Electronic Supplementary Material (ESI) for ChemComm.

Rh-catalyzed arylation of fluorinated ketones with arylboronic acids

Supporting Information

Luca S. Dobson and Graham Pattison*

Department of Chemistry, University of Warwick, Gibbet Hill Road, Coventry, CV4 7AL, UK.

Email: graham.pattison@warwick.ac.uk

Contents

1. General Considerations

Solvents and commercially available reagents were purchased from standard chemical suppliers (Fisher, Sigma-Aldrich, VWR, Fluorochem) and used as received without further purification or drying. Reactions were performed under an atmosphere of dry nitrogen gas. Thin layer chromatography (TLC) was performed on Merck DF-Alufoilien 60F254 0.2 mm precoated plates. Product spots were visualized by UV light at 254 nm, and subsequently developed using vanillin or potassium permanganate as appropriate. Flash column chromatography was carried out using silica gel (Apollo Scientific 60Å particle size 40-63 micron). Melting points are uncorrected. Infra-red spectra were recorded on a Bruker Alpha-P ATR instrument on the neat compound. NMR spectra were recorded on a Bruker DPX-300, Bruker Avance III HD 300 MHz or Bruker Avance III HD 500 MHz instrument. For ^{1}H NMR spectra, chemical shifts (δ) are quoted in parts per million (ppm) downfield of tetramethylsilane, using residual protonated solvent as internal standard ($CDCl_3$ at 7.26 ppm, d_6-acetone at 2.05 ppm). Abbreviations used in the description of resonances are: s (singlet), d (doublet), t (triplet), q, (quartet), app (apparent), br (broad). Coupling constants (J) are quoted to the nearest 0.1 Hz. For proton decoupled ^{13}C NMR spectra, chemical shifts (δ) are quoted in parts per million (ppm) downfield of tetramethylsilane, using deuterated solvent as internal standard ($CDCl_3$ at 77.16 ppm, d_6-acetone at 29.92 ppm). Assignments were made using DEPT or PENDANT pulse sequences. For proton-decoupled ^{19}F NMR spectra, chemical shifts (δ) are quoted in parts per million (ppm) downfield of $CFCl_3$, using residual protonated solvent as internal standard ($CFCl_3$ at 376.38 MHz with respect to tetramethylsilane at 400.00 MHz). Low resolution mass spectra were recorded using electrospray ionization (ESI) techniques on an Agilent 6130R instrument. High resolution mass spectra were recorded using electrospray ionization (ESI) techniques on a Bruker Maxis instrument.

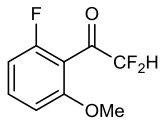
2. Preparation of difluoromethyl ketones.

These were prepared using General Procedure A following a literature method.[1] Data for compounds **1a-1m** was in agreement with that reported in the literature.

General Procedure A.

Selectfluor (24 mmol) and the 1,3-dicarbonyl derivativc (10 mmol) were dissolved in acetonitrile (10.4 mL). The mixture was heated to reflux at 80 °C for 3 hours, followed by the addition of water (20 mmol), then heated to reflux for a further 15 minutes. The solution was cooled to room temperature, triethylamine (50 mmol) was added and the mixture stirred overnight. The solvent was removed under vacuum and the resulting crude product was purified by column chromatography to afford the difluoromethyl ketone.

2,2-difluoro-1-(2-fluoro-6-methoxyphenyl)ethan-1-one (1n)



This compound was prepared by a modification of General Procedure A using the following quantities: 4,4,4-trifluoro-1-(2-methoxy-6-fluoro-phenyl)-1,3-butanedione (150 mg, 0.61 mmol) and Selectfluor (517 mg, 1.46 mmol) were dissolved in acetonitrile (0.6 mL) and heated to reflux at 80 °C for 3 hours, followed by the addition of water (22 µL, 1.22 mmol), then heated to reflux for a further 15 minutes. The solution was cooled to room temperature, triethylamine (0.43 mL, 3.05 mmol) was added and the mixture stirred overnight. The solvent was removed under vacuum and the resulting crude product was purified by column chromatography (5% Et_2O / hexane) to afford the difluoromethyl ketone **1n** as a white solid (111 mg, 90%); m.p. 65 – 67 °C; IR 1687, 1492, 1423, 1263, 1174, 1140, 1069, 1016, 821, 736 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.52 (1H, dd, *J* = 8.4, 3.2 Hz, Ar**H**), 7.29 (1H, ddd, *J* = 11, 8.4, 4.2 Hz, Ar**H**), 6.99 (1H, dd, *J* = 9.1, 3.9 Hz, Ar**H**), 6.59 (1H, t, *J* = 54 Hz, Ar**H**), 3.94 (3H, s, OC**H**$_3$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 188.0 (td, *J* = 25, 1.4 Hz, C), 157.0 (d, *J* = 242 Hz, C), 155.7 (d, *J* = 1.9 Hz, C), 124.0 (d, *J* = 6.5 Hz, C), 122.5 (d, *J* = 24 Hz, CH), 117.4 (d, *J* = 25 Hz, CH), 113.4 (d, *J* = 7.5 Hz, CH), 109.5 (t, *J* = 248 Hz, CF_2H), 56.5 (s, CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ -122.1 (1F, ddd, *J* = 4.1, 7.8, 11 Hz), -128.8 (2F, d, *J* = 54 Hz).

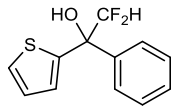
[1] D.J. Leng; C.M. Black; G. Pattison *Org. Biomol. Chem.* **2016**, *14,* 1531 - 1535

3. Racemic Arylation of Difluoromethyl and Monofluoromethyl Ketones.

General Procedure B

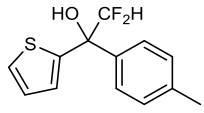
Difluoromethyl ketone (0.5 mmol), boronic acid (1.5 mmol), potassium carbonate (207 mg, 1.5 mmol) and $[Rh(cod)Cl]_2$ (6.2 mg, 0.0125 mmol, 2.5 mol%) were dissolved in toluene (2 mL) and the mixture stirred at 100 °C for 24 hours. After this period the mixture was cooled and the reaction quenched by the addition of 2M HCl (4 mL). The aqueous layer was washed with DCM (3 x 30 mL), and the organic layers collected, combined and dried with magnesium sulfate. The solvent was removed under reduced pressure and the crude purified by column chromatography.

2,2-difluoro-1-phenyl-1-(thiophen-2-yl)ethan-1-ol (2a)



The title compound was prepared according to General Procedure B from 2,2-difluoro-1-(thiophen-2-yl)ethan-1-one (81 mg, 0.5 mmol) and phenylboronic acid (183 mg, 1.5 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give an orange oil (87 mg, 69%). IR 3536, 1716, 1602, 1494, 1449, 1333, 1133, 1070, 1043, 837cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (2H, d, *J* = 7.1 Hz, Ar**H**), 7.44 – 7.32 (4H, m, Ar**H**), 7.15 (1H, d, *J* = 3.5 Hz, Ar**H**), 7.02 (1H, dd, *J* = 4.7, 4.0 Hz, Ar**H**), 6.12 (1H, t, *J* = 56 Hz, Ar**H**), 2.98 (1H, s, O**H**); ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.0 (C), 139.2 (C), 128.7 (CH), 128.3 (2 x CH), 126.8 (CH), 126.6 (2 x CH), 126.5 (t, *J* = 1.9Hz, CH), 126.4 (CH), 116.3 (t, J = 252 Hz, CF_2H), 76.9 (t, J = 22 Hz, C); ^{19}F NMR (282 MHz, $CDCl_3$) δ -126.6 (1F, d, J = 275 Hz, CF_2H), -127.7 (1F, d, J = 275 Hz, CF_2H); HRMS (ES^-): Exact mass calculated for $C_{12}H_{10}OF_2S$ $[M-H]^-$: 239.0348, found: 239.0345.

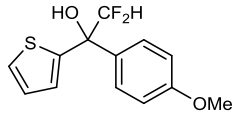
2,2-difluoro-1-(thiophen-2-yl)-1-(p-tolyl)ethan-1-ol (2b)



The title compound was prepared according to General Procedure B from 2,2-difluoro-1-(thiophen-2-yl)ethan-1-one (81 mg, 0.5 mmol) and *p*-tolylboronic acid (204 mg, 1.5 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give an orange oil (104

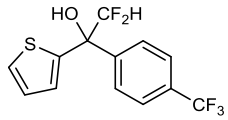
mg, 82%). IR 3339, 1132, 1071, 792, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (2H, d, *J* = 8.0 Hz, Ar**H**), 7.35 (1H, d, *J* = 5.0 Hz, Ar**H**), 7.22 (2H, d, *J* = 8.0 Hz, Ar**H**), 7.16 (1H, d, *J* = 3.5 Hz, Ar**H**), 7.03 (1H, dd, *J* = 5.0, 3.5 Hz, Ar**H**), 6.12 (1H, t, *J* = 56 Hz, CF_2**H**), 2.98 (1H, s, O**H**), 2.39 (3H, s, C**H**$_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 144.2 (C), 138.5 (C), 136.3 (C), 129.0 (2 x CH), 126.7 (CH), 126.5 (2 x CH), 126.4 (CH), 126.3 (CH), 116.3 (t, *J* = 252 Hz, CF_2H), 76.8 (t, *J* = 22 Hz, C), 21.0 (CH_3); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -126.7 (1F, dd, *J* = 275, 56 Hz, CF_2H), -127.7 (1F, dd, *J* = 275, 56 Hz, CF_2H); HRMS (ES^-): Exact mass calculated for $C_{13}H_{12}OF_2S$ $[M-H]^-$: 253.0504, found: 253.0503.

2,2-difluoro-1-(4-methoxyphenyl)-1-(thiophen-2-yl)ethan-1-ol (2c)



The title compound was prepared according to General Procedure B from 2,2-difluoro-1-(thiophen-2-yl)ethan-1-one (81 mg, 0.5 mmol) and 4-methoxyphenylboronic acid (228 mg, 1.5 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a colourless oil (119 mg, 88%). IR 2970, 1609, 1511, 1300, 1250, 1128, 1071, 946, 830 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (2H, d, *J* = 8.9 Hz), 7.34 (1H, dd, *J* = 5.1, 1.1 Hz, Ar**H**), 7.13 (1H, d, *J* = 3.6 Hz, Ar**H**), 7.01 (1H, dd, *J* = 5.1, 3.6 Hz, Ar**H**), 6.93 – 6.87 (2H, m, Ar**H**), 6.08 (1 H, t, *J* = 56 Hz, CF_2**H**), 3.82 (3H, s, OC**H**$_3$), 2.92 (1H, s, O**H**); ^{13}C NMR (126 MHz, $CDCl_3$) δ 159.7 (s, C), 144.4 (s, C), 131.3 (s, C), 128.1 (s, 2 x CH), 126.8 (s, CH), 126.4 (t, *J* = 1.8 Hz, CH), 126.3 (s, CH), 116.4 (t, *J* = 252 Hz, CF_2H), 113.6 (s, 2 x CH), 76.7 (t, *J* = 22 Hz, C), 55.3 (s, CH_3); ^{19}F NMR (282 MHz, $CDCl_3$) δ -126.4 (1F, dd, *J* = 274, 56 Hz), -127.4 (1F, dd, *J* = 274, 56 Hz); HRMS (ES^-): Exact mass calculated for $C_{13}H_{12}O_2F_2S$ $[M-H]^-$: 269.0453, found: 269.0458.

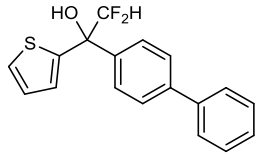
2,2-difluoro-1-(thiophen-2-yl)-1-(4-(trifluoromethyl)phenyl)ethan-1-ol (2d)



The title compound was prepared according to General Procedure B from 2,2-difluoro-1-(thiophen-2-yl)ethan-1-one (81.1 mg, 0.5 mmol) and (4-trifluoromethyl)phenylboronic acid (284.9 mg, 1.5 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a red oil (110 mg, 71%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (2H, d, *J* = 8.4 Hz, Ar**H**),

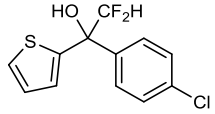
7.64 (2H, d, *J* = 8.4 Hz, Ar**H**), 7.37 (1H, dd, *J* = 5.1, 1.1 Hz, Ar**H**), 7.18 (1H, d, *J* = 3.6 Hz, Ar**H**), 7.03 (1H, dd, *J* = 5.1, 3.6 Hz, Ar**H**), 6.10 (1H, t, *J* = 55 Hz, CF_2**H**), 3.00 (1H, s, O**H**; ^{13}C NMR (126 MHz, $CDCl_3$) δ 143.3 (C), 142.9 (C), 130.8 (q, *J* = 32 Hz, **C**CF_3), 127.3 (2 x CH), 127.0 (CH), 126.9 (2 x CH), 126.7 (t, *J* = 1.8 Hz, CH), 125.3 (q, *J* = 4.0 Hz, 2 x CH), 123.8 (q, *J* = 272 Hz, CF_3), 116.0 (t, *J* = 252 Hz, CF_2H), 76.7 (t, *J* = 23 Hz, C); ^{19}F NMR (282 MHz, $CDCl_3$) δ -62.7 (3F, s, CF_3), -126.5 (1F, dd, *J* = 276, 55 Hz, CF_2H), -127.5 (1F, dd, *J* = 276, 55 Hz, CF_2H); HRMS (ES^-): Exact mass calculated for $C_{13}H_9OF_5S$ $[M-H]^-$: 307.0222, found: 307.0219.

1-([1,1'-biphenyl]-4-yl)-2,2-difluoro-1-(thiophen-2-yl)ethan-1-ol (2e)



The title compound was prepared according to General Procedure B from 2,2-difluoro-1-(thiophen-2-yl)ethan-1-one (81.1 mg, 0.5 mmol) and ([1,1'-biphenyl]-4-ylboronic acid (297.0 mg, 1.5 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a red oil (110 mg, 69%). mp: 113-114 ^oC; IR 3250, 1484, 1148, 1049, 789, 714, 696 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (4H, s, Ar**H**), 7.59 (2H, dd, *J* = 8.2, 0.8 Hz, Ar**H**), 7.44 (2H, t, *J* = 7.6 Hz, Ar**H**), 7.33-7.38 (2H, m, Ar**H**), 7.18 (1H, d, *J* = 3.6 Hz, Ar**H**), 7.03 (1H, dd, *J* = 5.0, 3.6 Hz, Ar**H**), 6.14 (1H, t, *J* = 56 Hz, CF_2**H**); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 144.0 (C), 141.5 (C), 140.4 (C), 138.2 (C), 128.8 (2 x CH), 127.6 (CH), 127.13 (2 x CH), 127.10 (2 x CH), 127.0 (2 x CH), 126.8 (CH), 126.6 (t, *J* = 1.8 Hz, CH), 126.5 (CH), 116.3 (t, *J* = 252 Hz, CF_2H), 76.9 (t, *J* = 22 Hz, C); ^{19}F NMR (376.5 MHz, $CDCl_3$) δ -126.6 (1F, dd, *J* = 274, 56 Hz, CF_2H), -127.4 (1F, dd, *J* = 274, 56 Hz, CF_2H); HRMS (ES^-): Exact mass calculated for $C_{18}H_{14}OF_2S$ $[M-H]^-$: 315.0661, found: 315.0659.

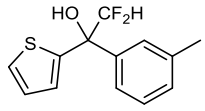
1-(4-chlorophenyl)-2,2-difluoro-1-(thiophen-2-yl)ethan-1-ol (2f)



The title compound was prepared according to General Procedure B from 2,2-difluoro-1-(thiophen-2-yl)ethan-1-one (81.1 mg, 0.5 mmol) and 4'-chlorophenylboronic acid (234.6 mg, 1.5 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a red

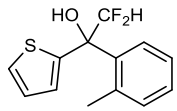
oil (102 mg, 74%). IR 1491, 1073, 1013, 824, 704 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49 (2H, d, *J* = 8.5 Hz, Ar**H**), 7.37 – 7.34 (3H, m, Ar**H**), 7.14 (1H, d, *J* = 3.6 Hz, Ar**H**), 7.02 (1H, dd, *J* = 5.1, 3.6 Hz, Ar**H**), 6.07 (1H, t, *J* = 55 Hz, CF_2**H**); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 143.6 (C), 137.7 (C), 134.8 (2 x C), 128.5 (2 x CH), 128.3 (2 x CH), 126.9 (CH), 126.7 (CH), 126.6 (CH), 116.1 (t, *J* = 253 Hz, CF_2H), 76.6 (t, *J* = 22.1 Hz, CHOH); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -127.1 (1F, dd, *J* = 276, 55 Hz, CF_2H), -127.4 (1F, dd, *J* = 276, 55 Hz, CF_2H); HRMS (ES^-): Exact mass calculated for $C_{12}H_9OClF_2S$ $[M-H]^-$: 272.9958, found: 272.9959.

2,2-difluoro-1-(thiophen-2-yl)-1-(m-tolyl)ethan-1-ol (2g)



The title compound was prepared according to General Procedure B from 2,2-difluoro-1-(thiophen-2-yl)ethan-1-one (81 mg, 0.5 mmol) and *m*-tolylboronic acid (204 mg, 1.5 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a red oil (81 mg, 64%). IR 1132 (C-O stretch), 1071 (C-F stretch), 773, 701 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (1H, s, Ar**H**), 7.36 – 7.32 (2H, m, Ar**H**), 7.26 (1H, t, *J* = 7.5 Hz, Ar**H**), 7.16 (1H, d, *J* = 7.5 Hz, Ar**H**), 7.12 (1H, d, *J* = 3.6 Hz, Ar**H**), 7.00 (1H, dd, *J* = 5.0, 3.6 Hz, Ar**H**), 6.10 (1H, t, *J* = 56 Hz, CF_2**H**), 3.06 – 2.95 (1H, m, O**H**), 2.35 (3H, s, C$\mathbf{H}_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 144.2 (C), 139.2 (C), 138.1 (C), 129.5 (CH), 128.2 (CH), 127.2 (CH), 126.8 (CH), 126.5 (CH), 126.4 (CH), 123.7 (CH), 116.3 (t, *J* = 253 Hz, CF_2H), 76.9 (t, *J* = 22 Hz, C), 21.6 (CH_3); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -126.7 (1F, dd, *J* = 274, 56 Hz, CF_2H), -127.7 (1F, *J* = 274, 56 Hz, CF_2H); HRMS (ES^-): Exact mass calculated for $C_{13}H_{12}OF_2S$ $[M-H]^-$: 253.0504, found: 253.0498.

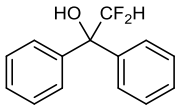
2,2-difluoro-1-(thiophen-2-yl)-1-(o-tolyl)ethan-1-ol (2h)



The title compound was prepared according to General Procedure B from 2,2-difluoro-1-(thiophen-2-yl)ethan-1-one (81 mg, 0.5 mmol) and o-tolylboronic acid (204 mg, 1.5 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a red oil (87 mg, 69%). IR 1137, 1069, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (1H, d, *J* = 7.6 Hz, Ar**H**), 7.33 (1H, dd, *J* = 5.5, 1.1 Hz, Ar**H**), 7.30 – 7.21 (2H, m, Ar**H**), 7.18 (1H, d, *J* = 7.3 Hz, Ar**H**),

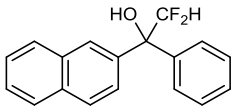
6.96 (1H, td, *J* = 4.6, 1.1 Hz, Ar**H**), 6.88 (1H, d, *J* = 3.1 Hz, Ar**H**), 6.25 (1H, t, *J* = 56 Hz, CF_2**H**), 2.17 (3H, s, C**H**$_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 143.8 (C), 138.2 (C), 137.3 (C), 132.9 (CH), 128.8 (CH), 126.7 (CH), 126.64 (CH), 126.57 (t, *J* = 2.9 Hz, CH), 126.4 (CH), 125.4 (CH), 116.0 (t, *J* = 251 Hz, CF_2H), 77.6 (t, *J* = 22 Hz, CHOH), 21.3 (CH_3); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -125.3 (1F, dd, *J* = 272, 56 Hz, CF_2H), -127.9 (1F, dd, *J* = 272, 56 Hz, CF_2H).

2,2-difluoro-1,1-diphenylethan-1-ol (2i)



The title compound was prepared according to General Procedure B from 2,2-difluoroacetophenone (78.0 mg, 0.5 mmol) and phenylboronic acid (182.9 mg, 1.5 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a white solid (92 mg, 79%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (4H, d, *J* = 7.5 Hz, Ar**H**), 7.24-7.32 (6H, m, Ar**H**), 6.16 (1H, t, *J* = 55 Hz, CF_2**H**), 2.71 (1H, s, O**H**); ^{13}C NMR (125.8 MHz, $CDCl_3$ δ 140.5 (2 x C), 128.4 (4 x CH), 128.2 (2 x CH), 127.0 (t, J = 1.2Hz, 4 x CH), 116.8 (CH, t, *J* = 251 Hz), 78.1 (t, *J* = 21 Hz, C); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -127.7 (2F, d, *J* = 55 Hz, CF_2H). Data is in agreement with that reported in the literature.[2]

2,2-difluoro-1-(naphthalen-2-yl)-1-phenylethan-1-ol (2j)

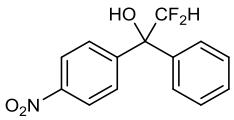


The title compound was prepared according to General Procedure B from 2,2-difluoro-1-(naphthalen-2-yl)ethan-1-one (103 mg, 0.5 mmol) and phenylboronic acid (183 mg, 1.5 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a colourless oil (92 mg, 65%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (1H, s, Ar**H**), 7.90-7.79 (3H, m, Ar**H**), 7.56-7.47 (4H, m, Ar**H**), 7.46 (1H, dd, *J* = 8.7, 1.5 Hz, Ar**H**), 7.42-7.33 (3H, m, Ar**H**), 6.33 (1H, t, *J* = 55 Hz, CF_2**H**), 2.88 (1H, s, O**H**); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 140.4 (C), 137.7 (C), 132.8 (C), 132.7 (C), 128.5 (CH), 128.4 (2 x CH), 128.3 (CH), 128.2 (CH), 127.5 (CH), 127.1 (2 x CH), 126.6 (CH), 126.4 (CH), 125.9 (CH), 125.1 (CH), 117.0 (t, *J* = 251 Hz, CH), 78.3 (t,

[2] P. Beier, A. V Alexandrova, M. Zibinsky and G. K. S. Prakash, *Tetrahedron*, 2008, **64**, 10977–10985.

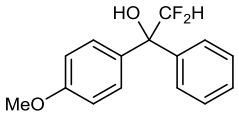
J = 21 Hz, C); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -127.2 (1F, dd, *J* = 276, 55 Hz, CF_2H), -127.9 (1F, dd, *J* = 276, 55 Hz, CF_2H); HRMS (ES^-): Exact mass calculated for $C_{18}H_{14}OF_2$ $[M-H]^-$: 283.0929, found: 284.9360.

2,2-difluoro-1-(4-nitrophenyl)-1-phenylethan-1-ol (2k)



The title compound was prepared according to General Procedure B using modified quantities: 2,2-difluoro-1-(4-nitrophenyl)ethan-1-one (123 mg, 0.609 mmol), phenylboronic acid (223 mg, 1.83 mmol), potassium carbonate (253 mg, 1.83 mmol) and $[Rh(cod)Cl]_2$ (7.5 mg, 0.015 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a yellow oil (159 mg, 94%). IR 3493, 1606, 1518, 1450, 1346, 1137, 1070, 904, 850, 806, 757, 697 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (2H, d, *J* = 8.9 Hz, Ar**H**), 7.69 (2H, d, *J* = 8.9 Hz, Ar**H**), 7.48 – 7.34 (5H, m, Ar**H**), 6.23 (1H, t, *J* = 55 Hz, CF_2**H**); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 147.6 (C), 147.1 (C), 139.6 (C), 128.9 (CH), 128.83 (CH), 128.76 (2 x CH), 128.3 (2 x CH), 126.8 (2 x CH), 123.3 (2 x CH), 116.3 (t, *J* = 251.0 Hz, CF_2H), 77.9 (t, *J* = 22 Hz, C); ^{19}F (283 MHz, $CDCl_3$) δ -126.7 (1F, dd, *J* = 278, 55 Hz), -127.7 (1F, dd, *J* = 278, 55 Hz, CF_2H); HRMS (ES^-): Exact mass calculated for $C_{14}H_{11}NO_3F_2$ $[M-H]^-$: 278.0634, found: 278.0643.

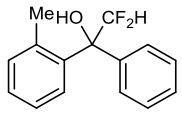
2,2-difluoro-1-(4-methoxyphenyl)-1-phenylethan-1-ol (2l)



The title compound was prepared according to General Procedure B using modified quantities: 2,2-difluoro-1-(4-methoxyphenyl)ethan-1-one (28 mg, 0.15 mmol), phenylboronic acid (55 mg, 0.45 mmol), potassium carbonate (62 mg, 0.45 mmol) and $[Rh(cod)Cl]_2$ (1.8 mg, 3.75 μmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a yellow oil (34 mg, 86 %). IR 3448, 1608, 1513, 1452, 1302, 1243, 1153, 1059, 971 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (2H, d, *J* = 7.5 Hz, Ar**H**), 7.41 – 7.30 (5H, m, Ar**H**), 6.88 (2H, d, *J* = 8.9 Hz, Ar**H**), 6.18 (1H, t, *J* = 55 Hz, CF_2**H**), 3.81 (1H, s, OC**H**$_3$), 2.72 (1H, s, O**H**); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 159.4 (C), 140.6 (C), 132.6 (C), 128.4 (2 x CH), 128.3 (2 x CH), 128.2 (CH), 127.1 (2 x CH), 116.9 (t, *J* = 250 Hz, CF_2H), 113.7 (2 x CH), 77.8 (t, *J* = 21 Hz, C), 55.2

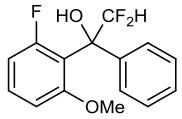
(CH_3); ^{19}F (283 MHz, $CDCl_3$) δ -127.4 (2F, d, *J* = 55 Hz); HRMS (ES^-): Exact mass calculated for $C_{15}H_{14}O_2F_2$ $[M-H]^-$: 263.0889, found: 263.0885.

