Electronic Supplementary Material (ESI) for Chemical Science.

Supporting Information

Pyridine Sulfinates as General Nucleophilic Coupling Partners in Palladium-Catalyzed Cross-Coupling Reactions with Aryl Halides

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1. General Experimental Methods

Reactions were performed under a nitrogen atmosphere with anhydrous solvent unless otherwise stated. All glassware was oven dried at > 100 °C, and allowed to cool to room temperature under a positive nitrogen pressure. Reactions were monitored by TLC or LCMS until deemed complete using aluminum backed silica plates. Plates were visualized under ultraviolet light (254 nm) and/or staining with $KMnO_4$.

Reagents were purchased from Sigma-Aldrich Chemical Co. Ltd., Alfa Aesar, Acros Organics Ltd., Fluorochem Ltd., Insights or Strem Chemicals Inc. and were used as supplied. THF and 1,4-dioxane were degassed with a flow of nitrogen and stored over activated 3 Å molecular sieves. Flash chromatography was carried out using matrix 60 silica. Petrol refers to the fraction of light petroleum ether boiling in the range 40-60 °C. Sodium 1-methyl 3-sulfinopropionate (SMOPS) was prepared according to Baskin and Wang.[1]

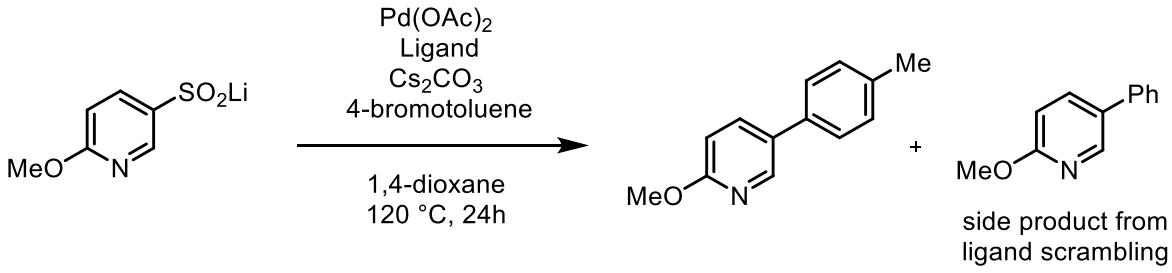
^{1}H NMR spectra were obtained on a Bruker AVIII400 (400 MHz) spectrometer using the residual solvent as an internal standard. ^{13}C NMR spectra were obtained on a Bruker AVIII400 (101 MHz) using the residual solvent as an internal standard. ^{19}F-NMR spectra were obtained on a Bruker AVIII400 (377 MHz) spectrometer. Chemical shifts (δ) were reported in parts per million (ppm) with the multiplicities of the resonances reported as following: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; app., apparent. Coupling constants (J) were given in Hertz (Hz).

Low resolution ESI mass spectra were recorded on a Waters LCT Premier spectrometer. High resolution mass spectrometry measurements were recorded on a Bruker Daltronics MicroTOF (ESI) spectrometer or on a Micromass LCT (FI) spectrometer by the internal service at Chemistry Research Laboratory, University of Oxford. Samples for mass spectra were prepared as 1 mg/mL solution in MeOH (LRMS, HRMS-ESI) or submitted neat (HRMS-FI).

Infrared spectra were recorded as thin films on a Bruker Tensor 27 FT-IR spectrometer. Melting points were determined using a Stuart Scientific Melting Point Apparatus SMP1. Reverse phase HPLC analysis was performed on Agilent Zorbax SB-C18 5µm column (4.6 x 150mm), eluted in 85% MeCN/H2O, 1 mL/min.

2. Optimization Screening Tables

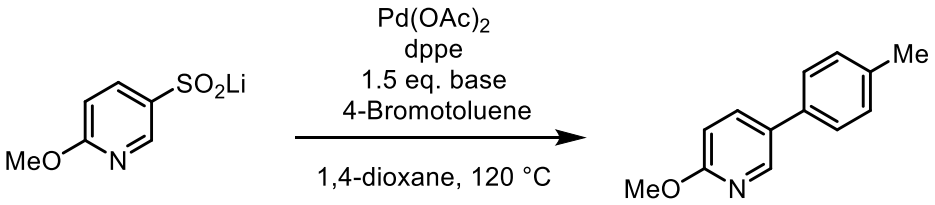
Table S1. Ligand Screening at 120 °C.[a]



Entry	Ligand	Yield [%][b]
1	XPhos	4
2	PCy_3	34
3	$P(^tBu)_3$	0
4	CataCXium A	22
5	RuPhos	9
6	DavePhos	13
7	BrettPhos	12
8	dppf	22 (3:1)[c]
9	XantPhos	15 (3:1)[c]
10	DPEPhos	15 (2.5:1)[c]
11	PPh_3	17
12	Ditertbutylmethylphosphine	30
13	BINAP	11
14	Tris(o-tolyl)phosphine	3
15	dppe	60 (3.5:1)[c]
16	dcpe	18
17	dppm	15
18	dppp	20
19	dppb	10
20	Phenanthroline	0
21	Bipyridine	0
22	*p*-CF_3-dppe	45 (5.5:1)[c]
23	*p*-OMe-dppe	66 (7:1)[c]
24	*o*-*i*Pr-dppe	21 (2:1)[c]

[a] Reaction conditions: 3-pyridyl lithium sulfinate (0.3 mmol, 1.5 eq.), caesium carbonate (0.3 mmol, 1.5 eq.), 4-bromotoluene (0.2 mmol, 1.0 eq.), palladium(II) acetate (5 mol%), Ligand (7.5-10 mol%), 1,4-dioxane (0.1 M). [b] Determined by HPLC using 4,4'-dimethylbiphenyl as an internal standard. [c] Ratio of products (desired product :side product).

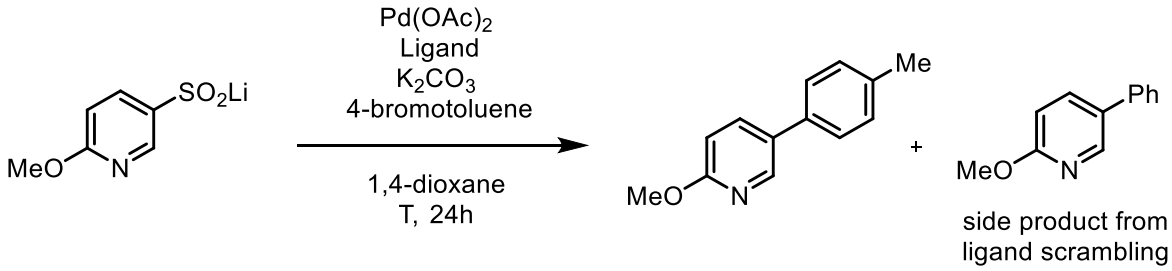
Table S2. Base and Metal Salt Screening at 120 °C.[a]



Entry	Ligand	Yield [%][b]
1	no base	0
2	Li_2CO_3	0
3	Na_2CO_3	19
4	K_2CO_3	64
5	Cs_2CO_3 (0.5 eq.)	32
6	Cs_2CO_3 (1.0 eq.)	55
7	Cs_2CO_3 (2.0 eq.)	60
8	Cs_2CO_3 (2.5 eq.)	58
9	Cs_2CO_3 (3.0 eq.)	59
10	Ag_2CO_3	0
11	$CaCO_3$	2
12	$CuCO_3$	0
13	KOAc	7
14	KF	11
15	CsF	16
16	K_3PO_4	28
17	NaO*t*Bu	20
18	KO*t*Bu	32
19	NaOH	9
20	KOH	23
21	CsOH	21
22	KCl	15
23	KBr	7
24	NaCl	0
25	NEt_3	0
26	DABCO	0
27	DBU	0

[a] Reaction conditions: 3-pyridyl lithium sulfinate (0.3 mmol, 1.5 eq.), base (0.3 mmol, 1.5 eq.), 4-bromotoluene (0.2 mmol, 1.0 eq.), palladium(II) acetate (5 mol%), Ligand (7.5 mol%), 1,4-dioxane (0.1 M). [b] Determined by HPLC using 4,4'-dimethylbiphenyl as an internal standard.

Table S3. Ligand Effects and Sulfinate Stochiometries at 130 and 150 °C.[a]

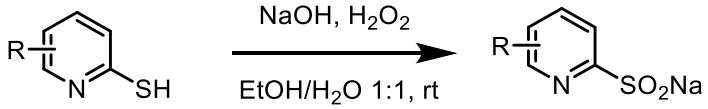


Entry	Ligand	Temp. [°C]	Equiv. Sulfinate	Yield [%][b]
1	dppe	130	1.5	64 (4:1)
2	dppe	130	2.0	55 (9:1)
3	dppe	150	1.5	71 (4.5:1)
4	dppe	150	2.0	73 (7:1)
5	*p*-OMe-dppe	130	1.5	78 (7:1)
6	*p*-OMe-dppe	130	2.0	82 (8:1)
7	*p*-OMe-dppe	150	1.5	82 (8:1)
8	*p*-OMe-dppe	150	2.0	92 (9:1)
9	PCy_3	150	1.5	88 (1:0)
10	PCy_3	150	2.0	99 (1:0)

[a] Reaction conditions: 3-pyridyl lithium sulfinate (0.3 or 0.4 mmol, 1.5 eq. or 2.0 eq.), potassium carbonate (0.3 mmol, 1.5 eq.), 4-bromotoluene (0.2 mmol, 1.0 eq.), palladium(II) acetate (5 mol%), Ligand (7.5-10 mol%), 1,4-dioxane (0.1 M). [b] Determined by HPLC using 4,4'-dimethylbiphenyl as an internal standard.

3. Synthetic Procedures and Characterization Data

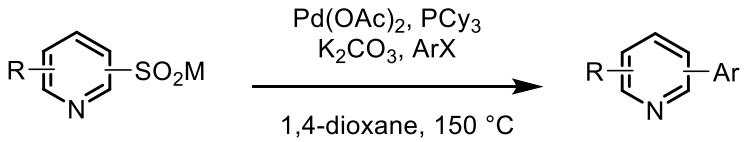
General Procedure (A) for the Pyridyl Thiol Oxidation



Modified procedure according to Kamiyama and Inoue.[2] Pyridyl thiol (4.5 mmol, 1.0 equiv.) was dissolved in a mixture of 20 mL of water containing sodium hydroxide (234.0 mg, 1.3 equiv.) and 20 mL of ethanol. An aqueous solution of hydrogen peroxide (0.5 mL, 1.1 equiv., 30% (*w*/*w*) in H_2O) was added dropwise at room temperature and stirred until completion. The solvent was removed under reduced pressure and the residue was washed with ethyl acetate (3 x 30 mL). The aqueous phase was then co-evaporated with acetonitrile to afford the corresponding sodium sulfinate salt. An analytical sample was obtained by preparative HPLC using Sunfire C18

column eluted with unmodified MeCN/H_2O gradient. **Note:** For preparative coupling chemistry – all sulfinates were used without further purification.

General Procedure (B) for the Desulfinylative Cross-Coupling Reaction



CAUTION: Sulfur dioxide gas formation during reaction. Pyridyl sulfinate (2.0 equiv.), aryl halide (1.0 eq.), potassium carbonate (41.4 mg, 0.3 mmol, 1.5 equiv.), palladium(II) acetate (2.2 mg, 5 mol%), tricyclohexylphosphine (5.6 mg, 10 mol%) were placed in a microwave vial under nitrogen atmosphere followed by the addition of 1,4-dioxane (2.0 mL, 0.1 M). The reaction was heated at 150 °C until completion. The mixture was then allowed to cool down to room temperature, filtered over a pad of Celite© and washed with ethyl acetate and H_2O. After separating the layers the aqueous phase was extracted with ethyl acetate (15 mL) and the combined organic phases were washed with brine, dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude material was purified by column chromatography to yield the corresponding coupling product.

General Procedure (B-1) for the Varenicline Library Cross-Couplings

A microwave vial was charged with **5** (34.2 mg, 0.10 mmol, 1.0 equiv.), potassium carbonate (27.6 mg, 0.20 mmol, 2.0 equiv.) and pyridyl-sulfinate (0.20 mmol, 2.0 equiv.). The vial was then sealed, and a nitrogen atmosphere was established. A precatalyst stock solution was prepared from palladium(II) acetate (13.9 mg, 5 mol%), tricyclohexylphosphine (26.4 mg, 7.5 mol%), and 1,4-dioxane (6.3 mL). The microwave vial was then charged with a portion of the stock precatalyst solution (0.5 mL) and the reaction mixture was heated at 150 °C for 16 h. After allowing the reaction mixture to cool to room temperature, 1 M aq. NaOH (0.5 mL) and EtOH (0.5 mL) were added and heating to 50 °C was commenced. After 1 h, heating was discontinued and the volatile components of the reaction were removed using a Genevac. The residue was purified by preparative HPLC (Sunfire C18 column eluted with a MeCN/H_2O gradient modified with TFA) to afford the corresponding coupling products.

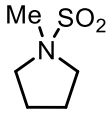
General Procedure (B-2a) for the Mepyramine Library Cross-Couplings (liquid Het-Br)

To a nitrogen-filled vial containing liquid Het-Br (0.10 mmol, 1.0 equiv.), 1.4 mL of a precatalyst stock solution from palladium(II) acetate (21.5 mg, 5 mol%), tricyclohexylphosphine (40.9 mg, 7.5 mol%) in dioxane (9.5 mL) was added. A portion (0.42 mL, 0.83 mmol) of the resulting solution was added to a nitrogen-filled microwave vial containing compound **6** (35.6 mg, 0.10 mmol, 1.2 equiv.) and K_2CO_3 (23.0 mg, 0.17 mmol, 2.0 equiv.). The resulting mixture was heated at 150 °C for 15 h. After cooling to room temperature, the reaction mixture was partitioned between EtOAc (2.0 mL) and half sat. brine (1.0 mL). The aqueous layer was further extracted with EtOAc (4 x 1.0 mL) and the combined organic layers were dried over sodium sulfate and concentrated to afford a brown oil. The residue was purified by preparative HPLC (Sunfire C18 column eluted with a MeCN/H_2O gradient modified with TFA) to afford the corresponding coupling products.

General Procedure (B-2b) for the Mepyramine Library Cross-Couplings (solid Het-Br)

A microwave vial was charged with **6** (35.6 mg, 0.10 mmol, 1.2 equiv.), K_2CO_3 (23.0 mg, 0.17 mmol, 2.0 equiv.) and solid Het-Br (0.083 mmol, 1.0 equiv.). The vial was then sealed, and a nitrogen atmosphere was established. A precatalyst stock solution was prepared from palladium(II) acetate (13.9 mg, 5 mol%), tricyclohexylphosphine (26.4 mg, 7.5 mol%), and 1,4-dioxane (6.3 mL). The microwave vial was then charged with a portion of the stock precatalyst solution (0.4 mL) and the reaction mixture was heated for at 150 °C for 16 h. After cooling to room temperature, the reaction mixture was partitioned between EtOAc (2.0 mL) and half sat. brine (1.0 mL). The aqueous layer was further extracted with EtOAc (4 x 1.0 mL) and the combined organic layers were dried over sodium sulfate and concentrated. The residue was purified by preparative HPLC (Sunfire C18 column eluted with a MeCN/H_2O gradient modified with TFA) to afford the corresponding coupling products.

3.1 Synthesis of *N*-methylpyrrolidine SO_2 adduct *TIMSO*

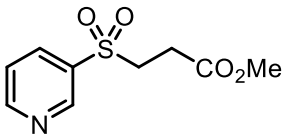


A 250 mL round bottom flask was fitted with a condenser, attached to a Dreschel bottle oil bubbler system and cooled under a flow of argon. *N*-methylpyrrolidine (15 mL, 144 mmol) was added to the flask and the system flushed with nitrogen for a further 5 minutes. A flow of sulfur dioxide gas was introduced into the system for 5 minutes. The reaction flask was cooled to -20 °C, the condenser to -78 °C and sulfur dioxide was condensed dropwise onto the *N*-methylpyrrolidine with stirring (approx. 120 mL). The gas flow was stopped and the flask allowed to warm up to -10 °C and left stirring at reflux for 1 hour. The flask was warmed to room temperature and the excess of sulfur dioxide allowed to evaporate through the bubbler overnight. The system was flushed fully with nitrogen to obtain *TIMSO* as a light yellow liquid (18.6 g, 87%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 2.82 (m, 4H), 2.35 (s, 3H), 1.89 – 1.78 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 52.9, 39.3, 24.0; IR υ_{max} (neat)/cm^{-1} 1455, 1227, 1091, 943, 764, 645; LRMS (ESI) *m*/*z* 150 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 150.0510 $[M+H]^+$, $C_5H_{12}NO_2S$ requires *m*/*z* 150.0511.

3.2 Synthesis of Pyridyl Sulfinate Salts using sodium 1-methyl 3-sulfinopropanoate (SMOPS)

Methyl 3-(pyridin-3-ylsulfonyl)propanoate

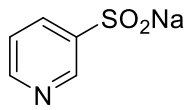


3-Iodopyridine (102.5 mg, 0.5 mmol, 1.0 equiv.) was added to a solution of CuI (285.5 mg, 1.5 mmol, 3.0 equiv.) and SMOPS (261.0 mg, 1.5 mmol, 3.0 equiv.) in DMSO (1 mL). The reaction was stirred under a nitrogen atmosphere at 110 °C for 12 h. The mixture was then cooled to room temperature, diluted with ethyl acetate (5 mL) and filtered through a

pad of silica. The filtrate was washed with H_2O (2 x 5 mL), brine (5 mL), dried over $MgSO_4$, filtered through a pad of silica and concentrated under reduced pressure. The product was purified by column chromatography (Gradient in PE/EA 4:1 to 1:1) and was obtained as a white solid (63.3 mg, 61%).

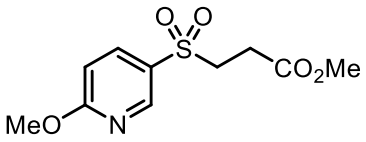
mp 161-162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.06 (dd, J = 2.4, 0.8 Hz, 1H), 8.85 (dd, J = 4.8, 1.6 Hz, 1H), 8.14 (ddd, J = 8.1, 2.4, 1.6 Hz, 1H), 7.48 (ddd, J = 8.1, 4.8, 0.8 Hz, 1H), 3.59 (s, 3H), 3.42 (t, J = 7.5 Hz, 2H), 2.75 (t, J = 7.5 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.1, 154.5, 149.1, 136.0, 124.0, 52.4, 51.8, 27.4; IR υ_{max} (neat)/cm^{-1} 2990, 1738, 1577, 1373, 1201, 1022, 818, 726, 618; LRMS (ESI) *m*/*z* 230 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 230.0482 $[M+H]^+$, $C_9H_{12}NO_4S$ requires *m*/*z* 230.0481.

Sodium pyridine-3-sulfinate (1b)



To a solution of the corresponding sulfone (100.0 mg, 0.4 mmol, 1.0 equiv.) in THF was added NaOMe (0.1 mL, 0.4 mmol, 1.0 equiv., 25% in MeOH) dropwise while stirring at room temperature. After 30 minutes the solvent was removed under reduced pressure and the resulting sulfinate salt **1a** was used without further purification.

Methyl 3-[(6-methoxypyridin-3-yl)sulfonyl]propanoate

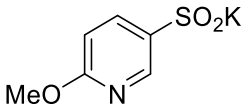


5-Bromo-2-methoxypyridine (0.13 mL, 1.0 mmol, 1.0 equiv.) was added to a solution of CuI (571.3 mg, 3.0 mmol, 3.0 equiv.) and SMOPS (522.0 mg, 3.0 mmol, 3.0 equiv.) in DMSO (2 mL). The reaction was stirred under a nitrogen atmosphere at 110 °C for 12 h. The mixture was then cooled to room temperature, diluted with ethyl acetate (10 mL) and filtered through a pad of silica. The filtrate was washed with H_2O (2 x 10 mL), brine (10 mL), dried over $MgSO_4$,

filtered through a pad of silica and concentrated under reduced pressure. The product was purified by column chromatography (Gradient in PE/EA 4:1 to 1:1) and was obtained as a white solid (191.0 mg, 74%).

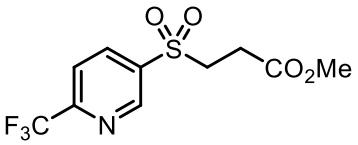
mp 149-152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (dd, *J* = 2.5, 0.5 Hz, 1H, Pyr-*H*), 8.00 (dd, *J* = 8.8, 2.5, 1H, Pyr-*H*), 6.88 (dd, *J* = 8.8, 0.5 Hz, 1H, Pyr-*H*), 4.04 (s, 3H, O*Me*), 3.67 (s, 3H, CO_2*Me*), 3.44 (t, *J* = 7.5 Hz, 2H, CH_2), 2.79 (t, *J* = 7.5 Hz, 2H, CH_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.3, 167.3, 148.9, 138.0, 127.7, 111.7, 54.5, 52.4, 52.0, 27.6; IR υ_{max} (neat)/cm^{-1} 2951, 1732, 1562, 1416, 1258, 1131, 989, 793, 697; LRMS (ESI) *m*/*z* 260 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 260.0514 $[M+H]^+$, $C_{10}H_{14}NO_5S$ requires *m*/*z* 260.0514.

Potassium 6-methoxypyridine-3-sulfinate (1c)



To a solution of the corresponding sulfone (100.0 mg, 0.4 mmol, 1.0 equiv.) in THF was added KOMe (0.1 mL, 0.4 mmol, 1.0 equiv., 25% in MeOH) dropwise while stirring at room temperature. After 30 minutes the solvent was removed under reduced pressure and the resulting sulfinate salt **1c** was used without further purification.

Methyl 3-{[6-(trifluoromethyl)pyridin-3-yl]sulfonyl}propanoate

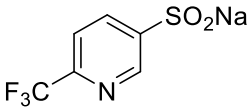


5-Bromo-2-(trifluoromethyl)pyridine (300.0 mg, 1.3 mmol, 1.0 equiv.) was added to a solution of CuI (726.0 mg, 4.0 mmol, 3.0 equiv.) and SMOPS (600.0 mg, 4.0 mmol, 3.0 equiv.) in DMSO (3 mL). The reaction was stirred under a nitrogen atmosphere at 110 °C for 12 h. The mixture was then cooled to room temperature, diluted with ethyl acetate (15 mL) and filtered through a pad of silica. The filtrate was washed with H_2O (2 x 15 mL), brine (15 mL), dried over $MgSO_4$, filtered through a pad of silica and concentrated under reduced pressure. The product was

purified by column chromatography (Gradient in PE/EA 4:1 to 1:1) and was obtained as a white solid (314.0 mg, 86%).

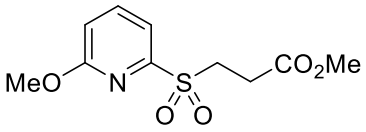
mp 167-169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.15 (dd, J = 2.6, 0.8 Hz, 1H), 8.35 (dd, J = 8.2, 2.2 Hz, 1H), 7.86 (dd, J = 8.2, 0.8 Hz, 1H), 3.58 (s, 3H), 3.47 (t, J = 7.4 Hz, 2H), 2.77 (t, J = 7.4 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.9, 149.5 (q, J = 35.5 Hz), 138.1, 137.9, 121.9, 120.9 (q, J = 275.6 Hz), 119.2, 52.5, 51.9, 27.2; ^{19}F NMR (377 MHz, $CDCl_3$) δ -68.27; IR υ_{max} (neat)/cm^{-1} 2957, 1731, 1587, 1439, 1262, 1151, 1017, 904, 802, 728, 633; LRMS (ESI) m/z 298 (100%, $[M+H]^+$); HRMS (ESI) found m/z 298.0356 $[M+H]^+$, $C_{10}H_{11}F_3NO_4S$ requires m/z 298.0355.

Sodium 6-(trifluoromethyl)pyridine-3-sulfinate (1d)



To a solution of the corresponding sulfone (100.0 mg, 0.4 mmol, 1.0 equiv.) in THF was added NaOMe (0.1 mL, 0.4 mmol, 1.0 equiv., 25% in MeOH) dropwise while stirring at room temperature. After 30 minutes the solvent was removed under reduced pressure and resulting sulfinate salt **1d** was used without further purification.

Methyl 3-[(6-methoxypyridin-2-yl)sulfonyl]propanoate

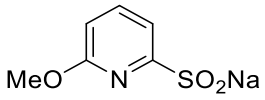


2-Bromo-6-methoxypyridine (300.0 mg, 1.0 mmol, 1.0 equiv.) was added to a solution of CuI (571.3 mg, 3.0 mmol, 3.0 equiv.) and SMOPS (522.0 mg, 3.0 mmol, 3.0 equiv.) in DMSO (2 mL). The reaction was stirred under a nitrogen atmosphere at 110 °C for 12 h. The mixture was then cooled to room temperature, diluted with ethyl acetate (10 mL) and filtered through a pad of silica. The filtrate was washed with H_2O (2 x 10 mL), brine (10 mL), dried over $MgSO_4$, filtered through a pad of silica and concentrated under reduced pressure. The product was

purified by column chromatography (Gradient in PE/EA 4:1 to 1:1) and was obtained as a white solid (207.2 mg, 80%).

mp 179-181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 9.0, 7.2, 1H), 7.67 (app dt, J = 7.2, 1.2 Hz, 1H), 7.01 (app dt, J = 8.4, 1.1 Hz, 1H), 4.01 (s, 3H), 3.70 (m, 5H), 2.86 (dd, J = 9.0, 7.2, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.5, 164.1, 153.5, 139.9, 116.3, 115.4, 54.2, 52.3, 47.2, 27.3; IR υ_{max} (neat)/cm^{-1} 1736, 1559, 1438, 1312, 1115, 1096, 983, 670; LRMS (ESI) m/z 282 (100%, $[M+Na]^+$); HRMS (ESI) found m/z 282.0405 $[M+Na]^+$, $C_{10}H_{13}NO_5SNa$ requires m/z 282.0406.

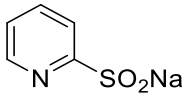
Sodium 6-methoxypyridine-2-sulfinate (1e)



To a solution of the corresponding sulfone (100.0 mg, 0.4 mmol, 1.0 equiv.) in THF was added NaOMe (0.1 mL, 0.4 mmol, 1.0 equiv., 25% in MeOH) dropwise while stirring at room temperature. After 30 minutes the solvent was removed under reduced pressure and resulting sulfinate salt **1e** was used without further purification.

3.3 Synthesis of Sodium Pyridyl Sulfinate Salts via Thiol Oxidation

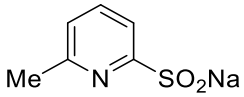
Sodium pyridine-2-sulfinate (1f)



General procedure A was followed using pyridine-2-thiol (499.5 mg, 4.5 mmol, 1.0 equiv.). Product **1f** was obtained as a white solid (504.9 mg, 69%)

mp 281-284 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.53 (dt, J = 5.0, 1.3 Hz, 1H), 7.97 (td, J = 7.6, 1.7 Hz, 1H), 7.91 (dt, J = 7.9, 1.2 Hz, 1H), 7.43 (ddd, J = 7.4, 4.9, 1.4 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 173.1, 147.9, 138.0, 124.3, 117.4; IR υ_{max} (neat)/cm^{-1} 1647, 1580, 1423, 1033, 971, 775, 573; HRMS (ESI) found m/z 144.0115 $[M+H]^+$, $C_5H_6NO_2S$ requires m/z 144.0114.

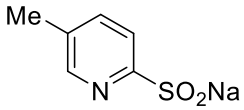
Sodium 6-methylpyridine-2-sulfinate (1g)



General procedure A was followed using 6-methylpyridine-2-thiol (562.5 mg, 4.5 mmol, 1.0 equiv.). Product **1g** was obtained as a white solid (644.4 mg, 80%).

mp > 285 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.83 (t, J = 7.7 Hz, 1H), 7.71 (dd, J = 7.7, 0.9 Hz, 1H), 7.28 (dd, J = 7.7, 1.0 Hz, 1H), 2.57 (s, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 172.6, 157.5, 138.0, 123.8, 114.0, 22.2; IR υ_{max} (neat)/cm^{-1} 1585, 1440, 1050, 991, 787, 614; HRMS (ESI) found m/z 161.0271 $[M+H]^+$, $C_6H_8NO_2S$ requires m/z 161.0271.

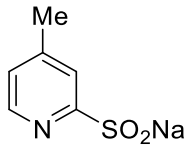
Sodium 5-methylpyridine-2-sulfinate (1h)



General procedure A was followed using 5-methylpyridine-2-thiol (562.5 mg, 4.5 mmol, 1.0 equiv.). Product **1h** was obtained as a white solid (644.9 mg, 81%).

mp > 285 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.42 – 8.31 (m, 1H), 7.84 – 7.73 (m, 2H), 2.40 (s, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 170.3, 148.1, 138.3, 134.5, 117.2, 16.8; IR υ_{max} (neat)/cm^{-1} 1566, 1463, 1367, 1064, 1029, 986, 830, 568; HRMS (ESI) found m/z 161.0233 $[M+H]^+$, $C_6H_8NO_2S$ requires m/z 161.0240.

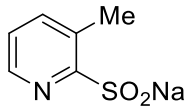
Sodium 4-methylpyridine-2-sulfinate (1i)



General procedure A was followed using 4-methylpyridine-2-thiol (562.5 mg, 4.5 mmol, 1.0 equiv.). Product **1i** was obtained as a white solid (612.1 mg, 76%).

mp > 285 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.37 (d, J = 5.0 Hz, 1H), 7.74 (dd, J = 1.8, 0.9 Hz, 1H), 7.27 (dd, J = 5.1, 1.8 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 172.8, 149.9, 147.6, 125.1, 117.9, 19.8; IR υ_{max} (neat)/cm^{-1} 1596, 1092, 1062, 982, 824; HRMS (ESI) found m/z 161.0270 $[M+H]^+$, $C_6H_8NO_2S$ requires m/z 161.0268.

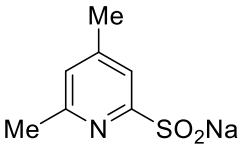
Sodium 3-methylpyridine-2-sulfinate (1j)



General procedure A was followed using 3-methylpyridine-2-thiol (562.5 mg, 4.5 mmol, 1.0 equiv.). Product **1j** was obtained as a white solid (588.0 mg, 73%).

mp 278-280 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.39 (dd, J = 4.9, 1.5 Hz, 1H), 7.64 (ddd, J = 7.6, 1.7, 0.9 Hz, 1H), 7.31 (dd, J = 7.7, 4.7 Hz, 1H), 2.64 (s, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 168.2, 146.0, 139.6, 131.2, 124.2, 15.4; IR υ_{max} (neat)/cm^{-1} 1570, 1401, 1035, 979, 816, 588; HRMS (ESI) found m/z 161.0236 $[M+H]^+$, $C_6H_8NO_2S$ requires m/z 161.0240.

Sodium 4,6-dimethylpyridine-2-sulfinate (1k)

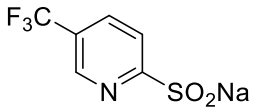


General procedure A was followed using 4,6-dimethylpyridine-2-thiol (625.5 mg, 4.5 mmol, 1.0 equiv.). Product **1k** was obtained as a white solid (694.8 mg, 80%)

mp > 285 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.55 (d, J = 1.9 Hz, 1H), 7.12 (d, J = 1.9 Hz, 1H), 2.52 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 172.5, 157.2, 149.8, 124.6, 114.6,

21.9, 19.7; IR υ_{max} (neat)/cm^{-1} 1603, 1442, 1053, 992, 625; HRMS (ESI) found *m*/*z* 174.0400 $[M+H]^+$, $C_7H_{10}NO_2S$ requires *m*/*z* 174.0398.

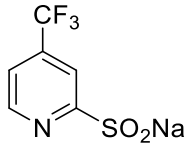
Sodium 5-(trifluoromethyl)pyridine-2-sulfinate (1l)



General procedure A was followed using 5-(trifluoromethyl)pyridine-2-thiol (805.5 mg, 4.5 mmol, 1.0 equiv.). Product **1l** was obtained as a white solid (884.5 mg, 84%)

mp > 285 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.86 (dd, *J* = 2.2, 1.1 Hz, 1H), 8.30 – 8.25 (m, 1H), 8.06 (dd, *J* = 8.2, 0.8 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 177.2, 145.3, 135.0 (q, *J* = 3.7 Hz), 123.5 (q, *J* = 271.6 Hz), 117.7, 113.1 (q, *J* = 3.7 Hz); ^{19}F NMR (377 MHz, CD_3OD) δ -63.87; IR υ_{max} (neat)/cm^{-1} 1594, 1335, 1129, 1104, 1066, 1019, 851, 707; HRMS (ESI) found *m*/*z* 211.9992 $[M+H]^+$, $C_6H_5NO_2S$ requires *m*/*z* 211.9988.

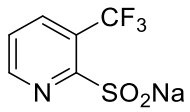
Sodium 4-(trifluoromethyl)pyridine-2-sulfinate (1m)



General procedure A was followed using 4-(trifluoromethyl)pyridine-2-thiol (805.5 mg, 4.5 mmol, 1.0 equiv.). Product **1m** was obtained as a white solid (768.5 mg, 73%)

mp > 285 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.80 (d, *J* = 5.1 Hz, 1H), 8.20 – 8.13 (m, 1H), 7.74 – 7.68 (m, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 175.5, 149.7, 139.9 (q, *J* = 34.4 Hz), 124.2 (q, *J* = 272.8 Hz), 119.6 (q, *J* = 3.1 Hz), 113.0; ^{19}F NMR (377 MHz, CD_3OD) δ -66.39; IR υ_{max} (neat)/cm^{-1} 1334, 1141, 1081, 1064, 988, 860; HRMS (ESI) found *m*/*z* 233.9796 $[M+Na]^+$, $C_6H_4NO_2SNa$ requires *m*/*z* 233.9807.

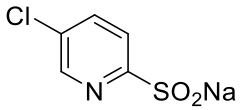
Sodium 3-(trifluoromethyl)pyridine-2-sulfinate (1n)



General procedure A was followed using 3-(trifluoromethyl)pyridine-2-thiol (805.5 mg, 4.5 mmol, 1.0 equiv.). Product **1n** was obtained as a white solid (773.2 mg, 75%)

mp > 285 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.93 – 8.83 (m, 1H), 8.12 (dd, J = 7.9, 1.6 Hz, 1H), 7.58 (ddd, J = 8.0, 4.8, 0.9 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 171.2, 153.0, 146.8, 134.3 (q, J = 5.3 Hz), 124.0 (q, J = 34.5 Hz), 118.7; ^{19}F NMR (377 MHz, CD_3OD) δ -58.83; IR υ_{max} (neat)/cm^{-1} 1568, 1417, 1317, 1255, 1127, 1114, 1051, 813, 601; HRMS (ESI) found *m*/*z* 211.9981 $[M+H]^+$, $C_6H_5NO_2S$ requires *m*/*z* 211.9988.

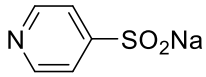
Sodium 5-chloropyridine-2-sulfinate (1o)



General procedure A was followed using 5-chloropyridine-2-thiol (652.5 mg, 4.5 mmol, 1.0 equiv.). Product **1o** was obtained as a white solid (582.1 mg, 65%)

mp > 285 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.53 (dd, J = 2.4, 0.8 Hz, 1H), 7.98 (dd, J = 8.4, 2.4 Hz, 1H), 7.87 (dd, J = 8.3, 0.8 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 171.7, 146.8, 137.4, 132.3, 118.7; IR υ_{max} (neat)/cm^{-1} 1453, 1096, 1060, 1017, 999, 829, 632; HRMS (ESI) found *m*/*z* 199.9540 $[M+Na]^+$, $C_5H_4NO_2SClNa$ requires *m*/*z* 199.9543.

Sodium pyridine-4-sulfinate (1p)

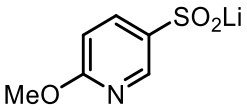


General procedure A was followed using pyridine-4-thiol (499.5 mg, 4.5 mmol, 1.0 equiv.). Product **1p** was obtained as an off-white solid (582.1 mg, 65%).

mp > 285 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 8.63 (d, J = 6.0 Hz, 2H), 7.68 (d, J = 6.0 Hz, 2H); ^{13}C NMR (101 MHz, CD_3OD) δ 165.1, 149.0, 119.1; IR υ_{max} (neat)/cm^{-1} 1648, 1581, 1406, 1085, 1031, 1000, 969, 818, 631; HRMS (ESI) found m/z 144.0111 $[M+H]^+$, $C_5H_6NO_2S$ requires m/z 144.0114.

3.4 Synthesis of Lithium Pyridyl Sulfinate Salts via Metallation

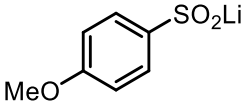
Lithium 6-methoxypyridine-3-sulfinate (1a)



To a solution of 5-bromo-2-methoxypyridine (2.5 mL, 19.3 mmol, 1.0 equiv.) in THF (100.0 mL, 0.2 M) at -78 °C, *n*BuLi (8.2 mL, 2.12 M in hexane, 17.4 mmol, 0.9 equiv.) as added slowly. The mixture was stirred for 40 minutes before *TIMSO* (2.9 g, 19.3 mmol, 1.0 equiv.) was added slowly. After complete addition, the solution was allowed to warm to room temperature and the crude product was collected by vacuum filtration and washed with acetone (2 x 20 mL) and Et_2O (2 x 20 mL) to yield the pyridine lithium sulfinate **1a** (3.4 g, 99%).

decomp 243 °C; ^{1}H NMR (400 MHz, D_2O) δ 8.14 (dd, J = 2.4, 0.8 Hz, 1H), 7.82 (dd, J = 8.6, 2.4 Hz, 1H), 6.84 (dd, J = 8.6, 0.8 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (101 MHz, D_2O) δ 164.7, 143.3, 142.3, 135.7, 110.9, 54.2; IR υ_{max} (neat)/cm^{-1} 2947, 1587, 1477, 1307, 1194, 1026, 827, 754, 632; LRMS (ESI) m/z: 172 $[M-Li]^-$; HRMS (ESI) found m/z 172.0068 $[M-Li]^-$, $C_6H_6NO_3S$ requires m/z 172.0062.

Lithium 4-methoxybenzenesulfinate (7)



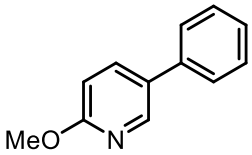
To a solution of 1-bromo-4-methoxybenzene (0.6 mL, 5.0 mmol, 1.0 equiv.) in THF (25 mL) at -78 °C, *n*BuLi (1.8 mL, 2.26 M in hexane, 4.3 mmol, 0.9 equiv.) was added slowly. The mixture was stirred for 40 minutes before *TIMSO* (0.7 g, 5.0 mmol, 1.0 equiv.) was added slowly. After

complete addition, the solution was allowed to warm to room temperature and the crude product was collected by vacuum filtration and washed with acetone (2 x 20 mL) and diethyl ether (2 x 20 mL) to yield sulfinate **7** (0.8 g, 99%) as a white powder.

mp 261-266 °C; ^{1}H NMR (400 MHz, D_2O) δ 7.59 (d, J = 8.8 Hz, 2H), 7.09 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H); ^{13}C NMR (101 MHz, D_2O): δ 162.2, 149.3, 126.8, 114.7, 55.8; IR υ_{max} (neat)/cm^{-1} 1593, 1440, 1301, 1170, 993, 836, 793, 626; LRMS (ESI) *m*/*z*: 171 [M-Li]$^-$; HRMS (ESI) found *m*/*z* 171.0115 [M-Li]$^-$, $C_6H_6NO_3S$ requires *m*/*z* 171.0114.

3.5 3-Pyridyl Sulfinate Cross-Couplings

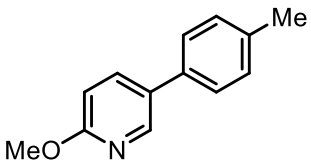
2-Methoxy-5-phenylpyridine (3p)



General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and bromobenzene (21.3 µL, 0.2 mmol, 1.0 equiv.) or chlorobenzene (20.3 µL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 10:1 to 5:1) yielded product **3p** (Br: 36.8 mg, 99%; Cl: 36.2 mg, 97%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (dd, J = 2.6, 0.8 Hz, 1H), 7.80 (dd, J = 8.6, 2.6 Hz, 1H), 7.60 – 7.30 (m, 5H), 6.83 (dd, J = 8.6, 0.8 Hz, 1H), 4.00 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 144.9, 137.9, 137.5, 130.1, 128.9, 127.3, 126.7, 110.8, 53.6; LRMS (ESI) *m*/*z* 186 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 186.0841 $[M+H]^+$, $C_{12}H_{12}NO$ requires *m*/*z* 186.0840. Data consistent with literature.[3]

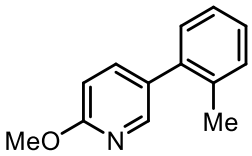
2-Methoxy-5-(*p*-tolyl)pyridine (2a)



General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 4-bromotoluene (34.7 mg, 0.2 mmol, 1.0 equiv.) or 4-chlorotoluene (23.7 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 10:1 to 5:1) yielded product **2a** (Br: 37.8 mg, 92%; Cl: 37.1 mg, 90%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dd, J = 2.5, 0.8 Hz, 1H), 7.69 (dd, J = 8.6, 2.5 Hz, 1H), 7.34 (d, J = 8.1 Hz, 2H), 7.20 – 7.14 (m, 2H), 6.72 (dd, J = 8.6, 0.8 Hz, 1H), 3.90 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 144.7, 137.3, 137.1, 135.0, 130.0, 129.7, 126.5, 115.2, 110.7, 53.5, 21.1; LRMS (ESI) m/z 200 (100%, $[M+H]^+$); HRMS (ESI) found m/z 200.0997 $[M+H]^+$, $C_{13}H_{14}NO$ requires m/z 200.0996. Data consistent with literature.[4]

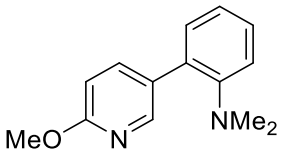
2-Methoxy-5-(*o*-tolyl)pyridine (3q)



General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 2-bromotoluene (24.0 μL, 0.2 mmol, 1.0 eq. equiv.) or 2-chlorotoluene (23.4 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 10:1 to 5:1) yielded product **3q** (Br: 37.8 mg, 99%; Cl: 37.8 mg, 99%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, J = 2.5, 0.8 Hz, 1H), 7.47 (dd, J = 8.6, 2.5 Hz, 1H), 7.26 – 7.09 (m, 4H), 6.72 (dd, J = 8.6, 0.8 Hz, 1H), 3.90 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.1, 146.5, 139.5, 138.1, 135.8, 130.5, 130.4, 127.6, 127.1, 126.0, 110.1, 53.4, 20.4; LRMS (ESI) m/z 200 (100%, $[M+H]^+$); HRMS (ESI) found m/z 200.0997 $[M+H]^+$, $C_{13}H_{14}NO$ requires m/z 200.0996. Data consistent with literature.[4]

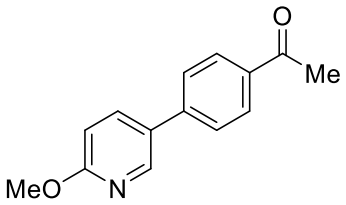
2-(6-Methoxypyridin-3-yl)-*N*,*N*-dimethylaniline (3u)



General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 2-bromo-*N*,*N*-dimethylaniline (40.01 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 3:1) yielded product **3u** (38.8 mg, 85%) as an off-white solid.

mp 146-147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, J = 2.5, 0.8 Hz, 1H), 7.82 (dd, J = 8.5, 2.5 Hz, 1H), 7.28 – 7.17 (m, 1H), 7.13 (dd, J = 7.5, 1.7 Hz, 1H), 7.05 – 6.87 (m, 2H), 6.70 (dd, J = 8.5, 0.8 Hz, 1H), 3.91 (s, 3H), 2.47 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.9, 151.6, 146.0, 139.2, 131.2, 131.0, 130.5, 128.4, 122.0, 118.1, 110.2, 53.4, 43.4; ; IR υ_{max} (neat)/cm^{-1} 1600, 1500, 1370, 1036, 944, 752, 611 ; LRMS (ESI) m/z 229 (100%, $[M+H]^+$); HRMS (ESI) found m/z 229.1336 $[M+H]^+$, $C_{14}H_{17}N_2O$ requires m/z 229.1335.

1-[4-(6-Methoxypyridin-3-yl]phenyl)ethan-1-one (3v)

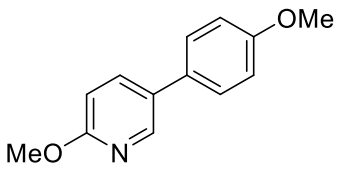


General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 4-bromoacetophenone (39.8 mg, 0.2 mmol, 1.0 equiv.) or 4-chloroacetophenone (25.9 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1) yielded product **3v** (Br: 44.5 mg, 98%; Cl: 44.5 mg, 98%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (dd, J = 2.6, 0.8 Hz, 1H), 8.06 – 7.98 (d, J = 8.0 Hz, 2H), 7.81 (dd, J = 8.6, 2.6 Hz, 1H), 7.64 – 7.57 (d, J = 8.0 Hz, 2H), 6.83 (dd, J = 8.6, 0.8 Hz, 1H), 3.98 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.5, 164.1, 145.3, 142.4, 137.3, 135.8, 130.2, 129.1, 126.5, 111.1, 53.6, 26.6; LRMS (ESI) m/z 228 (100%, $[M+H]^+$); HRMS

(ESI) found *m*/*z* 228.1018 $[M+H]^+$, $C_{14}H_{14}NO_2$ requires *m*/*z* 228.1019. Data consistent with literature.[5]

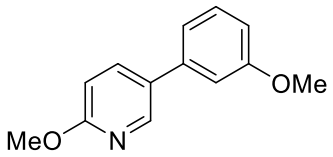
2-Methoxy-5-(4-methoxyphenyl)pyridine (3r)



General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 4-bromoanisole (25.0 μL, 0.2 mmol, 1.0 equiv.) or 4-chloroanisole (24.5 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1) yielded product **3r** (Br: 40.0 mg, 93%; Cl: 39.9 mg, 92%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (dd, *J* = 2.6, 0.8 Hz, 1H), 7.67 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.37 (d, *J* = 8.8 Hz, 2H), 6.91 (d, *J* = 8.8 Hz, 2H), 6.72 (dd, *J* = 8.6, 0.8 Hz, 1H), 3.90 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.2, 159.1, 144.5, 137.1, 130.4, 129.8, 127.7, 114.4, 110.7, 55.3, 53.5; LRMS (ESI) *m*/*z* 216 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 216.1018 $[M+H]^+$, $C_{13}H_{13}NO_2$ requires *m*/*z* 228.1019. Data consistent with literature.[5]

2-Methoxy-5-(3-methoxyphenyl)pyridine (3s)

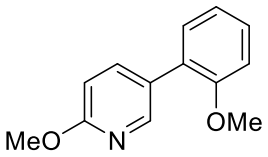


General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 3-bromoanisole (37.4 mg, 0.2 mmol, 1.0 equiv.) or 3-chloroanisole (24.5 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1) yielded product **3s** (Br: 38.7 mg, 90%; Cl: 38.0 mg, 86%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (dd, *J* = 2.6, 0.8 Hz, 1H), 7.68 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.26 (t, *J* = 8.0 Hz, 1H), 7.06 – 7.00 (m, 1H), 6.96 (t, *J* = 2.1 Hz, 1H), 6.80 (ddd, *J* = 8.3, 2.6, 0.9 Hz,

1H), 6.71 (dd, *J* = 8.6, 0.8 Hz, 1H), 3.89 (s, 3H), 3.76 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 160.0, 145.0, 139.3, 137.4, 130.0, 129.9, 119.1, 112.5, 112.4, 110.7, 55.2, 53.5; IR υ_{max} (neat)/cm^{-1} 1602, 1476, 1366, 1282, 1212, 1055, 928, 829; LRMS (ESI) *m*/*z* 216 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 216.1019 $[M+H]^+$, $C_{13}H_{14}NO_2$ requires *m*/*z* 216.1018.

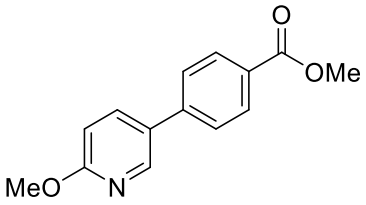
2-Methoxy-5-(2-methoxyphenyl)pyridine (3t)



General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 2-bromoanisole (24.9 μL, 0.2 mmol, 1.0 equiv.) or 2-chloroanisole (25.4 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 6:1) yielded product **3t** (Br: 36.1 mg, 84%; Cl: 36.9 mg, 89%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 – 8.20 (dd, *J* = 2.6, 0.8 Hz, 1H), 7.70 (dd, *J* = 8.6, 2.6 Hz, 1H), 7.33 – 7.19 (m, 2H), 7.02 – 6.87 (m, 2H), 6.71 (dd, *J* = 8.6, 0.8 Hz, 1H), 3.90 (s, 3H), 3.74 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.0, 156.5, 146.8, 139.9, 130.3, 128.9, 127.3, 127.0, 120.9, 111.1, 109.9, 55.5, 53.4; IR υ_{max} (neat)/cm^{-1} 1599, 1503, 1435, 1286, 1122, 1037, 793; LRMS (ESI) *m*/*z* 216 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 126.1019 $[M+H]^+$, $C_{13}H_{14}NO_2$ requires *m*/*z* 216.1030.

Methyl 4-(6-methoxypyridin-3-yl)benzoate (3w)

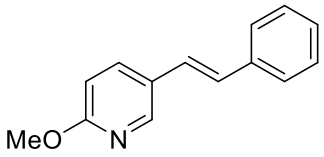


General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and methyl 4-bromobenzoate (43.0 mg, 0.2 mmol, 1.0 equiv.) or methyl 4-chlorobenzoate (34.1 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by

flash chromatography (Gradient in PE/EA 6:1) yielded product **3w** (Br: 43.8 mg, 90%; Cl: 43.8 mg, 90%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (dd, J = 2.6, 0.8 Hz, 1H), 8.03 (d, J = 8.4 Hz, 2H), 7.80 – 7.74 (dd, J = 8.6, 2.6 Hz, 1H), 7.52 (d, J = 8.5 Hz, 2H), 6.77 (dd, J = 8.6, 0.8 Hz, 1H), 3.92 (s, 3H), 3.87 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.8, 164.1, 145.3, 142.3, 137.4, 130.3, 128.9, 128.8, 126.4, 111.0, 53.6, 52.1; LRMS (ESI) m/z 244 (100%, $[M+H]^+$); HRMS (ESI) found m/z 244.0968 $[M+H]^+$, $C_{14}H_{14}NO_3$ requires m/z 244.0968. Data consistent with literature.[6]

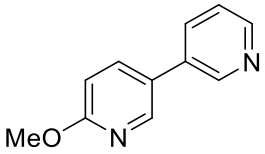
(*E*)-2-Methoxy-5-styrylpyridine (3x)



General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and bromostyrene (25.7 μL, 0.2 mmol, 1.0 equiv.), potassium carbonate (41.4 mg, 0.3 mmol, 1.5 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 10:1 to 6:1) yielded product **3x** (29.9 mg, 71%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, J = 2.6, 0.8 Hz, 1H), 7.73 (dd, J = 8.7, 2.6 Hz, 1H), 7.42 (d, J = 7.4 Hz, 2H), 7.29 (t, J = 7.6 Hz, 2H), 7.19 (t, J = 7.3 Hz, 1H), 7.06 – 6.86 (m, 2H), 6.69 (dd, J = 8.6, 0.8 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 145.8, 137.1, 135.3, 128.7, 127.9, 127.6, 126.6, 126.3, 124.7, 111.1, 53.5; LRMS (ESI) m/z 212 (100%, $[M+H]^+$); HRMS (ESI) found m/z 212.1070 $[M+H]^+$, $C_{14}H_{14}NO$ requires m/z 212.1069. Data consistent with literature.[7]

6-Methoxy-3,3'-bipyridine (4p)

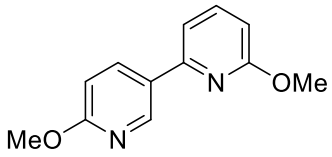


General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 3-bromopyridine (19.0 μL, 0.2 mmol, 1.0 equiv.) or 3-

chloropyridine (19.0 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **4p** (Br: 35.3 mg, 95%; Cl: 34.6 mg, 90%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (d, J = 2.3 Hz, 1H), 8.57 (dd, J = 2.6, 0.8 Hz, 1H), 8.30 (dd, J = 8.6, 0.8 Hz, 1H), 7.76 – 7.68 (m, 2H), 7.29 (ddd, J = 7.9, 4.8, 0.8 Hz, 1H), 6.78 (dd, J = 8.6, 0.8 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1, 148.5, 147.8, 145.1, 137.2, 133.8, 133.5, 126.7, 123.6, 111.2, 53.6; LRMS (ESI) m/z 187 (100%, $[M+H]^+$); HRMS (ESI) found m/z 187.0793 $[M+H]^+$, $C_{11}H_{11}N_2O$ requires m/z 187.0794. Data consistent with literature.[8]

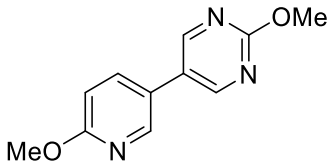
6,6'-Dimethoxy-2,3'-bipyridine (4q)



General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 2-bromo-6-methoxypyridine (24.6 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 3:1 to 1:1) yielded product **4q** (40.6 mg, 94%) as a white solid.

mp 171-173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 2.4 Hz, 1H), 8.15 (dd, J = 8.6, 2.5 Hz, 1H), 7.52 (dd, J = 8.2, 7.4 Hz, 1H), 7.22 – 7.11 (m, 1H), 6.74 (dd, J = 8.7, 0.7 Hz, 1H), 6.59 (d, J = 8.2 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.4, 163.8, 152.2, 145.5, 139.2, 136.9, 128.2, 111.8, 110.6, 109.1, 53.6, 53.2; IR υ_{max} (neat)/cm^{-1} 1601, 1500, 1410, 1332, 1254, 1011, 794; LRMS (ESI) m/z 217 (100%, $[M+H]^+$); HRMS (ESI) found m/z 217.0969 $[M+H]^+$, $C_{12}H_{13}N_2O_2$ requires m/z 217.0971.

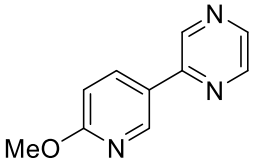
2-Methoxy-5-(6-methoxypyridin-3-yl)pyrimidine (4r)



General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 5-bromo-2-methoxypyrimidine (37.8 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 1:1) yielded product **4r** (35.2 mg, 81%) as a white solid.

mp 179-184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (s, 2H), 8.25 (dd, J = 2.6, 0.8 Hz, 1H), 7.65 (dd, J = 8.6, 2.6 Hz, 1H), 6.80 (dd, J = 8.6, 0.8 Hz, 1H), 3.99 (s, 3H), 3.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.1, 164.1, 156.9, 144.5, 136.8, 125.4, 123.5, 111.5, 55.1, 53.6; IR υ_{max} (neat)/cm^{-1} 1598, 1464, 1352, 1291, 1071, 827; LRMS (ESI) m/z 218 (100%, $[M+H]^+$); HRMS (ESI) found m/z 218.0925 $[M+H]^+$, $C_{11}H_{12}N_3O_2$ requires m/z 218.0924.

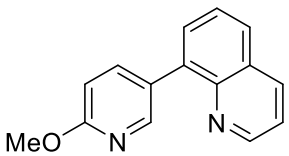
2-(6-Methoxypyridin-3-yl)pyrazine (4s)



General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 2-chloropyrazine (17.8 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 1:1) yielded product **4s** (32.9 mg, 88%) as a white solid.

mp 113-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, J = 1.6 Hz, 1H), 8.74 (dd, J = 2.6, 0.8 Hz, 1H), 8.54 (dd, J = 2.6, 1.6 Hz, 1H), 8.43 (d, J = 2.5 Hz, 1H), 8.18 (dd, J = 8.7, 2.6 Hz, 1H), 6.81 (dd, J = 8.7, 0.8 Hz, 1H), 3.94 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 150.6, 145.7, 144.2, 142.8, 141.3, 137.1, 125.6, 111.4, 53.8; IR υ_{max} (neat)/cm^{-1} 1607, 1504, 1409, 1279, 1036, 825; LRMS (ESI) m/z 188 (100%, $[M+H]^+$); HRMS (ESI) found m/z 188.0819 $[M+H]^+$, $C_{10}H_{10}N_3O$ requires m/z 188.0818.

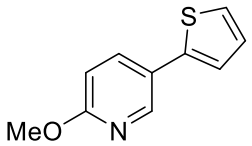
8-(6-Methoxypyridin-3-yl)quinolone (4t)



General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 8-chloroquinoline (25.4 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 1:1 to 1:3) yielded product **4t** (44.4 mg, 94%) as a pale yellow solid.

mp 204-206 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.85 (dd, J = 4.2, 1.8 Hz, 1H), 8.45 (dd, J = 2.5, 0.8 Hz, 1H), 8.11 (dd, J = 8.2, 1.8 Hz, 1H), 7.93 (dd, J = 8.6, 2.5 Hz, 1H), 7.74 (dd, J = 8.2, 1.6 Hz, 1H), 7.63 (dd, J = 7.2, 1.6 Hz, 1H), 7.52 (dd, J = 8.2, 7.1 Hz, 1H), 7.34 (dd, J = 8.3, 4.2 Hz, 1H), 6.80 (dd, J = 8.6, 0.8 Hz, 1H), 3.93 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.4, 150.2, 147.6, 146.0, 141.1, 137.2, 136.3, 129.7, 128.8, 128.3, 127.7, 126.4, 121.2, 110.0, 53.5; IR υ_{max} (neat)/cm^{-1} 1738, 1600, 1492, 1363, 1281, 1029, 825; LRMS (ESI) m/z 237 (100%, $[M+H]^+$); HRMS (ESI) found m/z 237.1023 $[M+H]^+$, $C_{15}H_{13}N_2O$ requires m/z 237.1022.

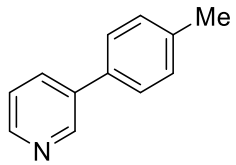
2-Methoxy-5-(thiophen-2-yl)pyridine (4u)



General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 2-bromothiophene (18.7 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 1:1) yielded product **4u** (31.3 mg, 82%) as a pale yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (dd, J = 2.6, 0.7 Hz, 1H), 7.71 (dd, J = 8.6, 2.6 Hz, 1H), 7.25 – 7.17 (m, 1H), 7.15 (dd, J = 3.6, 1.2 Hz, 1H), 7.01 (dd, J = 5.1, 3.6 Hz, 1H), 6.70 (dd, J = 8.6, 0.7 Hz, 1H), 3.90 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 143.9, 140.7, 136.5, 128.0, 124.6, 124.1, 122.9, 110.9, 53.6; LRMS (ESI) m/z 192 (100%, $[M+H]^+$); HRMS (ESI) found m/z 192.0478 $[M+H]^+$, $C_{10}H_{10}NOS$ requires m/z 192.0477. Data consistent with literature.[9]

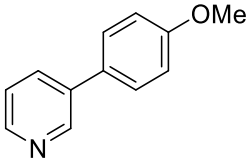
3-(*p*-Tolyl)pyridine (2m)



General procedure B was followed using sodium pyridine-3-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 4-bromotoluene (34.7 mg, 0.2 mmol, 1.0 equiv.) or 4-chlorotoluene (23.7 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 15:1 to 10:1) yielded product **2m** (Br: 30.4 mg, 90%; Cl: 30.4 mg, 90%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 2.6 Hz, 1H), 8.50 (dd, J = 4.6, 2.3 Hz, 1H), 7.78 (dt, J = 7.9, 2.0 Hz, 1H), 7.41 (d, J = 8.1 Hz, 2H), 7.27 (dd, J = 7.9, 4.8 Hz, 1H), 7.23 (d, J = 8.1 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.1, 138.0, 136.6, 134.9, 134.1, 129.8, 126.9, 123.5, 21.1; LRMS (ESI) m/z 170 (100%, $[M+H]^+$); HRMS (ESI) found m/z 170.0965 $[M+H]^+$, $C_{12}H_{12}N$ requires m/z 170.0964. Data consistent with literature.[9]

3-(4-Methoxyphenyl)pyridine (3m)

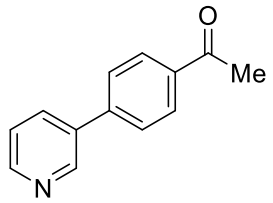


General procedure B was followed using sodium pyridine-3-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 4-bromoanisole (25.0 μL, 0.2 mmol, 1.0 equiv.) or 4-chloroanisole (24.5 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 6:1) yielded product **3m** (Br: 34.0 mg, 92%; Cl: 39.9 mg, 90%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 2.6 Hz, 1H), 8.47 (dd, J = 4.6, 2.3 Hz, 1H), 7.74 (dt, J = 8.1, 1.9 Hz, 1H), 7.43 (d, J = 8.7 Hz, 2H), 7.25 (dd, J = 7.9, 4.7 Hz, 1H), 6.93 (d, J = 8.7 Hz, 2H), 3.77 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.7, 147.9, 147.8, 136.2, 133.8, 130.2, 128.2,

123.5, 114.5, 55.3; LRMS (ESI) *m*/*z* 186 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 186.0914 $[M+H]^+$, $C_{12}H_{12}NO$ requires *m*/*z* 186.0913. Data consistent with literature.[10]

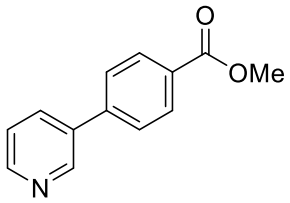
1-(4-(Pyridin-3-yl)phenyl)ethan-1-one (3n)



General procedure B was followed using sodium pyridine-3-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and methyl 4-bromobenzoate (43.0 mg, 0.2 mmol, 1.0 equiv.) or methyl 4-chlorobenzoate (34.1 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 3:1 to 1:1) yielded product **3n** (Br: 33.9 mg, 87%; Cl: 33.2 mg, 82%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, *J* = 2.6 Hz, 1H), 8.57 (dd, *J* = 4.6, 2.3 Hz, 1H), 7.98 (d, *J* = 8.5 Hz, 2H), 7.84 (dt, *J* = 7.9, 1.9 Hz, 1H), 7.61 (d, *J* = 8.5 Hz, 2H), 7.33 (ddd, *J* = 7.3, 4.8, 1.9 Hz, 1H), 2.57 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.5, 149.3, 148.3, 142.3, 136.5, 135.4, 134.4, 129.1, 127.2, 123.6, 26.7; LRMS (ESI) *m*/*z* 198 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 198.0914 $[M+H]^+$, $C_{13}H_{12}NO$ requires *m*/*z* 198.0913. Data consistent with literature.[11]

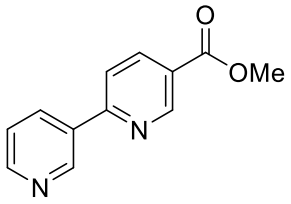
Methyl 4-(pyridin-3-yl)benzoate (3o)



General procedure B was followed using odium pyridine-3-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and methyl 4-bromobenzoate (43.0 mg, 0.2 mmol, 1.0 equiv.) or methyl 4-chlorobenzoate (34.1 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1) yielded product **3o** (Br: 38.3 mg, 90%; Cl: 37.5 mg, 85%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (d, J = 2.5 Hz, 1H), 8.56 (dd, J = 4.6, 2.3 Hz, 1H), 8.07 (d, J = 8.5 Hz, 2H), 7.91 – 7.78 (m, 1H), 7.58 (d, J = 8.5 Hz, 2H), 7.38 – 7.28 (m, 1H), 3.87 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 149.2, 148.3, 142.2, 135.5, 134.4, 130.3, 129.7, 127.0, 123.6, 52.2; LRMS (ESI) *m*/*z* 214 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 214.0862 $[M+H]^+$, $C_{13}H_{12}NO$ requires *m*/*z* 214.0862. Data consistent with literature.[13]

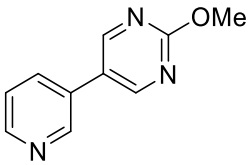
Methyl [2,3'-bipyridine]-5-carboxylate (4n)



General procedure B was followed using sodium pyridine-3-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and methyl 6-chloronicotinate (34.3 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 3:1 to 1:1) yielded product **4n** (35.9 mg, 84%) as a white solid.

mp 111-115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.23 (d, J = 2.5 Hz, 1H), 9.19 (s, 1H), 8.63 (d, J = 4.8 Hz, 1H), 8.40 – 8.25 (m, 2H), 7.83 – 7.70 (m, 1H), 7.37 (dd, J = 8.0, 4.8 Hz, 1H), 3.91 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 158.2, 151.2, 150.7, 148.5, 138.1, 134.7, 133.8, 124.9, 123.7, 119.9, 52.5; IR υ_{max} (neat)/cm^{-1} 1690, 1600, 1510, 1444, 1240, 1200, 1190, 967, 763 LRMS (ESI) *m*/*z* 215 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 215.0815 $[M+H]^+$, $C_{12}H_{11}N_2O_2$ requires *m*/*z* 215.0815.

2-Methoxy-5-(pyridin-3-yl)pyrimidine (4o)

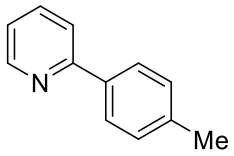


General procedure B was followed using sodium pyridine-3-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 5-bromo-2-methoxypyrimidine (37.8 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 3:1 to 1:1) yielded product **4o** (29.5 mg, 79%) as a white solid.

mp 99-100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 – 8.72 (d, J = 2.5 Hz, 1H), 8.67 (s, 2H8.62 – 8.59 (dd, J = 4.6, 2.3 Hz, 1H), 7.77 (dt, J = 7.9, 2.1 Hz, 1H), 7.39 – 7.33 (m, 1H), 4.01 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.5, 157.4, 149.4, 147.5, 133.8, 130.3, 125.2, 123.9, 55.2; IR υ_{max} (neat)/cm^{-1} 1600, 1466, 1355, 1301, 1075, 891; LRMS (ESI) m/z 188 (100%, $[M+H]^+$); HRMS (ESI) found m/z 188.0818 $[M+H]^+$, $C_{10}H_9N_3O$ requires m/z 188.0818.

3.6 2-Pyridyl Sulfinate Cross-Couplings

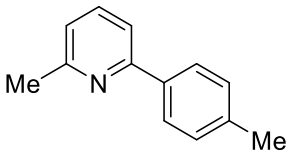
2-(*p*-Tolyl)pyridine (2b)



General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 4-bromotoluene (34.7 mg, 0.2 mmol, 1.0 equiv.) or 4-chlorotoluene (23.7 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **2b** (Br: 24.0 mg, 71%; Cl: 24.0 mg, 71%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 – 8.54 (m, 1H), 7.82 (d, J = 8.0 Hz, 2H), 7.70 – 7.58 (m, 2H), 7.21 (d, J = 8.0 Hz, 2H), 7.12 (ddd, J = 6.6, 4.8, 2.1 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.4, 149.6, 138.9, 136.7, 136.6, 129.4, 126.7, 121.8, 120.2, 21.2; LRMS (ESI) m/z 170 (100%, $[M+H]^+$); HRMS (ESI) found m/z 170.0964 $[M+H]^+$, $C_{12}H_{12}N$ requires m/z 170.0964. Data consistent with literature.[12]

2-Methyl-6-(*p*-tolyl)pyridine (2c)

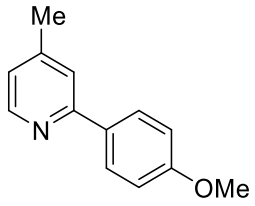


General procedure B was followed using sodium 6-methylpyridine-2-sulfinate (71.6 mg, 0.4 mmol, 2.0 equiv.) and 4-bromotoluene (34.7 mg, 0.2 mmol, 1.0 equiv.) or 4-chlorotoluene (23.7 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash

chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **2c** (Br: 29.6 mg, 81%; Cl: 30.0 mg, 83%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.0 Hz, 2H), 7.52 (t, J = 7.7 Hz, 1H), 7.45 – 7.36 (m, 1H) 7.23 – 7.13 (d, J = 8.0 Hz, 2H), 7.02 – 6.95 (m, 1H), 2.53 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.2, 156.9, 138.6, 136.8, 136.7, 129.4, 126.8, 121.2, 117.3, 24.8, 21.3; LRMS (ESI) m/z 184 (100%, $[M+H]^+$); HRMS (ESI) found m/z 184.1119 $[M+H]^+$, $C_{13}H_{14}N$ requires m/z 184.1120. Data consistent with literature.[13]

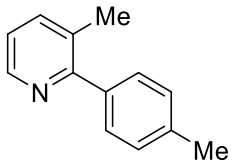
2-(4-Methoxyphenyl)-4-methylpyridine (2e)



General procedure B was followed using sodium 4-methylpyridine-2-sulfinate (71.6 mg, 0.4 mmol, 2.0 equiv.) and 4-bromoanisole (25.0 5 μL, 0.2 mmol, 1.0 equiv.) or 4-chloroanisole (24.5 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **2e** (Br: 33.8 mg, 85%; Cl: 33.8 mg, 85%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43 (d, J = 5.1 Hz, 1H), 7.86 (d, J = 8.8 Hz, 2H), 7.41 (s, 1H) 6.92 (m, J = 7.1, 4.8 Hz, 3H), 3.78 (s, 3H, O*Me*), 2.32 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.3, 157.0, 149.3, 147.6, 132.1, 128.1, 122.4, 120.7, 114.0, 55.3, 21.2; LRMS (ESI) m/z 200 (100%, $[M+H]^+$); HRMS (ESI) found m/z 200.1070 $[M+H]^+$, $C_{13}H_{14}NO$ requires m/z 200.1069. Data consistent with literature.[14]

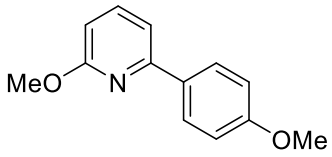
3-Methyl-2-(*p*-tolyl)pyridine (2f)



General procedure B was followed using sodium 3-methylpyridine-2-sulfinate (71.6 mg, 0.4 mmol, 2.0 equiv.) and 4-bromotoluene (34.7 mg, 0.2 mmol, 1.0 equiv.) or 4-chlorotoluene (23.7 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **2f** (Br: 32.0 mg, 87%; Cl: 32.6 mg, 89%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49 – 8.34 (m, 1H), 7.48 (dd, J = 7.7, 1.6 Hz, 1H), 7.35 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 7.07 (dd, J = 7.7, 4.7 Hz, 1H), Pyr-*H*, 2.32 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 146.9, 138.4, 137.6, 137.5, 130.7, 128.8, 128.7, 121.8, 21.3, 20.1; LRMS (ESI) *m*/*z* 184 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 184.1122 $[M+H]^+$, $C_{13}H_{14}N$ requires *m*/*z* 184.1120. Data consistent with literature.[15]

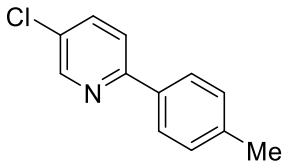
2-Methoxy-6-(4-methoxyphenyl)pyridine (2k)



General procedure B was followed using sodium 6-methoxypyridine-2-sulfinate (78.0 mg, 0.4 mmol, 2.0 equiv.) and 4-bromoanisole (25.0 5 μL, 0.2 mmol, 1.0 equiv.) or 4-chloroanisole (24.5 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **2k** (Br: 38.1 mg, 86%; Cl: 38.7 mg, 90%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.9 Hz, 2H), 7.51 (dd, J = 8.2, 7.5 Hz, 1H), 7.19 (dd, J = 7.5, 0.7 Hz, 1H), 6.90 (d, J = 8.9 Hz, 2H), 6.55 (dd, J = 8.2, 0.7 Hz, 1H), 3.95 (s, 3H), 3.78 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 160.3, 154.4, 139.1, 131.7, 127.9, 113.9, 111.9, 108.3, 55.3, 53.1; LRMS (ESI) *m*/*z* 216 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 216.1020 $[M+H]^+$, $C_{13}H_{14}NO_2$ requires *m*/*z* 216.1019. Data consistent with literature.[16]

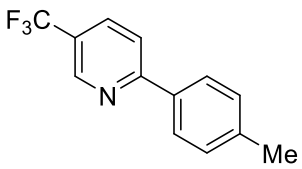
5-Chloro-2-(*p*-tolyl)pyridine (2l)



General procedure B was followed using sodium 5-chloropyridine-2-sulfinate (79.6 mg, 0.4 mmol, 2.0 equiv.) and 4-bromotoluene (34.7 mg, 0.2 mmol, 1.0 equiv.) or 4-chlorotoluene (23.7 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **2l** (Br: 36.9 mg, 91%; Cl: 36.0 mg, 87%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (dd, J = 2.4, 0.8 Hz, 1H), 7.78 (d, J = 8.2 Hz, 2H), 7.65 – 7.54 (m, 2H), 7.20 (d, J = 8.2 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.59, 148.40, 139.37, 136.38, 135.43, 130.22, 129.59, 126.67, 120.81, 21.31; LRMS (ESI) *m*/*z* 204 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 204.0575 $[M+H]^+$, $C_{12}H_{11}NCl$ requires *m*/*z* 204.0574. Data consistent with literature.[17]

2-(*p*-Tolyl)-5-(trifluoromethyl)pyridine (2h)

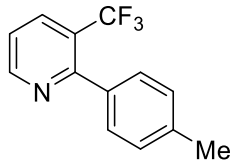


General procedure B was followed using sodium 5-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and 4-bromotoluene (34.7 mg, 0.2 mmol, 1.0 equiv.) or 4-chlorotoluene (23.7 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **2h** (Br: 36.9 mg, 88%; Cl: 36.0 mg, 87%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (dd, J = 2.2, 1.1 Hz, 1H), 7.85 (m, J = 8.2 Hz, 3H), 7.72 (d, J = 8.4 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.6, 146.5 (q, J = 4.1 Hz), 140.3, 135.1, 133.8 (q, J = 3.4 Hz), 129.7, 127.1, 124.6 (q, J = 33.0 Hz), 122.4 (q, J = 272.1 Hz), 119.5, 21.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.19; LRMS (ESI) *m*/*z*

238 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 238.0837 $[M+H]^+$, $C_{13}H_{11}NF_3$ requires *m*/*z* 238.0838. Data consistent with literature.[18]

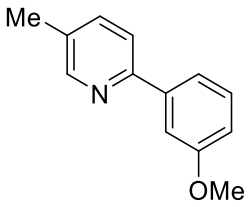
2-(*p*-Tolyl)-3-(trifluoromethyl)pyridine (2j)



General procedure B was followed using sodium 3-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and 4-bromotoluene (34.7 mg, 0.2 mmol, 1.0 equiv.) or 4-chlorotoluene (23.7 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **2j** (Br: 40.3 mg, 85%; Cl: 40.3 mg, 85%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (dd, *J* = 4.8, 1.6 Hz, 1H), 7.97 (dd, *J* = 7.9, 1.7 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.31 – 7.28 (m, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.5, 151.8, 138.7, 136.4, 134.7 (q, *J* = 5.1 Hz), 128.7, 128.5 (q, *J* = 3.4 Hz), 125.0 (q, *J* = 33.0 Hz), 123.7 (q, *J* = 273.3 Hz), 21.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.38; LRMS (ESI) *m*/*z* 238 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 238.0831 $[M+H]^+$, $C_{13}H_{11}NF_3$ requires *m*/*z* 238.0834. Data consistent with literature.[19]

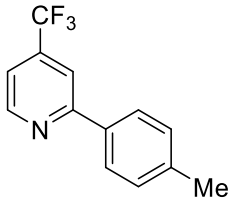
2-(3-Methoxyphenyl)-5-methylpyridine (2d)



General procedure B was followed using sodium 5-methylpyridine-2-sulfinate (71.6 mg, 0.4 mmol, 2.0 equiv.) and 3-bromoanisole (37.4 mg, 0.2 mmol, 1.0 equiv.) or 3-chloroanisole (24.5 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 8:1) yielded product **2d** (Br: 33.8 mg, 85%; Cl: 33.7 mg, 84%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, J = 2.2 Hz, 1H), 7.56 – 7.42 (m, 4H), 7.29 (t, J = 7.9 Hz, 1H), 6.87 (ddd, J = 8.2, 2.6, 0.9 Hz, 1H), 3.81 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 154.5, 150.0, 140.9, 137.3, 131.7, 129.6, 120.2, 119.1, 114.7, 111.7, 55.3, 18.1; LRMS (ESI) m/z 200 (100%, $[M+H]^+$); HRMS (ESI) found m/z 200.0997 $[M+H]^+$, $C_{13}H_{14}NO$ requires m/z 200.0999. Data consistent with literature.[22]

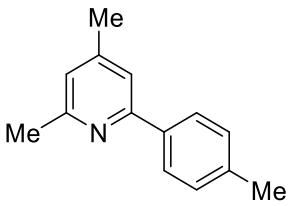
2-(*p*-Tolyl)-4-(trifluoromethyl)pyridine (2i)



General procedure B was followed using sodium 4-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and 4-bromotoluene (34.7 mg, 0.2 mmol, 1.0 equiv.) or 4-chlorotoluene (23.7 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 10:1 to 4:1) yielded product **2i** (Br: 23.3 mg, 84%; Cl: 23.6 mg, 86%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 5.1 Hz, 1H), 7.85 (d, J = 8.3 Hz, 2H), 7.82 – 7.81 (m, 1H), 7.32 (dd, J = 5.1, 1.5 Hz, 1H), 7.22 (d, J = 7.9 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 150.5, 140.0, 139.2 (q, J = 34.1 Hz), 135.2, 129.7, 126.9, 124.3 (q, J = 273.7 Hz), 117.2 (q, J = 3.3 Hz), 115.7 (q, J = 3.7 Hz), 21.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -64.83; LRMS (ESI) m/z 238 (100%, $[M+H]^+$); HRMS (ESI) found m/z 238.0838 $[M+H]^+$, $C_{13}H_{11}NF_3$ requires m/z 238.0838. Data consistent with literature.[20]

2,4-Dimethyl-6-(*p*-tolyl)pyridine (2g)

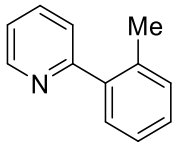


General procedure B was followed using sodium 4,6-dimethylpyridine-2-sulfinate (77.2 mg, 0.4 mmol, 2.0 equiv.) and 4-bromotoluene (34.7 mg, 0.2 mmol, 1.0 equiv.) or 4-

chlorotoluene (23.7 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 10:1) yielded product **2g** (Br: 27.2 mg, 69%; Cl: 26.5 mg, 64%) as a white solid.

mp 132-136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, J = 8.2 Hz, 2H), 7.20 – 7.16 (m, 3H), 6.83 (s, 1H), 2.50 (s, 3H), 2.32 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0, 156.9, 147.6, 138.4, 137.0, 129.3, 126.8, 122.3, 118.4, 24.5, 21.2, 21.1; IR υ_{max} (neat)/cm^{-1} 1593, 1485, 1404, 1331, 1032, 805; LRMS (ESI) *m*/*z* 198 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 198.1277 $[M+H]^+$, $C_{14}H_{16}N$ requires *m*/*z* 198.1277.

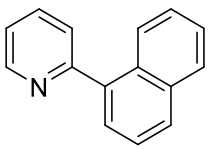
2-(*o*-Tolyl)pyridine (3a)



General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 2-bromotoluene (24.0 μL, 0.2 mmol, 1.0 equiv.) or 2-chlorotoluene (23.4 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 8:1 to 2:1) yielded product **3a** (Br: 29.7 mg, 88%; Cl: 30.0 mg, 90%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 7.67 (td, J = 7.7, 1.6 Hz, 1H), 7.36 – 7.31 (m, 2H7.27 – 7.17 (m, 4H), 2.29 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 149.2, 140.4, 136.0, 135.7, 130.7, 129.6, 128.2, 125.8, 124.1, 121.6, 20.3; LRMS (ESI) *m*/*z* 170 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 170.0962 $[M+H]^+$, $C_{12}H_{12}N$ requires *m*/*z* 170.0964. Data consistent with literature.[21]

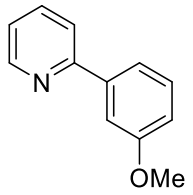
2-(Naphthalen-1-yl)pyridine (3b)



General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 1-bromonaphthalene (28.0 μL, 0.2 mmol, 1.0 equiv.) or 1-chloronaphthalene (27.2 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 4:1 to 2:1) yielded product **3b** (Br: 36.9 mg, 90%; Cl: 36.9 mg, 90%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H), 8.08 – 7.97 (m, 1H), 7.89 – 7.81 (m, 2H), 7.75 (td, J = 7.7, 1.8 Hz, 1H), 7.57 – 7.36 (m, 5H), 7.26 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 149.5, 138.5, 136.4, 133.9, 131.1, 128.8, 128.3, 127.4, 126.4, 125.8, 125.5, 125.3, 125.0, 122.0; LRMS (ESI) m/z 206 (100%, $[M+H]^+$); HRMS (ESI) found m/z 206.0965 $[M+H]^+$, $C_{15}H_{12}N$ requires m/z 206.0964. Data consistent with literature.[22]

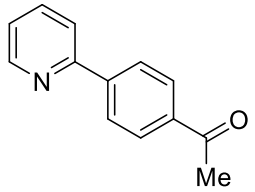
2-(3-Methoxyphenyl)pyridine (3c)



General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 3-bromoanisole (37.4 mg, 0.2 mmol, 1.0 equiv.) or 3-chloroanisole (24.5 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 4:1 to 2:1) yielded product **3c** (Br: 27.1 mg, 73%; Cl: 28.0 mg, 78%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 – 8.57 (m, 1H), 7.75 – 7.60 (m, 2H), 7.52 (dd, J = 2.6, 1.6 Hz, 1H), 7.47 (dt, J = 7.6, 1.2 Hz, 1H), 7.31 (t, J = 7.9 Hz, 1H), 7.21 – 7.13 (m, 1H), 6.90 (ddd, J = 8.2, 2.7, 1.0 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.0, 157.2, 149.6, 140.9, 136.7, 129.7, 122.2, 120.7, 119.3, 115.0, 111.9, 55.3; LRMS (ESI) m/z 204 (100%, $[M+Na]^+$); HRMS (ESI) found m/z 186.0914 $[M+H]^+$, $C_{12}H_{12}NO$ requires m/z 186.0913. Data consistent with literature.[23]

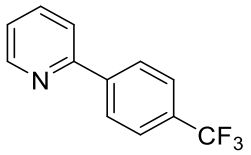
1-(4-(Pyridin-2-yl)phenyl)ethan-1-one (3d)



General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and methyl 4-bromobenzoate (43.0 mg, 0.2 mmol, 1.0 equiv.) or methyl 4-chlorobenzoate (34.1 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 3:1 to 1:1) yielded product **3d** (Br: 33.9 mg, 86%; Cl: 33.9 mg, 86%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (dt, J = 4.8, 1.4 Hz, 1H), 8.08 – 7.95 (m, 4H), 7.72 (m, 2H), 7.27 – 7.17 (m, 1H), 2.58 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.8, 156.0, 149.9, 143.6, 128.8, 128.7, 127.0, 122.9, 121.0, 26.7; LRMS (ESI) *m*/*z* 198 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 198.0913 $[M+H]^+$, $C_{13}H_{12}NO$ requires *m*/*z* 186.0913. Data consistent with literature.[24]

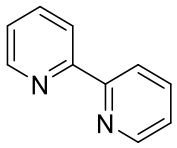
2-[4-(Trifluoromethyl)phenyl]pyridine (3e)



General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 4-bromobenzotrifluoride (28.0 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 3:1 to 1:1) yielded product **3e** (37.0 mg, 83%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 – 8.62 (m, 1H), 8.04 (m, 2H), 7.80 – 7.62 (m, 4H), 7.23 (ddd, J = 6.7, 4.8, 1.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.8, 149.9, 142.6, 136.9, 127.1 (q, J = 3.4 Hz), 125.6 (q, J = 3.7 Hz), 122.9, 120.8; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.57; LRMS (ESI) *m*/*z* 224 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 224.0682 $[M+H]^+$, $C_{12}H_9NF_3$ requires *m*/*z* 224.0681. Data consistent with literature.[28]

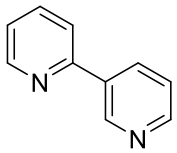
2,2'-Bipyridine (4a)



General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 2-bromopyridine (19.1 μL, 0.2 mmol, 1.0 equiv.) or 2-chloropyridine (18.9 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **4a** (Br: 22.3 mg, 76%; Cl: 21.5 mg, 69%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71 (ddd, J = 4.8, 1.8, 0.9 Hz, 2H), 8.42 (dt, J = 7.9, 1.1 Hz, 2H), 7.84 (td, J = 7.7, 1.8 Hz, 2H), 7.38 – 7.31 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1, 149.1, 136.9, 123.7, 121.0; LRMS (ESI) m/z 157 (100%, $[M+H]^+$); HRMS (ESI) found m/z 157.0760 $[M+H]^+$, $C_{10}H_9N_2$ requires m/z 157.0760. Data consistent with literature.[25]

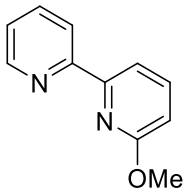
2,3'-Bipyridine (4c)



General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 3-bromopyridine (19.3 μL, 0.2 mmol, 1.0 equiv.) or 3-chloropyridine (19.0 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **4c** (Br: 26.2 mg, 84%; Cl: 25.4 mg, 79%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.13 (s, 1H), 8.66 (dt, J = 4.8, 1.4 Hz, 1H), 8.65 – 8.57 (m, 1H), 8.26 (dt, J = 8.0, 2.0 Hz, 1H), 7.81 – 7.64 (m, 2H), 7.35 (dd, J = 7.9, 4.7 Hz, 1H), 7.23 (ddd, J = 7.2, 4.8, 1.4 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.8, 150.1, 149.9, 148.2, 137.0, 134.8, 134.3, 123.6, 122.8, 120.6; LRMS (ESI) m/z 157 (100%, $[M+H]^+$); HRMS (ESI) found m/z 157.0760 $[M+H]^+$, $C_{10}H_9N_2$ requires m/z 157.0760. Data consistent with literature.[3]

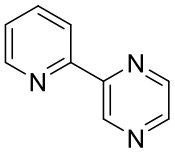
6-Methoxy-2,2'-bipyridine (4b)



General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 2-bromo-6-methoxypyridine (24.6 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 3:1 to 1:1) yielded product **4b** (26.4 mg, 71%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (ddd, J = 4.8, 1.8, 0.9 Hz, 1H), 8.34 (dt, J = 8.0, 1.1 Hz, 1H), 7.94 (dd, J = 7.4, 0.8 Hz, 1H), 7.73 (ddd, J = 8.0, 7.5, 1.8 Hz, 1H), 7.64 (dd, J = 8.2, 7.4 Hz, 1H), 7.25 – 7.20 (m, 1H), 6.71 (dd, J = 8.2, 0.8 Hz, 1H), 3.98 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.5, 156.0, 153.4, 149.0, 139.4, 136.7, 123.5, 120.9, 113.7, 111.0, 53.2; LRMS (ESI) *m*/*z* 187 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 187.0866 $[M+H]^+$, $C_{11}H_{11}N_2O$ requires *m*/*z* 187.0865. Data consistent with literature.[26]

2-(Pyridin-2-yl)pyrazine (4d)

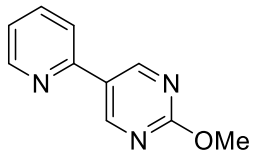


General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 2-bromopyrazine (18.0 μL, 0.2 mmol, 1.0 equiv.) or 2-chloropyrazine (17.8 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **4d** (Br: 24.8 mg, 77%; Cl: 25.1 mg, 80%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.57 (d, J = 1.5 Hz, 1H), 8.66 (ddd, J = 4.8, 1.8, 1.0 Hz, 1H), 8.60 – 8.51 (m, 2H), 8.33 – 8.25 (m, 1H), 7.80 (dd, J = 7.7, 1.8 Hz, 1H), 7.30 (ddd, J = 7.5, 4.8, 1.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.2, 151.1, 149.5, 144.4, 143.5, 143.3, 137.1, 124.4,

121.4; LRMS (ESI) *m*/*z* 158 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 158.0713 $[M+H]^+$, $C_9H_8N_3$ requires *m*/*z* 158.0712. Data consistent with literature.[26]

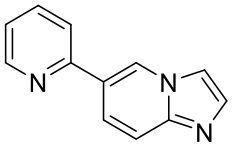
2-Methoxy-5-(pyridin-2-yl)pyrimidine (4e)



General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 5-bromo-2-methoxypyrimidine (37.8 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 3:1 to 1:1) yielded product **4e** (30.3 mg, 81%) as a white solid.

mp 134-134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.05 (s, 2H), 8.63 (ddd, *J* = 4.8, 1.9, 1.0 Hz, 1H), 7.72 (td, *J* = 7.7, 1.8 Hz, 1H), 7.60 (dt, *J* = 7.9, 1.0 Hz, 1H), 7.27 – 7.20 (m, 1H), 4.02 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 157.7, 152.3, 150.1, 137.0, 126.6, 122.7, 119.6, 55.2; IR υ_{max} (neat)/cm^{-1} 1593, 1485, 1404, 1331, 1032, 805; LRMS (ESI) *m*/*z* 188 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 188.0818 $[M+H]^+$, $C_{10}H_{10}N_3O$ requires *m*/*z* 188.0818.

6-(Pyridin-2-yl)imidazo[1,2-a]pyridine (4f)

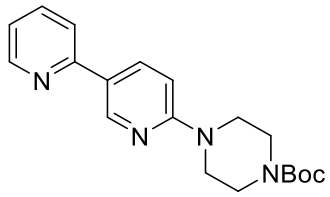


General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 6-bromoimidazo[1.2-a]pyridine (39.4 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 3:1 to 1:1) yielded product **4f** (27.3 mg, 70%) as a white solid.

mp 100-101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (s, 1H), 8.61 (dd, *J* = 5.1, 1.6 Hz, 1H), 7.79 – 7.58 (m, 6H), 7.26 – 7.16 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 149.8, 137.1, 134.5, 134.4, 124.9, 124.8, 123.4, 122.5, 119.9, 117.5; IR υ_{max} (neat)/cm^{-1} 1587, 1516, 1468, 1348,

1130, 776; LRMS (ESI) *m*/*z* 196 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 196.0871 $[M+H]^+$, $C_{12}H_{10}N_3$requires *m*/*z* 196.0869.

***Tert*-butyl 4-([2,3'-bipyridin]-6'-yl)piperazine-1-carboxylate (4j)**



General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and *tert*-butyl 4-(5-bromopyridin-2-yl)piperazine-1-carboxylate (68.2 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 3:1 to 1:1) yielded product **4j** (60.5 mg, 89%) as a white solid.

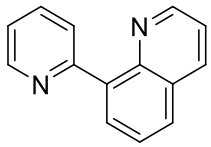
mp 192-194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 – 8.67 (m, 1H), 8.56 (ddd, *J* = 4.9, 1.8, 0.9 Hz, 1H), 8.12 (dd, *J* = 8.9, 2.5 Hz, 1H), 7.63 (td, *J* = 7.7, 1.8 Hz, 1H), 7.56 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.09 (ddd, *J* = 7.3, 4.9, 1.2 Hz, 1H), 6.71 – 6.63 (m, 1H), 3.55 (dd, *J* = 7.0, 3.7 Hz, 4H), 3.52 (dd, *J* = 7.0, 3.7 Hz, 4H), 1.42 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 155.3, 154.8, 149.7, 146.6, 136.7, 136.1, 124.9, 121.4, 119.1, 106.7, 80.0, 44.9, 43.4, 28.4; IR υ_{max} (neat)/cm^{-1} 1687, 1605, 1508, 1465, 1240, 1170, 1124, 934, 782; LRMS (ESI) *m*/*z* 341 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 341.1967 $[M+H]^+$, $C_{19}H_{25}N_4O_2$ requires *m*/*z* 341.1972.

3.6.1 Preparative Scale Synthesis of Bipyridine 4j

Pyridine-2-sulfinate (5.4 g, 32.9 mmol, 1.5 equiv.), *tert*-butyl 4-(5-bromopyridin-2-yl)piperazine-1-carboxylate (7.5 g, 21.9 mmol, 1.0 equiv.), potassium carbonate (6.1 g, 43.8 mmol, 2.0 equiv.), palladium(II) acetate (49.4 mg, 1 mol%), tricyclohexylphosphine (123.4 mg, 2 mol%) were placed in a 250-mL round bottom flask equipped with a reflux condenser , followed by the addition of dibutylether (75 mL, 0.3 M). The reaction was heated at 140 °C for 16 h. The mixture was then allowed to cool down to room temperature, filtered over a pad of Celite© and washed with ethyl acetate and H_2O. After separating the layers the aqueous phase was extracted with ethyl acetate (3 x 50 mL) and the combined organic phases were washed with brine, dried over $MgSO_4$ and the solvent was removed under reduced pressure.

