4-((2-Halogeno-5-pyridyl)dimethylsilyl)phenylboronic Acids: New Potential Building Blocks for the Synthesis of Silicon-Containing Drugs

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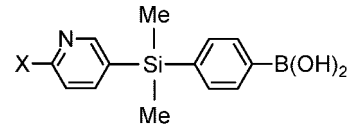
With the synthesis of 4-((2-fluoro-5-pyridyl)dimethylsilyl)phenylboronic acid (**1a**) and 4-((2-chloro-5-pyridyl)dimethylsilyl)phenylboronic acid (**1b**), new potential building blocks for the synthesis of silicon-containing drugs have been made available. Compounds **1a**,**b** were characterized by elemental analyses, multinuclear NMR experiments, and single-crystal X-ray diffraction studies. The synthetic potential of **1a** was demonstrated by the Suzuki−Miyaura coupling reaction with 4-bromophenol to give (2-fluoro-5-pyridyl)(4′-hydroxy-(1,1′-biphenyl)-4-yl)dimethylsilane (**2**).

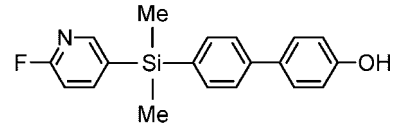
Boronic acids are extensively used as reagents in organic synthesis and thereby play an important role in the preparation of drugs and agrochemicals.[1] In this context, the palladium-catalyzed cross-coupling reaction of aryl- or heteroarylboronic acids with aryl- or heteroaryl halides or triflates (Suzuki−Miyaura coupling) has proved to be an efficient method for C−C bond formation.[2] In addition, boronic acids and their derivatives have many other applications: They can be used as catalysts,[3] as protecting groups for diols,[4] and as receptors and sensors for carbohydrates,[5] and they are of interest as enzyme inhibitors, BNCT agents, and drug release systems.[6] In spite of this importance of boronic acids, only a few examples of *p*-silyl-substituted phenylboronic acids have been described in the literature, mainly for applications in material sciences.[7]

In context with our systematic research on sila-substituted drugs,[8,9] we have now succeeded in synthesizing a series of novel *p*-silyl-substituted phenylboronic acids that contain silicon-bound 2-halogeno-5-pyridyl groups. Generally, halogenopyridyl groups are important building blocks in medicinal chemistry.[10] Thus, 4-((2-halogeno-5-pyridyl)silyl)phenylboronic acids are expected to be challenging reagents for the synthesis of novel biologically active organosilicon compounds. We report here on (i) the syntheses and crystal structure analyses of compounds **1a**,**b** and (ii) studies dealing with a model Suzuki−Miyaura coupling reaction of **1a** with 4-bromophenol to yield compound **2**.



1a: X = F

1b: X = Cl



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Results and Discussion

Syntheses of the Boronic Acids. The title compounds **1a**,**b** were prepared in multistep syntheses according to Scheme 1. Thus, lithiation of the respective 5-bromo-2-halopyridines with *n*-butyllithium in the presence of an excess of dimethoxydimethylsilane gave the corresponding (2-halogeno-5-pyridyl)-methoxydimethylsilanes **3a**,**b** (yields: **3a**, 52%; **3b**, 60%). Subsequent treatment of **3a**,**b** with (4-bromophenyl)lithium (obtained by lithiation of 1,4-dibromobenzene with *n*-butyllithium) gave the (4-bromophenyl)(2-halogeno-5-pyridyl)dimethylsilanes **4a**,**b**, respectively (yields: **4a**, 74%; **4b**, 71%). Metalation of **4a**,**b** with *tert*-butyllithium and subsequent treatment with 4,4,5,5-tetramethyl-2-propyloxy-1,3,2-dioxaborolane[11] afforded the corresponding (2-halogeno-5-

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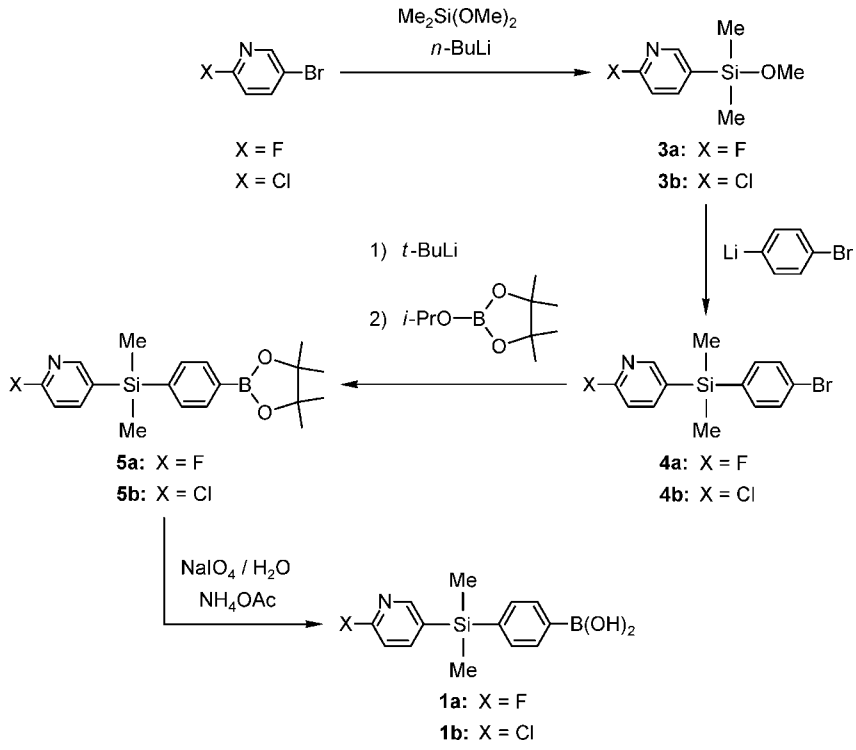
Scheme 1

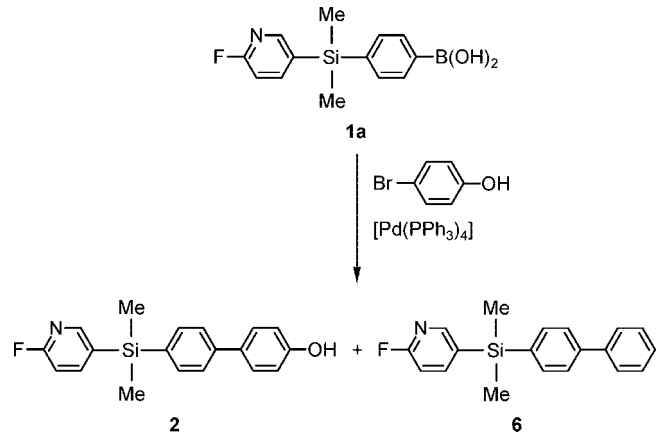


pyridyl)dimethyl(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)silanes **5a**,**b**, respectively (yields: **5a**, 57%; **5b**, 80%). Finally, treatment of **5a**,**b** with an aqueous solution of sodium periodate[12] and ammonium acetate yielded compounds **1a** (isolated as the solvate **1a**·0.5MeC(O)Me) and **1b**, respectively (yields: **1a**·0.5MeC(O)Me, 75%; **1b**, 75%).

