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Synthesis and Suzuki Cross-Coupling Reactions of 2,6-Bis(trifluoromethyl)pyridine-4-boronic Acid Pinacol Ester

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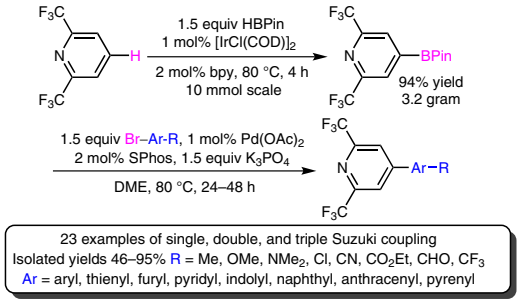

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Abstract Iridium-catalyzed aromatic borylation provides quick one-step access to 2,6-bis(trifluoromethyl)pyridine-4-boronic acid pinacol ester. Suzuki couplings of this highly electron-deficient pyridine-4-boronic ester with various (hetero)aryl bromides was successfully carried out and the coupled products were obtained in 46–95% isolated yields. Double and triple Suzuki couplings, with dibromo- and tribromoarenes, respectively, were also achieved. Thus demonstrating that this pyridine-4-boronic ester can be a useful source for the installation of one of the strongest electron-withdrawing aromatic group in organic compounds.

Key words iridium catalysis, C–H activation, borylation, boronic esters, Suzuki coupling, 2,6-bis(trifluoromethyl)pyridine, organic electronic materials

Organic compounds containing powerful electron-withdrawing (hetero)aromatic groups have important applications in various fields including organic electronics,[1] catalysis,[2] and sensors.[3] Aromatic rings can be decorated with various electron-withdrawing groups; however, recently fluorinated groups have become more common due to their increased stability and functional group compatibility. Important fluorinated electron-withdrawing aromatic groups include pentafluorophenyl, 4-(trifluoromethyl)phenyl, and 3,5-bis(trifluoromethyl)phenyl. Fluorinated tetraarylborates, such as 'BARF', behave as very weakly coordinating anions thereby enabling the formation of highly reactive cationic transition-metal complexes for various catalytic applications.[4] A frustrated Lewis pair consisting of tris[3,5-bis(trifluoromethyl)phenyl]borane and 2,2,6,6-tetramethylpiperidine has been reported to activate small molecules such as H_2.[5]

Taft's polar substituent constant, σ*, has been very useful in quantifying the electron-withdrawing capacity of various functional groups.[6] Taft's σ* values for 3,5-bis(trifluoromethyl)phenyl and pentafluorophenyl groups, which are currently widely used, are 1.18 and 1.50 respectively (Figure 1).[7] In comparison, the 2,6-bis(trifluoromethyl)pyridin-4-yl group, with a σ* value of 1.66, is the most powerful fluorinated electron-withdrawing aromatic group.[8] Recently, this functional group has been used to synthesize highly electron-deficient phosphine ligands.[8,9] However, 4-bromo-2,6-bis(trifluoromethyl)pyridine, which was employed for the incorporation of the 2,6-bis(trifluoromethyl)pyridin-4-yl group, requires a three-step synthesis from acyclic precursors. It will be advantageous to directly functionalize 2,6-bis(trifluoromethyl)pyridine for its utilization as a powerful electron-withdrawing group for the synthesis of organic materials. In particular, convenient synthesis of the 4-borylated derivative will be highly beneficial as the 4-arylpyridines[10] obtained after Suzuki coupling can have applications as materials for non-linear optics,[11] multi-photon absorption,[12] and biologically active molecules,[13] as well as replacing the 3,5-bis(trifluoromethyl)aryl group in known useful organic compounds.[14]

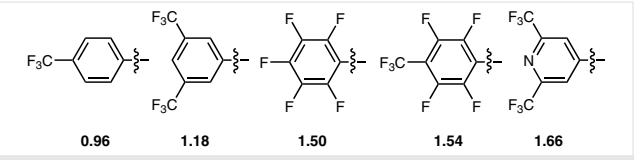
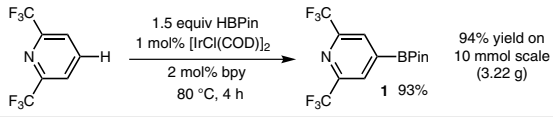


Figure 1 Taft's σ* values of selected fluorinated aromatic groups

Direct functionalization of the C–H bonds of 2,6-bis(trifluoromethyl)pyridine has remained a challenge. Despite being known for over fifty years, its chemistry has been mainly limited to *N*-oxide formation.[15] The highly electron-deficient nature of 2,6-bis(trifluoromethyl)pyridine precludes electrophilic aromatic substitution. Attempted di-

rected orthometalation using butyllithium gave a brown polymeric tar,[16] while controlled reaction with *tert*-butyllithium resulted in the nucleophilic addition of *t*-BuLi across the C–N bond of the pyridine ring, subsequently yielding the 1,2-dihydropyridine upon acidification. Very recently, Zheng et al. reported that 2,6-bis(trifluoromethyl)pyridine can be lithiated using LDA, however the lithiation was not selective, and resulted in a mixture of 3- and 4-lithiated products.[17] The lithiated intermediates were subsequently trapped with triisopropyl borate to yield the corresponding boronic acid mixture. The aforementioned limitations of the traditional functionalization methods have resulted in an under-utilization of this interesting group for its incorporation in organic materials, pharmaceuticals etc.

