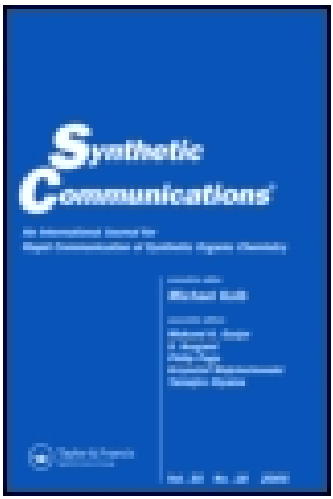

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Palladium-Catalyzed Synthesis of Arylamines from Diphenyliodonium Tetrafluoroborate and Secondary Amine

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PALLADIUM-CATALYZED SYNTHESIS OF ARYLAMINES FROM DIPHENYLIODONIUM TETRAFLUOROBORATE AND SECONDARY AMINE

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Abstract: The hetero-cross coupling reaction of diphenyliodonium tetrafluoroborate with secondary amine in the presence of $LiNTMS_2$ or NaO*t*Bu as base, $Pd_2(dba)_3{\cdot}CHCl_3$ as catalyst, and tri-*o*-tolylphosphine as ligand afforded arylamines at room temperature under mild conditions.

The arylamines are considerably important in a variety of synthetic and naturally occuring biologically active compounds. Synthetic methods for the construction of the carbon-nitrogen bond in arylamines are limited and these methods[1] rely on copper-mediated Ullmann condensation which needs

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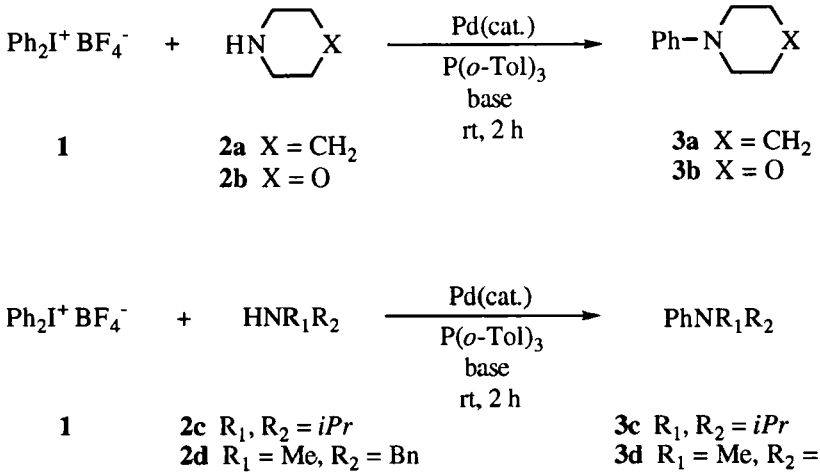
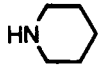
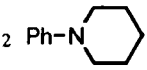
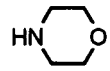
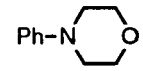
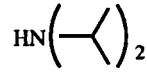
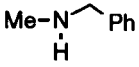
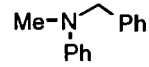
high temperature, or nucleophilic aromatic substitution of N-nucleophiles with activated aromatic substrates. In 1994, Hartwig[2] and Buchwald[3] indepently reported palladium-catalyzed amination of aryl bromides with aminostannanes to give arylamines by the modification of Migita's transamination reaction. [4] Recently, Buchwald[5] and Hartwig[6] reported the first catalytic aminations of aryl bromides with free amines. In these reactions, the coupling occurred in the presence of sterically hindered bases such as NaO*t*Bu and $LiNTMS_2$ at temperatures of 65~110℃. In our attempts to find an alternative to aryl bromides for reactions at mild conditions, we focused our attention to diphenyliodonium tetrafluoroborate.[7] We now report palladium-catalyzed hetero-coupling of diphenyliodonium tetrafluoroborate with secondary amines at ambient temperature, which is shown in Scheme 1.



Scheme 1

Table 1. Palladium-Catalyzed Amination of Diphenyliodonium Tetrafluoroborate (**1**)

Entry	Amine	Catalyst[a]	Ligand	Base	Product	Yield(%)[b]
1	 **2a**	$Pd_2(dba)_3{\cdot}CHCl_3$	P(*o*-Tol)$_3$	$LiNTMS_2$	 **3a**	62
2	**2a**	$Pd_2(dba)_3{\cdot}CHCl_3$	P(*o*-Tol)$_3$	NaOtBu	**3a**	64
3	**2a**	$Pd_2(dba)_3{\cdot}CHCl_3$	Ph_3As	$LiNTMS_2$	**3a**	61
4	**2a**	Pd/C	P(*o*-Tol)$_3$	$LiNTMS_2$	**3a**	61
5	**2a**	Pd/C	P(*o*-Tol)$_3$	NaOtBu	**3a**	65
6	 **2b**	$Pd_2(dba)_3{\cdot}CHCl_3$	P(*o*-Tol)$_3$	NaOtBu	 **3b**	69
7	 **2c**	$Pd_2(dba)_3{\cdot}CHCl_3$	P(*o*-Tol)$_3$	NaOtBu	PhN*i*Pr$_2$ **3c**	54
8	 **2d**	$Pd_2(dba)_3{\cdot}CHCl_3$	P(*o*-Tol)$_3$	NaOtBu	 **3d**	48

[a] $Pd_2(dba)_3{\cdot}CHCl_3$ (5 mol %) or Pd/C (10 mol %) was used.

