Supplementary Information

Design, synthesis and evaluation of a boronic acid based artificial receptor for L-DOPA in aqueous media

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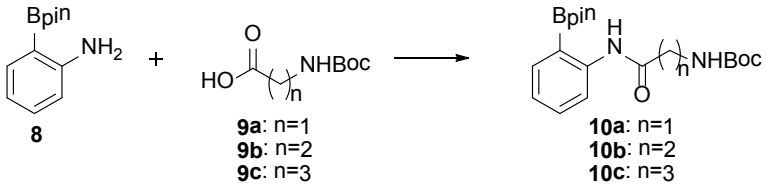
General methods for synthesis.

Melting points were determined on a micro hot-stage (Yanako MP-S3). ^{1}H and ^{13}C NMR spectra were recorded on a JEOL Lambda (300 MHz for ^{1}H) or JEOL ECA-500 (500 MHz for ^{1}H and 125 MHz for ^{13}C) spectrometer. ^{1}H NMR data are reported as follows; chemical shift in parts par million (ppm) downfield or upfield from tetramethylsilane (TMS) (δ 0.00) or D_2O (δ 4.79), integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, d = quartet, quint = quintet, and m = multiplet) and coupling constants (Hz). ^{13}C chemical shifts are reported in ppm downfield or upfield from $CDCl_3$ (δ 77.16) or external standard acetone (δ 30.89). ESI-TOF Mass spectra were measured on a Waters LCT premier XE. Silica gel TLC and column chromatography were performed on Merck TLC 60F-254 (0.25 mm) and Silica Gel 60 N (spherical, neutral, 40-50 μm) (Kanto Chemical Co., Inc.), respectively. Air- and/or moisture-sensitive reactions were carried out under an atmosphere of argon using oven-dried glassware. In general, organic solvents were purified and dried using an appropriate procedure, and evaporation and concentration were carried out under reduced pressure below 30 °C, unless otherwise noted.

Compounds 10a-c



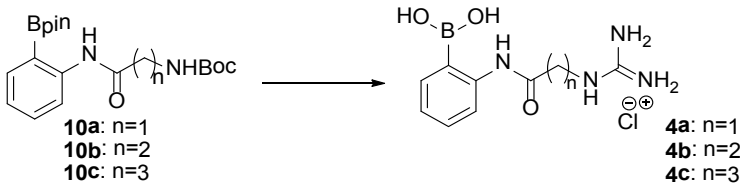
To a solution of 2-anilineboronic acid pinacol ester (**8**) (263 mg, 1.20 mmol) in MeOH (6.00 mL) were added **9a** (300 mg, 1.71 mmol) and DMT-MM (474 mg, 1.71 mmol). After the mixture was stirred at 40 °C for 5 h, the reaction was quenched by addition of a cooled solution of ethyl acetate (30 ml) and saturated aq. NH_4Cl (15 mL). The resulting mixture was extracted with ethyl acetate (30 mL×2). The extracts were washed with saturated aq. $NaHCO_3$ (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated in *vacuo*. Purification of the residue by silica gel column chromatography ($CHCl_3$/acetone = 5/1) gave **10a** (182 mg, 0.479 mmol) in 40% yield as a white solid; R_f 0.67 (7/1 $CHCl_3$/acetone); mp. 164-166 °C; ^{1}H NMR ($CDCl_3$, TMS) δ 9.59 (1H, br s), 7.39 (1H, m), 7.78 (1H, m), 7.47 (1H, t, J = 7.5 Hz), 7.10 (1H, t, J = 7.5 Hz), 5.19 (1H, br s), 4.02 (2H, s), 1.48 (9H, s), 1.38 (12H, s); ^{13}C NMR ($CDCl_3$) δ 167.4, 155.7, 144.0, 136.4, 133.0, 123.4, 119.9, 84.6, 80.2, 45.2, 28.5, 25.0; HRMS (ESI-TOF) *m/z* 377.2258 (377.2248 calcd. for $C_{19}H_{30}BN_2O_5$ $[M+H]^+$).

The compound **10b** was obtained as a white solid from **8** (40.6 mg, 0.185 mmol) and **9b** (50.0 mg, 0.264 mmol) according to the above procedure in 83% yield (59.7 mg, 0.153 mmol); R_f 0.19 (9/1 $CHCl_3$/acetone); mp. 74-76 °C; ^{1}H NMR ($CDCl_3$, TMS) δ 9.67 (1H, br s), 8.27 (1H, m), 7.75 (1H,

dd, J = 1.4 and J = 7.5 Hz), 7.43 (1H, dt, J = 1.4 and J = 7.5 Hz), 7.09 (1H, dt, J = 1.4 and J = 7.5 Hz), 5.29 (1H, br s), 3.49 (2H, m), 2.55 (2H, t, J = 5.4 Hz), 1.43 (9H, s), 1.37 (12H, s); ^{13}C NMR ($CDCl_3$) δ 170.1, 156.2, 143.5, 136.1, 132.4, 123.6, 119.0, 84.2, 79.4, 37.4, 36.4, 28.5, 25.1; HRMS (ESI-TOF) *m/z* 391.2416 (391.2426 calcd. for $C_{30}H_{31}BN_2O_5$ $[M+H]^+$).

The compound **10c** was obtained as a white solid from **8** (37.7 mg, 0.172 mmol) and **9c** (50.0 mg, 0.246 mmol) according to the above procedure in 63% yield (43.5 mg, 0.108 mmol); R_f 0.15 (9/1 $CHCl_3$/acetone); mp. 118-120 °C; ^{1}H NMR ($CDCl_3$, TMS) δ 9.97 (1H, br s), 8.12 (1H, m), 7.74 (1H, m), 7.39 (1H, t, J = 7.2 Hz), 7.10 (1H, t, J = 7.2 Hz), 4.82 (1H, br s), 3.19 (2H, m), 2.35 (2H, t, J = 6.9 Hz), 1.88 (2H, quint, J = 6.9 Hz), 1.43 (9H, s), 1.37 (12H, s); ^{13}C NMR ($CDCl_3$) δ 171.1, 156.4, 143.0, 135.7, 131.8, 123.8, 118.7, 83.7, 79.5, 40.0, 34.8, 28.5, 25.9, 25.0; HRMS (ESI-TOF) *m/z* 405.2549 (405.2542 calcd. for $C_{26}H_{33}BN_2O_5$ $[M+H]^+$).

Compounds 4a-c



To a solution of **10a** (182 mg, 0.484 mmol) in CH_2Cl_2 (1.80 mL) was added TFA (1.80 mL). After the mixture was stirred at room temperature for 1 h, the reaction mixture was concentrated in *vacuo*.

To a solution of the above residue was added acetone (1.00 mL) and water (1.00 mL). After the mixture was stirred at room temperature for 15 h, the reaction mixture was concentrated in *vacuo*. The resulting residue was diluted with H_2O (10 mL), extracted with diethyl ether (40 mL×4), and the water layer was concentrated in *vacuo*.

To a solution of the residue in MeCN (3.60 mL) and water (0.194 mL) were added *N,N'*-di-*tert*-buthoxycarbonyl-1H-pyrazole-1-carboxamidine (**12**) (120 mg, 0.387 mmol) and DIEA (0.279 mL, 1.60 mmol). After the mixture was stirred at room temperature for 2 h, the reaction was quenched by addition of a cooled solution of ethyl acetate (20 mL) and saturated aq. NH_4Cl (15 mL). The resulting mixture was extracted with ethyl acetate (20×2 mL). The extracts was washed with saturated aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over sodium sulfate, and concentrated in *vacuo*.

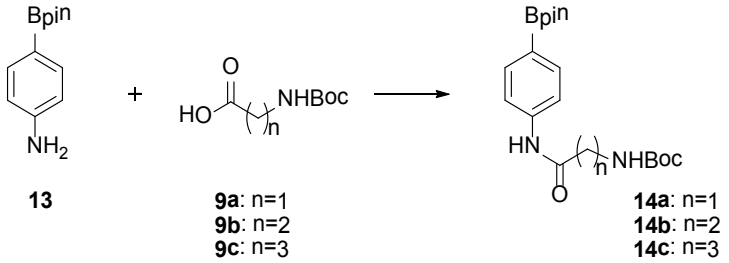
To the above residue was added 4 M HCl/1,4–dioxane (1.70 mL). After the reaction mixture was stirred at room temperature for 4 h, the mixture was concentrated in *vacuo*. Purification of the residue by reverse-phase silica gel column chromatography (H_2O/MeOH = 3/7) gave **4a** (57.2 mg, 0.210 mmol) in 43% yield in 4 steps as a colorless syrup; R_f 0.57; ^{1}H NMR (D_2O) δ 7.40 (1H, dd, J

= 2.1 and 6.6 Hz), 7.21 (2H, m), 7.00 (1H, m), 4.29 (2H, s); ^{13}C NMR (D_2O, acetone) δ 168.2, 158.4, 136.2, 132.3, 129.1, 127.9, 117.2, 43.7; HRMS (ESI-TOF) *m/z* 219.1055 (219.1053 calcd. for $C_9H_{12}BN_4O_2$ $[M+H]^+$).

The compound **4b** was obtained as a colorless syrup from **10b** (96.7 mg, 0.337 mmol) according to the above procedure in 27% yield in 4 steps (26.1 mg, 0.091 mmol). R_f 0.02 (1/1/0.3 $CHCl_3$/MeOH/H_2O); mp. 298-300 °C; ^{1}H NMR (D_2O) δ 7.38 (1H, dd, *J* = 1.8 and 6.6 Hz), 7.20 (2H, m), 6.91 (1H, m), 3.51 (2H, t, *J* = 6.2 Hz), 2.79 (2H, t, *J* = 6.2 Hz); ^{13}C NMR (D_2O, acetone) δ 170.3, 157.4, 136.2, 132.2, 128.9, 127.9, 116.7, 37.4, 34.3; HRMS (ESI-TOF) *m/z* 233.1216 (233.1210 calcd. for $C_{10}H_{14}BN_4O_2$ $[M+H]^+$).

The compound **4c** was obtained as a colorless syrup from **10c** (64.0 mg, 0.213 mmol) according to the above procedure in 47% yield in 4 steps (30.1 mg, 0.100 mmol); R_f 0.63 (1/1/0.3 $CHCl_3$/MeOH/H_2O); ^{1}H NMR (D_2O) δ 7.42 (1H, dd, *J* = 1.8 and 6.6 Hz), 7.23 (2H, m), 6.95 (1H, dd, *J* = 1.8 and 6.6 Hz), 3.20 (2H, t, *J* = 6.9 Hz), 2.60 (2H, t, *J* = 6.9 Hz), 1.96 (2H, quint, *J* = 6.9 Hz); ^{13}C NMR (D_2O, acetone) δ 172.4, 157.4, 136.4, 132.1, 128.9, 127.8, 116.6, 40.8, 32.0, 24.4; HRMS (ESI-TOF) *m/z* 247.1366 (247.1366 calcd. for $C_{11}H_{16}BN_4O_2$ $[M+H]^+$).

Compounds 14a-c

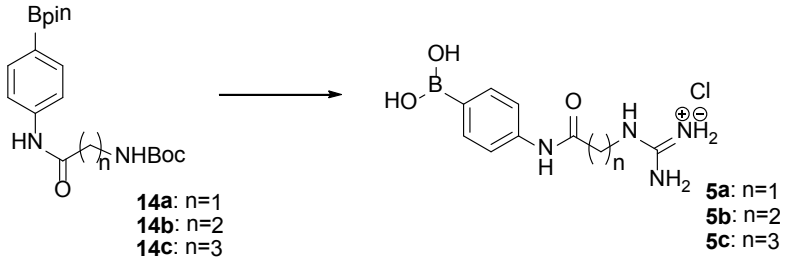


To a solution of 4-anilineboronic acid pinacol ester **13** (175 mg, 0.800 mmol) in MeOH (6.00 mL) were added **9a** (200 mg, 1.14 mmol) and DMT-MM (316 mg, 1.14 mmol). After the mixture was stirred at 40 °C for 3 h, the reaction was quenched by addition of a cooled solution of ethyl acetate (30 mL) and saturated aq. NH_4Cl (15 mL). The resulting mixture was extracted with ethyl acetate (30 mL×2). The extracts were washed with saturated aq. $NaHCO_3$ (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated in *vacuo*. Purification of the residue by silica gel column chromatography ($CHCl_3$/acetone = 5/1) gave **14a** (277 mg, 0.735 mmol) in 92% yield as a white solid; R_f 0.55 (7/1 $CHCl_3$/acetone); mp. 225-226 °C; ^{1}H NMR ($CDCl_3$, TMS) δ 8.24 (1H, br s), 7.77 (2H, d, *J* = 8.4 Hz), 7.52 (2H, d, *J* = 8.4 Hz), 5.25 (1H, br s), 3.92 (2H, d, *J* = 5.7 Hz), 1.40 (9H, s), 1.38 (12H, s); ^{13}C NMR ($CDCl_3$) δ 189.5, 167.4, 140.1, 136.0, 118.8, 83.9, 80.7, 45.9, 28.4, 25.0; HRMS (ESI-TOF) *m/z* 377.2235 (377.2248 calcd. for $C_{19}H_{30}BN_2O_5$ $[M+H]^+$).

The compound **14b** was obtained as a white solid from **13** (344 mg, 1.57 mmol) and **9b** (425 mg, 2.24 mmol) according to the above procedure in 62% yield (408 mg, 0.970 mmol); R_f 0.37 (7/1 $CHCl_3$/acetone); mp. 217-218 °C; ^{1}H NMR ($CDCl_3$, TMS) δ 7.77 (2H, d, J = 7.8 Hz), 7.69 (1H, br s), 7.54 (2H, d, J = 7.8 Hz), 5.16 (1H, br s), 3.50 (2H, m), 2.61 (2H, t, J = 5.9 Hz), 1.43 (9H, s), 1.34 (12H, s); ^{13}C NMR ($CDCl_3$) δ169.8, 156.4, 140.6, 135.9, 118.7, 83.9, 79.8, 37.9, 36.5, 28.5, 25.0; HRMS (ESI-TOF) m/z 391.2420 (391.2426 calcd. for $C_{30}H_{32}BN_2O_5$ $[M+H]^+$).

The compound **14c** was obtained as a white solid from **13** (302 mg, 1.38 mmol) and **10c** (400 mg, 1.97 mmol) according to the above procedure in 78% yield (449 mg, 1.07 mmol); R_f 0.55 (4/1 $CHCl_3$/acetone); mp. 190-191 °C; ^{1}H NMR ($CDCl_3$, TMS) δ 8.77 (1H, br s), 7.76 (2H, d, J = 8.4 Hz), 7.61 (2H, d, J = 8.4 Hz), 4.82 (1H, br, s), 3.24 (2H, m), 2.39 (2H, t, J = 6.9 Hz), 1.87 (2H, quint, J = 6.9 Hz), 1.46 (9H, s), 1.33 (12H, s); ^{13}C NMR ($CDCl_3$) δ 171.7, 157.4, 141.1, 135.8, 118.7, 83.8, 80.0, 39.4, 34.9, 28.5, 27.3, 25.0; HRMS (ESI-TOF) m/z 405.2566 (405.2582 calcd. for $C_{21}H_{33}BN_2O_3$ $[M+H]^+$).

Compounds 5a-c



To a solution of **14a** (277 mg, 0.736 mmol) in CH_2Cl_2 (2.80 mL) was added TFA (2.80 mL). After the mixture was stirred at room temperature for 3 h, the reaction mixture was concentrated in *vacuo*.

To a solution of the above residue was added acetone (2.80 mL) and water (2.80 mL). After the mixture was stirred at room temperature for 14 h, the reaction mixture was concentrated in *vacuo*. The resulting residue was diluted with H_2O (10 mL), extracted with diethyl ether (40 mL×4), and the water layer was concentrated in *vacuo*.

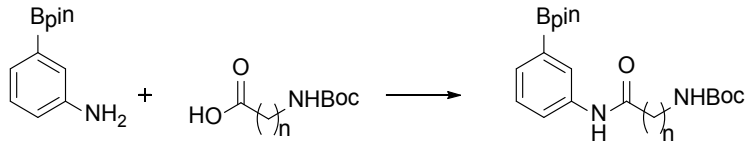
To a solution of the residue in MeCN (5.45 mL) and water (0.296 mL) were added *N,N'*-di-*tert*-buthoxycarbonyl-1H-pyrazole-1-carboxamidine (**12**) (183 mg, 0.589 mmol) and DIEA (0.423 ml, 2.43 mmol). After the mixture was stirred at room temperature for 5 h, the reaction was quenched by addition of a cooled solution of ethyl acetate (20 mL) and saturated aq. NH_4Cl (15 mL). The resulting mixture was extracted with ethyl acetate (20×2 mL). The extracts was washed with saturated aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over sodium sulfate, and concentrated in *vacuo*.

To the above residue was added 4 M HCl/1,4–dioxane (1.4 mL). After the reaction mixture was stirred at room temperature for 7 h, the mixture was concentrated in *vacuo*. Purification of the residue by reverse-phase silica gel column chromatography (H_2O/MeOH = 3/7) gave **5a** (65.0 mg, 0.239 mmol) in 32% yield in 4 steps as a white solid; R_f 0.53 (1/1/0.3 $CHCl_3$/MeOH/H_2O); mp. 146-147 °C; ^{1}H NMR (D_2O) δ 7.66 (2H, d, J = 8.4 Hz), 7.38 (2H, d, J = 8.4 Hz), 4.05 (2H, s); ^{13}C NMR (D_2O, acetone) δ 169.2, 158.3, 139.7 135.4, 121.2, 44.8; HRMS (ESI-TOF) *m/z* 237.1149 (237.1159 calcd. for $C_9H_{14}BN_4O_3$ $[M+H]^+$).

The compound **5b** was obtained as a white solid from **14b** (71.4 mg, 0.183 mmol) according to the above procedure in 48% yield in 4 steps (25.0 mg, 0.088 mmol); R_f 0.58 (1/1/0.3 $CHCl_3$/MeOH/H_2O); mp. 168-170 °C; ^{1}H NMR (D_2O) δ 7.63 (2H, d, J = 8.4 Hz), 7.34 (2H, d, J = 8.4 Hz), 3.42 (2H, t, J = 6.3 Hz), 2.59 (2H, t, J = 6.3 Hz); ^{13}C NMR (D_2O, acetone) δ 172.7, 157.7, 139.8, 135.4, 121.3, 38.0, 36.2; HRMS (ESI-TOF) *m/z* 251.1309 (251.1315 calcd. for $C_{10}H_{16}BN_4O_3$ $[M+H]^+$).

