ORGANIC LETTERS

2005
Vol. 7, No. 11
2209−2211

Arylation of Diarylamines Catalyzed by Ni(II)–PPh_3 System

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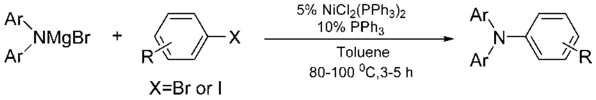
Received March 21, 2005

ABSTRACT



The cross-coupling of bromomagnesium diarylamides, generated in situ from diarylamines, with aryl bromides or iodides can be effected with a simple $NiCl_2(PPh_3)_2$–PPh_3 catalyst system under relatively mild conditions. This coupling reaction is an inexpensive, convenient, and practical method, functioning as an alternative to the corresponding Pd-catalyzed or Cu-mediated process for the synthesis of triarylamines.

Transition-metal-catalyzed cross-couplings between arylamines and aryl halides represent a powerful tool for the construction of triarylamines. These amines are an extremely important unit of organic materials with interesting electronic, photoelectronic, and magnetic properties and are extensively used in organic light-emitting diodes, photovoltaic cells, nonlinear optics, and organic photoconductors, etc.[1] So far, both the Ullmann-type reactions (Cu-mediated)[2] and the Buchwald−Hartwig methods (Pd-catalyzed)[3] have made remarkable advances in the formation of various C−N bonds, among which were syntheses of triarylamines from arylation of anilines and diarylamines.[4,5] However, in Pd-catalyzed processes, the high cost of palladium and the special ligands required to activate it limit its use at least in the large-scale preparation of triarylamines. And for Cu-catalyzed triarylamine syntheses, either expensive ligands or defined substrates such as aryl iodides are required to obtain good yields. In striking contrast, cheap and practical nickel-based catalysts, being a well-established partner of palladium catalysts in C−C bond-forming reactions, have not been fully developed in the C−N bond construction, and there are only a few reports on Ni-catalyzed halide amination in which dialkylamines and/or anilines were mainly involved.[6] Our desire to pursue an inexpensive, convenient, and mild procedure for scalable synthesis of triarylamine compounds prompted us to explore the feasibility of employing a combination of Ni-based catalysts and the most common ligands such as triphenylphosphine. To our knowledge, the Ni-catalyzed cross-coupling between diarylamines and aryl halides has not been reported. Herein, we describe our initial results on the first Ni-catalyzed arylation of diarylamines with unactivated aryl bromides or iodides.

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(1) (a) Louie, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1997**, *119*, 11695−11696. (b) Chou, M.-Y.; Leung, M.-K.; Su, Y. O.; Chiang, C. L.; Lin, C.-C.; Liu, J.-H.; Kuo, C.-K. Mou, C.-Y. *Chem. Mater.* **2004**, *16*, 654−661. For reviews, see: (c) Strohriegl, P.; Grazulevicius, J. V. *Adv. Mater.* **2002**, *14*, 1439−1452. (d) Shirota, Y. *J. Mater. Chem.* **2000**, *10*, 1−25.

(2) (a) Ullmann, F. *Chem. Ber.* **1903**, *36*, 2382−2384. For reviews, see: (b) Lindley, J. *Tetrahedron* **1984**, *40*, 1433−1456. (c) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337−2364.

(3) For reviews, see: (a) Muci, A. R.; Buchwald, S. L. Practical Palladium Catalysts for C−N and C−O Bond Formation. In *Topics in Current Chemistry*; Miyaura, N., Ed.; Springer-Verlag: Berlin, 2002; Vol. 219, p 133. (b) Hartwig, J. F. *Angew. Chem., Int. Ed.* **1998**, *37*, 2046−2067. (c) Tsuji, J. *Palladium Reagents and Catalysts: Innovations in Organic Synthesis*; Wiley: New York, 1996.

(4) For representative referenes: (a) Pd(0)/biphenyl-based phosphane system, see: Ali, M. H.; Buchwald, S. L. *J. Org. Chem.* **2001**, *66*, 2560−2565. (b) Pd(0)/P(t-Bu)$_3$ or DPPF system, see: Louie, J.; Hartwig, J. F. *Macromolecules* **1998**, *31*, 6737−6739. (c) Pd(0)/DPPF or P(o-tolyl)$_3$ system, see ref 1a.

