Electronic Supplementary Information

For

Catalytic *meta*-selective C-H functionalization to construct quaternary carbon centres.

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General Considerations:

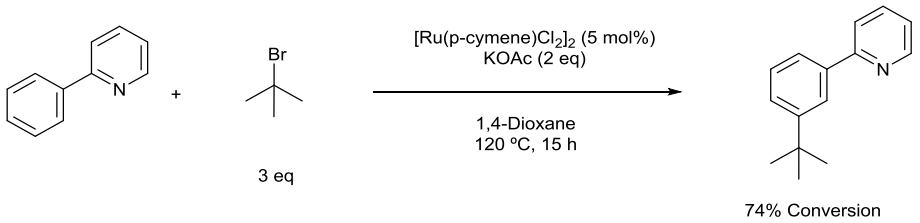
^{1}H, ^{13}C and ^{19}F nuclear magnetic resonance (NMR) spectra were recorded on an Agilent Technologies spectrometer (^{1}H NMR at 500 MHz, ^{13}C NMR at 126 MHz, and ^{19}F NMR at 470 MHz). Chemical shifts for protons are reported downfield from tetramethylsilane and are referenced to residual protium in the solvent (^{1}H NMR: $CHCl_3$ at 7.26 ppm). Chemical shifts for carbons are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent peak (^{13}C NMR: $CDCl_3$ at 77.0 ppm). Chemical shifts for fluorine resonances are reported in parts per million referenced to $CFCl_3$. NMR data are represented as follows: chemical shift (integration, multiplicity [s = singlet, bs = broad singlet, d = double, dd = doublet of doublet, t = triplet, q = quartet, hept = heptet, m = multiplet], coupling constants (Hz)). IR spectra were recorded on a Perkin-Elmer 1600 FT IR spectrophotometer, with absorbencies quoted as ν in cm^{-1}. High resolution mass spectrometry was performed on a Bruker Daltonik μTOF electrospray time-of-flight (ESI-TOF) mass spectrometer. HPLC analysis was conducted on an Agilent 1260 infinity quaternary LC instrument equipped with a Zorbax Eclipse XDB-C18 4.6 x 250 mm 5 μm analytical column. Analytical thin layer chromatography (TLC) were performed using aluminium-backed plates coated with Alugram® SIL G/UV_{254} purchased from Macherey-Nagel and visualised by UV light (254 nm) and/or $KMnO_4$, staining. Silica gel column chromatography was carried out using 60 Å, 200-400 mesh particle size silica gel purchased from Sigma-Aldrich.

Materials:

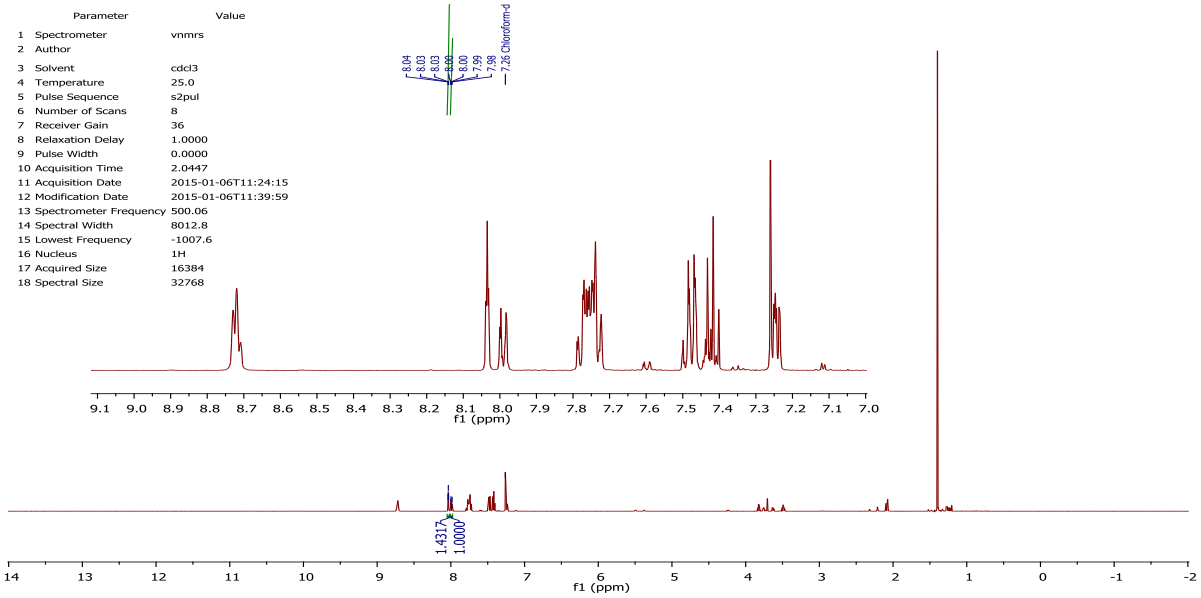
All reactions were carried out under an atmosphere of argon, in oven-dried glassware unless otherwise stated. Anhydrous solvents were used in all experiments and stored under an atmosphere of argon prior to use. $[RuCl_2(p\text{-cymene})]_2$ was purchased from Strem chemicals. Boronic acids were purchased from Fronteir Scientific. 2-chloro-2methylpropane, 2-bromo-2methylpropane, 2-bromo-2methylbutane, 1-bromo adamantine and 3-chloro-3-ethyl pentane were purchased from sigma Aldrich. All other chemicals were bought from Alfa Aesar. All commercially bought chemicals were used without further purification.

Reaction Conversions

Reaction conversions were calculated using ^{1}H NMR and confirmed using ^{19}F NMR where possible. With the exception of those carried out using ethyl 2-bromoisobutrate (**2c**) all reactions formed one product exclusively and thus conversions represent conversion of the starting material to the desired product. Suitably resolved signals in the crude reaction mixture were used for these calculations. Orthogonal analysis using TLC and HPLC-MS revealed negligible by-products. This is exemplified below.



Conversion by ^{1}H NMR of Crude Reaction Mixture: Signal at 8.05 ppm (dd, J = 1.8 Hz, 1H) from product **3a** and signal at 8.00 – 7.98 (m, J = 5.3, 3.4 Hz, 2H) from starting material **1a** used for conversion calculation.



HPLC analysis of the crude reaction mixture showing the major components: starting material **1a** (retention time 5.93 min) and product **3a** (retention time 11.28 min).

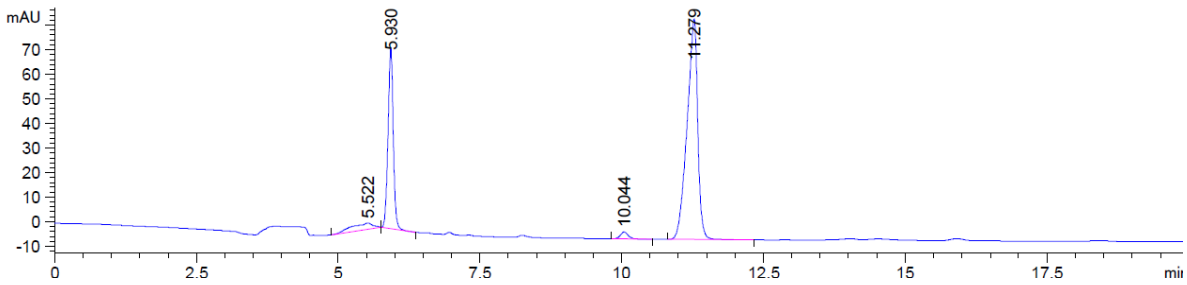
Sample prepared to approximate 10 µmol / mL in acetonitrile

Column: Zorbax Eclipse XDB-C18 4.6 x 250 mm 5 µm analytical column

Mobile Phase: Isocratic 70/30 acetonitrile/H_2O with 0.1% formic acid

Flow Rate: 0.5 mL / min

UV detection: 254 nm

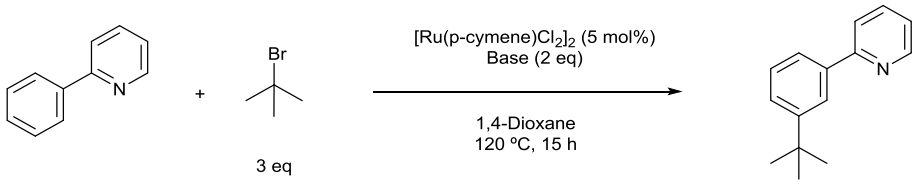


Reaction Optimisation

General Procedure

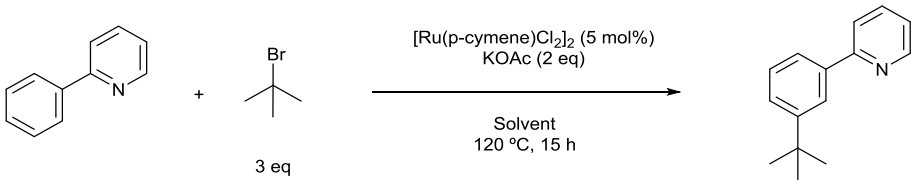
To an oven dried, argon purged ampule equipped with magnetic stirrer was added 2-phenylpyridine (1 mmol, 0.14 mL), a solvent (4 mL), 2-Bromo-2-methylpropane, $[RuCl_2(p\text{-cymene})]_2$ and a base in the amounts specified. The ampule was then sealed and refluxed on a carousel at 120 °C for the amount of time specified. After cooling to room temperature, aqueous $NaHCO_3$ (saturated) and EtOAc were added. A sample of the organic phase was taken, evaporated to dryness and then conversions analysed by ^1H NMR and HPLC-MS.

Base Screen



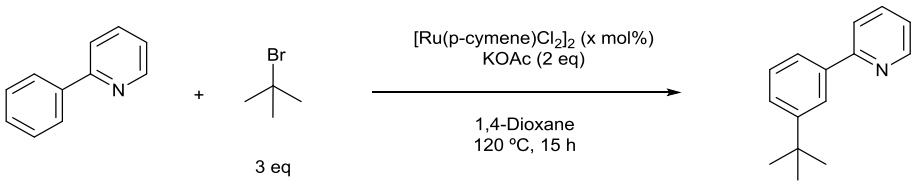
Base	Conversion (%)
No Base	0
K_2CO_3	12
NaOAc	31
KOAc	74
CsOAc	64
Bu_4NOAc	13
$Cu(OAc)_2$	0
AgOAc	0

Solvent Screen



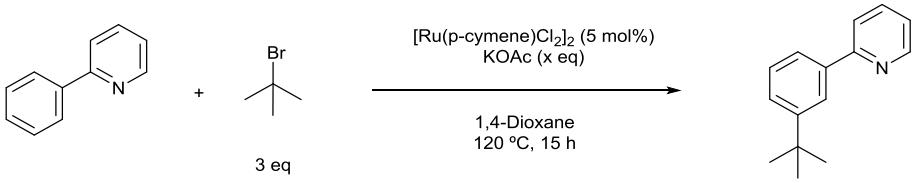
Solvent	Conversion (%)
No Solvent	69
2-Bromo-2-methylpropane	72
Acetonitrile	0
1,2-Dichloroethane	0
N-Methyl-2-pyrrolidone	0
2-methyl-2-butanol	61
H_2O	0
Toluene	66
Trifluoromethyl-benzene	70
Ethylene glycol	0
Dimethylformamide	0
Dimethoxyethane	56
Diglyme	43
Triglyme	44
THF	59
2-Methyltetrahydrofuran	68
Methyl tert-butyl ether	55
Cyclopentyl methyl ether	68
2-Butanone	61

Catalyst Loading



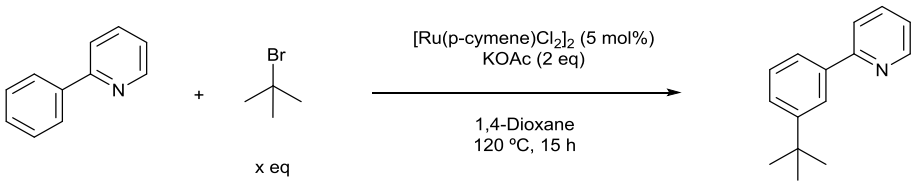
Catalyst Loading (mol %)	Conversion (%)
No Catalyst	0
0.5	7
1	50
2.5	58
5	74
7.5	68

KOAc Stoichiometry



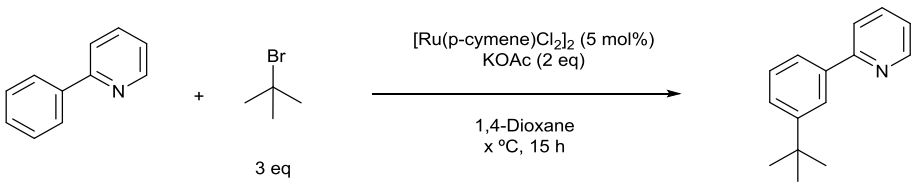
Base Equivalents	Conversion (%)
No Base	0
0.5	24
1.5	58
1.75	65
2	74
2.5	72
3	56
4	59

Alkyl Halide Stoichiometry



Alkyl Halide Equivalents	Conversion (%)
1	0
1.5	38
2	58
3	74
As solvent	72

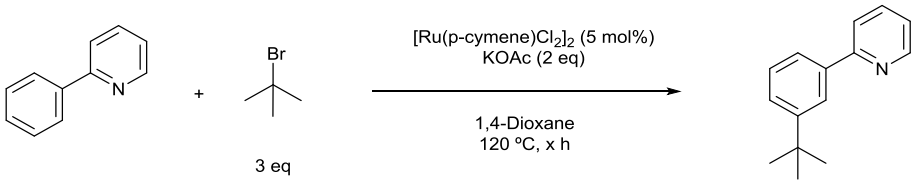
Temperature



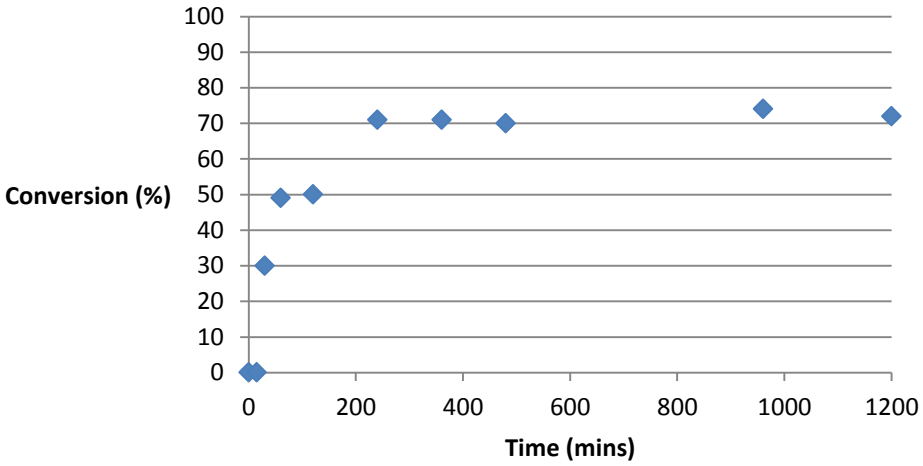
Temperature (°C)	Conversion (%)
25	0
80	18
100	50
120	74
135	65

Reaction Time

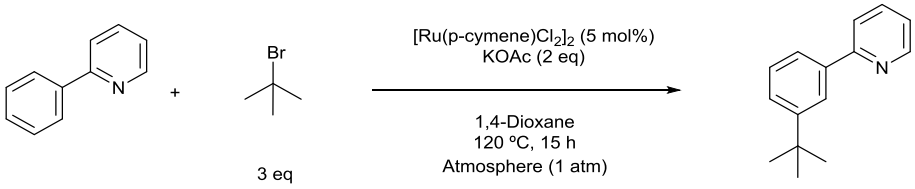
Multiple reactions were set up in series and after the designated reaction time were immediately cooled in an ice bath, worked up and analysed as per the general procedure.



Time (min)	Conversion (%)
0	0
15	0
30	30
60	49
120	50
240	71
360	71
480	70
960	74
1200	72



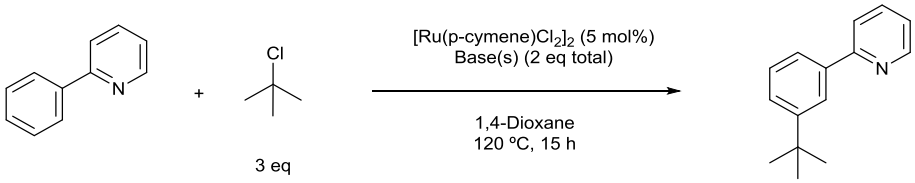
Reaction Atmosphere



Atmosphere (1 atm)	Conversion (%)
Argon	74
Air	25
Oxygen	0*

*****No formation of **3a**, starting material **1a** completely destroyed.

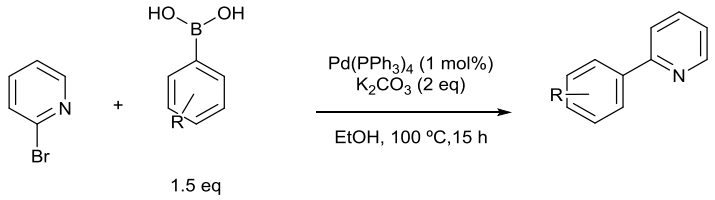
Optimisation for 2-Chloro-2-methylpropane



KOAc Equivalents	K_2CO_3 Equivalents	Conversion (%)
0	2	27
0.5	1.5	63
1	1	38
1.5	0.5	0
2	0	0

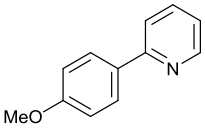
Synthesis of 2-Substituted Pyridine Derivatives

General Procedure



To an oven dried, argon purged flask equipped with magnetic stirrer and condenser was added $Pd(PPh_3)_4$ (1 mol%), K_2CO_3 (2 eq) and ethanol (1 M). A solution of the boronic acid (1.5 eq) in EtOH (1 M) was then added *via* a dropping funnel to the reaction vessel followed by the addition of 2-bromopyridine (1 eq). The reaction mixture was then heated to 100 °C and refluxed for 15 hours. After cooling to room temperature, aqueous NaOH (1 M) was added and extracted three times with EtOAc. The organic extracts were then combined, washed with brine, dried with $MgSO_4$ and then concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography (Hexane / EtOAc).

2-(4-methoxyphenyl)pyridine (1c)



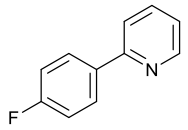
2-bromopyridine (25 mmol, 2.4 mL), 4-methoxyphenyl boronic acid (33 mmol, 5.0 g), $Pd(PPh_3)_4$ (0.25 mmol, 289 mg), K_2CO_3 (50 mmol, 6.90 g) were reacted together in EtOH (25 mL) according to the general procedure to afford the title compound as a white solid (4.4 g, 95%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.65 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H), 7.96 (d, *J* = 8.9 Hz, 2H), 7.76 – 7.64 (m, 2H), 7.17 (ddd, *J* = 7.2, 4.8, 1.3 Hz, 1H), 7.00 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.43, 157.08, 149.47, 136.67, 131.92, 128.15, 121.38, 119.79, 114.11, 55.34.

Data conforms to literature.[1]

2-(4-fluorophenyl)pyridine (1d)



2-bromopyridine (20 mmol, 1.9 mL), 4-fluorophenyl boronic acid (30 mmol, 4.20 g), $Pd(PPh_3)_4$ (0.2 mmol, 231 mg), and K_2CO_3 (40 mmol, 5.52 g) were reacted together in EtOH (20 mL) according to the general procedure to afford the title compound as a yellow / white crystalline solid (3.20 g, 92%).

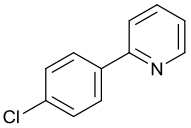
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (ddd, J = 4.8, 1.6, 0.9 Hz, 1H), 7.98 (dd, J = 8.9, 5.4 Hz, 2H), 7.77 – 7.72 (m, 1H), 7.68 (dt, J = 8.0, 1.0 Hz, 1H), 7.22 (ddd, J = 7.4, 4.8, 1.1 Hz, 1H), 7.16 (t, J = 8.7 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 163.51 (d, $^1J_{C\text{-}F}$ = 248.4 Hz), 135.51 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 128.68 (d, $^3J_{C\text{-}F}$ = 8.4 Hz), 115.63 (d, $^2J_{C\text{-}F}$ = 21.6 Hz).

^{19}F NMR (470 MHz, $CDCl_3$) δ -113.14 – -113.24 (m).

Data conforms to literature.[1]

2-(4-chlorophenyl)pyridine (1e)



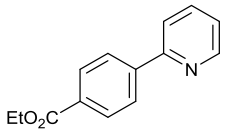
2-bromopyridine (13 mmol, 1.2 mL), 4-chlorophenyl boronic acid (20 mmol, 3.04 g), $Pd(PPh_3)_4$ (0.13 mmol, 150 mg), and K_2CO_3 (26 mmol, 3.58 g) were reacted together in EtOH (13 mL) according to the general procedure to afford the title compound as a pale yellow crystalline solid (1.20 g, 89%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (dd, J = 4.8, 0.8 Hz, 1H), 7.95 (d, J = 8.4 Hz, 2H), 7.81 – 7.74 (m, 1H), 7.71 (dd, J = 7.9, 0.9 Hz, 1H), 7.45 (d, J = 8.5 Hz, 2H), 7.29 – 7.24 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.97, 149.35, 137.31, 137.26, 135.30, 128.97, 128.23, 122.45, 120.49.

Data conforms to literature.[1]

2-(4-(ethoxycarbonyl)phenyl)pyridine (1f)



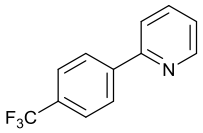
2-bromopyridine (13 mmol, 1.2 mL), 4-(methoxycarbonyl)phenyl boronic acid (20 mmol, 3.04 g), $Pd(PPh_3)_4$ (0.13 mmol, 150 mg), and K_2CO_3 (26 mmol, 3.58 g) were reacted together in EtOH (13 mL) according to the general procedure to afford the title compound as a white solid (2.42 g, 82%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (d, *J* = 4.6 Hz, 1H), 8.15 (d, *J* = 8.2 Hz, 2H), 8.07 (d, *J* = 8.3 Hz, 2H), 7.87 – 7.71 (m, 2H), 7.29 (dd, *J* = 8.3, 4.8 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 166.56, 156.38, 149.93, 143.42, 137.15, 130.90, 130.16, 126.95, 123.00, 121.19, 77.16, 61.22, 14.50.

Data conforms to literature.[1]

2-(4-(trifluoromethyl)phenyl)pyridine (1g)



2-bromopyridine (10 mmol, 0.92 mL), 4-(trifluoromethyl)phenyl boronic acid (15 mmol, 2.85 g), $Pd(PPh_3)_4$ (0.10 mmol, 115 mg), and K_2CO_3 (20 mmol, 2.76 g) were reacted together in EtOH (10 mL) according to the general procedure to afford the title compound as an off white solid (1.38 g, 62%).

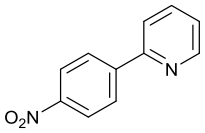
1H NMR (500 MHz, $CDCl_3$) δ 8.73 (d, J = 4.7 Hz, 1H), 8.11 (d, J = 8.2 Hz, 2H), 7.84 – 7.69 (m, 4H), 7.33 – 7.27 (m, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.98 (s), 150.03 (s), 142.77 (s), 137.13 (s), 130.91 (q, $^2J_{C\text{-}F}$ = 32.5 Hz), 127.31 (s), 125.81 (q, $^3J_{C\text{-}F}$ = 3.8 Hz), 124.32 (q, $^1J_{C\text{-}F}$ = 272.0 Hz), 123.09 (s), 121.00 (s).

^{19}F NMR (470 MHz, $CDCl_3$) δ -62.61 (s).

Data conforms to literature.[2]

2-(4-(trifluoromethyl)phenyl)pyridine (1h)



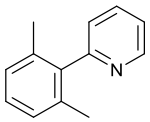
2-bromopyridine (4.5 mmol, 0.43 mL), 4-nitrophenyl boronic acid (6 mmol, 1.0 g), $Pd(PPh_3)_4$ (0.045 mmol, 52 mg), and K_2CO_3 (9 mmol, 1.24 g) were reacted together in EtOH (5 mL) according to the general procedure to afford the title compound as a yellow solid (609 mg, 68%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.7 Hz, 1H), 8.34 (d, *J* = 8.6 Hz, 2H), 8.19 (d, *J* = 8.6 Hz, 2H), 7.89 – 7.74 (m, 2H), 7.35 (t, *J* = 5.6 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 155.03, 150.30, 148.22, 145.41, 137.26, 127.83, 124.16, 123.66, 121.36

Data conforms to literature.[1]

2-(2,6-dimethylphenyl)pyridine (1i)



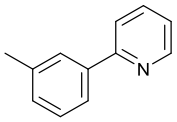
2-bromopyridine (13 mmol, 1.2 mL), 2,6-dimethylphenylboronic acid (20 mmol, 3.0 g), $Pd(PPh_3)_4$ (0.13 mmol, 150 mg), and K_2CO_3 (26 mmol, 3.59 g) were reacted together in EtOH (15 mL) according to the general procedure to afford the title compound as a red oil (1.96 g, 82%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 4.5 Hz, 1H), 7.82 (dd, *J* = 7.6 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.28 (d, *J* = 8.2 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 2H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.56, 149.17, 139.76, 137.09, 135.93, 128.25, 127.72, 124.93, 122.02, 77.16, 20.33.

Data conforms to literature.[3]

2-(3-dimethylphenyl)pyridine (1j)



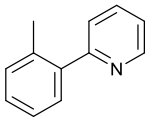
2-bromopyridine (5 mmol, 0.46 mL), 3-methylphenylboronic acid (7 mmol, 1.0 g), $Pd(PPh_3)_4$ (0.05 mmol, 58 mg), and K_2CO_3 (10 mmol, 1.38 g) were reacted together in EtOH (7.5 mL) according to the general procedure to afford the title compound as a yellow oil (772 mg, 91%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.73 (d, J = 4.7 Hz, 1H), 7.87 (s, 1H), 7.84 – 7.73 (m, 3H), 7.39 (dd, J = 7.6 Hz, 1H), 7.29 – 7.24 (m, 2H), 2.46 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.40, 149.18, 138.81, 138.50, 137.16, 129.94, 128.69, 127.72, 124.09, 122.11, 120.86, 21.51.

Data conforms to literature. [4]

2-(2-methylphenyl)pyridine (1l)



2-bromopyridine (20 mmol, 1.84 mL), 2-methylphenylboronic acid (30 mmol, 4.08 g), $Pd(PPh_3)_4$ (0.2 mmol, 231 mg), and K_2CO_3 (40 mmol, 5.52 g) were reacted together in EtOH (30 mL) according to the general procedure to afford the title compound as a yellow oil (2.96 g, 88%).

