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Synthesis of *N*-Substituted-2-Aminobenzothiazoles by Ligand-Free Copper(I)-Catalyzed Cross-Coupling Reaction of 2-Haloanilines with Isothiocyanates

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Keywords: Copper / Fused-ring systems / Domino reactions / Cross-coupling / Heterocycles

A novel and efficient formation of *N*-substituted-2-aminobenzothiazoles by a ligand-free copper(I)-catalyzed one-pot cascade process was developed. A variety of isothiocyanates coupled with 2-iodoanilines to give *N*-substituted-2-aminobenzothiazoles in moderate to excellent yields under mild conditions.

Introduction

2-Aminobenzothiazoles such as 2-anilinobenzothiazoles, 2-(*N*-alkylamino)benzothiazoles, and 2-(*N*-acylamino)benzothiazoles are important intermediates and broadly found in biological chemistry and medicinal areas.[1] A great amount of 2-anilinobenzothiazole derivatives are found to be anticancer active. For example, 2-anilinobenzothiazole (**A**; R116010) is a potential inhibitor of retinoic acid metabolism;[2] 2-anilinobenzothiazole (**B**) is claimed to possess activity for enhancing the atRA-induced expression of CYP26B1.[3] Many 2-(*N*-alkylamino)benzothiazoles (**C**)[1b,4] and 2-(*N*-acylamino)benzothiazole derivatives (**D**)[5] might also be biologically active and of pharmaceutical value (Figure 1).

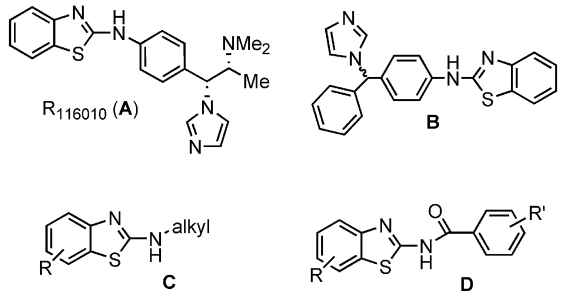

Figure 1. Several *N*-substituted-2-aminobenzothiazole derivatives reported as biologically active compounds and pharmaceutical products.

There are several methods to synthesize *N*-substituted-2-aminobenzothiazoles, including: (i) cyclization of arylthioureas with liquid bromine and benzyltrimethylammonium tribromide,[6,1b] (ii) coupling of arylamines with 2-halobenzothiazole,[7] (iii) coupling of 2-aminobenzothiazoles with aryl halides,[8] (iv) oxidative cyclization of the intermediates generated by 2-aminothiophenol with isothiocyanates,[9] and (v) intramolecular C–S bond formation for the synthesis of 2-aminobenzothiazoles catalyzed by Cu^{I}/Pd[10] and some multistep methods.[11] Although these reactions might proceed efficiently, they usually suffer from the use of highly toxic and corrosive reagents, high-costing metal catalysts, and specific ligands. These drawbacks make the methodologies difficult to be a choice in large- and industrial-scale applications. However, in recent years copper-catalyzed reactions, especially ligand-free reactions, have received considerable attention because of their efficiency and low costs.[12] Very recently, these copper-catalyzed strategies have been successfully applied to the synthesis of various heterocyclic compounds through one-pot strategies.[13] Our group is also interested in this copper-catalyzed one-pot strategy and developed a copper-catalyzed cascade addition/cyclization methodology for the synthesis of several types of heterocyclic compounds.[14] For example, *ortho*-iodophenol underwent the intermolecular addition/intramolecular C–S coupling reaction with isothiocyanate under catalysis of Cu^{I}–ligand–base to give 2-iminobenzo-1,3-oxathioles.