2,2-difluoro-1-phenyl-1-(o-tolyl)ethan-1-ol (2m)



The title compound was prepared according to General Procedure B using modified quantities: 2,2-difluoro-1-(*o*-tolyl)ethan-1-one (26 mg, 0.15 mmol), phenylboronic acid (55 mg, 0.45 mmol), potassium carbonate (62 mg, 0.45 mmol) and $[Rh(cod)Cl]_2$ (1.8 mg, 3.75 µmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a yellow oil (36 mg, 84 %). ^1H NMR (500 MHz, $CDCl_3$) δ 7.61 – 7.55 (1H, m, Ar**H**), 7.32 – 7.15 (7H, m, Ar**H**), 7.10 – 7.07 (1H, m, Ar**H**), 6.10 (1H, t, J = 55 Hz, CF_2**H**), 2.67 (1H, s, O**H**), 1.92 (3H, s, C**H**$_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 139.5 (C), 138.7 (C), 138.0 (C), 133.1 (CH), 128.5 (CH), 128.1 (2 x CH), 128.0 (CH), 127.0 (2 x CH), 126.8 (dd, *J* = 4.0, 2.7 Hz, CH), 125.2 (CH), 116.9 (t, *J* = 251 Hz, CF_2H), 78.8 (t, *J* = 20 Hz, C), 21.2 (CH_3); HRMS (ES^-): Exact mass calculated for $C_{15}H_{14}OF_2$ $[M-H]^-$: 247.0940, found: 247.0935.

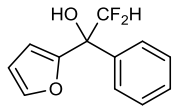
2,2-difluoro-1-phenyl-1-(o-tolyl)ethan-1-ol (2n)



The title compound was prepared according to General Procedure B using modified quantities: 2,2-difluoro-1-(*o*-tolyl)ethan-1-one (26 mg, 0.15 mmol), phenylboronic acid (55 mg, 0.45 mmol), potassium carbonate (62 mg, 0.45 mmol) and $[Rh(cod)Cl]_2$ (1.8 mg, 3.75 µmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a yellow oil (36 mg, 84 %). IR 3413, 1494, 1449, 1259, 1215, 1141, 1086, 1024, 852 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.41 (2H, d, *J* = 7.2 Hz, Ar**H**), 7.38 – 7.28 (4H, m, Ar**H**), 7.02 (1H, ddd, *J* = 9.0, 7.6, 3.1 Hz, Ar**H**), 6.85 (1H, dd, *J* = 9.0, 4.5 Hz, Ar**H**), 6.42 (1H, t, *J* = 55 Hz, CF_2**H**), 4.38 (1H, s, O**H**), 3.61 (3H, s, OC**H**$_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 157.0 (d, *J* = 240 Hz, CF), 152.9 (d, *J* = 2.5 Hz, C), 140.5 (C), 130.5 (d, *J* = 6.7 Hz, C), 128.12 (CH), 128.09 (2 x CH), 126.7 (2 x CH), 115.8 (t, *J* = 249 Hz, CF_2H), 115.5 (d, *J* = 22 Hz, CH), 115.4 (dt, *J* = 26, 2.7 Hz, CH), 78.1 (t, *J* = 21 Hz, C), 56.4 (CH_3); ^{19}F (282.4 MHz, $CDCl_3$) δ -121.8 (1F, s), -127.3 (1F, d, *J* =

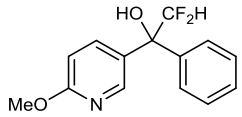
277 Hz), -128.7 (1F, d, *J* = 277 Hz); HRMS (ES^-): Exact mass calculated for $C_{15}H_{13}O_2F_3$ [M-H]$^-$: 281.0795, found: 281.0797.

2,2-difluoro-1-(furan-2-yl)-1-phenylethan-1-ol (2o)



The title compound was prepared according to General Procedure B from 2,2-difluoro-1-(furan-2-yl)ethan-1-one (93 mg, 0.5 mmol) and phenylboronic acid (183 mg, 1.5 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give an orange oil (107 mg, 95%). IR 3446, 1497, 1450, 1334, 1230, 1135, 1073, 1013 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.51 (2H, d, *J* = 6.7 Hz, Ar**H**), 7.45 (1H, d, *J* = 1.0 Hz, Ar**H**), 7.42 – 7.35 (3H, m, Ar**H**), 6.45 (1H, d, *J* = 3.2 Hz, Ar**H**), 6.41 (1H, dd, *J* = 3.3, 1.8 Hz, Ar**H**), 6.14 (1H, t, *J* = 55 Hz, CF_2**H**), 2.98 (1H, s, O**H**); δ_C (126 MHz, $CDCl_3$) 152.2 (C), 143.2 (CH), 137.1 (C), 128.7 (CH), 128.3 (2 x CH), 126.7 (2 x CH), 115.4 (t, *J* = 251 Hz, CF_2H), 110.4 (CH), 109.4 (t, *J* = 1.5 Hz, CH), 75.4 (t, *J* = 22.3 Hz, C); δ_F (282 MHz, $CDCl_3$) -128.4 (1F, d, *J* = 277 Hz), -129.5 (1F, d, *J* = 277 Hz); HRMS (ES^+): Exact mass calculated for $C_{12}H_{10}O_2F_2$ [M+Na]$^-$: 247.0541, found: 247.0540.

2,2-difluoro-1-(6-methoxypyridin-3-yl)-1-phenylethan-1-ol (2p)



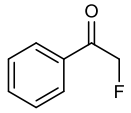
The title compound was prepared according to General Procedure B using modified quantities: 2,2-difluoro-1-(6-methoxypyridin-3-yl)ethan-1-one (75 mg, 0.4 mmol), phenylboronic acid (146 mg, 1.2 mmol), potassium carbonate (166 mg, 0.45 mmol) and $[Rh(cod)Cl]_2$ (4.9 mg, 0.01 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a colourless oil (84 mg, 79 %). IR 1606, 1493, 1379, 1288, 1132, 1069, 904, 833 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.22 (1H, d, *J* = 2.1 Hz, Ar**H**), 7.61 (1H, dd, *J* = 8.8, 2.5 Hz, Ar**H**), 7.45 (2H, d, *J* = 7.4 Hz, Ar**H**), 7.40 – 7.32 (3H, m, Ar**H**), 6.71 (1H, d, *J* = 8.7 Hz, Ar**H**), 6.13 (1H, t, *J* = 55 Hz, CF_2**H**), 3.92 (3H, s, OC**H**$_3$), 3.05 (1H, s, O**H**); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 163.8 (C), 145.7 (t, *J* = 2.0 Hz, CH), 139.9 (C), 138.2 (CH), 129.0 (C), 128.5 (3 x CH), 127.0 (2 x CH), 116.7 (t, *J* = 251 Hz, CF_2H), 110.6 (CH), 76.9 (t, *J* = 22 Hz, C), 53.6 (CH_3); ^{19}F (282.4 MHz,

$CDCl_3$) δ -126.8 (1F, d, *J* = 277 Hz), -127.8 (1F, d, *J* = 277 Hz); HRMS (ES^+): Exact mass calculated for $C_{14}H_{13}O_2NF_2$ $[M+H]^+$: 266.0987, found: 266.0985.

Synthesis of a monofluoromethyl ketones. General procedure C.

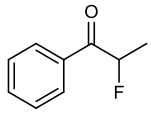
Acetophenone derivative (4 mmol), tetrabutylammonium fluoride trihydrate (2.524 g, 8 mmol) and pyridine (0.644 mL, 8 mmol) were dissolved in dioxane (40 mL) and heated at 80 °C for 24h. The solution was acidified with 2M HCl, extracted with diethyl ether and the solvent removed under reduced pressure, before purification by flash column chromatography.

2-fluoroacetophenone (3a)



The title compound was prepared according to General Procedure C from 2-bromoacetophenone (796 mg, 4.0 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a red solid (262 mg, 47%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.89 (2H, d, *J* = 7.5 Hz, Ar**H**), 7.57-7.62 (1H, m, Ar**H**), 7.49 (2H, t, *J* = 7.7 Hz, Ar**H**), 5.53 (2H, d, *J* = 47.0 Hz, CF**H**$_2$). Data is in agreement with that reported in the literature.[3]

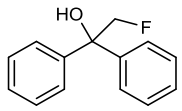
2-fluoropropiophenone (3b)



The title compound was prepared according to General Procedure C from 2-bromopropiophenone (852 mg, 4 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a yellow oil (543 mg, 89%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.00 (2H, dq, *J* = 8.5, 0.6 Hz, Ar**H**), 7.60-7.66 (1H, m, Ar**H**), 7.48-7.55 (2H, m, Ar**H**), 5.73 (1H, dq, *J* = 49.0, 6.8 Hz, CF**H**CH_3), 1.69 (3H, dd, *J* = 24.1, 6.8 Hz, C**H**$_3$); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -181.5 (1F, dq, *J* = 48.0, 24.5 Hz, $CFHCH_3$); LRMS (ES^+): m/z 175.1 ($[M+Na]^+$, 100%). Data is in agreement with that reported in the literature.[4]

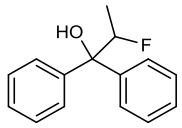
[3] T. H. Krane Thvedt, E. Fuglseth, E. Sundby and B. H. Hoff, *Tetrahedron*, 2009, **65**, 9550–9556.
[4] Y. Guo, G.-H. Tao, A. Blumenfeld and J. M. Shreeve, *Organometallics*, 2010, **29**, 1818-1823.

2-fluoro-1,1-diphenylethan-1-ol (4a)



The title compound was prepared according to General Procedure B from 2-fluoroacetophenone (69.1 mg, 0.5 mmol) and phenylboronic acid (183 mg, 1.5 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a white solid (77.0 mg, 67%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.05-7.65 (10H, m, Ar**H**), 4.85 (2H, d, *J* = 47.8 Hz, C**H**$_2$F); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 142.4 (d, *J* =2.7 Hz, C), 128.4 (2 x CH), 127.8 (CH), 126.7 (d, *J* = 0.9 Hz, 2 x CH), 87.4 (d, *J* =180 Hz, CFH_2), 77.8 (d, *J* = 19 Hz, C); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -218.7 (t, *J* = 48.5 Hz, CH_2F). Data is in agreement with that reported in the literature.[5]

2-fluoro-1,1-diphenylpropan-1-ol (4b)



The title compound was prepared according to General Procedure B from 2-fluoropropiophenone (76.1 mg, 0.5 mmol) and phenylboronic acid (183 mg, 1.5 mmol) and purified using column chromatography (0-10% EtOAc/Hexane) to give a white solid (77.0 mg, 67%). mp: 102-103 ºC; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (2H, d, *J* = 8.3 Hz, Ar**H**), 7.33 – 7.10 (8H, m, Ar**H**), 5.52 (1H, dq, *J* = 47, 6.4 Hz, CF**H**$_2$), 2.52 (1H, s, O**H**), 1.16 (3H, dd, *J* = 25, 6.3 Hz, C**H**$_3$); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 144.6 (C), 143.0 (d, *J* = 4.0 Hz, C), 128.2 (4 x CH), 127.3 (CH), 127.1 (CH), 126.8 (d, *J* = 1.5 Hz, 2 x CH), 125.8 (2 x CH), 92.5 (d, *J* = 176 Hz, **C**F), 79.1 (d, *J* = 20 Hz, C), 13.9 (d, *J* = 23 Hz, CH_3); ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -180.3 (dq, *J* = 47, 25 Hz, C**F**HCH_3); *m/z* (ES^-) 229 (100%, $[M-H]^-$)

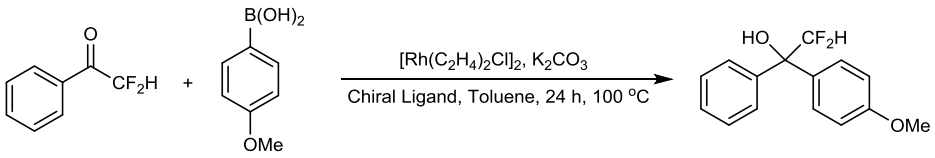
[5] G. Stavber, M. Zupan, M. Jereb and S. Stavber, *Org. Lett.*, 2004, **6**, 4973–4976.

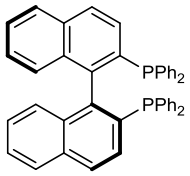
4. Competition Experiments

General Procedure D

A mixture of ketone A (0.2 mmol) and ketone B (0.2 mmol) were dissolved in dry toluene (1 mL) under nitrogen. This solution was added to a mixture of boronic acid (0.2 mmol), potassium carbonate (28 mg, 0.2 mmol) and $[Rh(cod)Cl]_2$. The mixture was heated to 100 °C for 16 hours before cooling, elution through a small plug of silica with chloroform and evaporation of the solvent. The ratio of products was determined by ^{19}F NMR.

5. Towards an asymmetric arylation of difluoromethyl ketones

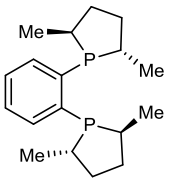




L1

(*S*)-BINAP

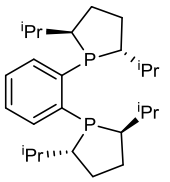
Conversion = 89.6%
e.e. = 20%



L2

(*S,S*)-Me-DUPHOS

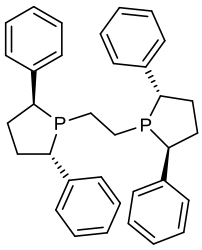
Conversion = 34.2%
e.e. = 55%



L3

(*S,S*)-^{i}Pr-DUPHOS

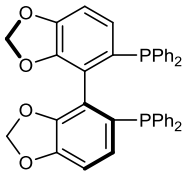
Conversion = 90.9%
e.e. = 36%



L4

(*S,S*)-Ph-BPE

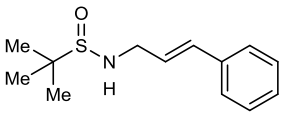
Conversion = 57.6%
e.e. = 3.1%



L5

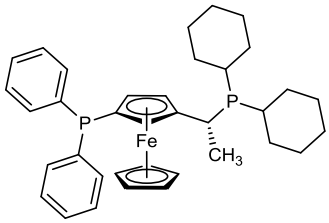
(*S*)-SEGPHOS

Conversion = 94.4%
e.e. = 28%



L6

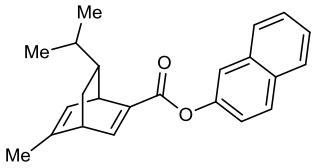
Conversion = 62.5%
e.e. = 20%



L7

(*R*)-(*S*)-Josiphos

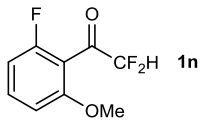
Conversion = 51.8%
e.e. = 9.3%



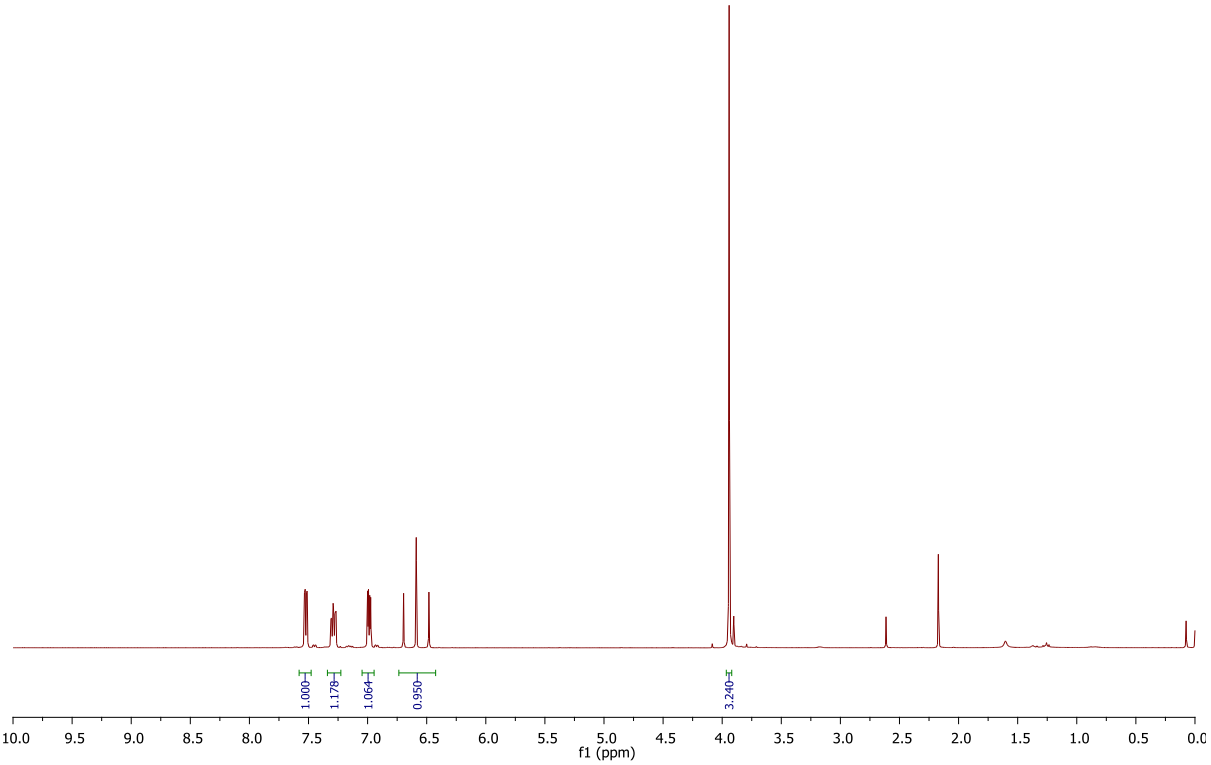
L8

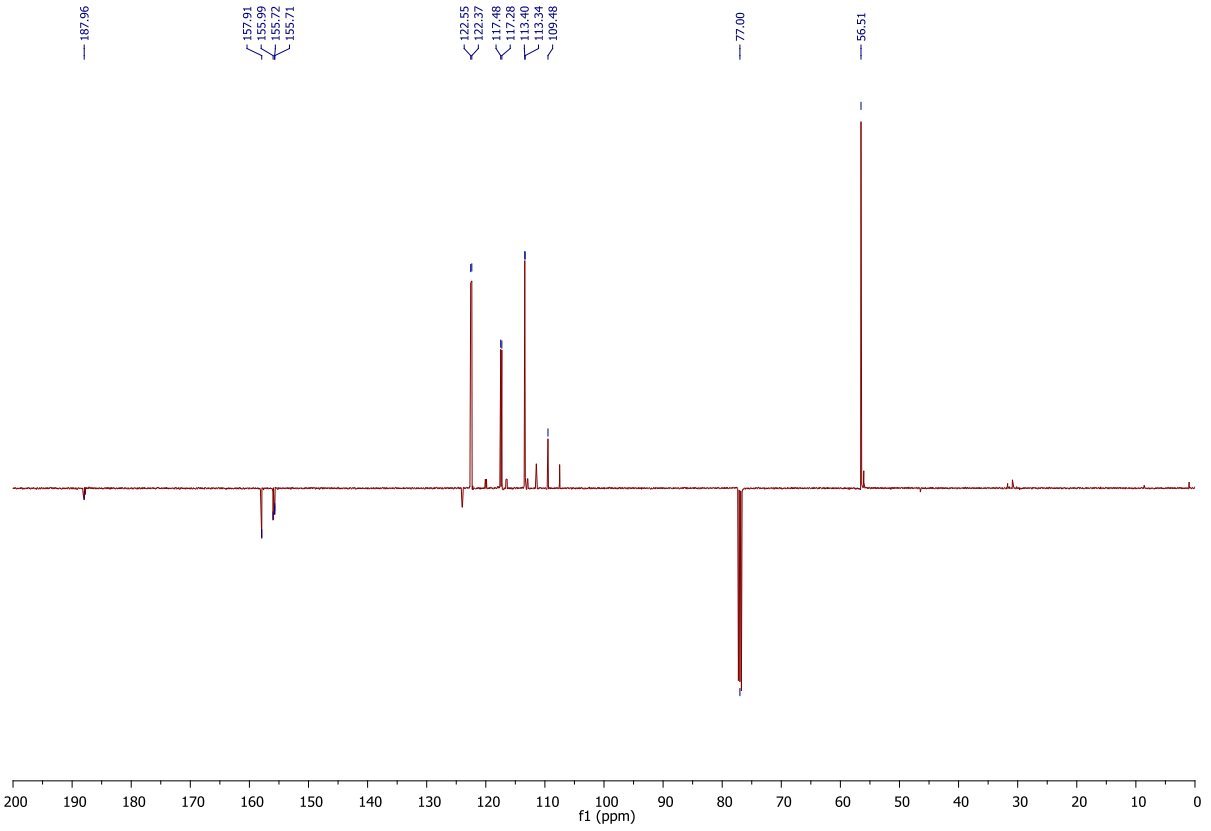
Conversion = 100%
e.e. = 0.5%

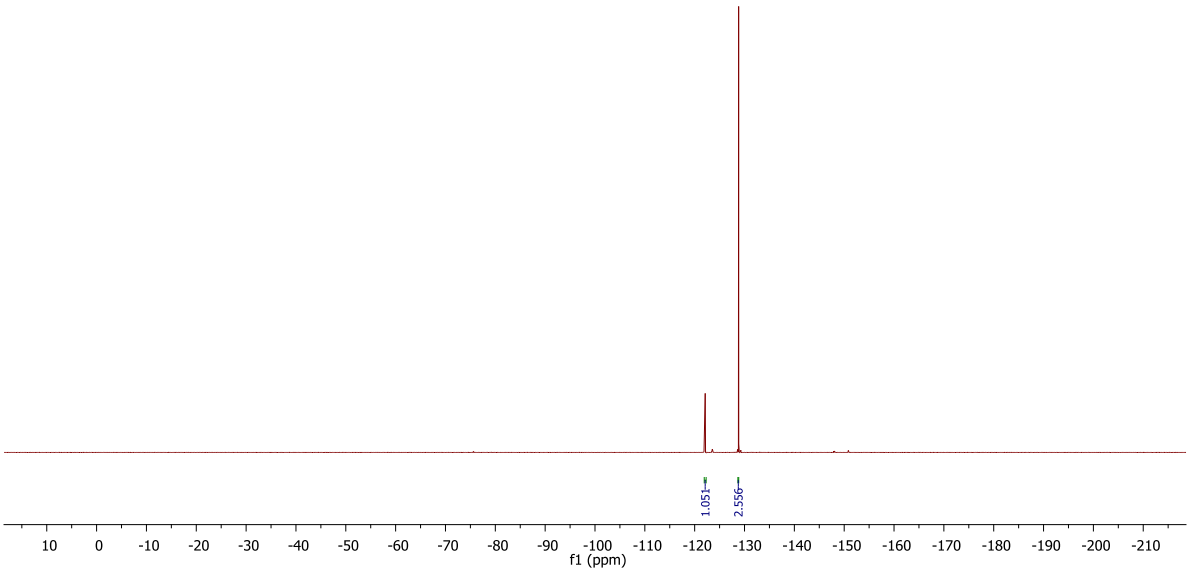
6. Copies of ^{1}H and ^{13}C NMR spectra for all new compounds

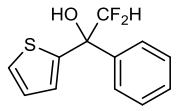

F
O
CF2H
OMe

1n

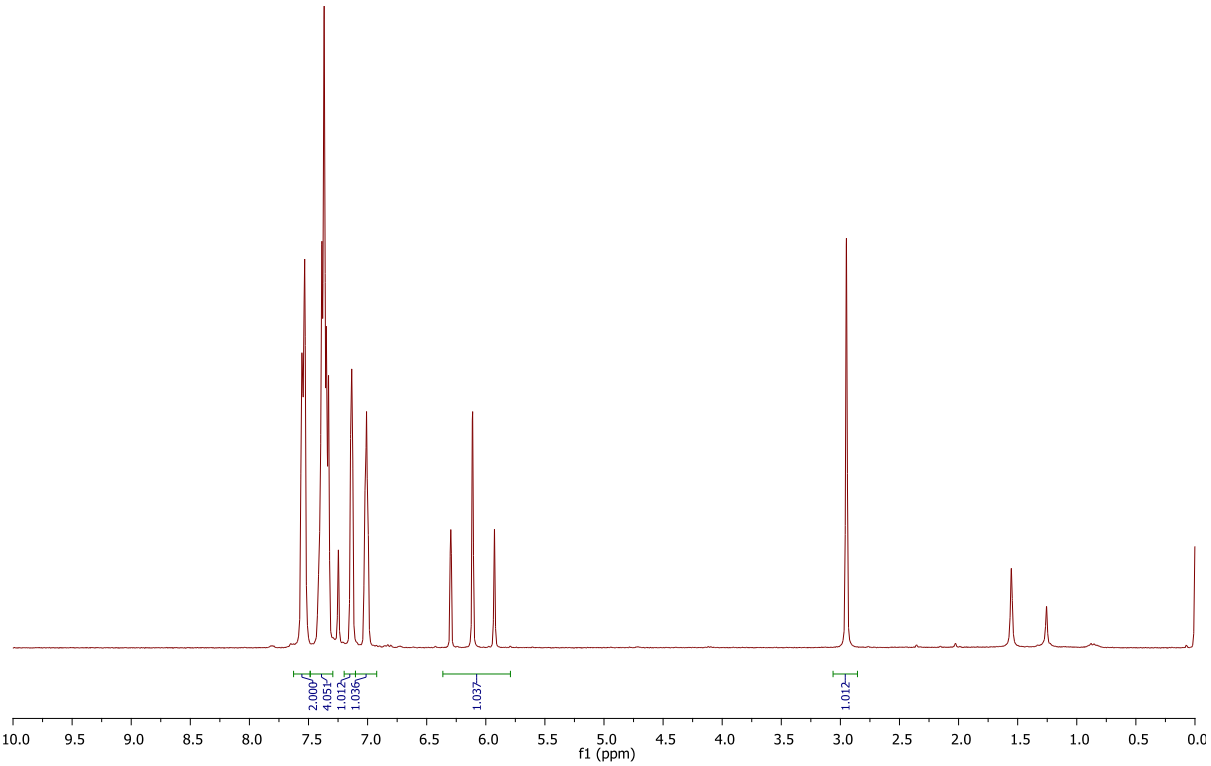

1.000
1.178
1.064
0.950
3.240
f1 (ppm)