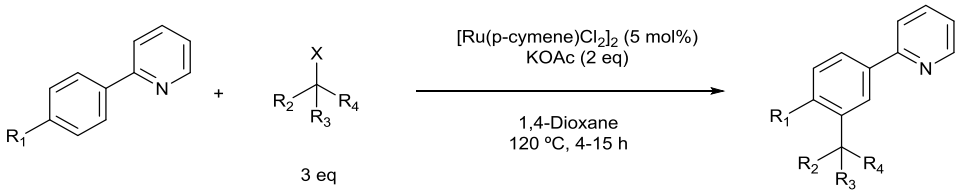
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (d, *J* = 3.9 Hz, 1H), 7.85 – 7.69 (m, 1H), 7.42 (dd, *J* = 13.6, 4.5 Hz, 2H), 7.33 – 7.25 (m, 4H), 2.29 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.67, 148.75, 139.86, 136.60, 135.77, 130.77, 129.64, 128.46, 125.91, 124.30, 121.76, 20.27.

Data conforms to literature. [3]

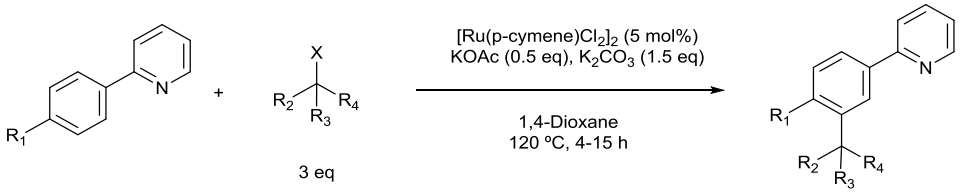
Synthesis of *meta*-Substituted 2-Phenylpyridine Derivatives.

General Procedure A



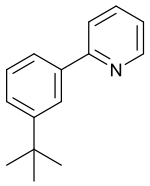
To an oven dried, argon purged ampule equipped with magnetic stirrer was added the 2-phenylpyridine derivative (1 mmol), the alkyl halide (3mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), KOAc (2 mmol, 196 mg) and 1,4-Dioxane (4 mL). The ampule was then sealed and refluxed on a carousel at 120 °C for the amount of time specified. After cooling to room temperature, aqueous $NaHCO_3$ (saturated) was added and then was extracted three times with EtOAc. The organic extracts were then combined, washed with brine, dried with $MgSO_4$ and then concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography (Hexane / EtOAc).

General Procedure B



To an oven dried, argon purged ampule equipped with magnetic stirrer was added the 2-phenylpyridine derivative (1 mmol), the alkyl halide (3mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg), K_2CO_3 (1.5 mmol, 207 mg) and 1,4-Dioxane (4 mL). The ampule was then sealed and refluxed on a carousel at 120 °C for the amount of time specified. After cooling to room temperature, aqueous $NaHCO_3$ (saturated) was added and then was extracted three times with EtOAc. The organic extracts were then combined, washed with brine, dried with $MgSO_4$ and then concentrated under reduced pressure. The crude product was then purified by silica gel column chromatography (Hexane / EtOAc).

2-(3-tert-butylphenyl)pyridine (3a)



2-phenylpyridine (1 mmol, 0.14 mL), 2-bromo-2-methylpropane (3 mmol, 0.34 mL), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford the title compound as a yellow oil (15 mg, 7%).

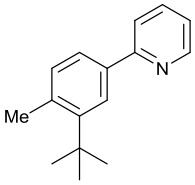
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (d, *J* = 4.8 Hz, 1H), 8.05 (dd, *J* = 1.8 Hz, 1H), 7.86 – 7.65 (m, 3H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.22 (ddd, *J* = 6.7, 4.9, 1.9 Hz, 1H), 1.40 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.19, 151.74, 149.75, 139.32, 136.78, 128.57, 126.20, 124.30, 124.10, 122.04, 120.90, 77.16, 35.01, 31.54.

HR-MS (ESI) *m/z*: calculated for $C_{15}H_{18}N$ $[M+H]^+$ 212.1439, found: 212.1395

ν_{max} (neat) / cm^{-1}; 2960, 1584, 1564, 1461

2-(3-tert-butyl-4-methylphenyl)pyridine (3b)



2-(4-methylphenyl)lpyridine (1 mmol, 0.17 mL), 2-bromo-2-methylpropane (3 mmol, 0.34 mL), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford the title compound as a colourless oil (12 mg, 5%).

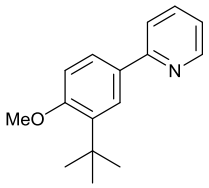
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (d, *J* = 4.0 Hz, 1H), 8.05 (s, 1H), 7.77 (dd, *J* = 7.4 Hz, 1H), 7.74 – 7.68 (m, 2H), 7.24 (d, *J* = 7.6 Hz, 2H), 2.60 (s, 3H), 1.49 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.83, 151.32, 149.12, 148.63, 137.41, 133.47, 125.07, 124.54, 122.86, 121.93, 120.90, 36.18, 30.98, 23.27.

HR-MS (ESI) *m/z*: calculated for $C_{16}H_{19}N$ $[M+H]^+$ 226.1596, found: 226.1594

ν_{max} (neat) / cm^{-1}; 2958, 1586, 1464, 1433

2-(3-tert-butyl-4-methoxyphenyl)pyridine (3c)



2-(4-methoxyphenyl)pyridine (1 mmol, 185 mg), 2-bromo-2-methylpropane (3 mmol, 0.34 mL), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford the title compound as a colourless oil (100 mg, 42%).

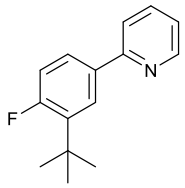
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (d, J = 4.7 Hz, 1H), 7.96 (d, J = 1.3 Hz, 1H), 7.83 (d, J = 8.4 Hz, 1H), 7.74 (t, J = 7.5 Hz, 1H), 7.68 (d, J = 7.9 Hz, 1H), 7.19 (br s, 1H), 6.98 (d, J = 8.5 Hz, 1H), 3.90 (s, 3H), 1.44 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.84, 157.66, 149.06, 138.70, 137.25, 126.05, 125.71, 121.40, 120.38, 111.84, 77.16, 55.29, 35.19, 29.84.

HR-MS (ESI) *m/z*: calculated for $C_{16}H_{19}NO$ $[M+H]^+$ 242.1545, found: 242.1549

ν_{max} (neat) / cm^{-1}; 2954, 1586, 1462, 1430

2-(3-tert-butyl-4-fluorophenyl)pyridine (3d)



2-(4-fluorophenyl)pyridine (1 mmol, 173 mg), 2-bromo-2-methylpropane (3 mmol, 0.34 mL), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K_2CO_3 (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a colourless oil (140 mg, 61%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4.6 Hz, 1H), 8.00 (d, *J* = 8.1 Hz, 1H), 7.79 – 7.74 (m, 1H), 7.70 (dd, *J* = 7.1 Hz, 1H), 7.65 (d, *J* = 7.9 Hz, 1H), 7.22 – 7.16 (m, 1H), 7.08 (dd, *J* = 12.0, 8.6 Hz, 1H), 1.46 (s, 9H).

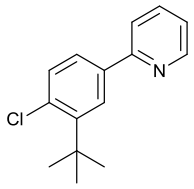
^{13}C NMR (126 MHz, $CDCl_3$) δ 162.83 (d, $^1J_{C\text{-}F}$ = 250.7 Hz), 157.14 (s), 149.60 (s), 137.41 (d, $^2J_{C\text{-}F}$ = 12.1 Hz), 136.82 (s), 135.13 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 126.29 (d, $^3J_{C\text{-}F}$ = 6.4 Hz), 126.25 (d, $^3J_{C\text{-}F}$ = 9.3 Hz), 121.89 (s), 120.43 (s), 116.64 (d, $^2J_{C\text{-}F}$ = 25.0 Hz), 34.53 (d, $^3J_{C\text{-}F}$ = 2.7 Hz), 29.97 (d, $^4J_{C\text{-}F}$ = 3.4 Hz).

^{19}F NMR (470 MHz, $CDCl_3$) δ -109.38 (s).

HR-MS (ESI) *m/z*: calculated for $C_{15}H_{16}NF$ $[M+H]^+$ 230.1345, found: 230.1342

ν_{max} (neat) / cm^{-1}; 2959, 1589, 1461, 1433

2-(3-tert-butyl-4-chlorophenyl)pyridine (3e)



2-4-(chlorophenyl)pyridine (1 mmol, 190 mg), 2-bromo-2-methylpropane (3 mmol, 0.34 mL), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford the title compound as a colourless oil (70 mg, 25%).

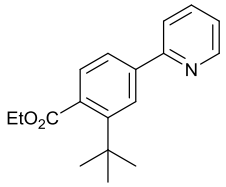
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 (d, *J* = 4.1 Hz, 1H), 8.10 (d, *J* = 2.2 Hz, 1H), 7.81 (td, *J* = 7.8, 1.8 Hz, 1H), 7.72 (d, *J* = 8.2 Hz, 1H), 7.72 (d, *J* = 8.3 Hz, 1H), 7.45 (d, *J* = 8.2 Hz, 1H), 7.29 (ddd, *J* = 7.3, 4.9, 0.8 Hz, 1H), 1.55 (s, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 156.47, 148.97, 146.95, 137.60, 136.82, 135.08, 132.37, 126.67, 125.65, 122.36, 120.91, 36.31, 29.58.

HR-MS (ESI) *m/z*: calculated for $C_{15}H_{16}NCl$ $[M+H]^+$ 246.1050, found: 246.1030

ν_{max} (neat) / cm^{-1}; 2960, 1586, 1459, 1431

ethyl 2-tert-butyl-4-(pyridin-2-yl)benzoate (3f)



2-(4-(ethoxycarbonyl)phenyl)pyridine (1 mmol, 190 mg), 2-bromo-2-methylpropane (3 mmol, 0.34 mL), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford the title compound as a colourless oil (23 mg, 8%).

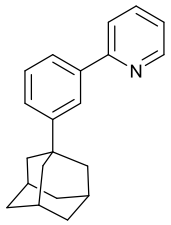
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, *J* = 3.7 Hz, 1H), 8.17 (s, 1H), 7.85 – 7.78 (m, *J* = 13.6, 7.5 Hz, 2H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 7.9 Hz, 1H), 7.33 – 7.28 (m, 1H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.48 (s, 9H), 1.40 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 171.75, 156.49, 149.00, 148.31, 139.50, 137.64, 133.94, 129.34, 125.93, 124.05, 122.62, 121.26, 61.48, 36.20, 31.36, 14.08.

HR-MS (ESI) *m/z*: calculated for $C_{18}H_{21}NO_2$ $[M+H]^+$ 284.1651, found: 284.1645

ν_{max} (neat) / cm^{-1}; 2965, 1722, 1586, 1464, 1434

2-(3-(adamantan-1-yl)phenyl)pyridine (4a)



2-Phenylpyridine (1 mmol, 140 µL), 1-adamantyl bromide (3.00 mmol, 645 mg), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K_2CO_3 (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a white solid (15 mg, 5%).

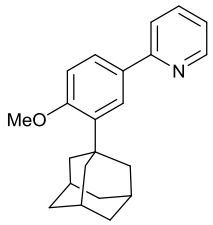
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.75 (d, *J* = 4.6 Hz, 1H), 8.14 – 7.96 (m, 1H), 7.85 – 7.74 (m, 3H), 7.50 – 7.42 (m, 2H), 7.31 – 7.24 (m, 1H), 2.14 (s, 3H), 2.02 (s, 6H), 1.85 – 1.76 (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.29, 152.00, 149.76, 139.35, 136.74, 128.60, 125.79, 124.36, 123.80, 122.00, 120.87, 43.34, 36.95, 36.54, 29.13.

HR-MS (ESI) *m*/*z*: calculated for $C_{21}H_{23}NO$ $[M+H]^+$ 290.1909, found: 290.1883

ν_{max} (neat) / cm^{-1}; 3252, 2898, 2856, 1622, 1584, 1564, 1461

2-(3-(adamantan-1-yl)-4-methoxyphenyl)pyridine (4c)



2-(4-Methoxyphenyl)pyridine (1 mmol, 185 mg), 1-adamantyl bromide (3.00 mmol, 645 mg), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K_2CO_3 (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a white solid (114 mg, 36%). Crystals large enough for single crystal X-ray analysis were generated using $CHCl_3$ / Hexane.

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (ddd, *J* = 4.9, 1.7, 1.0 Hz, 1H), 7.92 (d, *J* = 2.3 Hz, 1H), 7.81 (dd, *J* = 8.5, 2.3 Hz, 1H), 7.74 – 7.69 (m, 1H), 7.68 (ddd, *J* = 8.0, 1.2 Hz, 1H), 7.17 (ddd, *J* = 7.0, 4.9, 1.4 Hz, 1H), 6.97 (d, *J* = 8.5 Hz, 1H), 3.89 (s, 3H), 2.20 – 2.15 (m, *J* = 2.9 Hz, 6H), 2.09 (s, 3H), 1.79 (s, 6H).

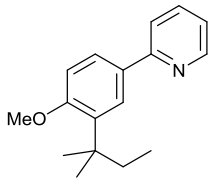
^{13}C NMR (126 MHz, $CDCl_3$) δ 159.99, 157.81, 149.31, 138.83, 136.95, 131.29, 125.67, 125.64, 121.32, 120.22, 111.90, 55.24, 40.64, 37.29, 37.25, 29.22

HR-MS (ESI) *m*/*z*: calculated for $C_{22}H_{25}NO$ $[M+H]^+$ 320.2014, found: 320.2008

Crystal Data 4c, C22H25NO (M = 319.43 g/mol): monoclinic, space group P21/c (no. 14), a = 12.82457(18), b = 6.61539(9), c = 20.0798(3) Å, β = 93.3829(13)°, U = 1700.59(4) Å3, Z = 4, T = 150(2) K, μ(CuKα) = 0.581 mm-1, Dcalc = 1.248 g/cm3, 17596 reflections measured (8.82° ≤ 2θ ≤ 143.96°), 3328 unique (Rint = 0.0403, Rsigma = 0.0297) which were used in all calculations. The final R1 was 0.0384 (I>2σ(I)) and wR2 was 0.0964 (all data).

Crystallographic data have been deposited with Cambridge Crystallographic Data Centre; CCDC-1064109. Copies of these data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; Fax: +44 1223 336033; email: deposit@ccdc.cam.ac.uk).

2-[4-methoxy-3-(2-methylbutan-2-yl)phenyl]pyridine (5c)



2-(4-Methoxyphenyl)pyridine (1 mmol, 185 mg), 2-chloro-2-methylbutane (367 µL, 3 mmol), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K_2CO_3 (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a colourless oil (139 mg, 54%).

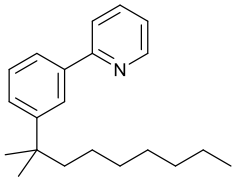
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.67 (ddd, J = 4.9, 1.7, 1.0 Hz, 1H), 7.90 (d, J = 2.3 Hz, 1H), 7.83 (dd, J = 8.5, 2.3 Hz, 1H), 7.73 – 7.69 (m, 1H), 7.68 (ddd, J = 8.0, 1.2 Hz, 1H), 7.21 – 7.05 (m, 1H), 6.96 (d, J = 8.5 Hz, 1H), 3.87 (s, 3H), 1.89 (q, J = 7.5 Hz, 2H), 1.41 (s, 6H), 0.66 (t, J = 7.5 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 159.68, 157.79, 149.33, 136.91, 136.87, 131.11, 126.92, 125.89, 121.30, 120.20, 111.62, 55.28, 38.79, 33.22, 28.01, 9.78.

HR-MS (ESI) *m/z*: calculated for $C_{17}H_{21}NO$ $[M+H]^+$ 256.1701, found: 256.1725

ν_{max} (neat) / cm^{-1}; 2979, 1602, 1585, 1562, 1460

2-[3-(2-methylnonan-2-yl)phenyl]pyridine (6a)



2-Phenylpyridine (1 mmol, 140 µL), 2-chloro-2-methylnonane (3 mmol, 530 mg), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K_2CO_3 (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a colourless oil (146 mg, 43%).

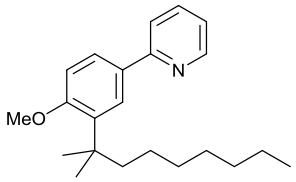
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.72 (d, *J* = 4.7 Hz, 1H), 8.00 – 7.96 (m, 1H), 7.83 – 7.71 (m, 3H), 7.46 – 7.39 (m, 2H), 7.28 – 7.22 (m, 1H), 1.70 – 1.62 (m, 2H), 1.37 (s, 6H), 1.30 – 1.04 (m, 10H), 0.84 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 157.85, 150.47, 149.20, 138.55, 137.09, 128.43, 126.85, 124.58, 124.14, 121.98, 120.95, 44.63, 37.90, 31.87, 30.31, 29.23, 29.01, 24.76, 22.65, 14.09.

HR-MS (ESI) *m/z*: calculated for $C_{21}H_{29}NO$ $[M+H]^+$ 296.2378, found: 296.2401

ν_{max} (neat) / cm^{-1}; 2957, 2926, 2855, 1584, 1564, 1461

2-[4-methoxy-3-(2-methylnonan-2-yl)phenyl]pyridine (6c)



2-(4-methoxyphenyl)pyridine (1 mmol, 185 mg), 2-chloro-2-methylnonane (3 mmol, 530 mg), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K_2CO_3 (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a colourless oil (139 mg, 54%).

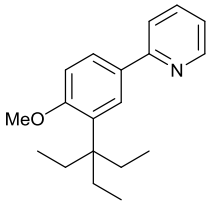
^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.67 (d, J = 4.6 Hz, 1H), 7.91 (d, J = 1.9 Hz, 1H), 7.84 (dd, J = 8.5, 2.3 Hz, 1H), 7.74 – 7.65 (m, 2H), 7.20 – 7.12 (m, 1H), 6.95 (d, J = 8.5 Hz, 1H), 3.87 (s, 3H), 1.93 – 1.78 (m, 2H), 1.44 (d, J = 6.7 Hz, 6H), 1.31 – 1.15 (m, 8H), 1.06 – 0.97 (m, 2H), 0.85 (t, J = 7.1 Hz, 3H).

^{13}C NMR: (126 MHz, $CDCl_3$) δ 159.59, 157.64, 149.17, 137.12, 136.84, 130.93, 126.64, 125.77, 121.20, 120.09, 111.51, 55.13, 40.80, 38.42, 31.89, 30.39, 29.21, 28.48, 25.26, 22.69, 14.12.

HR-MS (ESI) *m/z*: calculated for $C_{22}H_{31}NO$ $[M+H]^+$ 326.2484, found: 326.2521

ν_{max} (neat) / cm^{-1}; 2951, 2921, 2854, 1602, 1588, 1498, 1462

2-(3-(3-ethylpentan-3-yl)-4-methoxyphenyl)pyridine (7c)



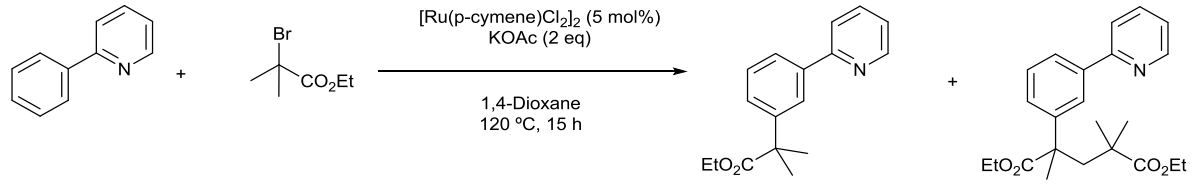
2-(4-methoxyphenyl)pyridine (1 mmol, 185 mg), 3-chloro-3-ethylpentane (1.70 mmol, 229 mg), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), KOAc (0.5 mmol, 49 mg) and K_2CO_3 (1.5 mmol, 207 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure B to afford the title compound as a colourless oil (139 mg, 54%).

^{1}H NMR: (500 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.95 – 7.68 (m, 4H), 7.22 (s, 1H), 6.97 (d, *J* = 6.2 Hz, 1H), 3.86 (s, 3H), 1.88 (q, *J* = 7.2 Hz, 6H), 0.66 (t, *J* = 7.3 Hz, 9H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 160.11, 157.43, 148.85, 137.83, 135.10, 129.89, 128.57, 126.10, 121.57, 120.67, 111.80, 77.16, 55.44, 44.78, 26.21, 8.65.

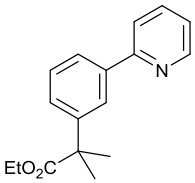
HR-MS (ESI) *m/z*: calculated for $C_{19}H_{25}NO$ $[M+H]^+$ 284.1936, found: 284.1949

ν_{max} (neat) / cm^{-1}; 2979, 2888, 1603, 1587, 1494, 1460



2-phenylpyridine (1 mmol, 0.14 mL), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A. The crude mixture was purified by flash column chromatography to yield products **8a** (125 mg, 46%) as a colourless oil and product **9a** (25 mg, 9%) as a colourless oil.

ethyl 2-methyl-2-[3-(pyridin-2-yl)phenyl]propanoate (8a)



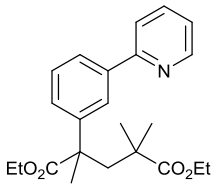
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (ddd, *J* = 4.9, 1.7, 1.0 Hz, 1H), 7.99 (dd, *J* = 1.9 Hz, 1H), 7.86 – 7.83 (m, 1H), 7.77 – 7.74 (m, 1H), 7.71 (ddd, *J* = 8.0, 1.1 Hz, 1H), 7.43 (dd, *J* = 7.7 Hz, 1H), 7.40 – 7.37 (m, 1H), 7.23 (ddd, *J* = 7.3, 4.9, 1.3 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 1.64 (s, 6H), 1.18 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 176.80, 157.50, 149.54, 145.50, 139.34, 137.05, 128.87, 126.72, 125.45, 124.36, 122.27, 120.92, 60.96, 46.73, 26.70, 14.18.

HR-MS (ESI) *m/z*: calculated for $C_{17}H_{19}NO_2$ $[M+H]^+$ 270.1494, found: 270.1533

ν_{max} (neat) / cm^{-1}; 2978, 1722, 1584, 1461, 1433

diethyl 2,2,3-trimethyl-3-[3-(pyridin-2-yl)benzyl]butanedioate (9a)

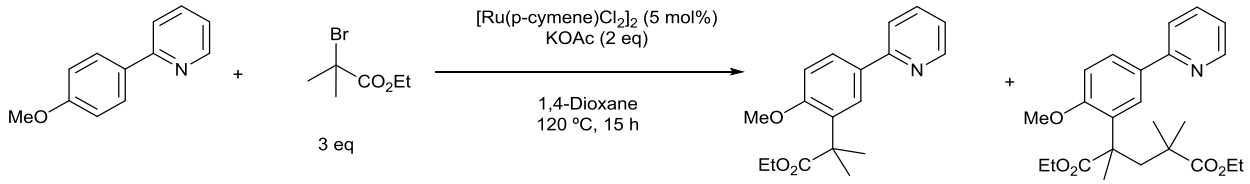


^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (d, J = 4.8 Hz, 1H), 8.02 (s, 1H), 7.86 (d, J = 7.3 Hz, 1H), 7.77 (dd, J = 7.6 Hz, 1H), 7.72 (d, J = 7.9 Hz, 1H), 7.47 – 7.39 (m, 2H), 7.26 – 7.23 (m, 1H), 4.24 – 3.98 (m, 4H), 2.64 (d, J = 14.5 Hz, 1H), 2.56 (d, J = 14.5 Hz, 1H), 1.57 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H), 1.20 (t, J = 7.1 Hz, 3H), 1.20 (s, 3H), 1.13 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 178.44, 176.08, 157.25, 149.16, 145.42, 137.59, 136.00, 128.97, 127.11, 125.76, 124.90, 122.43, 121.20, 61.19, 60.69, 49.64, 48.05, 41.92, 29.35, 23.99, 21.04, 14.20, 14.09.

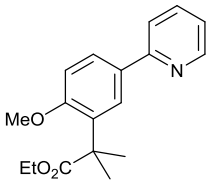
HR-MS (ESI) *m/z*: calculated for $C_{23}H_{29}NO_4Na$ $[M+Na]^+$ 406.1994, found: 406.1971

ν_{max} (neat) / cm^{-1}; 2979, 1721, 1584, 1461



2-(4-methoxyphenyl)pyridine (1 mmol, 185 mg), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A. The crude mixture was purified by flash column chromatography to yield products **8c** (170 mg, 57%) as a white amorphous solid and product **9c** (45 mg, 12%) as a colourless oil.

ethyl 2-[2-methoxy-5-(pyridin-2-yl)phenyl]-2-methylpropanoate (8c)



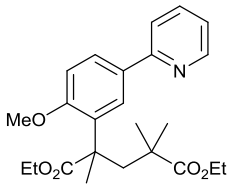
^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (d, *J* = 4.4 Hz, 1H), 7.99 (d, *J* = 2.1 Hz, 1H), 7.86 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.73 (dd, *J* = 7.5 Hz, 1H), 7.69 (d, *J* = 7.9 Hz, 1H), 7.21 – 7.14 (m, 1H), 6.94 (d, *J* = 8.5 Hz, 1H), 4.11 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 1.59 (s, 6H), 1.15 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 177.87, 157.87, 157.36, 149.31, 137.08, 134.68, 131.52, 126.70, 124.68, 121.55, 120.28, 110.96, 60.44, 55.37, 44.55, 25.74, 14.32.

HR-MS (ESI) *m/z*: calculated for $C_{18}H_{22}NO_3$ $[M+H]^+$ 300.1600, found: 300.1613

ν_{max} (neat) / cm^{-1}; 2979, 1727, 1587, 1465

diethyl 2-[2-methoxy-5-(pyridin-2-yl)phenyl]-2,3,3-trimethylbutanedioate (9c)

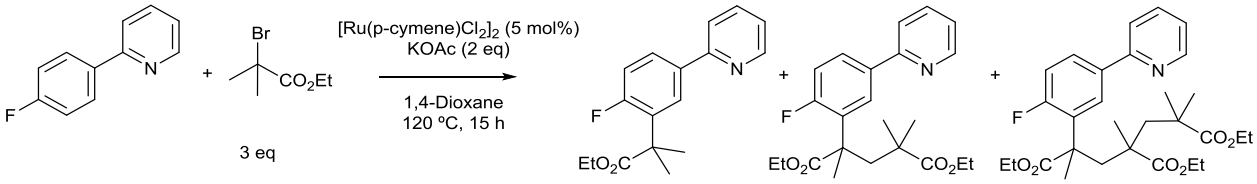


^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (ddd, *J* = 4.8, 1.7, 1.0 Hz, 1H), 7.91 (d, *J* = 2.2 Hz, 1H), 7.89 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.69 (ddd, *J* = 8.0, 1.3 Hz, 1H), 7.17 (ddd, *J* = 6.9, 4.8, 1.5 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 4.11 – 4.02 (m, 2H), 3.87 – 3.82 (m, *J* = 7.2, 1.5 Hz, 2H), 3.81 (s, 3H), 2.67 (d, *J* = 14.8 Hz, 1H), 2.50 (d, *J* = 14.8 Hz, 1H), 1.64 (s, 3H), 1.18 (s, 3H), 1.12 (t, *J* = 7.1 Hz, 3H), 1.11 (t, *J* = 7.1 Hz, 3H), 0.88 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 177.98, 177.32, 159.13, 156.04, 135.99, 132.74, 130.08, 128.28, 128.06, 127.10, 122.09, 121.53, 111.27, 60.67, 60.43, 55.50, 48.06, 44.59, 41.47, 28.10, 27.38, 23.16, 14.21, 14.11.

