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Palladium-copper-catalyzed desulfitative amination of benzo[*d*]oxazole C–H bond

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ABSTRACT

An efficient palladium-copper-catalyzed direct C–H amination of substituted benzoxazoles with various sulfamoyl chlorides as nitrogen group sources has been developed. The system does not need a strong base and tolerates a series of functional groups, such as chloro, methyl, and nitro groups, providing the amination products in moderate to excellent yields.

The transition-metal-catalyzed amination reaction of azoles is a highly important transformation in synthetic chemistry since these amination products are widely employed in biological, pharmaceutical, and material sciences.[1] In the past decades, remarkable results have been obtained in hydroamination,[2] allylic amination,[3] and oxidative amidation[4] of double or triple bonds. The palladium-catalyzed Buchwald–Hartwig coupling,[5] copper-catalyzed Ullmann and Goldberg couplings[6] and copper-promoted Chan–Lam coupling[7] are all powerful tools to fulfill these transformations. However, two functionalized precursors are required for the aforementioned transformation. To circumvent this drawback, the direct amination of heteroarenes C–H is undoubtedly the most straightforward strategy on such transformations.[8] As far as the nitrogen group sources are concerned, primary and secondary amines,[9] chloroamines,[10] and amides[11] have been successfully installed into the corresponding substrates via C–H activation. Despite the remarkable success that has been achieved, to the best of our knowledge, the desulfination of sulfamoyl chloride in the direct amination reaction via C–H bond cleavage followed by C–N bond formation has never been reported. Herein, we report the aerobic oxidative amination of azoles with sulfamoyl chlorides as nitrogen sources.

During the optimization of the reaction conditions, this amination reaction was performed using benzoxazole (**1a**) and dimethylsulfamoyl chloride (**2a**) as substrates as summarized in Table 1. Initially, the reaction was performed in dry PhCl at 150 °C in the presence of $Pd(O_2CCF_3)_2$/CuCN with $K_2Cr_2O_7$ as the oxidant, affording *N*,*N*-dimethylbenzo[*d*]oxazol-2-amine (**3aa**) in 34% yield (entry 1, Table 1). A series of palladium catalysts were screened, such as $Pd_2(dba)_3$, $PdCl_2(CH_3CN)_2$, $PdCl_2$ (entries 2–6, Table 1), and $bipyPdCl_2$ was found to be the best. Copper salts were crucial for the amination reaction. After a range of copper salts screened, CuCN was superior to others, such as $Cu(OAc)_2$, CuCl, CuI (entries 7–9, Table 1). The yield dramatically decreased to 10% without CuCN (entry 10, Table 1). Whereas CuCN was enhanced to 1.0 equiv, the yield did not improve significantly (entry 5, Table 1). We next examined the effect of oxidants on this reaction (entries 15 and 16, Table 1), and $K_2Cr_2O_7$ was the best. The base played an important role in the amination reaction and K_2CO_3 was superior to other bases (entries 5, 11–13, Table 1). The solvent had a significant impact on the reaction, replacing of PhCl with DMSO, 1,4-dioxane, or CH_3CN, the reaction became sluggish and provided poor conversions (entries 17–19, Table 1). To our delight, when 4 Å molecular sieves were added to the reaction mixture, the desired product **3aa** was obtained in 85% yield (entry 5, Table 1).

Further experiments showed that various substituted benzoxazoles allowed the direct amination reaction under the optimum reaction conditions (Table 2). Both electron-rich and electron-poor substituted benzoxazoles were successfully converted to the corresponding cross-coupling products in moderate to good yields. The procedure was a little sensitive to the electron-nature of the substituents on the aromatic ring of the benzoxazoles. For example, except for **3ca**, electron-withdrawing groups gave a slightly higher yield than electron-donating groups (**3da**, **3la** vs **3ba**, **3ea**, and **3fa**, Table 2). Notably, the *p*-methoxyphenyl, *p*-trifluoromethylphenyl, *p*-methoxycarbonylphenyl, and *p*-methylphenyl on benzoxazoles

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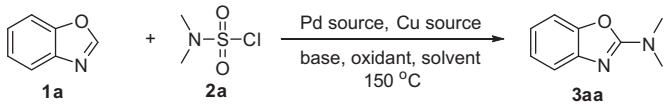
Table 1
Optimization of reaction conditions[a]