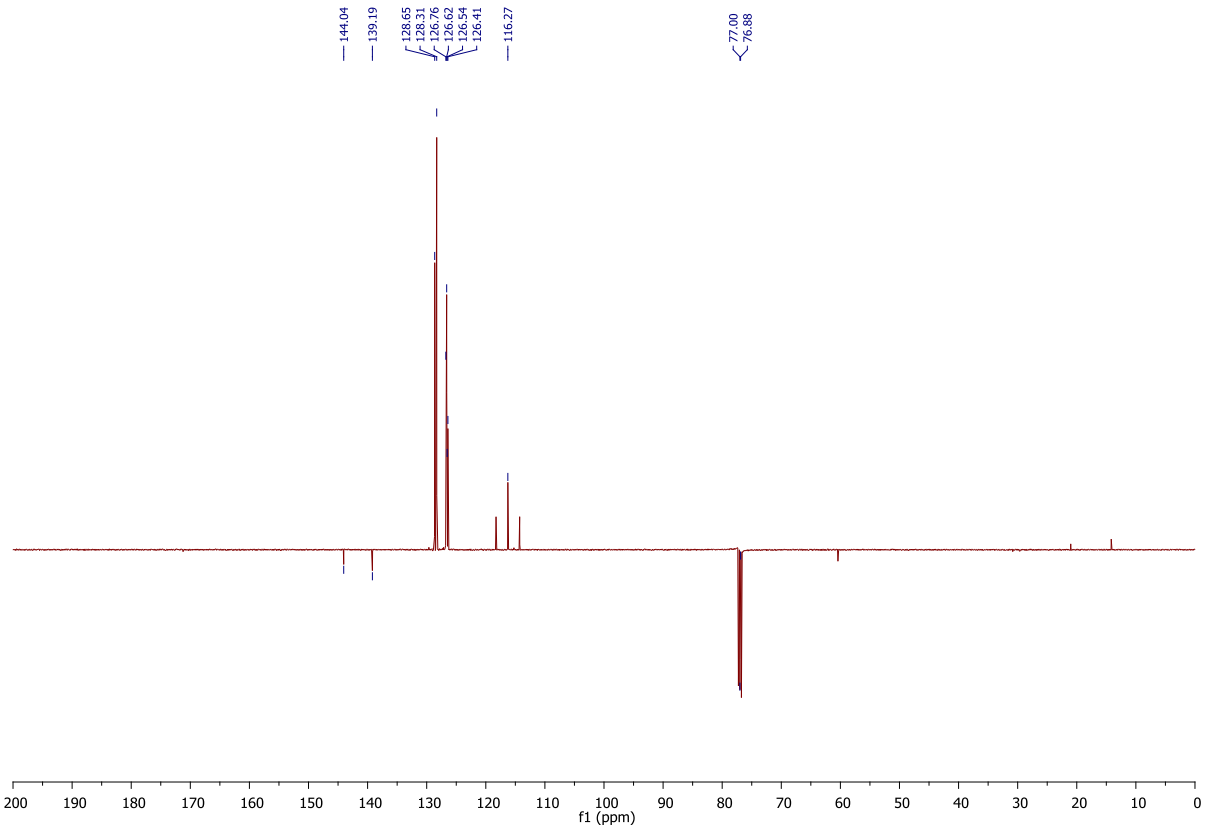

187.96
157.91
155.99
155.72
155.71
122.55
122.37
117.48
117.28
113.40
113.34
109.48
77.00
56.51
f1 (ppm)

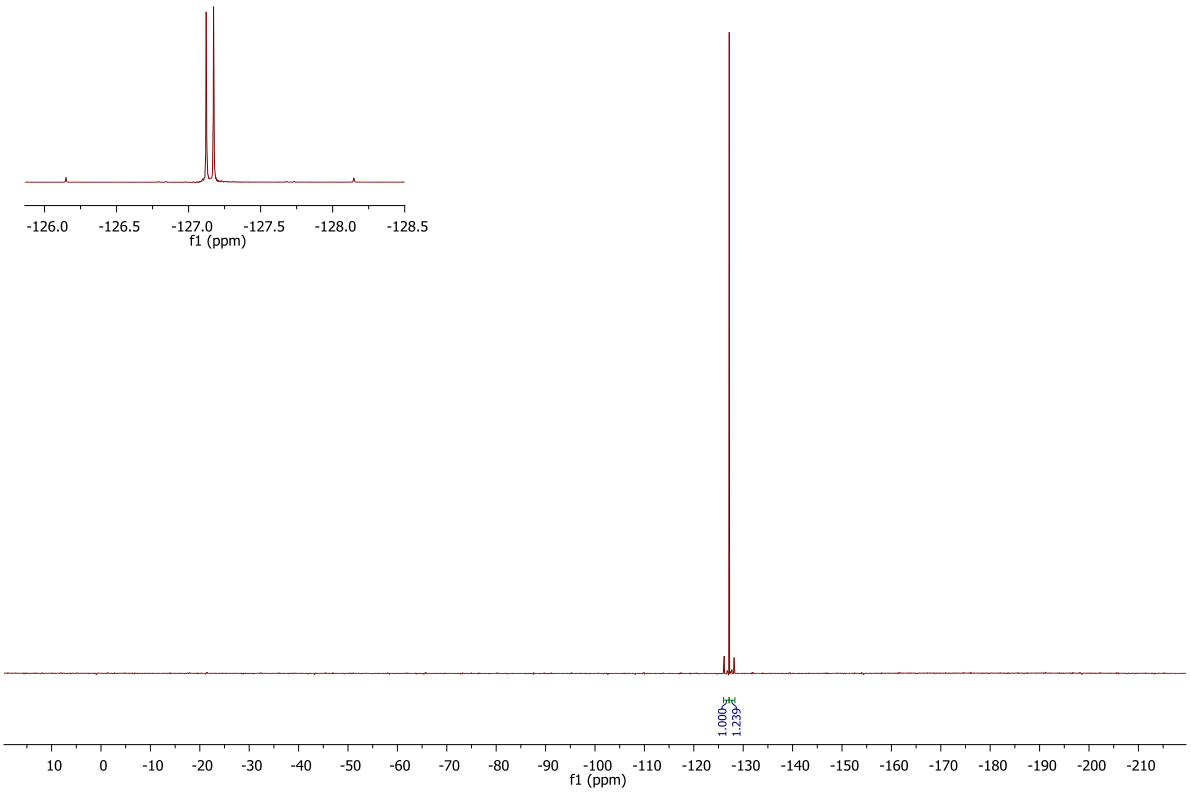

1.051
2.556
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

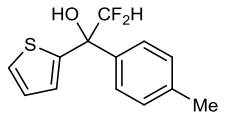

HO
CF2H
S

2a

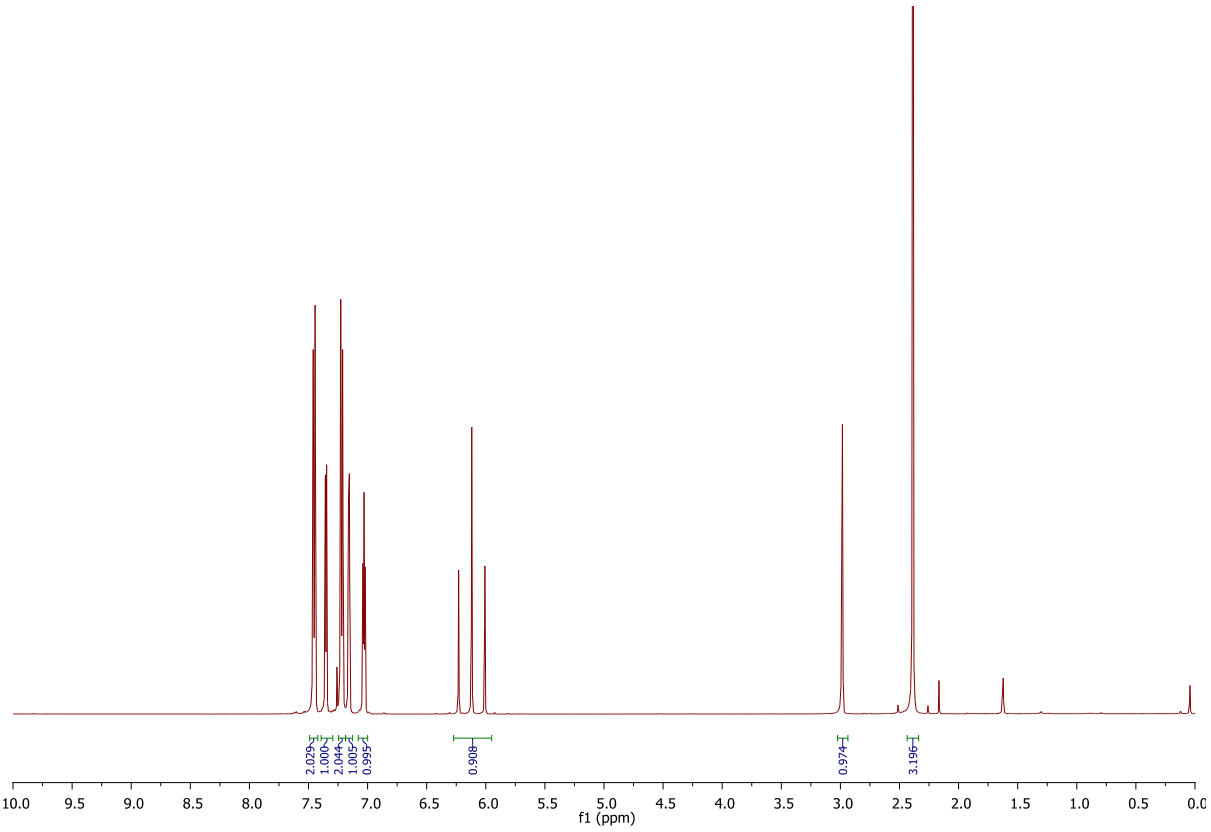

2.000
4.051
1.012
1.036
1.037
1.012
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

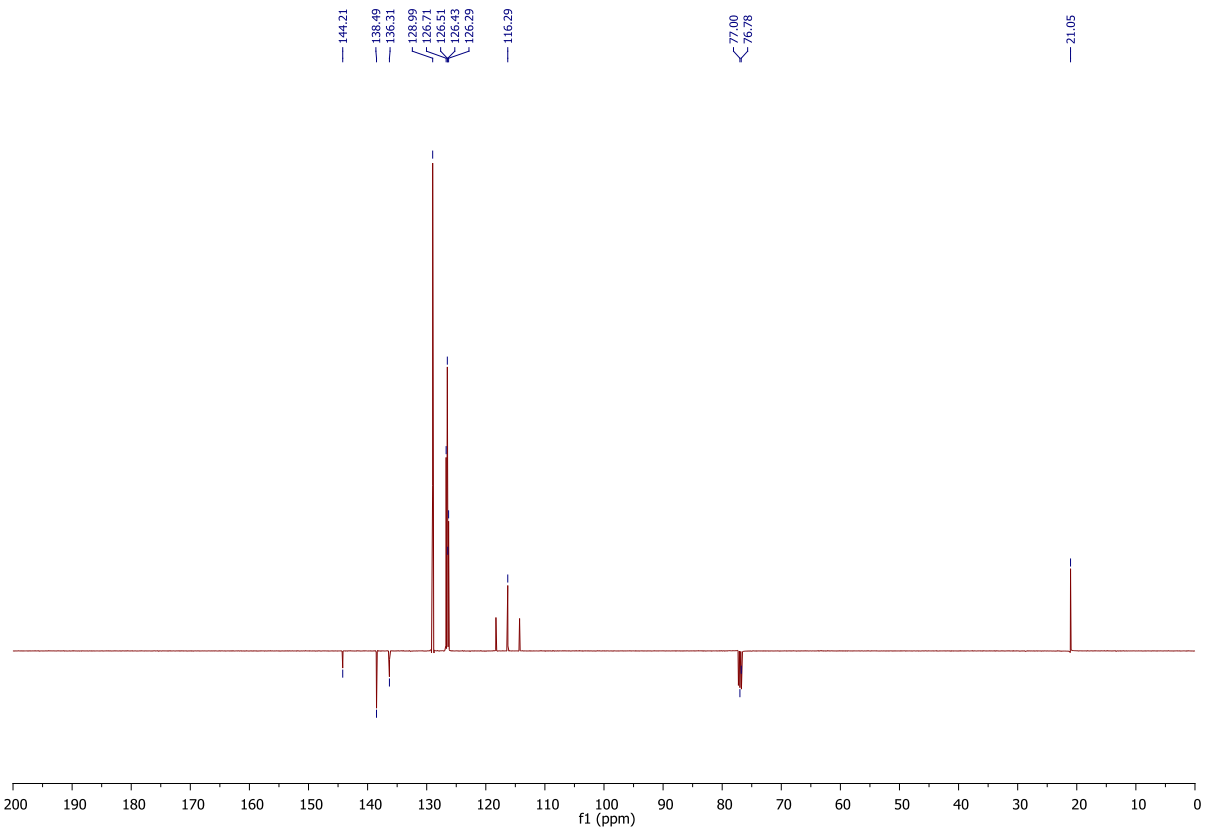

144.04
139.19
128.65
128.31
126.76
126.62
126.54
126.41
116.27
77.00
76.88
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

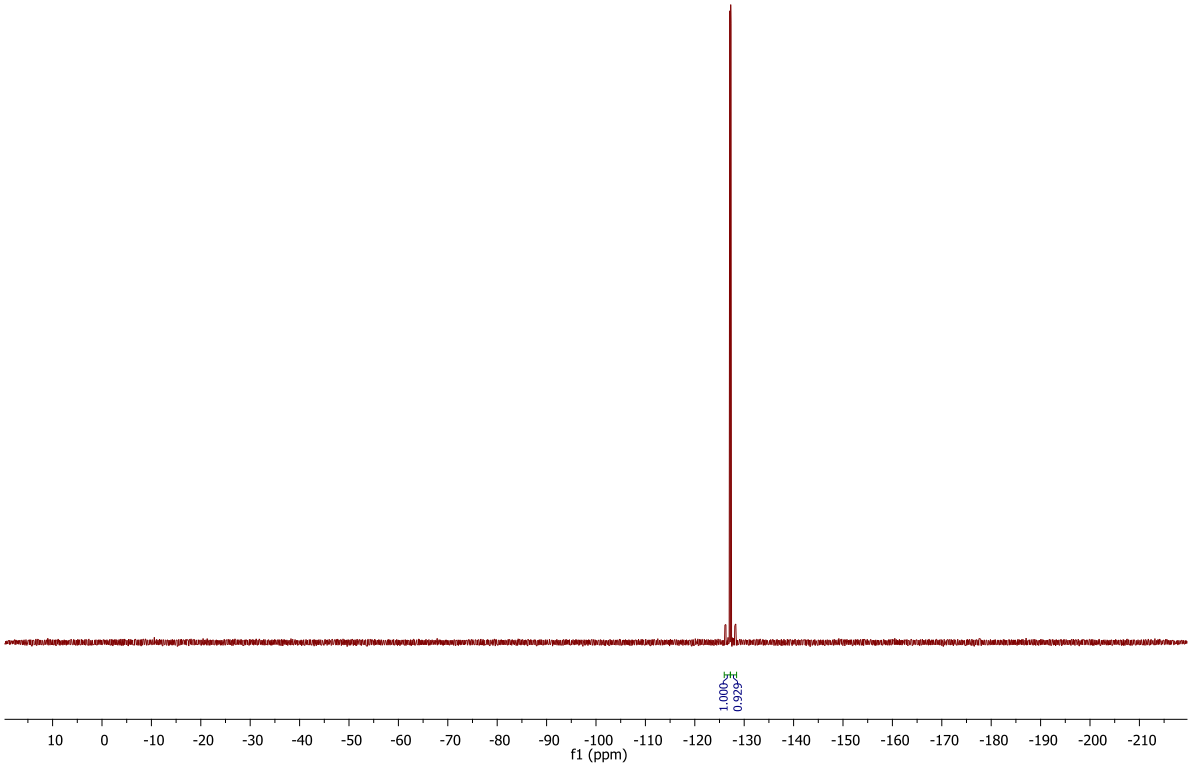

-126.0
-126.5
-127.0
-127.5
-128.0
-128.5
f1 (ppm)
1.000
1.239
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

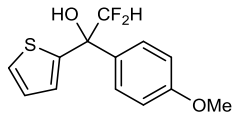

HO
CF2H
S
Me

2b

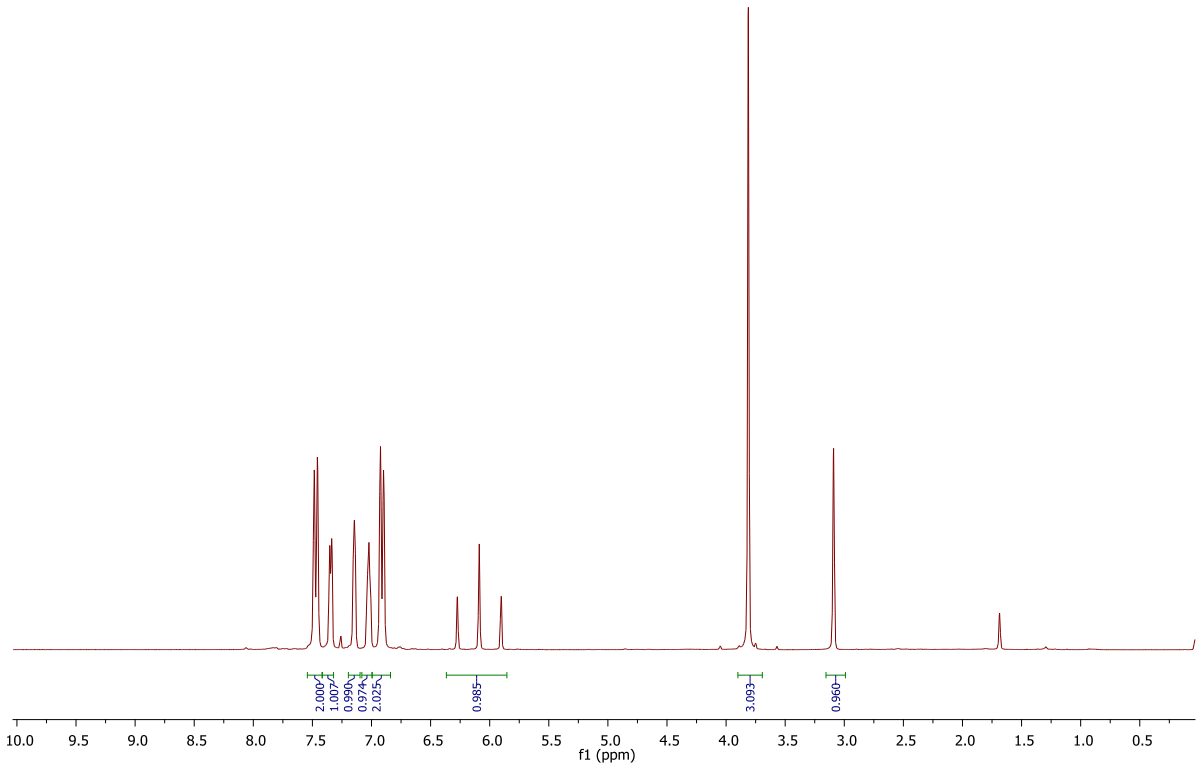

2.029
1.000
2.044
1.005
0.995
0.908
0.974
3.196
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

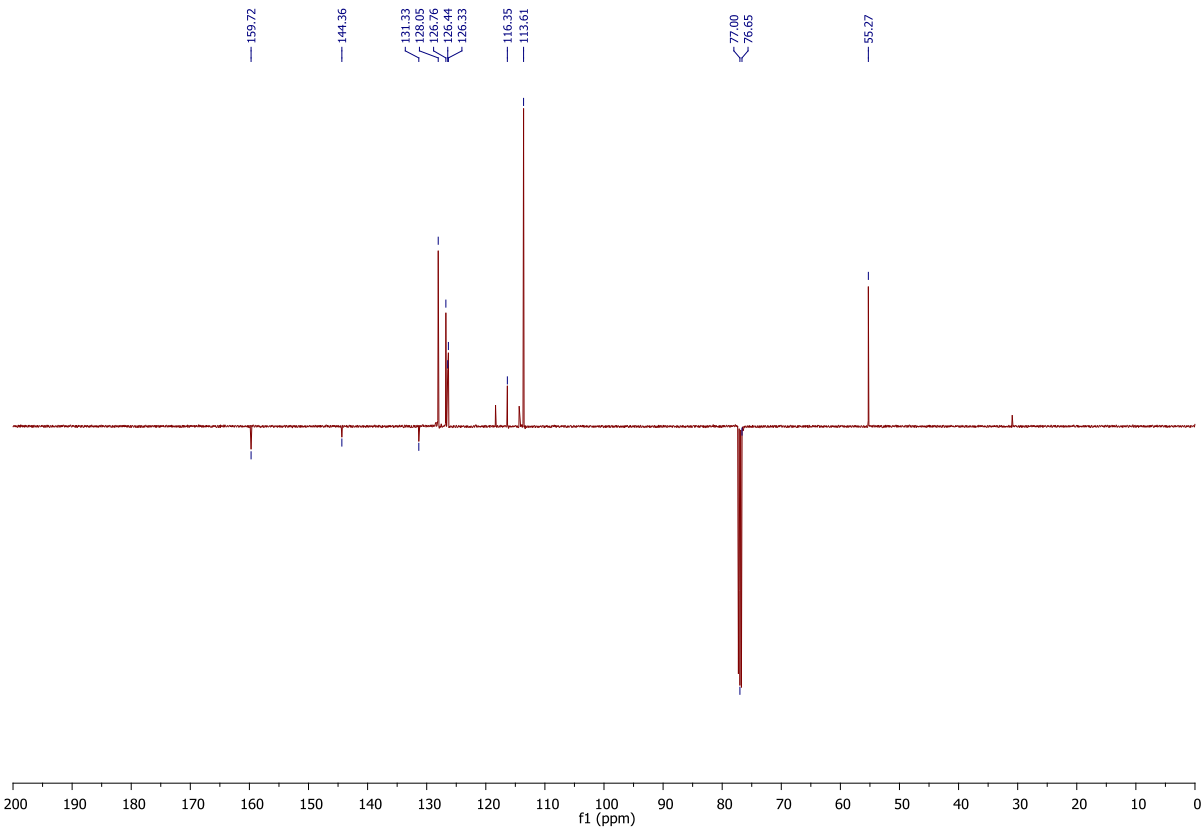

144.21
138.49
136.31
128.99
128.71
126.51
126.43
126.29
116.29
77.00
76.78
21.05
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

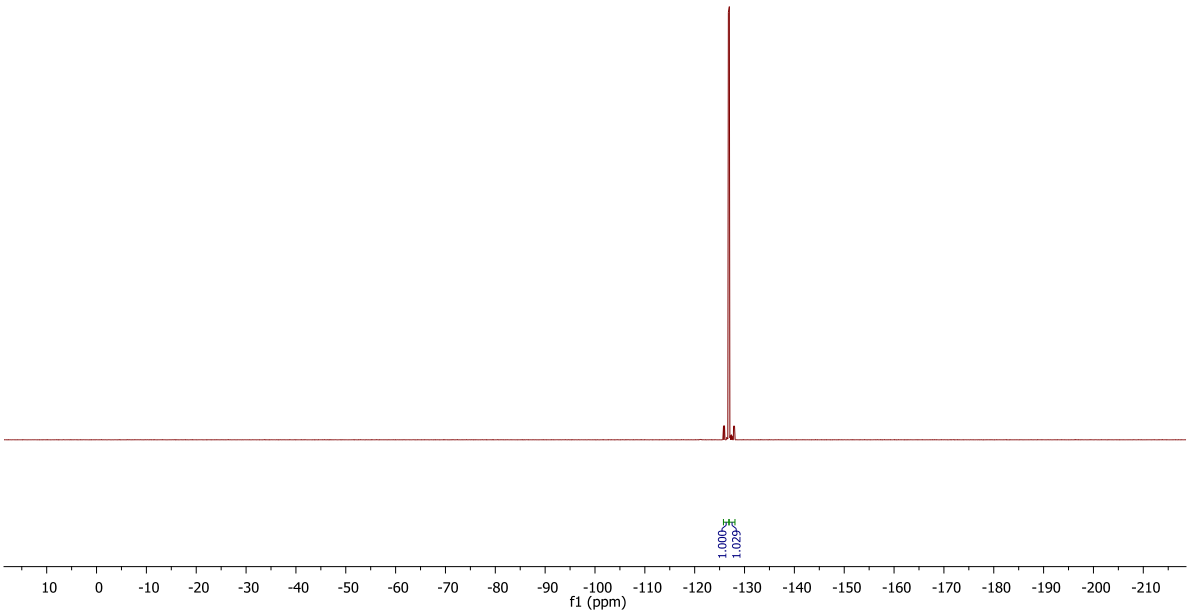

1.000
0.929
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


HO
CF2H
S
OMe

2c


2.000
1.007
0.990
0.974
2.025
0.985
3.093
0.960
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
f1 (ppm)


159.72
144.36
131.33
128.05
126.76
126.44
126.33
116.35
113.61
77.00
76.65
55.27
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


