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Deprotonative Silylation of Aromatic C−H Bonds Mediated by a Combination of Trifluoromethyltrialkylsilane and Fluoride

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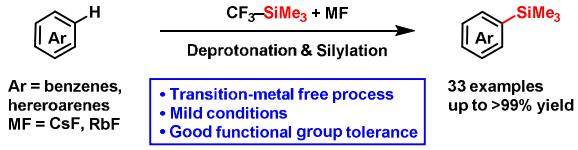


ABSTRACT: A method for the deprotonative silylation of aromatic C−H bonds has been developed using trifluoromethyltrimethylsilane (CF_3SiMe_3, Ruppert-Prakash reagent) and a catalytic amount of fluoride. In this reaction, CF_3SiMe_3 is considered to act as a base and a silicon electrophile. This process is highly tolerant to various functional groups on heteroarenes and benzenes. Furthermore, this method can be applied to the synthesis of trimethylsilyl group-containing analogs of TAC-101, which is a bioactive synthetic retinoid with selective affinity for RAR-α binding. We also report further transformations of the silylated products into useful derivatives.

The synthesis of arylsilanes is one of the most important research areas in organic chemistry. Arylsilanes are used as important synthetic intermediates for halogenation,[1] oxidation,[2] and the Hiyama coupling reaction.[3] Traditionally, methods for the construction of aromatic C−Si bonds involve the reaction of aryllithium or aryl Grignard reagents with an appropriate silyl electrophile.[4] However, this method limits the substrate scope because of the high nucleophilicity or basicity of these reagents. Additionally, this approach requires prefunctionalization of the arenes using pyrophoric organometallic species in stoichiometric quantities. Recently, methods for the synthesis of arylsilanes in high yield and with wide substrate compatibility have been developed using transition-metal-catalyzed coupling reactions of arylhalides with silanes.[5] However, the direct functionalization of aromatic C−H bonds is considered a more efficient and economical method. Therefore, the transition-metal catalyzed silylation of aromatic C−H bonds has emerged as an alternative strategy for synthesizing arylsilanes.[6] To obtain a product with high regioselectivity, the use of directing groups is needed in the reaction. Very recently, a transition-metal-free C−H silylation has been achieved using a *t*BuOK[7] catalyst or $B(C_6F_5)_3$.[8] However, these methods are applicable only to five-membered heteroarenes or *N*,*N*-substituted anilines. As another approach, deprotonative C−H silylation is considered a practical method for the synthesis of silylated aromatic compounds. Silylation has been accomplished using a combination of bases[9] (such as NaHMDS,[9a]

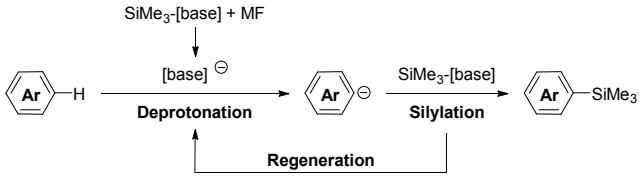


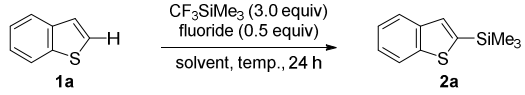
Figure 1. Working hypothesis for the deprotonative silylation of aromatic C−H bonds.

LiTMP,[9b] and LDA[9c,d]) and TMSCl. In conjunction with our recent studies on C−H functionalization using a reactive base generated *in situ* from a silylated base precursors and fluoride,[10] we started our research on deprotonative aromatic C−H silylation using a similar *in situ* generated base. As shown in Figure 1, the silylated base precursors act both as the base and the silylating agent. Consequently, trifluoromethyltrimethylsilane (CF_3SiMe_3) was found to be effective for the reaction. This reagent, now known as Ruppert-Prakash reagent, has been known to be a useful precursor of the CF_3 carbanion.[11] The pK_a value of CF_3H is reported to be around 30,[12] and its conjugate base, the CF_3 carbanion, is considered to have sufficient basicity to deprotonate aromatic ring protons.[13] In our previous report, we have described the deprotonative silylation of aromatic C−H bonds using Ruppert-Prakash reagent (CF_3SiMe_3) with a catalytic amount of fluoride.[13e] For some substrates (especially benzene derivatives), the yields of silylated products were low, therefore, development of improved method for the C−H silylation have been required. Herein, we report a method for the deprotonative C−H silyla-

tion which can be successfully applied to various heteroaromatic and benzene derivatives. Furthermore, the synthesis of biologically active TAC-101 analogs using this method and further transformation of the products silylated arenes are demonstrated.

We began our investigations using benzothiophene **1a** as a substrate to optimize the reaction conditions. The silylation of **1a** was first performed in the presence of CF_3SiMe_3 (3.0 equiv) and KF (0.5 equiv) at rt in 1,3-dimethyl-2-imidazolidinone (DMI). However, these conditions proved to be ineffective (entry 1). Subsequent lowering of the reaction temperature to 0 °C led to improved yield (entry 2). One possible reason for this increase in yield is that the decreased temperature prevented the decomposition of the pentacoordinated silicon species generated in the presence of the fluoride anion (F^-) into difluorocarbene and F^-.[14] The use of other amide solvents such as DMPU and NMP decreased the yield (entries 3 and 4). The following tests using various fluorides revealed that RbF and CsF were effective for the reaction (entries 5−7), and the reaction proceeded to completion within 2 h (entry 9). The substrate scope of the process was next investigated under the optimal conditions (Scheme 1). Benzothiophene derivatives gave moderate to high yields, regardless of the electron-donating or electron-withdrawing nature of the substituent (**2b**−**e**). This process was also applied to benzofuran (**2f**). Silylation of thiophenes possessing electron-withdrawing groups was achieved with good yields (**2g**−**j**). In addition to the trimethylsilylation of heteroaromatics, triethylsilylation and triphenylsilylation also proceeded smoothly, affording products **3** and **4**.

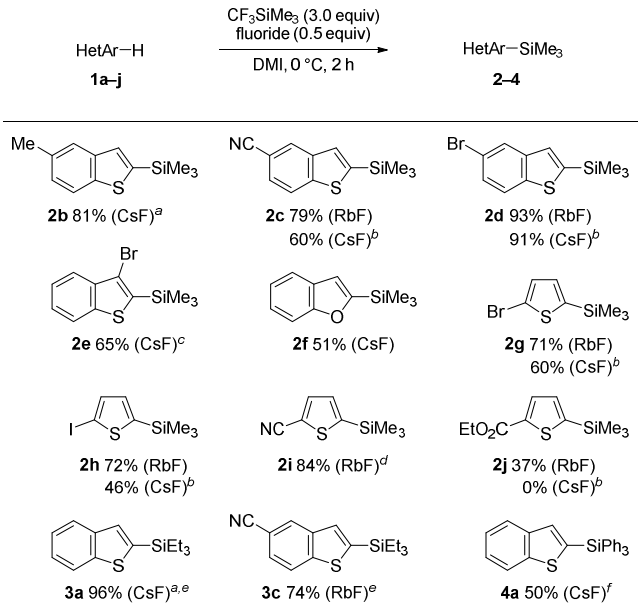
Table 1. Optimization Studies on the Reaction Parameters Using Substrate 1a



entry	fluoride	solvent	temp.	yield (%)[a]
1	KF	DMI	rt	14
2	KF	DMI	0 °C	51(41)[b]
3	KF	DMPU	0 °C	6
4	KF	NMP	0 °C	14
5	RbF	DMI	0 °C	86(83)[b]
6	CsF	DMI	0 °C	83(82)[b]
7	TMAF[c]	DMI	0 °C	trace
8	none	DMI	0 °C	0
9[d]	CsF	DMI	0 °C	97(94)[b]

[a] Determined by ^{1}H-NMR using 1,1,2-trichloroethane as an internal standard. [b] Isolated yields in parentheses. [c] TMAF = Tetramethylammonium fluoride. [d] The reaction time was 2 h.

Scheme 1. C−H Bond Silylation of Various Heteroarenes

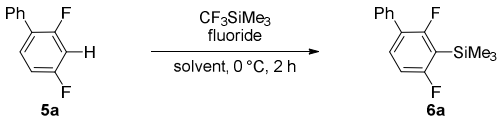


[a] The reaction was run for 24 h. [b] Determined by ^{1}H-NMR using 1,1,2-trichloroethane as an internal standard. [c] 5 equiv of CF_3SiMe_3 was used. [d] The reaction was conducted in THF/DMI (1:1) at –20 °C. [e] CF_3SiEt_3 was used instead of CF_3SiMe_3. [f] Reaction conditions: CF_3SiPh_3 (1.5 equiv), CsF (0.5 equiv), DMI, 0 °C to rt, 4h.

Next, we attempted to apply this process to benzene derivatives. 2,4-Difluorobiphenyl **5a** was selected as a substrate because its analog 1,3-difluorobenzene has a pK_a of 28.7 in DMSO[15] and is acidic enough to be deprotonated by the CF_3 anion. The previously determined optimum conditions furnished **6a** in quantitative yield (Table 2, entry 1); therefore, further investigation was conducted to decrease the amount of CF_3SiMe_3 and fluoride. Decreasing the amounts of CF_3SiMe_3 and CsF to 2.0 equiv and 0.2 equiv, respectively, had little effect on the yield (entry 4). We then conducted an evaluation of solvents (entries 4−8), and found that 1,2-dimethoxyethane (DME) gave the best results (entry 7). Among the fluoride sources investigated (entries 9−12), RbF was found to be effective for the reaction (entry 10), although it gave lower yield than CsF. This reaction proceeded to completion within 1 h (entry 13).

