ORGANIC LETTERS

2012
Vol. 14, No. 7
1748–1751

Copper-Catalyzed Alkylation of Benzoxazoles with Secondary Alkyl Halides

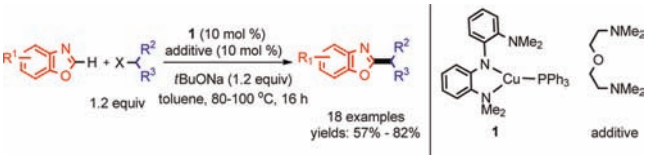
Peng Ren, Isuf Salihu, Rosario Scopelliti, and Xile Hu*

Laboratory of Inorganic Synthesis and Catalysis, Institute of Chemical Sciences and Engineering, Ecole Polytechnique Fédérale de Lausanne (EPFL), SB-ISIC-LSCI, BCH 3305, Lausanne 1015, Switzerland

xile.hu@epfl.ch

Received February 13, 2012

ABSTRACT



Copper-catalyzed direct alkylation of benzoxazoles using nonactivated secondary alkyl halides has been developed. The best catalyst is a new copper(I) complex (1), and the reactions are promoted by bis[2-(*N*,*N*-dimethylamino)ethyl] ether.

Aromatic heterocycles are important organic molecules because they often exhibit interesting biological, pharmaceutical, and material functions.[1] In recent years, direct C−H functionalization has emerged as one of the most straightforward and efficient methods for the derivatization of aromatic heterocycles. Significant progress has been made in direct arylation, alkenylation, and alkynylation.[2,3] Direct alkylation, however, proves to be more challenging, especially if the alkyl groups contain β-hydrogens.[4] This is likely due to the tendency of metal alkyl intermediates to undergo unproductive β-H elimination.[5]

Several approaches are now available for direct alkylation of aromatic heterocycles, including Friedel−Crafts,[6] radical alkylation,[7] insertion of C−H bonds into olefins,[8,9] coupling of heterocycles with tosylhydrozones,[10,11] and coupling of heterocycles with alkyl electrophiles.[12−14] Most reported methods only introduce a primary alkyl group. Metal-catalyzed hydroarylation of olefins is in principle an effective way to incorporate a secondary alkyl group onto heterocycles, yet current success is largely limited to the introduction of activated alkyl (e.g., benzyl and allyl) groups.[8] Wang et al. pioneered Cu-catalyzed direct benzylation and allylation of azoles with *N*-tosylhydrozones.[10]

(1) (a) Eicher, T.; Hauptmann, S. *The Chemistry of Heterocycles*; Wiley-VCH: Weinheim, 2003. (b) Carey, J. S.; Laffan, D.; Thomson, C.; Williams, M. T. *Org. Biomol. Chem.* **2006**, *4*, 2337–2347. (c) Kraft, A.; Grimsdale, A. C.; Holmes, A. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 402–428.

(2) (a) Campeau, L. C.; Fagnou, K. *Chem. Commun.* **2006**, 1253–1264. (b) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172–8174. (c) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068–5083. (d) Ackermann, L.; Althammer, A.; Fenner, S. *Angew. Chem., Int. Ed.* **2009**, *48*, 201–204. (e) Join, B.; Yamamoto, T.; Itami, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 3644–3647. (f) Besselievre, F.; Piguel, S. *Angew. Chem., Int. Ed.* **2009**, *48*, 9553–9556. (g) Brand, J. P.; Charpentier, J.; Waser, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 9346–9349. (h) Turner, G. L.; Morris, J. A.; Greaney, M. F. *Angew. Chem., Int. Ed.* **2007**, *46*, 7996–8000. (i) Matsuyama, N.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett.* **2009**, *11*, 4156–4159. (j) Hachiya, H.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 2202–2205. (k) Kitahara, M.; Hirano, K.; Tsurugi, H.; Satoh, T.; Miura, M. *Chem.—Eur. J.* **2010**, *16*, 1772–1775. (l) Messaoudi, S.; Brion, J. D.; Alami, M. *Eur. J. Org. Cherm.* **2010**, 6495–6516. (m) Li, H.; Sun, C. L.; Yu, M. A.; Yu, D. G.; Li, B. J.; Shi, Z. J. *Chem.—Eur. J.* **2011**, *17*, 3593–3597.