Herein, we wish to report a new example of the copper-catalyzed cascade addition/cyclization reaction to synthesize *N*-substituted-2-aminobenzothiazoles catalyzed by a copper(I) salt under ligand-free conditions. Our designed and proposed approach is similar to our previous reactions and is summarized in Scheme 1. The nucleophilic N atom of 2-iodoanilines **a** would attack the carbon atom of NCS on isothiocyanatobenzene **b**; intermediate **d** could then be formed in the presence of a proper base (step 1).[14c] With a proper copper(I) catalyst, the sulfur atom would take priority over the nitrogen atom in assaulting cyclization action and **d** might be converted into product **c** through intramolecular C–S coupling (step 2).[15]

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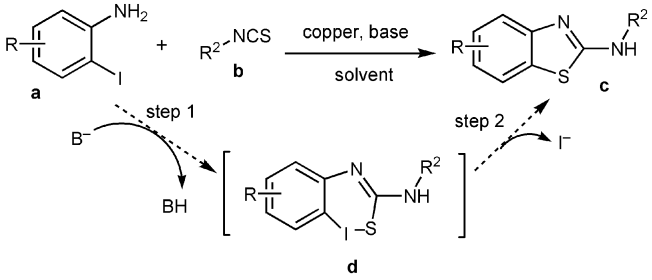
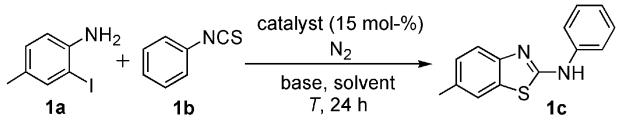


Scheme 1. Designed one-pot synthesis of *N*-substituted-2-aminobenzothiazoles through intermolecular addition/intramolecular C–S coupling.

Results and Discussion

Initially, 2-iodo-4-methylaniline (**1a**) and isothiocyanatobenzene (**1b**) were selected as the model substrates (Table 1). Catalyzed by CuI, different ligands, temperatures, bases, and solvents were examined to set up standard reaction conditions. The reaction was firstly carried out in DMSO with CuI (15 mol-%), 1,10-phenanthroline (30 mol-%) as the catalyst, Cs_2CO_3 (3.0 equiv.) as the base at 115 °C under a nitrogen atmosphere. The reaction was stopped 24 h later, and anticipated product **1c** was obtained in 45% yield after flash chromatography (Table 1, Entry 1). To increase the yield, the reaction temperature was set to 125 °C and 65% yield was obtained (Table 1, Entry 2). Besides DMSO, a number of other solvents such as NMP and *n*PrCN were also surveyed under these conditions, but the yield did not improve greatly (Table 1, Entries 3 and 4). Different ligands such as ethyl 2-oxocyclohexanecarboxylate (β-keto ester) and L-proline were also tested, and the yield changed a little (Table 1, Entries 5 and 6). We envisioned that the reaction should be efficient. As changes in the temperature, ligand, and solvent did not have much of an effect, we thought that maybe the base played an important role. The amount of the base was reduced to one equivalent. To our delight, the starting materials disappeared and product **1c** was formed in excellent yield after 24 h (Table 1, Entry 7). When a much cheaper base K_2CO_3 was used, an even higher yield was obtained (97%; Table 1, Entry 8). Considering that β-diaza compounds could serve as a ligand in the Cu^I-catalyzed coupling reactions,[16] we tried a "ligand-free" reaction, because the intermediate and the product in our reaction were β-diaza compounds. Only CuI and K_2CO_3 (1 equiv.) were added. The reaction was conducted in DMSO at 125 °C and the product was obtained in 97% yield (Table 1, Entry 9). By lowering the reaction temperature to 95 °C, the

Table 1. Optimization of the reaction conditions.



