Supporting Information

for

Synthesis of Pyrrolnitrin and Related Halogenated Phenylpyrroles

by

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GENERAL METHODS

NMR spectra were obtained on a Bruker Avance-300, Avance-400, or Avance-500 spectrometer and referenced to the deuterated solvent as indicated. High resolution mass spectra were obtained on a Waters / Micromass GCT mass spectrometer in EI mode. THF was dried with a Solvent Purification System from PureSolv. Butyllithiums (n- and t-) were purchased from Sigma-Aldrich and stored in septum-sealed containers under nitrogen atmosphere. For low temperature measurements, a Digi-Sense Dual JTEK Thermocouple Thermometer was used. All experiments were carried out under nitrogen in oven dried glassware, using syringe-septum cap techniques. Flash column chromatography was carried out using Silicycle Ultra Pure Silica Gel (particle size: 40-63 µm).

GENERAL PROCEDURES

General Procedure 1. Preparation of 2,6-Dihalobenzoic acids. To a solution of n-BuLi (1.4 equiv) in dry THF (2.0 mL/mmol dihalobenzene) at 0°C was added diisopropylamine (DIPA, 1.5 equiv), and the mixture was stirred at this temperature for 15 min before cooling to either -78°C (acetone/CO₂) or -100°C (ethyl ether/CO₂). To the mixture was added the dihalobenzene (1.0 equiv) dropwise while maintaining the temperature. After 1 h of reaction time, CO₂ was added subsurface via syringe/needle (place dry ice pellet in empty 10 mL syringe and plug needle with septum to accumulate CO₂ gas) The addition of CO₂ was continued until ΔT < 0.2°C, and the reaction was then left to warm to room temperature (ca. 2 h). The mixture was diluted with water (5–10 mL) and transferred to a separatory funnel where the mixture was extracted with sodium hydroxide (NaOH, 0.1 N, 3 x 10–20 mL). The aqueous layers were collected and then back-extracted with EtOAc (10–20 mL). This organic layer was discarded. The aqueous layer was
then acidified to pH 1 using 6 N hydrochloric acid (HCl), and subsequently extracted with EtOAc (3 x 10–20 mL). This organic layer was washed with sodium chloride (NaCl, 10–20 mL), dried over MgSO₄, and concentrated in vacuo to afford the product in high purity.

**General Procedure 2. Preparation of 2,6-Dihaloanilines.** A solution of 2,6-dihalobenzoic acid (1.0 equiv) in concentrated sulfuric acid (H₂SO₄, 2.5 mL/mmol dihalobenzoic acid) was heated to 60°C for 1.5 h. The solution was then cooled to rt before addition of sodium azide (NaN₃). The resulting mixture was left to stir at rt for 42 h before cooling to 0°C and basifying with concentrated ammonium hydroxide (NH₄OH). The organics were extracted with ethyl acetate (EtOAc, 3 x 10–20 mL). The organic layers were combined and washed with saturated sodium chloride (NaCl, 1 x 10–20 mL), dried with magnesium sulfate (MgSO₄) and concentrated under reduced pressure to afford the crude product.

**General Procedure 3. Preparation of 2,6-Dihalonitrobenzenes.** To a solution of 2,6-dihaloaniline (1.0 equiv) in anhydrous dichloroethane (DCE, 2.0 mL/mmol dihaloaniline) was added *meta*-chloroperbenzoic acid (*m*-CPBA, 4.0 equiv). The resulting mixture was heated at 70°C for 2 h (monitored reaction progress by TLC and GC/MS) while the reaction vessel was wrapped in aluminum foil to minimize light exposure. After the 2 h reaction period, the mixture was diluted with EtOAc (5 mL), transferred to a separatory funnel and extracted with 0.1 N NaOH (3–5 x 10–20 mL) to remove residual perbenzoic and benzoic acids. After rinsing with brine (10–20 mL), and drying over MgSO₄, the organic phase was concentrated in vacuo to yield the crude product.
**General Procedure 4. Preparation of TIPS-Protected Phenylpyrroles by Suzuki-Miyaura Cross-Coupling.** In an over-dried Schlenk flask, the solid starting materials were combined: phenyl halide (1.0 equiv), \( N \)-(TIPS)pyrrole pinacol boronate (1.2 equiv), palladium acetate \([\text{Pd(OAc)}_2, \ 0.05 \text{ equiv}]\), 2-Dicyclohexyl-phosphino-2',6'-dimethoxybiphenyl (SPhos, 0.10 equiv), and potassium phosphate (\( \text{K}_3\text{PO}_4, \ 2.0 \text{ equiv} \)). Note: when one of the starting materials was an oil at room temperature, it was dissolved in reaction solvent (e.g. \( n \)-butanol) and added with the rest of the solvent at a later stage. The Schlenk flask containing the solid materials was evacuated and back-filled with nitrogen (3 times), followed by addition of the solvent system (2.0 mL/mmol aryl halide), consisting of degassed \( n \)-butanol (\( n \)-BuOH) and degassed deionized water in the ratio of 2.5:1. The resulting mixture was heated at 35°C for 12 h. The crude reaction mixture was then filtered through a plug of silica gel using EtOAc eluent and concentrated in vacuo. Purification by column chromatography over deactivated silica gel (5% triethylamine, NEt₃) provided the desired TIPS-protected phenylpyrrole.

