Simple, Efficient Catalyst System for the Palladium-Catalyzed Amination of Aryl Chlorides, Bromides, and Triflates

John P. Wolfe,† Hiroshi Tomori, Joseph P. Sadighi,‡ Jingjun Yin, and Stephen L. Buchwald*

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Received October 29, 1999

Palladium complexes supported by (*o*-biphenyl)P(*t*-Bu)$_2$ (**3**) or (*o*-biphenyl)PCy$_2$ (**4**) are efficient catalysts for the catalytic amination of a wide variety of aryl halides and triflates. Use of ligand **3** allows for the room-temperature catalytic amination of many aryl chloride, bromide, and triflate substrates, while ligand **4** is effective for the amination of functionalized substrates or reactions of acyclic secondary amines. The catalysts perform well for a large number of different substrate combinations at 80−110 °C, including chloropyridines and functionalized aryl halides and triflates using 0.5−1.0 mol % Pd; some reactions proceed efficiently at low catalyst levels (0.05 mol % Pd). These ligands are effective for almost all substrate combinations that have been previously reported with various other ligands, and they represent the most generally effective catalyst system reported to date. Ligands **3** and **4** are air-stable, crystalline solids that are commercially available. Their effectiveness is believed to be due to a combination of steric and electronic properties that promote oxidative addition, Pd−N bond formation, and reductive elimination.

Owing to the many important applications of aniline derivatives, and the limitations of most methods for their synthesis, a considerable amount of effort has been recently devoted to the development of catalysts that are capable of effecting the cross-coupling of amines with aryl halides and sulfonates.[1] However, the proper choice of catalyst (Pd source, ligand choice) is crucial for the success of these reactions. It would be desirable to have one ligand (or a small class of ligands) that is capable of handling all possible substrate combinations. Our group, and others, have recently reported catalysts based on bulky, electron-rich phosphines that are capable of transforming inexpensive and readily available aryl chlorides (as well as aryl bromides) into aniline derivatives, thereby expanding the substrate scope of the palladium-catalyzed amination methodology.[2] Herein we disclose results of a detailed study of the use of these ligands in aryl amination processes.

Our first catalysts for the amination of aryl chlorides used ligands **1** and **2** (Figure 1).[2e] However, the preparation of these phosphines required a multistep synthesis. We recently reported that the simple phosphines **3** and

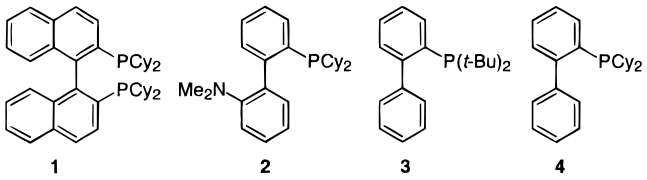


Figure 1.

4 (Figure 1) are excellent ligands for C−N,[3a] C−C,[3a,b] and C−O[3c] bond-forming reactions of aryl chloride substrates. Catalysts that employ **3** are sufficiently active to promote the room-temperature catalytic amination and Suzuki coupling of aryl chloride substrates,[3a,b,d,e] and catalysts derived from **4** are effective for the Suzuki coupling of hindered substrates.[3b] These ligands also promote some Suzuki coupling and catalytic amination reactions at very low catalyst levels (0.000001−0.1 mol % Pd).[3a] Ligands **3** and **4** are air-stable, crystalline solids that are prepared in a single step and are now commercially available.[4]

Although **3** is effective for the room-temperature amination of several aryl chloride substrates, the scope of aryl chloride aminations is much broader when ligands **3** or **4** are employed at higher temperatures (80−110 °C). This is particularly relevant for reactions of functionalized aryl halides, as the room-temperature reactions require the use of the strong base NaO*t*-Bu. Ligand **3** is effective for aminations of electron-rich or -neutral aryl chlorides with a wide variety of amine coupling partners;

† Present address: Department of Chemistry, University of California, Irvine, CA 92697-2025.

‡ Present address: Department of Chemistry, California Institute of Technology, Pasadena, CA, 91125.

(1) (a) Yang, B. H.; Buchwald, S. L. *J. Organomet. Chem.* **1999**, *576*, 125−146. (b) Hartwig, J. F. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2046−2067. (c) Wolfe, J. P.; Wagaw, S.; Marcoux, J.-F.; Buchwald, S. L. *Acc. Chem. Res.* **1998**, *31*, 805−818.

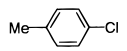
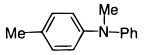
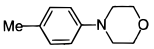
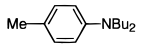
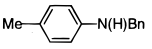
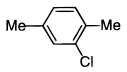
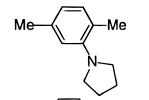
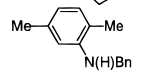
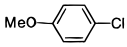
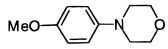
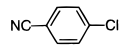
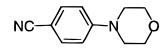
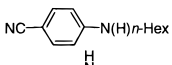
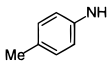
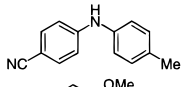
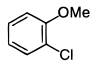
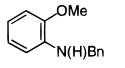
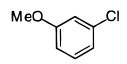
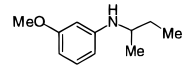
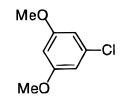
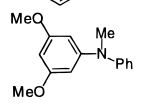
(2) (a) Nishiyama, M.; Yamamoto, T.; Koie, Y. *Tetrahedron Lett.* **1998**, *39*, 617−620. (b) Yamamoto, T.; Nishiyama, M.; Koie, Y. *Tetrahedron Lett.* **1998**, *39*, 2367−2370. (c) Reddy, N. P.; Tanaka, M. *Tetrahedron Lett.* **1997**, *38*, 4807−4810. (d) Hamann, B. C.; Hartwig, J. F. *J. Am. Chem. Soc.* **1998**, *120*, 7369−7370. (e) Old, D. W.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722−9723. (f) Bei, X.; Guram, A. S.; Turner, H. W.; Weinberg, W. H. *Tetrahedron Lett.* **1999**, *40*, 1237−1240. (g) Bei, X.; Uno, T.; Norris, J.; Turner, H. W.; Weinberg, W. H.; Guram, A. S.; Peterson, J. L. *Organometallics* **1999**, *18*, 1840−1853. (h) A procedure employing the Herrmann-Beller palladacycle has been used for some C−N bond-forming reactions of aryl chlorides at 135 °C; mixtures of regioisomers are often observed. Riermeier, T. H.; Zapf, A.; Beller, M. *Top. Catal.* **1997**, *4*, 301−309 and references therein.

(3) (a) A portion of this work has been previously communicated. See: Wolfe, J. P.; Buchwald, S. L. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 2413−2416. (b) Wolfe, J. P.; Singer, R. A.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 9550−9561. (c) Aranyos, A.; Old, D. W.; Kiyomori, A.; Wolfe, J. P.; Sadighi, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 4369−4378. (d) Hartwig has recently reported examples of room-temperature catalytic amination of aryl bromides and chlorides using P(*t*-Bu)$_3$. See: Hartwig, J. F.; Kawatsura, M.; Hauck, S. I.; Shaughnessy, K.; Alcazar-Roman, L. M. *J. Org. Chem.* **1999**, *64*, 5575−5580. (e) Nolan has also recently reported aminations of aryl chlorides using nucleophilic carbenes as ligand. See: Huang, J.; Grasa, G.; Nolan, S. P. *Org. Lett.* **1999**, *1*, 1307−1309.

(4) Ligands **3** and **4** are commercially available from Strem Chemical Co.

10.1021/jo991699y CCC: $19.00
Published on Web 02/02/2000

Table 1. Room-Temperature Catalytic Amination of Aryl Chlorides[a]

Entry	Halide	Amine	Product	%Pd	Rxn Time	Yield (%)
1				1.0	19 h	98
2				1.0	20 h	94
3		$HNBu_2$		2.0	18 h	81
4		H_2NBn		5.0	18 h	78[b]
5				1.0	21 h	98
6		H_2NBn		2.0	18 h	99
7				2.0	20 h	90
8				1.0	15 h	86
9		H_2NHex		5.0	17 h	71[c]
10				5.0	16 h	78[c]
11		H_2NBn		1.0	14 h	99
12		*s*-$BuNH_2$		5.0	20 h	92
13				1.0	16 h	97

[a] Reaction conditions: 1.0 equiv of aryl chloride, 1.2 equiv of amine, 1.4 equiv of NaO*t*-Bu, 1−2 mol % $Pd(OAc)_2$, 2−4 mol % **3**, toluene (1 mL/mmol halide), rt. Reaction times have not been minimized. Yields represent isolated yields (average of two or more experiments) of compounds estimated to be ≥95 % pure as judged by ^{1}H NMR and GC analysis (known compounds) and combustion analysis (new compounds). [b] The reaction was conducted with 1.5 equiv of benzylamine. [c] $Pd_2(dba)_3$ used in place of $Pd(OAc)_2$.

reactions involving secondary acyclic amines or aryl chlorides bearing base-sensitive functionality are typically more efficient using **4**. Aryl bromides and triflates are also effectively coupled with amines using catalysts based on **3** or **4**; the Pd/**4** catalyst is the most efficient system reported to date for the coupling of electron-rich aryl bromides with primary anilines.

Results

Room-Temperature Catalytic Amination of Aryl Chlorides. Initial attempts to effect the room-temperature catalytic amination of aryl chlorides using **2** were in general unsuccessful despite the utility of this ligand for room-temperature Suzuki coupling reactions of aryl chlorides.[2e] The one exception was when 4-chlorobenzonitrile, an activated aryl chloride, was combined with morpholine. However, use of ligand **3** provided catalysts with higher activity than was previously observed with **2**. Catalysts comprised of **3**/$Pd(OAc)_2$ were sufficiently reactive to promote the room-temperature catalytic amination of a variety of aryl chloride substrates.[3a] As shown in Table 1, the reaction is effective for both electron-rich and electron-deficient substrates, and a variety of amines are suitable coupling partners. For example, both *p*- and *o*-chloroanisole could be converted to aniline derivatives in ≥90% yield using 1−2 mol % catalyst (entries 7, 11). The reaction of benzylamine with 4-chlorotoluene was slow with 1−2 mol % catalyst; the desired product was obtained in good yield when 5 mol % of the palladium catalyst was employed (Table 1, entry 4). Excess benzylamine (1.5 equiv) was employed to minimize the formation of diaryl(alkyl) amine side products. Under these conditions a ratio of 8−9/1 diaryl/monoaryl product was observed. A larger amount of diarylated side product was formed at room-temperature than at 80 °C (see below). This procedure was also effective for the arylation of *s*-butylamine with *m*-chloroanisole (entry 12). In this case no diarylation was observed when 1.2 equiv of amine was employed. Use of $Pd(OAc)_2$ as the palladium source was required for most of the room-temperature reactions, although the reaction of *n*-hexylamine with the highly activated 4-chlorobenzonitrile gave the best results when $Pd_2(dba)_3$ was employed. In contrast to what has been previously observed,[5,6c] the reaction of a primary amine or primary aniline with an electron-deficient aryl halide afforded small amounts of diarylated side products; a ratio of ∼14−15/1 diarylamine/triarylamine was observed in the reaction of 4-chlorobenzonitrile with *n*-hexylamine or *p*-toluidine. The weak base K_3PO_4 was ineffective for the room-temperature reactions, even for highly activated substrates such as 4-chloronitrobenzene.

Unfortunately, the scope of the room-temperature reactions was somewhat limited. For example, the reaction of *m*-chloroanisole with *n*-hexylamine proceeded to only 19% conversion in 18 h. The requirement for $Pd(OAc)_2$ as a precatalyst precluded the use of primary anilines as coupling partners (see below), except for the reaction of *p*-toluidine with 4-chlorobenzonitrile, which was effective when 2.5 mol % of $Pd_2(dba)_3$ was employed as the palladium source. The functional group tolerance of the process is currently limited owing to the need to employ the strong base NaO*t*-Bu. However, nitrile functionality was tolerated even for arylations of primary anilines, which react with halobenzonitriles at higher temperatures (80 °C) in the presence of NaO*t*-Bu to form large amounts of amidine side products.

Catalytic Amination of Unactivated Aryl Chlorides at 80−110 °C. As shown in Table 2, the scope of the catalytic amination of aryl chlorides is considerably broader at 80−110 °C than at room temperature. A catalyst system derived from $Pd(OAc)_2$ or $Pd_2(dba)_3$ functions well for a variety of substrates including those that are electron-rich and/or ortho-substituted. Even the very hindered 2,6-dimethylchlorobenzene was a suitable substrate, although higher reaction temperatures and/or larger amounts of catalyst were required for reactions to proceed to completion in ≤24 h.

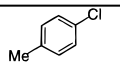
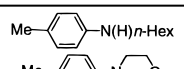
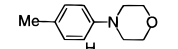
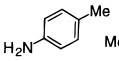
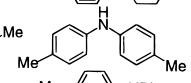
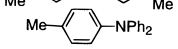
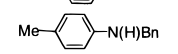
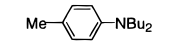
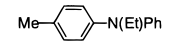
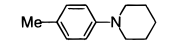
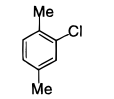
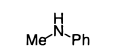
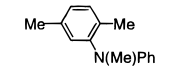
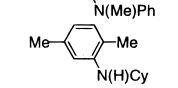
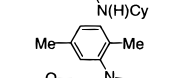
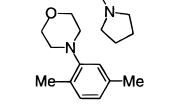
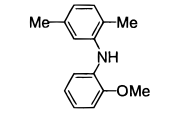
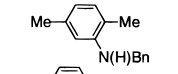
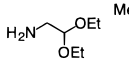
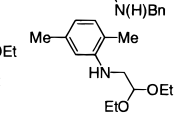
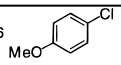
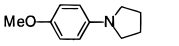
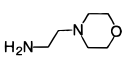
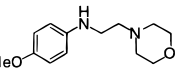
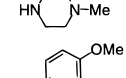
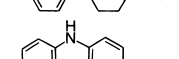
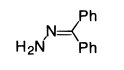
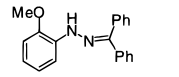
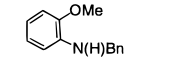
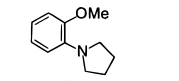
A variety of amine coupling partners may be used including primary and secondary anilines, primary amines, cyclic secondary amines, and diarylamines. Benzophenone imine, which serves as an NH_3 equivalent,[7] and

(5) Wolfe, J. P.; Wagaw, S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 7215−7216.

(6) (a) Guram, A. S.; Rennels, R. A.; Buchwald, S. L. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1348−1350. (b) Louie, J.; Hartwig, J. F. *Tetrahedron Lett.* **1995**, *36*, 3609−3612. (c) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 7217−7218. (d) Marcoux, J.-F.; Wagaw, S.; Buchwald, S. L. *J. Org. Chem.* **1997**, *62*, 1568−1569. (e) Sadighi, J. P.; Harris, M. C.; Buchwald, S. L. *Tetrahedron Lett.* **1998**, *39*, 5327−5330.

(7) Wolfe, J. P.; Åhman, J.; Sadighi, J. P.; Singer, R. A.; Buchwald, S. L. *Tetrahedron Lett.* **1997**, *38*, 6367−6370.

Table 2. Palladium-Catalyzed Amination of Unactivated Aryl Chlorides[a]

Entry	Halide	Amine	Product	mol % Pd	Rxn Time	Yield (%)
1		H_2NHex		0.5	19 h	85[e]
2				0.5	4 h	93
3				0.5	2.5 h	90[b]
4		$HNPh_2$		0.5	12 h	90
5		H_2NBn		0.5	5 h	89[e]
6		$HNBu_2$		1.0/**2** 0.5/**5** 0.5/**6**	6 h 22 h 22 h	95[b,f] 89[b] 91[b]
7		HN(Et)Ph		0.5	18 h	93
8				0.5	23 h	86
9				0.5	3 h	90
10		H_2NCy		1.0	19 h	98
11				0.5	3h	98
12				0.5	24 h	89
13				0.5	2.5 h	97[b]
14		H_2NBn		0.5	24 h	96
15				0.5	15 h	100[c]
16				1.0	23 h	92
17				0.5	24 h	86[d]
18				0.5/**4**	21 h	82[c]
19				0.5	8 h	94[b]
20				0.5	2.5 h	91[b]
21		H_2NBn		0.5	18 h	96
22				0.5	16 h	88
23				0.5	2.5 h	95[b]
24				1.0/**4**	18 h	>99[b]
25				1.0/**2**	20 h	86[d]
26		H_2NBn		1.0	24 h	86[d,e]
27				4.0	20 h	73[b]

[a] Reaction conditions: 1.0 equiv of aryl halide, 1.2 equiv of amine, 1.4 equiv of NaO*t*-Bu, cat. $Pd(OAc)_2$, cat. **3** (2L/Pd), toluene (2 mL/mmol halide), 80 °C. Reaction times have not been minimized. [b] $Pd_2(dba)_3$ used in place of $Pd(OAc)_2$. [c] The reaction was conducted at 100 °C. [d] The reaction was conducted at 110 °C. [e] The reaction was conducted with 1.5 equiv of amine. [f] A ratio of 1.5 L/Pd was employed.

benzophenone hydrazone[8] are also suitable substrates. Use of **2**, **5**, or **6** as ligands for the coupling of di-*n*-butylamine with 4-chlorotoluene gave higher yields than were obtained with **3** or **4** (entry 6); use of **3** or **4** resulted in the formation of aryl(*tert*-butyl)ether byproducts (~10%).