Entry	Catalyst/ligand	Base (equiv.)	Solvent	*T* [°C]	Yield [%][a]
1	CuI/1,10-phenanthroline	Cs_2CO_3 (3.0)	DMSO	115	45[b]
2	CuI/1,10-phenanthroline	Cs_2CO_3 (3.0)	DMSO	125	65[b]
3	CuI/1,10-phenanthroline	Cs_2CO_3 (3.0)	*n*PrCN	125	68[b]
4	CuI/1,10-phenanthroline	Cs_2CO_3 (3.0)	NMP	125	30[b]
5	CuI/L-proline	Cs_2CO_3 (3.0)	DMSO	125	30[b]
6	CuI/β-keto ester	Cs_2CO_3 (3.0)	DMSO	125	64[b]
7	CuI/1,10-phenanthroline	Cs_2CO_3 (1.0)	DMSO	125	96[c]
8	CuI/1,10-phenanthroline	K_2CO_3 (1.0)	DMSO	125	97[c]
9	CuI	K_2CO_3 (1.0)	DMSO	125	97[d]
10	CuI	K_2CO_3 (1.0)	DMSO	95	96[d]
11	CuI	K_2CO_3 (1.0)	DMSO	85	90[d]
12	CuI	K_2CO_3 (1.0)	DMSO	65	40[d]
13	CuI	K_2CO_3 (1.0)	DMF	95	94[d]
14	CuI	K_2CO_3 (1.0)	1,4-dioxane	95	40[d]
15	CuI	Et_3N (1.0)	DMSO	95	35[d]
16	–	K_2CO_3 (1.0)	DMSO	95	18
17	Cu_2O	K_2CO_3 (1.0)	DMSO	95	80[d]
18	CuBr	K_2CO_3 (1.0)	DMSO	95	92[d]
19	$Cu(OAc)_2$	K_2CO_3 (1.0)	DMSO	95	94[d]
20	CuI	K_2CO_3 (1.0)	DMSO	95	98[e]

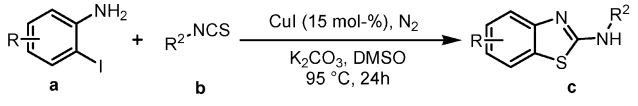
[a] Isolated yield after flash chromatography and based on 2-iodo-4-methylaniline.[b] Reaction conditions: CuI (0.06 mmol), ligand (0.12 mmol), 2-iodo-4-methylaniline (0.4 mmol), isothiocyanatobenzene (0.7 mmol), and base (1.2 mmol) in solvent (2.0 mL) under a nitrogen atmosphere. [c] Reaction conditions: CuI (0.06 mmol), ligand (0.12 mmol), 2-iodo-4-methylaniline (0.4 mmol), isothiocyanatobenzene (0.7 mmol), and base (0.4 mmol) in solvent (2.0 mL) under a nitrogen atmosphere. [d] Reaction conditions: copper salt (0.06 mmol), 2-iodo-4-methylaniline (0.4 mmol), isothiocyanatobenzene (0.7 mmol), and base (0.4 mmol) in solvent (2.0 mL) under a nitrogen atmosphere. [e] Reaction conditions: CuI (0.75 mmol), 2-iodo-4-methylaniline (5 mmol), isothiocyanatobenzene (8.75 mmol), and base (5 mmol) in solvent (10 mL) under a nitrogen atmosphere.

yield decreased only a little (Table 1, Entry 10). Obviously these are the best conditions. Et_3N was also tried but it was ineffective (Table 1, Entry 15). Interestingly, the product was obtained in 18% yield without the catalyst (Table 1, Entry 16). Some other catalysts such as Cu_2O, CuBr, and $Cu(OAc)_2$ were also tested (Table 1, Entries 17–19), but CuI provided the best yield. When the amount of 2-iodo-4-methylaniline was increased to 5 mmol (1.17 g), the yield increased to 98% (Table 1, Entry 20).

With the optimal condition established, we tried to investigate the scope of this methodology. Firstly, the reactions of 2-iodoanilines **a** with various substituted isothiocyanates **b** were examined (Table 2, Entries 1–13). The isothiocyanatobenzenes bearing both electron-donating groups (*o*-Me, *m*-Me, *p*-Me, and *p*-MeO) and electron-withdrawing groups (*p*-Cl) were able to couple with **1a** in moderate to excellent yields (Table 2, Entries 1–5). The yields of the reaction were not affected by the steric hindrance of both substrates (Table 2, Entries 1–4), but electron-withdrawing groups on the isothiocyanates were unfavorable to the reaction (Table 2, Entry 5). Besides the isothiocyanatobenzenes, some other isothiocyanates like benzoyl isothiocyanate and (isothiocyanatomethyl)benzene could also react well with 2-iodo-4-methylaniline (Table 2, Entries 6–8). These substrates enlarged the scope of this reaction. Furthermore, 2-iodoaniline was also investigated and good results were detected (Table 2, Entries 9–11). As for 2-iodoanilines bearing electron-withdrawing groups, the yields decreased obviously (Table 2, Entries 12 and 13).

