Photochemical, Halogen Atom Transfer (XAT) Mediated Three-Component Dichloromethylative Pyridylation of Styrenes

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Supporting Information

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1.0. General Information:

Unless otherwise noted, all chemicals were purchased from commercial sources and used without further purification. Yields refer to chromatographically pure material. All solvents were used as purchased, without purification. Chloroform and DMA was used as after drying. Reactions were monitored by Thin Layer Chromatography (TLC) performed on 0.25 mm Merck silica gel plates (60F-254) using UV light. Merck silica gel (mesh size 100-200) was used for flash column chromatography.

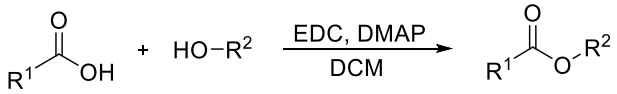
NMR spectra were recorded on JEOL 500 (^{1}H: 500MHz, ^{13}C: 125MHz) or 400 (^{1}H: 500MHz, ^{13}C: 125 MHz) spectrometer in $CDCl_3$ having TMS 0.03% as internal standard. ^{19}F NMR were recorded using $CDCl_3$ and $PhCF_3$ as reference standard. Mass spectrometric data were obtained using WATER- Q- TOF Premier- ESI-MS and GC-MS.

The following abbreviations were used to explain the multiplicities: s= singlet, d= doublet, t= triplet, q= quartet, dd= doublet of doublet, ddd= doublet of a doublet of doublet. m = multiplet. All starting material were prepared according to the literature reports[23].

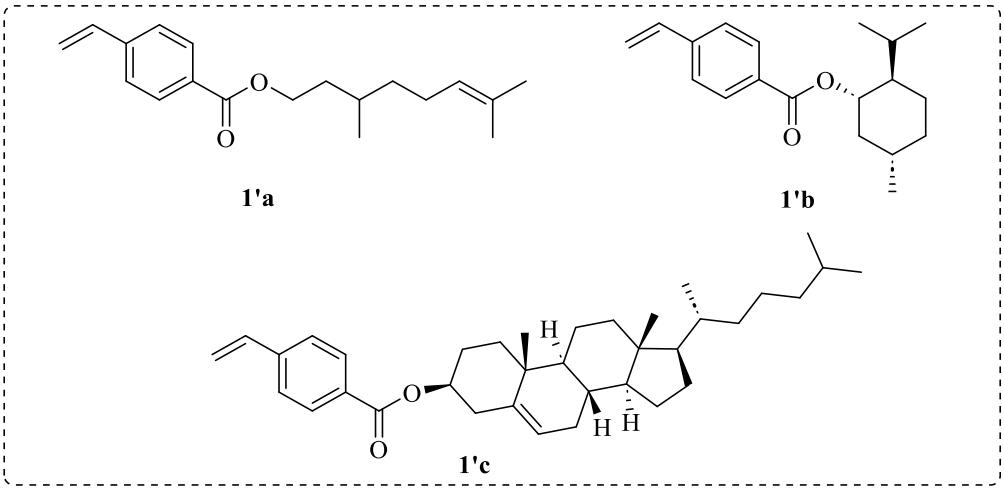
The reaction was carried out using two Kessil KSPR160L- 390nm lamps (manufactured by Kessil Lighting 1689 Regatta Blvd, Richmond, CA 9480, purchased from PR@kessil(PR160L) at 100% intensity. The Kessil KSPR160L (equipped with the linear reflector has an emission wavelength of 390 nm with a maximum power consumption of 40 W and average intensity 0f 352 Mw/cm^2 measured from 1 cm distance). The light source provides precise wavelength control (± 5nm). The reaction was conducted in a 7 ml glass vial Supelco, (product no: 27151) placed at room temperature under sideways irradiation of Kessil lamp at an approximate distance of 5 cm with fan cooling. No additional filters were used.

2.0. General Experimental Procedure:

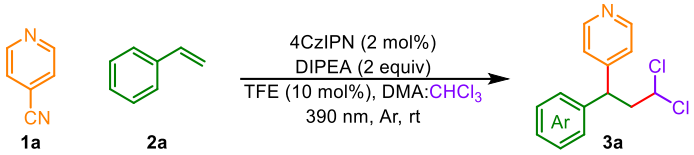
2.1. General Procedure for the Synthesis of **1'a, 1'b, 1'c**:



According to the reported procedure[23], a mixture of carboxylic acid compound (1.0 mmol), a hydroxyl compound (1.02 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (287.6 mg, 1.5 mmol), and DMAP (2.5 mg, 0.02 mmol) in CH_2Cl_2 (20.0 ml) was stirred at room temperature for 2.5 h. The reaction mixture was added to H_2O and extracted with CH_2Cl_2 (thrice). The organic layers were combined, washed with brine, dried over Na_2SO_4, filtered, and concentrated in vacuo to afford the crude product which was purified by flash chromatography.



2.2. General Procedure for Synthesis of Product (**3a**)



Isonicotinonitrile **1a** (0.48mmol, 1 equiv.), styrene **2a** (3 equiv.), DIPEA (2 equiv. 0.96mmol), 4CzIPN (2 mol%) and TFE (10 mol%) were added to an oven dried vial equipped with a magnetic stir bar. Under argon atmosphere, anhydrous (1:1) DMA and chloroform (2 mL) were added to this mixture and then the mixture was purged with Ar for 30 minutes. The reaction was stirred for 12-16 h at room temperature, under the irradiation of 390 nm Kessil LED equipped with a cooling fan. Upon completion of the reaction (monitored by TLC), the reaction mixture was concentrated and the residue was purified by column chromatography on silica gel using ethyl acetate in petroleum ether to afford the desired product **3a.**

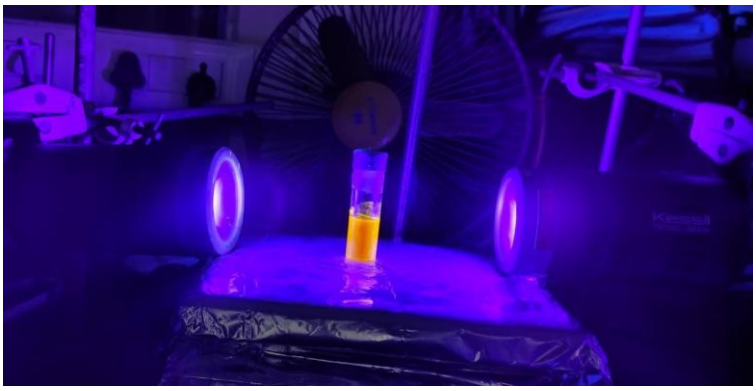
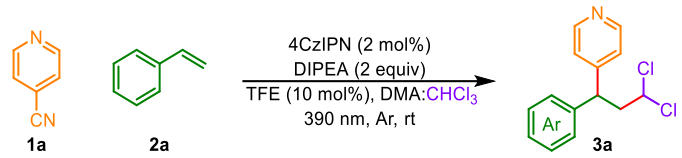


Figure S1: The set- up for the reaction.

2.3. General Procedure for Gram Scale Synthesis of **3a**:



In an oven dried reaction tube equipped with a magnetic stir bar, **1a** (1g, 9.6 mmol), **2a** (3 equiv.), DIPEA (2 equiv.), 4CzIPN (2 mol%) and TFE (10 mol%) were dissolved in (1:1) DMA and chloroform (20 mL). The reaction mixture was purged with Ar for 30 minutes and irradiated under 390 nm LED light source. On completion of the reaction (monitored by TLC) the solvent was reduced under reduced pressure and the product was purified by flash chromatography on silica gel using 25% ethyl acetate in petroleum ether to give the desired product **3a** as a brown viscous liquid.

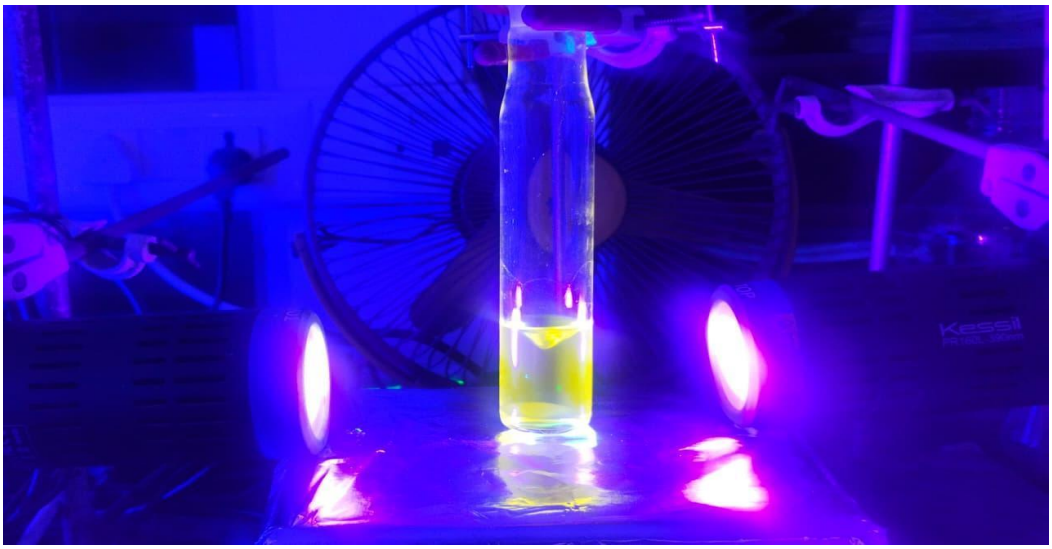
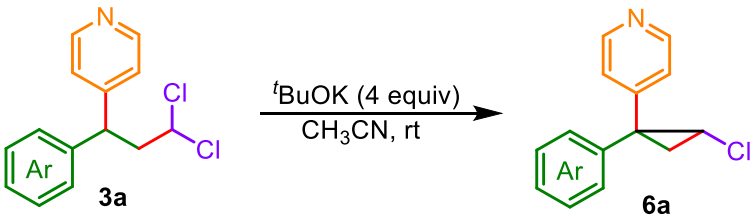


Figure S2: The set- up for gram scale reaction.

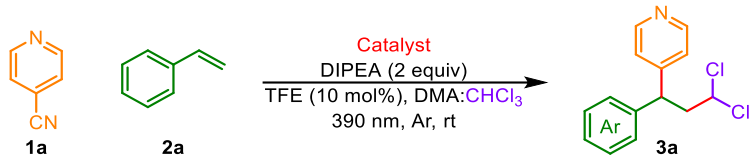
2.4. Procedure for conversion of obtained product:

According to general procedure 2.2, 4-(3,3-dichloro-1-phenylpropyl)pyridine (1 equiv, 0.2 mmol) and ^{t}BuOK (5 equiv, 0.7 mmol). The reaction was taken up in acetonitrile (2.0 ml) and was allowed to stir at room temperature until starting material was consumed based off TLC (4 h). Upon completion the reaction was concentrated under reduced pressure, and the crude material was purified by flash column chromatography.



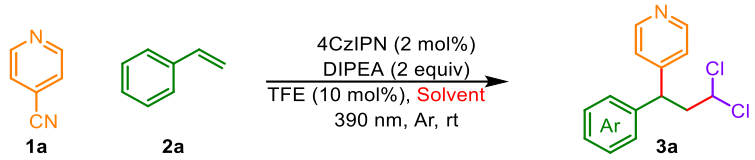
3.0. Reaction Optimization using 4-cyanopyridine, styrene and chloroform:

3.1. Screening of catalyst:



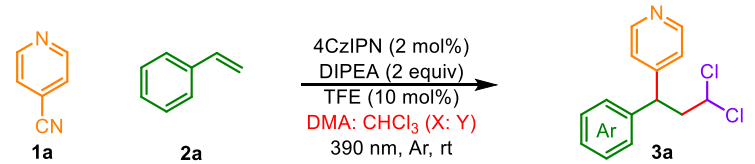
Entry	Catalyst (2 mol%)	Yield (%)
1	Eosin y	No reaction
2	Rose Bengal	36
3	$Ru(bpy)_3Cl_2 \cdot 6H_2O$	Trace
4	4CzIPN	75

3.2. Solvent study:



Entry	Solvent (1:1 mL)	Yield (%)
1	Acetone: $CHCl_3$	48
2	DMA: $CHCl_3$	75
3	DMF: $CHCl_3$	55
4	DCE: $CHCl_3$	36
5	DMSO: $CHCl_3$	52
6	MeCN: $CHCl_3$	16

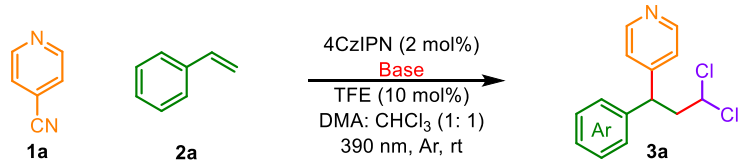
3.2: Solvent ratio optimization:



Entry	DMA: $CHCl_3$ (X: Y mL)	Yield (%)
1	1.5: 0.5	42
2	1.4: 0.6	44
3	1.3: 0.7	46

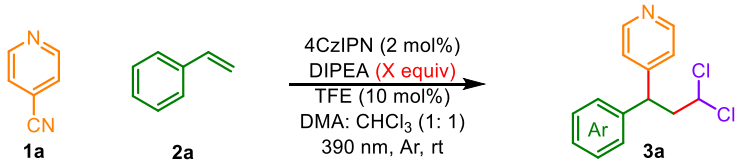
4	1.2: 0.8	53
5	1.1: 0.9	58
6	1.0: 1.0	75
7	0.0: 2.0	32

3.3: (a) Screening of Bases:



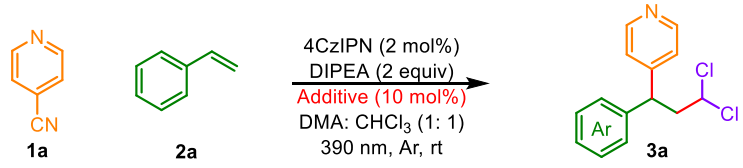
Entry	Base (2 equiv.)	Yield (%)
1	DIPEA	75
2	Et_3N	39
3	DBU	20
4	DABCO	Trace
5	TMG	16
6	K_2CO_3	34
7	Na_2CO_3	25
8	Bu_3N	30

3.3: (b) Screening of Base equivalent:



Entry	DIPEA (X equiv.)	Yield (%)
1	0.5	18
2	1.0	39
3	1.5	62
4	2.0	75
5	3.0	57

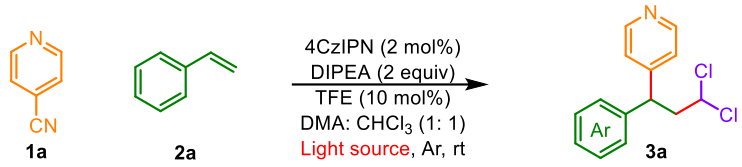
3.4: Screening of Additives:



Entry	Additive (10 mol%)	Yield (%)
1	AcOH	50

2	$Zn(OTf)_2$	69
3	Benzoic acid	74
4	CSA	73
5	$Cu(OTf)_2$	74
6	TFE	75

3.5. Light source Screening:

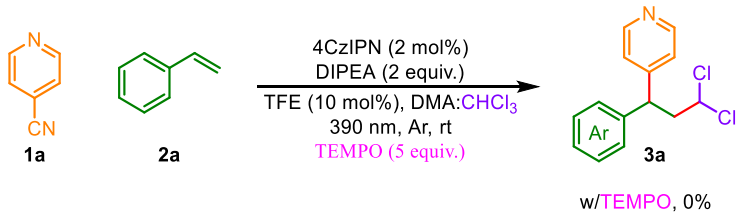


Entry	Light source	Yield (%)
1	456 nm	38
2	427 nm	15
3	390 nm	75
4	370 nm	56
5	450 nm	42
6	White LED lamp	No reaction

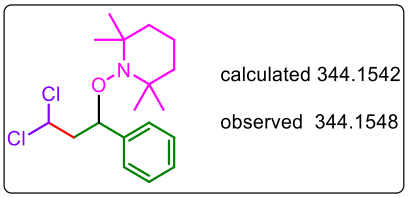
4.0. Control Experiments:

4.1. Procedure for experiment with TEMPO:

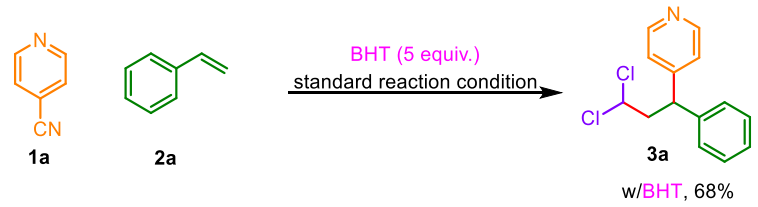
In an oven dried reaction vial equipped with a magnetic stir bar, **1a** (50 mg, 0.48 mmol),**2a** (3 equiv.), DIPEA (2 equiv,0.96 mmol), TEMPO (5 equiv.), and 10 mol% TFE were dissolved in anhydrous 2.0 mL DMA and $CHCl_3$ (1:1). The reaction mixture purged with Ar for 30 minutes and irradiated under blue LED. After 24 h TLC (Thin layer chromatography) showed no reaction. Benzyl radical was trapped by TEMPO which was detected by LC-MS. Exact mass calculated for $C_{18}H_{27}Cl_2NO^+$ $[M+H]^+$: 344.1548; found: 344.1542.



intermediates detected by mass spectrometry



4.2. Procedure for experiment with BHT:



In an oven dried reaction vial equipped with a magnetic stir bar, **1a** (50 mg, 0.48 mmol), **2a** (3 equiv.), DIPEA (2 equiv, 0.96 mmol), BHT (5 equiv.), TFE (10 mol%) and 4CzIPN catalyst (2 mol%) were dissolved in anhydrous 2.0 mL DMA and $CHCl_3$ (1:1). The reaction mixture was purged with Ar for 15 minutes and irradiated under 390 nm LED. After 24h, TLC (thin layer chromatography) indicated product formation. The reaction mixture was concentrated and the residue was purified by column chromatography on silica gel using ethyl acetate in petroleum ether to afford the desired product **3a** (87 mg, 68%).

5.0. Fluorescence Quenching Experiments:

Fluorescence spectra were recorded using Horiba Fluoromax spectrofluorometer. The Stern-Volmer fluorescence quenching studies were run with freshly prepared 4CzIPN (0.001 µM solution in DMA) at room temperature. The solution was irradiated at 450 nm and fluorescence was measured from 400 to 600 nm. Control experiment showed that 4CzIPN fluorescence was quenched by DIPEA.

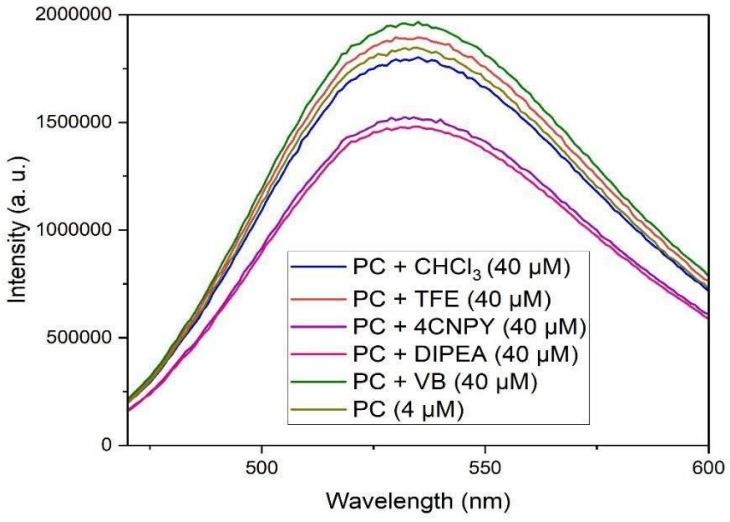


Figure S2: Fluorescence intensity of 4CzIPN solution (0.001 µM solution in DMA) containing DIPEA, Styrene, trifluoroethanol in DMA (excitation wavelength: 450 nm). Peak descriptors: 4CzIPN (4 µM) in DMA (dark yellow line), $CHCl_3$ (40 µM) in DMA (blue line), TFE (40 µM) in DMA (red line), 4CNPY (40 µM) in DMA (purple line), (DIPEA (40 µM) in DMA (pink line), VB (40 µM) in DMA (green line).

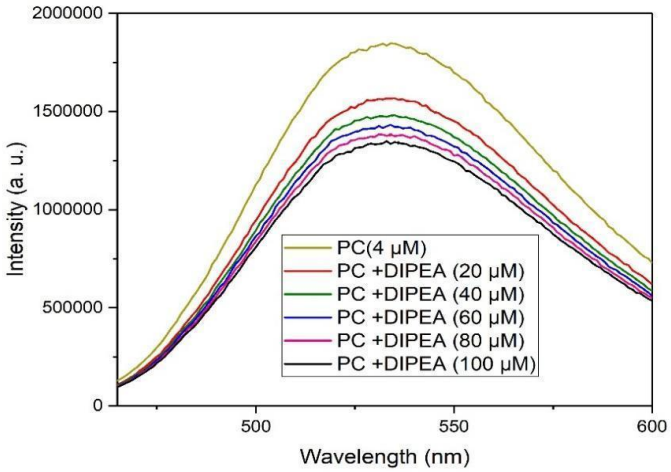


Figure S3: Fluorescence intensity of 4CzIPN solution (4 μM solution in DMA) containing varying amounts of DIPEA (excitation wavelength: 450 nm)

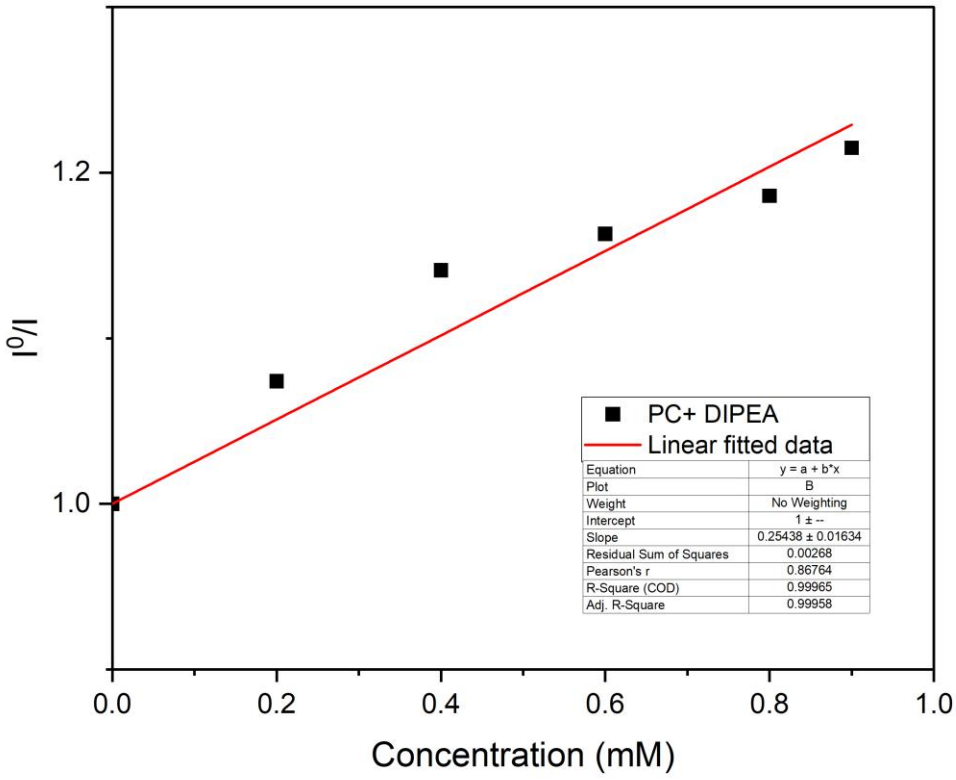


Figure S4: Stern-Volmer plot for the fluorescence quenching studies of 4CzIPN by DIPEA.

UV-Vis absorption experiments:

The UV/Vis absorption spectra of 4CNPy, photocatalyst, DIPEA, styrene, TFE and chloroform in acetonitrile is measured in quartz cuvettes with a 1 cm path length, respectively. In figure s5 UV-Vis absorption study of all reaction components was shown.

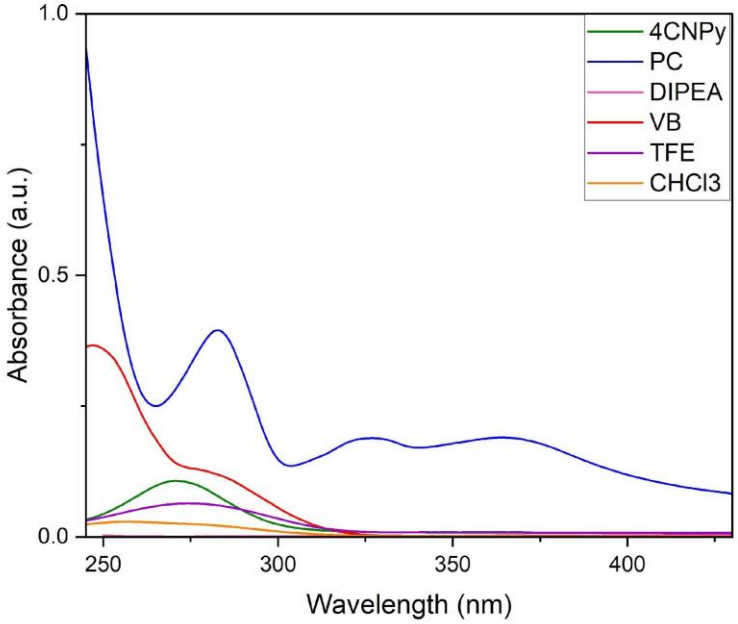


Figure S5: UV-Vis absorption study of all reaction components.

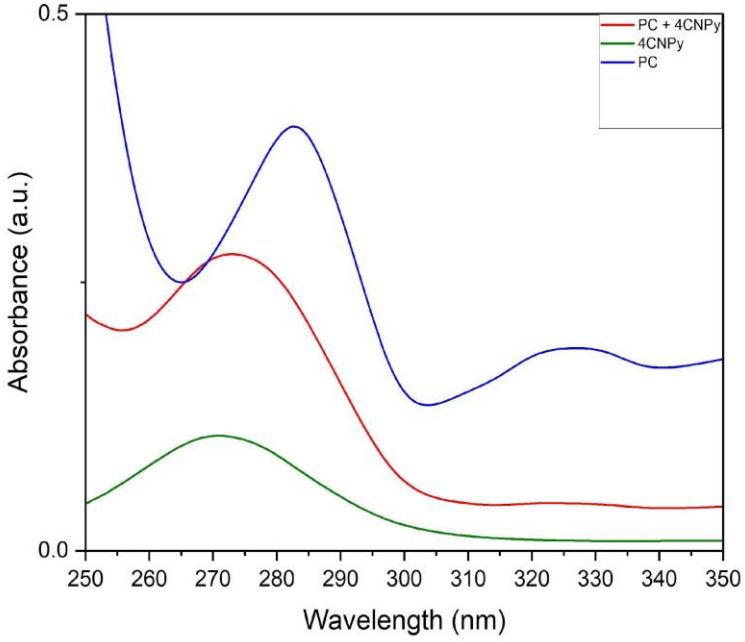


Figure S6: UV-Vis absorption study for EDA complex formation.

We measured the UV-Vis absorption spectra of the photocatalyst (4CzIPN), DIPEA, 4CNPy, TFE and styrene and their combinations to confirm the involvement of EDA complex formation in the reaction mixture (Figures S6, S7). To evaluate the possibility of EDA complex between DIPEA and 4CNPy, we recorded the UV-Vis absorption spectrum of their mixture. No bathochromic (red) shift or new absorption band was observed upon mixing the components (Figure S8). This indicates that DIPEA and 4CNPy do not form a detectable EDA complex under the studied conditions.

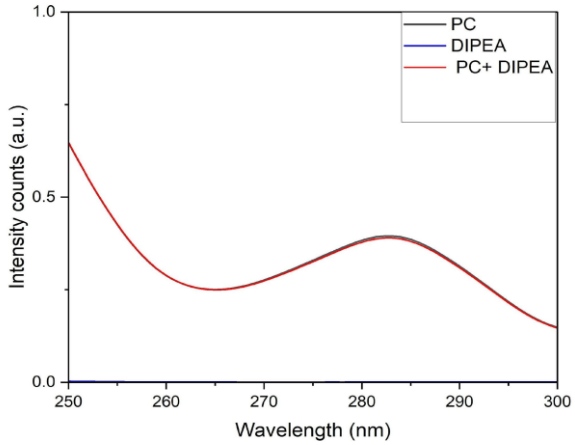


Figure S7: UV-Vis absorption study for EDA complex formation.

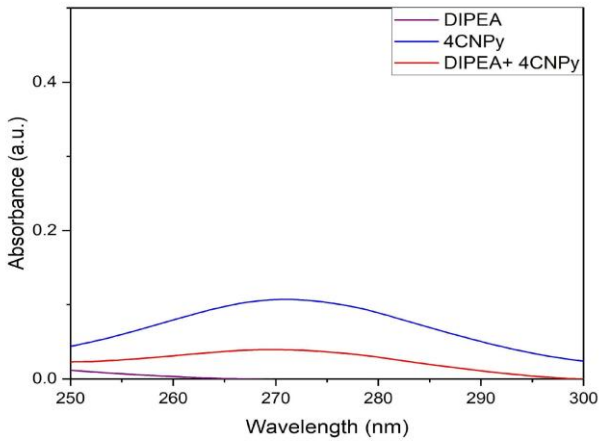
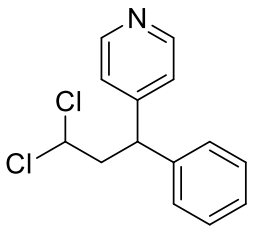


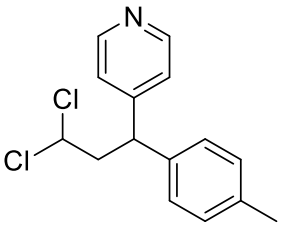
Figure S8: UV-Vis absorption study for EDA complex formation.

To evaluate the possibility of EDA complex between DIPEA and 4CNPy, we recorded the UV-Vis absorption spectrum of their mixture. No bathochromic (red) shift or new absorption band was observed upon mixing the components. This indicates that DIPEA and 4CNPy do not form a detectable EDA complex under the studied conditions.

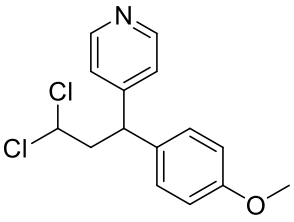
6.0. Analytical Data of Synthesized Products:



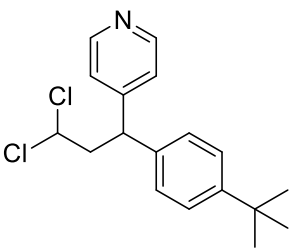
4-(3,3-Dichloro-1-phenylpropyl)pyridine (3a): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), styrene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3a** after flash chromatography as a brown liquid (96 mg, 75%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.51 (dd, *J* = 4.5, 1.8 Hz, 2H), 7.33 (ddd, *J* = 7.6, 6.2, 1.3 Hz, 2H), 7.28 – 7.24 (m, 1H), 7.23 – 7.19 (m, 2H), 7.17 – 7.13 (m, 2H), 5.35 (dd, *J* = 7.4, 6.1 Hz, 1H), 4.25 (t, *J* = 7.8 Hz, 1H), 2.95 – 2.85 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 151.4, 150.3, 140.3, 129.3, 127.9, 127.7, 123.0, 71.4, 48.4, 47.7. Exact mass calculated for $C_{14}H_{14}Cl_2N$ $[M+H]^+$ 266.0503, found 266.0507.



4-(3,3-Dichloro-1-(*p*-tolyl)propyl)pyridine (3b): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-methyl-4-vinylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3b** after flash chromatography as brown liquid (89 mg, 66%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.51 (d, *J* = 6.0 Hz, 2H), 7.16 – 7.13 (m, 4H), 7.09 (d, *J* = 8.5 Hz, 2H), 5.35 (t, *J* = 6.6 Hz, 1H), 4.21 (t, *J* = 7.9 Hz, 1H), 2.88 (td, *J* = 7.9, 7.0, 3.0 Hz, 2H), 2.32 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 151.7, 150.3, 137.5, 137.3, 129.9, 127.8, 123.0, 71.5, 48.5, 47.3, 21.1. Exact mass calculated for $C_{15}H_{16}Cl_2N$ $[M+H]^+$ 280.0660, found 280.0657.

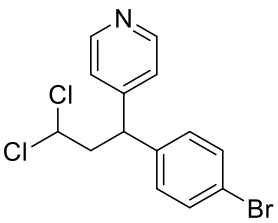


4-(3,3-Dichloro-1-(4-methoxyphenyl)propyl)pyridine (3c): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-methoxy-4-vinylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3c** after flash chromatography as brown liquid (89 mg, 62%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.53 – 8.49 (m, 2H), 7.16 – 7.12 (m, 4H), 7.11 – 7.08 (m, 2H), 5.36 (dd, *J* = 7.5, 6.0 Hz, 1H), 4.21 (t, *J* = 7.8 Hz, 1H), 2.94 – 2.83 (m, 2H), 2.32 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 159.0, 152.1, 150.1, 132.2, 129.0, 123.0, 114.7, 71.5, 55.4, 48.5, 47.0. Exact mass calculated for $C_{15}H_{16}Cl_2NO$ $[M+H]^+$ 296.0609, found 266.0608.

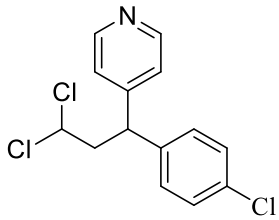


4-(1-(4-(*tert*-Butyl)phenyl)-3,3-dichloropropyl)pyridine (3d): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-(*tert*-butyl)-4-vinylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3d** after flash chromatography as brown liquid (67 mg, 43%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 – 8.50 (m, 2H), 7.35 – 7.32 (m, 2H), 7.17 – 7.12 (m, 4H), 5.36 (dd, *J* = 7.6, 5.9 Hz, 1H), 4.24 – 4.20 (m, 1H), 2.92 – 2.85 (m, 2H), 1.29 (s, 9H). ^{13}C{^{1}H}

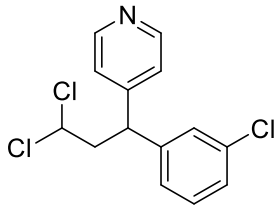
NMR (125 MHz, Chloroform-*d*) δ 151.8, 150.6, 150.2, 137.1, 127.5, 126.2, 123.1, 71.6, 48.5, 47.3, 34.6, 31.4. Exact mass calculated for $C_{18}H_{22}Cl_2N$ $[M+H]^+$ 322.1129, found 322.1132.



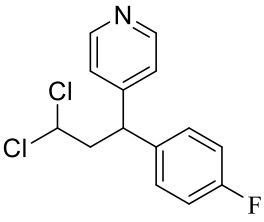
4-(1-(4-Bromophenyl)-3,3-dichloropropyl)pyridine (3e): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-bromo-4-vinylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3e** after flash chromatography as brown liquid (66 mg, 40 %). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.55 – 8.51 (m, 2H), 7.49 – 7.44 (m, 2H), 7.14 – 7.11 (m, 2H), 7.11 – 7.07 (m, 2H), 5.33 (t, *J* = 6.6 Hz, 1H), 4.22 (t, *J* = 7.9 Hz, 1H), 2.90 – 2.84 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 150.7, 150.4, 139.4, 132.4, 129.6, 122.9, 121.7, 71.1, 48.1, 47.1. Exact mass calculated for $C_{14}H_{13}BrCl_2N$ $[M+H]^+$ 343.9608, found 343.9609.



4-(3,3-Dichloro-1-(4-chlorophenyl)propyl)pyridine (3f): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-chloro-4-vinylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3f** after flash chromatography as brown liquid (51 mg, 35%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.54 (d, *J* = 4.8 Hz, 2H), 7.31 (d, *J* = 8.5 Hz, 2H), 7.14 (m, 4H), 5.33 (t, *J* = 6.6 Hz, 1H), 4.24 (t, *J* = 7.9 Hz, 1H), 2.88 (t, *J* = 7.3 Hz, 2H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 150.9, 150.4, 138.8, 133.6, 129.5, 129.3, 122.9, 71.1, 48.2, 47.1. Exact mass calculated for $C_{14}H_{13}Cl_3N$ $[M+H]^+$ 300.0114, found 300.0118.

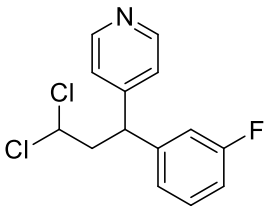


4-(3,3-Dichloro-1-(3-chlorophenyl)propyl)pyridine (3g): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-chloro-3-vinylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3g** after flash chromatography as brown liquid (58 mg, 40%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.53 (d, *J* = 5.9 Hz, 2H), 7.25 (d, *J* = 7.2 Hz, 2H), 7.18 (s, 1H), 7.13 (d, *J* = 5.9 Hz, 2H), 7.10 (dd, *J* = 6.8, 2.3 Hz, 1H), 5.34 (t, *J* = 6.8 Hz, 1H), 4.22 (t, *J* = 7.9 Hz, 1H), 2.88 (t, *J* = 7.2 Hz, 2H). ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 150.5, 150.4, 142.5, 135.2, 130.5, 128.1, 128.0, 126.1, 122.9, 71.0, 48.1, 47.4. Exact mass calculated for $C_{14}H_{13}Cl_3N$ $[M+H]^+$ 300.0114, found 300.0109.

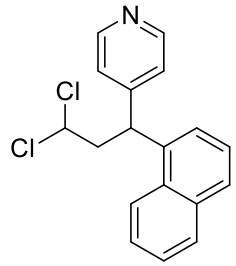


4-(3,3-Dichloro-1-(4-fluorophenyl) propyl) pyridine (3h): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-fluoro-4-vinylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3h** after flash chromatography as brown liquid (67 mg, 49%). Rf= 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.59 – 8.53 (m, 2H), 7.33 – 7.29 (m, 2H),

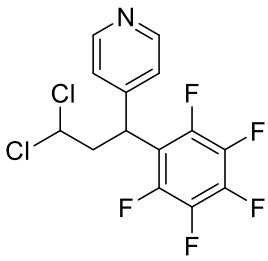
7.15 (d, J = 2.1 Hz, 2H), 7.13 (d, J = 2.9 Hz, 2H), 5.36 – 5.30 (m, 1H), 4.24 (t, J = 7.8 Hz, 1H), 2.89 – 2.86 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, Chloroform-*d*) δ 150.9, 150.4, 138.9, 133.7, 129.5, 129.3 (d, J = 24.1 Hz), 125.3, 123.5, 123.1, 71.1, 48.2, 47.1. ^{19}F NMR (471 MHz, Chloroform-*d*) δ -114.28- -11.22 (m). Exact mass calculated for $C_{14}H_{13}Cl_2FN$ $[M+H]^+$ 284.0409, found 284.0403.



4-(3,3-Dichloro-1-(3-fluorophenyl)propyl)pyridine (3i): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-fluoro-3-vinylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3i** after flash chromatography as brown liquid (70 mg, 51%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^1H NMR (500 MHz Chloroform-*d*) δ 8.55 (d, J = 5.4 Hz, 2H), 7.31 (d, J = 7.9, Hz, 1H), 7.17 – 7.11 (m, 2H), 7.03 – 6.93 (m, 2H), 6.90 (dd, J = 9.7, 2.4 Hz, 1H), 5.35 (t, J = 6.6 Hz, 1H), 4.25 (t, J = 7.9 Hz, 1H), 2.89 (t, J = 7.3 Hz, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, Chloroform-*d*) δ 164.2, 162.2, 150.6 (d, J = 20.3 Hz), 150.5, 150.4, 142.9, 142.9, 130.8, 123.7, 123.5, 123.0, 122.9, 115.1, 115.0, 114.9, 114.8 (dd, J = 29.7, 21.3 Hz), 114.6, 71.1, 48.2, 47.4. ^{19}F NMR (471 MHz, Chloroform-*d*) δ -111.40 (d, J = 91.1 Hz. Exact mass calculated for $C_{14}H_{13}Cl_2FN$ $[M+H]^+$ 284.0409, found 284.0404.

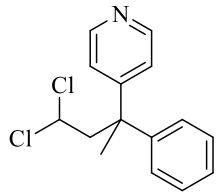


4-(3,3-Dichloro-1-(naphthalen-1-yl)propyl)pyridine (3j): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-vinylnaphthalene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3j** after flash chromatography as brown solid (94 mg, 62%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^1H NMR (500 MHz, Chloroform-*d*) δ 8.52 (d, J = 5.7 Hz, 2H), 8.07 – 7.98 (m, 1H), 7.90 – 7.84 (m, 1H), 7.81 (d, J = 8.2 Hz, 1H), 7.53 – 7.45 (m, 3H), 7.40 (d, J = 7.1 Hz, 1H), 7.21 (dd, J = 4.4, 1.7 Hz, 2H), 5.50 (t, J = 6.7 Hz, 1H), 5.10 (t, J = 7.7 Hz, 1H), 3.16 – 2.99 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, Chloroform-*d*) δ 157.3, 150.1, 142.3, 133.2, 132.3, 128.8, 128.2, 127.6, 126.7, 126.6, 125.9, 125.6, 122.3, 70.3, 54.3, 46.8, 27.5. Exact mass calculated for $C_{18}H_{16}Cl_2N$ $[M+H]^+$316.0660, found 316.0659.

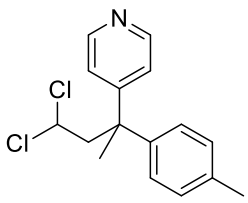


4-(3,3-Dichloro-1-(perfluorophenyl)propyl)pyridine(3k): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 2,3,4,5,6-pentafluoro styrene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3k** after flash chromatography as brown liquid (52 mg, 30%). R_f= 0.4 (25% ethyl acetate in petroleum ether). ^1H NMR (500 MHz, Chloroform-*d*) δ 8.58 (d, J = 5.4 Hz, 2H), 7.23 (d, J = 5.9 Hz, 2H), 5.51 (t, J = 6.3 Hz, 1H), 4.74 (t, J = 7.7 Hz, 1H), 3.07 (m, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, Chloroform-*d*) δ 150.7, 147.8, 146.4, 144.0, 139.1, 136.7, 122.7, 114.0, 70.6, 44.9, 37.6. 150.7, 150.4, 147.9, 146.4-146.1 (m), 144.4- 144.1 (m), 141.9-141.6 (m), 137.2-136.8 (m), 122.6, 114.1-113.8(m), 70.6, 45.0, 44.9, 37.6. ^{19}F NMR (471 MHz, Chloroform-*d*) δ -140.75 (d, J = 22.8 Hz), -153.27 (t, J = 19.9 Hz),

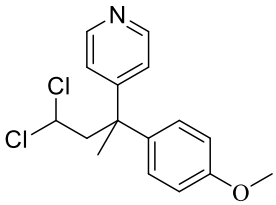
-159.94 (t, J = 22.8 Hz). -140.71 – -140.9 (m), -153.4 (q, J = 23.0, 22.2 Hz), -160.0 – -160.2 (m). Exact mass calculated for $C_{14}H_9Cl_2F_5N$ $[M+H]^+$ 356.0032, found 356.0028.



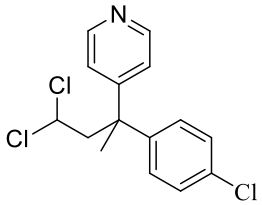
4-(4,4-Dichloro-2-phenylbutan-2-yl)pyridine (3l): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), alpha methyl styrene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3l** after flash chromatography as brown liquid (98 mg, 73%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 – 8.49 (m, 2H), 7.32 (td, J = 6.7, 1.7 Hz, 2H), 7.27 – 7.22 (m, 1H), 7.15 (dd, J = 7.2, 1.6 Hz, 2H), 7.08 – 7.05 (m, 2H), 5.34 (dd, J = 6.1, 5.2 Hz, 1H), 3.17 (dd, J = 5.7, 2.9 Hz, 2H), 1.79 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 157.3, 150.1, 145.2, 128.8, 127.2, 122.2, 70.3, 547, 46.6, 27.4. Exact mass calculated for $C_{15}H_{16}Cl_2N$ $[M+H]^+$280.0660, found 280.0654.



4-(4,4-Dichloro-2-(*p*-tolyl) butan -2-yl) pyridine (3m): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-methyl-4-(prop-1-en-2-yl) benzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3m** after flash chromatography as brown liquid (105 mg, 74%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 – 8.48 (m, 2H), 7.13 (d, J = 7.8 Hz, 2H), 7.08 – 7.05 (m, 2H), 7.05 – 7.02 (m, 2H), 5.34 (dd, J = 6.2, 5.1 Hz, 1H), 3.15 (dd, J = 5.6, 2.0 Hz, 2H), 2.32 (s, 3H), 1.77 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 157.7, 150.0, 142.1, 136.9, 129.5, 127.1, 122.2, 70.4, 54.6, 46.3, 27.5, 21.0. Exact mass calculated for $C_{16}H_{18}Cl_2N$ $[M+H]^+$294.0816, found 294.0815.

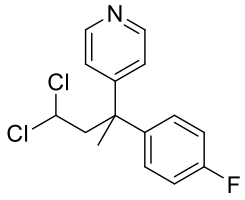


4-(4,4-Dichloro-2-(4-methoxyphenyl) butan-2-yl) pyridine (3n): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48mmol), 1-methoxy-4-(prop-1-en-2-yl)benzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3n** after flash chromatography as brown liquid (100 mg, 67%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.50 – 8.48 (m, 2H), 7.07 – 7.05 (m, 4H), 6.87 – 6.83 (m, 2H), 5.35 (t, J = 5.6 Hz, 1H), 3.79 (s, 3H), 3.14 (d, J = 5.7 Hz, 2H), 1.76 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 158.5, 157.9, 150.0, 136.9, 128.4, 122.2, 114.1, 70.4, 55.4, 54.8, 46.0, 27.6. Exact mass calculated for $C_{16}H_{18}Cl_2NO$ $[M+H]^+$310.0765, found 310.0768.

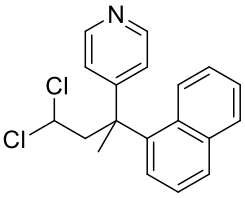


4-(4,4-Dichloro-2-(4-chlorophenyl)butan-2-yl)pyridine (3o): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-chloro-4-(prop-1-en-2-yl) benzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3o** after flash chromatography as brown liquid (107 mg, 71%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.53 – 8.48 (m, 2H), 7.28

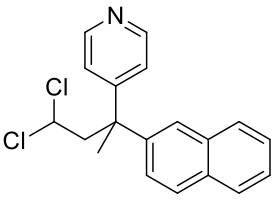
(d, *J* = 8.7 Hz, 2H), 7.07 (d, *J* = 8.6 Hz, 2H), 7.04 (d, *J* = 6.3 Hz, 2H), 5.33 (t, *J* = 5.6 Hz, 1H), 3.13 (d, *J* = 5.7 Hz, 2H), 1.76 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, Chloroform-*d*) δ 156.8, 150.2, 143.9, 133.2, 129.0, 128.7, 122.2, 70.0, 54.4, 46.3, 27.4. Exact mass calculated for $C_{15}H_{15}Cl_3N$ $[M+H]^+$314.0270, found 314.0268.



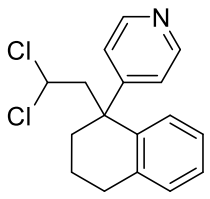
4-(4,4-Dichloro-2-(4-fluorophenyl) butan-2-yl) pyridine (3p): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-fluoro-4-(prop-1-en-2-yl) benzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3p** after flash chromatography as brown liquid (95 mg, 66%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 – 8.49 (m, 2H), 7.13 – 7.09 (m, 2H), 7.06 – 7.04 (m, 2H), 7.03 – 6.98 (m, 2H), 5.33 (t, *J* = 5.6 Hz, 1H), 3.14 (d, *J* = 5.7 Hz, 2H), 1.77 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, Chloroform-*d*) δ 162.7, 160.7, 157.1, 150.1, 141.0, 129.0 (d, *J* = 8.5 Hz), 122.1, 115.8, 70.1, 54.6, 46.2, 27.6. ^{19}F NMR (471 MHz, Chloroform-*d*) δ -115.1 (tt, *J* = 9.0, 4.5 Hz). Exact mass calculated for $C_{15}H_{15}Cl_2FN$ $[M+H]^+$ 298.0566, found 298.0566.



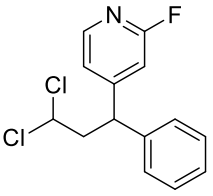
4-(4,4-dichloro-2-(naphthalen-1-yl)butan-2-yl)pyridine (3q): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-(prop-1-en-2-yl)naphthalene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3q** after flash chromatography as brown liquid (37 mg, 23%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.47 (d, *J* = 6.0 Hz, 2H), 7.86 (dd, *J* = 8.2, 3.9 Hz, 2H), 7.72 (d, *J* = 7.3 Hz, 1H), 7.54 (t, *J* = 7.9 Hz, 1H), 7.40 – 7.33 (m, 1H), 7.16 (d, *J* = 6.0 Hz, 2H), 7.04 (d, *J* = 6.0 Hz, 2H), 4.99 (dd, *J* = 7.9, 3.6 Hz, 1H), 3.68 (dd, *J* = 14.5, 3.6 Hz, 1H), 3.27 (dd, *J* = 15.1, 7.9 Hz, 1H), 1.94 (s, 3H). ^{13}C $\{^{1}H\}$ NMR (125 MHz, Chloroform-*d*) δ 159.4, 150.4, 137.7, 135.0, 130.7, 129.7, 129.5, 126.7, 126.0, 125.9, 125.5, 125.1, 120.9, 70.4, 52.9, 47.2, 31.8. Exact mass calculated for $C_{19}H_{18}Cl_2N$ $[M+H]^+$ 330.0816, found 330.0816.



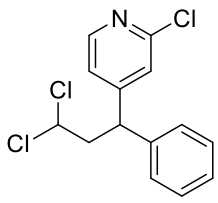
4-(4,4-dichloro-2-(naphthalen-2-yl)butan-2-yl)pyridine (3r): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 2-(prop-1-en-2-yl)naphthalene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3r** after flash chromatography as brown solid (130 mg, 82%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 6.3 Hz, 2H), 7.83 (ddd, *J* = 18.1, 7.3, 2.1 Hz, 2H), 7.77 (d, *J* = 9.2 Hz, 2H), 7.55 – 7.48 (m, 2H), 7.11 – 7.09 (m, 2H), 7.07 (d, *J* = 2.1 Hz, 1H), 5.37 (dd, *J* = 6.5, 4.8 Hz, 1H), 3.35 – 3.24 (m, 2H), 1.90 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, Chloroform-*d*) δ 159.7, 150.2, 137.6, 135.0, 130.6, 129.72, 129.6, 126.7, 126.0, 125.5, 125.1, 121.1, 70.4, 52.9, 47.2, 31.8. Exact mass calculated for $C_{19}H_{18}Cl_2N$ $[M+H]^+$330.0816, found 330.0820.