5 **6**

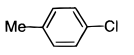
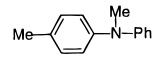
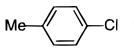
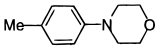
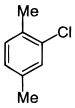
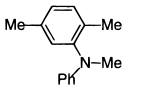
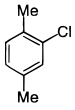
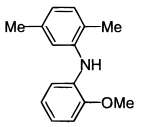
Reactions of primary aliphatic amines with unhindered aryl halides afforded good yields of the aryl(alkyl)amine products with the **3**/Pd catalyst at 80 °C; 1.5 equiv of amine was employed to minimize the formation of diarylated side products in these reactions. The ratios of monoaryl/diaryl products were typically ~10−20/1 for reactions of primary amines with *p*-substituted aryl chlorides, with *n*-hexylamine producing more diarylation (12/1 monoaryl/diaryl) than benzylamine (21/1 monoaryl/diaryl) in reactions with 4-chlorotoluene. Diarylated products were not observed with *o*-substituted aryl chlorides. Reactions of primary anilines were inefficient if $Pd(OAc)_2$ was employed as a precatalyst, but use of $Pd_2(dba)_3$ for these reactions provided excellent results.

Some substrate combinations that gave outstanding results with the BINAP catalyst system[5] (for the analogous aryl bromides) were either inefficient or required high temperatures or long reaction times. For example, the reaction of 4-bromobenzonitrile with *n*-hexylamine proceeds to completion rapidly and in essentially quantitative yield using the BINAP catalyst system (0.05 mol % Pd).[5] However, the reaction of 4-chlorobenzonitrile with *n*-hexylamine required 40 h at 110 °C to proceed to completion with 1 mol % Pd (see below in Table 5, entry 11).

For some substrates it was possible to conduct reactions with low catalyst loadings (0.05 mol % Pd),[3a] although to date these conditions are only effective for a limited number of substrate combinations (Table 3). For example, the reaction of *N*-methylaniline with 4-chlorotoluene proceeds to completion in 22 h using 0.025 mol % $Pd_2(dba)_3$ and 0.1 mol % **3** at 100 °C affording the

(8) The Pd-catalyzed arylation of benzophenone hydrazone and the subsequent transformation of the aryl hydrazone products to indoles have been previously reported by this group. See: (a) Wagaw, S.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 6621−6622. (b) Wagaw, S.; Yang, B. H.; Buchwald, S. L. *J. Am. Chem. Soc.* **1999**, *121*, 10251−10263. (c) Hartwig has also reported the catalyzed arylation step, but not the subsequent conversion into indoles: Hartwig, J. F. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2090−2093.

Table 3. Amination of Aryl Chlorides at Low Catalyst Loading[a]

Entry	Halide	Amine	Product	%Pd	Rxn Time	Yield
1				0.05	22 h	95[b]
2				0.05/**4**	19 h	89[b]
3				0.05	22 h	95
4				0.05	14 h	97[c]

[a] Reaction conditions: 1.0 equiv of aryl chloride, 1.2 equiv amine, 1.4 equiv of NaO*t*-Bu, 0.025 mol % $Pd_2(dba)_3$, 0.1 mol % **3**, toluene (1 mL/mmol halide), 110 °C. Reaction times have not been minimized. Yields represent isolated yields (average of two or more experiments) of compounds estimated to be ≥95 % pure as judged by ^{1}H NMR and GC analysis (known compounds) and combustion analysis (new compounds). [b] The reaction was conducted at 100 °C. [c] The reaction was conducted at 80 °C.

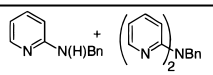
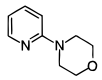
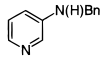
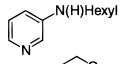
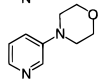
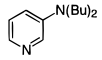
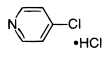
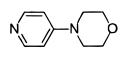
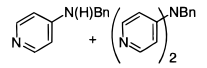
desired product in 95% yield. However, although the reaction of 4-chlorotoluene with *p*-toluidine is efficient with 0.5 mol % Pd (Table 2, entry 3), it only proceeds to 41% conversion in 48 h at 110 °C using 0.05 mol % Pd.

Catalytic Amination of Chloropyridines. Previous studies in our laboratory demonstrated that bromopyridine substrates were effective coupling partners in catalytic amination reactions provided that the chelating phosphine ligands BINAP or DPPP were employed;[9] nonchelating triarylphosphines were displaced from the metal by the pyridine substrate leading to catalyst deactivation.[9,10] Aminations of 2-chloropyridines were possible, although fairly high catalyst loadings (4 mol % Pd) were required.[9]

When the mixtures of $Pd(OAc)_2$ and **2**, **3**, or **4** were employed, 2-, 3-, and 4-chloropyridine proved to be viable substrates in catalytic amination reactions. While the chloropyridine derivatives reacted more slowly than other aryl halides, use of 1 mol % $Pd(OAc)_2$ at 100−110 °C provided acceptable results (Table 4). Despite the diminished reactivity of these substrates relative to other aryl chlorides, a variety of amines proved to be suitable coupling partners. Reactions catalyzed by Pd/**3**, that provided unacceptable results were usually more efficient if Pd/**4** or Pd/**2** were employed. Use of the Pd/**4** catalyst system necessitated the addition of excess amine (1.5−3.0 equiv) for reactions with primary amines in order to minimize the formation of doubly arylated products. As expected, aminations of the more reactive 2-chloropyridine were considerably faster than those of 3-chloropyridine. Use of the mild base K_3PO_4 was effective for the amination of 4-chloropyridine HCl with morpholine. The use of this base gave cleaner but slower reactions.

Catalytic Amination of Functionalized Aryl Chlorides. The use of the strong base NaO*t*-Bu in catalytic amination reactions leads to a relatively low level of functional group tolerance.[1] However, employment of

Table 4. Palladium-Catalyzed Amination of Chloropyridines[a]

Entry	Halide	Amine	Product	mol % Pd	Rxn Time	Yield (%)
1		H_2NBn		0.5	3.5h	98[b,c] (19:1)
2				0.5/**4**	4h	95[b]
3				1.0/**4** 1.0/**2**	22h 22h	97 94
4		H_2NBn		1.0	22h	86[c]
5		*n*-HexylNH_2 (3 eq)		1.0/**2**	22h	76[d]
6				1.0	22h	70
7		Bu_2NH		1.0/**2**	22h	77
8				1.0	14h	78[b,e,f]
9		H_2NBn		1.0/**4**	22h	70[b,g,h] (27/1)
10				1.0/**4**	22h	93[b,g,h]

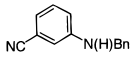
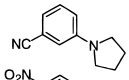
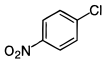
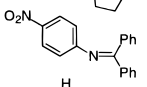
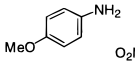
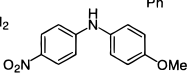
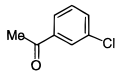
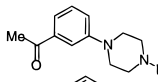
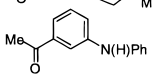
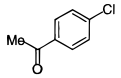
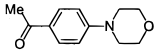
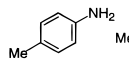
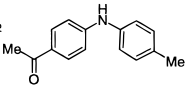
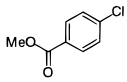
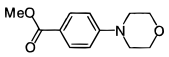
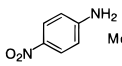
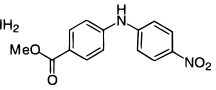
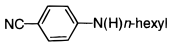
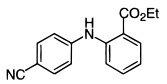
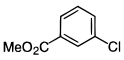
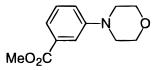
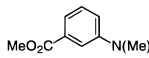
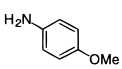
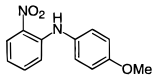
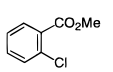
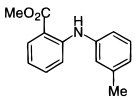
[a] Reaction conditions: 1.0 equiv of chloropyridine, 1.2 equiv of amine, 1.4 equiv of NaO*t*-Bu, cat. $Pd(OAc)_2$, cat. **3**, toluene (2 mL/mmol halide), 110 °C. [b] The reaction was conducted at 100 °C. [c] The reaction was conducted using 1.5 equiv of amine. [d] The reaction was conducted using 3.0 equiv amine. [e] 2.8 equiv of K_3PO_4 used in place of NaO*t*-Bu. [f] 1,4-Dioxane (1 mL/mmol halide) was used as the solvent. [g] 1,4-Dioxane (2 mL/mmol halide) was used as the solvent. [h] 2.8 equiv of NaO*t*-Bu was employed.

weaker bases such as Cs_2CO_3[11] or K_3PO_4[2e] greatly improves the functional group compatibility of these reactions.

Catalytic amination of aryl chloride substrates bearing a variety of base-sensitive functional groups was achieved using catalysts derived from **2**, **3**, and **4** when K_3PO_4 was employed as the stoichiometric base (Table 5). The reaction conditions tolerated the presence of enolizable ketones, methyl esters, nitriles, and nitro groups; a variety of amines were efficient coupling partners, but reactions of primary aliphatic amines usually required longer reaction times, higher temperatures, and/or larger catalyst loadings. Although the Pd/**3** catalyst was useful for some substrate combinations, the best results were generally obtained with either **2** or **4**; catalysts based on **2** were slightly more reactive than those derived from **4**. Reactions that proved to be inefficient when $Pd(OAc)_2$ was employed as a precatalyst usually gave better results when $Pd_2(dba)_3$ was used. Substrates that contained functional groups ortho to the aryl chloride were much less reactive. Acceptable yields were obtained for the reaction of 2-chloronitrobenzene or methyl-2-chlorobenzoate with primary anilines (entries 15, 16); however, reactions with aliphatic amines resulted in the formation of large amounts of side products arising from reduction and/or homocoupling of the aryl chloride, and typically proceeded to <80% conversion even with 10 mol % of the palladium catalyst. Despite the relatively low reactivity

(9) Wagaw, S.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 7240−7241.
(10) Hartwig has also demonstrated the displacement of triarylphosphines by pyridine in LPd(Ar)X complexes. See: Paul, F.; Patt, J.; Hartwig, J. F. *Organometallics* **1995**, *14*, 3030−3039.
(11) Wolfe, J. P.; Buchwald, S. L. *Tetrahedron Lett.* **1997**, *38*, 6359−6362.

Table 5. Palladium-Catalyzed Amination of Functionalized Aryl Chlorides[a]

Entry	Halide	Amine	Product	mol % Pd	Rxn Time	Yield (%)
1		H_2NBn		2.0	25 h	80[b,c]
2				1.0	40 h	81[c]
3				1.0/**2**	16 h	82
4				1.0/**3**	17 h	91
5				1.0/**2**	21 h	77
6				1.0 1.0/**2**	22 h 22 h	81 84
7				1.0/**3**	21 h	91[c,d]
8				1.0	18 h	95[d]
9				1.0	18 h	90[c,d]
10				1.0	18 h	81
11		*n*-HexylNH$_2$		1.0/**3**	40 h	72[e,g]
12				1.0	17 h	75
13				1.0	20 h	93
14				1.0 1.0/**2**	20 h 20 h	88[b] 83
15				5.0	16 h	69
16				5.0	17 h	80

[a] Reaction conditions: 1.0 equiv of aryl chloride, 1.2 equiv of amine, 1.4 equiv of K_3PO_4, cat. $Pd_2(dba)_3$, cat. **4**, DME (2 mL/mmol halide), 100 °C. [b] The reaction proceeded to 99% conversion. [c] $Pd(OAc)_2$ used in place of $Pd_2(dba)_3$. [d] The reaction was conducted at 80 °C. [e] The reaction was conducted at 110 °C. [f] The reaction was conducted with 3.0 equiv of amine. [g] NaO*t*-Bu, toluene used in place of K_3PO_4, DME.

of aryl chlorides containing ortho functional groups, a primary aniline with an ethyl ester in the ortho position was efficiently coupled with 4-chlorobenzonitrile using only 1 mol % Pd (entry 12). Other electron-deficient anilines such as 4-nitroaniline were also effectively arylated.

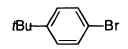
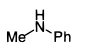
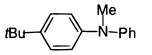
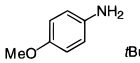
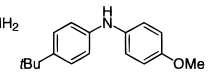
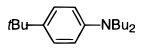
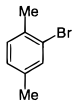
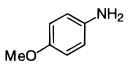
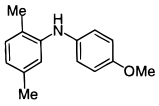
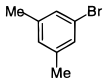
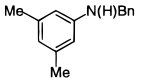
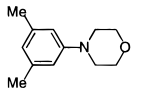
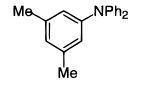
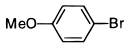
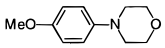
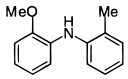
During the preparation of this article, a report was given by Hartwig and co-workers describing the application of tri-*tert*-butylphosphine,[3d] a ligand first used for aromatic amination by Nishiyama et al. at Tosoh,[2a,b] for the aminations of aryl chlorides and bromides under mild conditions. As such, a brief comparison of the "user friendliness" of the P(*t*-Bu)$_3$ system with the one reported in this paper, both of which are commercially available, is of interest. The chemistry that we report uses either $Pd(OAc)_2$ or $Pd_2(dba)_3$, both of which are commercially available, as the palladium source for the amination chemistry. The reactions that are described in the previous paper were "assembled in the drybox in sealed reaction vessels"; none of the reactions that we report involved the use of a glovebox. The exception to this is that bulk quantities of NaO*t*-Bu were stored in a glovebox. Smaller quantities were removed and used for 1−2 weeks while being stored in a desiccator between uses. Probably the largest difference between the two ligand types is the degree of their air sensitivity. To probe this, we prepared a solution of **3** in toluene and let it stir for 15 days in the air at room temperature. During this time an average of 3% of the ligand was oxidized to the phosphine oxide. We also compared the stability of P(*t*-Bu)$_3$ and **3** in side-by-side experiments by stirring toluene solutions of the two ligands (individually) for 2 h at room temperature in the air. Analysis by GC showed that all of **3** remained, while 97% of the P(*t*-Bu)$_3$ had been destroyed. Ligand **3** is a nicely crystalline material that is stable for at least six months in the solid state in the air (in a desiccator).

Catalytic Amination of Aryl Bromides. A number of catalyst systems have previously been developed for the palladium-catalyzed amination of aryl bromides.[1,2d,e,g,5,6] However, there remain several substrate combinations that are not efficiently handled by the available catalysts. For example, the coupling of primary anilines with electron-rich aryl bromides, such as 4-bromoanisole, is often problematic with catalysts based on triarylphosphine ligands (either chelating or monodentate). Additionally, for experimental simplicity, it is desirable to have a small family of ligands that are capable of transforming many different substrate combinations such that large libraries of ligands are not required to optimize reactions.

The reaction conditions that were effective for the room-temperature catalytic amination of aryl chlorides proved to be inefficient for aryl bromide substrates. However, use of a catalyst comprised of $Pd_2(dba)_3$/**3** allowed for the arylation of primary and secondary anilines at room temperature (Table 6). Room-temperature aminations of aryl bromides with aliphatic amines were slow under these conditions; however, use of 1.5−2.5 mol % $Pd_2(dba)_3$ with KO*t*-Bu as base in THF solvent allowed for the arylation of morpholine and benzylamine. It is worth noting that a significantly larger amount of double arylation of benzylamine was observed at room temperature (6/1 monoaryl/diaryl) than at 80 °C (29/1 monoaryl/diaryl) with 0.5 mol % Pd. The use of KO*t*-Bu/THF was unsatisfactory for the arylation of di-*n*-butylamine; however, this substrate was efficiently coupled with 4-*tert*-butylbromobenzene using $Pd_2(dba)_3$/**5** in DME solvent (NaO*t*-Bu as base). The functional group tolerance of the room-temperature reactions is currently limited owing to the requirement to employ a strong base.