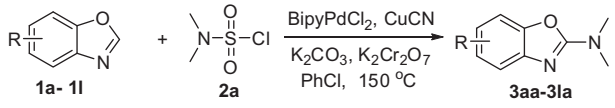


1a 2a 3aa

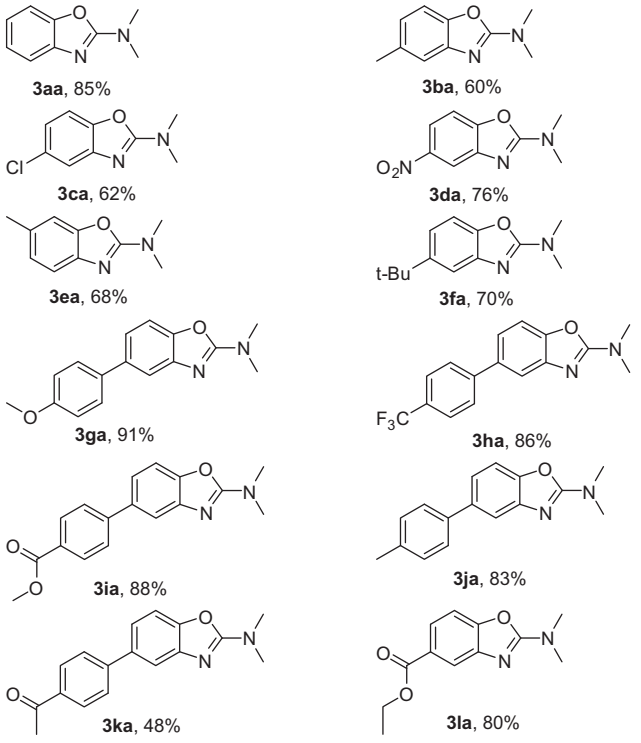
Entry	Pd source	Cu source	Base	Oxidant	Solvent	Yield[b] (%)
1	$Pd(O_2CCF_3)_2$	CuCN	K_2CO_3	$K_2Cr_2O_7$	PhCl	34
2	$Pd_2(dba)_3$	CuCN	K_2CO_3	$K_2Cr_2O_7$	PhCl	42
3	$PdCl_2(CH_3CN)_2$	CuCN	K_2CO_3	$K_2Cr_2O_7$	PhCl	75
4	$PdCl_2$	CuCN	K_2CO_3	$K_2Cr_2O_7$	PhCl	50
5	$BipyPdCl_2$	CuCN	K_2CO_3	$K_2Cr_2O_7$	PhCl	76 (85)[c] (76)[d]
6	—	CuCN	K_2CO_3	$K_2Cr_2O_7$	PhCl	66
7	$BipyPdCl_2$	$Cu(OAc)_2$	K_2CO_3	$K_2Cr_2O_7$	PhCl	60
8	$BipyPdCl_2$	CuCl	K_2CO_3	$K_2Cr_2O_7$	PhCl	62
9	$BipyPdCl_2$	CuI	K_2CO_3	$K_2Cr_2O_7$	PhCl	42
10	$BipyPdCl_2$	—	K_2CO_3	$K_2Cr_2O_7$	PhCl	10
11	$BipyPdCl_2$	CuCN	Na_2CO_3	$K_2Cr_2O_7$	PhCl	60
12	$BipyPdCl_2$	CuCN	*t*-BuOK	$K_2Cr_2O_7$	PhCl	18
13	$BipyPdCl_2$	CuCN	—	$K_2Cr_2O_7$	PhCl	65
14	$BipyPdCl_2$	CuCN	K_2CO_3	BQ	PhCl	<5
15	$BipyPdCl_2$	CuCN	K_2CO_3	DDQ	PhCl	53
16	$BipyPdCl_2$	CuCN	K_2CO_3	—	PhCl	50
17	$BipyPdCl_2$	CuCN	K_2CO_3	$K_2Cr_2O_7$	DMSO	40
18	$BipyPdCl_2$	CuCN	K_2CO_3	$K_2Cr_2O_7$	1,4-Dioxane	32
19	$BipyPdCl_2$	CuCN	K_2CO_3	$K_2Cr_2O_7$	CH_3CN	58

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), Pd source (10 mol %), Cu source (20 mol %), base (0.4 mmol), and oxidant (0.2 mmol), in dry PhCl (2 mL), air, 150 °C, sealed tube, 24 h.
[b] Isolated yield.
[c] 4 Å molecular sieves (50 mg).
[d] CuCN (1.0 equiv).

