Sequential N-Arylation of Primary Amines as a Route To Alkyldiarylamines

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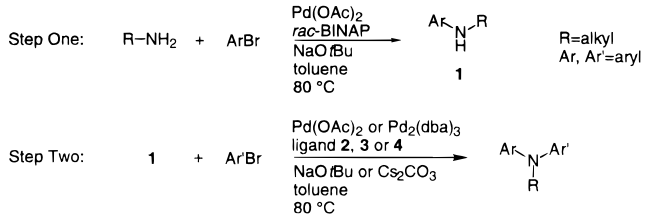
The synthesis of unsymmetrical alkyldiarylamines from a primary amine and two aryl bromides is described. A catalyst system composed of $Pd(OAc)_2$/(*rac*)-BINAP is used to prepare an alkylarylamine (**1**) from a primary amine and aryl bromide. The palladium-catalyzed arylation of **1**, by means of a different catalyst system, affords an alkyldiarylamine. The efficiency of each catalyst for the second step depends on the electronic nature of the substrates. This method has reasonable generality and compatiblity with base-sensitive functional groups.

Alkyldiarylamines are common structural elements found in many biologically active compounds. Examples include the antipsychotic agent mosapramine, the coronary vasodilator pretiadil, and the antiinflammatory agent mepheclocine.[1] Methods for the synthesis of alkyldiarylamines include the N-alkylation of diarylamines,[2] Cu-mediated couplings,[3] nucleophilic aromatic substitution,[4] and the Smiles rearrangement.[5] However, these methods often require high temperatures and/or harsh conditions, and in some cases the preparation of precursors is not trivial.

The palladium-catalyzed arylation of amines has been the focus of intensive research in recent years.[6] The cross-coupling of aryl halides with *N*-methylaniline[7] and *N*-ethylaniline[8] has been demonstrated previously. Attempts to couple *N*-alkylanilines where the alkyl is larger than ethyl resulted in the formation of large amounts of arene side product due to reduction of the aryl bromide. We therefore sought a more general route to alkyldiarylamines. We report herein a two-step procedure for the synthesis of alkyldiarylamines from primary amines and two different aryl bromides.

While it would be desirable to use the same catalyst system to effect both coupling reactions in one pot, we were unable to carry out the transformation in this manner. Catalyst systems which were efficient for one step were ineffective in the other. We therefore developed a protocol which employs different catalyst systems for each step of this two-step process (Scheme 1).

Scheme 1



The combination of $Pd(OAc)_2$ and (*rac*)-BINAP is an excellent catalyst system for the coupling of primary amines with aryl bromides[7] and is employed in the first step. The catalyst and excess ligand are removed from the reaction mixture by oxidation with hydrogen peroxide followed by filtration through silica gel and concentration. The crude secondary amine is used in the second step without further purification.

The proper choice of ligand for the second step is dependent on the electronic nature of both coupling partners, as depicted in Figures 1 and 2. Xantphos[9] (**2**) was found to be an effective ligand in the coupling of electronically neutral or electron-deficient *N*-alkylanilines with electron-deficient aryl bromides. Arylations of electron-rich *N*-alkylanilines are efficiently carried out using **3** as the ligand.

The scope of this method is further expanded by the use of the base Cs_2CO_3, allowing the coupling of aryl bromides which are incompatible with NaO*t*Bu.[10] The $Pd_2(dba)_3$/**2** catalyst system works well with Cs_2CO_3 at somewhat higher catalyst loadings and temperatures than those used with NaO*t*Bu. However, when Cs_2CO_3 was employed with the $Pd_2(dba)_3$/**3** catalyst system, extremely slow reactions or poor product:arene ratios were observed. In the course of ligand screening, we noted that the combination of $Pd_2(dba)_3$ with the ligand PPF−OMe[11] (**4**) displayed substrate scope and catalyst activity similar to those of the $Pd_2(dba)_3$/**3** catalyst system.[12] In

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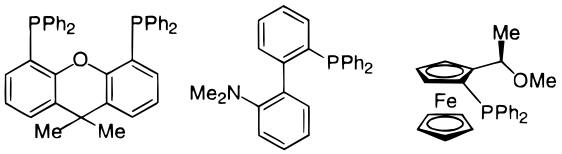


Xantphos (**2**) **3** PPF-OMe (**4**)

Figure 1. Ligands used in *N*-alkylaniline arylation.