As was observed for the catalytic amination of aryl chlorides, the scope of the amination reaction of aryl bromides was significantly broader at 80−100 °C (Table 7). Excellent results for the arylations of anilines with electron-rich or -neutral aryl bromides are obtained with catalysts comprised of $Pd_2(dba)_3$/**3**; this system appears to be the most effective catalyst developed to date for these types of substrates. While the **3**/Pd catalyst was usually less effective for reactions of aryl bromides with

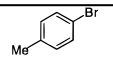
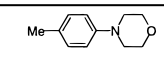
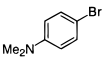
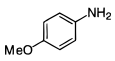
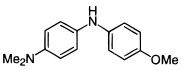
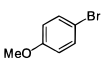
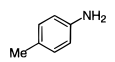
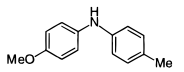
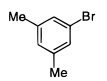
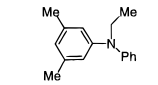
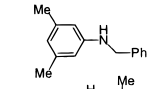
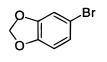
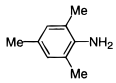
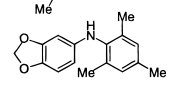
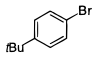
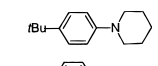
Table 6. Room-Temperature Catalytic Amination of Aryl Bromides[a]

Entry	Halide	Amine	Product	%Pd	Rxn Time	Yield (%)
1				1.0	21 h	92
2				1.0	28 h	87
3		$HNBu_2$		3.0/**5**	22 h	83[c]
4				1.0	48 h	88
5		H_2NBn		5.0	19 h	52[b]
6				3.0	20 h	80[b]
7		$NHPh_2$		1.0	23 h	89
8				3.0	20 h	83[b]
9				2.0	23 h	90

[a] Reaction conditions: 1.0 equiv of aryl bromide, 1.2 equiv of amine, 1.4 equiv of NaO*t*-Bu, 0.5−2.5 mol % $Pd_2(dba)_3$, (1−5 mol % Pd), 2−10 mol % **3**, toluene (1 mL/mmol halide), rt. Reaction times have not been minimized. [b] KO*t*-Bu and THF were used in place of NaO*t*-Bu and toluene. [c] DME used as solvent.

aliphatic amines, excellent results were obtained using a combination of **4** and $Pd_2(dba)_3$. This catalyst functioned well for reactions of both cyclic and acyclic secondary amines, although marginally better results were obtained in the reaction of di-*n*-butylamine with 4-*tert*-butylbromobenzene when **5** was employed. Substrates such as piperidine and di-*n*-butylamine, which often give poor results with the BINAP catalyst, were effectively coupled using the **4**/$Pd_2(dba)_3$ catalyst system. In contrast to what was observed for the reaction of 4-chlorotoluene with di-*n*-butylamine, only trace amounts (1−2%) of aryl(*tert*-butyl)ether side products were observed in the reaction of 4-*tert*-butylbromobenzene with di-*n*-butylamine. Use of **3** provided the best results for the amination of 5-bromo-*m*-xylene with benzylamine. The scope of reactions catalyzed by ligand **4** appears to be similar to the scope of catalytic amination processes that employ either BINAP or PPF−OMe as the ligand for palladium, although reactions of primary aliphatic amines require the use of **3**. Use of $Pd_2(dba)_3$ is essential for the success of most amination reactions of aryl bromide substrates using ligands **3**−**5**. For example, the reaction of 5-bromo-*m*-xylene with benzylamine proceeded to only 31% conversion after 22 h at 80 °C using $Pd(OAc)_2$/**3** as the catalyst (0.5 mol % Pd). Use of $Pd_2(dba)_3$ in place of $Pd(OAc)_2$ afforded the desired product in 90% yield after 17 h. Although high yields are obtained in reactions of aryl bromides with primary amines with the Pd/**3** catalyst, much faster reactions are observed when the BINAP ligand is used for these processes;[5] the reaction of 5-bromo-*m*-xylene with benzylamine is complete in ∼3 h using the $Pd_2(dba)_3$/BINAP catalyst system under similar

Table 7. Palladium-Catalyzed Amination of Aryl Bromides[a]

Entry	Halide	Amine	Product	mol % Pd	Rxn Time	Yield (%)
1				0.5	20 h	92[b]
2				0.5	2 h	93
3				0.5	2.5 h	90
4				0.5	3 h	82[b]
5				0.5	42 h	86
6				0.5	2 h	97
7				0.5/**4**	17 h	86
8		$HN(n\text{-}Bu)_2$		0.5/**4** 0.5/**5**	20 h 18 h	85 89
9				0.5/**4**	16 h	74
10		H_2N		0.5	6 h	92
11				1.0/**2**	20 h	86[c,d]
12				3.0/**4**	20 h	56[c,d,e]
13		H_2NBn		3.0/**4**	22 h	79[b,c,d,f,g]
14				1.0/**4**	23 h	96[c,d,f]
15				5.0/**4**	24 h	96[c,d,e]

[a] Reaction conditions: 1.0 equiv of aryl bromide, 1.2 equiv of amine, 1.4 equiv of NaO*t*-Bu, cat. $Pd_2(dba)_3$, cat. ligand **3**, toluene (2 mL/mmol halide), 80 °C. [b] $Pd(OAc)_2$ used in place of $Pd_2(dba)_3$. [c] The reaction was conducted at 100 °C. [d] K_3PO_4 used in place of NaO*t*-Bu. [e] DME (1 mL/mmol halide) was used as solvent. [f] Toluene (1 mL/mmol halide) was used as the solvent. [g] Contains ∼2.5% of 4,4′-dicyanobiphenyl.

reaction conditions (0.5 mol % Pd). The amination of functionalized aryl bromides proceeds in high yield using ligands **2** or **4** with K_3PO_4 as the stoichiometric base (entries 11−15).

The reactions of many aryl bromides with aliphatic amines using the **3**/Pd catalyst system are slower than the corresponding reactions of aryl chloride substrates. For example, the reaction of 4-chlorotoluene with morpholine is complete in <65 min at 80 °C with 0.5 mol % Pd, while the reaction of 4-bromotoluene with the same amine proceeds only to 29% conversion in the same amount of time. A competition experiment was conducted in which equimolar amounts of 4-bromotoluene and 4-chlorotoluene were reacted with 1.2 equiv of morpholine (Scheme 1). Not suprisingly, the bromide reacted considerably more rapidly than the chloride.

Higher yields were occasionally obtained for reactions of aryl chloride substrates. For example, the reaction of

Scheme 1

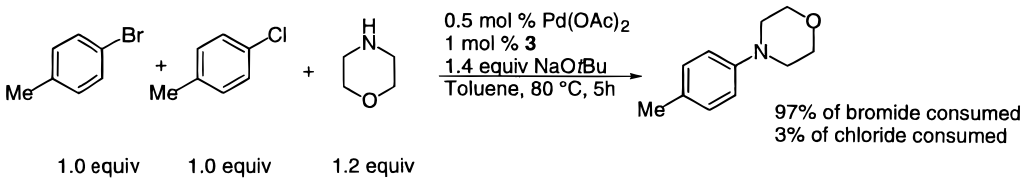
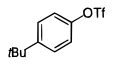
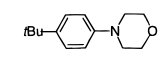
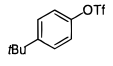
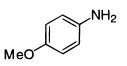
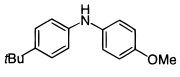
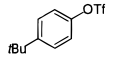
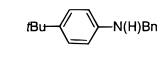
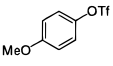
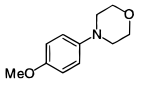
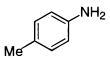
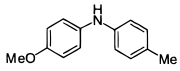
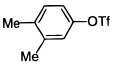
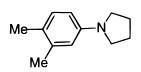


Table 8. Room-Temperature Catalytic Amination of Aryl Triflates[a]

Entry	Halide	Amine	Product	mol % Pd	Rxn Time	Yield (%)
1				1.0	24h	79
2				1.0	46h	74[b,c,d]
3		H_2NBn		1.0	22h	81
4				1.0	22h	81
5				1.0	48h	76[b]
6				1.0	22h	75

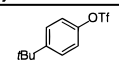
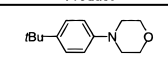
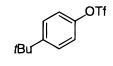
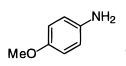
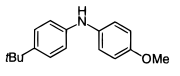
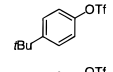
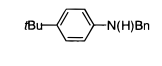
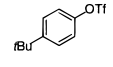
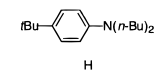
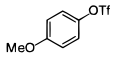
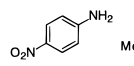
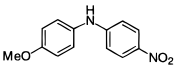
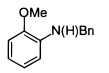
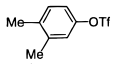
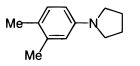
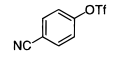
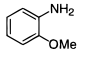
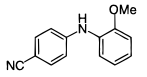
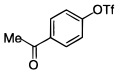
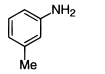
[a] Reaction conditions: 1.0 equiv of aryl triflate, 1.2 equiv of amine, 1.4 equiv of NaO*t*-Bu, cat. $Pd(OAc)_2$, cat ligand **3**, toluene (1 mL/mmol halide), rt. [b] $Pd_2(dba)_3$ used in place of $Pd(OAc)_2$. [c] Toluene (3 mL/mmol triflate) was used as solvent. [d] A L/Pd ratio of 1/0.8 was used.

2-bromo-*p*-xylene with *N*-methyl aniline afforded the desired product in good yield (75%) using ligand **4**; a 90% yield was obtained for the corresponding aryl chloride substrate with a catalyst comprised of Pd/**3** (see above).[12] However, for most comparable systems, both bromides and chlorides gave similar yields under optimized conditions.

Catalytic Amination of Aryl Triflates. Aryl triflates are desirable substrates owing to their ease of preparation from readily available phenols.[13] Catalytic aminations of aryl triflates have been previously effected using Pd/BINAP[14a,b] or Pd/dppf[14c] catalyst systems; these catalysts are usually inefficient for the arylation of secondary acyclic amines.[14] Reactions of electron-deficient aryl triflates often give low yields owing to NaO*t*-Bu-promoted cleavage of the triflate substrate; use of cesium carbonate with the Pd/BINAP catalyst gives improved results for these systems, although 3−5 mol % Pd was often required in these reactions.[14b]

The first room-temperature catalytic aminations of aryl triflates were accomplished using catalysts derived from **3** with NaO*t*-Bu as the base (Table 8). While this protocol was effective for the amination of electron-rich or -neutral aryl triflates, poor results were obtained for electron-deficient aryl triflates owing to base-promoted cleavage of the triflate substrate. Use of weaker bases such as K_3PO_4 or Cs_2CO_3 gave only small amounts of desired products; most of the starting aryl triflate remained unreacted.

Table 9. Palladium-Catalyzed Amination of Aryl Triflates[a]

Entry	Halide	Amine	Product	mol % Pd	Rxn Time	Yield (%)
1				1.0	26h	92[b,d]
2				1.0	16h	85
3		H_2NBn		1.0	19h	68[b,c,e]
4		$HN(n\text{-Bu})_2$		1.0/**4**	19h	73[b,c,e]
5				1.0	16h	76
6		H_2NBn		1.0	2h	81[b,c,e]
7				1.0/**4**	25h	88
8				1.0	1.5h	85[d]
9				1.0	1.5h	91
10				1.0	17h	76

[a] Reaction conditions: 1.0 equiv of aryl chloride, 1.2 equiv of amine, 1.4 equiv of K_3PO_4, cat. $Pd_2(dba)_3$, cat. ligand **3**, DME (2 mL/mmol halide), 80 °C. [b] $Pd(OAc)_2$ used in place of $Pd_2(dba)_3$. [c] NaO*t*-Bu used in place of K_3PO_4. [d] THF used as solvent. [e] Toluene used as solvent.

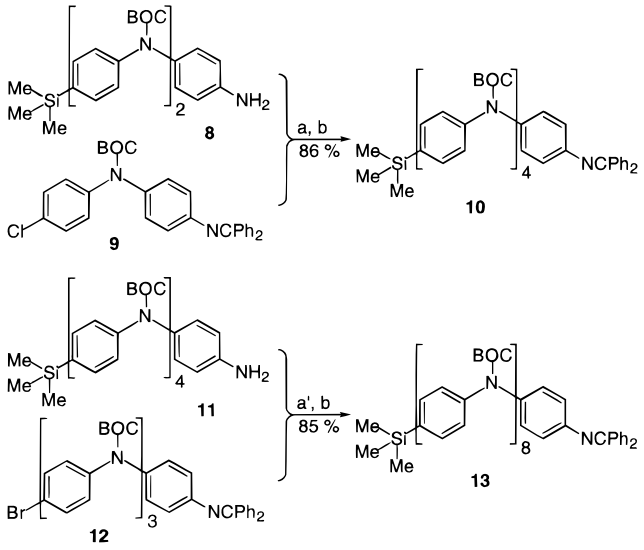
As expected, the scope of aryl triflate aminations was considerably broader at 80 °C (Table 9). Reactions of both electron-rich and electron-deficient aryl triflates proceeded in high yield using a catalyst comprised of Pd and **3** or **4** using K_3PO_4 as the stoichiometric base. As was observed for aryl bromide reactions, arylations of anilines were typically faster than those of aliphatic amines. Diaryl ether side products were occasionally observed (presumably arising from hydrolysis of the triflate followed by arylation of the resulting phenol). The reactions of 4-*tert*-butylphenyl triflate with benzylamine or di-*n*-butylamine were extremely slow when K_3PO_4 was used as base, even with up to 5 mol % of the palladium catalyst at 110 °C. However, use of NaO*t*-Bu in place of K_3PO_4 for these reactions provided acceptable yields of the desired products and required only 1 mol % Pd at 80 °C, although the yield for the reaction of benzylamine with 4-*tert*-butylphenyl triflate was higher at room temperature (77%) than at 80 °C (68%).

(12) Use of ligand **3** for the reaction of 2-bromo-*p*-xylene with *N*-methylaniline gave only 60% conversion.

(13) Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 5478−5486.

(14) (a) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **1997**, *62*, 1264−1267. (b) Åhman, J.; Buchwald, S. L. *Tetrahedron Lett.* **1997**, *38*, 6363−6366. (c) Louie, J.; Driver, M. S.; Hamann, B. C.; Hartwig, J. F. *J. Org. Chem.* **1997**, *62*, 1268−1273.

Scheme 2[a]



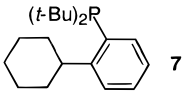
[a] Key: (a) $Pd_2(dba)_3$ (0.25 mol %), **3** (1.0 mol %), NaO-*t*-Bu (1.4 equiv), toluene, 80 °C; (a′) $Pd_2(dba)_3$ (0.5 mol %), **3** (2.0 mol %), NaO-*t*-Bu (1.4 equiv), toluene, 80 °C; (b) $(BOC)_2O$ (1.2−1.3 equiv), 4-DMAP (0.2−0.5 equiv), THF, 60 °C.

Applications Toward the Synthesis of Oligoanilines. The high reactivity of the $Pd_2(dba)_3$/**3** catalyst system toward electron-rich aryl chlorides and aryl bromides has proven useful in the synthesis of *p*-oligoaniline derivatives. We have previously demonstrated the synthesis of these compounds by palladium catalysis, using BINAP as the supporting ligand.[15] The less expensive chelating ligand DPEphos[6e,16] may also be used. Most of the aryl halide substrates were 4-bromo-*N*-(*tert*-butoxycarbonyl)diarylamines, which react relatively slowly with the triarylphosphine-ligated palladium catalysts; catalyst loadings in the range of 2−6 mol % palladium are typically necessary to achieve complete conversions. The combination of $Pd_2(dba)_3$ and ligand **3** is a far more active catalyst toward this class of aryl bromides; catalyst loadings of 1 mol % palladium are sufficient to achieve efficient coupling reactions. In addition, a dimer-derived aryl chloride, more readily obtained than the corresponding aryl bromide, may now be employed as a substrate. The synthesis of pentaaniline and nonaaniline derivatives is shown in Scheme 2.

