Supporting Information

Iridium-Catalyzed C-H Borylation of Pyridines

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Experimental

General

All reactions were carried out under a dry nitrogen atmosphere using standard Schlenk techniques or in an Innovative Technology Inc. System 1 double-length glove box. Glassware was oven dried before all borylation reactions. Solvents used for borylation reactions were anhydrous and degassed by multiple freeze-pump-thaw cycles. Unless otherwise stated DMF and DMAc used for tandem borylation Suzuki-Miyaura reactions was used without drying but with multiple freeze-pump-thaw degassing cycles.

Solvents

Methyl-tert-butyl-ether (MTBE) was purchased anhydrous from Sigma Aldrich. DMF and DMAc were purchased from Sigma-Aldrich. All other reaction solvents were dried using an Innovative Technology Solvent Purification System (SPS) and stored under argon. Deuterated chloroform ($CDCl_3$), deuterated benzene (C_6D_6) and deuterium oxide (D_2O) were purchased from Apollo Scientific. The former was dried over 4 Å molecular sieves and used without further treatment. Acetone-d_6 was purchased from ARMAR Chemicals, dried over 4 Å molecular sieves and used without further treatment. Ether refers to diethyl ether.

Reagents

2-Picoline, 2-phenylpyridine, 2,3-dimethylpyrazine and 2,5-dimethylpyrazine were dried over CaH_2. $[Ir(\mu\text{-}OMe)(COD)]_2$ was synthesised, as previously described,[1] from $IrCl_3.3H_2O$, obtained from Precious Metals Online. B_2pin_2 was supplied as a generous gift by AllyChem Co. Ltd. (P.R.China) and was used without further purification. All other

[1] R. Uson, L. A. Oro and J.A. Cabeza, *Inorg. Synth.,* 1985, **23**, 126-130.

compounds were obtained from Sigma-Aldrich, Alfa Aesar, Fluorochem, Acros, Apollo Scientific or Lancaster and used without further purification.

NMR Spectroscopy

NMR spectra were recorded at ambient temperature on Bruker Avance-400 (^{1}H, ^{11}B, ^{19}F), Varian Inova-500 (^{1}H, $^{13}C\{^{1}H\}$, HSQC, HMBC, COSY) or Varian VNMRS-700 (^{1}H, $^{13}C\{^{1}H\}$, HSQC, HMBC, COSY) spectrometers. The ^{1}H and ^{13}C chemical shifts are reported in ppm using the residual solvent signal of the deuterated solvents ($CDCl_3$: δH = 7.26 ppm, δC = 77.16 ppm; Acetone d_6: δH = 2.05 ppm, δC = 206.26/29.84 ppm). All chemical shifts are reported in parts per million relative to tetramethylsilane (δH = 0.00 ppm). ^{11}B NMR chemical shifts are referenced to external $BF_3 \bullet Et_2O$ (δB = 0.0 ppm). Multiplicities are reported using the following abbreviations; s (singlet), d (doublet), t (triplet), q (quartet), m (unresolved multiplet) and br (broad). Assignment of spectra was carried out using 2D COSY, HMBC, HSQC and NOESY techniques.

Elemental Analysis

Elemental analyses were conducted in the Department of Chemistry at the University of Durham using an Exeter Analytical Inc. CE-440 Elemental Analyser.

Mass Spectrometry

GC/MS analyses were performed on an Agilent 6890N gas chromatograph (column: HP-5MS, 10 m, Ø 0.25 mm, film 0.25 µm; injector: 250 °C; oven: 70 °C (2 min), 70 °C to 250 °C (20 °C min^{-1}), 250 °C (5 min); carrier gas: helium (1.6 mL min^{-1})) equipped with an Agilent 5973 inert mass selective detector operating in EI mode and a custom built Anatune liquid handling system functioning as autosampler/injector. Electrospray (ES) mass spectra were obtained on a Micromass LCT Mass Spectrometer. High Resolution mass spectra were obtained using a Thermo Finnigan LTQFT mass spectrometer or

Xevo QToF mass spectrometer (Waters UK, Ltd) by the Durham University Mass Spectrometry Service.

IR Spectroscopy

Infrared spectra were measured on a Perkin-Elmer Paragon 1000 FT-IR spectrometer *via* the use of a Diamond ATR (attenuated total reflection) accessory (Golden Gate). Assigned peaks are reported in wavenumbers (cm^{-1}).

Melting Points

Melting points were recorded using an Electrothermal 9100 capillary melting point apparatus.

Thin-Layer Chromatography (TLC)

TLC was performed on 'Polygram Sil G/UV' plastic-backed silica plates with a 0.2 mm silica gel layer doped with a fluorescent indicator. Plates were purchased from VWR International.

Flash Column Chromatography

Flash column chromatography refers to purification by automated operation using a Teledyne Isco CombiFlash Rf machine on pre-packed silica Redisep® Rf cartridges with the stated solvent gradient and at a constant flow rate of 35 mL/min.

Microwave Reactor

Microwave reactions were carried out in septum-containing, crimp-capped, sealed vials in a monomodal Emrys™ Optimizer reactor from Personal Chemistry. The wattage was automatically adjusted to maintain the desired temperature for the desired period of time.

General Procedures

General Procedure for the Preparation of a Catalyst Stock Solution for C-H Borylation

In a glovebox, a catalyst stock solution was prepared by weighing $[Ir(COD)OMe]_2$ (100 mg, 0.15 mmol), dtbpy (80 mg, 0.30 mmol) and B_2pin_2 (2.54 g, 10.0 mmol) into a volumetric flask followed by the addition of MTBE to make up the volume to 25 mL of solution. The flask was vigorously shaken until the solution developed a deep red colour and no more solid was visible. The solution was transferred to and stored in, a crimp-cap septum-sealed tube in a freezer and used within a week. A 2.5 mL aliquot of this equates to 1 mmol of B_2pin_2 and 1.5 mol% of the active Ir catalyst

NMR Reaction Monitoring

For all room temperature borylation reactions, an aliquot (0.5 mL) of the reaction mixture was removed and transferred (in a glovebox or by Schlenk techniques) to a Young's Tap-sealed NMR tube containing a coaxial tube filled with acetone-d_6. The reactions were monitored for 24 h or until full consumption of starting material was observed by NMR spectroscopy.

Conversion Calculation

Unless stated otherwise, conversions were calculated by NMR spectroscopic analysis by taking the ratios of integrals corresponding to products and starting materials. Where required, averages of integrals within a molecule were taken. NMR ratios are presented as a percentage.

General Procedure A: C-H Borylation of Pyridines in a Glovebox (using pre-prepared stock solution)

In a glovebox, a thick-walled microwave synthesis vial was charged with the corresponding pyridine (1.0 mmol) followed by the addition of 2.5 mL of stock solution. The vessel was sealed with a crimp top septum cap and shaken until all of the pyridine substrate was dissolved. The reaction mixture was stirred on a magnetic stirring block for the time stated. Upon completion, the vial was removed from the glovebox and the volatiles were removed *in vacuo* to afford the crude product. Where stated, the crude product was dry-loaded onto silica gel and purified by silica gel flash column chromatography using the stated conditions to afford the purified product.

General Procedure B: C-H Borylation of Pyridines using Schlenk Techniques (using pre-prepared stock solution)

A thick-walled microwave synthesis vial was charged with the corresponding pyridine (1.0 mmol). The vial was sealed with a crimp top septum cap and purged with three evacuation/refill cycles. Under argon, the vial was charged with an aliquot (2.5 mL) of stock solution and shaken until all of the pyridine dissolved. The reaction mixture was stirred on a magnetic stirring block for the time stated. Upon completion, the volatiles were removed *in vacuo* to afford the crude product. Where stated, the crude product was dry-loaded onto silica gel and purified by silica gel flash column chromatography using the stated conditions to afford the purified product.

General Procedure C: Procedure for Catalytic Borylations (without the use of stock solution)

In a glove box, to a premixed solution of $[Ir(\mu\text{-}OMe)COD]_2$ (X mol%) and dtbpy (X mol%) in 2 mL of solvent was added a mixture of boron reagent (Y mmol) and pyridine

derivative (Z mmol) in 3 mL of hexane (5 mL total solvent volume). The mixture was shaken vigorously to ensure complete mixing, and then the mixture was stirred at room temperature or transferred to ampoules sealed with a Teflon Young's tap and heated to 80 °C. The reactions were monitored by GC/MS.

General Procedure D: One-pot C-H Borylation/Suzuki-Miyaura Cross-Coupling Sequence A

The borylation step was carried out as per general procedure A or B. Upon completion, volatiles were removed *in vacuo*. To the crude mixture under N_2, was added $Pd(dppf)Cl_2$ (5 or 10 mol%), Cs_2CO_3 (2 eq.), CuI (1 eq.) and aryl halide (1.1 - 2 eq.) in DMF. The reaction was irradiated with stirring at 100 °C for 1 h in a microwave reactor. The reaction mixture was diluted with water and extracted into ether. The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the crude product. This was dry-loaded onto silica gel and purified by silica gel flash column chromatography using the stated solvent system.

General Procedure E: One-pot C-H Borylation/Suzuki-Miyaura Cross-Coupling Sequence B

Once the borylation product formed, as shown by *in situ* GC/MS analysis, the solvent was removed *in vacuo*, followed by addition of aryl halide (X mmol), K_2CO_3 (aq.) (Y equiv., (aq. = 1 mL water : 4.5-5 mL solvent), $[(PPh_3)_2PdCl_2]$ (Z mmol, 5 mol%) and 1,4-dioxane (15-20 ml). The mixture was transferred to a microwave reaction tube (20 mL volume), then sealed and heated for 1 h at 150 °C.

General Procedure F: "One-pot C-H borylation/Suzuki-Miyaura Cross-Coupling Sequence C using standard heating conditions

The borylation step was carried out as per general procedure A or B. Once the borylation product formed, as shown by *in situ* NMR spectroscopic analysis, the solvent was removed *in vacuo*, followed by addition of arylhalide (1.1 eq.), Cs_2CO_3 (2 eq.), $Pd(dppf)Cl_2$ (5 mol%) and DMF (5 mL). The mixture was heated for the stated time at 70 °C under a flow of nitrogen then worked up as per general procedure D.

Borylation of 2,6-Lutidine **(4)**

General procedure C was applied on a 1.9 mmol scale; $[Ir(\mu\text{-}OMe)COD]_2$ (30.7 mg, 92.6 x 10^{-3} mmol, 2.5 mol%), dtbpy (24.8 mg, 92.5 x 10^{-3} mmol, 5 mol%), B_2pin_2 (475 mg, 1.9 mmol, 1 equiv.) and **4** (200 mg, 1.9 mmol). After 16 h, the reaction was quenched with DMF (10 mL) and water (5 mL), extracted into ethyl acetate, and dried over ($MgSO_4$). Kugelrohr distillation (100-170 °C, 3 x 10^{-4} torr) gave 375 mg (1.6 mmol, 86%) of an analytically pure sample. Slow evaporation of a DCM solution, gave white crystals of **5** suitable for X-ray diffraction. m.p. 80-82 °C; Found, C 66.71; H 8.69; N 5.85; Calcd. for $C_{13}H_{20}BNO_2$, C 66.98; H 8.65; N 6.01. δ_H ($CDCl_3$, 400 MHz) 7.31 (s, 2H; 3,5-*H*), 2.52 (s, 6H; 2,6-C*H*$_3$), 1.33 (s, 12H; pin–C*H*$_3$); δ_C ($CDCl_3$, 100 MHz) 156.50 (2C, 2,5-*C*), 125.09 (2C, 3,5-C), 84.03 (O*C*CH_3), 24.50 (2,6-*C*H_3), 23.78 (s, pin–*C*H_3), the resonance for the carbon attached to boron was not observed; δ_B ($CDCl_3$, 128.4 MHz): δ 30.38 (s, br); MS (EI) m/z: 233 [M^+], 218 [$M\text{-}CH_3]^+$. All spectra identical with that previously reported.[2]

Tandem Borylation Suzuki-Miyaura Reaction using 2,6-Lutidine

General procedure E was applied to **4** on a 1.87 mmol scale to synthesise 2,6-dimethyl-4-naphthalen-1-yl-pyridine (**S1**). Once compound **5** formed completely, as shown by *in situ* GC/MS analysis. The solvent was removed *in vacuo* followed by addition of 1-iodonaphthalene (474 mg, 1.87 mmol, 1 equiv.), K_2CO_3 (aq.) (517 mg, 3.75 mmol, 2 equiv.), $[(PPh_3)_2PdCl_2]$ (65.5 mg, 93 x 10^{-3} mmol, 5 mol%) and 1,4-dioxane (20 ml). The mixture was transferred to a microwave tube (20 mL volume) as above, then sealed and heated for 1 h at 150 ^oC. The product was extracted into ethylacetate, dried ($MgSO_4$), and chromatographed on silica gel (hexane:ethylacetate, 90:10) to yield 400 mg (1.72

[2] P. Harrisson, J. Morris, T. B. Marder and P. G. Steel, *Org. Lett.*, 2009, **11**, 3586-3589.

mmol, 92%) of product. Slow evaporation of a diethylether solution gave white crystals suitable for X-ray diffraction. m.p. 90-92 ^{o}C; Found, C 87.37%, H 6.45%, N 6.14%; Calcd. for $C_{17}H_{15}N$, C 87.52%, H 6.48%, N 6.00%. δ_H (C_6D_6, 500 MHz) 8.30 (d, *J* = 8 Hz, 1H; 12), 7.39 (d, *J* = 7.8 Hz, 1H; 6), 7.36 (d, *J* = 8 Hz, 1H; 9), 6.97 (t, *J* = 8 Hz, 2H; 10,11), 6.86-6.92 (m, 2H; 7, 8), 6.51 (s, 2H, 3), 2.20 (s, 6H, 2,6-C*H*$_3$); δ_C (C_6D_6, 100 MHz) 158.14, 149.20, 138.67, 131.61, 131.61, 126.86, 126.63, 126.24, 125.97, 125.50, 121.55, 24.95 (CH_3), 24.58. m/z (EI) 233 [M^+], 218 [M-CH_3]$^+$.

Borylation of 2,6-dichloropyridine **(6)**: *Synthesis of 2,6-dichloro-4-(Bpin)-pyridine* **(7)**

General Procedure A was applied on a 1 mmol scale. Purification by silica flash-column chromatography eluting with 100% DCM afforded **7** as a pale pink solid (263 mg, 96%); m.p. 118 - 119 °C (from hexane); Found C 48.4%; H 5.2%; N 5.0%; Calcd. for $C_{11}H_{14}BCl_2NO_2$ C 48.2%; H 5.15%; N 5.1%. ν_{max} ($CHCl_3$) 2984, 1515, 1422, 1358, 1337, 1161, 1141, 965, 873, 802, 674 cm^{-1}. δ_H (400 MHz, $CDCl_3$) 7.59 (s, 2H, 3,5-*H*), 1.34 (s, 12H, pin-C*H*$_3$); δ_C (126 MHz, $CDCl_3$) 150.6 (2,6-*C*), 128.0 (3,5-*C*), 85.4 (pin-*C*(CH_3)$_2$), 25.0 (pin-*C*H$_3$); δ_B (128 MHz, $CDCl_3$) 29.58. *m/z* (GC-MS, EI) 277 (27%, [M^+($^{37}Cl^{37}Cl$)]), 275 (12%, [M^+($^{35}Cl^{37}Cl$)]), 273 (41%, [M^+($^{35}Cl^{35}Cl$)]), 262 (58%, M^+($^{37}Cl^{37}Cl$) -CH_3), 260 (24%, M^+($^{35}Cl^{37}Cl$) -CH_3), 258 (91%, [M^+($^{35}Cl^{35}Cl$)-CH_3]), 193 (10%), 191 (64%), 191 (100%). All spectra identical with that previously reported.[2]

Borylation of 2-phenylpyridine **(8)** *and Synthesis of 4-naphthalen-1-yl-2-phenyl-pyridine* **(S2)** *and 5-naphthalen-1-yl-2-phenyl-pyridine* **(S3)**

General Procedure E was followed using [Ir(μ-OMe)COD]$_2$ (22 mg, 66 x 10^{-3} mmol, 2.5 mol%), dtbpy (18 mg, 67 x 10^{-3} mmol, 5 mol%), B_2pin_2 (164 mg, 645 x 10^{-3} mmol, 0.5 equiv.) and **8** (200 mg, 1.3 mmol); 1-iodonaphthalene (328 mg, 1.3 mmol, 1 equiv.),

K_2CO_3 (aq.) (359 mg, 2.6 mmol, 2 equiv.), $(PPh_3)_2PdCl_2$ (45.3 mg, 65 x 10^{-3} mmol, 5 mol%) and 1,4-dioxane (20 ml). The reaction mixture was extracted with ethylacetate, dried ($MgSO_4$), and chromatographed on silica gel (hexane:ethylacetate, 95:5) to yield 220 mg of a mixture of the two isomers (0.783 mmol, 67%). The isolated yields of **S2** and **S3** were (100 mg, 356 x 10^{-3} mmol, 45%), and (120 mg, 427 x 10^{-3} mmol, 55%), respectively.

S2

m.p. 80-82 °C. δ_H (C_6D_6, 500 MHz) 8.67 (d, *J* = 4.9 Hz, 1H), 8.19 (2 overlapped d, *J* = 6.8 Hz, 2H), 7.76 (d, *J* = 8.3 Hz, 1H), 7.69 (s, 1H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.65 (d, *J* = 8.3 Hz, 1H), 7.23-7.28 (m, 4H), 7.02-7.07 (m, 3H), 6.94 (dd, *J* = 4.9, 1.5 Hz, 1H). δ_C NMR (C_6D_6, 125 MHz): 157.70, 150.09, 149.42, 139.69, 138.36, 134.26, 131.53, 129.62, 128.94, 128.91, 128.72, 127.39, 127.04, 126.87, 126.34, 125.79, 125.52, 123.57, 119.50. m/z (EI) 281 [M^+]; Anal. Calcd. for $C_{21}H_{15}N$: C 89.65%, H 5.37%, N 4.89%; found C 89.41%, H 5.56%, N 4.98%

S3

M.p. 130-132 °C. δ_H (C_6D_6, 500 MHz) 8.90 (s, 1H), 8.28 (2 overlapped d, *J* = 8.3 Hz, 1H), 7.83 (d, *J* = 8.8 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 8.3 Hz, 1H), 7.40-7.45 (m, 2H), 7.32 (m, 2H), 7.17-7.28 (m, 5H). δ_C (C_6D_6, 125 MHz) 156.32, 150.82, 139.56, 137.95, 136.89, 134.92, 134.40, 129.25, 129.15, 128.74, 128.57, 128.55, 127.57, 127.27, 126.71, 126.26, 125.82, 125.66, 119.46. m/z (EI) 281 [M^+]; Anal. Calcd. for $C_{21}H_{15}N$: C 89.65%, H 5.37%, N 4.89%; found C 89.42%, H 5.52%, N 4.79%.

Borylation-Cross-Coupling of 2-picoline **(11)** *and Synthesis of 2-methyl-4-phenyl-pyridine* **(S4)** *and 2-methyl-5-phenyl-pyridine* **(S5)**

General Procedure E was followed using $[Ir(\mu\text{-}OMe)COD]_2$ (17 mg, 51 x 10^{-3} mmol, 2.5 mol%), dtbpy (14 mg, 52 x 10^{-3} mmol, 5 mol%), B_2pin_2 (136 mg, 535 x 10^{-3} mmol, 0.5 equiv.) and **11** (100 mg, 1.1 mmol); 1-iodobenzene (219 mg, 1.1 mmol, 1 equiv.), K_2CO_3 (aq.) (279 mg, 2.2 mmol, 2 equiv.), $[(PPh_3)_2PdCl_2]$ (37.7 mg, 53.7 x 10^{-3} mmol, 5 mol%) and 1,4-dioxane (20 ml). The reaction mixture was extracted with ethyl acetate, dried ($MgSO_4$), and chromatographed on silica gel (hexanes:diethylether, 50:50) to yield 120 mg of a mixture of the two isomers (0.71 mmol, 67%). The isolated yield for **S4** and **S5** were (120 mg, 0.71 mmol, 49%) and (123 mg, 0.72 mmol, 51%) respectively.

S4

M.p. 42-44 °C. δ_H ($CDCl_3$, 500 MHz) 8.54 (d, *J* = 5.4 Hz, 1H, 6-*H*), 7.62 (d, $J_{H,H}$ = 7.7 Hz, 2H, 2',6'-*H*), 7.41-7.48 (m, 3H, 3',4',5'-*H*), 7.37 (s, 1H, 3-*H*), 7.31 (d, *J* = 5.4 Hz, 1H, 5-*H*), 2.63 (s, 3H, C*H*$_3$). δ_C ($CDCl_3$, 100 MHz) 158.45 (2-*C*), 149.12 (6'-*C*), 148.51 (4'-*C*), 138.13 (1'-*C*), 128.72, 128.61, 126.69 (2'-*C*), 120.93 (3-*C*), 118.56 (5-*C*), 24.11 (*C*H_3). m/z (EI) 169 [M^+], 155 [$M\text{-}CH_4$]$^+$. Anal. Calcd. for $C_{12}H_{11}N$: C 85.17%, H 6.55%, N 8.28%; found C 85.04%, H 6.60%, N 8.25%.

S5

M.p. 82-84 °C. δ_H (C_6D_6, 500 MHz) 8.78 (s, 1H, 6-*H*); 7.34 (m, 2H, 2',6'-*H*), 7.29 (d, *J* = 7.7 Hz, 1H, 4-*H*), 7.10-7.14 (m, 3H, 3', 4', 5'-*H*), 6.72 (d, *J* = 7.7 Hz, 1H, 3-*H*), 2.47 (s, 3H, C*H*$_3$). δ_C (C_6D_6, 100 MHz) 156.47 (2'-*C*), 146.82 (6'-*C*), 137.22 (5'-*C*), 133.15, 132.43, 127.87, 126.32, 125.76 (4'-*C*), 121.56 (3'-*C*), 22.83 (*C*H_3). m/z (EI) 169 [M^+],

155 $[M\text{-}CH_4]^+$. Anal. Calcd. for $C_{12}H_{11}N$: C 85.17%, H 6.55%, N 8.28%; found C 84.89%, H 6.56%, N 8.15%.

Borylation of 2,2'-bipyridine **(14):** *Synthesis of 4-(Bpin)-2,2'-bipyridine* **(15),** *5-(Bpin)-2,2'-bipyridine* **(16)**, *4,4'- bis(Bpin)-2,2'-bipyridine* (**S6**)

General procedure C was followed using $[Ir(\mu\text{-}OMe)COD]_2$ (11 mg, 33.2 x 10^{-3} mmol, 2.5 mol%), dtbpy (8.9 mg, 33.2 x 10^{-3} mmol, 5 mol%), B_2pin_2 (82 mg, 322 x 10^{-3} mmol, 0.5 equiv.) and **14** (100 mg, 641 x 10^{-3} mmol). The mixture was stirred at room temperature for 16 h. *In situ* GC/MS analysis showed full consumption of B_2pin_2 and a mixture of mono and bis borylated products in a ca. 52 : 48 ratio. The mono borylated products were formed in a 42:58 ratio of **15:16** whilst the bis borylated derivatives were tentatively assigned as a 15 : 77 : 8 mixture of 3,3': 4,4' : 3,4' isomers respectively. Fractional Kugelrohr distillation afforded an analytically pure sample of the major *4,4'- bis(Bpin)-2,2'-bipyridine* (**S6**) as confirmed by single crystal X-ray diffraction analysis. δ_H ($CDCl_3$, 500 MHz) 8.73 (d, *J* = 5.0 Hz, 2H, 3,3'-*H*), 8.70 (s, 2H, 6,6'-*H*), 7.46 (d, *J* = 5.0 Hz, 2H, 5,5'-*H*), 1.37 (s, 24H, pin-C*H*$_3$). m/z (EI) 408 $[M^+]$, 393 $[M\text{-}CH_3]^+$. Anal. Calcd. For $C_{22}H_{30}N_2B_2O_4$, C 64.75%, H 7.41%, N 6.86%; found C 64.64%, H 7.31%, N 6.60%.

Borylation of 2,3-dimethylpyrazine **(17)**: *Synthesis of 2,3-dimethyl-5-(Bpin)-pyrazine* **(18)**

General procedure C was followed using $[Ir(\mu\text{-}OMe)COD]_2$ (17 mg, 25 x 10^{-3} mmol, 2.5 mol%), dtbpy (13 mg, 50 x 10^{-3} mmol, 5 mol%), B_2pin_2 (254 mg, 1 mmol, 1 equiv.) and **17** (110 µL, 108 mg, 1 mmol). After stirring at room temperature for 24 h, NMR spectroscopic analysis revealed 90% conversion to **18**. The reaction was quenched with D_2O (2 drops) before being concentrated and analysed by both ^1H and ^2H NMR spectroscopy; δ_D (Acetone d_6, 92.1 MHz): 8.30 ppm (s, 1D).

Borylation-Cross-Coupling of 2,3-dimethylpyrazine **(17)**: *Synthesis of 2,3-dimethyl-5-thiophen-2'-yl-pyrazine* (**S7**)

Following general procedure E, borylation of **17** was carried out on a 1.85 mmol scale and, following complete conversion to the boronate ester (GC/MS), the solvent was removed *in vacuo* followed by addition of 2-bromothiophene (300 mg, 1.84 mmol, 1 equiv.), K_3PO_4 (aq.) (785 mg, 3.70 mmol, 2 equiv.), $[(PPh_3)_2PdCl_2]$ (65 mg, 93 x 10^{-3} mmol, 5 mol%) and DMF (20 ml). The reaction mixture was transferred to a microwave tube (20 mL volume), crimp sealed with a septum cap, and heated for 1 h at 150 ^oC. The product was extracted into ethylacetate, dried ($MgSO_4$), and concentrated. Chromatography on silica gel (hexane:ethylacetate, 9:1) afforded **S7** (120 mg, 0.632 mmol, 34%). M.p. 50-52 ^oC. δ_H ($CDCl_3$, 400 MHz) 8.62 (s, 1H, 6-*H*), 7.59 (dd, *J* = 4.0, 1.0 Hz, 1H, 5'-*H*), 7.39 (dd, *J* = 5.1, 1.0 Hz, 1H, 3'-*H*), 7.10 (dd, *J* = 4.0, 5.1 Hz, 1H, 4'-*H*), 2.52, 2.54 (6H, s, 2,3-C*H*$_3$); δ_C NMR ($CDCl_3$, 100 MHz) 151.67, 150.15, 145.0, 141.82, 136.6, 128.15, 127.61, 124.63, 21.98, 21.59. m/z (EI) 190 [M^+], 108 [M-C_4H_2S]$^+$. Anal. Calcd. For $C_{10}H_{10}N_2S$, C 63.13%, H 5.30%, N 14.72%; found C, 63.18%, H, 5.34%, N, 14.50%.

Borylation of 2-chloro-3-methylpyrazine **(19);** *Synthesis of 2-chloro-3-methyl-6-(Bpin)pyrazine* **(20)** *and 2-chloro-3-methyl-5-(Bpin)-pyrazine* **(21)**

General procedure C was followed using $[Ir(\mu\text{-}OMe)COD]_2$ (15 mg, 23 x 10^{-3} mmol, 2.5 mol%), dtbpy (13 mg, 47 x 10^{-3} mmol, 5 mol%), B_2pin_2 (236 mg, 0.9 mmol, 1 equiv.) and **19** (120 mg, 0.9 mmol). The reaction was stirred at room temperature for 24 h. NMR spectroscopic analysis of the crude mixture showed 30% conversion (based on **19**) to a 64:36 mixture of **20:21**.

Borylation of 2,5-dimethylpyrazine **(22)**: *Synthesis of 2,5-dimethyl-3-(4-methoxyphenyl)pyrazine* **(S8)**

General procedure C was followed using $[Ir(\mu\text{-OMe})COD]_2$ (33 mg, 5 x 10^{-2} mmol, 5 mol%), dtbpy (27 mg, 0.1 mmol, 10 mol%), B_2pin_2 (254 mg, 1 mmol, 1 equiv.) and **22** (110 µL, 108 mg, 1 mmol). The reaction was stirred at 80 °C for 16 h. NMR spectroscopic analysis of the crude mixture showed 56% conversion (based on **22**).

$Pd(dppf)Cl_2$ (37 mg, 5 x 10^{-2} mmol, 5 mol%), K_3PO_4 (420 mg, 2 mmol, 2 equiv.), 4-iodoanisole (260 mg, 1.1 mmol, 1.1 equiv.) and DMAc:H_2O (9:1) (5 mL) were added to the crude mixture and heated to 60 °C for 16 h. The reaction was worked up as per General Procedure D/F. Flash column chromatography (gradient elution 10-25% Ethyl Acetate in Heptane) provided **S8** as a pale yellow oil (59 mg, 28% based on **22**).

S8

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.28 (s, 1H, 6-*H*), 7.52 (m, 2H, 2'/6'-*H*), 7.00 (m, 2H, 3'/5'-*H*), 3.86 (s, 3H, O-CH_3), 2.58 (s, 3H, CH_3), 2.56 (s, 3H, CH_3); ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.1 (*C*-OCH_3), 152.6 (3-*C*), 150.4 (Ar*C*), 148.2 (Ar*C*), 141.5 (6-*C*), 131.5 (1'-*C*), 130.5 (2C, 2'/6'-*C*), 114.0 (2C, 3'/5'-*C*), 55.5 (O*C*H_3), 22.9 (2-C*C*H_3), 21.3 (5-C*C*H_3); ν_{max} (neat) 1610, 1513, 1448, 1407, 1372, 1290, 1249, 1176, 1161, 1068, 1033, 968, 908 cm^{-1}; Accurate Mass (ASAP) m/z found $[M+H]^+$ 215.1184 ($C_{13}H_{15}N_2O$) requires *M* 215.1183.

Borylation of 2-phenylpyrimidine **(24)**: *Synthesis of 2-phenyl-4-pyridin-3'-yl-pyrimidine* **(S9)**

General procedure C was followed using $[Ir(\mu\text{-OMe})COD]_2$ (20 mg, 3 x 10^{-2} mmol, 5 mol%), dtbpy (16 mg, 0.1 mmol, 10 mol%), B_2pin_2 (150 mg, 1 mmol, 1 equiv.) and **24**

(100 mg, 0.6 mmol). The reaction was stirred at RT for 24 h. NMR spectroscopic analysis of the crude mixture showed 65% conversion to **25**.

Pd(Amphos)Cl_2 (35 mg, 5 x 10^{-2} mmol, 5 mol%), K_3PO_4 (420 mg, 2 mmol, 2 equiv.), 3-iodopyridine (230 mg, 1.1 mmol, 1.1 equiv.) and DMAc:H_2O (9:1) (5 mL) were added to the crude mixture and heated to 70 °C for 2 h. The reaction was worked up as per General Procedure D/F. Flash column chromatography Heptane:Ethyl Acetate (1:1) provided **S9** as an orange solid (110 mg, 47% based on **24**).

S9

^{1}H NMR (700 MHz, $CDCl_3$) δ 9.03 (s, 2H, 4/6-*H)*, 8.92 (s, 2''-*H*), 8.72 (d, J = 4.6 Hz, 1H, 6''-*H*), 8.50 (m, 2H, 2', 6'-*H*), 7.95 (d, J = 7.8 Hz, 1H, 4''-*H*), 7.53 (m, 3H, 3', 5', 4'-*H*), 7.48 (dd, J = 7.8, 4.6 Hz, 1H, 5''-*H*); ^{13}C NMR (176 MHz, $CDCl_3$) δ 164.4 (2-*C*), 155.4 (2C, 4, 6-*C*), 150.0 (6''-*C*), 147.9 (2''-*C*), 137.1 (1'-*C*), 134.3 (4''-*C*), 131.2 (4'-*C*), 130-7 (5-*C*), 128.9 (3C, 3', 5', 3''-*C*), 128.4 (2C, 2', 6'-*C*), 124.2 (5''-*C*); v_{max} (neat) 1534, 1442, 1425, 1374, 1334 cm^{-1}; Accurate Mass (ASAP) m/z found $[M]^+$ 233.0953 ($C_{15}H_{11}N_3$) requires *M* 233.0954.

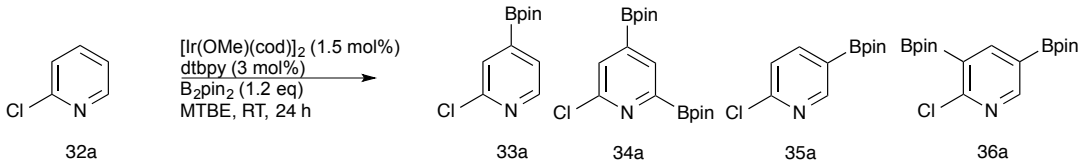
Borylation of 3-methylpyridazine **(26)**: *Synthesis of 3-methyl-5-naphthalen-2-ylpyridazine* **(S10)**

General procedure B was applied to 3-Methylpyridazine (**26**) on a 1 mmol scale. The reaction was stirred at RT for 24 h. NMR spectroscopic analysis showed full conversion to **27**. Pd(Amphos)Cl_2 (35 mg, 5 x 10^{-2} mmol, 5 mol%), K_3PO_4 (420 mg, 2 mmol, 2 equiv.), 2-bromonaphthalene (230 mg, 1.1 mmol, 1.1 equiv.) and DMAc:H_2O (9:1) (5 mL) were added to the crude mixture and heated to 70 °C for 2 h. The reaction was worked up as per General Procedure D/F. Flash column chromatography Heptane:Ethyl Acetate (4:6) provided **S10** as an orange solid (96 mg, 44% based on **26**).

S10

^{1}H NMR (700 MHz, $CDCl_3$) δ 9.43 (d, J = 2.0 Hz, 1H, 6-*H*), 8.16 (s, 1H, 1'-*H*), 8.00 (d, J = 8.5 Hz, 1H, 4'-*H*), 7.93 (m, 2H, 5', 8'-*H*), 7.75 (dd, J = 8.5, 1.7 Hz, 1H, 3'-*H*), 7.63 (d, J = 2.0 Hz, 1H, 4-*H*), 7.58 (m, 2H, 6', 7'-*H*) 2.83 (s, 3H, C*H*$_3$); ^{13}C NMR (176 MHz, $CDCl_3$) δ 160.0 (3-*C*), 148.0 (6-*C*), 138.5 (5-*C*), 133.7 (10'-*C*), 133.4 (9'-*C*), 132.0 (2'-*C*), 129.4 (4'-*C*), 128.5 (Ar*C*), 127.8 (Ar*C*), 127.4 (Ar*C*), 127.0 (Ar*C*), 126.9 (1'-*C*), 124.0 (3'-*C*), 123.8 (4-*C*), 22.4 (*C*H_3); v_{max} (neat) 1590 cm^{-1}; Accurate Mass (ASAP) m/z found $[M]^+$ 220.1000 ($C_{15}H_{12}N_2$) requires *M* 220.0999.

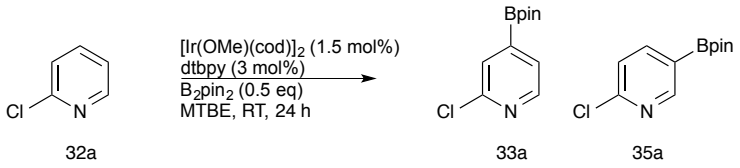
Borylation of 2-chloropyridine **(32a)**



32a 33a 34a 35a 36a

General procedure A was applied to 2-chloropyridine (**32a**) on a 1 mmol scale with additional B_2pin_2 (51 mg, 0.2 mmol). The reaction mixture was stirred at room temperature for 24 h giving full conversion (^{1}H NMR) to **33a**, **34a**, **35a** and **36a** in a 28:38:27:7 ratio.

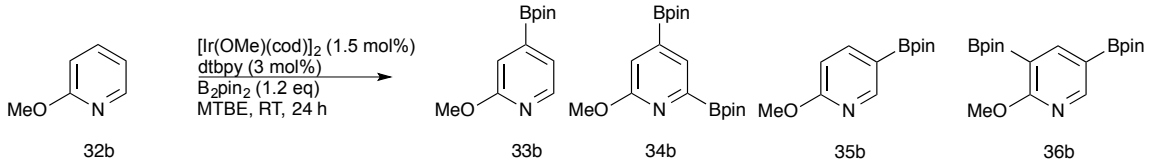
Borylation of 2-chloropyridine **(32a)** *under boron-limiting conditions*



32a 33a 35a

General procedure B was applied to 2-chloropyridine (**32a**) on a 1 mmol scale. The reaction mixture was stirred at room temperature for 24h giving 55% conversion (^{1}H NMR) to afford **33a** and **35a** in a 75:25 ratio.

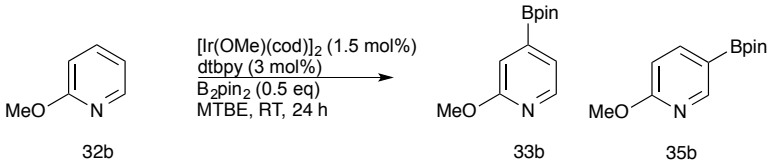
Borylation of 2-methoxypyridine **(32b)**



32b 33b 34b 35b 36b

General procedure A was applied to 2-methoxypyridine (**32b**) on a 1 mmol scale with additional B_2pin_2 (51 mg, 0.2 mmol). The reaction mixture was stirred at room temperature for 24 h giving full conversion (^{1}H NMR) to **33b**, **34b**, **35b** and **36b** in a 43:17:31:9 ratio.

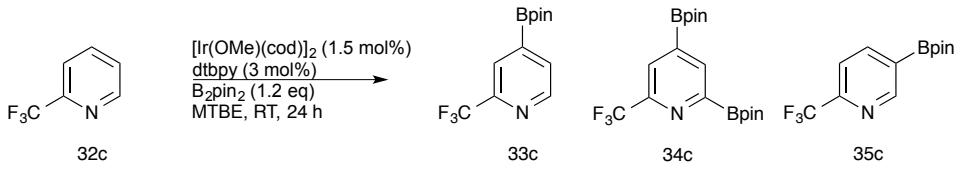
Borylation of 2-methoxypyridine **(32b)** *under boron-limiting conditions*



32b 33b 35b

General procedure B was applied to 2-methoxypyridine (**32b**) on a 1 mmol scale. The reaction mixture was stirred at room temperature for 24 h giving 42% conversion (^{1}H NMR) to afford **33b** and **35b** in a 73:27 ratio.

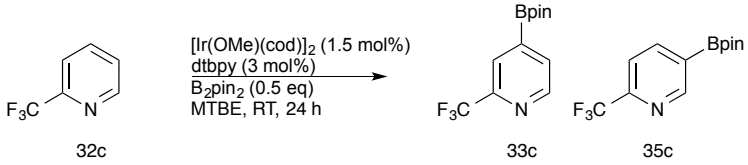
Borylation of 2-(trifluoromethyl)pyridine **(32c)**



32c 33c 34c 35c

General procedure A was applied to 2-(trifluoromethyl)pyridine (**32c**) on a 1 mmol scale with additional B_2pin_2 (51 mg, 0.2 mmol). The reaction mixture was stirred at room temperature for 24 h giving full conversion (^{1}H NMR) to **33c**, **34c** and **35c** in a 25:36:39 ratio.

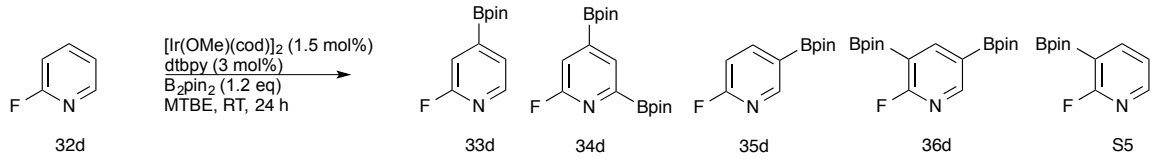
Borylation of 2-(trifluoromethyl)pyridine **(32c)** *under boron-limiting conditions*



32c 33c 35c

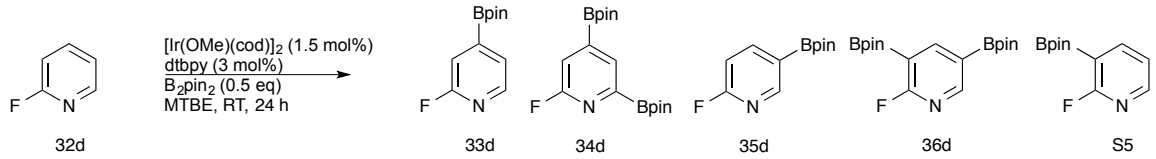
General procedure B was applied to 2-(trifluoromethyl)pyridine (**32c**) on a 1 mmol scale. The reaction mixture was stirred at room temperature for 24 h giving 83% conversion (^{1}H NMR) to afford **33c** and **35c** in a 65:35 ratio.

Borylation of 2-fluoropyridine **(32d)**



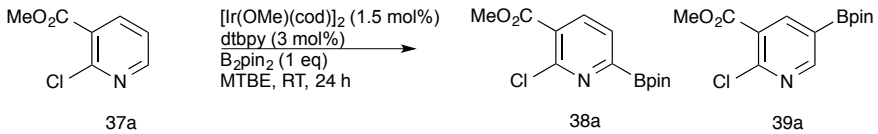
General procedure A was applied to 2-fluoropyridine (**32d**) on a 1 mmol scale with additional B_2pin_2 (51 mg, 0.2 mmol). The reaction mixture was stirred at room temperature for 24 h giving full conversion (^{1}H NMR) to afford **33d**, **34d**, **35d**, **36d** and **S11** in a 45:15:10:19:11 ratio.