Purification of the crude material by flash chromatography (Gradient in PE/EA 4:1 to 1:1) yielded product **4j** (6.9 g, 92%) as a white solid.

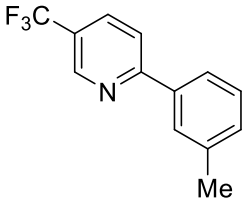
8-(Pyridin-2-yl)quinolone (4g)



General procedure B was followed using sodium pyridine-2-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 8-chloroquinoline (25.4 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 3:1 to 1:1) yielded product **4g** (33.7 mg, 82%) as a yellow solid.

mp 177-178 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (dd, J = 4.2, 1.8 Hz, 1H), 8.72 (dt, J = 5.0, 1.2 Hz, 1H), 8.16 (dd, J = 8.3, 1.9 Hz, 1H), 8.06 (dd, J = 7.2, 1.6 Hz, 1H), 8.01 (dd, J = 8.0, 1.1 Hz, 1H), 7.82 (dd, J = 8.2, 1.6 Hz, 1H), 7.75 (td, J = 7.7, 1.8 Hz, 1H), 7.60 (dd, J = 8.1, 7.2 Hz, 1H), 7.37 (dd, J = 8.3, 4.2 Hz, 1H), 7.24 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.1, 150.3, 149.5, 138.9, 138.0, 136.4, 135.5, 131.2, 128.8, 128.6, 126.8, 126.4, 122.1, 121.0; IR υ_{max} (neat)/cm^{-1} 1590, 1560, 1457, 1384, 1049, 972, 796, 617; LRMS (ESI) m/z 207 (100%, $[M+H]^+$); HRMS (ESI) found m/z 207.0918 $[M+H]^+$, $C_{14}H_{11}N_2$ requires m/z 207.0916.

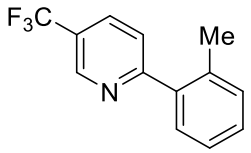
2-(*m*-Tolyl)-5-(trifluoromethyl)pyridine (3g)



General procedure B was followed using sodium 5-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and 3-bromotoluene (24.3 7 μL, 0.2 mmol, 1.0 equiv.) or 3-chlorotoluene (23.6 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **3g** (Br: 39.3 mg, 83%; Cl: 39.3 mg, 83%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (dd, J = 2.2, 1.1 Hz, 1H), 7.90 (dd, J = 8.3, 2.2 Hz, 1H), 7.81 – 7.70 (m, 3H), 7.33 (t, J = 7.6 Hz, 1H), 7.27 – 7.20 (m, 1H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.8, 146.5 (q, J = 4.1 Hz), 138.7, 137.9, 133.8 (q, J = 3.2 Hz), 130.8, 128.8, 127.9, 124.3 (q, J = 280.3 Hz), 120.0, 103.0, 99.9, 21.5; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.21; LRMS (ESI) m/z 238 (100%, $[M+H]^+$); HRMS (ESI) found m/z 238.0833 $[M+H]^+$, $C_{13}H_{11}NF_3$ requires m/z 238.0838. Data consistent with literature.[27]

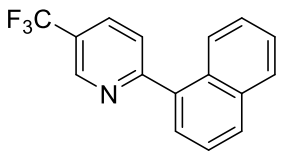
2-(*o*-Tolyl)-5-(trifluoromethyl)pyridine (3f)



General procedure B was followed using sodium 5-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and 2-bromotoluene (24.0 7 μL, 0.2 mmol, 1.0 equiv.) or 2-chlorotoluene (23.4 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **3f** (Br: 42.2 mg, 87%; Cl: 42.6 mg, 90%) as a white solid.

mp 113-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (dd, J = 2.2, 1.1 Hz, 1H), 7.91 (ddd, J = 8.2, 2.4, 0.8 Hz, 1H), 7.47 (d, J = 8.3 Hz, 1H), 7.37 – 7.20 (m, 4H), 2.31 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.55, 146.12 (q, J = 4.0 Hz), 139.0, 135.9, 133.3 (q, J = 3.5 Hz), 131.0, 129.6, 129.0, 126.1, 125.1, 124.3 (q, J = 33.0 Hz), 122.3 (q, J = 272.1 Hz), 20.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.20; IR υ_{max} (neat)/cm^{-1} 1738, 1605, 1327, 1241, 1164, 1083, 912, 734; LRMS (ESI) m/z 238 (100%, $[M+H]^+$); HRMS (ESI) found m/z 238.0838 $[M+H]^+$, $C_{13}H_{11}NF_3$ requires m/z 238.0839.

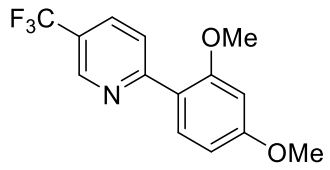
2-(Naphthalen-1-yl)-5-(trifluoromethyl)pyridine (3h)



General procedure B was followed using sodium 5-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and 1-bromonaphthalene (28.0 μL, 0.2 mmol, 1.0 equiv.) or 1-chloronaphthalene (33.4 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **3h** (Br: 43.9 mg, 82%; Cl: 43.7 mg, 80%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (dd, J = 2.2, 1.1 Hz, 1H), 8.03 – 7.96 (m, 2H), 7.93 – 7.80 (m, 2H), 7.66 (ddd, J = 8.2, 2.4, 0.8 Hz, 1H), 7.57 – 7.39 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8, 146.4 (q, J = 3.9 Hz), 137.0, 133.9, 133.6 (q, J = 3.3 Hz), 130.8, 129.8, 128.5, 127.8, 126.9, 126.1, 125.2, 125.1, 124.7, 122.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.16; LRMS (ESI) m/z 274 (100%, $[M+H]^+$); HRMS (ESI) found m/z 274.0835 $[M+H]^+$, $C_{16}H_{11}NF_3$ requires m/z 274.0838. Data consistent with literature.[27]

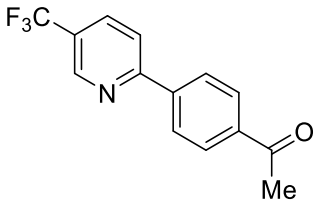
2-(2,4-Dimethoxyphenyl)-5-(trifluoromethyl)pyridine (3k)



General procedure B was followed using lithium 6-methoxypyridine-3-sulfinate (71.4 mg, 0.4 mmol, 2.0 equiv.) and 1-chloro-2,4-dimethoxybenzene (34.52 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 3:1) yielded product **3k** (54.3 mg, 96%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (dd, J = 2.2, 1.1 Hz, 1H), 7.91 (ddd, J = 8.2, 2.4, 0.8 Hz, 1H), 7.86 – 7.76 (m, 2H), 6.56 (dd, J = 8.6, 2.4 Hz, 1H), 6.48 (d, J = 2.3 Hz, 1H), 3.79 (s, 6H*e*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.1, 159.1, 158.5, 146.0 (q, J = 4.0 Hz), 132.6 (q, J = 3.4 Hz), 132.3, 125.2, 124.1 (q, J = 33.0 Hz), 122.5 (q, J = 272.0 Hz), 120.5, 105.3, 98.8, 55.4; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.17; IR υ_{max} (neat)/cm^{-1} 1602, 1580, 1465, 1327, 1290, 1209, 1122, 1054, 937, 773; LRMS (ESI) m/z 284 (100%, $[M+H]^+$); HRMS (ESI) found m/z 284.0893 $[M+H]^+$, $C_{14}H_{13}NO_2F_3$ requires m/z 284.0892.

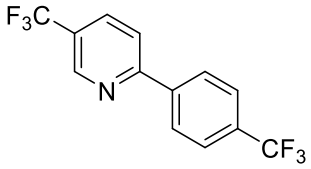
1-(4-(5-(Trifluoromethyl)pyridin-2-yl)phenyl)ethan-1-one (3i)



General procedure B was followed using sodium 5-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and methyl 4-bromobenzoate (43.0 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **3i** (Br: 36.3 mg, 70%; Cl: 36.0 mg, 68%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (dd, J = 2.2, 1.1 Hz, 1H), 8.08 (d, J = 8.6 Hz, 2H), 8.02 (d, J = 8.6 Hz, 2H), 7.98 – 7.93 (ddd, J = 8.2, 2.4, 0.8 Hz, 1H), 7.84 (d, J = 8.3 Hz, 1H), 2.59 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6, 159.2, 146.8 (q, J = 3.9 Hz), 141.9, 137.9, 134.1 (q, J = 3.3 Hz), 128.9, 127.4, 125.7, 125.4, 124.9, 120.4, 26.8; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.32; IR υ_{max} (neat)/cm^{-1} 1685, 1385, 1139, 1013, 828, 732;LRMS (ESI) m/z 266 (100%, $[M+H]^+$); HRMS (ESI) found m/z 266.0788 $[M+H]^+$, $C_{14}H_{11}NOF_3$ requires m/z 266.0787.

5-(Trifluoromethyl)-2-(4-(trifluoromethyl)phenyl)pyridine (3j)

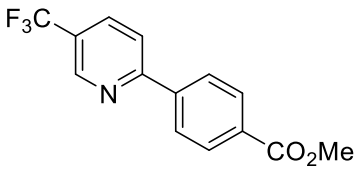


General procedure B was followed using sodium 5-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and 4-bromobenzotrifluoride (28.0 μL, 0.2 mmol, 1.0 equiv.).Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **3j** (36.0 mg, 62%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (dd, J = 2.2, 1.1 Hz, 1H), 8.09 (d, J = 8.8 Hz, 2H), 7.97 (dd, J = 8.3, 2.3 Hz, 1H), 7.82 (d, J = 8.3 Hz, 1H), 7.70 (d, J = 8.8 Hz, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.0, 146.8 (q, J = 4.0 Hz), 141.1, 134.2 (q, J = 3.3 Hz), 131.6 (q, J = 319.4 Hz), 127.6, 125.9 (q, J = 3.8 Hz), 125.5 (q, J = 280.1 Hz), 122.1; ^{19}F NMR (376 MHz, $CDCl_3$) δ -

62.36, -62.77; LRMS (ESI) *m*/*z* 292 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 292.0556 $[M+H]^+$, $C_{13}H_8NF_6$ requires *m*/*z* 292.0555. Data consistent with literature.[27]

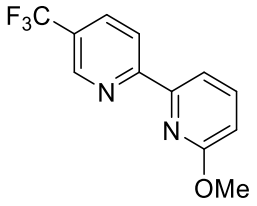
Methyl 4-(5-(trifluoromethyl)pyridin-2-yl)benzoate (3l)



General procedure B was followed using sodium 5-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and methyl 4-bromobenzoate (43.0 mg, 0.2 mmol, 1.0 equiv.).Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **3l** (42.1 mg, 75%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (dd, *J* = 2.2, 1.1 Hz, 1H), 8.10 (d, *J* = 8.7 Hz, 2H), 8.04 (d, *J* = 8.6 Hz, 2H), 8.00 (ddd, *J* = 8.2, 2.4, 0.8 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 1H), 3.88 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 159.4, 146.7 (q, *J* = 3.9 Hz), 141.8, 134.1 (q, *J* = 3.3 Hz), 131.3, 130.1, 127.2, 124.9 (q, *J* = 33.0 Hz), 122.2 (q, *J* = 272.0 Hz), 120.4, 52.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.32; IR υ_{max} (neat)/cm^{-1} 1680, 1577, 1361, 1166, 1132, 1013, 843, 720; LRMS (ESI) *m*/*z* 282 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 282.0734 $[M+H]^+$, $C_{14}H_{11}NO_2F_3$ requires *m*/*z* 282.0736.

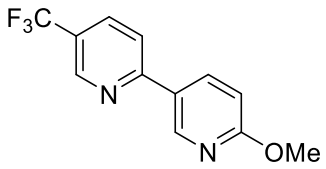
6'-Methoxy-5-(trifluoromethyl)-2,2'-bipyridine (4k)



General procedure B was followed using sodium 5-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and 2-bromo-6-methoxypyridine (24.6 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **4k** (40.1 mg, 79%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.86 (dd, J = 2.2, 1.1 Hz, 1H), 8.45 (dt, J = 8.5, 0.8 Hz, 1H), 7.99 (dd, J = 7.4, 0.8 Hz, 1H), 7.94 (ddd, J = 8.3, 2.4, 0.8 Hz, 1H), 7.65 (dd, J = 8.2, 7.4 Hz, 1H), 6.76 (dd, J = 8.2, 0.8 Hz, 1H), 3.97 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.6, 159.2, 151.9, 146.0 (q, J = 4.0 Hz), 139.5, 133.8 (q, J = 3.6 Hz), 125.8, 122.3 (q, J = 272.4 Hz), 120.4, 114.5, 112.3, 53.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.31; IR υ_{max} (neat)/cm^{-1} 1603, 1566, 1467, 1323, 1265, 1124, 1075, 858; LRMS (ESI) m/z 255 (100%, $[M+H]^+$); HRMS (ESI) found m/z 255.0740 $[M+H]^+$, $C_{12}H_{10}N_2OF_3$ requires m/z 255.0739.

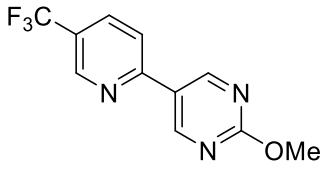
6'-Methoxy-5-(trifluoromethyl)-2,3'-bipyridine (4i)



General procedure B was followed using sodium 5-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and 3-bromo-6-methoxypyridine (25.0 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **4i** (35.5 mg, 70%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.87 (dd, J = 2.2, 1.1 Hz, 1H), 8.74 (dd, J = 2.5, 0.8 Hz, 1H), 8.22 (dd, J = 8.7, 2.5 Hz, 1H), 7.97 – 7.87 (m, 1H), 7.71 (dt, J = 8.3, 0.8 Hz, 1H), 6.80 (dd, J = 8.7, 0.8 Hz, 1H), 3.94 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.2, 158.2, 146.7 (q, J = 4.0 Hz), 146.1, 137.5, 134.0 (q, J = 3.4 Hz), 127.1, 125.0, 124.8, 118.9, 111.2, 53.8; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.28; LRMS (ESI) m/z 255 (100%, $[M+H]^+$); HRMS (ESI) found m/z 255.0740 $[M+H]^+$, $C_{12}H_{10}N_2OF_3$ requires m/z 255.0739. Data consistent with literature.[10]

2-Methoxy-5-(5-(trifluoromethyl)pyridin-2-yl)pyrimidine (4l)

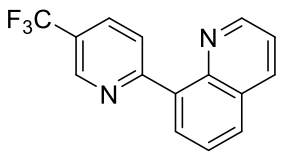


General procedure B was followed using sodium 5-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and 5-bromo-2-methoxypyrimidine (37.8 mg,

0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **4l** (37.7 mg, 74%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (s, 2H), 8.89 (dd, *J* = 2.2, 1.1 Hz, 1H), 7.95 (ddd, *J* = 8.2, 2.4, 0.8 Hz, 1H), 7.74 (d, *J* = 8.3 Hz, 1H), 4.04 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 158.2, 155.6, 147.0 (q, *J* = 4.0 Hz), 134.3 (q, *J* = 3.3 Hz), 125.3 (q, *J* = 33.0 Hz), 122.1, 118.8, 55.4; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.38; IR υ_{max} (neat)/cm^{-1} 1602, 1573, 1422, 1327, 1120, 1091, 801; LRMS (ESI) *m*/*z* 256 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 256.0692 $[M+H]^+$, $C_{11}H_9N_3F_3$ requires *m*/*z* 256.0692.

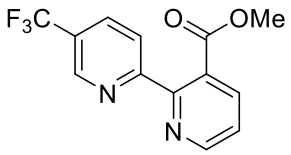
8-(5-(Trifluoromethyl)pyridin-2-yl)quinolone (4m)



General procedure B was followed using sodium 5-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and 8-chloroquinoline (25.4 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **4m** (49.8 mg, 91%) as a yellow solid.

mp 200-203 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (dd, *J* = 2.2, 1.1 Hz, 1H), 8.88 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.23 (dt, *J* = 8.3, 0.8 Hz, 1H), 8.17 (dd, *J* = 8.3, 1.8 Hz, 1H), 8.11 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.96 (ddd, *J* = 8.3, 2.4, 0.8 Hz, 1H), 7.86 (dd, *J* = 8.2, 1.5 Hz, 1H), 7.61 (dd, *J* = 8.2, 7.2 Hz, 1H), 7.38 (dd, *J* = 8.3, 4.2 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.4, 150.5, 146.3 (q, *J* = 4.1 Hz), 145.6, 137.4, 136.6, 132.5 (q, *J* = 3.4 Hz), 131.5, 129.7, 128.6, 127.3, 126.7, 126.5, 124.9 (d, *J* = 33.2 Hz), 121.3; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.24; IR υ_{max} (neat)/cm^{-1} 1602, 1324, 1124, 1080, 1014, 829, 706; LRMS (ESI) *m*/*z* 275 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 275.0788 $[M+H]^+$, $C_{15}H_{10}N_2F_3$ requires *m*/*z* 275.0790.

Methyl 5'-(trifluoromethyl)-[2,2'-bipyridine]-3-carboxylate (4h)

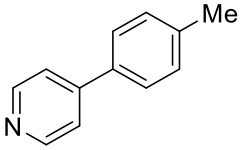


General procedure B was followed using sodium 5-(trifluoromethyl)pyridine-2-sulfinate (93.2 mg, 0.4 mmol, 2.0 equiv.) and methyl 2-bromonicotinate (43.0 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **4h** (38.9 mg, 69%) as a white solid.

mp 112-116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (dd, J = 2.2, 1.1 Hz, 1H), 8.71 (dd, J = 4.8, 1.7 Hz, 1H), 8.22 (d, J = 8.3 Hz, 1H), 8.01 (dd, J = 8.3, 2.3 Hz, 1H), 7.94 (dd, J = 7.7, 1.7 Hz, 1H), 7.38 (dd, J = 7.8, 4.8 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.9, 159.3, 153.9, 150.5, 145.2 (q, J = 4.2 Hz), 137.1, 134.0 (q, J = 3.3 Hz), 128.8, 126.5, 126.1 (d, J = 33.0 Hz), 123.5, 122.5, 52.5; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.35; IR υ_{max} (neat)/cm^{-1} 1732, 1605, 1327, 1165, 1129, 859; LRMS (ESI) m/z 283 (100%, $[M+H]^+$); HRMS (ESI) found m/z 283.0680 $[M+H]^+$, $C_{13}H_{10}N_2O_2F_3$ requires m/z 283.0688.

3.7 4-Pyridyl Sulfinate Cross-Couplings

4-(*p*-Tolyl)pyridine (2o)

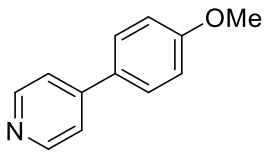


General procedure B was followed using sodium pyridine-4-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 4-bromotoluene (34.7 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **2o** (29.0 mg, 86%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 – 8.50 (m, 2H), 7.47 (d, J = 8.2 Hz, 2H), 7.44 – 7.40 (m, 2H), 7.22 (d, J = 7.9 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.2, 149.3, 148.2,

139.2, 135.1, 129.8, 121.4, 21.2; LRMS (ESI) *m*/*z* 170 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 170.0964 $[M+H]^+$, $C_{12}H_{12}N$ requires *m*/*z* 170.0964. Data consistent with literature.[29]

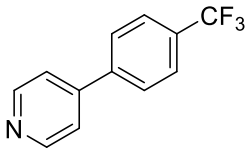
4-(4-Methoxyphenyl)pyridine (3z)



General procedure B was followed using sodium pyridine-4-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 4-bromoanisole (24.6 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **3z** (30.3 mg, 82%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 – 8.52 (m, 2H), 7.53 (d, J = 8.8 Hz, 2H), 7.39 (m, 2H), 6.94 (d, J = 8.9 Hz, 2H), 3.79 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.5, 150.2, 147.7, 137.3, 130.3, 128.1, 121.0, 55.4; LRMS (ESI) *m*/*z* 186 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 186.0914 $[M+H]^+$, $C_{12}H_{12}NO$ requires *m*/*z* 186.0913. Data consistent with literature.[25]

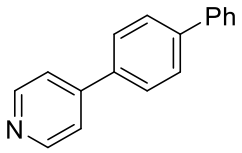
4-(4-(Trifluoromethyl)phenyl)pyridine (3aa)



General procedure B was followed using sodium pyridine-4-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 4-bromobenzotrifluoride (28.0 μL, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **3aa** (30.0 mg, 74%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 – 8.61 (m, 2H), 7.67 (s, 4H), 7.48 – 7.38 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.5, 146.9, 141.7, 131.2, 130.8, 127.4, 126.0 (q, J = 3.7 Hz), 122.6 (q, J = 3.8 Hz), 121.7; ^{19}F NMR (377 MHz, $CDCl_3$) δ -62.67; LRMS (ESI) *m*/*z* 224 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 224.0682 $[M+H]^+$, $C_{12}H_9NF_3$ requires *m*/*z* 224.0681. Data consistent with literature.[30]

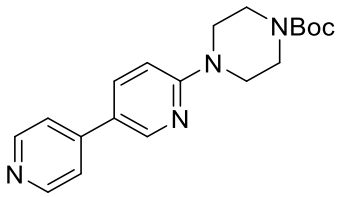
4-([1,1'-Biphenyl]-4-yl)pyridine (3y)



General procedure B was followed using sodium pyridine-4-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 4-bromo-1,1'-biphenyl (46.4 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 5:1 to 1:1) yielded product **3y** (30.5 mg, 66%) as a white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 5.0 Hz, 2H), 7.66 (s, 4H), 7.62 – 7.56 (m, 2H), 7.53 – 7.46 (m, 2H), 7.46 – 7.38 (m, 2H), 7.37 – 7.28 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.3, 147.8, 142.0, 140.2, 136.9, 128.9, 127.8, 127.8, 127.7, 127.1, 121.4; LRMS (ESI) *m*/*z* 232 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 232.1121 $[M+H]^+$, $C_{17}H_{14}N$ requires *m*/*z* 232.1120. Data consistent with literature.[27]

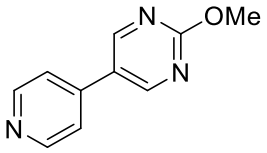
***Tert*-butyl 4-([3,4'-bipyridin]-6-yl)piperazine-1-carboxylate (4v)**



General procedure B was followed using sodium pyridine-4-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and *tert*-butyl 4-(5-bromopyridin-2-yl)piperazine-1-carboxylate (68.2 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 3:1 to 1:1) yielded product **4v** (57.1 mg, 84%) as a white solid.

mp 231-232 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (d, J = 5.2 Hz, 2H), 8.45 (d, J = 2.6 Hz, 1H), 7.71 (dd, J = 8.9, 2.6 Hz, 1H), 7.43 – 7.33 (m, 2H), 6.66 (d, J = 8.8 Hz, 1H), 3.60 – 3.55 (m, 4H), 3.54 – 3.49 (m, 4H), 1.42 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.2, 154.7, 150.3, 146.4, 145.4, 135.8, 122.8, 120.2, 106.8, 80.1, 44.8, 43.1, 28.4; IR υ_{max} (neat)/cm^{-1} 1692, 1596, 1537, 1484, 1284, 1239, 1083, 807; LRMS (ESI) *m*/*z* 341 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 341.1970 $[M+H]^+$, $C_{19}H_{25}N_4O_2$ requires *m*/*z* 341.1972.

2-Methoxy-5-(pyridin-4-yl)pyrimidine (4w)

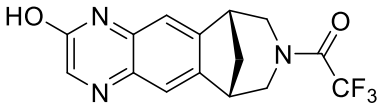


General procedure B was followed using sodium pyridine-4-sulfinate (66.0 mg, 0.4 mmol, 2.0 equiv.) and 5-bromo-2-methoxypyrimidine (37.8 mg, 0.2 mmol, 1.0 equiv.). Purification of the crude material by flash chromatography (Gradient in PE/EA 3:1 to 1:1) yielded product **4w** (26.5 mg, 71%) as a white solid.

mp 143-145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 2H), 8.38 – 8.29 (m, 2H, Pyr-*H*), 6.91 – 6.80 (m, 2H), 4.03 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.4, 156.9, 149.7, 148.6, 120.4, 117.5, 55.6; IR υ_{max} (neat)/cm^{-1} 1572, 1469, 1398, 1328, 1034, 801; LRMS (ESI) *m*/*z* 188 (100%, $[M+H]^+$); HRMS (ESI) found *m*/*z* 188.0820 $[M+H]^+$, $C_{10}H_{10}N_3O$ requires *m*/*z* 188.0818.

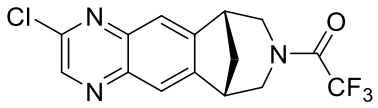
3.8 Varenicline Chloride Synthesis and Cross-Couplings

2,2,2-Trifluoro-1-[(6*S*,10*R*)-2-hydroxy-6,7,9,10-tetrahydro-8*H*-6,10-methanoazepino[4,5-*g*]quinoxalin-8-yl]ethan-1-one



Prepared according to Pfizer Patent.[31] Methyl 2-hydroxy-2-methoxyacetate (1.33 g, 4.4 mmol, 1.1 equiv.) was added to a solution of *rac*-1-((1*R*,5*S*)-7,8-diamino-1,2,4,5-tetrahydro-3*H*-1,5-methanobenzo[*d*]azepin-3-yl)-2,2,2 trifluoroethan-1-one (1.17 g, 4.1 mmol, 1.0 equiv.) in EtOH (8.2 mL) and the resulting mixture was heated at 75 °C. After 21 h, evaporation of the reaction mixture afforded a pale yellow solid, which was evaporated from MeCN and dried under dynamic vacuum to afford 1.5 g of the product, which was used without further purification.

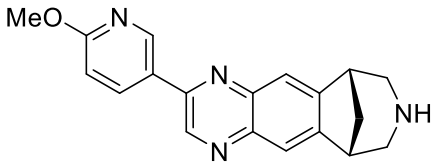
1-[(6*S*,10*R*)-2-Chloro-6,7,9,10-tetrahydro-8*H*-6,10-methanoazepino[4,5-*g*]quinoxalin-8-yl]-2,2,2-trifluoroethan-1-one (5)



A suspension of 2,2,2-Trifluoro-1-[(6*S*,10*R*)-2-hydroxy-6,7,9,10-tetrahydro-8*H*-6,10-methanoazepino[4,5-*g*]quinoxalin-8-yl]ethan-1-one (1.4 g, 4.2 mmol, 1.0 equiv.) in $POCl_3$ (4.0 mL, 43 mmol, 10.2 equiv.) was heated to 85 °C for 45 minutes. After allowing the reaction mixture to cool to room temperature, excess $POCl_3$ was quenched by portionwise addition of the reaction mixture to a stirred solution of 86% phosphoric acid (1.7 g), water (25 mL), methyl orange indicator solution (2 drops), and 50 wt. % aq. NaOH to reach the turning point of the indicator. During the quench, added ice was necessary to maintain the internal workup mixture temperature below 35 °C and additional 50 wt. % aq. NaOH was added to maintain the pH of the workup mixture at the turning point of the indicator. The mixture was then extracted with EtOAc (2 x 50 mL), and the combined organic layers were washed with brine, dried over sodium sulfate and evaporated to afford a light brown solid (1.26 g). MPLC purification on a 120 g RediSep Gold silica gel column using an EtOAc/heptane gradient (15% to 60% EtOAc) furnished compound **5** (1.2 g, 89% over two steps) as a white solid.

mp 198-199 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.73 (d, J = 8.3 Hz, 1H), 7.92 (s, 1H), 7.83 (s, 1H), 4.53 – 4.44 (m, 1H), 4.09 – 4.02 (m, 1H), 3.68 (dd, J = 12.8, 1.6 Hz, 1H), 3.57 – 3.55 (m, 1H), 3.53 – 3.50 (m, 1H), 3.28 (d, J = 13.1 Hz, 1H, C*H*), 2.57 – 2.48 (m, 1H), 2.15 (d, J = 11.3 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 157.2 (q, J = 36.1 Hz), 148.3, 147.7, 147.1, 146.9, 146.8, 146.6, 142.4, 142.3, 141.4, 141.2, 122.7, 122.5, 122.0, 121.8, 116.9 (q, J = 288.5 Hz), 50.7, 48.5, 41.8, 41.79, 39.9, 39.8, 39.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -68.57; IR υ_{max} (neat)/cm^{-1} 1688, 1463, 1222, 1186, 1144, 959, 756, 544; HRMS (ESI) found m/z 342.0542 $[M+H]^+$, $C_{15}H_{12}N_3OF_3Cl$ requires m/z 342.0539.

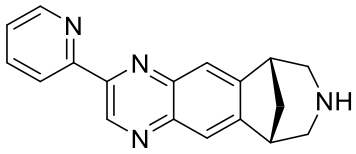
(6*S*,10*R*)-2-(6-Methoxypyridin-3-yl)-7,8,9,10-tetrahydro-6*H*-6,10-methanoazepino[4,5-*g*]quinoxaline (5a)



General procedure B-1 was followed using lithium 5-methoxypyridine-2-sulfinate (34.4 mg, 0.191 mmol). Purification using automated preparative HPLC afforded compound **5a** as a light yellow CF_3CO_2H salt (34.2 mg, 80%).

decomp. 232 °C; ^{1}H NMR (600 MHz, CD_3OD) δ 9.38 (s, 1*H*), 9.04 (d, J = 2.4 Hz, 1H), 8.56 (dd, J = 8.7, 2.5 Hz, 1H), 8.11 (s, 1H), 8.06 (s, 1H), 6.99 (d, J = 8.7 Hz, 1H), 4.02 (s, 3H), 3.69 – 3.65 (m, 2H), 3.55 – 3.51 (m, 2H), 3.38 – 3.35 (m, 2H), 2.51 – 2.49 (m, 1H), 2.29 (d, J = 11.6 Hz, 1H); ^{13}C NMR (151 MHz, CD_3OD) δ 165.5, 149.3, 146.2, 145.6, 144.7, 142.9, 141.9, 141.7, 137.6, 125.8, 123.8, 123.2, 110.7, 53.0, 40.2, 38.6, 38.59; IR υ_{max} (neat)/cm^{-1} 3422, 1674, 1603, 1502, 1474, 1372, 1268, 1199, 1133, 1020, 833, 720; HRMS (ESI) found m/z 319.1555 $[M+H]^+$, $C_{19}H_{19}N_4O$ requires m/z 319.1557.

(6*S*,10*R*)-2-(Pyridin-2-yl)-7,8,9,10-tetrahydro-6*H*-6,10-methanoazepino[4,5-*g*]quinoxaline (5b)

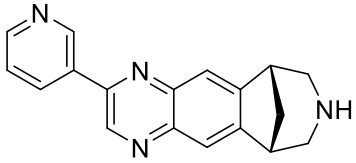


General procedure B-1 was followed using sodium pyridine-2-sulfinate (33.1 mg, 0.191 mmol). Purification using automated preparative HPLC afforded compound **5b** as a CF_3CO_2H salt (4.6 mg, 12%).

decomp. 190 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 9.87 (s, 1H), 8.82 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H), 8.68 – 8.62 (m, 1H), 8.22 (s, 1H), 8.15 (s, 1H), 8.10 (td, J = 7.8, 1.8 Hz, 1H), 7.60 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H), 3.78 – 3.71 (m, 2H), 3.67 – 3.49 (m, 2H), 3.41- 3.39 (m, 2H), 2.61 – 2.50 (m, 1H), 2.33 (d, J = 11.6 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 153.6, 149.6, 149.0, 145.8, 145.8, 142.9, 137.9, 125.0, 124.2, 123.3, 121.9, 48.9, 40.2, 38.6, 38.59; IR υ_{max} (neat)/cm^{-1} 3410,

1671, 1474, 1199, 1131, 1075, 866, 744, 609; HRMS (ESI) found *m*/*z* 289.1449 $[M+H]^+$, $C_{18}H_{17}N_4$ requires *m*/*z* 289.1445.

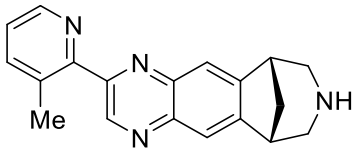
(6*S*,10*R*)-2-(Pyridin-3-yl)-7,8,9,10-tetrahydro-6*H*-6,10-methanoazepino[4,5-*g*]quinoxaline (5c)



General procedure B-1 was followed using sodium pyridine-3-sulfinate (33.1 mg, 0.191 mmol). Purification using automated preparative HPLC afforded compound **5c** as a CF_3CO_2H salt (10.6 mg, 27%).

mp 176-177 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 9.47 (s, 1H), 9.44 (dd, *J* = 2.3, 0.9 Hz, 1H), 8.74 (ddd, *J* = 8.0, 2.3, 1.6 Hz, 1H), 8.71 (dd, *J* = 5.0, 1.6 Hz, 1H), 8.20 (s, 1H), 8.11 (s, 1H), 7.67 (ddd, *J* = 8.0, 4.9, 0.9 Hz, 1H), 3.71 – 3.68 (m, 2H), 3.59 – 3.54 (m, 2H), 3.45 – 3.36 (m, 2H), 2.60 – 2.47 (m, 1H), 2.31 (d, *J* = 11.6 Hz, 1H): ^{13}C NMR (101 MHz, CD_3OD) δ 149.7, 148.7, 147.5, 146.0, 145.7, 142.9, 142.3, 142.2, 135.6, 132.7, 124.3, 124.1, 123.3, 48.9, 40.1, 38.6, 38.59; IR υ_{max} (neat)/cm^{-1} 3295, 1465, 1190, 1070, 1025, 916, 858, 704, 606; HRMS (ESI) found *m*/*z* 289.1447 $[M+H]^+$, $C_{18}H_{17}N_4$ requires *m*/*z* 289.1450.

(6*S*,10*R*)-2-(3-Methylpyridin-2-yl)-7,8,9,10-tetrahydro-6*H*-6,10-methanoazepino[4,5-*g*]quinoxaline (5d)

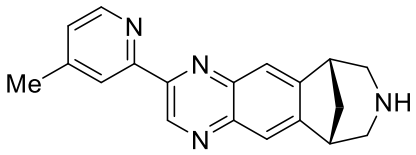


General procedure B-1 was followed using sodium 3-methylpyridine-2-sulfinate (34.1 mg, 0.190 mmol). Purification using automated preparative HPLC afforded compound **5d** as a CF_3CO_2H salt (35.6 mg, 86%).

decomp. 190 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 9.39 (s, 1H), 8.71 – 8.65 (m, 1H), 8.20 (s, 1H), 8.18 (s, 1H), 8.05 (ddd, *J* = 7.9, 1.7, 0.8 Hz, 1H), 7.61 (dd, *J* = 7.8, 4.9 Hz, 1H), 3.75 -3.71 (m,

2H), 3.59 – 3.55 (m, 2H), 3.42 – 3.38 (m, 2H), 2.70 (s, 3H), 2.62 – 2.51 (m, 1H), 2.34 (d, *J* = 11.6 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 151.8, 151.2, 146.2, 145.9, 145.5, 145.0, 141.9, 141.8, 141.6, 134.8, 128.2, 125.7, 125.0, 48.9 40.2, 38.7, 38.6, 18.6; IR υ_{max} (neat)/cm^{-1} 3400, 1673, 1473, 1198, 1132, 720, 594; HRMS (ESI) found *m*/*z* 303.1602 $[M+H]^+$, $C_{19}H_{19}N_4$ requires *m*/*z* 303.1600.

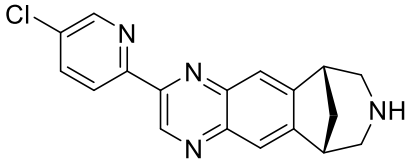
(6*S*,10*R*)-2-(4-Methylpyridin-2-yl)-7,8,9,10-tetrahydro-6*H*-6,10-methanoazepino[4,5-*g*]quinoxaline (5e)



General procedure B-1 was followed using sodium 4-methylpyridine-2-sulfinate (34.1 mg, 0.190 mmol). Purification using automated preparative HPLC afforded compound **5e** as a CF_3CO_2H salt (20.3 mg, 49%).

decomp. 179 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 9.82 (s, 1H), 8.71 (d, *J* = 5.3 Hz, 1H), 8.62 (dt, *J* = 1.7, 0.9 Hz, 1H), 8.24 (s, 1*H*), 8.17 (s, 1H), 7.67 – 7.58 (m, 1H), 3.75 – 3.71 (m, 2H), 3.60 – 3.55 (m, 2H), 3.42 – 3.39 (m, 2H), 2.65 (s, 3H), 2.56 (m, 1H), 2.34 (d, *J* = 11.6 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 153.2, 151.4, 147.5, 146.9, 146.5, 146.2, 143.1, 142.8, 142.4, 126.4, 124.2, 123.6, 123.5, 48.9, 40.1, 38.7, 38.69, 20.2; IR υ_{max} (neat)/cm^{-1} 3410, 1676, 1632, 1197, 1131, 970, 833, 720, 546; HRMS (ESI) found *m*/*z* 303.1603 $[M+H]^+$, $C_{19}H_{19}N_4$ requires *m*/*z* 303.1600.

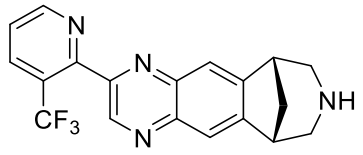
(6*S*,10*R*)-2-(5-Chloropyridin-2-yl)-7,8,9,10-tetrahydro-6*H*-6,10-methanoazepino[4,5-*g*]quinoxaline (5f)



General procedure B-1 was followed using sodium 5-chloropyridine-2-sulfinate (40.8 mg, 0.204 mmol). Purification using automated preparative HPLC afforded compound **5f** as a CF_3CO_2H salt (19.5 mg, 45%).

decomp. 232 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 9.82 (s, 1H), 8.75 (dd, J = 2.5, 0.7 Hz, 1H), 8.58 (dd, J = 8.6, 0.7 Hz, 1H), 8.15 (s, 1H), 8.10 (s, 1H), 8.05 (dd, J = 8.6, 2.5 Hz, 1H), 3.70 (dt, J = 5.4, 1.9 Hz, 2H), 3.56 (dt, J = 12.6, 1.5 Hz, 2H), 3.38 (ddd, J = 12.5, 3.2, 1.7 Hz, 2H), 2.52 (m, 1H), 2.30 (d, J = 11.6 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 152.3, 149.0, 148.0, 145.8, 145.8, 142.7, 142.7, 142.5, 137.0, 133.4, 124.1, 123.3, 122.5, 48.9, 40.1, 38.6, 38.59; IR υ_{max} (neat)/cm^{-1} 3403, 1674, 1468, 1354, 1199, 1132, 1109, 831, 580; HRMS (ESI) found m/z 323.1061 $[M+H]^+$, $C_{18}H_{16}N_4Cl$ requires m/z 323.1062.

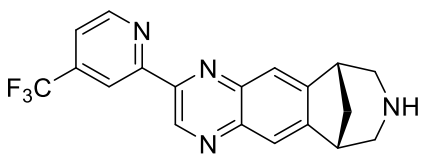
(6*S*,10*R*)-2-[3-(Trifluoromethyl)pyridin-2-yl]-7,8,9,10-tetrahydro-6*H*-6,10-methanoazepino[4,5-*g*]quinoxaline (5g)



General procedure B-1 was followed using sodium 3-trifluoromethylpyridine-2-sulfinate (44.0 mg, 0.189 mmol). Purification using automated preparative HPLC afforded compound **5g** as a CF_3CO_2H salt (43.1 mg, 93%).

decomp. 230 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 9.29 (s, 1H), 9.00 (ddd, J = 4.8, 1.5, 0.8 Hz, 1H), 8.43 (dd, J = 8.1, 1.5 Hz, 1H), 8.19 (s, 1H), 8.17 (s, 1H), 7.80 (ddd, J = 8.0, 4.8, 1.0 Hz, 1H), 3.74 – 3.70 (m, 2H), 3.63 – 3.56 (m, 2H), 3.41 – 3.37 (m, 2H), 2.62 – 2.51 (m, 1H), 2.33 (d, J = 11.6 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 153.4 (q, J = 1.7 Hz), 151.9, 151.9, 151.1, 146.4, 146.1, 144.4, 142.3, 141.7, 136.0 (q, J = 5.1 Hz), 127.4, 125.6 (q, J = 33.1 Hz), 125.0 (q, J = 273.0 Hz), 124.0, 123.4, 122.1, 48.83, 48.8, 40.2, 38.7, 38.6; ^{19}F NMR (377 MHz, CD_3OD) δ -59.13; IR υ_{max} (neat)/cm^{-1} 3403, 1673, 1461, 1233, 1170, 1135, 1071, 834, 721, 556; HRMS (ESI) found m/z 357.1323 $[M+H]^+$, $C_{19}H_{16}N_4F_3$ requires m/z 357.1318.

(6*S*,10*R*)-2-[4-(Trifluoromethyl)pyridin-2-yl]-7,8,9,10-tetrahydro-6*H*-6,10-methanoazepino[4,5-*g*]quinoxaline (5h)

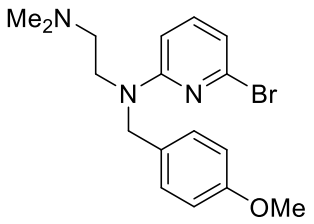


General procedure B-1 was followed using sodium 4-trifluoromethylpyridine-2-sulfinate (44.0 mg, 0.189 mmol). Purification using automated preparative HPLC afforded compound **5h** as a CF_3CO_2H salt (24.5 mg, 53%).

decomp. 249 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 9.93 (s, 1H), 9.04 (dd, J = 5.0, 0.8 Hz, 1H), 8.89 – 8.82 (m, 1H), 8.24 (s, 1H), 8.16 (s, 1H), 7.88 – 7.81 (m, 1H), 3.78 – 3.73 (m, 2H), 3.62 – 3.57 (m, 2H), 3.42 - 3.38 (m, 2H), 2.62 – 2.50 (m, 1H), 2.34 (d, J = 11.6 Hz, 1H); ^{13}C NMR (101 MHz, CD_3OD) δ 155.6, 150.8, 148.5, 146.3, 146.0, 143.1, 142.7, 142.5, 139.4 (q, J = 34.2 Hz) 124.3, 123.4, 120.1 (q, J = 3.5 Hz), 118.3 (q, J = 293.0 Hz), 116.8 (q, J = 3.8 Hz), 48.9, 40.1, 38.7, 38.6; ^{19}F NMR (377 MHz, CD_3OD) δ - 66.45; IR υ_{max} (neat)/cm^{-1} 2981, 1675, 1357, 1200, 1134, 833, 592; HRMS (ESI) found m/z 357.1324 $[M+H]^+$, $C_{19}H_{16}N_4F_3$requires m/z 357.1321.

3.8 Mepyramine Sulfinate Synthesis and Cross-Couplings

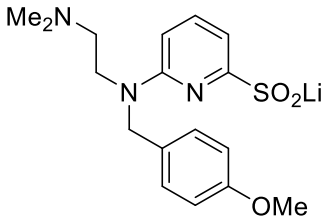
***N*^{1}-(6-Bromopyridin-2-yl)-*N*^{1}-(4-methoxybenzyl)-*N*^{2},*N*^{2}-dimethylethane-1,2-diamine**



Prepared according to US patents.[32-33] A suspension of 6-bromo-*N*-(4-methoxybenzyl)pyridin-2-amine (1.8 g, 6.2 mmol, 1.0 equiv.) and 2-chloro-*N*,*N*-dimethylethan-1-amine hydrochloride (1.1 g, 7.6 mmol, 1.2 equiv.) in toluene (28 mL) was heated at 140 °C under nitrogen flow to distill 4 mL of toluene. After cooling to room temperature, LiHMDS (1.0 M in THF, 16 mL, 16 mmol, 2.5 equiv.) was added in one portion. After heating for 16 h in at 115 °C, the reaction was allowed to cool and then quenched by the addition of sodium carbonate. Brine (16 mL) was added to the mixture and the layers were separated. The aqueous layer was extracted with EtOAc (2 x 50 mL), and the combined organic layers were dried over sodium sulfate and evaporated to afford a viscous oil. Purification by MPLC (222.0 g RediSep Gold silica column, EtOAc/heptane gradient from 0% to 30%) afforded the titled compound (1.6 g, 72%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 – 7.07 (m, 3H), 6.84 – 6.80 (m, 2H), 6.67 (dd, J = 7.4, 0.5 Hz, 1H), 6.32 (dd, J = 8.4, 0.6 Hz, 1H), 4.64 (s, 2H), 3.78 (s, 3H), 3.65 – 3.59 (m, 2H), 2.51 – 2.43 (m, 2H), 2.27 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 158.0, 140.0, 139.2, 129.9, 128.2, 114.6, 113.9, 104.0, 56.4, 55.2, 51.4, 46.4, 45.7; HRMS (ESI) found m/z 364.0946 $[M+H]^+$, $C_{17}H_{23}N_3OBr$ requires m/z 364.0946.

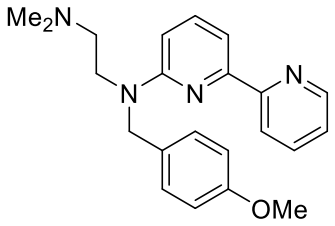
Lithium 6-{[(2-(dimethylamino)ethyl](4-methoxybenzyl)amino}pyridine-2-sulfinate (6)



To a solution of N^1-(6-bromopyridin-2-yl)-N^1-(4-methoxybenzyl)-N^2,N^2-dimethylethane-1,2-diamine (460.0 mg, 1.3 mmol, 1.0 equiv.) in THF (7.6 mL) at -78 °C, *t*BuLi (0.5 mL, 2.8 M in heptane, 1.5 mmol, 1.1 equiv.) was added dropwise. After 15 min, *TIMSO* (0.3 mL, 1.9 mmol, 1.5 equiv.) was added slowly and the mixture was allowed to stir for additional 15 minutes at the same temperature. Addition of heptane (1.5 mL) caused precipitation of white solid which was isolated by vacuum filtration and washed with 2-methyltetrahydrofuran (3 x 2.0 mL). The crude material was evaporated from EtOH and MeCN (2 x). Purification by reverse-phase chromatography, eluting an unmodified MeCN/H_2O gradient afforded compound **6** (321.0 mg, 71%) as a white solid.

Decomp. 180 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 7.63 (dd, J = 8.5, 7.2 Hz, 1H), 7.18 – 7.14 (m, 2H), 6.98 (dd, J = 7.2, 0.7 Hz, 1H), 6.89 – 6.83 (m, 2H), 6.81 (d, J = 8.2 Hz, 1H), 4.66 (s, 2H), 3.92 – 3.84 (m, 2H), 3.76 (s, 3H), 3.26 – 3.18 (t, J = 7.1 Hz, 2H), 2.86 (s, 6H); ^{13}C NMR (101 MHz, CD_3OD) δ 169.3, 159.2, 158.1, 139.1, 129.0, 127.7, 113.8, 109.9, 108.3, 59.8, 54.2, 53.1, 45.8, 43.1; IR υ_{max} (neat)/cm^{-1} 3385, 1591, 1511, 1495, 1247, 1029, 968, 791; HRMS (ESI) found m/z 350.1519 $[M+H]^+$, $C_{17}H_{23}N_3O_3S$ requires m/z 350.1518.

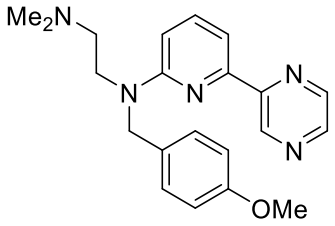
N^1-([2,2'-Bipyridin]-6-yl)-N1-(4-methoxybenzyl)-N^2,N^2-dimethylethane-1,2-diamine (6a)



General procedure B-2a was followed using 2-bromopyridine (45.3 mg). Purification using automated preparative HPLC afforded compound **6a** as a CF_3CO_2H salt (23.2 mg, 58%).

^{1}H NMR (400 MHz, CD_3OD) δ 8.82 (ddd, J = 5.1, 1.7, 0.9 Hz, 1H), 8.27 (dt, J = 8.1, 1.0 Hz, 1H), 8.13 (td, J = 7.8, 1.7 Hz, 1H), 7.73 (dd, J = 8.6, 7.5 Hz, 1H), 7.62 (ddd, J = 7.6, 5.1, 1.1 Hz, 1H), 7.53 (d, J = 7.4 Hz, 1H), 7.21 – 7.18 (m, 1H), 6.91 (dd, J = 8.7, 5.4 Hz, 3H), 4.74 (s, 2H), 4.02 (m, 2H), 3.77 (s, 3H), 3.43 – 3.37 (m, 2H), 2.97 (s, 6H); ^{13}C NMR (101 MHz, CD_3OD) δ 159.2, 158.3, 154.0, 150.9, 147.6, 139.8, 139.2, 128.9, 127.7, 124.4, 122.3, 113.9, 111.2, 109.1, 58.8, 54.3, 52.9, 45.1, 42.8; IR υ_{max} (neat)/cm^{-1} 1676, 1598, 1513, 1479, 1249, 1198, 1176, 1131, 813, 720; HRMS (ESI) found m/z 363.2165 $[M+H]^+$, $C_{22}H_{27}N_4O$ requires m/z 363.2169.

N^1-(4-Methoxybenzyl)-N^2,N^2-dimethyl-N1-[6-(pyrazin-2-yl)pyridin-2-yl]ethane-1,2-diamine (6b)

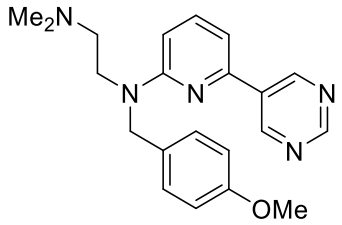


General procedure B-2a was followed using 2-bromopyrazine (19.7 mg). Purification using automated preparative HPLC afforded compound **6b** as a CF_3CO_2H salt (21.1 mg, 53%).

^{1}H NMR (400 MHz, CD_3OD) δ 9.42 (d, J = 1.5 Hz, 1H), 8.83 (dd, J = 2.6, 1.5 Hz, 1H), 8.70 (d, J = 2.5 Hz, 1H), 7.77 (dd, J = 8.6, 7.5 Hz, 1H), 7.65 (dd, J = 7.5, 0.7 Hz, 1H), 7.23 – 7.20 (m, 2H), 6.97 (d, J = 8.6, 1H), 6.93 – 6.88 (m, 2H), 4.77 (s, 2H), 4.08 – 3.98 (m, 2H), 3.79 (s, 3H), 3.49 – 3.43 (m, 2H), 3.02 (s, 6H); ^{13}C NMR (101 MHz, CD_3OD) δ 159.3, 158.6, 151.1, 150.5, 144.2, 144.1, 143.0, 139.2, 128.8, 127.7, 113.9, 111.4, 109.4, 59.1, 54.3, 52.9, 45.3, 42.9; IR υ_{max}

(neat)/cm^{-1} 1677, 1603, 1512, 1410, 1199, 1176, 1134, 1018, 796, 613; HRMS (ESI) found *m*/*z* 364.2106 $[M+H]^+$, $C_{21}H_{26}N_5O$ requires *m*/*z* 364.2101.

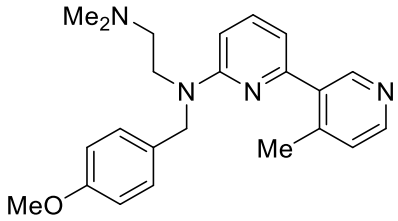
N^1-(4-Methoxybenzyl)-N^2,N^2-dimethyl-N^1-[6-(pyrimidin-5-yl)pyridin-2-yl]ethane-1,2-diamine (6c)



General procedure B-2b was followed using 5-bromopyrimidine (13.2 mg, 0.0830 mmol). Purification using automated preparative HPLC afforded compound **6c** as a CF_3CO_2H salt (4.3 mg, 11%).

^{1}H NMR (400 MHz, CD_3OD) δ 9.40 (s, 2H), 9.20 (s, 1H), 7.69 (dd, *J* = 8.6, 7.4 Hz, 1H), 7.34 (d, *J* = 7.4 Hz, 1H), 7.22 – 7.20 (m, 2H), 6.92 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 1H), 4.78 (s, 2H), 4.21 (t, *J* = 6.9 Hz, 2H), 3.79 (s, 3H), 3.48 (t, *J* = 6.9 Hz, 2H), 2.98 (s, 6H); ^{13}C NMR (101 MHz, CD_3OD) δ 159.2, 158.1, 157.4, 154.8, 149.4, 138.8, 133.2, 128.9, 127.6, 113.9, 110.1, 107.6, 55.0, 54.3, 51.1, 43.1, 42.7; IR υ_{max} (neat)/cm^{-1} 3421, 1676, 1599, 1512, 1417, 1248, 1201, 1174, 1131, 832, 720, 532; HRMS (ESI) found *m*/*z* 393.2276 $[M+H]^+$, $C_{21}H_{26}N_5O$ requires *m*/*z* 393.2285.

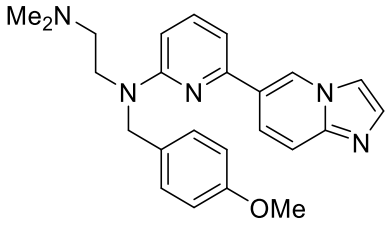
N^1-(4-Methoxybenzyl)-N^2,N^2-dimethyl-N1-(4'-methyl-[2,3'-bipyridin]-6-yl)ethane-1,2-diamine (6d)



General procedure B-2a was followed using 3-bromo-4-methylpyridine (25.0 mg). Purification using automated preparative HPLC afforded compound **6d** as a CF_3CO_2H salt (33.7 mg, 84%).

^{1}H NMR (400 MHz, CD_3OD) δ 8.71 (s, 1H), 8.58 (d, J = 5.5 Hz, 1H), 7.78 (dd, J = 8.6, 7.4 Hz, 1H), 7.68 (d, J = 5.5 Hz, 1H), 7.22 (d, J = 8.6 Hz, 2H), 7.02 – 6.91 (m, 3H), 6.87 (dd, J = 8.7, 0.6 Hz, 1H), 4.77 (s, 2H), 4.07 (t, J = 6.4 Hz, 2H), 3.80 (s, 3H), 3.38 (t, J = 6.4 Hz, 2H), 2.84 (s, 6H), 2.58 (s, 3H); ^{13}C NMR (101 MHz, CD_3OD) δ 159.2, 158.1, 152.2, 150.5, 145.8, 144.7, 138.5, 138.1, 128.7, 127.6, 126.9, 113.9, 113.7, 106.8, 56.0, 54.3, 51.3, 43.6, 42.5, 19.1; IR υ_{max} (neat)/cm^{-1} 1672, 1593, 1566, 1455, 1246, 1197, 1171, 1124, 1030, 796, 738; HRMS (ESI) found m/z 376.2263 $[M+H]^+$, $C_{23}H_{29}N_4O$ requires m/z 376.2262.

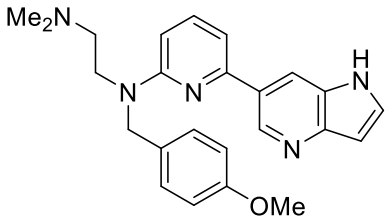
N^1-(6-(Imidazo[1,2-*a*]pyridin-6-yl)pyridin-2-yl)-N^1-(4-methoxybenzyl)-N^2,N^2-dimethylethane-1,2-diamine (6e)



General procedure B-2b was followed using 6-bromoimidazo[1,2-*a*]pyridine (16.4 mg, 0.0832 mmol). Purification using automated preparative HPLC afforded compound **6e** as a CF_3CO_2H salt (25.0 mg, 48%).

mp 114-123 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 9.48 (dd, J = 1.6, 1.0 Hz, 1H), 8.65 (dd, J = 9.5, 1.6 Hz, 1H), 8.33 (dd, J = 2.2, 0.8 Hz, 1H), 8.09 (d, J = 2.2 Hz, 1H), 8.03 (d, J = 9.5 Hz, 1H), 7.71 (dd, J = 8.6, 7.5 Hz, 1H), 7.36 (d, J = 7.4 Hz, 1H), 7.23 – 7.20 (m, 2H), 6.92 – 6.88 (m, 2H), 6.85 (d, J = 8.6 Hz, 1H), 4.81 (s, 2H), 4.23 (t, J = 7.0 Hz, 2H), 3.78 (s, 3H), 3.48 (t, J = 7.0 Hz, 2H), 2.97 (s, 6H); ^{13}C NMR (101 MHz, CD_3OD) δ 159.2, 157.9, 149.5, 139.8, 138.9, 132.6, 130.4, 129.1, 127.7, 126.8, 122.8, 115.9, 113.8, 111.4, 109.8, 107.5, 54.8, 54.3, 51.1, 43.0, 42.7; IR υ_{max} (neat)/cm^{-1} 1671, 1567, 1488, 1241, 1197, 1175, 1130, 1031, 830, 720; HRMS (ESI) found m/z 402.2258 $[M+H]^+$, $C_{24}H_{28}N_5O$ requires m/z 402.2255.

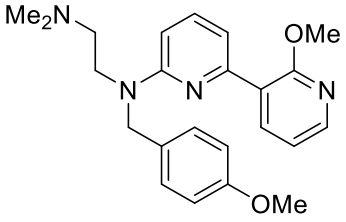
N^1-[6-(1*H*-Pyrrolo[3,2-*b*]pyridin-6-yl)pyridin-2-yl]-N^1-(4-methoxybenzyl)-N^2,N^2-dimethylethane-1,2-diamine (6f)



General procedure B-2b was followed using 6-bromo-1*H*-pyrrolo[3,2-*b*]pyridine (12.1 mg, 0.0614 mmol). Purification using automated preparative HPLC afforded compound **6f** as a CF_3CO_2H salt (12.7 mg, 33%).

mp 167-169 °C; ^{1}H NMR (400 MHz, CD_3OD) δ 9.29 (d, J = 1.6 Hz, 1H), 9.14 (t, J = 1.2 Hz, 1H), 8.18 (d, J = 3.2 Hz, 1H), 7.72 (dd, J = 8.6, 7.5 Hz, 1H), 7.42 (d, J = 7.5 Hz, 1H), 7.24 (m, 2H), 6.97 – 6.91 (m, 3H), 6.85 (d, J = 8.6 Hz, 1H), 4.83 (s, 2H), 4.23 (t, J = 7.1 Hz, 2H), 3.79 (s, 3H), 3.55 – 3.44 (m, 2H), 2.98 (s, 6H); ^{13}C NMR (101 MHz, CD_3OD) δ 159.2, 157.9, 150.2, 139.0, 137.2, 136.0, 133.5, 132.7, 129.6, 129.1, 127.7, 124.5, 113.9, 109.5, 107.1, 96.4, 54.7, 54.3, 51.1, 43.1, 42.7; IR υ_{max} (neat)/cm^{-1} 3087, 1673, 1612, 1512, 1357, 1200, 1131, 1032, 834, 575; HRMS (ESI) found m/z 402.2258 $[M+H]^+$, $C_{24}H_{28}N_5O$ requires m/z 402.2215.

N^1-(2'-Methoxy-[2,3'-bipyridin]-6-yl)-N^1-(4-methoxybenzyl)-N^2,N^2-dimethylethane-1,2-diamine (6g)



General procedure B-2a was followed using 3-bromo-2-methoxypyridine (34.7 mg). Purification using automated preparative HPLC afforded compound **6g** as a CF_3CO_2H salt (38.4 mg, 90%).

^{1}H NMR (400 MHz, CD_3OD) δ 8.20 (dd, J = 5.0, 1.9 Hz, 1H), 8.10 (dd, J = 7.4, 1.9 Hz, 1H), 7.61 (dd, J = 8.6, 7.5 Hz, 1H), 7.23 – 7.18 (m, 3H), 7.10 (dd, J = 7.4, 5.0 Hz, 1H), 6.90 (m, 2H), 6.78 – 6.73 (m, 1H), 4.71 (s, 2H), 4.05 (t, J = 6.0 Hz, 2H), 3.97 (s, 3H), 3.76 (s, 3H), 3.37 (t, J =

6.0 Hz, 2H), 2.82 (s, 6H); ^{13}C NMR (101 MHz, CD_3OD) δ 160.9, 159.2, 157.7, 151.5, 146.6, 138.9, 138.5, 128.8, 127.7, 123.0, 117.0, 114.0, 113.9, 106.5, 56.9, 54.3, 52.7, 51.7, 44.0, 42.7; IR υ_{max} (neat)/cm^{-1} 1675, 1594, 1465, 1397, 1247, 1199, 1135, 1015, 788, 608; HRMS (ESI) found *m*/*z* 393.2276 $[M+H]^+$, $C_{23}H_{29}N_4O_2$ requires *m*/*z* 393.2285.

4. References

1. J. M. Baskin, Z. Wang *Tetrahedron Lett*. **2002**, *43*, 8479.

2. T. Kaniyama, S. Enomoto, M. Inoue *Chem. Pharm. Bull*. **1988**, *36*, 2653.

3. N. Kudo, M. Perseghini, G. C. Fu *Angew. Chem. Int. Ed*. **2006**, *45*, 1282.

4. C. Liu, Q. Ni, F. Bao, J. Qiu *Green Chem.* **2011**, *13*, 1260.

5. J. L. Bolliger, C. M. Frech *Chem. Eur. J.* **2010**, *16*, 110702.

6. T. Abe, T. Mino, K. Watanabe, F. Yagishita, M. Sakamoto *Eur. J. Org. Chem*. **2014**, 3909.

7. D. J. Augeri, S. A. Baumeister, M. Bruncko, D. A. Dickman, H. Ding, J. Dinges, S. W. Fesik, P. J. Hajduk, A. R. Kunzer, W. McClellan, D. G Nettesheim, T. Oost, A. M Petros, S. H. Rosenberg, W. Shen, S. A. Thomas, X. Wang, M. D. Wendt *US Pat.*, US2002/55631 A1 **2002**.

8. Z Liu, Y. Yao, M. Kogiso, B. Zheng, L. Deng, J. J. Qiu, S. D., Hua Lv, J. M. Gallo, X. Li, Y. Song *J. Med. Chem*. **2014**, *57*, 8307.

9. L. Y. Liao, K. M. Liu, X. F. Duan *J. Org. Chem*. **2015**, *80*, 9856.

10. P. R. Parry, C. Wang, A. S. Batsanov, M. R. Bryce, B. Tarbit *J. Org. Chem*. **2002**, *67*, 7541.

11. C. Liu, N. Han, X. Song, J. Qiu *Eur. J. Org. Chem*. **2010**, 5548.

12. A. Gavryushin, C. Konfik, G. Manolikakes, P. Knochel *Org. Lett*. **2005**, *7*, 4871.

13. F. Beaumard, G. A. Molander *Org. Lett*. **2010**, *12*, 4022.

14. G-J. Chen, F-S. Han *Eur. J. Org. Chem*. **2012**, 3575.

15. Z. Xi, B. Liu, W. Chen *J. Org. Chem*. **2008**, *73*, 3954.

16. Y. Yuen, S. M. Wong, K. F. Chan, C. M. So, F. Y. Kwong *Synthesis* **2014**, *46*, 2826.

17. M. L. N. Rao, R. J. Dhanorkar *Eur. J. Org. Chem*. **2014**, 5214.

18. J. K. Laha, K. P. Jethava, S. Patel *Org. Lett*. **2015**, *17*, 5890.

19. N. A. Isley, F. Gallou, B. H. Lipshutz *J. Am. Chem. Soc*. **2013**, *135*, 17707.

20. S.Brumfield, J. J. Matasi, D. Tulshia, M. Czarniecki, W. Greenlee, C. Garlisi, H. Qiu, K. Devit, S.-C. Chen., Y. Sun, R. Bertorelli, J. Ansell, W. Geiss, Van-Duc Le, G. S. Martin, S. A. Vellekoop, J. Haber, M. L. Allard *Bioorg. Med. Chem. Lett*. **2011**, *21*, 7287.

21. J-J. Dai, C. Fang, B. Xiao, J. Yi, J. Xu, Z-J. Liu, X. Lu, L. Liu, Y. Fu *J. Am. Chem. Soc.* **2013**, *135*, 8436.

22. C. A. Blum, X. Zheng, H. Brielmann, K. J. Hodgetts, R. Bakthavatchalam, J. Chandrasekhar, J. E. Krause, D. Cortright, D. Matson, M. Crandall, C. K. Ngo, L. Fung, M. Day, M. Kershaw, S. De Lombaert , B. L. Chenard *Bioorg. Med. Chem. Lett*. **2008**, *18*, 4573.

23. I. Sasaki, L. Vendier, A. Sournia-Saquet, P. G. Lacroix *Eur. J. Inorg. Chem*. **2006**, 3294.

24. A. Deb, S. Manna, A. Maji, U. Dutta, D. Maiti *Eur. J. Org. Chem*. **2013**, 5251.

25. J. Park, S. Chang *Angew. Chem. Int. Ed*. **2015**, *54*, 14103.

26. O. Navarro, N. Marion, J. Mei, S. P. Nolan *Chem. Eur. J.* **2006**, *12*. 5142.

27. L-C. Campeau, S. Rosseaux, K. Fagnou *J. Am. Chem. Soc*. **2005**, *127*, 18020.

28. G. R. Dick, E. M. Woerly, M. D. Burke *Angew. Chem. Int. Ed*. **2012**, *51*, 2667.

29. S. Wübbolt, M. Oestreich *Angew. Chem. Int. Ed*. **2015**, *54*, 15876.

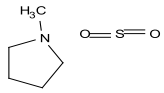
30. D. Channe, S. Abiraj *Synlett* **2004**, *5*, 877.

31. Pfizer Products Inc. WO2006/90236 A1, **2006**.

32. B. C. Askew, M. J. Breslin, M. E. Duggan, J. H. Hutchinson, R. S. Meissner, J. J. Perkins, T. G. Steele, M. A. Patane US2001/53853 A1, **2001**.

33. Merck and Co., Inc. US6410526 B1, **2002**.

5. Spectra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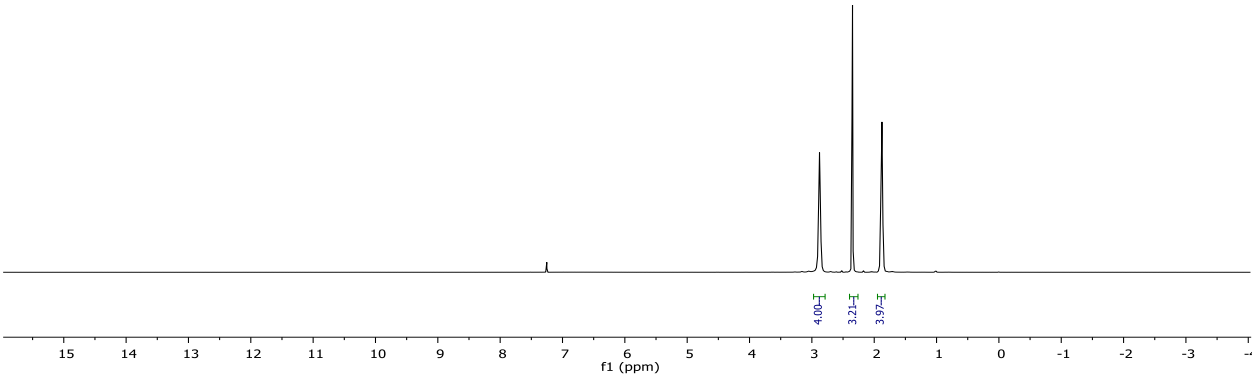
N
O
S
O


4.00
3.21
3.97
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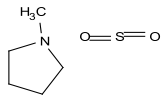
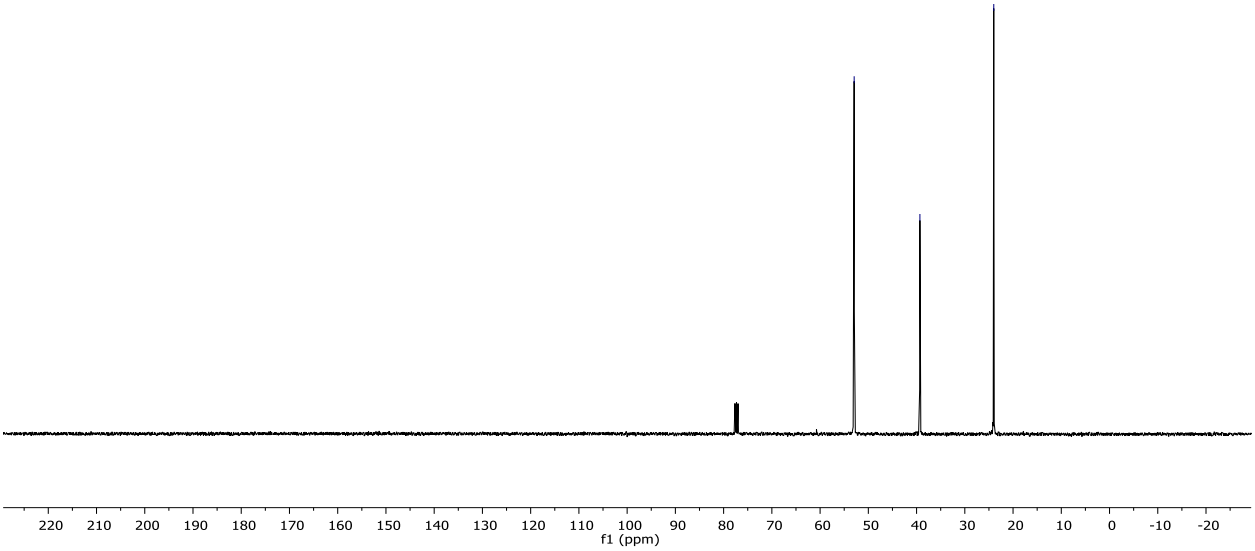
f1 (ppm)


H3C
N
O
S
O


52.94
39.31
24.00
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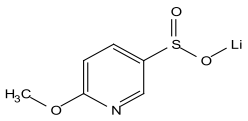
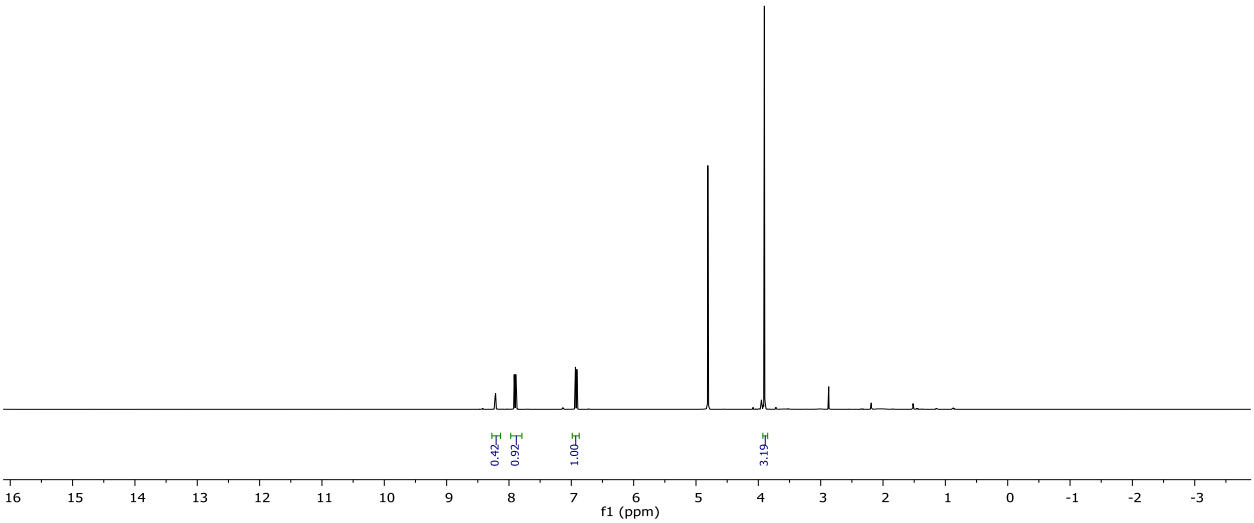
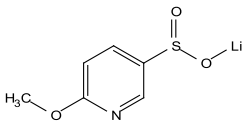
f1 (ppm)


O
S
Li
O
H_3C
O
N


0.42
0.92
1.00
3.19
16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
f1 (ppm)


O
S
Li
O
H_3C
O
N

164.92
143.09
142.84
135.67
111.04
54.30
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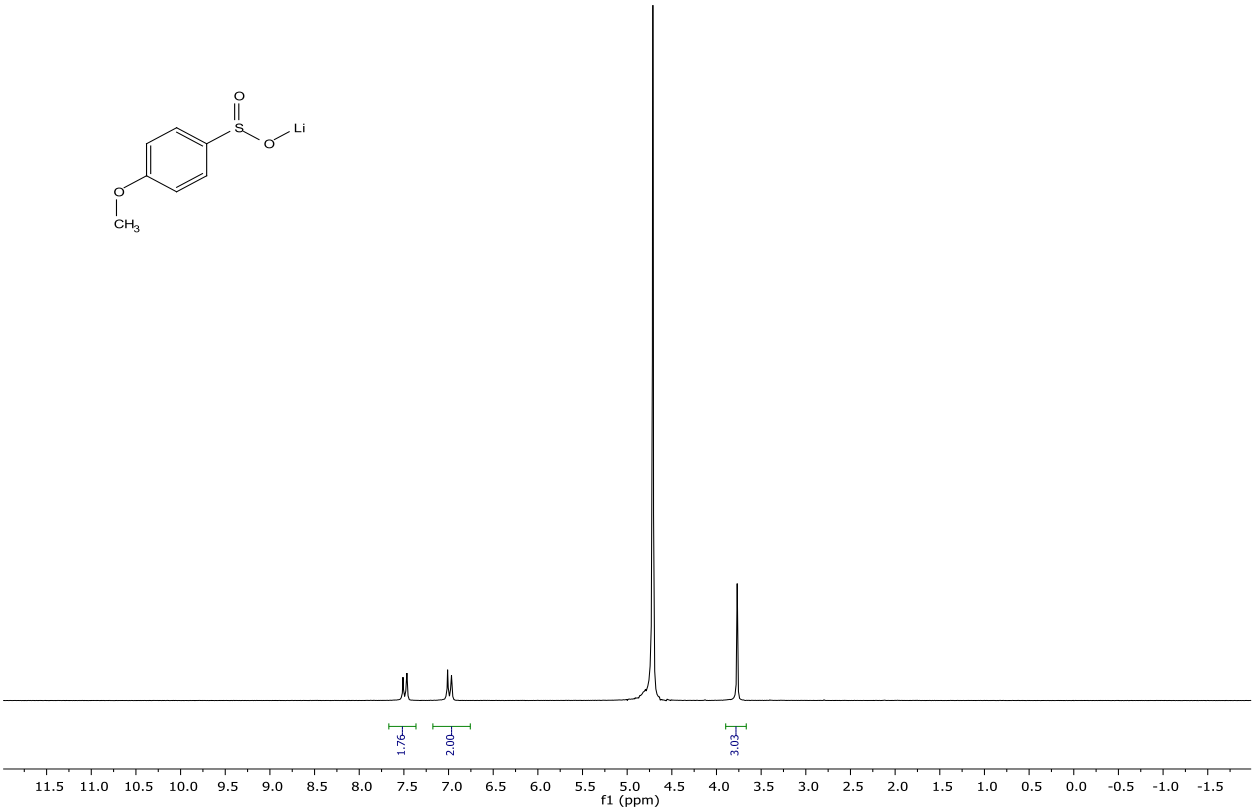
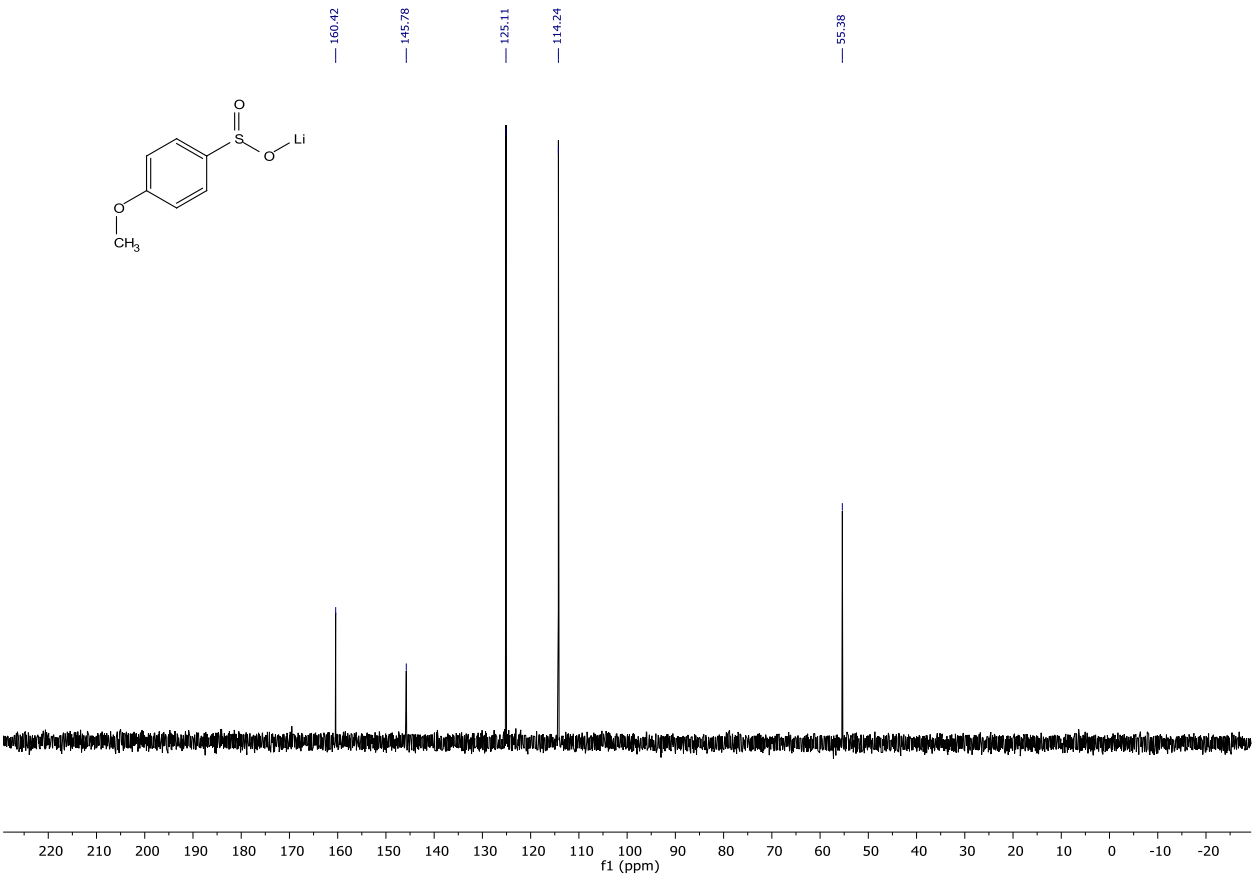
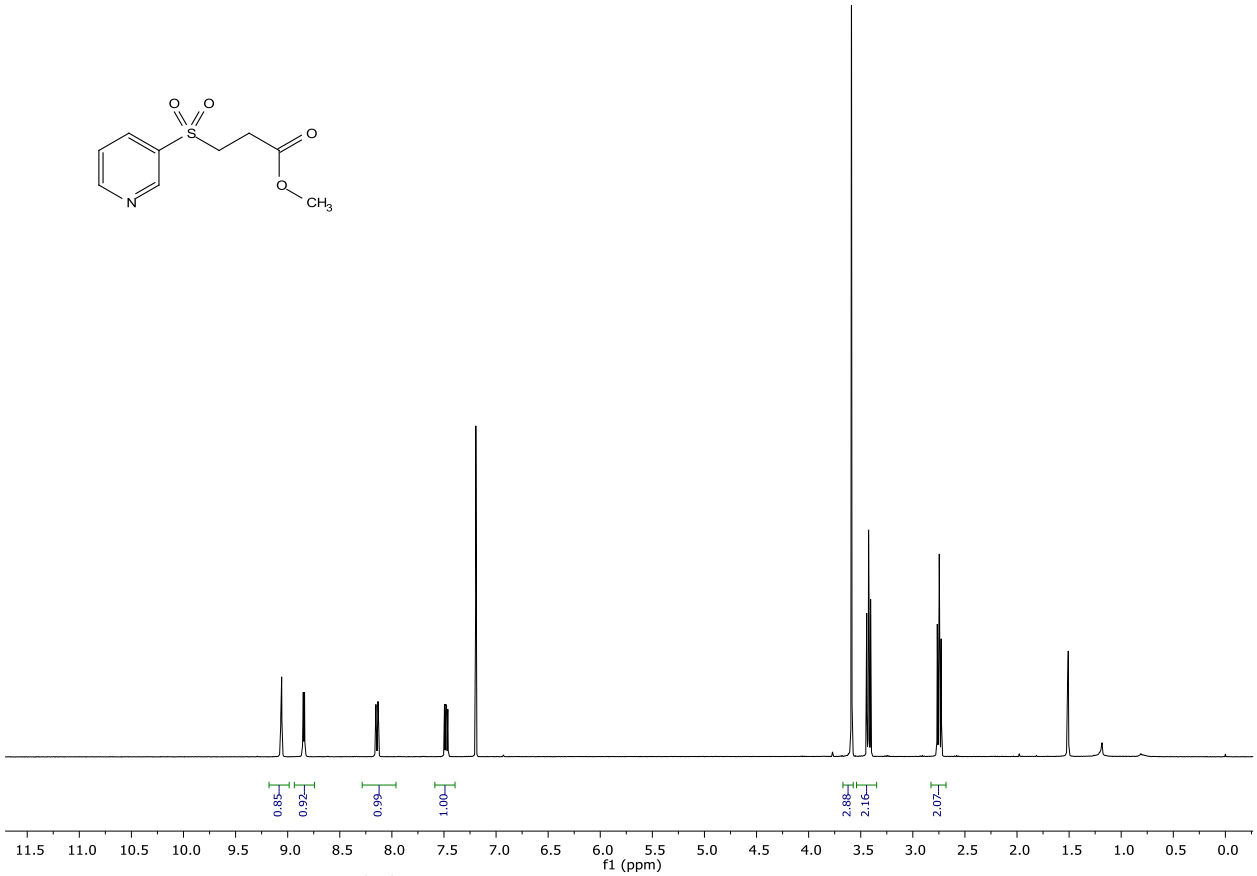
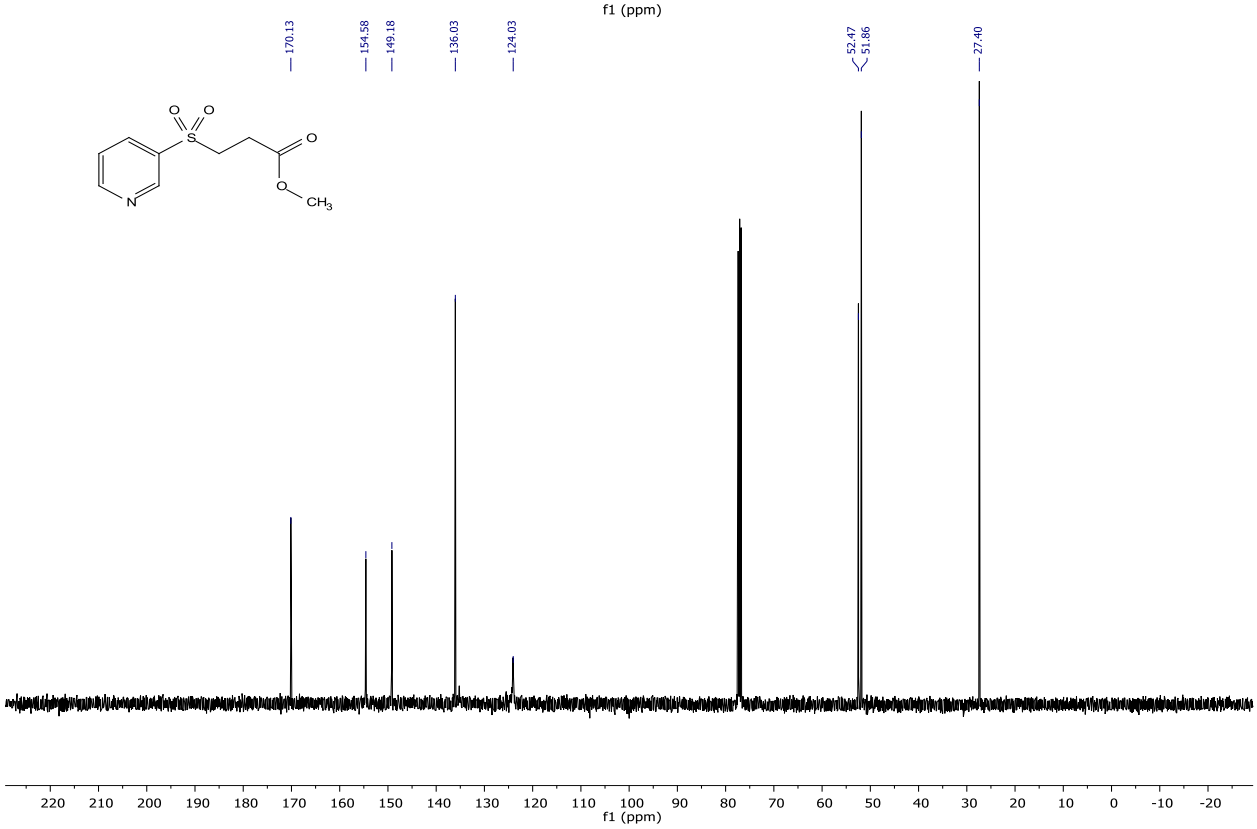
f1 (ppm)


O
S
O
Li
O
CH3
1.76
2.00
3.03
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)


160.42
145.78
125.11
114.24
55.38
O
S
O
Li
O
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


0.85
0.92
0.99
1.00
2.88
2.16
2.07
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


170.13
154.58
149.18
136.03
124.03
52.47
51.86
27.40
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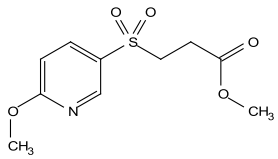
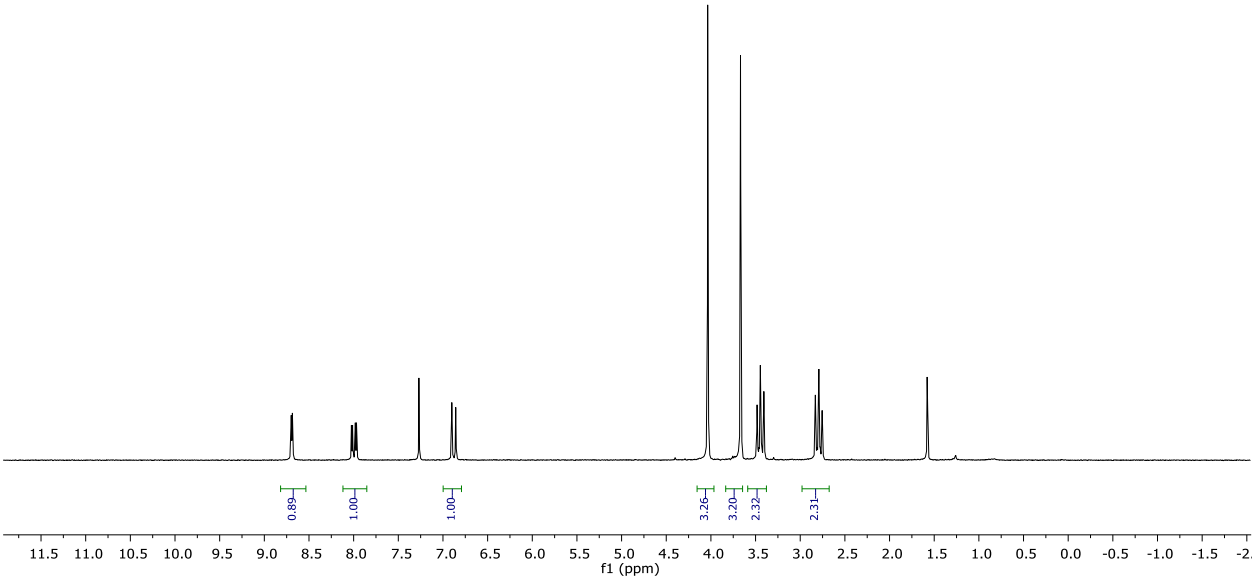
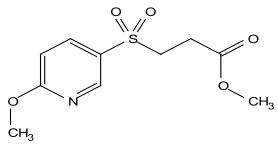
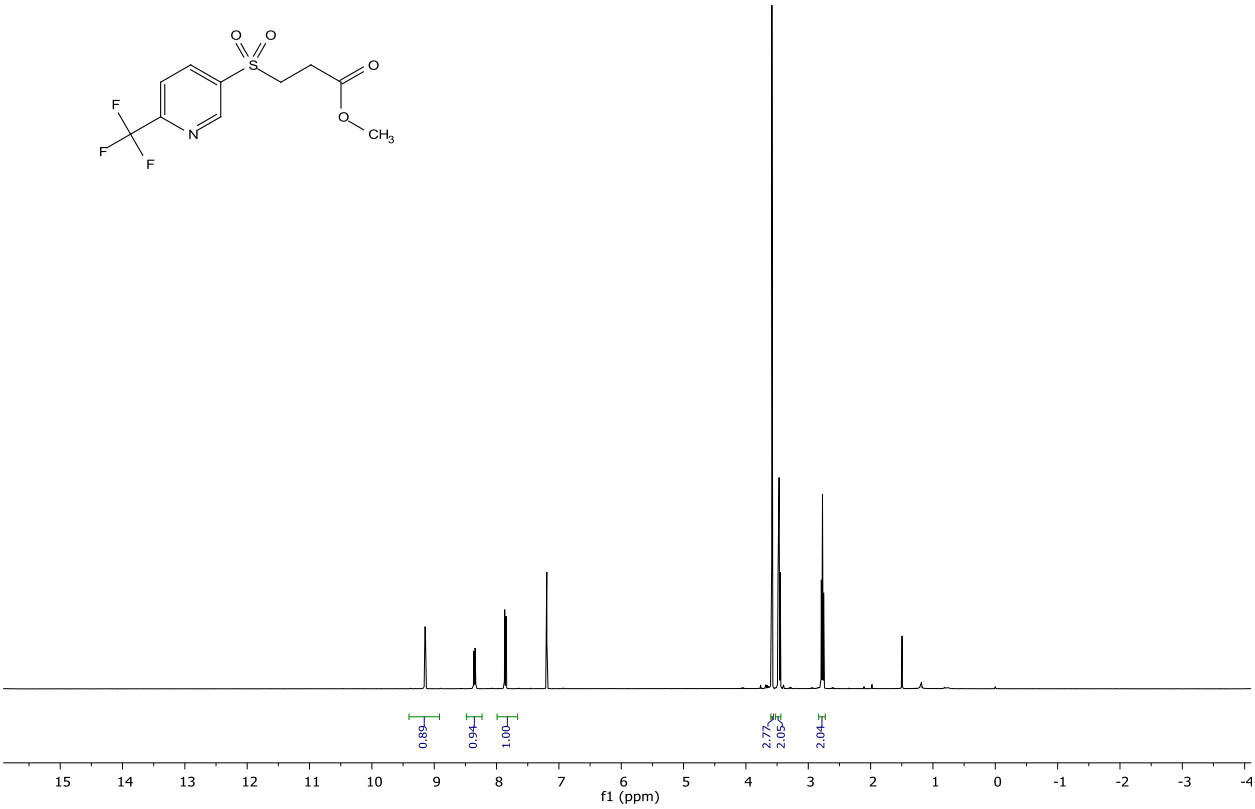
f1 (ppm)

