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sp^3 Carbon–Fluorine Bond Activation in 2,2-Difluorohomoallylic Alcohols via Nucleophilic 5-*endo-trig* Cyclisation: Synthesis of 3-Fluorinated Furan Derivatives

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Supporting Information

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1. General Statement

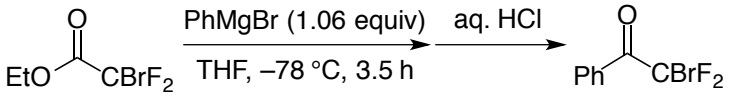
^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded on a Bruker Avance 500 spectrometer. Chemical shift values are given in ppm relative to internal Me_4Si (for ^{1}H NMR: δ = 0.00 ppm), $CDCl_3$ (for ^{13}C NMR: δ = 77.0 ppm) and C_6F_6 (for ^{19}F NMR: δ = 0.00 ppm; –164.9). IR spectra were recorded on a Horiba FT-300S spectrometer by the attenuated total reflectance (ATR) method. Mass spectra were measured on a JEOL JMS-T100GCV or a JEOL JMS-T100CS spectrometer. Elemental analyses were carried out at Elemental Analysis Laboratory, Division of Chemistry, Faculty of Pure and Applied Sciences, University of Tsukuba. Melting points were measured on a Yanaco micro melting point apparatus and were uncorrected.

Column chromatography was conducted on Florisil (Wako Pure Chemical Industries, Ltd., 75–150 μm) or silica gel (Silica Gel 60 N, Kanto Chemical Co., Inc., 63–210 μm). All the reactions were conducted under argon or nitrogen.

Tetrahydrofuran (THF) was purified by a solvent-purification system (GlassContour) equipped with columns of activated alumina and supported-copper catalyst (Q-5) before use. *N*,*N*-Dimethylformamide (DMF) was distilled from CaH_2, and stored over activated molecular sieves 4A. Potassium hydride was washed with dry hexane three times, dried under vacuum and stored in a glove box. Unless otherwise noted, materials were obtained from commercial sources and used directly without further purifications.

2. Preparation of Bromodifluoromethyl Ketones 2

2-Bromo-2,2-difluoro-1-phenylethan-1-one (2a)

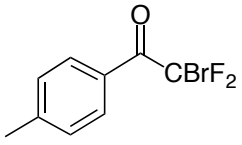


2a

To a THF (30 mL) solution of ethyl bromodifluoroacetate (6.1 g, 30 mmol) was added phenylmagnesium bromide, prepared from bromobenzene (5.0 g, 32 mmol), magnesium turnings (0.80 g, 33 mmol) and THF (30 mL), at –78 °C over 0.5 h. After stirring for 3 h at –78 °C, the reaction was quenched with an aqueous HCl solution (2 M, 30 mL). Organic materials were extracted with ether three times. The combined extracts were washed with brine and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by passing through a short column of silica gel (hexane/ethyl acetate = 50/1) to give **2a** (6.3 g, 90%) as a colourless liquid.

Spectral data for this compound showed good agreement with the literature data.[1]

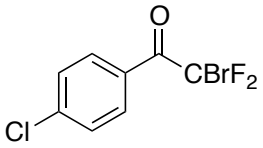
2-Bromo-2,2-difluoro-1-(4-methylphenyl)ethan-1-one (2b)



Bromodifluoromethyl ketone **2b** was prepared by the method described for **2a** using ethyl bromodifluoroacetate (6.1 g, 30 mmol), 4-bromotoluene (5.38 g, 31.5 mmol) and magnesium turnings (802 mg, 33.0 mmol). Passing through a short column of silica gel (hexane/ethyl acetate = 10/1) gave **2b** (6.90 g, 93%) as a colourless liquid.

Spectral data for this compound showed good agreement with the literature data.[2]

2-Bromo-1-(4-chlorophenyl)-2,2-difluoroethan-1-one (2c)

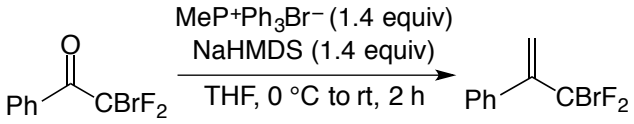


Bromodifluoromethyl ketone **2c** was prepared by the method described for **2a** using ethyl bromodifluoroacetate (3.05 g, 15.0 mmol), 1-bromo-4-chlorobenzene (3.03 g, 15.8 mmol) and magnesium turnings (401 mg, 16.5 mmol). Passing through a short column of silica gel (hexane/ethyl acetate = 10/1) gave **2c** (1.84 g, 45%) as a colourless liquid.

Spectral data for this compound showed good agreement with the literature data.[3]

3. Preparation of 3-Bromo-3,3-difluoropropenes 3

(3-Bromo-3,3-difluoroprop-1-en-2-yl)benzene (3a)

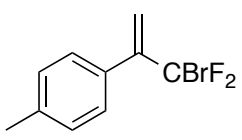


2a **3a**

To a THF (60 mL) solution of methyltriphenylphosphonium bromide (5.0 g, 14 mmol) was added NaHMDS (1.9 M in THF, 7.5 mL, 14 mmol) at –78 °C over 0.5 h. After stirring –78 °C for 1 h, the mixture was warmed to 0 °C. After stirring at 0 °C for 1 h, bromodifluoromethyl ketone **2a** (2.4 g, 10 mmol) was added to the reaction mixture. After stirring at room temperature for 2 h, the reaction was quenched with an aqueous HCl solution (2 M, 30 mL). Organic materials were extracted with ether three times. The combined extracts were washed with brine and dried over Na_2SO_4. After the solvent was removed under reduced pressure, the residue was purified by silica gel column chromatography (hexane) to give **3a** (1.5 g, 65%) as a colourless liquid.

Spectral data for this compound showed good agreement with the literature data.[4]

1-(3-Bromo-3,3-difluoroprop-1-en-2-yl)-4-methylbenzene (3b)

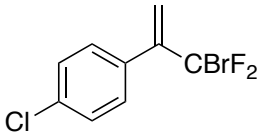


3-Bromo-3,3-difluoropropene **3b** was prepared by the method described for **3a** using methyl triphenylphosphonium bromide (5.1 g, 14 mmol), NaHMDS (1.9 M in THF, 7.5 mL, 14 mmol) and

bromodifluoromethyl ketone **2b** (2.5 g, 10 mmol). Purification by silica gel column chromatography (hexane) gave **3b** (1.6 g, 65%) as a colourless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 2.38 (s, 3H), 5.51 (s, 1H), 5.84 (s, 1H), 7.20 (d, J = 7.6 Hz, 2H), 7.38 (d, J = 7.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.2, 117.7 (t, J_{CF} = 7 Hz), 118.3 (t, J_{CF} = 303 Hz), 128.1, 129.1, 131.2, 139.0, 145.5 (t, J_{CF} = 22 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 115.7 (s). IR (neat): ν 2923, 1504, 1151, 1070, 914, 821, 742, 571 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{10}H_9{}^{79}BrF_2$ $[M]^+$: 245.9856; Found: 245.9856.

1-(3-Bromo-3,3-difluoroprop-1-en-2-yl)-4-chlorobenzene (3c)

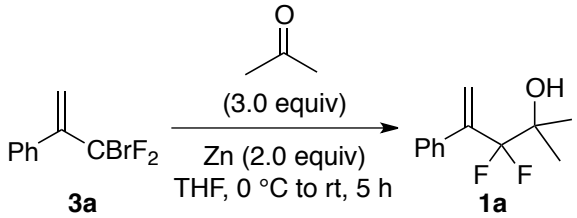


3-Bromo-3,3-difluoropropene **3c** was prepared by the method described for **3a** using methyl triphenylphosphonium bromide (3.38 g, 9.46 mmol), NaHMDS (1.9 M in THF, 5.0 mL, 9.5 mmol) and bromodifluoromethyl ketone **2c** (1.84 g, 6.83 mmol). Purification by silica gel column chromatography (hexane) gave **3c** (578 mg, 32%) as a colourless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.51 (t, J_{HF} = 1.8 Hz, 1H), 5.87 (s, 1H), 7.33–7.40 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 117.7 (t, J_{CF} = 306 Hz), 118.7 (t, J_{CF} = 7 Hz), 128.6, 129.6, 133.0, 135.1, 144.6 (t, J_{CF} = 21 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 116.4 (s). IR (neat): ν 1491, 1155, 1093, 1072, 922, 833, 555 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_9H_6{}^{79}BrClF_2$ $[M]^+$: 265.9309; Found: 265.9315.