Compounds **1a**·0.5MeC(O)Me, **1b**, **4b**, and **5a**,**b** were obtained as crystalline solids, whereas **3a**,**b** and **4a** were isolated as liquids. The identities of all these compounds were established by elemental analyses and multinuclear NMR spectroscopy. In addition, compounds **1a**·0.5MeC(O)Me, **1b**, **4b**, and **5a** were structurally characterized by single-crystal X-ray diffraction.

Suzuki−Miyaura Cross-Coupling Reaction. The cross-coupling reaction of **1a** with 4-bromophenol in the presence of tetrakis(triphenylphosphine)palladium(0)[13] gave the corresponding

Scheme 2



1,1′-biphenyl-4-ol derivative **2** in 45% yield (Scheme 2). In addition, the formation of a related coupling product, the 1,1′-biphenyl derivative **6** (55% yield), was observed (Scheme 2). The low yield of **2** is similar to those observed for comparable coupling reaction products obtained from 4-bromophenol.[13a]

Compounds **2** and **6** were isolated as colorless crystalline solids. Their identities were established by elemental analyses and NMR spectroscopy, and **2** was additionally characterized by single-crystal X-ray diffraction.

Crystal Structure Analyses. Compounds **1a**·0.5MeC(O)Me, **1b**, **2**, **4b**, and **5a** were structurally characterized by single-crystal X-ray diffraction. The crystal data and the experimental parameters used for these studies are given in Table 1. The molecular structures of **1a** and **2** are depicted in Figures 1 and

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Table 1. Crystal Data and Experimental Parameters for the Crystal Structure Analyses of 1a·0.5MeC(O)Me, 1b, 2, 4b, and 5a

	1a·0.5MeC(O)Me	**1b**	**2**	**4b**	**5a**
empirical formula	$C_{14.5}H_{18}BFNO_{2.5}Si$	$C_{13}H_{15}BClNO_2Si$	$C_{19}H_{18}FNOSi$	$C_{13}H_{13}BrClNSi$	$C_{19}H_{25}BFNO_2Si$
formula mass, g mol^{-1}	304.20	291.61	323.43	326.69	357.30
collection T, K	193(2)	100(2)	193(2)	100(2)	193(2)
λ(Mo Kα), Å	0.710 73	0.710 73	0.710 73	0.710 73	0.710 73
cryst syst	monoclinic	monoclinic	orthorhombic	triclinic	monoclinic
space group (No.)	$P2_1/n$ (14)	$C2/c$ (15)	$Pbcn$ (60)	$P\bar{1}$ (2)	$P2_1/c$ (14)
a, Å	6.6964(10)	20.5093(8)	15.218(3)	6.2696(13)	12.0086(15)
b, Å	22.190(3)	15.6888(6)	9.2640(10)	9.6147(19)	12.2203(14)
c, Å	11.1528(17)	9.7982(4)	24.984(3)	12.194(2)	13.4878(18)
α, deg	90	90	90	95.37(3)	90
β, deg	97.817(18)	105.419(2)	90	100.82(3)	92.594(16)
γ, deg	90	90	90	98.07(3)	90
V, Å^3	1641.8(4)	3039.3(2)	3522.3(9)	709.4(2)	1977.3(4)
Z	4	8	8	2	4
D(calcd), g cm^{-3}	1.231	1.275	1.220	1.529	1.200
μ, mm^{-1}	0.158	0.326	0.146	3.148	0.139
F(000)	640	1216	1360	328	760
cryst dimens, mm	0.5 × 0.4 × 0.2	0.230 × 0.095 × 0.047	0.5 × 0.4 × 0.2	0.403 × 0.258 × 0.192	0.5 × 0.3 × 0.1
2θ range, deg	5.20−58.12	3.32−66.82	5.36−58.22	3.42−65.88	5.56−58.22
index ranges	$-9 \le h \le 9$	$-30 \le h \le 31$	$-20 \le h \le 20$	$-9 \le h \le 9$	$-16 \le h \le 16$
	$-30 \le k \le 30$	$-24 \le k \le 24$	$-12 \le k \le 12$	$-14 \le k \le 14$	$-16 \le k \le 16$
	$-15 \le l \le 15$	$-15 \le l \le 15$	$-34 \le l \le 34$	$-18 \le l \le 18$	$-18 \le l \le 18$
no. of collected rflns	23 419	48 634	48 816	41 227	20 682
no. of indep rflns	4240	5811	4704	5247	5269
R_{int}	0.0371	0.0566	0.0410	0.0488	0.0498
no. of rflns used	4240	5811	4704	5247	5269
no. of restraints	9	0	0	6	14
no. of params	207	180	214	163	304
S^a	1.037	1.045	1.066	1.045	1.052
weight params a/b^b	0.0737/0.4762	0.0480/2.3900	0.0654/0.7362	0.0342/0.1475	0.0681/0.1642
$R1^c$ ($I > 2\sigma(I)$)	0.0441	0.0379	0.0410	0.0239	0.0455
$wR2^d$ (all data)	0.1274	0.1058	0.1198	0.0659	0.1276
max/min residual electron density, e Å^{-3}	+0.335/−0.384	+0.622/−0.385	+0.329/−0.374	+0.754/−0.375	+0.328/− 0.314

[a] $S = \{\sum[w(F_o^2 - F_c^2)^2]/(n - p)\}^{0.5}$; n = no. of reflections; p = no. of parameters. [b] $w^{-1} = \sigma^2(F_o^2) + (aP)^2 + bP$, with $P = [\max(F_o^2,0) + 2F_c^2]/3$. [c] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$. [d] $wR2 = \{\sum[w(F_o^2 - F_c^2)^2]/\sum[w(F_o^2)^2]\}^{0.5}$.