The compound **5c** was obtained as a white solid from **14c** (74.8 mg, 0.178 mmol) according to the above procedure in 60% yield in 4 steps (32.1 mg, 0.107 mmol); R_f 0.08 (1/1/0.3 $CHCl_3$/MeOH/H_2O); mp. 173-175 °C; ^{1}H NMR (D_2O) δ 7.63 (2H, d, J = 8.4 Hz), 7.35 (2H, d, J = 8.4 Hz), 3.13 (2H, t, J = 6.9 Hz), 2.37 (2H, t, J = 6.9 Hz), 1.83 (2H, quint, J = 6.9 Hz); ^{13}C NMR (D_2O, acetone) δ175.1, 157.7, 139.8, 135.3, 121.3, 41.1, 34.0, 24.7; HRMS (ESI-TOF) *m/z* 265.1464 (265.1472 calcd. for $C_{11}H_{18}BN_4O_3$ $[M+H]^+$).

Compounds 16a-c



15 **9a**: n=1 **9b**: n=2 **9c**: n=3 **16a**: n=1 **16b**: n=2 **16c**: n=3

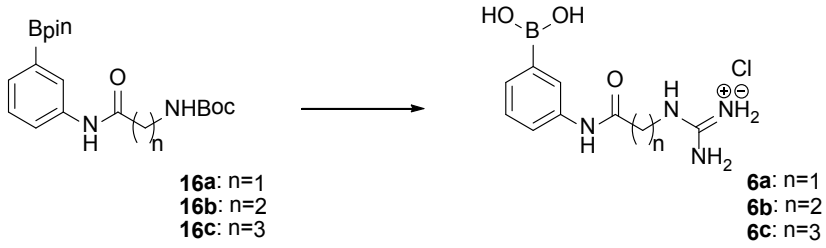
To a solution of 3-anilineboronic acid pinacol ester **15** (262 mg, 1.20 mmol) in MeOH (6.00 mL) were added **9a** (300 mg, 1.71 mmol) and DMT-MM (473 mg, 1.71 mmol). After the mixture was stirred at 40 °C for 1 h, the reaction was quenched by addition of a cooled solution of ethyl acetate (30 mL) and saturated aq. NH_4Cl (15 mL). The resulting mixture was extracted with ethyl acetate (30 mL×2). The extracts were washed with saturated aq. $NaHCO_3$ (30 mL) and brine (30 mL), dried over sodium sulfate, and concentrated in *vacuo*. Purification of the residue by silica gel column chromatography ($CHCl_3$/acetone = 5/1) gave **16a** (312 mg, 0.829 mmol) in 69% yield as a white solid; R_f 0.52 (7/1 $CHCl_3$/acetone); mp. 160-161 °C; ^{1}H NMR ($CDCl_3$, TMS) δ 7.97 (1H, br s), 7.88

(1H, br d, J = 7.8 Hz), 7.65 (1H, d, J = 1.8 Hz), 7.56 (1H, d, J = 7.8 Hz), 7.35 (1H, t, J = 7.8 Hz), 5.17 (1H, br s), 3.93 (2H, d, J = 5.7 Hz), 1.49 (9H, s), 1.38 (12H, s); ^{13}C NMR ($CDCl_3$) δ 167.8, 156.4, 137.0, 131.0, 128.8, 126.0, 123.3, 84.1, 80.9, 45.6, 28.5, 25.0; HRMS (ESI-TOF) *m/z* 377.2246 (377.2248 calcd. for $C_{19}H_{30}BN_2O_5$ $[M+H]^+$).

The compound **16b** was obtained as a white solid from **15** (139 mg, 0.634 mmol) and **9b** (172 mg, 0.909 mmol) according to the above procedure in 65% yield (161 mg, 0.412 mmol); R_f 0.38 (7/1 $CHCl_3$/acetone); mp. 164-166 °C; ^{1}H NMR ($CDCl_3$) δ 7.78 (2H, m), 7.55 (1H, d, J = 7.2 Hz), 7.48 (1H, br s), 5.18 (1H, br s), 3.49 (2H, m), 2.59 (2H, t, J = 5.9 Hz), 1.44 (9H, s), 1.34 (12H, s); ^{13}C NMR ($CDCl_3$) δ 169.8, 156.4, 137.3, 130.8, 128.6, 126.0, 123.1, 84.0, 79.6, 37.5, 36.5, 28.5, 25.0; HRMS (ESI-TOF) *m/z* 391.2402 (391.2404 calcd. for $C_{30}H_{32}BN_2O_5$ $[M+H]^+$).

The compound **16c** was obtained as a white solid from **15** (93.5 mg, 0.427 mmol) and **9c** (124 mg, 0.610 mmol) according to the above procedure in 82% yield (147 mg, 0.350 mmol); R_f 0.27 (7/1 $CHCl_3$/acetone); mp. 166-168 °C; ^{1}H NMR ($CDCl_3$) δ 8.36 (1H, br, s), 7.86 (2H, m), 7.54 (1H, m), 7.35 (1H, m), 4.80 (1H, br s), 3.24 (2H, m), 2.37 (2H, t, J = 6.9 Hz), 2.00 (2H, m), 1.46 (9H, s), 1.33 (12H, s); ^{13}C NMR ($CDCl_3$) δ 171.2, 157.0, 137.9, 130.5, 128.6, 126.0, 123.1, 84.0, 79.8, 39.6, 34.8, 28.5, 27.0, 25.0; HRMS (ESI-TOF) *m/z* 405.2553 (405.2542 calcd. for $C_{26}H_{33}BN_2O_3$ $[M+H]^+$).

Compounds 6a-c



16a: n=1
16b: n=2
16c: n=3

6a: n=1
6b: n=2
6c: n=3

To a solution of **16a** (311 mg, 0.827 mmol) in CH_2Cl_2 (3.00 mL) was added TFA (3.00 mL). After the mixture was stirred at room temperature for 4 h, the reaction mixture was concentrated in *vacuo*.

To a solution of the above residue was added acetone (1.62 mL) and water (1.62 mL). After the mixture was stirred at room temperature for 17 h, the reaction mixture was concentrated in *vacuo*. The resulting residue was diluted with H_2O (10 mL), extracted with diethyl ether (40 mL×4), and the water layer was concentrated in *vacuo*.

To a solution of the residue in MeCN (6.14 mL) and water (0.330 mL) were added *N,N'*-di-*tert*-buthoxycarbonyl-1H-pyrazole-1-carboxamidine (**12**) (165 mg, 0.531 mmol) and DIEA (0.381 ml, 2.19 mmol). After the mixture was stirred at room temperature for 2 h, the reaction was quenched by addition of a cooled solution of ethyl acetate (20 mL) and saturated aq. NH_4Cl (15 mL).

The resulting mixture was extracted with ethyl acetate (20×2 mL). The extracts was washed with saturated aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over sodium sulfate, and concentrated in *vacuo*.

To the above residue was added 4 M HCl/1,4–dioxane (2.00 mL). After the reaction mixture was stirred at room temperature for 4 h, the mixture was concentrated in *vacuo*. Purification of the residue by reverse-phase silica gel column chromatography (H_2O/MeOH = 3/7) gave **6a** (100 mg, 0.367 mmol) in 44% yield in 4 steps as a white solid; R_f 0.53 (1/1/0.3 $CHCl_3$/MeOH/H_2O); mp. 198-200 °C; ^{1}H NMR (D_2O) δ 7.61 (1H, s), 7.46 (2H, m), 7.34 (1H, t, J = 7.8 Hz), 4.09 (2H, s); ^{13}C NMR (D_2O, acetone) δ 169.2, 158.3, 136.6 131.6, 129.6, 127.5, 125.1, 44.8; HRMS (ESI-TOF) *m/z* 237.1154 (237.1159 calcd. for $C_9H_{14}BN_4O_3$ $[M+H]^+$).

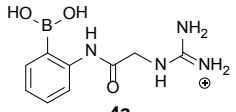
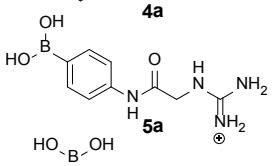
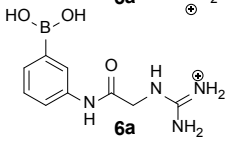
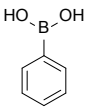
The compound **6b** was obtained as a white solid from **16b** (100 mg, 0.256 mmol) according to the above procedure in 47% yield in 4 steps (34.6 mg, 0.121 mmol); R_f 0.71 (1/1/0.3 $CHCl_3$/MeOH/H_2O); mp. 174-175 °C; ^{1}H NMR (D_2O) δ 7.61 (1H, s), 7.46 (2H, m), 7.35 (1H, t, J = 7.5 Hz), 3.45 (2H, t, J = 6.3 Hz), 2.62 (2H, t, J = 6.3 Hz); ^{13}C NMR (D_2O, acetone) δ 172.7, 157.5, 136.9, 131.4, 129.5, 127.4, 125.0, 38.1, 36.1; HRMS (ESI-TOF) *m/z* 251.1311 (251.1315 calcd. for $C_{10}H_{16}BN_4O_3$ $[M+H]^+$).

The compound **6c** was obtained as a colorless syrup from **16c** (69.2 mg, 0.165 mmol) according to the above procedure in 34% yield in 4 steps (16.9 mg, 0.0562 mmol); R_f 0.80 (1/1/0.3 $CHCl_3$/MeOH/H_2O); ^{1}H NMR (D_2O) δ 7.56 (1H, s), 7.42 (2H, m), 7.30 (1H, t, J = 7.5 Hz), 3.12 (2H, t, J = 6.9 Hz), 2.35 (2H, t, J = 6.9 Hz), 1.82 (2H, quint, J = 6.9 Hz); ^{13}C NMR (D_2O, acetone) δ 174.8, 157.4, 137.1, 131.2, 129.4, 127.2, 124.8, 41.1, 33.9, 24.8; HRMS (ESI-TOF) *m/z* 265.1479 (265.1472 calcd. for $C_{11}H_{18}BN_4O_3$ $[M+H]^+$).

^{11}B NMR chemical shifts of 4a, 5a, 6a and 7.

^{11}B NMR spectra were recorded on a JEOL ECA-500 (160 MHz for ^{11}B) spectrometer. To avoid the broad signal from the boron incorporated in glasses, measurements were carried out in a 5 mm tube made of poly(tetrafluoroethylene). The ^{11}B NMR spectrum of each compound (1.0 mM) was measured in 0.1 M phosphate buffer (D_2O, pH 7.4) at 298 K. For these compounds, a resonance at ca. 5-10 ppm on the $B(OH)_3$ scale is indicative of a sp^2 hybridized neutral boron atom, while one in the −10 to −15 ppm range is indicative of a sp^3 hybridized anionic borate center.[1]

Table S1 ^{11}B NMR chemical shifts of **4a**, **5a**, **6a**, and **7**.

Compound	Chemical Shift (ppm)[a]
 **4a**	8.04 -12.41 (major peak)
 **5a**	8.19
 **6a**	7.51
 **7**	8.79

[a]Chemical shifts in ppm downfield (positive) or upfield (negative) of external standard $B(OH)_3$

General procedure for ^{1}H NMR titration.[2]

A 5.0 mM receptor stock solution (solution A) and 10 mM stock solution of each guest molecule (solution B) were prepared in phosphate buffered D_2O (100 mM, pH 7.4). And then, solution B was titrated into solution A in order to make mixtures with a constant concentration of the receptor (1.0 mM) and a range of concentration of each guest. In general, three different concentrations (1.0, 1.5 and 2.0 mM) were made.

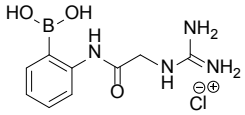
The slow dissociation of the complex compared to the NMR timescale led to two different sets of signals for the free receptor and the complexed receptor. The concentrations of the free and the complexed receptor were determined by the integral ratio of these peaks considering the known total concentration. In general, the signal set of the aromatic protons of the receptor were used for determination of the binding constants (K_a).

The equilibrium constant for the complexation of the receptor with the guest is defined as

$$K_a = [\text{complexed receptor}]_{area}/([S][\text{free receptor}]_{area}) \quad (1)$$

$$[S] = [S_0] - [\text{complexed receptor}], \quad [S_0] \text{ denotes the total guest.} \quad (2)$$

Table S2



4a

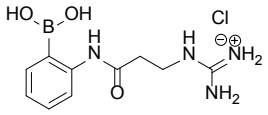
L-DOPA			
4a (mmol)	L-DOPA (mmol)	integral of	
		free **4a**	complexed **4a**
1	1	1	ND
1	1.5	1	ND
1	2	1	ND
		K_a	<10 M^{-1}

Dopamine			
4a (mmol)	Dopamine (mmol)	integral of	
		free **4a**	complexed **4a**
1	1	1	ND
1	1.5	1	ND
1	2	1	ND
		K_a	<10 M^{-1}

Catechol			
4a (mmol)	Catechol (mmol)	integral of	
		free **4a**	complexed **4a**
1	1	1	ND
1	1.5	1	ND
1	2	1	ND
		K_a	<10 M^{-1}

ND = not detected.

Table S3



4b

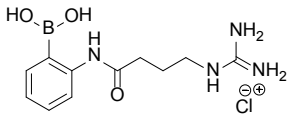
L-DOPA			
4b (mmol)	L-DOPA (mmol)	integral of	
		free **4b**	complexed **4b**
1	1	1	ND
1	1.5	1	ND
1	2	1	ND
		K_a	<10 M^{-1}

Dopamine			
4b (mmol)	Dopamine (mmol)	integral of	
		free **4b**	complexed **4b**
1	1	1	ND
1	1.5	1	ND
1	2	1	ND
		K_a	<10 M^{-1}

Catechol			
4b (mmol)	Catechol (mmol)	integral of	
		free **4b**	complexed **4b**
1	1	1	ND
1	1.5	1	ND
1	2	1	ND
		K_a	<10 M^{-1}

ND = not detected.

Table S4



4c

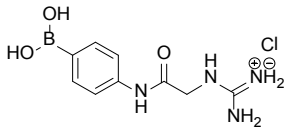
L-DOPA			
4c (mmol)	L-DOPA (mmol)	integral of	
		free **4c**	complexed **4c**
1	1	1	ND
1	1.5	1	ND
1	2	1	ND
		K_a	<10 M^{-1}

Dopamine			
4c (mmol)	Dopamine (mmol)	integral of	
		free **4c**	complexed **4c**
1	1	1	ND
1	1.5	1	ND
1	2	1	ND
		K_a	<10 M^{-1}

Catechol			
4c (mmol)	Catechol (mmol)	integral of	
		free **4c**	complexed **4c**
1	1	1	ND
1	1.5	1	ND
1	2	1	ND
		K_a	<10 M^{-1}

ND = not detected.

Table S5

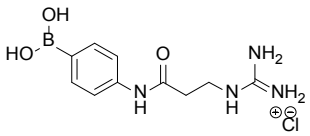


5a

L-DOPA			
5a (mmol)	L-DOPA (mmol)	integral of	
		free **5a**	complexed **5a**
1	1	1	0.63
1	1.5	1	1.22
1	2	1	1.65
		K_a	1228 M^{-1}

Dopamine				**Catechol**			
5a (mmol)	Dopamine (mmol)	integral of		**5a** (mmol)	Catechol (mmol)	integral of	
		free **5a**	complexed **5a**			free **5a**	complexed **5a**
1	1	1	0.75	1	1	1	0.48
1	1.5	1	1.08	1	1.5	1	0.82
1	2	1	1.58	1	2	1	1.14
		K_a	1115 M^{-1}			K_a	783 M^{-1}

Table S6

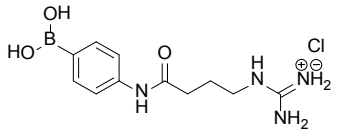


5b

L-DOPA			
5b (mmol)	L-DOPA (mmol)	integral of	
		free **5b**	complexed **5b**
1	1	1	0.62
1	1.5	1	0.98
1	2	1	1.54
		K_a	1115 M^{-1}

Dopamine				**Catechol**			
5b (mmol)	Dopamine (mmol)	integral of		**5b** (mmol)	Catechol (mmol)	integral of	
		free **5b**	complexed **5b**			free **5b**	complexed **5b**
1	1	1	0.68	1	1	1	0.52
1	1.5	1	1.15	1	1.5	1	0.76
1	2	1	1.59	1	2	1	1.2
		K_a	1157 M^{-1}			K_a	799 M^{-1}

Table S7

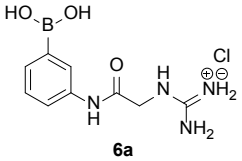


5c

L-DOPA			
5c (mmol)	L-DOPA (mmol)	integral of	
		free **5c**	complexed **5c**
1	1	1	0.62
1	1.5	1	1
1	2	1	1.5
		K_a	1060 M^{-1}

Dopamine				**Catechol**			
5c (mmol)	Dopamine (mmol)	integral of		**5c** (mmol)	Catechol (mmol)	integral of	
		free **5c**	complexed **5c**			free **5c**	complexed **5c**
1	1	1	0.67	1	1	1	0.5
1	1.5	1	1.06	1	1.5	1	0.82
1	2	1	1.61	1	2	1	1.16
		K_a	1147 M^{-1}			K_a	793 M^{-1}

Table S8

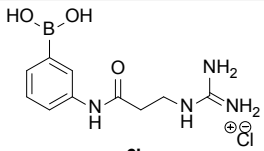


6a

L-DOPA			
6a (mmol)	L-DOPA (mmol)	integral of	
		free **6a**	complexed **6a**
1	1	1	1.09
1	1.5	1	1.77
1	2	1	3.16
		K_a	2467 M^{-1}

Dopamine				**Catechol**			
6a (mmol)	Dopamine (mmol)	integral of		**6a** (mmol)	Catechol (mmol)	integral of	
		free **6a**	complexed **6a**			free **6a**	complexed **6a**
1	1	1	0.99	1	1	1	0.83
1	1.5	1	1.81	1	1.5	1	1.53
1	2	1	2.48	1	2	1	2.19
		K_a	1963 M^{-1}			K_a	1686 M^{-1}

Table S9

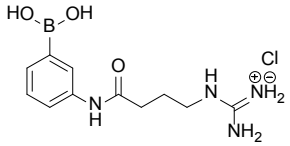


6b

L-DOPA			
6b (mmol)	L-DOPA (mmol)	integral of	
		free **6b**	complexed **6b**
1	1	1	0.97
1	1.5	1	1.81
1	2	1	2.63
		K_a	2085 M^{-1}

Dopamine				**Catechol**			
6b (mmol)	Dopamine (mmol)	integral of		**6b** (mmol)	Catechol (mmol)	integral of	
		free **6b**	complexed **6b**			free **6b**	complexed **6b**
1	1	1	0.99	1	1	1	0.75
1	1.5	1	1.96	1	1.5	1	1.35
1	2	1	2.82	1	2	1	2.15
		K_a	1826 M^{-1}			K_a	1620 M^{-1}

