6] *N*-acylamidines,[7] and simple amines,[8] have been used in the Suzuki cross-coupling reaction. Most of these reactions were performed in traditional organic solvents and resulted in considerable environmental pollution. Due to environmental, economical, and safety concerns, many research groups have focused on the use of water as a solvent for the Suzuki reaction.[9]

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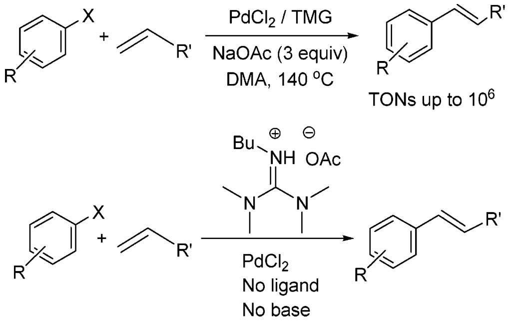
10.1021/jo0626257 CCC: $37.00

There are problems associated with the use of an aqueous solvent. These include solubility of substrates and stability of the metal catalysts in water. Although the application of phase-transfer catalysts[10,8e] and water-soluble phosphine ligands[11] has been developed, most of these systems require harsh conditions. Also, fewer catalytic systems could perform the cross-coupling reaction of aryl bromides or aryl chlorides at room temperature.

In previous studies,[12] we found that tetramethylguanidine (TMG) was a highly efficient ligand for the palladium-catalyzed Heck reaction. Its use resulted in high turnover numbers (TONs) (up to 10^6 TONs for the reaction of iodobenzene and butyl acrylate). Furthermore, the Brønsted guanidine acid−base ionic liquids could act as ligand, base, and solvent in the Heck reaction. This offered the advantages of high activities and reusability in this environmentally benign process (eq 1).



(1)

Although there are high activities obtained in the guanidine/Pd-catalyzed Heck reaction, a high reaction temperature (140 °C) was still required to afford high yield of the product. From these promising results, we endeavored to examine the efficiency of these types of ligands on palladium-catalyzed Suzuki cross-coupling reactions. We are especially interested in the possibility of using these types of ligands for room temperature Suzuki cross-coupling reactions in aqueous solvent under air conditions.

Results and Discussion

Screening of the Ligands. The synthesis of tetraalkylguanidines (TAGs) and pentaalkylguanidines (PAGs) was according to literature methods,[13] and the structure of TAGs and PAGs is outlined in Figure 1. The chemical structure and elemental composition of the guanidines were confirmed by elemental analysis and ^{1}H NMR spectroscopies (see the Supporting Information). To examine the efficiency of $Pd(OAc)_2$/guanidine as a catalyst in the Suzuki cross-coupling reaction, a model coupling reaction of 4-bromoanisole with phenylboronic acid was initially tested. The results are summarized in Table 1. These data show that these guanidines are effective ligands for the palladium-catalyzed Suzuki reaction. In the absence of ligands, only a 42% yield of the cross-coupling product was isolated in the presence of 1.5 mol % of $Pd(OAc)_2$ and 3 equiv of K_2CO_3 in CH_3CN at 80 °C (entry 1). The yield of the product increased sharply upon addition of guanidine (entries 2−10). Among the guanidines investigated, TAGs showed moderate efficiency, which gave the coupling product in 74−83% yield (entries 2−6). PAGs were found to be the best ligands, which gave the coupling product in nearly quantitative yield (entries 7−10). To further evaluate the influence of the steric bulk of the guanidine ligands, the coupling reaction of the less active chlorobenzene with phenylboronic acid, in the presence of 2.0 mol % of $Pd(OAc)_2$ and 3 equiv of K_2CO_3 in CH_3CN at 80 °C, was also tested. The results are summarized in Table 2. 1,1,3,3-Tetramethylguanidine (**1a**) displayed less efficiency, giving the coupling product in 12% yield. The more bulky PAGs were found to be better ligands. 1,1,3,3-Tetramethyl-2-*n*-butylguanidine (**1f**) afforded the product in 31% yield. The more bulky 1,1,3,3-tetramethyl-2-*sec*-butylguanidine (**1g**) was found to be the best ligand, giving the product in 45% yield in 10 h. However, the more bulky guanidine, 1,1,3,3-tetramethyl-2-*tert*-butylguanidine (**1h**), furnished the product in a lower yield