Encouraged by the above results, we further investigated the scope and the generality of the method by varying the 2-iodoanilines to 2-bromoanilines and 2,6-dibromopyridin-

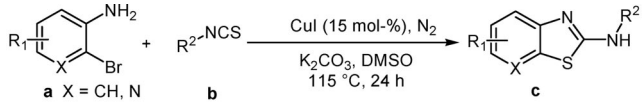
Table 2. CuI-catalyzed one-pot synthesis of *N*-substituted-2-aminobenzothiazoles from 2-iodoanilines **a** and isothiocyanates **b**.[a]



Entry	R	R^2	Product	Yield [%][b]
1	4-CH_3	2-$CH_3C_6H_4$	**2c**	84
2	4-CH_3	3-$CH_3C_6H_4$	**3c**	90
3	4-CH_3	4-$CH_3C_6H_4$	**4c**	81
4	4-CH_3	4-$CH_3OC_6H_4$	**5c**	92
5	4-CH_3	4-ClC_6H_4	**6c**	65
6	4-CH_3	C_6H_5CO	**7c**	83
7	4-CH_3	4-$CH_3OC_6H_4CO$	**8c**	60
8	4-CH_3	$C_6H_5CH_2$	**9c**	78
9	H	C_6H_5	**10c**	91
10	H	4-$CH_3C_6H_4$	**11c**	80
11	H	$C_6H_5CH_2$	**12c**	73
12	Cl	C_6H_5	**13c**	69
13	4-CH_3,6-I	C_6H_5	**14c**	60

[a] Reaction conditions: CuI (0.06 mmol), 2-iodo-4-methylaniline (0.4 mmol), isothiocyanates (0.7 mmol), and base (0.4 mmol) in DMSO (2.0 mL) at 95 °C under a nitrogen atmosphere. [b] Isolated yield after flash chromatography based on 2-iodoanilines.

Table 3. CuI-catalyzed one-pot synthesis of *N*-substituted-2-aminobenzothiazoles from 2-bromoaniline **a** and isothiocyanates **b**.[a]

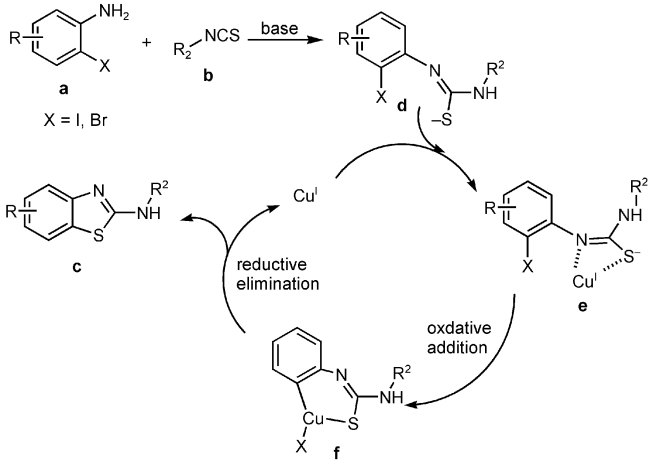


Entry	X	R_1	R^2	Product	Yield [%][b]
1	CH	H	C_6H_5	**10c**	90
2	CH	H	C_6H_5CO	**15c**	70
3	CH	H	$C_6H_5CH_2$	**12c**	65
4	CH	4-CH_3	C_6H_5	**1c**	80
5	CH	H	4-$CH_3OC_6H_4$	**16c**	84
6	N	6-Br	4-$CH_3C_6H_4$	**17c**	74
7	N	6-Br	C_6H_5	**18c**	70

[a] Reaction conditions: CuI (0.06 mmol), 2-iodo-4-methylaniline (0.4 mmol), isothiocyanates (0.7 mmol), and base (0.4 mmol) in DMSO (2.0 mL) at 115 °C under a nitrogen atmosphere. [b] Isolated yield after flash chromatography based on 2-bromoanilines.