Table S10

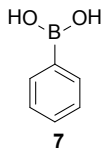


6c

L-DOPA			
6c (mmol)	L-DOPA (mmol)	integral of	
		free **6c**	complexed **6c**
1	1	1	0.96
1	1.5	1	1.65
1	2	1	2.84
		K_a	2209 M^{-1}

Dopamine				**Catechol**			
6c (mmol)	Dopamine (mmol)	integral of		**6c** (mmol)	Catechol (mmol)	integral of	
		free **6c**	complexed **6c**			free **6c**	complexed **6c**
1	1	1	0.98	1	1	1	0.80
1	1.5	1	1.77	1	1.5	1	1.40
1	2	1	2.85	1	2	1	1.99
		K_a	2252 M^{-1}			K_a	1504 M^{-1}

Table S11



7

L-DOPA			
7 (mmol)	L-DOPA (mmol)	integral of	
		free **7**	complexed **7**
1	1	1	0.49
1	1.5	1	0.83
1	2	1	1.12
		K_a	771 M^{-1}

Dopamine			
7 (mmol)	Dopamine (mmol)	integral of	
		free **7**	complexed **7**
1	1	1	0.49
1	1.5	1	0.79
1	2	1	1.19
		K_a	803 M^{-1}

Catechol			
7 (mmol)	Catechol (mmol)	integral of	
		free **7**	complexed **7**
1	1	1	0.41
1	1.5	1	0.64
1	2	1	0.89
		K_a	579 M^{-1}

^{1}H NMR titration of receptor 6a with L-DOPA

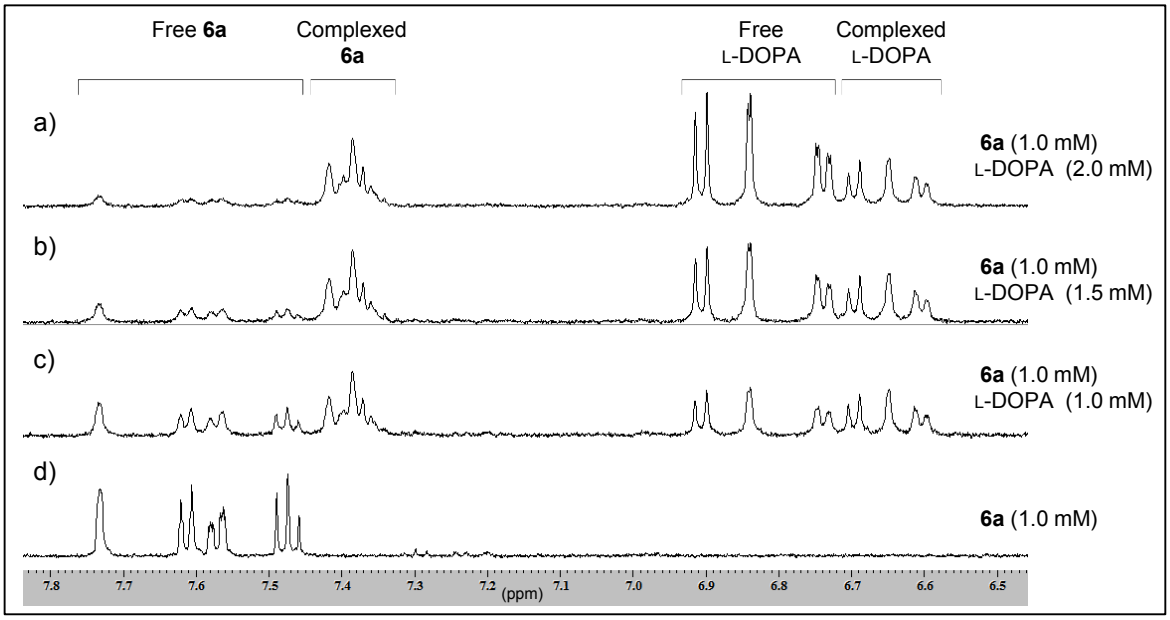


Figure S1a ^{1}H NMR titration of receptor **6a** (1.0 mM) with increasing concentrations (bottom to top) of L-DOPA in phosphate buffered D_2O (100 mM, pH 7.4). L-DOPA concentration is a) 2.0 mM, b) 1.5 mM, c) 1.0 mM, and d) 0 mM. The aromatic regions of the spectra are shown.

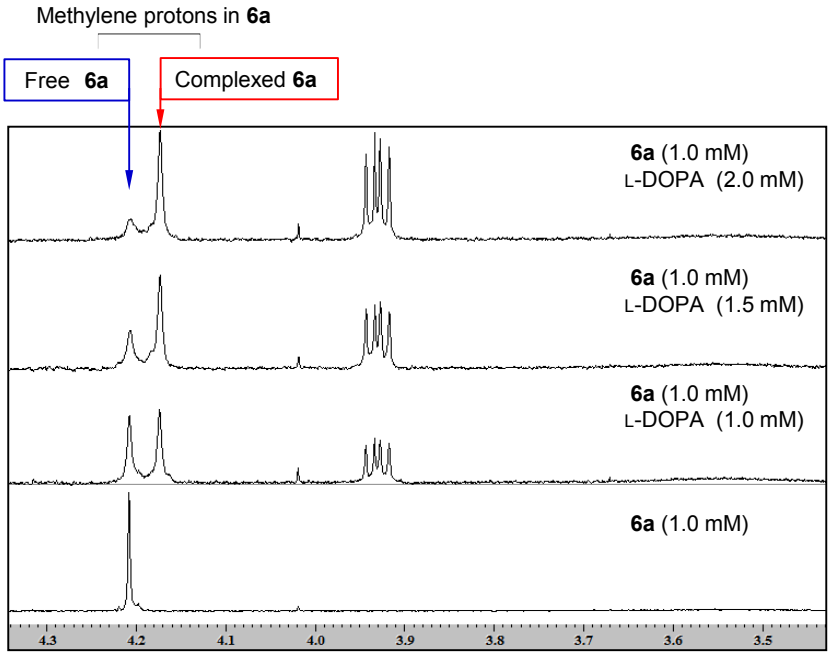


Figure S1b ^{1}H NMR titration of receptor **6a** (1.0 mM) with increasing concentrations (bottom to top) of L-DOPA in phosphate buffered D_2O (100 mM, pH 7.4) (aromatic region). L-DOPA concentration is a) 2.0 mM, b) 1.5 mM, c) 1.0 mM, and d) 0 mM. The aliphatic regions of the spectra are shown.

^{11}B NMR of receptor 6a with L-DOPA

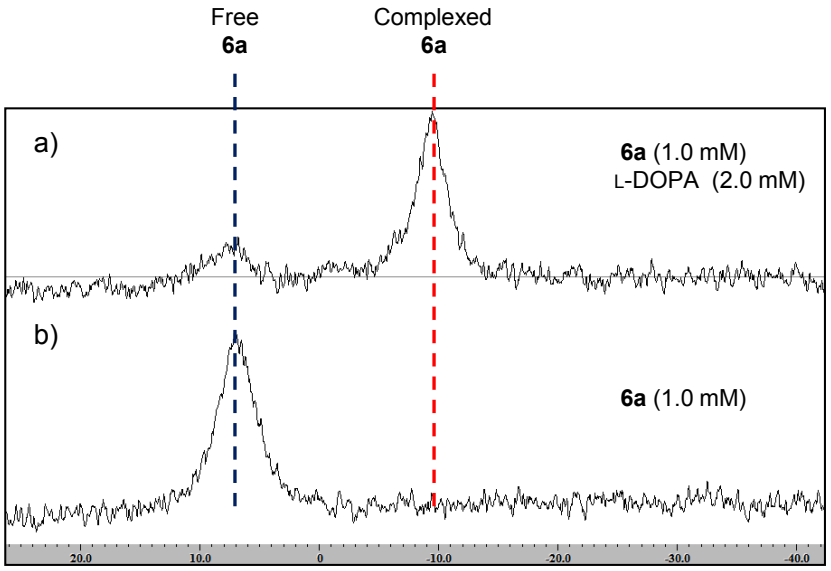


Figure S2 ^{11}B NMR of receptor **6a** (1.0 mM) a) with L-DOPA (2.0 mM), b) without L-DOPA in

phosphate buffered D_2O (100 mM, pH 7.4).

Inhibition assay of L-DOPA decarboxylase.[3]

The 5.0 mM stock solutions of L-DOPA, pyridoxal-5'-phosphate (PLP), and **4a** or **6a** in 50 mM HEPES buffer (containing 100 mM NaCl, pH 7.2) were prepared. In addition, the stock solution of DDC (Sino Biological Inc.) (20 μg/mL) in 50 mM HEPES buffer (pH 7.2) was prepared. The DDC enzymatic reaction was started by combining of the above stock solutions in 50 mM HEPES buffer (pH 7.2) at 37 °C. The final concentrations in the incubation mixture were DDC 3.5 μg/mL, L-DOPA 1.0 mM, PLP 0.10 mM, and **4a** or **6a** 1.0 mM. The resulting mixture was incubated at the same temperature for 30 or 60 min. The enzymatic reaction was stopped by heating to 100 °C for 2 min, and then cooled on ice for 2 min. To the reaction mixture was added TNBS (5% in H_2O), and the mixture was incubated for 20 min at 37 °C. And then, TNP-dopamine, which was formed by the reaction between dopamine and TNBS, was extracted by benzene. The progress of the DDC enzymatic reaction was monitored by UV analysis (340 nm) of the extracted TNP-dopamine.

Cell culture.

Human human lung fibroblast WI-38 cells were grown at 37 °C in 5% CO_2 in air in DMEM medium supplemented with phenol red, L-glutamine (2 mM), penicillin (100 Units/mL), kanamycin (100 μg/mL) and 10% fetal bovine serum.

MTT assay.

Cells were seeded at 8.0×10^3 cells per well in 96-well in 10% FBS DMEM. After 24 h, samples were incubated with the indicated concentration of **6a** or cisplatin. Cells were then kept for 24 h at 37 °C and in 5% CO_2 in air, and then MTT reagent was added to each well and cells were incubated for up to 3 additional hours at 37 °C. The absorbance at a single wavelength of 540 nm was read on a plate reader SAFIRE (TECAN Inc.).

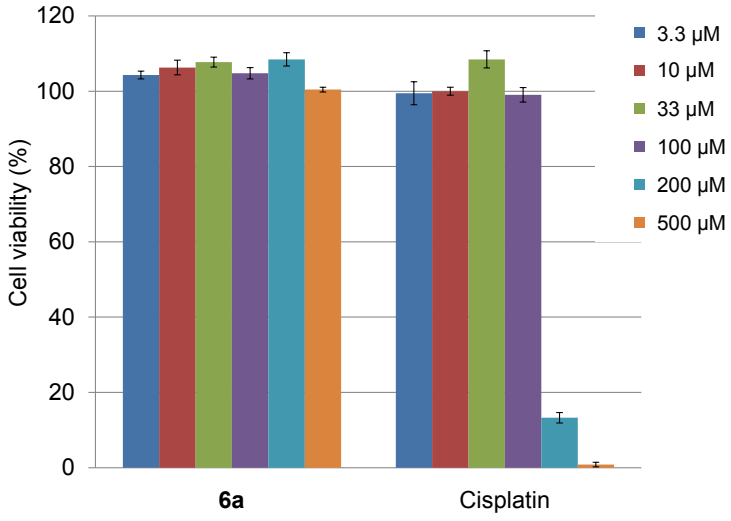


Figure S3 Effect of compound **6a** and cisplatin on WI-38 cell viability.

References.

1. (a) P. M. Groziak, A. D. Ganguly and P. D. Robinson, *J. Am. Chem. Soc.*, 1994, **116**, 7597; (b) K. Djanashvili, L. Frullano and J. A. Peters, *Chem. Eur. J.* 2005, **11**, 4010.
2. M. Maue and T. Schrader, *Angew. Chem. Int. Ed.*, 2005, **44**, 2265.
3. A. Charteris and R. John, *Anal. Biochem.*, 1975, **66**, 365.

