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# Palladium-Catalyzed Regioselective Direct Arylation of Benzofurazans at C4 Position

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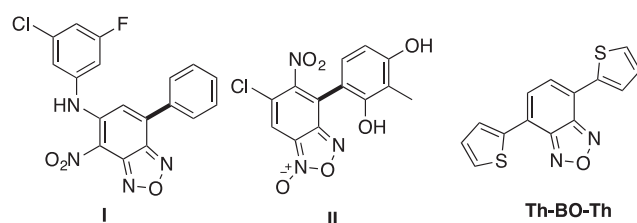
**Abstract.** The palladium-catalyzed direct arylation of benzofurazans with aryl bromides to access 4-arylbenzofurazans proceeds in moderate-to-high yields using phosphine-free palladium acetate as the catalyst and potassium acetate as an inexpensive base. A wide variety of (hetero)aryl bromides, including bromopyridine and bromothiophene derivatives has been successfully employed.

Palladium-catalyzed one-pot C4,C7-diarylation of benzofurazane was also described using a larger amount of aryl bromide. Moreover, the derivatization of 4-arylbenzofurazans into 4-arylquinaxolines is also reported.

**Keywords:** Benzofurazans; C–H activation; Catalysis; Palladium; Quinaxolines.

## Introduction

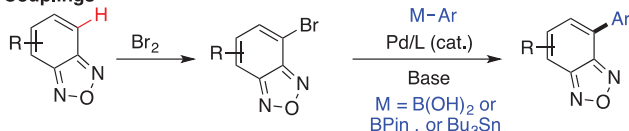
Benzofurazan is an important unit, which found applications in materials sciences. Especially C4 or/and C7 (hetero)aryl benzofurazans are involved in the molecular design of photovoltaic materials (Figure 1).<sup>[1]</sup> Some 4-arylbenzofurazans also displayed important biological activities such as **I**, which inhibits the PAS-B domain of the hypoxia inducible factor 2 $\alpha$ ;<sup>[2]</sup> or the benzo[*c*][1,2,5]oxadiazole-1-oxide **II**, which has been synthesized for its antimicrobial properties.<sup>[3]</sup> Recently, electron donor–acceptor type organic semiconductors were designed based on 4-heteroarylbenzofurazan (Th-BO-Th) for application as organo-photocatalysts (Figure 1).<sup>[4]</sup>



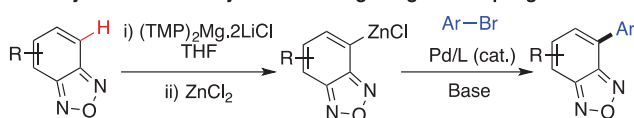
**Figure 1.** Examples of Useful Molecules Containing a 4-Arylbenzofurazan Unit.

One of the most common access to 4-arylbenzofurazan derivatives is through a bromination of benzofurazan followed by palladium catalyzed Suzuki<sup>[5]</sup> or Stille<sup>[6]</sup> cross-coupling reactions (Scheme 1a). Oligomers have also been synthesized from 4,7-dibromofurazan and an organometallic reagent.<sup>[7]</sup> Negishi reactions with an organozinc reagent prepared from benzofurazan through a magnesiation with bis(2,2,6,6-tetramethylpiperidin-1-yl)magnesium–lithium chloride complex (TMP<sub>2</sub>Mg·2LiCl) followed by transmetalation with zinc chloride, have also been reported (Scheme 1b).<sup>[8]</sup> Since the discovery by Nakamura<sup>[9]</sup> and Otha<sup>[10]</sup> of the Pd-catalyzed C–H bond arylation of heteroarenes using aryl halides, this technology has emerged as one of the most powerful method for the formation of C–C bonds for the access to a wide variety of arylated heterocycles as no prefunctionalization is required.<sup>[11]</sup> However, examples of palladium-catalyzed non-directed C–H bond arylation of 6-membered rings remains scarce.<sup>[12]</sup> Recent examples on the arylation of activated benzothiadiazole *via* C–H bond activation have been reported using palladium catalysis.<sup>[13]</sup> To the best of our knowledge there is no example of direct arylation of benzofurazan in the literature, to date (Scheme 1c).

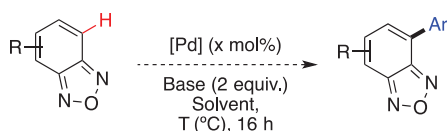
**a. 4-Arylbenzofurazan Synthesis through Suzuki-Miyaura or Stille Couplings<sup>5-7</sup>**



**b. 4-Arylbenzofurazan Synthesis through Negishi Coupling<sup>8</sup>**



**c. Palladium-Catalyzed Direct Arylation of Benzofurazan (this work)**



**Scheme 1.** Previous Strategies to Synthesize 4-Arylbenzofurazans.

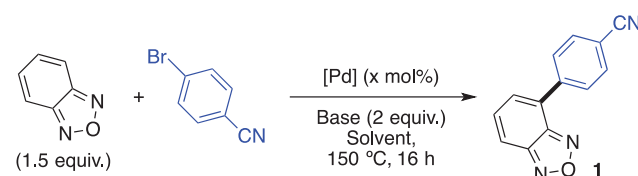
As part of our continuing efforts concerning the functionalization of benzene rings fused to heterocycles *via* palladium-catalyzed C–H bond arylation, we recently reported an efficient protocol for the synthesis of benzothiazoles and benzoxazoles arylated at the C7 position.<sup>[14]</sup> Based on these results, we examined the reactivity of benzofurazan in palladium-catalyzed direct arylation using aryl bromides as aryl source.

## Results and Discussion

We began our investigations by fine-tuning the conditions using benzofurazan and 4-bromobenzonitrile as model substrates in 1.5:1 ratio (Table 1). We were pleased to find that the reaction occurred regioselectively at the C4 position to afford **1** in good yields using 2 mol% of a diphosphine-palladium catalyst in the presence of KOAc as base in DMA at 150 °C or even at 120 °C (Table 1, entries 1 and 2). More interestingly, we found that the reaction is also operative using 2 mol% of phosphine-free Pd(OAc)<sub>2</sub> catalyst in a comparable yield (Table 1, entry 3). A lower catalyst loading of 1 mol% of Pd(OAc)<sub>2</sub> gave **1** in 85% yield; while partial conversion was obtained if only 0.5 mol% catalyst loading was used (Table 1, entries 4 and 5). Other inorganic bases, such as PivOK, K<sub>2</sub>CO<sub>3</sub> or Cs<sub>2</sub>CO<sub>3</sub> did not allow to improve the yield in **1** (Table 1, entries 6–8). When the reaction was performed using 1 mol% Pd(OAc)<sub>2</sub> at 120 °C, the C4-arylated benzofurazan **1** was obtained in 87% yield (Table 1, entry 9). Under these conditions, the excess of benzofurazan can be decreased up to 1.15 equivalents, as the desired product **1** was isolated in 89% yield (Table 1, entry 10). Then, we employed greener solvents than DMA such as cyclopentylmethyl ether, 1-pentanol or diethylcarbonate,<sup>[15]</sup> but no reaction occurred (Table 1, entries 11–13). No reaction occurred when 4-chlorobenzonitrile was used as aryl

source (Table 1, entry 14). It should also be mentioned that using the optimized reaction conditions, benzothiadiazole was unreactive.