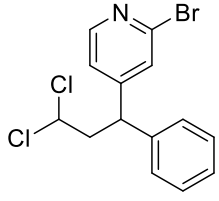
4-(1-(2,2-Dichloroethyl)-1,2,3,4-tetrahydronaphthalen-1-yl) pyridine (3s): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-methylene-1,2,3,4-tetrahydronaphthalene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3s** after flash chromatography as brown solid (109 mg, 74%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.45 (s, 2H), 7.27 – 7.19 (m, 3H), 7.01 (dd, *J* = 7.0, 2.8 Hz, 1H), 6.90 (d, *J* = 6.3 Hz, 2H), 5.56 (t, *J* = 5.3 Hz, 1H), 3.20 (d, *J* = 5.3 Hz, 2H), 2.85 (ddd, *J* = 16.8, 10.9, 5.9 Hz, 1H), 2.76 (dt, *J* = 16.8, 4.7 Hz, 1H), 2.49 (ddd, *J* = 13.7, 12.2, 3.1 Hz, 1H), 2.07 – 2.00 (m, 1H), 1.77 – 1.70 (m, 1H), 1.48 – 1.36 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 158.3, 149.8, 139.2, 136.7, 130.3, 128.6, 127.4, 126.5, 122.6, 70.6, 54.3, 47.2, 36.2, 29.9, 19.0. Exact mass calculated for $C_{17}H_{18}Cl_2N$ $[M+H]^+$ 330.0816, found 306.0812.



4-(3,3-dichloro-1-phenylpropyl)-2-fluoropyridine (3t): According to general procedure 2.2, 2-fluoroisonicotinonitrile (1 equiv, 0.48 mmol), styrene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3t** after flash chromatography as brown liquid (50 mg, 43%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 5.3 Hz, 1H), 7.36 (ddd, *J* = 7.6, 6.2, 1.3 Hz, 2H), 7.31 – 7.28 (m, 1H), 7.22 – 7.20 (m, 2H), 7.05 (dt, *J* = 5.3, 1.7 Hz, 1H), 6.79 (s, 1H), 5.35 (dd, *J* = 7.7, 5.6 Hz, 1H), 4.29 (dd, *J* = 9.0, 6.7 Hz, 1H), 2.94 – 2.87 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 164.3 (d, *J* = 239.5 Hz), 157.5 (d, *J* = 7.6 Hz), 148.1 (d, *J* = 15 Hz), 139.6, 129.5, 128.0, 127.9, 120.8 (d, *J* = 3.75 Hz), 108.6 (d, *J* = 37.76 Hz), 71.1, 48.2, 47.6. ^{19}F NMR (471 MHz, Chloroform-*d*) δ -67.17. Exact mass calculated for $C_{14}H_{13}Cl_2FN$ $[M]^+$ 284.0409, found 284.0408.

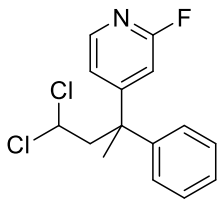


2-Chloro-4-(3,3-dichloro-1-phenylpropyl)-2-chloropyridine (3u): According to general procedure 2.2, 2-chloroisonicotinonitrile (1 equiv, 0.48 mmol), styrene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3u** after flash chromatography as brown liquid (49 mg, 45%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.30 (d, *J* = 5.4 Hz, 1H), 7.38 – 7.33 (m, 2H), 7.32 – 7.26 (m, 1H), 7.20 (dd, *J* = 7.0, 2.0 Hz, 3H), 7.08 (dd, *J* = 5.2, 2.0 Hz, 1H), 5.34 (dd, *J* = 7.7, 5.4 Hz, 1H), 4.25 (dd, *J* = 9.1, 6.8 Hz, 1H), 2.96 – 2.83 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 154.9, 152.2, 150.1, 139.5, 129.5, 128.0, 127.9, 123.4, 121.8, 71.1, 48.1, 47.5. Exact mass calculated for $C_{14}H_{13}Cl_3N$ $[M+H]^+$ 300.0114, found 300.0109.

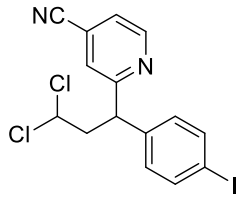


2-Bromo-4-(3,3-dichloro-1-phenylpropyl)-2-bromopyridine (3v): According to general procedure 2.2, 2-bromoisonicotinonitrile (1 equiv, 0.48 mmol), styrene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3v** after flash chromatography as brown liquid (33 mg, 35%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.28 (d, *J* = 4.8 Hz, 1H), 7.36 (q, *J* = 5.1, 3.0 Hz, 3H), 7.30 (d, *J* = 7.3 Hz, 1H), 7.20 (d, *J* = 7.3 Hz, 2H), 7.11 (d, *J* = 4.8 Hz, 1H), 5.38 – 5.31 (m, 1H), 4.23 (t, *J* = 7.9 Hz, 1H), 2.88 (q, *J* = 8.2 Hz, 2H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-

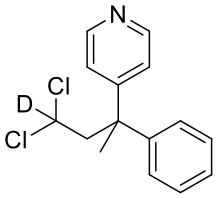
d) δ 154.6, 150.5, 143.0, 139.4, 129.5, 128.0, 127.9, 127.2, 122.2, 71.1, 48.1, 47.5. Exact mass calculated for $C_{14}H_{13}BrCl_2N$ $[M+H]^+$ 343.9608, found 343.9604.



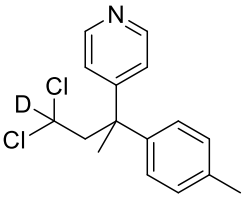
4-(4,4-Dichloro-2-phenylbutan-2-yl)-2-fluoropyridine (3w): According to general procedure 2.2, 2-fluoroisonicotinonitrile (1 equiv, 0.48 mmol), alpha methyl styrene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3w** after flash chromatography as brown liquid (56 mg, 46%). R_f = 0.4 (25% ethyl acetate in petroleum ether) ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 5.4 Hz, 1H), 7.36 (t, *J* = 7.6 Hz, 2H), 7.30 (d, *J* = 6.6 Hz, 1H), 7.16 (d, *J* = 7.9 Hz, 2H), 6.93 (d, *J* = 5.4 Hz, 1H), 6.73 (s, 1H), 5.38 – 5.31 (m, 1H), 3.17 (t, *J* = 6.0 Hz, 2H), 1.81 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 163.6 (J_{C-F} = 147.8, 147.7, 144.4, 129.0, 127.5, 127.1, 120.2, 108.2, 107.9, 70.0, 54.5, 46.9, 27.4. ^{19}F NMR (471 MHz, Chloroform-*d*) δ -67.26. Exact mass calculated for $C_{15}H_{15}Cl_2FN$ $[M+H]^+$ 298.0566, found 298.0569.



4-(3,3-Dichloro-1-(4-iodophenyl)propyl)picolinonitrile (3y): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 4-iodostyrene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **3y** after flash chromatography as brown liquid (18 mg, 10%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.76 (d, *J* = 4.8 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.38 (dd, *J* = 4.8, 1.8 Hz, 1H), 7.34 (s, 1H), 7.08 – 7.02 (m, 2H), 5.45 (t, *J* = 6.6 Hz, 1H), 4.36 (t, *J* = 7.6 Hz, 1H), 3.17 (dt, *J* = 14.5, 7.3 Hz, 1H), 2.90 (ddd, *J* = 14.5, 8.5, 6.0 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 162.3, 150.5, 139.9, 138.4, 130.1, 125.3, 123.6, 121.3, 116.3, 93.5, 71.6, 49.9, 47.8. Exact mass calculated for $C_{15}H_{12}Cl_2IN$ $[M+H]^+$ 416.9417, found 416.9427.

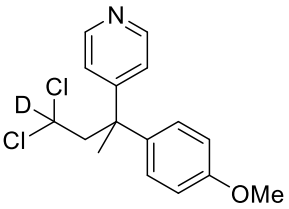


4-(4,4-Dichloro-2-phenylbutan-2-yl-4-d)pyridine (4a): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), prop-1-en-2-ylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4mmol) provided **4a** after flash chromatography as brown liquid (74 mg, 55%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 6.3 Hz, 2H), 7.33 (dd, *J* = 6.7, 1.7 Hz, 2H), 7.29 – 7.26 (m, 1H), 7.16 (dd, *J* = 7.1, 1.5 Hz, 2H), 7.09 – 7.05 (m, 2H), 3.18 (d, *J* = 2.9 Hz, 2H), 1.80 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 157.4, 150.1, 145.2, 128.9, 127.2, 122.3, 71. (t, *J* = 27.2), 54.5, 46.6, 27.4. Exact mass calculated for $C_{15}H_{15}DCl_2N$ $[M+H]^+$ 281.0723, found 281.0713.

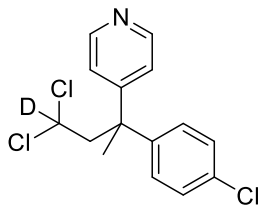


4-(4,4-Dichloro-2-(*p*-tolyl)butan-2-yl-4-d)pyridine (4b): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-methyl-4-(prop-1-en-2-yl)benzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4mmol) provided **4b** after flash chromatography as brown liquid (81 mg, 57%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.50 – 8.46 (m, 2H), 7.12 (d, *J* = 8.0 Hz, 2H), 7.07 – 7.05 (m, 2H), 7.04 – 7.01 (m, 2H), 5.34 (dd, *J* =

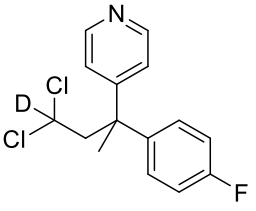
6.2, 5.1 Hz, 1H), 3.15 (dd, *J* = 5.6, 1.8 Hz, 2H), 2.31 (s, 3H), 1.76 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, Chloroform-*d*) δ 157.7, 150.0, 142.1, 136.8, 129.5, 127.1, 122.25, 70.4 (t, *J* = 31.2 Hz), 54.7, 46.3, 27.5, 21.0. Exact mass calculated for $C_{16}H_{17}DCl_2N$ $[M]^+$ 295.0874, found 294.0869.



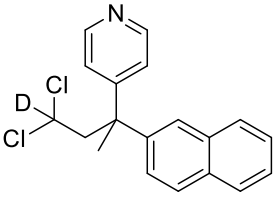
4-(4,4-Dichloro-2-(4-methoxyphenyl)butan-2-yl-4-d)pyridine (4c): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-methoxy-4-(prop-1-en-2-yl)benzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **4c** after flash chromatography as brown liquid (78 mg, 52%). R_f= 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.49 – 8.47 (m, 2H), 7.07 – 7.06 (m, 2H), 7.06 – 7.04 (m, 2H), 6.86 – 6.83 (m, 2H), 3.77 (s, 3H), 3.13 (s, 2H), 1.75 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, Chloroform-*d*) δ 158.5, 157.9, 145.0, 136.9, 128.4, 122.2, 114.1, 73.3 (t, *J* = 33.7 Hz), 55.3, 54.6, 46.0, 27.6. Exact mass calculated for $C_{16}H_{17}DCl_2NO$ $[M+H]^+$ 311.0828, found 311.0837**.**



4-(4,4-Dichloro-2-(4-chlorophenyl)butan-2-yl-4-d)pyridine (4d) : According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48mmol), 1-chloro-4-(prop-1-en-2-yl)benzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **4d** after flash chromatography as brown liquid (88 mg, 58%). R_f= 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 – 8.51 (m, 2H), 7.31 – 7.28 (m, 2H), 7.10 – 7.06 (m, 2H), 7.06 – 7.04 (m, 2H), 3.14 (s, 2H), 1.77 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, Chloroform-*d*) δ 156.7, 150.2, 143.9, 133.2, 129.0, 128.7, 122.1, 70.1 (t, *J* = 27.5 Hz), 54.3, 46.3, 27.4. Exact mass calculated for $C_{15}H_{14}DCl_3N$ $[M+H]^+$ 315.0327, found 315.0339.

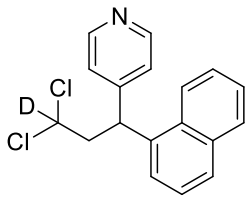


4-(4,4-Dichloro-2-(4-fluorophenyl)butan-2-yl-4-d)pyridine (4e) : According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-fluoro-4-(prop-1-en-2-yl)benzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **4e** after flash chromatography as brown liquid (102 mg, 71%). R_f= 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.50 – 8.48 (m, 2H), 7.12 – 7.08 (m, 2H), 7.06 – 7.03 (m, 2H), 7.02 – 6.97 (m, 2H), 3.13 (s, 2H), 1.76 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, Chloroform-*d*) δ 162.7, 160.7, 157.2, 150.0, 141.0, 129.0 (d, *J* = 8.5 Hz), 122.2, 115.7 (d, *J* = 21.7 Hz), 70.3 (t, J = 27.5 Hz), 46.2, 27.6. ^{19}F NMR (471 MHz, Chloroform-*d*) δ -115.09 (dq, *J* = 9.0, 4.9, 4.5 Hz). Exact mass calculated for $C_{15}H_{14}DCl_2FN$ $[M+H]^+$ 299.0623, found 299.0628.

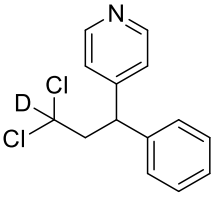


4-(4,4-Dichloro-2-(naphthalen-2-yl)butan-2-yl-4-d)pyridine (4f): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 2-(prop-1-en-2-yl)naphthalene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **4f** after flash chromatography as brown liquid (129 mg, 81%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*)

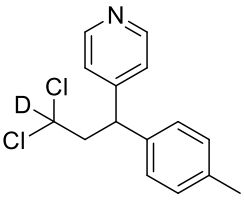
δ 8.52 (dd, *J* = 4.6, 1.9 Hz, 2H), 7.86 – 7.80 (m, 3H), 7.77 (s, 1H), 7.76 (s, 1H), 7.51 (ddd, *J* = 7.2, 5.0, 1.7 Hz, 2H), 7.10 (d, *J* = 1.7 Hz, 1H), 7.09 (d, *J* = 1.9 Hz, 1H), 7.07 (d, *J* = 2.1 Hz, 1H), 3.29 (d, *J* = 9.7 Hz, 2H), 1.90 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, Chloroform-*d*) δ 157.4, 150.1, 142.4, 133.2, 132.3, 128.8, 128.3, 127.7, 126.7, 126.6, 125.9, 125.7, 122.3, 70.1 (t, *J*= 33.75 Hz), 54.2, 46.8, 27.5. Exact mass calculated for $C_{19}H_{17}DCl_2N$ $[M+H]^+$ 331.0879, found 331.0861.



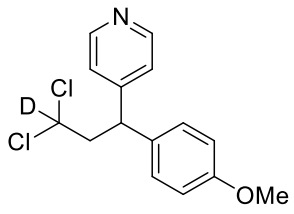
4-(3,3-Dichloro-1-(naphthalen-1-yl)propyl-3-d)pyridine (4g): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-vinylnaphthalene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **4g** after flash chromatography as brown liquid (93 mg, 61%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 6.0 Hz, 2H), 8.06 – 7.98 (m, 1H), 7.87 (dd, *J* = 6.3, 3.3 Hz, 1H), 7.82 (d, *J* = 8.5 Hz, 1H), 7.49 (dq, *J* = 8.5, 3.9 Hz, 3H), 7.40 (d, *J* = 7.3 Hz, 1H), 7.21 (d, *J* = 6.0 Hz, 2H), 5.10 (t, *J* = 7.6 Hz, 1H), 3.14 – 2.98 (m, 2H). $^{13}C\{^{1}H\}$ NMR (125 MHz, Chloroform-*d*) δ 151.4, 150.4, 136.0, 134.4, 131.4, 129.3, 128.6, 126.9, 126.4, 126.1, 125.5, 124.7, 123.2, 123.1, 71.5, (t, *J* = 6.7 Hz), 48.6, 43.0. Exact mass calculated for $C_{18}H_{15}DCl_2N$ $[M+H]^+$ 317.0717, found 317.0709.



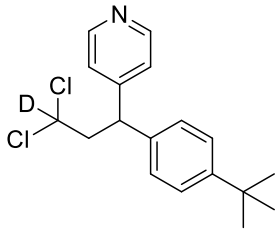
4-(3,3-Dichloro-1-phenylpropyl-3-d) pyridine (4h): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48mmol), styrene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **4h** after flash chromatography as brown liquid (61 mg, 48%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.53 (d, *J* = 5.1 Hz, 2H), 7.36 – 7.32 (m, 2H), 7.29 – 7.27 (m, 1H), 7.21 (dd, *J* = 6.9, 1.5 Hz, 2H), 7.17 – 7.15 (m, 2H), 4.25 (t, *J* = 7.8 Hz, 1H), 2.90 (dd, *J* = 7.9, 3.1 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (125 MHz, Chloroform-*d*) δ 151.8, 150.0, 140.2, 129.3, 127.7, 123.1, 72.4 (t, *J* = 27.5 Hz), 48.2, 47.7. Exact mass calculated for $C_{14}H_{13}DCl_2N$ $[M+H]^+$ 267.0561, found 267.0572.



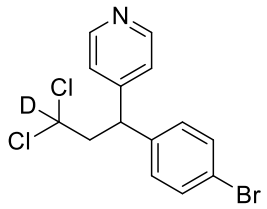
4-(3-3-Dichloro-1-(*p*-tolyl) propyl-3-*d*) pyridine (4i): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-(methyl)-4-vinylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **4i** after flash chromatography as brown liquid (80 mg, 59%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*), δ 8.52 – 8.50 (m, 2H), 7.15 (d, *J* = 1.7 Hz, 2H), 7.14 (d, *J* = 2.9 Hz, 2H), 7.09 (d, *J* = 8.2 Hz, 2H), 4.23 (t, 1H), 2.88 (dd, *J* = 7.8, 3.4 Hz, 2H), 2.31 (s, 3H). 13C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 151.8, 150.2, 137.5, 137.2, 129.9, 127.8, 123.0, 72.0 – 70.5 (t), 48.3, 47.3, 21.1. Exact mass calculated for $C_{15}H_{15}DCl_2N$ $[M+H]^+$ 281.0717, found 281.0719.



4-(3,3-Dichloro-1-(4-methoxyphenyl) propyl-3-d) pyridine (4j): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48mmol), 1-(methoxy)-4-vinylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **4j** after flash chromatography as brown liquid (57 mg, 40%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 – 8.49 (m, 2H), 7.15 – 7.10 (m, 4H), 6.88 – 6.84 (m, 2H), 4.19 (t, *J* = 7.8 Hz, 1H), 3.77 (s, 3H), 2.86 (d, *J* = 8.0 Hz, 2H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 159.0, 151.9, 150.3, 132.2, 129.0, 122.9, 114.6, 71.6 (t, *J* = 26.25 Hz), 55.4, 48.4, 46.9. Exact mass calculated for $C_{15}H_{15}DCl_2NO$ $[M+H]^+$ 297.0666, found 297.0678.

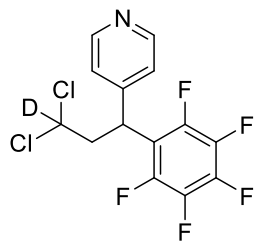


4-(1-(4-(*tert*-Butyl)phenyl)-3,3-dichloropropyl-3-d)pyridine: (4k) According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48mmol), 1-(*tert*-Butyl)-4-vinylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **4k** after flash chromatography as brown liquid (53 mg, 34%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) 8.52 (d, *J* = 6.0 Hz, 2H), 7.34 (d, *J* = 8.5 Hz, 2H), 7.17 (d, *J* = 6.0 Hz, 2H), 7.13 (d, *J* = 8.5 Hz, 2H), 4.21 (t, *J* = 7.9 Hz, 1H), 2.95 – 2.82 (m, 2H), 1.29 (s, 9H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 151.8, 150.6, 150.2, 137.1, 127.5, 126.2, 123.1, 71.8 (t, *J* = 26.25 Hz), 48.4, 47.3, 34.6, 31.4. Exact mass calculated for $C_{18}H_{21}DCl_2N$ $[M+H]^+$ 323.1187, found 323.1189.

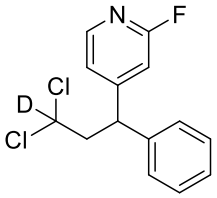


4-(1-(4-Bromophenyl)-3,3-dichloropropyl-3-d)pyridine (4l): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 1-bromo-4-vinylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **4l** after flash chromatography as brown liquid (68 mg, 41%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.54 (s, 2H), 7.49 – 7.44 (m, 2H), 7.13 (d, *J* = 6.1 Hz, 2H), 7.10 – 7.07 (m, 2H), 4.22 (t, *J* = 7.6 Hz, 1H), 2.89 – 2.84 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 150.8, 150.4, 139.4, 132.4, 129.6, 122.9, 121.7, 70.8, 70.6 (t, *J* = 26.25 Hz), 48.0, 47.2. Exact mass calculated for $C_{14}H_{12}DBrCl_2N$ $[M+H]^+$ 344.966, found 344.968.

4-(3,3-Dichloro-1-(perfluorophenyl)propyl-3-d)pyridine (4m): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48mmol), 1,2,3,4,5-pentafluoro-6-vinylbenzene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **4m** after flash chromatography as brown liquid (62 mg, 36%). R_f = 0.4 (25% ethyl acetate in petroleum ether).^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.58 (d, *J* = 2.9 Hz, 2H), 7.22 (d, *J* = 6.1 Hz, 2H), 4.74 (t, *J* = 7.8 Hz, 1H), 3.08 (d, *J* = 8.1 Hz, 2H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 150.7, 147.9, 146.4, 144.0, 142.2, 139.3, 136.7, 122.7, 114.1, 70.3 (t, *J* = 26.25 Hz), 44.8, 37.6.

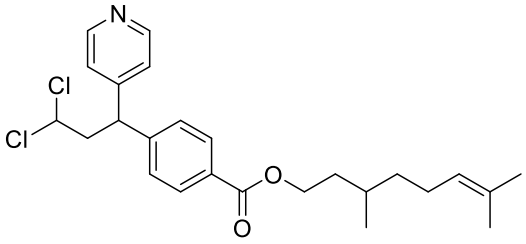


^{19}F NMR (471 MHz, Chloroform-*d*) δ -140.73 – -140.89 (m), -153.28 – -153.51 (m), -159.94 – -160.17 (m). Exact mass calculated for $C_{14}H_8DCl_2F_5N$ $[M+H]^+$357.0095, found 357.0089.

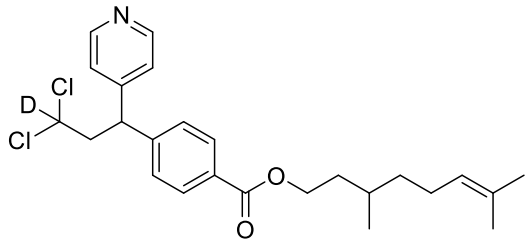


4-(3,3-Dichloro-1-phenylpropyl-3-d)-2-fluoropyridine (4n): According to general procedure 2.2, 2-fluoro isonicotinonitrile (1 equiv, 0.48 mmol), styrene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **4n** after flash chromatography as brown liquid (36 mg, 31%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.13 (d, *J* = 5.1 Hz, 1H), 7.37 – 7.33 (m, 2H), 7.32 – 7.26 (m, 1H), 7.21 (dd, *J* = 7.0, 1.6 Hz, 2H), 7.05 (dt, *J* = 5.1, 1.7 Hz, 1H), 6.79 (s, 1H), 4.32 – 4.27 (m, 1H), 2.93 – 2.88 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 164.3 (d, J_{C-F} = 240.2 Hz), 157.6, 148.1 (d, J_{C-F} = 14.4 Hz), 139.6, 129.5, 128.0, 127.9, 120.8 (d, J_{C-F} = 4.8 Hz), 108.6 (d, J_{C-F} = 37.4 Hz), 48.0, 47.5. ^{19}F NMR (471 MHz, Chloroform-*d*) δ -67.18. Exact mass calculated for $C_{14}H_{12}DCl_2FN$ $[M]^+$ 285.0466, found 285.0473.

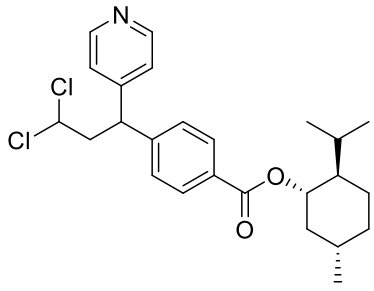
2-Chloro-4-(3,3-dichloro-1-phenylpropyl-3-d)pyridine (4o): According to general procedure 2.2, 2-chloro isonicotinonitrile (1 equiv, 0.48 mmol), styrene (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **4o** after flash chromatography as brown liquid (49 mg, 45%). R_f= 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.30 (d, *J* = 5.1 Hz, 1H), 7.36 (td, *J* = 6.5, 5.9, 1.4 Hz, 3H), 7.31 – 7.29 (m, 1H), 7.21 (d, *J* = 1.7 Hz, 1H), 7.19 (d, *J* = 1.3 Hz, 2H), 7.08 (dd, *J* = 5.2, 1.6 Hz, 1H), 4.25 (dd, *J* = 9.1, 6.6 Hz, 1H), 2.89 (dd, *J* = 10.5, 7.8 Hz, 2H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 150.8, 150.4, 139.4, 132.4, 129.2, 122.9, 121.7, 72.0 (t, *J* = 27.5 Hz), 48.0, 47.2. Exact mass calculated for $C_{14}H_{12}DCl_3F_5N$ $[M+H]^+$ 301.0171, found 301.0172.



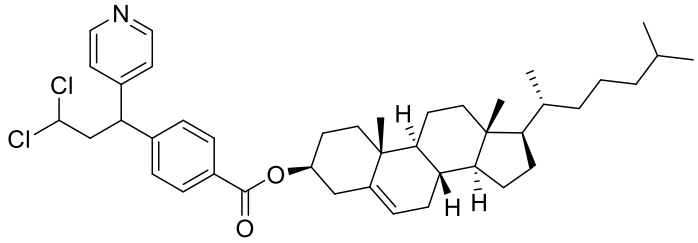
3,7-Dimethyloct-6-en-1-yl 4-(3,3-dichloro-1-(pyridin-4-yl) propyl) benzoate (5a): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 3,7-dimethyloct-6-en-1-yl 4-vinylbenzoate (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **5a** after flash chromatography as yellow liquid (57 mg, 26%). Rf= 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ) δ 8.54 (d, *J* = 6.0 Hz, 2H), 8.00 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H), 7.14 (d, *J* = 6.0 Hz, 2H), 5.33 (t, *J* = 7.0 Hz, 1H), 5.07 (t, *J* = 7.3 Hz, 1H), 4.33 (dd, *J* = 7.6, 3.3 Hz, 2H), 2.92 (t, *J* = 7.3 Hz, 2H), 2.04 – 1.91 (m, 2H), 1.83 – 1.74 (m, 1H), 1.67 – 1.50 (m, 10H), 1.37 (ddt, *J* = 12.1, 9.1, 6.0 Hz, 1H), 0.94 (d, *J* = 6.0 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, Chloroform-*d*) δ 166.1, 150.6, 150.4, 145.3, 131.5, 130.5, 130.1, 128.0, 124.6, 123.0, 71.0, 63.7, 48.1, 47.7, 37.0, 35.5, 29.8, 29.6, 25.8, 25.5, 19.6, 17.8. Exact mass calculated for $C_{25}H_{32}Cl_2NO_2$ $[M+H]^+$ 448.1805, found 448.1808.



3,7-Dimethyloct-6-en-1-yl-4-(3,3-dichloro-1-(pyridin-4-yl)propyl-3-d)benzoate (5b): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 3,7-dimethyloct-6-en-1-yl4-vinylbenzoate (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) and $CDCl_3$ (5 equiv, 2.4 mmol) provided **5b** after flash chromatography as yellow liquid (63 mg, 29%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.54 (d, *J* = 6.3 Hz, 2H), 8.01 (d, *J* = 10.5 Hz, 2H), 7.31 – 7.27 (m, 2H), 7.14 (dd, *J* = 4.5, 1.8 Hz, 2H), 5.11 – 5.03 (m, 1H), 4.35 – 4.31 (m, 2H), 2.92 (d, J = 7.8 Hz, 2H), 2.04 – 1.93 (m, 2H), 1.81 – 1.75 (m, 1H), 1.72 (s, 1H), 1.65 (s, 3H), 1.58 (s, 5H), 1.44 – 1.35 (m, 1H), 0.95 (d, *J* = 6.5 Hz, 3H), 0.06 (s, 1H).^{13}C{^{1}H} (125 MHz, Chloroform-*d*) δ 166.1, 150.5, 150.4, 145.3, 131.5, 130.5, 130.1, 128.0, 124.7, 70.6 (t, J = 26.25 Hz), 63.7, 47.9, 47.7, 37.0, 35.6, 29.6, 25.8, 25.5, 19.6, 17.7. Exact mass calculated for $C_{25}H_{31}DCl_2NO_2$ $[M+H]^+$ 449.1867, found 449.1868.

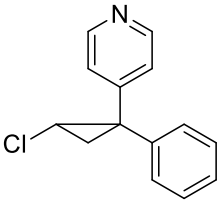


3,7-Dimethyloct-6-en-1-yl 4-(3,3-dichloro-1-(pyridin-4-yl) propyl) benzoate (5c): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol), 2-isopropyl-5-methylcyclohexyl 4-vinylbenzoate (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **5c** after flash chromatography as yellow liquid (80 mg, 37%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.54 (d, *J* = 5.4 Hz, 2H), 8.01 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.15 (d, *J* = 5.4 Hz, 2H), 5.33 (t, *J* = 6.6 Hz, 1H), 4.91 (td, *J* = 10.9, 4.8 Hz, 1H), 4.32 (d, *J* = 15.7 Hz, 1H), 2.92 (t, *J* = 7.3 Hz, 2H), 2.09 (d, *J* = 11.5 Hz, 1H), 1.96 – 1.86 (m, 1H), 1.71 (dd, *J* = 13.6, 3.9 Hz, 3H), 1.52 (dt, *J* = 10.3, 3.0 Hz, 2H), 1.14 – 1.02 (m, 2H), 0.90 (t, *J* = 6.3 Hz, 6H), 0.77 (d, *J* = 6.6 Hz, 3H). ^{13}C{^{1}H} NMR (126 MHz, Chloroform-*d*) δ 165.6, 150.6, 150.5, 145.2, 130.5, 130.4, 128.0, 122.9, 75.1, 71.1, 48.1, 47.7, 47.3, 41.0, 34.4, 31.5, 26.6, 23.7, 22.1, 20.9, 16.6. Exact mass calculated for $C_{25}H_{32}Cl_2NO_2$ $[M+H]^+$ 448.1805, found 448.1808.



(1*S*,2*R*)-2-Isopropyl-5-methylcyclohexyl 4-(3,3-dichloro-1-(pyridin-4-yl) propyl) benzoate (5d): According to general procedure 2.2, isonicotinonitrile (1 equiv, 0.48 mmol),(3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-((R)-6-methylheptan-2-yl)2,3,4,7,8,9,10,11,12,13,14,15,16,17-tetradecahydro-1Hcyclopenta[a]phenanthren-3-yl 4-vinylbenzoate vinylbenzoate (3 equiv, 1.4 mmol), DIPEA (2 equiv, 0.96 mmol) provided **5d** after flash chromatography as brown liquid (140 mg, 43%). R_f = 0.4 (25% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.55 (d, *J* = 6.0 Hz, 2H), 8.01 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.15 (d, *J* = 6.0 Hz, 2H), 5.40 (d, *J* = 4.8 Hz, 1H), 5.33 (t, *J* = 6.8 Hz, 1H), 4.88 – 4.79 (m, 1H), 4.33 (t, *J* = 7.7 Hz, 1H), 2.93 (t, *J* = 7.3 Hz, 2H), 2.43

(d, J = 7.3 Hz, 2H), 2.04 – 1.87 (m, 4H), 1.77 – 1.65 (m, 2H), 1.56 (t, J = 8.9 Hz, 2H), 1.53 – 1.45 (m, 4H), 1.44 (d, J = 4.8 Hz, 1H), 1.42 (t, J = 2.9 Hz, 1H), 1.18 – 1.07 (m, 8H), 1.05 (s, 3H), 0.99 (ddd, J = 18.1, 7.4, 4.1 Hz, 5H), 0.91 (d, J = 6.3 Hz, 3H), 0.85 (dd, J = 6.6, 2.1 Hz, 6H), 0.67 (s, 3H). $^{13}C\{^{1}H\}$ NMR (126 MHz, Chloroform-*d*) δ 165.5, 150.4, 145.2, 139.6, 130.5, 130.4, 127.9, 123.0, 71.0, 56.8, 56.2, 50.1, 48.1, 47.7, 42.4, 39.8, 39.6, 38.3, 37.1, 36.7, 36.3, 35.9, 32.0, 29.8, 28.3, 28.1, 28.0, 24.3, 23.9, 22.9, 22.6, 21.1, 19.4, 18.8, 14.2, 11.9, 10.1.Exact mass calculated for $C_{42}H_{58}Cl_2NO_2$ $[M+H]^+$ 678.3839, found 678.3831.



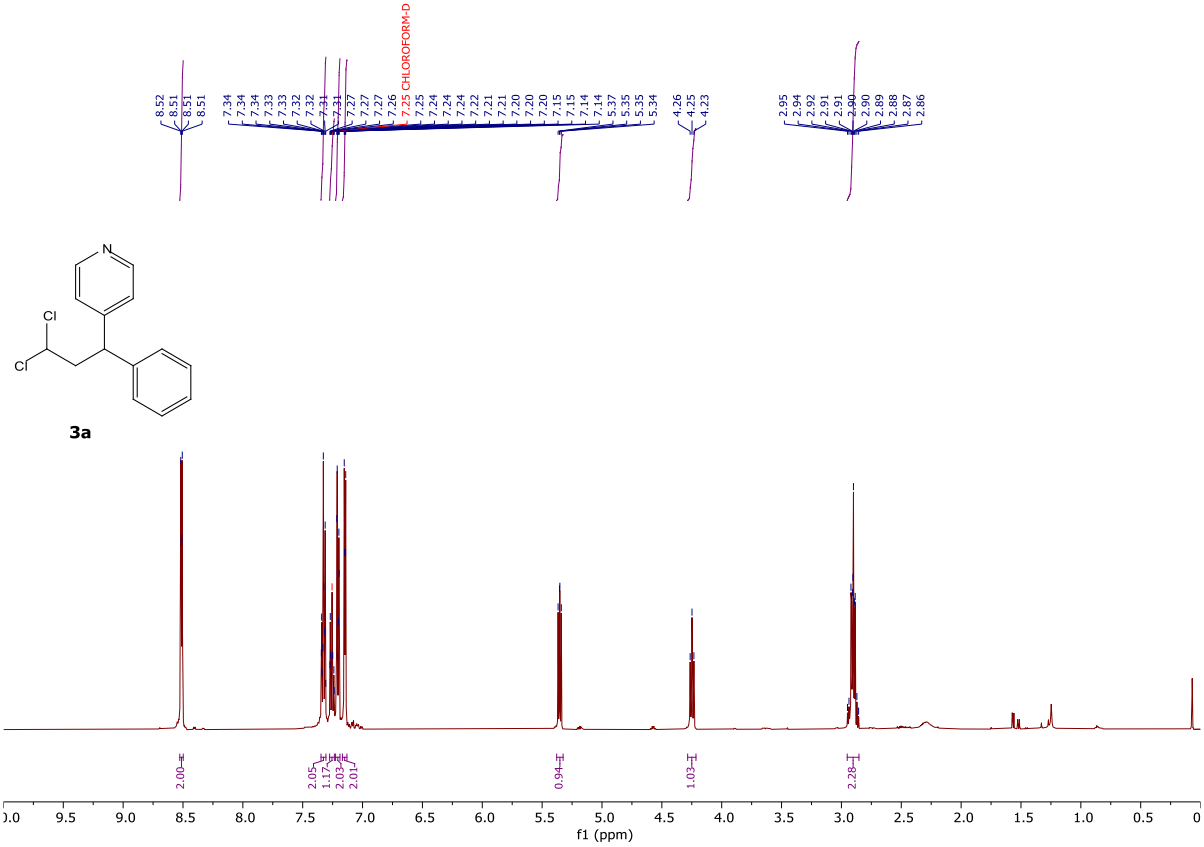
4-(2-Chloro-1-phenylcyclopropyl)pyridine (6a): According to general procedure 2.4, 4-(3,3-dichloro-1-phenylpropyl)pyridine (1 equiv, 0.2 mmol) and ^{t}BuOK (5 equiv, 0.7 mmol) provided **6a** after flash chromatography as white solid (31 mg, 72%). R_f = 0.4 (30% ethyl acetate in petroleum ether). ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.45 – 8.43 (m, 2H), 7.40 – 7.33 (m, 5H), 6.97 – 6.95 (m, 2H), 3.71 (dd, J = 7.2, 5.2 Hz, 1H), 1.87 – 1.82 (m, 2H). ^{13}C NMR (100 MHz, 500 MHz, Chloroform-*d*) δ 153.1, 150.0, 137.4, 131.2, 128.7, 127.9, 121.8, 39.8, 35.7, 25.3. Exact mass calculated for $C_{14}H_{13}ClN$ $[M+H]^+$ 230.0731, found 230.0739.

7.0. References:

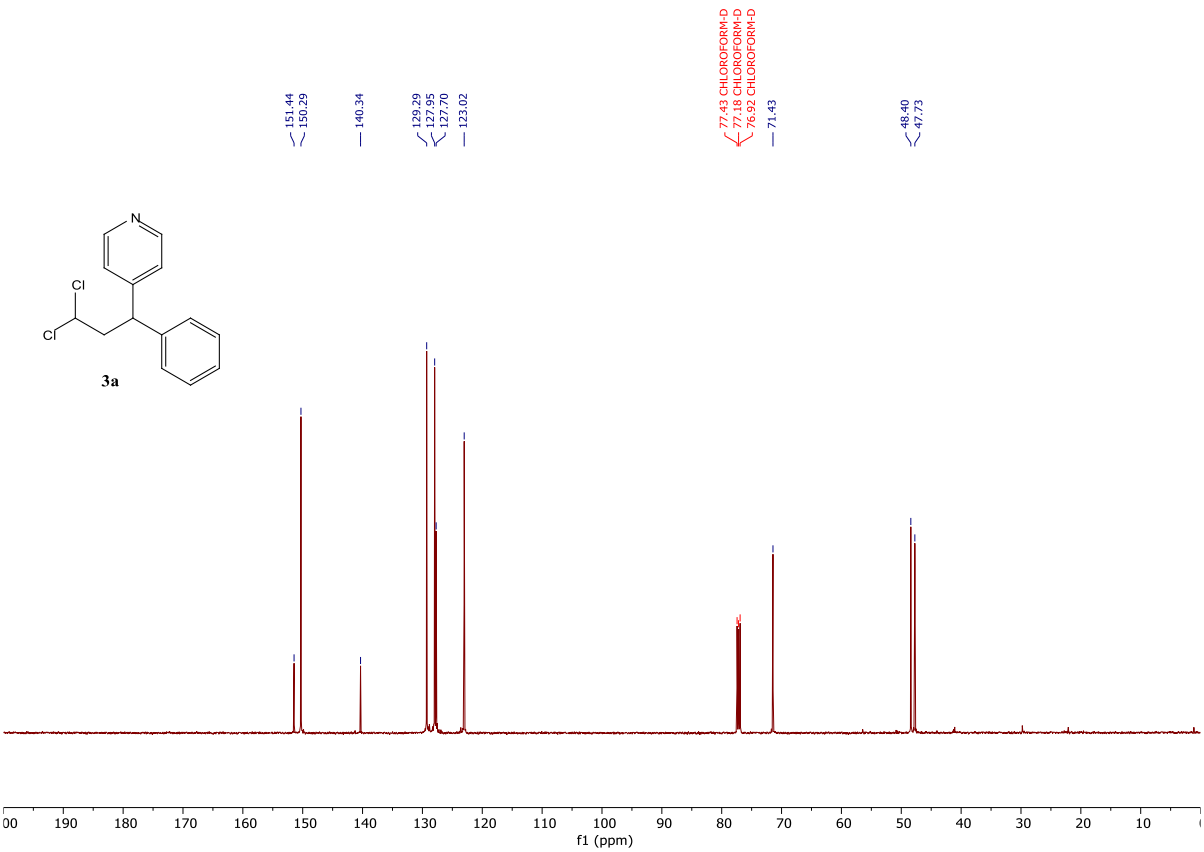
1. G. W. Gribble, *Accounts of Chemical Research*, 1998, **31**, 141-152.
2. P. A. Cohen and G. H. N. Towers, *Journal of Natural Products*, 1995, **58**, 520-526.
3. G. W. Gribble, *Journal of Natural Products*, 1992, **55**, 1353-1395.
4. N. Kambe, T. Iwasaki and J. Terao, *Chemical Society Reviews*, 2011, **40**, 4937-4947.
5. A. Jordan, P. Stoy and H. F. Sneddon, *Chemical Reviews*, 2021, **121**, 1582-1622.
6. C.-L. Ji, X. Zhai, Q.-Y. Fang, C. Zhu, J. Han and J. Xie, *Chemical Society Reviews*, 2023, **52**, 6120-6138.
7. K. Komeyama, T. Michiyuki and I. Osaka, *ACS Catalysis*, 2019, **9**, 9285-9291.
8. B. Gál, C. Bucher and N. Z. Burns, *Marine Drugs*, 2016, **14**, 206.
9. A. Tlili and J. Schranck, in *Solvents as Reagents in Organic Synthesis*, 2017, DOI: https://doi.org/10.1002/9783527805624.ch4, pp. 125-159.
10. M. S. Kharasch, E. V. Jensen and W. H. Urry, *Science*, 1945, **102**, 128-128.
11. B. Das, B. Sahana and D. P. Hari, *JACS Au*, 2025, **5**, 291-301.
12. T. Constantin, M. Zanini, A. Regni, N. S. Sheikh, F. Juliá and D. Leonori, *Science*, 2020, **367**, 1021-1026.
13. R. K. Neff, Y.-L. Su, S. Liu, M. Rosado, X. Zhang and M. P. Doyle, *Journal of the American Chemical Society*, 2019, **141**, 16643-16650.
14. Y.-L. Su, L. Tram, D. Wherritt, H. Arman, W. P. Griffith and M. P. Doyle, *ACS Catalysis*, 2020, **10**, 13682-13687.
15. S. Liu, Y.-L. Su, T.-Y. Sun, M. P. Doyle, Y.-D. Wu and X. Zhang, *Journal of the American Chemical Society*, 2021, **143**, 13195-13204.
16. C. M. Marshall, J. G. Federice, C. N. Bell, P. B. Cox and J. T. Njardarson, *Journal of Medicinal Chemistry*, 2024, **67**, 11622-11655.
17. R. U. McVicker and N. M. O'Boyle, *Journal of Medicinal Chemistry*, 2024, **67**, 2305-2320.

18. J. Chen, S. Zhu, J. Qin and L. Chu, *Chemical Communications*, 2019, **55**, 2336-2339.
19. J. Shen, Y. Zhang, Y. Yu and M. Wang, *Organic Chemistry Frontiers*, 2021, **8**, 901-907.
20. D. Louvel, A. Souibgui, A. Taponard, J. Rouillon, M. ben Mosbah, Y. Moussaoui, G. Pilet, L. Khrouz, C. Monnereau, J. C. Vantourout and A. Tlili, *Advanced Synthesis & Catalysis*, 2022, **364**, 139-148.
21. D.-D. Tang, Y.-Z. Wang, C. Liu, Y. Xia and Y. Li, *Organic Letters*, 2024, **26**, 6477-6481.
22. J. Cao, L. Gao, G. Wang and S. Li, *Green Chemistry*, 2024, **26**, 4785-4791.
23. J. Shen, J. Li, M. Chen and Y. Chen, *Organic Chemistry Frontiers*, 2023, **10**, 1166-1172.
24. Z. Zhang, J. Wang, C. Yu, J. Tan, H. Du and N. Chen, *Organic Letters*, 2024, **26**, 4727-4732.
25. C.-H. Ma, Y. Ji, J. Zhao, X. He, S.-T. Zhang, Y.-Q. Jiang and B. Yu, *Chinese Journal of Catalysis*, 2022, **43**, 571-583.
26. A. Wang, Y. Ma, J.-H. Jin, L.-Q. Wang, D.-D. Li, Z.-W. Xi, C. Shen and Y.-M. Shen, *The Journal of Organic Chemistry*, 2024, **89**, 17382-17388.
27. J.-m. Yu, L.-w. Zhu, X.-y. Hong, H. Gao and T.-t. Chen, *Organic & Biomolecular Chemistry*, 2021, **19**, 5642-5648.
28. W. Yu, H. Wang, K. Zhao, W. Li, T. Wang and J. Fu, *The Journal of Organic Chemistry*, 2024, **89**, 1703-1708.
29. C. Jian, Z. Li, Y. Mao, Y. Zhu, W. Yu, J. Wu and S. Li, *Organic Letters*, 2025, **27**, 2576-2581.
30. T. Singh, S. R. Nasireddy, G. C. Upreti, S. Arora and A. Singh, *Organic Letters*, 2023, **25**, 5558-5562.
31. G. C. Upreti, T. Singh, K. Khanna, D. Sahoo and A. Singh, *Organic Letters*, 2024, **26**, 3652-3656.
32. Hao, T.; Shen, J.;Wei, Y.; Shi, M. J. C. C., 2023**,** ***3*** (12).(Synthesis of **6a**)

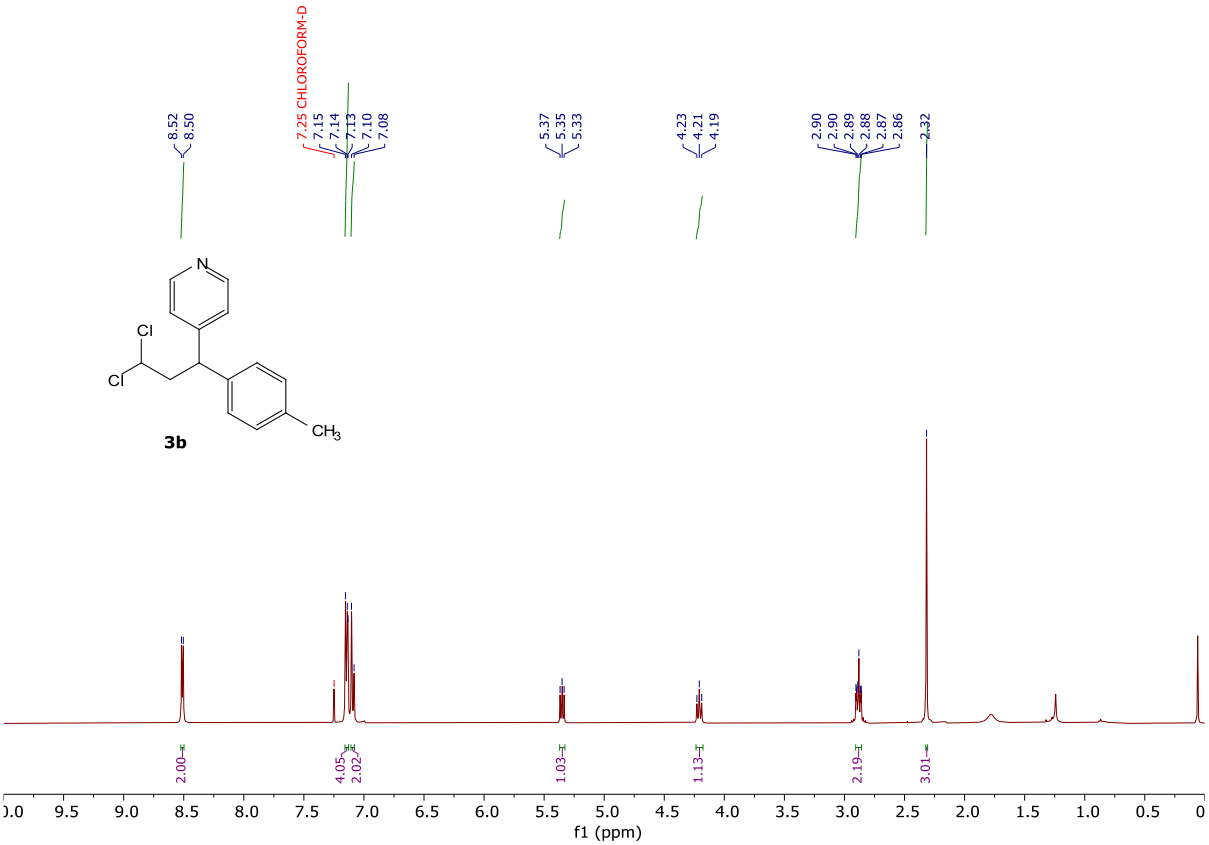
8.0. ^{1}H, $^{13}C\{^{1}H\}$, ^{19}F Spectra of Products:



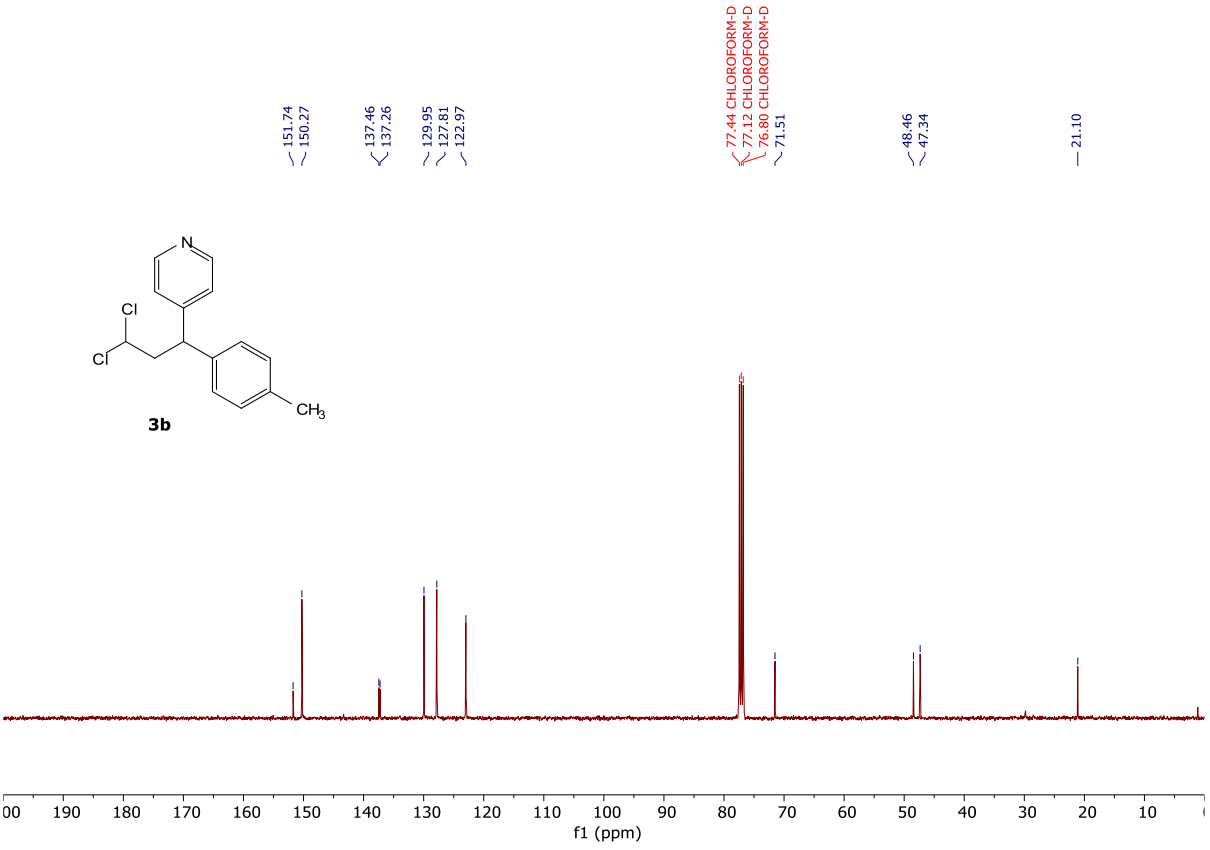
^{1}H NMR (400MHz) spectrum of compound **3a** in $CDCl_3$