With the optimized conditions in hand, we investigated the substrate scope of the silylation using benzene derivatives (Scheme 2). 2,4-Difluorobenzene derivatives bearing electron-donating or electron-withdrawing substituents on the benzene rings gave the silylated products in good yields (**6b**−**j**). When

Table 2. Optimization Studies on the Reaction Parameters Using Substrate 5a

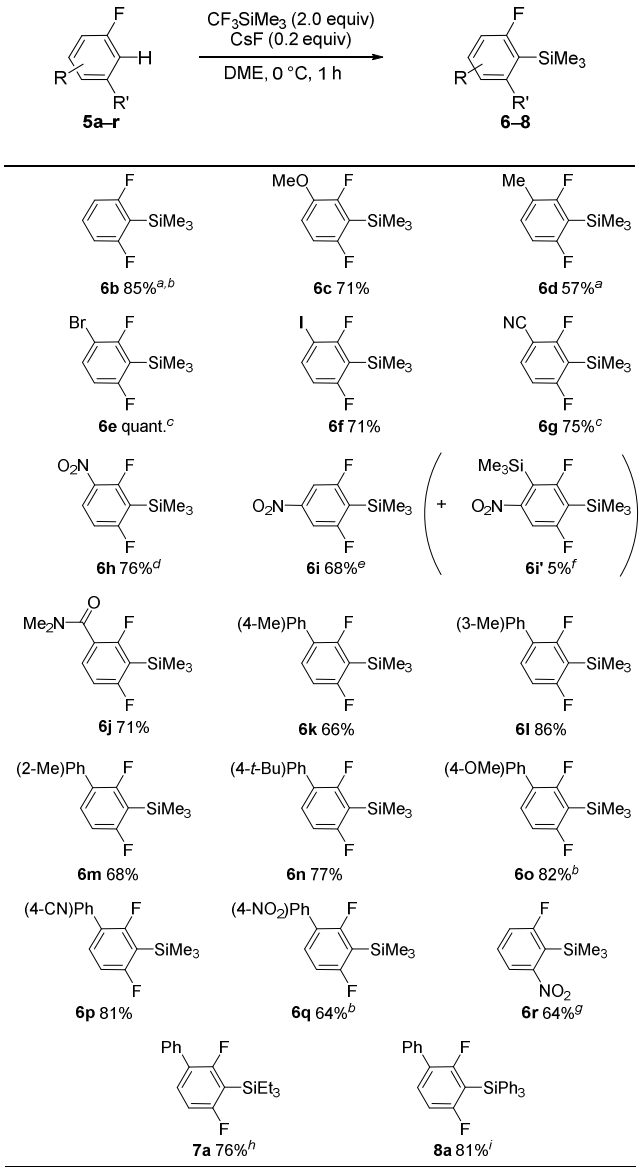


entry	CF_3SiMe_3 (equiv)	fluoride (equiv)	solvent	yield (%)[a]
1	3.0	CsF (0.5)	DMI	100
2	3.0	CsF (0.2)	DMI	100
3	3.0	CsF (0.1)	DMI	50
4	2.0	CsF (0.2)	DMI	83
5	2.0	CsF (0.2)	DMF	0
6	2.0	CsF (0.2)	THF	23
7	2.0	CsF (0.2)	DME	86

8	2.0	CsF (0.2)	toluene	0
9	2.0	KF (0.2)	DME	0
10	2.0	RbF (0.2)	DME	69
11	2.0	TMAF (0.2)	DME	8
12	2.0	none	DME	0
13[b]	2.0	CsF (0.2)	DME	90(90)[c]

[a] Determined by ^{19}F-NMR using 4-fluorotoluene as an internal standard. [b] The reaction time was 1 h. [c] Isolated yield in parentheses.

Scheme 2. C−H Bond Silylation of Various Benzenes



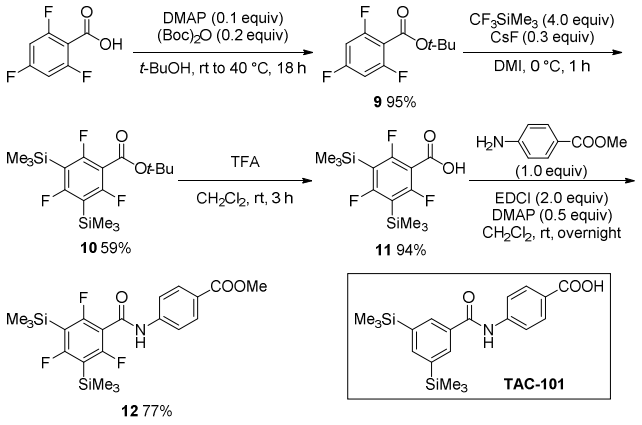
[a] Determined by ^{19}F-NMR using 4-fluorotoluene as an internal standard for volatile products. [b] 0.5 equiv of CsF was used. [c] 0.1 equiv of CsF was used. [d] 0.3 equiv of RbF was used instead of CsF. [e] 0.2 equiv of RbF was used instead of CsF. [f] Determined by ^{19}F-NMR using 4-fluorotoluene as an internal standard. [g] 0.3 equiv of CsF was used. [h] CF_3SiEt_3 was used instead of CF_3SiMe_3. [i] CF_3SiPh_3 was used instead of CF_3SiMe_3.

the silylation of 1,3-difluoro-5-nitrobenzene **5i** was conducted using RbF, a small amount of the disilylated product **6i'** was obtained in addition to the desired compound **6i**. Reactions of 2,4-difluorobiphenyls proceeded smoothly, regardless the electronic nature of the substituents (**6k**−**q**). Besides 2,4-difluorobenzene derivatives, this process could be extended to 1-fluoro-3-nitrobenzene (**6r**). In addition to the trimethylsilylation of benzene derivatives, triethylsilylation and triphenylsilylation proceeded smoothly, providing the products **7a** and **8a**.

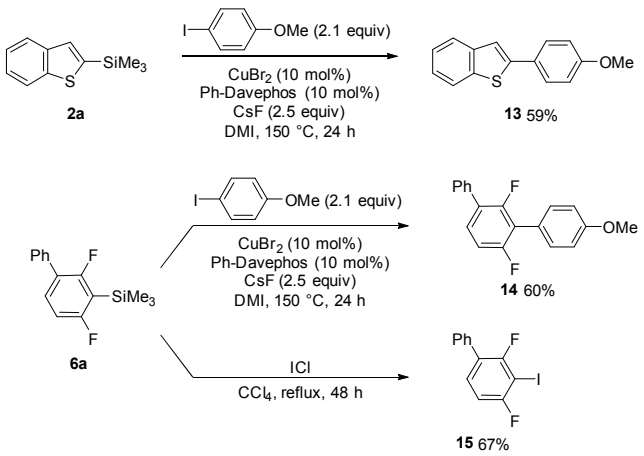
The synthesis of analogs of natural products and biologically active compounds is an important focus of research in medicinal chemistry. In particular, the introduction of fluorine atoms into compounds is known to alter their physicochemical and physiological properties[16]; therefore, this strategy has been researched actively.[17] TAC-101 (4-[3,5-bis(trimethylsilyl)benzamido]benzoic acid) is a synthetic retinoid that shows selective affinity for RAR-α binding.[18] We attempted to apply this method to the synthesis of TAC-101 analogs containing fluorine atoms (Scheme 3). 2,4,6-Trifluorobenzoic acid was selected as a starting material to synthesize compound **12**. First, esterification of the benzoic acid was conducted to obtain **9**. Subsequently, trimethylsilylation of the aromatic C−H bonds was achieved by using a combination of CF_3SiMe_3 and CsF. After hydrolysis of **10**, the condensation of **11** with methyl 4-aminobenzoate yielded TAC-101 analog **12**.

Arylsilylated compounds are shown to undergo various further transformations (Scheme 4). For example, the silylated compounds (**2a** and **6a**) obtained from this process were subjected to a copper-catalyzed cross coupling reaction with an iodoarene to produce compounds **13** and **14**, respectively.[19] Silylarene **6a** also underwent iodination to form compound **15** in good yield.[1b]

Scheme 3. Synthesis of TAC-101 Analogs



Scheme 4. Further Transformation of Arylsilanes



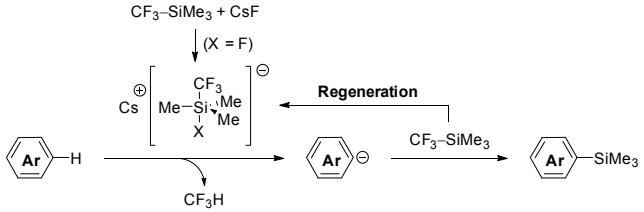


Figure 2. Presumptive mechanism for the silylation of aromatic C−H bonds.

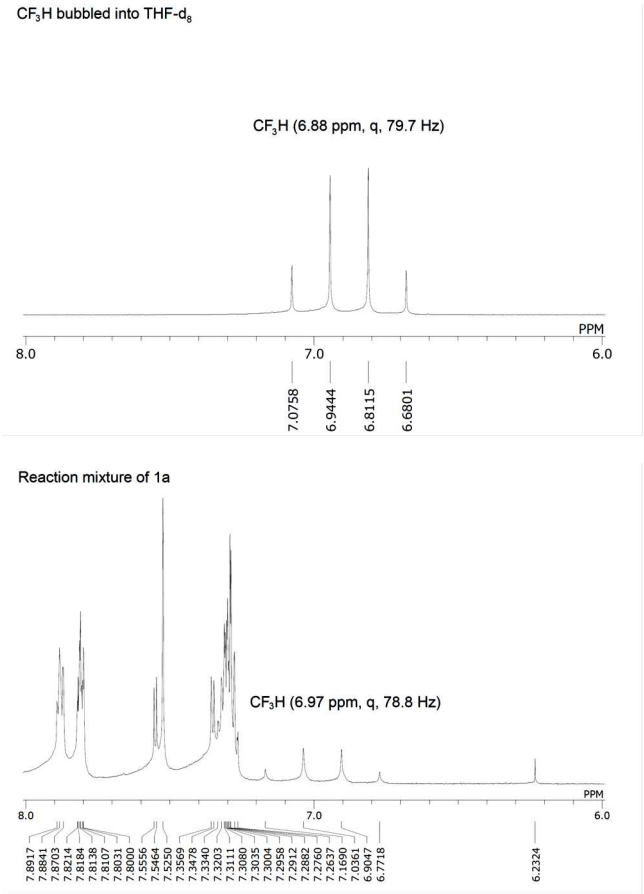


Figure 3. ^{1}H NMR spectra of CF_3H and the reaction mixture of substrate **1a** under optimum conditions (Table 1, entry 9).

