Supplementary Material (ESI) for Chemical Communications

Copper-Catalyzed Arene C-H Bond Cross-Coupling

SUPPORTING INFORMATION

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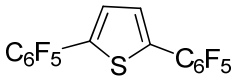
Experimental Section

General considerations. Reactions were performed in 1-dram vials with PTFE/Liner caps (from SUPELCO). Flash chromatography was performed on 60Å silica gel (Sorbent Technologies). Purification by preparative HPLC was performed on a Shimadzu Prominence LC (LC-20AB) equipped with a SPD-20A UV-Vis detector and a Varian Dynamax (250 mm x 21.4 mm) column. GC-MS analyses were performed on a Shimadzu GCMS-QP5000 chromatograph equipped with a Restek column (Rtx-XLB, 30 m x 0.25 mm I.D.). The ^{1}H, and ^{19}F NMR were recorded on a GE QE-300 spectrometer using residual solvent peak as a reference. Hexafluorobenzene (1% in C_6D_6, δ = -164.9) was employed as an external standard in ^{19}F NMR spectra. ^{13}C NMR was recorded on a JEOL ECX-400 spectrometer using residual solvent peak as a reference. Elemental analyses were performed by Atlantic Microlab Inc. of Norcross, GA. IR spectra were obtained using ThermoNicolet Avatar 370 FT-IR instrument. Analytical thin layer chromatography was performed on silica gel IB-F (Baker-flex) by J. T. Baker.

Materials. The following starting materials were obtained from commercial sources and were used without further purification: pentafluorobenzene, 2,3-dihydrobenzofuran, and 2-bromothiophene were bought from Oakwood. Anisole, diphenyl ether, *t*-butylbenzene, 1-methylindole, copper(I) iodide, and anhydrous potassium phosphate were obtained from Acros. 1,3-Dinitrobenzene, *m*-xylene, 3,5-dichloropyridine, and *N*,*N*-dimethylaniline were purchased from Aldrich. Azulene, 3,3-dimethyl-1-butyne, 1-methylpyrazole, 2-chlorothiophene, 1-methoxynaphthalene, and iodine monochloride were from Alfa Aesar. 2-Methylthiophene, 2,3,5,6-tetrafluoroanisole, 3,5-difluorobenzonitrile, 1,2,4,5-tetrafluorobenzene, 1-methyl-1,2,4-triazole, 2,3,5,6-tetrafluoropyridine, and 2,3,5,6-tetrafluorotoluene were obtained from Matrix Scientific. Lithium *t*-butoxide was bought from Strem. Iodine was from EM Science. *N*,*N*-Dimethylformamide and dichloromethane were purchased from Mallinckrodt Chemicals.

General procedure: A 15 mL recovery flask was equipped with a magnetic stir bar was charged with iodine (25.4 mg, 0.1 mmol), DCM/DMF mixture, and ICl. The flask was fitted with a reflux condenser. To the stirred mixture was **quickly added in one portion** the first substrate through the condenser. The reaction mixture was stirred at 50^{o}C (bath temperature) for 2.5 hours followed by CH_2Cl_2 removal under reduced pressure. In most cases, *N*,*N*-

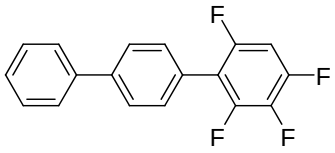
dimethylaniline (121 mg, 1.0 mmol) was added followed by stirring for another 30 minutes. Commercial, non-anhydrous DMF (0.6 mL) was added to reaction mixture followed by transfer to a 1 dram vial. It is important to use the specified vial caps due to volatility of some reactants. Phenanthroline (18.0 mg, 0.1 mmol) and the second substrate (1.0-3.0 mmol) were subsequently added. The vial was flushed with argon, capped and placed inside a glovebox. To this mixture was added CuI (19 mg, 0.1 mmol) and base. The sealed vial was taken out of the glovebox, stirred at 50 ^{o}C for 5 min and placed in a preheated oil bath (125-135 ^{o}C) for indicated time. The reaction mixture was allowed to cool to room temperature and diluted with ethyl acetate (50 mL). The resulting solution was washed with brine (1 x 15 mL), dried over anhydrous $MgSO_4$, and concentrated under vacuum to a volume of about 2 mL. The mixture containing the product was subjected to flash chromatography on silica gel (hexanes followed by appropriate solvent to elute the products). After concentrating the fractions containing the product, the residue was dried under reduced pressure.