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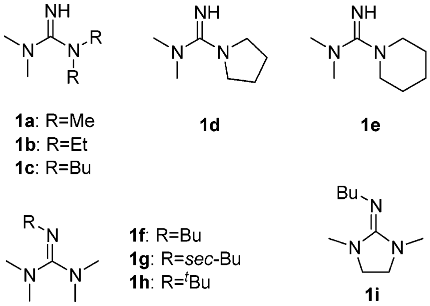
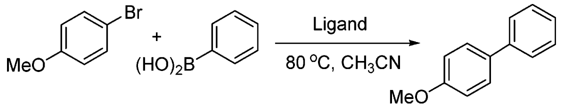


FIGURE 1. Structures of guanidine ligands.

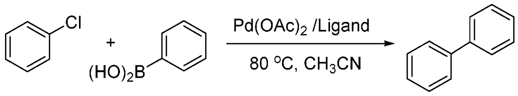
TABLE 1. Screening of the Ligands on the Suzuki Reaction of 4-Bromoanisole with Phenylboronic Acid[a]



entry	ligand	yield (%)[b]	entry	ligand	yield (%)[b]
1	none	42	6	**1e**	80
2	**1a**	74	7	**1f**	99
3	**1b**	78	8	**1g**	100
4	**1c**	81	9	**1h**	100
5	**1d**	83	10	**1i**	98

[a] Reaction conditions: 1.5 mol % of Pd(OAc)$_2$, 3.0−6.0 mol % of ligand, 1.0 mmol of 4-bromoanisole, 1.2 mmol of phenylboronic acid, 3.0 mmol of K_2CO_3, 3.0 mL of CH_3CN, 80 °C, 2 h. [b] Isolated yield.

TABLE 2. Evaluation of the Steric Bulk Effect of the Ligands on the Suzuki Reaction of Chlorobenzene with Phenylboronic Acid[a]

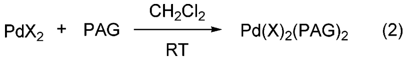


	entries 1−9								
	1	2	3	4	5	6	7	8	9
ligand	**1a**	**1b**	**1c**	**1d**	**1e**	**1f**	**1g**	**1h**	**1i**
yield (%)[b]	12	15	18	16	17	31	45	30	34

[a] Reaction conditions: 2.0 mol % of Pd(OAc)$_2$, 4.0-8.0 mol % of ligand, 1.0 mmol of chlorobenzene, 1.2 mmol of phenylboronic acid, 3.0 mmol of K_2CO_3, 3.0 mL of CH_3CN, 80 °C, 10 h. [b] Isolated yield.

(30%). These results suggested steric bulk was important to the activity of the catalyst as has been previously reported for phosphine ligands.[2b] These results also suggested that other factors than steric bulk might be involved in the observed activity of these guanidine ligands. For instance, **1h** afforded a lower yield of the coupling product than **1g** despite the fact that the former is more bulky than the latter.

To evaluate the difference in the catalytic activities between TAGs and PAGs ligands, two kinds of PAGs/Pd(II) complexes were synthesized from PAGs and Pd(OAc)$_2$ (or PdCl$_2$) (eq 2).



$$\mathrm{PdX_2} + \mathrm{PAG} \xrightarrow[\mathrm{RT}]{\mathrm{CH_2Cl_2}} \mathrm{Pd(X)_2(PAG)_2} \qquad (2)$$

X = OAc, PAG = **1f** $\quad$ Pd(OAc)$_2$·(**1f**)$_2$

X = Cl, PAG = **1i** $\quad$ PdCl$_2$·(**1i**)$_2$

These catalysts are water soluble and stable under air conditions.[14] Their structures were confirmed by X-ray crystallography (see Figure 2 and the Supporting Information). The X-ray data show that two PAGs ligands lie on opposite sides of the palladium center. This is in contrast to our previous finding that four molecules of TMG could coordinate simultaneously to a Pd(II) center.[12a] The structural difference between PAGs/Pd and TMG/Pd may help to explain the different activity in these catalytic systems.

