Nickel-Catalyzed Amination of Aryl Chlorides

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Abstract: Aryl chlorides are converted to aniline derivatives using catalytic amounts of $Ni(COD)_2$ (COD = 1,5-cyclooctadiene) and DPPF (DPPF = 1,1′-bis(diphenylphosphino)ferrocene) or 1,10-phenanthroline in the presence of sodium *tert*-butoxide. This procedure has a broad substrate scope: electron-rich or electron-poor aryl chlorides, as well as chloropyridine derivatives, can be combined with primary and secondary amines to give the desired aryl amine products in moderate to excellent yields. Additionally, a procedure which utilizes the air-stable precatalysts $(DPPF)NiCl_2$ or $(1,10\text{-phenanthroline})NiCl_2$ is also described.

The palladium-catalyzed amination of aryl bromides,[1a−g] iodides,[1g,h] and triflates[1i,j] with primary and secondary amines and anilines has provided a new route to a wide variety of aryl amines. Our desire to expand the aryl amination methodology to include aryl chlorides stems from the fact that they are both the least expensive and the most widely available aryl halides. Many of the methods used to extend the scope of palladium-catalyzed carbon−carbon bond-forming reactions to include aryl chlorides are limited by the need for substrates that are activated by electron-withdrawing groups or by complexed transition metal fragments.[2,3] While electron-rich phosphines have been utilized,[2,4] these do not appear to be viable ligands for palladium-catalyzed aminations; increased electron density on the metal center decreases the rate of reductive elimination relative to β-hydride elimination, leading to lower yields of coupled products and increased amounts of arene side products (see below).[5]

Our initial attempts to utilize aryl chlorides as substrates with palladium catalysts resulted in low conversion when $P(o\text{-tolyl})_3$ or BINAP-based[7] catalyst systems were employed as ligands. For example, the reaction of 4-chlorotoluene and *N*-methylbenzylamine at 100 °C resulted in low conversion (<10%) when a $Pd_2(dba)_3/P(o\text{-tolyl})_3$ catalyst system was employed (4 mol % Pd). When $P(cyclohexyl)_3$ was used as the phosphine ligand, the reaction proceeded to completion, but the yield of desired product was low (<30% by GC).

Nickel complexes have been shown to catalyze carbon−carbon bond-forming reactions which use aryl chlorides as coupling partners.[2] This prompted us to investigate their utility in catalyzing carbon−nitrogen bond-forming reactions with aryl chloride substrates, and herein, we report our initial results.[6] This process, which proceeds at moderate temperatures (70−100 °C), is capable of converting a wide variety of aryl chlorides to substituted anilines.

After some initial experimentation, we found that mixtures of $Ni(COD)_2$ (COD = cyclooctadiene) and DPPF[7] effectively promote the coupling of aryl chlorides with amines (eq 1). For

$$\text{Ar-Cl} + \text{HN(R)R}' \xrightarrow[\text{toluene, } 70-100\ ^\circ\text{C}]{\text{cat. Ni(COD)}_2\text{, ligand, NaO}t\text{Bu}} \text{Ar-N(R)R}' \quad (1)$$

example, 4-chlorotoluene and *N*-methylaniline (Table 1, entry 1) give the desired tertiary amine in 80% yield by employing 2 mol % $Ni(COD)_2$/4 mol % DPPF in the presence of a stoichiometric amount of NaO*t*Bu at 100 °C in toluene. This method effectively couples both electron-rich (entries 1−10) and electron-poor aryl chlorides (entries 11−12), as well as chloropyridine derivatives (entries 13−14), with amines in moderate to excellent yields (Table 1). The reaction conditions are sufficiently mild to tolerate a variety of functional groups including ethers, nitriles, acetals, and non-enolizable ketones,

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(1) (a) Kosugi, M.; Kameyama, M.; Migita, T. *Chem. Lett.* **1983**, 927−928. (b) Guram, A. S.; Rennels, R. A.; Buchwald, S. L. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1348−1350. (c) Wolfe, J. P.; Rennels, R. A.; Buchwald, S. L. *Tetrahedron* **1996**, *52*, 7525−7546. (d) Wolfe, J. P.; Wagaw. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 7215−7216. (e) Wagaw, S.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 7240−7241. (f) Louie, J.; Hartwig, J. F. *Tetrahedron Lett.* **1995**, *36*, 3609−3612. (g) Driver, M. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **1996**, *118*, 7217−7218. (h) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 1133−1135. (i) Wolfe, J. P.; Buchwald, S. L. *J. Org. Chem.* **1997**, *62*, 1264−1267. (j) Louie, J.; Driver, M. S.; Hamann, B. C.; Hartwig, J. F. *J. Org. Chem.* **1997**, *62*, 1268−1273.