(3) (a) Daugulis, O.; Do, H. Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074–1086. (b) Hirano, K.; Miura, M. *Synlett* **2011**, 294–307.

(4) For representative examples of direct alkylation of nonheterocyclic substrates, see: (a) Ackermann, L.; Novak, P.; Vicente, R.; Hofmann, N. *Angew. Chem., Int. Ed.* **2009**, *48*, 6045–6048. (b) Ackermann, L.; Hofmann, N.; Vicente, R. *Org. Lett.* **2011**, *13*, 1875–1877. (c) Zhang, Y. H.; Shi, B. F.; Yu, J. Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 6097–6100. (d) Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2010**, *132*, 3965–3972. (e) Zhao, Y. S.; Chen, G. *Org. Lett.* **2010**, *13*, 4850–4853. (f) Altenhoff, G.; Wurtz, S.; Glorius, F. *Tetrahedron Lett.* **2006**, *47*, 2925–2928. (g) Eckhardt, M.; Fu, G. C. *J. Am. Chem. Soc.* **2003**, *125*, 13642–13643.

(5) (a) Frisch, A. C.; Beller, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 674–688. (b) Netherton, M. R.; Fu, G. C. *Adv. Synth. Catal.* **2004**, *346*, 1525–1532. (c) Rudolph, A.; Lautens, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 2656–2670. (d) Ackermann, L. *Chem. Commun.* **2010**, *46*, 4866–4877. (e) Hu, X. L. *Chem. Sci.* **2011**, *2*, 1867–1886.

10.1021/ol300348w
Published on Web 03/09/2012

Miura et al. reported Ni- and Co-catalyzed alkylation of azoles with *N*-tosylhydrozones, which was the first general method to couple nonactivated secondary alkyl groups with azoles.[11] We and others recently developed metal-catalyzed direct alkylation of azoles and thiazoles using nonactivated alkyl halides.[10,13,14] Unfortunately, only primary alkyl halides could be used. Herein we describe Cu-catalyzed alkylation of benzoxazoles with secondary alkyl halides. An important additive is also identified.

Earlier work from our group showed that a Ni pincer complex, [($^{Me}N_2N$)NiCl],[15,16] was an active (pre)catalyst for cross coupling of nonactivated alkyl halides[17,18] and direct C−H alkylation.[13,19] We then became interested in the chemistry of analogous Cu complexes. The anionic bis(amino)amide ligand N_2N alone was not sufficient to stabilize the Cu(I) ion, as the reactions of [($^{Me}N_2N$)Li]$_2$[15] with a Cu(I) precursor (e.g., CuI, CuCl, [Cu(CH_3CN)$_4$]PF_6) led to the formation of copper mirror and protonated ligand H$^{Me}N_2N$. Triphenylphosphine, however, could be used as a coligand to form a stable Cu(I) complex. Thus, reaction of [($^{Me}N_2N$)Li]$_2$ with [Cu(PPh_3)Cl]$_4$ yielded [($^{Me}N_2N$)Cu(PPh_3)] (**1**).[20] The solid-state molecular structure of **1** was established by X-ray crystallography (Figure 1). The Cu ion is in a distorted trigonal planar ligand environment. The N_2N ligand is bidentate, with one of the amine donors being noncoordinating (N3−Cu1 = 3.290(2) Å). The Cu−N (amide) distance (1.9406(16) Å) is significantly shorter than the Cu−N (amine) distance (2.1339(16) Å).