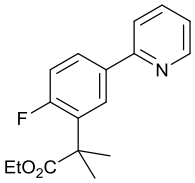
HR-MS (ESI) *m/z*: calculated for $C_{24}H_{31}NO_5Na$ $[M+Na]^+$ 436.2100, found: 436.2096

ν_{max} (neat) / cm^{-1}; 2979, 1727, 1587, 1465



2-(4-fluorophenyl)pyridine (1 mmol, 173 mg), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A. The crude mixture was purified by flash column chromatography to yield products **8c** (135 mg, 47%) as a colourless oil, product **9c** (50 mg, 13%) as a colourless oil and product **9d** (15 mg, 3%).

ethyl 2-[2-fluoro-5-(pyridin-2-yl)phenyl]-2-methylpropanoate (8d)



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, *J* = 4.1 Hz, 1H), 8.03 (dd, *J* = 7.7, 2.2 Hz, 1H), 7.82 (ddd, *J* = 8.3, 4.8, 2.2 Hz, 1H), 7.77 (dd, *J* = 7.6 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 1.63 (s, 6H), 1.17 (t, *J* = 7.1 Hz, 3H).

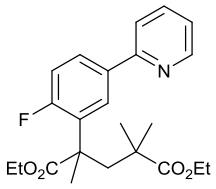
^{13}C NMR (126 MHz, $CDCl_3$) δ 176.65 (s), 161.64 (d, $^{1}J_{C\text{-}F}$ = 249.7 Hz), 156.59 (s), 149.40 (s), 137.32 (s), 135.14 (s), 133.31 (d, $^{2}J_{C\text{-}F}$ = 14.0 Hz), 127.19 (d, $^{3}J_{C\text{-}F}$ = 9.2 Hz), 125.76 (d, $^{3}J_{C\text{-}F}$ = 5.2 Hz), 122.24 (s), 120.70 (s), 116.00 (d, $^{2}J_{C\text{-}F}$ = 23.2 Hz), 61.03 (s), 44.37 (s), 25.84 (d, $^{4}J_{C\text{-}F}$ = 0.7 Hz), 14.14 (s).

^{19}F NMR (470 MHz, $CDCl_3$) δ -112.82.

HR-MS (ESI) *m/z*: calculated for $C_{17}H_{18}FNO_2Na$ $[M+H]^+$ 288.1400, found: 288.1402

ν_{max} (neat) / cm^{-1}; 2980, 1723, 1589, 1464

diethyl 2-[2-fluoro-5-(pyridin-2-yl)phenyl]-2,3,3-trimethylbutanedioate (9d)



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.69 (d, *J* = 4.1 Hz, 1H), 7.96 (dd, *J* = 7.7, 2.2 Hz, 1H), 7.89 (ddd, *J* = 8.2, 4.7, 2.2 Hz, 1H), 7.79 (dd, *J* = 7.1 Hz, 1H), 7.71 (d, *J* = 7.9 Hz, 1H), 7.31 – 7.23 (m, 1H), 7.09 (dd, *J* = 11.3, 8.5 Hz, 1H), 4.19 – 4.07 (m, 2H), 3.98 – 3.80 (m, 2H), 2.61 (d, *J* = 14.9 Hz, 1H), 2.58 (d, *J* = 14.9 Hz, 1H), 1.65 (s, 3H), 1.20 (s, 3H), 1.18 (t, *J* = 7.2 Hz, 3H), 1.16 (t, *J* = 7.2 Hz, 3H), 0.96 (s, 3H).

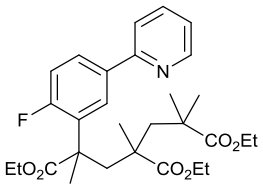
^{13}C NMR (126 MHz, $CDCl_3$) δ 177.83 (s), 176.17 (s), 161.89 (d, $^{1}J_{C\text{-}F}$ = 249.9 Hz), 156.36 (s), 149.19 (s), 137.60 (s), 131.69 (d, $^{2}J_{C\text{-}F}$ = 12.9 Hz), 127.63 (d, $^{3}J_{C\text{-}F}$ = 9.4 Hz), 127.40 (d, $^{3}J_{C\text{-}F}$ = 5.0 Hz), 122.32 (s), 120.85 (s), 116.12 (d, $^{2}J_{C\text{-}F}$ = 23.9 Hz), 61.22 (s), 60.53 (s), 47.98 (s), 45.44 (d, $^{3}J_{C\text{-}F}$ = 2.8 Hz), 41.49 (s), 27.63 (s), 27.13 (s), 22.48 (s), 14.04 (s), 14.03 (s).

^{19}F NMR (470 MHz, $CDCl_3$) δ -110.60.

HR-MS (ESI) *m/z*: calculated for $C_{23}H_{28}FNO_4Na$ $[M+Na]^+$ 424.1900, found: 424.1905

ν_{max} (neat) / cm^{-1}; 2980, 1723, 1589, 1463

triethyl 2-[2-fluoro-5-(pyridin-2-yl)phenyl]-3,5-dimethylhexane-2,3,5-tricarboxylate (9e)



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.72 (s, 1H), 8.03 – 7.89 (m, J = 21.0, 11.2, 4.3 Hz, 2H), 7.86 (s, 1H), 7.77 (s, 1H), 7.36 – 7.28 (m, J = 10.0, 5.7 Hz, 1H), 7.16 – 7.04 (m, 1H), 4.21 – 3.95 (m, 4H), 3.73 – 3.56 (m, J = 46.8, 10.8, 7.2 Hz, 2H), 2.83 – 2.65 (m, 1H), 2.42 – 2.29 (m, J = 25.8, 13.9 Hz, 1H), 2.21 – 2.09 (m, 1H), 2.09 – 1.95 (m, 1H), 1.71 – 1.59 (m, 3H), 1.31 – 1.05 (m, 15H), 1.03 – 0.95 (m, 3H).

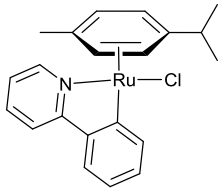
^{19}F NMR (470 MHz, $CDCl_3$) δ -109.10.

HR-MS (ESI) *m/z*: calculated for $C_{29}H_{38}FNO_6Na$ $[M+Na]^+$ 538.2580, found: 538.2611

ν_{max} (neat) / cm^{-1}; 2980, 1723, 1589, 1464

Mechanistic Studies

Synthesis of Complex A



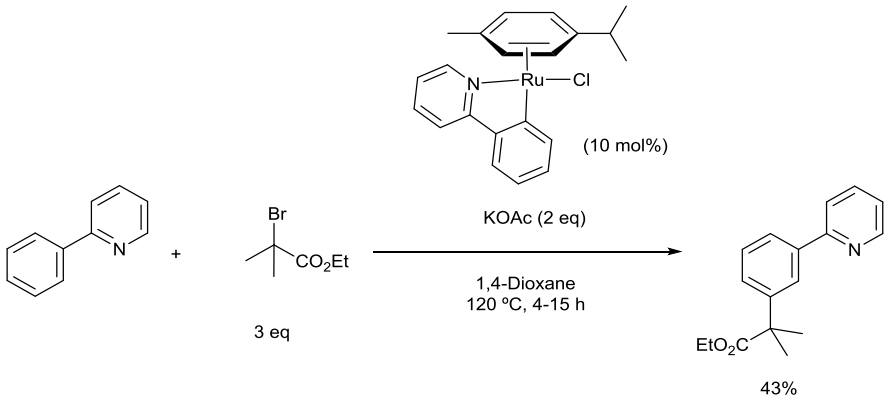
Complex A was synthesised according to literature procedure.[5] To an oven dried, argon purged round bottom flask was added $[RuCl_2(p\text{-cymene})]_2$ (1.5 mmol, 918 mg), KOAc (6 mmol, 588 mg) followed by 2-phenylpyridine (3 mmol, 0.42 mL) and dry MeOH (30 mL). The reaction was stirred at room temperature for 48 h. The reaction was then concentrated to dryness, dissolved in a minimal amount of EtOAc and then purified through neutral alumina with EtOAc as the solvent to yield the title compound as a yellow solid (1.1 g, 86%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 9.23 (d, J = 5.5 Hz, 1H), 8.15 (d, J = 7.5 Hz, 1H), 7.70 (d, J = 7.9 Hz, 1H), 7.65 (dd, J = 7.6 Hz, 1H), 7.60 (d, J = 7.6 Hz, 1H), 7.17 (dd, J = 7.3 Hz, 1H), 7.06 – 6.99 (m, 2H), 5.58 (d, J = 5.8 Hz, 1H), 5.55 (d, J = 5.9 Hz, 1H), 5.17 (d, J = 5.9 Hz, 1H), 4.98 (d, J = 5.8 Hz, 1H), 2.43 (hept, J = 6.8 Hz, 1H), 2.04 (s, 3H), 0.98 (d, J = 6.9 Hz, 3H), 0.88 (d, J = 6.9 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 181.50, 165.44, 154.70, 143.41, 139.67, 136.70, 129.53, 123.96, 122.57, 121.48, 118.87, 100.73, 100.59, 90.83, 89.72, 84.24, 82.27, 30.89, 22.61, 21.81, 18.85.

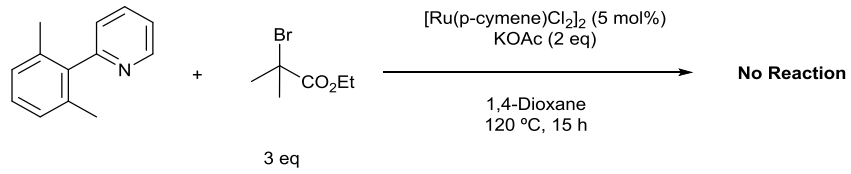
Data conforms to literature.[5]

Catalytic Reaction using Complex A

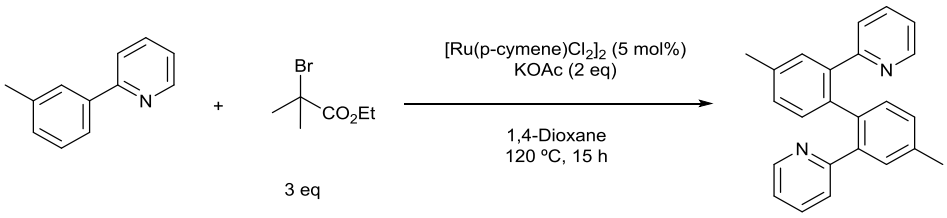


2-phenylpyridine (1 mmol, 0.14 mL), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), Complex A (10 mol%, 41 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A. The crude mixture was purified by flash column chromatography to yield product **8a** as a colourless oil (115 mg, 43%). Data in accordance with previous synthesis.

Reactions with Substrates 1j-1l

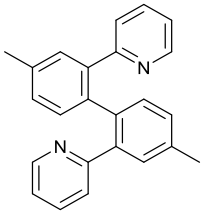


2-(2,6-dimethylphenyl)pyridine (1 mmol, 183 mg), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A. No conversion of the starting material was observed.



2-(3-methylphenyl)pyridine (1 mmol, 169 mg), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford product **10** as a yellow solid (60 mg 35%).

2,2'-(4,4'-dimethylbiphenyl-2,2'-diyl)dipyridine (10)

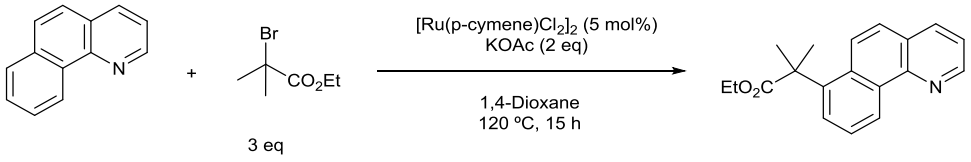


^{1}H NMR (500 MHz, $CDCl_3$) δ 8.34 (d, J = 2.7 Hz, 2H), 7.43 – 7.33 (m, 4H), 7.29 (d, J = 7.7 Hz, 2H), 7.25 (t, J = 6.7 Hz, 2H), 7.06 (bs, 1H), 6.80 (d, J = 7.7 Hz, 2H), 2.40 (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 157.80, 148.48, 138.98, 137.69, 136.81, 136.07, 131.42, 130.80, 129.78, 124.80, 121.52, 21.17.

HR-MS (ESI) *m/z*: calculated for $C_{24}H_{20}N_2$ $[M+Na]^+$ 359.1524, found: 359.1533

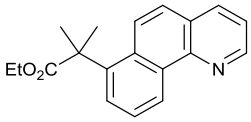
Data conforms to literature.[6]



22%

Benzoquinoline (1 mmol, 179 mg), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A. The crude mixture was purified by flash column chromatography to yield product **11** as a colourless oil (63 mg, 22%)

ethyl 2-(benzo[h]quinolin-7-yl)-2-methylpropanoate (11)

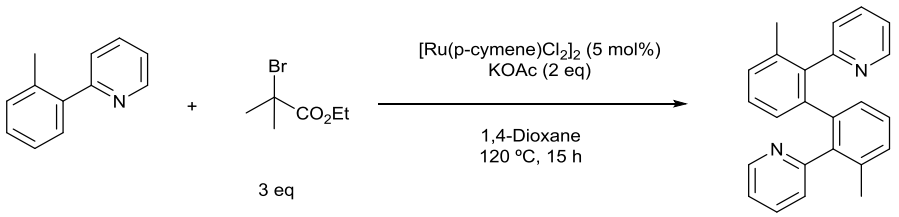


^{1}H NMR (500 MHz, $CDCl_3$) δ 9.38 (d, *J* = 8.0 Hz, 1H), 9.00 (dd, *J* = 4.4, 1.8 Hz, 1H), 8.15 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.90 (d, *J* = 9.3 Hz, 1H), 7.77 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.74 – 7.70 (m, 1H), 7.66 (d, *J* = 9.3 Hz, 1H), 7.50 (dd, *J* = 8.0, 4.4 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 1.80 (s, 7H), 1.02 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 178.85, 148.81, 146.83, 141.08, 135.81, 132.46, 131.42, 126.65, 125.53, 125.22, 125.07, 124.07, 123.96, 121.96, 61.15, 46.58, 27.88, 14.05.

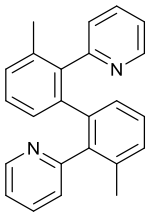
HR-MS (ESI) *m/z*: calculated for $C_{19}H_{19}NO_2$ $[M+H]^+$ 294.1494, found: 294.1517

ν_{max} (neat) / cm^{-1}; 2979, 1718, 1592, 1428



2-(2-methylphenyl)pyridine (1 mmol, 169 mg), ethyl 2-bromoisobutrate (3 mmol, 0.44 mL), $[RuCl_2(p\text{-cymene})]_2$ (5 mol%, 30 mg), and KOAc (2 mmol, 196 mg) were reacted together in 1,4-Dioxane (4 mL) according to general procedure A to afford product **12** as a white solid (50 mg 29%).

2,2'-(3,3'-dimethylbiphenyl-2,2'-diyl)dipyridine (12)



^{1}H NMR (500 MHz, $CDCl_3$) δ 8.57 (d, *J* = 4.2 Hz, 2H), 7.55 (t, *J* = 7.1 Hz, 2H), 7.36 – 7.30 (m, *J* = 6.2 Hz, 2H), 7.10 – 7.06 (m, 2H), 7.04 (d, *J* = 7.5 Hz, 2H), 6.93 (t, *J* = 7.6 Hz, 2H), 6.77 (d, *J* = 7.6 Hz, 2H), 2.10 (s, 6H).

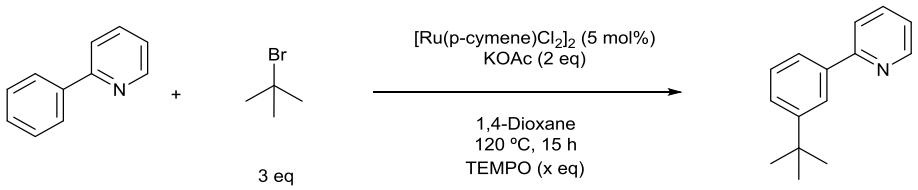
^{13}C NMR (126 MHz, $CDCl_3$) δ 159.38, 148.63, 140.35, 139.62, 136.03, 135.83, 128.89, 128.75, 126.83, 125.87, 121.40, 20.64.

HR-MS (ESI) *m/z*: calculated for $C_{24}H_{20}N_2$ $[M+Na]^+$ 359.1524, found: 359.1517

Data conforms to literature.[6]

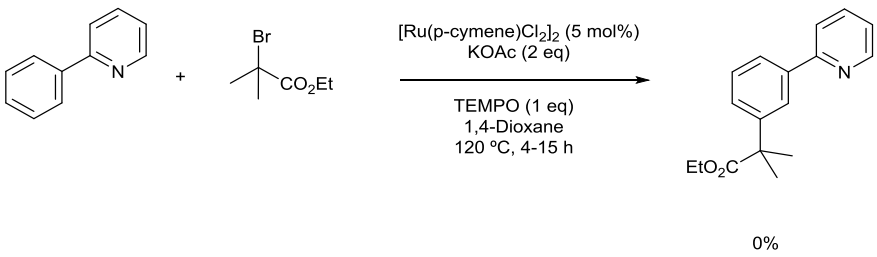
Reactions with TEMPO

Reactions were carried out as per general procedure A.



TEMPO stoicheometry	Conversion (%)
0	71
0.1	41
1	0
3	0

Reaction with ethyl 2-bromoisobutrate carried out as per general procedure A. No trapped TEMPO adducts could be observed or isolated.



0%

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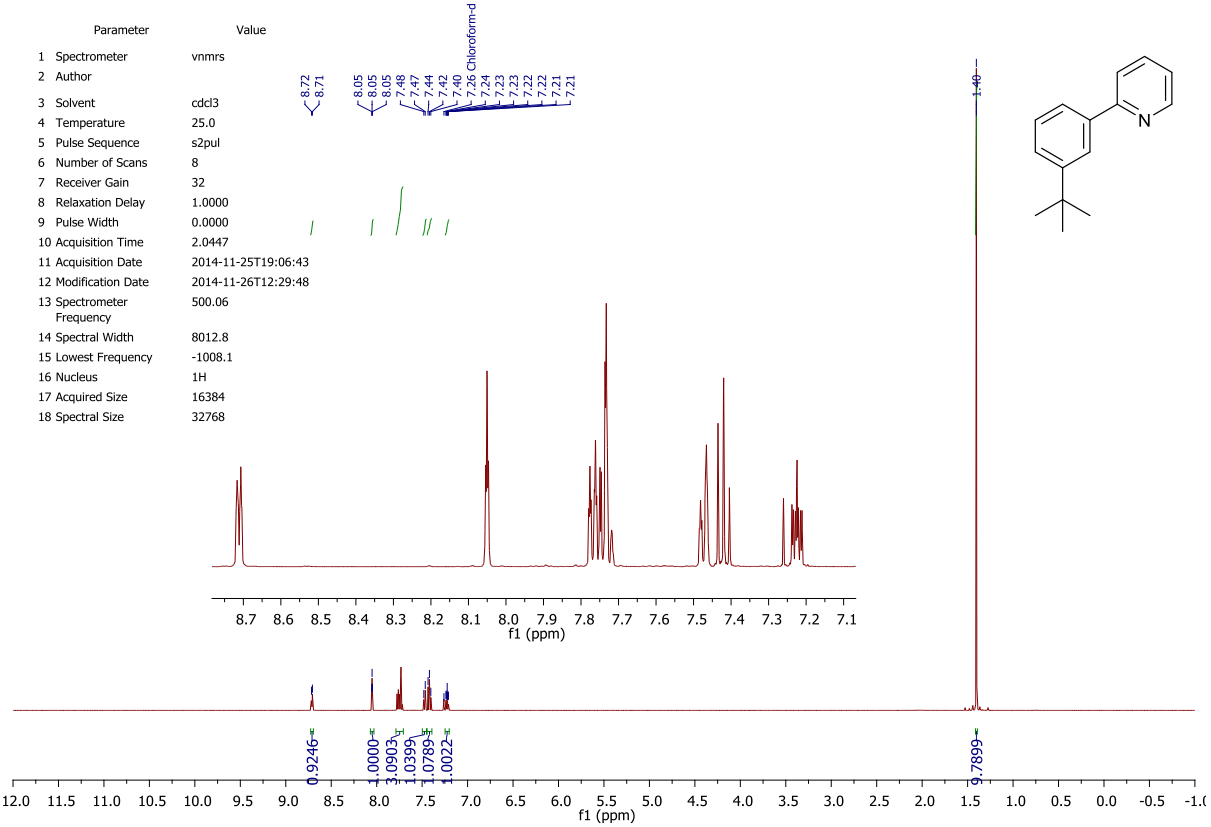
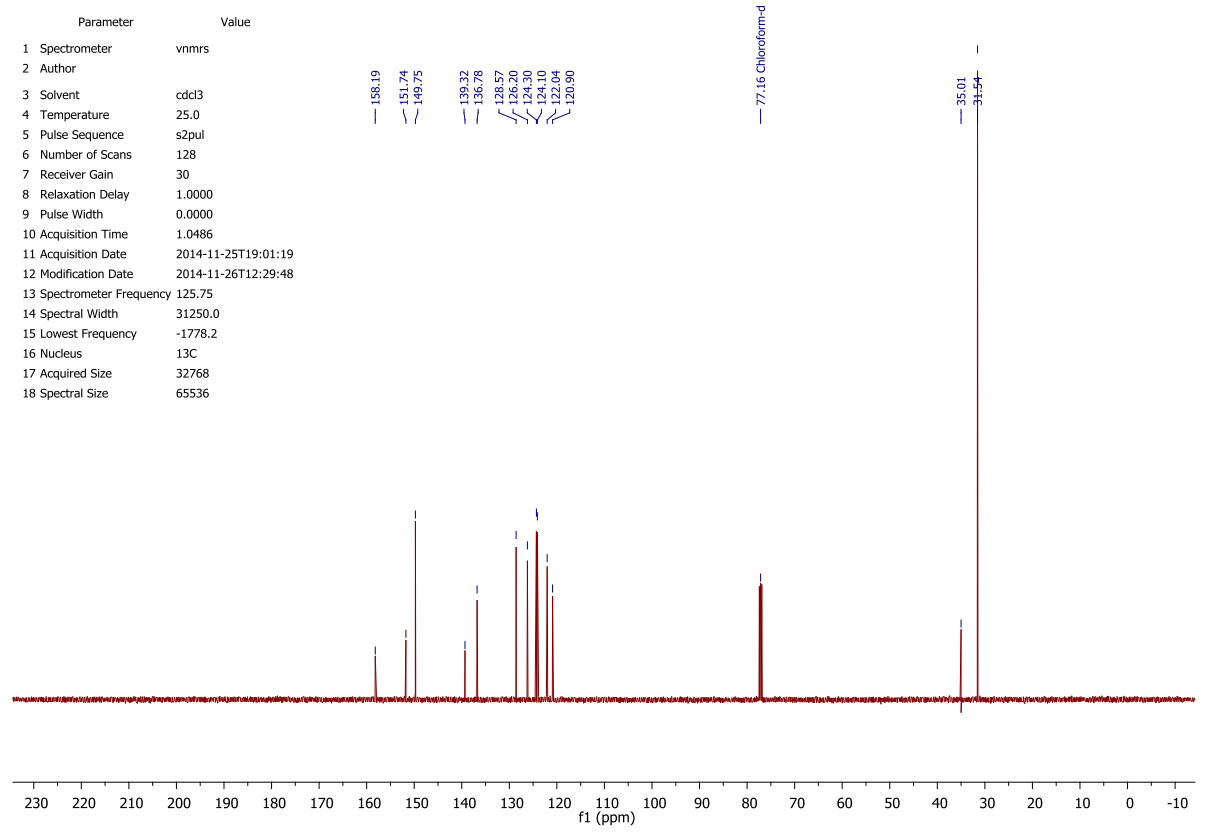
NMR Spectra

2-(3-tert-butylphenyl)pyridine (3a)

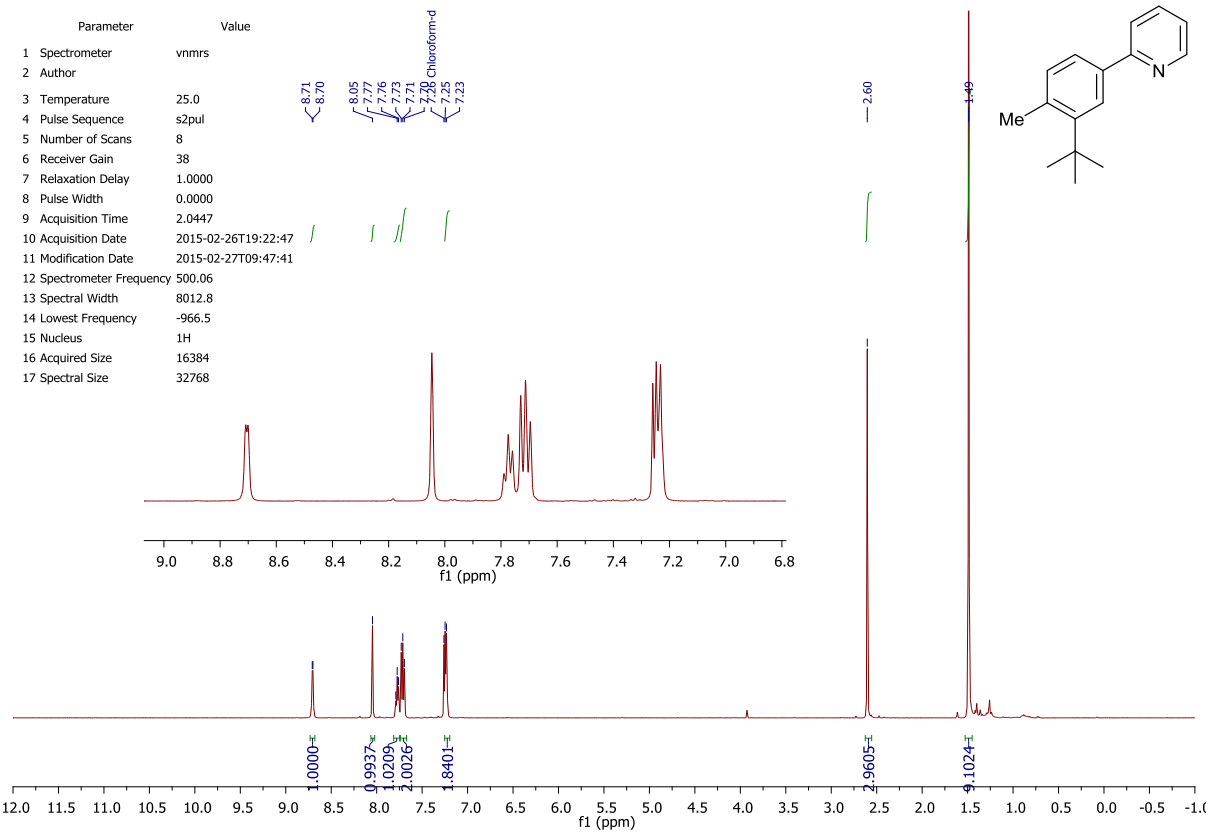
	Parameter	Value
1	Spectrometer	vnmrs
2	Author	
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Number of Scans	8
7	Receiver Gain	32
8	Relaxation Delay	1.0000
9	Pulse Width	0.0000
10	Acquisition Time	2.0447
11	Acquisition Date	2014-11-25T19:06:43
12	Modification Date	2014-11-26T12:29:48
13	Spectrometer Frequency	500.06
14	Spectral Width	8012.8
15	Lowest Frequency	-1008.1
16	Nucleus	1H
17	Acquired Size	16384
18	Spectral Size	32768

