http://dx.doi.org/10.5012/bkcs.2013.34.1.42

Functionalization of Organotrifluoroborates *via* Cu-Catalyzed C-N Coupling Reaction

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Received September 11, 2012, Accepted September 12, 2012

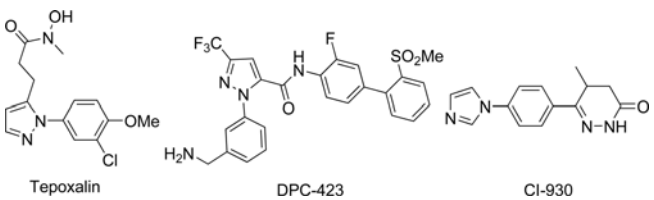
Potassium *N*-heterobiaryltrifluoroborates were successfully prepared *via* a selective Cu-catalyzed C-N coupling reaction. The BF_3K moiety was well tolerated under the reaction conditions involving CuI and dimethylethylenediamine (DMEDA) in the presence of DMSO. The Pd-catalyzed Suzuki-Miyaura cross couplings of potassium *N*-heterobiaryltrifluoroborates with bromoarenes were studied to prepare the *N*-heterotriaryl compounds. Moreover, homocoupling, iodination, and hydroxylation of potassium *N*-heterobiaryltrifluoroborates provided the corresponding products in high yields.

Key Words : Organotrifluoroborate, Potassium *N*-heterobiaryltrifluoroborates, Cu-catalyzed C-N coupling, Chan-Lam coupling, *N*-Heterobiarene

Introduction

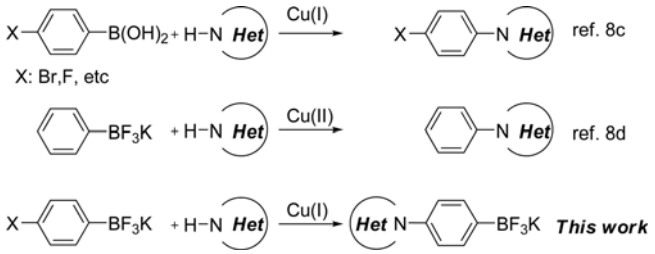
N-Heterobiarenes are ubiquitous in many bioactive natural products,[1] pharmaceutical drugs,[2] and organic materials.[3] For example, Tepoxalin, a *N*-aryl pyrazole derivative, has been reported as a novel dual inhibitor of COX (COX-1 and COX-2) and LOX.[4] DPC-423, developed by Bristol Myers Squibb, shows antithrombotic effects in human plasma.[5] The parent compound of Meribendan, CI 930 inhibits the action of the phosphodiesterase enzyme PDE3 (Scheme 1).

One of the most powerful synthetic methods to prepare *N*-heterobiarenes is the Cu-catalyzed C-N coupling reaction.[7] A large number of this Ullmann-type coupling reaction with various coupling partners (nucleophiles), including not only arylhalides but also arylboronic acids and aryltrifluoroborates, have been reported. Particularly, Cu-catalyzed C-N bond formation employing the arylboronic acids as a coupling partner are known as the Chan-Lam coupling and it has been widely demonstrated by various research groups.[8] Sreedhar and co-workers developed a Cu_2O-catalyzed C-N cross-coupling of arylboronic acids with *N*-heteroarenes.[8c] Surprisingly, bromophenylboronic acids and imidazole were used as coupling partners, bromo-substituted *N*-heterobiarene was obtained as a major product. Moreover, Batey



Scheme 1. Selected examples of the biologically active *N*-heterobiarenes.

[a]These authors contributed equally to this work.



Scheme 2. Our synthetic route for the selective preparation of *N*-heterobiaryltrifluoroborates.

and co-workers reported that potassium aryltrifluoroborates could be utilized in $Cu(OAc)_2$-catalyzed C-N bond coupling.[8d] However, to the best of our knowledge, there is no reports on the preparation of the potassium *N*-heterobiaryltrifluoroborates by the selective Cu-catalyzed Ullmann-type reaction with halobenzene derivatives bearing a BF_3K moiety on the phenyl ring.

Over the last decade, organotrifluoroborate salts have attracted a great deal of attention because of their excellent air and moisture stability as well as their remarkable tolerance to harsh conditions in numerous synthetic reactions. For instance, direct functionalizations of organotrifluoroborates *via* epoxidation,[9a] Jones oxidation,[9b] Wittig olefination,[9c] click reaction[9d] or halogen-lithium exchange[9e] have been successfully performed without elimination of the BF_3K group. In addition, numerous transformations of the BF_3K group in the reactions, such as Suzuki-Miyaura coupling, halogenation,[10] hydroxylation,[11] and C-N bond formation[8d] have been investigated.

Developing a synthetic method employing various organotrifluoroborate, thus, would be important for expanding the scope of organotrifluoroborate chemistry. In here, we report the synthesis of potassium *N*-heterobiaryltrifluoroborates using the selective Cu-catalyzed Ullmann-type condensation

of halophenyltrifluoroborates with *N*-heteroarenes (Scheme 2).

