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Radical Trideuteromethylation in the Synthesis of Heterocycles and Labelled Building Blocks

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General

Unless otherwise noted, all commercially available compounds were used as provided without further purification. Solvents for chromatography were technical grade. Analytical thin-layer chromatography (TLC) was performed on Merck silica gel aluminium plates with F-254 indicator. Compounds were visualized by irradiation with UV light or potassium permanganate staining. Column chromatography was performed using silica gel Merck 60 (particle size 0.040-0.063 mm). Solvent mixtures are understood as volume/volume. ^{1}H-NMR and ^{13}C-NMR were recorded on a Bruker DRX500 (500 MHz) and Bruker DRX600 (600 MHz) using CDCl3, CD_3OD or DMSO-$d_6$as solvent. Data are reported in the following order: chemical shift (δ) values are reported in ppm with the solvent resonance as internal standard (CDCl3: δ = 7.26 ppm for ^{1}H, δ = 77.16 ppm for ^{13}C; CD_3OD: δ = 3.31 ppm for ^{1}H, δ = 49.00 ppm for ^{13}C; DMSO-d_6: δ = 2.50 ppm for ^{1}H, δ = 39.52 ppm for ^{13}C); multiplicities are indicated br s (broadened singlet), s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), quin (quintet); coupling constants (*J*) are given in Hertz (Hz). High resolution mass spectra were recorded on a LTQ Orbitrap mass spectrometer coupled to an Acceka HPLC-System (HPLC column: Hypersyl GOLD, 50 mm x 1 mm, particle size 1.9 µm, ionization method: electron spray ionization). Fourier transform infrared spectroscopy (FT-IR) spectra were obtained with a Bruker Tensor 27 spectrometer (ATR, neat) and are reported in terms of frequency of absorption (cm^{-1}).

Method Afor the preparation of Trideuteromethylated compounds (2b-2k)

To a screw capped reaction vial containing quinoline or isoquinoline (0.5 mmol) in DMSO-d_6 (1 mL) $FeCl_2$ (0.25 mmol) and TFA (0.75 mmol) were added. Then H_2O_2 (30 % in water) (2.50 mmol) was added slowly and portion-wise and the reaction was stirred at room temperature under air until full conversion monitored by TLC and GC-MS. Afterwards residual trifluoacetic acid was neutralized by adding NEt_3 (1 mmol) and the reaction mixture was diluted with water. The aqueous phase was extracted three times with ethyl acetate and the combined organic layers were dried over $MgSO_4$. Subsequently, column chromatography of the reaction mixture provided the pure product using petroleum ether/EtOAc or dichloromethane/MeOH as eluent system.

Method B for the preparation of Trideuteromethylated compounds (4a-4j, 8)

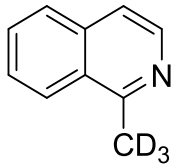
To a screw capped reaction vial containing *N*-arylacrylamide (0.2 mmol) in DMSO-d_6 (1 mL) $FeCl_2$ (0.10 mmol) and TFA (0.20 mmol) were added. Then H_2O_2 (30 % in water) (1 mmol) was added slowly and portion-wise and the reaction was stirred at room temperature under air until full conversion monitored by TLC and GC-MS. Afterwards residual trifluoacetic acid was neutralized by adding NEt_3 (0.50 mmol) and the reaction mixture was diluted with water. The aqueous phase was extracted three times with ethyl acetate and the combined organic layers were dried over $MgSO_4$. Subsequently, column chromatography of the reaction mixture provided the pure product using petroleum ether/EtOAc as eluent system.

Method C for the preparation of Trideuteromethylated compounds (6a-6d)

To a screw capped reaction vial containing activated alkenes (0.5 mmol) in DMSO-d_6 (1 mL) $FeCl_2$ (0.25 mmol) and TFA (0.75 mmol) were added. Then H_2O_2 (30 % in water) (2.50 mmol) was added slowly and portion-wise and the reaction was stirred at room temperature under air until full conversion monitored by TLC and GC-MS. Afterwards residual trifluoacetic acid was neutralized by adding NEt_3 (1 mmol) and the reaction mixture was diluted with water. The aqueous phase was extracted three times with ethyl acetate and the combined organic layers were dried over $MgSO_4$. Subsequently, column chromatography of the reaction mixture provided the pure product using petroleum ether/EtOAc as eluent system.

Characterization of products

Substrates were prepared according to literature procedure[1].



(2b)

1-[$^2H_3$]-Methylisoquinoline

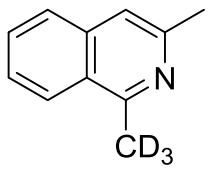
Prepared according to the method A; the product was obtained as colorless oil (yield 83%); R_f= 0.43 (petroleum ether/EtOAc = 70/30 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 8.39 (d, *J* = 5.8 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.72-7.66 (m, 1H), 7.63-7.58 (m, 1H), 7.52 ppm (d, *J* = 5.8 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$) δ 158.69, 141.69, 136.04, 130.20, 127.35, 127.25, 125.82, 125.80, 119.51, 22.12 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 2959, 2922, 2852, 1562, 1417, 1259 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{10}H_7{}^2H_3N$: 147.09961 found: 147.09951.



(2c)

1-[$^2H_3$]-Methyl-3-methylisoquinoline

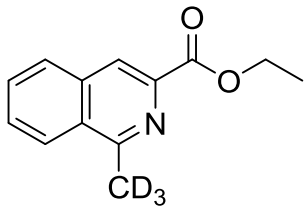
Prepared according to the method A; the product was obtained as pale yellow solid (yield 55%); R_f= 0.37 (petroleum ether/EtOAc = 50/50 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 8.05 (d, *J* = 8.4 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 1H), 7.63-7.58 (m, 1H), 7.53-7.47 (m, 1H), 7.33 (s, 1H), 2.65 ppm (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 158.11, 150.26, 136.74, 130.04, 126.70, 126.15, 125.69, 125.66, 117.33, 24.33, 21.65 (quin, *J* = 19.5 Hz) ppm.

FT-IR:$\tilde{\nu}$ = 3048, 2981, 2918, 1589, 1565, 1359 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{11}H_9{}^2H_3N$: 161.11526 found: 161.11531.



(2d)

Ethyl 1-[$^{2}H_{3}$-]-Methyl-isoquinoline-3-carboxylate

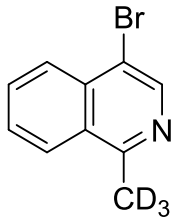
Prepared according to the method A; the product was obtained as pale yellow solid (yield 65%); R_f= 0.5 (petroleum ether/EtOAc = 50/50 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 8.43 (s, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.78-7.69 (m, 2H), 4.51 (q, *J* = 7.1 Hz, 2H), 1.46 ppm (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 165.96, 159.50, 140.48, 135.54, 130.91, 129.54, 129.02, 128.79, 125.93, 123.05, 61.94, 21.91 (quin, *J* = 19.5 Hz),14.49 ppm.

FT-IR:$\tilde{\nu}$ = 3064, 2988, 2924, 1727, 1498, 1316, 1237, 1022 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{13}H_{11}{}^{2}H_3O_2N$: 219.12074 found: 219.12110.



(2e)

1-[$^{2}H_{3}$]-Methyl-4-bromoisoquinoline

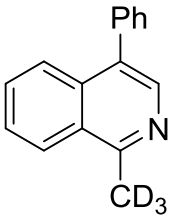
Prepared according to the method A; the product was obtained as white solid (yield 65%); R_f= 0.28 (petroleum ether/EtOAc = 70/30 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 8.58 (s, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.80 (t, *J* = 7.7 Hz, 1H), 7.67 ppm (t, *J* = 7.7 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 158.27, 143.35, 134.68, 131.41, 128.84, 128.17, 126.72, 126.21, 118.01 ppm.

FT-IR:$\tilde{\nu}$ = 3068, 3036, 2989, 1556, 1378, 1271 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{10}H_6{}^{2}H_3N^{79}Br$: 225.01012 found: 225.01096; calc. for $[M+H]^+$ $C_{10}H_6{}^{2}H_3N^{81}Br$: 227.00807 found: 227.00857.



(2f)

1-[$^{2}H_{3}$-]-Methyl-4-phenylisoquinoline

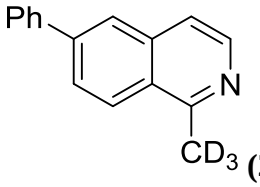
Prepared according to the method A; the product was obtained aspale white solid (yield 73%); R_f= 0.5 (petroleum ether/EtOAc = 50/50 v/v).

^{1}H NMR (600 MHz, CDCl$_3$)δ 8.36 (s, 1H), 8.20 (d, *J* = 8.0 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.67-7.62 (m, 2H), 7.55-7.44 ppm (m, 5H).

^{13}C NMR (151 MHz, CDCl$_3$)δ 158.01, 141.42, 137.39, 134.52, 132.22, 130.35, 130.28 (2C), 128.67 (2C), 127.91, 127.29, 127.09, 126.02, 125.66, 21.95 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 3063, 3028, 1554, 1507, 1387, 1073 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{16}H_{11}{}^{2}H_3N$: 223.13091 found: 223.13121.



(2g)

1-[$^{2}H_{3}$]-Methyl-6-phenylisoquinoline

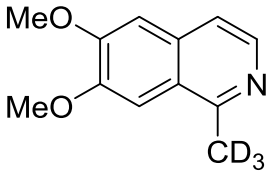
Prepared according to the method A; the product was obtained as pale yellow oil (yield 71%); R_f= 0.34 (petroleum ether/EtOAc = 50/50 v/v).

^{1}H NMR (500 MHz, CDCl$_3$)δ 8.40 (d, *J* = 5.7 Hz, 1H), 8.28-8.23 (m, 1H), 7.95-7.90 (m, 1H), 7.86 (t, *J* = 8.3 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 2H), 7.55-7.47 (m, 3H), 7.45-7.37 ppm (m, 1H).

^{13}C NMR (126 MHz, CDCl$_3$)δ 158.02, 152.14, 142.99, 141.54, 137.40, 134.43, 132.12, 130.33, 130.20, 128.65 (2C), 127.87 (2C), 127.03, 125.98, 125.61 ppm.

FT-IR:$\tilde{\nu}$ = 3050, 3031, 1587, 1489, 1281, 1076 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{16}H_{11}{}^{2}H_3N$: 223.13091 found: 223.13081.



(2h)

1-[$^{2}H_3$]-Methyl-6,7-dimethoxy-isoquinoline

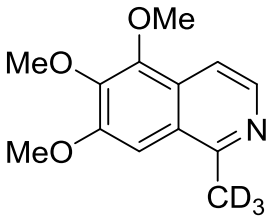
Prepared according to the method A; the product was obtained as pale yellow solid (yield 62%); R_f= 0.55 (dichloromethane/MeOH = 90/10 v/v).

^{1}H NMR (500 MHz, CD_3OD)δ 8.20 (d, *J* = 6.6 Hz, 1H), 8.06 (d, *J* = 6.6 Hz, 1H), 7.64 (s, 1H), 7.60 (s, 1H), 4.10 (s, 3H), 4.09 ppm (s, 3H).

^{13}C NMR (126 MHz, CD_3OD)δ 159.18, 154.37 (2C), 137.92, 129.94, 124.23, 122.85, 107.25, 105.97, 57.36, 57.04, 17.36 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 3068, 2918, 2845, 1507, 1233, 1168, 1114, 1016 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{12}H_{11}{}^{2}H_3O_2N$: 207.12074 found: 207.12123.



(2i)

1-[$^{2}H_3$]-Methyl-5,6,7-trimethoxy-isoquinoline

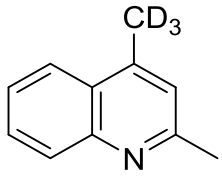
Prepared according to the method A; the product was obtained as pale yellow solid (yield 77%); R_f= 0.28 (dichloromethane/MeOH = 95/5 v/v).

^{1}H NMR (500 MHz, $CDCl_3$+ CD_3OD)δ 8.41-8.26 (m, 1H), 8.00 (d, *J* = 6.0 Hz, 1H), 7.16 (s, 1H), 4.05 (s, 3H), 4.03 ppm (s, 6H).

^{13}C NMR (126 MHz, $CDCl_3$+ CD_3OD)^{13}C NMR (126 MHz, $CDCl_3$) δ 155.44, 154.41, 146.86, 146.76, 129.72, 124.18, 116.06, 100.38, 100.05, 61.88, 61.48, 56.43, 41.91 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 2889, 1507, 1280, 1146, 1017 cm^{-1};

HRMS: calc. for $[M+H]^+$ $C_{13}H_{13}{}^{2}H_3O_3N$: 237.13130 found: 237.13117.



(2j)

4-[$^{2}H_{3}$]-Methyl-2-methylquinoline

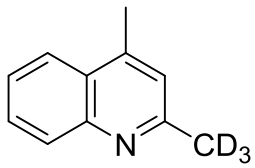
Prepared according to the method A; the product was obtained as pale yellow solid (yield 73%); R_f= 0.5 (petroleum ether/EtOAc = 50/50 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 8.01 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.67-7.64 (m, 1H), 7.50-7.47 (t, *J* = 7.6 Hz, 1H), 7.11 (s, 1H), 2.69 ppm (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 158.73, 147.64, 144.29, 129.24, 129.11, 126.65, 125.53, 123.70, 122.83, 25.30, 17.93 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 3059, 2989, 2915, 1506, 1338, 1220 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{11}H_9{}^2H_3N$: 161.11526 found: 161.11535.



(2k)

2-[$^{2}H_{3}$]-Methyl-4-methyl-quinoline

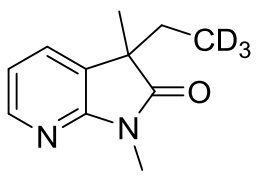
Prepared according to the method A; the product was obtained as pale yellow oil (yield 53%); R_f= 0.5 (petroleum ether/EtOAc = 50/50 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 8.02 (d, *J* = 8.4 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 1H), 7.12 (s, 1H), 2.66 ppm (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 158.69, 147.65, 144.39, 129.26, 129.13, 126.64, 125.55, 123.70, 122.83, 24.61 (quin, *J* = 19.5 Hz), 18.73 ppm.

FT-IR:$\tilde{\nu}$ = 3059, 2974, 1560, 1508, 1343 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{11}H_9{}^2H_3N$: 161.11526 found: 161.11517.



(4a)

3-[2-$^2H_3$]-Ethyl-1,3-dimethyl-1,3-dihydro-2*H*-pyrrolo[2,3-*b*]pyridin-2-one

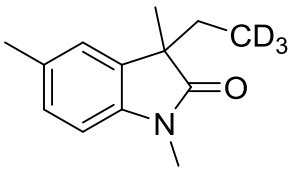
Prepared according to the method B; the product was obtained ascolorless oil (yield 91%); R_f= 0.43 (petroleum ether/EtOAc = 60/40 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 8.17 (dd, *J* = 5.3, 1.5 Hz, 1H), 7.39 (dd, *J* = 7.2, 1.5 Hz, 1H), 6.95 (dd, *J* = 7.2, 5.3 Hz, 1H), 3.29 (s, 3H), 1.92 (d, *J* = 13.5 Hz, 1H), 1.76 (d, *J* = 13.5 Hz, 1H), 1.36 ppm (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 180.47, 157.09, 146.61, 130.02, 128.38, 118.15, 48.69, 30.88, 25.36, 22.83, 8.14 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 2868, 2923, 1716, 1592, 1468, 1346, 1136, 1027 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{11}H_{12}{}^2H_3ON_2$: 194.13672 found: 194.13680.



(4b)

3-[2-$^2H_3$]-Ethyl-1,3,5-trimethylindolin-2-one

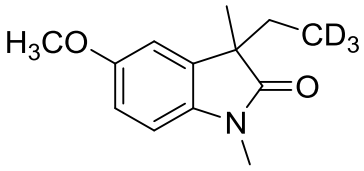
Prepared according to the method B; the product was obtained as pale yellow oil (yield 61%); R_f= 0.55 (petroleum ether/EtOAc = 70/30 v/v).

^{1}H NMR (500 MHz,$CDCl_3$)δ 7.05 (d, *J* = 7.8 Hz, 1H), 6.98 (s, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 3.19 (s, 3H), 2.35 (s, 3H), 1.90 (d, *J* = 13.5 Hz, 1H), 1.73 (d, *J* = 13.5 Hz, 1H), 1.34 ppm (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 180.83, 141.18, 134.08, 131.98, 127.90, 123.48, 107.63, 49.07, 31.32, 26.20, 23.50, 21.29, 8.18 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 2965, 2919, 1703, 1601, 1499, 1349, 1152, 1135 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{13}H_{15}{}^2H_3ON$: 207.15712 found: 207.15722.



(4c)

3-[2-$^2H_3$]-Ethyl-5-methoxy-1,3-dimethylindolin-2-one

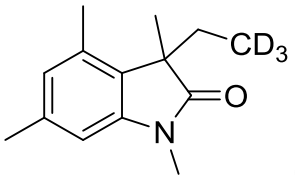
Prepared according to the method B; the product was obtained as colorless oil (yield 65%); R_f= 0.40 (petroleum ether/EtOAc = 70/30 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 6.79-6.76 (m, 2H), 6.72 (d, *J* = 9.1 Hz, 1H), 3.79 (s, 3H), 3.17 (s, 3H), 1.89 (d, *J* = 13.5 Hz, 1H), 1.70 (d, *J* = 13.5 Hz, 1H), 1.32 ppm (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 180.48, 156.08, 137.11, 135.48, 111.47, 110.37, 108.10, 55.86, 49.46, 31.33, 26.25, 23.52, 8.14 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 2920, 1700, 1598, 1497, 1290, 1118, 1039 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{13}H_{15}{}^{2}H_3O_2N$: 223.15204 found: 223.15240.



(4d)

3-[2-$^{2}H_3$)]-Ethyl-1,3,4,6-tetramethylindolin-2-one

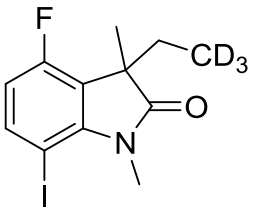
Prepared according to the method B; the product was obtained as pale yellow oil (yield 70%); R_f= 0.53 (petroleum ether/EtOAc = 70/30 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 6.65 (s, 1H), 6.51 (s, 1H), 3.18 (s, 3H), 2.34 (s, 3H), 2.31 (s, 3H), 1.96 (s, 2H), 1.40 ppm (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 181.17, 143.96, 137.55, 133.95, 127.46, 125.60, 106.73, 50.01, 29.27, 26.25, 22.37, 21.67, 18.11, 8.54 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 2927, 1708, 1618, 1454, 1238, 1059 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{14}H_{17}{}^{2}H_3ON$: 221.17277 found: 221.17338.



(4e)

3-[2-$^{2}H_3$]-Ethyl-4-fluoro-7-iodo-1,3-dimethylindolin-2-one

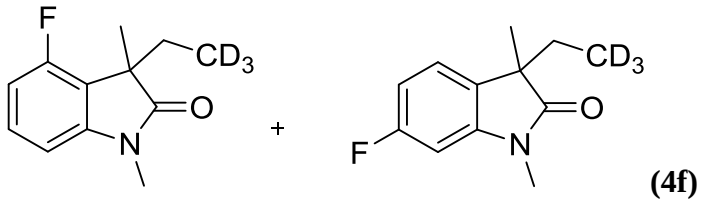
Prepared according to the method B; the product was obtained as pale white solid (yield 76%); R_f= 0.47 (petroleum ether/EtOAc = 80/20 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 7.37-7.31 (m, 1H), 7.24-7.21 (m, 1H), 3.62-3.30 (m, 3H), 1.90 (d, *J* = 13.5 Hz, 1H), 1.69 (d, *J* = 13.5 Hz, 1H), 1.33 ppm (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 179.66, 147.43 (d, *J* = 248.9 Hz), 139.03 (d, *J* = 3.2 Hz), 130.23 (d, *J* = 7.9 Hz), 127.63 (d, *J* = 3.2 Hz), 124.82 (d, *J* = 21.8 Hz), 83.47 (d, *J* = 6.6 Hz), 49.54, 31.53, 28.63 (d, *J* = 5.6 Hz), 23.63, 8.15 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 2929, 2859, 1708, 1621, 1417, 1258 cm^{-1}.

HRMS: calc. for $[M+H]^+C_{12}H_{11}{}^2H_3ONFI$: 337.02869 found:337.02910.



(4f)

3-[2-$^2H_3$]-Ethyl-4-fluoro-1,3-dimethylindolin-2-one and 3-[2-$^2H_3$]-ethyl-6-fluoro-1,3-dimethylindolin-2-one, 4f-major and 4f-minor

Prepared according to the method B; the product was obtained as colorless oil as a mixture of regioisomers (r.r. = 1.5:1; yield 90%); R_f= 0.57 (petroleum ether/EtOAc = 70/30 v/v).

For major regioisomer: **^{1}H NMR (500 MHz, $CDCl_3$)**δ 7.26-7.20 (m, 1H), 6.73 (t, *J* = 7.7 Hz, 1H), 6.64 (d, *J* = 7.7 Hz, 1H), 3.20 (s, 3H), 1.95 (q, *J* = 13.5 Hz, 2H), 1.44 ppm (s, 3H).

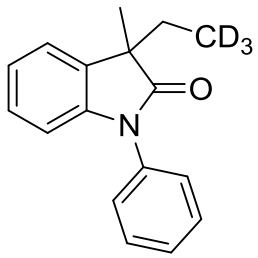
^{13}C NMR (126 MHz, $CDCl_3$)δ 180.24, 159.02 (d, *J* = 246.8 Hz), 145.60 (d, *J* = 10.5 Hz), 129.47 (d, *J* = 8.6 Hz), 123.47 (d, *J* = 9.7 Hz), 110.21 (d, *J* = 21.2 Hz), 104.11 (d, *J* = 3.1 Hz), 48.71, 29.90, 26.63, 22.23, 8.39 ppm (quin, *J* = 19.5 Hz).

For minor regioisomer: **^{1}H NMR (500 MHz, $CDCl_3$)**δ 7.10-7.05 (m, 1H), 6.73 (t, *J* = 8.6 Hz, 1H), 6.58 (dd, *J*= 8.6, 2.3 Hz, 1H), 3.19 (s, 3H), 1.88 (d, *J* = 13.5 Hz, 1H), 1.72 (d, *J* = 13.5 Hz, 1H), 1.33 ppm (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 181.16, 162.86 (d, *J* = 243.8 Hz), 144.96 (d, *J* = 11.5 Hz) 129.21 (d, *J* = 2.9 Hz), 118.88 (d, *J* = 20.1 Hz), 108.42 (d, *J* = 22.2 Hz), 96.82 (d, *J* = 27.4 Hz), 49.50, 31.35, 26.32, 23.52, 8.39 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 2970, 1711, 1618, 1474, 1377, 1235, 1046 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{12}H_{12}{}^2H_3ONF$: 211.13205 found: 211.13247.