**General Procedure 5. Preparation of Iodinated \( N \)-(TIPS)pyrroles.** To a solution of the starting \( N \)-(TIPS)pyrrole (1.0 equiv) in acetone (2.0 mL/mmol SM) was added \( N \)-iodosuccinimide (NIS, 1.0 equiv). The reaction flask was covered in aluminum foil and the mixture was stirred at room temperature for 7–12 h. Note: on TLC plates, the iodinated products often had a very similar \( R_f \) to the starting material, so it was useful to monitor the reaction progress by GC-MS. To do this, a pipette tip full of reaction mixture was filtered through a micro-plug of cotton and silica in a separate pipette using EtOAc eluent. Once the reaction had finished, the crude mixture was reduced in vacuo. The product was then taken up in either hexane or pentane, filtered through a plug of neutral alumina, and concentrated in vacuo to give the product in high purity.
General Procedure 6. Preparation of Brominated N-(TIPS)pyrroles. To a solution of the starting N-(TIPS)pyrrole (1.0 equiv) in THF (2.0 mL/mmol SM) at -78°C was added N-bromosuccinimide (NBS, 1.0 equiv). While the reaction mixture remained exposed to light and air, stirring was continued at -78°C for 1–2 h. Note: on TLC plates, the brominated products often had a very similar R_f to the starting material, so it was useful to monitor the reaction progress by GC-MS. To do this, a pipette tip full of reaction mixture was filtered through a micro-plug of cotton and silica in a separate pipette using EtOAc as eluent. Once the reaction had finished, the crude mixture was reduced in vacuo. The product was then taken up in either hexane or pentane, filtered through a plug of neutral alumina, and concentrated in vacuo to yield crude product.

General Procedure 7. Metalation of Halogenated N-(TIPS)pyrroles. To a solution of 3-X-N-(TIPS)pyrrole (1.0 equiv, X = Br or I) in THF (2.0 mL/mmol SM) at -78°C, was added t-BuLi (2.05 equiv of a 1.7 M solution in hexanes) dropwise. This mixture was kept at -78°C for 0.5 h (X = I) or 1 h (X = Br). A solution of the electrophile (2.0 equiv) in THF (3.0 mL/mmol SM) was then added dropwise, and the resulting mixture was left to react at -78°C for 0.5 h before warming to RT (ca. 1 h). The reaction mixture was quenched with saturated ammonium chloride (NH₄Cl) solution and the resulting biphasic mixture was transferred to a separatory funnel. The organic and aqueous layers were separated and the aqueous layer was extracted with ethyl acetate. The organic layers were combined and washed with saturated sodium chloride, dried with magnesium sulfate (MgSO₄) and concentrated under reduced pressure to afford the crude product. The crude product was purified by column chromatography over deactivated silica gel (5% NEt₃) using pentane as the eluent.
**General Procedure 8. Preparation of N-(TIPS)pyrrole Pinacol Boronates.** In an oven-dried Schlenk flask, the solid SMs were combined: 3-X-N-(TIPS)pyrrole (1.0 equiv, X = Br or I), bis(acetonitrile)dichloropalladium(II) [PdCl₂(CH₃CN)₂, 0.03 equiv], and SPhos (0.09 equiv). Note: when one of the starting materials was an oil at room temperature, it was dissolved in reaction solvent (e.g. toluene) and added with the rest of the solvent at a later stage. The Schlenk flask containing the solid SMs was evacuated and back-filled with nitrogen (3 times), followed by addition of dry toluene (2.0 mL/mmol 3-X-N-(TIPS)pyrrole), degassed NEt₃ (2.5 equiv), and finally pinacol borane (HBPin, 1.2 equiv). The resulting mixture was heated at 90°C for ca. 3 h. The crude reaction mixture was then filtered through a plug of neutral alumina using EtOAc eluent and reduced in vacuo. Purification by column chromatography over deactivated silica gel (5% NEt₃) provided the desired N-(TIPS)pyrrole pinacol boronate. Note: column chromatography must be performed quickly to minimize product decomposition. It is helpful to use shorter and thicker column lengths of silica gel.

**General Procedure 9. Fluoride-Induced Desilylation of TIPS-Protected Phenylpyrroles.** To a solution of TIPS-protected phenylpyrrole (1.0 equiv) in THF (2.0 mL/mmol SM) at room temperature was added tetrabutylammonium fluoride (TBAF, 1.0 M in THF, 2.0 equiv) dropwise. With the reaction vessel was covered in aluminum foil to minimize light exposure, the mixture was stirred at room temperature for ca. 1 h (reaction progress monitored by TLC). The reaction mixture was quenched with saturated ammonium chloride (NH₄Cl) solution and the resulting biphasic mixture was transferred to a separatory funnel. The organic and aqueous layers were separated and the aqueous layer was extracted with ethyl acetate. The organic layers were combined and washed with saturated sodium chloride, dried with magnesium sulfate (MgSO₄)
and concentrated under reduced pressure to afford the crude product. Subsequent purification by column chromatography over deactivated silica gel (5% NEt₃) afforded the desilylated product.

3-Chloro-N-(TIPS)pyrrole (8)

Following General Procedure 7, 8 was prepared from 3-bromo-N-(TIPS)pyrrole (6.00 g, 19.9 mmol). The crude residue was purified by column chromatography, affording 8 as a colorless oil in 87% yield. ¹H NMR [400 MHz, (CD₃)₂CO] δ ppm 1.10 (d, J = 8.78 Hz, 18H), 1.58-1.47 (m, 3H), 6.21 (dd, J = 2.51, 1.75 Hz, 1H), 6.81 (dd, J = 3.09, 1.93 Hz, 2H); ¹³C NMR [400 MHz, (CD₃)₂CO] δ ppm 126.25, 122.60, 115.37, 112.51, 19.02, 13.12; HRMS (EI) m/z: calcd for C₁₃H₂₄ClNSi: 257.1367. Found: 257.1376.

