Copper-Catalyzed Direct Amination of Polyfluoroarenes and Azoles with Hydroxylamines and Its Application to the Synthesis of 3-Aminobenzoheteroles

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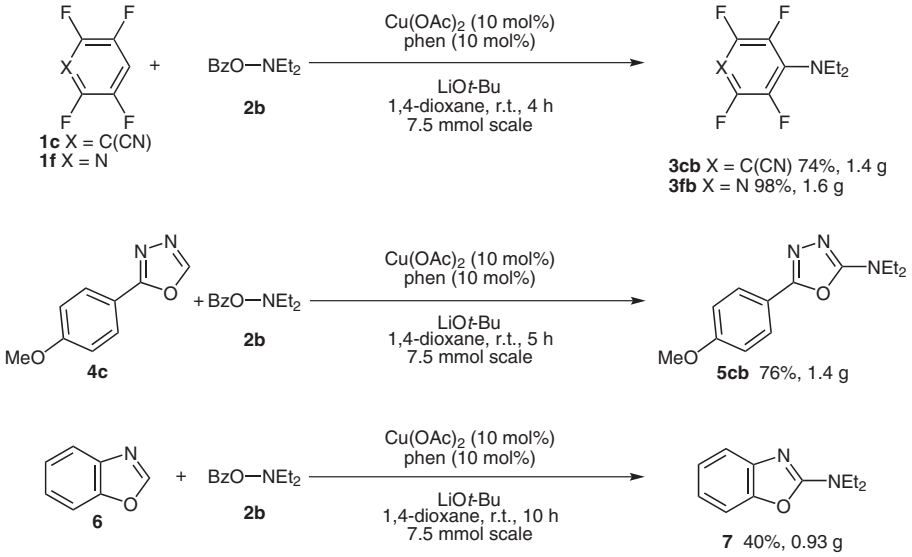
Received 9 January 2012

PSP No 223

Abstract: A copper-catalyzed electrophilic, umpolung amination strategy for the direct C–H amination of polyfluoroarenes and 1,3-azoles has been developed. The copper-based amination reaction is robust and can be easily scaled up on a gram scale. Its application to an annulative electrophilic amination of *o*-alkynylphenols and -anilines for the synthesis of 3-aminobenzofurans and -indoles is also described.

Key words: copper, electrophilic amination, C–H functionalization, polyfluoroarenes, heterocycles



Scheme 1

Introduction

Since aryl- and heteroarylamines frequently occur in pharmaceuticals, biologically active compounds, and functional materials,[1] the development of an aromatic carbon–nitrogen bond-forming reaction is one of longstanding central topics in organic synthesis. Significant advances in palladium-[2] and copper-catalyzed[3] aminations of aryl halides with amines now provide a powerful and convergent approach to the target motifs. On the other hand, we have recently focused on the unique reactivity of O-acylated hydroxylamines[4] as a class of electrophilic amination reagents and succeeded in performing a copper-catalyzed C–H amination of polyfluoroarenes and some 1,3-azoles even at room temperature.[5] The electrophilic, umpolung amination is robust and easily carried out on a gram scale (Scheme 1). Moreover, the copper-based amination protocol can be applied to an annulative electrophilic amination of *o*-alkynylphenols and -anilines for the synthesis of 3-aminobenzofurans and -indoles.[6]

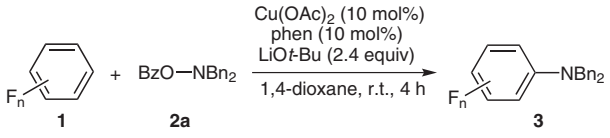
Scope and Limitation

Treatment of pentaflurobenzene (**1a**; 0.30 mmol, 1.2 equiv) with *O*-benzoyl-*N*,*N*-dibenzylhydroxylamine (**2a**; 0.25 mmol) in the presence of 10 mol% of $Cu(OAc)_2$/phen (0.025 mmol/0.025 mmol, phen = 1,10-phenanthroline) and LiO*t*-Bu (0.60 mmol, 2.4 equiv) in 1,4-dioxane (1.5 mL) at room temperature for 4 hours afforded *N*,*N*-dibenzyl-2,3,4,5,6-pentafluoroaniline (**3aa**) in 65% yield (Table 1, entry 1). 2,3,5,6-Tetrafluorobenzenes **1b** and **1c** bearing an electron-withdrawing group showed a good reactivity similar to **1a** (entries 2 and 3), whereas the introduction of an electron-donating group decreased the reaction efficiency (entries 4 and 5). A pyridine analogue