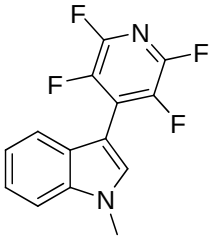
2,5-Diperfluorophenylthiophene (Entry 1, Table 1, large scale reaction, 10 mmol) :

A 25 mL Schlenk flask was equipped with a magnetic stir bar was charged with iodine (254 mg, 1 mmol), DCM/DMF mixture (8/2, 2 mL), ICl (1970 mg, 12 mmol). The flask was fitted with a reflux condenser. To the stirred mixture was **quickly added in one portion** 2-bromothiophene (1630 mg, 10.0 mmol). The reaction mixture was stirred at 50^{o}C for 2.5 hours following by CH_2Cl_2 removal under reduced pressure. The residue was dissolved in DMF/*m*-xylene (1/1, 7 mL) and transfered to a 100 mL Kontes flask. Subsequently, phenanthroline (180 mg, 1 mmol) and pentafluorobenzene (5880 mg, 35 mmol) were added. The flask was flushed with argon, capped and placed inside a glovebox. To this mixture was added CuI (191 mg, 1 mmol) and K_3PO_4 (8480 mg, 40 mmol). The sealed flask was taken out of the glovebox, stirred at 50 ^{o}C for 5 min and placed in a preheated oil bath (130 ^{o}C) for 24 hours. The reaction mixture was allowed to cool to room temperature and diluted with ethyl acetate (300 mL). The resulting solution was washed with brine (1 x 50 mL), dried over anhydrous $MgSO_4$, and concentrated under vacuum. The mixture was subjected to flash chromatography on silica gel. After column chromatography (hexanes) 1620 mg (63%) of a colorless solid was obtained. R_f = 0.44 (SiO_2, hexanes). This compound is known.[1] ^{1}H NMR

(300 MHz, $CDCl_3$) δ 7.60 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 109.2 (dt, J_{C-F} = 15.3 Hz, 4.1 Hz;), 129.3, 130.3 (t, J_{C-F} = 5.2 Hz), 136.6-139.8 (m), 138.8-142.0 (m), 142.7-145.7 (m).

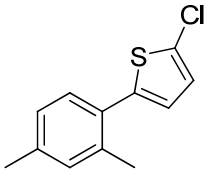


2,3,4,6-Tetrafluoro-4'-phenylbiphenyl (Entry 2, Table 1): Iodine (25 mg, 0.1 mmol), DCM/DMF (9.5/0.5, 0.2 mL), iodine monochloride (164 mg, 1.0 mmol), biphenyl (231 mg, 1.5 mmol in 0.3 mL DCM), 50 ^oC, 2.5 hours then *N*,*N*-dimethylaniline (121 mg, 1.0 mmol), DMF (0.6 mL), 1,10-phenanthroline (18 mg, 0.1 mmol), 1,2,3,5-tetrafluorobenzene (300 mg, 2.0 mmol), copper(I) iodide (19 mg, 0.1 mmol), K_3PO_4 (488 mg, 2.3 mmol), 130 ^oC, 24 hours. After column chromatography (hexanes, then 2% ethyl acetate in hexanes) 135 mg (45%) of a colorless solid was obtained. R_f = 0.27 (SiO_2, hexanes). This compound is known.[2] ^1H NMR (300 MHz, $CDCl_3$) δ 6.83-6.95 (m, 1H; C_6F_4**H**), 7.34-7.55 (m, 5H), 7.60-7.74 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 101.1 (ddd, J_{C-F} = 29.7 Hz, 20.9 Hz, 3.8 Hz), 115.5-116.1 (m, 1C), 126.5, 127.3, 127.4, 127.8, 129.0, 130.7, 137.6 (dtd, J_{C-F} = 246.4 Hz, 31.3 Hz, 4.7 Hz), 140.4, 141.8, 147.4-150.5 (m), 148.2-151.3 (m), 152.8-155.8 (m).