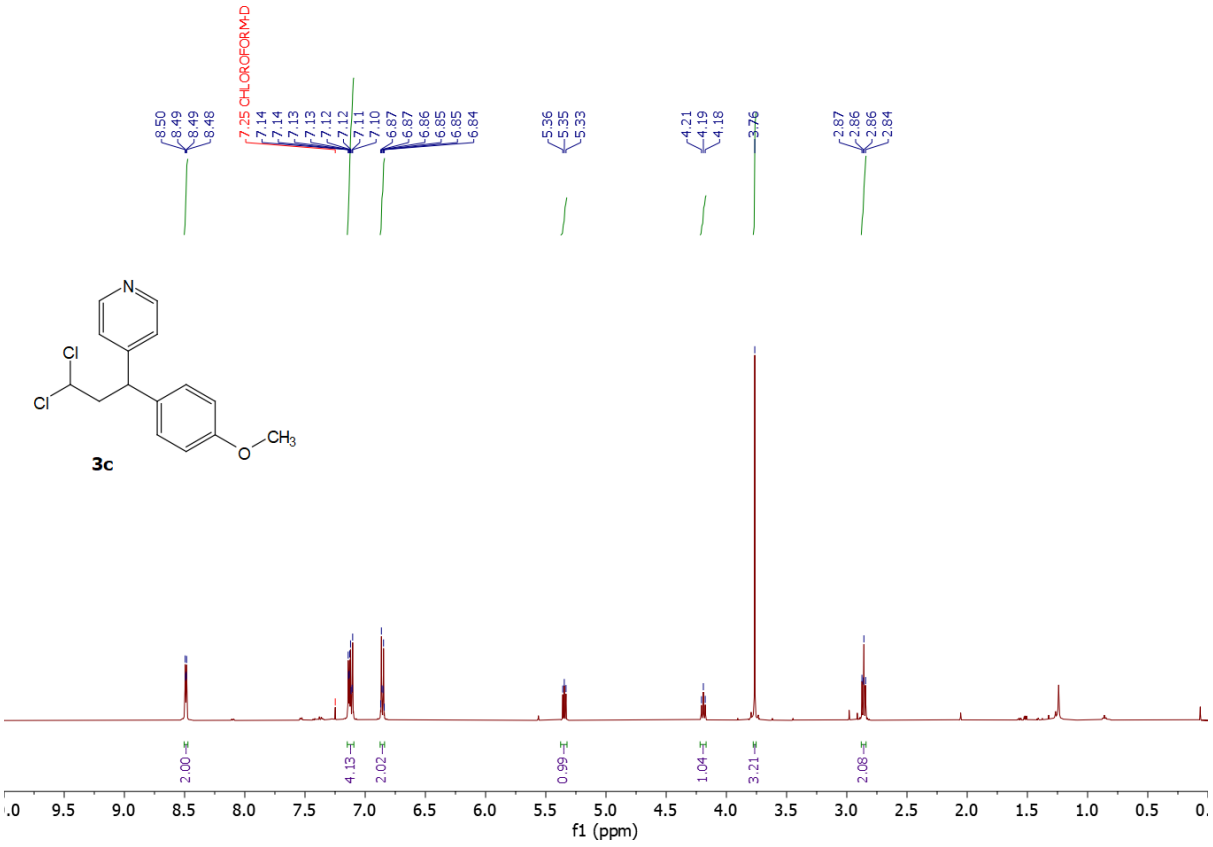
$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **3a** in $CDCl_3$



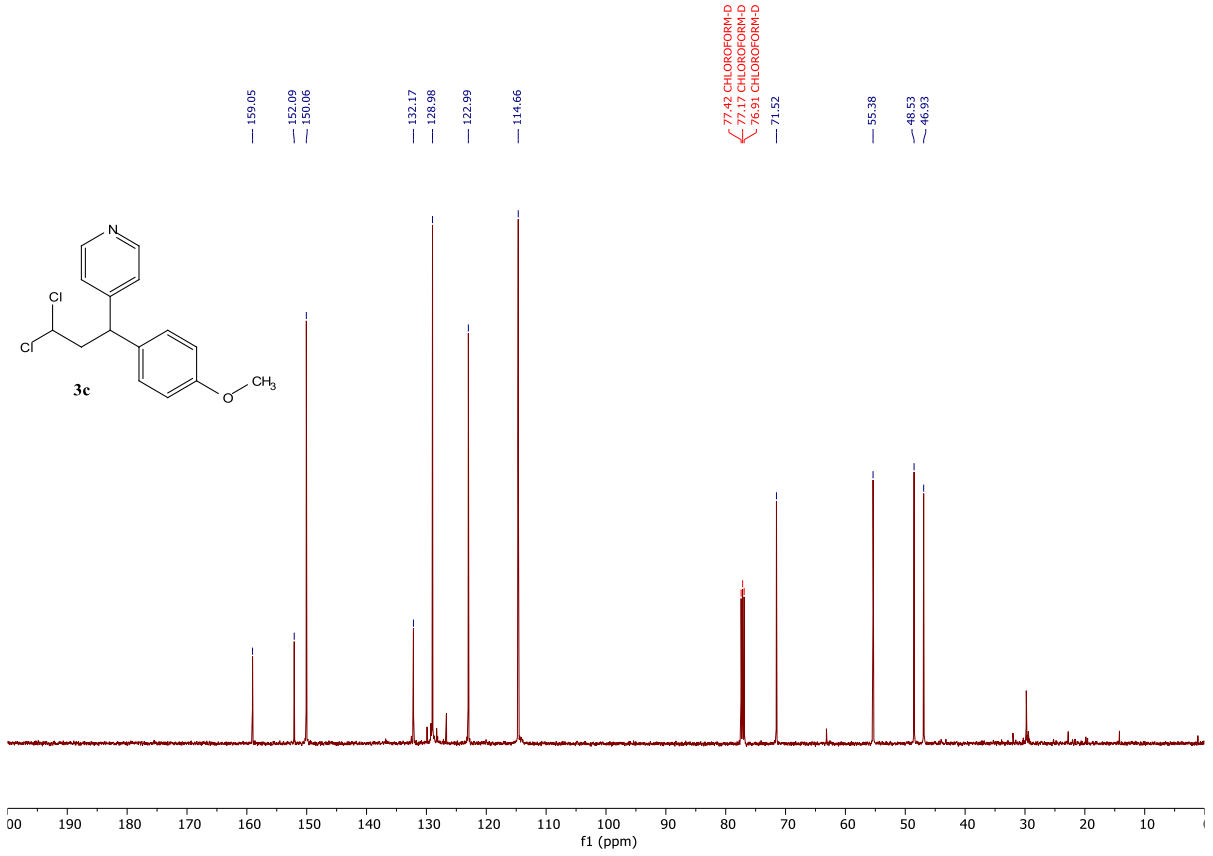
^{1}H NMR (400MHz) spectrum of compound **3b** in $CDCl_3$



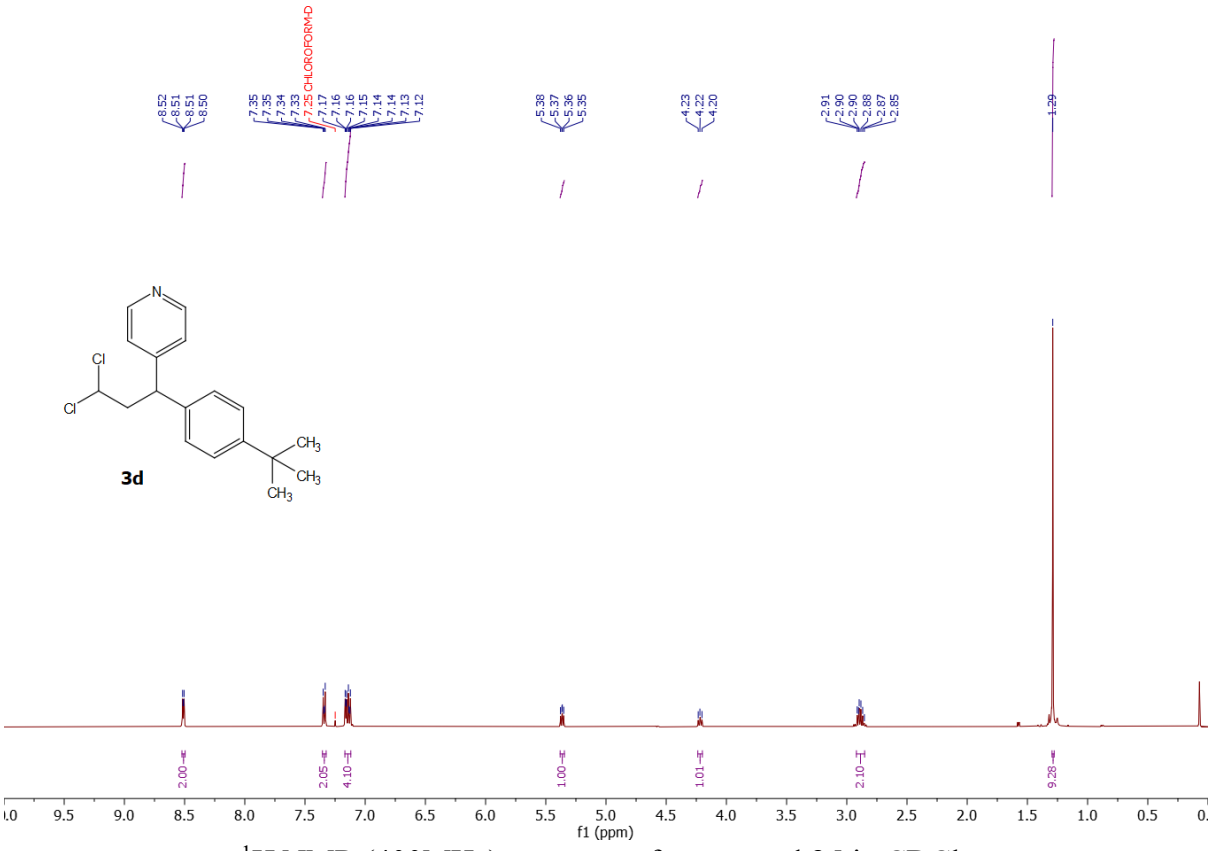
^{13}C{^{1}H} NMR (125MHz) spectrum of compound **3b** in $CDCl_3$



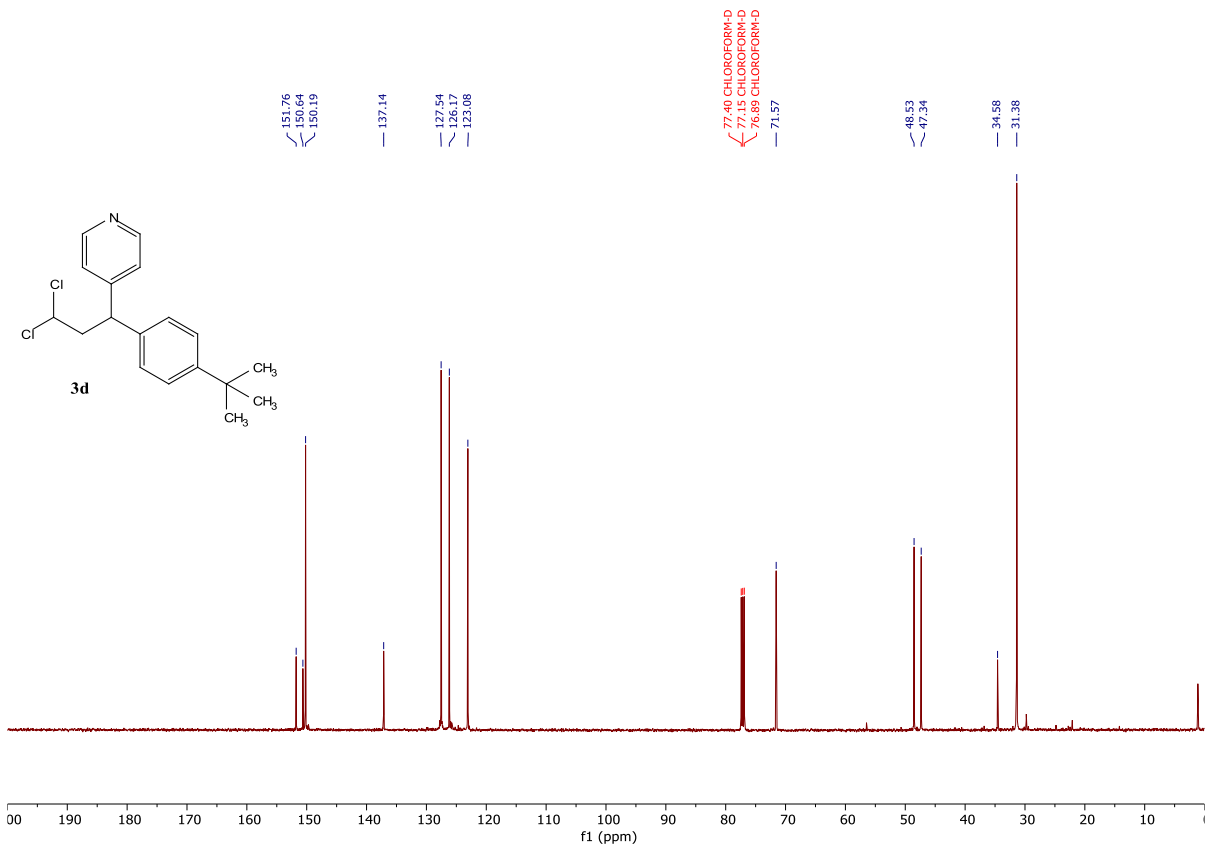
^{1}H NMR (400MHz) spectrum of compound **3c** in $CDCl_3$



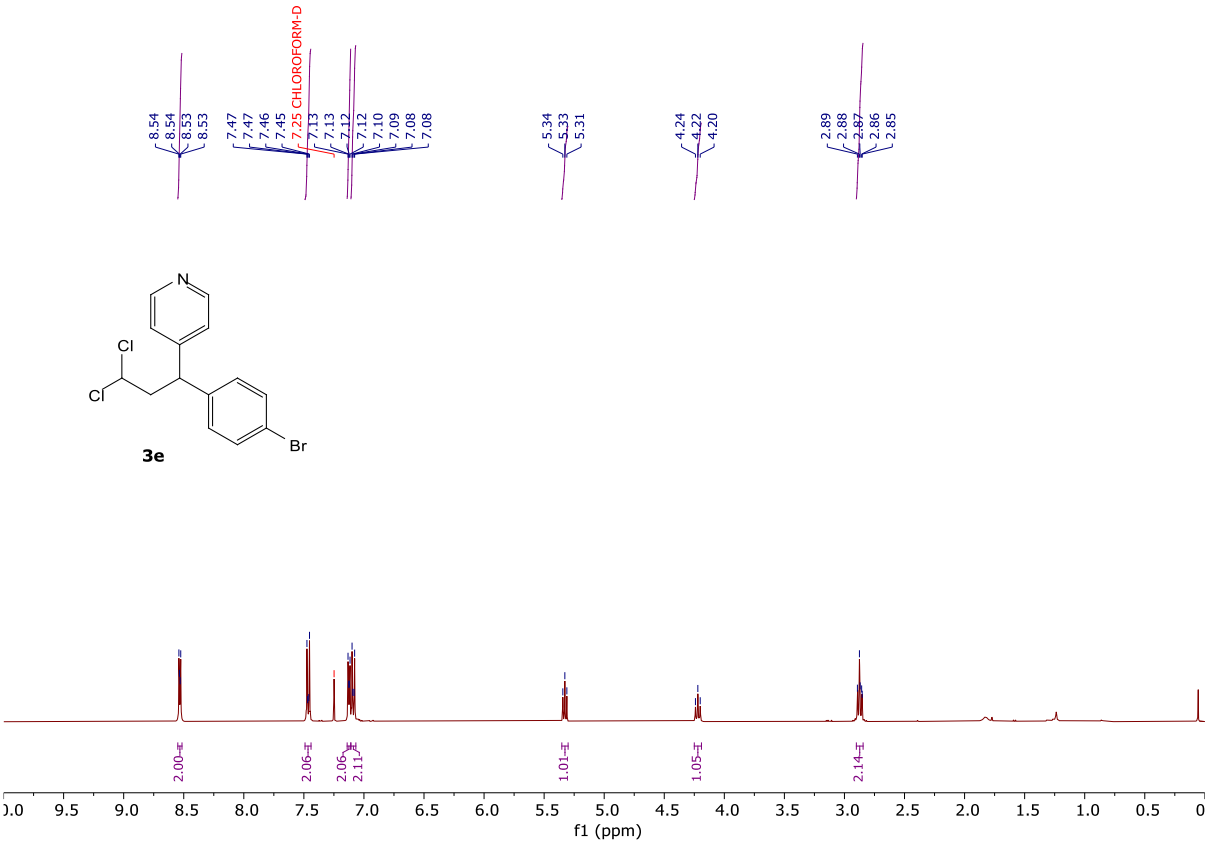
^{13}C{^{1}H} NMR (125MHz) spectrum of compound **3c** in $CDCl_3$



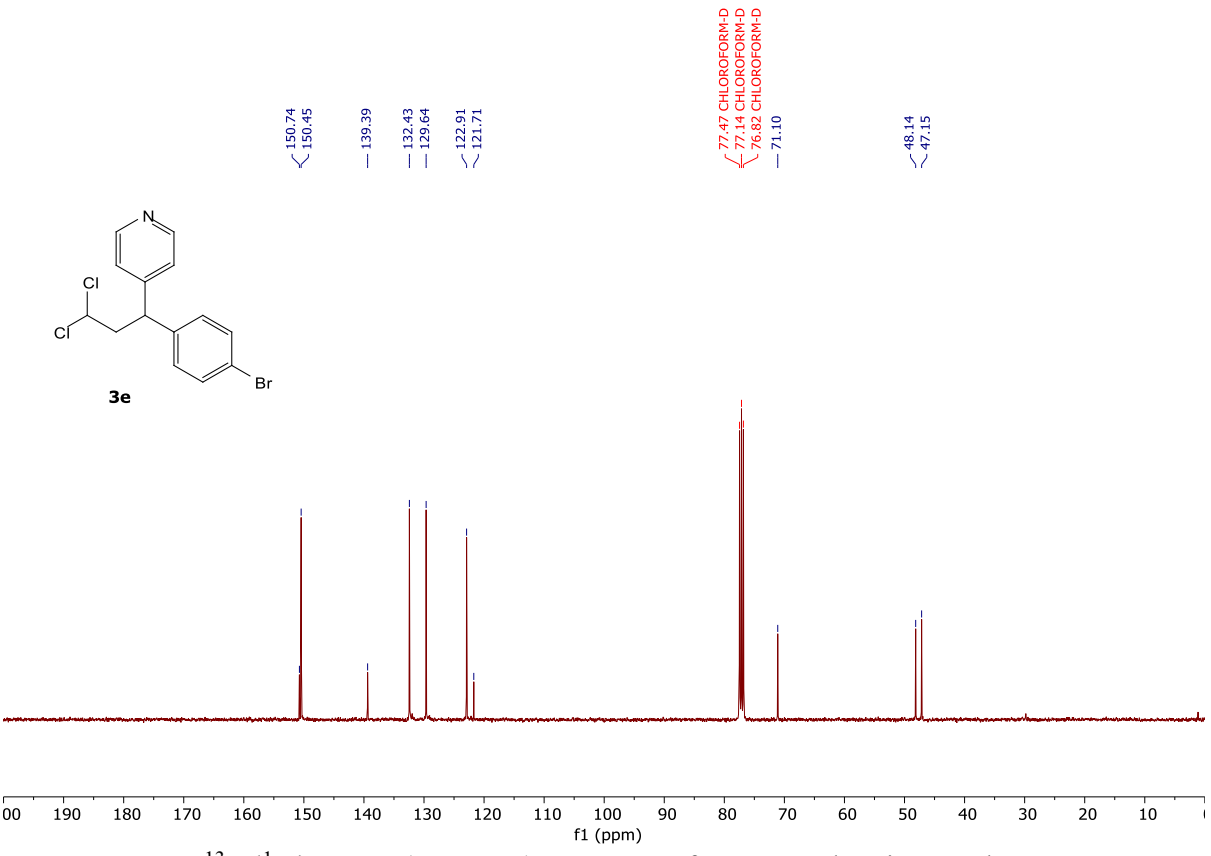
^{1}H NMR (400MHz) spectrum of compound **3d** in $CDCl_3$



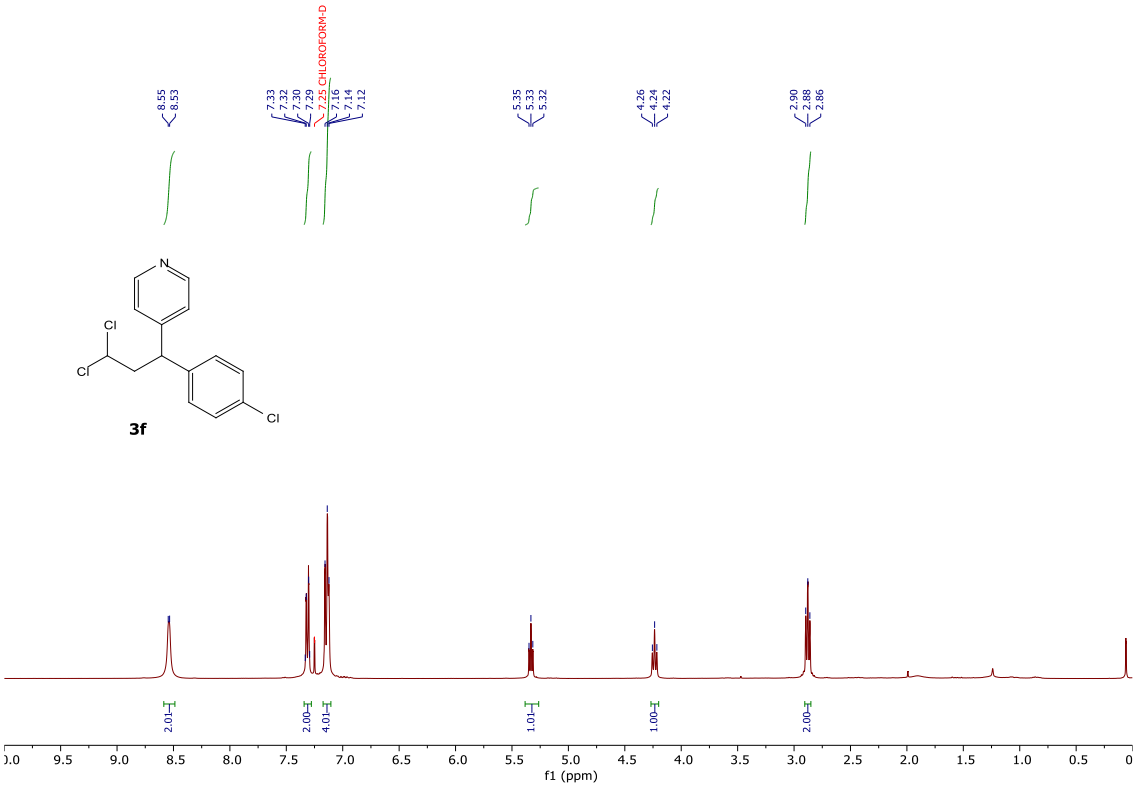
^{13}C{^{1}H} NMR (125MHz) spectrum of compound **3d** in $CDCl_3$



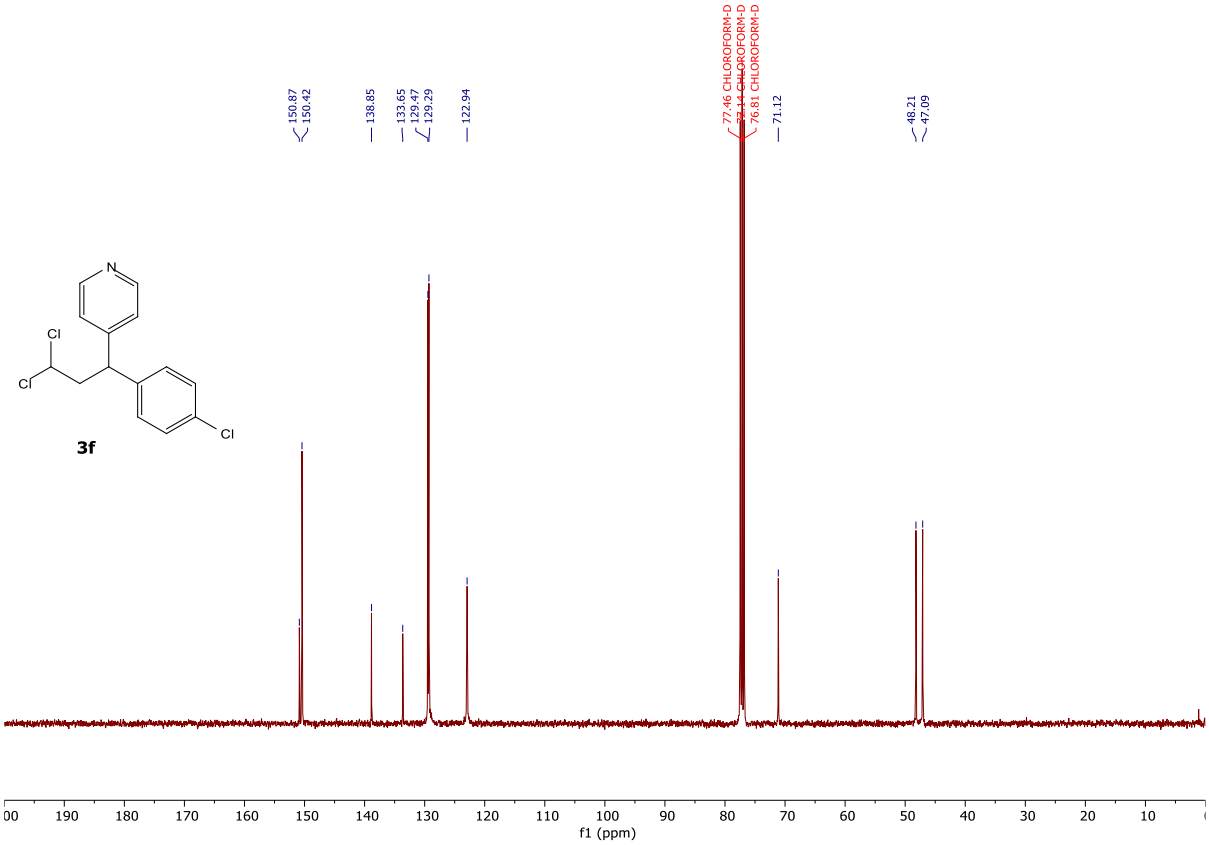
^{1}H NMR (400MHz) spectrum of compound **3e** in $CDCl_3$



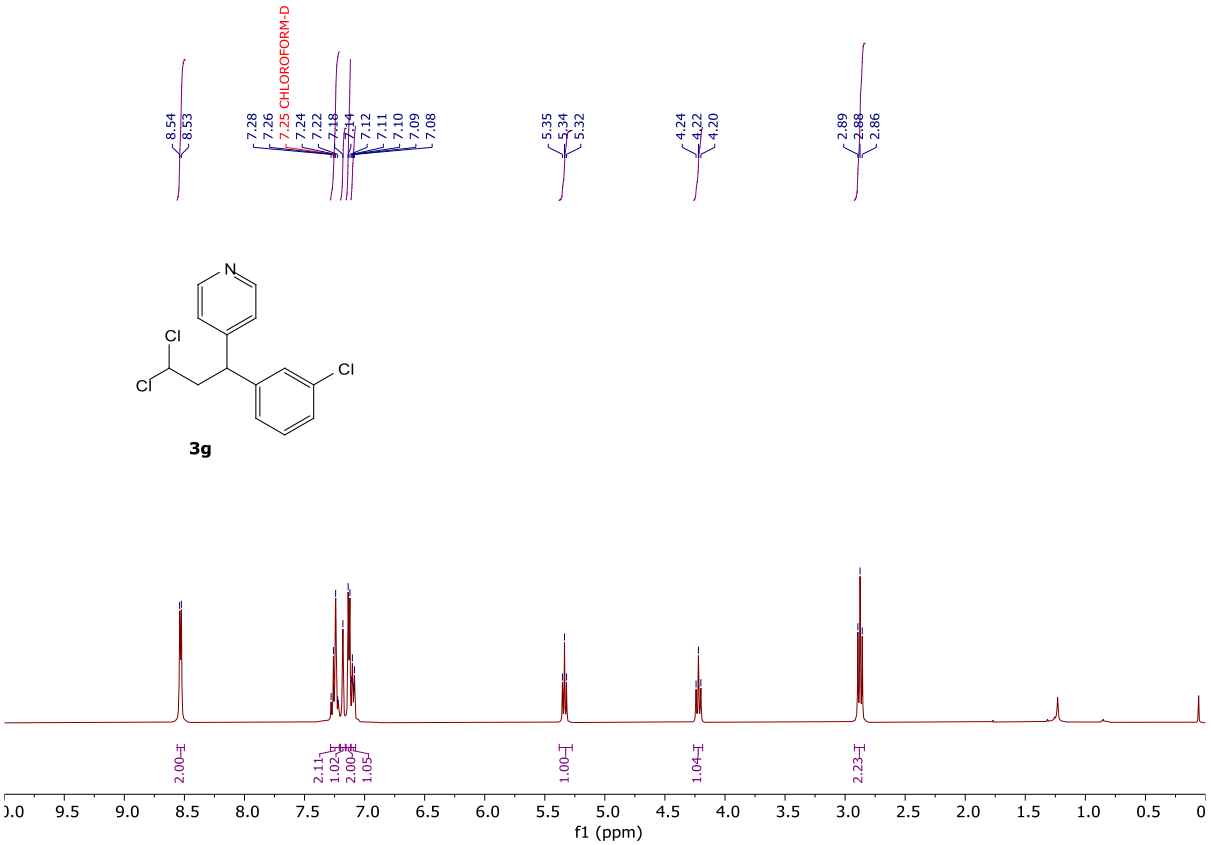
^{13}C{^{1}H} NMR (125MHz) spectrum of compound **3e** in $CDCl_3$



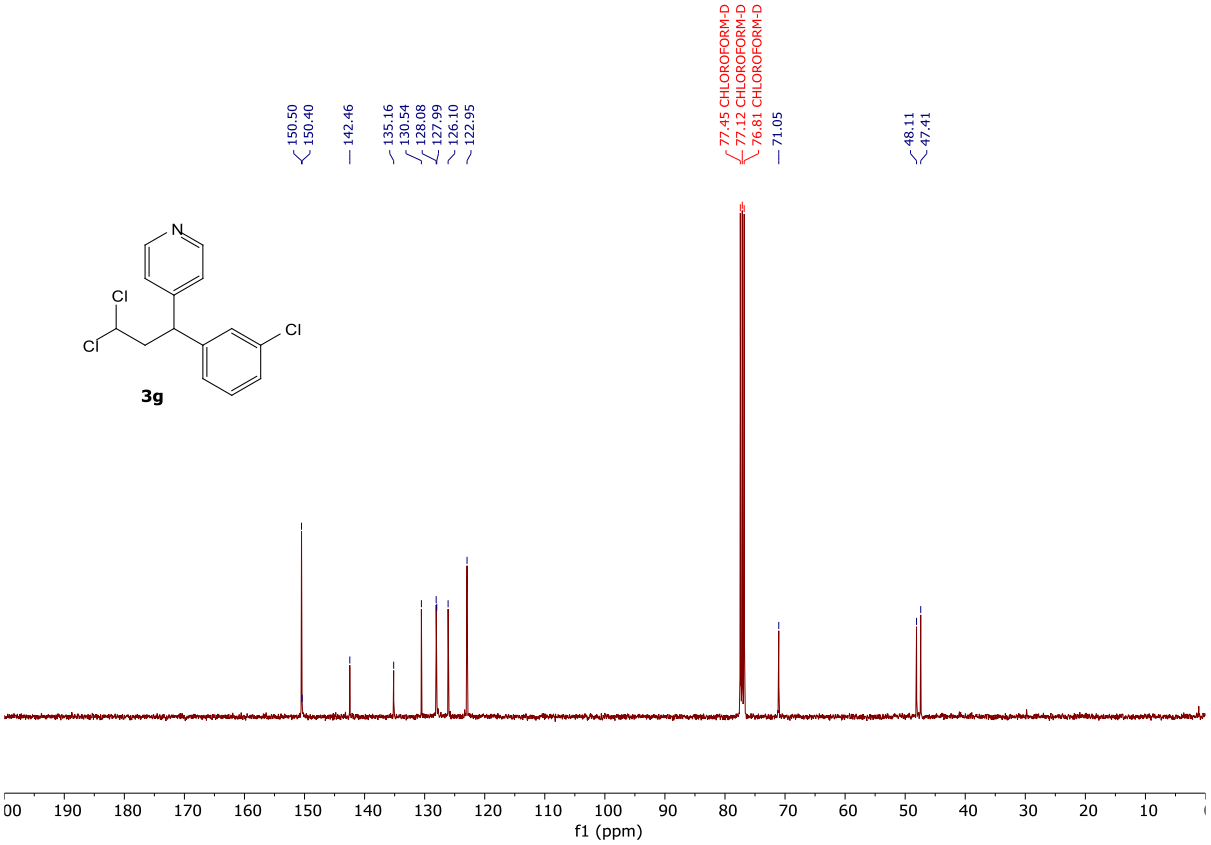
^{1}H NMR (400MHz) spectrum of compound **3f** in $CDCl_3$



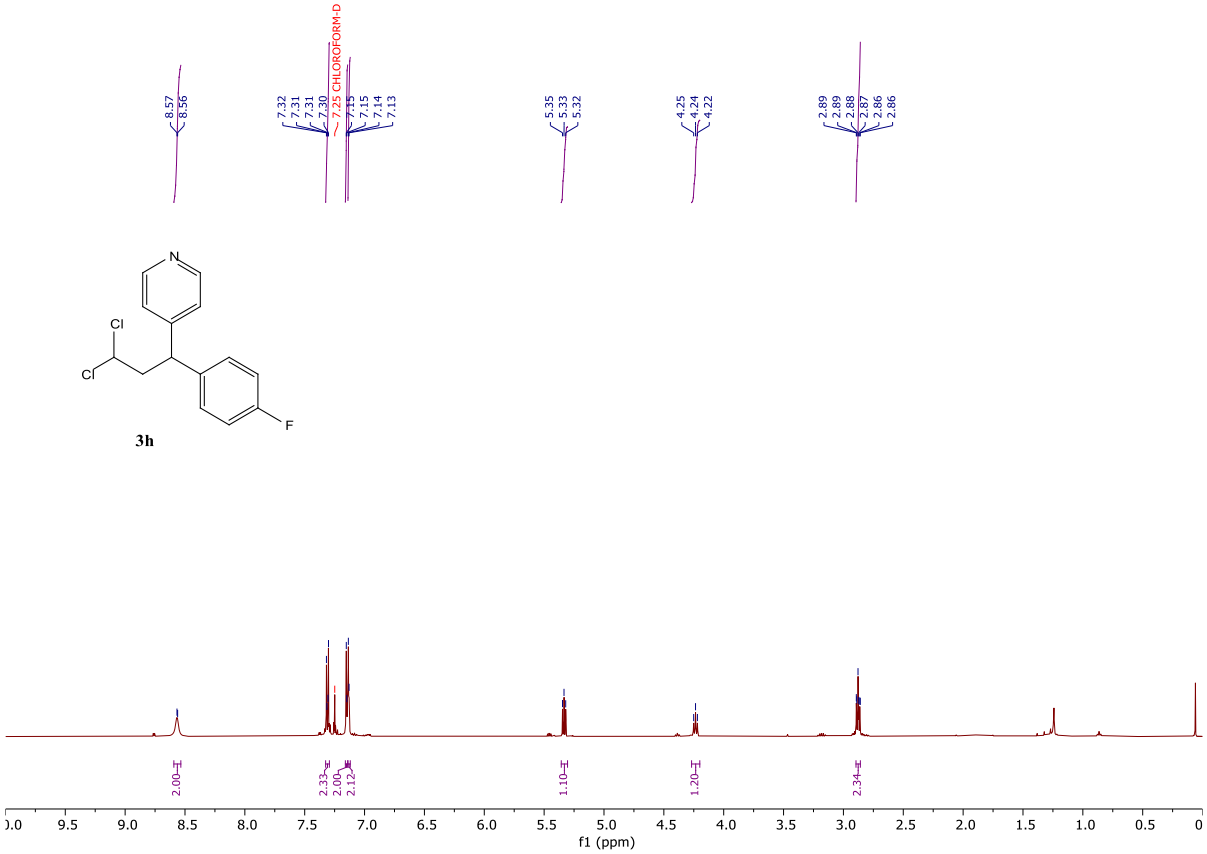
^{13}C {^{1}H} NMR (125MHz) spectrum of compound **3f** in $CDCl_3$



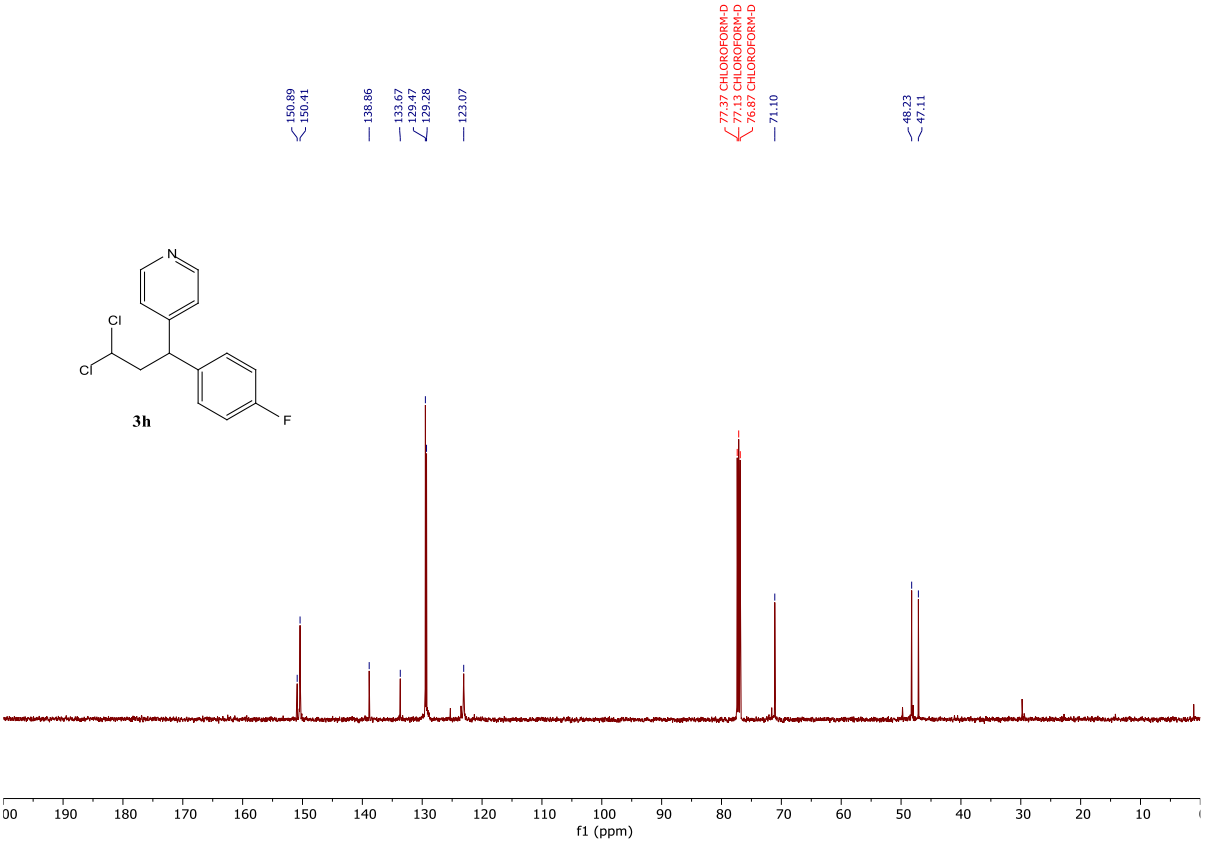
^{1}H NMR (400MHz) spectrum of compound **3g** in $CDCl_3$



^{13}C{^{1}H} NMR (125MHz) spectrum of compound **3g** in $CDCl_3$



^{1}H NMR (400MHz) spectrum of compound **3h** in $CDCl_3$



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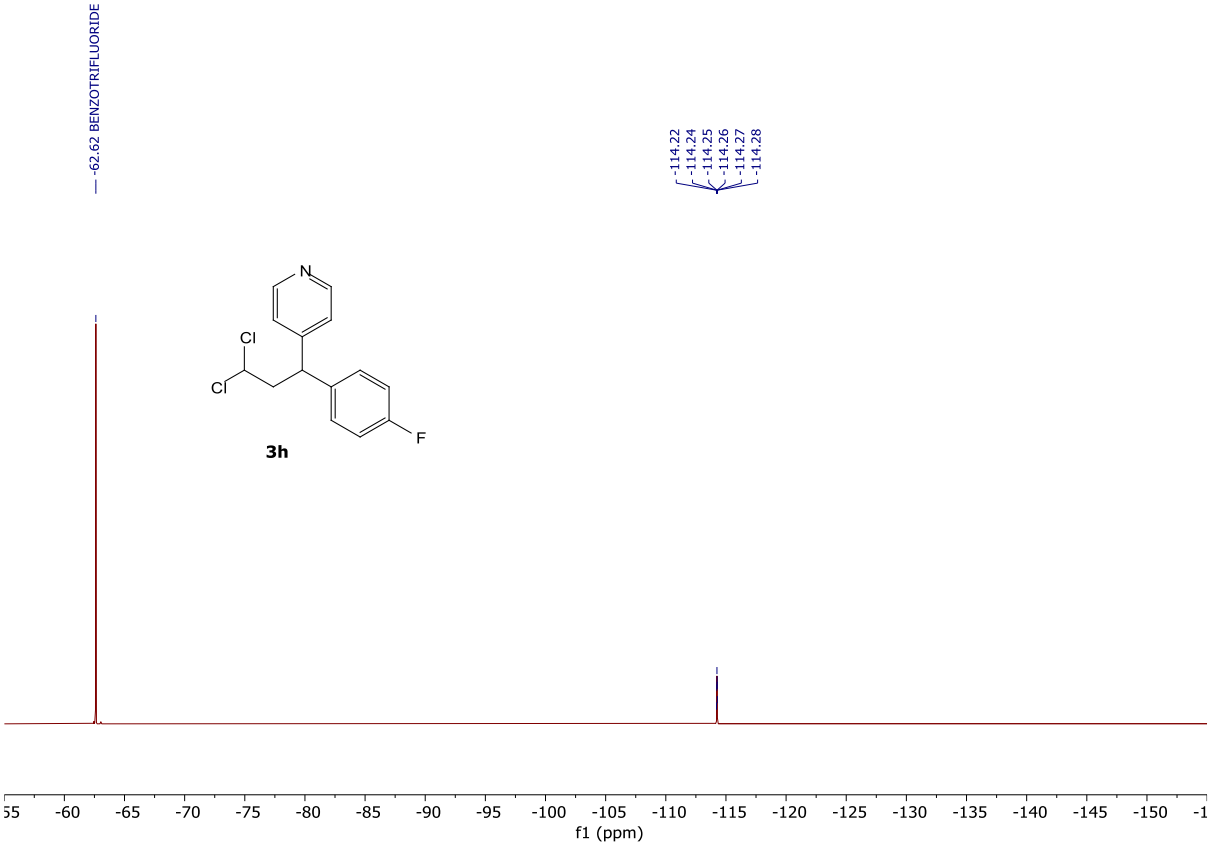
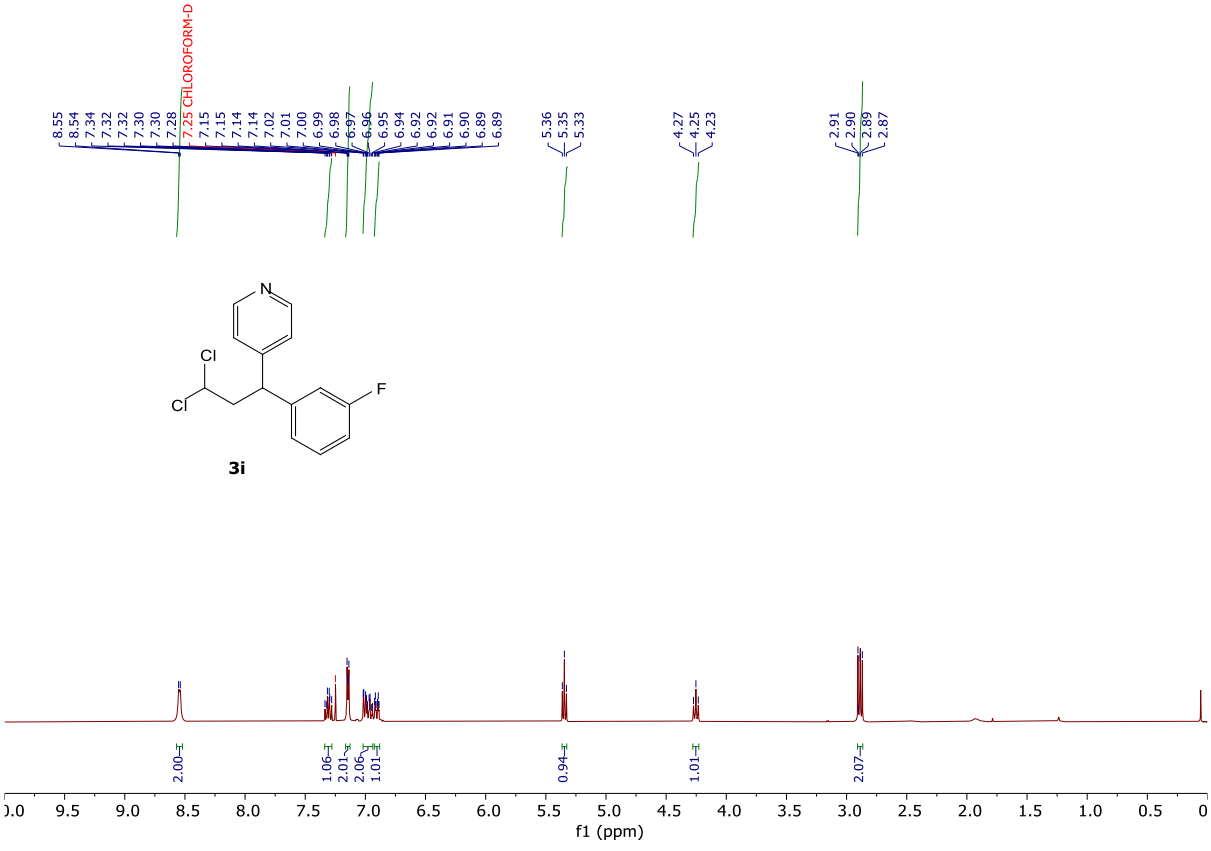
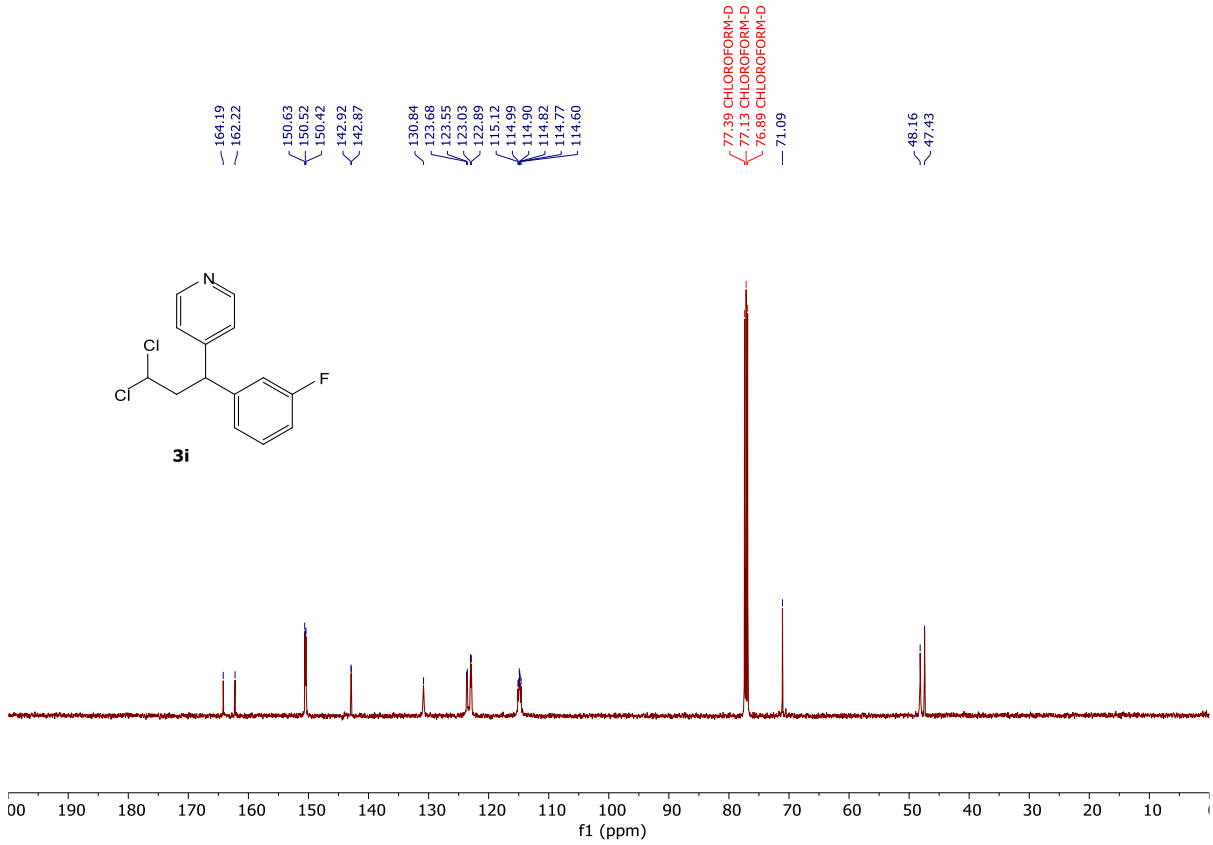