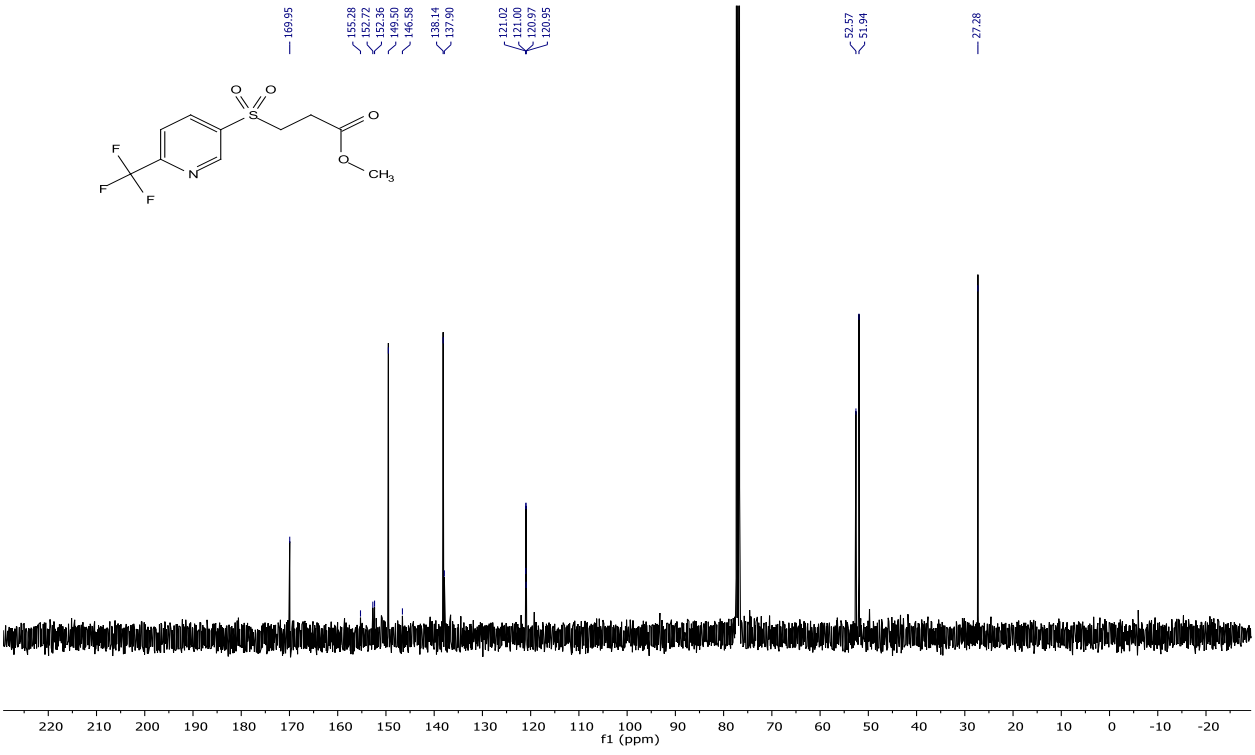

O
O
S
O
O
CH3
N
O
CH3

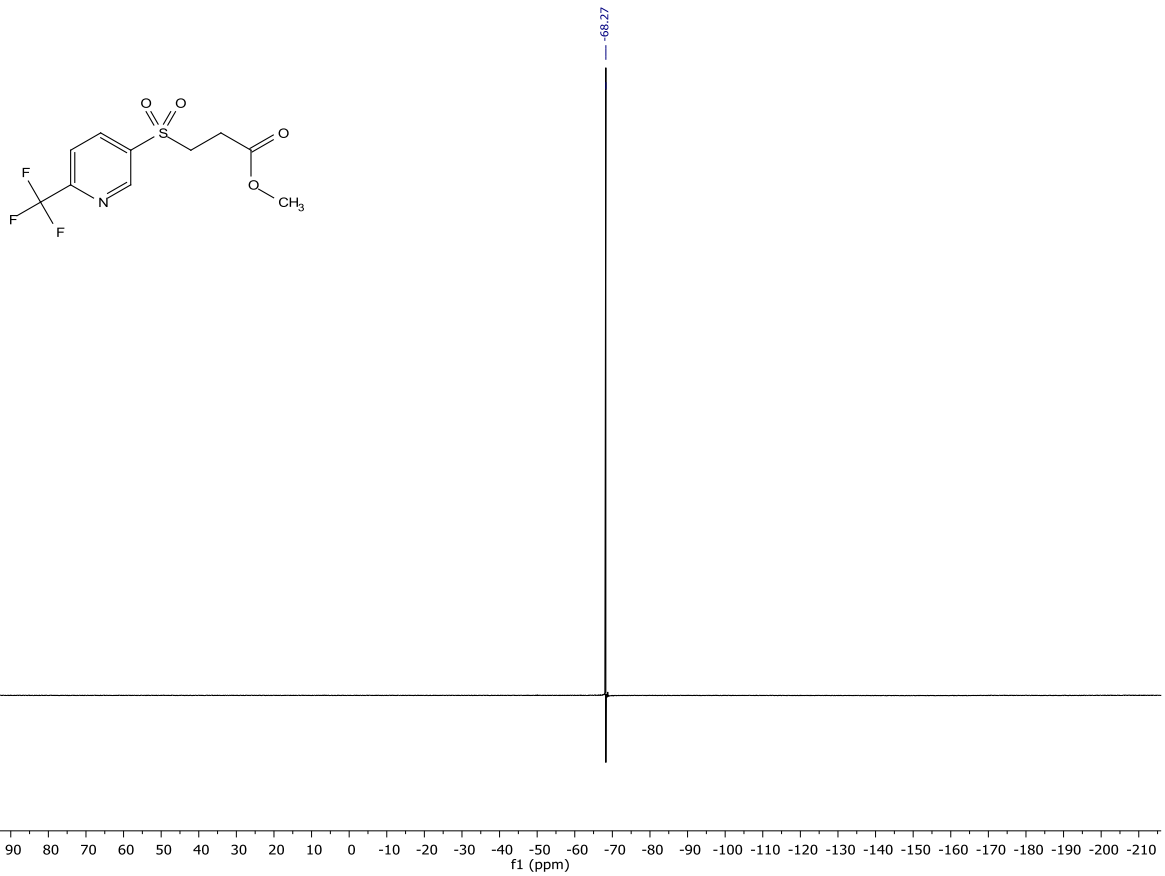

0.89
1.00
1.00
3.26
3.20
2.32
2.31
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)


O
O
S
O
O
CH3
N
O
CH3

220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


O
O
S
O
F
F
F
N
O
CH3
0.89
0.94
1.00
2.77
2.05
2.04
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


169.95
155.28
152.72
152.36
149.50
146.58
138.14
137.90
121.02
121.00
120.97
120.95
52.57
51.94
27.28
O
O
S
O
F
F
F
N
O
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


-68.27
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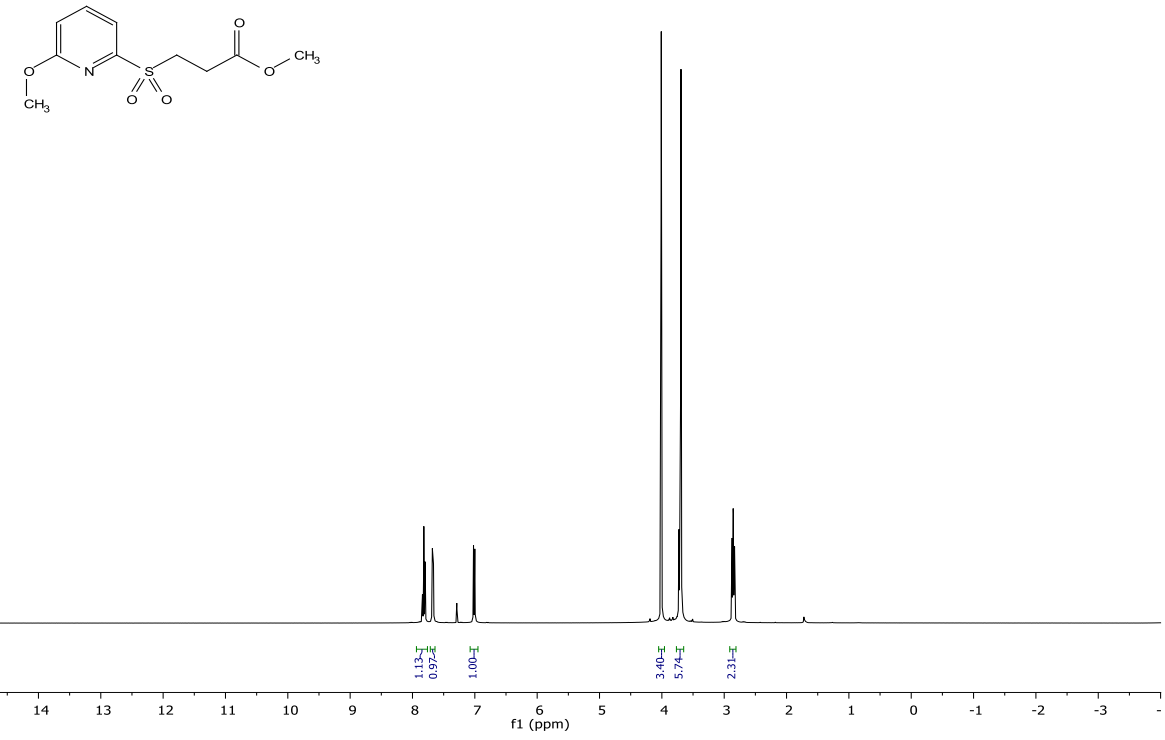
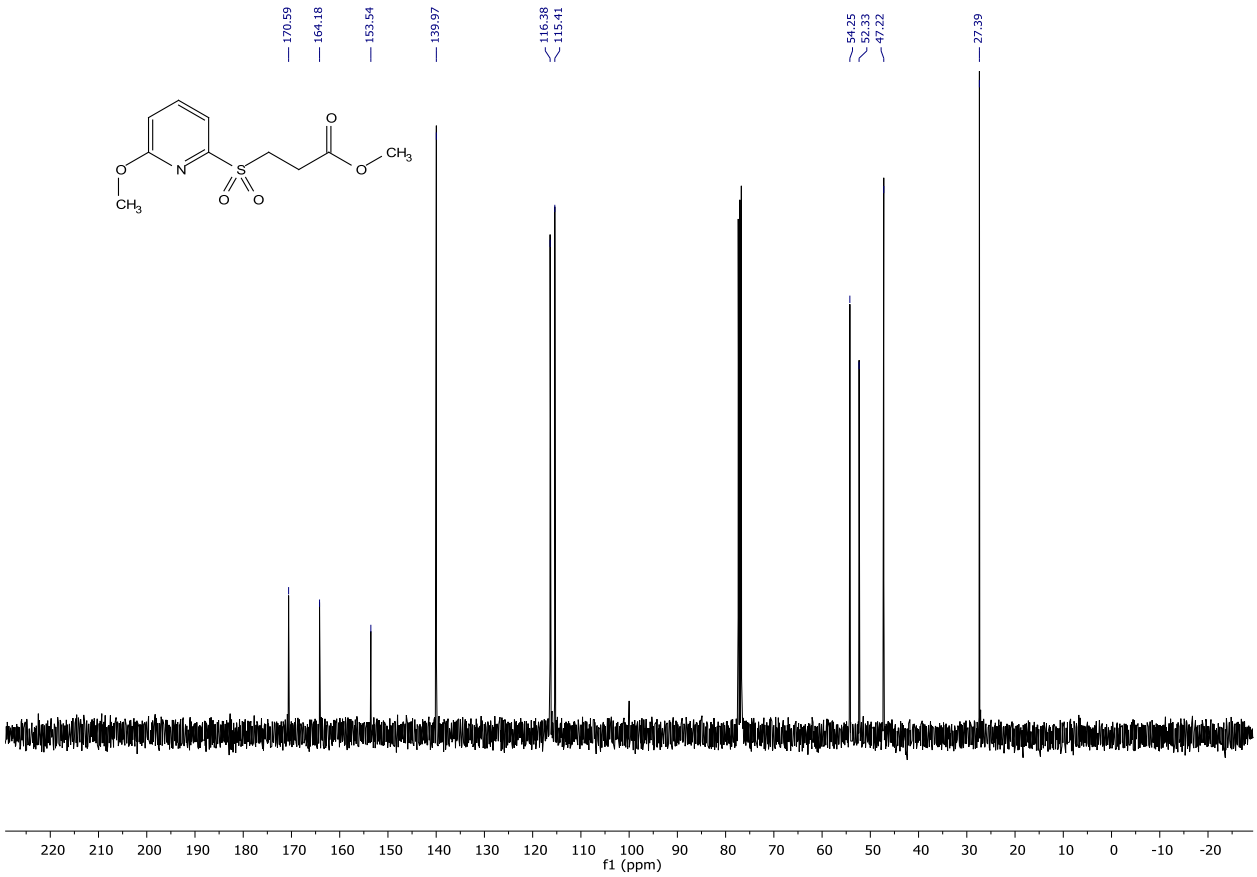
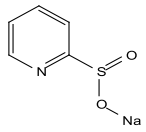
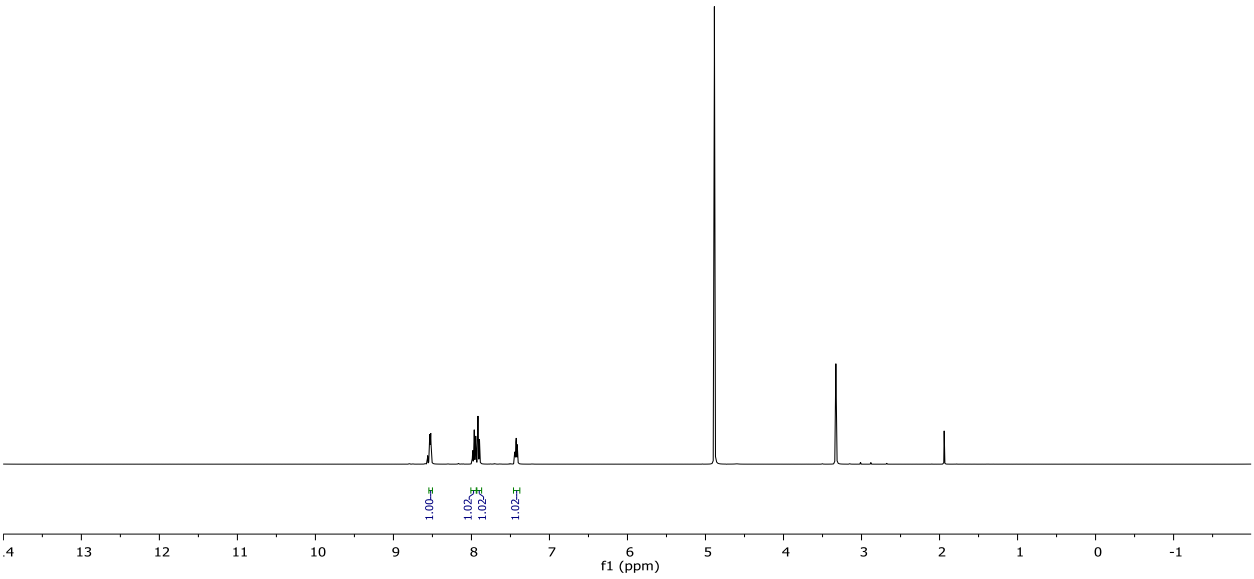
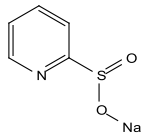

1.13
0.97
1.00
3.40
5.74
2.31
f1 (ppm)

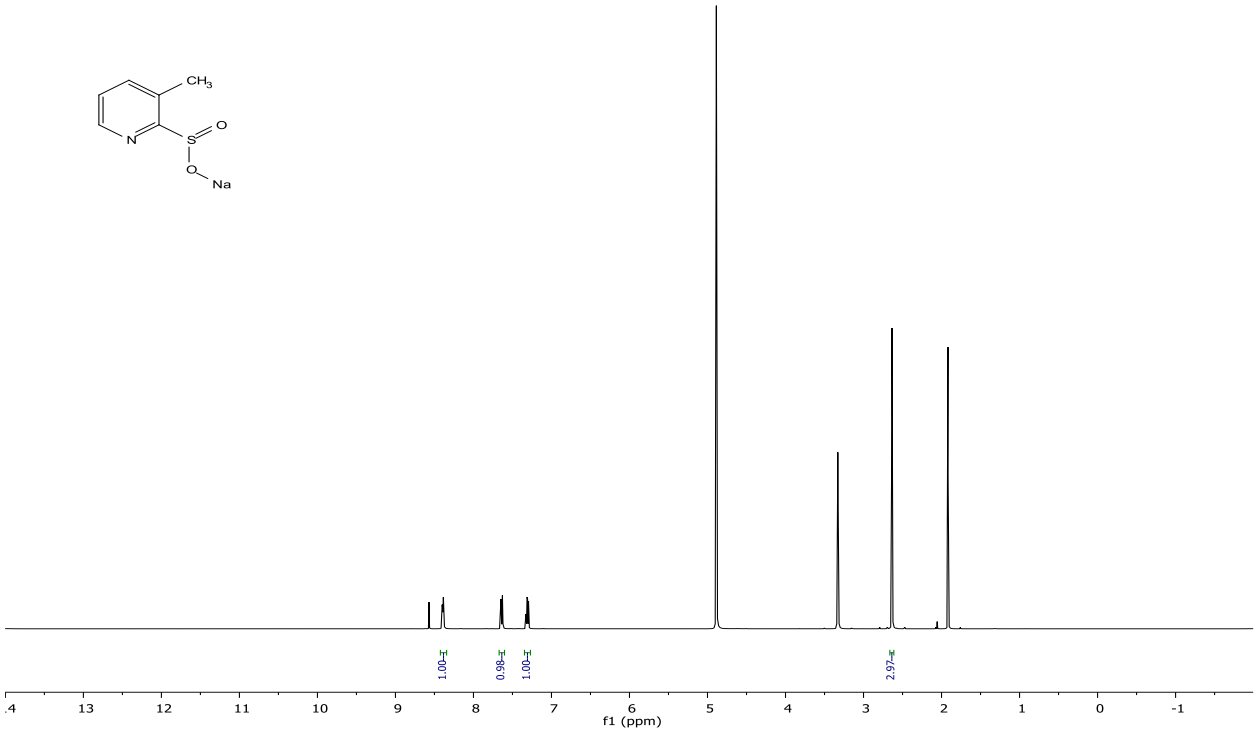

170.59
164.18
153.54
139.97
116.38
115.41
54.25
52.33
47.22
27.39
O
O
CH3
O
N
S
O
O
O
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


N
S
O
O
Na


1.00
1.02
1.02
1.02
f1 (ppm)


N
S
O
O
Na

173.16
147.97
138.00
124.30
117.42
f1 (ppm)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S
O
O
Na
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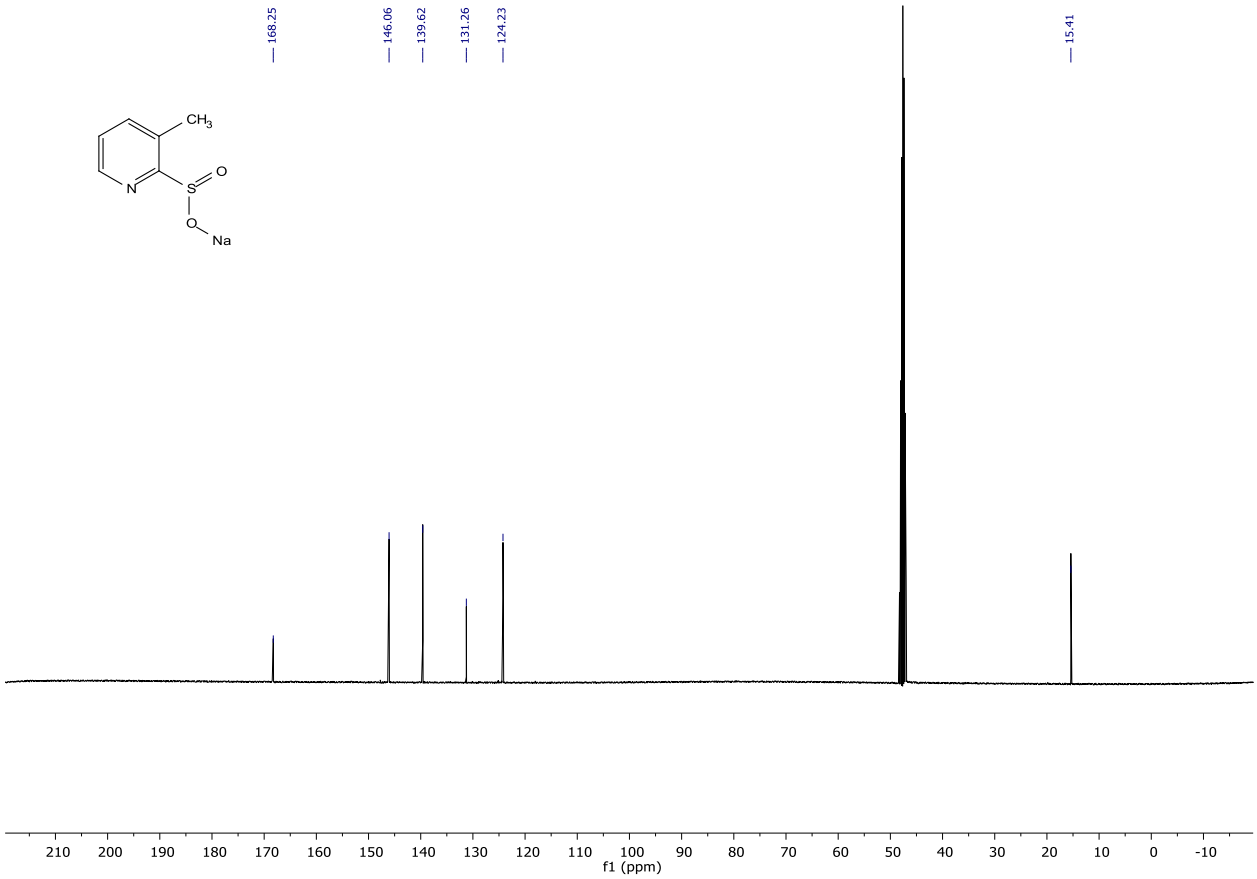
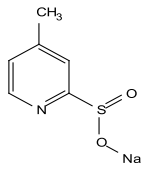
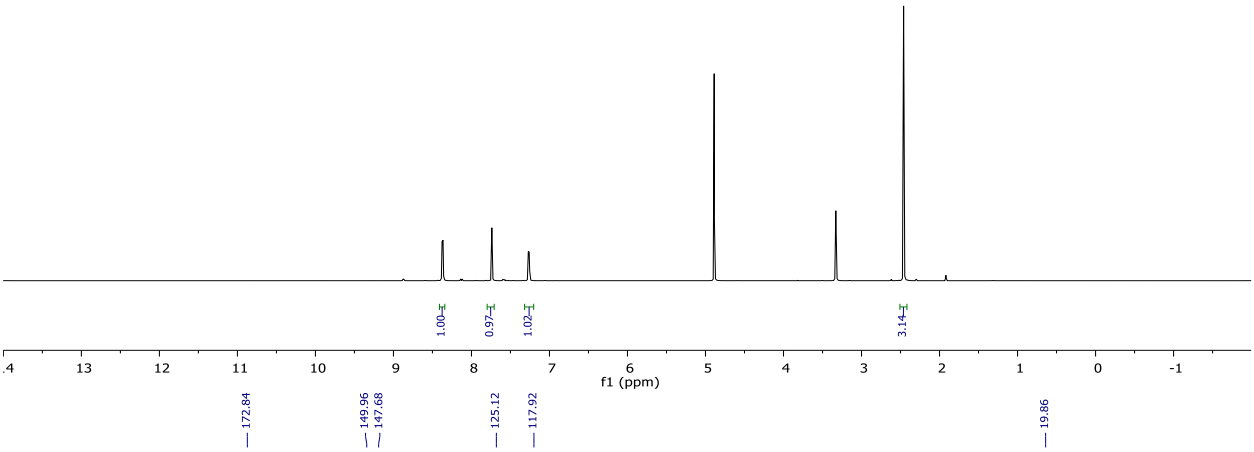
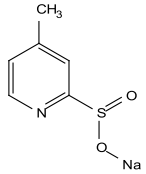
0.98
1.00
2.97
f1 (ppm)

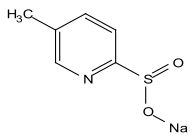

168.25
146.06
139.62
131.26
124.23
15.41
CH3
N
S
O
O
Na
f1 (ppm)





172.84
149.96
147.68
125.12
117.92
19.86




H3C
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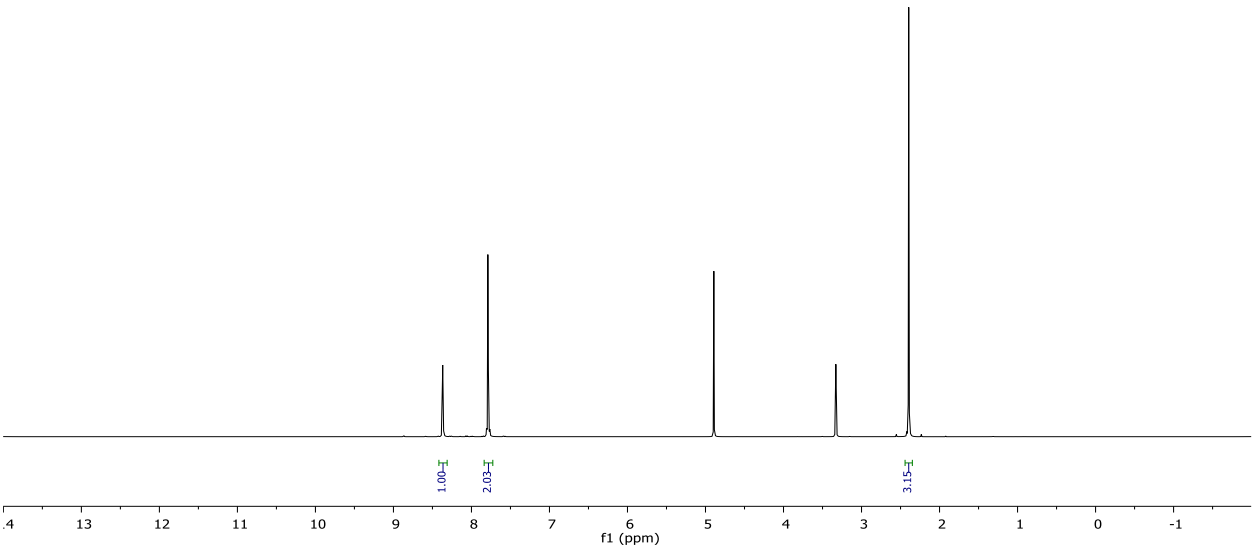
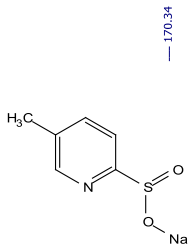
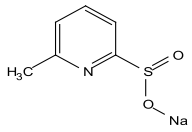
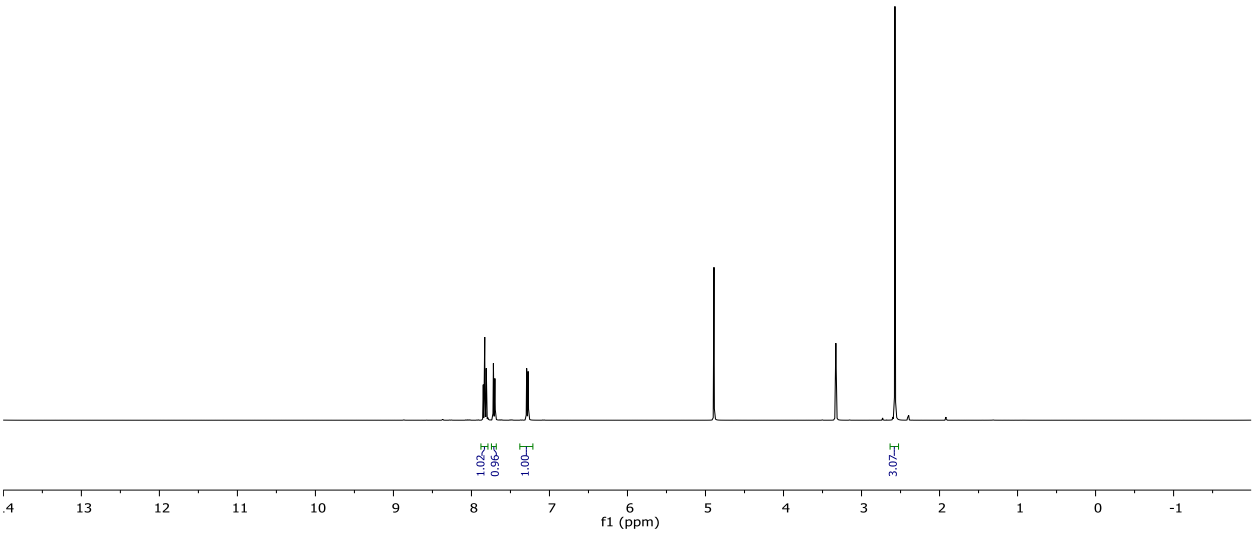
S
O
O
Na

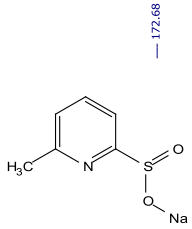

1.00
2.03
3.15
.4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


H3C
N
S
O
O
Na

170.34
148.16
138.32
134.54
117.21
16.81
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


H3C
N
S
O
O
Na


1.02
0.96
1.00
3.07
.4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


H3C
N
S
O
O
Na

172.68
157.56
138.03
123.89
114.08
22.24
210
200
190
180
170
160
150
140
130
120
110
100
90
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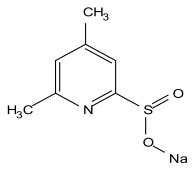
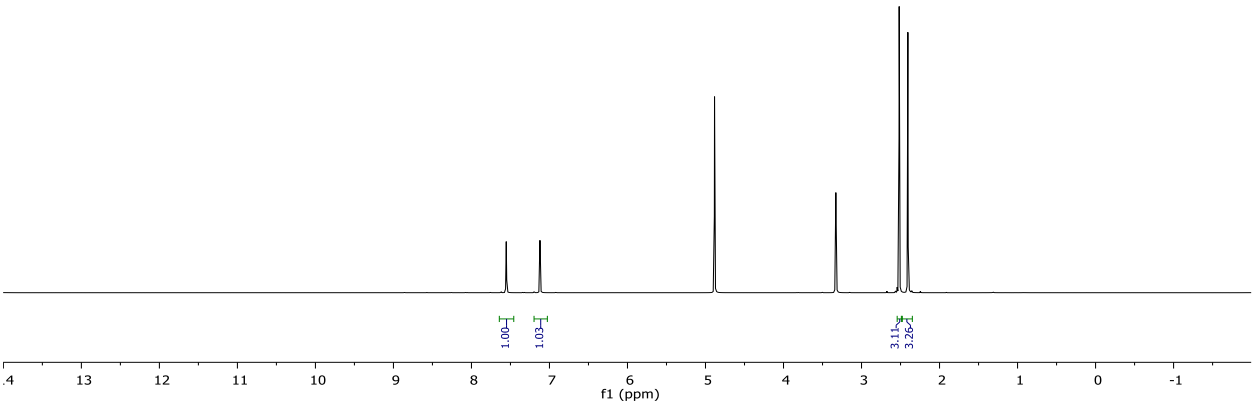
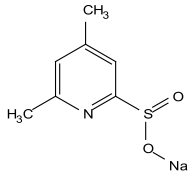
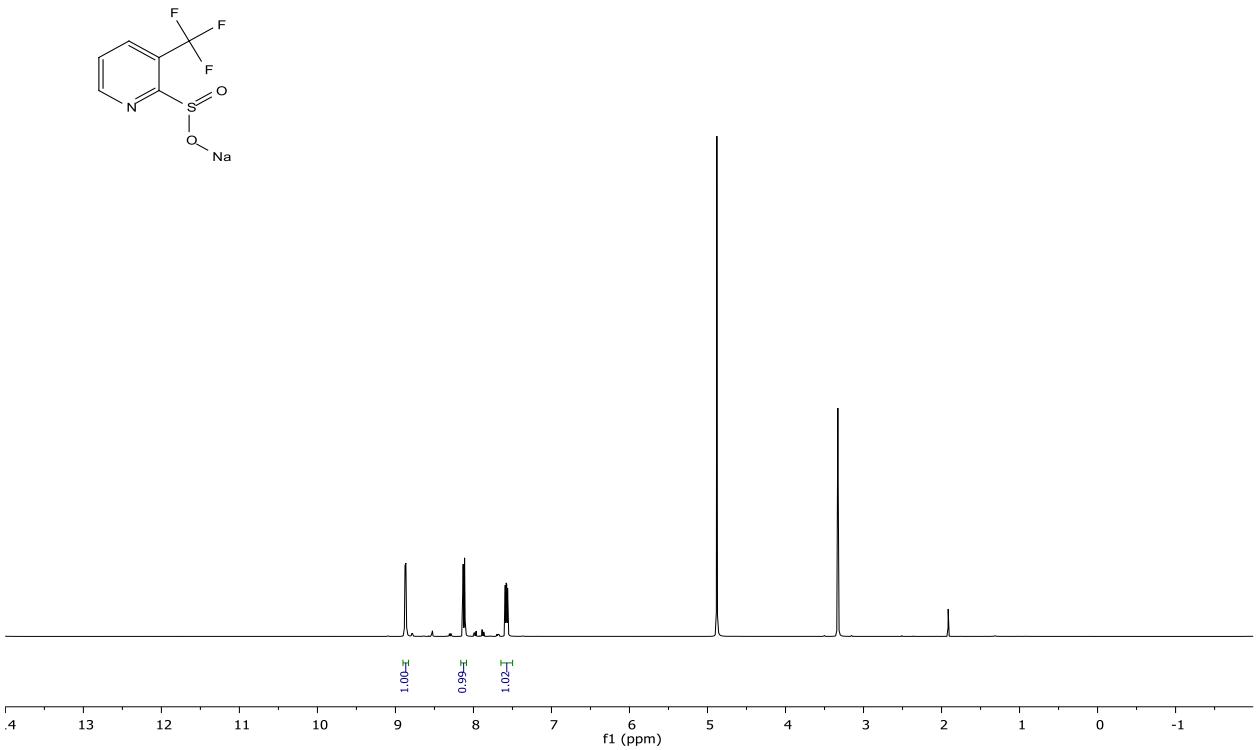
70
60
50
40
30
20
10
0
-10
f1 (ppm)

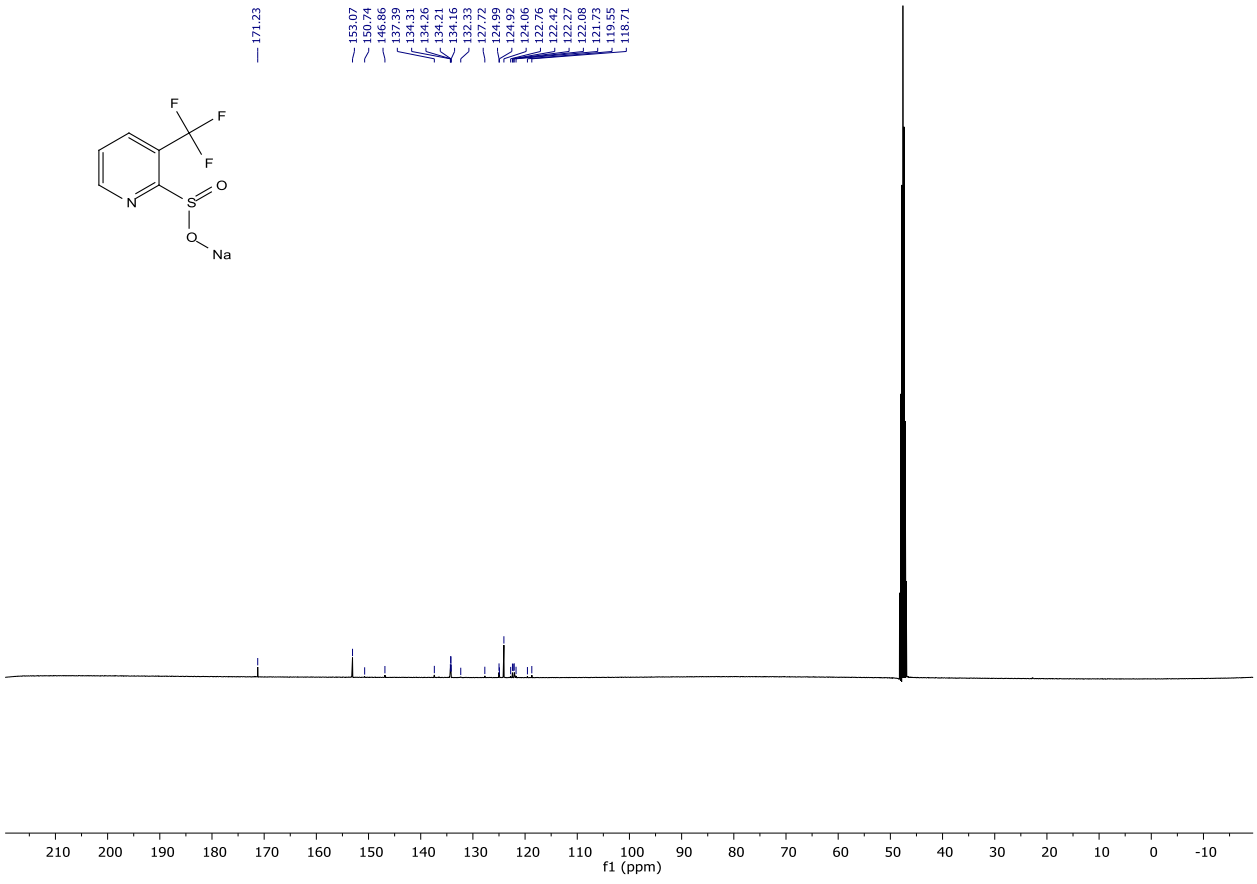

CH3
H3C
N
S
O
O
Na

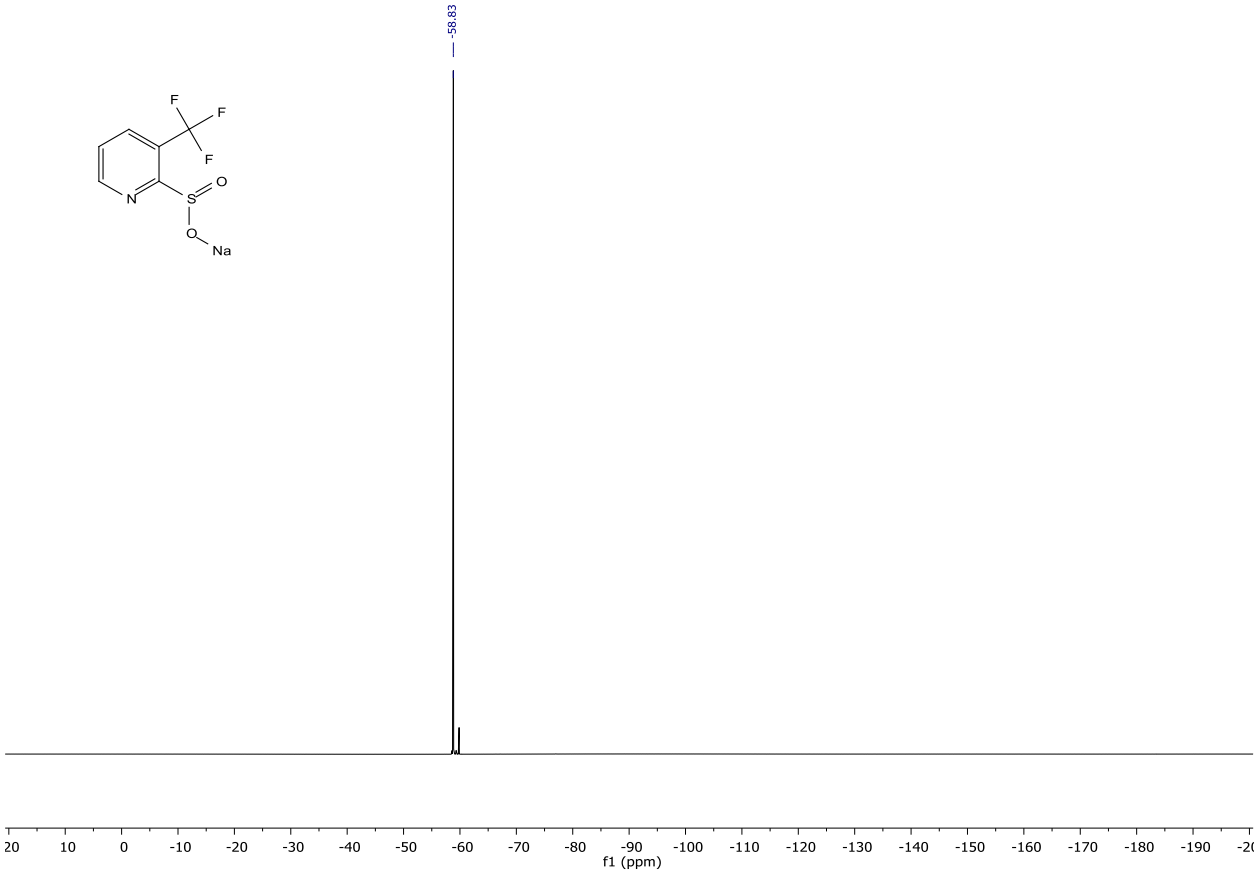

1.00
1.03
3.11
3.26
f1 (ppm)

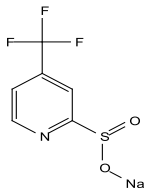

CH3
H3C
N
S
O
O
Na

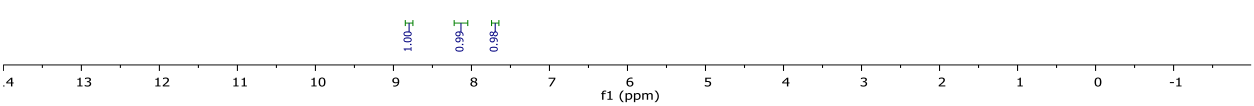
172.50
157.22
149.88
124.67
114.59
21.97
19.75
f1 (ppm)

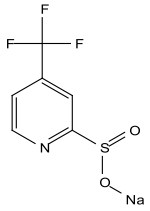

F
F
F
N
S
O
O
Na
1.00
0.99
1.02
.4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


171.23
153.07
150.74
146.86
137.39
134.31
134.26
134.21
134.16
132.33
127.72
124.99
124.92
124.06
122.76
122.42
122.27
122.08
121.73
119.55
118.71
F
F
F
N
S
O
O
Na
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

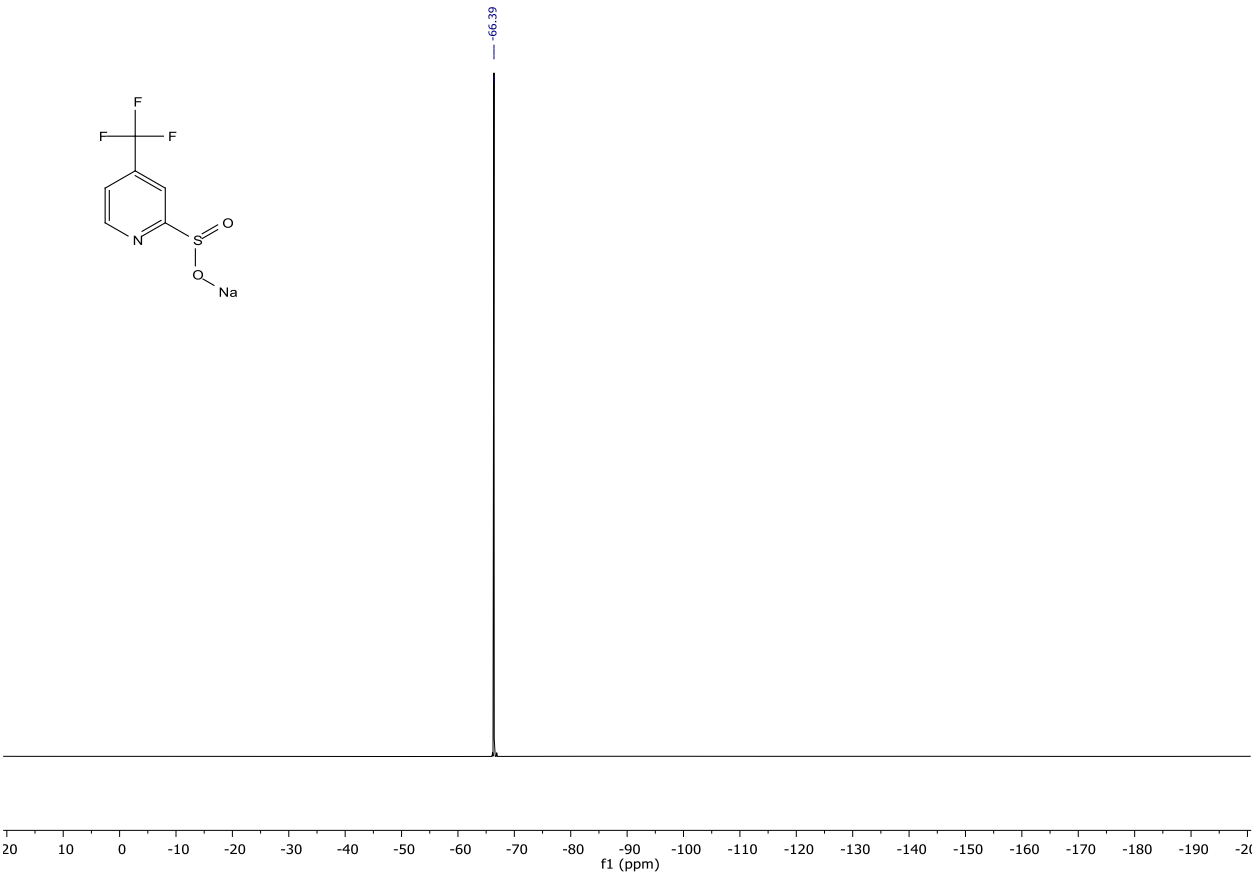

-58.83
F
F
F
N
S
O
O
Na
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

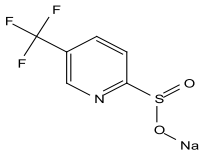

F
F
F
N
S
O
O
Na

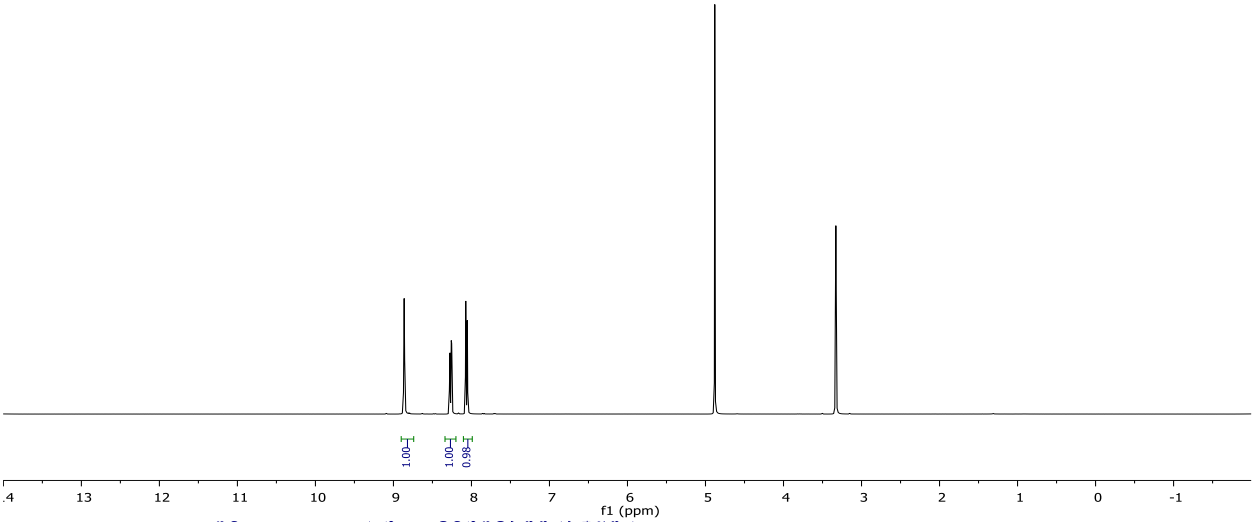

1.00
0.99
0.98
.4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

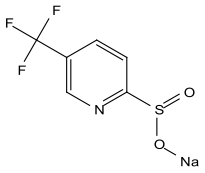

F
F
F
N
S
O
O
Na

149.74
138.95
139.61
139.27
138.93
127.00
124.29
121.58
119.61
118.86
113.09
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

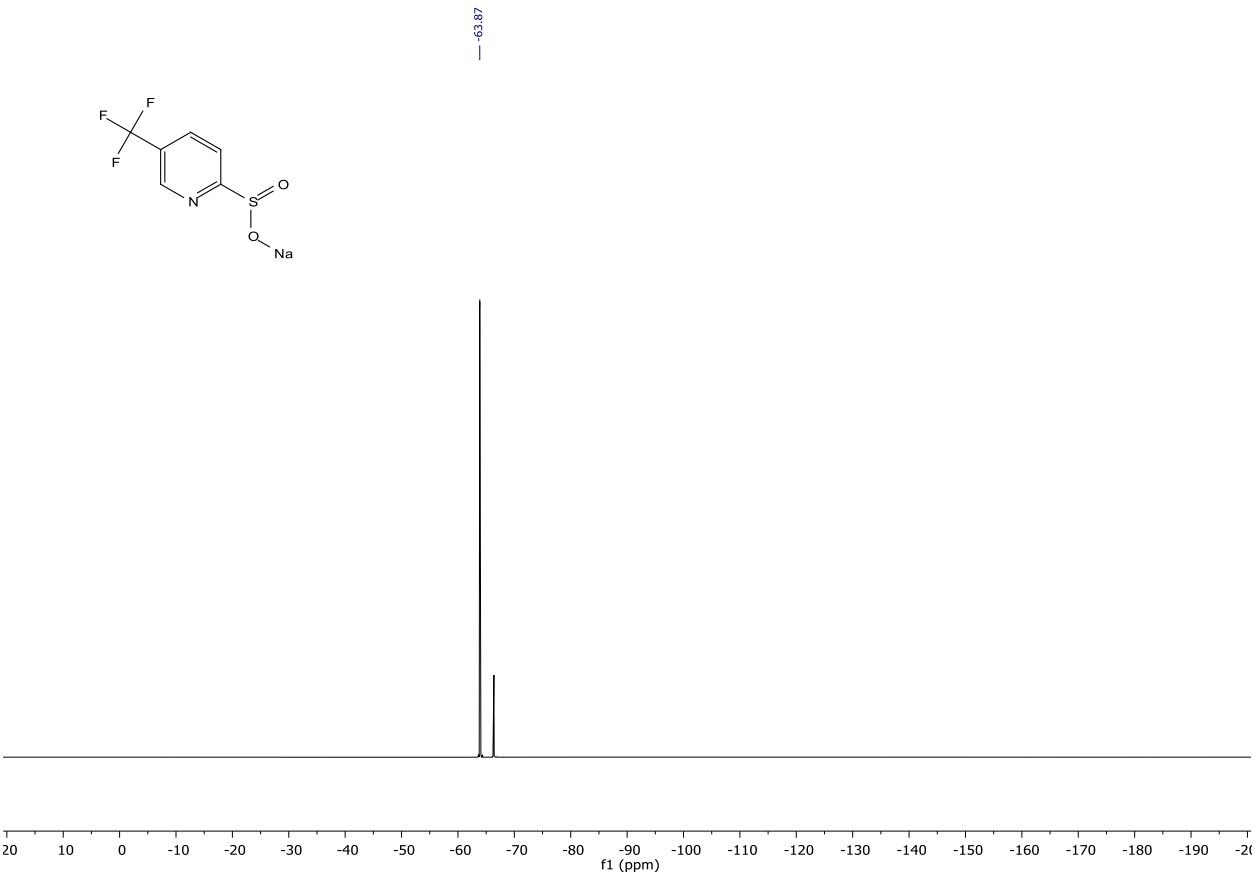

-66.39
F
F
F
N
S
O
O
Na
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

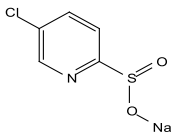

F
F
F
N
S
O
O
Na

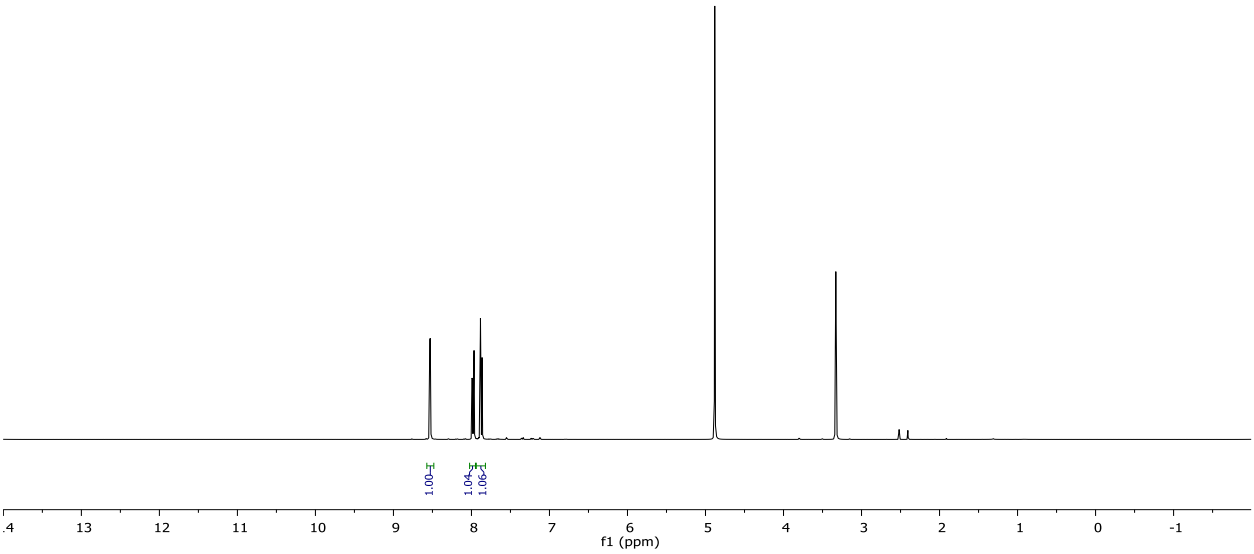

1.00
1.00
0.98
.4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

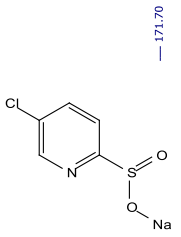

F
F
F
N
S
O
O
Na

177.23
175.49
149.81
145.26
135.00
127.59
127.16
126.83
126.50
126.17
124.88
122.18
119.61
119.57
117.74
113.22
113.18
113.11
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

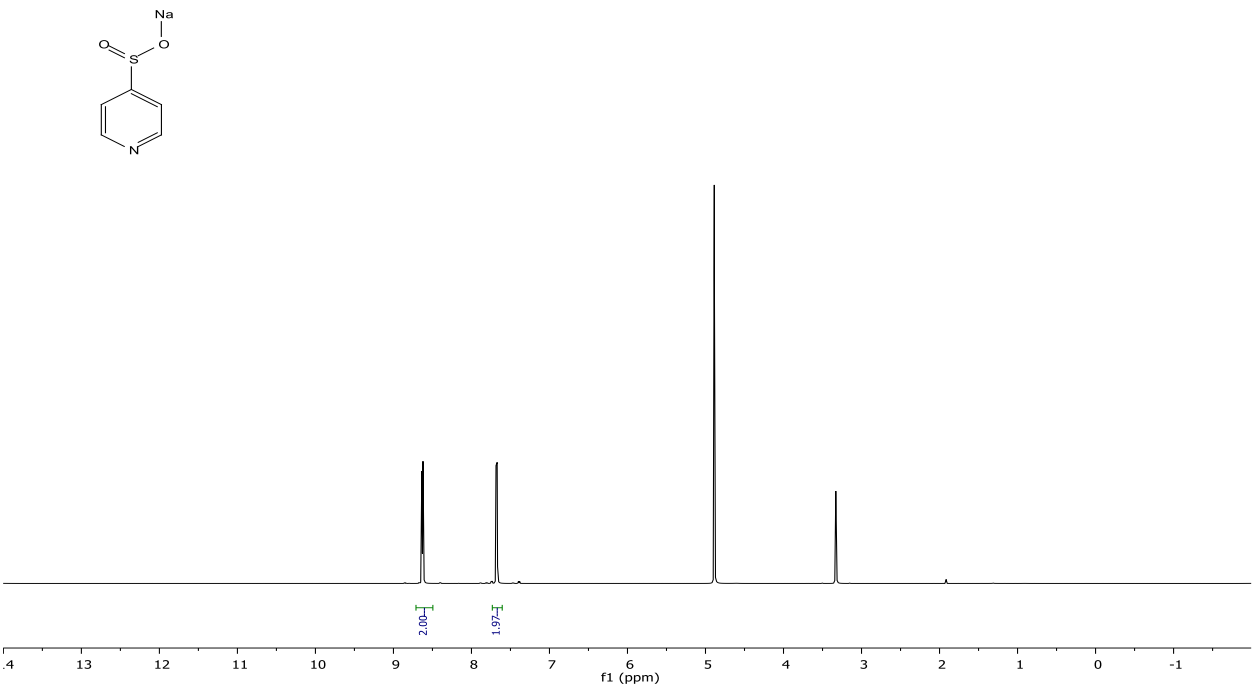

-63.87
F
F
F
N
S
O
O
Na
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

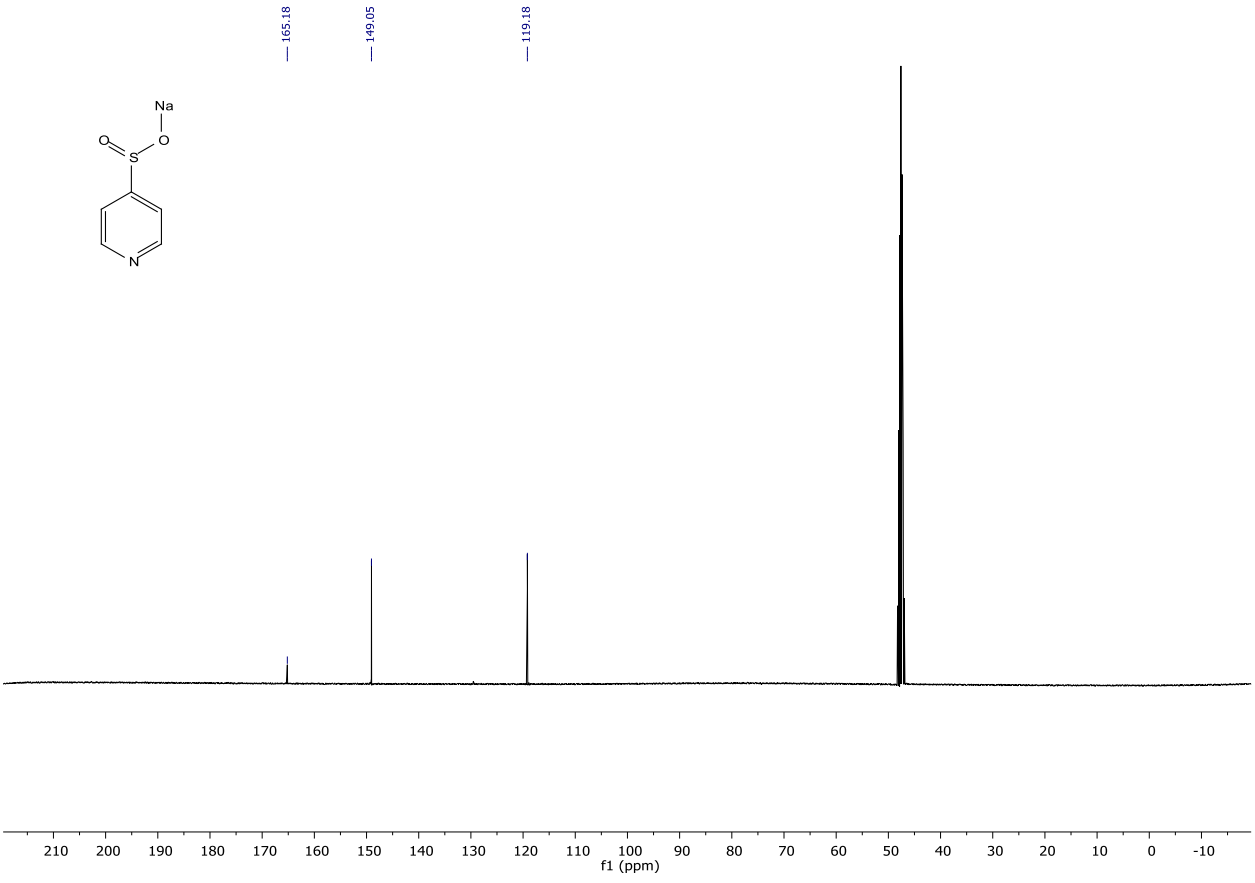

Cl
N
S
O
O
Na

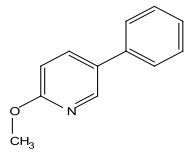

1.00
1.04
1.06
.4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

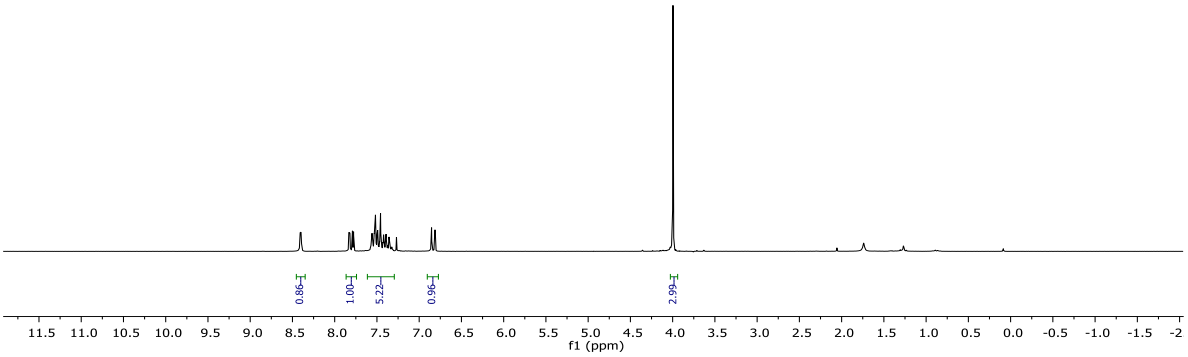

Cl
N
S
O
O
Na

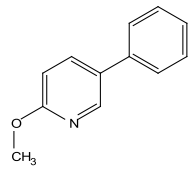
171.70
146.88
137.40
132.34
118.76
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Na
O
S
O
N
2.00
1.97
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

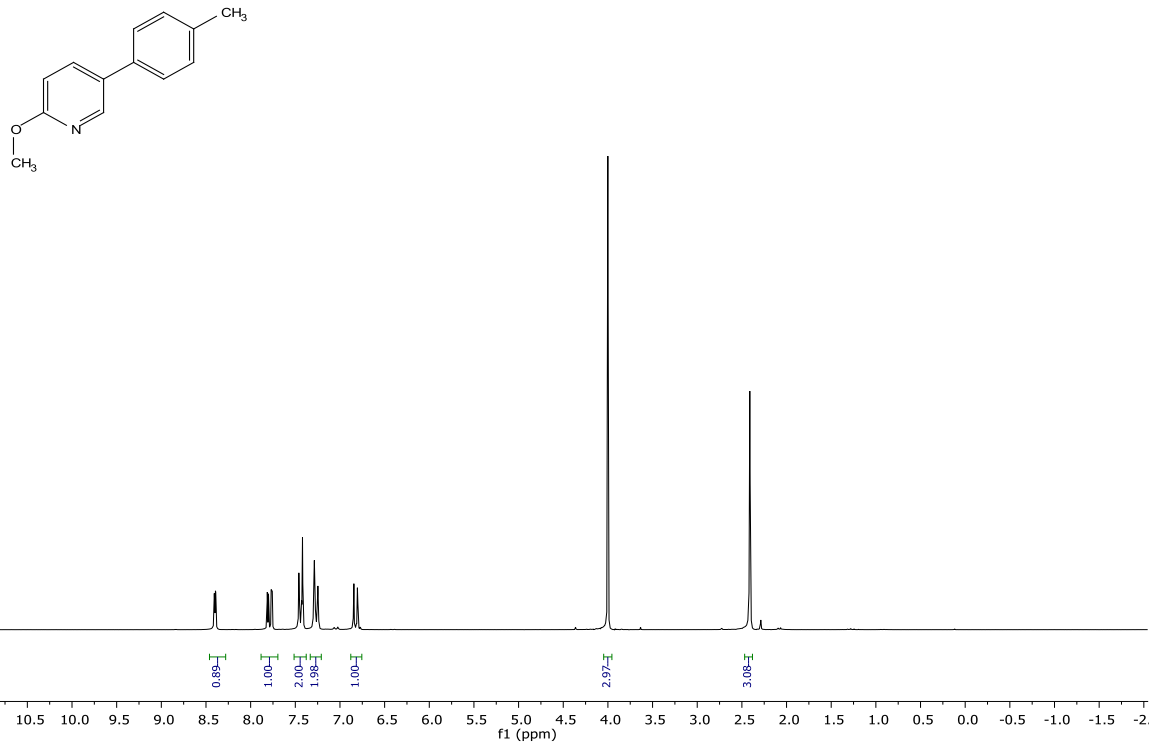

165.18
149.05
119.18
Na
O
S
O
N
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

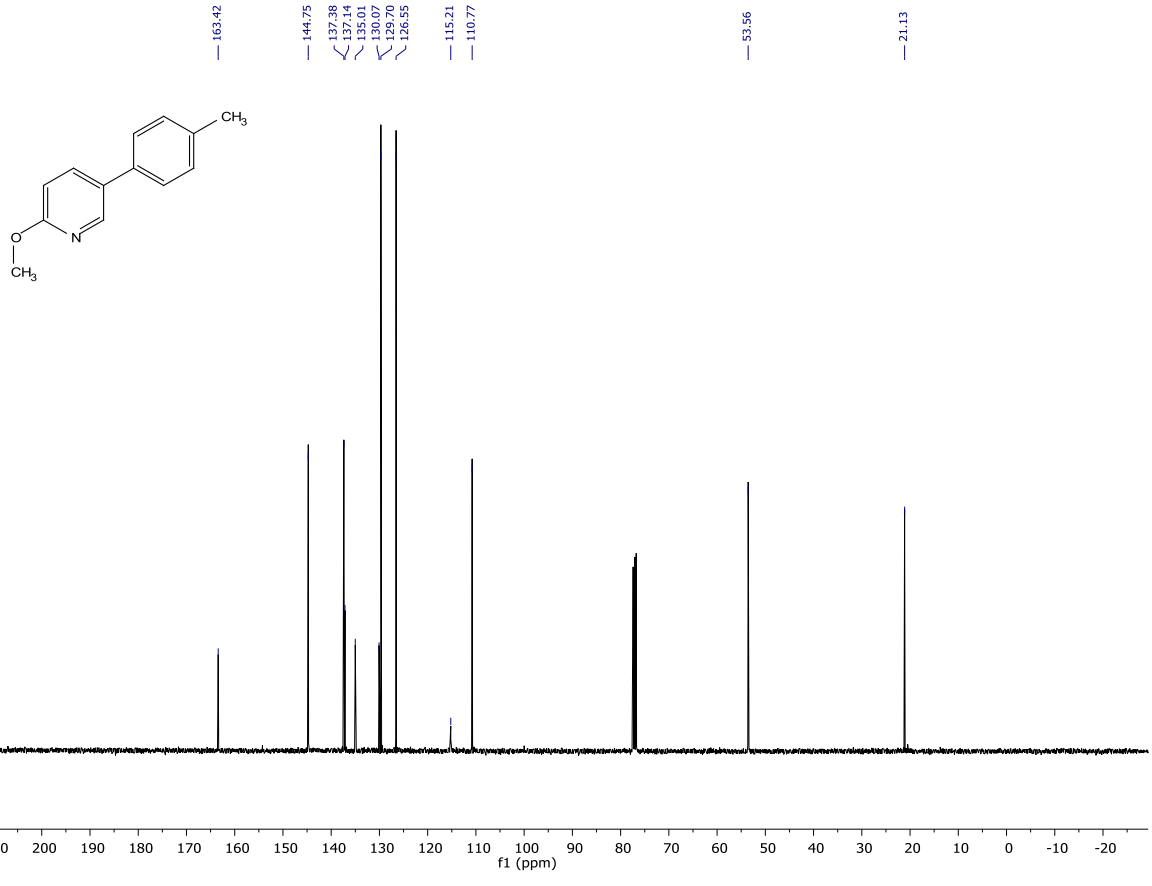

O
N
CH3

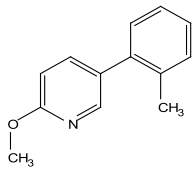

0.86
1.00
5.22
0.96
2.99
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5 -2
f1 (ppm)

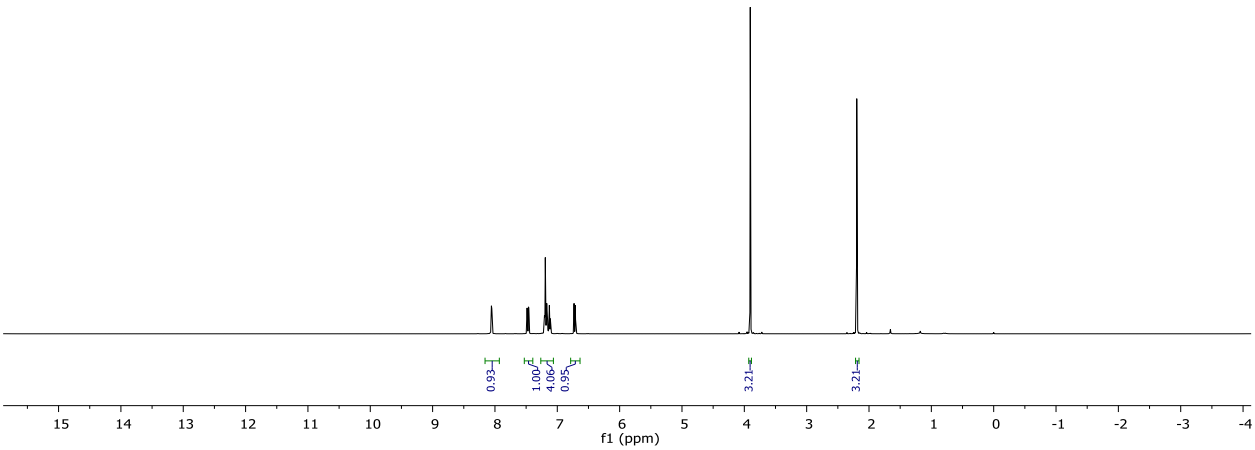

O
N
CH3

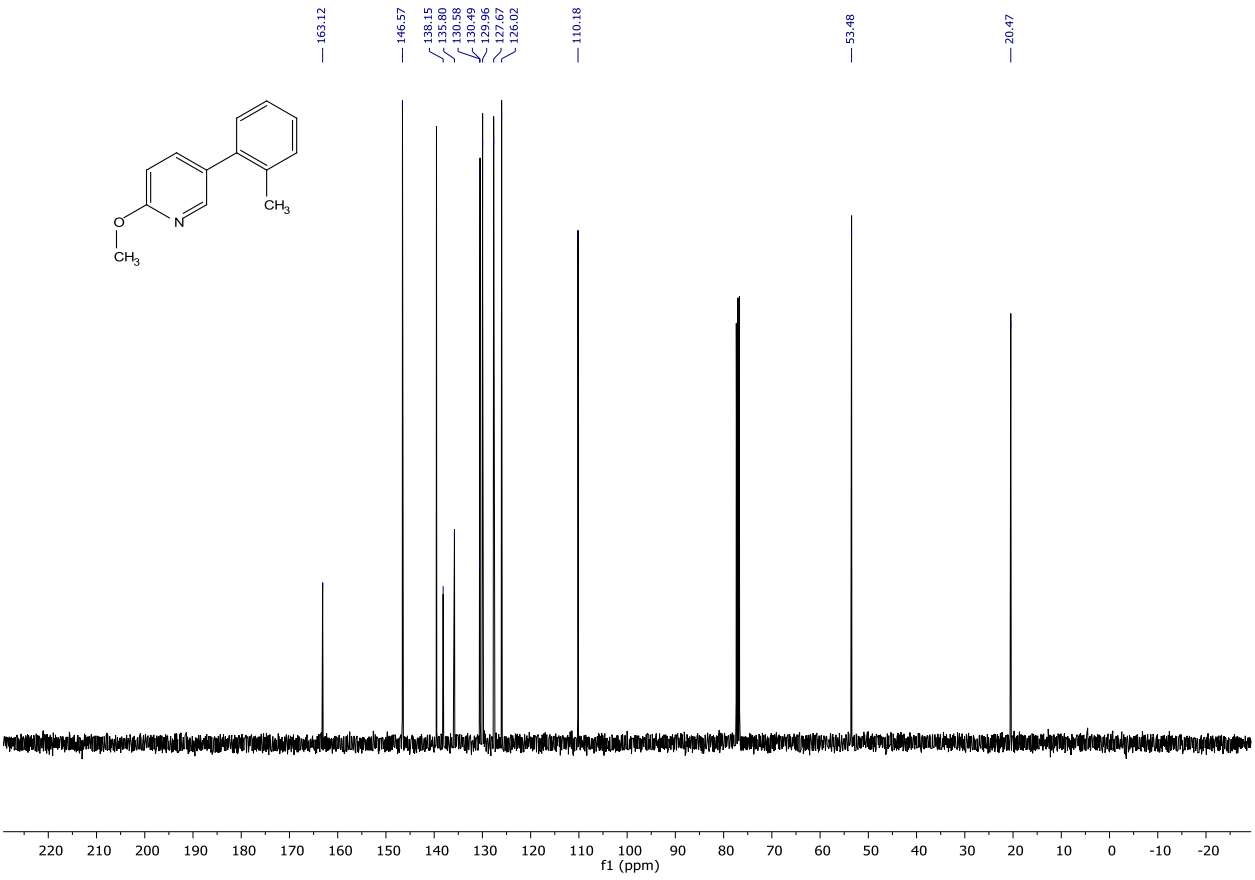
163.59
144.97
137.91
137.52
130.11
128.99
127.34
126.70
110.84
53.60
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

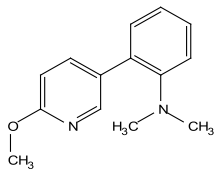

CH3
O
N
CH3
0.89
1.00
2.00
1.98
1.00
2.97
3.08
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)

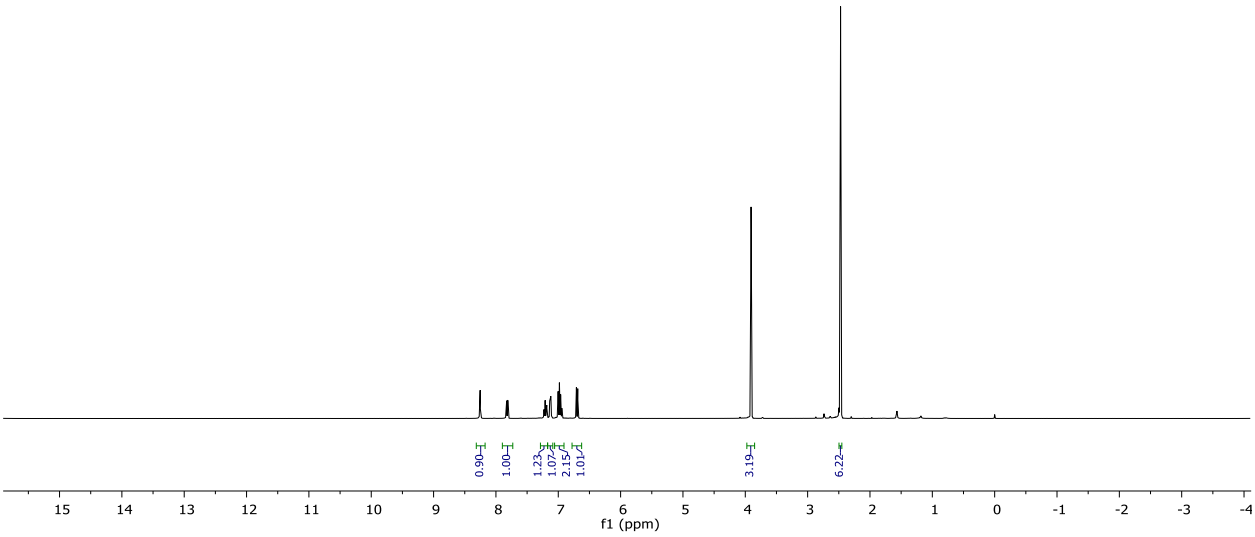

163.42
144.75
137.38
137.14
135.01
130.07
129.70
126.55
115.21
110.77
53.56
21.13
CH3
O
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

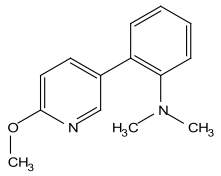

O
N
CH3
CH3


0.93
1.00
4.06
0.95
3.21
3.21
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

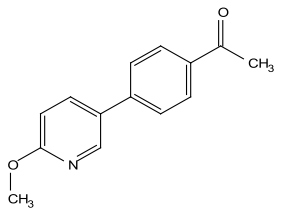

163.12
146.57
138.15
135.80
130.58
130.49
129.96
127.67
126.02
110.18
53.48
20.47
O
N
CH3
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

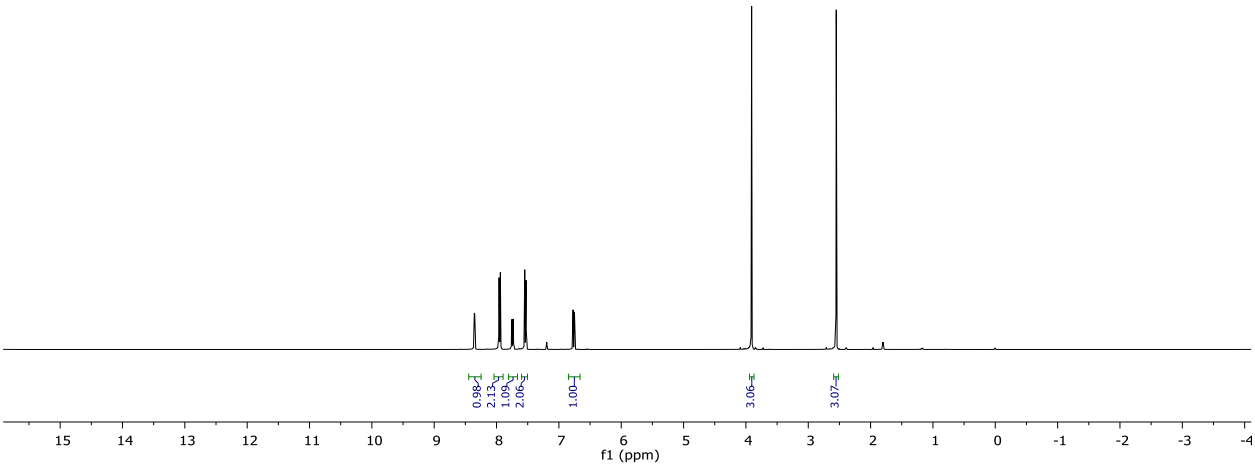

O
N
CH3
H3C
N
CH3

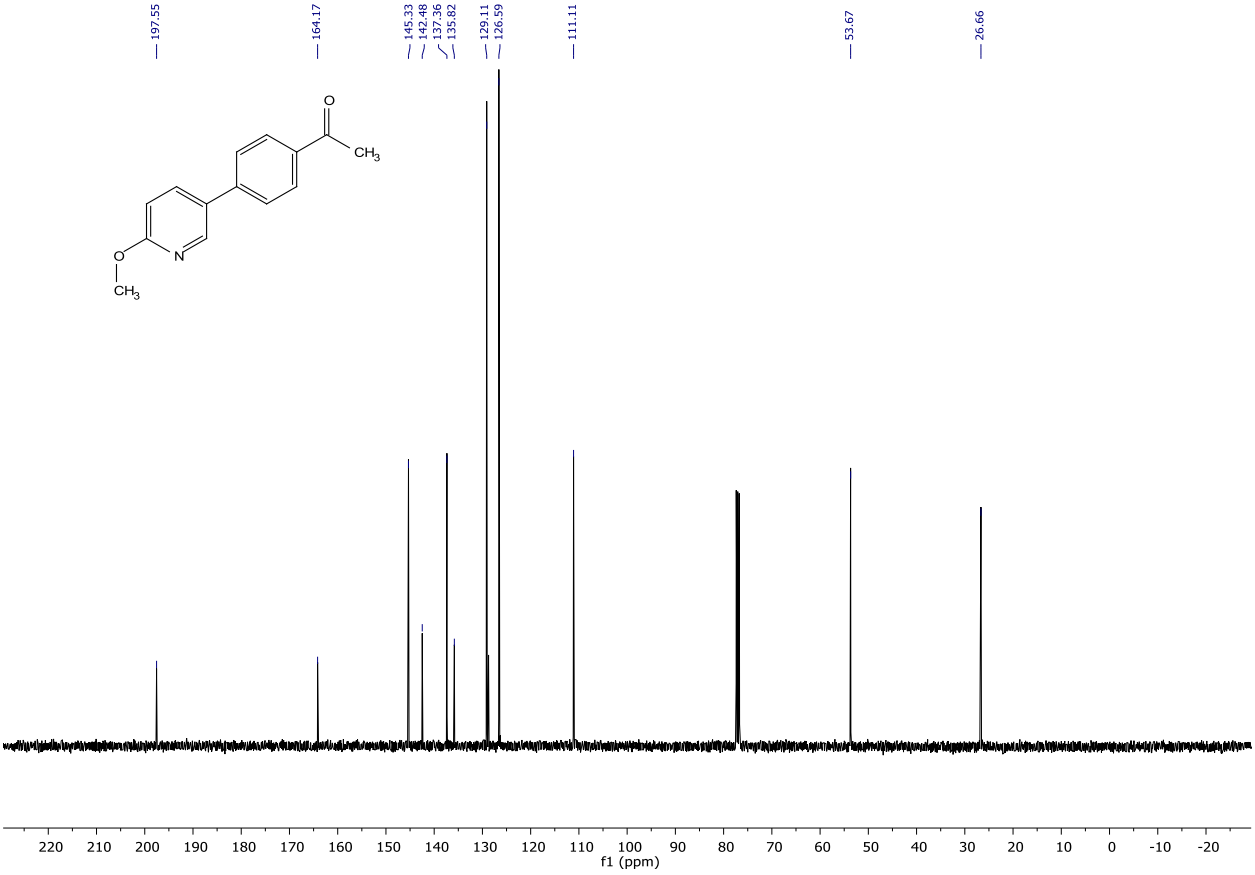

0.90
1.00
1.23
1.07
2.15
1.01
3.19
6.22
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

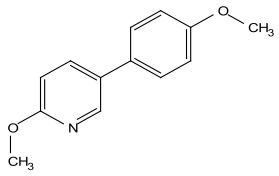

O
N
CH3
H3C
N
CH3

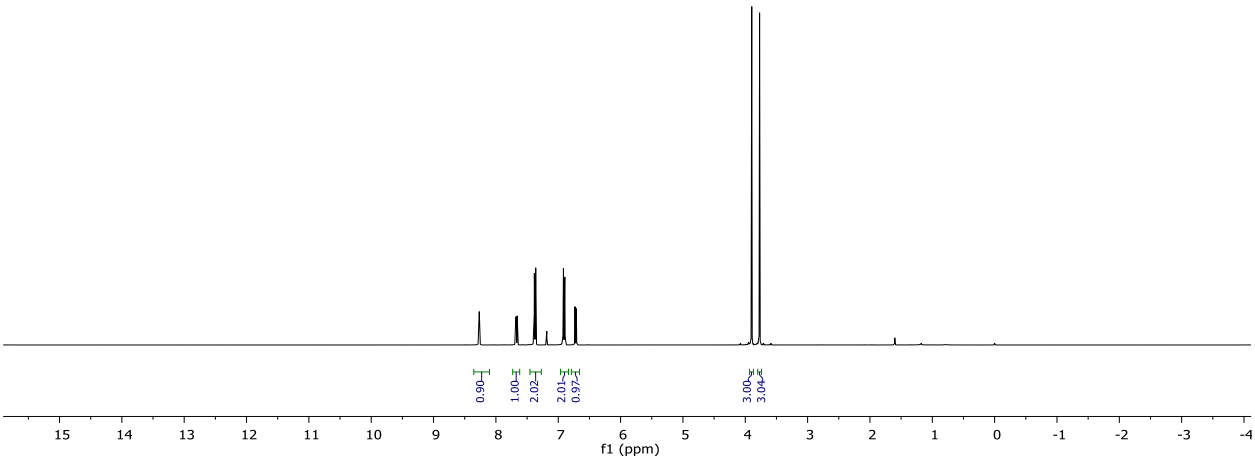
162.92
151.64
146.03
139.26
131.20
130.52
128.41
122.08
118.17
110.26
53.40
43.40
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

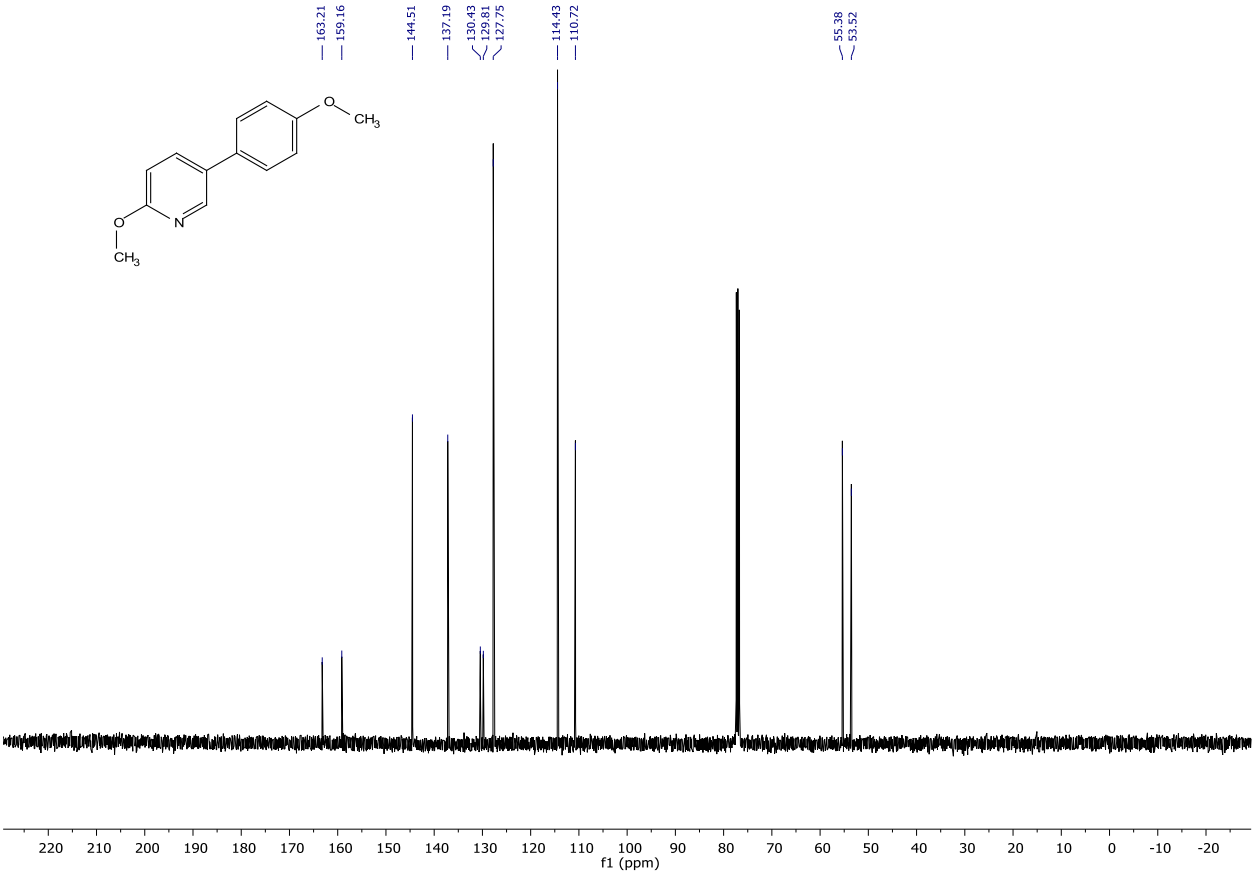

O
CH3
O
N
CH3

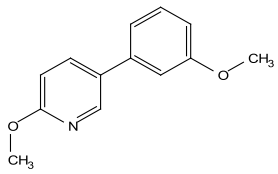

0.98
2.13
1.09
2.06
1.00
3.06
3.07
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

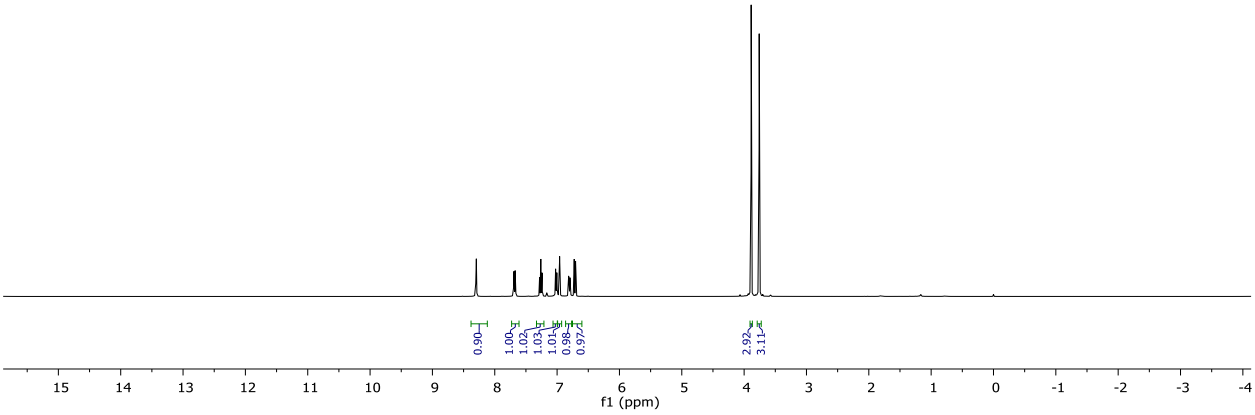

197.55
164.17
145.33
142.48
137.36
135.82
129.11
126.59
111.11
53.67
26.66
O
CH3
O
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

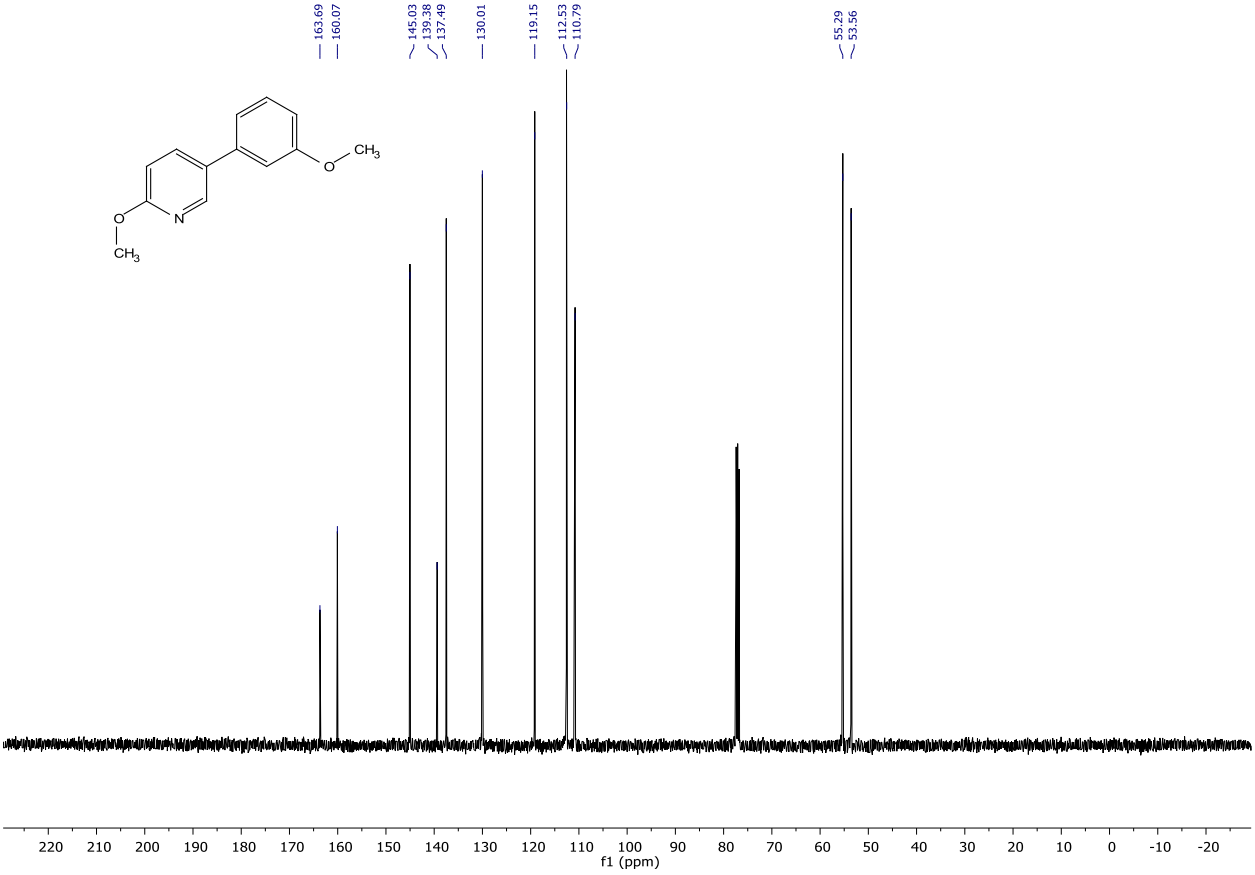

O
CH3
O
N
CH3

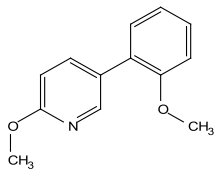

0.90
1.00
2.02
2.01
0.97
3.00
3.04
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