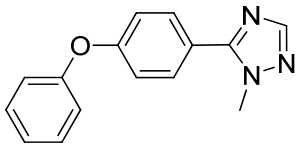


1-Methyl-3-(perfluoropyridin-4-yl)-1H-indole (Entry 3, Table 1): Outside the glovebox a 1-dram vial equipped with a magnetic stir bar was charged with iodine (25.4 mg, 0.1 mmol), DMF (0.5 mL), iodine monochloride (164 mg, 1.0 mmol), and 1-methylindole (201 mg, 1.5 mmol). The vial was flushed with argon, capped and placed inside a glovebox. To this mixture was added K_3PO_4 (742 mg, 3.5 mmol). The reaction mixture was stirred at 70 ^oC for 2.5 hours then 1,10-phenanthroline (18 mg, 0.1 mmol), 2,3,5,6-tetrafluoropyridine (302 mg, 2.0 mmol), and copper(I) iodide (19 mg, 0.1 mmol) were added. The sealed vial was taken out of the glovebox, stirred at 50 ^oC for 5 min and placed in a preheated oil bath (130 ^oC) for 24 hours. Workup and isolation of product was performed as described in general procedure. After column chromatography (hexanes, then 20% ethyl acetate in hexanes) 200 mg (71%) of

a colorless solid was obtained. R_f = 0.26 (SiO_2, 1/9 ethyl acetate/hexanes), mp 172-175 ^oC (from AcOEt/hexanes 1/9). ^1H NMR (300 MHz, $CDCl_3$) δ 3.93 (s, 3H; N-C**H**$_3$), 7.26-7.47 (m, 3H), 7.53-7.57 (m, 1H; C**H**-indole), 7.63-7.70 (m, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -145.9- -145.5 (m, 2F), -95.5- -95.2 (m, 2F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.5, 100.5, 109.9, 120.9 (t, J_{C-F} = 5.2 Hz), 121.3, 122.9, 125.7, 128.4 (t, J_{C-F} = 15.7 Hz), 131.9 (t, J_{C-F} = 3.8 Hz), 137.0, 137.2-140.4 (m), 142.7-145.6 (m). FT-IR (neat, cm^{-1}) υ 1641, 1540, 1481, 1452, 1187, 1139, 1067, 1022. Anal calcd for $C_{14}H_8F_4N_2$ (280.22 g/mol): C, 60.01; H, 2.88; N, 10.00; Found. C, 60.19; H, 2.67; N, 10.00.

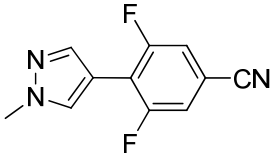


2-Chloro-5-(2,4-dimethylphenyl)thiophene (Entry 4, Table 1): Iodine (25 mg, 0.1 mmol), DCM/DMF (9.5/0.5, 0.2 mL), iodine monochloride (164 mg, 1.0 mmol), *m*-xylene (212 mg, 2.0 mmol), 50 ^oC, 2.5 hours; then *N*,*N*-dimethylaniline (121 mg, 1.0 mmol), DMF (0.6 mL), 1,10-phenanthroline (18 mg, 0.1 mmol), 2-chlorothiophene (237 mg, 2.0 mmol), copper(I) iodide (19 mg, 0.1 mmol), *t*BuOLi (160 mg, 2.0 mmol), 130 ^oC, 24 hours. After column chromatography (hexanes) 155 mg (70%) of an isomer mixture (12/1) was obtained. Pure major isomer (140 mg, 63%) can be obtained as a colorless oil by preparative HPLC (hexanes). R_f = 0.47 (SiO_2, hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 2.35 (s, 3H), 2.39 (s, 3H), 6.79 (d, *J* = 4.5 Hz, 1H), 6.89 (d, *J* = 3.8 Hz, 1H), 7.01-7.11 (m, 2H), 7.24 (d, *J* = 7.7 Hz, 1H; xylene C**H** *ortho* to thiophene). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 21.1, 125.4, 126.1, 126.7, 128.9, 130.2, 130.5, 131.6, 135.9, 138.1, 141.9. FT-IR (neat, cm^{-1}) υ 1496, 1446, 1066, 1003. Anal calcd for $C_{12}H_{11}ClS$ (222.73 g/mol): C, 64.71; H, 4.98; Found. C, 64.69; H, 4.93.