^{1}H and ^{13}C NMR spectra

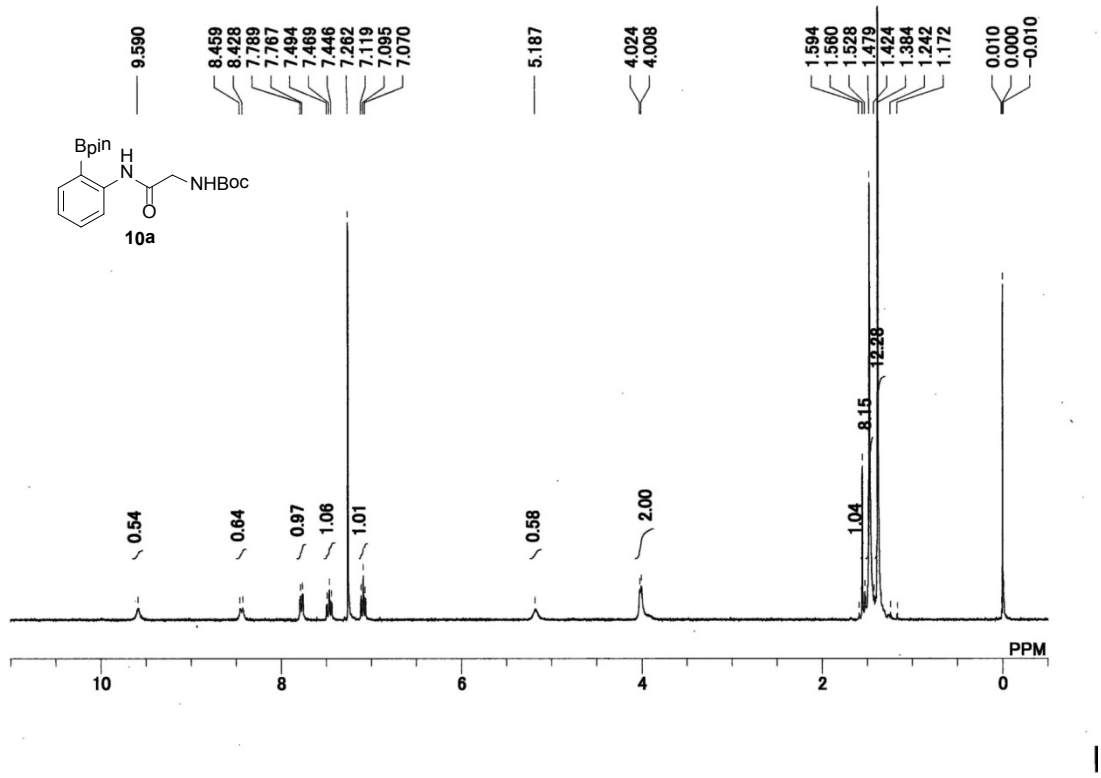


Figure S2 ^{1}H NMR spectrum of **10a**

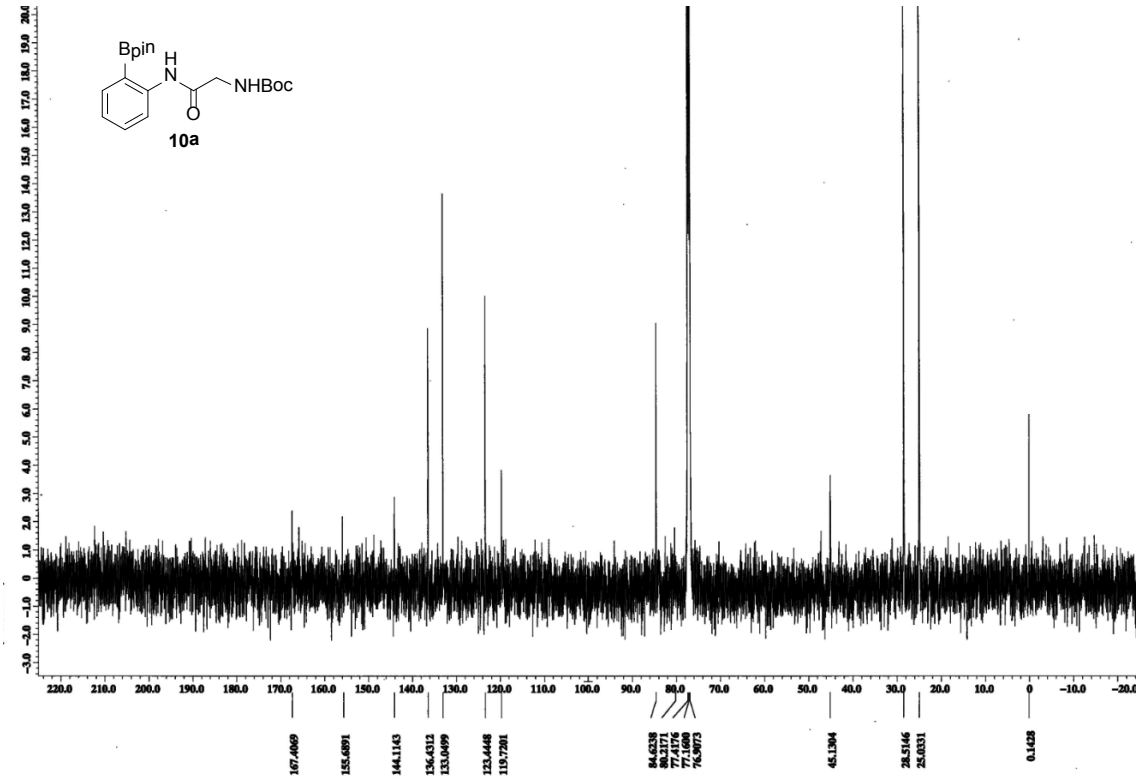


Figure S3 ^{13}C NMR spectrum of **10a**

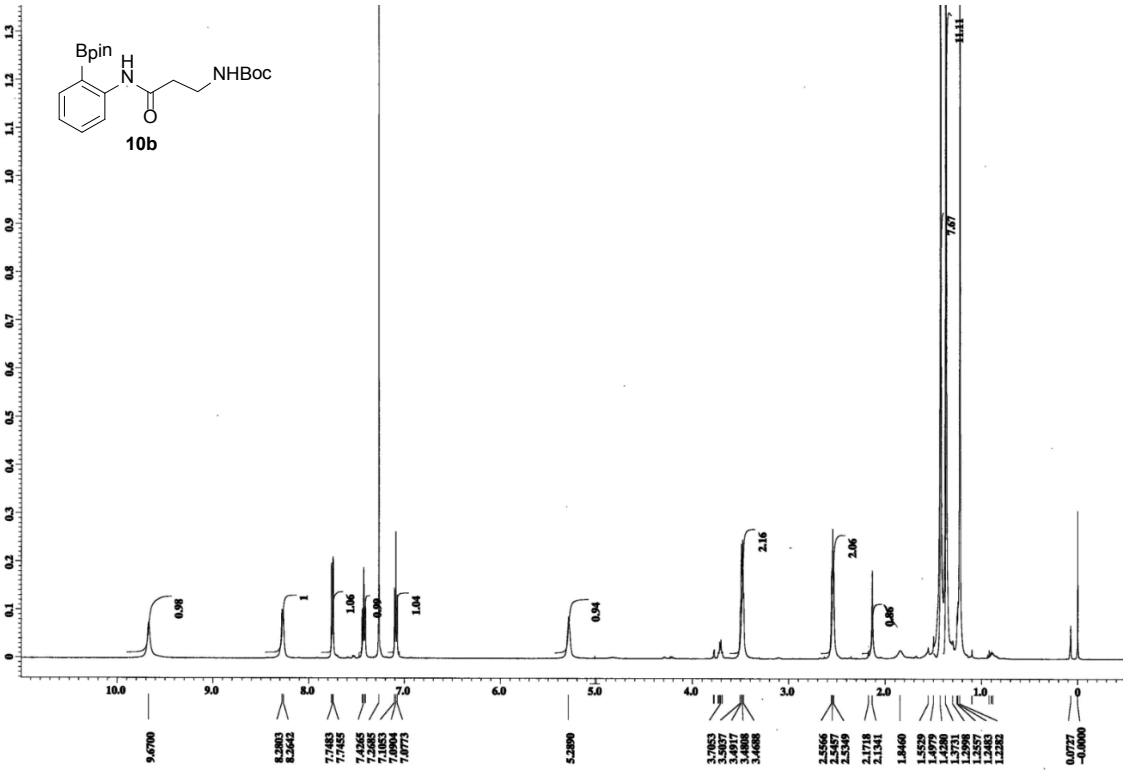


Figure S4 ^{1}H NMR spectrum of **10b**

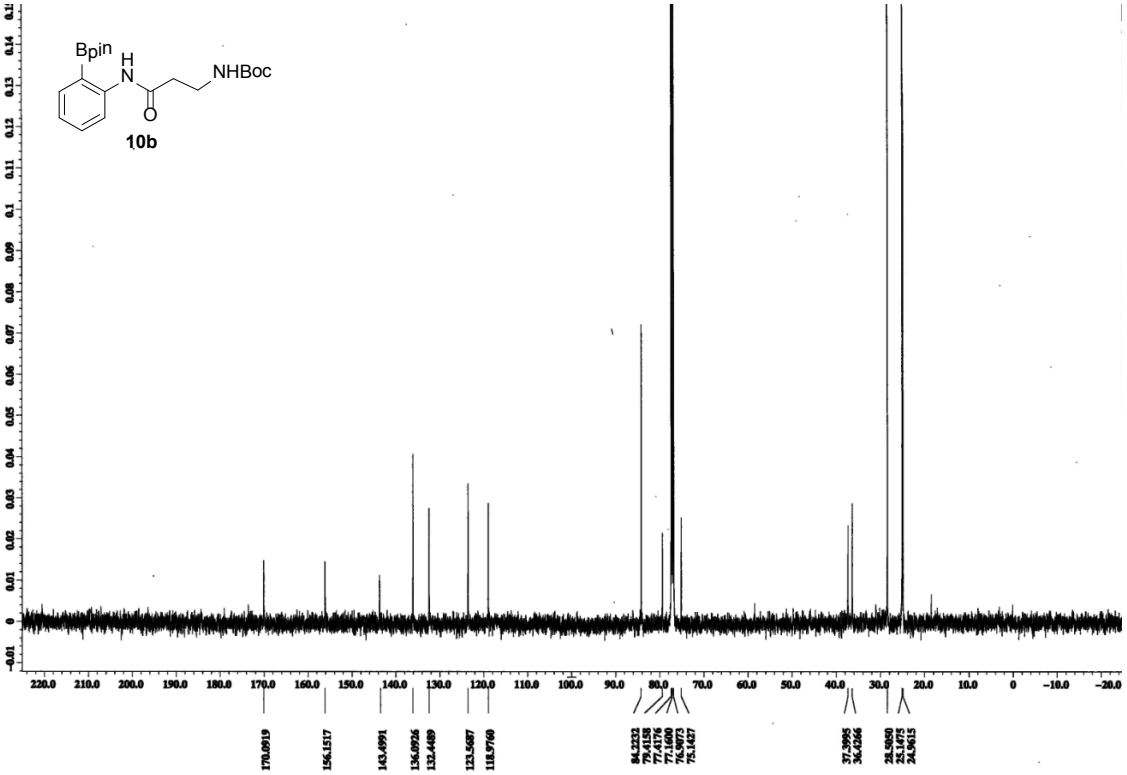


Figure S5 ^{13}C NMR spectrum of **10b**

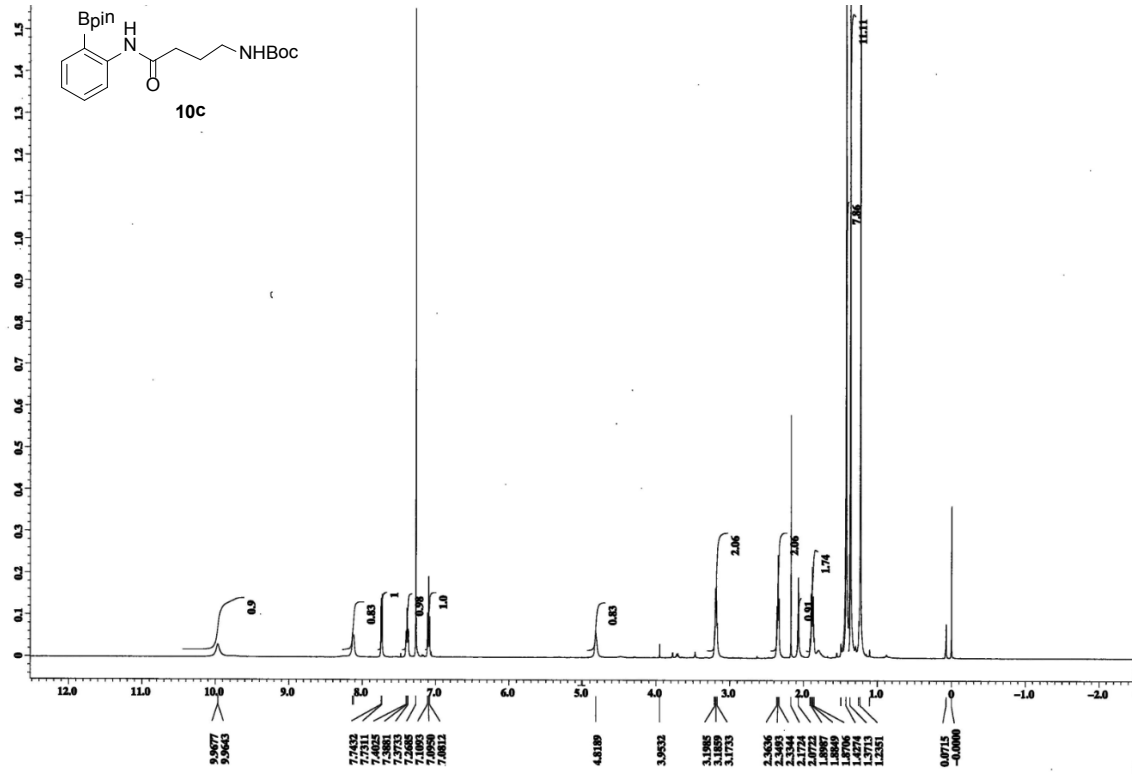


Figure S6 ^{1}H NMR spectrum of **10c**

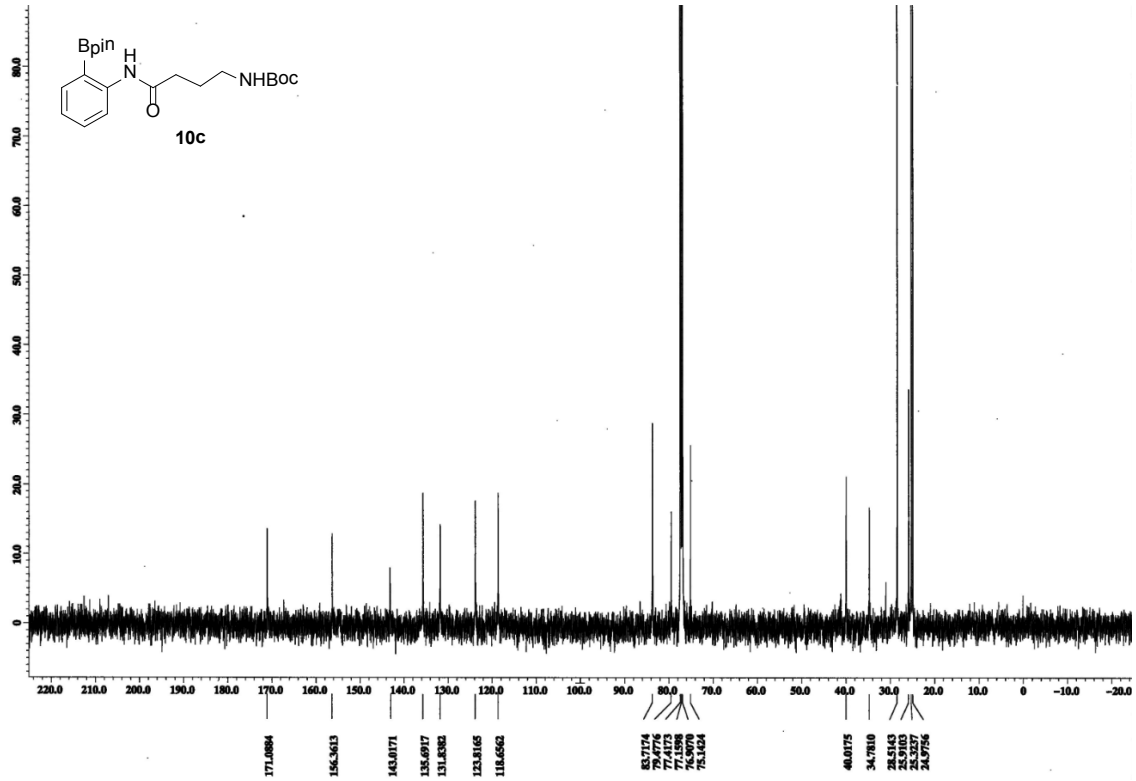


Figure S7 ^{13}C NMR spectrum of **10c**

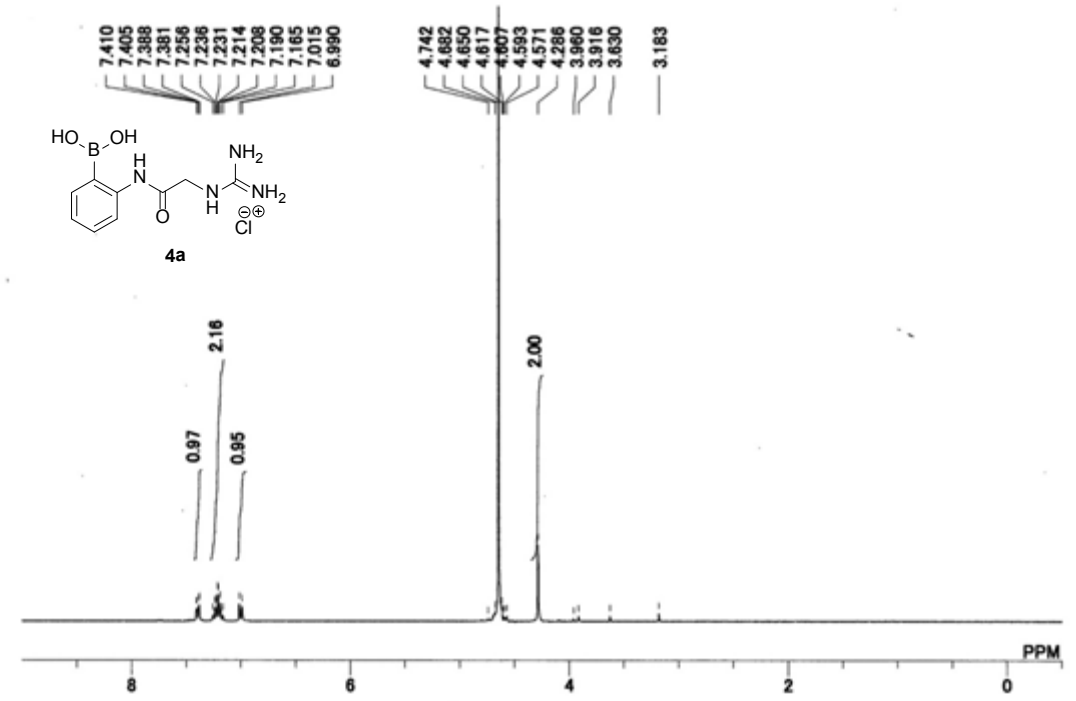


Figure S8 ^{1}H NMR spectrum of **4a**

