Electronic Supplementary Material (ESI) for Chemical Communications.

Fluorine containing cyclopropanes: Synthesis of aryl substituted all-cis 1,2,3-trifluorocylopropanes, a facially polar motif

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Contents

General information

All chemicals were purchased from Sigma-Aldrich or Fluorochem except the $CHFI_2$ and $CHFBr_2$. which were synthesised as described in the corresponding reference.[1] All the reactions were carried out in oven-dried PTFE flask or normal glassware under the atmosphere of argon, unless stated otherwise.

The progress of reactions was followed by thin-layer chromatography (TLC) using aluminium plates coated with silica gel ($60F_{245}$ Merck). TLC plates were examined under UV light at 254 and 266 nm. Column chromatography was performed on Merck Geduran silica gel (250-400 mesh) under a positive pressure of compressed air eluting with solvents as supplied.

Proton (^1H) and proton-decoupled nuclear magnetic resonance spectra ($^{19}F\{^1H\}$, $^{13}C\{^1H\}$) were recorded on a Bruker AV 300, Bruker AV 400, Bruker AVII 400, Bruker AVIII-HD 500 or Bruker AVIII 500 instrument. Chemical shifts are reported in parts per million (ppm).

Tetramethylsilane (δ = 0 ppm) functioned as an external standard for **^{1}H** and **^{13}C NMR** experiments. $CFCl_3$ was used as an external standard for **^{19}F NMR** experiments. Coupling constants (*J*) are reported in Hz.

High-resolution mass spectrometry was acquired using electrospray ionisation (ESI), on a ThermoFisher Excalibur Orbitrap Spectrometer, operating in positive and negative mode, from solutions of the analyte in methanol or acetonitrile. Mass analyses were done at the University of St Andrews. Additional data was obtained at the EPSRC UK National Mass Spectrometry Facility at Swansea University, UK.

X-ray crystal structures were obtained on a Rigaku XtaLAB P200 diffractometer, using multi-layer mirror monochromated Mo-Kα radiation, at the University of St Andrews by Prof. Alexandra Slawin and Dr David Cordes. Data was analysed by using CrystalMaker.

The measurement of Log P values is based on the method reported in the reference[2] using a Shimadzu HPLC.

Synthetic procedure, analytical and NMR data

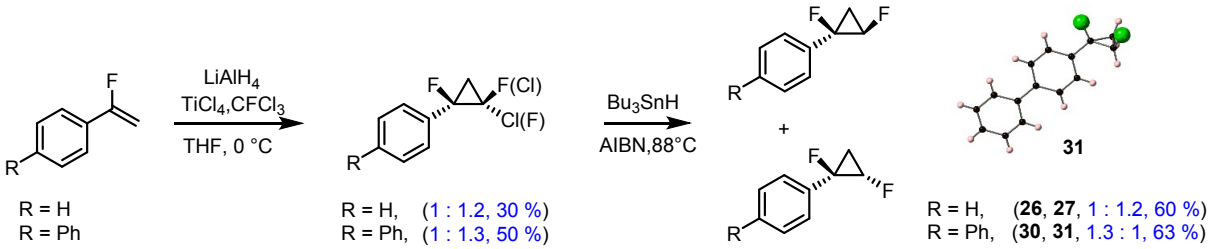
General procedure A for CFBr: or CFI: carbene addition to olefin

To a well-stirred mixture of alkene, $CHBr_2F$ (2 equiv.) or CHI_2F (2 equiv.), TEBAB (0.1 equiv.) and CH_2Cl_2 (0.25 mL per 1 mmol of alkene), a 50 percent solution of NaOH (4 equiv.) was added dropwise at 0 ^oC. The reaction mixture was then stirred further at RT for overnight, while the reaction progress was controlled by TLC. Then it was diluted with water and extracted with CH_2Cl_2. The organic mixture was dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure (500 mbar) at room temperature. The residue was purified by silica gel chromatography (pentane) to give the desired product.

General procedure B for reduction of Halofluorocyclopropanes

Tri-n-butyltin hydride (1.2 equiv) and AIBN (0.1 equiv) were added to the Halofluorocyclopropane (1 equiv). The reaction was reacted at 88 °C for chlorofluorocyclopropane or at RT for bromofluorocyclopropane and iodofluorocyclopropane for overnight. After reaction, the mixture was poured into the potassium fluoride aqueous solution and extracted with pentane (25 mL x 3). The combined organic extracts were dried over sodium sulphate, filtered, and concentrated under reduced pressure (500 mbar) at room temperature. The residue was purified by silica gel chromatography (pentane) to give the desired product.

General procedure C for synthesis of compounds 26, 27 and their derivatives



R = H
R = Ph

R = H, (1 : 1.2, 30 %)
R = Ph, (1 : 1.3, 50 %)

R = H, (**26**, **27**, 1 : 1.2, 60 %)
R = Ph, (**30**, **31**, 1.3 : 1, 63 %)

Titanium tetrachloride (3 equiv) was slowly added to anhydrous THF solution at 0 ℃ under nitrogen atmosphere. The addition was exothermic and the white vapour was produced along with a yellow precipitate. Lithium aluminium hydride (3 equiv) in 50 mL anhydrous THF was carefully added to the mixture to remain temperature below 10 ℃. The reaction was exothermic and gas was evolved. Upon addition, a brown colour was produced and disappeared again, the reaction mixture became green and finally dark brown. Then the mixture was allowed to stir as it slowly warmed to 20 °C over a period of 30 min. The flask was cooled again in an ice bath. When the temperature had fallen to 0 °C, fluorinated olefin (1 equiv) was added. Then, a solution of fluorotrichloromethane (3 equiv) in 10 mL of dry THF was added slowly so that the temperature remained at or below 0 °C. The mixture was allowed to stir at 0 °C for 1h. After reaction, the cold mixture was carefully poured into 100 mL of 10% aqueous hydrochloric acid, containing some ice, in a 600-mL beaker. Rapid stirring was maintained during this hydrolysis. The brown aqueous mixture was extracted with pentane (50 mL x 3), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure (500 mbar) at room temperature. The residue was purified by silica gel chromatography (pentane) to give the chlorofluorocyclopropanes as the mixture. Then following the general procedure **B** to generate the desired products.

(1-azidovinyl)benzene 10

^{1}H NMR (500 MHz, $CDCl_3$) δ_H 4.96 (d, *J* = 2.0 Hz, 1H), 5.43 (d, *J* = 2.0 Hz, 1H), 7.35-7.37 (m, 3H), 7.55-7.57 (m, 2H). Data agreement with the literature.[3]

4-(1-azidovinyl)-1,1'-biphenyl 11

^{1}H NMR (500 MHz, $CDCl_3$) δ_H 5.00 (d, *J* = 2.0 Hz, 1H), 5.51 (d, *J* = 2.0 Hz, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 2H), 7.58-7.63 (m, 4H), 7.65-7.68 (m, 2H); Data agreement with the literature.[3]

2-fluoroacetophenone 12

^{1}H NMR (400 MHz, $CDCl_3$):δ_H 7.89–7.87 (m, 2H), 7.62–7.59 (m, 1H), 7.50–7.46 (m, 2H), 5.51 (d, *J* = 47.0 Hz, 2H); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ−230.8 (s, 1F); Data agreement with the literature.[4]

1-(Biphenyl-4-yl)-2-fluoroethanone 13

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.98 (d, *J* = 8.1 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.63 (d, *J* = 7.4 Hz, 2H), 7.49 (t, *J* = 7.3 Hz, 2H), 7.46 – 7.39 (m, 1H), 5.56 (d, *J* = 46.9 Hz, 2H). **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ -230.33 (s, 1F). Data agreement with the literature.[4]

1-phenyl-1,1,2-trifluoroethane 14

^{1}H NMR (400 MHz, $CDCl_3$) δ_H 4.63 (dt, 2 H, $^2J_{HF}$ = 46.2 Hz, $^3J_{HF}$ = 12.0 Hz), 7.44-7.54 (m, 5 H, arom.); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ_F -107.9 (d, 2 F, *J* = 18 Hz), -231.7 (t, 1 F, *J* = 18 Hz). Data agreement with the literature.[5]

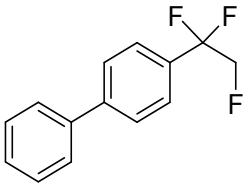
***cis*-α,β-Difluorstyrene 16**

^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.95(dd, 1 H, $^2J_{HF}$ = 71 Hz, $^3J_{HF}$ = 17.0 Hz), 7.36-7.41 (m, 5 H, arom.); **^{19}F {^{1}H} NMR** (282 MHz, $CDCl_3$) δ_F -142.1 (d, 1 F, $^3J_{FF}$ = 11 Hz), -164.4 (d, 1 F, *J* = 11 Hz); **^{19}F NMR** (282 MHz, $CDCl_3$) δ_F -142.1(dd, 1 F, $^3J_{HF}$ = 17.0 Hz, $^3J_{FF}$ = 11 Hz, PhCF), -164.4 (dd, 1 F, $^2J_{HF}$ = 71 Hz, $^3J_{FF}$ = 11 Hz, CHF). Data agreement with the literature.[5]

(2,2-Difluorocyclopropyl)benzene 28

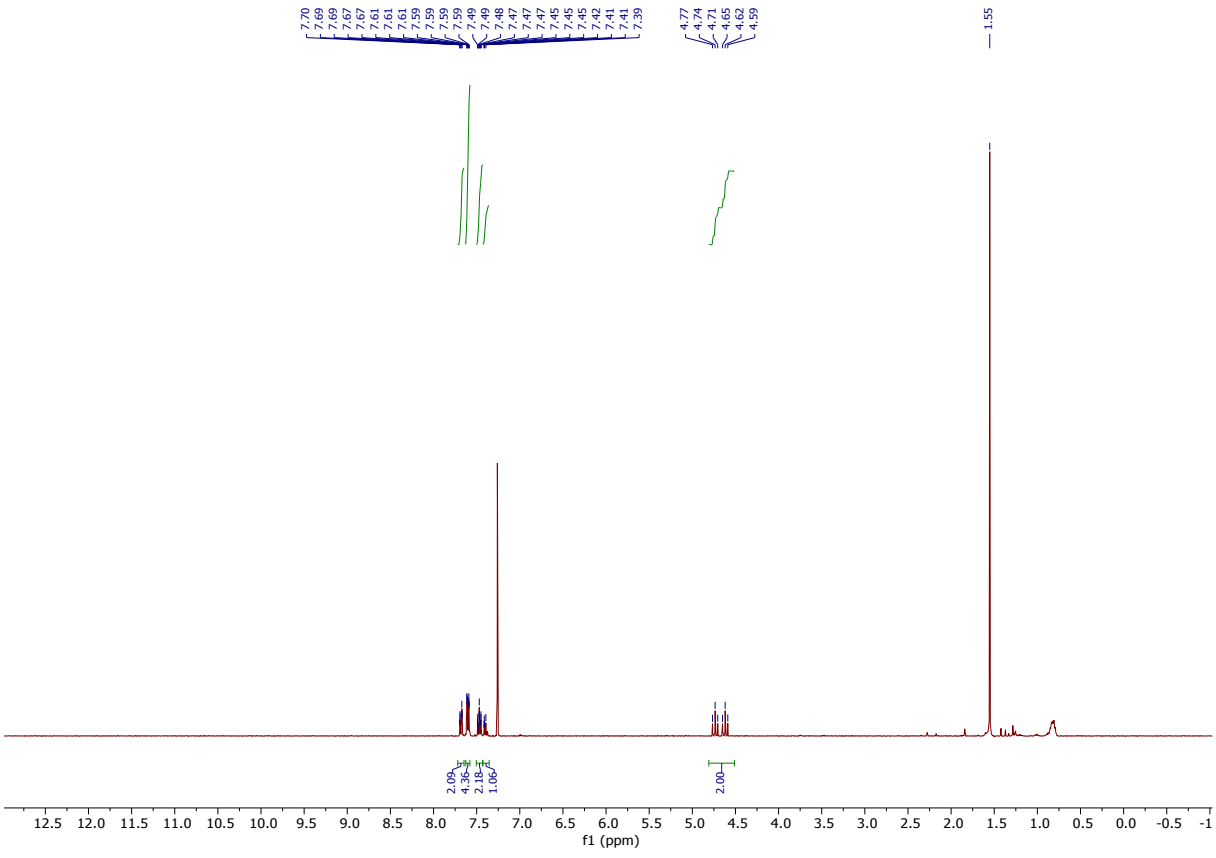
^{1}H NMR (400 MHz, $CDCl_3$) δ_H 7.46–7.18 (m, 5H), 2.87–2.65 (m, 1H), 1.92–1.71 (m, 1H), 1.70–1.54 (m, 1H). **^{19}F NMR** (376 MHz, $CDCl_3$): δ_F 124.5–125.5 (m, 1F), 141.1–142.1 (m, 1F). Data agreement with the literature.[6]

4-(1,1,2-trifluoroethyl)-1,1'-biphenyl 15

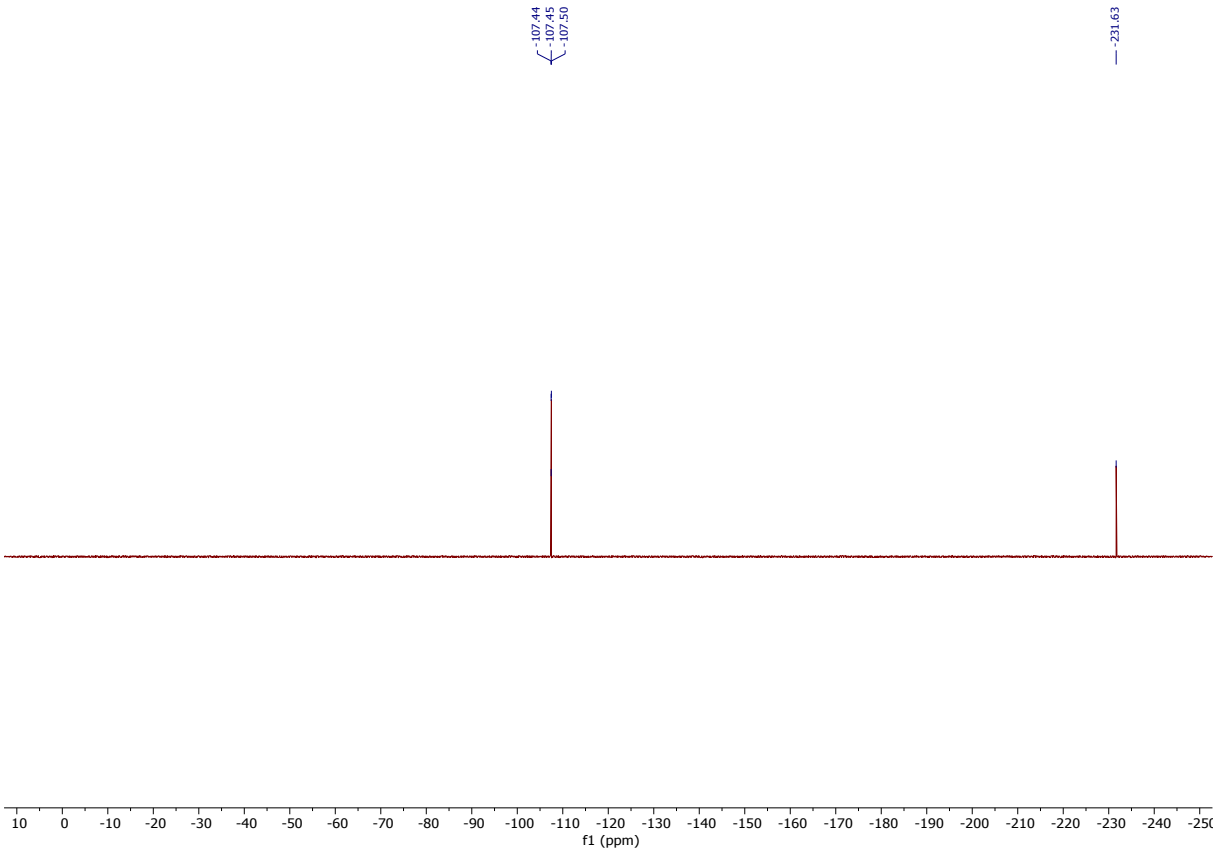


Mp. = 62 °C ; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 4.67 (dt, 2 H, $^{2}J_{HF}$ = 46.5 Hz, $^{3}J_{HF}$ = 12.2 Hz), 7.39 (m, 1 H, arom.), 7.46 (m, 2 H, arom.), 7.60 (m, 4 H, arom.), 7.69 (d, 2 H, *J* = 8.2 Hz, arom.); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ_F -107.5 (d, 2 F, *J* = 18 Hz), -231.6 (t, 1 F, *J* = 18 Hz); **^{19}F NMR** (376 MHz, $CDCl_3$) δ_F -107.5 (dt, 2 F, *J* = 18, 12 Hz), -231.6 (m, 1 F); **^{13}C NMR** (125 MHz, $CDCl_3$) δc 82.6 (dt, J_{CF} = 186 Hz, $^{2}J_{CF}$ = 36 Hz, CHF), 118.6 (m, CF_2), 126.0 (t, *J* = 6.3 Hz), 127.2, 127.4, 127.9, 128.9, 131.9 (t, *J* = 25 Hz), 140, 143.7; **HRMS** (ASAP^{+}) m/z calcd for $C_{14}H_{11}F_3$ [M] 236.0813, found 236.0816, calcd $C_{14}H_{12}F_3$ [M+H] 237.0847, found 237.0849.

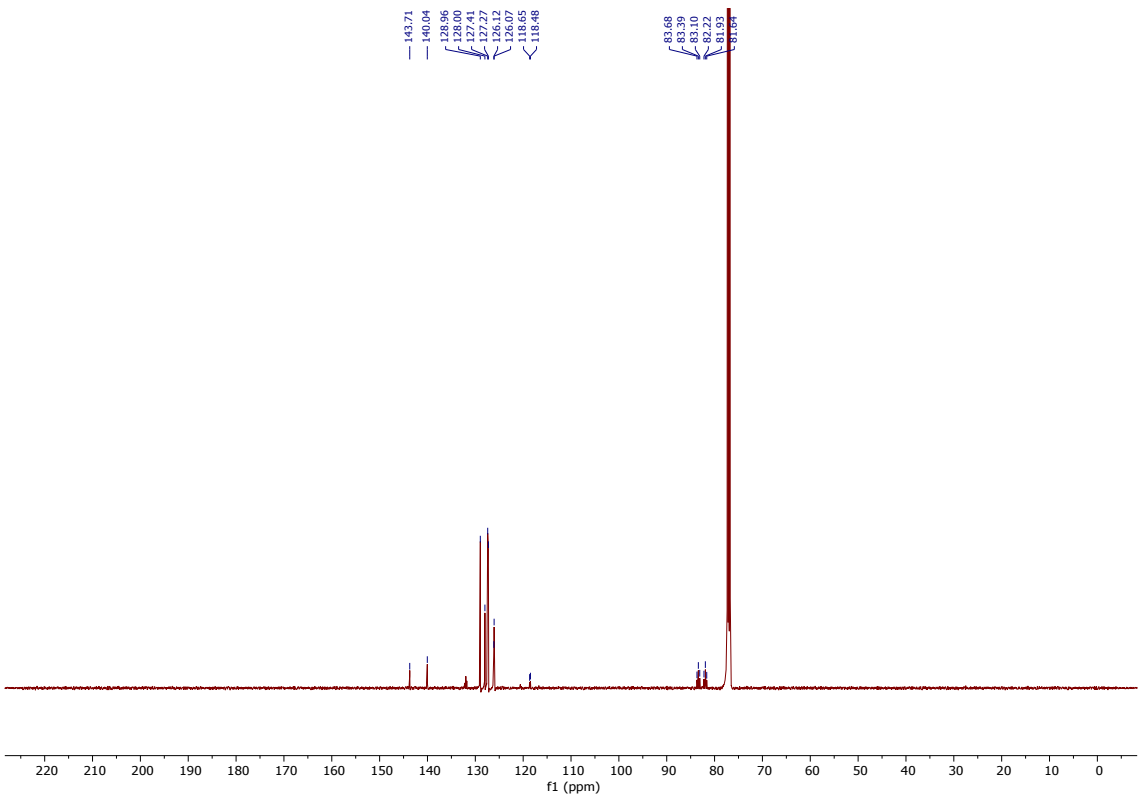
^{1}H NMR



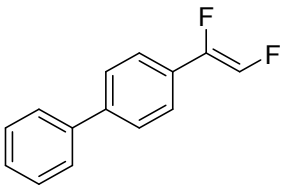
^{19}F {^{1}H} NMR



^{13}C NMR

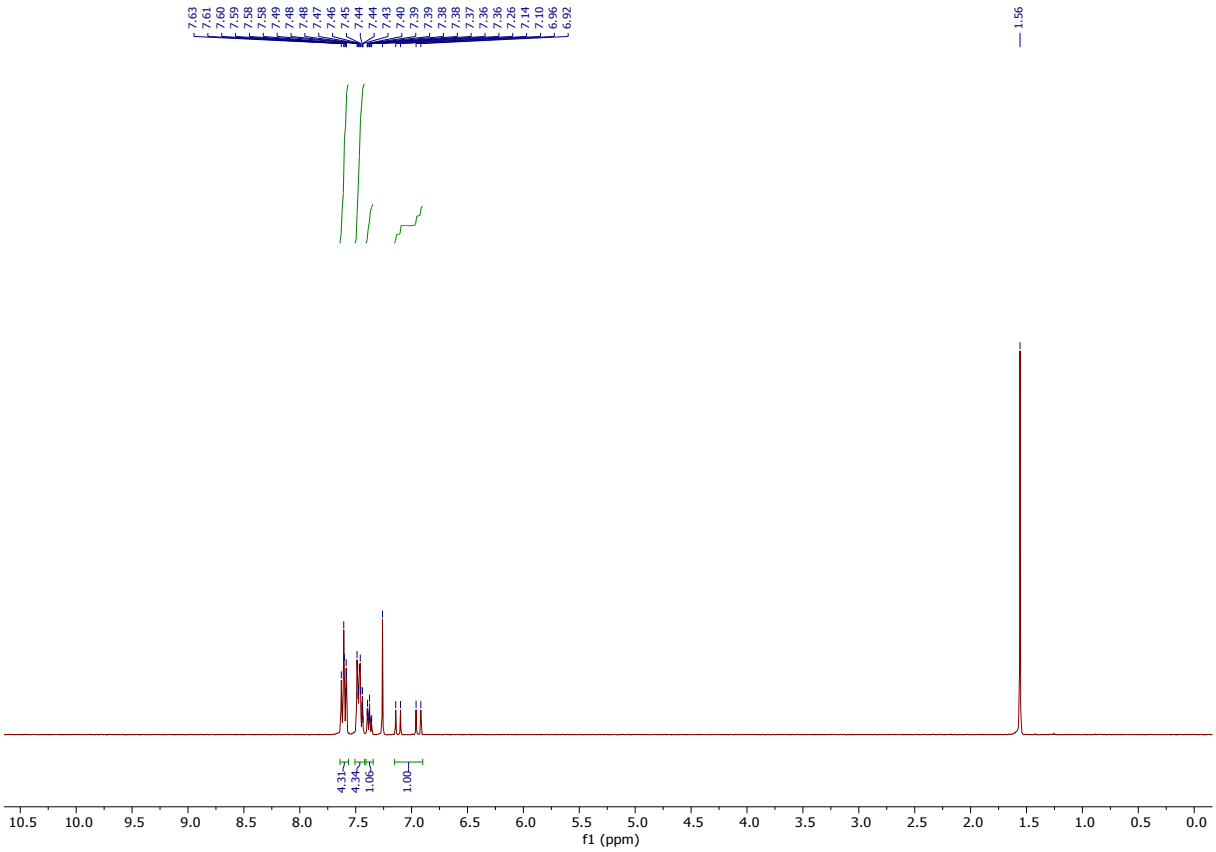


(Z)-4-(1,2-difluorovinyl)-1,1'-biphenyl 17



Mp. = 102 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.03 (dd, 1 H, $^{2}J_{HF}$ = 72 Hz, $^{3}J_{HF}$ = 17 Hz), 7.37 (m, 1 H, arom.), 7.46 (m, 4 H, arom.), 7.60 (m, 4 H, arom.); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ_F -142.1 (d, 1 F, $^{3}J_{FF}$ = 11 Hz, PhCF), -164.4 (d, 1 F, *J* = 11 Hz, CHF); **^{19}F NMR** (376 MHz, $CDCl_3$) δ_F -142.1(dd, 1 F, $^{3}J_{HF}$ = 17.0 Hz, $^{3}J_{FF}$ = 11 Hz, PhCF), -164.4 (dd, 1 F, $^{2}J_{HF}$ = 71 Hz, $^{3}J_{FF}$ = 11 Hz, CHF); **^{13}C NMR** (125 MHz, $CDCl_3$) δc 124.1 (t, *J* = 5.5 Hz), 127.0, 127.4, 127.8, 128.9, 134.1 (dd, $^{1}J_{CF}$ = 257 Hz, $^{2}J_{CF}$ = 15.6 Hz, CHF), 140.1, 142.18, 142.20, 148.3 (dd, $^{1}J_{CF}$ = 246 Hz, $^{2}J_{CF}$ = 10 Hz, CF). **HRMS** (ASAP^{+}) m/z calcd for $C_{14}H_{10}F_2$ [M] 216.0751, found 216.0748, calcd $C_{14}H_{11}F_2$ [M+H] 217.0829, found 217.0813.