(2) Grushin, V. V.; Alper, H. *Chem. Rev.* **1994**, *94*, 1047−1062. Nickel-catalyzed C−S bond formation has also been reported: (a) Takagi, K. *Chem. Lett.* **1987**, 2221−2224. (b) Cristau, H. J.; Chabaud, B.; Chene, A.; Christol, H. *Synthesis* **1981**, 892−894.

(3) Carpentier, J. F.; Petit, F.; Mortreux, A.; Dufaud, V.; Basset, J.-M.; Thivolle-Cazat, J. *J. Mol. Catal.* **1993**, *81*, 1−15.

(4) (a) Portnoy, M.; Milstein, D. *Organometallics* **1993**, *12*, 1665−1673 and references therein. (b) The most effective ligands for Pd-catalyzed reactions of aryl chlorides[2] are chelating bis(diisopropylphosphine) complexes such as 1,3-bis(diisopropylphosphino)propane (dippp). However, these ligands are not commercially available and can be difficult to prepare due to the air-sensitive nature of small, basic phosphines.

(5) (a) Hegedus, L. S. *Transition Metals in the Synthesis of Complex Organic Molecules*; University Science Books: Mill Valley, CA, 1994; p 27. (b) Marcoux, J.-F.; Wagaw, S.; Buchwald, S. L. *J. Org. Chem.* **1997**, *62*, 1568−1569. (c) Hartwig, J. F.; Richards, S.; Barañano, D.; Paul, F. *J. Am. Chem. Soc.* **1996**, *118*, 3626−3633.

(6) Previous reports of nickel-catalyzed aryl carbon−nitrogen bond formation consist of a few examples with no isolated yields of products given. The only example of nickel-catalyzed amination of an aryl chloride was the reaction of chlorobenzene with dimethylamine, which required 10 equiv of dimethylamine and only proceeded to 68% conversion after 6 h at 200 °C. (a) Cramer, R.; Coulson, D. R. *J. Org. Chem.* **1975**, *40*, 2267−2273. (b) Christau, H. J.; Desmurs, J. R. *Ind. Chem. Libr.* **1995**, *7*, 240. (c) In the report by Cristau and Desmurs, no specific aryl halides were referred to. Instead, the generic example "Ar-Br" was used. Additionally, no experimental details were given. (d) After the submission of this manuscript, Beller reported the coupling of electron-deficient aryl chlorides with amines in the presence of a palladacycle catalyst, potassium *tert*-butoxide, and lithium bromide at 135−140 °C. The aniline products were obtained as mixtures of regioisomers resulting from a competing benzyne pathway. Beller, M.; Reirmeier, T. H.; Reisinger, C.-P.; Herrmann, W. A. *Tetrahedron Lett.* **1997**, *38*, 2073−2074.

(7) Abbreviations used: dba = dibenzylideneacetone, DPPF= 1,1′-bis-(diphenylphosphino)ferrocene, BINAP = 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl, PPFA = *N*,*N*-dimethyl-1-[2-(diphenylphosphino)ferrocenyl]-ethylamine, PPFE = 1-[2-(diphenylphosphino)ferrocenyl]ethyl methyl ether, DPPP = 1,3-bis(diphenylphosphino)propane, and DPPE = 1,2-bis(diphenylphosphino)ethane.

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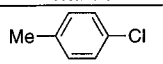
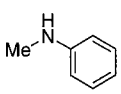
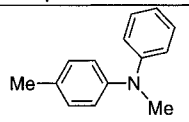
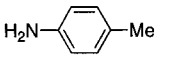
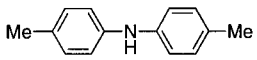
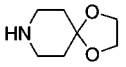
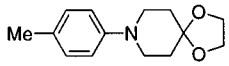
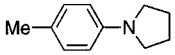
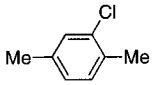
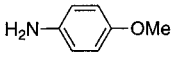
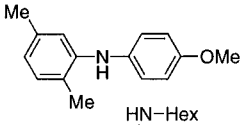
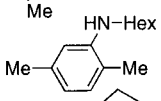
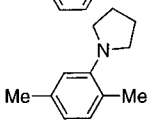
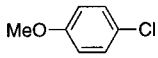
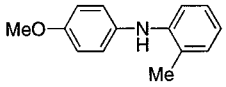
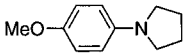
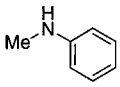
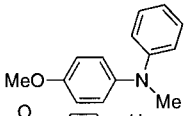
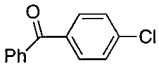
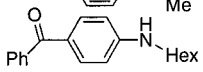
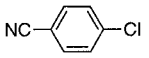
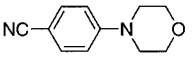
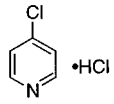
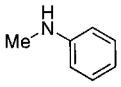
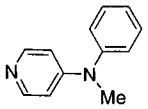
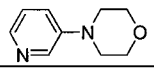
Table 1. Nickel-Catalyzed Amination of Aryl Chlorides