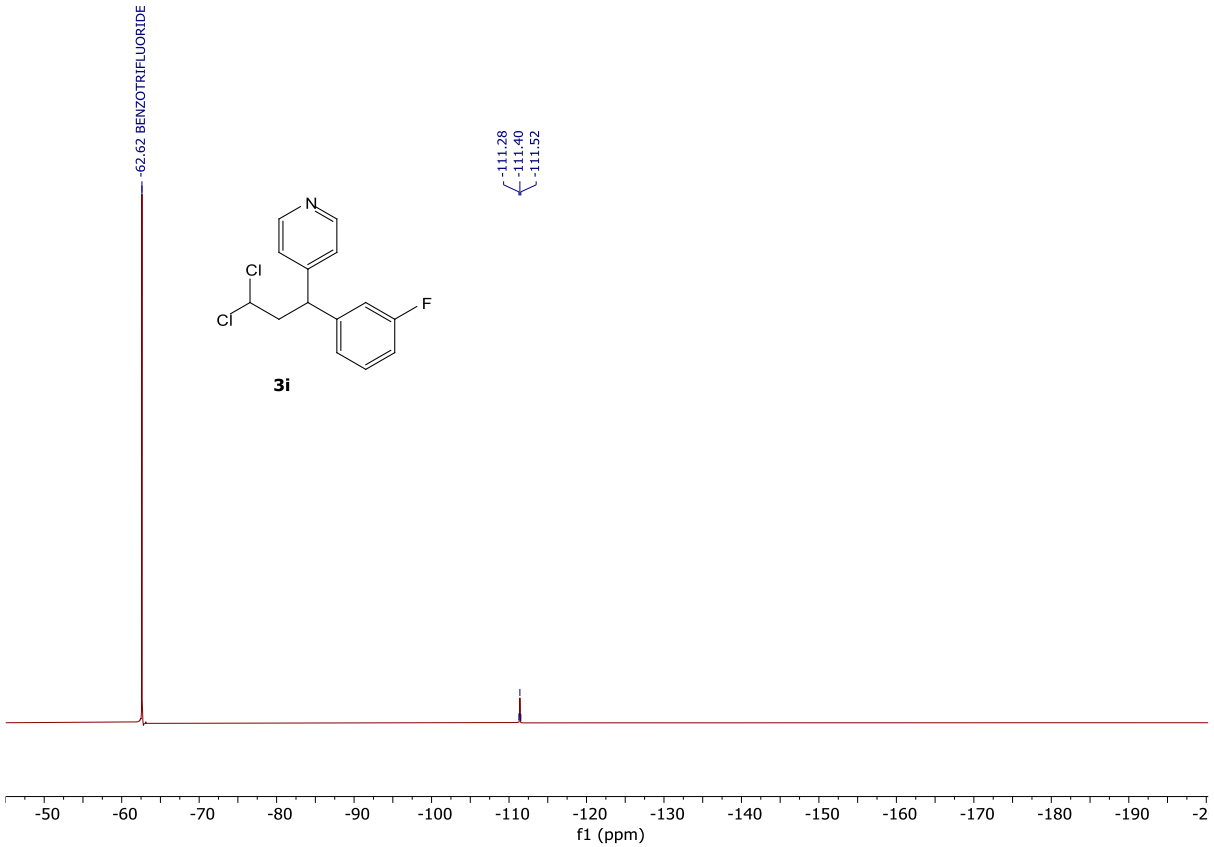
^{19}F NMR (471 MHz) spectrum of compound **3h** in $CDCl_3$



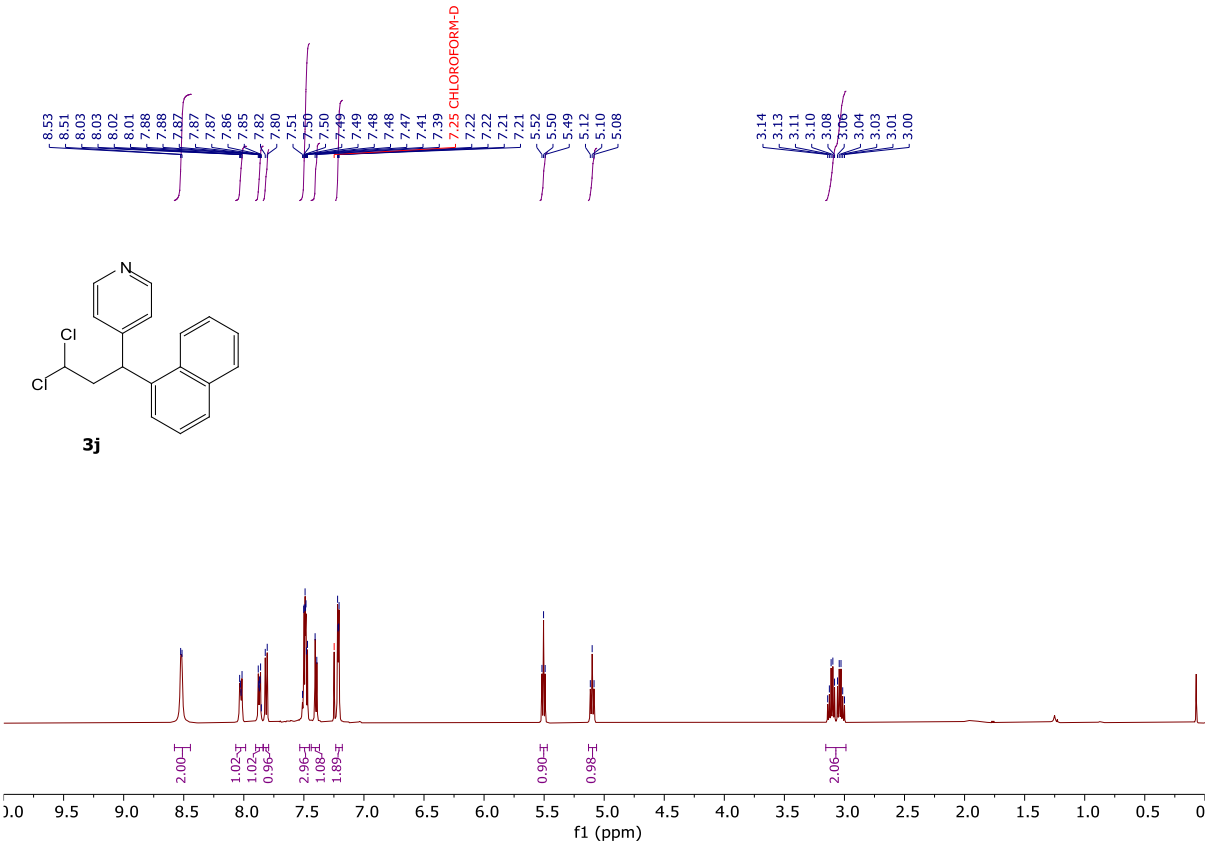
^{1}H NMR (400MHz) spectrum of compound **3i** in $CDCl_3$



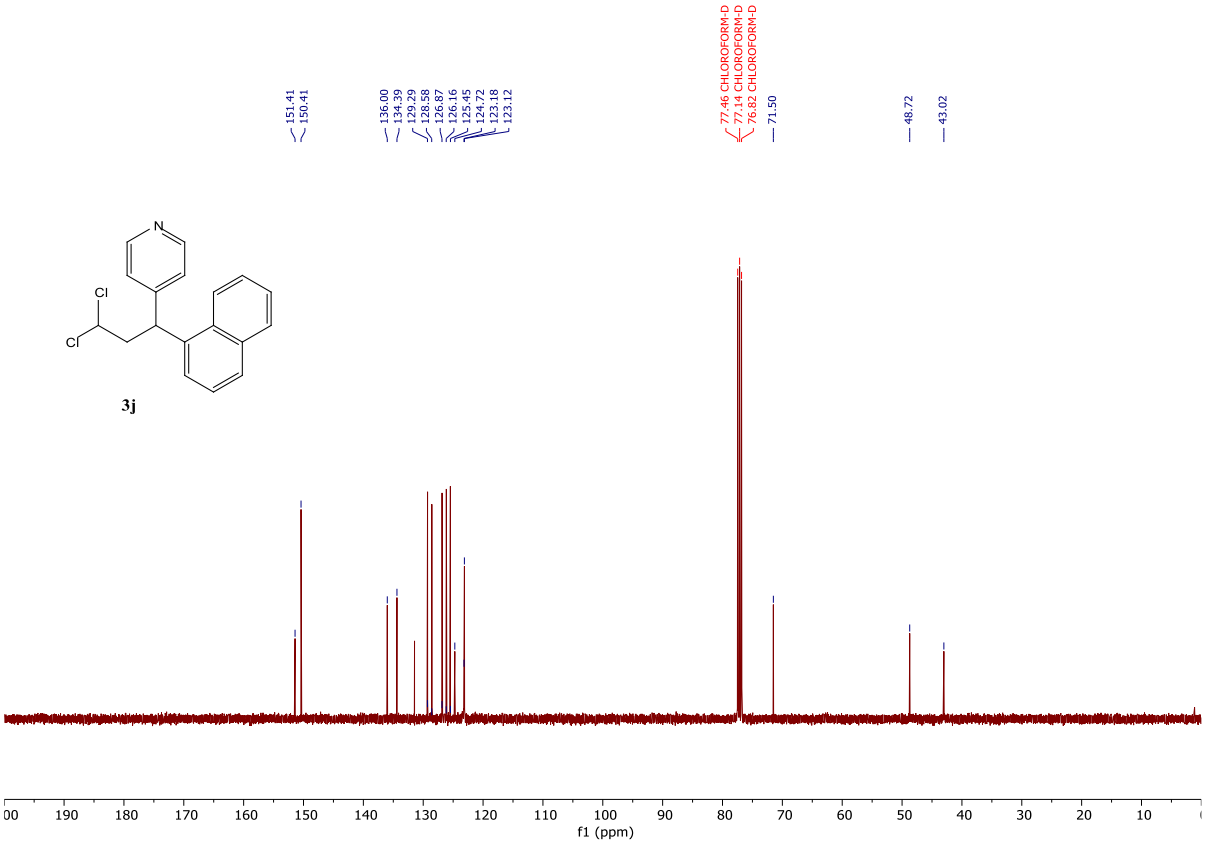
^{13}C {^{1}H} NMR (125MHz) spectrum of compound **3i** in $CDCl_3$



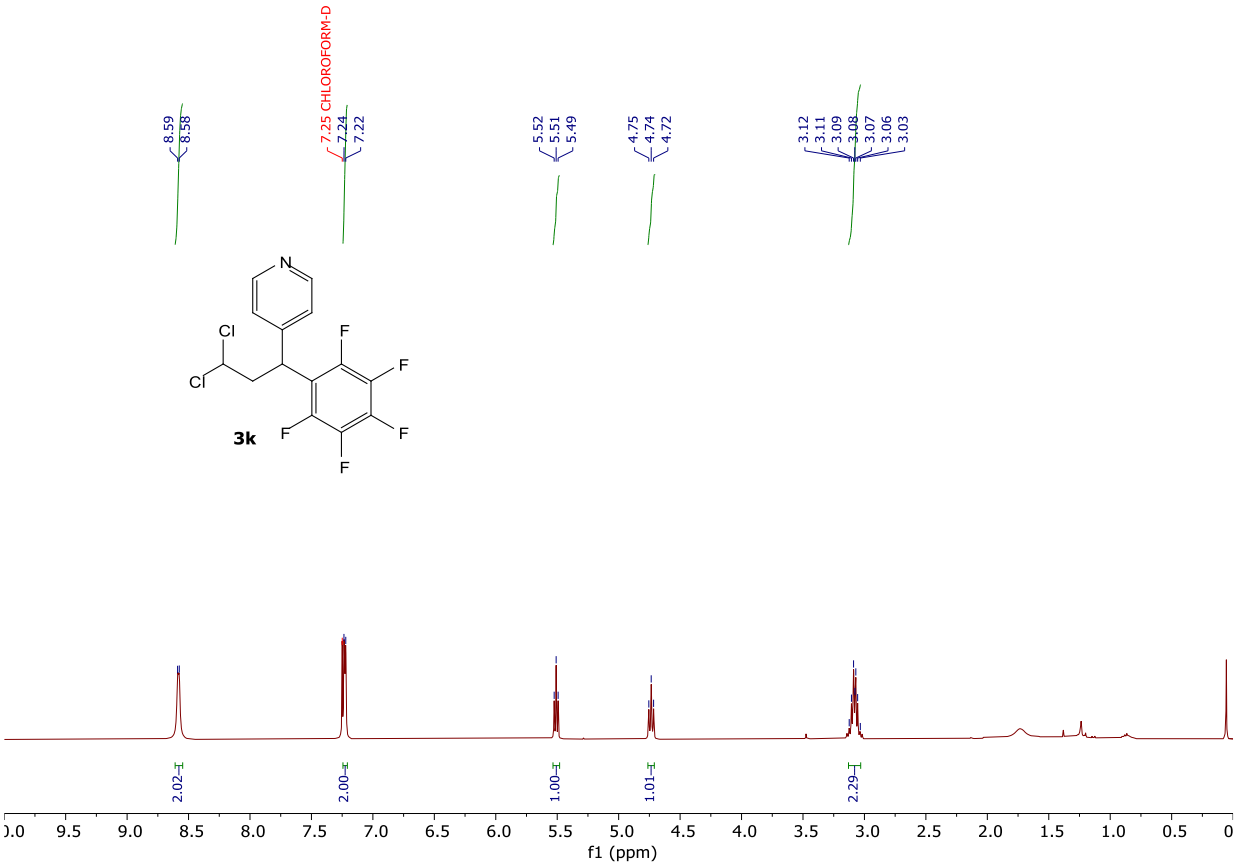
^{19}F NMR (471 MHz) spectrum of compound **3i** in $CDCl_3$



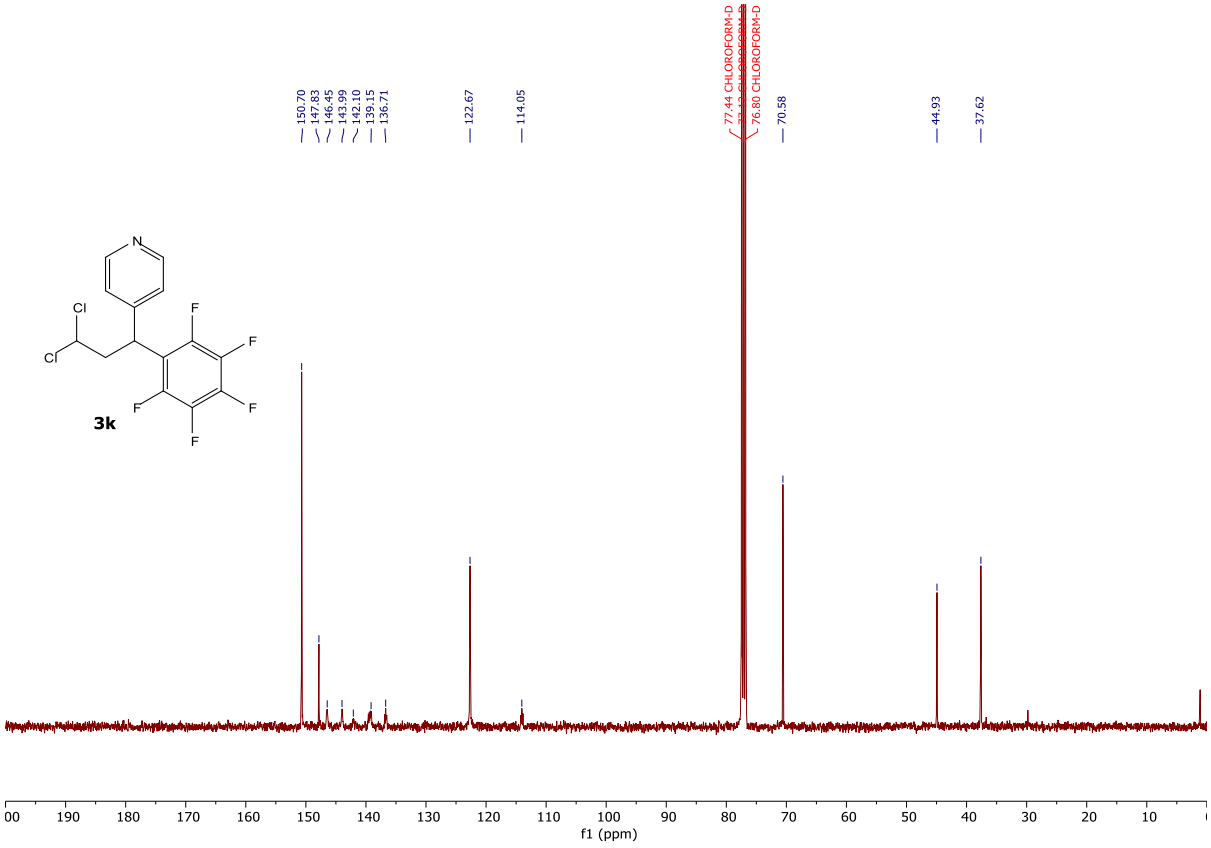
^{1}H NMR (400MHz) spectrum of compound **3j** in $CDCl_3$



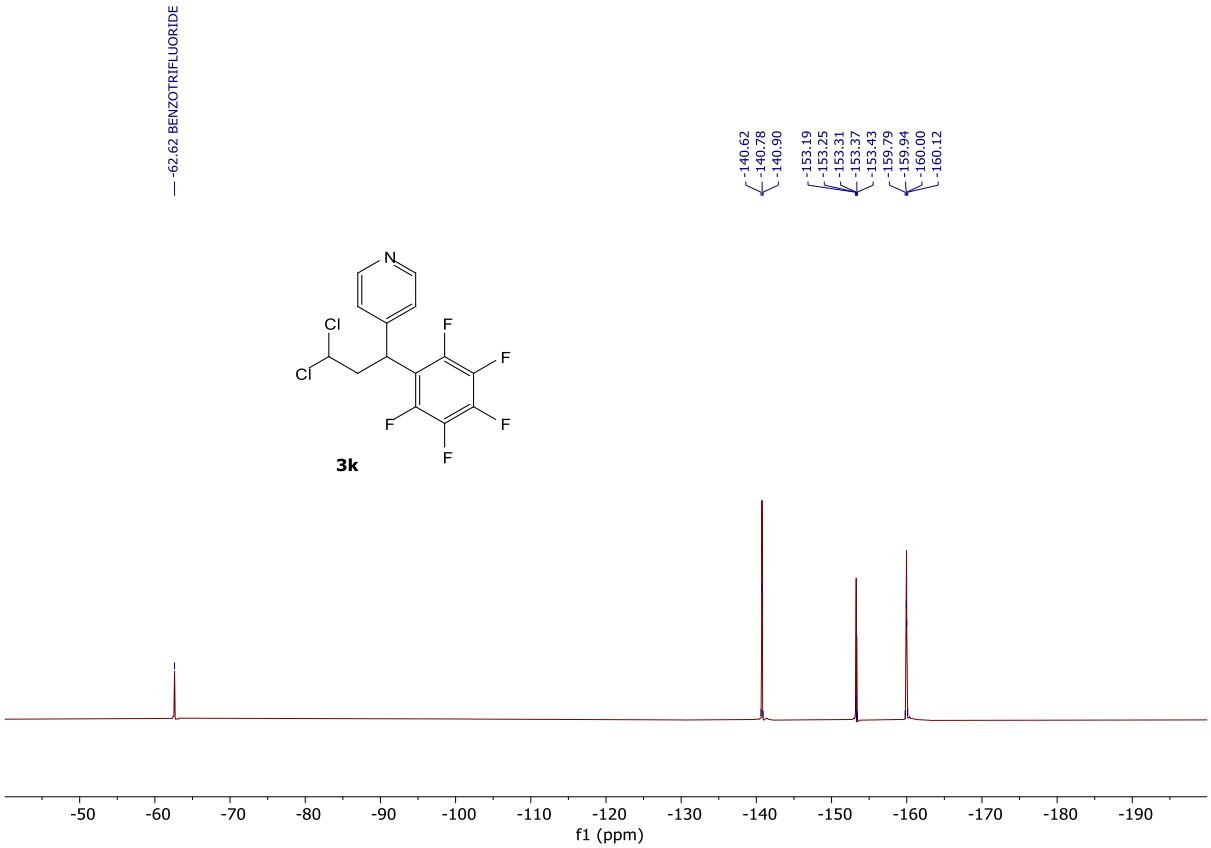
^{13}C{^{1}H} NMR (125MHz) spectrum of compound **3j** in $CDCl_3$



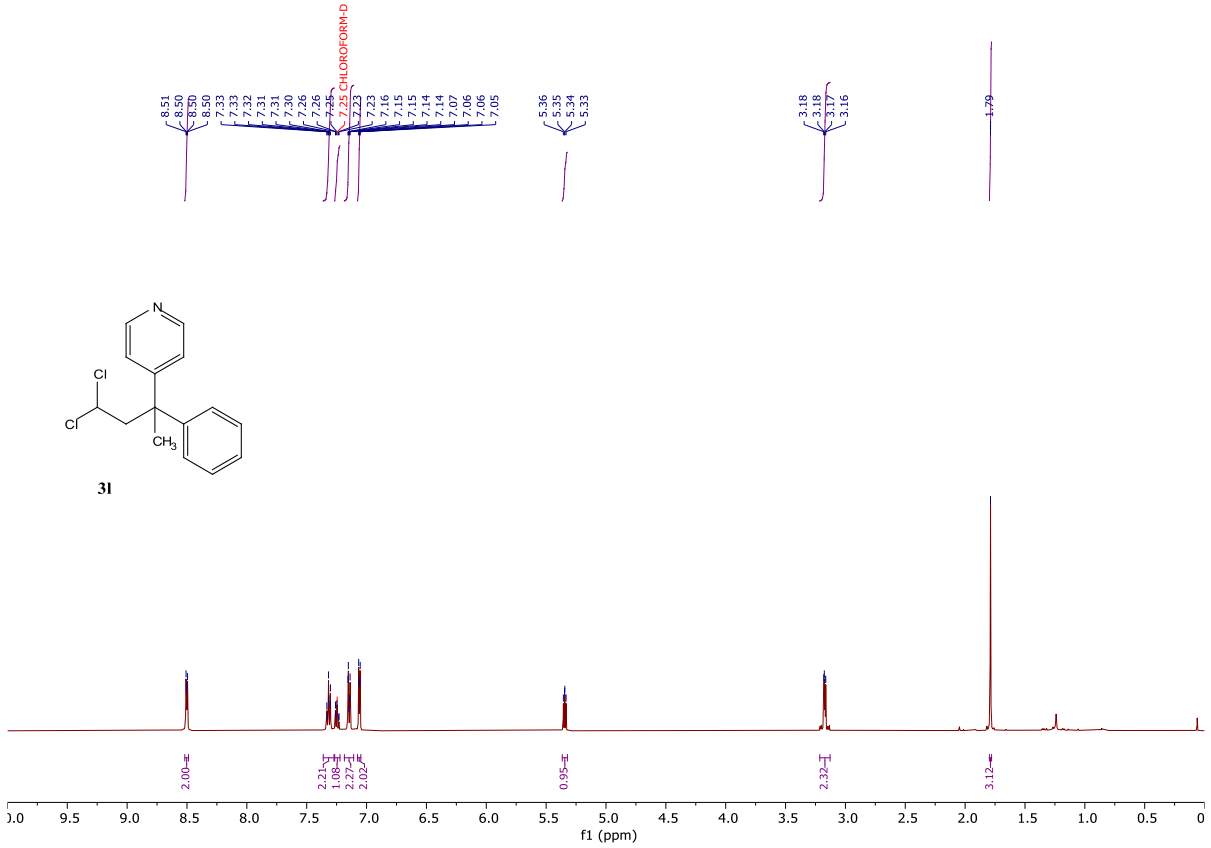
^{1}H NMR (400MHz) spectrum of compound **3k** in $CDCl_3$



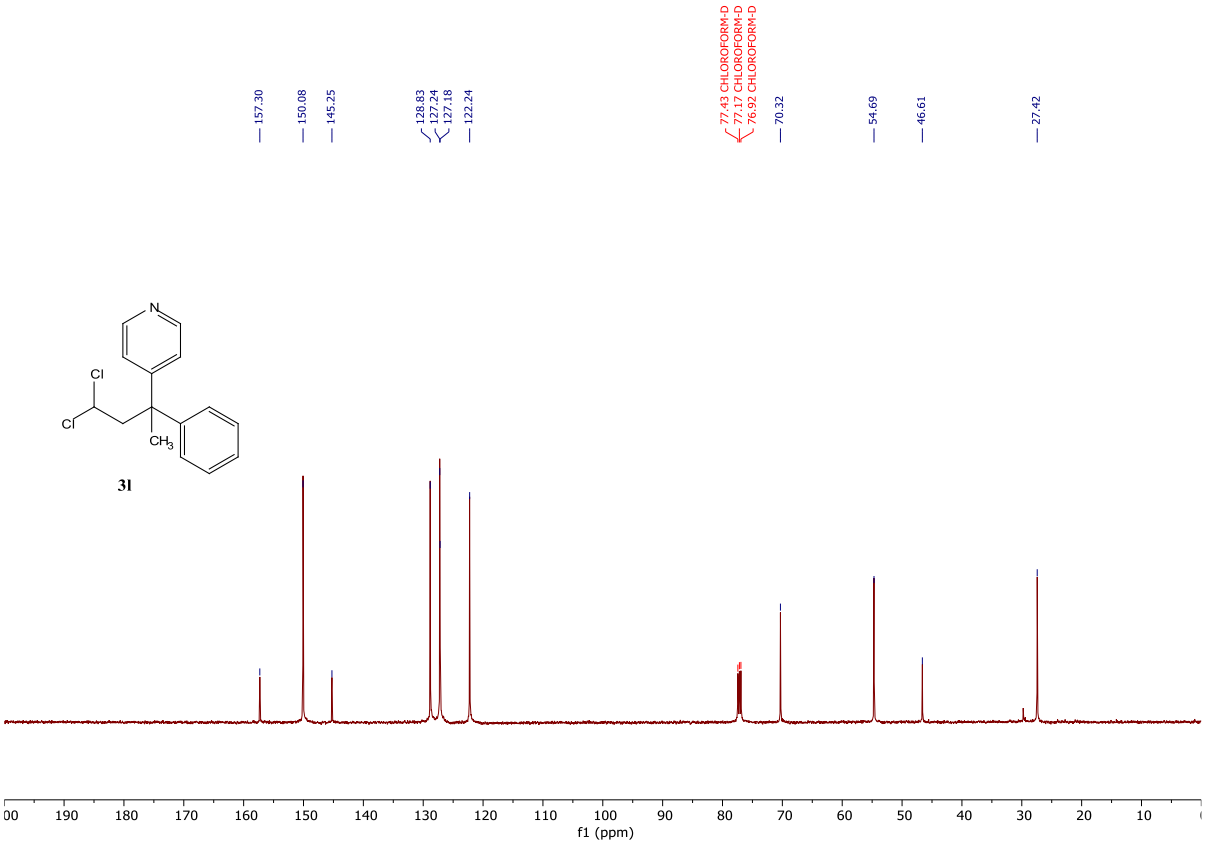
^{13}C {^{1}H} NMR (125MHz) spectrum of compound **3k** in $CDCl_3$



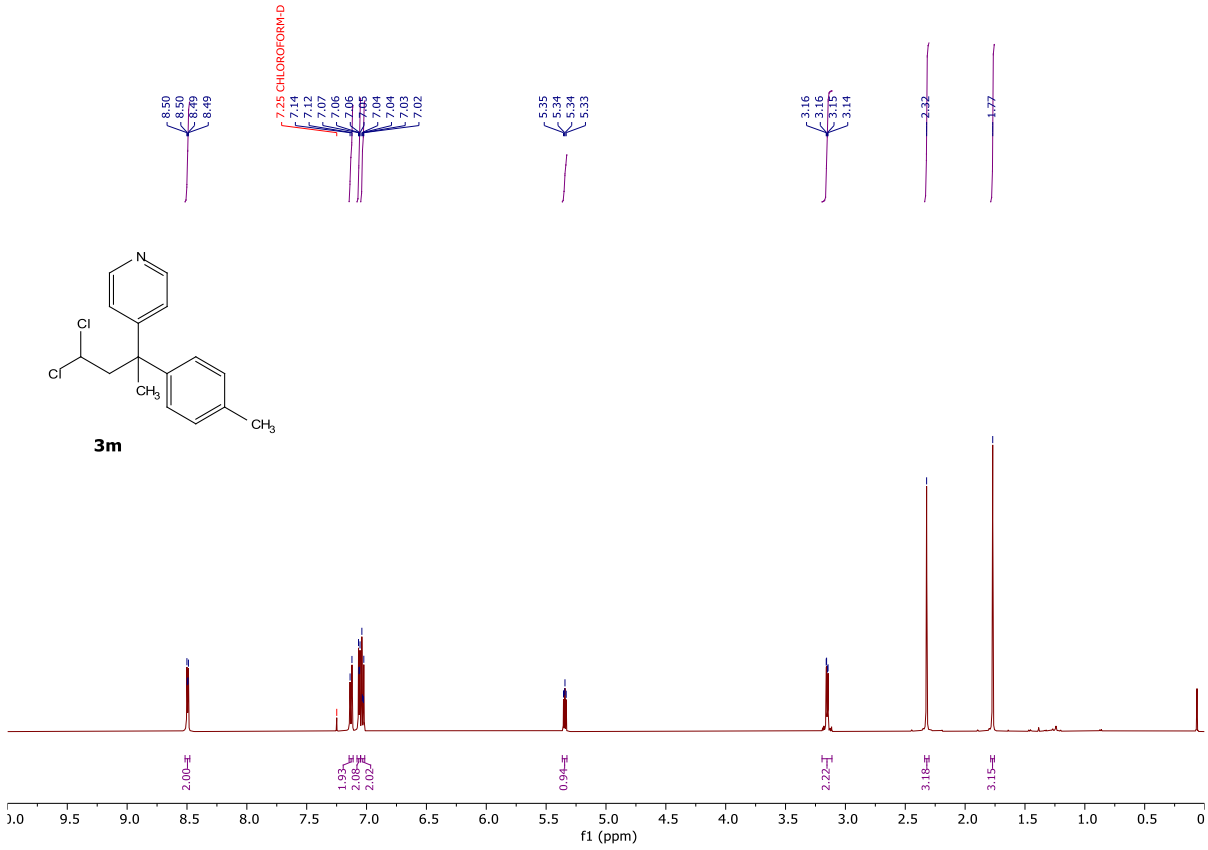
^{19}F NMR (471 MHz) spectrum of compound **3k** in $CDCl_3$



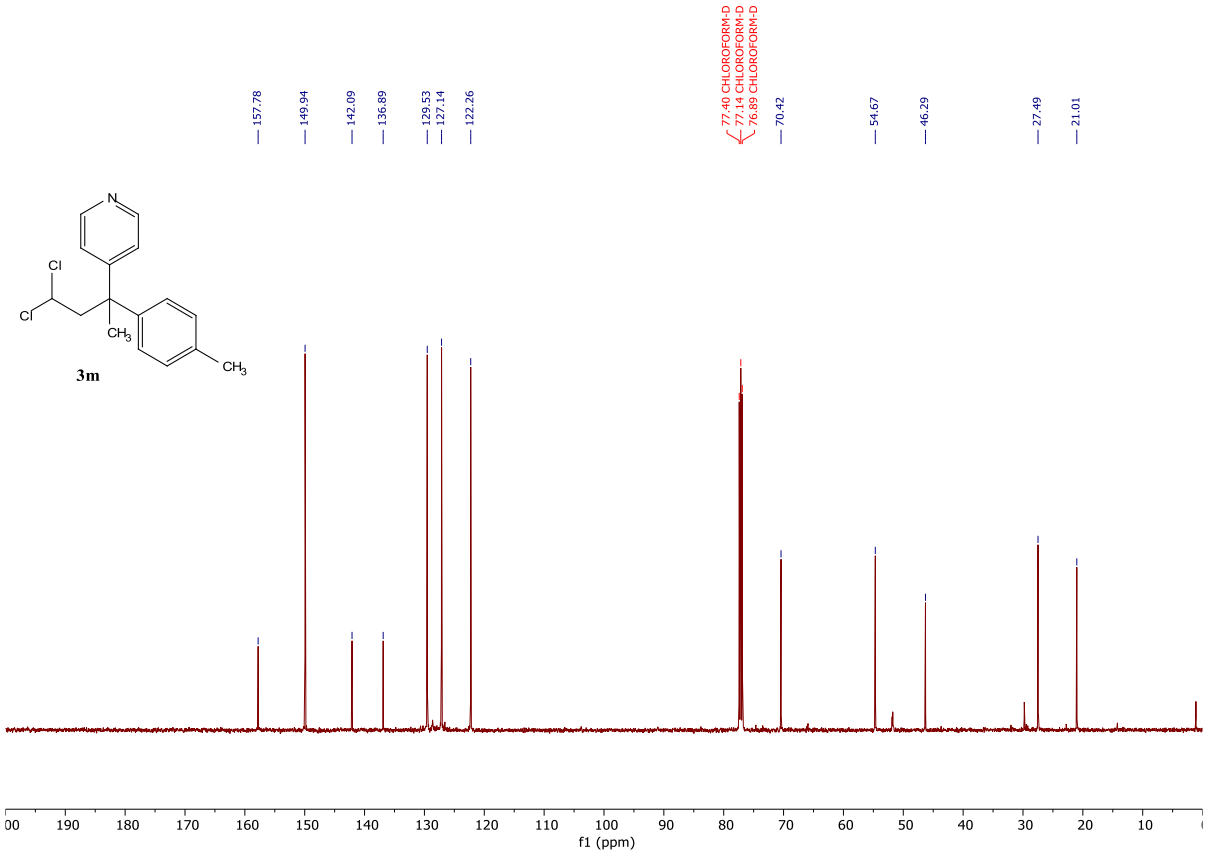
^{1}H NMR (400MHz) spectrum of compound **3l** in $CDCl_3$



$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **3l** in $CDCl_3$



^{1}H NMR (400MHz) spectrum of compound **3m** in $CDCl_3$



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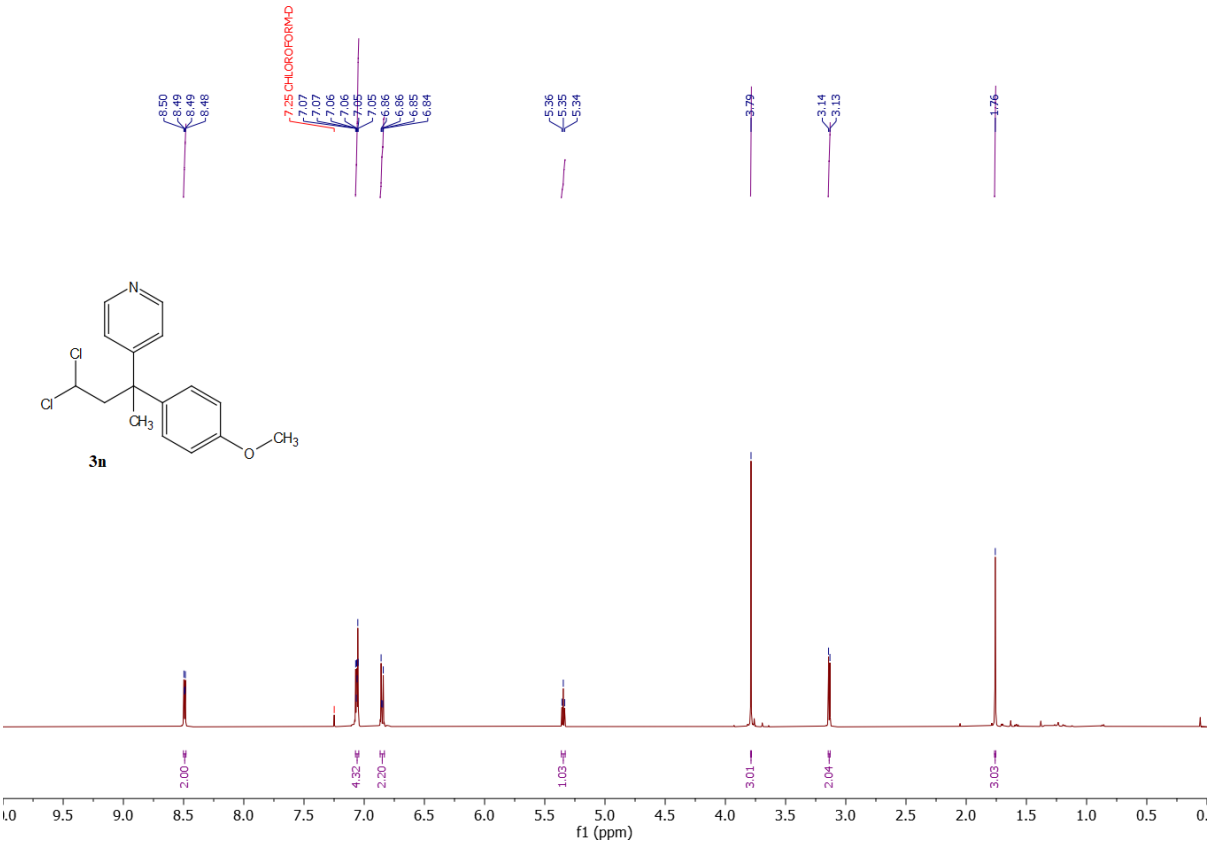

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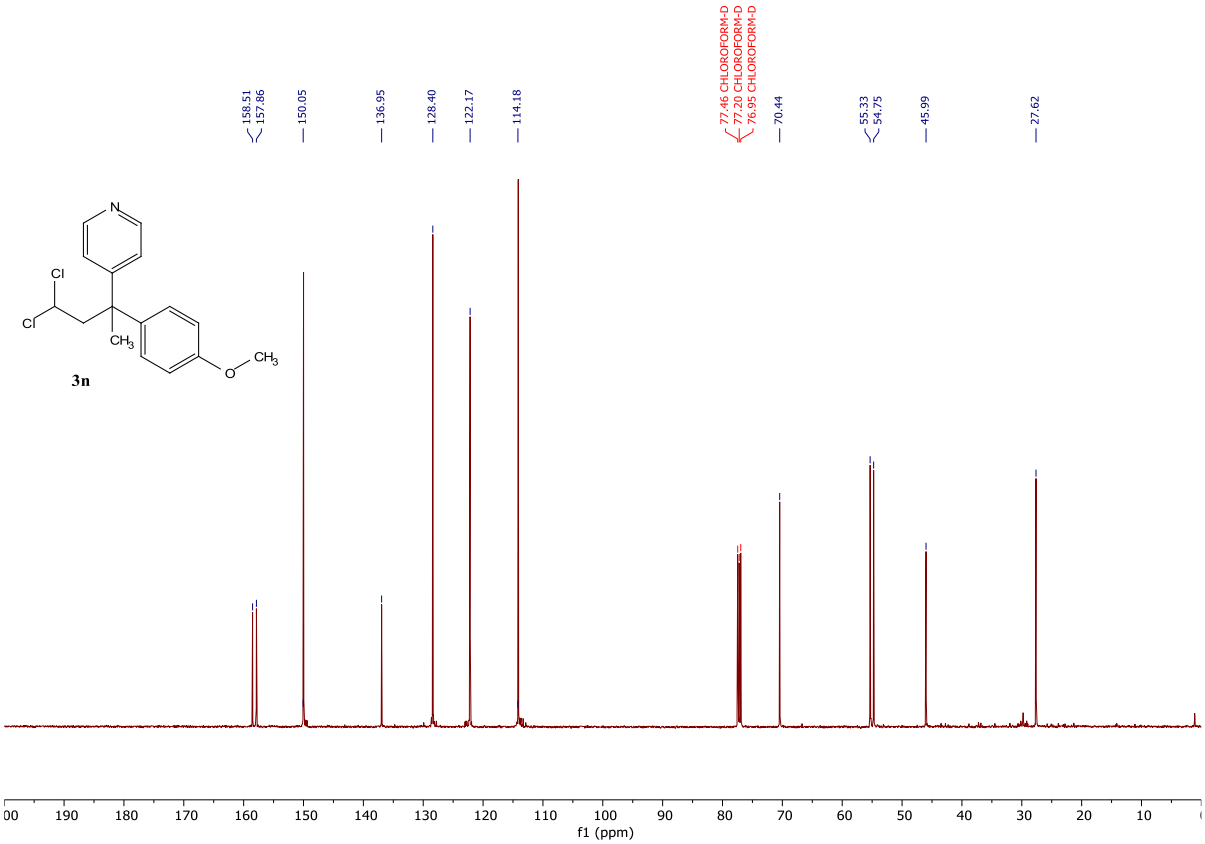
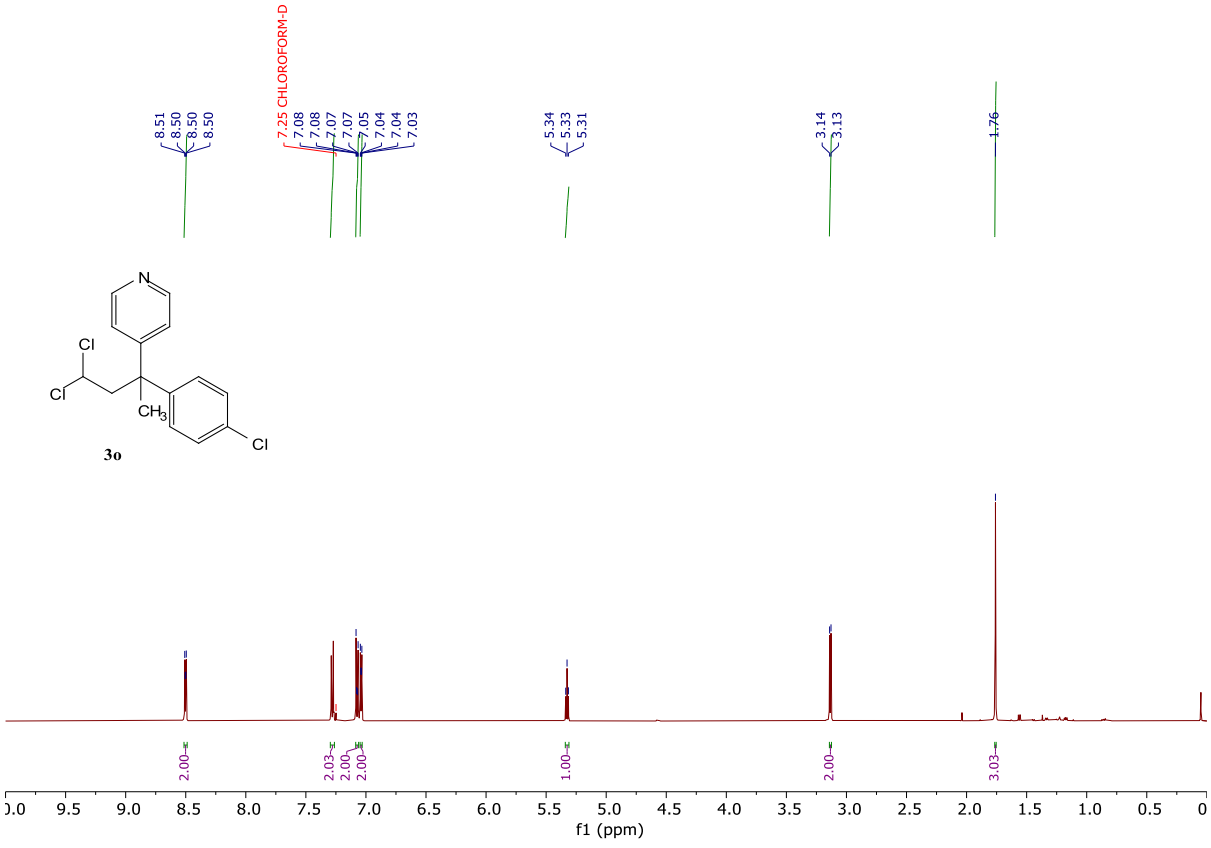


$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **3n** in $CDCl_3$



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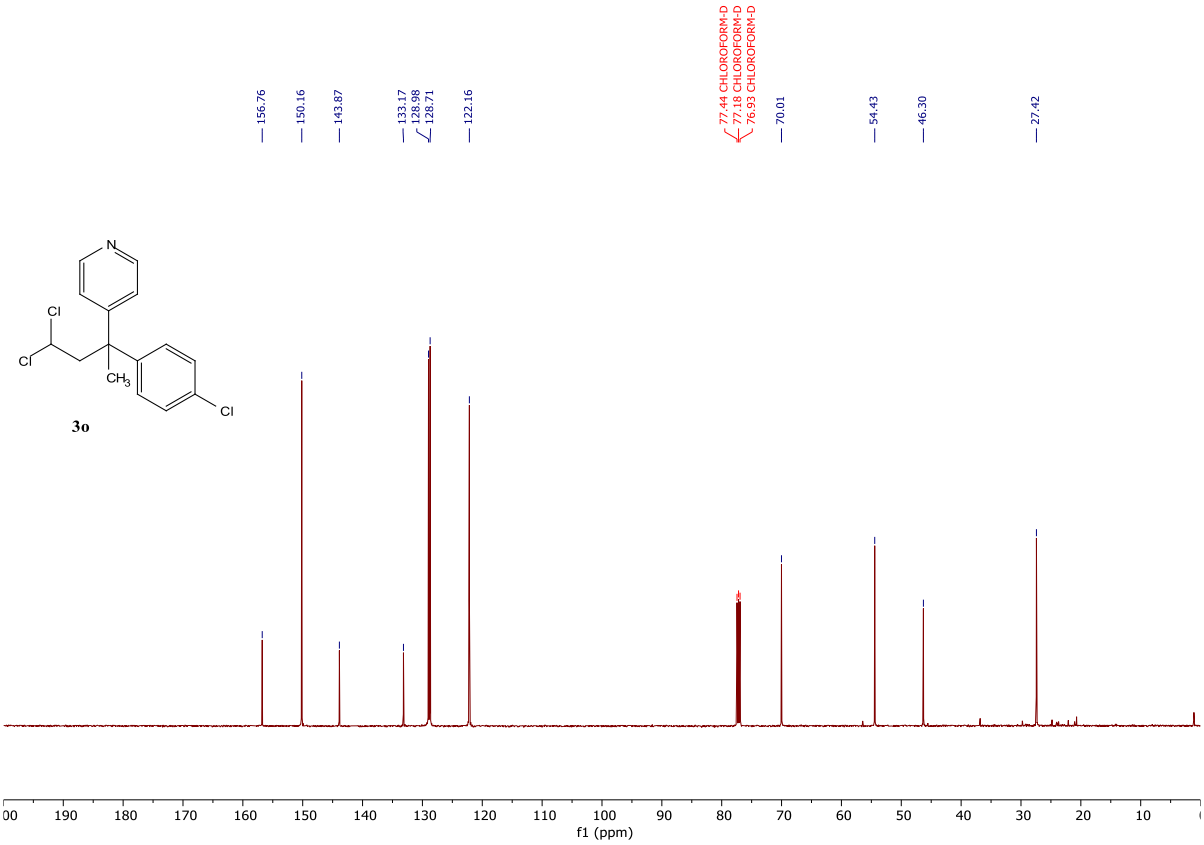
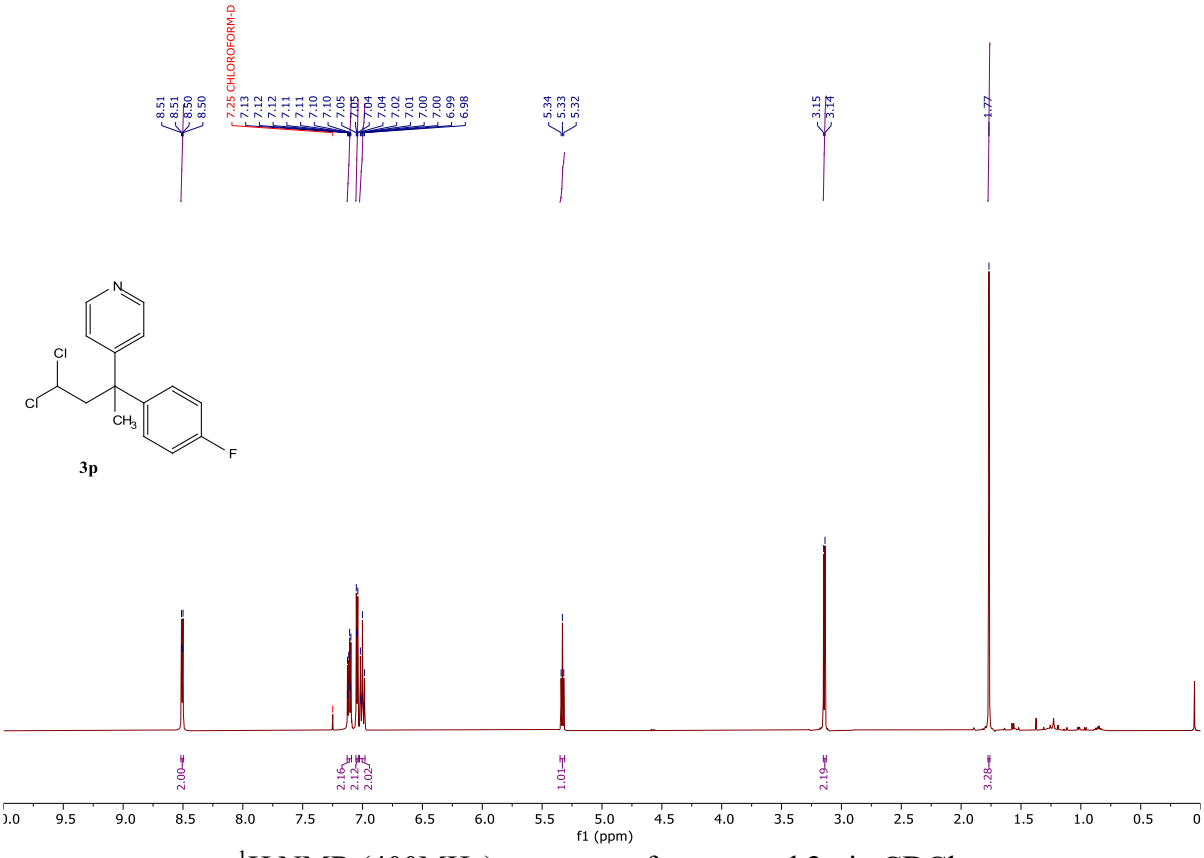
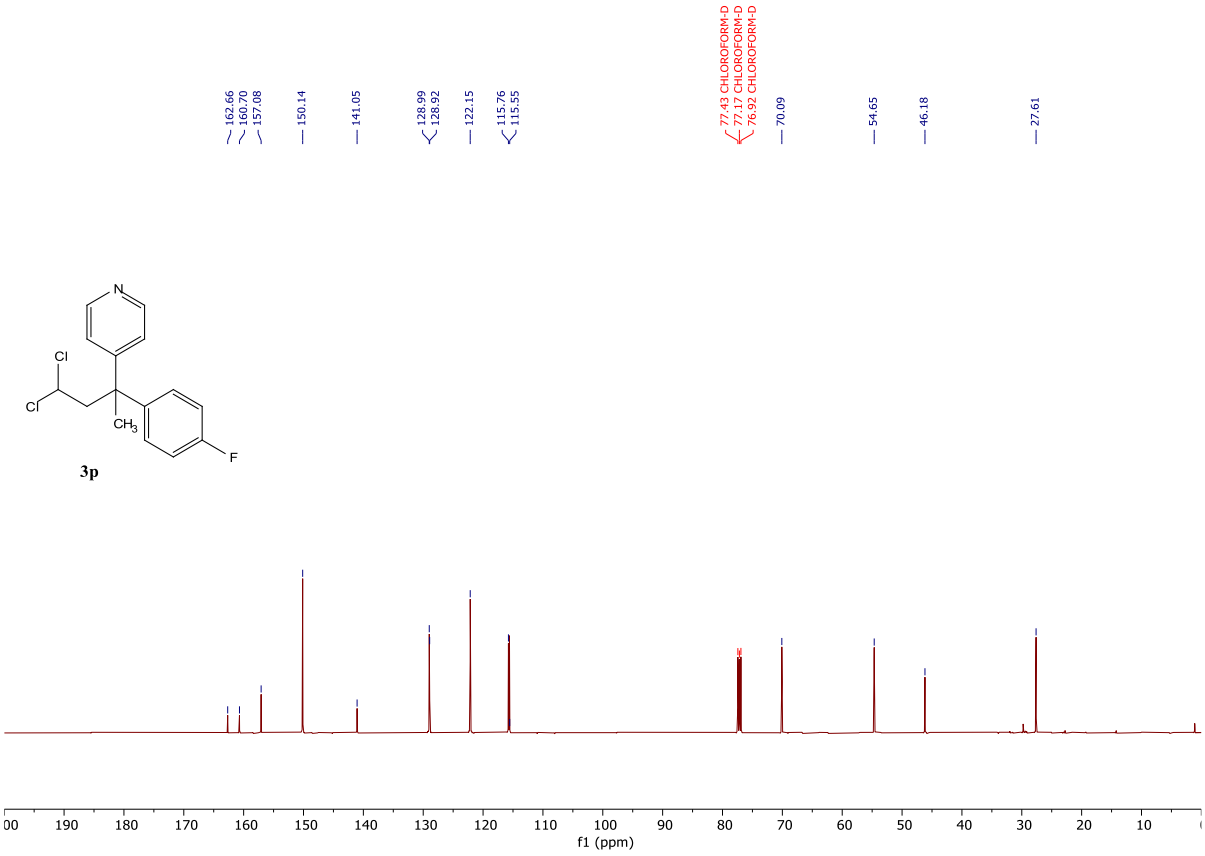