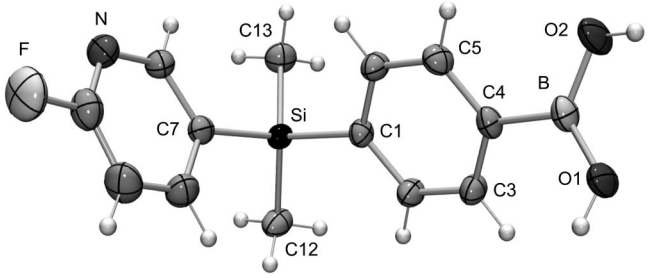

Figure 1. Molecular structure of **1a** in the crystal of **1a**·0.5MeC(O)Me (probability level of displacement ellipsoids 50%). Selected bond distances (Å), bond angles (deg), and torsion angles (deg): Si−C1 = 1.8804(14), Si−C7 = 1.8894(16), Si−C12 = 1.8615(17), Si−C13 = 1.8711(17), O1−B = 1.364(2), O2−B = 1.352(2), C4−B = 1.580(2); C1−Si−C7 = 104.57(6), C1−Si−C12 = 110.45(7), C1−Si−C13 = 109.40(7), C7−Si−C12 = 110.36(8), C7−Si−C13 = 109.97(8), C12−Si−C13 = 111.84(8), O1−B−O2 = 119.96(14), O1−B−C4 = 123.09(14), O2−B−C4 = 116.95(15); O1−B−C4−C3 = −30.5(2), O1−B−C4−C5 = 149.20(16), O2−B−C4−C3 = 149.98(16), O2−B−C4−C5 = −30.3(2).

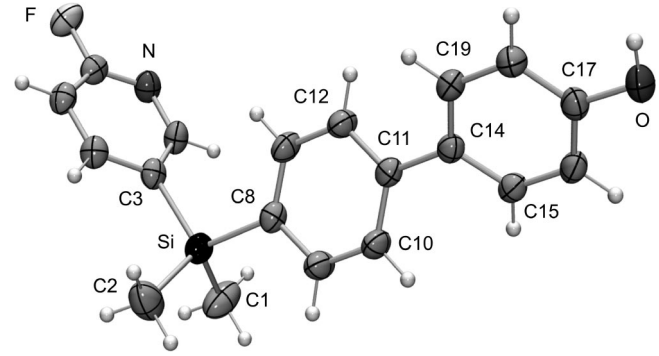

Figure 2. Molecular structure of **2** in the crystal (probability level of displacement ellipsoids 50%). Selected bond distances (Å), bond angles (deg), and torsion angles (deg): Si−C1 = 1.8649(17), Si−C2 = 1.8722(18), Si−C3 = 1.8849(13), Si−C8 = 1.8776(13), O−C17 = 1.3670(15), C11−C14 = 1.4857(16); C1−Si−C2 = 110.17(10), C1−Si−C3 = 109.14(7), C1−Si−C8 = 110.61(7), C2−Si−C3 = 109.40(7), C2−Si−C8 = 108.89(7), C3−Si−C8 = 108.60(6); C10−C11−C14−C15 = 33.50(18), C10−C11−C14−C19 = −144.28(13), C12−C11−C14−C15 = −148.37(12), C12−C11−C14−C19 = 33.85(18). Intermolecular O−H···N hydrogen bonds lead to the formation of infinite chains in the crystal of **2**. Distances (Å) and angles (deg) of the hydrogen-bonding system:[14] O−H = 0.886(19), H···N = 2.021(19), O···N = 2.8855(17); O−H···N = 165.0(19).

2; selected interatomic distances, bond angles, and torsion angles are given in the respective figure legends (for further details of the crystal structure analyses, see the Supporting Information).

The crystal structures of **1a**·0.5MeC(O)Me, **1b**, **2**, **4b**, and **5a** (Figures 1 and 2 and the Supporting Information) do not show any special features and therefore do not need a detailed discussion, except for the hydrogen-bonding systems observed for **1a**·0.5MeC(O)Me and **1b**. In both cases, intermolecular O−H···O hydrogen bonds lead to the formation of centrosymmetric dimers of the boronic acid, which are further connected by intermolecular O−H···N hydrogen bonds, resulting in a

(14) The hydrogen-bonding systems were analyzed by using the program system PLATON: (a) Spek, A. L., PLATON; University of Utrecht, Utrecht, The Netherlands, 1998. (b) Spek, A. L. *Acta Crystallogr., Sect. A* **1990**, *46* (Supplement), C34.

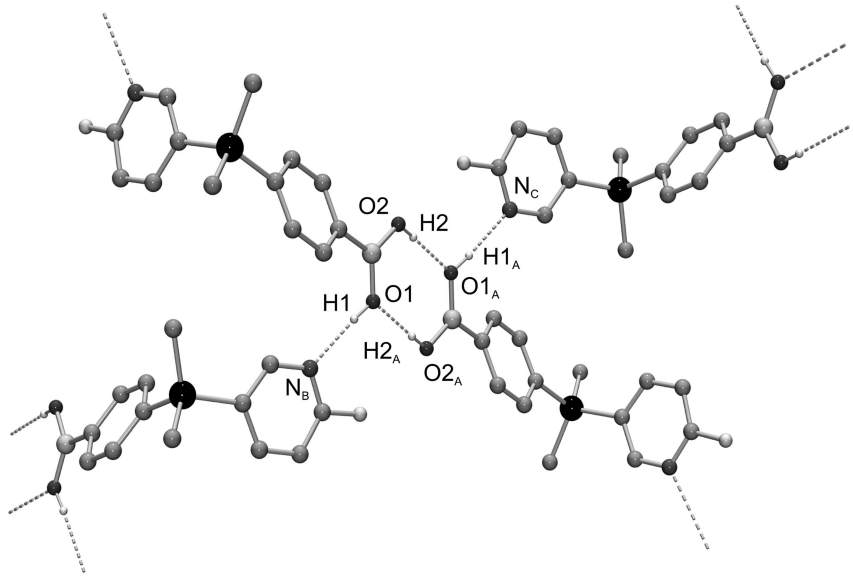

Figure 3. Two-dimensional hydrogen-bonding network in the crystal of **1a**·0.5MeC(O)Me. The dashed lines indicate intermolecular O−H···O and O−H···N hydrogen bonds, respectively, leading to the formation of centrosymmetric dimeric units of the boronic acid, which are further connected to form a corrugated layer structure. The acetone molecules and the hydrogen atoms (except for the O*H* atoms) are omitted for clarity. Distances (Å) and angles (deg) of the hydrogen-bonding system:[14] O1−H1 = 0.83(3), H1···N_B = 2.00(3), O1···N_B = 2.820(2), O1−H1···N_B = 174(2); O2−H2 = 0.80(3), H2···$O1_A$ = 1.97(3), O2···$O1_A$ = 2.7628(18), O2−H2···$O1_A$ = 174(3).

corrugated layer structure. This is shown exemplarily for **1a**·0.5MeC(O)Me in Figure 3.