Borylation of 2-fluoropyridine **(32d)** *under boron-limiting conditions*



General procedure B was applied to 2-fluoropyridine (**32d**) on a 1 mmol scale. The reaction mixture was stirred at room temperature for 24 h giving 89% conversion (^{1}H NMR) to afford **33d**, **34d**, **35d**, **36d** and **S11** in a 57:2:19:5:17 ratio.

Borylation of methyl-2-chloronicotinate **(37a)**; synthesis of methyl-2-chloro-5-(Bpin)-nicotinate **(39a)**



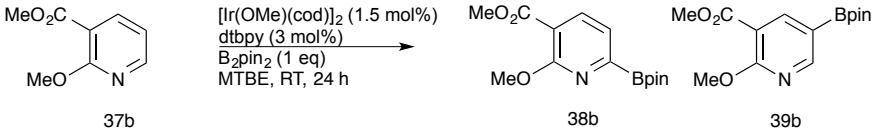
General procedure B was applied to methyl-2-chloronicotinate (**37a**) on a 1 mmol scale. The reaction mixture was stirred at room temperature for 24 h giving 75% conversion (^{1}H NMR) to afford **38a** and **39a** in a 6:94 ratio. The crude mixture was dry loaded onto C_{18} silica and purified by reverse phase column chromatography (0-100% MeCN in H_2O) using a Biotage SNAP KP-C_{18}-HS cartridge. Fractions with the same R_f were combined,

concentrated and the aqueous residue extracted with ethyl acetate. Concentration of the solvent gave **39a** as a white solid (0.93 g, 52%).

39a

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (m, br, 6-*H*), 8.49 (d, J = 1.9 Hz, 1H, 4-*H*), 3.95 (s, 3H, CO_2CH_3), 1.36 (s, 12H, pin-CH_3); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1 (CO_2CH_3), 157.4 (6-*C*), 152.6 (2-*C*), 146.3 (4-*C*), 126.2 (3-*C*), 84.8 (2C, pin-$C(CH_3)_2$), 52.8 (CO_2CH_3), 24.9 (4C, pin-CH_3); ^{11}B NMR (128 MHz, $CDCl_3$) δ 30.2; ν_{max} (neat) 1738, 1694, 1588, 1548, 1426, 1359, 1255, 1138, 1108, 1062, 971 cm^{-1}; Accurate Mass (AP$^+$-TOF) m/z found $[M]^+$ 297.1047 ($C_{13}H_{18}{}^{10}B^{35}ClNO_4$) requires *M* 297.1054.

Borylation of methyl-2-methoxynicotinate **(37b)***: Synthesis of methyl-2-methoxy-5-(4-methoxyphenyl)nicotinate* **(S12)**



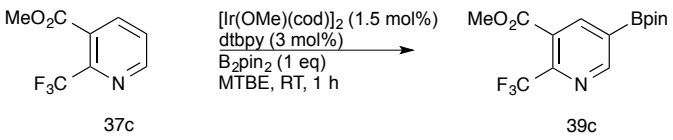
37b 38b 39b

General procedure F was applied to Methyl-2-methoxynicotinate (**37b**) on a 1.1 mmol scale; $Pd(dppf)Cl_2$ (0.04g, 0.05 mmol, 5 mol%), Cs_2CO_3 (0.72 g, 2.2 mmol) and 4-iodoanisole (0.28 g, 1.2 mmol) The reaction mixture was stirred at room temperature for 24 h giving full conversion (^{1}H NMR) to **38b** and **39b** in a 7:93 ratio. Suzuki-Miyaura step was carried out for 2 h. Crude material was purified by flash column chromatography (0-15% EtOAc in Heptane) to give **S12** as a white solid (0.22 g, 76%).

S12

^{1}H NMR (700 MHz, $CDCl_3$) δ 8.48 (d, J = 2.6 Hz, 1H, 6-*H*), 8.33 (d, J = 2.6 Hz, 1H, 4-*H*), 7.47 (m, 2H, 2', 6'-*H*), 6.99 (m, 2H, 3', 5'-*H*), 4.08 (s, 3H, 2-COCH_3), 3.93 (s, 3H, CO_2CH_3), 3.85 (s, 3H, 4'-COCH_3); ^{13}C NMR (176 MHz, $CDCl_3$) δ 165.7 (CO_2CH_3), 161.5 (2-*C*), 159.6 (4'-*C*), 148.4 (6-*C*), 139.6 (4-*C*), 129.8 (5-*C*), 129.4 (1'-*C*), 127.9 (2C, 2', 6'-*C*), 114.7 (2C, 3', 5'-*C*), 113.7 (3-*C*), 55.5 (4'-COCH_3), 54.4 (2-COCH_3), 52.5 (CO_2CH_3); ν_{max} (neat) 1732, 1606, 1563, 1519, 1474, 1417, 1327, 1285, 1245, 1181, 1087, 1060, 1014 cm^{-1}; Accurate Mass (ASAP) m/z found $[M+H]^+$ 274.1079 ($C_{15}H_{16}NO_4$) requires *M* 274.1075.

Borylation of methyl-2-(trifluoromethyl)nicotinate **(37c)**: *Synthesis of methyl-2-(trifluoromethyl)-5-(4-methoxyphenyl)nicotinate* **(S13)**



37c 39c

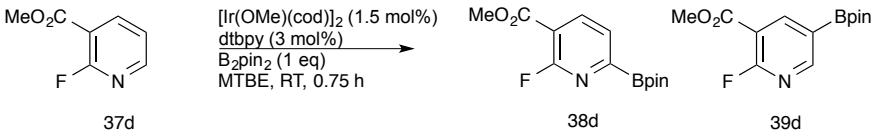
General procedure F was applied to Methyl-2-(trifluoromethyl)nicotinate (**37c**) on a 1.4 mmol scale; $Pd(dppf)Cl_2$ (0.05 g, 0.07 mmol), Cs_2CO_3 (0.91 g, 2.8 mmol) and 4-iodoanisole (0.36 g, 1.5 mmol). The reaction mixture was stirred at room temperature for 1h giving full conversion (^{1}H NMR) to **39c**. Suzuki-Miyaura step carried out for 3 h. Purification by preparative HPLC provided **S13** as a white solid (0.33 g, 75%).

S13

^{1}H NMR (700 MHz, $CDCl_3$) δ 8.96 (d, J = 2.1 Hz, 1H, 6-*H*), 8.22 (d, J = 2.1 Hz, 1H, 4-*H*), 7.58 (m, 2H, 2', 6'-*H*), 7.05 (m, 2H, 3', 5'-*H*), 3.99 (s, 3H, CO_2CH_3), 3.88 (s, 3H, COCH_3); ^{13}C NMR (176 MHz, $CDCl_3$) δ 166.2 (CO_2CH_3), 161.0 (4'-*C*), 148.6 (6-*C*), 143.4 (m, 2-*C*), 138.9 (5-*C*), 135.7 (4-*C*), 128.7 (2C, 2', 6'-*C*), 127.8 (3-*C*), 127.6 (1'-*C*), 121.4 (q, J =

274.6, CF_3), 115.1 (2C, 3', 5'-*C*), 55.6 ($CO\mathit{C}H_3$), 53.4 ($CO_2\mathit{C}H_3$); ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.3 (s); ν_{max} (neat) 1738, 1609, 1519, 1440, 1324, 1252, 1142, 1065, 1049 cm^{-1}; Accurate Mass (ASAP) m/z found $[M]^+$ 311.0769 ($C_{15}H_{12}F_3NO_3$) requires *M* 311.0768.

Borylation of methyl 2-fluoronicotinate **(37d)**: *Synthesis of methyl-2-fluoro-5-(3-methoxyphenyl)nicotinate* **(S14)**



37d 38d 39d

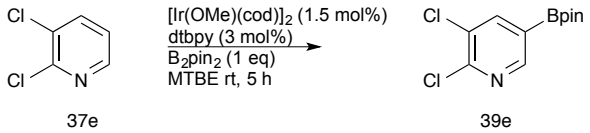
General procedure F was applied to Methyl-2-fluoronicotinate (**37d**) on a 4.4 mmol scale; $Pd(dppf)Cl_2$ (0.16 g, 0.22 mmol), Cs_2CO_3 (2.87 g, 8.8 mmol) and 3-iodoanisole (1.13 g, 4.8 mmol). The reaction mixture was stirred at room temperature for 45 min giving full conversion (^{1}H NMR) to **38d** and **39d** in a 9:91 ratio. The Suzuki-Miyaura step was carried out for 2 h. Crude material was purified by flash column chromatography (0-20% EtOAc in Heptane) to give **S14** as an off-white solid (0.71 g, 62%).

S14

^{1}H NMR (700 MHz, $CDCl_3$) δ 8.54 (m, 2H, 4, 6-*H*), 7.40 (t, J = 7.9 Hz, 1H, 5'-*H*), 7.13 (d, J = 7.9 Hz, 1H, 6'-*H*), 7.07 (t, J = 2.3 Hz, 1H, 2'-*H*), 6.97 (dd, J = 7.9, 2.3 Hz, 1H, 4'-*H*), 3.98 (s, 3H, $CO_2C\mathit{H}_3$), 3.87 ($COC\mathit{H}_3$); ^{13}C NMR (176 MHz, $CDCl_3$) δ 163.8 (d, J = 8.1 Hz, $\mathit{C}O_2CH_3$), 161.0 (d, J = 249.8 Hz, 2-*C*), 160.4 (3'-*C*), 149.6 (d, J = 15.6 Hz, Ar*C*), 141.7 (d, J = 1.7 Hz, Ar*C*), 137.0 (1'-*C*), 135.2 (d, J = 5.3 Hz, 5-*C*), 130.5 (5'-*C*), 119.5 (6'-*C*), 114.0 (4'-*C*), 113.4 (d, J = 26 Hz, 3-*C*), 113.0 (2'-*C*), 55.5 ($COC\mathit{H}_3$), 53.0 ($CO_2\mathit{C}H_3$); ^{19}F

NMR (376 MHz, $CDCl_3$) δ -65.2 (m); v_{max} (neat) 1722, 1603, 1459, 1446, 1327, 1292, 1249, 1179, 1089, 1042, 977 cm^{-1}; Accurate Mass (ASAP) m/z found $[M]^+$ 261.0801 ($C_{14}H_{12}FNO_3$) requires *M* 261.0824

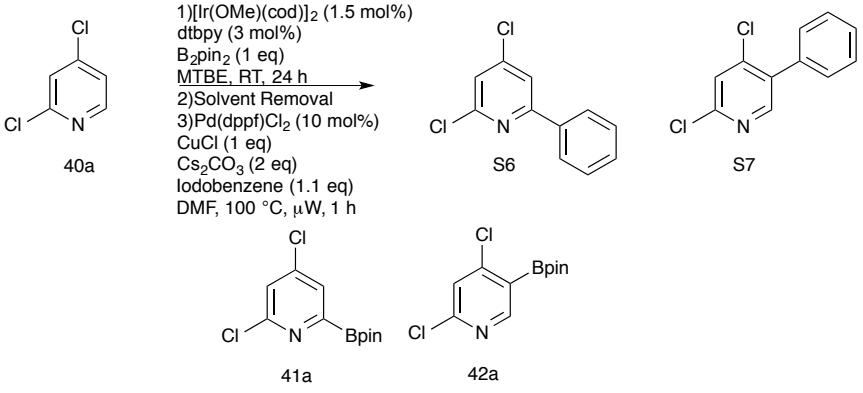
Borylation of 2,3-dichloropyridine **(37e)**: *Synthesis of 2,3-dichloro-5(Bpin)-pyridine* **(39e)**



37e 39e

General procedure B was applied to 2,3-dichloropyridine (**37e**) on a 1 mmol scale. The reaction mixture was stirred at room temperature for 5 h giving full conversion (^{1}H NMR) to **39e**. The crude product was filtered through an SCX column before being purified by flash column chromatography (eluent; 0-5% MeOH in DCM) to give **39e** (0.12 g, 44%) as a white solid. δ_H (700 MHz, $CDCl_3$) 8.57 (1H, d, J = 1.5 Hz, 6-*H*), 8.09 (1H, d, J = 1.5 Hz, 4-*H*), 1.33 (12H, s, C*H*$_3$); δ_C (176 MHz, $CDCl_3$) 152.9 (6-*C*), 151.8 (2-*C*), 144.6 (4-*C*), 130.5 (3-*C*), 84.9 (pin-*C*$(CH_3)_2$), 25.0 (pin-*C*H_3); δ_B (128 MHz, $CDCl_3$) 30.0 (s, br). m/z (GCMS-EI) 277 ($[M(^{37}Cl_2)]^+$), (275 ($[M(^{37}Cl^{35}Cl)]^+$), 273 ($[M(^{35}Cl_2)]^+$), 262 ($[M(^{37}Cl_2)$-$CH_3]^+$)260 ($[M(^{37}Cl^{35}Cl)$-$CH_3]^+$ ^{37}Cl), 258 ($[M(^{35}Cl_2)$-$CH_3]^+$). HRMS (ASAP) found $[M+H]^+$ 273.0609, $C_{11}H_{15}{}^{10}BNO_2{}^{35}Cl_2$ requires *M* 273.0625.

Borylation-cross-coupling of 2,4-dichloropyridine **(40a)**: *Synthesis of 2,4-dichloro-6-phenylpyridine* (**S15**) and *2,4-dichloro-5-phenylpyridine* (**S16**)



40a S6 S7

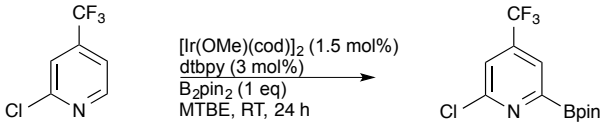
41a 42a

General procedure D was applied to 2,4-dichloropyridine (**40a**) on a 2 mmol scale using iodobenzene (449 mg, 2.2 mmol) as the cross-coupling partner. ^{1}H NMR analysis after the C-H borylation step showed 92% conversion to a 50:50 mixture of **41a** and **42a**. Purification by flash column chromatography (24 g column, 0-10% EtOAc/hexane, 25 column volumes) afforded **S15** (179 mg, 40%) and **S16** (125 mg, 28%), both as colourless liquids.

S15: ν_{max} (ATR) 3058, 2928, 1742, 1568, 1542, 1408, 1369, 1157, 1068, 844, 800, 796, cm^{-1}. δ_H (700 MHz, $CDCl_3$) 7.98 (m, 2H, 2',6'-*H*), 7.66 (d, *J* = 1.4, 1H, 5-*H*), 7.46-7.50 (m, 3H, 3',4',5'-*H*) 7.30 (d, *J* = 1.4, 1H, 3-*H*); δ_C (176 MHz, $CDCl_3$) 159.1 (6-*C*), 152.1 (1'-*C*), 146.4 (4-*C*), 136.8 (2-*C*), 130.4 (4'-*C*), 129.1 (3',5'-*C*), 127.2 (2',6'-*C*), 122.4 (3-*C*), 119.4 (5-*C*); *m/z* (GCMS-EI) 227 ([M]$^+$, ^{37}Cl^{37}Cl), 225 ([M]$^+$, ^{37}Cl^{35}Cl), 223 ([M]$^+$, ^{35}Cl^{35}Cl), 190 ([M-Cl]$^+$, ^{37}Cl), 188 ([M-Cl]$^+$, ^{35}Cl), 153 [M-2Cl]$^+$; HRMS (ASAP) found [M]$^+$ 222.9953, $C_{11}H_7{}^{35}Cl_2N$ requires *M* 222.9950.

S16: ν_{max} (ATR) 3058, 2928, 1742, 1568, 1542, 1408, 1369, 1157, 1068, 844, 800, 796, cm^{-1}. δ_H (700 MHz, $CDCl_3$) 8.34 (s, 1H, 6-*H*), 7.49-7.46 (m, 4H), 7.42 (d, *J* = 2.0, 2H); δ_C (176 MHz, $CDCl_3$) 150.8, 150.7, 144.3, 135.6, 134.4, 129.6, 128.7, 124.9. *m/z* (GCMS-EI) 227 ([M]$^+$, ^{37}Cl^{37}Cl), 225 ([M]$^+$, ^{37}Cl^{35}Cl), 223 ([M]$^+$, ^{35}Cl^{35}Cl), 190 [M-Cl]$^+$, ^{37}Cl), 188 ([M-Cl]+, ^{35}Cl), 153 [M-2Cl]$^+$; HRMS (ASAP) found [M]$^+$ 222.9955, $C_{11}H_7{}^{35}Cl_2N$ requires *M* 222.9950.

Borylation of 2-chloro-4-(trifluoromethyl)pyridine **(40b)**: *Synthesis of 2-chloro-4-(trifluoromethyl)-6-(3-methoxyphenyl)pyridine* **(S17)**



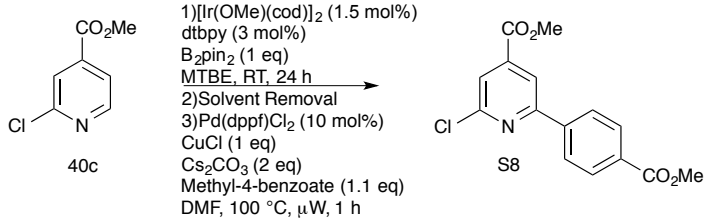
40b 41b

General procedure F was applied to 2-Chloro-4-(trifluoromethyl)pyridine (**40b**) on a 1 mmol scale; $Pd(dppf)Cl_2$ (37 mg, 0.05 mmol), Cs_2CO_3 (650 mg, 2 mmol) and 3-iodoanisole (260 mg, 1.1 mmol). The reaction mixture was stirred at room temperature for 24 h giving 72% conversion (^{1}H NMR) to **41b**. The Suzuki-Miyaura step was carried out for 3 h. Crude material was purified by flash column chromatography (0-3% Et_2O in Heptane) to give **S17** as an off-white solid (148 mg, 51% based on **40b**).

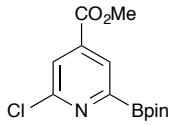
S17

^{1}H NMR (700 MHz, $CDCl_3$) δ 7.83 (s, 1H, 5-*H*), 7.59 (t, J = 2.3 Hz, 1H, 2'-*H*), 7.58 (d, J = 7.9 Hz, 1H, 6'-*H*), 7.48 (s, 1H, 3-*H*), 7.41 (t, J = 7.9 Hz, 1H, 5'-*H*), 7.03 (dd, J = 7.9, 2.3 Hz, 1H, 4'-*H*), 3.91 (s, 3H, OCH_3); ^{13}C NMR (176 MHz, $CDCl_3$) δ 160.4 (3'-*C*), 159.4 (6-*C*), 152.4 (2-*C*), 141.8 (q, J = 34.3 Hz, 4-*C*), 138.0 (1'-*C*), 130.2 (5'-*C*), 122.3 (q, J = 274 Hz, *C*F_3), 119.6 (6'-*C*), 118.7 (q, J = 3.7 Hz, 3-*C*), 116.6 (4'-*C*), 114.8 (q, J = 3.5 Hz, 5-*C*), 112.6 (2'-*C*), 55.6 (O*C*H_3); ν_{max} (neat) 1600, 1561, 1459, 1400, 1333, 1274, 1221, 1177, 1142, 1102 cm^{-1}; Accurate Mass (ASAP) m/z found $[M]^+$ 287.0325 ($C_{13}H_9{}^{35}ClF_3NO$) requires *M* 287.0330.

Borylation-cross-coupling of methyl-2-chloroisonicotinate **(40c)**: *Synthesis of methyl 2-chloro-6-(4-(methoxycarbonyl)phenyl)isonicotinate* (**S18**)



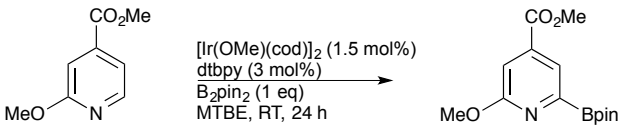
40c S8



41c

General procedure D was applied to methyl 2-chloroisonicotinate (**40c**) on a 1 mmol scale using methyl 4-iodobenzoate (288 mg, 1.1 mmol) as the cross-coupling partner. ^{1}H NMR analysis after the C-H borylation step showed 73% conversion to **41c**. Purification by flash column chromatography (40 g column, 0-40% ether in hexanes, 20 column volumes) afforded **S18** as a white solid (70 mg, 53%). m.p. 167 - 168 °C; ν_{max} (ATR) 1720, 1551, 1402, 1315, 1266, 1108, 968, 763 cm^{-1}. δ_H (700 MHz, $CDCl_3$) 8.25 (1H, d, *J* = 1.4, 5-*H*), 8.15-8.12 (4H, m, 2',3',5',6'-*H*), 7.85 (1H, d, *J* = 1.4, 3-*H*), 4.00 (3H, s, Py-CO_2CH_3), 3.95 (3H, s, Ph-CO_2CH_3). δ_C (176 MHz, $CDCl_3$) 166.7 (4'-CO_2), 164.5 (4-CO_2), 157.8 (6-*C*), 152.5 (4-*C*), 141.2 (2-*C*), 141.0 (1'-*C*), 131.6 (4'-*C*), 130.3 (2C,3', 5'-*C*), 127.2 (2C,2', 6'-*C*), 123.0 (3-*C*), 118.7 (5-*C*), 53.3 (4-CO_2CH_3), 52.4 (4'-CO_2CH_3). *m/z* (GCMS-EI) 307 ($[M]^+$, ^{37}Cl), 305 ($[M]^+$, ^{35}Cl), 276 ($[M\text{-}OCH_3]^+$, ^{37}Cl), 274 ($[M\text{-}OCH_3]^+$, ^{35}Cl), 248 ($[M\text{-}CO_2CH_3]^+$, ^{37}Cl), 246 ($[M\text{-}CO_2CH_3]^+$, ^{35}Cl), 189 ($[M\text{-}(CO_2CH_3)_2]^+$, ^{37}Cl), 187 ($[M\text{-}(CO_2CH_3)_2]^+$, ^{35}Cl), 152 $[M\text{-}(CO_2CH_3)_2Cl]^+$. HRMS (ASAP) found $[M]^+$ 305.0451, $C_{15}H_{12}{}^{35}ClNO_4$ requires *M* 305.0449.

Borylation of methyl 2-methoxyisonicotinate (**40d**): Synthesis of *methyl-2-methoxy-6-(3-methoxyphenyl)isonicotinate* **(S19)**



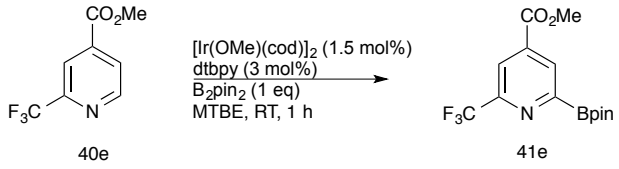
40d **41d**

General procedure F applied to Methyl-2-methoxyisonicotinate (**40d**) on a 1 mmol scale; $Pd(dppf)Cl_2$ (37 mg, 0.05 mmol), Cs_2CO_3 (650 mg, 2 mmol) and 3-iodoanisole (260 mg, 1.1 mmol). The reaction mixture was stirred at room temperature for 24 h giving 57% conversion (^{1}H NMR) to **41d.** The Suzuki-Miyaura step was carried out for 16 h. Crude material was purified by flash column chromatography (7% EtOAc in Heptane) to give **S19** as an off-white solid (111 mg, 41% based on **40e**).

S19

^{1}H NMR (700 MHz, $CDCl_3$) δ 7.88 (s, 1H, 5-*H*), 7.67 (m, 2H, 2', 6'-*H*), 7.38 (t, J = 8.0 Hz, 1H, 5'-*H*), 7.25 (s, 1H, 3-*H*), 6.97 (dd, J = 8.0, 2.4 Hz, 1H, 4'-*H*), 4.07 (s, 3H, 2-COCH_3), 3.96 (s, 3H,CO_2CH_3), 3.89 (s, 3H, 3'-COCH_3); ^{13}C (176 MHz, $CDCl_3$) δ 165.9 (CO_2CH_3), 164.5 (2-*C*), 160.1 (3'-*C*), 155.5 (*6*-*C*), 141.0 (4-*C*), 139.9 (1'-*C*), 129.8 (5'-*C*), 119.4 (6'-*C*), 115.0 (4'-*C*), 112.6 (2'-*C*), 112.3 (5-*C*), 109.8 (3-*C*), 55.5 (2-COCH_3), 53.9 (3'-COCH_3), 52.8 (CO_2CH_3); ν_{max} (neat) 1731, 1568, 1452, 1386, 1354, 1258, 1225, 1208, 1108, 1045 cm^{-1}; Accurate Mass (ASAP) m/z found $[M]^+$ 273.1001 ($C_{15}H_5NO_4$) requires *M* 273.1008.

Borylation of methyl 2-(trifluoromethyl)isonicotinate **(40e)***: Synthesis of methyl-2-(trifluoromethyl)-6-(4-methoxyphenyl)isonicotinate* **(S20)**



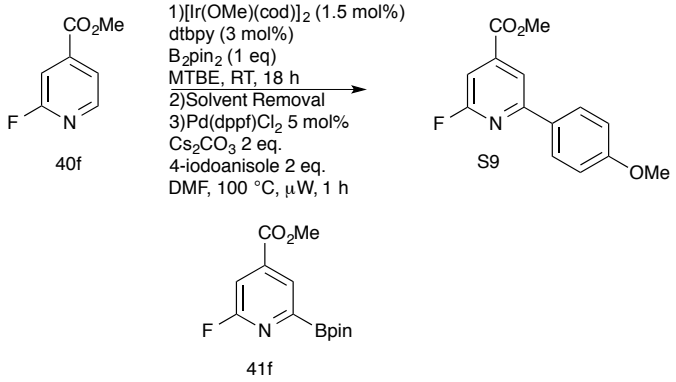
General procedure A applied to methyl-2-(trifluoromethyl)isonicotinate (**40e**) on a 0.2 mmol scale. The reaction mixture was stirred at room temperature for 1 h giving 93% conversion (^{1}H NMR) to **41e.** $Pd(dppf)Cl_2$ (15 mg, 2 x 10^{-2} mmol, 5 mol%), K_3PO_4 (170 mg, 0.8 mmol, 2 equiv.), 4-iodoanisole (100 mg, 0.44 mmol, 1.1 equiv.) and DMAc:H_2O

(9:1) (5 mL) were added to the crude mixture and heated to 60 °C for 16 h. The reaction was worked up as per General Procedure D/F. Flash column chromatography (3% Ethyl Acetate in Heptane) provided **S20** as a white solid (82 mg, 66% based on **40e**).

S20

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (s, 1H, 5-*H*), 8.10 (m, 2H, 2', 6'-*H*), 8.05 (d, J = 0.9 Hz, 1H, 3-*H*), 7.02 (m, 2H, 3', 5'-*H*), 4.02 (s, 3H, CO_2CH_3), 3.88 (s, 3H, OCH_3); ^{13}C (151 MHz, $CDCl_3$) δ 164.9 (CO_2CH_3), 161.7 ($COCH_3$), 158.8 (6-*C*), 149.1 (q, J = 35 Hz, 2-*C*), 139.8 (4-*C*), 129.7 (1'-*C*), 128.8 (2C, 2', 6'-*C*), 121.5 (5-*C*), 121.5 (m, CF_3), 117.1 (q, J = 2.7 Hz, 3-*C*), 114.5 (2C, 3', 5'-*C*), 55.6 (OCH_3), 53.2 (CO_2CH_3); ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.2 (s); ν_{max} (neat) 1735, 1609, 1565, 1519, 1429, 1373, 1257, 1187, 1144, 1072, 1032, 979, 914 cm^{-1}; Accurate Mass (ASAP) m/z found $[M]^+$ 311.0769 ($C_{15}H_{12}F_3NO_3$) requires *M* 311.0784.

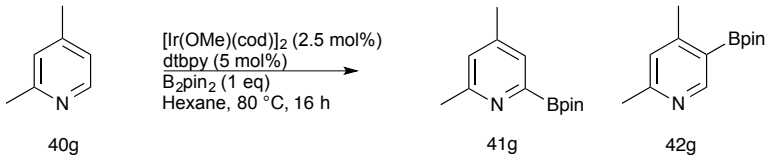
Borylation-Cross-Coupling of methyl 2-fluoroisonicotinate **(40f)**: *Synthesis of methyl 2-fluoro-6-(4'-(methoxycarbonyl)phenyl)isonicotinate* (**S21**)



General procedure D was applied to methyl 2-fluoroisonicotinate (**40f**) on a 1.1 mmol scale using 4-iodoanisole (0.51 g, 2.2 mmol, 2 eq.) as the cross-coupling partner in the absence of CuCl. ^{1}H NMR analysis after the C-H borylation step showed full conversion to **41f** in 18 h. Purification by flash column chromatography (0-20% ethyl acetate in

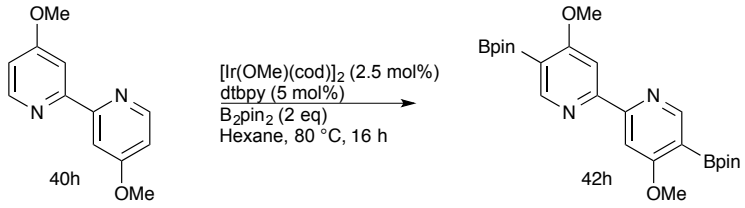
hexanes) afforded **S21** as a colourless oil (157 mg, 55%). ν_{max} (neat) 1733, 1608, 1568, 1520, 1420, 1396, 1352, 1252, 1206 1177 cm^{-1}. δ_H (700 MHz, $CDCl_3$) 8.13 (1H, m, 5-*H*), 8.03 (2H, m, 2', 6'-*H*), 7.32 (1H, m, 3-*H*), 7.00 (2H, m, 3', 5'-*H*), 4.00 (3H, s, CO_2CH_3), 3.88 (3H, s, $COCH_3$). δ_C (176 MHz, $CDCl_3$) 164.8 (d, J = 4.2 Hz, 4-CO_2Me), 162.3 (d, J = 247 Hz, 2-*C*), 161.5 (4'-*C*), 157.2 (d, J = 14 Hz, 6-*C*), 143.4 (d, J = 8 Hz, 4-*C*), 129.5 (1'-*C*), 128.6 (2C, 2', 6'-*C*), 116.3 (d, J = 5 Hz, 5-*C*), 114.4 (2C, 3', 5'-*C*), 106.7 (d, J = 40 Hz, 3-*C*), 55.6 (CO_2CH_3), 53.1 ($COCH_3$); δ_F (400 MHz, $CDCl_3$) -66.2. *m/z* (GCMS-EI) 261 $[M]^+$, 246 $[M\text{-}CH_3]^+$, 230 $[M\text{-}OCH_3]$, 218, 203, 187, 159.

Borylation of 2,4-lutidine **(40g)**



General procedure C was applied to 2,4-lutidine (**40g**) using [Ir(μ-OMe)COD]$_2$ (17 mg, 2.5 x 10^{-2} mmol), dtbpy (13 mg, 5 x 10^{-2} mmol), B_2pin_2 (254 mg, 1 mmol) and **40g** (107 mg, 1 mmol). The reaction mixture was stirred at 80 °C for 16 h giving 45% conversion (^{1}H NMR) to afford a 75:25 mixture of **41g**:**42g**.

Borylation of 4,4'-dimethoxy-2,2'-bipyridine **(40h)**



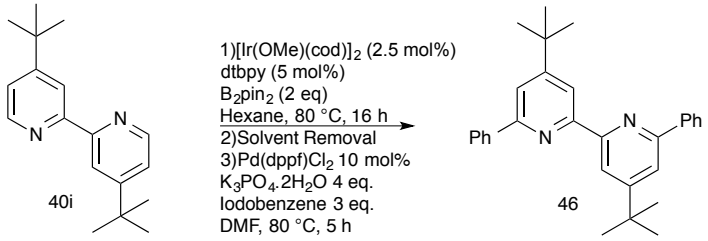
General procedure C applied to 4,4'-dimethoxy-2,2'-bipyridine (**40h**) on a 0.2 mmol scale; [Ir(μ-OMe)COD]$_2$ (8 mg, 24.1 x 10^{-3} mmol), dtbpy (7 mg, 26.1 x 10^{-3} mmol), B_2pin_2 (118 mg, 465 x 10^{-3} mmol, 2 equiv) and **40h** (50 mg, 231 x 10^{-3} mmol). The reaction mixture was stirred at 80 °C for 16 h then analysed by GC-MS which showed 85% conversion to **42h**. The solvent was removed *in vacuo*, and the residue was redissolved in 10 mL of hexanes, then passed through a celite pad, and the solvent was evaporated to afford a mixture of *3,3'-bisBpin-4,4'-dimethoxy-2,2'-bipyridine* **(42h)** accompanied by small amounts of *3-Bpin-4,4'-dimethoxy-2,2'-bipyridine* residual boron reagents. A crystal sample of **42h** suitable for single crystal X-ray diffraction was obtained by slow evaporation of a CH_2Cl_2 solution. δ_H (C_6D_6, 400 MHz) 1.10 (24H, s, CC*H*$_3$), 3.36 (6H, s,

OC*H*$_3$), 8.49 (2H, s, 3,3'-*H*), 9.51 (2H, s, 6,6'-*H*); δ_C ($CDCl_3$, 100 MHz) 24.57, 55.83, 83.82, 111.11, 150.05, 156.70, 167.73. m/z (EI) 468 [M^+], 453 [$M-CH_3$]$^+$.

Borylation of 4,4'-di-tert-butyl-2,2'-bipyridine **(40i)**

General procedure C applied to 4,4'-di-tert-butyl-2,2'-bipyridine (**40i**) on a 0.2 mmol scale; [Ir(μ-OMe)COD]$_2$ (6.2 mg, 18.7 x 10^{-3} mmol), dtbpy (5 mg, 18.6 x 10^{-3} mmol), B_2pin_2 (95 mg, 374 x 10^{-3} mmol, 2 equiv.) and **40i** (50 mg, 187 x 10^{-3} mmol). The reaction mixture was stirred at 80 °C for 16 h then analysed by GC-MS which showed full conversion to **41i**. The solvent was removed *in vacuo*, dry C_6D_6 was added, and the mixture was analysed by NMR spectroscopy. δ_H (C_6D_6, 500 MHz), 9.28 (d, *J* = 2.0 Hz, 2H, 3, 3'-*H*), 8.24 (d, *J* = 2.0 Hz, 2H, 5, 5'-*H*), 1.14 (s, 18H, C(C*H*$_3$)$_3$), 1.10 (s, 24H, pin-C*H*$_3$); δ_C (C_6D_6, 125 MHz) 159.16, 158.00, 120.63, 84.12, 34.75, 30.50, 25.01,; δ_B (C_6D_6, 128.4 MHz) 31.24. m/z (EI) 520 [M^+], 505 [M-Me]$^+$.

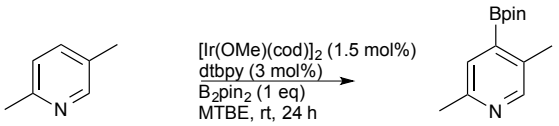
Borylation-cross-coupling of 4,4'-di-tert-butyl-2,2'-bipyridine **(40i)**: *Synthesis of 4,4'-di-tert-butyl-6,6'-diphenyl-2,2'-bipyridine* **(46)**



Borylation of *4,4'-di-tert-butyl-2,2'-bipyridine* **40i** was undertaken as described above on a 0.2 mmol scale. On complete consumption of **40i**, (GC/MS), the solvent was removed *in vacuo*, and PhI (114 mg, 0.56 mmol, 3 equiv.), K_3PO_4•$2H_2O$ (185 mg, 0.75 mmol, 4 equiv.), [(dppf)$PdCl_2$] (15 mg, 18 x 10^{-3} mmol, 10 mol%) and dry DMF (8 ml) added. The

mixture was heated at 80 °C for 5 h. The product was extracted into hexane, dried ($MgSO_4$) and concentrated. Chromatography on silica gel (hexane:diethylether, 9:1) afforded **46** (52 mg, 0.098 mmol, 67%). m.p. 182-184 °C. δ_H ($CDCl_3$, 400 MHz) 8.61 (d, *J* = 1.5 Hz, 2H, 3-*H*), 8.17 (d, *J* = 7.6 Hz, 4H, 2"-*H*), 7.78 (d, *J* = 1.5 Hz, 2H, 5, 5'-*H*), 7.53 (t, *J* = 7.6 Hz, 4H, 3"-*H*), 7.45 (t, *J* = 7.6 Hz, 2H, 4"-*H*), 1.47 (s, 18H, C(CH_3)$_3$); δ_C ($CDCl_3$, 100 MHz) 161.68, 156.57, 140.07, 128.87, 128.82, 127.26, 117.63, 117.13, 34.17, 29.76; m/z (EI) 420 [M^+], 405 [M-Me]$^+$; Anal. Calcd. for $C_{30}H_{32}N_2$: C 85.76%, H 7.67%, N 6.66%; found C 85.61%, H 7.66%, N 6.55%.;

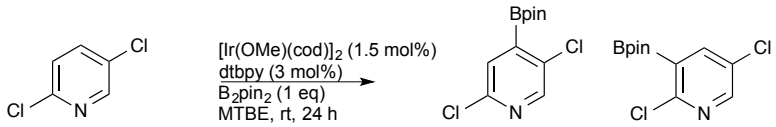
Borylation of 2,5-lutidine **(43a)**



43a 44a

General procedure B was applied to 2,5-lutidine (**43a**), on a 1 mmol scale. The reaction mixture was stirred at room temperature for 24 h giving 10% conversion (^{1}H NMR) to **44a**.

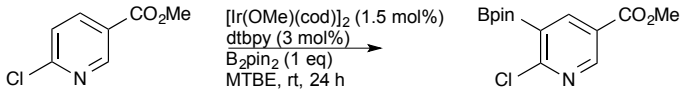
Borylation of 2,5-dichloropyridine **(43b)**



43b 44b 45b

General procedure B was applied to 2,5-dichloropyridine (**43b**), on a 1 mmol scale. The reaction mixture was stirred at room temperature for 24 h giving 93% conversion (^{1}H NMR) to **44b** and **45b** in a 84:16 ratio. GCMS analysis showed trace amounts of bis-borylated products.

Borylation of methyl 6-chloronicotinate **(43c)**; *Synthesis of methyl-5-(3-methoxyphenyl)-6-chloro-nicotinate* **(S22)**



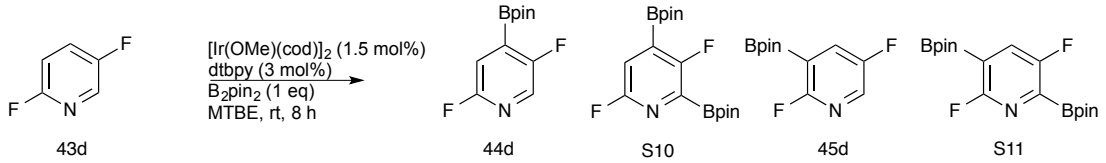
43c 45c

General procedure F was applied to Methyl-6-chloronicotinate (**43c**), on a 1 mmol scale; $Pd(dppf)Cl_2$ (0.04 g, 0.05 mmol), Cs_2CO_3 (0.65 g, 2 mmol) and 3-iodoanisole (0.26 g, 1.1 mmol). The reaction mixture was stirred at room temperature for 24 h giving 46% conversion (^{1}H NMR) to **45c**. The Suzuki-Miyaura step was carried out over 1 h. Crude material was purified by flash column chromatography 0-15% EtOAc in Heptane to give **S22** as a white solid (89 mg, 32% based on 43c).

S22

^{1}H (700 MHz, $CDCl_3$) δ 8.98 (d, J = 2.2 Hz, 1H, 2-*H*), 8.27 (d, J = 2.2 Hz, 1H, 4-*H*), 7.39 (m, 1H, 5'-*H*), 7.03 (m, 1H, 6'-*H*), 6.99 (m, 2H, 2', 4'-*H*), 3.97 (s, 3H, CO_2CH_3), 3.86 (s, 3H, $COCH_3$); ^{13}C (176 MHz, $CDCl_3$) δ 165.2 (CO_2Me), 159.7 (3'-*C*), 153.9 (6-*C*), 149.6 (2-*C*), 140.5 (4-*C*), 137.9 (1'-*C*), 136.9 (5-*C*), 129.8 (5'-*C*), 125.4 (3-*C*), 121.7 (6'-*C*), 115.1 (Ar*C*), 114.4 (Ar*C*), 55.5 ($COCH_3$), 52.8 (CO_2CH_3) δ; ν_{max} (neat) 1728, 1590, 1394, 1316, 1265, 1228, 1129, 1036,907; Accurate Mass (ASAP) m/z found $[M+H]^+$ 277.0506 ($C_{14}H_{12}{}^{35}ClNO_3$) requires *M* 277.0497.