(4g)

3-[2-$^{2}H_3$]-Ethyl-3-methyl-1-phenylindolin-2-one

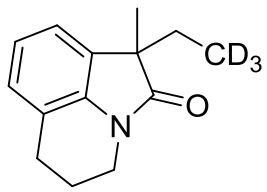
Prepared according to the method B; the product was obtained as colorless oil (yield 89%); R_f= 0.61 (petroleum ether/EtOAc = 70/30 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 7.55-7.49 (m, 2H), 7.43-7.38 (m, 3H), 7.24 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.19 (td, *J* = 7.7, 1.2 Hz, 1H), 7.11 (td, *J* = 7.7, 1,2 Hz, 1H), 6.84 (d, *J* = 7.9 Hz, 1H), 2.04 (d, *J* = 13.5 Hz, 1H), 1.84 (d, *J* = 13.5 Hz, 1H), 1.48 ppm (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 180.31, 143.49, 134.76, 133.80, 129.66 (2C), 128.01, 127.63, 126.68 (2C), 123.01, 122.93, 109.27, 49.09, 31.94, 23.75. 8.22 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 2966, 2920, 1718, 1499, 1373, 1175 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{17}H_{15}{}^{2}H_3ON$: 255.15712 found: 255.15735.



(4h)

1-[2-$^{2}H_3$]-Ethyl-1-methyl-5,6-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-2(1*H*)-one

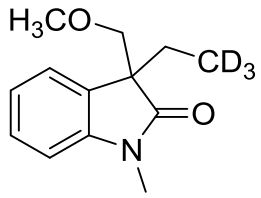
Prepared according to the method B; the product was obtained as colorless oil (yield 79%); R_f= 0.37 (petroleum ether/EtOAc = 70/30 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 7.02-6.98 (m, 2H), 6.97-6.92 (m, 1H), 3.71 (t, *J* = 5.9 Hz, 2H), 2.81-2.77 (m, 2H), 2.02-1.98 (m, 2H), 1.87 (d, *J* = 13.5 Hz, 1H), 1.75 (d, *J* = 13.5 Hz, 1H), 1.35 ppm (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 179.78, 139.25, 132.57, 126.49, 121.91, 120.52, 119.98, 50.35, 38.77, 31.03, 24.74, 23.03, 21.41, 8.21 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 2962, 2923, 1480, 1371, 1239, 1165, 1023 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{14}H_{15}{}^{2}H_3ON$: 219.15712 found: 219.15768.



(4i)

3-[2-$^{2}H_3$]-Ethyl-3-(methoxymethyl)-1-methylindolin-2-one

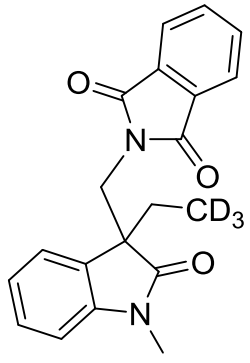
Prepared according to the method B; the product was obtained as colorless oil (yield 85%); R_f= 0.29 (eluent petroleum ether/EtOAc = 70/30 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 7.30-7.26 (m, 1H), 7.25-7.21 (m, 1H), 7.08 (td, *J* = 7.7, 1,2 Hz, 1H), 6.84 (d, *J* = 7.7 Hz, 1H), 3.65 (q, *J* = 8.9 Hz, 2H), 3.22 (s, 3H), 3.21 (s, 3H), 1.86 (d, *J* = 13.5 Hz, 1H), 1.78 ppm (d, *J* = 13.5 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 178.53, 144.42, 130.95, 128.06, 123.11, 122.53, 107.96, 76.93, 59.65, 54.65, 26.73, 26.26, 7.35 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 3054, 2921, 1706, 1611, 1469, 1349, 1196, 1097 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{13}H_{15}{}^{2}H_3O_2N$: 223.15204 found: 223.15260.



(4j)

2-{[3-[2-$^{2}H_3$]-Ethyl-1-methyl-2-oxoindolin-3-yl]methyl}isoindoline-1,3-dione

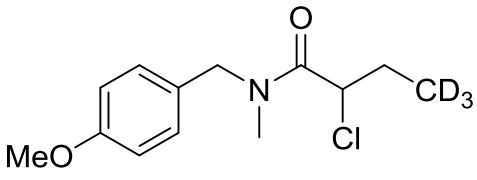
Prepared according to the method B; the product was obtained ascolorless oil (yield 87%); R_f= 0.17 (petroleum ether/EtOAc = 70/30 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 7.75 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.65 (dd, *J* = 5.5, 3.1 Hz, 2H), 7.20 (dt, *J* = 7.7, 3.9 Hz, 1H), 7.18-7.14 (m, 1H), 6.97 (td, *J* = 7.8, 0.6 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 4.04 (d, *J* = 1.2 Hz, 2H), 3.20 (s, 3H), 2.10 (d, *J* = 13.5 Hz, 1H), 1.93 ppm (d, *J* = 13.5 Hz, 1H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 178.00, 168.14, 144.31, 134.03 (2C), 131.79, 129.02, 128.53, 123.73 (2C), 123.43 (2C), 122.35, 108.02, 53.56, 43.21, 28.62, 26.39, 7.88ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 3056, 2919, 1706, 1610, 1468, 1392, 1068 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{20}H_{16}{}^2H_3O_3N_2$: 338.15785 found: 338.15784.



(6a)

2-Chloro-*N*-(4-methoxybenzyl)-*N*-methyl-[4-$^2H_3$]-butanamide

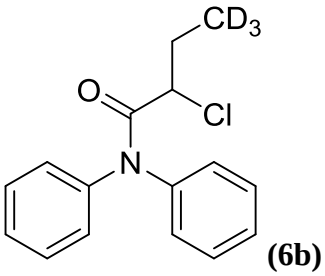
Prepared according to the method C; the product was obtained as colorless oil(yield 75%); R_f= 0.40 (petroleum ether/EtOAc = 70/30 v/v).

^{1}H NMR (500 MHz, DMSO-d_6, 90 °C) δ 7.17 (d, *J* = 8.5 Hz, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 4.82-4.75 (m, 1H), 4.54 (s, 2H), 3.76 (s, 3H), 3.04 (s, 3H), 2.00 (dd, *J* = 13.5, 6.3 Hz, 1H), 1.84 ppm (dd, *J* = 13.5, 6.3 Hz, 1H).

^{13}C NMR (126 MHz, DMSO-d_6, 25 °C)δ 168.21, 168.06, 158.68, 158.52, 129.12, 128.94, 128.72, 128.34, 114.12, 113.97, 55.92, 55.38, 55.13, 55.08, 51.79, 49.77, 34.52, 33.59, 27.78, 27.35, 9.87 ppm (quin, *J* = 17.6 Hz).

FT-IR:$\tilde{\nu}$ = 2934, 1651, 1511, 1244, 1175, 1031 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{13}H_{16}{}^2H_3O_2N^{35}Cl$: 259.12871 found: 259.12890; calc. for $[M+H]^+$ $C_{13}H_{16}{}^2H_3O_2N^{37}Cl$: 261.12576 found: 261.12554.



(6b)

2-Chloro-*N*,*N*-diphenyl-[4-$^2H_3$]-butanamide

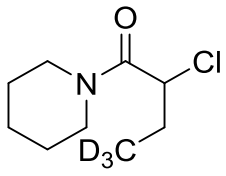
Prepared according to the method C; the product was obtained as pale yellow oil (yield 56%); R_f = 0.47 (petroleum ether/EtOAc = 90/10 v/v).

^{1}H NMR (600 MHz, $CDCl_3$)^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51-7.29 (m, 8H), 7.24-7.16 (m, 2H), 4.21 (t, *J* = 7.3 Hz, 1H), 2.15 (dd, *J* = 13.8, 7.5 Hz, 1H), 1.93 ppm (dd, *J* = 13.8, 7.0 Hz, 1H).

^{13}C NMR (151 MHz, $CDCl_3$)δ 169.20, 142.35, 142.05, 130.17 (2C), 129.13 (2C), 128.76 (2C), 128.50, 126.66, 126.32 (2C), 56.52, 28.23, 10.26 ppm (quin, *J* = 20.16 Hz).

FT-IR:$\tilde{\nu}$ = 3062, 3039, 1679, 1489, 1325, 1235 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{16}H_{14}{}^2H_3ON^{35}Cl$: 277.11815 found: 277.11775; calc. for $[M+H]^+$ $C_{16}H_{14}{}^2H_3ON^{37}Cl$: 279.11520 found: 279.11466.



(6c)

2-Chloro-1-(piperidin-1-yl)-[4-$^2H_3$]-butan-1-one

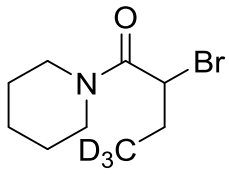
Prepared according to the method C; the product was obtained aspale white solid (yield 65%); R_f= 0.57 (petroleum ether/EtOAc = 50/50 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 4.34 (dd, *J* = 7.8, 6.1 Hz, 1H), 3.73-3.64 (m, 1H), 3.59-3.50 (m, 1H), 3.50-3.39 (m, 2H), 2.07 (dd, *J* = 14.2, 6.1 Hz, 1H), 1.94 (dd, *J* = 14.2, 7.8 Hz, 1H), 1.74-1.51 ppm (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 166.91, 55.98, 47.14, 43.64, 27.78, 26.53, 25.63, 24.58, 10.41 ppm (quin, *J* = 19.5 Hz).

FT-IR:$\tilde{\nu}$ = 2937, 2856, 1645, 1441, 1274, 1137, 1010 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_9H_{14}{}^2H_3ON^{35}Cl$: 193.11815 found: 193.11827; calc. for $[M+H]^+C_9H_{14}{}^2H_3ON^{37}Cl$: 195.11520 found: 195.11495.



(6d)

2-Bromo-1-(piperidin-1-yl)-[4-$^2H_3$]-butan-1-one

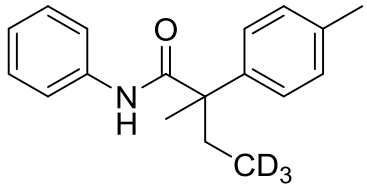
Prepared according to the method C; the product was obtained aspale colorless oil(yield 91%); R_f= 0.66 (petroleum ether/EtOAc = 50/50 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 4.37-4.31 (m, 1H), 3.66 (dd, *J* = 9.0, 4.5 Hz, 1H), 3.53-3.43 (m, 2H), 3.43-3.35 (m, 1H), 2.12 (dd, *J* = 14.3, 6.4 Hz, 1H), 2.02 (dd, *J* = 14.3, 6.4 Hz, 1H), 1.77-1.48 ppm (m, 6H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 167.09, 47.32, 45.83, 43.60, 28.18, 26.27, 25.56, 24.52, 11.58 ppm (quin, *J* = 18.9 Hz).

FT-IR:$\tilde{\nu}$ = 2935, 2859, 1632, 1442, 1214, 1120, 1025 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_9H_{14}{}^2H_3ON^{79}Br$: 237.06763 found: 237.06844; calc. for $[M+H]^+$ $C_9H_{14}{}^2H_3ON^{81}Br$: 239.06559 found: 239.06601.



(8)

2-Methyl-*N*-phenyl-2-(4-methylphenyl)-[4-$^2H_3$]-butanamide

Prepared according to the method B; the product was obtained as white solid (yield 67%); R_f= 0.33 (petroleum ether/EtOAc = 90/10 v/v).

^{1}H NMR (500 MHz, $CDCl_3$)δ 7.39-7.34 (m, 2H), 7.31-7.24 (m, 4H), 7.20 (d, *J* = 8.0 Hz, 2H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.81 (br s, 1H), 2.36 (s, 3H), 2.09 (q, *J* = 13.5 Hz, 2H), 1.59 ppm (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$)δ 175.66, 140.44, 138.13, 137.08, 129.75 (2C), 129.00 (2C), 127.07 (2C), 124.15, 119.73 (2C), 51.63, 31.35, 23.48, 21.13, 8.16 ppm (quin, *J* = 18.9 Hz).

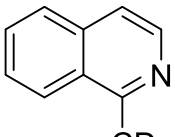
FT-IR:$\tilde{\nu}$ = 3311, 2932, 1663, 1528, 1498, 1311, 1242, 1071 cm^{-1}.

HRMS: calc. for $[M+H]^+$ $C_{18}H_{19}{}^2H_3ON$: 271.18842found:271.18797.

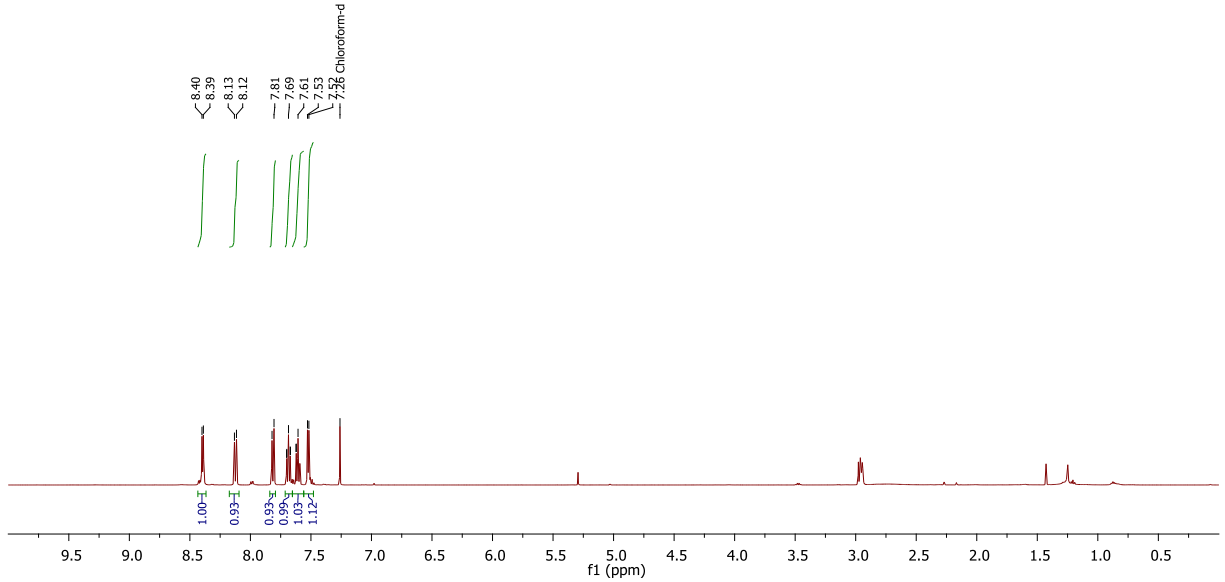
References:

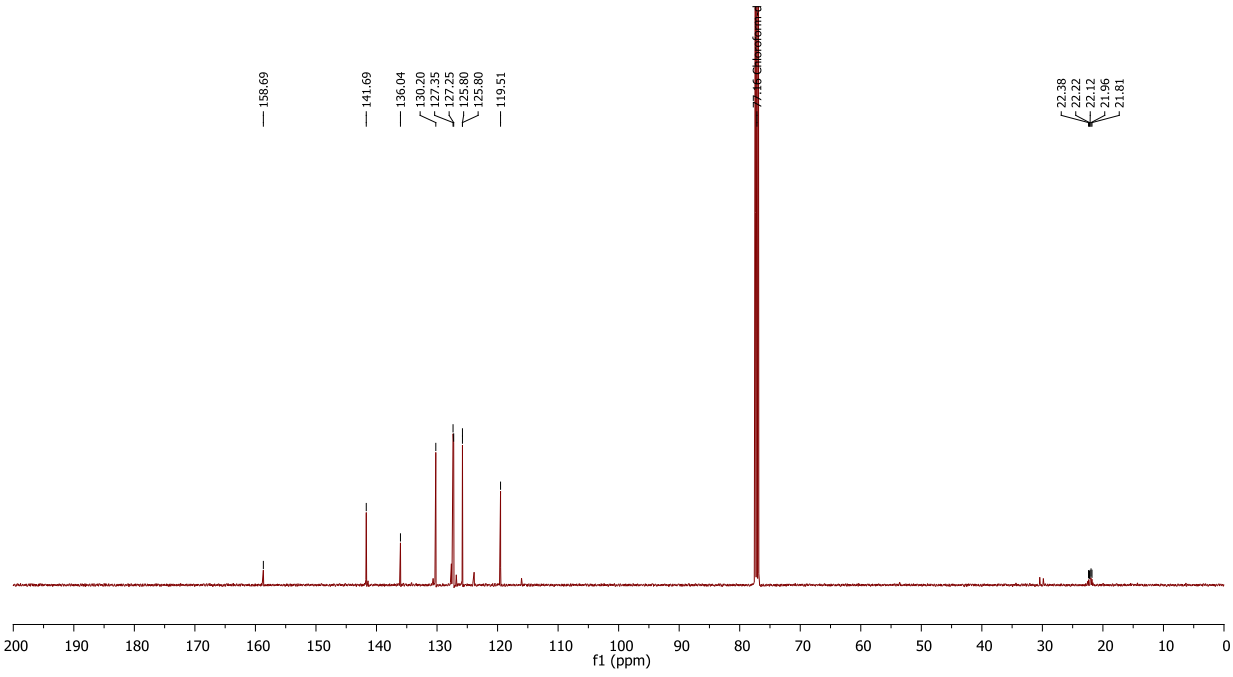
[1]a) Mu, X.; Wu, T.; Wang, H.-y.; Guo, Y.-l.; Liu, G. *J. Am. Chem. Soc*. **2011**, *134*, 878-881; b) Pigge, F. C.; Dhanya, R. and Hoefgen, Erik R. *Angew. Chem. Int. Ed.* **2007**, *46*, 2887-2890; c) Friesen, R. W.; Trimble, L. A., *Can. J. Chem.* **2004**,*82*, 206-214; d) Liu, Q.; Zhu, F.-P.; Jin, X.-L.; Wang, X.-J.; Chen, H. and Wu, L.-Z. *Chem. Eur. J*.**2015**,*21*, 10326-10329; e) Wang, S.; Huang, X.; Wen, Y.; Ge, Z.; Wang, X.; Li, R.*Tetrahedron*, **2015**, *71*, 8117-8122.

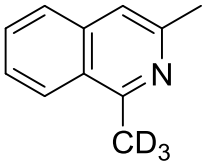
Copiesof spectra



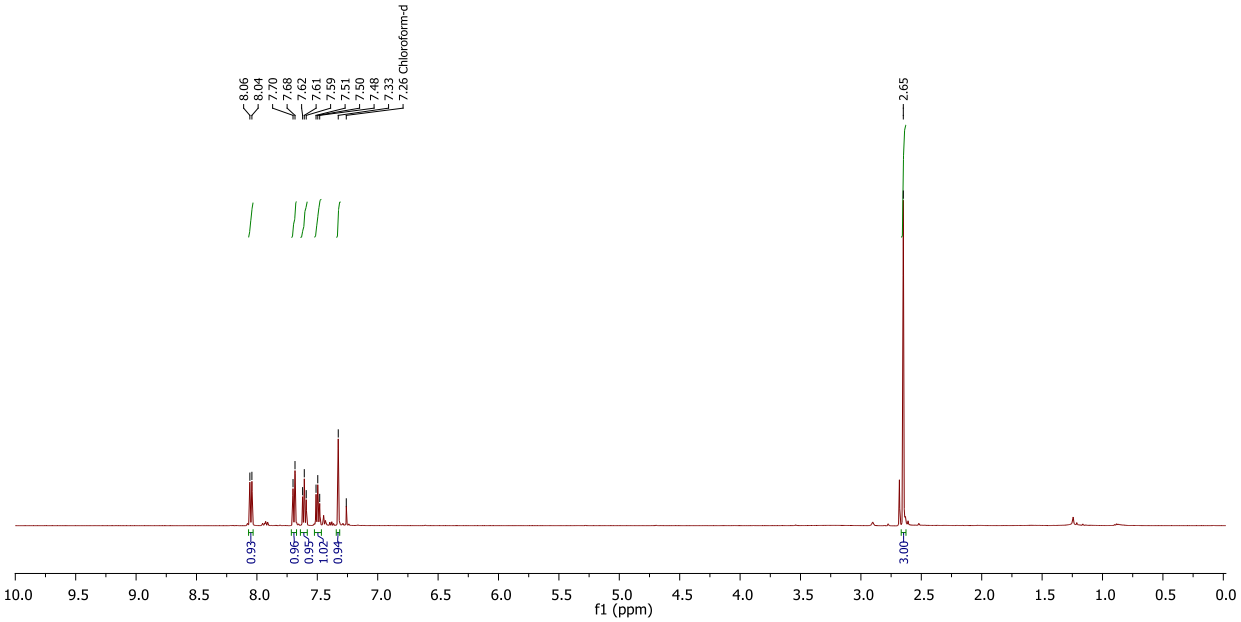
(2b)

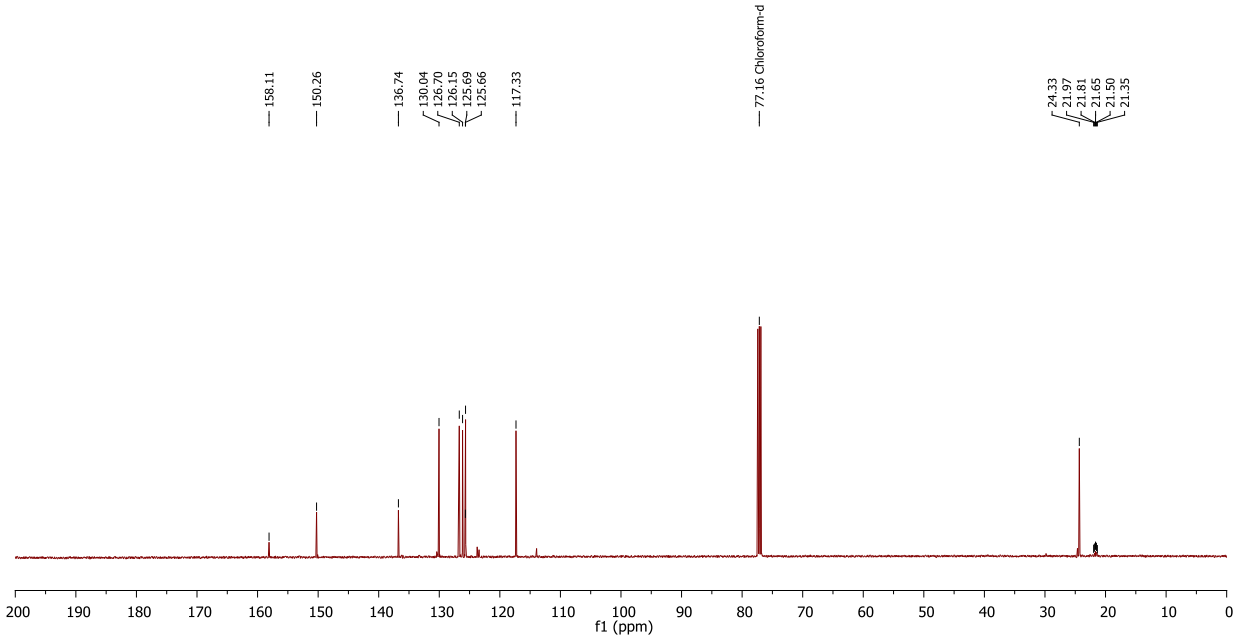





N
CD3

(2c)


8.06
8.04
7.70
7.68
7.62
7.61
7.59
7.51
7.50
7.48
7.33
7.26 Chloroform-d
2.65
0.93
0.96
0.95
1.02
0.94
3.00
f1 (ppm)


