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N-Heterocyclic Carbene Copper(I) Complex-Catalyzed Synthesis of 2-Aryl Benzoxazoles and Benzothiazoles.

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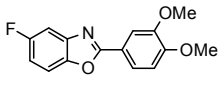
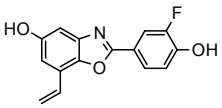
A new and efficient synthesis of 2-aryl benzoxazoles and benzothiazoles using cooper *N*-heterocyclic carbene complex is described. In a simple protocol a variety of 2-substituted benzoxazoles and benzothiazoles were obtained via intramolecular coupling cyclization of 2-haloanilides/ 2-halothioanilides in good to excellent yields.

Introduction

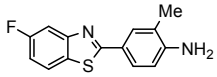
The 2-aryl-substituted benzoxazole and benzothiazole scaffolds are present in many compounds with useful biological and pharmaceutical properties, including antitumor agents,[1a,b] estrogen receptor-β agonist[1c] and anti-trypanocidal agents.[1d] (Figure 1) Traditional methods to obtain 2-aryl-substituted- benzoxazoles and benzothiazoles involve condensation of 2-aminophenols/and 2-aminothiophenols with carboxylic acids or aldehydes under oxidative conditions.[2,3] In the last decades, transition-metal-catalyzed processes for carbon-heteroatom bond formations have been developed to obtain these heterocyclic systems.[4] For example copper-,[5] palladium-,[6] cobalt-[7] and iron-catalyzed[8] intramolecular cyclization of 2-haloanilides/2-halothioanilides have been used for the synthesis of benzoxazoles and benzothiazoles.[9,10]



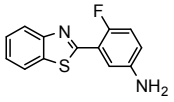
antitumor activity



estrogen receptor-β agonist



antitumor activity



trypanocidal activity

Figure 1 Examples of some biologically active 2-aryl-benzoxazoles and benzothiazoles.

However, these approaches often require complex ligands and long reaction times. Therefore, development of more efficient methods to obtain benzoxazoles and benzothiazoles remains as an important synthetic objective. Recently, *N*-heterocyclic carbene (NHC) metal complexes have emerged as a powerful tool as homogeneous catalysts in organic synthesis.[11] Interestingly, copper(I) complexes with NHC ligands have demonstrated excellent catalytic activity in the synthesis of 2-substituted oxazolines,[12] substituted vinylboronates,[13] *N*-methylation of amines,[14] 1,3-halogen migrations,[15] hydrosilylation of ketones,[16] carboxylation of organoboronic esters[17] and many others.[18] Nevertheless, Ullmann-type reactions have scarcely been explored and only the arylation of phenols and hydroxylation of aryl iodides have been described.[19] Considering these precedents we became interested in using a copper-NHC complex for an intramolecular Ullmann-type reaction to obtain benzoxazole and benzothiazole derivatives. The copper-NHC complex with the ligand 1,3-bis(2,6-diisopropylphenyl)imidazol (IPr) was chosen for our study because it showed excellent catalytic activity in other processes.[12,17] Interestingly, an efficient and inexpensive synthesis of these catalysts have been recently described.[20]

Results and discussion

The (IPr)CuCl (**2**) complex was easily obtained by reaction of 1,3-bis(2,6-diisopropylphenyl)imidazolium chloride[21] (**1**) with Cu_2O in dioxane. To start our study, *N*-(2-iodophenyl)benzamide **3** was chosen as model substrate to carry out optimization of the reaction conditions.

According to classical conditions of Ullmann reactions,[5,11d,22] MeCN, DMSO and DMF were chosen as solvents, and K_2CO_3 or Cs_2CO_3 as bases at 80-110 °C. Initially, the intramolecular cyclization of benzamide **3** (0.3 mmol) in the presence of (IPr)CuCl (10 mol%), using Cs_2CO_3 (2.0 equiv.) in acetonitrile for 6 h under reflux gave