Table 2
Palladium-copper-catalyzed direct amination of benzoxazole with dimethylsulfamoyl chloride[a]

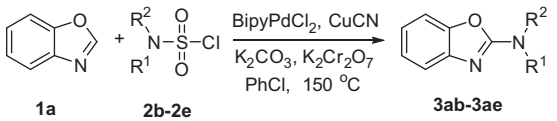


1a- 1l 2a 3aa-3la

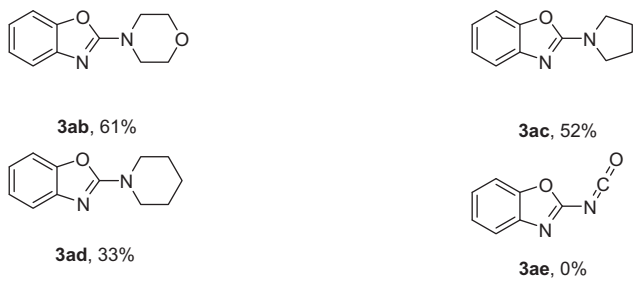


[a] Reaction conditions: **1** (0.2 mmol), **2a** (0.3 mmol), $BipyPdCl_2$ (10 mol %), CuCN (20 mol %), K_2CO_3 (0.4 mmol) and $K_2Cr_2O_7$ (0.2 mmol), in dry PhCl (2 mL), air, 150 °C, sealed tube, 24 h, 4 Å MS (50 mg).

Table 3
Palladium-copper-catalyzed direct amination of benzoxazole with sulfamoyl chloride [a]



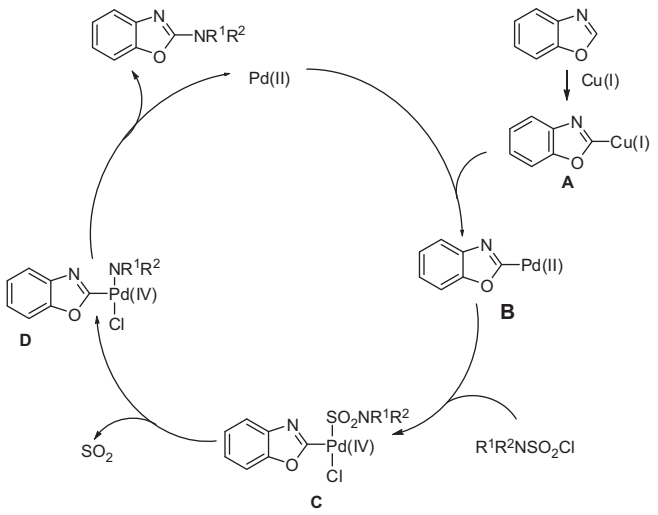
1a 2b-2e 3ab-3ae



[a] Reaction conditions: **1a** (0.2 mmol), **2** (0.3 mmol), $BipyPdCl_2$ (10 mol %), CuCN (20 mol %), K_2CO_3 (0.4 mmol) and $K_2Cr_2O_7$ (0.2 mmol), in dry PhCl (2 mL), air, 150 °C, sealed tube, 24 h, 4 Å MS (50 mg).

were all well tolerated under these reaction conditions and the desired products were obtained in good yields (**3ga–3ja**, Table 2). The *p*-acetylphenyl on benzoxazole which had an electron-withdrawing group only provided the product in 48% yield (**3ka**, Table 2). It was regrettable that benzothiazole, benzofuran and *N*-methylindole did not work under the optimum reaction conditions.

Next, some sulfamoyl chlorides were tested for the direct amination of benzoxazole (Table 3). Sulfamoyl chloride including morpholine-4-sulfonyl chloride, pyrrolidine-1-sulfonyl chloride, and piperidine-1-sulfonyl chloride were tolerated under the optimal reaction conditions, and the desired products were obtained in



Scheme 1. Plausible mechanism.

moderate yields (**3ab–3ad**, Table 3). Unfortunately, no desired product was obtained when chlorosulfonyl isocyanate was employed under the reaction conditions, which may be caused by the SO_2 extrusion from chlorosulfonyl isocyanate unsuccessfully (**3ae**, Table 3).