Fu[2b] and Buchwald[15] have reported that bulky phosphines are more efficient ligands in the palladium-catalyzed C−C bond or C−N bond formation reactions, respectively. The active catalyst involved in these coupling reactions is generally believed to be the monophosphine species LPd(0). This is derived from the dissociation of a phosphine ligand in L$_2$Pd(0). They found that both the size and the electron-rich character of *P*-ligands played a key role in facilitating the formation of the species involved in the catalytic cycle. As shown in Table 1, more bulky PAGs are more efficient ligands than TAGs in the Suzuki cross-coupling reaction. These results suggest steric bulk is important to the activity of the catalyst, as has been reported for phosphine ligands. If the active catalyst was LPd(0) (L = G), the unusual cross-coupling activity furnished by PAGs might therefore be attributed to both its size and electron richness: the steric bulk and the electron-donating ability of PAGs favored dissociation (relative to less bulky TAGs) to a monoligand complex more easily. Another proposed active species in the Suzuki cross-coupling reaction is L$_2$Pd(0), where L is the ligand triphenylphosphine.[1f] If L$_2$Pd(0) (L = TMGs or PAGs) was present in the catalytic cycle, the L$_2$Pd(0) (L = PAGs) was the active catalyst, but the dissociation of the TAG from L$_4$Pd(X)$_2$ was required for catalyst activation. This activation process might result in a slower reaction rate than that of PAGs ligands. It is unclear whether the guanidine played a role similar to phosphine in the Suzuki coupling reaction reported herein, and further mechanistic studies are in progress in our laboratory.

Optimization of Reaction Conditions. Preliminary studies showed that PAGs were the best ligands for palladium-catalyzed Suzuki cross-coupling reaction. Other reaction conditions, such as solvents, bases, and reaction temperature, have also been tested. In the presence of 1.5 mol % of Pd(OAc)$_2$·(**1f**)$_2$, the cross-coupling reaction of bromobenzene with phenylboronic acid was investigated in commonly used solvents in air (Table 3). When the reaction was tested at room temperature, the nonpolar solvent toluene gave a low yield. The polar aprotic solvents, such as DMF, DMSO, dioxane, and acetone, also afforded low yields of the coupling product. On the other hand, the polar protic solvents such as methanol, ethanol, and poly(ethylene glycol)-400 furnished the coupling product in good to excellent yields. Although a low yield was obtained when H$_2$O was used as solvent, the high yield was still acquired when a suitable amount of EtOH, as cosolvent, was added (Table 3, entry 12). The influence of cosolvent on the Suzuki cross-coupling reaction has previously been reported in the literature.[16] Herein, the high efficiency of the EtOH cosolvent may be due to both the increased solubility of the reagents and the fast

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(14) The catalyst could be stable in the air for two months, without loss of catalyst activity.

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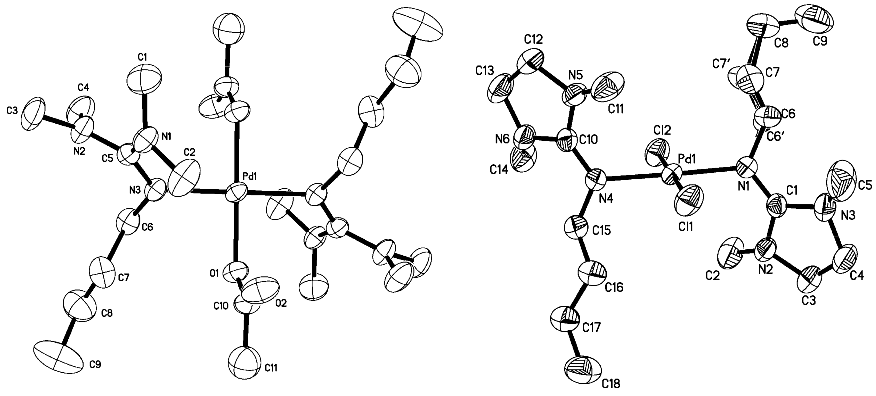
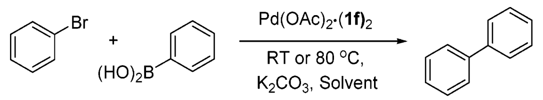


FIGURE 2. ORTEP plot of Pd(OAc)$_2$·(**1f**)$_2$ (left) and PdCl$_2$·(**1i**)$_2$ (right).