^{1}H NMR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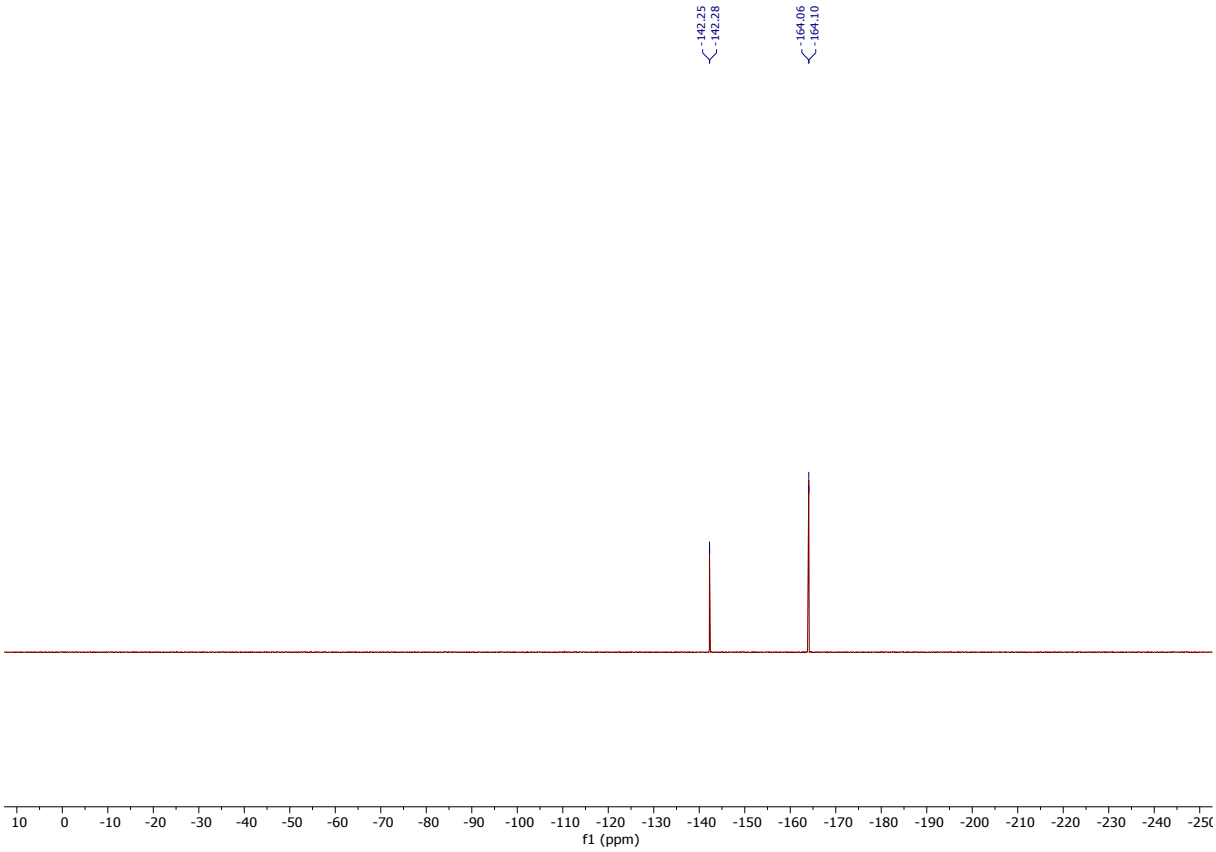
7.14
7.10
6.96
6.92
1.56
4.31
4.34
1.06
1.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^{19}F {^{1}H} NMR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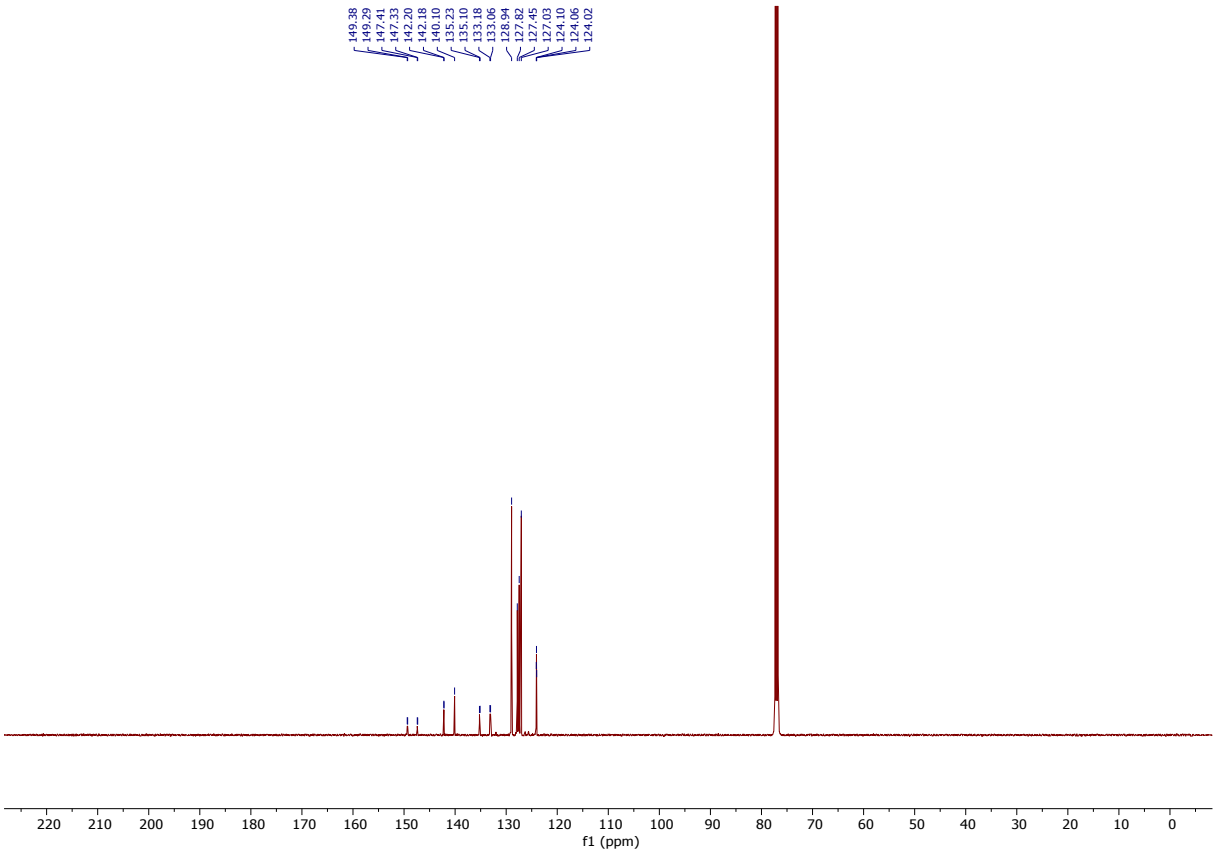
-142.28
-164.06
-164.10
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -250
f1 (ppm)

^{13}C NMR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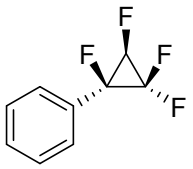
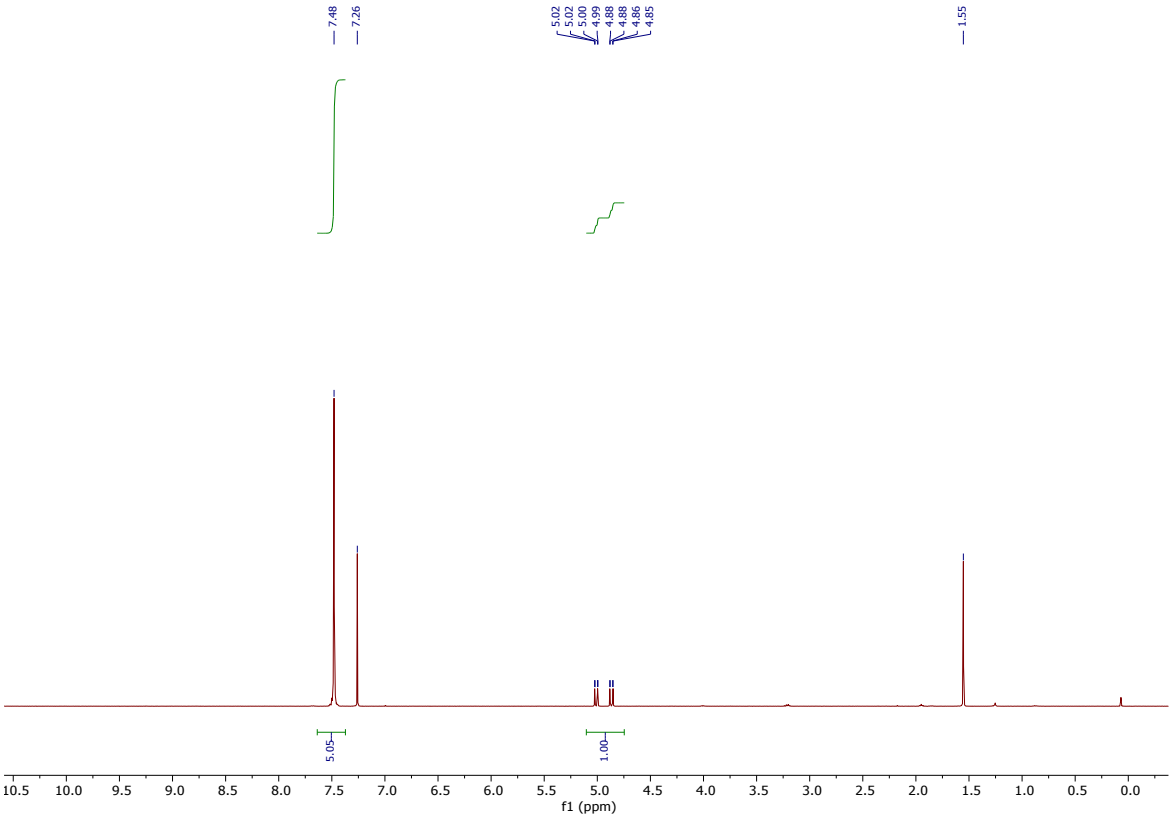
128.94
127.82
127.45
127.03
124.10
124.06
124.02
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

1,2,2,3-tetrafluorocyclopropylbenzene 18

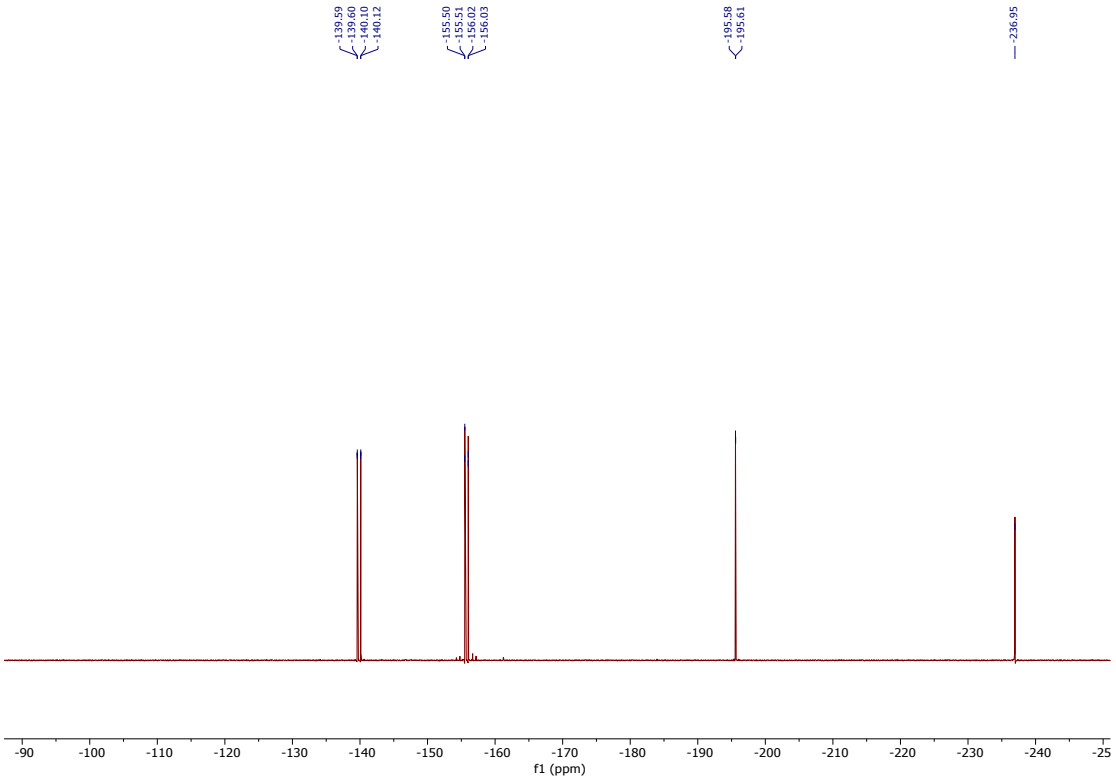


To a solution of *cis*-α,β-Difluorstyrene **16** (40 mg, 0.28 mmol, 1 equiv) and $TMSCF_3$ (101.4 mg, 0.71 mmol, 2.5 equiv) in anhydrous THF, NaI (106 mg, 0.71 mmol, 2.5 equiv) was added. The resulting suspension was stirred at 75 ^oC for 20 h under N_2 atmosphere. After completion, the reaction mixture was allowed to cool to RT and solvent was removed *in vacuo*. The crude residue was diluted with pentane (50 mL) and washed with distilled water (50 mL). The phases were separated and the aqueous layer was extracted with pentane (2 x 50 mL). The combined organic phases were washed sequentially with saturated aqueous solutions of Na_2SO_3 and $NaHCO_3$, followed by drying over Na_2SO_4, filtration and concentrated under reduced pressure (500 mbar). Purification by flash column chromatography (pentane) gave the desired product as the white oil (21.4 mg, 40 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.48 (s, 5 H, arom), 4.94 (ddd, J = 57.0, 11.0, 1.3 Hz, 1 H), **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ_F -139.9 (dd, 1 F, *J* = 193.1, 6.9 Hz, CF_2), -155.7 (dd, 1 F, *J* = 193.1, 3.6 Hz, CF_2), -195.6 (d, 1 F, J = 10.2 Hz, PhCF), -236.9 (ddd, 1 F, *J* = 10.5, 6.8, 3.3 Hz, CHF), **^{19}F NMR** (376 MHz, $CDCl_3$), -139.9 (ddd, 1 F, *J* = 193.1, 11.0, 6.9 Hz, CF_2), -155.7 (ddd, 1 F, *J* = 193.1, 3.2, 1.3 Hz, CF_2), -195.6 (d, 1 F, J = 10.2 Hz, PhCF), -236.9 (m, 1 F, CHF). **^{13}C NMR** (125 MHz, $CDCl_3$) δc 130.7 (d, *J* = 3.0 Hz), 129.1, 128.16, 128.13, 103.9 (m), 76.9 (m), 71.3 (m); **HRMS** ($ASAP^+$) m/z calcd for $C_9H_6F_4$ 190.0400, found 190.0398.

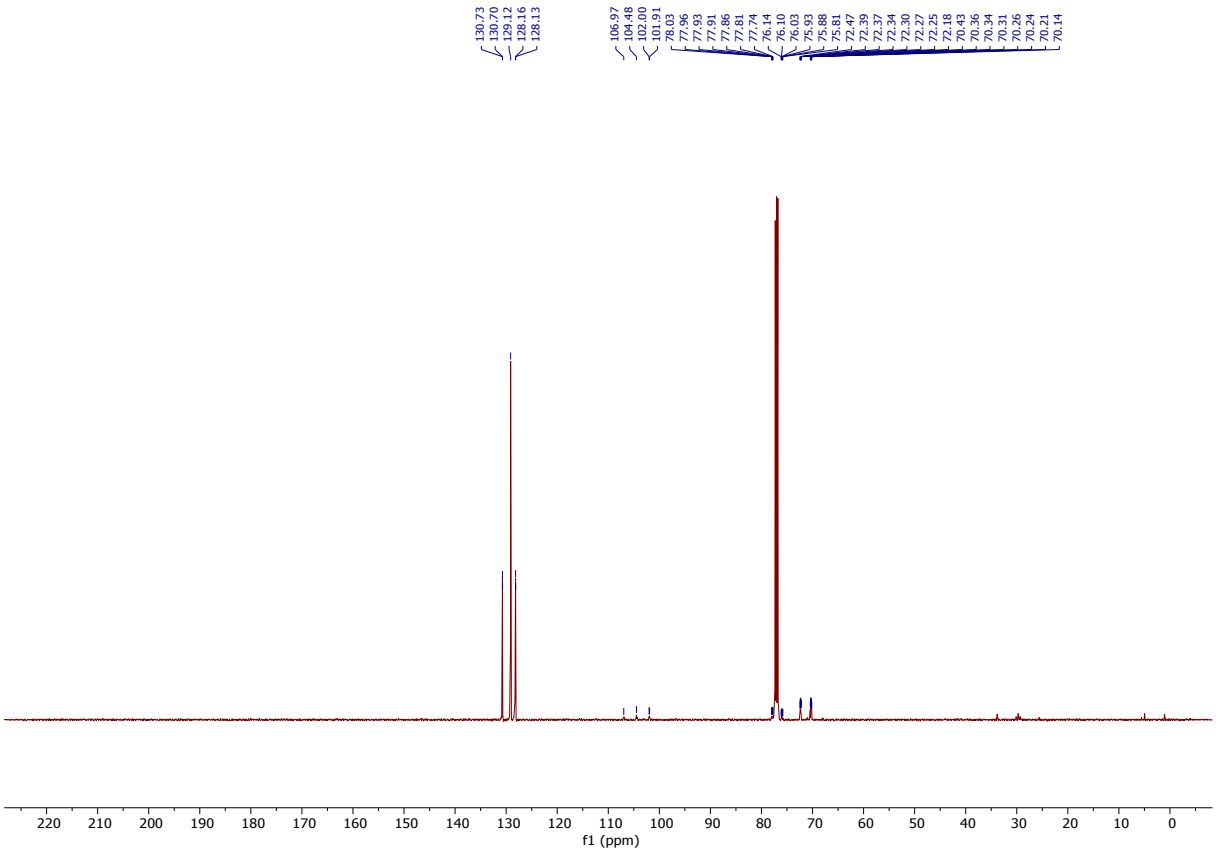
^{1}H NMR



^{19}F {^{1}H} NMR



^{13}C NMR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75.88
75.81
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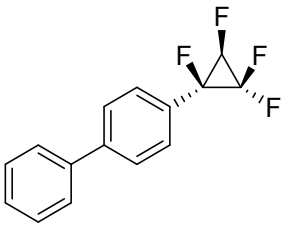
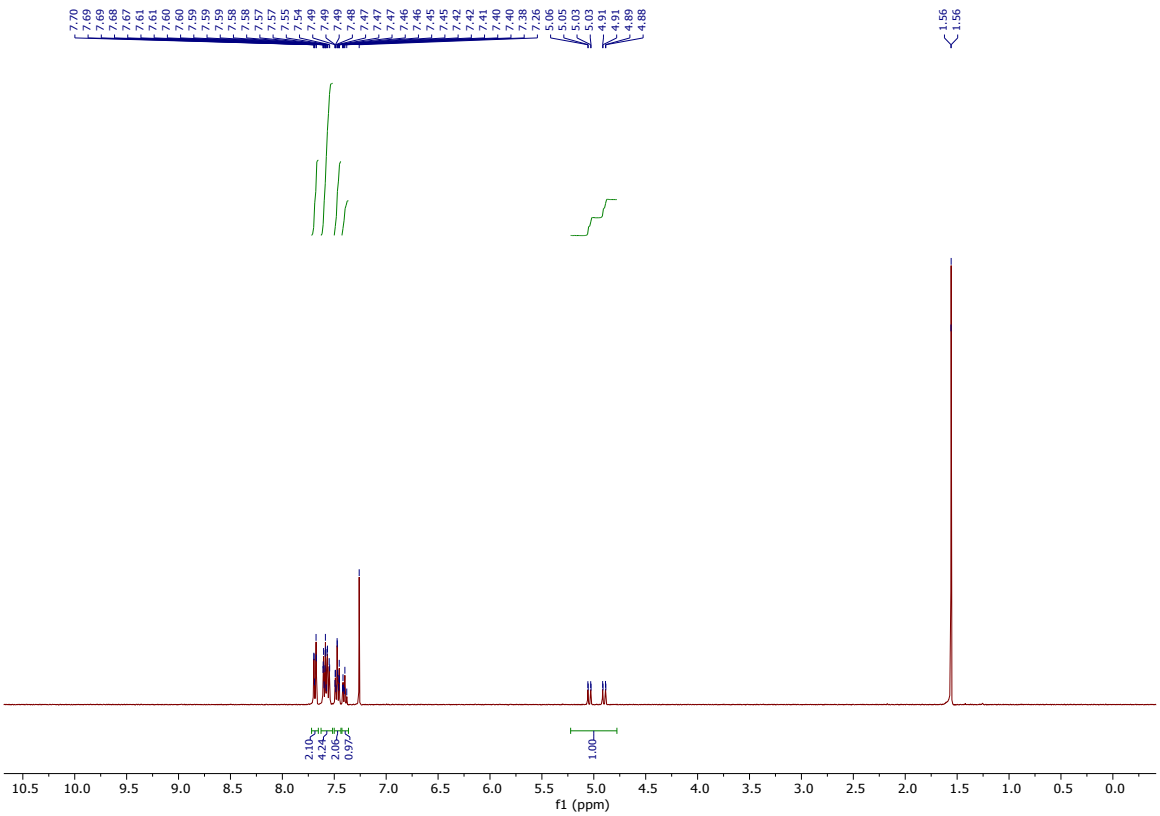
70.43
70.36
70.34
70.31
70.26
70.24
70.21
70.14
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

