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Simple Amine/$Pd(OAc)_2$-Catalyzed Suzuki Coupling Reactions of Aryl Bromides under Mild Aerobic Conditions

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A new palladium catalyst (DAPCy) made from $Pd(OAc)_2$ and commercially available, inexpensive dicyclohexylamine has been developed for the Suzuki coupling reaction of aryl bromides with boronic acids to give the coupling products in good to high yields. The air-stable catalyst was characterized and well-defined by X-ray crystallography. A catalytic system involving DAPCy in dioxane demonstrates a temperature-dependent reactivity toward aryl bromides with different electronic substituents, and selectively couples electron-deficient aryl bromides with boronic acids over electron-rich ones at room temperature. Another catalytic system employing DAPCy in EtOH provides a general and convenient method to prepare biaryls from aryl bromides and boronic acids with a broad range of functional groups at room temperature and under aerobic conditions.

Introduction

The palladium-catalyzed Suzuki coupling reaction, involving aryl electrophiles (such as halides or pseudohalides) with boronic acids, is one of the most powerful, popular, and convenient synthetic methods to prepare biaryls,[1] important structural units found in natural products, pharmaceuticals, catalyst ligands, and advanced materials.[2] The reaction is normally promoted by a palladium catalyst precursor, a ligand that binds to the palladium center to stabilize and/or activate the catalyst during the reaction process, and a base that captures the boronic acid. Among all the influencing factors the ligand plays a pivotal role in the successful execution of the coupling reaction. Therefore, a large amount of research work has been done and is ongoing to develop new efficient ligands. In addition to the original ligand, triphenyl phosphine,[3] electron-rich bulky phosphines[4−7] (such as trialkylphosphines and dialkyl biphenylphosphines), phosphine-based palladacycles,[8] and phosphine oxides[9] have recently been introduced as effective ligands. These new phosphorus-based ligands greatly enlarge the scope of the Suzuki coupling reaction,[10] along with applications to other related coupling reactions.[11,12] While modified phosphine-based ligands are still the subject of ongoing research efforts, there are some promising developments for phosphine-free ligands, such as C-based

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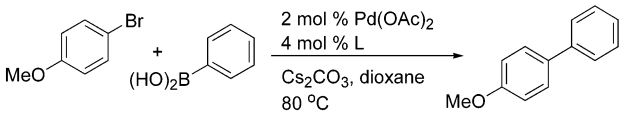
heterocyclic carbenes,[13] C,N-based 2-aryl-2-oxazolines,[14] aryloximes,[15] arylimines,[16] and N,N-based diimines.[17] These nonphosphine ligands have the potential to overcome the disadvantages of the catalyst instability and environmental concerns, especially for large-scale industrial applications.

On the other hand, most of these new phosphine- and nonphosphine-based ligands are not readily available, and some are cumbersome to synthesize; and of those that are commercially available many are expensive. Simple, inexpensive, easily accessible, and stable catalysts are desired. Furthermore, from the practical standpoint, it is convenient to conduct reactions at ambient temperature under aerial conditions, avoiding heating and inert gas protection. We recently described the first palladium−amine catalyst (DAPCy) from commercially available, inexpensive dicyclohexylamine (Cy_2NH) for the Suzuki coupling reaction of aryl bromides and boronic acids, and its temperature-dependent activity toward aryl bromides with different electronic substituents.[18] Herein we report the synthesis and characterization of DAPCy, and optimization studies of a new catalytic system for selective coupling reactions of aryl bromides with different functional groups. Furthermore, conditions are described which smoothly afford the desired products in good to high yields at room temperature and under aerobic conditions, with great tolerance to a broad range of functional groups on both partners.