1.000
1.029
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
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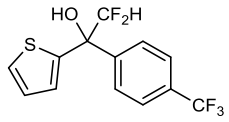
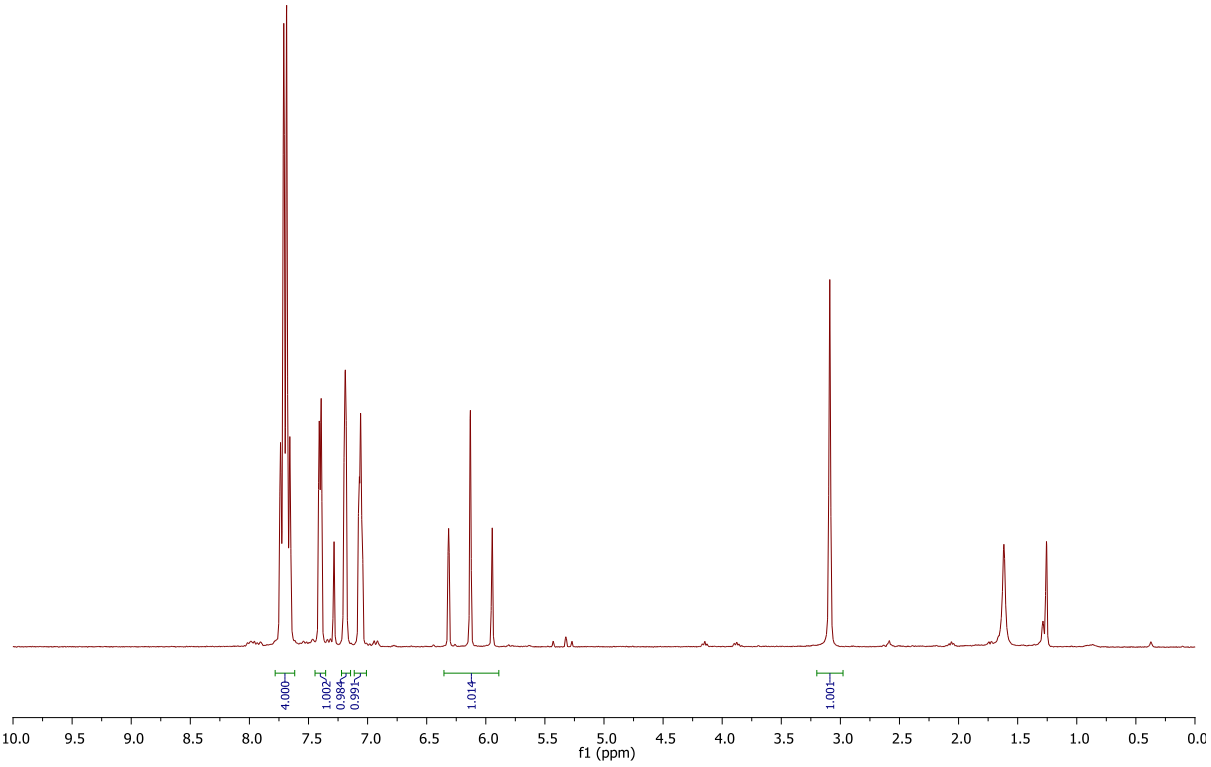
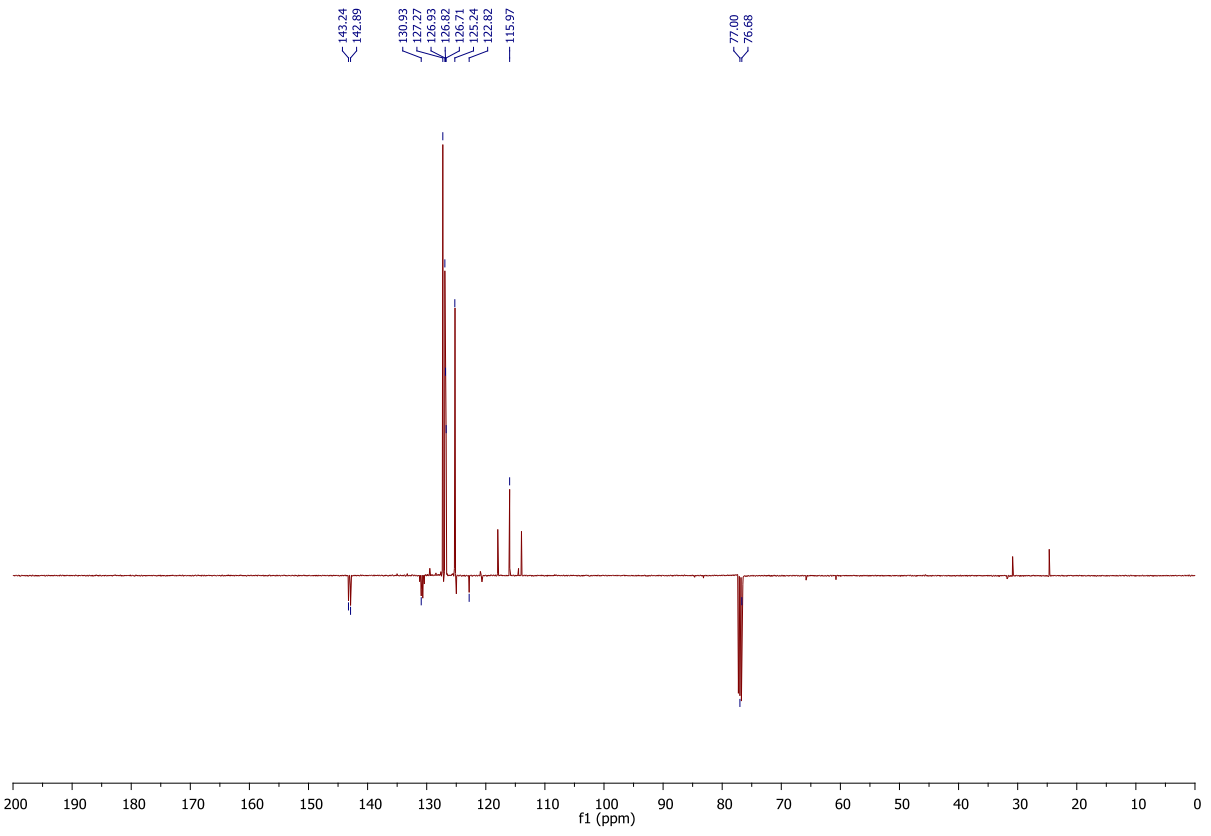
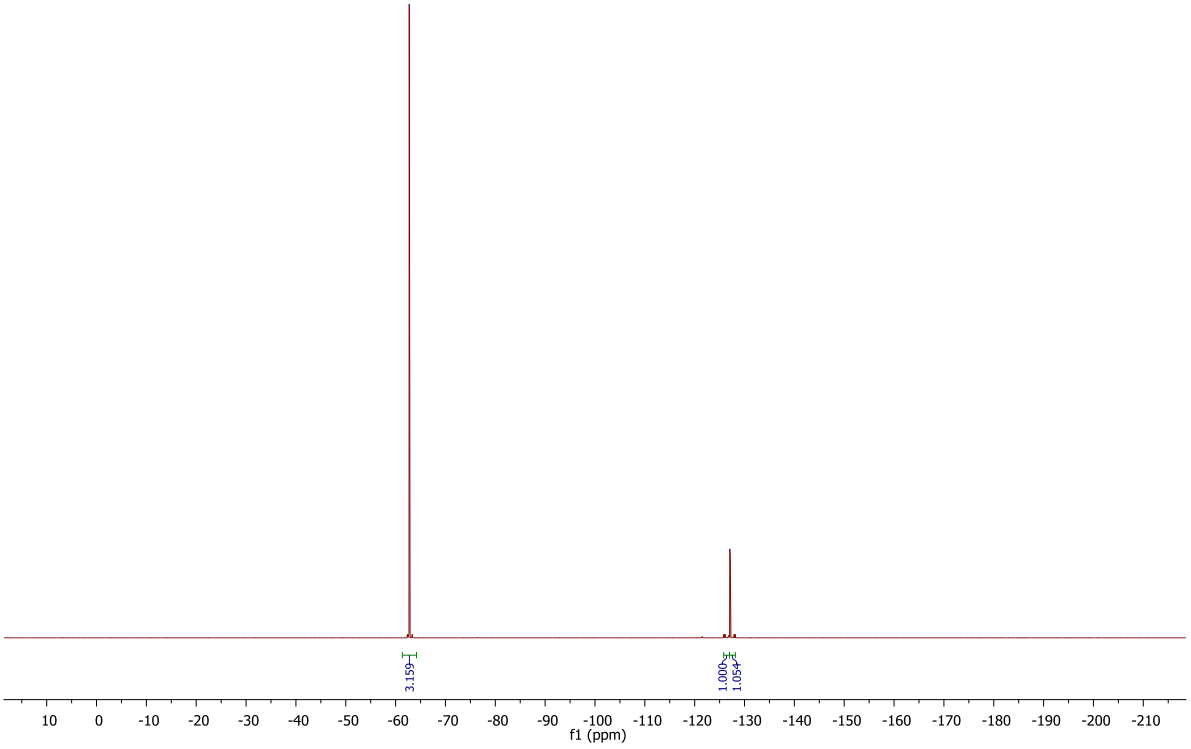
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

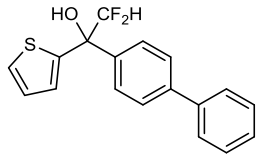

HO
CF2H
S
CF3

2d

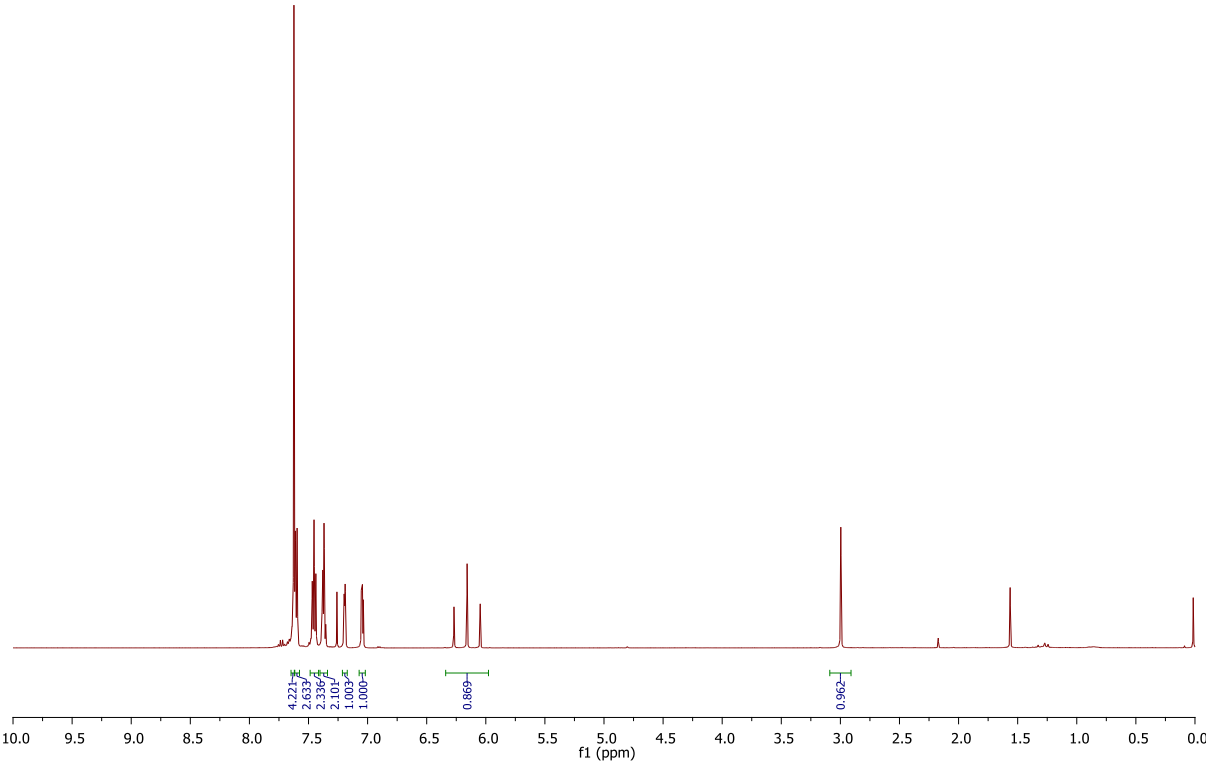

4.000
1.002
0.984
0.991
1.014
1.001
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

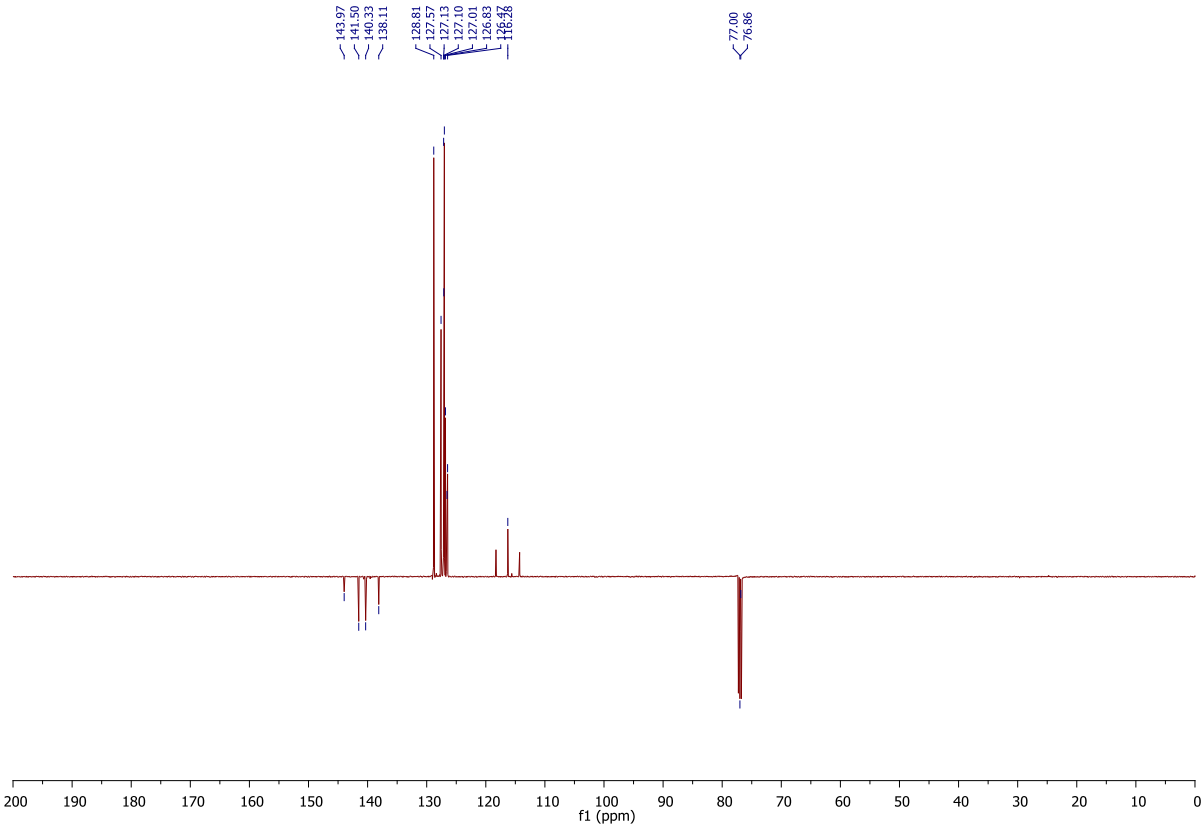

143.24
142.89
130.93
127.27
126.93
126.82
126.71
125.24
122.82
115.97
77.00
76.68
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

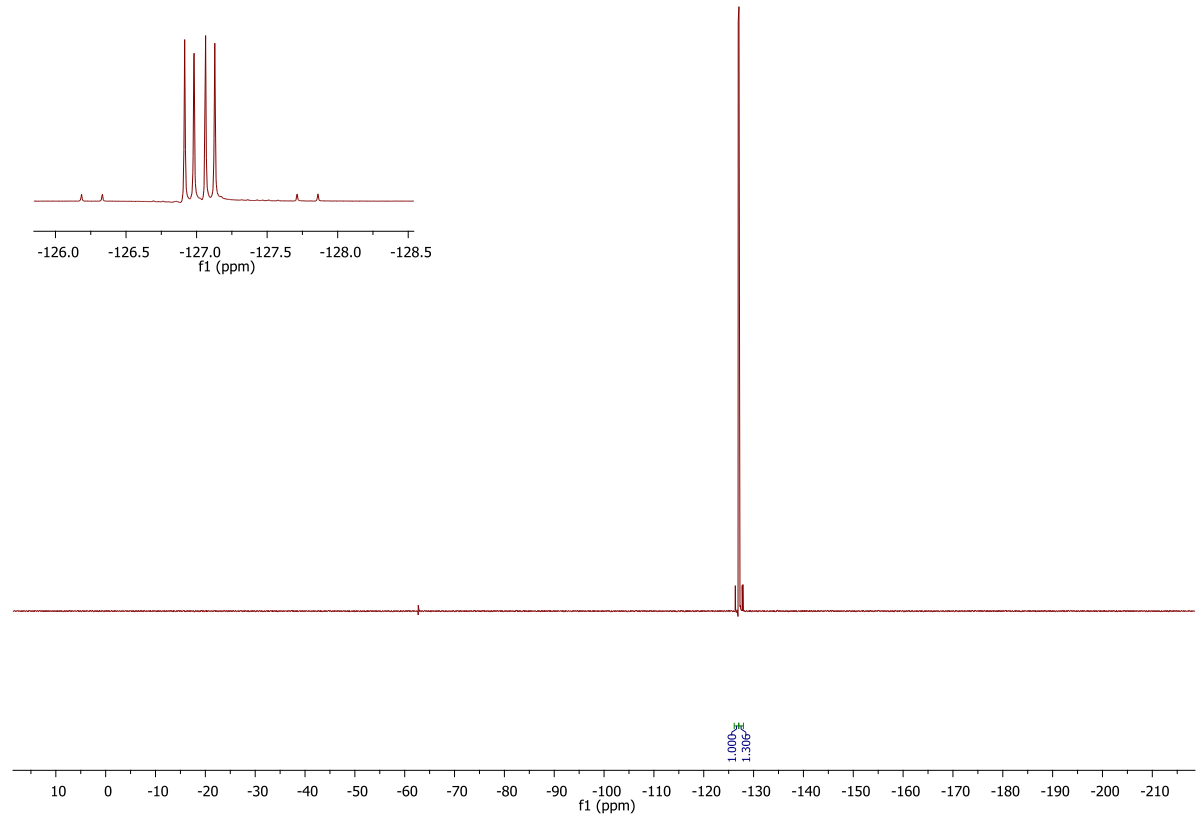

3.159
1.000
1.054
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

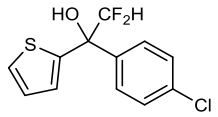

HO
CF2H
S

2e

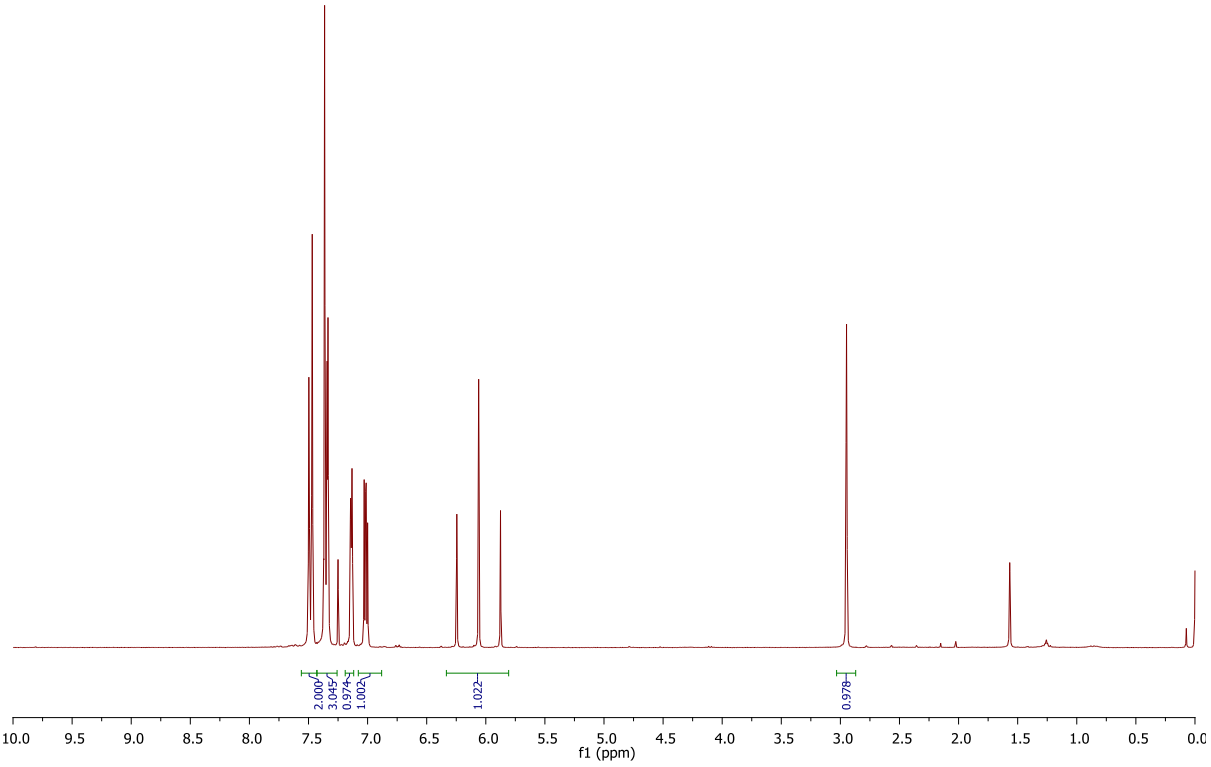

4.221
2.633
2.336
2.101
1.003
1.000
0.869
0.962
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

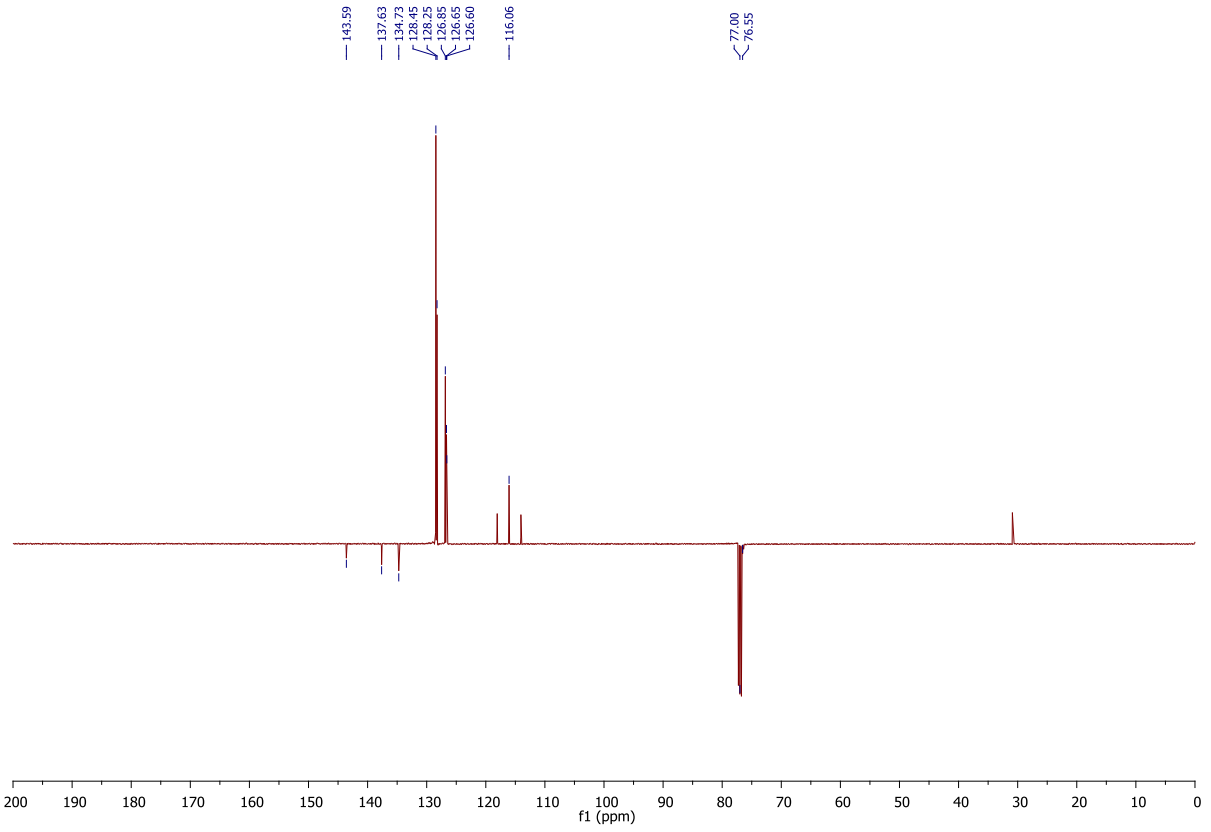

143.97
141.50
140.33
138.11
128.81
127.57
127.13
127.10
127.01
126.83
77.00
76.86
f1 (ppm)

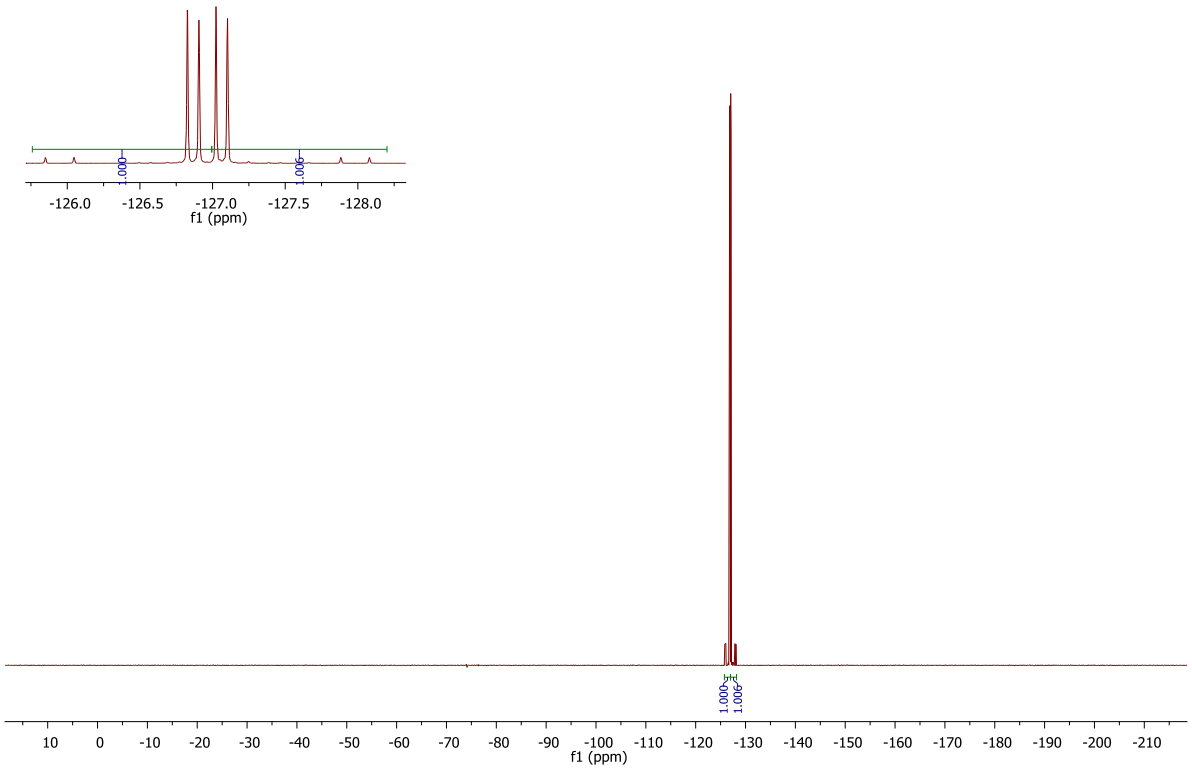

-126.0
-126.5
-127.0
-127.5
-128.0
-128.5
f1 (ppm)
1.000
1.306
f1 (ppm)