The proposed mechanism for the reaction is shown in Figure 2. A fluoride activates trifluoromethyltrimethylsilane, forming a CF_3^- equivalent species. Subsequently, a base generated from the CF_3^- species deprotonates the C−H bond of the aromatic compound, followed by coupling with a silyl source, to give a silylated product. To provide evidence for the proposed mechanism, we confirmed the formation of CF_3H. The reaction of benzothiophene **1a** under the optimum conditions (Table 1, entry 9) was monitored by ^{1}H and ^{19}F NMR. The chemical shifts in the NMR spectra showed good agreement with the shifts from the sample of THF-d_8 resulting from bubbled CF_3H gas (Figures 3 and 4).

CONCLUSION

In summary, the deprotonative silylation of aromatic C−H bonds was achieved using trifluoromethyltrimethylsilane (CF_3SiMe_3) and a catalytic amount of fluoride. This process could be successfully applied to the synthesis of heteroarenes and benzenes possessing various functional groups. Moreover, we demonstrated the utility of the method by the synthesis of biologically active TAC-101 analogs and further transformation of the silylated arenes. Studies aimed at expanding the substrate scope and elucidating the reaction mechanism are underway.

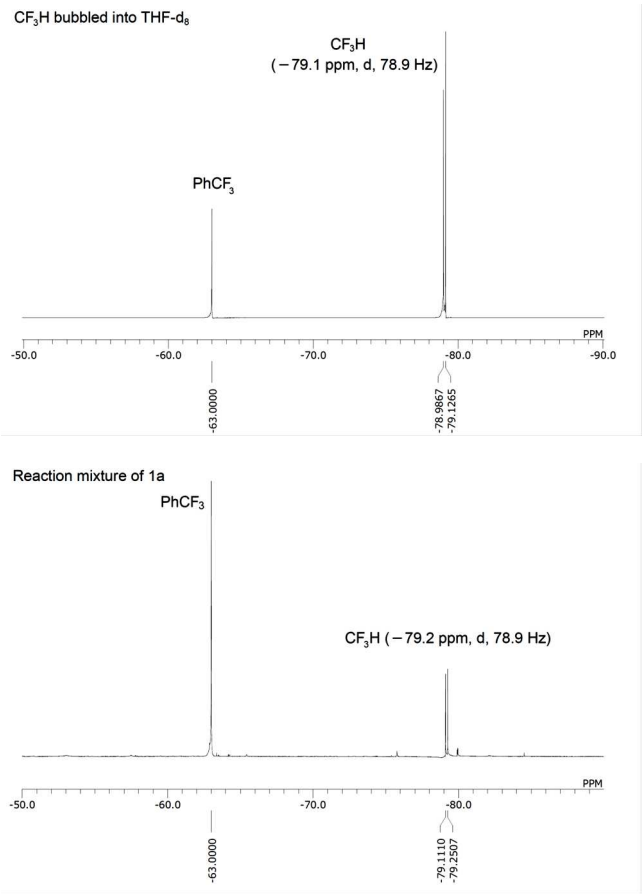


Figure 4. ^{19}F NMR spectra of CF_3H and the reaction mixture of substrate **1a** under optimum conditions (Table 1, entry 9).

EXPERIMENTAL SECTION

General Comments. Melting points (mp) were determined with a Yazawa micro melting point apparatus and uncorrected. Infrared (IR) data were recorded on a SHIMADZU IRAffinity. Absorbance frequencies are reported in reciprocal centimeters (cm^{-1}). NMR data were recorded on a JEOL AL400 (400 MHz) or JEOL ECA600 (600 MHz) spectrometer. Chemical shifts are expressed in δ (parts per million, ppm) values and coupling constants are expressed in herts (Hz). ^1H NMR spectra were referenced to tetramethylsilane as an internal standard or to a solvent signal ($CDCl_3$: δ = 7.26 ppm). ^{13}C NMR spectra were referenced to a solvent signal ($CDCl_3$: δ = 77.0 ppm). ^{19}F NMR spectra were referenced to 4-fluorotoluene (δ = –118.0 ppm) or α,α,α-trifluorotoluene (δ = –63.0 ppm) as an internal standard. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = double doublet, br.s. = broad singlet. Low and high resolution mass spectra (LRMS and HRMS) were obtained from Mass Spectrometry Resource, Graduate School of Pharmaceutical Sciences, Tohoku University, on a JEOL JMS-DX 303 and JMS-700/JMS-T 100 GC spectrometer respectively.

Preparation of Starting Materials.

Method A. To a solution of aryl iodide (1.0 equiv) in toluene (14.3 M) was added 2,4-difluorophenylboronic acid (2.0 equiv) dissolved in EtOH (1.0 M relative to 2,4-difluorophenylboronic acid). 2 M Na_2CO_3 aq. (2.5 M) and $Pd(PPh_3)_4$ (4.0 mol%) were added to the reaction mixture. The mixture was stirred at 60 °C for 17 h and then cooled to room temperature. The reaction mixture was extracted with CH_2Cl_2 (10 mL × 3) and the organic layer was washed with brine (15 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by SiO_2 column chromatography (eluent; ethyl acetate/hexane = 1/10) to afford the biphenyl.

Method B. A mixture of 2,4-difluorobromobenzene (1.0 equiv), arylboronic acid (1.5 equiv), $PdCl_2$ (0.13 mol%) and K_2CO_3 (2.0 equiv) was stirred in distilled water (1.0 M) and ethanol (1.0 M) at room temperature under air for the several hours. After the completion of reaction, the mixture was diluted with brine (15 mL) and extracted with diethyl ether (10 mL × 4), and then the combined organic layer was dried over $MgSO_4$. The solvent was concentrated under reduced pressure and the residue was purified by SiO_2 column chromatography (eluent; ethyl acetate/hexane = 1/10) to afford the biphenyl.

*2,4-Difluoro-4'-methylbiphenyl (**5k**)*. According to Method B, 279.1 mg (68%, 2.0 mmol scale). Recrystallized from acetone/hexane, colorless crystals, mp. 38 °C. ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 2.40 (s, 3H), 6.87−6.95 (m, 2H), 7.24−7.26 (m, 2H), 7.35−7.40 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 21.1, 104.2 (dd, J_{FC} = 27.2, 25.5 Hz), 111.4 (dd, J_{FC} = 20.6, 3.3 Hz), 125.3 (dd, J_{FC} = 14.0, 4.1 Hz), 128.7 (d, J_{FC} = 3.3 Hz), 129.2, 131.2−131.3 (m), 132.1 (d, J_{FC} = 16.5 Hz), 137.5, 159.7 (dd, J_{FC} = 235.4, 12.4 Hz), 162.2 (dd, J_{FC} = 234.6, 12.4 Hz); LRMS (EI) *m/z*: 204 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_{13}H_{10}F_2$: 204.0751, found: 204.0741; IR (neat): 724, 732, 805, 851, 960, 1010, 1098, 1138, 1221, 1262, 1271, 1400, 1427, 1492, 1591, 603, 1613, 2863, 2923, 3028 cm^{-1}.

*2,4-Difluoro-3'-methylbiphenyl (**5l**)*. According to Method A, 243.4 mg (76%, 1.6 mmol scale), colorless oil. ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 2.41 (s, 3H), 6.87–6.95 (m, 2H), 7.18 (d, *J* = 7.3 Hz, 1H), 7.30–7.41 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 21.4, 104.3 (dd, J_{FC} = 27.2, 25.5 Hz), 111.4 (dd, J_{FC} = 21.4, 4.1 Hz), 125.5 (dd, J_{FC} = 14.0, 4.1 Hz), 126.0 (d, J_{FC} = 2.5 Hz), 128.4 (d, J_{FC} = 9.1 Hz), 129.6 (d, J_{FC} = 2.5 Hz), 131.4–131.5 (m, 2C), 134.9, 138.1, 159.7 (dd, J_{FC} = 246.3, 12.4 Hz), 162.3 (dd, J_{FC} = 245.3, 12.3 Hz); LRMS (EI) *m/z*: 204 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{13}H_{10}F_2$: 204.0751, found: 204.0773; IR (neat): 719, 783, 848, 965, 1092, 1102, 1139, 1263, 1275, 1405, 1481, 1507, 1596, 1608, 1620, 2858, 2922, 3034, 3079 cm^{-1}.

*2,4-Difluoro-2'-methylbiphenyl (**5m**)*. According to Method A, 201.6 mg (44%, 2.2 mmol scale). Recrystallized from acetone/hexane, colorless crystals, mp. 52–55 °C. ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 2.19 (s, 3H), 6.86–6.96 (m, 2H), 7.17–7.30 (m, 5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 19.9, 103.8 (t, J_{FC} = 26.3 Hz), 111.1 (dd, J_{FC} = 21.4, 4.1 Hz), 125.7, 128.1, 130.0, 130.2, 132.0–132.2 (m, 2C), 134.8, 136.7, 159.6 (dd, J_{FC} = 249.4, 12.4 Hz), 162.3 (dd, J_{FC} = 260.9, 11.5 Hz); LRMS (EI) *m/z*: 204 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{13}H_{10}F_2$: 204.0751, found: 204.0764; IR (neat): 729, 759, 823, 857, 957, 1097, 1138, 1264, 1277, 1416, 1484, 1506, 1591 cm^{-1}.