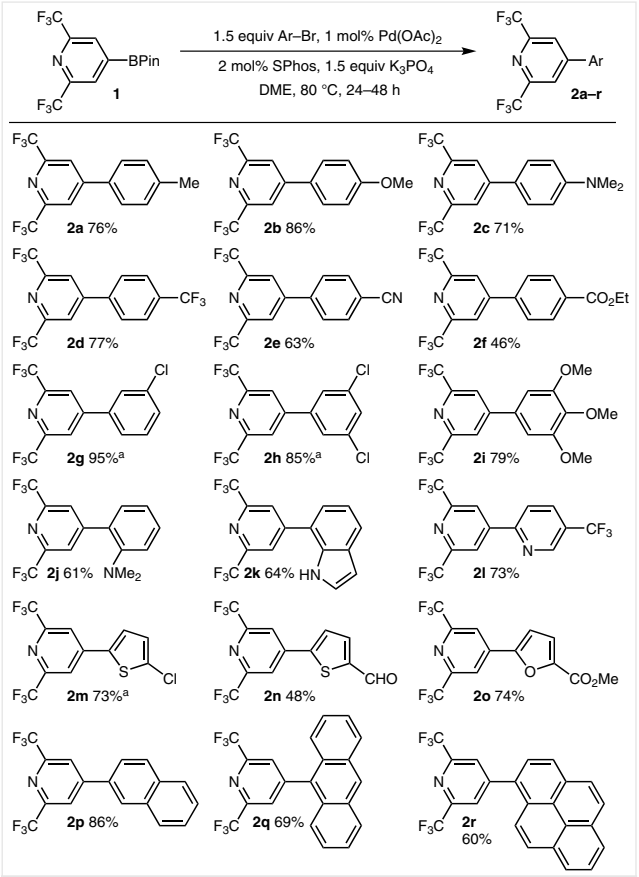
Apart from the traditional functionalization methods for aromatic compounds, the newly developed transition-metal-catalyzed C–H functionalizations provide alternative protocols. Specially, the iridium-catalyzed C–H borylation reaction, developed by the groups of Smith–Maleczka and Hartwig–Miyuara, has revolutionized the art of aromatic functionalization.[18] Generally sterics, not electronics, dictate the product regioselectivity in this new reaction. Interestingly, electron-deficient arenes react faster than electron-rich ones,[19] a characteristic useful for the functionalization of pyridines. This new methodology, when applied to 2,6-disubstituted pyridines, has been reported to yield 4-borylated pyridines as a single product.[18a,19a,20] We therefore decided to apply iridium-catalyzed C–H borylation to 2,6-bis(trifluoromethyl)pyridine, expecting it to yield a single 4-borylated product isomer (Scheme 1) which could potentially be a highly useful coupling agent for the Suzuki reaction.



Scheme 1 Iridium-catalyzed borylation of 2,6-bis(trifluoromethyl)pyridine

Catalytic borylation of 2,6-bis(trifluoromethyl)pyridine was attempted using the [IrCl(COD)]/bpy catalyst system,[18b] without employing a glovebox or Schlenk line.[21] We were pleased to observe that the borylation was complete in 4 hours at 80 °C, and the 4-borylated pyridine **1** was readily isolated in excellent yield by eluting the crude reaction mixture through a short silica plug using dichloromethane as a solvent. Isolated yield was reproducible (94%, 3.22 g) when the reaction was scaled-up to 10 mmol even though the catalyst loading was reduced to half. While our work was in progress, Lahm et al. also reported a similar route, employing high catalyst loading (10 mol% Ir/bpy), B_2Pin_2, and heptane solvent, for the preparation of 4-borylated 2,6-bis(trifluoromethyl)pyridine.[22] They coupled the 4-borylated product with a bromoalkene to synthesize a styrene derivative. Studies on the Suzuki coupling reactions of 2,6-bis(trifluoromethyl)pyridine-4-boronic acid pinacol ester with (hetero)aryl halides for the synthesis of biaryls are lacking. Herein, we describe the scope of Suzuki coupling reactions of this pyridine-4-boronic ester with various (hetero)aryl halides.

After synthesizing the 2,6-bis(trifluoromethyl)pyridine-4-boronic acid pinacol ester (**1**), a major concern was the feasibility of its use in the Suzuki coupling reaction, since the Suzuki coupling reaction of electron-deficient pyridineboronic esters has been known to be problematic.[13a] We were pleased to observe that this highly electron-deficient pyridineboronic ester easily underwent Suzuki couplings with (hetero)aryl bromides using Buchwald's $Pd(OAc)_2$/SPhos catalyst system[23] as well as by the $Pd(PPh_3)_4$ catalyst (Scheme 2).

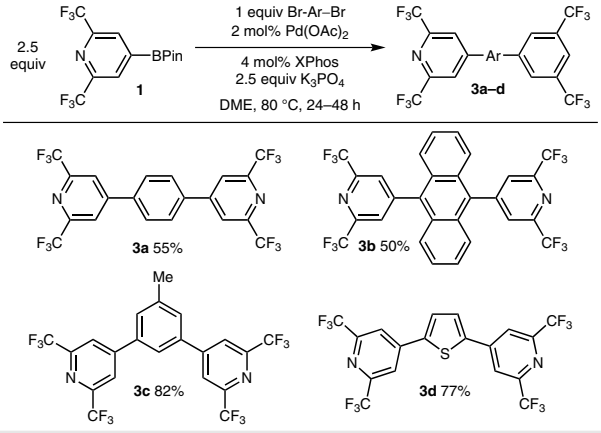


Scheme 2 Suzuki cross-coupling reactions of **1** with (hetero)aryl bromides [a] 3 mol% $Pd(PPh_3)_4$ was used as catalyst.

Both, electron-rich (**2a–c,i,j**) and electron-deficient coupling partners (**2d–f,l**) gave good yields of the Suzuki coupled product. Homocoupling of the pyridineboronic ester was observed as a minor side product (<5%) for reactions with electron-rich aryl bromides. Fused polycyclic aryl bro-

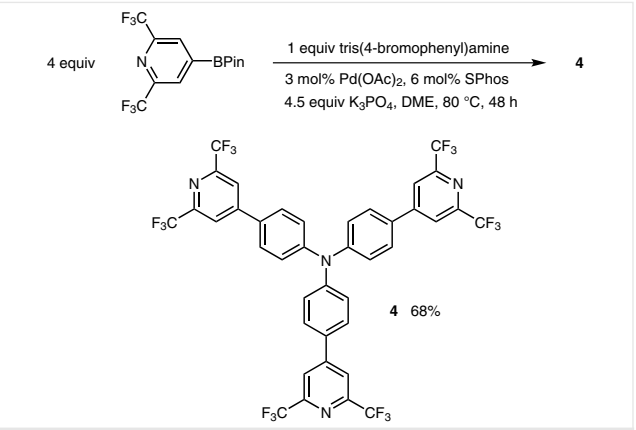
mides such as those of naphthalene, anthracene, and pyrene also proved to be good coupling partner (**2p–r**). However, steric hindrance in case of 9-bromoanthracene and 1-bromopyrene resulted in reduced yields of the Suzuki products. For chloro-substituted aryl bromides (**2g**,**h**,**m**), Suzuki coupling was carried out using $Pd(PPh_3)_4$, which resulted in the formation of small amounts of phenyl-transfer product from PPh_3, however the desired pure products were isolated in good yields. In addition to aryl bromides, heteroaryl bromides such as those of indole, thiophene, furan, and pyridine were also utilized as coupling partners and the corresponding Suzuki products were isolated in good yields (**2k–o**). All the heterobiaryl Suzuki products were solid at room temperature, and some were colored (**2c**,**m**,**n**: light yellow; **2k**: faint purple; **2r**: light orange). Some of the synthesized biaryl products can be potentially interesting organic materials. For example, **2c** due to its photophysical properties,[12b,24] and **2l** for its use in the synthesis of OLEDs.[17]

