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A Facile and Efficient Synthesis of *N*,*N*-Dimethylarylamines from Aryl Bromides

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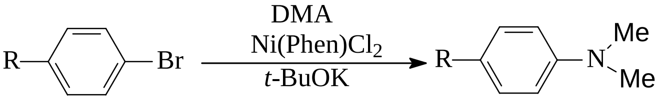
Abstract: Catalytic amination of aryl bromides with *in situ* generated dimethylamines from *N*, *N*-dimethylacetamide (DMA) has been successfully carried out using Ni(Phen)Cl_2 as catalyst. Both electron-rich and electron-poor aromatic system reacted smoothly under the conditions to give *N*,*N*-dimethylarylamines in good yields.

Keywords: Amination, nickel-catalyzed, cross-coupling reaction, *N*, *N*-dimethylarylamine.

The *N*-aryl moiety represents an important motif in natural products[1] and pharmaceuticals[2], as well as in polymers and materials[3]. Since Misita and co-workers reported the first example of the palladium-catalyzed transformation of aryl bromide to aryl amine *via* the use of amine stannanes[4], various of palladium-catalyzed synthetic methods for the preparation of aniline derivatives have been reported[5]. Now palladium-catalyzed synthesis of *N*-substituted anilines using aryl halides or halide equivalents has proven to be a very useful and versatile method in organic synthesis [6]. However, to the best of our knowledge, fewer efforts were devoted to nickel-catalyzed C-N bond formation reactions[7]. Inspired by the catalysis capability of nickel complexes[8] and Buchwald's works[9], we examined nickel complexes for their ability to promote the amination of aryl bromides with *in situ* generated dimethylamine from *N*, *N*-dimethylacetamide (DMA) and found that Ni (Phen)Cl_2 was an efficient catalyst for this transformation in mild conditions.

Scheme 1



R = H, Me, MeO, Cl, Br or NO_2

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As shown in **Scheme 1**, a solution of aryl bromides, 2% mol of Ni(Phen)Cl_2 and a hindered base such as ^{t}BuOK in DMA was stirred at 80°C for 8 h to give coupling products in good yields. We examined the amination of several substituted aryl bromides under the optimized conditions and found that *in situ* generated dimethylamine could successfully react with either electron-rich or electron-neutral aromatic system (**Table 1**, entry 1~5). This catalyst was more active for electron-poor aromatic system than for the electron-rich or electron-neutral aromatic system (**Table 1**, entry 6). The amination of 1, 4-dihalidebenzene also proceeded smoothly with *N*, *N*, *N'*, *N'*-tetramethyl -1, 4-phenylenediamine as the major by-product (**Table1**, entry 4~5).

General procedure: A solution of aryl bromide (2 mmol), ^{t}BuOK (4 mmol) and Ni(Phen)Cl_2 (0.04 mmol) in DMA (5 mL) was stirred at 80°C for 8 h. The reaction mixture was cooled to room temperature, diluted with water (10 mL), and extracted with EtOAc (3×10 mL). The combined organic layer was dried over anhydrous Na_2SO_4. The crude product was purified by silica gel chromatography.

Table 1 The yields of amination of aryl bromides with *in situ* generated dimethylaimne

Entry	Substrate	Product	Isolated Yield
1	C_6H_5Br	$C_6H_5NMe_2$	76%
2	4-Me-C_6H_5Br	4-Me-$C_6H_5NMe_2$	74%
3	4-MeO-C_6H_5Br	4-MeO-$C_6H_5NMe_2$	72%
4	4-Cl-C_6H_5Br	4-Cl-$C_6H_5NMe_2$	70%[a]
5	4-Br-C_6H_5Br	4-Br-$C_6H_5NMe_2$	73%[a]
6	4-O_2N-C_6H_5Br	4-O_2N-$C_6H_5NMe_2$	85%

a. The major by-product was *N*, *N*, *N'*, *N'*-tetramethyl-1, 4-phenylenediamine.

In conclusion, we have successfully developed a facile and efficient procedure for the synthesis of *N*, *N*-dimethylaniline derivatives from aryl bromides. Both electron-rich and electron-poor aromatic system reacted smoothly to give amination products in good yields.

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