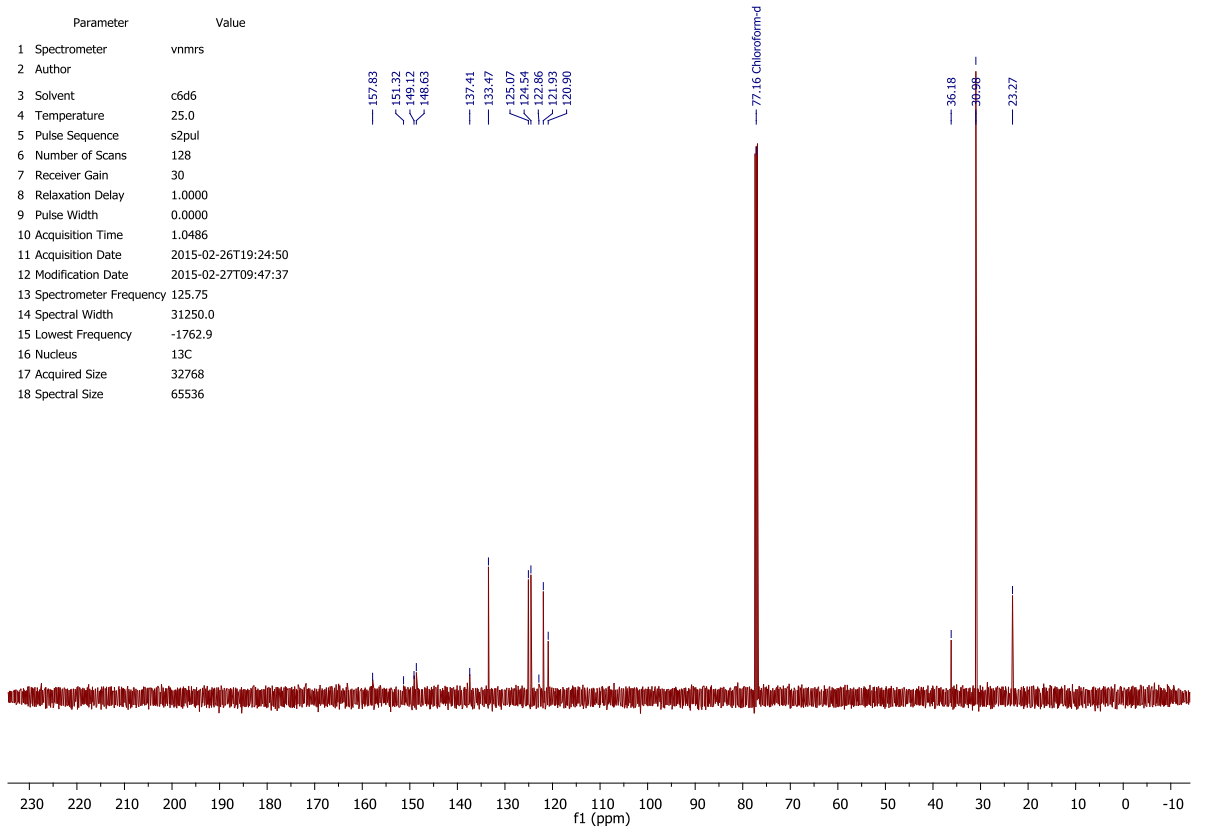


	Parameter	Value
1	Spectrometer	vnmrs
2	Author	
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Number of Scans	128
7	Receiver Gain	30
8	Relaxation Delay	1.0000
9	Pulse Width	0.0000
10	Acquisition Time	1.0486
11	Acquisition Date	2014-11-25T19:01:19
12	Modification Date	2014-11-26T12:29:48
13	Spectrometer Frequency	125.75
14	Spectral Width	31250.0
15	Lowest Frequency	-1778.2
16	Nucleus	13C
17	Acquired Size	32768
18	Spectral Size	65536

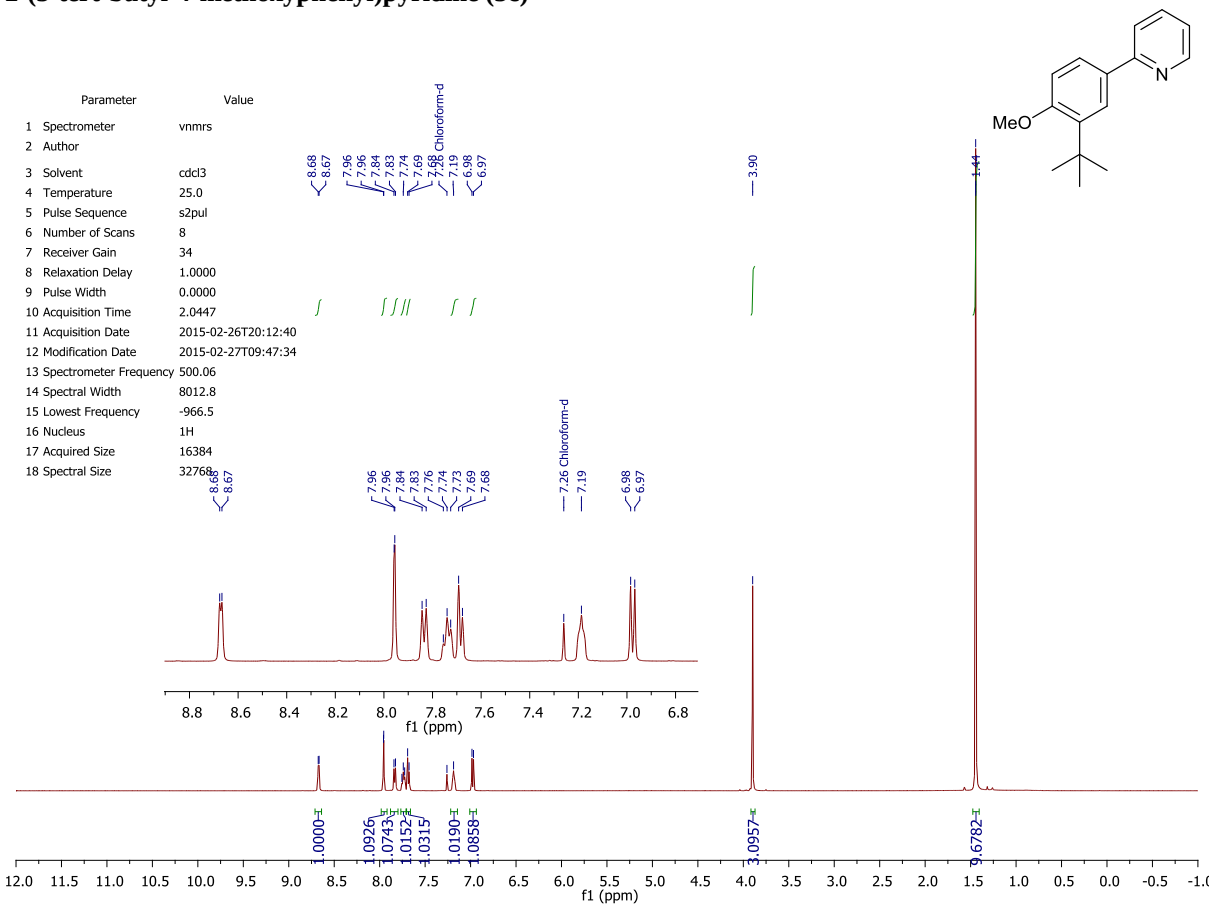


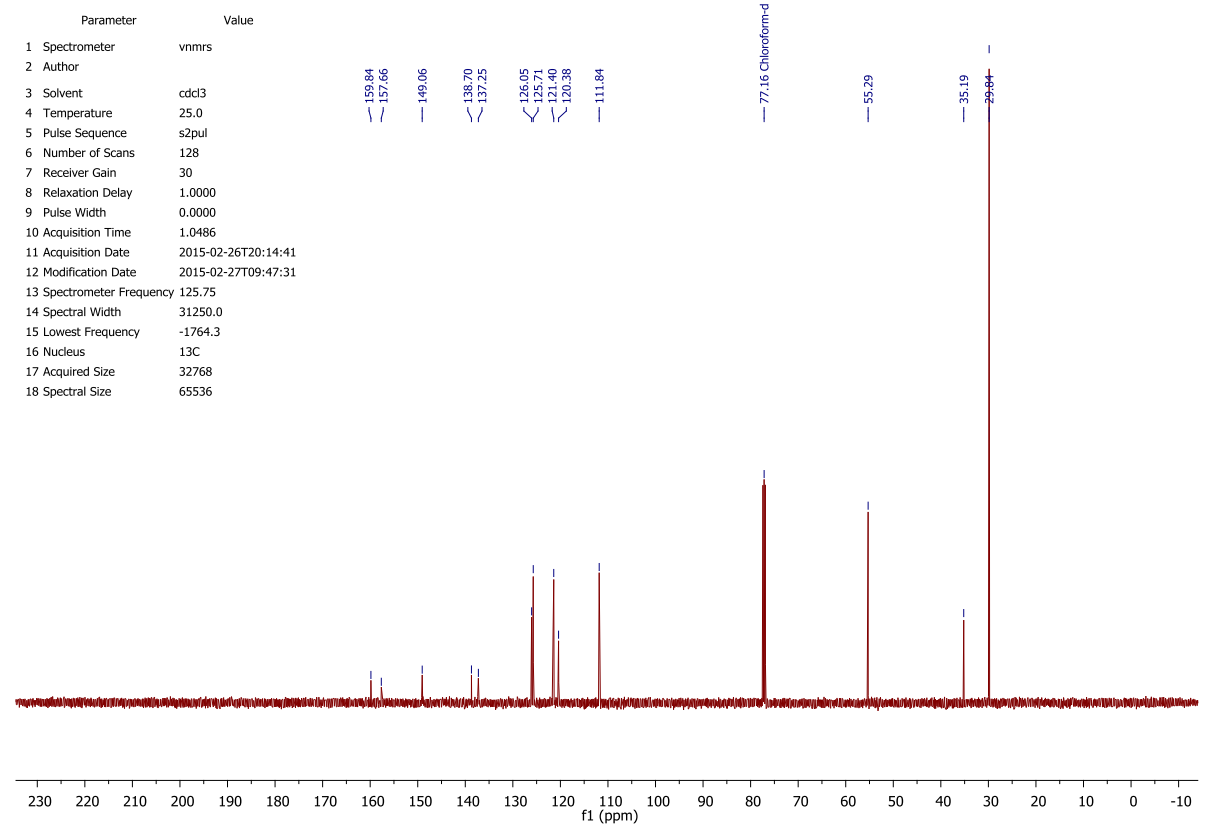
2-(3-tert-butyl-4-methylphenyl)pyridine (3b)



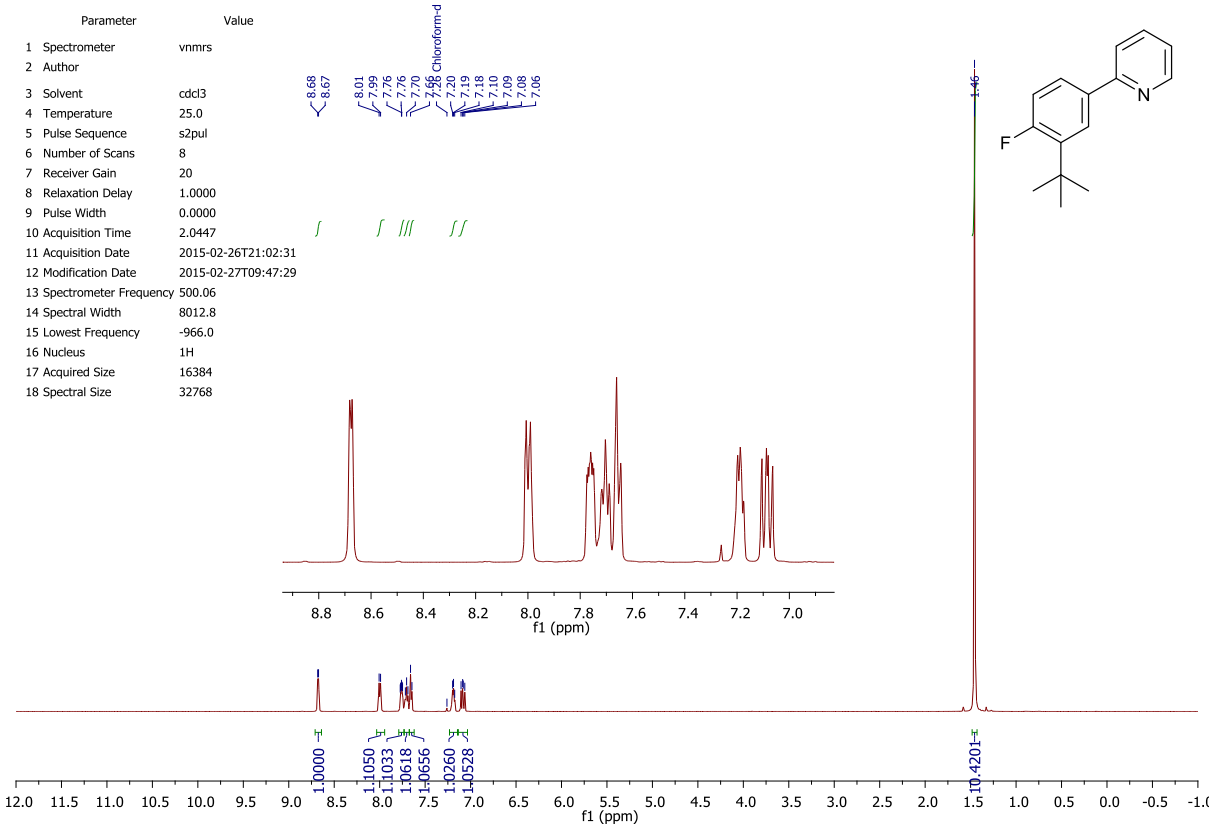


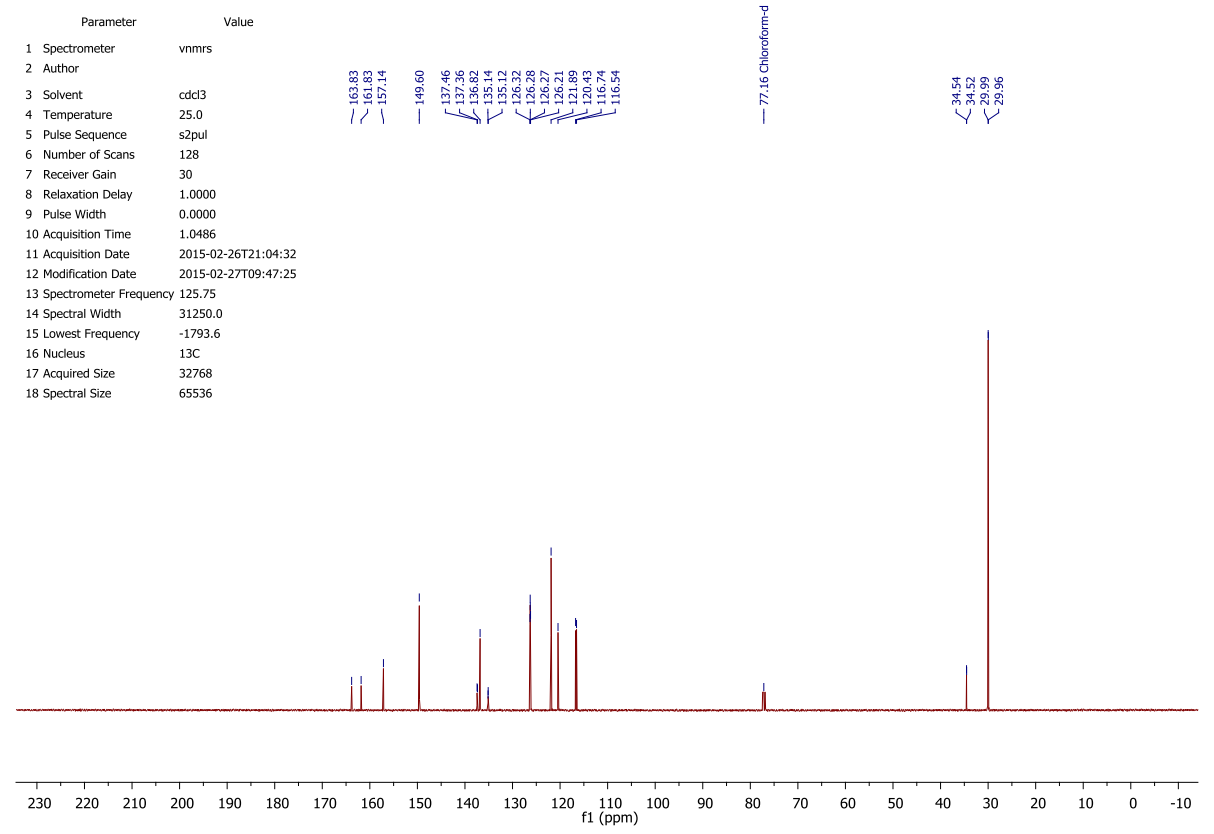
2-(3-tert-butyl-4-methoxyphenyl)pyridine (3c)



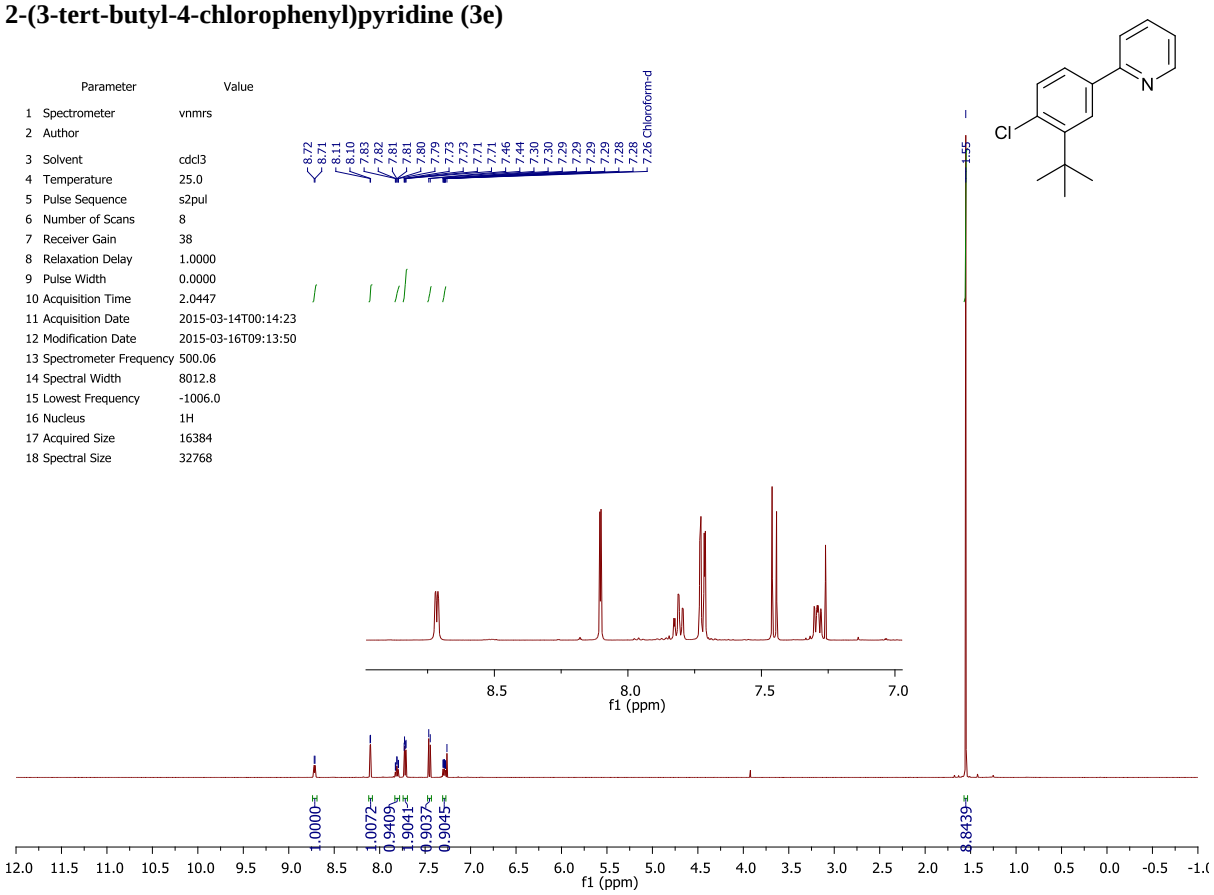


2-(3-tert-butyl-4-fluorophenyl)pyridine (3d)

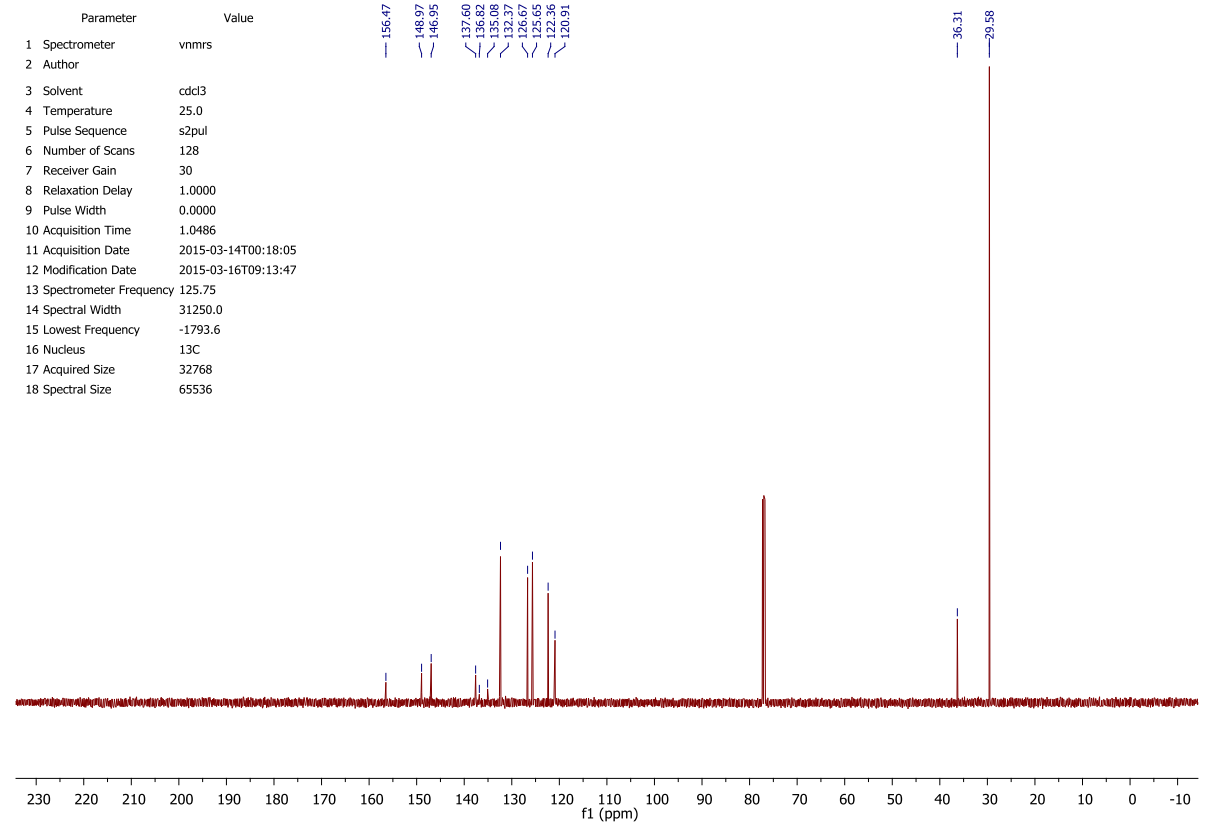




2-(3-tert-butyl-4-chlorophenyl)pyridine (3e)



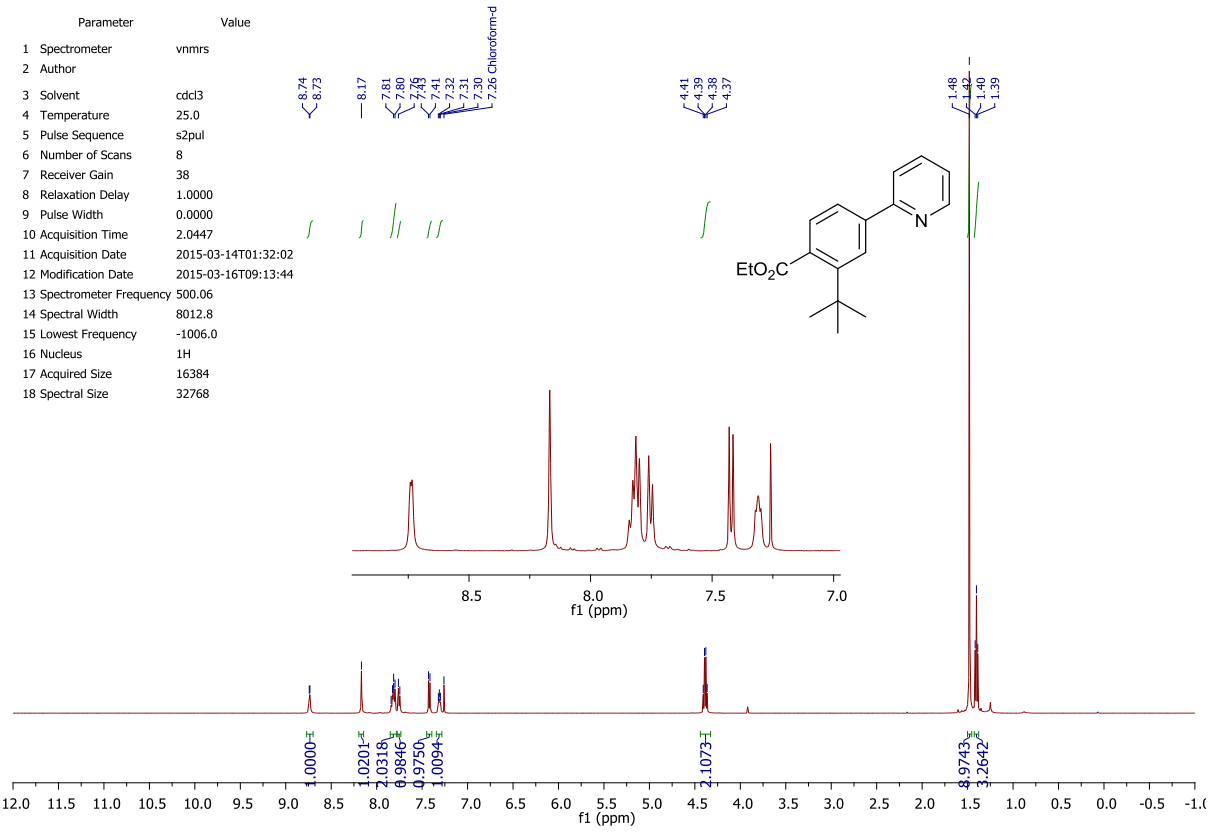
Parameter	Value
1 Spectrometer	vnmrs
2 Author	
3 Solvent	cdcl3
4 Temperature	25.0
5 Pulse Sequence	s2pul
6 Number of Scans	8
7 Receiver Gain	38
8 Relaxation Delay	1.0000
9 Pulse Width	0.0000
10 Acquisition Time	2.0447
11 Acquisition Date	2015-03-14T00:14:23
12 Modification Date	2015-03-16T09:13:50
13 Spectrometer Frequency	500.06
14 Spectral Width	8012.8
15 Lowest Frequency	-1006.0
16 Nucleus	1H
17 Acquired Size	16384
18 Spectral Size	32768