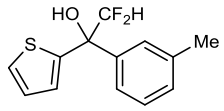

HO
CF2H
S
Cl

2f

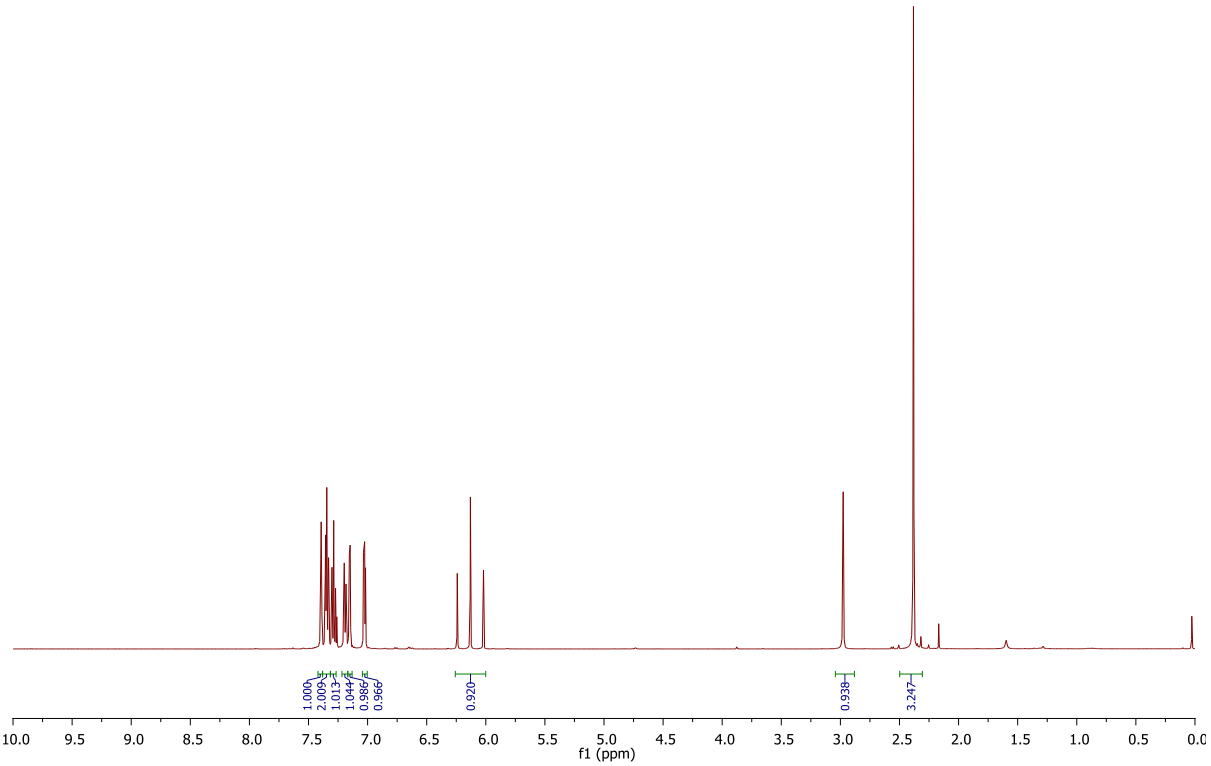

2.000
3.045
0.974
1.002
1.022
0.978
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

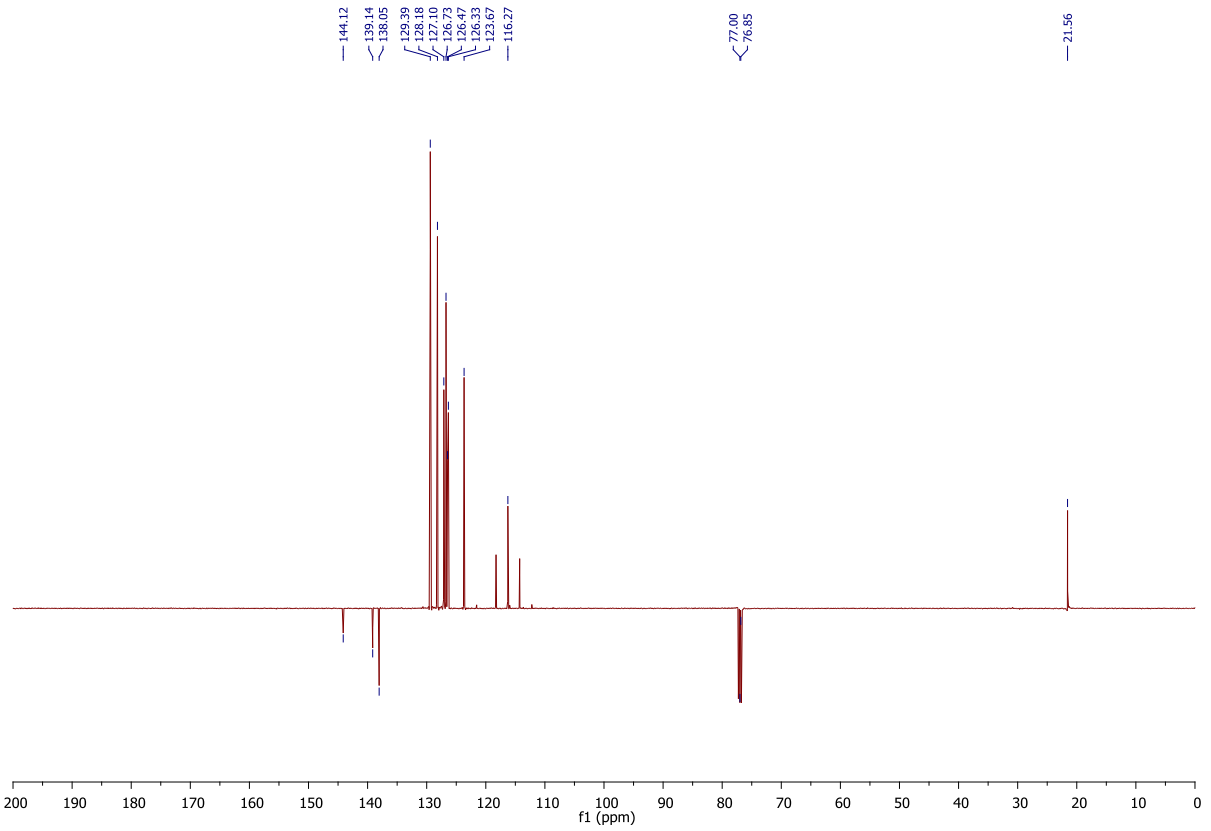

143.59
137.63
134.73
128.45
128.25
126.85
126.65
126.60
116.06
77.00
76.55
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

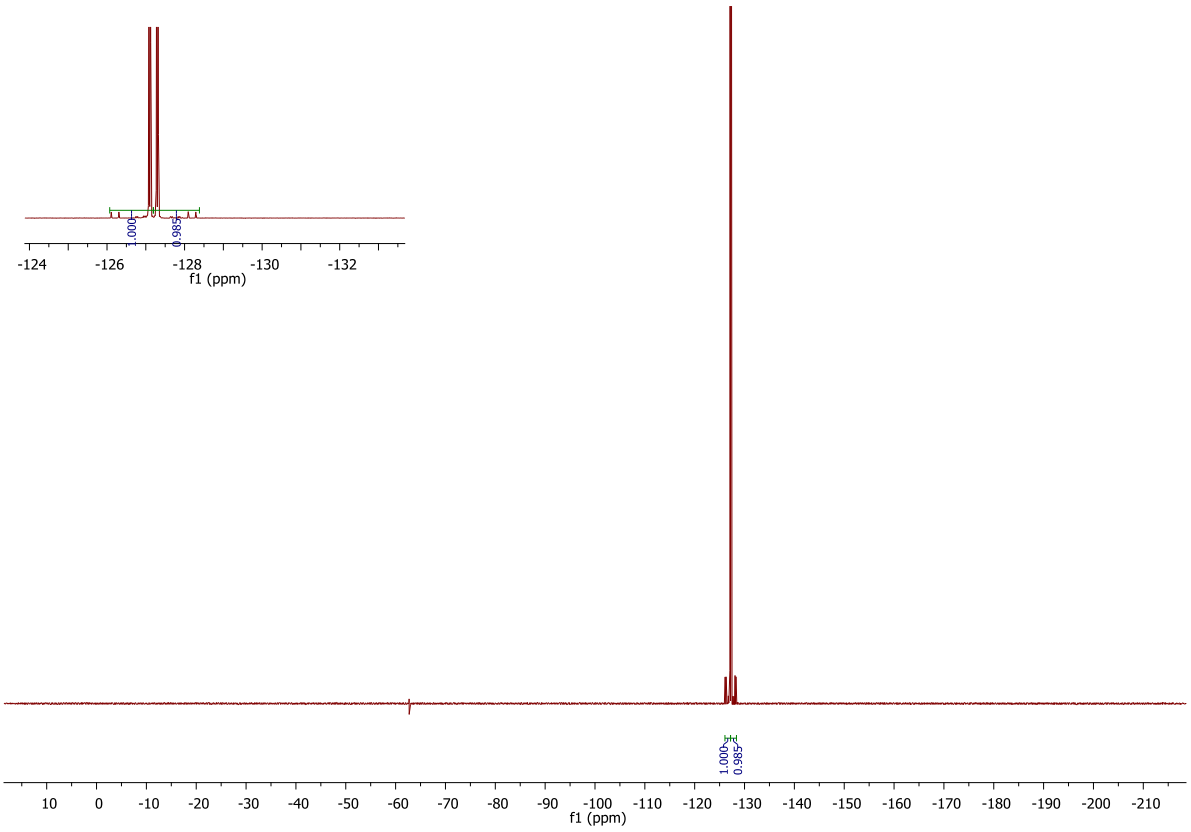

1.000
1.006
-126.0
-126.5
-127.0
-127.5
-128.0
f1 (ppm)
1.000
1.006
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


HO
CF2H
S
Me

2g


1.000
2.009
1.013
1.044
0.986
0.966
0.920
0.938
3.247
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)


144.12
139.14
138.05
129.39
128.18
127.10
126.73
126.47
126.33
123.67
116.27
77.00
76.85
21.56
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


1.000
0.985
-124
-126
-128
-130
-132
f1 (ppm)
1.000
0.985
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
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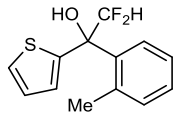
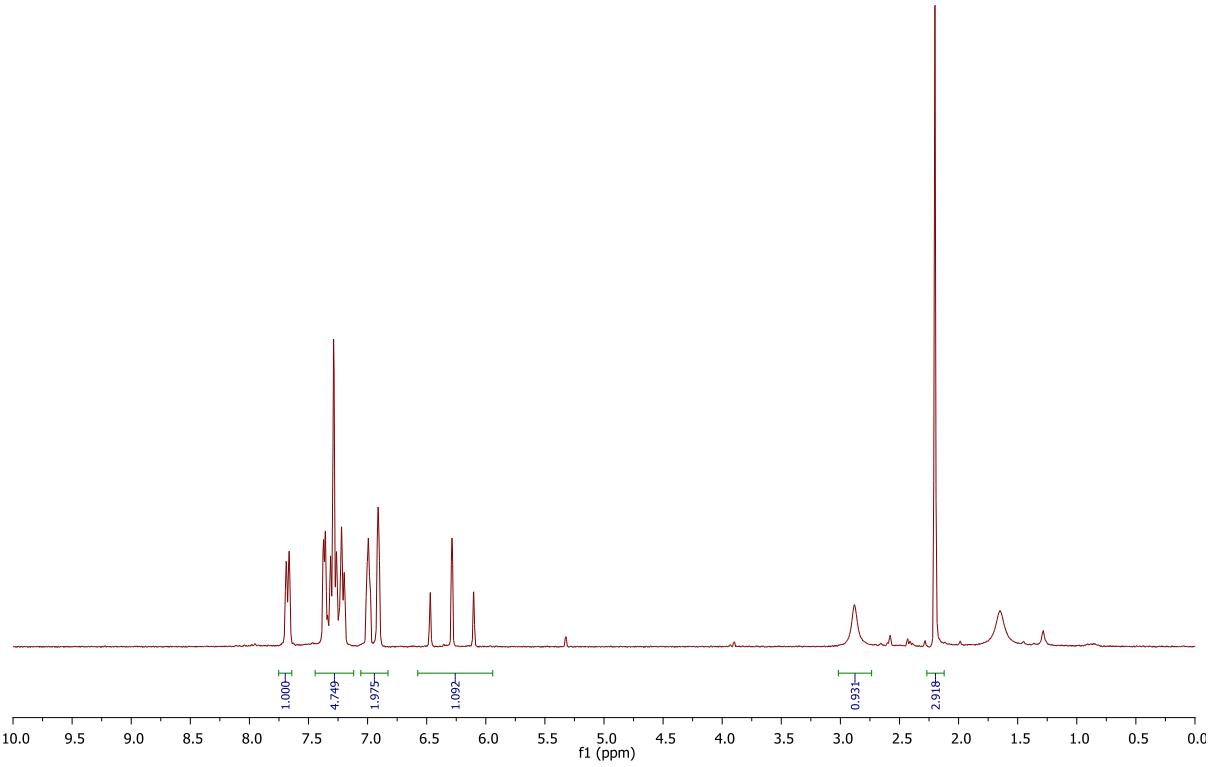
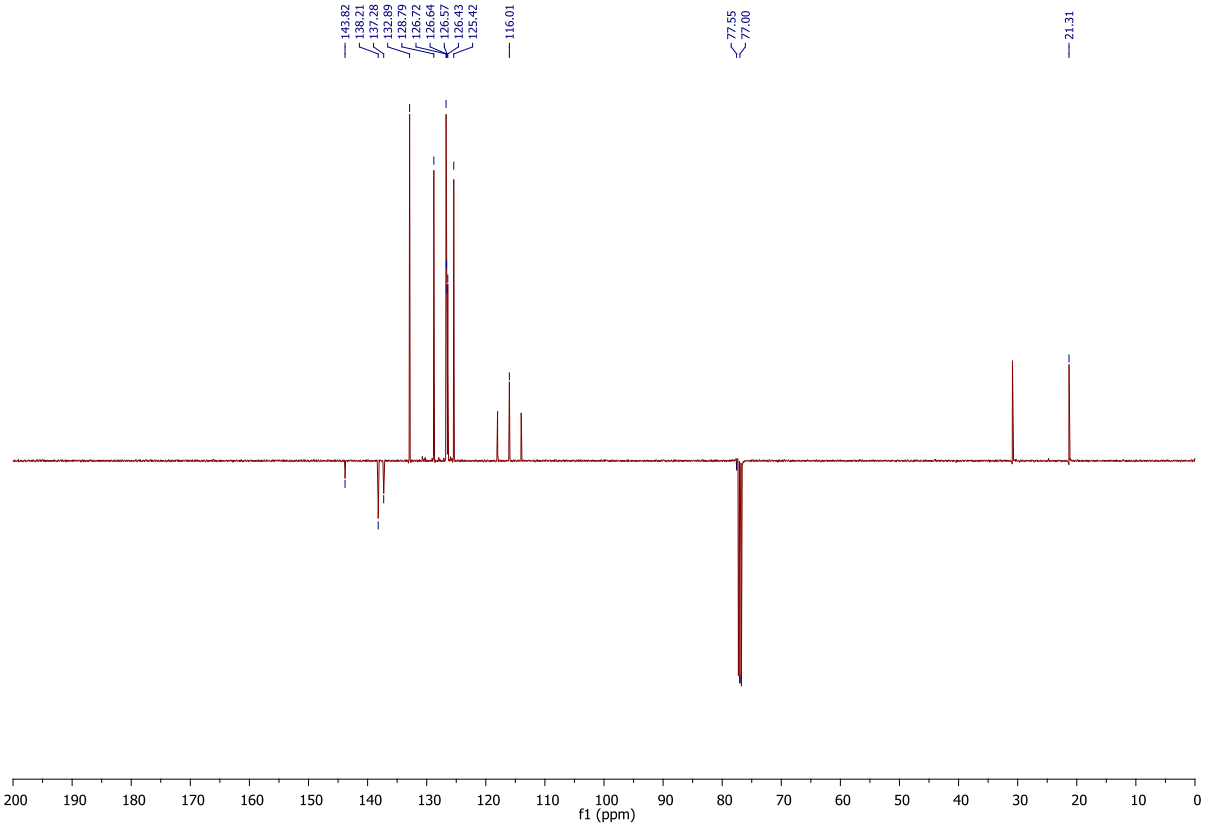
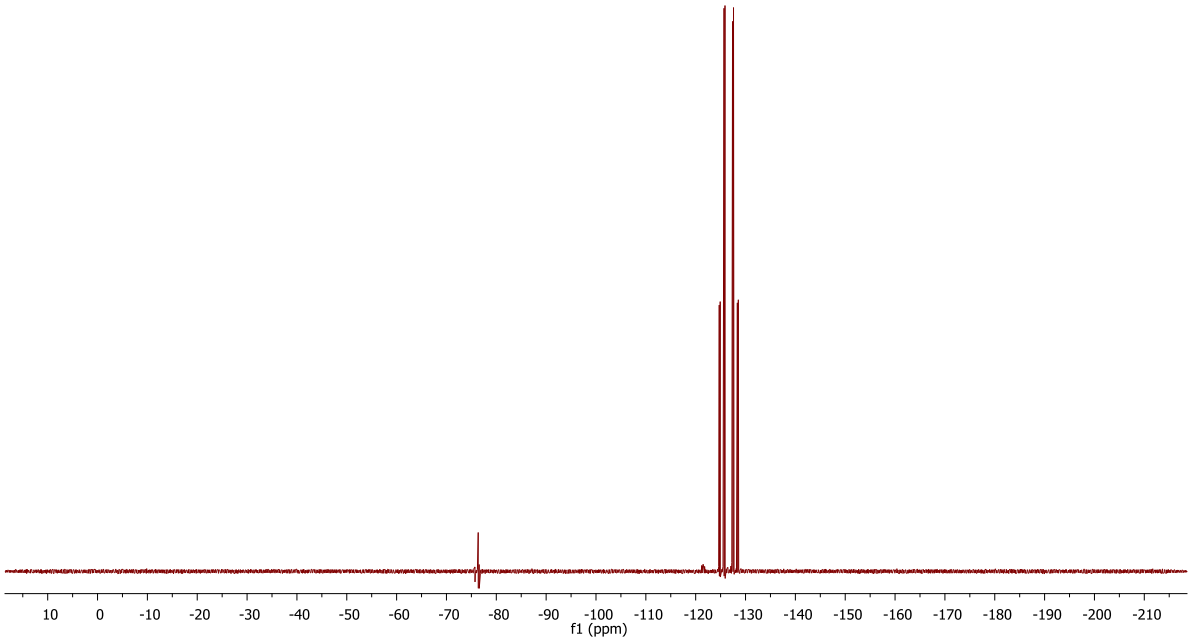
-160
-170
-180
-190
-200
-210
f1 (ppm)

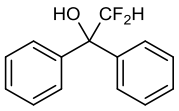

HO
CF2H
S
Me

2h

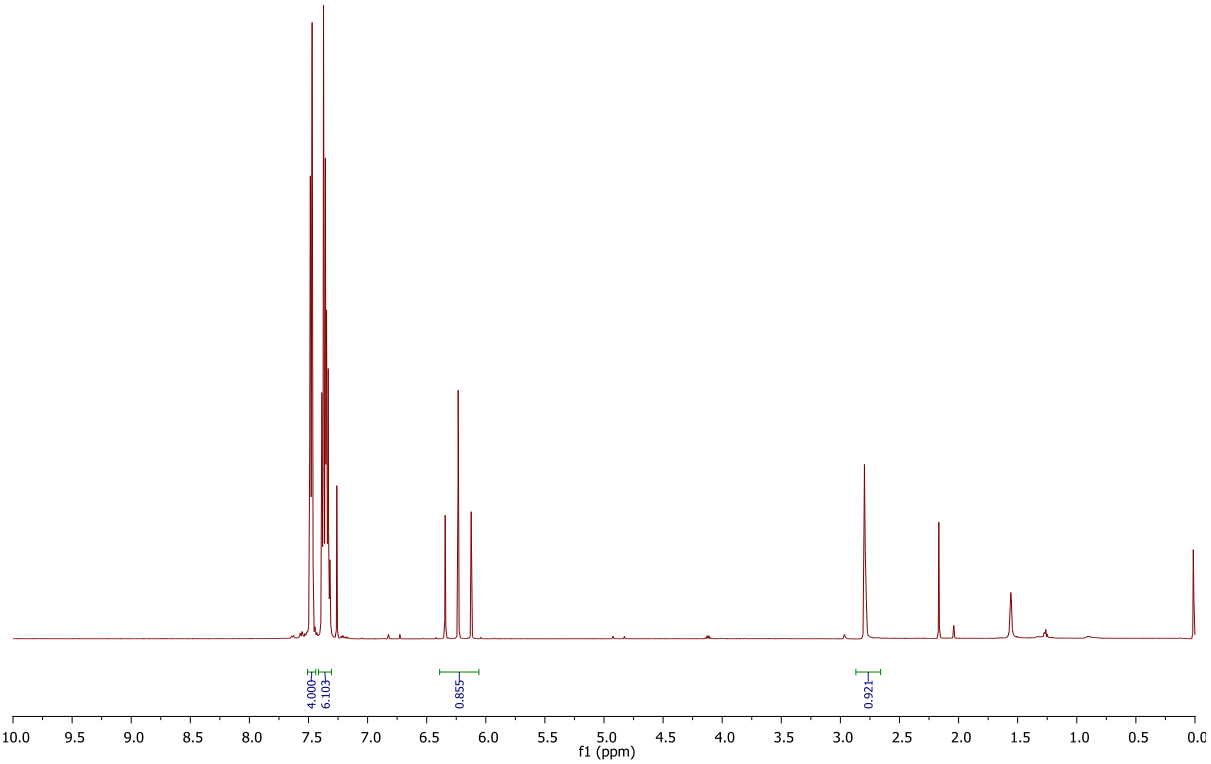

1.000
4.749
1.975
1.092
0.931
2.918
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

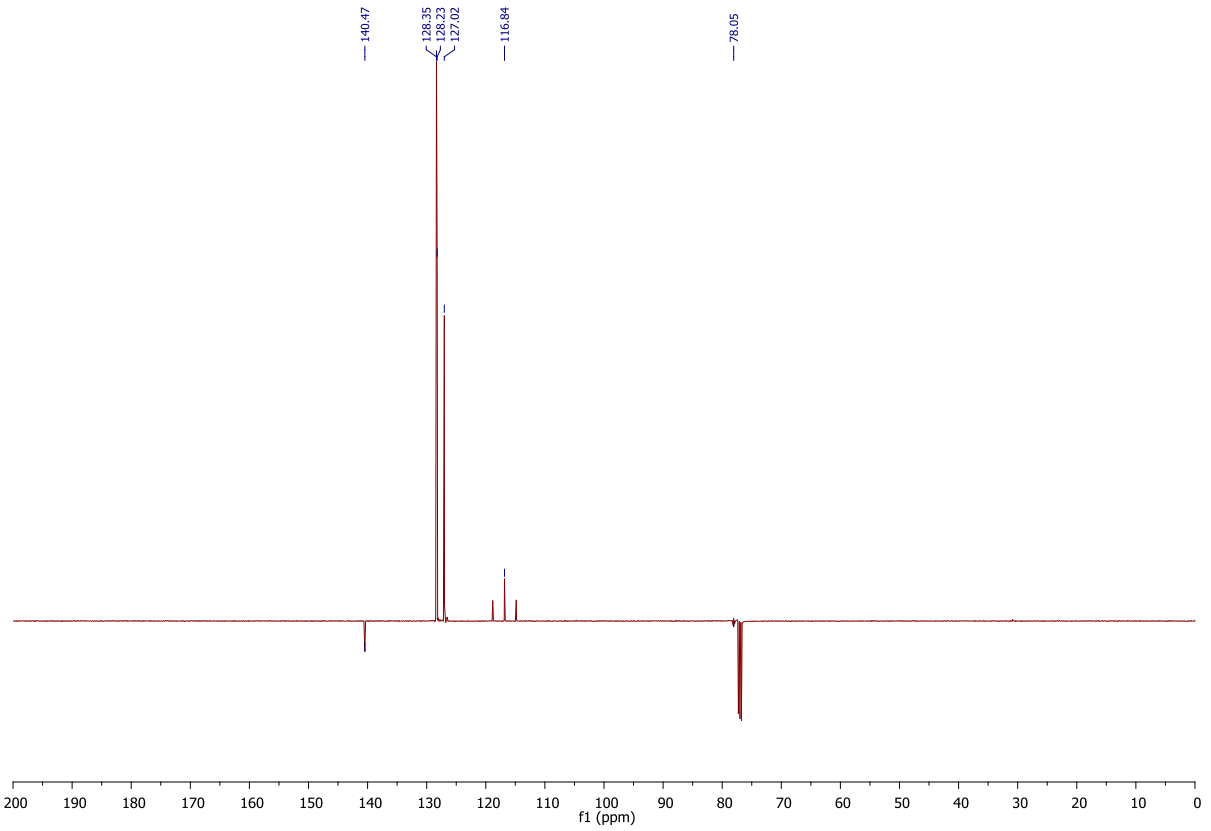

143.82
138.21
137.28
132.89
128.79
126.72
126.64
126.57
126.43
125.42
116.01
77.55
77.00
21.31
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