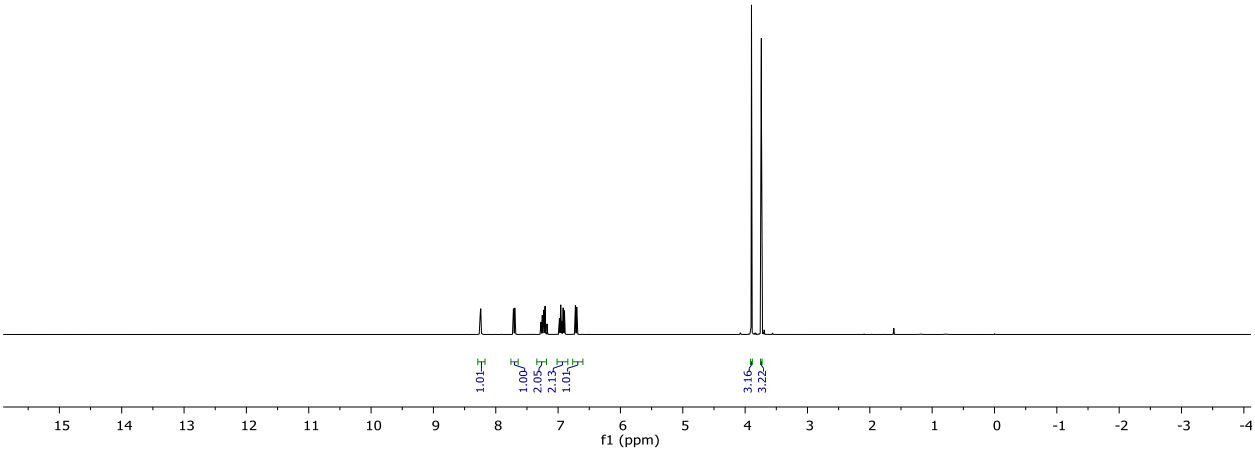

163.21
159.16
144.51
137.19
130.43
129.81
127.75
114.43
110.72
55.38
53.52
O
CH3
O
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

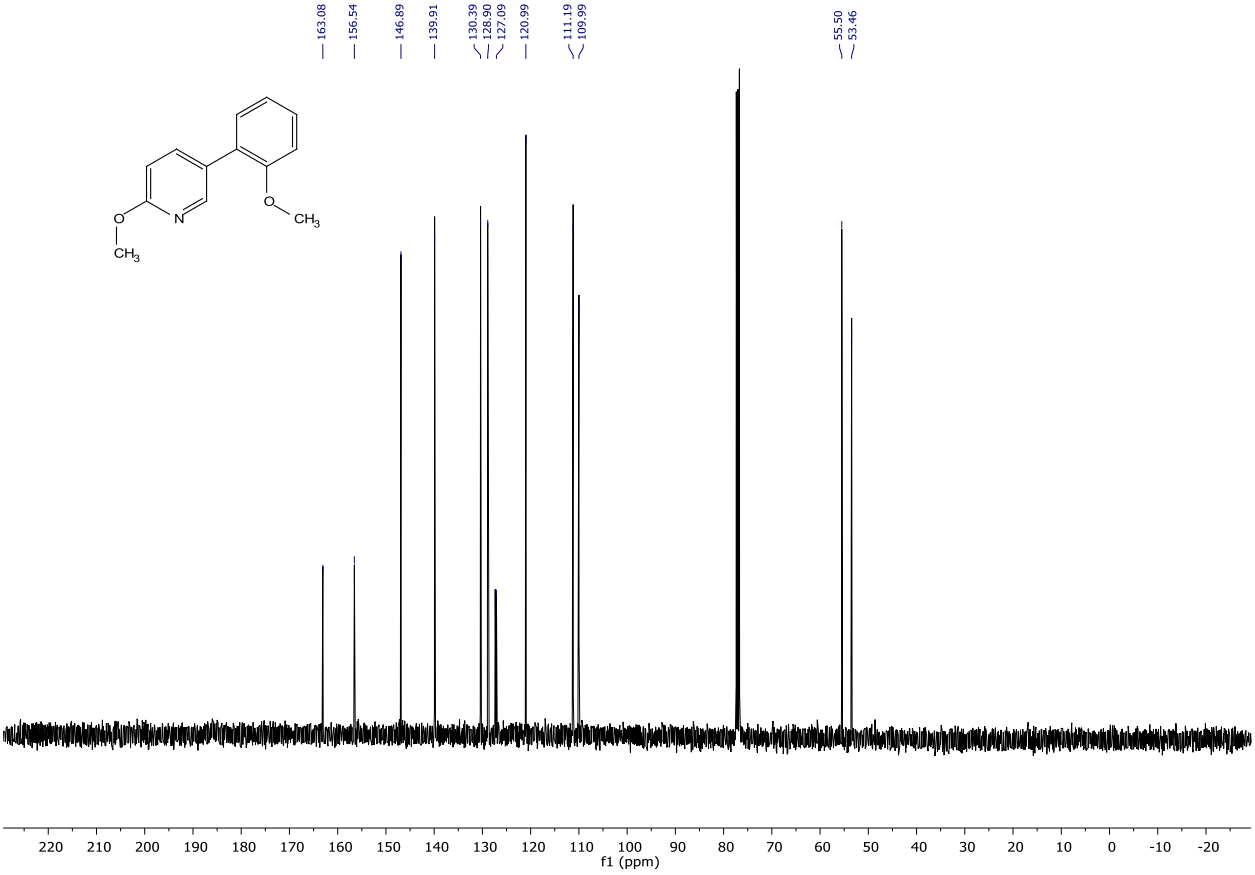

O
CH3
O
N
CH3


0.90
1.00
1.02
1.03
1.01
0.98
0.97
2.92
3.11
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


163.69
160.07
145.03
139.38
137.49
130.01
119.15
112.53
110.79
55.29
53.56
O
CH3
O
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


O
N
O
CH3
O
CH3


1.01
1.00
2.05
2.13
1.01
3.16
3.22
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


163.08
156.54
146.89
139.91
130.39
128.90
127.09
120.99
111.19
109.99
55.50
53.46
O
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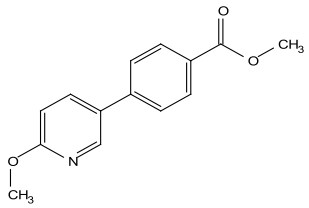
O
CH3
O
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)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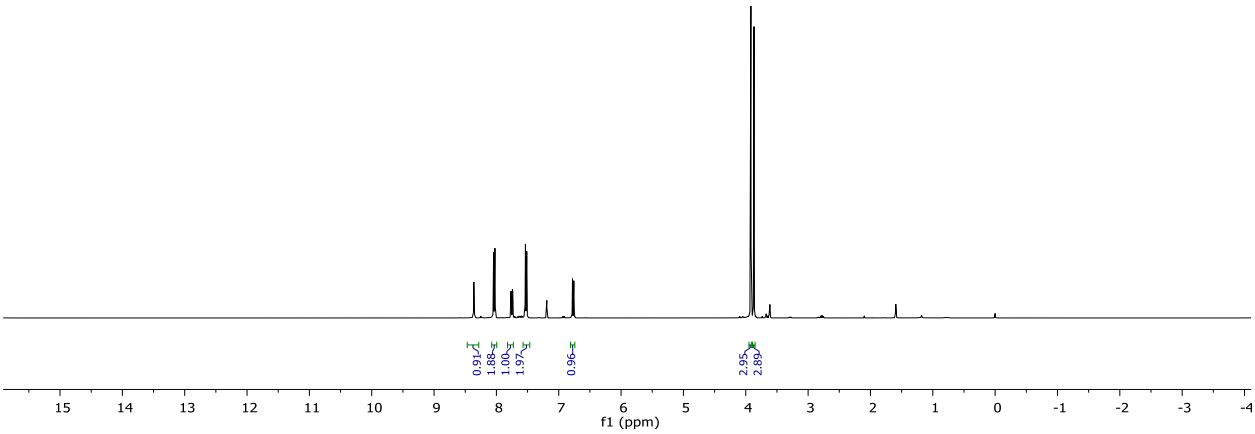
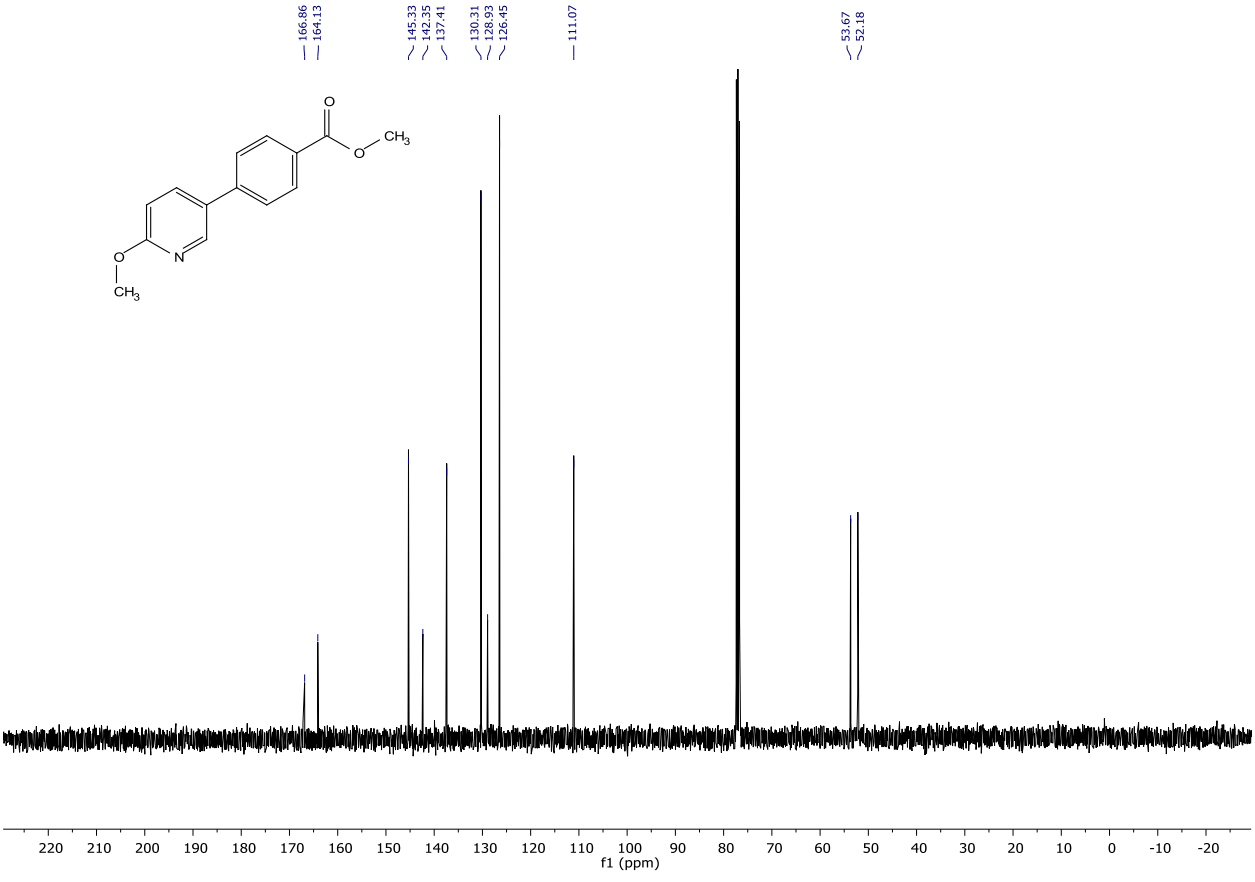
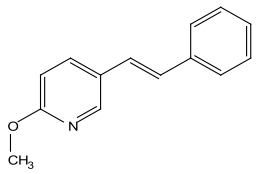
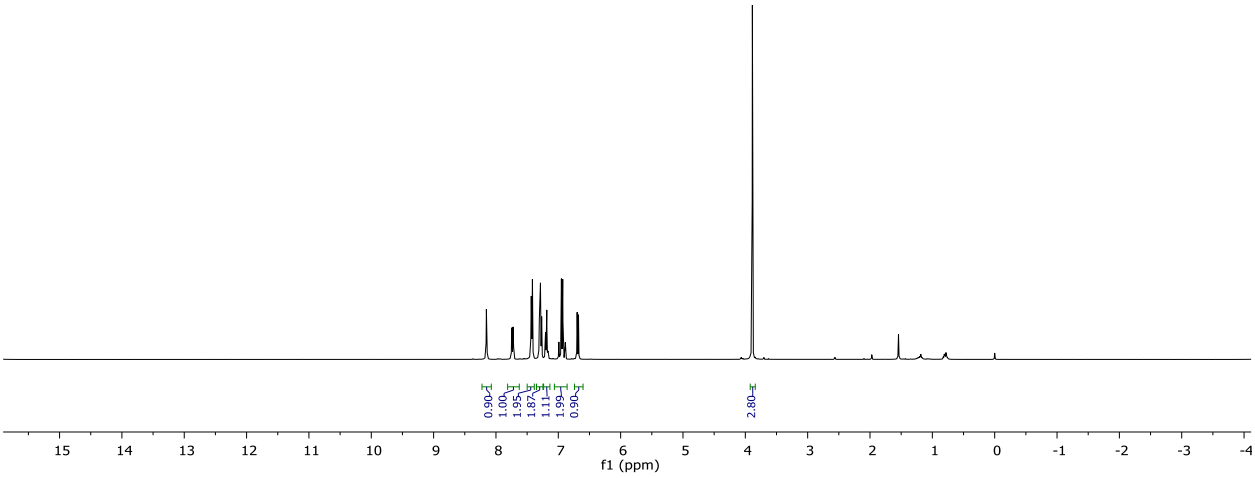
O
CH3
O
N
O
CH3


0.91
1.88
1.00
1.97
0.96
2.95
2.89
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


166.86
164.13
145.33
142.35
137.41
130.31
128.93
126.45
111.07
53.67
52.18
O
O
CH3
O
N
O
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


O
N
CH3


0.90
1.00
1.95
1.87
1.11
1.99
0.90
2.80
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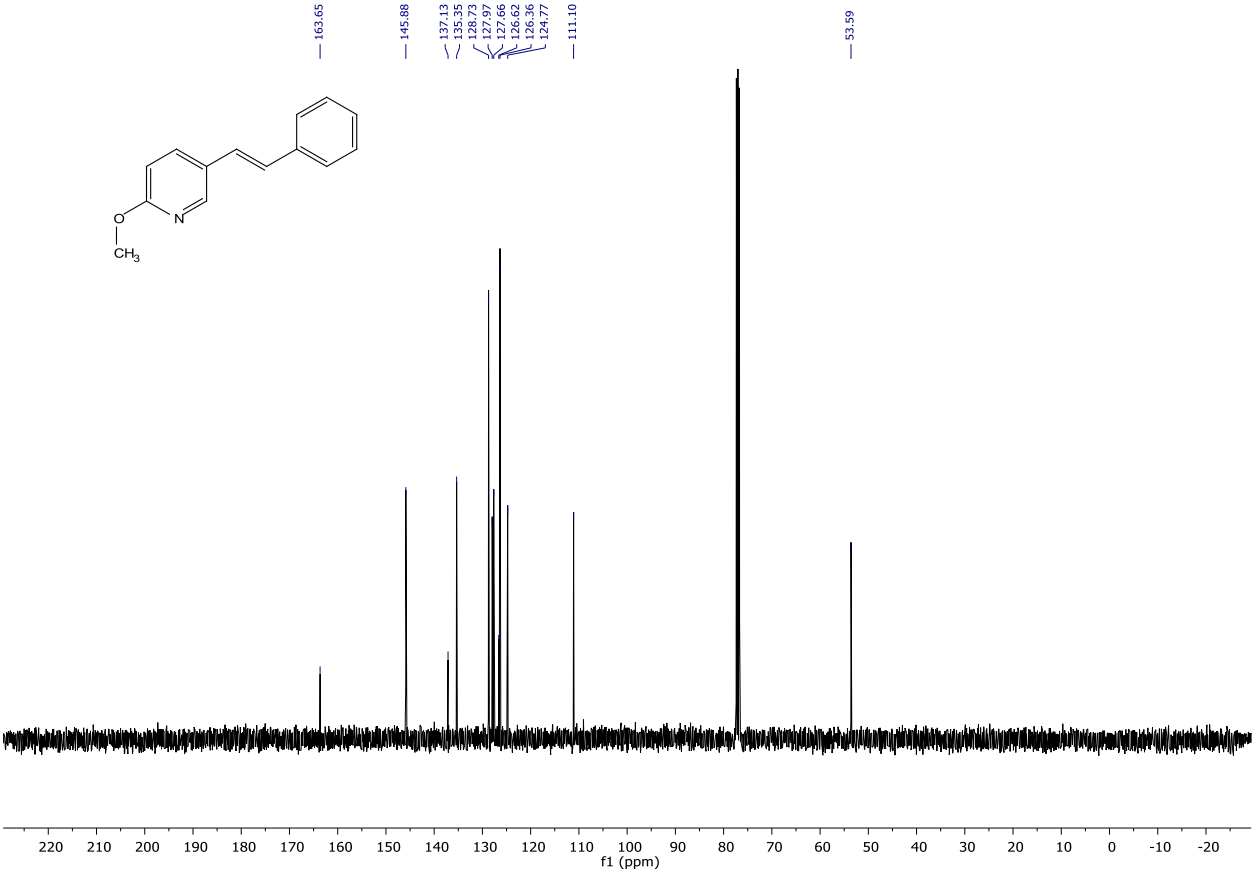
f1 (ppm)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128.73
127.97
127.66
126.62
126.36
124.77
111.10
53.59
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N
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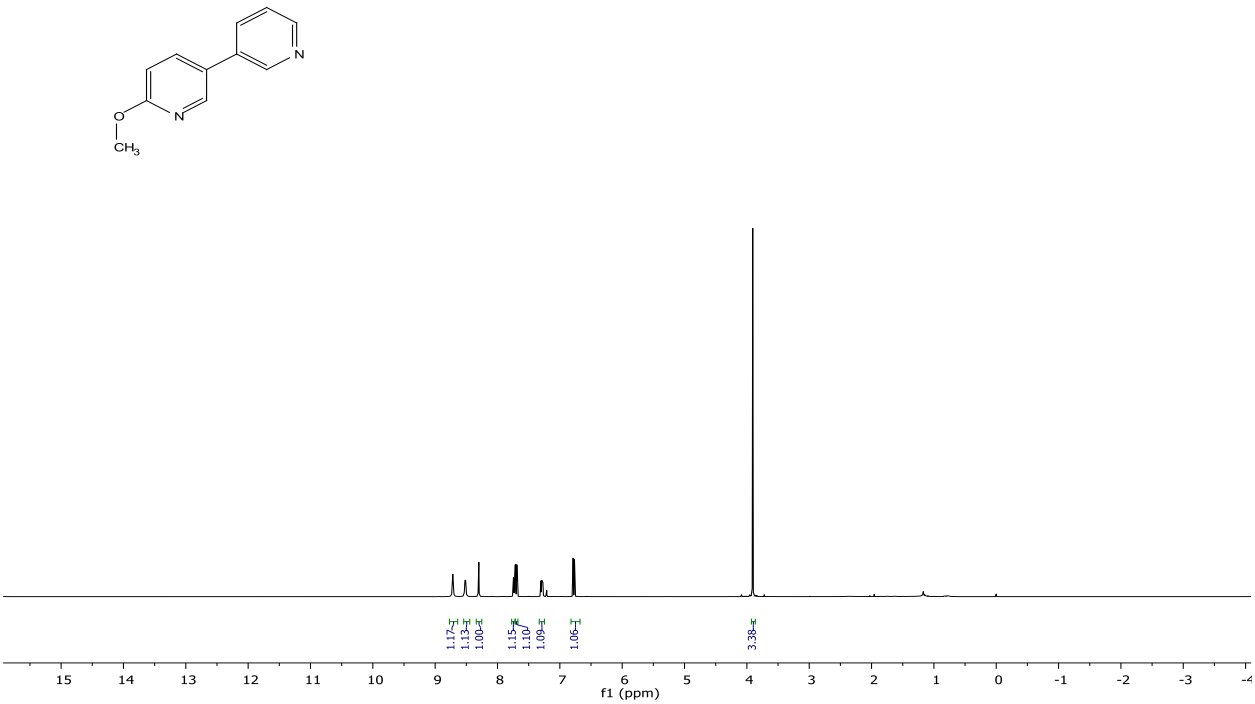
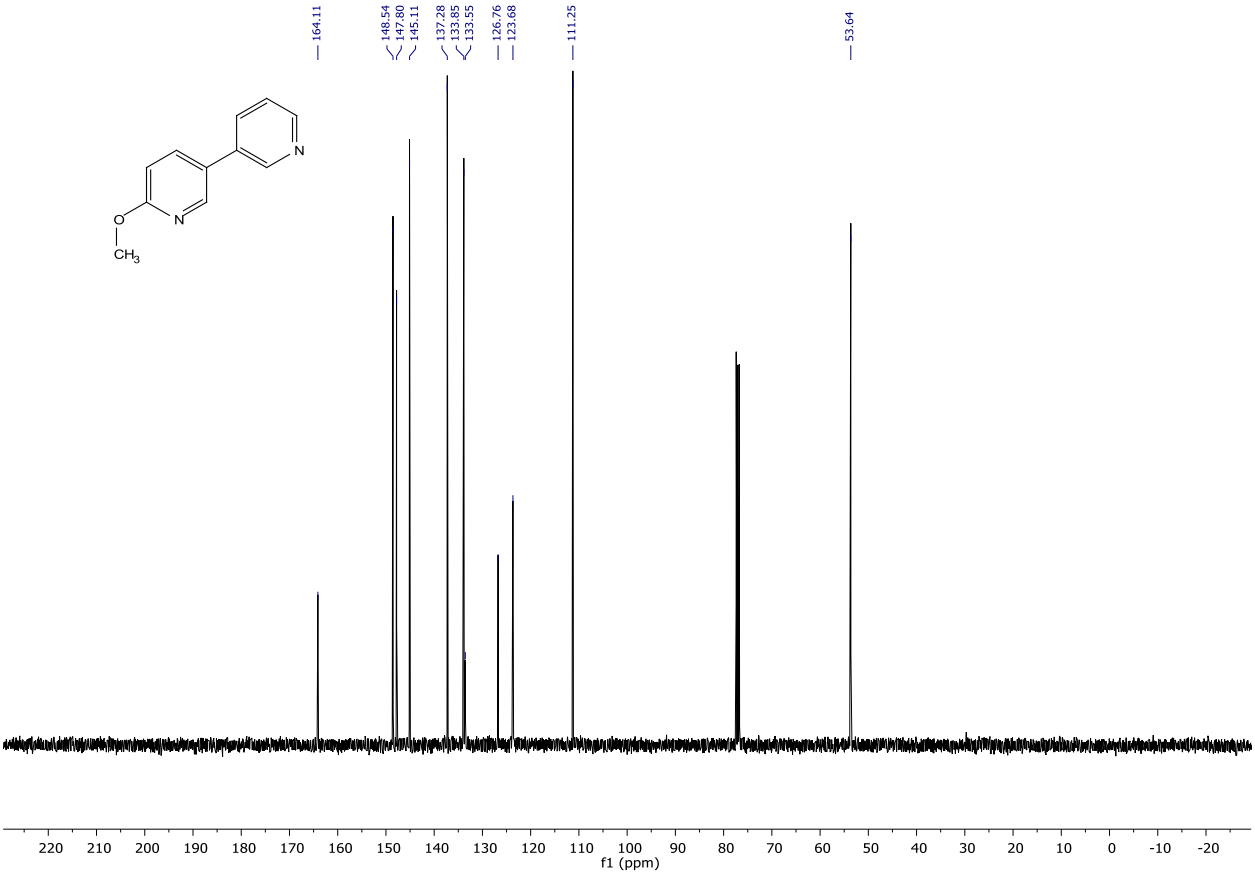
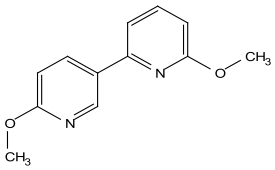
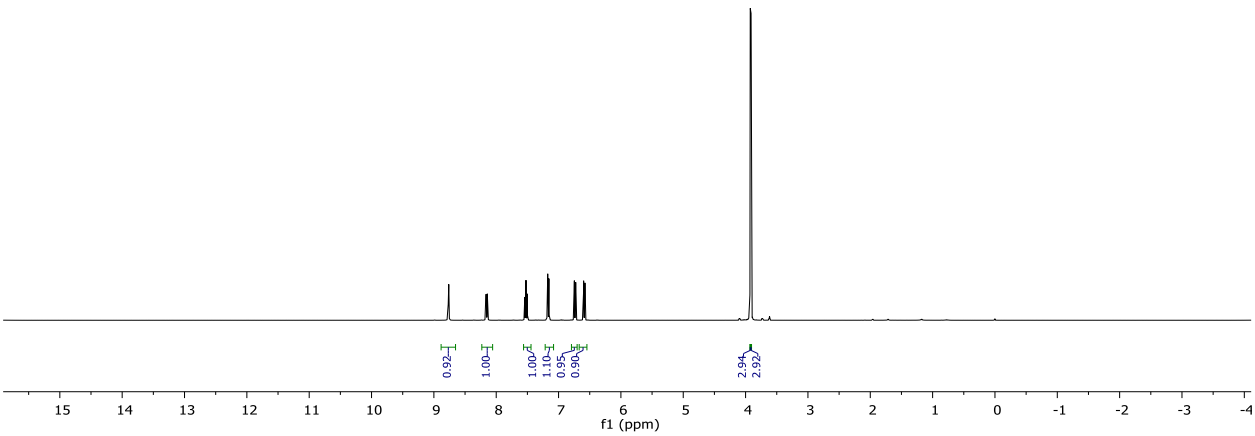
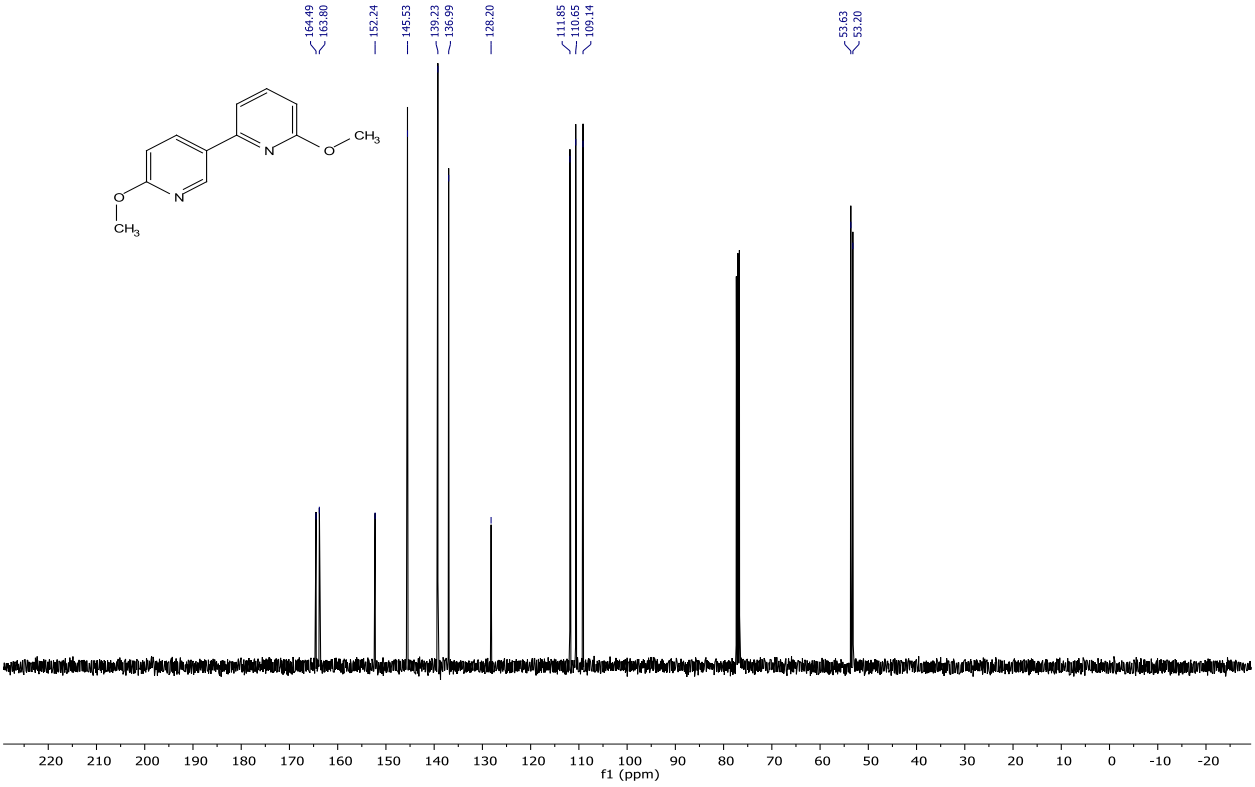
f1 (ppm)

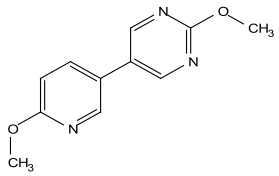

N
O
N
CH3
1.17
1.13
1.00
1.15
1.10
1.09
1.06
3.38
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
f1 (ppm)

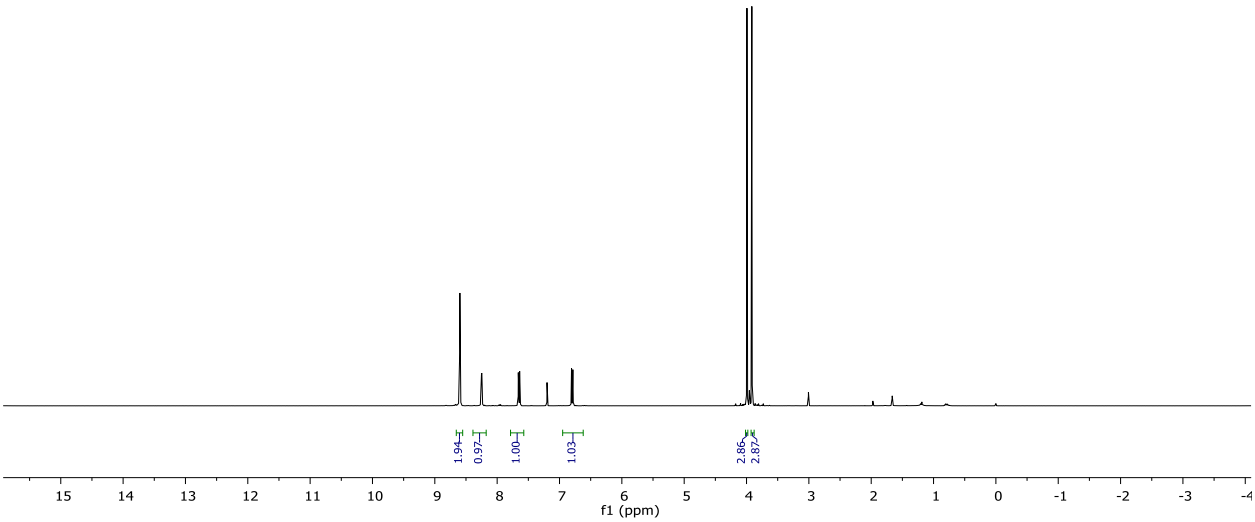

164.11
148.54
147.80
145.11
137.28
133.85
133.55
126.76
123.68
111.25
53.64
N
O
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

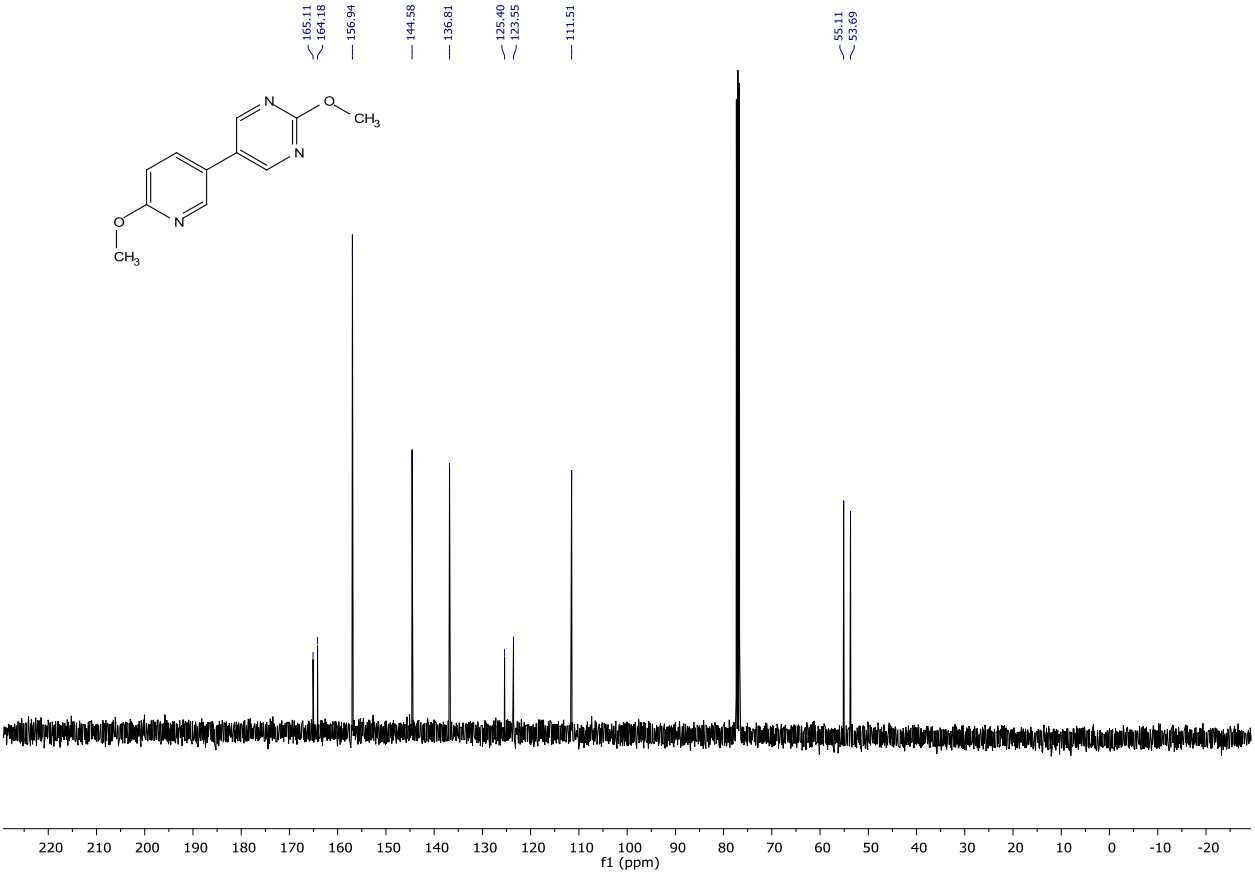

N
O
CH3
O
N
CH3

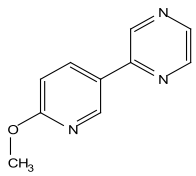

0.92
1.00
1.00
1.10
0.95
0.90
2.94
2.92
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

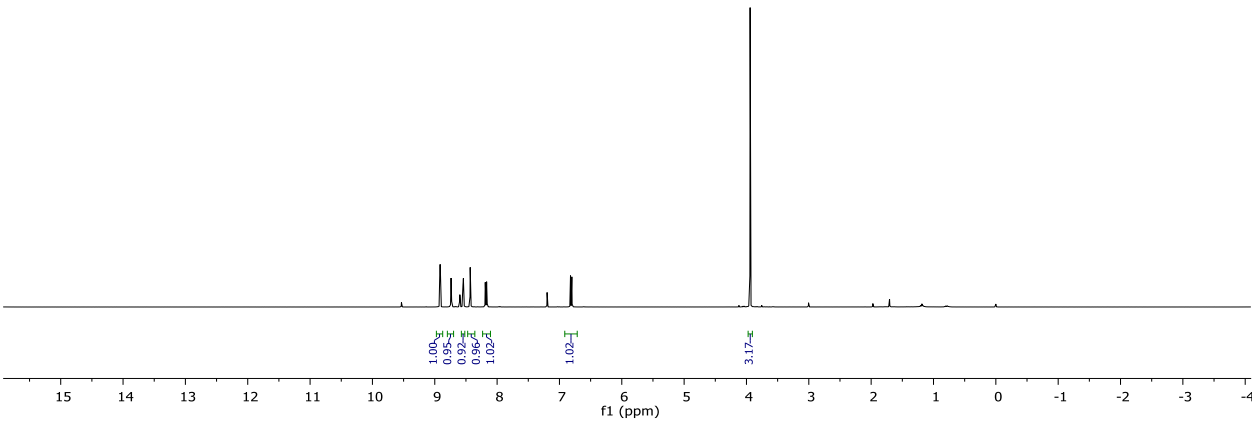

164.49
163.80
152.24
145.53
139.23
136.99
128.20
111.85
110.65
109.14
53.63
53.20
N
O
CH3
O
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

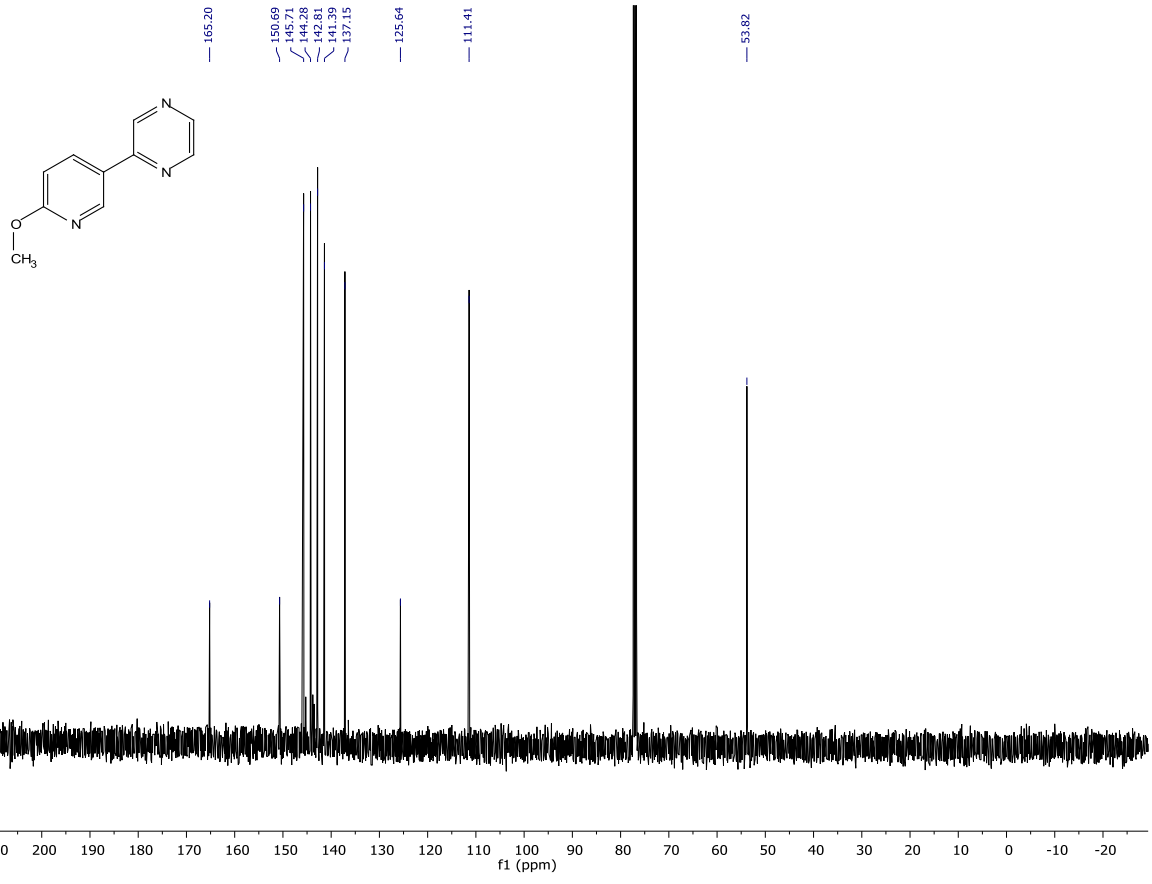

N
O
CH3
N
O
N
CH3

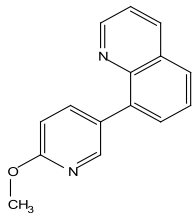

1.94
0.97
1.00
1.03
2.86
2.87
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

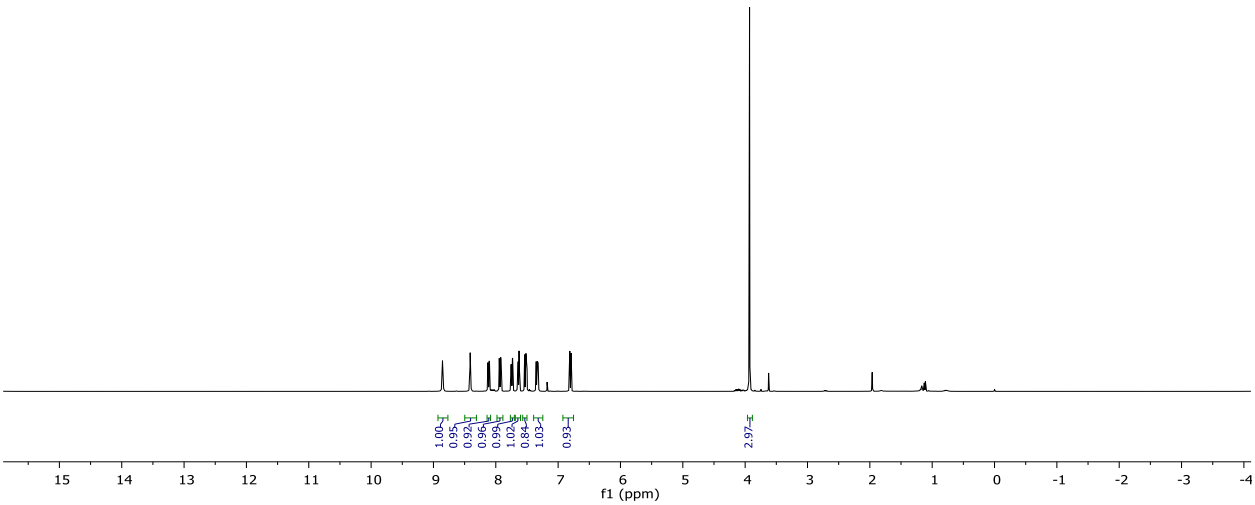

165.11
164.18
156.94
144.58
136.81
125.40
123.55
111.51
55.11
53.69
N
O
CH3
N
O
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

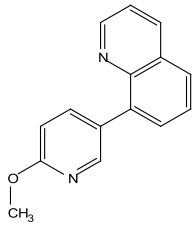

N
N
O
N
CH3


1.00
0.95
0.92
0.96
1.02
1.02
3.17
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
f1 (ppm)

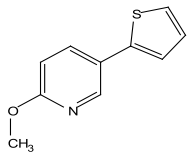

165.20
150.69
145.71
144.28
142.81
141.39
137.15
125.64
111.41
53.82
N
N
O
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

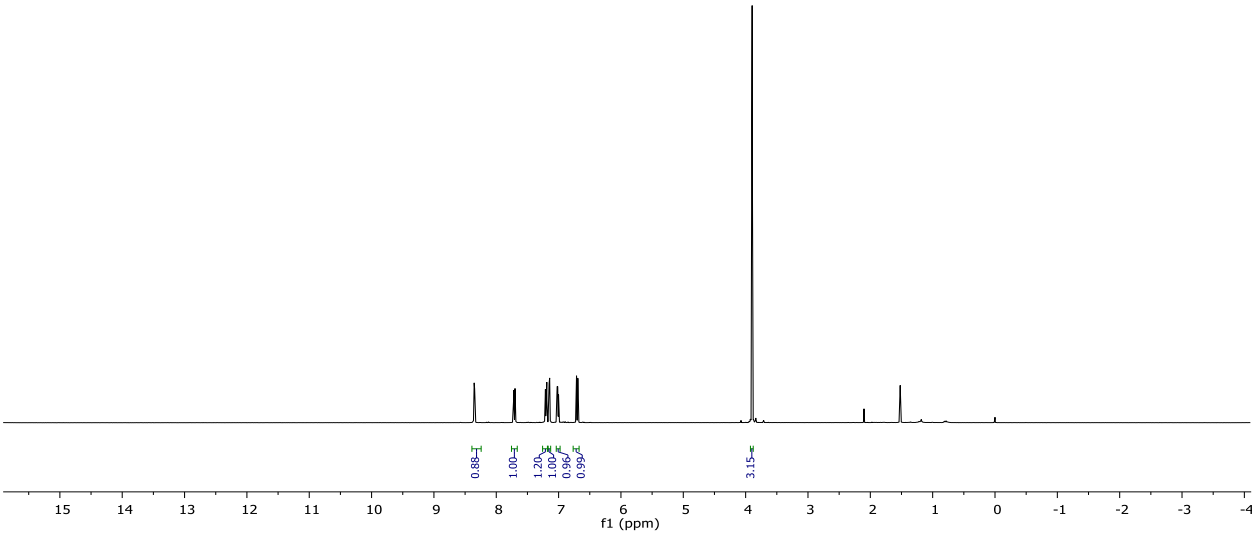

N
O
N
CH3

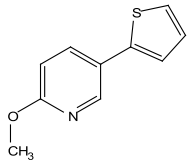

1.00
0.95
0.92
0.96
0.99
1.02
0.84
1.03
0.93
2.97
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


N
O
N
CH3

163.49
150.25
147.64
146.00
141.19
137.27
136.34
129.79
129.47
128.80
128.34
127.78
126.41
121.21
110.03
53.55
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


S
N
O
CH3


0.88
1.00
1.20
1.00
0.96
0.99
3.15
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


S
N
O
CH3

143.96
140.76
136.56
128.07
124.67
124.10
122.94
110.95
53.62
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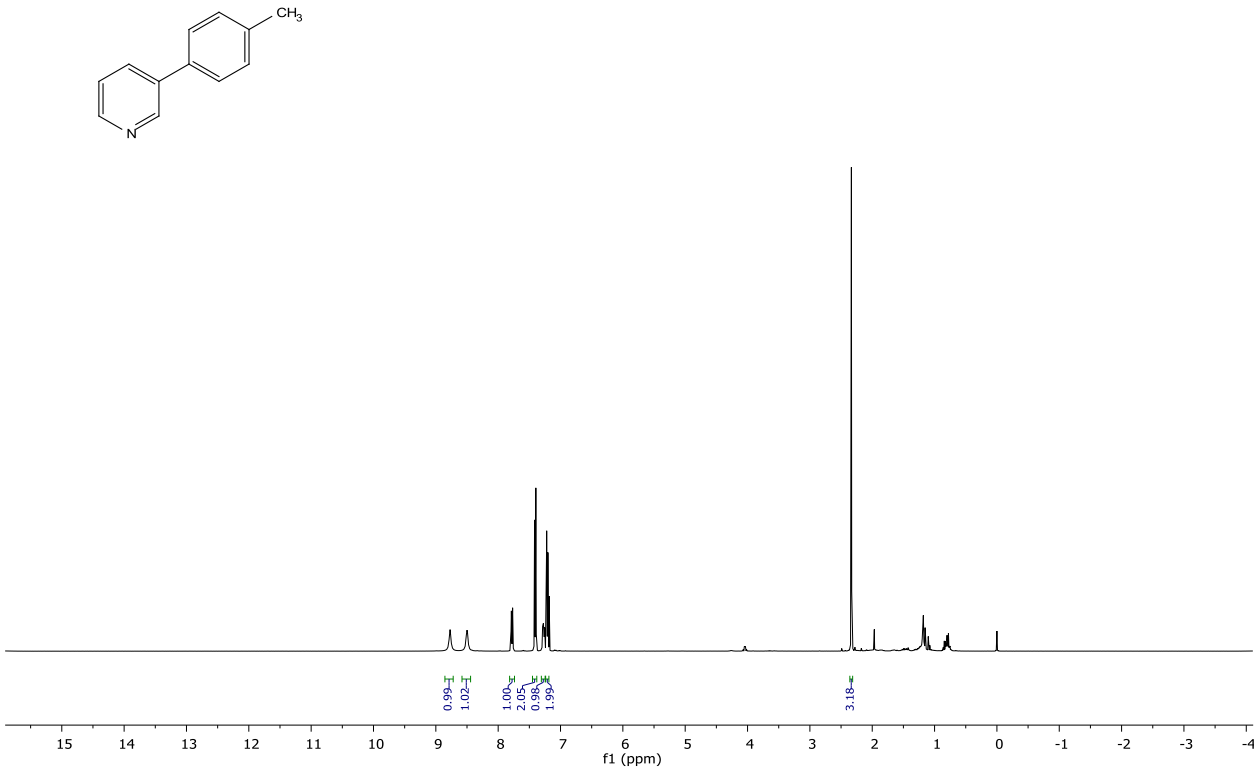
f1 (ppm)


CH3
N
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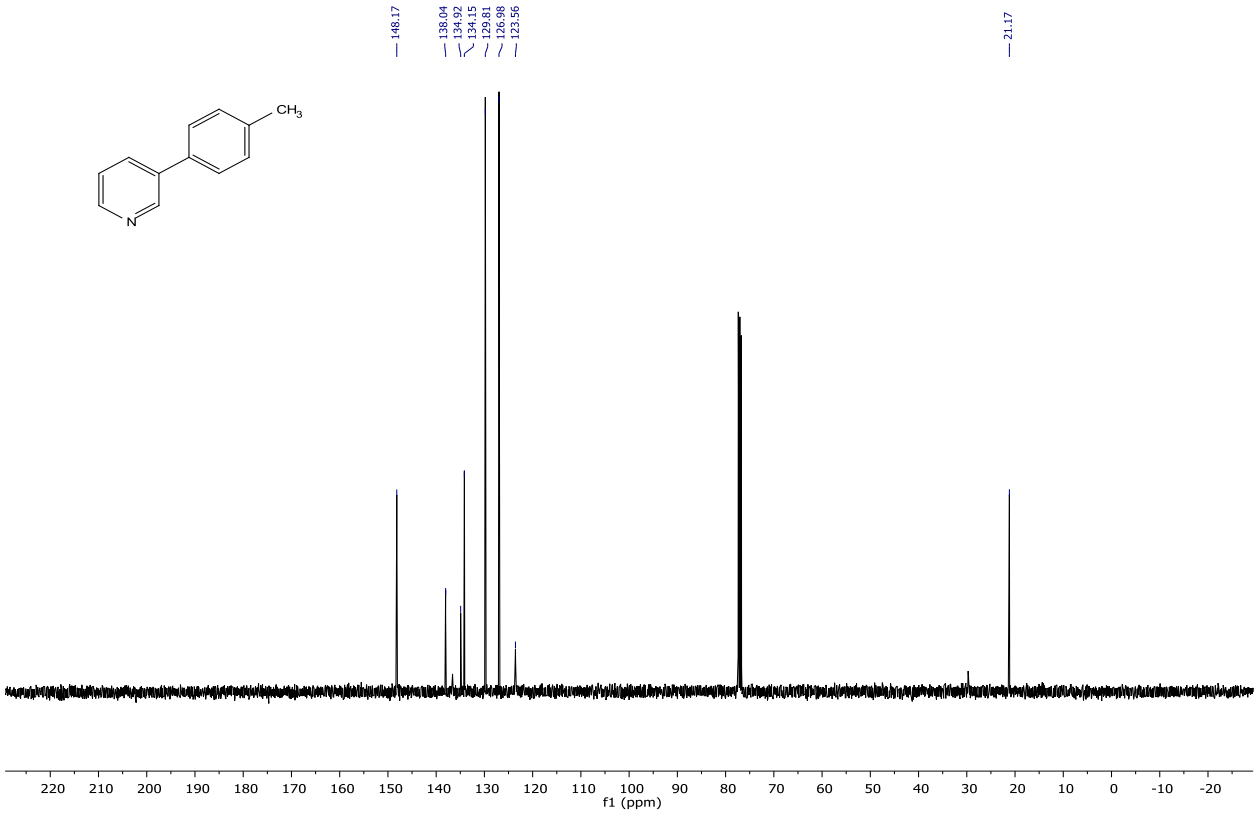
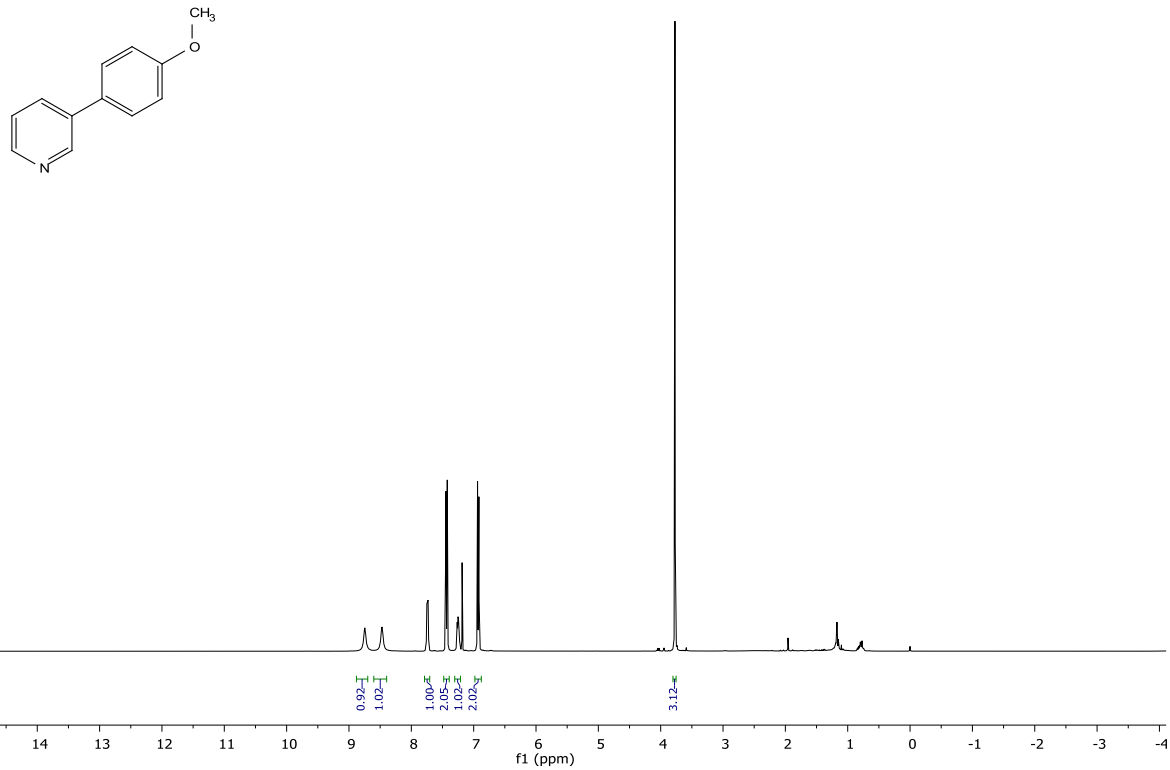
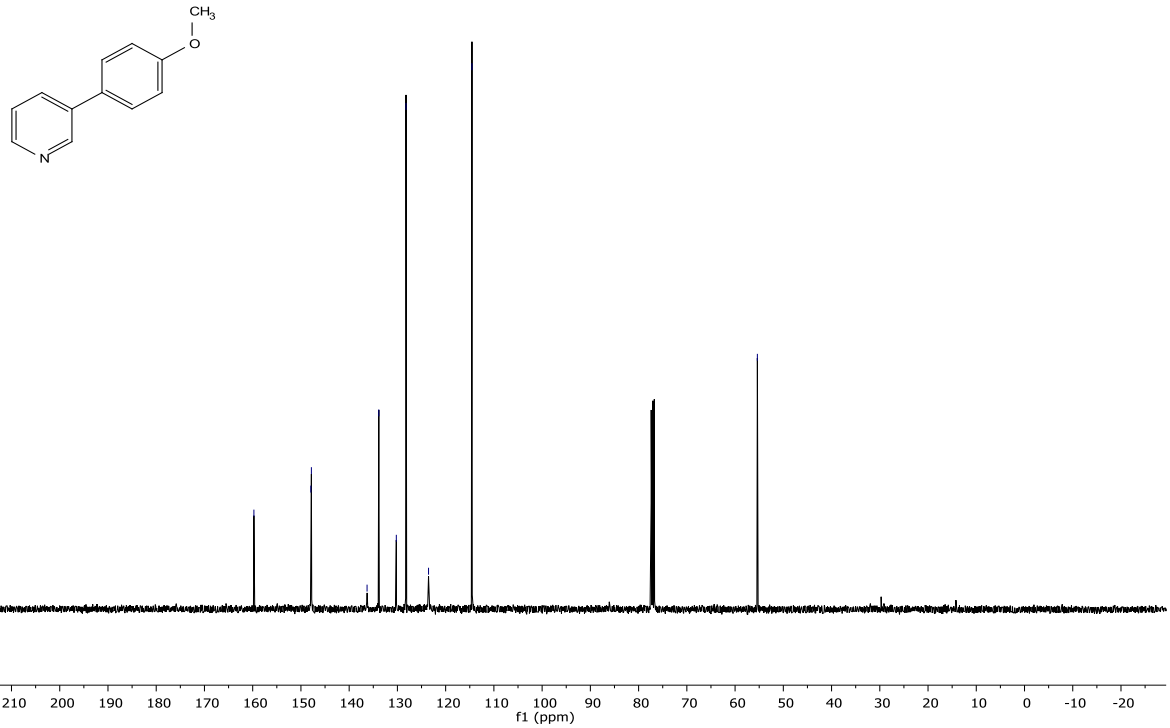
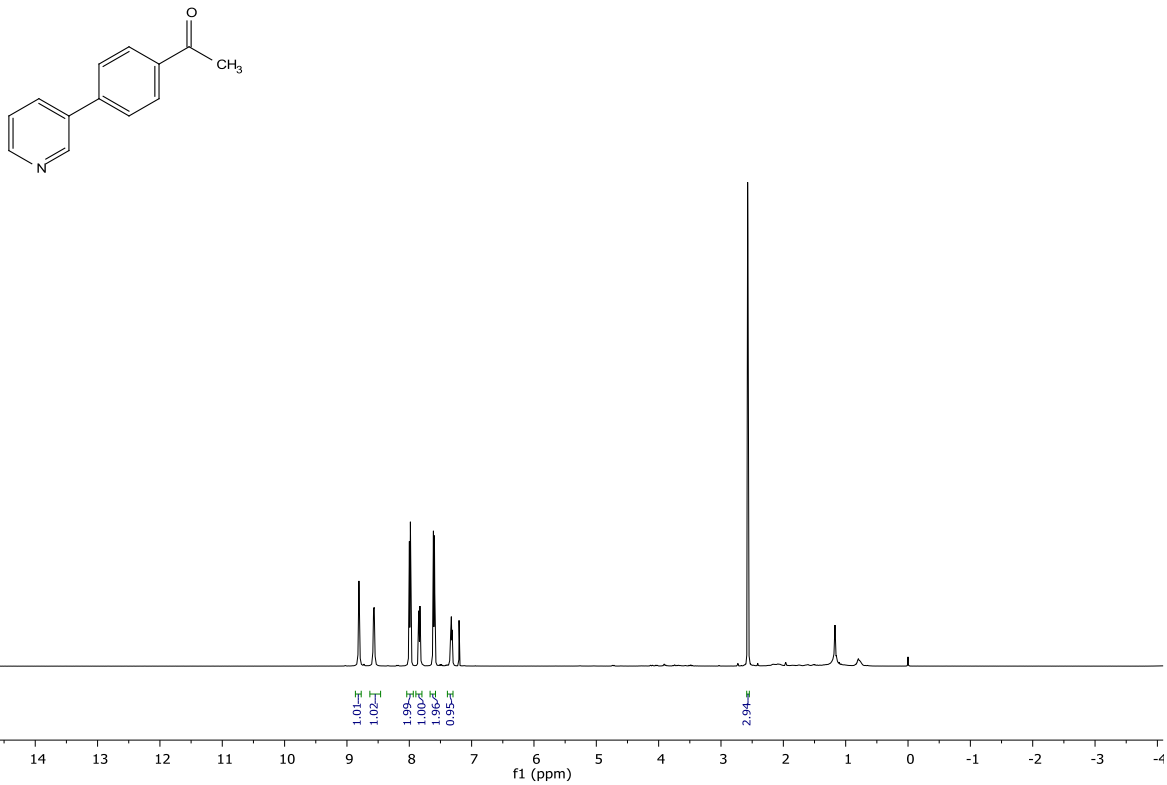
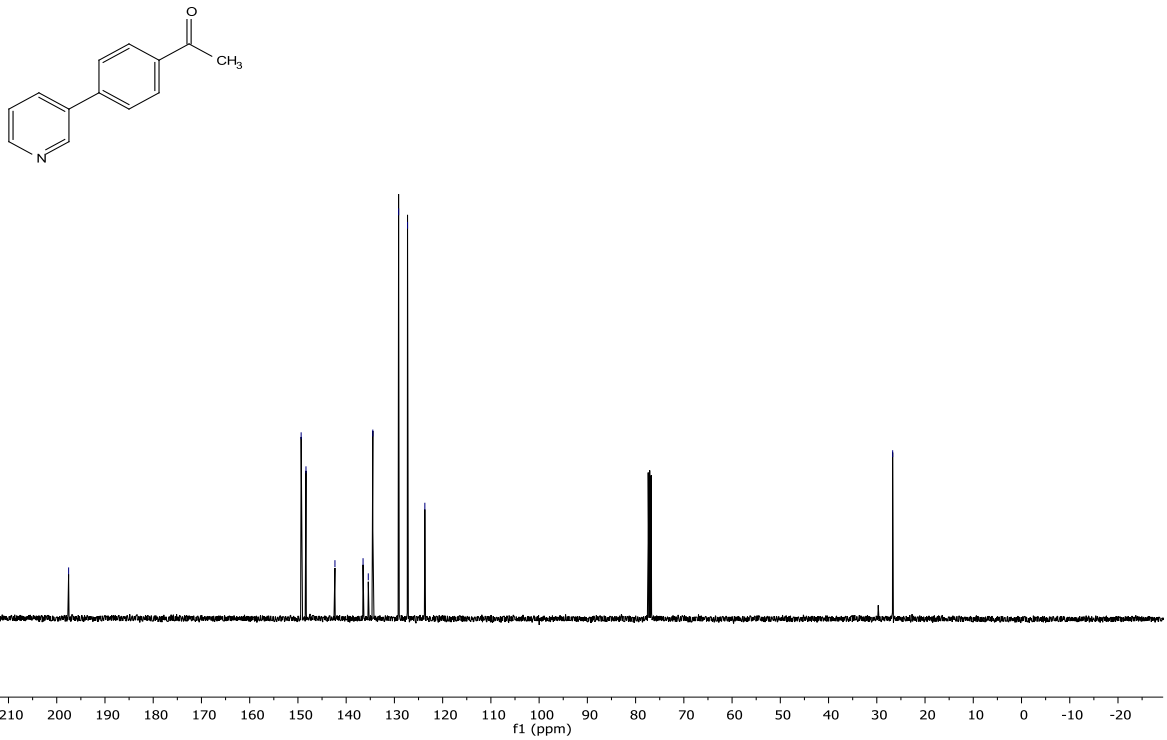
1.02
1.00
2.05
0.98
1.99
3.18
f1 (ppm)


148.17
138.04
134.92
134.15
129.81
126.98
123.56
21.17
CH3
N
f1 (ppm)


CH3
O
N
0.92
1.02
1.00
2.05
1.02
2.02
3.12
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


CH3
O
N
159.75
147.95
147.83
136.29
133.86
130.22
128.22
123.55
114.55
55.38
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


O
CH3
N
1.01
1.02
1.99
1.00
1.96
0.95
2.94
f1 (ppm)


O
CH3
N
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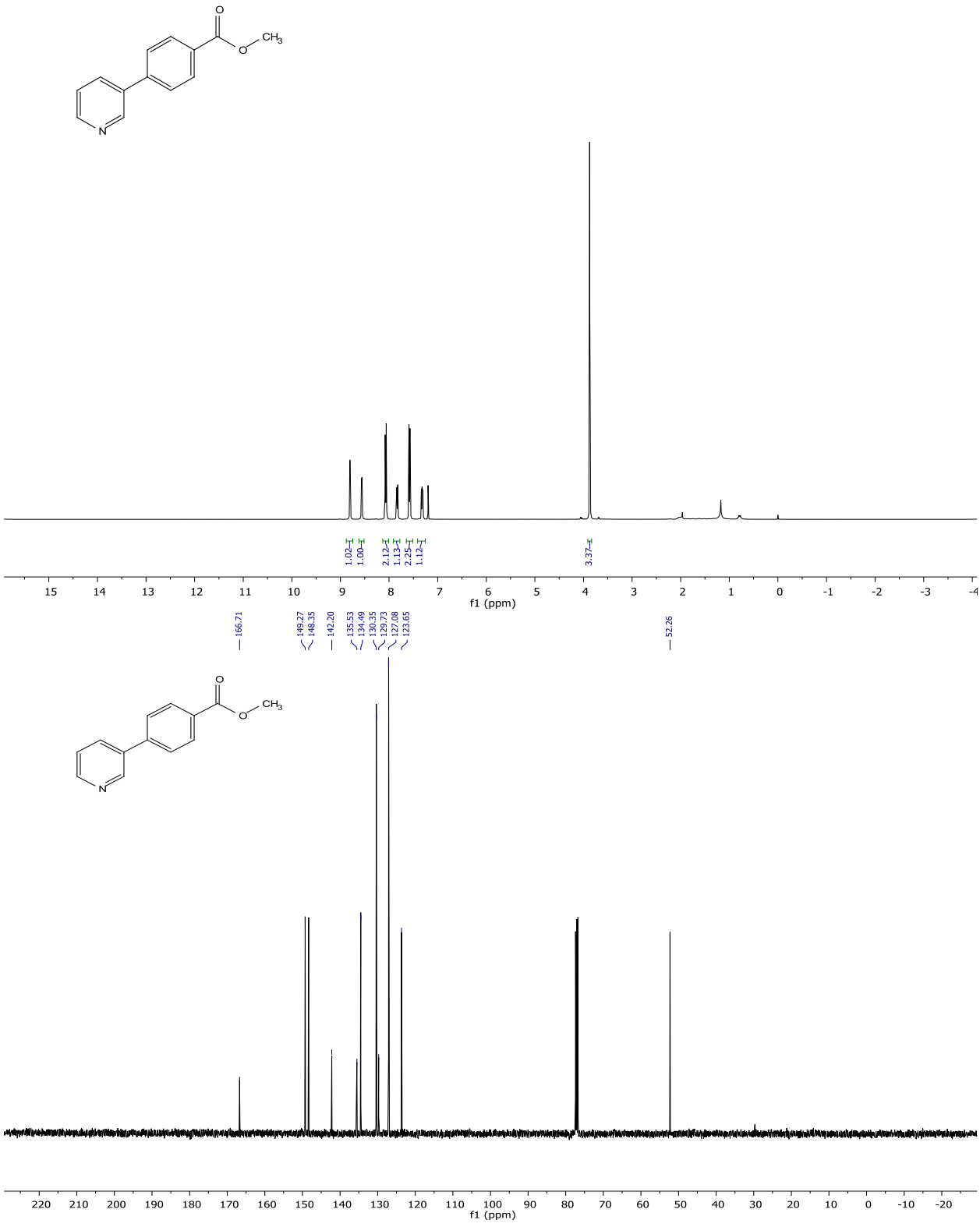
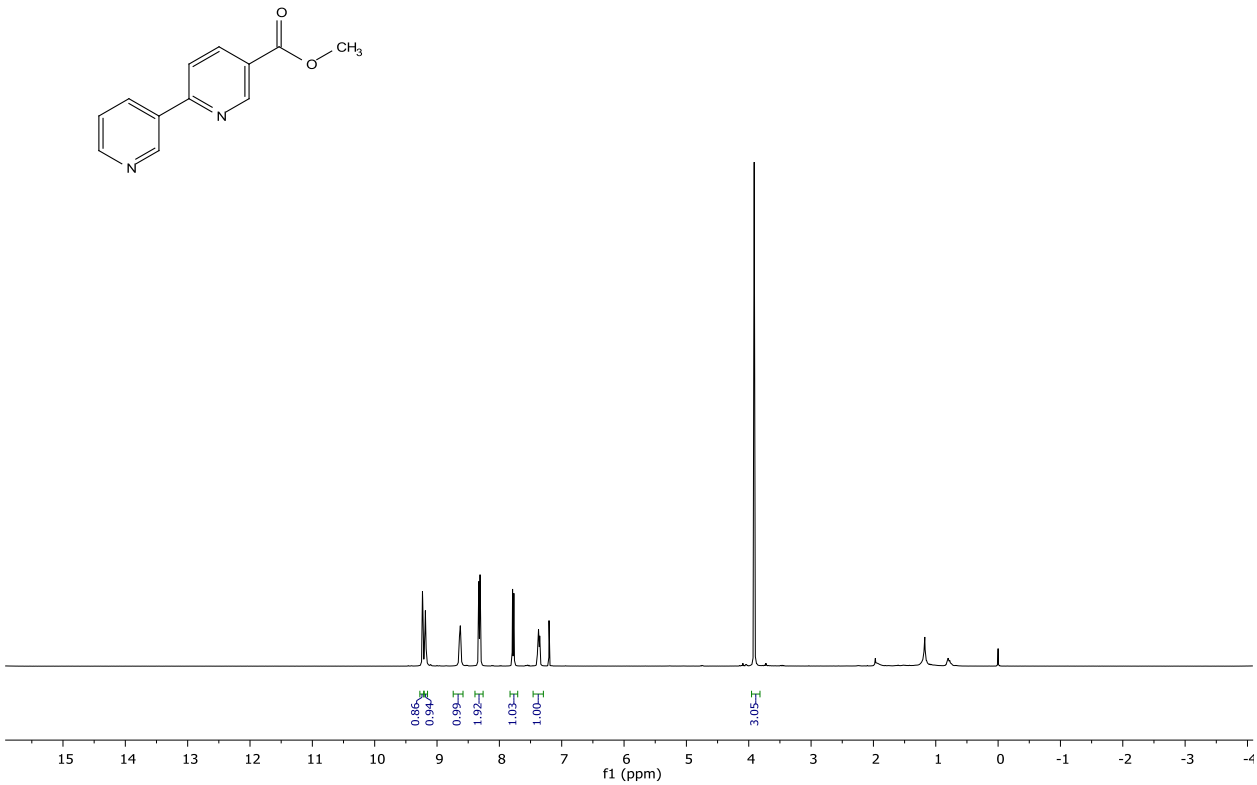
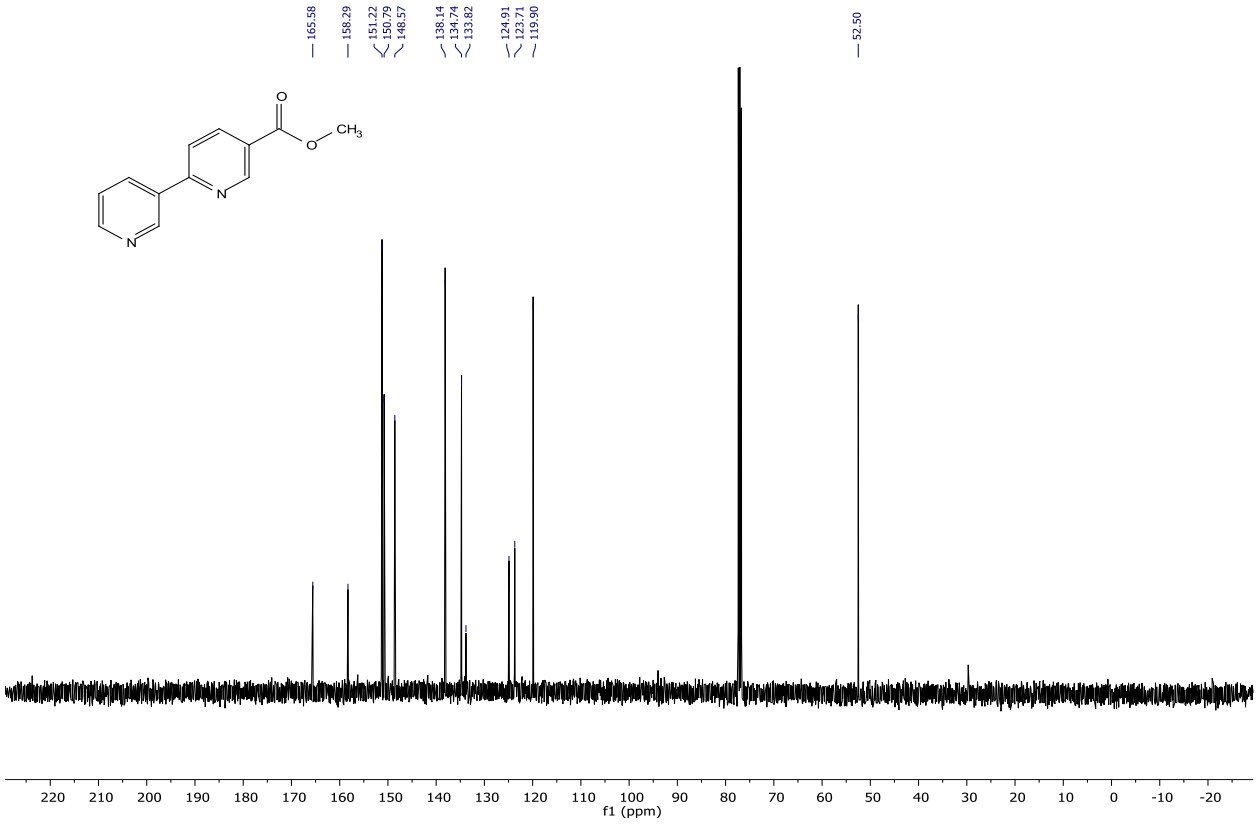
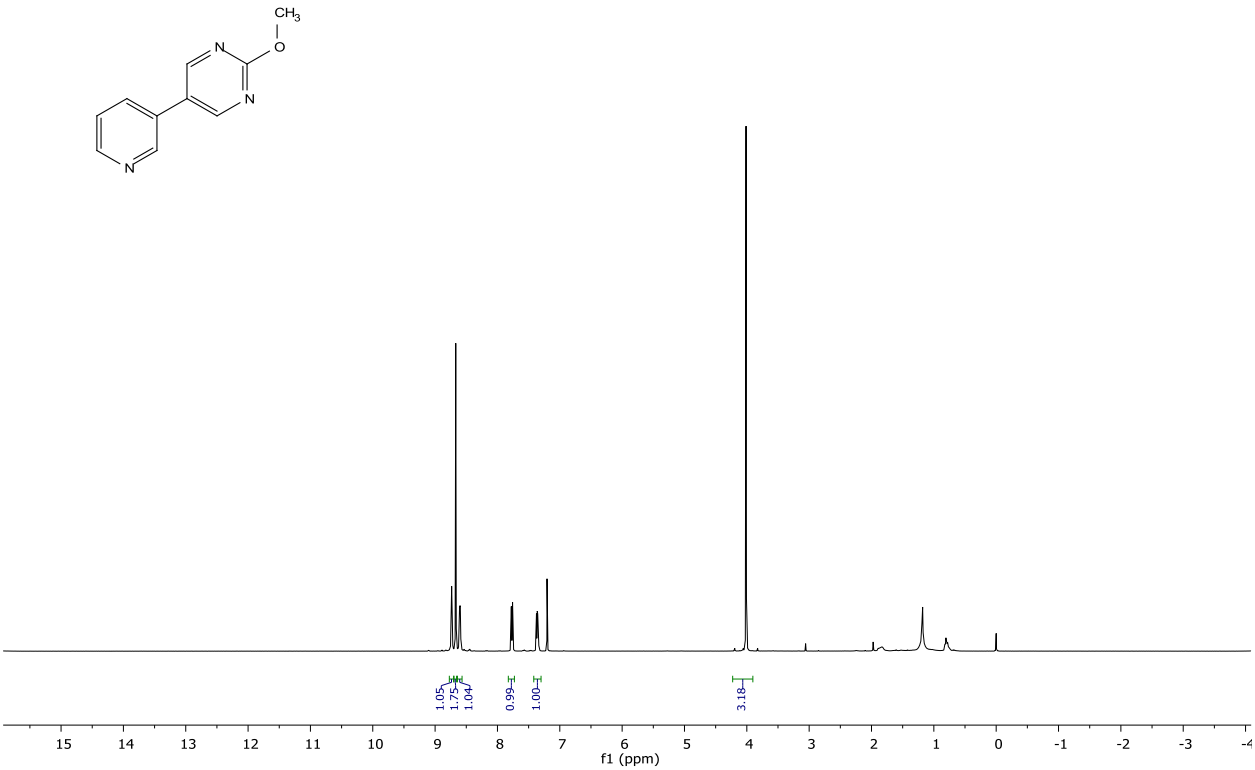
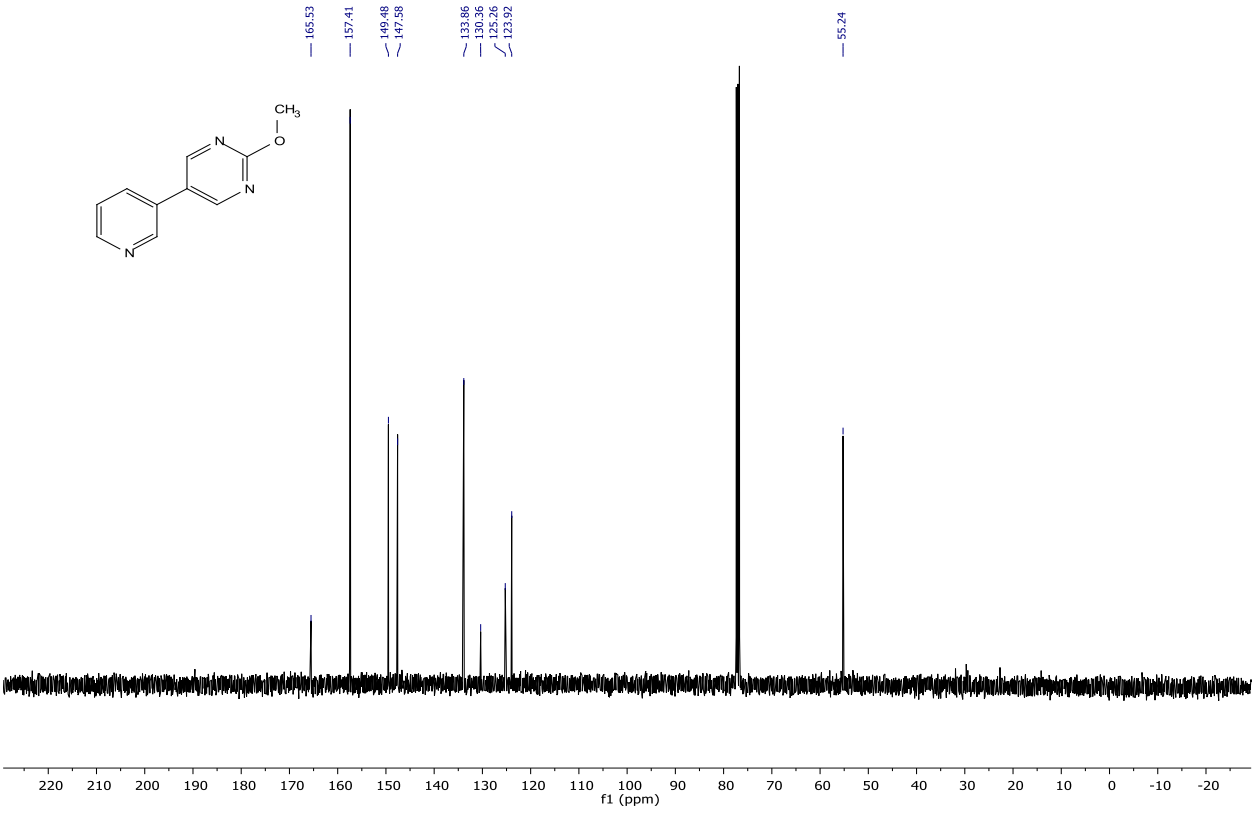
149.33
148.33
142.33
136.50
135.41
134.47
129.13
127.28
123.69
26.71
f1 (ppm)

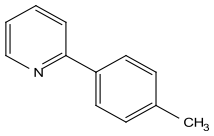

O
O
CH3
N
1.02
1.00
2.12
1.13
2.25
1.12
3.37
f1 (ppm)
166.71
149.27
148.35
142.20
135.53
134.49
130.35
129.73
127.08
123.65
52.26
f1 (ppm)

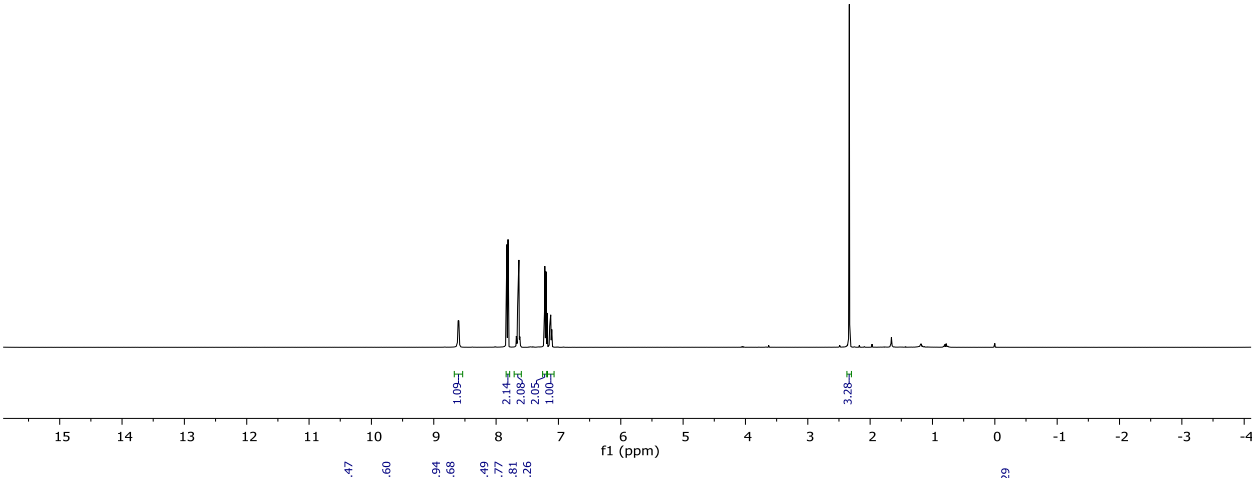

O
O
CH3
N
N
0.86
0.94
0.99
1.92
1.03
1.00
3.05
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
f1 (ppm)

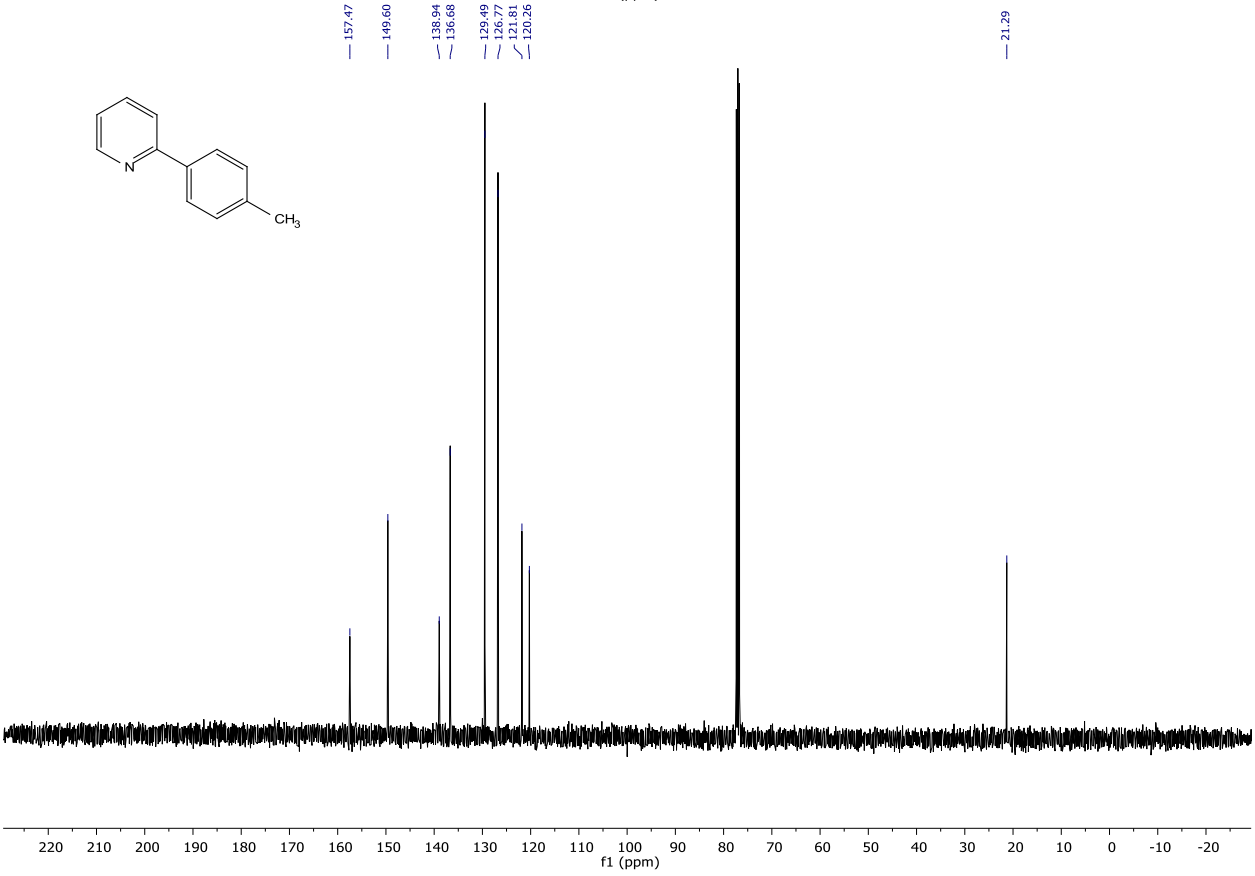

165.58
158.29
151.22
150.79
148.57
138.14
134.74
133.82
124.91
123.71
119.90
52.50
O
O
CH3
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

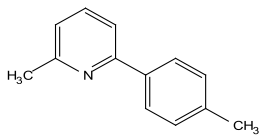

CH3
O
N
N
N
1.05
1.75
1.04
0.99
1.00
3.18
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3
f1 (ppm)

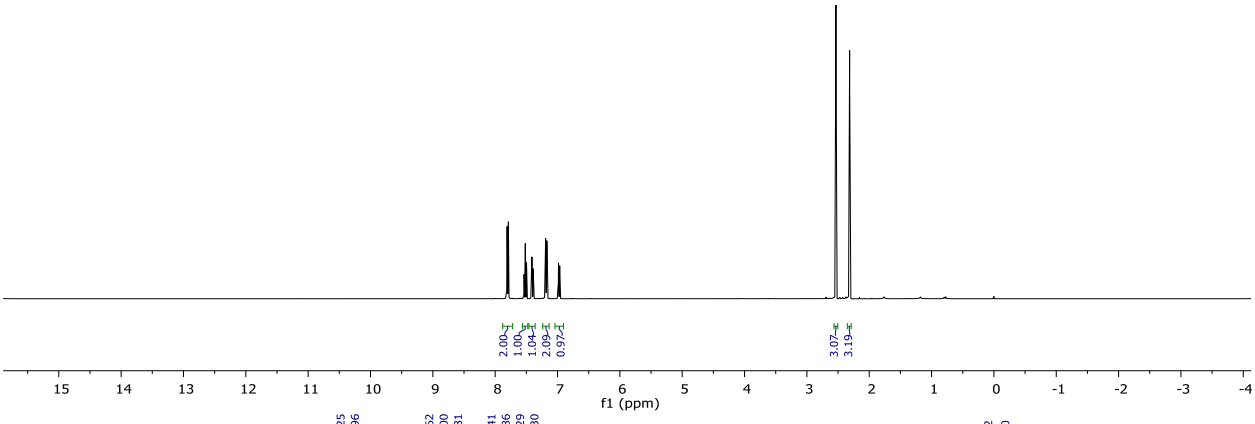

165.53
157.41
149.48
147.58
133.86
130.36
125.26
123.92
55.24
CH3
O
N
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

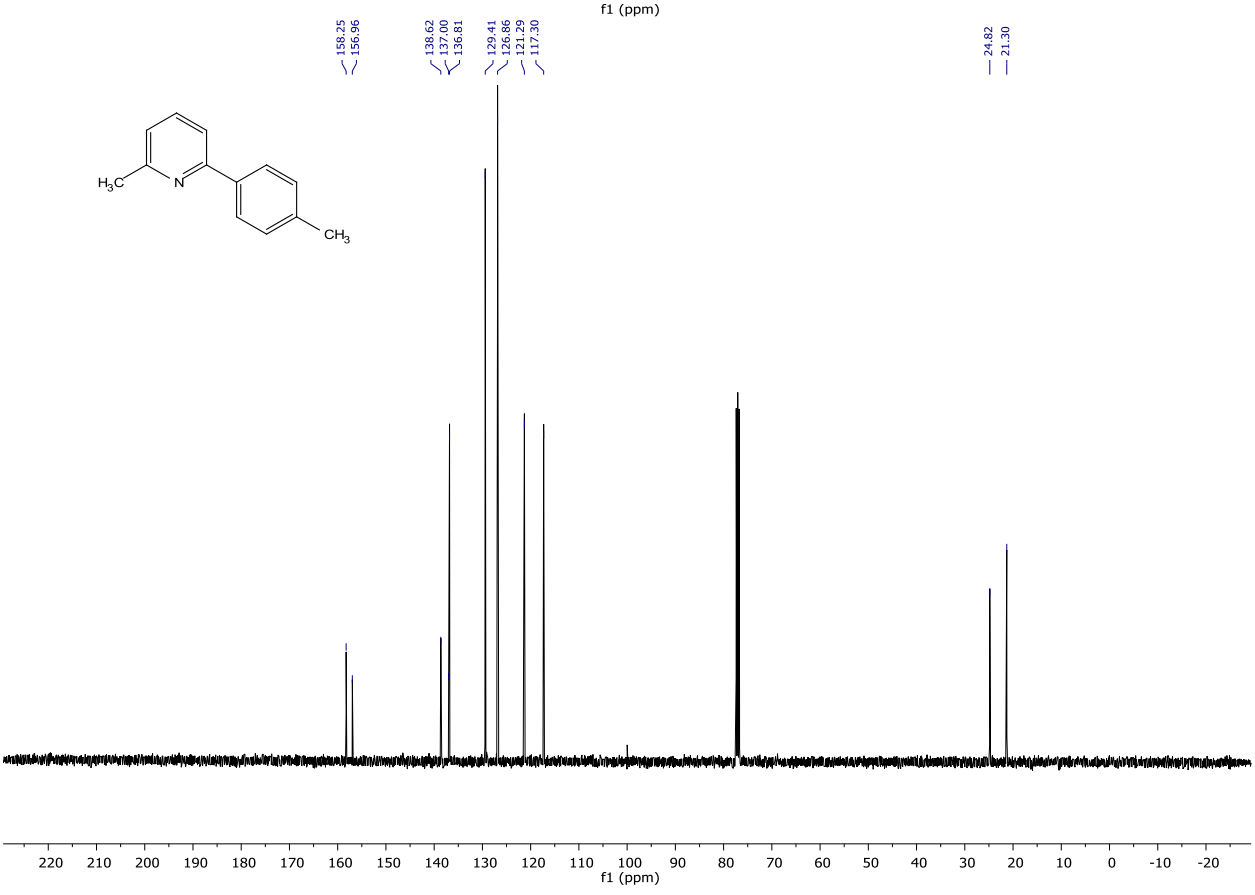

N
CH3


1.09
2.14
2.08
2.05
1.00
3.28
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


157.47
149.60
138.94
136.68
129.49
126.77
121.81
120.26
21.29
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