Discussion

The catalytic cycle for the amination reactions is presumably similar to that postulated for the palladium-catalyzed amination of aryl bromides using the Pd/P(*o*-tol)$_3$ catalyst system. Although the reasons for the high reactivity of catalysts based on **2**−**6** are not completely understood, several structural features of these ligands appear to contribute to their effectiveness. The electron-rich phosphine group serves to accelerate the oxidative addition process and allows for the transformation of aryl chloride substrates that react sluggishly when palladium complexes bearing triarylphosphine ligands are used.[17] The steric bulk of the ligands may accelerate the C−N bond-forming reductive elimination,[18a] as well as promote the rate of N−Pd bond formation via the formation of (monophosphine)palladium complexes.[1b,18b−g] Although attempts to isolate palladium complexes of these ligands have thus far been unsuccessful owing to the high solubility of these complexes as well as a competing cyclometalation reaction, circumstantial evidence suggests that monophosphine complexes are involved in these reactions. The room-temperature amination of 4-chlorotoluene with *N*-methylaniline proceeds at roughly the same rate regardless of the ratio of **3**/Pd that is employed; the reaction proceeds to 75 ± 9% conversion after 2 h when a L/Pd ratio of 1.2/1 is employed, and to 69 ± 1% conversion after 2 h with a L/Pd ratio of 2/1.

We believe that other factors may also be of importance; for example, the π-system of the ortho aromatic group on these ligands may participate in an interaction with the unoccupied metal d-orbital.[19] Examination of molecular models suggest that this interaction is sterically favorable (Figure 2), and further circumstantial evidence for this interaction is provided by the fact that room-temperature reactions conducted with ligand **7** are



7

generally much less efficient than those that employ **3**. For example, the reaction of 4-chlorotoluene with morpholine proceeds to completion in 20 h and affords the desired product in 94% isolated yield when **3** is employed. Use of **7** for this coupling afforded only 33% conversion (33% GC yield) in 22 h. This trend was observed for several substrate combinations. The metal−arene interaction presumably serves to stabilize the catalyst. Of importance is that it forces the arene derived from the aryl halide substrate into an orientation in which it is pependicular to the N−Pd bond. Such an orientation should stereoelectronically favor reductive elimination (Figure 2).[20]

The lower reactivity of chloropyridine derivatives relative to other aryl chlorides may be due to the ability of the pyridine nitrogen to coordinate strongly to palladium, (as observed for (*o*-tol)$_3$PPd(Ar)X complexes),[9,10] thereby

(15) Sadighi, J. P.; Singer, R. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 4960−4976.

(16) Kranenburg, M.; van der Burgt, Y. E. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Goubitz, K.; Fraanje, J. *Organometallics* **1995**, *14*, 3081−3089.

(17) Grushin, V. V.; Alper, H. *Chem. Rev.* **1994**, *94*, 1047−1062.

(18) (a) Hartwig, J. F.; Richards, S.; Baranano, D.; Paul, F. *J. Am. Chem. Soc.* **1996**, *118*, 3626−3633. (b) Hartwig, J. F.; Paul, F. *J. Am. Chem. Soc.* **1995**, *117*, 5373−5374. (c) Paul, F.; Patt, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1994**, *116*, 5969−5970. (d) Louie, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1995**, *117*, 11598-11599. (e) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1995**, *117*, 4708−4709. (f) Louie, J.; Paul, F.; Hartwig, J. F. *Organometallics* **1996**, *15*, 2794−2805. (g) Hartwig, J. F. *Synlett* **1997**, 329−340. (h) Jones has demonstrated that steric bulk facilitates C−C bond-forming reductive elimination in ruthenium complexes, see: Jones, W. D.; Kuykendall, V. L. *Inorg. Chem.* **1991**, *30*, 2615−2622.

(19) Metal−π interactions have been observed in other palladium complexes. (a) Ossor, H.; Pfeffer, M.; Jastrzebski, J. T. B. H.; Stam, C. H. *Inorg. Chem.* **1987**, *26*, 1169−1171. (b) Falvello, L. R.; Fornies, J.; Navarro, R.; Sicilia, V.; Tomas, M. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 891−893. (c) Sommovigo, M.; Pasquali, M.; Leoni, P.; Braga, D.; Sabatino, P. *Chem. Ber.* **1991**, *124*, 97−99. (d) Li, C.-S.; Cheng, C.-H.; Liao, F.-L.; Wang, S.-L. *J. Chem. Soc., Chem. Commun.* **1991**, 710−712. (e) Kannan, S.; James, A. J.; Sharp, P. R. *J. Am. Chem. Soc.* **1998**, *120*, 215−216. (f) Kočovský, P.; Vyskočil, S.; Císařová, I.; Sejbal, J.; Tišlerová, I.; Smrčina, M.; Lloyd-Jones, G. C.; Stephen, S. C.; Butts, C. P.; Murray, M.; Langer, V. *J. Am. Chem. Soc.* **1999**, *121*, 7714−7715.

(20) Biaryl-forming reductive elimination from Pt(II) has been postulated to occur via a transition state in which both arenes are perpendicular to the coordination plane. See: Braterman, P. S.; Cross, R. J.; Young, G. B. *J. Chem. Soc., Dalton Trans.* **1977**, 1892−1897.

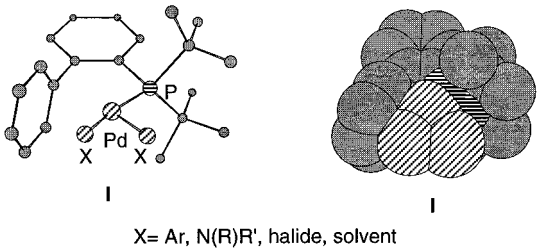


Figure 2. Chem 3-D representation of hypothetical $LPdX_2$.

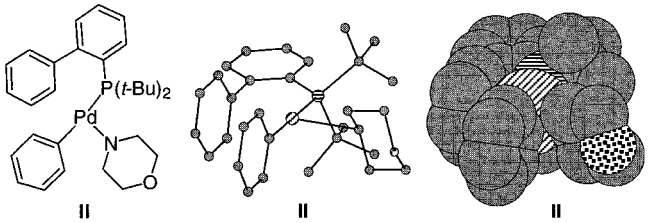


Figure 3. Chem 3-D representation of hypothetical LPd(Ar-)(morpholine).

decreasing the rate of one or more steps in the catalytic cycle. However, the fact that aminations of chloropyridines proceed effectively at 110 °C suggests that the pyridine nucleophile is not capable of irreversibly displacing the basic phosphine ligand from the metal.[9,10]

The selectivity for the reaction of an aryl bromide in the presence of an aryl chloride (in the competition experiment described above) demonstrates that while the overall process is faster for aryl chloride substrates, as expected, the oxidative addition of the aryl bromide substrate is faster than that of the aryl chloride. The reductive elimination processes should proceed at the same rate for both aryl chlorides and aryl bromides; thus, the Pd−N bond-forming step must be slower for the LPd(Ar)Br complex than for the LPd(Ar)Cl complex and is presumably rate-limiting for the reactions of aryl bromides with aliphatic amines. In contrast, NMR experiments have shown that oxidative addition is most likely the rate-limiting step in catalytic amination reactions that employ Pd/BINAP or Pd/DPPF catalysts.[2d,21] Arylations of aniline substrates were faster for aryl bromides than for the analogous aryl chlorides. It is possible that the increased acidity of anilines relative to aliphatic amines increases the rate of Pd−N bond formation to the point that oxidative addition becomes rate-limiting.

In conclusion, use of **2**−**6** allows for the efficient palladium-catalyzed amination of aryl chloride substrates. Catalysts based on **3** effect this transformation at room temperature for some substrate combinations and work well for reactions of primary amines with unhindered aryl chlorides and arylations of aniline substrates at 80 °C. Reactions of functionalized substrates with potassium phosphate as the base at 80−100 °C are most effective with **2** and **4**; these ligands frequently work for reactions of secondary amines that are inefficient with **3**. Reactions of di-*n*-butylamine are improved with the use of **5** or **6**. Certain substrate combinations react efficiently at low catalyst loadings (0.05 mol % Pd), although most reactions require moderate levels of palladium (0.5−1.0 mol %). Ligands **3** and **4** are also effective for the amination of aryl bromides and triflates, although the rates of reactions of aliphatic amines with aryl bromides are slower with catalysts supported by these ligands than with the Pd/BINAP catalyst system. In general, reactions of aryl bromides and triflates with primary aliphatic amines and primary anilines are more efficient with **3**; ligand **4** provides the best results for reactions of these substrates with secondary aliphatic amines.

The effectiveness of these ligands is believed to be due to a unique combination of steric and electronic properties. Their electron-rich nature promotes oxidative addition; their steric bulk facilitates reductive elimination and promotes reactivity via monophosphine intermediates, which presumably promotes all steps of the catalytic cycle.

The family of ligands **3** and **4** exhibit excellent generality in catalytic amination reactions, and their scope encompasses nearly all of the transformations that can be effected with P(*o*-tol)$_3$, BINAP, PPF−OMe, DPPF, and P(*t*-Bu)$_3$. Furthermore, their ease of preparation, commercial availability, and exceptional air stability are substantial benefits over other catalyst systems for reactions of aryl chloride, bromide, and triflate substrates.

Experimental Section

General Considerations. All reactions were carried out under an argon atmosphere in oven-dried glassware. Elemental analyses were performed by Atlantic Microlabs Inc, Norcross, GA, or E&R Microanalytical Laboratory, Parsippany, NJ. Toluene was distilled under nitrogen from molten sodium. Anhydrous DME was purchased from Aldrich Chemical Co. and was used without further purification. THF was distilled under argon from sodium benzophenone ketyl. Aryl halides were purchased from commercial sources and were used without further purification with the exception of 2-chloro-*p*-xylene and 5-bromo-*m*-xylene, which were passed through alumina to remove colored impurities. Aryl triflates were prepared according to previously published procedures.[13,14] Amines were purchased from commercial sources and were passed through alumina before use. Ligands **2**−**6** were prepared as previously described.[2e,3a−c] Palladium acetate and tris(dibenzylideneacetone)dipalladium(0) were purchased from Strem Chemical company. Sodium *tert*-butoxide was purchased from Aldrich Chemical Co.; the bulk of this material was stored under nitrogen in a Vacuum Atmospheres glovebox. Small portions (1−2 g) were removed from the glovebox in glass vials, stored in the air in desiccators filled with anhydrous calcium sulfate, and weighed in the air. Tribasic potassium phosphate was purchased from Fluka Chemical Company. Tetramer bromide (**12**) (see Scheme 2) was prepared according to previously published procedures.[15] IR spectra reported in this paper were obtained by placing neat samples directly on the DiComp probe of an ASI REACTIR in situ IR instrument. Yields in Tables 1−9 refer to isolated yields (average of two runs) of compounds estimated to be ≥95% pure as determined by ^{1}H NMR and GC analysis or combustion analysis. Compounds previously reported by this group were characterized by ^{1}H NMR; their purity was confirmed by GC analysis. Compounds that are described in more than one table (or more than once in the same table) were completely characterized once. Other samples of these compounds were characterized by comparing their ^{1}H NMR spectra to those of the fully characterized product; their purity was confirmed by GC analysis. The *characterization data of known compounds are given in the Supporting Information*. The procedures described in this section are representative, thus the yields may differ from those given in Tables 1−9.

***o*-(Di-*tert*-butylphosphino)cyclohexylbenzene (7).** An oven-dried Schlenk flask was allowed to cool to room temper-

(21) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **2000**, *65*, 1144.

ature under an argon purge and was charged with 1,2-dibromobenzene (1.2 mL, 10.0 mmol), ether (20 mL), and THF (20 mL). The mixture was cooled to −119 °C with stirring using an ethanol/N_2 cold bath. A solution of *n*-butyllithium in hexanes (1.6 M, 5.8 mL, 9.3 mmol) was added slowly dropwise. The mixture was stirred at −119 °C for 45 min, and then cyclohexanone (0.98 mL, 9.5 mmol) was added to the mixture. The mixture was stirred at −119 °C for 30 min, then warmed to room temperature, and stirred for 17 h. The mixture was quenched with saturated aqueous ammonium chloride (20 mL), diluted with ether (50 mL), and poured into a separatory funnel. The layers were separated, and the aqueous phase was extracted with ether (20 mL). The organic layers were combined and washed with brine (20 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel to afford 1.91 g of 1-(*o*-bromophenyl)cyclohexanol, which was judged to be ~86% pure by GC analysis. This material was used without further purification.

A round-bottomed flask was purged with argon and charged with 1-(*o*-bromophenyl)cyclohexanol (1.78 g, 7.0 mmol), dichloromethane (28 mL), triethylsilane (1.5 mL, 9.1 mmol), and trifluoroacetic acid (1.1 mL, 14.7 mmol). The mixture was stirred at room temperature for 1.5 h, and then was quenched with solid potassium carbonate (ca. 2 g). The mixture was diluted with ether (50 mL) and transferred to a separatory funnel. The mixture was washed with saturated aqueous $NaHCO_3$ (50 mL), and the organic phase was dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford a mixture of 1-bromo-2-cyclohexylbenzene and 1-(2-bromophenyl)cyclohexene. The crude material was placed into a round-bottomed flask, and the flask was purged with argon. THF (2 mL) was added, and the mixture was cooled to 0 °C with stirring. A solution of BH_3 in THF (1 M, 7.0 mL, 7.0 mmol) was added dropwise to the mixture. The mixture was stirred at 0 °C for 1.5 h, then warmed to room temperature, and stirred for 19 h. Acetic acid (4 mL) was added, and the mixture was stirred at room temperature for 6 h. The mixture was then diluted with ether (50 mL) and poured into a separatory funnel. The mixture was washed with aqueous NaOH (1 M, 50 mL), the layers were separated, and the aqueous phase was extracted with ether (50 mL). The combined organic phases were washed with brine (50 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel to afford 555 mg of 1-bromo-2-cyclohexylbenzene, which was judged to be 93% pure by GC analysis. This material was used without further purification.

An oven-dried Schlenk flask was cooled to room temperature under an argon purge and was charged with magnesium turnings (27 mg, 1.1 mmol), THF (1 mL), and 1,2-dibromoethane (8 μL). The mixture was stirred at room temperature for 10 min, and then 1-bromo-2-cyclohexylbenzene (239 mg, 1.0 mmol) was added in one portion. The mixture was stirred at room temperature for 20 min and then immersed in a 60 °C oil bath for 15 min. The mixture was cooled to room temperature, the septum was removed from the flask, and copper(I) chloride (104 mg, 1.05 mmol) was added. The flask was capped with the septum and purged with argon for 1 min. The flask was charged with di-*tert*-butylchlorophosphine (0.23 mL, 1.2 mmol) and additional THF (1 mL). The mixture was immersed in a 60 °C oil bath with stirring for 26 h, then cooled to room temperature, and filtered, and the solids were washed with 1:1 ether:hexanes (50 mL). The organic solution was poured into a separatory funnel and washed with 30% aqueous ammonium hydroxide solution (3 × 50 mL) and brine (50 mL). The organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel to afford the title compound as a white solid (141 mg), which was judged to be 92% pure by GC analysis. This material was recrystallized from methanol to afford 101 mg (~3% overall from 1,2-dibromobenzene) of the title compound as a white, crystalline solid, mp 101−102 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75−7.65 (m, 1H), 7.40−7.20 (m, 2H), 7.15−7.05 (m, 1H), 4.05−3.90 (m, 1H), 1.85−1.60 (m, 5H), 1.51−1.25 (m, 5H), 1.14 (d, 18H, J = 11.6 Hz); ^{31}P NMR (121 MHz, $CDCl_3$) δ 13.0; ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.7, 155.4, 135.0, 134.7, 128.8, 126.34, 126.27, 123.85, 40.8, 40.3, 34.4, 32.3, 31.9, 30.7, 30.5, 26.7, 26.3; IR (neat, cm^{-1}) 2927, 1461, 1175, 768. Anal. Calcd for $C_{20}H_{33}P$: C, 78.90; H, 10.93. Found: C, 78.96; H, 11.31.