158.11
150.26
136.74
130.04
126.70
126.15
125.69
125.66
117.33
77.16 Chloroform-d
24.33
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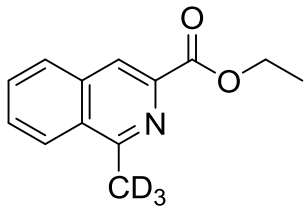
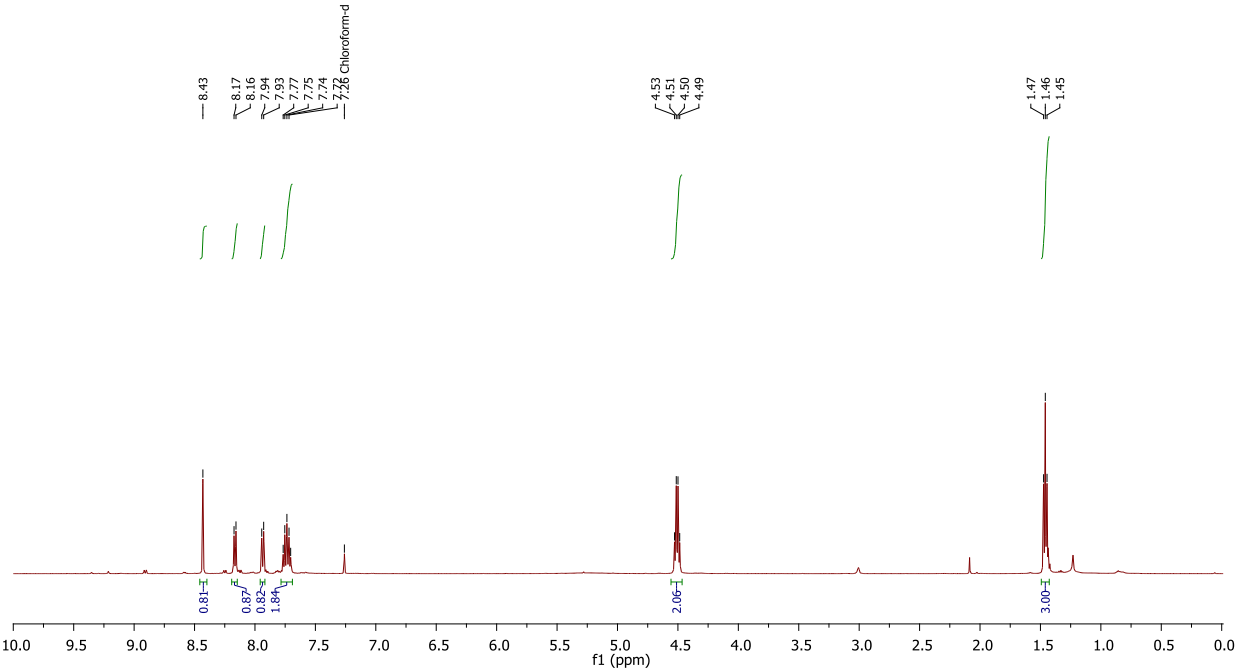
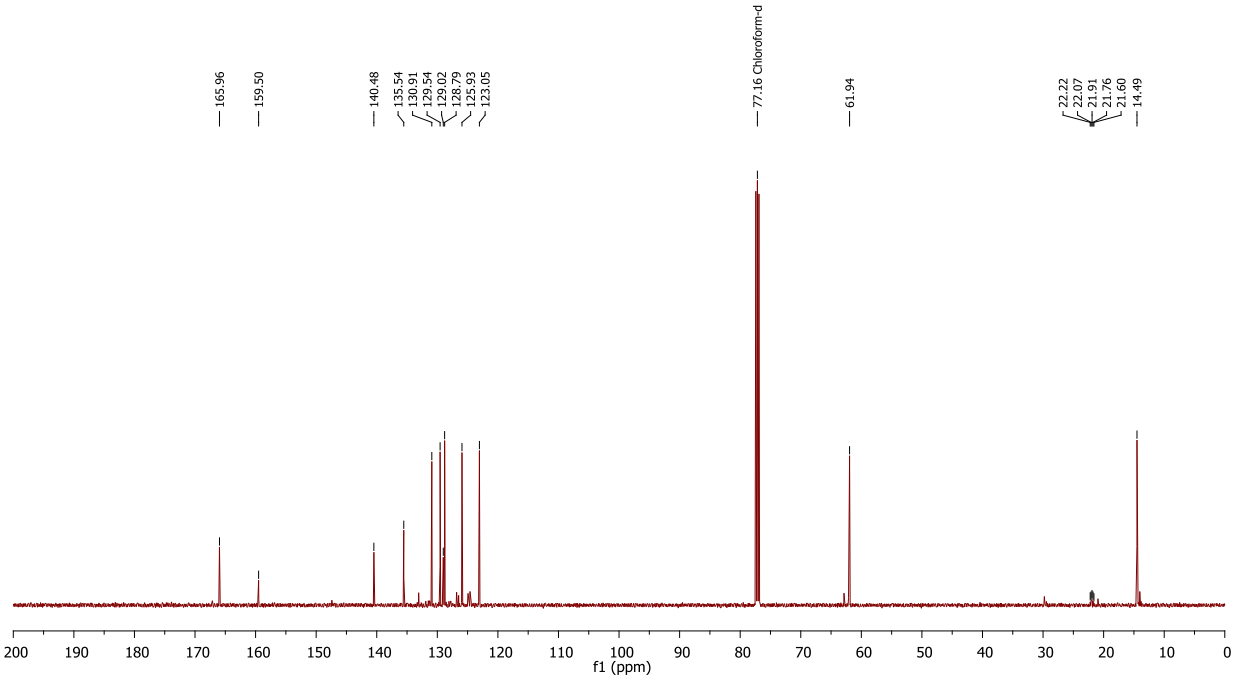
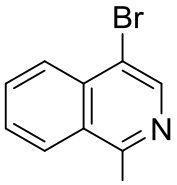
21.81
21.65
21.50
21.35
f1 (ppm)


O
O
N
CD3

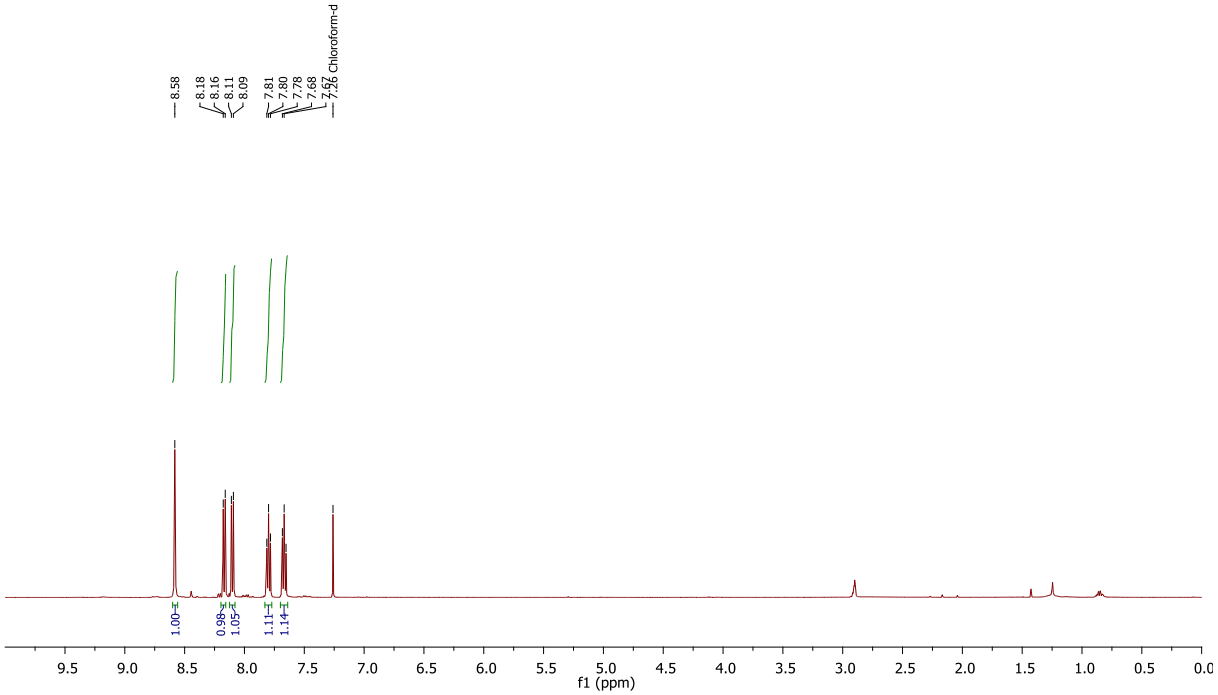
(2d)

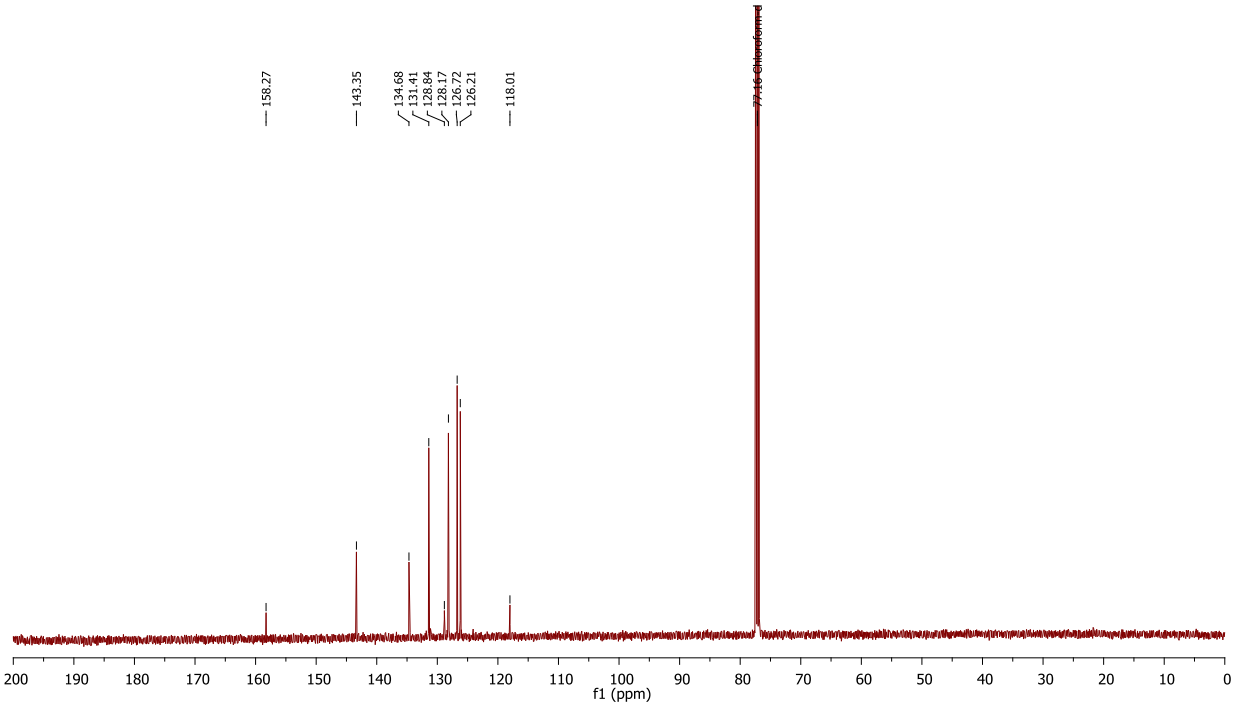

8.43
8.17
8.16
7.94
7.93
7.77
7.75
7.74
7.72
7.26 Chloroform-d
4.53
4.51
4.50
4.49
1.47
1.46
1.45
0.81
0.87
0.82
1.84
2.06
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

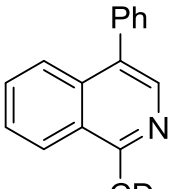

165.96
159.50
140.48
135.54
130.91
129.54
129.02
128.79
125.93
123.05
77.16 Chloroform-d
61.94
22.22
22.07
21.91
21.76
21.60
14.49
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Br
N
CD3

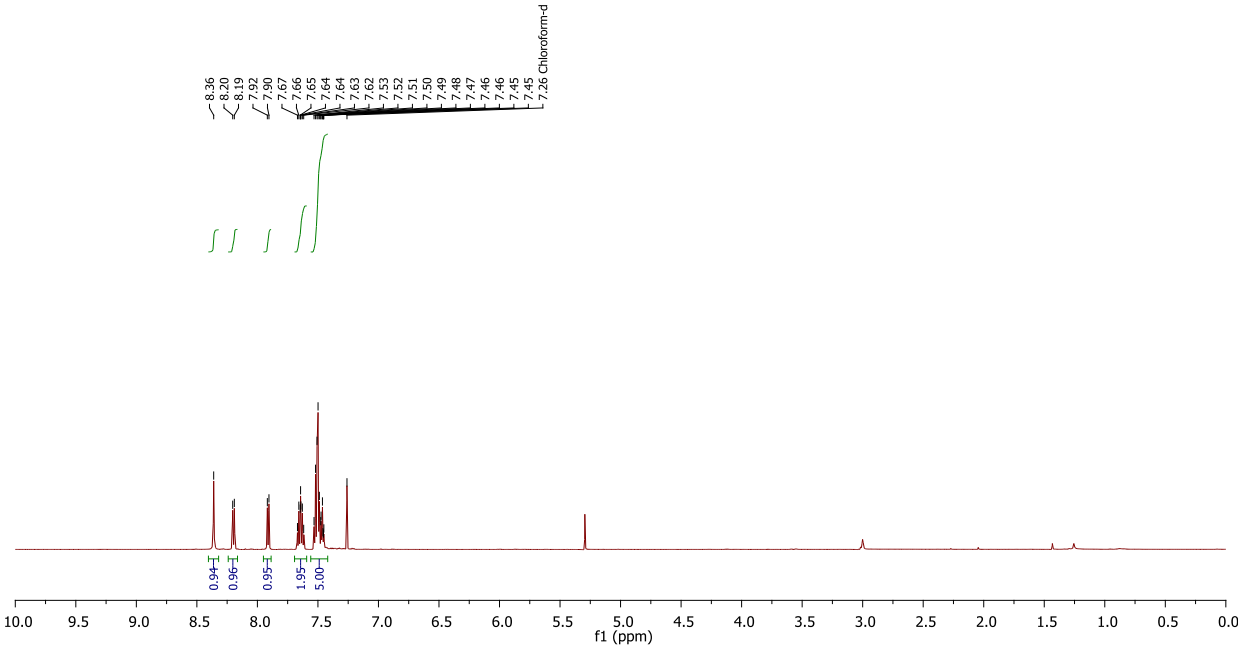
(2e)

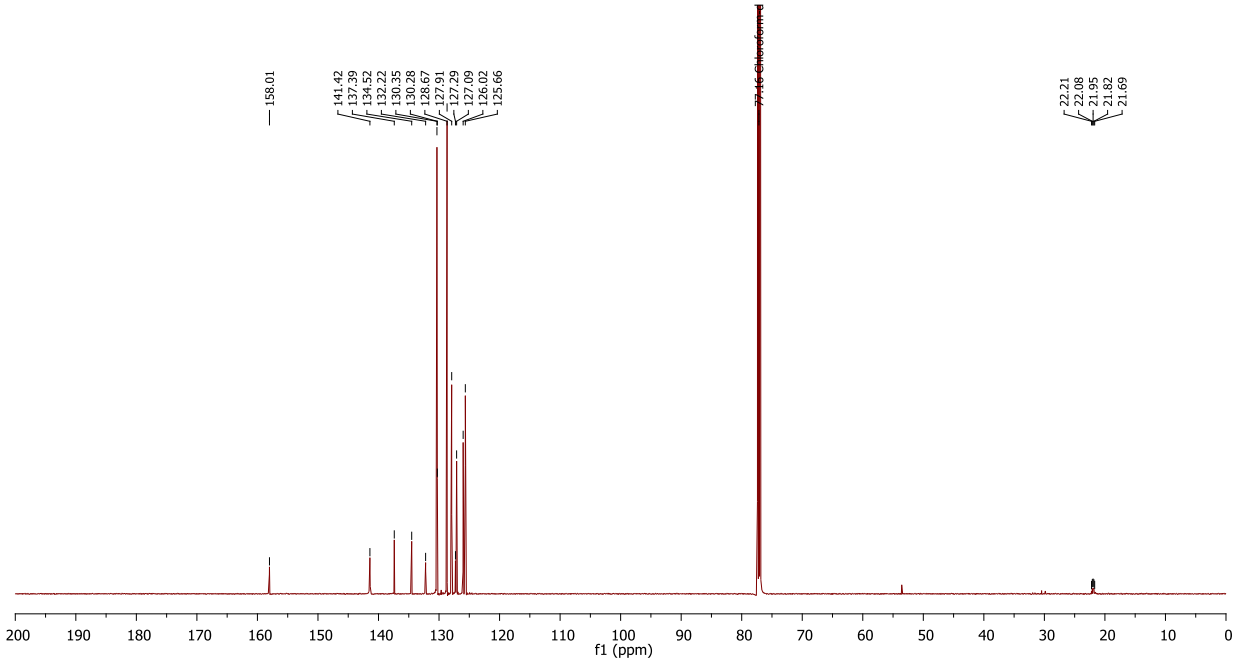

8.58
8.18
8.16
8.11
8.09
7.81
7.80
7.78
7.68
7.52
7.26 Chloroform-d
1.00
0.98
1.05
1.11
1.14
f1 (ppm)

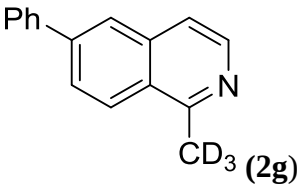

158.27
143.35
134.68
131.41
128.84
128.17
126.72
126.21
118.01
77.16 Chloroform-d
f1 (ppm)


Ph
N
CD3

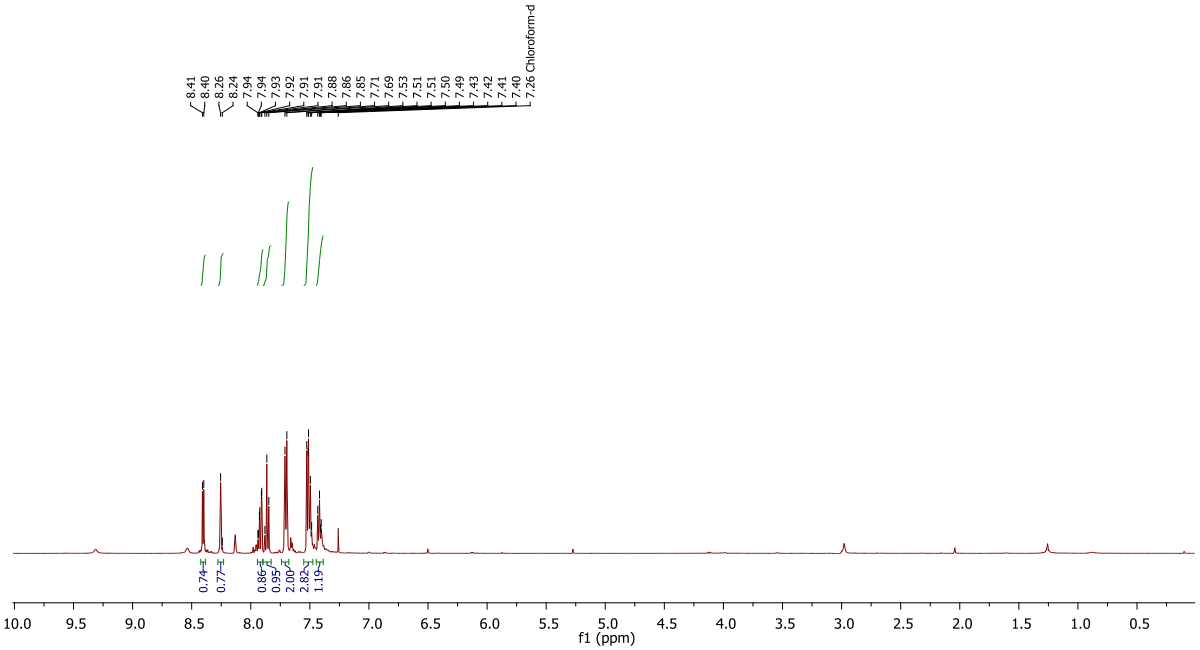
(2f)

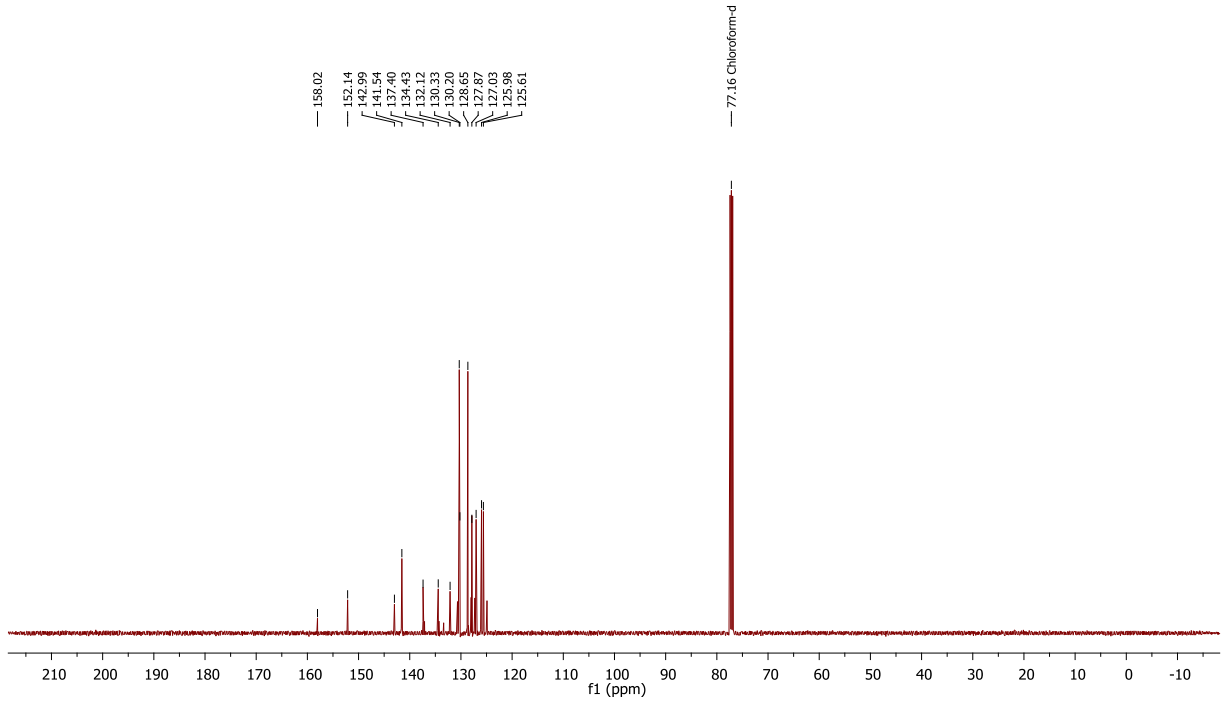

8.36
8.20
8.19
7.92
7.90
7.67
7.66
7.65
7.64
7.64
7.63
7.62
7.53
7.52
7.51
7.50
7.49
7.48
7.47
7.46
7.46
7.45
7.45
7.26 Chloroform-d
0.94
0.96
0.95
1.95
5.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