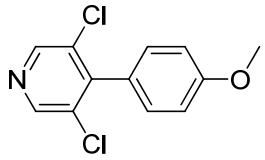
1-Methyl-5-(4-phenoxyphenyl)-1H-1,2,4-triazole (Entry 5, Table 1): Iodine (25 mg, 0.1 mmol), DCM/DMF (9.5/0.5, 0.2 mL), iodine monochloride (164 mg, 1.0 mmol), diphenyl ether (340 mg, 2.0 mmol), 50 ^oC, 2.5 hours; then *N*,*N*-dimethylaniline (121 mg, 1.0 mmol),

DMF (0.6 mL), 1,10-phenanthroline (18 mg, 0.1 mmol), 1-methyl-1,2,4-triazole (166 mg, 2.0 mmol), copper(I) iodide (19 mg, 0.1 mmol), *t*BuOLi (200 mg, 2.5 mmol), 130 ^{o}C, 20 hours. After column chromatography (hexanes, then 30% hexanes in ethyl acetate) and preparative HPLC (30% hexanes in ethyl acetate) 140 mg (56%) of a colorless solid was obtained. R_f = 0.21 (SiO_2, 1/1 ethyl acetate/hexanes), mp 78-80 ^{o}C (from AcOEt/hexanes 2/8). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.00 (s, 3H; N-C**H**$_3$), 7.04-7.21 (m, 5H), 7.35-7.43 (m, 2H), 7.61-7.67 (m, 2H), 7.92 (s, 1H; triazole C**H**). ^{13}C NMR (100 MHz, $CDCl_3$) δ 37.0, 118.3, 119.8, 122.2, 124.3, 130.0, 130.3, 150.6, 154.2, 156.0, 159.3. FT-IR (neat, cm^{-1}) υ 1589, 1487, 1286, 1244, 1169, 1002. Anal calcd for $C_{15}H_{13}N_3O$ (251.28 g/mol): C, 71.70; H, 5.21; N, 16.72; Found. C, 71.11; H, 5.18; N, 16.59.

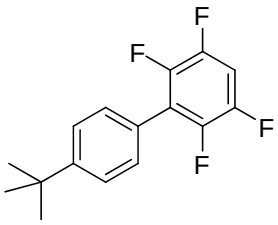


3,5-Difluoro-2-(1-methyl-1H-pyrazol-4-yl)benzonitrile (Entry 6, Table 1): Outside the glovebox a 1-dram vial equipped with a magnetic stir bar was charged with iodine (25.4 mg, 0.1 mmol), DMF (0.25 mL), iodine monochloride (247 mg, 1.5 mmol), and 1-methypyrazole (82 mg, 1.0 mmol). The vial was flushed with argon, capped and placed inside a glovebox. To this mixture was added K_3PO_4 (318 mg, 1.5 mmol). The reaction mixture was stirred at 70 ^{o}C for 2.5 hours followed by addition of DMF (0.3 mL), 1,10-phenanthroline (18 mg, 0.1 mmol), 3,5-difluorobenzonitrile (278 mg, 2.0 mmol), K_3PO_4 (530 mg, 2.5 mmol), and copper(I) iodide (19 mg, 0.1 mmol). The sealed vial was taken out of the glovebox, stirred at 50 ^{o}C for 5 min and placed in a preheated oil bath (130 ^{o}C) for 24 hours. Workup and isolation of product were performed as described in general procedure. After column chromatography (hexanes, then 40% ethyl acetate in hexanes) 130 mg (59%) of a light tan solid was obtained. R_f = 0.36 (SiO_2, 1/1 ethyl acetate/hexanes), mp 147-150 ^{o}C (from AcOEt/hexanes 1/9). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.98 (s, 3H; N-C**H**$_3$), 7.20-7.31 (m, 2H; phenyl C**H**), 7.93-7.96 (m, 1H), 8.00-8.04 (m, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -110.0 (d, J_F = 7.0 Hz, 2F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.3, 108.7, 109.2 (t, $J_{C\text{-}F}$ = 12.4 Hz), 115.6-116.1 (m, 1C) 116.3 (t, $J_{C\text{-}F}$ = 17.2 Hz), 116.9 (t, $J_{C\text{-}F}$ = 3.5 Hz), 131.2 (t, $J_{C\text{-}F}$ = 7.6 Hz), 140.0 (t, $J_{C\text{-}F}$ = 7.6 Hz), 159.2 (dd, $J_{C\text{-}F}$ = 250.1 Hz, 9.5 Hz). FT-IR (neat, cm^{-1}) υ 2229, 1558, 1429, 1318, 1251, 1189, 1070, 1024. Anal calcd for $C_{11}H_7F_2N_3$ (219.19 g/mol): C, 60.28; H,

3.22; N, 19.17; Found. C, 60.28; H, 3.09; N, 18.97. The connectivity was verified by X-ray crystallography analysis; however, structure was not fully refined.