		Ar(R)NH	
		e-poor	e-rich
Ar'Br	e-poor	**2**	**3**
	e-rich	n/a	**3**

Figure 2. Ligand choice in second step.

contrast to the latter, the $Pd_2(dba)_3$/PPF-OMe system is an effective catalyst in the presence of Cs_2CO_3,[10] as demonstrated by the synthesis of an alkyldiarylamine from ethyl-4-bromobenzoate (entry 13).

The method presented here is fairly general with respect to the steric as well as electronic properties of the substrates. Alkyldiarylamines bearing a secondary alkyl group were prepared in several cases, although an acyclic primary amine substrate gave a lower yield (entry 2). The reaction of a primary alkylamine with two ortho-substituted aryl bromides has also been demonstrated (entry 6).

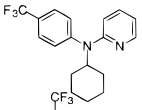
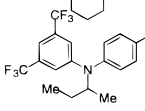
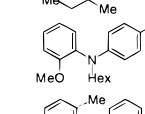
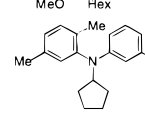
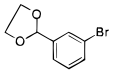
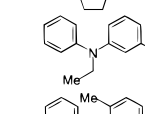
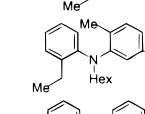
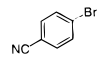
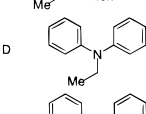
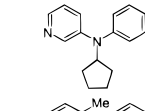
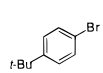
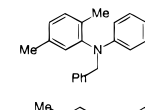
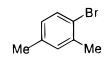
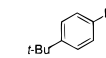
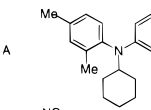
The coupling of certain substrates, however, is not straightforward. For example, in the attempted reaction of the very hindered *N*-(*sec*-butyl)-2-ethylaniline with 4-bromobiphenyl, a large proportion of 4-*tert*-butoxybiphenyl was formed. In the attempted coupling of *N*-hexyl-2-methyl-4-methoxy-aniline with 3-bromobenzonitrile, using the $Pd_2(dba)_3$/**3** catalyst system, only starting materials were observed after prolonged reaction times. By contrast, an analogous reaction with this aryl bromide, using the $Pd(OAc)_2$/**2** catalyst system, proceeded effectively (entry 12). In certain cases the order in which the aryl bromides are coupled is crucial. For example, if the sequence in entry 2 is reversed, a precipitous decrease in yield is observed due to the formation of a large amount of reduced arene side product in the second step. In another instance we were unable to successfully couple alkylaminopyridines with an aryl bromide, while the combination of *N*-alkylanilines with bromopyridines proceeded in moderate yield (entry 8).[13]

Other limitations included the inability to couple 2-bromobenzaldehyde, 4-(4′-bromophenyl)-2-butanone or 4′-bromoacetophenone with *N*-alkylanilines (alkyl > Me). We are currently attempting to determine the cause of our somewhat surprising failure to utilize the latter two substrates and to overcome this limitation.

In conclusion, we have developed a palladium-catalyzed method for the two-step synthesis of a wide range of alkyldiarylamines from alkylamines and two aryl bromides. This catalytic process displays broad scope

(13) Alkyldipyridylamines have been synthesized in a one pot procedure using $Pd_2(dba)_3$/(*rac*)-BINAP: Wagaw, S.; Buchwald, S. L. *J. Org. Chem.* **1996**, *61*, 7240.