SYNTHESIS 2012, 44, 1792–1797
Advanced online publication: 15.02.2012
DOI: 10.1055/s-0031-1289715; Art ID: Z003111SS

1f also coupled with **2a** very smoothly to furnish **3fa** in 84% yield (entry 6). In the cases of **1g** and **1h**, which possess the equally reactive two C–H bonds, the selective monoamination occurred to give **3ga** and **3ha**, respectively, albeit with moderate yields (entries 7 and 8). In a sharp contrast to the above tetrafluorobenzenes, the reaction of 1,2,4-trifluorobenzene (**1i**) was sluggish (entry 9). The result suggest that the efficiency of the direct amination highly depends on the acidity of C–H bond.[7] Indeed, fluoroarenes containing less than three fluorine atoms did not undergo the amination at all.

Table 1 Copper-Catalyzed Direct Amination of Polyfluoroarenes **1** with *O*-Benzoyl-*N*,*N*-dibenzylhydroxylamine (**2a**)



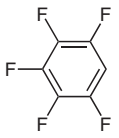
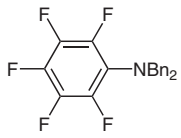
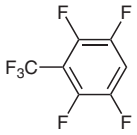
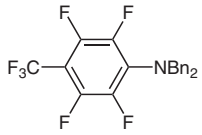
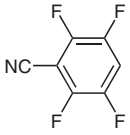
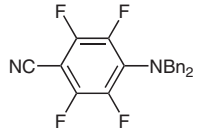
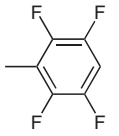
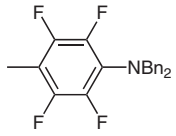
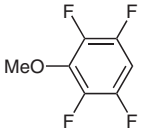
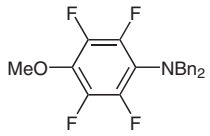
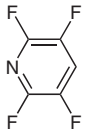
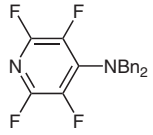
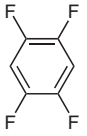
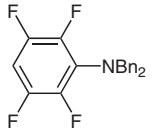
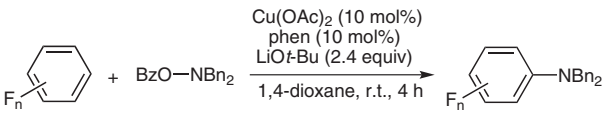
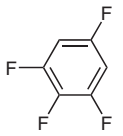
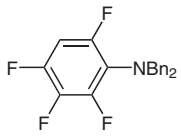
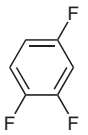
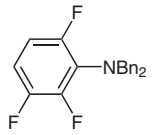
Entry	Polyfluoroarenes **1**	**3**, Yield (%)[a]
1	 **1a**	 **3aa**, 65
2	 **1b**	 **3ba**, 74
3	 **1c**	 **3ca**, 60
4[b]	 **1d**	 **3da**, 44
5	 **1e**	 **3ea**, 43
6	 **1f**	 **3fa**, 84
7	 **1g**	 **3ga**, 50

Table 1 Copper-Catalyzed Direct Amination of Polyfluoroarenes **1** with *O*-Benzoyl-*N*,*N*-dibenzylhydroxylamine (**2a**) (continued)



Entry	Polyfluoroarenes **1**	**3**, Yield (%)[a]
8[b]	 **1h**	 **3ha**, 31
9	 **1i**	 **3ia**, 3

[a] Yield of isolated product.
[b] At 50 °C.