H3C
N
CH3


2.00
1.00
1.04
2.09
0.97
3.07
3.19
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)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156.96
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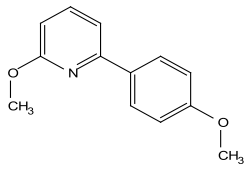
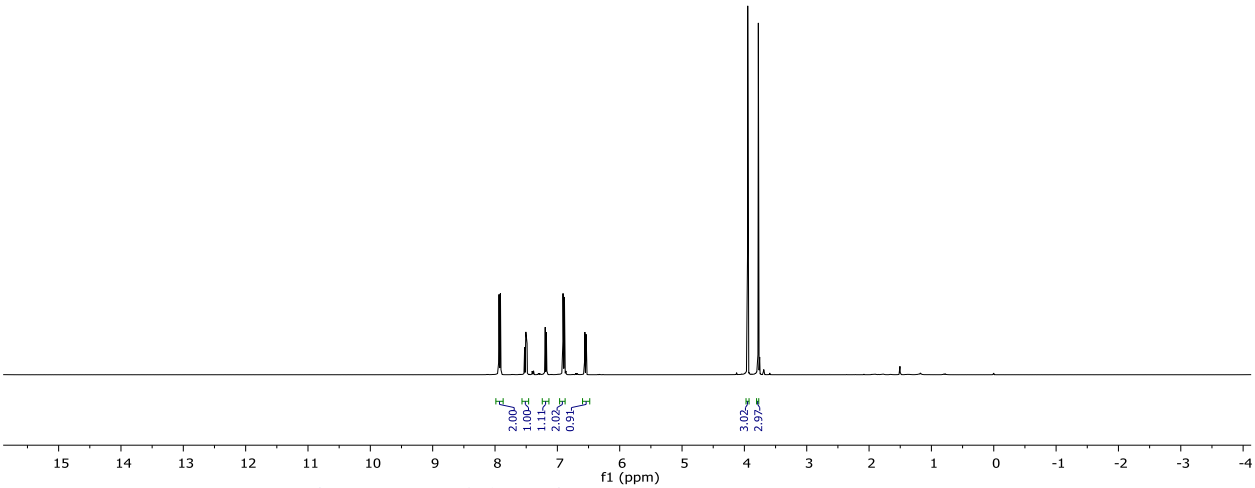
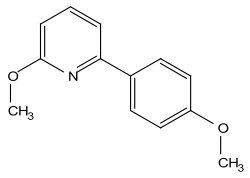
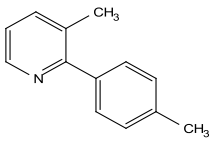
137.00
136.81
129.41
126.86
121.29
117.30
24.82
21.30
H3C
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

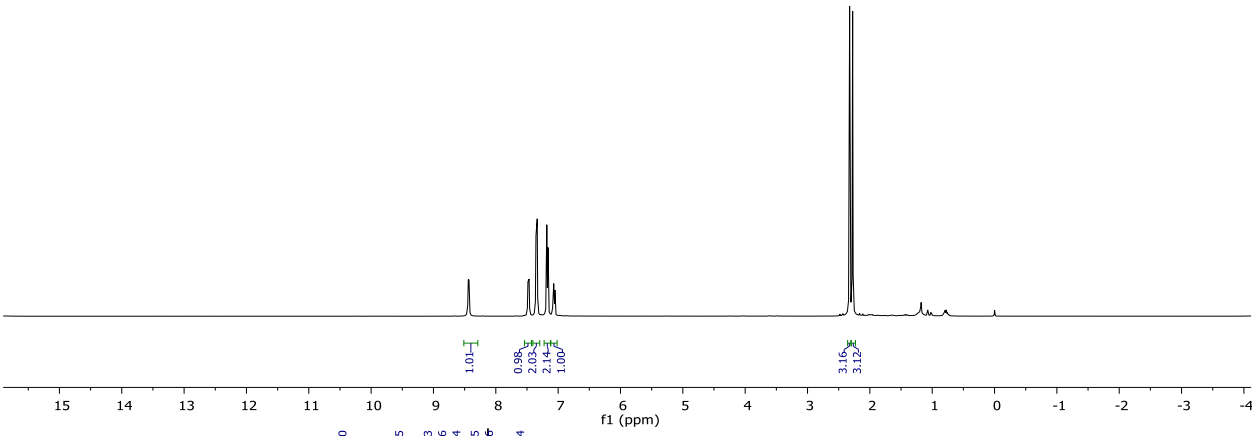

O
N
CH3
O
CH3


2.00
1.00
1.11
2.02
0.91
3.02
2.97
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


O
N
CH3
O
CH3

163.66
160.35
154.41
139.13
131.77
127.98
113.96
111.93
108.32
55.36
53.16
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


CH3
N
CH3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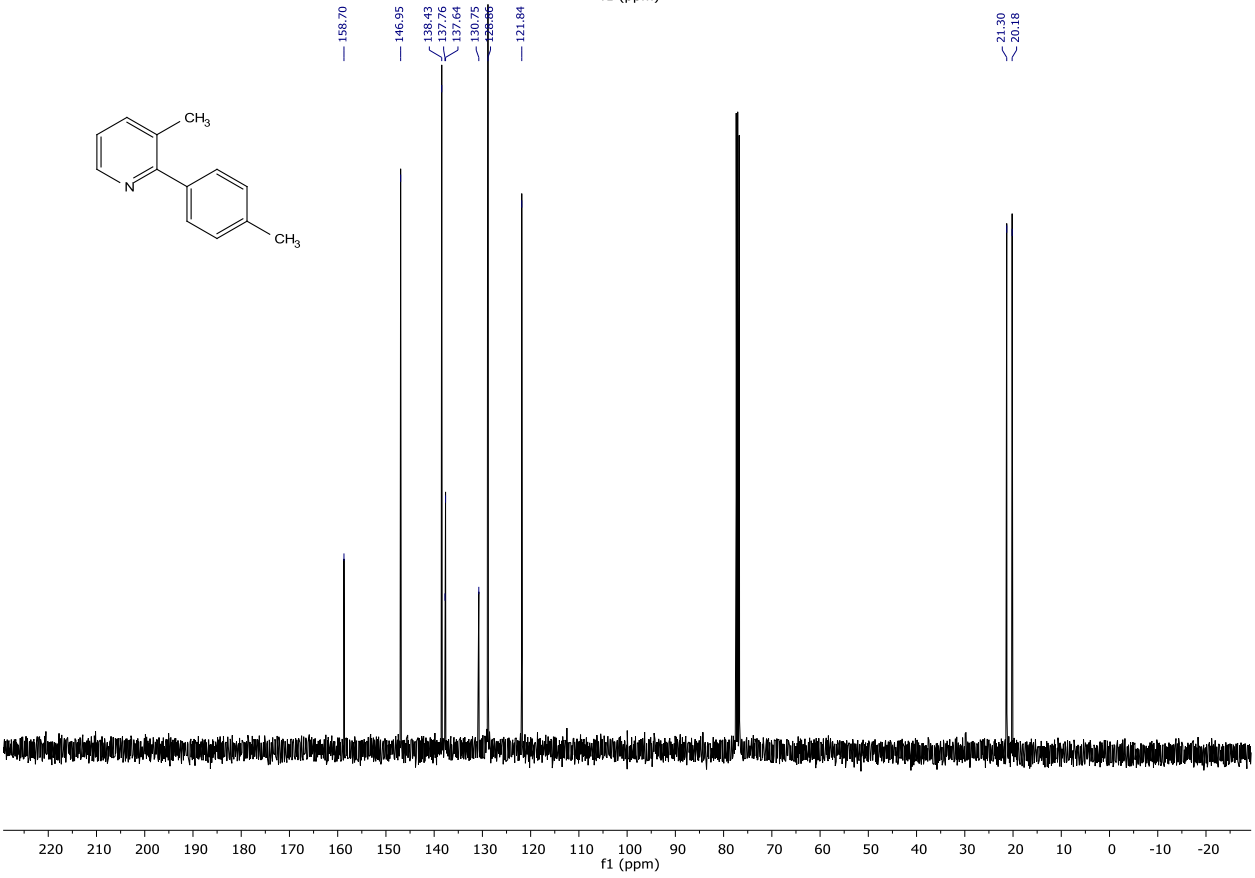
0.98
2.03
2.14
1.00
3.16
3.12
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)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137.64
130.75
121.84
21.30
20.18
CH3
N
CH3
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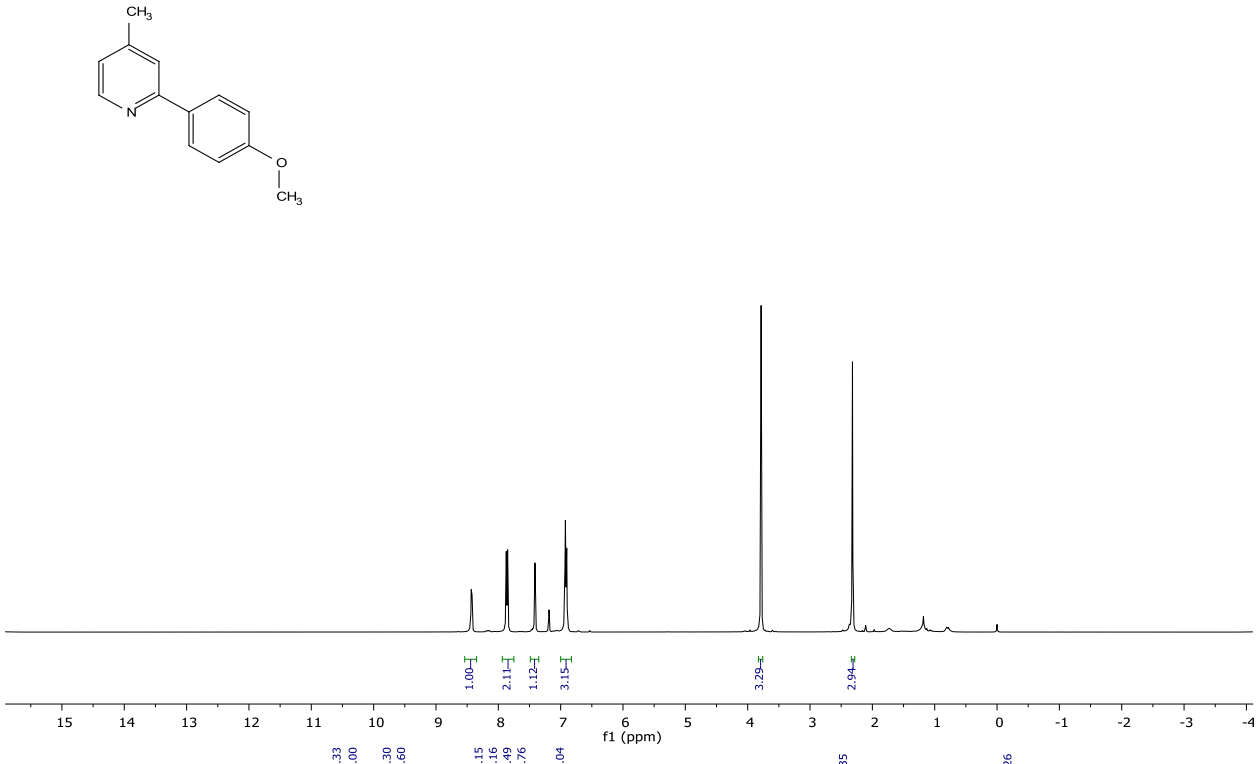
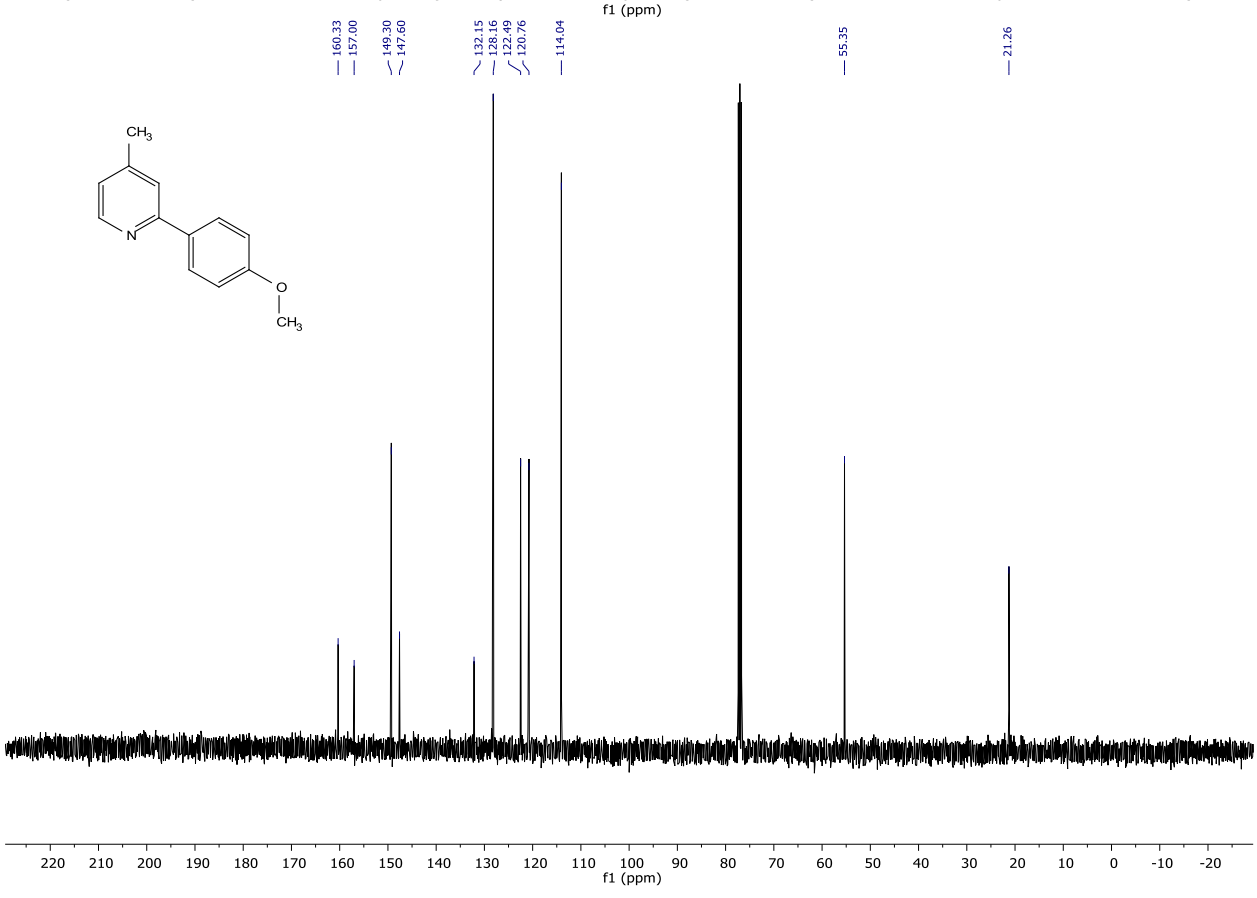
f1 (ppm)


CH3
N
O
CH3
1.00
2.11
1.12
3.15
3.29
2.94
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)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147.60
132.15
128.16
122.49
120.76
114.04
55.35
21.26
CH3
N
O
CH3
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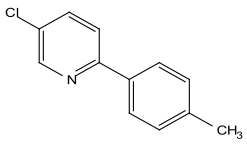
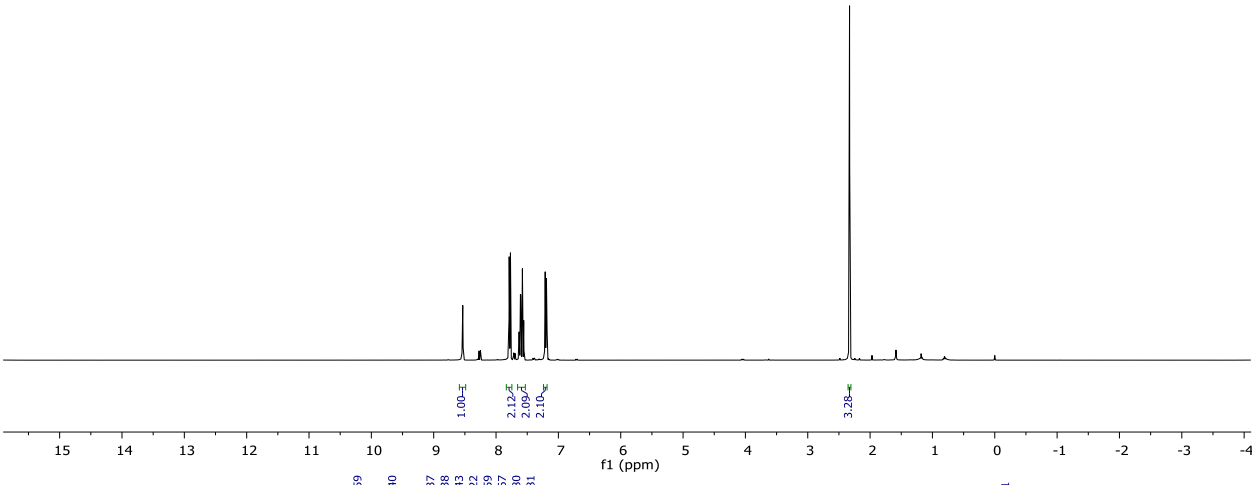
f1 (ppm)


Cl
N
CH3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2.12
2.09
2.10
3.28
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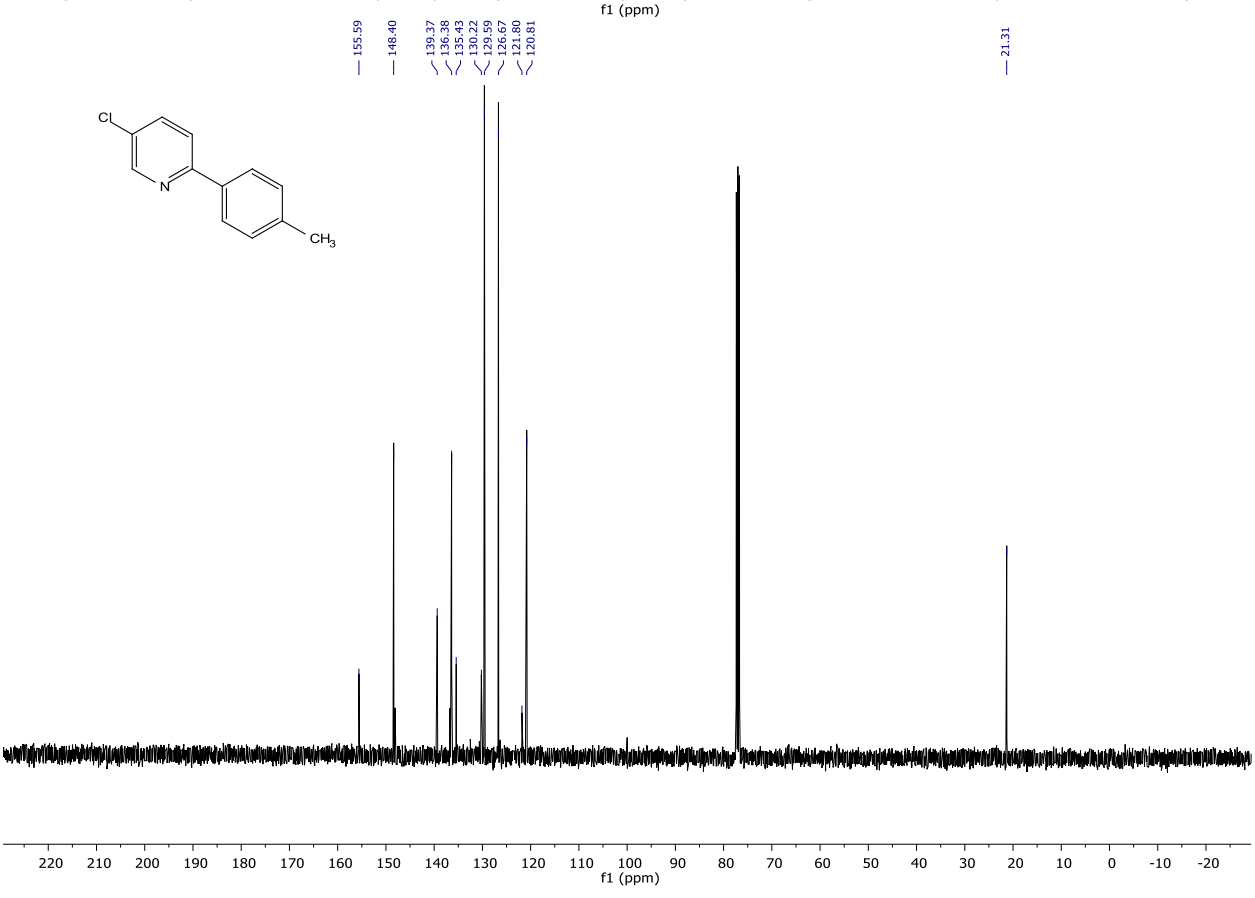
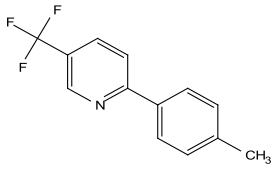
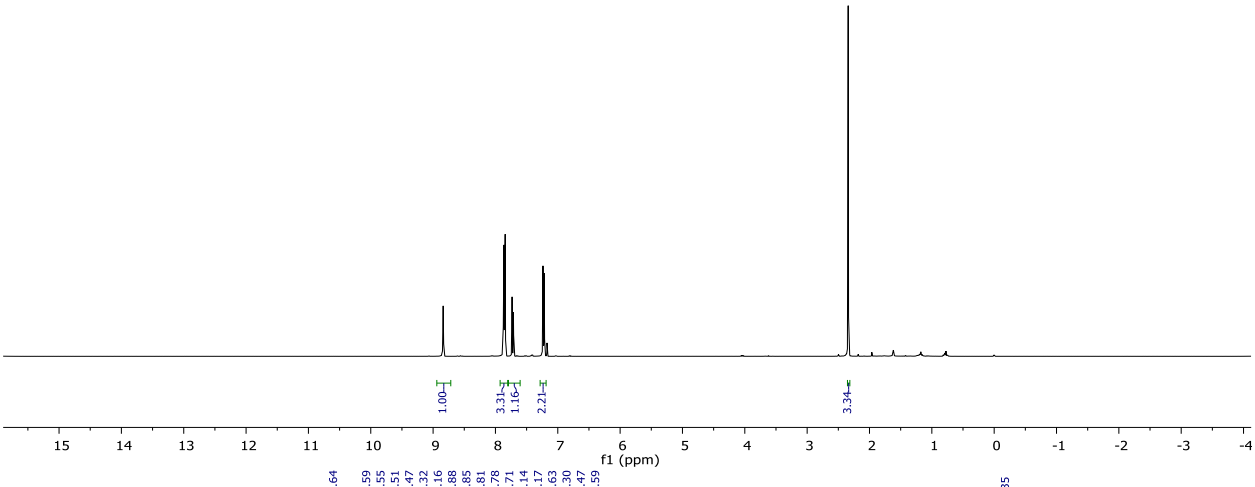
f1 (ppm)


155.59
148.40
139.37
136.38
135.43
130.22
129.59
126.67
121.80
120.81
21.31
Cl
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


F
F
F
N
CH3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3.31
1.16
2.21
3.34
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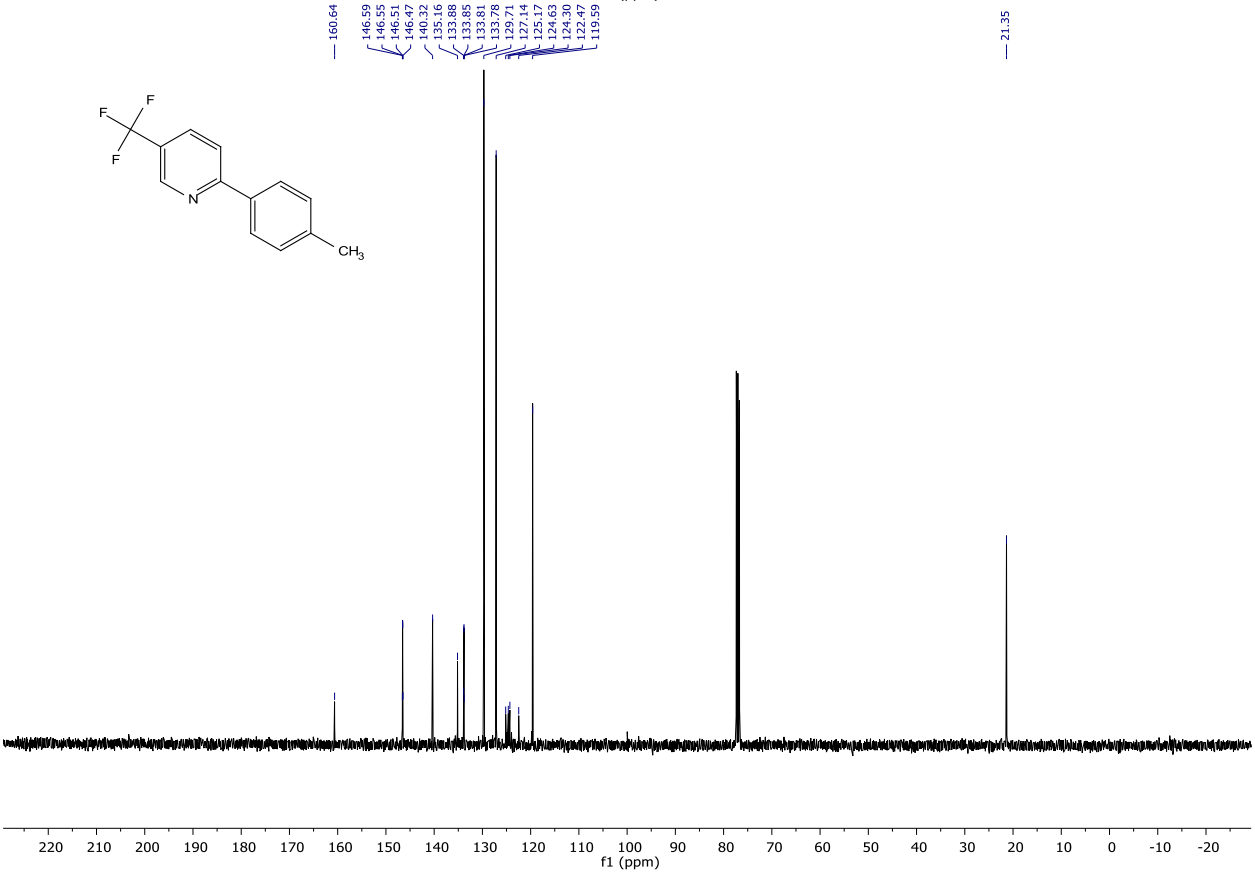
f1 (ppm)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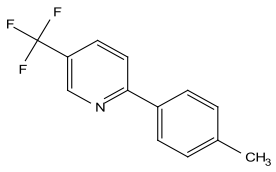
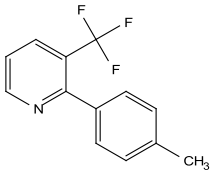
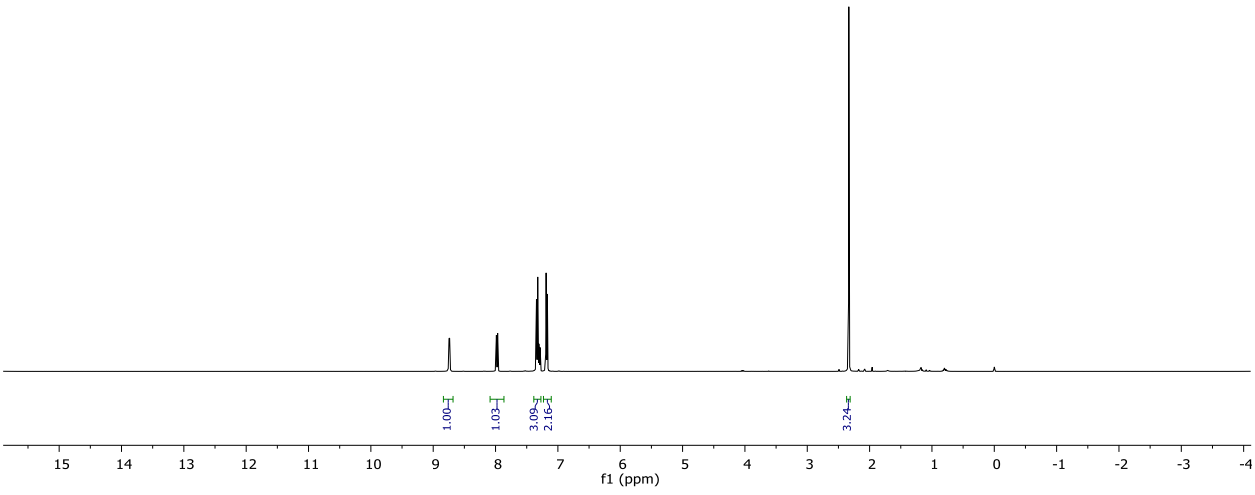
146.55
146.51
146.47
140.32
135.16
133.88
133.85
133.81
133.78
129.71
127.14
125.17
124.63
124.30
122.47
119.59
21.35
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

F
F
F
N
CH3


F
F
F
N
CH3

-62.19
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)


F
F
F
N
CH3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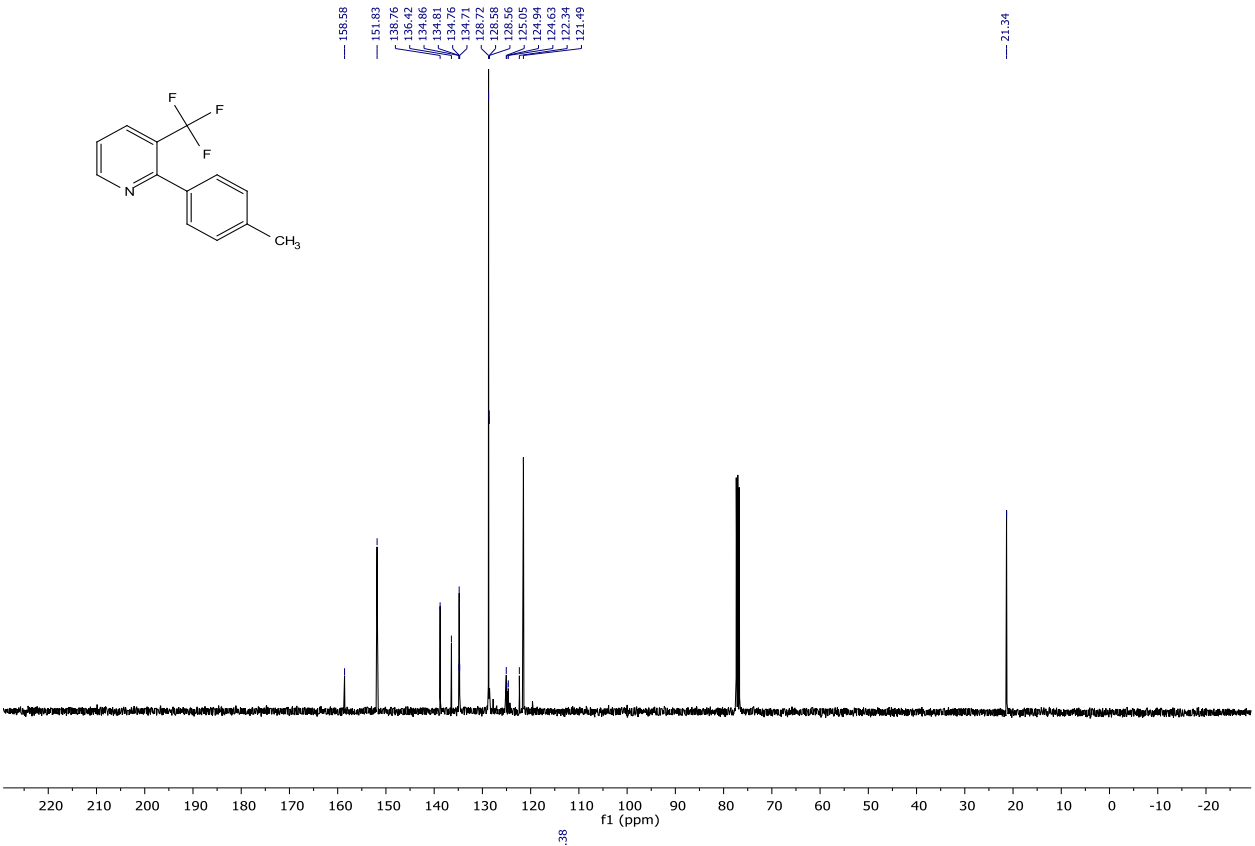
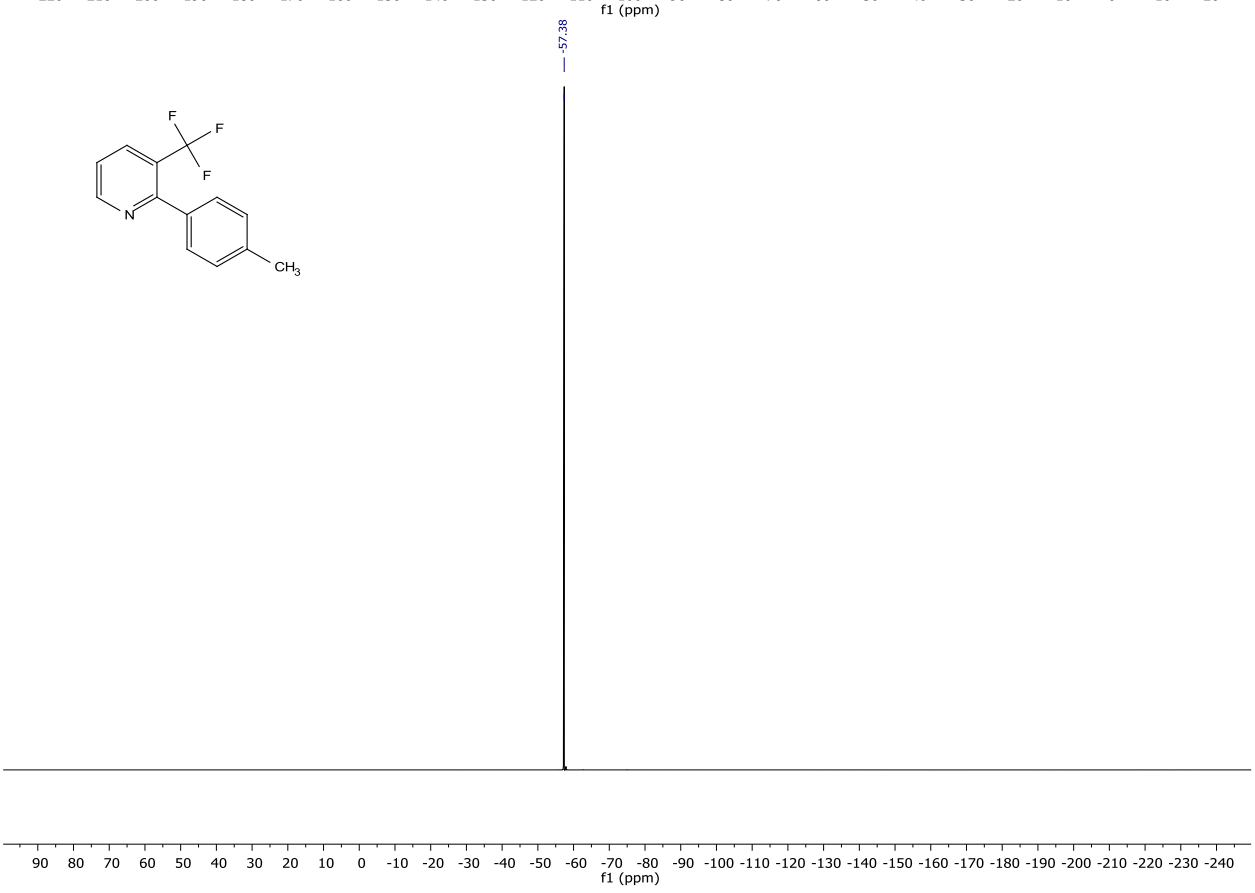
1.03
3.09
2.16
3.24
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


158.58
151.83
138.76
136.42
134.86
134.81
134.76
134.71
128.72
128.58
128.56
125.05
124.94
124.63
122.34
121.49
21.34
F
F
F
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


-57.38
F
F
F
N
CH3
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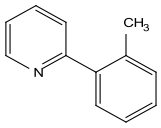
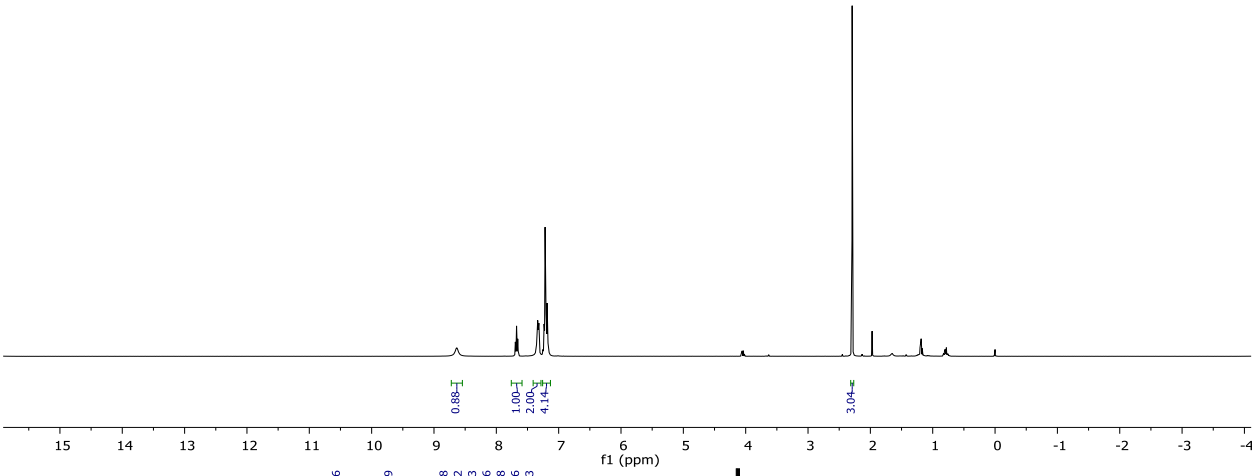
f1 (ppm)


CH3
N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2.00
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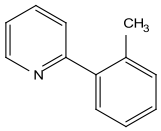
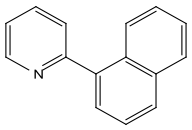
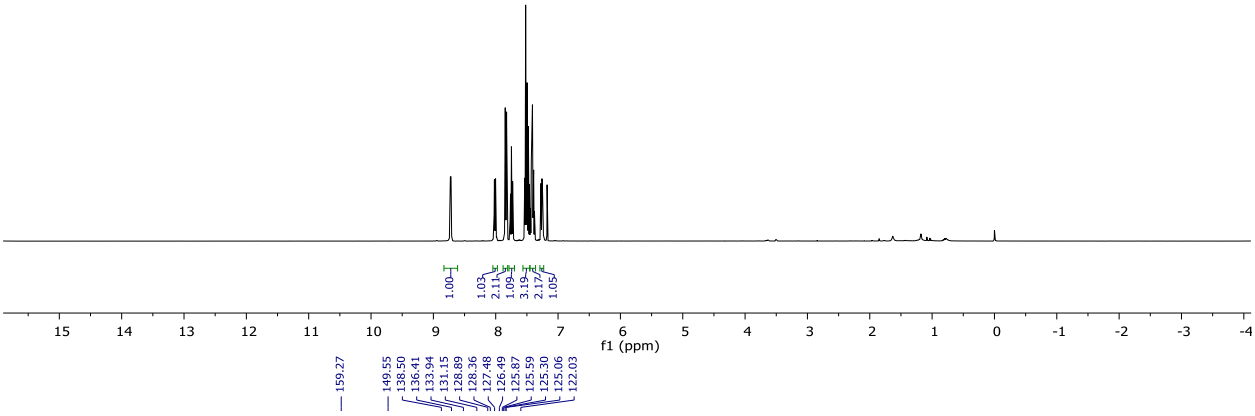
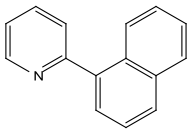
f1 (ppm)


CH3
N

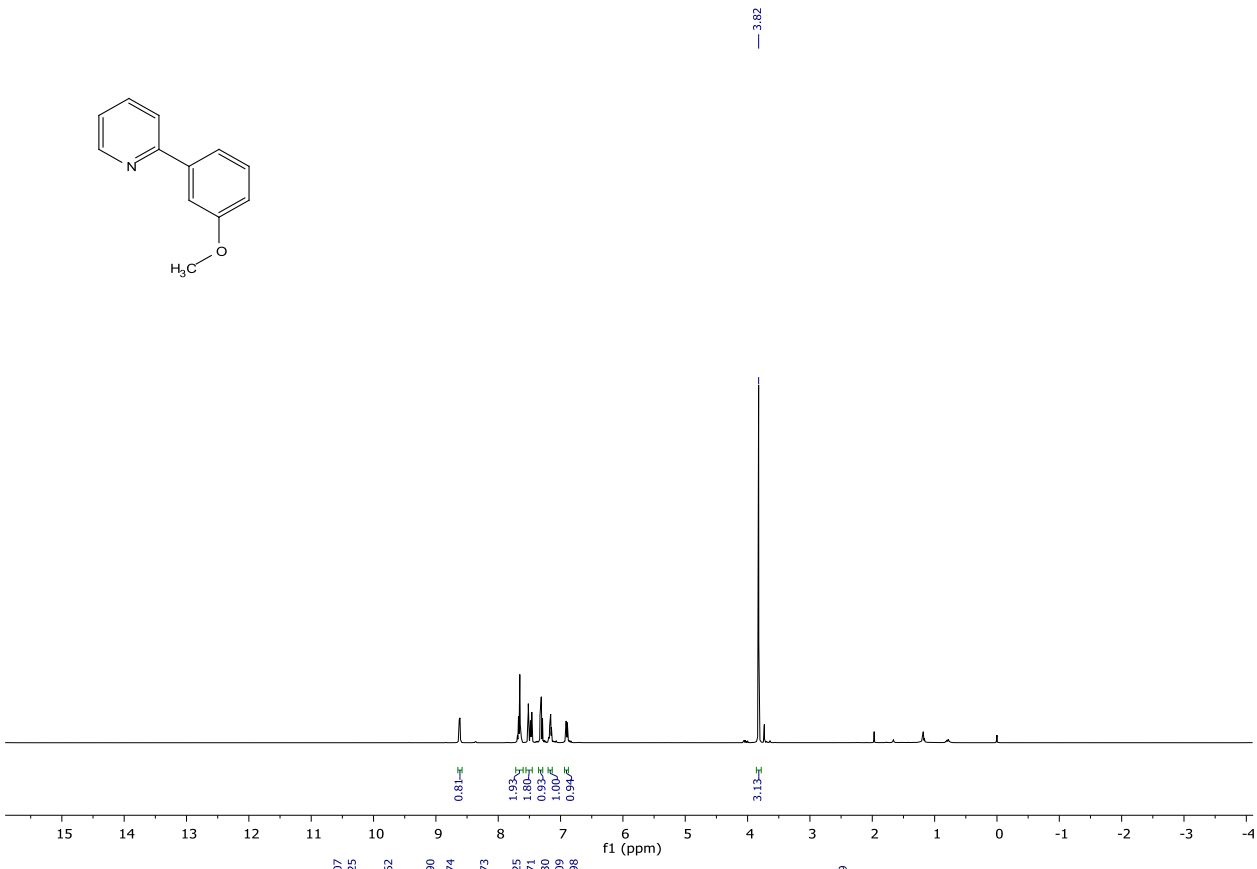
160.06
149.19
136.08
135.72
130.73
128.26
125.88
124.16
121.63
20.30
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)




1.00
1.03
2.11
1.09
3.19
2.17
1.05
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)



159.27
149.55
138.50
136.41
133.94
131.15
128.89
128.36
127.48
126.49
125.87
125.59
125.30
125.06
122.03
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


3.82
N
O
H3C
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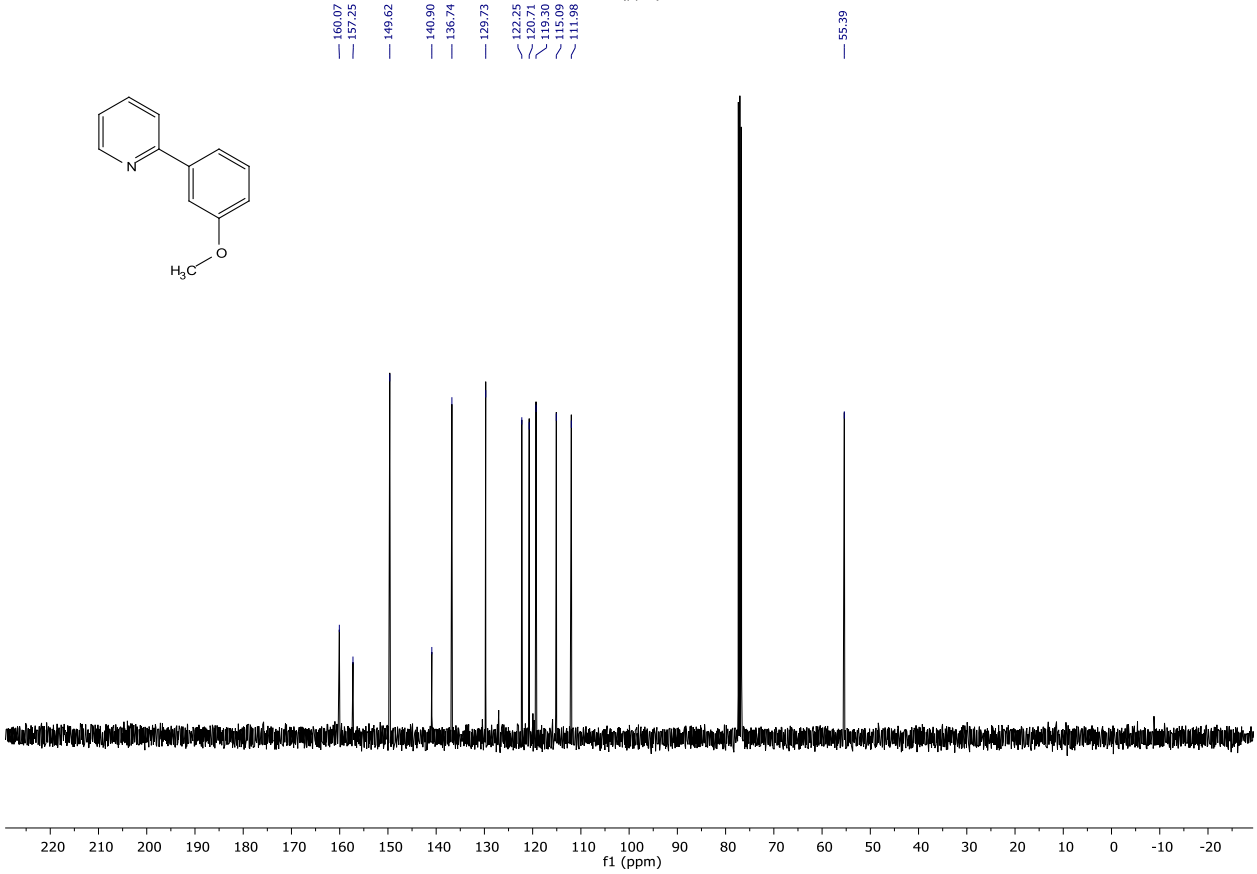
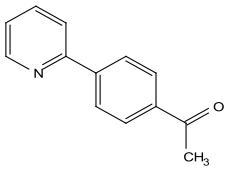
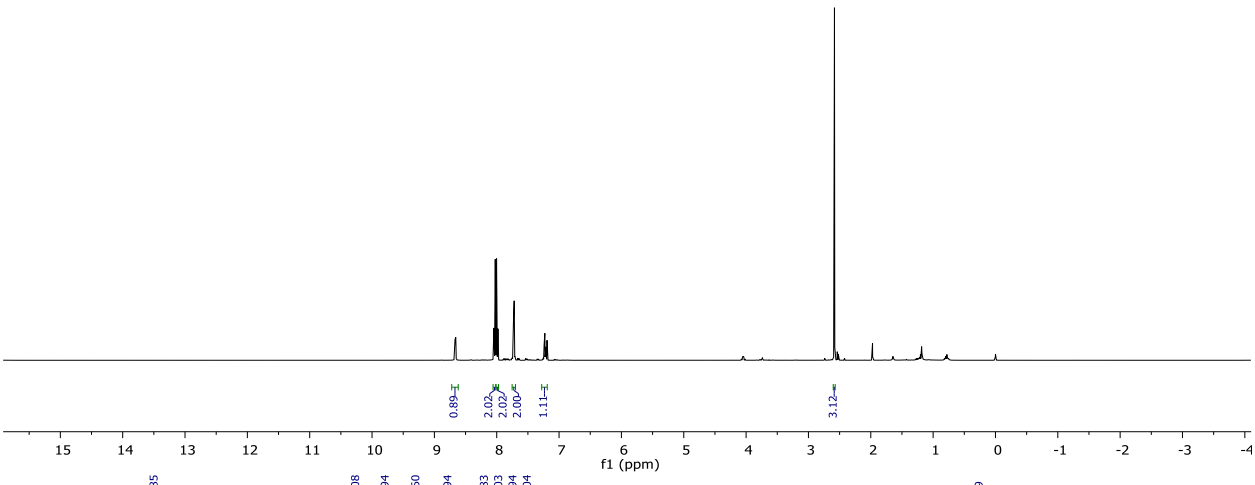
1.93
1.80
0.93
1.00
0.94
3.13
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


160.07
157.25
149.62
140.90
136.74
129.73
122.25
120.71
119.30
115.09
111.98
55.39
N
O
H3C
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


N
O
CH3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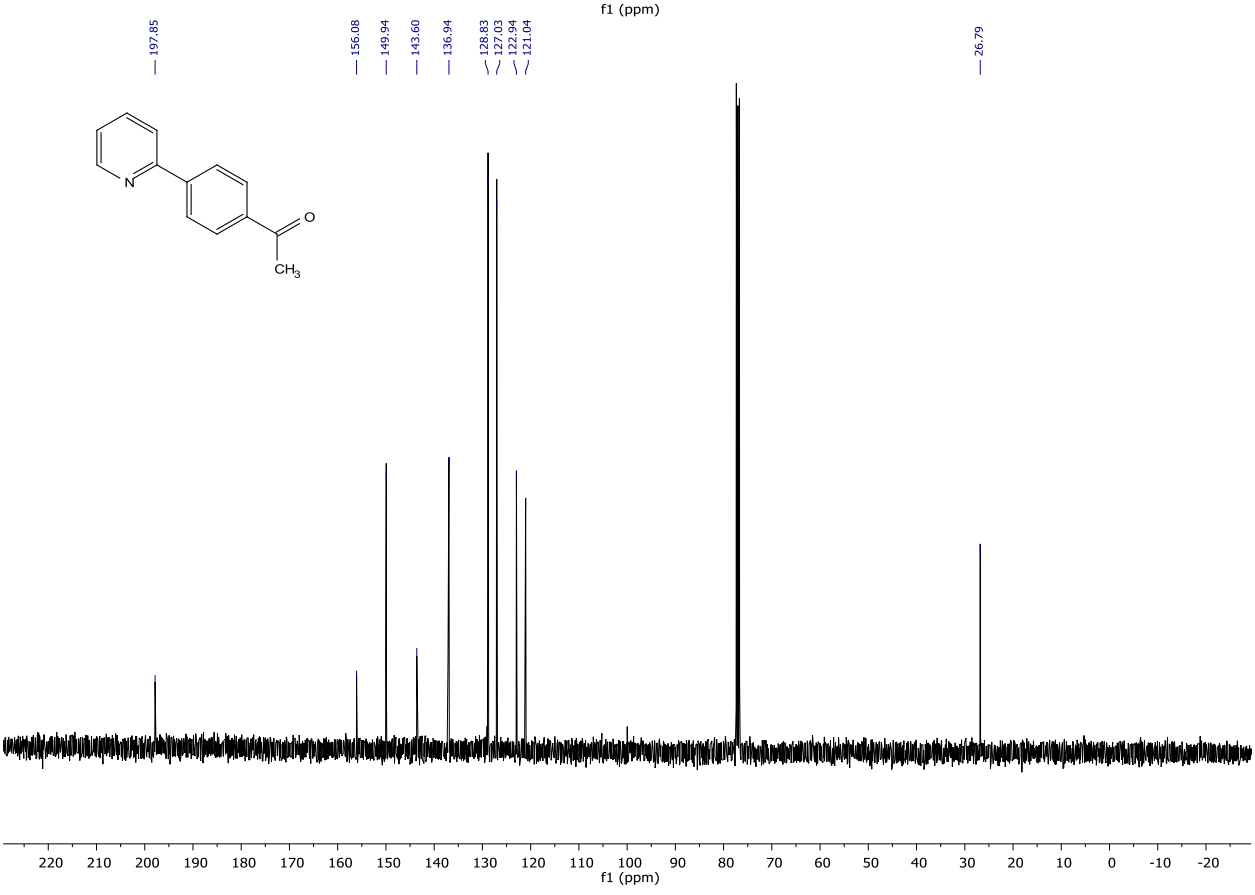
2.02
2.02
2.00
1.11
3.12
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)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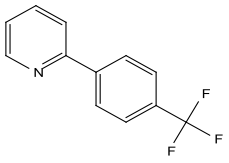
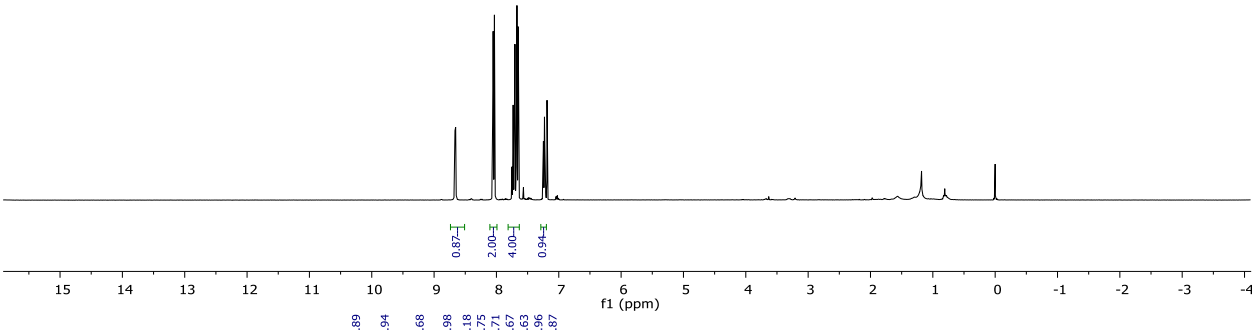
149.94
143.60
136.94
128.83
127.03
122.94
121.04
26.79
N
O
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


N
F
F
F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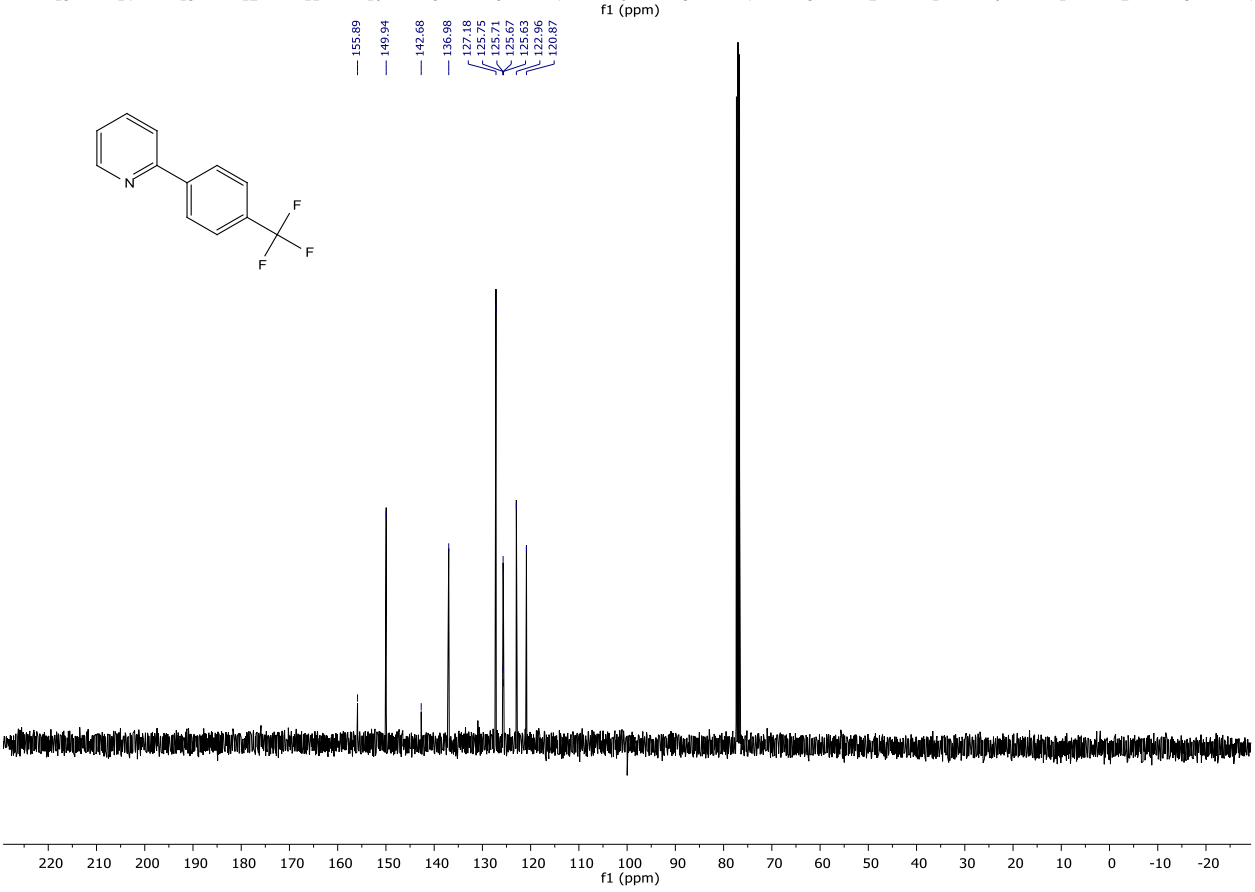
2.00
4.00
0.94
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)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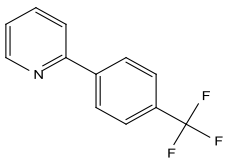
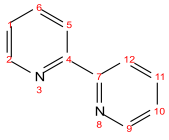
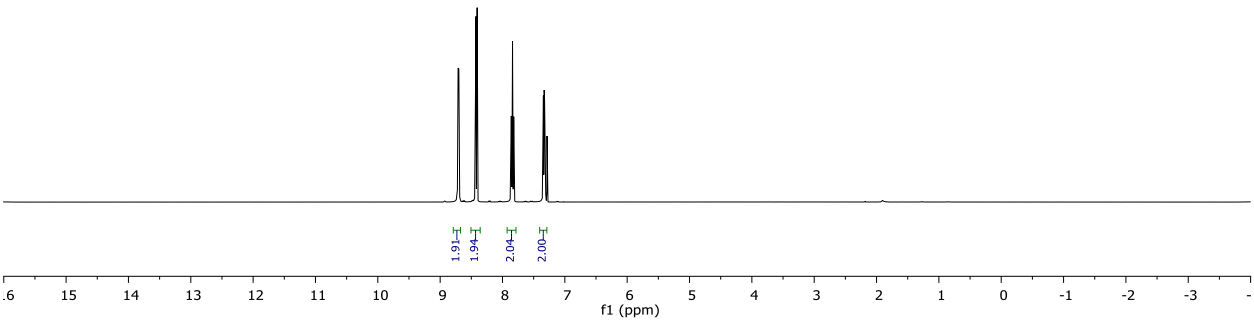
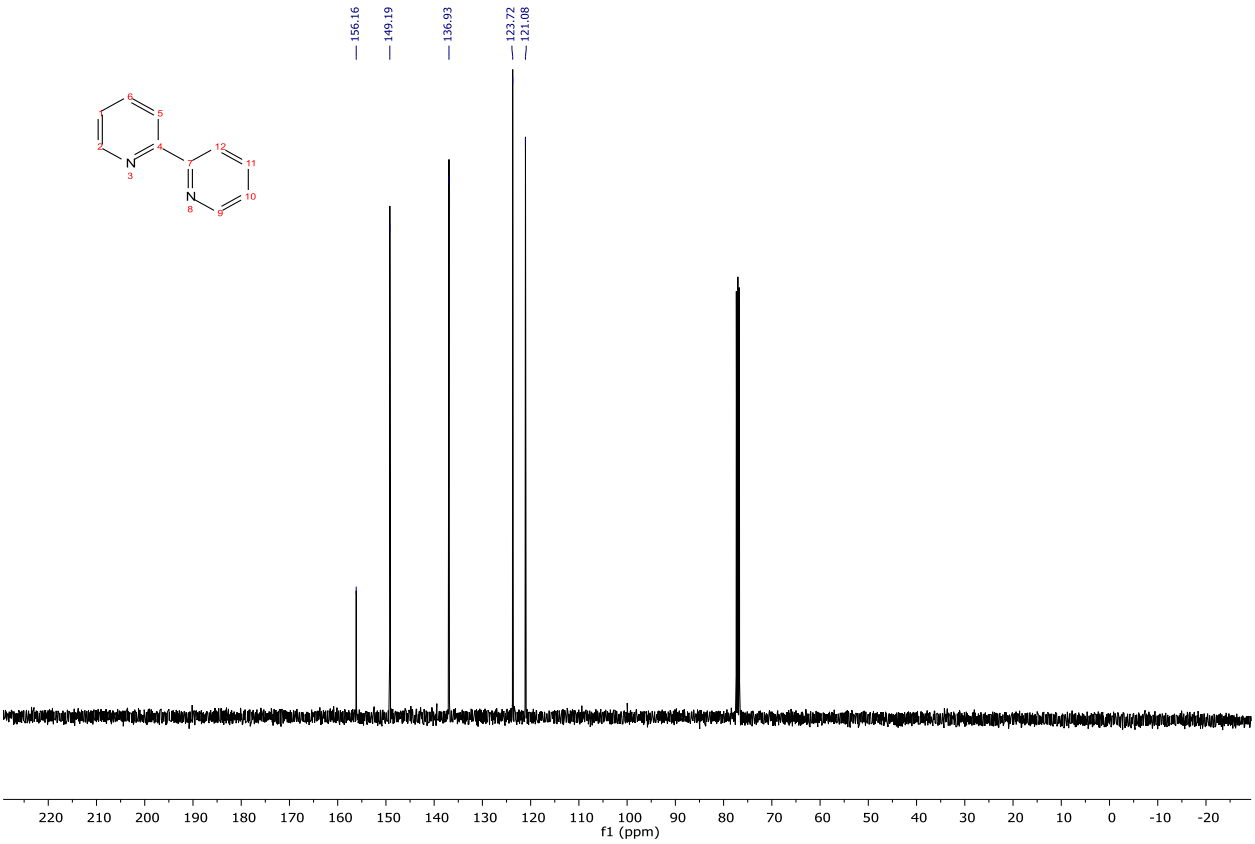
149.94
142.68
136.98
127.18
125.75
125.71
125.67
125.63
122.96
120.87
N
F
F
F
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


N
F
F
F

-62.57
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)


1
2
N
3
4
5
6
7
8
N
9
10
11
12


1.91
1.94
2.04
2.00
.6 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -
f1 (ppm)


156.16
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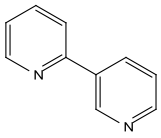
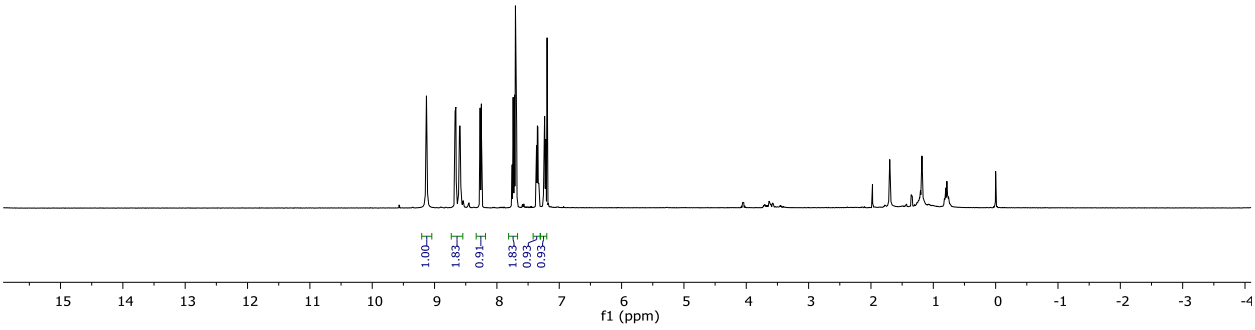
136.93
123.72
121.08
f1 (ppm)

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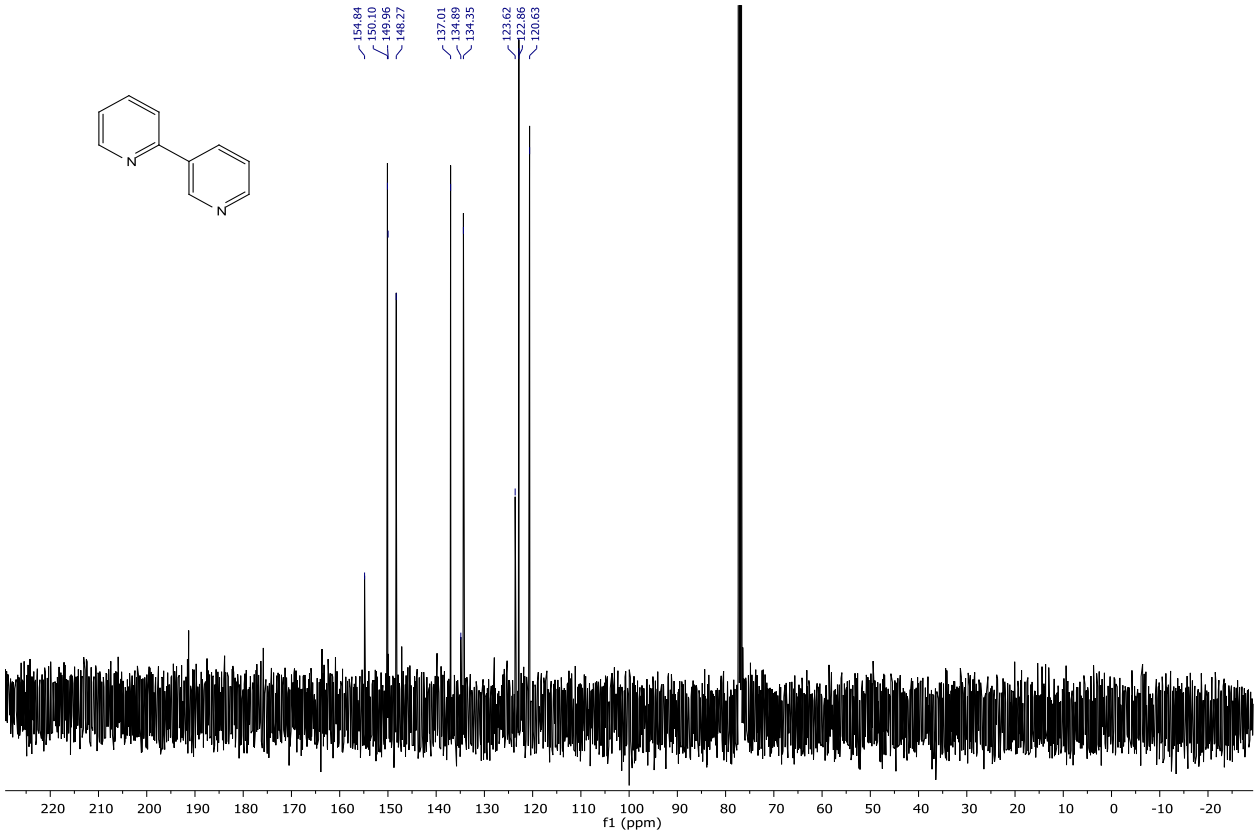
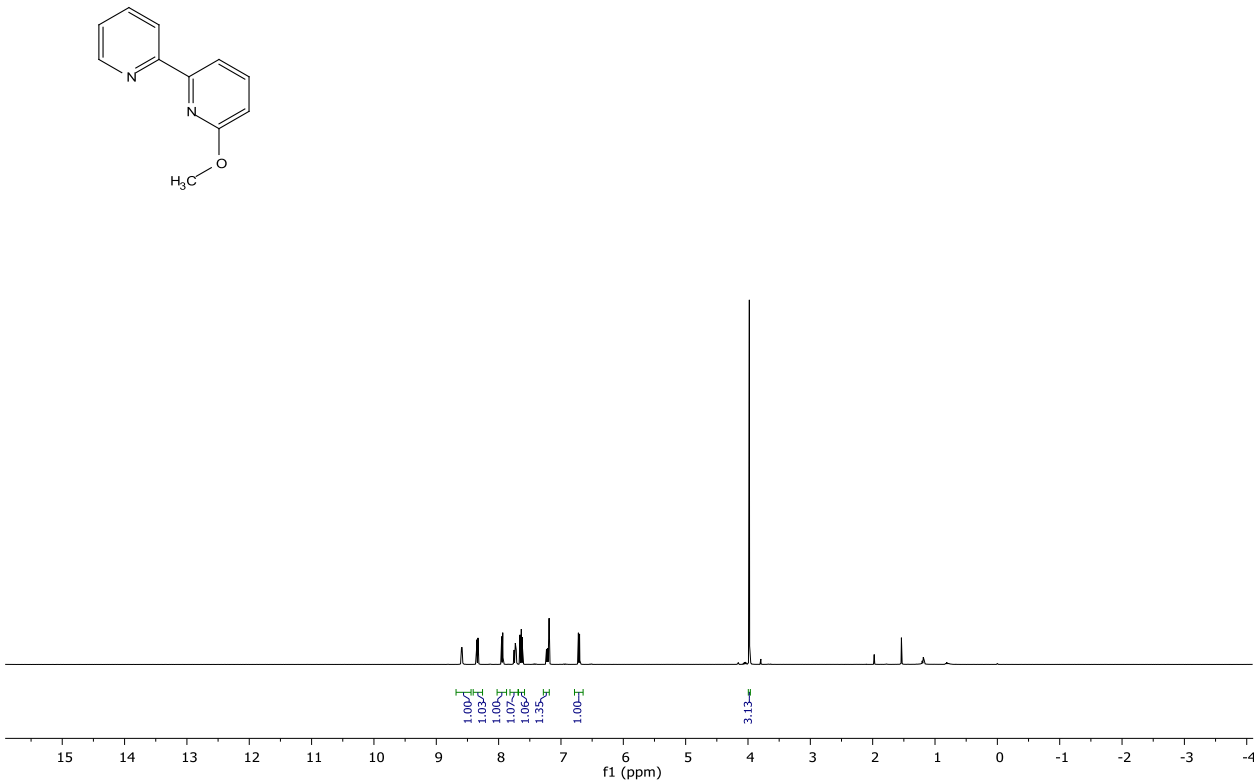
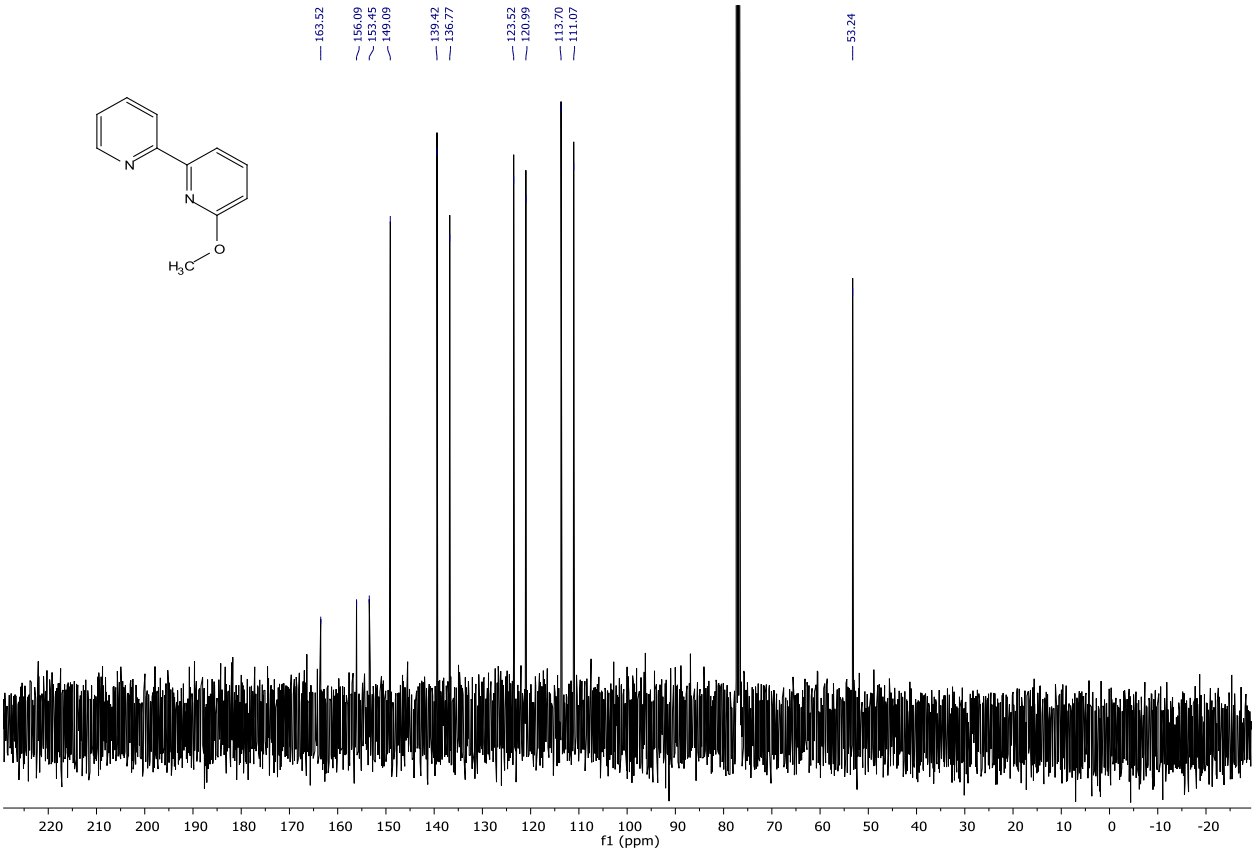
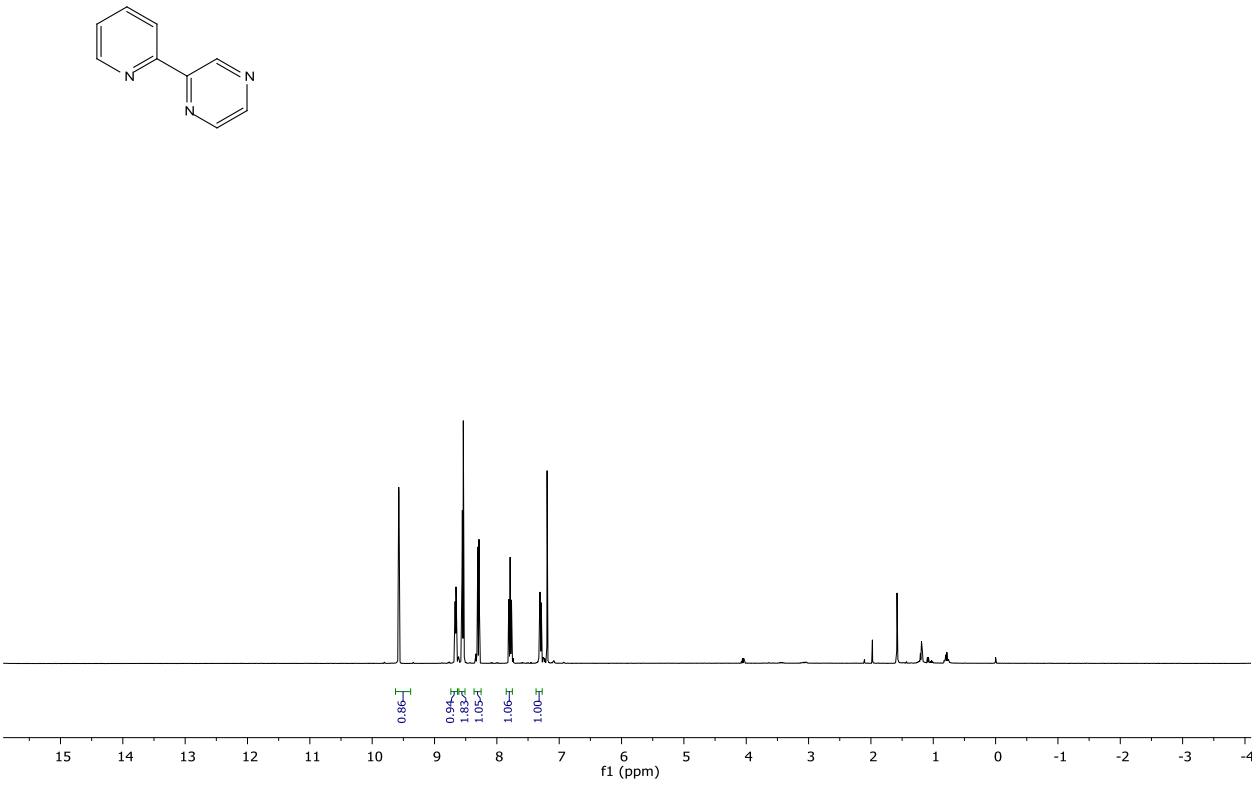
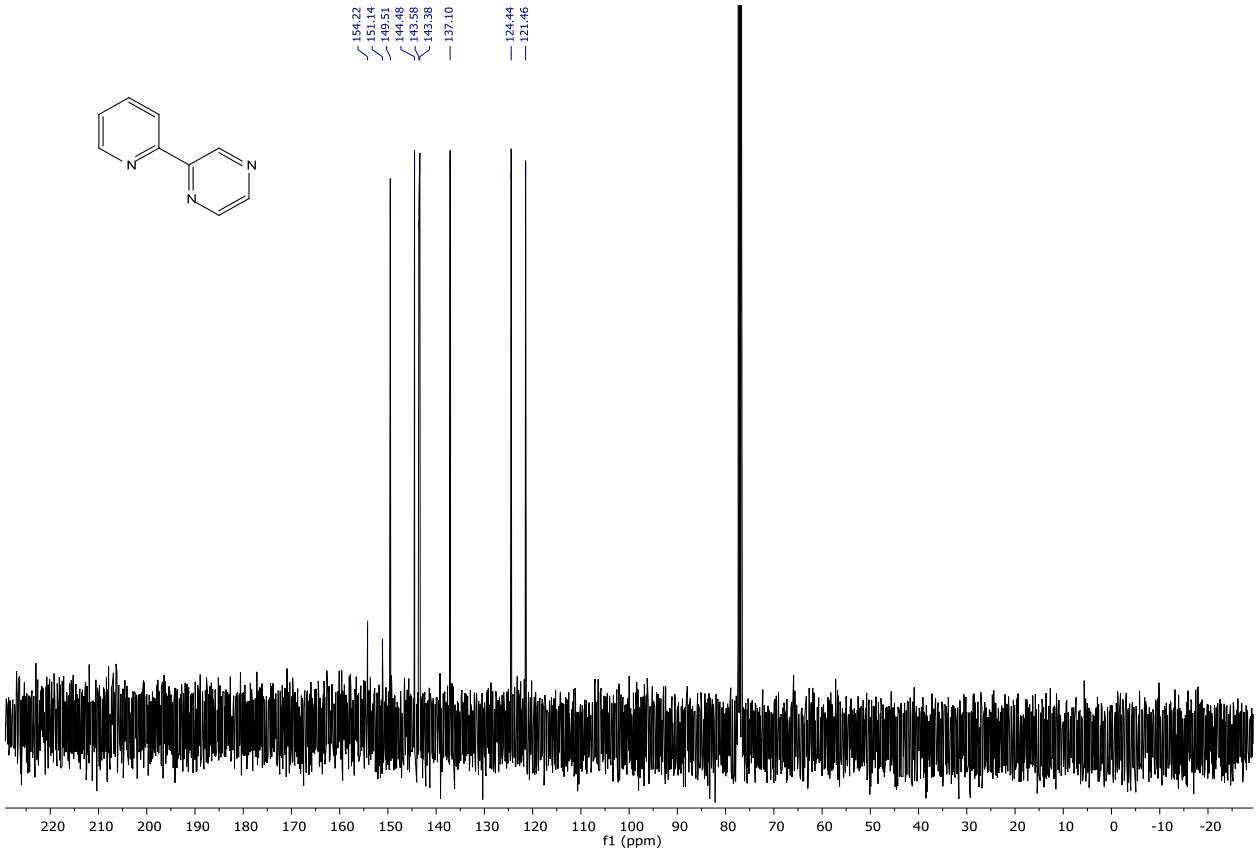
1.83
0.91
1.83
0.93
0.93
f1 (ppm)

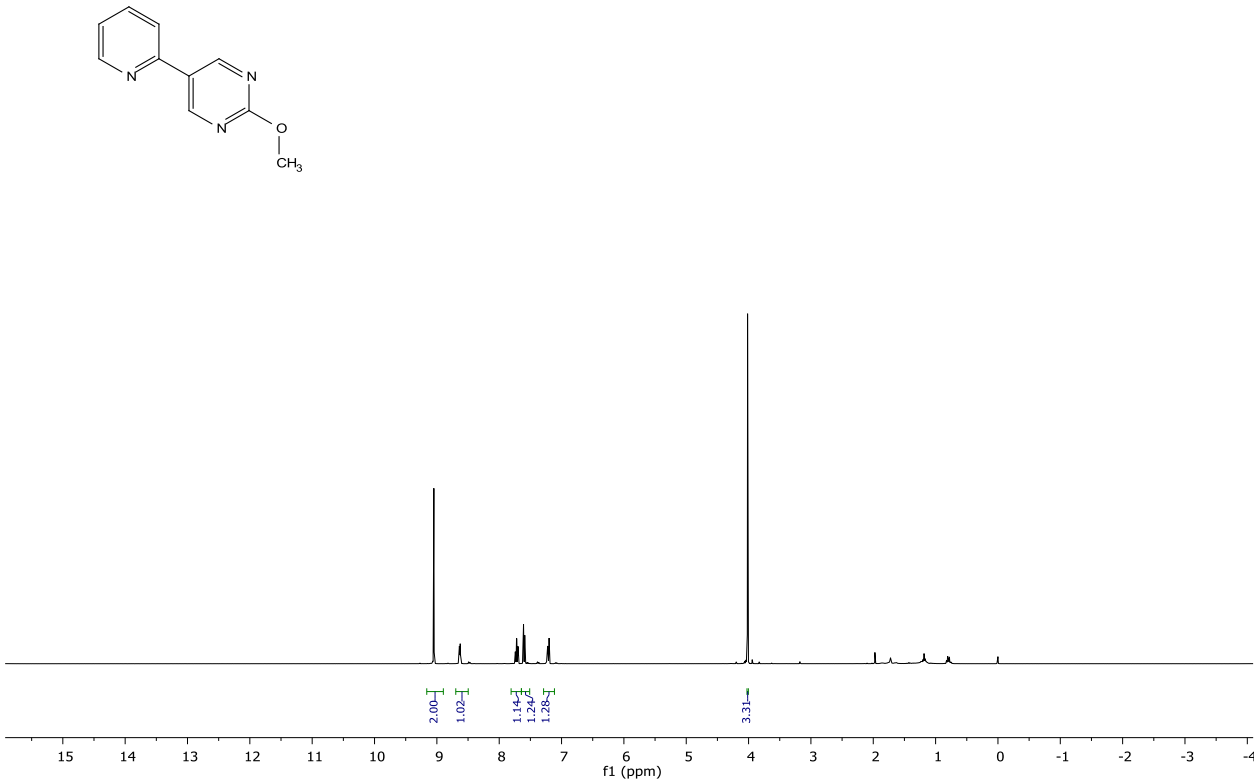

154.84
150.10
149.96
148.27
137.01
134.89
134.35
123.62
122.86
120.63
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

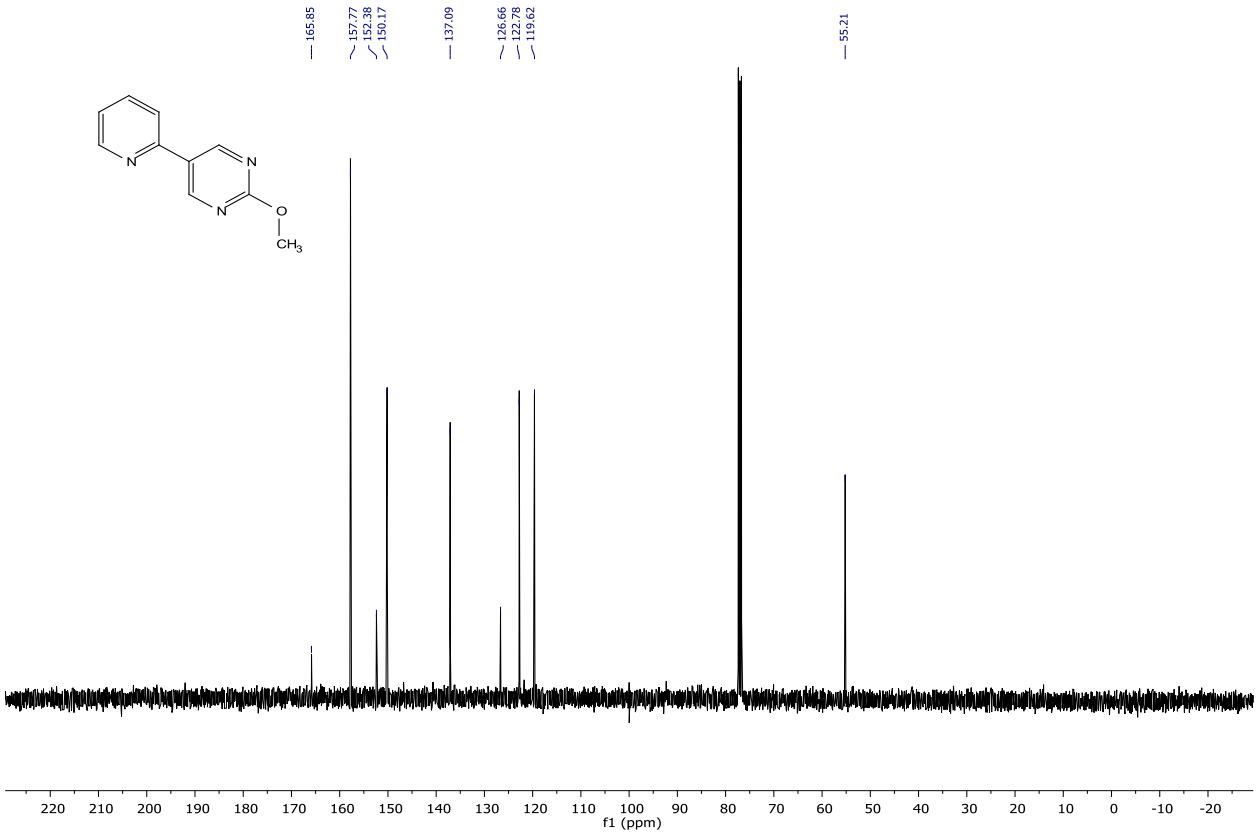

N
N
O
H3C
1.00
1.03
1.00
1.07
1.06
1.35
1.00
3.13
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

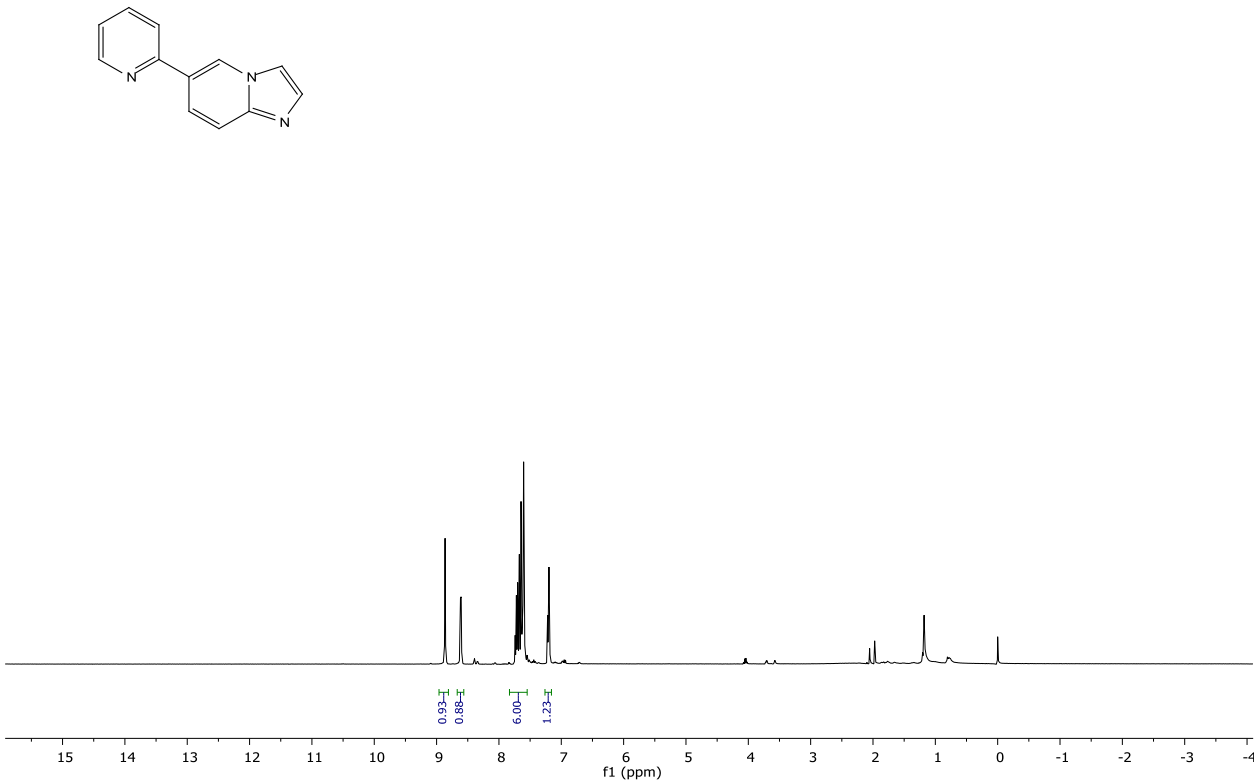

163.52
156.09
153.45
149.09
139.42
136.77
123.52
120.99
113.70
111.07
53.24
N
N
O
H3C
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

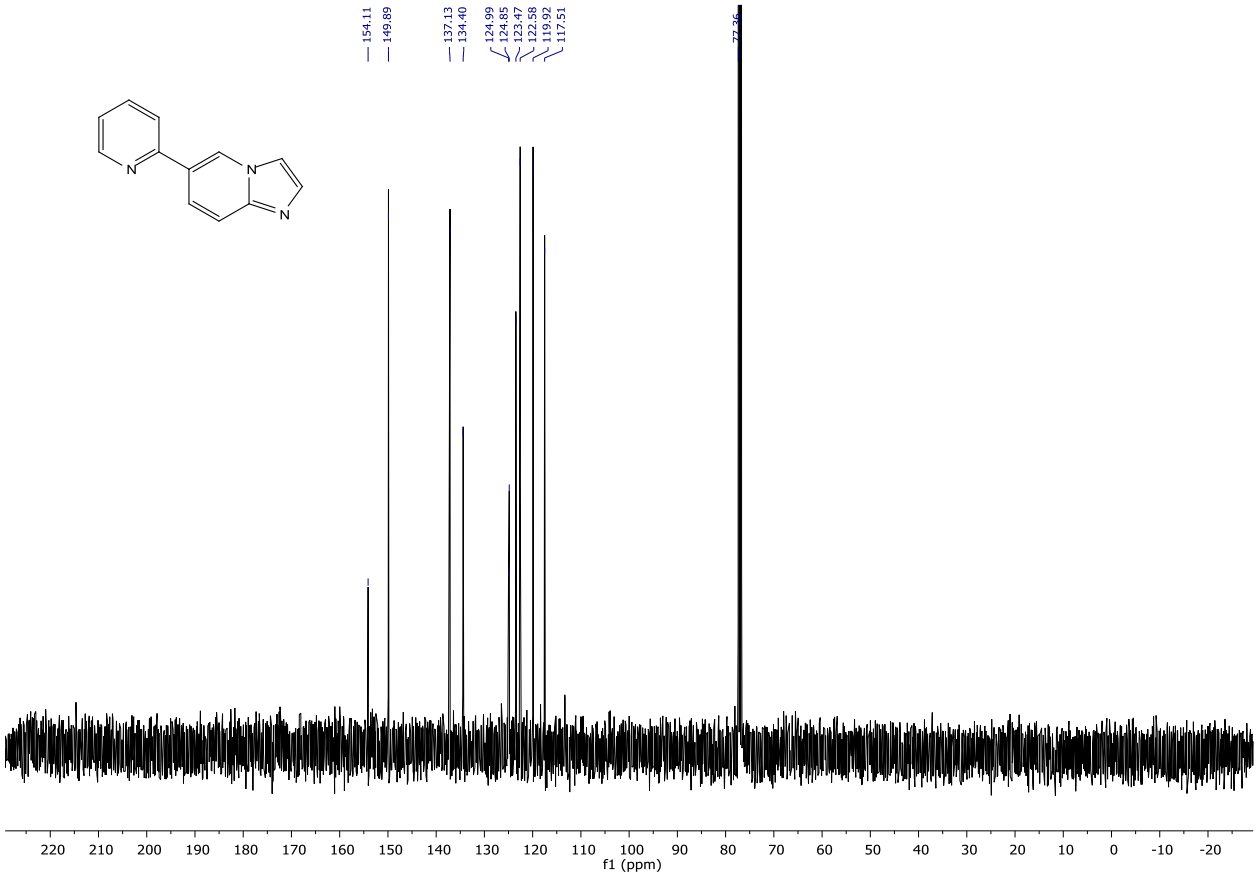

N
N
N
0.86
0.94
1.83
1.05
1.06
1.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