3-Bromo-4-chloro-N-(TIPS)pyrrole (10)

Following General Procedure 6, 10 was prepared from 8 (2.50 g, 9.70 mmol). Recrystallization from methanol afforded 10 as a white solid in 85% yield. ¹H NMR [400 MHz, (CD₃)₂CO] δ ppm 1.12 (d, J = 7.5 Hz, 18H), 1.56 (td, J = 14.99, 7.51 Hz, 3H), 6.95 (t, J = 8.8, Hz, 2H); ¹³C NMR [400 MHz, (CD₃)₂CO] δ ppm 125.73, 123.43, 116.12, 99.97, 18.93, 12.93; HRMS (EI) m/z: calcd for C₁₃H₂₃BrClNSi: 335.0472. Found 335.0482.

3-Chloro-4-iodo-N-(TIPS)pyrrole (11)

Following General Procedure 5, 11 was prepared from 8 (2.50 g, 9.70 mmol). The title compound was a white solid. ¹H NMR [400 MHz, (CD₃)₂CO] δ ppm 1.12 (d, J = 8.78 Hz, 18H), 1.55 (tt, J = 7.34, 5.21 Hz, 3H), 6.97 (dd, J = 10.22, 2.46 Hz, 2H); ¹³C
NMR [400 MHz, (CD3)2CO] δ ppm 130.95, 123.28, 120.07, 67.99, 18.94, 12.94; HRMS (EI) m/z: calcd for C13H23ClINSi: 383.0333. Found 383.0344.


Following General Procedure 8, 12 was prepared from 3-chloro-4-iodo-N-(TIPS)pyrrole (4.45 g, 11.6 mmol). The crude residue was purified by column chromatography, affording 12 as an off-white solid in 80% yield. 1H NMR [400 MHz, (CD3)2CO] δ ppm 7.11 (d, J = 2.3, 1H), 6.85 (d, J = 2.3, 1H), 1.54 (dq, J = 7.5, 14.8, 3H), 1.11 (d, J = 7.5, 18H); 13C NMR [500 MHz, (CD3)2CO] δ ppm 135.68, 124.16, 120.94, 112.50, 84.46, 26.18, 19.00, 13.08; HRMS (EI) m/z: calcd for C19H35BClNO2Si: 383.2219. Found 383.2222.

2-Bromo-6-fluorobenzoic acid (13)

Following General Procedure 1, 13 was prepared from 1-bromo-3-fluorobenzene (2.23 g, 10.0 mmol). The white crystalline product was obtained in 92% yield. Found 217.9378. The analytical and spectral data were in accordance with those previously reported.2

2-Bromo-6-fluorobenzoic acid (14)

Following General Procedure 2, 14 was prepared from 1-bromo-3-fluorobenzene (860 mg, 4.5 mmol). The white crystalline product was obtained in 86% yield. 1H NMR [400 MHz, (CD3)2CO] δ 7.22 (dd, J = 1.0, 8.2, 1H), 7.00 (ddd, J = 0.9, 1.0, 8.2 Hz 1H), 6.57 (td, J = 5.5, 8.2, 1H), 4.86 (s, 2H) 13C NMR [400 MHz, (CD3)2CO] δ 164.08,
159.08 (d, J = 1000 Hz), 132.18 (d, J = 35 Hz), 128.75 (d, J = 14 Hz), 125.46 (d, J = 84 Hz),
119.14 (d, J = 19 Hz), 114.96 (d, J = 85 Hz); HRMS (EI) m/z: calcd for C7H5NFBr: 188.9589.
Found 188.9591.

2-Bromo-6-fluorobenzoic acid (15)

Following General Procedure 3, 15 was prepared from 1-bromo-3-fluorobenzene
(322 mg, 1.46 mmol). The white crystalline product was obtained in 88% yield.
1H NMR [400 MHz, CDCl3] δ 77.51 (dt, J = 1.1, 8.2 Hz, 1H), 7.40 (dt, J = 5.5,
8.3, 1H), 7.26(td, J = 1.1, 8.7 Hz, 1H). 13C NMR [400 MHz, CDCl3] δ 154.07 (d, J = 1036 Hz)
140.68 (d, J = 138 Hz), 132.26 (d, J = 33 Hz), 129.24 (d, J = 14 Hz), 116.38 (d, J = 76 Hz),
114.25; HRMS (EI) m/z: calcd for C6H3NO2FBr: 218.9318. Found 218.9321.

2-Bromo-6-chlorobenzoic acid (16)

Following General Procedure 1, 16 was prepared from 1-bromo-3-chlorobenzene
(5.00 g, 26.1 mmol). The off-white crystalline product was obtained in
quantitative yield. The analytical and spectral data were in accordance with those
previously reported.3

2-Bromo-6-chloroaniline (17)

Following General Procedure 2, 17 was prepared from 2-bromo-6-chlorobenzoic
acid (5.00 g, 24.2 mmol). The crude crystalline material was purified by column
chromatography, affording 17 as a light brown solid in 92% yield. 1H NMR [400
MHz, CDCl3] δ ppm 5.10 (s, 2H), 6.58 (t, J = 8.00 Hz, 1H), 7.26 (dd, J = 7.97, 1.16 Hz, 1H),
7.38 (dd, \( J = 8.01, 1.19 \) Hz, 1H); \(^{13}\)C NMR [500 MHz, CDCl\(_3\)] \( \delta \) ppm 143.86, 133.05, 130.45, 120.38, 119.97, 110.20; HRMS (EI) \( m/z \): calcd for C\(_6\)H\(_5\)BrClN: 204.9294. Found 204.9295.