Double Suzuki coupling with dibromoarenes was also carried out (Scheme 3). Small amounts (5–10%) of mono-Suzuki coupling appeared as a side product during these double Suzuki coupling reactions. However, we were successful in isolating the pure dicoupled products in moderate to good yields (**3a–d**). Finally, tris(4-bromophenyl)amine was used as coupling partner and the triple Suzuki product was isolated in 68% yield (Scheme 4). Structurally related tris[(pyridin-4-yl)phenyl]amine molecules lacking the CF_3 groups have been studied as octupolar push–pull molecules,[25] and as fluorescent pH sensors.[26]



Scheme 3 Double Suzuki cross-coupling reactions of **1** with dibromoarenes

In conclusion, iridium-catalyzed borylation provides ready access to 2,6-bis(trifluoromethyl)-4-pyridine-4-boronic acid pinacol ester. Suzuki coupling of this pyridineboronic ester provides a convenient route for the incorporation of the most electron-deficient 2,6-bis(trifluoromethyl)pyridin-4-yl group in various organic molecules. It is expected that this new route will be highly beneficial for the synthesis of new organic electronic materials, catalysts, and bioactive molecules.



Scheme 4 Triple Suzuki cross-coupling reaction of **1** with tris(4-bromophenyl)amine

All reactions were carried out under N_2 atmosphere, without the use of glovebox or Schlenk line. All commercially available chemicals and reagents were used without further purification unless otherwise noted. EtOAc, hexanes, and CH_2Cl_2 were distilled before use. Reactions were carried out in air-free 25-mL Schlenk flask (0–4 mm Valve, 175-mm OAH). Analytical TLC was carried out using 250-µm thick SiliaPlate™ TLC Plates. Visualization was achieved under a UV lamp (254 nm and 365 nm). Column chromatography was carried out using SiliaFlash® (particle size: 40–63 µm, 230–400 mesh). All reported yields are for isolated materials. Reaction times and yields are not optimized. SPhos = 2-dicyclohexylphosphino-2′,6′-dimethoxybiphenyl; XPhos = 2-dicyclohexylphosphino-2′,4′,6′-triisopropylbiphenyl; HBPin = pinacolborane.

Infrared spectra were recorded as neat using a Bruker Alpha-P IR instrument in the ATR geometry with a diamond ATR unit. Melting points were taken on Electrothermal IA9100 melting point apparatus. Reactions were monitored by a GC-MS operating in EI mode. Accurate mass determinations (HRMS) were obtained using an Orbitrap mass spectrometer. ^1H NMR spectra were recorded at 700.130 MHz and ^{13}C NMR spectra were recorded at 176.048 MHz at ambient temperatures. The chemical shifts in ^1H NMR spectra are reported using TMS as internal standard and were referenced with the residual proton resonances of the corresponding deuterated solvent ($CDCl_3$: δ = 7.26). The chemical shifts in the ^{13}C NMR spectra are reported relative to TMS (δ = 0) or the central peak of $CDCl_3$ (δ = 77.23) for calibration.

4-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2,6-bis(trifluoromethyl)pyridine (1)

In a fume hood, an oven-dried Schlenk flask equipped with magnetic stirring bar was filled with N_2 and evacuated (three cycles). Under N_2 atmosphere, $[IrCl(COD)]_2$ (6.7 mg, 0.01 mmol, 2 mol% Ir), 2,2′-bipyridyl (3.1 mg, 0.02 mmol, 2 mol%), HBPin (218 µL, 192 mg, 1.5 mmol, 1.5 equiv), and 2,6-bis(trifluoromethyl)pyridine (215 mg, 1 mmol, 1 equiv) were added. The Schlenk flask was closed and the mixture was heated at 80 °C for 4 h in an oil bath. After 4 h, the Schlenk flask was

cooled to r.t. and exposed to air. The mixture was taken out by dissolving in CH_2Cl_2 and the volatiles were removed under reduced pressure. The crude product was purified by column chromatography; white solid; yield: 318 mg (93%); mp 87–88 °C; R_f = 0.5 (CH_2Cl_2).

FT-IR (ATR): 2983, 2963, 1310, 1272, 1139, 964, 912, 875, 844 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.21 (s, 2 H), 1.38 (br s, 12 H, 4 CH_3 of BPin).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 148.1 (q, $^2J_{C-F}$ = 35.7 Hz, 2 C), 128.1 (2 CH), 121.0 (q, $^1J_{C-F}$ = 274.6 Hz, 2 CF_3), 85.6 (2 C), 24.8 (4 CH_3 of BPin). Carbon atom attached to the boron atom of BPin group not observed due to broadening from and coupling with boron.

GC-MS (EI): *m*/z (%) = 341 (5) $[M]^+$, 326 (100), 322 (15), 299 (14), 281 (9), 255 (11).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{13}H_{15}BF_6NO_2$: 342.10945; found: 342.10860.

Suzuki Coupling; General Procedure

In a fume hood, an oven-dried Schlenk flask equipped with magnetic stirring bar was filled with N_2 and evacuated (three cycles). Under N_2 atmosphere, $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 1 mol% Pd), SPhos (4.1 mg, 0.01 mmol, 2 mol%), K_3PO_4 (160 mg, 1.5 mmol, 1.5 equiv), 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,6-bis(trifluoromethyl)pyridine (**1**, 171 mg, 0.5 mmol, 1 equiv), aryl bromide (0.75 mmol, 1.5 equiv), and DME (2 mL) were added in order. The Schlenk flask was closed and the mixture was heated at 80 °C in an oil bath for 24–48 h. The progress of reaction was monitored by GC-MS and TLC. Upon completion of reaction, the Schlenk flask was cooled to r.t. and exposed to air. The mixture was extracted into EtOAc, washed with water and brine, and dried (anhyd Na_2SO_4). The crude product was purified by column chromatography (silica gel).