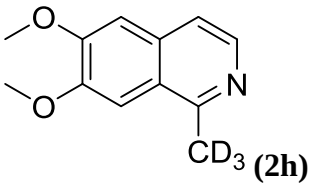

158.01
141.42
137.39
134.52
132.22
130.35
130.28
128.67
127.91
127.29
127.09
126.02
125.66
77.16 Chloroform-d
22.21
22.08
21.95
21.82
21.69
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Ph
N
CD3

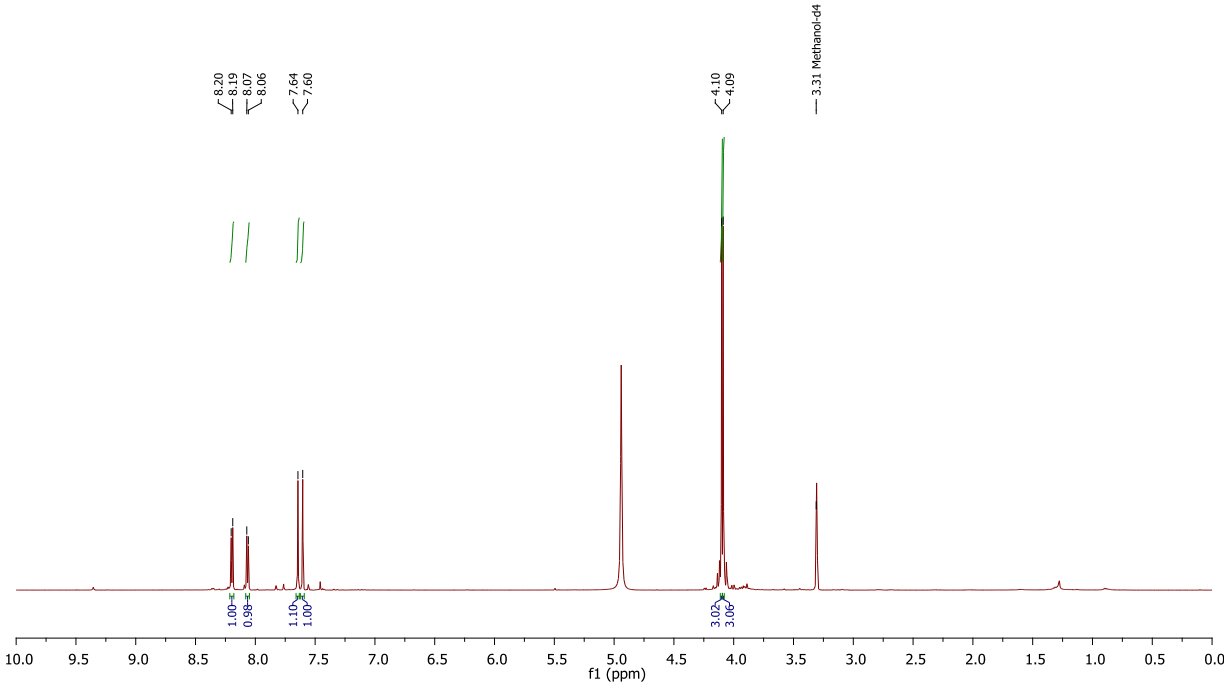
(2g)

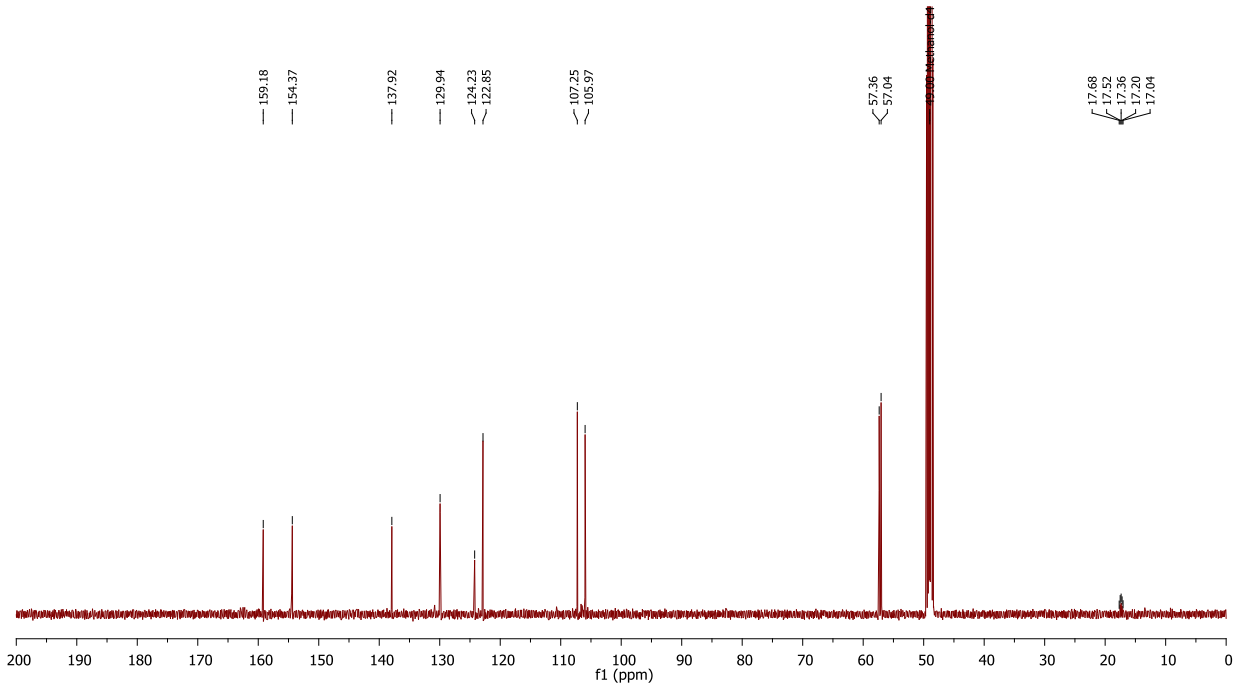

8.41
8.40
8.26
8.24
7.94
7.94
7.93
7.92
7.91
7.91
7.88
7.86
7.85
7.71
7.69
7.53
7.51
7.51
7.50
7.49
7.43
7.42
7.41
7.40
7.26 Chloroform-d
0.74
0.77
0.86
0.95
2.00
2.82
1.19
f1 (ppm)

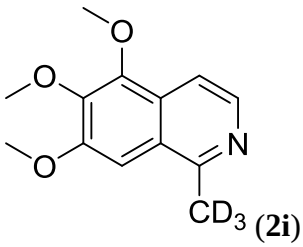

158.02
152.14
142.99
141.54
137.40
134.43
132.12
130.33
130.20
128.65
127.87
127.03
125.98
125.61
77.16 Chloroform-d
f1 (ppm)


O
O
N
CD3

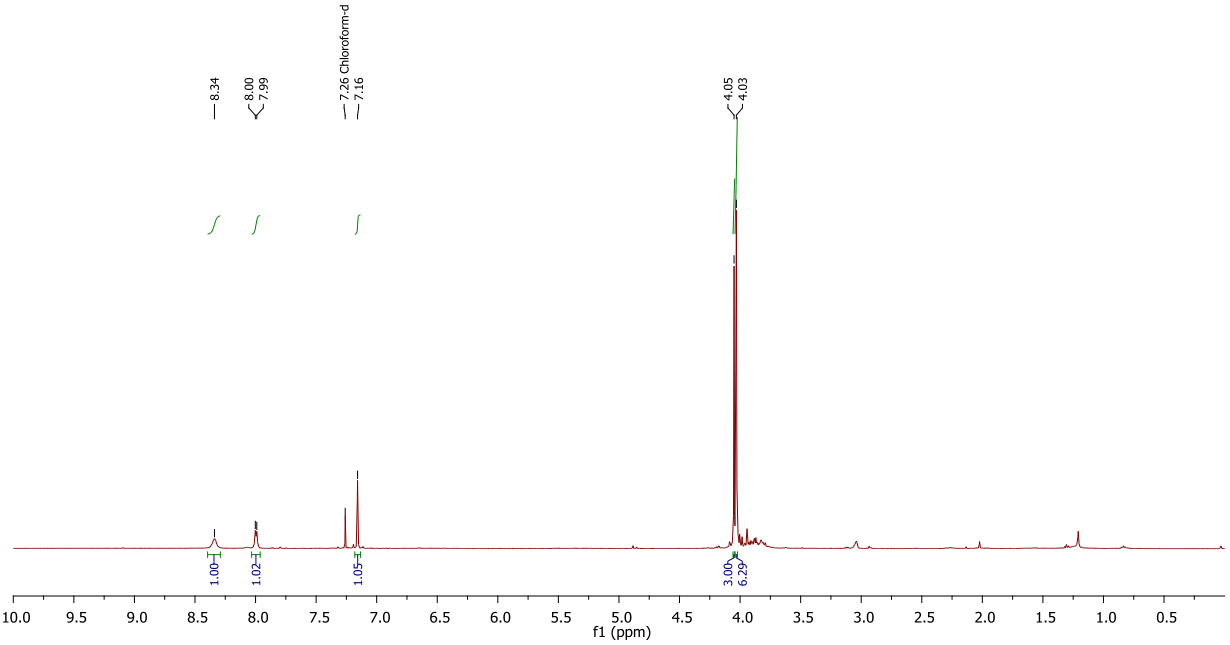
(2h)

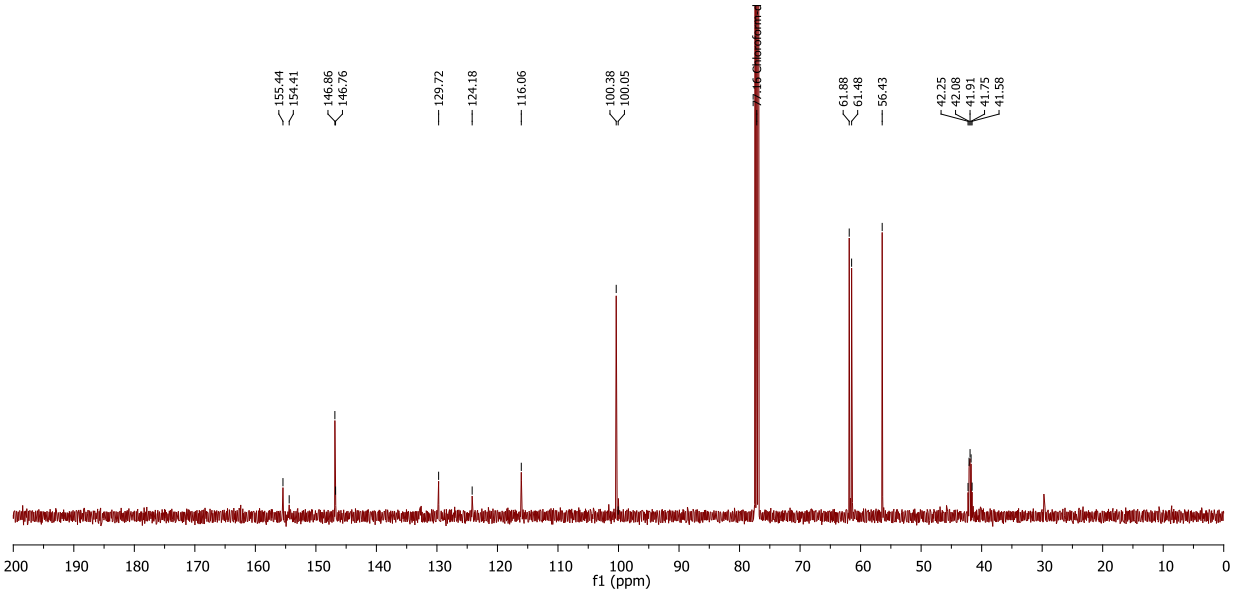

8.20
8.19
8.07
8.06
7.64
7.60
4.10
4.09
3.31 Methanol-d4
1.00
0.98
1.10
1.00
3.02
3.06
f1 (ppm)

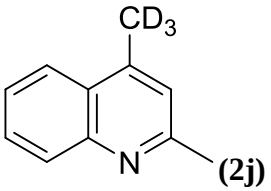

159.18
154.37
137.92
129.94
124.23
122.85
107.25
105.97
57.36
57.04
49.00 Methanol-d4
17.68
17.52
17.36
17.20
17.04
f1 (ppm)


O
O
O
N
CD3

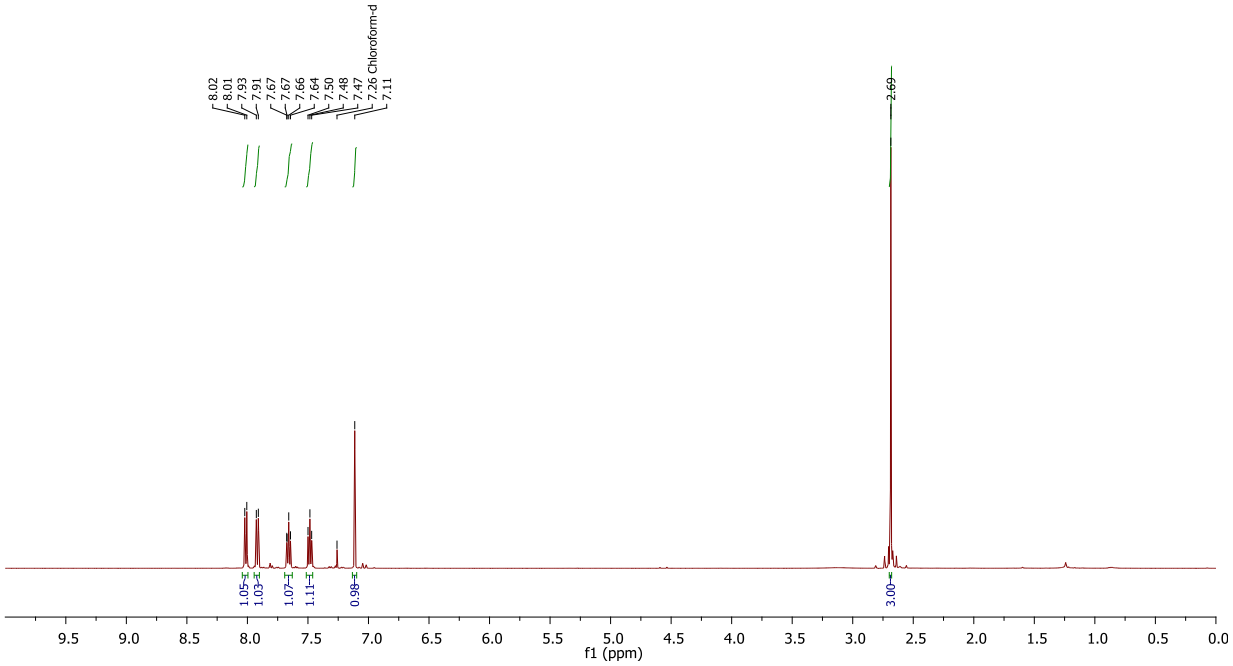
(2i)

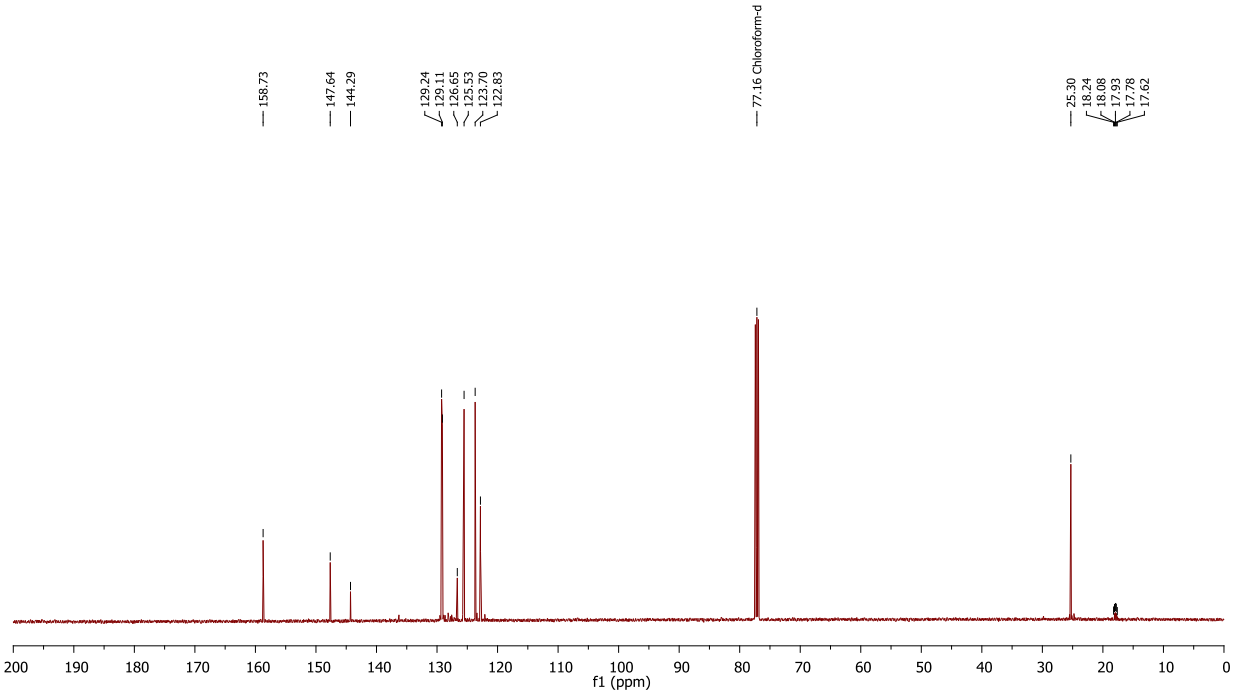

8.34
8.00
7.99
7.26 Chloroform-d
7.16
4.05
4.03
1.00
1.02
1.05
3.00
6.29
f1 (ppm)

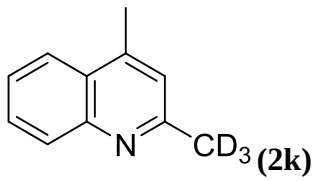

155.44
154.41
146.86
146.76
129.72
124.18
116.06
100.38
100.05
77.16 Chloroform-d
61.88
61.48
56.43
42.25
42.08
41.91
41.75
41.58
f1 (ppm)


CD3
N

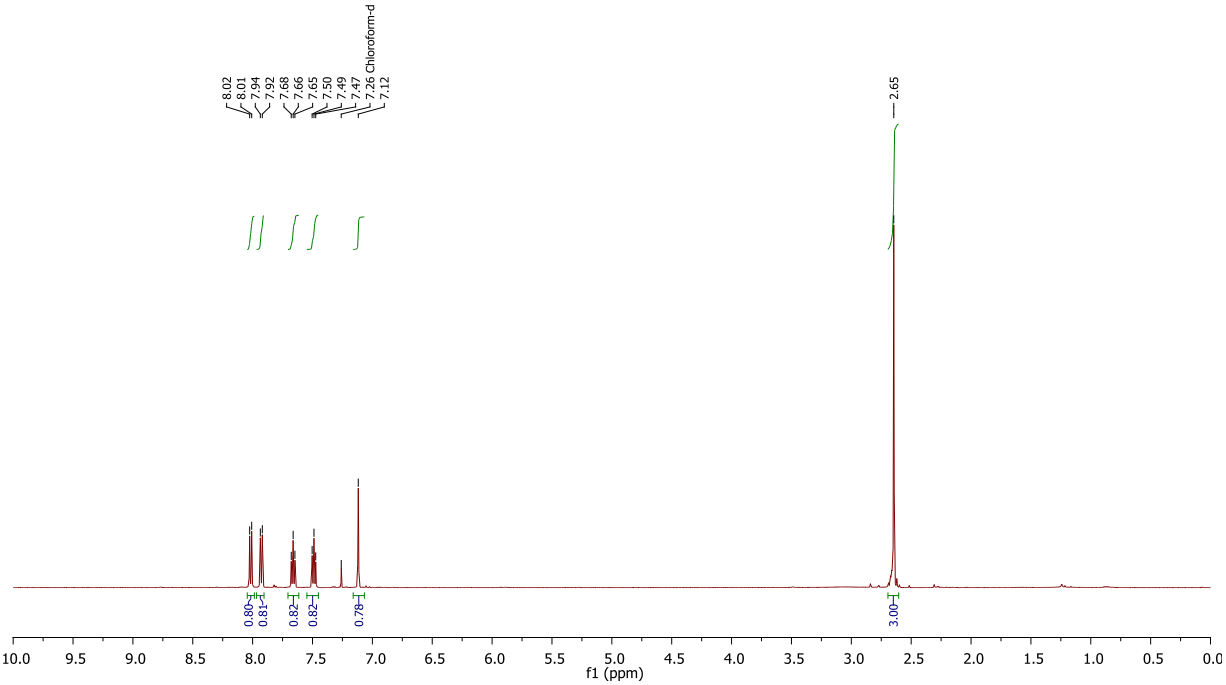
(2j)

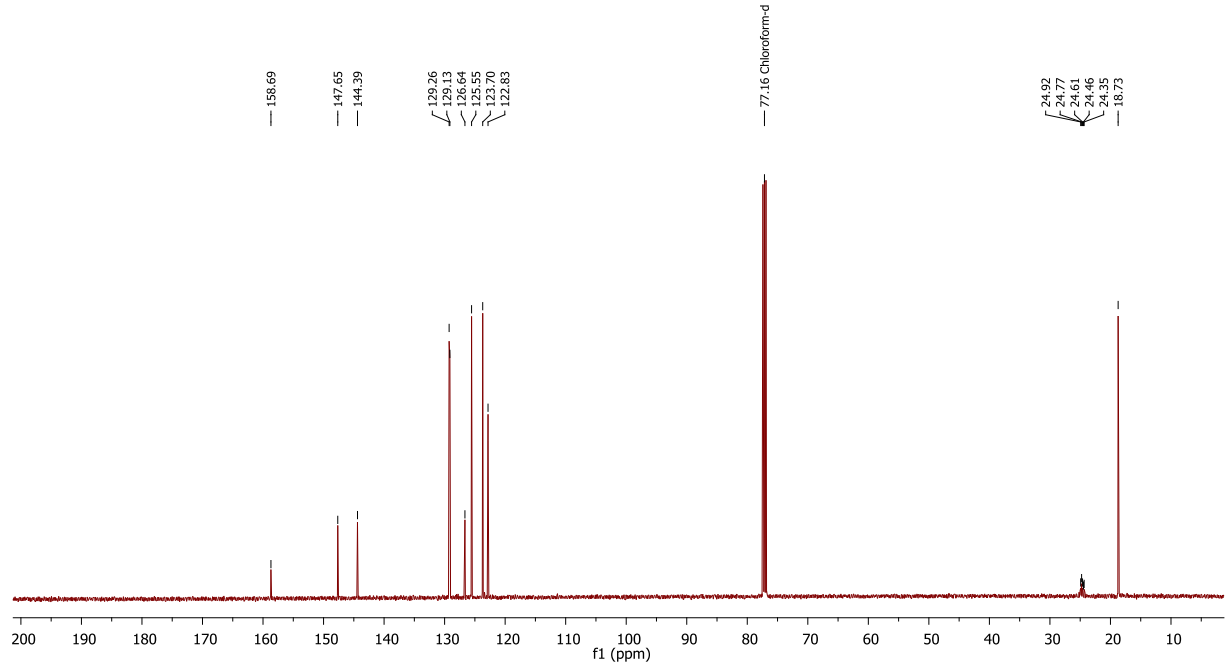

8.02
8.01
7.93
7.91
7.67
7.67
7.66
7.64
7.50
7.48
7.47
7.26 Chloroform-d
7.11
2.69
1.05
1.03
1.07
1.11
0.98
3.00
f1 (ppm)