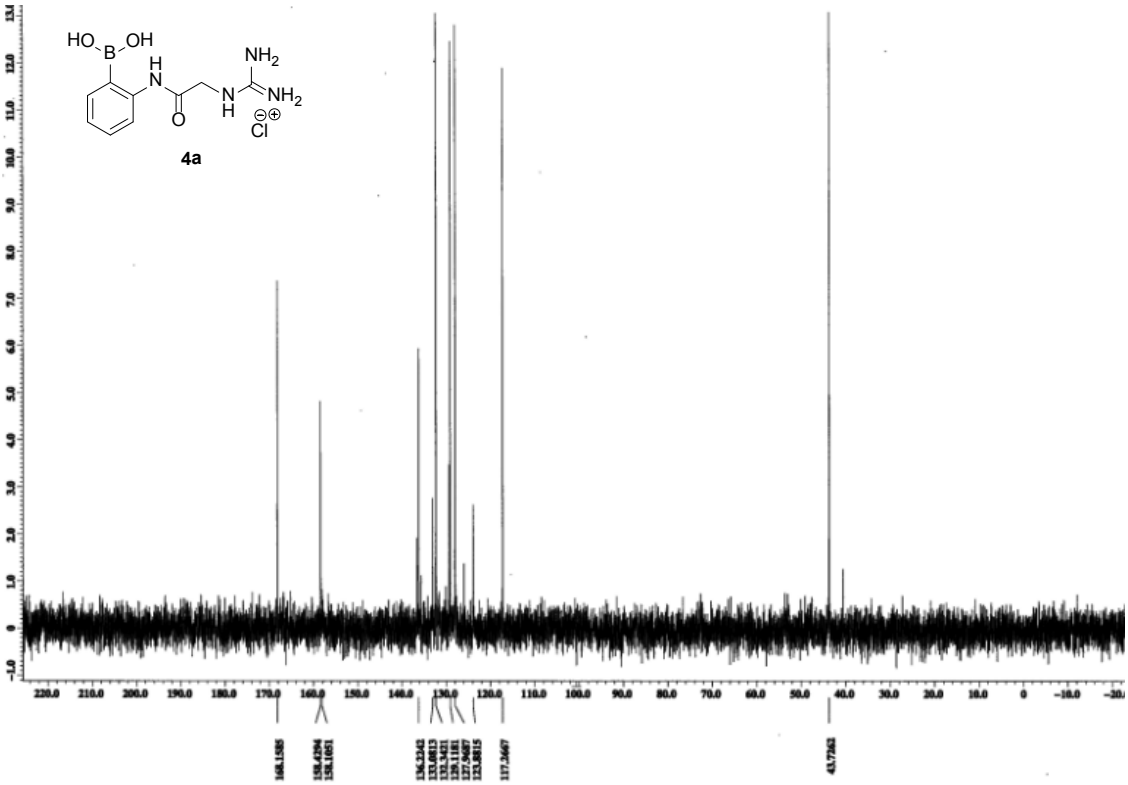


Figure S9 ^{13}C NMR spectrum of **4a**

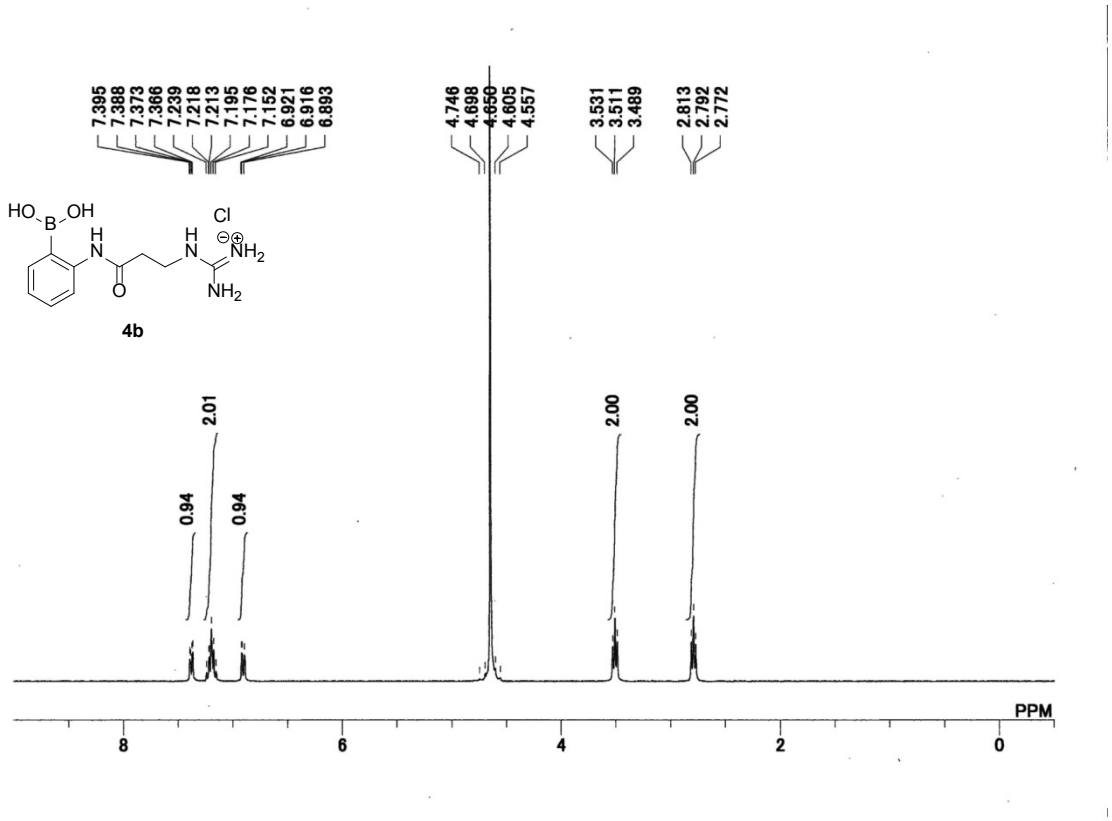


Figure S10 ^{1}H NMR spectrum of **4b**

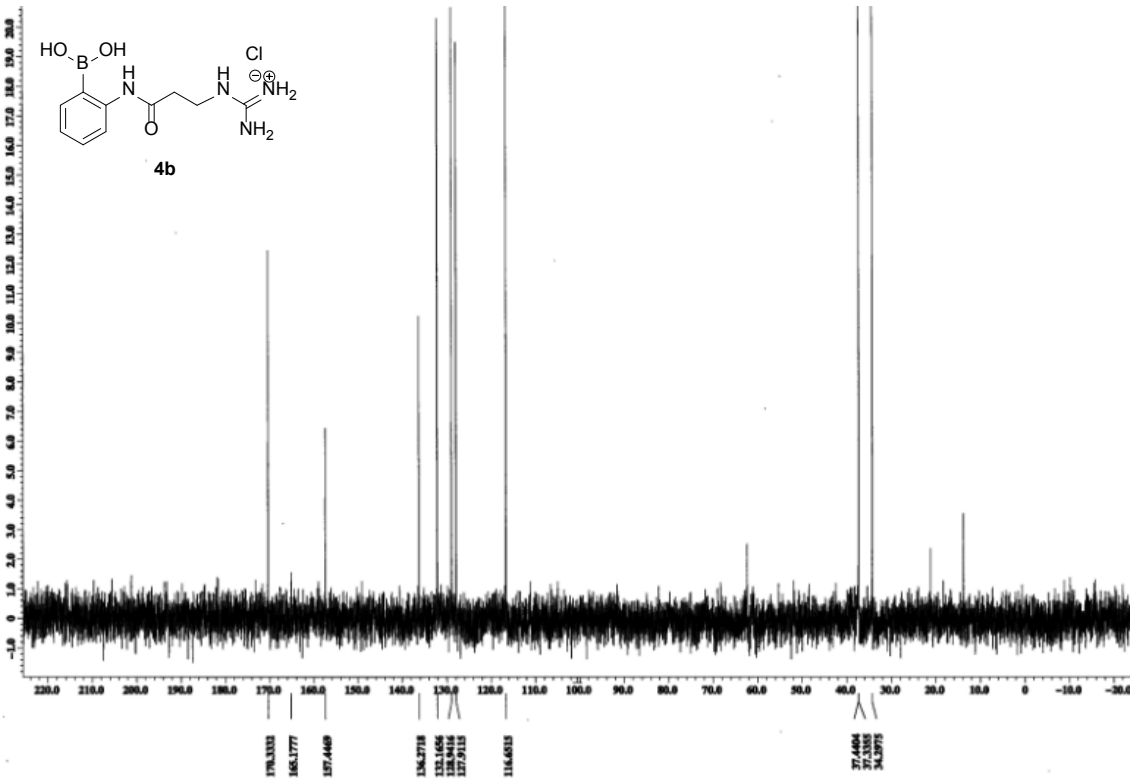


Figure S11 ^{13}C NMR spectrum of **4b**

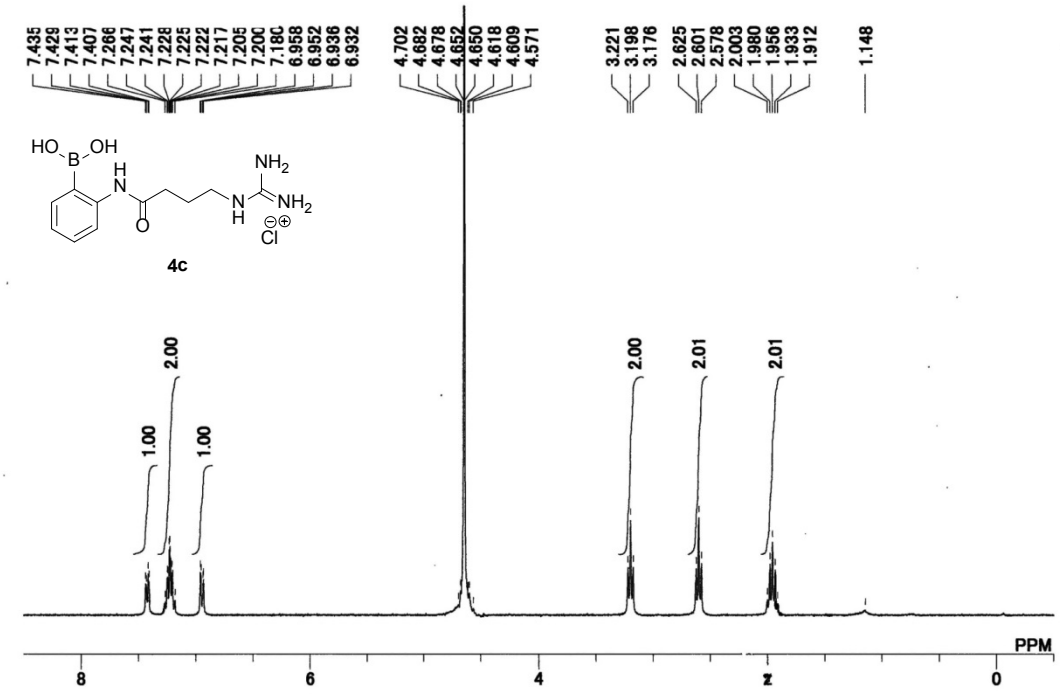


Figure S12 ^{1}H NMR spectrum of **4c**

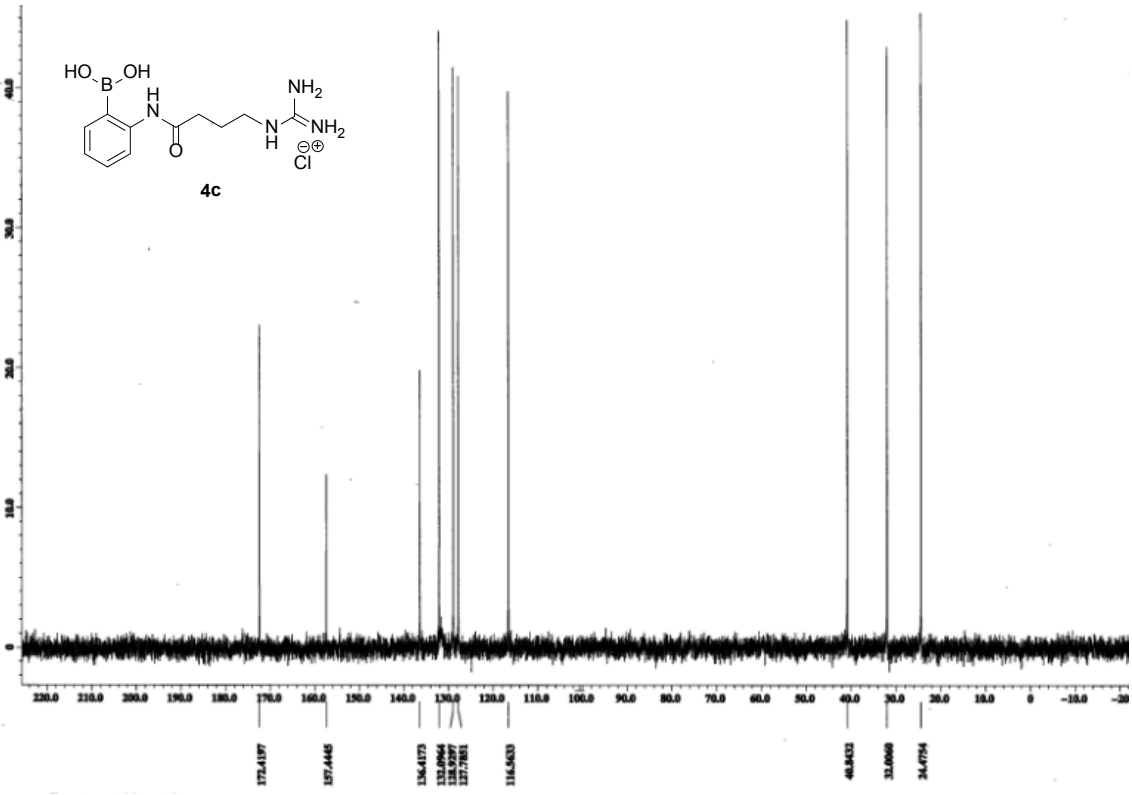


Figure S13 ^{13}C NMR spectrum of **4c**

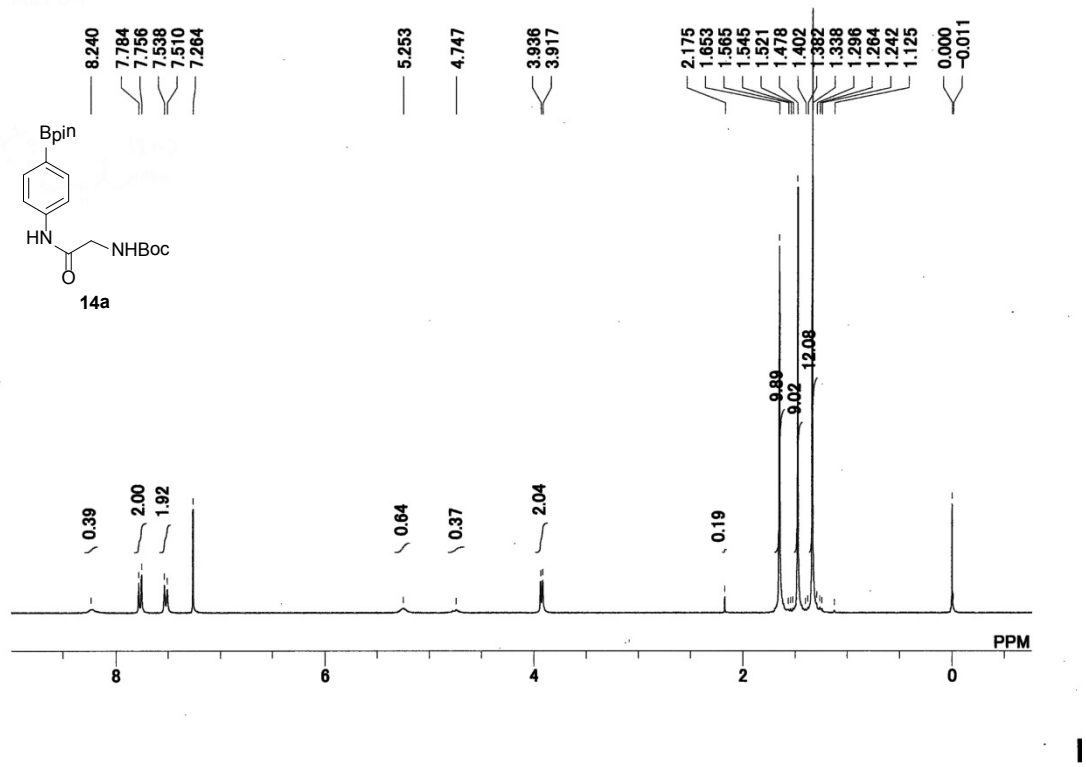


Figure S14 ^{1}H NMR spectrum of **14a**

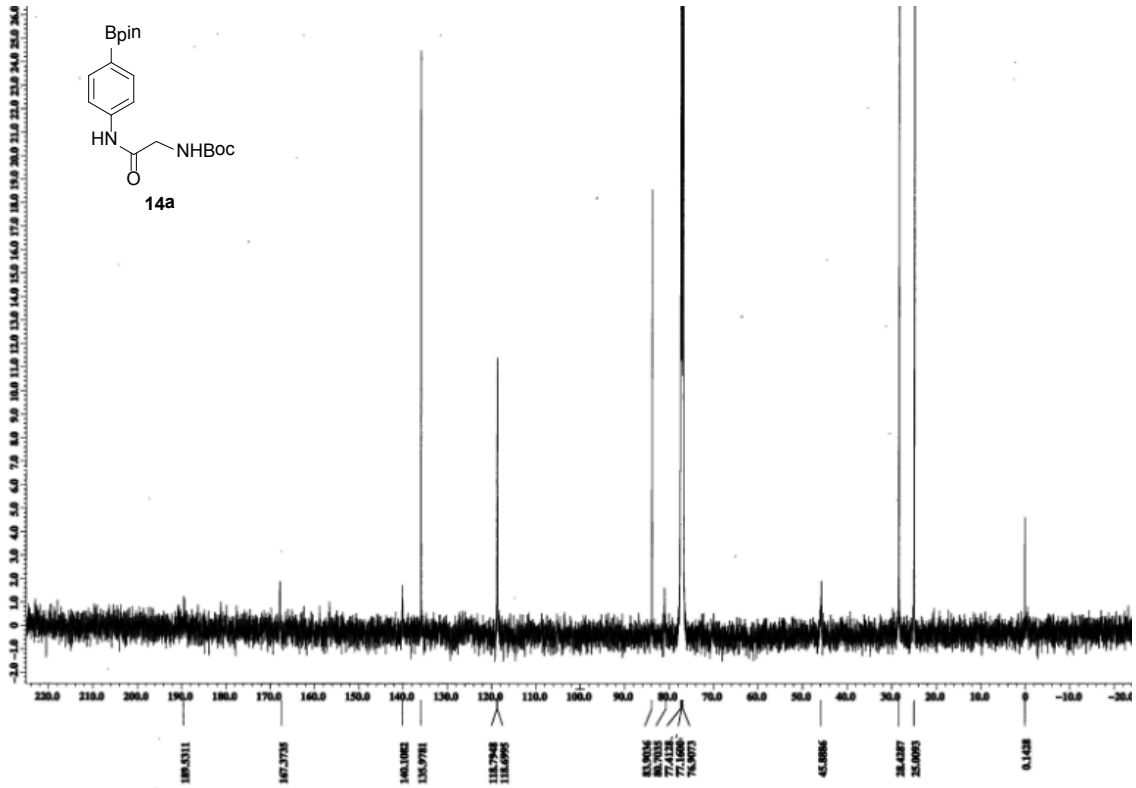


Figure S15 ^{13}C NMR spectrum of **14a**

