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SUPPORTING INFORMATION

Title: (Dimethoxy- and Dihalopyridyl)boronic Acids and Highly Functionalized Heteroarylpyridines by Suzuki Cross-Coupling Reactions

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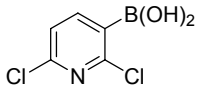
Ref. No.: O200701156

General Information

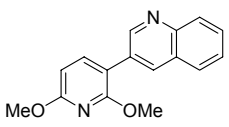
For chlorine-containing compounds MS data are quoted for the ^{35}Cl isotope.

2,6-Dichloro-3-pyridylboronic acid (8)



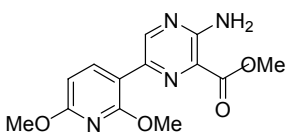
To a solution of diisopropylamine (5.2 mL, 37.2 mmol) in anhydrous THF (50 mL) at 0 °C, *n*BuLi (2.5 M in hexane, 15.2 mL, 38.0 mol) was added dropwise. The reaction was stirred for 0.5 h at 0 ºC and was then cooled to –78 °C before 2,6-dichloropyridine **7** (5.0 g, 33.8 mmol) in anhydrous THF (25 mL) was added dropwise. The reaction was stirred for 3 h at –78 °C then triisopropylborate (9.3 mL, 40.5 mmol) was added slowly. The reaction mixture was stirred at –78 °C for another 1 h, then quenched with water (50 mL) and allowed to warm to room temperature with stirring overnight. The organic solvent was evaporated *in vacuo* and then filtered. The filtrate was washed with diethyl ether (3 × 50 mL) to remove unreacted starting material. The aqueous layer was then acidified to pH 6 (with 48% HBr) to precipitate **8** as white solid (4.7 g, 73%) mp 155.2-156.0 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 7.88 (d, ^{3}J =8.0 Hz, 1H), 7.48 (d, ^{3}J =8.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ = 151.5, 149.1, 146.2, 122.8 ppm. $C_5H_4BCl_2NO_2$ (191.8) calcd. C 31.31, H 2.10, N 7.30; found: C 31.11, H 2.05, N 7.40. Recrystallisation of the product from toluene increased the melting point to 275.1-276.3 ºC. This is presumably due to the formation of the anhydride.

3-(2,6-Dimethoxypyridin-3-yl)quinoline (16)



Boronic acid **2** (311 mg, 1.7 mmol), 3-bromoquinoline **11** (312 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 24 h; eluent DCM:EtOAc (1:1 v/v) gave **16** as a white solid (333 mg, 83%), mp 98.0-98.7 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 9.06 (d, ^{5}J = 2.0 Hz, 1H), 8.42 (d, ^{5}J = 2.0 Hz, 1H), 8.02 (d, ^{3}J = 8.0 Hz, 1H), 7.97 (d, ^{3}J = 8.0 Hz. 1H), 7.91 (t, ^{3}J = 8.0 Hz, 1H), 7.73 (t, ^{3}J = 8.0 Hz, 1H), 7.60 (t, ^{3}J = 8.0 Hz, 1H), 6.55 (d, ^{3}J = 8.0 Hz, 1H), 3.94 (s, 3H), 3.91 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 162.4, 159.2, 151.1, 146.2, 142.2, 134.5, 129.5, 129.3, 128.6, 128.1, 127.5, 126.8, 111.7, 101.9, 53.5, 53.5 ppm. MS (EI) *m/z* 266.1 (M^+). $C_{16}H_{14}N_2O_2$ (266.1) calcd. C 72.16, H 5.30, N 10.52; found: C 71.67, H 5.28, N 10.50.

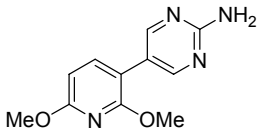
Methyl 3-amino-6-(2,6-dimethoxypyridin3-yl)pyrazine-2-carboxylate (17)



Boronic acid **2** (311 mg, 1.7 mmol), methyl 3-amino-6-bromopyrazine-2-carboxylate **12** (348 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 15 min; eluent EtOAc gave **17** as yellow needles (320 mg, 74%), mp 191.8-192.3 °C (from toluene). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.79 (s, 1H), 8.08 (d, ^{3}J = 8.0 Hz, 1H), 7.36 (br. s, 2H), 6.54 (d, ^{3}J = 8.0 Hz, 1H), 3.98 (s, 3H), 3.91 (s, 3H), 3.87 (s, 3H) ppm. ^{13}C

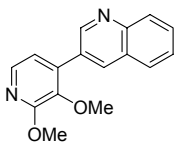
NMR (100 MHz, DMSO-d_6) δ = 166.5, 162.2, 158.9, 154.0, 147.7, 141.2, 137.1, 122.0, 111.0 102.0, 53.50, 53.49, 52.2 ppm. MS (EI) *m/z* 290.2 (M^+). $C_{13}H_{14}N_4O_4$ (290.3) calcd. C 53.79, H 4.86, N 19.30; found: C 53.64, H 4.81, N, 19.07.