Table 1. Sequential Arylation of Alkylamines to Alkyldiarylamines

Entry	Amine	ArBr	Ar'Br	Method[a]	Product	Yield(%)[b]
1				B		46[c]
2				B		55
3				A A'		96 95
4				A		78
5				B		74
6				A		53[d,e]
7				C or D		85
8				B		51[c]
9				A A'		79 80
10				A		69
11				B B'		91 82
12				B		75
13				C'		74
14				D		70
15				B		80
16				D'		51

[a] First coupling: 1 mol % $Pd(OAc)_2$, (*rac*)-BINAP/$Pd(OAc)_2$ (1.5/1), 0.5 M in aryl halide. Second coupling, method A: 0.5 mol % $Pd_2(dba)_3$, **3**/$Pd_2(dba)_3$ (1.5/1), 0.5 M in aryl halide, Ar′Br is limiting reagent. Method A′: same as method A, but ArBr is limiting reagent. Method B: 1 mol % $Pd(OAc)_2$, Xantphos/$Pd(OAc)_2$ (1.5/1), 0.5 M in aryl halide, Ar′Br is limiting reagent. Method B′: same as method B, but ArBr is limiting reagent. Method C (Cs_2CO_3 as base): 1 mol % $Pd_2(dba)_3$, PPF-OMe/$Pd_2(dba)_3$ (1.5/1), 0.5 M in aryl halide, Ar′Br is limiting reagent. Method C′: same as method C, but ArBr is limiting reagent. Method D (Cs_2CO_3 as base): 1 mol % $Pd_2(dba)_3$, Xantphos/$Pd_2(dba)_3$ (1.5/1), 0.5 M in aryl halide, Ar′Br is limiting reagent. method D′: same as method D, but ArBr is limiting reagent. [b] Yields represent isolated yields based on either ArBr or Ar′Br, depending on method used (average of 2 runs). [c] 2 mol % Pd used in second step. [d] Reaction proceeded to 97% completion. [e] 4 mol % Pd used in second step.

with respect to the steric and electronic properties of the substrate combinations and is compatible with many base-sensitive functional groups.

Experimental Section

General. All reactions were carried out under an argon atmosphere in oven-dried glassware. Elemental analyses were performed by E&R Microanalytical Laboratory Inc., Parsippany, NJ. Toluene was distilled under nitrogen from molten sodium. Substrates were purchased from Aldrich Chemical Co., except 4-bromo-*m*-xylene (Lancaster) and 2-bromonaphthalene (Alfa-Aesar), and used without further purification. Sodium *tert*-butoxide was purchased from Aldrich Chemical Co. and stored in a Vacuum Atmospheres glovebox under nitrogen. Small amounts were removed from the glovebox as needed, stored in a desiccator for up to one week, and weighed in the air. Palladium acetate, tris(dibenzylideneacetone)dipalladium-(0), and (*rac*)-BINAP were purchased from Strem Chemical Co. and used as supplied. Hydrogen peroxide (30%) was purchased from Fisher. Preparative flash chromatography was performed on ICN Flash silica gel 230−400 mesh. The 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 combustion analysis. The procedures described in the Experimental Section are representative; thus, the yields may differ from those given in Table 1.

General Procedure for the Synthesis of *N*-Alkylanilines. First coupling: A Schlenk tube was charged with palladium acetate (2.2 mg, 0.01 mmol, 1 mol % Pd), (*rac*)-BINAP (9.3 mg, 0.015 mmol, 1.5 mol %), evacuated, backfilled with argon, and fitted with a rubber septum. Alkylamine (1.4 mmol), aryl bromide (1.2 mmol), and toluene (1 mL) were added via syringe. The resulting mixture was stirred for 5 min at room temperature. The septum was removed, and solid sodium *tert*-butoxide (163 mg, 1.7 mmol) was added. The septum was replaced, toluene (1 mL) was added via syringe so as to wash down any base on the sides of the tube and the tube was purged with argon for 5 min. The reaction mixture was then heated to 80 °C with stirring until the aryl bromide had been consumed as judged by GC analysis (2−8 h), then cooled to room temperature, taken up in diethyl ether (3 mL), washed with brine, and concentrated. Aqueous hydrogen peroxide (30%, 10 μL, 0.088 mmol) was added to the residual oil, and the resulting mixture was stirred vigorously for 1 h. Excess hydrogen peroxide was destroyed by adding saturated aqueous ferrous sulfate (20 μL) to the mixture. Diethyl ether (25 mL) was added, and the resulting mixture was filtered through a pad of silica gel and concentrated. Analysis by ^{31}P NMR showed no signal for BINAP or its oxidation products.