2-Bromo-6-chloronitrobenzene (18)

Following General Procedure 3, 18 was prepared from 2-bromo-6-aniline (5.00 g, 21.2 mmol). The crude crystalline material was purified by column chromatography, affording 18 as an orange solid in 94% yield. \(^1\)H NMR [400 MHz, CDCl\(_3\)] \( \delta \) ppm 7.61 (dd, \( J = 1.1, 8.1 \) Hz, 1H), 7.50 (dd, \( J = 1.1, 8.2 \) Hz, 1H), 7.33 (t, \( J = 8.2 \) Hz, 1H); \(^{13}\)C NMR [500 MHz, (CD\(_3\))\(_2\)CO] \( \delta \) ppm 151.65, 134.52, 134.48, 131.93, 127.19, 115.02; HRMS (EI) \( m/z \): calcd for C\(_6\)H\(_5\)BrClNO\(_2\): 234.9036. Found 234.9047.

2,6-Dibromobenzoic acid (19)

Following General Procedure 1, 19 was prepared from 1,3-dibromobenzene (3.00 g, 12.7 mmol). The off-white crystalline product was obtained in 85% yield. The analytical and spectral data were in accordance with those previously reported.\(^4\)

2,6-Dibromoaniline (20)

Following General Procedure 2, 20 was prepared from 2,6-dibromobenzoic acid (2.50 g, 8.93 mmol). The crude crystalline material was purified by column chromatography, affording 20 as an off-white solid in 78% yield. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.39 (d, \( J = 8.0 \), 2H), 6.51 (t, \( J = 8.0 \), 1H). \(^{13}\)C NMR (400 MHz, CDCl\(_3\)) \( \delta \) 142.00, 131.74, 119.39, 108.86; HRMS (EI) \( m/z \): calcd for C\(_6\)H\(_5\)Br\(_2\)N: 248.8789. Found 248.8781.
2,6-Dibromonitrobenzene (21)

Following General Procedure 3, 21 was prepared from 2,6-dibromo-aniline (2.00 g, 7.12 mmol). The crude crystalline material was purified by column chromatography, affording 21 as an orange solid in 82% yield. $^1$H NMR [500 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 7.31 (t, $J = 8.1$ Hz, 1H), 7.68 (d, $J = 8.1$ Hz, 2H); $^{13}$C NMR [400 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 167.87, 140.37, 133.58, 133.54, 120.58; HRMS (EI) $m/z$: calcd for C$_6$H$_3$Br$_2$NO$_2$: 278.8531. Found 278.8544.

2-Bromo-6-iodobenzoic acid (22)

Following General Procedure 1, 22 was prepared from 1-bromo-3-iodo-benzene (3.00 g, 10.6 mmol). The off-white crystalline product was obtained in 80% yield as a 5:1 mixture of it and 3-bromobenzoic acid. $^1$H NMR [400 MHz, CDCl$_3$] $\delta$ ppm 7.83 (d, $J = 8.0$ Hz, 1H), 7.61 (d, $J = 8.6$ Hz, 1H), 7.01(t, $J = 8.0$ Hz, 1H); $^{13}$C NMR [500 MHz, CDCl$_3$] $\delta$ ppm 169.27, 140.13, 134.20, 133.73, 133.63, 119.72, 93.15; HRMS (EI) $m/z$: calcd for C$_7$H$_4$BrIO$_2$: 325.8439. Found 325.8427.

2-Bromo-6-iodoaniline (23)

Following General Procedure 2, 23 was prepared from 2-bromo-6- chlorobenzoic acid (2.30 g, 7.04 mmol). The crude crystalline material was purified by column chromatography, affording 23 as a white solid in 58% yield. $^1$H NMR [400 MHz, CDCl$_3$] $\delta$ ppm 7.60 (d, $J = 7.9$ Hz, 1H), 7.41 (d, $J = 7.9$ Hz, 1H), 6.35 (t, $J = 7.9$ Hz, 1H) $^{13}$C NMR [500 MHz, CDCl$_3$] $\delta$ ppm 144.03, 138.20, 132.74, 120.34, 107.31, 83.08; HRMS (EI) $m/z$: calcd for C$_6$H$_5$BrIN: 296.8650. Found 296.8648.
2-Bromo-6-iodonitrobenzene (24)

Following General Procedure 3, 24 was prepared from 2-bromo-6-iodoaniline (1.50 g, 5.04 mmol). The crude crystalline material was purified by column chromatography, affording 24 as a colored solid in 56% yield. $^1$H NMR [400 MHz, CDCl₃] δ ppm 7.84 (d, $J = 8.0$ Hz, 1H), 7.64 (d, $J = 8.1$ Hz, 1H), 7.06 (t, $J = 8.0$ Hz, 1H); $^{13}$C NMR [500 MHz, CDCl₃] δ ppm 155.35, 139.09, 133.55, 131.97, 112.96, 85.57; HRMS (EI) m/z: calcd for C₆H₃BrINO₂: 326.8392. Found 326.8391.

3-(2'-aminophenyl)-N-(TIPS)pyrrole (26)

Following General Procedure 4, 26 was prepared from 25 (125 mg, 0.357 mmol) and commercially available 2-iodoaniline (65.3 mg, 0.298 mmol). The crude residue was purified by column chromatography, affording 26 as a light yellow oil in 85% yield. $^1$H NMR [400 MHz, (CD₃)₂CO] δ 1.16 (d, $J = 8.78$ Hz, 18H), 1.57 (td, $J = 14.95$, 7.51 Hz, 3H), 4.45 (s, 2H), 6.50 (dd, $J = 2.60$, 1.40 Hz, 1H), 6.63 (d, $J = 1.00$ Hz, 1H), 6.77-6.73 (m, 1H), 6.97-6.92 (m, 2H), 7.04 (s, 1H), 7.17 (dd, $J = 7.57$, 1.35 Hz, 1H); $^{13}$C NMR [400 MHz, (CD₃)₂CO] δ ppm 143.60, 129.64, 126.85, 124.66, 123.81, 122.52, 122.27, 118.48, 115.41, 110.66, 17.81, 11.63; HRMS (EI) m/z: calcd for C₁₉H₃₀N₂Si: 314.2178. Found 314.2193.