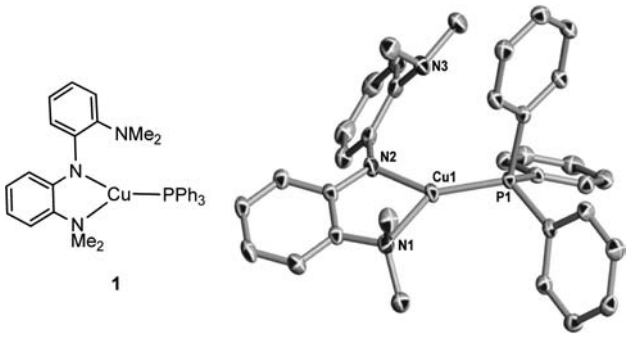


Figure 1. (Left) Structural formula for complex **1**. (Right) X-ray structure of **1**. The thermal ellipsoids are displayed in 50% probability. Selected bond lengths (Å) and angles (deg): Cu1−N1, 2.1339(16); Cu1−N2, 1.9406(16); Cu1−P1, 2.1492(6); N1−Cu1−N2, 85.00(6); N2−Cu1−P1, 143.42(5); P1−Cu1−N1, 131.34(5).

Complex **1** turned out to be a good catalyst for direct alkylation. The coupling of benzoxazole with cyclopentyl iodide was used as the test reaction (Table 1). The Ni/Cu based method, which was efficient for direct coupling of azoles with primary alkyl halides,[13] was inefficient for this reaction. After modification, it gave a maximum yield of 4% (entry 1, Table 1). Replacing [($^{Me}N_2N$)NiCl] with **1** improved the yield to 32% (entry 2, Table 1). Increasing the loading of **1** to 10 mol % further increased the yield to 50% (entry 3, Table 1). The yields were similar when the reactions were run at 80 or 100 °C. ^{t}BuONa and toluene were the best base and solvent combination. Other combinations such as ^{t}BuOLi + dioxane, ^{t}BuOLi + DMF, Cs_2CO_3 + toluene gave no or inferior yields. Interestingly, without CuI as cocatalyst, the yield was only 11% (entry 4, Table 1). CuI alone did not catalyze the reaction (entry 5, Table 1).

In our previous studies of Ni-catalyzed Kumada-type coupling reactions, we found that bis[(2-(*N*,*N*-dimethylaminoethyl)]ether (BDMAEE, previously abbreviated as O-TMEDA) often promoted the catalysis.[18] Out of curiosity, we tested the effect of BDMAEE for direct alkylation. To our delight, addition of 5 mol % or 0.2 equiv of BDMAEE led to a coupling yield of 77% (entry 6, Table 1). Slightly lower yields were obtained when the loadings of BDMAEE were between 1 and 5 equiv. Lowering the temperature from 100 to 80 °C further increased the yield to 87% (entry 7, Table 1). CuI was no longer necessary under these conditions, and when **1** was replaced by CuI (15 mol %) the yield decreased to 62%. When another soluble Cu(I) complex, [Cu(Phen)(PPh_3)$_2$]NO_3 (phen = phenanthroline) or Cu(S(CH_3)$_2$)Br or [Cu(PPh_3)Cl]$_4$, was used as precatalyst, the yield was about 60% (entry 9, Table 1). These results indicate a superior catalytic activity for complex **1**. On the other hand, [($^{Me}N_2N$)NiCl] was still a poor catalyst even with BDMAEE as additive (compare entries 1 and 10, Table 1). A control experiment showed

(6) Roberts, R. M.; Khalaf, A. A. *Friedel−Crafts Alkylation Chemistry. A Century of Discovery*; Marcel Dekker: New York, 1984.

(7) (a) Minisci, F.; Vismara, E.; Fontana, F. *Heterocycles* **1989**, *28*, 489–519. (b) Molander, G. A.; Colombel, V.; Braz, V. A. *Org. Lett.* **2011**, *13*, 1852–1855. (c) Bowman, W. R.; Storey, J. M. D. *Chem. Soc. Rev.* **2007**, *36*, 1803–1822.