4. Preparation of 2,2-Difluorohomoallylic Alcohols 1

3,3-Difluoro-2-methyl-4-phenylpent-4-en-2-ol (1a)

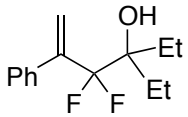


To the mixture of acetone (517 mg, 8.90 mmol) and zinc powder (activated with an aqueous HCl solution, 390 mg, 5.96 mmol) in THF (4.0 mL) was added a THF (4.0 mL) solution of 3-bromo-3,3-difluoropropene **3a** (699 mg, 3.00 mmol) at 0 °C over 30 min. Then, the reaction mixture was warmed to room temperature, and stirred at room temperature for 5 h. The reaction was quenched with an aqueous HCl solution (2 M, 5 mL). Organic materials were extracted with dichloromethane three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 10/1) to give **1a** (575 mg, 90%) as a colourless liquid.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.20 (s, 6H), 5.53 (d, J = 2.3 Hz, 1H), 5.78 (d, J = 2.3 Hz, 1H), 7.30–7.34 (m, 3H), 7.40–7.43 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 24.1, 74.1 (t, J_{CF} = 28 Hz),

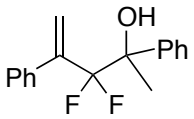
122.0 (t, J_{CF} = 9 Hz), 122.3 (t, J_{CF} = 252 Hz), 128.0, 128.2, 128.6, 138.4, 142.9 (t, J_{CF} = 22 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 52.7 (s). IR (neat): ν 3442, 2989, 1494, 1147, 1070, 775, 698, 590 cm^{-1}. HRMS (ESI+): *m*/*z* Calcd for $C_{12}H_{14}F_2NaO$ $[M + Na]^+$: 235.0910; Found: 235.0914.

3-Ethyl-4,4-difluoro-5-phenylhex-5-en-3-ol (1b)



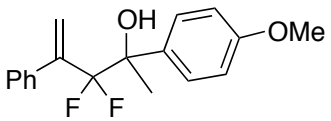
2,2-Difluorohomoallylic alcohol **1b** was prepared by the method described for **1a** using diethyl ketone (258 mg, 3.00 mmol), zinc powder (131 mg, 2.0 mmol) and 3-bromo-3,3-difluoropropene **3a** (231 mg, 0.996 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave **1b** (186 mg, 78%) as a colourless liquid.
^{1}H NMR (500 MHz, $CDCl_3$): δ 0.84 (t, *J* = 7.5 Hz, 6H), 1.28 (s, 1H), 1.55–1.66 (m, 4H), 5.49 (s, 1H), 5.77 (s, 1H), 7.30–7.32 (m, 3H), 7.40–7.42 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 7.4, 25.6, 77.7 (t, J_{CF} = 27 Hz), 121.5 (t, J_{CF} = 9 Hz), 123.2 (t, J_{CF} = 253 Hz), 127.8, 128.0, 128.5, 138.4, 143.4 (t, J_{CF} = 21 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 58.0 (s). IR (neat): ν 3585, 3482, 2972, 2949, 2887, 1496, 1463, 1078, 1027, 935, 775, 700 cm^{-1}. HRMS (ESI+): *m*/*z* Calcd for $C_{14}H_{18}F_2NaO$ $[M + Na]^+$: 262.1223; Found: 262.1224.

3,3-Difluoro-2,4-diphenylpent-4-en-2-ol (1c)



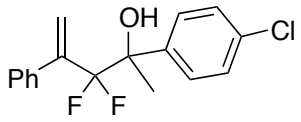
2,2-Difluorohomoallylic alcohol **1c** was prepared by the method described for **1a** using acetophenone (132 mg, 1.1 mmol), zinc powder (126 mg, 1.9 mmol) and 3-bromo-3,3-difluoropropene **3a** (235 mg, 1.01 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave **1c** (148 mg, 53%) as a colourless liquid.
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.67 (s, 3H), 2.05 (s, 1H), 5.31 (d, *J* = 0.8 Hz, 1H), 5.37 (d, *J* = 0.8 Hz, 1H), 7.21–7.28 (m, 8H), 7.43–7.45 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 24.6 (dd, J_{CF} = 2, 2 Hz), 77.6 (dd, J_{CF} = 27, 27 Hz), 121.6 (dd, J_{CF} = 254, 254 Hz), 122.5 (dd, J_{CF} = 9, 9 Hz), 126.4, 127.6, 127.7, 127.7, 127.9, 128.6, 138.2, 140.6, 142.6 (dd, J_{CF} = 24, 24 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 56.3 (d, J_{FF} = 248 Hz, 1F), 58.6 (d, J_{FF} = 248 Hz, 1F). IR (neat): ν 3566, 3483, 3059, 2993, 2941, 1495, 1448, 1070, 1028, 933, 760, 698 cm^{-1}. HRMS (ESI+): *m*/*z* Calcd for $C_{17}H_{17}F_2O$ $[M + H]^+$: 275.1247; Found: 275.1239.

3,3-Difluoro-2-(4-methoxyphenyl)-4-phenylpent-4-en-2-ol (1d)



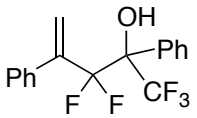
2,2-Difluorohomoallylic alcohol **1d** was prepared by the method described for **1a** using 4'-methoxyacetophenone (331 mg, 2.20 mmol), zinc powder (261 mg, 3.99 mmol) and 3-bromo-3,3-difluoropropene **3a** (466 mg, 2.00 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave **1d** (275 mg, 45%) as a colourless oil.
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.65 (s, 3H), 2.08 (s, 1H), 3.80 (s, 3H), 5.33 (s, 1H), 5.38 (s, 1H), 6.79–6.80 (m, 2H), 7.25–7.27 (m, 5H), 7.34 (d, J = 8.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 24.5, 55.2, 77.3 (dd, J_{CF} = 29, 29 Hz), 113.0, 121.8 (t, J_{CF} = 254 Hz), 122.5 (t, J_{CF} = 9 Hz), 127.67, 127.70, 127.9, 128.6, 132.8, 138.3, 142.7 (t, J_{CF} = 24 Hz), 159.0. ^{19}F NMR (470 MHz, $CDCl_3$): δ 56.4 (d, J_{FF} = 242 Hz, 1F), 58.7 (d, J_{FF} = 242 Hz, 1F). IR (neat): ν 3494, 2999, 2941, 2839, 1612, 1514, 1252, 1028, 775, 700 cm^{-1}. HRMS (ESI+): *m*/*z* Calcd for $C_{18}H_{18}F_2NaO$ [M + Na]$^+$: 327.1173; Found: 327.1166.