3-(2'-aminophenyl)pyrrole (27)

Following General Procedure 9, 27 was prepared from 26 (79.6 mg, 0.253 mmol). The crude residue was purified by column chromatography, affording 27 as a light yellow oil in 79% yield. $^1$H NMR [500 MHz, (CD₃)₂CO] δ ppm
10.20 (s, 1H), 7.15 (dd, J = 1.5, 7.5, 1H), 7.01 (dd, J = 1.8, 4.1, 1H), 6.93 (td, J = 1.5, 7.9, 1H),
6.88 (dd, J = 2.6, 4.7, 1H), 6.74 (dd, J = 1.0, 7.9, 1H), 6.62 (td, J = 1.2, 7.4, 1H), 6.34 (dd, J =
2.5, 4.1, 1H), 4.46 (s, 2H); \(^{13}\)C NMR [500 MHz, \((\text{CD}_3)_2\text{CO}\)] \(\delta\) ppm 146.67, 131.03, 128.18,
123.10, 123.59, 120.14, 119.09, 117.77, 116.92, 109.45; HRMS (EI) \(m/z\): calcd for C\(_{10}\)H\(_{10}\)N\(_2\):
158.0844. Found 158.0845.

3-(2’-nitrophenyl)-N-(TIPS)pyrrole (28)

Following General Procedure 4, 28 was prepared from 25 (125 mg, 0.357
mmol) and commercially available 2-bromonitrobenzene (60.2 mg, 0.298
mmol). The crude residue was purified by column chromatography,
affording 28 as a light yellow oil in 81% yield. \(^1\)H NMR [400 MHz, \((\text{CD}_3)_2\text{CO}\)] \(\delta\) ppm 7.66 (ddd,
\(J = 1.0, 3.2, 4.8, 1H\), 7.58 (td, \(J = 1.3, 7.6, 1H\), 7.40 (ddd, \(J = 1.4, 7.4, 8.1, 1H\), 7.05 (t, \(J = 1.6,
1H\), 6.91 (t, \(J = 2.2, 1H\), 6.41 (dd, \(J = 1.5, 2.8, 1H\), 1.55 (dq, \(J = 7.5, 15.0, 3H\), 1.13 (d, \(J =
7.5, 18H\) ); \(^{13}\)C NMR [500 MHz, \((\text{CD}_3)_2\text{CO}\)] \(\delta\) ppm 151.28, 133.20, 132.27, 130.98, 128.23,
127.14, 124.72, 124.64, 122.74, 111.94, 19.07, 13.23; HRMS (EI) \(m/z\): calcd for C\(_{19}\)H\(_{28}\)N\(_2\)O\(_2\)Si:

3-(2’-nitrophenyl)pyrrole (29)

Following General Procedure 9, 29 was prepared from 28 (83.0 mg, 0.241
mmol). The crude residue was purified by column chromatography, affording
29 as a light yellow oil in 81% yield. \(^1\)H NMR [500 MHz, \((\text{CD}_3)_2\text{CO}\)] \(\delta\) ppm 10.39 (s, 1H), 7.66 – 7.61 (m,
1H), 7.57 (ddd, \(J = 1.3, 7.7, 8.8, 1H\), 7.38 (ddd, \(J = 1.5, 7.5, 7.9, 1H\), 7.05 (d, \(J = 1.5, 1H\), 6.87 (dd, \(J = 1.8, 2.8, 1H\), 6.25 (dd, \(J = 1.8, 2.6, 1H\); \(^{13}\)C NMR [500

MHz, (CD$_3$)$_2$CO] $\delta$ ppm 151.23, 133.15, 132.20, 131.31, 127.98, 124.66, 120.99, 120.06, 118.73, 109.05; HRMS (EI) m/z: calcd for C$_{10}$H$_8$N$_2$O$_2$: 188.06. Found 188.059.

3-(2'-amino-3'-chlorophenyl)-N-(TIPS)pyrrole (30)

Following General Procedure 4, 30 was prepared from 25 (125 mg, 0.357 mmol) and 17 (61.5 mg, 0.298 mmol). The crude residue was purified by column chromatography, affording 30 as a light yellow oil in 82% yield. $^1$H NMR [400 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 7.13 (ddd, $J = 1.4, 6.6, 8.1, 1$H), 7.07 (d, $J = 1.5, 1$H), 6.97 (d, $J = 2.6, 1$H), 6.65 (t, $J = 7.8, 1$H), 6.51 (dd, $J = 1.4, 2.7, 1$H), 4.68 (s, 2H), 1.58 (dq, $J = 7.5, 15.0, 3$H), 1.14 (d, $J = 7.5, 18$H); $^{13}$C NMR [500 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 142.93, 129.93, 128.58, 126.92, 125.58, 125.55, 124.24, 120.59, 119.48, 112.39, 19.12, 13.32; HRMS (EI) m/z: calcd for C$_{19}$H$_{29}$ClN$_2$Si: 348.1789. Found 348.1785.