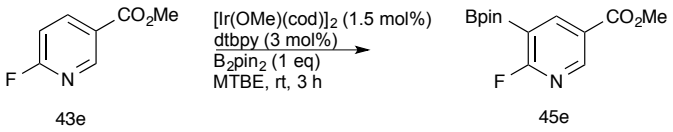
Borylation of 2,5-difluoropyridine **(43d)**



43d 44d S10 45d S11

General procedure B was applied to 2,5-difluoropyridine (**43d**), on a 1 mmol scale. The reaction mixture was stirred at room temperature for 8 h giving full conversion (^{1}H NMR) to afford mono and bis borylated products **44d**:**S23**:**45d**:**S24** in a ratio of 72:3:19:6.

Borylation of methyl 6-fluoronicotinate **(43e)**: Synthesis of *methyl 3-(Bpin)-2-fluoronicotinate **(45e)***



43e 45e

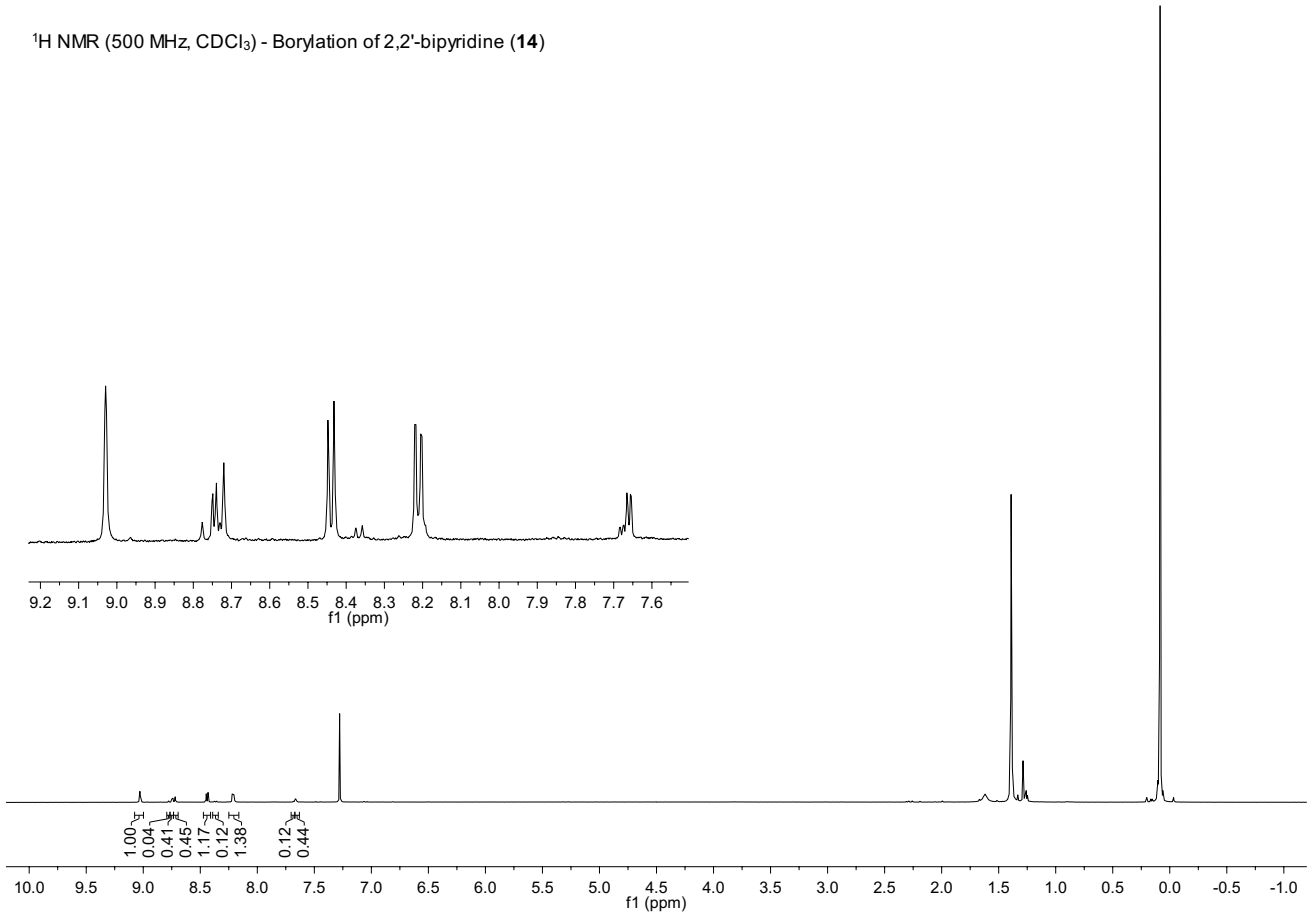
General procedure B was applied to methyl 6-fluoronicotinate (**43e**), on a 0.7 mmol scale. The reaction mixture was stirred at room temperature for 3 h giving full conversion (^{1}H NMR) to **45e**. Following concentration *in vacuo* and absorption onto silica, purification by flash column chromatography (0-10% MeOH in DCM) afforded **45e** (141 mg, 77%) as a white solid. ν_{max} (ATR) 1722, 1604, 1578, 1444, 1421, 1393, 1392, 1390, 1349, 1336, 1260, 1215, 1188, 1171, 1145, 1123, 1079 cm^{-1}. δ_H (600 MHz, $CDCl_3$) 8.91 (d, J = 2.5 Hz, 1H, 6-*H*), 8.74 (dd, J = 7.9, 2.5 Hz, 1H, 4-*H*), 3.93 (s, 3H, $CO_2C\mathit{H}_3$), 1.36 (s, 12H, pin-CH_3); δ_C (151 MHz, $CDCl_3$) 169.1 (d, J = 251 Hz, *C*-F), 164.9 ($\mathit{C}O_2CH_3$), 153.1 (d, J = 17 Hz, 6-*C*), 150.0 (d, J = 9 Hz, 4-*C*), 124.2 (d, J = 5 Hz, 5-*C*), 84.9 (pin$\mathit{C}(CH_3)_2$), 52.5, ($CO_2\mathit{C}H_3$), 24.9 (pin-$\mathit{C}H_3$); δ_B (128 MHz, $CDCl_3$) 29.7; δ_F (564 MHz, $CDCl_3$) -52.2. m/z (EI) 281 $[MH]^+$, 266 $[M\text{-}CH_3]$, 250 $[M\text{-}OCH_3]^+$, 238, 222 $[M\text{-}CO_2CH_3]^+$, 208, 197, 182, 150; HRMS (ASAP) found $[M+H]^+$ 281.1349 ($C_{13}H_{18}{}^{10}BNO_4F$) requires *M* 281.1340.

Tandem borylation/Suzuki-Miyaura cross coupling/reductive dechlorination reaction of 2-chloroisonicotinate **(40c)**: *Synthesis of methyl 2-(4'-methoxyphenyl)isonicotinate* **(48)**

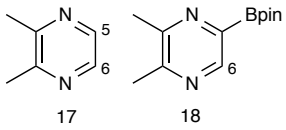
General procedure D was applied to **40c** on a 2 mmol scale using 4-iodoanisole (0.94 g, 4 mmol, 4equiv.) as the cross-coupling partner. ^{1}H NMR analysis after C-H borylation step showed 73% conversion to **41c**. Without purification, the crude cross-coupling reaction product was dissolved in ethanol (20 mL) and ammonium formate (40 mmol, 20equiv.) was added. The reaction vessel was evacuated and backfilled with nitrogen (x 3 cycles) before 10% Pd/C was slowly added under a positive pressure of nitrogen. The reaction was stirred at room temperature for 2 h then filtered through a plug of celite and absorbed onto silica. Purification by flash column chromatography (0-20 % ethyl acetate in hexane) afford **48** as a white solid (0.23 g, 47%) (yield based on 40c). ν_{max} (ATR) 1730, 1607, 1580, 1557, 1516, 1467, 1436, 1421, 1390, 1301, 1274, 1249, 1176, 1111, 1060, 1031 cm^{-1}. δ_H (700 MHz, $CDCl_3$) 8.76 (1H, m, 2-*H*), 8.21 (1H, s, 5-*H*), 8.00 (2H, m, 2', 6'-*H*), 7.68 (1H, dd, J = 6.8, 2.1, 3-*H*), 6.99 (2H, m, 3', 5'-*H*), 3.96 (3H, s, CO_2CH_3), 3.85 (3H, s, OCH_3); δ_C (176 MHz, $CDCl_3$) 166.0 (CO_2Me), 161.0 (4'-*C*), 158.2 (6-*C*), 150.4 (2-*C*), 138.1 (4-*C*), 131.2 (1'-*C*), 128.4 (2C, 2',6'-*C*), 120.4 (3-*C*), 119.0 (5-*C*), 114.3 (2C, 3',5'-*C*), 55.5 (OCH_3), 52.8 (CO_2CH_3). HRMS (ASAP) found $[M+H]^+$ 244.0974, $C_{14}H_{14}NO_3$ requires *M* 244.0957.

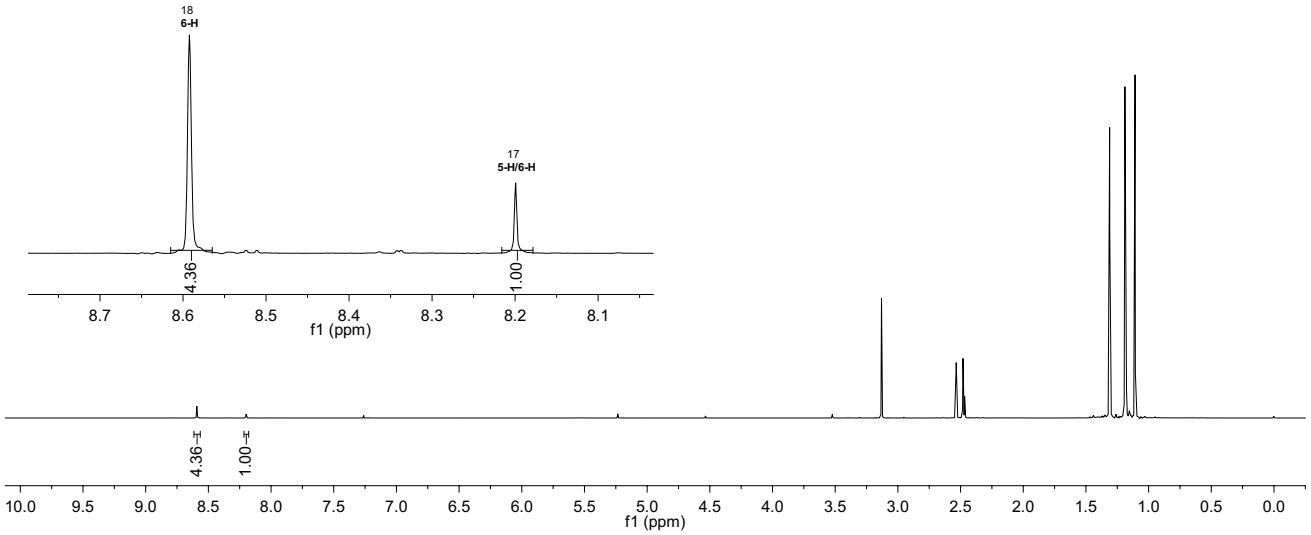
^{1}H, ^{13}C, ^{11}B, ^{19}F NMR Spectra

^{1}H NMR (500 MHz, $CDCl_3$) - Borylation of 2,2'-bipyridine (**14**)

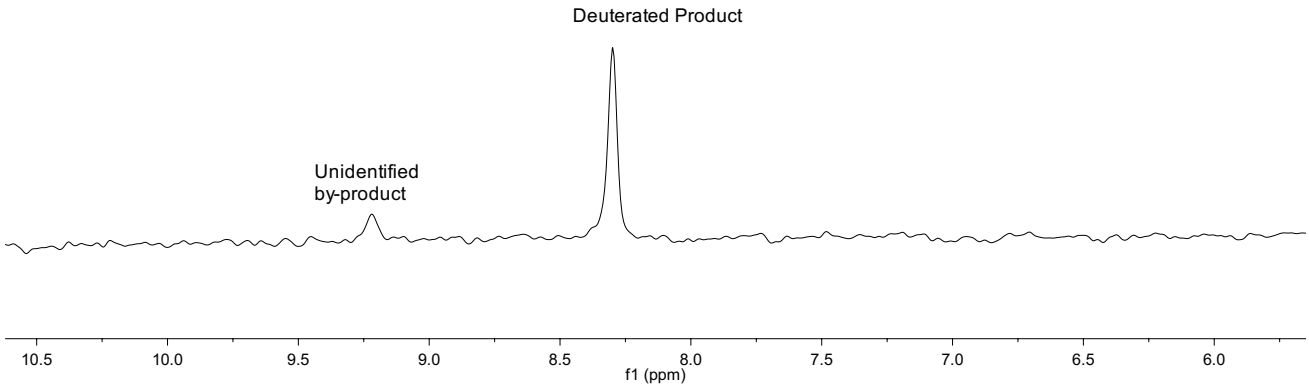


^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2,3-dimethylpyrazine (**17**)

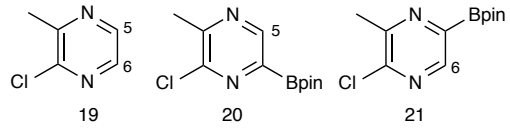


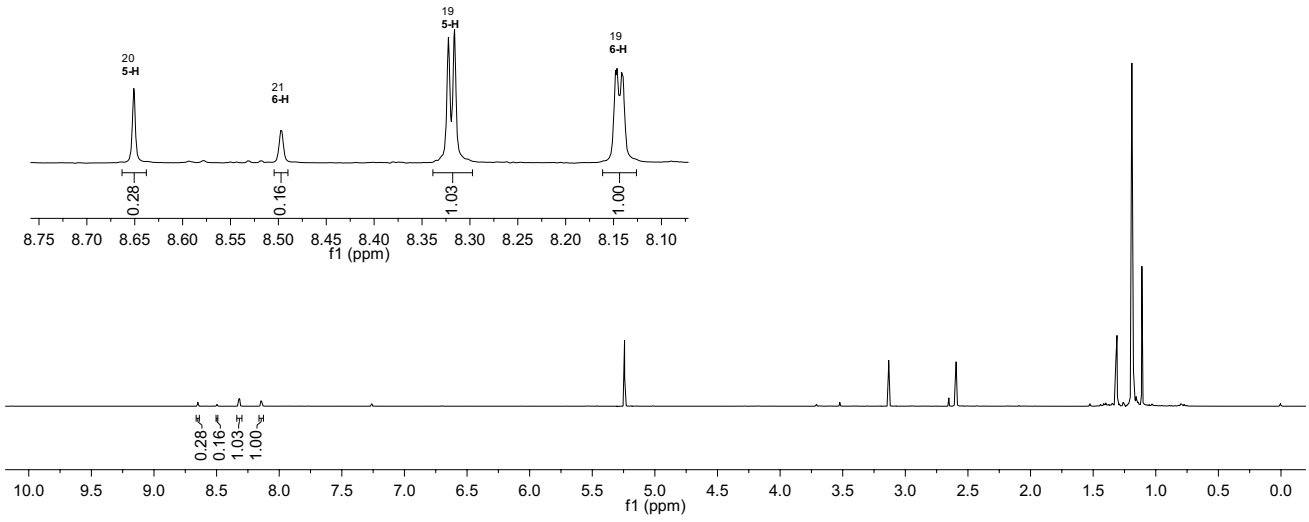


^{2}H NMR (92.1 MHz $(CD_3)_2CO$) - Deuteration of 2,3-dimethylpyrazine (**17**)

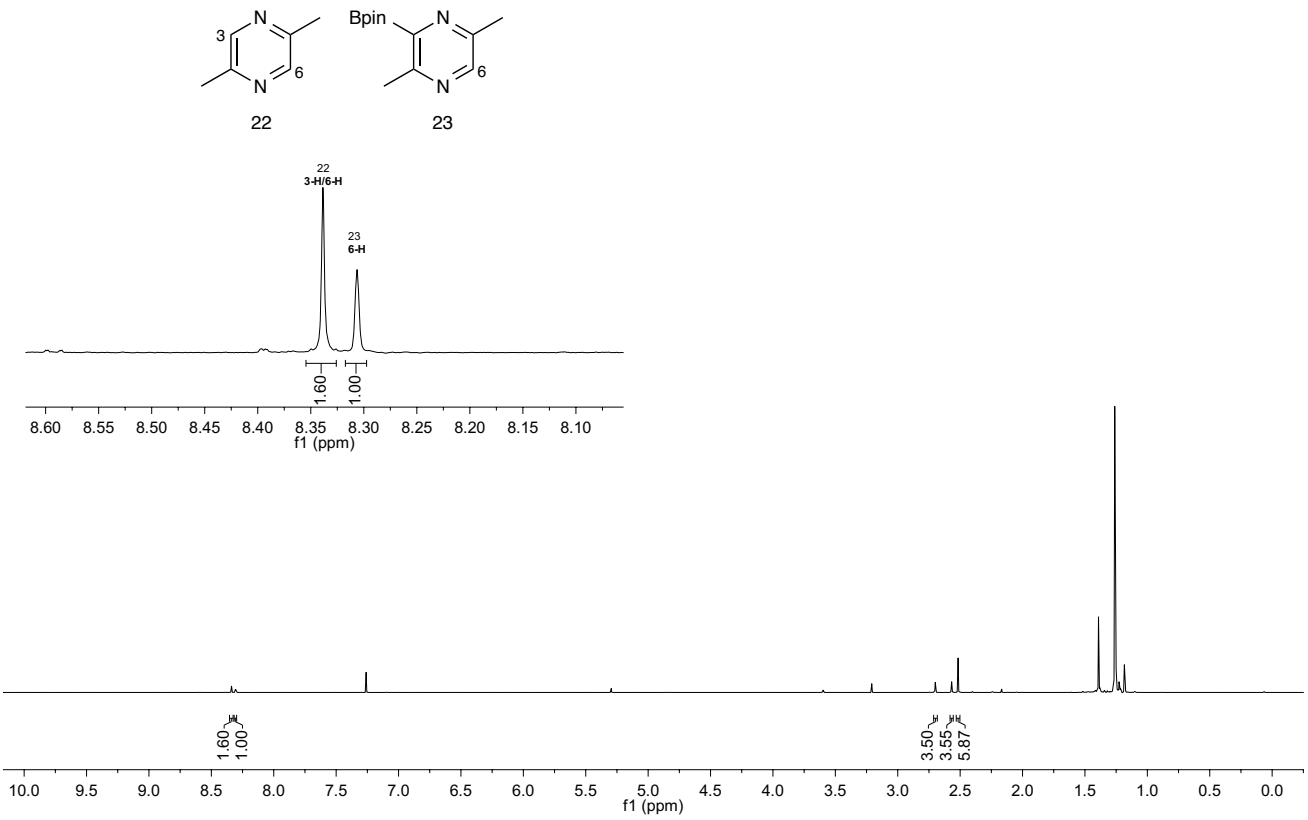


^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2-chloro-3-methylpyrazine (**19**)

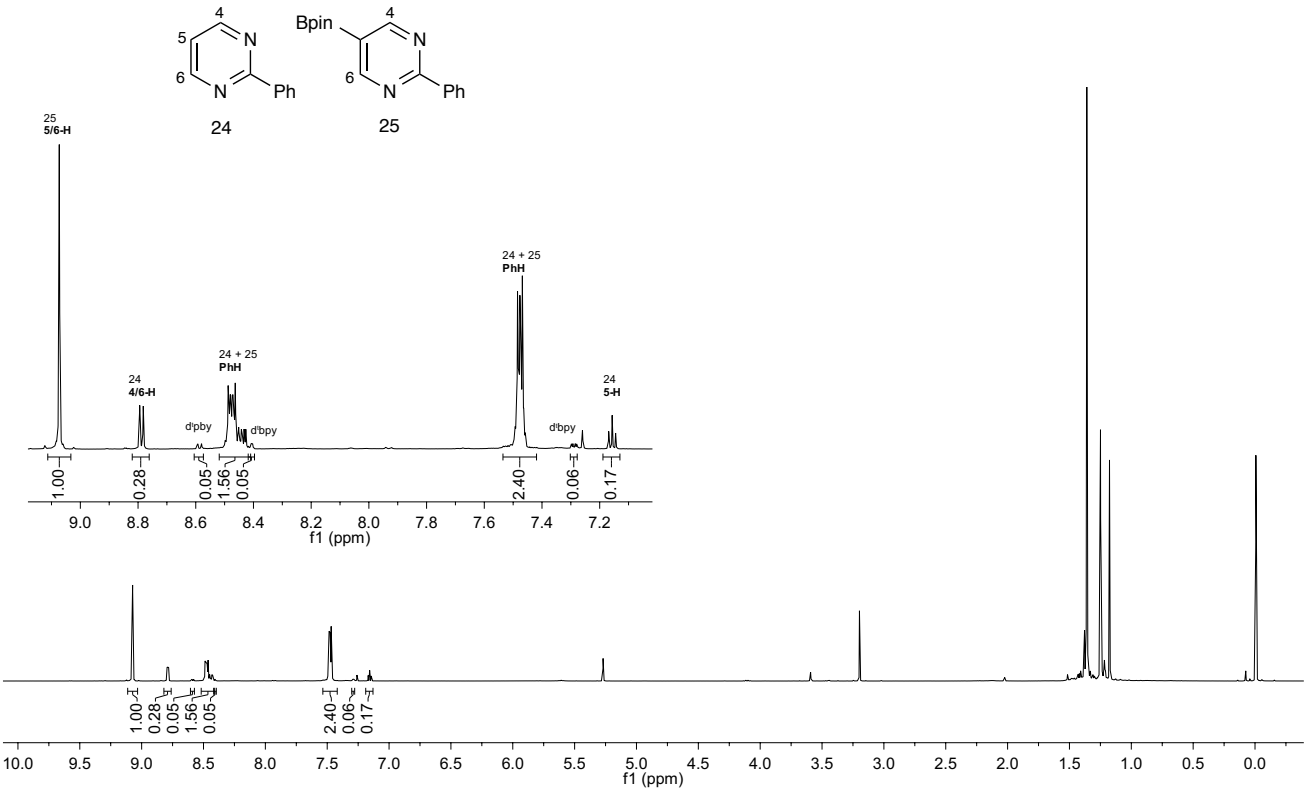




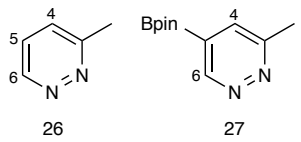
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2,5-dimethylpyrazine (**22**)



^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2-phenylpyrimidine (**24**)

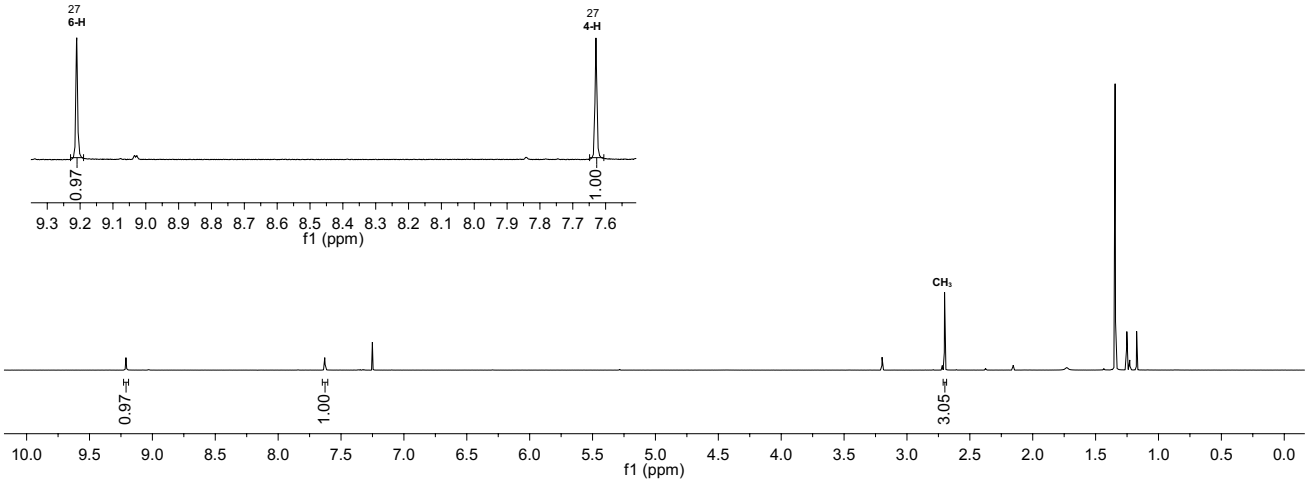


^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 3-methypyridazine (**26**)

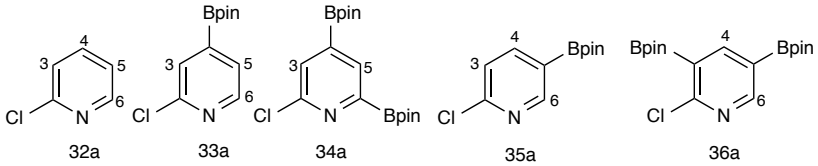


26

27



^{1}H NMR (600 MHz, $CDCl_3$) - Borylation of 2-chloropyridine (**32a**)



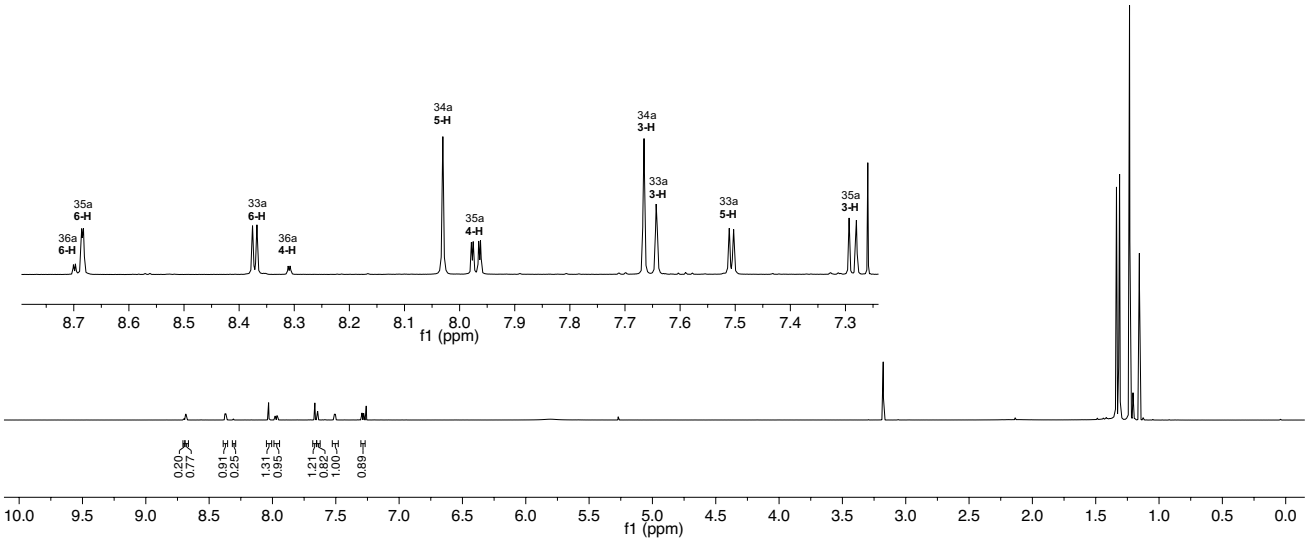
32a

33a

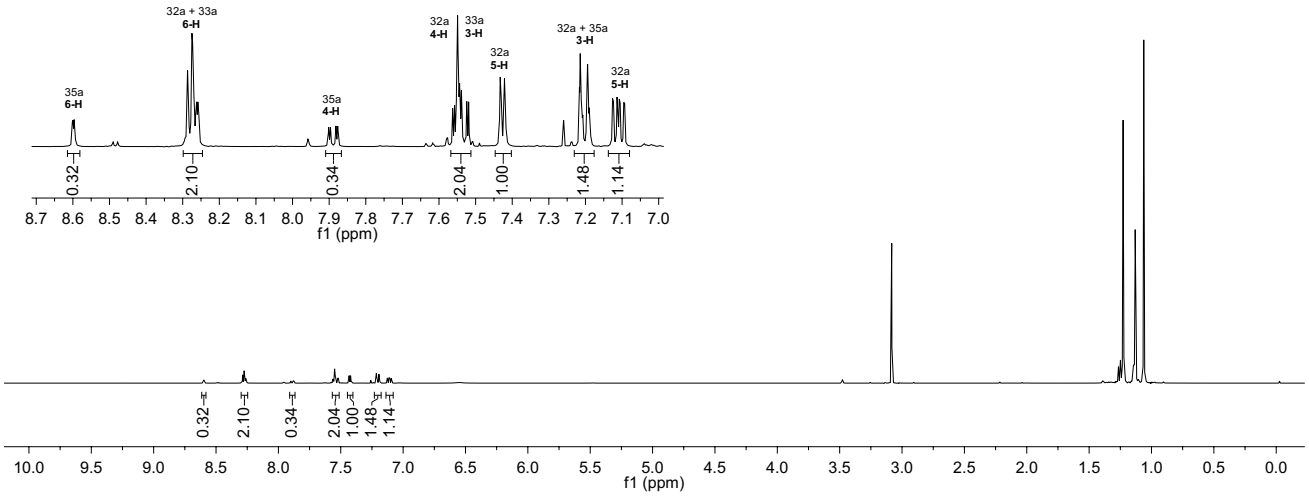
34a

35a

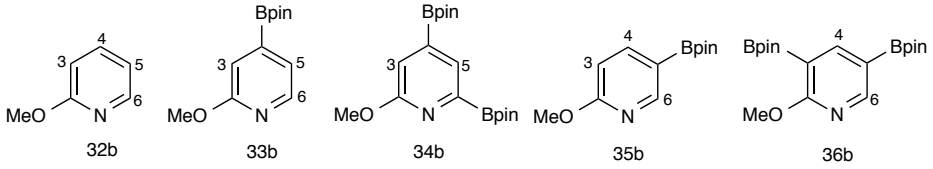
36a

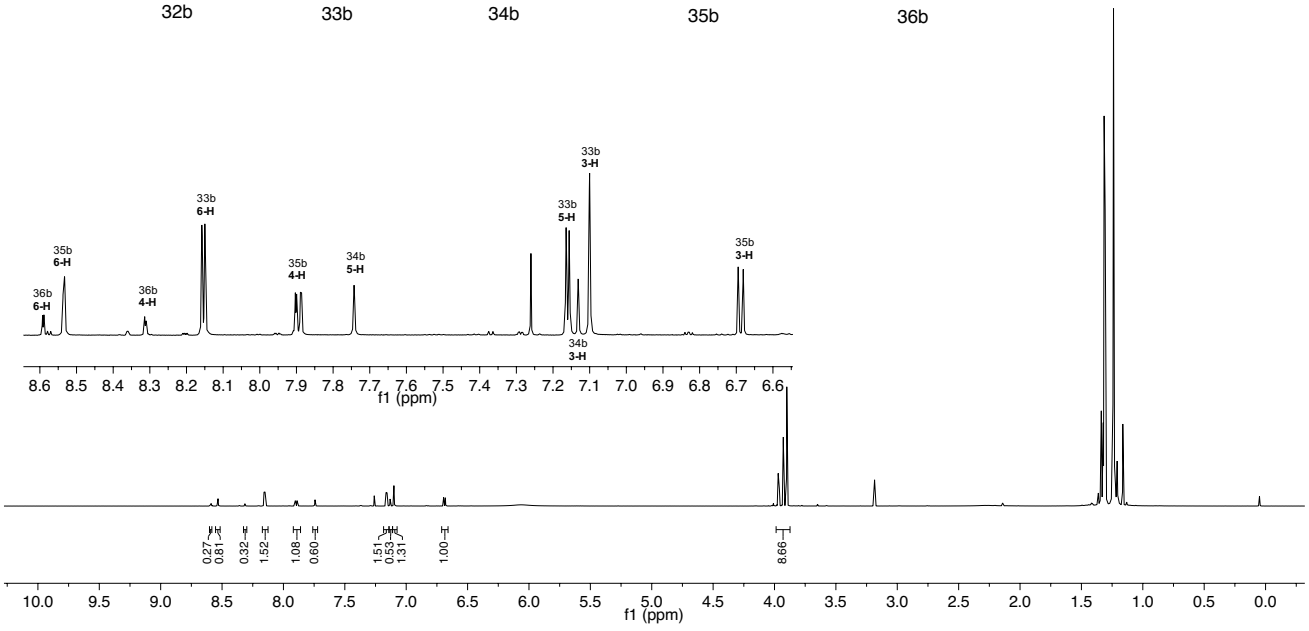


^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2-chloropyridine (**32a**)
Boron-limiting conditions

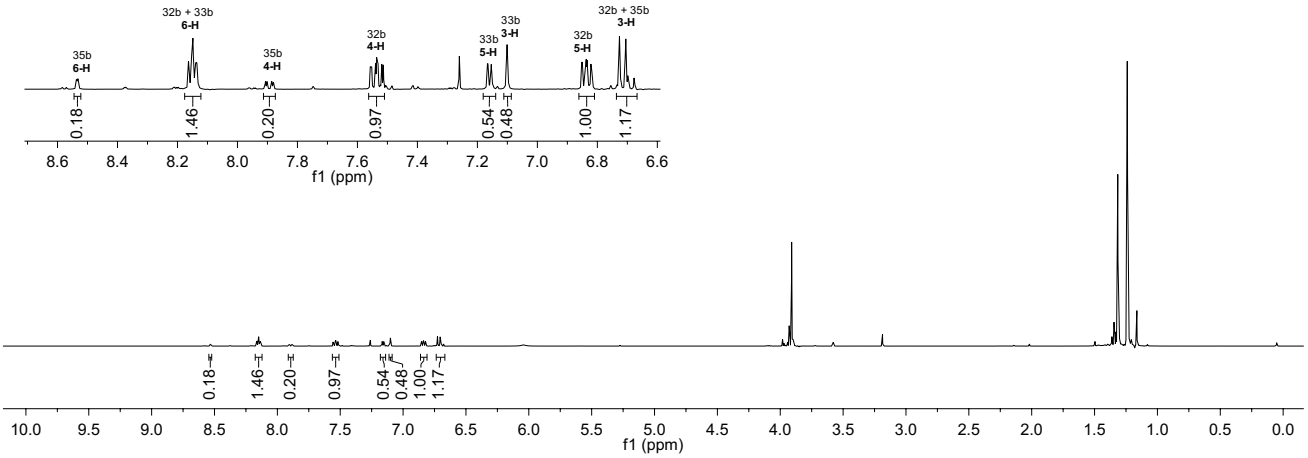


^{1}H NMR (600 MHz, $CDCl_3$) - Borylation of 2-methoxypyridine (**32b**)

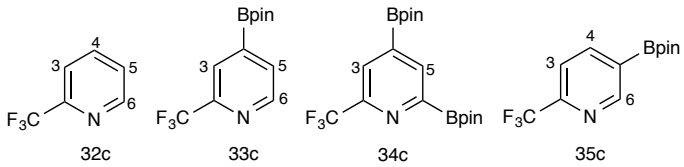




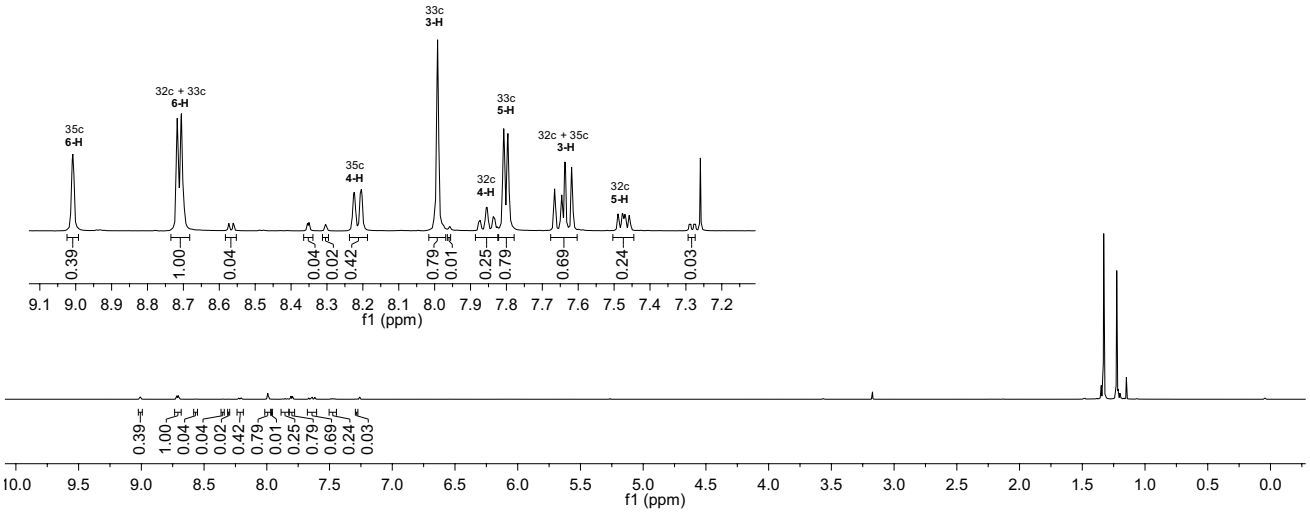
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2-methoxypyridine (**32b**)
(Boron-limiting conditions)



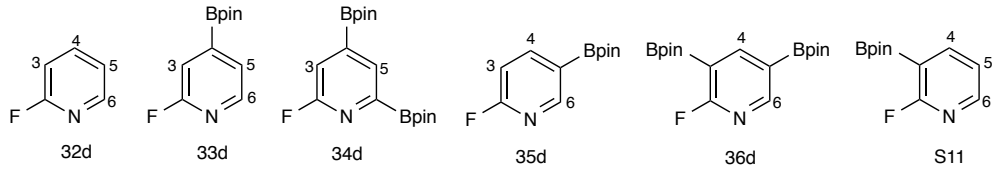
^{1}H NMR (600 MHz, $CDCl_3$) - Borylation of 2-(trifluoromethyl)pyridine (**32c**)

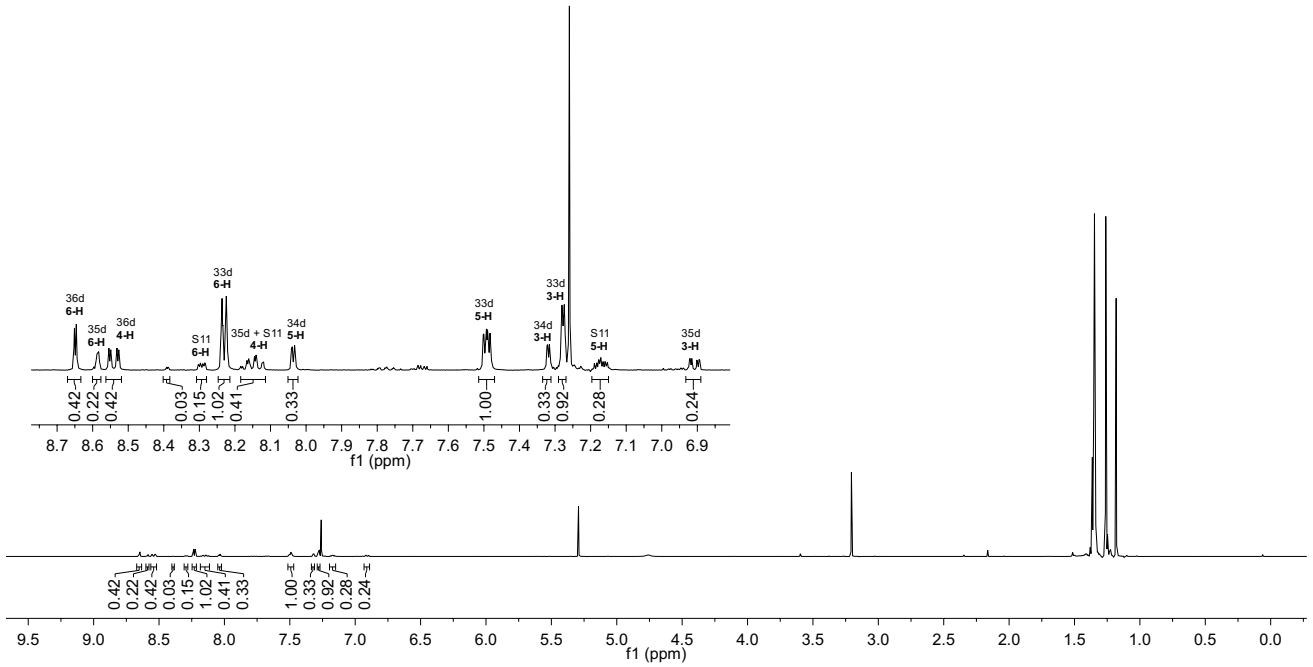


^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2-(trifluoromethyl)pyridine (**32c**)
(Boron-limiting conditions)