A wide range of hydroxylamines **2** could be employed for the C–N coupling. Representative data are shown in Table 2. The tetrafluoropyridine **1f** underwent the amination with acyclic amines **2b**–**d** such as *N*,*N*-diethyl-, *N*-benzyl-*N*-methyl-, and *N*,*N*-diallylamines (Table 2, entries 1–3). The resultant benzylic and allylic moieties can be readily deprotected and undergo further orthogonal manipulations.[8] The copper catalyst accommodated cyclic systems: pyrrolidine, piperidine, and morpholine frameworks were directly installed to the fluorinated aromatic core (entries 4–6). In addition, the Boc-protected piperazine and bicyclic tetrahydroisoquinoline could participate in the reaction (entries 7 and 8). Particularly notable is the tolerance toward the secondary amine **2j** (entry 9). Moreover, the reaction with **2b** could be performed on a 30-fold scale, indicating the good reliability and reproducibility of the amination process (entry 1). A gram scale synthesis of **3cb** was also achieved (entry 10).

Similarly, the amination of some acidic 1,3-azoles[7] was catalyzed by the $Cu(OAc)_2$/phen system (Scheme 2). 2-Aryl-1,3,4-oxadiazoles **4** reacted with **2b** effectively to furnish good yields of the corresponding heteroarylamines **5** of medicinal and pharmaceutical interest. Benzoxazole (**6**) and benzothiazole (**8**) were also reacted with **2b** to furnish amines **7** and **9**. It is worth noting that a gram-scale synthesis of **5cb** and **7** was possible without any difficulty.

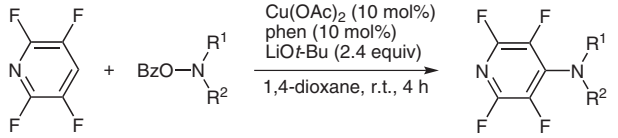
Some mechanistic studies with an isolated (phen)CuC_6F_5 complex **10**[9] support an electrophilic amination process of a (hetero)arylcopper species with hydroxylamines in the C–N bond-forming step (Scheme 3).

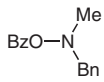
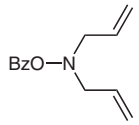
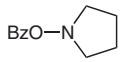
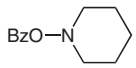
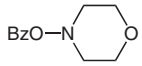
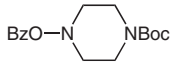
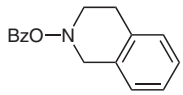
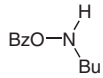
Our attention was turned next to the direct amination of other heterocycles such as benzofuran. However, no detectable amount of aminated product was observed. The failure was attributed to lack of formation of the corre-

assisted direct cupration could be difficult owing to the lower acidity of benzofuran C–H bonds than that of polyfluoroarene and 1,3-azole C–H bonds (Scheme 4). Thus, we envisioned an alternative, catalytic approach to this key intermediate from *o*-alkynylphenols; an electrophilic activation of the alkynyl moiety through the π coordination to the Cu center could trigger an annulative cupration to generate the desirable 3-benzofurylcopper in situ.[10]

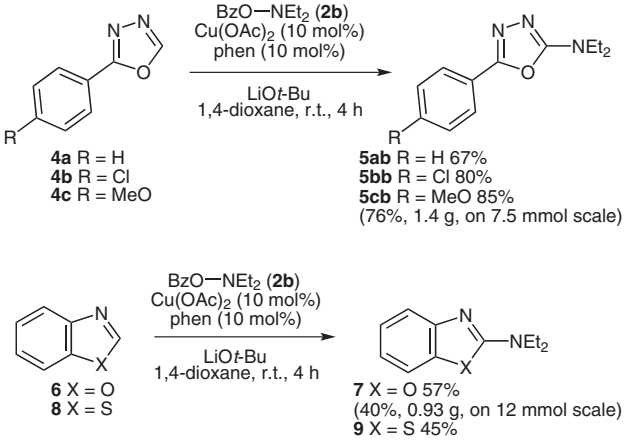
In accordance with the above assumption, extensive optimization studies were performed, and we were pleased to find that the annulative amination of 2-(phenylethynyl)phenol (**11a**, 0.50 mmol) with *O*-benzoyl-*N*,*N*-diethyl-