General Procedure for the Coupling of *N*-Alkylanilines with Aryl Bromides. Methods A and B: A Schlenk tube was charged with $Pd_2(dba)_3$ (4.6 mg, 0.005 mmol, 1 mol %), **3** (5.7 mg, 0.015 mmol, 1.5 mol %) (method A) or $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 1 mol %), **2** (8.7 mg, 0.015 mmol, 1.5 mol %) (method B), evacuated, backfilled with argon, and fitted with a rubber septum. A solution of the crude alkylamine (1.2 mmol) in toluene (0.5 mL) was added via syringe followed by the aryl bromide (1.0 mmol) and toluene (0.5 mL). The resulting mixture was stirred for 5 min at room temperature. The septum was removed, and solid sodium *tert*-butoxide (1.4 mmol) was added, followed by toluene (1 mL) via syringe. The tube was purged with argon for 5 min and the reaction heated to 80 °C with stirring until the aryl bromide had been consumed as judged by GC analysis (6−24 h). The reaction mixture was then cooled to room temperature, taken up in diethyl ether (3 mL), washed with brine, and concentrated. The product was purified by flash chromatography on silica gel using a mixture of hexanes and ethyl acetate as eluent.

General Procedure for the Coupling of *N*-Alkylanilines with Base-Sensitive Aryl Bromides. Methods C and D: A Schlenk tube was charged with cesium carbonate (456 mg, 1.4 mmol), $Pd_2(dba)_3$ (4.6 mg, 0.01 mmol, 2 mol %), **4** (5.7 mg, 0.03 mmol, 3 mol %) (method C) or **2** (8.7 mg, 0.03 mmol, 3 mol %) (method D), evacuated, backfilled with argon, and fitted with a rubber septum. A solution of the crude alkylamine (1.2 mmol) in toluene (0.5 mL) was added via syringe followed by the aryl bromide (1.0 mmol) and toluene (0.5 mL). The resulting mixture was stirred for 5 min at room temperature. The reaction mixture was heated to 80 °C with stirring until the aryl bromide had been consumed as judged by GC analysis (6−24 h). The reaction mixture was cooled to room temperature, taken up in diethyl ether (3 mL), washed with brine, and concentrated. The product was purified by flash chromatography on silica gel using a mixture of hexanes and ethyl acetate as eluent.[14]

(1) *N*-(2-Pyridyl)-*N*-[4-(trifluoromethyl)phenyl]cyclohexylamine. The general procedure was used (method B), except 2 mol % $Pd(OAc)_2$ and 3 mol % **2** were used in the second step to afford the product as white crystals (0.153 g, 48%), mp 102−104 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, J = 6.9 Hz, 1H), 7.69 (d, J = 8.4 Hz, 2H), 7.27−7.22 (m, 3H), 6.58 (t, J = 7.2 Hz, 1H), 5.98 (d, J = 8.4 Hz, 1H), 4.90−4.75 (m, 1H), 1.97−1.93 (m, 2H), 1.79−1.75 (m, 2H), 1.66−1.40 (m, 3H), 1.18−0.94 (m, 3H); ^{13}C ($CDCl_3$) δ 158.5, 147.9, 136.9, 131.6, 126.9, 126.9, 126.9, 113.2, 109.7, 54.7, 32.2, 26.2, 25.8; Anal. Calcd for $C_{18}H_{19}F_3N_2$: C, 67.49; H, 5.98. Found: C, 67.44; H, 6.09.