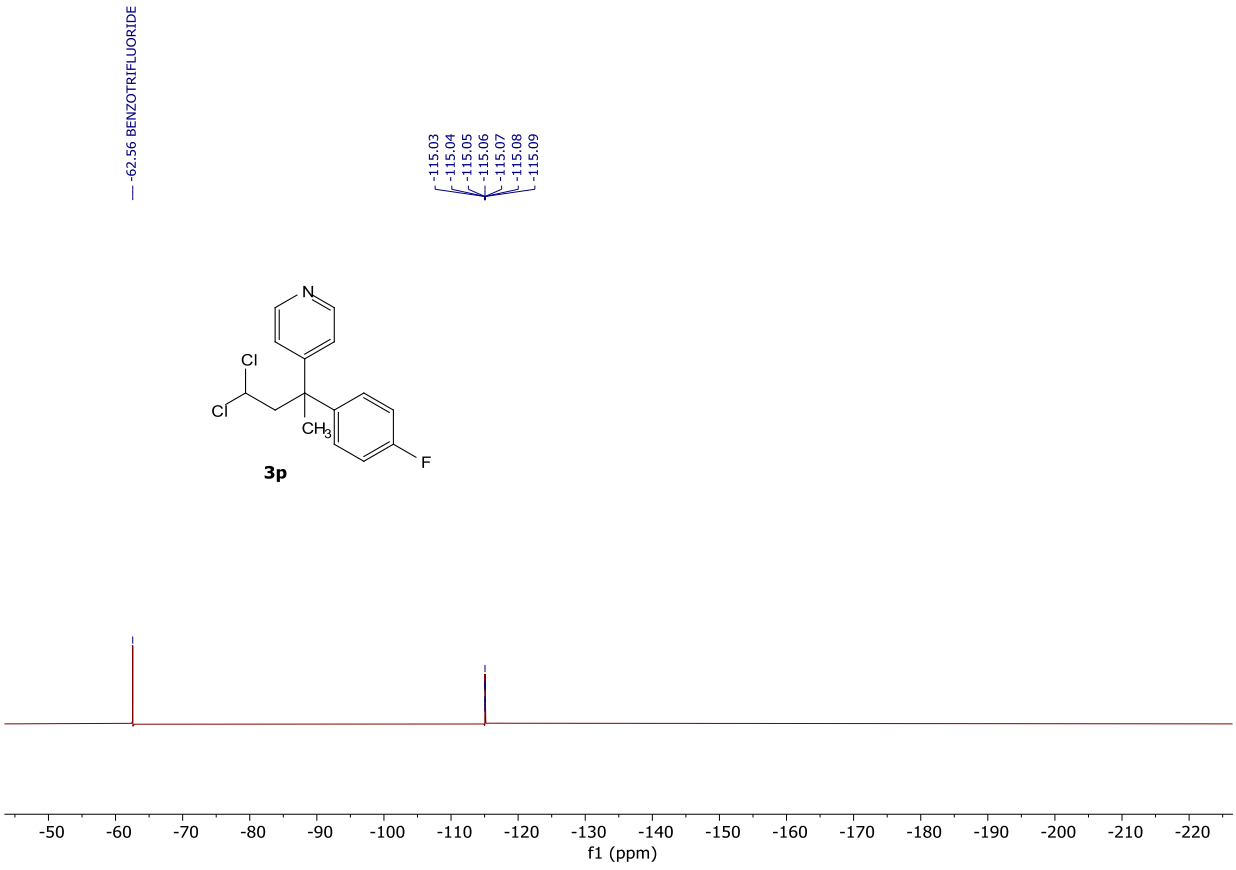
$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **3o** in $CDCl_3$



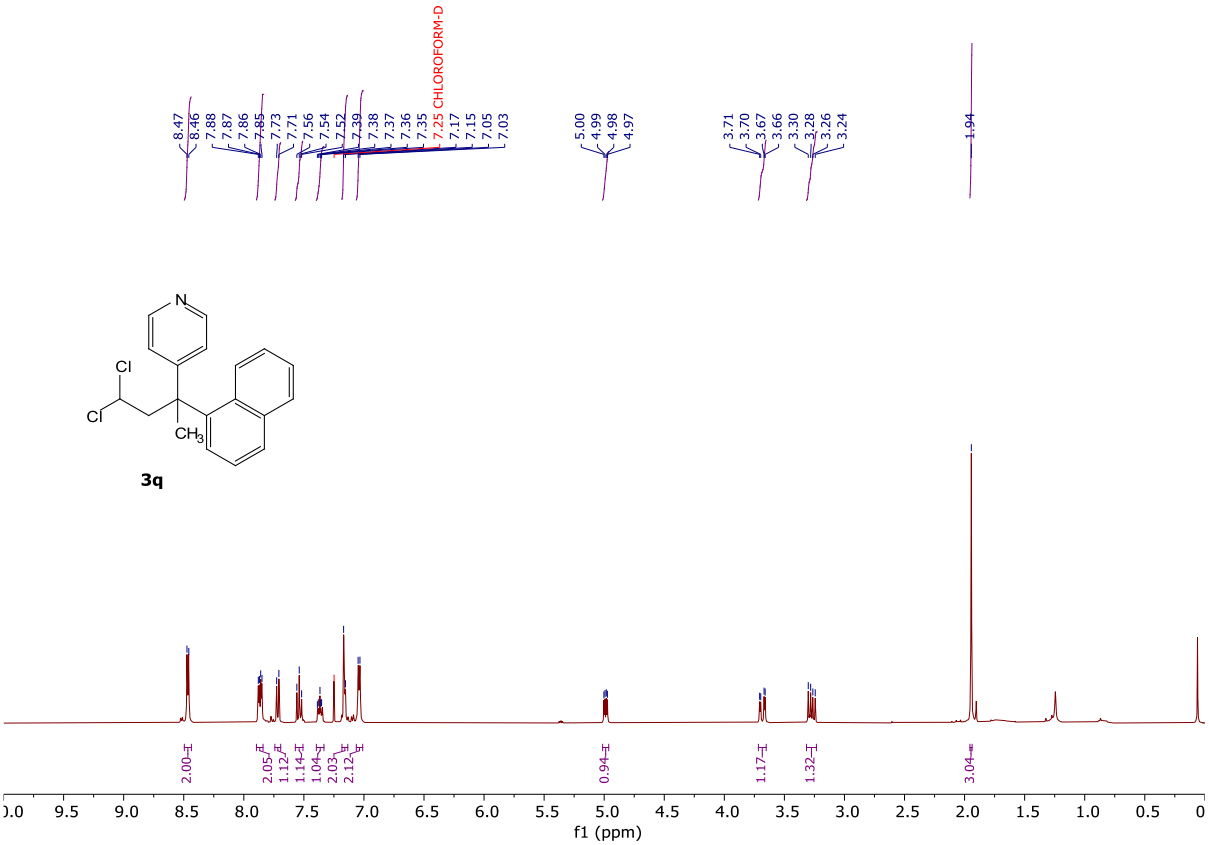
^{1}H NMR (400MHz) spectrum of compound **3p** in $CDCl_3$



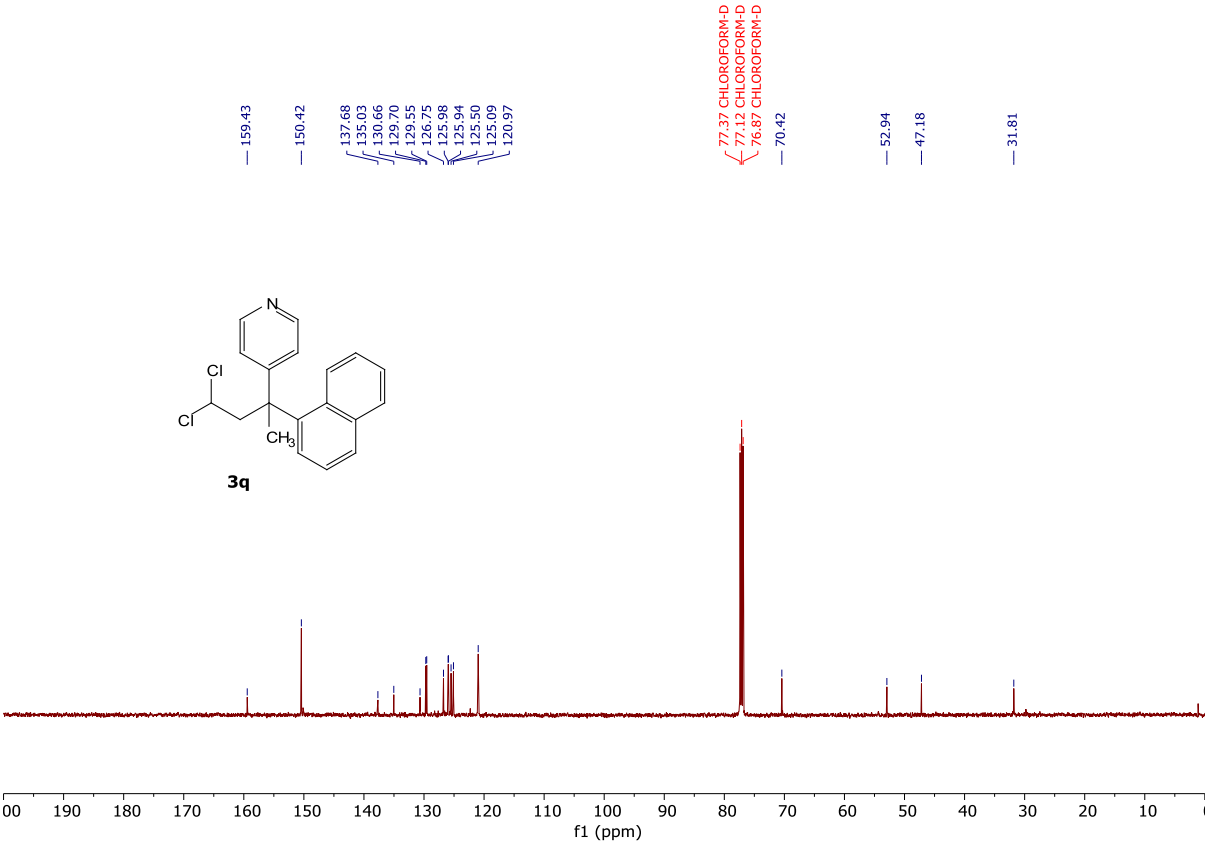
^{13}C {^{1}H} NMR (125MHz) spectrum of compound **3p** in $CDCl_3$



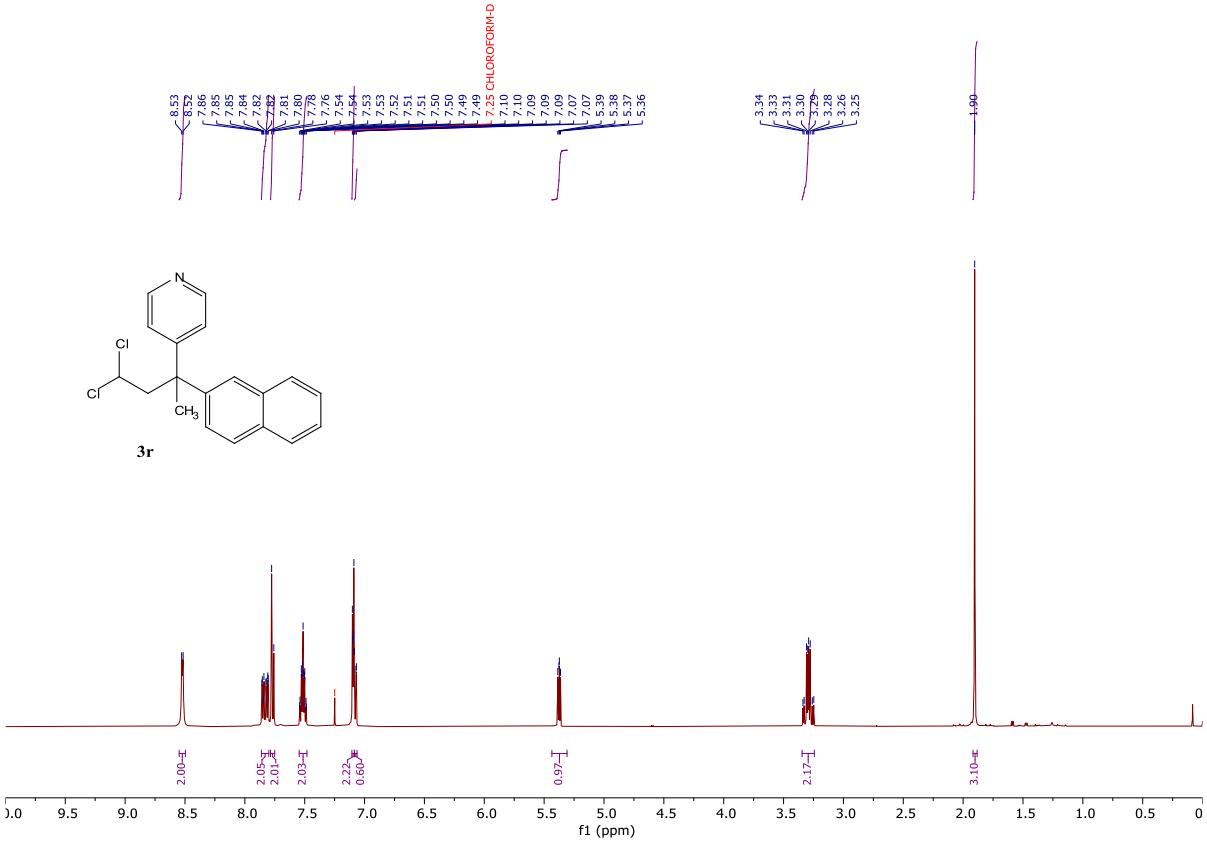
^{19}F NMR (471 MHz) spectrum of compound **3p** in $CDCl_3$



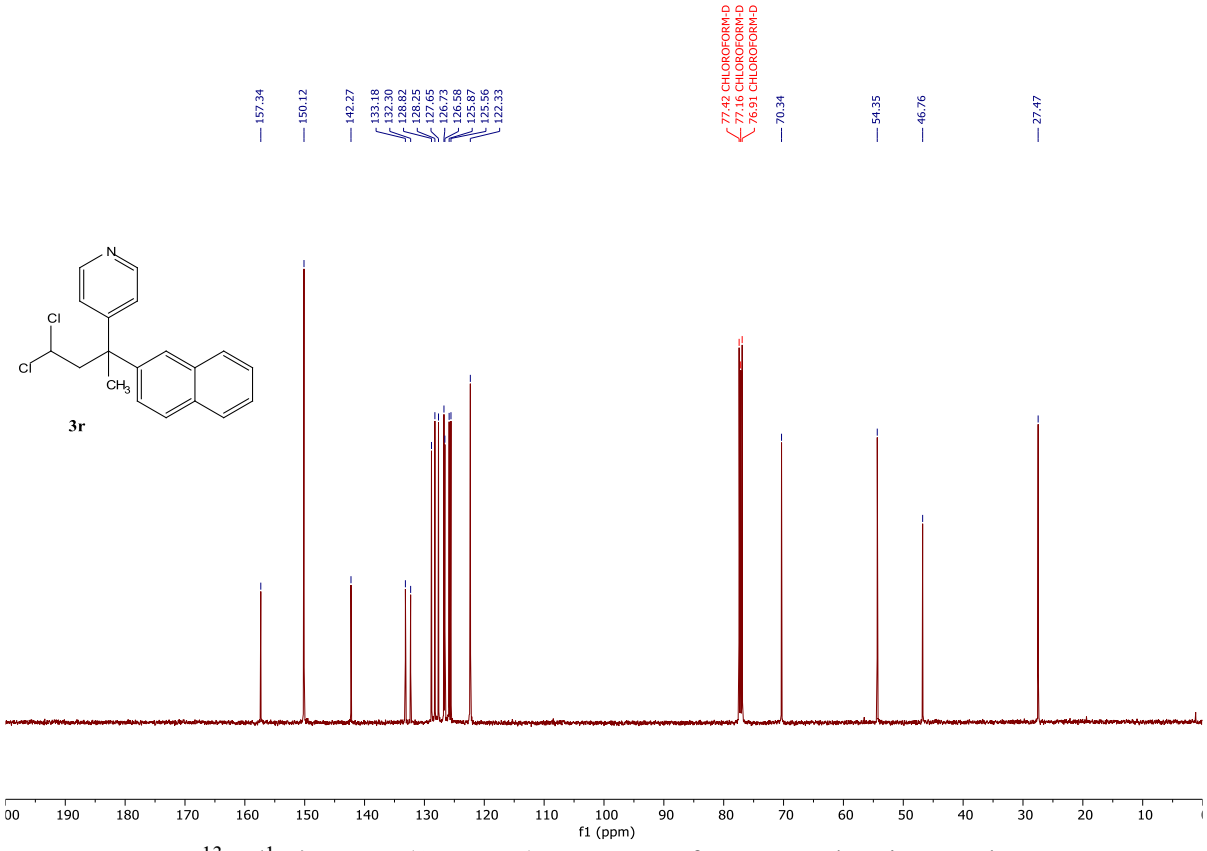
^{1}H NMR (400MHz) spectrum of compound **3q** in $CDCl_3$



^{13}C {^{1}H} NMR (125MHz) spectrum of compound **3q** in $CDCl_3$



^{1}H NMR (400MHz) spectrum of compound **3r** in $CDCl_3$



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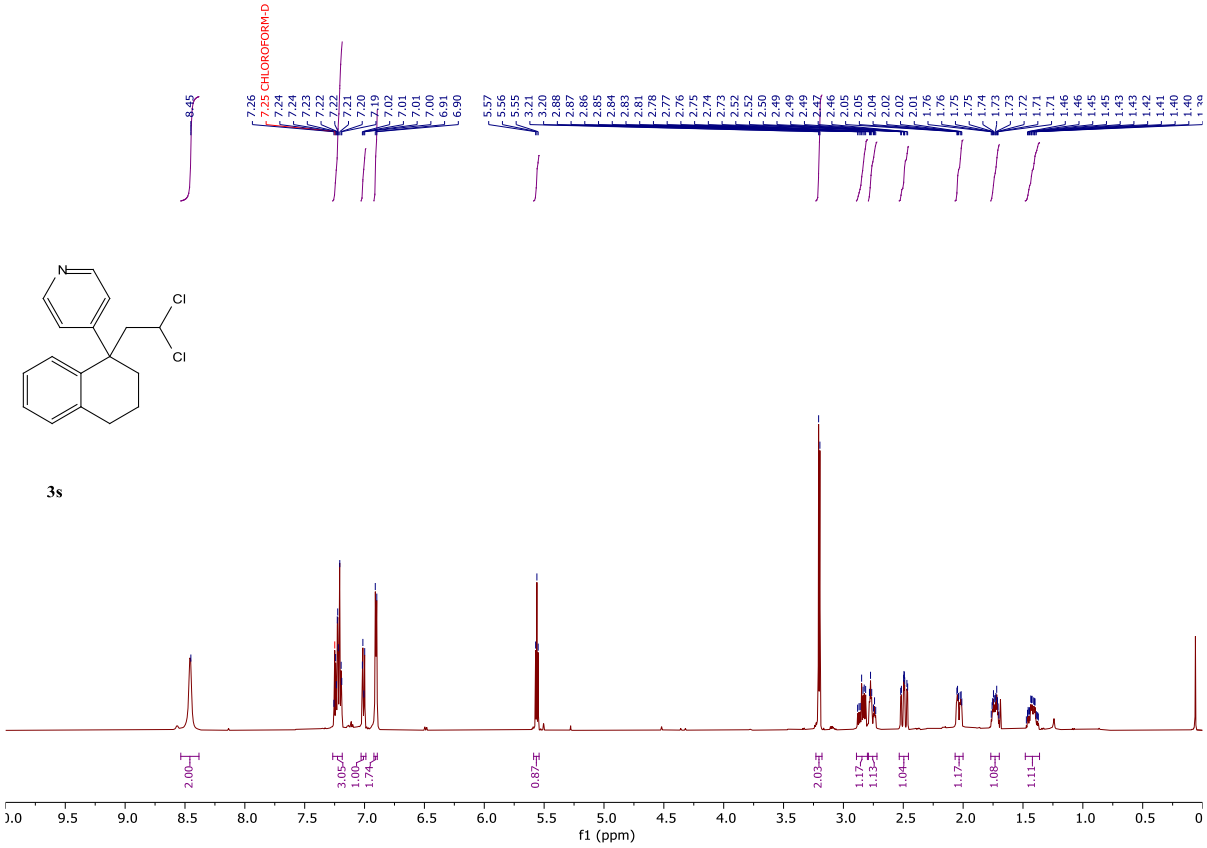
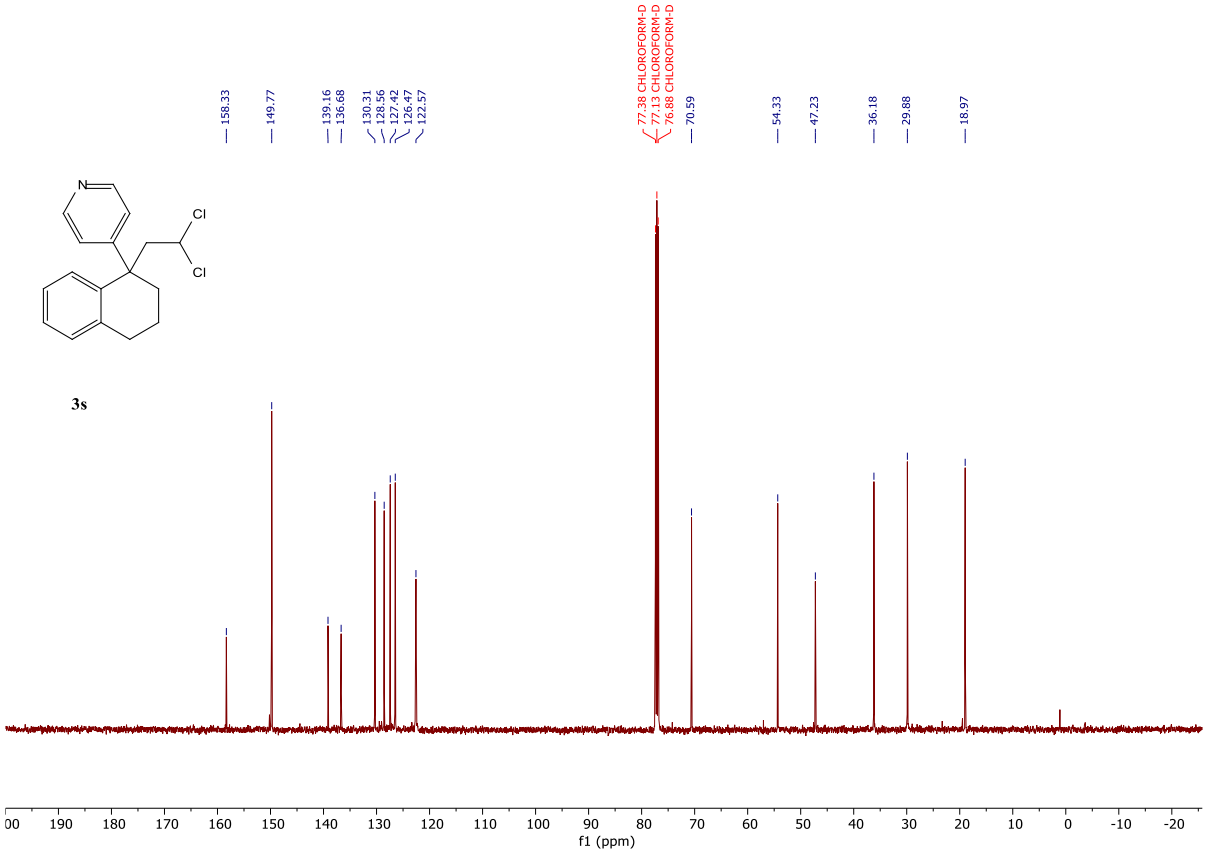


^{1}H NMR (400MHz) spectrum of compound **3s** in $CDCl_3$



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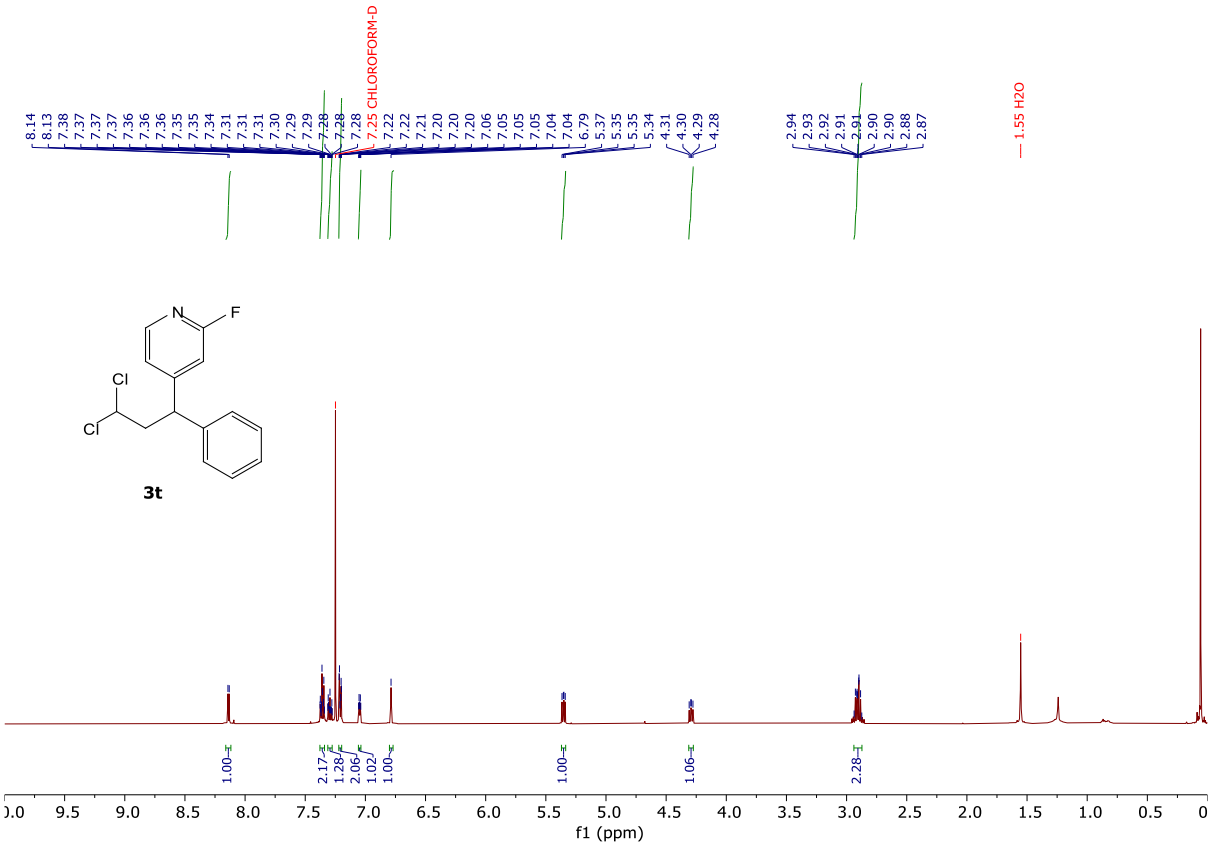
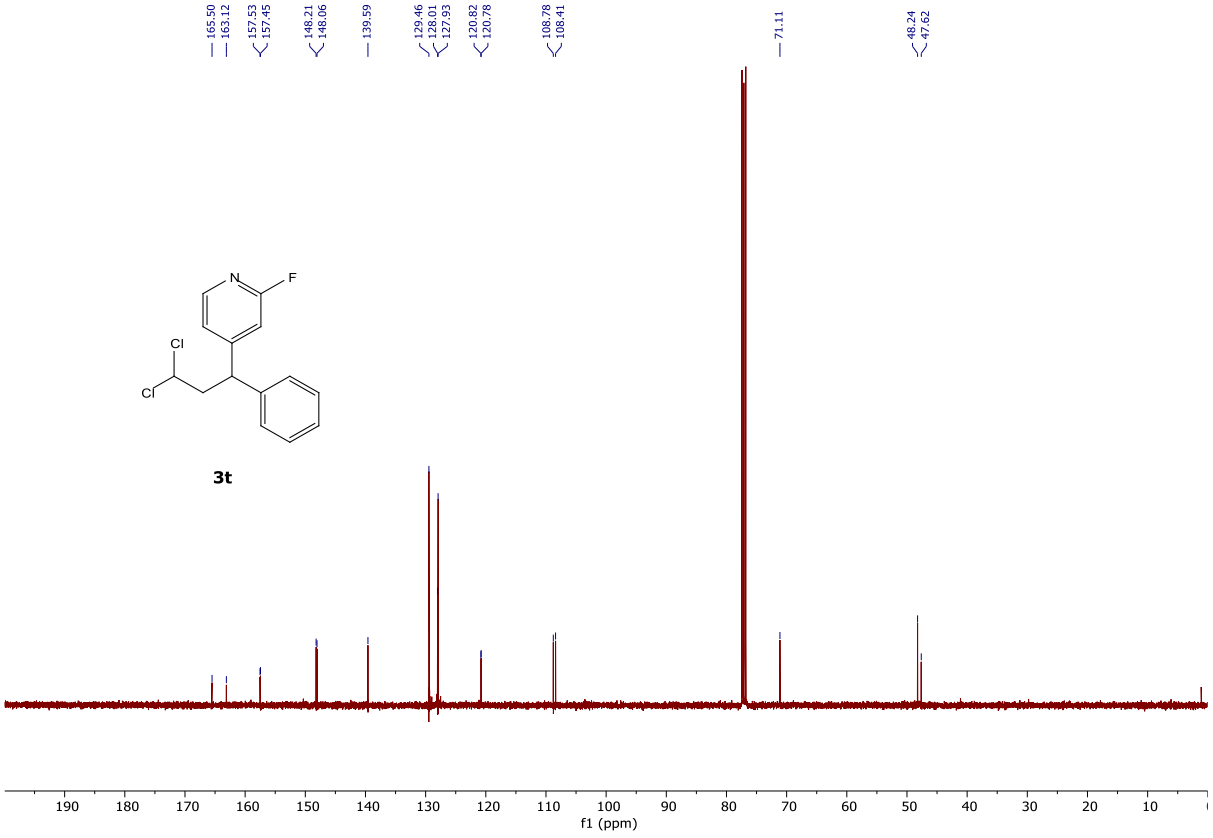
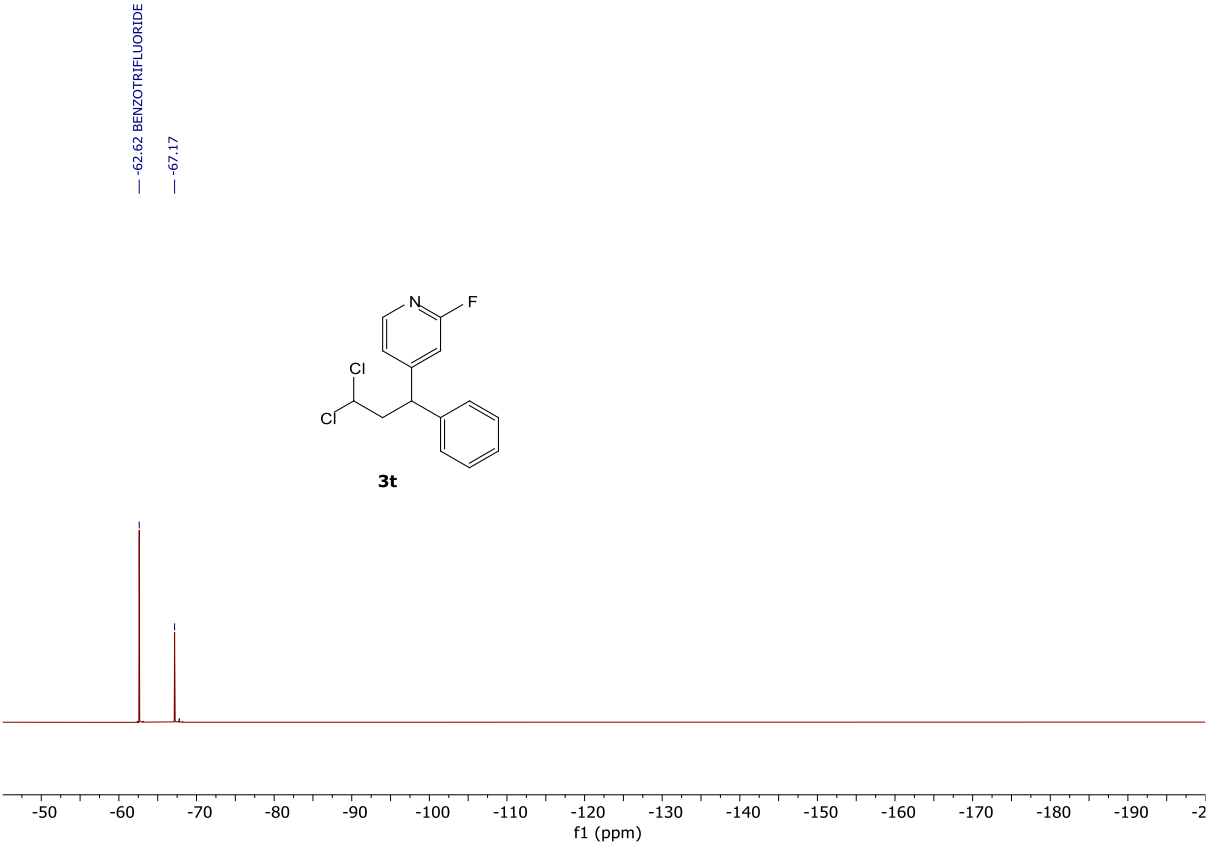


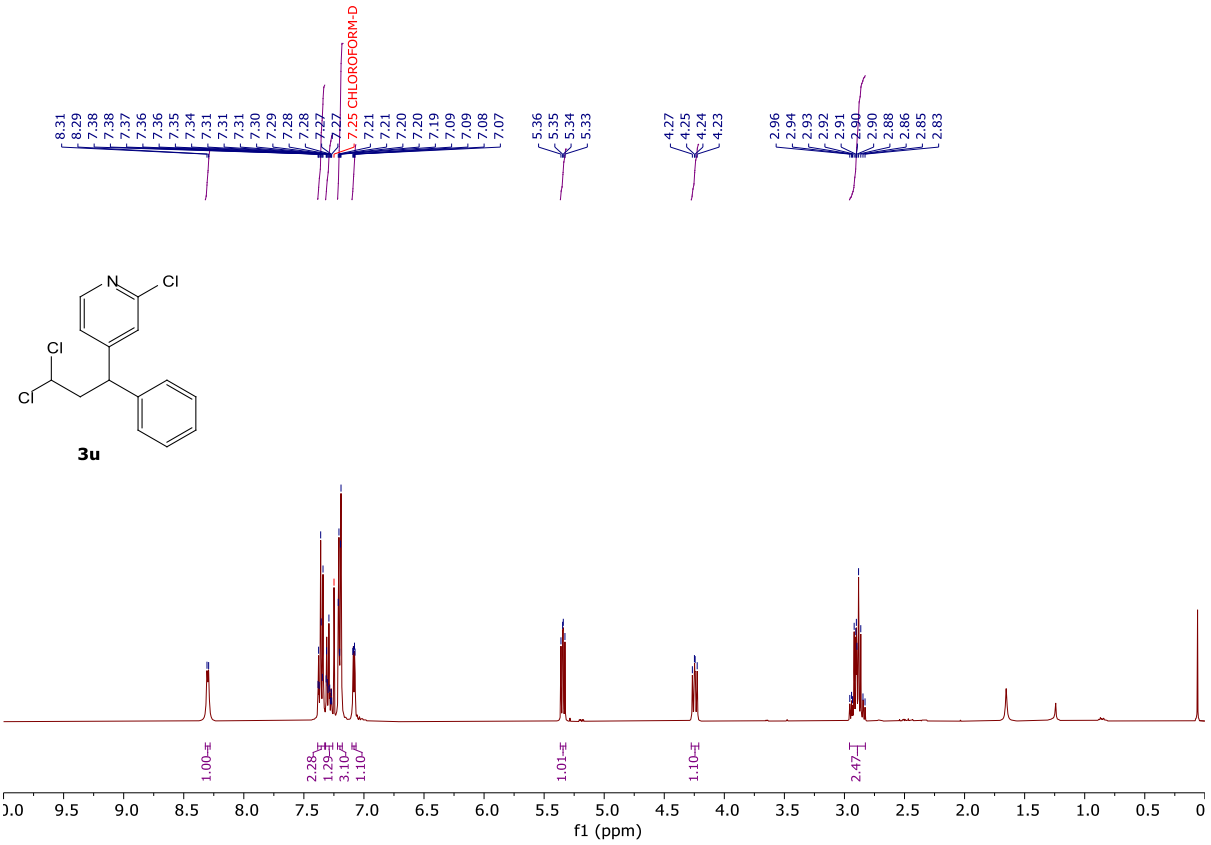
^{1}H NMR (400MHz) spectrum of compound **3t** in $CDCl_3$



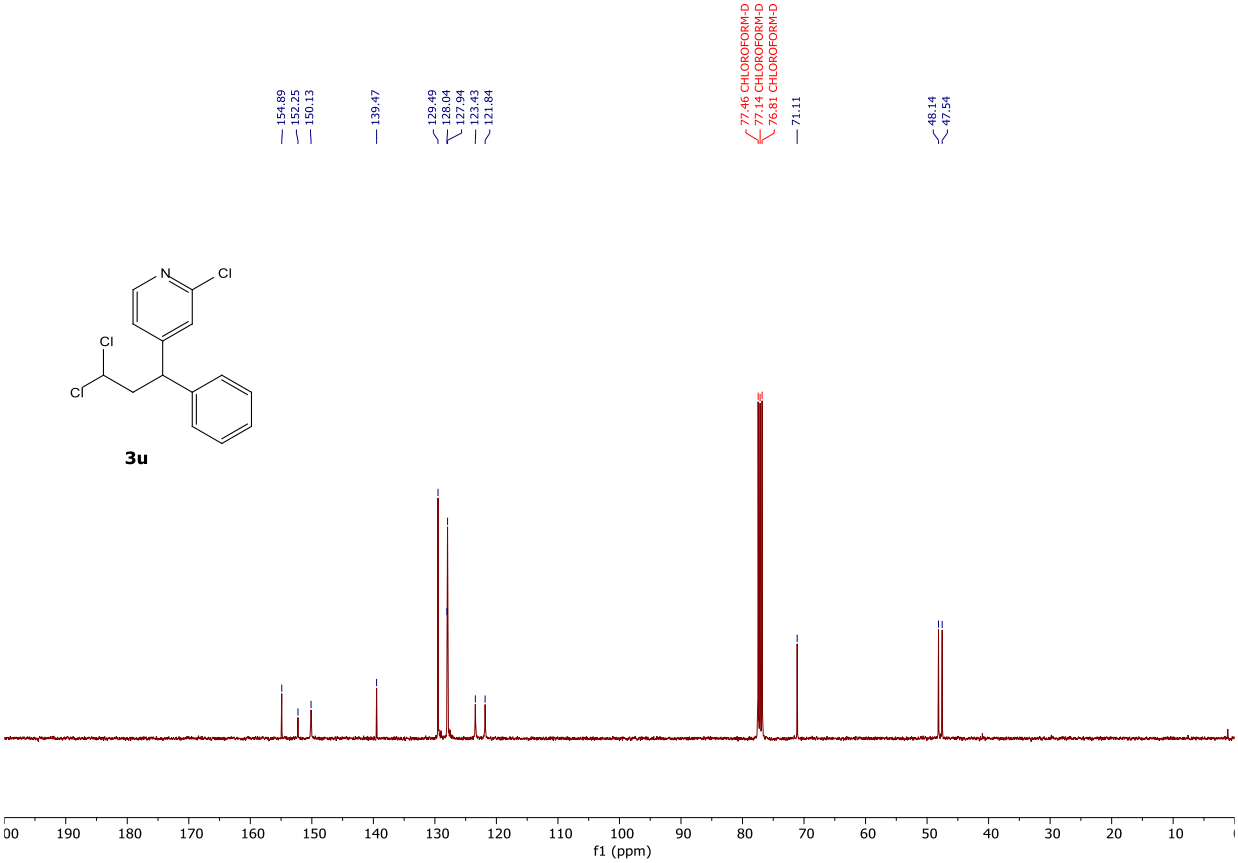
^{13}C{^{1}H} NMR (125MHz) spectrum of compound **3t** in $CDCl_3$



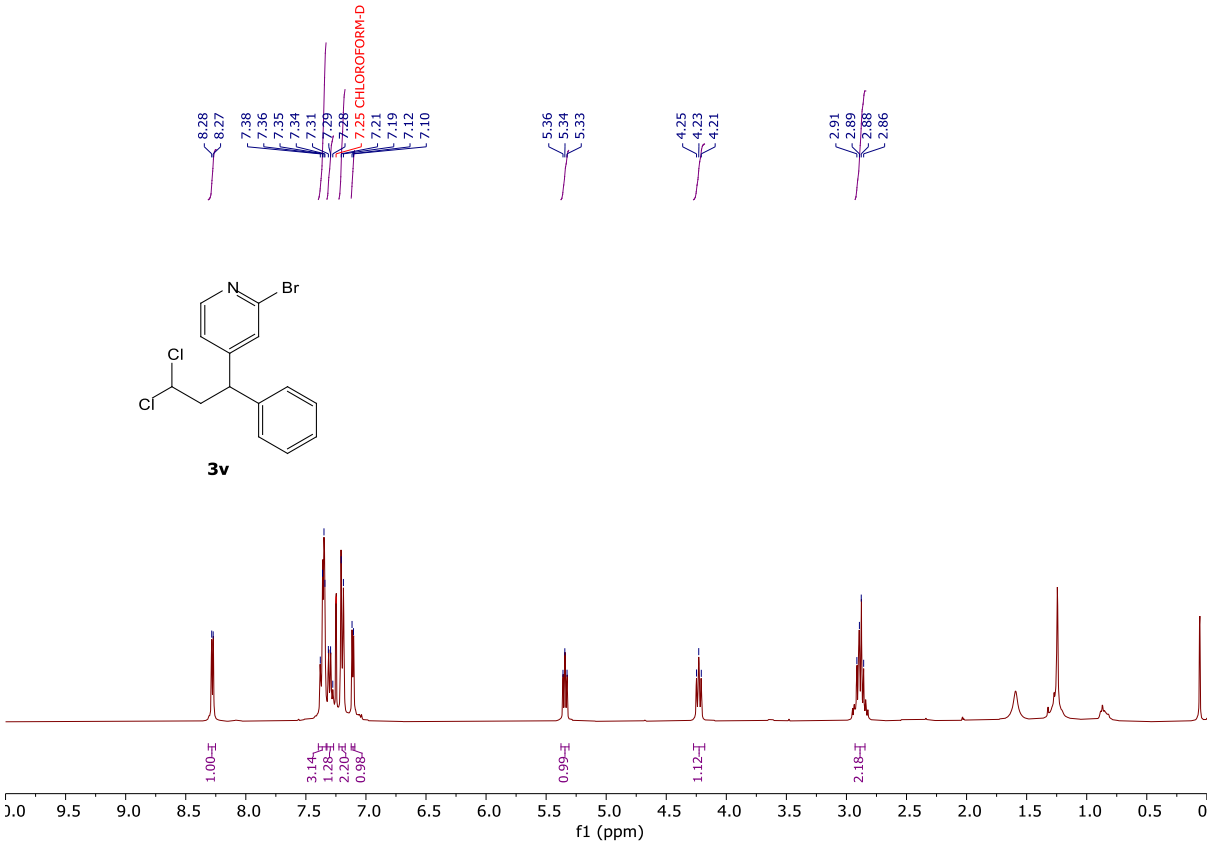
^{19}F NMR (471MHz) spectrum of compound **3t** in $CDCl_3$



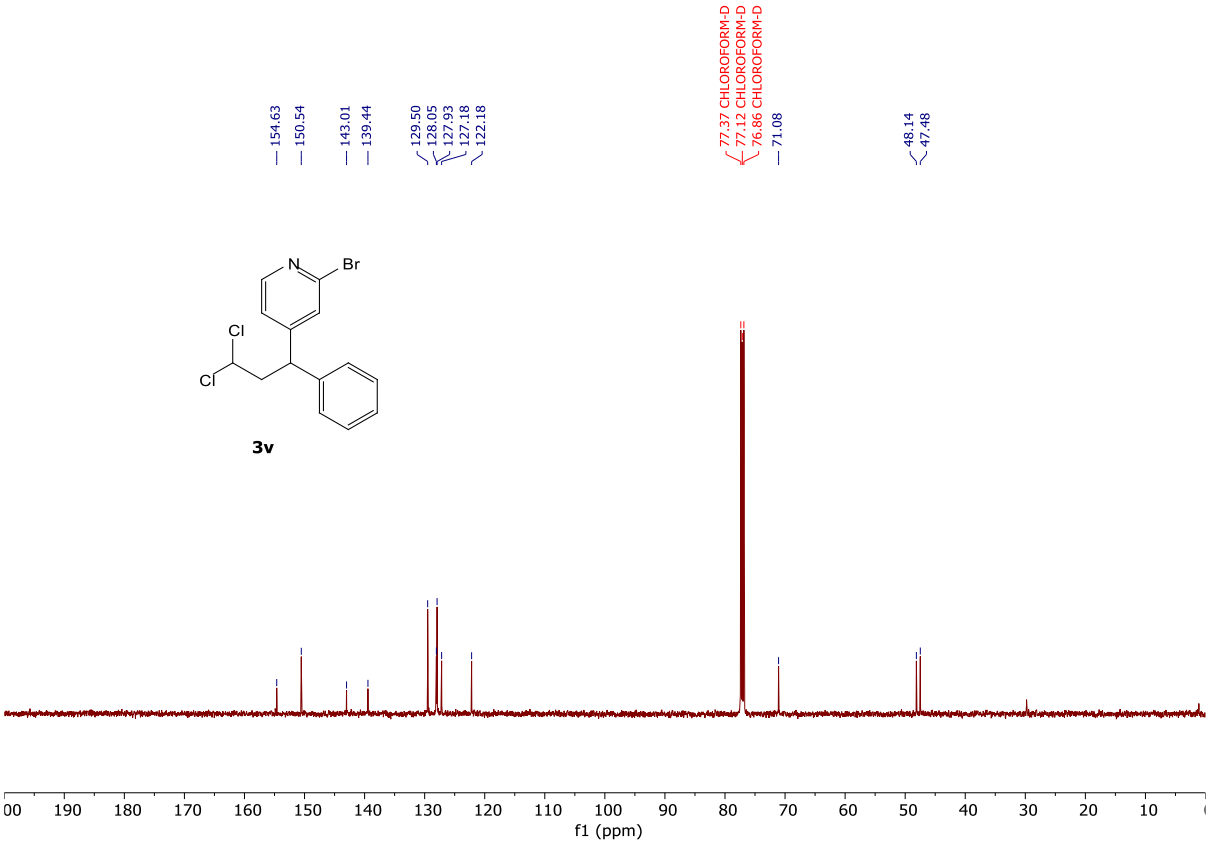
^{1}H NMR (400MHz) spectrum of compound **3u** in $CDCl_3$



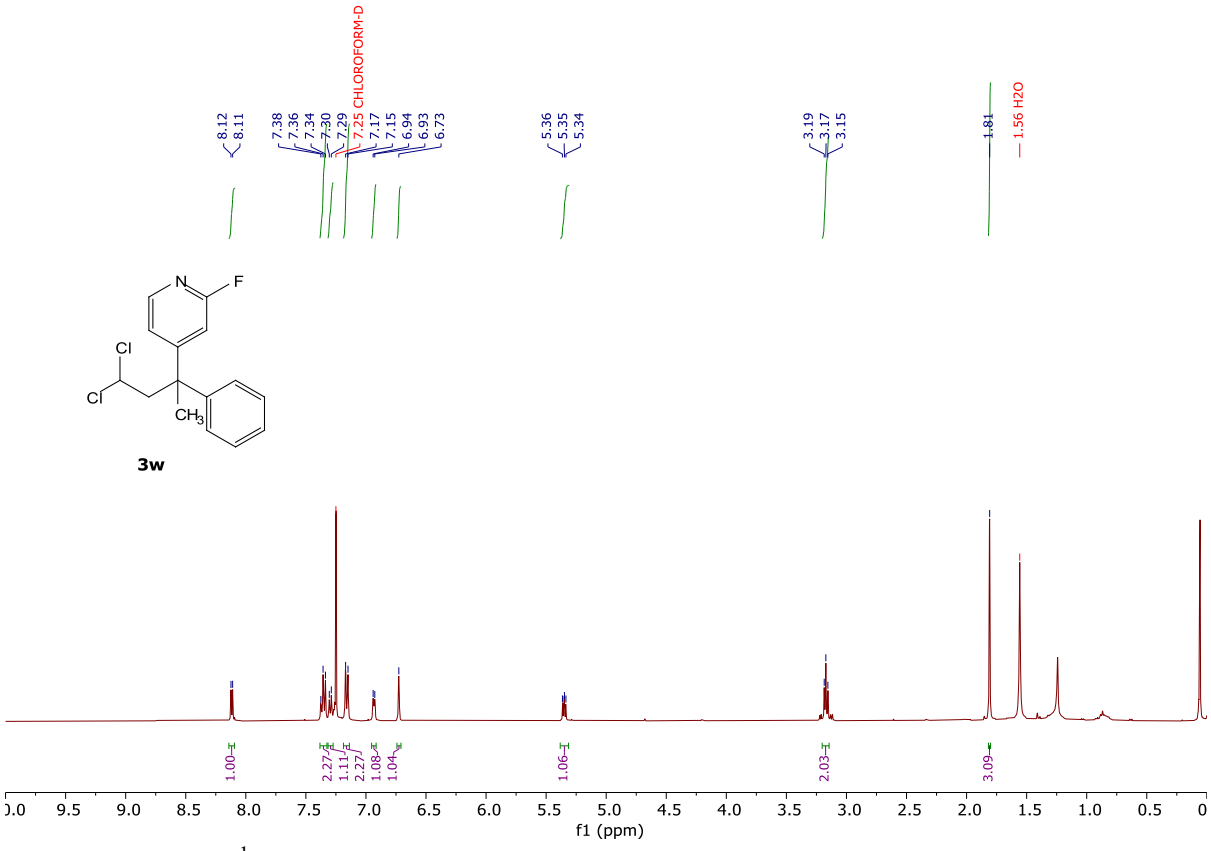
^{13}C {^{1}H} NMR (125MHz) spectrum of compound **3u** in $CDCl_3$