**Table 1.** Optimization of the Reaction Conditions

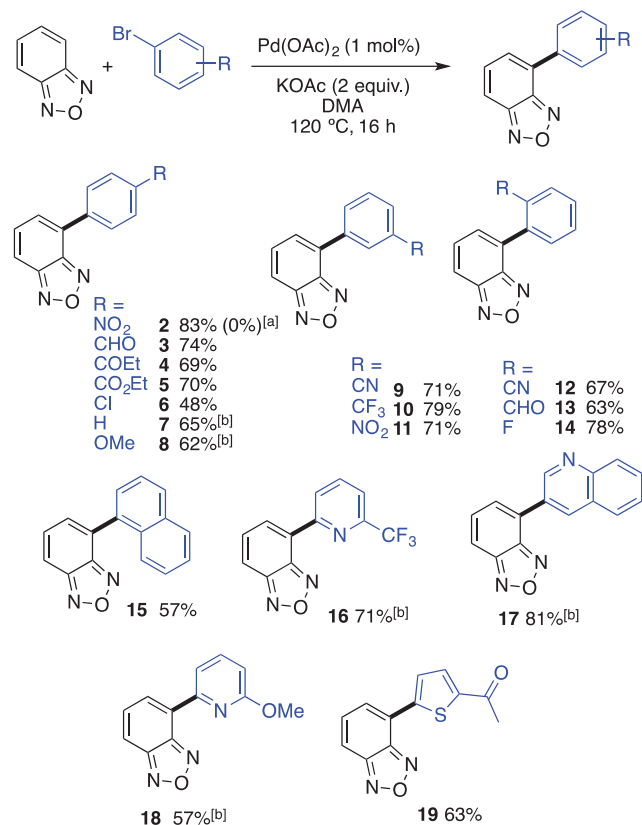


Entry	Pd (x mol%)	Base	Solvent	Conv. (%) <sup>[a]</sup>	Yield in <b>1</b> (%) <sup>[a]</sup>
1	PdCl(C <sub>3</sub> H <sub>5</sub> ) <sub>2</sub> (dppb) (2)	KOAc	DMA	100	75
2 <sup>[b]</sup>	PdCl(C <sub>3</sub> H <sub>5</sub> ) <sub>2</sub> (dppb) (2)	KOAc	DMA	100	74
3	Pd(OAc) <sub>2</sub> (2)	KOAc	DMA	100	82
4	Pd(OAc) <sub>2</sub> (1)	KOAc	DMA	100	85
5	Pd(OAc) <sub>2</sub> (0.5)	KOAc	DMA	83	79
6	Pd(OAc) <sub>2</sub> (1)	PivOK	DMA	80	53
7	Pd(OAc) <sub>2</sub> (1)	K <sub>2</sub> CO <sub>3</sub>	DMA	95	12
8	Pd(OAc) <sub>2</sub> (1)	Cs <sub>2</sub> CO <sub>3</sub>	DMA	67	0
9 <sup>[b]</sup>	Pd(OAc) <sub>2</sub> (1)	KOAc	DMA	100	87
10 <sup>[b,c]</sup>	Pd(OAc) <sub>2</sub> (1)	KOAc	DMA	100	89
11 <sup>[b]</sup>	Pd(OAc) <sub>2</sub> (1)	KOAc	CPME	0	0
12 <sup>[b]</sup>	Pd(OAc) <sub>2</sub> (1)	KOAc	pentan-1-ol	0	0
13 <sup>[b]</sup>	Pd(OAc) <sub>2</sub> (1)	KOAc	DEC	0	0
14 <sup>[d]</sup>	Pd(OAc) <sub>2</sub> (1)	KOAc	DMA	0	0

[a] Determined by GC-MS analysis using dodecane as internal standard. [b] Reaction performed at 120 °C. [c] Reaction performed using 1.15 equiv. of benzofurazan. [d] 4-Chlorobenzonitrile was used instead of 4-bromobenzonitrile. DMA = Dimethylacetamide; CPME = Cyclopentylmethyl ether; DEC = Diethylcarbonate

With the best conditions in hands, namely 1 mol% phosphine-free Pd(OAc)<sub>2</sub> associated to KOAc as base in DMA at 120 °C, we turned our attention to the scope of the reaction (Scheme 2). First, we examined the reactivity of *para*-substituted aryl bromides. The coupling of benzofurazan with 4-bromonitrobenzene, 4-bromobenzaldehyde, 4-bromopropiophenone, and ethyl 4-bromobenzoate proceeded nicely to afford **2–5** in 69–83% yields. A moderate yield in the desired 4-aryl benzofurazan **6** was obtained from the less electron-deficient 4-bromochlorobenzene owing a partial conversion of this aryl bromide. For bromobenzene and electron-rich 4-bromoanisole, as their oxidative addition to palladium is more challenging,<sup>[16]</sup> the reactions were conducted at a more elevated temperature of 150 °C to afford the

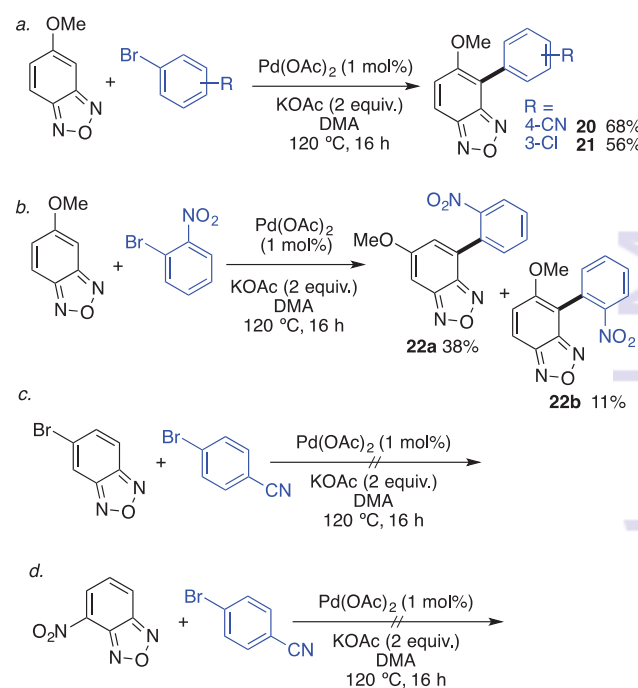
desired products **7** and **8** in 65% and 62% yields, respectively. It should be noted that no additional phosphine ligand is required to perform such couplings. The electron-deficient *meta*-substituted aryl bromides 3-bromobenzonitrile, 3-(trifluoromethyl)bromobenzene and 3-bromonitrobenzene were also very reactive using 1 mol% Pd(OAc)<sub>2</sub> as the catalyst at 120 °C and afforded **9–11** in yields of 71–79%. Then, we investigated the effect of an *ortho* substituent on the aryl bromide. 2-Nitrile-, 2-formyl-, and 2-fluorobromobenzenes allowed the formation of the desired 4-arylated benzofurazans **12–14** in good yields. Under the standard reaction conditions, more sterically demanding 1-bromonaphthalene was also efficiently coupled with benzofurazan to deliver **15** in 57% yield. *N*-containing heteroaryl bromides (e.g., 2-bromo-6-(trifluoromethyl)pyridine, 3-bromoquinoline, or 2-bromo-6-methoxypyridine) nicely reacted in the presence of 1 mol% Pd(OAc)<sub>2</sub> at 150 °C to afford the desired products **16–18** in good yields. In addition, this methodology allowed the synthesis 4-thiophen-2-ylfurazan **19**, which is a useful intermediate in the design of organic materials, in 63% yield.