(5) For representative references: (a) CuI/P(Bu)$_3$ system, see: Patil, N. M.; Kelkar, A. A.; Nabi, Z.; Chaudhari, R. V. *Chem. Commun.* **2003**, 2460−2461. (b) Cu(I)/neocufroine, see: Gujadhur, R. K.; Bates, C. G.; Venkataraman, D. *Org. Lett.* **2001**, *3*, 4315−4317. (c) Cu(I)/1,10-phenanthroline system, see: Goodbrand, H. B.; Hu, N. X. *J. Org. Chem.* **1999**, *64*, 670−674.

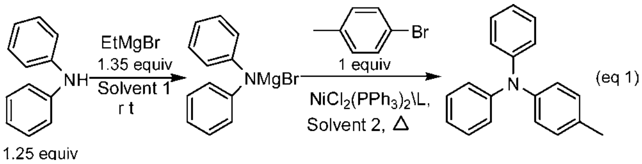
(6) For recent selected literature, see: (a) Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 6054−6058. (b) Brenner, E.; Schneider, R.; Fort, Y. *Tetrahedron* **1999**, *55*, 12829−12842. (c) Lipshutz, B. H.; Ueda, H. *Angew. Chem., Int. Ed.* **2000**, *39*, 4492−4494. (d) Tasler, S.; Lipshutz, B. H. *J. Org. Chem.* **2003**, *68*, 1190−1199.

10.1021/ol050608i CCC: $30.25 © 2005 American Chemical Society
Published on Web 04/28/2005

Ni(II) complexes such as $NiCl_2(PPh_3)_2$ or $Ni(acac)_2$ were chosen as precatalysts in view of the fact that they are readily available and conveniently manipulated due to their insensitivity to air and moisture. However, generating the catalytically active Ni(0) species in situ for the subsequent catalytic cycle would be a problem with the use of Ni(II) precatalysts because it is fundamental to reduce Ni(II) to Ni(0) for success of cross-coupling reactions.[6a,c,7] Learning from the Kumada−Corriu reaction[8] and considering the nature of diarylamines with a relatively acidic proton on the N−H group, we proposed a protocol to employ Grignard reagents both as the base for producing nucleophilic amides and as the reducing reagent for Ni(II) complex in this "two-step/one-pot" reaction (eq 1).

Initially, the whole reaction was performed in the same solvent. Although the Kumada−Corriu reaction of Grignard reagents with aryl halides readily took place in THF or ether,[8] the cross-coupling of bromomagnesium diphenylamide with *p*-bromotoluene using THF as reaction solvents gave only a low yield of the desired product (Table 1, entries 1 and 2), and no desired product was obtained with ether as a reaction solvent (entry 3). In addition, increasing the catalyst loading did not seem to be very favorable for this reaction (comparing entry 2 with entry 1). Next, we attempted to use a cosolvent of THF/toluene (1:3 v/v) to elevate the coupling reaction temperature to 90 °C, resulting in a yield of 67% (entry 4). With this result in hand, we tried to remove THF entirely under vacuum after deprotonation of diphenylamine and then added dried toluene as the reaction solvent, performing the reaction at 100 °C. As a result, a better yield of 71% was

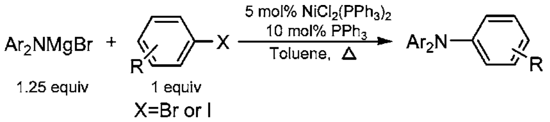
Table 1. Screening of Conditions for Ni-Catalyzed Arylation of Diphenylamine[a]