entry	halide	amine	product	catalyst loading	method[a]	rxn time	iso. yield
1				2 mol%	A	18.5 h	80%
2				2 mol%	A	19 h	91%
3				5 mol%	A	21.5 h	81%
4				2 mol% 5 mol% 2 mol% 7 mol%	A B C D	15 h 19 h 19 h 21 h	58% 84% 54% 86%
5				2 mol% 3 mol%	A C	19 h 21.5 h	96% 83%
6		$HexNH_2$		5 mol% 6 mol%	A[b] B[b]	15 h 30 h	50% 63%
7				5 mol%	B	18 h	82%
8				3 mol%	A	15 h	88%
9				5 mol%	B	36 h	56%
10				3 mol%	A	23 h	55%
11		$HexNH_2$		2 mol% 2 mol%	A C	22 h 16 h	91% 85%
12				2 mol% 2 mol%	A B	15 h 5 h	86% 82%
13				5 mol%	A	20 h	79%
14				5 mol%	A	19 h	87%

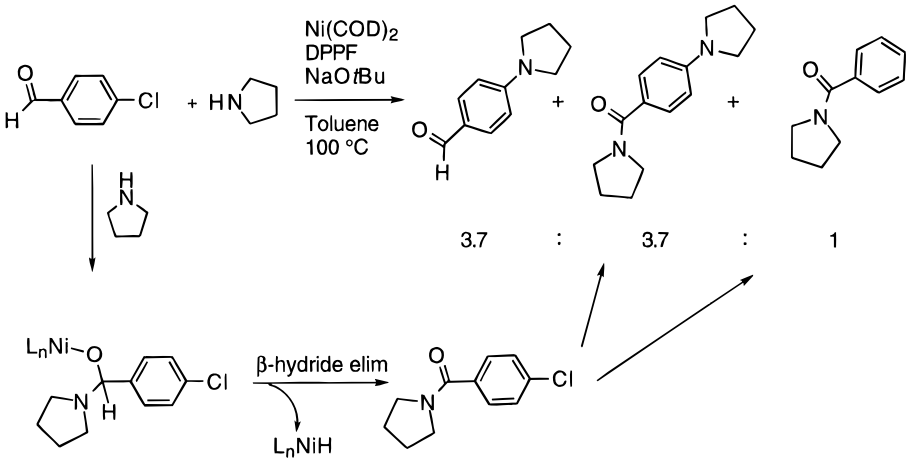
[a] Method A: 1 equiv of halide, 1.2 equiv of amine, 1.4 equiv of NaO*t*Bu, 2−5 mol % $Ni(COD)_2$, 4−10 mol % DPPF, toluene (0.25 M), 100 °C. Method B: 1 equiv of halide, 1.2 equiv of amine, 1.4 equiv of NaO*t*Bu, 2−5 mol % $Ni(COD)_2$, 4−10 mol % 1,10-phenanthroline, pyridine (0.25 M), 100 °C. Method C: Same as method A, but $(DPPF)NiCl_2$/MeMgBr used in place of $Ni(COD)_2$. Method D: Same as method B, but $(Phen)NiCl_2$/MeMgBr used in place of $Ni(COD)_2$. [b] 3.0 equiv of amine used.

and reactions may be run at temperatures as low as 70 °C. The main side products of the reaction are arenes resulting from reduction of the aryl halides, although in some cases small amounts of homocoupled arenes were produced. Attempts to couple 4-chlorobenzaldehyde with pyrrolidine resulted in the formation of amide side products which may arise from β-hydride elimination of a hemi-aminal intermediate as shown in Scheme 1. Primary amines with β-hydrogens give large amounts of reduced side products, unless electron-deficient aryl chlorides are used as coupling partners. Additionally, when primary amines with β-hydrogens are coupled with electronically-neutral aryl chlorides, imine side products resulting from oxidation of the coupled amine were also detected. Formation of these side products is significantly decreased when the couplings were performed with an excess (3 equiv) of the amine.