Conclusions

With the syntheses of the 4-((2-halogeno-5-pyridyl)dimethylsilyl)phenylboronic acids **1a**,**b**, two new silicon-containing boronic acids have been made accessible. Compounds **1a**,**b** were prepared in four-step syntheses, starting from the corresponding 5-bromo-2-halogenopyridine. The key step in the synthesis of **1a**,**b** is the low-temperature coupling reaction of dimethoxydimethylsilane with a (2-halogeno-5-pyridyl)lithium reagent, generated in situ from the respective 5-bromo-2-halopyridine and *n*-butyllithium in diethyl ether. Owing to their synthetically valuable boronic acid functionality and their 2-halogeno-5-pyridyl group, compounds **1a**,**b** are promising building blocks for the synthesis of new silicon-based drugs. The synthetic potential of **1a** has been exemplarily demonstrated by the Suzuki−Miyaura cross-coupling reaction with 4-bromophenol to give the (1,1′-biphenyl-4-yl)(2-halogeno-5-pyridyl)dimethylsilanes **2** and **6**.

Experimental Section

General Procedures. All syntheses were carried out under dry nitrogen. The organic solvents used were dried and purified according to standard procedures and stored under dry nitrogen. A Büchi GKR-51 apparatus was used for the bulb-to-bulb distillations. Melting points were determined with a Büchi B-540 melting point apparatus using samples in sealed glass capillaries. The ^{1}H, ^{13}C, ^{11}B, ^{19}F, and ^{29}Si NMR spectra were recorded at 23 °C on a Bruker DRX-300 (^{1}H, 300.1 MHz; ^{13}C, 75.5 MHz; ^{29}Si, 59.6 MHz), Bruker Avance 400 (^{1}H, 400.1 MHz; ^{13}C, 100.6 MHz; ^{19}F, 376.5 MHz; ^{29}Si, 79.5 MHz), or Bruker Avance 500 NMR spectrometer (^{1}H, 500.1 MHz; ^{13}C, 125.8 MHz; ^{11}B, 160.5 MHz; ^{29}Si, 99.4 MHz). $CDCl_3$ or [D_6]DMSO was used as the solvent. Chemical shifts (ppm) were determined relative to internal $CHCl_3$ (^{1}H, δ 7.24; $CDCl_3$), internal $CDCl_3$ (^{13}C, δ 77.0; $CDCl_3$), internal [D_5]DMSO (^{1}H, δ 2.49; [D_6]DMSO), internal [D_6]DMSO (^{13}C, δ 39.5; [D_6]DMSO), external BF_3·Et_2O (^{11}B, δ 0; $CDCl_3$, [D_6]DMSO), external $CFCl_3$ (^{19}F, δ 0; $CDCl_3$, [D_6]DMSO), or external TMS (^{29}Si, δ 0; $CDCl_3$, [D_6]DMSO). Analysis and assignment of the ^{1}H NMR data were supported by ^{1}H,^{1}H COSY, ^{13}C,^{1}H HMQC, and ^{13}C,^{1}H HMBC experiments. Assignment of the ^{13}C NMR data was supported by DEPT 135, ^{13}C,^{1}H HMQC, and ^{13}C,^{1}H HMBC experiments.

Preparation of 4-((2-Fluoro-5-pyridyl)dimethylsilyl)phenylboronic Acid−Hemiacetone (1a·0.5MeC(O)Me). A solution of sodium periodate (7.20 g, 33.7 mmol) and ammonium acetate (2.60 g, 33.7 mmol) in water (300 mL) was added in a single portion at 20 °C to a stirred solution of **5a** (3.00 g, 8.40 mmol) in acetone (420 mL), and the resulting mixture was then stirred at 20 °C for 6 days. The organic solvent was removed under reduced pressure, and the aqueous solution was adjusted to pH 3 with 2 M hydrochloric acid. Ethyl acetate (400 mL) was added, the organic layer was separated, and the aqueous phase was extracted with ethyl acetate (2 × 400 mL). The organic extracts were combined, the solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (silica gel, 32−63 μm (ICN 02826); eluent, *n*-hexane/acetone (2:1 (v/v))) to afford a yellowish oily product, which was crystallized from *n*-hexane/acetone/water (30:10:1 (v/v/v)) (82 mL; crystallization at 20 °C over a period of 8 days by slow evaporation of the solvent). The precipitate was isolated by filtration, washed with *n*-hexane (3 × 10 mL), and dried in vacuo (0.05 mbar, 20 °C, 6 h) to give **1a**·0.5MeC(O)Me in 75% yield as a colorless crystalline solid (1.92 g, 6.31 mmol); mp 73−74 °C. ^{1}H NMR (500.1 MHz, [D_6]DMSO): δ 0.57 (s, 6 H, SiCH_3), 2.07 (s, 3 H, CCH_3, $CH_3C(O)CH_3$), 7.14−7.16 (m, 1 H, *H*-3, C_5H_3N), 7.48−7.53 (m, 2 H, *H*-3/*H*-5, C_6H_4), 7.77−7.86 (m, 2 H, *H*-2/*H*-6, C_6H_4), 8.01−8.05 (m, 1 H, *H*-4, C_5H_3N), 8.1 (br. s, 2 H, BO*H*), 8.29−8.30 (m, 1 H, *H*-6, C_5H_3N). ^{13}C NMR (125.8 MHz, [D_6]DMSO): δ −3.0 (SiCH_3), 30.7 (CCH_3, $CH_3C(O)CH_3$), 109.3 (d, $^2J_{CF}$ = 35.2 Hz, *C*-3, C_5H_3N), 131.0 (d, $^4J_{CF}$ = 4.6 Hz, *C*-5, C_5H_3N), 132.8 (*C*-3/*C*-5, C_6H_4), 133.5 (*C*-2/*C*-6, C_6H_4), 138.5 (*C*-1, C_6H_4), 147.6 (d, $^3J_{CF}$ = 7.5 Hz, *C*-4, C_5H_3N), 152.5 (d, $^3J_{CF}$ = 13.7 Hz, *C*-6, C_5H_3N), 164.0 (d, $^1J_{CF}$ = 236.9 Hz, *C*-2, C_5H_3N), 206.4 (*C*═O, $CH_3C(O)CH_3$), B*C* not detected. ^{11}B NMR (160.5 MHz, [D_6]DMSO): δ 27.2. ^{19}F NMR (376.5 MHz, [D_6]DMSO): δ −67.6. ^{29}Si NMR (99.4 MHz, [D_6]DMSO): δ −8.5 (d, $^5J_{SiF}$ = 1.8 Hz). Anal. Calcd for

$C_{13}H_{15}BFNO_2Si \cdot 0.5C_3H_6O$: C, 57.25; H, 5.96; N, 4.60. Found: C, 57.08; H, 5.82; N, 4.66.