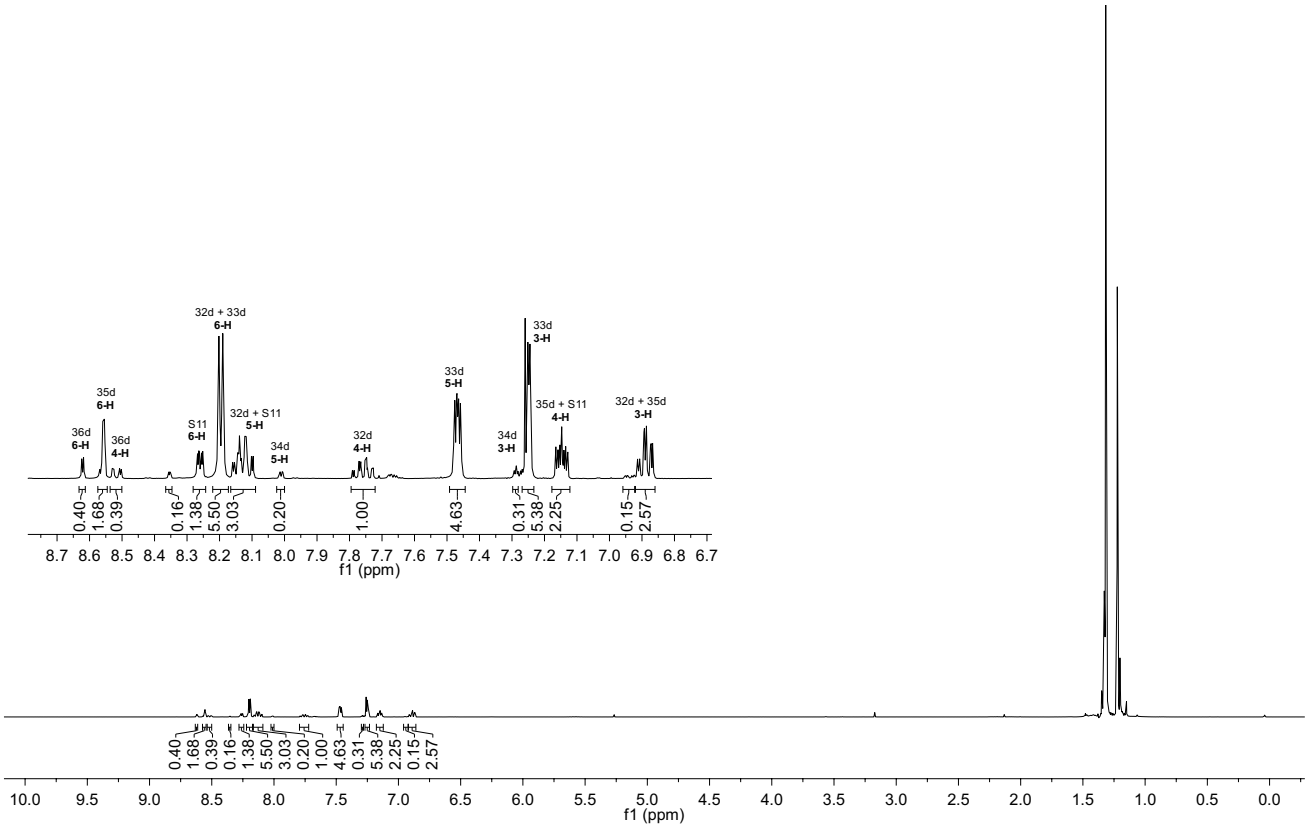


^{1}H NMR (400 MHz, $CDCl_3$)- Borylation of 2-fluoropyridine **(32d)**

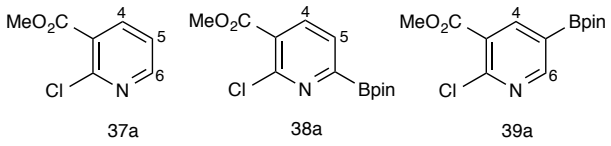


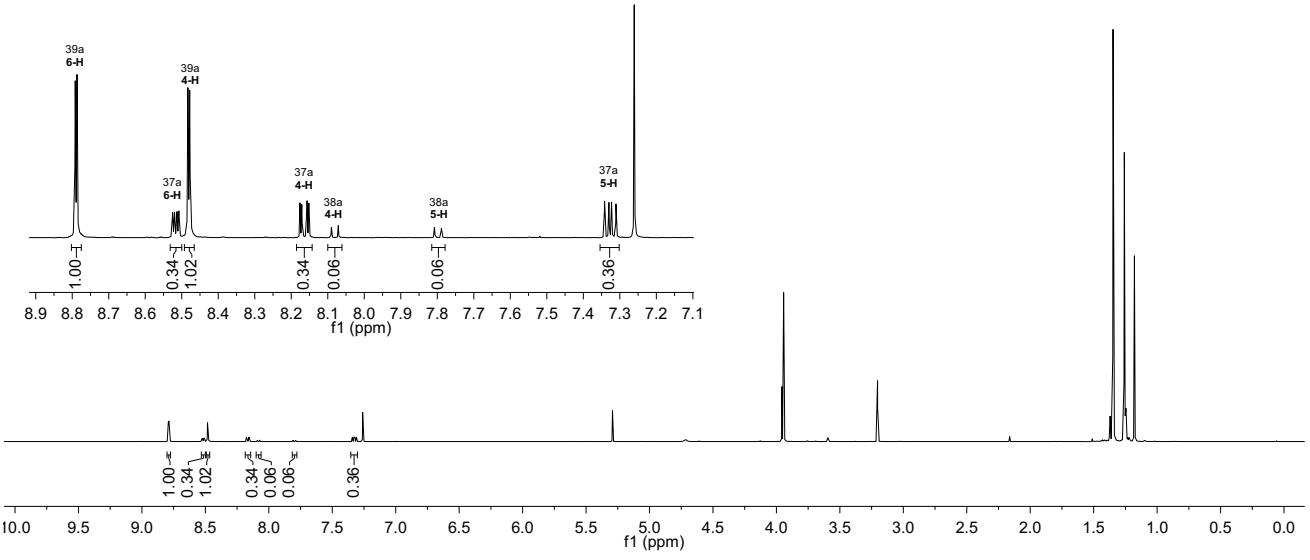


^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2-fluoropyridine (**32d**)
Boron-limiting conditions

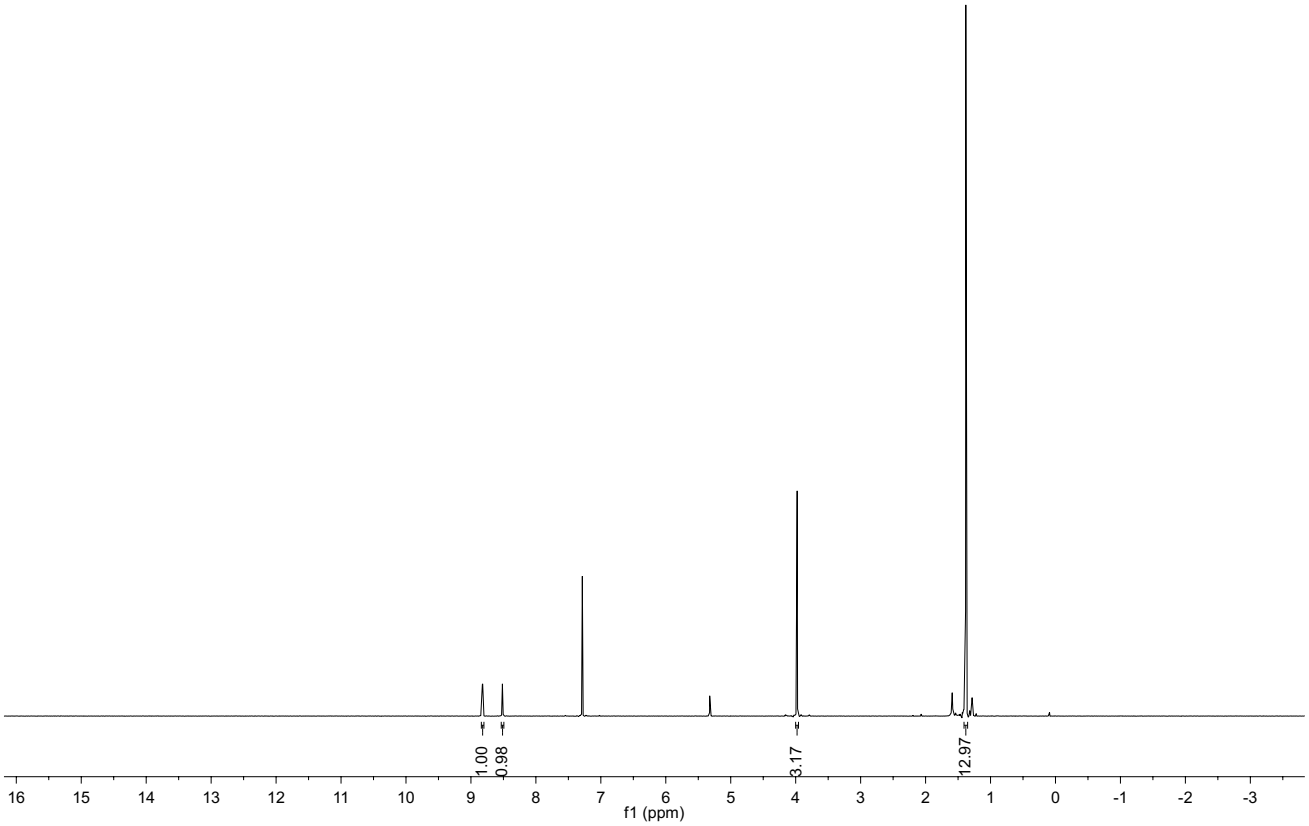


^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of methyl-2-chloronicotinate (**37a**)

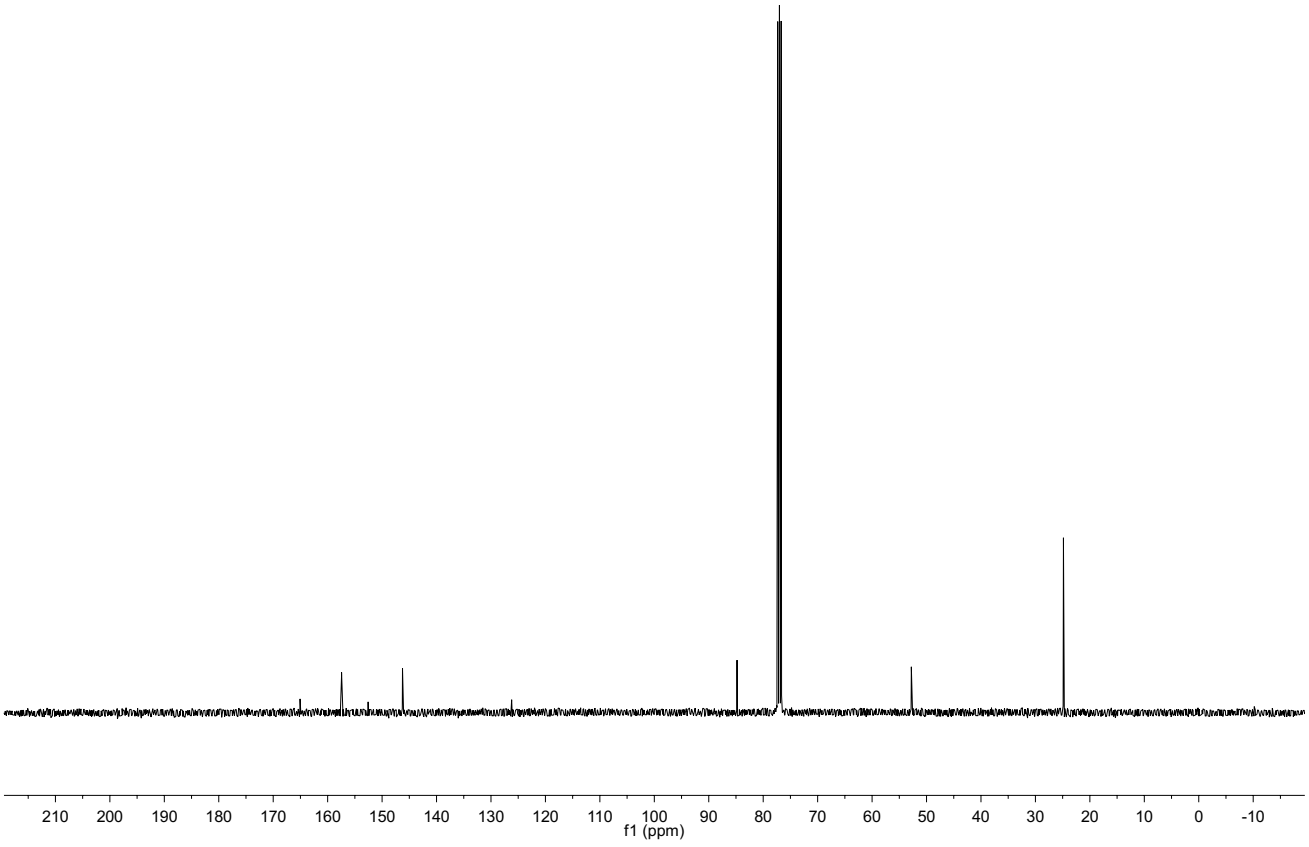




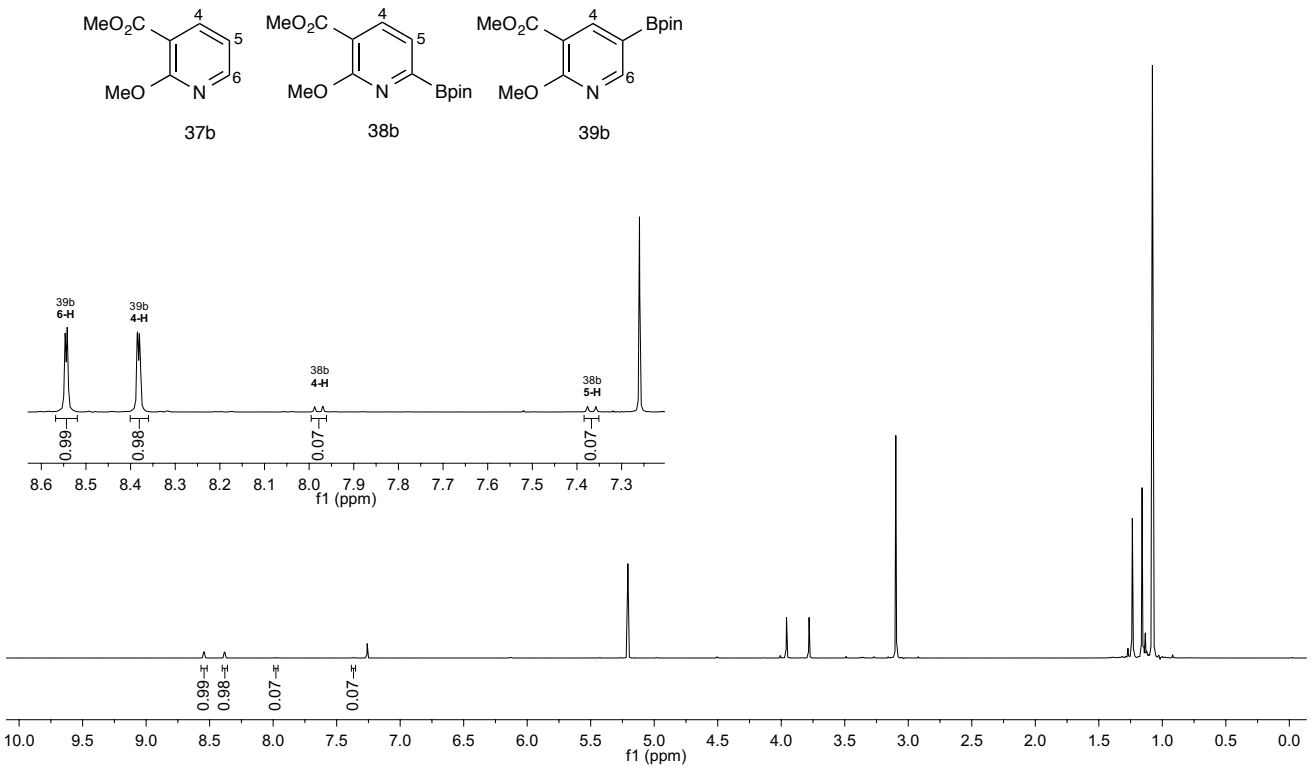
^{1}H NMR (400 MHz, $CDCl_3$) **39a**



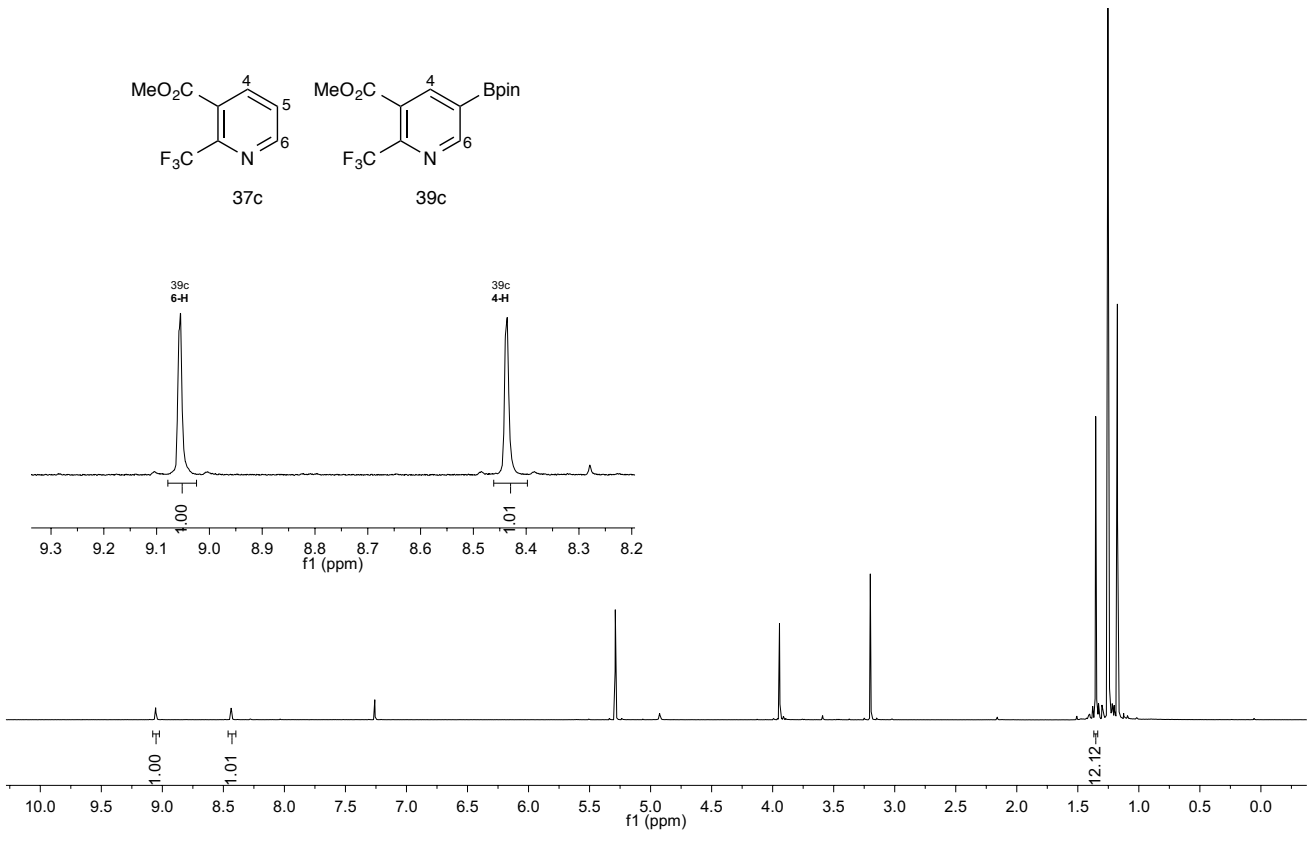
^{13}C NMR (101 MHz, $CDCl_3$) - **39a**



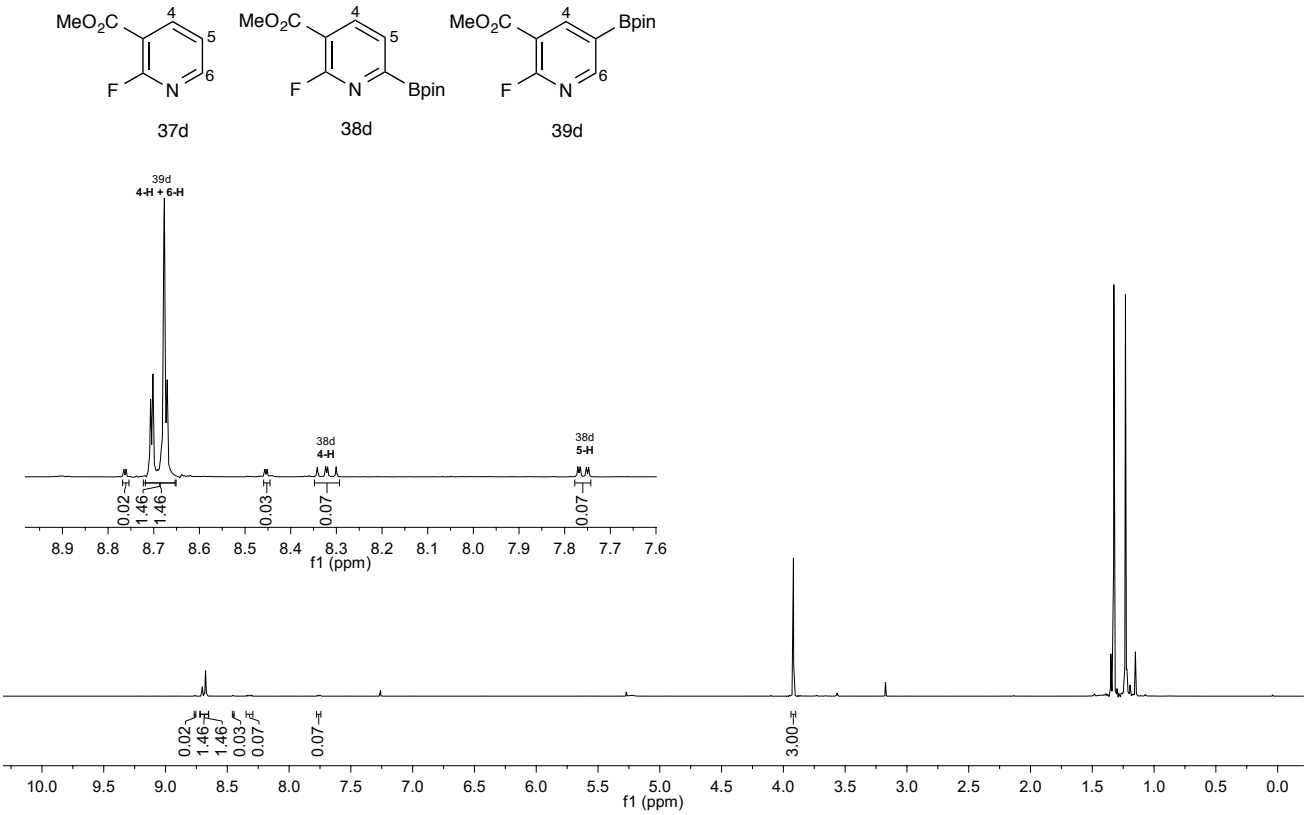
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of methyl-2-methoxynicotinate (**37b**)



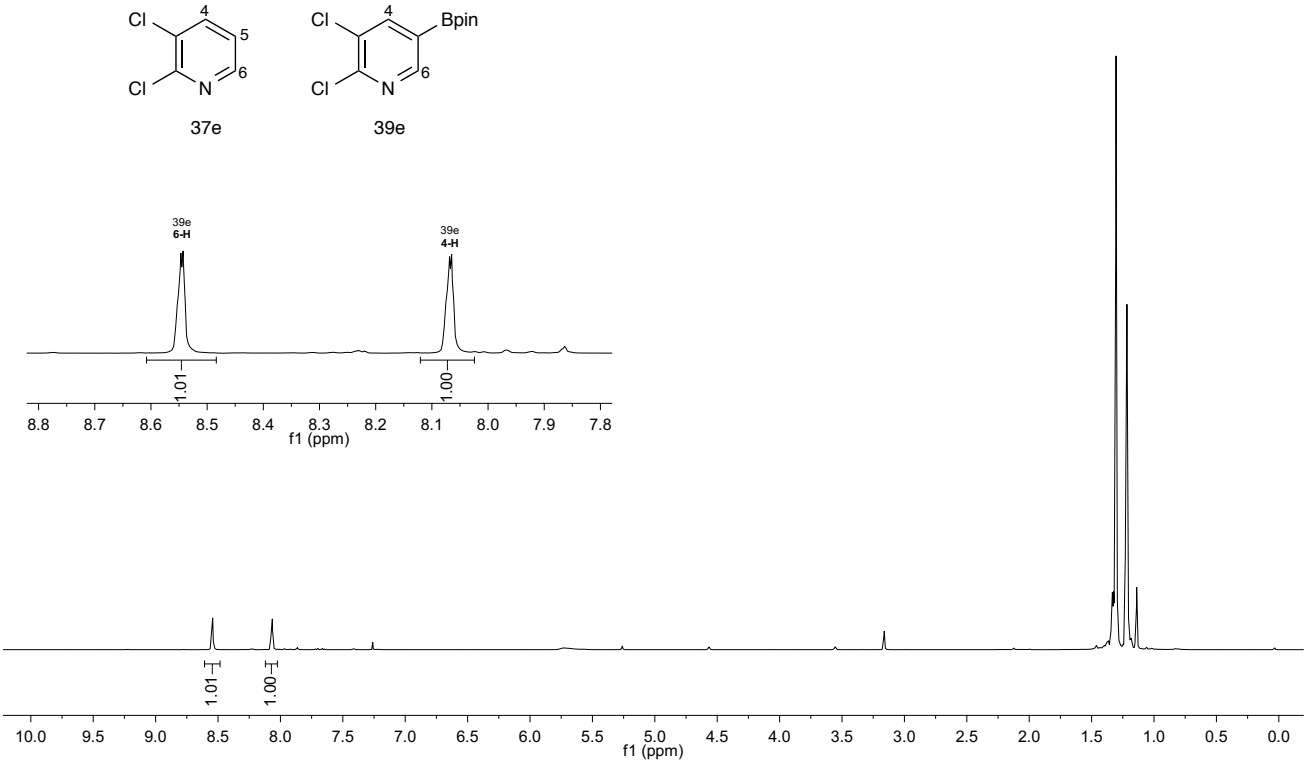
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of methyl-2-(trifluoromethyl)nicotinate (**37c**)



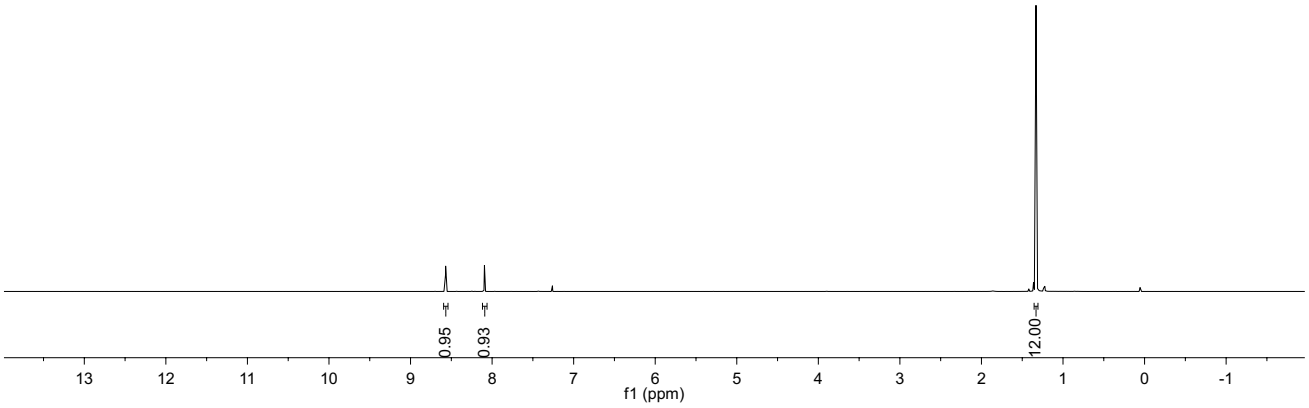
^{1}H NMR (400MHz, $CDCl_3$) - Borylation of methyl-2-fluoronicotinate **(37d)**



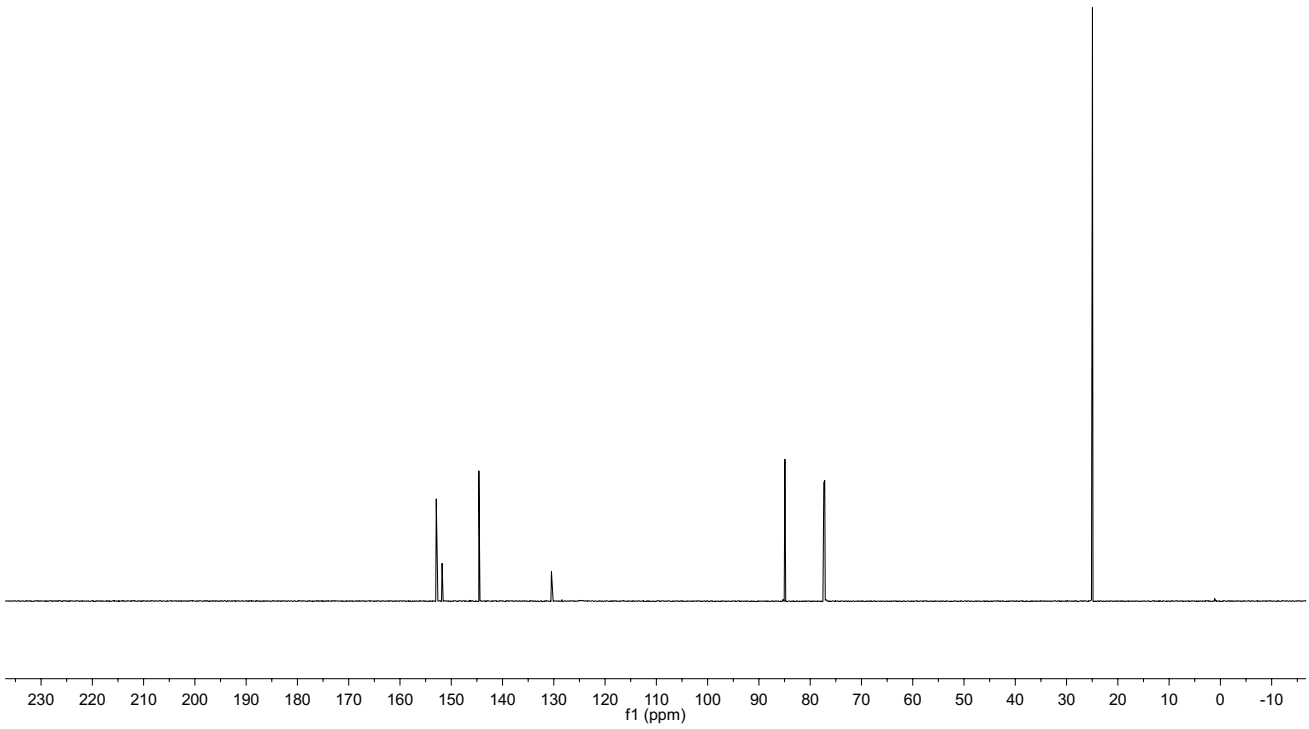
^{1}H NMR (400MHz, $CDCl_3$) - Borylation of 2,3-dichloropyridine (**37e**)



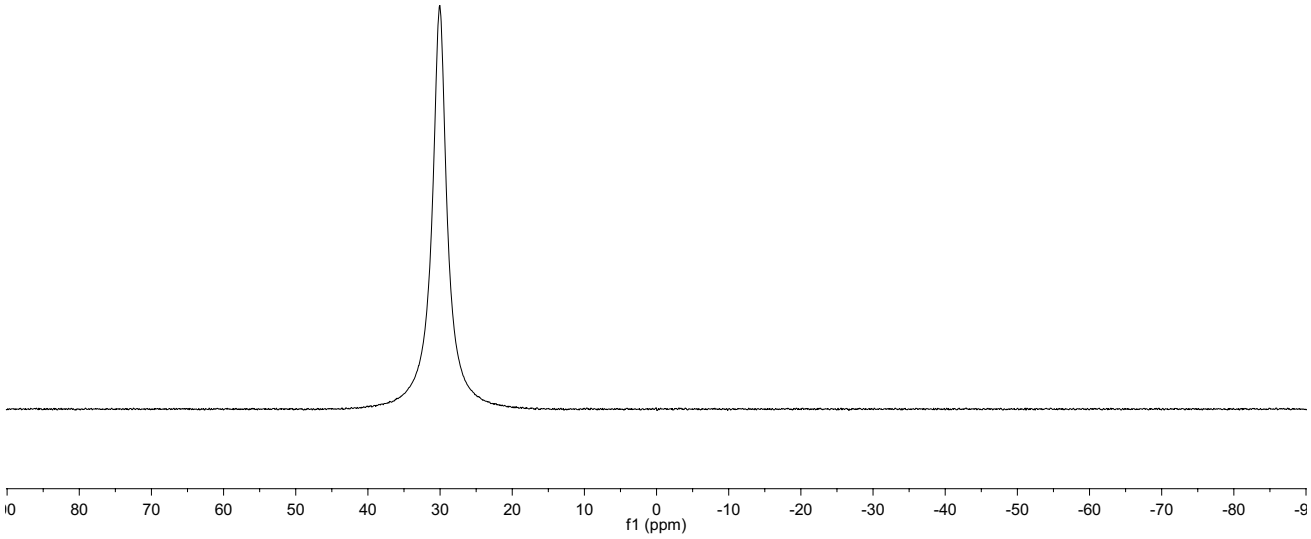
^{1}H NMR (700 MHz, $CDCl_3$) - 2,3-dichloro-5-(Bpin)pyridine (**39e**)



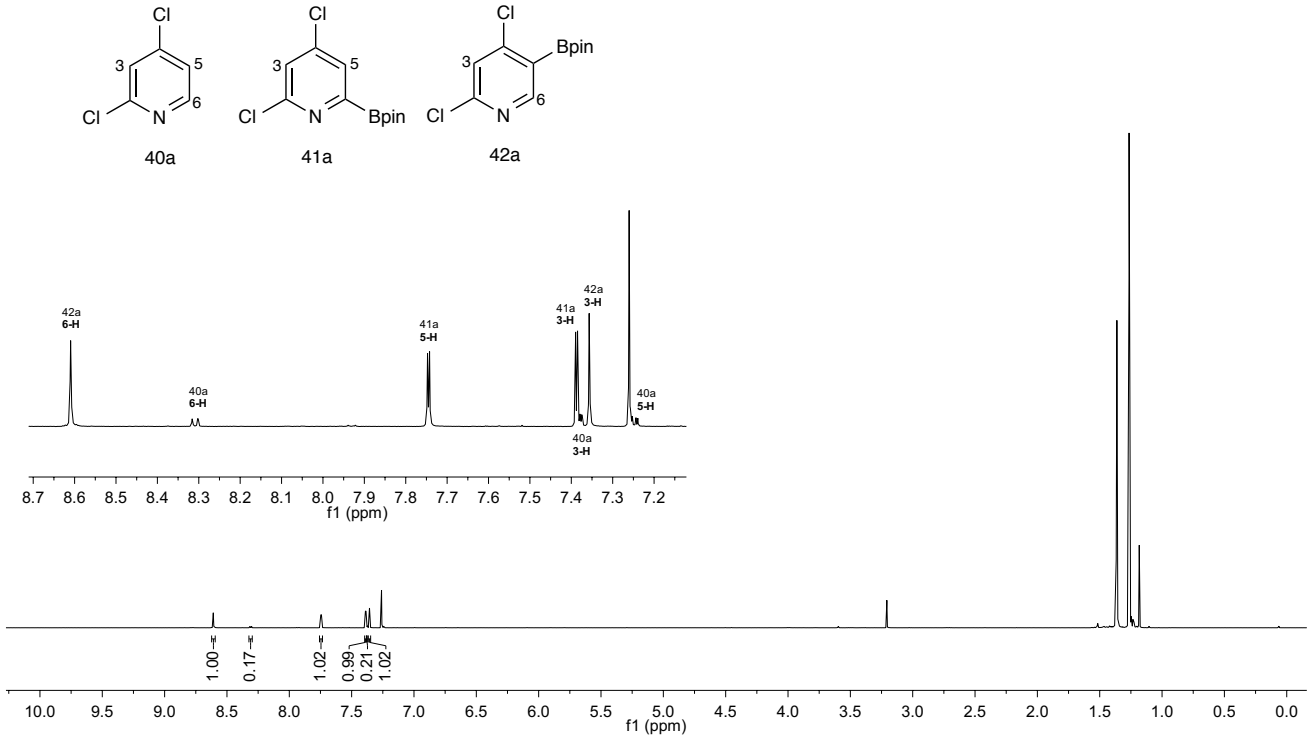
^{13}C NMR (176 MHz, $CDCl_3$) - 2,3-dichloro-5-(Bpin)pyridine (**39e**)



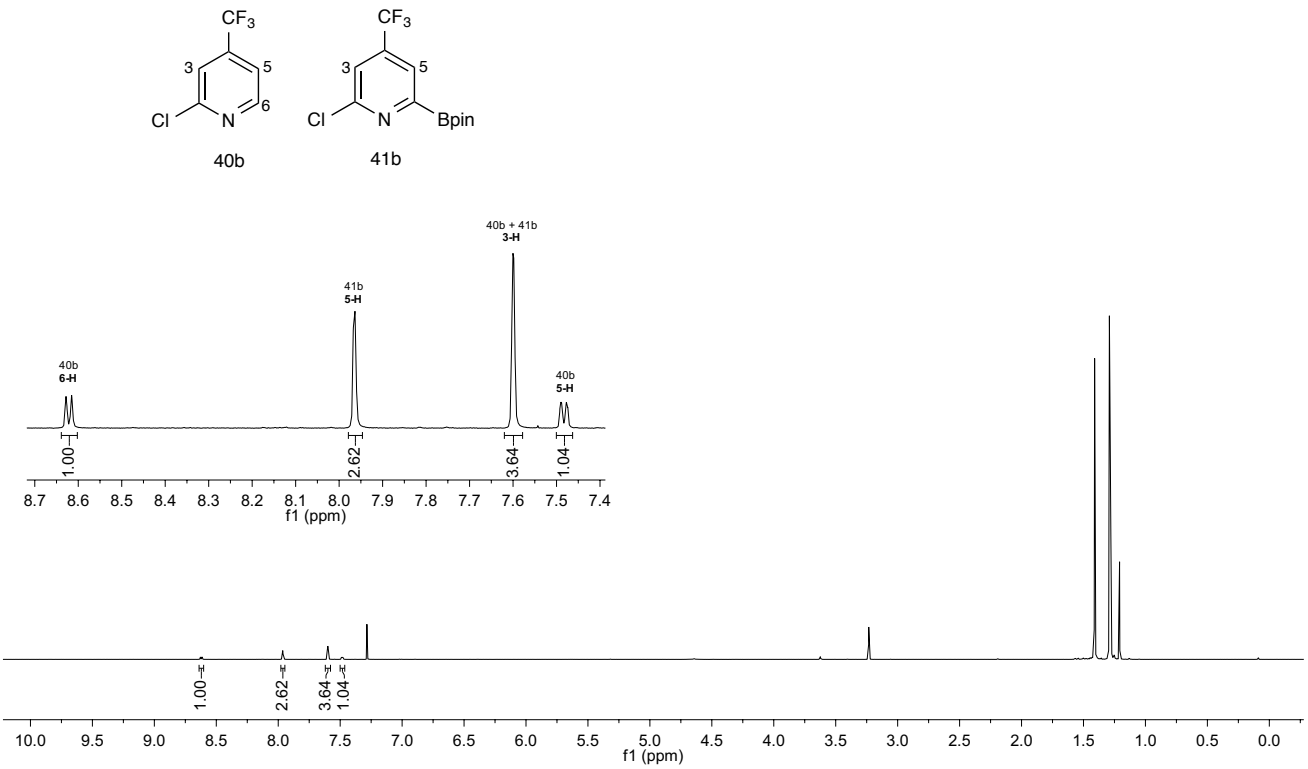
^{11}B NMR (128 MHz, $CDCl_3$) - 2,3-dichloro-5-(Bpin)-pyridine (**39e**)