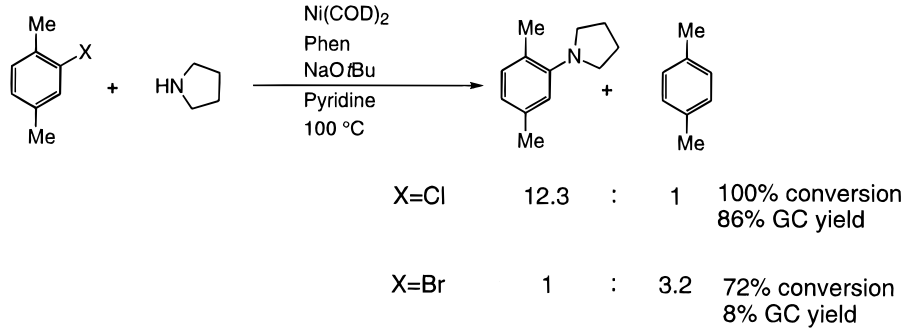
Other phosphine ligands examined (BINAP, PPFA, PPFE, DPPP, DPPE, PPh_3, and $P(o\text{-tolyl})_3$)[7] gave either low conversion or poor product/reduced substrate ratios for the coupling reaction. However, the chelating nitrogen ligand 1,10-phenanthroline (phen), which was not an effective ligand in palladium-catalyzed aminations, proved quite useful for nickel-catalyzed C−N bond-forming procedures (Table 1, entries 4, 6, 7, 9, and 12). With this ligand, substantially higher yields of desired products could be obtained for some substrates than with the $Ni(COD)_2$/DPPF catalyst system. For example, the attempted reaction of 2-chloro-*p*-xylene with pyrrolidine afforded a 1:2 ratio[8] of the desired product/arene side product using the $Ni(COD)_2$/DPPF combination. With the $Ni(COD)_2$/1,10-phenanthroline catalyst, a 12:1 ratio of desired product/arene was obtained; *N*-(2,5-xylyl)pyrrolidine was isolated in 84%. In most cases, reactions which employed 1,10-phenanthroline required a larger catalyst loading than those using DPPF (5% vs 2%). In addition, it was necessary to employ pyridine as a solvent to obtain complete consumption of the starting aryl chloride. However, 1,10-phenanthroline is much less expensive than either

(8) Ratios are not corrected for GC response factors.

Scheme 1



Scheme 2



BINAP or DPPF, and its high polarity allows for its easy chromatographic separation from the desired products.[9] The use of other 1,10-phenanthroline derivatives such as neocuproine hydrate and 2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline afforded little or no desired products. While 1,10-phenanthroline proved to be a superior ligand for some coupling reactions, attempts to use it in procedures to couple aryl chlorides with anilines failed under these conditions, giving mainly homocoupled byproducts.

Due to the air sensitivity and thermal instability of $Ni(COD)_2$, we felt it would be desirable to develop conditions to carry out this transformation with air stable $(L-L)NiCl_2$ precatalysts. Attempts to directly employ these complexes without additional additives resulted in no reaction. Use of activated zinc[2a,10] to reduce the Ni(II) precatalysts *in situ* also failed, resulting in low conversion of the aryl chloride to the desired aniline. However, MeMgBr (2 equiv/Ni) proved to be an effective reagent for the activation of these complexes (eq 2).[11] Use of

$$\text{Ar-Cl} + \text{HN(R)R}' \xrightarrow[\text{NaO}t\text{Bu, toluene, 100 °C}]{\text{cat. (L-L)NiCl}_2\text{, cat. MeMgBr, ligand}} \text{Ar-N(R)R}' \quad (2)$$

the *in situ* generated catalyst provided yields which were generally comparable to those obtained with $Ni(COD)_2$, although sometimes slightly higher catalyst levels were required. While this method proved satisfactory for some coupling reactions (Table 1, entries 4, 5, and 11), it did not provide reproducible results for the attempted combination of 4-chloroanisole with *o*-toluidine.