**Scheme 2.** Scope of Aryl Bromides in Palladium-Catalyzed Direct C4 Arylation of Benzofurazan. [a] 4-Chloronitrobenzene was used instead of 4-bromonitrobenzene. [b] Reaction performed at 150 °C.

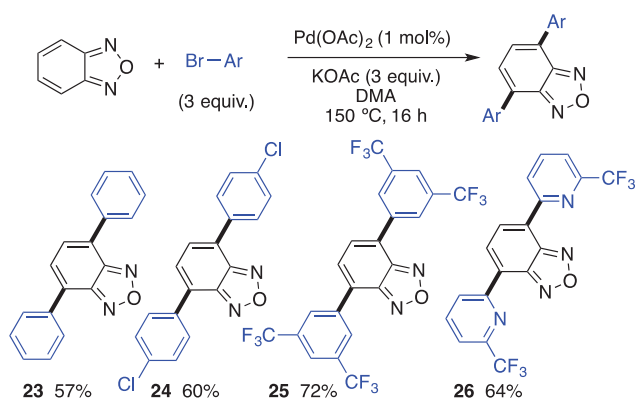
Next, we investigated the reactivity of 4- and 5-substituted benzofurazans (Scheme 3). Benzofurazan

substituted by an electron-donating group such as a methoxy at C5 position underwent Pd(OAc)<sub>2</sub>-catalyzed direct arylation. The reaction was completely regioselective with 4-bromobenzonitrile or 3-chlorobromobenzene and the arylation took place exclusively at the C4 position to afford products **20** and **21** in 68% and 56% yields, respectively (Scheme 3a). Conversely, the reaction was not regioselective using 2-bromonitrobenzene, probably because of its greater steric hindrance. The major regioisomer **22a** was isolated in 38% yield and resulted from the C–H bond activation at the less sterically hindered C7 position of the benzofurazan (Scheme 1b); whereas, the C4-arylation regioisomer **22b** was formed in less than 11% yield, making its isolation difficult. In contrast, benzofurazans substituted by an electron-withdrawing group such as 5-bromobenzofurazan or 4-nitrobenzofurazan were not reactive under our reaction conditions, even at 150 °C or in the presence of PdCl(C<sub>3</sub>H<sub>5</sub>)(dppb) catalyst (Scheme 3c and 3d).



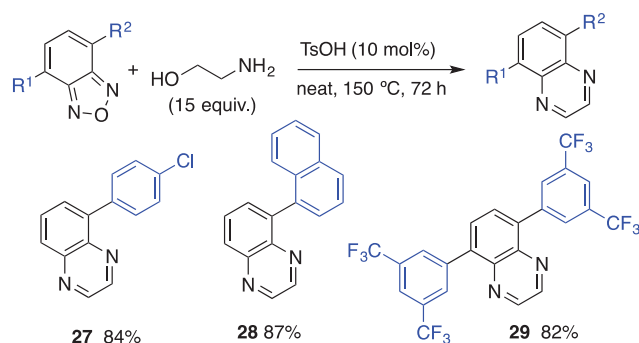
**Scheme 3.** Reactivities of Substituted Benzofurazans in Palladium-Catalyzed Direct Arylation.

Using the same reaction conditions, but in the presence of an excess amount of aryl bromides and base (3 equivalents), benzofurazan has been diarylated at both C4 and C7 carbons in one pot (Scheme 4). From bromobenzene, 4-chlorobromobenzene and 3,5-bis(trifluoromethyl)bromobenzene the diarylated products **23–26** were isolated in a range of yield of 57–72%. Again, it is important to note that this procedure did not require the use of a phosphine ligand.



**Scheme 4.** Scope of Palladium-Catalyzed C<sub>4</sub>,C<sub>7</sub> Diarylation of Benzofurazan

It is known that furazan unit of benzofurazans can easily undergo a ring opening in the presence of ethanolamines under acidic conditions to yield quinoxaline derivatives.<sup>[17]</sup> Quinoxaline is an important motif, which is present in many pharmaceuticals.<sup>[18]</sup> Therefore, we investigated the synthesis of some quinoxalines from arylated benzofurazans. Using the Samsonov conditions,<sup>[17]</sup> namely, 10 mol% *para*-toluenesulfonic acid in the presence of 1-aminoethanol, the arylated benzofurazans **6**, **15** and **25** were converted into 5-aryl quinoxalines **27-29** in 82-87% yields.



**Scheme 5.** Synthesis of 5-Arylated cc from Arylated Benzofurazans

## Conclusion

In summary, we disclose here an elegant route to access 4-arylated benzofurazans from commercially available benzofurazan through palladium-catalyzed regioselective C–H bond arylation. Our phosphine-free procedure using Pd(OAc)<sub>2</sub> catalyst, KOAc as inexpensive base in the presence of aryl bromides as coupling partners promotes the C<sub>4</sub> arylation or the C<sub>4</sub>,C<sub>7</sub>-diarylation of benzofurazan depending of the aryl bromide stoichiometry. A wide range of functions such as methoxy, fluoro, formyl, propionyl, carboxylate, nitrile or nitro on the aryl bromide is tolerated. Some sterically hindered aryl bromides,

and sulfur or nitrogen containing heteroaromatic substrates have also been employed successfully. In addition, some of these 4-arylated benzofurazans were successfully transformed into quinoxaline derivatives.

## Experimental Section

**General Methods:** All reactions were carried out under argon atmosphere with standard Schlenk techniques. DMA was purchased from Acros Organics and were not purified before use. Benzofurazans were purchased from Sigma-Aldrich. <sup>1</sup>H NMR spectra were recorded on Bruker GPX (400 MHz) spectrometer. Chemical shifts (δ) were reported in parts per million relative to residual chloroform (7.28 ppm for <sup>1</sup>H; 77.23 ppm for <sup>13</sup>C), constants were reported in Hertz. <sup>1</sup>H NMR assignment abbreviations were the following: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of triplets (dt), and multiplet (m). <sup>13</sup>C NMR spectra were recorded at 100 MHz on the same spectrometer and reported in ppm. All reagents were weighed and handled in air.

### Procedure A (Palladium-catalyzed direct C<sub>4</sub> arylation):

To a 5 mL oven dried Schlenk tube, benzofurazan derivative (1.15 mmol), aryl bromide (1 mmol), AcOK (196 mg, 2 mmol), DMA (4 mL) and Pd(OAc)<sub>2</sub> (2.2 mg, 0.01 mmol, 2 mol%) were successively added. The reaction mixture was evacuated by vacuum-argon cycles (5 times) and stirred at 120-150 °C (oil bath temperature) for 16 hours (see tables and schemes). After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography to afford the desired arylated products.

#### 4-(Benzo[*c*][1,2,5]oxadiazol-4-yl)benzonitrile (**1**):

Following the general procedure A using 4-bromobenzonitrile (182 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-CH<sub>2</sub>Cl<sub>2</sub>, 60-40) to afford the desired compound **1** (197 mg, 89%) as a white solid (Mp = 180-184 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.13 (d, *J* = 8.5 Hz, 2H), 7.91 (d, *J* = 8.9 Hz, 1H), 7.82 (d, *J* = 8.5 Hz, 2H), 7.66 (d, *J* = 7.0 Hz, 1H), 7.56 (dd, *J* = 7.0, 9.0 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 149.7, 148.1, 139.4, 132.7, 131.6, 129.3, 128.9, 128.4, 118.5, 116.8, 112.8. Elemental analysis: calcd (%) for C<sub>13</sub>H<sub>7</sub>N<sub>3</sub>O (221.22): C 70.58, H 3.19; found: C 70.85, H 3.46.