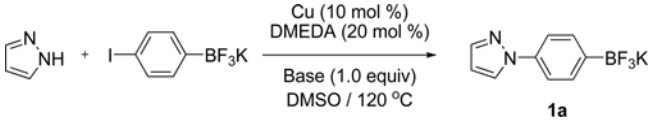
Results and Discussion

We first focused on the synthesis of potassium 4-(1*H*-pyrazolyl)phenyltrifluoroborate (**1a**) employing potassium 4-iodoaryltrifluoroborate with pyrazole (Table 1).[12]

In our previous study,[13] we found that Cu-catalyzed azidation of potassium 4-haloaryltrifluoroborates could be effective without loss of the BF_3K moiety. *N*,*N*′-Dimethylethylenediamine (DMEDA) was the best ligand among all the amine ligands tested, and it provided the highest conversion yield in shortest time. Thus, DMEDA was chosen as the ligand in the present study and the reaction was carried out in DMSO-d_6 in an NMR tube. The reaction was monitored by ^{1}H NMR. Various catalysts, including Cu(I) and Cu(II) salts were screened for the C-N bond formation (Table 1, entries 1-6). The reactions were carried out in the presence of Cu (II) catalyst such as $Cu(acac)_2$ and $Cu(OAc)_2$ (Table 1, entries 1 and 2). However, the reactions did not complete even after heating at 120 °C for 4 h. In contrast, the reaction proceeded at a faster rate in the presence of CuBr or CuO_2, and full conversion was observed within 4 h. Nevertheless, the best catalyst was CuI as it afforded the product in excellent isolated yield (Table 1, entry 6) in 2 h. Test reactions using a variety of bases (cf. Cs_2CO_3, K_3PO_4, K_2CO_3, NaO*t*Bu, and KO*t*Bu) indicated Cs_2CO_3 to be the best (Table 1, entries 6-10). The reaction rate decreased considerably when the reaction temperature was lowered to 100 °C (Table 1, entry 11).

We applied these optimized conditions to various nitrogen-containing heteroarenes to explore the scope of the CuI-catalyzed coupling reaction (Table 2). In most cases, the desired potassium *N*-heterobiaryltrifluoroborates were obtain-

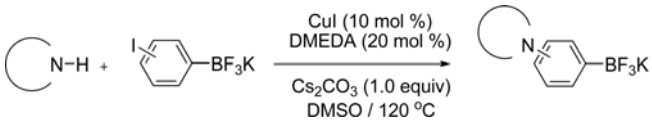
Table 1. Preparation of the preparation potassium 4-(1*H*-pyrazolyl)phenyltrifluoroborate (**1a**)[a]



Entry	Catalyst	Base	Time (h)	Conversion yield (%)[b]
1	$Cu(acac)_2$	Cs_2CO_3	4	79
2	$Cu(OAc)_2$	Cs_2CO_3	4	81
3	$CuBrSMe_2$	Cs_2CO_3	4	64
4	CuBr	Cs_2CO_3		100 (93)[c]
5	Cu_2O	Cs_2CO_3	4	100 (98)[c]
6	**CuI**	**Cs_2CO_3**	**2**	**100 (98)[c]**
7	CuI	K_3PO_4	4	80
8	CuI	K_2CO_3	4	47
9	CuI	NaO^{t}Bu	4	54
10	CuI	KO^{t}Bu	4	< 5
11[d]	CuI	Cs_2CO_3	9	70

[a]All reactions were performed with 0.1 mmol of potassium 4-iodophenyltrifluoroborate and 1.1 equiv of pyrazole in 0.5 mL of DMSO-d_6. [b]The conversion yield was based on the integration of ^{1}H NMR peaks at 8.35 ppm (potassium 4-iodophenyltrifluoroborate) and 7.15 ppm (**1a**), respectively. [c]Isolated yields. [d]Reaction temperature was 100 °C.

Table 2. Preparation of *N*-heterobiaryltrifluoroborates *via* Cu-catalyzed C-N coupling reaction[a]



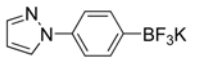
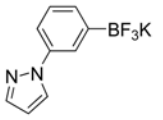
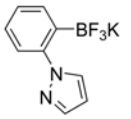
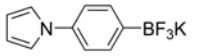
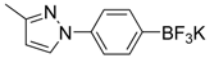
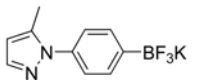
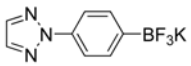
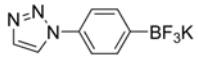
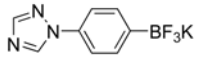
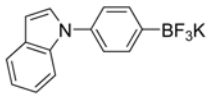
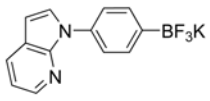
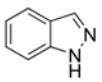
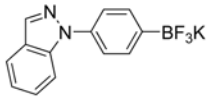
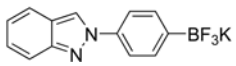
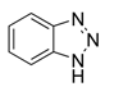
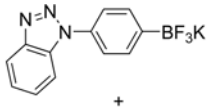
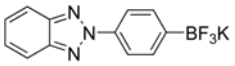
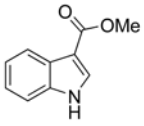
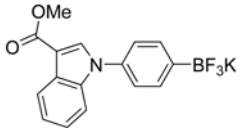
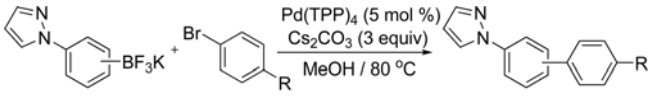
Entry	*N*-Heteroarene	Time (h)	Product		Yield (%)[b]
1		2		**1a**	98
2		3		**1b**	97
3		16		**1c**	40
4		5		**1d**	55
5		4		**1e**	
			+		99 (5 : 1)
				**1f**	
6		8		**1g**	
			+		90 (4 : 1)
				**1h**	
7[c]		8		**1i**	94
8		4		**1j**	72
9		6		**1k**	83
10		2		**1l**	
			+		94 (2 : 1)
				**1m**	