5-(2,6-Dimethoxypyridin-3-yl)pyrimidin-2-amine (18)



Boronic acid **2** (311 mg, 1.7 mmol), 2-amino-5-bromopyrimidine **13** (261 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 65 h; eluent EtOAc gave **18** as a pale yellow solid (261 mg, 75%), mp 201.2-202.5 °C (from toluene). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.36 (s, 2H), 7.70 (d, ^3J = 8.0 Hz, 1H), 6.67 (s, 2H), 6.45 (d, ^3J = 8.0 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ = 162.2, 161.6, 158.7, 157.2, 140.5, 118.3, 109.8, 101.4, 53.3, 53.2 ppm. MS (ES^+) *m/z* 233.1 ($[M+1]^+$). $C_{11}H_{12}N_4O_2$ (232.2) calcd. C 56.89, H 5.21, N 24.12; found: C 57.18, H 5.21, N 24.08.

3-(2,3-Dimethoxypyridin-4-yl)quinoline (19)



Boronic acid **4** (311 mg, 1.7 mmol), 3-bromoquinoline **11** (312 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 1.25 h; eluent EtOAc gave **19** as a clear oil which solidified to a white solid (383 mg, 96%), mp 99.4-102.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.12 (d, ^5J = 2.4 Hz, 1H), 8.33 (d, ^5J = 2.0 Hz, 1H), 8.12 (d, ^3J = 8.4 Hz, 1H), 7.97 (d, ^3J = 5.2 Hz. 1H), 7.85 (d, ^3J = 8.0 Hz, 1H), 7.72 (t, ^3J = 8.0 Hz, 1H), 7.55 (t, ^3J = 8.0 Hz, 1H), 6.97 (d, ^3J = 5.2 Hz, 1H), 4.05 (s, 3H), 3.67 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 150.7, 147.6, 141.2, 141.2, 138.9, 135.9, 130.1, 129.3, 129.1, 128.2, 127.7, 127.1, 118.0, 60.6, 53.8 ppm. MS (ES^+) *m/z* 267.3 ($[M+1]^+$), 289.3 ($[M+Na]^+$). $C_{16}H_{14}N_2O_2$ (266.1) calcd. C 72.16, H 5.30, N 10.52; found: C 71.96, H 5.29, N 10.46. Crystals for X-ray analysis were grown from ethyl acetate. *Crystal data*: $C_{16}H_{14}N_2O_2$, *M*=266.29, *T*=120 K, triclinic, space group $P\bar{1}$ (No. 2), *a*=5.4857(8), *b*=11.2295(16), *c*=11.3018(16) Å, α=101.86(2), β=102.48(2), γ=96.51(2)º, *U*=656.11(16) Å^3, *Z*=2, μ=0.09 mm^{-1}, Mo-K_α radiation ($\bar{\lambda}$ =0.71073 Å), SMART 1K CCD area detector, 7851 reflections (2θ≤58º), 3482 unique, R_{int}=0.026, *R*=0.038 [3068 data with $I \geq 2\sigma(I)$], w$R(F^2)$=0.111 (all data): CCDC-662747.

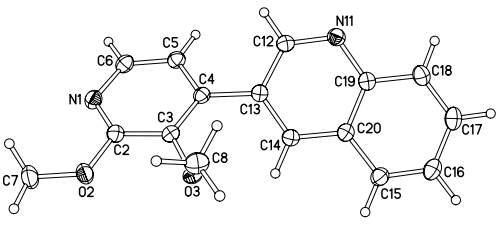
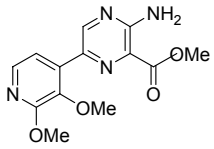


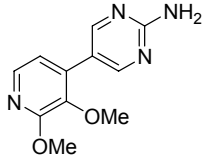
Figure S1. X-ray molecular structure of **19** (50% probability thermal ellipsoids). Dihedral angle between the pyridine and quinoline planes is 36.5°, torsion angles N(1)-C(2)-O(2)-C(7) 6.9(1)°, C(4)-C(3)-O(3)-C(8) 90.5(1)°.