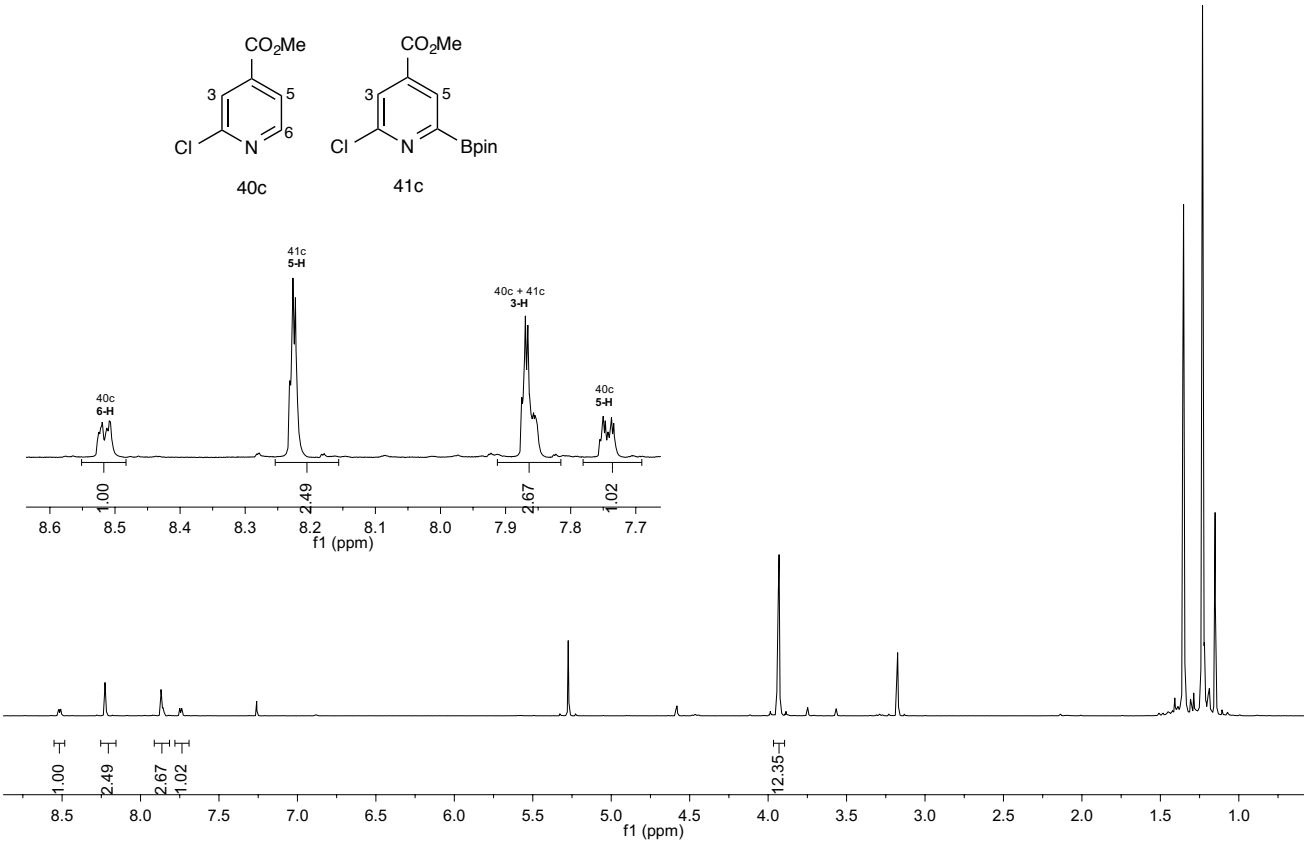
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2,4-dichloropyridine (**40a**)



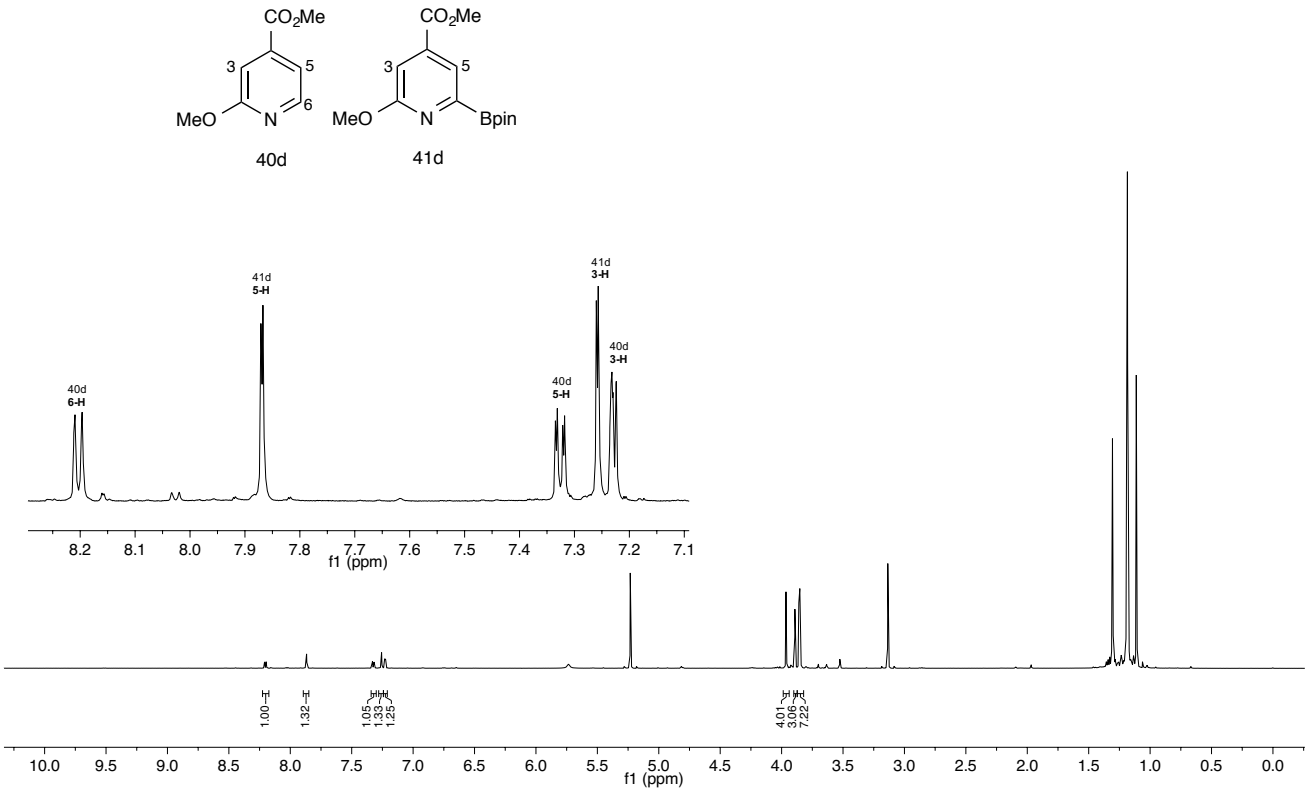
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2-chloro-4-(trifluoromethyl)pyridine (**40b**)



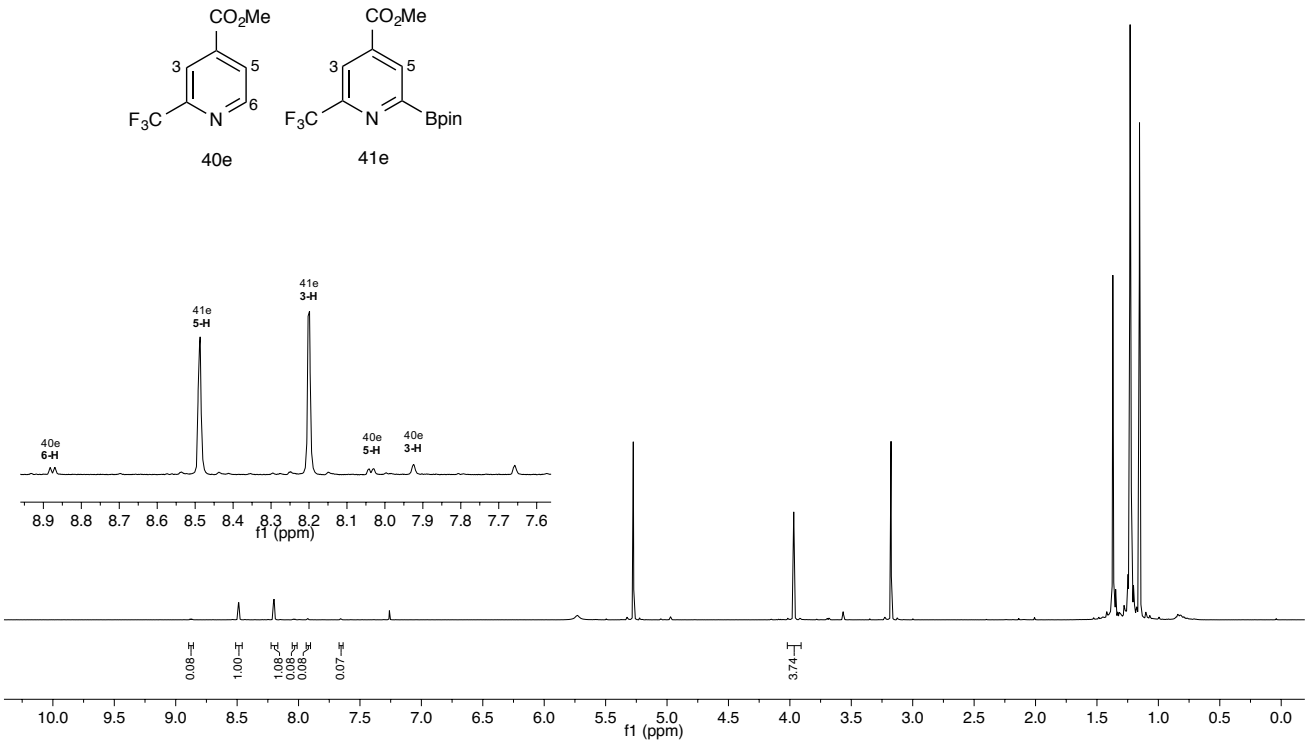
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of methyl-2-chloroisonicotinate (40c)



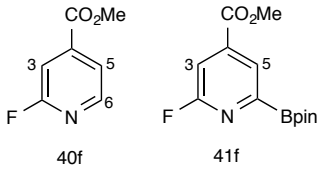
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of methyl-2-methoxyisonicotinate (**40d**)



^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of methyl-2-(trifluoromethyl)isonicotinate (**40e**)

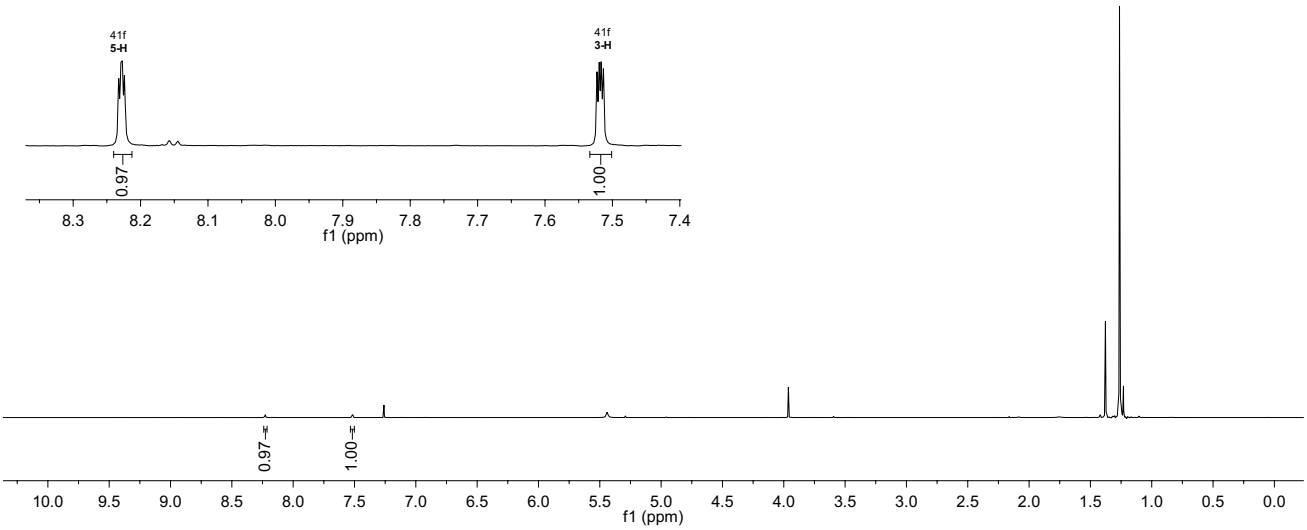


^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of methyl-2-fluoroisonicotinate (**40f**)

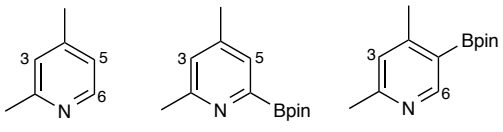


40f

41f



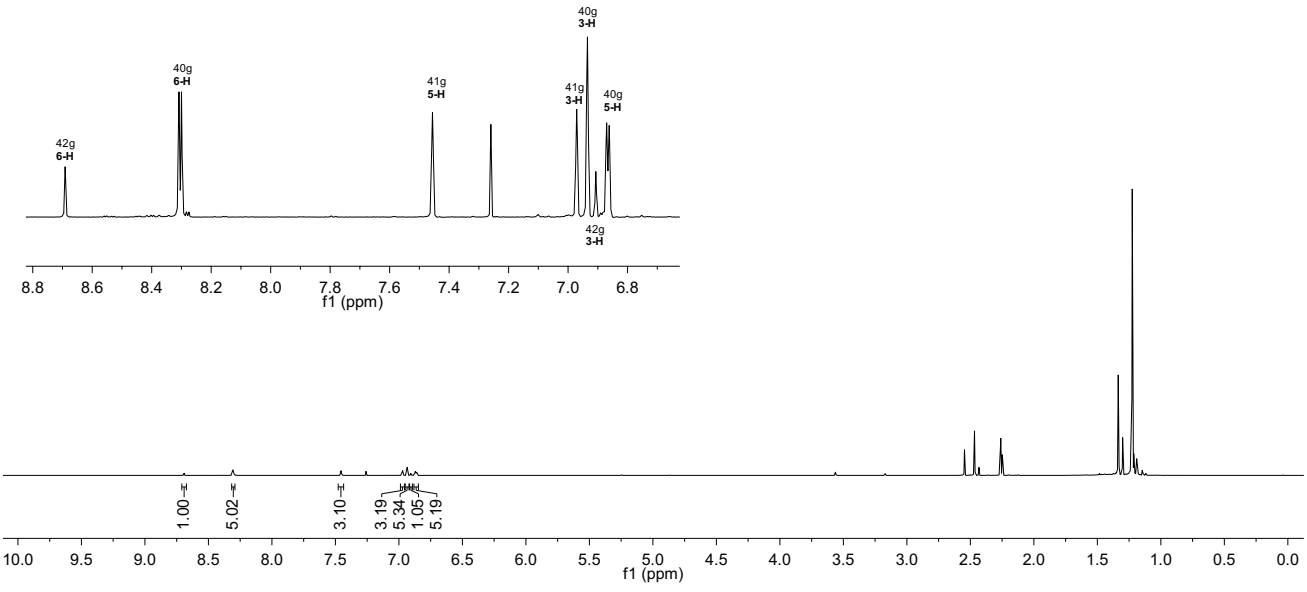
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2,4-lutidine (**40g**)



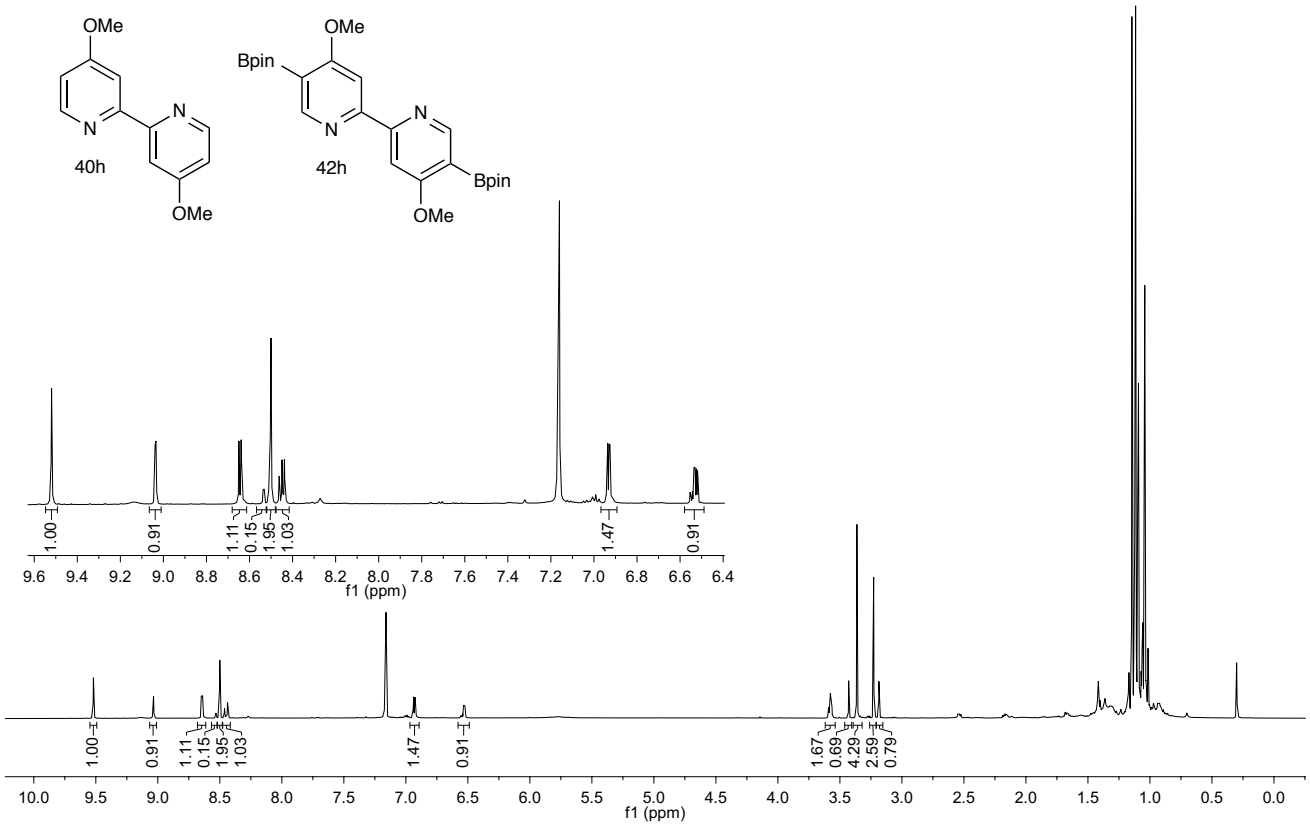
40g

41g

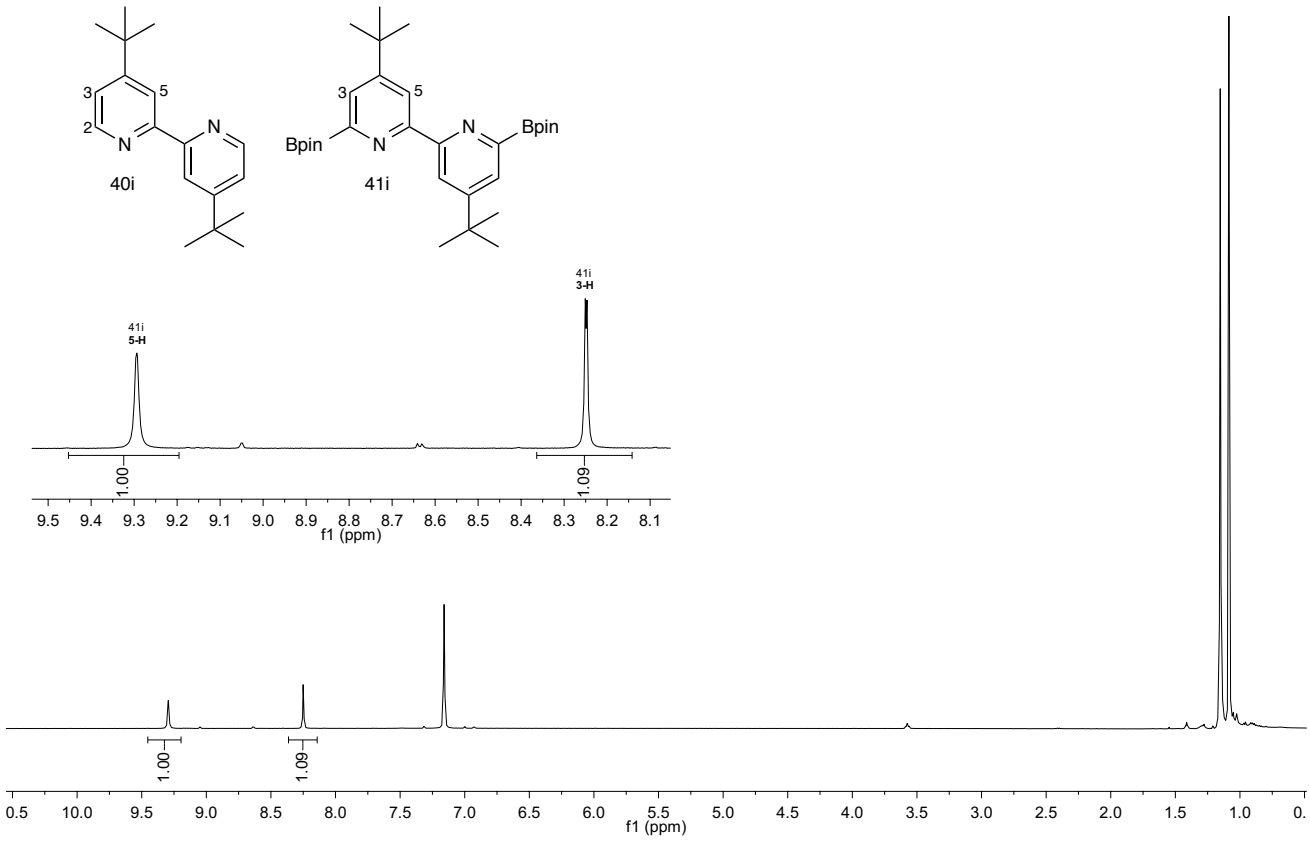
42g



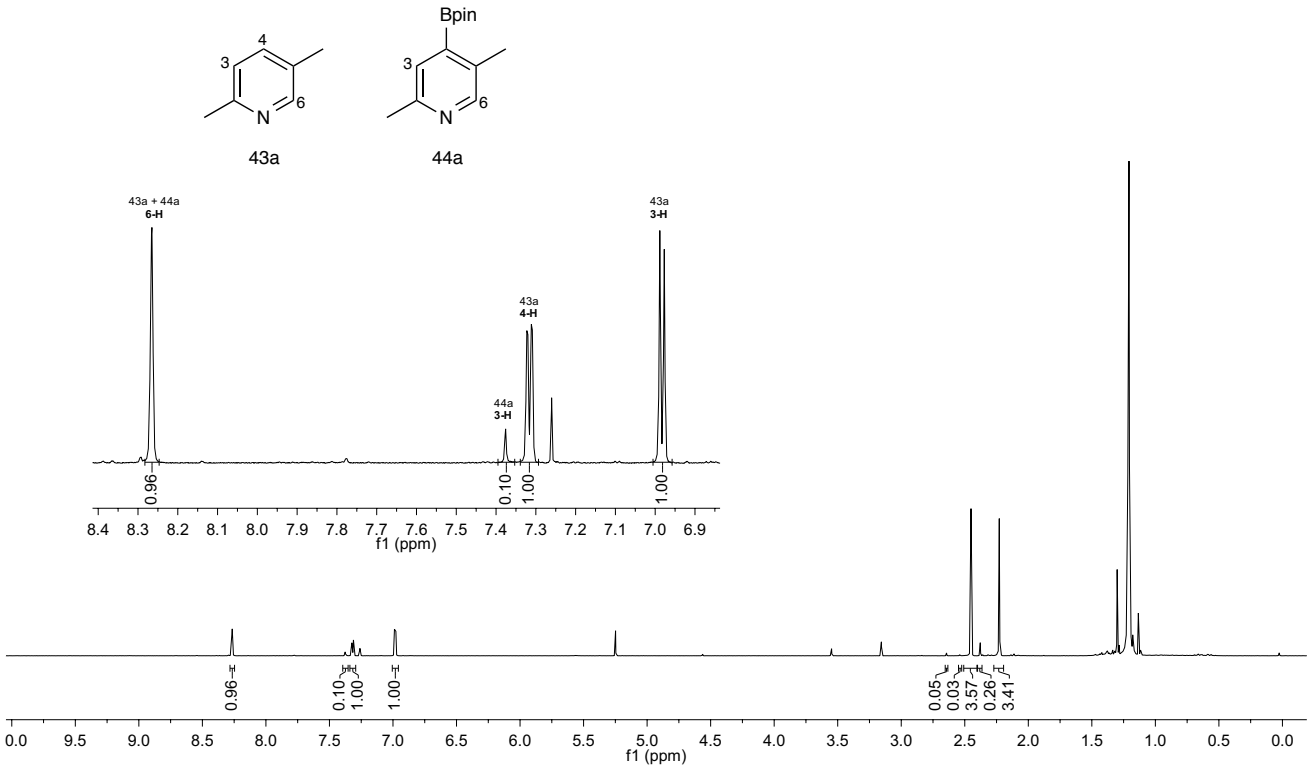
^{1}H NMR (500 MHz, C_6D_6) - Borylation of 4,4'-dimethoxy-2,2'-bipyridine (**40h**)



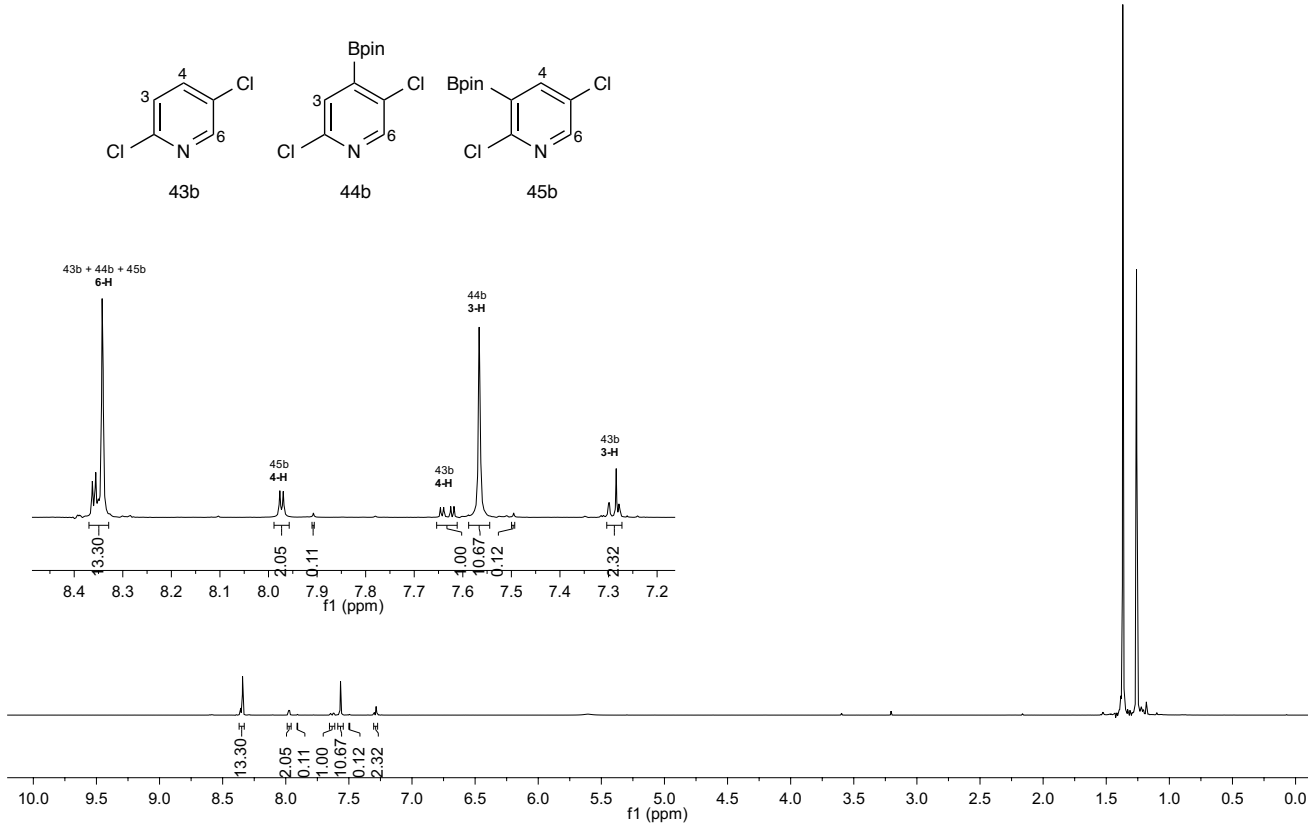
^{1}H NMR (500 MHz, C_6D_6) - Borylation 4,4'-di-tertbutyl-2,2'-bipyridine (**40i**)



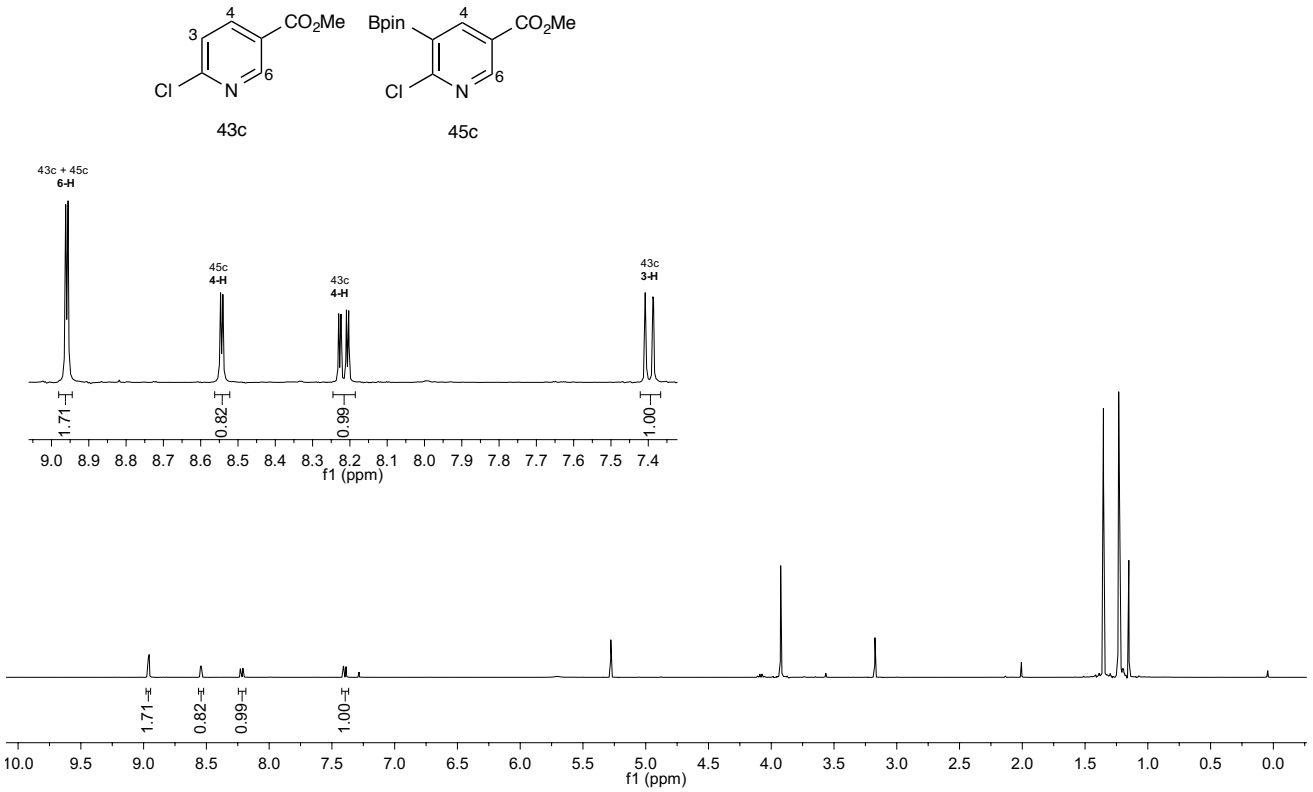
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2,5-lutidine (**43a**)



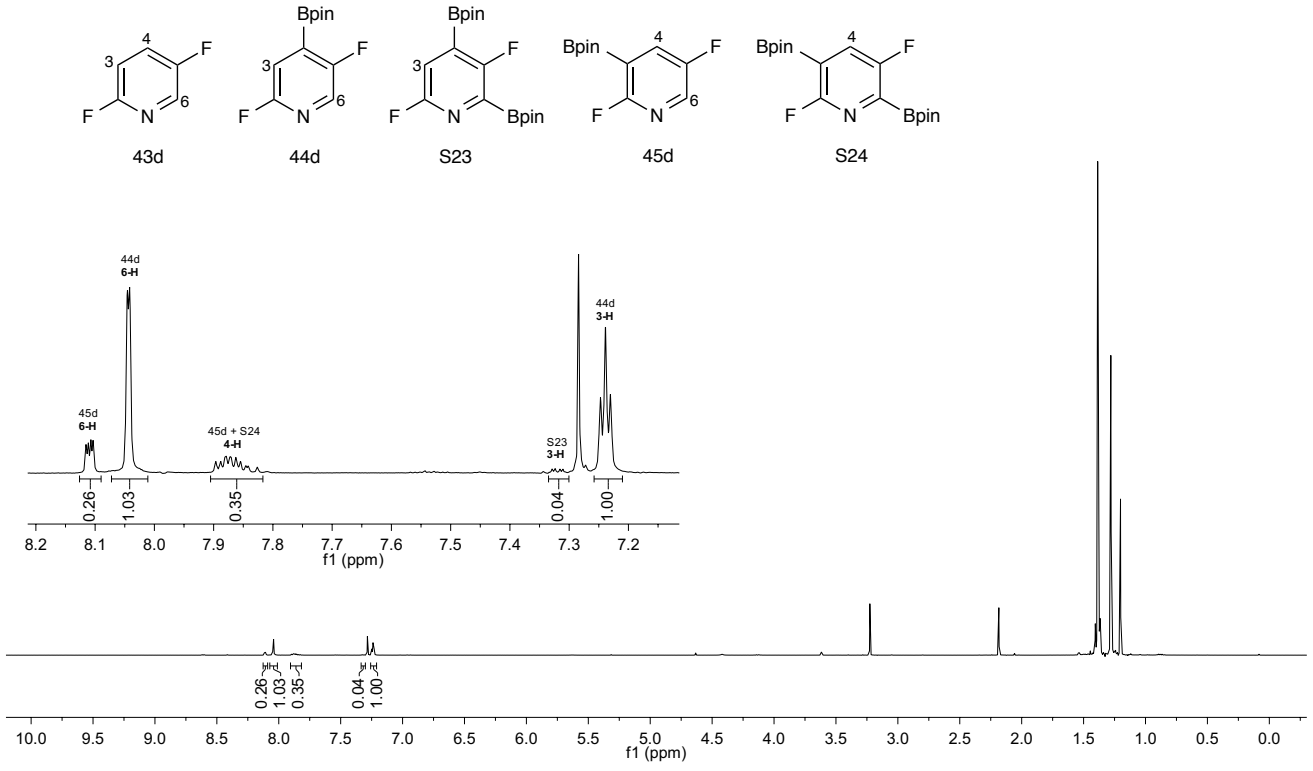
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2,5-dichloropyridine (**43b**)



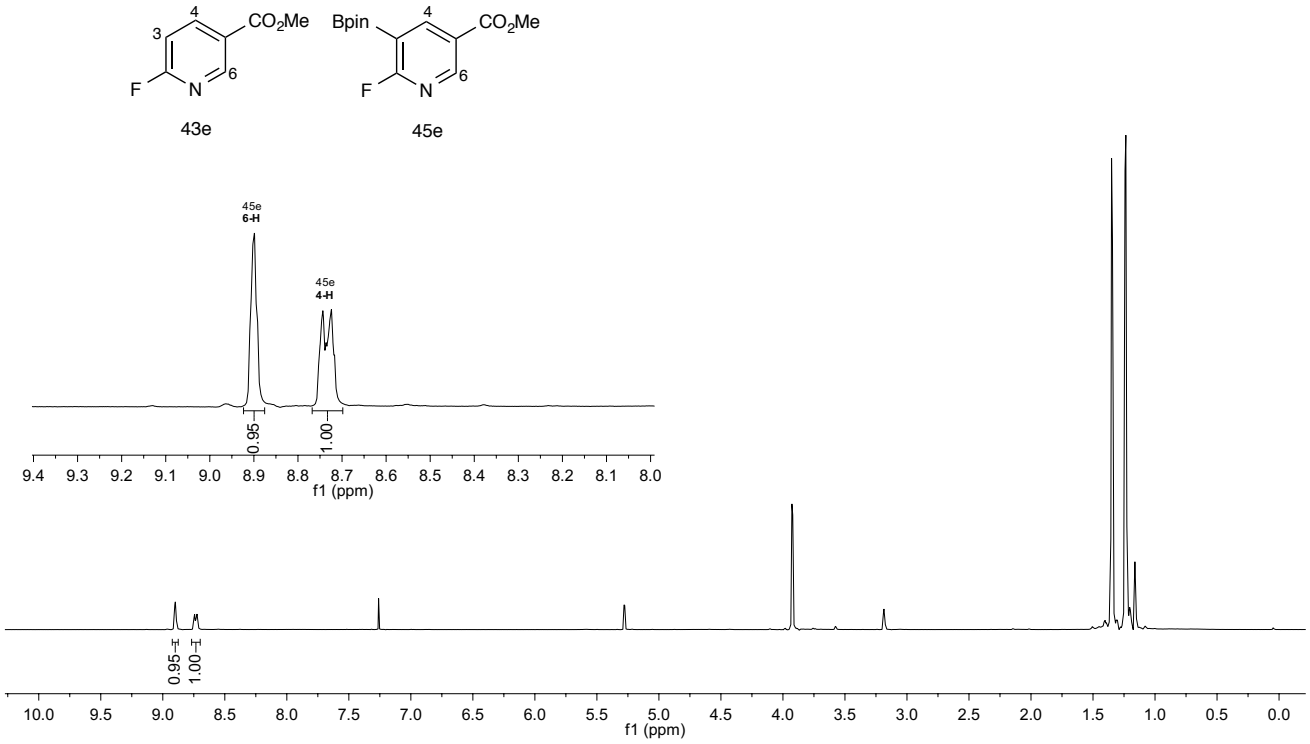
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of methyl-6-chloronicotinate (**43c**)



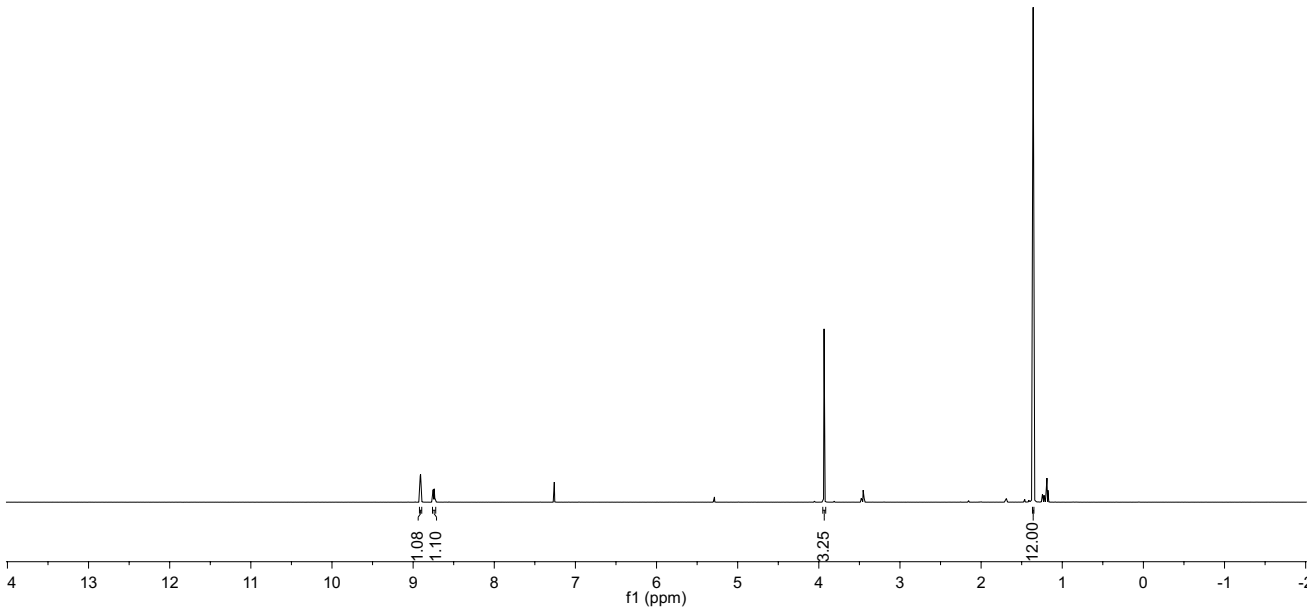
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of 2,5-difluoropyridine (**43d**)