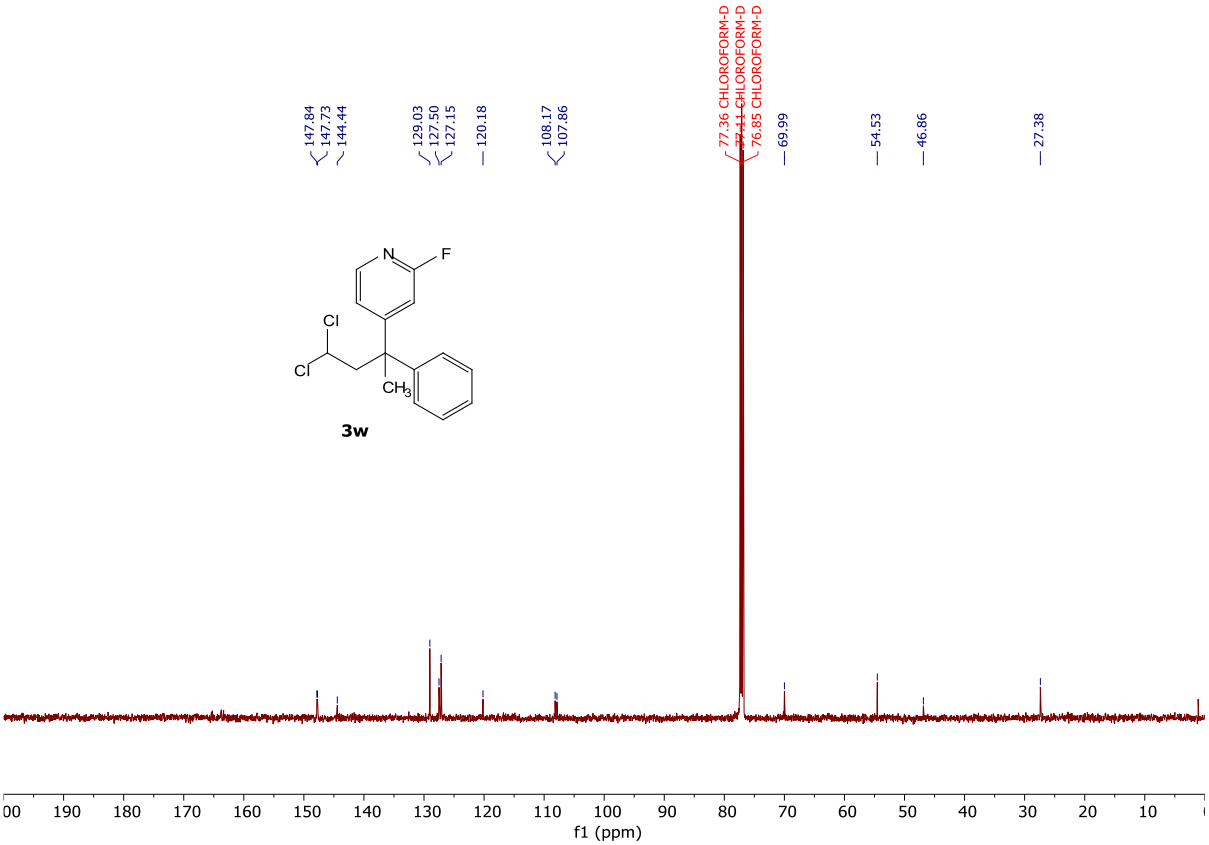
^{1}H NMR (400MHz) spectrum of compound **3v** in $CDCl_3$



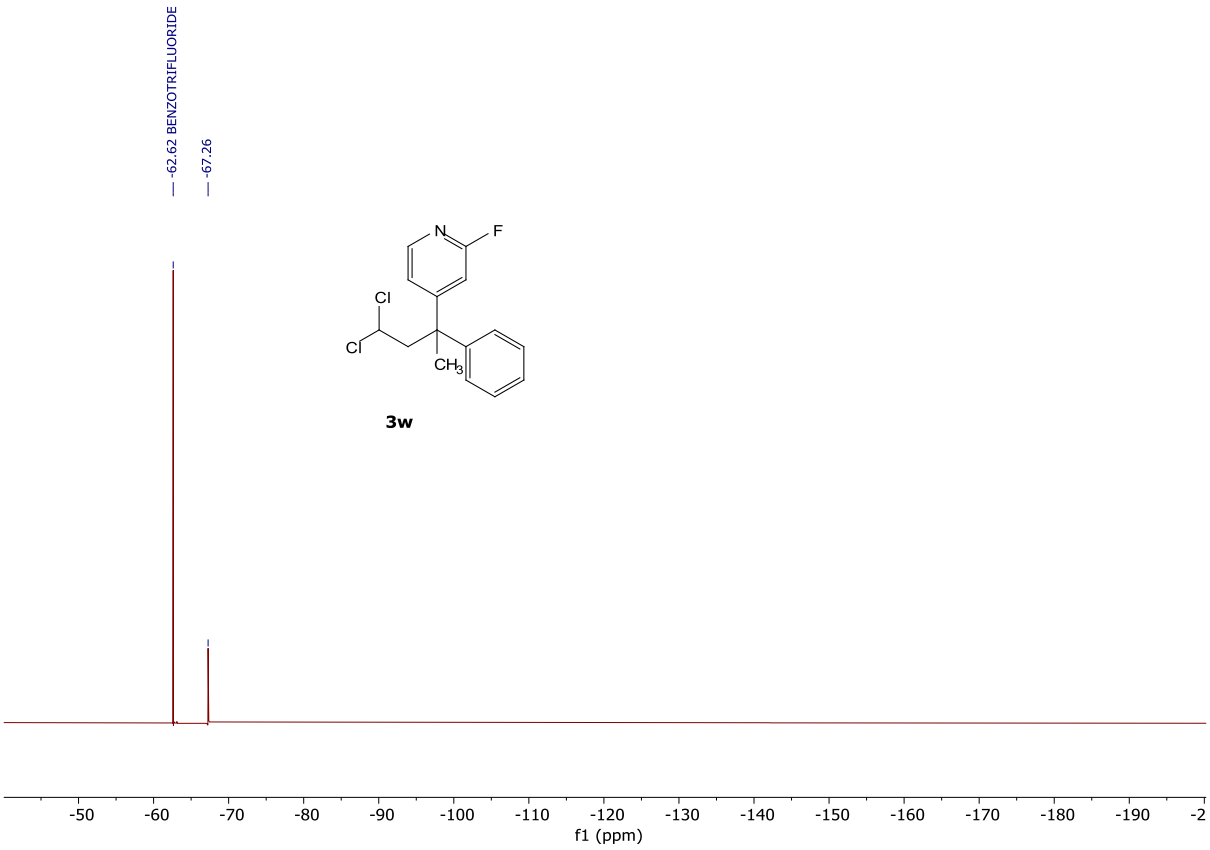
$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **3v** in $CDCl_3$



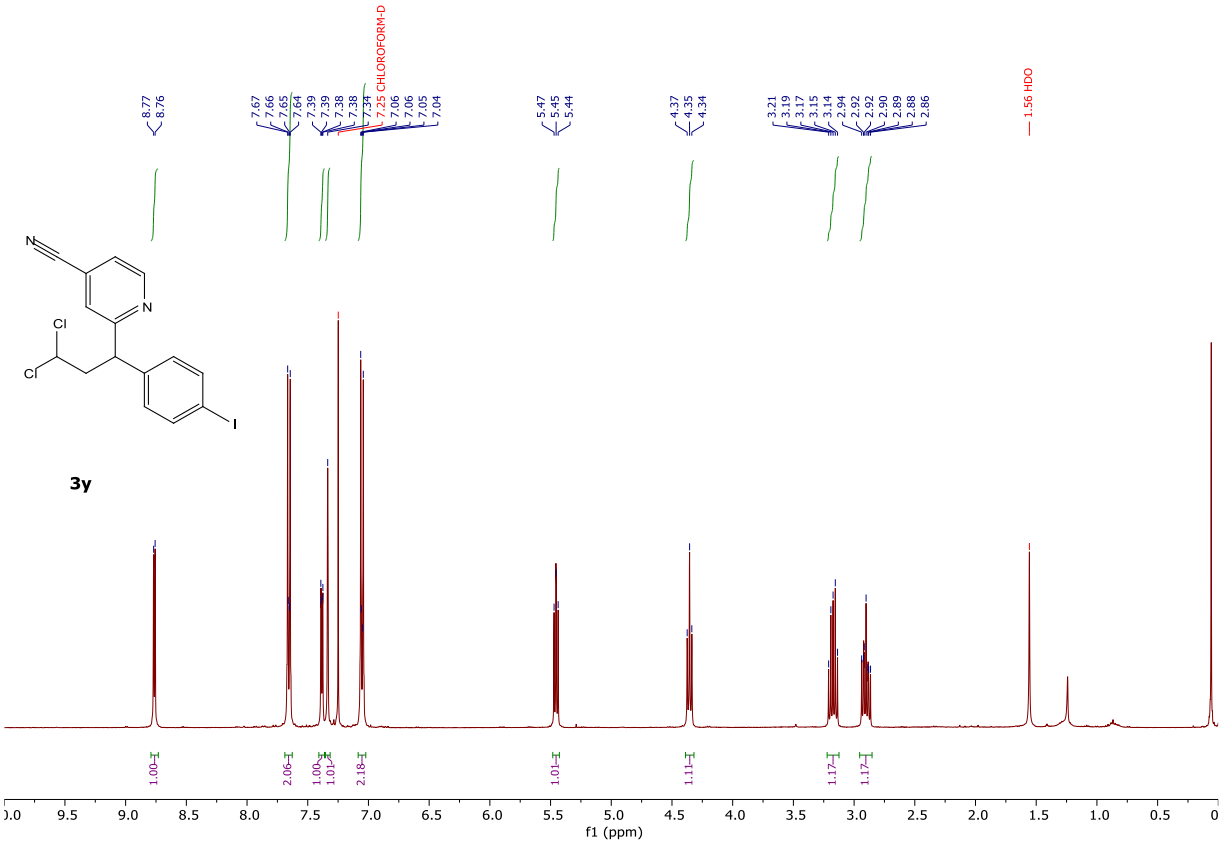
^{1}H NMR (400MHz) spectrum of compound **3w** in $CDCl_3$



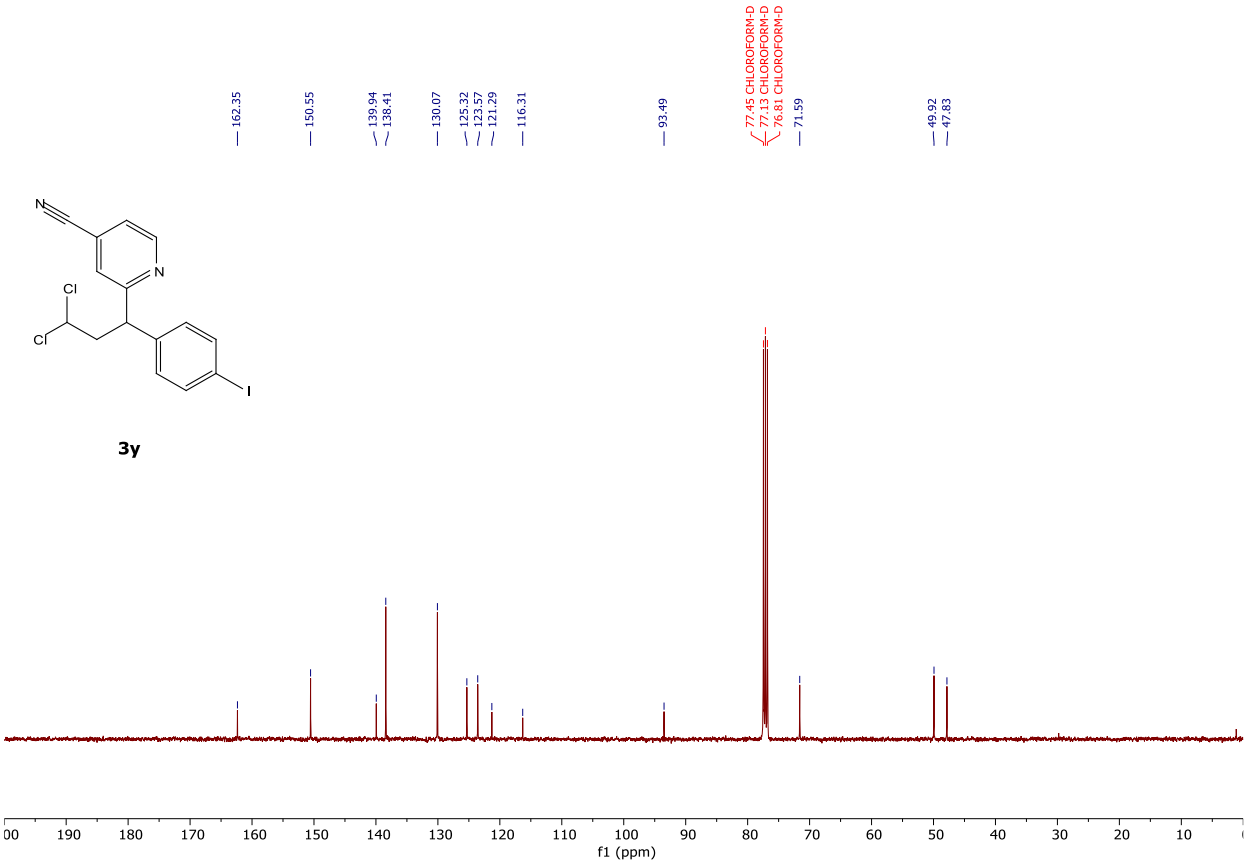
^{13}C {^{1}H} NMR (125MHz) spectrum of compound **3w** in $CDCl_3$



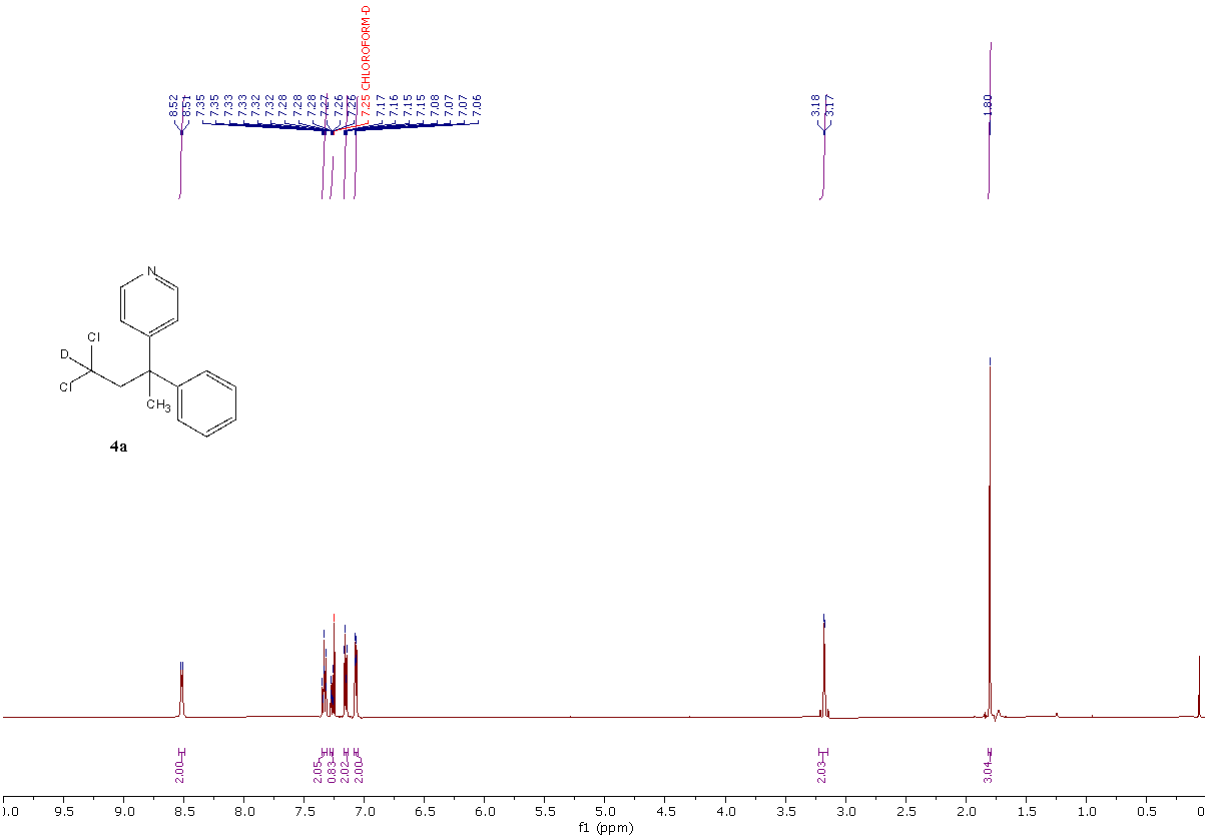
^{19}F NMR (471 MHz) spectrum of compound **3w** in $CDCl_3$



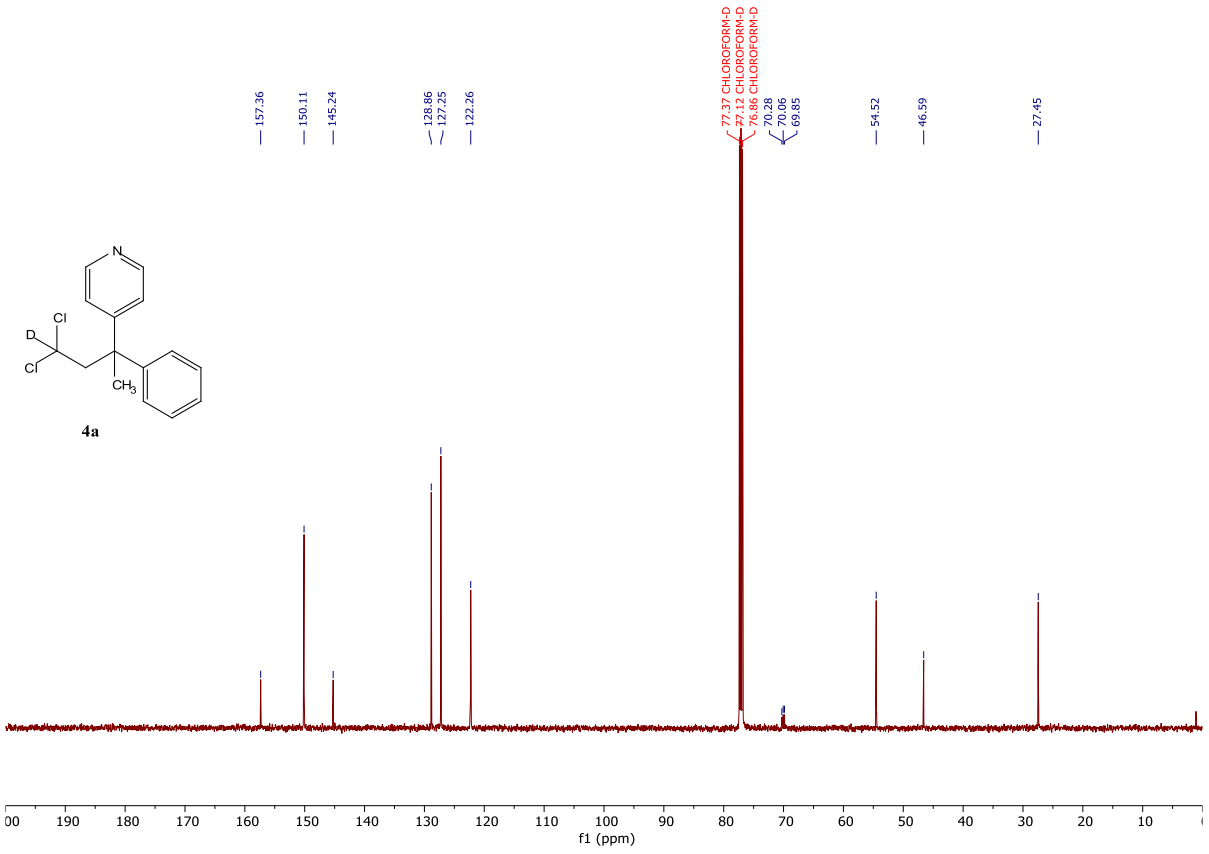
^{1}H NMR (400MHz) spectrum of compound **3y** in $CDCl_3$



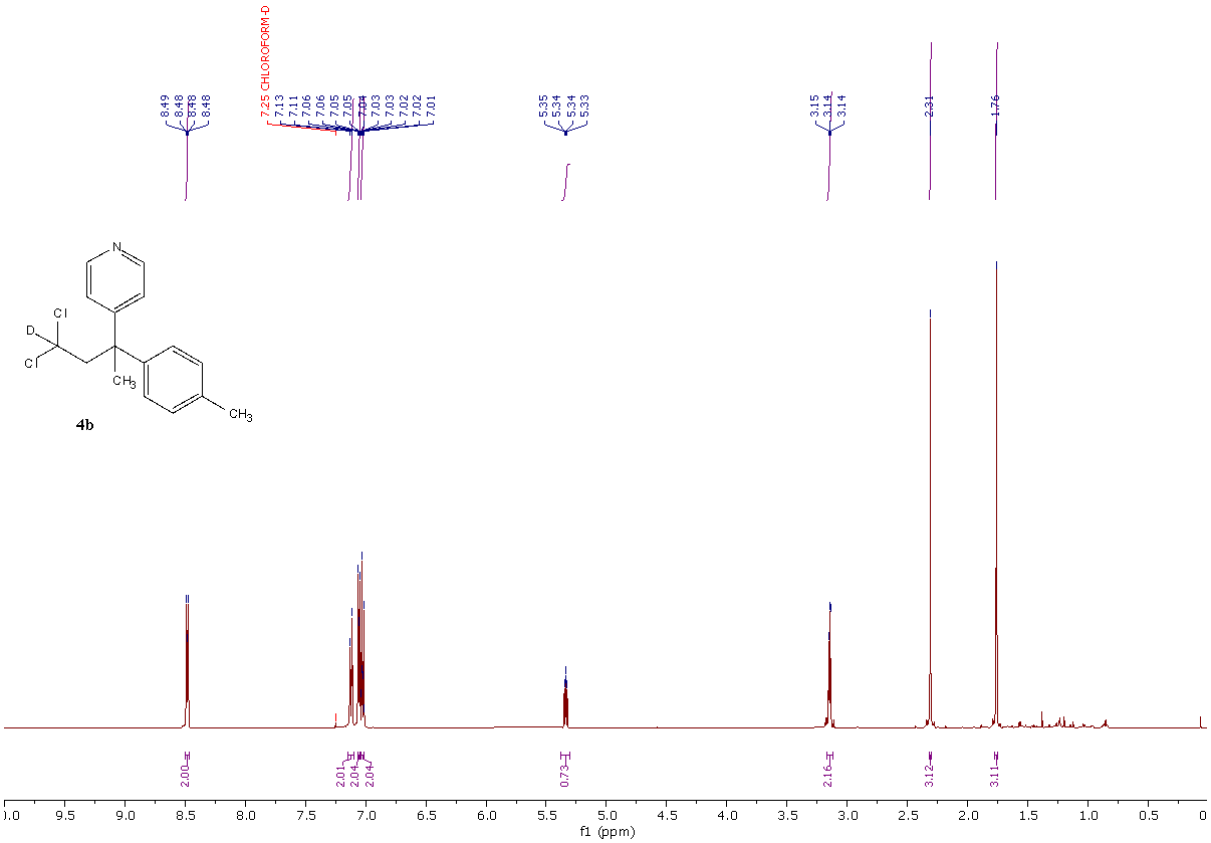
^{13}C{^{1}H} NMR (100MHz) spectrum of compound **3y** in $CDCl_3$



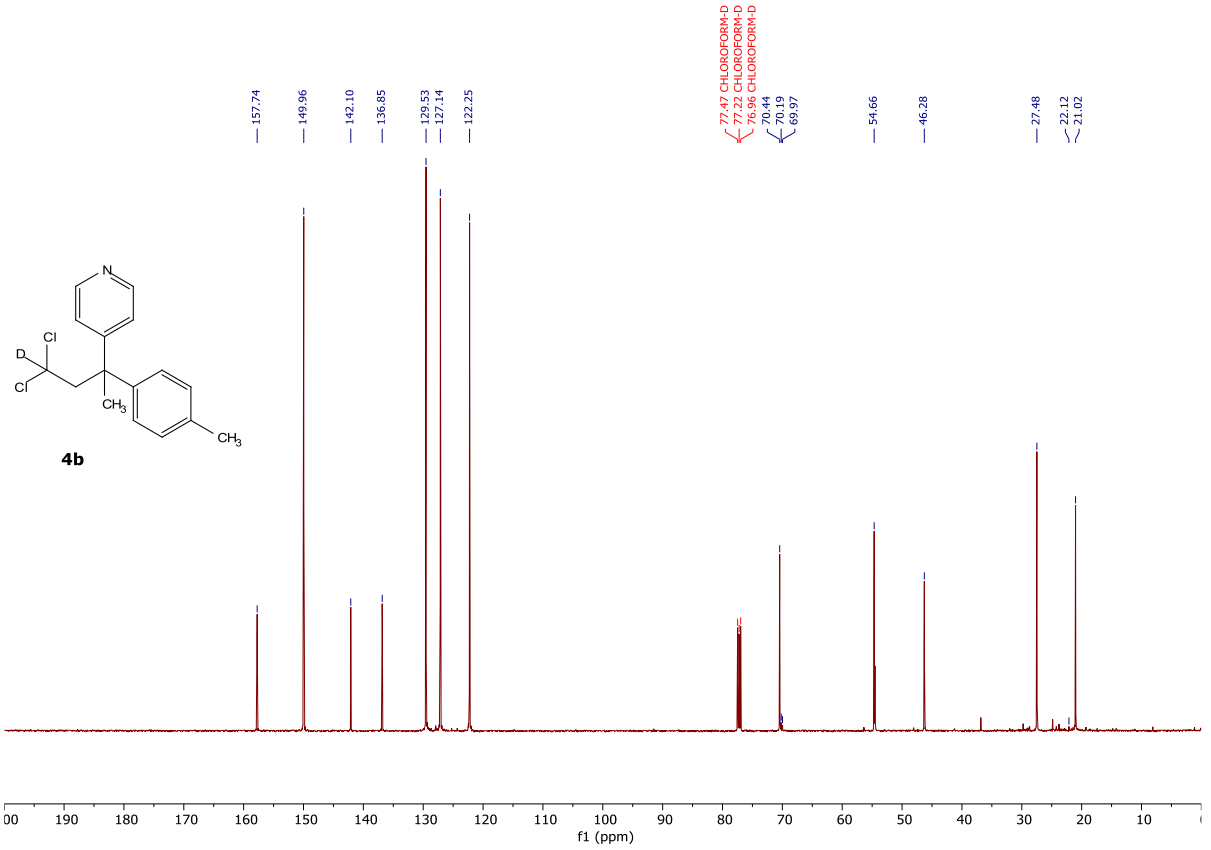
^{1}H NMR (400MHz) spectrum of compound **4a** in $CDCl_3$



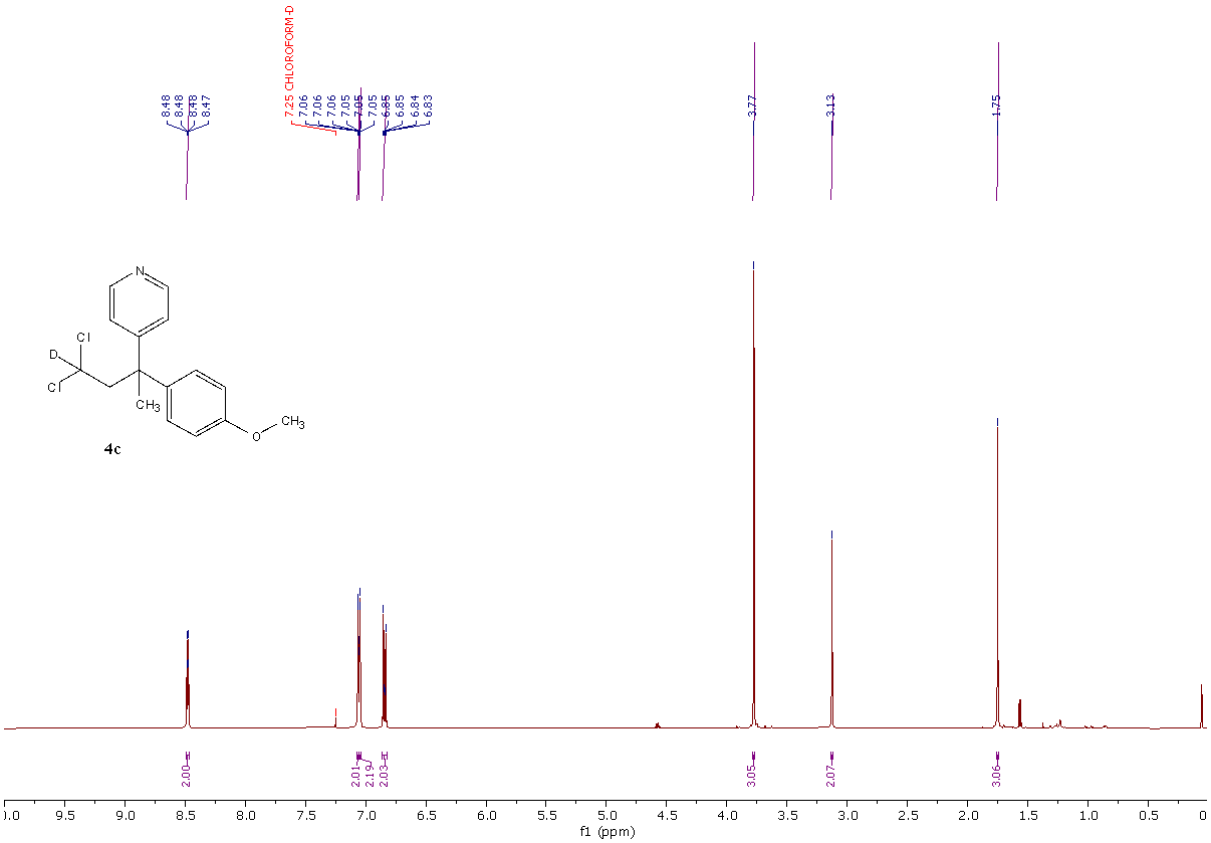
^{13}C{^{1}H} NMR (125MHz) spectrum of compound **4a** in $CDCl_3$



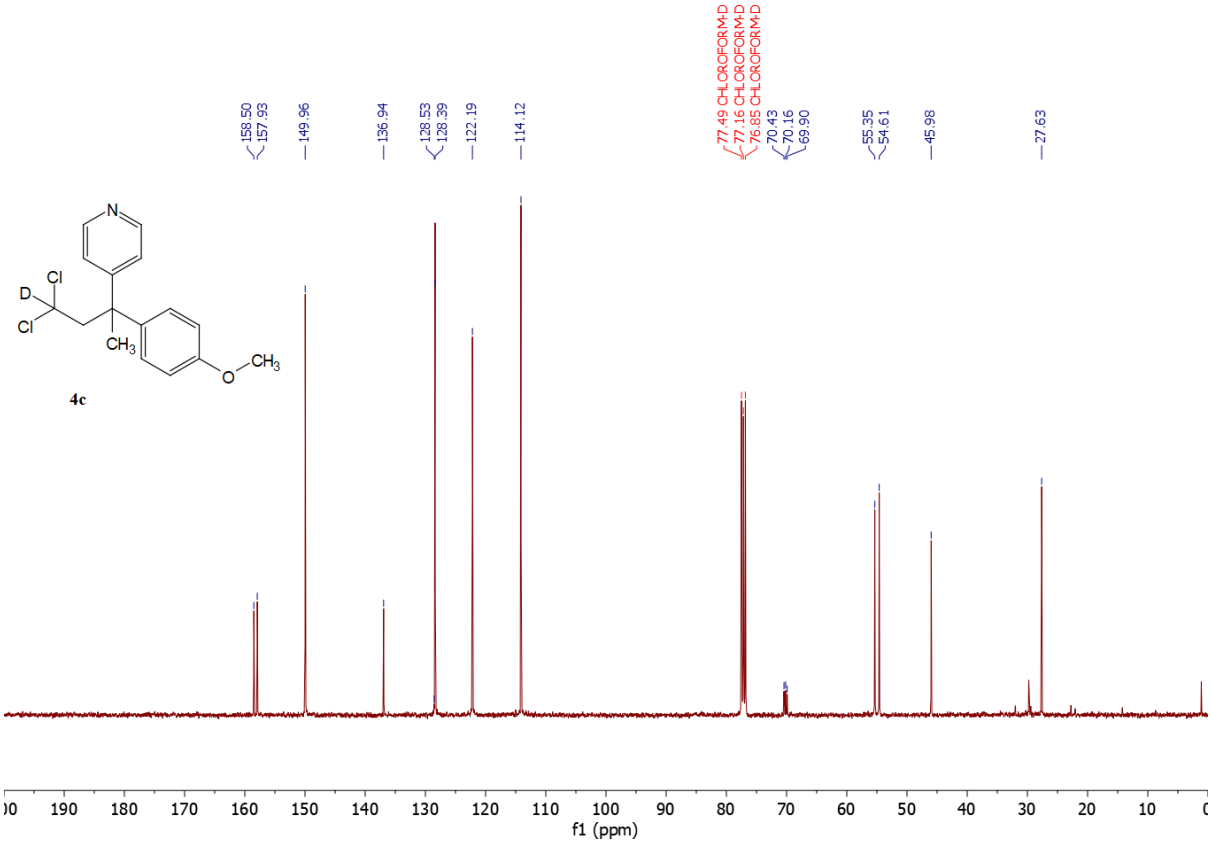
^{1}H NMR (400MHz) spectrum of compound **4b** in $CDCl_3$



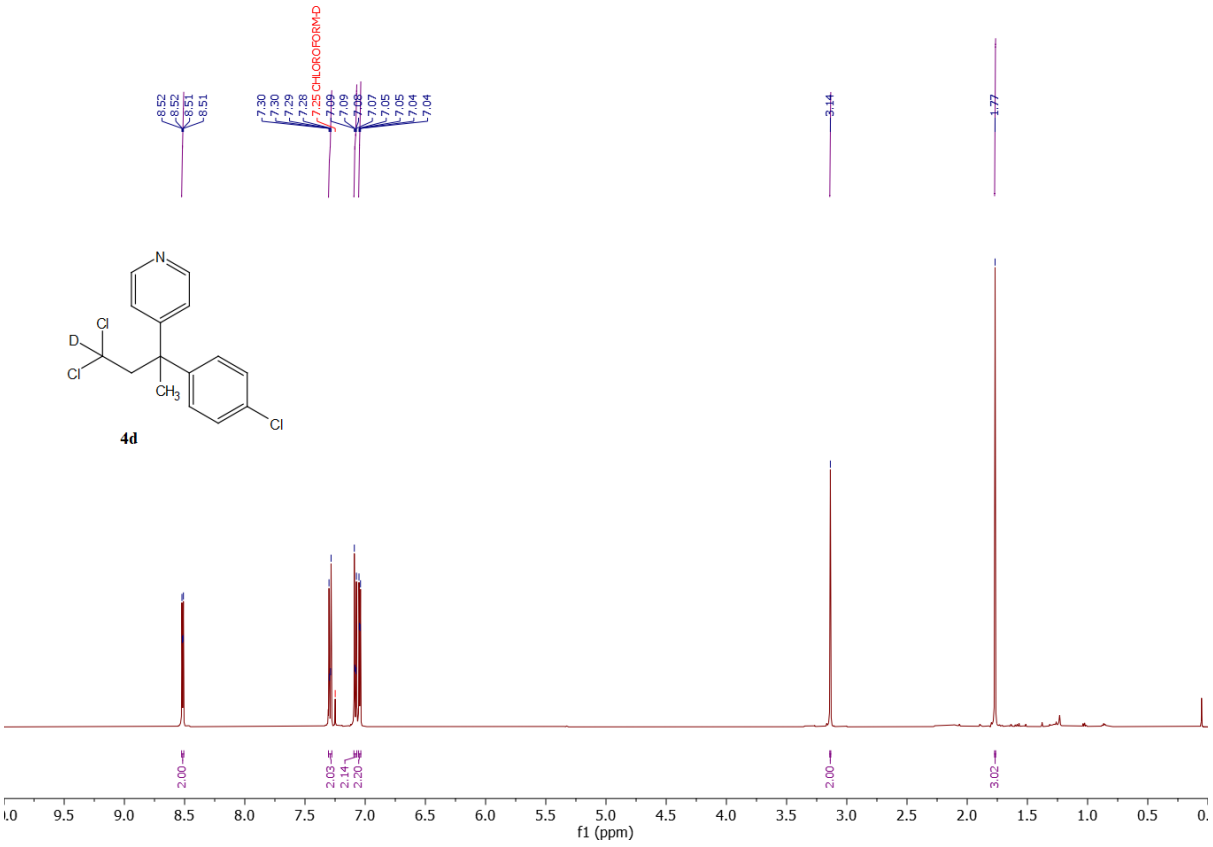
^{13}C{^{1}H} NMR (125MHz) spectrum of compound **4b** in $CDCl_3$



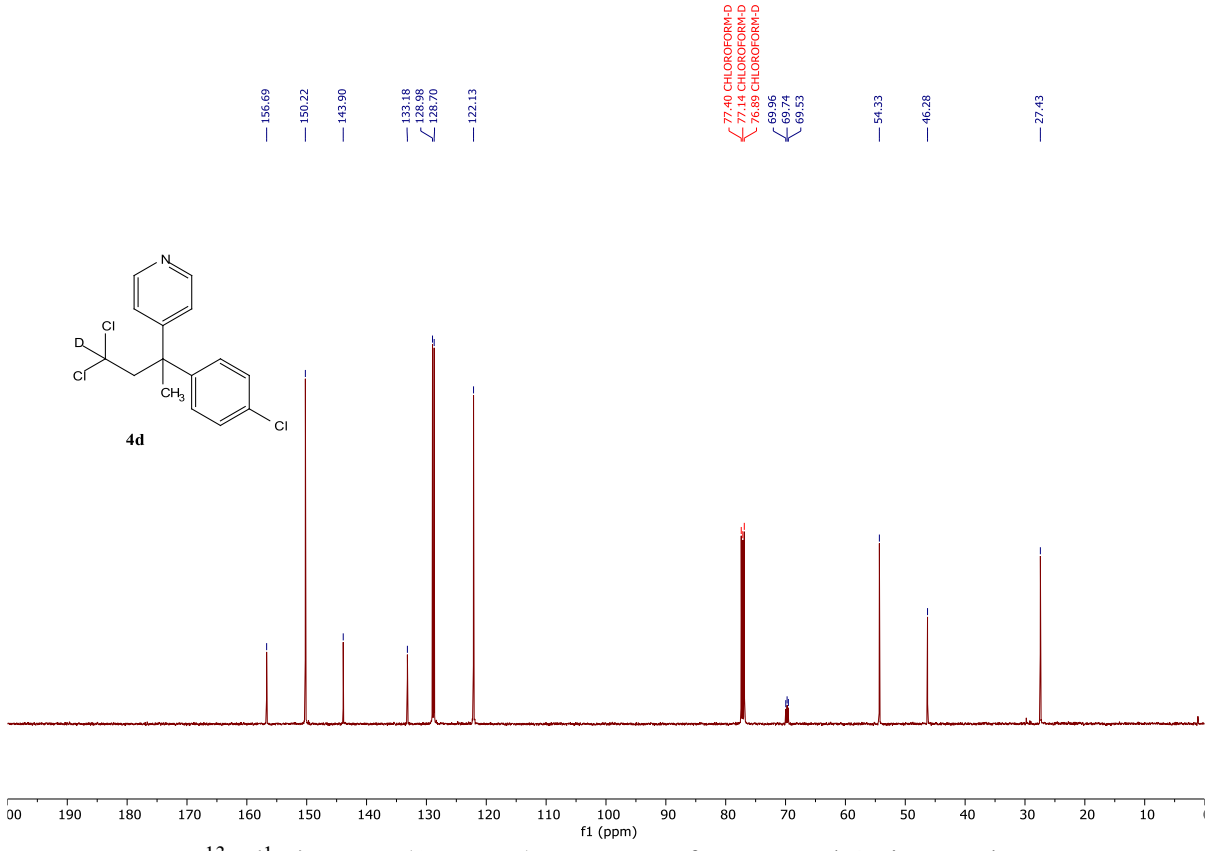
^{1}H NMR (400MHz) spectrum of compound **4c** in $CDCl_3$



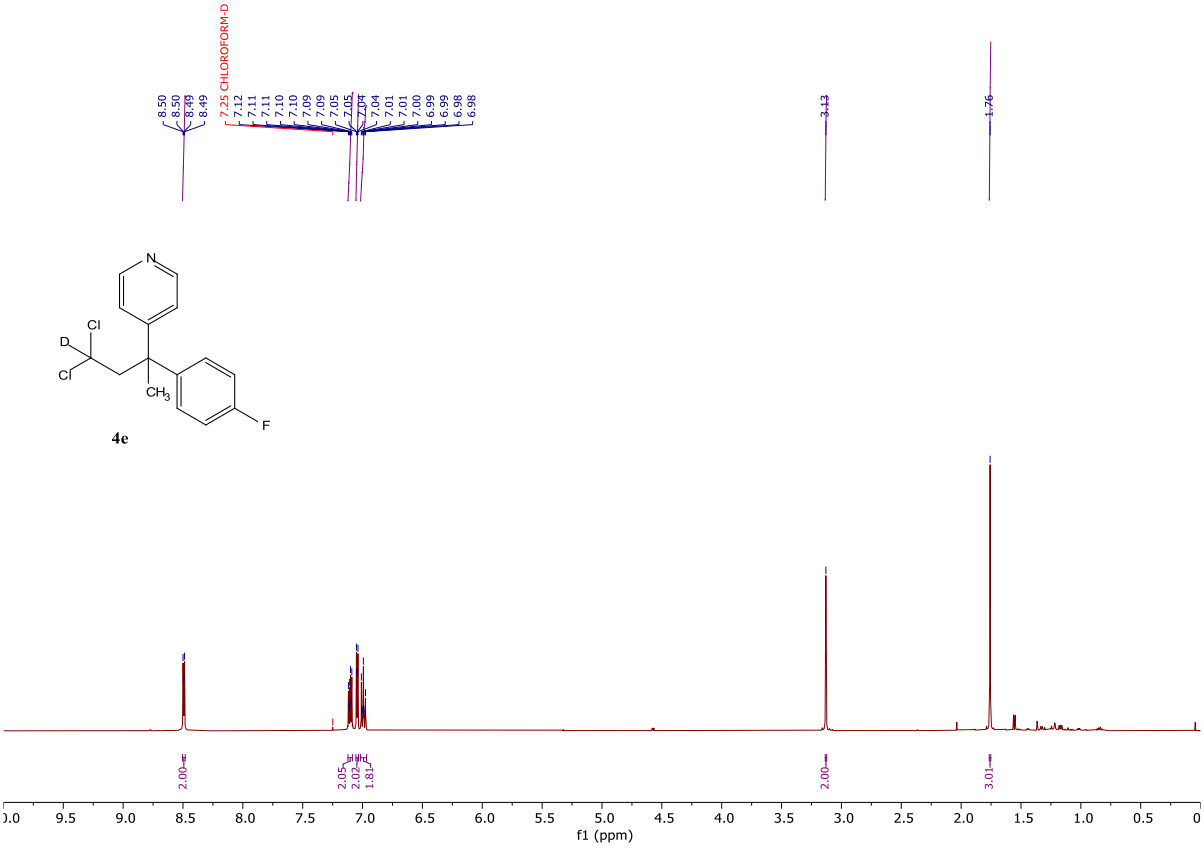
^{13}C{^{1}H} NMR (125MHz) spectrum of compound **4c** in $CDCl_3$



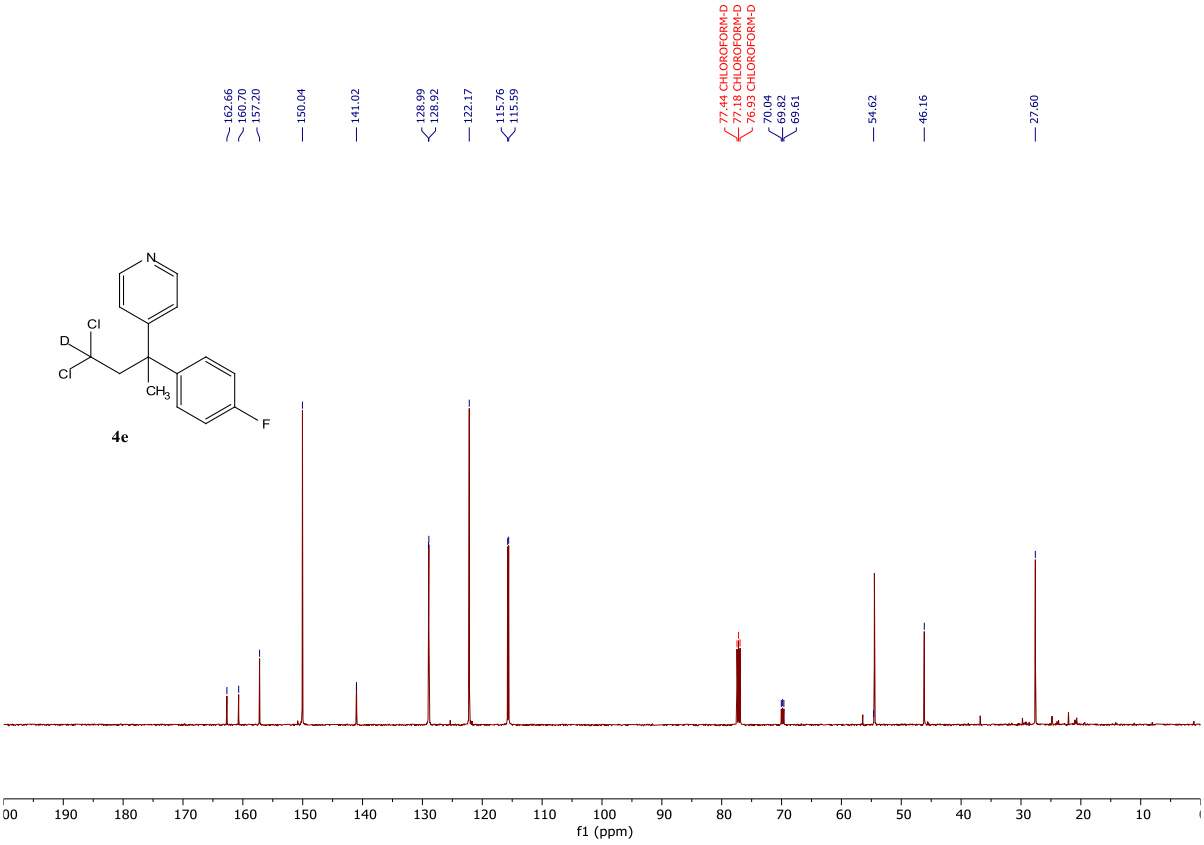
^{1}H NMR (400MHz) spectrum of compound **4d** in $CDCl_3$



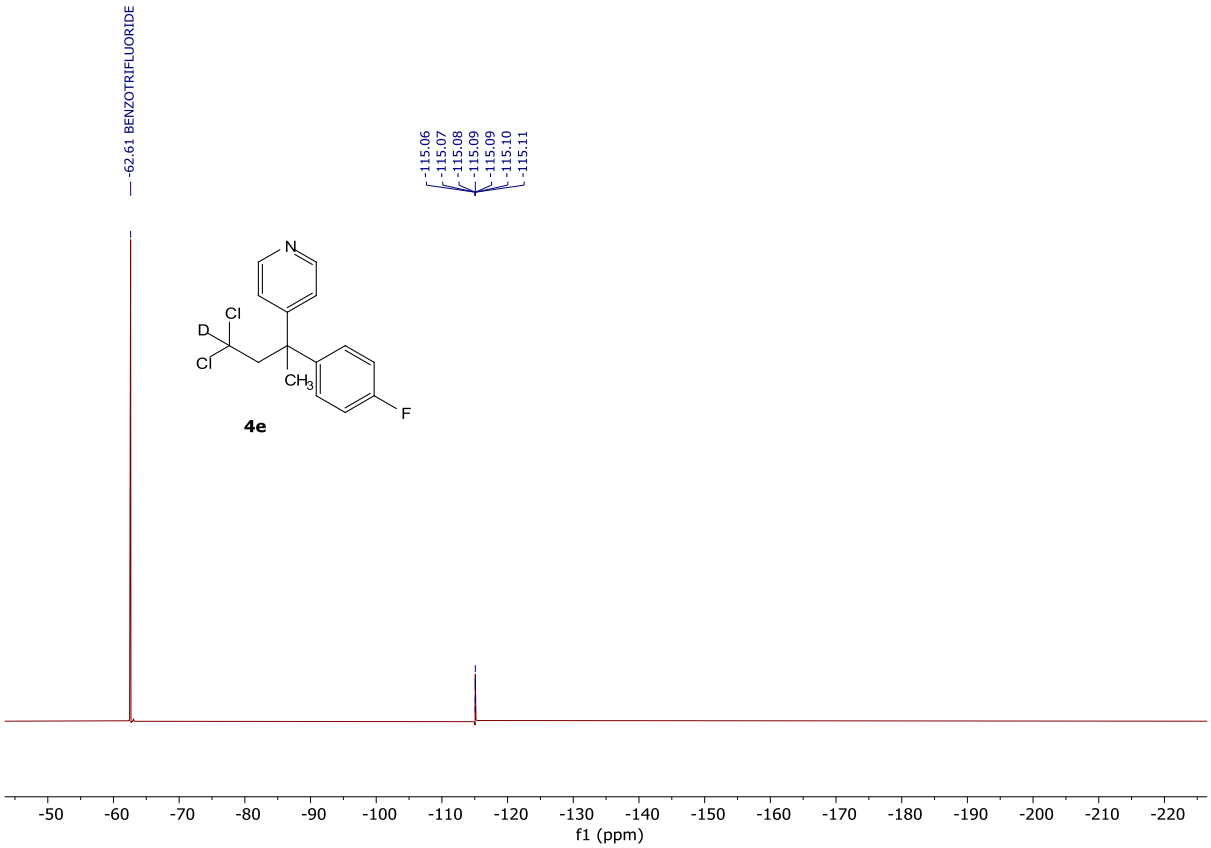
^{13}C{^{1}H} NMR (125MHz) spectrum of compound **4d** in $CDCl_3$



