ORGANIC LETTERS

2012
Vol. 14, No. 16
4182–4185

Nickel-Catalyzed Amination of Aryl Sulfamates and Carbamates Using an Air-Stable Precatalyst

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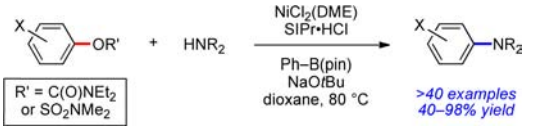
Received July 5, 2012

ABSTRACT



A facile nickel-catalyzed method to achieve the amination of synthetically useful aryl sulfamates and carbamates is reported. Contrary to most Ni-catalyzed amination reactions, this user-friendly approach relies on an air-stable Ni(II) precatalyst, which, when employed with a mild reducing agent, efficiently delivers aminated products in good to excellent yields. The scope of the method is broad with respect to both coupling partners and includes heterocyclic substrates.

Nickel-catalyzed cross-couplings of phenol-based electrophiles have received considerable attention in recent years.[1] Attractive aspects of such processes include the low cost of Ni and the many benefits that pertain to utilizing phenol derivatives. Of the substrates widely explored, aryl carbamates and sulfamates are particularly attractive because of their pronounced stability and capacity to direct the installation of functional groups onto an aromatic ring through directed ortho-metalation[1−3] or electrophilic aromatic substitution processes.[2d] Although carbon−carbon bond forming reactions using aryl sulfamates and carbamates

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10.1021/ol301847m
Published on Web 07/31/2012

have been most widely studied,[4,5] several reports of carbon−nitrogen bond formation are available.[6−9] Aminations of aryl sulfamates and carbamates are facile and proceed in synthetically useful yields; however, the air sensitivity of the nickel precatalyst employed in all cases (i.e., $Ni(cod)_2$)[10] limits the widespread use of these C−N bond forming processes.

We report the development of sulfamate and carbamate aminations using an inexpensive air-stable nickel(II) precatalyst (Figure 1). When used in combination with phenylboronic acid pinacol ester (Ph−B(pin)) as a mild reducing agent, this procedure provides an efficient and user-friendly means to achieve amination reactions across a range of aryl substrates and amine coupling partners.

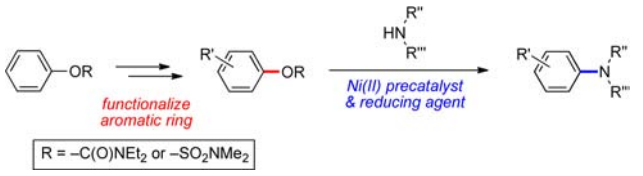
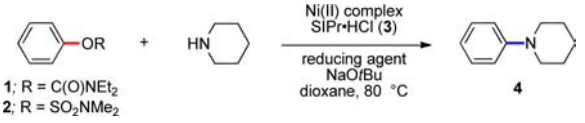


Figure 1. Amination of aryl carbamates and sulfamates using Ni(II) precatalyst.

A key challenge in developing the desired amination reaction using a Ni(II) precatalyst is the difficulty in reducing Ni(II) to Ni(0). Although Pd(II) precatalysts readily undergo in situ reduction with amines or phosphines in Pd-catalyzed Buchwald−Hartwig couplings, the corresponding reduction of Ni(II) is less facile. Ni-catalyzed amination methodologies that use Ni(II) precatalysts are only available for aryl halides and typically use Zn or hydrides as reducing agents.[11]

We selected phenylcarbamate **1** and phenylsulfamate **2** as substrates for the desired amination and then surveyed Ni(II) complexes in the presence of the NHC ligand SIPr•HCl (**3**)[12] and various reducing agents. Key results are summarized in Table 1, where piperidine was employed as the amine coupling partner. Reaction conditions utilizing Zn dust proved ineffective (entries 1 and 2), while the use of triethylsilane gave either poor or modest results (entries 3 and 4). Inspired by Suzuki−Miyaura coupling methodologies of sulfamates and carbamates, where boronic acids serve to reduce Ni(II) to Ni(0) in situ,[4a−4f] we tested the use of $Ph-B(OH)_2$ in the amination reaction. Gratifyingly, good to excellent yields could be obtained (entries 5 and 6), and the $NiCl_2(DME)$ complex[13] was identified as the optimal Ni precatalyst (entry 6). Although these results were promising, we found that the corresponding coupling of sulfamate **2** gave inconsistent results (entry 7). Nonetheless, it was observed that boronic esters could be used in place of $Ph-B(OH)_2$ or boroxines to give more consistent results (entries 8 and 9). By using Ph−B(pin) as the reducing agent with $NiCl_2(DME)$ as the precatalyst, a 94% yield of the desired aminated product **4** was obtained. These conditions were also found to be useful for the coupling of carbamate **1** (entry 10).