*2,4-Difluoro-4'-tert-butylbiphenyl (**5n**)*. According to Method B, 218.1 mg (41%, 2.1 mmol scale). Recrystallized from acetone/hexane, colorless crystals, mp. 73–77 °C. ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 1.36 (s, 9H), 6.87–6.96 (m, 2H), 7.37–7.54 (m, 5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 31.3, 34.6, 104.3 (dd, J_{FC} = 26.3, 25.1 Hz), 111.4 (dd, J_{FC} = 20.6, 3.3 Hz), 125.2 (dd, J_{FC} = 14.0, 4.1 Hz), 125.5, 128.5 (d, J_{FC} = 3.3 Hz), 131.3 (q, J_{FC} = 4.9 Hz), 132.0, 150.8, 159.8 (dd, J_{FC} = 239.5, 11.5 Hz), 162.1 (dd, J_{FC} = 249.4, 11.5 Hz); LRMS (EI) *m/z*: 246 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_{16}H_{16}F_2$: 246.1220, found: 246.1230; IR (neat): 711, 731, 760, 769, 807, 839, 845, 960, 1006, 1099, 1136, 1261, 1274, 1394, 1492, 1591, 1610, 2896, 2966 cm^{-1}.

*2,4-Difluoro-4'-methoxybiphenyl (**5o**)*. According to Method A, 309.1 mg (70%, 2.0 mmol scale). Recrystallized from acetone/hexane, colorless crystals, mp. 71–72 °C. ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 3.85 (s, 3H), 6.87–6.99 (m, 4H), 7.35–7.44 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 55.2, 104.3 (dd, J_{FC} = 27.0, 25.4 Hz), 111.4 (dd, J_{FC} = 21.4, 4.1 Hz), 114.0, 125.0 (dd, J_{FC} = 13.9, 4.1 Hz), 127.3, 130.0 (d, J_{FC} = 2.5 Hz), 131.0−131.2 (m), 159.3, 159.5 (dd, J_{FC} = 226.3, 12.3 Hz), 162.0 (dd, J_{FC} = 224.7, 11.5 Hz); LRMS (EI) *m/z*: 220 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{13}H_{10}F_2O$: 220.0700, found: 220.0714; IR (neat): 732, 800, 809, 841, 869, 961, 967, 1034, 1102, 1145, 1177, 1227, 1244, 1263, 1436, 1456, 1477, 1494, 1605, 2360, 2842, 2940, 2973, 3073 cm^{-1}.

*2,4-Difluoro-4'-cyanobiphenyl (**5p**)*. According to Method A, 286.9 mg (89%, 1.5 mmol scale). Recrystallized from acetone/hexane, colorless needless, mp. 120−121 °C. ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 6.92−7.02 (m, 2H), 7.38−7.44 (m, 1H), 7.61 (dd, *J* = 8.8, 1.5 Hz, 2H), 7.73 (d, *J* = 8.3 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 104.7 (dd, J_{FC} = 27.0, 25.4 Hz), 111.5, 112.1 (dd, J_{FC} = 21.3, 4.1 Hz), 118.6, 123.4 (dd, J_{FC} = 13.1, 4.1 Hz), 129.5 (d, J_{FC} = 3.3 Hz), 131.2−131.4 (m), 132.3, 139.5 (d, J_{FC} = 1.6 Hz), 159.7 (dd, J_{FC} = 253.5, 12.3 Hz), 163.0 (dd, J_{FC} = 251.8, 12.3 Hz); LRMS (EI) *m/z*: 215 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{13}H_7F_2N$: 215.0547, found: 215.0553; IR (neat): 732, 807, 841, 963, 1098, 1139, 1265, 1273, 1301, 1401, 1492, 1592, 1619, 2238, 3060, 3075 cm^{-1}.

*2,4-Difluoro-4'-nitrobiphenyl (**5q**)*. According to Method A, 397.2 mg (84%, 2.0 mmol scale). Recrystallized from acetone/hexane, colorless needless, mp. 92−93 °C. ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 6.94−7.04 (m, 2H), 7.42−7.48 (m, 1H), 7.68 (dd, *J* = 8.8, 1.4 Hz, 2H), 8.31 (d, *J* = 9.3 Hz, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 104.9 (t, J_{FC} = 26.0 Hz), 112.2 (dd, J_{FC} = 21.7, 2.9 Hz), 123.1 (dd, J_{FC} = 13.7, 3.6 Hz), 123.8, 129.7 (d, J_{FC} = 2.9 Hz), 131.4 (dd, J_{FC} = 10.1, 4.3 Hz),

141.5, 147.3, 159.0−160.7 (m), 163.2 (dd, J_{FC} = 250.7, 15.2 Hz); LRMS (EI) *m/z*: 235 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{12}H_7F_2NO_2$: 235.0445, found: 235.0464; IR (neat): 713, 728, 842, 856, 966, 1095, 1141, 1265, 1345, 1507, 1602, 2360, 2954, 3073 cm^{-1}.

Synthesis of Trifluoromethyltriphenylsilane.

Under an Ar atmosphere, diethyl ether (70 mL) was cooled to –78 °C and stirred at that temperature for 10 minutes. After 10 minutes, CF_3H was bubbled into this ether solution until saturated solution (About 5 minutes). After bubbled, triphenylchlorosilane (4.4 g, 15 mmol) was added to the reaction mixture dropwise and the resulting reaction mixture was stirred at –78 °C for 10 minutes. A solution of potassium hexamethyldisilazide (3.7 g, 18 mmol) in diethyl ether (26 mL) was added dropwise to the reaction mixture and the resulting yellowish reaction mixture was stirred at –78 °C for 2 h, and then was gradually warmed to room temperature and stirred at room temperature for 1 h. The solvent was removed under reduced pressure and the residue was dissolved in pentane (75 mL). The organic layer was washed with water (15 mL) and cold concentrated sulfuric acid (98%) (7.5 mL × 4) to remove most of the siloxane and silanols formed in the reaction. The organic layer was then washed with water (25 mL × 5) until pH of the water showed neutral and dried over Na_2SO_4. The organic layer was concentrated under reduced pressure and the residue was recrystallized from acetone/hexane to afford trifluoromethyltriphenylsilane (3.7 g, 76%).

White solid, mp. 161–165 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.44 (t, *J* = 7.3 Hz, 6H), 7.51–7.55 (m, 3H), 7.63 (d, *J* = 6.8 Hz, 6H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 127.7, 128.4, 130.8 (q, J_{FC} = 318.8 Hz), 131.2, 136.1; LRMS (EI) *m/z*: 328 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{19}H_{15}F_3Si$: 328.0895, found: 328.0902; IR (neat): 739, 835, 1052, 1114, 1198, 1430, 1559, 2363, 3071, 3750, 3854 cm^{-1}.

Representative Procedure for Silylation of Heteroaromatics (Table 1, Entry 9).

In a globe box, a mixture of benzo[*b*]thiophene (**1a**) (40.3 mg, 0.30 mmol), CsF (22.8 mg, 0.15 mmol) and CF_3SiMe_3 (133 μL, 0.90 mmol) in DMI (0.3 mL) was stirred at 0 °C for 2 h. The reaction mixture was quenched with saturated NH_4Cl aq. and extracted with diethyl ether (10 mL × 3). The combined organic phase was washed with brine and dried over $MgSO_4$. The organic phase was concentrated under reduced pressure and the residue was purified by SiO_2 column chromatography (1% AcOEt in hexane) to give 2-trimethylsilylbenzo[*b*]thiophene (**2a**).

*2-Trimethylsilylbenzo[b]thiophene (**2a**)*. Yellow oil. 60.0 mg (94%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.38 (s, 9H), 7.28−7.35 (m, 2H), 7.46 (s, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.87−7.89 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): –0.3, 122.2, 123.4, 124.0, 124.1, 130.8, 141.1, 142.1, 143.5; LRMS (EI) *m/z*: 206 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_{11}H_{14}SSi$: 206.0585, found: 206.0573; IR (neat): 726, 742, 755, 826, 869, 1017, 1249, 1453, 1493, 2900, 2956, 3075 cm^{-1}.

*5-Methyl-2-trimethylsilylbenzo[b]thiophene (**2b**)*. Colorless oil. 53.2 mg (81%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.36 (s, 9H), 2.45 (s, 3H), 7.13 (d, *J* = 8.3 Hz, 1H), 7.37 (s, 1H), 7.58 (s, 1H), 7.74 (d, *J* = 8.3 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): –0.3, 21.3, 121.8, 123.3, 126.0, 130.4, 133.6, 140.8, 141.5, 142.3; LRMS (EI) *m/z*: 220 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{12}H_{16}SSi$: 220.0742, found: 220.0739; IR (neat): 754, 794, 828, 834, 973, 1070, 1449, 1502, 2910, 2956, 3050, 3075 cm^{-1}.

*5-Carbonitrile-2-trimethylsilylbenzo[b]thiophene (**2c**)*. Recrystallized from acetone/hexane, colorless solid, mp 88–90 °C. 56.2 mg (79%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.40 (s, 9H), 7.50–7.52 (m, 2H), 7.95 (d, *J* = 9.3 Hz, 1H), 8.12 (s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): –0.5, 107.6, 119.5, 123.1, 125.9, 127.9, 130.3, 140.8, 146.0, 147.5; LRMS (EI) *m/z*: 231 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{12}H_{13}NSSi$: 231.0538, found: 231.0512; IR (neat): 756, 805, 835, 973, 1069, 1243, 1250, 1285, 1408, 2218, 2897, 2955 cm^{-1}.