3-amine (Table 3, Entries 1–8). To our delight, generally the reactions proceeded successfully in moderate to excellent yields, although higher temperatures were required. Several 2-bromoanilines were coupled with various isothiocyanates from moderate to excellent yields (Table 3, Entries 1–5). Finally, 2,6-dibromopyridin-3-amine was also tested. The yield was relatively lower than that of the 2-bromoanilines, probably because the electronic effect of 2,6-dibromopyridin-3-amine (6-Br) influenced the intramolecular coupling process (Table 3, Entries 6 and 7).

A plausible mechanism, which accounts for the formation of the *N*-substituted-2-aminobenzothiazoles from the 2-iodoanilines and isothiocyanates, is shown in Scheme 2. The nucleophilic N atom of 2-iodoanilines **a** would attack the carbon atom on NCS and intermediate **d** could be formed in the presence of a proper base. Coordination of copper to **d** gave **e**. Reductive elimination released product **c** with concomitant regeneration of the catalyst.



Scheme 2. Plausible mechanism.

Conclusions

In summary, we have developed a novel, efficient, and concise method to synthesize *N*-substituted-2-aminobenzothiazoles under ligand-free copper(I)-catalyzed conditions. A simple "one-pot" operation was conducted, readily available starting materials were employed, and relatively mild conditions were applied. Various *N*-substituted-2-aminobenzothiazoles, which might be potentially applicable in the pharmaceutical and biochemical areas, were conveniently synthesized in moderate to excellent yields. The reaction is also a good example of a ligand-free copper(I)-catalyzed one-pot cascade process.

Experimental Section

General Procedure: An oven-dried Schlenk tube equipped with a Teflon valve was charged with a magnetic stir bar, K_2CO_3 (0.4 mmol, 100 mol-%), CuI (0.06 mmol, 15 mol-%), and 2-haloanilines (0.4 mmol). The tube was evacuated and backfilled with N_2 (this procedure was repeated 3 times). Under a counter flow of N_2, DMSO (2.0 mL) was added by syringe. Then, isothiocyanates (0.7 mmol) were added by syringe under a counter flow of N_2. The reaction mixture was stirred for 24 h at 95(115) °C. The reaction was monitored by TLC. After the starting material was consumed completely, the reaction was stopped and cooled to room temperature. H_2O (20 mL) was added to the solvent, and the mixture was extracted with EtOAc (3×15 mL). The extracts were combined and washed with water (2×10 mL) and brine (15 mL) and dried ($MgSO_4$). After evaporating the solvent under reduced pressure, the residue was purified by column chromatography on silica gel to give the pure product.

Supporting Information (see footnote on the first page of this article): Spectroscopic data and copies of the ^1H and ^{13}C NMR spectra.

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[1] a) A. C. Gyorkos, C. P. Corrette, S. Y. Cho, T. M. Turner, S. A. Pratt, K. Aso, M. Kori, M. Gyoten, Worldwide Patent 2005, 044, 793, **2005**; [*Chem. Abstr.* **2005**, *142*, 482]; b) A. D. Jordan, C. Luo, A. B. Reitz, *J. Org. Chem.* **2003**, *68*, 8693; c) A. R. Katritzky, D. O. Tymoshenko, D. Monteux, V. Vvedensky, G. Nikonov, C. B. Cooper, M. Deshpande, *J. Org. Chem.* **2000**, *65*, 8059; d) R. A. Glennon, J. J. Gaines, M. E. Rogers, *J. Med. Chem.* **1981**, *24*, 766.