(8) (a) Rueping, M.; Nachtsheim, B. J.; Scheidt, T. *Org. Lett.* **2006**, *8*, 3717–3719. (b) Kischel, J.; Jovel, I.; Mertins, K.; Zapf, A.; Beller, M. *Org. Lett.* **2006**, *8*, 19–22. (c) Wang, M. Z.; Wong, M. K.; Che, C. M. *Chem.—Eur. J.* **2008**, *14*, 8353–8364. (d) Nakao, Y.; Yamada, Y.; Kashihara, N.; Hiyama, T. *J. Am. Chem. Soc.* **2010**, *132*, 13666–13668. (e) Nakao, Y.; Kashihara, N.; Kanyiva, K. S.; Hiyama, T. *Angew. Chem., Int. Ed.* **2010**, *49*, 4451–4454. (f) Nakao, Y.; Idei, H.; Kanyiva, K. S.; Hiyama, T. *J. Am. Chem. Soc.* **2009**, *131*, 15996–15997. (g) Mukai, T.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74*, 6410–6413.

(9) Lewis, J. C.; Bergman, R. G.; Ellman, J. A. *Acc. Chem. Res.* **2008**, *41*, 1013–1025.

(10) Zhao, X.; Wu, G. J.; Zhang, Y.; Wang, J. B. *J. Am. Chem. Soc.* **2011**, *133*, 3296–3299.

(11) Yao, T.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 775–779.

(12) (a) Verrier, C.; Hoarau, C.; Marsais, F. *Org. Biomol. Chem.* **2009**, *7*, 647–650. (b) He, T.; Yu, L.; Zhang, L.; Wang, L.; Wang, M. *Org. Lett.* **2011**, *13*, 5016–5019. (c) Ackermann, L.; Barfusser, S.; Kornhaass, C.; Kapdi, A. R. *Org. Lett.* **2011**, *13*, 3082–3085.

(13) Vechorkin, O.; Proust, V.; Hu, X. L. *Angew. Chem., Int. Ed.* **2010**, *49*, 3061–3064.

(14) (a) Yao, T.; Hirano, K.; Satoh, T.; Miura, M. *Chem.—Eur. J.* **2010**, *16*, 12307–12311. (b) Ackermann, L.; Punji, B.; Song, W. F. *Adv. Synth. Catal.* **2011**, *353*, 3325–3329.

(15) Csok, Z.; Vechorkin, O.; Harkins, S. B.; Scopelliti, R.; Hu, X. L. *J. Am. Chem. Soc.* **2008**, *130*, 8156–8157.

(16) Vechorkin, O.; Csok, Z.; Scopelliti, R.; Hu, X. L. *Chem.—Eur. J.* **2009**, *15*, 3889–3899.

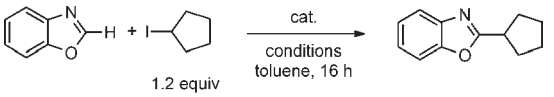
(17) Vechorkin, O.; Hu, X. L. *Angew. Chem., Int. Ed.* **2009**, *48*, 2937–2940.

(18) (a) Vechorkin, O.; Proust, V.; Hu, X. L. *J. Am. Chem. Soc.* **2009**, *131*, 9756–9766. (b) Vechorkin, O.; Scopelliti, R.; Hu, X. L. *Angew. Chem., Int. Ed.* **2011**, *50*, 11777–11781.

(19) Vechorkin, O.; Barmaz, D.; Proust, V.; Hu, X. L. *J. Am. Chem. Soc.* **2009**, *131*, 12078–12079.

(20) See the Supporting Information.