General Procedure for Room-Temperature Catalytic Amination of Aryl Chlorides and Triflates. An oven-dried resealable Schlenk flask was evacuated and backfilled with argon. The flask was charged with $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 1 mol %), **3** (6.0 mg, 0.02 mmol, 2 mol %), and NaO*t*-Bu (135 mg, 1.4 mmol). The flask was evacuated and backfilled with argon and then capped with a rubber septum. Toluene (0.5 mL), the aryl chloride or triflate (1.0 mmol), the amine (1.2 mmol), and additional toluene (0.5 mL) were added through the septum (aryl halides or amines that were solids at room temperature were added as solids following the addition of NaO*t*-Bu). The septum was replaced with a Teflon screwcap, the flask was sealed, and the mixture was stirred at room temperature until the starting aryl chloride or triflate had been completely consumed as judged by GC analysis. During the course of the reaction, the mixture was observed to form a gel (at around 50% conversion) and then liquefy again as the reaction proceeded to completion. Following the complete consumption of the aryl chloride or triflate starting material, the mixture was diluted with ether (20 mL), filtered through Celite, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel.

Workup Method B. Following complete consumption of the aryl chloride or triflate starting material, the mixture was diluted with ether (50 mL) and transferred to a separatory funnel. The mixture was washed with aqueous HCl (1 M, 2 × 20 mL), washed with brine (20 mL), dried over anhydrous magnesium sulfate, filtered and, concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

Aryl Chlorides.

***N*-Methyl-*N*-phenyl-*p*-toluidine**[22] (Table 1, entry 1). The general procedure using workup method B gave 197 mg (100%) of the title compound as a colorless oil.

***N*-(4-Methylphenyl)morpholine**[22,23] (Table 1, entry 2). The general procedure gave 166 mg (94%) of the title compound as a white solid.

***N*,*N*-Dibutyl-*p*-toluidine**[22,24] (Table 1, entry 3). The general procedure was modified such that 2 mol % $Pd(OAc)_2$ and 3 mol % **3** were employed. When the 4-chlorotoluene had been completely consumed, 30% H_2O_2 (1 mL) was added to the reaction mixture in order to oxidize the phosphine ligand. The mixture was stirred at room temperature for 5 min, then diluted with ether (20 mL), and transferred to a separatory funnel. The layers were separated, and the organic layer was washed with water (20 mL) and saturated aqueous $Fe(SO)_4$ (20 mL). The combined aqueous layers were extracted with ether; the organic extracts were combined, and the aqueous layer was discarded. The combined organic extracts were extracted with aqueous HCl (1 M, 4 × 50 mL), the organic layer was discarded, and the aqueous extracts were combined and basified to pH 14. The aqueous layer was extracted with ether (4 × 50 mL), and the combined organic extracts were washed with brine, dried over anhydrous magnesium sulfate, filtered through a plug of silica gel, and concentrated in vacuo to afford 172 mg (79%) of the title compound as a colorless oil.

***N*-Benzyl-*p*-toluidine** (Table 1, entry 4).[2e] The general procedure was followed using 5 mol % $Pd(OAc)_2$ and 1.5 equiv of benzylamine. When the 4-chlorotoluene had been completely consumed as judged by GC analysis, the reaction mixture was diluted with THF (5 mL), and 30% aqueous hydrogen peroxide (5 mL) was added to oxidize the phosphine. The mixture was stirred at room temperature for 5 min, then diluted with ether (50 mL), and transferred to a separatory funnel. The layers were separated, and the organic layer was washed with water

(22) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 1133−1135.

(20 mL) and saturated aqueous $FeSO_4$ (20 mL). The aqueous washes were discarded, the organic phase was extracted with aqueous 1M HCl (4 × 50 mL), and the organic layer was discarded. The combined aqueous layers were basified to pH 14 with aqueous 6 M NaOH and then extracted with ether (3 × 50 mL). The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated to afford 158 mg (80%) of a colorless oil.

***N*-(2,5-Xylyl)pyrrolidine**[25,26] (Table 1, entry 5). The general procedure gave 169 mg (97%) of the title compound as a colorless oil, which was determined to contain ≤1% of **3** as judged by ^{1}H NMR and GC analysis.

***N*-(2,5-Xylyl)benzylamine** (Table 1, entry 6). The general procedure was modified such that 2 mol % $Pd(OAc)_2$ and 4 mol % **3** were employed. When the aryl halide had been completely consumed, 30% H_2O_2 (2 mL) and THF (1 mL) were added to the reaction mixture. The mixture was stirred at room temperature for 5 min, then diluted with ether (20 mL), and transferred to a separatory funnel. The layers were separated, and the organic layer was washed with water (20 mL) and saturated aqueous $Fe(SO)_4$ (20 mL). The combined aqueous layers were extracted with ether; the organic extracts were combined, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude material was then purified by flash chromatography on silica gel to afford 196 mg (99%) of the title compound as a colorless oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.41−7.26 (m, 5H), 6.96 (d, 1H, J = 7.3 Hz), 6.51−6.46 (m, 2H), 4.36 (s, 2H), 3.790 (s, br, 1H), 2.26 (s, 3H), 2.12 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.9, 139.5, 129.9, 128.6, 127.6, 127.2, 118.9, 117.8, 110.8, 48.3, 21.5, 17.1; IR (neat, cm^{-1}) 3438, 1582, 1453, 795. Anal. Calcd for $C_{15}H_{17}N$: C, 85.26; H, 8.11. Found: C, 85.14; H, 8.12.

***N*-(4-Methoxyphenyl)morpholine**[22,23] (Table 1, entry 7). The general procedure was modified such that 2 mol % $Pd(OAc)_2$ and 4 mol % **3** were employed. The procedure afforded 173 mg (90%) of the title compound as a white solid.

***N*-(4-Cyanophenyl)morpholine**[25,27] (Table 1, entry 8). The general procedure gave 158 mg (84%) of the title compound as a white solid.

***N*-(4-Cyanophenyl)-*n*-hexylamine** (Table 1, entry 9).[5] The general procedure using 2.5 mol % $Pd_2(dba)_3$ gave 144 mg (71%) of the title compound as a white solid.

***N*-(4-Cyanophenyl)-*p*-toluidine** (Table 1, entry 10).[11] The general procedure using 2.5 mol % $Pd_2(dba)_3$ gave 169 mg (81%) of the title compound as a tan solid.

***N*-(2-Methoxyphenyl)benzylamine**[28] (Table 1, entry 11). The general procedure gave 211 mg (99%) of the title compound as a colorless oil.

***N*-(3-Methoxyphenyl)-*s*-butylamine** (Table 1, entry 12). The general procedure using 5 mol % $Pd(OAc)_2$ gave 159 mg (89%) of the title compound as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.06 (t, 1H, J = 8.0 Hz), 6.25−6.12 (m, 3H), 3.77 (s, 3H), 3.55 (s, br, 1H), 3.41−3.31 (m, 1H), 1.63−1.43 (m, 2H), 1.16 (d, 3H, J = 6.3 Hz), 0.94 (t, 3H, J = 7.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.7, 148.9, 129.8, 106.2, 101.6, 98.9, 55.0, 49.8, 29.7, 20.3, 10.5; IR (neat, cm^{-1}) 3397, 1613, 1208, 1158, 1050 Anal. Calcd for $C_{11}H_{17}NO$: C, 73.70; H, 9.56. Found: C, 73.77; H, 9.65.

***N*-Methyl-*N*-(3,5-dimethoxyphenyl)aniline** (Table 1, entry 13). The general procedure gave 238 mg (98%) of the title compound as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32−7.26 (m, 2H), 7.10−7.01 (m, 3H), 6.12−6.06 (m, 3H), 3.73 (s, 6H), 3.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.3, 150.9, 148.6, 129.2, 122.3, 97.5, 92.4, 55.2, 40.3; IR (neat, cm^{-1}) 2939, 1586, 1150, 1065, 700. Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04. Found: C, 73.90; H, 7.01.

Aryl Triflates.

***N*-(4-*tert*-Butylphenyl)morpholine** (Table 8, entry 1).[29] The general procedure gave 170 mg (78%) of the title compound as a white solid.

***N*-(4-*tert*-Butylphenyl)-*p*-anisidine** (Table 8, entry 2). The general procedure using $Pd_2(dba)_3$ and 3 mL toluene/mmol aryl triflate gave 195 mg (76%) of the title compound as a pale yellow solid.

***N*-(4-*tert*-Butylphenyl)benzylamine** (Table 8, entry 3). The general procedure gave 184 mg (77%) of the title compound as a colorless oil.

***N*-(4-Methoxyphenyl)morpholine** (Table 8, entry 4).[22,23] The general proceudre gave 170 mg (88%) of the title compound as a white solid.

***N*-(*p*-Tolyl)-*p*-anisidine** (Table 8, entry 5).[30] The general procedure using $Pd_2(dba)_3$ gave 151 mg (71%) of the title compound as a pale yellow solid.

***N*-(3,4-Dimethylphenyl)pyrrolidine** (Table 8, entry 6). The general procedure gave 132 mg (75%) of the title compound as a colorless oil.

General Procedure for Room-Temperature Catalytic Amination of Aryl Bromides. An oven-dried resealable Schlenk flask was evacuated and backfilled with argon. The flask was charged with $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol, 1 mol % Pd), **3** (6.0 mg, 0.02 mmol, 2 mol %), and NaO*t*-Bu (135 mg, 1.4 mmol). The flask was evacuated and backfilled with argon and then capped with a rubber septum. Toluene (0.5 mL), the aryl bromide (1.0 mmol), the amine (1.2 mmol), and additional toluene (0.5 mL) were added through the septum (aryl bromides or amines that were solids at room temperature were added as solids following the addition of NaO*t*-Bu). The septum was replaced with a Teflon screwcap, the flask was sealed, and the mixture was stirred at room temperature until the starting aryl bromide had been completely consumed as judged by GC analysis. During the course of the reaction, the mixture was observed to form a gel (at around 50% conversion) and then liquefy again as the reaction proceeded to completion. Following the complete consumption of the aryl bromide starting material, the mixture was diluted with ether (20 mL), filtered through Celite, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel.

Workup Method B. Following complete consumption of the aryl bromide starting material, the mixture was diluted with ether (50 mL) and transferred to a separatory funnel. The mixture was washed with aqueous HCl (1 M, 2 × 20 mL), washed with brine (20 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

***N*-Methyl-*N*-(4-*tert*-butylphenyl)aniline** (Table 6, entry 1).[29] The general procedure using workup method B gave 221 mg (92%) of the title compound as a colorless oil.

***N*-(4-*tert*-Butylphenyl)-*p*-anisidine** (Table 6, entry 2). The general procedure using workup method B gave 224 mg (88%) of the title compound as a pale yellow solid.

***N*,*N*-Dibutyl-4-*tert*-butylaniline** (Table 6, entry 3).[6d] The general procedure using 1.5 mol % $Pd_2(dba)_3$, ligand **5**, and DME solvent gave 214 mg (82%) of the title compound as a colorless oil.

***N*-(2,5-Xylyl)-*p*-anisidine** (Table 6, entry 4).[25] The general procedure using workup method B gave 206 mg (91%) of the title compound as a colorless oil.

***N*-Benzyl-3,5-xylidene** (Table 6, entry 5).[5] The general procedure was followed using 2.5 mol % $Pd_2(dba)_3$, KO*t*-Bu, 1.5 equiv of benzylamine, and THF as solvent. When the aryl bromide had been completely consumed as judged by GC analysis, the reaction mixture was diluted with THF (5 mL), and 30% aqueous hydrogen peroxide (5 mL) was added to oxidize the phosphine. The mixture was stirred at room

(23) Tsuji, Y.; Huh, K. T.; Ohsugi, Y.; Watanabe, Y. *J. Org. Chem.* **1985**, *50*, 1365−1370.
(24) Watanabe, Y.; Tsjui, Y.; Ige, H.; Ohsuji, Y.; Ohta, T. *J. Org. Chem.* **1984**, *49*, 3359−3363.
(25) Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 6054−6058.
(26) Walkup, R. E.; Searles, S., Jr. *Tetrahedron* **1985**, *41*, 101−106.
(27) Kotsuki, H.; Kobayashi, S.; Suenaga, H.; Nishizawa, H. *Synthesis* **1990**, 1145−1147.
(28) Pratt, E. F.; McGovern, T. P. *J. Org. Chem.* **1964**, *29*, 1540−1543.
(29) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **1997**, *62*, 6066−6068.
(30) Barton, D. H. R.; Donnelly, D. M. X.; Finet, J.-P.; Guiry, P. T. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2095−2102.

temperature for 5 min, then diluted with ether (50 mL), and transferred to a separatory funnel. The layers were separated, and the organic layer was washed with water (20 mL) and saturated aqueous $FeSO_4$ (20 mL). The aqueous washes were discarded, the organic phase was extracted with aqueous 1 M HCl (4 × 50 mL), and the organic layer was discarded. The combined aqueous layers were basified to pH 14 with aqueous 6 M NaOH and then extracted with ether (3 × 50 mL). The combined organic layers were washed with brine, dried over anhydrous magnesium sulfate, filtered, and concentrated to afford 110 mg (52%) of the title compound as a colorless oil.

***N*-(3,5-Xylyl)morpholine** (Table 6, entry 6).[31] The general procedure using 1.5 mol % $Pd_2(dba)_3$, KO*t*-Bu, and THF solvent gave 151 mg (79%) of the title compound as a colorless oil. This material contained <3% 3,5-dimethylphenol as judged by GC analysis.

3,5-Dimethyltriphenylamine (Table 6, entry 7).[32] The general procedure was followed; the product was isolated by recrystallization from ethanol instead of chromatography to give 238 mg (88%) of the title compound as a white solid.

***N*-(4-Methoxyphenyl)morpholine** (Table 6, entry 8).[22,23] The general procedure using 1.5 mol % $Pd_2(dba)_3$, KO*t*-Bu, and THF solvent afforded 159 mg (82%) of the title compound as a white solid.

2-Methoxy-2′-methyldiphenylamine (Table 6, entry 9).[30] The general procedure using 2 mol % $Pd(OAc)_2$ and workup method B gave 197 mg (92%) of the title compound as a pale yellow oil.

General Procedure for the Catalytic Amination of Aryl Chlorides at 80−110 °C. An oven-dried resealable Schlenk flask was evacuated and backfilled with argon. The flask was charged with palladium acetate (0.5 mol %), **3** (1.0 mol %), and NaO*t*-Bu (1.4 equiv) and evacuated and backfilled with argon. The flask was capped with a rubber septum, and toluene (2 mL/mmol halide), the aryl chloride (1.0 equiv), and the amine (1.2 equiv) were added through the septum (aryl chlorides or amines that were solids at room temperature were added as solids following the addition of NaO*t*-Bu). The septum was replaced with a Teflon screwcap, the flask was sealed, and the mixture was heated to 80 °C with stirring until the starting aryl halide had been completely consumed as judged by GC analysis. The mixture was cooled to room temperature, diluted with ether (30 mL), filtered through Celite, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

Workup Method B. Following complete consumption of the aryl halide starting material, the mixture was diluted with ether (50 mL) and transferred to a separatory funnel. The mixture was washed with aqueous HCl (1 M, 2 × 20 mL), washed with brine (20 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

***N*-(4-Methylphenyl)hexylamine** (Table 2, entry 1).[22] The general procedure was conducted on a 2 mmol scale using 1.5 equiv of amine. Following completion of the reaction, the mixture was cooled to room temperature, diluted with ether (40 mL), and extracted with 1 M aqueous HCl (3 × 50 mL). The organic phase was discarded, and the aqueous layer was basified to pH 14 with 6 M aqueous NaOH. The aqueous phase was extracted with ether (3 × 50 mL), and the ether layers were combined, dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo to afford 318 mg (83%) of the title compound as a white solid. This material contained 1% **3** as judged by GC and ^{1}H NMR analysis.

***N*-(4-Methylphenyl)morpholine**[22,23] (Table 2, entry 2). The general procedure conducted on a 2 mmol scale gave 316 mg (95%) of the title compound as a white solid.

Di-*p*-tolylamine (Table 2, entry 3).[25,33] The general procedure using $Pd_2(dba)_3$ gave 185 mg (93%) of the title compound as a white solid.

***N*-(*p*-Tolyl)diphenylamine** (Table 2, entry 4).[34] The general procedure gave 242 mg (93%) of the title compound as a pale yellow solid.