Table 1. Optimization of Amination Using Ni(II) Precatalyst[a]



entry	substrate	Ni source	reducing agent	yield[b]
1	**1**	$Ni(acac)_2$	Zn dust[c]	0%
2	**1**	$NiCl_2(DME)$	Zn dust[c]	0%
3	**1**	$Ni(acac)_2$	$H-SiEt_3$[c]	0%
4	**1**	$NiCl_2(DME)$	$H-SiEt_3$[c]	51%
5	**1**	$Ni(acac)_2$	$Ph-B(OH)_2$	57%
6	**1**	$NiCl_2(DME)$	$Ph-B(OH)_2$	98%
7	**2**	$NiCl_2(DME)$	$Ph-B(OH)_2$	variable
8	**2**	$NiCl_2(DME)$	$(Ph-BO)_3$	58%
9	**2**	$NiCl_2(DME)$	Ph−B(pin)	94%
10	**1**	$NiCl_2(DME)$	Ph−B(pin)	92%

[a] Conditions: Ni(II) complex (5 mol %), **3** (10 mol %), sulfamate/carbamate substrate (1 equiv), piperidine (1.2 equiv), reducing agent (0.55 equiv), NaO*t*Bu (1.85 equiv), hexamethylbenzene (0.1 equiv), 3 h. [b] Yield determined by ^1H NMR analysis of the crude reaction mixtures using hexamethylbenzene as an internal standard. [c] Reducing agent (0.8 equiv) and NaO*t*Bu (1.4 equiv).

(6) For examples of sulfamate and carbamate amination, see: (a) Mesganaw, T.; Silberstein, A. L.; Ramgren, S. D.; Fine Nathel, N. F.; Hong, X.; Liu, P.; Garg, N. K. *Chem. Sci.* **2011**, *2*, 1766–1771. (b) Ramgren, S. D.; Silberstein, A. L.; Yang, Y.; Garg, N. K. *Angew. Chem., Int. Ed.* **2011**, *50*, 2171–2173. (c) Ackermann, L.; Sandmann, R.; Song, W. *Org. Lett.* **2011**, *13*, 1784–1786.

(7) For examples of the amination of aryl sulfonates, see: (a) Hamann, B. C.; Hartwig, J. F. *J. Am. Chem. Soc.* **1998**, *120*, 7369–7370. (b) Roy, A. H.; Hartwig, J. F. *J. Am. Chem. Soc.* **2003**, *125*, 8704–8705. (c) Ogata, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 13848–13849. (d) Gao, C.-Y.; Yang, L.-M. *J. Org. Chem.* **2008**, *73*, 1624–1627. (e) Fors, B. P.; Watson, D. A.; Biscoe, M. R.; Buchwald, S. L. *J. Am. Chem. Soc.* **2008**, *130*, 13552–13554. (f) So, C. M.; Zhou, Z.; Lau, C. P.; Kwong, F. Y. *Angew. Chem., Int. Ed.* **2008**, *47*, 6402–6406.

(8) For the amination of aryl methyl ethers, see: Tobisu, M.; Shimasaki, T.; Chatani, N. *Chem. Lett.* **2009**, *38*, 710–711.

(9) For the amination of aryl pivalates, see: Shimasaki, T.; Tobisu, M.; Chatani, N. *Angew. Chem., Int. Ed.* **2010**, *49*, 2929–2932.

(10) $Ni(cod)_2$ is commercially available from Strem Chemicals Inc. or Sigma-Aldrich (CAS # 1295-35-8). For more information on this catalyst, see: Wender, P. A.; Smith, T. E.; Zuo, G.; Duong, H. A.; Louie, J. *Encyclopedia of Reagents for Organic Synthesis* **2006**, DOI: 10.1002/047084289X.rb118.pub2.