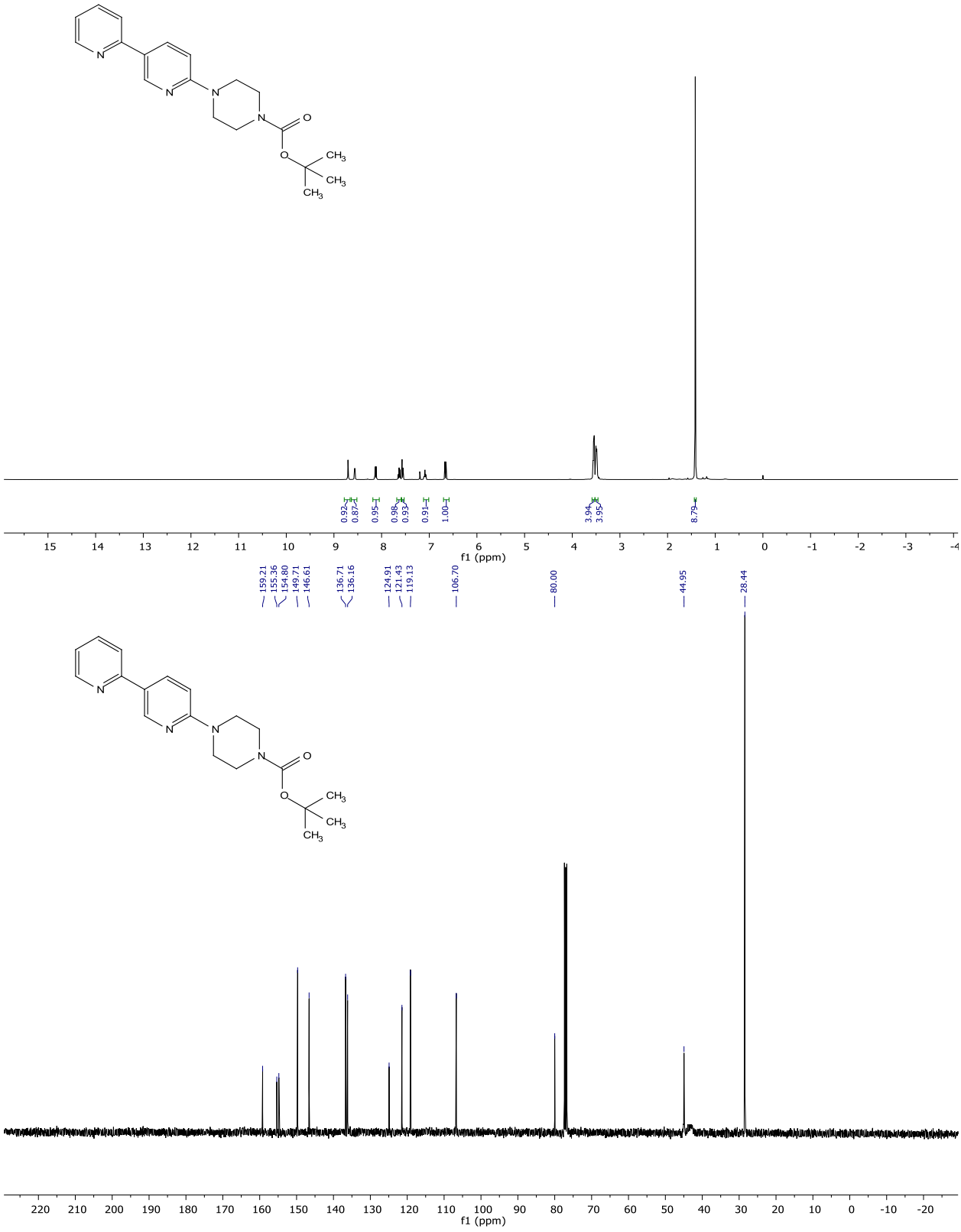

154.22
151.14
149.51
144.48
143.58
143.38
137.10
124.44
121.46
N
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

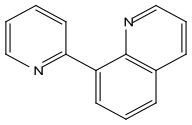

N
N
N
O
CH3
2.00
1.02
1.14
1.24
1.28
3.31
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

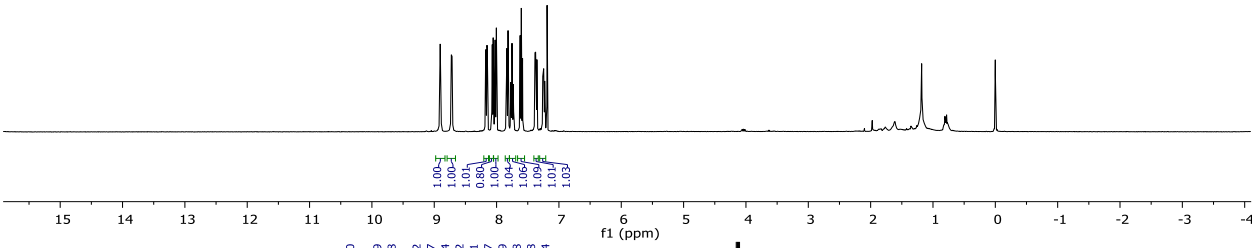

165.85
157.77
152.38
150.17
137.09
126.66
122.78
119.62
55.21
N
N
N
O
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

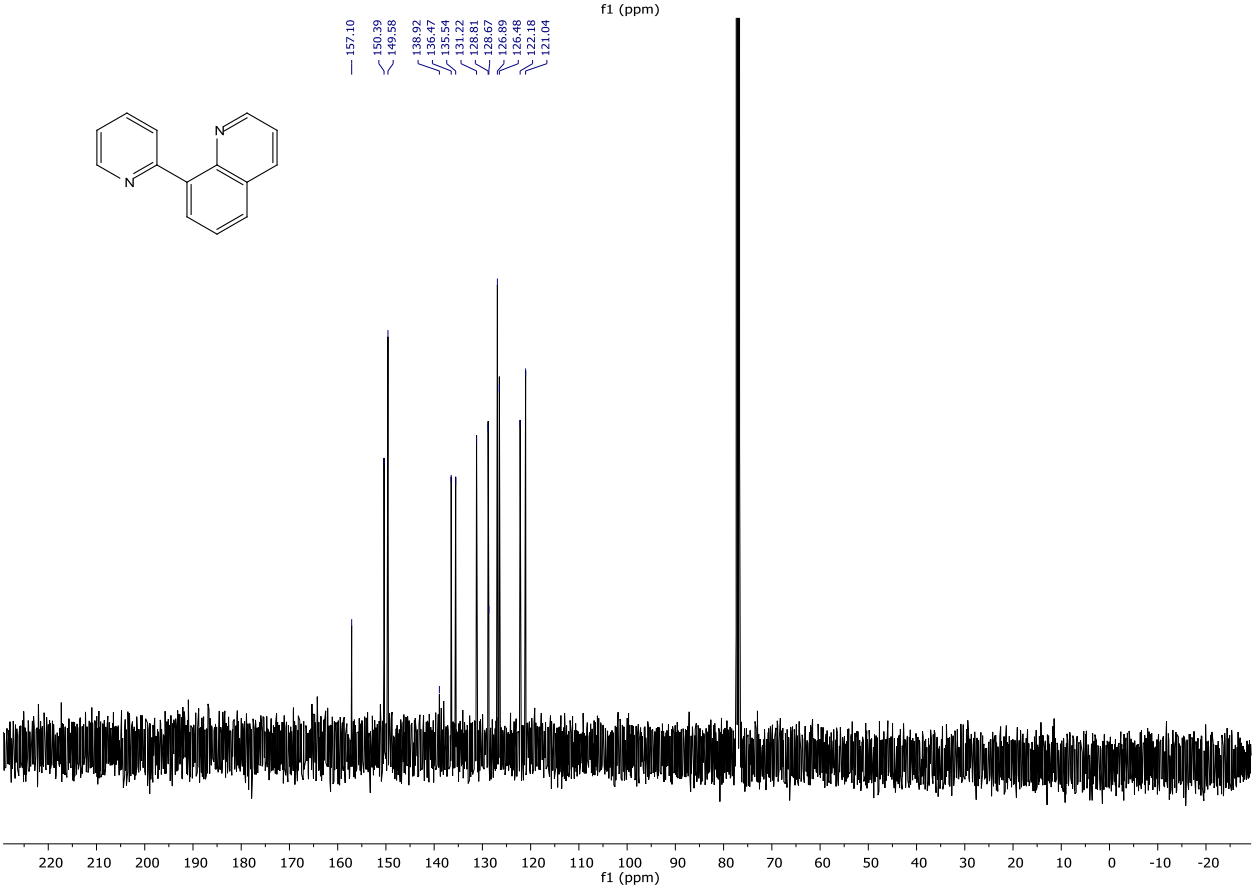

N
N
N
0.93
0.88
6.00
1.23
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

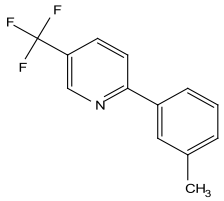

154.11
149.89
137.13
134.40
124.99
124.85
123.47
122.58
119.92
117.51
77.26
N
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

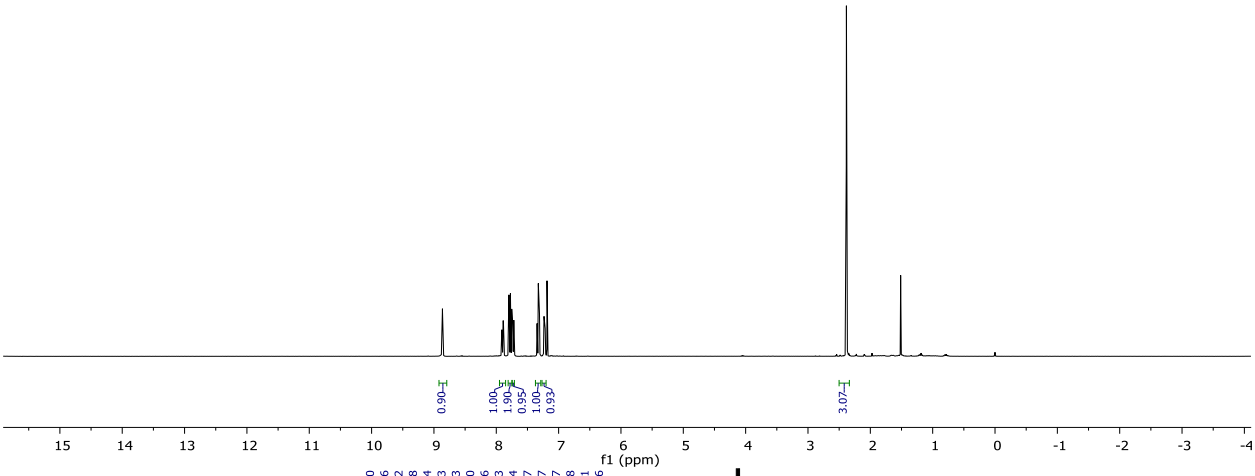

0.92
0.87
0.95
0.98
0.93
0.91
1.00
3.94
3.95
8.79
f1 (ppm)
159.21
155.36
154.80
149.71
146.61
136.71
136.16
124.91
121.43
119.13
106.70
80.00
44.95
28.44
f1 (ppm)

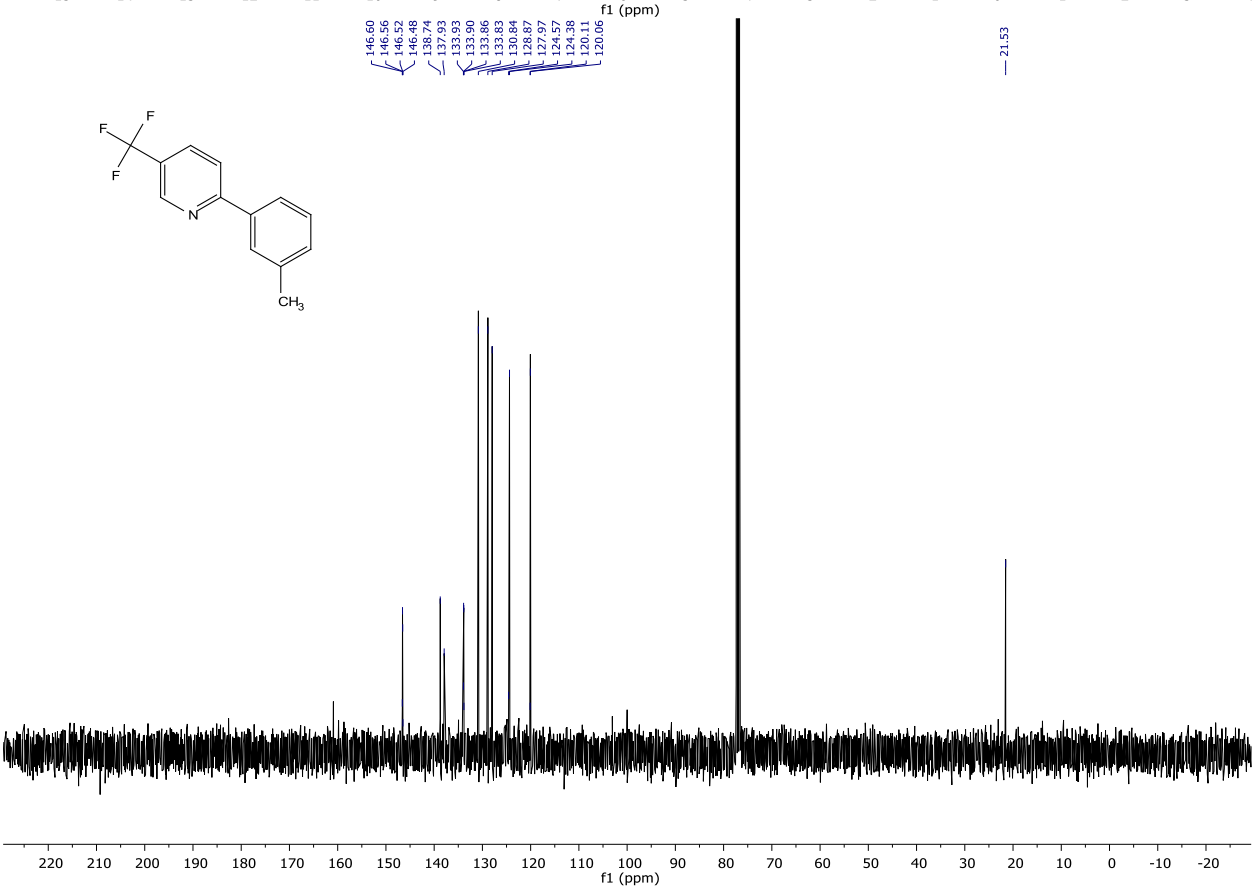

N
N

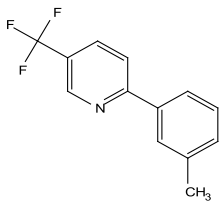

1.00
1.00
1.01
0.80
1.00
1.04
1.06
1.09
1.01
1.03
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


157.10
150.39
149.58
138.92
136.47
135.54
131.22
128.81
128.67
126.89
126.48
122.18
121.04
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

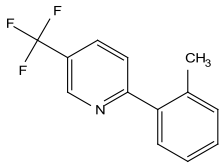

F
F
F
N
CH3

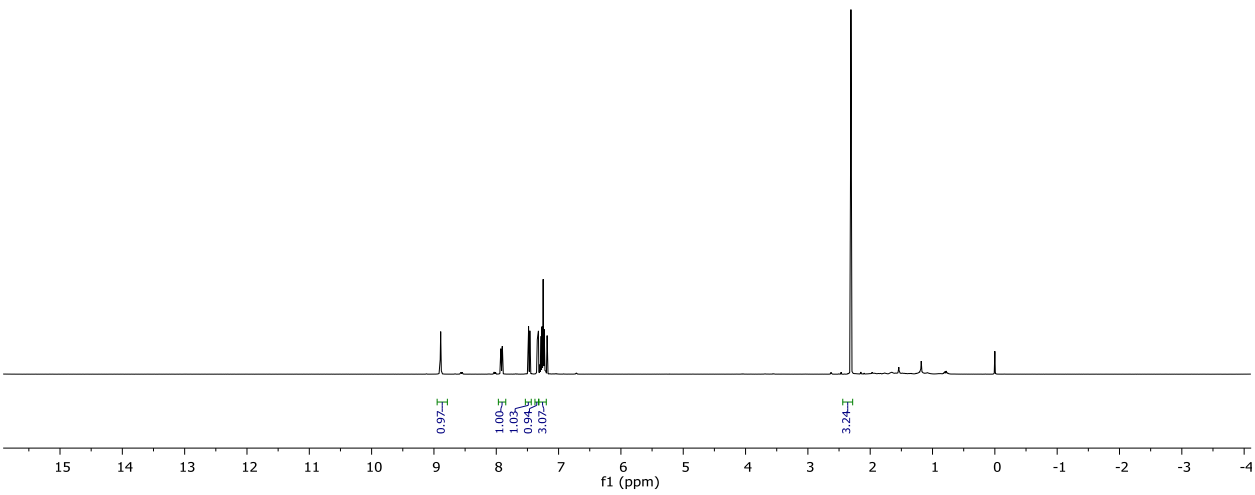

0.90
1.00
1.90
0.95
1.00
0.93
3.07
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

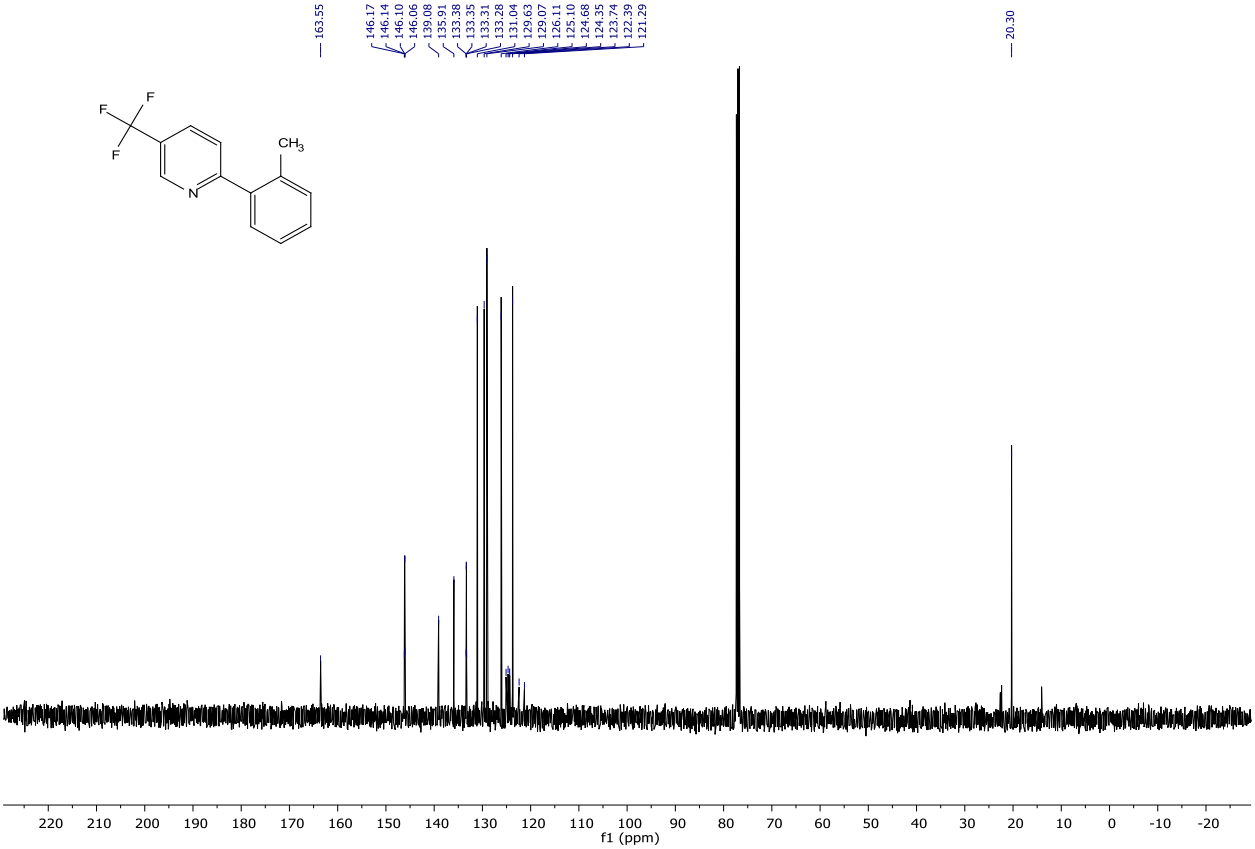

146.60
146.56
146.52
146.48
138.74
137.93
133.93
133.90
133.86
133.83
130.84
128.87
127.97
124.57
124.38
120.11
120.06
21.53
F
F
F
N
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

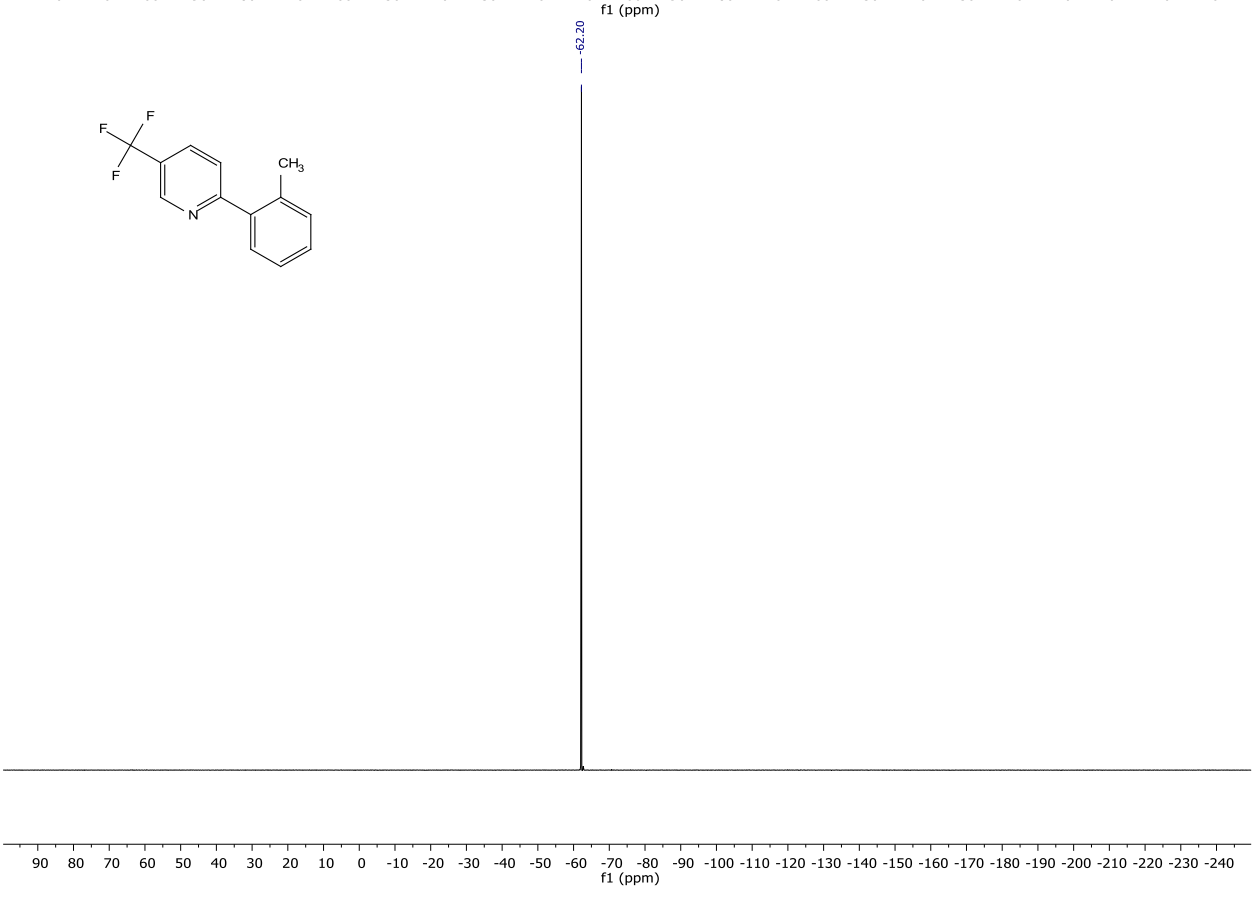

F
F
F
N
CH3

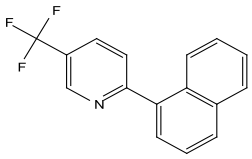
-62.21
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

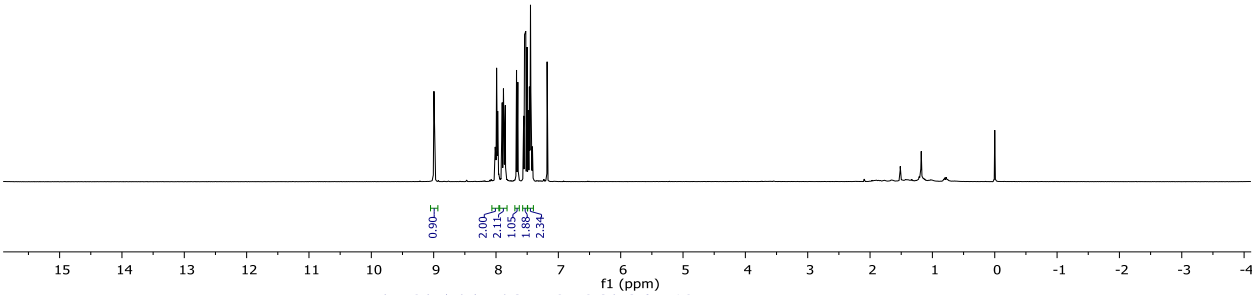

F
F
F
N
CH3

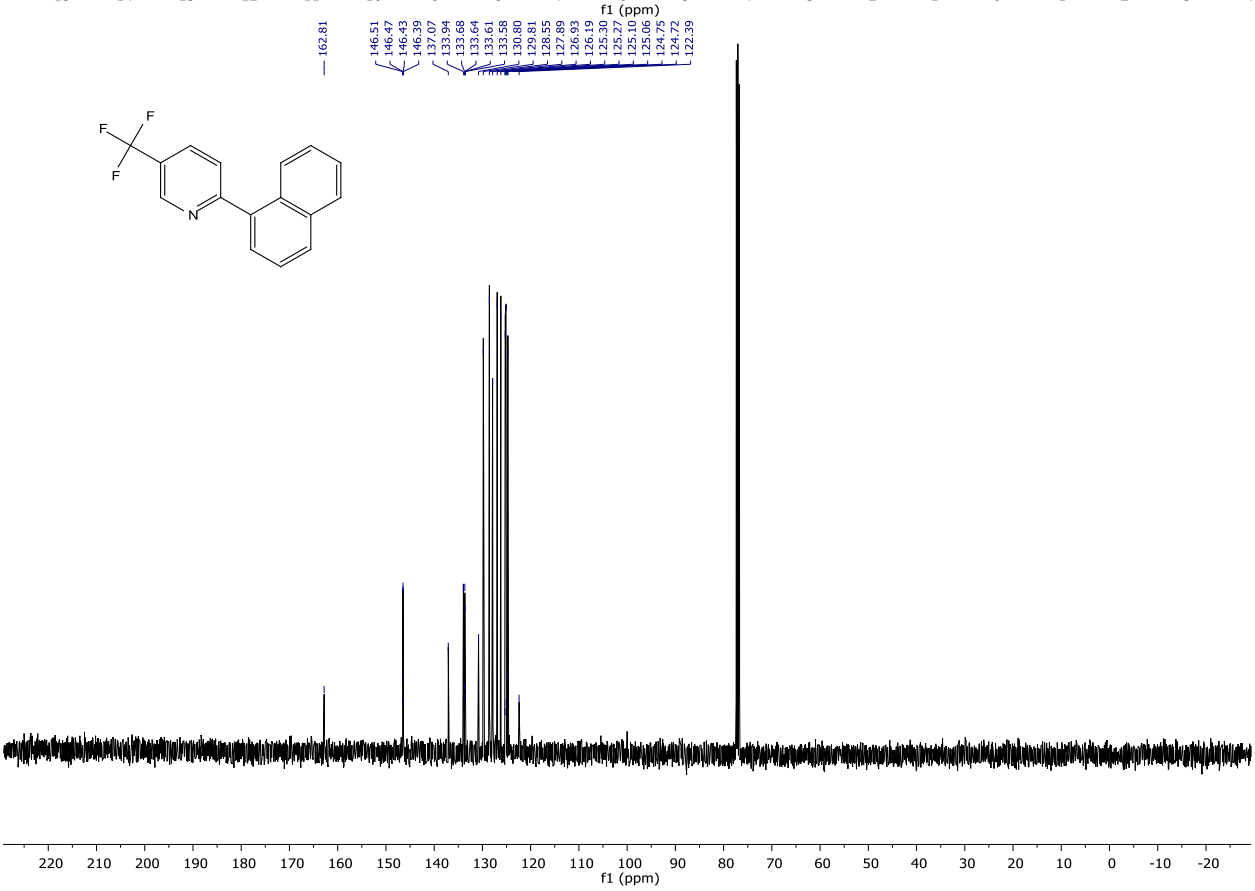

0.97
1.00
1.03
0.94
3.07
3.24
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

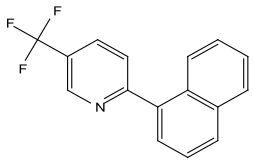

163.55
146.17
146.14
146.10
146.06
139.08
135.91
133.38
133.35
133.31
133.28
131.04
129.63
129.07
126.11
125.10
124.68
124.35
123.74
122.39
121.29
20.30
F
F
F
CH3
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


-62.20
F
F
F
CH3
N
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

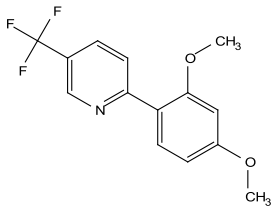

F
F
F
N

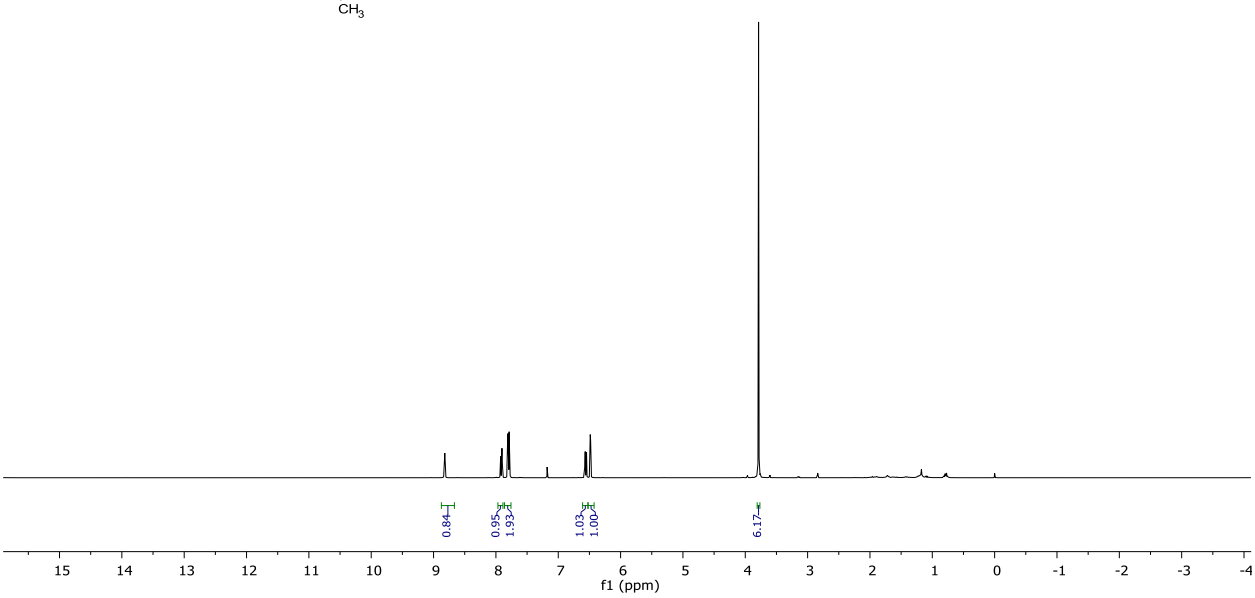

0.90
2.00
2.11
1.05
1.88
2.34
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

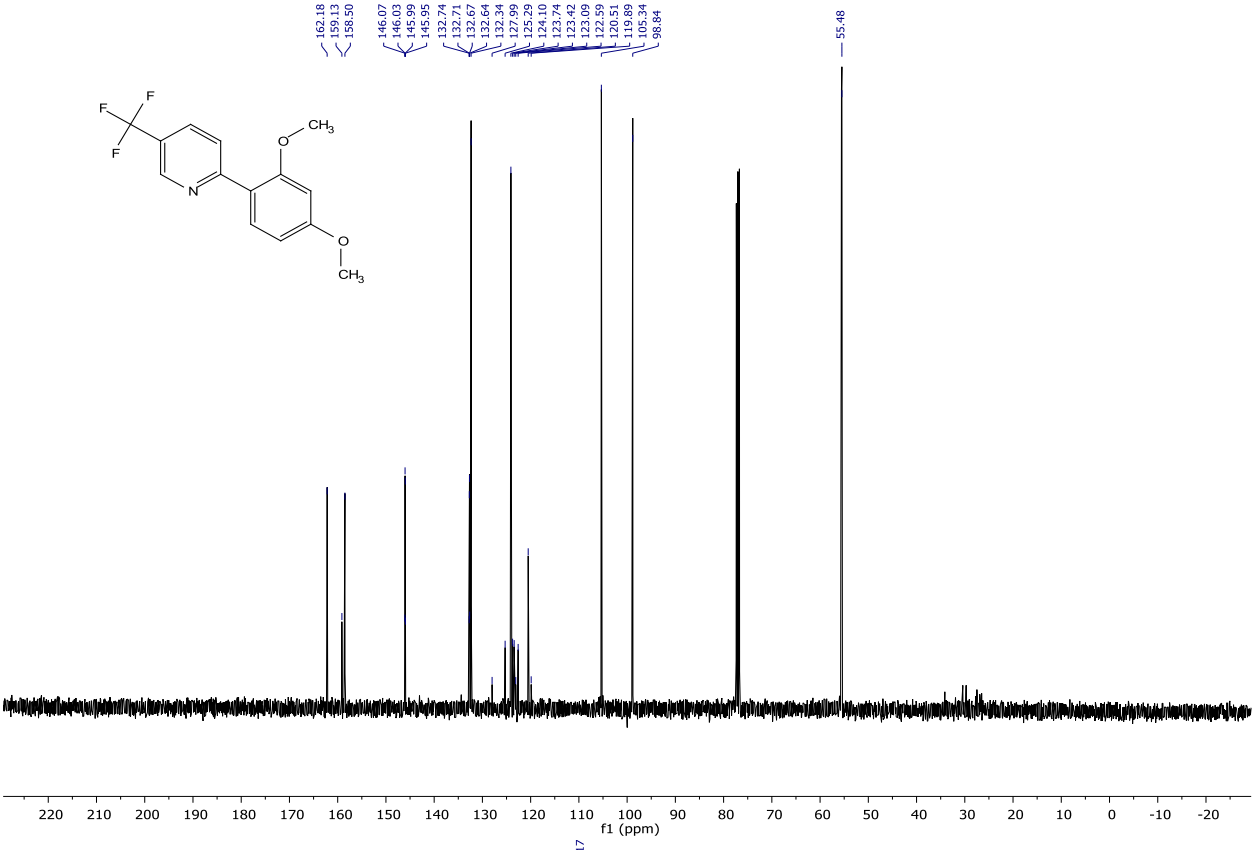

162.81
146.51
146.47
146.43
146.39
137.07
133.94
133.68
133.64
133.61
133.58
130.80
129.81
128.55
127.89
126.93
126.19
125.30
125.27
125.10
125.06
124.75
124.72
122.39
F
F
F
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

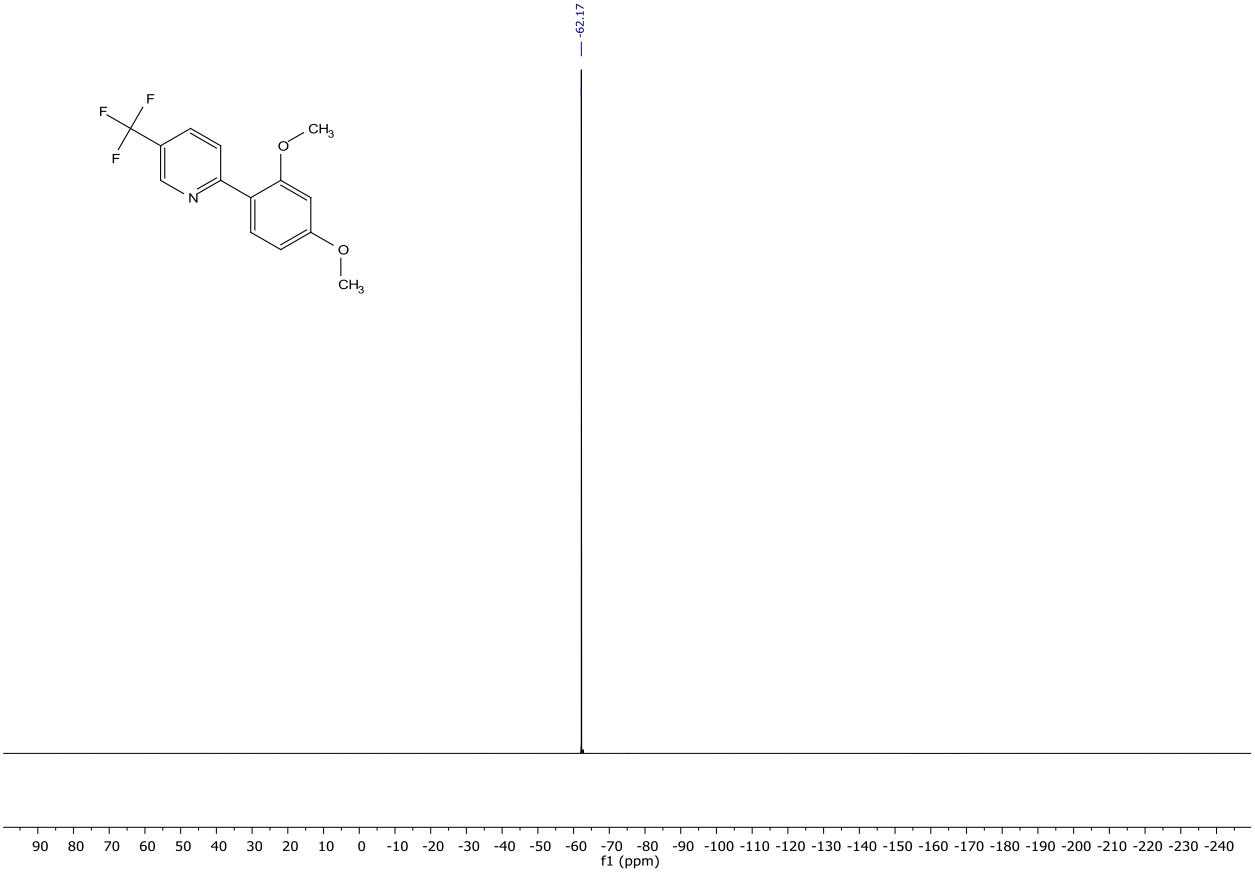

F
F
F
N

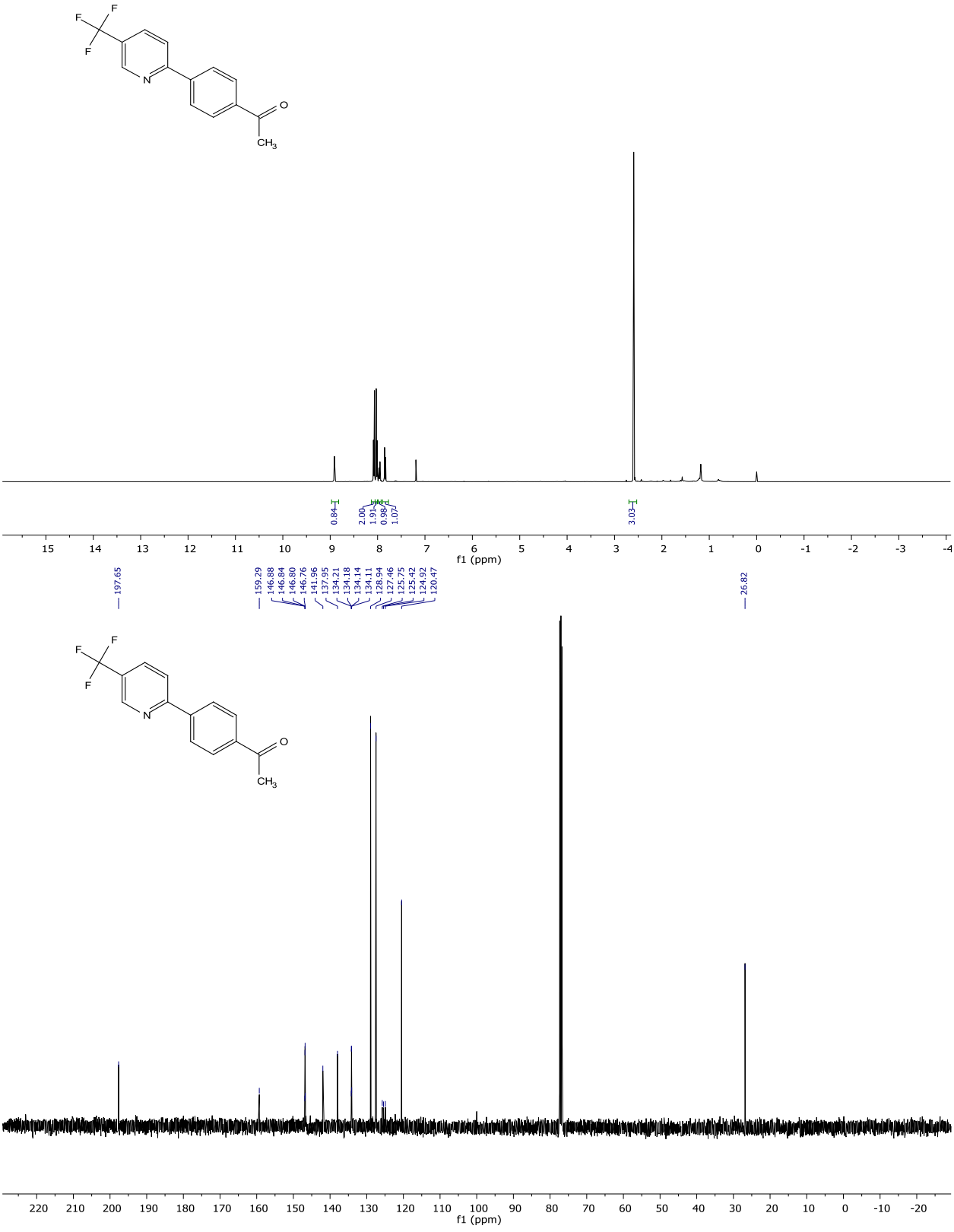
-62.16
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

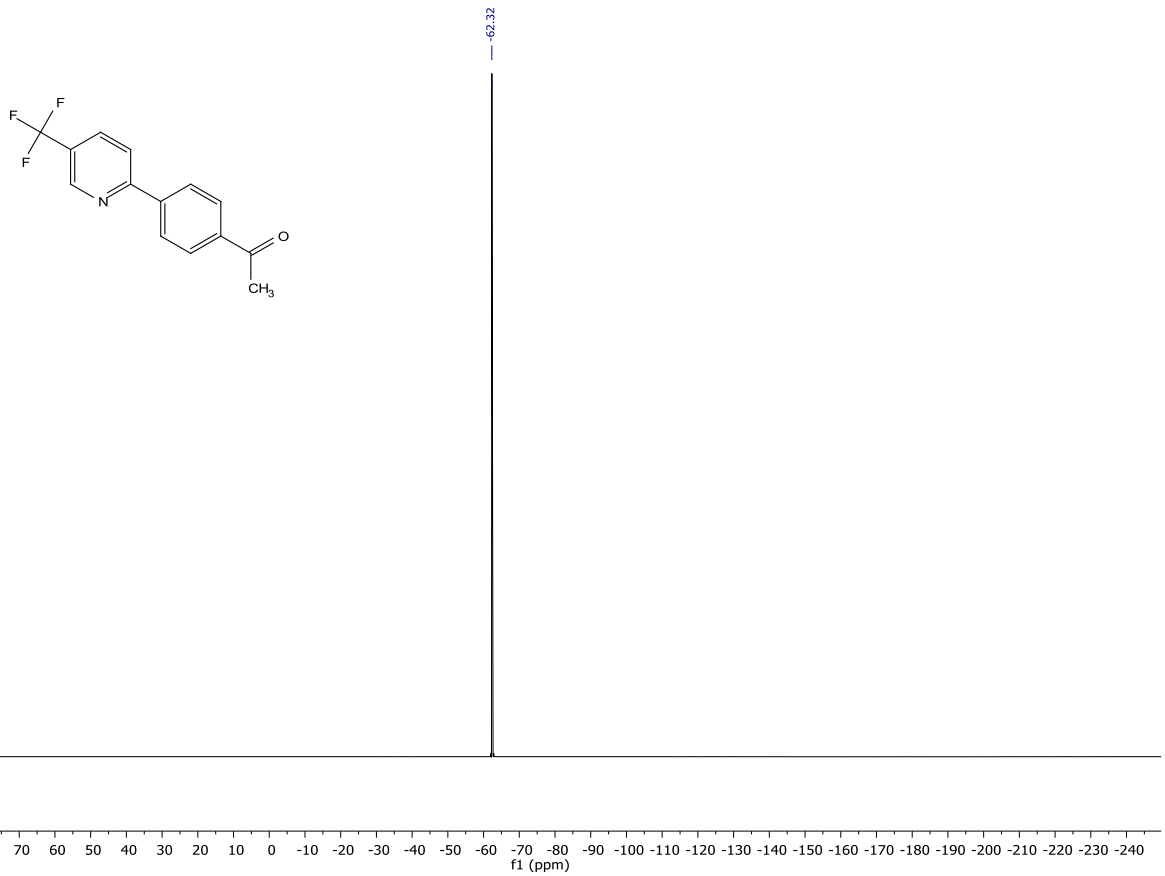

F
F
F
N
O
CH3
O
CH3

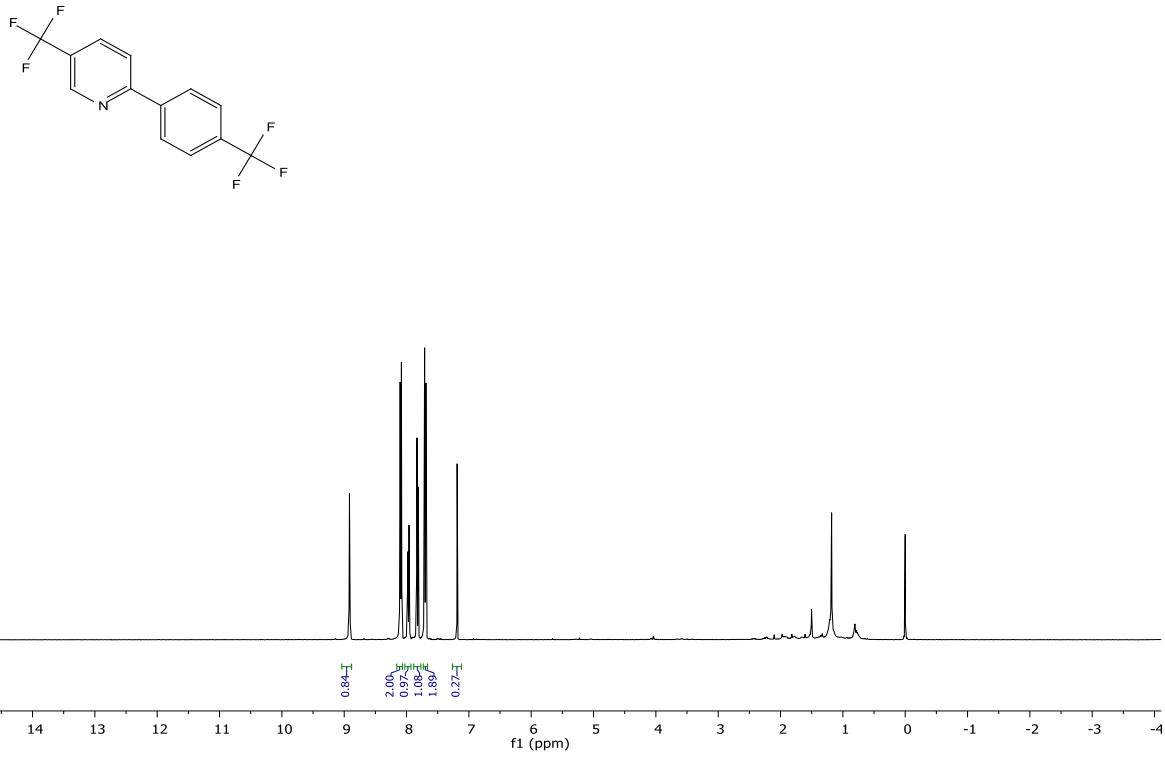

0.84
0.95
1.93
1.03
1.00
6.17
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

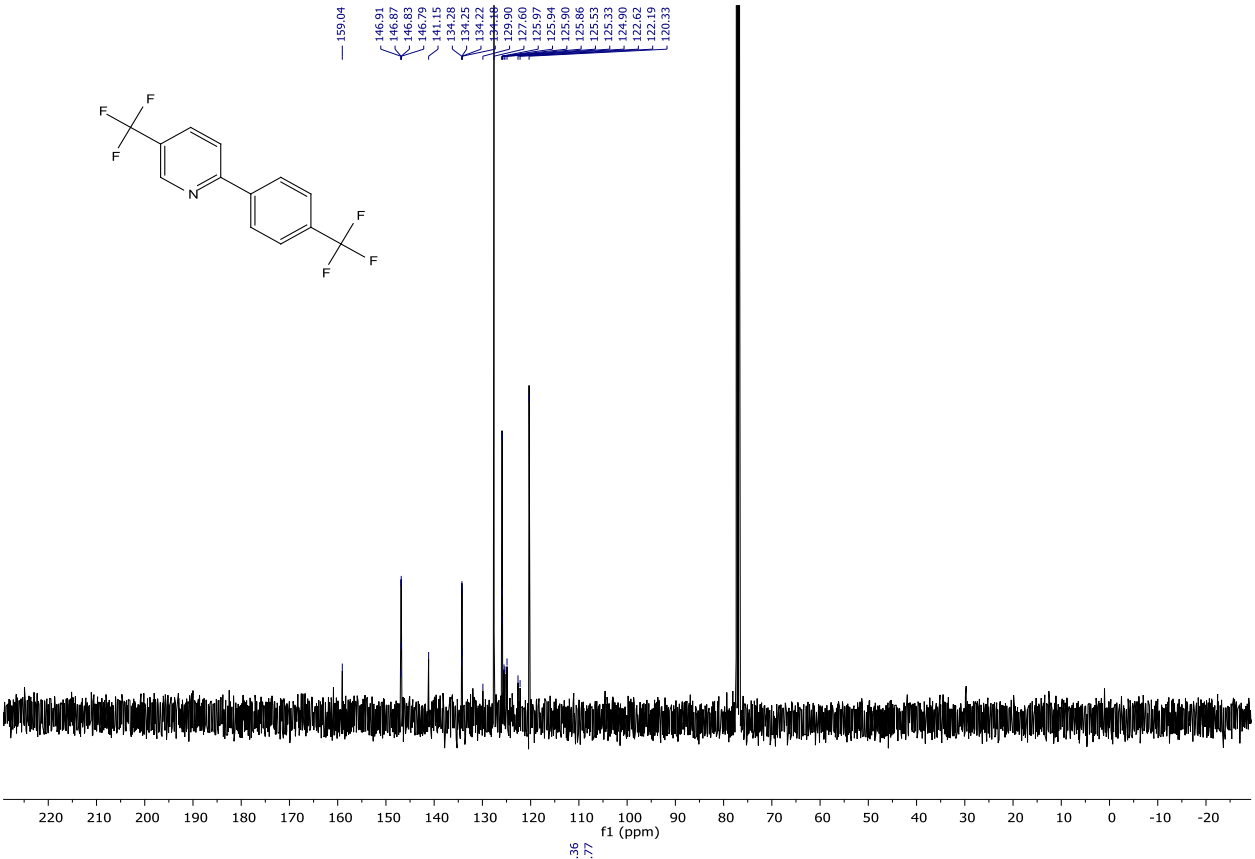

162.18
159.13
158.50
146.07
146.03
145.99
145.95
132.74
132.71
132.67
132.64
132.34
127.99
125.29
124.10
123.74
123.42
123.09
122.59
120.51
119.89
105.34
98.84
55.48
F
F
F
N
O
CH3
O
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

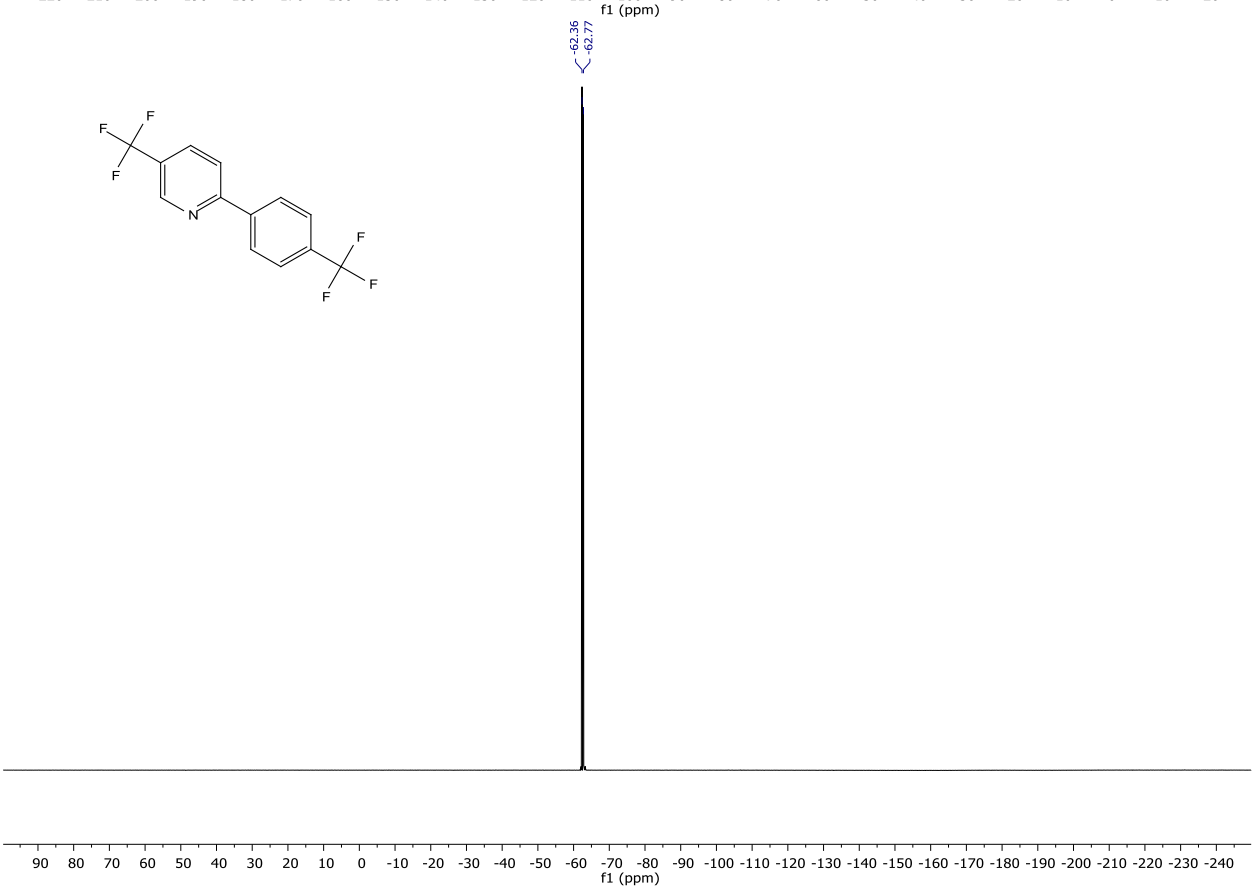

-62.17
F
F
F
N
O
CH3
O
CH3
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

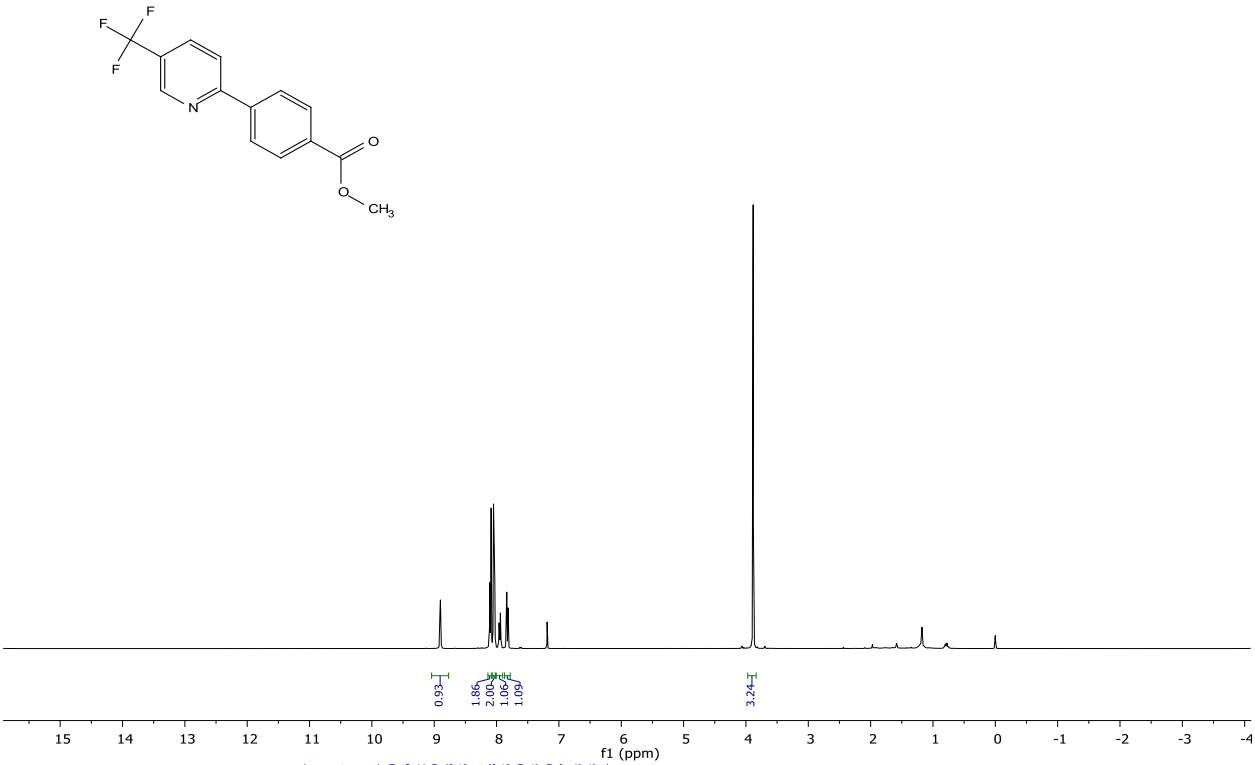

F
F
F
N
O
CH3
0.84
2.00
1.91
0.98
1.07
3.03
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)
197.65
159.29
146.88
146.84
146.80
146.76
141.96
137.55
134.21
134.18
134.14
134.11
128.94
127.46
125.75
125.42
124.92
120.47
26.82
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

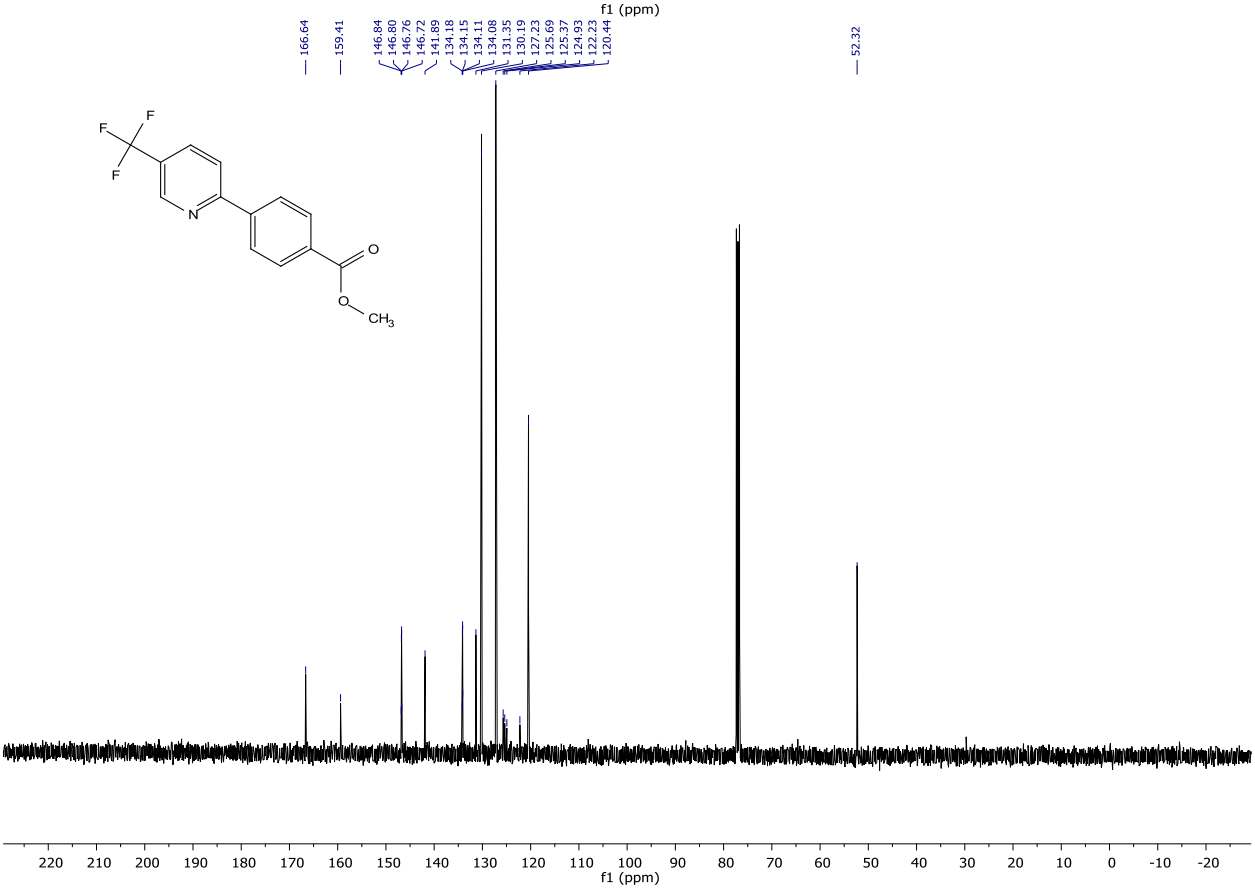

-62.32
F
F
F
N
O
CH3
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

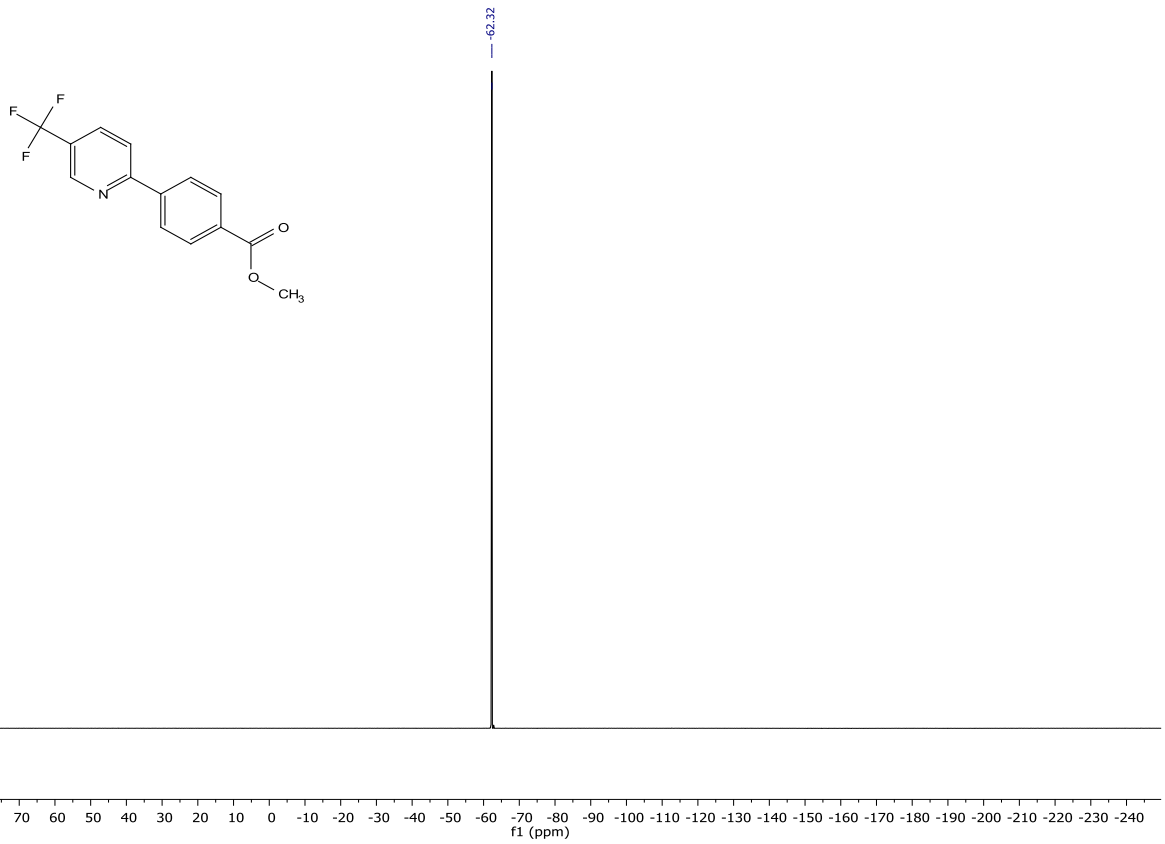

F
F
F
N
F
F
0.84
2.00
0.97
1.08
1.89
0.27
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

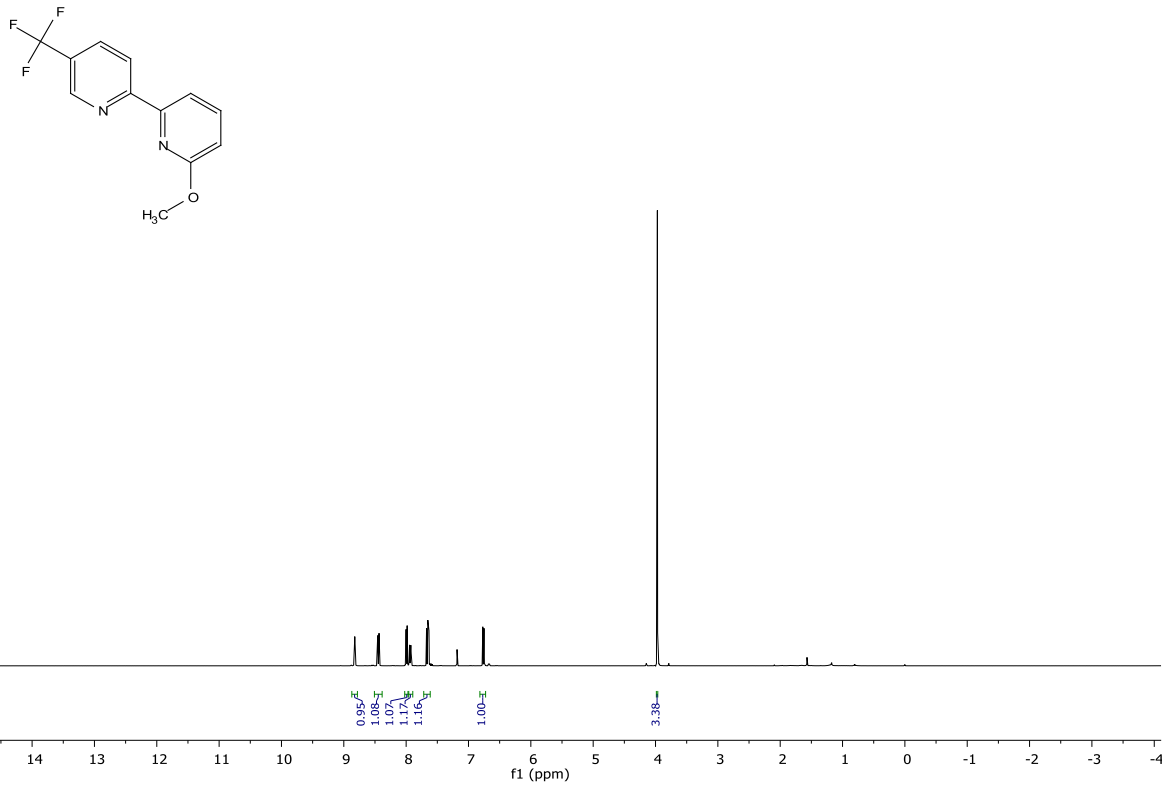

159.04
146.91
146.87
146.83
146.79
141.15
134.28
134.25
134.22
129.90
127.60
125.97
125.94
125.90
125.86
125.53
125.33
124.90
122.62
122.19
120.33
F
F
F
N
F
F
F
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

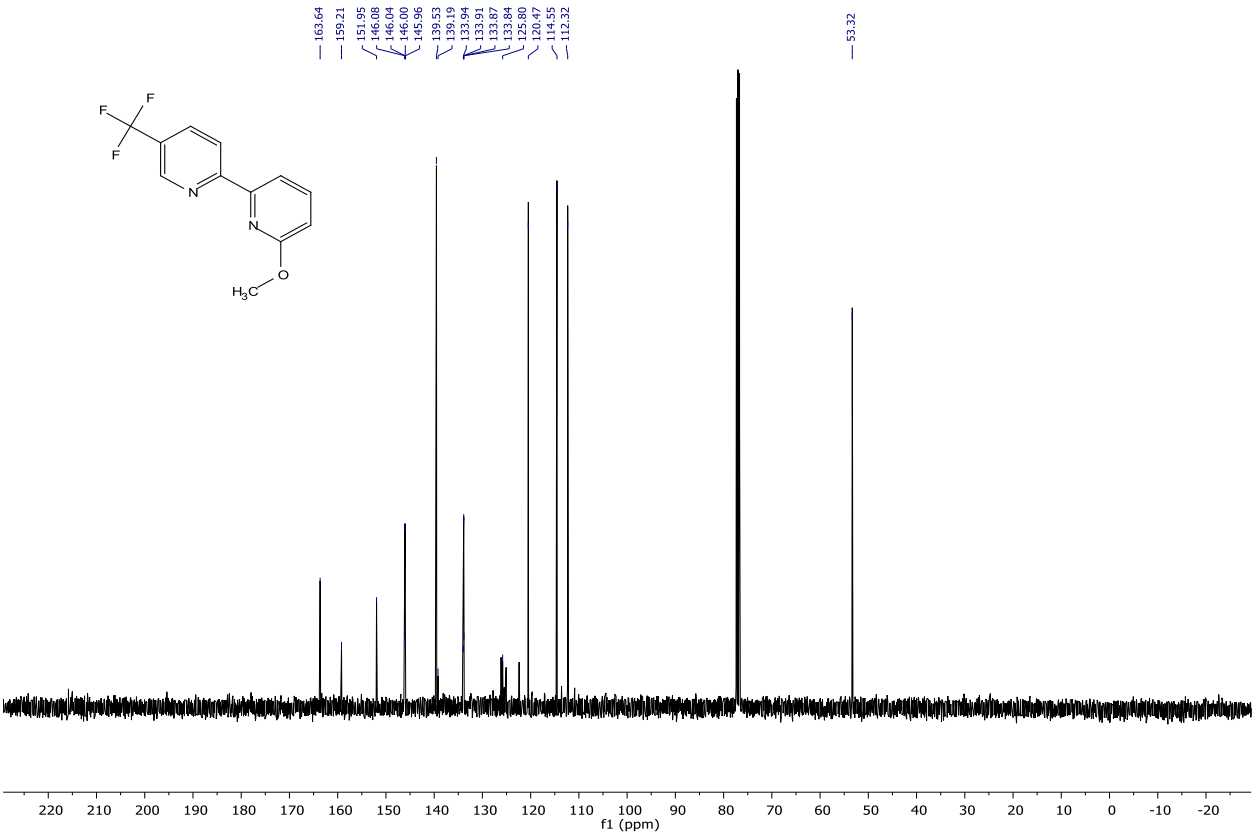

-62.36
-62.77
F
F
F
N
F
F
F
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

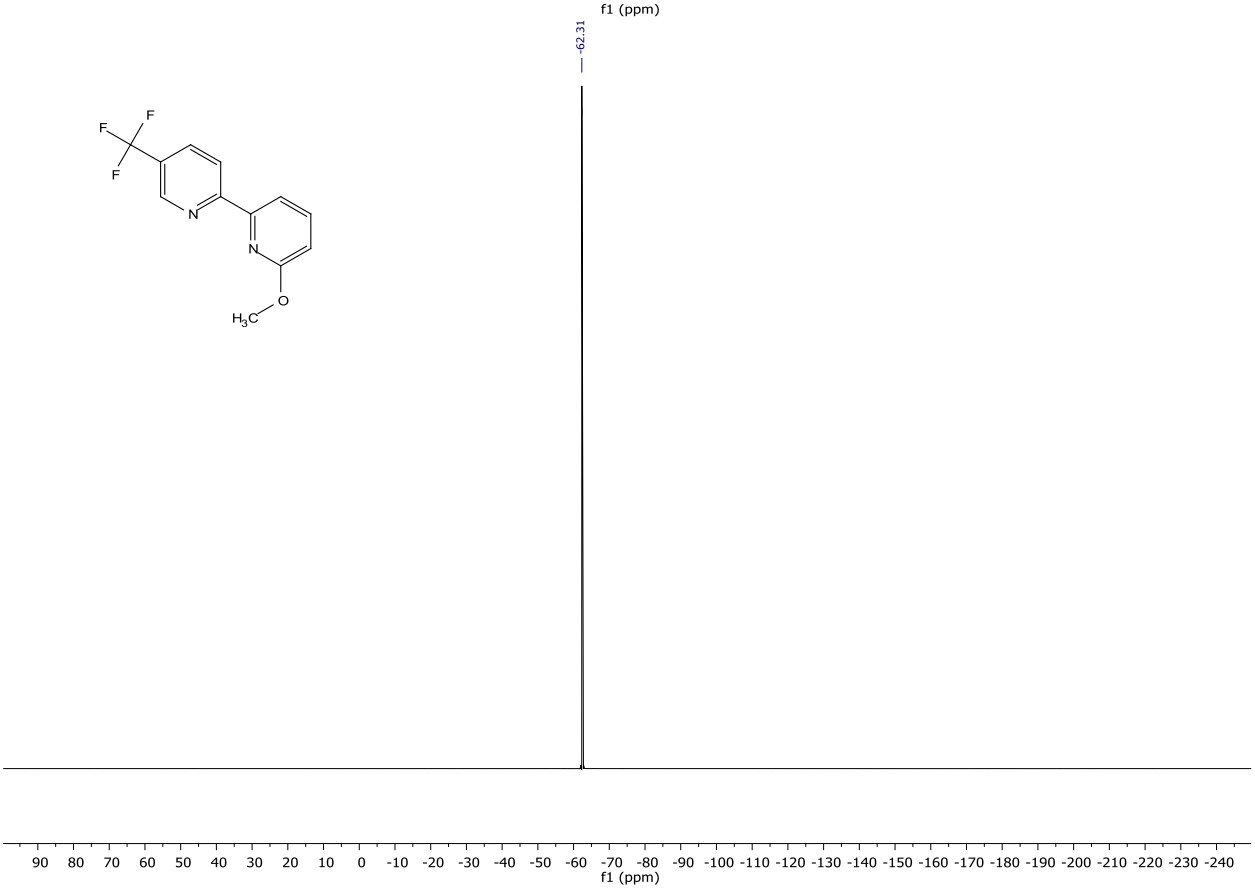

F
F
F
N
O
O
CH3
0.93
1.86
2.00
1.06
1.09
3.24
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

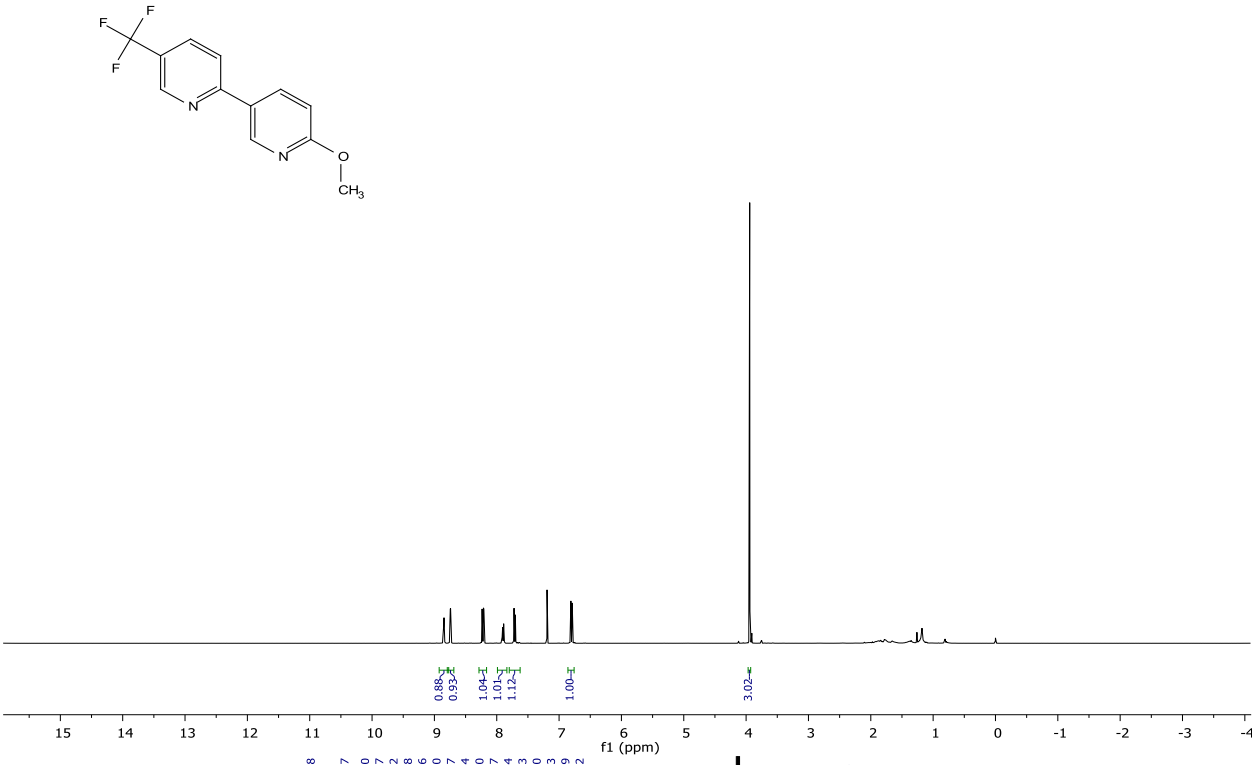

166.64
159.41
146.84
146.80
146.76
146.72
141.89
134.18
134.15
134.11
134.08
131.35
130.19
127.23
125.69
125.37
124.93
122.23
120.44
52.32
F
F
F
N
O
O
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

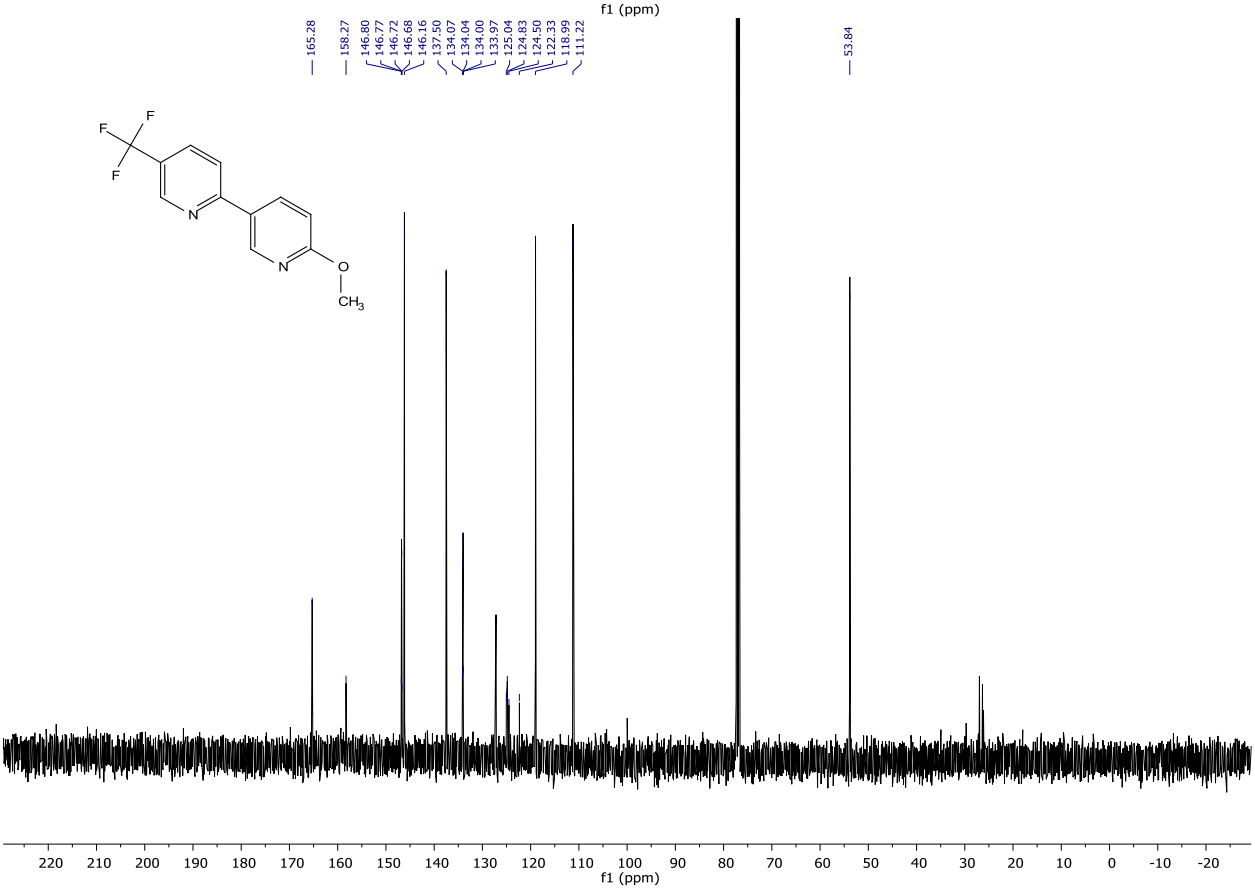

-62.32
F
F
F
N
O
O
CH3
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)


F
F
F
N
N
O
H3C
0.95
1.08
1.07
1.17
1.16
1.00
3.38
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


163.64
159.21
151.95
146.08
146.04
146.00
145.96
139.53
139.19
133.94
133.91
133.87
133.84
125.80
120.47
114.55
112.32
53.32
F
F
F
N
N
O
H3C
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)


-62.31
F
F
F
N
N
O
H3C
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)


F
F
F
N
N
O
CH3
0.88
0.93
1.04
1.01
1.12
1.00
3.02
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)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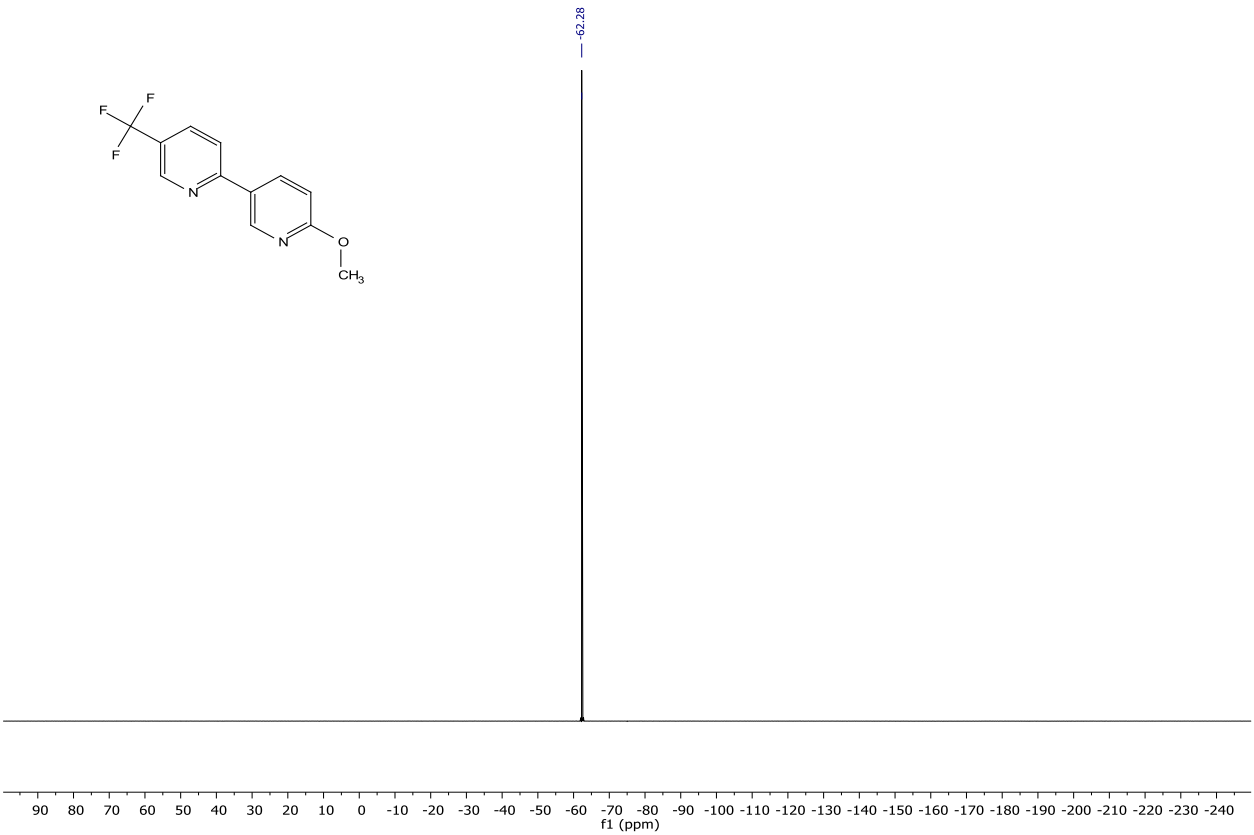
158.27
146.80
146.77
146.72
146.68
146.16
137.50
134.07
134.04
134.00
133.97
125.04
124.83
124.50
122.33
118.99
111.22
53.84
F
F
F
N
N
O
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)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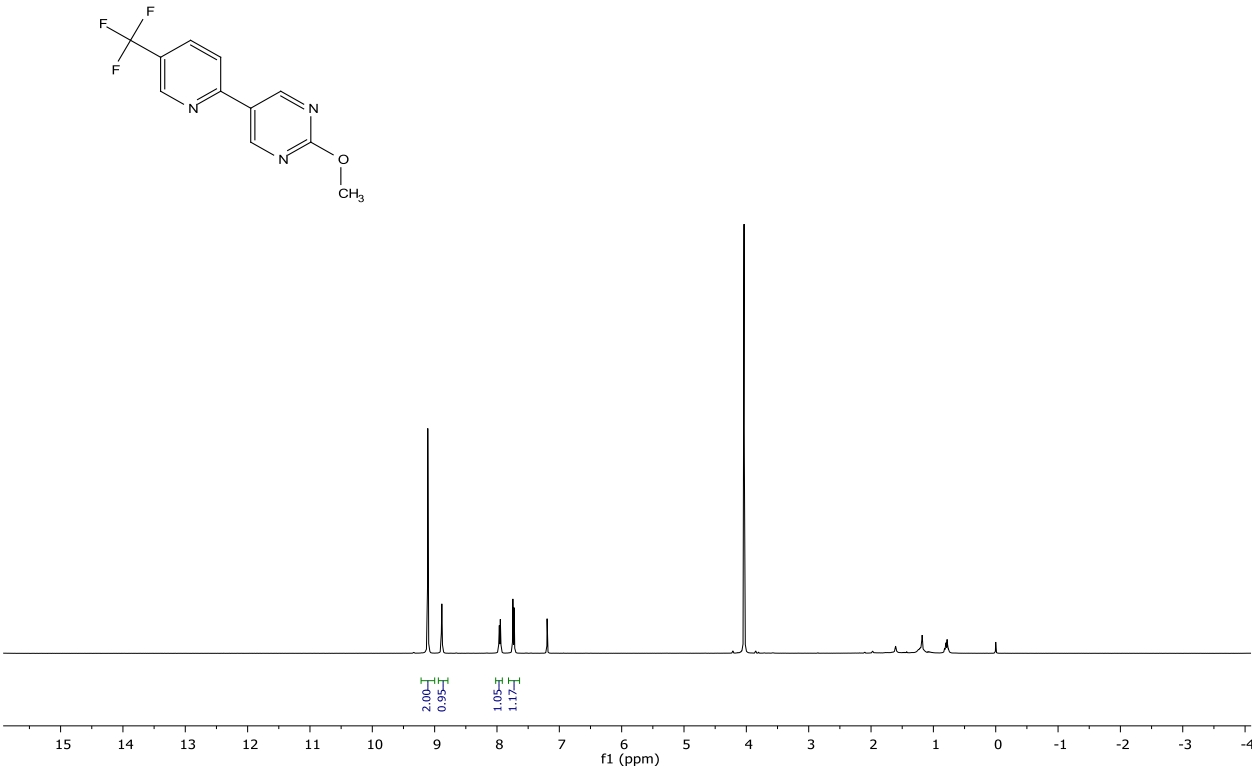
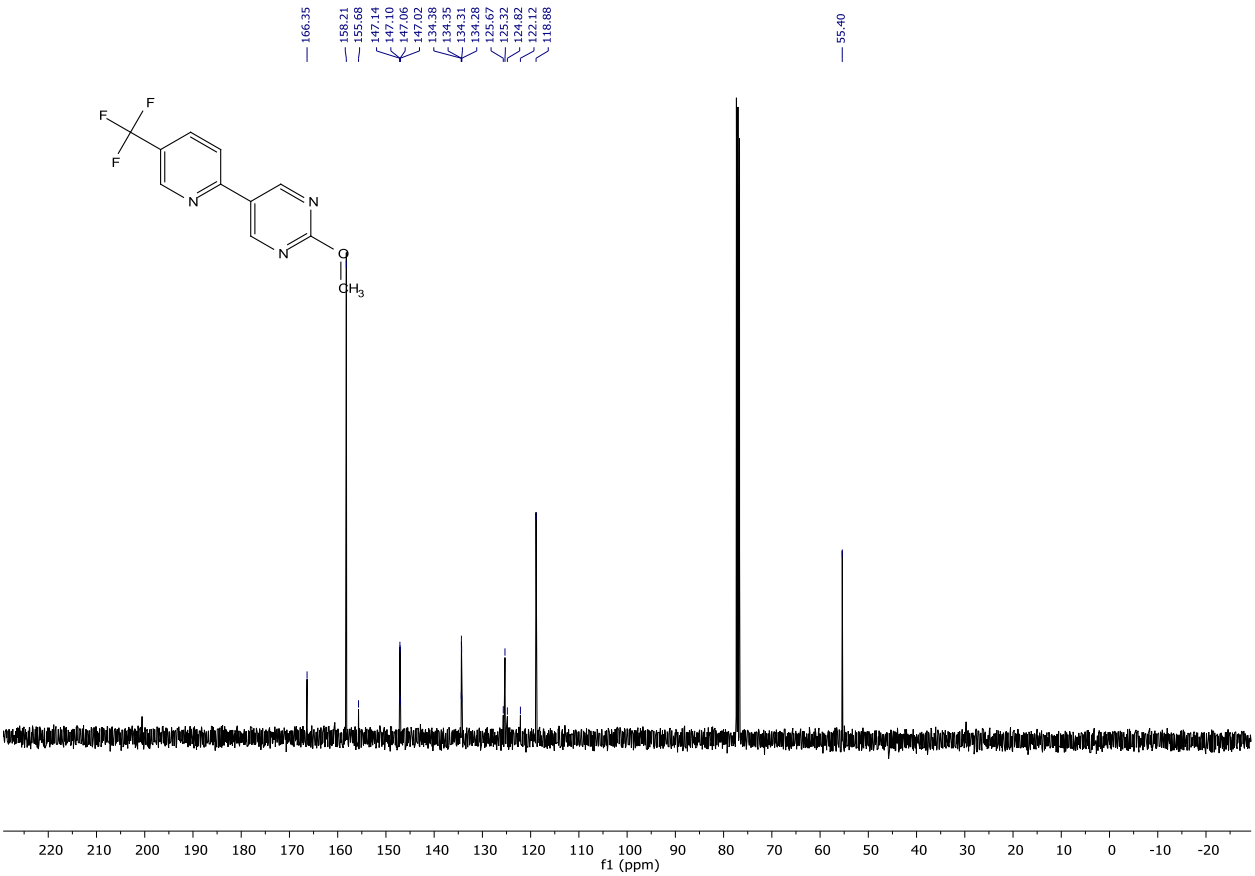
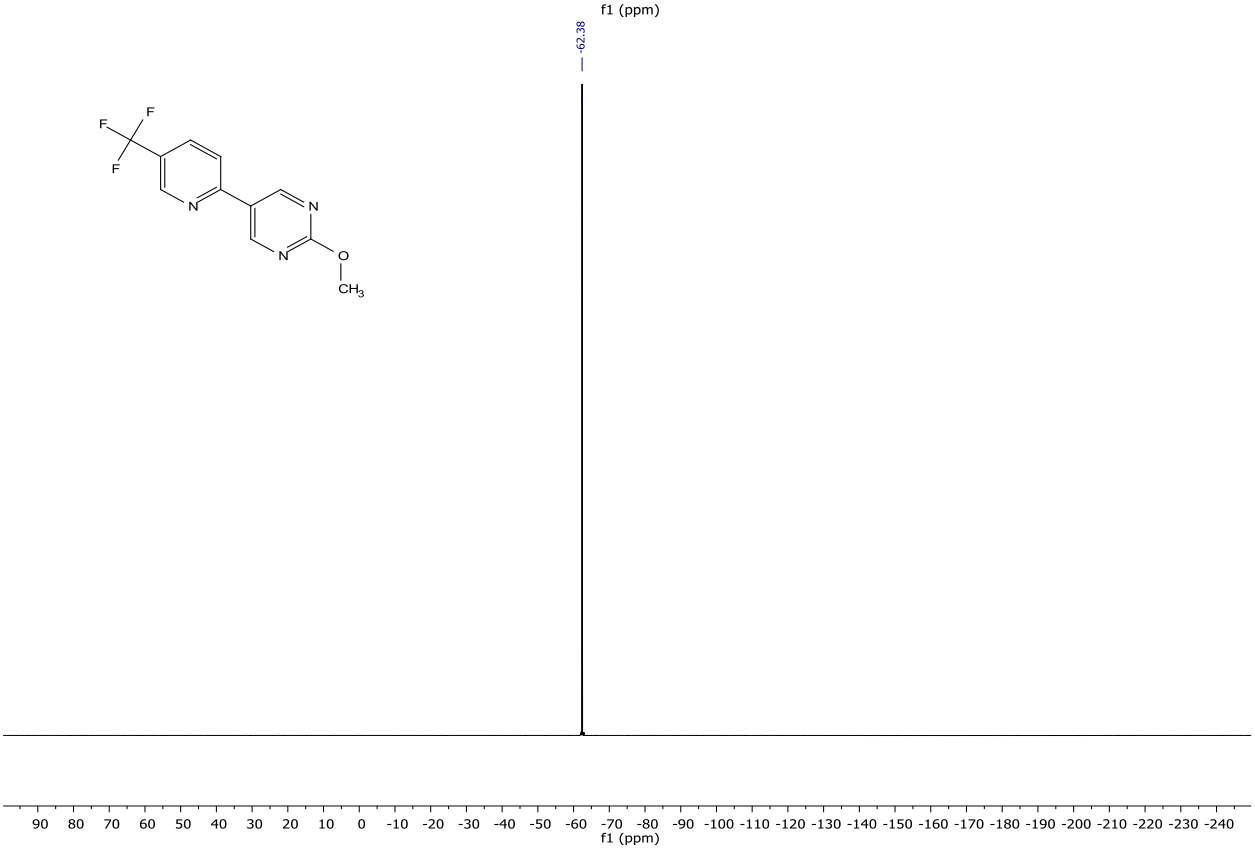
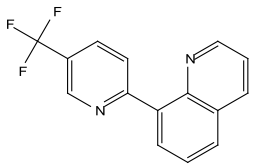
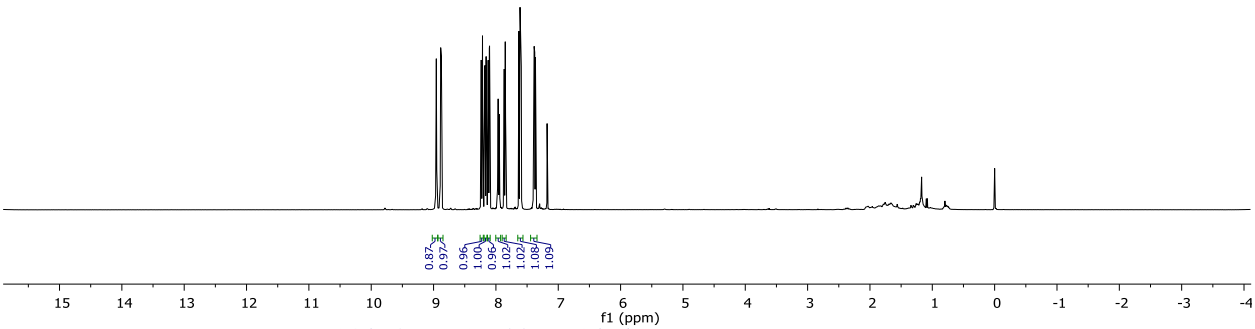
F
F
F
N
N
O
CH3
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