Results and Discussion

Screening of Ligands. Many N-based compounds[14−17] have been reported to be efficient ligands for the Suzuki reaction. Tetrabutylammonium bromide has also been used as a promoter in "ligandless" coupling reactions in 20−100% equiv of aryl halide.[19] Recently, triethylamine (TEA) has also been reported as a base in ligandless coupling reactions.[20] However, simple amines have not been reported as ligands for C−C bond-forming coupling reactions. In view of these developments,[14−17] we reasoned that simple amines could be used as ligands for the reaction. So, several simple and commercially available amines were screened as potential ligands, using a model coupling reaction of 4-bromoanisole and phenylboronic acid in the presence of 2 mol % of $Pd(OAc)_2$, 4 mol % of amine, and 2 equiv of Cs_2CO_3 in dioxane at 80 °C. Among the amines investigated, common amines, such as TEA, diisopropylethylamine (DIEA), aniline, and pyridine, showed no or low activity. Diisopropylamine (DIA) displayed moderate efficiency, giving the coupling product in 66% yield. More bulky amines were found to be better ligands. Cyclohexylamine ($CyNH_2$) afforded the product in 83% yield. Cy_2NH was found to be the best ligand, giving the coupling product in nearly quantitative yield in 2 h. However, the more bulky amine, dicyclohexylmethylamine (Cy_2NMe) furnished the product in a lower yield. Another bulky amine, 1-adamantaneamine ($AdNH_2$), gave a comparable yield to that of Cy_2NH. These results suggest steric bulk is important to the activity of the catalyst as has been reported for phosphine ligands.[4b] The catalytic activity increases with increasing bulk around the nitrogen ligands. For example, the more bulky DIEA gave a higher yield of the product than TEA (Table 1, entries 2 vs 5). Similarly, Cy_2NH was found to be a better ligand than $CyNH_2$ (Table 1, entries 7 vs 8), and $AdNH_2$ was more efficient than $CyNH_2$ (Table 1, entries 10 vs 7). These results also suggest other factors than steric bulk may be involved in the observed activity of these amine ligands. For instance, DIEA afforded a lower yield of the coupling product than *i*-Pr_2NH (Table 1, entries 5 vs 6) despite the fact that the former is more bulky than the latter. The more bulky Cy_2NMe was also less effective than the less bulky Cy_2NH (Table 1, entries 9 vs 8). Bulky primary and secondary amines appear to be better ligands than comparable bulky tertiary amines, probably because the former has a greater ability to stabilize the catalytic active Pd species responsible for the catalytic cycle. Actually, we found that the bulky primary and secondary amines reacted readily with $Pd(OAc)_2$ to form stable complexes, while the tertiary amines, such as NEt_3 and Cy_2NMe, did not afford the corresponding complexes under similar conditions. In contrast, Pd black was formed in these latter reactions. The effect of amines on activating the catalyst has been demonstrated in the Pd-catalyzed C−N bond formation reaction, which is closely related to the Suzuki coupling reaction, and often the same catalysts can be used for both types of reactions. Buchwald and co-workers[21] have recently reported that both the added amines and the size of the P-ligands play a role in facilitating the formation of the catalytic species involved in the catalytic cycle. It is plausible that the amines play a similar role in the Suzuki coupling reactions reported herein.

TABLE 1. Screening of Ligands[a]



entry	amine	yield (%)[b]	entry	amine	yield (%)[b]
1	no L	19	6	*i*-Pr_2NH	66
2	NEt_3	12	7	$CyNH_2$	83
3	aniline	14	8	Cy_2NH	94
4	pyridine	43	9	Cy_2NMe	77
5	DIEA	39	10	1-$AdNH_2$	93

[a] Reaction conditions: 1.0 mmol of aryl bromide, 1.2 mmol of boronic acid, 2.0 mmol of Cs_2CO_3, 3.0 mL of dioxane, 3 h. [b] Isolated yield.

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Synthesis and Characterization of DAPCy. From the mechanistic standpoint, it is advantageous to have defined single-component catalysts. Reactions involving defined catalysts should give a clearer picture of the reaction and thus provide key information about its details. Although many in situ catalytic systems are available, only a few catalysts are well-defined.[22] We sought to isolate the complexes of amines and $Pd(OAc)_2$. As shown in eq 1, $Pd(OAc)_2$ readily reacted with 2 equiv

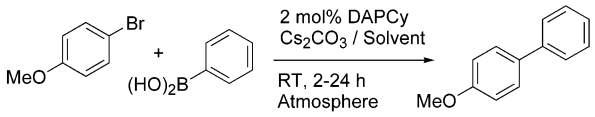
$$Pd(OAc)_2 + 2\ Amine \xrightarrow[RT]{Dioxane} trans\text{-}Pd(OAc)_2(Amine)_2 \qquad (1)$$