Methyl 3-amino-6-(2,3-dimethoxypyridin-4-yl)pyrazine-2-carboxylate (20)



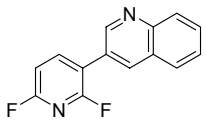
Boronic acid **4** (311 mg, 1.7 mmol), methyl 3-amino-6-bromopyrazine-2-carboxylate **12** (348 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 15 min; eluent EtOAc gave **20** as yellow crystals (375 mg, 86%), mp 195.6-196.1 °C (from toluene); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.79 (s, 1H), 7.94 (d, ^3J = 5.2 Hz, 1H), 7.60 (br s, 2H), 7.31 (d, ^3J = 5.2 Hz, 1H), 3.94 (s, 3H), 3.88 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 166.16, 157.89, 154.76, 148.29, 140.58, 140.41, 136.87, 135.89, 122.58, 116.55, 60.136, 53.43, 52.26; HRMS (EI) calcd for $C_{13}H_{14}N_4O_4$ (M^+) 290.1015, found 290.1015.

5-(2,3-Dimethoxypyridin-4-yl)pyrimidin-2-amine (21)



Boronic acid **4** (311 mg, 1.7 mmol), 2-amino-5-bromopyrimidine **13** (261 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 1.25 h; eluent EtOAc followed by recrystallisation from touene gave **21** as a pale yellow solid (278 mg, 80%), mp 179.2-181.9 °C (from toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.60 (s, 2H), 7.92 (d, ^3J = 5.6 Hz, 1H), 6.85 (d, ^3J = 5.2 Hz, 1H), 5.29 (s, 2H), 4.04 (s, 3H), 3.72 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ = 162.6, 158.6, 158.4, 141.4, 140.8, 136.4, 120.0, 116.7, 60.4, 53.8 ppm. MS (ES^+) *m/z* 233.2 ($[M+1]^+$). $C_{11}H_{12}N_4O_2$ (232.2) calcd. C 56.89, H 5.21, N 24.12; found: C 56.78, H 5.20, N 24.02.

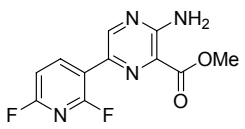
3-(2,6-Difluoropyridin-3-yl)quinoline (22)



Boronic acid **6** (270 mg, 1.7 mmol), 3-bromoquinoline **11** (312 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 24 h; eluent DCM:EtOAc (1:1 v/v) gave **22** as a white solid (303 mg, 84%), mp 155.5-156.2 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 9.10 (t, ^5J = 2.0 Hz, 1H), 8.61 (s, 1H), 8.54 (q, ^3J = 8.0 Hz, 1H), 8.06 (t, ^3J = 8.0 Hz, 2H), 7.82 (t, ^3J = 8.0 Hz, 1H), 7.67 (t, ^3J = 8.0 Hz, 1H), 7.38 (dd, ^3J = 8.0 Hz, ^5J = 2.4 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ = 160.1 (dd, ^1J = 244 Hz, ^3J = 15 Hz, 1C), 157.4 (dd, ^1J = 244 Hz, ^3J = 15 Hz, 1C), 150.0 (d, ^3J = 8 Hz, 1C), 147.0 (d, ^3J = 8 Hz, 1C), 147.0 (d, ^4J = 6 Hz, 1C), 135.8 (d, ^4J = 3 Hz, 1C), 130.4, 128.7, 128.5, 127.3, 127.1, 125.6 (d, ^4J = 5 Hz, 1C), 117.3 (dd, ^2J = 26 Hz, ^4J = 5 Hz, 1C), 107.6 (dd, ^2J =

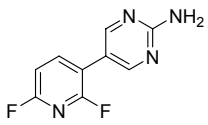
34 Hz, ^4J = 6 Hz, 1C) ppm. MS (EI) *m/z* 242.1 (M^+). $C_{14}H_8F_2N_2$ (242.2) calcd. C 69.19, H 3.22, N 11.57; found: C 69.19, H 3.22, N 11.35.

Methyl 3-amino-6-(2,6-difluoropyridin-3-yl)pyrazine-2-carboxylate (23)



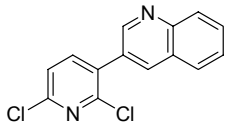
Boronic acid **6** (270 mg, 1.7 mmol), methyl 3-amino-6-bromopyrazine-2-carboxylate **12** (348 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 15 min; eluent EtOAc gave **23** as a yellow powder (327 mg, 82%), mp 201.8-202.3 °C (from toluene). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.68 (d, ^5J = 2.4 Hz, 1H), 8.52 (q, ^3J = 8.0 Hz, 1H), 7.63 (br. s, 2H), 7.32 (dd, ^3J = 8.0 Hz, ^5J = 2.4 Hz, 1H), 3.88 (s, 3H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ = 166.0, 154.7, 147.4, 147.3, 145.5, 133.3, 122.8, 107.6, 107.3, 107.2, 52.3 ppm. MS (ES^+) *m/z* 267.0 ($[M+1]^+$). $C_{11}H_8F_2N_4O_2$ (266.2) calcd. C 49.63, H 3.03, N 21.05; found: C 49.46, H 2.76, N 20.95.