TABLE 3. Solvent and Temperature Effects on the Suzuki Coupling of Bromobenzene with Phenylboronic Acid[a]



		yield (%)[b]				yield (%)[b]	
entry	solvent	rt	80 °C	entry	solvent	rt	80 °C
1	DMF	19.3	96.6	7	EtOH	98.6	100
2	DMA	20.1	95.4	8	*i*-PrOH	96.5	100
3	acetone	9.8	96.8	9	MeOH	94.9	99
4	H_2O	32.1	83.2	10	CH_3CN	13.2	100
5	toluene	10.1	78	11	PEG-400	95.3	99
6	DMSO	14.5	85	12[c]	H_2O/EtOH	95	100

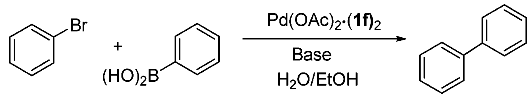
[a] Reaction conditions: 1.0 mmol of bromobenzene, 1.2 mmol of phenylboronic acid, 3.0 mmol of K_2CO_3, 1.5 mol % of Pd(OAc)$_2$·(**1f**)$_2$, 3.0 mL of solvent, reaction time 1 h. [b] Isolated yield. [c] H_2O/EtOH = 3:2 mL.

reduction of Pd^{2+} to Pd(0).[17] While the reactions were performed at high temperature (80 °C), all solvents displayed high efficiency and the coupling product was obtained in a high yields. The observed solvent and temperature effects were similar to those for bulky amine-based ligands, which were reported in the literature,[8a] but the solvent effects described displayed a different trend from that involving phosphine-based ligands, where nonpolar solvents generally facilitated the reaction.[2b,d]

While the reactions proceed with various bases (Table 4), the best results were obtained with cesium carbonate as the base in H_2O/EtOH solvent at room temperature. K_2CO_3, K_3PO_4, and other hydroxide bases all furnished the coupling products in good yields. A similar beneficial effect of strong bases on coupling reactions was also observed for other *N*-, *P*-based ligand systems.[18]

With the optimized conditions in hand, we screened a representative range of aryl halides for the reaction. The results are summarized in Table 5. The Pd(OAc)$_2$·(**1f**)$_2$/K_2CO_3 system was effective for the coupling of various aryl halides with arylboronic acids in H_2O/EtOH media at room temperature. The coupling reaction of activated or deactivated aryl iodide with phenylboronic acid could be performed smoothly, even though the catalyst loadings were decreased to 0.0001 mol %. In the presence of 0.0001 mol % of Pd(OAc)$_2$·(**1f**)$_2$, 1-iodo-4-nitrobenzene was coupled with phenylboronic acid efficiently to give an 85% yield of the corresponding product. The TONs achieved could be up to 850 000 (entry 3). For the coupling of deactivated 4-iodoanisole with phenylboronic acid, a 72% yield of the coupling product was also isolated after prolonging the reaction time to 30 h (entry 2). However, for the coupling of aryl bromides, lower yields of the coupling product were obtained in the presence of 0.001 mol % of Pd(OAc)$_2$·(**1f**)$_2$ (entry 4). Good yields of the products could be obtained for the coupling of 4-bromoanisole with phenylboronic acid when the catalyst loading was increased to 1.0 mol % (entry 6).