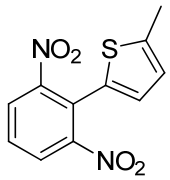


3,5-Dichloro-4-(4-methoxyphenyl)pyridine (Entry 7, Table 1): Iodine (25 mg, 0.1 mmol), DCM/DMF (9/1, 0.2 mL), iodine monochloride (164 mg, 1.0 mmol), anisole (216 mg, 2.0 mmol), 50 ^{o}C, 2.5 hours; then *N*,*N*-dimethylaniline (121 mg, 1.0 mmol), DMF (0.6 mL), 1,10-phenanthroline (18 mg, 0.1 mmol), 3,5-dichloropyridine (222 mg, 1.5 mmol), copper(I) iodide (19 mg, 0.1 mmol), *t*BuOLi (160 mg, 2.0 mmol), 130 ^{o}C, 24 hours. After column chromatography (hexanes, then 15% ethyl acetate in hexanes) 140 mg (55%) of an isomer mixture (12/1) was obtained. Pure major isomer (125 mg, 49%) can be obtained as a colorless solid by preparative HPLC (10% ethyl acetate in hexanes). R_f = 0.33 (SiO_2, 1/9 ethyl acetate/hexanes), mp 52-54 ^{o}C (from hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.86 (s, 3H; OC**H**$_3$), 6.98-7.04 (m, 2H), 7.19-7.24 (m, 2H), 8.55 (s, 2H; pyridine C**H**). ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.4, 114.0, 126.0, 130.5, 132.4, 146.4, 147.8, 160.1. FT-IR (neat, cm^{-1}) υ 1610, 1516, 1438, 1392, 1297, 1255, 1213, 1184, 1040. Anal calcd for $C_{12}H_9Cl_2NO$ (254.11 g/mol): C, 56.72; H, 3.57; N, 5.51; Found. C, 56.80; H, 3.45; N, 5.48.

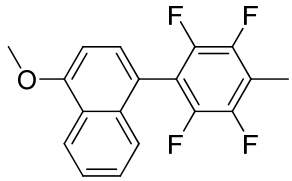


4'-*tert*-Butyl-2,3,5,6-tetrafluorobiphenyl (Entry 8, Table 1): Iodine (25 mg, 0.1 mmol), DCM/DMF (9/1, 0.2 mL), iodine monochloride (247 mg, 1.5 mmol), *t*-butylbenzene (134 mg, 1.0 mmol), 50 ^{o}C, 2.5 hours; then DMF (0.6 mL), *N*,*N*-dimethylaniline (121 mg, 1.0 mmol), 1,10-phenanthroline (18 mg, 0.1 mmol), 1,2,4,5-tetrafluorobenzene (450 mg, 3.0 mmol), copper(I) iodide (19 mg, 0.1 mmol), K_3PO_4 (636 mg, 3.0 mmol), 130 ^{o}C, 24 hours. After column chromatography (hexanes) 180 mg (64%) of an isomer mixture (32/1) was obtained. Pure major isomer (160 mg, 57%) can be obtained as a colorless solid by preparative HPLC (hexanes). R_f = 0.40 (SiO_2, hexanes), mp 84-86 ^{o}C (from hexanes). ^{1}H

NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 9H; C(C**H**$_3$)$_3$), 6.98-7.12 (m, 1H; C_6F_4**H**), 7.41 (d, J = 8.0 Hz, 2H), 7.52 (d, J = 8.0 Hz, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -147.2- -146.9 (m, 2F), -142.5- -142.3 (m, 2F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 31.2, 34.8, 104.5 (t, J_{C-F} = 22.4 Hz), 121.4 (t, J_{C-F} = 16.2 Hz), 124.5, 125.6, 129.8, 142.4-145.2 (m), 144.7-147.7 (m), 152.3. FT-IR (neat, cm^{-1}) υ 2968, 1503, 1492, 1173, 1159. Anal calcd for $C_{16}H_{14}F_4$ (282.28 g/mol): C, 68.08; H, 5.00; Found. C, 68.00; H, 4.95.