2-(4-Chlorophenyl)-3,3-difluoro-4-phenylpent-4-en-2-ol (1e)



2,2-Difluorohomoallylic alcohol **1e** was prepared by the method described for **1a** using 4'-chloroacetophenone (340 mg, 2.20 mmol), zinc powder (261 mg, 3.99 mmol) and 3-bromo-3,3-difluoropropene **3a** (467 mg, 2.00 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave **1e** (293 mg, 47%) as a colourless oil.
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.66 (s, 3H), 2.09 (s, 1H), 5.35 (s, 1H), 5.42 (s, 1H), 7.20–7.37 (m, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 24.5 (t, J_{CF} = 2 Hz), 77.2 (dd, J_{CF} = 29, 29 Hz), 121.4 (t, J_{CF} = 255 Hz), 122.6 (t, J_{CF} = 9 Hz), 125.3, 127.7, 127.8, 127.9, 128.5, 133.6, 139.09, 139.11, 142.3 (t, J_{CF} = 24 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 55.0 (d, J_{FF} = 243 Hz, 1F), 57.4 (d, J_{FF} = 243 Hz, 1F). IR (neat): ν 3581, 1495, 1095, 1012, 941, 798, 700, 548 cm^{-1}. HRMS (ESI+): *m*/*z* Calcd for $C_{17}H_{15}ClF_2NaO$ [M + Na]$^+$: 331.0677; Found: 331.0678.

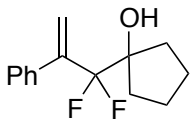
1,1,1,3,3-Pentafluoro-2,4-diphenylpent-4-en-2-ol (1f)



2,2-Difluorohomoallylic alcohol **1f** was prepared by the method described for **1a** using 2,2,2-trifluoroacetophenone (96 mg, 0.55 mmol), zinc powder (65 mg, 0.99 mmol) and 3-bromo-3,3-difluoropropene **3a** (116 mg, 0.50 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave **1f** (106 mg, 65%) as a colourless liquid.
^{1}H NMR (500 MHz, $CDCl_3$): δ 2.88 (s, 1H), 5.51 (d, J = 2.0 Hz, 1H), 5.52 (d, J = 2.0 Hz, 1H), 7.06–7.07 (m, 2H), 7.21–7.35 (m, 6H), 7.54–7.56 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 79.0 (dd, J_{CF} = 26, 26 Hz), 119.7 (dd, J_{CF} = 260, 256 Hz), 123.69 (dd, J_{CF} = 9, 9 Hz), 123.72 (q, J_{CF} = 291 Hz), 127.0, 127.8, 127.9, 128.0, 128.6, 129.2, 131.3, 136.9, 141.4 (dd, J_{CF} = 23, 23 Hz). ^{19}F NMR

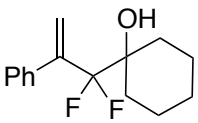
(470 MHz, $CDCl_3$): δ 57.9 (dq, J_{FF} = 249 Hz, J_{FF} = 12 Hz, 2F), 58.9 (dq, J_{FF} = 249 Hz, J_{FF} = 12 Hz, 2F), 89.5 (dd, J_{FF} = 12, 12 Hz). IR (neat): ν 3589, 3548, 1259, 1205, 1173, 1074, 916, 901, 729, 698 cm^{-1}. Elem. Anal. Calcd for $C_{17}H_{13}F_5O$: C, 62.20; H, 3.99. Found: C, 62.22; H, 4.20.

1-(1,1-Difluoro-2-phenylallyl)cyclopentan-1-ol (1g)



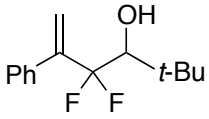
2,2-Difluorohomoallylic alcohol **1g** was prepared by the method described for **1a** using cyclopentanone (190 mg, 2.3 mmol), zinc powder (266 mg, 4.07 mmol) and 3-bromo-3,3-difluoropropene **3a** (468 mg, 2.01 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave **1g** (245 mg, 51%) as a colourless liquid.
^1H NMR (500 MHz, $CDCl_3$): δ 1.42–1.48 (m, 2H), 1.57–1.63 (m, 2H), 1.70–1.79 (m, 2H), 1.84–1.89 (s, 2H), 5.51 (s, 1H), 5.81 (s, 1H), 7.32–7.33 (m, 3H), 7.33–7.41 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 24.0, 35.6, 85.1 (t, J_{CF} = 29 Hz), 121.5 (t, J_{CF} = 9 Hz), 121.9 (t, J_{CF} = 287 Hz), 128.0, 128.1, 128.7, 138.3, 143.5 (t, J_{CF} = 22 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 55.9 (s). IR (neat): ν 3593, 3464, 2958, 2875, 1153, 1030, 1016, 937, 775, 698 cm^{-1}. HRMS (ESI+): *m*/*z* Calcd for $C_{14}H_{16}F_2NaO$ $[M + Na]^+$: 261.1067; Found: 261.1073.

1-(1,1-Difluoro-2-phenylallyl)cyclohexan-1-ol (1h)



2,2-Difluorohomoallylic alcohol **1h** was prepared by the method described for **1a** using cyclohexanone (389 mg, 3.96 mmol), zinc powder (240 mg, 3.67 mmol) and 3-bromo-3,3-difluoropropene **3a** (471 mg, 2.02 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave **1h** (424 mg, 83%) as a colourless liquid.
^1H NMR (500 MHz, $CDCl_3$): δ 1.14 (s, 1H), 1.36–1.56 (m, 10H), 5.45 (s, 1H), 5.66 (s, 1H), 7.24–7.25 (m, 3H), 7.34–7.35 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 20.6, 25.2, 30.6, 74.8 (t, J_{CF} = 27 Hz), 121.8 (t, J_{CF} = 10 Hz), 122.3 (t, J_{CF} = 254 Hz), 127.8, 128.1, 128.5, 138.5, 142.8 (t, J_{CF} = 24 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 52.4 (s). IR (neat): ν 3575, 3482, 2937, 2862, 1446, 1263, 1139, 1041, 987, 775, 698, 590 cm^{-1}. Elem. Anal. Calcd for $C_{15}H_{18}F_2O$: C, 71.41; H, 7.19. Found: C, 71.46; H, 7.28.

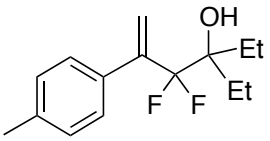
4,4-Difluoro-2,2-dimethyl-5-phenylhex-5-en-3-ol (1i)



2,2-Difluorohomoallylic alcohol **1i** was prepared by the method described for **1a** using

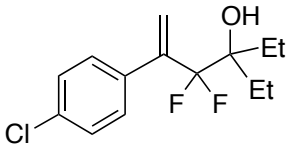
2,2-dimethylpropanal (95 mg, 1.1 mmol), zinc powder (133 mg, 2.0 mmol) and 3-bromo-3,3-difluoropropene **3a** (230 mg, 0.987 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave **1i** (106 mg, 45%) as a colourless liquid.
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.05 (s, 9H), 1.74 (s, 1H), 3.43 (dd, J_{HF} = 22.0, 5.3 Hz, 1H), 5.53 (d, J = 3.3 Hz, 1H), 5.81 (d, J = 3.3 Hz, 1H), 7.34–7.35 (m, 3H), 7.43–7.44 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 26.9 (dd, J_{CF} = 3, 3 Hz), 34.9, 77.2 (dd, J_{CF} = 26, 26 Hz), 119.2 (dd, J_{CF} = 11, 8 Hz), 122.6 (dd, J_{CF} = 254, 249 Hz), 128.1, 128.2, 128.4, 137.0 (d, J_{CF} = 4 Hz), 144.6 (dd, J_{CF} = 21, 21 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 50.4 (dd, J_{FF} = 248 Hz, J_{FH} = 22 Hz, 1F), 66.4 (d, J_{FF} = 248 Hz, 1F). IR (neat): ν 3600, 3496, 2960, 2912, 2877, 1496, 1369, 1180, 1049, 1016, 935, 779, 698 cm^{-1}. HRMS (ESI+): *m*/*z* Calcd for $C_{14}H_{18}F_2NaO$ [M + Na]$^+$: 263.1223; Found: 263.1222.