Amine = Cy_2NH, 91% DAPCy
1-$AdNH_2$, 94% DAPAd-1

of both $CyNH_2$ and $AdNH_2$ in dioxane at room temperature to give the stable complexes *trans*-$(Cy_2NH)_2Pd(OAc)_2$ (DAPCy) and *trans*-$(1\text{-}AdNH_2)_2Pd(OAc)_2$ (DAPAd-1) in 91% and 94% yields, respectively, after crystallization from hexane/dichloromethane. Both DAPCy and DAPAd-1 are yellow solids and stable at room temperature.[23] They are fully characterized by ^1H, ^{13}C NMR spectra and elemental analyses. As mentioned before, tertiary amines such as TEA and Cy_2NMe did not form stable compounds with $Pd(OAc)_2$ under similar conditions and Pd black formation was observed for these reactions. Furthermore, the structure of the trans isomer of DAPCy was confirmed by X-ray crystallography (see Figure 1 and Supporting Information). The X-ray data show that the two Cy_2NH ligands lie on opposite sides of the palladium center. The bond angles of N(1)−Pd−N(1A) and O(1)−Pd−O(1A) are 180°. Also as expected, the Pd−N bonds are longer than the Pd−O bonds (2.079 vs 2.016 Å), indicating that the Pd−N bonds are weaker than the Pd−O bonds. Another interesting feature of the complex is that hydrogen bonds form between the two O's of the acetyl groups and the two H's connecting the N's of the amine ligands (O(2) and H(1N), O(2A) and H(1NA)). Since tertiary amines do not form stable complexes with $Pd(OAc)_2$ under similar conditions, intramolecular hydrogen bonding may be a factor contributing to the stability of the complex.

Optimization of Reaction Conditions. With the well-defined and air-stable complexes available, we performed optimization studies to determine how solvents, bases, and temperature affect the coupling reaction involving DAPCy. DAPAd-1 gave the coupling products in comparable yields in some reactions (data not shown) and it is expected to behave similarly with DAPCy. Although many catalytic systems are known, most require harsh conditions such as high temperature and strong bases. We sought reaction conditions under mild temperatures and without the need of inert gas protection. Such extremely mild conditions would provide easy operations and, most importantly, allow a wider range of applications due to greater tolerance of sensitive functional groups on the coupling partners. The same coupling reaction for the ligand-screening experiments was used as a model for the optimization studies, only under much milder conditions. In the presence of 2 mol % of DAPCy at room temperature and in the open air, many commonly used solvents were tested (Table 2). The nonpolar solvent toluene and polar solvent water both gave low yields. The polar aprotic solvents, such as DMF, DMSO, dioxane, and acetone, afforded none or very little of the coupling product. On the other hand, the polar protic solvents, such as methanol, ethanol, 1-propanol, and 2-propanol, furnished the coupling product in various yields. Ethanol and 1-propanol gave the coupling product in excellent yields. Both methanol and 2-propanol, though, gave lower yields of the product, perhaps due to their different activity from the other alcohols in the β-elimination reactions from the Pd−alcohol complexes.[24] These results show a profound solvent effect on the reaction and that polar protic solvents greatly benefit the reaction. The observed solvent effect displays a different trend from that involving phosphine-based ligands, where nonpolar solvents generally facilitate the reaction.[4b]

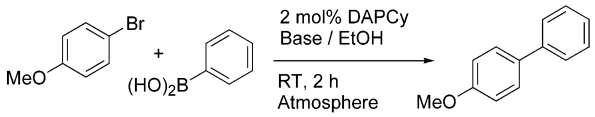
TABLE 2. Solvent Effect[a]



entry	solvent	yield (%)[b]	entry	solvent	yield (%)[b]
1	toluene	17	6	MeOH	83
2	acetone	0	7	EtOH	93
3	dioxane	0	8	1-PrOH	95
4	DMF	0	9	2-PrOH	30
5	DMSO	0	10	H_2O	32

[a] Reaction conditions: 1.0 mmol of aryl bromide, 1.2 mmol of boronic acid, 2.0 mmol of Cs_2CO_3, 2 mol % of DAPCy, 3.0 mL of solvent. [b] Isolated yield.