*5-Bromo-2-trimethylsilylbenzo[b]thiophene (**2d**)*. Yellow oil. 78.1 mg (93%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.37 (s, 9H), 7.37–7.40 (m, 2H), 7.72 (d, *J* = 8.3 Hz, 1H), 7.93–7.94 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): –0.4, 118.0, 123.4, 125.9, 127.1, 129.8, 142.1, 142.7, 144.7; LRMS (EI) *m/z*: 284 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_{11}H_{13}{}^{79}BrSSi$: 283.9691, found: 283.9672; IR (neat): 755, 795, 836, 881, 969, 1068, 1249, 1491, 1578, 2900, 2955, 3075 cm^{-1}.

*3-Bromo-2-trimethylsilylbenzo[b]thiophene (**2e**)*. Yellow oil. 53.6 mg (65%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.47 (s, 9H), 7.37 (t, *J* = 7.8 Hz, 1H), 7.43 (t, *J* = 7.8 Hz, 1H), 7.83 (dd, *J* = 7.8, 3.9 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): –0.8, 114.7, 122.1, 122.9, 124.8, 125.1, 136.1, 139.8, 141.4; LRMS (EI) *m/z*: 284 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_{11}H_{13}{}^{79}BrSSi$: 283.9691, found: 283.9669; IR (neat): 726, 749, 835, 881, 991, 1020, 1242, 1248, 1290, 1482, 2897, 2956, 3057 cm^{-1}.

*2-Trimethylsilylbenzo[b]furan (**2f**)*. Colorless oil. 30.5 mg (51%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.35 (s, 9H), 6.96 (s, 1H), 7.19 (t, *J* = 7.8 Hz, 1H), 7.24–7.28 (m, 1H), 7.50 (d, *J* = 8.3 Hz, 1H), 7.56 (d, *J* = 7.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): –1.8, 111.3, 116.0, 120.9, 122.3, 124.3, 128.0, 158.1, 163.5; LRMS (EI) *m/z*: 190 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_{11}H_{14}OSi$: 190.0814, found: 190.0789; IR (neat): 740, 750, 837, 920, 1066, 1111, 1250, 1443, 1471, 1529, 2926, 2960, 3065 cm^{-1}.

*2-Bromo-5-trimethylsilylthiophene (**2g**)*. Yellow oil. 49.2 mg (71%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.29 (s, 9H), 6.98 (d, *J* = 3.4 Hz, 1H), 7.08 (d, *J* = 3.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): –0.3, 116.7, 131.1, 134.3, 143.3; LRMS (EI) *m/z*: 234 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_7H_{11}{}^{79}BrSSi$: 233.9534, found: 233.9533; IR (neat): 754, 794, 834, 954, 1067, 1203, 1250, 1406, 2900, 2956 cm^{-1}.

*2-Iodo-5-trimethylsilylthiophene (**2h**)*. Red oil. 61.4 mg (72%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.29 (s, 9H), 6.91 (d, *J* = 3.4 Hz, 1H), 7.25 (d, *J* = 3.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): –0.2, 78.0, 135.5, 138.1, 148.1; LRMS (EI) *m/z*: 282 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_7H_{11}ISSi$: 281.9395, found: 281.9397; IR (neat): 754, 795, 834, 936, 990, 1067, 1202, 1248, 1396, 2875, 2900, 2955 cm^{-1}.

*2-Cyano-5-trimethylsilylthiophene (**2i**)*. Yellow oil. 44.8 mg (84%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.35 (s, 9H), 7.20 (d, *J* = 3.9 Hz, 1H), 7.65 (d, *J* = 3.9 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): –0.4, 114.1, 114.4, 133.7, 137.9, 150.5; LRMS (EI) *m/z*: 181 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_8H_{11}NSSi$: 181.0381, found: 181.0379; IR (neat): 757, 821, 840, 873, 1003, 1252, 2211, 2900, 2958 cm^{-1}.

*Ethyl 5-trimethylsilylthiophene-2-carboxylate (**2j**)*. Yellow oil. 22.1 mg (37%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.34 (s, 9H), 1.37 (t, *J* = 7.3 Hz, 3H), 4.34 (q, *J* = 7.3 Hz, 2H), 7.20 (d, *J* = 3.7 Hz, 1H), 7.81 (d, *J* = 3.7 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): –0.3, 14.3, 61.0, 134,0, 134.1, 138.6, 149.2, 162.2; LRMS (EI) *m/z*: 228 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{10}H_{16}O_2SSi$: 228.0640, found: 228.0649; IR (neat): 750, 838, 988, 1089, 1239, 1274, 1312, 1426, 1519, 1710, 2900, 2958 cm^{-1}.

*2-Triethylsilylbenzo[b]thiophene (**3a**)*. Yellow oil. 74.3 mg (96%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.87 (q, *J* = 7.8 Hz, 6H), 1.03 (t, *J* = 7.8 Hz, 9H), 7.28–7.35 (m, 2H), 7.47 (s, 1H), 7.82 (dd, *J* = 6.6, 2.0 Hz, 1H), 7.88 (d, *J* = 6.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 4.2, 7.3, 122.1, 123.3, 123.9, 124.0, 131.5, 139.0, 141.0, 143.6; LRMS (EI) *m/z*: 248 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_{14}H_{20}SSi$: 248.1055, found: 248.1042; IR (neat): 737, 1018, 1071, 1242, 1290, 1414, 1453, 1493, 2874, 2910, 2936, 2954, 3075 cm^{-1}.

*5-Carbonitrile-2-triethylsilylbenzo[b]thiophene (**3c**)*. Yellow oil. 61.7 mg (74%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.88 (q, *J* = 7.8 Hz, 6H), 1.03 (t, *J* = 7.8 Hz, 9H), 7.50–7.52 (m, 2H), 7.95 (d, *J* = 8.3 Hz, 1H), 8.13 (d, *J* = 1.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 4.1, 7.2, 107.5, 119.5, 123.0, 125.8, 127.9, 131.0, 140.7, 142.9, 147.5; LRMS (EI) *m/z*: 273 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{15}H_{19}NSSi$: 273.1007, found: 273.0990; IR (neat): 736, 807, 1068, 1243, 1409, 1437, 1457, 2228, 2875, 2909, 2936, 2955, 3075 cm^{-1}.

*2-Triphenylsilylbenzo[b]thiophene (**4a**)*. Recrystallized from acetone/hexane, colorless needles, mp 156–158 °C. 55.5 mg (50%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 7.28–7.33 (m, 2H), 7.36–7.46 (m, 9H), 7.55 (s, 1H), 7.64 (d, *J* = 7.8 Hz, 6H), 7.76–7.78 (m, 1H), 7.84–7.86 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 122.1, 123.8, 124.1, 124.6, 128.0, 130.0, 133.5, 135.5, 136.2 (2C), 140.8, 144.6; LRMS (EI) *m/z*: 392 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_{26}H_{20}SSi$: 392.1055, found: 392.1040; IR (neat): 745, 834, 967, 1107, 1293, 1426, 1483, 3065 cm^{-1}.

Representative Procedure for Silylation of Benzene Derivatives (Table 2, entry 13).

In a glove box, a mixture of 2,4-difluoro-1,1'-biphenyl (**5a**) (57.0 mg, 0.30 mmol), CsF (9.1 mg, 0.060 mmol) and CF_3SiMe_3 (93 μL, 0.60 mmol) in DME (0.3 mL) was stirred at 0 °C for 1 h. The reaction mixture was diluted with saturated NH_4Cl aq. and extracted with diethyl ether (10 mL × 3). The combined organic phase was washed with brine (10 mL) and dried over $MgSO_4$. The organic layer was concentrated under reduced pressure and the residue was purified by SiO_2 column chromatography (eluent; 1% CH_2Cl_2 in hexane) to give 2,4-difuoro-3-trimethylsilylbiphenyl (**6a**).

*2,4-Difluoro-3-trimethylsilylbiphenyl (**6a**)*. Yellow oil. 70.3 mg (90%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.40 (t, *J* = 1.4 Hz, 9H), 6.87 (t, *J* = 8.3 Hz, 1H), 7.33–7.49 (m, 6H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 0.3 (t, J_{FC} = 3.3 Hz), 111.3 (dd, J_{FC} = 27.0, 4.1 Hz), 114.0 (t, J_{FC} = 35.2 Hz), 125.1 (dd, J_{FC} = 18.8, 4.1 Hz), 127.5, 128.4, 129.1 (d, J_{FC} = 2.5 Hz), 132.9 (dd, J_{FC} = 10.2, 5.3 Hz), 135.7, 163.4 (dd, J_{FC} = 245.4, 16.0 Hz), 166.3 (dd, J_{FC} = 244.1, 15.6 Hz); LRMS (EI) *m/z*: 262 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_{15}H_{16}F_2Si$: 262.0989, found: 262.0991; IR (neat): 719, 768, 807, 842, 987, 1094, 1125, 1207, 1225, 1252, 1389, 1445, 1600, 2902, 2957 cm^{-1}.

*2,4-Difluoro-3-trimethylsilylanisole (**6c**)*. Yellow oil. 45.0 mg (71%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.37 (t, *J* = 1.4 Hz, 9H), 3.85 (s, 3H), 6.70–6.75 (m, 1H), 6.87–6.93 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 0.1 (t, J_{FC} = 2.9 Hz), 56.8, 110.0 (dd, J_{FC} = 28.0, 3.6 Hz), 114.6 (dd, J_{FC} = 35.9, 30.1 Hz), 115.1 (dd, J_{FC} = 10.0, 2.9 Hz), 143.9–144.0 (m), 155.6 (dd, J_{FC} = 243.1, 15.1 Hz), 160.0 (dd, J_{FC} = 238.1, 15.8 Hz); LRMS (EI) *m/z*: 216 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{10}H_{14}F_2OSi$: 216.0782, found: 216.0784; IR (neat): 723, 767, 800, 823, 843, 867, 984, 1054, 1132, 1234, 1251, 1310, 1412, 1437, 1464, 1581, 1621, 2839, 2903, 2959 cm^{-1}.