3-(2'-amino-3'-chlorophenyl)pyrrole (3)

Following General Procedure 9, 3 was prepared from 30 (85.2 mg, 0.244 mmol). The crude residue was purified by column chromatography, affording 3 as a light yellow oil in 80% yield. The analytical and spectral data were in accordance with those previously reported.$^5$

3-(3'-chloro-2'-nitrophenyl)-N-(TIPS)pyrrole (31)

Following General Procedure 4, 31 was prepared from 25 (125 mg, 0.357 mmol) and 18 (70.5 mg, 0.298 mmol). The crude residue was purified by column chromatography, affording 31 as a light yellow oil in 87% yield. $^1$H NMR
[500 MHz, (CD$_3$)$_2$CO] δ ppm 7.68 (dd, $J = 1.2, 7.9$, 1H), 7.56 (d, $J = 8.0$, 1H), 7.49 (dd, $J = 1.2, 8.0$, 1H), 7.08 (d, $J = 1.5$, 1H), 6.95 (t, $J = 2.2$, 1H), 6.47 (dd, $J = 1.5, 2.7$, 1H), 1.54 (dq, $J = 7.5, 15.0$, 3H), 1.12 (d, $J = 7.5$, 18H); $^{13}$C NMR [500 MHz, (CD$_3$)$_2$CO] δ ppm 132.92, 132.15, 130.30, 127.82, 127.55, 125.99, 124.98, 124.74, 121.41, 111.60, 19.12, 13.23; HRMS (EI) m/z: calcd for C$_{19}$H$_{27}$ClN$_2$O$_2$Si: 378.1530. Found 378.1526.

3-(3’-chloro-2’-nitrophenyl)pyrrole (32)

Following General Procedure 9, 32 was prepared from 31 (98.2 mg, 0.259 mmol). The crude residue was purified by column chromatography, affording 32 as a light yellow oil in 64% yield. $^1$H NMR [500 MHz, (CD$_3$)$_2$CO] δ ppm 6.35-6.30 (m, 1H), 6.91 (dd, $J = 4.66, 2.57$ Hz, 1H), 7.09 (d, $J = 1.07$ Hz, 1H), 7.48 (dd, $J = 7.99, 1.11$ Hz, 1H), 7.55 (d, $J = 7.97$ Hz, 1H), 7.64 (dd, $J = 7.90, 1.10$ Hz, 1H), 10.539 (s, 1H); $^{13}$C NMR [500 MHz, (CD$_3$)$_2$CO] δ ppm 132.91, 132.56, 130.25, 128.60, 125.98, 121.56, 119.07, 118.79, 108.83; HRMS (EI) m/z: calcd for C$_{10}$H$_7$ClN$_2$O$_2$: 222.0196. Found 222.0192.

3-Chloro-4-(2’-aminophenyl)-N-(TIPS)pyrrole (33)

Following General Procedure 4, 33 was prepared from 12 (137 mg, 0.357 mmol) and commercially available 2-iodoaniline (65.3 mg, 0.298 mmol). The crude residue was purified by column chromatography, affording 33 as a light yellow oil in 81% yield. $^1$H NMR [500 MHz, (CD$_3$)$_2$CO] δ ppm 1.15 (d, $J = 7.56$ Hz, 18H), 1.57 (td, $J = 14.96, 7.51$ Hz, 3H), 4.34 (s, 2H), 6.68-6.64 (m, 1H), 6.78 (dd, $J = 8.01, 0.95$ Hz, 1H), 6.91 (d, $J = 2.46$ Hz, 1H), 6.98 (d, $J = 2.47$ Hz, 1H), 7.04 (dt, $J = 7.99, 1.55$ Hz, 1H),
7.11 (dd, $J = 7.53, 1.47$ Hz, 1H); $^{13}$C NMR [500 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 147.80, 132.93, 129.71, 124.93, 123.61, 120.30, 118.56, 116.65, 115.22, 19.09, 13.08; HRMS (EI) $m/z$: calcd for C$_{19}$H$_{29}$ClN$_2$Si: 348.1789. Found 348.1772.

3-Chloro-4-(2'-aminophenyl)pyrrole (34)

Following General Procedure 9, 34 was prepared from 33 (84.1 mg, 0.241 mmol). The crude residue was purified by column chromatography, affording 33 as a light yellow oil in 75% yield. $^1$H NMR [500 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 4.38 (s, 2H), 6.64 (dt, $J = 7.41, 1.14$ Hz, 1H), 6.77 (dd, $J = 8.01, 0.98$ Hz, 1H), 6.90-6.87 (m, 1H), 6.95 (t, $J = 2.60$, Hz, 1H), 7.02 (dt, $J = 8.01, 1.56$ Hz, 1H), 7.08 (dd, $J = 7.52, 1.49$ Hz, 1H), 10.38 (s, 1H); $^{13}$C NMR [500 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 147.94, 133.08, 129.58, 120.83, 120.56, 119.04, 118.46, 118.03, 116.58, 112.57; HRMS (EI) $m/z$: calcd for C$_{10}$H$_9$ClN$_2$: 192.0454. Found 192.0452.

3-Chloro-4-(2'-nitrophenyl)-N-(TIPS)pyrrole (35)

Following General Procedure 4, 35 was prepared from 12 (137 mg, 0.357 mmol) and commercially available 2-bromonitrobenzene (60.2 mg, 0.298 mmol). The crude residue was purified by column chromatography, affording 35 as a light yellow oil in 86% yield. $^1$H NMR [500 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 1.15 (d, $J = 7.51$ Hz, 18H), 1.57 (td, $J = 11.59, 7.50$ Hz, 3H), 6.96 (dd, $J = 5.82, 2.46$ Hz, 2H), 7.58 (dd, $J = 11.84, 4.46$ Hz, 2H), 7.73-7.69 (m, 1H), 7.96-7.88 (m, 1H); $^{13}$C NMR [500 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 174.96, 134.71, 133.89, 129.91, 129.54, 125.64, 125.16, 123.81, 122.11, 114.93, 19.01, 13.06; HRMS (EI) $m/z$: calcd for C$_{19}$H$_{27}$ClN$_2$O$_2$Si: 344.1920. Found 344.1922.
3-Chloro-4-(2'-nitrophenyl)pyrrole (36)

Following General Procedure 9, 36 was prepared from 35 (97.0 mg, 0.256 mmol). The crude residue was purified by column chromatography, affording 35 as a light yellow oil in 78% yield. $^1$H NMR [400 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 6.95 (td, $J = 5.21$, 2.35 Hz, 2H), 7.55 (ddd, $J = 6.59$, 5.46, 3.84 Hz, 2H), 7.70 (dd, $J = 7.58$, 6.23 Hz, 1H), 7.90 (dd, $J = 7.98$, 0.88 Hz, 1H), 10.53 (s, 1H); $^{13}$C NMR [400 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 134.83, 133.87, 129.83, 129.71, 125.64, 119.43, 119.31, 118.33, 112.46; HRMS (EI) $m/z$: calcd for C$_{10}$H$_7$ClN$_2$O$_2$: 222.0196. Found 222.0194.