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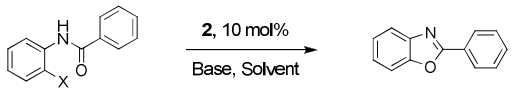
benzoxazole **4** in 4% yield (Table 1, entry 1). Changing the base to K_2CO_3 under similar conditions the yield was increased to 10% (Table 1, entry 2). When the reaction was performed with the other selected solvents, the best choice was DMF and K_2CO_3 at 110 °C for 6 h that afforded 99% yield for the coupling cyclization. (Table 1, entries 3-6). The effect of the catalyst loading was also examined and using 5 mol% of (IPr)CuCl the reaction provided **4** in 71% yield. (Table 1, entry 7). A control experiment confirmed that, in the absence of catalyst, the formation of **4** was not observed. (Table 1, entry 8). Accordingly, the optimal conditions for the intramolecular coupling cyclization of 2-halobenzanilide **3** (X = I) were (IPr)CuCl (10 mol%), K_2CO_3 (2.0 equiv.) in DMF at 110 °C for 6 h. (Table 1, entry 6). Next the influence of the halide in the coupling reaction was evaluated, and the bromine derivative **3** (X = Br) afforded benzoxazole **4** in excellent yields (98%) while the chlorine derivative **3** (X = Cl) was not reactive. (Table 1, entries 9, 10). Therefore the reactivity for 2-halobenzanilides **3** followed the order ArI>ArBr>ArCl, which is characteristic of the Ullmann coupling reaction.[11c,23]

Then, to investigate the scope of this approach, the intramolecular *O*-arylation of various substituted 2-haloanilides under the optimized conditions was examined. As shown in Table 2, this methodology is appropriated for a broad range of substrates having substituents on either of the aryl moieties of anilides **5**. Substrates possessing electron donating substituents such as 4-Me (**5a**) and electron withdrawing substituents such as 4-Cl (**5b**), 4-CN (**5c**) and 4-F(**5d**) on the phenylamino moiety reacted efficiently, giving high yields of the corresponding benzoxazoles **6 a-d**. (Table 2, entries 1-4).

Table 1 Optimization of reaction conditions.



3 X=I, Br, Cl — **4**

entry	X	base	solvent	temp. (ºC)	Time (h)	Yield (%)[a]
1	I	Cs_2CO_3	MeCN	82	6	4
2	I	K_2CO_3	MeCN	82	6	10
3	I	Cs_2CO_3	DMSO	110	6	17
4	I	K_2CO_3	DMSO	110	6	76
5	I	Cs_2CO_3	DMF	110	6	63
6	I	K_2CO_3	DMF	110	6	99
7	I	K_2CO_3	DMF	110	6	71[b]
8	I	K_2CO_3	DMF	110	6	0[c]
9	Br	K_2CO_3	DMF	110	18	98
10	Cl	K_2CO_3	DMF	110	24	0

[a] Isolated yields. [b] (IPr)CuCl (5 mol%), [c] Reaction performed without catalysts.

The 2-haloanilide with the 4-nitro group (**5e**) was less reactive and gave 55% yield of benzoxazole **6e**. (Table 2, entry 5) Additionally, substrates having substituents such as 4-Cl (**5f**), 4-OMe (**5g**), 3,4-di-OMe (**5h**) and 4-Me (**5i**) on the benzoyl moiety gave good yields of the corresponding benzoxazoles **6f-i.** (Table 2, entries 6-9). The reactivity exhibited by the 2-methyl substituted substrate (5j) was reduced probably due to steric hindrance and the yield of the respective benzoxazole **6j** was 56-62%. (Table 2, entry 10).

After the successful synthesis of benzoxazoles **6** from various iodo- and bromobenzanilides **5**, the utility of the (IPr)CuCl (**2**) catalytic system for the preparation of benzothiazoles was investigated. The 2-halothioanilides **7** precursors were readily obtained by reaction of the corresponding amides **5** with Lawesson's reagent.[24] The intramolecular coupling cyclization of 2-halothioanilides **7**, under the optimized reactions conditions (IPr)CuCl (10 mol%), K_2CO_3 (2.0 equiv.) in DMF at 110 °C used in the synthesis of benzoxazoles, was evaluated.