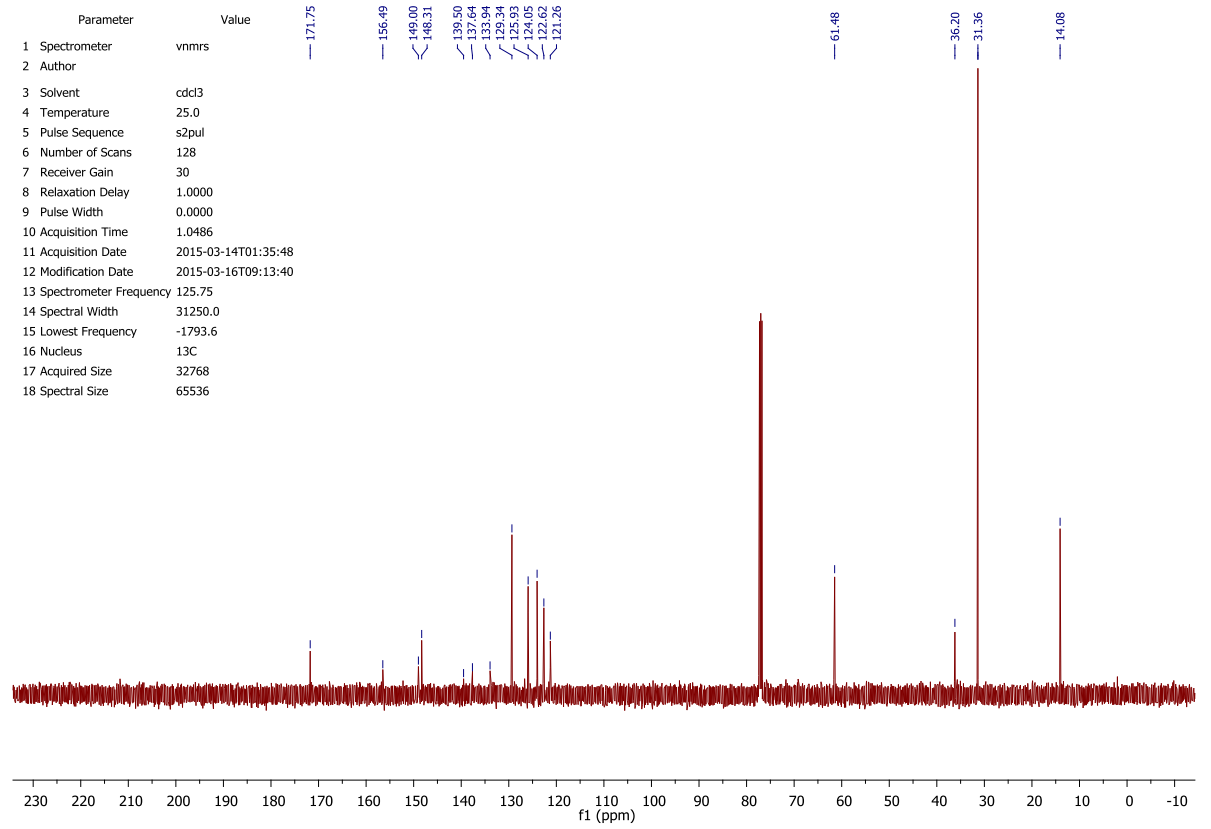
Parameter	Value
1 Spectrometer	vnmrs
2 Author	
3 Solvent	cdcl3
4 Temperature	25.0
5 Pulse Sequence	s2pul
6 Number of Scans	128
7 Receiver Gain	30
8 Relaxation Delay	1.0000
9 Pulse Width	0.0000
10 Acquisition Time	1.0486
11 Acquisition Date	2015-03-14T00:18:05
12 Modification Date	2015-03-16T09:13:47
13 Spectrometer Frequency	125.75
14 Spectral Width	31250.0
15 Lowest Frequency	-1793.6
16 Nucleus	13C
17 Acquired Size	32768
18 Spectral Size	65536

ethyl 2-tert-butyl-4-(pyridin-2-yl)benzoate (3f)

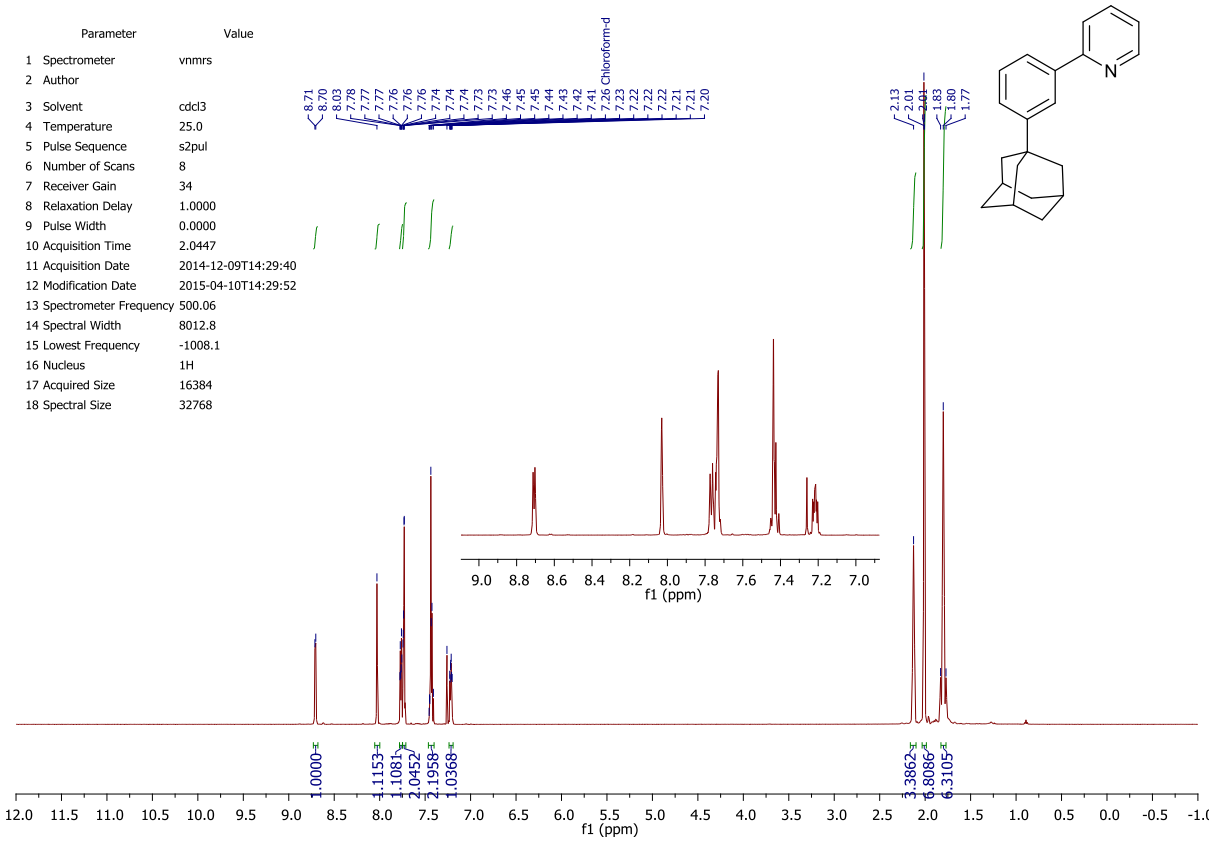
	Parameter	Value
1	Spectrometer	vnmrs
2	Author	
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Number of Scans	8
7	Receiver Gain	38
8	Relaxation Delay	1.0000
9	Pulse Width	0.0000
10	Acquisition Time	2.0447
11	Acquisition Date	2015-03-14T01:32:02
12	Modification Date	2015-03-16T09:13:44
13	Spectrometer Frequency	500.06
14	Spectral Width	8012.8
15	Lowest Frequency	-1006.0
16	Nucleus	1H
17	Acquired Size	16384
18	Spectral Size	32768

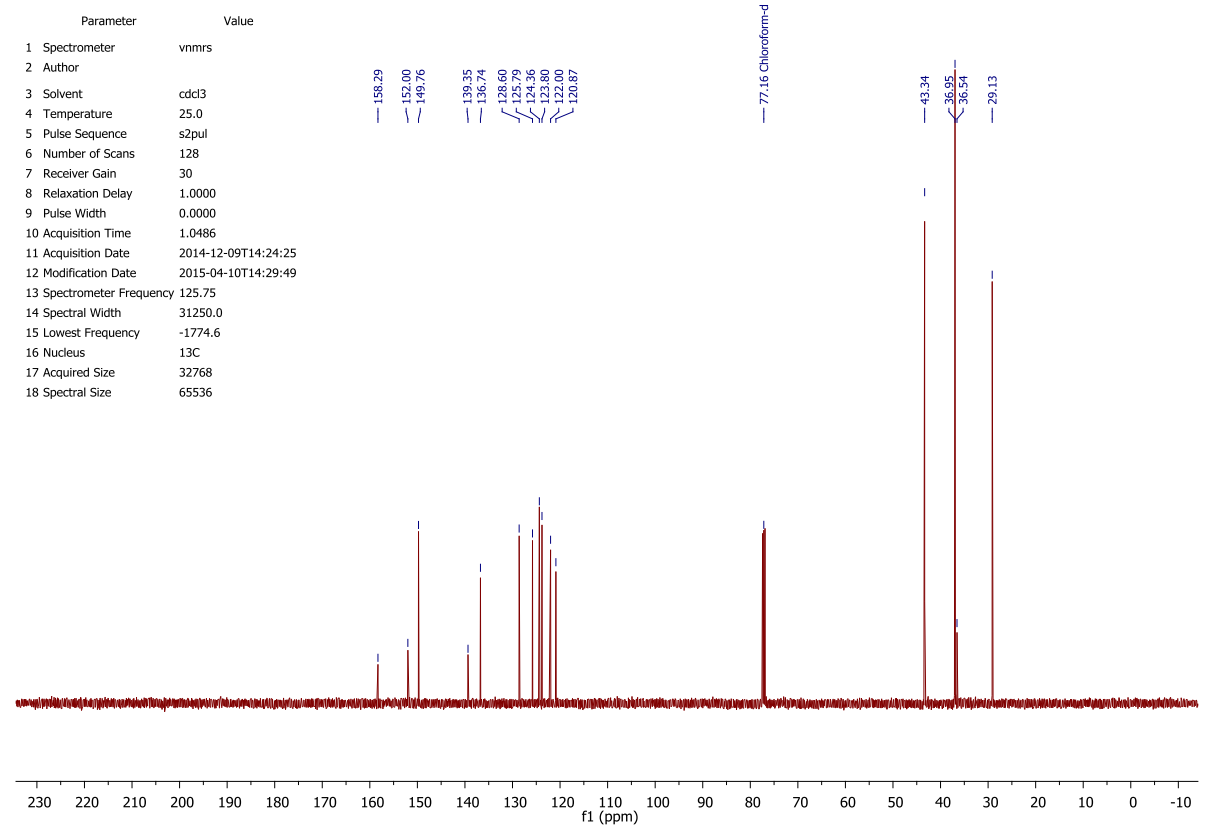


	Parameter	Value
1	Spectrometer	vnmrs
2	Author	
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Number of Scans	128
7	Receiver Gain	30
8	Relaxation Delay	1.0000
9	Pulse Width	0.0000
10	Acquisition Time	1.0486
11	Acquisition Date	2015-03-14T01:35:48
12	Modification Date	2015-03-16T09:13:40
13	Spectrometer Frequency	125.75
14	Spectral Width	31250.0
15	Lowest Frequency	-1793.6
16	Nucleus	13C
17	Acquired Size	32768
18	Spectral Size	65536

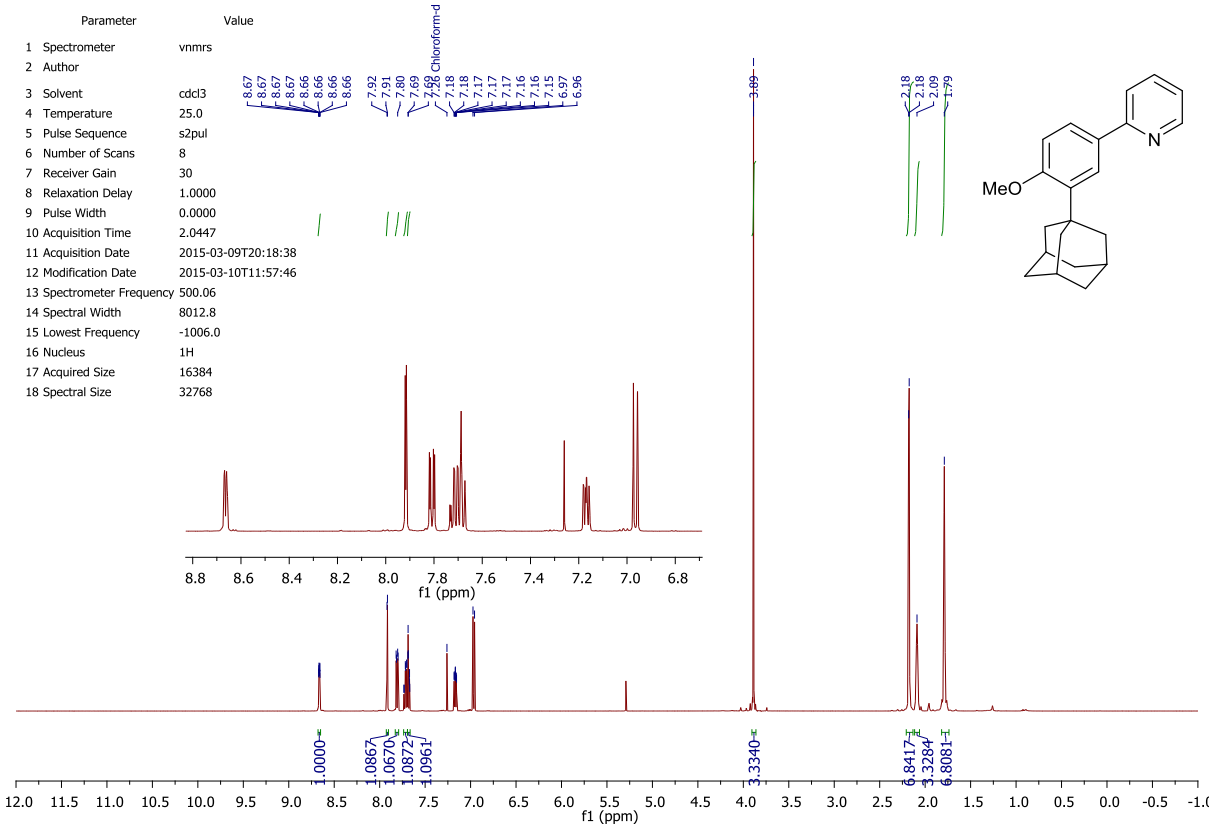


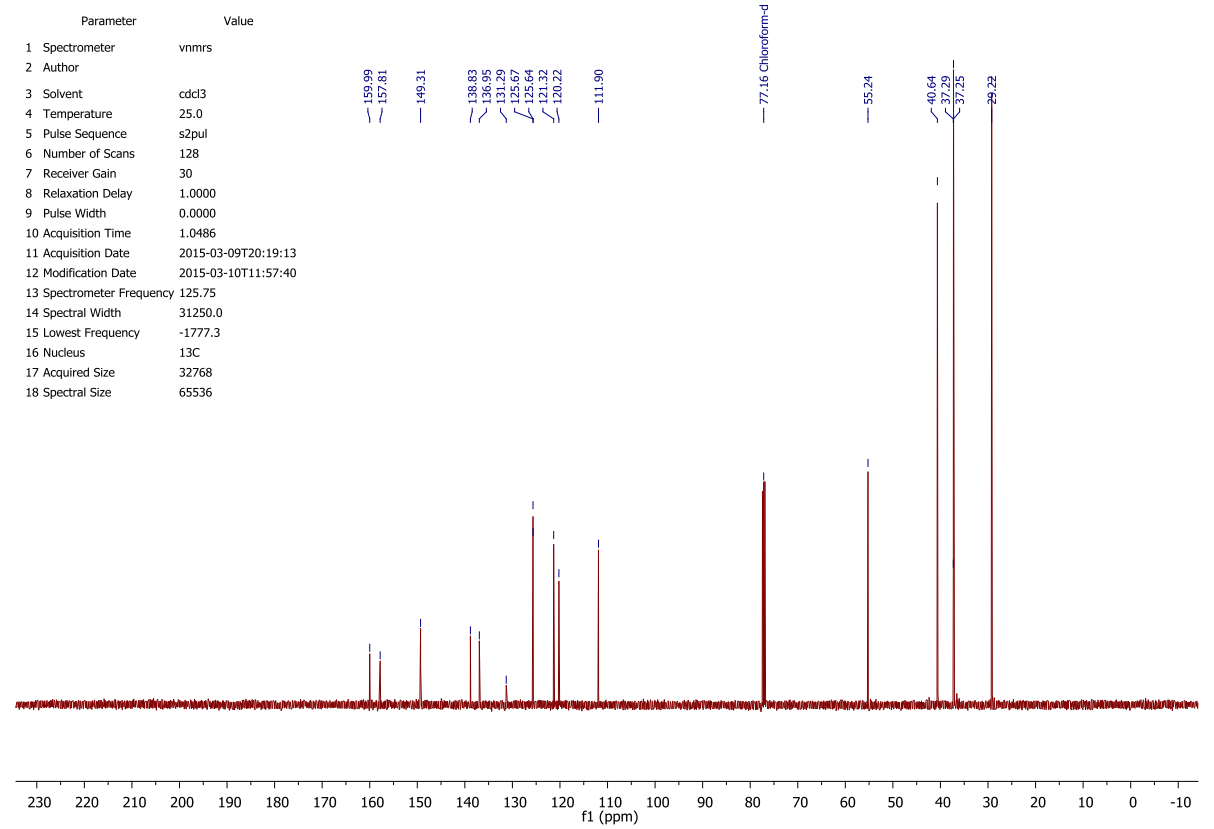
2-(3-(adamantan-1-yl)phenyl)pyridine (4a)



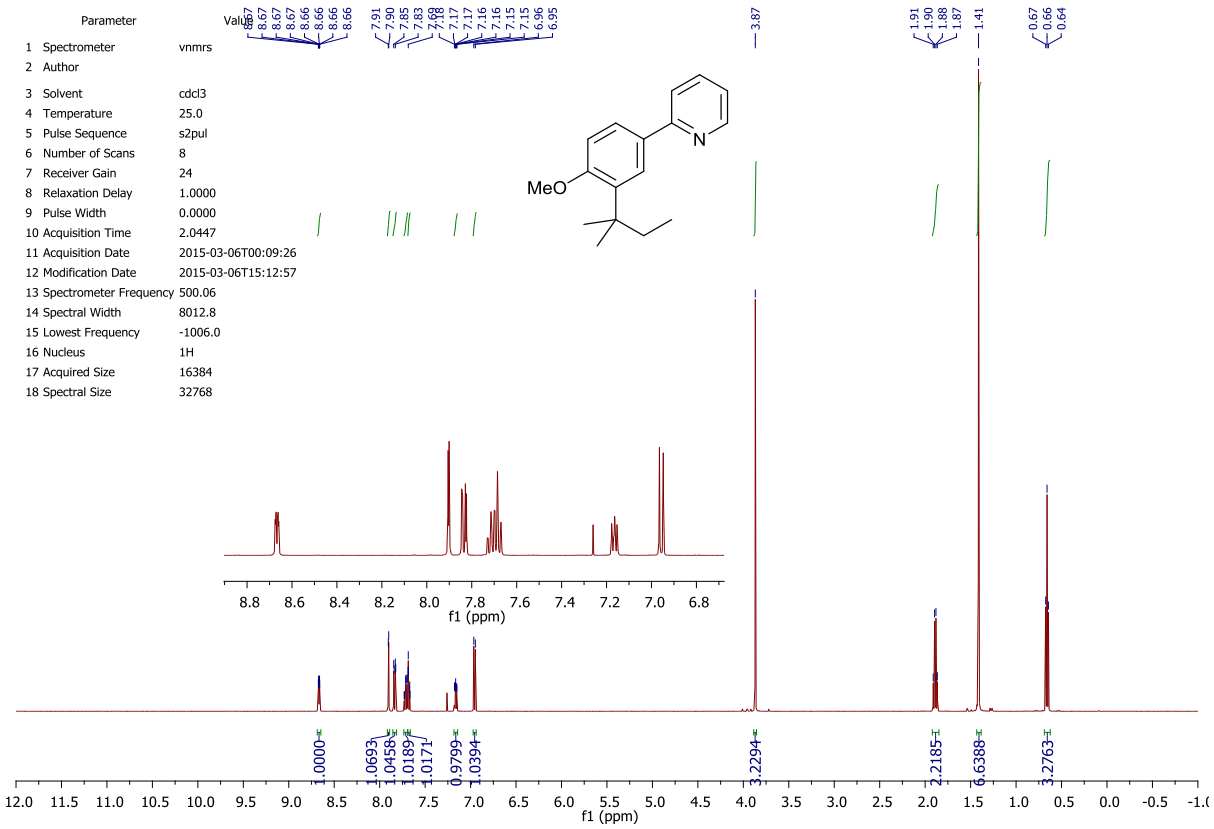


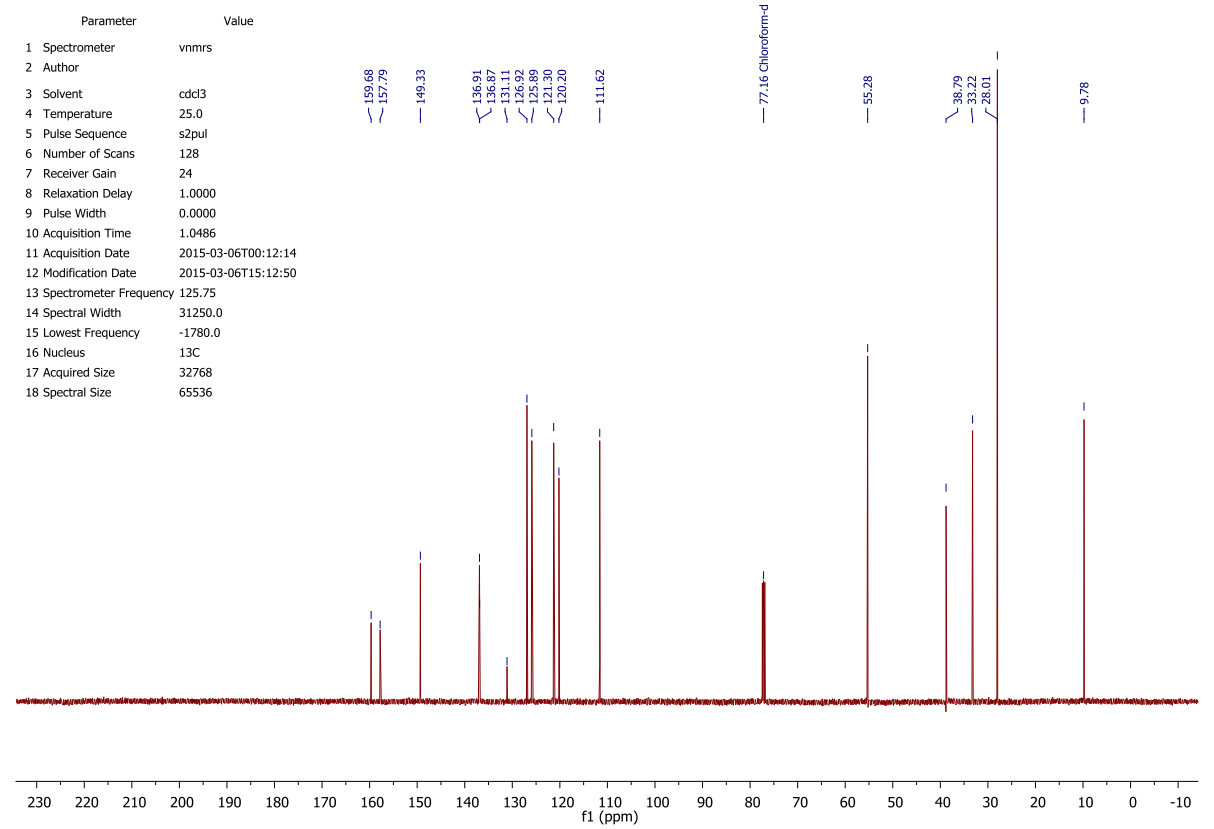
2-(3-(adamantan-1-yl)-4-methoxyphenyl)pyridine (4c)