Table 2. (continued)

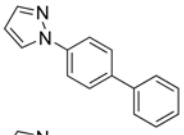
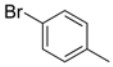
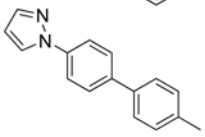
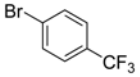
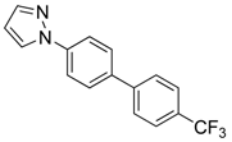
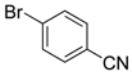
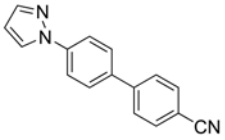
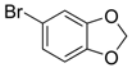
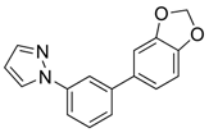
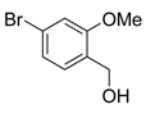
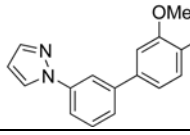
Entry	*N*-Heteroarene	Time (h)	Product	Yield (%)[b]
11		6	 **1n** +  **1o**	84 (8 : 1)
12		20	 **1p**	73

[a]All reactions were performed with a 0.5 mmol of potassium iodophenyltrifluoroborate and 1.1 equiv of pyrazole in 2 mL of DMSO. [b]Isolated yields. [c]Reaction temperature was 130 °C.

Table 3. Suzuki-Miyaura cross-coupling of potassium pyrazolylphenyltrifluoroborates with bromoarenes[a]

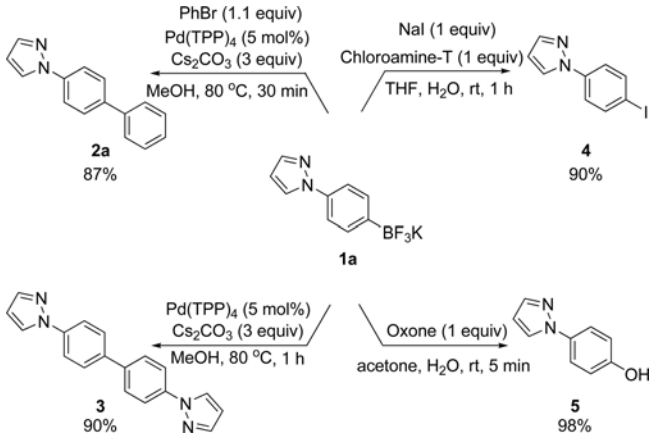


1a or **1b** **2**

Entry	ArBr	Time (min)	Product	Yield (%)[b]
1		30	 **2a**	87
2		30	 **2b**	81
3		10	 **2c**	83
4		20	 **2d**	96
5		30	 **2e**	82
6		60	 **2f**	51

[a]All reactions were performed with a 0.3 mmol of 4-(1*H*-pyrazol-1-yl)phenyltrifluoroborate (0.3 mmol) and 1.1 equiv of arylbromide in 2 mL of MeOH. [b]Isolated yield.

ed in good to excellent yields. However, coupling of 2-iodoaryltrifluoroborate and pyrazole furnished the product



Scheme 3. Various functionalization of potassium 4-(1*H*-pyrazolyl)phenyltrifluoroborate (**1a**).

1c in 40% yield, probably due to the steric effect (Table 2, entry 3). Two regioisomers, **1e** and **1f** were obtained when 3-methylpyrazole was used as the coupling partner due to the electron-donating effect of the methyl group (Table 2, entry 5).[14] Moreover, the regioisomers (**1g**/**1h**, **1l**/**1m**, and **1n**/**1o**) were obtained in a ratio of 2:1 to 8:1 when 1,2,3-triazole, indazole, and benzotriazole were used as the coupling partners (Table 2, entries 6, 10 and 11).

N-arylpyrazoles are well known core framework in drug development.[2] For example, Rimonabant,[15] an anorectic anti-obesity drug, and Celecoxib,[16] a sulfa-NSAID, commonly contain the *N*-arylpyrazole skeleton. In our ongoing project, we also studied on the synthesis of biologically active compound libraries including the *N*-arylpyrazole core. We were interested in the functionalization of *N*-arylpyrazole compounds bearing a BF_3K moiety by Suzuki-Miyaura cross coupling with bromoarenes. Under the optimized conditions that we developed,[17] we conducted the cross coupling reaction of potassium 4- or 3-(1*H*-pyrazolyl)-phenyltrifluoroborate (**1a** or **1b**) with bromoarenes bearing various functional groups. As illustrated in Table 3, all the reactions proceeded to 100% completion within 1 h to afford the desired *N*-heterotriaryl compounds in good to excellent yields.

Finally, we further attempted functionalization reactions of **1a** towards homocoupling, iodination, and hydroxylation. The results are summarized in Scheme 3. Homocoupling of **1a** under the same conditions used for cross coupling without bromoarenes afforded the desired homocoupled product **3** in 90% yield. Iodination[10] of the BF_3K group of **1a** was also successfully accomplished to give the product **4** in 90% yield. Furthermore, hydroxylation[11] of **1a** using oxone gave the corresponding phenol derivative **5** in high yield.