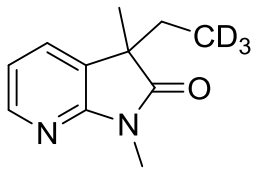

158.73
147.64
144.29
129.24
129.11
126.65
125.53
123.70
122.83
77.16 Chloroform-d
25.30
18.24
18.08
17.93
17.78
17.62
f1 (ppm)


N
CD3

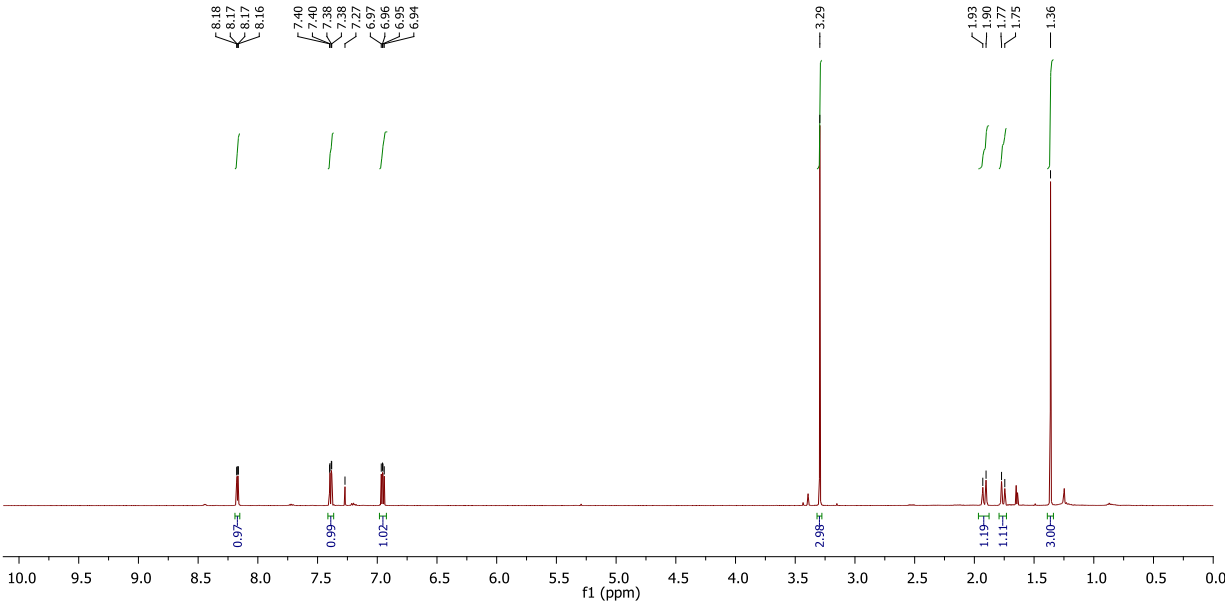
(2k)

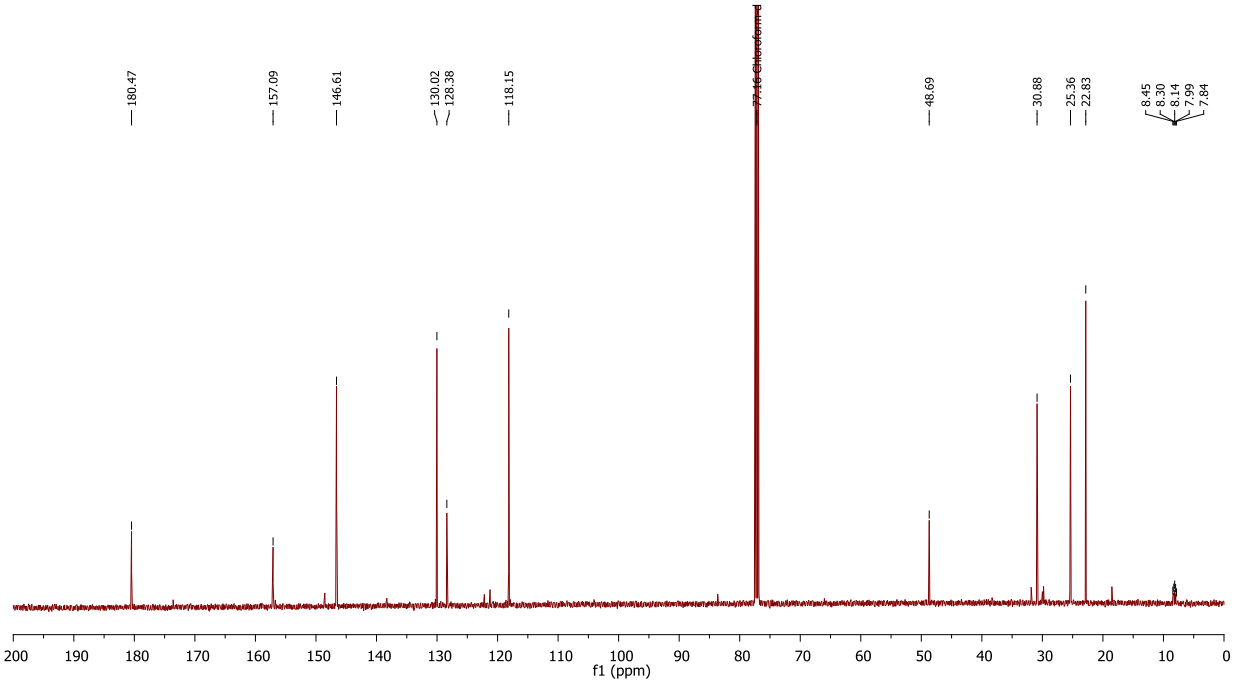

8.02
8.01
7.94
7.92
7.68
7.66
7.65
7.50
7.49
7.47
7.26 Chloroform-d
7.12
2.65
0.80
0.81
0.82
0.82
0.78
3.00
f1 (ppm)

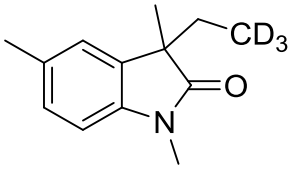

158.69
147.65
144.39
129.26
129.13
126.64
125.55
123.70
122.83
77.16 Chloroform-d
24.92
24.77
24.61
24.46
24.35
18.73
f1 (ppm)


CD3
O
N
N

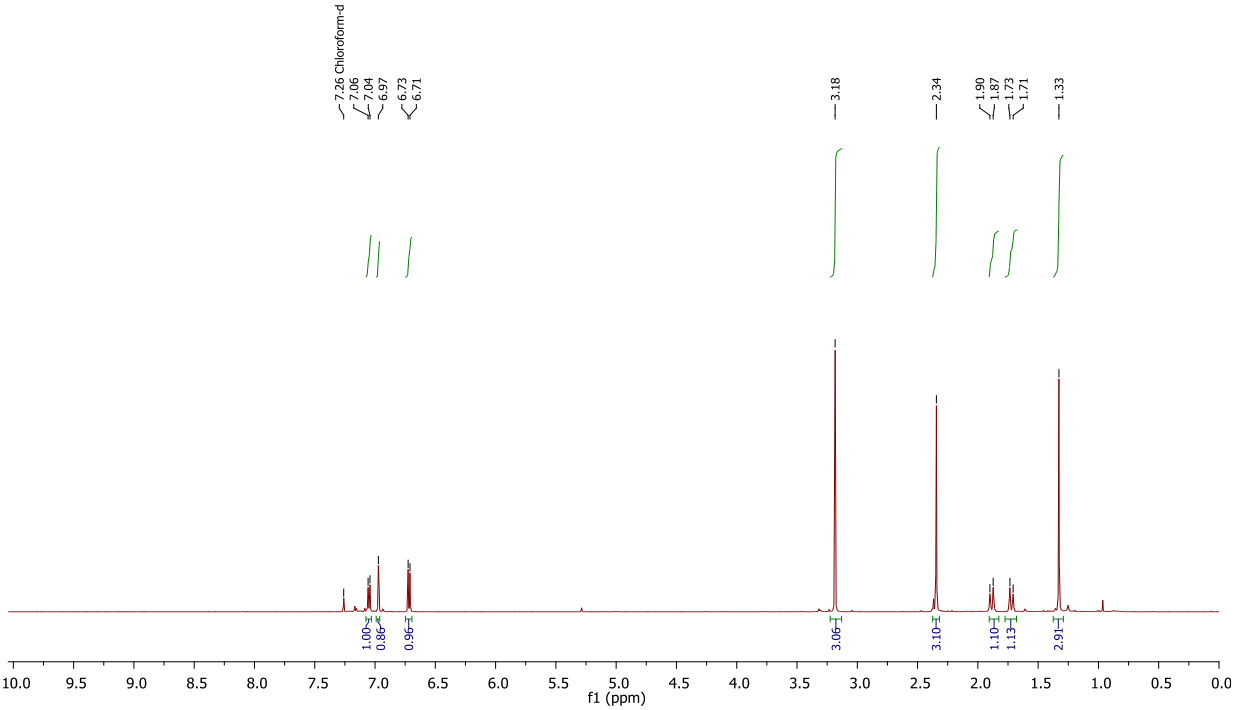
(4a)

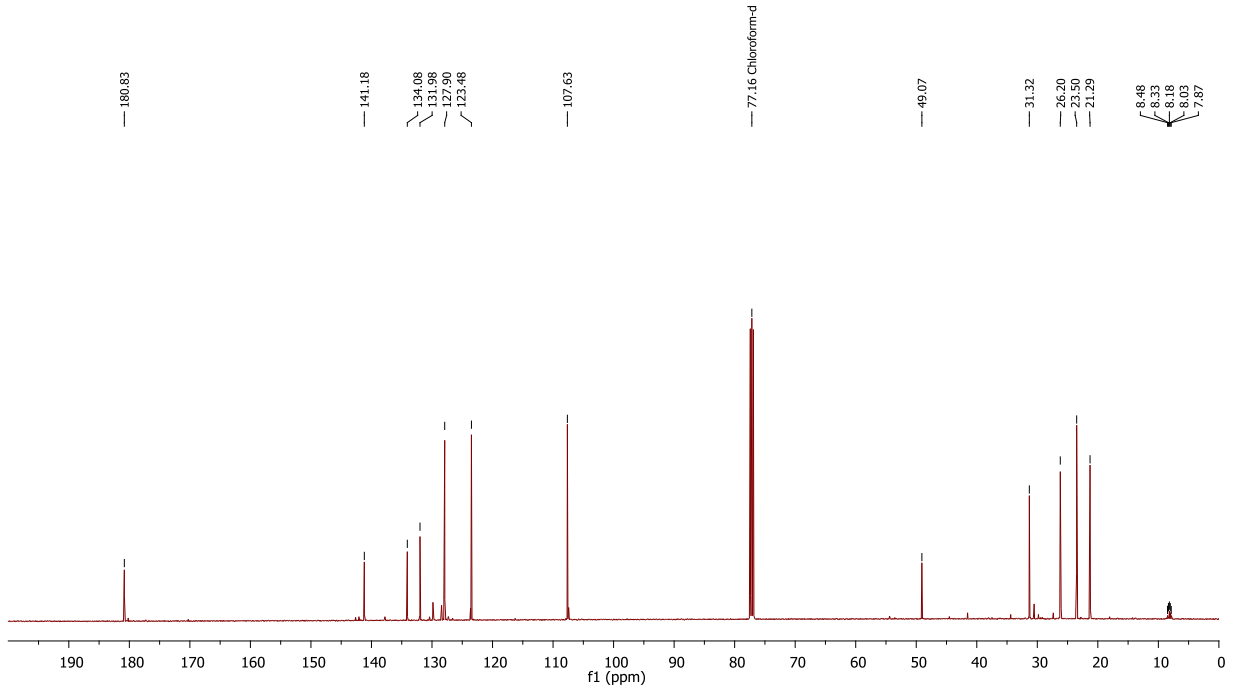

8.18
8.17
8.17
8.16
7.40
7.40
7.38
7.38
7.27
6.97
6.96
6.95
6.94
3.29
1.93
1.90
1.77
1.75
1.36
0.97
0.99
1.02
2.98
1.19
1.11
3.00
f1 (ppm)

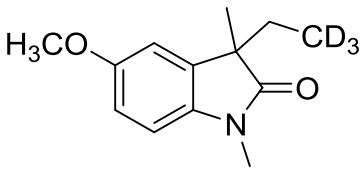

180.47
157.09
146.61
130.02
128.38
118.15
77.16 Chloroform
48.69
30.88
25.36
22.83
8.45
8.30
8.14
7.99
7.84
f1 (ppm)


CD3
O
N

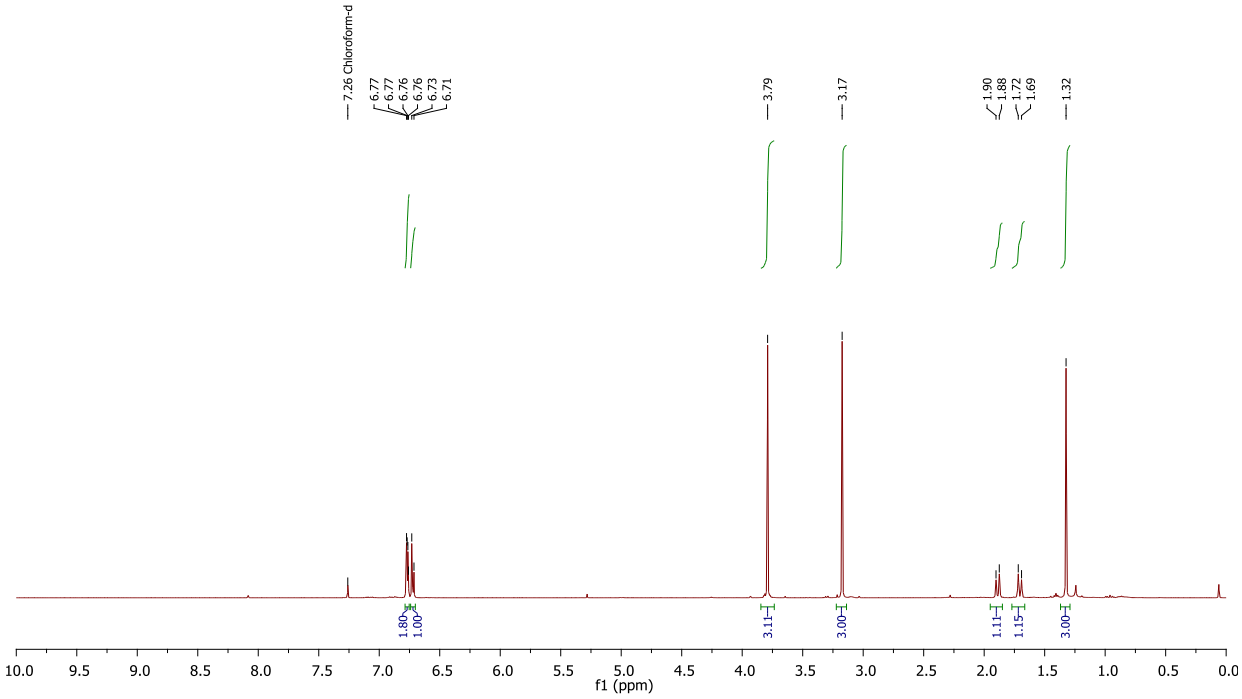
(4b)

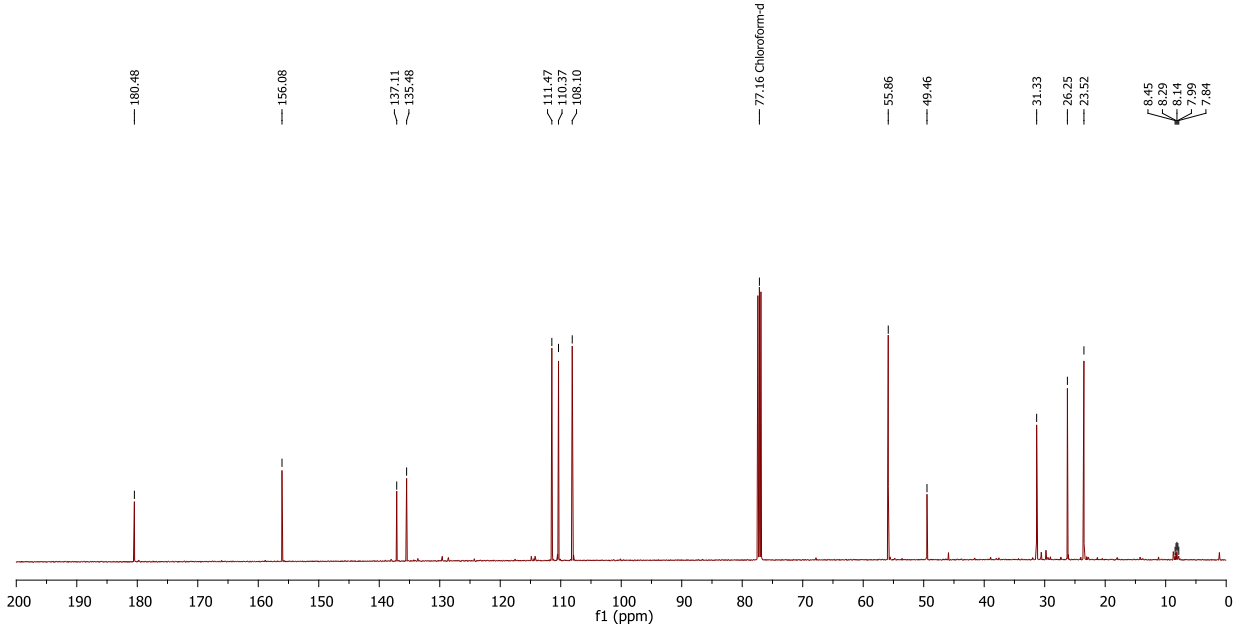

7.26 Chloroform-d
7.06
7.04
6.97
6.73
6.71
3.18
2.34
1.90
1.87
1.73
1.71
1.33
1.00
0.86
0.96
3.06
3.10
1.10
1.13
2.91
f1 (ppm)

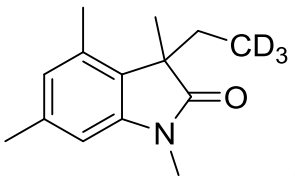

180.83
141.18
134.08
131.98
127.90
123.48
107.63
77.16 Chloroform-d
49.07
31.32
26.20
23.50
21.29
8.48
8.33
8.18
8.03
7.87
f1 (ppm)


H3CO
CD3
O
N

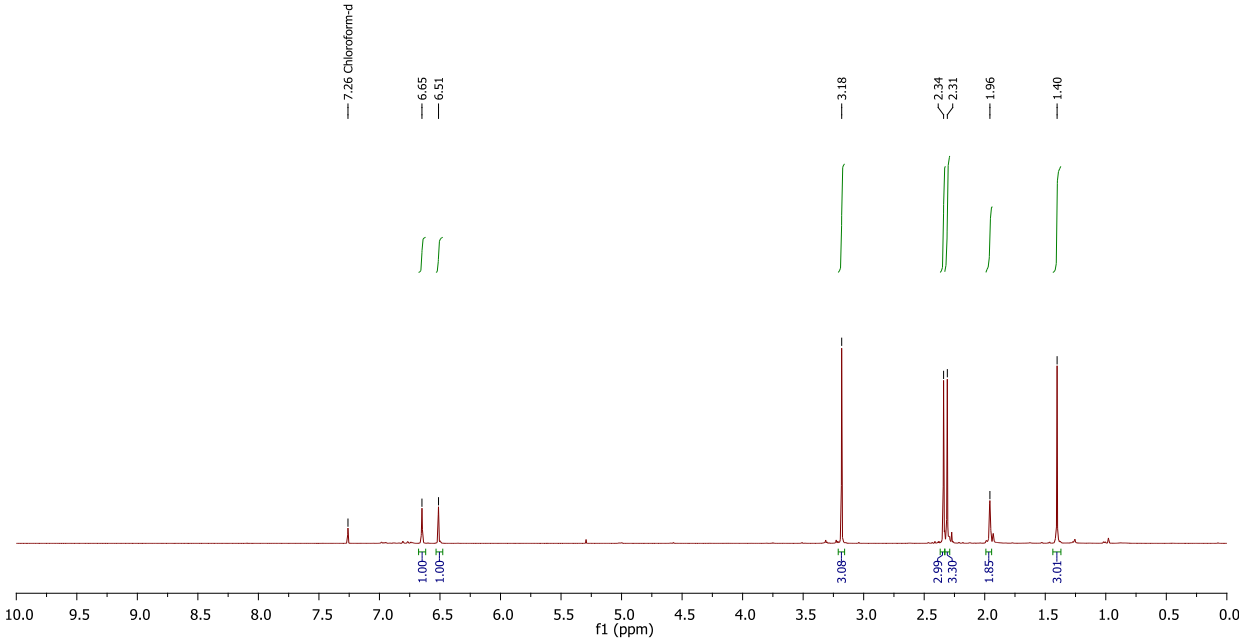
(4c)

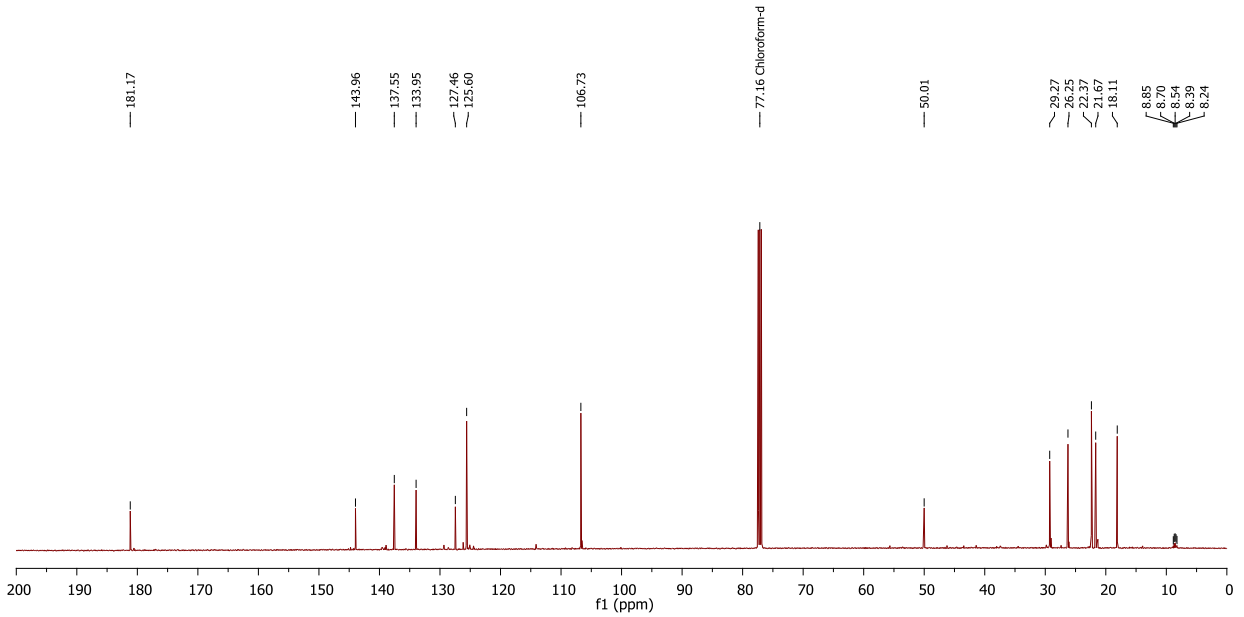

7.26 Chloroform-d
6.77
6.77
6.76
6.76
6.73
6.71
3.79
3.17
1.90
1.88
1.72
1.69
1.32
1.80
1.00
3.11
3.00
1.11
1.15
3.00
f1 (ppm)