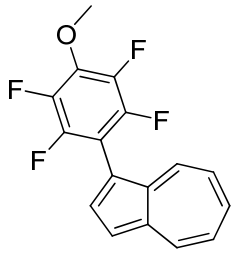


2-(2,6-dinitrophenyl)-5-methylthiophene (Entry 9, Table 1): Iodine (25 mg, 0.1 mmol), DCM/DMF (9.5/0.5, 0.2 mL), iodine monochloride (246 mg, 1.5 mmol), 2-methylthiophene (245 mg, 2.5 mmol), 50 ^{o}C, 2.5 hours; then *N*,*N*-dimethylaniline (121 mg, 1.0 mmol), DMF (0.6 mL), 1,10-phenanthroline (18 mg, 0.1 mmol), 1,3-dinitrobenzene (168 mg, 1.0 mmol), copper(I) iodide (19 mg, 0.1 mmol), K_3PO_4 (636 mg, 3.0 mmol), 125 ^{o}C, 20 hours. After column chromatography (hexanes, then 25% ethyl acetate in hexanes) and preparative HPLC (25% ethyl acetate in hexanes) 135 mg (51%) of a yellow solid was obtained. R_f = 0.57 (SiO_2, 1/1 ethyl acetate/hexanes), mp 94-95 ^{o}C (from AcOEt/hexanes 1/9). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.50 (s, 3H; C**H**$_3$), 6.72-6.75 (m, 1H; thiophene C**H** *ortho* to CH_3), 6.86 (d, J = 3.3 Hz, 1H; thiophene C**H** *ortho* to dinitroaryl), 7.62-7.70 (m, 1H; C**H** *meta* to nitro), 7.88-7.94 (m, 2H; C**H** *ortho* to nitro). ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.3, 123.3, 125.8, 125.9, 126.1, 129.7, 129.8, 144.2, 151.5. FT-IR (neat, cm^{-1}) υ 1536, 1356. Anal calcd for $C_{11}H_8N_2O_4S$ (264.26 g/mol): C, 50.00; H, 3.05; N, 10.60; Found. C, 49.93; H, 2.94; N, 10.45.



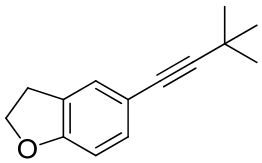
1-Methoxy-4-(2,3,5,6-tetrafluoro-4-methylphenyl)naphthalene (Entry 10, Table 1): Iodine (25 mg, 0.1 mmol), DCM/DMF (9/1, 0.4 mL), iodine monochloride (197 mg, 1.2 mmol), 1-methoxynaphthalene (158 mg, 1.0 mmol), 50 ^{o}C, 2.5 hours; then *N*,*N*-dimethylaniline (121 mg, 1.0 mmol), DMF (0.6 mL), 1,10-phenanthroline (18 mg, 0.1

mmol), 2,3,5,6-tetrafluorotoluene (410 mg, 2.5 mmol), copper(I) iodide (19 mg, 0.1 mmol), K_3PO_4 (636 mg, 3.0 mmol), 130 ^oC, 24 hours. After column chromatography (hexanes, then 5% ethyl acetate in hexanes) and preparative HPLC (3% ethyl acetate in hexanes) 230 mg (72%) of a colorless solid was obtained. R_f = 0.47 (SiO_2, 1/9 ethyl acetate/hexanes), mp 145-147 ^oC (from hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 2.38 (t, J = 2.0 Hz, 3H; $C_6F_4C\mathbf{H}_3$), 4.05 (s, 3H; $OC\mathbf{H}_3$), 6.91 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 8.0 Hz, 1H), 7.46-7.57 (m, 3H), 8.35-8.40 (m, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -147.2- -147.0 (m, 2F), -145.0- -144.8 (m, 2F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.7, 55.6, 103.3, 115.4 (t, J_{C-F} = 19.1 Hz), 116.6 (t, J_{C-F} = 19.6 Hz), 117.1, 122.5, 124.7, 125.5, 125.7, 127.2, 129.1, 132.5, 142.8-145.7 (m), 143.7-146.6 (m), 156.5. FT-IR (neat, cm^{-1}) υ 1583, 1479, 1462, 1374, 1299, 1216, 1097, 1066. Anal calcd for $C_{18}H_{12}F_4O$ (320.28 g/mol): C, 67.50; H, 3.78; Found. C, 67.26; H, 3.60.