(2) *N*-(4-Cyanophenyl)-*N*-[3,5-bis(trifluoromethyl)phenyl]-*sec*-butylamine. The general procedure was used (method B) to afford the product as off-white crystals (0.213 g, 55%), mp 74−76 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.52 (d, J = 8.4 Hz, 2H), 7.45 (s, 2H), 6.73 (d, J = 8.4 Hz, 2H), 4.12−4.04 (m, 1H), 1.77−1.64 (m, 1H), 1.46−1.34 (m, 1H), 1.20 (d, J = 6.3 Hz, 3H), 1.01 (t, J = 7.4 Hz, 3H); ^{13}C ($CDCl_3$) δ 150.5, 145.3, 133.9, 133.6, 133.6, 127.4, 124.2, 122.0, 119.6, 119.0, 119.0, 119.0, 118.9, 118.6, 103.2, 56.1, 28.4, 18.7, 11.7; Anal. Calcd for $C_{19}H_{16}F_6N_2$: C, 59.07; H, 4.17. Found: C, 58.99; H, 4.24.

(3) *N*-(2-Methoxyphenyl)-*N*-[4-(trifluoromethyl)phenyl]-hexylamine. The general procedure was used (method A) to afford the product as a yellow oil (0.333 g, 74%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.27 (m, 3H), 7.16 (d, J = 6.9 Hz, 3H), 7.01 (d, J = 9.0 Hz, 2H), 6.53 (d, J = 9.0 Hz, 2H), 3.70 (s, 3H), 3.55 (t, J = 7.5 Hz, 2H), 1.70−1.60 (m, 2H), 1.34−1.24 (m, 6H), 0.87 (t, J = 6.6 Hz, 3H); ^{13}C ($CDCl_3$) δ 156.5, 151.3, 134.0, 130.9, 128.3, 126.4, 126.3, 126.3, 126.3, 126.2, 121.5, 112.8, 112.0, 55.7, 51.7, 31.9, 27.4, 26.9, 22.8, 14.2. Anal. Calcd for $C_{20}H_{24}F_3NO$: C, 68.36; H, 6.88. Found: C, 68.32; H, 6.78.

(4) *N*-(2,5-Dimethylphenyl)-*N*-[3-(trifluoromethyl)phenyl]cyclopentylamine. The general procedure was used (method A) to afford the product as a colorless oil (0.259 g, 77%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24−7.16 (m, 2H), 7.14 (d, J = 7.8 Hz, 1H), 6.87−6.84 (m, 2H), 6.71 (s, 1H), 6.48 (d, J = 7.8 Hz, 1H), 4.30−4.15 (m, 1H), 2.31 (s, 3H), 2.04 (s, 3H), 1.61−1.54 (m, 4H), 1.42−1.39 (m, 4H); ^{13}C ($CDCl_3$) δ 149.3, 141.7, 137.2, 135.7, 131.8, 131.2, 129.3, 128.5, 116.3, 112.5, 112.5, 108.9, 108.9, 60.1, 30.6, 23.5, 21.1, 17.8. Anal. Calcd for $C_{20}H_{22}F_3N$: C, 71.40; H, 7.49. Found: C, 71.53; H, 7.29.

(5) *N*-[3-(1,3-Dioxolan-2-yl)phenyl]-*N*-ethylaniline. The general procedure was used (method B) to afford the product as a colorless oil (0.199 g, 74%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29−7.22 (m, 4H), 7.09 (s, 1H), 7.05−6.92 (m, 4H), 5.73 (s, 1H), 4.13−3.98 (m, 4H), 3.78 (q, J = 7.2 Hz, 2H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C ($CDCl_3$) δ 148.0, 147.7, 139.1, 129.4, 121.7, 121.6, 121.4, 118.9, 118.3, 104.0, 65.4, 46.6, 12.9; Anal. Calcd for $C_{17}H_{19}N_2O_2$: C, 75.81; H, 7.11. Found: C, 75.83; H, 7.02.