*2,4-Difluoro-3-trimethylsilylbromobenzene (**6e**)*. Colorless oil. 82.7 mg (100%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.38 (t, *J* = 1.5 Hz, 9H), 6.73 (t, *J* = 8.8 Hz, 1H), 7.46–7.52 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 0.05 (t, J_{FC} = 2.9 Hz), 103.8 (dd, J_{FC} = 26.2, 4.1 Hz), 112.6 (dd, J_{FC} = 28.7, 4.1 Hz), 115.5 (t, J_{FC} = 35.6 Hz), 134.9 (dd, J_{FC} = 11.0, 1.7 Hz), 162.3 (dd, J_{FC} = 243.7, 16.0 Hz), 166.0 (dd, J_{FC} = 244.1, 14.7 Hz); LRMS (EI) *m/z*: 264 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_9H_{11}{}^{79}BrF_2Si$: 263.9781, found: 263.9753; IR (neat): 767, 807, 842, 987, 1094, 1207, 1251, 1388, 1444, 1600, 1743, 2957 cm^{-1}.

*2,4-Difluoro-3-trimethylsilyliodobenzene (**6f**)*. Yellow oil. 65.0 mg (71%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.37 (t, *J* = 1.4 Hz, 9H), 6.64 (t, *J* = 8.3 Hz, 1H), 7.66–7.71 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 0.1 (t, J_{FC} = 2.9 Hz), 75.1 (dd, J_{FC} = 31.1, 4.1 Hz), 113.2 (dd, J_{FC} = 27.9, 4.1 Hz), 114.9 (d, J_{FC} = 2.5 Hz), 140.7 (dd, J_{FC} = 9.8, 3.3 Hz), 164.9 (dd, J_{FC} = 239.1, 16.5 Hz), 167.4 (dd, J_{FC} = 241.6, 14.0 Hz); LRMS (EI) *m/z*: 312 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_9H_{11}F_2ISi$: 311.9643, found: 311.9644; IR (neat): 718, 768, 807, 843, 985, 1081, 1123, 1209, 148, 1269, 1380, 1439, 1548, 1583, 2346, 2372, 2852, 2902, 2957 cm^{-1}.

*2,4-Difluoro-3-trimethylsilylbenzonitrile (**6g**)*. Recrystallized from acetone/hexane, pale yellow crystals, mp 35−40 °C. 47.7 mg (75%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.40 (s, 9H), 6.92 (t, *J* = 7.8 Hz, 1H), 7.62 (q, *J* = 7.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): –0.2, 97.5–97.7 (m), 112.5 (dd, J_{FC} = 28.8, 3.3 Hz), 113.8, 116.2 (d, J_{FC} = 32.9 Hz), 135.7 (d, J_{FC} = 11.5 Hz), 167.8 (dd, J_{FC} = 254.4, 17.3 Hz), 169.6 (dd, J_{FC} = 252.7, 15.7 Hz); LRMS (EI) *m/z*: 211 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{10}H_{11}F_2NSi$: 211.0629, found: 211.0638; IR (neat): 717, 765, 817, 829, 844, 865, 994, 1129, 1183, 1234, 1253, 1403, 1454, 1569, 1602, 1910, 2233, 2904, 2961, 3091 cm^{-1}.

*1,3-Difluoro-4-nitro-2-(trimethylsilyl)benzene (**6h**)*. Yellow oil. 51.2 mg (76%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.42 (t, *J* = 1.5 Hz, 9H), 6.91–6.95 (m, 1H), 8.05–8.10 (m, 1H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): –0.1 (t, J_{FC} = 3.6 Hz), 112.0 (dd, J_{FC} = 30.1, 4.3 Hz), 117.4 (t, J_{FC} = 35.1 Hz), 129.0 (d, J_{FC} = 11.5 Hz), 134.3 (d, J_{FC} = 11.5 Hz), 159.8 (dd, J_{FC} = 261.0, 17.2 Hz), 169.3 (dd, J_{FC} = 255.3, 15.8 Hz); LRMS (EI) *m/z*: 231 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_9H_{11}F_2NO_2Si$: 231.0527, found: 231.0506; IR (neat): 773, 834, 844, 1001, 1122, 1252, 1342, 1410, 1522, 1574, 1608, 2965, 3094 cm^{-1}.

*3,5-Difluoro-4-trimethylsilylnitrobenzene (**6i**)*. Recrystallized from ethanol, colorless needless, mp 85−87 °C. 57.5 mg (68%). ^{1}H NMR (400 MHz, acetone-d_6) δ (ppm): 0.41 (s, 9H), 7.65–7.67 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): –0.2, 106.9 (dd, J_{FC} = 28.0, 7.9 Hz), 122.3 (t, J_{FC} = 35.1 Hz), 150.1 (t, J_{FC} = 12.2 Hz), 166.6 (dd, J_{FC} = 248.1, 18.6 Hz); LRMS (EI) *m/z*: 231 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_9H_{11}F_2O_2NSi$: 231.0527, found: 231.0522; IR (neat): 707, 746, 769, 786, 840, 875, 1013, 1093, 1254, 1286, 1349, 1401, 1495, 1522, 1600, 2904, 2958, 3109 cm^{-1}.

*3,5-Difluoro-2,4-ditrimethylsilylnitrobenzene (**6i'**)*. Yellow oil. ^{1}H NMR (600 MHz, acetone-d_6) δ (ppm): 0.38 (d, *J* = 2.0 Hz, 9H), 0.45 (t, *J* = 1.3 Hz, 9H), 7.52 (d, *J* = 8.3 Hz, 1H); ^{13}C{^{1}H}NMR (150 MHz, $CDCl_3$/TMS) δ(ppm); –0.02, 0.2 (d, J_{FC} = 4.3 Hz), 107.3 (d, J_{FC} = 31.6 Hz), 116.7 (dd, J_{FC} = 41.6, 4.3 Hz), 119.1 (dd, J_{FC} = 41.6, 31.6 Hz), 157.7 (dd, J_{FC} = 15.1, 9.3 Hz), 167.3 (dd, J_{FC} = 248.1, 18.6 Hz), 171.4 (dd, J_{FC} = 243.8, 15.8 Hz); LRMS (EI) *m/z*: 288 $(M–CH_3)^+$; HRMS (EI-EB) *m/z*: $(M–CH_3)^+$ Calcd. for $C_{11}H_{16}F_2NO_2Si_2$: 288.0688, found: 288.0687; IR (neat): 786, 841, 1022, 1251, 1339, 1531, 1585, 1734, 2958 cm^{-1}.

*2,4-Difluoro-3-trimethylsilyl-N,N-dimethylbenzamide (**6j**)*. Colorless oil. 35.5 mg (71%, 0.20 mmol scale). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.37 (t, *J* = 1.5 Hz, 9H), 2.93 (d, *J* = 1.5

Hz, 3H), 3.12 (s, 3H), 6.86 (t, J = 8.3 Hz, 1H), 7.32–7.38 (m, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 0.1 (t, J_{FC} = 2.9 Hz), 35.0, 38.3 (d, J_{FC} = 2.9 Hz), 111.7 (dd, J_{FC} = 27.5, 4.3 Hz), 114.2 (t, J_{FC} = 35.4 Hz), 120.5 (dd, J_{FC} = 23.1, 4.3 Hz), 131.2–131.3 (m), 162.2 (dd, J_{FC} = 244.9, 16.6 Hz), 166.7, 167.4 (dd, J_{FC} = 246.4, 15.2 Hz); LRMS (EI) *m/z*: 257 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{12}H_{17}F_2NOSi$: 257.1047, found: 257.1078; IR (neat): 778, 842, 991, 1089, 1189, 1247, 1398, 1606, 1639, 2957 cm^{-1}.

2,4-Difluoro-4'-methyl-3-trimethylsilylbiphenyl ***(6k)***. Colorless oil. 55.2 mg (66%). ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.39 (s, 9H), 2.39 (s, 3H), 6.86 (td, J = 8.8, 1.0 Hz, 1H), 7.23–7.25 (m, 2H), 7.33–7.39 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 0.29 (t, J_{FC} = 3.3 Hz), 21.2, 111.2 (dd, J_{FC} = 27.0, 4.1 Hz), 113.8 (dd, J_{FC} = 36.0, 33.6 Hz), 124.9 (dd, J_{FC} = 18.8, 3.3 Hz), 128.9 (d, J_{FC} = 2.5 Hz), 129.1, 132.6–132.8 (m, 2C), 137.3, 163.3 (dd, J_{FC} = 245.0, 15.6 Hz), 166.1 (dd, J_{FC} = 244.4, 15.6 Hz); LRMS (EI) *m/z*: 276 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{16}H_{18}F_2Si$: 276.1146, found: 276.1152; IR (neat): 718, 741, 771, 806, 842, 980, 1020, 1053, 1112, 1127, 1196, 1242, 1380, 1413, 1456, 1605, 1896, 2363, 2949, 2957 cm^{-1}.

2,4-Difluoro-3'-methyl-3-trimethylsilylbiphenyl ***(6l)***. Colorless oil. 71.5 mg (86%). ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.39 (t, J = 1.4 Hz, 9H), 2.40 (s, 3H), 6.86 (t, J = 8.3 Hz, 1H), 7.16 (d, J = 7.3 Hz, 1H), 7.23–7.39 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 0.3 (t, J_{FC} = 2.9 Hz), 21.5, 111.2 (dd, J_{FC} = 26.9, 3.7 Hz), 113.8 (dd, J_{FC} = 35.6, 33.1 Hz), 125.1 (dd, J_{FC} = 18.6, 3.7 Hz), 126.2 (d, J_{FC} = 2.5 Hz), 128.3 (d, J_{FC} = 2.5 Hz), 129.8 (d, J_{FC} = 2.5 Hz), 132.8–132.9 (m, 2C), 135.6 (d, J_{FC} = 1.7 Hz), 138.0, 163.3 (dd, J_{FC} = 245.8, 15.7 Hz), 166.2 (dd, J_{FC} = 244.1, 15.7 Hz); LRMS (EI) *m/z*: 276 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{16}H_{18}F_2Si$: 276.1146, found: 276.1127; IR (neat): 700, 786, 842, 877, 1126, 1241, 1377, 1458, 1606, 2957 cm^{-1}.