Preparation of 4-((2-Chloro-5-pyridyl)dimethylsilyl)phenylboronic Acid (1b). A solution of sodium periodate (13.7 g, 64.1 mmol) and ammonium acetate (5.00 g, 64.9 mmol) in water (600 mL) was added in a single portion at 20 °C to a stirred solution of **5b** (6.00 g, 16.1 mmol) in acetone (840 mL), and the resulting mixture was then stirred at 20 °C for 10 days. The organic solvent was removed under reduced pressure, and the aqueous solution was adjusted to pH 3 with 2 M hydrochloric acid. Ethyl acetate (600 mL) was added, the organic layer was separated, and the aqueous phase was extracted with ethyl acetate (2 × 600 mL). The organic extracts were combined, the solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (silica gel, 32−63 μm (ICN 02826); eluent, *n*-hexane/acetone (2:1 (v/v))) to afford a solid product, which was recrystallized from *n*-hexane/acetone/water (700:300:1 (v/v/v)) (100 mL; crystallization at 20 °C over a period of 10 days by slow evaporation of the solvent). The precipitate was isolated by filtration, washed with *n*-hexane (2 × 10 mL), and dried in vacuo (0.05 mbar, 20 °C, 3 h) to give **1b** in 75% yield as a colorless crystalline solid (3.49 g, 12.0 mmol); mp 185−186 °C. ^{1}H NMR (500.1 MHz, [D$_6$]DMSO): δ 0.57 (s, 6 H, SiC*H*$_3$), 7.47−7.53 (m, 3 H, *H*-3/*H*-5, C_6H_4, *H*-3, C_5H_3N), 7.77−7.86 (m, 2 H, *H*-2/*H*-6, C_6H_4), 7.88 (dd, $^3J_{HH}$ = 8.0 Hz, $^4J_{HH}$ = 2.1 Hz, 1 H, *H*-4, C_5H_3N), 8.1 (br s, 2 H, BO*H*), 8.45 (dd, $^4J_{HH}$ = 2.1 Hz, $^5J_{HH}$ = 0.7 Hz, 1 H, *H*-6, C_5H_3N). ^{13}C NMR (125.6 MHz, [D$_6$]DMSO): δ −3.1 (Si*C*H$_3$), 123.9 (*C*-3, C_5H_3N), 132.4 (*C*-5, C_5H_3N), 132.9 (*C*-3/*C*-5, C_6H_4), 133.5 (*C*-2/*C*-6, C_6H_4), 138.2 (*C*-1, C_6H_4), 145.1 (*C*-4, C_5H_3N), 151.6 (*C*-2, C_5H_3N), 154.4 (*C*-6, C_5H_3N), B*C* not detected. ^{11}B NMR (160.5 MHz, [D$_6$]DMSO): δ 27.6. ^{29}Si NMR (99.4 MHz, [D$_6$]DMSO): δ −8.3. Anal. Calcd for $C_{13}H_{15}BClNO_2Si$: C, 53.54; H, 5.18; N, 4.80. Found: C, 53.51; H, 5.10; N, 4.80.

Preparation of (2-Fluoro-5-pyridyl)(4′-hydroxy-(1,1′-biphenyl)-4-yl)dimethylsilane (2) and ((1,1′-Biphenyl)-4-yl)(2-fluoro-5-pyridyl)dimethylsilane (6). A 2 M aqueous solution of sodium carbonate (1.7 mL) was added to a suspension of **1a**·0.5$CH_3C(O)CH_3$ (300 mg, 986 μmol), 4-bromophenol (358 mg, 2.07 mmol), and tetrakis(triphenylphosphine)palladium(0) (72.0 mg, 62.3 μmol) in 1,2-dimethoxyethane (5 mL), and the resulting mixture was heated under reflux for 23 h. Ethyl acetate (25 mL) and 2 M hydrochloric acid (25 mL) were added, the organic layer was separated, and the aqueous phase was extracted with ethyl acetate (3 × 25 mL). The organic extracts were combined and dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel (silica gel, 32−63 μm (ICN 02826); eluent, *n*-hexane/ethyl acetate (2:1 (v/v))). The relevant first fractions (GC control) were combined, and the solvent was removed under reduced pressure to give **6** in 55% yield as a colorless solid (166 mg, 540 μmol); mp 81−82 °C. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 0.61 (s, 6 H, SiC*H*$_3$), 6.91−6.92 (m, 1 H, *H*-3, C_5H_3N), 7.34−7.37 (m, 1 H, *H*-4′, C_6H_5), 7.42−7.46 (m, 2 H, *H*-3′/*H*-5′, C_6H_5), 7.56−7.61 (m, 6 H, *H*-2/*H*-3/*H*-5/*H*-6, SiC_6H_4, *H*-2′/*H*-6′, C_6H_5), 7.85−7.89 (m, 1 H, *H*-4, C_5H_3N), 8.33−8.34 (m, 1 H, *H*-6, C_5H_3N). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ −2.5 (Si*C*H$_3$), 109.3 (d, $^2J_{CF}$ = 35.2 Hz, *C*-3, C_5H_3N), 126.8 (*C*-2/*C*-6, SiC_6H_4), 127.1 (*C*-2′/*C*-6′, C_6H_5), 127.6 (*C*-4′, C_6H_5), 128.8 (*C*-3′/*C*-5′, C_6H_5), 130.7 (d, $^4J_{CF}$ = 4.6 Hz, *C*-5, C_5H_3N), 134.5 (*C*-3/*C*-5, SiC_6H_4), 135.2 (*C*-4, SiC_6H_4), 140.7 (*C*-1′, C_6H_5), 142.4 (*C*-1, SiC_6H_4), 146.9 (d, $^3J_{CF}$ = 7.0 Hz, *C*-4, C_5H_3N), 153.0 (d, $^3J_{CF}$ = 10.5 Hz, *C*-6, C_5H_3N), 164.6 (d, $^1J_{CF}$ = 242.1 Hz, *C*-2, C_5H_3N). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −66.9. ^{29}Si NMR (99.4 MHz, $CDCl_3$): δ −8.2 (d, $^5J_{SiF}$ = 1.8 Hz). Anal. Calcd for $C_{19}H_{18}FNSi$: C, 74.23; H, 5.90; N, 4.56. Found: C, 74.10; H, 5.96; N, 4.66.