Based upon the previous literature, a plausible mechanism was outlined in Scheme 1. A Pd(IV/II) catalytic cycle may be involved in this transformation. Firstly, the cupration of benzoxazole took place to form Cu(I) species **A**.[12] Meanwhile, the oxidative addition of sulfamoyl chloride of Pd(II) formed a Pd(II) species **B**. Secondly, the transmetallation of Cu(I) to Pd formed the new Pd(IV) species **C**. The intermediate **C** released SO_2 to yield intermediate **D**.[13] Finally, the reductive elimination of intermediate **D** released the aminated product, along with the Pd(II) to enter the catalytic cycle. However, we could not thoroughly rule out the possibility of a Pd(0)/Pd(II) mechanism.[14]

In summary, an efficient and palladium-copper-catalyzed direct C–H amination of substituted benzoxazoles with sulfamoyl chlorides as nitrogen group sources has been developed in moderate to excellent yields. The reaction provides a novel methodology allowing for a wide functional group tolerance. Further studies aimed at obtaining a better understanding of the reaction mechanism and at expanding the substrate scope of the reaction are underway.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2012.09.044.

References and notes

1. (a) *Amino Group Chemistry, From Synthesis to the Life Sciences*; Ricci, A., Ed.; Wiley-VCH: Weinheim, 2007; (b) Seregin, I. V.; Gevorgan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173; (c) Hili, R.; Yudin, A. K. *Nat. Chem. Biol.* **2006**, *2*, 284.
2. (a) Muller, T. E.; Hultzsch, K. C.; Yus, M.; Foubelo, F.; Tada, M. *Chem. Rev.* **2008**, *108*, 3795; (b) Xu, H.-C.; Moeller, K. D. *Org. Lett.* **2010**, *12*, 5174; (c) Reznichenko, A. L.; Nguyen, H. N.; Hultzsch, K. C. *Angew. Chem., Int. Ed.* **2010**, *49*, 8984; (d) Wang, L.-G.; Yu, X.-Q.; Feng, X.-J.; Bao, M. *Org. Lett.* **2012**, *14*, 2418; (e) Kulshrestha, A.; Marzijarani, N. S.; Ashtekar, K. D.; Staples, R.; Borhan, B. *Org. Lett.* **2012**, *14*, 3592.
3. (a) Takemoto, Y.; Miyabe, H. In *Comprehensive Organometallic Chemistry*; Crabtree, R. H., Mingos, D. M. P., Eds.; Elsevier: Oxford, 2007; Vol. 10, (b) Johannsen, M.; Jorgensen, K. A. *Chem. Rev.* **1998**, *98*, 1689; (c) Yin, G.; Wu, Y.; Liu, G. *J. Am. Chem. Soc.* **2010**, *132*, 11978; (d) Lin, C.-F.; Ojima, I. *J. Org. Chem.* **2011**, *76*, 6240; (e) Souto, J. A.; Zian, D.; Muniz, K. *J. Am. Chem. Soc.* **2012**, *134*, 7242.
4. (a) Brice, J. L.; Harang, J. E.; Timokhin, V. I.; Anastasi, N. R.; Stahl, S. S. *J. Am. Chem. Soc.* **2005**, *127*, 2868; (b) Lee, J. M.; Ahn, D.-S.; Jung, D. Y.; Lee, J.; Do, Y.; Kim, S. K.; Chang, S. *J. Am. Chem. Soc.* **2006**, *128*, 12954; (c) Mcdonald, R. I.; White, P. B.; Weinstein, A. B.; Tam, C. P.; Stahl, S. S. *Org. Lett.* **2011**, *13*, 2830; (d) Panda, N.; Jena, A. K.; Raghavender, M. *ACS Catal.* **2012**, *2*, 539.
5. (a) Muci, A. R.; Buchwald, S. L. *Top. Curr. Chem.* **2002**, *219*, 131; (b) Surry, D. S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 6338; (c) Hartwig, J. F. *Acc. Chem. Res.* **2008**, *41*, 1534; (d) Bouhlel, A.; Curti, C.; Khoumeri, O.; Vanelle, P. *Tetrahedron. Lett.* **2011**, *52*, 1919; (e) Mitsudo, K.; Shimohara, S.; Mizoguchi, J.; Mandia, H.; Suga, S. *Org. Lett.* **2012**, *14*, 2702.
6. Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400.