Conclusion

In summary, Cu-catalyzed functionalization of potassium iodoaryltrifluoroborates with *N*-heteroarenes was successfully accomplished without loss of the BF_3K moiety. The intact BF_3K moiety could be further utilized in Suzuki-Miyaura cross coupling to afford *N*-heterotriaryl compounds.

Moreover, homocoupling, iodination, and hydroxylation were investigated. Further applications and developments based on this methodology are currently under investigation.

Experimental Section

General Information. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded at 400, 100, and 376 MHz, respectively. ^{19}F NMR chemical shifts were referenced to external $CFCl_3$ (0.0 ppm). ^{11}B NMR spectra at 128 MHz were obtained on a spectrometer equipped with the appropriate decoupling accessories. All ^{11}B NMR chemical shifts were referenced to external $BF_3{\cdot}OEt_2$ (0.0 ppm) with a negative sign indicating an upfield shift. Mass spectra of potassium 1,2,3-triazoletrifluoroborates were recorded on LCQ Fleet Ion Trap Mass Spectrometer (ESI-MS) using negative ESI mode at the mass spectrometry facilities in KIST-Gangneung Institute. IR spectra were obtained using Nicolet iS10 FT-IR spectrometer. Melting points were performed on recrystallized solids and recorded on Stanford Research Systems OptiMelt MPA100 melting point apparatus and are uncorrected. Commercially available reagents were used without purification unless noted otherwise.

General Procedure I (Preparation of Potassium *N*-Heterobiaryltrifluoroborate, Table 2). To a solution of potassium iodophenyltrifluoroborate (0.5 mmol), CuI (10 mol %), DMEDA (20 mol %), and Cs_2CO_3 (0.5 mmol) in DMSO (2 mL) was added corresponding *N*-heteroarenes (0.55 mmol) under atmospheric conditions. The reaction mixture was stirred in an oil bath at 120 °C. After completion of the reaction, the solvent was removed *in vacuo* at 60-70 °C. The residual product was dissolved in dry acetone (3 mL), and the insoluble salts were removed by filtration through Celite. The solvent was concentrated on a rotary evaporator. The addition of Et_2O led to the precipitation of the product. The product was filtered and dried *in vacuo* to afford the desired product.

Potassium 4-(1*H*-pyrazol-1-yl)phenyltrifluoroborate (1a). White solid; mp 250 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.19 (d, 1H, J = 2.4 Hz), 7.61 (d, 1H, J = 1.2 Hz), 7.58 (d, 2H, J = 10.4 Hz), 7.56 (d, 2H, J = 10.4 Hz), 6.44 (t, 1H, J = 4.0 Hz); ^{13}C NMR (100 MHz, acetone-d_6) δ 140.6(C2), 133.3, 127.3, 117.8, 107.4; ^{19}F NMR (376 MHz, acetone-d_6) δ −141.4; ^{11}B NMR (128 MHz, acetone-d_6) δ 3.72. FT-IR (ATR): 1603, 1524, 1431, 1396, 1331, 1221, 1118, 1019, 966, 933, 825, 741 cm^{-1}; ESIMS: *m/z* calcd for $C_{13}H_{15}BF_3O_2$ $[M\text{-}K^+]^-$ 211.07, found 211.01.

Potassium 3-(1*H*-pyrazol-1-yl)phenyltrifluoroborate (1b). Brown solid; mp 250 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.19 (d, 1H, J = 2.4 Hz), 7.85 (s, 1H), 7.62 (d, 1H, J = 1.2 Hz), 7.52 (d, 1H, J = 8.0 Hz), 7.43 (d, 1H, J = 7.2 Hz), 7.22 (t, 1H, J = 15.2 Hz), 6.44 (t, 1H, J = 4.0 Hz); ^{13}C NMR (100 MHz, acetone-d_6) δ 140.7(C2), 130.9, 128.0, 127.6, 122.9, 117.0, 107.5; ^{19}F NMR (376 MHz, acetone-d_6) δ −140.7; ^{11}B NMR (128 MHz, acetone-d_6) δ 3.22. FT-IR (ATR): 2927, 2854, 1581, 1518, 1460, 1404, 1330, 1198, 1050, 1026, 985 cm^{-1}; ESIMS: *m/z* calcd for $C_{13}H_{15}BF_3O_2$ $[M\text{-}K^+]^-$ 211.07, found 211.04.

Potassium 2-(1*H*-pyrazol-1-yl)phenyltrifluoroborate (1c). Brown solid; mp 250 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.49 (s, 1H), 7.74 (d, 1H, J = 6.8 Hz), 7.51 (s, 1H), 7.48 (d, 1H, J = 7.6 Hz), 7.18 (t, 1H, J = 14.8 Hz), 7.12 (t, 1H, J = 14.0 Hz), 6.26 (s, 1H); ^{13}C NMR (100 MHz, acetone-d_6) δ 145.2, 139.4, 135.2, 132.6, 127.0, 126.1, 124.5, 105.3; ^{19}F NMR (376 MHz, acetone-d_6) δ −135.9; ^{11}B NMR (128 MHz, acetone-d_6) δ 3.02; FT-IR (ATR): 3444, 2925, 2854, 2359, 2341, 1588, 1519, 1456, 1402, 1123, 1083, 756 cm^{-1}; ESIMS: *m/z* calcd for $C_{13}H_{15}BF_3O_2$ $[M\text{-}K^+]^-$ 211.07, found 211.03.