Table 1. Optimization of Conditions for the Coupling of Benzoxazole with Cyclopentyl-I[a]



entry	catalysts	conditions	yield[b] (%)
1	5 mol % of [(^{Me}N$_2$N)NiCl] and 5 mol % of CuI	1.4 equiv of ^{t}BuONa, 140 °C	4
2	5 mol % of **1** and 5 mol % of CuI	1 equiv of ^{t}BuONa, 100 °C	32
3	10 mol % of **1** and 5 mol % of CuI	1.2 equiv of ^{t}BuONa, 80 or 100 °C	50
4	10 mol % of **1**	1.2 equiv of ^{t}BuONa, 80 °C	11
5	5 mol % of CuI	1.2 equiv of ^{t}BuONa, 80 °C	0
6	10 mol % of **1** and 5 mol % of CuI	5 mol % or 0.2 equiv of BDMAEE, 1.2 equiv of ^{t}BuONa, 100 °C	77
7	10 mol % of **1**	0.2 equiv of BDMAEE, 1.2 equiv of ^{t}BuONa, 80 °C	**87/80**[c]
8	15 mol % of CuI	0.2 equiv of BDMAEE, 1.2 equiv of ^{t}BuONa, 80 °C	62
9	10 mol % of [Cu(Phen)(PPh$_3$)$_2$]NO$_3$, Cu(S(CH$_3$)$_2$)Br, or [Cu(PPh$_3$)Cl]$_4$	0.2 equiv of BDMAEE, 1.2 equiv of ^{t}BuONa, 80 °C	57−61
10	10 mol % of [(^{Me}N$_2$N)NiCl] and 5 mol % of CuI	0.2 equiv of BDMAEE, 1.2 equiv of ^{t}BuONa, 80 °C	10
11	none	0.2 equiv of BDMAEE, 1.2 equiv of ^{t}BuONa, 80 °C	0
12	6.5 mol % of [(BDMAEE)Cu$_2$I$_2$]	0.2 equiv of BDMAEE, 1.2 equiv of ^{t}BuONa, 80 °C	61
13	10 mol % of **1**	0.2 equiv of TMEDA, 1.2 equiv of ^{t}BuONa, 80 °C	44
14	15 mol % of CuI	0.2 equiv of TMEDA, 1.2 equiv ^{t}BuONa, 80 °C	0
15	10 mol % of [(TMEDA)CuI]	1.2 equiv of ^{t}BuONa, 80 °C	0

[a] See the Supporting Information for experimental details. [b] GC yield relative to benzoxazole. [c] Isolated yield.

that without a Cu catalyst, BDMAEE did not catalyze the coupling (entry 11, Table 1). Finally, a preparative reaction under the optimized conditions (entry 7, Table 1) gave the alkylated product in an isolated yield of 80%.

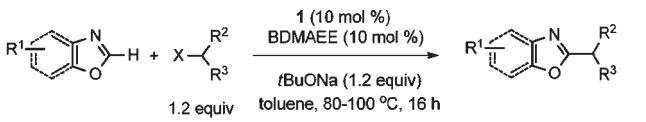
As BDMAEE was essential for achieving high yields in the Cu-catalyzed direct alkylation, its roles were investigated. Obviously BDMAEE is a potential ligand. When CuI or Cu(S(CH$_3$)$_2$)Br was used as precatalyst (entries 8 and 9, Table 1), the real catalyst most likely was a Cu−BDMAEE complex. Reaction of CuI with BDMAEE produced a copper complex that appeared to be [(BDMAEE)Cu$_2$I$_2$] according to NMR and elemental analysis.[20] Using this complex as catalyst, the coupling of benzoxazole with cyclopentyl iodide had a yield of 61%, similar to those obtained using CuI or Cu(S(CH$_3$)$_2$)Br in conjunction with BDMAEE. However, BDMAEE was not a ligand when complex **1** was used as catalyst, as no reaction occurred between **1** and BDMAEE. Furthermore, using **1** as catalyst, the yield was significantly higher (87%) than using [(BDMAEE)Cu$_2$I$_2$] as catalyst. Under these conditions, BDMAEE must have another important role. It is possible that BDMAEE partially solubilizes the inorganic base and promotes the deprotonation of azole. It is also possible that BDMAEE facilitates the transmetalation of azole anions to the Cu center in **1**. These roles might be replaced by CuI, albeit with a lower efficiency. In fact, the combination of **1** and CuI gave a coupling yield of about 50% (entry 3, Table 1), much higher than that of 11% using **1** alone (entry 4, Table 1). TMEDA (tetramethylethylenediamine) was another poor substitute for BDMAEE, resulting in a yield of 40% (entry 13, Table 1). The combination of CuI and TMEDA alone was not catalytically active (entries 14 and 15, Table 1).