#### 4-(4-Nitrophenyl)benzo[*c*][1,2,5]oxadiazole (**2**):

Following the general procedure A using 4-bromonitrobenzene (202 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-EtOAc, 90-10) to afford the desired compound **2** (200 mg, 83%) as a yellow solid (MP = 198-202 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.42 (d, *J* = 8.9 Hz, 2H), 8.23 (d, *J* = 8.9 Hz, 2H), 7.96 (d, *J* = 9.0 Hz, 1H), 7.73 (d, *J* = 6.8 Hz, 1H), 7.60 (dd, *J* = 6.8, 9.0 Hz, 1H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 149.7, 148.2, 148.1, 141.2, 131.5, 129.7, 129.2, 128.1, 124.2, 117.1. Elemental analysis: calcd (%) for C<sub>12</sub>H<sub>7</sub>N<sub>3</sub>O<sub>3</sub> (241.21): C 59.75, H 2.93; found: C 59.81, H 3.19.

**4-(Benzo[c][1,2,5]oxadiazol-4-yl)benzaldehyde (3):** Following the general procedure **A** using 4-bromobenzaldehyde (185 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-Et<sub>2</sub>O, 70-30) to afford the desired compound **3** (166 mg, 74%) as a pale yellow solid (MP = 128-130 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 10.14 (s, 1H), 8.22 (d, *J* = 8.4 Hz, 2H), 8.07 (d, *J* = 8.4 Hz, 2H), 7.93 (d, *J* = 9.0 Hz, 1H), 7.72 (d, *J* = 6.8 Hz, 1H), 7.58 (dd, *J* = 6.8, 9.0 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 191.6, 149.8, 148.3, 140.9, 136.5, 131.6, 130.2, 129.3, 129.1, 129.0, 116.5. Elemental analysis: calcd (%) for C<sub>13</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub> (224.21): C 69.64, H 3.60; found: C 69.52, H 3.75.

**1-(4-(Benzo[c][1,2,5]oxadiazol-4-yl)phenyl)propan-1-one (4):** Following the general procedure **A** using 4-bromopropiophenone (213 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-CH<sub>2</sub>Cl<sub>2</sub>, 50-50) to afford the desired compound **4** (174 mg, 69%) as a white solid (MP = 161-165 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.14 (s, 4H), 7.90 (d, *J* = 9.0 Hz, 1H), 7.69 (d, *J* = 6.8 Hz, 1H), 7.57 (dd, *J* = 6.8, 9.0 Hz, 1H), 3.09 (q, *J* = 7.3 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 200.2, 149.8, 148.4, 139.3, 137.1, 131.6, 129.3, 128.9, 128.6, 128.5, 116.1, 32.0, 8.2. Elemental analysis: calcd (%) for C<sub>15</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub> (252.27): C 71.42, H 4.79; found: C 71.56, H 3.81.

**Ethyl 4-(benzo[c][1,2,5]oxadiazol-4-yl)benzoate (5):** Following the general procedure **A** using ethyl 4-bromobenzoate (229 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-CH<sub>2</sub>Cl<sub>2</sub>, 40-60) to afford the desired compound **5** (188 mg, 70%) as an orange solid (MP = 105-108 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.22 (d, *J* = 8.2 Hz, 2H), 8.11 (d, *J* = 8.2 Hz, 2H), 7.89 (d, *J* = 9.0 Hz, 1H), 7.68 (d, *J* = 6.8 Hz, 1H), 7.56 (dd, *J* = 6.8, 9.0 Hz, 1H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.46 (t, *J* = 7.1 Hz, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 166.1, 149.8, 148.4, 139.3, 131.6, 131.0, 130.1, 129.4, 128.9, 128.3, 116.0, 61.2, 14.4. Elemental analysis: calcd (%) for C<sub>15</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub> (268.27): C 67.16, H 4.51; found: C 66.98, H 4.79.

**4-(4-Chlorophenyl)benzo[c][1,2,5]oxadiazole (6):** Following the general procedure **A** using 1-bromo-4-chlorobenzene (191 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-CH<sub>2</sub>Cl<sub>2</sub>, 80-20) to afford the desired compound **6** (111 mg, 48%) as a yellow solid (MP = 95-97 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 7.98 (d, *J* = 8.5 Hz, 2H), 7.85 (d, *J* = 8.9 Hz, 1H), 7.59 (d, *J* = 6.8 Hz, 1H), 7.57 – 7.44 (m, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 149.8, 148.4, 135.4, 133.6, 131.7, 129.6, 129.2, 129.2, 128.0, 115.5. Elemental analysis: calcd (%) for C<sub>12</sub>H<sub>7</sub>ClN<sub>2</sub>O (230.65): C 62.49, H 3.06; found: C 62.53, H 3.00.

**4-(Phenyl)benzo[c][1,2,5]oxadiazole (7):** Following the general procedure **A** using bromobenzene (157 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-toluene, 80-20) to afford the desired compound **7** (127 mg, 65%) as a yellow solid (MP = 58-60 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.04 – 7.98 (m, 2H), 7.87 – 7.80 (m, 1H), 7.60 (td, *J* = 1.0, 6.8 Hz, 1H), 7.57 –

7.46 (m, 4H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 149.8, 148.6, 135.3, 131.8, 130.5, 129.3, 129.0, 128.4, 128.0, 115.0. Elemental analysis: calcd (%) for C<sub>12</sub>H<sub>8</sub>N<sub>2</sub>O (196.21): C 73.46, H 4.11; found: C 73.69, H 3.90.

**4-(4-methoxyphenyl)benzo[c][1,2,5]oxadiazole (8):** Following the general procedure **A** using 4-bromoanisole (187 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-toluene, 80-20) to afford the desired compound **8** (140 mg, 62%) as an orange solid (MP = 118-121 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.00 (d, *J* = 8.8 Hz, 2H), 7.77 (dd, *J* = 1.3, 8.5 Hz, 1H), 7.58 – 7.47 (m, 2H), 7.08 (d, *J* = 8.8 Hz, 2H), 3.92 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 160.5, 149.9, 148.7, 131.9, 130.1, 129.7, 127.7, 126.7, 114.4, 114.1, 55.4. This is a known compound and the spectral data are identical to those reported in literature.<sup>[5a]</sup>

**3-(Benzo[c][1,2,5]oxadiazol-4-yl)benzonitrile (9):** Following the general procedure **A** using 3-bromobenzonitrile (182 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-toluene, 80-20) to afford the desired compound **9** (157 mg, 71%) as a yellow solid (MP = 156-159 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.34 – 8.24 (m, 2H), 7.92 (d, *J* = 8.9 Hz, 1H), 7.78 (dt, *J* = 1.4, 7.7 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.67 – 7.63 (m, 1H), 7.58 (dd, *J* = 6.8, 8.9 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 149.7, 148.2, 136.4, 132.6, 132.5, 131.8, 131.6, 129.9, 128.9, 128.1, 118.4, 116.5, 113.4. Elemental analysis: calcd (%) for C<sub>13</sub>H<sub>7</sub>N<sub>3</sub>O (221.22): C 70.58, H 3.19; found: C 70.41, H 3.29.