Potassium 4-(1*H*-pyrazol-1-yl)phenyltrifluoroborate (1d). Brown solid; mp 208.7 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 7.56 (d, 2H, J = 8.0 Hz), 7.25 (d, 2H, J = 7.6 Hz), 7.17 (s, 2H), 6.22 (s, 2H); ^{13}C NMR (100 MHz, acetone-d_6) δ 139.0, 133.7, 119.8, 119.0, 110.3; ^{19}F NMR (376 MHz, acetone-d_6) δ −140.5; ^{11}B NMR (128 MHz, acetone-d_6) δ 3.46. FT-IR (ATR): 1604, 1520, 1476, 1401, 1328, 1216, 1123, 960, 918, 823, 719 cm^{-1}; ESIMS: *m/z* calcd for $C_{13}H_{15}BF_3O_2$ $[M\text{-}K^+]^-$ 210.07, found 211.01.

Potassium 4-(3-Methyl-1*H*-pyrazol-1-yl)phenyltrifluoroborate (1e) and Potassium 4-(5-Methyl-1*H*-pyrazol-1-yl)phenyl-trifluoroborate (1f). White solid; mp 250 °C; **1e**: ^{1}H NMR (400 MHz, acetone-d_6) δ 8.08 (s, 1H), 7.54 (d, 2H, J = 12.8 Hz), 7.52 (d, 2H, J = 13.2 Hz), 6.22 (s, 1H), 2.27 (s, 3H); **1f**: ^{1}H NMR (400 MHz, acetone-d_6) δ 7.59 (d, 2H, J = 7.6 Hz), 7.43 (s, 1H), 7.21 (d, 2H, J = 7.6 Hz), 6.17 (s, 1H), 2.31 (s, 3H); ^{19}F NMR (376 MHz, acetone-d_6) δ −140.18; ^{11}B NMR (128 MHz, acetone-d_6) δ 3.31; FT-IR (ATR): 2925, 1606, 1533, 1445, 1411, 1365, 1217, 966, 946, 826, 747 cm^{-1}; ESIMS: *m/z* calcd for $C_{13}H_{15}BF_3O_2$ $[M\text{-}K^+]^-$ 225.08, found 225.00; The 5:1 ratio of **1e** and **1f** was based on the integration of peaks at 6.22 (**1e**) and 6.17 (**1f**) ppm, respectively.

Potassium 4-(2*H*-1,2,3-Triazol-2-yl)phenyltrifluoroborate (1g) and Potassium 4-(1*H*-1,2,3-triazol-1-yl)phenyltrifluoro-borate (1h). White solid; mp 206.2 °C; **1g**: ^{1}H NMR (400 MHz, acetone-d_6) δ 7.90 (s, 2H), 7.83 (d, 2H, J = 7.6 Hz), 7.66-7.61 (m, 2H); **1h**: ^{1}H NMR (400 MHz, acetone-d_6) δ 8.49 (s, 1H), 7.84 (s, 1H), 7.66-7.61 (m, 4H); ^{19}F NMR (376 MHz, acetone-d_6) δ −140.9; ^{11}B NMR (128 MHz, acetone-d_6) δ 3.23; FT-IR (ATR): 3136, 2926, 1706, 1601, 1511, 1411, 1379, 1219, 961, 945, 829 cm^{-1}; ESIMS: *m/z* calcd for $C_{13}H_{15}BF_3O_2$ $[M\text{-}K^+]^-$ 212.06, found 212.02; The 4:1 ratio of **1g** and **1h** was based on the integration of peaks at 7.89 (**1g**) and 8.49 (**1h**) ppm, respectively.

Potassium 4-(1*H*-1,2,4-Triazol-1-yl)phenyltrifluoroborate (1i). White solid; mp 250 °C; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.96 (s, 1H), 8.05 (s, 1H), 7.63 (d, 2H, J = 8.0 Hz), 7.58 (d, 2H, J = 8.0 Hz); ^{13}C NMR (100 MHz, acetone-d_6) δ 152.8, 142.2, 135.8, 133.6, 118.6; ^{19}F NMR (376 MHz, acetone-d_6) δ −140.6; ^{11}B NMR (128 MHz, acetone-d_6) δ 3.38; FT-IR (ATR): 3122, 3039, 1603, 1522, 1207, 951, 877, 820, 675, 652 cm^{-1}; ESIMS: *m/z* calcd for $C_{13}H_{15}BF_3O_2$ $[M\text{-}K^+]^-$ 212.06, found 212.09.

Potassium 4-(1*H*-Indol-1-yl)phenyltrifluoroborate (1j).

Brown solid; mp 250 ºC; ^{1}H NMR (400 MHz, acetone-d_6) δ 7.68 (d, 2H, J = 7.6 Hz), 7.64 (d, 1H, J = 8.0 Hz), 7.55 (d, 1H, J = 8.0 Hz), 7.47 (d, 1H, J = 2.8 Hz), 7.30 (d, 2H, J = 7.6 Hz), 7.17 (t, 1H, J = 15.2 Hz), 7.09 (t, 1H, J = 14.8 Hz), 6.64 (d, 1H, J = 2.8 Hz); ^{13}C NMR (100 MHz, acetone-d_6) δ 137.8, 136.9, 133.7, 130.2, 129.3, 123.1, 122.7, 121.7, 120.6, 111.4, 103.3; ^{19}F NMR (376 MHz, acetone-d_6) δ −142.1; ^{11}B NMR (128 MHz, acetone-d_6) δ 3.24; FT-IR (ATR): 3027, 2924, 1602, 1517, 1455, 1333, 1210, 949, 830, 738, 586 cm^{-1}; ESIMS: *m/z* calcd for $C_{13}H_{15}BF_3O_2$ [M-K$^+$]$^-$ 260.09, found 260.02.