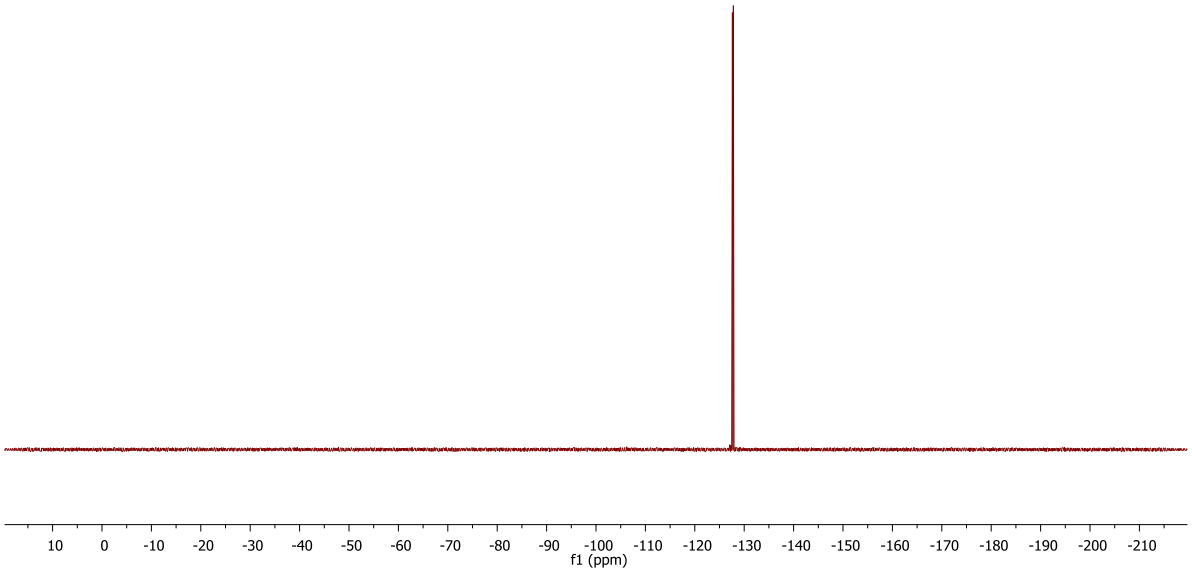

10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

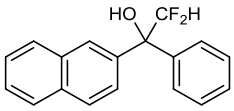

HO
CF2H

2i

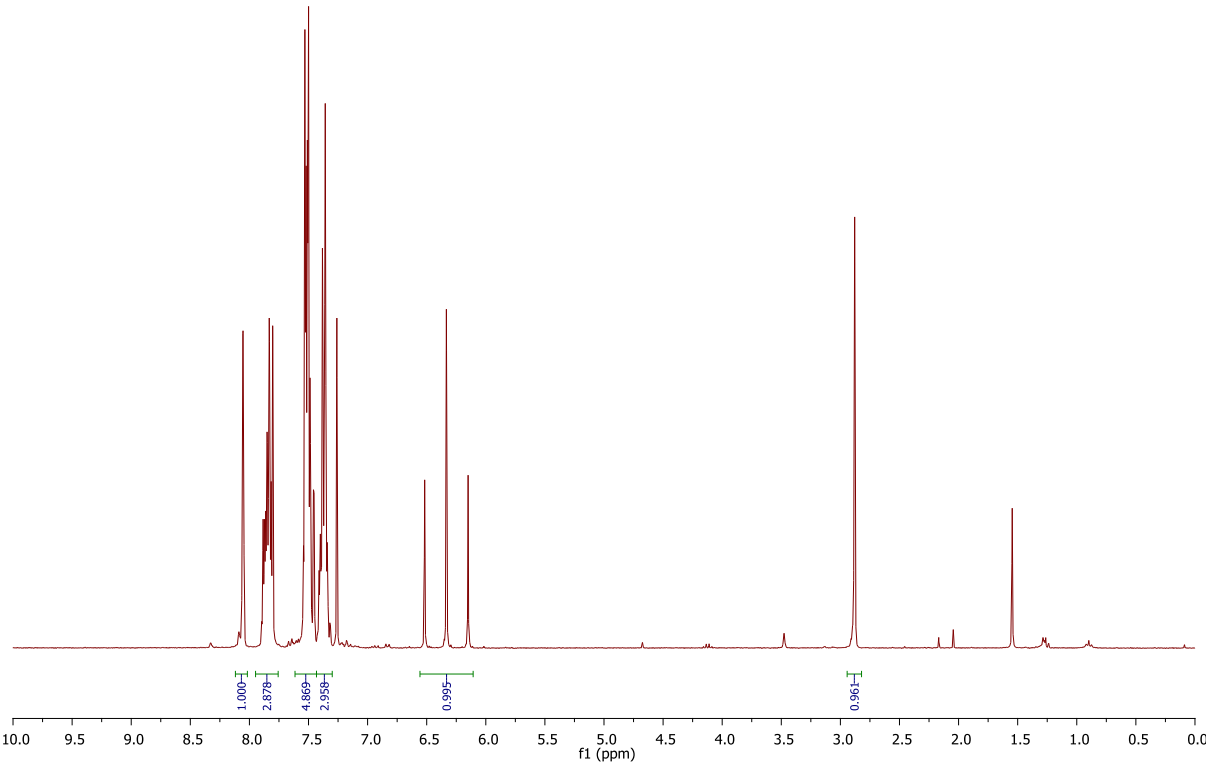

4.000
6.103
0.855
0.921
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

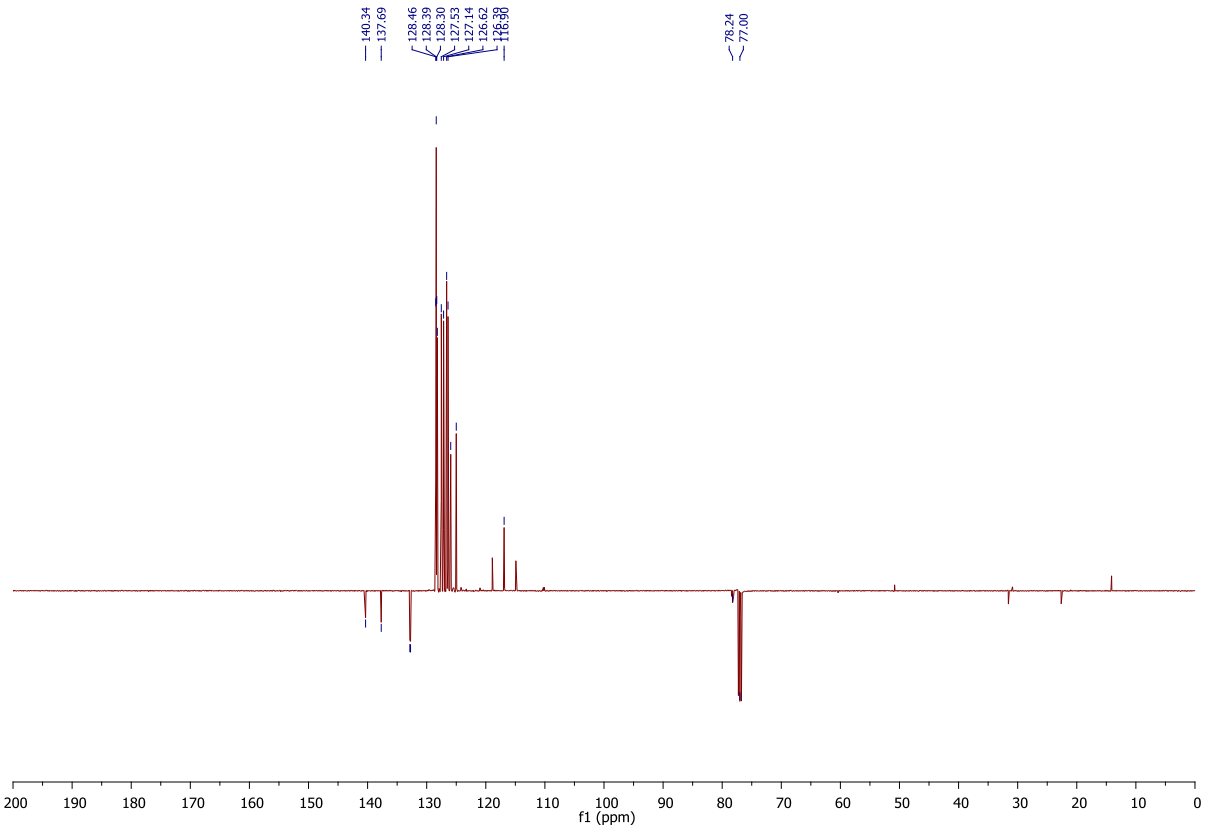

140.47
128.35
128.23
127.02
116.84
78.05
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

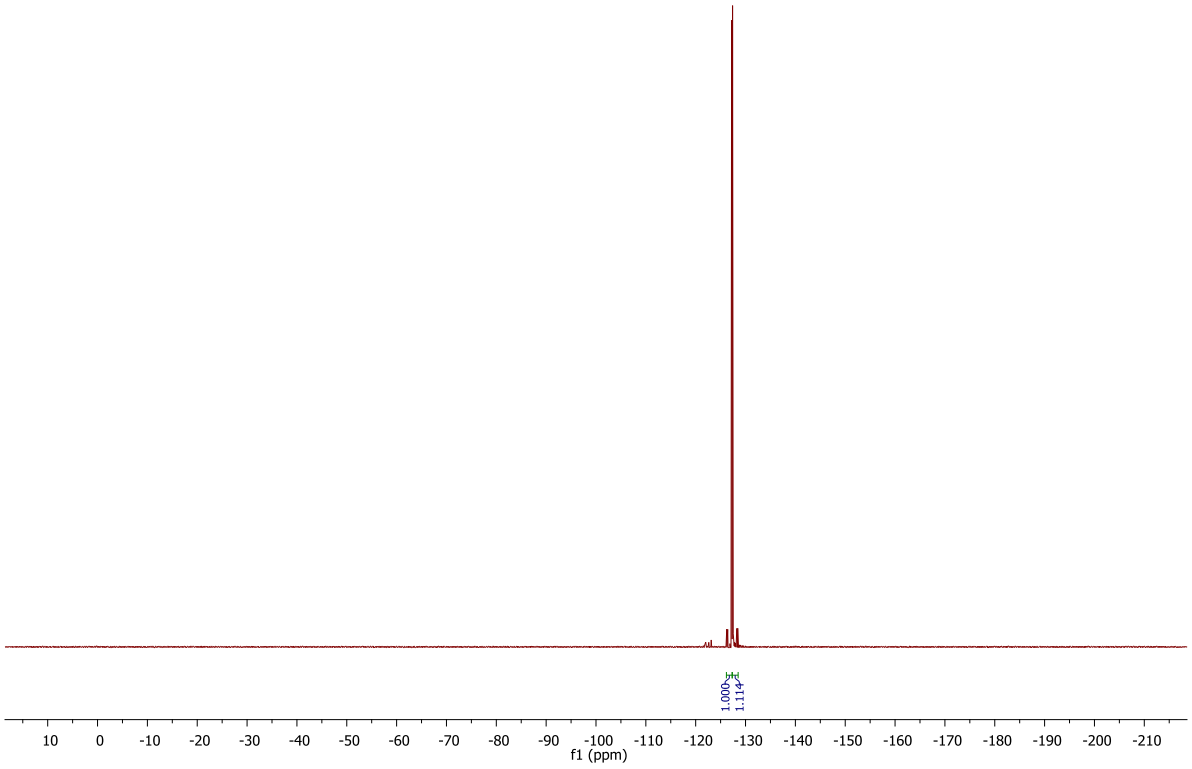

10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

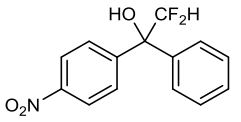

HO
CF2H

2j

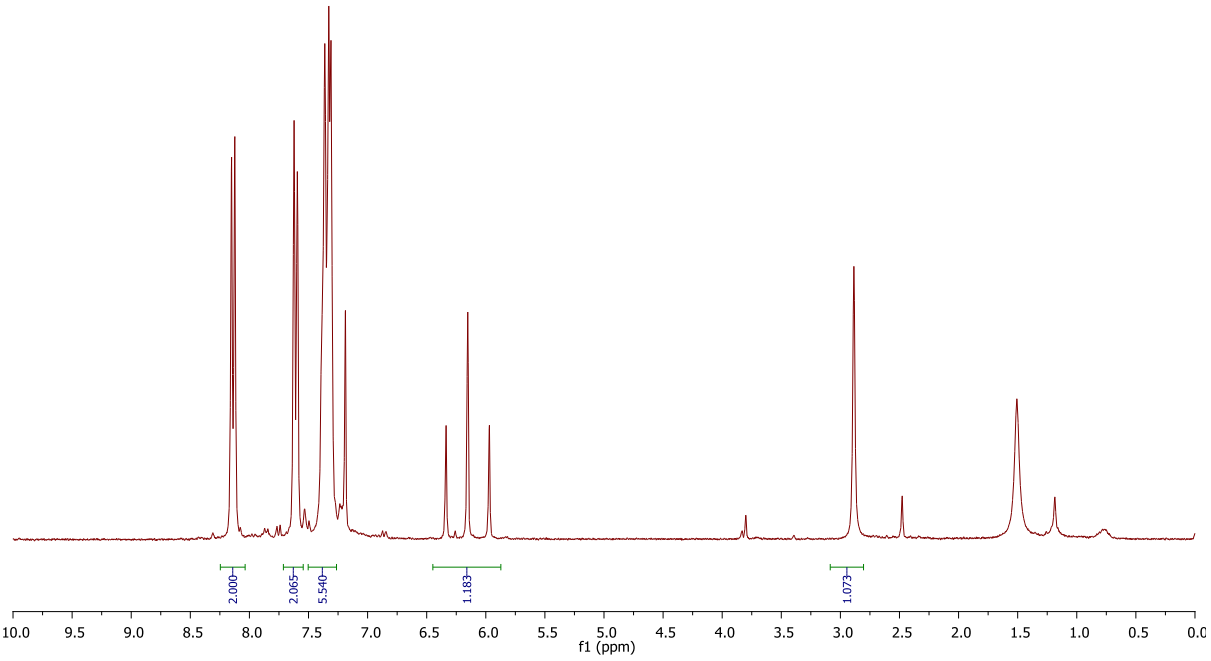

1.000
2.878
4.869
2.958
0.995
0.961
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

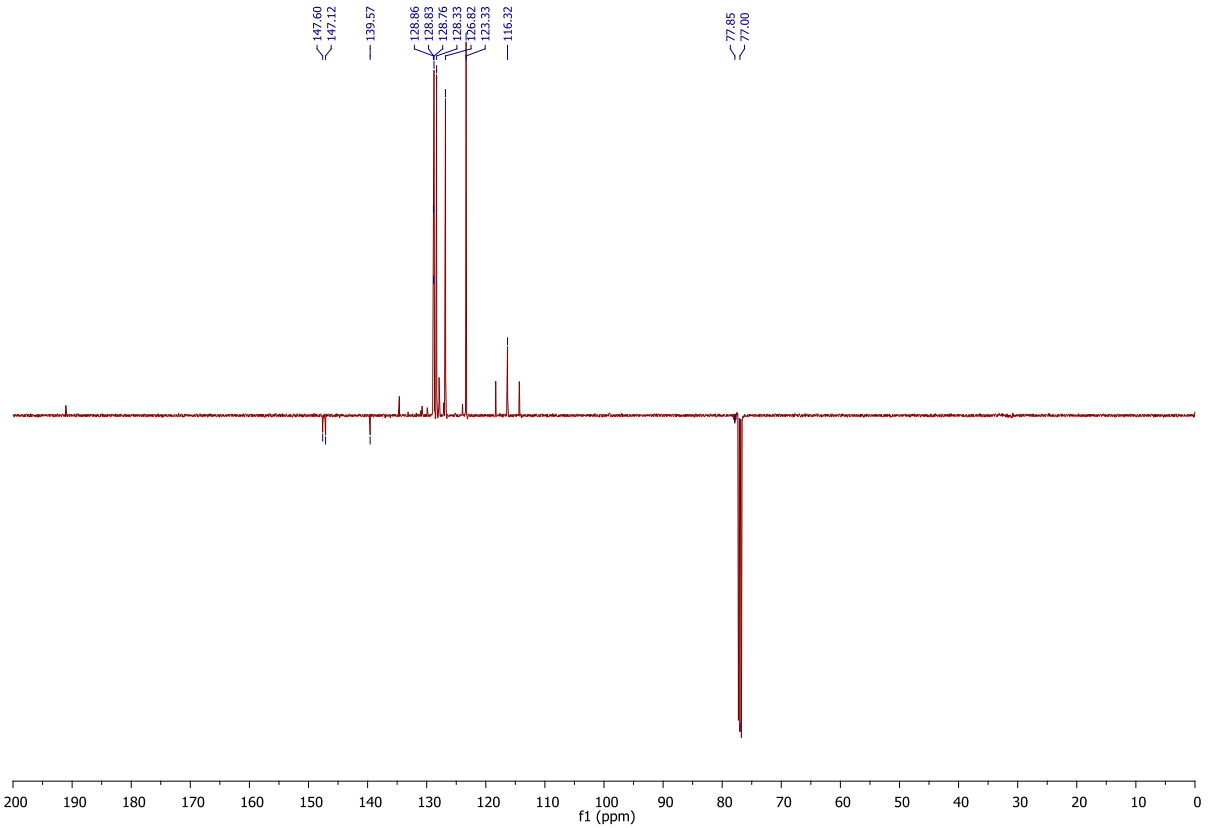

140.34
137.69
128.46
128.39
128.30
127.53
127.14
126.62
78.24
77.00
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

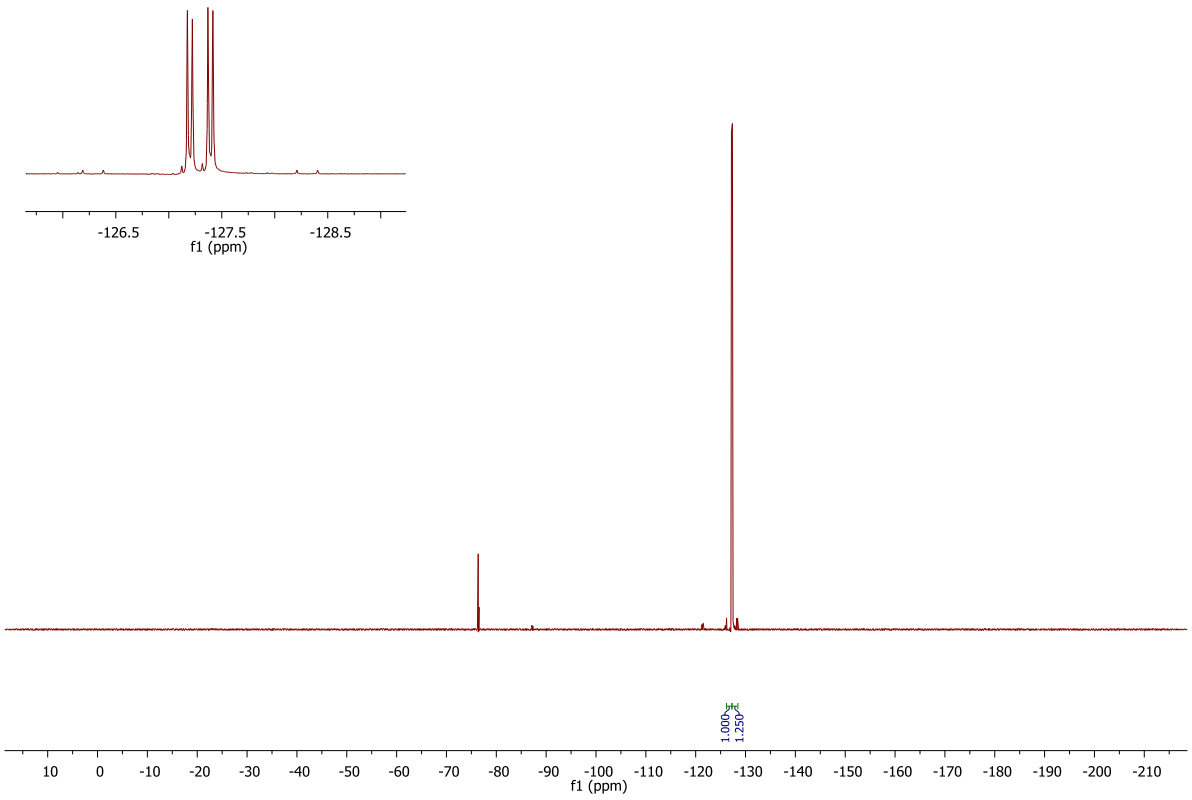

1.000
1.114
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

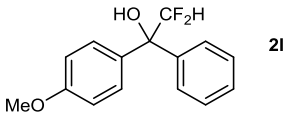

HO
CF2H
O2N

2k

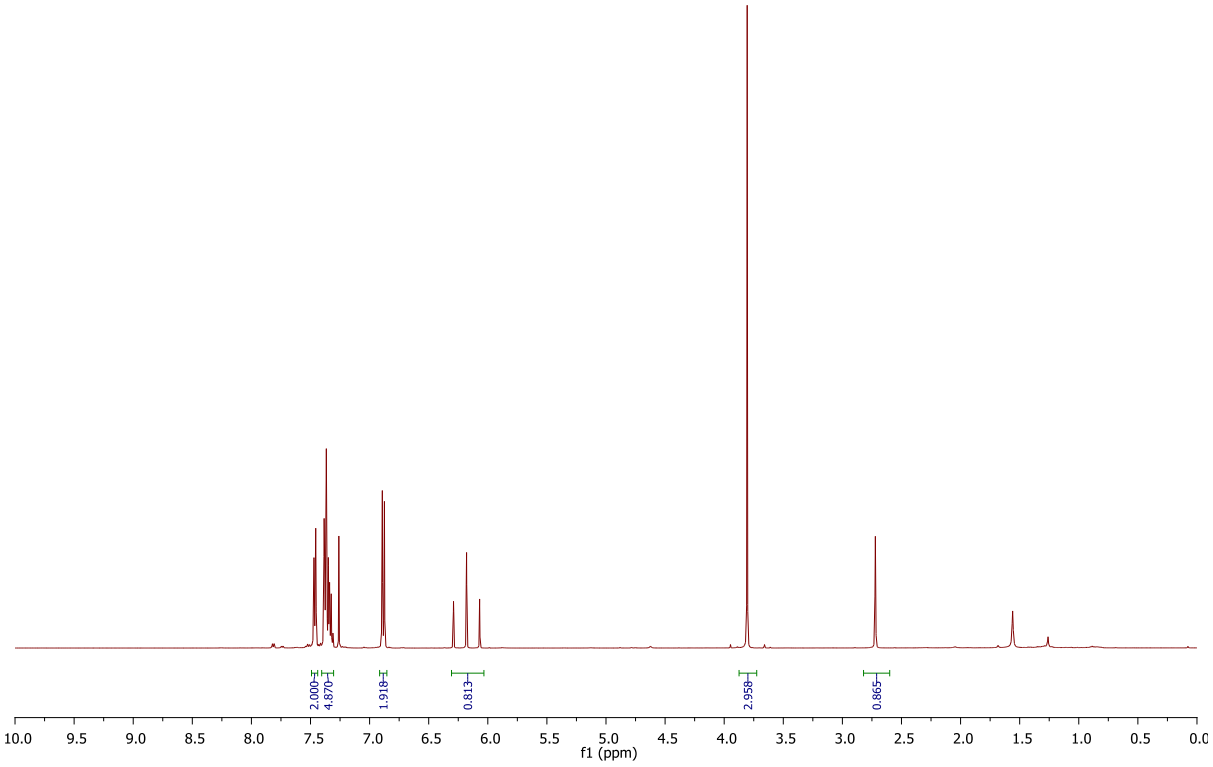

2.000
2.065
5.540
1.183
1.073
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

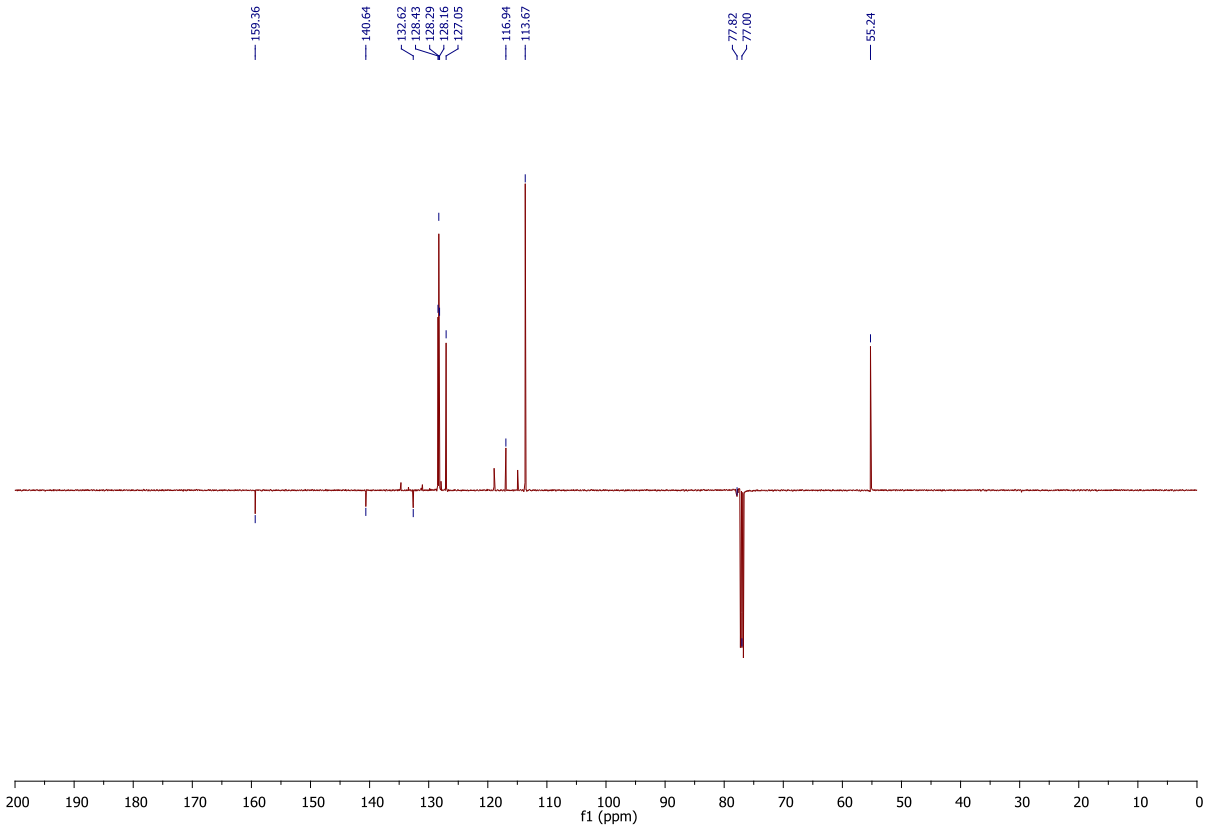

147.60
147.12
139.57
128.86
128.83
128.76
128.33
126.82
123.33
116.32
77.85
77.00
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