TABLE 4. Effect of Base on the Suzuki Coupling of Bromobenzene with Phenylboronic Acid[a]



entry	base	yield (%)[b]	entry	base	yield (%)[b]
1	K_2CO_3	90	6	K_3PO_4	86
2	Cs_2CO_3	99	7	NaOH	90
3	Na_2CO_3	46	8	KOH	92
4	NaOAc	40	9	LiOH	86
5	KF	75	10	$NaHCO_3$	12

[a] Reaction conditions: 1.0 mmol of bromobenzene, 1.2 mmol of boronic acid, 3.0 mmol of base, 1.5 mol % of Pd(OAc)$_2$·(**1f**)$_2$, 3.0 mL of H_2O/EtOH (3:2), reaction time 0.5 h, rt. [b] Isolated yield.

It is worth mentioning that the system was effective for coupling of activated aryl chlorides. In the presence of 2.0 mol % of Pd(OAc)$_2$·(**1f**)$_2$, moderate yields were obtained for the reaction of phenylboronic acid with 1-chloro-4-nitrobenzene (entry 9). The results showed that tetrabutylammonium bromide (TBAB)[8d,19] was required to improve the Suzuki cross-coupling reaction of aryl chlorides. An attempt to couple chlorobenzene with phenylboronic acid was not successful at room temperature. This reaction afforded 34% yield of the corresponding coupled product after adding 0.1 equiv of TBAB (entry 11). In the absence of TBAB, only a 33% yield of the coupled product was isolated from the reaction of chlorobenzene with phenylboronic acid at 80 °C after 48 h. A 66% yield was obtained

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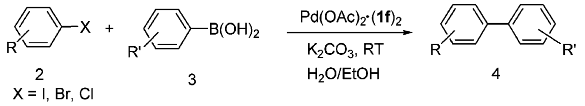
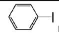
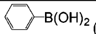
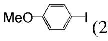
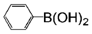
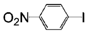
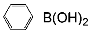
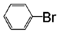
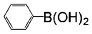
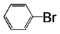
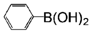
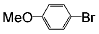
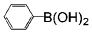
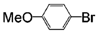
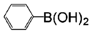
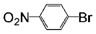
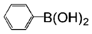
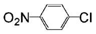
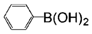
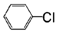
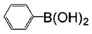
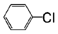
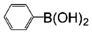
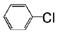
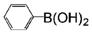
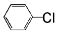
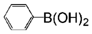
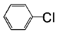
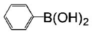
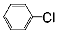
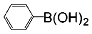
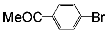
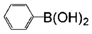
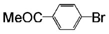
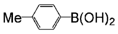
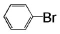
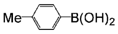
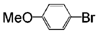
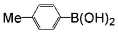
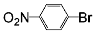
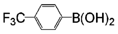
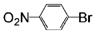
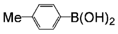
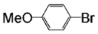
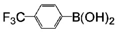
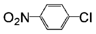
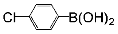
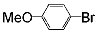
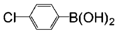
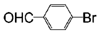
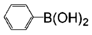
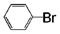
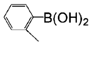
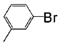
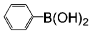
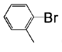
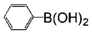
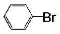
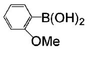
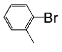
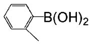
(17) (a) Kim, S.-W.; Park, J.-N.; Jang, Y.-J.; Chung, Y.-H.; Hwang, S.-J.; Hyeon, T. *Nano Lett.* **2003**, *3*, 1289. (b) Artuso, F.; D'Archivio, A. A.; Lora, S.; Jerabek, K.; Králik, M.; Corain, B. *Chem. Eur. J.* **2003**, *9*, 5292. (c) Teranishi, T.; Miyake, M. *Chem. Mater.* **1998**, *10*, 594.

(18) (a) Wallow, T. I.; Novak. B. M. *J. Org. Chem.* **1994**, *59*, 5034. (b) Miyaura, N.; Ishiyama, T.; Sasaki, H.; Ishikawa, M.; Sato, M.; Suzuki, A. *J. Am. Chem. Soc.* **1989**, *111*, 314.