Potassium 4-(1*H*-Pyrrolo[2,3-*b*]pyridin-1-yl)phenyltrifluoroborate (1k). White solid; mp 248.7 ºC; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.29 (d, 1H, J = 4.0 Hz), 8.03 (d, 1H, J = 7.6 Hz), 7.75 (d, 1H, J = 3.2 Hz), 7.65 (d, 2H, J = 8.0 Hz), 7.60 (d, 2H, J = 8.0 Hz), 7.14 (dd, 1H, J = 8.0 Hz, 4.8 Hz), 6.65 (d, 1H, J = 3.6 Hz); ^{13}C NMR (100 MHz, acetone-d_6) δ 148.5, 143.8, 136.9, 133.1, 129.5, 129.4, 122.8, 122.4, 117.1, 101.6; ^{19}F NMR (376 MHz, acetone-d_6) δ −140.2; ^{11}B NMR (128 MHz, acetone-d_6) δ 3.61; FT-IR (ATR): 3034, 1606, 1593, 1577, 1421, 1356, 1216, 958, 894, 830, 792, 771, 713 cm^{-1}; ESIMS: *m/z* calcd for $C_{13}H_{15}BF_3O_2$ [M-K$^+$]$^-$ 261.08, found 261.06.

Potassium 4-(1*H*-Indazol-1-yl)phenyltrifluoroborate (1l) and Potassium 4-(2*H*-indazol-2-yl)phenyltrifluoroborate (1m). White solid; mp 250 ºC; **1l**: ^{1}H NMR (400 MHz, acetone-d_6) δ 8.20 (s, 1H), 7.85-7.77 (m, 2H), 7.69 (d, 2H, J = 8.0 Hz), 7.50 (d, 2H, J = 7.6 Hz), 7.44 (t, 1H, J = 7.6 Hz), 7.22 (t, 1H, J = 7.4 Hz); **1m**: ^{1}H NMR (400 MHz, acetone-d_6) δ 8.78 (s, 1H), 7.85 (d, 2H, J = 8.0 Hz), 7.85-7.77 (m, 1H), 7.75 (d, 1H, J = 8.4 Hz), 7.67 (d, 2H, J = 8.0 Hz), 7.28 (t, 1H, J = 8.0 Hz), 7.09 (t, 1H, J = 8.0 Hz); ^{19}F NMR (376 MHz, acetone-d_6) δ −141.3; ^{11}B NMR (128 MHz, acetone-d_6) δ 3.49; FT-IR (ATR): 3062, 2926, 1605, 1515, 1464, 1422, 1379, 1223, 1199, 1023, 965, 905, 828, 737 cm^{-1}; ESIMS: *m/z* calcd for $C_{13}H_{15}BF_3O_2$ [M-K$^+$]$^-$ 261.08, found 261.05; The 2:1 ratio of **1l** and **1m** was based on the integration of peaks at 8.20 (**1l**) and 8.77 (**1m**) ppm, respectively.

Potassium 4-(1*H*-Benzo[*d*][1,2,3]triazol-1-yl)phenyl-trifluoroborate (1n) and Potassium 4-(2*H*-benzo[*d*][1,2,3]-triazol-2-yl)phenyltrifluoroborate (1o). White solid; mp 162 ºC; **1n**: ^{1}H NMR (400 MHz, acetone-d_6) δ 8.11 (d, 1H, J = 8.4 Hz), 7.88 (d, 1H, J = 8.4 Hz), 7.79 (d, 2H, J = 8.4 Hz), 7.63 (t, 1H, J = 16.4 Hz), 7.58 (d, 2H, J = 7.6 Hz), 7.49 (t, 1H, J = 15.2 Hz); **1o**: ^{1}H NMR (400 MHz, acetone-d_6) δ 8.15 (d, 2H, J = 8.0 Hz), 7.97 (dd, 2H, J = 6.6, Hz, 3.2 Hz), 7.73 (d, 2H, J = 8.4 Hz), 7.52-7.45 (m, 2H); ^{19}F NMR (376 MHz, acetone-d_6) δ −141.2; ^{11}B NMR (128 MHz, acetone-d_6) δ 3.41; FT-IR (ATR): 3031, 2928, 1601, 1502, 1452, 1211, 1069, 1007, 953, 828, 784, 766, 742 cm^{-1}; ESIMS: *m/z* calcd for $C_{13}H_{15}BF_3O_2$ [M-K$^+$]$^-$ 262.08, found 262.09; The 8:1 ratio of **1n** and **1o** was based on the integration of peaks at 7.78 (**1n**) and 7.73 (**1o**) ppm, respectively.