7. (a) Qiao, J. X.; Lam, P. Y. S. *Synthesis* **2011**, 829; (b) He, C.; Chen, C.; Cheng, J.; Liu, C.; Liu, W.; Li, Q.; Lei, A.-W. *Angew. Chem., Int. Ed.* **2008**, *47*, 6414; (c) Matsuda, N.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 3642; (d) Rucker, R. P.; Whittaker, A. M.; Dang, H.; Lalic, G. *Angew. Chem., Int. Ed.* **2012**, *51*, 3953.
8. For reviews on direct C–H bond amination reactions, see: (a) Collet, F.; Dodd, R. H.; Dauban, P. *Chem. Commun.* **2009**, 5061; (b) Zalatan, D. N.; Bois, J. D. *Top. Curr. Chem.* **2010**, *292*, 347; (c) Armstrong, A.; Collins, J. C. *Angew. Chem., Int. Ed.* **2010**, *49*, 2282; (d) Thansandote, P.; Lautens, M. *Chem. Eur. J.* **2009**, *15*, 5874.
9. Selected recent literatures: (a) Yoo, E. J.; Ma, S.; Mei, T.-S.; Chan, K. S. L.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 7652; (b) Monguchi, D.; Fujiwara, T.; Furukawa, H.; Mori, A. *Org. Lett.* **2009**, *11*, 1607; (c) Lamani, M.; Prabhu, K. R. *J. Org. Chem.* **2011**, *76*, 7938; (d) Wertz, S.; Kodama, S.; Studer, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 11511; (e) Thu, H.-Y.; Yu, W.-Y.; Che, C.-M. *J. Am. Chem. Soc.* **2006**, *128*, 9048; (f) John, A.; Nicholas, K. M. *J. Org. Chem.* **2011**, *76*, 4158; (g) Li, Y.; Xie, Y.; Zhang, R.; Jin, K.; Wang, X.; Duan, C. *J. Org. Chem.* **2011**, *76*, 5444; (h) Bercovici, D. A.; Brewer, M. *J. Am. Chem. Soc.* **2012**, *134*, 9890.
10. Selected recent literatures: (a) Matsuda, N.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2011**, *13*, 2860; (b) Kawano, T.; Hirano, K.; Satoh, T.; Miura, M. *J. Am. Chem. Soc.* **2010**, *132*, 6900; (c) Liu, X.-Y.; Gao, P.; Shen, Y.-W.; Liang, Y.-M. *Org. Lett.* **2011**, *13*, 4196; (d) Ng, K.-H.; Zhou, Z.; Yu, W.-Y. *Org. Lett.* **2012**, *14*, 272; (e) Grohmann, C.; Wang, H.; Glorius, F. *Org. Lett.* **2012**, *14*, 656.
11. Selected recent literatures: (a) Miyasaka, M.; Hirano, K.; Satoh, T.; Kowalczyk, R.; Bolm, C.; Miura, M. *Org. Lett.* **2011**, *13*, 359; (b) Xiao, B.; Gong, T.-J.; Xu, J.; Liu, Z.-J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 1466; (c) Wang, J.; Hou, J.-T.; Wen, J.; Zhang, J.; Yu, X.-Q. *Chem. Commun.* **2011**, *47*, 3652; (d) Li, J.-J.; Mei, T.-S.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2008**, *47*, 6452; (e) Tan, Y.; Hartwig, J. F. *J. Am. Chem. Soc.* **2010**, *132*, 3676.
12. (a) Do, H.-Q.; Daugulis, O. *Org. Lett.* **2010**, *12*, 2517; (b) Do, H.-Q.; Daugulis, O. *J. Am. Chem. Soc.* **2007**, *129*, 12404; (c) Fukuzawa, S.; Shimizu, E.; Atsuumi, Y.; Haga, M.; Ogata, K. *Tetrahedron Lett.* **2009**, *50*, 2374; (d) Zhao, X.; Wu, G.-J.; Zhang, Y.; Wang, J.-B. *J. Am. Chem. Soc.* **2011**, *133*, 3296.
13. (a) Zhao, X.-D.; Dimitrijević, E.; Dong, V. M. *J. Am. Chem. Soc.* **2009**, *131*, 3466; (b) Zhao, X.-D.; Dong, V. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 932.
14. Some recent papers about desulfitative arylation of azoles via Pd(0)/Pd(II) mechanism: (a) Chen, R.; Liu, S.; Liu, X.; Yang, L.; Deng, G.-J. *Org. Biomol. Chem.* **2011**, *9*, 7675; (b) Liu, B.; Guo, Q.; Cheng, Y.; Lan, J.; You, J. *Chem. Eur. J.* **2011**, *17*, 13415; (c) Wang, M.; Li, D.; Zhou, W.; Wang, L. *Tetrahedron* **1926**, *2012*, 68; (d) Liu, B.; Li, J.; Song, F.; You, J. *Chem. Eur. J.* **2012**, *18*, 10830; (e) Yu, X.; Li, X.; Wan, B. *Org. Biomol. Chem.* **2012**, *10*, 7479.