Upon further elution with *n*-hexane/ethyl acetate (2:1 (v/v)), the relevant fractions (GC control) were combined, and the solvent was removed under reduced pressure to give **2** in 45% yield as a colorless solid (145 mg, 448 μmol); mp 132−133 °C. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 0.60 (s, 6 H, SiC*H*$_3$), 6.2 (br. s, 1 H, O*H*), 6.90−6.94 (m, 3 H, *H*-3, C_5H_3N, *H*-3′/*H*-5′, C_6H_4OH), 7.44−7.47 (m, 2 H, *H*-2′/*H*-6′, C_6H_4OH), 7.51−7.55 (m, 4 H, *H*-2/*H*-3/*H*-5/*H*-6, SiC_6H_4), 7.87−7.91 (m, 1 H, *H*-4, C_5H_3N), 8.31−8.32 (m, 1 H, *H*-6, C_5H_3N). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ −2.5 (Si*C*H$_3$), 109.4 (d, $^2J_{CF}$ = 34.1 Hz, *C*-3, C_5H_3N), 115.8 (*C*-3′/*C*-5′, C_6H_4OH), 126.3 (*C*-2/*C*-6, SiC_6H_4), 128.3 (*C*-2′/*C*-6′, C_6H_4OH), 131.1 (d, $^4J_{CF}$ = 4.8 Hz, *C*-5, C_5H_3N), 133.1 (*C*-4, SiC_6H_4), 134.1 (*C*-1′, C_6H_4OH), 134.5 (*C*-3/*C*-5, SiC_6H_4), 142.1 (*C*-1, SiC_6H_4), 147.3 (d, $^3J_{CF}$ = 7.5 Hz, *C*-4, C_5H_3N), 152.7 (d, $^3J_{CF}$ = 12.6 Hz, *C*-6, C_5H_3N), 155.8 (*C*-4′, C_6H_4OH), 164.5 (d, $^1J_{CF}$ = 242.1 Hz, *C*-2, C_5H_3N). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −67.5. ^{29}Si NMR (99.4 MHz, $CDCl_3$): δ −8.2 (d, $^5J_{SiF}$ = 1.8 Hz). Anal. Calcd for $C_{19}H_{18}FNOSi$: C, 70.56; H, 5.61; N, 4.33. Found: C, 70.22; H, 5.68; N, 4.11.

Preparation of (2-Fluoro-5-pyridyl)methoxydimethylsilane (3a). A 2.5 M solution of *n*-butyllithium in hexanes (28.4 mL, 71.0 mmol of *n*-BuLi) was added dropwise at −70 °C (±5 °C, temperature measurement within the flask) within 3 h to a stirred mixture of dimethoxydimethylsilane (12.8 g, 106 mmol), 5-bromo-2-fluoropyridine (12.5 g, 71.0 mmol), and diethyl ether (120 mL) (the *n*-butyllithium solution was added via a special horizontally elongated side neck of the three-necked flask, which itself was immersed in the cooling bath to ensure precooling of the *n*-butyllithium solution before making contact with the reaction mixture). After the addition was complete, the resulting mixture was stirred at −75 °C for 5 h and then warmed to 20 °C within 17 h. The precipitate was removed by filtration, washed with diethyl ether (2 × 20 mL), and discarded. The filtrate and washings were combined, the solvent was removed under reduced pressure, and the residue was purified by fractional distillation to give **3a** in 52% yield as a colorless liquid (6.87 g, 37.1 mmol); bp 96 °C/10 mbar. ^{1}H NMR (400.1 MHz, $CDCl_3$): δ 0.36 (s, 6 H, SiC*H*$_3$), 3.41 (s, 3 H, OC*H*$_3$), 6.89−6.92 (m, 1 H, *H*-3, C_5H_3N), 7.87−7.92 (m, 1 H, *H*-4, C_5H_3N), 8.29−8.30 (m, 1 H, *H*-6, C_5H_3N). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ −2.3 (Si*C*H$_3$), 50.6 (O*C*H$_3$), 109.3 (d, $^2J_{CF}$ = 34.9 Hz, *C*-3, C_5H_3N), 129.9 (d, $^4J_{CF}$ = 4.7 Hz, *C*-5, C_5H_3N), 146.3 (d, $^3J_{CF}$ = 7.3 Hz, *C*-4, C_5H_3N), 152.5 (d, $^3J_{CF}$ = 13.4 Hz, *C*-6, C_5H_3N), 164.8 (d, $^1J_{CF}$ = 241.2 Hz, *C*-2, C_5H_3N). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −66.1. ^{29}Si NMR (59.6 MHz, $CDCl_3$): δ 9.0 (d, $^5J_{SiF}$ = 1.8 Hz). Anal. Calcd for $C_8H_{12}FNOSi$: C, 51.86; H, 6.53; N, 7.56. Found: C, 51.47; H, 6.40; N, 7.99.

Preparation of (2-Chloro-5-pyridyl)methoxydimethylsilane (3b). A 2.5 M solution of *n*-butyllithium in hexanes (30 mL, 75.0 mmol of *n*-BuLi) was added dropwise at −70 °C (±5 °C, temperature measurement within the flask) within 2 h to a stirred mixture of dimethoxydimethylsilane (10.2 g, 84.8 mmol), 5-bromo-2-chloropyridine (10.9 g, 56.6 mmol), and diethyl ether (130 mL) (the *n*-butyllithium solution was added via a special horizontally elongated side neck of the three-necked flask, which itself was immersed in the cooling bath to ensure precooling of the *n*-butyllithium solution before making contact with the reaction mixture). After the addition was complete, the mixture was stirred at −70 °C for 5 h and then warmed to 20 °C within 15 h. The precipitate was removed by filtration, washed with diethyl ether (5 × 20 mL), and discarded. The filtrate and washings were combined, the solvent was removed under reduced pressure, and the residue was purified by bulb-to-bulb distillation (80−85 °C/0.09 mbar) to give **3b** in 60% yield as a colorless liquid (6.86 g, 34.0 mmol). ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 0.35 (s, 6 H, SiC*H*$_3$), 3.40 (s, 3 H, OC*H*$_3$), 7.28 (dd, $^3J_{HH}$ = 7.9 Hz, $^5J_{HH}$ = 0.9 Hz, 1 H, *H*-3, C_5H_3N), 7.73 (dd, $^3J_{HH}$ = 7.9 Hz, $^4J_{HH}$ = 2.0 Hz, 1 H, *H*-4, C_5H_3N), 8.44 (dd, $^4J_{HH}$ = 2.0 Hz, $^5J_{HH}$ = 0.9 Hz, 1 H, *H*-6, C_5H_3N). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ −2.3 (Si*C*H$_3$), 50.7 (O*C*H$_3$), 123.9 (*C*-3, C_5H_3N), 131.1 (*C*-5, C_5H_3N), 143.7 (*C*-4, C_5H_3N), 153.0 (*C*-2, C_5H_3N), 154.0 (*C*-6, C_5H_3N). ^{29}Si NMR (99.4 MHz, $CDCl_3$): δ