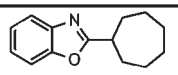
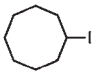
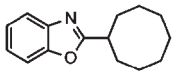
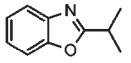
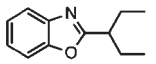
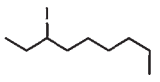
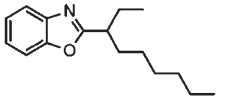
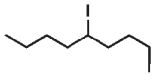
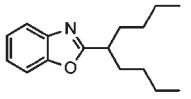
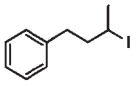
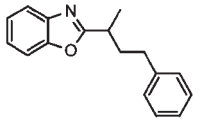
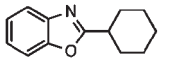
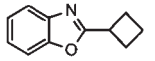
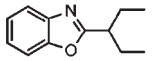
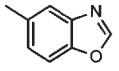
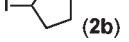
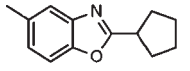
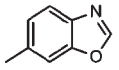
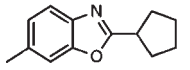
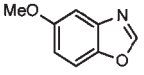
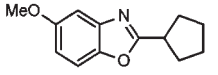
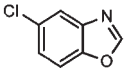
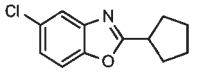
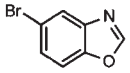
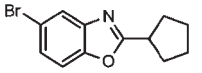
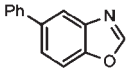
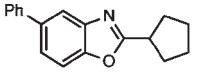
The scope of the Cu-catalyzed alkylation was then explored (Table 2). Cycloheptyl- and cyclooctyl-I were coupled to benzoxazole in high yields (entries 1−2, Table 2). Acyclic secondary alkyl iodides were also suitable substrates, and the reactions were insensitive to the length of the alkyl chains (entries 3−7, Table 2). Secondary alkyl bromides could be coupled (entries 8−10, Table 2). Addition of a catalytic amount of CuI increased the yield substantially, probably because CuI mediated an I/Br exchange reaction.[21] Other iodide sources were not as effective. Unfortunately secondary alkyl chlorides did not react even in the presence of ^{n}Bu$_4$NI. Cl/I exchange must be difficult for secondary alkyl chlorides under these conditions. Substituted benzoxazoles could also be alkylated in high yields (entries 11−16, Table 2). Both electron-donating Me and MeO groups and electron withdrawing Cl and Br groups were tolerated. The aryl-Cl and aryl-Br moieties in the products (entries 14 and 15, Table 2) leave room for further functionalization by traditional cross coupling methods. Interestingly, for some unknown reasons, the coupling of primary alkyl halides was not efficient (Table S1, Supporting Information). Fortunately, such coupling could be achieved using previously reported Ni-catalysis.[10,13,14] Oxazoles other than benzoxazoles could not be coupled with high efficiency either.

The catalytic cycle of the Cu-catalyzed alkylation reaction might be similar to those proposed for Cu-catalyzed direct arylation and alkynylation of aromatic heterocycles.[2c,3] The azoles are deprotonated and transmetalated to Cu, and the resulting organometallic Cu species react with alkyl halides to give the coupling products. We showed earlier by a Hg-test

(21) In the coupling reactions of alkyl bromides, trace amounts of alkyl iodides could be observed by GC in the product mixture.