[2] J. Van Heusden, R. Van Ginckel, H. Bruwiere, P. Moelans, B. Janssen, W. Floren, B. J. van der Leede, J. van Dun, G. Sanz, M. Venet, L. Dillen, C. Van Hove, G. Willemsens, M. Janicot, W. Wouters, *Br. J. Cancer* **2002**, *86*, 605.

[3] M. S. Gomaa, J. L. Armstrong, B. Bobillon, G. J. Veal, A. Brancale, C. P. F. Redfern, C. Simons, *Bioorg. Med. Chem.* **2008**, *16*, 8301.

[4] a) C. Liu, J. Lin, S. Pitt, R. F. Zhang, J. S. Sack, S. E. Kiefer, K. Kish, A. M. Doweyko, H. Zhang, P. H. Marathe, J. Trzaskos, M. Mckinnon, J. H. Dodd, J. C. Barrish, G. L. Schieven, K. Leftheris, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 1874; b) K. Takagi, *Chem. Lett.* **1986**, 265.

[5] a) E. Y. Song, N. Kaur, M. Y. Park, Y. Jin, K. Lee, G. Kim, K. Y. Lee, J. S. Yang, J. H. Shin, K. Y. Nam, K. T. No, G. Han, *Eur. J. Med. Chem.* **2008**, *43*, 1519; b) P. L. Sangwan, J. L. Koul, S. Koul, M. V. Reddy, N. Thota, I. A. Khan, A. Kumar, N. P. Kallia, G. N. Qazi, *Bioorg. Med. Chem.* **2008**, *16*, 9847; c) D. Armenise, N. de Laurentis, A. Reho, A. Rosato, F. Morlacchi, *J. Heterocycl. Chem.* **2004**, *41*, 771.

[6] J. M. Sprague, A. H. Land in *Heterocyclic Compounds* (Ed.: R. C. Elderfield), Wiley, New York, **1957**, vol. 5, ch. 8, p. 484.

[7] a) T. Suzuki, S. Igari, A. Hirasawa, M. Hata, M. Ishiguro, H. Fujieda, Y. Itoh, T. Hirano, H. Nakagawa, M. Ogura, M. Makishima, G. Tsujimoto, N. Miyata, *J. Med. Chem.* **2008**, *51*, 7640; b) H. F. Motiwala, R. Kumar, A. K. Chakraborti, *Aust. J. Chem.* **2007**, *60*, 369; c) F. Delmas, A. Avellaneda, C. Di Giorgio, M. Robin, E. De Clercq, P. Timon-David, J. P. Galy, *Eur. J. Med. Chem.* **2004**, *39*, 685; d) J. Das, R. V. Moquin, J. Lin, C. J. Liu, A. M. Doweyko, H. F. DeFex, Q. Fang, S. Pang, S. Pitt, D. R. Shen, G. L. Schieven, J. C. Barrish, J. Wityak, *Bio. Med. Chem. Lett.* **2003**, *13*, 2587; e) H. Tanikawa, K. Ishii, S. Kubota, S. Yagai, A. Kitamura, T. Karatsu, *Tetrahedron Lett.* **2008**, *49*, 3444.

[8] a) Z. Li, S. X. Xiao, G. Q. Tian, A. G. Zhu, X. Feng, J. Liu, *Phosphorus Sulfur Silicon* **2008**, *183*, 1124; b) Q. L. Shen, T. Ogata, J. F. Hartwig, *J. Am. Chem. Soc.* **2008**, *130*, 6586; c) J. J. Yin, M. M. Zhao, M. A. Huffman, J. M. McNamara, *Org. Lett.* **2002**, *4*, 3481.