(6) *N*-(2,5-Dimethylphenyl)-*N*-(2-ethylphenyl)hexylamine. The general procedure was used (method A), except 2 mol % $Pd_2(dba)_3$ and 6 mol % **3** were used in the second step (97% conversion). The title compound was obtained as a colorless oil (0.160 g, 52%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, J = 7.5 Hz, 1H), 7.18−7.08 (m, 1H), 7.05−6.95 (m, 3H),

(14) Note: The first aryl bromide has also been used as the limiting reagent. The procedure is identical to that given, except that the stoichiometry for the first arylation is 1.4:1.2:1.0 (base:amine:aryl halide). In the second arylation, the aryl bromide is used in 20% excess. The modified procedures are denoted as A′, B′, C′ or D′.

6.74 (d, $J = 7.5$ Hz, 1H), 6.66 (s, 1H), 3.35 (t, $J = 7.8$ Hz, 2H), 2.45 (q, $J = 7.5$ Hz, 2H), 2.22 (s, 3H), 2.02 (s, 3H), 1.70−1.52 (m, 2H), 1.38−1.20 (m, 6H), 1.10 (t, $J = 7.5$ Hz, 3H), 0.86 (t, $J = 7.2$ Hz, 3H); ^{13}C ($CDCl_3$) δ 149.4, 148.3, 139.5, 135.8, 131.4, 130.0, 129.3, 126.1, 123.6, 123.6, 123.5, 123.4, 54.0, 31.8, 28.2, 27.0, 23.7, 22.8, 21.3, 18.5, 14.2, 14.1. Anal. Calcd for $C_{22}H_{31}N$: C, 85.38; H, 10.10. Found: C, 85.67; H, 10.36.

(7) *N*-(4-Cyanophenyl)-*N*-ethylaniline. The general procedure was used (method D) to afford the product as a yellow oil (0.181 g, 81%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.36 (m, 3H), 7.28 (t, $J = 7.5$ Hz, 1H), 7.18 (d, $J = 7.5$ Hz, 2H), 6.65 (d, $J = 6.9$ Hz, 2H), 3.77 (q, $J = 7.2$ Hz, 2H), 1.24 (t, $J = 7.2$ Hz, 3H); ^{13}C ($CDCl_3$) δ 151.2, 145.3, 133.4, 130.3, 127.7, 126.6, 120.6, 113.7, 98.8, 46.8, 12.4. Anal. Calcd for $C_{15}H_{14}N$: C, 81.05; H, 6.35. Found: C, 81.42; H, 6.68.

(8) *N*-(4-Chlorophenyl)-*N*-(3-pyridyl)cyclopentylamine. The general procedure was used (method B), except 2 mol % $Pd(OAc)_2$ and 3 mol % **2** were used in the second step, to afford the product as a yellow oil (0.134 g, 49%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17−8.14 (m, 2H), 7.28 (d, $J = 9.0$ Hz, 2H), 7.16−7.12 (m, 1H), 7.07−7.02 (m, 1H), 6.88 (d, $J = 6.9$ Hz, 2H), 4.30−4.15 (m, 1H), 2.10−1.95 (m, 2H), 1.70−1.58 (m, 4H), 1.50−1.30 (m, 2H); ^{13}C ($CDCl_3$) δ 144.3, 144.1, 142.8, 142.0, 129.7, 129.4, 127.5, 126.9, 123.7, 60.2, 30.5, 23.1. Anal. Calcd for $C_{16}H_{17}ClN_2$: C, 69.93; H, 6.97. Found: C, 70.23; H, 6.68.