TABLE 3. Base Effect[a]



entry	base	yield (%)[b]	entry	base	yield (%)[b]
1	Cs_2CO_3	93	6	$LiOH\cdot H_2O$	97
2	K_2CO_3	53	7	NaOH	92
3	Na_2CO_3	14	8	KOH	94
4	K_3PO_4	94	9	$CsOH\cdot H_2O$	90
5	K_2HPO_4	7	10	KF	85

[a] Reaction conditions: 1.0 mmol of aryl bromide, 1.2 mmol of boronic acid, 2.0 mmol of base, 2 mol % of DAPCy, 3.0 mL of EtOH. [b] Isolated yield.

Data in Table 3 show that for this system, the use of a stronger base generally leads to higher yields for the coupling reaction. Cs_2CO_3, K_2CO_3, and Na_2CO_3 gave the product in 93%, 53%, and 14%, respectively. The contrast in yield for simple changes in base is more profound for K_3PO_4 and K_2HPO_4 (94% vs 7%). The four hydroxide bases all afforded the coupling product in excellent yields. A similar beneficial effect of strong bases on coupling reactions was also observed for phosphine-based systems.[25]

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(23) Both catalysts retain the same activity after being stored at room temperature over 4 months without any precautions to exclude air.

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TABLE 4. Different Reactivities of Electron-Deficient and Electron-Rich Bromides Catalyzed by DAPCy in Dioxane

Entry	Ar-Br	Ar'-B(OH)$_2$	Product[a]	T(°C)/Time (h)[b]	Yield (%)[c]
1	MeO–Br	B(OH)$_2$	MeO–	RT/30	0
2				80/3	94
3	MeO–Br	B(OH)$_2$ (Me)	MeO– (Me)	RT/30	0
4				80/16	81
5	Me–Br	B(OH)$_2$	Me–	RT/24	0
6				80/3	92
7	OHC–Br	B(OH)$_2$	OHC–	RT/16	89
8	O_2N–Br	B(OH)$_2$	O_2N–	RT/10	98
9	O_2N–Br	B(OH)$_2$ (Me)	O_2N– (Me)	RT/24	87
10	NC–Br	O_2N B(OH)$_2$	NC– (NO_2)	RT/10	92
11	NC Br	B(OH)$_2$	NC	RT/20	93
12	Br (CN)	*p*-Ph-PhB(OH)$_2$	(CN)	RT/30	90

[a] Reaction conditions: 1.0 mmol of aryl bromide, 1.5 mmol of boronic acid, 2.0 mmol of Cs_2CO_3, 2 mol % of DAPCy, 3.0 mL of 1,4-dioxane. [b] Reaction time not optimized. [c] Isolated yield.

Different Reactivities of Electron-Deficient and Electron-Rich Aryl Bromides. As discussed before, in the screening test the coupling reaction in dioxane proceeded in high yield at 80 °C with Pd(OAc)$_2$ and Cy$_2$-NH in the presence of Cs_2CO_3 (Table 1, entry 8), while the reaction catalyzed by DAPCy did not occur at room temperature (Table 2, entry 3). To eliminate the possibility of discrepancy with the catalyst, substituting Pd(OAc)$_2$ and Cy$_2$NH with DAPCy in the former reaction afforded virtually the same amount of product (data not shown). This indicates that the difference of the rate of the coupling reaction in dioxane between 80 °C and room temperature indeed results from the temperature effect, not from the catalyst difference. This observation is quite general to other electron-rich aryl bromides (See Table 4). Like 4-bromoanisole, they did not react with boronic acid at room temperature even after 24 h. High temperature was required for the coupling reactions of these electron-rich bromides. These coupling reactions took place at 80 °C to give the products in good yields (Table 4, entries 2, 4, and 6). While the coupling reactions of electron-rich aryl bromides with boronic acids in dioxane require *elevated temperature*, electron-deficient ones react *at room temperature*. As shown in Table 4, at room temperature the reactions with electron-withdrawing bromides gave the coupling products in good to high yields (Table 4, entries 7−12) in the presence of 2% of DAPCy in 10−30 h. While the electronic properties of the bromides greatly influenced the ease of the coupling reactions, those of the boronic acids have little effect (Table 4). Both electron-deficient and electron-rich boronic acids gave the coupling products in good to high yields. These results reflect the different reactivity of electron-deficient and electron-rich aryl bromides under the reaction conditions.