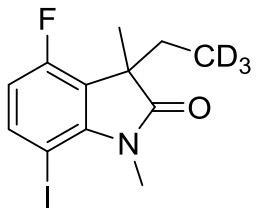

180.48
156.08
137.11
135.48
111.47
110.37
108.10
77.16 Chloroform-d
55.86
49.46
31.33
26.25
23.52
8.45
8.29
8.14
7.99
7.84
f1 (ppm)


CD3
O
N

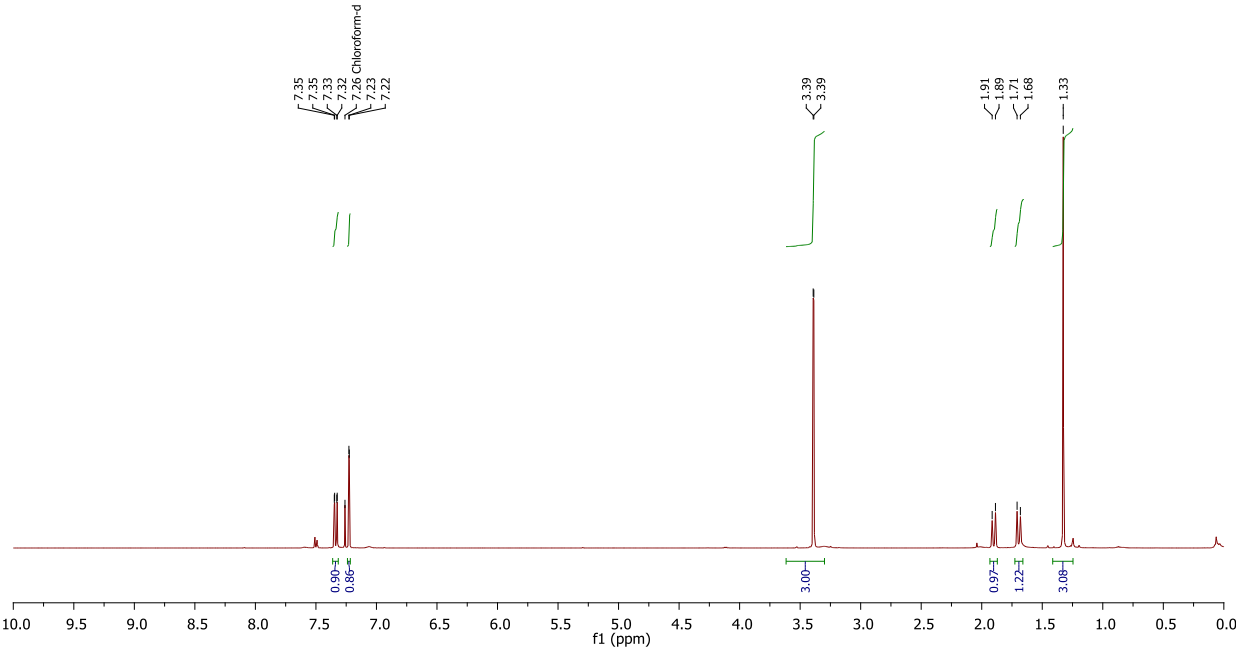
(4d)

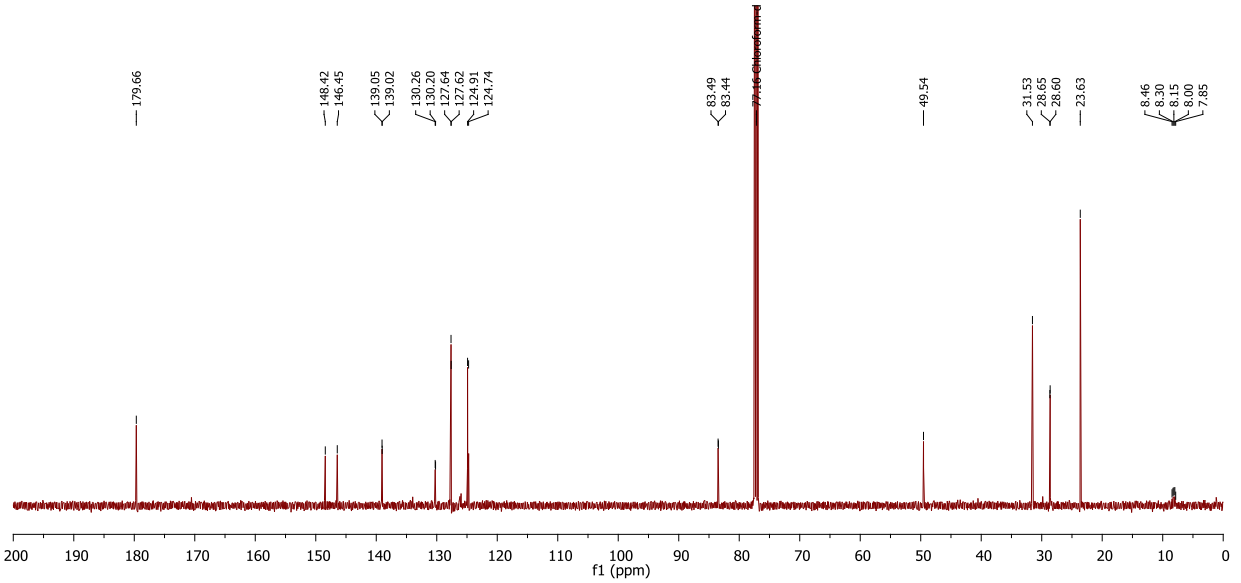

7.26 Chloroform-d
6.65
6.51
3.18
2.34
2.31
1.96
1.40
1.00
1.00
3.08
2.99
3.30
1.85
3.01
f1 (ppm)

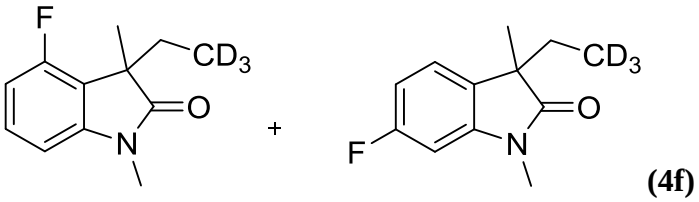

181.17
143.96
137.55
133.95
127.46
125.60
106.73
77.16 Chloroform-d
50.01
29.27
26.25
22.37
21.67
18.11
8.85
8.70
8.54
8.39
8.24
f1 (ppm)


F
CD3
O
N
I

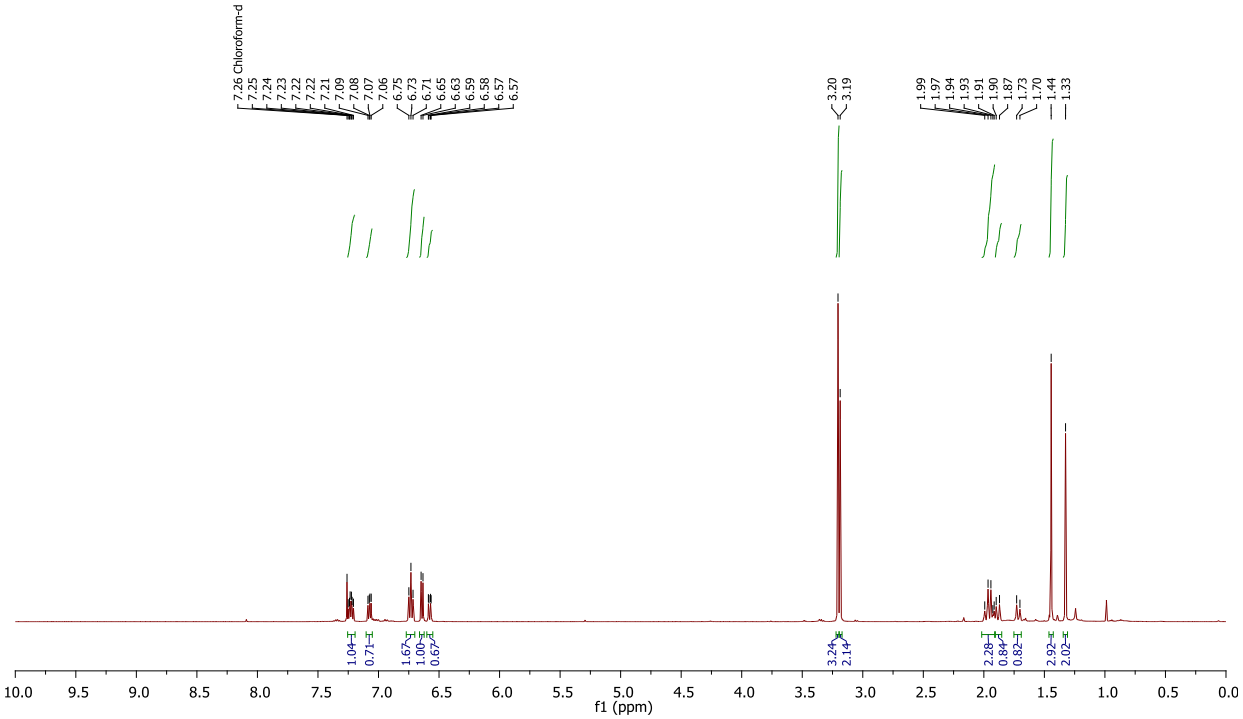
(4e)

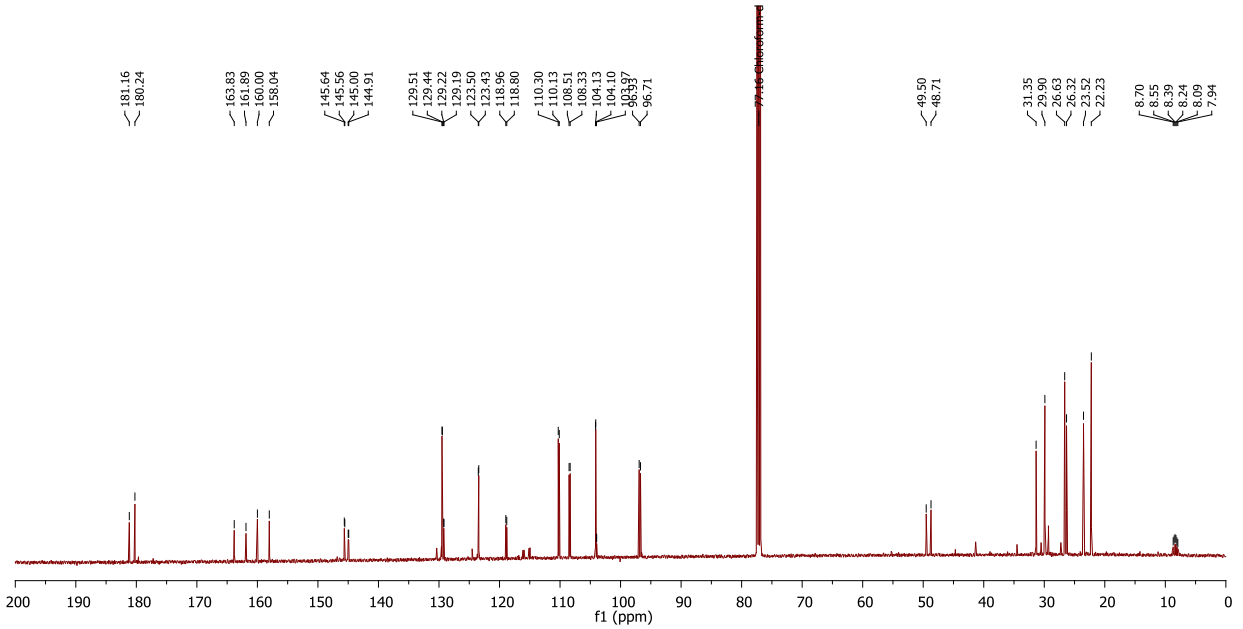

7.35
7.35
7.33
7.32
7.26 Chloroform-d
7.23
7.22
3.39
3.39
1.91
1.89
1.71
1.68
1.33
0.90
0.86
3.00
0.97
1.22
3.08
f1 (ppm)

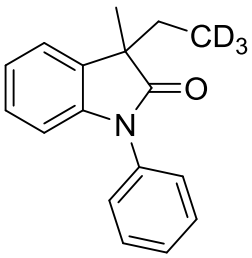

179.66
148.42
146.45
139.05
139.02
130.26
130.20
127.64
127.62
124.91
124.74
83.49
83.44
77.16 Chloroform-d
49.54
31.53
28.65
28.60
23.63
8.46
8.30
8.15
8.00
7.85
f1 (ppm)



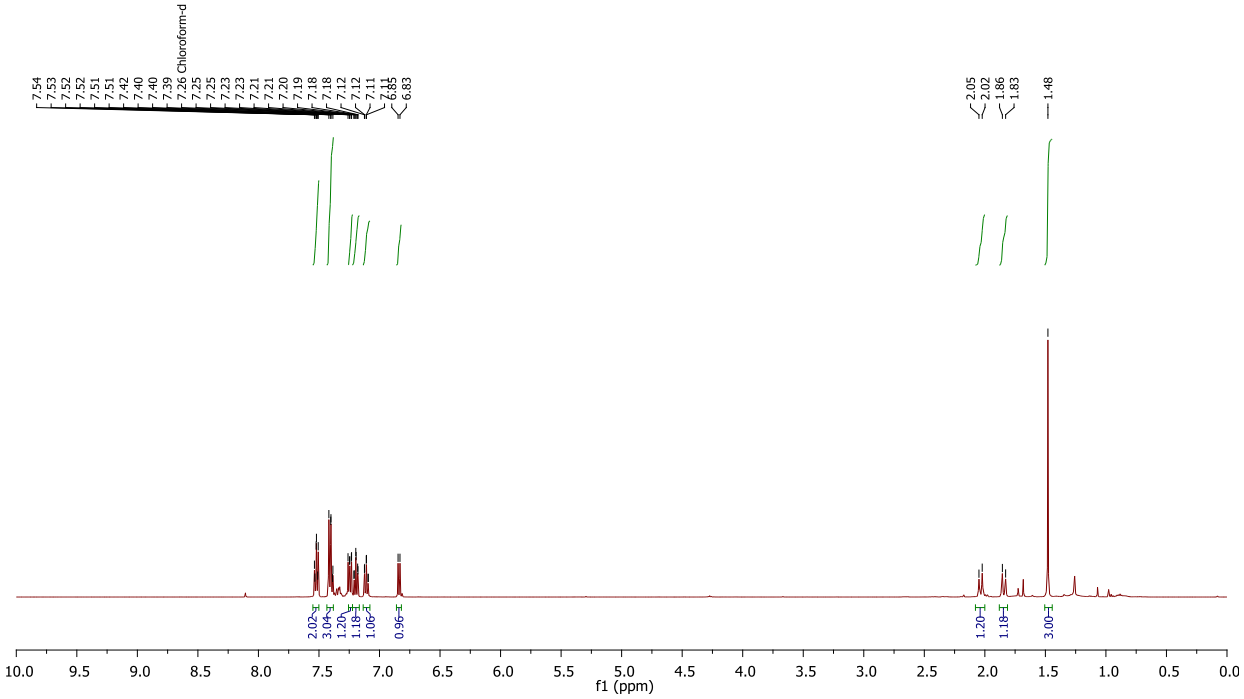
(4f)

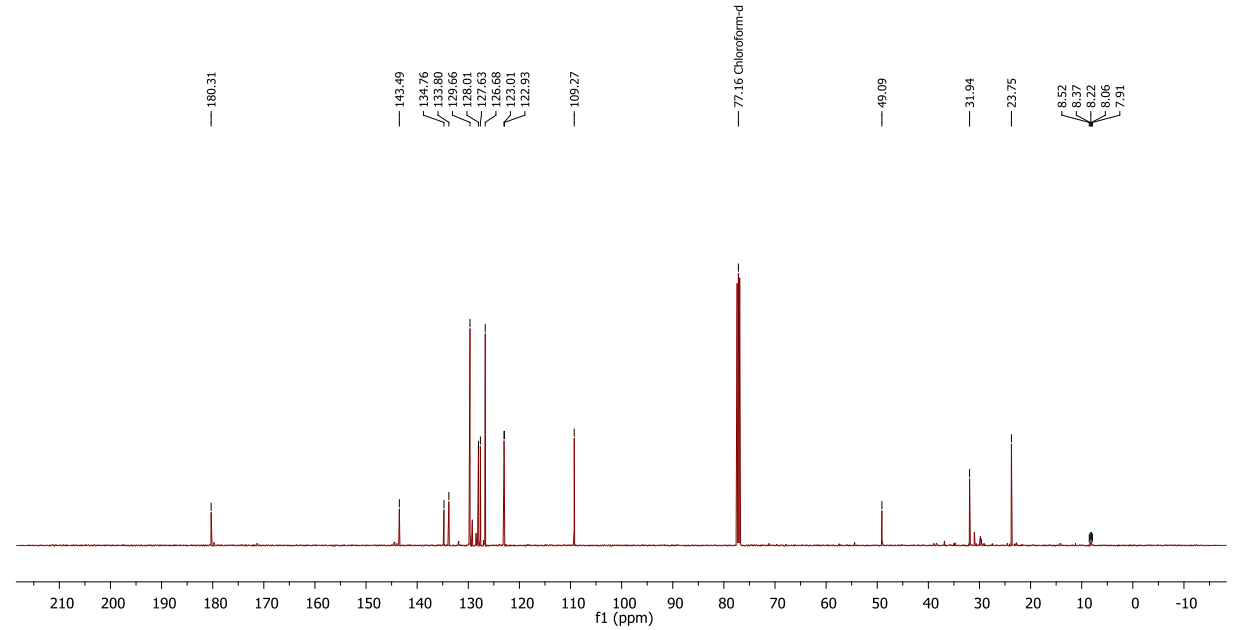

7.26 Chloroform-d
7.25
7.24
7.23
7.22
7.22
7.21
7.09
7.08
7.07
7.06
6.75
6.73
6.71
6.65
6.63
6.59
6.58
6.57
6.57
3.20
3.19
1.99
1.97
1.94
1.93
1.91
1.90
1.87
1.73
1.70
1.44
1.33
1.04
0.71
1.67
1.00
0.67
3.24
2.14
2.28
0.84
0.82
2.92
2.02
f1 (ppm)

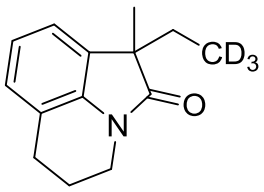

181.16
180.24
163.83
161.89
160.00
158.04
145.64
145.56
145.00
144.91
129.51
129.44
129.22
129.19
123.50
123.43
118.96
118.80
110.30
110.13
108.51
108.33
104.13
104.10
98.33
96.71
77.16 Chloroform-d
49.50
48.71
31.35
29.90
26.63
26.32
23.52
22.23
8.70
8.55
8.39
8.24
8.09
7.94
f1 (ppm)


CD3
O
N

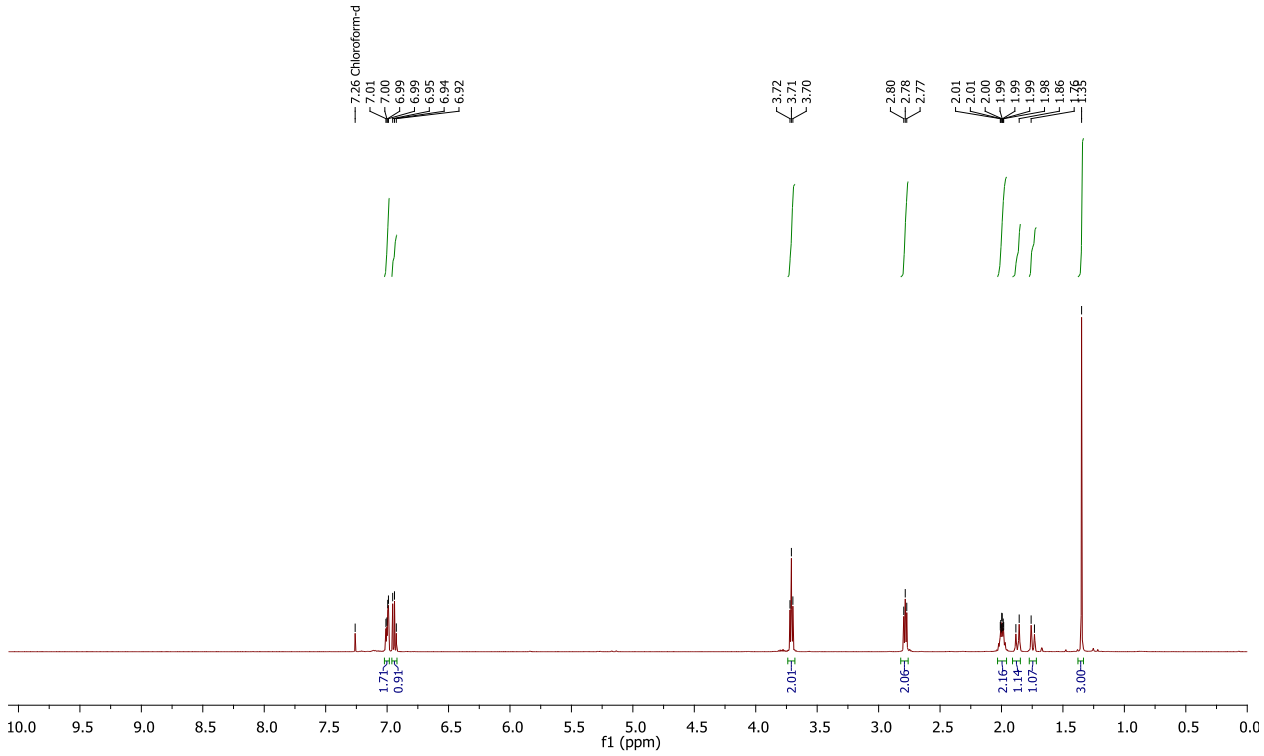
(4g)