***N*-Benzyl-*p*-toluidine** (Table 2, entry 5).[2e] The general procedure was conducted on a 2 mmol scale using 1.5 equiv of amine. The reaction was subjected to the same workup described above for *N*-(4-methylphenyl)hexylamine to afford 344 mg (87%) of the title compound as a pale yellow oil. This material contained 1% **3** as judged by GC and ^{1}H NMR analysis.

***N*,*N*-Dibutyl-*p*-toluidine** (Table 2, entry 6).[22,24] The general procedure using $Pd_2(dba)_3$ and **5** gave 193 mg (88%) of the title compound as a pale yellow oil.

***N*,*N*-Dibutyl-*p*-toluidine** (Table 2, entry 6).[22,24] The general procedure using $Pd_2(dba)_3$ and **6** gave 199 mg (91%) of the title compound as a pale yellow oil.

***N*-Ethyl-*N*-phenyl-*p*-toluidine** (Table 2, entry 7).[32] The general procedure gave 196 mg (93%) of the title compound as a pale yellow oil.

***N*-(4-Methylphenyl)piperidine** (Table 2, entry 8).[22] The general procedure gave 149 mg (85%) of the title compound as a colorless oil.

***N*-Methyl-*N*-phenyl-2,5-xylidene** (Table 2, entry 9).[5] The general procedure conducted on a 2 mmol scale gave 374 mg (89%) of the title compound as a colorless oil.

***N*-(2,5-Xylyl)cyclohexylamine** (Table 2, entry 10). The general procedure using 1 mol % $Pd(OAc)_2$ gave 197 mg (97%) of the title compound as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.92 (d, 1H, J = 7.4 Hz), 6.45−6.40 (m, 2H), 3.35−3.25 (m, 2H), 2.28 (s, 3H), 2.08 (s, br, 5H), 1.80−1.55 (m, 3H), 1.45−1.10 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1, 136.6, 130.0, 118.6, 116.8, 110.9, 51.4, 33.6, 26.0, 25.0, 21.6, 17.1; IR (neat, cm^{-1}) 3427, 2927, 1520, 789. Anal. Calcd for $C_{14}H_{21}N$: C, 82.70; H, 10.41. Found: C, 82.51; H, 10.78.

***N*-(2,5-Xylyl)pyrrolidine** (Table 2, entry 11).[25,26] The general procedure conducted on a 2 mmol scale gave 346 mg (99%) of the title compound as a colorless oil.

***N*-(2,5-Xylyl)morpholine** (Table 2, entry 12).[2e] The general procedure conducted on a 2 mmol scale gave 340 mg (89%) of the title compound as a colorless oil.

2-Methoxy-2′,4′-dimethyldiphenylamine (Table 2, entry 13). The general procedure using $Pd_2(dba)_3$ gave 228 mg (94%) of the title compound as a white solid, mp 90−91.5 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16 (s, 1H), 7.12 (d, J = 7.5 Hz, 1H), 7.05 (dd, J = 7.66, 2.2 Hz, 1H), 6.93−6.84 (m, 3H), 6.79 (d, J = 7.6 Hz, 1H), 5.86 (s, 1H), 3.93 (s, 3H), 2.31 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.2, 140.8, 136.5, 134.2, 130.9, 126.4, 123.1, 121.0, 120.4, 119.3, 114.6, 110.5, 55.8, 21.4, 17.7; IR (neat, cm^{-1}) 3411, 3062, 3045, 3006, 2964, 2933, 2919, 2856, 2836, 1598, 1576, 1521, 1501, 1449, 1412, 1341, 1293, 1243, 1220, 1179, 1115, 1048, 1030, 1000, 886, 809, 772, 741, 708. Anal. Calcd for $C_{15}H_{17}NO$: C, 79.26; H, 7.54. Found: C, 79.18; H, 7.56.

***N*-Benzyl-2,5-xylidene** (Table 2, entry 14). The general procedure conducted on a 2 mmol scale gave 387 mg (92%) of the title compound as a colorless oil.

***N*-(2,5-Dimethylphenyl)aminoacetoaldehyde Diethyl Acetal** (Table 2, entry 15). The general procedure conducted on a 2 mmol scale using a reaction temperature of 100 °C gave 474 mg (100%) of the title compound as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.93 (d, 1 H, J = 7.4 Hz), 6.48 (d, 1 H, J = 7.4 Hz), 6.45 (s, 1 H), 4.74 (t, 1H, J = 5.8 Hz), 3.80−3.52 (m, 5 H), 3.28 (d, 2 H, J = 5.7 Hz), 2.28 (s, 3 H), 2.10 (s,3 H), 1.25 (t, 6 H J = 7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.8, 136.8, 130.1, 119.4, 118.0, 111.1, 101.0, 62.4, 46.4, 21.8, 17.2, 15.6. IR (neat, cm^{-1}) 3421, 1522, 1125, 1059, 793; Anal. Calcd for $C_{14}H_{23}NO_2$: C, 70.85; H, 9.77. Found: C,70.70; H, 9.84.

***N*-*p*-Anisidylpyrrolidine** (Table 2, entry 16).[14a] The general procedure using 1 mol % $Pd(OAc)_2$ gave 159 mg (90%) of the title compound as a white solid.

(31) Vernaudon, P.; Rajoharison, H. G.; Roussel, C. *Bull. Chem. Soc. Fr.* **1987**, 205−211.
(32) Haga, K.; Oohashi, M.; Kaneko, R. *B. Chem. Soc. Jpn.* **1984**, *57*, 1586−1590.
(33) *Dictionary of Organic Compounds*, 6th ed.; Cadogan, J. I. G., Ley, S. V., Pattenden, G., Raphael, R. A., Rees, C. W., Eds.; Chapman & Hill: London, 1996; p 2611.
(34) Marsden, R. J. B. *J. Chem. Soc.* **1937**, 627.

4-[2-(*p*-Anisidyl)ethyl]morpholine (Table 2, entry 17). The general procedure conducted on a 2 mmol scale gave 420 mg (89%) of the title compound as a pale yellow oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.79 (d, 2 H, J = 9.0 Hz), 6.61 (m, 2 H, J = 9.0 Hz), 4.04 (br, s, 1 H), 3.75 (s, 3 H), 3.72 (m, 4 H, J = 4.5 Hz), 3.12 (t, 2 H, J = 6.0 Hz), 2.62 (t, 2 H, J = 6.0 Hz), 2.47 (m, 4 H, J = 4.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.3, 142.9, 115.1, 114.4, 67.1, 56.0, 57.5, 53.6, 41.1; IR (neat, cm^{-1}) 3367, 2950, 1235, 1115, 1036. Anal. Calcd for $C_{13}H_{20}N_2O_2$: C, 66.07; H, 8.53. Found: C, 65.87; H, 8.62.

1-(4-Methoxyphenyl)-4-methylpiperazine (Table 2, entry 18).[35] The general procedure conducted on a 2 mmol scale using ligand **4** gave 341 mg (83%) of the title compound as a yellow solid.

4,4′-Dimethoxydiphenylamine (Table 2, entry 19).[30] The general procedure using $Pd_2(dba)_3$ gave 217 mg (95%) of the title compound as a pale yellow solid.

Benzophenone *N*-(2-Methoxyphenyl)hydrazone (Table 2, entry 20).[36] The general procedure using $Pd_2(dba)_3$ gave 278 mg (92%) of the title compound as a pale yellow solid.

***N*-(2-Methoxyphenyl)benzylamine** (Table 2, entry 21).[28] The general procedure conducted on a 2 mmol scale gave 423 mg (99%) of the title compound as a colorless oil.

***N*-(2-Methoxyphenyl)pyrrolidine** (Table 2, entry 22).[37] The general procedure conducted on a 2 mmol scale gave 314 mg (89%) of the title compound as a colorless oil.

***N*-(*p*-Tolyl)-3,5-dimethoxyaniline** (Table 2, entry 23). The general procedure using $Pd_2(dba)_3$ gave 228 mg (94%) of the title compound as a white solid, mp 66.5−67.5 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.11 (d, J = 8.6 Hz, 2H), 7.04 (d, J = 8.5 Hz, 2H), 6.20 (d, J = 2.1 Hz, 2H), 6.05 (t, J = 2.2 Hz, 1H), 5.64 (s, 1H), 3.77 (s, 6H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8, 146.3, 139.9, 131.6, 130.0, 120.0, 95.1, 92.5, 55.4, 20.9; IR (neat, cm^{-1}) 3367, 3012, 966, 2937, 2840, 1594, 1513, 1478, 1459, 1254, 1200, 1189, 1165, 1144, 1057, 924, 822, 810, 770, 720, 683. Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04. Found: C, 74.06; H, 7.23.

***N*-Benzhydrilidene-3,5-dimethoxyaniline** (Table 2, entry 24). The general procedure using $Pd_2(dba)_3$ (1 mol % Pd) and ligand **4** gave 316 mg (100%) of the title compound as a pale yellow solid, mp 101−102 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76−7.71 (m, 2 H), 7.49−7.12 (m, 8 H), 6.06 (t, 1 H, J = 2.1), 5.91 (d, 2 H, J = 2.1 Hz), 3.62 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.5, 160.8, 153.14, 139.6, 136.3, 130.9, 129.5, 129.4, 128.8, 128.3, 128.1, 99.4, 96.1, 55.4; IR (neat, cm^{-1}) 1594, 1208, 1154, 1123, 704. Anal. Calcd for $C_{21}H_{19}NO_2$: C, 79.47; H, 6.03. Found: C, 79.61; H, 6.19.

***N*-(2,6-Dimethylphenyl)morpholine** (Table 2, entry 25). The general procedure using 1 mol % $Pd(OAc)_2$, ligand **2**, and a reaction temperature of 110 °C gave 162 mg (86%) of the title compound as a white solid, mp 86−87 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01−6.92 (m, 3 H), 3.79 (m, 4 H, J = 4.5 Hz), 3.08 (m, 4 H, J = 4.5 Hz), 2.34 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.1, 137.1, 129.2, 125.5, 68.3, 50.2, 19.8; IR (neat, cm^{-1}) 1260, 1109, 939, 843, 782. Anal. Calcd for $C_{12}H_{17}NO$: C, 75.36; H, 8.96. Found: C, 75.35; H, 9.26.

***N*-(2,6-Dimethylphenyl)benzylamine** (Table 2, entry 26).[38] The general procedure using 1 mol % $Pd(OAc)_2$ and 1.5 equiv of benzylamine gave 183 mg (87%) of the title compound as a colorless oil.

2,6-Diisopropyl-2′,6′-dimethyldiphenylamine (Table 2, entry 27).[6e] The general procedure using $Pd_2(dba)_3$ (4 mol % Pd) gave 212 mg (75%) of the title compound as a white solid.

Chloropyridine Derivatives.

***N*-Benzyl-2-aminopyridine** (Table 4, entry 1).[39] The general procedure conducted on a 2 mmol scale using 1.5 equiv of benzylamine and a reaction temperature of 100 °C gave 358 mg (97%) of a white solid, which was determined to be a 19/1 mixture (by ^{1}H NMR) of the title compound and bis(2-pyridyl)-benzylamine.

***N*-(2-Pyridyl)morpholine** (Table 4, entry 2).[9] The general procedure conducted on a 2 mmol scale using a reaction temperature of 100 °C and ligand **4** gave 319 mg (97%) of the title compound as a pale yellow oil.

***N*-Methyl-*N*-(3-pyridyl)aniline** (Table 4, entry 3).[9] The general procedure using 1 mol % $Pd(OAc)_2$, ligand **4**, and a reaction temperature of 110 °C gave 178 mg (97%) of the title compound as a pale yellow oil.

***N*-Methyl-*N*-(3-pyridyl)aniline** (Table 4, entry 3).[9] The general procedure using 1 mol % $Pd(OAc)_2$, ligand **2**, and a reaction temperature of 110 °C gave 176 mg (96%) of the title compound as a pale yellow oil.

***N*-Benzyl-3-aminopyridine** (Table 4, entry 4).[40] The general procedure using 1 mol % $Pd(OAc)_2$, 1.5 equiv of benzylamine, and a reaction temperature of 110 °C gave 161 mg (88%) of the title compound as a pale green solid.

***N*-Hexyl-3-aminopyridine** (Table 4, entry 5).[9] The general procedure using 3 equiv of hexylamine, 1 mol % $Pd(OAc)_2$, ligand **2**, and a reaction temperature of 100 °C gave 134 mg (75%) of the title compound as a white solid.

***N*-(3-Pyridyl)morpholine** (Table 4, entry 6).[9] The general procedure using 1 mol % $Pd(OAc)_2$ and a reaction temperature of 110 °C gave 116 mg (71%) of the title compound as a pale yellow oil.

***N*,*N*-Dibutyl-3-aminopyridine** (Table 4, entry 7).[6d] The general procedure using 1 mol % $Pd(OAc)_2$, ligand **2**, and a reaction temperature of 110 °C gave 171 mg (83%) of the title compound as a pale yellow oil.

***N*-(4-Pyridyl)morpholine** (Table 4, entry 8).[9] The general procedure using 1 mol % $Pd(OAc)_2$, 2 mol % **3**, 2.8 equiv of K_3PO_4, dioxane solvent, and a reaction temperature of 100 °C gave 124 mg (76%) of the title compound as a white solid.

***N*-Benzyl-4-aminopyridine** (Table 4, entry 9).[41] The general procedure using 1 mol % $Pd(OAc)_2$, 2 mol % **4**, 2.8 equiv of NaO*t*-Bu, dioxane solvent, and a reaction temperature of 100 °C gave 132 mg (72%) of a white solid, mp 108−110 °C (CH_2Cl_2/hexanes) (lit. mp 110.5−111 °C),[41] which was determined to contain 3.6% of bis(4-pyridyl)benzylamine by ^{1}H NMR analysis.

***N*-Methyl-*N*-(4-pyridyl)aniline** (Table 4, entry 10).[25] The general procedure using 1 mol % $Pd(OAc)_2$, 2 mol % **4**, 2.8 equiv of NaO*t*-Bu, dioxane solvent, and a reaction temperature of 100 °C gave 171 mg (93%) of a yellow oil.

General Procedure for the Catalytic Amination of Aryl Bromides at 80−110 °C. An oven-dried resealable Schlenk flask was evacuated and backfilled with argon. The flask was charged with $Pd_2(dba)_3$ (2.3 mg, 0.0025 mmol, 0.5 mol % Pd), **3** (3.0 mg, 0.01 mmol, 1.0 mol %), and NaO*t*-Bu (135 mg, 1.4 mmol) and evacuated and backfilled with argon. The flask was capped with a rubber septum, and toluene (2 mL/mmol halide), the aryl bromide (1.0 mmol), and the amine (1.2 mmol) were added through the septum (aryl bromides or amines that were solids at room temperature were added as solids following the addition of NaO*t*-Bu). The septum was replaced with a Teflon screwcap, the flask was sealed, and the mixture was heated to 80 °C with stirring until the starting aryl bromide had been completely consumed as judged by GC analysis. The mixture was cooled to room temperature, diluted with ether (30 mL), filtered through Celite, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

Workup Method B. Following complete consumption of the aryl halide starting material, the mixture was diluted with ether (50 mL) and transferred to a separatory funnel. The mixture was washed with aqueous HCl (1 M, 2 × 20 mL) and then with brine (20 mL), dried over anhydrous magnesium

(35) Davis, W.; Ross, W. C. J. *J. Chem. Soc.* **1949**, 2831−2834.
(36) Busch, M.; Kunder, H. *Ber. Dtsch. Chem. Ges.* **1916**, *49*, 317−334.
(37) Shim, S. C.; Huh, K. T.; Park, W. H. *Tetrahedron* **1986**, *42*, 259−263.
(38) Maccarone, E.; Mamo, A.; Torre, M. *J. Org. Chem.* **1979**, *44*, 1143−1145.
(39) Sprinzak, Y. *Org. Synth. Coll. Vol. IV* **1963**, 91−92.
(40) Trifonov, L. S.; Orahovats, A. S. *Helv. Chim. Acta* **1987**, *90*, 1732−1736.
(41) Okuda, S.; Robison, M. M. *J. Org. Chem.* **1959**, *24*, 1008−1011.

sulfate, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

***N*-(4-Methylphenyl)morpholine** (Table 7, entry 1).[22,23] The general procedure conducted on a 2 mmol scale using $Pd(OAc)_2$ gave 329 mg (93%) of the title compound as a white solid.