We currently have little mechanistic information about this transformation. The reaction sequence may be similar to the one proposed for the palladium-catalyzed amination of aryl halides,[1d] or it may proceed through Ni(I) and Ni(III) intermediates as proposed by Kochi for the nickel-catalyzed coupling of aryl halides with Grignard reagents.[12] A mechanism which involves electron transfer from Ni to an aryl halide is consistent with the fact that reaction of 2-bromo-*p*-xylene with pyrrolidine afforded mainly xylene and only a small amount of the desired product under conditions which gave excellent yields for the coupling of the corresponding chloride (Scheme 2). These results are consistent with the observations made by Kumada on reactions of halobenzenes with *n*-butylmagnesium bromide, although the differences between the results obtained with the aryl chloride and aryl bromide are more dramatic in this case.[11]

In conclusion, we have demonstrated the first nickel-catalyzed amination of aryl chlorides which allows for the coupling of a wide variety of substrates under relatively mild conditions. Studies are underway to further expand the scope of this methodology, as well as to ascertain mechanistic details of the nickel-catalyzed process.

Experimental Section

General. All reactions were carried out under an argon atmosphere in oven dried glassware. Reactions catalyzed by mixtures of $Ni(COD)_2$ and DPPF or 1,10-phenanthroline were run in Schlenk tubes equipped with a Teflon screwcap and were mixed and sealed in a Vacuum Atmospheres glovebox prior to heating in an oil bath outside of the glovebox. Reactions in which $(L-L)NiCl_2$ complexes were employed

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as catalysts were run in Schlenk tubes equipped with rubber septa and were assembled outside of the glovebox. Elemental analyses were performed by E & R Microanalytical Laboratory Inc., Corona, NY. Toluene was distilled under nitrogen from molten sodium, degassed under vacuum, and stored under argon in a Vacuum Atmospheres glovebox. Pyridine was distilled under argon from CaH_2, degassed under vacuum, and stored under argon in a Vacuum Atmospheres glovebox. All amines were purchased from commercial sources. Amines which were liquids at ambient temperature were distilled from CaH_2 under argon or vacuum, degassed under vacuum, and stored under argon in a Vacuum Atmospheres glovebox. Amines which were solids at ambient temperature were stored under argon in a Vacuum Atmospheres glovebox and used without further purification. Sodium *tert*-butoxide was purchased from Aldrich chemical company and stored in a Vacuum Atmospheres glovebox under nitrogen or argon. For reactions which employed (L−L)$NiCl_2$ precatalysts, small amounts of sodium *tert*-butoxide were removed from the glovebox, stored in a dessicator for up to 1 week, and weighed in the air. Solvents for these reactions were taken directly from solvent stills using standard syringe techniques. Bis(1,5-cyclooctadiene)nickel was purchased from Strem Chemical Company, stored in the freezer of a Vacuum Atmospheres glovebox under argon, and used without further purification. DPPF was purchased from Strem Chemical Company and used without further purification. 1,10-Phenanthroline was purchased from Lancaster Synthesis, Inc., and used without further purification. Aryl chlorides were purchased from commercial sources, degassed under vacuum, and stored under argon in a Vacuum Atmospheres glovebox. Methylmagnesium bromide (3 M solution in Et_2O) was purchased from Aldrich. The paramagnetic complexes (DPPF)$NiCl_2$[13] and (phen)$NiCl_2$[14] were prepared by slightly modified literature procedures and characterized by IR spectroscopy and elemental analysis. For example, the (phen)-$NiCl_2$ obtained from the literature procedure was found to contain large amounts of alcohol by IR analysis. This compound was dried under vacuum at 180 °C overnight. The preparation of (DPPF)$NiCl_2$ was carried out in a 1:1:1 mixture of ethanol/*n*-butanol/CH_2Cl_2 due to the low solubility of the phosphine in ethanol. Preparative flash chromatography was performed on ICN Biomedicals Silitech 32−63d silica gel. Yields in Table 1 refer to isolated yields (average of two runs) of compounds estimated to be ≥95% pure as determined by ^{1}H NMR and either capillary GC (known compounds) or combustion analysis (new compounds). The procedures described below are representative; thus, the yields may differ from those given in Table 1.

General Procedure for the Catalytic Amination of Aryl Chlorides. (A) Method A. A sealable Schlenk tube was charged with bis(1,5-cyclooctadiene)nickel (6 mg, 0.02 mmol, 2 mol %), DPPF (22 mg, 0.04 mmol, 4 mol %), and sodium *tert*-butoxide (135 mg, 1.4 mmol) under argon in a Vacuum Atmospheres glovebox. Toluene (1 mL) was added, followed by the aryl chloride (1.0 mmol), the amine (1.2 mmol), and additional toluene (3 mL). The tube was sealed, removed from the glovebox, and heated to 100 °C with stirring until the starting halide had been consumed as judged by GC analysis.