Table 2 Copper-Catalyzed Direct Amination of 2,3,5,6-Tetrafluoropyridine (**1f**) with Various Hydroxylamines **2**

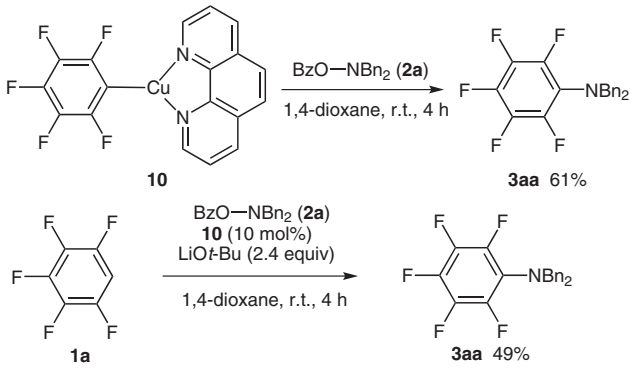


Entry	**2**	**3**, Yield (%)[a]
1	BzO—NEt_2 **2b**	**3fb**, 83 (98)[b]
2	 **2c**	**3fc**, 79
3	 **2d**	**3fd**, 67
4	 **2e**	**3fe**, 66
5	 **2f**	**3ff**, 57
6	 **2g**	**3fg**, 71
7	 **2h**	**3fh**, 52
8	 **2i**	**3fi**, 37
9	 **2j**	**3fj**, 46
10[c]	**2b**	**3cb**, 84 (74)[b]

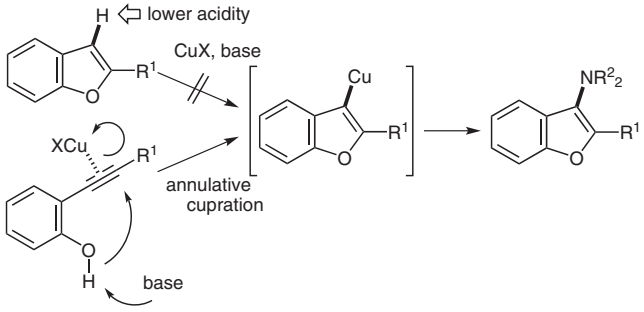
[a] Yield of isolated product.
[b] On a 30-fold scale.
[c] With **1c** instead of **1f**.



Scheme 2



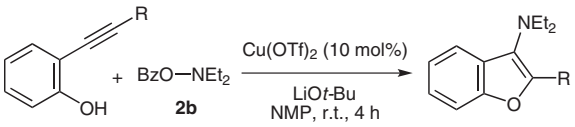
Scheme 3



Scheme 4

hydroxylamine (**2b**, 0.60 mmol, 1.2 equiv) proceeded in the presence of 10 mol% $Cu(OTf)_2$ (0.050 mmol) and LiO*t*-Bu (1.0 mmol, 2.0 equiv) in NMP at room temperature to produce the expected 3-aminobenzofuran **12ab** in 61% yield (Scheme 5). At alkyne terminus, an electron-donating methoxyphenyl and heterocyclic thienyl groups were compatible (**12bb** and **12cb**). It should be noted that the copper catalysis accommodated an alkyl substituent (**12dd**). Moreover, this type of transformation can be extended to nitrogen analogues, *o*-alkynylanilines **13**, directed toward the synthesis of 3-aminoindoles **14** (Scheme 6). As seen in the reaction of phenols **11**, electronically and sterically diverse substitution patterns were tolerated to obtain the corresponding indoles in good to excellent yields. The annulative electrophilic amination

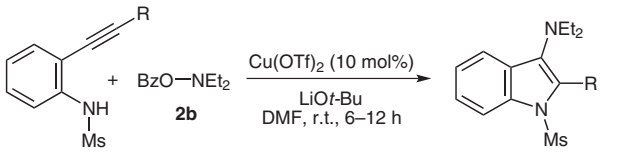
could provide a new and unique approach to 3-aminobenzoheteroles as a promising candidate for the drug design.[11]