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(12) NHC ligand **3** has been employed in the Ni-catalyzed amination of sulfamates and carbamates; see refs 6a and 6b.

(13) $NiCl_2(DME)$ is commercially available from Strem Chemicals Inc. (CAS #29046-78-4) at an approximate cost of $13 USD/gram.

(14) Although the optimal reaction conditions shown in Table 1 (entries 9 and 10) are generally useful across a range of substrates, further optimization of reaction conditions for individual substrates led to improved yields. The optimized conditions and results are shown in Figures 2 and 3.

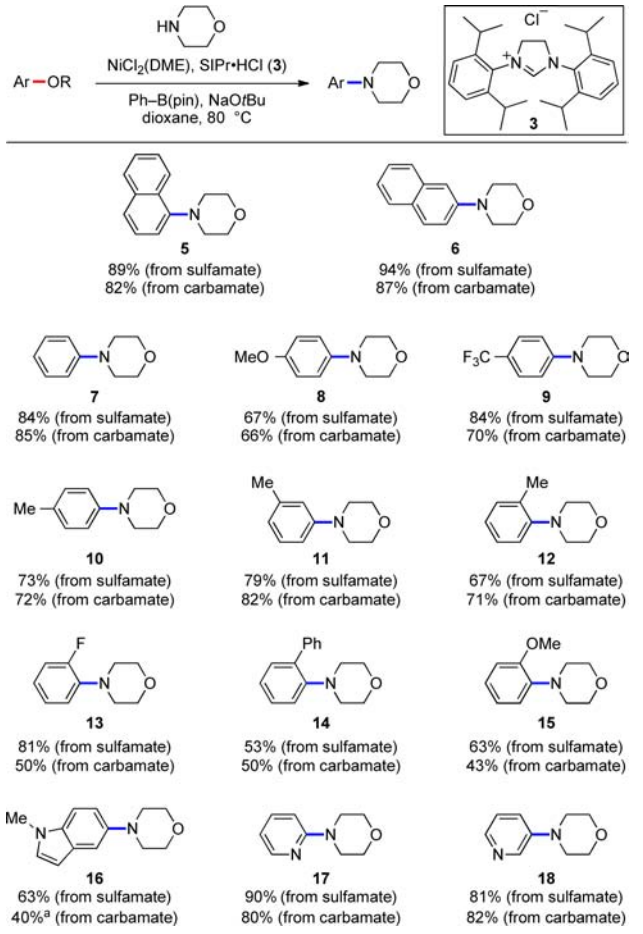


Figure 2. Amination of aryl sulfamates and carbamates using morpholine. Reaction conditions: $NiCl_2$(DME) (5−20 mol %), **3** (10−40 mol %), sulfamate/carbamate substrate (1 equiv), morpholine (1.2−2.4 equiv), Ph−B(pin) (0.15−1.4 equiv), NaO*t*Bu (1.4−3.75 equiv), 3 h. Unless otherwise noted, yields reflect those of isolated product. [a]Yield determined by ^{1}H NMR analysis with hexamethylbenzene as the internal standard.

Having identified optimal reaction conditions,[14] we examined the scope of aryl sulfamates and carbamates, using morpholine as the amine coupling partner (Figure 2). Fused arenes were tolerated, as demonstrated by the smooth formation of **5** and **6**. The ability to form **7**−**12** in good yields shows the methodology's tolerance to nonfused arenes with a variety of substituent patterns. It should also be noted that ortho-substituted substrates, which are readily accessible by ortho-functionalization of phenyl sulfamates or carbamates,[2,3] underwent the desired coupling to give **12**−**15**. Heterocycles such as indoles and pyridines were also tolerated, as revealed by the formation of products **16**−**18**. In many cases, sulfamates and carbamates perform equally well in this amination methodology.