Concerning the 2-halide substituent, the order of reactivity for 2-halothioanilides **7a** was ArI > ArBr > ArCl, but in this case the chloro derivative **7a** (X = Cl) gave 84% yield of benzothiazole **8a**. (Table 3, entry 1). The different reactivity observed for chlorine derivatives **3** and **7a** is probably due to the better donating capacity of thioamides than amides.[6a,25] This result is of particular interest because the literature reports for copper-catalysed intramolecular cyclization of 2-chlorothioanilides to the corresponding benzothiazoles requires high temperature and long reaction times. Regarding substrates with electron-donating as well as electron-withdrawing substituents on either of the aryl moieties (**7b-f**) were well tolerated and the corresponding benzothiazoles (**8b-f**) were obtained in excellent yields. (Table 3, entries 2-6).

Finally, based on our results that the reactivity order of the substrates was ArI>ArBr> ArCl and on literature reports[5e,23,26] of Cu-catalyzed C-X bond formations, probably the reaction proceeds via two-electron Cu(I)/Cu(III) catalytic cycle for the intramolecular cyclization of 2-halobenzanilides **3** to give benzoxazoles **4**.

Additionally, when the reaction of 2-iodobenzanilide **3** was performed in the presence of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as a radical scavenger, no inhibition of the intramolecular cyclization was observed.

Conclusions

In summary, we have reported the first (NHC)-copper-catalyzed intramolecular cyclization of 2-halobenzanilides as an efficient approach for the synthesis of 2-arylbenzoxazoles. In addition, the (NHC)-copper catalytic system has been successfully applied for the synthesis of 2-arylbenzothiazoles via intramolecular cyclization of 2-halothiobenzanilides. All products were obtained in good to excellent yields through a simple and efficient protocol without adding specific ligands or complex bases. This work demonstrates the versatility of copper-NHC complexes in a new catalytic process.

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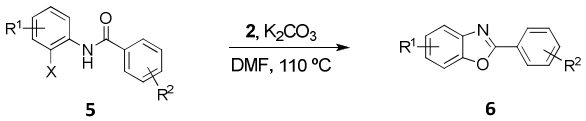
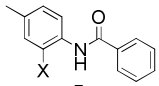
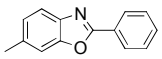
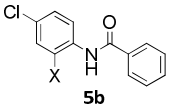
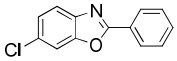
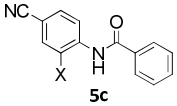
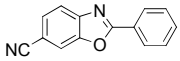
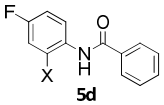
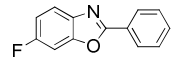
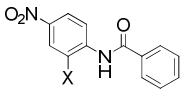
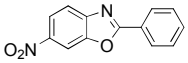
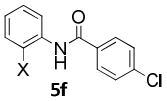
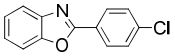
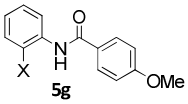
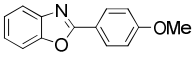
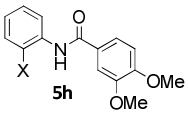
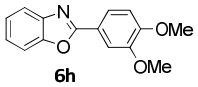
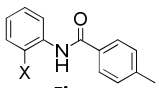
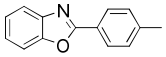
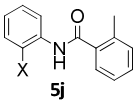
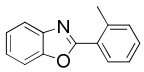
Table 2 (NHC)-copper-catalyzed synthesis of benzoxazoles **6** from 2-haloanilides **5**



5 **6**

Entry	5	6	X	Time (h)	Yield (%)[b]
1	 **5a**	 **6a**	I	10	92
			Br	18	83
2	 **5b**	 **6b**	I	8	95
			Br	18	90
3	 **5c**	 **6c**	I	12	86
4	 **5d**	 **6d**	I	12	80
5	 **5e**	 **6e**	I	12	55
6	 **5f**	 **6f**	I	14	86
			Br	18	77
7	 **5g**	 **6g**	I	10	82
			Br	16	75
8	 **5h**	 **6h**	I	12	86
9	 **5i**	 **6i**	I	12	87
			Br	18	79
10	 **5j**	 **6j**	I	12	62
			Br	24	56

[a] Reaction conditions: *N*-(2-halophenyl)benzamide (0.3 mmol), (IPr)CuCl (10 mol%), K_2CO_3 (0.6 mmol), DMF. [b] Isolated yield