1-(2,3,5,6-Tetrafluoro-4-methoxyphenyl)azulene (Entry 11, Table 1): Outside the glovebox a 1-dram vial equipped with a magnetic stir bar was charged with azulene (128, 1 mmol) and DMF (0.3 mL). To the stirred mixture was added a solution of iodine monochloride (197 mg, 1.2 mmol) in DMF (0.3 mL). The resulting mixture was stirred at 50 ^oC for 1 hour followed by the addition of 1,10-phenanthroline (18 mg, 0.1 mmol) and 2,3,5,6-tetrafluoroanisole (540 mg, 3.0 mmol). The vial was flushed with argon, capped and placed inside a glovebox. To this mixture was added copper(I) iodide (19 mg, 0.1 mmol) and K_3PO_4 (636 mg, 3.0 mmol). The sealed vial was taken out of the glovebox, stirred at 50 ^oC for 5 min and placed in a preheated oil bath (135 ^oC) for 24 hours. Workup and isolation of product were performed as described in general procedure. After column chromatography (hexanes, then 10% ethyl acetate in hexanes) 160 mg (52%) of a dark blue solid was obtained. R_f = 0.44 (SiO_2, 1/9 ethyl acetate/hexanes), mp 104-106 ^oC (from hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 4.15 (s, 3H; $OC\mathbf{H}_3$), 7.22-7.35 (m, 2H), 7.50 (d, J = 4.5 Hz, 1H), 7.69 (t, J = 10.0 Hz, 1H), 7.95 (d, J = 4.5 Hz, 1H), 8.11 (d, J = 10.0 Hz, 1H), 8.43 (d, J = 9.4 Hz, 1H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -161.5- -161.3 (m, 2F), -144.9- -144.7 (m, 2F). ^{13}C

NMR (100 MHz, $CDCl_3$) δ 62.3 (t, J_{C-F} = 3.3 Hz), 110.4 (t, J_{C-F} = 19.0 Hz), 114.2, 118.0, 124.1, 124.4, 135.4, 136.7, 137.1 (t, J_{C-F} = 12.0 Hz), 137.5, 138.4, 138.6, 139.9-142.8 (m), 142.0, 143.1-146.0 (m). FT-IR (neat, cm^{-1}) υ 1516, 1497, 1481, 1433, 1397, 1200, 1109. Anal calcd for $C_{17}H_{10}F_4O$ (306.25 g/mol): C, 66.67; H, 3.29; Found. C, 66.85; H, 3.29.



5-(3,3-Dimethylbut-1-ynyl)-2,3-dihydrobenzofuran (Entry 12, Table 1): Iodine (25 mg, 0.1 mmol), DCM/DMF (9/1, 0.3 mL), iodine monochloride (197 mg, 1.2 mmol), 2,3-dihydrobenzofuran (120 mg, 1.0 mmol), 50 ^oC, 1.5 hours; then DMF (0.6 mL), 1,10-phenanthroline (18 mg, 0.1 mmol), 3,3-dimethyl-1-butyne (205 mg, 2.5 mmol), copper(I) iodide (19 mg, 0.1 mmol), K_3PO_4 (636 mg, 3.0 mmol), 135 ^oC, 24 hours. After column chromatography (hexanes, then 10% ethyl acetate in hexanes) 180 mg (90%) of the isomer mixture (24/1) was obtained. Pure major isomer (160 mg, 80%) can be obtained as a colorless solid by preparative HPLC (2% ethyl acetate in hexanes). R_f = 0.52 (SiO_2, 1/9 ethyl acetate/hexanes), mp 75-76 ^oC (from hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 1.29 (s, 9H; $C(C\mathbf{H}_3)_3$), 3.16 (t, J = 8.8 Hz, 2H; benzylic $C\mathbf{H}_2$), 4.56 (t, J = 8.8 Hz, 2H; $OC\mathbf{H}_2$), 6.68 (d, J = 7.7 Hz, 1H; aryl C**H** *ortho* to O), 7.12-7.18 (m, 1H), 7.21-7.24 (m, 1H; aryl C**H** *ortho* to alkyne and alkyl). ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.0, 29.5, 31.3, 71.4, 79.1, 96.3, 109.2, 115.9, 127.1, 128.3, 131.9, 159.6. FT-IR (neat, cm^{-1}) υ 2965, 1608, 1491, 1477, 1455, 1236, 1100. Anal calcd for $C_{14}H_{16}O$ (200.28 g/mol): C, 83.96; H, 8.05; Found. C, 83.88; H, 8.01.

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(2) Do, H.-Q.; Khan, R. M. K.; Daugulis, O. *J Am Chem Soc* **2008**, *130*, 15185.