Workup Method 1. The reaction mixture was cooled to room temperature, diluted with ether (10 mL), filtered, and concentrated. The crude product was purified by flash chromatography on silica gel. Products which were inseparable from DPPF by silica gel chromatography were purified according to one of the following workup procedures.

Workup Method 2. The reaction mixture was cooled to room temperature, diluted with ether (20 mL), and poured into a separatory funnel. The mixture was extracted with 1 M HCl (3 × 10 mL). The organic layer was discarded after confirming that no desired product remained. The aqueous extracts were then combined and taken to pH 12 with 3 M NaOH. The aqueous solution was extracted with ether (3 × 20 mL), and the combined ether extracts were washed with brine (20 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated.

Workup Method 3. The reaction mixture was cooled to room temperature, diluted with ether (10 mL), filtered, and concentrated. The product was then taken up in ether (20 mL), and 30% H_2O_2 (5 mL) was added to oxidize the phosphine. The mixture was stirred at room temperature for 10 min and then poured into a separatory funnel. The aqueous layer was drained, and the ether layer was washed with distilled water (10 mL) and saturated aqueous $FeSO_4$ (20 mL). (CAUTION: The reaction between H_2O_2 and $FeSO_4$ is vigorously exothermic, and both the washing of the organic layer with aqueous $FeSO_4$ and the mixing of the aqueous washes should be done with care.) The aqueous washes were combined, and the aqueous mixture was allowed to cool to room temperature and then was extracted with ether (3 × 20 mL). The combined organic extracts were washed with brine (20 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated. The crude product was then purified by flash chromatography on silica gel.

(B) Method B. A sealable Schlenk tube was charged with bis(1,5-cyclooctadiene)nickel (15 mg, 0.05 mmol, 5 mol %), 1,10-phenanthroline (18 mg, 0.10 mmol, 10 mol %), and sodium *tert*-butoxide (135 mg, 1.4 mmol) under argon in a Vacuum Atmospheres glovebox. Pyridine (1 mL) was added, followed by the aryl chloride (1.0 mmol), the amine (1.2 mmol), and additional pyridine (3 mL). The tube was sealed, removed from the glovebox, and heated to 100 °C with stirring until the starting halide had been consumed as judged by GC analysis. The mixture was cooled to room temperature, taken up in ether (10 mL), filtered, and concentrated. The crude product was purified by flash chromatography on silica gel.

(C) Method C. A Schlenk tube was charged with (DPPF)$NiCl_2$ (14mg, 0.02 mmol, 2 mol %), DPPF (11mg, 0.02 mmol, 2 mol %), and sodium *tert*-butoxide (135 mg, 1.4 mmol) and purged with argon. Toluene (2 mL) was added, followed by methylmagnesium bromide (13 μL, 3.0 M in diethyl ether, 0.04 mmol, 4 mol %), and additional toluene (2 mL). The mixture was stirred at room temperature for 15 min, and then the aryl halide (1.0 mmol) and amine (1.2 mmol) were added. The mixture was heated to 100 °C with stirring until the starting aryl halide had been consumed as judged by GC analysis. The mixture was cooled to room temperature, taken up in ether (10 mL), filtered, and concentrated. The crude product was purified by flash chromatography on silica gel.

(D) Method D. A Schlenk tube was charged with (phen)$NiCl_2$ (22 mg, 0.07 mmol, 7 mol %), 1,10-phenanthroline (13 mg, 0.07 mmol, 7 mol %), and sodium *tert*-butoxide (135 mg, 1.4 mmol) and purged with argon. Pyridine (2 mL) was added, followed by methylmagnesium bromide (47 μL, 3.0 M in diethyl ether, 0.14 mmol, 14 mol %) and additional pyridine (2 mL). The mixture was stirred at room temperature for 15 min, and then the aryl halide (1.0 mmol) and amine (1.2 mmol) were added. The mixture was heated to 100 °C with stirring until the starting aryl halide had been consumed as judged by GC analysis. The mixture was cooled to room temperature, taken up in ether (10 mL), filtered, and concentrated. The crude product was purified by flash chromatography on silica gel.

Di-*p*-tolylamine.[15] The general procedure A using workup 1 gave 186 mg (94%) of a white solid: mp 77 °C (lit.[15] mp 77−78 °C); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.29 (s, 6H), 5.54 (s, br, 1H), 6.93 (d, 4H, J = 8.5 Hz), 7.06 (d, 4H, J = 8.6 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 20.6, 117.9, 129.7, 130.1, 141.1; IR (KBr, cm^{-1}) 3418, 1610, 1518, 1320, 807.