For chloro-substituted bromoarenes (**2g**, **2h**, and **2m**), $Pd(PPh_3)_4$ (23 mg, 0.02 mmol, 4 mol% Pd) was used (for 1-mmol scale reaction) in place of $Pd(OAc)_2$ and SPhos. Unless otherwise noted, reactions were performed on a 0.5-mmol 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,6-bis(trifluoromethyl)pyridine (**1**) scale.

4-(*p*-Tolyl)-2,6-bis(trifluoromethyl)pyridine (2a)

Colorless solid, 1-mmol scale; yield: 233 mg (76%); mp 57–58 °C; R_f = 0.6 (hexanes–CH_2Cl_2 4:1).

FT-IR (ATR): 2927, 2857, 1608, 1391, 1288, 1262, 1138, 1097, 1063, 896, 856, 816, 717, 695 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.04 (s, 2 H), 7.61 (d, *J* = 7.9 Hz, 2 H), 7.37 (d, *J* = 7.9 Hz, 2 H), 2.45 (s, 3 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 152.4 (C), 149.3 (q, $^2J_{C-F}$ = 35.6 Hz, 2 C), 141.3 (C), 132.7 (C), 130.4 (2 CH), 127.1 (2 CH), 121.0 (q, $^1J_{C-F}$ = 274.7 Hz, 2 CF_3), 120.6 (2 CH), 21.4 (CH_3).

GC-MS (EI): *m*/z (%) = 305 (65) $[M]^+$, 286 (10), 236 (92), 216 (100), 189 (17), 167 (9).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{10}F_6N$: 306.07120; found: 306.07030.

4-(4-Methoxyphenyl)-2,6-bis(trifluoromethyl)pyridine (2b)

Colorless solid; yield: 138 mg (86%); mp 81–84 °C; R_f = 0.6 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 2977, 2944, 2919, 2848, 1604, 1521, 1464, 1390, 1265, 1133, 1064, 1023, 897, 855, 828, 718, 696 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.01 (s, 2 H), 7.67 (d, *J* = 8.6 Hz, 2 H), 7.06 (d, *J* = 8.6 Hz, 2 H), 3.90 (s, 3 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 161.8 (C), 151.9 (C), 149.3 (q, $^2J_{C-F}$ = 35.5 Hz, 2 C), 128.6 (2 CH), 127.7 (C), 121.0 (q, $^1J_{C-F}$ = 274.8 Hz, 2 CF_3), 120.1 (2 CH), 115.1 (2 CH), 55.6 (OCH_3).

GC-MS (EI): *m*/z (%) = 321 (95) $[M]^+$, 306 (14), 291 (19), 278 (100), 252 (18), 238 (18), 189 (12).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{10}F_6NO$: 322.06611; found: 322.06486.

4-[2,6-Bis(trifluoromethyl)pyridin-4-yl]-*N*,*N*-dimethylaniline (2c)

Light yellow (needles) solid; yield: 118 mg (71%); mp 128–132 °C; R_f = 0.5 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 2952, 2923, 2869, 1589, 1537, 1389, 1281, 1125, 1060, 996, 887, 853, 812, 694 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 7.98 (s, 2 H), 7.63 (d, *J* = 8.8 Hz, 2 H), 6.79 (d, *J* = 8.8 Hz, 2 H), 3.08 (s, 6 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 152.0 (C), 151.9 (C), 149.0 (q, $^2J_{C-F}$ = 35.2 Hz, 2 C), 128.0 (2 CH), 121.9 (C), 121.2 (q, $^1J_{C-F}$ = 274.7 Hz, 2 CF_3), 118.8 (2 CH), 112.4 (2 CH), 40.2 (2 CH_3).

GC-MS (EI): *m*/z (%) = 334 (97) $[M]^+$, 333 (100), 318 (10), 317 (12), 315 (9), 290 (8), 270 (24), 220 (30), 202 (9), 195 (9).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{13}F_6N_2$: 335.09774; found: 335.09647.

2,6-Bis(trifluoromethyl)-4-[4-(trifluoromethyl)phenyl]pyridine (2d)

Colorless solid; yield: 136 mg (77%); mp 82–83 °C; R_f = 0.6 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 2924, 2854, 1611, 1395, 1325, 1296, 1273, 1195, 1110, 1054, 1015, 905, 835, 725, 695 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.07 (s, 2 H), 7.84 (d, *J* = 8.4 Hz, 2 H), 7.82 (d, *J* = 8.4 Hz, 2 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 151.1 (C), 149.7 (q, $^2J_{C-F}$ = 35.9 Hz, 2 C), 139.2 (C), 132.6 (q, $^2J_{C-F}$ = 33.0 Hz, C), 127.8 (2 CH), 126.7 (q, $^3J_{C-F}$ = 3.7 Hz, 2 CH), 123.6 (q, $^1J_{C-F}$ = 272.3 Hz, CF_3), 121.2 (d, $^4J_{C-F}$ = 1.4 Hz, 2 CH), 120.8 (q, $^1J_{C-F}$ = 274.7 Hz, 2 CF_3).

GC-MS (EI): *m*/z (%) = 359 (51) $[M]^+$, 340 (15), 309 (10), 290 (100), 270 (46), 243 (11), 220 (31), 201 (9), 145 (6).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_7F_9N$: 360.04293; found: 360.04173.

4-[2,6-Bis(trifluoromethyl)pyridin-4-yl]benzonitrile (2e)

Colorless solid, 1-mmol scale; yield: 198 mg (63%); mp 194 °C; R_f = 0.25 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3086, 3042, 2238, 1615, 1392, 1294, 1270, 1194, 1117, 1064, 918, 835, 708, 694, 558 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.07 (s, 2 H), 7.89–7.88 (m, 2 H), 7.83–7.82 (m, 2 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 150.6 (C), 149.8 (q, $^2J_{C-F}$ = 35.9 Hz, 2 C), 139.9 (C), 133.4 (2 CH), 128.0 (2 CH), 121.2 (2 CH), 120.7 (q, $^1J_{C-F}$ = 274.7 Hz, 2 CF_3), 117.8 (C), 114.5 (C).

GC-MS (EI): *m*/z (%) = 316 (68) $[M]^+$, 297 (7), 247 (100), 227 (37), 220 (6), 207 (12), 200 (19), 197 (5), 177 (11), 170 (4), 158 (22), 151 (9).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{14}H_7F_6N_2$: 317.05079; found: 317.05029.