5-(2,6-Difluoropyridin-3-yl)pyrimidin-2-amine (24)



Boronic acid **6** (270 mg, 1.7 mmol), 2-amino-5-bromopyrimidine **13** (261 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 24 h; eluent EtOAc gave **24** as a white solid (215 mg, 69%), mp 221.1-222.0 °C (from toluene). ^{1}H NMR (400 MHz, acetone-d_6) δ = 8.51 (d, ^5J = 1.6 Hz, 2H), 8.28 (dt, ^3J = 8.0 Hz, ^5J = 1.6 Hz, 1H), 7.18 (dd, ^3J = 8.0 Hz, $^3J_{H\text{-}F}$ = 2.8 Hz, 1H), 6.33 (s, 2H) ppm. ^{13}C NMR (100 MHz, acetone-d_6) δ = 164.2, 160.9 (dd, ^1J = 195 Hz, ^3J = 11 Hz, 1C), 158.4 (dd, ^1J = 195 Hz, ^3J = 11 Hz, 1C), 158.3 (d, ^3J = 3 Hz, 1C), 145.6 (dd, ^3J = 6 Hz, ^3J = 4 Hz, 1C), 116.6 (d, ^2J = 68 Hz, 1C), 116.1 (d, ^2J = 21 Hz, 1C), 106.7 (dd, ^2J = 90 Hz, ^4J = 6 Hz, 1C) ppm. MS (ES^+) *m/z* 208.2 (M^+). $C_9H_6F_2N_4$ (208.2) calcd. C 51.93, H 2.91, N 26.91; found: C 52.06, H 3.03, N 27.01%.

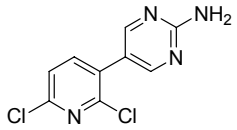
3-(2,6-Dichloropyridin-3-yl)quinoline (25)



Boronic acid **8** (326 mg, 1.7 mmol), 3-bromoquinoline **11** (312 mg, 1.5 mmol), $Pd(OAc)_2$ (19.0 mg, 0.085 mmol), tri-*t*-butylphosphane (30 mg, 0.15 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 24 h; eluent DCM:EtOAc (1:1 v/v) gave **25** as a white solid (235 mg, 57%), mp 162.2-163.0 °C (from toluene). ^{1}H NMR (400 MHz, acetone-d_6) δ = 9.03 (d, ^5J = 2.0 Hz, 1H), 8.48 (d, ^5J = 2.0 Hz, 1H), 8.13 (s, 1H), 8.11 (s, 1H), 8.05 (d, ^3J = 8.0 Hz, 1H), 7.84 (t, ^3J = 8.0 Hz, 1H), 7.68 (m, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 150.4, 148.5, 147.8, 146.9, 143.8, 136.5, 132.6, 130.5, 129.1, 128.7, 128.5,

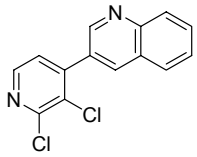
127.4, 126.9, 124.1 ppm. MS (EI) *m/z* 274.0 (M^+). $C_{14}H_8Cl_2N_2$ (275.1) calcd. C 61.12, H 2.93, N 10.18; found: C 60.79, H 2.92, N 10.09.

5-(2,6-Dichloropyridin-3-yl)pyrimidin-2-amine (26)



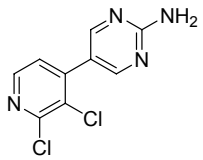
Boronic acid **8** (326 mg, 1.7 mmol), 2-amino-5-bromopyrimidine **13** (261 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), tri-*t*-butylphosphane (30 mg, 0.15 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 24 h; eluent EtOAc gave **26** as a pale yellow solid (166 mg, 46%), mp 245.2-245.9 °C (from toluene). ^{1}H NMR (400 MHz, DMSO-d_6) δ = 8.38 (s, 2H), 7.99 (d, ^3J = 8.0 Hz, 1H), 7.65 (d, ^3J = 8.0 Hz, 1H), 7.00 (s, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ 163.0, 158.1, 147.6, 147.5, 142.8, 130.9, 124.0, 118.0 ppm. MS (ES^+) *m/z* 240.0 (M^+). $C_9H_6Cl_2N_4$ (241.1) calcd. C 44.84, H 2.51, N 23.24; found: C 44.76, H 2.52, N 22.88.