4-Methoxy-4′-(dimethylamino)diphenylamine (Table 7, entry 2).[42] The general procedure gave 229 mg (95%) of the title compound as a pale yellow solid.

***N*-(*p*-Tolyl)-*p*-anisidine** (Table 7, entry 3).[30] The general procedure gave 194 mg (91%) of the title compound as a pale yellow solid.

***N*-Ethyl-*N*-(3,5-dimethylphenyl)aniline** (Table 7, entry 4).[6d] The general procedure using $Pd(OAc)_2$ gave 188 mg (84%) of the title compound as a pale yellow oil.

***N*-Benzyl-3,5-xylidene** (Table 7, entry 5).[5] The general procedure using 1.5 equiv benzylamine gave 174 mg (82%) of the title compound as a colorless oil.

***N*-Mesityl-3,4-(methylenedioxy)aniline** (Table 7, entry 6).[30] The general procedure gave 245 mg (96%) of the title compound as a pale yellow solid.

***N*-(4-*tert*-Butylphenyl)piperidine** (Table 7, entry 7).[14a] The general procedure using ligand **4** gave 185 mg (85%) of the title compound as a white solid.

***N*,*N*-Dibutyl-4-*tert*-butylaniline** (Table 7, entry 8).[6d] The general procedure using ligand **4** gave 222 mg (85%) of the title compound as a colorless oil.

***N*,*N*-Dibutyl-4-*tert*-butylaniline** (Table 7, entry 8).[6d] The general procedure using ligand **5** gave 237 mg (91%) of the title compound as a colorless oil.

***N*-Methyl-*N*-phenyl-2,5-xylidene** (Table 7, entry 9).[5] The general procedure using ligand **4** gave 159 mg (75%) of the title compound as a colorless oil.

***N*-Allyl-2,5-xylidene** (Table 7, entry 10).[43] The general procedure gave 149 mg (93%) of the title compound as a colorless oil.

General Procedure for the Catalytic Amination of Aryl Triflates at 65−80 °C. An oven-dried resealable Schlenk flask was evacuated and backfilled with argon. The flask was charged with $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol, 1.0 mol % Pd), **3** (6.0 mg, 0.02 mmol, 2.0 mol %), and K_3PO_4 (297 mg, 1.4 mmol) and evacuated and backfilled with argon. The flask was capped with a rubber septum, and DME (2 mL/mmol halide), the aryl triflate (1.0 mmol), and the amine (1.2 mmol) were added through the septum (aryl triflates or amines that were solids at room temperature were added as solids following the addition of K_3PO_4). The septum was replaced with a Teflon screwcap, the flask was sealed, and the mixture was heated to 80 °C with stirring until the starting aryl triflate had been completely consumed as judged by GC analysis. The mixture was cooled to room temperature, diluted with ether (30 mL), filtered through Celite, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

Workup Method B. Following complete consumption of the aryl halide starting material, the mixture was diluted with ether (50 mL) and transferred to a separatory funnel. The mixture was washed with aqueous HCl (1 M, 2 × 20 mL) and then with brine (20 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

***N*-(4-*tert*-Butylphenyl)morpholine** (Table 9, entry 1).[29] The general procedure using $Pd(OAc)_2$, THF as solvent, and a reaction temperature of 65 °C gave 201 mg (92%) of the title compound as a white solid.

***N*-(4-*tert*-Butylphenyl)-*p*-anisidine** (Table 9, entry 2). The general procedure using workup method B gave 221 mg (87%) of the title compound as a pale yellow solid, mp 80−82 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30−7.20 (m, 2H), 7.10−6.75 (m, 6H), 5.50 (s, br, 1H), 3.20 (s, 3H), 1.29 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.8, 142.6, 142.4, 136.6, 126.0, 121.3, 115.7, 114.6, 55.5, 34.0, 31.5; IR (neat, cm^{-1}) 3381, 2961, 1509, 1235, 1031, 818. Anal. Calcd for $C_{17}H_{21}NO$: C, 79.96; H, 8.29. Found: C, 79.85; H, 8.29.

***N*-(4-*tert*-Butylphenyl)benzylamine** (Table 9, entry 3). The general procedure using $Pd(OAc)_2$,1.5 equiv of benzylamine, NaO*t*-Bu, and toluene as solvent gave 163 mg (68%) of the title compound as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.26 (m, 5H), 7.20 (d, 2H, J = 6.7 Hz), 6.60 (d, 2H, J = 6.5 Hz), 4.31 (s, 2H), 3.95 (s, br, 1H), 1.27 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.8, 140.3, 139.6, 128.6, 127.5, 127.1, 126.0, 112.5, 48.6, 33.8, 31.5; IR (neat, cm^{-1}) 3416, 2961, 1613, 1521, 818. Anal. Calcd for $C_{17}H_{21}N$: C, 85.30; H, 5.85. Found: C, 85.37; H, 8.91.

***N*,*N*-Dibutyl-*p*-*tert*-butylaniline** (Table 9, entry 4).[6d] The general procedure using $Pd(OAc)_2$, 2 mol % **4**, NaO*t*-Bu, and toluene as solvent gave 185 mg (71%) of the title compound as a colorless oil.

4-Methoxy-4′-nitrodiphenylamine (Table 9, entry 5).[44] The general procedure using K_3PO_4 as the base, 0.5 mol % $Pd_2(dba)_3$, and DME as solvent (the material was purified by crystallization from ethanol instead of by flash chromatography) gave 183 mg (75%) of the title compound as a yellow solid.

***N*-(2-Methoxyphenyl)benzylamine** (Table 9, entry 6).[28] The general procedure using 1.0 mol % $Pd(OAc)_2$ gave 172 mg (81%) of the title compound as a colorless oil.

***N*-(3,4-Dimethylphenyl)pyrrolidine** (Table 9, entry 7). The general procedure using ligand **4** gave 155 mg (89%) of the title compound as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.97 (d, 1H, J = 8.1 Hz), 6.40−6.33 (m, 2H), 3.26−3.21 (m, 4H), 2.23 (s, 3H), 2.16 (s, 3H), 2.00−1.94 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.6, 137.0, 130.1, 113.3, 109.2, 47.8, 25.4, 20.2, 18.6; IR (neat, cm^{-1}) 2922, 1613, 1363, 796. Anal. Calcd for $C_{12}H_{17}N$: C, 82.23; H, 9.78. Found: C, 82.37; H, 9.81.

2-Methoxy-4′-cyanodiphenylamine (Table 9, entry 8). The general procedure using THF solvent (the product was purified by recrystallization from ethanol/hexanes instead of by chromatography) gave 194 mg (87%) of the title compound as a pale yellow solid, mp 108−109 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 8.7 Hz, 2H), 7.37 (d, J = 7.5 Hz, 1H), 7.08−6.94 (m, 5H), 6.38 (s, 1H), 3.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.2, 147.6, 133.8, 129.7, 123.4, 120.9, 120.1, 118.9, 115.6, 111.2, 101.8, 55.8; IR (neat, cm^{-1}) 3321, 3045, 3002, 2968, 2929, 2831, 2217, 1611, 1598, 1586, 1522, 1507, 1488, 1459, 1341, 1328, 1295, 1248, 1175, 1111, 1028, 830, 820, 741. Anal. Calcd for $C_{14}H_{12}N_2O$: C, 74.98; H, 5.39. Found: C, 74.95; H, 5.32.

***N*-(4-Acetylphenyl)-*m*-toluidine** (Table 9, entry 9). The general procedure using workup method B gave 211 mg (94%) of the title compound as a yellow solid, mp 89−91 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.86 (d, 2H, J = 6.9 Hz), 7.23 (t, 1H, J = 6.6 Hz), 6.97−6.87 (m, 4H), 6.11 (s, 1H), 2.53 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.4, 148.5, 140.5, 139.4, 130.6, 129.2, 128.7, 124.1, 121.3, 117.7, 114.3, 26.1, 21.4; IR (neat, cm^{-1}) 3312, 3053, 1656, 1583, 1278, 1166, 764. Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71. Found: C, 79.77; H, 6.64.

***N*-(4-Nitrophenyl)piperidine** (Table 9, entry 10).[11,45] The general procedure gave 168 mg (82%) of the title compound as a yellow solid.

Procedures for the Catalytic Amination of Aryl Chlorides at Low Catalyst Loadings. *N*-Methyl-*N*-phenyl-*p*-toluidine[22] (Table 3, entry 1). An oven-dried Schlenk flask was evacuated and backfilled with argon. The flask was charged with NaO*t*-Bu (270 mg, 2.8 mmol) and then evacuated and backfilled with argon, and toluene (1 mL), 4-chlorotoluene (0.24 mL, 2.0 mmol), and *N*-methylaniline (0.26 mL, 2.4 mmol) were added through a rubber septum. A separate flask was charged with $Pd_2(dba)_3$ (9.2 mg, 0.01 mmol) and ligand **3** (12.0 mg, 0.04 mmol) and was purged with argon. Toluene (4 mL) was added, the mixture was stirred for 1 min at room temperature, and then 200 μL of this solution (0.05 mol % Pd,

(42) Wieland, H. *Ber. Dtsch. Chem. Ges.* **1920**, *53*, 1313−1328.
(43) Hussein, F. A.; Kazandji, S. Y. *J. Indian Chem. Soc.* **1966**, *43*, 663−668.
(44) Ullmann, F.; Jüngel, K. *Ber. Dtsch. Chem. Ges.* **1909**, *42*, 1077−1083.
(45) Verardo, G.; Giumanini, A. G.; Favret, G.; Strazzolini, P. *Synthesis* **1991**, 447−450.

0.1 mol % ligand **3**) was added to the Schlenk flask followed by additional toluene (1 mL). The septum was removed; the flask was sealed with a Teflon screwcap and the mixture was stirred at room temperature for 2 min and then heated to 100 °C with stirring until the starting aryl chloride had been completely consumed as judged by GC analysis. The mixture was cooled to room temperature, diluted with ether, and filtered through Celite. The crude product was purified by flash chromatography on silica gel to give 378 mg (96%) of the title compound as a colorless oil.

***N*-(4-Methylphenyl)morpholine**[22,23] (Table 3, entry 2). An oven-dried Schlenk flask was evacuated and backfilled with argon. The flask was charged with NaO*t*-Bu (270 mg, 2.8 mmol) and then evacuated and backfilled with argon, and toluene (1 mL), 4-chlorotoluene (0.24 mL, 2.0 mmol), and morpholine (0.20 mL, 2.4 mmol) were added through a rubber septum. A separate flask was charged with $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol) and ligand **4** (7.0 mg, 0.02 mmol) and was purged with argon. THF (1 mL) was added, the mixture was stirred for 1 min at room temperature, and then 100 μL of this solution (0.05 mol % Pd, 0.1 mol % ligand **4**) was added to the Schlenk flask followed by additional toluene (1 mL). The septum was removed; the flask was sealed with a Teflon screwcap, and the mixture was stirred at room temperature for 2 min and then heated to 100 °C with stirring until the starting aryl chloride had been completely consumed as judged by GC analysis. The mixture was cooled to room temperature, diluted with ether, and filtered through Celite. The crude product was purified by flash chromatography on silica gel to give 311 mg (88%) of the title compound as a white solid.

***N*-Methyl-*N*-phenyl-2,5-xylidene**[5] (Table 3, entry 3). An oven-dried Schlenk flask was evacuated and backfilled with argon. The flask was charged with NaO*t*-Bu (270 mg, 2.8 mmol) and then evacuated and backfilled with argon, and toluene (1 mL), 2-chloro-*p*-xylene (0.24 mL, 2.0 mmol), and *N*-methylaniline (0.26 mL, 2.4 mmol) were added through a rubber septum. A separate flask was charged with $Pd_2(dba)_3$ (9.2 mg, 0.01 mmol) and ligand **3** (12.0 mg, 0.04 mmol) and was purged with argon. Toluene (4 mL) was added, the mixture was stirred for 1 min at room temperature, and then 200 μL of this solution (0.05 mol % Pd, 0.1 mol % ligand **3**) was added to the Schlenk flask followed by additional toluene (1 mL). The septum was removed; the flask was sealed with a Teflon screwcap, and the mixture was stirred at room temperature for 2 min and then heated to 100 °C with stirring until the starting aryl chloride had been completely consumed as judged by GC analysis. The mixture was cooled to room temperature, diluted with ether, and filtered through Celite. The crude product was purified by flash chromatography on silica gel to give 391 mg (93%) of the title compound as a colorless oil.

2-Methoxy-2′,4′-dimethyldiphenylamine (Table 3, entry 4). An oven-dried, resealable Schlenk tube equipped with a Teflon screwcap was evacuated and backfilled with argon. The cap was removed, and the tube was charged with sodium *tert*-butoxide (1.35 g, 14.0 mmol), tris(dibenzylideneacetone) dipalladium (2.3 mg, 0.0025 mmol, 0.05 mol % Pd), and **3** (3.0 mg, 0.010 mmol, 0.10 mol %). The tube was capped with the Teflon screwcap, evacuated, and backfilled with argon. The screwcap was replaced with a rubber septum, and *o*-anisidine (1.35 mL, 12.0 mmol) was added via syringe, followed by 2-chloro-*p*-xylene (1.34 mL, 10.0 mmol) and toluene (5 mL). The tube was purged with argon for 3 min, and then the septum was replaced with a Teflon screwcap; the tube was sealed, and the contents were heated to 80 °C with stirring. Analysis by gas chromatography after 14 h indicated complete consumption of the aryl chloride. The reaction mixture was cooled to room temperature, diluted with diethyl ether (50 mL), and washed with a 1 M aqueous solution of phosphoric acid (50 mL), followed by water (50 mL). The resulting solution was dried over anhydrous potassium carbonate, filtered, and concentrated in vacuo. The residue was purified by recrystallization from methanol to give 2.20 g (97%) of the title compound as white crystals.

General Procedure for the Catalytic Amination of Functionalized Aryl Halides. An oven-dried resealable Schlenk flask was evacuated and backfilled with argon. The flask was charged with $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol, 1 mol % Pd), **4** (7.0 mg, 0.02 mmol, 2 mol %), and K_3PO_4 (297 mg, 1.4 mmol). The flask was evacuated and backfilled with argon and capped with a rubber septum. DME (2 mL), the aryl halide (1.0 mmol), and the amine (1.2 mmol) were added through the septum (aryl halides or amines that were solids at room temperature were added as solids following the addition of K_3PO_4). The septum was removed, and the flask was sealed with a Teflon screwcap. The mixture was heated to 100 °C with stirring until the starting aryl halide had been completely consumed as judged by GC analysis. The mixture was cooled to room temperature, diluted with ether or 1/1 ether/ethyl acetate (40 mL), filtered through Celite, and concentrated in vacuo. The crude material was purified by flash chromatography on silica gel.

Aryl Chlorides.

***N*-(3-Cyanophenyl)benzylamine** (Table 5, entry 1). The general procedure using 2 mol % $Pd(OAc)_2$ and 4 mol % **4** gave 163 mg (78%) of the title compound as a white solid, mp 69−70 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40−7.14 (m, 6 H), 6.97 (ddd, 1 H, 7.5, 1.4, 1.0 Hz), 6.83−6.78 (m, 2 H), 4.37 (br s, 1 H), 4.33 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.4, 138.3, 129.9, 128.9, 127.6, 127.4, 120.8, 119.6, 117.3, 115.1, 112.9, 47.8; IR (neat, cm^{-1}) 3386, 2229, 1600, 776, 691. Anal. Calcd for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81. Found: C, 80.89; H, 5.66.

***N*-(3-Cyanophenyl)pyrrolidine** (Table 5, entry 2).[46] The general procedure using $Pd(OAc)_2$ gave 144 mg (84%) of the title compound as a pale yellow solid, mp 85−86 °C.

***N*-(Diphenylmethylene)-4-nitroaniline** (Table 5, entry 3).[47] The general procedure using ligand **2** was followed; the product was purified by recrystallization from toluene/ethanol rather than chromatography to give 249 mg (82%) of the title compound as a pale yellow solid.

4-Methoxy-4′-nitrodiphenylamine (Table 5, entry 4).[44] The general procedure using ligand **3** was followed; the product was purified by recrystallization from toluene/ethanol rather than chromatography to give 222 mg (91%) of the title compound as an orange solid.