Table 2. Scope of Cu-Catalyzed Alkylation of Benzoxazoles[a]



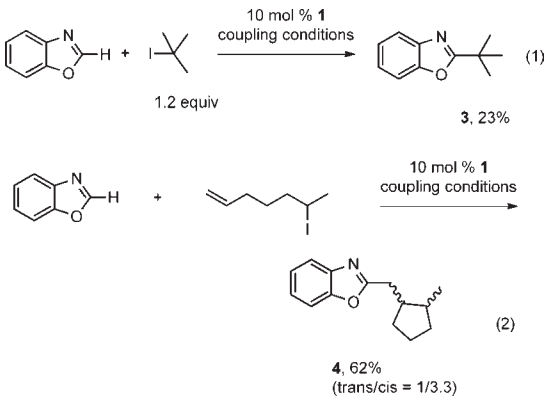
entry	azole	alkyl-x	product	yield (%)[b]
1	**2a**			73
2	**2a**			75
3	**2a**			81
4	**2a**			71
5	**2a**			81
6	**2a**			82
7	**2a**			76
8	**2a**			66[c]
9	**2a**			57
10	**2a**			60[c]
11		 **(2b)**		63
12		**2b**		62
13		**2b**		64
14		**2b**		73
15		**2b**		69
16		**2b**		64

[a] 80 °C for alkyl-I and 100 °C for alkyl-Br. See the Supporting Information for experimental details. [b] Isolated yield. [c] 10 mol % of **1** + 20 mol % of CuI + 40 mol % of BDMAEE were used.

experiment that Ni particles were the active species for Ni-catalyzed direct alkylation.[13] A similar Hg-test was conducted for the Cu catalysis. Thus, the coupling of benzoxazole with cyclopentyl-I was conducted in the presence of 10 equiv of Hg. The yield was 74%, close to the value obtained in the absence of Hg. This result suggests, albeit does not prove, that homogeneous Cu complexes are the active species.

A few experiments were carried out to probe the activation process of alkyl halides. Coupling of benzoxazole with *tert*-butyl-I gave **3** in a yield of 23% (eq 1, Scheme 1). While the yield is too low to be synthetically useful, the result rules out the possibility of a S_N2 process for the alkylation. The reaction of benzoxazole with 6-iodohept-1-ene gave the ring-closed product **4** in a yield of 62% (eq 2, Scheme 1). This result indicates that the activation of secondary alkyl halides occurs via a radical process. Furthermore, the recombination of the resulting secondary carbon radical with the catalyst is slower than the ring-closing rearrangement of the hept-6-en-2-radical, which has a first-order rate constant of about 10^5 s^{-1}.[22] When the coupling of benzoxazole with cyclopentyl-I was conducted in the presence of 1 equiv of a radical inhibitor, TEMPO, the yield was zero. This result is consistent with a radical mechanism for the alkylation.

Scheme 1. Alkylation Reactions Using Mechanistic Probes (Isolated Yields Are Reported)



In conclusion, we have developed a Cu-catalyzed direct alkylation of benzoxazoles. While the scope is limited and remains to be improved, to the best of our knowledge, this is the first time nonactivated secondary alkyl halides have been used as electrophiles. The well-defined Cu complex **1** is the best catalyst. The higher efficiency of **1** relative to other copper catalysts might result from a hemilabile property of the pincer ligand, which is subject to further elucidation and exploitation. The alkylation is promoted by a catalytic amount of BDMAEE. A similar promotion might be found for other C−H functionalization reactions.

Acknowledgment. This work is supported by the Swiss National Science Foundation (Project No. 20021_126498).

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

(22) Fossey, J. S.; Lefort, D.; Sorba, J. *Free Radicals in Organic Chemistry*; Wiley: New York, 1995.

The authors declare no competing financial interest.