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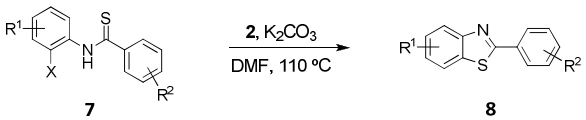
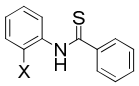
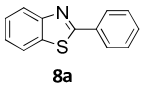
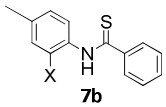
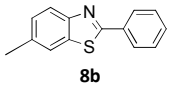
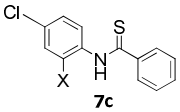
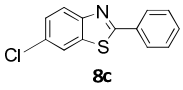
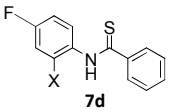
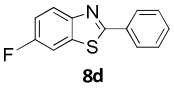
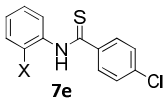
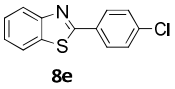
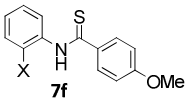
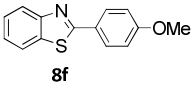
Table 3 (NHC)-copper-catalyzed synthesis of benzothiazoles from 2-halothioanilides.



7 8

Entry	7	8	X	Time (h)	Yield (%)[b]
1	 7a	 8a	I	2.5	99
			Br	5	98
			Cl	18	84
2	 7b	 8b	I	3.5	98
3	 7c	 8c	I	3	90
4	 7d	 8d	I	3	90
5	 7e	 8e	Br	3	97
6	 7f	 8f	Br	2	92

[a] Reaction conditions: *N*-(2-halophenyl)benzothiamide (0.3 mmol), (IPr)CuCl (10 mol%), K_2CO_3 (0.6 mmol), DMF. [b] Isolated yield

Experimental

General Information

All reagents were used as purchased from commercial sources without further purification. 2-Halobenzanilides were obtained from the corresponding 2-haloanilines according to literature methods.[5c] Thiobenzanilides were prepared by reaction of the respective anilides with Lawesson's reagent.[24] All reactions were performed under an air atmosphere in standard dried glassware and monitored by thin-layer chromatography using E. Merck silica gel 60 F254 pre-coated plates (0.25 mm). Flash chromatography was performed using silica gel (230-400 mesh, Merck). ^{1}H and ^{13}C NMR spectra were recorded on BRUKER AVANCE III HD-400 (11.74 T, 400 MHz to ^{1}H and 126 MHz to ^{13}C) NMR spectrometers using the residual proton or the carbon signal of the deuterated solvent as an internal standard.

General procedure for synthesis of Benzoxazoles/Benzothiazoles

A mixture of *N*-(2-halophenyl)benzamide/benzothiamide (1.0 equiv.), (IPr)CuCl (10 mol%), K_2CO_3 (2.0 equiv.) in DMF was stirred at 110 °C for the appropriate time (Tables 2 and 3). The reaction progress was monitored by TLC. After cooling, the reaction mixture was concentrated under vacuum and the residue was dissolved in ethyl acetate and washed with brine. The organic layer was dried and concentrated to give a residue, which was purified by flash chromatography on silica gel eluting with 2-10% ethyl acetate/hexane.

2-Phenylbenzoxazole (4)

N-(2-iodophenyl)benzamide (104.2 mg, 0.32 mmol, 1.0 equiv.), K_2CO_3 (89 mg, 0.64 mmol, 2.0 equiv.), (IPr)CuCl (15.8 mg, 0.032 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 99% (62.4 mg, 0.32 mmol).

N-(2-bromophenyl)benzamide (104.2 mg, 0.38 mmol, 1.0 equiv.), K_2CO_3 (104.2 mg, 0.76 mmol, 2.0 equiv.), (IPr)CuCl (18.4 mg, 0.038 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 98% (72.6 mg, 0.37 mmol).