4-(1,2,2,3-tetrafluorocyclopropyl)-1,1'-biphenyl 19

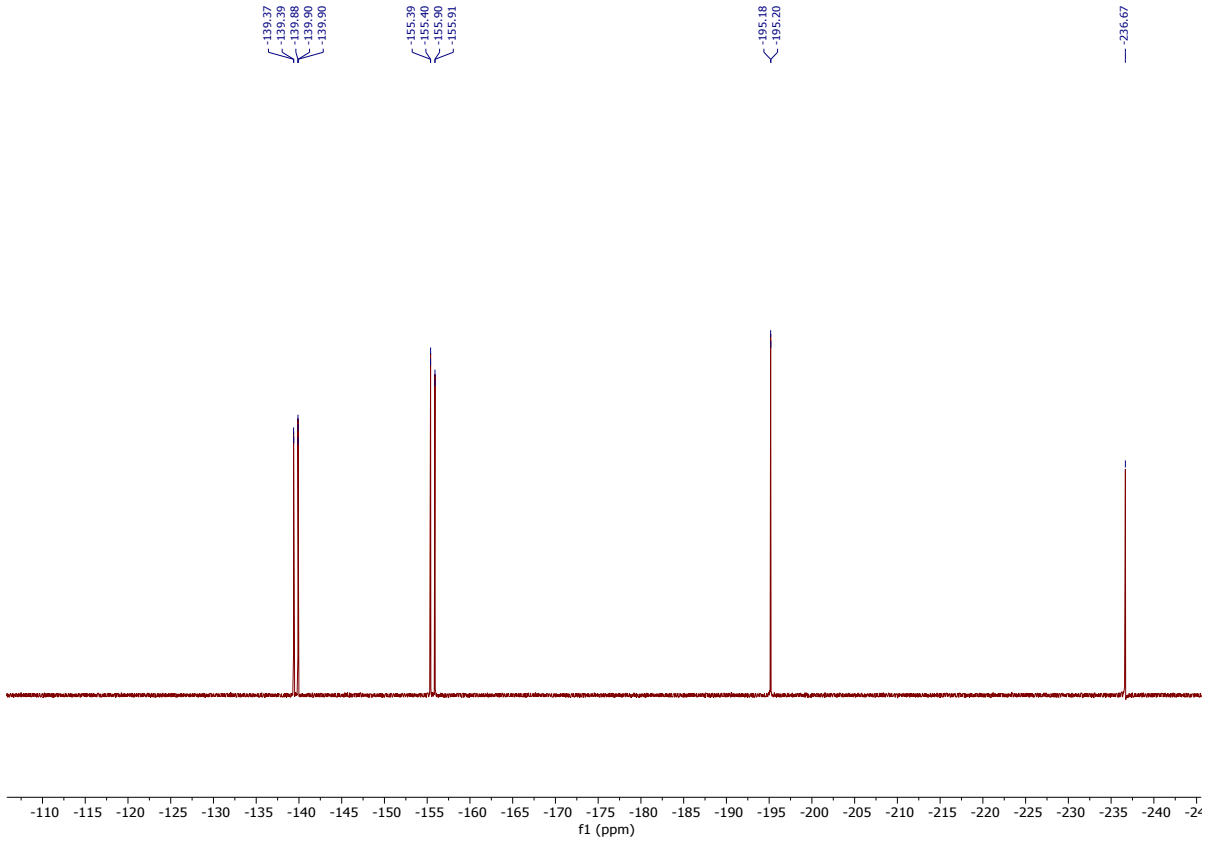


To a solution of compound **17** (90 mg, 0.42 mmol, 1 equiv) and $TMSCF_3$ (147.49 mg, 1.04 mmol, 2.5 equiv) in anhydrous THF, NaI (155 mg, 1.04 mmol, 2.5 equiv) was added. The resulting suspension was stirred at 75 °C for 20 h under N_2 atmosphere. After completion, the reaction mixture was allowed to cool to RT and solvent was removed *in vacuo*. The crude residue was diluted with diethyl ether (50 mL) and washed with distilled water (50 mL). The phases were separated and the aqueous layer was extracted with diethyl ether (2 x 50 mL). The combined organic phases were washed sequentially with saturated aqueous solutions of Na_2SO_3 and $NaHCO_3$, followed by drying over Na_2SO_4, filtration and concentrated under reduced pressure. Purification by flash column chromatography (pentane) gave the desired product as a colourless solid (53.6 mg, 48.1 %). **Mp**. = 102-103°C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.74-7.66 (m, 2 H, arom), 7.57 (m, 4 H, arom), 7.52-7.44 (m, 2 H, arom), 7.43-7.39 (m, 1 H, arom), 4.97 (ddd, *J* = 57.1, 10.9, 1.3 Hz, 1 H). **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ_F -139.6 (dd, 1 F, *J* = 193.1, 6.9 Hz, CF_2), -155.7 (dd, 1 F, *J* = 193.1, 3.3 Hz, CF_2), -195.2 (d, 1 F, J = 9.6 Hz, PhCF), -236.9 (ddd, 1 F, *J* = 9.9, 6.9, 3.1 Hz, CHF), **^{19}F NMR** (376 MHz, $CDCl_3$), -139.6 (ddd, 1 F, *J* = 193.1, 10.8, 6.9 Hz, CF_2), -155.7 (dd, 1 F, *J* = 193.1, 3.4 Hz, CF_2), -195.6 (d, 1 F, J = 10.0 Hz, PhCF), -236.9 (m, 1 F, CHF); **^{13}C NMR** (125 MHz, $CDCl_3$) δc 143.7(2 x C), 139.8, 129, 128.7 (d, *J* = 3.7 Hz), 128.1, 127.8, 127.2, 104.5 (m), 76.9 (m), 71.3 (m); **HRMS** ($ASAP^+$) m/z calcd for $C_{15}H_{10}F_4$ 260.0719, found 260.0719.

^{1}H NMR



^{19}F {^{1}H} NMR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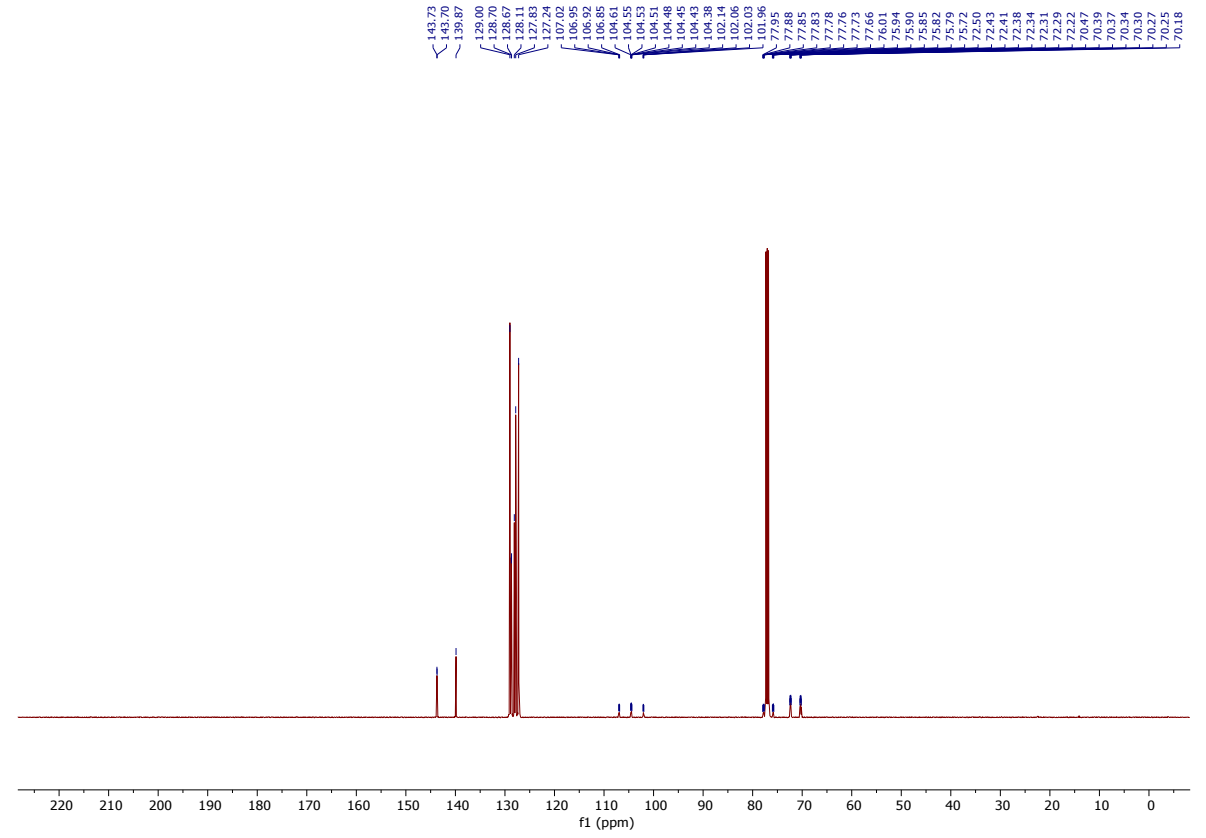
-236.67
f1 (ppm)

^{13}C NMR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77.95
77.88
77.85
77.83
77.78
77.76
77.73
77.66
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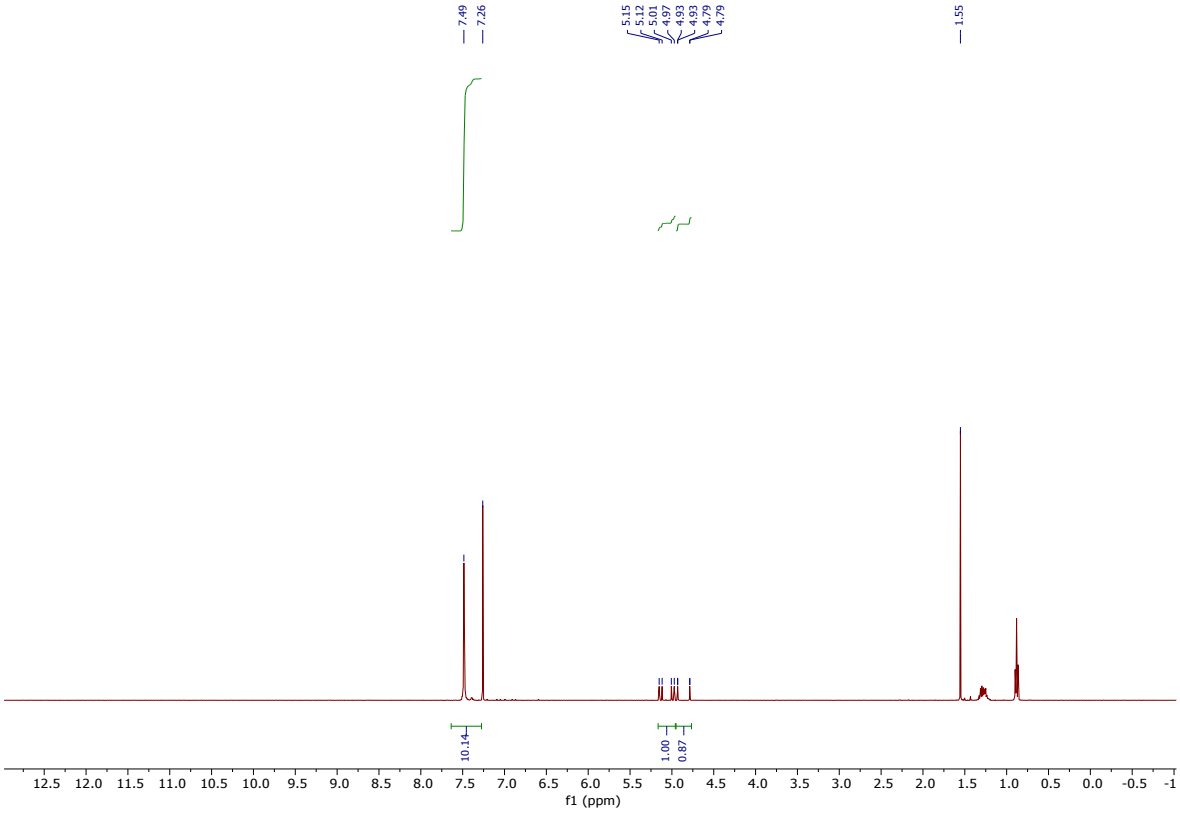
75.85
75.82
75.79
75.72
72.50
72.43
72.41
72.38
72.34
72.31
72.29
72.22
70.47
70.39
70.37
70.34
70.30
70.27
70.25
70.18
f1 (ppm)

(2-chloro-1,2,3-trifluorocyclopropyl)benzene 20a and 20b

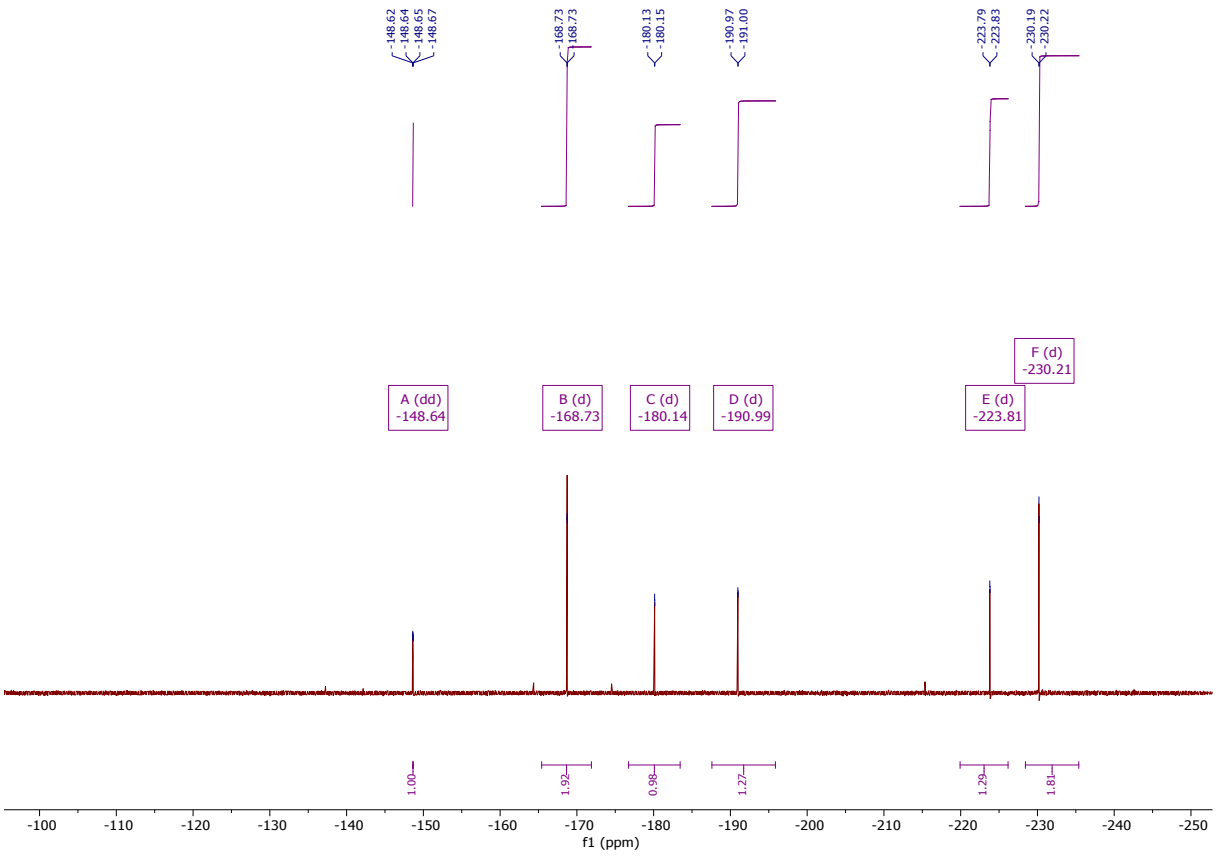
Following the procedure **C**. Titanium tetrachloride (1.22 g, 6.42 mmol,3 equiv) was slowly added to anhydrous THF solution at 0 ℃ under nitrogen atmosphere. The addition was exothermic and the white vapour was produced along with a yellow precipitate. Lithium aluminium hydride (244 mg, 6.42 mmol,3 equiv) in 50 mL anhydrous THF was carefully added to the mixture to remain temperature below 10 ℃. The reaction was exothermic and gas was evolved. Upon addition, a brown colour was produced and disappeared again, the reaction mixture became green and finally dark brown. Then the mixture was allowed to stir as it slowly warmed to 20 °C over a period of 30 min. The flask was cooled again in an ice bath. When the temperature had fallen to 0 °C, *cis*-α,β-Difluorstyrene **16** (300mg, 2.14 mmol, 1 equiv) was added. Then, a solution of fluorotrichloromethane (880 mg, 6.42 mmol, 3 equiv) in 10 mL of dry THF was added slowly so that the temperature remained at or below 0 °C. The mixture was allowed to stir at 0 °C for 1h. After reaction, the cold mixture was carefully poured

into 100 mL of 10% aqueous hydrochloric acid, containing some ice, in a 600-mL beaker. Rapid stirring was maintained during this hydrolysis. The brown aqueous mixture was extracted with pentane (50 mL x 3), dried over anhydrous sodium sulfate, filtered, and concentrated under reduced pressure (500 mbar) at room temperature. Purification by flash column chromatography (pentane) gave the desired products as a mixture (Rf = 0.3 in PE, liquid, 110 mg, 25 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 4.86 (1 H, d, $^{2}J_{CF}$ = 57.9 Hz, CHF,), 5.06 (1H, dd, *J* = 57.9, 14.2 Hz CHF), 7.49 (10 H, m, arom., *20a* and *20b*); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ_F -148.6(dd, J = 13.7, 7.1 Hz), -168.7(d, *J* = 2.6 Hz), -180 (d, *J* = 7.3 Hz), -190.9 (d, *J* = 9.3 Hz), -223.8 (d, *J* = 13.7 Hz), -230.21 (d, *J* = 9.3 Hz). **HRMS** (GC-EI-MS) m/z calcd for $C_9H_6{}^{35}ClF_3$ 206.0110, found 206.0118.

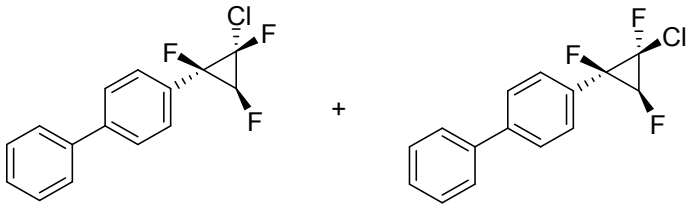
^{1}H NMR



^{19}F {^{1}H} NMR

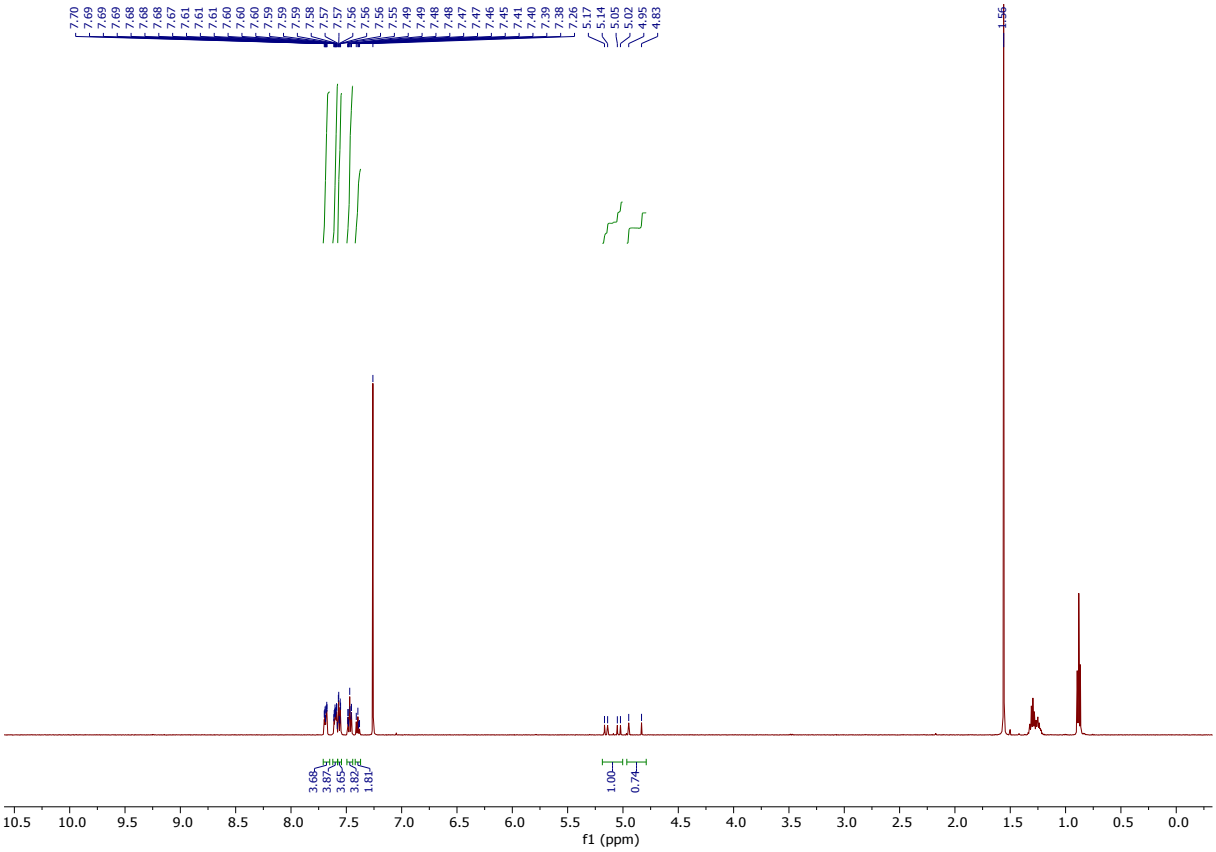


4-(2-chloro-1,2,3-trifluorocyclopropyl)-1,1'-biphenyl 21a and 21b

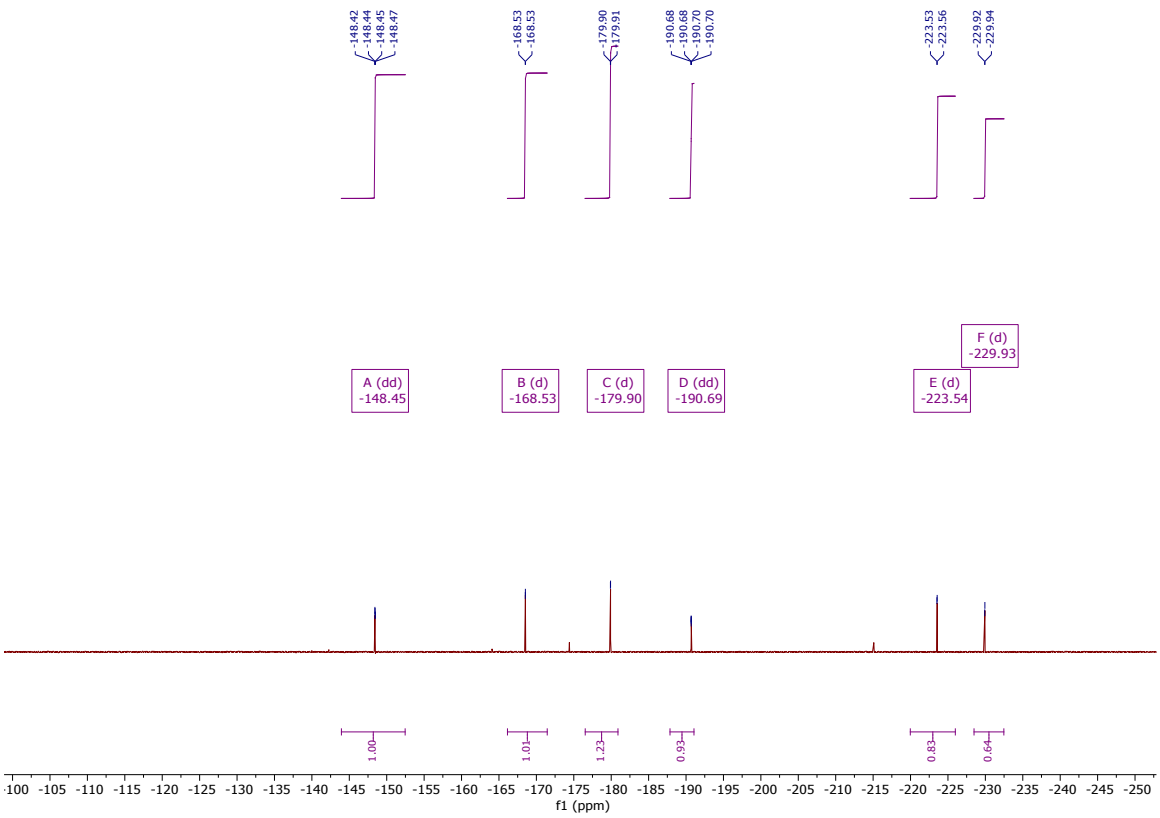


Following the general procedure **C**. The residue was purified by silica gel chromatography (pentane) to give the desired products as a mixture (Rf = 0.3 in PE, solid, 23.5 mg, 30 %). **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 4.89 (1 H, d, $^{2}J_{HF}$ = 57.9 Hz, CHF), 5.06 (1H, dd, *J* = 58.1, 14.1 Hz CHF), 7.40 (2H, m, arom.), 7.45-7.52 (4H, m, arom.), 7.54-7.73 (8H, m, arom.), 7.66-7.71 (4H, m, arom.); **^{19}F {^{1}H} NMR** (470 MHz, $CDCl_3$) δ_F -148.5(dd, J = 13.4, 7.6 Hz), -168.5(d, *J* = 2.9 Hz), -179.9 (d, *J* = 7.6 Hz), -190.7 (dd, *J* = 8.9, 2.5 Hz), -223.5 (d, *J* = 14.3 Hz), -229.9 (d, *J* = 9.3 Hz).