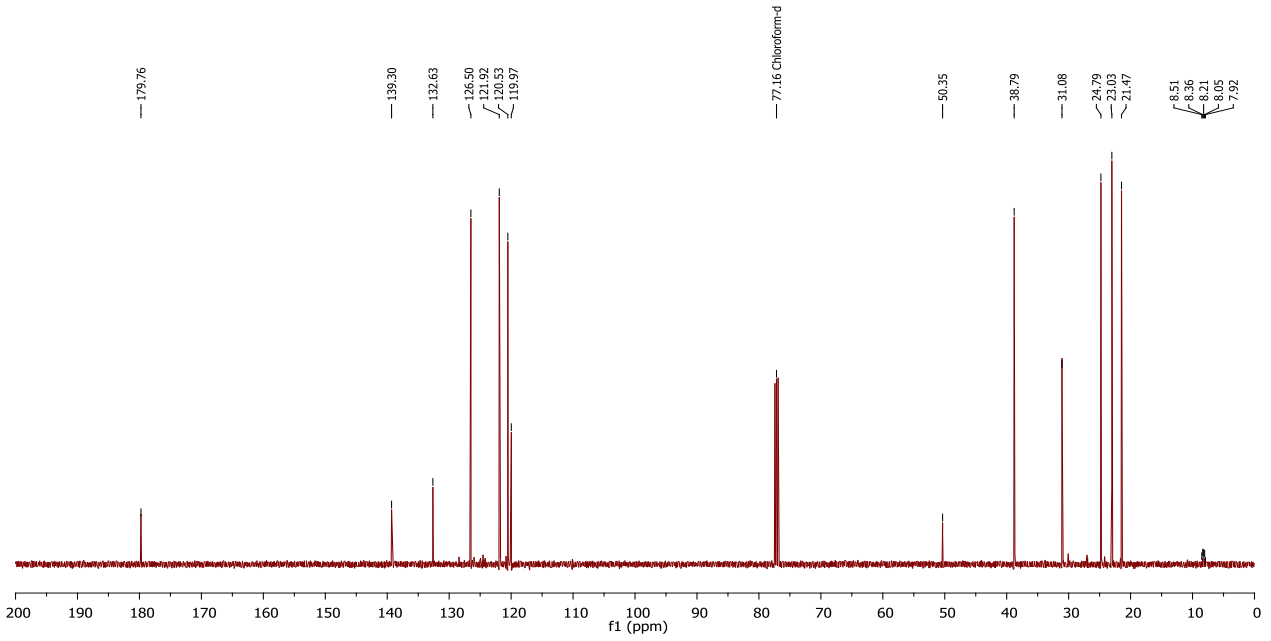

7.54
7.53
7.52
7.52
7.52
7.51
7.51
7.42
7.40
7.40
7.39
7.26 Chloroform-d
7.25
7.25
7.23
7.23
7.21
7.21
7.20
7.19
7.18
7.18
7.12
7.12
7.11
6.85
6.83
2.05
2.02
1.86
1.83
1.48
2.02
3.04
1.20
1.18
1.06
0.96
1.20
1.18
3.00
f1 (ppm)

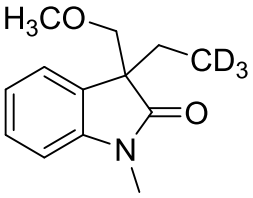

180.31
143.49
134.76
133.80
129.66
128.01
127.63
126.68
123.01
122.93
109.27
77.16 Chloroform-d
49.09
31.94
23.75
8.52
8.37
8.22
8.06
7.91
f1 (ppm)


CD3
O
N

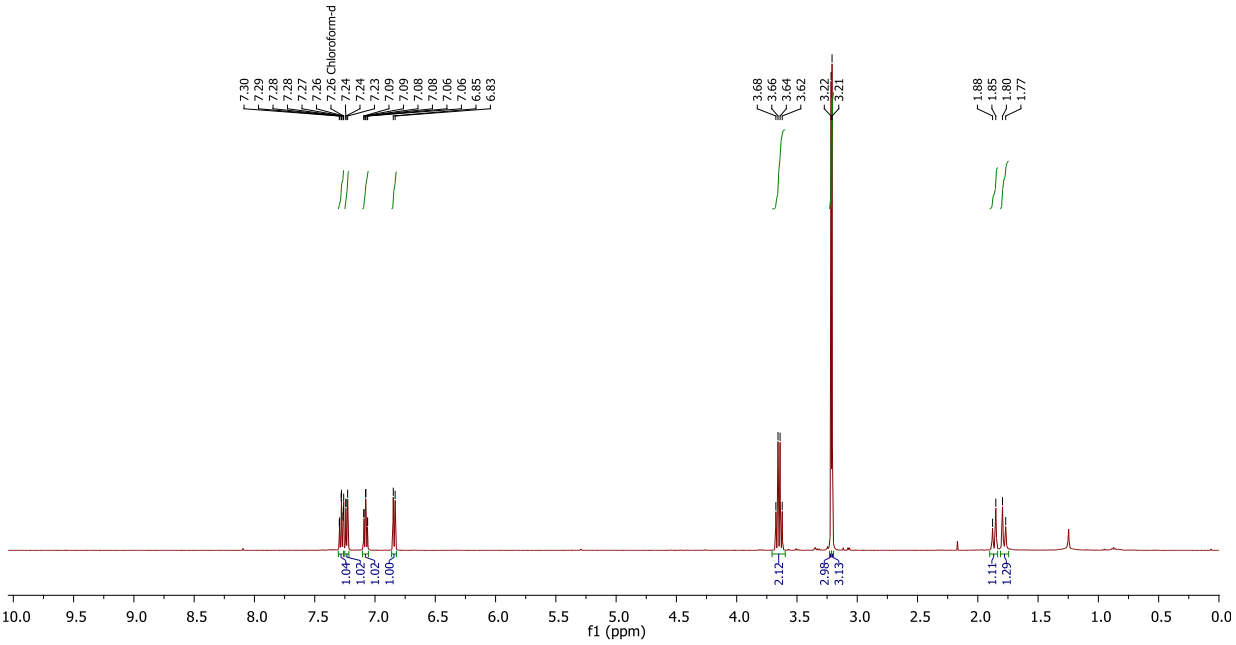
(4h

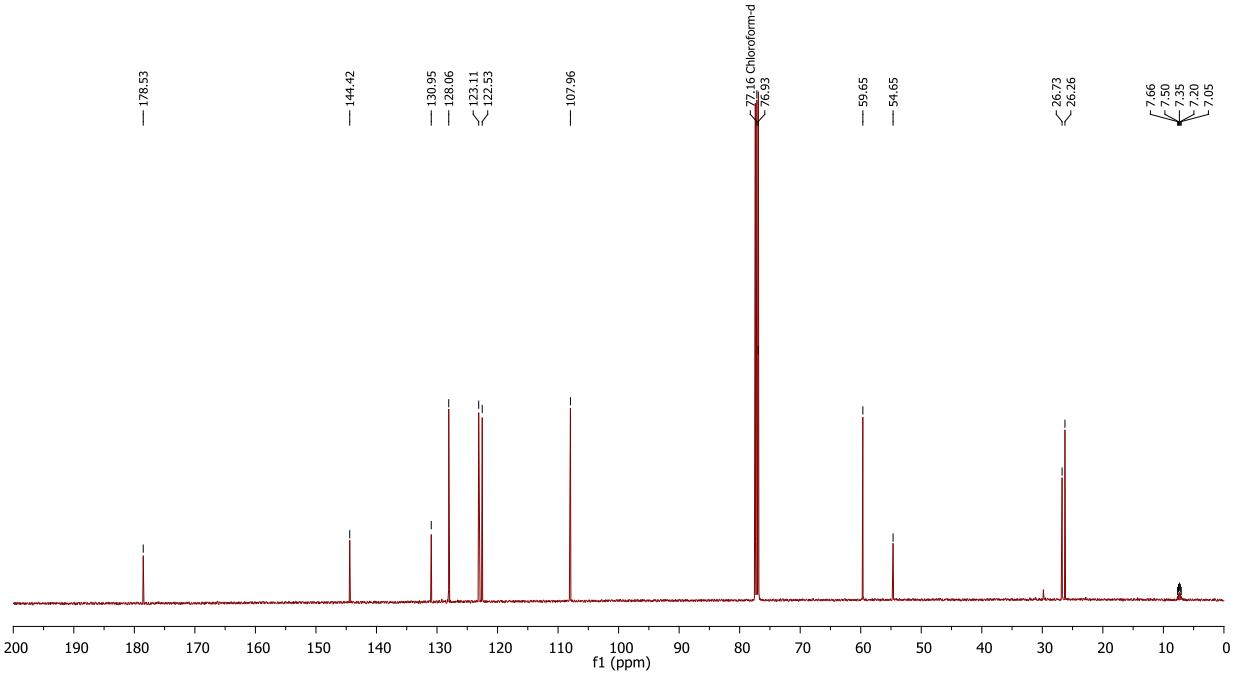

7.26 Chloroform-d
7.01
7.00
6.99
6.99
6.95
6.94
6.92
3.72
3.71
3.70
2.80
2.78
2.77
2.01
2.01
2.00
1.99
1.99
1.99
1.98
1.86
1.76
1.35
1.71
0.91
2.01
2.06
2.16
1.14
1.07
3.00
f1 (ppm)

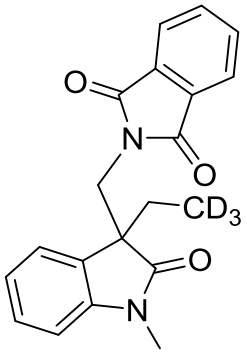

179.76
139.30
132.63
126.50
121.92
120.53
119.97
77.16 Chloroform-d
50.35
38.79
31.08
24.79
23.03
21.47
8.51
8.36
8.21
8.05
7.92
f1 (ppm)


H3CO
CD3
O
N

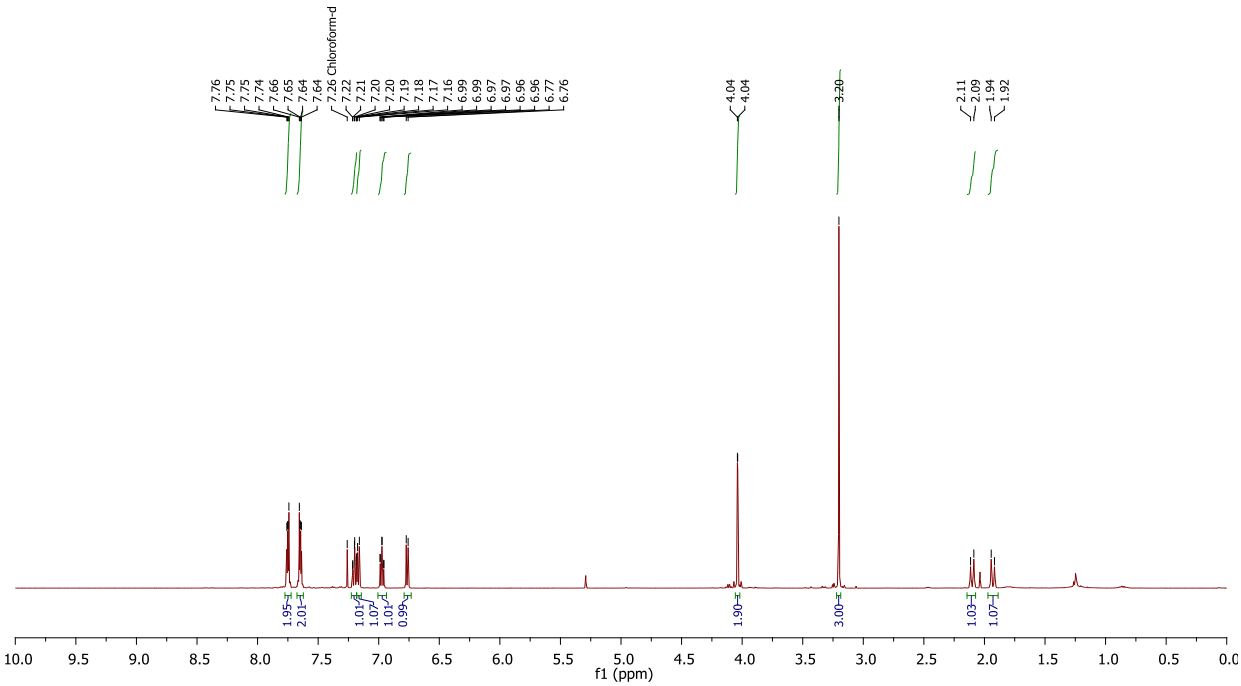
(4i)

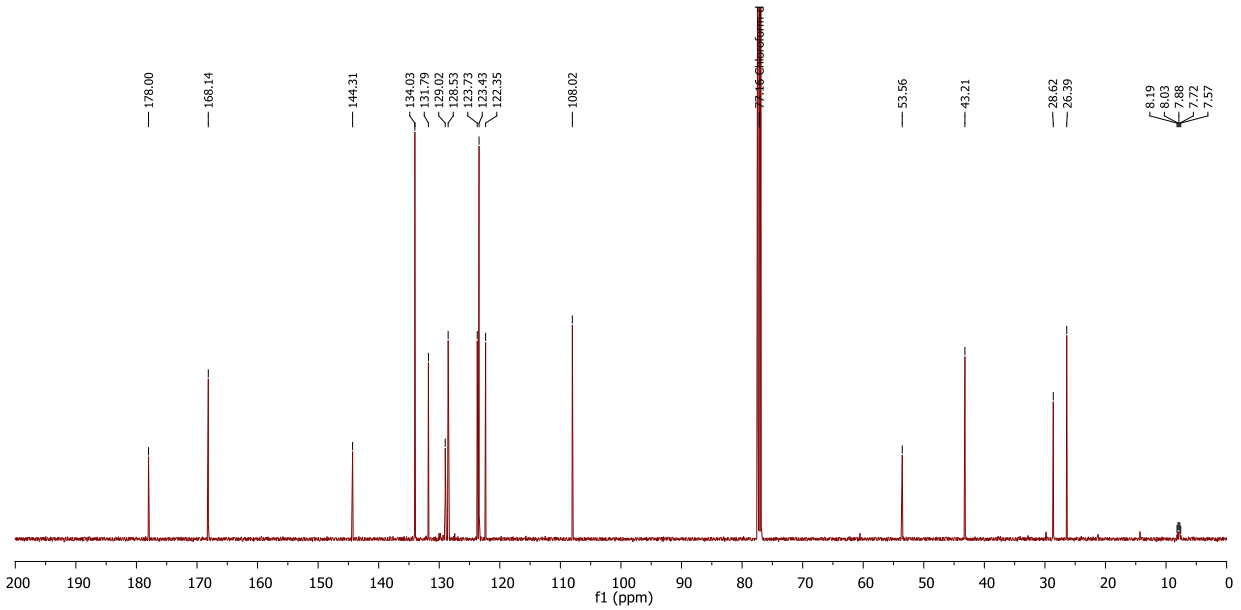

7.30
7.29
7.28
7.28
7.27
7.26
7.26 Chloroform-d
7.24
7.24
7.23
7.09
7.09
7.08
7.08
7.06
7.06
6.85
6.83
3.68
3.66
3.64
3.62
3.22
3.21
1.88
1.85
1.80
1.77
1.04
1.02
1.02
1.00
2.12
2.98
3.13
1.11
1.29
f1 (ppm)

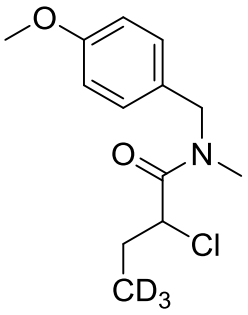

178.53
144.42
130.95
128.06
123.11
122.53
107.96
77.16 Chloroform-d
76.93
59.65
54.65
26.73
26.26
7.66
7.50
7.35
7.20
7.05
f1 (ppm)



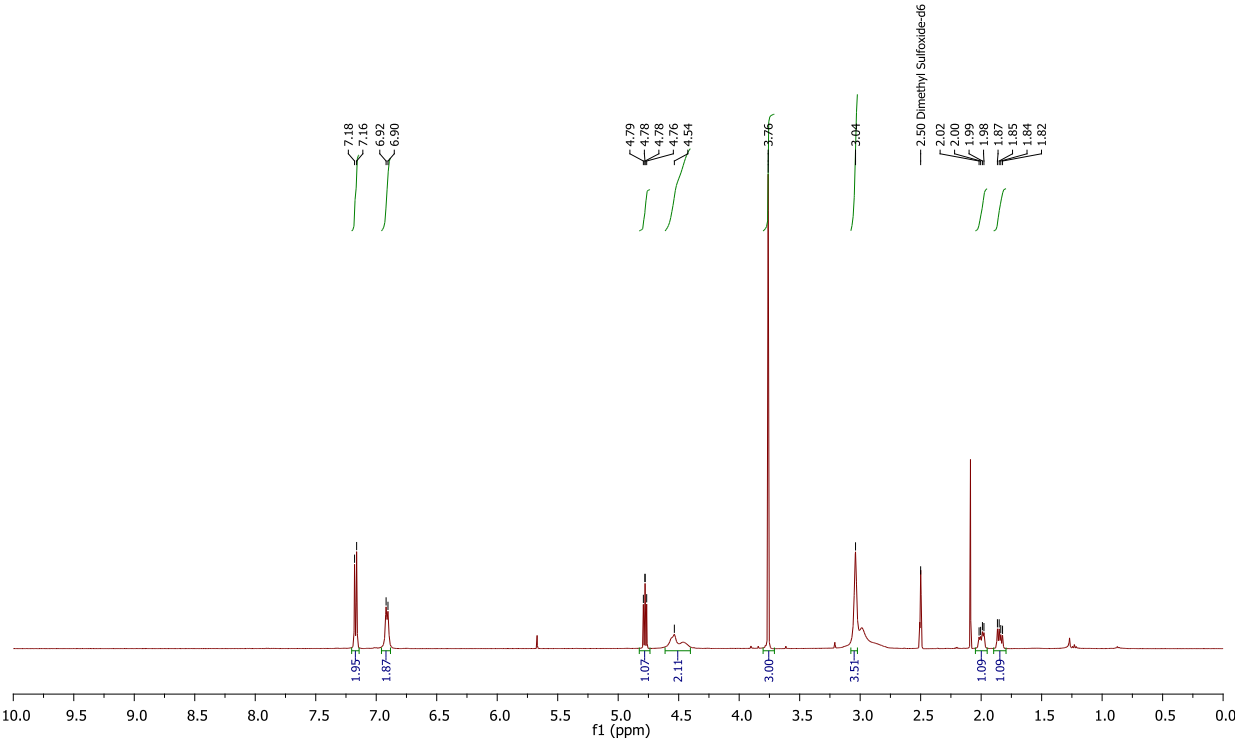
(4j)

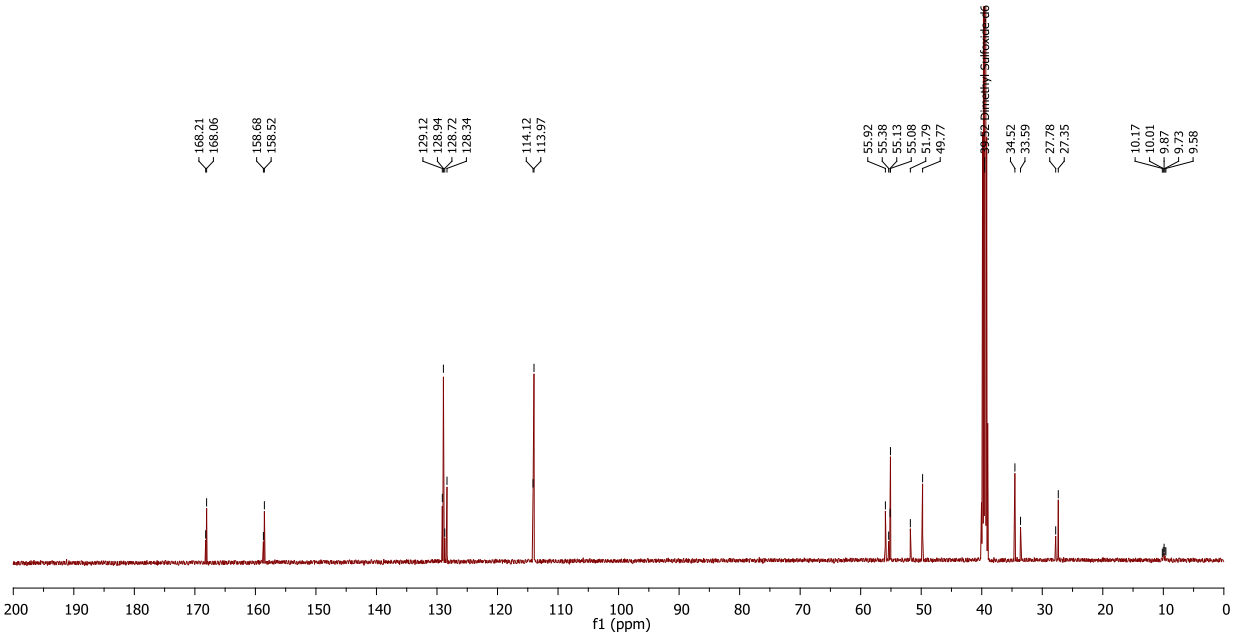

7.76
7.75
7.75
7.74
7.66
7.65
7.64
7.64
7.26 Chloroform-d
7.22
7.21
7.20
7.20
7.19
7.18
7.17
7.16
6.99
6.99
6.97
6.97
6.96
6.96
6.77
6.76
4.04
4.04
3.20
2.11
2.09
1.94
1.92
1.95
2.01
1.01
1.07
1.01
0.99
1.90
3.00
1.03
1.07
f1 (ppm)

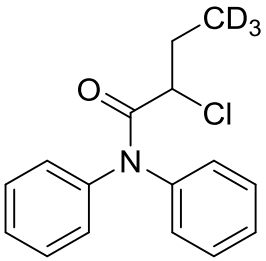

178.00
168.14
144.31
134.03
131.79
129.02
128.53
123.73
123.43
122.35
108.02
77.16 Chloroform-d
53.56
43.21
28.62
26.39
8.19
8.03
7.88
7.72
7.57
f1 (ppm)