**4-(3-(Trifluoromethyl)phenyl)benzo[c][1,2,5]oxadiazole (10):** Following the general procedure **A** using 1-bromo-3-(trifluoromethyl)benzene (225 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-toluene, 90-10) to afford the desired compound **10** (209 mg, 79%) as pale yellow oil. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.28 – 8.24 (m, 2H), 7.90 (d, *J* = 8.9 Hz, 1H), 7.77 – 7.73 (m, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 7.67 (d, *J* = 6.8 Hz, 1H), 7.57 (dd, *J* = 6.8, 9.0 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 149.7, 148.4, 135.9, 131.7, 131.6, 131.5 (q, *J* = 32.8 Hz), 129.5, 129.0, 128.7, 125.9 (q, *J* = 4.1 Hz), 125.0 (q, *J* = 4.1 Hz), 123.9 (q, *J* = 272.4), 116.1. Elemental analysis: calcd (%) for C<sub>13</sub>H<sub>7</sub>F<sub>3</sub>N<sub>2</sub>O (264.21): C 59.10, H 2.67; found: C 59.33, H 2.51.

**4-(3-Nitrophenyl)benzo[c][1,2,5]oxadiazole (11):** Following the general procedure **A** using 3-bromonitrobenzene (202 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-EtOAc, 90-1510) to afford the desired compound **11** (171 mg, 71%) as a brown solid (MP = 150-153 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.86 (s, 1H), 8.45 (d, *J* = 7.5 Hz, 1H), 8.35 (d, *J* = 7.9 Hz, 1H), 7.94 (d, *J* = 9.1 Hz, 1H), 7.81 – 7.68 (m, 2H), 7.64 – 7.53 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 149.7, 148.8, 148.2, 136.7, 134.4, 131.6, 130.1, 129.1, 127.9, 123.8, 123.0, 116.7. Elemental analysis: calcd (%) for C<sub>12</sub>H<sub>7</sub>N<sub>3</sub>O<sub>3</sub> (241.21): C 59.75, H 2.93; found: C 59.98, H 3.07.

**2-(Benzo[c][1,2,5]oxadiazol-4-yl)benzonitrile (12):** Following the general procedure **A** using 2-bromobenzonitrile (182 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash

chromatography on silica gel (pentane-CH<sub>2</sub>Cl<sub>2</sub>, 60-40) to afford the desired compound **12** (148 mg, 67%) as a white solid (MP = 164-166 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 7.97 (d, *J* = 9.1 Hz, 1H), 7.93 (d, *J* = 7.8 Hz, 1H), 7.90 (d, *J* = 7.2 Hz, 1H), 7.79 (dt, *J* = 1.4, 7.7 Hz, 1H), 7.72 (d, *J* = 6.7 Hz, 1H), 7.65 – 7.57 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 149.5, 148.6, 138.7, 134.1, 133.0, 131.7, 131.4, 131.1, 129.3, 126.9, 118.0, 117.0, 111.7. Elemental analysis: calcd (%) for C<sub>13</sub>H<sub>7</sub>N<sub>3</sub>O (221.22): C 70.58, H 3.19; found: C 70.39, H 3.30.

#### 2-(Benzo[c][1,2,5]oxadiazol-4-yl)benzaldehyde

**(13):** Following the general procedure **A** using 2-bromobenzaldehyde (185 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-Et<sub>2</sub>O, 70-30) to afford the desired compound **13** (141 mg, 63%) as an orange solid (MP = 140-143 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 9.97 (s, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.94 (d, *J* = 9.0 Hz, 1H), 7.77 (dt, *J* = 1.5, 7.5 Hz, 1H), 7.71 – 7.63 (m, 2H), 7.57 (dd, *J* = 6.6, 9.1 Hz, 1H), 7.36 (d, *J* = 6.6 Hz, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 190.8, 149.6, 149.1, 138.1, 134.4, 133.9, 131.8, 131.3, 131.2, 129.7, 129.5, 128.0, 116.4. Elemental analysis: calcd (%) for C<sub>13</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub> (224.21): C 69.64, H 3.60; found: C 69.72, H 3.88.

#### 4-(2-Fluorophenyl)benzo[c][1,2,5]oxadiazole

**(14):** Following the general procedure **A** using 1-bromo-2-fluorobenzene (175 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-toluene, 90-10) to afford the desired compound **14** (167 mg, 78%) as a yellow solid (MP = 119-121 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 7.91 – 7.84 (m, 2H), 7.62 (d, *J* = 6.9 Hz, 1H), 7.54 (dd, *J* = 6.8, 9.0 Hz, 1H), 7.51 – 7.44 (m, 1H), 7.34 (td, *J* = 1.2, 7.6 Hz, 1H), 7.30 – 7.24 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 159.9 (d, *J* = 249.5 Hz), 149.5, 148.7, 131.5, 131.2 (d, *J* = 5.4 Hz), 130.8 (d, *J* = 8.6 Hz), 124.9, 124.5, 124.5, 123.1 (d, *J* = 12.8 Hz), 116.4 (d, *J* = 20.9 Hz), 115.8. Elemental analysis: calcd (%) for C<sub>12</sub>H<sub>7</sub>FN<sub>2</sub>O (214.20): C 67.29, H 3.29; found: C 67.18, H 3.45.

#### 4-(Naphthalen-1-yl)benzo[c][1,2,5]oxadiazole

**(15):** Following the general procedure **A** using 1-bromonaphthalene (207 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-toluene, 95-15) to afford the desired compound **15** (140 mg, 57%) as a yellow solid (MP = 68-71 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.03 – 7.96 (m, 2H), 7.94 (d, *J* = 8.9 Hz, 1H), 7.74 (d, *J* = 8.9 Hz, 1H), 7.69 – 7.63 (m, 1H), 7.63 – 7.56 (m, 2H), 7.55 – 7.50 (m, 2H), 7.50 – 7.43 (m, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 149.9, 149.5, 133.9, 133.5, 131.6, 131.6, 131.3, 130.1, 129.5, 128.6, 127.9, 126.6, 126.2, 125.3, 125.3, 115.5. Elemental analysis: calcd (%) for C<sub>16</sub>H<sub>10</sub>N<sub>2</sub>O (246.27): C 78.03, H 4.09; found: C 78.45, H 4.19.

#### 4-(6-(Trifluoromethyl)pyridin-2-

yl)benzo[c][1,2,5]oxadiazole **(16):** Following the general procedure **A** using 2-bromo-6-(trifluoromethyl)pyridine (225 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-toluene, 80-20) to afford the desired compound **16** (188 mg, 71%) as a yellow solid (MP = 148-150 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.89 (d, *J* = 8.0 Hz, 1H), 8.64 (d, *J* = 6.9 Hz, 1H), 8.15 – 8.05 (m, 1H),

7.97 (dd, *J* = 0.8, 8.9 Hz, 1H), 7.74 (dd, *J* = 0.9, 7.8 Hz, 1H), 7.64 (dd, *J* = 6.9, 9.0 Hz, 1H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 152.1, 149.9, 148.3 (q, *J* = 34.9 Hz), 147.7, 138.8, 131.9, 131.2, 126.8, 126.5, 121.4 (q, *J* = 274.7 Hz), 119.9, 117.7. Elemental analysis: calcd (%) for C<sub>12</sub>H<sub>6</sub>F<sub>3</sub>N<sub>3</sub>O (265.20): C 54.35, H 2.28; found: C 64.43, H 2.37.