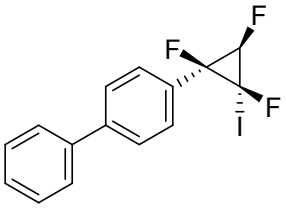
^{1}H NMR


7.70 7.69 7.69 7.69 7.68 7.68 7.68 7.67 7.61 7.61 7.60 7.60 7.60 7.59 7.59 7.59 7.58 7.57 7.57 7.56 7.56 7.56 7.55 7.49 7.49 7.48 7.48 7.47 7.47 7.46 7.45 7.41 7.40 7.39 7.38 7.26 5.17 5.14 5.05 5.02 4.95 4.83
1.56
3.68 3.87 3.65 3.82 1.81
1.00 0.74
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

^{19}F {^{1}H} NMR

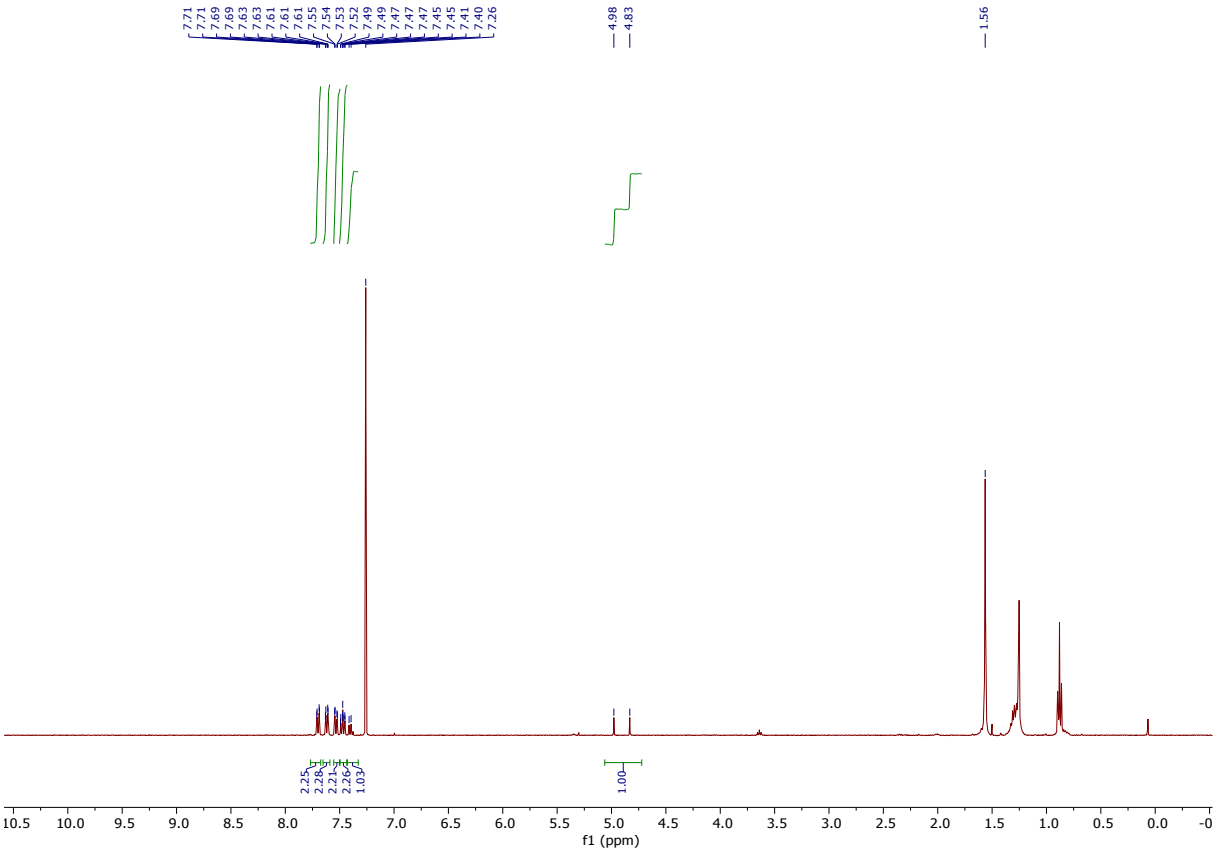


4-((1S,2S,3R)-1,2,3-trifluoro-2-iodocyclopropyl)-1,1'-biphenyl 22a

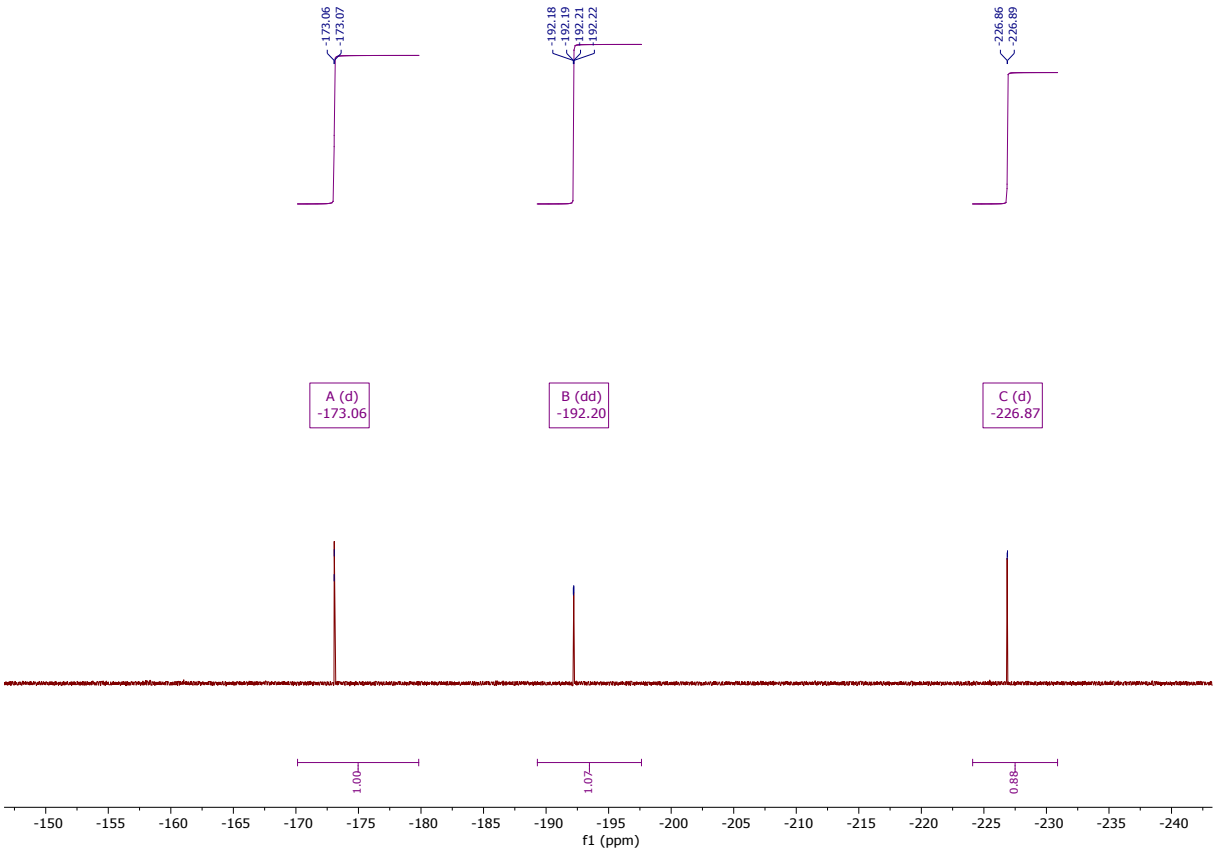


Following the general procedure A. **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.73-7.66 (m,2H), 7.65-7.58 (m, 2H), 7.57-7.50 (m, 2H), 7.47(m, 2H), 7.44-7.35 (m, 1H), 4.91 (d, *J* = 58.7 Hz, 1 H, CHF); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ_F -173.0 (d, *J* = 3.4 Hz), -192.2 (dd, *J* = 10.7, 3.1 Hz), -226.8 (d, *J* = 10.2 Hz). **HRMS** (ASAP^{+}) m/z calcd for [M-F] $C_{15}H_{10}F_3I$ 354,9795, found 354.9793.

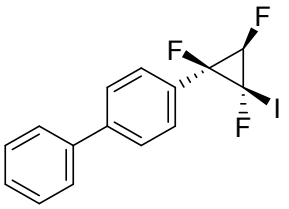
^{1}H NMR



^{19}F {^{1}H} NMR

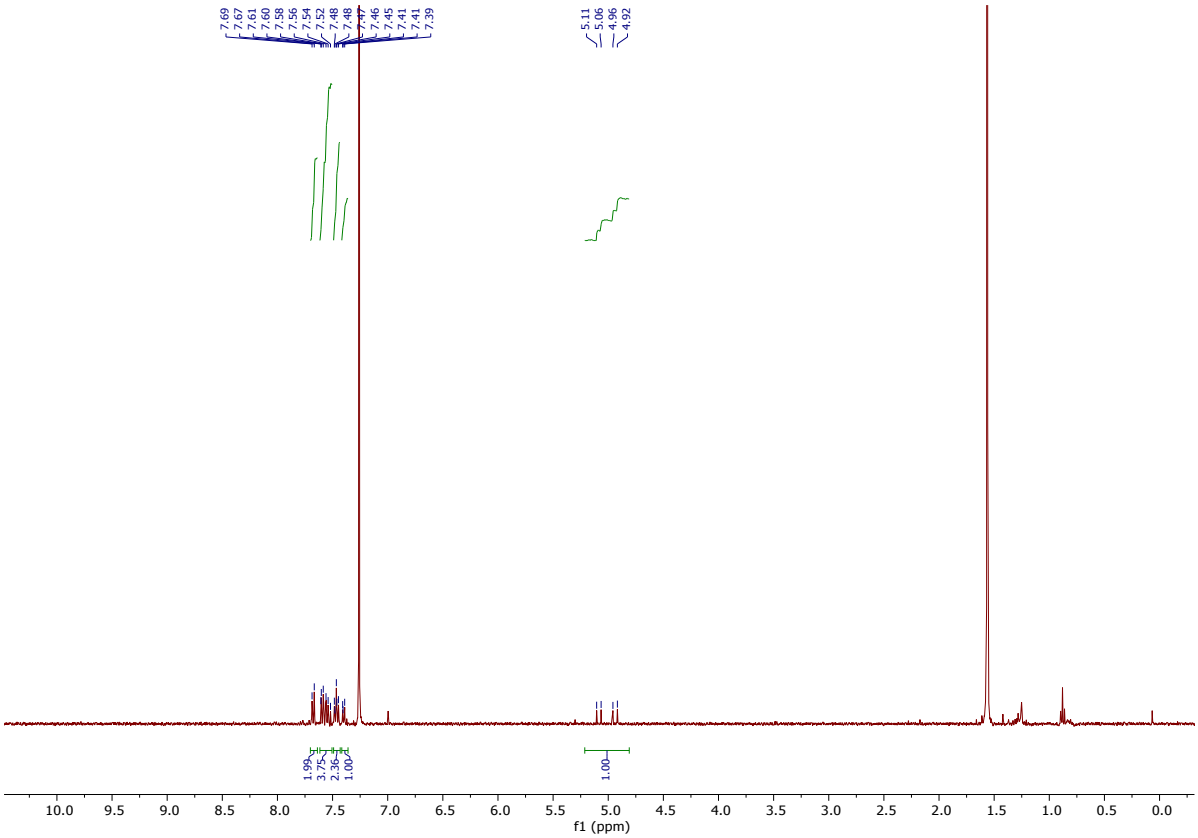

-173.06
-173.07
-192.18
-192.19
-192.21
-192.22
-226.86
-226.89
A (d)
-173.06
B (dd)
-192.20
C (d)
-226.87
1.00
1.07
0.88
-150
-155
-160
-165
-170
-175
-180
-185
-190
-195
-200
-205
-210
-215
-220
-225
-230
-235
-240
f1 (ppm)

4-((1S,2R,3R)-1,2,3-trifluoro-2-iodocyclopropyl)-1,1'-biphenyl 22 b

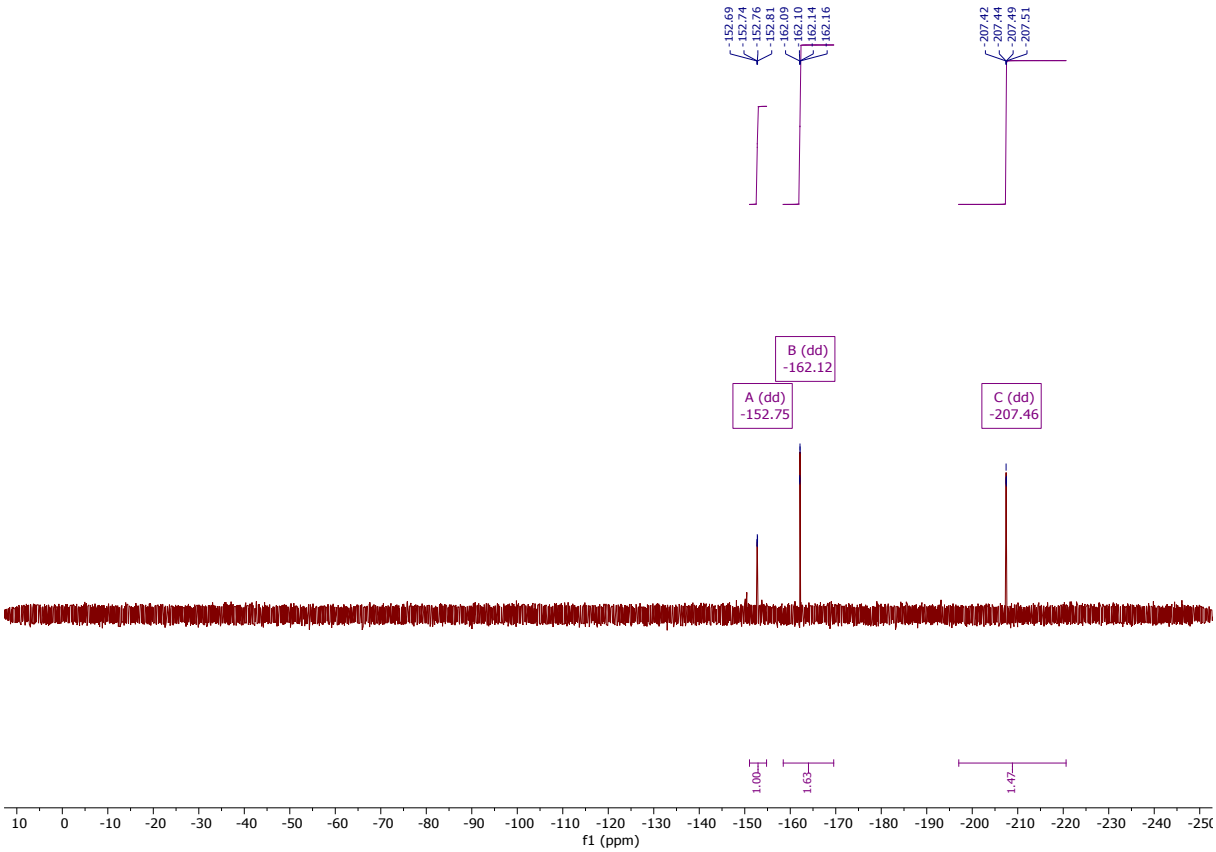


Following the general procedure A. **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.68 (d, *J* = 8.1 Hz), 7.62-7.51 (m, 4H), 7.49-7.44 (m, 2H), 7.42-7.36 (m, 1H), 5.01 (1 H, dd, *J* = 59.1, 16.2 Hz, CHF); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ_F -152.7 (dd, *J* = 24.9, 19.1 Hz), -162.12 (dd, *J* = 19.6, 5.6 Hz), -207.5 (dd, *J* = 25.1, 5.8 Hz). **HRMS** (ASAP^{+}) m/z calcd for [M-F] $C_{15}H_{10}F_3I$ 354,9795, found 354.9793.

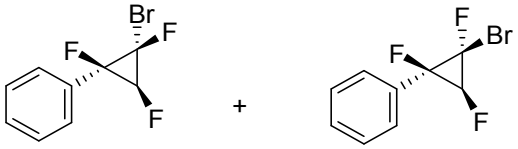
^{1}H NMR



^{19}F {^{1}H} NMR

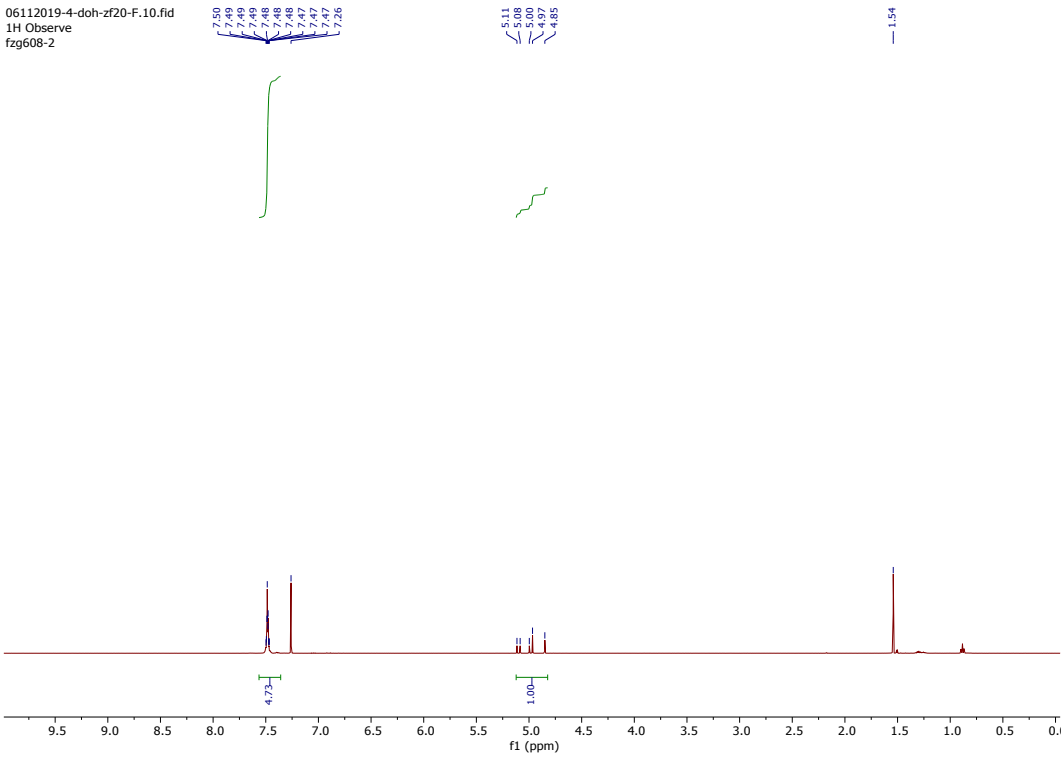


(2-bromo-1,2,3-trifluorocyclopropyl)benzene 23a and 23b

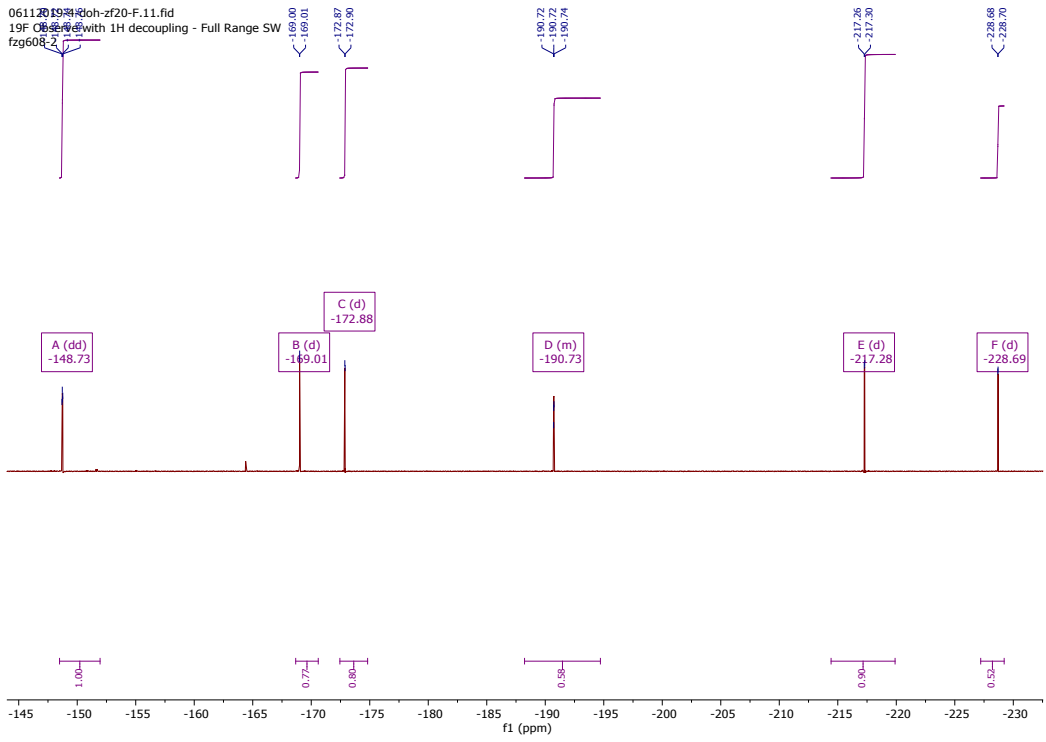


Following the general procedure A. The residue was purified by silica gel chromatography (pentane) to give the desired products as a mixture (liquid, 70 mg, 21.6 %). **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 4.91 (1 H, d, $^{2}J_{HF}$ = 58.4 Hz, CHF), 5.04 (1 H, dd, *J* = 58.6, 15.1 Hz, CHF), 7.48(5 H, m, arom.); **^{19}F {^{1}H} NMR** (470 MHz, $CDCl_3$) δ_F -148.7(dd, *J* = 18.8, 13.0 Hz), -169.0(d, *J* = 2.6 Hz), -172.9 (d, *J* = 13.0 Hz), -190.7 (dd, *J* = 10.5, 2.6 Hz), -217.3 (d, *J* = 18.8 Hz), -228.7 (d, *J* = 10.5 Hz). **HRMS** (EI^+) m/z calcd for [M] $C_9H_6F_3{}^{79}Br$ 249.9600, found 249.9574.