***N*-Methyl-*N*-phenyl-*p*-toluidine.**[1h] The general procedure A using workup 1 gave 152 mg (77%) of a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.32 (s, 3H), 3.28 (s, 3H), 6.86−7.25 (m, 9H).

***N*-(*p*-Methylphenyl)-1,4-dioxa-8-azaspiro[4.5]decane.**[1h] The general procedure A but using 5 mol % Ni(COD)$_2$, 10 mol % DPPF, and workup 1 gave 188 mg (88%) of a white solid: mp 65 °C (lit.[1h] mp 64.8−65.6 °C); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.84 (t, 1H, J = 5.7 Hz), 2.26 (s, 3H), 3.26 (t, 4H, J = 5.9 Hz), 3.98 (s, 4H), 6.86 (d, 2H, J = 9.1 Hz), 7.05 (d, 2H, J = 8.5 Hz).

***N*-*p*-Tolylpyrrolidine.**[16] The general procedure A using workup 2 gave 91 mg (57%) of a tan solid: mp 34−35 °C (lit.[16] oil); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.95−2.05 (m, 4H), 2.25 (s, 3H), 3.22−3.29 (m, 4H), 6.50 (d, 2H, J = 8.2 Hz), 7.03 (d, 2H, J = 8.1 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 20.3, 25.4, 47.8, 111.7, 124.4, 129.6, 146.1; IR (KBr, cm^{-1}) 2964, 1624, 1523, 1370, 1187, 801.

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***N*-(2,5-Dimethylphenyl)-*p*-anisidine.**[17] The general procedure A using workup 1 gave 216 mg (95%) of a pale yellow solid: mp 37 °C (lit,[17] mp 34−35 °C); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.20 (s, 3H), 2.23 (s, 3H), 3.80 (s, 3H), 5.17 (s, br, 1H), 6.63 (d, 1H, J = 7.0 Hz), 6.82−6.89 (m, 3H), 7.02 (m, 3H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 17.3, 21.2, 55.5, 114.6, 115.9, 120.7, 122.0, 122.3, 130.5, 136.4, 143.1, 154.9; IR (KBr, cm^{-1}) 3419, 2928, 1526, 1509, 1246, 826.

***N*-(2,5-Dimethylphenyl)hexylamine.**[1h] The general procedure A but using 3 mmol of amine, 5 mol % $Ni(COD)_2$, 10 mol % DPPF, and workup 3 gave 107 mg (52%) of a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.91−0.93 (m, 3H), 1.32−1.69 (m 8H), 2.09 (s, 3H), 2.29 (s, 3H), 3.13 (t, 2H, J = 7.2 Hz), 3.40 (s br, 1H), 6.44−6.47 (m, 2H), 6.92 (d, 12H, J = 7.5 Hz).

***N*-(2-Methylphenyl)-*p*-anisidine.** The general procedure A but using 3 mol % $Ni(COD)_2$, 6 mol % DPPF, and workup 1 gave 187 mg (88%) of a white solid: mp 78 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.25 (s, 3H), 3.80 (s, 3H), 5.20 (s, br, 1H), 6.67−7.16 (m, 8H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 17.7, 55.5, 114.6, 115.1, 119.9, 122.0, 125.2, 126.7, 130.7, 136.2, 143.3, 155.0; IR (KBr, cm^{-1}) 3392, 2997, 1514, 1236. Anal Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 78.85; H, 6.83.

***N*-Methyl-*N*-phenyl-*p*-anisidine.** The general procedure A but using 3 mol % $Ni(COD)_2$, 6 mol % DPPF, and workup 3 gave 120 mg (56%) of a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.26 (s, 3H), 3.81 (s, 3H), 6.76−7.20 (m, 9H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 40.4, 55.5, 114.7, 115.7, 118.3, 126.2, 128.9, 142.2, 149.7, 156.2; IR (neat, cm^{-1}) 2932, 1596, 1508, 1243. Anal Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09. Found: C, 78.77; H, 7.22.