11a R = Ph
11b R = 4-MeOC$_6$H$_4$
11c R = 3-thienyl
11d R = Bu

12ab R = Ph 61%
12bb R = 4-MeOC$_6$H$_4$ 71%
12cb R = 3-thienyl 77%
12db R = Bu 74%

Scheme 5



13a R = Ph
13b R = 4-MeOC$_6$H$_4$
13c R = 3-thienyl
13d R = Bu

14ab R = Ph 74%
14bb R = 4-MeOC$_6$H$_4$ 80%
14cb R = 3-thienyl 69%
14db R = Bu 93%

Scheme 6

In summary, we have developed a copper-catalyzed direct amination of polyfluoroarenes and 1,3-azoles with O-acylated hydroxylamines. The umpolung, electrophilic amination protocol enables the room temperature C–H amination of aromatics, which is a significant advantage compared to the precedent metal-mediated direct aminations.[12] Owing to the simplicity and mildness of the procedure, the amination reaction could be easily scaled up. Moreover, the copper-based catalysis can be applicable to an annulative electrophilic amination of *o*-alkynylphenols and -anilines for a new and convergent access to 3-aminobenzoheteroles.

All reactions were carried out under N_2 atmosphere in dried glassware. All starting materials were purchased from commercial suppliers and used without further purification, unless otherwise noted. 1,4-Dioxane was freshly distilled from sodium benzophenone ketyl. NMP and DMF were distilled from CaH_2 prior to use. *O*-Benzoylhydroxylamines **2**,[4] *o*-alkynylphenols **11**,[13] and *o*-alkynylanilines **13**[10] were readily accessible according to the literature. Silica gel column chromatography was performed using Wakogel 200 mesh and silica gel 60 N (spherical neutral) from Wako Pure Chemical Co. and Kanto Chemical, respectively. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded at 400 MHz, 100 MHz, and 373 MHz, respectively, for $CDCl_3$ solutions. MS data were obtained by EI. GC analysis was carried out using a silicon OV-17 column (i. d. 2.6 mm × 1.5 m) or a CBP-1 capillary column (i. d. 0.5 mm × 25 m).

Amination of Polyfluoroarenes and Azoles with Hydroxylamines; General Procedure 1 (Tables 1 and 2, and Scheme 2)

$Cu(OAc)_2$ (4.5 mg, 0.025 mmol), 1,10-phenanthroline (4.5 mg, 0.025 mmol), and LiO*t*-Bu (48 mg, 0.60 mmol) were placed in a 20 mL two-necked reaction flask, which was filled with N_2 by using the standard Schlenk technique. 1,4-Dioxane (0.50 mL) was then added to the flask, and the suspension was stirred for 15 min at r.t. Finally, a solution of polyfluoroarene **1**, or 1,3-azole **3** or **4** (0.30 mmol), *O*-benzoylhydroxylamine **2** (0.25 mmol), and 1-methylnaphthalene (ca. 25 mg, internal standard) in 1,4-dioxane (1.0 mL) was added dropwise. The solution was stirred at r.t. for additional 4 h, and the consumption of **2** was then confirmed by gas chromatographic analysis. The resulting mixture was quenched with H_2O (50 mL). The mixture was extracted with EtOAc (4 × 15 mL), and the combined organic layers were dried (Na_2SO_4). Concentration in vacuo and subsequent column chromatography (Wakogel, 200 mesh) with hexane–EtOAc (150:1 to 0:1, v/v) gave the corresponding arylamine **3**, **5**, **7**, or **9**.

Representative analytical and spectral data for **3aa** are provided below. Data for other products can be found in reference 5a.

***N*,*N*-Dibenzyl-2,3,4,5,6-pentafluoroaniline (3aa)**

Yield: 59 mg (0.16 mmol, 65%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.23 (s, 4 H), 7.21–7.29 (m, 10 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 57.3, 125.0 (tm, *J* = 12.2 Hz), 127.8, 128.6, 128.7, 137.8, 138.0 (dm, *J* = 249.7 Hz), 138.4 (dm, *J* = 250.4 Hz), 145.3 (dm, *J* = 247.3 Hz).

^{19}F NMR (373 MHz, $CDCl_3$): δ = –163.5 (t, *J* = 18.2 Hz), –160.8 (t, *J* = 18.2 Hz), –147.1 (d, *J* = 18.2 Hz).