#### 4-(Quinolin-3-yl)benzo[c][1,2,5]oxadiazole

**(17):** Following the general procedure **A** using 3-bromoquinoline (208 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-EtOAc, 70-30) to afford the desired compound **17** (200 mg, 81%) as an orange solid (MP = 143-145 °C). <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 9.53 (d, *J* = 2.4 Hz, 1H), 9.06 (d, *J* = 2.0 Hz, 1H), 8.18 – 8.10 (m, 4H), 7.87 (ddd, *J* = 1.4, 6.9, 8.4 Hz, 1H), 7.81 (dd, *J* = 6.8, 9.0 Hz, 1H), 7.72 (ddd, *J* = 1.2, 6.9, 8.1 Hz, 1H). <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>) δ (ppm) 150.1, 150.0, 148.7, 147.8, 135.9, 133.6, 131.0, 130.9, 129.3, 129.2, 128.3, 127.9, 127.7, 126.3, 116.3. Elemental analysis: calcd (%) for C<sub>15</sub>H<sub>9</sub>N<sub>3</sub>O (247.26): C 72.87, H 3.67; found: C 72.98, H 3.54.

#### 4-(6-Methoxypyridin-2-

yl)benzo[c][1,2,5]oxadiazole **(18):** Following the general procedure **A** using 2-bromo-6-methoxypyridine (188 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-toluene, 90-10) to afford the desired compound **18** (130 mg, 57%) as a yellow solid (MP = 140-143 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.53 (d, *J* = 6.9 Hz, 1H), 8.32 (d, *J* = 7.5 Hz, 1H), 7.89 (d, *J* = 8.9 Hz, 1H), 7.79 (dd, *J* = 7.4, 8.3 Hz, 1H), 7.60 (dd, *J* = 6.9, 9.0 Hz, 1H), 6.85 (d, *J* = 8.3 Hz, 1H), 4.09 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 163.5, 150.0, 148.8, 147.9, 139.6, 131.8, 129.5, 128.1, 117.7, 116.4, 111.7, 53.3. Elemental analysis: calcd (%) for C<sub>12</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub> (227.22): C 63.43, H 3.99; found: C 63.68, H 4.13.

#### 1-(5-(Benzo[c][1,2,5]oxadiazol-4-yl)thiophen-2-

yl)ethan-1-one **(19):** Following the general procedure **A** using 1-(5-bromothiophen-2-yl)ethan-1-one (205 mg, 1 mmol) and benzofurazan (138 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-EtOAc, 80-20) to afford the desired compound **19** (154 mg, 63%) as a yellow solid (MP = 205-207 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.17 (d, *J* = 4.0 Hz, 1H), 7.90 – 7.83 (m, 1H), 7.78 (d, *J* = 4.0 Hz, 1H), 7.75 (d, *J* = 6.8 Hz, 1H), 7.51 (dd, *J* = 6.8, 9.0 Hz, 1H), 2.64 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 190.6, 149.5, 147.3, 145.1, 144.7, 133.3, 131.6, 129.8, 127.6, 123.3, 116.3, 26.8. Elemental analysis: calcd (%) for C<sub>12</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub>S (244.26): C 59.01, H 3.30; found: C 58.87, H 3.11.

#### 4-(5-Methoxybenzo[c][1,2,5]oxadiazol-4-

yl)benzotrile **(20):** Following the general procedure **A** using 4-bromobenzotrile (182 mg, 1 mmol) and 6-methoxybenzofurazan (173 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-Et<sub>2</sub>O, 60-40) to afford the desired compound **20** (172 mg, 68%) as an orange solid (MP = 195-197 °C). <sup>1</sup>H NMR (300 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ (ppm) 8.02 – 7.89 (m, 3H), 7.81 (d, *J* = 8.7 Hz, 2H), 7.58 (d, *J* = 9.8 Hz, 1H), 4.02 (s, 3H). <sup>13</sup>C NMR (100 MHz, CD<sub>2</sub>Cl<sub>2</sub>) δ (ppm) 156.4, 150.0, 146.9, 137.3, 131.8, 131.0, 123.6, 118.7, 117.9, 111.5, 110.0, 57.6. Elemental analysis: calcd (%) for C<sub>14</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub> (251.25): C 66.93, H 3.61; found: C 67.05, H 3.88.

#### 4-(3-Chlorophenyl)-5-

**methoxybenzo[c][1,2,5]oxadiazole (21):** Following the general procedure **A** using 1-bromo-3-chlorobenzene (191 mg, 1 mmol) and 6-methoxybenzofurazan (173 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-Et<sub>2</sub>O, 90-10) to afford the desired compound **21** (169 mg, 65%) as a yellow solid (MP = 76-79 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 7.89 (d, *J* = 9.7 Hz, 1H), 7.79 (d, *J* = 1.5 Hz, 1H), 7.69 (td, *J* = 1.5, 7.5 Hz, 1H), 7.51 (d, *J* = 9.7 Hz, 1H), 7.48 – 7.42 (m, 1H), 7.42 – 7.38 (m, 1H), 3.98 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 155.7, 150.3, 146.9, 134.1, 133.9, 130.3, 129.4, 128.5, 128.3, 123.9, 117.1, 111.3, 57.7. Elemental analysis: calcd (%) for C<sub>13</sub>H<sub>9</sub>ClN<sub>2</sub>O<sub>2</sub> (260.68): C 59.90, H 3.48; found: C 60.12, H 3.27.

#### 6-Methoxy-4-(2-

**nitrophenyl)benzo[c][1,2,5]oxadiazole (22a):** Following the general procedure **A** using 2-bromonitrobenzene (191 mg, 1 mmol) and 6-methoxybenzofurazan (173 mg, 1.15 mmol), the residue was purified by flash chromatography on silica gel (pentane-Et<sub>2</sub>O, 60-40) to afford the desired compound **22a** (103 mg, 38%) as a yellow solid (MP = 200-202 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.20 (d, *J* = 8.1 Hz, 1H), 7.77 (t, *J* = 7.6 Hz, 1H), 7.68 (t, *J* = 7.9 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 2.0 Hz, 1H), 6.92 (d, *J* = 2.0 Hz, 1H), 3.99 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 161.4, 150.1, 146.6, 133.5, 132.0, 130.3, 130.2, 128.8, 127.2, 125.2, 89.6, 56.2. Elemental analysis: calcd (%) for C<sub>13</sub>H<sub>9</sub>N<sub>3</sub>O<sub>4</sub> (271.23): C 57.57, H 3.34; found: C 57.21, H 3.56. **22b** <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.10 (d, *J* = 8.1 Hz, 1H), 7.95 (d, *J* = 9.7 Hz, 1H), 7.75 (t, *J* = 7.5 Hz, 1H), 7.70 (d, *J* = 7.5 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.46 (d, *J* = 9.7 Hz, 1H), 3.90 (s, 3H).

**Procedure B (Palladium-catalyzed one-pot direct C4,C7-diarylation):** To a 5 mL oven dried Schlenk tube, benzofurazan derivative (1 mmol), aryl bromide (3 mmol), AcOK (294 mg, 3 mmol), DMA (4 mL) and Pd(OAc)<sub>2</sub> (2.2 mg, 0.01 mmol, 2 mol%) were successively added. The reaction mixture was evacuated by vacuum-argon cycles (5 times) and stirred at 150 °C (oil bath temperature) for 16 hours. After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography to afford the desired diarylated products.