Ethyl 4-[2,6-Bis(trifluoromethyl)pyridin-4-yl]benzoate (2f)

Colorless solid, 1-mmol scale; yield: 167 mg (46%); mp 134 °C; R_f = 0.3 (hexanes–CH_2Cl_2 2:1).

FT-IR (ATR): 3082, 2990, 2922, 1710, 1609, 1465, 1445, 1392, 1369, 1286, 1258, 1183, 1124, 1061, 1016, 910, 860, 825, 773 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.24–8.23 (m, 2 H), 8.09 (s, 2 H), 7.77–7.76 (m, 2 H), 4.44 (q, *J* = 7.1 Hz, 2 H), 1.44 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 165.7 (C=O), 151.5 (C), 149.5 (q, $^2J_{C-F}$ = 35.9 Hz, 2 C), 139.6 (C), 132.4 (C), 130.8 (2 CH), 127.3 (2 CH), 121.1 (2 CH), 120.8 (q, $^1J_{C-F}$ = 274.7 Hz, 2 CF_3), 61.6 (CH_2), 14.3 (CH_3).

GC-MS (EI): *m*/z (%) = 363 (11) $[M]^+$, 344 (6), 335 (62), 318 (94), 290 (10), 270 (68), 220 (100), 200 (11), 175 (6), 171 (7), 152 (7), 149 (7).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{12}F_6NO_2$: 364.07667; found: 364.07595.

4-(3-Chlorophenyl)-2,6-bis(trifluoromethyl)pyridine (2g)

Colorless solid, 1-mmol scale; yield: 310 mg (95%); mp 94–95 °C; R_f = 0.8 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3099, 1610, 1560, 1389, 1284, 1126, 906, 883, 868, 853, 795 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.04 (s, 2 H), 7.67 (app t, *J* = 1.6 Hz, 1 H), 7.58 (dt, *J* = 7.2, 1.6 Hz, 1 H), 7.54 (dt, *J* = 8.1, 1.6 Hz, 1 H), 7.51 (app t, *J* = 7.9 Hz, 1 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 151.2 (C), 149.6 (q, $^2J_{C-F}$ = 35.9 Hz, 2 C), 137.4 (C), 135.8 (C), 131.0 (CH), 130.7 (CH), 127.4 (CH), 125.4 (CH), 121.0 (2 CH), 120.8 (q, $^1J_{C-F}$ = 275 Hz, 2 CF_3).

GC-MS (EI): *m*/z (%) = 325 (84) $[M]^+$, 327 (26) $[M + 2]^+$, 306 (9), 258 (29), 256 (100), 236 (30), 220 (30), 200 (15), 167 (20).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{13}H_7ClF_6N$: 326.01657; found: 326.01568.

4-(3,5-Dichlorophenyl)-2,6-bis(trifluoromethyl)pyridine (2h)

Colorless solid; yield: 153 mg (85%); mp 131–133 °C; R_f = 0.8 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3063, 1611, 1557, 1444, 1382, 1275, 1125, 1088, 869, 851, 802 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.01 (s, 2 H), 7.56 (d, *J* = 1.5 Hz, 2 H), 7.55 (t, *J* = 1.5 Hz, 1 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 149.9 (C), 149.7 (q, $^2J_{C-F}$ = 36 Hz, 2 C), 138.6 (C), 136.5 (2 C), 130.5 (CH), 125.7 (2 CH), 121.0 (2 CH), 120.7 (q, $^1J_{C-F}$ = 275 Hz, 2 CF_3).

GC-MS (EI): *m*/z (%) = 359 (88) $[M]^+$, 361 (54) $[M + 2]^+$, 340 (8), 304 (16), 290 (100), 270 (23), 255 (31), 235 (15), 220 (53), 201 (29).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{13}H_6Cl_2F_6N$: 359.97760; found: 359.97646.

2,6-Bis(trifluoromethyl)-4-(3,4,5-trimethoxyphenyl)pyridine (2i)

Colorless solid, 1-mmol scale; yield: 300 mg (79%); mp 129–132 °C; R_f = 0.5 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 2955, 2829, 1589, 1509, 1462, 1394, 1278, 1241, 1191, 1122, 992, 909, 828 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 7.99 (s, 2 H), 6.83 (s, 2 H), 3.97 (s, 6 H), 3.93 (s, 3 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 154.1 (2 C), 152.6 (C), 149.2 (q, $^2J_{C-F}$ = 35.6 Hz, 2 C), 140.2 (C), 131.1 (C), 120.9 (q, $^1J_{C-F}$ = 274.7 Hz, 2 CF_3), 120.8 (2 CH), 104.5 (2 CH), 61.1 (OCH_3), 56.4 (2 OCH_3).

GC-MS (EI): *m*/z (%) = 381 (50) $[M]^+$, 366 (32), 338 (56), 323 (27), 306 (46), 295 (16), 286 (23), 278 (66), 252 (100), 220 (10), 214 (10).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{14}F_6NO_3$: 382.08724; found: 382.08609.

2-[2,6-Bis(trifluoromethyl]pyridin-4-yl)-*N*,*N*-dimethylaniline (2j)

Very light greenish solid; yield: 102 mg (61%); mp 111–113 °C; R_f = 0.6 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3084, 3013, 2987, 2919, 2795, 1607, 1573, 1495, 1391, 1189, 1101, 947, 899, 831, 765, 716, 694 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.17 (s, 2 H), 7.41 (t, *J* = 7.5 Hz, 1 H), 7.28 (d, *J* = 7.6 Hz, 1 H), 7.15 (d, *J* = 7.6 Hz, 1 H), 7.11 (t, *J* = 7.6 Hz, 1 H), 2.59 (s, 6 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 153.9 (C), 151.6 (C), 149.0 (q, $^2J_{C-F}$ = 35.5 Hz, 2 C), 131.3 (CH), 131.1 (CH), 128.5 (C), 122.6 (2 CH), 121.1 (q, $^1J_{C-F}$ = 274.7 Hz, 2 CF_3), 118.7 (CH), 43.9 (2 CH_3). One CH carbon peak overlapped with any of the other CH peaks.