HRMS (EI): *m*/*z* (M^+) calcd for $C_{20}H_{14}F_5N$: 363.1046; found: 363.1048.

Annulative Electrophilic Amination of *o*-Alkynylphenols; General Procedure 2 (Scheme 5)

$Cu(OTf)_2$ (18 mg, 0.050 mmol) and LiO*t*-Bu (80 mg, 1.0 mmol) were placed in a 20 mL two-necked reaction flask, which is filled with N_2 using the standard Schlenk technique. NMP (1.0 mL) was added, and the suspension was stirred for 10 min at r.t. A solution of *o*-alkynylphenol **11** (0.50 mmol) and *O*-benzoyl-*N*,*N*-diethylhydroxylamine (**2b**; 116 mg, 0.60 mmol) in NMP (2.0 mL) was then added dropwise. After stirring for 4 h at the same temperature, the resulting mixture was poured into brine (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Subsequent purification by column chromatography (silica gel 60 N, spherical neutral) with hexane–EtOAc–Et_3N (200:0:1–160:8:1, v/v/v) afforded the corresponding 3-aminobenzofuran **12**.

Representative analytical and spectral data for **12ab** are provided below. Data for other products can be found in reference 6b.

***N*,*N*-Diethyl-2-phenylbenzofuran-3-amine (12ab)**

Yield: 81 mg (0.31 mmol, 61%); pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.05 (t, *J* = 7.4 Hz, 6 H), 3.26 (q, *J* = 7.4 Hz, 4 H), 7.16 (t, *J* = 7.3 Hz, 1 H), 7.26–7.31 (m, 2 H), 7.40–7.49 (m, 3 H), 7.66 (d, *J* = 7.8 Hz, 1 H), 8.40 (d, *J* = 7.8 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 48.8, 111.7, 121.0, 122.0, 124.0, 125.9, 127.1, 127.7, 127.9, 128.2, 131.1, 149.2, 153.3.

HRMS (EI): *m*/*z* (M^+) calcd for $C_{18}H_{19}NO$: 265.1467; found: 265.1466.

Annulative Electrophilic Amination of *o*-Alkynylanilines; General Procedure 3 (Scheme 6)

$Cu(OTf)_2$ (9.0 mg, 0.025 mmol) and LiO*t*-Bu (40.0 mg, 0.50 mmol) were placed in a 20 mL two-necked reaction flask, which was filled with N_2 by using the standard Schlenk technique. DMF (0.5 mL) was then added to the flask, and the suspension was stirred for 15 min at r.t. Finally, a solution of *o*-alkynylaniline **13** (0.25 mmol), *O*-benzoyl-*N*,*N*-diethylhydroxylamine (**2b**; 58 mg, 0.30 mmol), and 1-methylnaphthalene (ca. 25 mg, internal standard) in DMF (1.0 mL) was added dropwise. The solution was stirred at r.t. for additional 6 h. The resulting mixture was quenched with H_2O (20 mL). Aq 4 M

HCl (60 mL) was added to the mixture. The aqueous layer was washed with Et_2O (4 × 15 mL), neutralized with aq 6 M NaOH, and then extracted with Et_2O (4 × 15 mL). The combined organic layers were dried (Na_2SO_4). Concentration in vacuo and subsequent purification by column chromatography (silica gel 60 N, spherical neutral) with hexane–EtOAc (5:1, v/v) as an eluent gave the corresponding 3-aminoindole **14**.

Representative analytical and spectral data for **14ab** are provided below. Data for other products can be found in reference 6b.

***N*,*N*-Diethyl-1-methanesulfonyl-2-phenylindol-3-amine (14ab)**
Yield: 63 mg (0.19 mmol, 74%); orange oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91 (t, *J* = 7.3 Hz, 6 H), 2.76 (s, 3 H), 3.01 (q, *J* = 7.3 Hz, 4 H), 7.29–7.49 (m, 7 H), 7.69 (d, *J* = 8.3 Hz, 1 H), 8.14 (d, *J* = 8.3 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 39.7, 48.1, 116.1, 120.5, 124.0, 125.2, 127.6, 128.7, 129.7, 131.6, 131.8, 133.0, 134.8, 136.5.