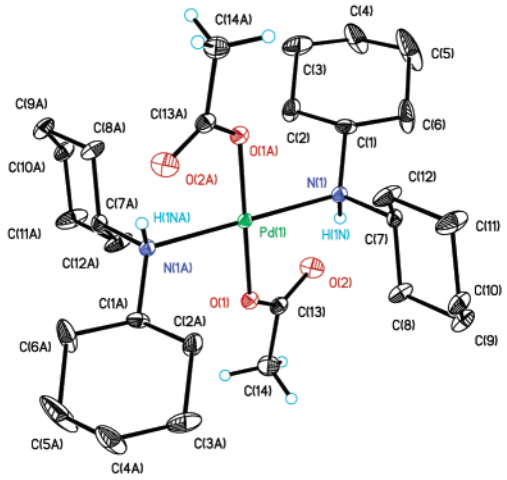

FIGURE 1. ORTEP drawing of DAPCy (the H's on the Cy rings are omitted for clarity). Select distances and angles (Å, deg): Pd−N(1), 2.079(2); Pd−O(1), 2.016(2); N(1)−Pd−N(1A), 180.0; O(1)−Pd−O(1A), 180.0; O(2)- - -H(1N), 1.95.

Selective Coupling Reactions. On the basis of the different reactivities demonstrated above, electron-deficient aryl bromides are expected to selectively couple with boronic acids over electron-rich ones in dioxane at room temperature. To test this point, two competitive coupling reactions were carried out as shown in Figure 2. The reaction of the electron-rich 4-bromotoluene (1.0 mmol) and the electron-deficient 4-bromonitrobenzene

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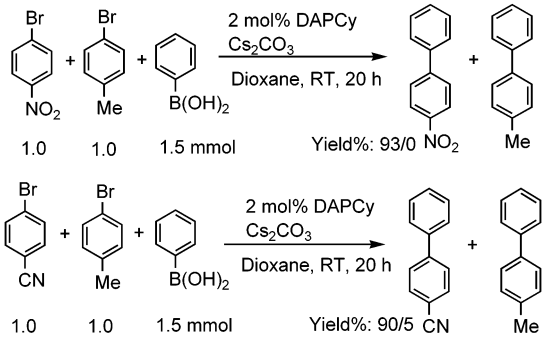


FIGURE 2. Selective coupling reactions of electron-deficient bromides over electron-rich ones.

(1.0 mmol) with phenylboronic acid (1.5 mmol) gave exclusively 4-nitrobiphenyl, from the electron-deficient bromide, in 93% yield, with no detectable 4-phenyltoluene formed from the electron-rich bromide. A similar result of high selectivity was also observed from the competitive reaction of 4-bromobenzonitrile and 4-bromotoluene with phenylboronic acid, affording the products from the electron-deficient bromide and from the electron-rich one in a ratio of 90%:5%. These results indicate that DAPCy in dioxane has the ability to distinguish between electron-deficient and electron-rich aryl bromides at room temperature. It should be pointed out that solvent plays a profound role in distinguishing between different bromides, since both electron-deficient and electron-rich bromides couple with boronic acids smoothly in EtOH at room temperature (as discussed later), whereas in dioxane only the electron-deficient ones couple at room temperature. Fu and co-workers[4b] reported moderately selective coupling reactions between aryl and alkenyl halides with a boronic acid. Nevertheless, these results represent the first direct, unambiguous demonstration that electron-deficient aryl bromides are more active than electron-rich ones for the Suzuki coupling reaction.

To gain some insight into the nature of the catalyst, a ^{1}H NMR study was performed. The reaction progress of phenylboronic acid with the electron-rich 4-bromoanisole in EtOH-d_6 and in dioxane-d_8 (for details, see Supporting Information) and that of the electron-deficient methyl bromobenzoate in dioxane-d_8 were monitored. The study revealed that no product was formed while DAPCy was still intact. When the product was detected, the DAPCy (at least some of it) was no longer completely in the original form. These results suggest that DAPCy itself is not the active catalytic species. It also shows that polar solvents such as EtOH help to convert DAPCy to an active catalytic species.[1] Rising temperature also facilities the formation of the active species from DAPCy during the reaction process. Nolan and co-workers[26] have recently proposed that 2-propanol (solvent) helps to convert a Pd catalyst to the active species involved in Suzuki reactions. Further study is required to develop a better understanding of the reaction mechanism.