GC-MS (EI): *m*/z (%) = 334 (90) $[M]^+$, 333 (45), 318 (27), 316 (69), 293 (12), 265 (100), 249 (28), 245 (23), 223 (17), 220 (19), 196 (23).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_{13}F_6N_2$: 335.09774; found: 335.09620.

7-[2,6-Bis(trifluoromethyl)pyridin-4-yl]-1*H*-indole (2k)

Light purplish-white solid; yield: 105 mg (64%); mp 129–131 °C; R_f = 0.4 (hexanes–CH_2Cl_2 5:1).

FT-IR (ATR): 3471, 3139, 3113, 1611, 1425, 1330, 1190, 1129, 966, 894, 857, 798, 736 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.40 (s, NH), 8.15 (s, 2 H), 7.81 (d, *J* = 7.33 Hz, 1 H), 7.33 (app t, *J* = 2.7 Hz, 1 H), 7.31–7.28 (m, 2 H), 6.71 (app t, *J* = 2.7 Hz, 1 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 151.6 (C), 149.7 (q, $^2J_{C-F}$ = 35.8 Hz, 2 C), 132.8 (C), 129.4 (C), 125.4 (CH), 123.4 (CH), 122.7 (CH), 122.1 (CH), 120.9 (q, $^1J_{C-F}$ = 275 Hz, 2 CF_3), 120.8 (CH), 120.1 (C), 104.0 (CH).

GC-MS (EI): *m*/z (%) = 330 (43) $[M]^+$, 309 (37), 260 (11), 241 (100), 221 (13), 191 (8).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{15}H_9F_6N_2$: 331.06644; found: 331.06495.

2′,5,6′-Tris(trifluoromethyl)-2,4′-bipyridine (2l)

Colorless solid; yield: 132 mg (73%); mp 91–93 °C; R_f = 0.5 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3103, 1605, 1385, 1328, 1278, 1128, 1066, 1015, 911, 845, 775, 727, 694 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 9.07 (s, 1 H), 8.55 (s, 2 H), 8.17 (dd, *J* = 8.2, 1.7 Hz, 1 H), 8.07 (d, *J* = 8.2 Hz, 1 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 154.9 (C), 149.8 (q, $^2J_{C-F}$ = 35.9 Hz, 2 C),148.9 (C), 147.5 (q, $^3J_{C-F}$ = 3.8 Hz, CH), 135.0 (q, $^3J_{C-F}$ = 3.7 Hz, CH), 127.9 (q, $^2J_{C-F}$ = 34.0 Hz, C), 123.1 (q, $^1J_{C-F}$ = 273.2 Hz, CF_3), 120.8 (q, $^1J_{C-F}$ = 274.8 Hz, 2 CF_3), 120.8 (CH), 120.7 (2 CH).

GC-MS (EI): *m*/z (%) = 360 (22) $[M]^+$, 341 (10), 291 (100), 271 (47), 221 (14), 202 (12), 194 (6).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{13}H_6F_9N_2$: 361.03818; found: 361.03683.

4-(5-Chlorothiophen-2-yl)-2,6-bis(trifluoromethyl)pyridine (2m)

Light yellow solid, 1-mmol scale; yield: 243 mg (73%); mp 81–83 °C; R_f = 0.6 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3108, 3086, 1607, 1427, 1384, 1281, 1178, 1135, 990, 895, 854, 799, 713 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 7.88 (s, 2 H), 7.47 (d, J = 4.0 Hz, 1 H), 7.04 (d, J = 4.0 Hz, 1 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 149.7 (q, $^2J_{C–F}$ = 35.9 Hz, 2 C), 144.5 (C), 136.7 (C), 135.0 (C), 128.3 (CH), 127.1 (CH), 120.7 (q, $^1J_{C–F}$ = 274.7 Hz, 2 CF_3), 118.3 (2 CH).

GC-MS (EI): m/z (%) = 331 (100) $[M]^+$, 333 (36) $[M + 2]^+$, 312 (10), 292 (12), 276 (27), 262 (35), 252 (51), 242 (18), 227 (30), 182 (10).

HRMS (ESI-Orbitrap): m/z $[M + H]^+$ calcd for $C_{11}H_5ClF_6NS$: 331.97299; found: 331.97202.

5-[2,6-Bis(trifluoromethyl)pyridin-4-yl]thiophene-2-carbaldehyde (2n)

Light yellow solid, 1-mmol scale; yield: 156 mg (48%); mp 114 °C; R_f = 0.5 (hexanes–CH_2Cl_2 2:1).

FT-IR (ATR): 3108, 3081, 2826, 1672, 1612, 1530, 1382, 1321, 1282, 1124, 1066, 989, 905, 855, 785, 755 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 10.01 (s, 1 H), 8.07 (s, 2 H), 7.87 (d, J = 4.0 Hz, 1 H), 7.76 (d, J = 4.0 Hz, 1 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 182.6 (C=O), 149.9 (q, $^2J_{C–F}$ = 35.9 Hz, 2 $^1J_{C–F}$ = 274.7 Hz, 2 CF_3), 119.5 (2 CH).

GC-MS (EI): m/z (%) = 325 (60) $[M]^+$, 324 (76) $[M–1]^+$, 306 (7), 297 (6), 258 (4), 252 (100), 233 (4), 228 (8), 212 (5), 208 (12), 202 (6), 182 (9), 163 (4), 152 (4), 137 (4).

HRMS (ESI-Orbitrap): m/z $[M + H]^+$ calcd for $C_{12}H_6OF_6NS$: 326.00688; found: 326.0679.

Methyl 5-[2,6-Bis(trifluoromethyl)pyridin-4-yl]furan-2-carboxylate (2o)

Colorless solid; yield: 125 mg (74%); mp 168–170 °C; R_f = 0.5 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3129, 3087, 2967, 1725, 1689, 1616, 1460, 1376, 1285, 1134, 1034, 987, 902, 855, 821, 764, 712 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.14 (s, 2 H), 7.33 (br s, 1 H), 7.18 (br s, 1 H), 3.97 (s, 3 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 158.5 (C), 151.7 (C), 149.7 (q, $^2J_{C–F}$ = 36.2 Hz, 2 C), 146.5 (C), 139.9 (C), 120.7 (q, $^1J_{C–F}$ = 274.9 Hz, 2 CF_3), 119.7 (CH), 117.7 (CH), 112.7 (CH), 52.5 (CH_3).

GC-MS (EI): m/z (%) = 339 (36) $[M]^+$, 308 (100), 281 (16), 252 (72), 182 (9).