3-Ethyl-4,4-difluoro-5-(4-methylphenyl)hex-5-en-3-ol (1j)



2,2-Difluorohomoallylic alcohol **1j** was prepared by the method described for **1a** using diethyl ketone (277 mg, 3.22 mmol), zinc powder (388 mg, 5.93 mmol) and 3-bromo-3,3-difluoropropene **3b** (744 mg, 3.01 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave **1j** (598 mg, 78%) as a colourless liquid.
^{1}H NMR (500 MHz, $CDCl_3$): δ 0.85 (t, J = 7.6 Hz, 6H), 1.53–1.68 (m, 4H), 2.34 (s, 3H), 5.48 (d, J = 2.4 Hz 1H), 5.74 (d, J = 2.4 Hz 1H), 7.13 (d, J = 7.9 Hz, 2H), 7.32 (d, J = 7.9 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 7.5, 21.1, 25.8, 77.8 (t, J_{CF} = 2 Hz), 121.0 (t, J_{CF} = 9 Hz), 123.3 (t, J_{CF} = 252 Hz), 128.5, 128.9, 135.6, 137.8, 143.3 (t, J_{CF} = 23 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 56.9 (s). IR (neat): ν 3597, 2974, 2887, 1084, 912, 742 cm^{-1}. HRMS (ESI+): *m*/*z* Calcd for $C_{15}H_{20}F_2NaO$ [M + Na]$^+$: 277.1380; Found: 277.1382.

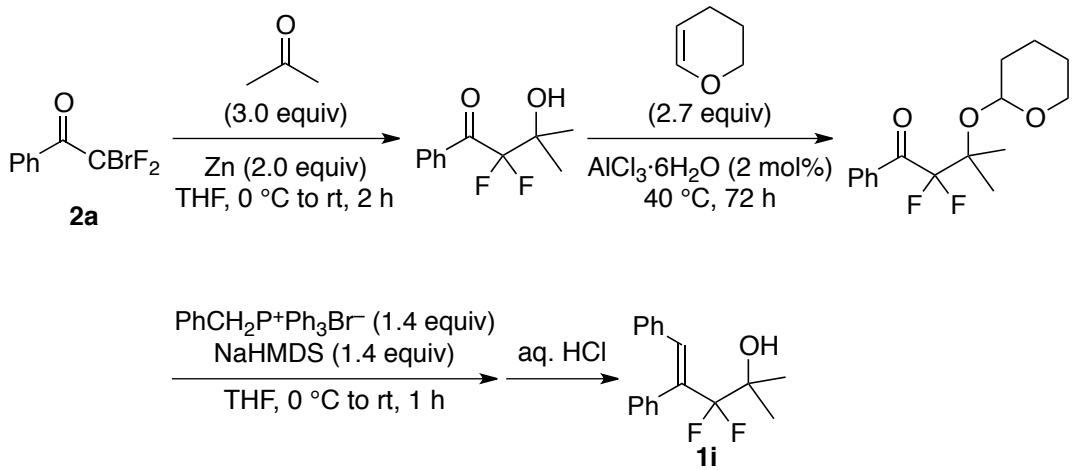
5-(4-Chlorophenyl)-3-ethyl-4,4-difluorohex-5-en-3-ol (1k)



2,2-Difluorohomoallylic alcohol **1k** was prepared by the method described for **1a** using diethyl ketone (261 mg, 3.03 mmol), zinc powder (131 mg, 2.0 mmol) and 3-bromo-3,3-difluoropropene **3c** (267 mg, 0.998 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1) gave **1k** (93 mg, 34%) as a colourless oil.
^{1}H NMR (500 MHz, $CDCl_3$): δ 0.86 (t, J = 7.6 Hz, 6H), 1.57–1.65 (m, 4H), 5.50 (s, 1H), 5.78 (s, 1H), 7.28–7.32 (m, 2H), 7.36 (d, J = 8.5 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 7.4, 25.6, 77.7 (t, J_{CF} = 26 Hz), 122.0 (t, J_{CF} = 9 Hz), 122.0 (t, J_{CF} = 254 Hz), 128.2, 130.0, 133.9, 137.0, 142.6 (t, J_{CF}

= 24 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 58.1 (s). IR (neat): ν 3587, 3469, 2974, 2887, 1493, 1092, 835 cm^{-1}. HRMS (ESI+): *m*/*z* Calcd for $C_{14}H_{17}ClF_2NaO$ $[M + H]^+$: 275.1014; Found: 275.1009.

3,3-Difluoro-2-methyl-4,5-diphenylpent-4-en-2-ol (1l)



2a **1i**

To the mixture of acetone (870 mg, 15.0 mmol) and zinc powder (activated with an aqueous HCl solution, 645 mg, 9.87 mmol) in THF (5.0 mL) was added a THF (5.0 mL) solution of bromodifluorodifluoromethyl ketone **2a** (1.17 g, 4.98 mmol) at 0 °C over 30 min. Then, the reaction mixture was warmed to room temperature and stirred at room temperature for 2 h. The reaction was quenched with aqueous HCl solution (2 M, 5 mL). Organic materials were extracted with dichloromethane three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 10/1) to give 2,2-difluoro-3-hydroxy-3-methyl-phenylbutan-1-one (423 mg, 40%) as a colourless liquid.

Spectral data for this compound showed good agreement with the literature data.[5]

To the mixture of 2,2-difluoro-3-hydroxy-3-methyl-phenylbutan-1-one (513 mg, 2.39 mmol) and 3,4-dihydro-2*H*-pyran (546 mg, 6.49 mmol) was added $AlCl_3 \cdot 6H_2O$ (12 mg, 0.050 mmol) at room temperature. After stirring at 40 °C for 72 h, the reaction was quenched with water. Organic materials were extracted with dichloromethane three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 10/1) to give 2,2-difluoro-3-methyl-1-phenyl-3-[(tetrahydro-2*H*-pyran-2-yl)oxy]butan-1-one (687 mg, 96%) as a colourless liquid.

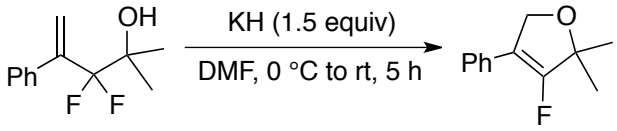
2,2-Difluoro-3-methyl-1-phenyl-3-[(tetrahydro-2*H*-pyran-2-yl)oxy]butan-1-one: ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.26–1.57 (m, 12H), 3.39–3.43 (m, 1H), 3.68–3.73 (m, 1H), 4.91 (dd, *J* = 3.4, 3.4 Hz, 1H), 7.44 (dd, *J* = 8.1, 7.5 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 8.13 (d, *J* = 8.1 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 18.82, 18.85, 21.9 (dd, J_{CF} = 3, 3 Hz), 25.0, 30.9, 61.7, 78.8 (dd, J_{CF} = 26, 26 Hz), 93.2, 118.5 (dd, J_{CF} = 260, 260 Hz), 127.9, 130.5, 133.5, 134.6, 191.8 (dd, J_{CF} = 28, 28 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 50.9 (d, J_{FF} = 253 Hz, 1F), 51.5 (d, J_{FF} = 253 Hz, 1F). IR (neat): ν

2947, 1695, 1138, 1108, 1024, 897, 715 cm^{-1}. HRMS (ESI+): *m*/*z* Calcd for $C_{16}H_{20}F_2NaO_3$ $[M + Na]^+$: 321.1278; Found: 321.1268.