3-(2,3-Dichloropyridin-4-yl)quinoline (27)



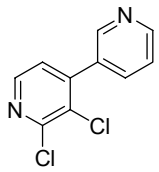
Boronic acid **10** (326 mg, 1.7 mmol), 3-bromoquinoline **11** (312 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), tri-*t*-butylphosphane (30 mg, 0.15 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 24 h; eluent DCM:EtOAc (3:7 v/v) gave **27** as a white solid (236 mg, 57%), mp 162.2-163.0 °C. ^{1}H NMR (400 MHz, acetone-d_6) δ = 9.03 (d, ^5J = 2.0 Hz, 1H), 8.60 (d, ^5J = 2.0 Hz, 1H), 8.52 (d, ^3J = 4.8 Hz, 1H), 8.10 (t, ^3J = 8.0 Hz, 2H), 7.87 (t, ^3J = 8.0 Hz, 1H), 7.71 (m, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ = 149.8, 149.0, 147.7, 147.7, 147.2, 136.5, 130.9, 129.4, 128.8, 128.7, 128.0, 127.5, 126.8, 125.9 ppm. MS (EI) *m/z* 274.0 (M^+). $C_{14}H_8Cl_2N_2$ (275.1) calcd. C 61.12, H 2.93, N 10.18; found: C 60.94, H 2.75, N 9.89.

5-(2,3-Dichloropyridin-4-yl)pyrimidin-2-amine (28)



Boronic acid **10** (326 mg, 1.7 mmol), 2-amino-5-bromopyrimidine **13** (261 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), tri-*t*-butylphosphane (30 mg, 0.15 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 24 h; eluent EtOAc gave **28** as a yellow solid (151 mg, 42%), mp 197.5-198.9 °C (from toluene). ^{1}H NMR (400 MHz, acetone-d_6) δ = 8.49 (s, 2H), 8.38 (d, ^3J = 4.8 Hz, 1H), 7.49 (d, ^3J = 4.8 Hz, 1H), 6.46 (s, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ = 163.3, 158.1, 149.0, 147.5, 145.9, 127.3, 124.7, 118.4 ppm. MS (ES^+) *m/z* 240.0 (M^+). $C_9H_6Cl_2N_4$ (241.1) calcd. C 44.84, H 2.51, N 23.24; found: C 44.76, H 2.52, N 22.68.

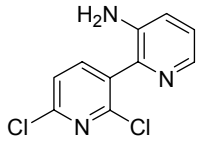
3-(2,3-Dichloropyridin-4-yl)pyridine (29)



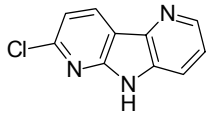
Boronic acid **10** (326 mg, 1.7 mmol), 3-bromopyridine **14** (237 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), tri-*t*-butylphosphane (30 mg, 0.15 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 24 h; eluent EtOAc gave **29** as a off white solid (138 mg, 41%), mp 192.2-193.0 °C (from hexane). ^{1}H NMR (500 MHz, acetone-d_6) δ = 8.72 (s, 1H), 8.69 (d, ^3J = 5.0 Hz, 1H), 8.48 (d, ^5J = 5.0 Hz, 1H), 7.99 (d, ^3J = 8.0 Hz, 1H), 7.57 (m, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ = 150.2, 149.0, 147.64, 147.61, 136.6, 132.1, 127.9, 125.5, 123.4 ppm. MS (EI) *m/z* 224.0 (M^+). $C_{10}H_6Cl_2N_2$ (225.1) calcd. C 53.36, H 2.69, N 12.45; found: C 53.72, H 2.92, N, 12.09.

When the reaction was repeated using 3-iodopyridine, compound **29** (169 mg, 50%) was obtained.

2-(2,6-Dichloropyridin-3-yl)pyridin-3-amine (31) and 7-chloro-5*H*-pyrrolo[2,3-b:4,5-b']dipyridine (32)



Boronic acid **8** (326 mg, 1.7 mmol), 2-chloro-3-aminopyridine **30** (193 mg, 1.5 mmol), $Pd(PPh_3)_2Cl_2$ (59.6 mg, 0.085 mmol), tri-*t*-butylphosphane (30 mg, 0.15 mmol), 1,4-dioxane (10 mL) and Na_2CO_3 (1 M, 4 mL); reaction time 24 h; eluent EtOAc gave **31** as a white solid (54 mg, 15%). ^{1}H NMR (400 MHz, acetone-d_6) δ = 7.90 (m, 2H), 7.67 (m, 1H), 7.14 (m, 1H), 5.23 (s, 2H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ = 143.8, 143.6, 138.8, 138.4, 129.6, 125.1, 124.6, 124.3, 122.7, 122.2. HRMS calcd. for $C_{10}H_7Cl_2N_3$ 239.0017 (M^+), found: 239.0018.