Room-Temperature Coupling Reactions Involving Partners with Various Functional Groups. Harsh conditions (high temperatures and strong bases, etc.) used in many Suzuki coupling reactions are not compatible with some sensitive functional groups, and preclude these functional groups from being present in coupling reactions. In anticipation of overcoming these problems, the coupling reactions catalyzed by DAPCy were studied in the presence of 2 mol % of DAPCy and 2 equiv of K_3PO_4 in ethanol at room temperature and open to the atmosphere. Although the hydroxides gave comparable or even better yields of the coupling product as indicated in Table 3, K_3PO_4 was chosen as the base for these studies because of concerns about the functional groups' instability under strong basic reaction conditions. Under these conditions, a series of substituted aryl bromides bearing both electron-donating and electron-withdrawing groups readily coupled with arylboronic acids to give products in good to high yields in 2−6 h (Table 5). This new catalytic system is tolerant to a broad range of sensitive functional groups, such as NO_2, NH_2, CHO, $CONH_2$, COOH, OH, CH_2OH, COMe, and CN. The reactions proceeded smoothly to afford the products in excellent yields even in the presence of very sensitive groups, such as CHO, COOH, NH_2, and OH groups without any protection. Although many catalytic systems have been reported, few[27] have shown tolerance to such a wide range of functional groups such as those listed in Table 5. In addition to substituted aryl bromides, the coupling reactions with heterocyclic bromides also led to the formation of the desired products in high yields (Table 5, entries 13−15). It is also worth noting that these reactions can be performed in a short reaction time (2−6 h) under extremely mild conditions (room temperature) and without inert gas protection. As a result, this new catalytic system provides an easy, quick, and convenient procedure for conducting these reactions. Finally, although several defined C,N-, C,P-based palladacycle complexes have been reported as catalysts for the Suzuki and Heck reactions they all exist in a dimeric form in terms of the palladium center.[9,16a,21] Mono-Pd-centered catalysts are rare, other than the original $Pd(PPh_3)_4$ catalyst,[3] and only recently have the very bulky P-[5c] and C-based[13e] mono-Pd-centered catalysts been reported. DAPCy represents the first simple amine-based mono-palladium-centered catalyst for the Suzuki reaction.

Conclusions

We have developed a simple amine/$Pd(OAc)_2$ catalyst for the Suzuki coupling reaction of aryl bromides. It is inexpensive, air-stable, and easy to make. A new catalytic system (K_3PO_4 as base in EtOH) provides mild and aerial conditions for the coupling of aryl bromides in good to excellent yields, and demonstrates great tolerance to a wide range of sensitive functional groups on both substrates. The catalyst also shows a special ability to selectively couple electron-deficient bromides with boronic acids over electron-rich ones in dioxane at room temperature.

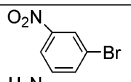
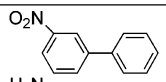
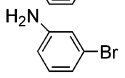
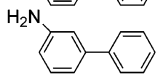
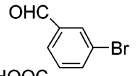
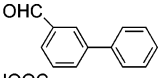
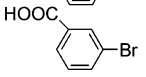
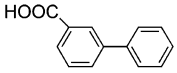
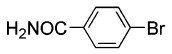
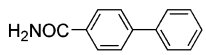
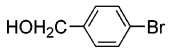
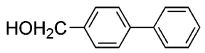
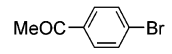
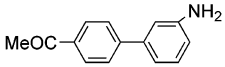
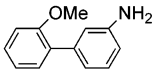
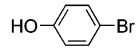
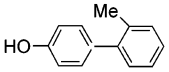
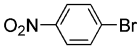
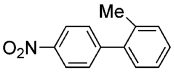
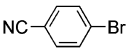
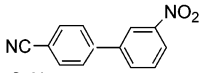
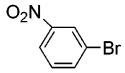
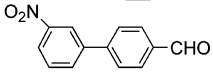
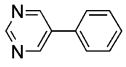
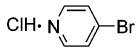
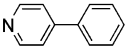
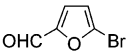
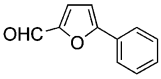
Experimental Section

Synthesis of *trans*-$(Cy_2NH)_2Pd(OAc)_2$ (DAPCy). Under a nitrogen atmosphere, Cy_2NH (0.725 g, 4.0 mmol) was added dropwise into a solution of $Pd(OAc)_2$ (0.449 g, 2.0 mmol) in

(26) Navarro, O.; Kelly, R. A., III; Nolan, S. P. *J. Am. Chem. Soc.* **2003**, *125*, 16194.