To a THF (5.0 mL) solution of benzyltriphenylphosphonium bromide (603 mg, 1.39 mmol) was added NaHMDS (1.9 M in THF, 0.750 mL, 1.4 mmol) at –78 °C over 0.5 h. After stirring at –78 °C for 1 h, the reaction mixture was warmed to 0 °C. After stirring at 0 °C for 1 h, a THF (1.0 mL) solution of 2,2-difluoro-3-methyl-1-phenyl-3-[(tetrahydro-2*H*-pyran-2-yl)oxy]butan-1-one (305 mg, 1.02 mmol) was added to the reaction mixture at 0 °C over 0.5 h. After stirring at room temperature for 1 h, the reaction was quenched with an aqueous HCl solution (2 M, 5 mL). Organic materials were extracted with ether and were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by silica gel column gel chromatography (hexane/ethyl acetate = 1/1) to give **1l** (230 mg, 78%, *E*/*Z* = 99/1) as white solid.
(*E*)-**1i**: mp 76.5–77.2 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.31 (s, 6H), 2.17 (s, 1H), 6.89 (m, 2H), 7.06–7.13 (m, 4H), 7.30–7.33 (m, 5H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 24.2, 74.8 (t, J_{CF} = 29 Hz), 122.2 (t, J_{CF} = 253 Hz), 127.5 (t, J_{CF} = 64 Hz), 127.8, 127.9, 128.5, 129.8, 130.5, 133.3 (t, J_{CF} = 10 Hz), 134.6 (t, J_{CF} = 23 Hz), 134.9, 135.9. ^{19}F NMR (470 MHz, $CDCl_3$): δ 55.2 (s). IR (neat): ν 3560, 3477, 3059, 2987, 1448, 1225, 1151, 1066, 943, 719, 696 cm^{-1}. HRMS (ESI+): *m*/*z* Calcd for $C_{18}H_{19}F_2O$ $[M + H]^+$: 289.1404; Found: 289.1399.

5. Synthesis of 3-Fluoro-2,5-dihydrofurans 4

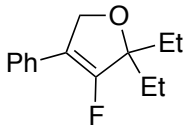
3-Fluoro-2,2-dimethyl-4-phenyl-2,5-dihydrofuran (4a)



1a **4a**

To the suspension of potassium hydride (9.1 mg, 0.23 mmol) in DMF (2 mL) was slowly added 2,2-difluorohomoallylic alcohol **1a** (32 mg, 0.15 mmol) at 0 °C. Then, the reaction mixture was warmed to room temperature and stirred at 0 °C for 5 h. Organic materials were extracted with ether three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by silica gel column gel chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) to give **4a** (24 mg, 85%) as a colourless oil.
^{1}H NMR (500 MHz, $CDCl_3$): δ 1.45 (s, 6H), 4.92 (d, J_{HF} = 4.9 Hz, 2H), 7.26–7.29 (m, 1H), 7.35–7.39 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 25.6, 69.9 (d, J_{CF} = 10 Hz), 82.0 (d, J_{CF} = 25 Hz), 107.9 (d, J_{CF} = 4 Hz), 126.3 (d, J_{CF} = 6 Hz), 127.6 (d, J_{CF} = 1 Hz), 128.6, 130.2 (d, J_{CF} = 5 Hz), 157.7 (d, J_{CF} = 286 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 24.1 (t, J_{FH} = 5 Hz). IR (neat): ν 2966, 914, 744, 669, 656 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{12}H_{13}FO$ $[M]^+$: 192.0950; Found: 192.0960.

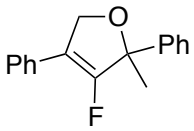
2,2-Diethyl-3-fluoro-4-phenyl-2,5-dihydrofuran (4b)



3-Fluoro-2,5-dihydrofurans **4b** was synthesised by the method described for **4a** using potassium hydride (18 mg, 0.45 mmol) and 2,2-difluorohomoallylic alcohol **1b** (72 mg, 0.30 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave **4b** (56 mg, 86%) as a colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.95 (t, J = 7.4 Hz, 6H), 1.65–1.77 (m, 4H), 4.94 (d, J_{HF} = 4.8 Hz, 2H), 7.25–7.30 (m, 1H), 7.35–7.41 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 7.8, 30.7 (d, J_{CF} = 3 Hz), 72.0 (d, J_{CF} = 10 Hz), 88.4 (d, J_{CF} = 23 Hz), 110.5 (d, J_{CF} = 4 Hz), 126.3 (d, J_{CF} = 6 Hz), 127.5 (d, J_{CF} = 2 Hz), 128.6, 130.2 (d, J_{CF} = 6 Hz), 154.4 (d, J_{CF} = 285 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 25.6 (t, J_{FH} = 5 Hz). IR (neat): ν 2970, 2854, 1704, 912, 733, 650 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{14}H_{13}FO$ $[M]^+$: 220.1263; Found: 220.1268.

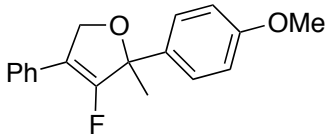
3-Fluoro-2-methyl-2,4-diphenyl-2,5-dihydrofuran (4c)



3-Fluoro-2,5-dihydrofurans **4c** was synthesised by the method described for **4a** using potassium hydride (9.1 mg, 0.23 mmol) and 2,2-difluorohomoallylic alcohol **1c** (41 mg, 0.15 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave **4c** (28 mg, 74%) as a colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.81 (s, 3H), 5.05 (d, J = 10.8 Hz, J_{HF} = 4.9 Hz, 1H), 5.08 (d, J = 10.8 Hz, J_{HF} = 5.0 Hz, 1H), 7.24–7.31 (m, 2H), 7.33–7.40 (m, 6H), 7.51–7.53 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 25.4 (d, J_{CF} = 3 Hz), 70.6 (d, J_{CF} = 10 Hz), 84.8 (d, J_{CF} = 24 Hz), 108.8 (d, J_{CF} = 4 Hz), 124.9, 126.4 (d, J_{CF} = 6 Hz), 127.6, 127.7 (d, J_{CF} = 1 Hz), 128.4, 128.6, 129.9 (d, J_{CF} = 5 Hz), 143.2 (d, J_{CF} = 4 Hz), 156.1 (d, J_{CF} = 289 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 27.5 (dd, J_{FH} = 5, 5 Hz). IR (neat): ν 3089, 3060, 3030, 2935, 2979, 2852, 1699, 1498, 1446, 1072, 1022, 762, 692 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{17}H_{15}FO$ $[M]^+$: 254.1107; Found: 254.1112.

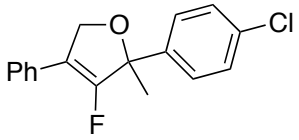
3-Fluoro-2-(4-methoxyphenyl)-2-methyl-4-phenyl-2,5-dihydrofuran (4d)



3-Fluoro-2,5-dihydrofurans **4d** was synthesised by the method described for **4a** using potassium hydride (9.1 mg, 0.23 mmol) and 2,2-difluorohomoallylic alcohol **1d** (46 mg, 0.15 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave **4d** (40 mg, 93%) as a colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.78 (s, 3H), 3.79 (s, 3H), 5.03 (dd, J = 10.6 Hz, J_{HF} = 4.9 Hz, 1H), 5.06 (dd, J = 10.6 Hz, J_{HF} = 4.9 Hz, 1H), 6.89–6.90 (m, 2H), 7.24–7.27 (m, 1H), 7.33–7.42 (m, 4H), 7.42–7.44 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 25.2 (d, J_{CF} = 3 Hz), 55.2, 70.5 (d, J_{CF} = 10 Hz), 84.6 (d, J_{CF} = 24 Hz), 108.6 (d, J_{CF} = 4 Hz), 113.7, 126.36 (d, J_{CF} = 3 Hz), 126.42, 127.7, 128.6, 130.0 (d, J_{CF} = 5 Hz), 135.4 (d, J_{CF} = 4 Hz), 156.4 (d, J_{CF} = 289 Hz), 159.1. ^{19}F NMR (470 MHz, $CDCl_3$): δ 27.7 (dd, J_{FH} = 5, 5 Hz). IR (neat): ν 2979, 2836, 1699, 1610, 1508, 1250, 1024, 829, 762, 692 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{18}H_{17}FO$ $[M]^+$: 284.1213; Found: 284.1204.