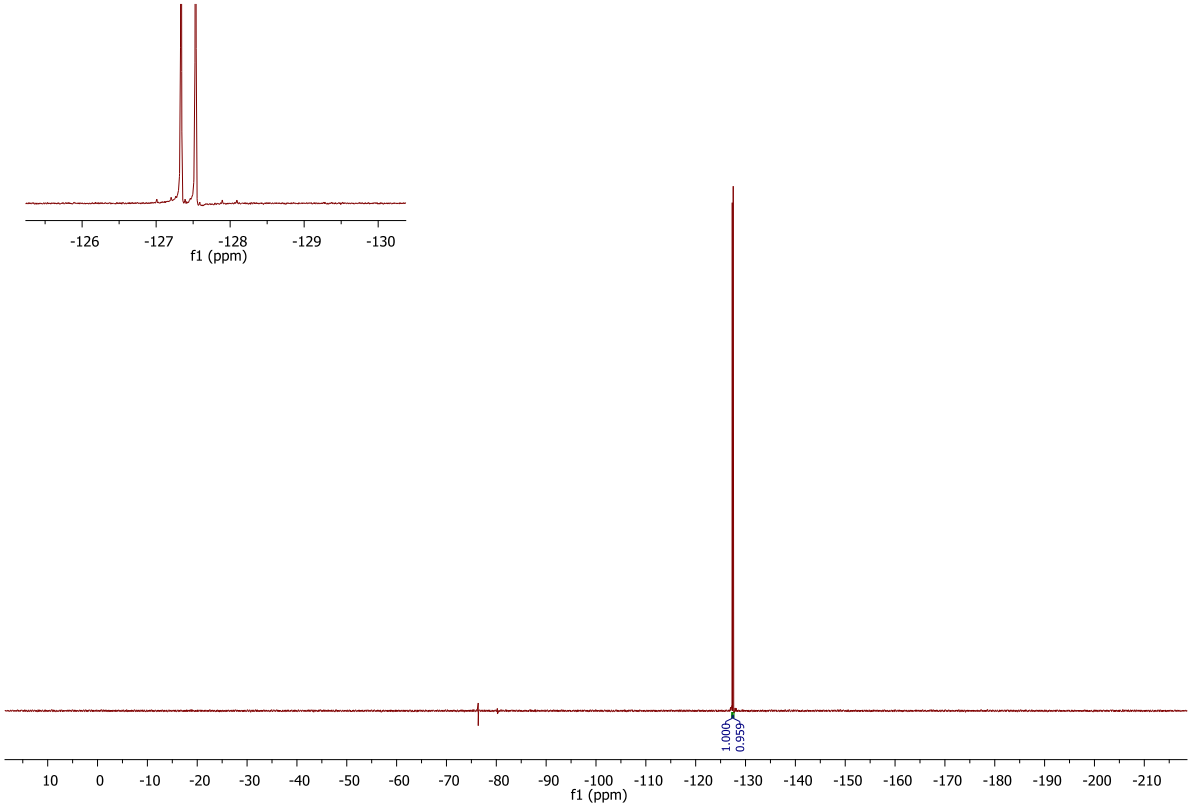

-126.5
-127.5
-128.5
f1 (ppm)
1.000
1.250
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

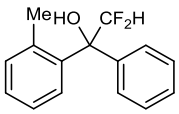

HO
CF2H
MeO

2l

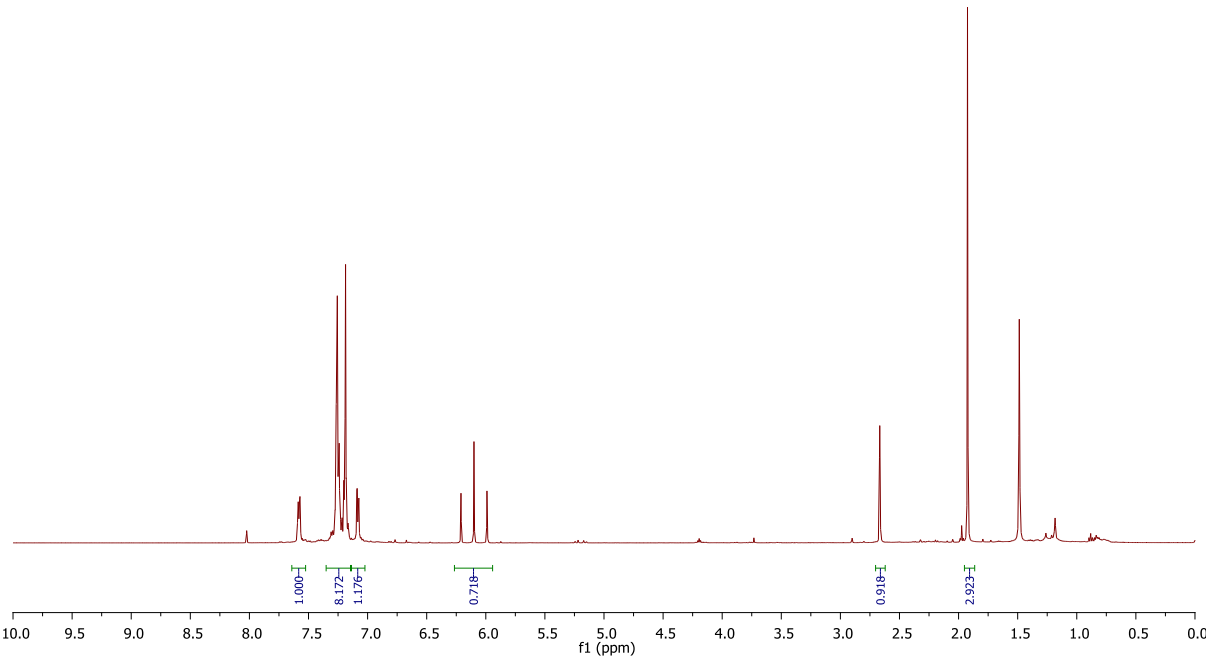

2.000
4.870
1.918
0.813
2.958
0.865
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

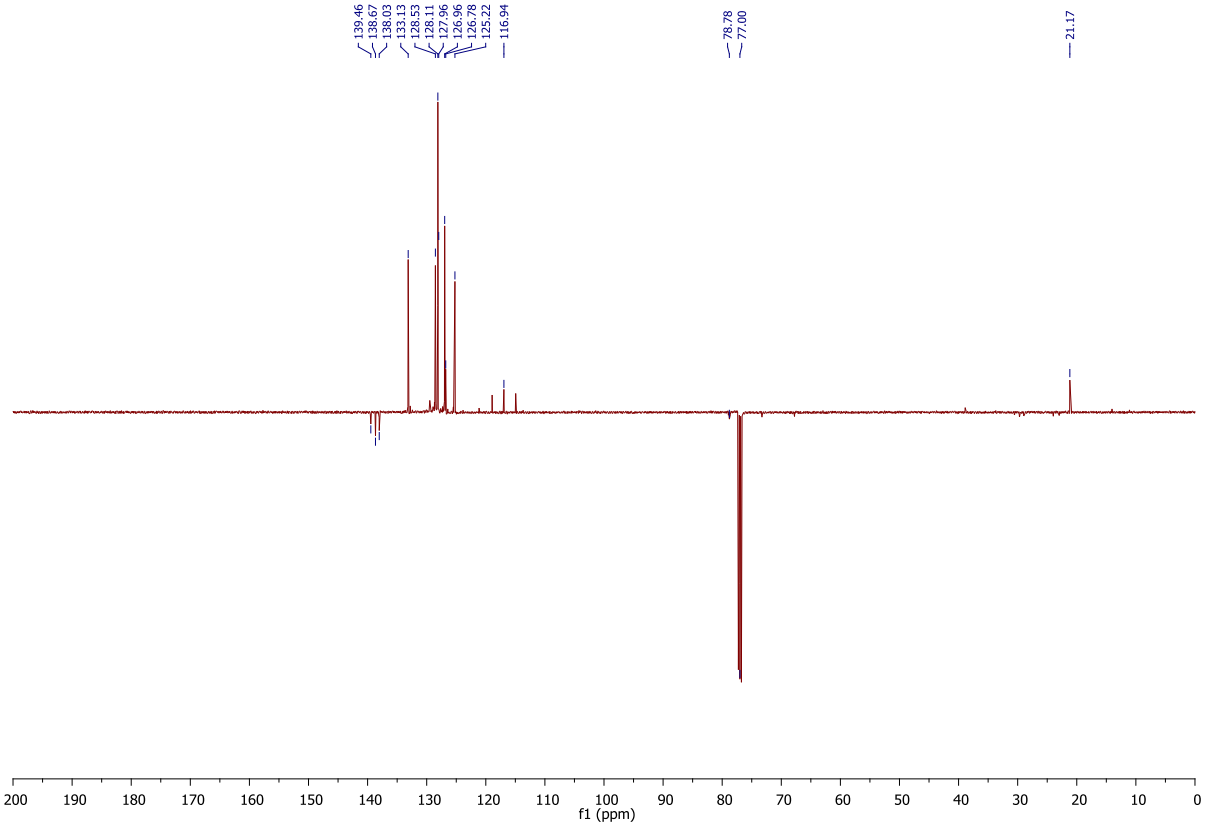

159.36
140.64
132.62
128.43
128.29
128.16
127.05
116.94
113.67
77.82
77.00
55.24
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

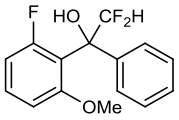

-126
-127
-128
-129
-130
f1 (ppm)
1.000
0.999
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


Me
HO
CF2H

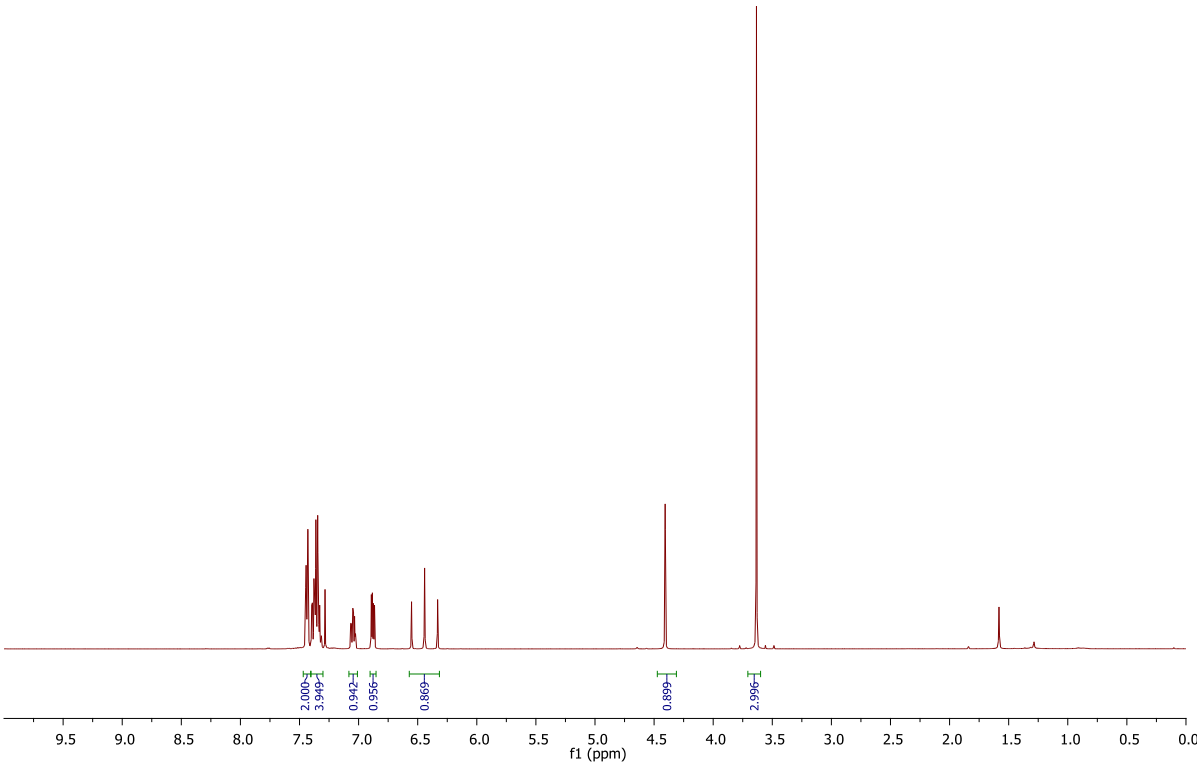
2m

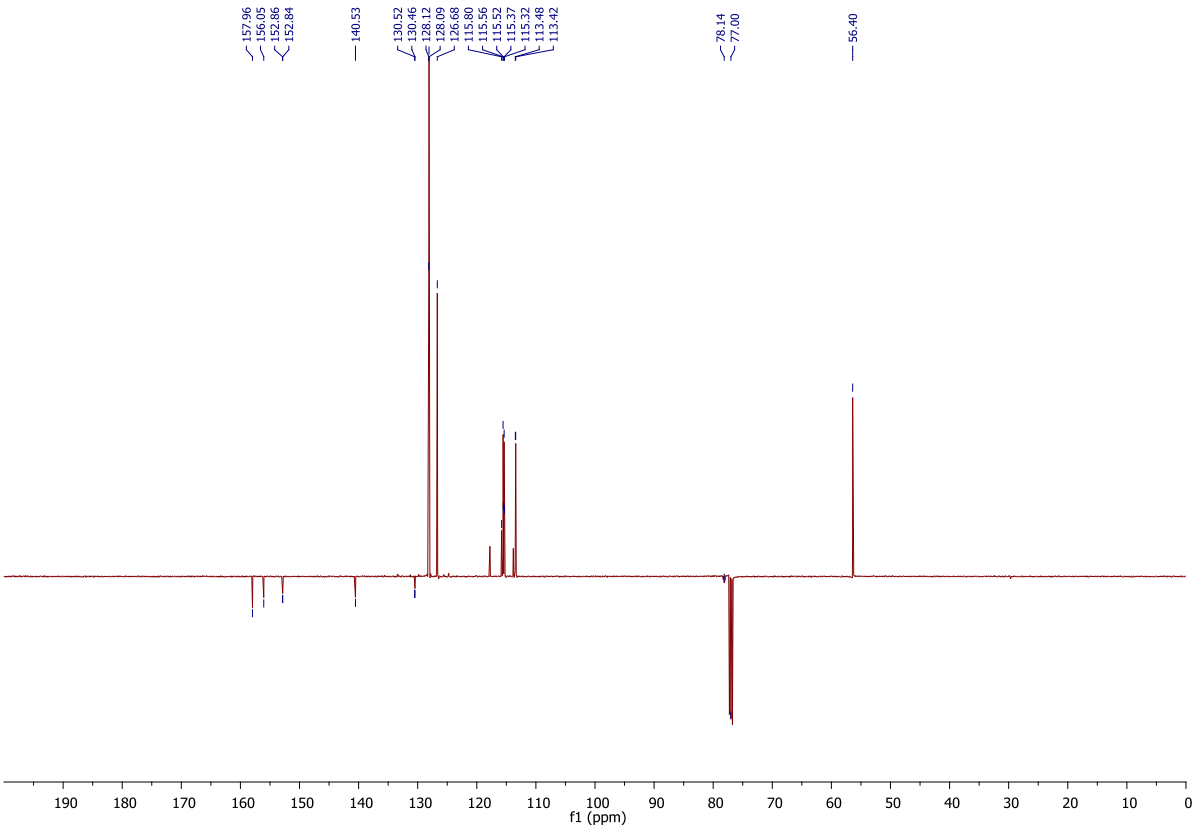

1.000
8.172
1.176
0.718
0.918
2.923
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

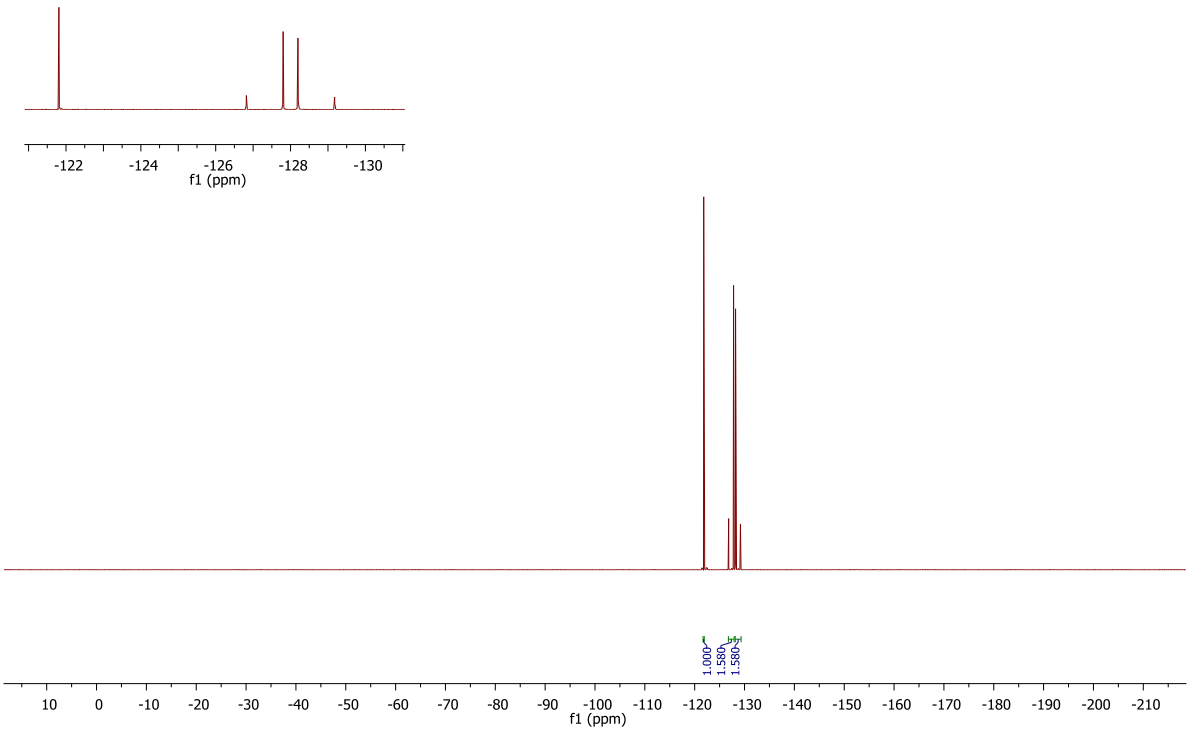

139.46
138.67
138.03
133.13
128.53
128.11
127.96
126.96
126.78
125.22
116.94
78.78
77.00
21.17
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

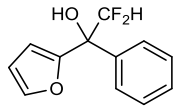

F
HO
CF2H
OMe

2n

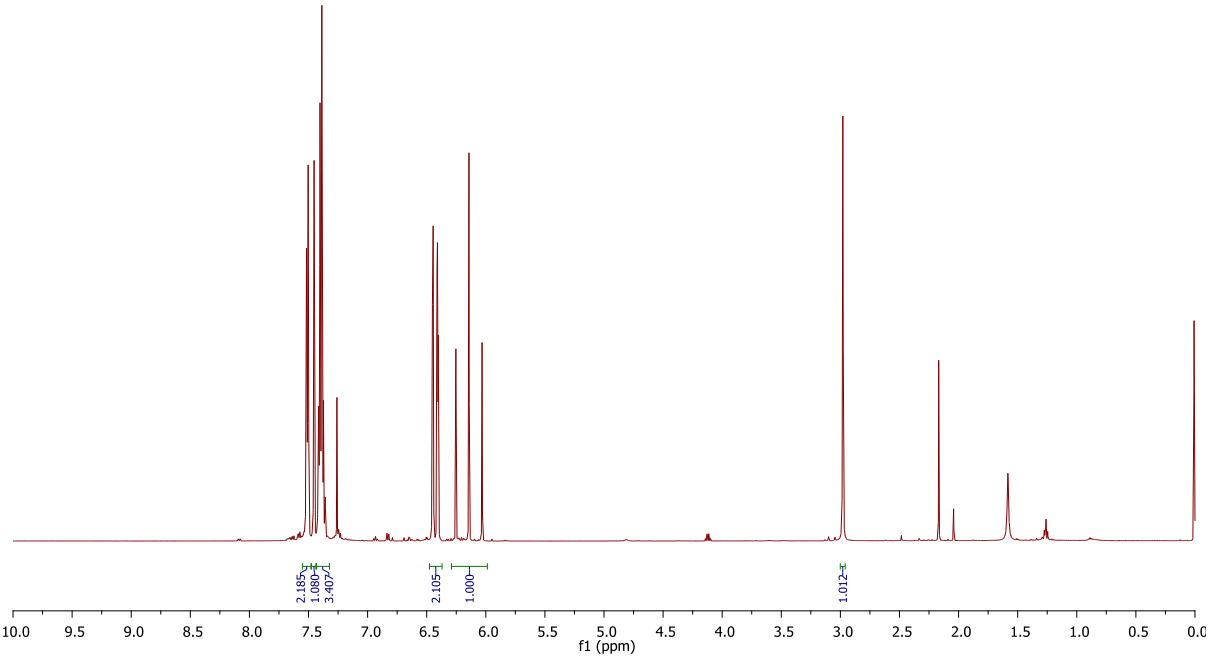

2.000
3.949
0.942
0.956
0.869
0.899
2.996
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

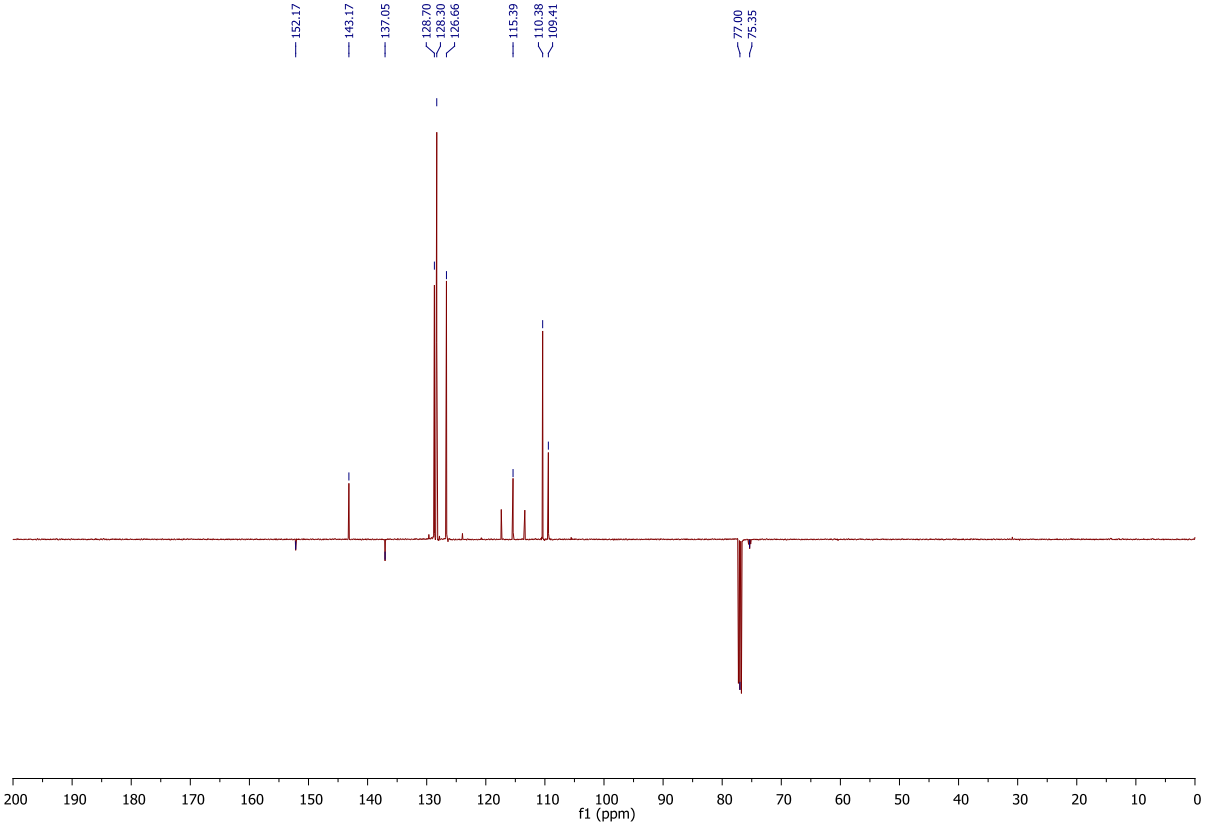

157.96
156.05
152.86
152.84
140.53
130.52
130.46
128.12
128.09
126.68
115.80
115.56
115.52
115.37
115.32
113.48
113.42
78.14
77.00
56.40
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

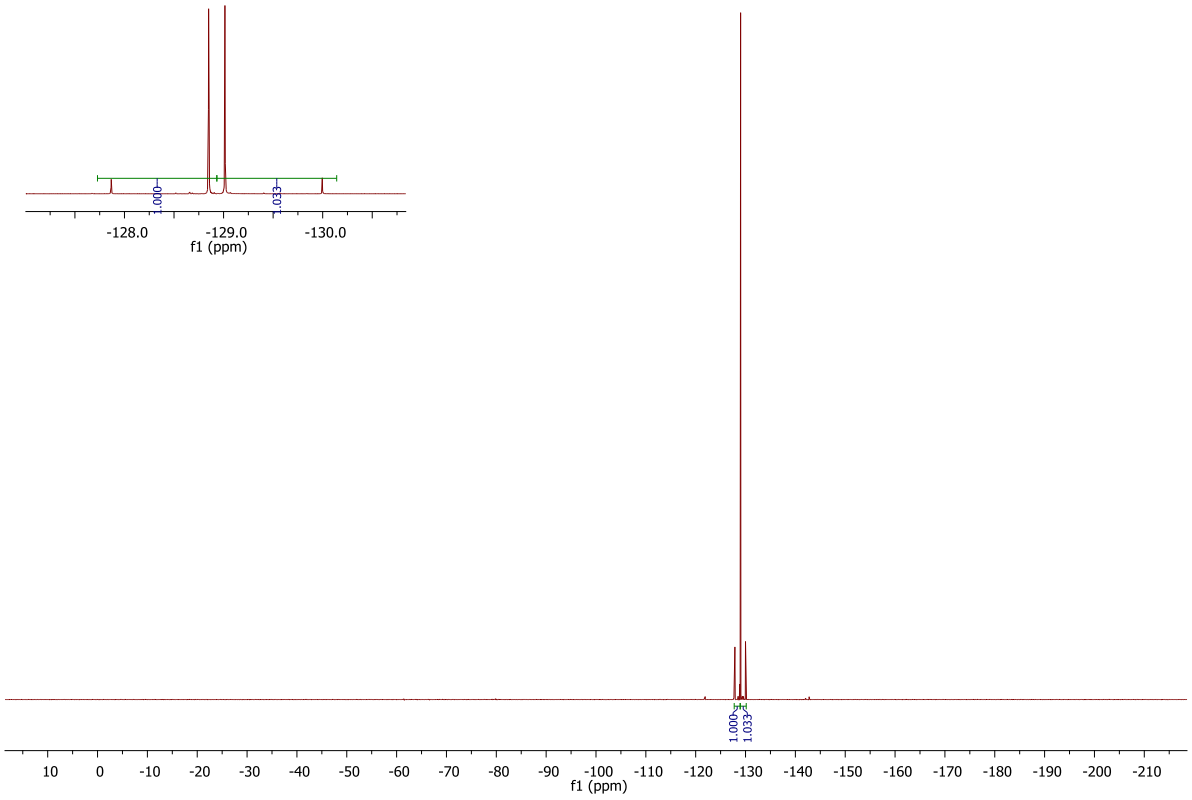

-122
-124
-126
-128
-130
f1 (ppm)
1.000
1.580
1.580
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