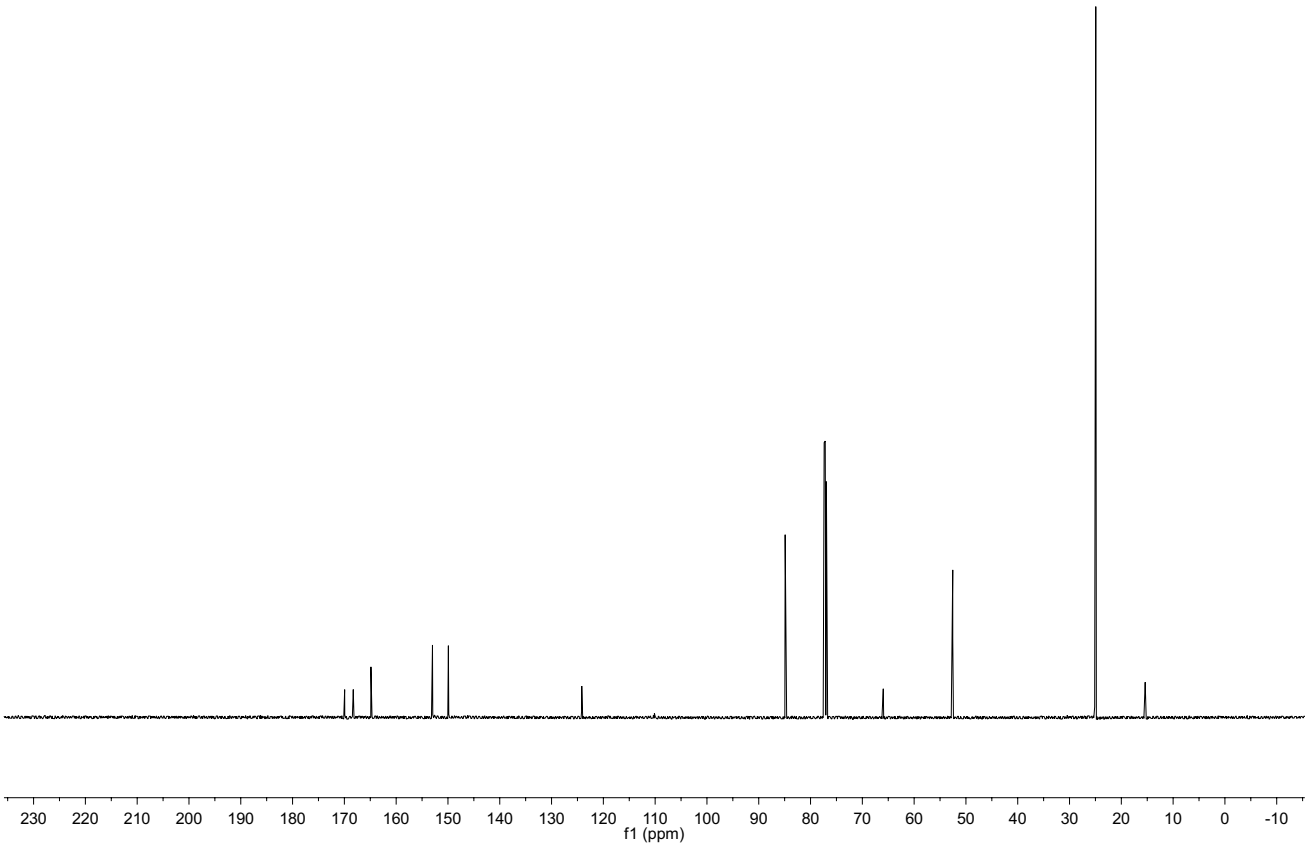
^{1}H NMR (400 MHz, $CDCl_3$) - Borylation of methyl-6-fluoronicotinate (**43e**)



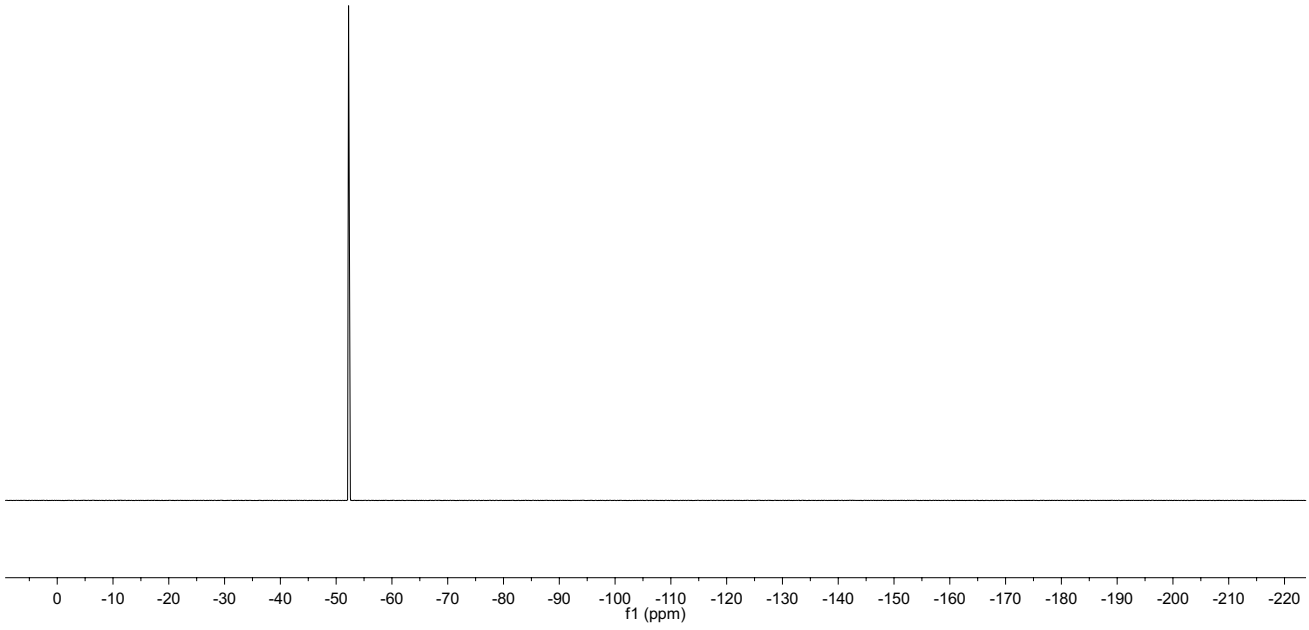
^{1}H NMR (600 MHz, $CDCl_3$) - methyl-5-(Bpin)-6-fluoronicotinate (Pure) (**45e**)



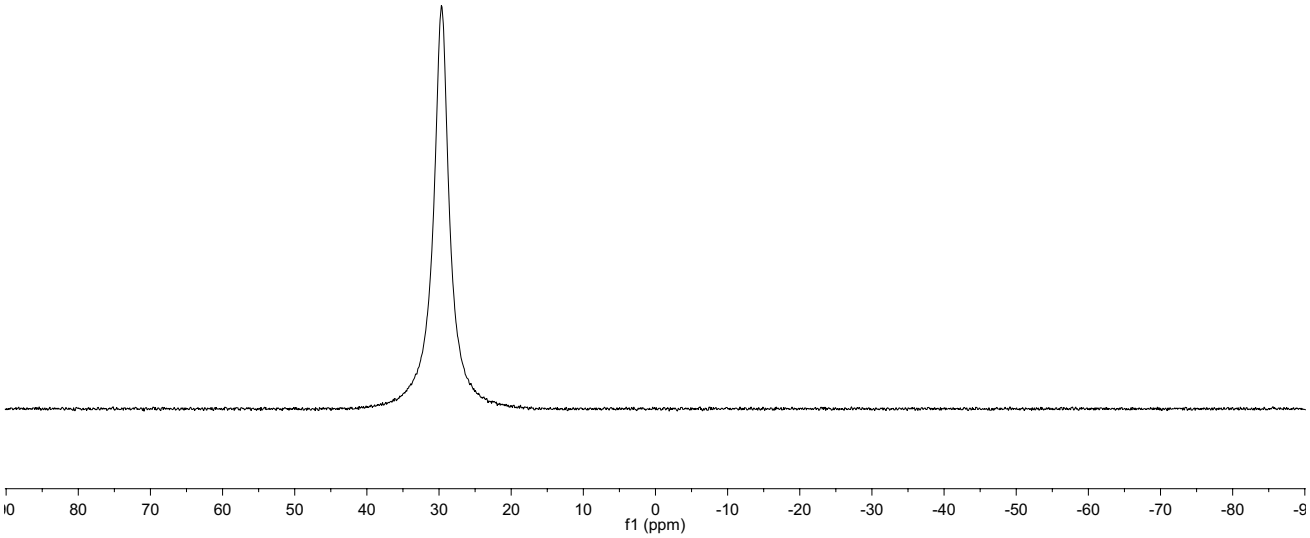
^{13}C NMR (151 MHz, $CDCl_3$) - methyl-5-(Bpin)-6-fluoronicotinate (Pure) (**45e**)



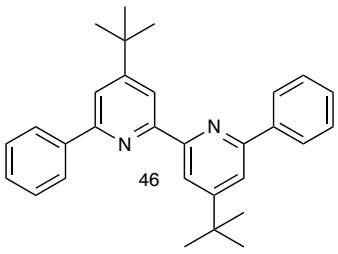
^{19}F NMR (564 MHz, $CDCl_3$) - methyl-5-(Bpin)-6-fluoronicotinate (Pure) (**45e**)



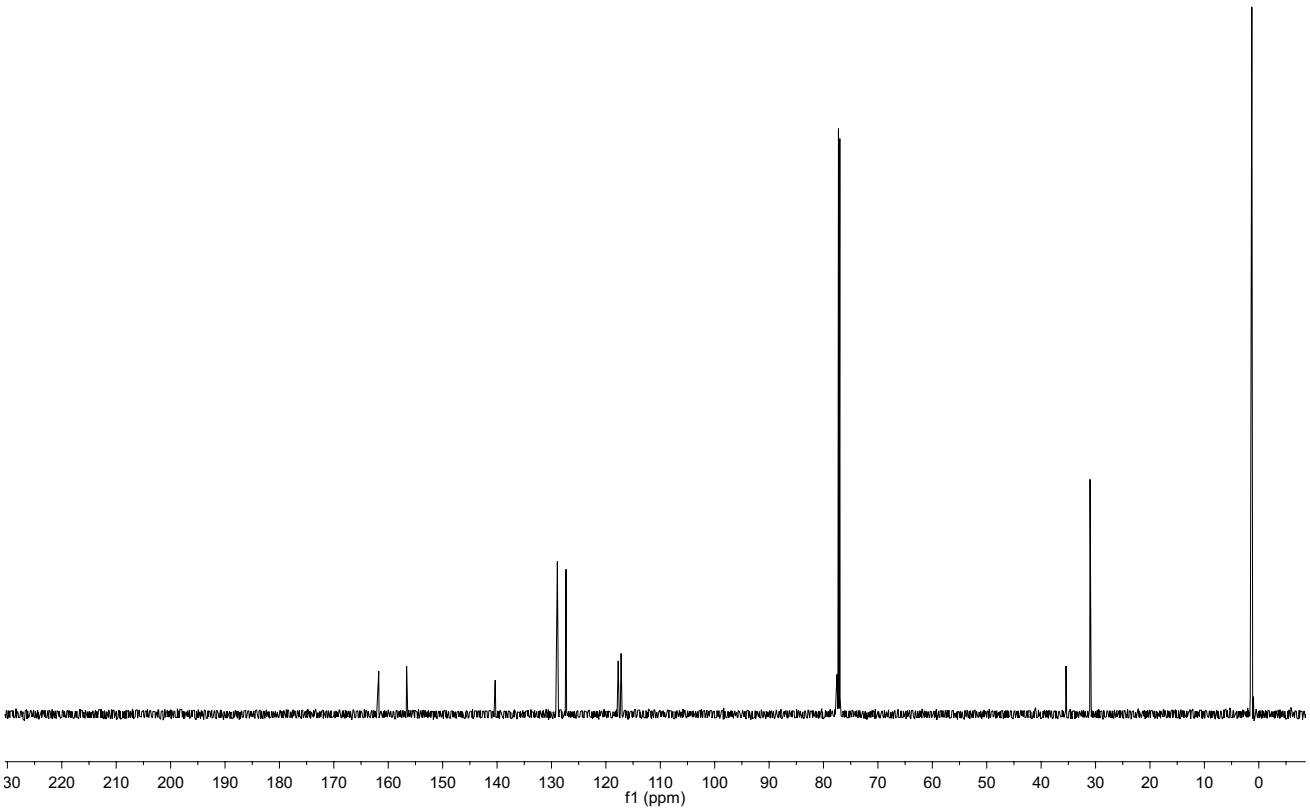
^{11}B NMR (128 MHz, $CDCl_3$) - methyl-5-(Bpin)-6-fluoronicotinate (Pure) (**45e**)



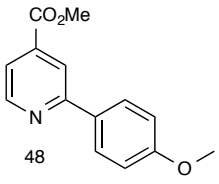
^{1}H NMR (500 MHz, $CDCl_3$) - 4,4'-di-tertbutyl-6,6'-diphenyl-2,2'-bipyridine (**46**)

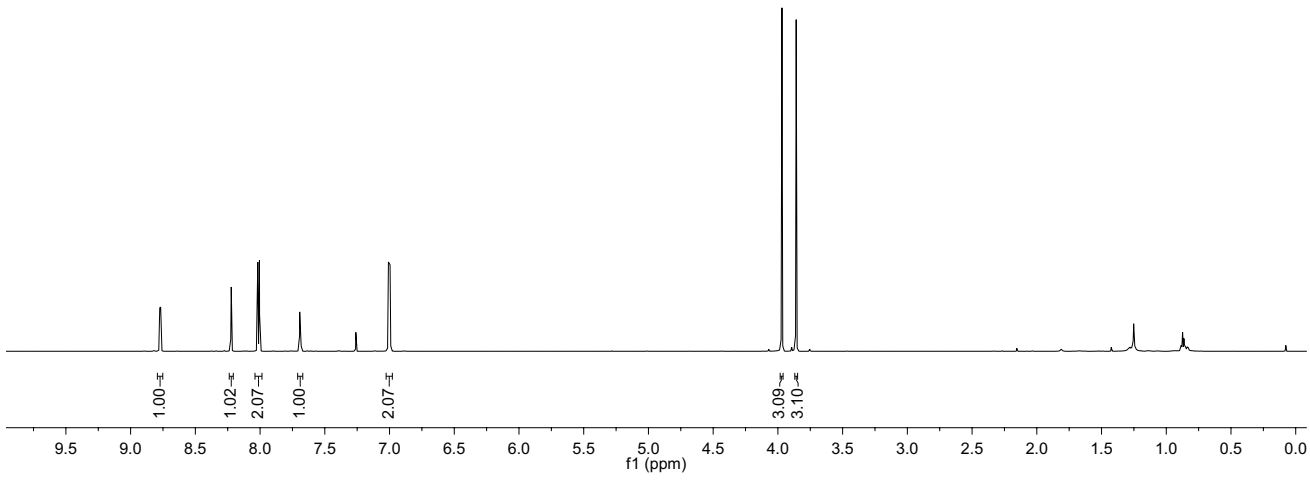


^{13}C NMR (126MHz, $CDCl_3$) – 4,4'-di-tertbutyl-6,6'-diphenyl-2,2'-bipyridine (**46**)

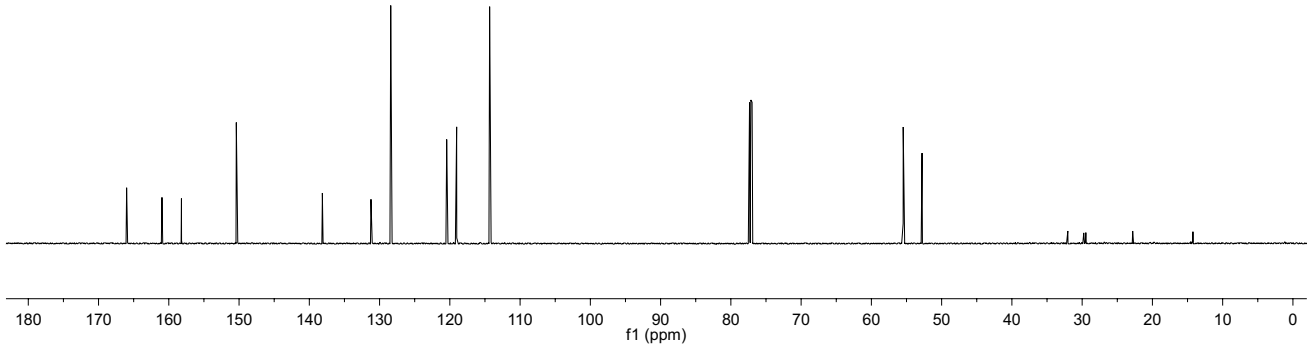


^{1}H NMR (700 MHz, $CDCl_3$) - **48**

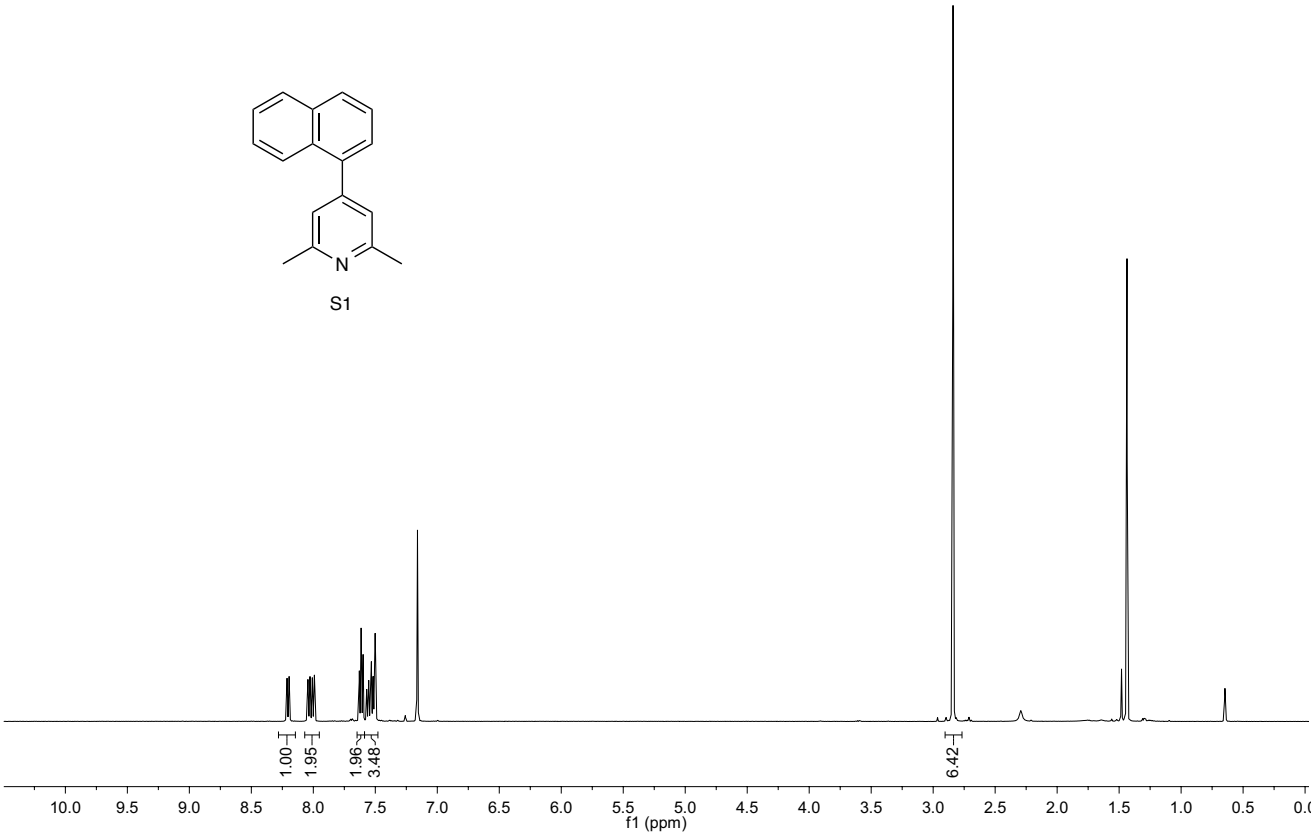




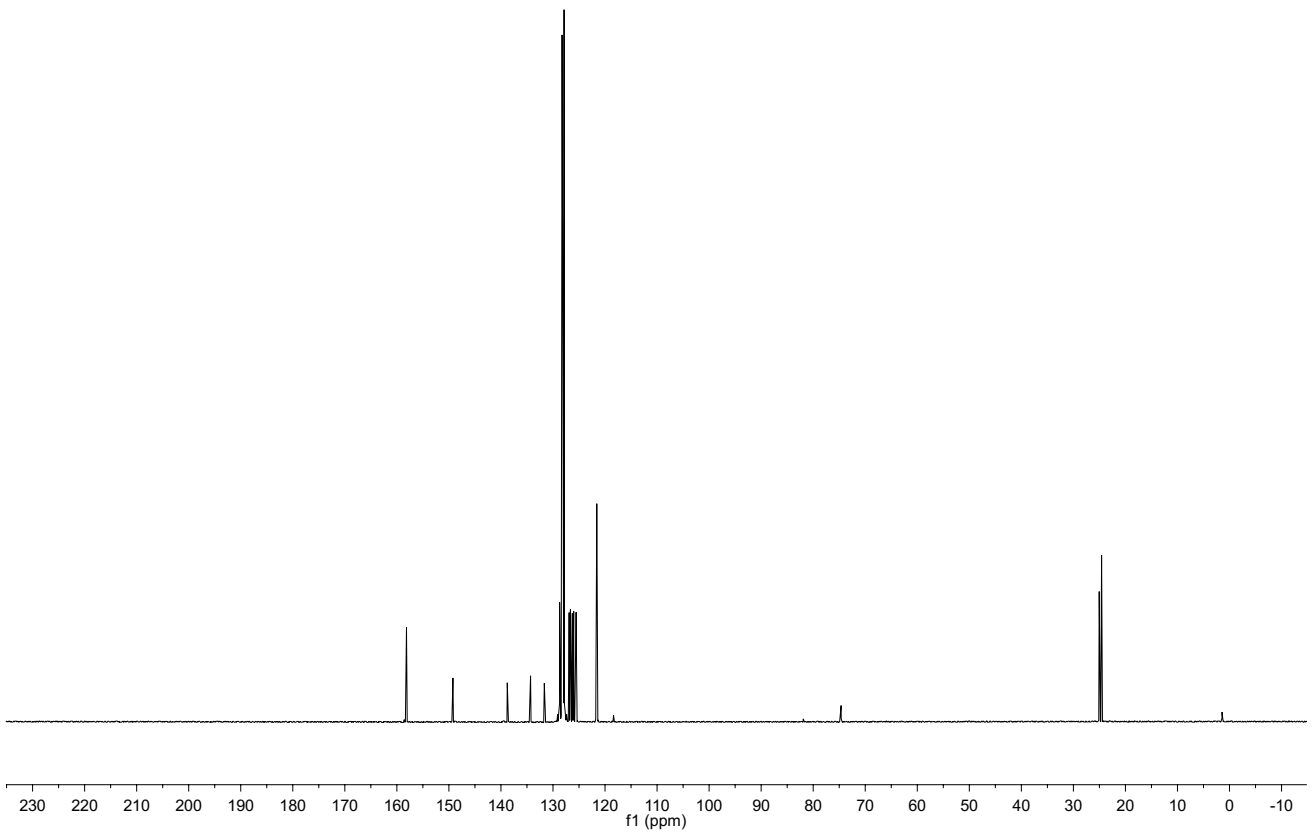
^{13}C NMR (176 MHz, $CDCl_3$) - **48**



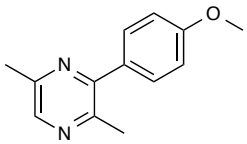
^{1}H NMR (500MHz, C_6D_6) - **S1**



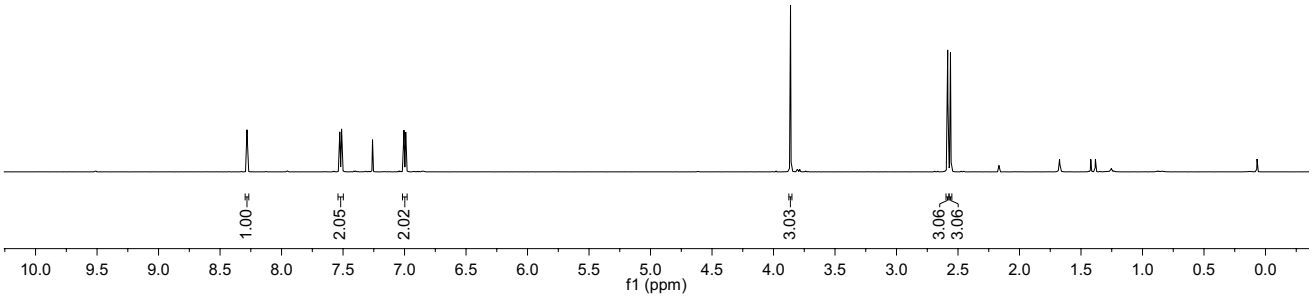
^{13}C NMR (126MHz, C_6D_6) - **S1**



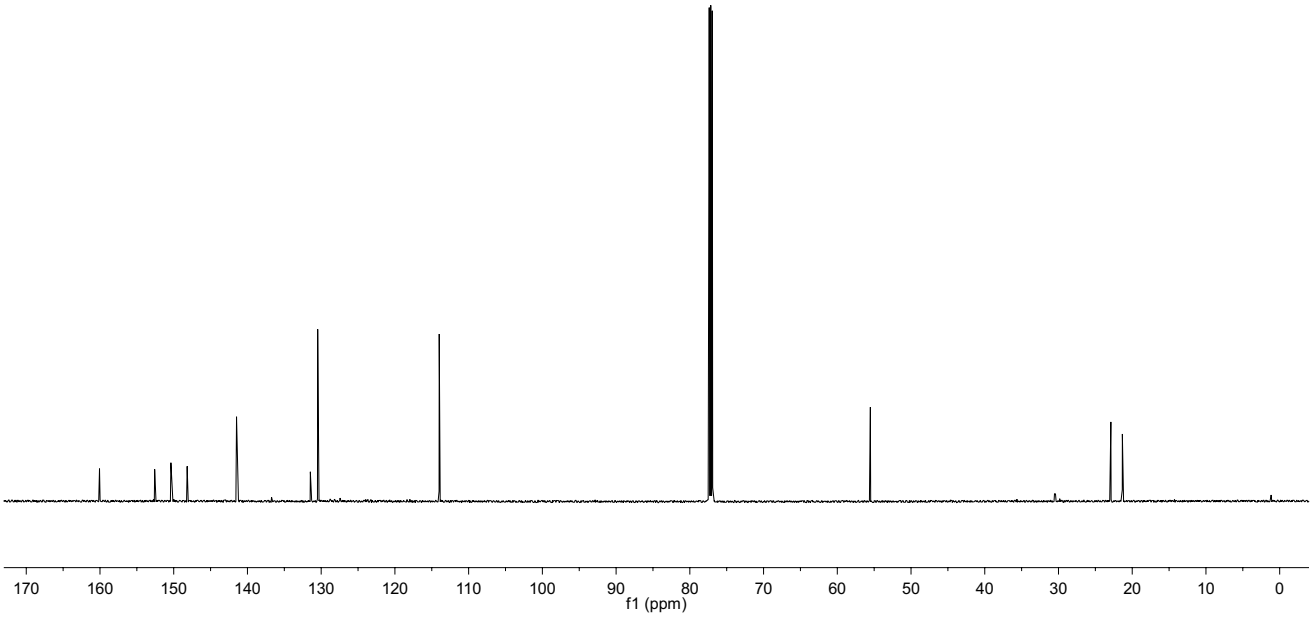
^{1}H NMR (600 MHz, $CDCl_3$) - **S8**



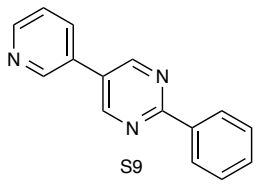
S8



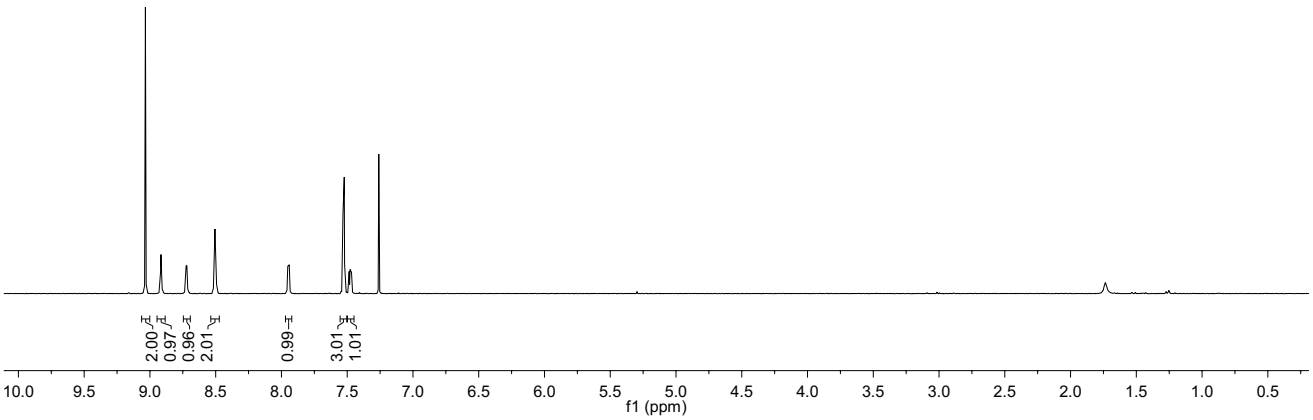
^{13}C NMR (151 MHz, $CDCl_3$) - **S8**



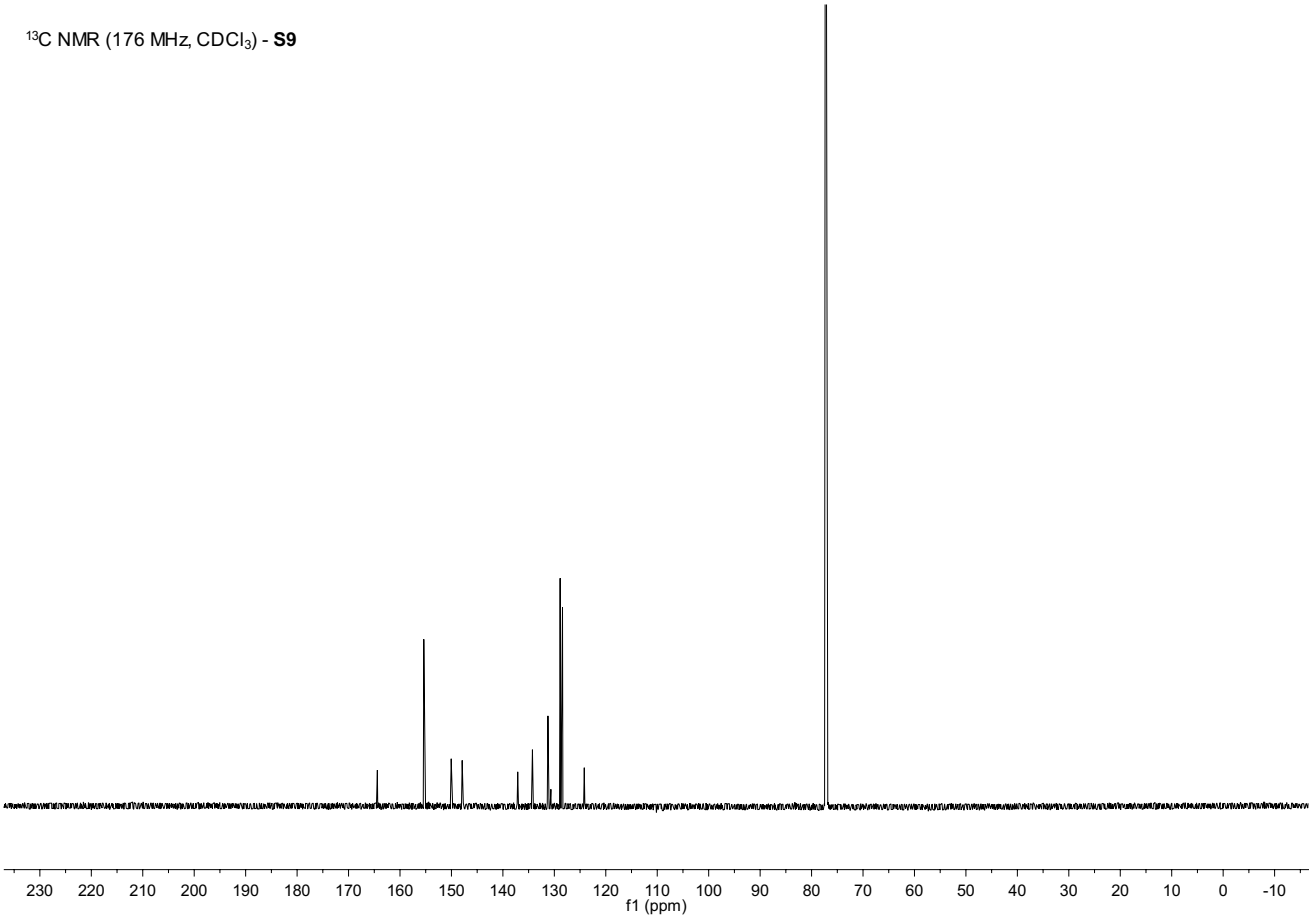
^{1}H NMR (700 MHz, $CDCl_3$) - **S9**



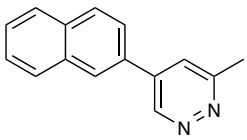
S9



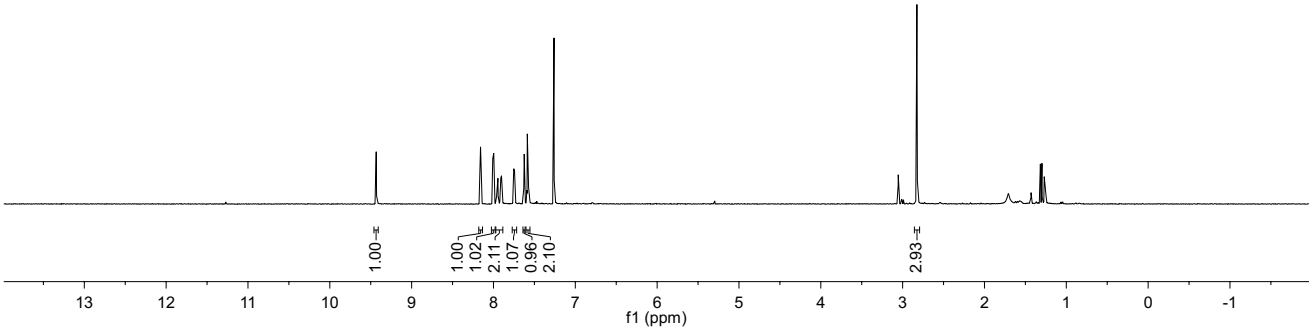
^{13}C NMR (176 MHz, $CDCl_3$) - **S9**



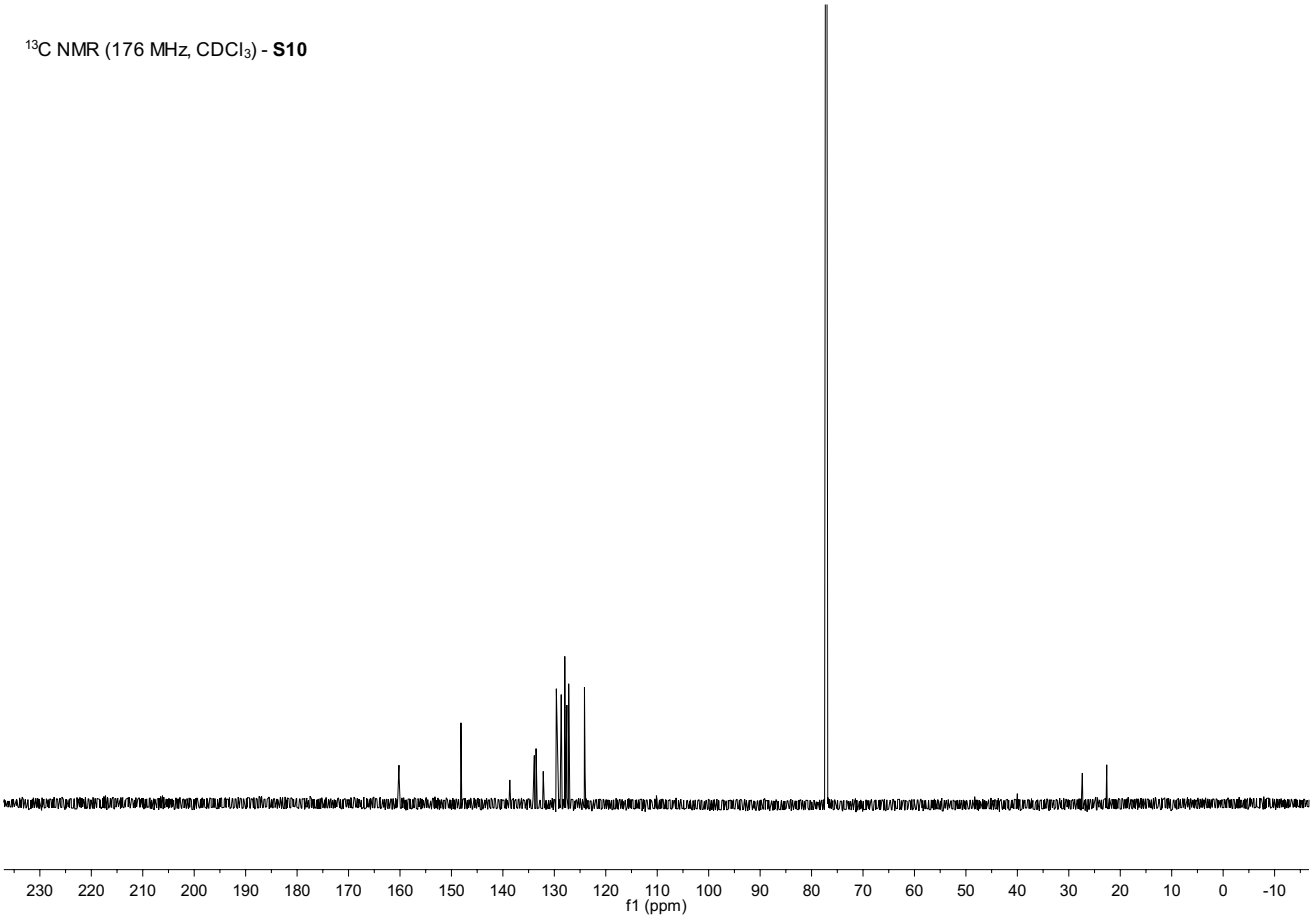
^{1}H NMR (700 MHz, $CDCl_3$) - **S10**



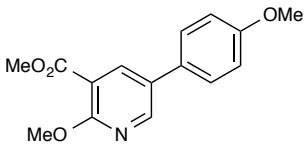
S10



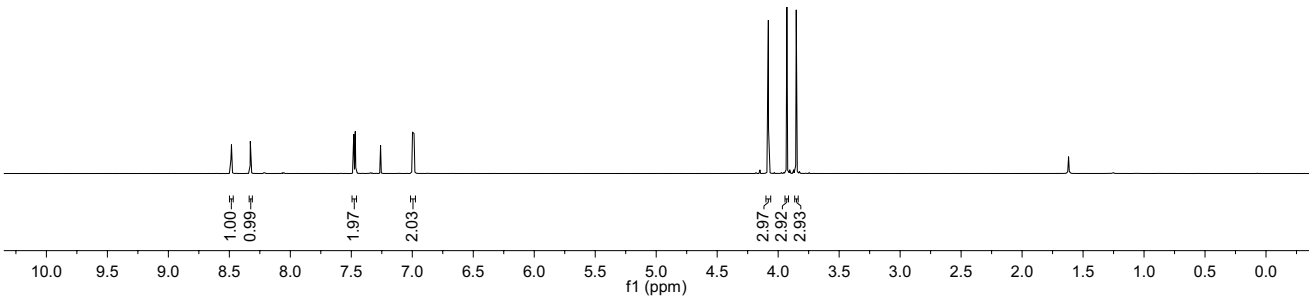
^{13}C NMR (176 MHz, $CDCl_3$) - **S10**