8.8. Anal. Calcd for $C_8H_{12}ClNOSi$: C, 47.63; H, 6.00; N, 6.94. Found: C, 47.87; H, 5.93; N, 7.34.

Preparation of (4-Bromophenyl)(2-fluoro-5-pyridyl)dimethylsilane (4a). A 2.5 M solution of *n*-butyllithium in hexanes (4.7 mL, 11.8 mmol of *n*-BuLi) was added dropwise at −70 °C within 20 min to a stirred solution of 1,4-dibromobenzene (2.77 g, 11.7 mmol) in diethyl ether (35 mL). After the addition was complete, the mixture was stirred at −75 °C for 2 h. Subsequently, a solution of **3a** (2.19 g, 11.8 mmol) in diethyl ether (10 mL) was added dropwise at −75 °C within 1 h, and the resulting mixture was stirred at −75 °C for 30 min and then warmed to 20 °C within 18 h. Water (45 mL) was added, the organic layer was separated, and the aqueous phase was extracted with diethyl ether (3 × 40 mL). The organic extracts were combined and dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure, and the residue was purified by bulb-to-bulb distillation (150 °C/0.1 mbar) to give **4a** in 74% yield as a colorless liquid (2.71 g, 8.74 mmol). ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 0.55 (s, 6 H, SiCH_3), 6.86−6.90 (m, 1 H, *H*-3, C_5H_3N), 7.31−7.34 (m, 2 H, *H*-3/*H*-5, C_6H_4), 7.46−7.49 (m, 2 H, *H*-2/*H*-6, C_6H_4), 7.77−7.81 (m, 1 H, *H*-4, C_5H_3N), 8.24−8.25 (m, 1 H, *H*-6, C_5H_3N). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ −2.7 (SiCH_3), 109.3 (d, $^2J_{CF}$ = 34.9 Hz, *C*-3, C_5H_3N), 124.5 (*C*-1, C_6H_4), 130.0 (d, $^4J_{CF}$ = 4.7 Hz, *C*-5, C_5H_3N), 131.2 (*C*-2/*C*-6, C_6H_4), 135.3 (*C*-4, C_6H_4), 135.5 (*C*-3/*C*-5, C_6H_4), 146.8 (d, $^3J_{CF}$ = 7.3 Hz, *C*-4, C_5H_3N), 152.9 (d, $^3J_{CF}$ = 13.4 Hz, *C*-6, C_5H_3N), 164.6 (d, $^1J_{CF}$ = 240.9 Hz, *C*-2, C_5H_3N). ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −66.6. ^{29}Si NMR (59.6 MHz, $CDCl_3$): δ −7.5 (d, $^5J_{SiF}$ = 1.8 Hz). Anal. Calcd for $C_{13}H_{13}BrFNSi$: C, 50.33; H, 4.22; N, 4.51. Found: C, 50.52; H, 4.49; N, 4.91.

Preparation of (4-Bromophenyl)(2-chloro-5-pyridyl)dimethylsilane (4b). A 2.5 M solution of *n*-butyllithium in hexanes (18 mL, 45.0 mmol of *n*-BuLi) was added dropwise at −70 °C within 45 min to a stirred solution of 1,4-dibromobenzene (10.5 g, 44.5 mmol) in diethyl ether (110 mL). After the addition was complete, the mixture was stirred at −70 °C for 2 h. Subsequently, a solution of **3b** (9.00 g, 44.6 mmol) in diethyl ether (40 mL) was added dropwise at −70 °C within 2 h, and the resulting mixture was stirred at −70 °C for 30 min and then warmed to 20 °C within 19 h. Water (160 mL) was added, the organic layer was separated, and the aqueous phase was extracted with diethyl ether (3 × 120 mL). The organic extracts were combined and dried over anhydrous sodium sulfate, and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel (silica gel, 32−63 μm (ICN 02826); eluent, *n*-hexane/ethyl acetate (9:1 (v/v))) to afford **4b** in 71% yield as a yellowish crystalline solid (10.4 g, 31.8 mmol); mp 65−66 °C. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ 0.55 (s, 6 H, SiCH_3), 7.27 (dd, $^3J_{HH}$ = 7.9 Hz, $^5J_{HH}$ = 0.9 Hz, 1 H, *H*-3, C_5H_3N), 7.30−7.34 (m, 2 H, *H*-3/*H*-5, C_6H_4), 7.47−7.51 (m, 2 H, *H*-2/*H*-6, C_6H_4), 7.64 (dd, $^3J_{HH}$ = 7.9 Hz, $^4J_{HH}$ = 2.1 Hz, 1 H, *H*-4, C_5H_3N), 8.40 (dd, $^4J_{HH}$ = 2.1 Hz, $^5J_{HH}$ = 0.9 Hz, 1 H, *H*-6, C_5H_3N). ^{13}C NMR (75.5 MHz, $CDCl_3$): δ −2.7 (SiCH_3), 124.0 (*C*-3, C_5H_3N), 124.7 (*C*-1, C_6H_4), 131.3 (*C*-2/*C*-6, C_6H_4), 131.4 (*C*-5, C_5H_3N), 135.0 (*C*-4, C_6H_4), 135.5 (*C*-3/*C*-5, C_6H_4), 144.3 (*C*-4, C_5H_3N), 152.9 (*C*-2, C_5H_3N), 154.5 (*C*-6, C_5H_3N). ^{29}Si NMR (59.6 MHz, $CDCl_3$): δ −7.2. Anal. Calcd for $C_{13}H_{13}BrClNSi$: C, 47.79; H, 4.01; N, 4.29. Found: C, 47.80; H, 3.93; N, 4.31.