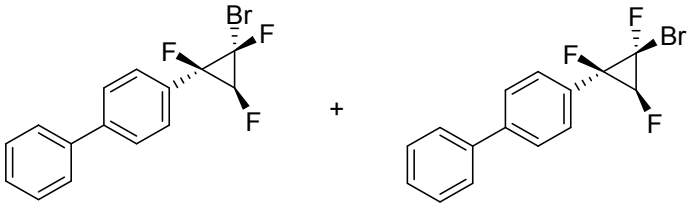
^{1}H NMR



^{19}F {^{1}H} NMR

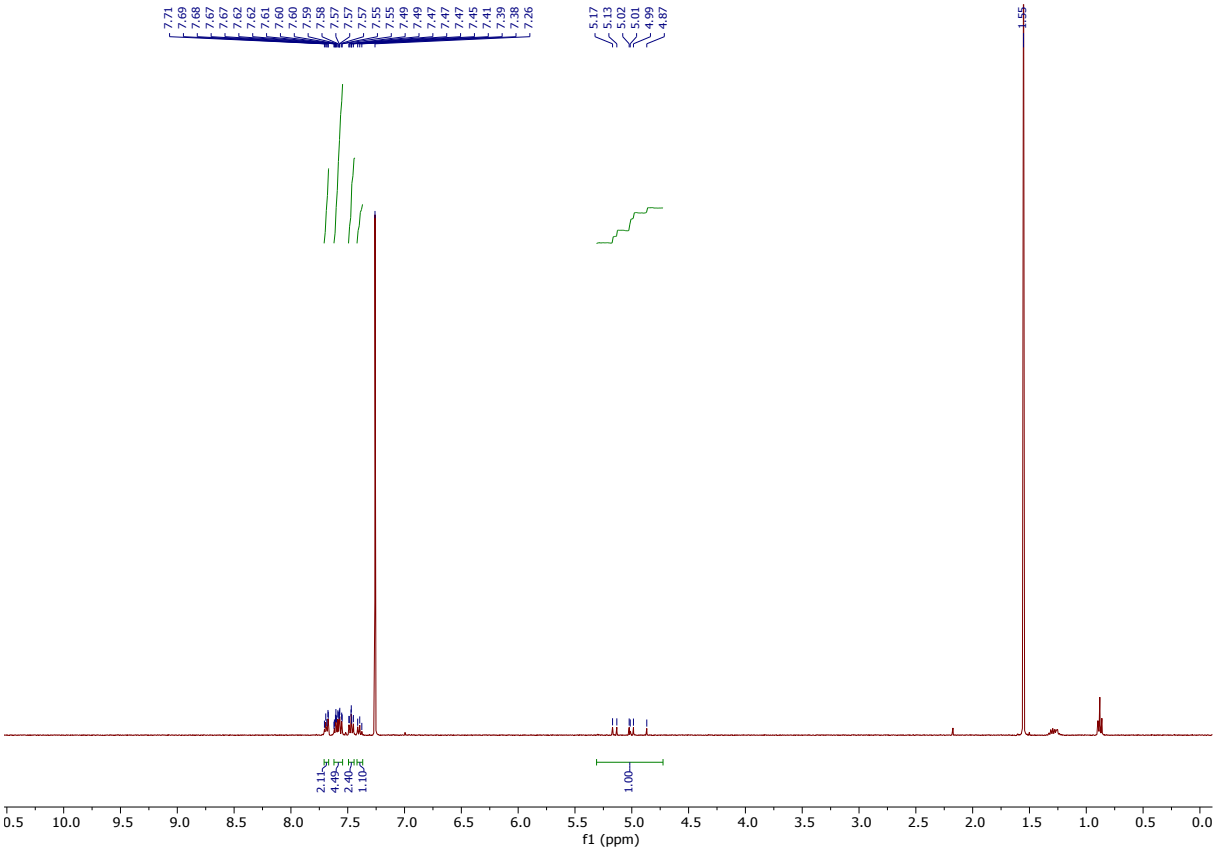


4-(2-bromo-1,2,3-trifluorocyclopropyl)-1,1'-biphenyl 24a and 24b

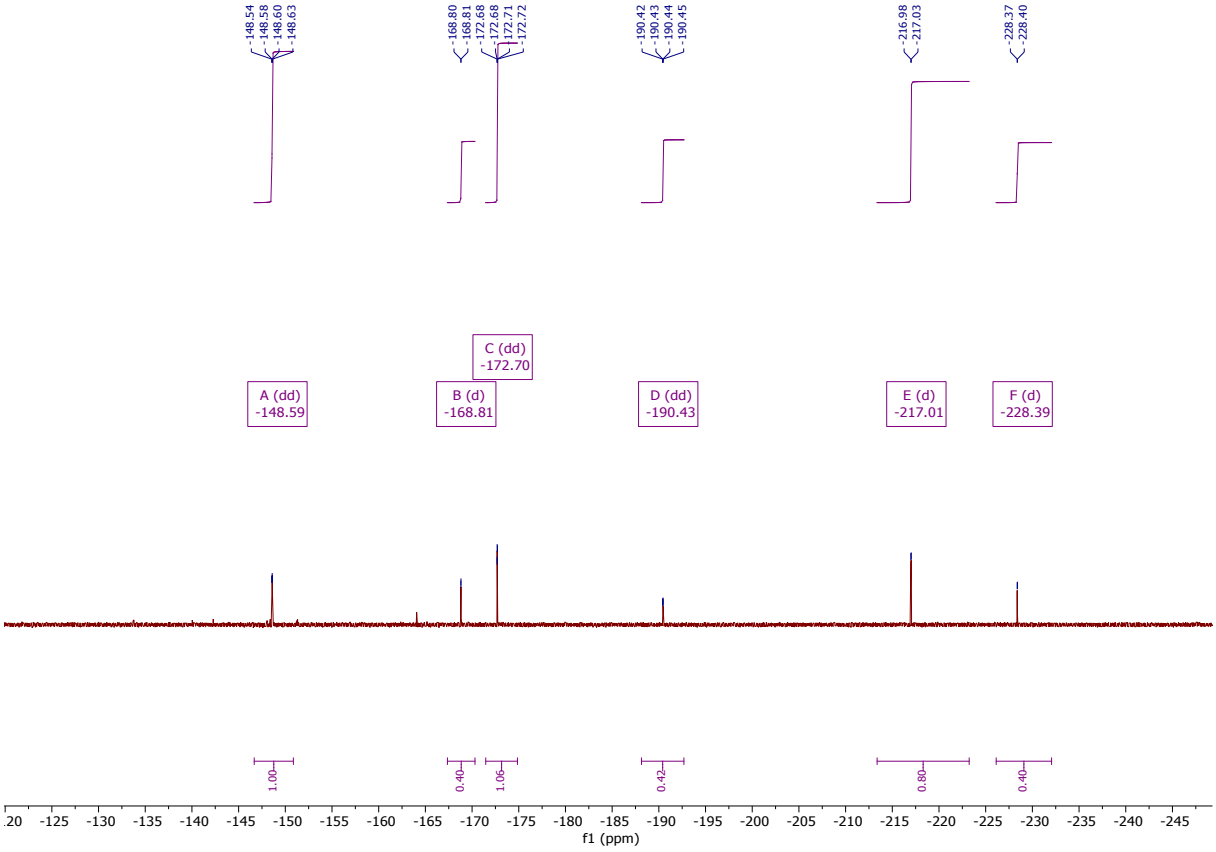


Following the above procedure. The residue was purified by silica gel chromatography (pentane) to give the desired products as a mixture (solid, 20 mg, 26.5 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 4.94 (1 H, d, $^{2}J_{HF}$ = 58.0 Hz, CHF), 5.07 (1 H, dd, *J* = 58.5, 15.1 Hz, CHF), 7.38-7.41(2 H, m, arom.), 7.45-7.47 (4 H, m, arom.), 7.55-7.62 (8H, m, arom.), 7.68-7.71 (4H, m, arom.); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ_F -148.6(dd, *J* = 19.1, 13.0 Hz), -168.8(d, *J* = 3.4 Hz), -172.0 (dd, *J* = 13.0, 1.9 Hz), -190.4 (dd, *J* = 10.0, 3.4 Hz), -217.0 (d, *J* = 19.1 Hz), -228.4 (d, *J* = 10.0 Hz). **HRMS** (EI^{+}) m/z calcd for [M] $C_{15}H_{10}F_3{}^{79}Br$ 325.9918, found 325.9917.

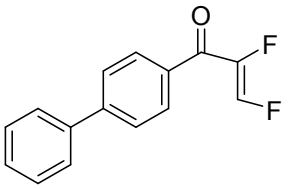
^{1}H NMR



^{19}F {^{1}H} NMR

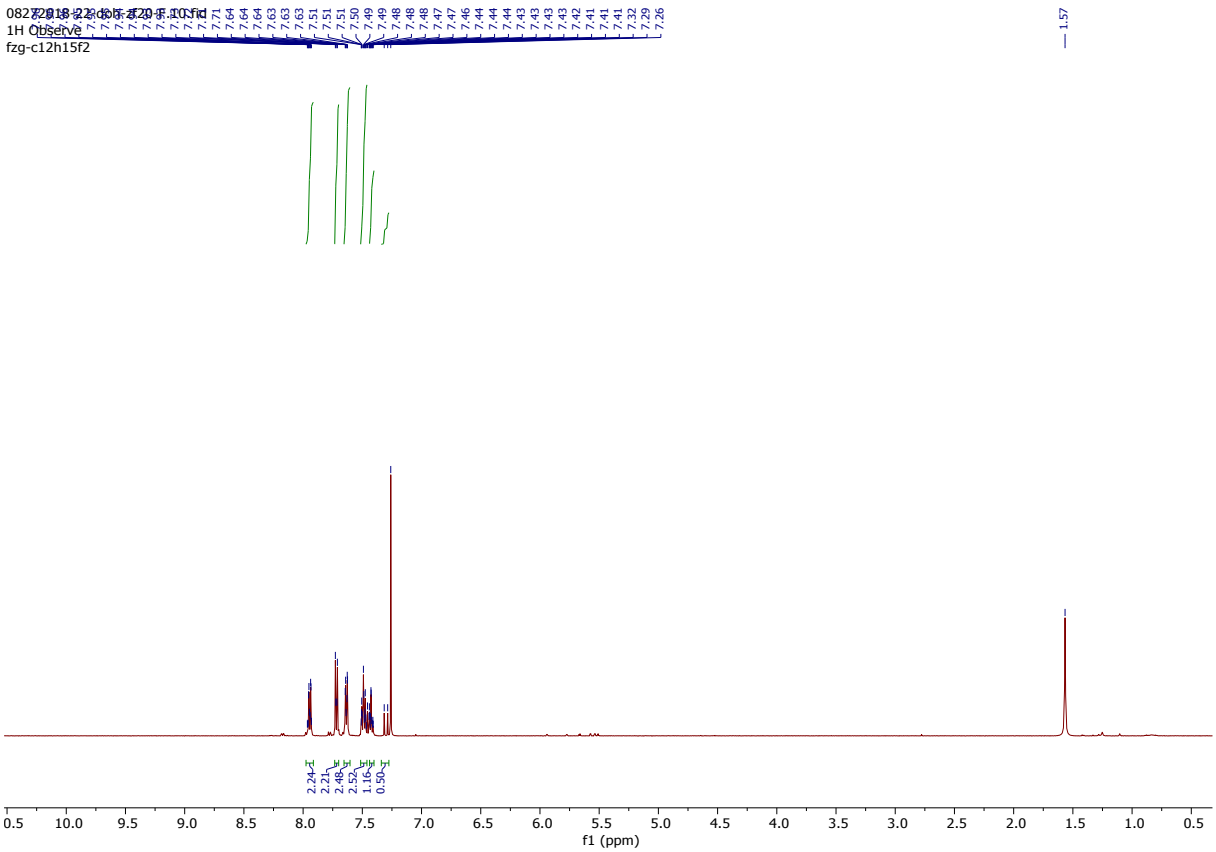


(Z)-1-([1,1'-biphenyl]-4-yl)-2,3-difluoroprop-2-en-1-one 25

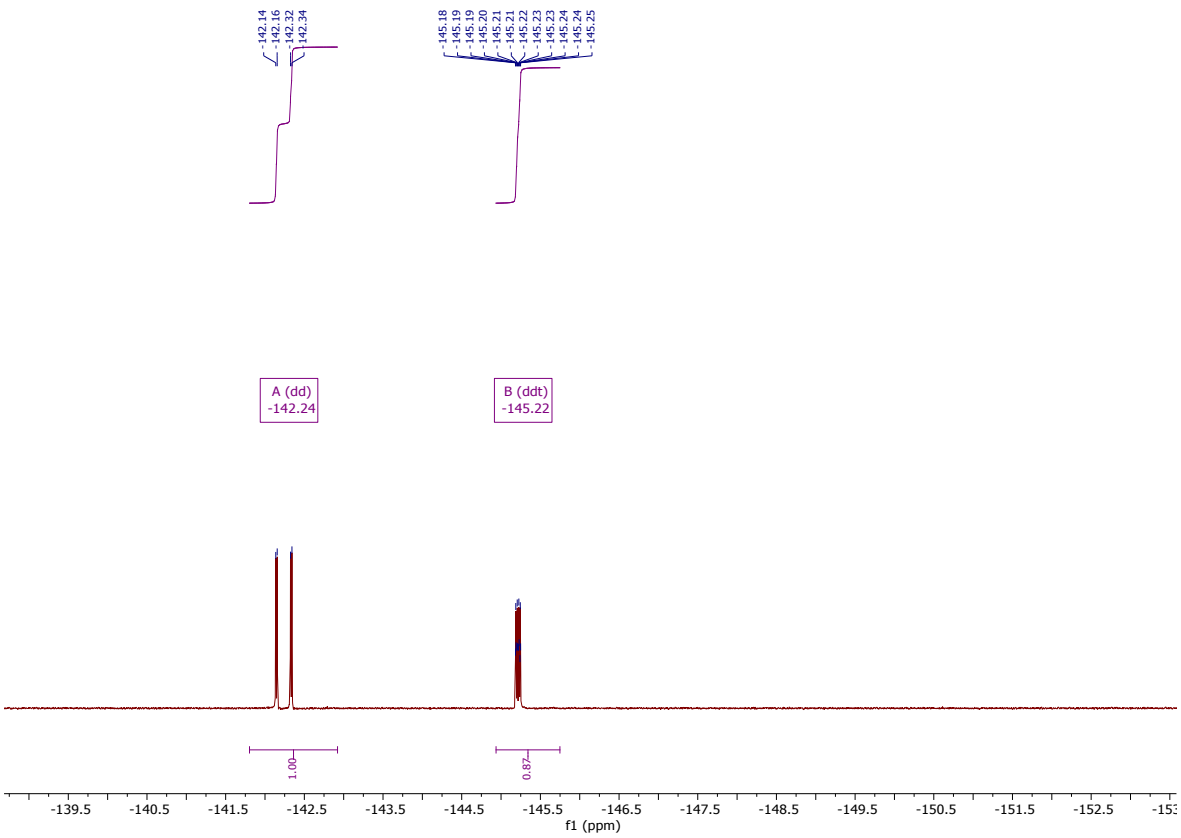


Mp. = 86-87 ^{o}C.**^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 7.96-7.93 (m, 2H), 7.73-7.71 (m, 2H), 7.64-7.63 (m, 2H), 7.51-7.47 (m, 2H), 7.44-7.41(m, 1H), 7.37 (dd, *J* = 70.6, 14.6 Hz, 1H, CHF), **^{19}F NMR** (470 MHz, $CDCl_3$) δ_F -142.2 (dd, *J* = 70.6, 6.8 Hz, CHF), -145.2 (ddt, *J* = 14.6, 6.8, 1.4 Hz, CF); **^{13}C NMR** (125 MHz, $CDCl_3$) δc 185.7 (dd, J = 22.3, 6.7 Hz, CO), 146.9 (dd, *J* = 265.7, 7.9 Hz, CF=CHF), 146.5, 145.8 (dd, J = 280.9, 11.9 Hz), 139.5, 129.7, 129.7, 129.0, 128.5, 127.38, 127.33.. **HRMS** (ASAP^{+}) m/z calcd for [M+H] $C_{15}H_{11}OF_2$ 245.0778, found 245.0780.

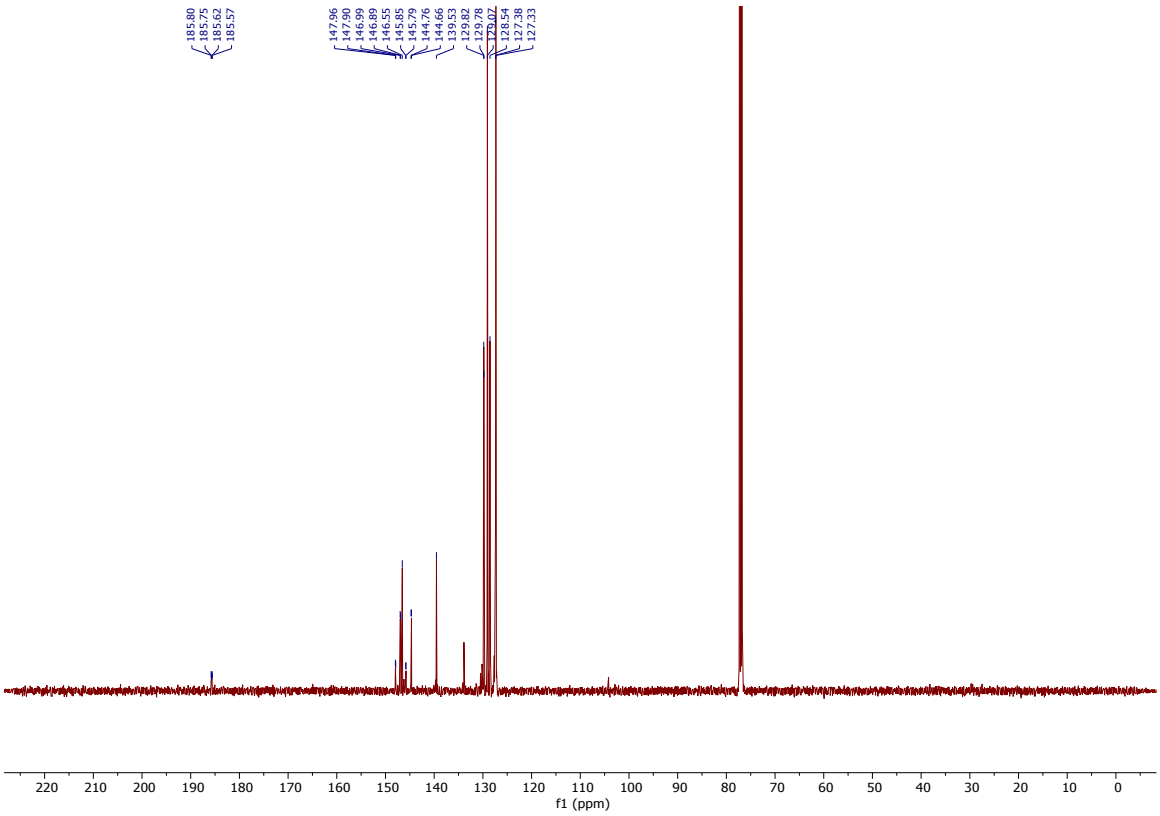
^{1}H NMR



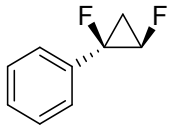
^{19}F NMR



^{13}C NMR

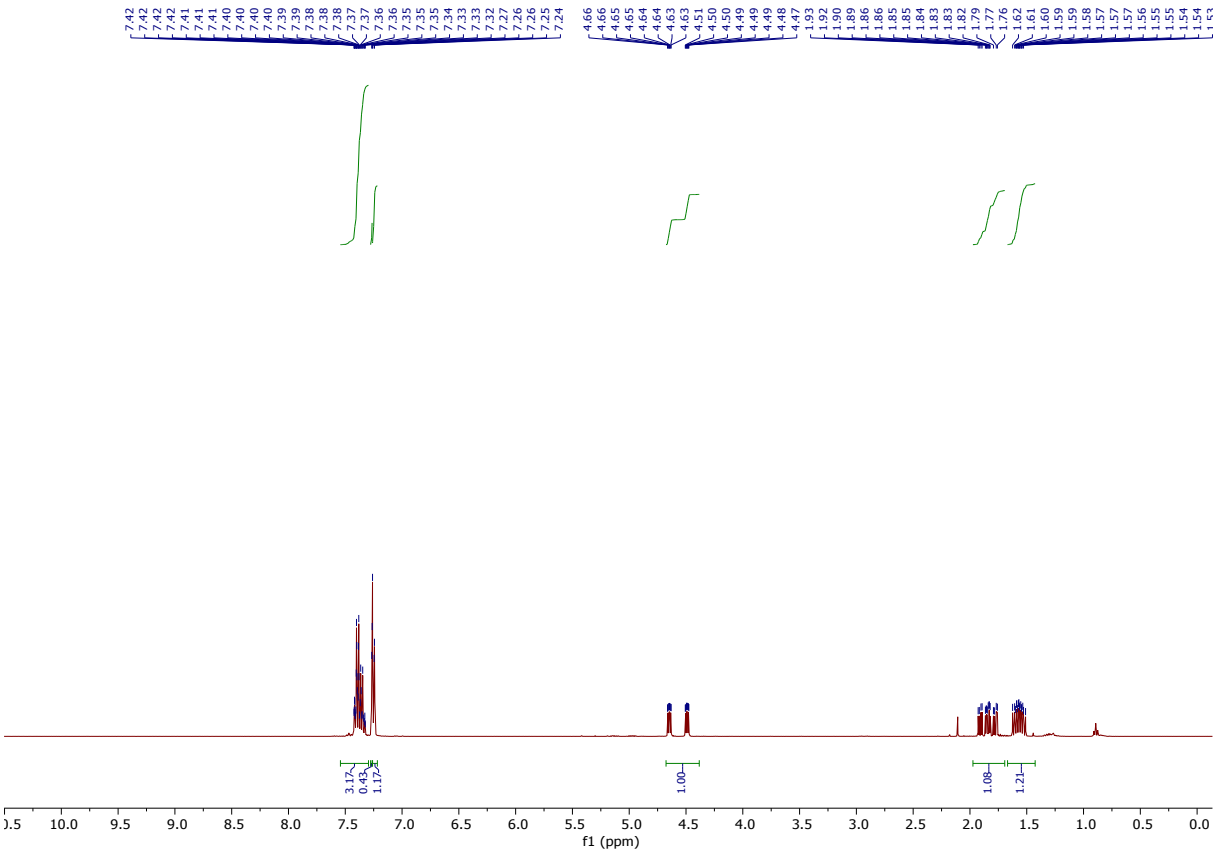


Cis-1,2-diflurocyclopropylbenzene 26

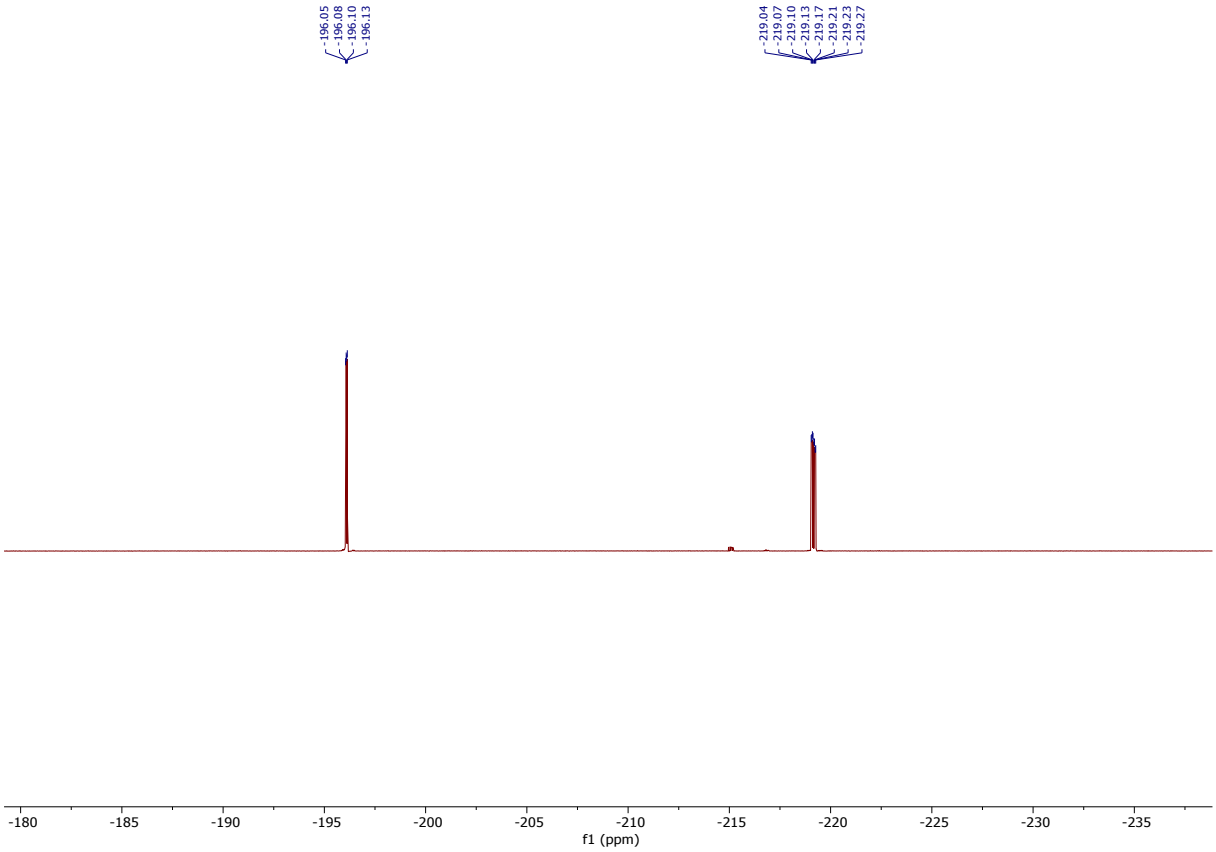


^{1}H NMR (400 Hz, $CDCl_3$) δ_H 1.51-1.62 (m, 1 H, CH_2), 1.75-1.92 (m, 1 H, CH_2), 4.55 (m, 1 H, CHF, $^{2}J_{CF}$ = 62.6 Hz), 7.23- 7.26(m, 2 H, arom.), 7.34-7.41 (m, 3 H, arom.); **^{19}F {^{1}H} NMR** (376 Hz, $CDCl_3$) δ_F -196.06 (s,1 F, CFPh), -219.19 (s, CFH); **^{19}F NMR** δ_F -196.07(dd, 1 F, CFPh, *J* = 25.6, 13.7 Hz), -219.20 (ddd, 1 F, CFH, *J* = 62.6, 28.3, 14.9 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) δc 18.7 (t, CH_2, *J* = 10 Hz), 73.1 (dd, CFH, *J* = 236, 9.1Hz), 76.6 (dd, CFPh, *J* = 222, 9.1Hz), 124.6 (d, C-arom., *J* = 5.5 Hz), 128.3 (s, C-arom.), 128.6 (s, C-arom.), 136.5 (dd, C-arom., *J* = 20.8, 1.8 Hz); **HRMS** (ASAP^{+}) m/z calcd for $C_9H_8F_2$ [M] 154.0550, found 154.0591, calcd $C_9H_7F_2$ [M-H] 153.0516, found 153.0520.