Next to elute was **32** as a white solid (98 mg, 32%), mp dec 310 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ = 12.27 (s, 1H), 8.58 (dd, ^3J = 8.8 Hz, ^6J = 0.8 Hz, 1H), 8.61 (d, ^3J = 8.0 Hz, 1H), 7.93 (dd, ^3J = 8.0 Hz, ^4J = 1.6 Hz, 1H), 7.49 (dd, ^3J = 8.0 Hz, ^3J = 4.8 Hz, 1H), 7.35 (d, ^3J = 8.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, DMSO-d_6) δ = 151.9, 148.9, 143.6, 139.2, 133.3, 132.3, 122.3, 119.8, 116.4, 114.0 ppm. MS (ES^+) *m/z* 204.1 (M^+). HRMS calcd. for $C_{11}H_6ClN_3$: 203.6277 (M^+), found: 203.6278.

NMR Spectra of Compound 32.

The ^{1}H NMR spectrum of **32** in DMSO-d_6 (Fig. S2) showed five aromatic protons plus a singlet at δ 12.27 ppm with an integral of one proton from the NH group.

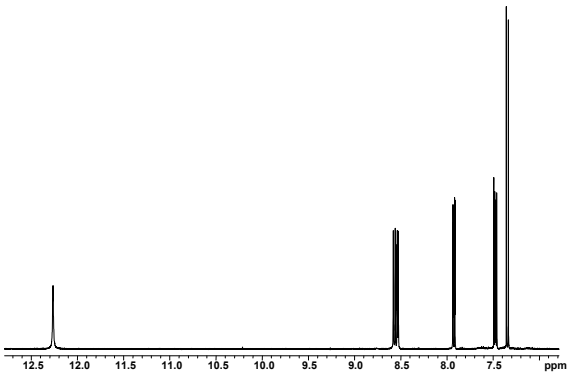


Figure S2 ^{1}H NMR spectrum of **32** in DMSO-d_6.

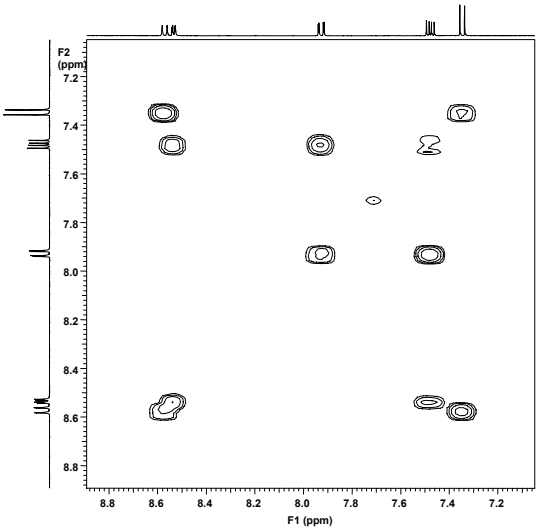


Figure S3: ROESY spectrum of **32**.

The ROESY spectrum (Figure S3) confirmed that the protons giving the two doublets at δ 8.6 and 7.3 ppm are on adjacent carbons, and the quartet at 7.5 ppm is from a proton on the carbon adjacent to both carbons that carry protons, causing the doublet of doublets at 7.9 and 8.5 ppm. Overall this is consistent with two protons attached to one ring and three protons attached to the other ring.

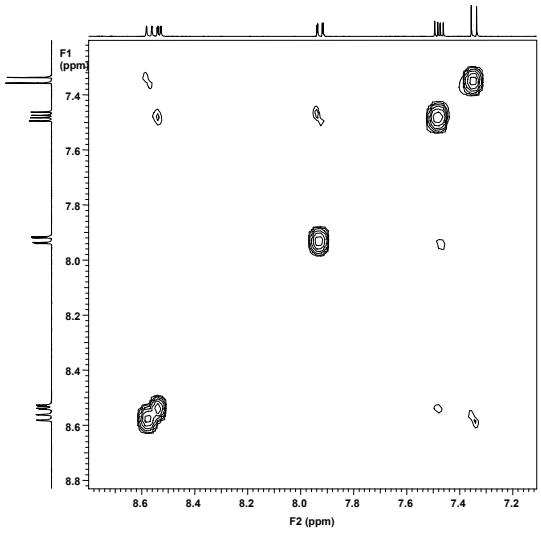


Figure S4: COSY spectrum of **32**.