Preparation of (2-Fluoro-5-pyridyl)dimethyl(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)silane (5a). A 1.6 M solution of *tert*-butyllithium in *n*-pentane (43.5 mL, 69.6 mmol of *t*-BuLi) was added dropwise at −75 °C within 90 min to a stirred solution of **4a** (16.7 g, 53.8 mmol) in tetrahydrofuran (310 mL), and the mixture was stirred at this temperature for 2 h. Subsequently, 4,4,5,5-tetramethyl-2-propyloxy-1,3,2-dioxaborolane[11] (12.9 g, 69.3 mmol) was added dropwise at −75 °C within 30 min, and the mixture was stirred at this temperature for 2 h and then warmed to 20 °C within 18 h. The solvent was removed under reduced pressure, diethyl ether (400 mL) and water (400 mL) were added, the organic layer was separated, and the aqueous phase was extracted with diethyl ether (3 × 400 mL). The organic extracts were combined and dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure, the solid residue was recrystallized from boiling *n*-hexane (90 mL; crystallization at −20 °C over a period of 24 h), and the precipitate was isolated by filtration and washed with cold (0 °C) *n*-hexane (40 mL). This purification step was repeated three times, followed by drying of the product in vacuo (11 mbar, 20 °C, 2 h) to give **5a** in 57% yield (11.0 g, 30.8 mmol) as a colorless crystalline solid; mp 131−132 °C. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 0.56 (s, 6 H, SiCH_3), 1.32 (s, 12 H, CCH_3), 6.85−6.88 (m, 1 H, *H*-3, C_5H_3N), 7.48−7.50 (m, 2 H, *H*-3/*H*-5, C_6H_4), 7.77−7.81 (m, 3 H, *H*-2/*H*-6, C_6H_4, *H*-4, C_5H_3N), 8.26−8.27 (m, 1 H, *H*-6, C_5H_3N). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ −2.6 (SiCH_3), 24.8 (CCH_3), 83.9 (*C*CH_3), 109.2 (d, $^2J_{CF}$ = 34.9 Hz, *C*-3, C_5H_3N), 130.5 (d, $^4J_{CF}$ = 4.8 Hz, *C*-5, C_5H_3N), 133.3 (*C*-3/*C*-5, C_6H_4), 134.1 (*C*-2/*C*-6, C_6H_4), 140.0 (*C*-1, C_6H_4), 146.9 (d, $^3J_{CF}$ = 7.3 Hz, *C*-4, C_5H_3N), 153.0 (d, $^3J_{CF}$ = 13.4 Hz, *C*-6, C_5H_3N), 164.6 (d, $^1J_{CF}$ = 240.7, *C*-2, C_5H_3N), B*C* not detected. ^{11}B NMR (160.5 MHz, $CDCl_3$): δ 30.1. ^{19}F NMR (376.5 MHz, $CDCl_3$): δ −67.0. ^{29}Si NMR (99.4 MHz, $CDCl_3$): δ −8.2 (d, $^5J_{SiF}$ = 1.8 Hz). Anal. Calcd for $C_{19}H_{25}BFNO_2Si$: C, 63.87; H, 7.05; N, 3.92. Found: C, 63.65; H, 7.01; N, 4.09.

Preparation of (2-Chloro-5-pyridyl)dimethyl(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)silane (5b). A 1.6 M solution of *tert*-butyllithium in *n*-pentane (25 mL, 40.0 mmol of *t*-BuLi) was added dropwise at −75 °C within 90 min to a stirred solution of **4b** (10.3 g, 31.5 mmol) in tetrahydrofuran (220 mL), and the mixture was stirred at this temperature for 2 h. Subsequently, 4,4,5,5-tetramethyl-2-propyloxy-1,3,2-dioxaborolane[11] (7.60 g, 40.8 mmol) was added dropwise at −75 °C within 30 min, and the mixture was stirred at this temperature for 2 h and then warmed to 20 °C within 18 h. The solvent was removed under reduced pressure, diethyl ether (240 mL) and water (240 mL) were added, the organic layer was separated, and the aqueous phase was extracted with diethyl ether (3 × 240 mL). The organic extracts were combined and dried over anhydrous sodium sulfate, the solvent was removed under reduced pressure, the solid residue was recrystallized from boiling *n*-hexane (200 mL; crystallization at −20 °C over a period of 24 h), and the precipitate was isolated by filtration and washed with cold (0 °C) *n*-hexane (30 mL). The product was dried in vacuo (0.05 mbar, 20 °C, 4 h) to give **5b** in 80% yield (9.38 g, 25.1 mmol) as a yellowish crystalline solid; mp 155−156 °C. ^{1}H NMR (500.1 MHz, $CDCl_3$): δ 0.56 (s, 6 H, SiCH_3), 1.32 (s, 12 H, CCH_3), 7.25 (dd, $^3J_{HH}$ = 7.9 Hz, $^5J_{HH}$ = 0.8 Hz, 1 H, *H*-3, C_5H_3N), 7.47−7.49 (m, 2 H, *H*-3/*H*-5, C_6H_4), 7.64 (dd, $^3J_{HH}$ = 7.9 Hz, $^4J_{HH}$ = 2.0 Hz, 1 H, *H*-4, C_5H_3N), 7.78−7.79 (m, 2 H, *H*-2/*H*-6, C_6H_4), 8.42 (dd, $^4J_{HH}$ = 2.0 Hz, $^5J_{HH}$ = 0.8 Hz, 1 H, *H*-6, C_5H_3N). ^{13}C NMR (125.8 MHz, $CDCl_3$): δ −2.7 (SiCH_3), 24.8 (CCH_3), 83.9 (*C*CH_3), 123.9 (*C*-3, C_5H_3N), 131.9 (*C*-5, C_5H_3N), 133.3 (*C*-3/*C*-5, C_6H_4), 134.2 (*C*-2/*C*-6, C_6H_4), 139.7 (*C*-1, C_6H_4), 144.4 (*C*-4, C_5H_3N), 152.7 (*C*-2, C_5H_3N), 154.7 (*C*-6, C_5H_3N), B*C* not detected. ^{11}B NMR (160.5 MHz, $CDCl_3$): δ 30.1. ^{29}Si NMR (99.4 MHz, $CDCl_3$): δ −7.9. Anal. Calcd for $C_{19}H_{25}BClNO_2Si$: C, 61.06; H, 6.74; N, 3.75. Found: C, 61.33; H, 6.78; N, 3.78.

Crystal Structure Analyses. Suitable single crystals of **1a**·0.5MeC(O)Me, **1b**, **2, 4b**, and **5a** were obtained by crystallization at 20 °C from *n*-hexane/acetone/water (30:10:1 (v/v/v) (**1a**); 700:300:1 (v/v/v) (**1b**)), at 20 °C from *n*-hexane/diethyl ether (1:2 (v/v) (**2**)), at 20 °C from *n*-hexane (**4b**), and at −20 °C from *n*-hexane (**5a**), respectively. The crystals were mounted in inert oil (perfluoropolyalkyl ether, ABCR) on a glass fiber and then transferred to the cold nitrogen gas stream of the diffractometer (**1a**·0.5MeC(O)Me, **2**, and **5a**, Stoe IPDS, graphite-monochromated Mo Kα radiation (λ = 0.710 73 Å); **1b** and **4b**, Bruker-Nonius Kappa-APEX2 CCD system with Göbel mirror, Mo Kα radiation

($\lambda = 0.710\ 73$ Å)). The structures were solved by direct methods.[15] All non-hydrogen atoms were refined anisotropically.[16] A riding model was employed in the refinement of the hydrogen atoms.

Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with The Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-729170 (**1a**·0.5MeC(O)Me), CCDC-729171 (**1b**), CCDC-729172 (**2**), CCDC-729173 (**4b**), and CCDC-729174 (**5a**). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax, (+44)1223/336033; e-mail, deposit@ccdc.cam.ac.uk).

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Supporting Information Available: Figures, tables, and CIF files, the latter giving atomic coordinates and equivalent isotropic displacement parameters, anisotropic displacement parameters, experimental details of the X-ray diffraction studies, and bond lengths and angles of **1a**·0.5MeC(O)Me, **1b**, **2**, **4b**, and **5a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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