(9) *N*-(4-*tert*-Butylphenyl)-*N*-(2,5-dimethylphenyl)benzylamine. The general procedure was used (method A′) to afford the product as a colorless oil (0.274 g, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (d, $J = 8.0$ Hz, 1H), 7.37−7.21 (m, 3H), 7.16−7.10 (m, 4H), 7.05 (s, 1H), 6.98 (d, $J = 7.5$ Hz, 1H), 6.44 (d, $J = 9.0$ Hz, 2H), 4.80 (s, 2H), 2.27 (s, 3H), 2.11 (s, 3H), 1.24 (s, 9H); ^{13}C ($CDCl_3$) δ 146.6, 146.3, 139.8, 137.2, 133.8, 131.4, 129.9, 128.6, 127.3, 127.1, 126.8, 125.8, 113.2, 56.8, 33.9, 31.7, 21.1, 18.2. Anal. Calcd for $C_{25}H_{29}N$: C, 87.41; H, 8.51. Found: C, 87.45; H, 8.46.

(10) *N*-(4-*tert*-Butylphenyl)-*N*-(2,4-dimethylphenyl)cyclohexylamine. The general procedure was used (method A) to afford the product as a colorless oil (0.230 g, 69%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14−7.10 (m, 2H), 7.02 (d, $J = 8.1$ Hz, 1H), 6.95 (d, $J = 8.1$ Hz, 1H), 6.35 (d, $J = 9.0$ Hz, 2H), 3.90−3.75 (m, 1H), 2.34 (s, 3H), 2.09 (s, 3H), 2.09−1.99 (m, 2H), 1.82−1.74 (m, 2H), 1.70−1.30 (m, 3H), 1.25 (s, 9H), 1.22−1.00 (m, 3H); ^{13}C ($CDCl_3$) δ 146.1, 139.5, 139.3, 138.2, 136.5, 131.9, 131.8, 127.7, 125.9, 112.2, 57.5, 33.8, 31.7, 31.7, 26.4, 26.1, 21.2, 18.7. Anal. Calcd for $C_{24}H_{33}N$: C, 85.91; H, 9.91. Found: C, 85.97; H, 9.47.

(11) *N*-(4-Cyanophenyl)-*N*-[4-(trifluoromethyl)phenyl]benzylamine. The general procedure was used (method B′) to afford the product as a colorless oil (0.295 g, 84%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60 (d, $J = 8.1$ Hz, 2H), 7.46 (d, $J = 8.7$ Hz, 2H), 7.35−7.24 (m, 7H), 6.98 (d, $J = 9.0$ Hz, 2H), 5.06 (s, 2H); ^{13}C ($CDCl_3$) δ 150.7, 137.0, 133.7, 129.1, 127.7, 127.3, 127.2, 127.2, 127.2, 126.3, 119.6, 117.7, 102.8, 56.2; Anal. Calcd for $C_{21}H_{15}F_3N_2$: C, 71.58; H, 4.29. Found: C, 71.85; H, 4.27.

(12) *N*-(3-Cyanophenyl)-*N*-[3-(1,3-dioxolan-2-yl)phenyl]hexylamine. The general procedure was used (method B) to afford the product as a colorless oil (0.271 g, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (t, $J = 7.8$ Hz, 1H), 7.30−7.18 (m, 3H), 7.11 (d, $J = 7.2$ Hz, 1H), 7.04−6.94 (m, 3H), 5.78 (s, 1H), 4.15−4.01 (m, 4H), 3.65 (t, $J = 7.8$ Hz, 2H), 1.63−1.57 (m, 2H), 1.37−1.26 (m, 6H), 0.88 (t, $J = 6.9$ Hz, 3H); ^{13}C ($CDCl_3$) δ 148.8, 146.6, 140.1, 130.1, 129.9, 126.3, 123.4, 123.0, 121.9, 121.7, 119.5, 119.1, 113.0, 103.4, 65.5, 52.6, 31.7, 27.2, 26.7, 22.7, 14.1. Anal. Calcd for $C_{22}H_{26}N_2O_2$: C, 75.40; H, 7.48. Found: C, 75.12; H, 7.33.

