

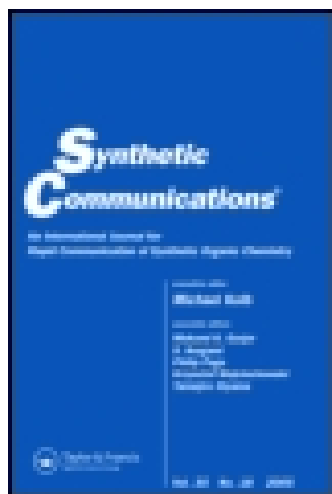
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Palladium-Catalyzed Synthesis of Arylamines from Diphenyliodonium Tetrafluoroborate and Secondary Amine

Suk-Ku Kang^a, Hong-Woo Lee^{a,b}, Won-Kyu Choi^a,
Ryung-Kee Hong^a & Jae-Sun Kim^a

^a Department of Chemistry, Sung Kyun Kwan University, Natural Science Campus, Suwon, 440-746, Korea

^b Chong Kun Dang Pharm. Co. Ltd.

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

Suk-Ku Kang,* Hong-Woo Lee,[†] Won-Kyu Choi, Ryung-Kee Hong,
and Jae-Sun Kim

Department of Chemistry, Sung Kyun Kwan University,
Natural Science Campus, Suwon 440-746, Korea

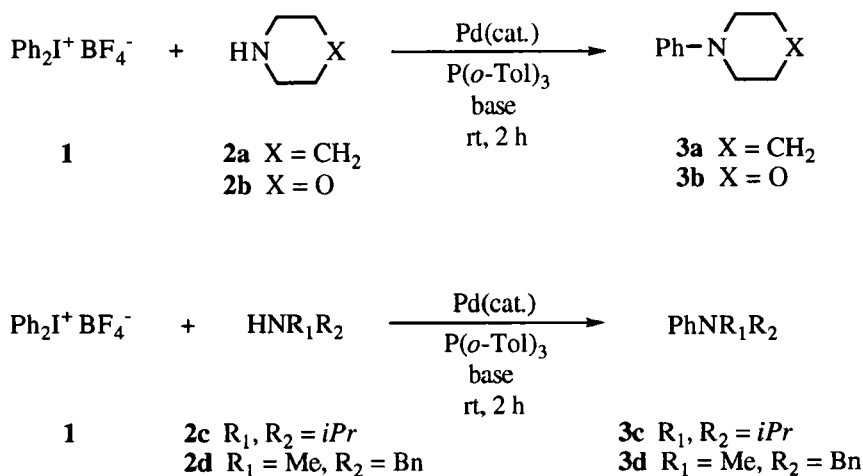
Abstract: The hetero-cross coupling reaction of diphenyliodonium tetrafluoroborate with secondary amine in the presence of LiNTMS_2 or $\text{NaO}t\text{Bu}$ as base, $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ as catalyst, and tri-*o*-tolylphosphine as ligand afforded arylamines at room temperature under mild conditions.

The arylamines are considerably important in a variety of synthetic and naturally occurring biologically active compounds. Synthetic methods for the construction of the carbon-nitrogen bond in arylamines are limited and these methods¹ rely on copper-mediated Ullmann condensation which needs

*To whom correspondence should be addressed.


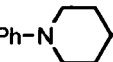

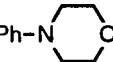
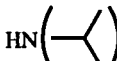
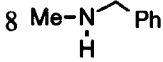
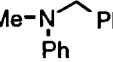
[†]Current Address: Chong Kun Dang Pharm. Co. Ltd.

high temperature, or nucleophilic aromatic substitution of N-nucleophiles with activated aromatic substrates. In 1994, Hartwig² and Buchwald³ independently reported palladium-catalyzed amination of aryl bromides with aminostannanes to give arylamines by the modification of Migita's transamination reaction.⁴ Recently, Buchwald⁵ and Hartwig⁶ 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 NaOtBu and LiNTMS₂ at temperatures of 65~110 °C. 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		$\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$	$\text{P}(o\text{-Tol})_3$	LiNTMS_2		62
	2a				3a	
2	2a	$\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$	$\text{P}(o\text{-Tol})_3$	NaOtBu	3a	64
3	2a	$\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$	Ph_3As	LiNTMS_2	3a	61
4	2a	Pd/C	$\text{P}(o\text{-Tol})_3$	LiNTMS_2	3a	61
5	2a	Pd/C	$\text{P}(o\text{-Tol})_3$	NaOtBu	3a	65
6		$\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$	$\text{P}(o\text{-Tol})_3$	NaOtBu		69
	2b				3b	
7		$\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$	$\text{P}(o\text{-Tol})_3$	NaOtBu	PhNiPr_2	54
	2c				3c	
8		$\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$	$\text{P}(o\text{-Tol})_3$	NaOtBu		48
	2d				3d	

^a $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ (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, $\text{Pd}_2(\text{dba})_3 \cdot \text{CHCl}_3$ and Pd/C were suitable as $\text{Pd}(0)$ source. Of the ligands tested, $\text{P}(o\text{-tolyl})_3$ and Ph_3As were the best choices. The

reactions were carried out in the presence of stoichiometric amounts of sterically hindered LiNTMS_2 or NaOtBu . Diphenyliodonium tetrafluoroborate **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 NaOtBu 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 NaOtBu 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-phenylmorpholine (**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 $\text{Pd}_2(\text{dba})_3\cdot\text{CHCl}_3$ (14 mg, 5 mol %) and $\text{P}(o\text{-tolyl})_3$ (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,

R_f = 0.62) to afford N-phenyl piperidine (27 mg, 62%). ¹H NMR (CDCl₃, 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, SiO₂, ethyl acetate/hexane = 1 : 10, R_f = 0.54. ¹H NMR (CDCl₃, 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, SiO₂, ethyl acetate/hexane = 1 : 10, R_f = 0.78. ¹H NMR (CDCl₃, 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, SiO₂, ethyl acetate/hexane = 1 : 10, R_f = 0.56. ¹H NMR (CDCl₃, 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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