HRMS (ESI-Orbitrap): m/z $[M + H]^+$ calcd for $C_{13}H_8F_6NO_3$: 340.04029; found: 340.03889.

4-(Naphthalen-2-yl)-2,6-bis(trifluoromethyl)pyridine (2p)

Colorless solid; yield: 146 mg (86%); mp 153–154 °C; R_f = 0.7 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3095, 3065, 1614, 1396, 1276, 1178, 1128, 1059, 885, 864, 815, 748 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.19 (s, 3 H), 8.03 (d, J = 8.5 Hz, 1 H), 7.99–7.92 (m, 2 H), 7.70 (dd, J = 8.5, 1.7 Hz, 1 H), 7.62–7.60 (m, 2 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 152.4 (C), 149.4 (q, $^2J_{C–F}$ = 35.6 Hz, 2 C), 134.0 (C), 133.3 (C), 132.7 (C), 129.7 (CH), 128.7 (CH), 127.86 (CH), 127.82 (CH), 127.34 (CH), 127.31 (CH), 123.8 (CH), 121.0 (2 CH), 120.96 (q, $^1J_{C–F}$ = 275 Hz, 2 CF_3).

GC-MS (EI): m/z (%) = 341 (100) $[M]^+$, 320 (14), 272 (15), 252 (63), 232 (19), 202 (23), 176 (8).

HRMS (ESI-Orbitrap): m/z $[M + H]^+$ calcd for $C_{17}H_{10}F_6N$: 342.07120; found: 342.06992.

4-(Anthracen-9-yl)-2,6-bis(trifluoromethyl)pyridine (2q)

Very light greenish-yellow solid; yield: 135 mg (69%); mp 227–230 °C; R_f = 0.6 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3084, 3051, 2924, 2852, 1608, 1331, 1273, 1189, 1127, 982, 900, 856, 788, 738 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.64 (s, 1 H), 8.12 (d, J = 8.5 Hz, 2 H), 8.01 (s, 2 H), 7.54 (ddd, J = 8.4, 6.5, 0.9 Hz, 2 H), 7.48 (ddd, J = 8.7, 6.5, 1.2 Hz, 2 H), 7.40 (dd, J = 8.7, 0.7 Hz, 2 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 152.1 (C), 149.3 (q, $^2J_{C–F}$ = 35.8 Hz, 2 C), 131.1 (2 C), 130.3 (C), 129.3 (2 C), 129.1 (CH), 128.9 (2 CH), 127.2 (2 CH), 126.0 (2 CH), 125.7 (2 CH), 124.7 (2 CH), 121.0 (q, $^1J_{C–F}$ = 274.8 Hz, 2 CF_3).

GC-MS (EI): m/z (%) = 391 (87) $[M]^+$, 370 (20), 322 (51), 302 (100), 282 (30), 251 (48), 225 (20).

HRMS (ESI-Orbitrap): m/z $[M + H]^+$ calcd for $C_{21}H_{12}F_6N$: 392.08685; found: 392.08564.

4-(Pyren-1-yl)-2,6-bis(trifluoromethyl)pyridine (2r)

Light orange solid; yield: 125 mg (60%); mp 212–214 °C; R_f = 0.8 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3083, 3042, 2917, 1605, 1394, 1274, 1190, 1121, 841, 759, 722 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.29 (d, J = 7.5 Hz, 1 H), 8.28 (d, J = 7.8 Hz, 1 H), 8.26 (d, J = 7.5 Hz, 1 H), 8.20 (d, J = 8.9 Hz, 1 H), 8.17 (s, 2 H), 8.16 (d, J = 9.1 Hz, 1 H), 8.14 (d, J = 8.9 Hz, 1 H), 8.10 (t, J = 7.6 Hz, 1 H), 7.99 (d, J = 9.1 Hz, 1 H), 7.96 (d, J = 7.8 Hz, 1 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 153.5 (C), 149.0 (q, $^2J_{C–F}$ = 35.7 Hz, 2 C), 132.4 (C), 131.4 (C), 131.3 (C), 130.7 (C), 129.5 (CH), 129.0 (CH), 128.1 (C), 127.2 (CH), 127.0 (CH), 126.7 (CH), 126.4 (CH), 125.9 (CH), 125.0 (CH), 124.9 (C), 124.8 (CH), 124.5 (C), 122.9 (CH), 121.0 (q, $^1J_{C–F}$ = 274.8 Hz, 2 CF_3).

GC-MS (EI): m/z (%) = 415 (100) $[M]^+$, 394 (27), 345 (20), 326 (56), 306 (16), 276 (28).

HRMS (ESI-Orbitrap): m/z $[M + H]^+$ calcd for $C_{23}H_{12}F_6N$: 416.08685; found: 416.08519.

Double Suzuki Coupling; General Procedure

In a fume hood, an oven-dried Schlenk flask equipped with magnetic stirring bar was filled with N_2 and evacuated (three cycles). Under N_2 atmosphere, $Pd(OAc)_2$ (1.1 mg, 0.005 mmol, 2 mol% Pd), XPhos (4.8 mg, 0.01 mmol, 4 mol%), K_3PO_4 (133 mg, 0.625 mmol, 2.5 equiv), 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,6-bis(trifluoromethyl)pyridine (**1**, 213 mg, 0.625 mmol, 2.5 equiv), aryl bromide (0.25 mmol, 1 equiv), and DME (2 mL) were added in order. The Schlenk flask was closed and the mixture was heated at 80 °C in an oil bath for 24–48 h. The progress of reaction was monitored by GC-MS and TLC. Upon completion of reaction, the Schlenk flask was cooled to r.t. and exposed to air. The mixture was extracted into EtOAc, washed with

water and brine, and dried (anhyd Na_2SO_4). The crude product was purified by column chromatography (silica gel). All experiments below were conducted on a 0.25-mmol aryl bromide scale.

1,4-Bis[2,6-bis(trifluoromethyl)pyridin-4-yl]benzene (3a)

Colorless solid; yield: 69 mg (55%); mp 215–217 °C; R_f = 0.7 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3105, 1608, 1385, 1293, 1264, 1191, 1126, 1070, 904, 836, 809, 717, 695 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.11 (s, 4 H), 7.91 (s, 4 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 151.1 (2 C), 149.7 (q, $^2J_{C–F}$ = 35.9 Hz, 4 C), 137.9 (2 C), 128.6 (4 CH), 121.0 (d, $^3J_{C–F}$ = 1.4 Hz, 4 CH), 120.8 (q, $^1J_{C–F}$ = 274.8 Hz, 4 CF_3).