(27) Alonso, D. A.; Najera, C.; Pacheco, M. C. *J. Org. Chem.* **2002**, *67*, 5588.

TABLE 5. Suzuki Couplings of Functional Aryl Bromides Catalyzed by DAPCy in EtOH at Room Temperature under Aerobic Conditions[a]

Entry	Aryl bromide	Boronic acid	Product	Time (h)[b]	Yield (%)[c]
1		$PhB(OH)_2$		2	91
2		$PhB(OH)_2$		2	92
3		$PhB(OH)_2$		2	94
4		$PhB(OH)_2$		3	91
5		$PhB(OH)_2$		6	89[d]
6		$PhB(OH)_2$		2	93
7		3-$H_2NPhB(OH)_2$		2	84
8		3-$H_2NPhB(OH)_2$		4	74
9		2-$MePhB(OH)_2$		2	90
10		2-$MePhB(OH)_2$		2	77
11		3-$O_2NPhB(OH)_2$		4	88
12		4-$OHCPhB(OH)_2$		3	82
13		$PhB(OH)_2$		4	90
14		$PhB(OH)_2$		2	88
15		$PhB(OH)_2$		6	91

[a] Reaction conditions: 1.0 mmol of aryl bromide, 1.2 mmol of boronic acid, 2.0 mmol of base, 2 mol % of DAPCy, 3.0 mL of EtOH. [b] Time not optimized. [c] Isolated yield. [d] 70 °C.

dioxane (20 mL) at room temperature. The mixture was stirred at rt for 3 h, during which a yellow precipitate occurred. The solvent was removed under reduced pressure. The resulting solid was crystallized from dichloromethane/hexane to give the final product. Yield 1.17 g (91%); mp 140 °C dec. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.94−6.92 (m, 2H), 2.82−2.79 (m, 4H), 2.48−2.36 (m, 4H), 1.91−1.66 (m, 30H), 1.29−1.17(m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 180.5, 55.0, 32.1, 32.0, 26.1, 25.9, 25.7, 24.2. Anal. Calcd for $C_{28}H_{52}N_2O_4Pd$: C, 57.27; H, 8.93; N, 4.77. Found: C, 57.19; H, 8.98; N, 4.74.

Synthesis of *trans*-(1-AdNH$_2$)$_2$Pd(OAc)$_2$. *trans*-(1-AdNH$_2$)$_2$-Pd(OAc)$_2$ was prepared following the above procedure for DAPCy. Yield 94%; mp 246 °C dec. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.84 (bs, 4H), 2.07−2.04 (m, 6H), 1.84 (s, 6H), 1.81−1.79 (m, 12H), 1.66−1.57 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.8, 52.6, 43.6, 35.8, 29.4, 23.6. Anal. Calcd for $C_{22}H_{40}N_2O_4Pd$: C, 54.67; H, 7.65; N 5.32. Found: C, 54.47; H, 7.70; N, 5.24.

Synthesis of 2-Cyanoterphenyl (Table 4, entry 12). Method C was followed. The reaction gave the title compound (90%) as a white solid. Mp 114−115 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 7.8 Hz, 1H), 7.72 (d, J = 7.8 Hz, 2H), 7.69−7.63 (m, 5H), 7.56 (d, J = 7.8 Hz, 1H), 7.50−7.42 (m, 3H), 7.37 (dd, J = 7.2, 7.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 141.6, 140.3, 137.0, 133.8, 132.8, 130.0, 129.2, 128.9, 127.6, 127.4, 127.2, 118.8, 111.1. Anal. Calcd for $C_{19}H_{13}N$: C, 89.38; H, 5.13. Found: C, 89.27; H, 5.08.

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Supporting Information Available: Procedures for the Suzuki coupling reactions, ^{1}H and ^{13}C NMR data for all the compounds synthesized, and ^{1}H NMR spectra of the model coupling reaction in dioxane-d_8 and EtOH-d_6, as well as X-ray crystallographic data for DAPCy (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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