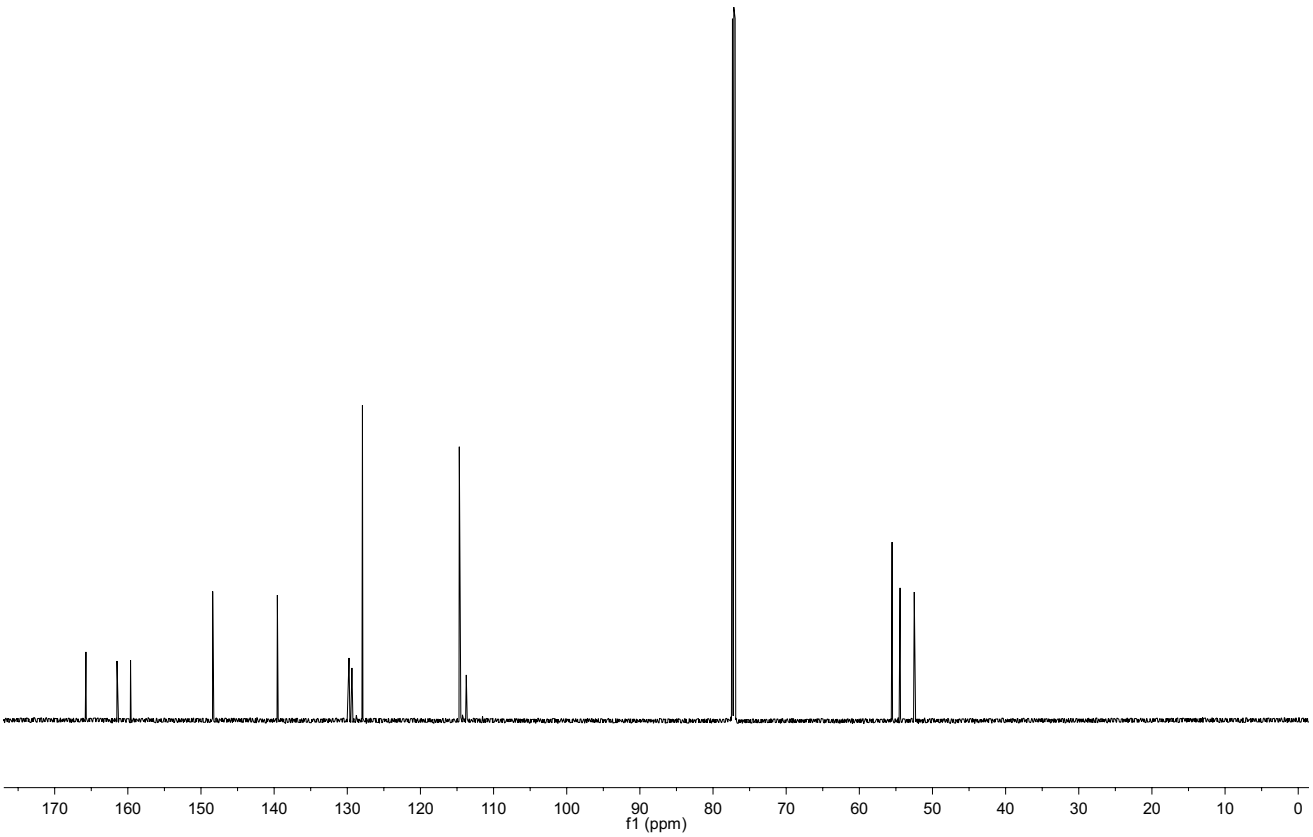
^{1}H NMR (700 MHz, $CDCl_3$) - **S12**



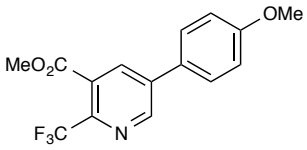
S12



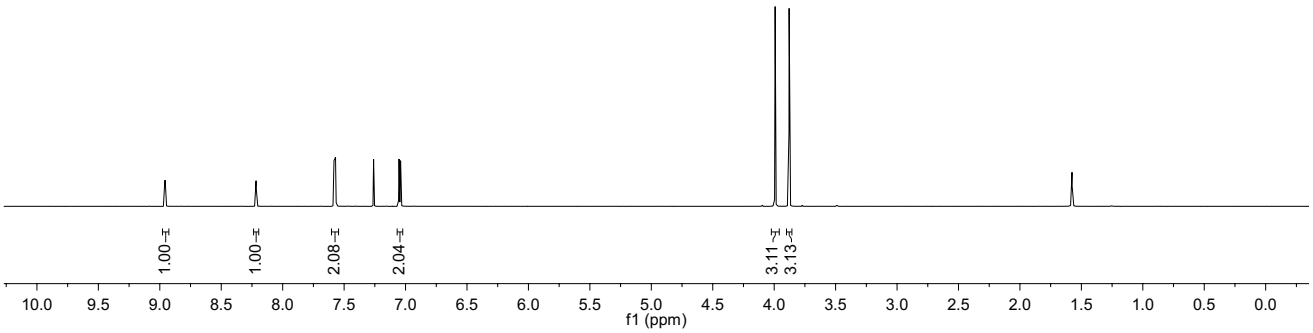
^{13}C NMR (176 MHz, $CDCl_3$) - **S12**



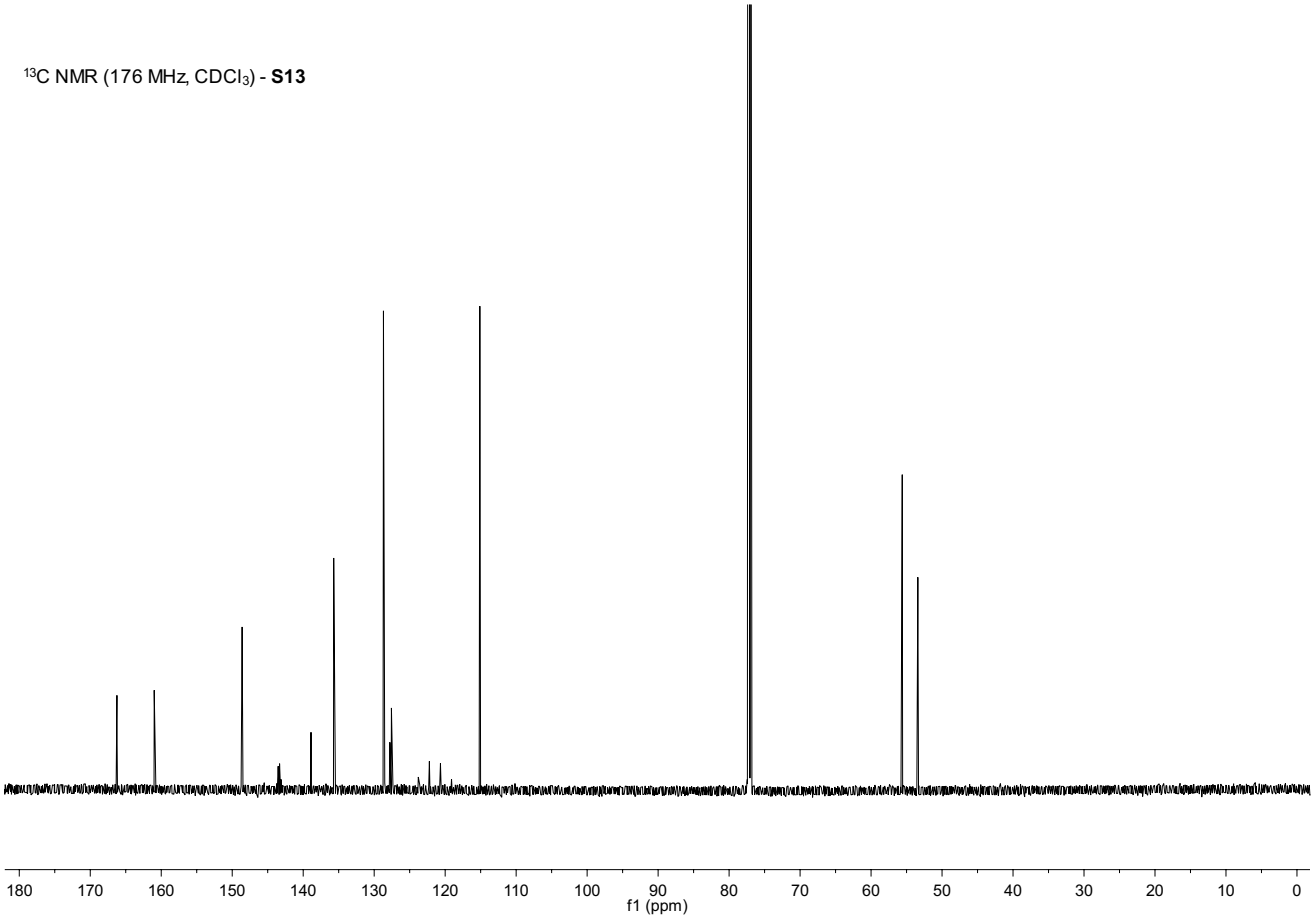
^{1}H NMR (700 MHz, $CDCl_3$) - **S13**



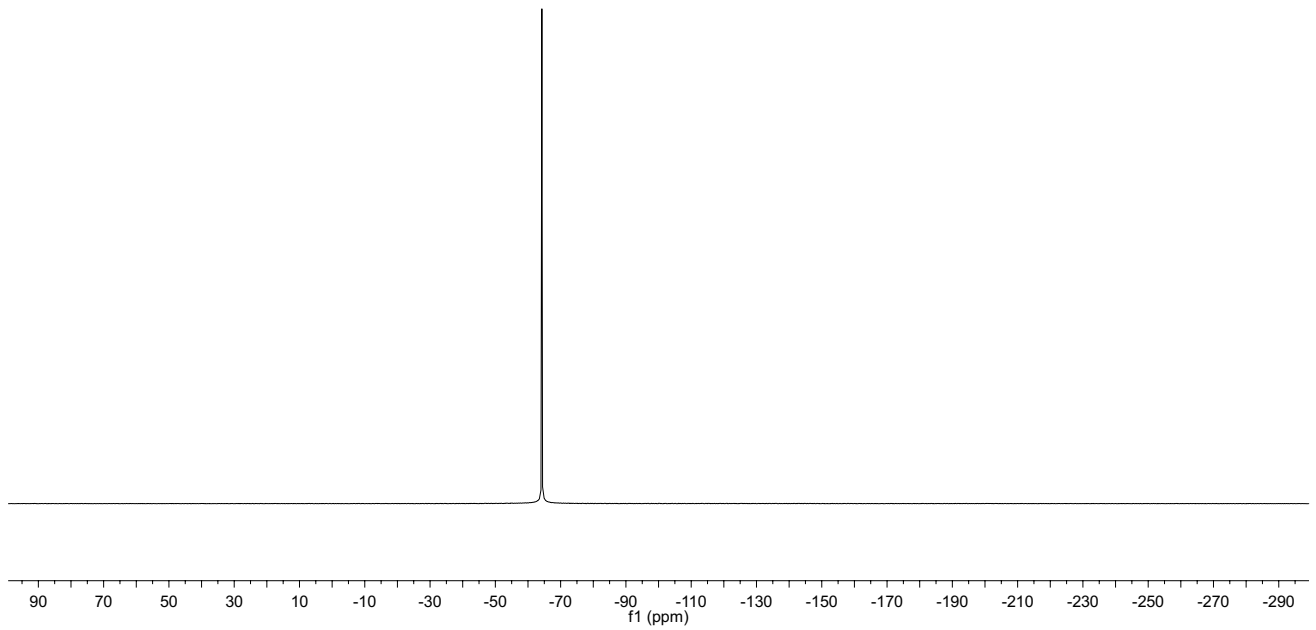
S13



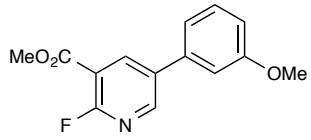
^{13}C NMR (176 MHz, $CDCl_3$) - **S13**



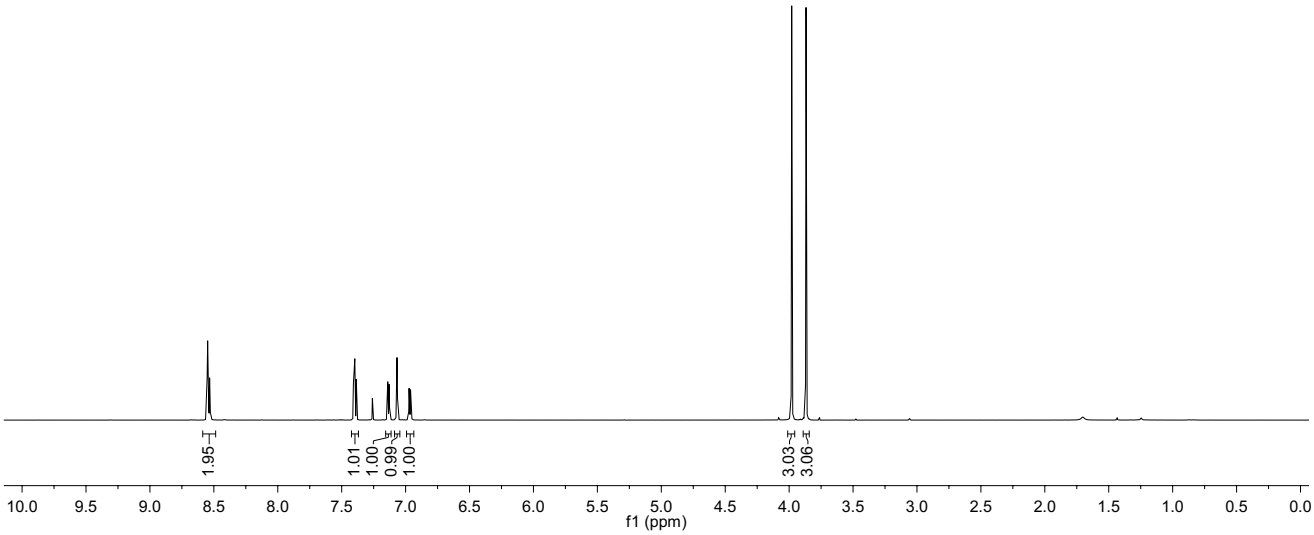
^{19}F NMR (376 MHz, $CDCl_3$) - S**13**



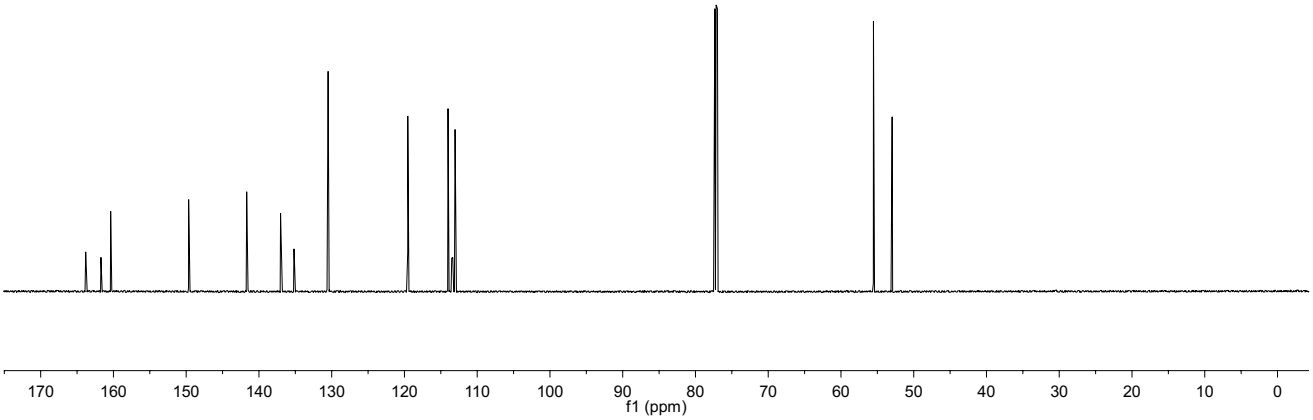
^{1}H NMR (700 MHz, $CDCl_3$) - **S14**



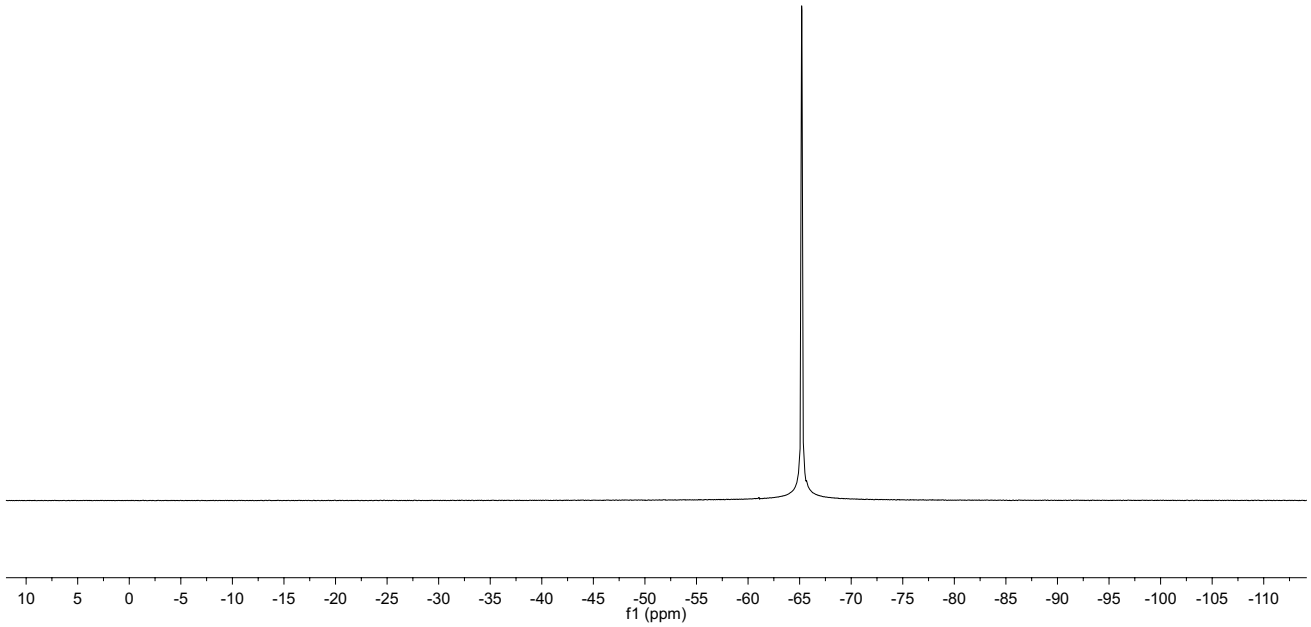
S14



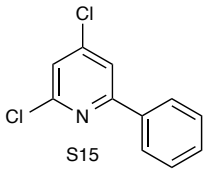
13C NMR (176 MHz, CDCl3) - **S14**



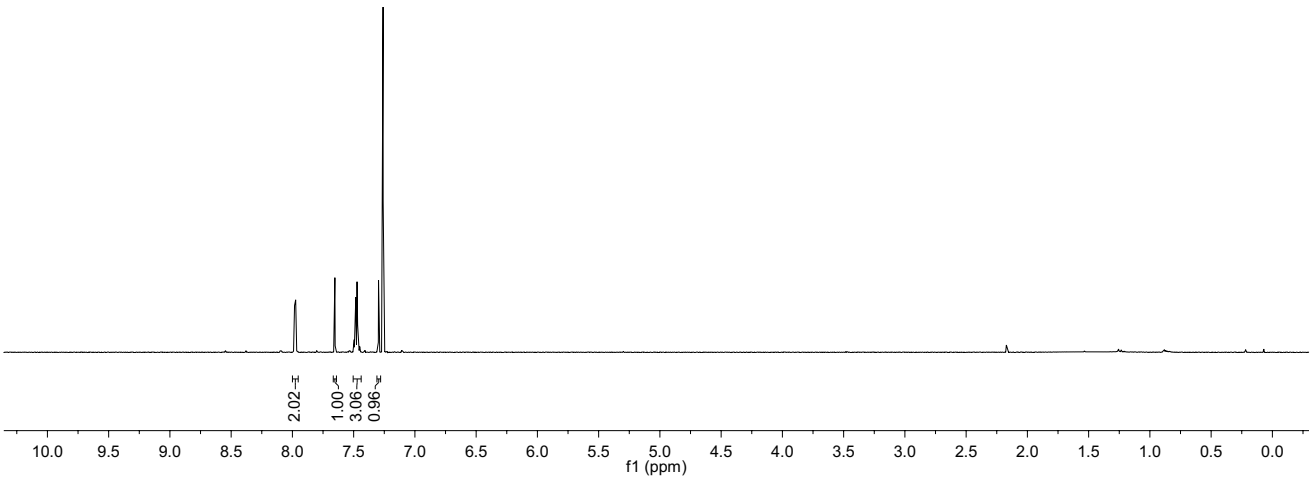
^{19}F NMR (376 MHz, $CDCl_3$) - **S14**



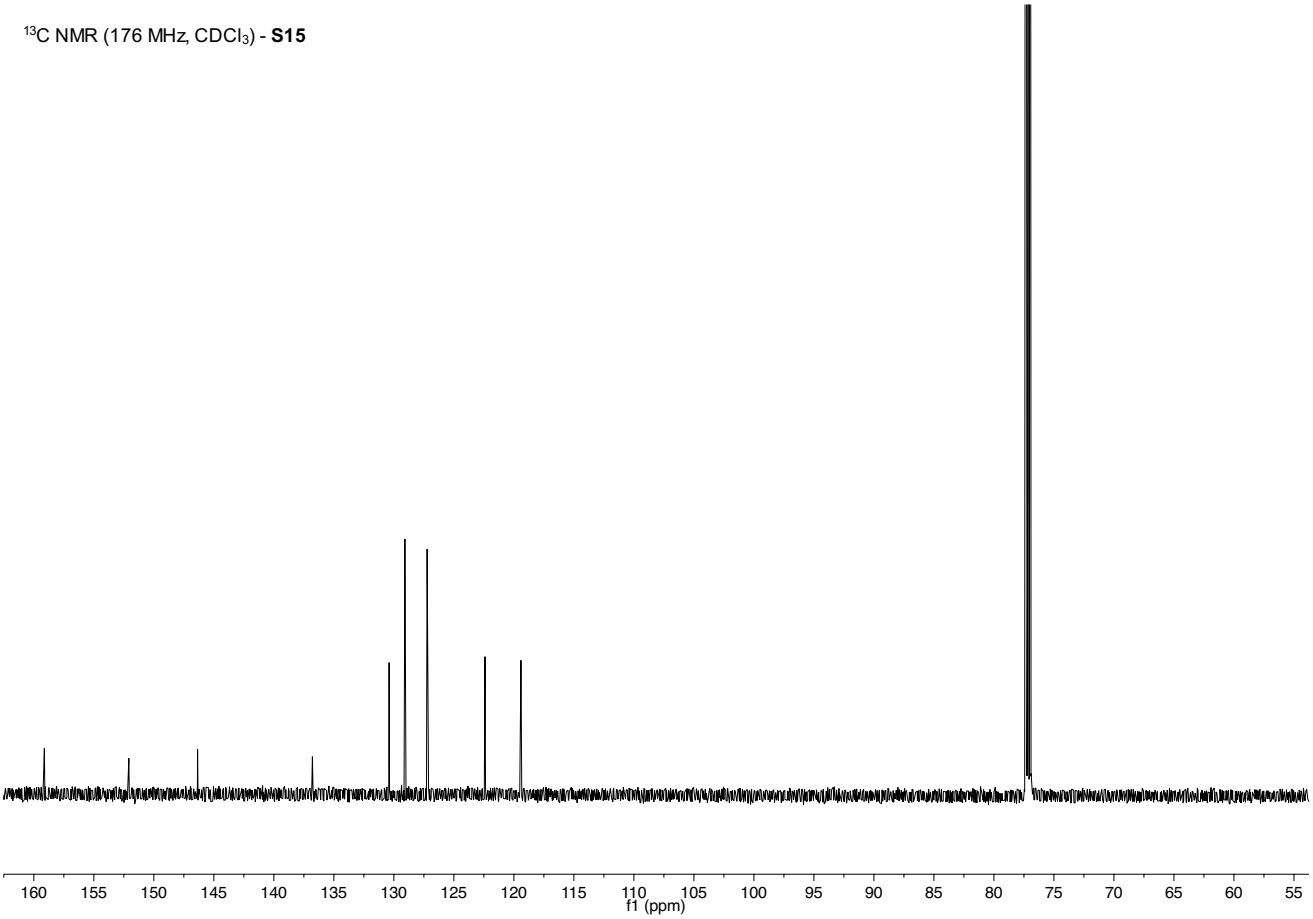
^{1}H NMR (700 MHz, $CDCl_3$) - **S15**



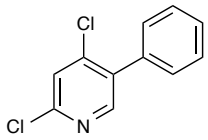
S15



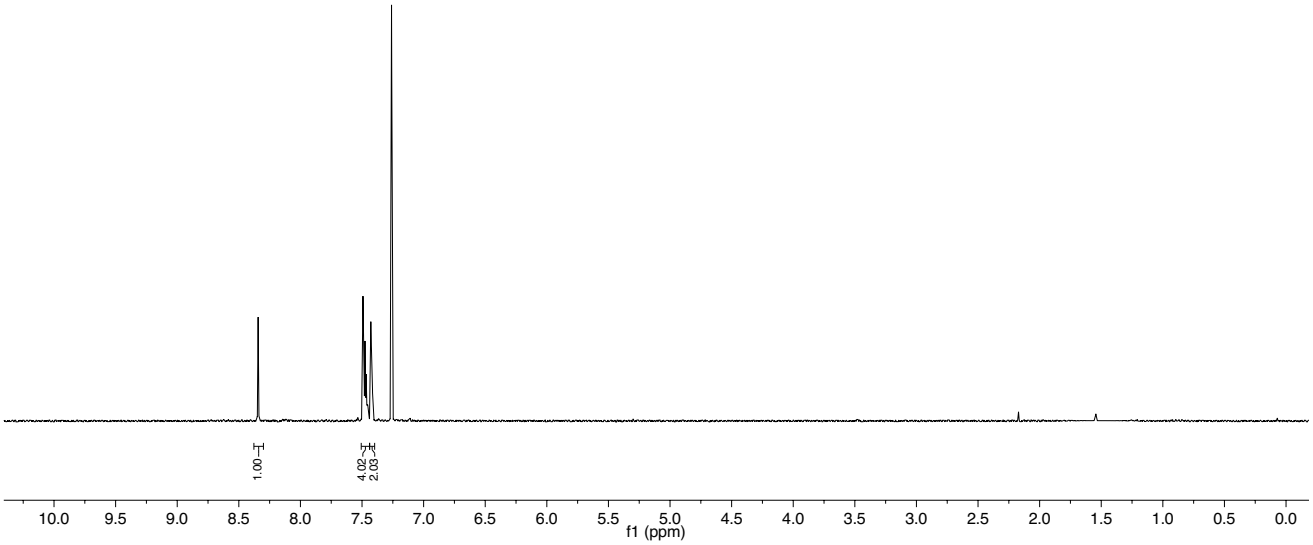
^{13}C NMR (176 MHz, $CDCl_3$) - **S15**



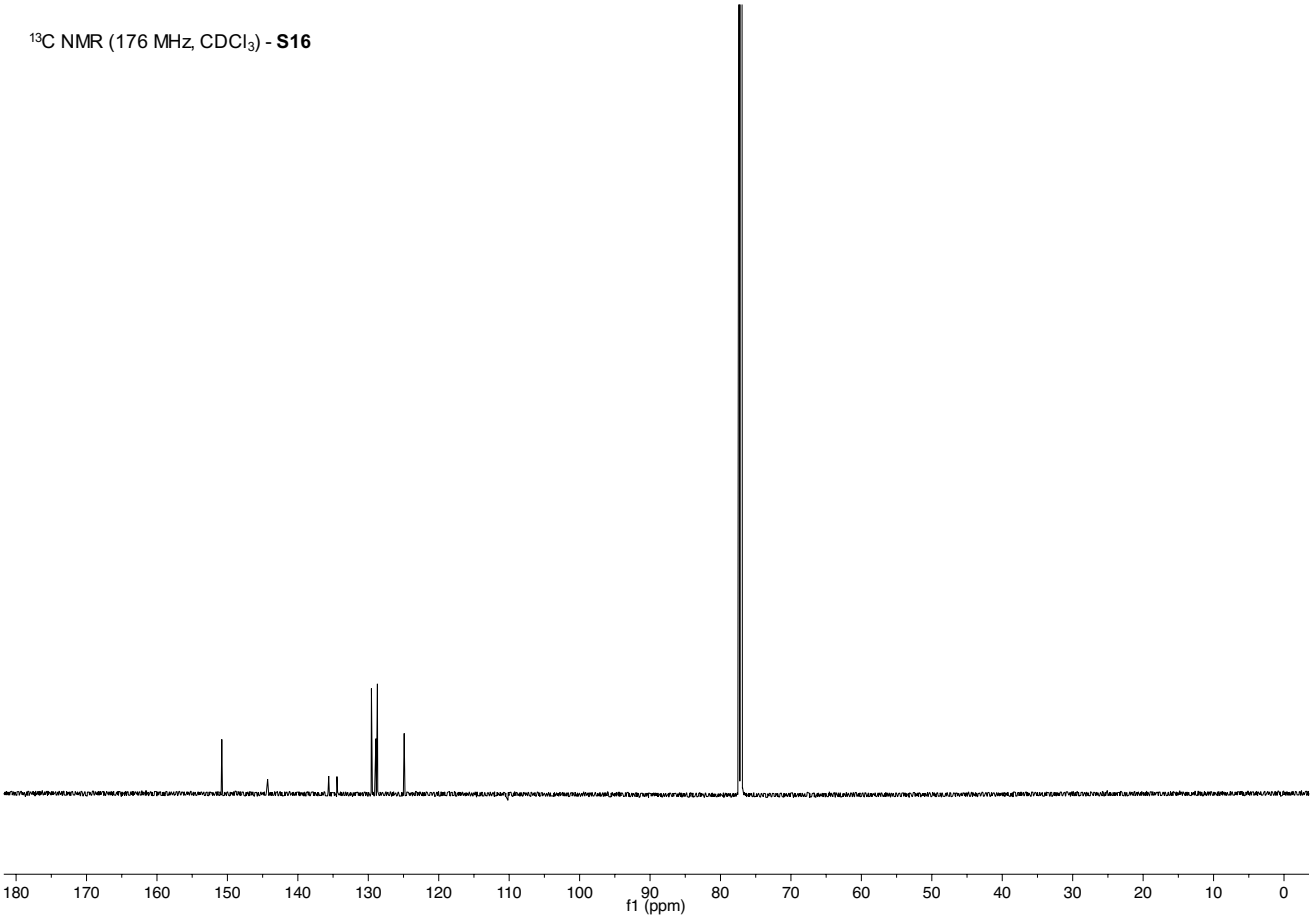
1H NMR (700 MHz, $CDCl_3$) - **S16**



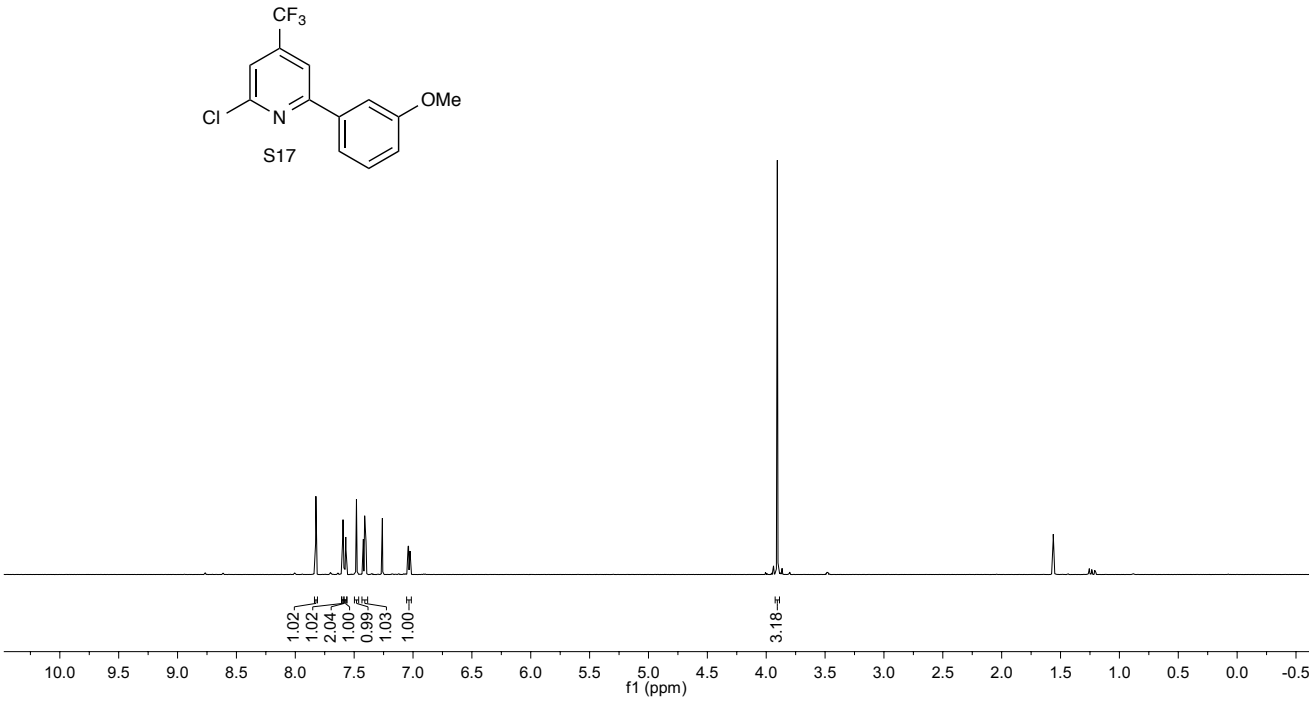
S16



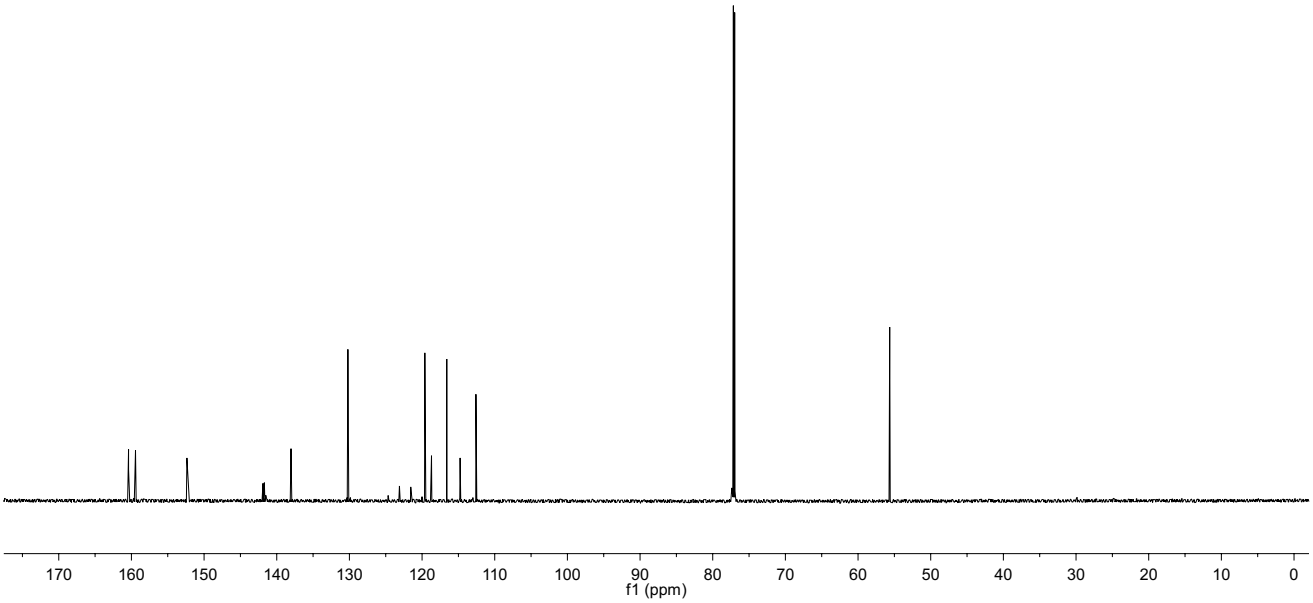
^{13}C NMR (176 MHz, $CDCl_3$) - **S16**



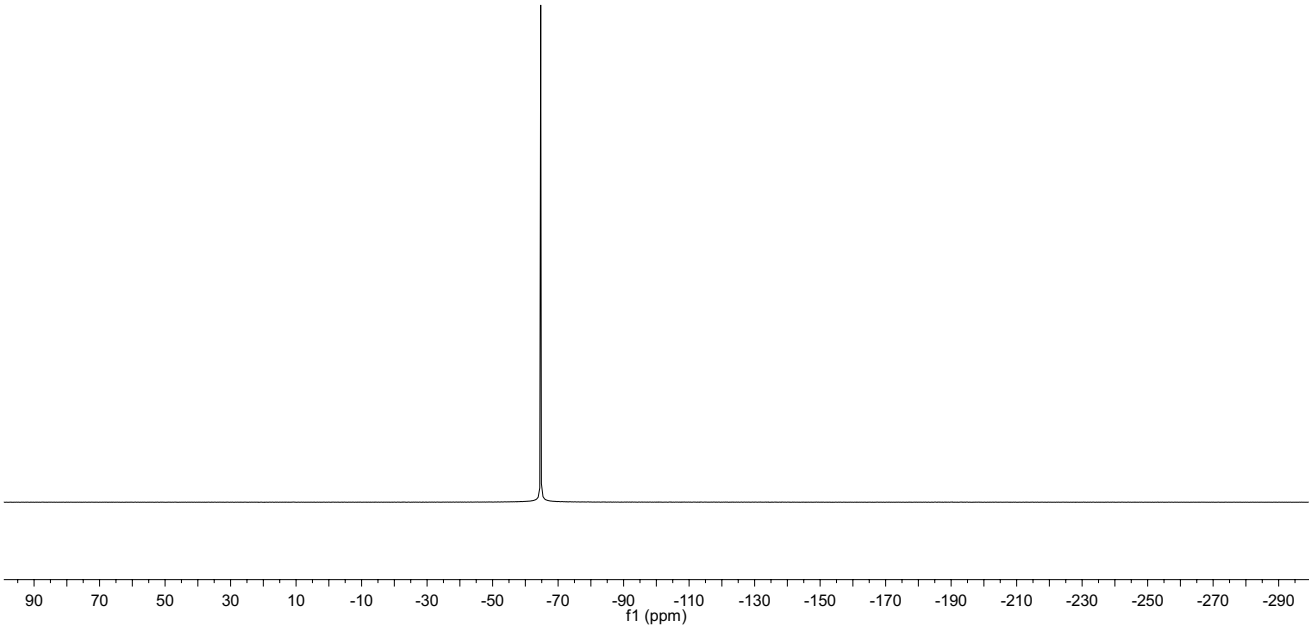
^{1}H NMR (700 MHz, $CDCl_3$) - **S17**



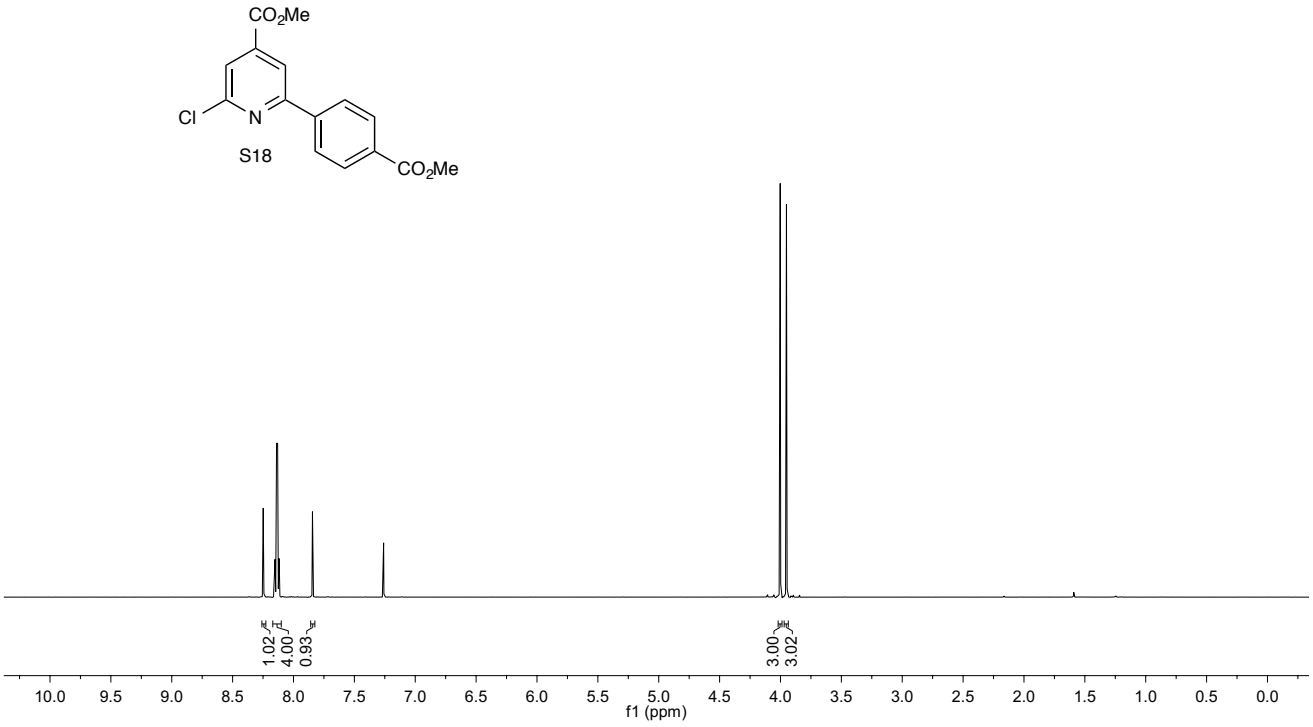
^{13}C NMR (176 MHz, $CDCl_3$) - **S17**