The scope with respect to the amine coupling partner is provided in Figure 3. In addition to morpholine, the cyclic amines piperidine and pyrrolidine underwent the desired coupling to furnish **4** and **19**. Acyclic secondary amines and

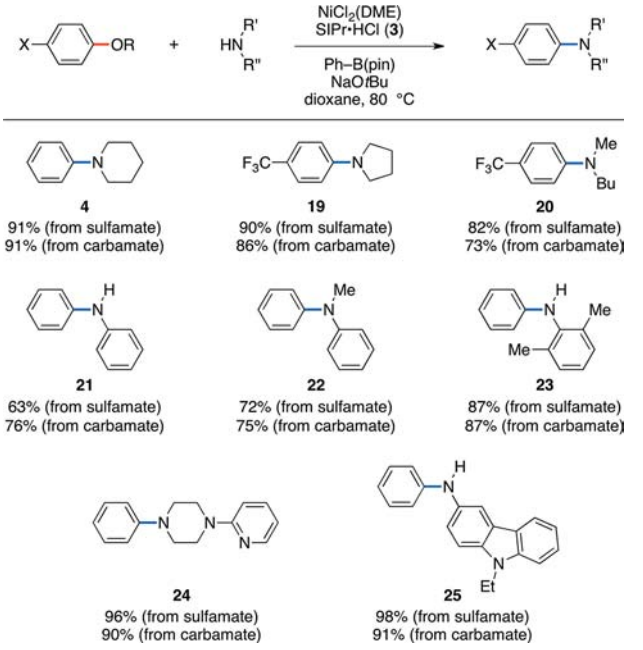
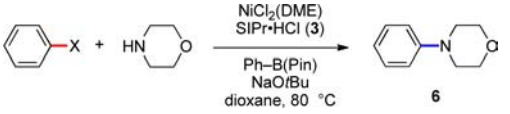


Figure 3. Amination of various amines. Reaction conditions: $NiCl_2$(DME) (5−20 mol %), **3** (10−40 mol %), sulfamate/carbamate substrate (1 equiv), amine (1.2−2.4 equiv), Ph−B(pin) (0.15−1.05 equiv), NaO*t*Bu (1.4−3.75 equiv), 3 h. Unless otherwise noted, yields reflect those of isolated product.

Table 2. Survey of Halide and Pseudohalide Substrates[a]



entry	X	yield[b]
1	OCO_2tBu	15%
2	OPiv	44%
3	OTs	63%
4	OTf	4%
5	I	25%
6	Br	33%
7	Cl	98%

[a] Conditions: $NiCl_2$(DME) (5 mol %), **3** (10 mol %), substrate (1 equiv), morpholine (1.8 equiv), Ph−B(pin) (0.35 equiv), NaO*t*Bu (2.25 equiv), hexamethylbenzene (0.1 equiv), 3 h. [b] Yield determined by ^{1}H NMR analysis with hexamethylbenzene as the internal standard.

anilines reacted successfully, as shown by the formation of **20**−**23**. Finally, amines with appended heterocycles were also tolerated, thus giving rise to **24**−**25**.

Given that most Ni-catalyzed amination reactions employ Ni(0) precatalysts, we tested the generality of our optimal reaction conditions on other electrophilic substrate classes using morpholine as the coupling partner (Table 2). Although modest results were obtained using *tert*-butyl phenyl carbonate and phenyl pivalate (entries

1 and 2), the use of phenyl tosylate was more promising, giving a 63% yield of product (entry 3). Phenyl triflate was not a suitable coupling partner (entry 4), and low yields were observed using iodobenzene or bromobenzene as the substrate (entries 5 and 6). On the other hand, chlorobenzene coupled smoothly under our reaction conditions to furnish the desired aminated product in 98% yield (entry 7).

In summary, we have developed a facile Ni-catalyzed method to achieve the amination of synthetically useful aryl sulfamates and carbamates. Our user-friendy approach employs $NiCl_2$(DME) as a bench-stable Ni(II) precatalyst, in addition to the mild reducing agent Ph−B(pin), to furnish aminated products in good to excellent yields. Given the attractive features of aryl sulfamates and carbamates, coupled with the transformation's broad scope, this Ni(II)-based methodology is expected to find use in various applications that require C−N bond construction.

Acknowledgment. The authors are grateful to Boehringer Ingelheim, DuPont, Eli Lilly, Amgen, AstraZeneca, Roche, the A. P. Sloan Foundation, the Foote family (fellowship to S.D.R.), and the University of California, Los Angeles for financial support. We thank Qi Liu for experimental assistance. These studies were supported by shared instrumentation grants from the NSF (CHE-1048804) and the National Center for Research Resources (S10RR025631).

Supporting Information Available. Experimental details and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.