HRMS (EI): *m*/*z* (M^+) calcd for $C_{19}H_{22}N_2O_2S$: 342.1402; found: 342.1400.

Gram-Scale Syntheses (Scheme 1)
4-(Diethylamino)-2,3,5,6-tetrafluorobenzonitrile (3cb)
$Cu(OAc)_2$ (0.14 g, 0.75 mmol), 1,10-phenanthroline (0.14 g, 0.75 mmol), and LiO*t*-Bu (1.4 g, 18 mmol) were placed in a 100 mL two-necked reaction flask, which was filled with N_2 by using the standard Schlenk technique. 1,4-Dioxane (15 mL) was then added to the flask, and the suspension was stirred for 15 min at r.t. Finally, a solution of 2,3,5,6-tetrafluorobenzonitrile (**1c**; 1.6 g, 9.0 mmol) and *O*-benzoyl-*N*,*N*-diethylhydroxylamine (**2b**; 1.4 g, 7.5 mmol) in 1,4-dioxane (30 mL) was added dropwise. The solution was stirred at r.t. for additional 4 h. The resulting mixture was quenched with H_2O (100 mL). The mixture was extracted with EtOAc (4 × 20 mL), and the combined organic layers were dried (Na_2SO_4). Concentration in vacuo and subsequent column chromatography (silica gel 60 N, spherical neutral) with hexane–EtOAc (40:1, v/v) as an eluent gave **3cb** as a white solid; yield: 1.4 g (5.5 mmol, 74%); mp 48–49 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.19 (t, *J* = 7.3 Hz, 6 H), 3.39 (q, *J* = 7.3 Hz, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.9, 47.0 (t, *J* = 4.8 Hz), 82.7 (tm, *J* = 8.2 Hz), 109.0 (t, *J* = 3.8 Hz), 135.5 (tt, *J* = 10.5, 2.9 Hz), 140.8 (dm, *J* = 249.2 Hz), 148.4 (dm, *J* = 251.1 Hz).

^{19}F NMR (373 MHz, $CDCl_3$): δ = –149.9 (d, *J* = 17.4 Hz), –135.1 (d, *J* = 17.4 Hz).

HRMS (EI): *m*/*z* (M^+) calcd for $C_{11}H_{10}F_4N_2$: 246.0780; found: 246.0777.

***N*,*N*-Diethyl-2,3,5,6-tetrafluoropyridin-4-amine (3fb)**
$Cu(OAc)_2$ (0.14 g, 0.75 mmol), 1,10-phenanthroline (0.14 g, 0.75 mmol), and LiO*t*-Bu (1.4 g, 18 mmol) were placed in a 100 mL two-necked reaction flask, which was filled with N_2 by using the standard Schlenk technique. 1,4-Dioxane (15 mL) was then added to the flask, and the suspension was stirred for 15 min at r.t. Finally, a solution of 2,3,5,6-tetrafluoropyridine (**1f**; 1.4 g, 9.0 mmol) and *O*-benzoyl-*N*,*N*-diethylhydroxylamine (**2b**; 1.4 g, 7.5 mmol) in 1,4-dioxane (30 mL) was added dropwise. The solution was stirred at r.t. for additional 4 h. The resulting mixture was quenched with H_2O (100 mL). The mixture was extracted with Et_2O (4 × 20 mL), and the combined organic layers were dried (Na_2SO_4). Concentration in vacuo and subsequent column chromatography (silica gel 60 N, spherical neutral) with hexane–EtOAc (40:1, v/v) as an eluent gave **3fb** as a colorless oil; yield: 1.6 g (7.3 mmol, 98%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (t, *J* = 7.3 Hz, 6 H), 3.44 (qt, *J* = 7.3, 1.4 Hz, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.1, 46.8 (t, *J* = 4.8 Hz), 134.59 (dm, *J* = 247.3 Hz), 139.5–139.7 (m), 145.4 (dm, *J* = 237.7 Hz).