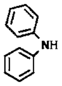
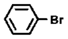
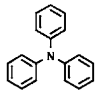
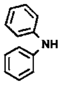
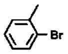
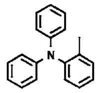
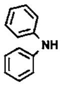
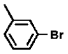
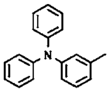
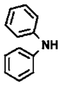
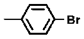
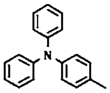
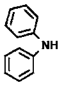
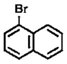
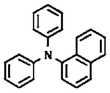
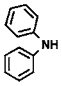
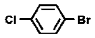
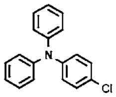
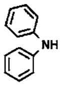
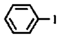
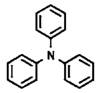
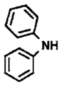
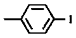
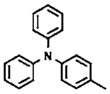
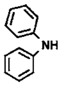
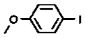
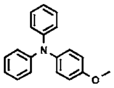
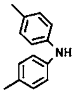
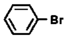
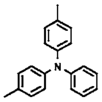
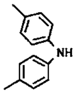
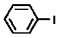
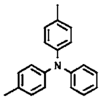
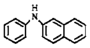
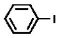
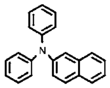
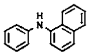
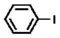
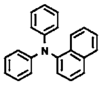
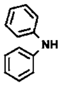
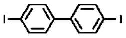
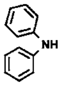


entry	solvent 1	catalyst (mol %)	ligand (mol %)	solvent 2	yield (%)[b]
1	THF	$NiCl_2(PPh_3)_2$ (3)	PPh_3 (6)	THF	25
2	THF	$NiCl_2(PPh_3)_2$ (5)	PPh_3 (10)	THF	33
3	ether	$NiCl_2(PPh_3)_2$ (5)	PPh_3 (10)	ether	none
4	THF	$NiCl_2(PPh_3)_2$ (5)	PPh_3 (10)	THF−Tol	67
5	THF	$NiCl_2(PPh_3)_2$ (5)	PPh_3 (10)	toluene	71
6	THF	$NiCl_2(PPh_3)_2$ (5)	none	toluene	58
7	THF	$Ni(acac)_2$ (5)	PPh_3 (10)	toluene	42
8	THF	$NiCl_2(PPh_3)_2$ (5)	$(C_2H_5O)_3P$ (10)	toluene	57
9	THF	$NiCl_2(PPh_3)_2$ (5)	COD (10)	toluene	69
10	THF	none	none	toluene	none

[a] Reaction conditions: a mixture of diphenylamine deprotonated in solvent 1 by EtMgBr and *p*-bromotoluene in solvent 2 was heated in the presence of Ni(II) precatalyst and ligand. [b] Isolated yields.

Table 2. $NiCl_2(PPh_3)_2$−PPh_3-Catalyzed Cross-Coupling of Bromomagnesium Diarylamides with Aryl Halides



entry	amine	aryl halide[a]	product	isolated yield(%)
1				90 (88[d])
2				91
3				77
4				71 (67[d])
5				91
6				73[b]
7				96 (96[d])
8				88
9				78
10				76
11				84
12				58
13				13
14			TPB	77[c]
15			DDP	64[c]

[a] Reactions: at 100 °C for 5 h for aryl bromides and at 80°C for 3 h for aryl iodides, respectively. [b] At 80 °C for 5 h. [c] Molar ratio of amine to halide was 2.2:1. [d] Reactons in a mixed solvent of THF−toluene (1:3).

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(7) (a) Percec, V.; Bae, J.-Y.; Hill, D. H. *J. Org. Chem.* **1995**, *60*, 1060−1065. (b) Galland, J. P.; Savignac, M.; Genet, J. P. *Tetrahedron Lett.* **1999**, *40*, 2323−2326. (c) Sato, S.; Oh-tani, S.; Miyaura, N. *J. Org. Chem.* **1997**, *62*, 8024−8030.