White solid; mp 100-102 °C (lit.[5a] 101-102 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.29-8.24 (m, 2H), 7.80-7.77 (m, 1H), 7.60-7.56 (m, 1H), 7.54-7.50 (m, 3H), 7.37-7.33 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 150.8, 142.1, 131.5, 128.9, 127.6, 127.2, 125.1, 124.6, 120.0, 110.6.

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6-Methyl-2-phenylbenzoxazole (6a)

N-(2-iodo-4-methylphenyl)benzamide (100 mg, 0.30 mmol, 1.0 equiv.), K_2CO_3 (95.2 mg, 0.69 mmol, 2.0 equiv.), (IPr)CuCl (16.9 mg, 0.030 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 92% (57 mg, 0.27 mmol).

N-(2-bromo-4-methylphenyl)benzamide (100 mg, 0.35 mmol, 1.0 equiv.), K_2CO_3 (104.2 mg, 0.76 mmol, 2.0 equiv.), (IPr)CuCl (18.4 mg, 0.035 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 83% (60 mg, 0.29 mmol).

White solid; mp 91-92 °C (lit.[25a] 91-92 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28-8.20 (m, 2H), 7.64 (d, *J* = 8.1 Hz, 1H), 7.52-7.48 (m, 2H), 7.36 (s, 1H), 7.16 (d, *J* = 8.1 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6, 151.1, 140.0, 135.6, 131.3, 128.9, 127.5, 127.4, 125.8, 119.4, 110.8, 21.8.

6-Chloro-2-phenylbenzoxazole (6b)

N-(4-chloro-2-iodophenyl)benzamide (100.5 mg, 0.28 mmol, 1.0 equiv.), K_2CO_3 (77.7 mg, 0.56 mmol, 2.0 equiv.), (IPr)CuCl (13.7 mg, 0.028 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 95% (61 mg, 0.27 mmol).

N-(4-chloro-2-bromophenyl)benzamide (95 mg, 0.31 mmol, 1.0 equiv.), K_2CO_3 (84.6 mg, 0.61 mmol, 2.0 equiv.), (IPr)CuCl (15 mg, 0.031 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 90% (63 mg, 0.27 mmol).

White solid; mp 104-105 °C (lit.[25a] 104-105 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (dd, *J* = 7.7, 1.6 Hz, 2H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.57 (s, 1H), 7.55-7.47 (m, 3H), 7.31 (dd, *J* = 8.5, 1.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7, 150.9, 140.9, 131.8, 130.7, 129.0, 127.7, 126.7, 125.3, 120.5, 111.2.

6-Ciano-2-phenylbenzoxazole (6c)

N-(4-cyano-2-iodophenyl)benzamide (125 mg, 0.36 mmol, 1.0 equiv.), K_2CO_3 (99.2 mg, 0.72 mmol, 2.0 equiv.), (IPr)CuCl (17.5 mg, 0.036 mmol, 0.1 equiv.), DMF (3.0 mL). Yield: 86% (68 mg, 0.31 mmol).

White solid; mp 197-198 °C (lit.[25a] 198-199 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 7.5 Hz, 2H), 7.86 (s, 1H), 7.80 (d, *J* = 8.2 Hz, 1H), 7.67-7.49 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 149.9, 145.9, 132.7, 129.1, 128.9, 128.1, 125.9, 120.9, 118.8, 114.8, 108.1.

6-Fluoro-2-phenylbenzoxazole (6d)

N-(4-fluoro-2-iodophenyl)benzamide (100 mg, 0.29 mmol, 1.0 equiv.), K_2CO_3 (81 mg, 0.59 mmol, 2.0 equiv.), (IPr)CuCl (14.3 mg, 0.029 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 80% (50 mg, 0.23 mmol).

White solid; mp 105 °C (lit.[25a] 106-107 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25-8.16 (m, 2H), 7.71-765 (m, 1H), 7.57-7.45 (m, 3H), 7.29 (dd, *J* = 7.9, 2.0 Hz, 1H), 7.14-7.05 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7, 161.9, 159.5, 150.8, 150.6, 138.4, 131.6, 128.9, 127.5, 126.9, 120.3, 120.2, 112.7, 112.4, 98.8, 98.5.