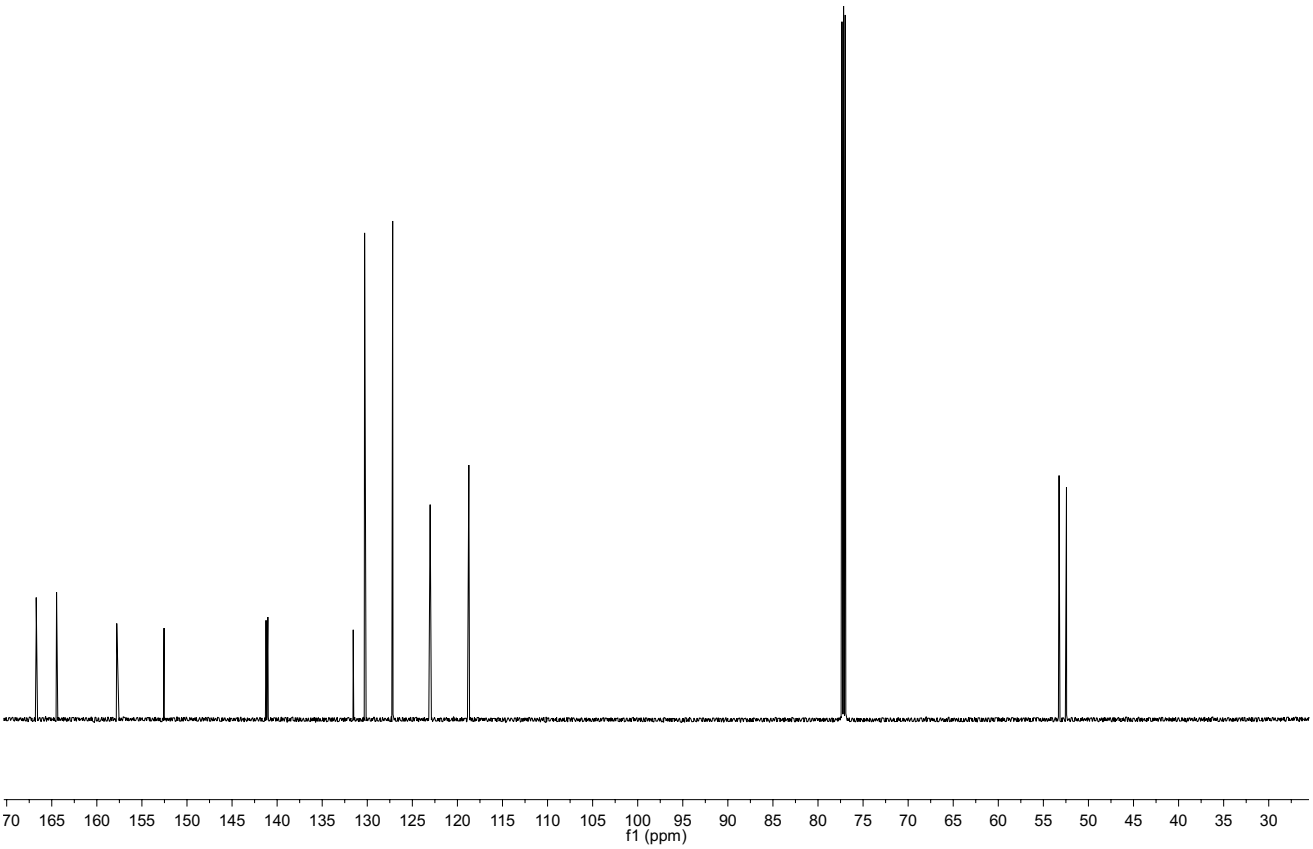
^{19}F NMR (376 MHz, $CDCl_3$) - **S17**



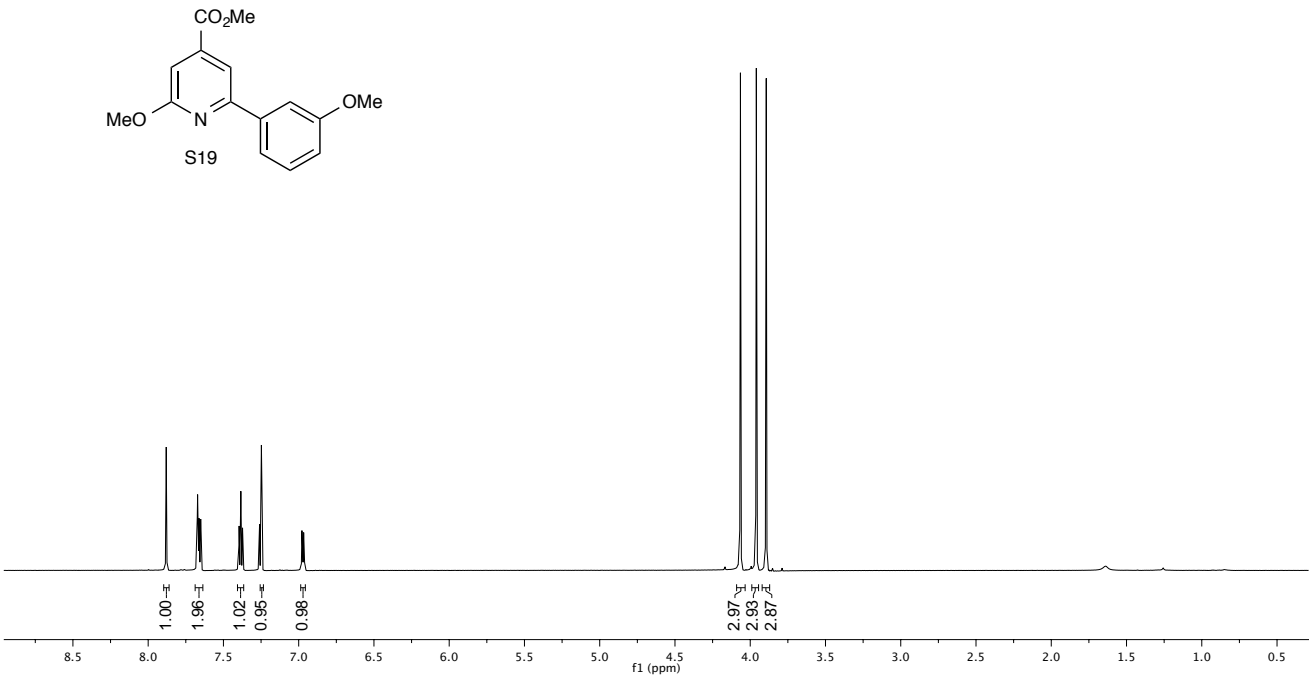
^{1}H NMR (700 MHz, $CDCl_3$) - **S18**



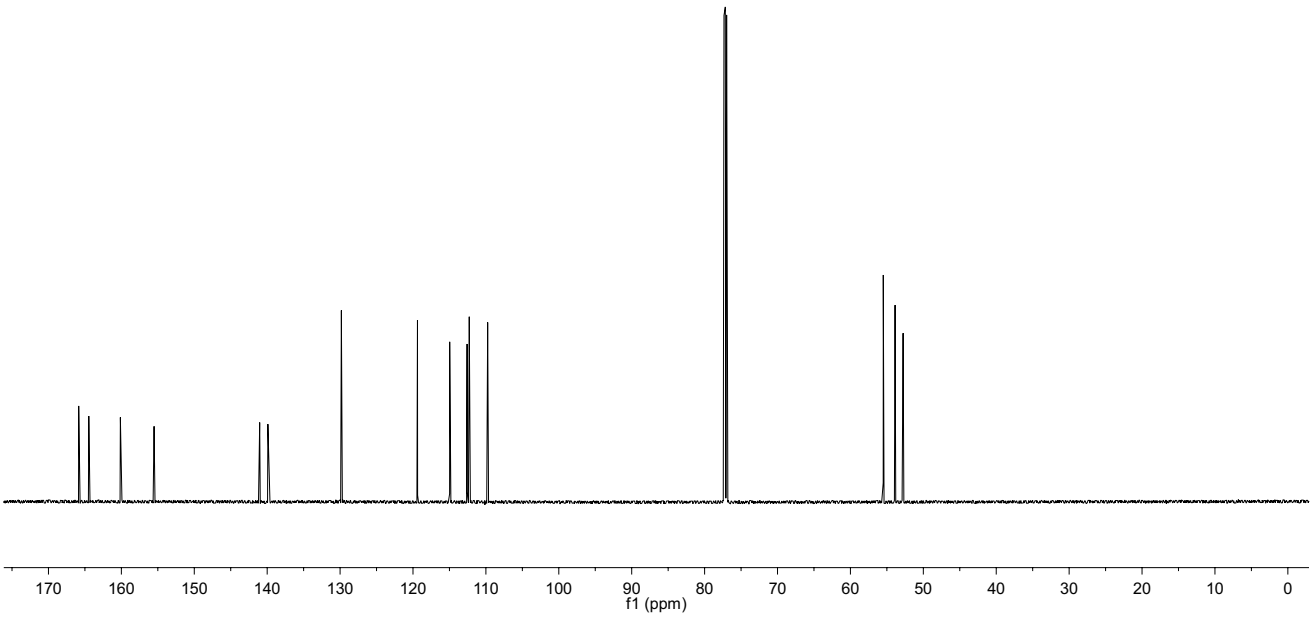
^{13}C NMR (176 MHz, $CDCl_3$) - **S18**



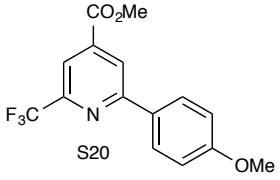
^{1}H NMR (700 MHz, $CDCl_3$) - **S19**



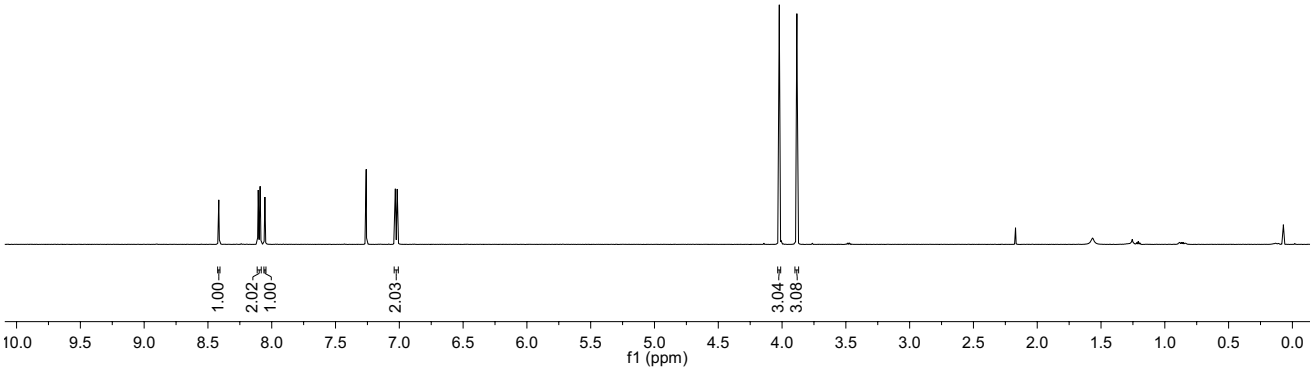
^{13}C NMR (176 MHz, $CDCl_3$) - **S19**



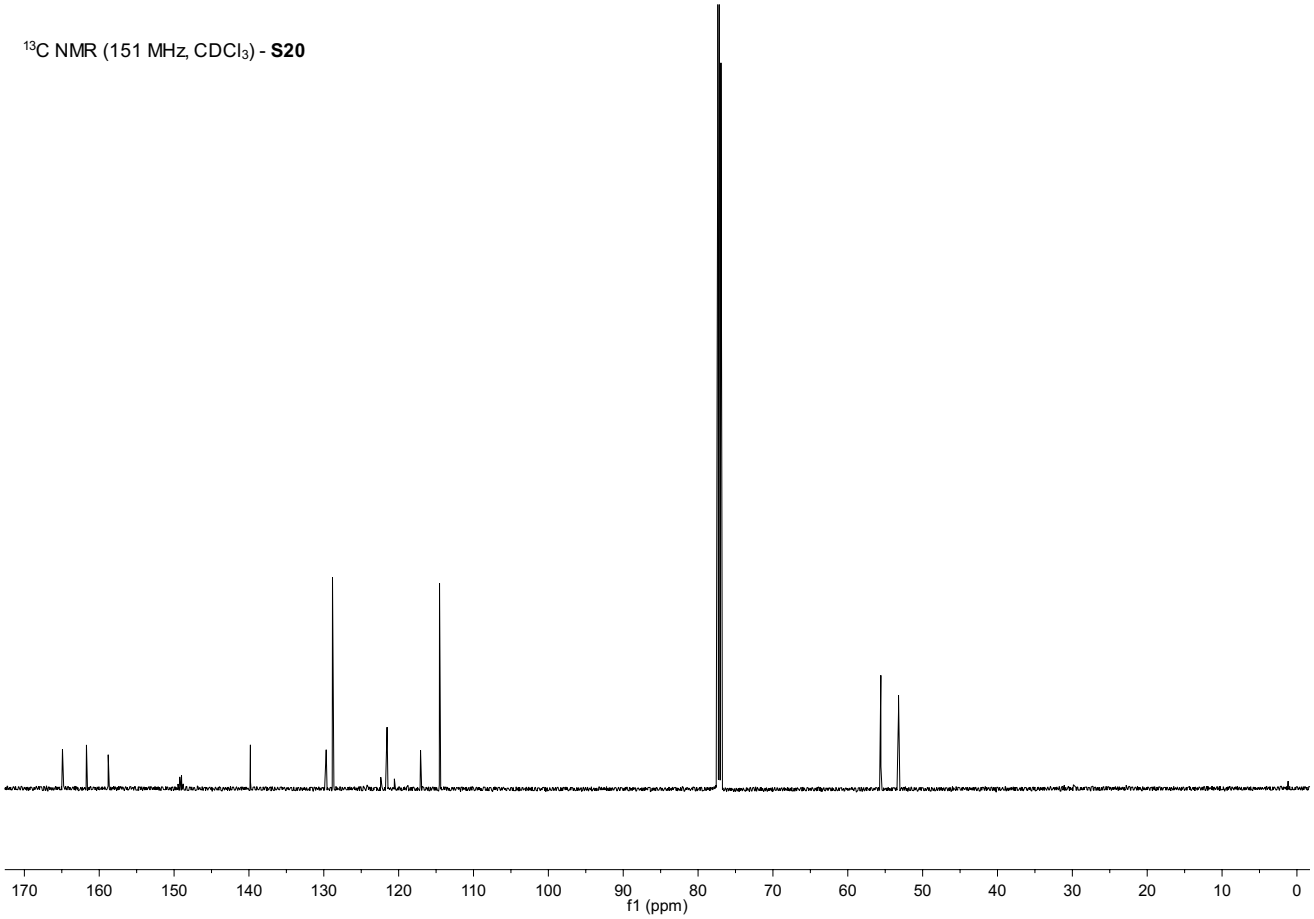
^{1}H NMR (600 MHz, $CDCl_3$) - **S20**



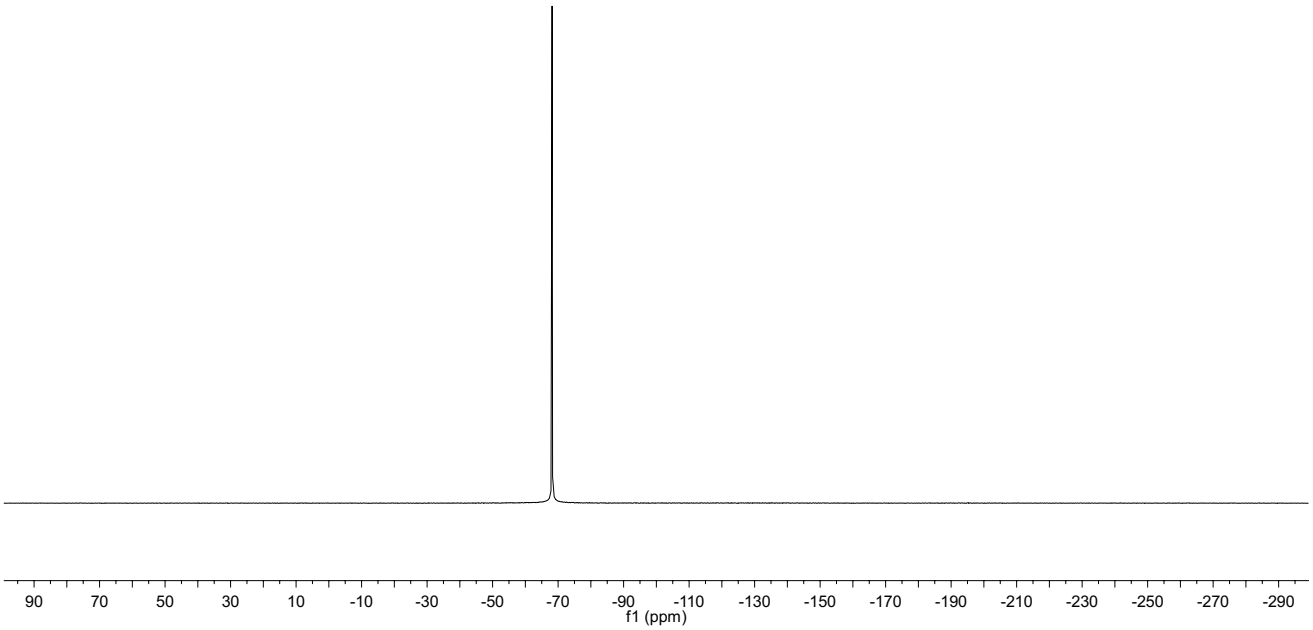
S20



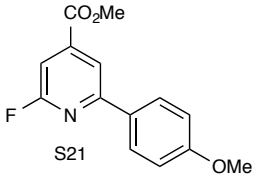
^{13}C NMR (151 MHz, $CDCl_3$) - **S20**



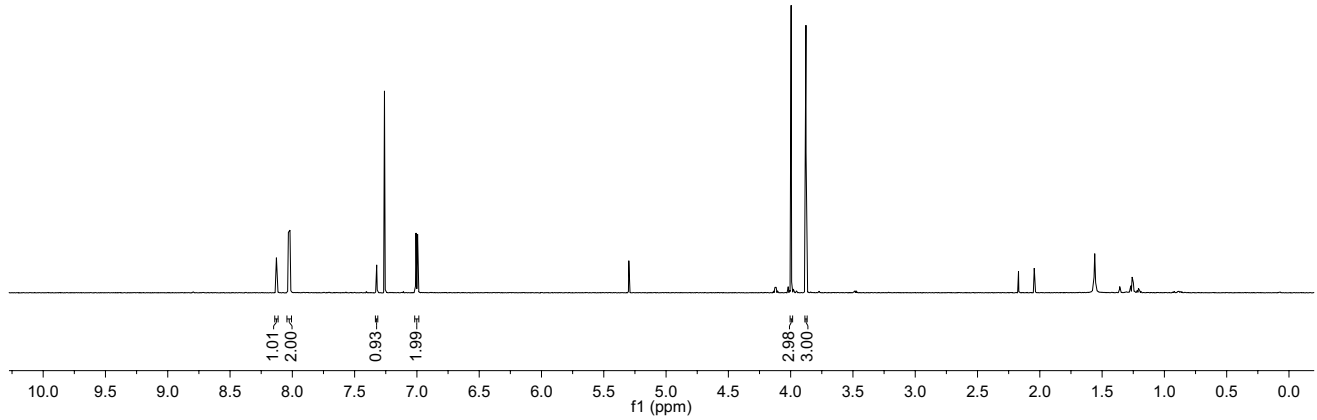
^{19}F NMR (376 MHz, $CDCl_3$) - **S20**



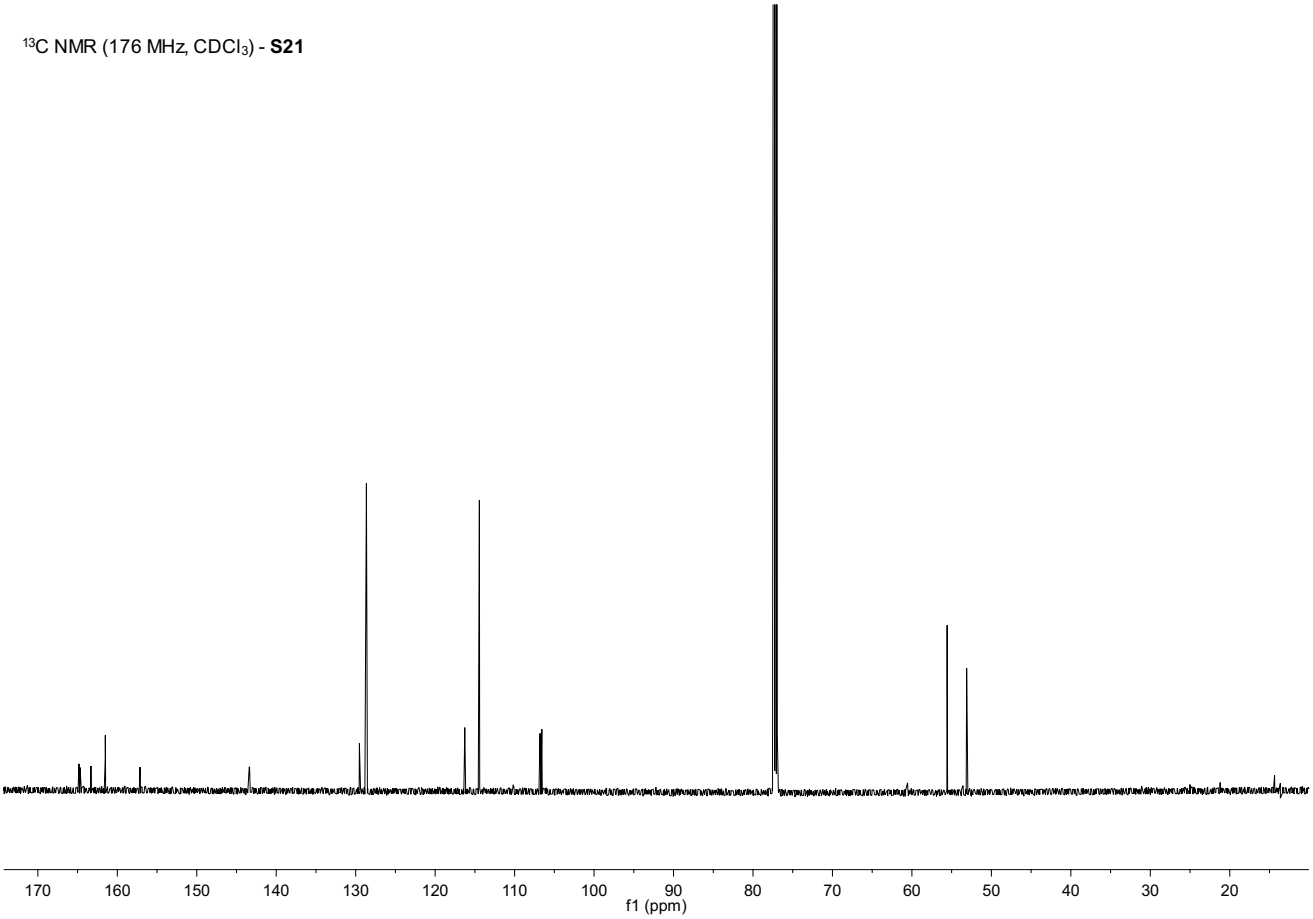
^{1}H NMR (700 MHz, $CDCl_3$) - **S21**



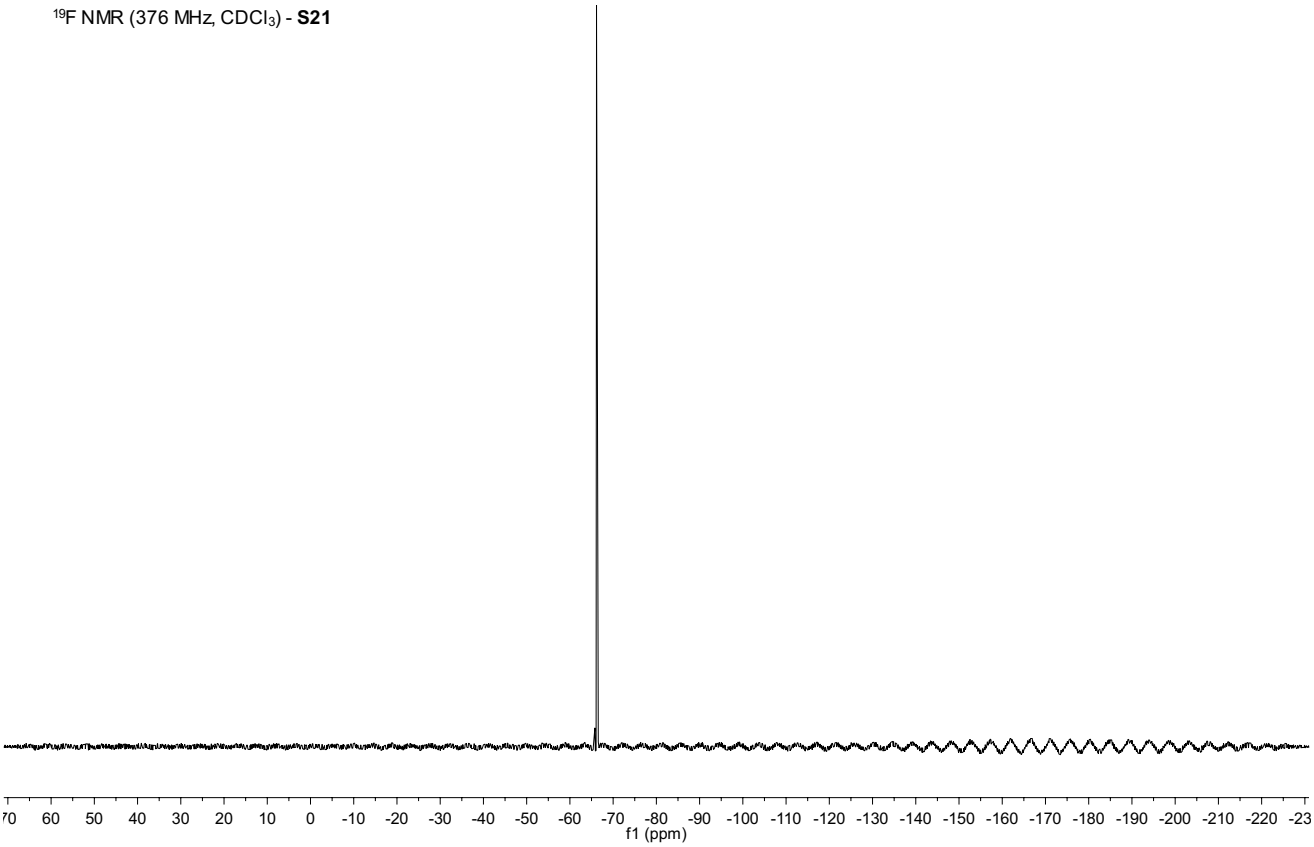
S21



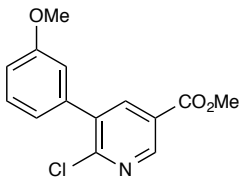
^{13}C NMR (176 MHz, $CDCl_3$) - **S21**



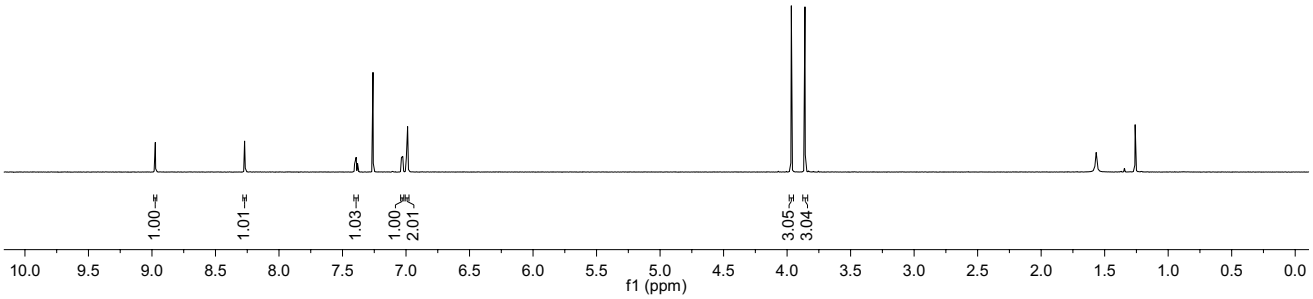
^{19}F NMR (376 MHz, $CDCl_3$) - **S21**



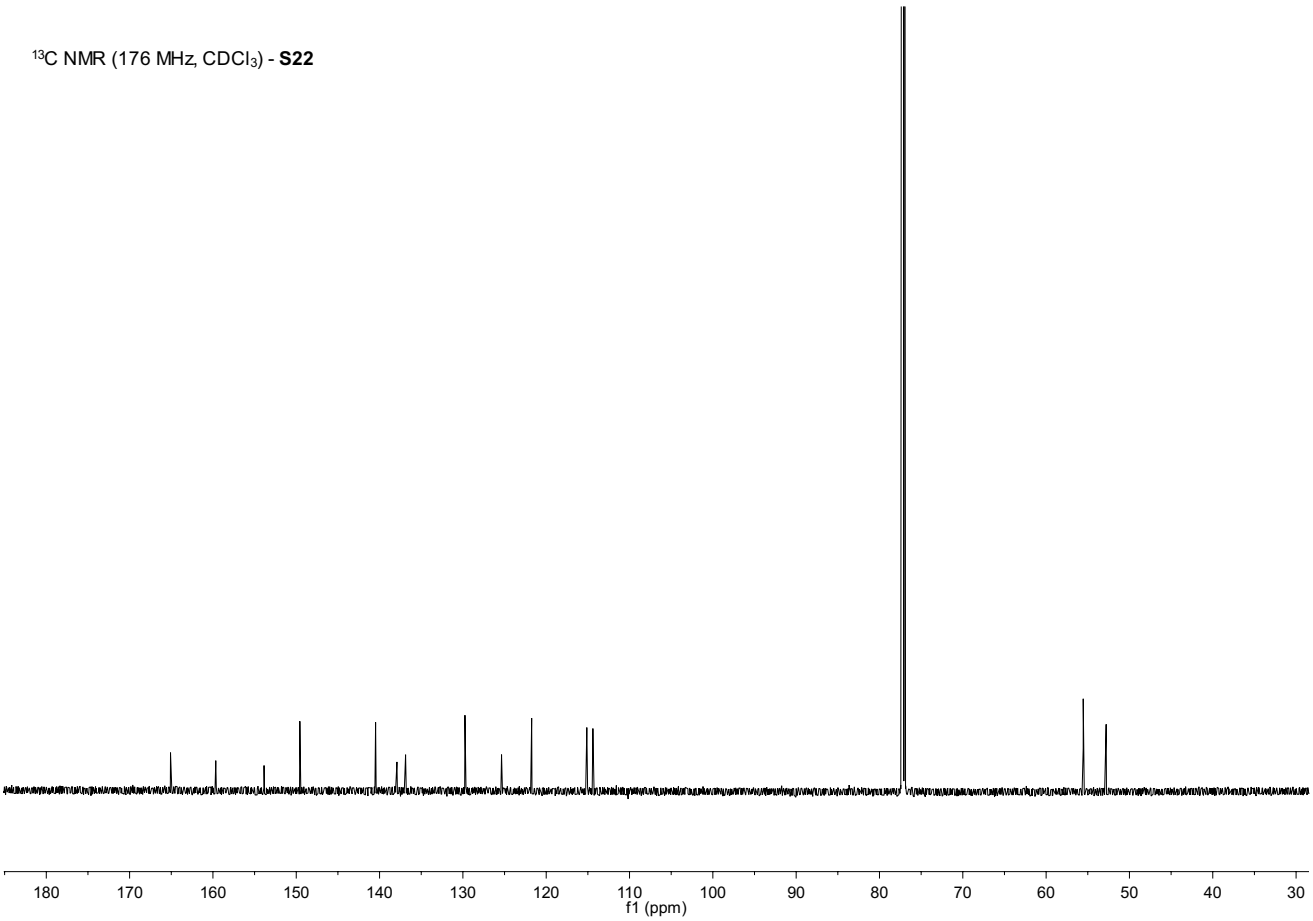
^{1}H NMR (700 MHz, $CDCl_3$) - **S22**



S22

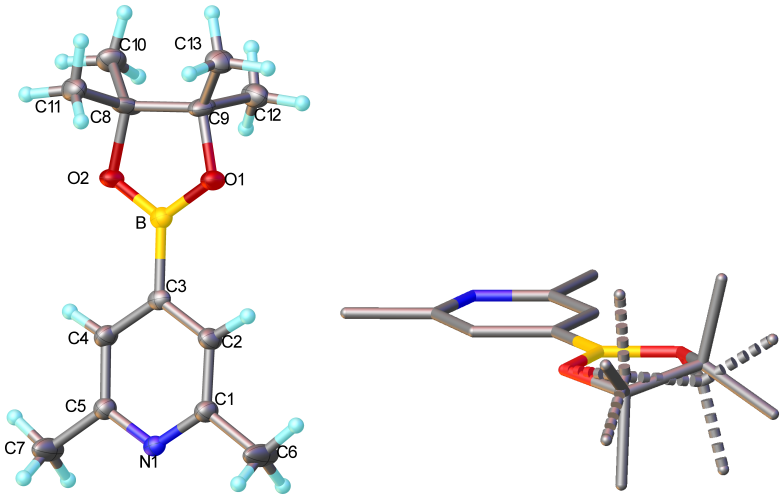


^{13}C NMR (176 MHz, $CDCl_3$) - **S22**



X-Ray Crystallography

The X-ray data were collected on Bruker 3-circle diffractometers with CCD area detectors ProteumM APEX (**5**), SMART 6000 (**39e**, **S4**, **S1**) and SMART 1000 (**S6, S7**), using graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å) from a sealed tube or (for **5**) a 60W Mo-target microfocus Bede Microsource X-ray generator with glass polycapillary X-ray optics. Crystals were cooled using Cryostream (Oxford Cryosystems) open flow N_2 cryostats. Reflection intensities were integrated using SAINT program.[3] The structures were solved by direct methods and refined by full matrix least squares (non-H atoms anisotropic, H atoms in riding model) against F^2 of all data, using OLEX2[4] and SHELXTL software[5] Crystal data and other experimental details are listed in Table X1, molecular structures are shown in Figs X1–X4. Molecule **5** lies on a crystallographic mirror (*m*) plane, which passes through B and O atoms, the pyridine ring and two adjacent methyl carbons. The C_2Me_4 moiety is disordered between two positions related via this plane and corresponding to two oppositely twisted conformations of the Bpin ring. Structure **S3** contains two symmetrically independent molecules of similar conformation. The absolute polarity of structure **S6** could not be established.

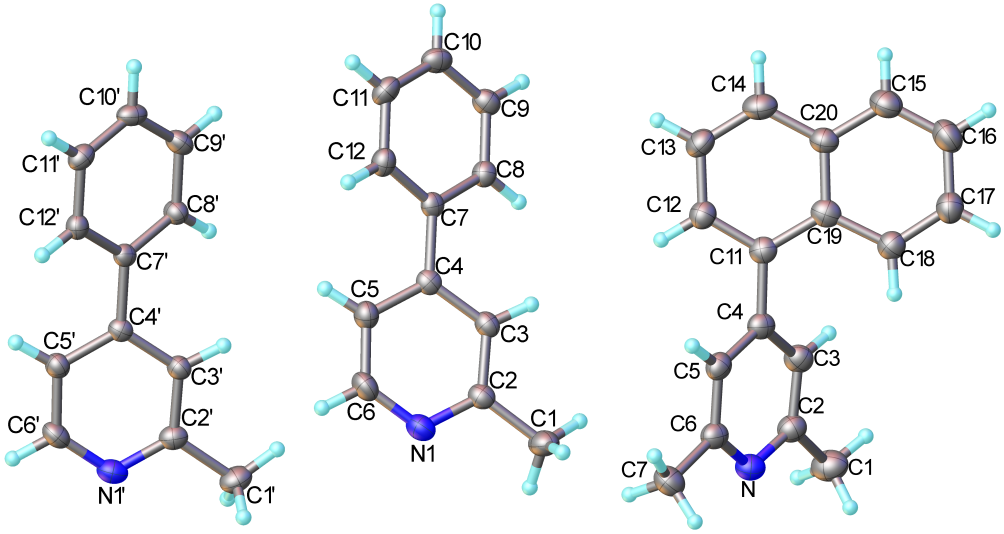


[3] SAINT version 6.45, Bruker AXS, Madison, WI, 2001

[4] Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.

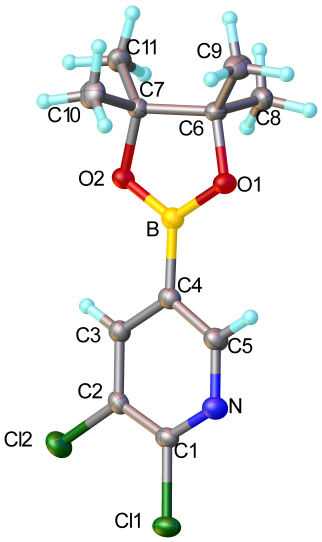
[5] Sheldrick, G.M. (2008). Acta Cryst. A64, 112-122

Fig. X1. Molecular structure of **5** in the crystal: Unique conformation (left) and disorder (right). Here and below thermal ellipsoids are drawn at 50% probability level.



(a) (b) (c)

Fig. X2. Two independent molecules of **S4** (a, b) and molecule of **S1** (c) in the crystal. Angles between arene and pyridine planes: 24.7º (a), 28.7º (b) and 51.2º (c).



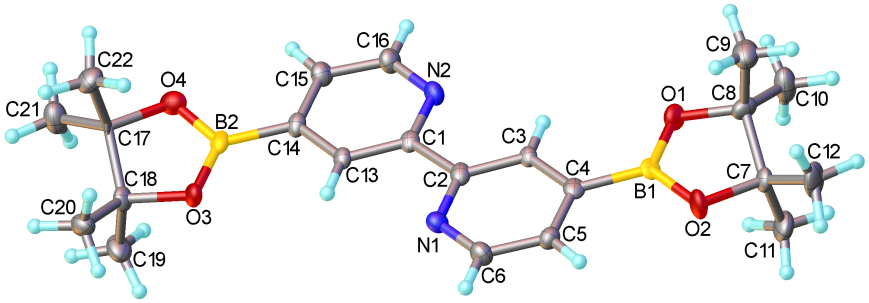


Fig. X3. Molecular structures of **39e** (left) and **S6** in the crystals. Boron atoms have planar-trigonal geometry. Angles between CBO_2 planes and the adjacent pyridine rings are 7.9º in **39e**, 6.0º and 9.4º in **S6**, that between pyridine rings in **S6** is 1.1º.

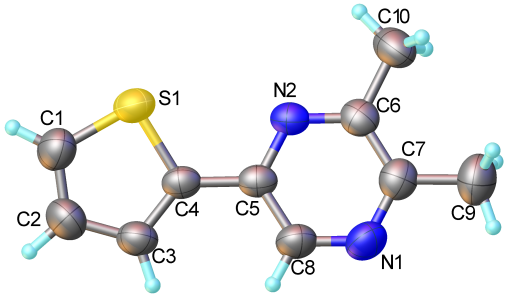


Fig. X4. Molecular structure of **S7** in the crystal. The heterocycles form an interplanar angle of 10.3º.

Table X1. Crystal data

Compound	**5**	**39e**	**S4**	**S1**	**S6**	**S7**
CCDC	988600	988601	988602	988603	988604	988605
Formula	$C_{13}H_{20}BNO_2$	$C_{11}H_{14}BCl_2NO_2$	$C_{12}H_{11}N$	$C_{17}H_{15}N$	$C_{22}H_{30}B_2N_2O_4$	$C_{10}H_{10}N_2S$
$D_{calc.}$/ g cm^{-3}	1.157	1.385	1.224	1.222	1.231	1.293
Formula weight	233.11	273.94	169.22	233.30	408.10	190.26
T/K	120	120	120	120	120	250
Crystal system	monoclinic	monoclinic	orthorhombic	monoclinic	orthorhombic	monoclinic
Space group	$P2_1/m$ (#11)	$P2_1/n$ (#14)	Pbca (#61)	$P2_1/c$ (#14)	$Pna2_1$ (#33)	$P2_1/c$ (#14)
a/Å	7.9952(15)	6.5381(4)	7.4760(6)	11.2252(16)	20.849(4)	7.1352(19)
b/Å	6.8431(13)	21.3579(12)	20.8897(14)	15.438(2)	6.6532(12)	12.292(3)
c/Å	12.251(2)	9.4192(5)	23.5283(17)	7.6917(12)	15.874(3)	11.175(3)
β/°	93.085(4)	93.137(2)	90	107.874(4)	90	94.168(4)
V/Å^3	669.3(2)	1313.33(13)	3674.4(5)	1268.6(3)	2201.9(7)	977.5(4)
Z	2	4	16	4	4	4
$2\Theta_{max}$/°	53	61	55	50.5	50	50
Measured refls.	3959	18635	30673	11358	10891	7011
Unique refls.	1496	4008	4220	2236	3720	1720
Refls with I>2σ(I)	1310	3283	2868	1286	2515	1411
R_{int}	0.020	0.028	0.060	0.088	0.080	0.024
Parameters	121	162	239	167	287	122
Dr max/min, *e*/Å^3	0.29, -0.25	0.36, -0.17	0.29, -0.19	0.21, -0.19	0.58, -0.25	0.16, -0.20
wR_2 (all data)	0.143	0.083	0.107	0.122	0.172	0.108
R_1 [I>2σ(I)]	0.055	0.031	0.039	0.045	0.069	0.037