The COSY spectrum (Figure S4) further supported a structure with two independent ring systems: no interaction was observed between the two ring systems grouped previously by the ROESY spectrum.

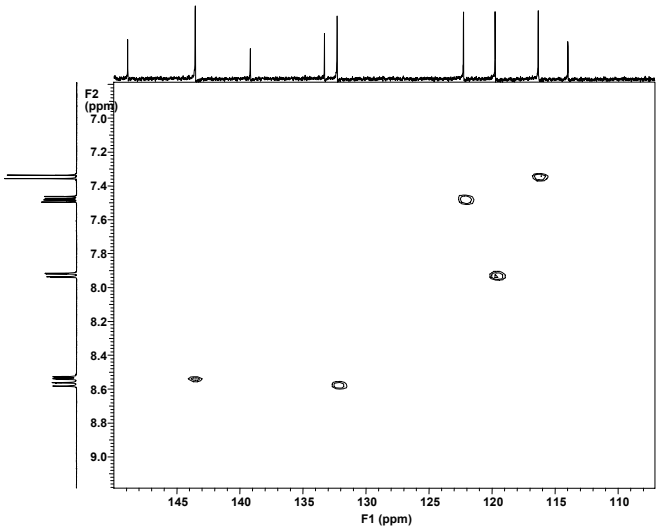


Figure S5 HSQC spectrum of **32**.

The HSQC spectrum (Figure S5) assigned the carbons to which each of the five aromatics protons are attached, and identified those carbons not bearing protons.

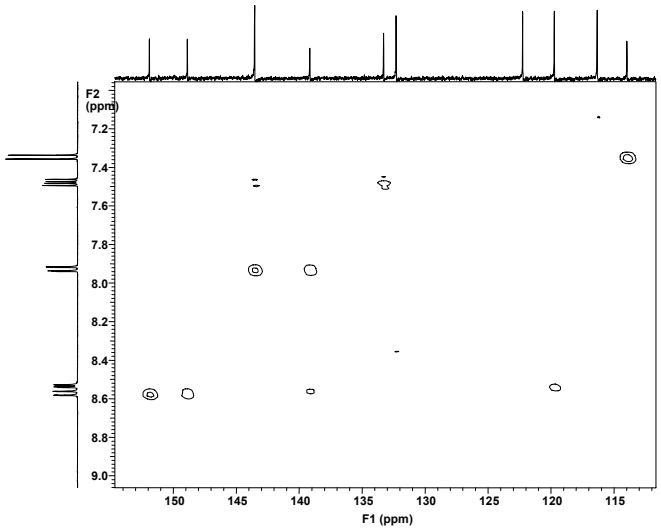


Figure S6. HMBC spectrum of **32**.

The HMBC spectrum (Figure S6) identified which carbons the five aromatic protons couple with through 2 or 3 bonds. Quaternary carbons can sometimes be observed by this technique. Taken together, all the data point unambiguously to structure **32**.

X-ray Crystallography. Single-crystal diffraction experiments (Table S1) were carried out on Bruker 3-circle diffractometers with CCD area detectors SMART 1K (**4**, **8**, **19**), SMART 6K (**2**) and APEX ProteumM (**10**), using graphite-monochromated Mo-K_α radiation (λ=0.71073 Å) from a sealed tube or (for **10**) a 60W Mo-target microfocus Bede Microsource® X-ray generator with glass polycapillary X-ray optics. The crystals were cooled with Cryostream (Oxford Cryosystems) open-flow N_2 cryostats. The diffraction of **2** was very weak (mean $I/\sigma(I)$=3.25) hence poor refinement. The structures were solved by direct methods and refined by full-matrix least squares (non-H atoms anisotropic; H atoms 'riding' in **2** and refined isotropically elsewhere) against F^2 of all data, using SHELXTL software.[1] Full crystallographic data, excluding structure factors, have been deposited at the Cambridge Crystallographic Data Centre.

Table S1 Crystal data (T=120 K)

Compound	**2**	**4**	**8**	**10**
CCDC dep. no.	656186	662746	656187	656188
Formula	$C_7H_{10}BNO_4$	$C_7H_{10}BNO_4$	$C_5H_4BCl_2NO_2$ ·½ H_2O	$C_5H_4BCl_2NO_2$
Formula weight	182.97	182.97	200.81	191.80
Symmetry	orthorhombic	orthorhombic	monoclinic	monoclinic
Space group	*Pbca* (# 61)	$Pna2_1$ (#)	$P2_1/n$ (# 14)	$P2_1/n$ (# 14)
a, Å	6.8615(6)	14.7587(6)	6.828(1)	8.970(2)
b, Å	15.8254(15)	3.8738(2)	31.106(4)	8.666(2)
c, Å	32.167(3)	14.7443(6)	7.797(1)	10.216(8)
β, °	90	90	95.25(3)	106.22(1)
V, Å^3	3492.9(6)	842.96(7)	1649.1(4)	762.5(3)
Z	16	4	8	4
μ, mm^{-1}	0.11	0.12	0.74	0.79
Refls total, unique	28059, 3079	9194, 1273	16845, 3769	9068, 2225
R_{int}, %	16.1	2.4	3.3	4.2
R_1, wR_2, %	9.1. 23.9	2.6, 7.0	3.6, 8.4	3.5, 7.8