6-Nitro-2-phenylbenzoxazole (6e)

N-(2-iodo-4-nitrophenyl)benzamide (100 mg, 0.27 mmol, 1.0 equiv.), K_2CO_3 (75.1 mg, 0.54 mmol, 2.0 equiv.), (IPr)CuCl (13.3 mg, 0.027 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 55% (36 mg, 0.15 mmol).

White solid; mp 150 °C (lit.[25b] 150 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (d, *J* = 1.7 Hz, 1H), 8.31 (dd, *J* = 8.8, 1.9 Hz, 1H), 8.27 (d, *J* = 7.4 Hz, 2H), 7.83 (d, *J* = 8.8 Hz, 1H), 7.65-7.53 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.4, 149.9, 147.4, 145.1, 132.9, 129.2, 128.3, 126.0, 120.1, 119.8, 107.2.

2-(4-Chlorophenyl)-benzoxazole (6f)

4-chloro-*N*-(2-iodophenyl)benzamide (100 mg, 0.28 mmol, 1.0 equiv.), K_2CO_3 (77.3 mg, 0.56 mmol, 2.0 equiv.), (IPr)CuCl (13.7 mg, 0.028 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 86% (55 mg, 0.24 mmol).

4-chloro-*N*-(2-bromophenyl)benzamide (70 mg, 0.23 mmol, 1.0 equiv.), K_2CO_3 (62.3 mg, 0.45 mmol, 2.0 equiv.), (IPr)CuCl (11 mg, 0.023 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 77% (40 mg, 0.17 mmol).

White solid; mp 148-150 °C (lit.[5a] 148-151 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22-8.13 (m, 2H), 7.79-7.73 (m, 1H), 7.59-7.53 (m, 1H), 7.52-7.44 (m, 2H), 7.39-7.32 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.2, 150.9, 142.1, 137.9, 129.4, 129.0, 125.8, 125.4, 124.9, 120.2, 110.7.

2-(4-Methoxyphenyl)-benzoxazole (6g)

N-(2-iodophenyl)-4-methoxybenzamide (100 mg, 0.28 mmol, 1.0 equiv.), K_2CO_3 (78.3 mg, 0.57 mmol, 2.0 equiv.), (IPr)CuCl (13.8 mg, 0.028 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 82% (52 mg, 0.23 mmol).

N-(2-bromophenyl)-4-methoxybenzamide (100 mg, 0.32 mmol, 1.0 equiv.), K_2CO_3 (90.3 mg, 0.65 mmol, 2.0 equiv.), (IPr)CuCl (16 mg, 0.033 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 75% (55 mg, 0.24 mmol).

White solid; mp 99-100 °C (lit.[5a] 99 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 8.5 Hz, 2H), 7.97-7.92 (m, 1H), 7.75 (d, *J* = 6.9 Hz, 2H), 7.56-7.49 (m, 2H), 7.22 (d, *J* = 8.8, 2H), 4.07 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 162.3, 150.7, 142.3, 129.4, 124.6, 124.4, 119.7, 119.6, 114.4, 110.4, 55.4.

2-(3,4-Dimethoxyphenyl)-benzoxazole (6h)

N-(2-iodophenyl)-3,4-dimethoxybenzamide (100 mg, 0.26 mmol, 1.0 equiv.), K_2CO_3 (72 mg, 0.52 mmol, 2.0 equiv.), (IPr)CuCl (12.8 mg, 0.026 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 87% (58 mg, 0.23 mmol).

White solid; mp 110 °C (lit.[5a] 109-110 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86-7.78 (m, 1H), 7.76-7.68 (m, 2H), 7.56-7.48 (m, 1H), 7.35-7.27 (m, 2H), 6.99-6.90 (m, 1H), 3.99 (s, 3H), 3.92 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 152.0, 149.2, 142.2, 124.7, 121.2, 119.8, 119.6, 111.0, 110.4, 110.0, 56.1, 56.0.

2-(*p*-Tolyl)-benzoxazole (6i)

N-(2-iodophenyl)-4-methylbenzamide (70 mg, 0.21 mmol, 1.0 equiv.), K_2CO_3 (57.4 mg, 0.42 mmol, 2.0 equiv.), (IPr)CuCl (10.1 mg, 0.021 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 87% (38 mg, 0.18 mmol).