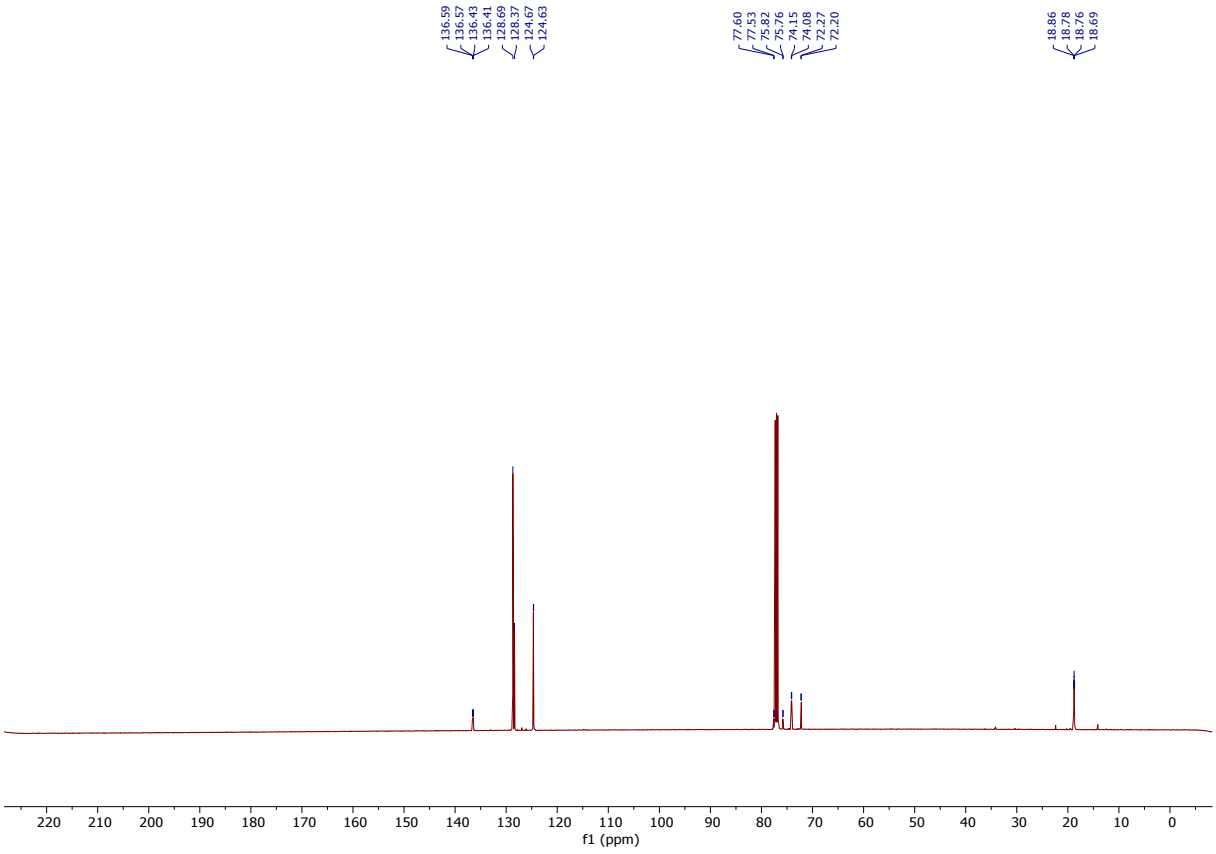
^{1}H NMR



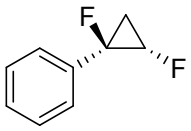
^{19}F NMR


-196.05
-196.08
-196.10
-196.13
-219.04
-219.07
-219.10
-219.13
-219.17
-219.21
-219.23
-219.27
-180
-185
-190
-195
-200
-205
-210
-215
-220
-225
-230
-235
f1 (ppm)

^{13}C NMR

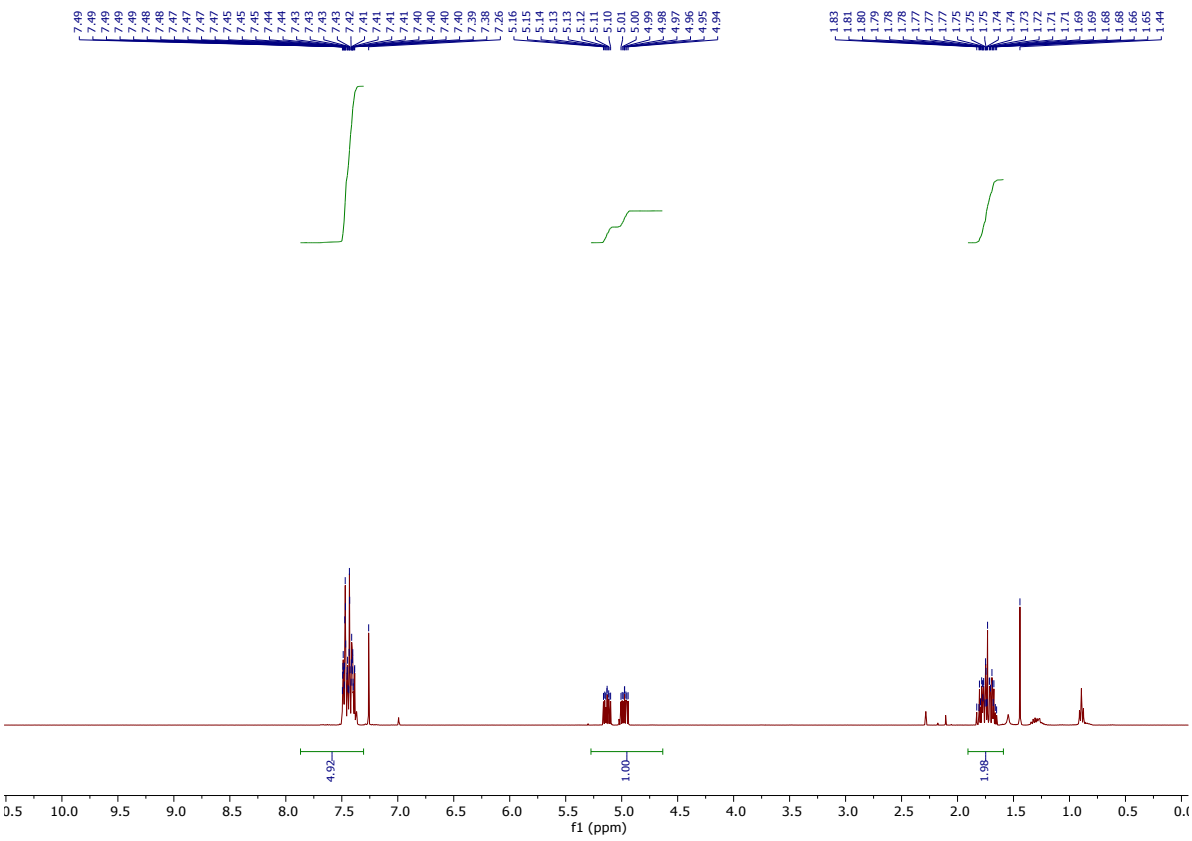

136.59
136.57
136.43
136.41
128.69
128.37
124.67
124.63
77.60
77.53
75.82
75.76
74.15
74.08
72.27
72.20
18.86
18.78
18.76
18.69
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

***Trans*-1,2-diflurocyclopropylbenzene 27**

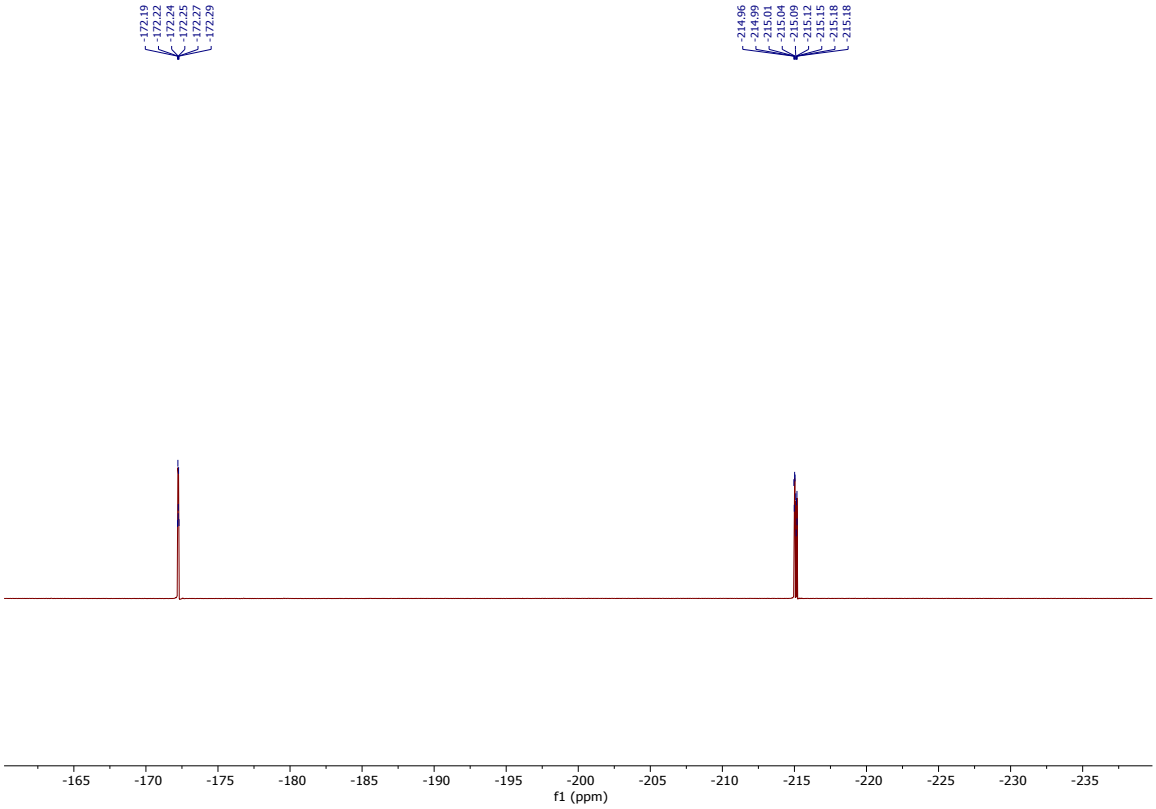


^{1}H NMR (400 Hz, $CDCl_3$) δ_H 1.67-1.80 (m, 2 H, CH_2), 5.08 (m, 1 H, CHF, $^{2}J_{CF}$ = 62.6 Hz), 7.30-7.48 (m, 5 H, arom.); **^{19}F {^{1}H} NMR** (376 Hz, $CDCl_3$) δ_F -172.21 (s,1 F, CFPh), -215.05 (s, CFH); **^{19}F NMR** δ_F -172.2 (dt, 1 F, CFPh, *J* = 22.6, 12.5 Hz), -219.20 (ddd, 1 F, CFH, *J* = 62.6, 24.8, 13.2 Hz); **^{13}C NMR** (125 MHz, $CDCl_3$) δc 19.5 (t, CH_2, *J* = 12.6 Hz), 73.5 (dd, CFH, *J* = 234, 19.1Hz), 78.7 (dd, CFPh, *J* = 221, 10 Hz), 126.9 (d, C-arom., *J* = 5.5 Hz), 128.4 (s, C-arom.), 128.7 (dd, C-arom., *J* = 1.7 Hz), 133.1 (d, C-arom., *J* = 19 Hz); **HRMS** (ASAP^{+}) m/z calcd for $C_9H_8F_2$ [M] 154.0550, found 154.0591, calcd $C_9H_7F_2$ [M-H] 153.0516, found 153.0520.

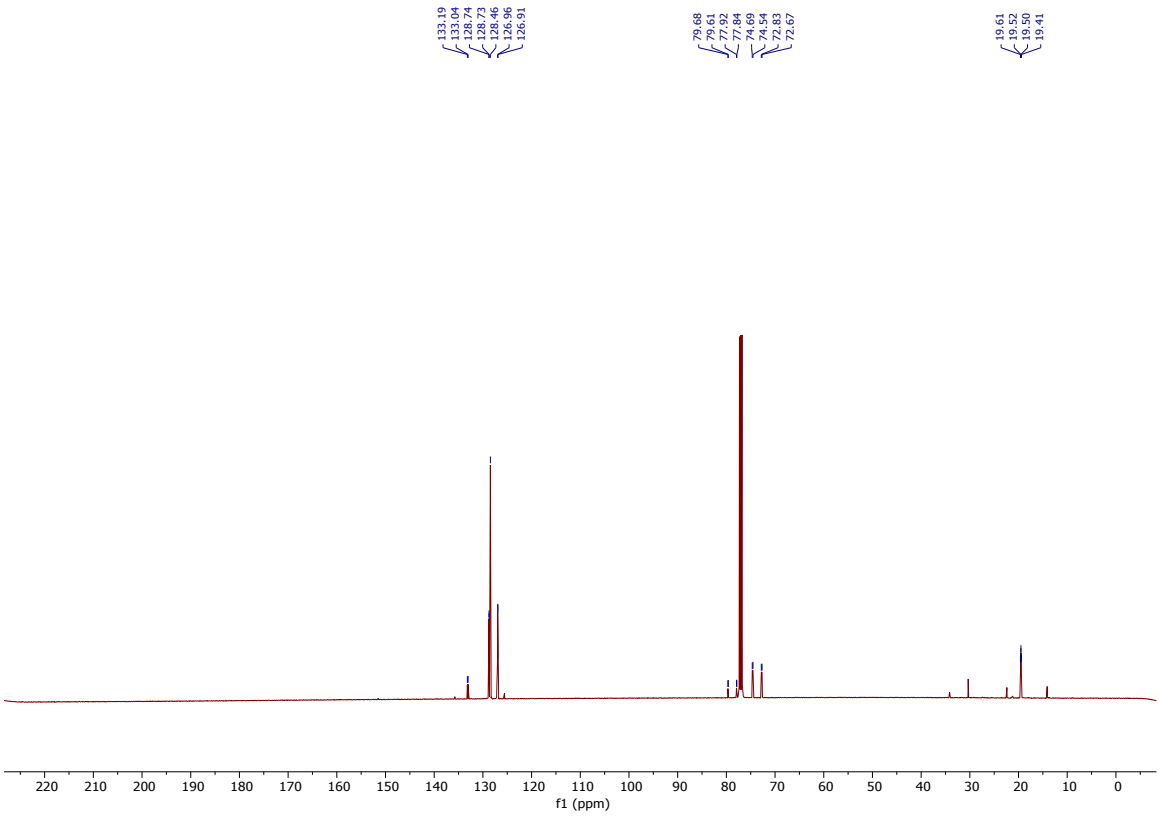
^{1}H NMR



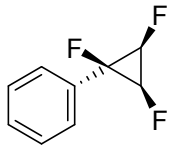
^{19}F NMR



^{13}C NMR

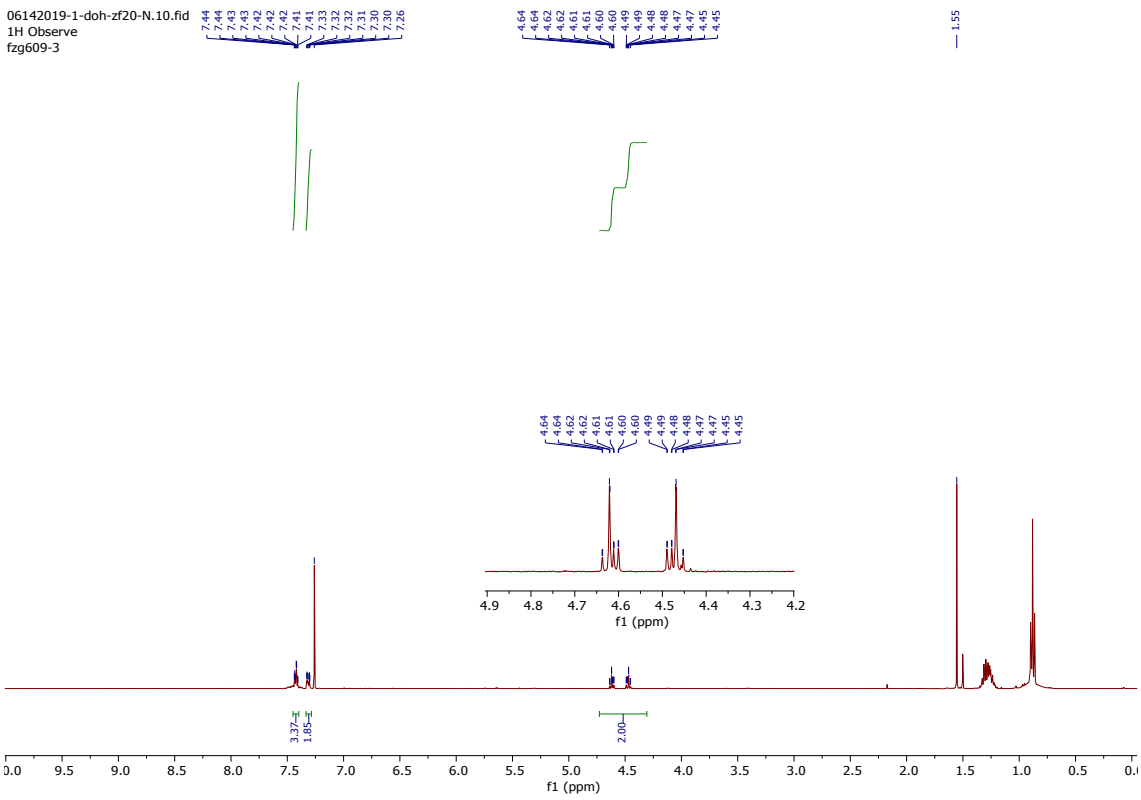


((1s,2R,3S)-1,2,3-trifluorocyclopropyl)benzene 3a

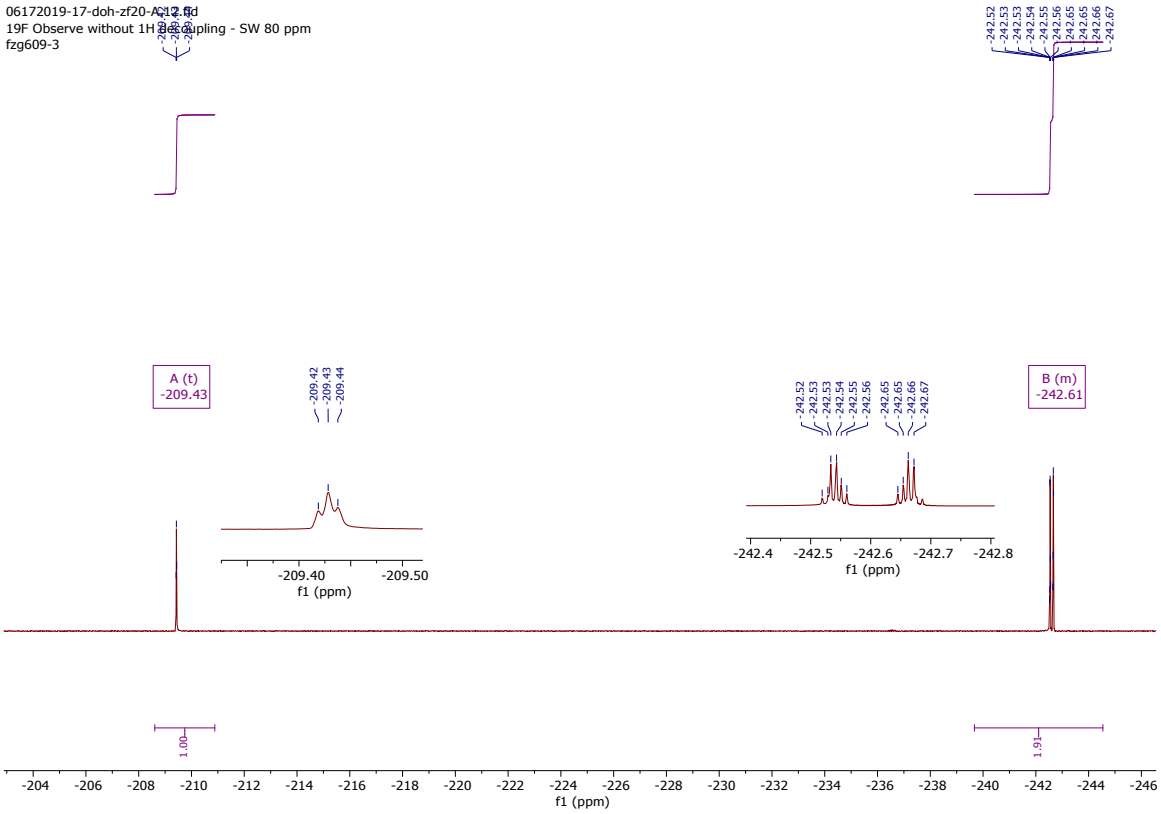


Following the general procedure **B**. Purification by flash column chromatography (pentane) gave the desired product as the liquid (volatile, Rf = 0.2 in PE, 14 mg, 15.4 %, volatile). **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 7.44 (m, 3H, arom), 7.31 (m, 2H, arom), 4.55 (m, 2H); **^{19}F {^{1}H} NMR** (470 MHz, $CDCl_3$) δ_F -209.4 (t, 1 F, *J* = 4.7 Hz, PHCF), -242.6 (d, 2 F, *J* = 4.7 Hz, CHF); **^{19}F NMR** (470 MHz, $CDCl_3$) δ_F -209.4 (t, 1 F, *J* = 4.7 Hz, PHCF), -242.6 (m, 2 F, CHF); **^{13}C NMR** (125 MHz, $CDCl_3$) δc 132.6 (tertiary), 129.0, 126.8, 125.9, 68.8.; **HRMS** (EI^+) m/z calcd for [M] $C_9H_7F_3$ 172.0494, found 172.0455.