[9] D. Fajkusova, P. Pazdera, *Synthesis* **2008**, *8*, 1297.
[10] L. L. Joyce, G. Evindar, R. A. Batey, *Chem. Commun.* **2004**, 446–447.
[11] a) J. Garin, E. Melendez, F. L. Merchan, P. Merino, J. Orduna, R. Tejedor, T. Tejero, *J. Heterocycl. Chem.* **1990**, *27*, 221; b) A. R. Katritzky, D. O. Tymoshenko, D. Monteux, V. Vvedensky, G. Nikonov, C. B. Cooper, M. Deshpande, *J. Org. Chem.* **2000**, *65*, 8059.
[12] a) A. V. Kel'in, A. W. Sromek, V. Gevorgyan, *J. Am. Chem. Soc.* **2001**, *123*, 2074; b) I. P. Beletskaya, A. V. Cheprakov, *Coord. Chem. Rev.* **2004**, *248*, 2337; c) C. Koradin, K. Polborn, P. Knochel, *Angew. Chem.* **2002**, *114*, 2651; *Angew. Chem. Int. Ed.* **2002**, *41*, 2535; d) F. Himo, T. Lovell, R. Hilgraf, V. V. Rostovtsev, L. Noodleman, K. B. Sharpless, V. V. Fokin, *J. Am. Chem. Soc.* **2005**, *127*, 210; e) A. Kondoh, H. Yorimitsu, K. Oshima, *J. Am. Chem. Soc.* **2007**, *129*, 4099; f) H. Isobe, K. Cho, N. Solin, D. B. Werz, P. H. Seeberger, E. Nakamura, *Org. Lett.* **2007**, *9*, 4611; g) A. Klapars, S. Parris, K. W. Anderson, S. L. Buchwald, *J. Am. Chem. Soc.* **2004**, *126*, 3529; h) L. Ackermann, H. K. Potukuchi, D. Landsberg, R. Vicente, *Org. Lett.* **2008**, *10*, 3081; i) J. F. Hartwig, *Angew. Chem.* **1998**, *110*, 2154.
[13] Selected examples for the synthesis of heterocycles by a copper-catalyzed one-pot process: a) J. Zhu, H. Xie, Z. Chen, S. Li, Y. Wu, *Chem. Commun.* **2009**, 2338; b) L. Li, M. Wang, X. Zhang, Y. Jiang, D. Ma, *Org. Lett.* **2009**, *11*, 1309; c) A. K. Verma, T. Kesharwani, J. Singh, V. Tandon, R. C. Larock, *Angew. Chem. Int. Ed.* **2009**, *48*, 1138; d) P.-Y. Yao, Y. Zhang, R. P. Hsung, K. Zhao, *Org. Lett.* **2008**, *10*, 4275; e) Y. Ohta, H. Chiba, S. Oishi, N. Fujii, H. Ohno, *Org. Lett.* **2008**, *10*, 3535; f) B. Wang, B. Lu, Y. Jiang, Z. Zhang, D. Ma, *Org. Lett.* **2008**, *10*, 2761; g) Y. Chen, Y. Wang, Z. Sun, D. Ma, *Org. Lett.* **2008**, *10*, 625; h) D. Yang, H. Fu, L. Hu, Y. Jiang, Y. Zhao, *J. Org. Chem.* **2008**, *73*, 7841; i) Q. Yuan, D. Ma, *J. Org. Chem.* **2008**, *73*, 5159; j) R. D. Viirre, G. Evindar, R. A. Batey, *J. Org. Chem.* **2008**, *73*, 3452.
[14] a) X. Lv, W. Bao, *J. Org. Chem.* **2009**, *74*, 5618–5621; b) W. Bao, Y. Liu, X. Lv, W. Qian, *Org. Lett.* **2008**, *10*, 3899–3902; c) X. Lv, Y. Liu, W. Qian, W. Bao, *Adv. Synth. Catal.* **2008**, *350*, 2507–2512.
[15] a) K. Takagi, *Chem. Lett.* **1986**, *15*, 265–266; b) Z. Duan, S. Ranjit, P. Zhang, X. Liu, *Chem. Eur. J.* **2009**, *15*, 3666–3669.
[16] G. Evano, N. Blanchard, M. Toumi, *Chem. Rev.* **2008**, *108*, 3054.

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