***N*-Methyl-*N*-(4-pyridyl)aniline.** A sealable Schlenk tube was charged with 4-chloropyridine hydrochloride (150 mg, 1.0 mmol), NaO*t*Bu (135 mg, 1.4 mmol), and toluene (1 mL) under argon in a Vacuum Atmospheres glovebox. The mixture was stirred for 2 min at ambient temperature, and then $Ni(COD)_2$ (15 mg, 0.05 mmol, 5 mol %), DPPF (55 mg, 0.10 mmol, 10 mol %), NaO*t*Bu (96 mg, 1.0 mmol), and toluene (3 mL) were added. The tube was sealed, removed from the glovebox, and heated to 100 °C with stirring until the halide had been consumed as judged by GC analysis. The product was isolated using workup 1 to give 138 mg (75%) of a pale yellow oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.32 (s, 3H), 6.54 (d, 2H, J = 5.2 Hz), 7.19−7.26 (m, 3H), 7.40−7.45 (m, 2H), 8.21 (s br, 2H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 39.3, 108.2, 126.3, 126.6, 129.9, 146.1, 149.8, 153.6; IR (neat, cm^{-1}) 3030, 1587, 1504, 1363. Anal Calcd for $C_{12}H_{12}N_2$: C, 78.23; H, 6.57. Found: C, 78.34; H, 6.54.

***N*-(3-Pyridyl)morpholine.**[1e] The general procedure A but using 5 mol % $Ni(COD)_2$, 10 mol % DPPF, and workup 1 gave a yellow oil which contained slight impurities as judged by ^{1}H NMR. The oil was then Kügelrohr distilled to give 141 mg (86%) of a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.17−3.21 (m, 4H), 3.86−3.90 (m, 4H), 7.17−7.19 (m, 2H), 8.13 (t, 1H, J = 3.0 Hz), 8.30−8.32 (m, 1H).

***N*-(4-Benzoylphenyl)hexylamine.**[1b] The general procedure A using workup 1 gave 262 mg (93%) of a yellow solid: mp 55−56 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.91 (t, 3H, J = 6.8 Hz), 1.30−1.69 (m, 8H), 3.19 (t, 2H, J = 7.3 Hz), 4.22 (s, br, 1H), 6.57 (d, 2H, J = 8.8 Hz), 7.42−7.52 (m, 3H), 7.71−7.79 (m, 4H); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 14.0, 22.5, 26.7, 29.2, 31.5, 43.2, 111.1, 125.6, 127.9, 129.4, 131.1, 133.0, 139.2, 152.3, 195.0; IR (KBr, cm^{-1}) 3354, 2924, 1635, 1586, 1321, 1285. Anal Calcd for $C_{19}H_{23}NO$: C, 81.10; H, 8.24. Found: C, 81.35; H, 8.02.

***N*-(4-Cyanophenyl)morpholine.**[18] The general procedure A using workup 1 gave 163 mg (87%) of a white solid: mp 77−78 °C (lit.[18] mp 75−76.5 °C); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.28 (t, 4H, J = 5.2 Hz), 3.85 (t 4H, J = 5.1 Hz), 6.86 (d, 2H, J = 8.5 Hz), 7.51 (d, 2H, J = 8.2 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 47.2, 66.4, 100.8, 114.0, 119.8, 133.4, 153.4; IR (KBr, cm^{-1}) 2981, 2217, 1606, 1518, 1245.

***N*-(4-Methoxyphenyl)pyrrolidine.**[16] The general procedure B gave a white solid which was contaminated with the byproduct 4,4′-dimethoxybiphenyl. This material was taken up in ether (20 mL) and extracted with 1 M HCl (3 × 10 mL). The organic layer was discarded after confirming that no desired product remained. The aqueous extracts were then combined and taken to pH 12 with 3 M NaOH. The aqueous solution was extracted with ether (3 × 20 mL), and the combined ether extracts were washed with brine (20 mL), dried over anhydrous magnesium sulfate, filtered, and concentrated to give 98 mg (55%) of a white solid: mp 41 °C (lit.[16] oil); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.96−2.01 (m, 4H), 3,23−3.26 (m, 4H), 3.76 (s, 3H), 6.53 (d, 2H, J = 8.8 Hz), 6.84 (d, 2H, J = 9.1 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 25.3, 48.1, 55.9, 112.5, 114.9, 143.1, 150.7; IR (KBr, cm^{-1}) 2960, 1516, 1238, 1044.

***N*-(2,5-Xylyl)pyrrolidine.**[19] The general procedure B gave 143 mg (82%) of a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.89−1.93 (m, 4H), 2.28 (s, 3H), 2.29 (s, 3H), 3.15−3.20 (m, 4H), 6.64 (d, 1H, J = 7.5 Hz), 6.69 (s, 1H), 6.99 (d, 2H, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 300 MHz) δ 20.1, 21.2, 24.9, 50.9, 116.5, 120.8, 125.5, 131.5, 135.6, 149.2; IR (neat, cm^{-1}) 2964, 1505, 1312. Anal Calcd for $C_{12}H_{17}N$: C, 82.23; H, 9.78. Found: C, 82.30; H, 9.71.

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