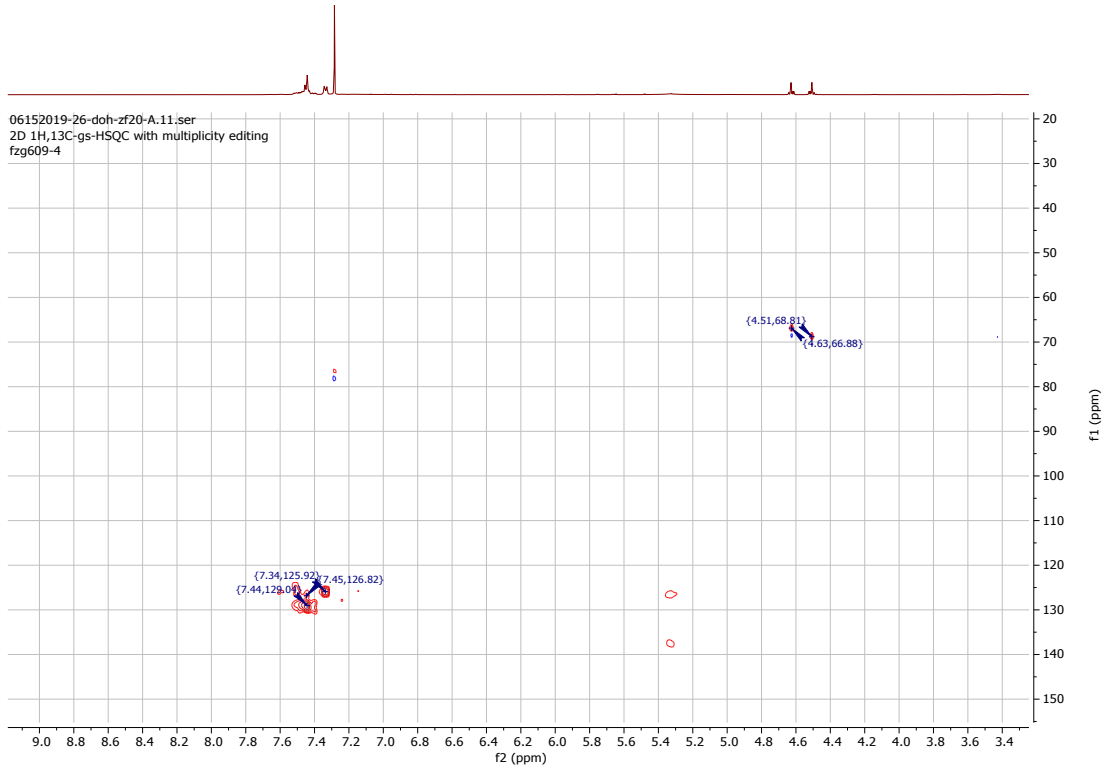
^{1}H NMR



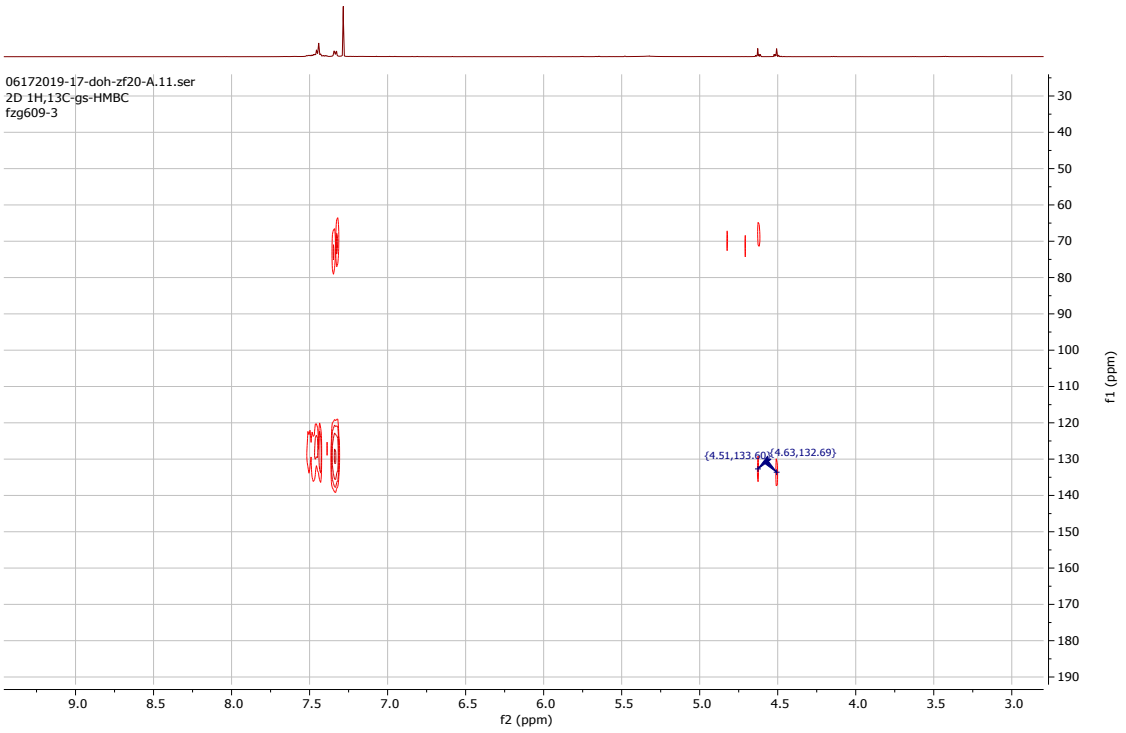
^{19}F NMR


06172019-17-doh-zf20-A.12.fid
19F Observe without 1H decoupling - SW 80 ppm
fzg609-3
A (t)
-209.43
B (m)
-242.61
f1 (ppm)
1.00
1.91

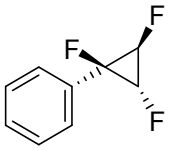
HSQC


06152019-26-doh-zf20-A.11.ser
2D 1H,13C-gs-HSQC with multiplicity editing
fzg609-4
{4.51,68.81}
{4.63,66.88}
{7.34,125.92}
{7.45,126.82}
f2 (ppm)
f1 (ppm)

HMBC

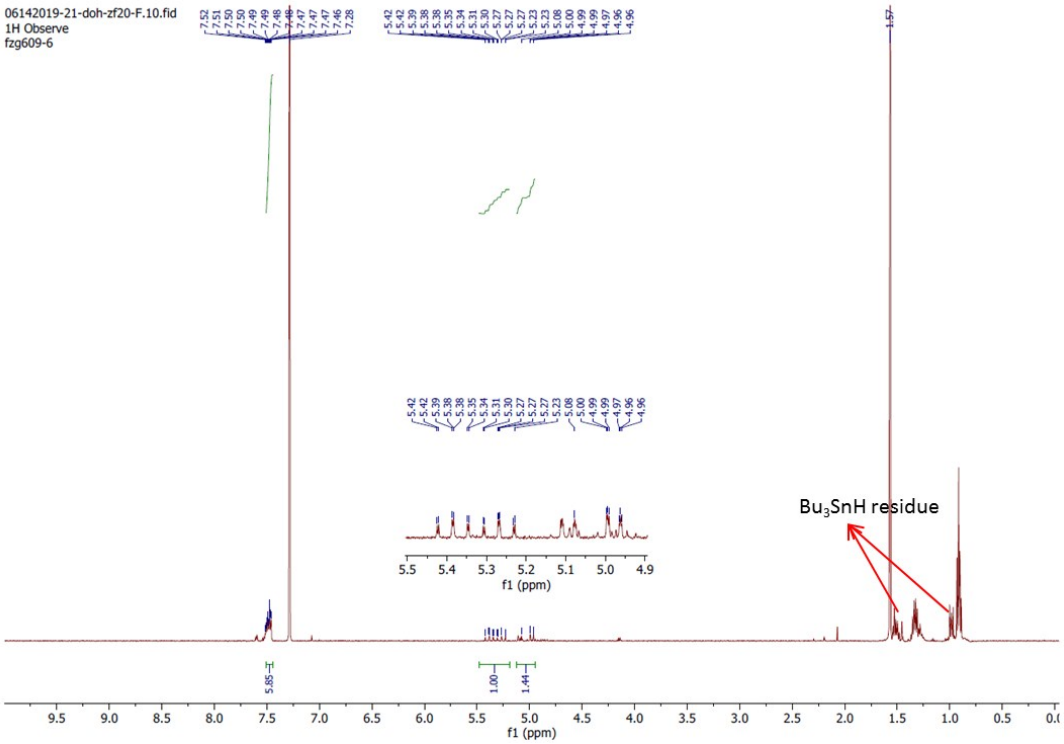


((2S,3S)-1,2,3-trifluorocyclopropyl)benzene 3b

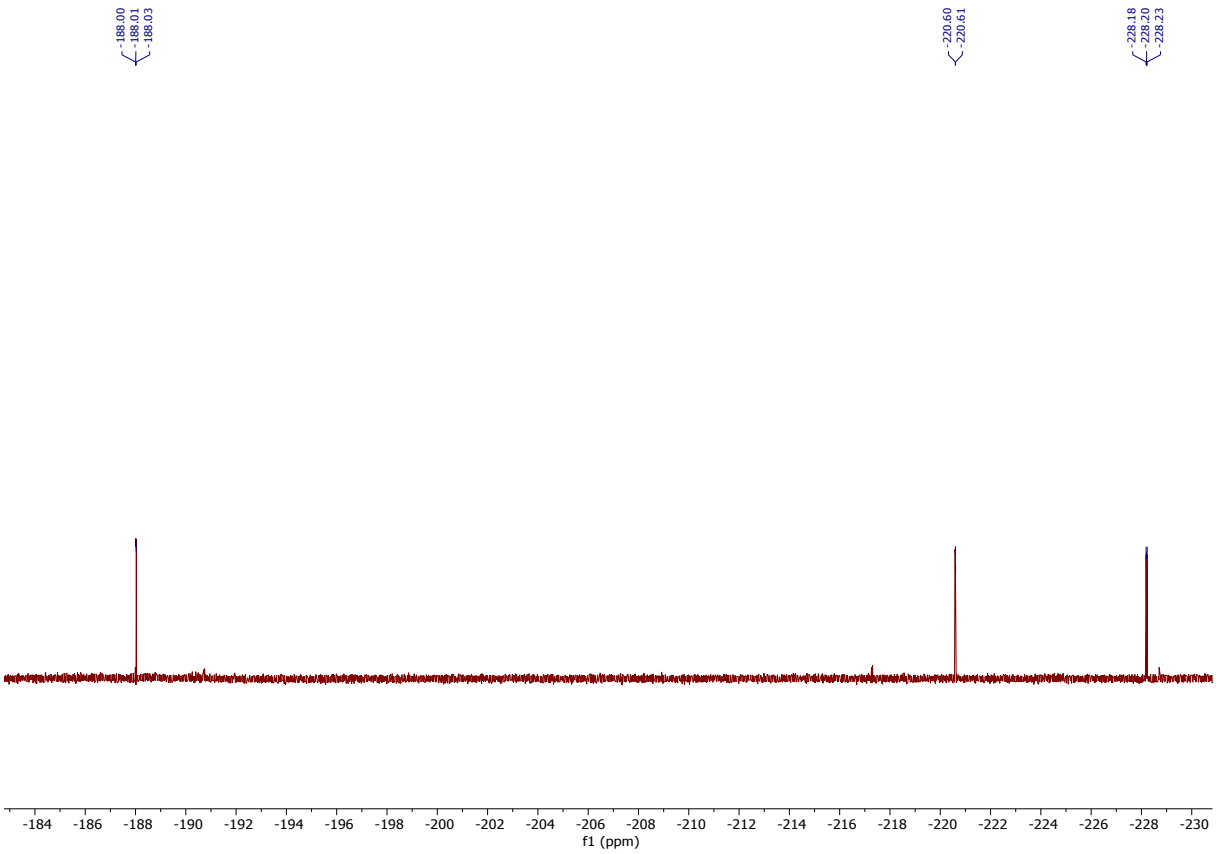


Following the general procedure **B**. Purification by flash column chromatography (pentane) gave the desired product as the liquid (volatile, Rf = 0.7 in PE, 20 mg, 22 %, volatile). **^{1}H NMR** (400 MHz, $CDCl_3$) δ_H 7.46 (m, 5H, arom), 5.31 (dddd, *J* = 58.0, 19.4, 18.7, 1.9 Hz, 1H, arom), 5.02 (dddd, *J* = 57.7, 16.0, 1.9, 1.2 Hz, 1H); **^{19}F {^{1}H} NMR** (376 MHz, $CDCl_3$) δ_F -188.2 (dd, *J* = 3.2, 12.2 Hz, 1F, PhCF), -220.7 (dd, *J* = 7.7, 3.0 Hz, 1F, CHF), -228.3 (dd, *J* = 12.2, 7.6 Hz, CHF); **^{19}F NMR** (376 MHz, $CDCl_3$) δ_F -188.2 (m, 1F, PhCF), -220.7 (m, 1F, CHF), -228.3 (m, 1F, CHF); **HRMS** (EI^+) m/z calcd for [M] $C_9H_7F_3$ 172.0494, found 172.0475.

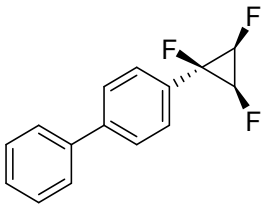
^{1}H NMR



^{19}F {^{1}H} NMR

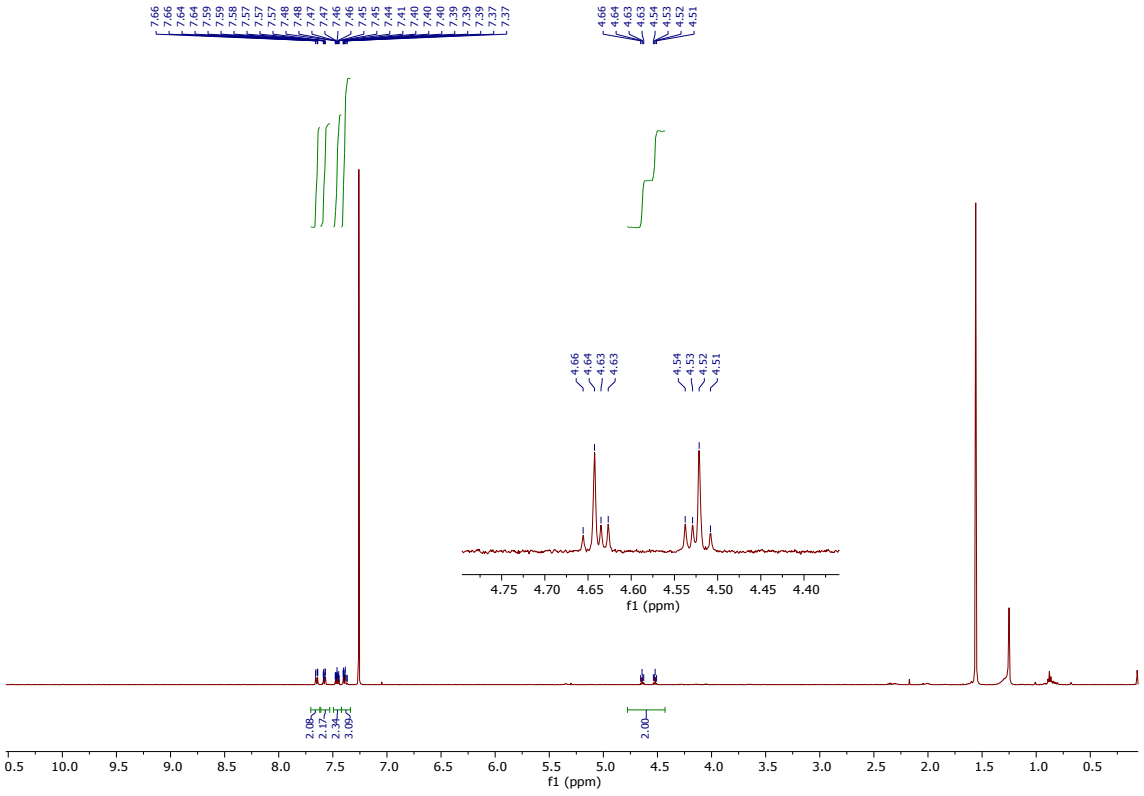

-188.00
-188.01
-188.03
-220.60
-220.61
-228.18
-228.20
-228.23
-184
-186
-188
-190
-192
-194
-196
-198
-200
-202
-204
-206
-208
-210
-212
-214
-216
-218
-220
-222
-224
-226
-228
-230
f1 (ppm)

4-((1s,2R,3S)-1,2,3-trifluorocyclopropyl)-1,1'-biphenyl 4a

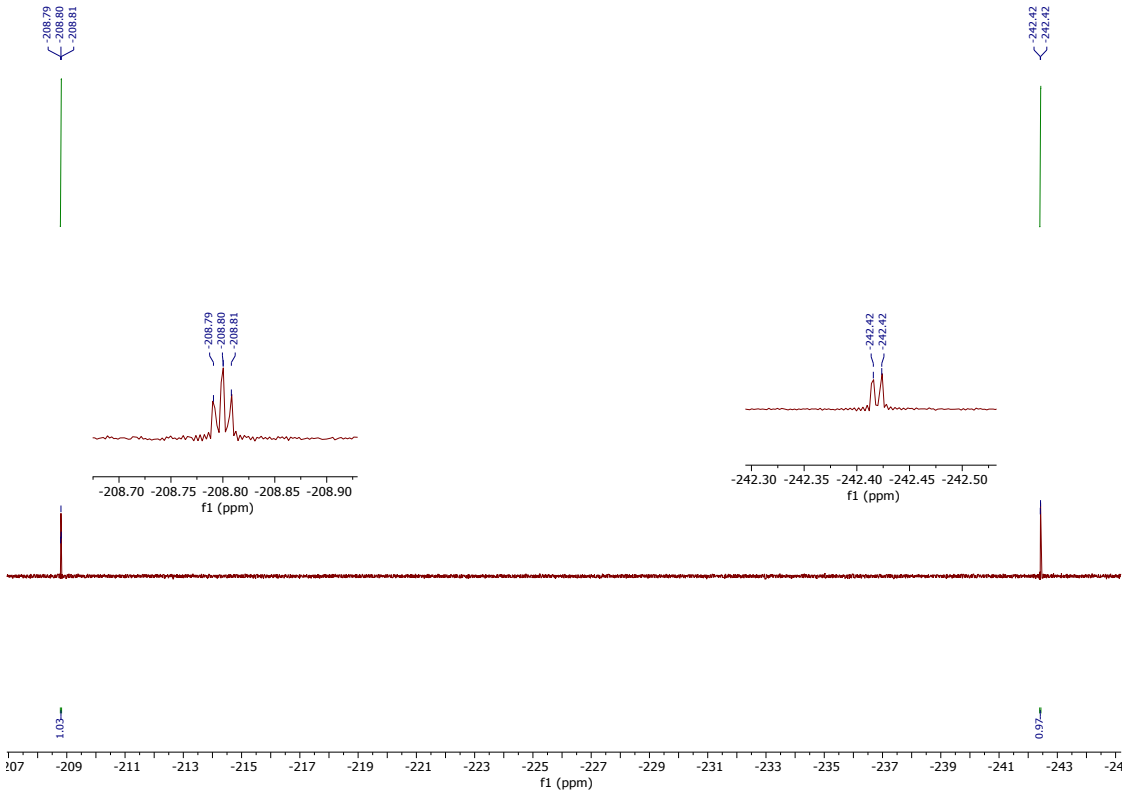


Following the general procedure **B**. The final product was obtained as the solid (2.7 mg, 17.7 %, volatile). **M.p.** = 84-85 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ_H 7.69– 7.63 (m, 2H), 7.59– 7.55 (m, 2H), 7.49 – 7.43 (m, 2H), 7.41-7.35 (m, 3H), 4.77 – 4.37 (m, 2H), 7; **^{19}F {^{1}H} NMR** (470 MHz, $CDCl_3$) δ_F -208.8 (t, *J* = 4.7 Hz, 1F, PhCF), -242.4 (d, *J* = 4.7 Hz, 2F, CHF); **^{19}F NMR** (376 MHz, $CDCl_3$) δ_F -208.8 (m, 1F, PhCF), -242.4 (m, 2F, CHF); **^{13}C NMR** (176 MHz, $CDCl_3$) δ_c 142.7, 140.0, 132.1, 128.9, 127.8, 127.7, 127.2, 126.6, 71.8, 67.8; **HRMS** (EI^+) m/z calcd for [M] $C_{15}H_{11}F_3$ 248.0807, found 248.0803.

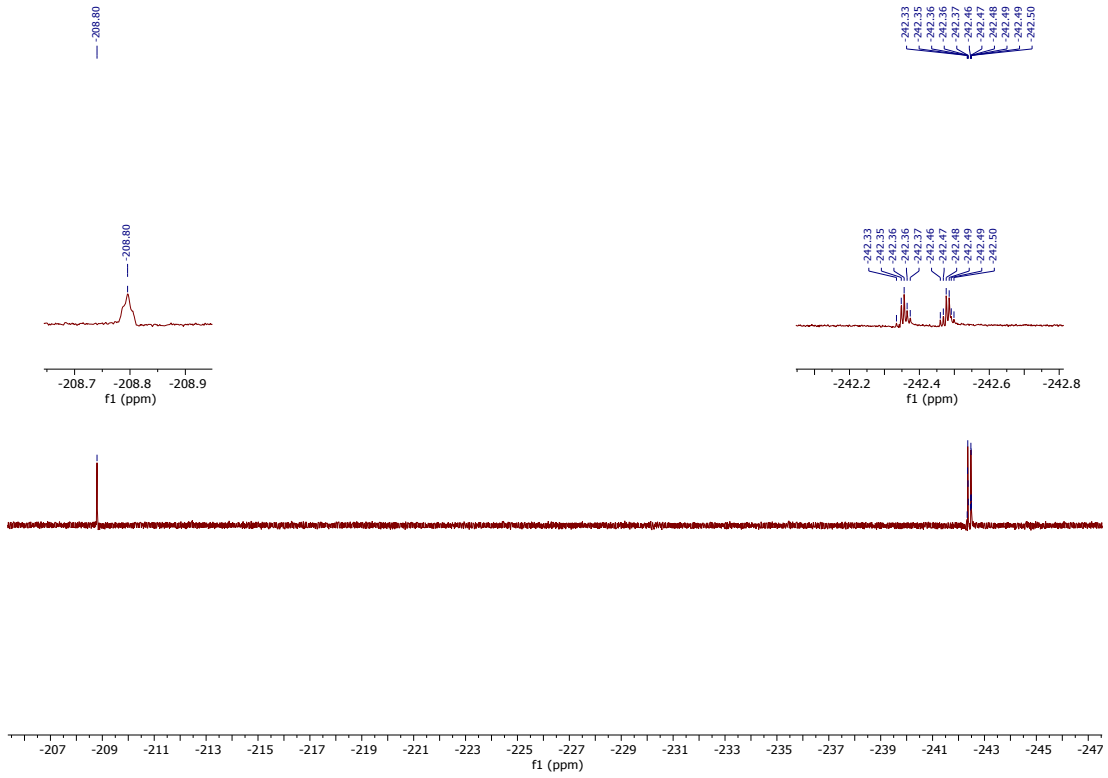
^{1}H NMR



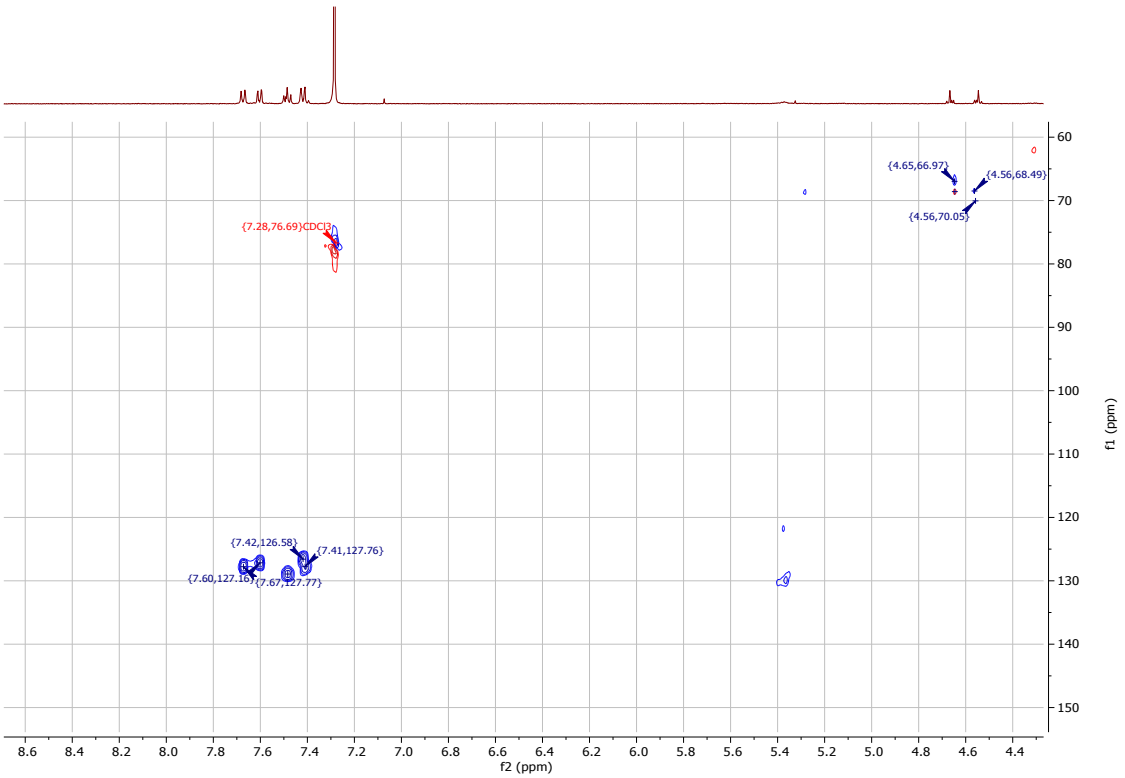
^{19}F {^{1}H} NMR



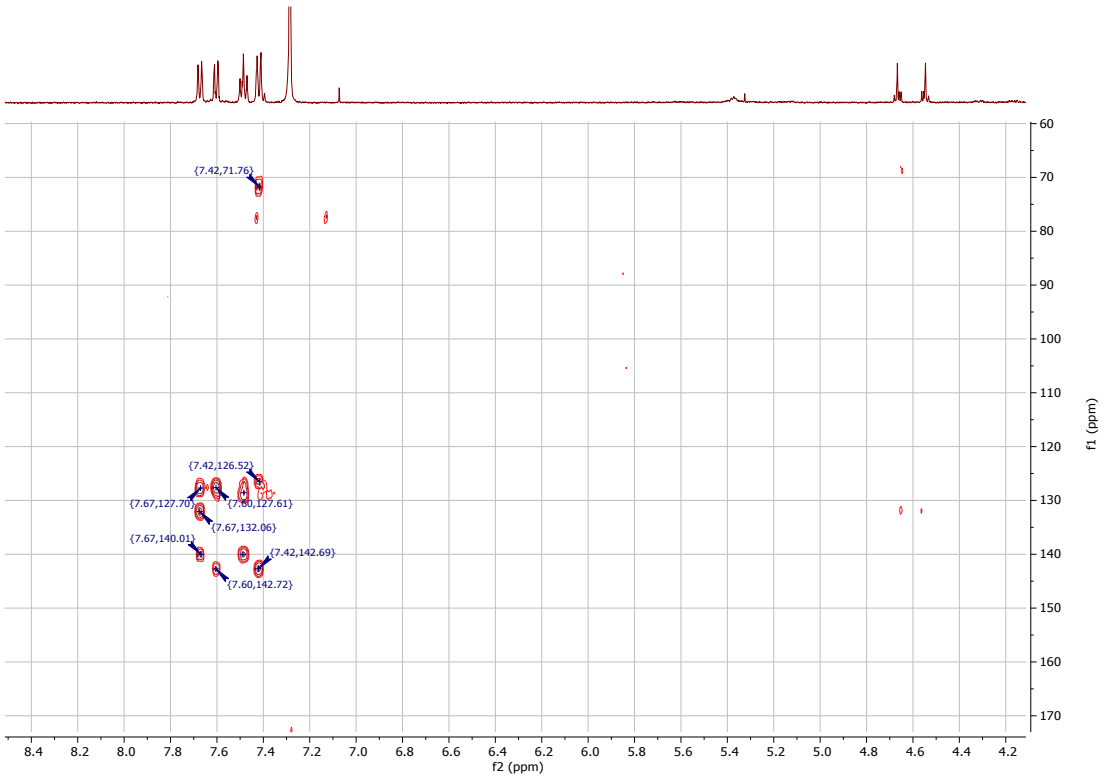
^{19}F NMR



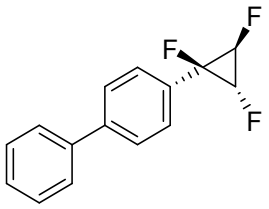
HSQC


{7.28,76.69}CDCl3
{4.65,66.97}
{4.56,68.49}
{4.56,70.05}
{7.42,126.58}
{7.41,127.76}
{7.60,127.16}
{7.67,127.77}
f2 (ppm)
f1 (ppm)