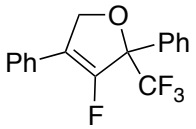
2-(4-Chlorophenyl)-3-fluoro-2-methyl-4-phenyl-2,5-dihydrofuran (4e)



3-Fluoro-2,5-dihydrofurans **4e** was synthesised by the method described for **4a** using potassium hydride (9.2 mg, 0.23 mmol) and 2,2-difluorohomoallylic alcohol **1e** (46 mg, 0.15 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave **4e** (30 mg, 69%) as a colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.76 (s, 3H), 5.02 (dd, J = 10.8 Hz, J_{HF} = 4.9 Hz, 1H), 5.06 (dd, J = 10.8 Hz, J_{HF} = 4.9 Hz, 1H), 7.24–7.35 (m, 7H), 7.43–7.44 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 25.5 (d, J_{CF} = 3 Hz), 70.7 (d, J_{CF} = 10 Hz), 84.5 (d, J_{CF} = 24 Hz), 109.1 (d, J_{CF} = 4 Hz), 126.4, 126.5, 127.9 (d, J_{CF} = 1 Hz), 128.6, 128.7, 129.7 (d, J_{CF} = 5 Hz), 133.5, 141.9 (d, J_{CF} = 3 Hz), 155.6 (d, J_{CF} = 289 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 27.0 (br s). IR (neat): ν 2981, 2854, 1701, 1489, 1092, 1012, 829, 762, 692 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{17}H_{14}ClFO$ $[M]^+$: 288.0717; Found: 288.0722.

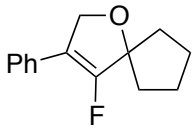
3-Fluoro-2,4-diphenyl-2-(trifluoromethyl)-2,5-dihydrofuran (4f)



3-Fluoro-2,5-dihydrofurans **4f** was synthesised by the method described for **4a** using potassium hydride (17 mg, 0.42 mmol) and 2,2-difluorohomoallylic alcohol **1f** (90 mg, 0.27 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave **4f** (51 mg, 60%) as a colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.11 (dd, J = 11.0 Hz, J_{HF} = 5.4 Hz, 1H), 5.24 (dd, J = 11.0 Hz, J_{HF} = 5.2 Hz, 1H), 7.32–7.46 (m, 8H), 7.72 (d, J = 7.4 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 72.3 (d, J_{CF} = 9 Hz), 114.9, 124.0 (qd, J_{CF} = 288, 4 Hz), 125.9, 126.8 (d, J_{CF} = 6 Hz), 127.9 (q, J_{CF} = 12 Hz), 128.5, 128.6 (q, J_{CF} = 15 Hz), 128.77, 128.81 (d, J_{CF} = 2 Hz), 129.2, 134.1 (d, J_{CF} = 4 Hz), 148.2 (d, J_{CF} = 289 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 27.7 (s, 1F), 85.4 (s, 3F). IR (neat): ν 3066, 2877, 2852, 1701, 1263, 1172, 912, 733, 690 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{17}H_{12}F_4O$ $[M]^+$: 308.0824; Found: 308.0827.

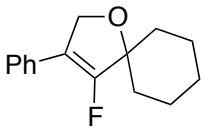
4-Fluoro-3-phenyl-1-oxaspiro[4.4]non-3-ene (4g)



3-Fluoro-2,5-dihydrofurans **4g** was synthesised by the method described for **4a** using potassium hydride (12 mg, 0.30 mmol) and 2,2-difluorohomoallylic alcohol **1g** (48 mg, 0.20 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave **4g** (23 mg, 52%) as a colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.65–1.75 (m, 2H), 1.78–1.96 (m, 6H), 4.87 (d, J_{HF} = 5.0 Hz, 2H), 7.23–7.27 (m, 1H), 7.33–7.38 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 24.7, 36.6 (d, J_{CF} = 3 Hz), 70.1 (d, J_{CF} = 1 Hz), 92.1 (d, J_{CF} = 25 Hz), 108.7 (d, J_{CF} = 4 Hz), 126.2 (d, J_{CF} = 6 Hz), 127.4 (d, J_{CF} = 1 Hz), 128.5, 130.2 (d, J_{CF} = 6 Hz), 155.4 (d, J_{CF} = 285 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 25.2 (s). IR (neat): ν 2960, 2871, 2850, 1700, 1362, 1078, 993, 761, 692 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{14}H_{15}FO$ $[M]^+$: 218.1107; Found: 218.1111.

4-Fluoro-3-phenyl-1-oxaspiro[4.5]dec-3-ene (4h)



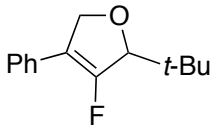
3-Fluoro-2,5-dihydrofurans **4h** was synthesised by the method described for **4a** using potassium hydride (15 mg, 0.37 mmol) and 2,2-difluorohomoallylic alcohol **1h** (63 mg, 0.25 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 25/1/1) gave **4h** (40 mg, 70%) as a white solid.

mp 58.6–59.2 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.21–1.31 (m, 1H), 1.63–1.77 (m, 9H), 4.90 (d, J_{HF} = 4.9 Hz, 2H), 7.24–7.28 (m, 1H), 7.33–7.39 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.9, 24.9, 34.0 (d, J_{CF} = 3 Hz), 69.8 (d, J_{CF} = 10 Hz), 83.1 (d, J_{CF} = 23 Hz), 108.1 (d, J_{CF} = 4 Hz), 126.3 (d, J_{CF} = 6 Hz), 127.4 (d, J_{CF} = 1 Hz), 128.6, 130.4 (d, J_{CF} = 5 Hz), 158.3 (d, J_{CF} = 286 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 25.4 (s). IR (neat): ν 3060, 2933, 2852, 1703, 1078, 906, 731, 692 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{15}H_{17}FO$ $[M]^+$: 232.1263; Found: 232.1261.

<1 mmol scale>

3-Fluoro-2,5-dihydrofurans **4h** was synthesised by the method described for **4a** using potassium hydride (61 mg, 1.5 mmol) and 2,2-difluorohomoallylic alcohol **1h** (252 mg, 0.999 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave **4h** (117 mg, 50%) as a white solid.

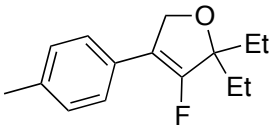
2-(*tert*-Butyl)-3-fluoro-4-phenyl-2,5-dihydrofuran (4i)



3-Fluoro-2,5-dihydrofurans **4i** was synthesised by the method described for **4a** using potassium hydride (9.1 mg, 0.23 mmol) and 2,2-difluorohomoallylic alcohol **1i** (37 mg, 0.15 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave **4i** (26 mg, 77%) as a colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.01 (s, 9H), 4.47 (ddd, J_{HF} = 4.6 Hz, J = 4.6, 4.6 Hz 1H), 4.92 (dd, J = 10.8 Hz, J_{HF} = 4.2 Hz, 1H), 4.95 (dd, J = 10.8 Hz, J_{HF} = 4.6 Hz, 1H), 7.25–7.30 (m, 1H), 7.35–7.40 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 25.2 (d, J_{CF} = 2 Hz), 35.8 (d, J_{CF} = 4 Hz), 72.3 (d, J_{CF} = 10 Hz), 87.8 (d, J_{CF} = 22 Hz), 111.5 (d, J_{CF} = 4 Hz), 126.3 (d, J_{CF} = 6 Hz), 127.6 (d, J_{CF} = 2 Hz), 128.6, 130.0 (d, J_{CF} = 5 Hz), 154.2 (d, J_{CF} = 287 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 33.9 (s). IR (neat): ν 2956, 2850, 1697, 1498, 1363, 1078, 760, 692 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{14}H_{17}FO$ $[M]^+$: 220.1263; Found: 220.1258.