O
O
N
Cl
CD3

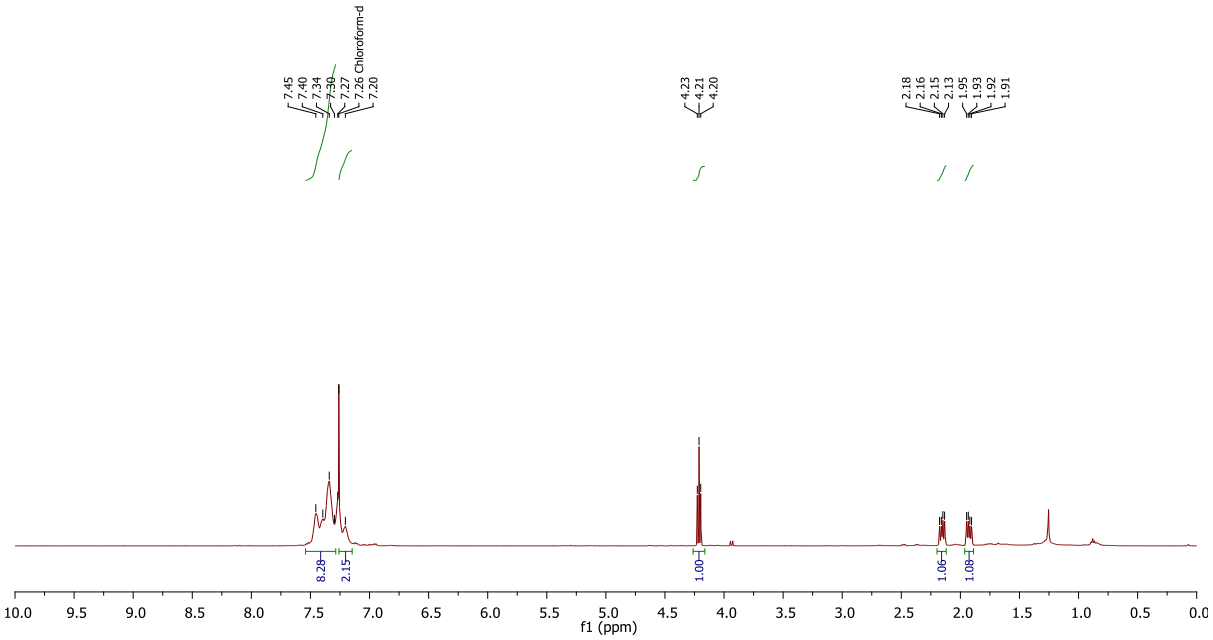
(6a)

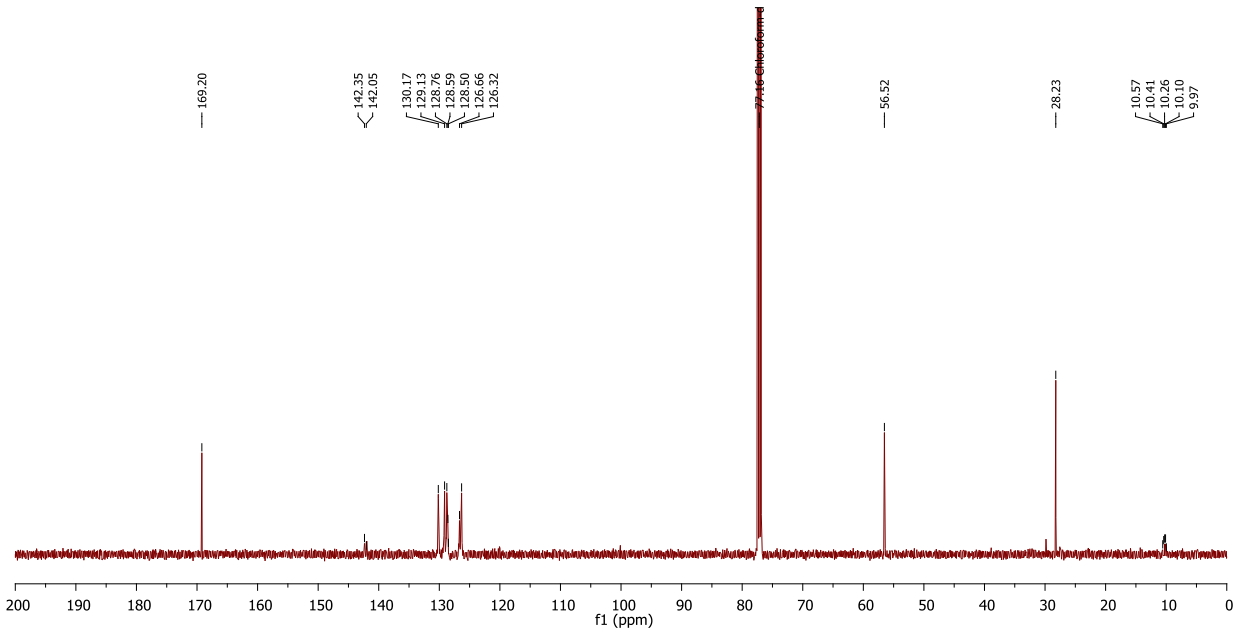

7.18
7.16
6.92
6.90
4.79
4.78
4.78
4.76
4.54
3.76
3.04
2.50 Dimethyl Sulfoxide-d6
2.02
2.00
1.99
1.98
1.87
1.85
1.84
1.82
1.95
1.87
1.07
2.11
3.00
3.51
1.09
1.09
f1 (ppm)

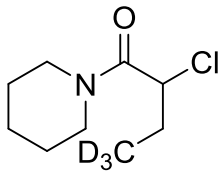

168.21
168.06
158.68
158.52
129.12
128.94
128.72
128.34
114.12
113.97
55.92
55.38
55.13
55.08
51.79
49.77
39.52 Dimethyl Sulfoxide-d6
34.52
33.59
27.78
27.35
10.17
10.01
9.87
9.73
9.58
f1 (ppm)


CD3
O
Cl
N

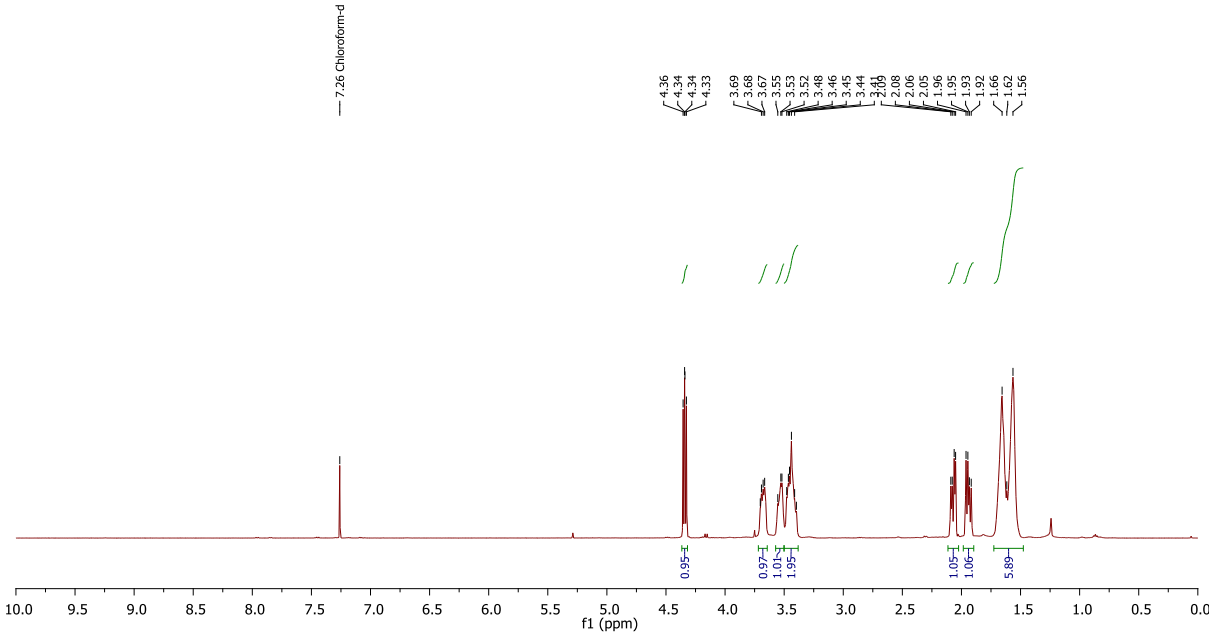
(6b)

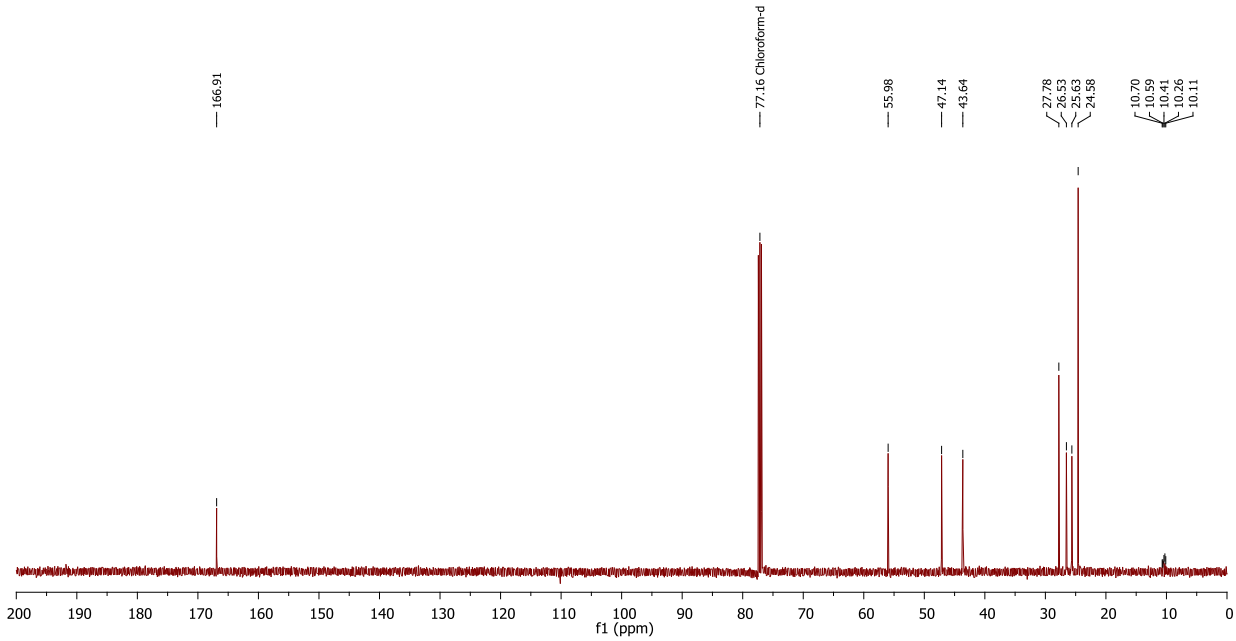

7.45
7.40
7.34
7.30
7.27
7.26 Chloroform-d
7.20
4.23
4.21
4.20
2.18
2.16
2.15
2.13
1.95
1.93
1.92
1.91
8.28
2.15
1.00
1.06
1.08
f1 (ppm)

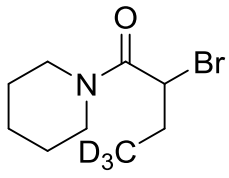

169.20
142.35
142.05
130.17
129.13
128.76
128.59
128.50
126.66
126.32
77.16 Chloroform-d
56.52
28.23
10.57
10.41
10.26
10.10
9.97
f1 (ppm)


O
N
Cl
D3C

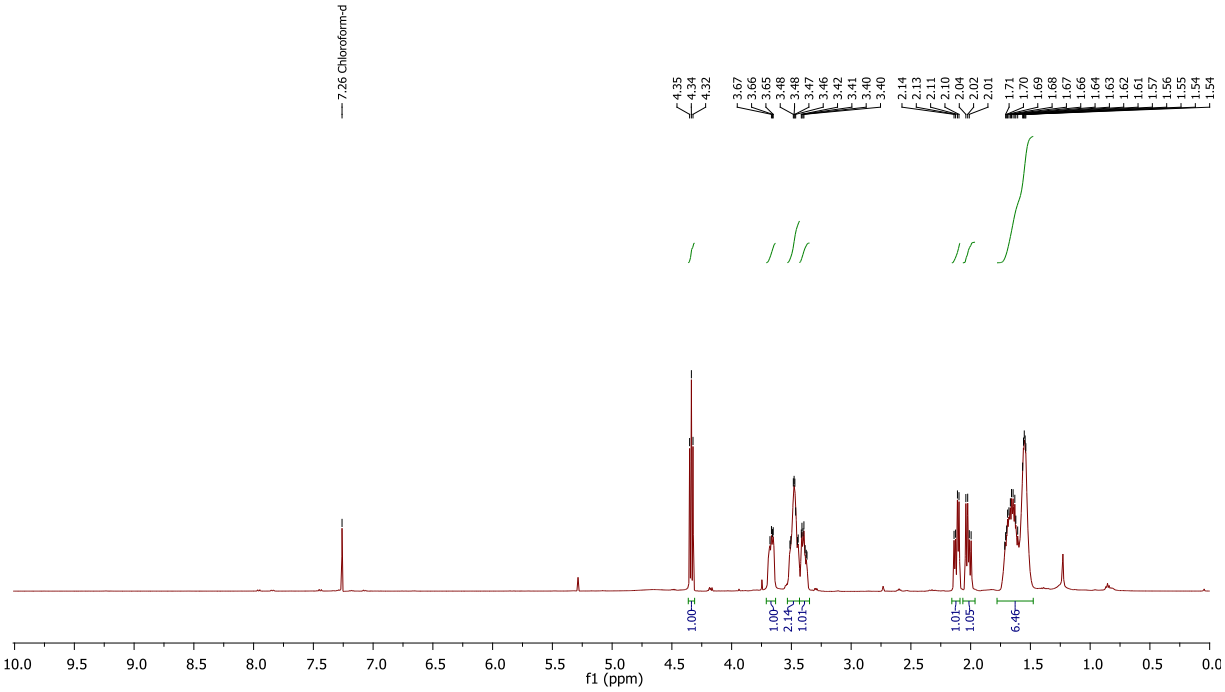
(6c)

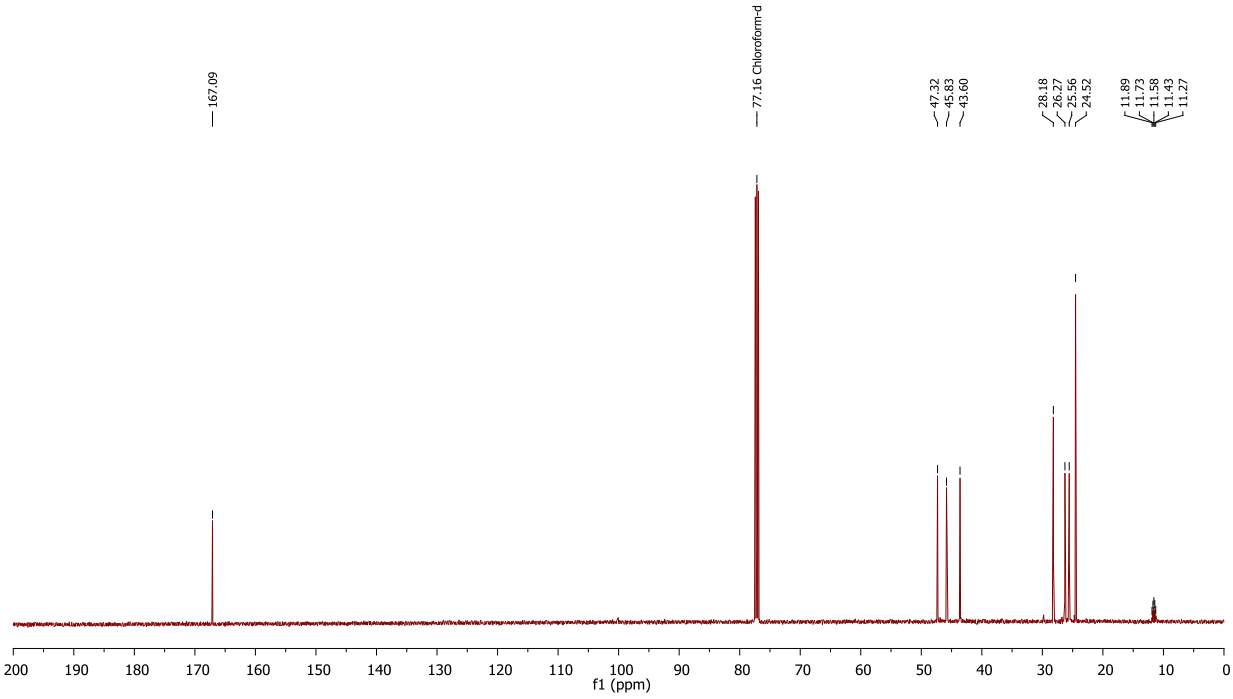

7.26 Chloroform-d
4.36
4.34
4.34
4.33
3.69
3.68
3.67
3.55
3.53
3.52
3.48
3.46
3.45
3.44
3.41
2.09
2.08
2.06
2.05
1.96
1.95
1.93
1.92
1.66
1.62
1.56
0.95
0.97
1.01
1.95
1.05
1.06
5.89
f1 (ppm)

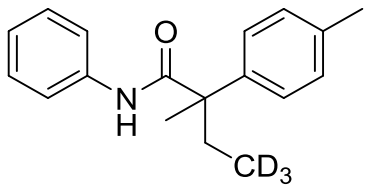

166.91
77.16 Chloroform-d
55.98
47.14
43.64
27.78
26.53
25.63
24.58
10.70
10.59
10.41
10.26
10.11
f1 (ppm)


O
Br
N
D3C

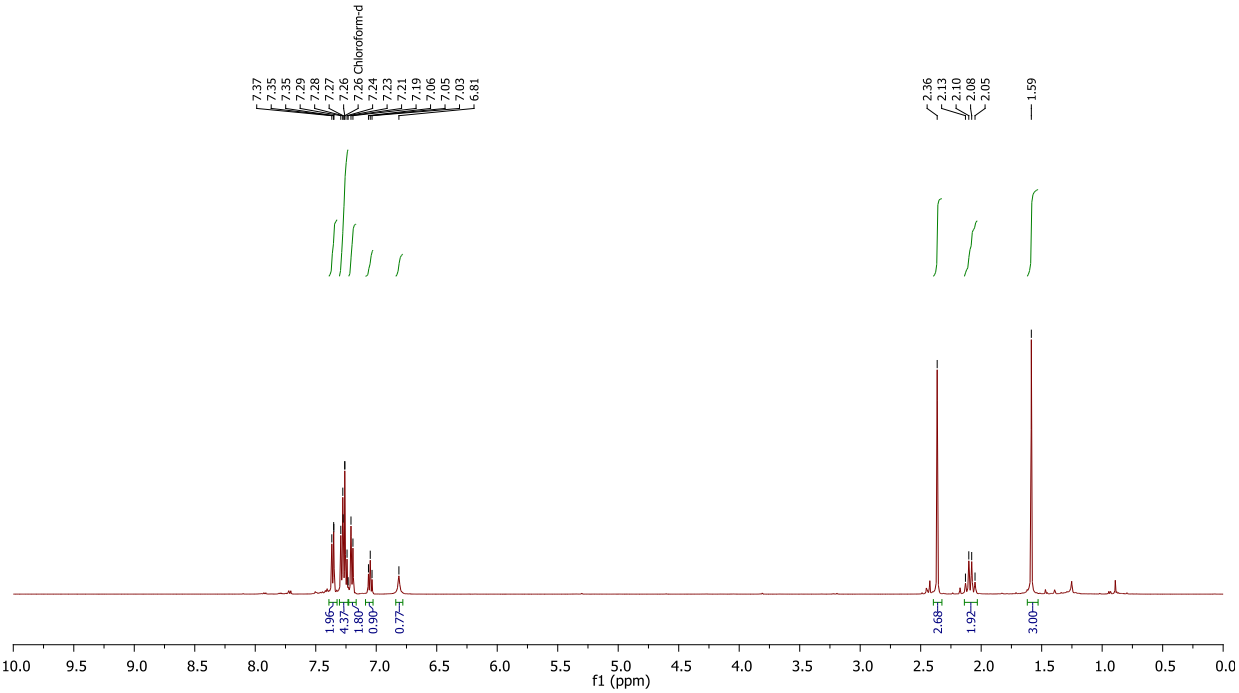
(4d)

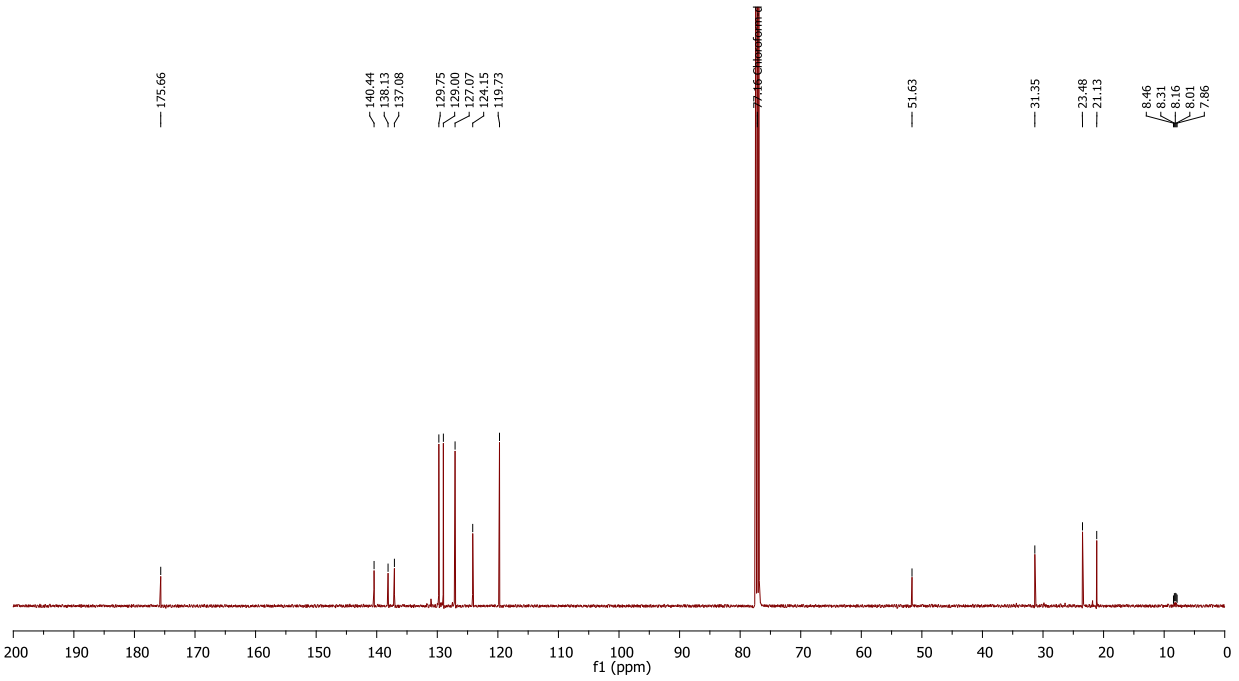

7.26 Chloroform-d
4.35
4.34
4.32
3.67
3.66
3.65
3.48
3.47
3.46
3.42
3.41
3.40
2.14
2.13
2.11
2.10
2.04
2.02
2.01
1.71
1.70
1.69
1.68
1.67
1.66
1.64
1.63
1.62
1.61
1.57
1.56
1.55
1.54
1.54
1.00
1.00
2.14
1.01
1.01
1.05
6.46
f1 (ppm)


167.09
77.16 Chloroform-d
47.32
45.83
43.60
28.18
26.27
25.56
24.52
11.89
11.73
11.58
11.43
11.27
f1 (ppm)


O
N
H
CD3

(8)


7.37
7.35
7.35
7.29
7.28
7.27
7.26
7.26 Chloroform-d
7.24
7.23
7.21
7.19
7.06
7.05
7.03
6.81
2.36
2.13
2.10
2.08
2.05
1.59
1.96
4.37
1.80
0.90
0.77
2.68
1.92
3.00
f1 (ppm)


175.66
140.44
138.13
137.08
129.75
129.00
127.07
124.15
119.73
77.16 Chloroform-d
51.63
31.35
23.48
21.13
8.46
8.31
8.16
8.01
7.86
f1 (ppm)