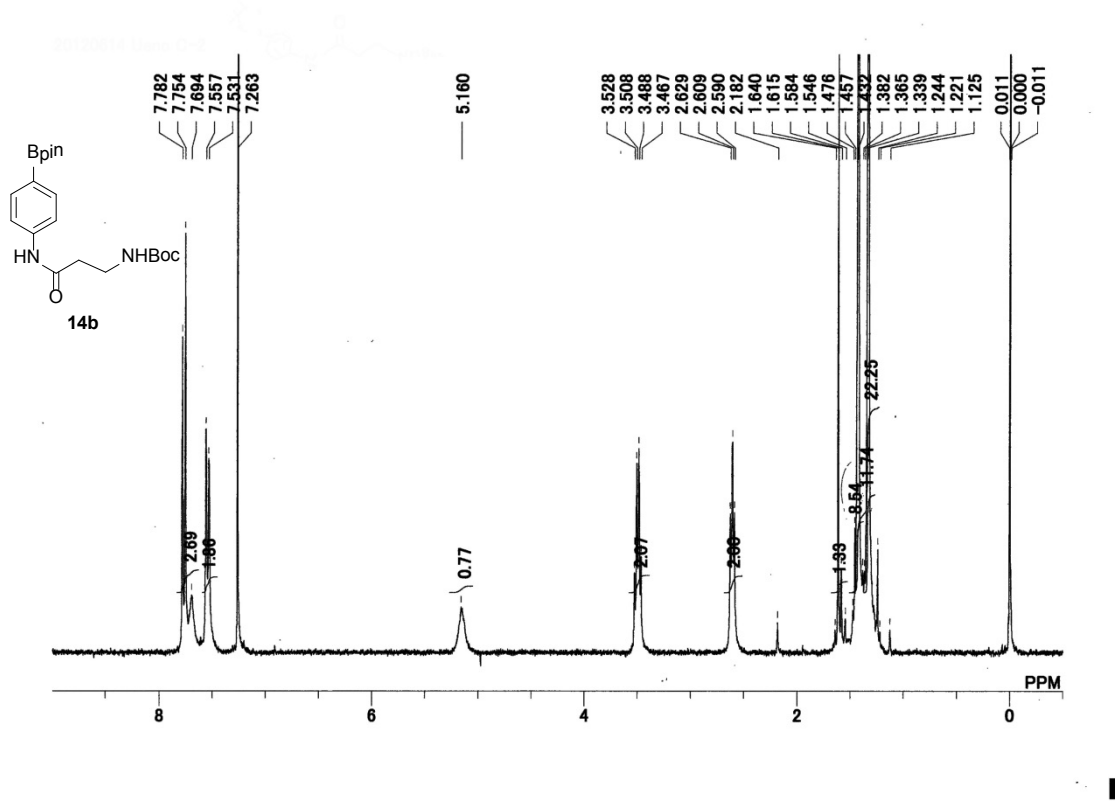


Figure S16 ^{1}H NMR spectrum of **14b**

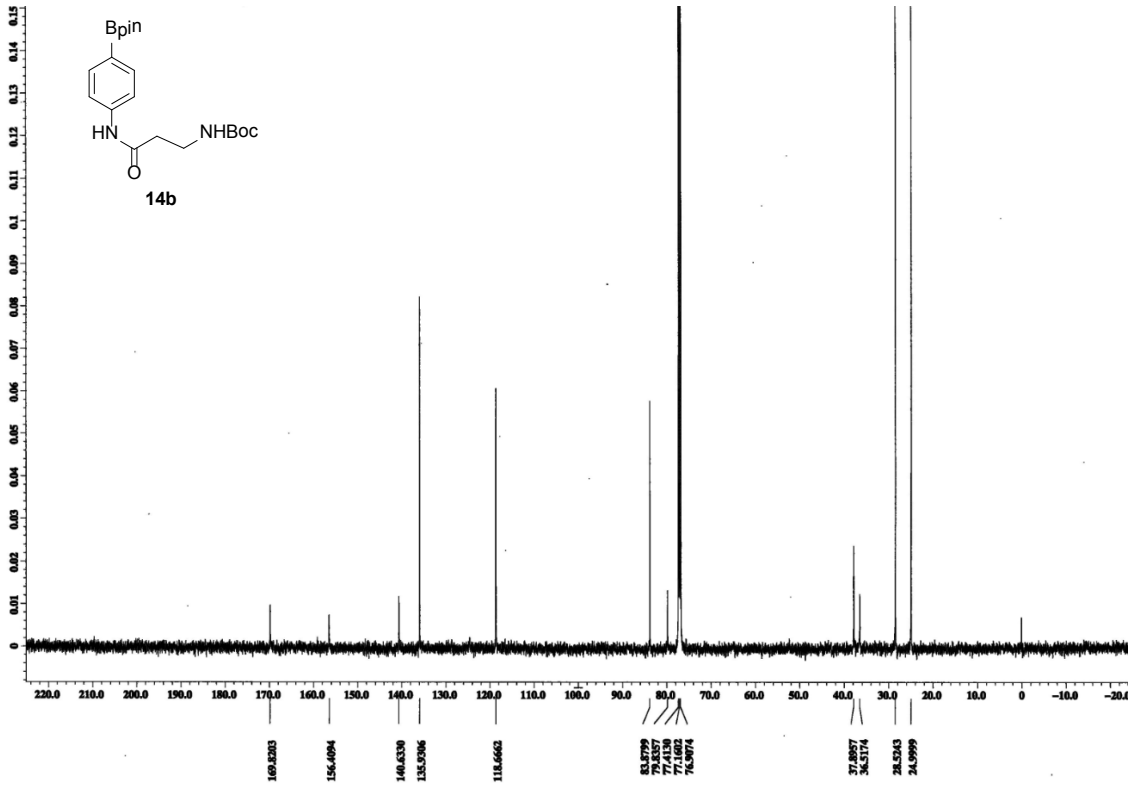


Figure S17 ^{1}H NMR spectrum of **14b**

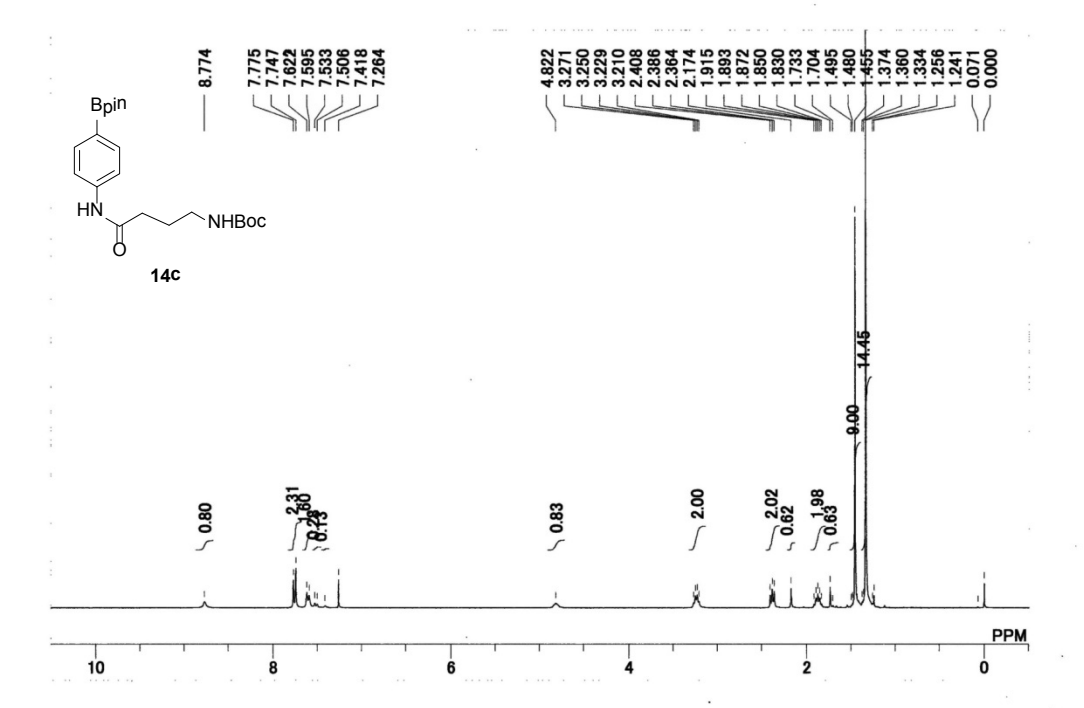


Figure S18 ^{1}H NMR spectrum of **14c**

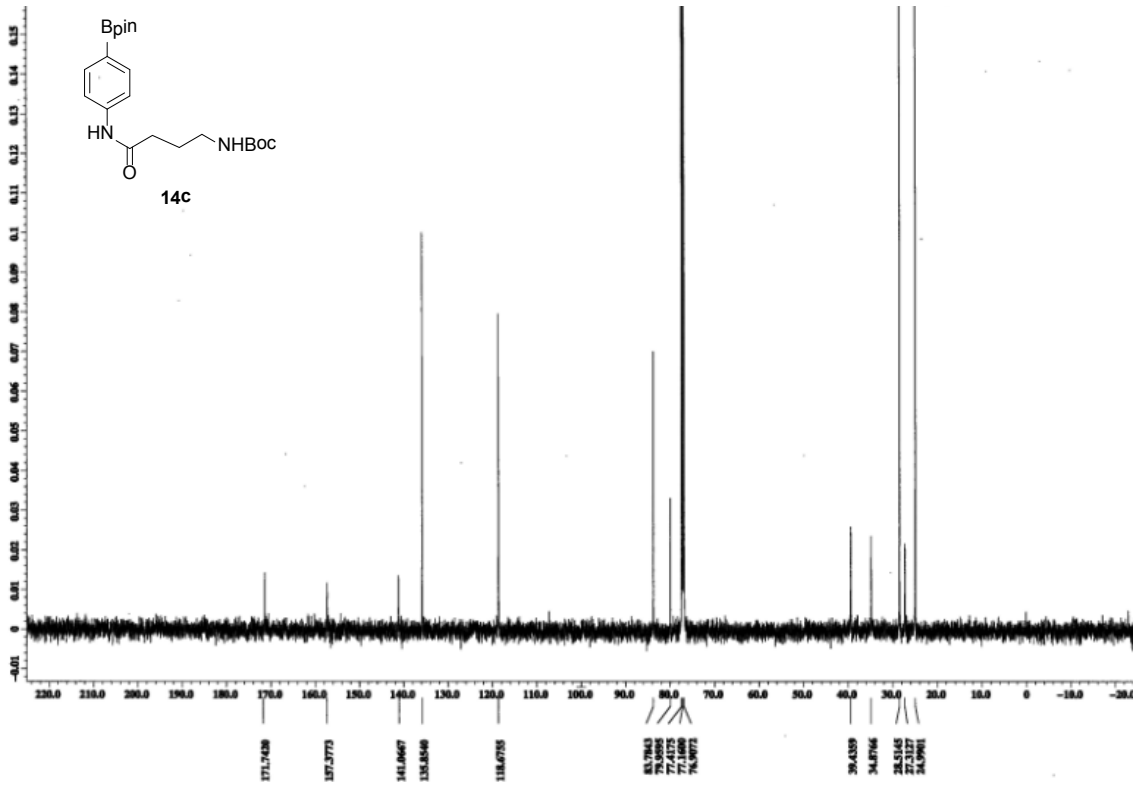


Figure S19 ^{13}C NMR spectrum of **14c**

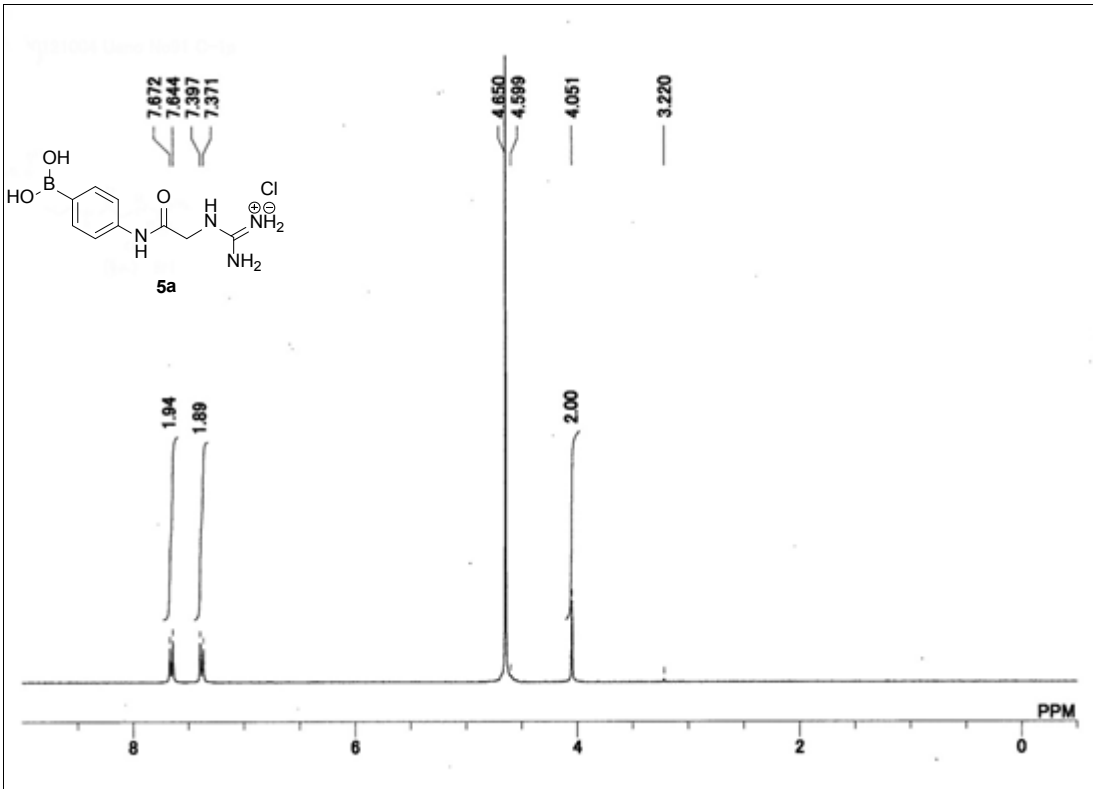


Figure S20 ^{1}H NMR spectrum of **5a**

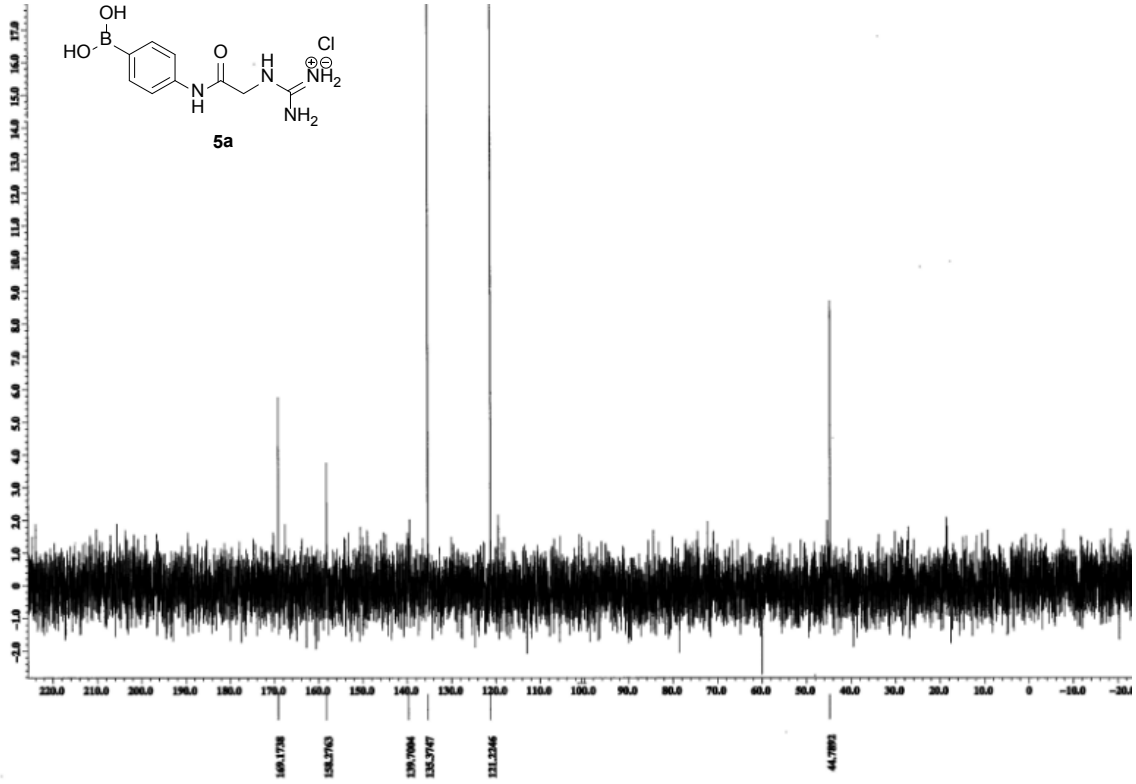


Figure S21 ^{13}C NMR spectrum of **5a**

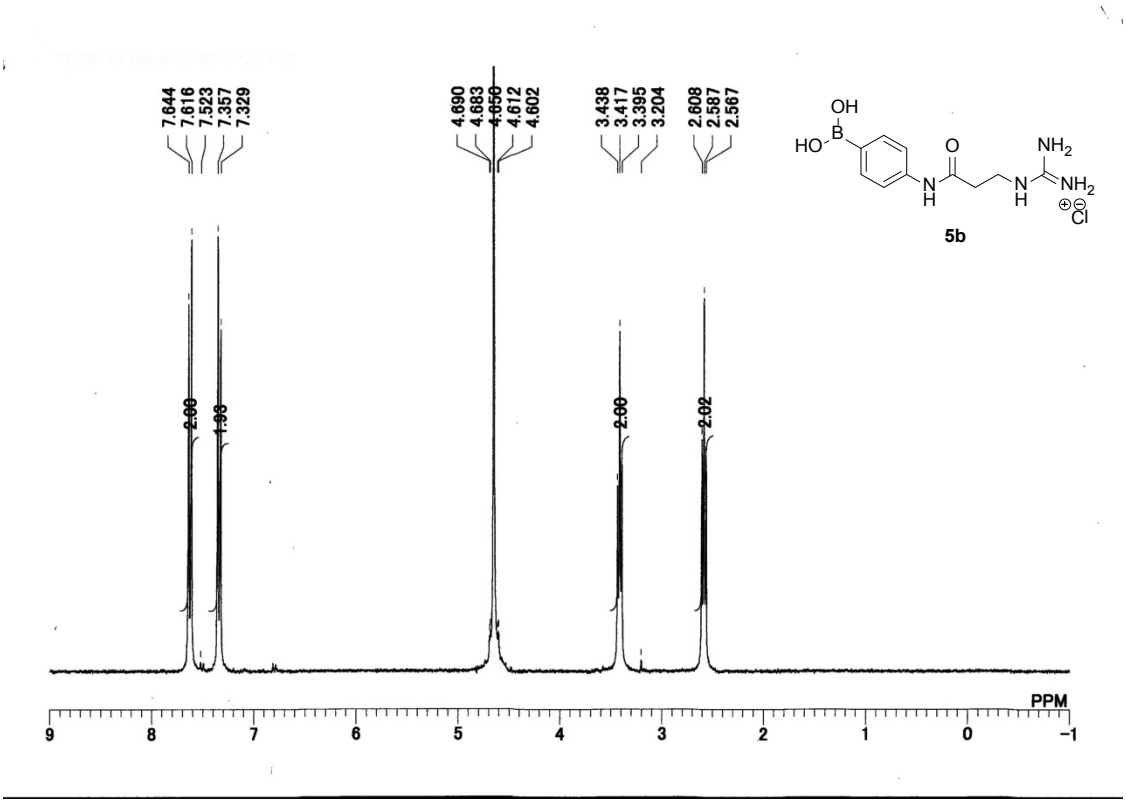


Figure S22 ^{1}H NMR spectrum of **5b**

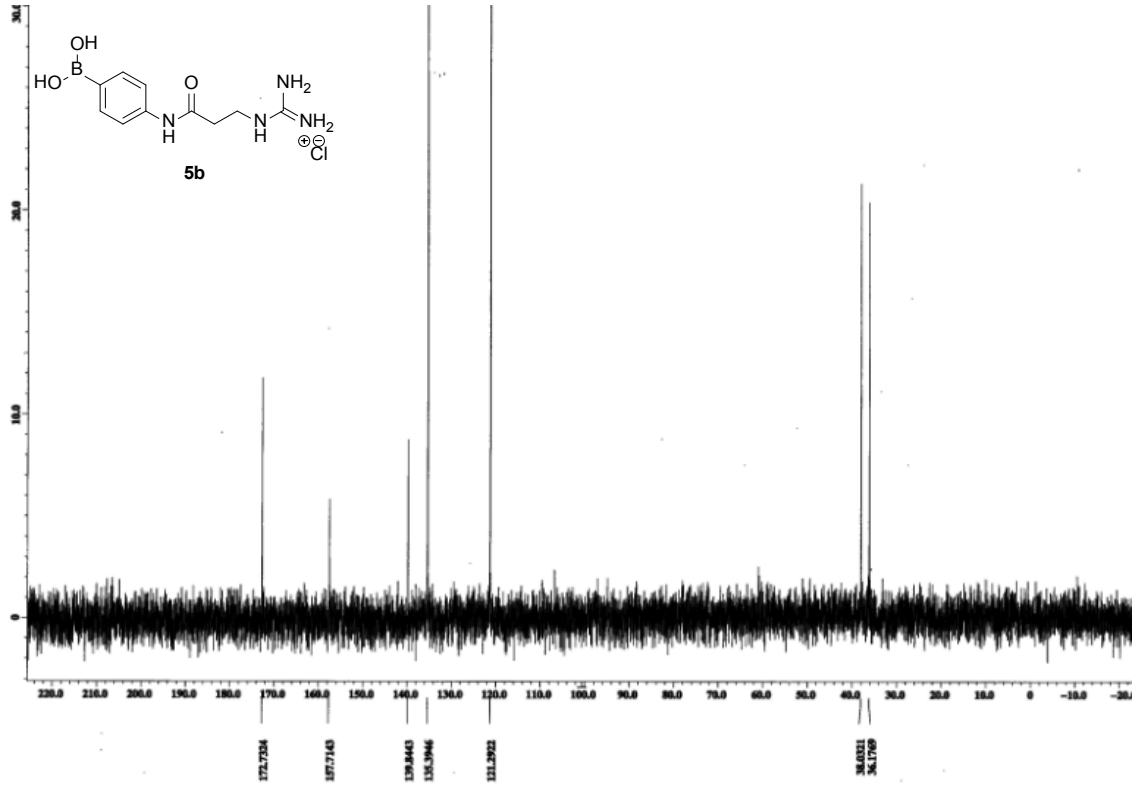