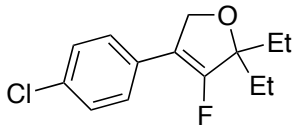
2,2-Diethyl-3-fluoro-4-(4-methylphenyl)-2,5-dihydrofuran (4j)



3-Fluoro-2,5-dihydrofurans **4j** was synthesised by the method described for **4a** using potassium hydride (46 mg, 1.1 mmol) and 2,2-difluorohomoallylic alcohol **1j** (190 mg, 0.75 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave **4j** (126 mg, 72%) as a colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.94 (t, J = 7.4 Hz, 6H), 1.64–1.76 (m, 4H), 2.35 (s, 3H), 4.94 (d, J_{HF} = 4.8 Hz, 2H), 7.18 (d, J = 8.2 Hz, 2H), 7.28 (d, J = 8.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 8.0, 21.2, 30.8 (d, J_{CF} = 3 Hz), 72.1 (d, J_{CF} = 11 Hz), 88.4 (d, J_{CF} = 24 Hz), 110.4 (d, J_{CF} = 4 Hz), 126.18, 126.23, 129.3, 137.4, 153.8 (d, J_{CF} = 284 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 24.4 (t, J_{FH} = 5 Hz). IR (neat): ν 2970, 2854, 1704, 912, 733, 650 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{15}H_{19}FO$ $[M]^+$: 234.1420; Found: 234.1428.

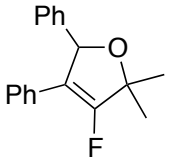
4-(4-Chlorophenyl)-2,2-diethyl-3-fluoro-2,5-dihydrofuran (4k)



3-Fluoro-2,5-dihydrofurans **4k** was synthesised by the method described for **4a** using potassium hydride (9.2 mg, 0.23 mmol) and 2,2-difluorohomoallylic alcohol **1k** (42 mg, 0.15 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave **4k** (28 mg, 71%) as a colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 0.92 (t, J = 7.4 Hz, 6H), 1.66–1.71 (m, 4H), 4.88 (d, J_{HF} = 4.9 Hz, 2H), 7.28–7.33 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 7.9, 30.7 (d, J_{CF} = 4 Hz), 71.8 (d, J_{CF} = 10 Hz), 88.5 (d, J_{CF} = 23 Hz), 109.7, 127.5 (d, J_{CF} = 6 Hz), 128.6 (d, J_{CF} = 5 Hz), 128.8, 133.2, 155.0 (d, J_{CF} = 289 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 27.9 (t, J_{FH} = 5 Hz). IR (neat): ν 2968, 2924, 2879, 2850, 1701, 1496, 1088, 1030, 827 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{14}H_{16}ClFO$ $[M]^+$: 254.0874; Found: 254.0870.

3-Fluoro-2,2-dimethyl-4,5-diphenyl-2,5-dihydrofuran (4l)

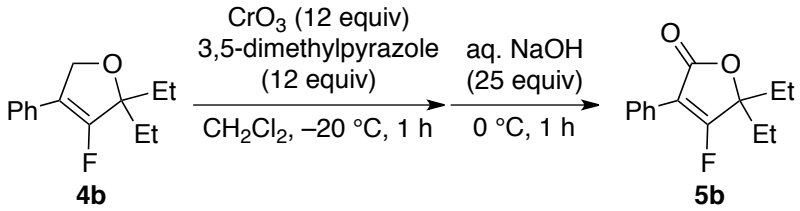


3-Fluoro-2,5-dihydrofurans **4l** was synthesised by the method described for **4a** using potassium hydride (18 mg, 0.45 mmol) and 2,2-difluorohomoallylic alcohol **1l** (*E*/*Z* = 99/1, 86 mg, 0.30 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave **4l** (42 mg, 52%) as a colourless oil.

^{1}H NMR (500 MHz, $CDCl_3$): δ 1.50 (s, 3H), 1.53 (s, 3H), 6.03 (d, J_{HF} = 4.5 Hz), 7.14–7.18 (m, 1H), 7.21–7.25 (m, 2H), 7.27–7.34 (m, 5H), 7.38–7.41 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 26.1 (d, J_{CF} = 3 Hz), 26.9 (d, J_{CF} = 3 Hz), 81.1 (d, J_{CF} = 24 Hz), 83.2 (d, J_{CF} = 10 Hz), 110.5, 127.27 (d, J_{CF} = 6 Hz), 127.30, 128.1, 128.4, 128.5, 128.7, 130.2 (d, J_{CF} = 5 Hz), 140.6, 159.7 (d, J_{CF} = 290 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 27.0 (d, J_{FH} = 5 Hz). IR (neat): ν 3064, 3030, 2978, 2927, 2886, 1695, 1496, 1448, 1142, 1016, 760, 692, 611 cm^{-1}. HRMS (EI): *m*/*z* Calcd for $C_{18}H_{17}FO$ $[M]^+$: 268.1263; Found: 268.1269.

6. Synthesis of 4-Fluorofuranones 5

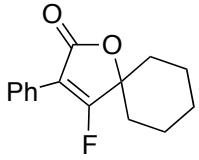
5,5-Diethyl-4-fluoro-3-phenylfuran-2(5*H*)-one (5b)



To the suspension of CrO_3 (60 mg, 0.60 mmol) in dichloromethane (0.5 mL) was added 3,5-dimethylpyrazole (59 mg, 0.61 mmol) at –20 °C. After stirring at –20 °C for 15 min, 3-fluoro-2,5-dihydrofurans **4b** (11 mg, 0.050 mmol) was added. After stirring at –20 °C for 1 h, an aqueous NaOH solution (5.0 M, 0.25 mL, 1.3 mmol) was added to the reaction mixture. Stirring at 0 °C for 1 h, the reaction was quenched with an aquous HCl solution (2 M, 0.5 mL). Organic materials were extracted with dichloromethane three times. The combined extracts were washed with brine and dried over Na_2SO_4. After removal of the solvent under reduced pressure, the residue was purified by silica gel column chromatography (hexane/ethyl acetate/Et_3N = 20/2/1) to give **5b**

(7.4 mg, 63%) as a colourless liquid.
^{1}H NMR (500 MHz, $CDCl_3$): δ 0.94 (t, J = 7.4 Hz, 6H), 1.88–2.05 (m, 4H), 7.38 (t, J = 7.4 Hz, 1H), 7.44 (dd, J = 7.4, 7.2 Hz, 2H), 7.90 (d, J = 7.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 7.3, 28.4 (d, J_{CF} = 3 Hz), 84.8 (d, J_{CF} = 21 Hz), 108.1, 126.4 (d, J_{CF} = 4 Hz), 127.7 (d, J_{CF} = 5 Hz), 128.6, 129.0, 169.1 (d, J_{CF} = 23 Hz), 176.2 (d, J_{CF} = 304 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 55.0 (s). IR (neat): ν 2978, 1755, 1689, 1703, 1198, 904, 727, 650 cm^{-1}. HRMS (EI): m/z Calcd for $C_{14}H_{15}FO_2$ $[M]^+$: 234.1056; Found: 234.1045.