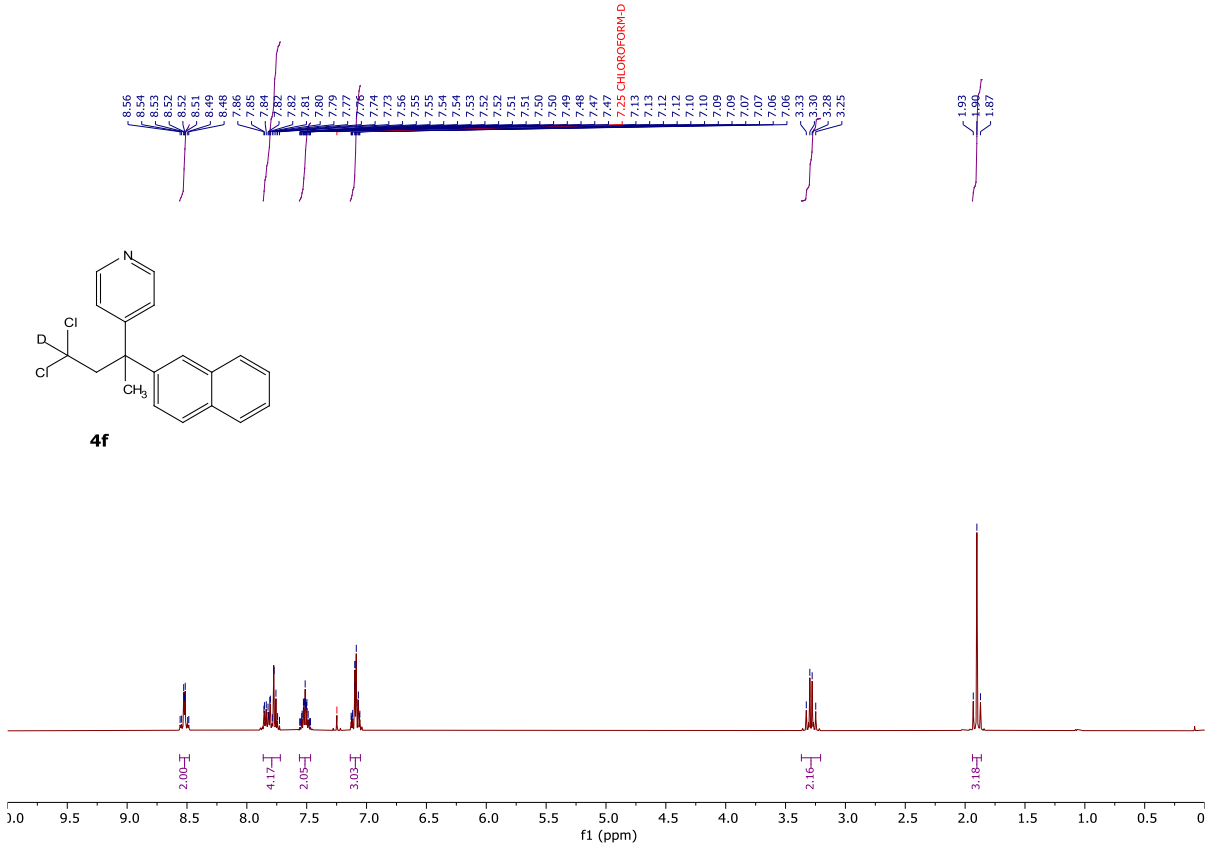
^{1}H NMR (400MHz) spectrum of compound **4e** in $CDCl_3$



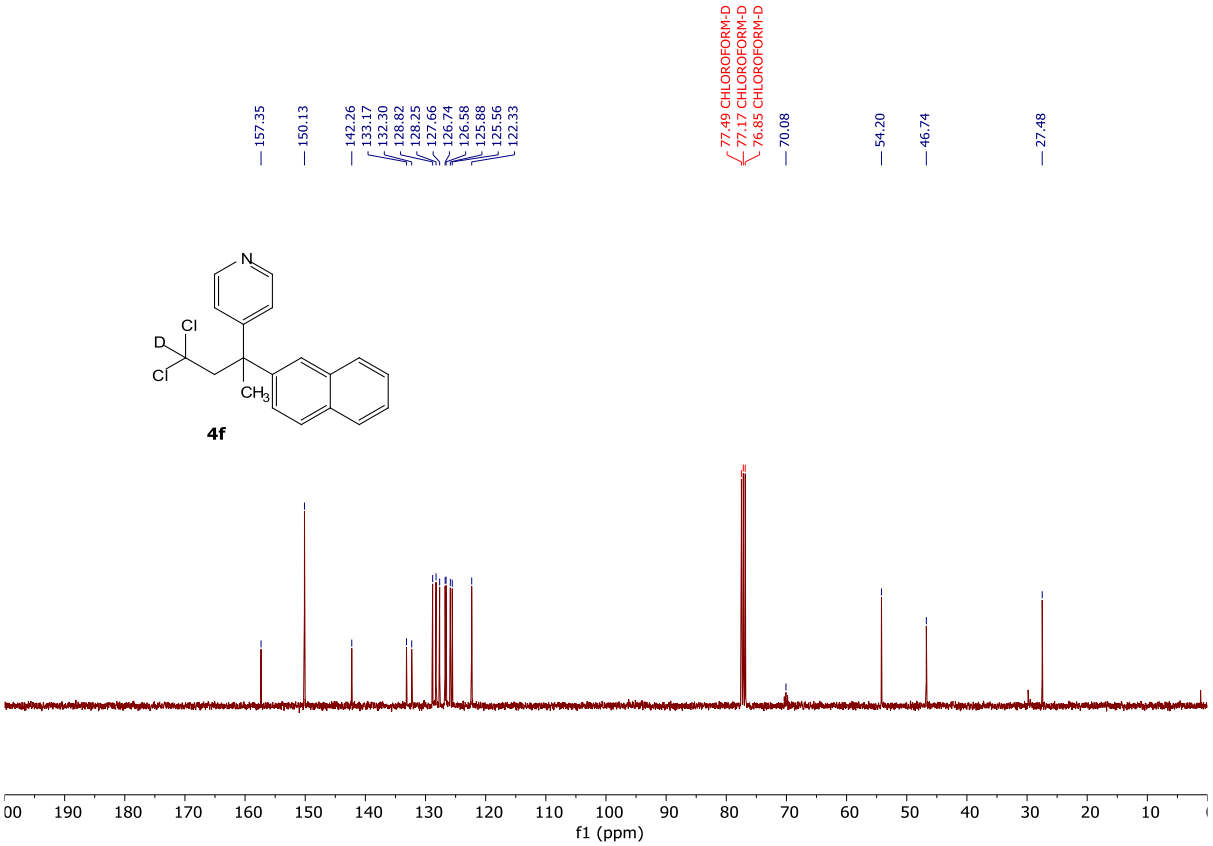
^{13}C{^{1}H} NMR (125MHz) spectrum of compound **4e** in $CDCl_3$



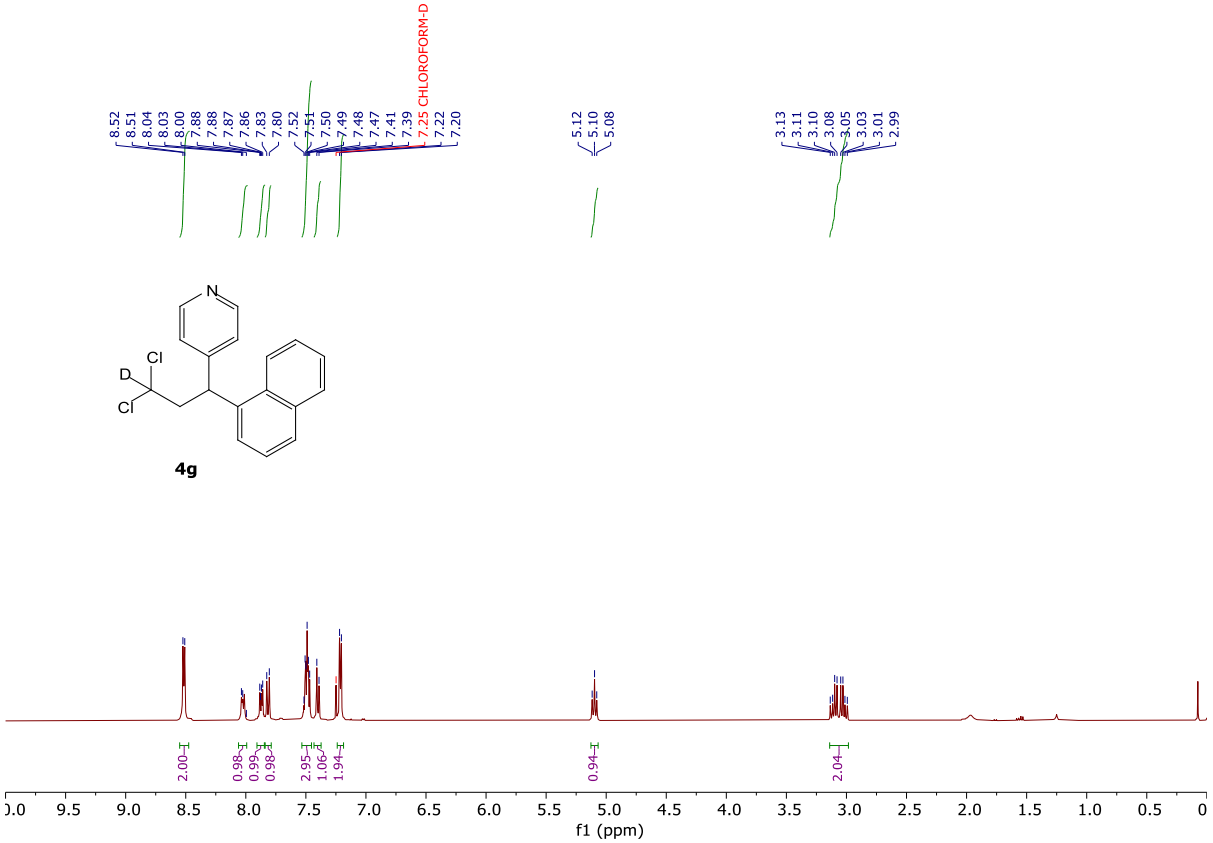
^{19}F NMR (471 MHz) spectrum of compound **4e** in $CDCl_3$



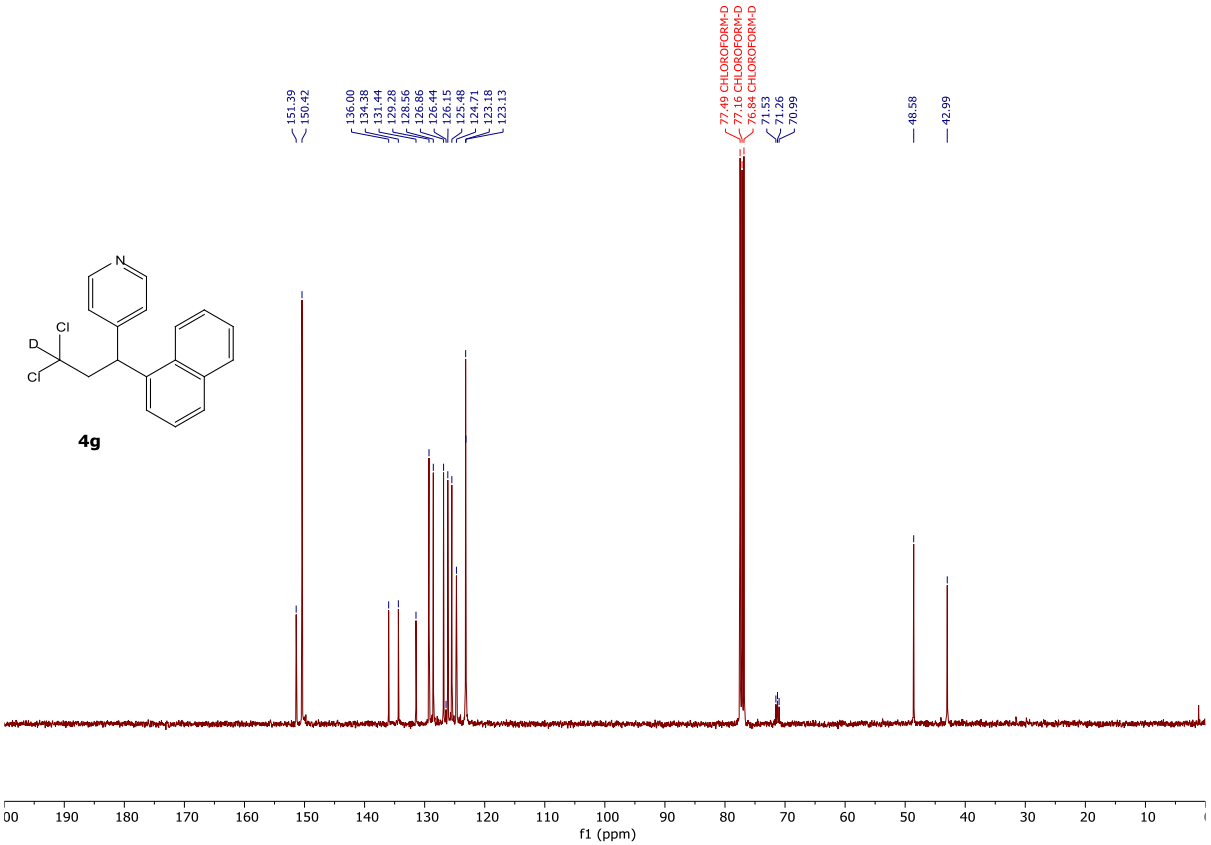
^{1}H NMR (400MHz) spectrum of compound **4f** in $CDCl_3$



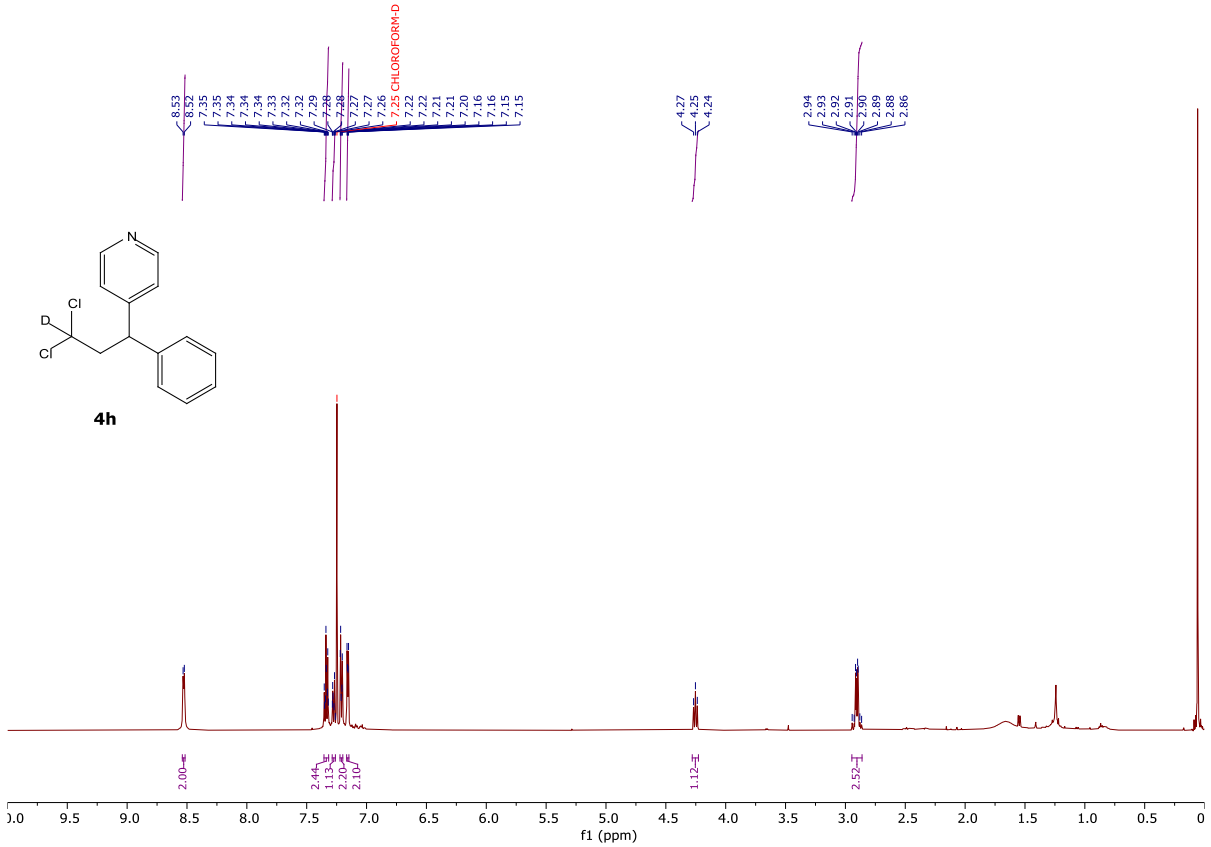
$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **4f** in $CDCl_3$



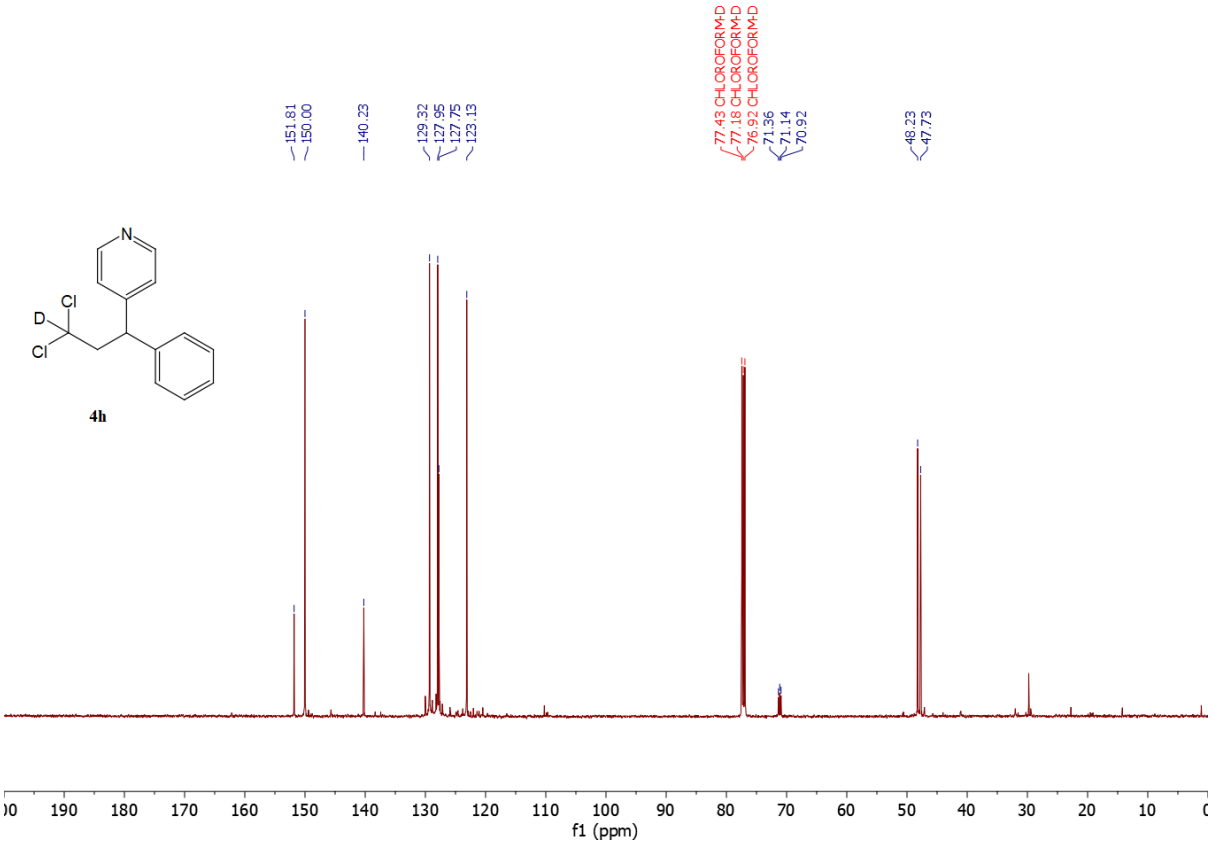
^{1}H NMR (400MHz) spectrum of compound **4g** in $CDCl_3$



^{13}C {^{1}H} NMR (125MHz) spectrum of compound **4g** in $CDCl_3$

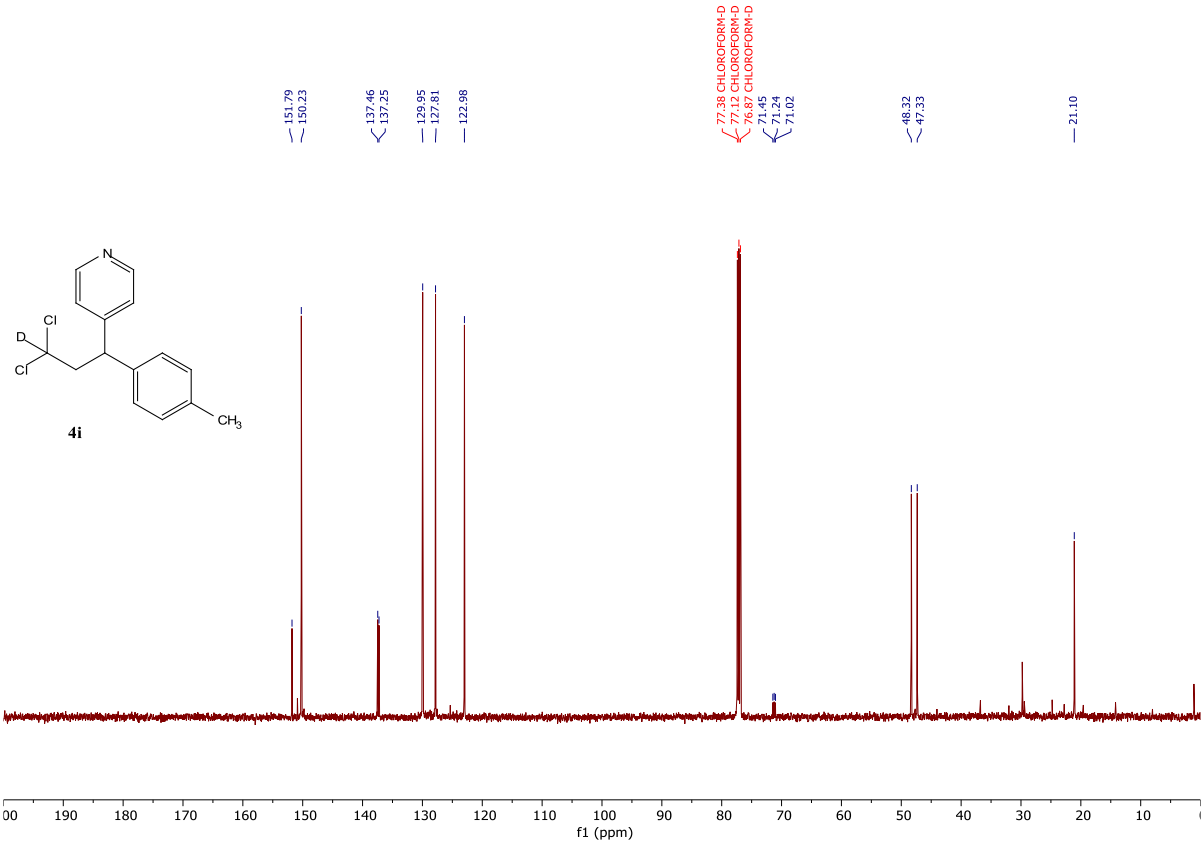


^{1}H NMR (400MHz) spectrum of compound **4h** in $CDCl_3$

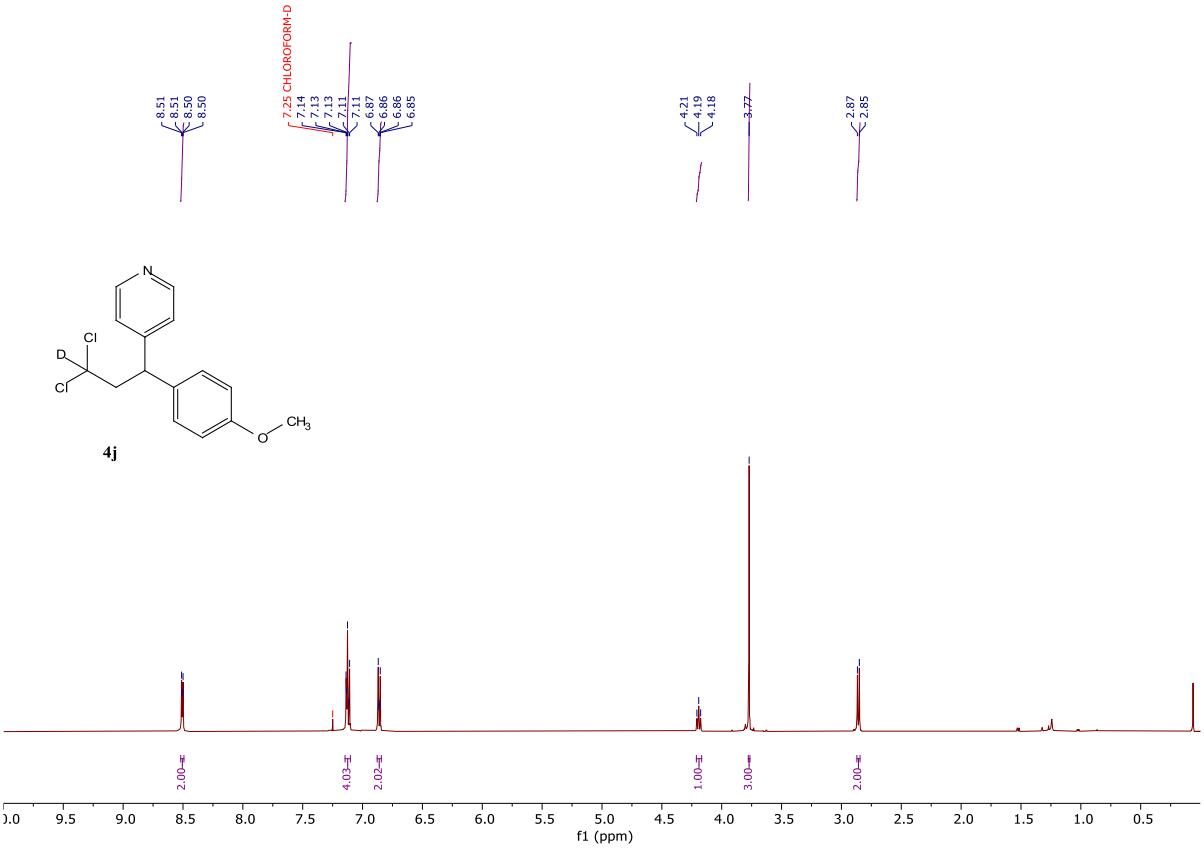


$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **4h** in $CDCl_3$

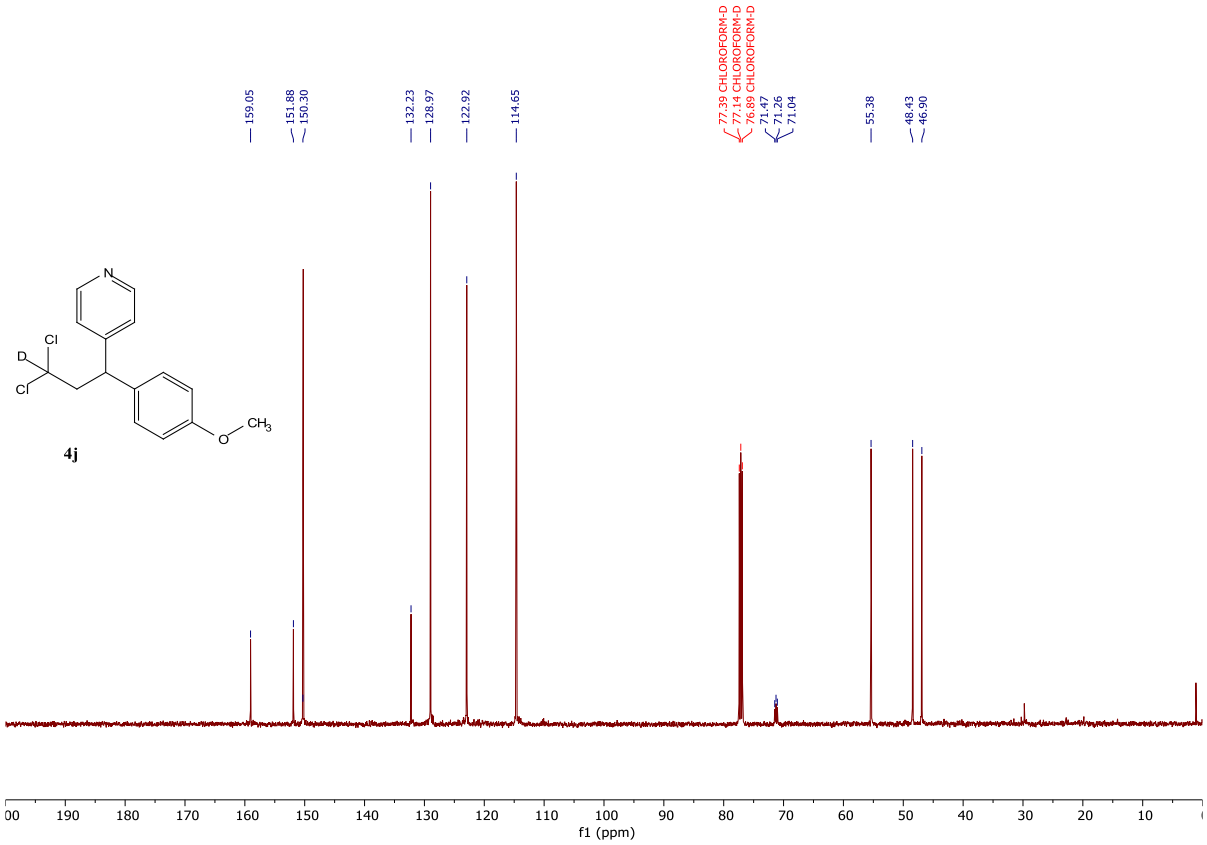
^{1}H NMR (400MHz) spectrum of compound **4i** in $CDCl_3$



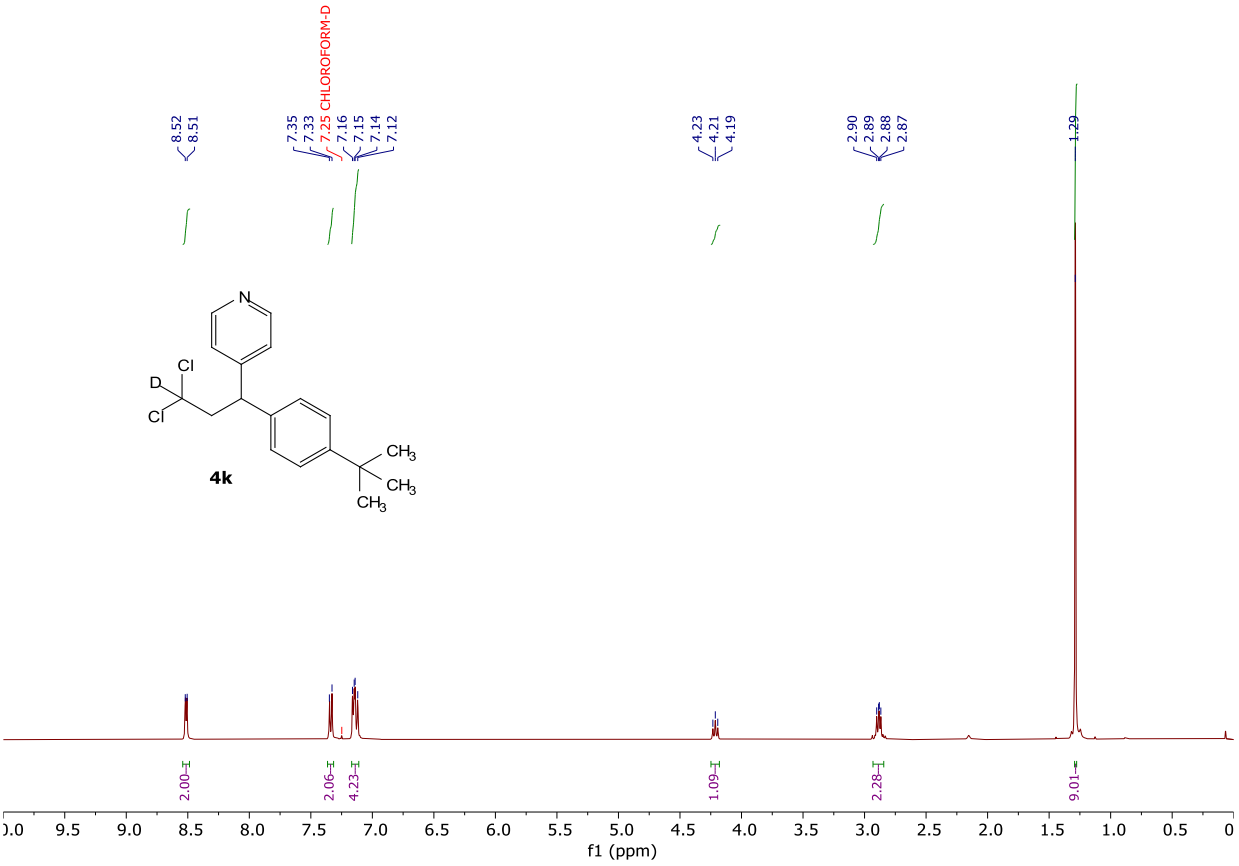
$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **4i** in $CDCl_3$



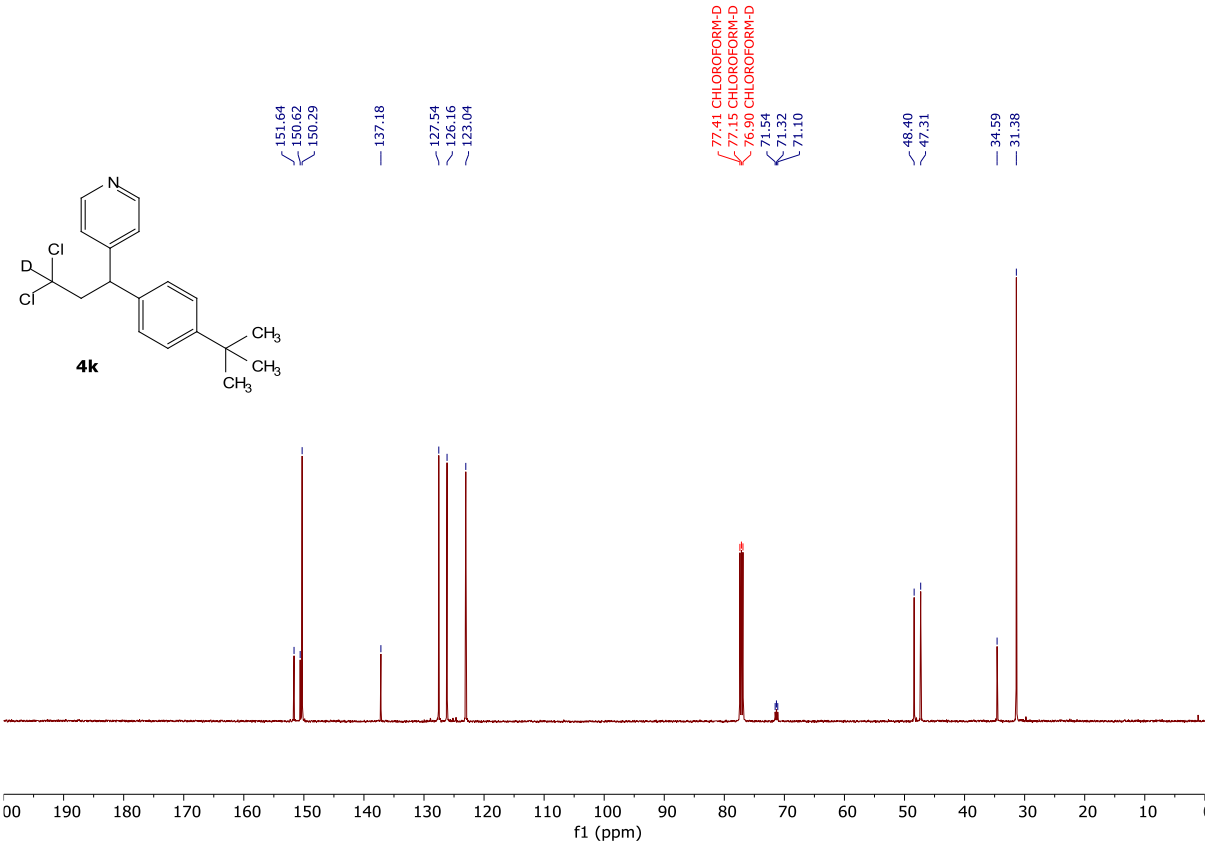
^{1}H NMR (400MHz) spectrum of compound **4j** in $CDCl_3$



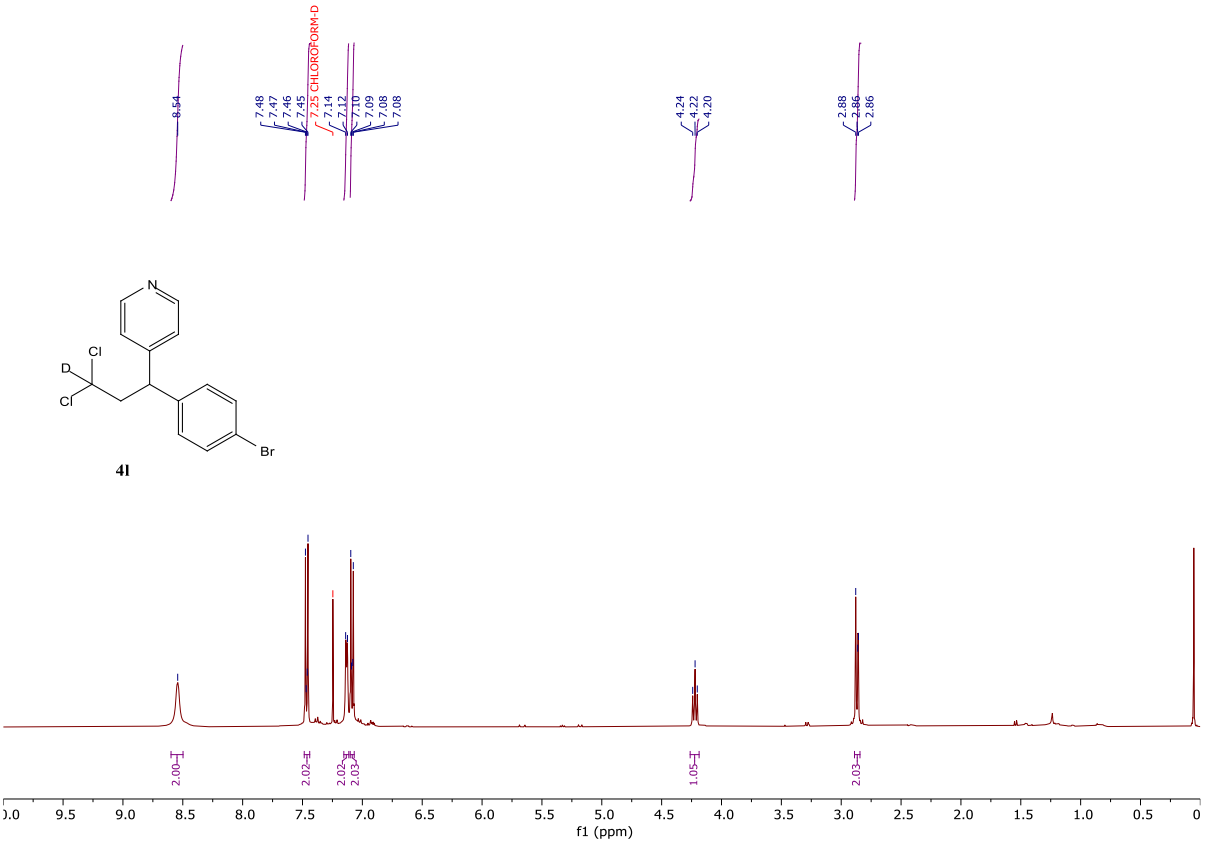
$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **4j** in $CDCl_3$



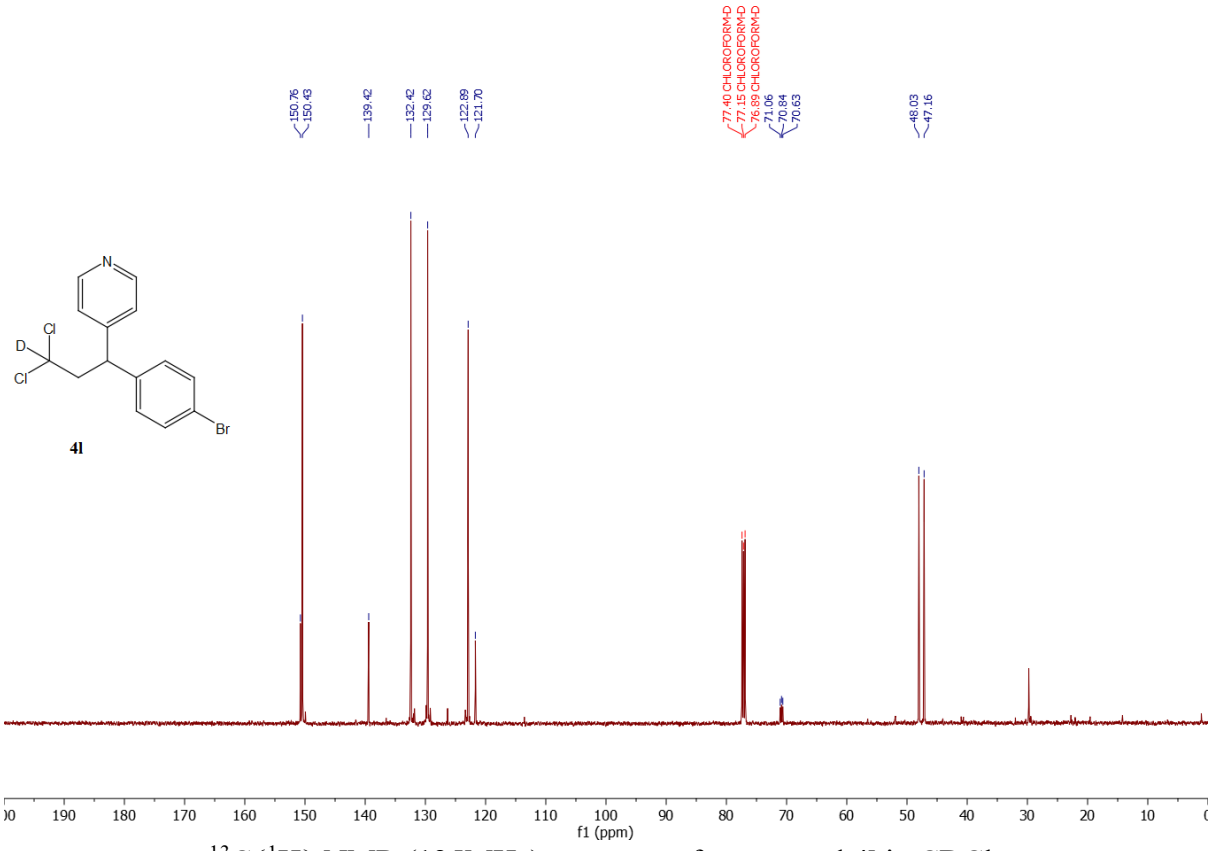
^{1}H NMR (400MHz) spectrum of compound **4k** in $CDCl_3$



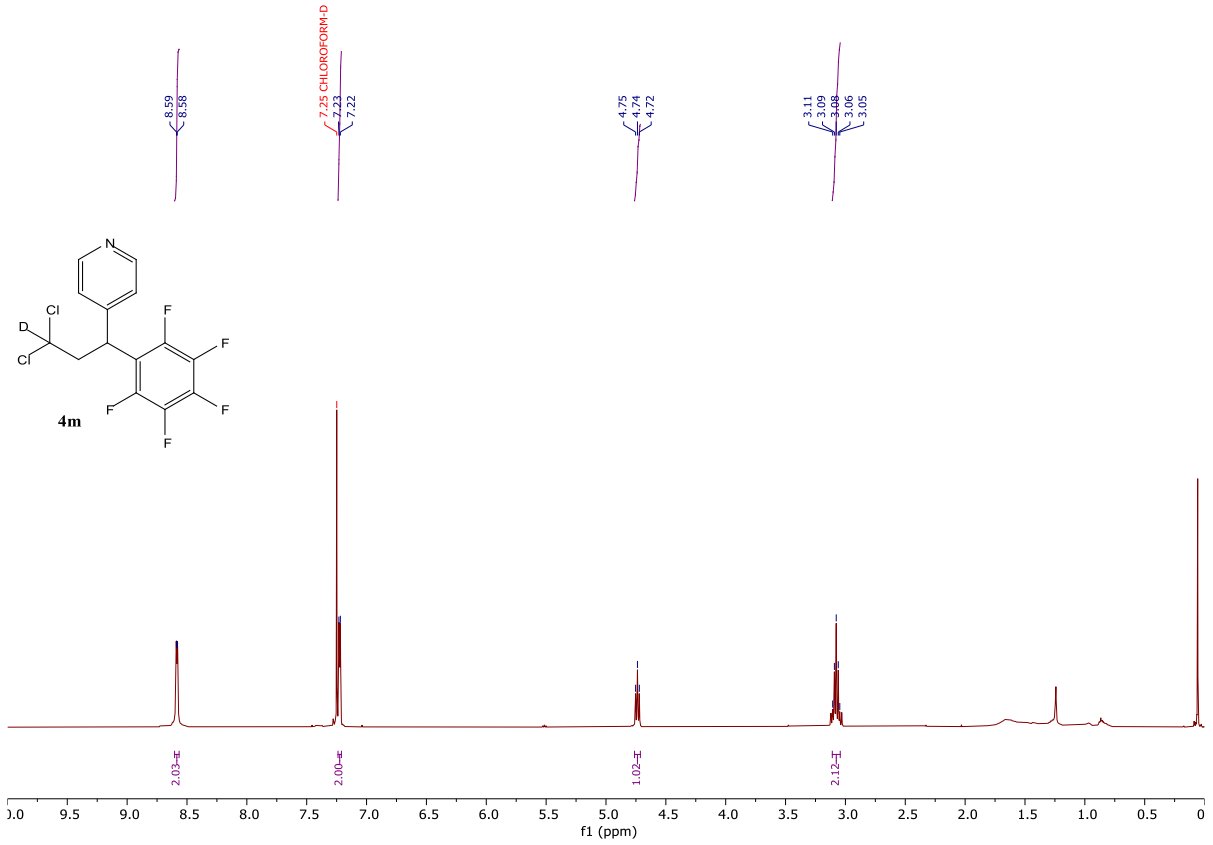
^{13}C {^{1}H} NMR (125MHz) spectrum of compound **4k** in $CDCl_3$



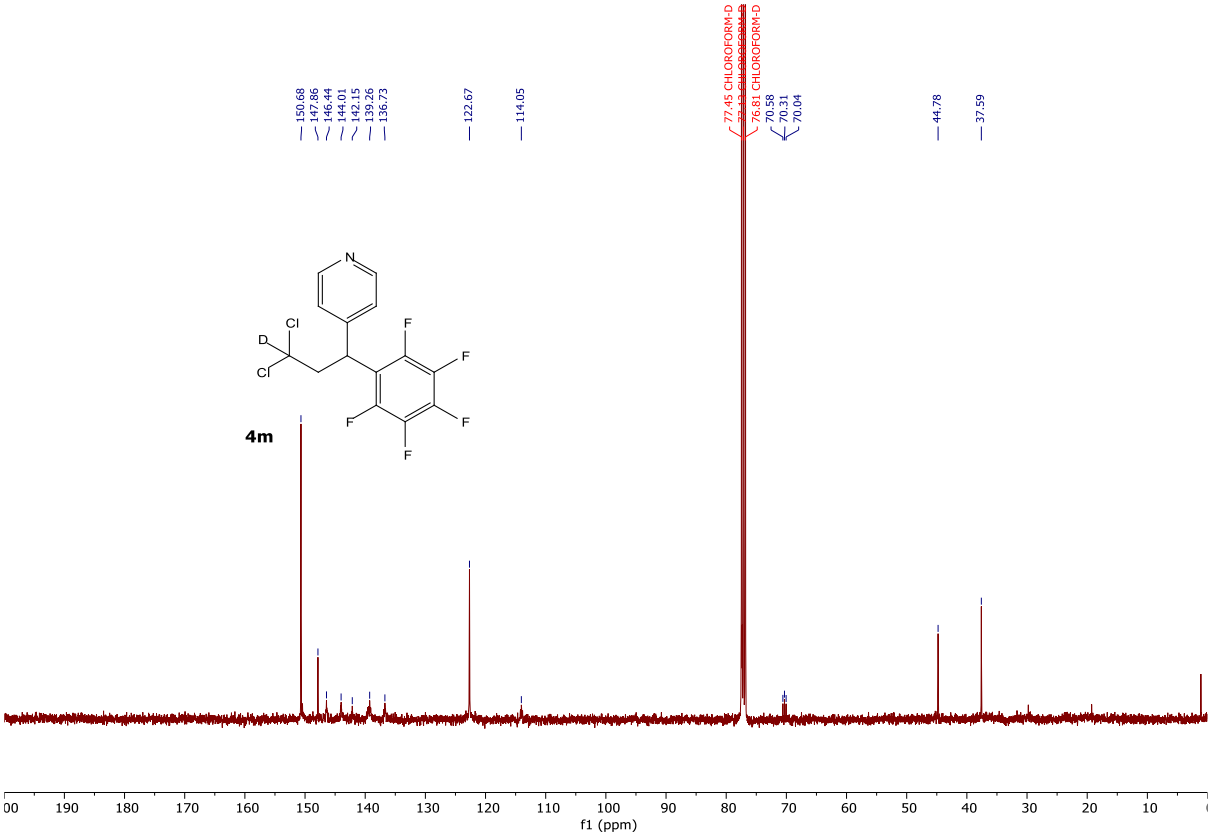
^{1}H NMR (400MHz) spectrum of compound **4l** in $CDCl_3$



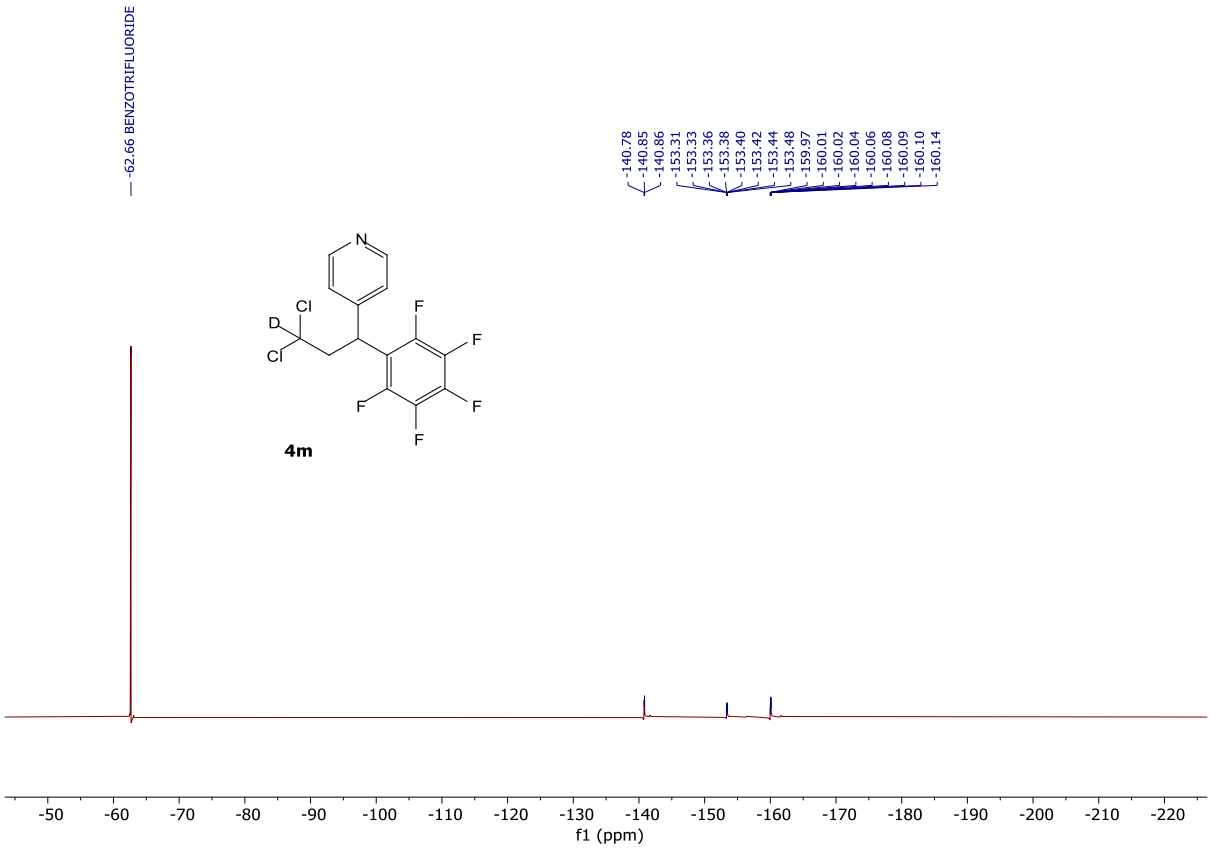
$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **4l** in $CDCl_3$