3-Chloro-4-(2'-amino-3'-chlorophenyl)-N-(TIPS)pyrrole (37)

Following General Procedure 4, 37 was prepared from 12 (137 mg, 0.357 mmol) and 17 (61.5 mg, 0.298 mmol). The crude residue was purified by column chromatography, affording 37 as a light yellow oil in 82% yield. $^1$H NMR [500 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 1.15 (d, $J = 7.52$ Hz, 18H), 1.59 (td, $J = 11.39$, 7.51 Hz, 3H), 4.57 (s, 2H), 6.67 (t, $J = 7.76$, 7.76 Hz, 1H), 6.96 (d, $J = 2.47$ Hz, 1H), 7.01 (d, $J = 2.46$ Hz, 1H), 7.05 (dd, $J = 7.54$, 1.38 Hz, 1H), 7.20 (dd, $J = 7.97$, 1.41 Hz, 1H); $^{13}$C NMR [400 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 144.26, 131.84, 129.94, 125.30, 123.99, 122.93, 122.19, 120.26, 118.93, 115.11, 19.08, 13.09; HRMS (EI) $m/z$: calcd for C$_{19}$H$_{28}$Cl$_2$N$_2$Si: 382.1399. Found 382.1408.

3-Chloro-4-(2'-amino-3'-chlorophenyl)pyrrole (4)

Following General Procedure 9, 4 was prepared from 37 (93.6 mg, 0.244 mmol). The crude residue was purified by column chromatography,
affording 4 as a light yellow oil in 73% yield. The analytical and spectral data were in accordance with those previously reported.\(^5\)

3-Chloro-4-(3’-chloro-2’-nitrophenyl)-N-(TIPS)pyrrole (38)

Following General Procedure 4, 38 was prepared from 12 (137 mg, 0.357 mmol) and 18 (70.5 mg, 0.298 mmol). The crude residue was purified by column chromatography, affording 38 as a light yellow oil in 89% yield. \(^1\)H NMR [500 MHz, (CD\(_3\))\(_2\)CO] \(\delta\) ppm 1.12 (d, \(J = 7.51\) Hz, 18H), 1.55 (td, \(J = 14.99, 7.51\) Hz, 3H), 6.87 (d, \(J = 2.37\) Hz, 1H), 7.03 (d, \(J = 2.38\) Hz, 1H), 7.69-7.61 (m, 3H); \(^13\)C NMR [500 MHz, (CD\(_3\))\(_2\)CO] \(\delta\) ppm 132.73, 132.44, 130.62, 129.74, 125.86, 125.53, 124.41, 119.01, 114.69, 18.93, 13.01; HRMS (EI) \(m/z\): calcd for C\(_{19}\)H\(_{26}\)Cl\(_2\)N\(_2\)O\(_2\)Si: 412.1141. Found 412.1143.

3-Chloro-4-(3’-chloro-2’-nitrophenyl)pyrrole (5)

Following General Procedure 9, 5 was prepared from 38 (110 mg, 0.265 mmol). The crude residue was purified by column chromatography, affording 5 as a light yellow oil in 74% yield. The analytical and spectral data were in accordance with those previously reported.\(^5\)

3-Bromo-4-iodo-N-(TIPS)pyrrole (39)

Following General Procedure 5, 39 was prepared from 3-bromo-N-(TIPS)pyrrole (2.93 g, 9.70 mmol). The title compound was a white solid. \(^1\)H NMR [400 MHz, (CD\(_3\))\(_2\)CO] \(\delta\) ppm 1.11 (d, \(J = 7.5\) Hz, 18H), 1.56 (dt, \(J = 7.5, 15\) Hz, 3H), 6.98 (dd, \(J = 2.45\) Hz, 1H), 7.07 (d, \(J = 2.45\) Hz, 1H); HRMS (EI) \(m/z\): calcd for C\(_{19}\)H\(_{26}\)BrI\(_2\)N\(_2\)O\(_2\)Si: 522.0617. Found 522.0614.
= 8.1, 2.4 Hz, 2H); $^{13}$C NMR [400 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 131.58, 126.18, 106.90, 70.85, 18.95, 13.00; HRMS (EI) $m/z$: calcd for C$_{13}$H$_{23}$BrINSi: 426.9828. Found 426.9834.

3-Bromo-4-(4',4',5',5'-tetramethyl-1',3',2'-dioxaborolan-2'-yl)-N-(TIPS)pyrrole (40)

Following General Procedure 8, 40 was prepared from 3-bromo-4-iodo-N-(TIPS)pyrrole (4.97 g, 11.6 mmol). The crude residue was purified by column chromatography, affording 40 as a white solid in 79% yield. $^1$H NMR [400 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 1.11 (d, $J = 7.53$ Hz, 18H), 1.29 (s, 12H), 1.56 (ddd, $J$ = 9.44, 5.59, 3.40 Hz, 3H), 6.90 (d, $J = 2.26$ Hz, 1H), 7.13 (d, $J = 2.27$ Hz, 1H); $^{13}$C NMR [500 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 136.28, 126.85, 114.77, 105.47, 84.45, 26.18, 19.00, 13.08; HRMS (EI) $m/z$: calcd for C$_{19}$H$_{35}$BBrNO$_2$Si: 427.1713. Found 427.1717.