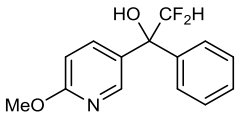

HO
CF2H
O

2o

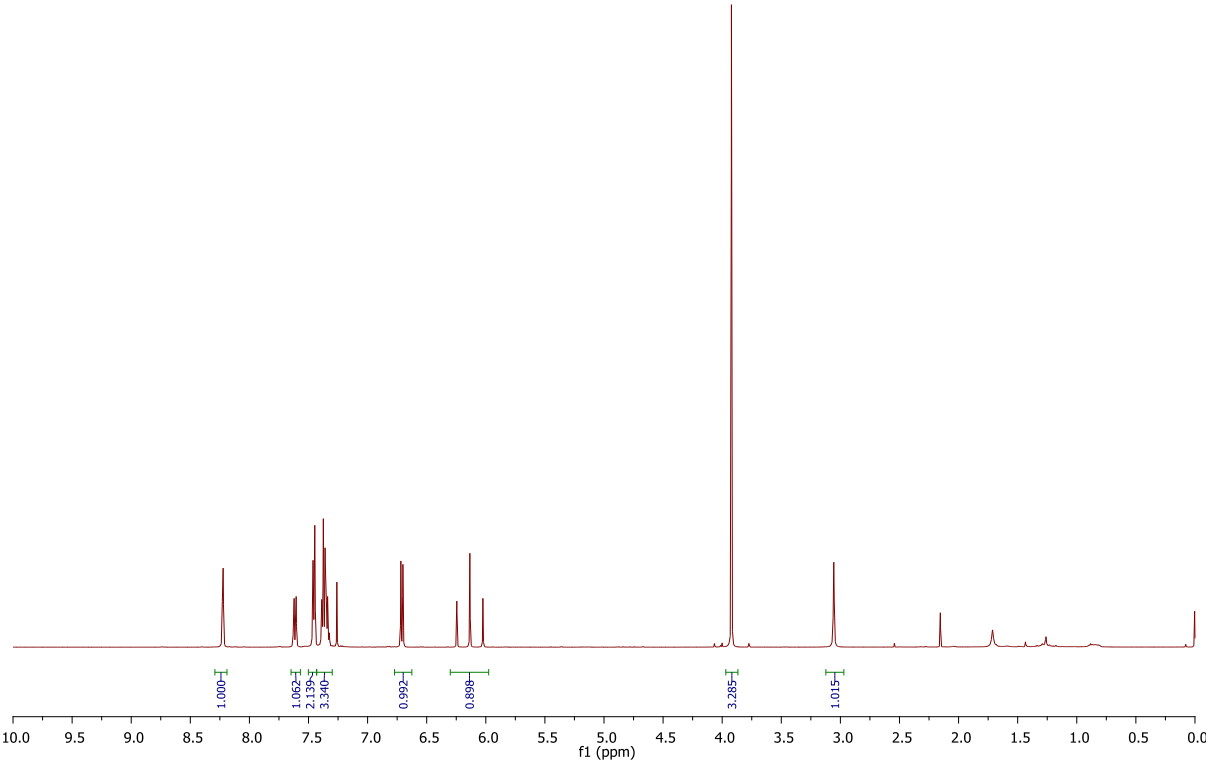

2.185
1.080
3.407
2.105
1.000
1.012
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

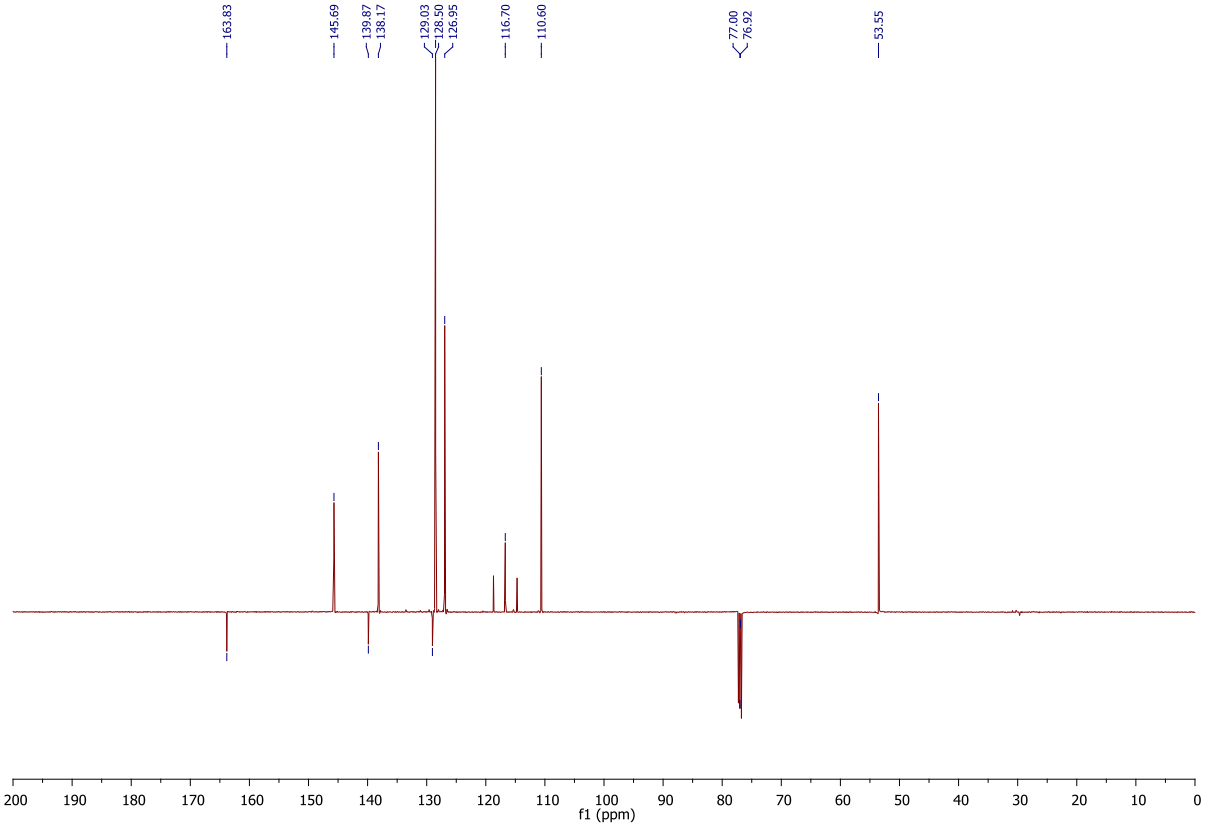

152.17
143.17
137.05
128.70
128.30
126.66
115.39
110.38
109.41
77.00
75.35
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

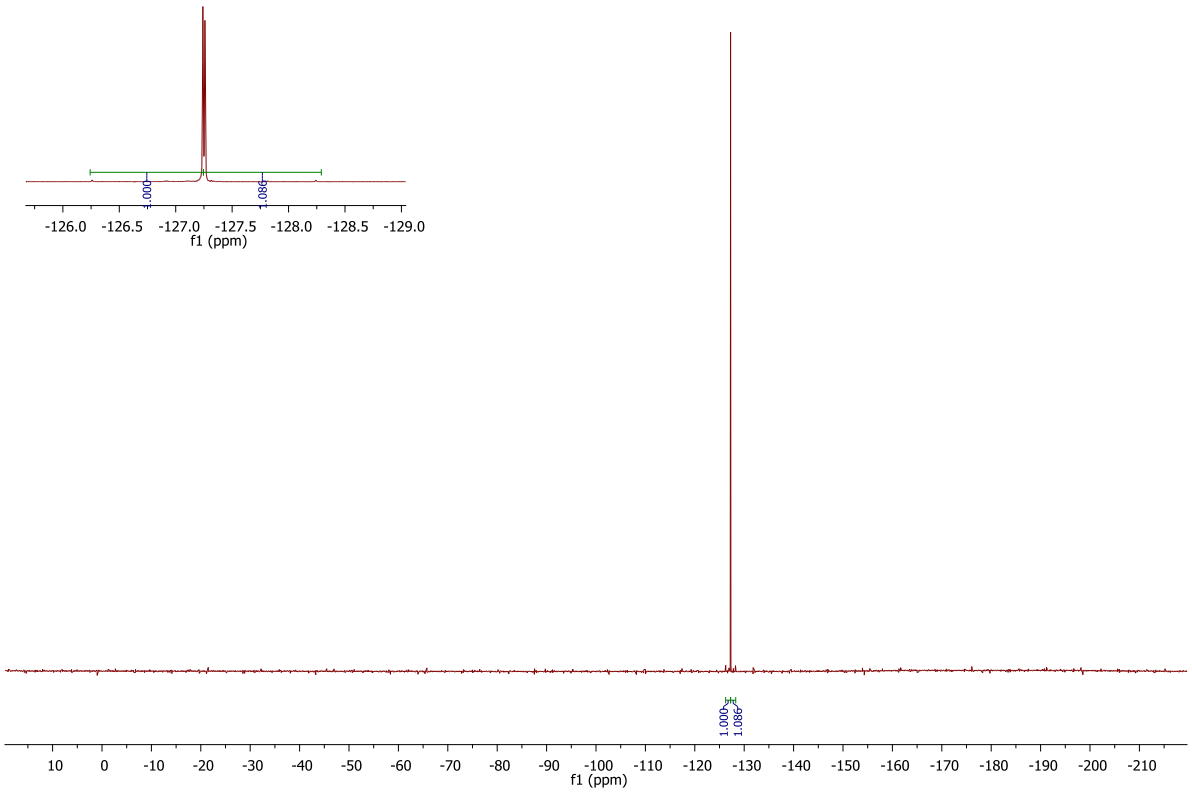

1.000
1.033
-128.0
-129.0
-130.0
f1 (ppm)
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

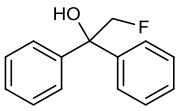

HO
CF2H
MeO
N

2p

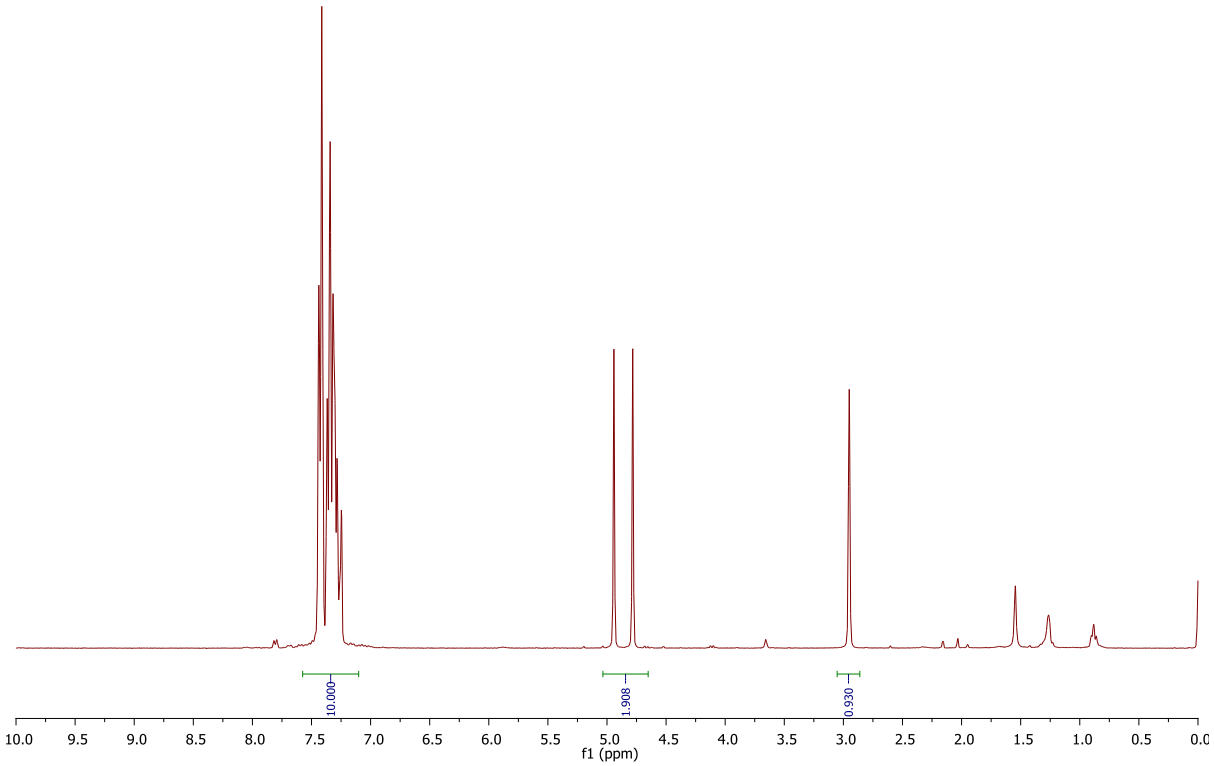

1.000
1.062
2.139
3.340
0.992
0.899
3.285
1.015
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

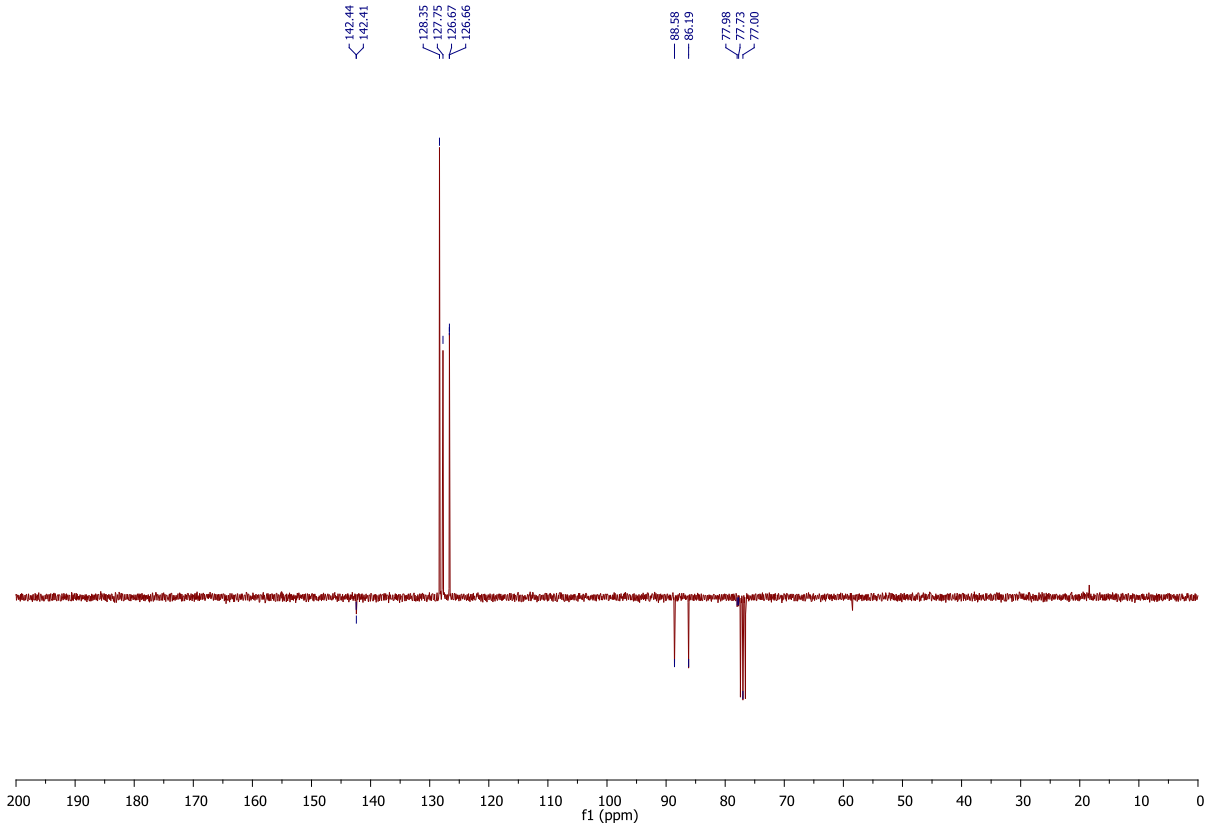

163.83
145.69
139.87
138.17
129.03
128.50
126.95
116.70
110.60
77.00
76.92
53.55
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

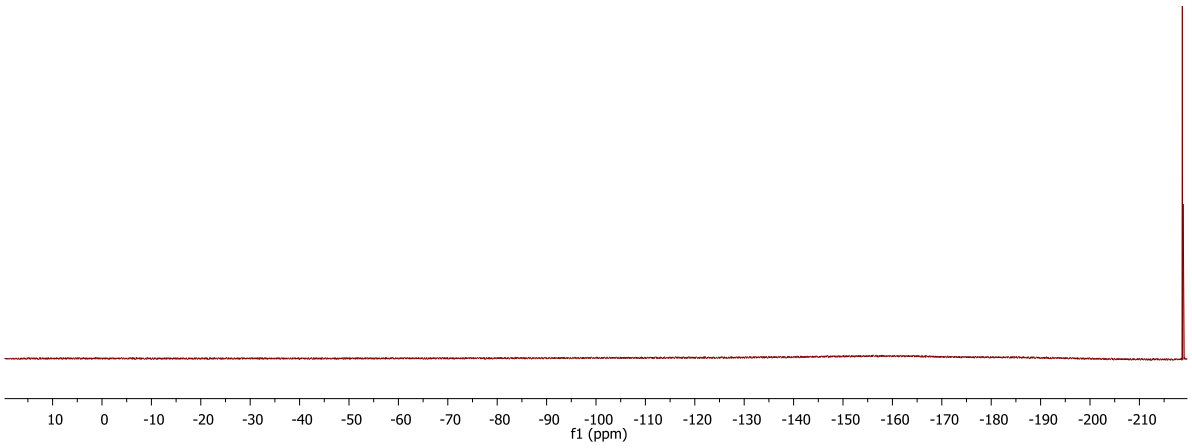

1.000
1.086
-126.0 -126.5 -127.0 -127.5 -128.0 -128.5 -129.0
f1 (ppm)
1.000
1.086
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

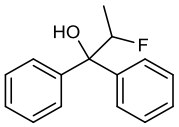

HO
F

3a

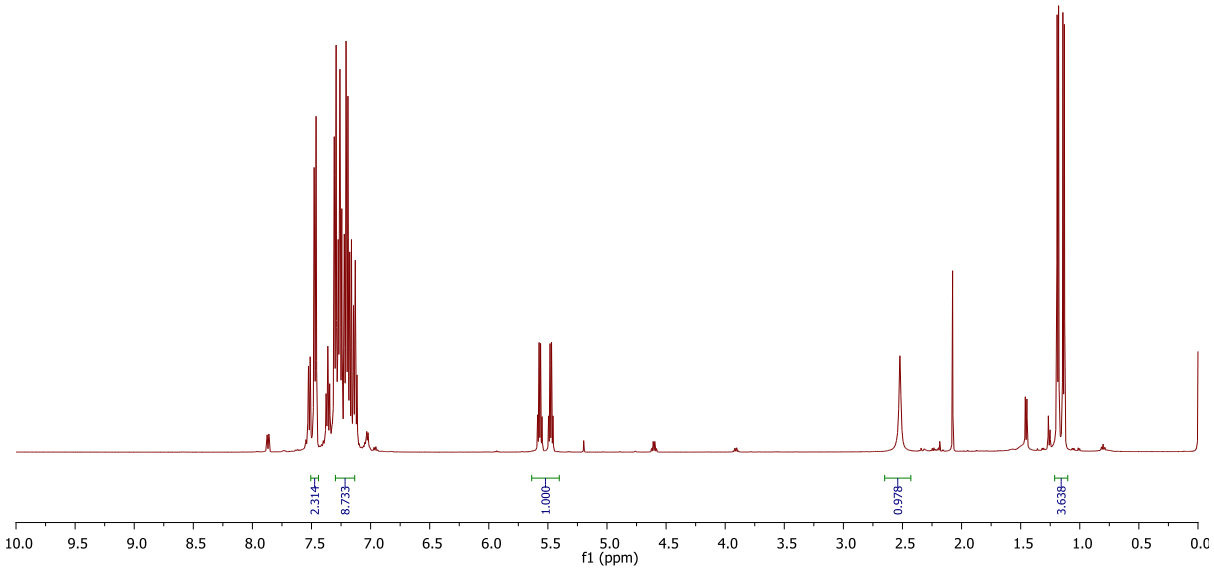

10.000
1.908
0.930
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

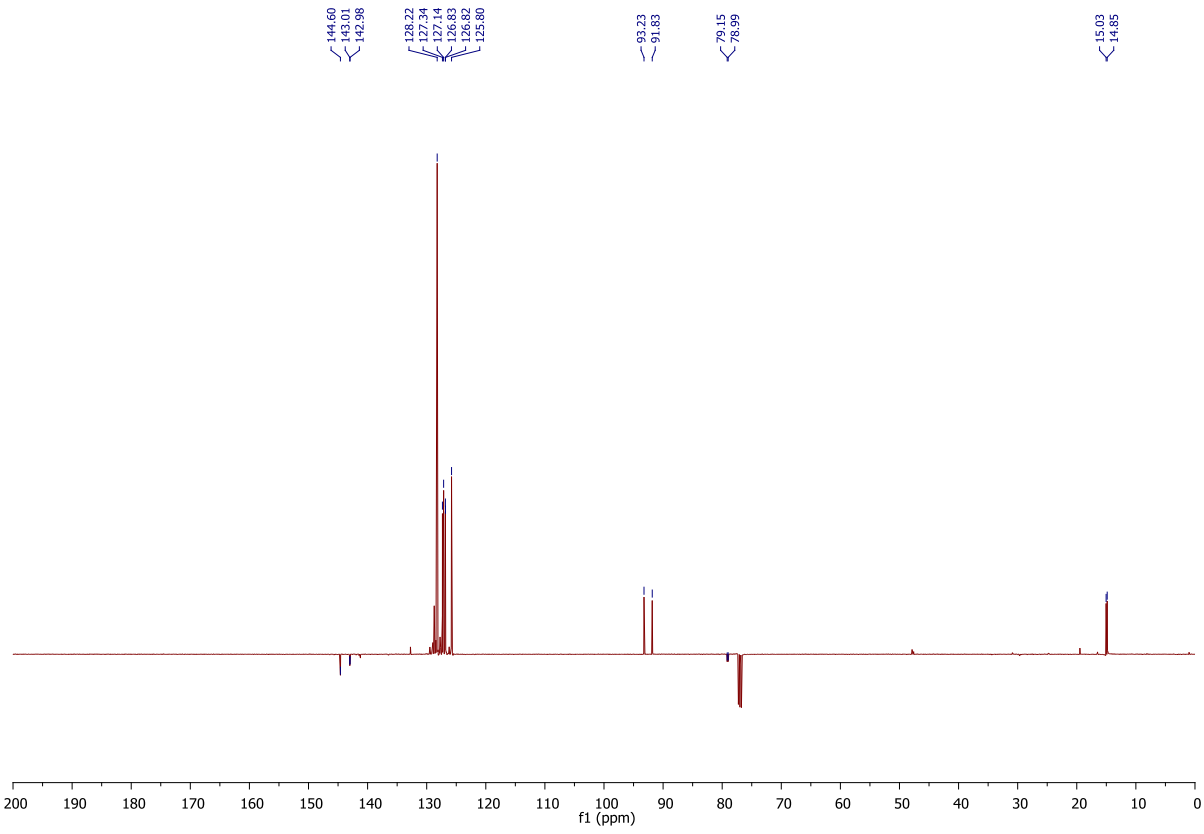

142.44
142.41
128.35
127.75
126.67
126.66
88.58
86.19
77.98
77.73
77.00
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

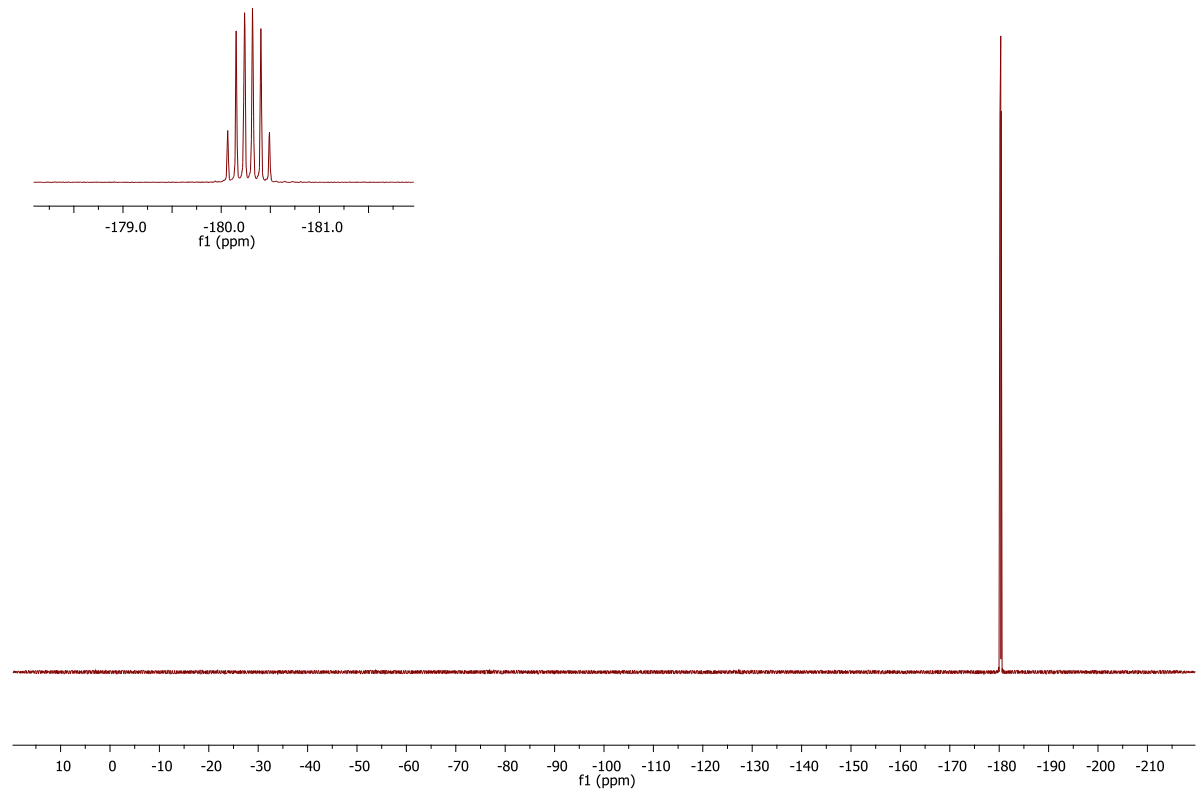

10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


HO
F

3b


2.314
8.733
1.000
0.978
3.638
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)


144.60
143.01
142.98
128.22
127.34
127.14
126.83
126.82
125.80
93.23
91.83
79.15
78.99
15.03
14.85
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-179.0
-180.0
-181.0
f1 (ppm)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)