HMBC

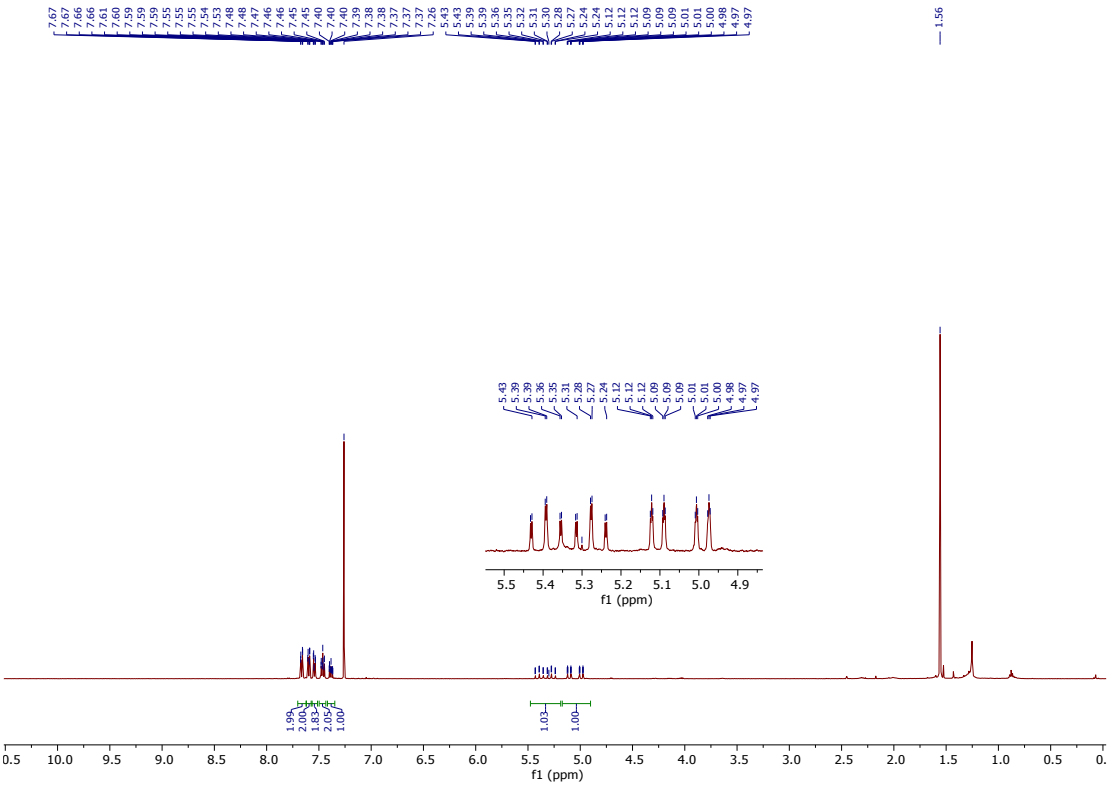

{7.42,71.76}
{7.42,126.52}
{7.67,127.70}
{7.60,127.61}
{7.67,132.06}
{7.67,140.01}
{7.42,142.69}
{7.60,142.72}
f2 (ppm)
f1 (ppm)

4-((2S,3S)-1,2,3-trifluorocyclopropyl)-1,1'-biphenyl 4b

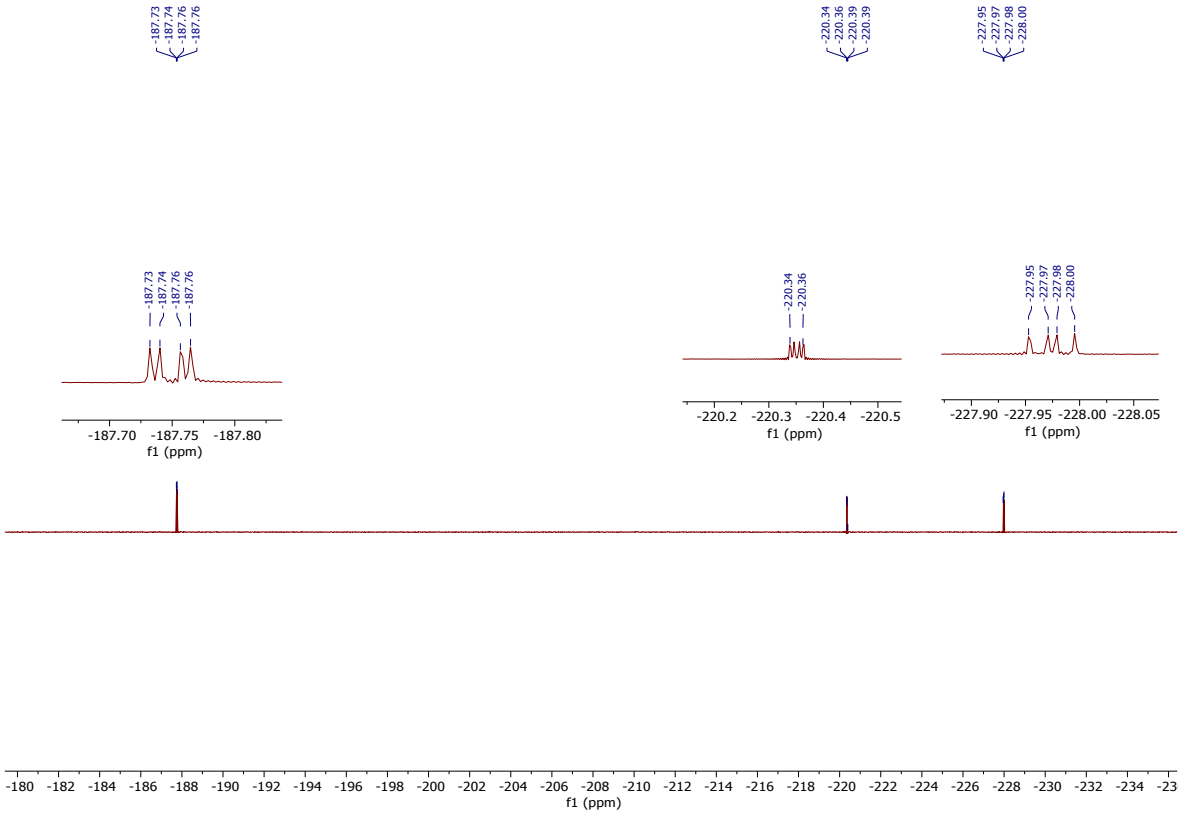


Following the general procedure **B**. The final product was obtained as the solid (3.7 mg, 24.3 %, volatile). **M.p.** = 76-77 °C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.70 – 7.64 (m, 2H), 7.62 – 7.58 (m, 2H), 7.54 (dd, J = 8.3, 1.6 Hz, 2H), 7.50 – 7.44 (m, 2H), 7.41 – 7.36 (m, 1H), 5.33 (m, *J* = 58.0, 18.9, 1.9 Hz, 1H), 5.05 (m, *J* = 57.7, 16.0, 1.6 Hz, 1H).; **^{19}F {^{1}H} NMR** (470 MHz, $CDCl_3$) δ_F -187.7 (dd, *J* = 11.5, 3.8 Hz, 1F, PhCF), -220.4 (dd, *J* = 8.6, 3.8 Hz, 1F, CHF), -227.9 (dd, *J* = 11.5, 8.6 Hz, CHF); **^{19}F NMR** (376 MHz, $CDCl_3$) δ_F -188.7 (m, 1F, PhCF), -220.4 (m, 1F, CHF), -227.9 (m, 1F, CHF); **^{13}C NMR** (126 MHz, $CDCl_3$) δ_c 142.9, 140.2, 132.1, 128.9, 128.2, 127.9, 127.6, 127.2, 80.8, 75.8, 75.5; **HRMS** (EI^+) m/z calcd for [M] $C_{15}H_{11}F_3$ 248.0807, found 248.0800.

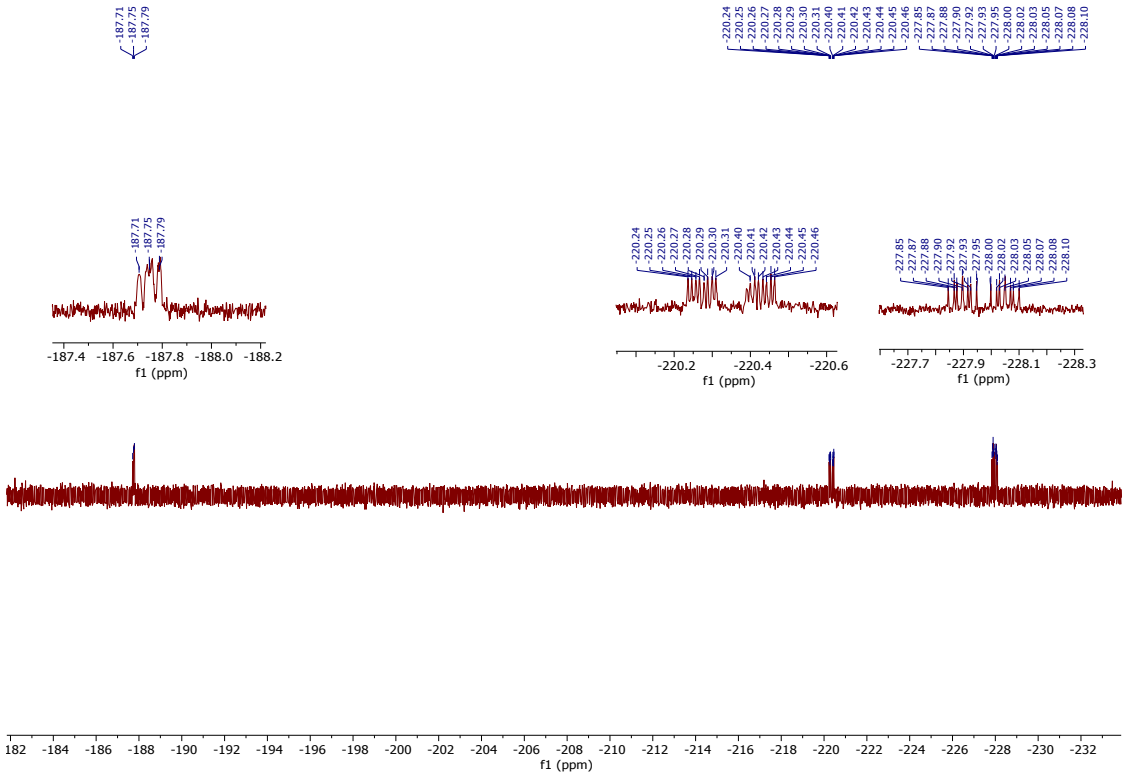
^{1}H NMR



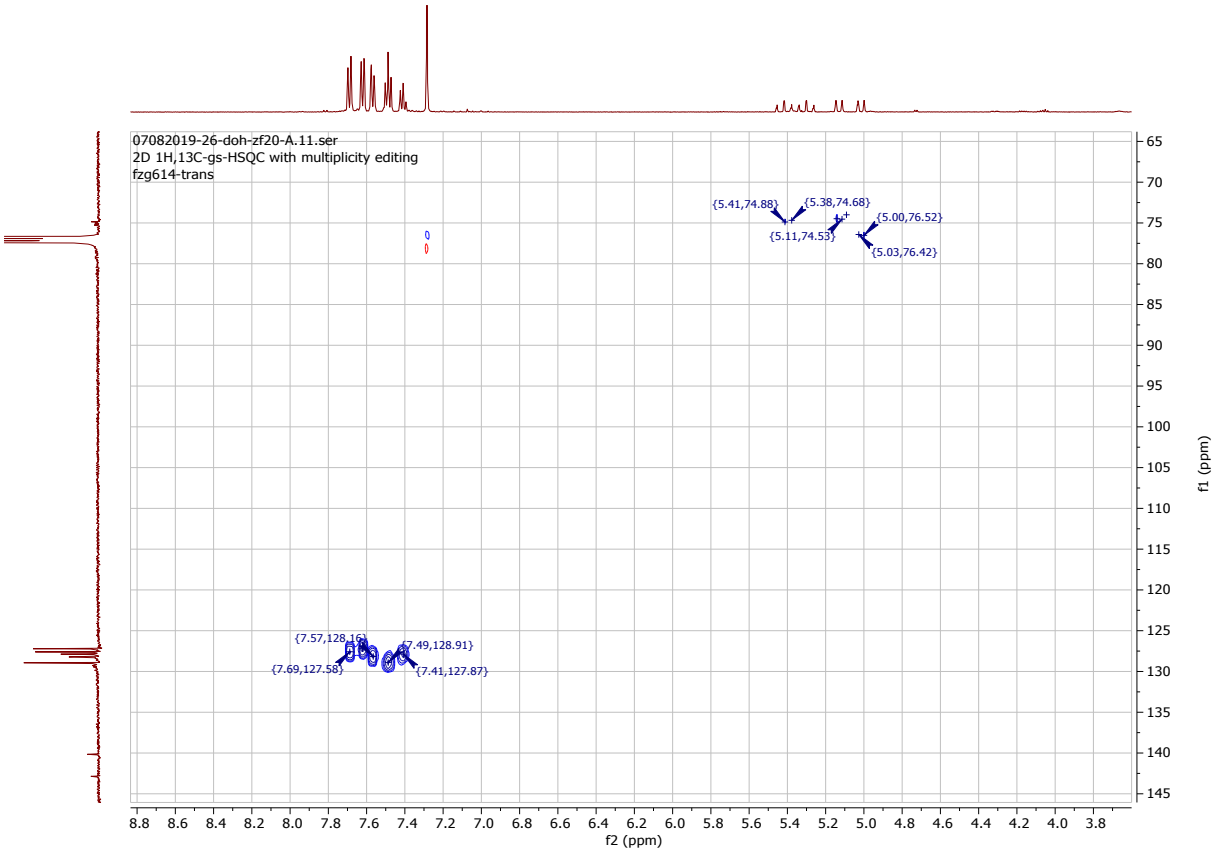
^{19}F {^{1}H} NMR



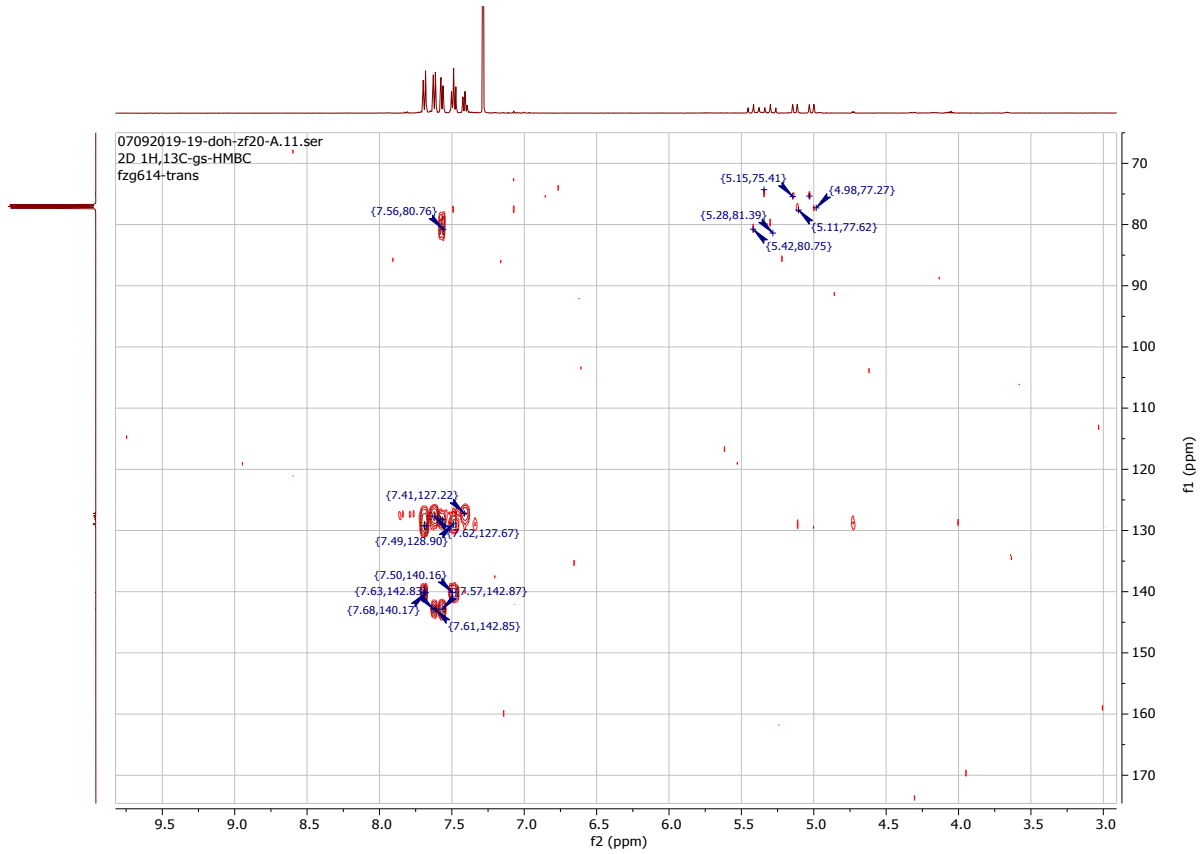
^{19}F NMR



HSQC


07082019-26-doh-zf20-A.11.ser
2D 1H,13C-gs-HSQC with multiplicity editing
fzg614-trans
{5.41,74.88}
{5.38,74.68}
{5.00,76.52}
{5.11,74.53}
{5.03,76.42}
{7.57,128.16}
{7.49,128.91}
{7.69,127.58}
{7.41,127.87}
f2 (ppm)
f1 (ppm)

HMBC



Computational study

Full geometry optimisation was performed in the gas phase using 6-311+G(d,p) basis.

Optimised Cartesian Coordinates

2a

C	2.78527400	-1.20779400	-0.09231800
C	3.47914100	0.00000000	-0.14992100
C	2.78526700	1.20779100	-0.09228700
C	1.39812600	1.20752500	0.02233600
C	0.69840000	-0.00001000	0.08241900
C	1.39813200	-1.20753800	0.02232300
H	3.32422400	-2.14677300	-0.13735700
H	4.55897800	0.00000400	-0.24227800
H	3.32421500	2.14677200	-0.13730700
H	0.85316800	2.14365300	0.07038400
H	0.85318400	-2.14367200	0.07036500
C	-0.77979700	0.00000300	0.25372400
C	-1.68887500	0.75683400	-0.68819500
C	-1.68888600	-0.75690500	-0.68812000
H	-1.26998500	1.30141000	-1.52703200

H	-1.27001300	-1.30156200	-1.52691300
F	-2.77795400	-1.37527600	-0.15047000
F	-1.18792200	0.00010000	1.56891300
F	-2.77795400	1.37525800	-0.15062500

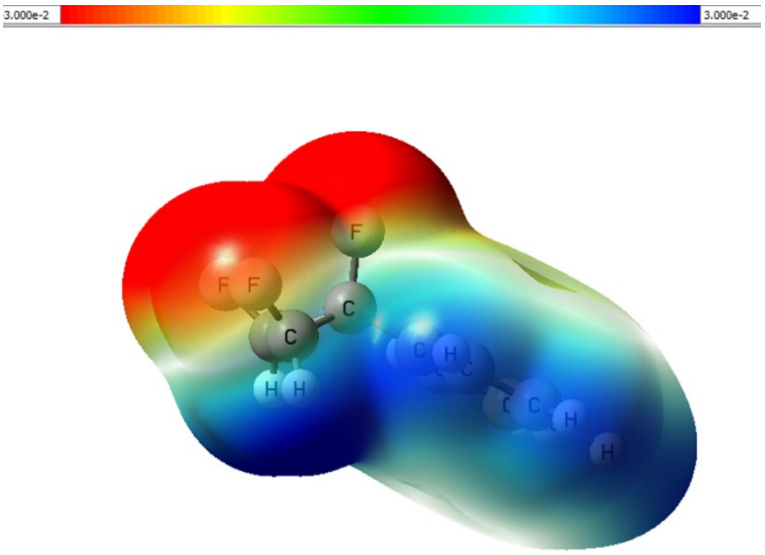


Figure S1: Electrostatic potential map for **3a** at the B3LYP/6-311+G(d,p) level, plotted on a colour scale from -0.03 a.u. (red) to +0.03 a.u. (blue) and mapped onto an isodensity surface ($\rho = 4 \times 10^{-4}$ a.u.).

Reference.

1. J. Hine, R. Butterworth and P. B. Langford. *J. Am. Chem. Soc.,* 1958, 80, 819-822.
2. A. Rodil, S. Bosisio and M. S. Ayoup *et al. Chem. Sci.,* 2018. **11**. 3023-3027.
3. Z. Liu, P. Liao and X. Bi. *Org.Lett.,* 2014, **16**, 3668-3671.
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5. J. Leroy. *J. Org. Chem*., 1981, **46**, 206-209.
6. Y. Chang, C. Cai. *Chem. Lett*. 2005, **34**, 1440-1441.