(13) 4-[*N*-(2,4-Dimethylphenyl)-*N*-hexyl]aminobenzoic Acid Ethyl Ester. The general procedure was used (method C′) to afford the product as a colorless oil (0.264 g, 75%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, $J = 9.0$ Hz, 2H), 7.12 (s, 1H), 7.08 (d, $J = 7.8$ Hz, 1H), 7.00 (d, $J = 7.8$ Hz, 1H), 6.40 (d, $J = 9.0$ Hz, 2H), 4.29 (q, $J = 6.0$ Hz, 2H), 3.60−3.45 (m, 2H), 2.36 (s, 3H), 2.04 (s, 3H), 1.67−1.56 (m, 2H), 1.36−1.20 (m, 9H), 0.88 (t, $J = 6.6$ Hz, 3H); ^{13}C ($CDCl_3$) δ 167.0, 152.0, 141.5, 137.1, 136.6, 132.4, 131.3, 129.3, 128.4, 117.6, 111.2, 60.2. 52.2, 31.8, 27.4, 26.9, 22.9, 21.3, 17.9, 14.7, 14.3. Anal. Calcd for $C_{23}H_{31}NO_2$: C, 78.13; H, 8.84. Found: C,78.28; H, 8.68.

(14) 3-[*N*-Ethyl-*N*-phenyl]aminobenzoic Acid Methyl Ester. The general procedure was used (method D) to afford the product as a colorless oil (0.170 g, 66%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.53 (d, $J = 8.4$ Hz, 1H), 7.33−7.23 (m, 3H), 7.09−7.00 (m, 4H), 3.88 (s, 3H), 3.80 (q, $J = 6.9$ Hz, 2H), 1.22 (t, $J = 7.2$ Hz, 3H); ^{13}C ($CDCl_3$) δ 167.3, 148.0, 147.2, 131.2, 129.6, 129.2, 123.7, 122.9, 122.7, 121.1, 119.5, 52.2, 46.6, 12.8. Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.26; H, 6.72. Found: C, 74.89; H, 6.49.

(15) *N*-[3,5-(Bistrifluoromethyl)phenyl]-*N*-(2-naphthyl)cyclopentylamine. The general procedure was used (method B) to afford the product as yellow needles (0.338 g, 80%), mp 90−92 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95−7.82 (m, 3H), 7.60−7.52 (m, 3H), 7.19−7.15 (m, 2H), 6.95 (s, 2H), 4.40−4.25 (m, 1H), 2.15−2.05 (m, 2H), 1.62−1.43 (m, 6H); ^{13}C ($CDCl_3$) δ 150.2, 139.9, 134.4, 132.5, 132.3, 132.0, 130.4, 129.1, 128.7, 128.1, 128.0, 126.7, 126.7, 124.9, 122.8, 114.0, 110.2, 110.2, 110.1, 60.7, 30.6, 23.2. Anal. Calcd for $C_{23}H_{19}F_6N$: C, 64.94; H, 4.98. Found: C, 65.18; H, 4.94.

(16) 4-{*N*-Cyclopentyl-*N*-[4-(trifluoromethyl)phenyl]amino}benzaldehyde. The general procedure was used (method D) to afford the product as a colorless oil (0.188 g, 57%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.77 (s, 1H), 7.72−7.66 (m, 4H), 7.21 (d, $J = 8.7$ Hz, 2H), 6.66 (d, $J = 9.0$ Hz, 2H), 4.41−4.26 (m, 1H), 2.14−2.00 (m, 2H), 1.71−1.59 (m, 4H), 1.45−1.30 (m, 2H); ^{13}C ($CDCl_3$) δ 190.5, 153.6, 146.3, 131.7, 129.9, 127.4, 127.2, 127.1, 115.4, 60.5, 30.6, 23.0. Anal. Calcd for $C_{19}H_{18}F_3NO$: C, 68.44; H, 5.45. Found: C, 68.47; H, 5.52.

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