2,4-Difluoro-2'-methyl-3-trimethylsilylbiphenyl ***(6m)***. Colorless oil. 56.2 mg (68%). ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.38 (t, J = 1.5 Hz, 9H), 2.18 (s, 3H), 6.86 (t, J = 8.3 Hz, 1H), 7.17–7.31 (m, 5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 0.2 (t, J_{FC} = 2.5 Hz), 19.9 (d, J_{FC} = 2.5 Hz), 110.9 (dd, J_{FC} = 26.5, 4.1 Hz), 113.5 (t, J_{FC} = 34.8 Hz), 124.8 (dd, J_{FC} = 21.9, 3.7 Hz), 125.7, 127.9, 130.0, 130.1 133.2–133.4 (m), 135.5, 136.7, 163.3 (dd, J_{FC} = 243.3, 15.7 Hz), 166.3 (dd, J_{FC} = 244.1, 15.7 Hz); LRMS (EI) *m/z*: 276 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{16}H_{18}F_2Si$: 276.1146, found: 276.1142; IR (neat): 726, 759, 842, 980, 1036, 1120, 1194, 1241, 1386, 1458, 1608, 2957 cm^{-1}.

2,4-Difluoro-4'-tert-butyl-3-trimethylsilylbiphenyl ***(6n)***. Recrystallized from hexane, colorless crystals, mp 62–65 °C. 73.2 mg (77%). ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.39 (s, 9H), 1.35 (s, 9H), 6.86 (t, J = 8.3 Hz, 1H), 7.34–7.47 (m, 5H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 0.3 (t, J_{FC} = 2.9 Hz), 31.3, 34.6, 111.3 (dd, J_{FC} = 27.0, 4.1 Hz), 113.7 (d, J_{FC} = 34.4 Hz), 125.0, 125.4, 128.7 (d, J_{FC} = 3.3 Hz), 132.7–132.8 (m, 2C), 150.5, 163.4 (dd, J_{FC} = 244.1, 15.6 Hz), 166.1 (dd, J_{FC} = 244.1, 15.6 Hz); LRMS (EI) *m/z*: 318 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{19}H_{24}F_2Si$: 318.1615, found: 318.1598; IR (neat): 771, 814, 840, 980, 1015, 1112, 1127, 1194, 1240, 1248, 1380, 1454, 1602, 2861, 2919, 2957 cm^{-1}.

2,4-Difluoro-4'-methoxy-3-trimethylsilylbiphenyl ***(6o)***. Brown oil. 72.0 mg (82%). ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.39 (d, J = 1.5 Hz, 9H), 3.85 (s, 3H), 6.85 (t, J = 8.3 Hz, 1H), 6.95–6.98 (m, 2H), 7.31–7.42 (m, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 0.3 (t, J_{FC} = 2.9 Hz), 55.3, 111.2 (dd, J_{FC} = 26.5, 3.6 Hz), 113.8 (t, J_{FC} = 35.1 Hz), 113.9, 124.6 (dd, J_{FC} = 18.6, 2.9 Hz), 128.0, 130.2 (d, J_{FC} = 2.9 Hz), 132.6 (dd, J_{FC} = 10.0, 5.7 Hz), 159.1, 163.3 (dd, J_{FC} = 245.2, 15.8 Hz), 166.0 (dd, J_{FC} = 243.8, 15.8 Hz); LRMS (EI) *m/z*: 292 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{16}H_{18}F_2OSi$: 292.1095, found: 292.1099; IR (neat): 772, 809, 837, 980, 1031, 1178, 1196, 1239, 1287, 1381, 1456, 1516, 1602, 2837, 2957 cm^{-1}.

2,4-Difluoro-4'-cyano-3-trimethylsilylbiphenyl ***(6p)***. Recrystallized from acetone/hexane, pale yellow needless, mp 55 °C. 68.9 mg (81%). ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.40 (t, J = 1.4 Hz, 9H), 6.92 (t, J = 7.8 Hz, 1H), 7.35–7.41 (m, 1H), 7.59 (dd, J = 8.5, 1.7 Hz, 2H), 7.72 (d, J = 8.3 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 0.2, 111.2, 111.8 (dd, J_{FC} = 27.3, 3.3 Hz), 114.6 (t, J_{FC} = 35.2 Hz), 118.7, 123.1 (dd, J_{FC} = 18.2, 4.1 Hz), 129.7 (d, J_{FC} = 3.3 Hz), 132.1, 132.6 (dd, J_{FC} = 10.8, 5.0 Hz), 140.3, 163.3 (dd, J_{FC} = 246.6, 15.7 Hz), 167.0 (dd, J_{FC} = 246.6, 16.6 Hz); LRMS (EI) *m/z*: 287 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_{16}H_{15}F_2NSi$: 287.0942, found: 287.0937; IR (neat): 744, 764, 772, 815, 841, 983, 1050, 1132, 1196, 1241, 1250, 1378, 1460, 1607, 1734, 2225, 2367, 2861, 2962 cm^{-1}.

2,4-Difluoro-4'-nitro-3-trimethylsilylbiphenyl ***(6q)***. Recrystallized from acetone/hexane, pale yellow needless, mp 67–70 °C. 58.7 mg (64%). ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.41 (s, 9H), 6.94 (t, J = 8.3 Hz, 1H), 7.38–7.44 (m, 1H), 7.65 (dd, J = 8.8, 2.0 Hz, 2H), 8.29 (d, J = 8.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 0.16–0.22 (m), 111.9 (td, J_{FC} = 22.9, 2.9 Hz), 114.7 (t, J_{FC} = 35.1 Hz), 122.8 (dd, J_{FC} = 18.6, 4.3 Hz) 123.6 (d, J_{FC} = 17.2 Hz), 129.9 (d, J_{FC} = 8.6 Hz), 132.5–132.8 (m), 142.3, 147.1, 163.3 (dd, J_{FC} = 246.7, 15.8 Hz), 167.2 (dd, J_{FC} = 246.0, 16.5 Hz); LRMS (EI) *m/z*: 307 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{15}H_{15}F_2NO_2Si$: 307.0840, found: 307.0827; IR (neat): 731, 773, 816, 842, 984, 1012, 1097, 1110, 1129, 1243, 1346, 1456, 1509, 1598, 2356, 2452, 2958, 3079 cm^{-1}.

3-Fluoro-2-trimethylsilylnitrobenzene ***(6r)***. Yellow oil. 41.1 mg (64%). ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.38 (d, J = 2.4 Hz, 9H), 7.21–7.26 (m, 1H), 7.44–7.49 (m, 1H), 7.63 (d, J = 7.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 0.2 (d, J_{FC} = 4.9 Hz), 119.4 (d, J_{FC} = 3.3 Hz), 119.7, 120.0, 121.8 (d, J_{FC} = 34.4 Hz), 131.4 (d, J_{FC} = 9.8 Hz), 167.0 (d, J_{FC} = 246.6 Hz); LRMS (EI) *m/z*: 198 $(M–CH_3)^+$; HRMS (EI-TOF) *m/z*: $(M–CH_3)^+$ Calcd. for $C_8H_9FNO_2Si$: 198.0387, found: 198.0367; IR (neat): 707, 741, 805, 842, 934, 1107, 1234, 1356, 1441, 1529, 2902, 2957 cm^{-1}.

2,4-Difluoro-3-triethylsilylbiphenyl ***(7a)***. Yellow oil. 68.3 mg (76%). ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.92–0.99 (m, 15H), 6.88 (t, J = 8.3 Hz, 1H), 7.35–7.49 (m, 6H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 4.4, 7.4, 111.3 (dd, J_{FC} = 27.2, 2.9 Hz), 111.6 (d, J_{FC} = 37.3 Hz), 125.0 (dd, J_{FC} = 18.6, 4.3 Hz), 127.5, 128.4, 129.1 (d, J_{FC} = 2.9 Hz), 132.9 (dd, J_{FC} = 10.5, 5.0 Hz), 135.8, 163.7 (dd, J_{FC} = 245.2, 15.8 Hz), 166.7 (dd, J_{FC} = 243.8, 15.8 Hz); LRMS (EI) *m/z*: 304 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{18}H_{22}F_2Si$: 304.1459, found: 304.1470; IR (neat): 718, 733, 767, 796, 818, 981, 1003, 1022, 1058, 1126, 1196, 1243, 1381, 1452, 1605, 2875, 2955, 3034 cm^{-1}.

2,4-Difluoro-3-triphenylsilylbiphenyl ***(8a)***. Recrystallized from acetone/hexane, colorless prisms, mp 119–121 °C. 36.3 mg (81%, 0.10 mmol scale). ^1H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 6.93 (t, J = 8.3 Hz, 1H), 7.30–7.44 (m, 14H), 7.52 (q, J = 8.3 Hz, 1H), 7.62 (d, J = 7.3 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 109.9 (dd, J_{FC} = 33.6, 31.1 Hz), 111.9 (dd, J_{FC} = 26.2, 4.1 Hz), 125.5 (dd, J_{FC} = 18.0, 4.1 Hz), 127.6, 127.8, 128.4, 129.1 (d, J_{FC} = 2.5 Hz), 129.6, 133.8 (d, J_{FC} = 1.6 Hz), 134.4 (dd, J_{FC} = 10.2, 5.3 Hz), 135.3 (d, J_{FC} = 1.6 Hz), 136.0, 163.4 (dd, J_{FC} = 250.3, 13.5 Hz), 166.4 (dd, J_{FC} = 248.2, 13.9 Hz); LRMS (EI) *m/z*: 448 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_{30}H_{22}F_2Si$: 448.1459, found: 448.1454; IR (neat): 706, 765, 813,

982, 1109, 1198, 1247, 1378, 1429, 1456, 1603, 2366, 3068, 3635, 3676, 3744 cm^{-1}.