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N-(2-bromophenyl)-4-methylbenzamide (72 mg, 0.25 mmol, 1.0 equiv.), K_2CO_3 (68.6 mg, 0.50 mmol, 2.0 equiv.), (IPr)CuCl (12 mg, 0.025 mmol, 0.1 equiv.), DMF (2.0 mL). Yield: 79% (41 mg, 0.20 mmol).
White solid; mp 117 °C (lit.[5a] 117-118 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.0 Hz, 2H), 7.80-7.73 (m, 1H), 7.60-7.52 (m, 1H), 7.37-7.29 (m, 4H), 2.42 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 150.8, 142.3, 142.1, 129.7, 127.7, 125.0, 124.6, 124.5, 120.0, 110.6, 21.7.

2-(*o*-Tolyl)-benzoxazole (6j)
N-(2-iodophenyl)-2-methylbenzamide (111.6 mg, 0.34 mmol, 1.0 equiv.), K_2CO_3 (91.6 mg, 0.66 mmol, 2.0 equiv.), (IPr)CuCl (16.2 mg, 0.034 mmol, 0.1 equiv.), DMF (3.0 mL). Yield: 62% (43 mg, 0.21 mmol).
N-(2-bromophenyl)-2-methylbenzamide (111.8 mg, 0.38 mmol, 1.0 equiv.), K_2CO_3 (106.4 mg, 0.78 mmol, 2.0 equiv.), (IPr)CuCl (19 mg, 0.038 mmol, 0.1 equiv.), DMF (3.0 mL). Yield: 56% (45 mg, 0.22 mmol).
White solid; mp 65 °C (lit.[8a] 68-69 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 7.6 Hz, 1H), 7.86-7.79 (m, 1H), 7.63-7.56 (m, 1H), 7.46-7.31 (m, 5H), 2.83 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 150.3, 142.2, 138.9, 131.8, 131.0, 130.0, 126.3, 126.1, 125.0, 124.4, 120.2, 110.5, 22.2.

2-Phenylbenzothiazole (8a)
N-(2-iodophenyl)benzothioamide (150 mg, 0.44 mmol, 1.0 equiv.), K_2CO_3 (122 mg, 0.88 mmol, 2.0 equiv.), (IPr)CuCl (21.6 mg, 0.044 mmol, 0.1 equiv.), DMF (3.0 mL). Yield: 99% (108 mg, 0.51 mmol).
N-(2-bromophenyl)benzothioamide (100 mg, 0.34 mmol, 1.0 equiv.), K_2CO_3 (94.6 mg, 0.68 mmol, 2.0 equiv.), (IPr)CuCl (16.5 mg, 0.034 mmol, 0.1 equiv.), DMF (3.0 mL). Yield: 98% (71 mg, 0.34 mmol).
N-(2-chlorophenyl)benzothioamide (130 mg, 0.53 mmol, 1.0 equiv.), K_2CO_3 (145 mg, 1.05 mmol, 2.0 equiv.), (IPr)CuCl (25.6 mg, 0.053 mmol, 0.1 equiv.), DMF (3.0 mL). Yield: 84% (93 mg, 0.44 mmol).
White solid; mp 111 °C (lit.[25b] 111 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99-7.91 (m, 3H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.52-7.47 (m, 4H), 7.23 (t, *J* = 7.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.1, 154.2, 135.1, 133.7, 131.0, 129.0, 127.6, 126.3, 125.2, 123.3, 121.7.

6-Methyl-2-phenylbenzothiazole (8b)
N-(2-iodo-4-methylphenyl)benzothioamide (120 mg, 0.34 mmol, 1.0 equiv.), K_2CO_3 (94 mg, 0.68 mmol, 2.0 equiv.), (IPr)CuCl (17 mg, 0.034 mmol, 0.1 equiv.), DMF (3.0 mL). Yield: 98% (75 mg, 0.33 mmol).
White solid; mp 123-124 °C (lit.[25a] 124-125 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12-8.05 (m, 2H), 7.97 (d, *J* = 8.3 Hz, 1H), 7.67 (s, 1H), 7.53-7.44 (m, 3H), 7.30 (d, *J* = 8.3, 1H), 2.49 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.0, 152.3, 135.4, 135.3, 133.8, 130.8, 129.0, 128.0, 127.5, 122.8, 121.4, 21.6.