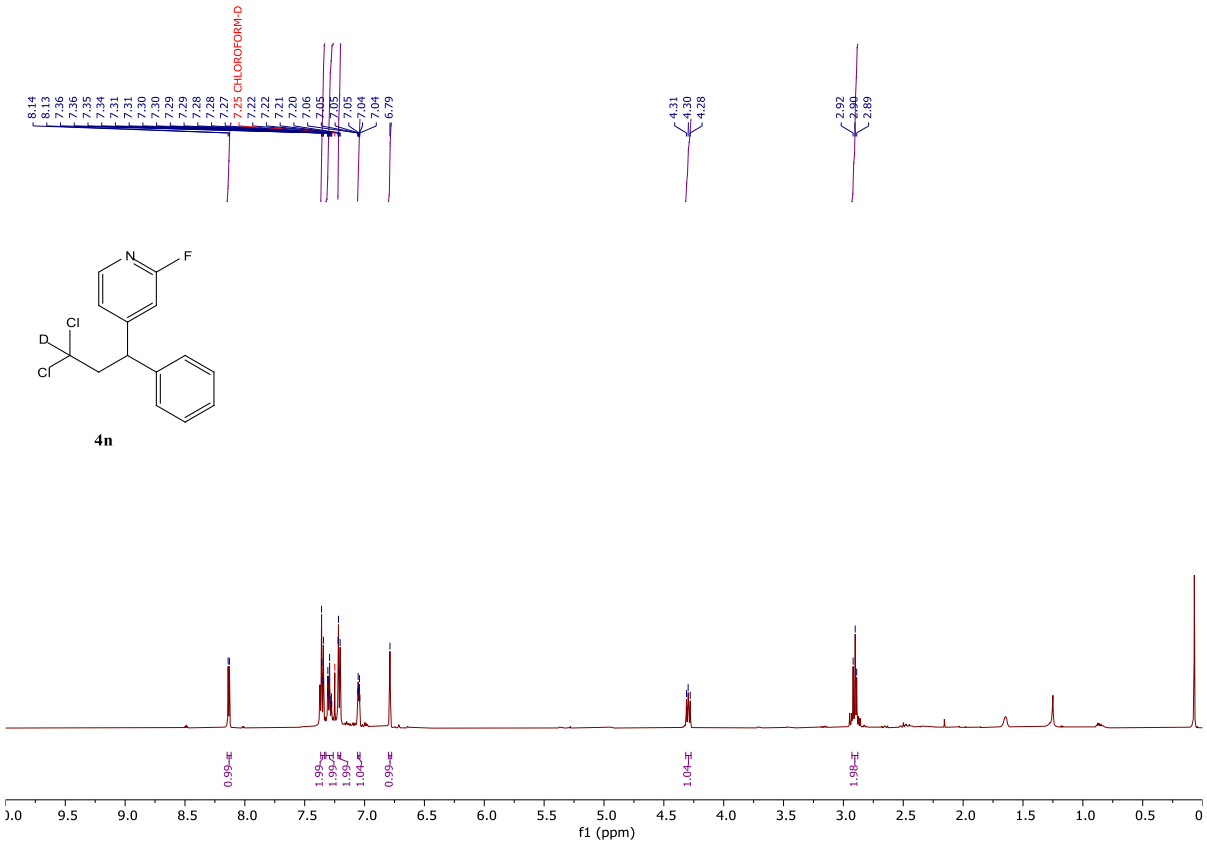
^{1}H NMR (400MHz) spectrum of compound **4m** in $CDCl_3$



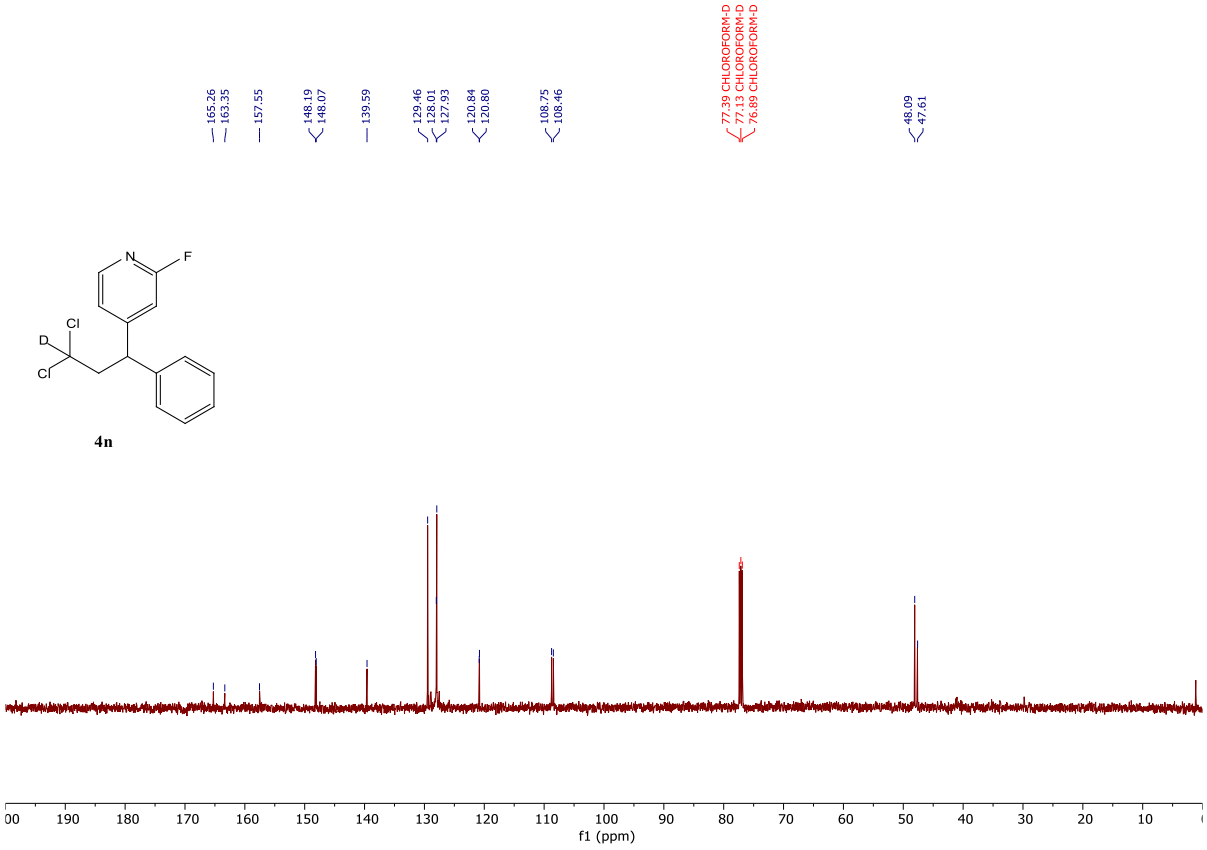
$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **4m** in $CDCl_3$



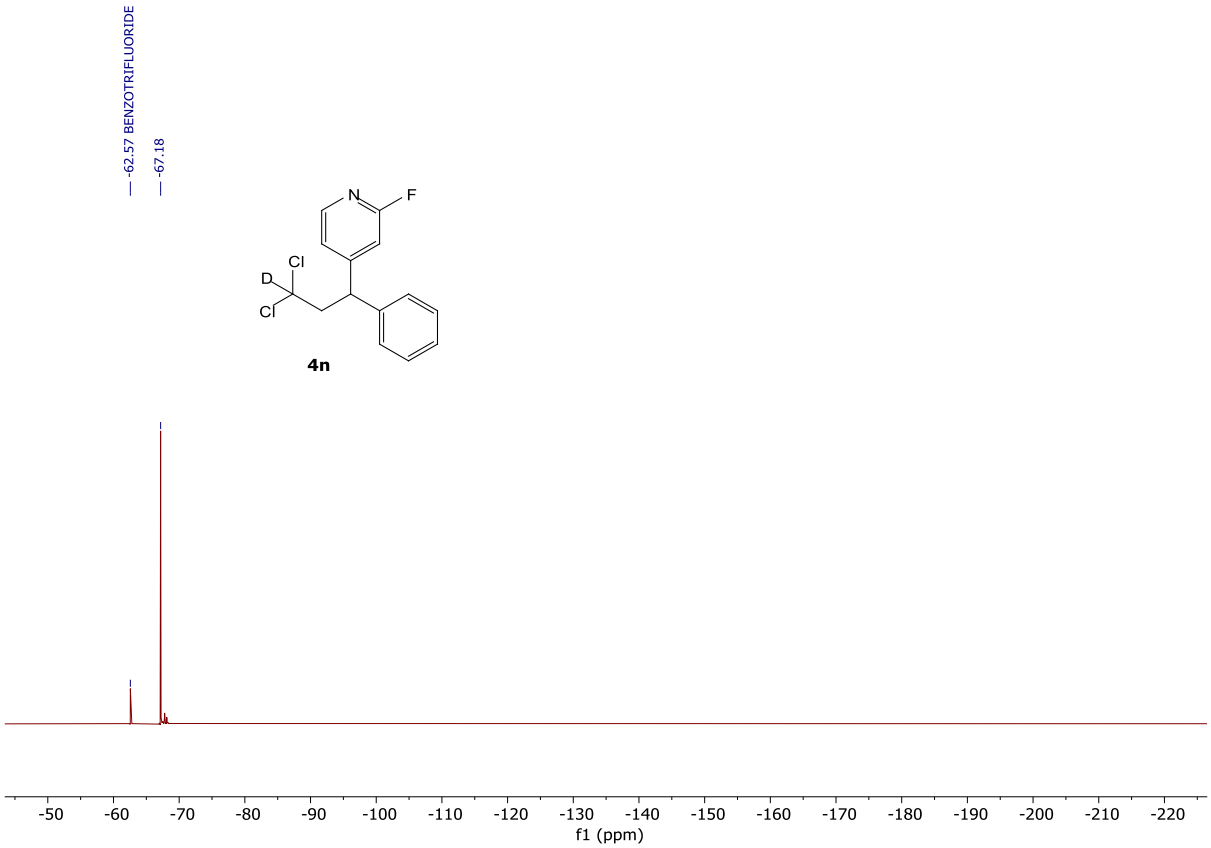
^{19}F NMR (471 MHz) spectrum of compound **4m** in $CDCl_3$



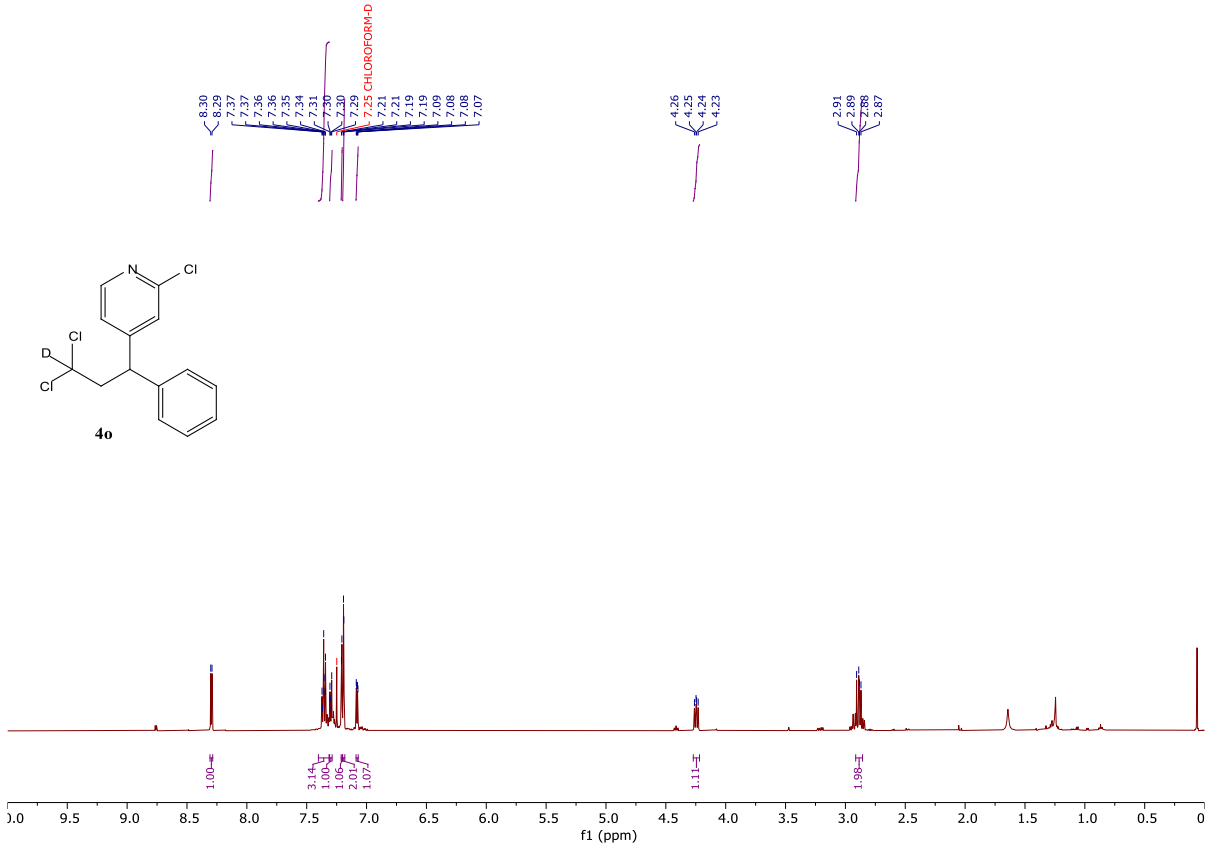
^{1}H NMR (400MHz) spectrum of compound **4n** in $CDCl_3$



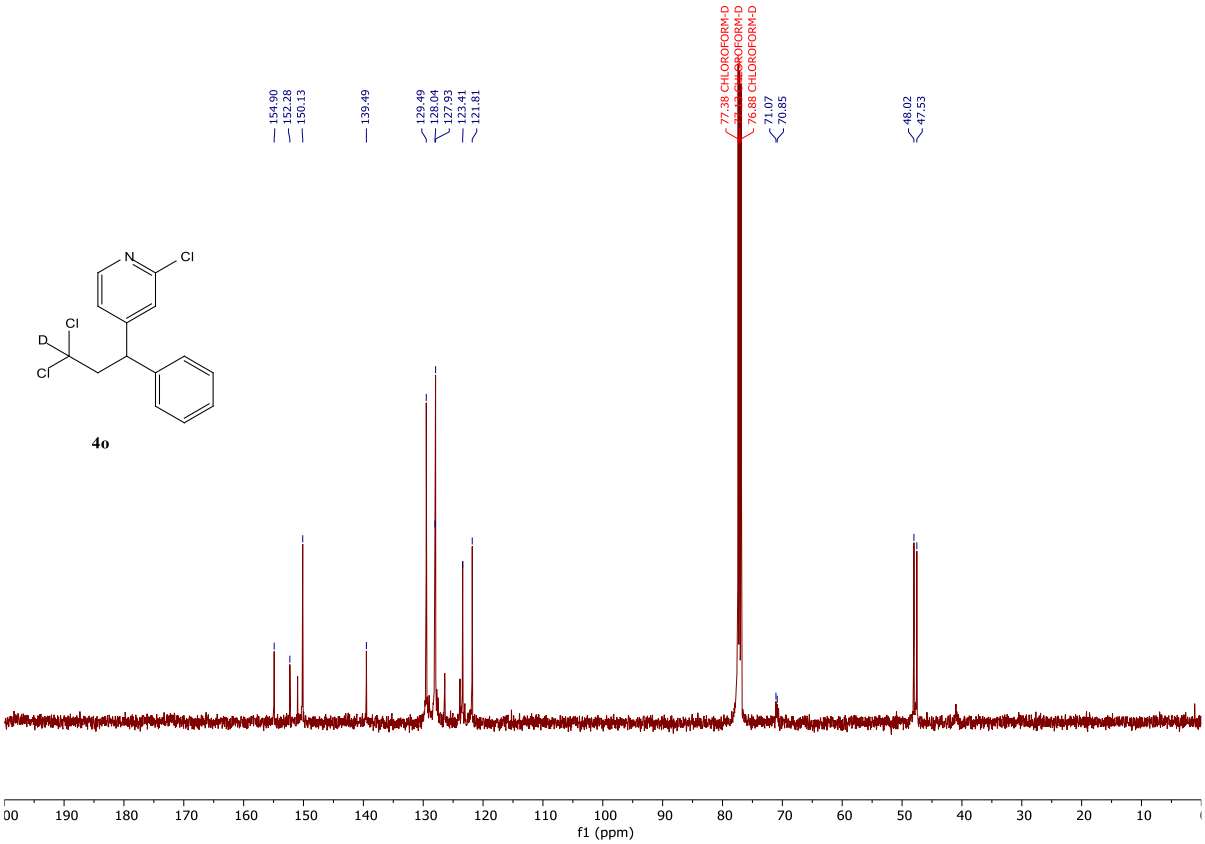
^{13}C{^{1}H} NMR (125MHz) spectrum of compound **4n** in $CDCl_3$



^{19}F NMR (471 MHz) spectrum of compound **4n** in $CDCl_3$

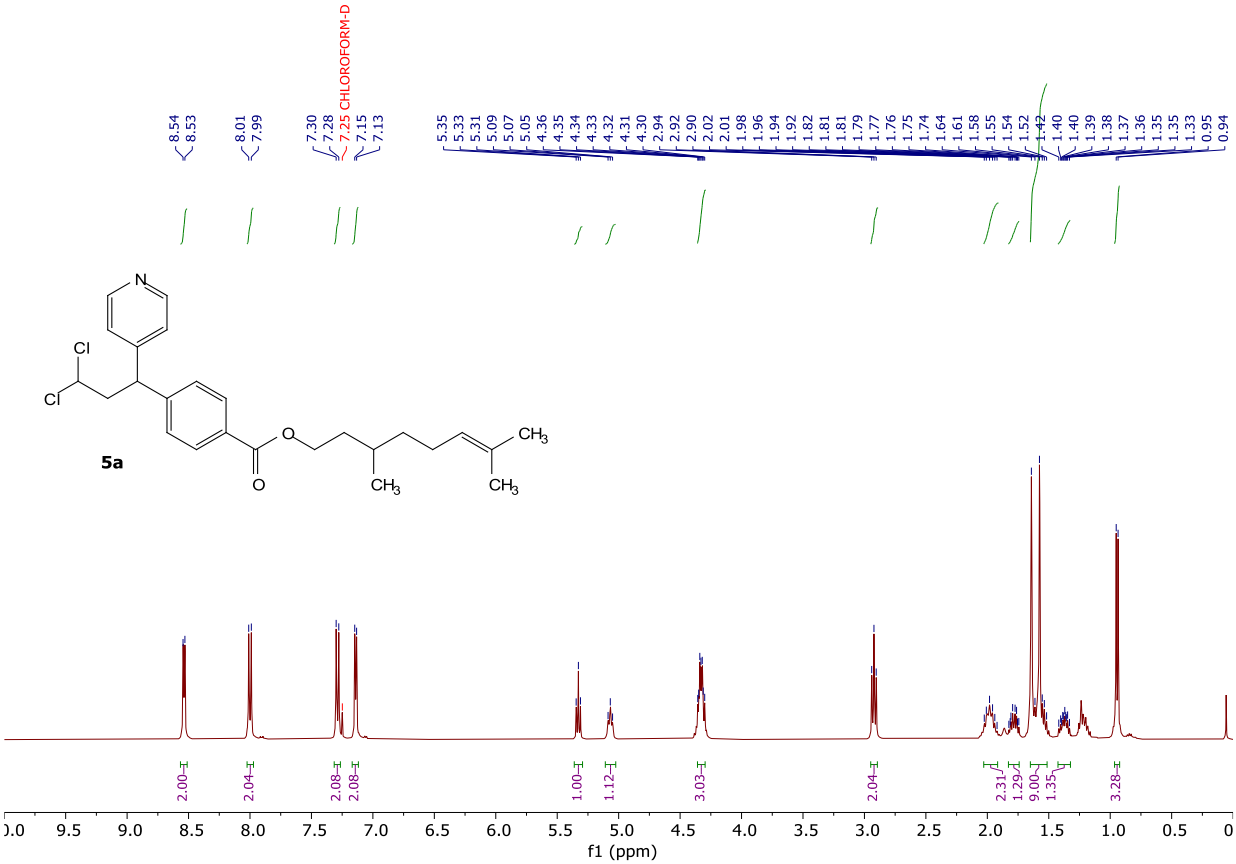


^{1}H NMR (400MHz) spectrum of compound **4o** in $CDCl_3$



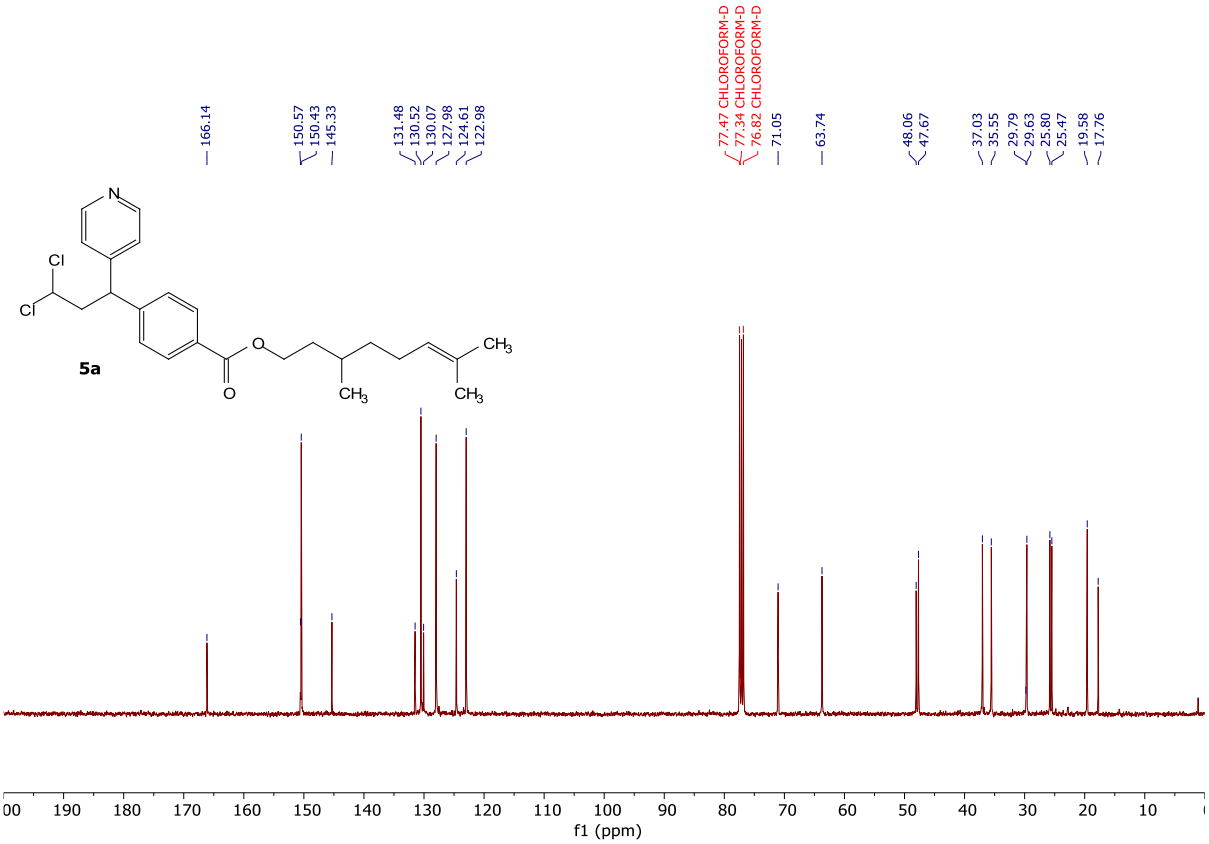
4o

$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **4o** in $CDCl_3$

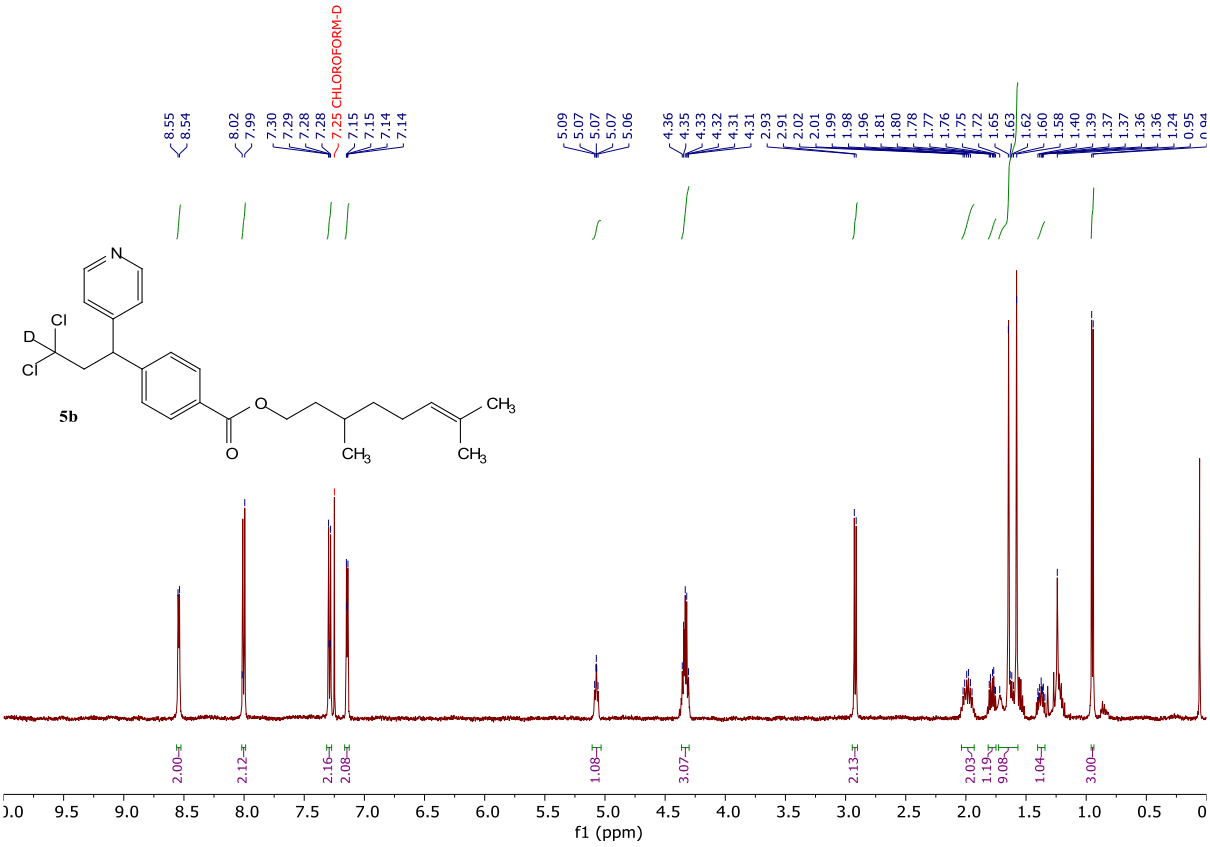


5a

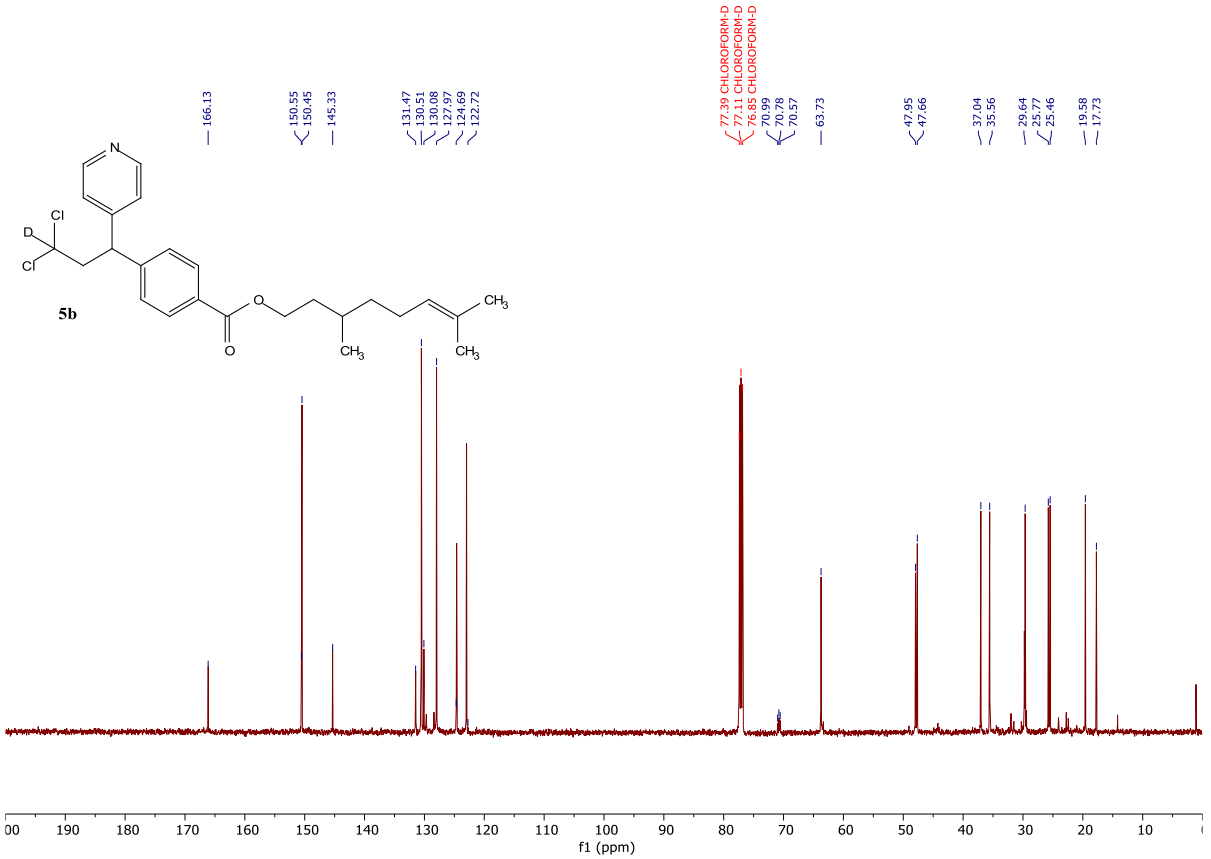
^{1}H NMR (400MHz) spectrum of compound **5a** in $CDCl_3$



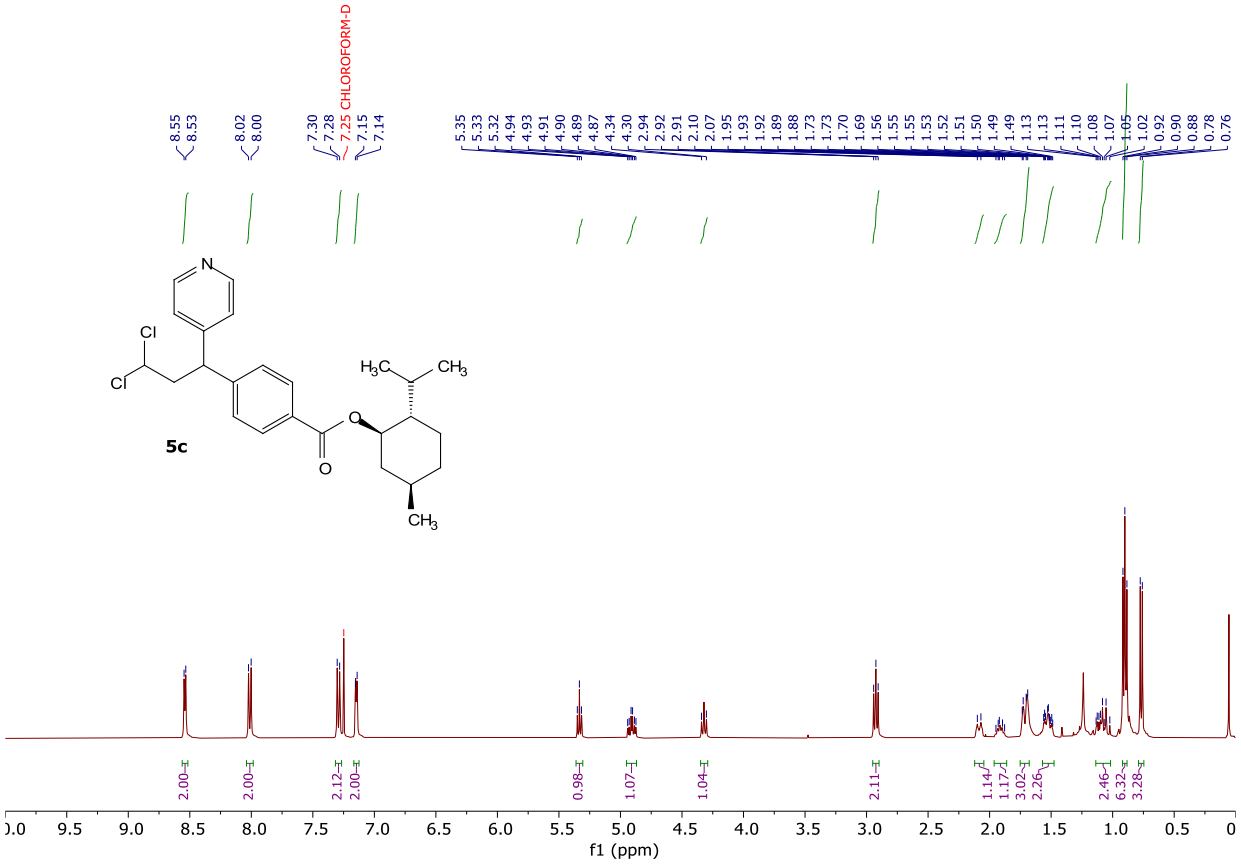
$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **5a** in $CDCl_3$



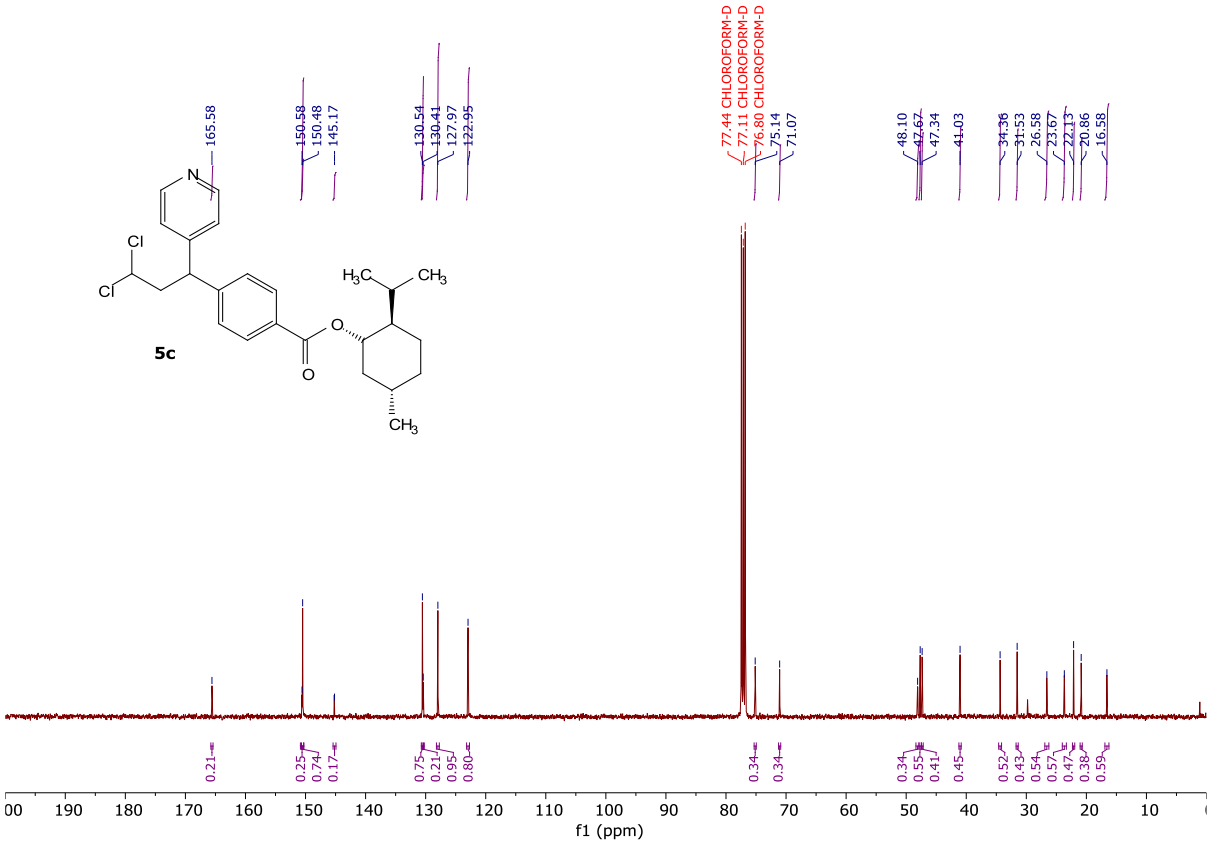
^{1}H NMR (400MHz) spectrum of compound **5b** in $CDCl_3$



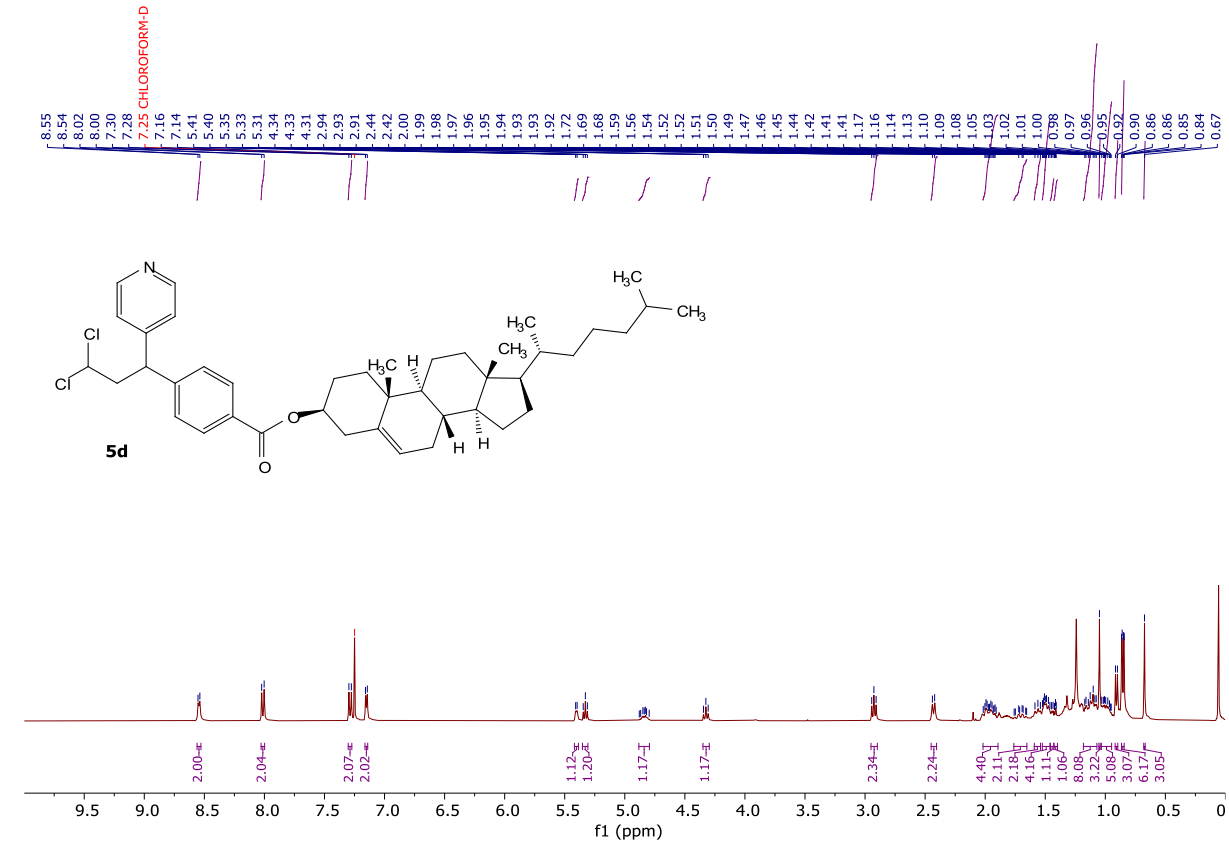
$^{13}C\{^{1}H\}$ NMR (125MHz) spectrum of compound **5b** in $CDCl_3$



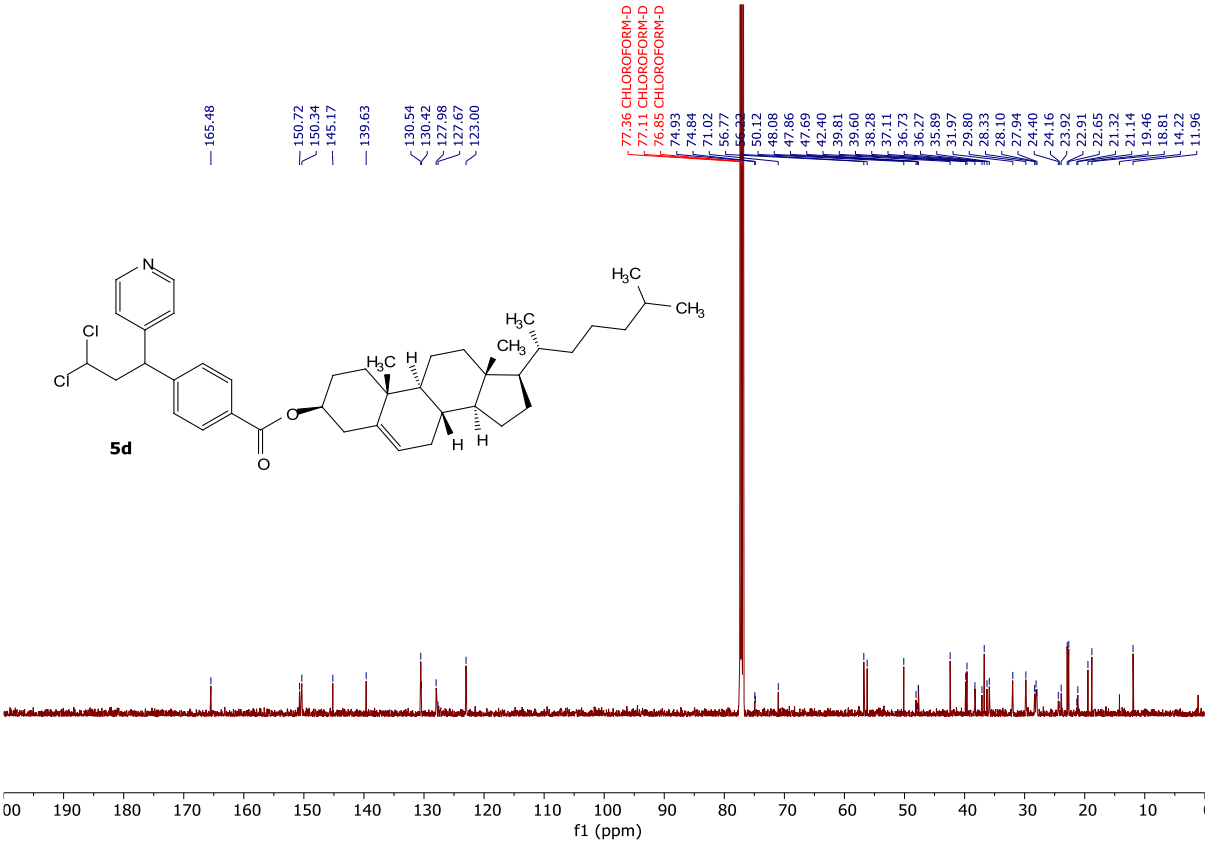
^{1}H NMR (400MHz) spectrum of compound **5c** in $CDCl_3$



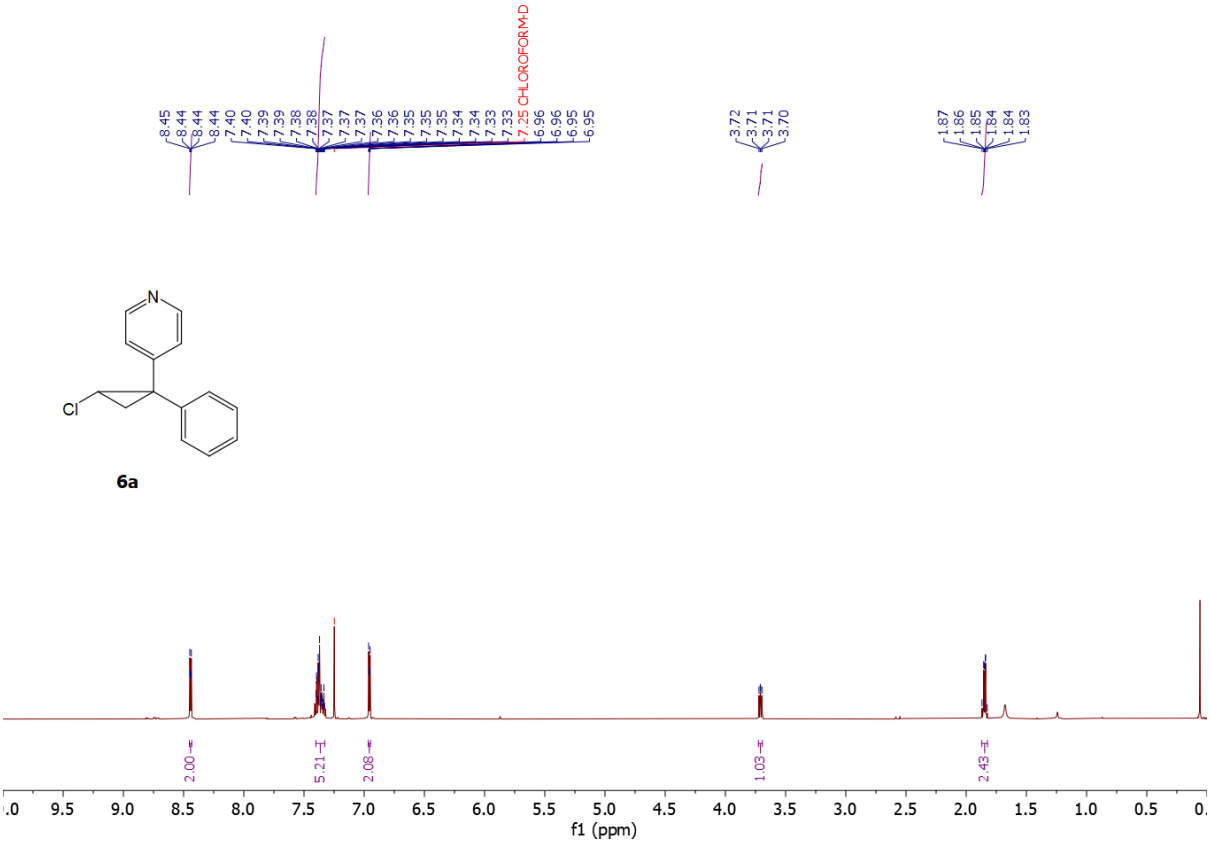
^{13}C {^{1}H} NMR (125MHz) spectrum of compound **5c** in $CDCl_3$



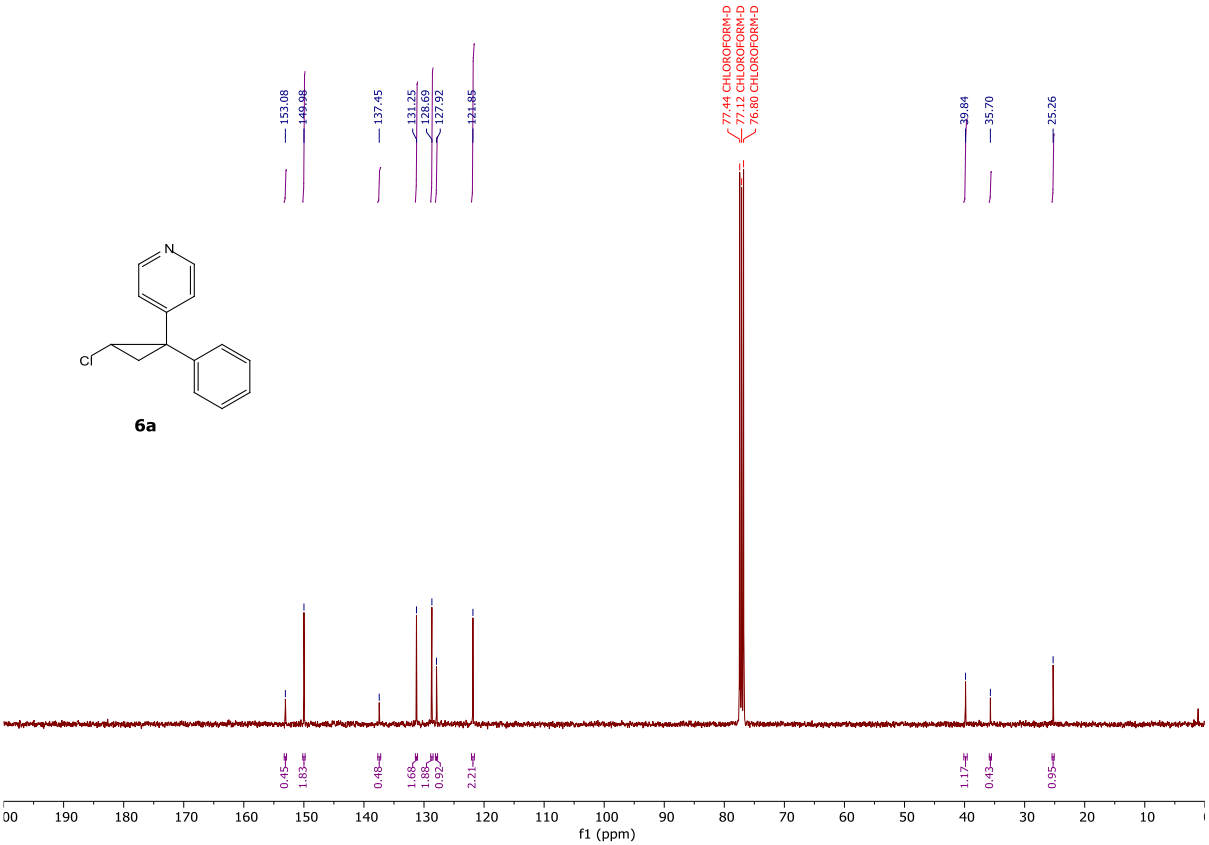
^{1}H NMR (400MHz) spectrum of compound **5d** in $CDCl_3$



^{13}C {^{1}H} NMR (125MHz) spectrum of compound **5d** in $CDCl_3$



^{1}H NMR (400MHz) spectrum of compound **6a** in $CDCl_3$



^{13}C {^{1}H} NMR (125MHz) spectrum of compound **6a** in $CDCl_3$