[b] The yields are isolated yields.

The results are summarized in Scheme 1 and Table 1. To optimize the reaction conditions, a series of experiments have been carried out (entries 1-5). The palladium catalyst, $Pd_2(dba)_3{\cdot}CHCl_3$ and Pd/C were suitable as Pd(0) source. Of the ligands tested, P(*o*-tolyl)$_3$ and Ph_3As were the best choices. The

reactions were carried out in the presence of stoichiometric amounts of sterically hindered $LiNTMS_2$ or NaO*t*Bu. Diphenyliodonium tetrafloroborate **1** was reacted with piperidine in the presence of palladium(0) bis(tri-*o*-tolylphosphine) complex and $LiNTMS_2$ at room temperature for 2 h to obtain **3a**[8] in 62% yield(entry 1 in Table 1). Under similar conditions with NaO*t*Bu as base, N-phenylpiperidine **3a** was obtained in 64% yield (entry 2). As ligand, triphenylarsine could also be used (entry 3). With Pd/C as Pd(0) source, in the presence of ligand bis(tri-*o*-tolylphosphine)complex and $LiNTMS_2$ or NaO*t*Bu as base, compound **3a** was obtained in 61% and 65% respectively (entries 4 and 5). Morpholine and diisopropylamine were also utilized as secondary amine components for hetero-cross coupling with diphenyliodonium tetrafluoroborate **1** to furnish N-phenylmorpoholine (**3b**)[8] and diisopropylphenylamine(**3c**),[9] respectively (entries 6 and 7). Finally, N-benzylaniline was coupled with diphenyliodonium tetrafluoroborate to afford N,N-diphenylbenzylamine(**3d**)[10] (entry 8).

Experimental Section

Typical procedure. Preparation of N-phenylpiperidine (**3a**). To a stirred solution of diphenyliodonium tetrafluoroborate (**1**) (100 mg, 0.27 mmol) in dioxane (4 mL) was added $Pd_2(dba)_3{\cdot}CHCl_3$ (14 mg, 5 mol %) and P(*o*-tolyl)$_3$ (8 mg, 10 mol %) followed by piperidine (35 mg, 0.41 mmol) and 1 M $LiNTMS_2$ in tetrahydrofuran (0.32 mL, 0.32 mmol) and stirred for 2 h at room temperature. The solvent was evaporated *in vacuo* and the crude product was purified by SiO_2 column chromatography (ethyl acetate/hexane = 1 : 10,

Rf = 0.62) to afford N-phenyl piperidine (27 mg, 62%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.59 (m, 2H), 1.72 (m, 4H), 3.16 (t, 4H, *J* = 5.3 Hz), 6.83 (t, 1H, *J* =3.5 Hz), 6.76 (d, 2H, *J* = 7.1 Hz), 7.25 (m, 2H). IR (neat) 3204, 3056, 1600, 1453, 1205, 739 cm^{-1}. MS (m/e) 161 (M^+), 160 (base peak), 77.

N-Phenylmorpholine (**3b**). TLC, SiO_2, ethyl acetate/hexane = 1 : 10, Rf = 0.54. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.16 (t, 4H, *J* = 4.8 Hz), 3.87 (t, 4H, *J* = 4.8 Hz), 6.90 (m, 3H), 7.28 (m, 2H). IR (KBr) 3267, 3055, 1603, 1459, 740 cm^{-1}. MS (m/e) 163 (M^+), 105 (base peak).

N,N-Diisopropylaniline (**3c**). TLC, SiO_2, ethyl acetate/hexane = 1 : 10, Rf = 0.78. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.20 (d, 12H, *J* = 6.7 Hz), 3.76 (sept, 2H, *J* = 6.7 Hz), 6.77 (t, 1H, *J* = 7.2 Hz), 6.91 (d, 2H, *J* = 8.6 Hz), 7.19 (dd, 2H, *J* = 8.6, 7.2 Hz). IR (neat) 3057, 2960, 1600, 1453, 1121, 703 cm^{-1}. MS (m/e) 177 (M^+), 120 (base peak).

N-Methyl-N-phenyl-benzenemethanamine (**3d**). TLC, SiO_2, ethyl acetate/ hexane = 1 : 10, Rf = 0.56. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.02 (s, 3H), 4.54 (s, 2H), 6.74 (m, 3H), 7.20~7.31 (m, 7H). IR (neat) 3042, 2870, 1608, 1484, 1312, 758 cm^{-1}. MS (m/e) 197 (M+), 91 (base peak).

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