$R_1=\Sigma||F_o| - |F_c||/\Sigma|F_o|$, on data with $I>2\sigma(I)$; $wR_2=\{\Sigma[w(F_o^2 - F_c^2)^2/\Sigma[w(F_o^2)^2]\}^{1/2}$

Crystal Structures

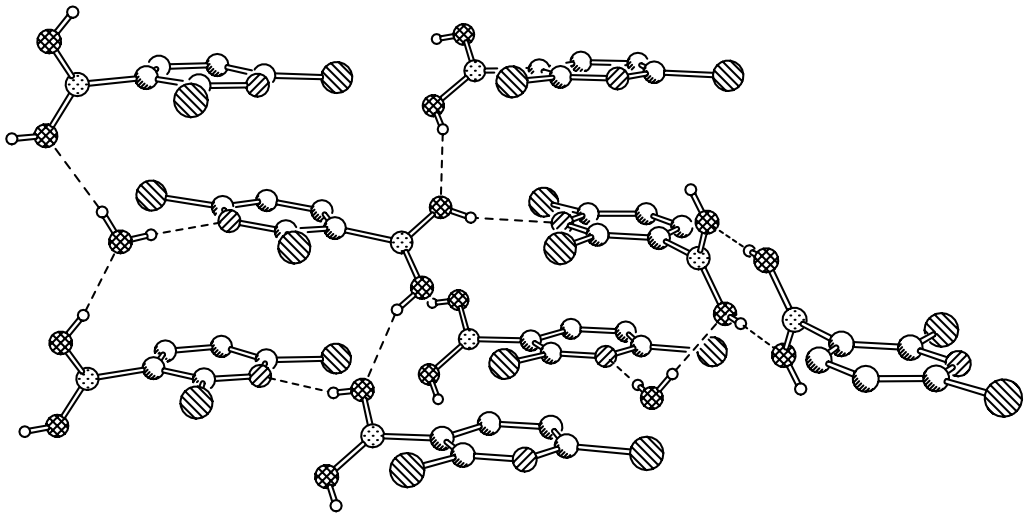


Figure S7. Hydrogen bonding in the structure of **8**·½ H_2O.

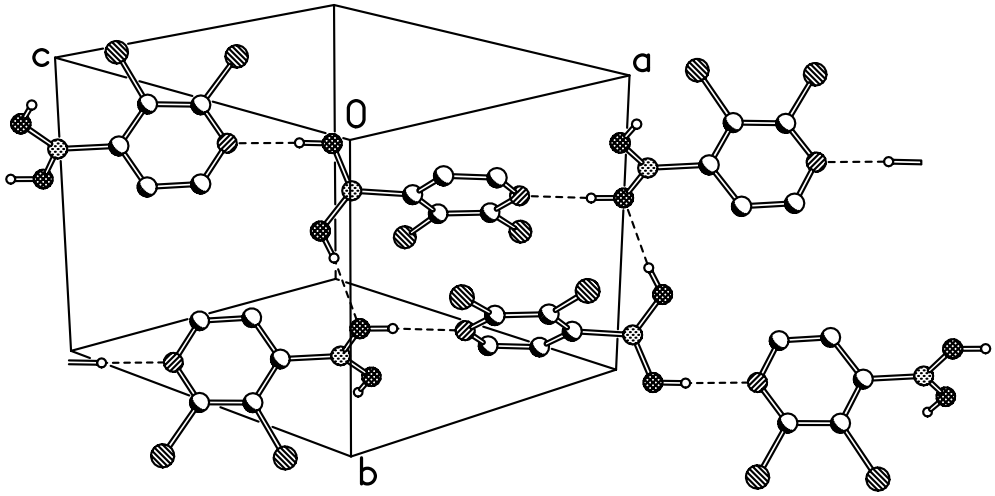


Figure S8. Hydrogen bonding in the structure of **10**.

[1] G. M. Sheldrick, SHELXTL, version 6.12, Bruker AXS, Madison, Wisconsin, U.S.A., **2003**.