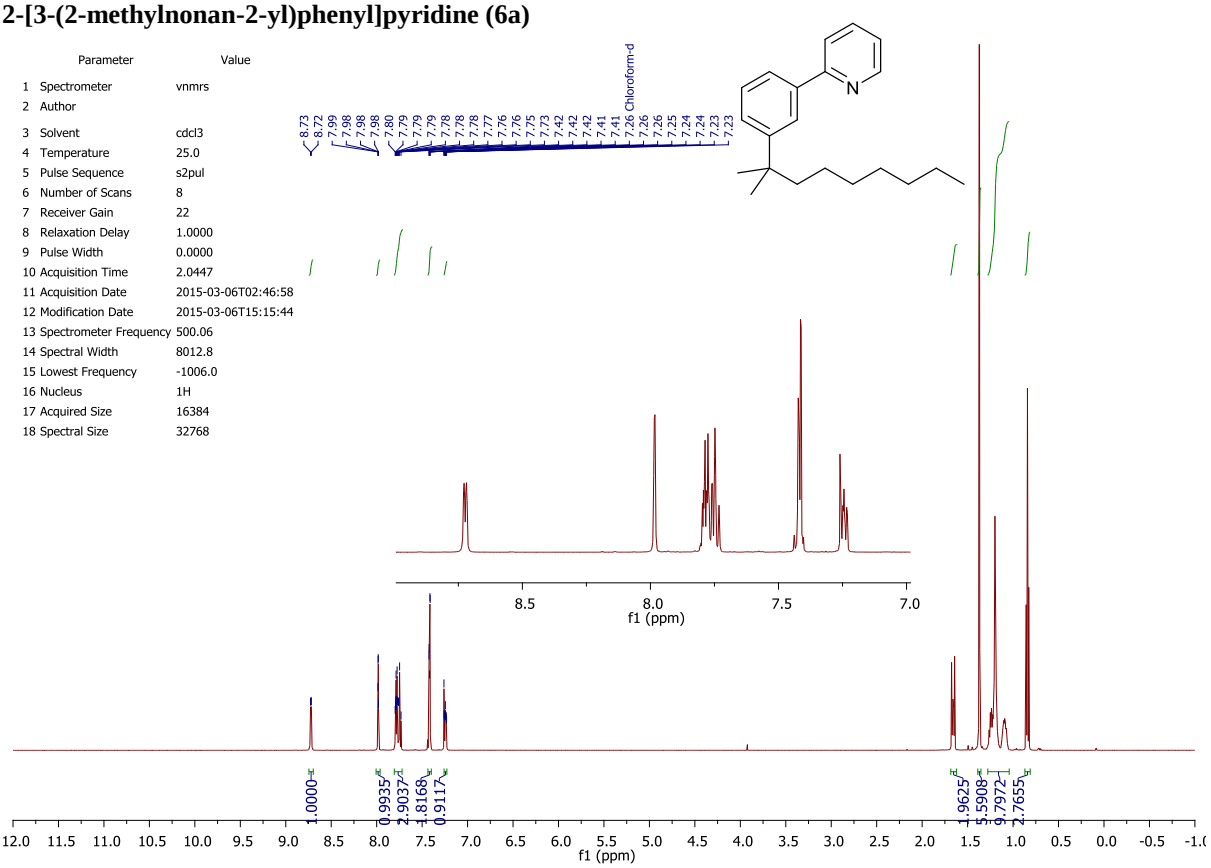
2-[4-methoxy-3-(2-methylbutan-2-yl)phenyl]pyridine (5c)



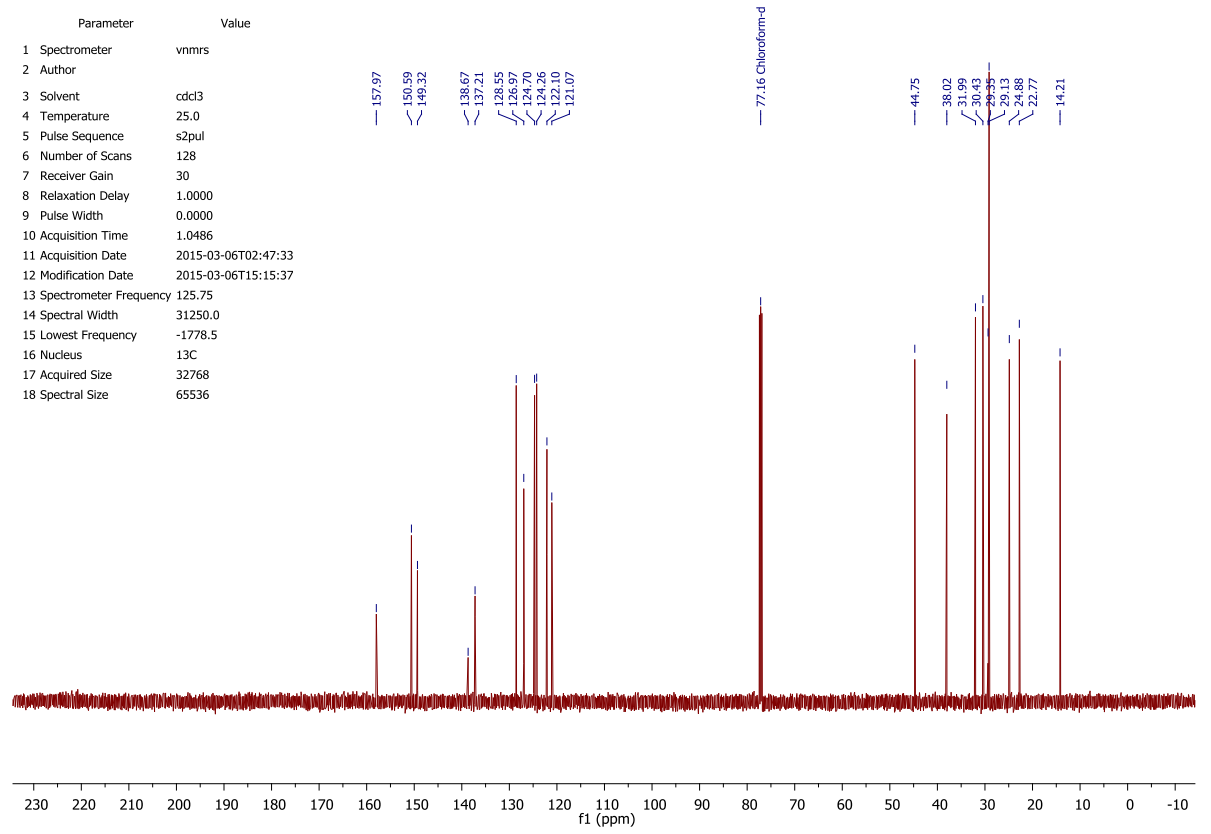


2-[3-(2-methylnonan-2-yl)phenyl]pyridine (6a)

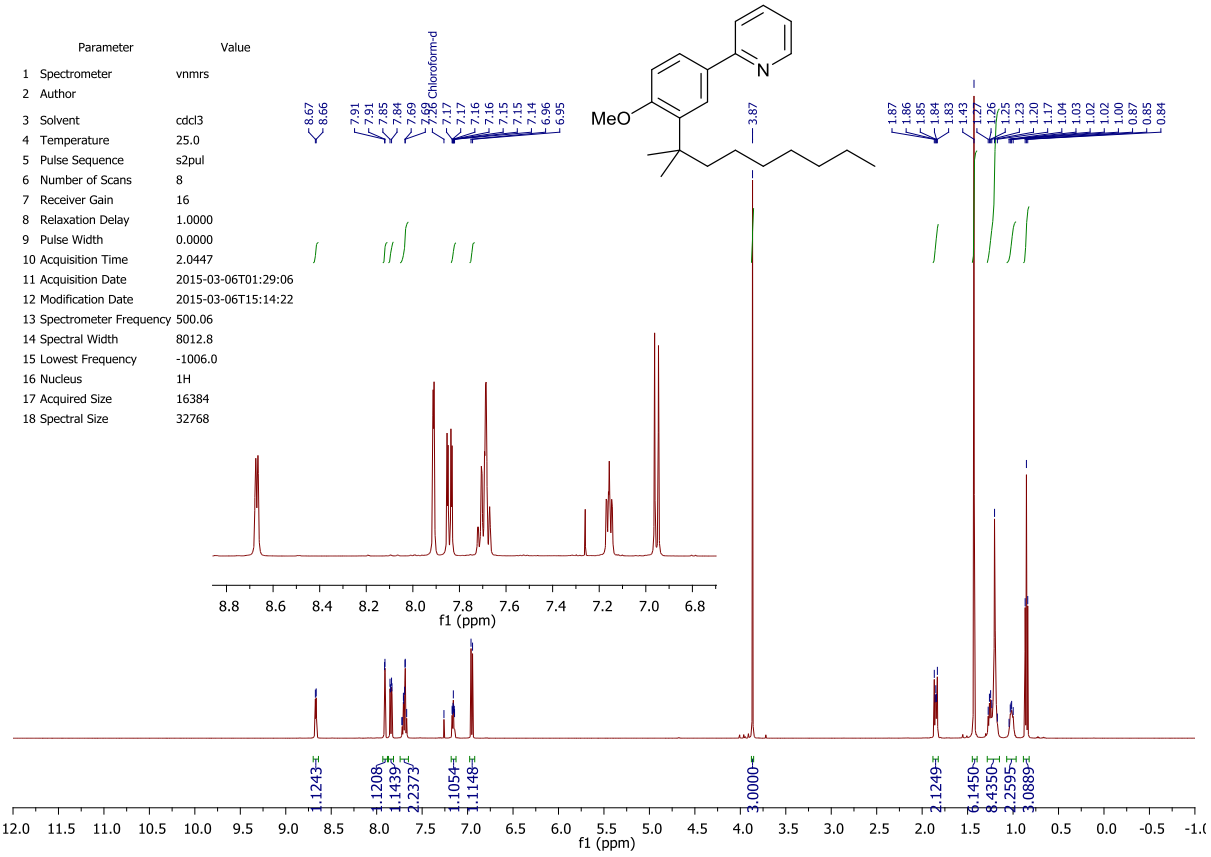
	Parameter	Value
1	Spectrometer	vnmrs
2	Author	
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Number of Scans	8
7	Receiver Gain	22
8	Relaxation Delay	1.0000
9	Pulse Width	0.0000
10	Acquisition Time	2.0447
11	Acquisition Date	2015-03-06T02:46:58
12	Modification Date	2015-03-06T15:15:44
13	Spectrometer Frequency	500.06
14	Spectral Width	8012.8
15	Lowest Frequency	-1006.0
16	Nucleus	1H
17	Acquired Size	16384
18	Spectral Size	32768

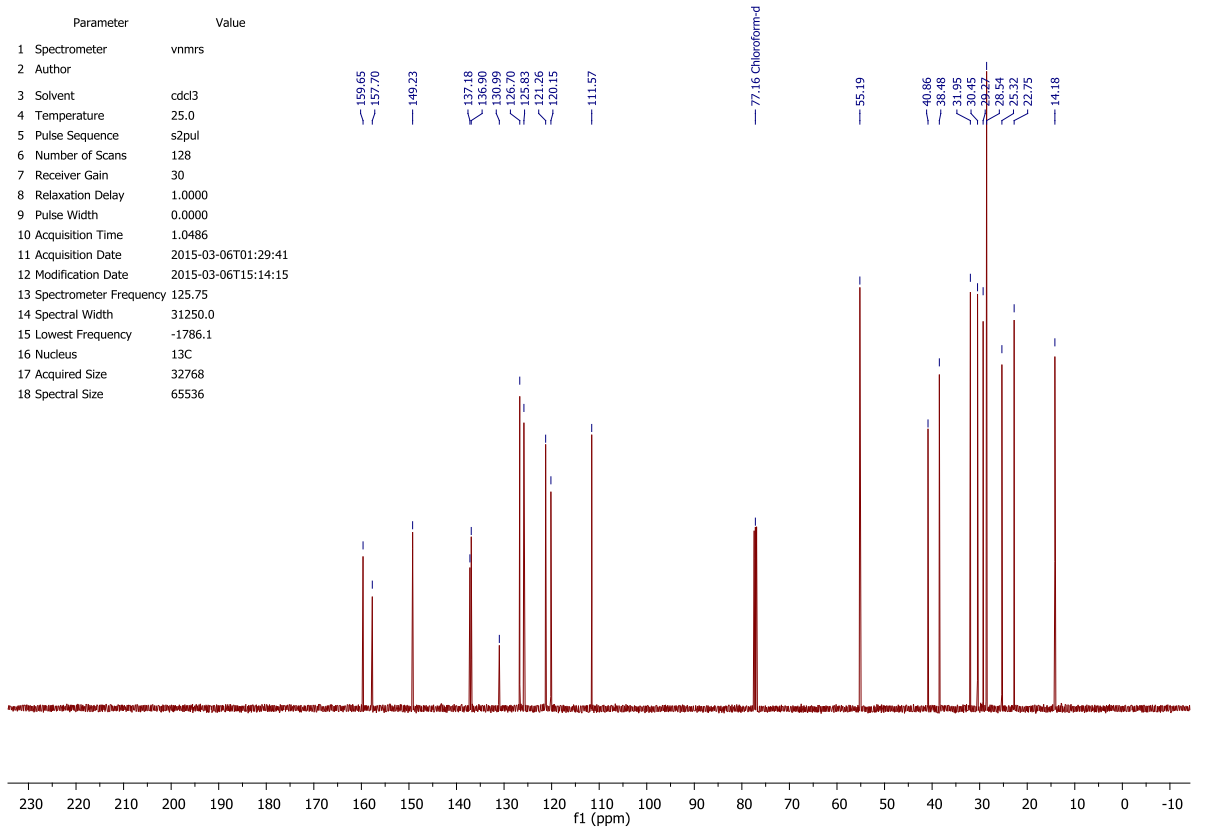


	Parameter	Value
1	Spectrometer	vnmrs
2	Author	
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Number of Scans	128
7	Receiver Gain	30
8	Relaxation Delay	1.0000
9	Pulse Width	0.0000
10	Acquisition Time	1.0486
11	Acquisition Date	2015-03-06T02:47:33
12	Modification Date	2015-03-06T15:15:37
13	Spectrometer Frequency	125.75
14	Spectral Width	31250.0
15	Lowest Frequency	-1778.5
16	Nucleus	13C
17	Acquired Size	32768
18	Spectral Size	65536

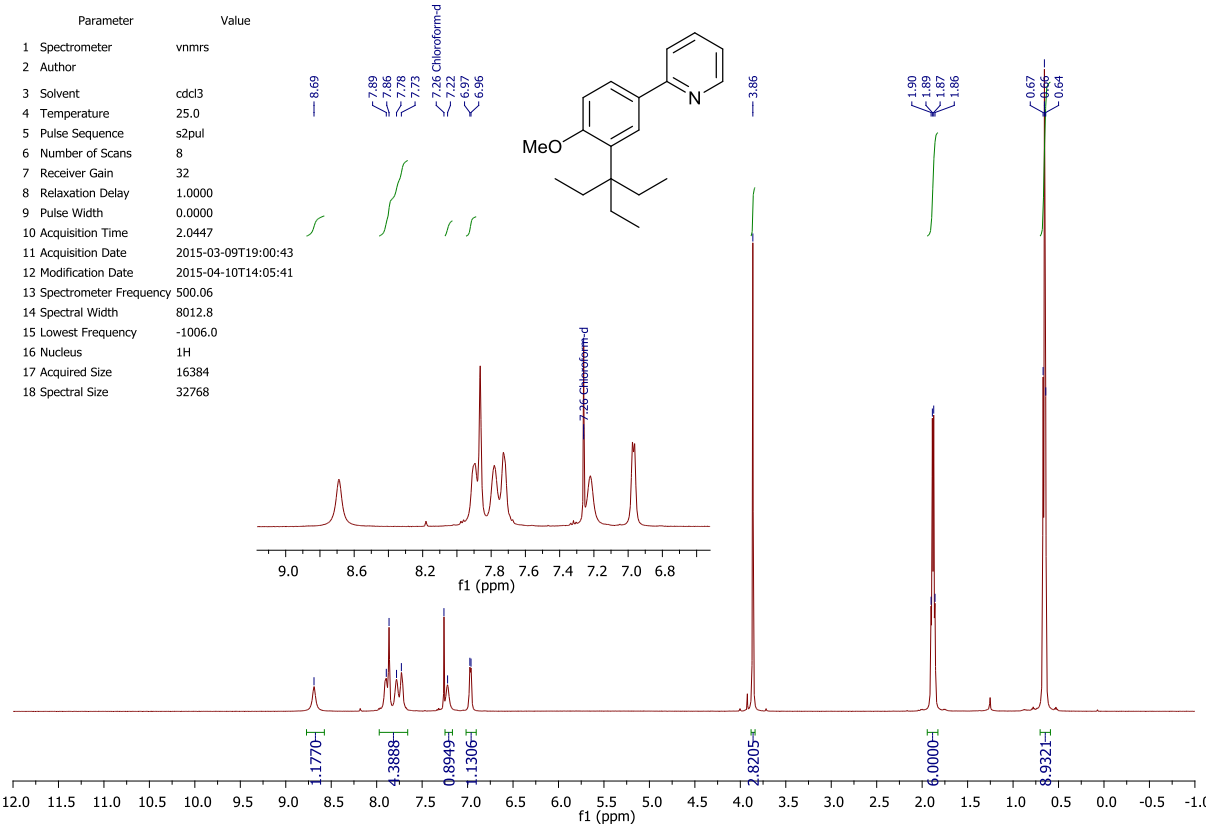


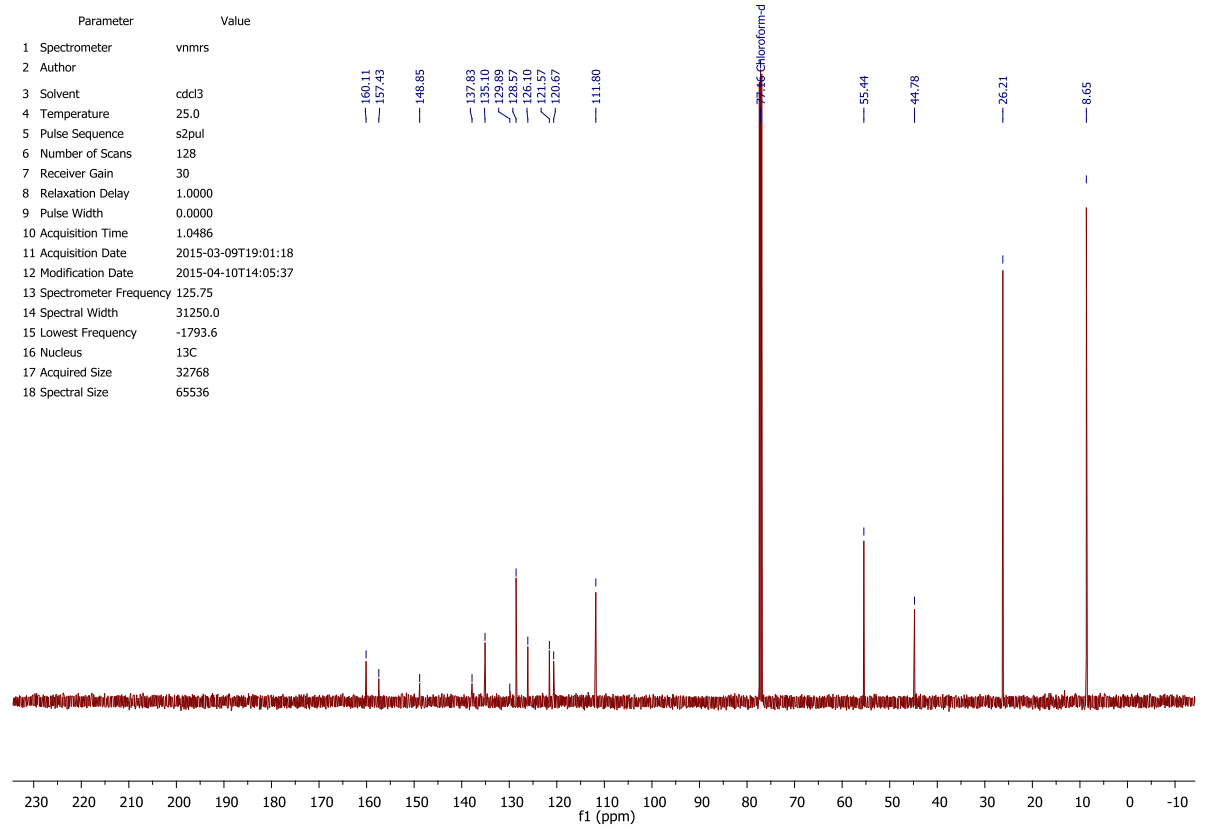
2-[4-methoxy-3-(2-methylnonan-2-yl)phenyl]pyridine (6c)





2-(3-(3-ethylpentan-3-yl)-4-methoxyphenyl)pyridine (7c)





ethyl 2-methyl-2-[3-(pyridin-2-yl)phenyl]propanoate (8a)

Parameter	Value
1 Spectrometer	vnmrs
2 Author	
3 Solvent	cdcl3
4 Temperature	25.0
5 Pulse Sequence	s2pul
6 Number of Scans	8
7 Receiver Gain	26
8 Relaxation Delay	1.0000
9 Pulse Width	0.0000
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11 Acquisition Date	2015-03-26T21:15:59
12 Modification Date	2015-03-27T09:25:04
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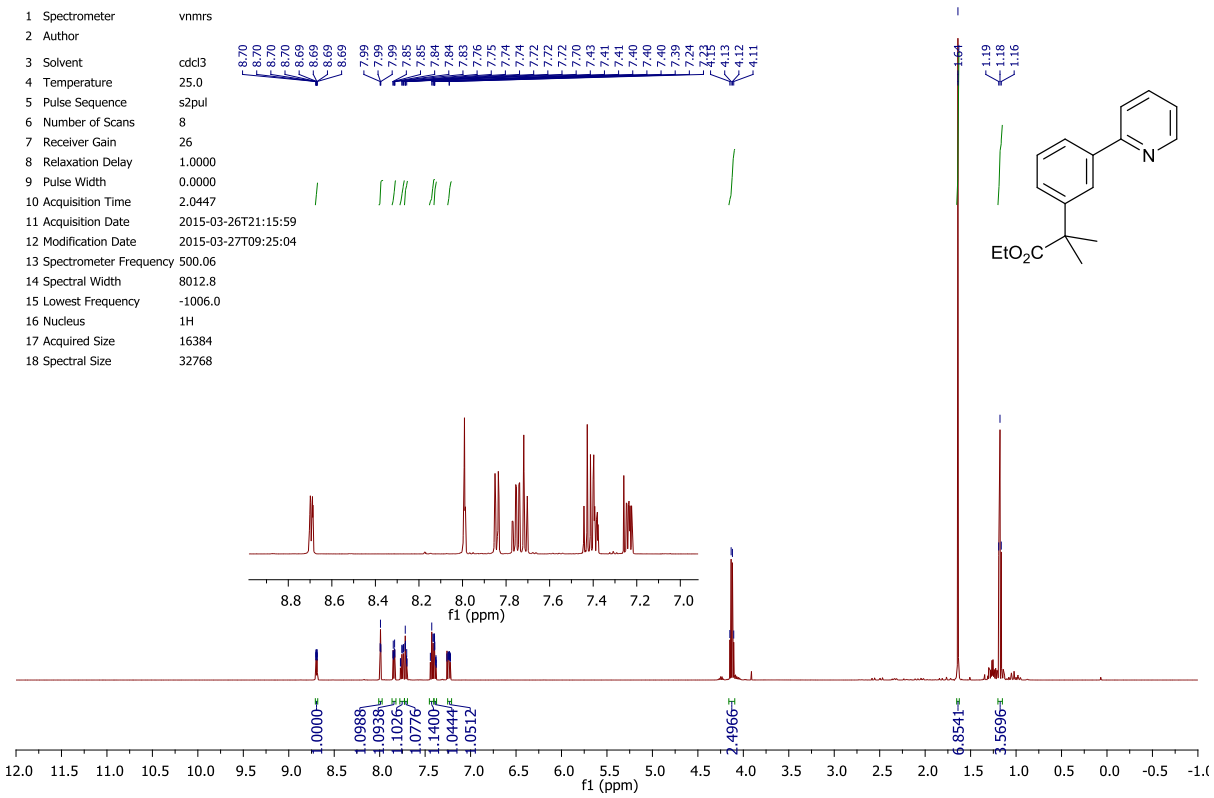
14 Spectral Width	8012.8
15 Lowest Frequency	-1006.0
16 Nucleus	1H
17 Acquired Size	16384
18 Spectral Size	32768