Potassium 4-(3-(Methoxycarbonyl)-1*H*-indol-1-yl)phenyl-trifluoroborate (1p). White solid; mp 154 ºC; ^{1}H NMR (400 MHz, acetone-d_6) δ 8.24-8.18 (m, 1H), 8.09 (s, 1H), 7.73 (d, 2H, J = 8.0 Hz), 7.52-7.50 (m, 1H), 7.35 (d, 2H, J = 8.0 Hz), 7.31-7.25 (m, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, acetone-d_6) δ 165.6, 137.9, 136.4, 135.3, 133.9, 127.9, 124.0, 123.6, 122.9, 122.2, 112.3, 108.7, 51.2; ^{19}F NMR (376 MHz, acetone-d_6) δ −141.12; ^{11}B NMR (128 MHz, acetone-d_6) δ 3.49; FT-IR (ATR): 3036, 2947, 1687, 1601, 1533, 1456, 1202, 1111, 952, 832, 776, 746 cm^{-1}; ESIMS: *m/z* calcd for $C_{13}H_{15}BF_3O_2$ [M-K$^+$]$^-$ 318.09, found 318.11.

General Procedure II (Suzuki-Miyaura Cross-Coupling Reactions, Table 3). To a solution of potassium 4-(1*H*-pyrazol-1-yl)phenyltrifluoroborate (0.3 mmol), Cs_2CO_3 (0.9 mmol), Pd(TPP)$_4$ (5 × 10^{-3} mmol, 5 mol %) in methanol (2 mL) was added aryl bromide (0.33 mmol). The reaction was conducted at 80 ºC. After the reaction was finished, water (5 mL) was added and organic layer was extracted with EtOAc (5 mL × 3). The crude product was purified by column chromatography to give pure product.

1-(Biphenyl-4-yl)-1*H*-pyrazole (2a). White solid; mp 124 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (brs, 1H), 7.78 (d, 2H, J = 8.8 Hz), 7.77 (s, 1H), 7.68 (d, 2H, J = 8.4 Hz), 7.62 (d, 2H, J = 8.4 Hz), 7.46 (t, 2H, J = 7.6 Hz), 7.37 (t, 1H, J = 7.4 Hz), 6.51 (brs, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 141.2, 140.1, 139.4, 139.4, 128.9, 128.1, 127.5, 127.0, 127.0, 119.5, 107.7; FT-IR (ATR): 3130, 3107, 2923, 2853, 1607, 1528, 1484, 1393, 1332, 938, 834, 760, 698 cm^{-1}; ESIMS: *m/z* calcd for $C_{15}H_{13}N_2$ [M+H]$^+$ 221.10, found 221.10.

1-(4'-Methylbiphenyl-4-yl)-1*H*-pyrazole (2b). White solid; mp 155 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.76 (d, 2H, J = 8.0 Hz), 7.75 (s, 1H), 7.67 (d, 2H, J = 8.4 Hz), 7.52 (d, 2H, J = 8.0 Hz), 7.27 (d, 2H, J = 8.0 Hz), 6.50 (s, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 139.3, 139.2, 137.3, 129.6, 128.1, 127.8, 126.8, 126.5, 119.5, 107.7, 21.1; FT-IR (ATR): 3110, 3033, 2915, 2856, 1610, 1515, 1497, 1393, 1050, 937, 805, 744 cm^{-1}; ESIMS: *m/z* calcd for $C_{16}H_{15}N_2$ [M+H]$^+$ 235.12, found 235.10.

1-(4'-(Trifluoromethyl)biphenyl-4-yl)-1*H*-pyrazole (2c). White solid; mp 189 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.82 (d, 2H, J = 8.0 Hz), 7.76 (s, 1H), 7.69 (m, 6H), 6.51 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 141.6, 140.2, 137.9, 129.7 (q, J = 32.0 Hz), 128.4, 127.4, 126.9, 126.0 (q, J = 3.7 Hz), 124.4 (q, J = 270.0 Hz), 119.7. 108.1; FT-IR (ATR): 3136, 2923, 1606, 1392, 1328, 1165, 1108, 1075, 1047, 935, 813, 753, 742, 669 cm^{-1}; ESIMS: *m/z* calcd for $C_{16}H_{12}F_3N_2$ [M+H]$^+$ 289.09, found 289.10.

4'-(1*H*-Pyrazol-1-yl)biphenyl-4-carbonitrile (2d). White solid; mp 183 ºC; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, 1H), 8.02 (d, 2H, J = 8.8 Hz), 7.95 (d, 2H, J = 8.4 Hz), 7.84 (m, 4H), 7.76 (s, 1H), 6.57 (t, 1H, J = 4.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 141.6, 140.4, 137.1, 132.7, 128.3, 127.5, 126.8, 119.5, 118.9, 111.1, 108.2; FT-IR (ATR): 3150, 3134, 3053, 2923, 2852, 2225, 1604, 1526, 1493, 1435, 1388, 1333, 1034, 931, 818, 749, 736 cm^{-1}; ESIMS: *m/z* calcd for $C_{16}H_{12}N_3$ [M+H]$^+$ 246.10, found 246.10.

1-(3-(Benzo[*d*][1,3]dioxol-5-yl)phenyl)-1*H*-pyrazole (2e).