(19) For the representative papers on TBAB-promoted cross coupling reactions, see: (a) Selvakumar, K.; Zapf, A.; Beller, M. *Org. Lett.* **2002**, *4*, 3031. (b) Yang, D.; Chen, Y.-C.; Zhu, N.-Y. *Org. Lett.* **2004**, *6*, 1557 and references cited therein.

TABLE 5. Palladium-Catalyzed Suzuki Coupling of Aryl Halides with Arylboronic Acids in Aqueous Solution [a]



entry	ArX	ArB(OH)$_2$	Pd (mol %) / T(°C)	time (h)	yield (%)[b]
1	 (2a)	 (3a)	0.001/ RT	20	99(4a)
2	 (2b)	 (3a)	0.001/ RT	30	72(4c)
3	 (2c)	 (3a)	0.0001/RT	20	85(4d)
4	 (2d)	 (3a)	0.001/RT	30	35(4a)
5	 (2d)	 (3a)	0.1/RT	2	88(4a)
6	 (2e)	 (3a)	1.0/RT	1	98(4c)
7	 (2e)	 (3a)	0.5/RT	2	90(4c)
8	 (2f)	 (3a)	0.1/RT	5	81(4d)
9	 (2g)	 (3a)	2.0/RT	10	67(4d)
10	 (2h)	 (3a)	2.0/RT	20	0(4a)
11[c]	 (2h)	 (3a)	2.0/RT	20	34(4a)
12	 (2h)	 (3a)	2.0/80	48	33(4a)
13[c]	 (2h)	 (3a)	2.0/80	10	66(4a)
14[d]	 (2h)	 (3a)	2.0/80	48	56(4a)
15[c,d]	 (2h)	 (3a)	2.0/80	10	73(4a)
16	 (2i)	 (3a)	1.0/RT	5	>99(4e)
17	 (2i)	 (3b)	1.0/RT	5	>99(4f)
18	 (2d)	 (3b)	1.0/RT	20	>99(4b)
19	 (2e)	 (3b)	1.0/RT	20	97(4g)
20	 (2f)	 (3c)	0.1/80	1	100(4h)
21	 (2f)	 (3b)	1.0/RT	1	91(4i)
22	 (2e)	 (3c)	1.0/RT	10	96(4j)
23	 (2g)	 (3d)	2.0/80	20	100(4k)
24	 (2e)	 (3d)	1.0/RT	20	95(4l)
25	 (2j)	 (3a)	0.1/RT	4	99(4m)
26	 (2d)	 (3e)	0.5/RT	10	95(4n)
27	 (2k)	 (3a)	0.5/RT	10	86(4o)
28	 (2l)	 (3a)	0.5/RT	10	74(4n)
29	 (2d)	 (3f)	0.5/RT	10	94(4p)
30	 (2l)	 (3e)	0.5/RT	10	83(4q)

[a] Reaction conditions: 1.0 mmol of aryl halide, 1.2 mmol of boronic acid, 3.0 mmol of base, 3.0 mL of H_2O/EtOH (3:2). [b] Isolated yield. [c] TBAB (0.1 equiv) as the additive. [d] The ligand **1g** was used in place of the ligand **1f**.

after 10 h when 0.1 equiv of TBAB was added at the same reaction temperature (entries 12 and 13). The coupling reaction of chlorobenzene with phenylboronic acid using **1g** as ligand was also tested. The results indicated that the yield of the coupling product was increased from 33% to 56% when the ligand **1g** was used in place of the ligand **1f** (entry 14). The yield of the coupling product was also increased from 66% to 73% when adding 0.1 equiv of TBAB (entry 15).

It was also demonstrated that the catalytic systems have great tolerance to a wide range of sensitive functional groups, such as CHO, NO_2, OMe, CF_3, and COMe on both substrates (entries 16−25) at room temperature. Furthermore, some meta-substituted or ortho-substituted aryl bromides or arylboronic acids could be formed easily in these catalytic systems. Moderate to good yields of the products were obtained when the catalyst loading was 0.5 mol % (Table 5, entries 26−30).