GC-MS (EI): *m*/z (%) = 504 (100) $[M]^+$, 485 (12), 435 (51), 415 (47), 395 (12), 365 (18), 345 (29), 295 (14), 277 (16), 270 (15), 252 (25), 250 (16), 220 (15), 218 (24), 208 (21), 183 (35), 173 (16).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{20}H_9F_{12}N_2$: 505.05686; found: 505.05524.

9,10-Bis[2,6-bis(trifluoromethyl)pyridin-4-yl]anthracene (3b)

Colorless solid; yield: 76 mg (50%); mp 314–315 °C; R_f = 0.6 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3044, 2922, 2850, 1606, 1426, 1338, 1278, 1186, 1132, 983, 915, 855, 805, 762 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.03 (s, 4 H), 7.54 (dd, *J* = 6.8, 3.1 Hz, 4 H), 7.47 (dd, *J* = 6.8, 3.1 Hz, 4 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 151.5 (2 C), 149.5 (q, $^2J_{C–F}$ = 36.1 Hz, 4 C), 132.9 (2 C), 128.9 (4 C), 127.4 (4 CH), 125.7 (4 CH), 125.6 (4 CH), 120.9 (q, $^1J_{C–F}$ = 275 Hz, 4 CF_3).

GC-MS (EI): *m*/z (%) = 604 (100) $[M]^+$, 585 (10), 535 (26), 515 (342), 390 (20), 370 (56), 321 (32), 320 (23), 300 (41), 282 (21), 275 (15), 251 (46), 247 (20), 222 (20).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{28}H_{13}F_{12}N_2$: 605.08816; found: 605.08593.

4,4′-(5-Methyl-1,3-phenylene)bis[2,6-bis(trifluoromethyl)pyridine] (3c)

Colorless solid; yield: 106 mg (82%); mp 189–192 °C; R_f = 0.7 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3097, 2928, 1613, 1421, 1359, 1281, 1188, 1133, 993, 891, 852, 765 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.10 (s, 4 H), 7.72 (s, 1 H), 7.66 (m, 2 H), 2.62 (s, 3 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 151.7 (2 C), 149.6 (q, $^2J_{C–F}$ = 36.0 Hz, 4 C), 141.4 (C), 137.6 (2 C), 130.1 (2 CH), 123.3 (CH), 121.2 (d, $^3J_{C–F}$ = 1.3 Hz, 4 CH), 120.8 (q, $^1J_{C–F}$ = 274.8 Hz, 4 CF_3), 21.6 (CH_3).

GC-MS (EI): *m*/z (%) = 518 (61) $[M]^+$, 499 (10), 450 (20), 429 (73), 402 (12), 380 (13), 304 (32), 284 (23), 264 (23), 259 (27), 215 (51), 190 (44).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{11}F_{12}N_2$: 519.07251; found: 519.07092.

2,5-Bis[2,6-bis(trifluoromethyl)pyridin-4-yl]thiophene (3d)

Light orange solid; yield: 98 mg (77%); mp 164–168 °C; R_f = 0.7 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 3102, 1609, 1383, 1279, 1184, 1127, 1096, 1031, 890, 856, 814, 788, 711 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.05 (s, 4 H), 7.78 (s, 2 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 149.9 (q, $^2J_{C–F}$ = 35.9 Hz, 4 C), 143.9 (2 C), 141.7 (2 C), 128.9 (2 CH), 120.6 (q, $^1J_{C–F}$ = 275 Hz, 4 CF_3), 118.9 (d, $^3J_{C–F}$ = 1.5 Hz, 4 CH).

GC-MS (EI): *m*/z (%) = 510 (M^+, 100), 491 (12), 441 (22), 421 (24), 371 (13), 351 (15), 283 (13), 271 (10), 258 (80), 252 (20), 207 (18).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_7F_{12}N_2S$: 511.01328; found: 511.01118.

Tris{4-[2,6-bis(trifluoromethyl)pyridin-4-yl]phenyl}amine (4)

In a fume hood, an oven-dried Schlenk flask equipped with magnetic stirring bar was filled with N_2 and evacuated (three cycles). Under N_2 atmosphere, $Pd(OAc)_2$ (1.7 mg, 0.0075 mmol, 3 mol% Pd), SPhos (6.2 mg, 0.015 mmol, 6 mol%), K_3PO_4 (239 mg, 1.125 mmol, 4.5 equiv), 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,6-bis(trifluoromethyl)pyridine (341 mg, 1 mmol, 4 equiv), tris(4-bromophenyl)amine (121 mg, 0.25 mmol, 1 equiv), and DME (2 mL) were added in order. The Schlenk flask was closed and the mixture was heated at 80 °C in an oil bath for 48 h. The progress of reaction was monitored by GC-MS and TLC. Upon completion of reaction, the Schlenk flask was cooled to r.t. and exposed to air. The mixture was extracted into EtOAc, washed with water and brine, and dried (anhyd Na_2SO_4). The crude product was purified by column chromatography (silica gel); light yellow solid; yield: 151 mg (0.25 mmol, 68%); mp 262–263 °C; R_f = 0.4 (hexanes–CH_2Cl_2 1:1).

FT-IR (ATR): 1593, 1515, 1389, 1329, 1260, 1187, 1129, 1064, 898, 855, 824, 725 cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 8.05 (s, 6 H), 7.69 (d, *J* = 8.6 Hz, 6 H), 7.34 (d, *J* = 8.6 Hz, 6 H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 151.3 (3 C), 149.4 (q, $^2J_{C–F}$ = 35.6 Hz, 6 C), 148.6 (3 C), 131.0 (3 C), 128.7 (6 CH), 125.1 (6 CH), 120.9 (q, $^1J_{C–F}$ = 274.7 Hz, 6 CF_3), 120.3 (6 CH).

GC-MS (EI): *m*/z (%) = 884 (100) $[M]^+$, 865 (10), 756 (7), 670 (11), 554 (27), 432 (32), 301 (38).

HRMS (ESI-Orbitrap): *m*/*z* $[M + H]^+$ calcd for $C_{39}H_{19}F_{18}N_4$: 885.13168; found: 885.12840.

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Supporting Information

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