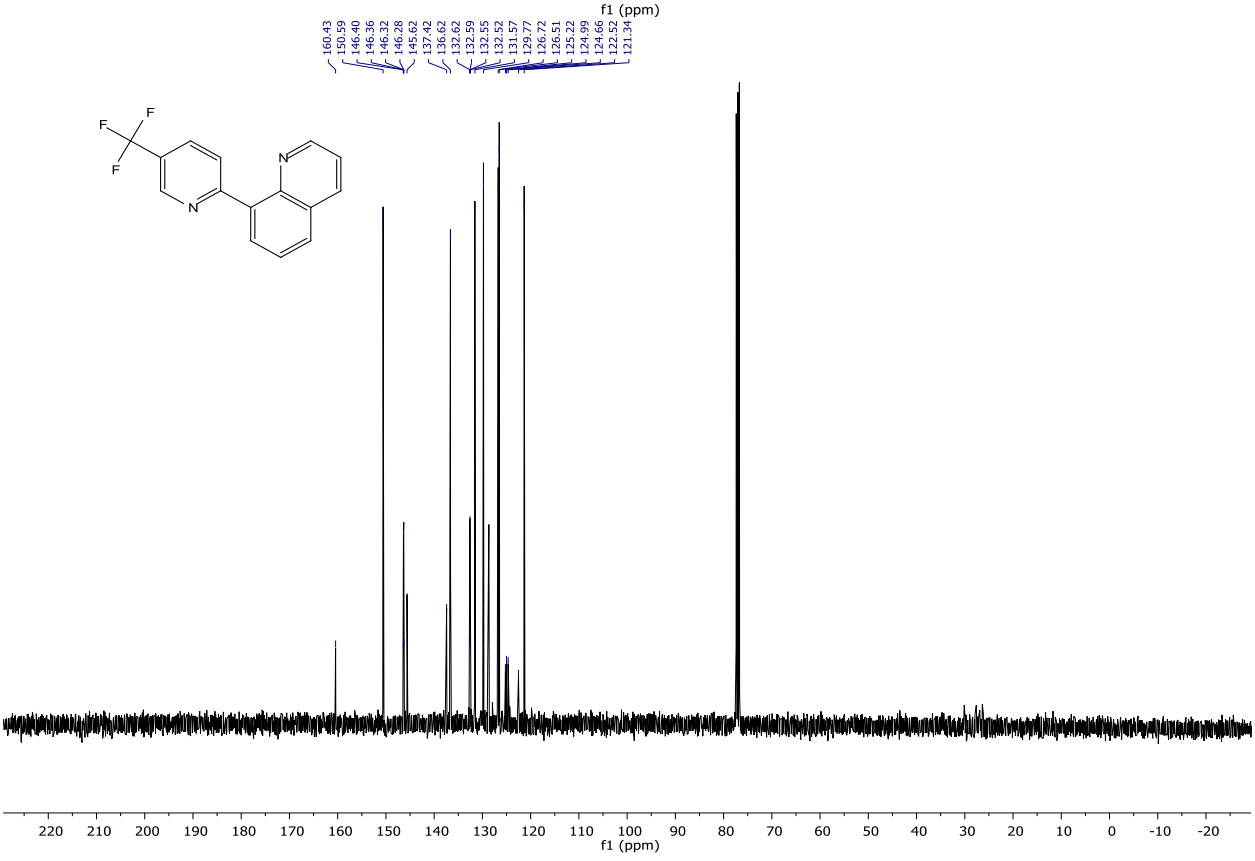

F
F
F
N
N
N
O
CH3
2.00
0.95
1.05
1.17
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

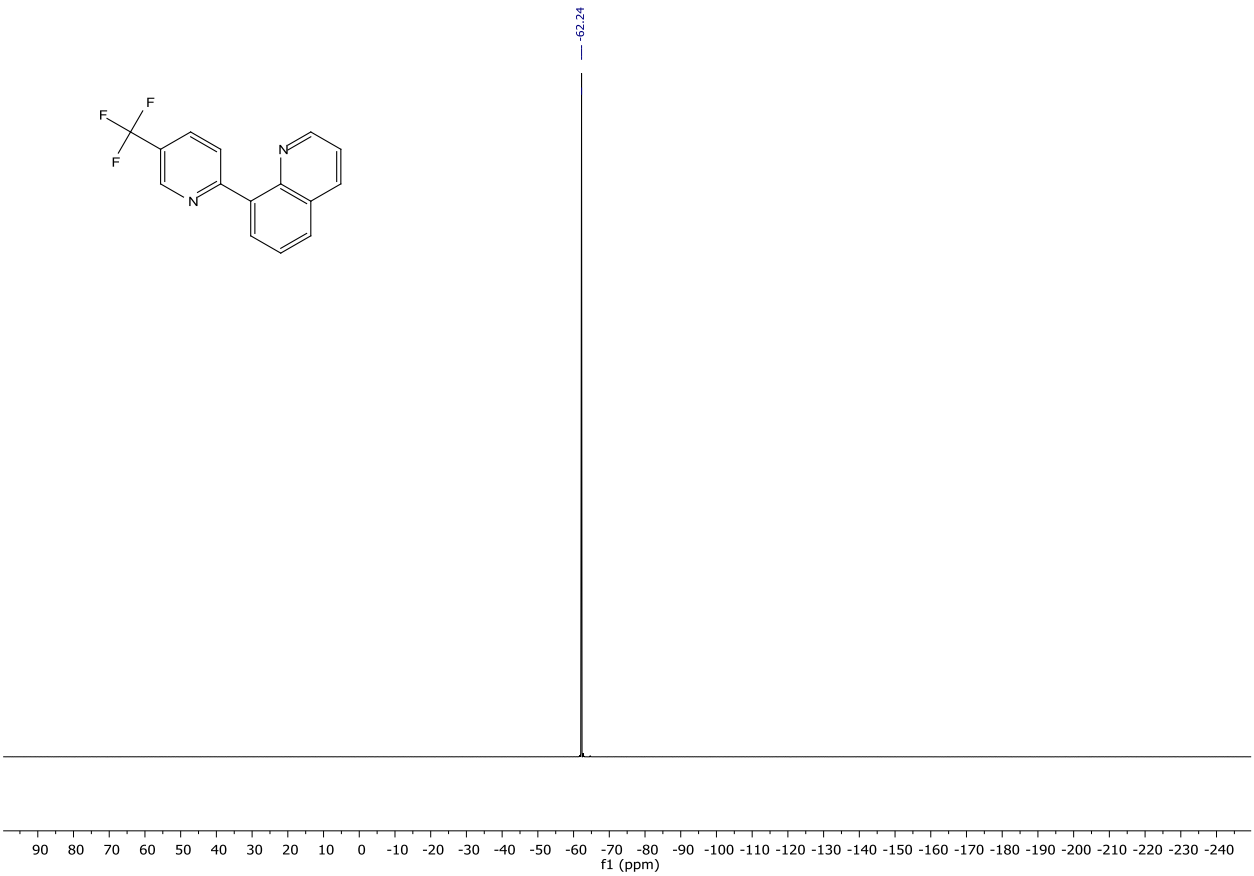

166.35
158.21
155.68
147.14
147.10
147.06
147.02
134.38
134.35
134.31
134.28
125.67
125.32
124.82
122.12
118.88
55.40
F
F
F
N
N
N
O
CH3
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

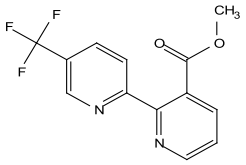

-62.38
F
F
F
N
N
N
O
CH3
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

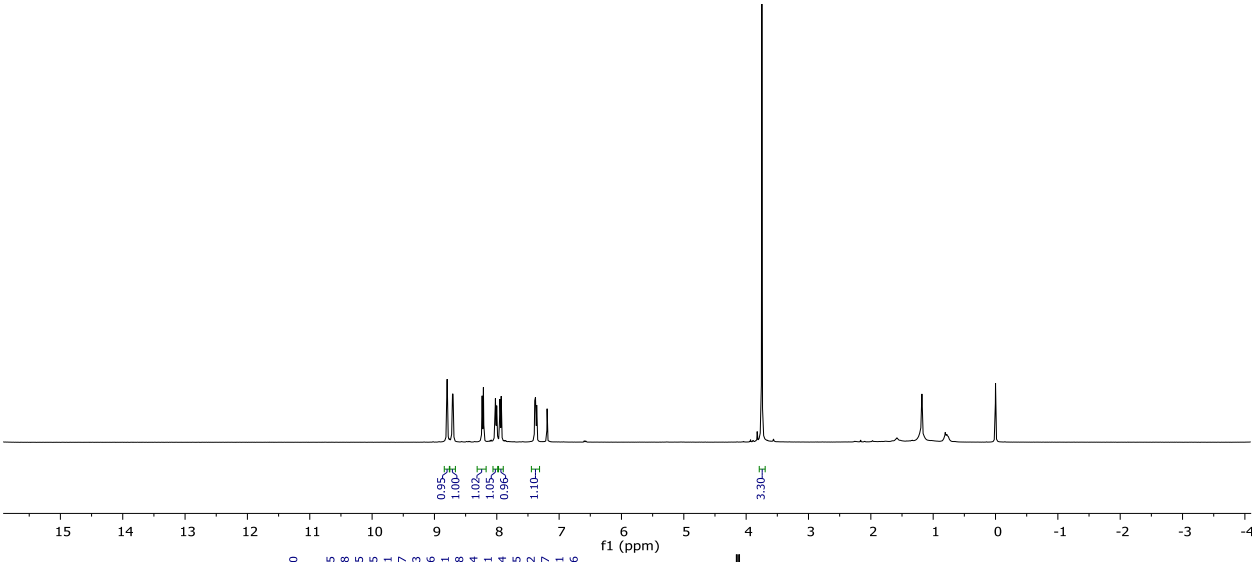

F
F
F
N
N

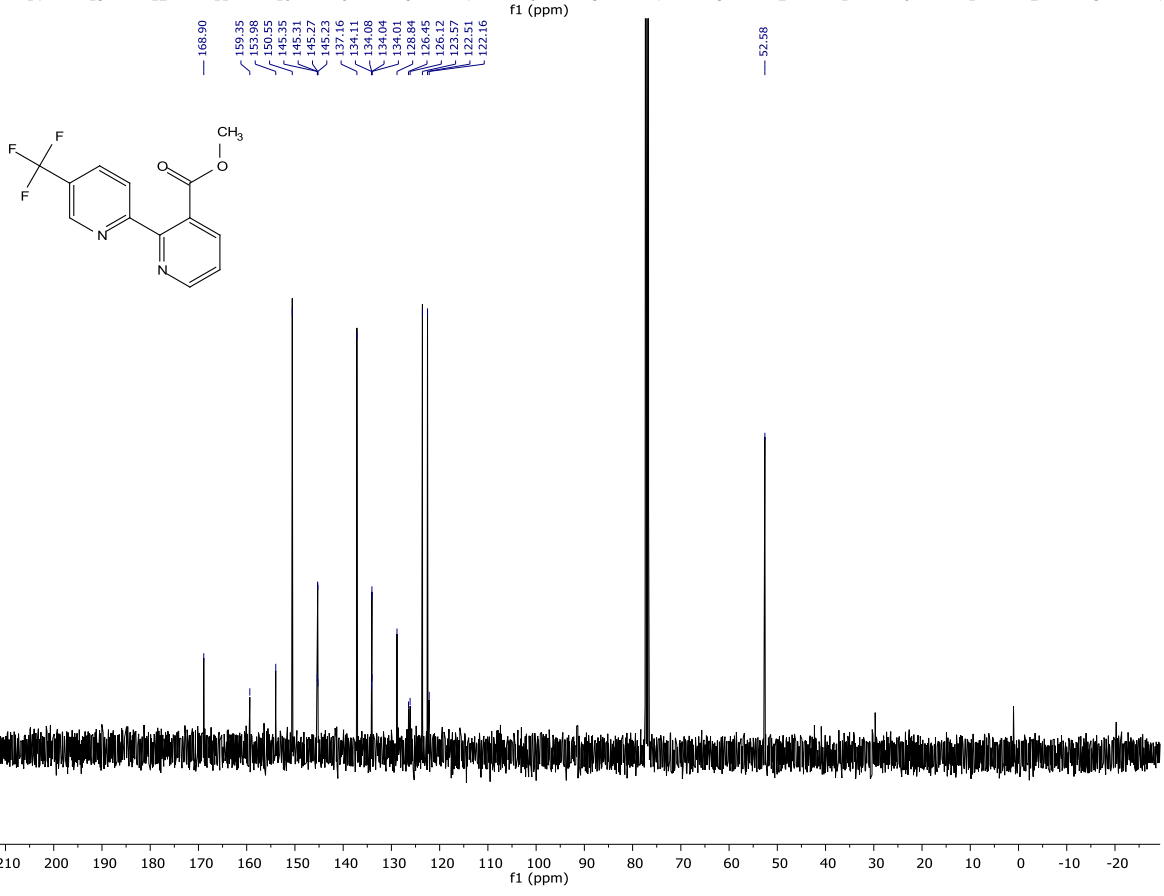

0.87
0.97
0.96
1.00
0.96
1.02
1.02
1.08
1.09
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)


160.43
150.59
146.40
146.36
146.32
146.28
145.62
137.42
136.62
132.62
132.59
132.55
132.52
131.57
129.77
126.72
126.51
125.22
124.99
124.66
122.52
121.34
F
F
F
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

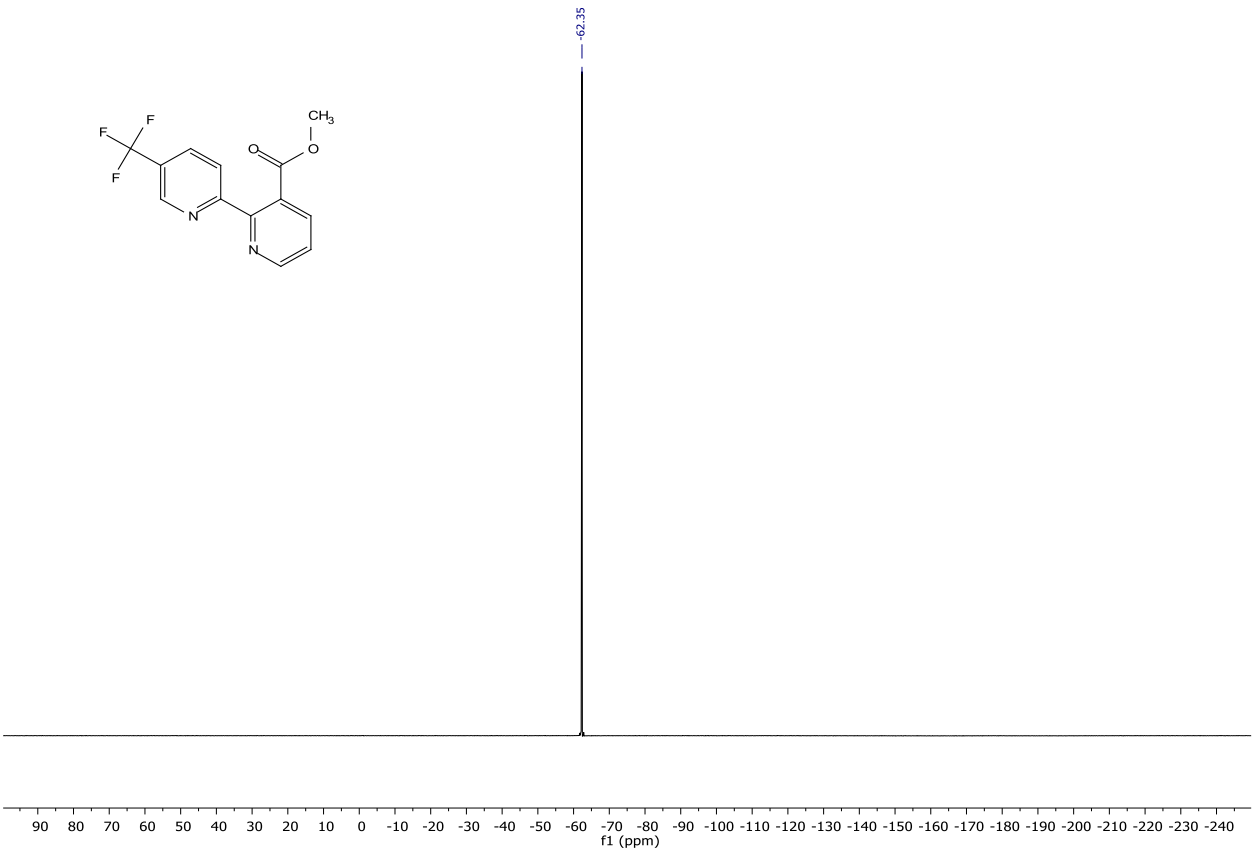

-62.24
F
F
F
N
N
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

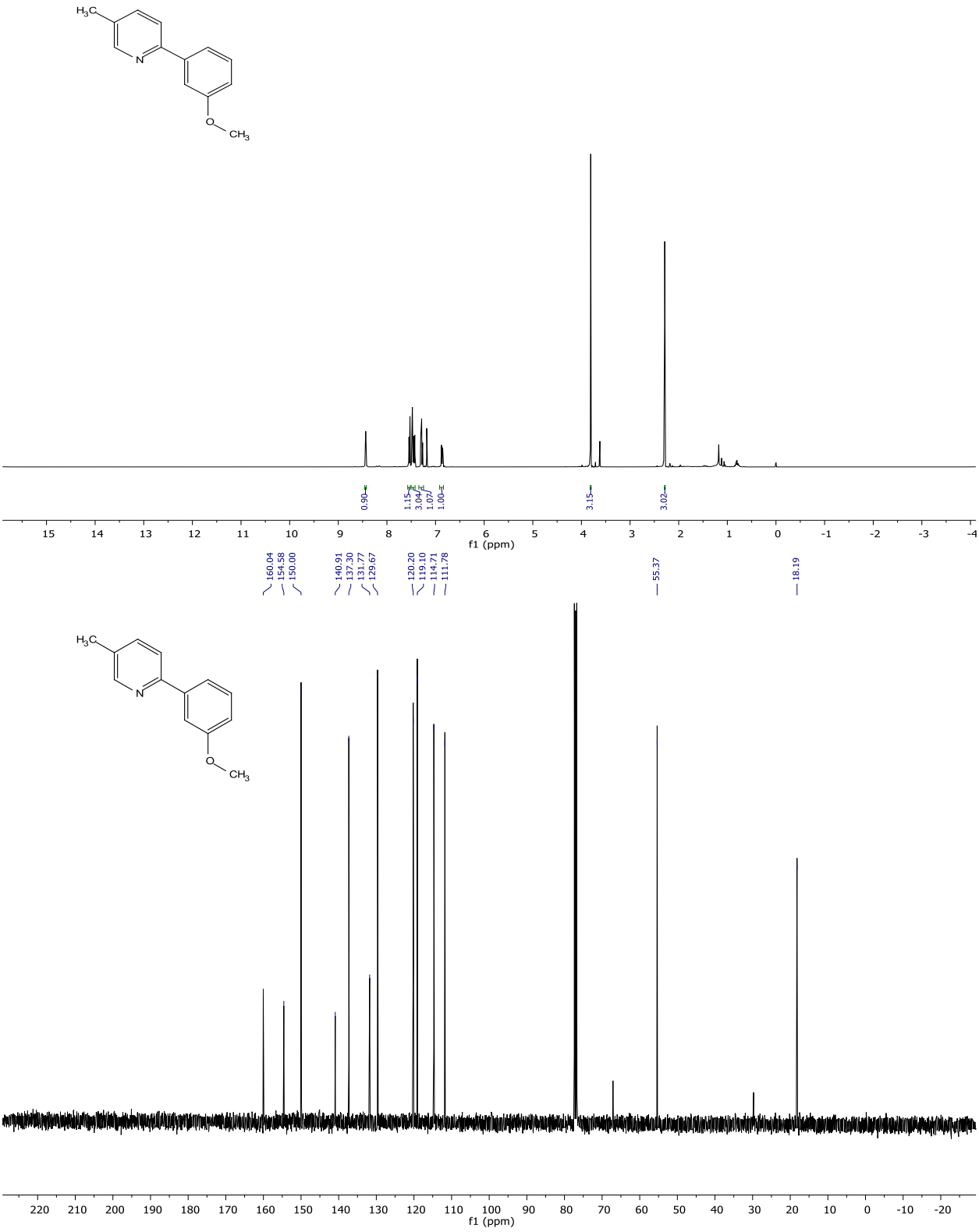

F
F
F
N
O
O
CH3
N

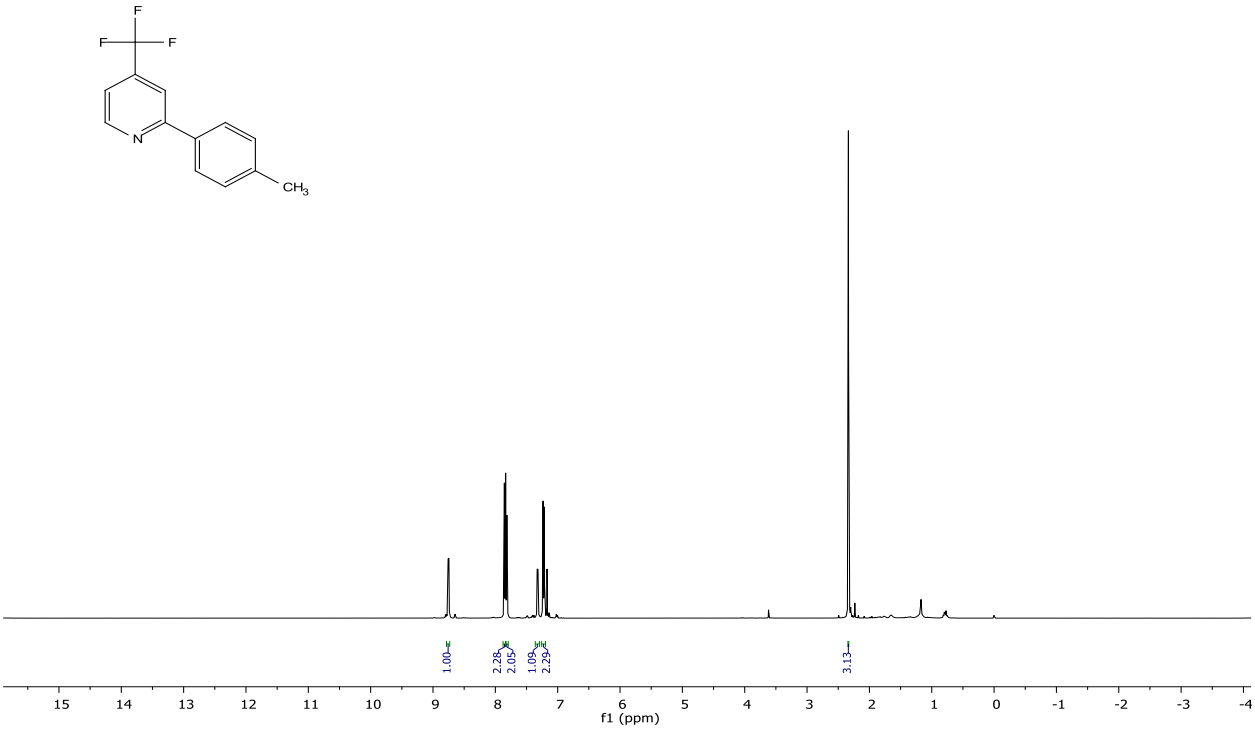

0.95
1.00
1.02
1.05
0.96
1.10
3.30
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

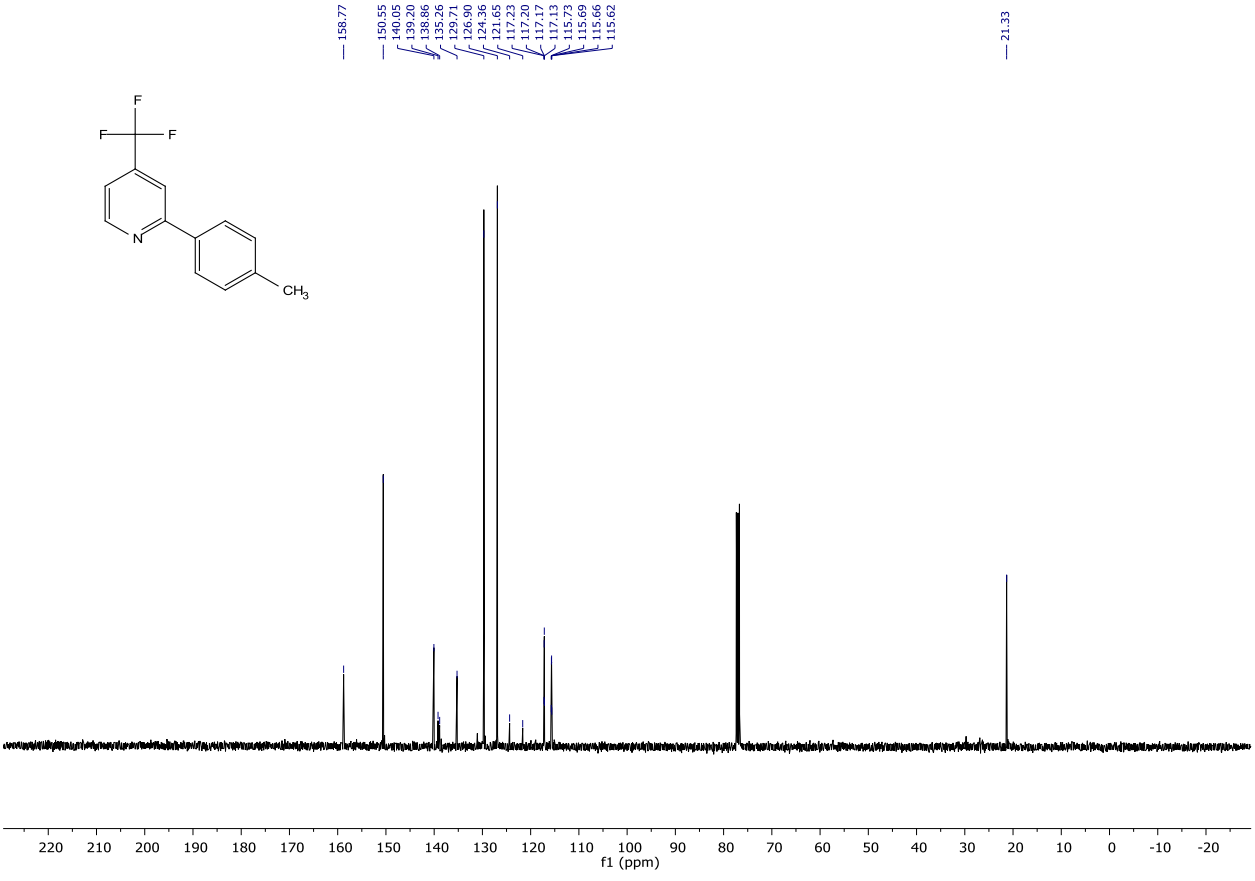

168.90
159.35
153.98
150.55
145.35
145.31
145.27
145.23
137.16
134.11
134.08
134.04
134.01
128.84
126.45
126.12
123.57
122.51
122.16
52.58
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

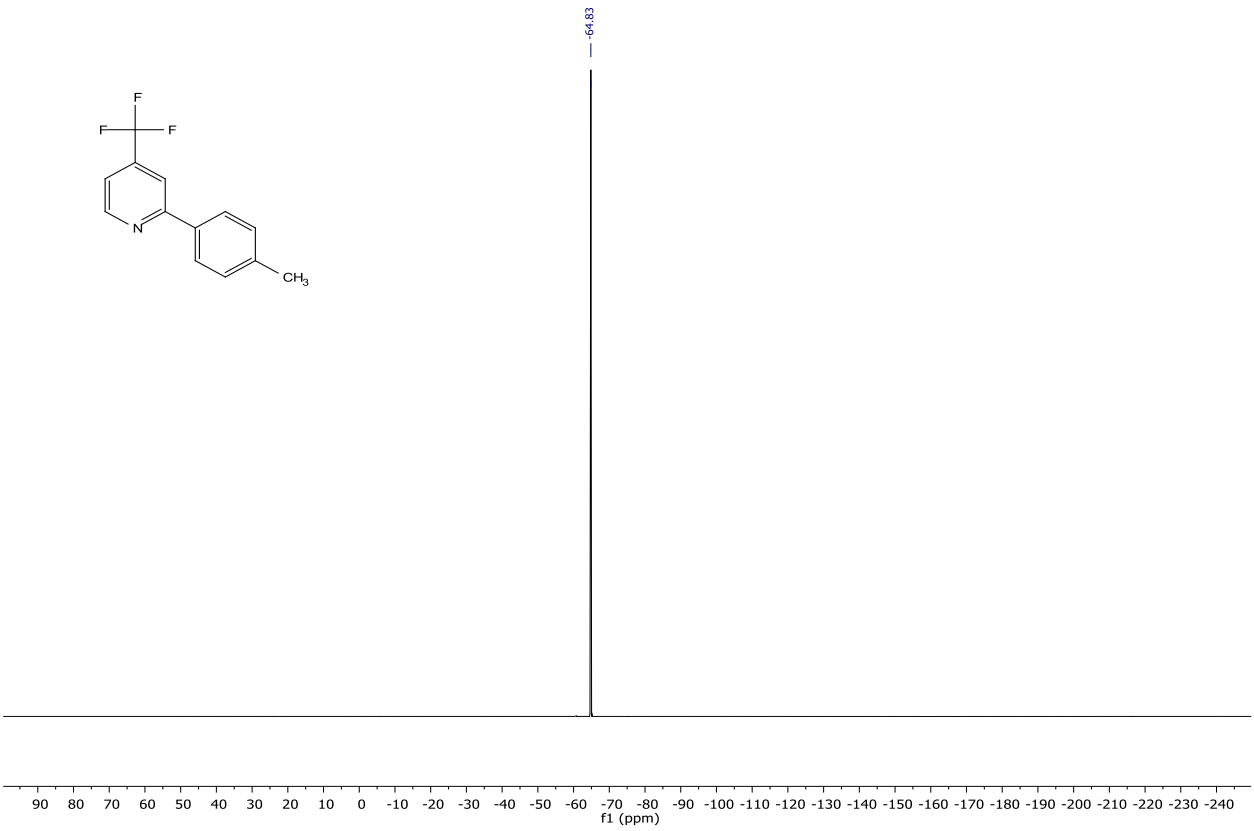
F
F
F
N
O
O
CH3
N

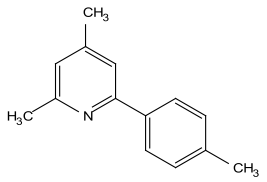

-62.35
F
F
F
N
N
O
O
CH3
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

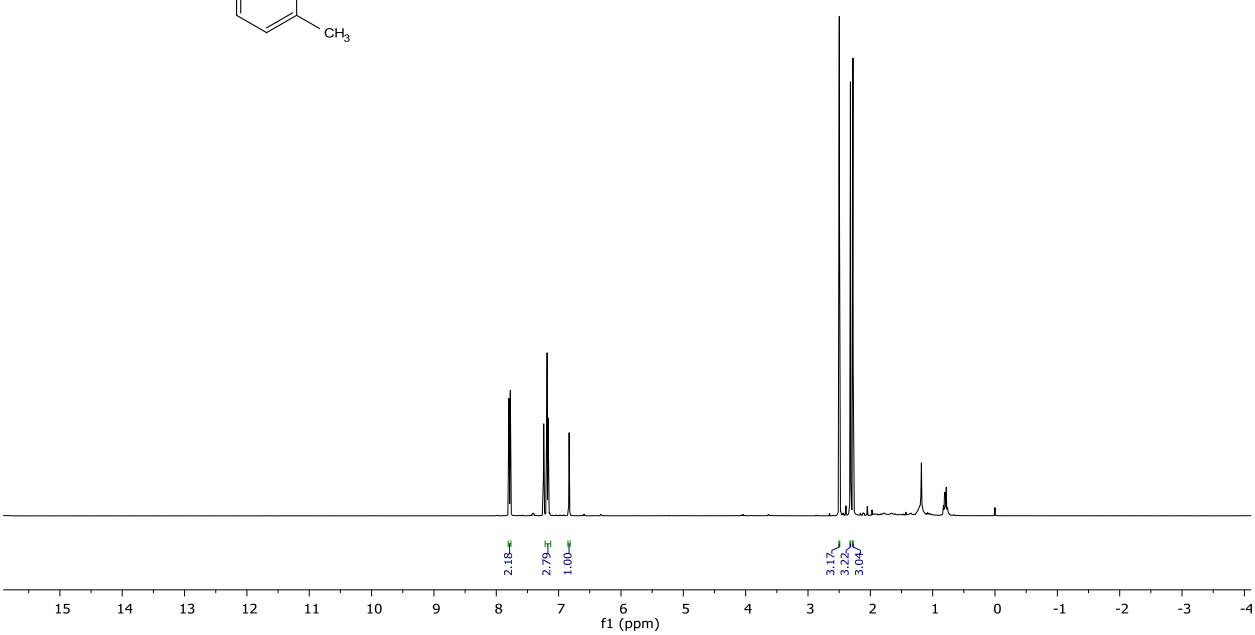

H3C
N
O
CH3
0.90
1.15
3.04
1.07
1.00
3.15
3.02
f1 (ppm)
160.04
154.58
150.00
140.91
137.30
131.77
129.67
120.20
119.10
114.71
111.78
55.37
18.19
f1 (ppm)


F
F
F
N
CH3
1.00
2.28
2.05
1.09
2.29
3.13
f1 (ppm)

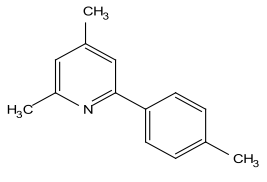

158.77
150.55
140.05
139.20
138.86
135.26
129.71
126.90
124.36
121.65
117.23
117.20
117.17
117.13
115.73
115.69
115.66
115.62
21.33
F
F
F
N
CH3
f1 (ppm)

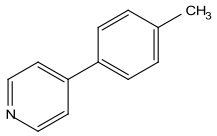

-64.83
F
F
F
N
CH3
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

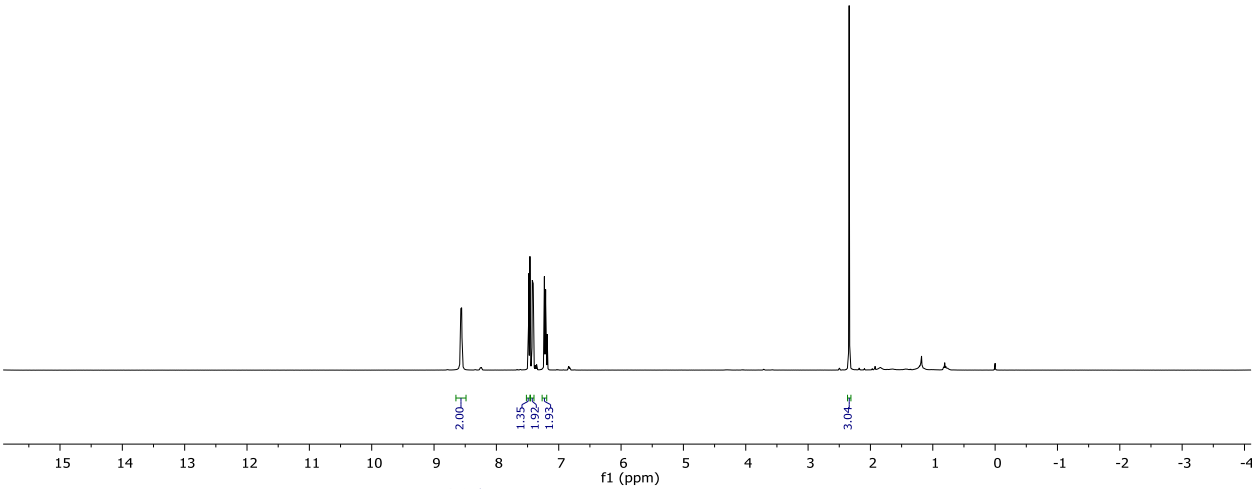


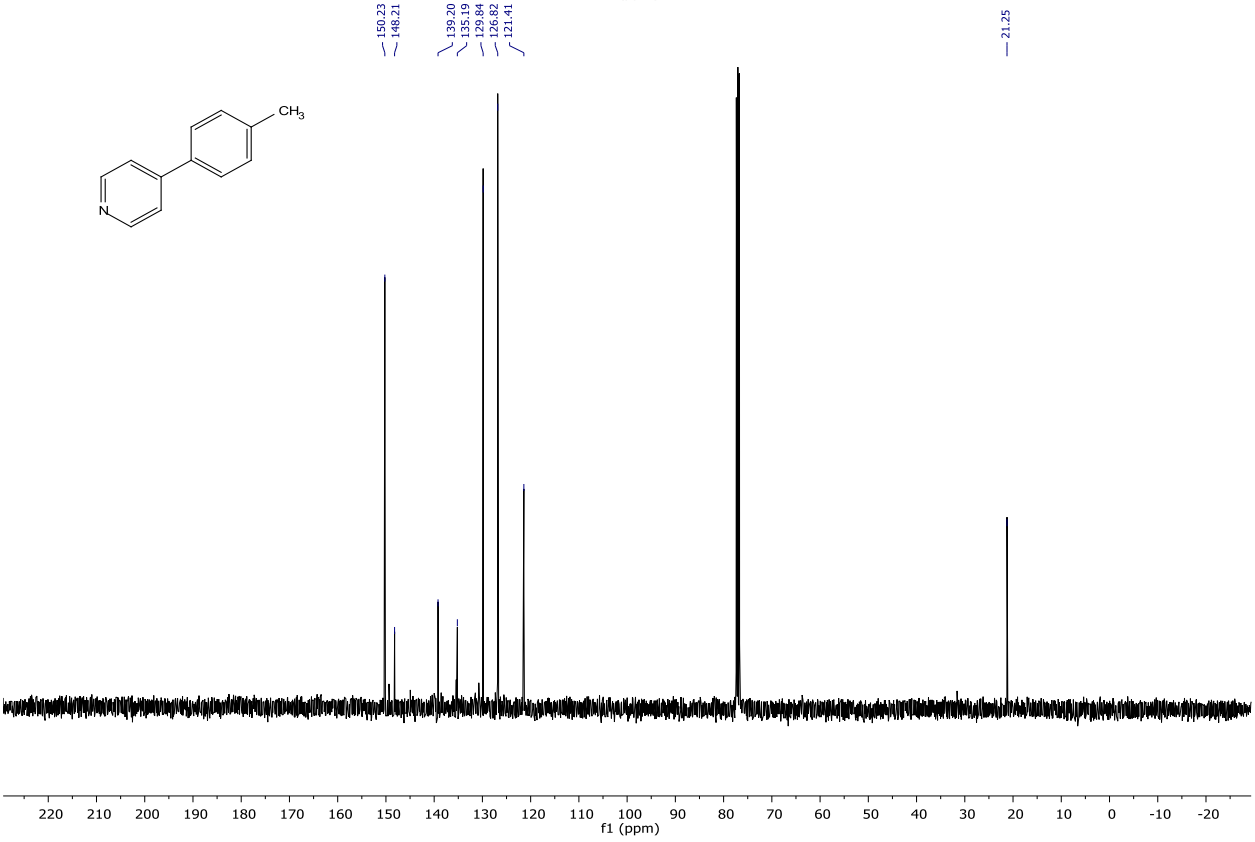


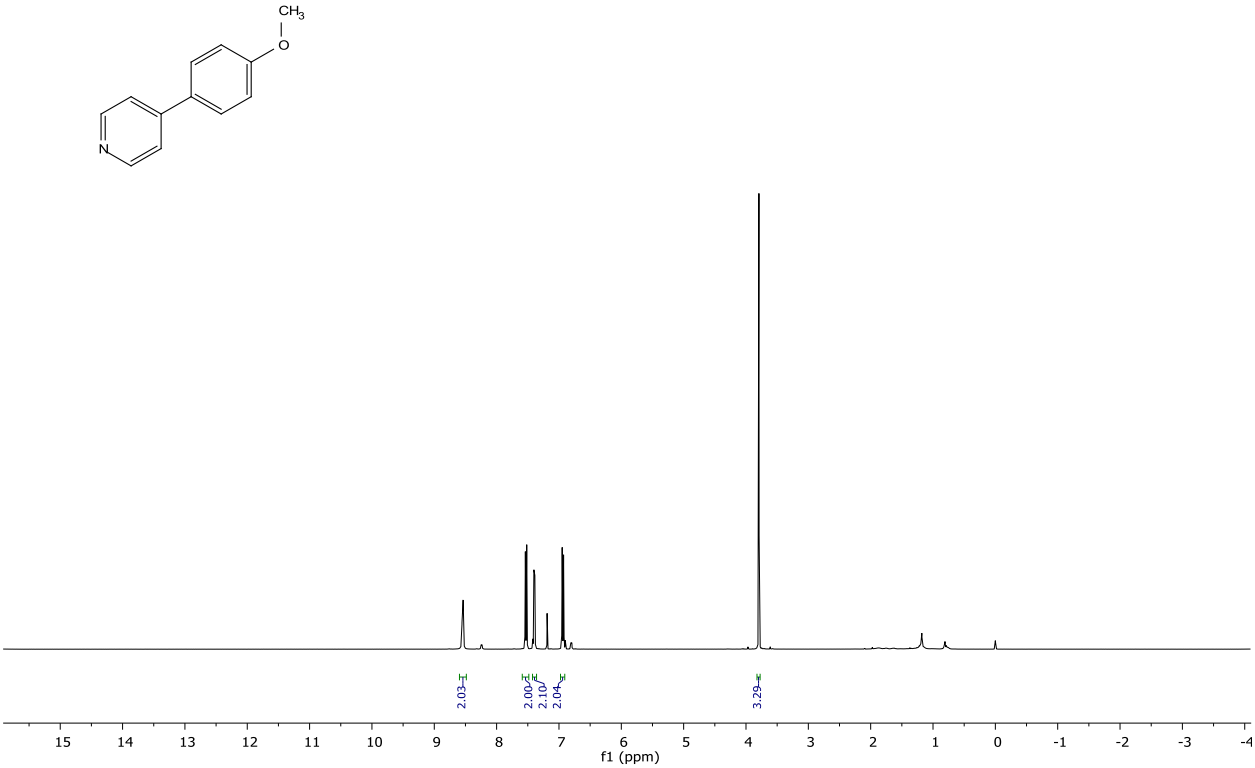
158.00
156.93
147.65
138.45
137.09
129.34
126.88
122.34
118.43
24.59
21.28
21.11

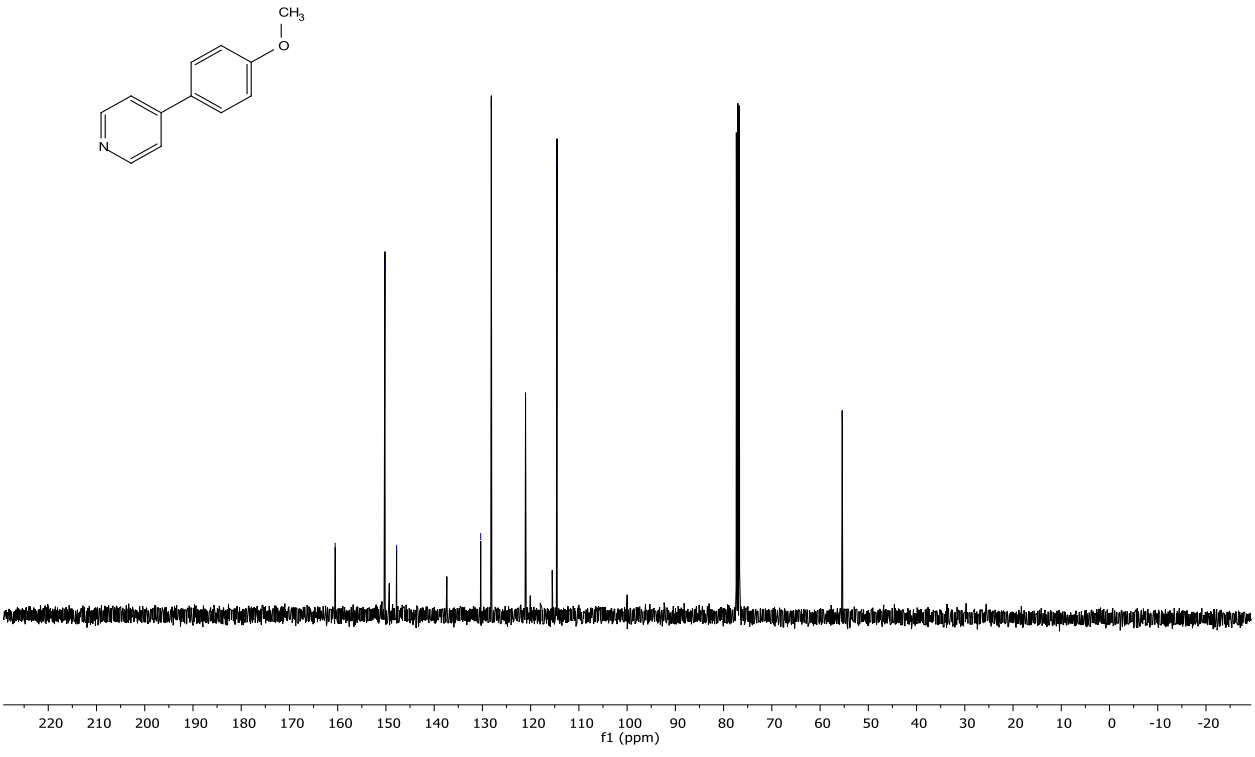


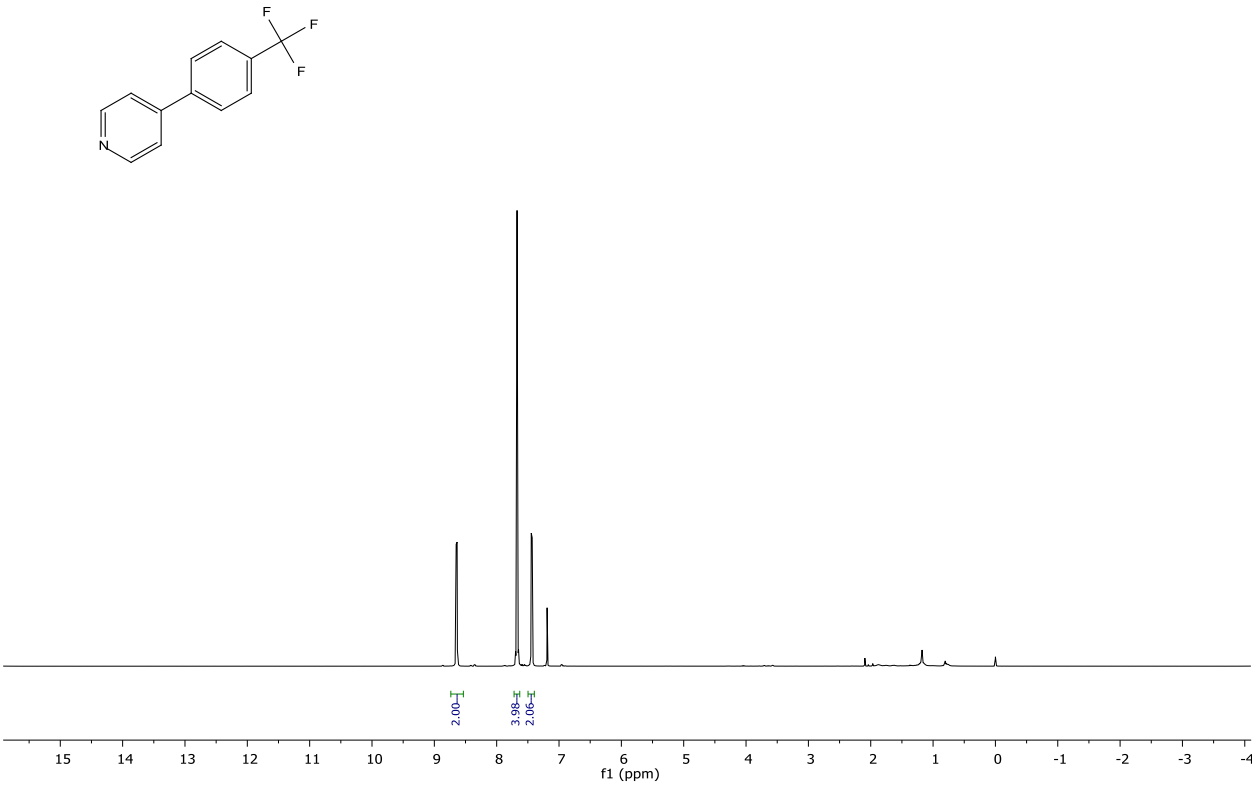

CH3
N

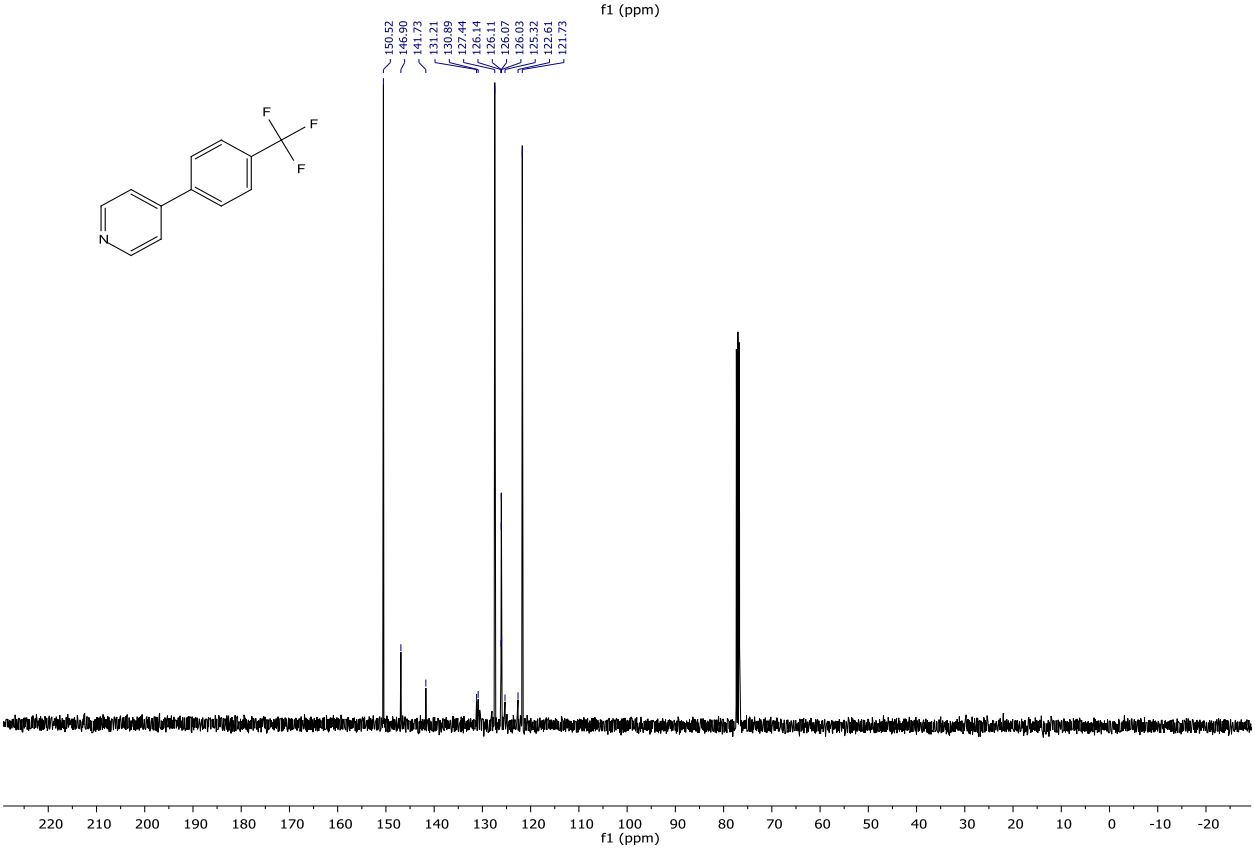

2.00
1.35
1.92
1.93
3.04
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

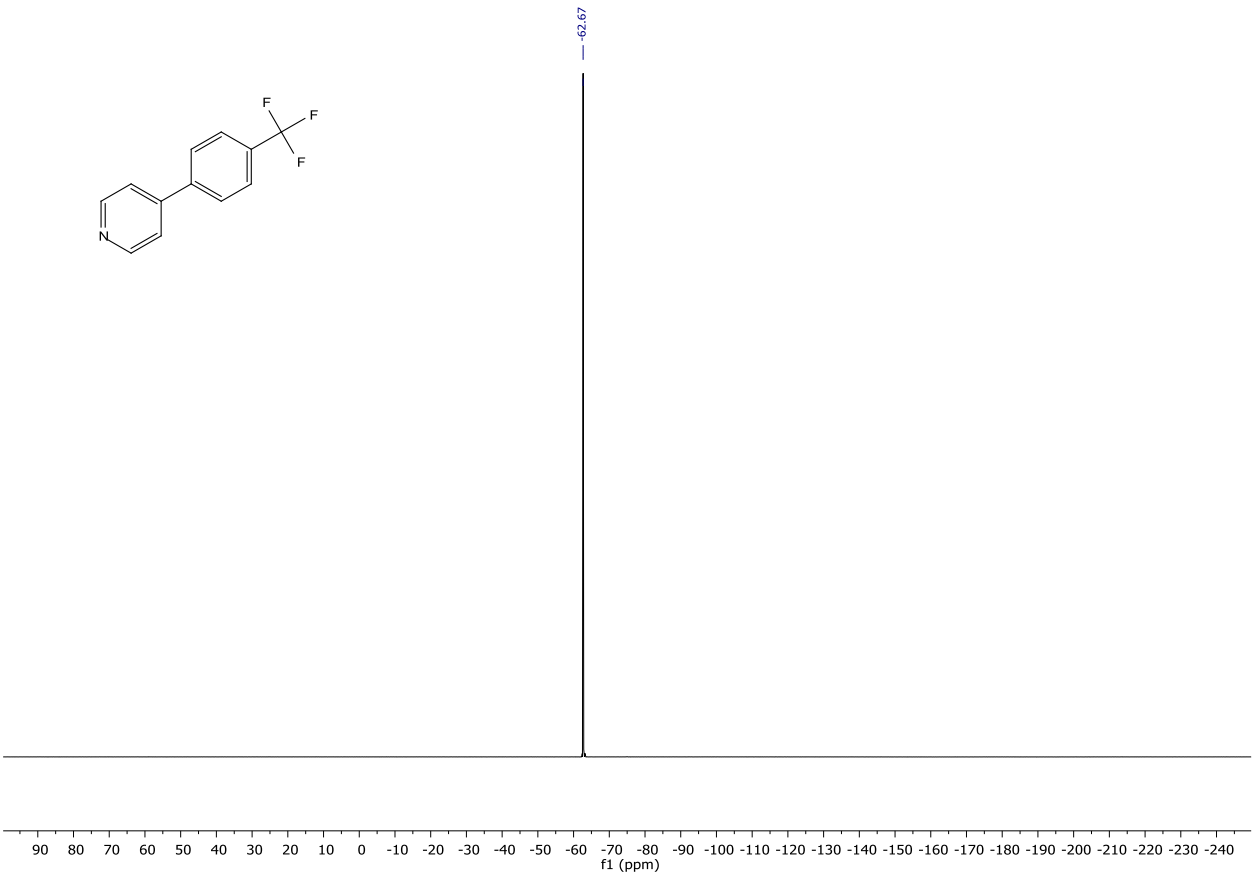

150.23
148.21
139.20
135.19
129.84
126.82
121.41
21.25
CH3
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

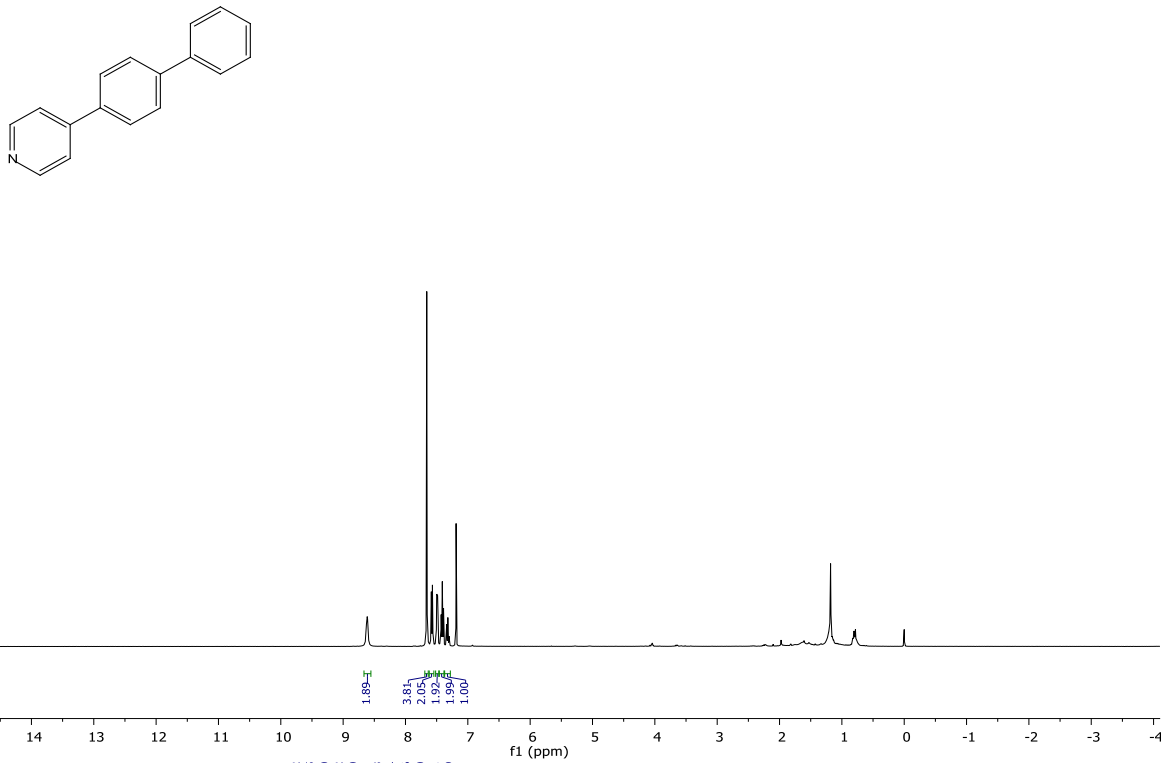

CH3
O
N
2.03
2.00
2.10
2.04
3.29
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

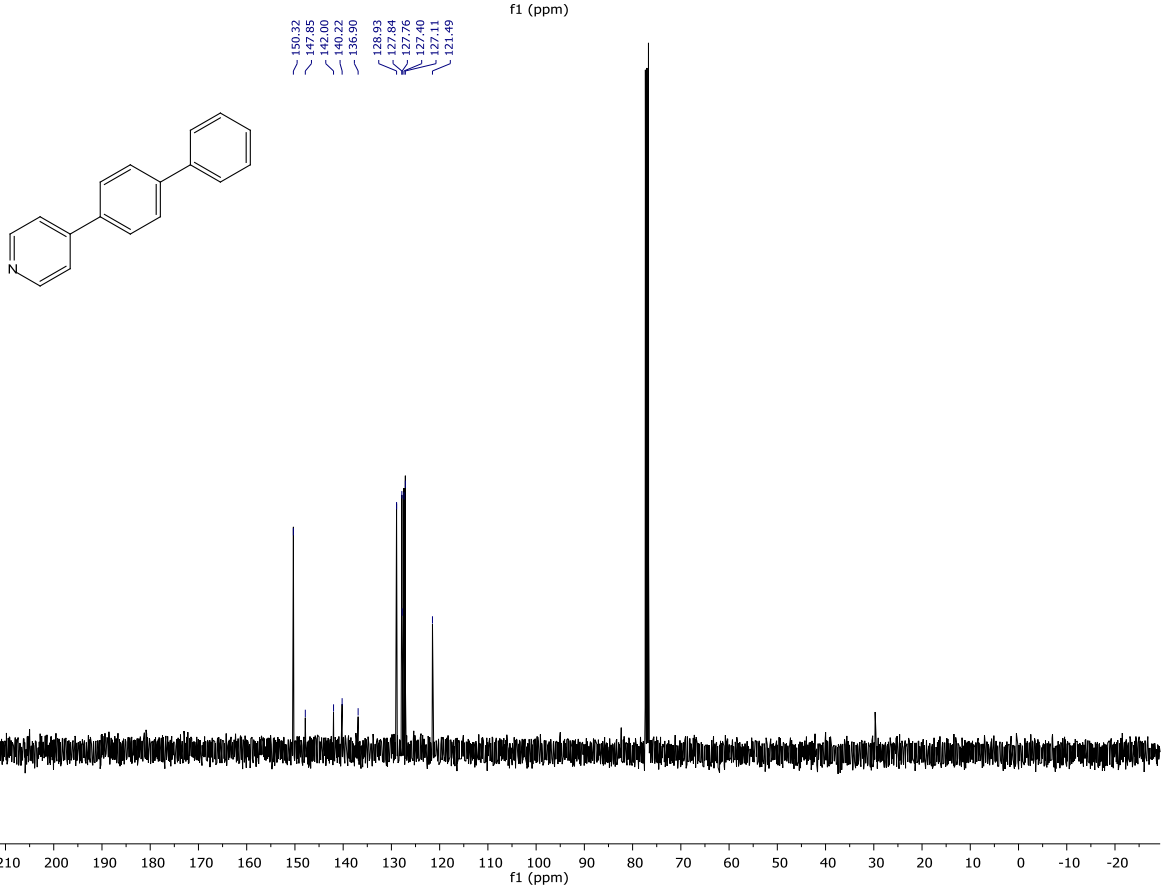

CH3
O
N
160.52
150.20
147.78
130.35
128.15
121.06
114.54
55.41
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

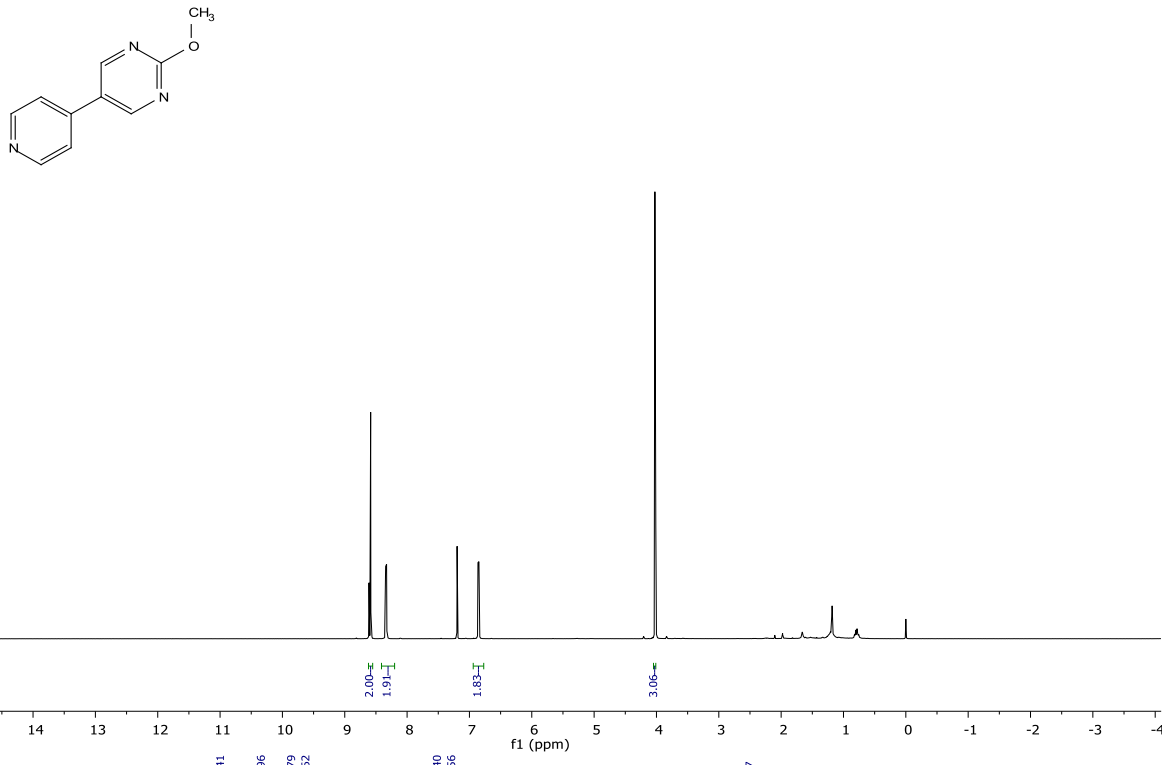

F
F
F
N
2.00
3.98
2.06
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

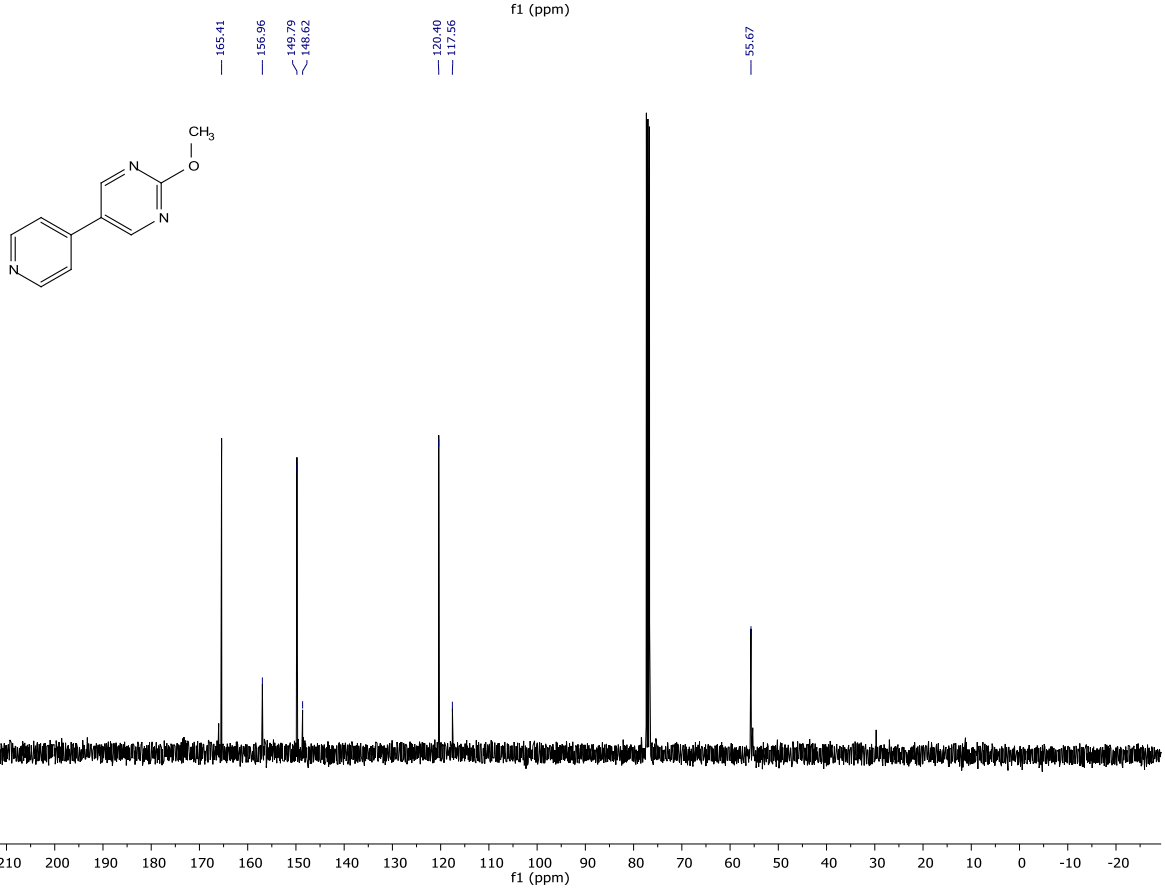

150.52
146.90
141.73
131.21
130.89
127.44
126.14
126.11
126.07
126.03
125.32
122.61
121.73
F
F
F
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

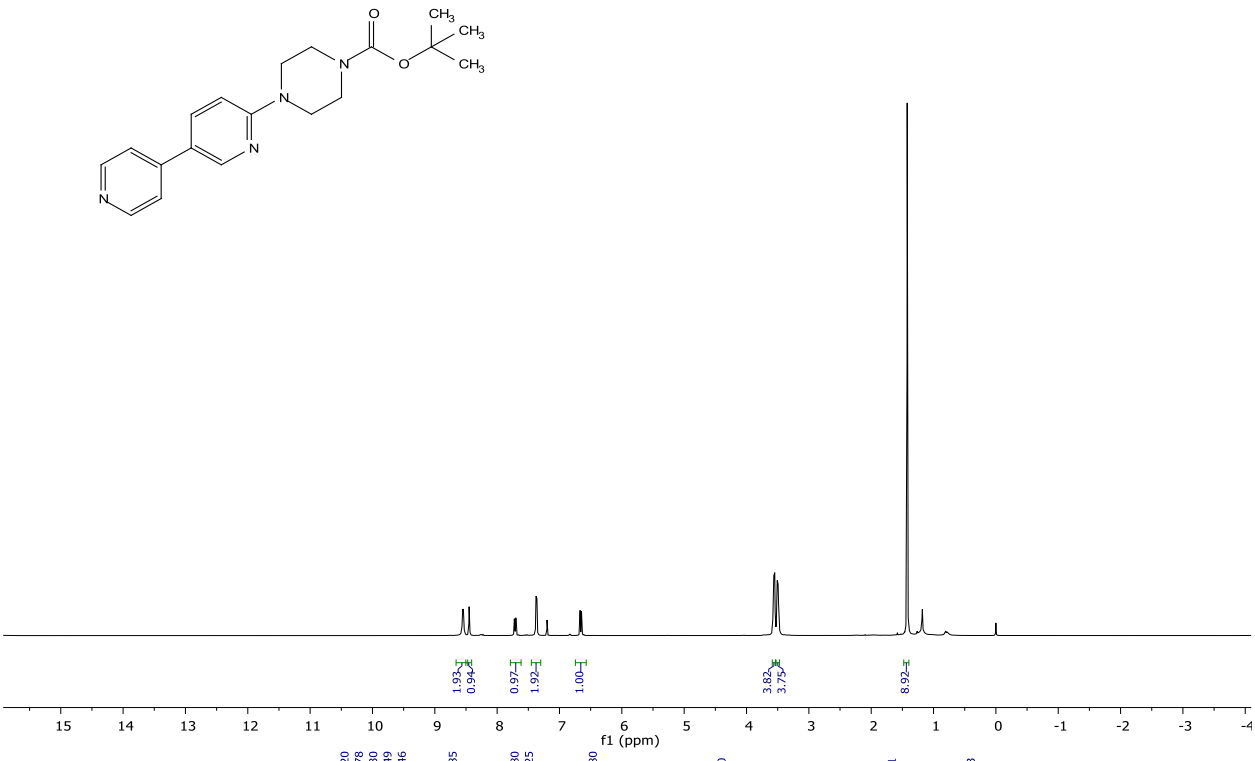

-62.67
F
F
F
N
90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240
f1 (ppm)

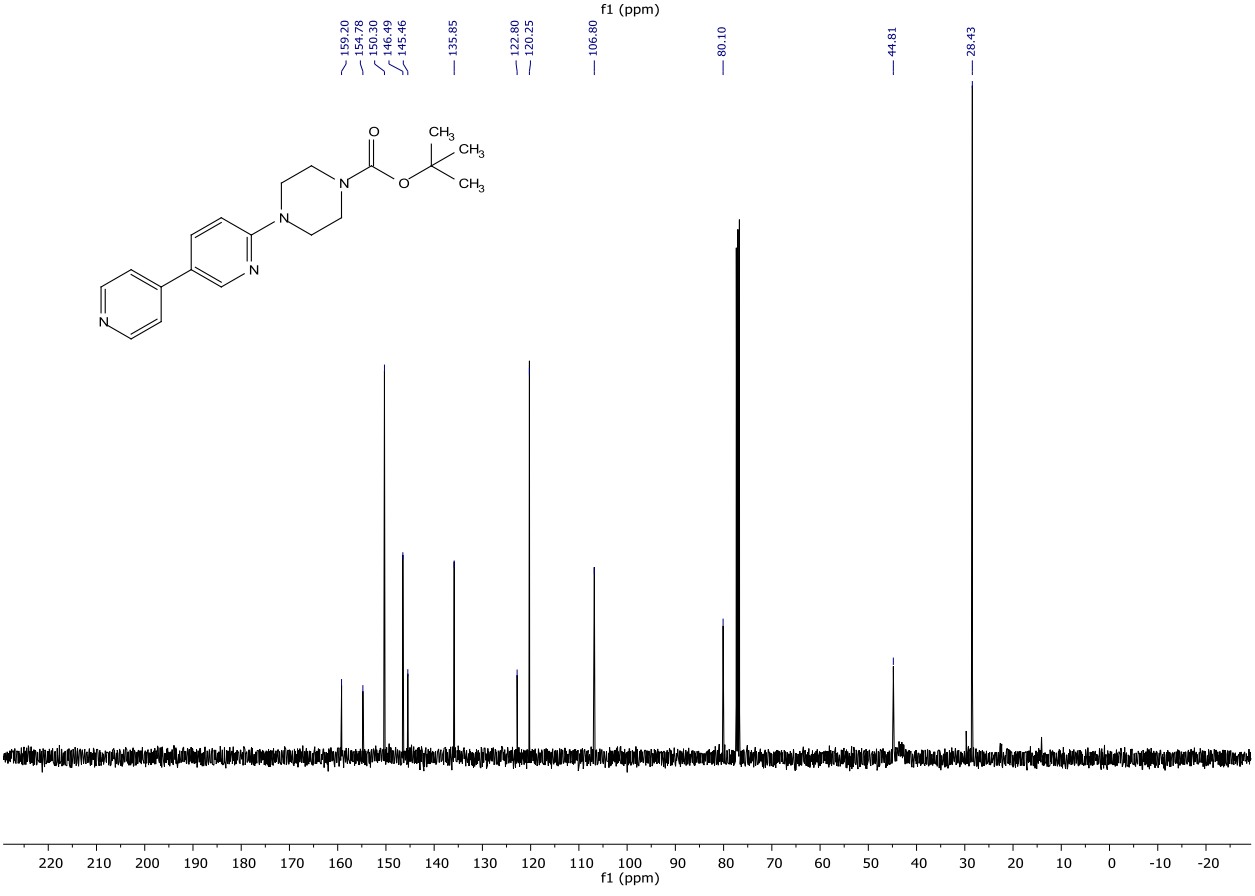

N
1.89
3.81
2.05
1.92
1.99
1.00
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

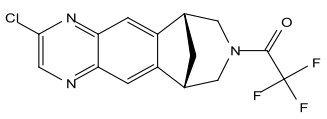

150.32
147.85
142.00
140.22
136.90
128.93
127.84
127.76
127.40
127.11
121.49
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

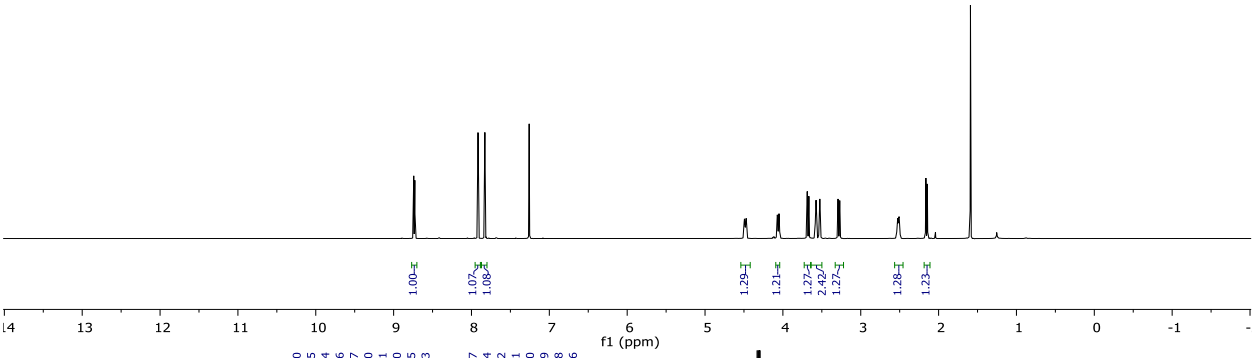

CH3
O
N
N
N
2.00
1.91
1.83
3.06
15 14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1 -2 -3 -4
f1 (ppm)

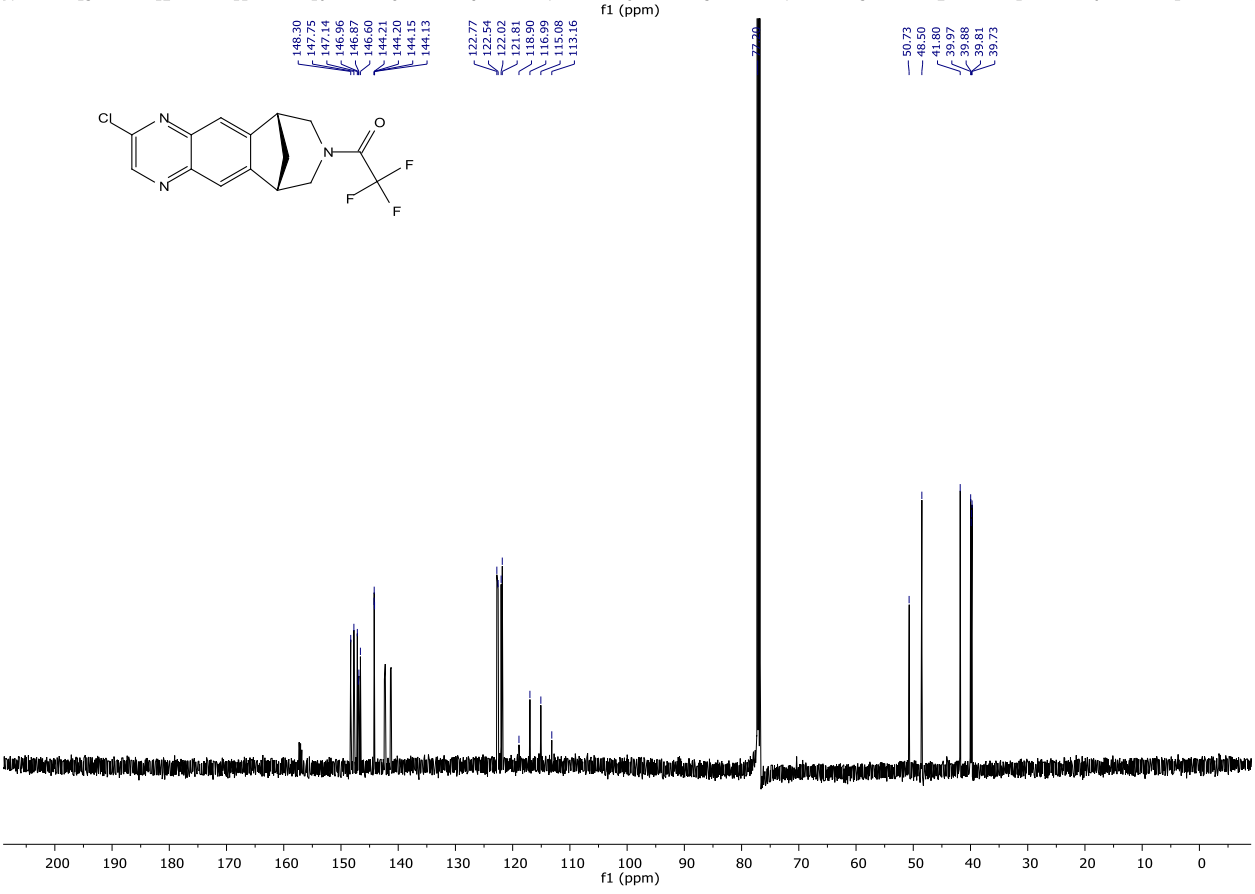

165.41
156.96
149.79
148.62
120.40
117.56
55.67
CH3
O
N
N
N
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

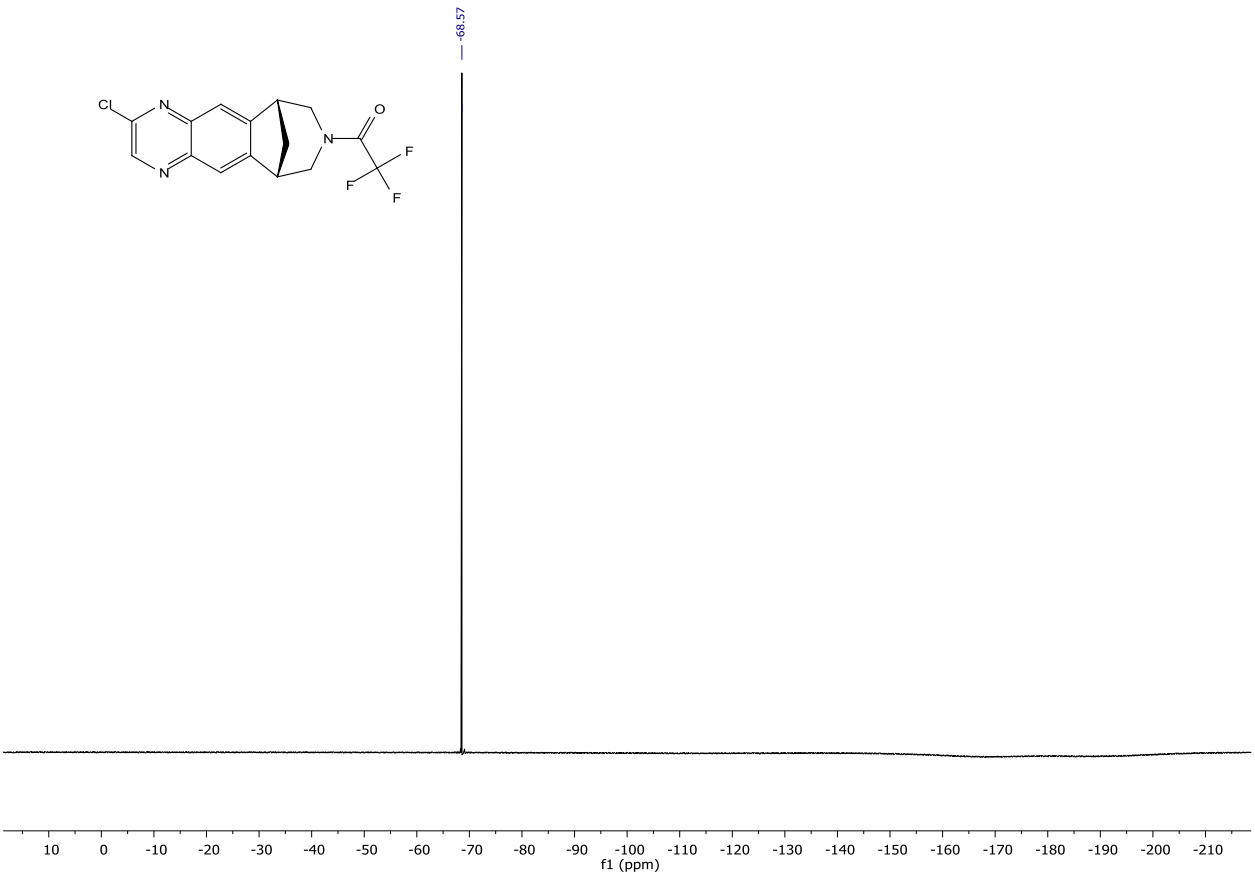

1.93
0.94
0.97
1.92
1.00
3.82
3.75
8.92
f1 (ppm)

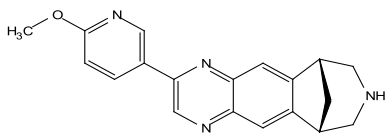

159.20
154.78
150.30
146.49
145.46
135.85
122.80
120.25
106.80
80.10
44.81
28.43
f1 (ppm)

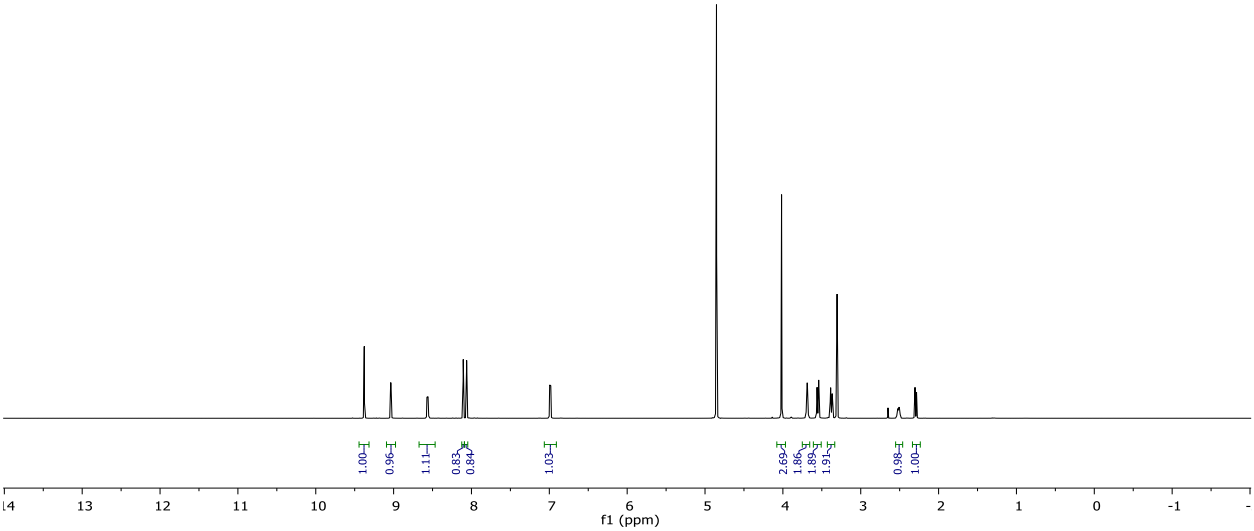

Cl
N
N
O
N
F
F
F

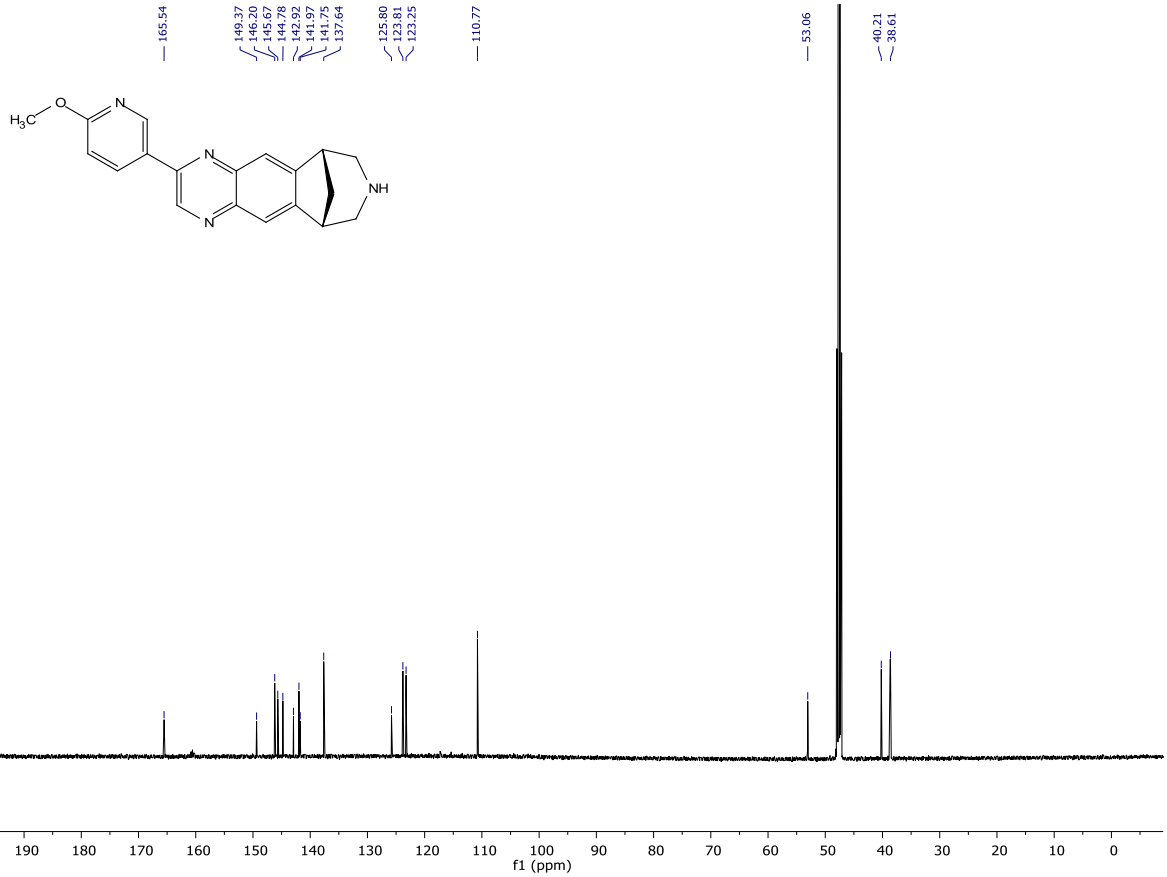

1.00
1.07
1.08
1.29
1.21
1.27
2.42
1.27
1.28
1.23
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