3-Bromo-4-D-N-(TIPS)pyrrole (41)

Following General Procedure 7, 41 was prepared from 3-bromo-4-iodo-N-(TIPS)pyrrole (1.71 g, 4.00 mmol). The title compound was a colorless oil. $^1$H NMR [400 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 1.10 (d, $J = 7.51$ Hz, 18H), 1.53 (td, $J = 14.96, 7.51$ Hz, 3H), 6.84 (dd, $J = 12.68, 2.26$ Hz, 2H); $^{13}$C NMR [400 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 126.81, 125.13, 114.78, 99.39 (d, $J = 40$ Hz), 19.02, 13.12; HRMS (EI) $m/z$: calcd for C$_{13}$H$_{23}$DBrNSi: 302.0924. Found 302.0920.
3-D-4-(4’,4’,5’,5’-tetramethyl-1’,3’,2’-dioxaborolan-2’-yl)-N-(TIPS)pyrrole (42)

Following General Procedure 8, 42 was prepared from 3-bromo-4-D-N-(TIPS)pyrrole (1.05 g, 3.00 mmol). The crude residue was purified by column chromatography, affording 42 as a white solid in 79% yield. 

$^1$H NMR [500 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 1.11 (d, $J = 7.57$ Hz, 18H), 1.28 (s, 12H), 1.54 (dd, $J = 9.44$, 5.59 Hz, 3H), 6.85 (d, $J = 1.84$ Hz, 1H), 7.19 (d, $J = 1.86$ Hz, 1H); 

$^{13}$C NMR [500 MHz, (CD$_3$)$_2$CO] $\delta$ ppm 134.97, 126.20, 117.47 (t, $J = 100$ Hz), 104.96, 84.07, 26.23, 19.12, 13.28; 

HRMS (EI) m/z: calcd for C$_{19}$H$_{35}$DBNO$_2$Si: 350.2671. Found 350.2678.

2-(1-(triisopropylsilyl)-1-D-pyrrol-3-yl)benzeneamine (43)

Following general procedure 4, 43 was prepared from 2-amino-1-bromobenzene (42 mg, 0.24 mmol) and 42 (102 mg, 0.29 mmol). The crude residue was purified by column chromatography, affording 43 as a yellow oil in 90% yield. 

$^1$H NMR [400 MHz, CDCl$_3$] $\delta$ ppm 7.19 (d, $J = 1.3$, 1H), 6.98 (td, $J = 1.4$, 7.7, 1H), 6.88 (d, $J = 2.0$, 1H), 6.77 (d, $J = 1.9$, 1H), 6.69 (t, $J = 7.2$, 1H), 3.48 (s, 1H), 1.40 (dt, $J = 7.5$, 14.9, 3H), 1.05 (d, $J = 7.5$, 18H); 

$^{13}$C NMR [400 MHz, CDCl$_3$] $\delta$ ppm 143.54, 129.69, 126.89, 124.62, 123.74, 122.63, 122.32, 118.60, 115.50, 110.47 (t, $J = 86$ Hz), 17.84, 11.68; 

HRMS (EI) m/z: Calculated for C$_{19}$H$_{27}$DN$_2$O$_2$Si: 315.2241. Found 315.2240.

3-Bromo-1-(triisopropylsilyl)-4-(2-nitrophenyl)-1H-pyrrole (44)

Following general procedure 4, 44 was prepared from 1-bromo-2-nitrobenzene (18 mg, 0.09 mmol) and 42 (47 mg, 0.11 mmol). The crude residue was purified by preparative TLC, affording 44 as a pale yellow oil in

520
18% yield. $^1$H NMR [400 MHz, CDCl$_3$] δ ppm 7.83 (dd, $J = 8.09$, 1.07 Hz, 1H), 7.58 (dt, $J = 7.52$, 7.35, 1.26 Hz, 1H), 7.53 (dd, $J = 7.70$, 1.52 Hz, 1H), 7.46-7.40 (m, 1H), 6.82 (d, $J = 2.40$ Hz, 1H), 6.77 (d, $J = 2.39$ Hz, 1H), 1.45 (td, $J = 14.92$, 7.50 Hz, 3H), 1.13 (d, $J = 7.48$ Hz, 18H); $^{13}$C NMR [400 MHz, CDCl$_3$] δ ppm 149.93, 133.02, 131.60, 128.66, 127.57, 124.29, 123.75, 123.32, 121.51, 98.96, 17.67, 11.49; HRMS (EI) $m$/z: Calculated for C$_{19}$H$_{27}$N$_2$O$_2$Si:Br 422.1025. Found 422.1024.
Copies of $^1$H and $^{13}$C NMR Spectra

for

Synthesis of Pyrroline and Related Halogenated Phenylpyrroles

by

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(11)
NO_2

Br

F

(15)
\[ \text{NO}_2 \quad (21) \]

\[ \text{Br} \quad \text{Br} \]

\[ \begin{align*}
\delta (\text{ppm}) & \quad \text{ppm} \\
7.6914 & \quad 7.6752 \\
7.3371 & \quad 7.3249 \\
7.2925 & \quad 7.3087 \\
7.2925 & \quad 7.3249 \\
7.6914 & \quad 7.2925 \\
7.3371 & \quad 7.6752 \\
7.2925 & \quad 7.3087 \\
7.6914 & \quad 7.2925 \\
7.3371 & \quad 7.6752 \\
7.2925 & \quad 7.3087
\end{align*} \]
(23)
(26)

NH₂

N-TIPS
Cl\(\text{NO}_2\)N-TIPS

(35)
References