^{19}F NMR (373 MHz, $CDCl_3$): δ = –156.0 to –156.2 (m), –94.4 to –94.3 (m).

HRMS (EI): *m*/*z* (M^+) calcd for $C_9H_{10}F_4N_2$: 222.0780; found: 222.0784.

***N*,*N*-Diethyl-5-(4-methoxyphenyl)-1,3,4-oxadiazol-2-amine (5cb)**
$Cu(OAc)_2$ (0.14 g, 0.75 mmol), 1,10-phenanthroline (0.14 g, 0.75 mmol), and LiO*t*-Bu (1.4 g, 18 mmol) were placed in a 100 mL two-necked reaction flask, which was filled with N_2 by using the standard Schlenk technique. 1,4-Dioxane (15 mL) was then added to the flask, and the suspension was stirred for 15 min at r.t. Finally, a solution of 2-(4-methoxyphenyl)-1,3,4-oxadiazole (**4c**; 1.6 g, 9.0 mmol) and *O*-benzoyl-*N*,*N*-diethylhydroxylamine (**2b**; 1.4 g, 7.5 mmol) in 1,4-dioxane (30 mL) was added dropwise. The solution was stirred at r.t. for additional 5 h. The resulting mixture was quenched with H_2O (100 mL). The mixture was extracted with EtOAc (4 × 20 mL), and the combined organic layers were dried (Na_2SO_4). Concentration in vacuo and subsequent column chromatography (silica gel 60 N, spherical neutral) with hexane–EtOAc (1:2, v/v) as an eluent gave **5cb** as a colorless oil; yield: 1.4 g (5.7 mmol, 76%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 (t, *J* = 7.3 Hz, 6 H), 3.51 (q, *J* = 7.3 Hz, 4 H), 3.85 (s, 3 H), 6.95 (d, *J* = 8.7 Hz, 2 H), 7.84 (d, *J* = 8.7 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.3, 43.4, 55.5, 114.3, 117.7, 127.4, 158.8, 161.3, 163.7.

HRMS (EI): *m*/*z* (M^+) calcd for $C_{13}H_{17}N_3O_2$: 247.1321; found: 247.1320.

***N*,*N*-Diethylbenzoxazol-2-amine (7)**
$Cu(OAc)_2$ (0.22 g, 1.2 mmol), 1,10-phenanthroline (0.22 g, 1.2 mmol), and LiO*t*-Bu (2.3 g, 29 mmol) were placed in a 100 mL two-necked reaction flask, which was filled with N_2 by using the standard Schlenk technique. 1,4-Dioxane (24 mL) was then added to the flask, and the suspension was stirred for 15 min at r.t. Finally, a solution of benzoxazole (**6**; 1.7 g, 14 mmol) and *O*-benzoyl-*N*,*N*-diethylhydroxylamine (**2b**; 2.3 g, 12 mmol) in 1,4-dioxane (48 mL) was added dropwise. The solution was stirred at r.t. for additional 10 h. The resulting mixture was quenched with H_2O (100 mL). The mixture was extracted with Et_2O (4 × 20 mL), and the combined organic layers was dried (Na_2SO_4). Concentration in vacuo and subsequent column chromatography (silica gel 60 N, spherical neutral) with hexane–EtOAc (5:1, v/v) as an eluent gave **7** as a colorless oil; yield: 0.93 g (4.9 mmol, 40%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, *J* = 7.3 Hz, 6 H), 3.59 (q, *J* = 7.3 Hz, 4 H), 6.98 (t, *J* = 7.8 Hz, 1 H), 7.14 (t, *J* = 7.8 Hz, 1 H), 7.24 (d, *J* = 7.8 Hz, 1 H), 7.35 (d, *J* = 7.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 13.7, 43.1, 108.7, 116.0, 120.1, 124.0, 143.9, 149.0, 162.4.

HRMS (EI): *m*/*z* (M^+) calcd for $C_{11}H_{14}N_2O$: 190.1106; found: 190.1101.

Acknowledgment

This work was supported by Grants-in-Aid for Scientific Research from MEXT and JSPS, Japan. K. H. acknowledges Kansai Research Foundation for the Promotion of Science.

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