Parameter	Value
1 Spectrometer	vnmrs
2 Author	
3 Solvent	cdcl3
4 Temperature	25.0
5 Pulse Sequence	s2pul
6 Number of Scans	128
7 Receiver Gain	30
8 Relaxation Delay	1.0000
9 Pulse Width	0.0000
10 Acquisition Time	1.0486
11 Acquisition Date	2015-03-26T21:16:34
12 Modification Date	2015-03-27T09:25:01
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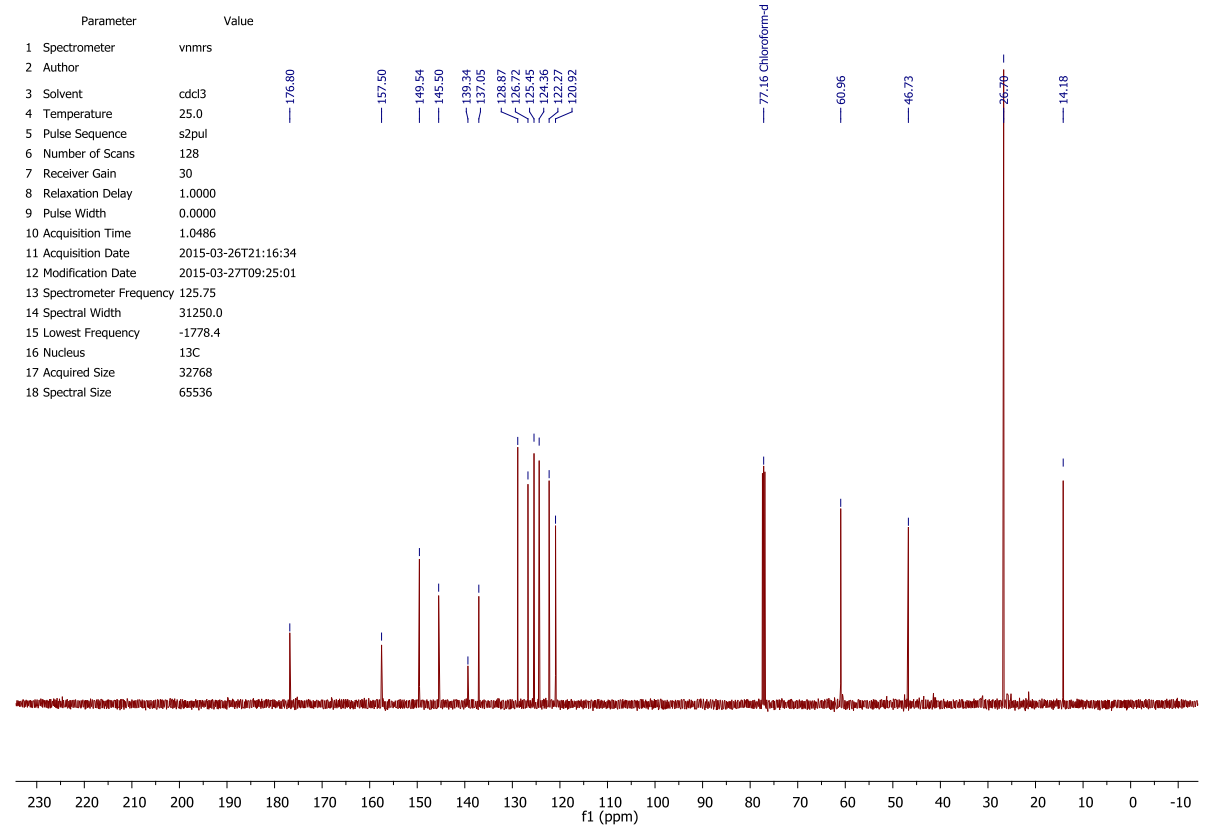
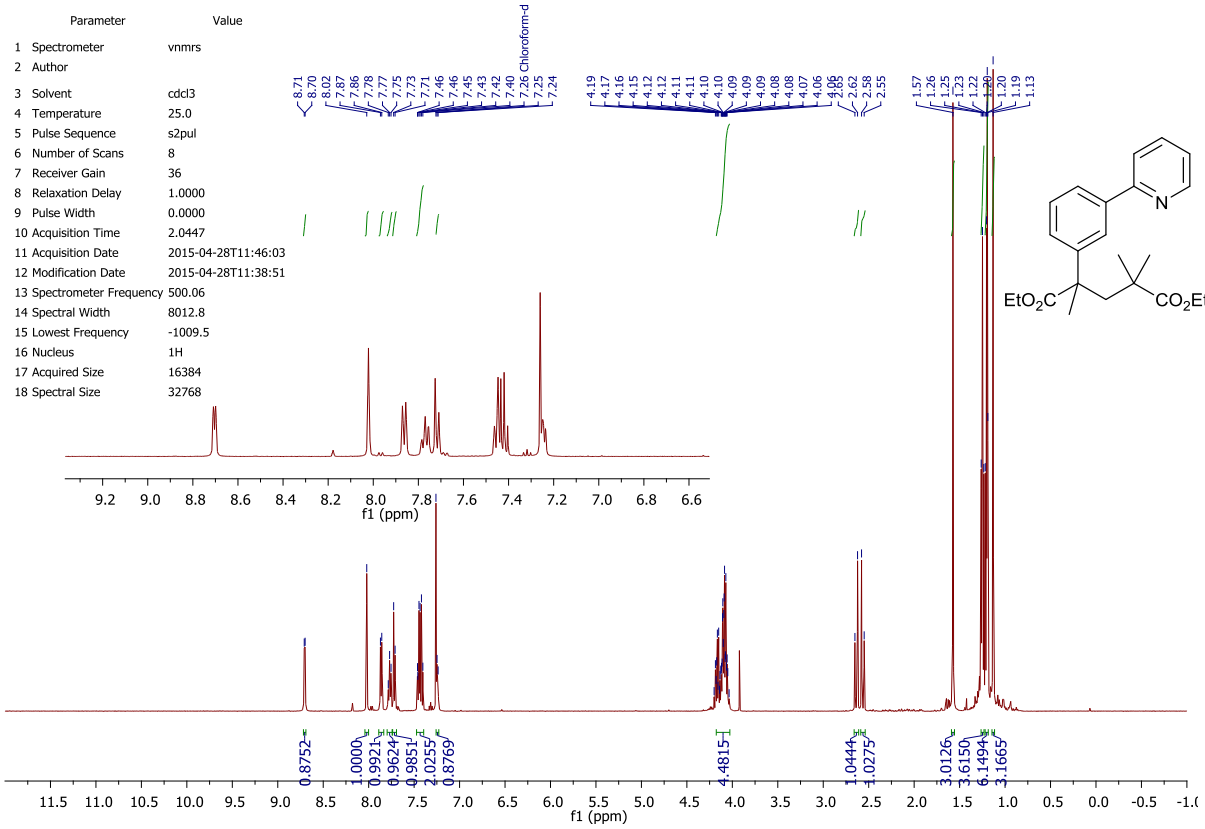
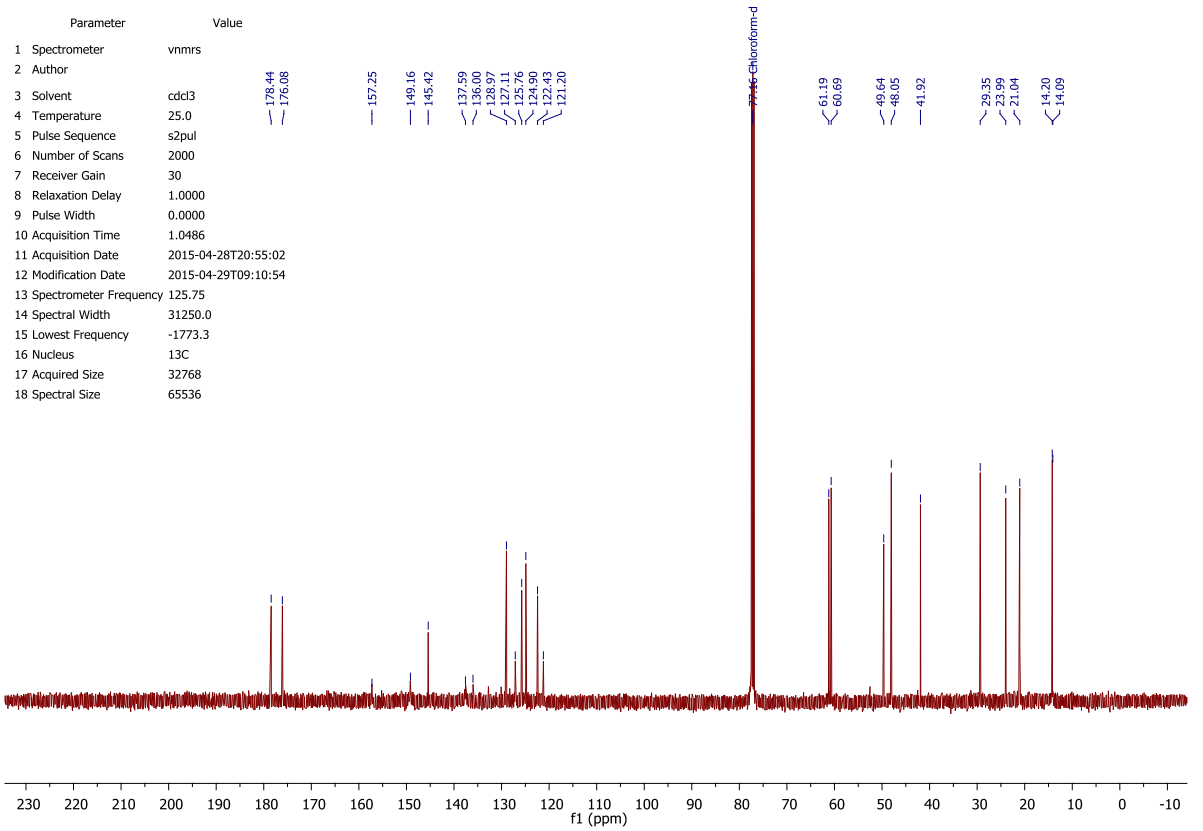
14 Spectral Width	31250.0
15 Lowest Frequency	-1778.4
16 Nucleus	13C
17 Acquired Size	32768
18 Spectral Size	65536

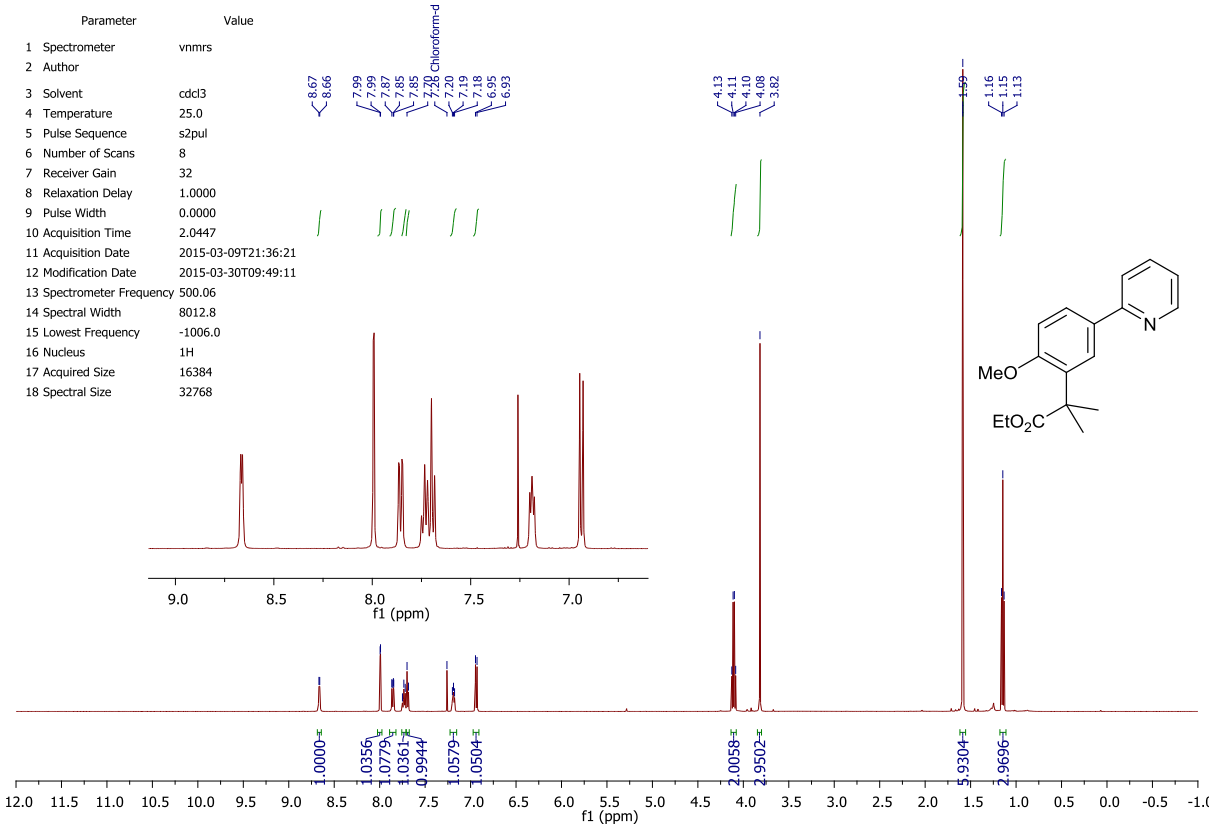


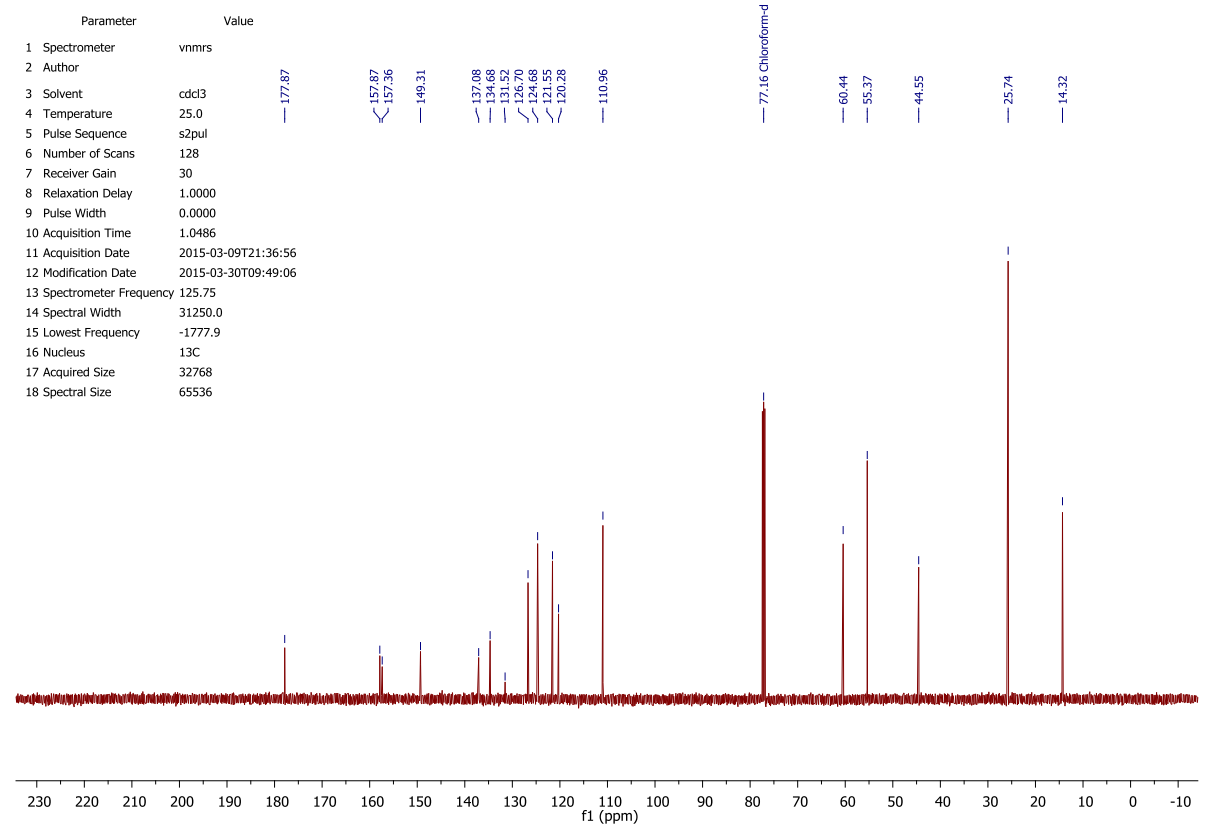
diethyl 2,2,3-trimethyl-3-[3-(pyridin-2-yl)benzyl]butanedioate (9a)



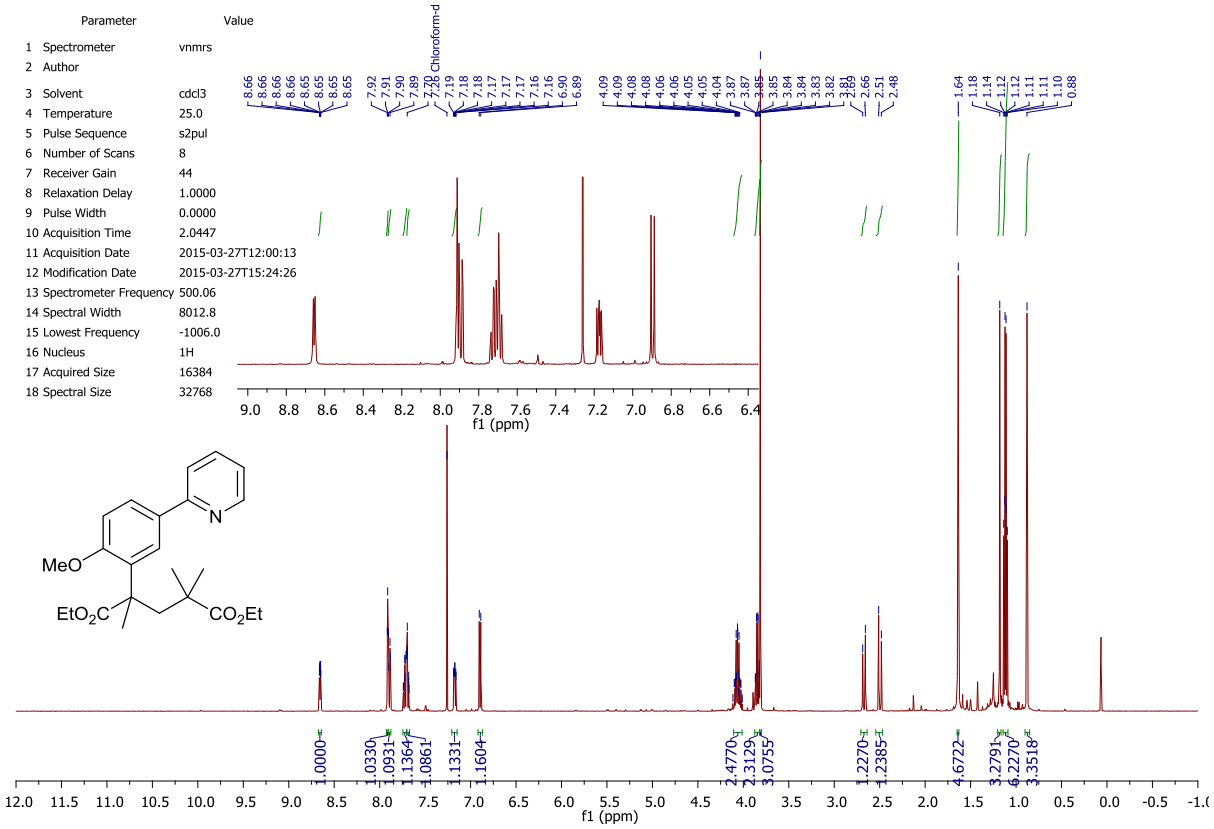


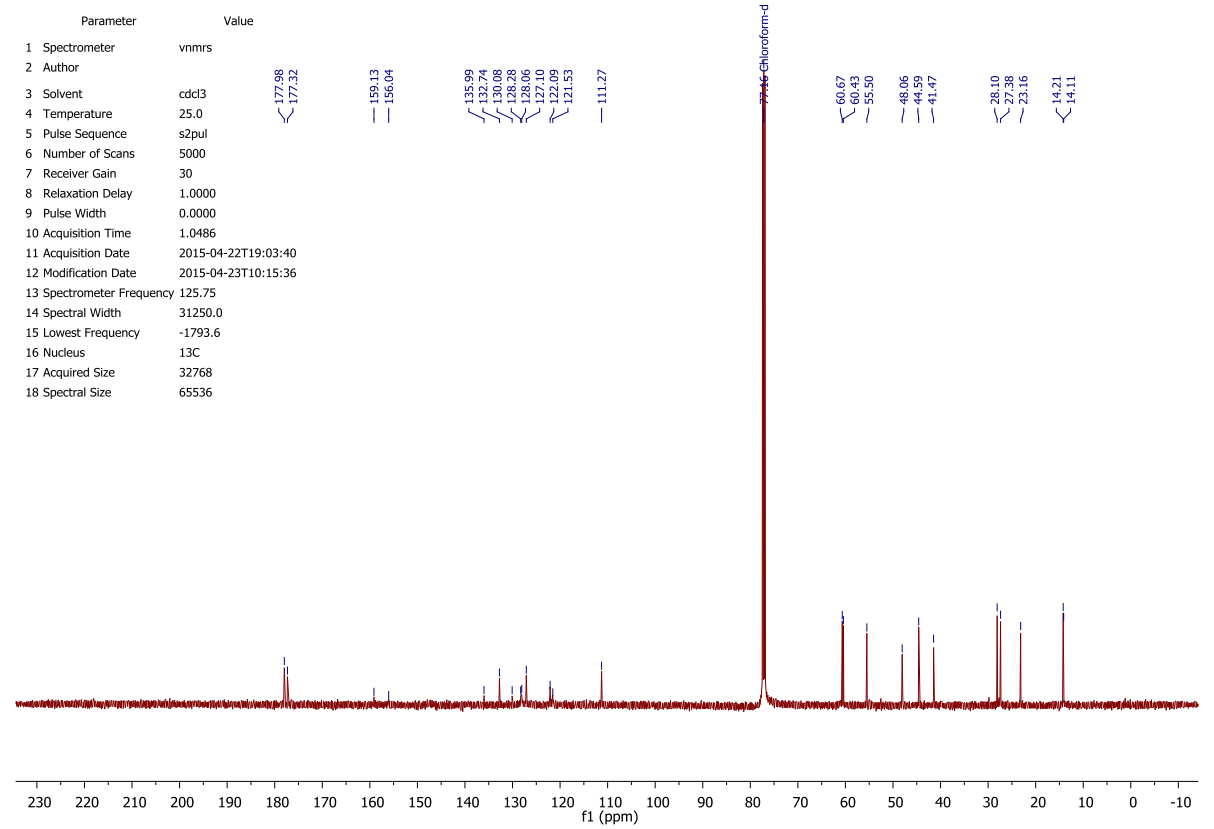
ethyl 2-[2-methoxy-5-(pyridin-2-yl)phenyl]-2-methylpropanoate (8c)



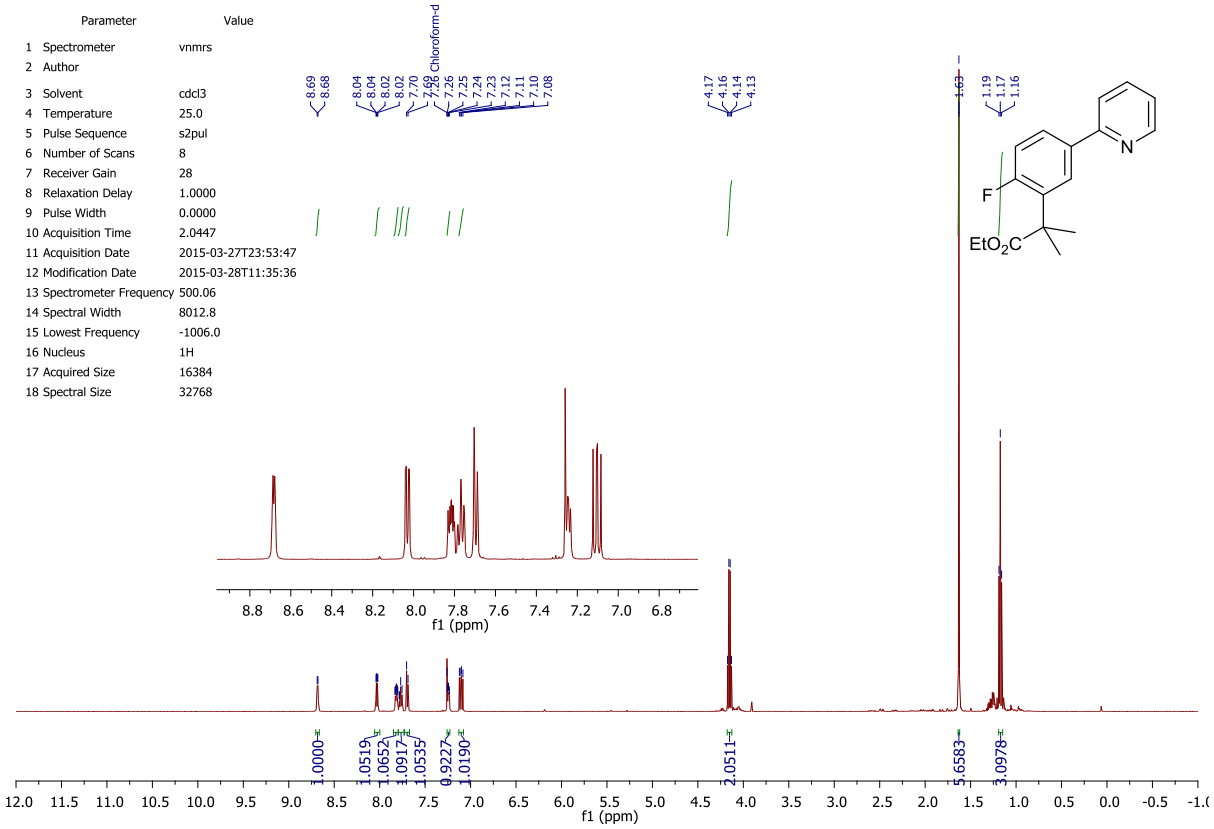


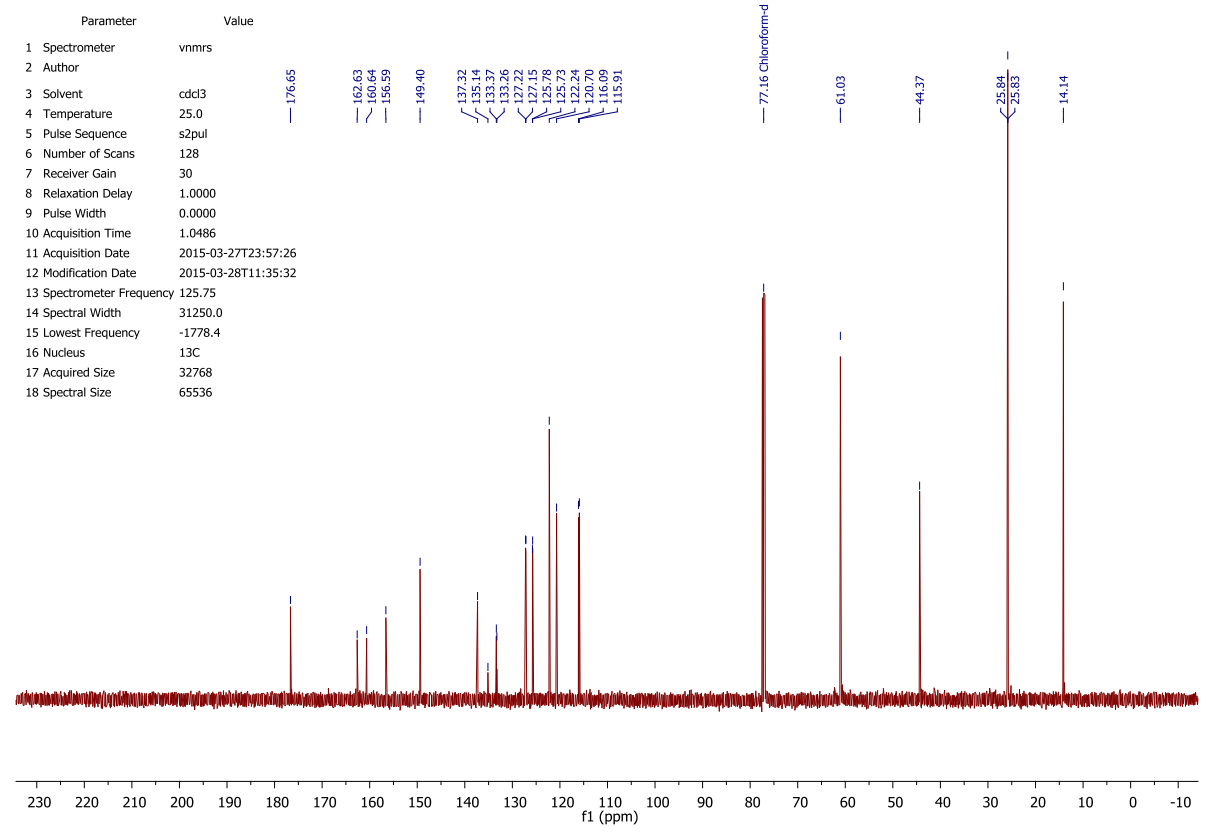
diethyl 2-[2-methoxy-5-(pyridin-2-yl)phenyl]-2,3,3-trimethylbutanedioate (9c)