Figure S23 ^{13}C NMR spectrum of **5b**

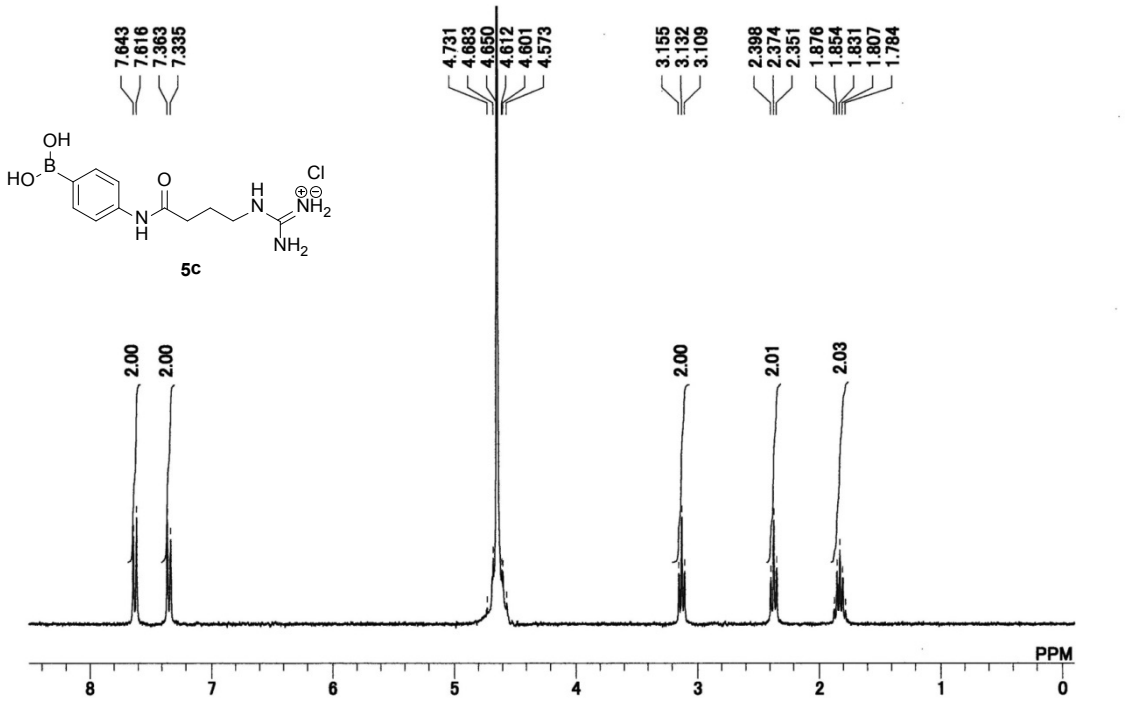


Figure S24 ^{1}H NMR spectrum of **5c**

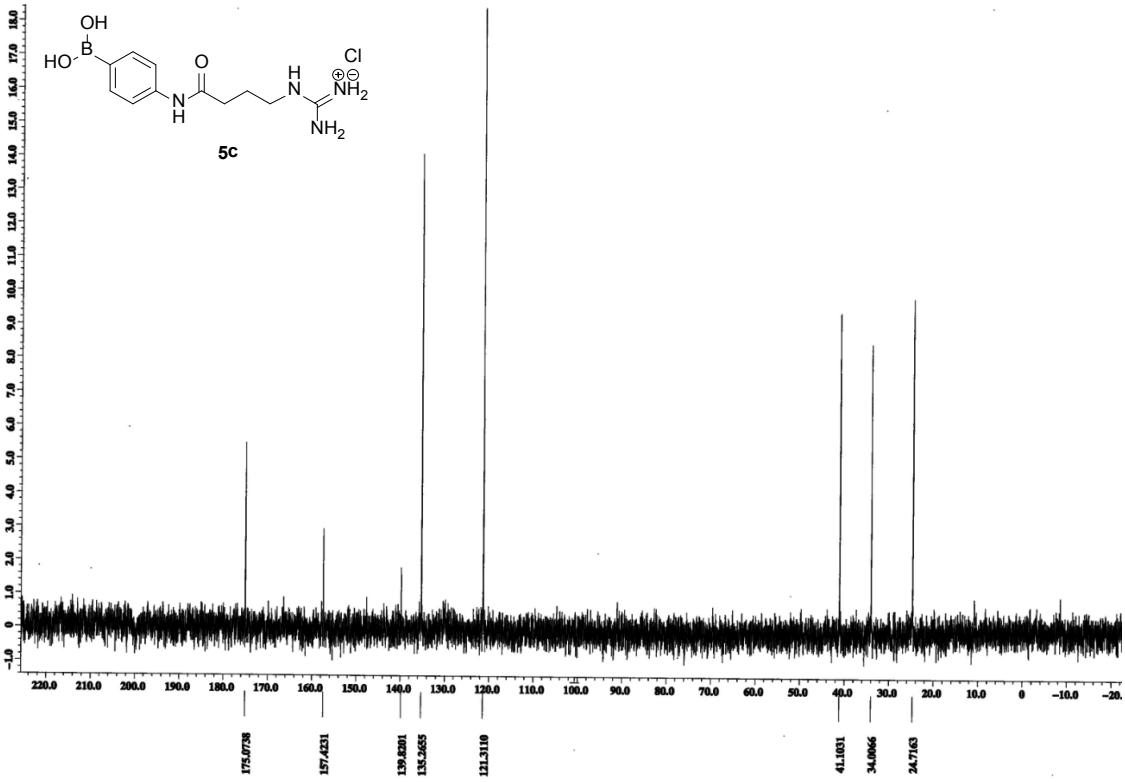


Figure S25 ^{13}C NMR spectrum of **5c**

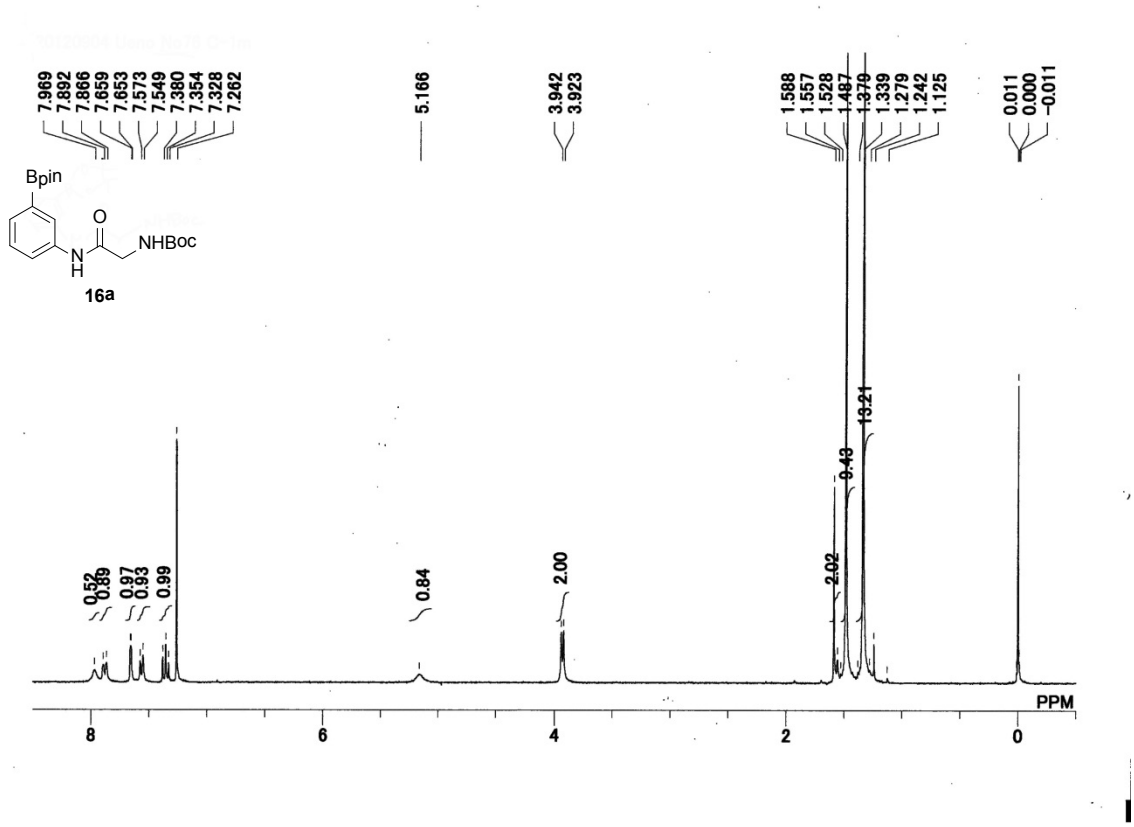


Figure S26 ^{1}H NMR spectrum of **16a**

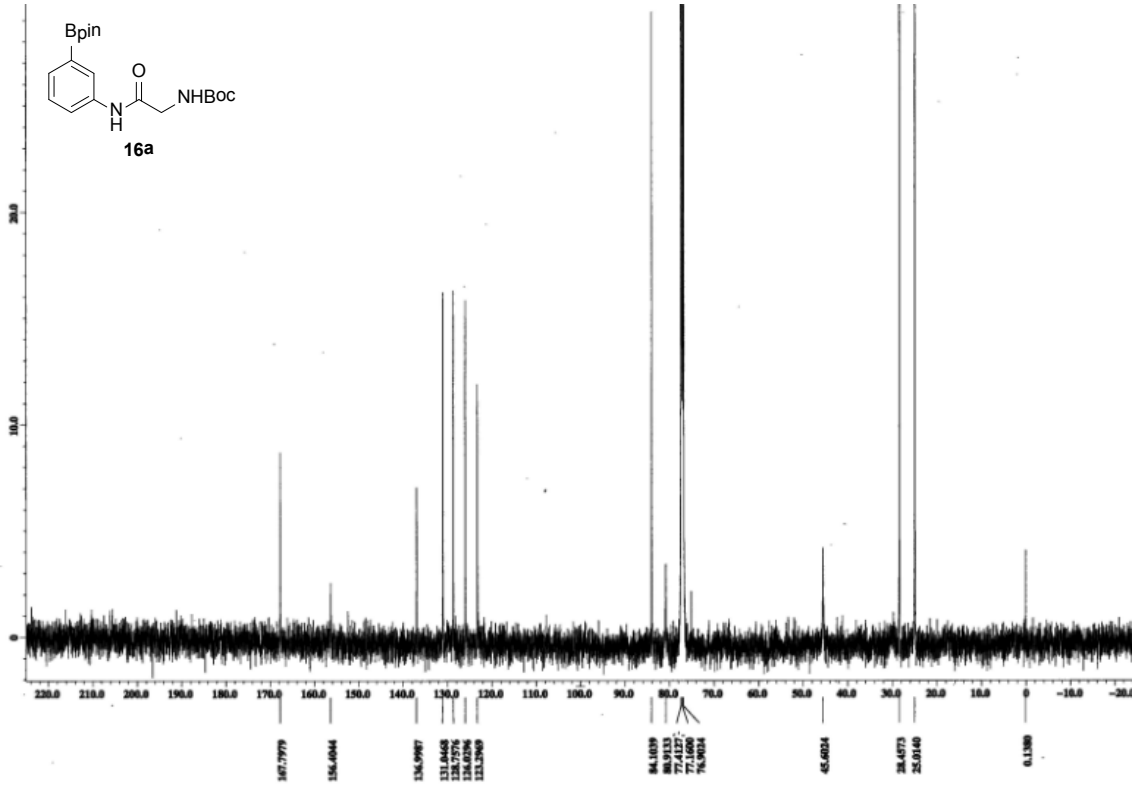


Figure S27 ^{13}C NMR spectrum of **16a**

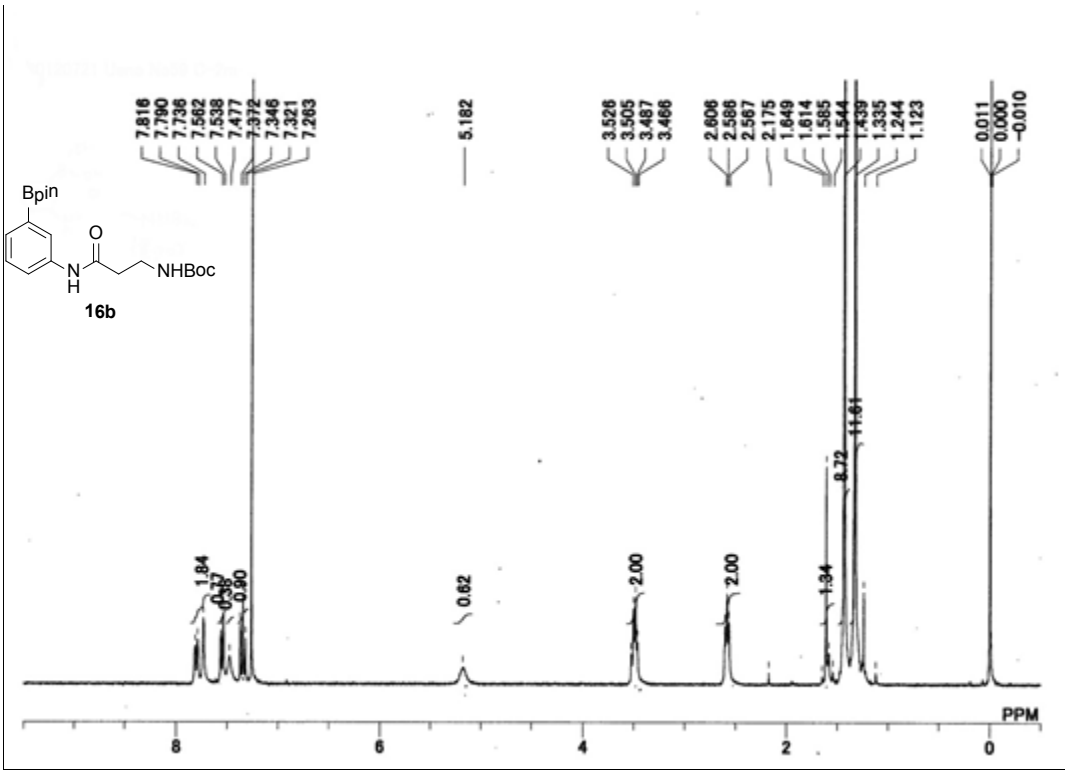


Figure S28 ^{1}H NMR spectrum of **16b**

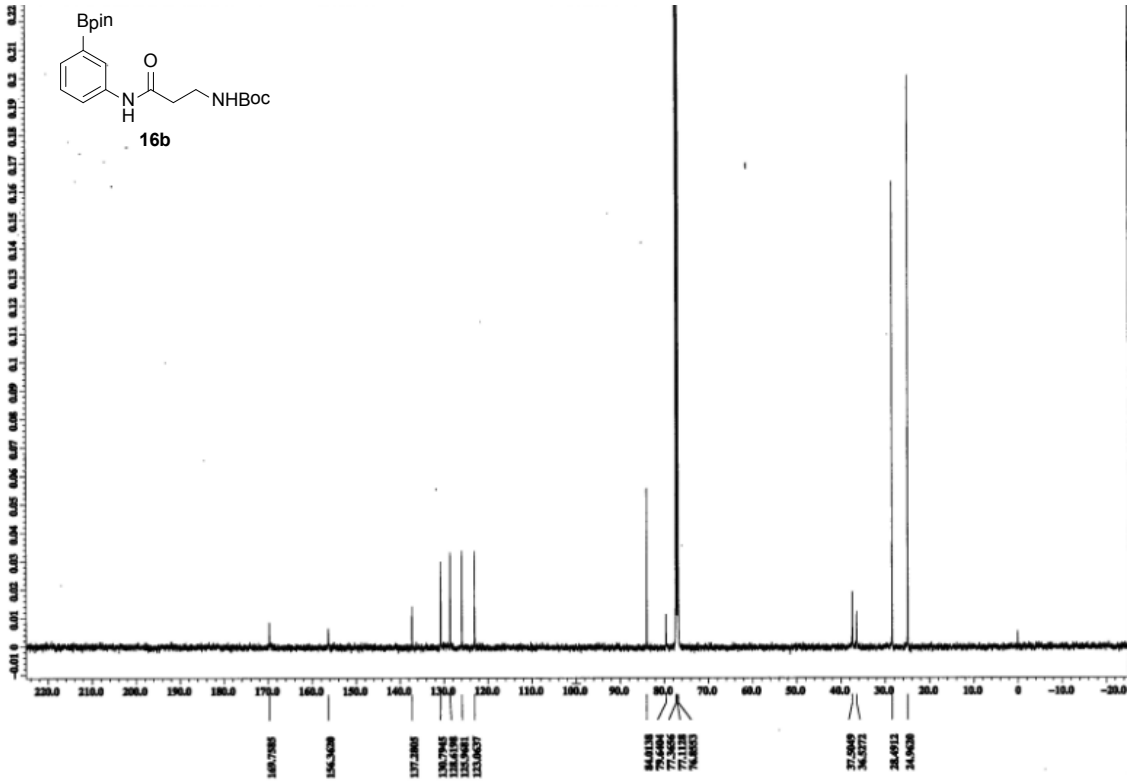


Figure S29 ^{13}C NMR spectrum of **16b**

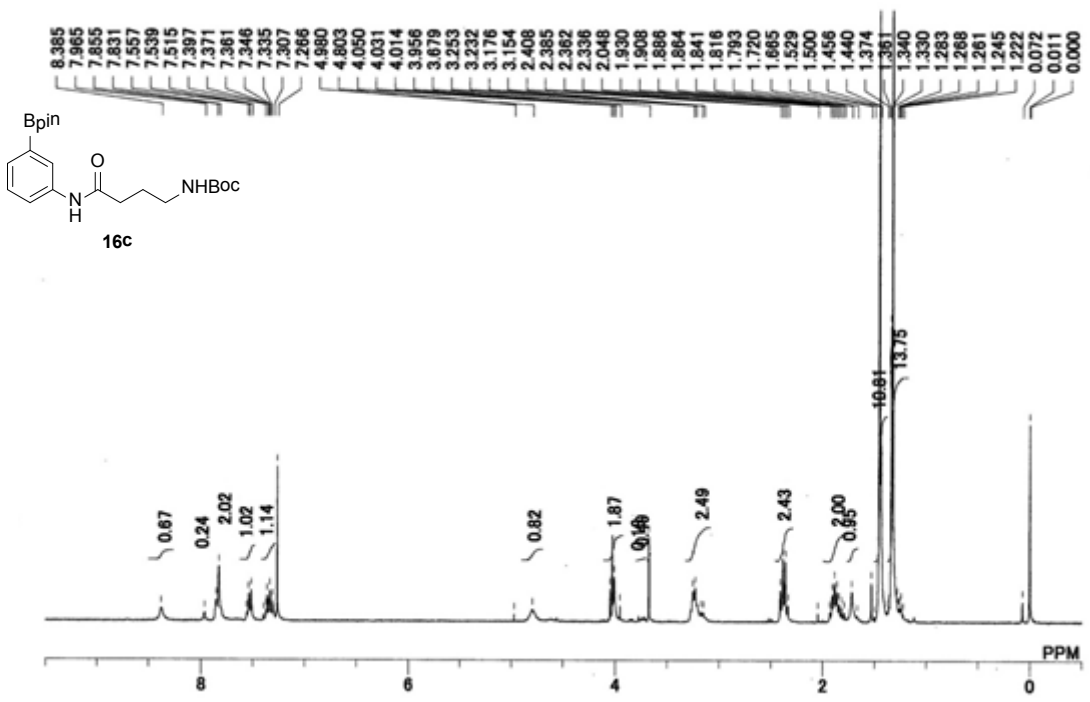