To the best of our knowledge, there are relatively few examples of Suzuki cross-couplings of aryl bromides or aryl chlorides that proceed at room temperature and under phosphine-free ligand conditions.[2h,8b,20] Although Boykin et al.[8b] have reported that bulky dicyclohexylamine could act as an efficient ligand for the Suzuki cross-coupling reactions of aryl bromides at room temperature in EtOH, the catalyst loading, however, was higher (2.0 mol %) than in our procedures (1.0−0.1 mol %), and their catalytic systems were not suitable for the coupling of aryl chlorides. Therefore, this protocol has furnished a new phosphine-free catalyst system and provided mild conditions for the coupling of aryl bromides or activated aryl chlorides in good to excellent yields. Moreover, these reactions can be performed in air conditioning and without the need for any special experimental precautions, rendering this method highly attractive for small- and large-scale synthesis.

Conclusions

In summary, a highly efficient $Pd(OAc)_2$/guanidine aqueous system for the Suzuki cross-coupling reaction has been developed (TONs up to 850 000 for the reaction of 1-iodo-4-nitrobenzene and phenylboronic acid). Results from these studies indicated that a wide range of aryl halides, including aryl iodides, aryl bromides, and even activated aryl chlorides, could couple with arylboronic acids smoothly by using this water-soluble catalyst $Pd(OAc)_2$·(**1f**)$_2$ at room temperature under aerial conditions. Furthermore, this catalytic system could tolerate a broad range of functional groups under mild reaction conditions.

Experimental Section

Synthesis of $Pd(OAc)_2$·(1f)$_2$. Under a nitrogen atmosphere, 1,1,3,3-tetramethyl-2-*n*-butylguanidine (**1f**, 0.684 g, 4.0 mmol) was added dropwise into a solution of $Pd(OAc)_2$ (0.449 g, 2.0 mmol) in dichloromethane (100 mL) at room temperature. The mixture was stirred for 3 h and the solvent was removed by distillation. Crystallization from dichloromethane/hexane gave $Pd(OAc)_2$·(**1f**)$_2$. Yield 0.96 g (85%); ^1H NMR (300 MHz, $CDCl_3$) δ 3.18 (t, 4H, J = 8.0 Hz), 3.03 (s, 12H), 2.90 (s, 12H), 1.98 (s, 6H), 1.65 (m, 4H, J = 7.6 Hz), 1.34 (m, 4H, J = 7.2 Hz), 0.92 (t, 6H, J = 8.0 Hz). Anal. Calcd for $C_{22}H_{48}N_6O_4Pd$: C 46.60, H 8.53, N 14.82. Found: C 46.96, H 8.31, N 14.38. Single crystals of $Pd(OAc)_2$·(**1f**)$_2$ suitable for X-ray diffraction were obtained by slow diffusion of hexane into a dichloromethane solution of $Pd(OAc)_2$·(**1f**)$_2$.

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(20) (a) Marion, N.; Navarro, O.; Mei, J.-G.; Stevens, E. D.; Scott, N. M.; Nolan, S. P. *J. Am. Chem. Soc.* **2006**, *128*, 4101. (b) Zim, D.; Gruber, A. S.; Ebeling, G.; Dupont, J.; Monteiro, A. L. *Org. Lett.* **2000**, *2*, 2881.

General Experimental Procedure for the Pd(OAc)$_2$·(1f)$_2$-Catalyzed Suzuki Cross-Coulping Reactions. In air conditioning, Pd(OAc)$_2$·(**1f**)$_2$ (8.5 mg, 0.015 mmol) was dissolved in a solvent (3 mL), followed by the addition of aryl halide **2** (1.0 mmol), arylboronic acid **3** (1.2 mmol), and K_2CO_3 (3 equiv). The mixture was stirred at room temperature for the desired time until complete consumption of starting material as judged by TLC. After the mixture was extracted and evaporated, the residue was purified by flash column chromatography (hexane/ethyl acetate) to afford the final product.

Acknowledgment. This research was financially supported by the national basic research program of China (2003CB615704).

Supporting Information Available: Analytical data and spectra (^{1}H NMR) for all the products, as well as X-ray crystallographic data for Pd(OAc)$_2$·(**1f**)$_2$ (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

JO0626257