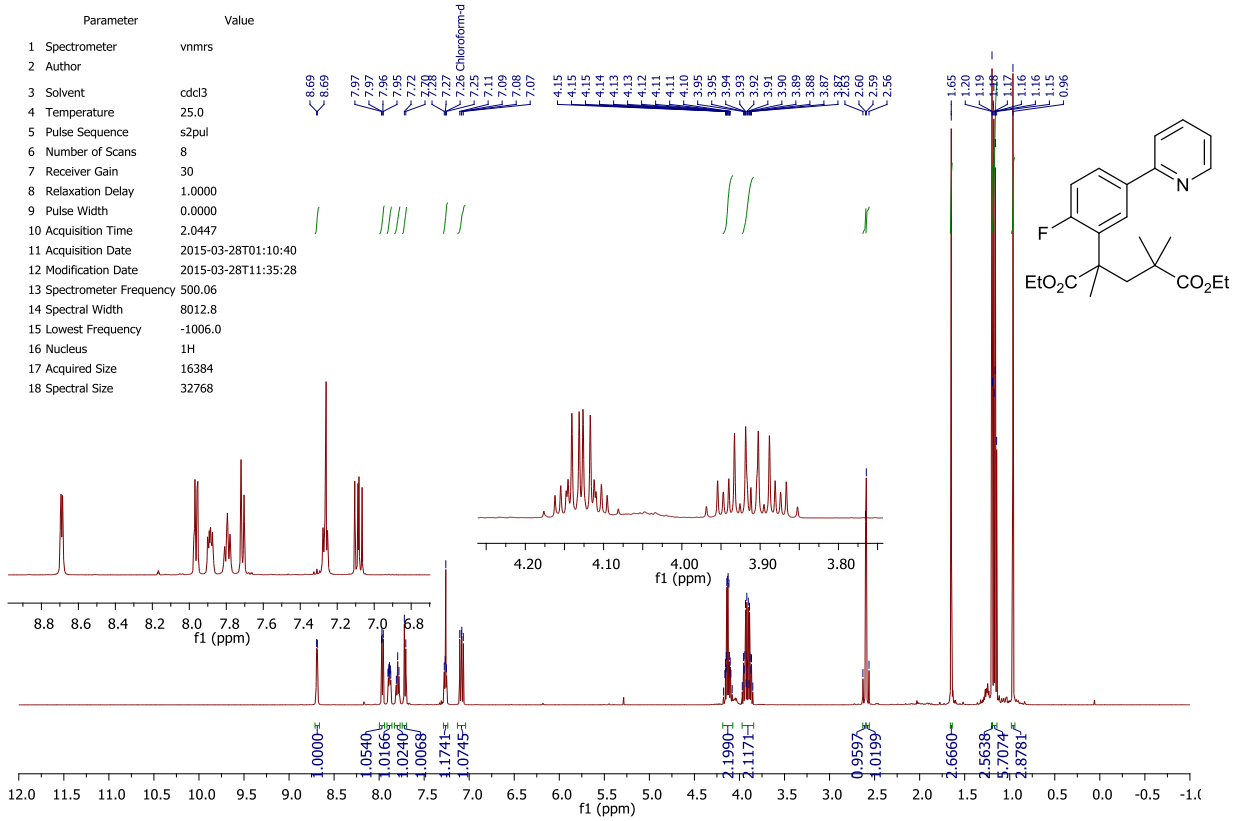


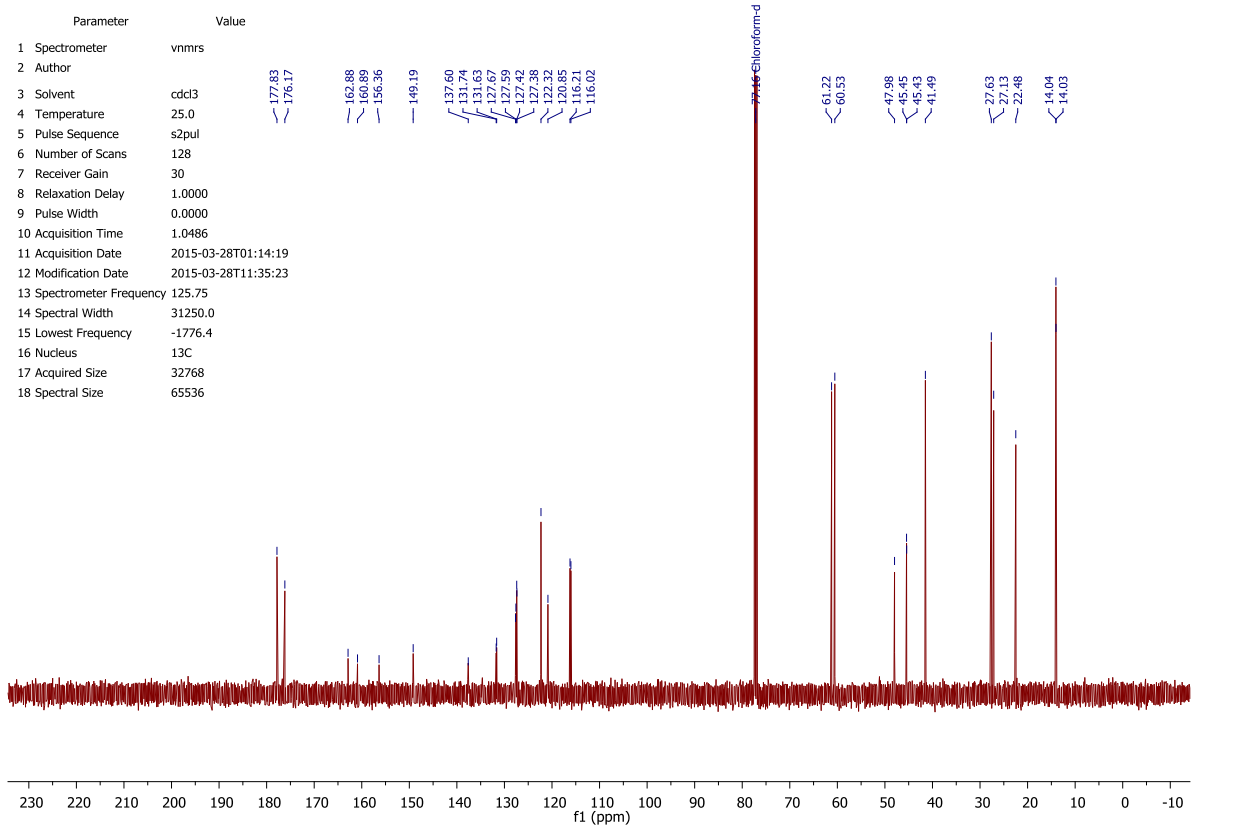
ethyl 2-[2-fluoro-5-(pyridin-2-yl)phenyl]-2-methylpropanoate (8d)



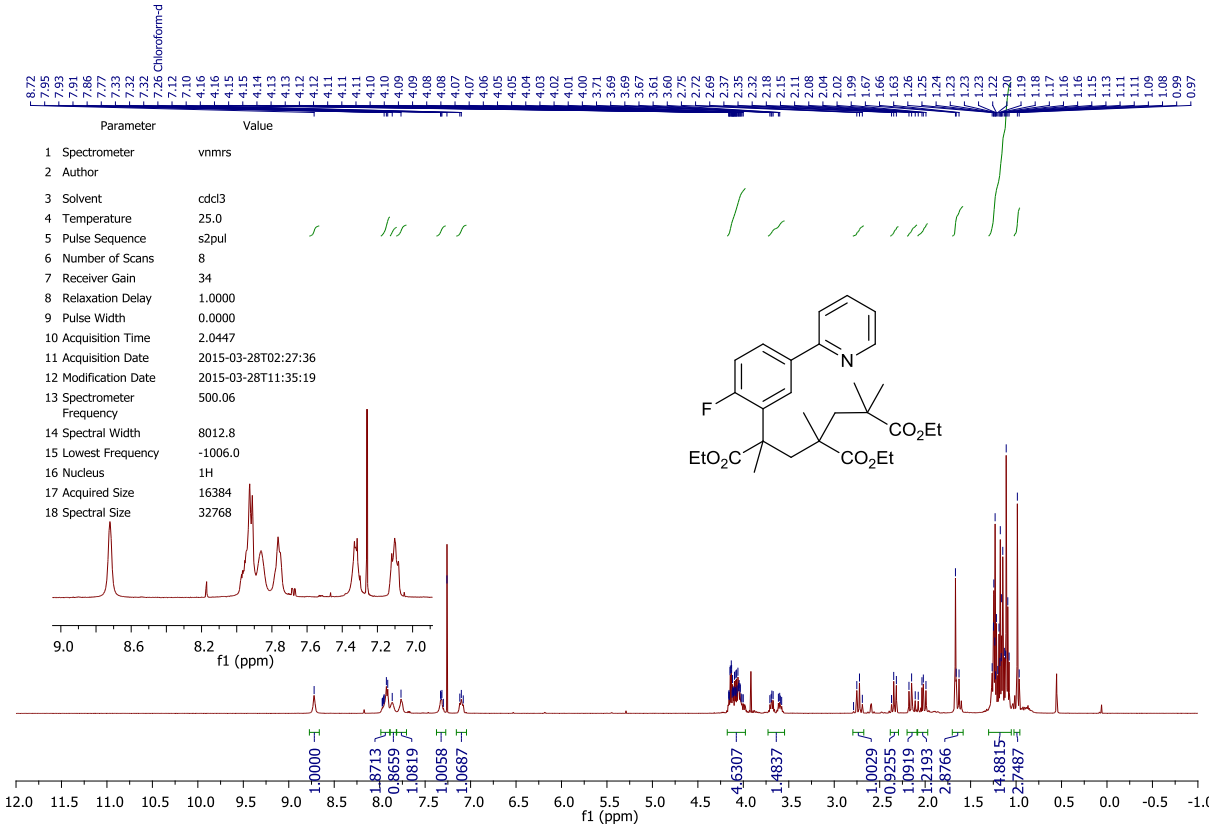


diethyl 2-[2-fluoro-5-(pyridin-2-yl)phenyl]-2,3,3-trimethylbutanedioate (9d)

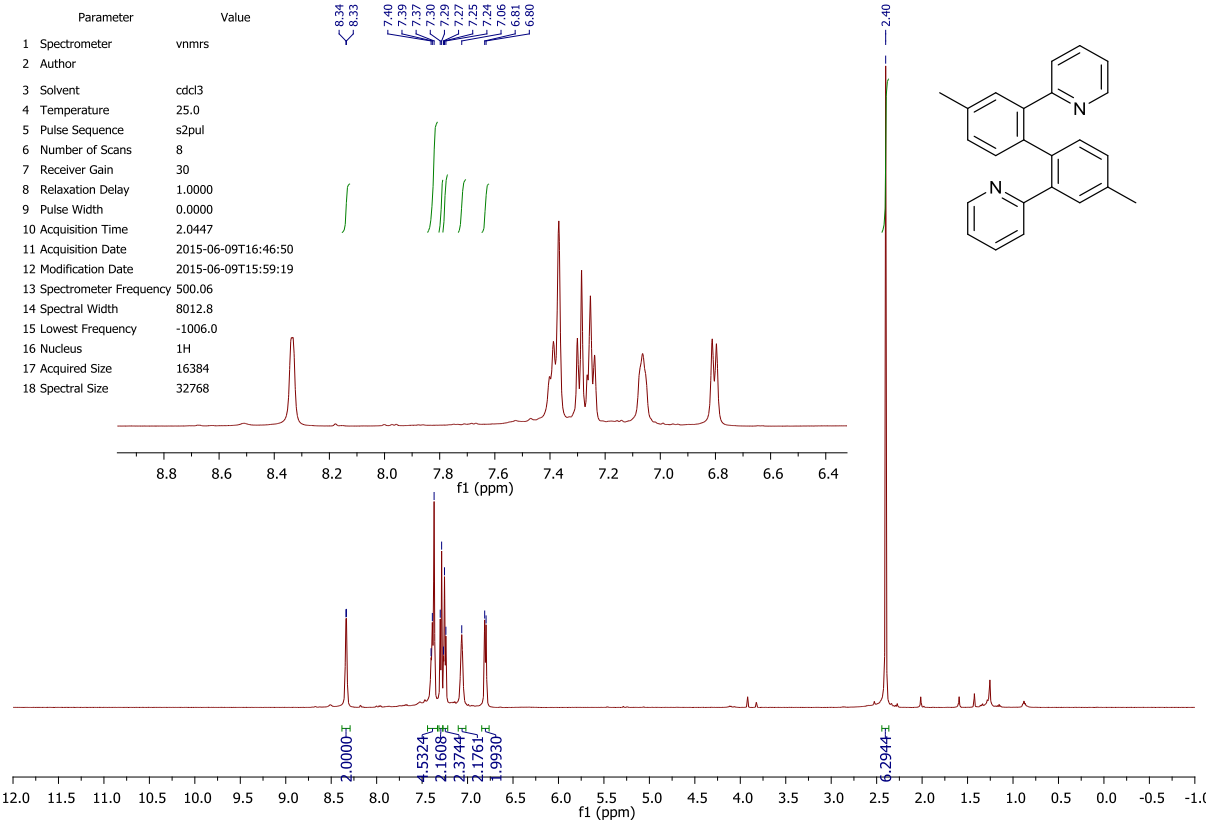


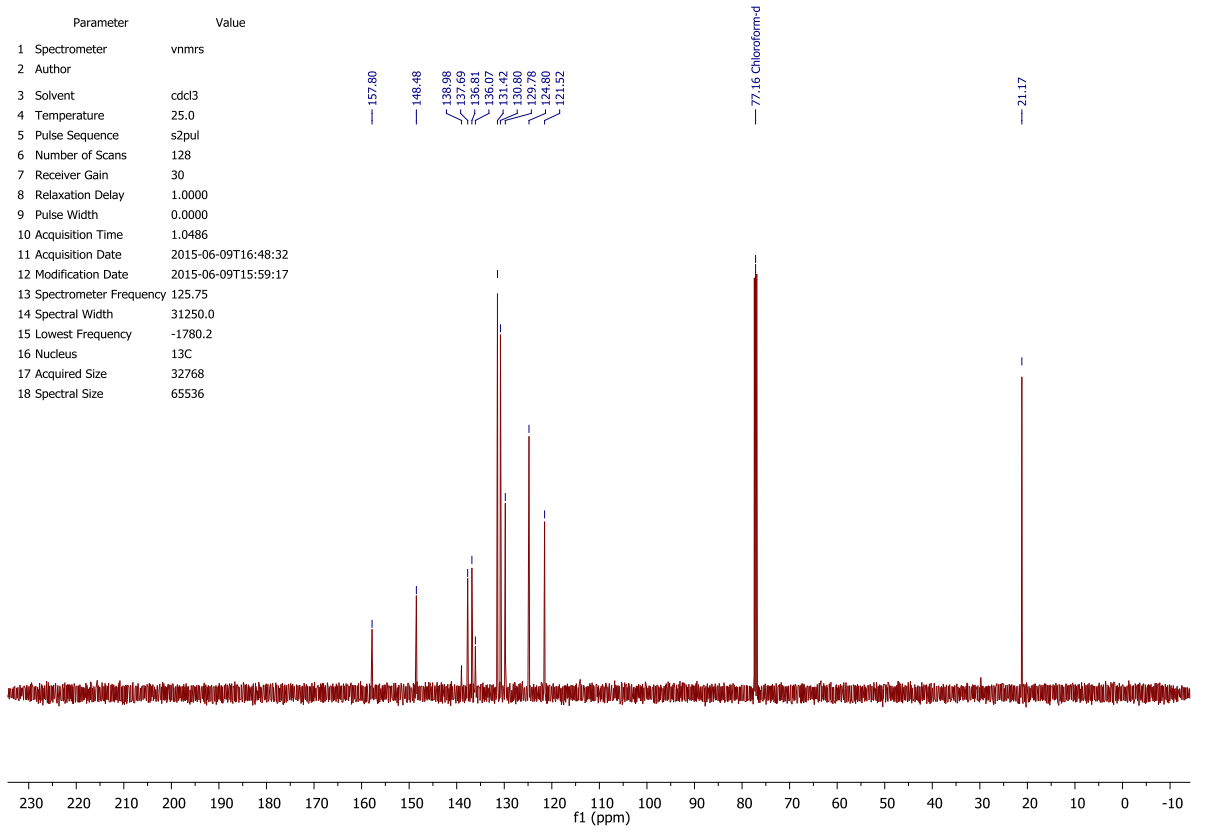


triethyl 2-[2-fluoro-5-(pyridin-2-yl)phenyl]-3,5-dimethylhexane-2,3,5-tricarboxylate (9e)

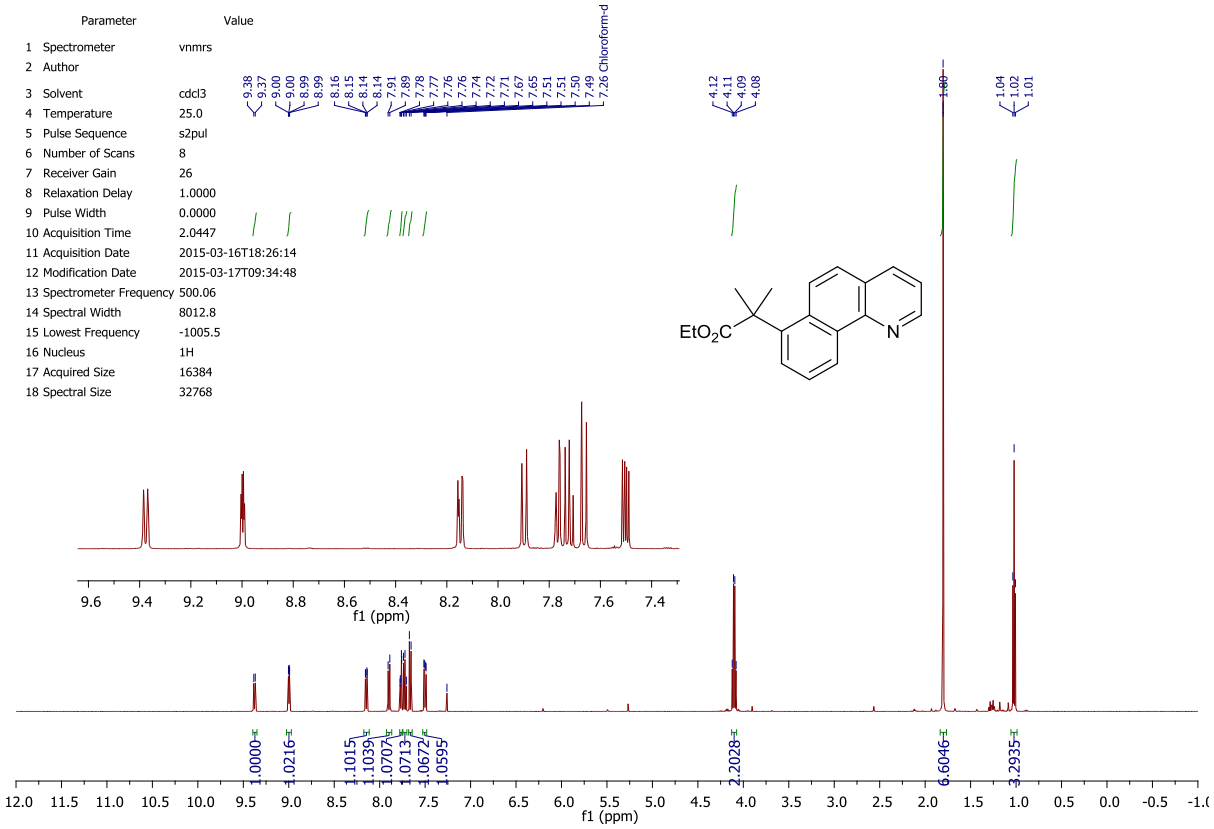


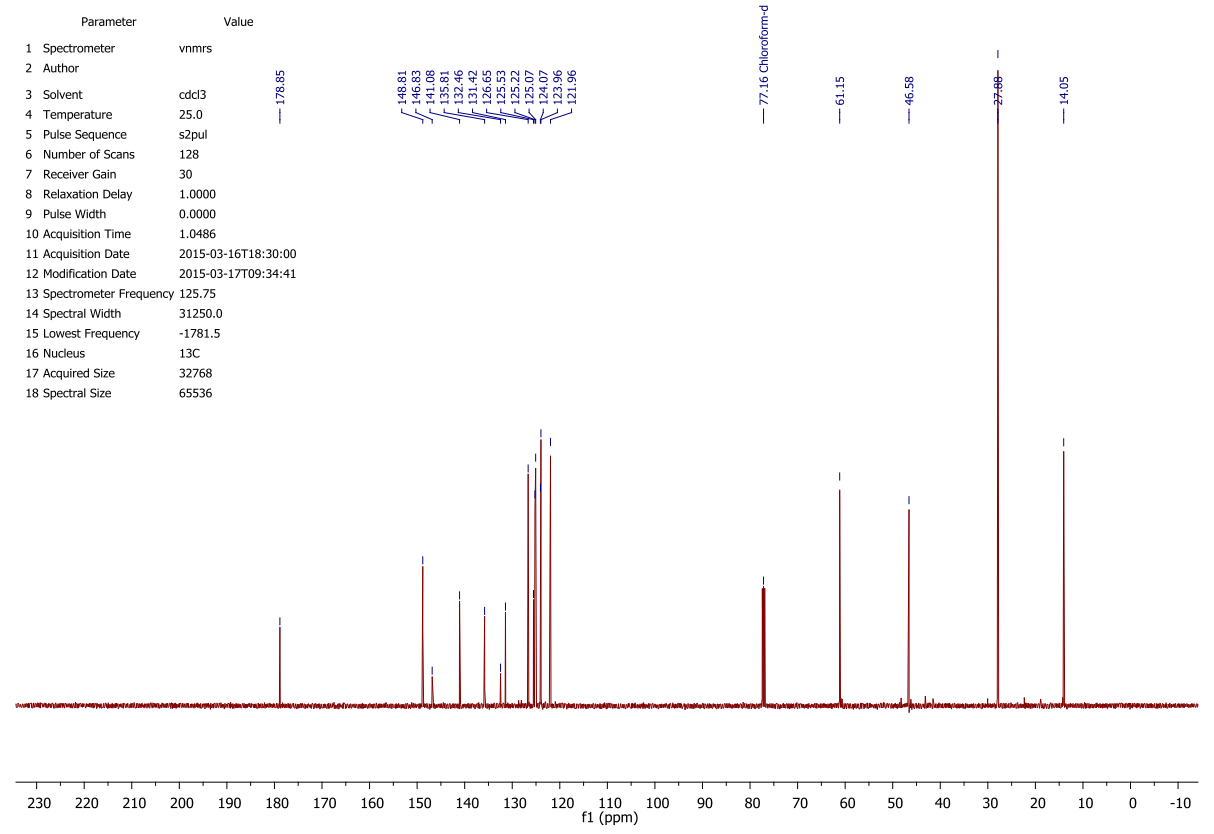
2,2'-(4,4'-dimethylbiphenyl-2,2'-diyl)dipyridine (10)





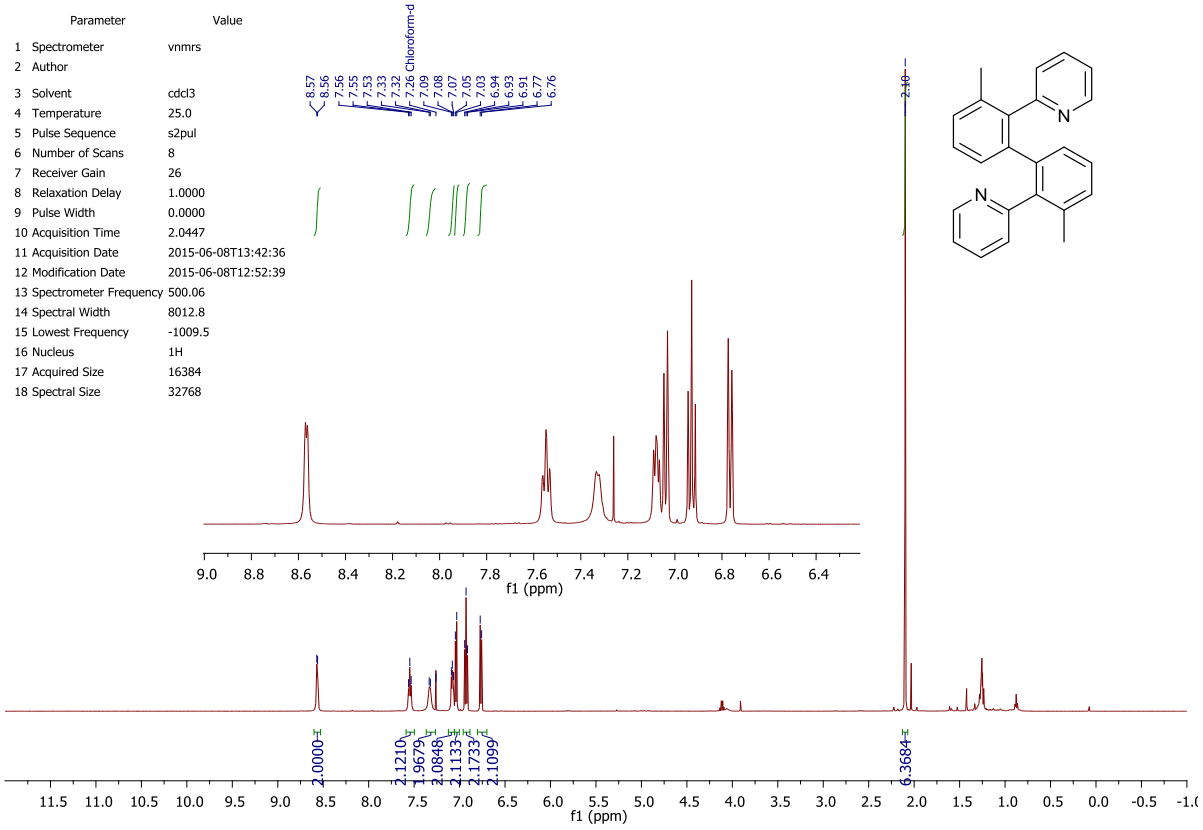
ethyl 2-(benzo[h]quinolin-7-yl)-2-methylpropanoate (11)





2,2'-(3,3'-dimethylbiphenyl-2,2'-diyl)dipyridine (12)

	Parameter	Value
1	Spectrometer	vnmrs
2	Author	
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Number of Scans	8
7	Receiver Gain	26
8	Relaxation Delay	1.0000
9	Pulse Width	0.0000
10	Acquisition Time	2.0447
11	Acquisition Date	2015-06-08T13:42:36
12	Modification Date	2015-06-08T12:52:39
13	Spectrometer Frequency	500.06
14	Spectral Width	8012.8
15	Lowest Frequency	-1009.5
16	Nucleus	1H
17	Acquired Size	16384
18	Spectral Size	32768



	Parameter	Value
1	Spectrometer	vnmrs
2	Author	
3	Solvent	cdcl3
4	Temperature	25.0
5	Pulse Sequence	s2pul
6	Number of Scans	128
7	Receiver Gain	30
8	Relaxation Delay	1.0000
9	Pulse Width	0.0000
10	Acquisition Time	1.0486
11	Acquisition Date	2015-06-08T13:43:17
12	Modification Date	2015-06-08T12:52:38
13	Spectrometer Frequency	125.75
14	Spectral Width	31250.0
15	Lowest Frequency	-1779.3
16	Nucleus	13C
17	Acquired Size	32768
18	Spectral Size	65536