6-Chloro-2-phenylbenzothiazole (8c)
N-(4-chloro-2-iodophenyl)benzothioamide (150 mg, 0.40 mmol, 1.0 equiv.), K_2CO_3 (111 mg, 0.80 mmol, 2.0 equiv.), (IPr)CuCl (19.6 mg, 0.040 mmol, 0.1 equiv.), DMF (3.5 mL). Yield: 90% (89 mg, 0.36 mmol).
White solid; mp 156 °C (lit.[25a] 156-157 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09-8.02 (m, 2H), 7.96 (d, *J* = 8.7 Hz, 1H), 7.85 (s, 1H), 7.51-7.47 (m, 3H), 7.44 (dd, *J* = 8.7, 1.9 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.5, 152.7, 136.2, 133.2, 131.3, 131.1, 129.1, 127.6, 127.1, 124.0, 121.2.

6-Fluoro-2-phenylbenzothiazole (8d)
N-(4-fluoro-2-iodophenyl)benzothioamide (100 mg, 0.28 mmol, 1.0 equiv.), K_2CO_3 (77.4 mg, 0.56 mmol, 2.0 equiv.), (IPr)CuCl (13.7 mg, 0.028 mmol, 0.1 equiv.), DMF (3.0 mL). Yield: 90% (58 mg, 0.25 mmol).
White solid; mp 135 °C (lit.[25a] 133-134 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10-7.98 (m, 3H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.50 (s, 1H), 7.22 (t, *J* = 8.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.8, 167.7, 161.7, 159.3, 150.8, 136.1, 136.0, 133.4, 131.0, 129.1, 127.4, 124.2, 124.1, 115.1, 114.8, 108.0, 107.7.

2-(4-Chlorophenyl)-benzothiazole (8e)
4-chloro-*N*-(2-bromophenyl)benzothioamide (150 mg, 0.46 mmol, 1.0 equiv.), K_2CO_3 (127 mg, 0.92 mmol, 2.0 equiv.), (IPr)CuCl (22.4 mg, 0.046 mmol, 0.1 equiv.), DMF (3.5 mL). Yield: 97% (109 mg, 0.44 mmol).
White solid; mp 115-116 °C (lit.[25c] 116-117 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.2 Hz, 1H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.89 (d, *J* = 8.0 Hz, 1H), 7.54-7.43 (m, 3H), 7.39 (t, *J* = 8.4 Hz, 1H); .^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 154.1, 137.0, 135.1, 132.1, 129.3, 128.7, 126.5, 125.4, 123.3, 121.7.

2-(4-Methoxyphenyl)-benzothiazole (8f)
N-(2-bromophenyl)-4-methoxybenzothioamide (100 mg, 0.31 mmol, 1.0 equiv.), K_2CO_3 (86 mg, 0.62 mmol, 2.0 equiv.), (IPr)CuCl (15 mg, 0.031 mmol, 0.1 equiv.), DMF (3.0 mL). Yield: 92% (69 mg, 0.28 mmol).
White solid; mp 121-122 °C (lit.[25c] 122-123 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06-8.00 (m, 3H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 6.98 (d, *J* = 8.7 Hz, 2H), 3.85 (s, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 167.9, 161.9, 154.3, 134.9, 129.1, 126.4, 126.2, 124.8, 122.8, 121.5, 114.4, 55.4.

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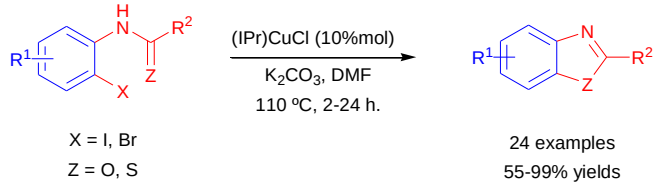
A new an efficient synthesis of 2-aryl benzoxazoles and benzothiazoles by intramolecular cyclization of 2-haloanilides/2-halothioanilides using a copper(I)-NHC complex is described.



X = I, Br
Z = O, S

24 examples
55-99% yields