#### 4,7-Diphenylbenzo[c][1,2,5]oxadiazole (23):

Following the general procedure **B** using 1-bromobenzene (471 mg, 3 mmol) and benzofurazan (120 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (pentane-Et<sub>2</sub>O, 95-5) to afford the desired compound **23** (155 mg, 57%) as a yellow solid (MP = 190-191 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.11 – 8.03 (m, 4H), 7.71 (s, 2H), 7.62 – 7.54 (m, 4H), 7.53 – 7.47 (m, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 149.3, 135.3, 129.2, 129.0, 128.9, 128.7, 128.4. Elemental analysis: calcd (%) for C<sub>18</sub>H<sub>12</sub>N<sub>2</sub>O (272.31): C 79.39, H 4.44; found: C 79.57, H 4.60.

#### 4,7-Bis(4-chlorophenyl)benzo[c][1,2,5]oxadiazole

**(24):** Following the general procedure **B** using 1-bromo-4-chlorobenzene (574 mg, 3 mmol) and benzofurazan (120 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (pentane-CH<sub>2</sub>Cl<sub>2</sub>, 80-20) to afford the desired compound **24** (205 mg, 60%) as a yellow solid (MP = 230-232 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ

(ppm) 8.02 (d, *J* = 8.3 Hz, 4H), 7.69 (s, 2H), 7.55 (d, *J* = 8.3 Hz, 4H).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 149.0, 135.4, 133.5, 129.6, 129.2, 128.5, 128.0. Elemental analysis: calcd (%) for C<sub>18</sub>H<sub>10</sub>Cl<sub>2</sub>N<sub>2</sub>O (341.19): C 63.37, H 2.95; found: C 63.18, H 3.09.

#### 4,7-Bis(3,5-

#### bis(trifluoromethyl)phenyl)benzo[c][1,2,5] oxadiazole

**(25):** Following the general procedure **B** using 1-bromo-3,5-bis(trifluoromethyl)benzene (879 mg, 3 mmol) and benzofurazan (120 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (pentane-toluene, 90-10) to afford the desired compound **25** (392 mg, 72%) as a yellow solid (MP = 156-159 °C). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm) 8.53 (s, 4H), 8.02 (s, 2H), 7.86 (s, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 148.6, 136.5, 132.7 (q, *J* = 33.6 Hz), 129.6, 128.4 (d, *J* = 2.6 Hz), 127.7, 123.2 (m), 123.1 (q, *J* = 270.1 Hz). Elemental analysis: calcd (%) for C<sub>22</sub>H<sub>8</sub>F<sub>12</sub>N<sub>2</sub>O (544.30): C 48.55, H 1.48; found: C 48.62, H 1.54.

#### 4,7-Bis(6-(trifluoromethyl)pyridin-2-

#### yl)benzo[c][1,2,5]oxadiazole (26):

Following the general procedure **B** using 2-bromo-6-(trifluoromethyl)pyridine (678 mg, 3 mmol) and benzofurazan (120 mg, 1 mmol), the residue was purified by flash chromatography on silica gel (pentane-toluene, 80-20) to afford the desired compound **26** (263 mg, 64%) as a yellow solid (MP = 209-211 °C). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm) 8.96 (d, *J* = 8.0 Hz, 2H), 8.84 (s, 2H), 8.14 (d, *J* = 8.0 Hz, 2H), 7.78 (d, *J* = 8.0 Hz, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 150.7, 147.5, 147.4 (q, *J* = 34.9 Hz), 137.8, 130.8, 126.2, 126.0, 120.3 (q, *J* = 275.7 Hz), 119.2. Elemental analysis: calcd (%) for C<sub>18</sub>H<sub>8</sub>F<sub>6</sub>N<sub>4</sub>O (410.28): C 52.70, H 1.97; found: C 52.89, H 1.63.

#### Procedure C (acid-promoted the formation of

**quinoxalines):** To a 5 mL oven dried Schlenk tube, arylated benzofurazan derivative (0.5 mmol), *p*-toluenesulfonic acid (8.6 mg, 0.05 mmol), 2-aminoethan-1-ol (0.45 mL, 7.5 mmol) were successively added. The reaction mixture was stirred at 150 °C (oil bath temperature) for 72 hours. After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography to afford the desired arylated products.

#### 5-(4-Chlorophenyl)quinoxaline (27):

Following the general procedure **C** using 4-(4-chlorophenyl)benzo[c][1,2,5]oxadiazole (**6**) (115 mg, 0.5 mmol), the residue was purified by flash chromatography on silica gel (pentane-CH<sub>2</sub>Cl<sub>2</sub>, 70-30) to afford the desired compound **27** (101 mg, 84%) as a brown solid (MP = 109-111 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.97 – 8.85 (m, 2H), 8.20 (dd, *J* = 1.6, 8.3 Hz, 1H), 7.88 (t, *J* = 7.1 Hz, 1H), 7.82 (dd, *J* = 1.6, 7.2 Hz, 1H), 7.63 (d, *J* = 8.5 Hz, 2H), 7.51 (d, *J* = 8.5 Hz, 2H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (ppm) 144.9, 144.7, 143.1, 140.9, 140.0, 136.5, 134.1, 131.9, 130.5, 129.9, 129.3, 128.4. Elemental analysis: calcd (%) for C<sub>14</sub>H<sub>9</sub>ClN<sub>2</sub> (240.69): C 69.86, H 3.77; found: C 69.90, H 4.02.

#### 5-(Naphthalen-1-yl)quinoxaline (28):

Following the general procedure **C** using 4-(naphthalen-1-yl)benzo[c][1,2,5]oxadiazole (**15**) (123 mg, 0.5 mmol), the residue was purified by flash chromatography on silica gel (pentane-CH<sub>2</sub>Cl<sub>2</sub>, 70-30) to afford the desired compound **28** (111 mg, 87%) as a brown solid (MP = 100-103 °C). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (ppm) 8.88 (d, *J* = 1.8 Hz, 1H),



8.77 (d,  $J = 1.8$  Hz, 1H), 8.28 (dd,  $J = 1.5, 8.4$  Hz, 1H), 8.01 – 7.91 (m, 3H), 7.86 (dd,  $J = 1.5, 7.1$  Hz, 1H), 7.63 (dd,  $J = 7.0, 8.2$  Hz, 1H), 7.53 (dd,  $J = 1.3, 7.0$  Hz, 1H), 7.49 (ddd,  $J = 2.0, 6.0, 8.1$  Hz, 1H), 7.38 – 7.30 (m, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 144.9, 142.9, 142.3, 140.5, 136.5, 133.5, 132.7, 132.0, 129.7, 129.4, 128.5, 128.3, 128.1, 126.3, 125.9, 125.7, 125.2. Elemental analysis: calcd (%) for  $\text{C}_{18}\text{H}_{12}\text{N}_2$  (256.31): C 84.35, H 4.72; found: C 84.14, H 4.96.

**5,8-Bis(3,5-bis(trifluoromethyl)phenyl)quinoxaline (29):** Following the general procedure C using 4,7-bis(3,5-bis(trifluoromethyl)phenyl)benzo[*c*][1,2,5] oxadiazole (25) (272 mg, 0.5 mmol), the residue was purified by flash chromatography on silica gel (pentane- $\text{CH}_2\text{Cl}_2$ , 80-20) to afford the desired compound 29 (227 mg, 82%) as a brown solid (MP = 200-203 °C).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 8.98 (s, 2H), 8.30 – 8.16 (m, 4H), 8.01 (s, 2H), 8.00 (s, 2H).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) 145.3, 140.7, 139.6, 138.9, 131.5 (q,  $J = 33.7$  Hz), 130.8, 130.3, 123.4 (q,  $J = 273.4$  Hz), 121.8. Elemental analysis: calcd (%) for  $\text{C}_{24}\text{H}_{10}\text{F}_{12}\text{N}_2$  (554.34): C 52.00, H 1.82; found: C 52.18, H 2.07.