White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.87 (s, 1H), 7.74 (s, 1H), 7.61 (d, 1H, J = 7.6 Hz), 7.51-7.41 (m, 2H), 7.12 (s, 2H), 6.89 (d, 1H, J = 8.4 Hz), 6.49 (s, 1H), 6.02 (d, 2H, J = 1.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.2, 147.5, 142.4, 141.2, 140.6, 134.7, 129.8, 126.9, 124.9, 120.9, 117.9, 117.6, 108.6, 107.7, 101.3, 29.7; FT-IR (ATR): 2924, 2853, 2359, 2341, 1586, 1519, 1506, 1468, 1242, 1222, 1040, 945, 786 cm^{-1}; ESIMS: *m/z* calcd for $C_{16}H_{13}N_2O_2$ $[M+H]^+$ 265.09, found 265.20.

(3-Methoxy-3'-(1*H*-pyrazol-1-yl)biphenyl-4-yl)methanol (2f). White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.97 (s, 1H), 7.79 (s, 1H), 7.70-6.65 (m, 1H), 7.58-7.51 (m, 2H), 7.39 (d, 1H, J = 7.6 Hz), 7.25 (dd, 1H, J = 7.6 Hz, 1.2 Hz), 7.16 (s, 1H), 6.53 (t, 1H, J = 2.0 Hz), 4.77 (d, 2H, J = 5.2 Hz), 3.98 (s, 3H), 2.32 (t, 1H, J = 2.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 142.7, 141.6, 141.2, 140.5, 129.8, 129.1, 128.8, 126.9, 125.3, 119.7, 118.2, 118.1, 109.3, 107.7, 61.9, 55.5; FT-IR (ATR): 3386, 2925, 2854, 2360, 2342, 1605, 1572, 1518, 1397, 1218, 1083, 1044, 947, 787, 747 cm^{-1}; ESIMS: *m/z* calcd for $C_{17}H_{17}N_2O_2$ $[M+H]^+$ 281.12, found 281.20.

4,4'-Di(1*H*-pyrazol-1-yl)biphenyl (3). To a solution of potassium 4-(1*H*-pyrazol-1-yl)phenyltrifluoroborate (75.0 mg, 0.3 mmol), Cs_2CO_3 (293.2 mg, 0.9 mmol) and $Pd(TPP)_4$ (17.3 mg, 5 × 10^{-3} mmol, 5 mol %) was added dry methanol (2 mL). The reaction was conducted at 80 °C. After 1 h, the solvent was removed under vacuum. After the reaction was finished, water (5 mL) was added and organic layer was extracted with EtOAc (5 mL × 3). The crude product was purified by column chromatography to give pure product (77.3 mg, a white solid) in 90% yield; mp 249.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 2H), 7.79 (d, 4H, J = 8.0 Hz), 7.76 (s, 2H), 7.71 (d, 4H, J = 8.0 Hz), 6.50 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2, 139.5, 138.2, 127.9, 126.7, 119.5, 107.8; FT-IR (ATR): 3135, 3119, 1608, 1518, 1498, 1390, 1332, 1049, 935, 814, 760, 744 cm^{-1}; ESIMS: *m/z* calcd for $C_{18}H_{15}N_4$ $[M+H]^+$ 287.12, found 287.10.

1-(4-Iodophenyl)-1*H*-pyrazole (4). To a solution of potassium 4-(1*H*-pyrazol-1-yl)phenyltrifluoroborate (75.0 mg, 0.3 mmol) in THF and H_2O (1 mL, respectively) were added NaI (45.0 mg, 0.3 mmol) and Chloroamine-T (84.5 mg, 0.3 mmol). The reaction mixture was stirred at rt for 1 h. The aqueous layer was extracted with EtOAc (5 mL × 3). The EtOAc layer was dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography to give pure product (72.9 mg, a white solid) in 90% yield; mp 89.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.76 (d, 2H, J = 8.8 Hz), 7.73 (s, 1H), 7.46 (d, 2H, J = 8.4 Hz), 6.48 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.4, 139.9, 138.4, 126.6, 120.8, 108.1, 90.5; FT-IR (ATR): 3149, 3087, 2923, 2852, 1585, 1517, 1487, 1396, 1386, 1334, 1307, 1248, 1197, 1121, 1000, 808, 744 cm^{-1}; ESIMS: *m/z* calcd for $C_9H_8IN_2$ $[M+H]^+$ 270.97, found 271.10.

4-(1*H*-Pyrazol-1-yl)phenol (5). To a solution of potassium 4-(1*H*-pyrazol-1-yl)phenyltrifluoroborate (75.0 mg, 0.3 mmol) in acetone and H_2O (0.5 mL, respectively) was added Oxane (184.4 mg, 0.3 mmol). The reaction mixture was stirred at rt for 5 min. The aqueous layer was extracted with EtOAc (5 mL × 3). The EtOAc layer was dried (Na_2SO_4) and concentrated. The crude product was purified by column chromatography to give pure product (47.1 mg, pale yellow oil) in 98% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.71 (s, 1H), 7.44 (d, 2H, J = 8.8 Hz), 6.83 (d, 2H, J = 8.4 Hz), 6.45 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.4, 140.5, 133.3, 127.7, 121.8, 116.2, 107.2; FT-IR (ATR): 3425, 2922, 2359, 1600, 1524, 1462, 1402, 1274, 1123, 1083, 833, 755 cm^{-1}; ESIMS: *m/z* calcd for $C_9H_9N_2O$ $[M+H]^+$ 161.06, found 161.06.

Acknowledgments. This research was supported by the KIST Institutional Program, Republic of Korea. This work was also supported by the Ewha Womans University Research Grant of 2012. We are grate to Professor Gary A. Molander (University of Pennsylvania) for his scientific advice.

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