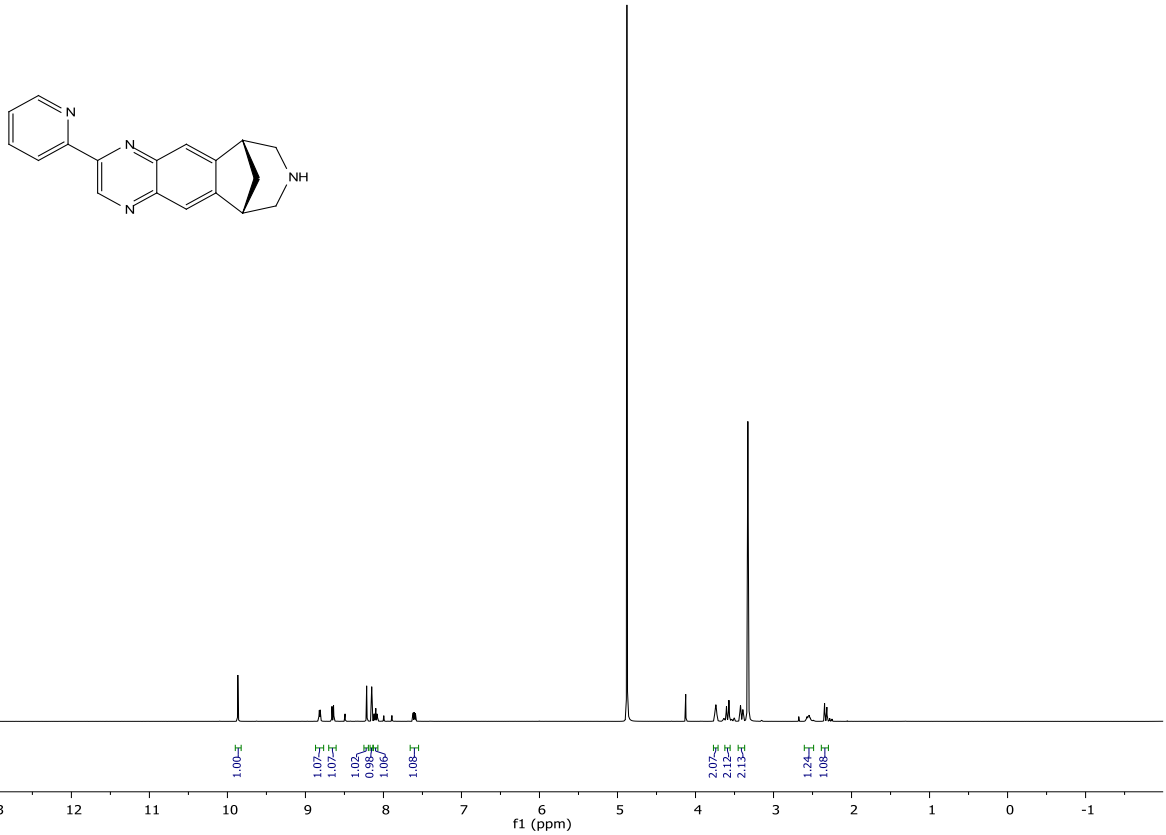

148.30
147.75
147.14
146.96
146.87
146.60
144.21
144.20
144.15
144.13
122.77
122.54
122.02
121.81
118.90
116.99
115.08
113.16
77.30
50.73
48.50
41.80
39.97
39.88
39.81
39.73
Cl
N
N
O
N
F
F
F
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

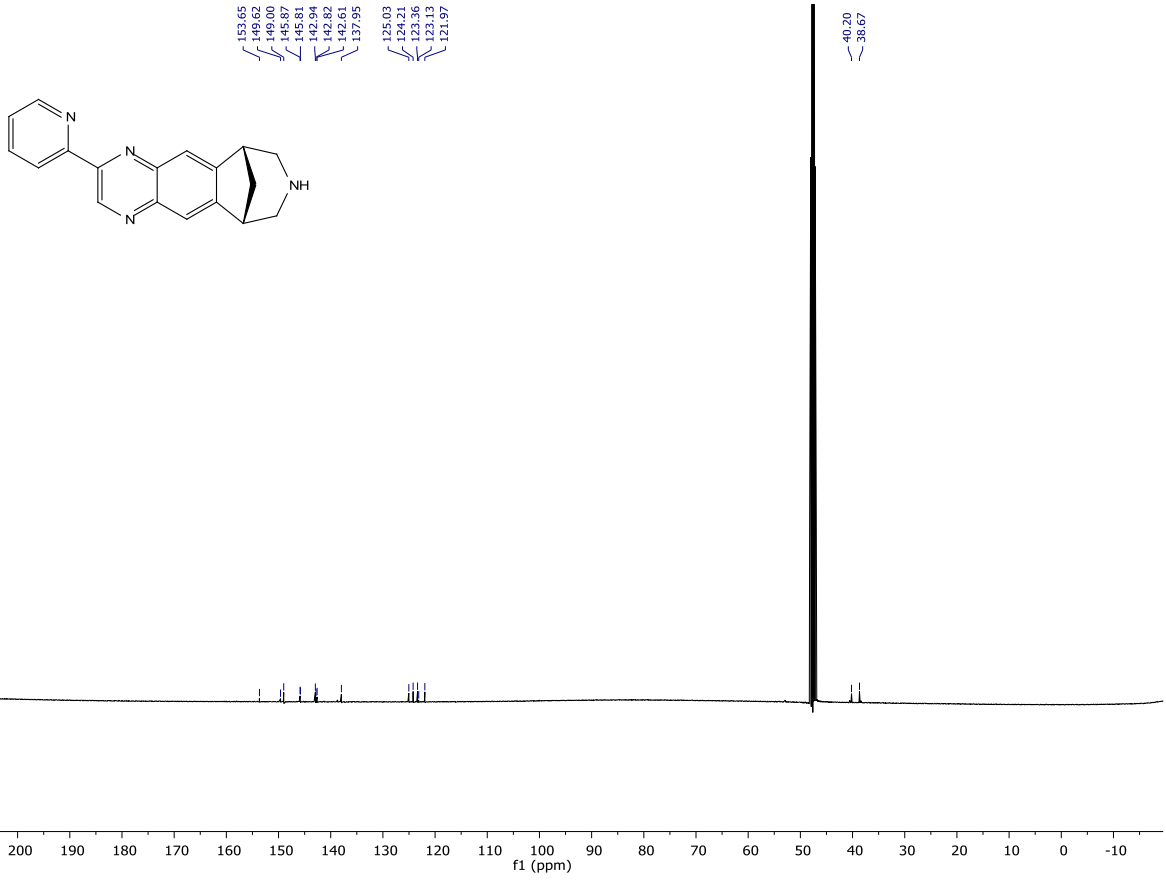

-68.57
Cl
N
N
N
O
F
F
F
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

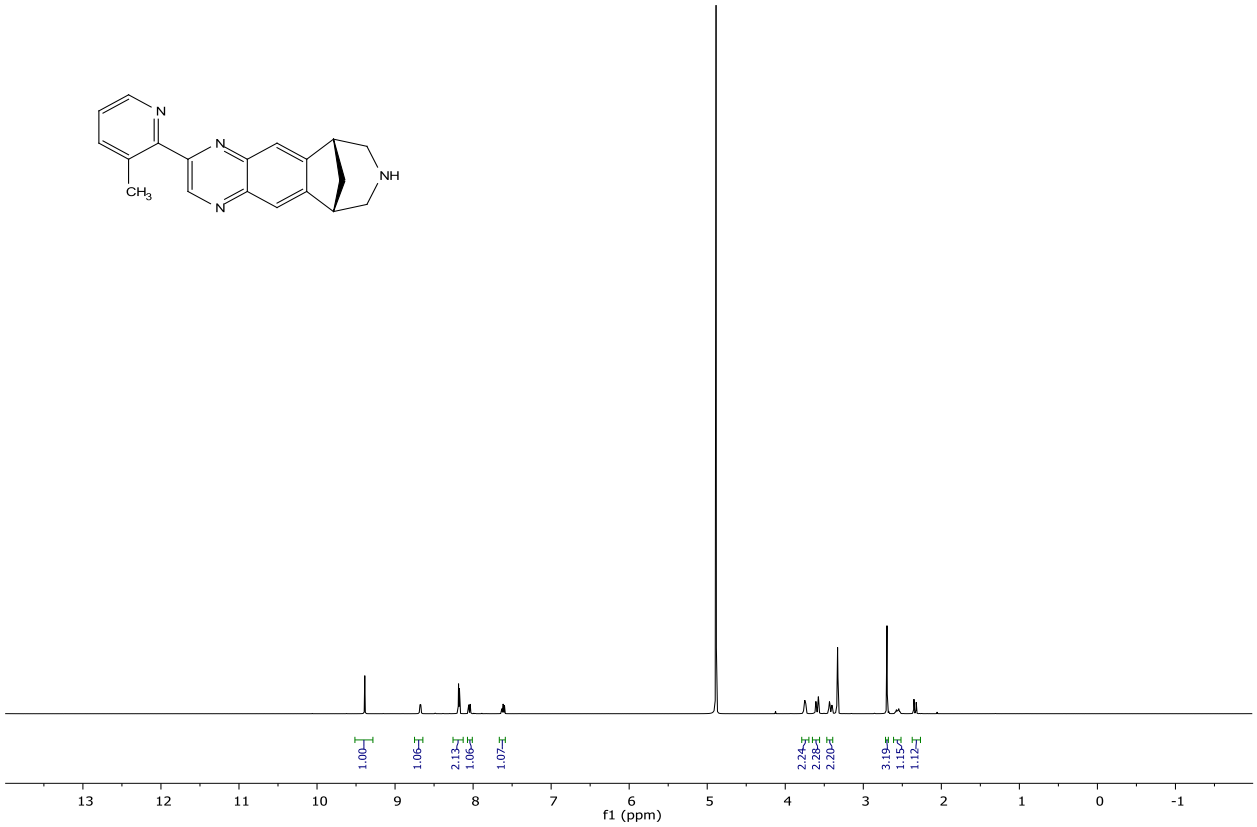

O
N
H_3C
N
N
NH

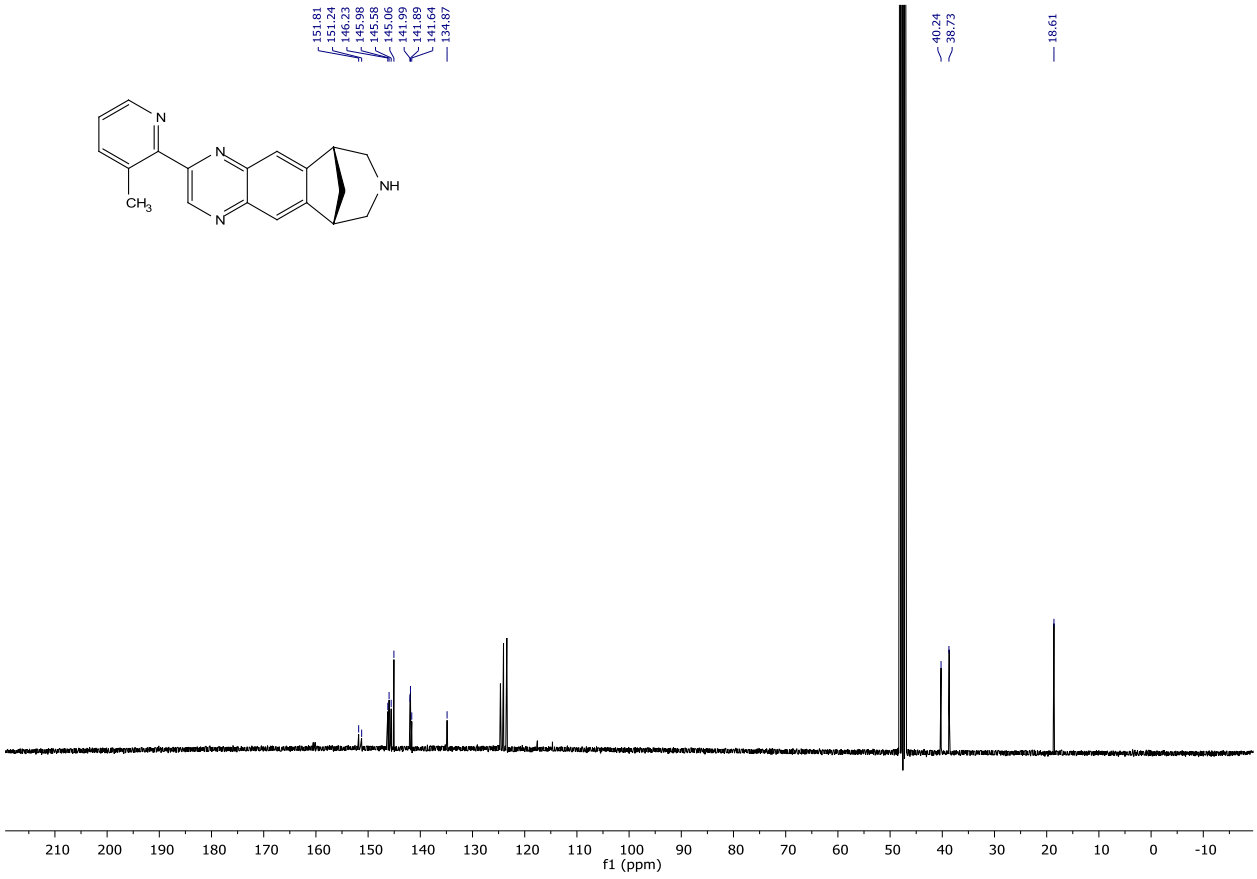

1.00
0.96
1.11
0.83
0.84
1.03
2.69
1.86
1.89
1.91
0.98
1.00
f1 (ppm)

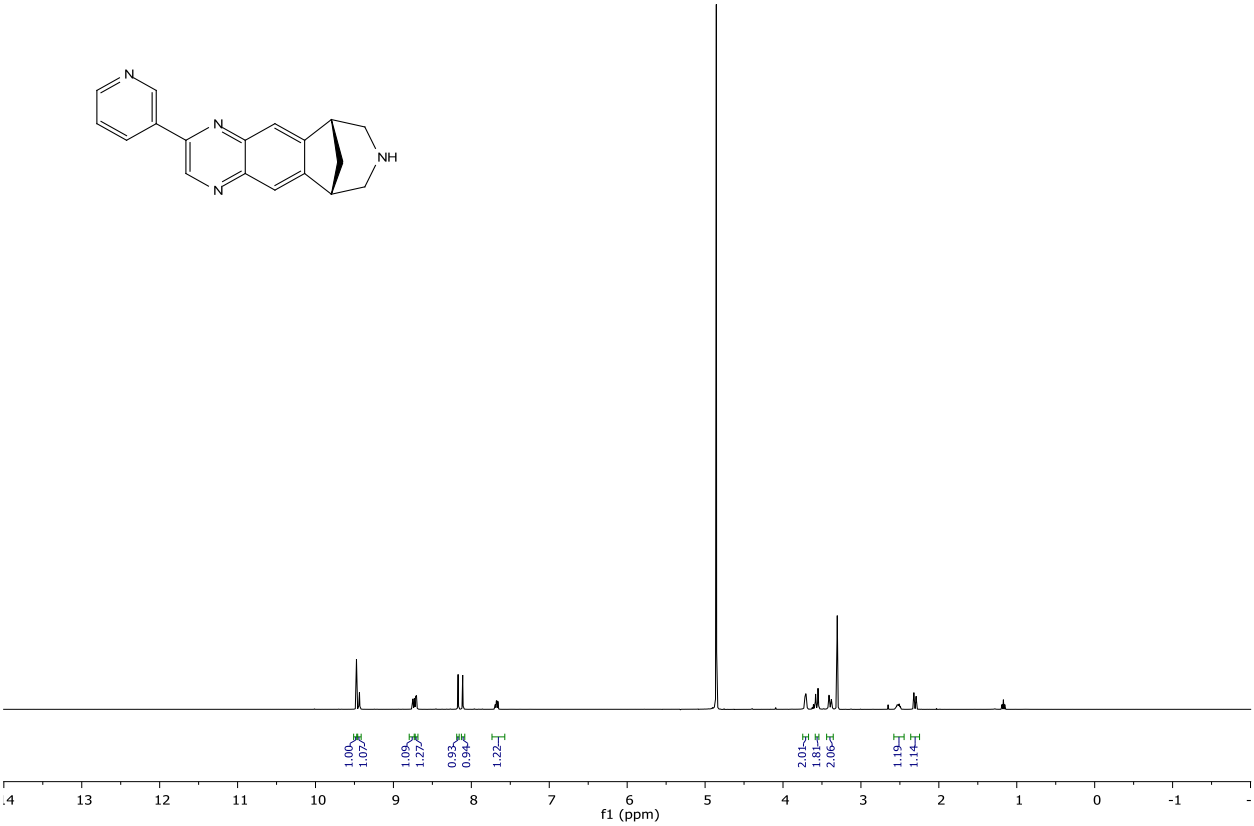

165.54
149.37
146.20
145.67
144.78
142.92
141.97
141.75
137.64
125.80
123.81
123.25
110.77
53.06
40.21
38.61
O
N
H_3C
N
N
NH
f1 (ppm)

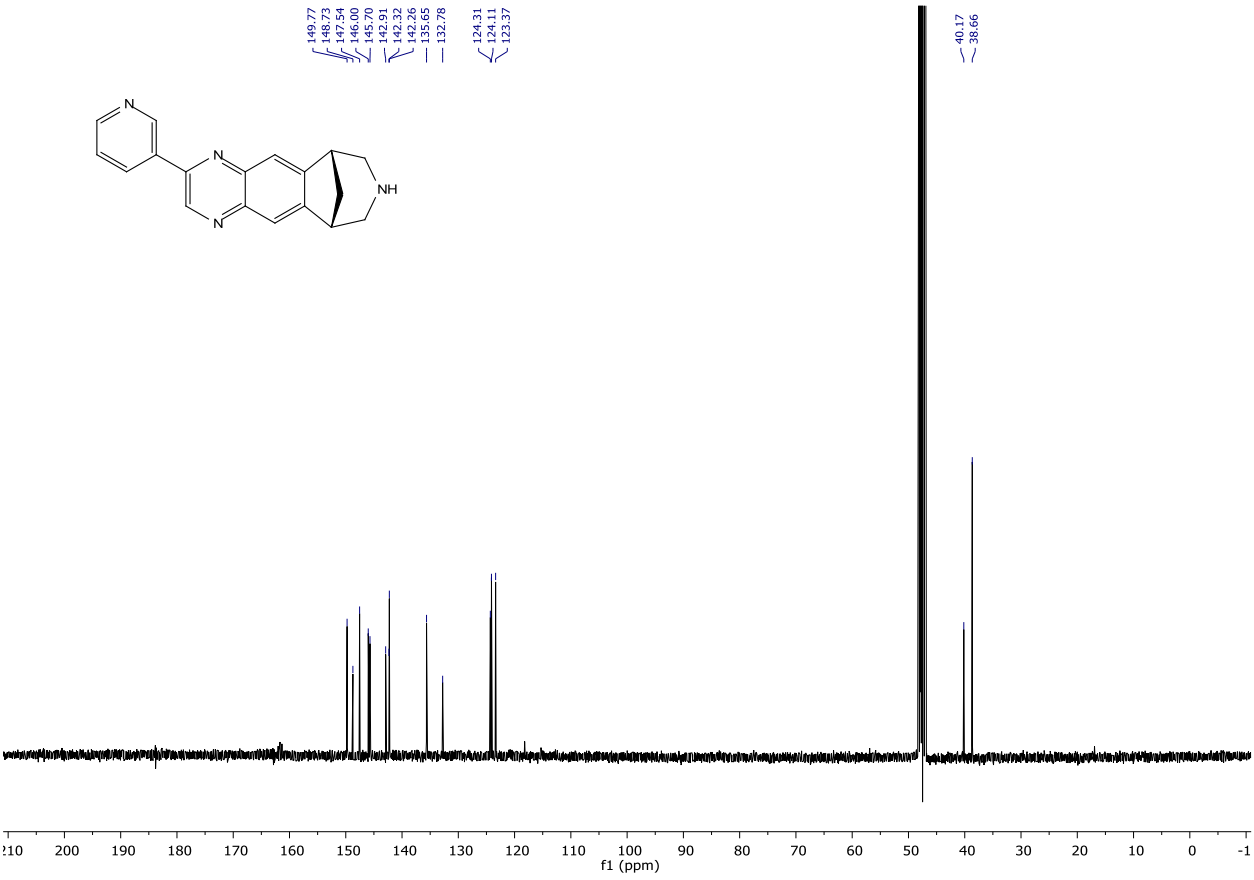

N
N
N
NH
1.00
1.07
1.07
1.02
0.98
1.06
1.08
2.07
2.12
2.13
1.24
1.08
f1 (ppm)

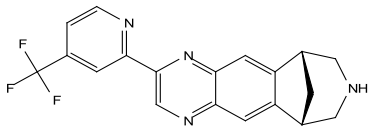

153.65
149.62
149.00
145.87
145.81
142.94
142.82
142.61
137.95
125.03
124.21
123.36
123.13
121.97
40.20
38.67
N
N
N
NH
f1 (ppm)

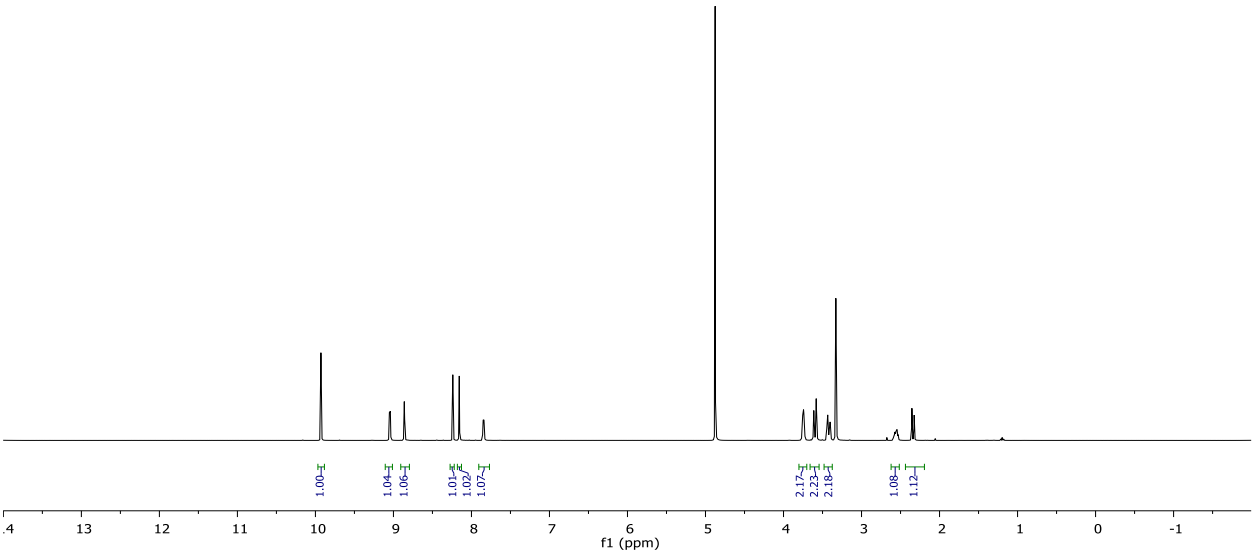

N
N
N
NH
CH3
1.00
1.06
2.13
1.06
1.07
2.24
2.28
2.20
3.19
1.15
1.12
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

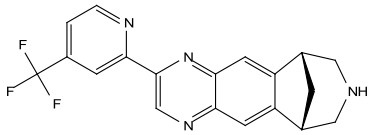

151.81
151.24
146.23
145.98
145.58
145.06
141.99
141.89
141.64
134.87
40.24
38.73
18.61
N
N
N
NH
CH3
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


N
N
N
NH
1.00
1.07
1.09
1.27
0.93
0.94
1.22
2.01
1.81
2.06
1.19
1.14
f1 (ppm)

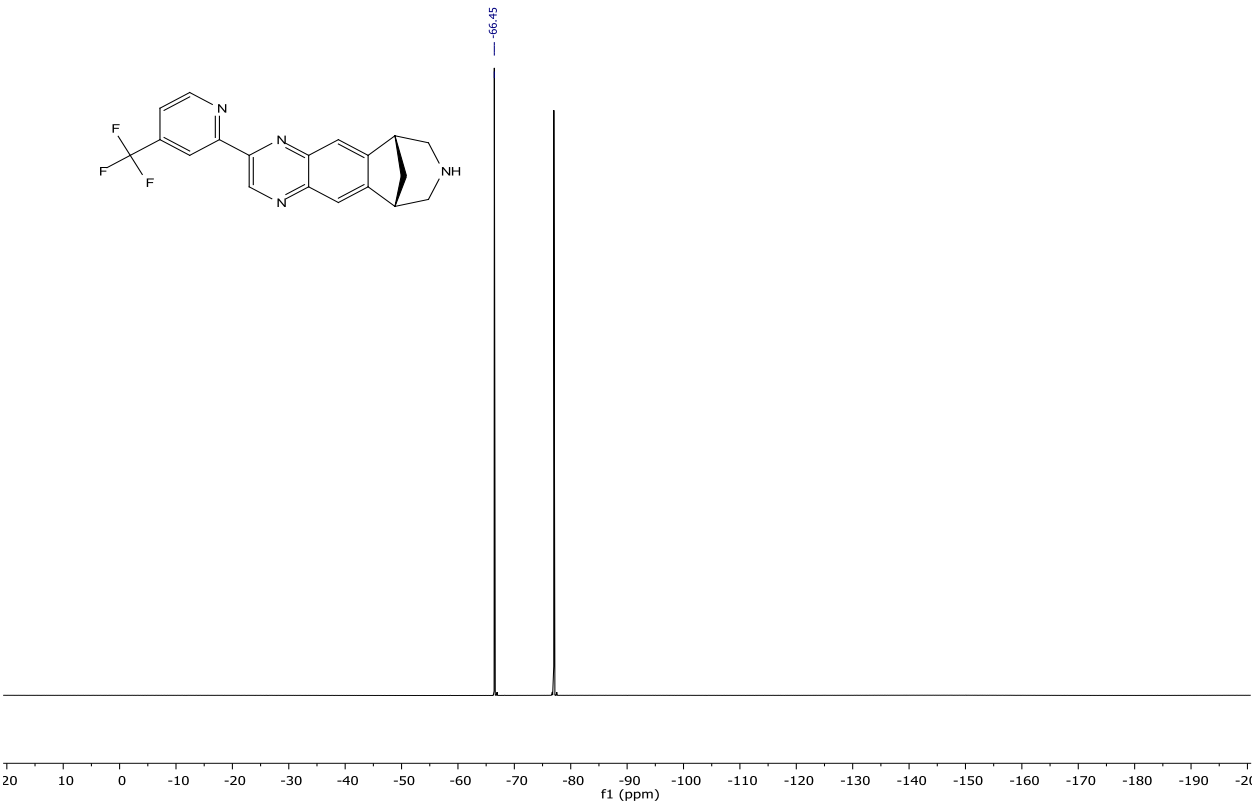

149.77
148.73
147.54
146.00
145.70
142.91
142.32
142.26
135.65
132.78
124.31
124.11
123.37
40.17
38.66
N
N
N
NH
f1 (ppm)

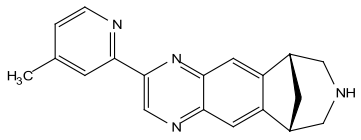

F
F
F
N
N
N
NH

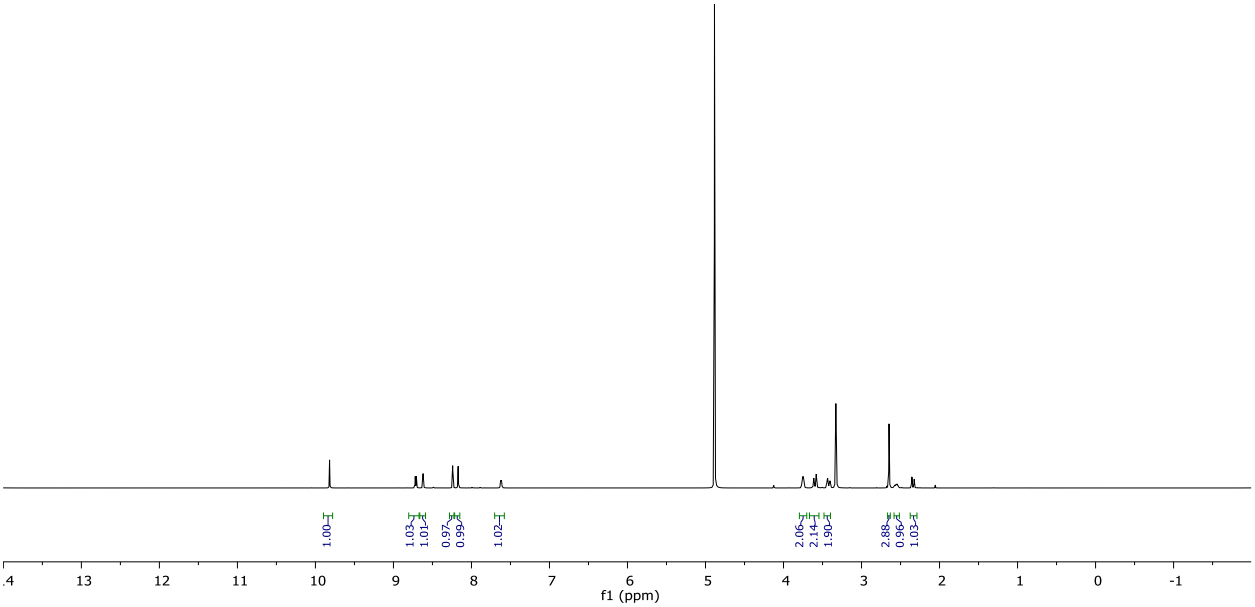

1.00
1.04
1.06
1.01
1.02
1.07
2.17
2.23
2.18
1.08
1.12
f1 (ppm)

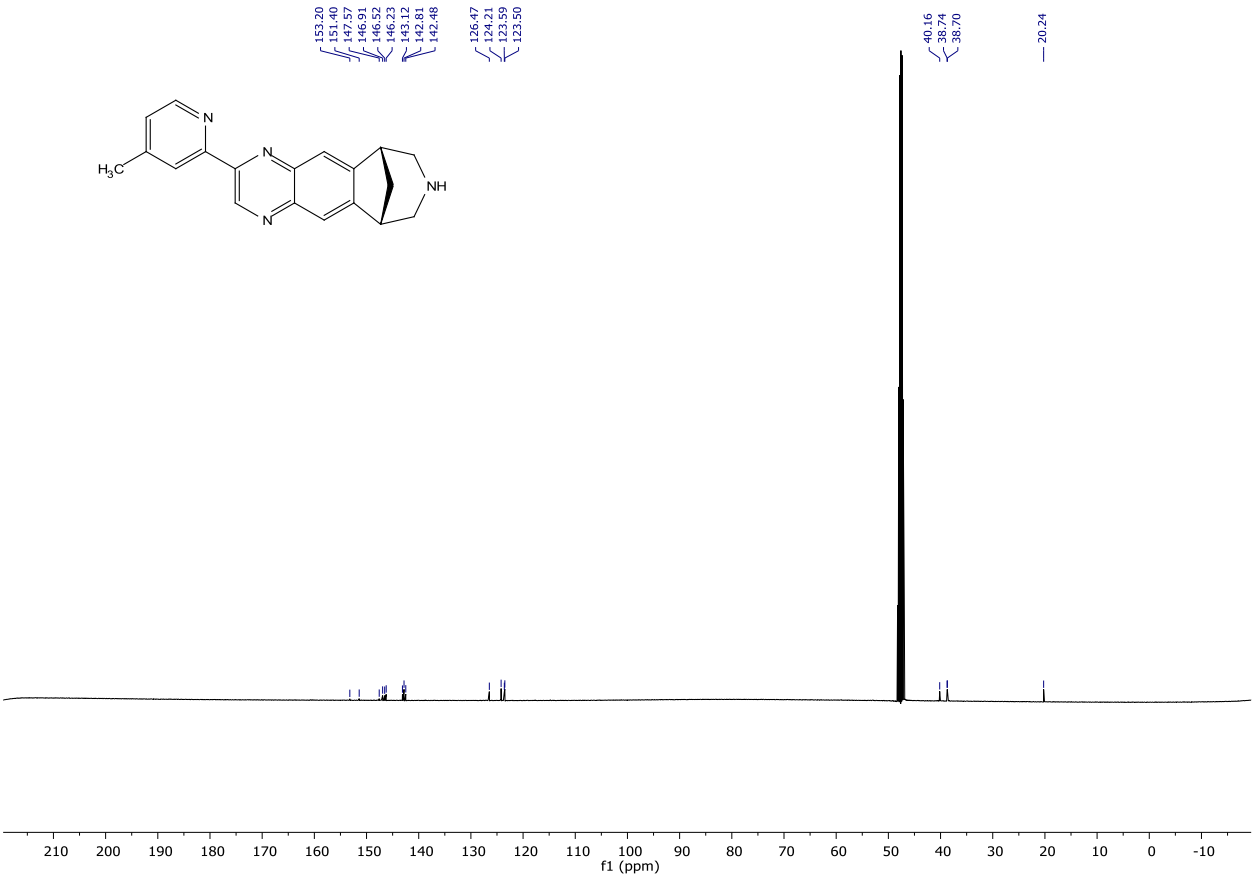

F
F
F
N
N
N
NH

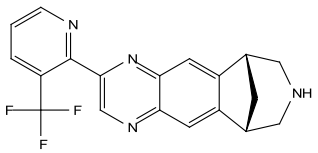
155.69
150.83
148.55
146.34
146.02
143.19
142.75
142.52
139.79
139.45
139.11
138.77
124.34
123.43
120.11
120.08
120.04
120.01
116.86
116.82
116.78
116.75
40.17
38.73
38.68
f1 (ppm)

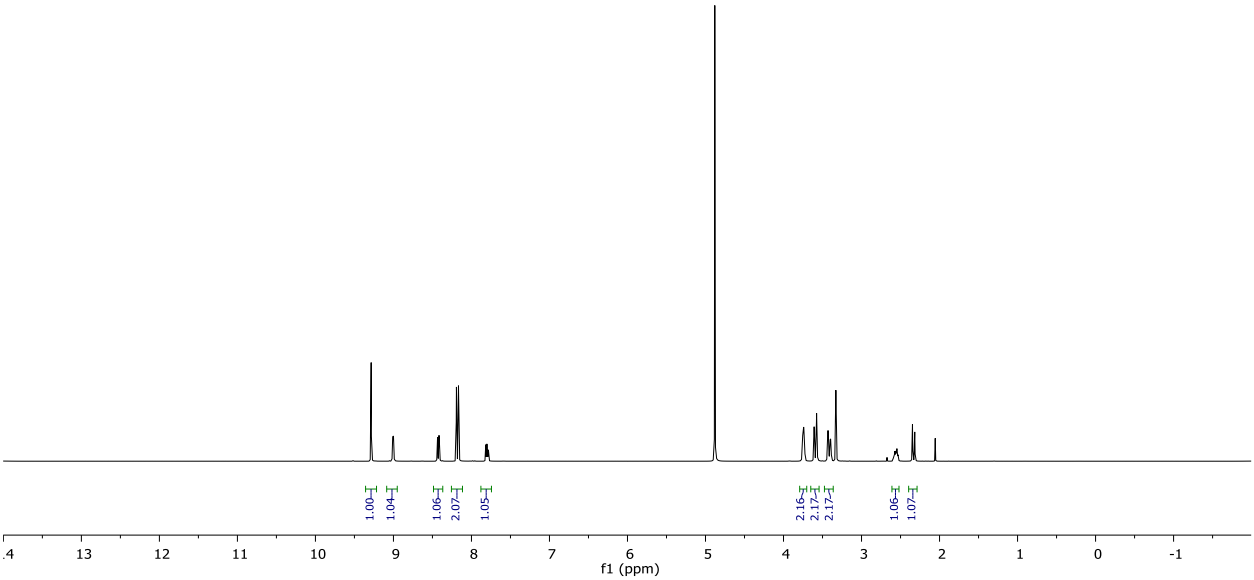

-66.45
F
F
F
N
N
N
NH
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

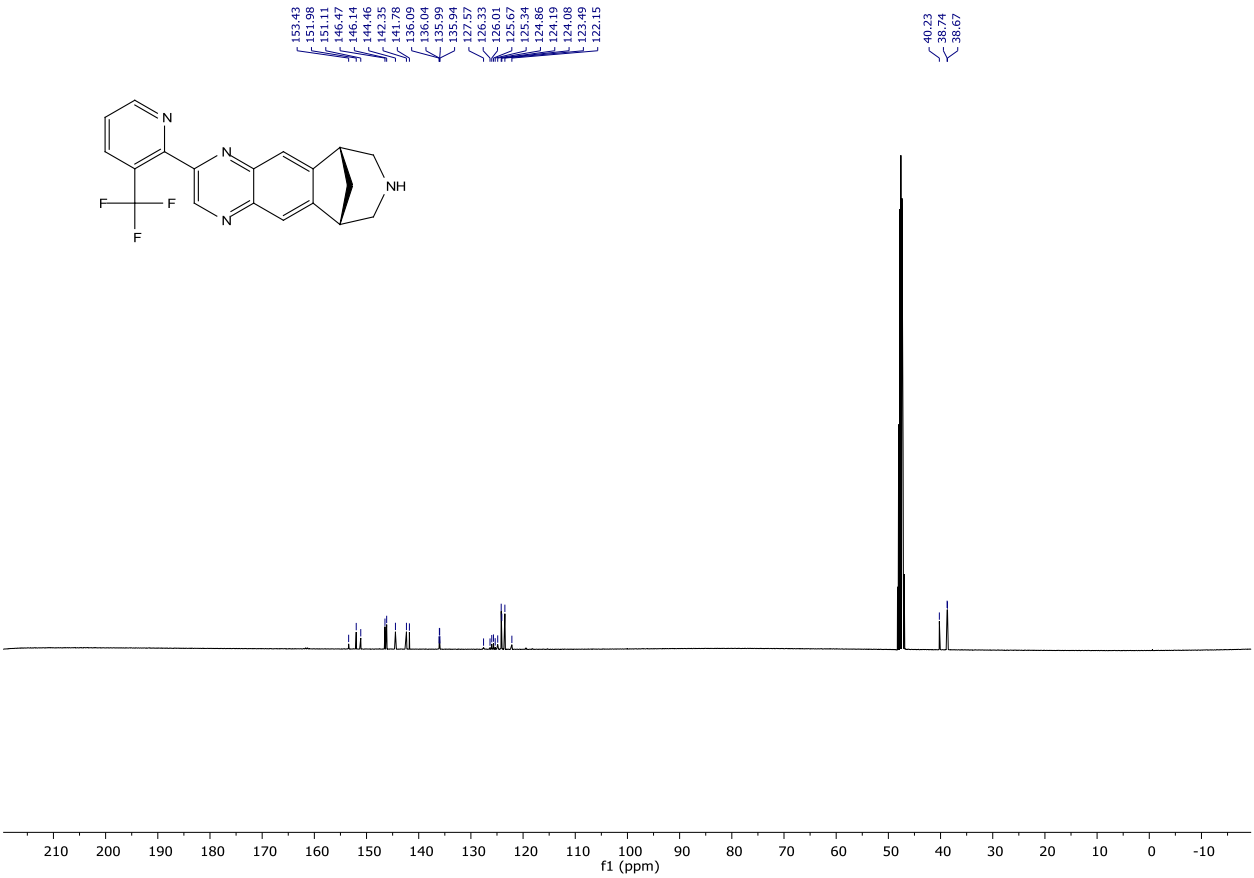

N
H3C
N
N
NH


1.00
1.03
1.01
0.97
0.99
1.02
2.06
2.14
1.90
2.88
0.96
1.03
.4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

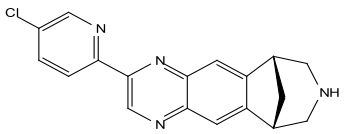

153.20
151.40
147.57
146.91
146.52
146.23
143.12
142.81
142.48
126.47
124.21
123.59
123.50
40.16
38.74
38.70
20.24
N
N
N
NH
H3C
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

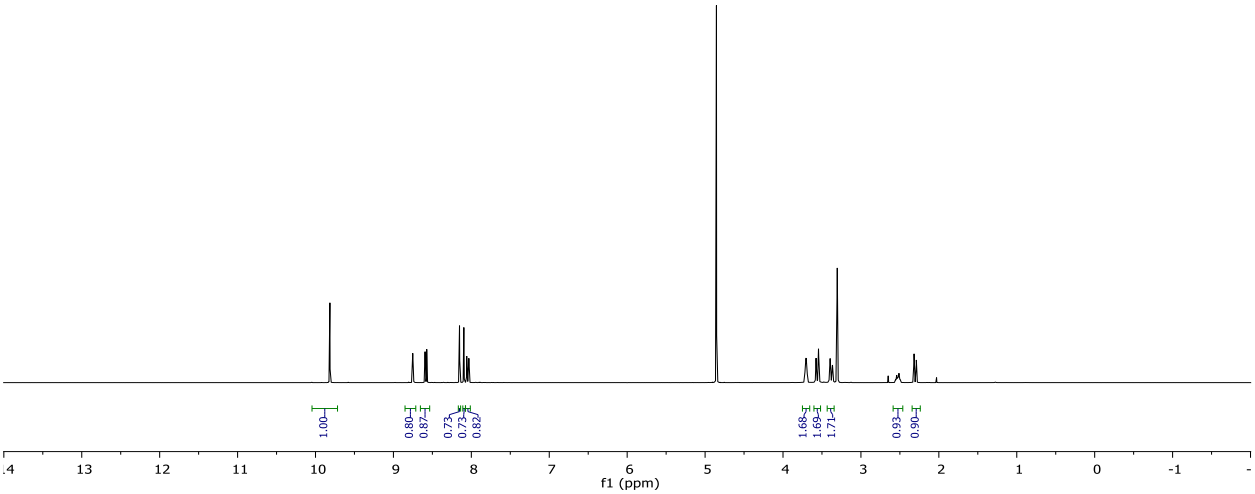

N
N
N
NH
F
F
F

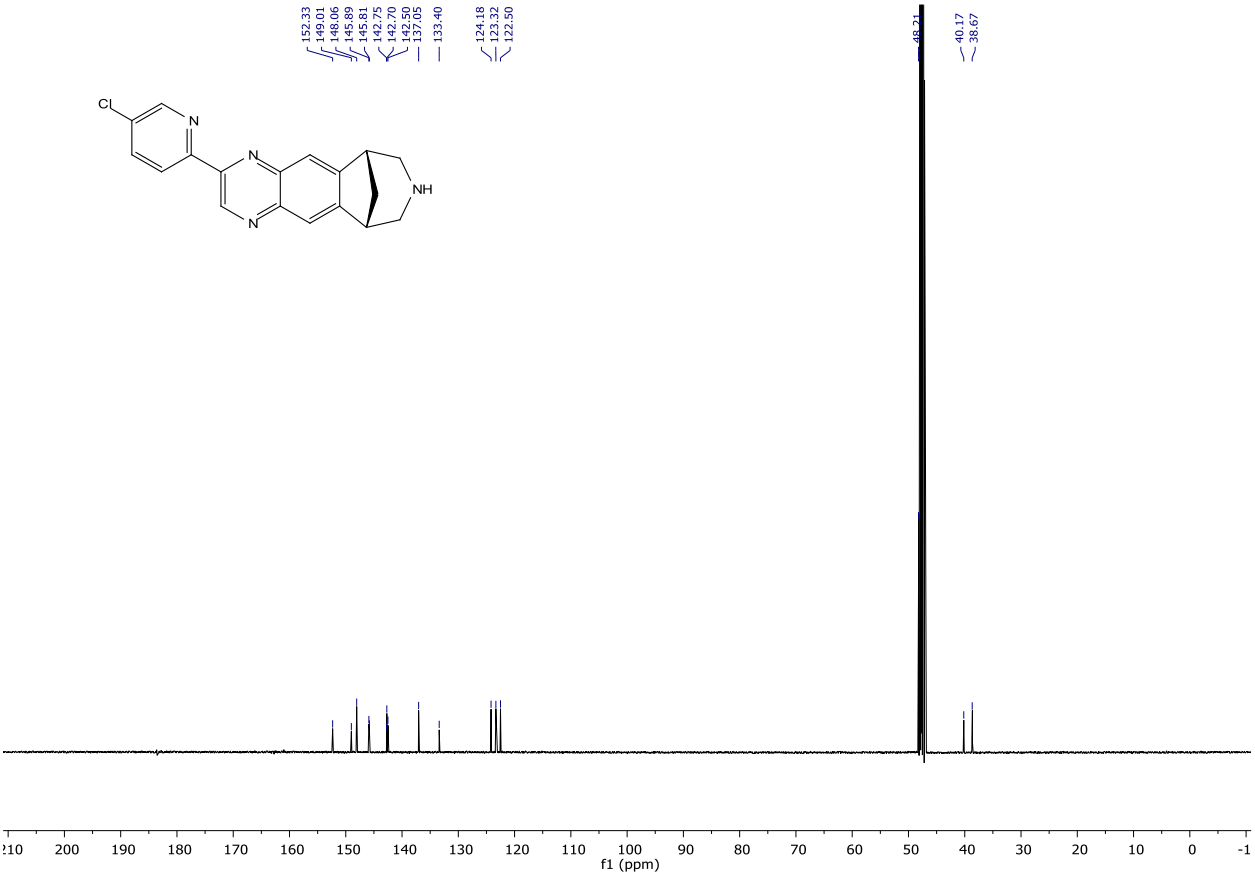

1.00
1.04
1.06
2.07
1.05
2.16
2.17
2.17
1.06
1.07
.4
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

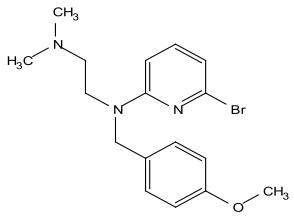

153.43
151.98
151.11
146.47
146.14
144.46
142.35
141.78
136.09
136.04
135.99
135.94
127.57
126.33
126.01
125.67
125.34
124.86
124.19
124.08
123.49
122.15
40.23
38.74
38.67
N
N
N
NH
F
F
F
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

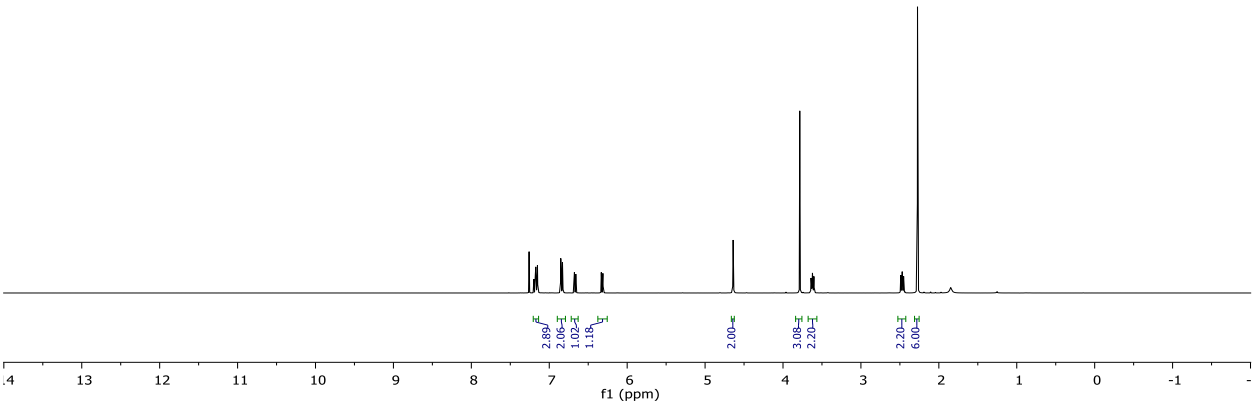

-59.13
N
N
N
NH
F
F
F
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


Cl
N
N
N
NH

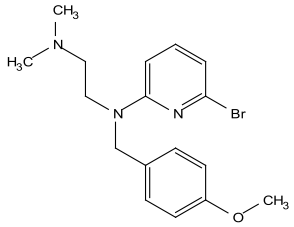

1.00
0.80
0.87
0.73
0.73
0.82
1.68
1.69
1.71
0.93
0.90
f1 (ppm)


152.33
149.01
148.06
145.89
145.81
142.75
142.70
142.50
137.05
133.40
124.18
123.32
122.50
48.21
40.17
38.67
f1 (ppm)

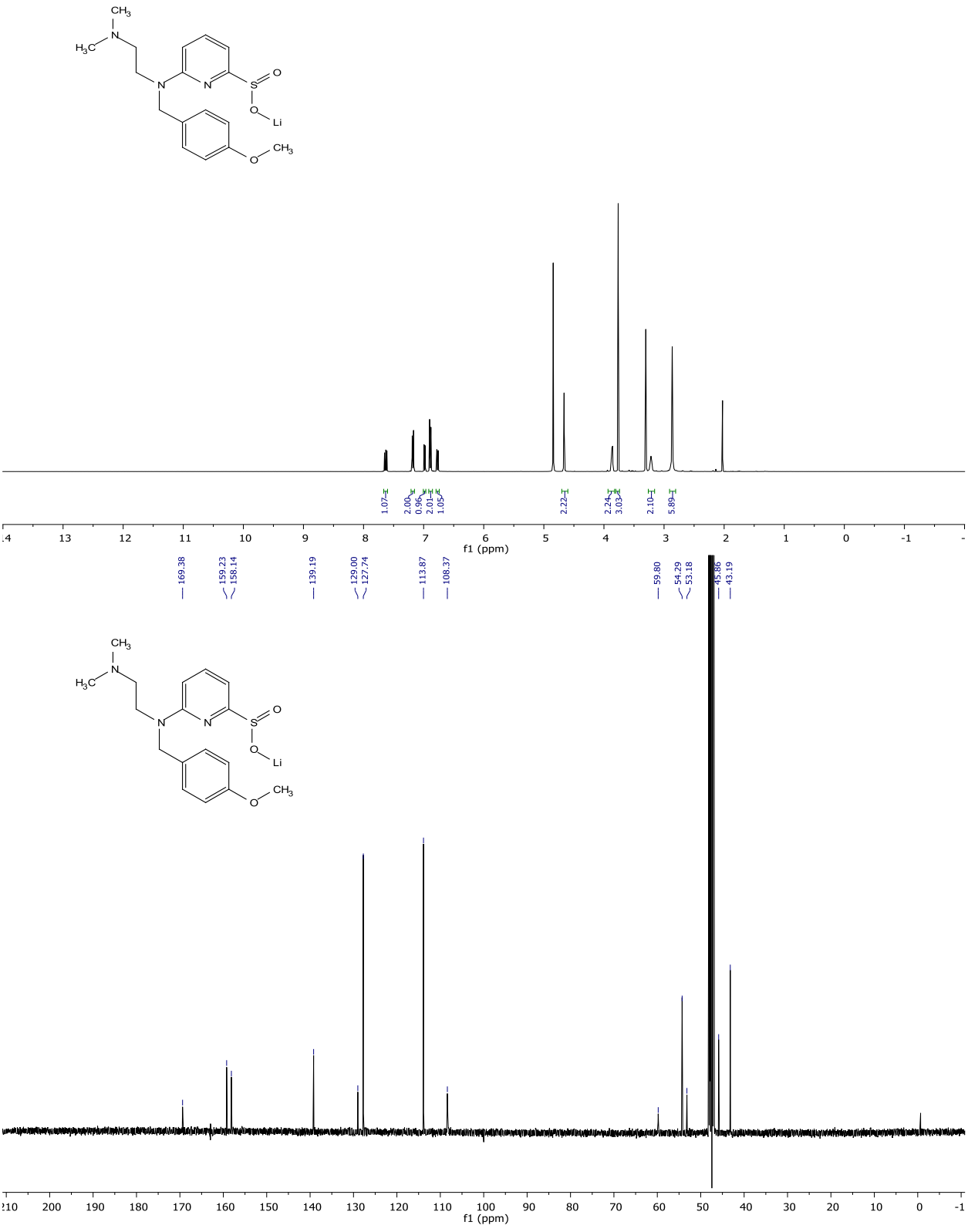

CH3
N
H3C
N
Br
O
CH3

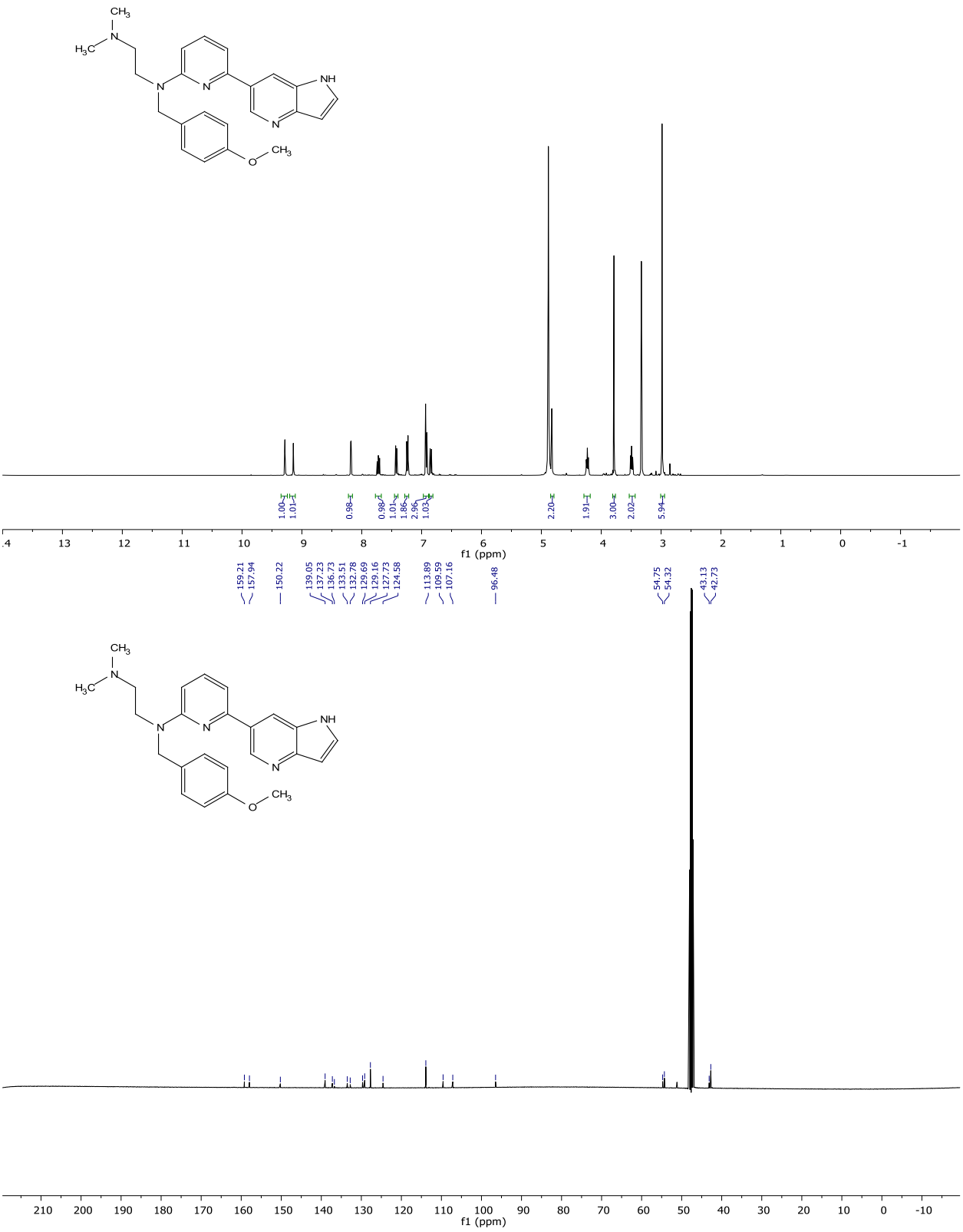

2.89
2.06
1.02
1.18
2.00
3.08
2.20
2.20
6.00
f1 (ppm)

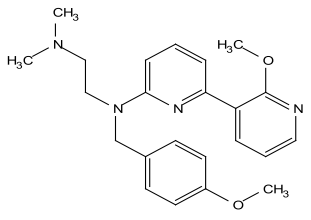

158.76
158.04
140.08
139.22
129.95
128.27
114.61
113.98
104.03
56.47
55.26
51.45
46.45
45.78

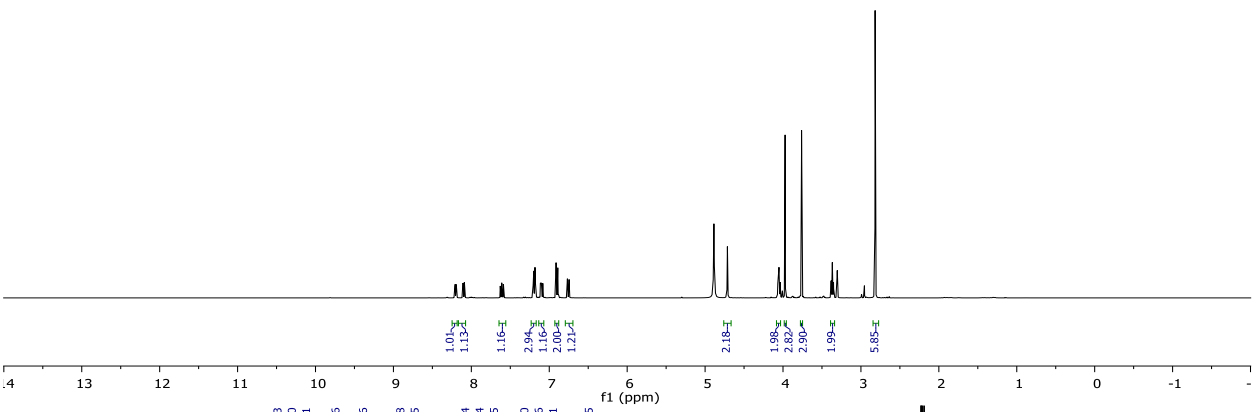

CH3
N
H3C
N
Br
O
CH3

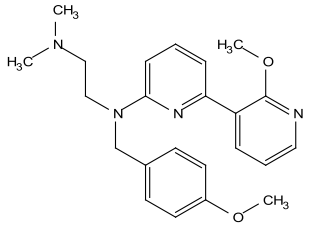
f1 (ppm)


CH3
N
H3C
N
N
S
O
O
Li
O
CH3
1.07
2.00
0.96
2.01
1.05
2.22
2.24
3.03
2.10
5.89
f1 (ppm)
169.38
159.23
158.14
139.19
129.00
127.74
113.87
108.37
59.80
54.29
53.18
45.86
43.19
f1 (ppm)

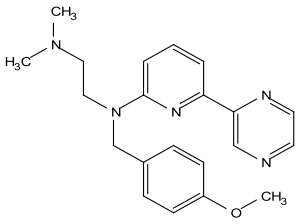

CH3
N
H3C
N
N
NH
N
O
CH3
1.00
1.01
0.98
0.98
1.01
1.86
2.96
1.03
2.20
1.91
3.00
2.02
5.94
f1 (ppm)
159.21
157.94
150.22
139.05
137.23
136.73
133.51
132.78
129.69
129.16
127.73
124.58
113.89
109.59
107.16
96.48
54.75
54.32
43.13
42.73
f1 (ppm)

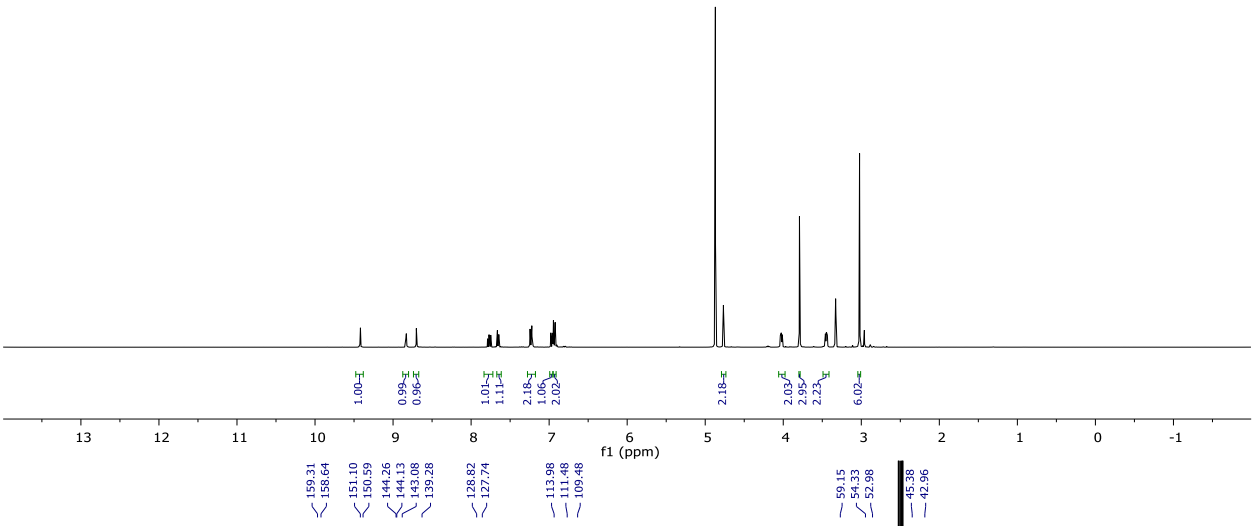


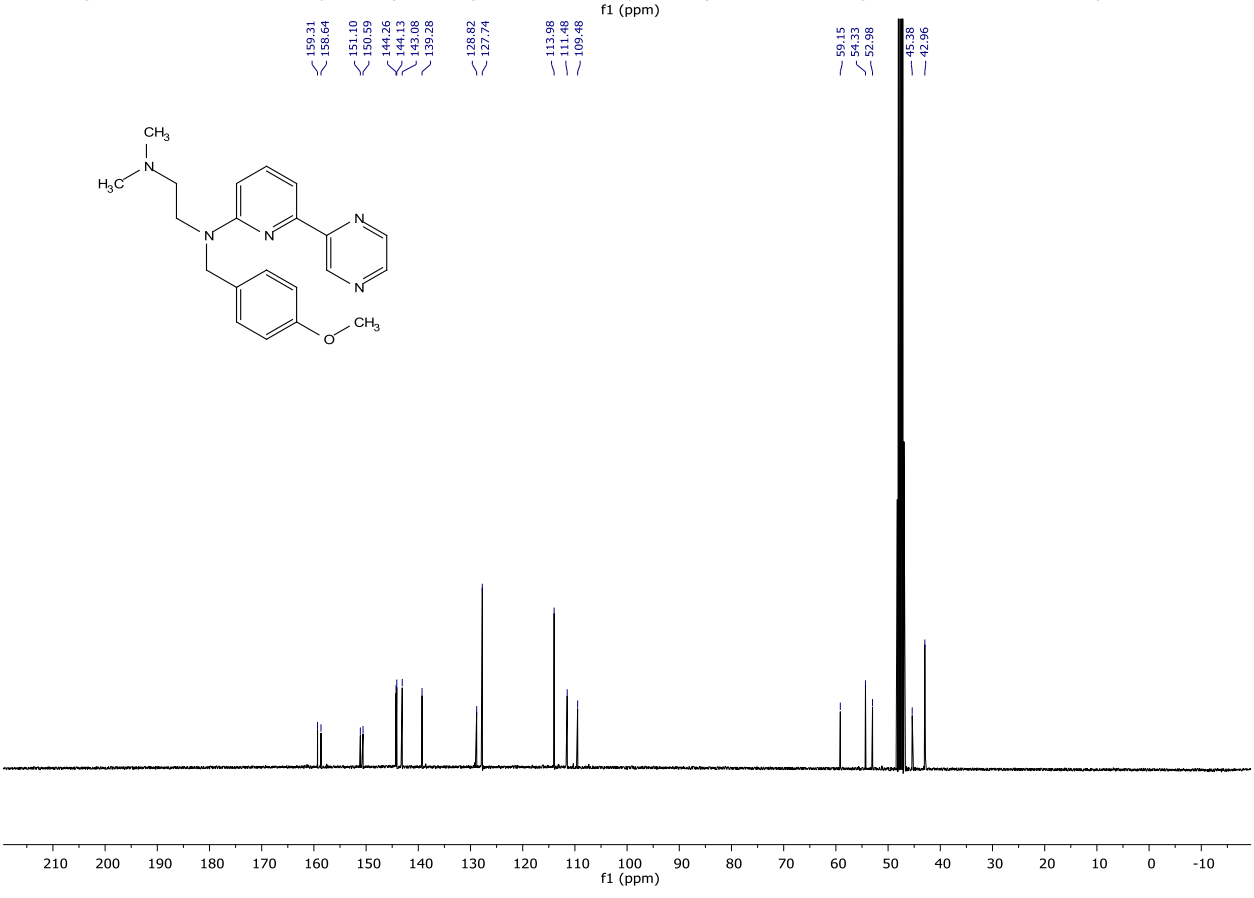

1.01
1.13
1.16
2.94
1.16
2.00
1.21
2.18
1.98
2.82
2.90
1.99
5.85
f1 (ppm)

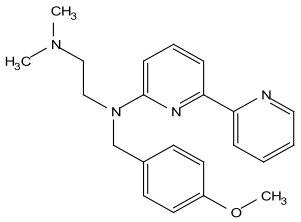


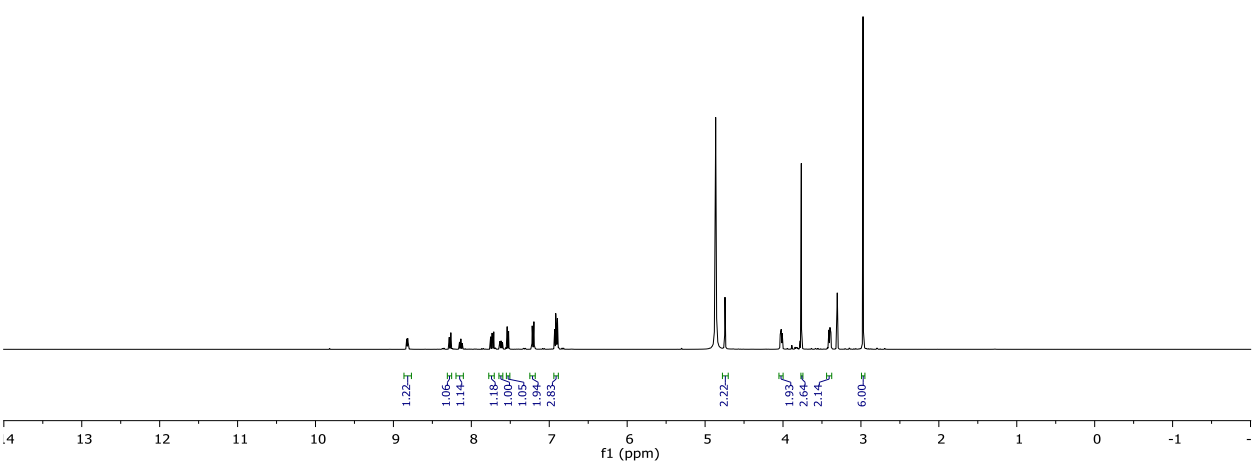
160.93
159.20
157.71
151.56
146.66
138.98
138.55
128.84
127.74
123.05
117.00
114.06
113.91
106.55
56.95
54.31
52.78
51.72
44.08
42.70
f1 (ppm)



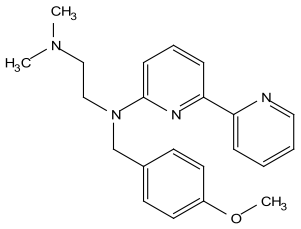

1.00
0.99
0.96
1.01
1.11
2.18
1.06
2.02
2.18
2.03
2.95
2.23
6.02
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)

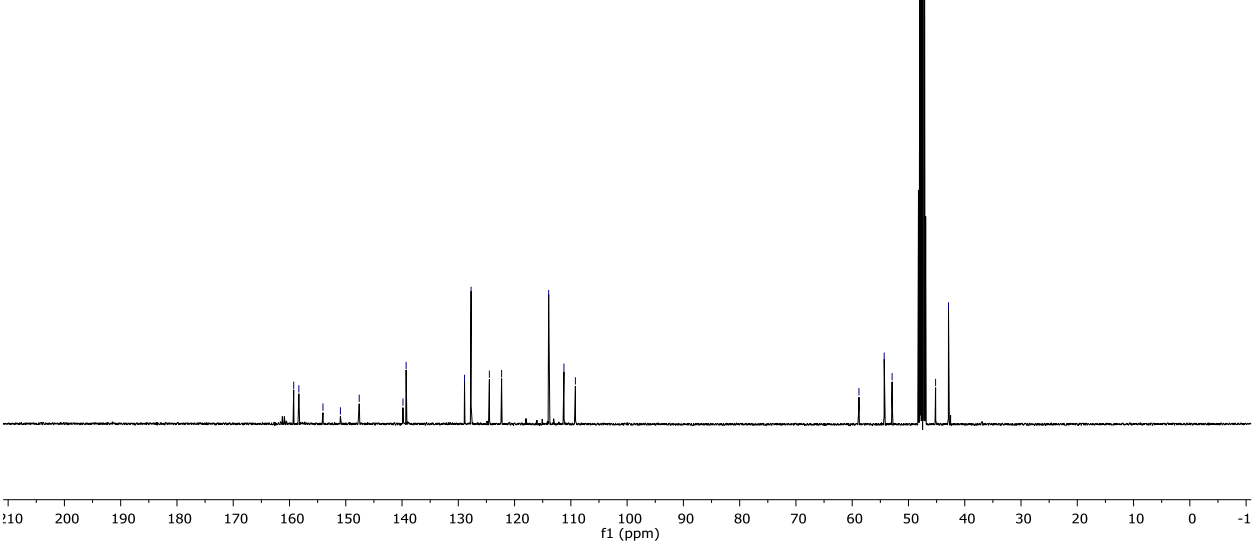

159.31
158.64
151.10
150.59
144.26
144.13
143.08
139.28
128.82
127.74
113.98
111.48
109.48
59.15
54.33
52.98
45.38
42.96
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

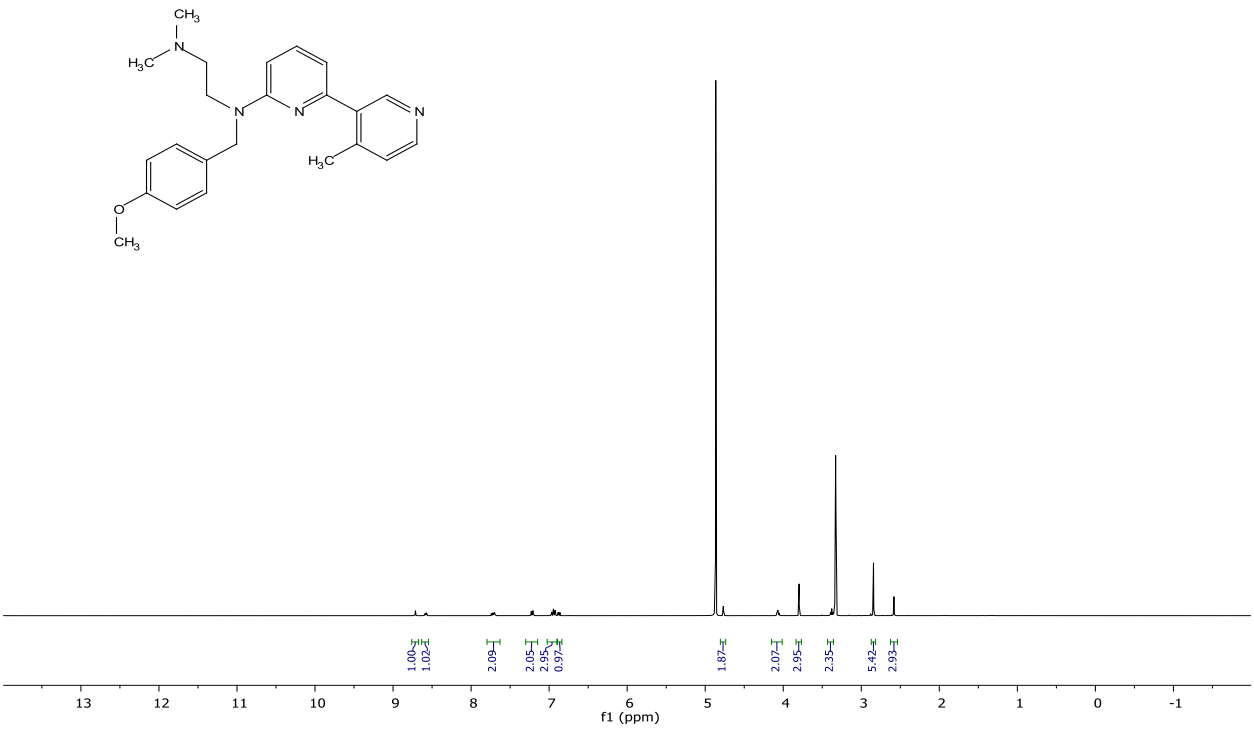


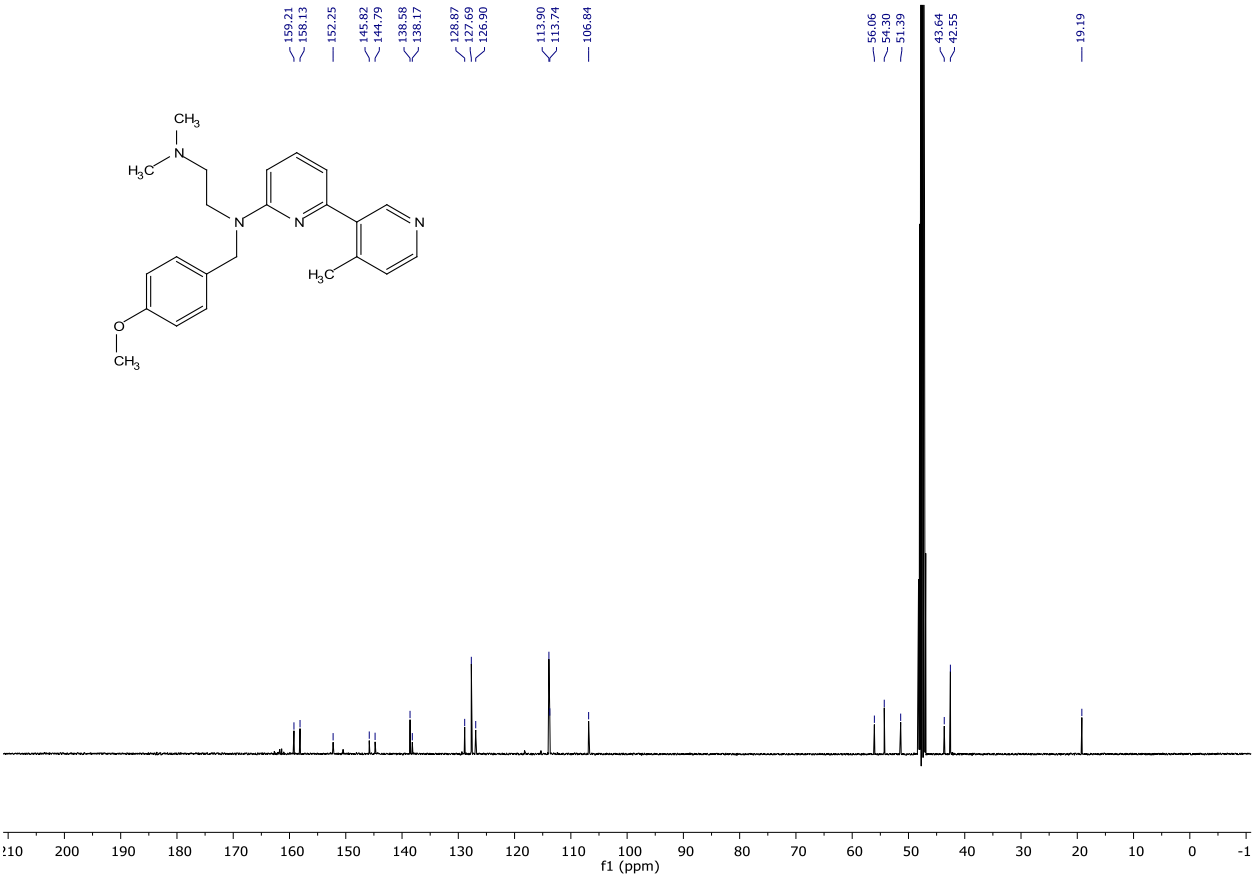

1.22
1.06
1.14
1.18
1.00
1.05
1.94
2.83
2.22
1.93
2.64
2.14
6.00
f1 (ppm)

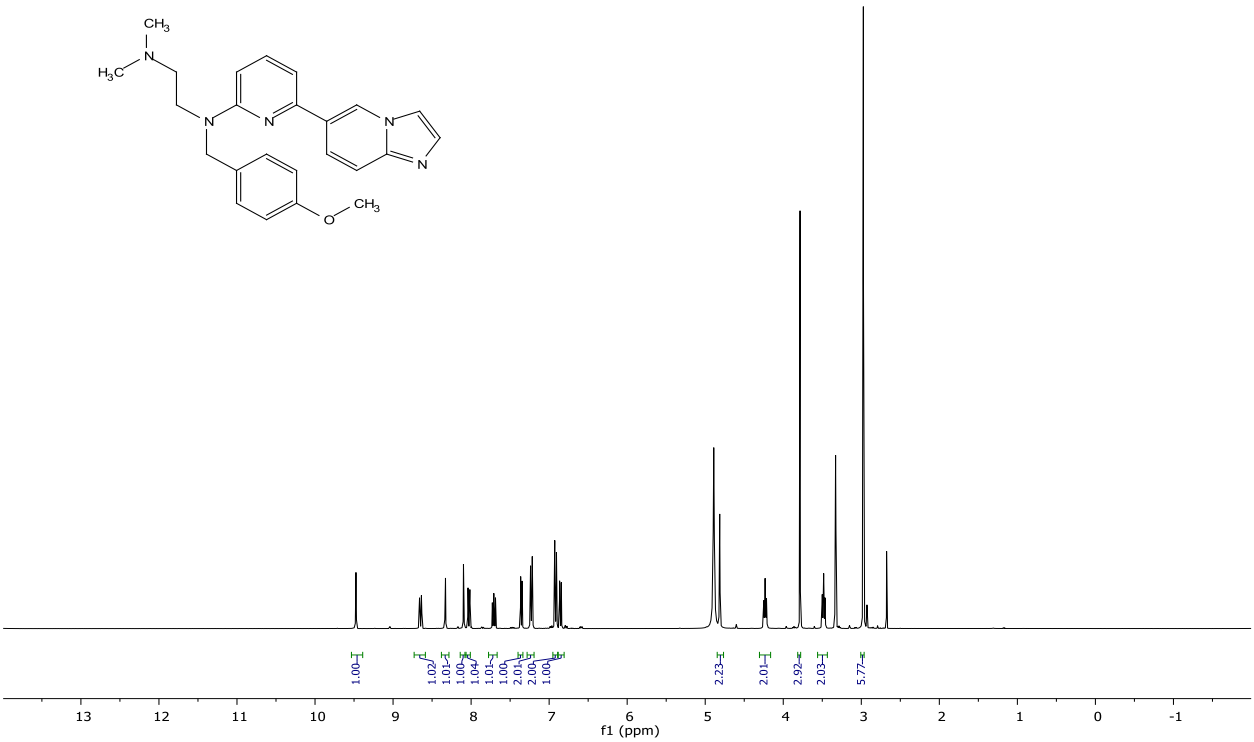

159.26
158.34
154.05
150.95
147.61
139.83
139.27
128.90
127.73
124.48
122.31
113.94
111.23
109.19
58.80
54.31
52.91
45.18
42.89

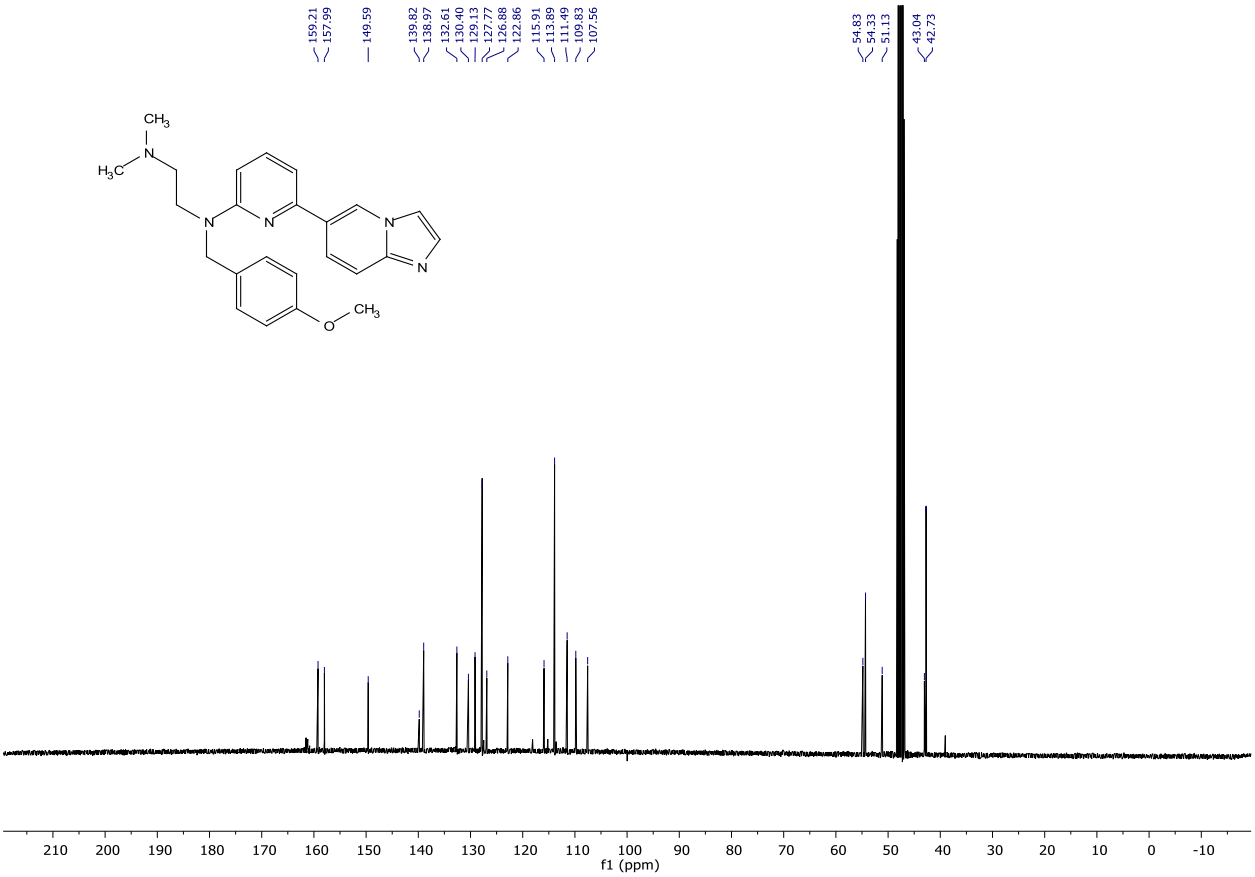


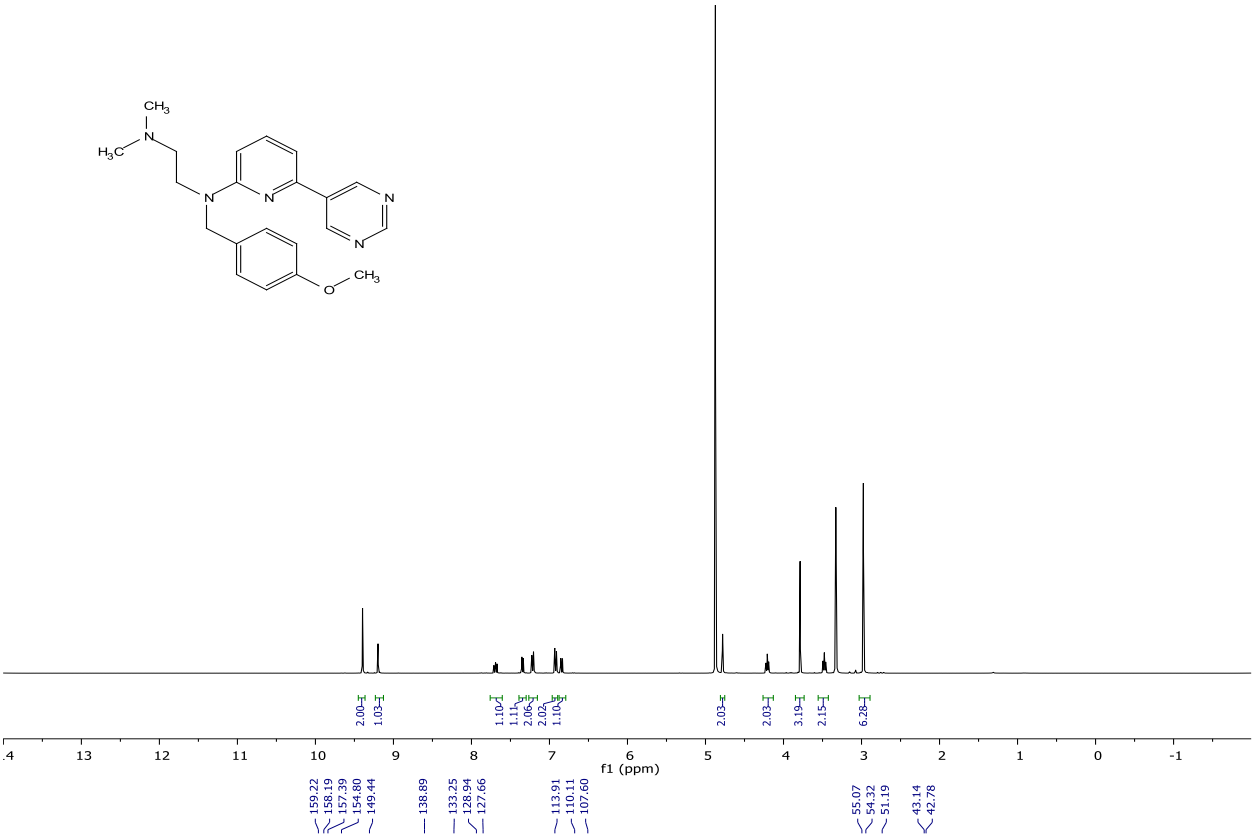

f1 (ppm)

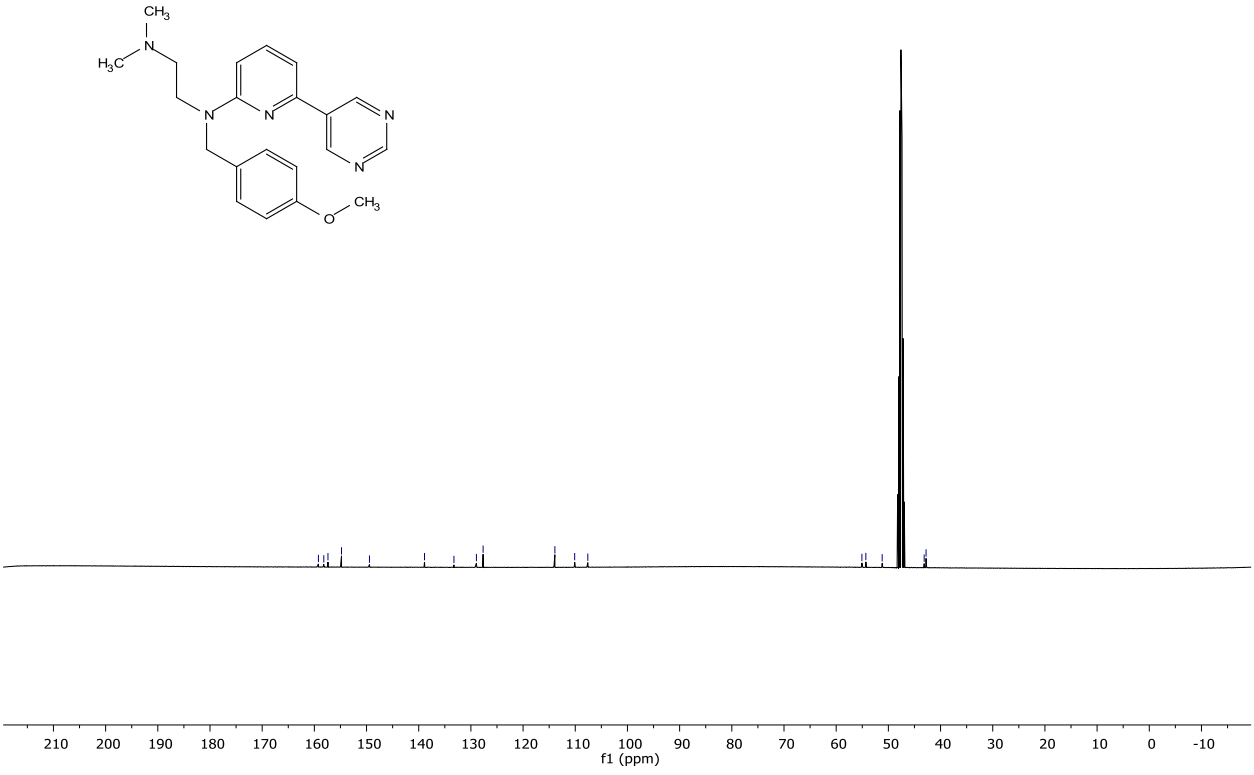

1.00
1.02
2.09
2.05
2.95
0.97
1.87
2.07
2.95
2.35
5.42
2.93
f1 (ppm)


159.21
158.13
152.25
145.82
144.79
138.58
138.17
128.87
127.69
126.90
113.90
113.74
106.84
56.06
54.30
51.39
43.64
42.55
19.19
f1 (ppm)


1.00
1.02
1.01
1.00
1.04
1.01
1.00
2.01
2.00
1.00
2.23
2.01
2.92
2.03
5.77
13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)


159.21
157.99
149.59
139.82
138.97
132.61
130.40
129.13
127.77
126.88
122.86
115.91
113.89
111.49
109.83
107.56
54.83
54.33
51.13
43.04
42.73
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


CH3
H3C
N
N
N
N
O
CH3
2.00
1.03
1.10
1.11
2.06
2.02
1.10
2.03
2.03
3.19
2.15
6.28
f1 (ppm)
159.22
158.19
157.39
154.80
149.44
138.89
133.25
128.94
127.66
113.91
110.11
107.60
55.07
54.32
51.19
43.14
42.78


CH3
H3C
N
N
N
N
O
CH3
f1 (ppm)