Synthesis of *tert*-Butyl-2,4,6-trifluorobenzoate (9).

A mixture of 2,4,6-trifluorobenzoic acid (254 mg, 1.4 mmol), DMAP (17.5 mg, 0.14 mmol) and di-*tert*-butyldicarbonate (628 mg, 0.23 mmol) in *tert*-butanol (4.0 mL) was stirred at 40°C for 18 h. The mixture was diluted with 1M HCl (10 mL) and extracted with ethyl acetate (15 mL × 3). The combined organic layer was washed with 1M NaOH (10 mL) and brine (15 mL), and then the solvent was removed under reduced pressure to afford **9** as pale yellow oil (317 mg, 95%).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 1.59 (s, 9H), 6.65–6.72 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 28.0, 83.4, 100.4–101.0 (m), 109.7 (td, J_{FC} = 18.9, 4.9 Hz), 159.7–162.6 (m, 2C), 164.9 (t, J_{FC} = 14.8 Hz); LRMS (EI) *m/z*: 217 $(M–CH_3)^+$; HRMS (EI-TOF) *m/z*: $(M–CH_3)^+$ Calcd. for $C_{10}H_8F_3O_2$: 217.0476, found: 217.0449; IR (neat): 841, 1043, 1109, 1170, 1283, 1602, 1640, 1730, 2982 cm^{-1}.

Synthesis of *tert*-Butyl-2,4,6-trifluoro-3,5-bis(trimethylsilyl)benzoate (10)

According to the representative procedure (4.0 equiv of CF_3SiMe_3 was used), obtained as yellow oil (65.5 mg, 59%).

^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.34 (s, 18H), 1.58 (s, 9H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 0.2, 28.1, 83.2, 109.1–119.8 (m), 161.3, 164.6–166.4 (2C), 171.5 (dt, J_{FC} = 242.8, 19.4 Hz); LRMS (EI) *m/z*: 376 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{17}H_{27}F_3O_2Si_2$: 376.1502, found: 376.1499; IR (neat): 841, 1055, 1135, 1252, 1571, 1597, 1732, 2331, 2980, 3854 cm^{-1}.

Synthesis of 2,4,6-Trifluoro-3,5-bis(trimehylsilyl)benzoic acid (11).

A solution of **10** (167.7 mg, 0.44 mmol) in CH_2Cl_2 (0.60 mL) was added trifluoroacetic acid (0.30 mL) and the reaction mixture was stirred for 3 h. The solvent was removed under reduced pressure to afford **11** as white solid (134.3 mg, 94%).

Mp. 154 °C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.37 (s, 18H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 0.2, 106.1, 110.2 (t, J_{FC} = 39.4 Hz), 166.7 (dq, J_{FC} = 254.6, 9.8 Hz, 2C), 172.9 (dt, J_{FC} = 245.0, 20.0 Hz); LRMS (EI) *m/z*: 320 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{13}H_{19}F_3O_2Si_2$: 320.0876, found: 320.0858; IR (neat): 842, 1059, 1262, 1569, 1694, 2901, 2957 cm^{-1}.

Synthesis of Methyl-4-{{3,5-bis(trimethylsilyl)phenyl}carboxamido}benzoate (12).

A mixture of **11** (38.6 mg, 0.12 mmol), ethyl-4-aminobenzoate (181 mg, 0.12 mmol), DMAP (73.3 mg, 0.060 mmol) and EDCI (46 mg, 0.24 mmol) in CH_2Cl_2 was stirred overnight. The reaction mixture was diluted with CH_2Cl_2 (15 mL) and washed with 1M HCl (10 mL), saturated $NaHCO_3$ aq. (10 mL) and brine (15 mL). The organic layer was dried over $MgSO_4$ and the solvent was removed under reduced pressure. The residue was purified by column chromatography (eluent; ethyl acetate/hexane = 2/3) to afford **12** as white solid (41.9 mg, 77 %).

Mp. 189 °C; ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 0.36 (s, 18H), 3.90 (s, 3H), 7.70 (d, *J* = 8.8 Hz, 2H), 7.84 (br.d, *J* = 7.8 Hz, 1H), 8.03 (d, *J* = 8.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$/TMS) δ (ppm): 0.2, 52.0, 110.0–110.5 (m), 119.1, 126.2, 130.8, 141.6, 159.1, 165.2 (dq, J_{FC} = 248.5, 10.3 Hz, 2C), 166.5, 171.8 (dt, J_{FC} = 245.7, 19.7 Hz); LRMS (EI) *m/z*: 453 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{21}H_{26}F_3NO_3Si_2$: 453.1403, found: 453.1419; IR (neat): 770, 844, 1051, 1251, 1278, 1539, 1601, 1718, 2957, 3077, 3122, 3243 cm^{-1}.1602, 2360, 2954, 3073 cm^{-1}.

General Procedure for Cu(II)-catalyzed Double Cross Coupling Using Trimethylsilylarenes as a Substrate.

In a glove box, trimethylsilylarene (0.31 mmol) was added to a solution of $CuBr_2$ (6.7 mg, 30 μmol), Ph-Davephos (11.5 mg, 30 μmol), CsF (115 mg, 0.76 mmol) and 4-iodoanisole (148 mg, 0.63 mmol) in DMI (0.2 mL). The mixture was stirred at 150 °C for 24 h in a sealed tube. The reaction mixture was diluted with CH_2Cl_2 and filtered. The filtrate was removed under reduced pressure. The residue was purified by SiO_2 column chromatography (eluent; CH_2Cl_2/hexane = 1/3) to afford the biaryl compound.

*2-(4-Methoxyphenyl)benzo[b]thiophene (**13**)*. White solid, mp. 196–200 °C. 43.4 mg (59%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 3.86 (s, 3H), 6.96 (d, *J* = 8.8 Hz, 2H), 7.28–7.35 (m, 2H), 7.43 (s, 1H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.74 (d, *J* = 7.3 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 55.4, 114.3, 118.2, 122.2, 123.2, 123.9, 124.4, 127.1, 127.7, 139.2, 140.9, 144.1, 159.8; LRMS (EI) *m/z*: 240 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{15}H_{12}OS$: 240.0609, found: 240.0638; IR (neat): 745, 819, 1030, 1112, 1253, 1434, 1496, 1602, 2835, 2960 cm^{-1}.

*2',6'-Difluoro-4-methoxy-1,1':4',1''-terphenyl (**14**)*. White solid, mp. 98–100 °C. 53.8 mg (60%). ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 3.86 (s, 3H), 6.99–7.06 (m, 3H), 7.31–7.39 (m, 2H), 7.42–7.46 (m, 4H), 7.53 (d, *J* = 7.8 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 55.2, 111.6 (dd, J_{FC} = 22.9, 4.1 Hz), 113.8, 118.4 (t, J_{FC} = 19.3 Hz), 121.4, 125.6 (dd, J_{FC} = 15.6, 4.1 Hz), 127.7, 128.4, 129.0 (d, J_{FC} = 3.3 Hz), 129.2–129.4 (m), 131.6 (t, J_{FC} = 2.0 Hz), 135.4, 156.7 (dd, J_{FC} = 249.5, 7.0 Hz), 159.4 (dd, J_{FC} = 248.2, 6.6 Hz), 159.5; LRMS (EI) *m/z*: 296 (M^+); HRMS (EI-EB) *m/z*: (M^+) Calcd. for $C_{19}H_{14}F_2O$: 296.1013, found: 296.1022; IR (neat): 771, 833, 994, 1176, 1250, 1400, 1471, 1611, 2363, 2933 cm^{-1}.

Procedure for Iodination of 2,4-Difluoro-3-trimethylsilylbiphenyl.

ICl dissolved in CCl_4 (0.9 M) was added dropwise to a solution of 2,4-difluoro-3-trimethylsilylbiphenyl (**6a**) (78.7 mg, 0.30 mmol) in CCl_4 (5 mL) at room temperature. The mixture was refluxed for 48 h. After cooling to room temperature, the mixture was diluted with water and extracted with diethyl ether (10 mL × 3). The organic layer was washed with saturated $Na_2S_2O_3$ aq. (10 mL) and brine (15 mL), and then dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by SiO_2 column chromatography (eluent; CH_2Cl_2/hexane = 1/50) to afford 2,4-difluoro-3-iodobiphenyl (**15**) (61.3 mg, 67%).

White solid, mp. 38 °C. ^{1}H NMR (400 MHz, $CDCl_3$/TMS) δ (ppm): 6.95–6.99 (m, 1H), 7.36–7.49 (m, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$/TMS) δ (ppm): 71.7–72.3 (m), 111.4 (dd, J_{FC} = 24.0, 4.1 Hz), 125.8 (dd, J_{FC} = 16.6, 4.1 Hz), 128.1, 128.6, 128.9 (d, J_{FC} = 3.3 Hz), 131.4–131.5 (m), 134.5 (d, J_{FC} = 4.5 Hz), 159.1 (dd, J_{FC} = 248.3, 6.6 Hz), 161.9 (dd, J_{FC} = 247.9, 4.6 Hz); LRMS (EI) *m/z*: 316 (M^+); HRMS (EI-TOF) *m/z*: (M^+) Calcd. for $C_{12}H_7F_2I$: 315.9560, found: 315.9566; IR (neat): 763, 822, 993, 1202, 1256, 1403, 1470, 1602, 2956 cm^{-1}.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/**.**

^{1}H and ^{13}C NMR spectra of all isolated products and new compounds.

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Notes

The authors declare no competing financial interest.

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