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## References

- [1] Y. Li, *Acc. Chem. Res.* **2012**, *45*, 723-733.
- [2] J. L. Rogers, L. Bayeh, T. H. Scheuermann, J. Longgood, J. Key, J. Naidoo, L. Melito, C. Shokri, D. E. Frantz, R. K. Bruick, K. H. Gardner, J. B. MacMillan, U. K. Tambar, *J. Med. Chem.* **2013**, *56*, 1739-1747.
- [3] E. A. Chugunova, N. I. Akylbekov, A. D. Voloshina, N. V. Kulik, V. V. Zobov, V. M. Babaev, N. V. Gavrilov, A. R. Burilov, *Synth. Commun.* **2016**, *46*, 1560-1565.
- [4] L. Wang, W. Huang, R. Li, D. Gehrig, P. W. M. Blom, K. Landfester, K. A. I. Zhang, *Angew. Chem. Int. Ed.* **2016**, *55*, 9783-9787.
- [5] a) A. A. Vasil'ev, M. I. Struchkova, A. B. Sheremetev, F. S. Levinson, R. V. Varganov, K. A. Lyssenko, *Russ. Chem. Bull.* **2011**, *60*, 2306-2314; b) J. L. Rogers, L. Bayeh, T. H. Scheuermann, J. Longgood, J. Key, J. Naidoo, L. Melito, C. Shokri, D. E. Frantz, R. K. Bruick, K. H. Gardner, J. B. MacMillan, U. K. Tambar, *J. Med. Chem.* **2013**, *56*, 1739-1747; c) C. Song, Y. Ling, L. Jin, M. Zhang, D.-L. Chen, Y. He, *Dalton Trans.* **2016**, *45*, 190-197.
- [6] a) H.-C. Ting, Y.-H. Chen, L.-Y. Lin, S.-H. Chou, Y.-H. Liu, H.-W. Lin, K.-T. Wong, *ChemSusChem* **2014**, *7*, 457-465; b) H.-C. Ting, Y.-T. Yang, C.-H. Chen, J.-H. Lee, J.-H. Chang, C.-I. Wu, T.-L. Chiu, C.-F. Lin, C.-L. Chung, K.-T. Wong, *ChemSusChem* **2016**, *9*, 1433-1441.
- [7] J. Bouffard, T. M. Swager, *Macromolecules* **2008**, *41*, 5559-5562.
- [8] H. Langhals, P. Knochel, A. Walter, S. Zimdars, *Synthesis* **2012**, *44*, 3465-3477.
- [9] N. Nakamura, Y. Tajima, K. Sakai, *Heterocycles* **1982**, *17*, 235-245.
- [10] a) A. Ohta, Y. Akita, T. Ohkuwa, M. Chiba, R. Fukunaga, A. Miyafuji, T. Nakata, N. Tani, Y. Aoyagi, *Heterocycles* **1990**, *31*, 1951-1958; b) Y. Aoyagi, A. Inoue, I. Koizumi, R. Hashimoto, K. Tokunaga, K. Gohma, J. Komatsu, K. Sekine, A. Miyafuji, J. Kunoh, *Heterocycles* **1992**, *33*, 257-272.
- [11] a) F. Kakiuchi, T. Kochi, *Synthesis* **2008**, 3013-3039; b) L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem. Int. Ed.* **2009**, *48*, 9792-9826; c) F. Bellina, R. Rossi, *Tetrahedron* **2009**, *65*, 10269-10310; d) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2009**, *48*, 5094-5115; e) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147-1169; f) E. M. Beck, M. J. Gaunt, *Top. Curr. Chem.* **2010**, *292*, 85-121; g) T. Satoh, M. Miura, *Synthesis* **2010**, 3395-3409; h) C.-L. Sun, B.-J. Li, Z.-J. Shi, *Chem. Commun.* **2010**, *46*, 677-685; i) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068-5083; j) N. Kuhl, M. N. Hopkinson, J. Wencel-Delord, F. Glorius, *Angew. Chem. Int. Ed.* **2012**, *51*, 10236-10254; k) B.-J. Li, Z.-J. Shi, *Chem. Soc. Rev.* **2012**, *41*, 5588-5598; l) M. C. White, *Synlett* **2012**, *23*, 2746-2748; m) J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem. Int. Ed.* **2012**, *51*, 8960-9009; n) S. I. Kozhushkov, L. Ackermann, *Chem. Sci.* **2013**, *4*, 886-896; o) R. Rossi, F. Bellina, M. Lessi, C. Manzini, *Adv. Synth. Catal.* **2014**, *356*, 17-117; p) M. Zhang, Y. Zhang, X. Jie, H. Zhao, G. Li, W. Su, *Org. Chem. Front.* **2014**, *1*, 843-895; q) M. R. Yadav, R. K. Rit, M. Shankar, A. K. Sahoo, *Asian J. Org. Chem.* **2015**, *4*, 846-864; r) K. Hirano, M. Miura, *Chem. Lett.* **2015**, *44*, 868-873; s) K. Yuan, J.-F. Soulé, H. Doucet, *ACS Catal.* **2015**, *5*, 978-991; t) C. B. Bheeter, L. Chen, J.-F. Soulé, H. Doucet, *Catal. Sci. Technol.* **2016**, *6*, 2005-2049.
- [12] J. F. Hartwig, M. A. Larsen, *ACS Cent. Sci.* **2016**, *2*, 281-292.
- [13] a) J. Zhang, W. Chen, A. J. Rojas, E. V. Jucov, T. V. Timofeeva, T. C. Parker, S. Barlow, S. R. Marder, *J. Am. Chem. Soc.* **2013**, *135*, 16376-16379; b) J. Zhang, T. C. Parker, W. Chen, L. Williams, V. N. Khrustalev, E. V. Jucov, S. Barlow, T. V. Timofeeva, S. R. Marder, *J. Org. Chem.* **2016**, *81*, 360-370.
- [14] F. Abdellaoui, C. Youssef, H. Ben Ammar, T. Roisnel, J.-F. Soulé, H. Doucet, *ACS Catal.* **2016**, *6*, 4248-4252.
- [15] S. Chikhi, S. Djebbar, J.-F. Soulé, H. Doucet, *Chem. Asian J.* **2016**, *11*, 2443-2452.
- [16] A. Jutand, M. Medio-Simons, B. Noverges Pedro, *ChemCatChem* **2017**, DOI: 10.1002/cctc.201700041.
- [17] V. A. Samsonov, *Russ. Chem. Bull.* **2007**, *56*, 2510-2512.
- [18] a) O. S. Moustafa, *J. Chin. Chem. Soc.* **2003**, *50*, 1205-1208; b) G. Sakata, K. Makino, Y. Kurasawa, *Heterocycles* **1988**, *27*, 2481-2515; c) J. A. Pereira, A. M. Pessoa, M. N. D. Cordeiro, R. Fernandes, C. Prudêncio, J. P. Noronha, M. Vieira, *Eur. J. Med. Chem.* **2015**, *97*, 664-672.



## Palladium-Catalyzed Regioselective Direct Arylation of Benzofurazans at C4 Position

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