Figure S30 ^{1}H NMR spectrum of **16c**

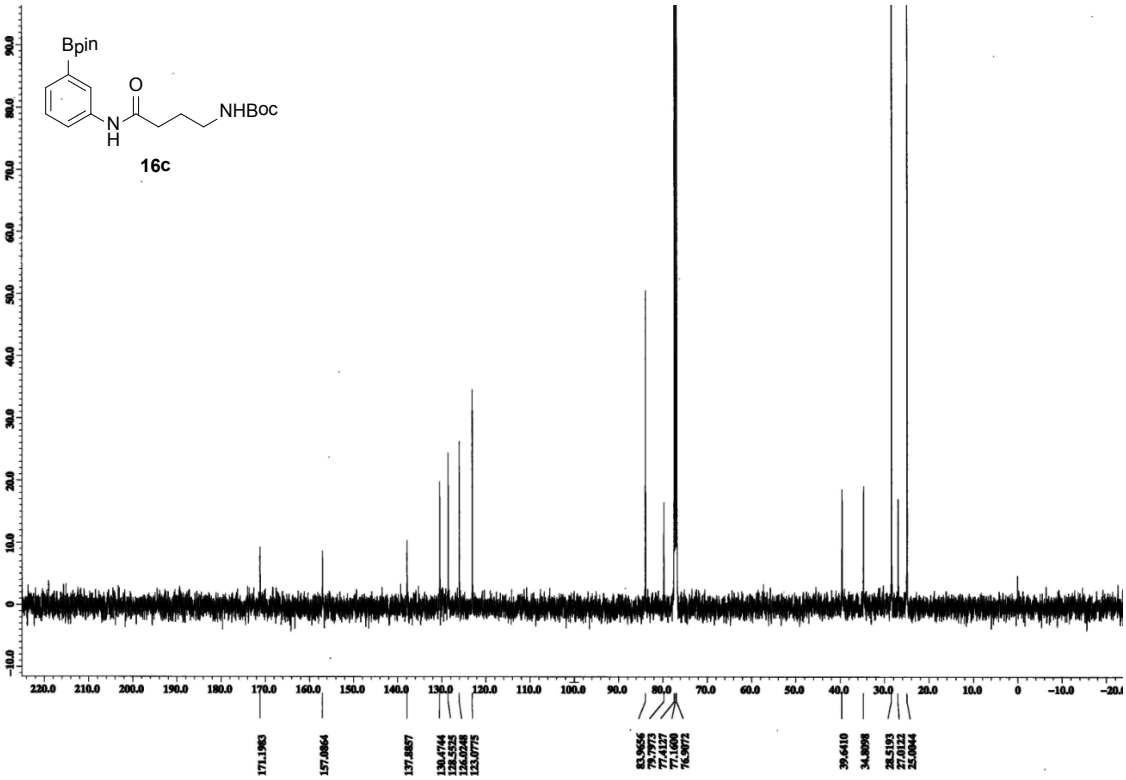


Figure S31 ^{13}C NMR spectrum of **16c**

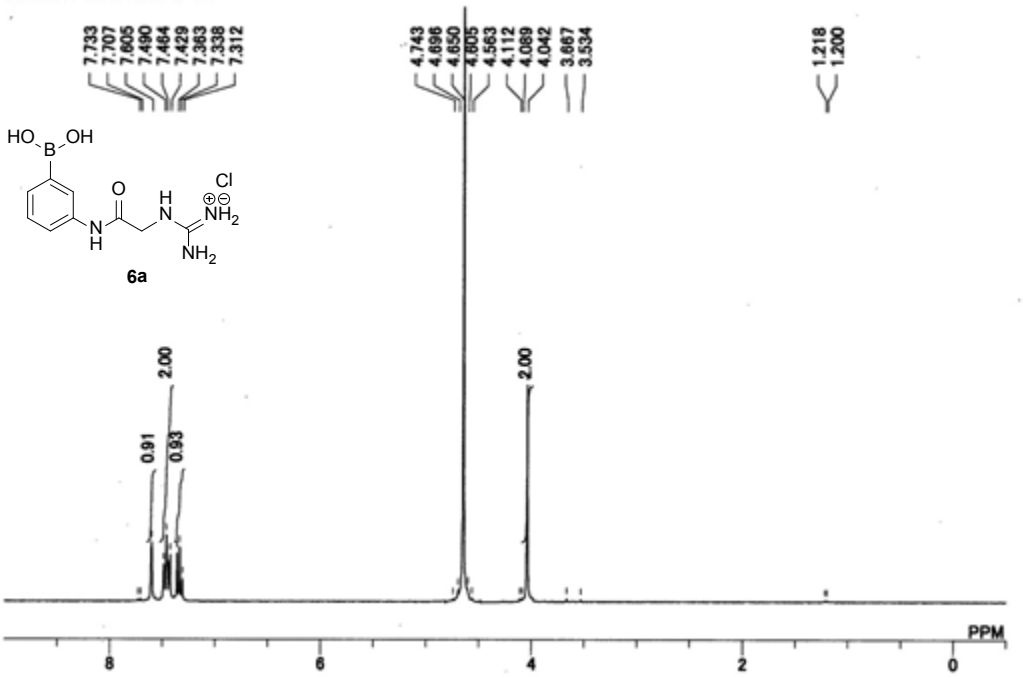


Figure S32 ^{1}H NMR spectrum of **6a**

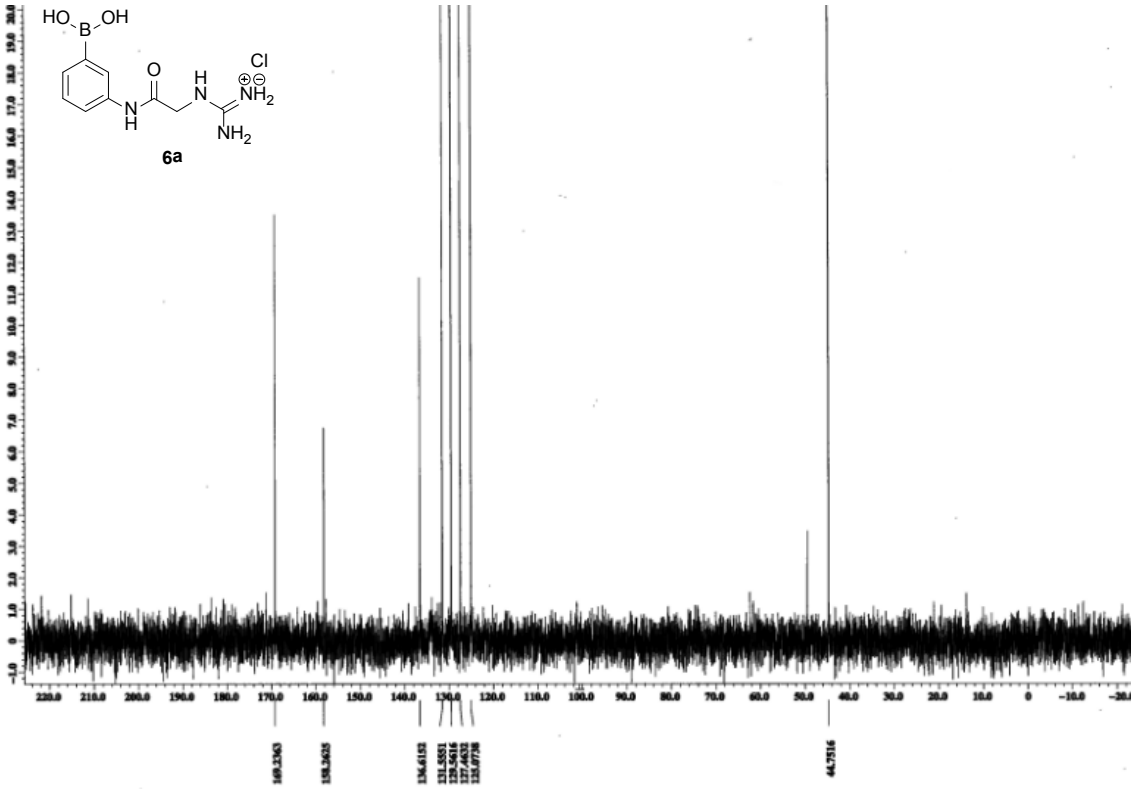


Figure S33 ^{13}C NMR spectrum of **6a**

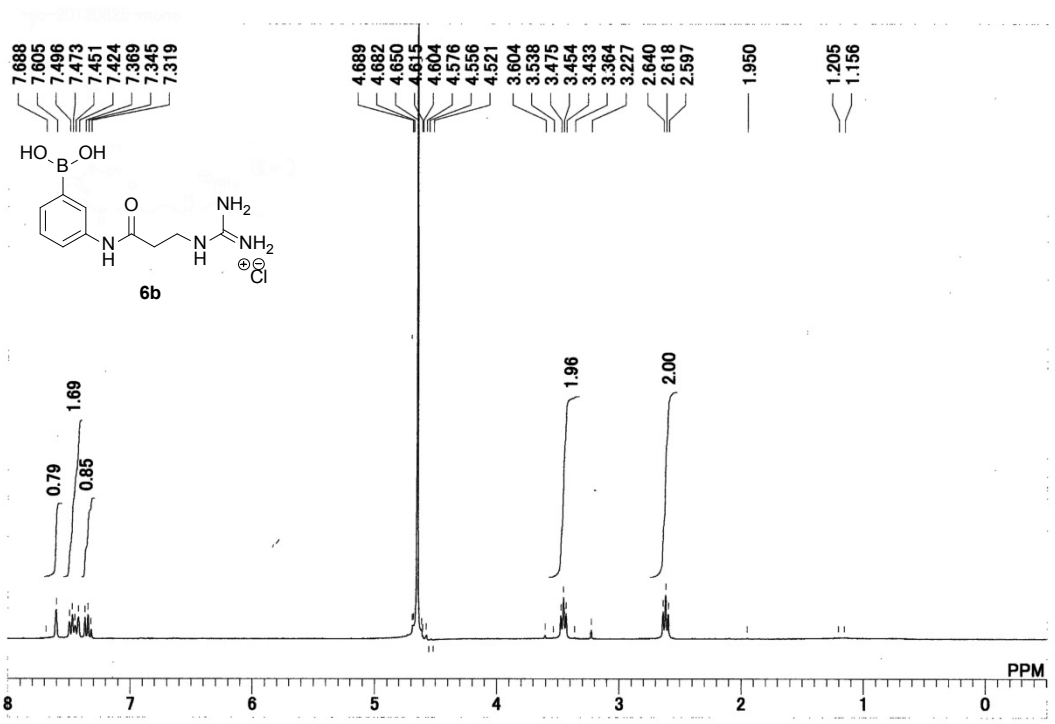


Figure S34 [1]H NMR spectrum of **6b**

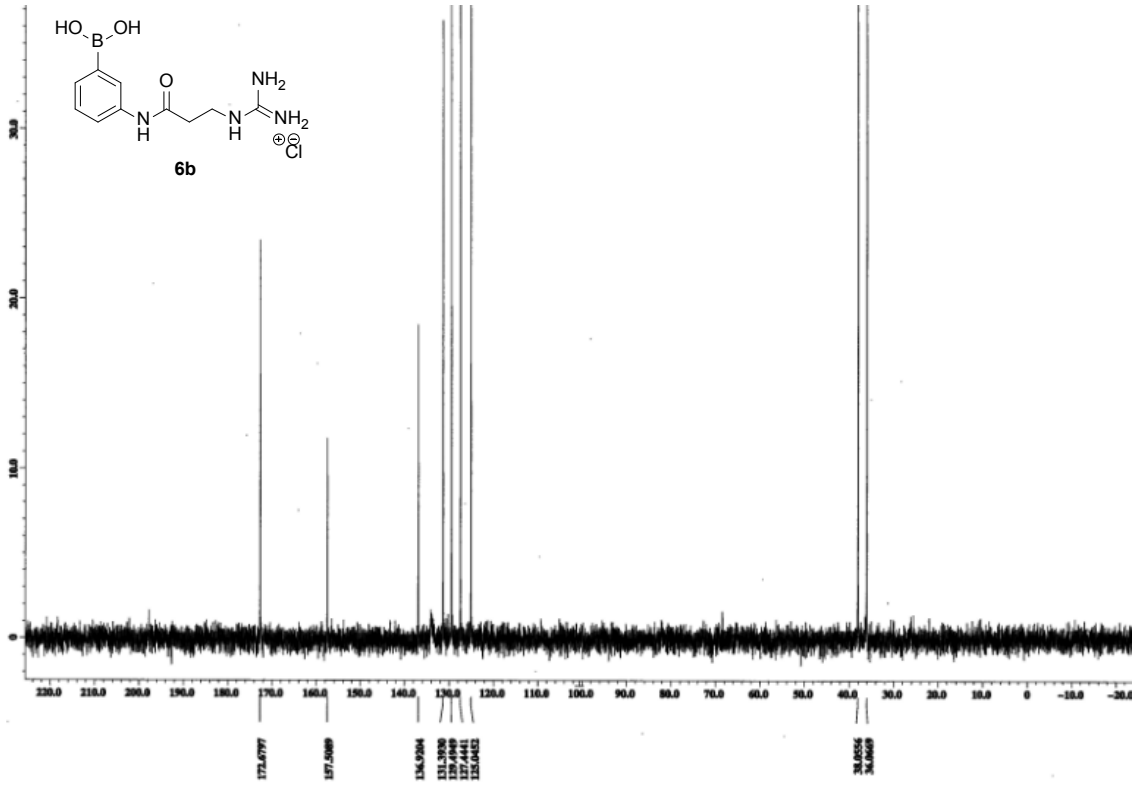


Figure S35 [13]C NMR spectrum of **6b**

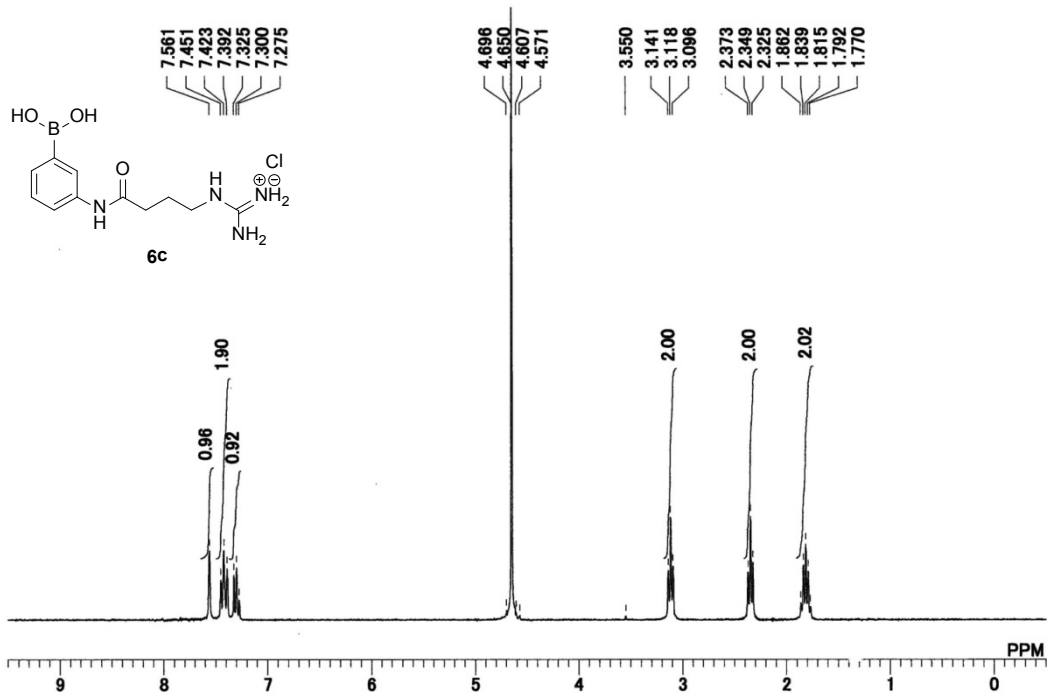


Figure S36 ^{1}H NMR spectrum of **6c**

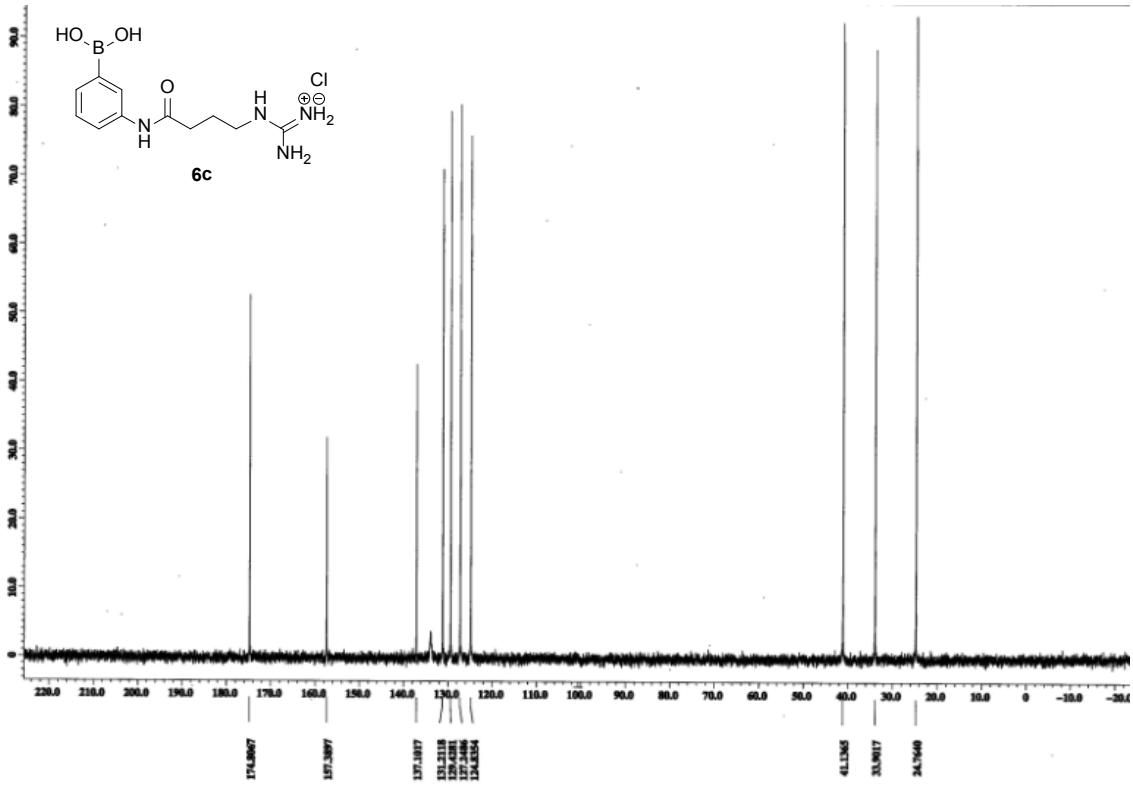


Figure S37 ^{13}C NMR spectrum of **6c**