1-(3-Acetylphenyl)-4-methylpiperazine (Table 5, entry 5). The general procedure using ligand **2** gave 163 mg (75%) of the title compound as a pale orange oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (dd, 1 H, J = 2.2, 1.5 Hz), 7.41 (ddd, 1 H, J = 8.0, 1.5, 1.1 Hz), 7.33 (dd, 1 H, J = 8.0, 8.0 Hz), 7.12 (ddd, 1 H, J = 8.0, 2.2, 1.1 Hz), 3.27 (m, 4 H, J = 4.8 Hz), 2.58 (m, 4 H, J = 4.8 Hz), 2.58 (s, 3 H), 2.36 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 198.6, 151.5, 138.0, 129.3, 120.6, 120.0, 27.0, 114.8, 55.2, 49.0, 46.3; IR (neat, cm^{-1}) 1681, 1441, 1296, 1260, 687; HRMS calcd for $C_{13}H_{18}N_2O$: 218.1419. Found: 218.1415.

***N*-(3-Acetylphenyl)aniline** (Table 5, entry 6).[48] The general procedure gave 174 mg (82%) of the title compound as a yellow solid.

***N*-(3-Acetylphenyl)aniline** (Table 5, entry 6).[48] The general procedure using ligand **2** gave 179 mg (85%) of the title compound as a yellow solid.

***N*-(4-Acetylphenyl)morpholine** (Table 5, entry 7).[2e,49] The general procedure using $Pd(OAc)_2$, ligand **3**, and a reaction temperature of 80 °C gave 187 mg (91%) of the title compound as a pale yellow solid.

***N*-(4-Acetylphenyl)-*p*-toluidine** (Table 5, entry 8).[11,50] The general procedure gave 211 mg (94%) of the title compound as a pink solid.

***N*-(4-Carbomethoxyphenyl)morpholine** (Table 5, entry 9).[2e] The general procedure using $Pd(OAc)_2$ and a reaction temperature of 80 °C gave 198 mg (90%) of the title compound as a pale yellow solid.

(46) Sznaidman, M. L.; Meade, E. A.; Beauchamp, L. M.; Russell, S.; Tisdale, M. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 565−568.
(47) Reddelien, G. *Ber. Dtsch. Chem. Ges.* **1914**, *47*, 1355−1364.
(48) Elson, L. A.; Gibson, C. S. *J. Chem. Soc.* **1931**, 2381−2388.
(49) Kotsuki, H.; Kobayashi, S.; Matsumoto, K.; Suenaga, H.; Nishizawa, H. *Synthesis* **1990**, 1147−1148.
(50) Iter, J.; Casadevall, A. *Bull. Chem. Soc. Fr.* **1969**, 2342−2355.

4-Carbomethoxyphenyl-4′-nitrodiphenylamine (Table 5, entry 10). The general procedure was followed; the product was isolated by recrystallization from methanol rather than by chromatography to give 224 mg (82%) of the title compound as a pale yellow solid, mp 160 °C: ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (d, 2H, J = 9.1 Hz), 8.04 (d, 2H, J = 8.8 Hz), 7.21 (d, 2H, J = 8.8 Hz), 7.12 (d, 2H, J = 9.1 Hz), 6.54 (s, br, 1H), 3.92 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4, 148.0, 144.3, 140.8, 131.4, 126.0, 124.4, 118.4, 115.6, 52.1; IR (neat, cm^{-1}) 3347, 2957, 1687, 1586, 1486, 1108, 830. Anal. Calcd for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44. Found: C, 61.75; H, 4.52.

***N*-(4-Cyanophenyl)hexylamine** (Table 5, entry 11).[5] The general procedure using NaO*t*-Bu, toluene solvent, and a reaction temperature of 110 °C gave 153 mg (76%) of the title compound as a pale yellow solid.

4-Cyano-2′-carboethoxydiphenylamine (Table 5, entry 12).[11,14b] The general procedure was followed; the product purified by recrystallization from ethanol instead of by chromatography gave 195 mg (73%) of the title compound as a yellow solid.

***N*-(3-Carbomethoxyphenyl)morpholine** (Table 5, entry 13).[11,14b] The general procedure gave 201 mg (91%) of the title compound as a pale yellow oil.

***N*-(3-Carbomethoxyphenyl)-*N*-methylaniline** (Table 5, entry 14). The general procedure gave 215 mg (89%) of the title compound as a pale orange oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (dd, 1 H, J = 2.7, 1.2 Hz), 7.56 (ddd, 1 H, J = 7.8, 2.7, 1.2 Hz), 7.35−7.25 (m, 3 H), 7.13 (ddd, 1 H, J = 7.2, 2.7, 1.2 Hz), 7.10−7.01 (m, 3 H), 3.88 (s, 3 H), 3.34 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.4, 149.3, 148.7, 131.3, 129.6, 129.1, 123.4, 122.9, 122.3, 121.5, 119.4, 52.2, 40.4; IR (neat, cm^{-1}) 1723, 1592, 1289, 1262, 1111. Anal. Calcd for $C_{15}H_{15}NO_2$: C, 74.67; H, 6.27. Found: C, 74.65; H, 6.13.

***N*-(3-Carbomethoxyphenyl)-*N*-methylaniline** (Table 5, entry 14). The general procedure using ligand **2** gave 189 mg (78%) of the title compound as a pale orange oil.

2-Nitro-4′-methoxydiphenylamine (Table 5, entry 15).[51] The general procedure was followed using 2.5 mol % $Pd_2(dba)_3$; the product was isolated by recyrstallization from methanol instead of by chromatogrophy to give 165 mg (68%) of the title compound as a yellow solid.

2-Carbomethoxy-3′-methyldiphenylamine (Table 5, entry 16).[52] The general procedure using 2.5 mol % $Pd_2(dba)_3$ gave 195 mg (81%) of the title compound as a colorless oil.

Aryl Bromides.

***N*-(3-Carbomethoxyphenyl)morpholine** (Table 7, entry 11). The general procedure using ligand **2** gave 193 mg (87%) of the title compound as a pale yellow oil.

***N*-(3-Carbomethoxyphenyl)-*N*-methylaniline** (Table 7, entry 12). The general procedure using 1.5 mol % $Pd_2(dba)_3$, ligand **4**, and 1 mL of DME/mmol bromide gave 140 mg (58%) of the title compound as a pale yellow oil.

***N*-(4-Cyanophenyl)benzylamine** (Table 7, entry 13).[53] The general procedure using 3 mol % $Pd(OAc)_2$ and 1 mL of toluene/mmol bromide gave 165 mg (79%) of the title compound as a white solid.

4-Acetyl-4′-methyldiphenylamine (Table 7, entry 14). The general procedure using 1 mL of toluene/mmol bromide gave 210 mg (93%) of the title compound as a pale yellow solid.

2-Carbomethoxy-3′-methyldiphenylamine (Table 7, entry 15). The general procedure using 2.5 mol % $Pd_2(dba)_3$, ligand **4**, and 1 mL of DME/mmol halide gave 236 mg (98%) of the title compound as a pale yellow oil.

Oligoanilines.

***N*-(4-Aminophenyl)-*N*′-[4-(trimethylsilyl)phenyl]-*N*,*N*′-bis(*tert*-butoxycarbonyl)-1,4-phenylenediamine (Trimer Amine 8).** Prepared by analogy to previously reported procedures.[15] Obtained as a white solid: mp 161.5−163 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J = 8.4 Hz, 2H), 7.18−7.11 (m, 6H), 6.98 (d, J = 8.7 Hz 2H), 6.62 (d, J = 8.7 Hz, 2H), 3.66 (s, 2H), 1.46 (s, 9H), 1.44 (s, 9H), 0.249 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.4, 154.0, 144.8, 143.5, 141.1, 139.8, 137.6, 134.0, 133.9, 128.7, 127.3, 126.4, 126.1, 115.4, 81.4, 81.1, 28.5, 28.4, −0.9; IR (neat, cm^{-1}) 3456, 3367, 2979, 1704, 1688, 1521, 1511, 1370, 1335, 1285, 1248, 1164, 1057, 857, 839, 820, 766, 754. Anal. Calcd for $C_{31}H_{41}N_3O_4Si$: C, 67.97; H, 7.54. Found: C, 68.10; H, 7.54.

***N*-(4-Chlorophenyl)-*N*-(*tert*-butoxycarbonyl)-*N*′-(diphenylmethylene)-1,4-phenylenediamine (Dimer Chloride 9).** Palladium-catalyzed cross-coupling of 4-chloroaniline with *N*-(diphenylmethylene)-4-bromoaniline was carried out using DPEphos as the supporting ligand, under previously reported conditions.[6e] The resulting diarylamine was converted to its BOC-derivative under previously reported conditions.[15] The title compound was obtained as yellow crystals in 81% yield (two steps): mp 166−168 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, J = 8.2 Hz, 2H), 7.49−7.42 (m, 3H), 7.29−7.22 (m, 5H), 7.15−7.08 (m, 4H), 6.96 (d, J = 8.8 Hz, 2H), 6.69 (d, J = 8.8 Hz, 2H), 1.41 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.0, 153.7, 149.6, 141.9, 139.6, 138.0, 136.2, 131.1, 130.5, 129.7, 129.5, 128.9, 128.7, 128.4, 128.1, 127.7, 127.3, 121.6, 81.4, 28.3; IR (neat, cm^{-1}) 3056, 3033, 3024, 3002, 2973, 1698, 1613, 1594, 1573, 1494, 1337, 1293, 1223, 1158, 1142, 1088, 1056, 1015, 959, 853, 836, 787, 768, 697, 677, 666. Anal. Calcd for $C_{30}H_{27}ClN_2O_2$: C, 74.60; H, 5.63. Found: C, 74.70; H, 5.62.

Pentamer 10. Trimer amine **8** (0.845 g, 1.54 mmol), dimer chloride **9** (0.676 g, 1.40 mmol), sodium *tert*-butoxide (0.188 g, 1.96 mmol), tris(dibenzylideneacetone) dipalladium (3.2 mg, 0.0035 mmol, 0.5 mol % Pd), and **3** (4.2 mg, 0.014 mmol, 1.0 mol %) were placed in an oven-dried, resealable Schlenk tube. The tube was fitted with a Teflon screwcap, evacuated, and backfilled with argon. The screwcap was replaced with a rubber septum, and toluene (4 mL) was added via syringe. The septum was replaced with the Teflon screwcap; the tube was sealed, and the reaction mixture was heated to 80 °C with stirring. Analysis by TLC after 12 h indicated the complete consumption of the aryl chloride starting material. The reaction mixture was cooled to room temperature, taken up in dichloromethane (50 mL), washed with water (50 mL), dried over anhydrous potassium carbonate, and filtered. The resulting solution was transferred to an oven-dried Schlenk flask and converted to its BOC-derivative under previously reported conditions.[15] The resulting orange solid was crystallized from ethanol, and the product was recrystallized from a mixture of toluene and ethanol, affording the title compound as pale yellow microcrystals, 1.32 g (86%): mp 191−193 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 8.3 Hz, 2H), 7.46−7.41 (m, 5H), 7.29−7.26 (m, 3H), 7.19−7.09 (m, 16H), 6.97 (d, J = 8.5 Hz, 2H), 6.69 (d, J = 8.5 Hz, 2H), 1.46 (s, 9H), 1.45 (s, 18H), 1.40 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.8, 153.9, 153.8, 153.8, 149.2, 143.3, 140.6, 140.4, 140.3, 140.2, 140.2, 139.6, 138.1, 137.6, 136.1, 133.9, 131.0, 129.6, 129.4, 128.8, 128.3, 128.0, 127.6, 127.4, 127.1, 127.0, 126.2, 126.0, 121.5, 81.5, 81.5, 81.2, 28.4, −0.9; IR (neat, cm^{-1}) 3002, 2975, 2935, 1706, 1511, 1368, 1328, 1293, 1252, 1160, 1059, 861, 839, 824, 766, 699. Anal. Calcd for $C_{66}H_{75}N_5O_8Si$: C, 72.43; H, 6.91. Found: C, 72.25; H, 6.94.

Pentamer Amine 11. Prepared by analogy to previously reported procedures.[15] Obtained as a white solid: mp 145−147 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44 (d, J = 8.3 Hz, 2H), 7.19−7.07 (m, 14H), 6.97 (d, J = 8.4 Hz, 2H), 6.63 (d, J = 8.4 Hz), 3.67 (broad s, 2H), 1.46 (s, 9H), 1.44 (s, 27H), 0.254 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2, 153.8, 144.7, 143.3, 141.1, 140.3, 140.2, 140.1, 139.4, 137.6, 133.8, 133.7, 128.5, 127.4, 127.1, 127.0, 126.3, 126.0, 115.3, 81.5, 81.4, 81.0, 28.4, −0.9; IR (neat, cm^{-1}) 3444, 3371, 2977, 1710, 1513, 1368, 1322, 1287, 1252, 1162, 1059, 841, 830, 764. Anal. Calcd for $C_{53}H_{67}N_5O_8Si$: C, 68.43; H, 7.26. Found: C, 68.38; H, 7.26.

Nonamer 13. Pentamer amine **11** (0.424 g, 0.456 mmol), tetramer bromide **12**[15] (0.395 g, 0.434 mmol), sodium *tert*-butoxide (0.0584 g, 0.608 mmol), tris(dibenzylideneacetone) dipalladium (2.0 mg, 0.0022 mmol, 1.0 mol % Pd), and **3** (2.6 mg, 0.0088 mg, 2.0 mol %) were placed in an oven-dried, resealable Schlenk tube. The tube was fitted with a Teflon screwcap, evacuated, and backfilled with argon. The screwcap

(51) Gale, D. J.; Wilshire, J. F. *Aust. J. Chem.* **1972**, *25*, 2145−2154.
(52) Legrand, L.; Lozac'h, N. *Bull. Chem. Soc. Fr.* **1969**, 1173−1182.
(53) Grigg, R.; Mitchell, T. R. B.; Tongpenyai, N. *Synthesis* **1981**, 442−444.

was replaced with a rubber septum, and toluene (1.6 mL) was added via syringe. The septum was replaced with the Teflon screwcap; the tube was sealed, and the reaction mixture was heated to 60 °C with stirring. Analysis by TLC after 8 h indicated the complete consumption of the aryl bromide starting material. The reaction mixture was cooled to room temperature, taken up in dichloromethane (50 mL), and washed with water (50 mL). The aqueous phase was extracted with dichloromethane (15 mL). The combined organic portions were dried over anhydrous potassium carbonate and filtered; the resulting solution was transferred to an oven-dried Schlenk flask and converted to its BOC-derivative under previously reported conditions.[15] The resulting orange solid was crystallized from a mixture of toluene and ethanol, affording the title compound as pale yellow microcrystals, 0.687 g (85%): mp 183−186 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 7.3 Hz, 2H), 7.46−7.40 (m, 5H), 7.28−7.27 (m, 3H), 7.19−7.10 (m, 32H), 6.97 (d, J = 8.3 Hz, 2H), 6.68 (d, J = 8.3 Hz, 2H), 1.45 (s, 63H), 1.40 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.7, 153.8, 153.7, 153.7, 149.2, 143.2, 140.6, 140.4, 140.3, 140.2, 140.2, 140.1, 139.5, 138.0, 137.6, 136.1, 133.8, 130.9, 129.6, 129.4, 128.8, 128.3, 128.0, 127.5, 127.3, 127.1, 127.0, 126.2, 125.9, 121.5, 81.5, 81.4, 81.4, 81.1, 28.4, −0.9; IR (neat, cm^{-1}) 2975, 2933, 1708, 1509, 1368, 1328, 1310, 1289, 1252, 1156, 1054, 1017, 837, 766, 697. Anal. Calcd for $C_{110}H_{127}N_9O_{16}Si$: C, 71.06; H, 6.88. Found: C, 70.95; H, 6.81.

Acknowledgment. We thank the National Institutes of Health (GM 58160), the National Cancer Institute (training grant NCI CI T32CA09112), and the Office of Naval Research for financial support of this work. We also acknowledge Pfizer, Merck, and Novartis for additional unrestricted support. J.P.W. is grateful for a fellowship from the Organic Division of the American Chemical Society sponsored by Schering-Plough. H.T. thanks Sankyo Co. Ltd. for support. We thank Mr. John Kowalski for conducting initial experiments on the room-temperature catalytic amination of aryl bromides using ligand **3**.

Supporting Information Available: The characterization data of known compounds. This material is available free of charge via the Internet: http://pubs.acs.org.

JO991699Y