(8) (a) Tamao, K.; Sumitani, K.; Kumada, M. *J. Am. Chem. Soc.* **1972**, *94*, 4374−4376. (b) Corriu, R. J. P.; Masse, J. P. *J. Chem. Soc., Chem. Commun.* **1972**, 144.

achieved (entry 5). Several other combinations, $NiCl_2(PPh_3)_2$ (entry 6), $Ni(acac)_2-PPh_3$ (entry 7), $NiCl_2(PPh_3)_2-P(OEt)_3$ (entry 8), and $NiCl_2(PPh_3)_2-COD$ (entry 9), were not as effective as the $NiCl_2(PPh_3)_2-PPh_3$ system in this reaction. Finally, our "normal" reaction procedure was that diarylamine was treated in THF with a small excess of EtMgBr, and then THF was replaced with toluene[9] before addition of $NiCl_2(PPh_3)_2$, PPh_3, and aryl halide, followed by heating the reaction mixture.

With the optimal conditions, several representative diarylamines and a range of unactivated aryl bromides and iodides were examined in this reaction (Table 2). In most cases, the cross-coupling reaction proceeded in good to excellent yields (Table 2, entries 1−11, 14, and 15). For aryl halides, electron-neutral aryl halides gave higher yields than electron-rich ones (compare entry 1 with entry 4 and entry 7 with entries 8 and 9). In the case of 2-bromotoluene (entry 2), the ortho position effect of the methyl group can increase the stability of the catalytic intermediate by lowering the energy of the highest filled orbital so as to facilitate the reaction;[10] a similar effect can be observed in the case of 1-bromonaphthalene (entry 5). Generally, iodide substrates reacted more quickly and gave higher yields than bromides. The coupling of chlorobenzene with the diphenylamide was sluggish even in refluxing toluene and gave only 23% yield of triphenylamine. Therefore, a selective amination of 4-bromo-1-chlorobenzene can be carried out in good yield at lower reaction temperature (entry 6). As for diarylamines, the effect of the steric factor on this reaction appeared to be far greater than that of the electronic factor (compare with entries 7, 11, 12, and 13). For instance, the sterically hindered (2-naphthyl)phenylamine coupled with aryl iodide to afford the product only in moderate yield (entry 12), and the cross-coupling almost did not take place with the use of more hindered (1-naphthyl)phenylamine (entry 13). The double cross-coupling proceeded in good yields under similar conditions when dihaloarene was treated with over 2 equiv of bromomagnesium diphenylamide (entries 14 and 15). In this reaction, the main side reaction was homocoupling of aryl halides to form biaryls. The mechanism of this reaction should follow the catalytic cycle in the transition-metal-catalyzed coupling reaction. However, the rate-controlling step of the reactions cannot be determined by results of the current experiment and presumably may be related to oxidative addition in the catalytic cycle.

In conclusion, a simple and practical method for the Ni-catalyzed arylation of diarylamines has been developed for the synthesis of triarylamines, which provides an alternative to the similar Pd-catalyzed or Cu-mediated process. This process involves the use of amido-Mg as a nucleophilic species, not reported before in Pd- and Ni-catalyzed cross-couplings of C−N bond formation.[11] This offers us an inspiration to develop new species of amido-metals and explore new reaction conditions in transition-metal-catalyzed C−N bond-forming reactions. Further investigation into this cross-coupling in synthetic and mechanistic aspects is underway.

Acknowledgment. This work was supported by the National 863 Program of China (715-Z36-1-98).

Supporting Information Available: Detailed experimental procedure and characterization of the products. This material is available free of charge via the Internet at http://pubs.acs.org.

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[9] Similar yield was obtained when the reaction of *p*-bromotoluene and diphenylamine was performed at 100 °C in dioxane in place of toluene. In addition, it was indicated in three cases that this coupling reaction, for the sake of convenience, may be run in a cosolvent of THF−toluene so long as the reaction temperature could reach over 90 °C for the aryl bromide or over 80 °C for the aryl iodide, albeit sometimes with slightly reduced yields (see entries 1, 4, and 7 in Table 2).

[10] (a) Chatt, J.; Shaw, B. L. *J. Chem. Soc.* **1960**, 1718−1729. (b) Moss, J. R.; Shaw, B. L. *J. Chem. Soc.* **1966**, 1793−1795.

[11] For amido-lithiums, see ref 1a. For amido-tins, see: (a) Paul, F.; Patt, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1994**, *116*, 5969−5970. (b) Guram, A. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 7901−7902.