4-Fluoro-3-phenyl-1-oxaspiro[4.5]dec-3-ene-2-one (5h)



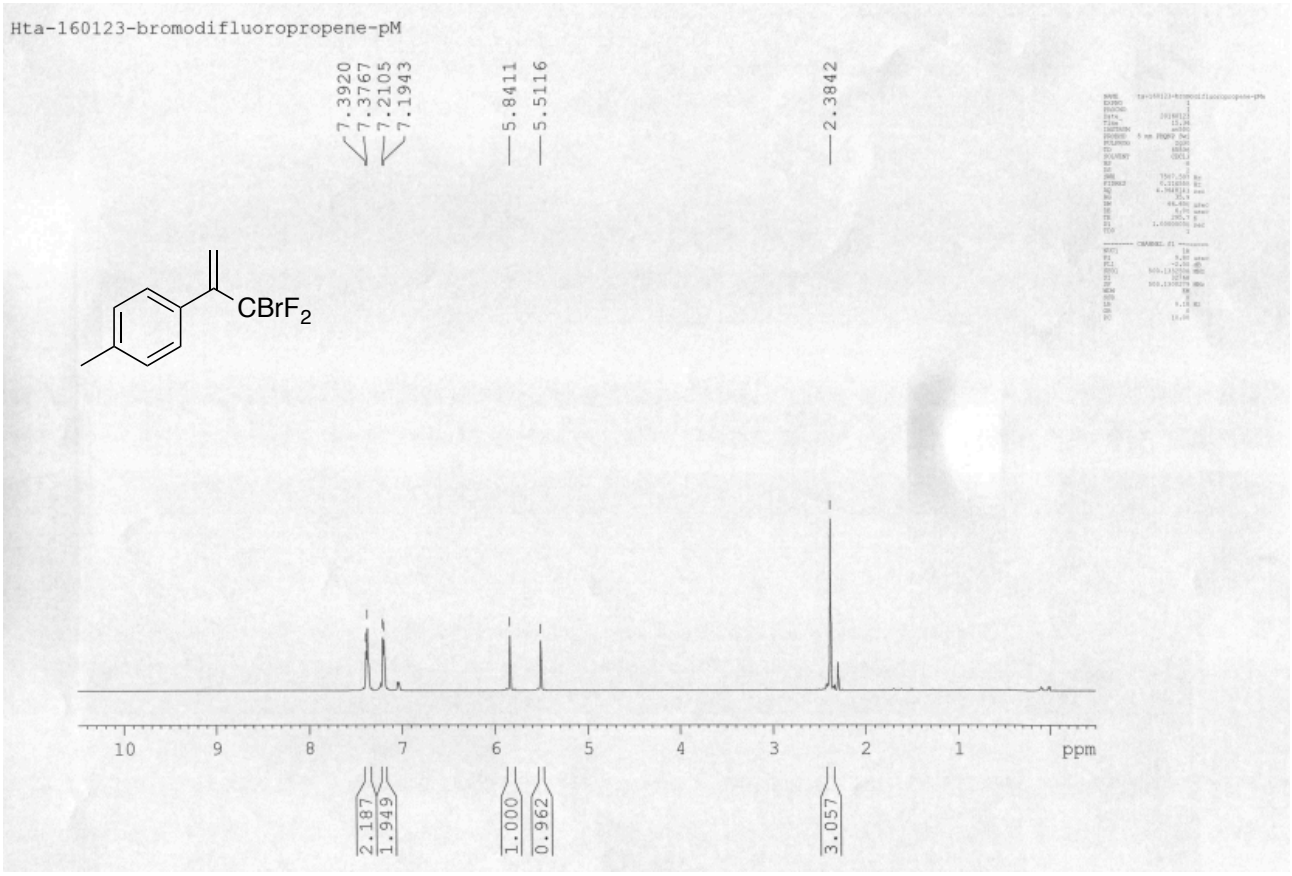
4-Fluorofuranone **5h** was synthesised by the method described for **5b** using CrO_3 (60 mg, 0.60 mmol), 3,5-dimethylpyrazole (59 mg, 0.62 mmol), 3-fluoro-2,5-dihydrofurans **4h** (13 mg, 0.056 mmol) and an aqueous NaOH solution (5.0 M, 0.25 mL, 1.3 mmol). Purification by silica gel column chromatography (hexane/ethyl acetate/triethylamine = 20/2/1) gave **5h** (10 mg, 76%) as a colourless oil.
mp 112.4–113.2 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 1.23–1.30 (m, 2H), 1.77–1.79 (m, 6H), 1.87–1.91 (m, 2H), 7.35–7.37 (m, 1H), 7.40–7.43 (m, 2H), 7.86–7.88 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 21.5, 24.2, 32.6 (d, J_{CF} = 2 Hz), 80.7 (d, J_{CF} = 21 Hz), 105.7, 126.6 (d, J_{CF} = 5 Hz), 127.7 (d, J_{CF} = 5 Hz), 128.5, 128.9, 168.7 (d, J_{CF} = 21 Hz), 179.1, (d, J_{CF} = 305 Hz). ^{19}F NMR (470 MHz, $CDCl_3$): δ 55.4 (s). IR (neat): ν 2941, 2858, 1757, 1699, 1362, 1192, 1126, 958, 787, 694 cm^{-1}. HRMS (EI): m/z Calcd for $C_{15}H_{15}FO_2$ $[M]^+$: 246.1056; Found: 246.1061.

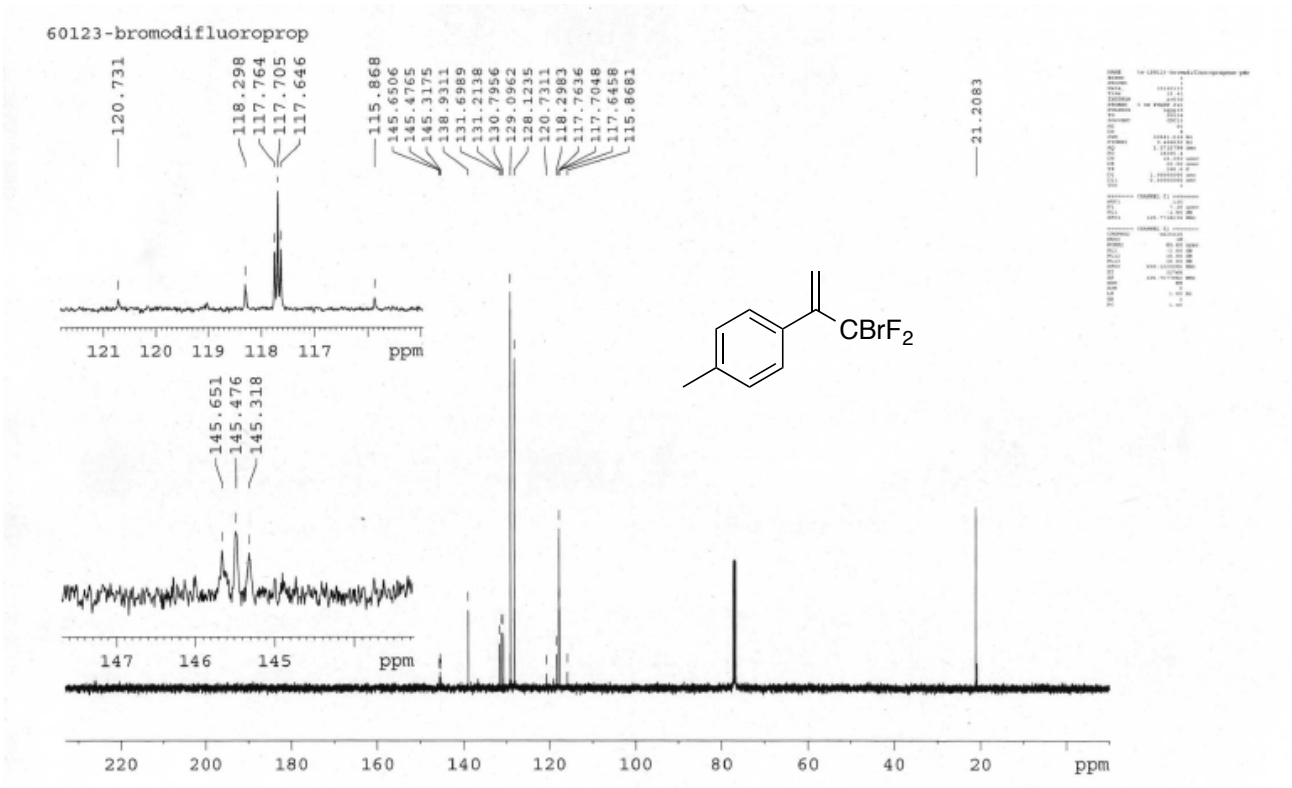
7. References

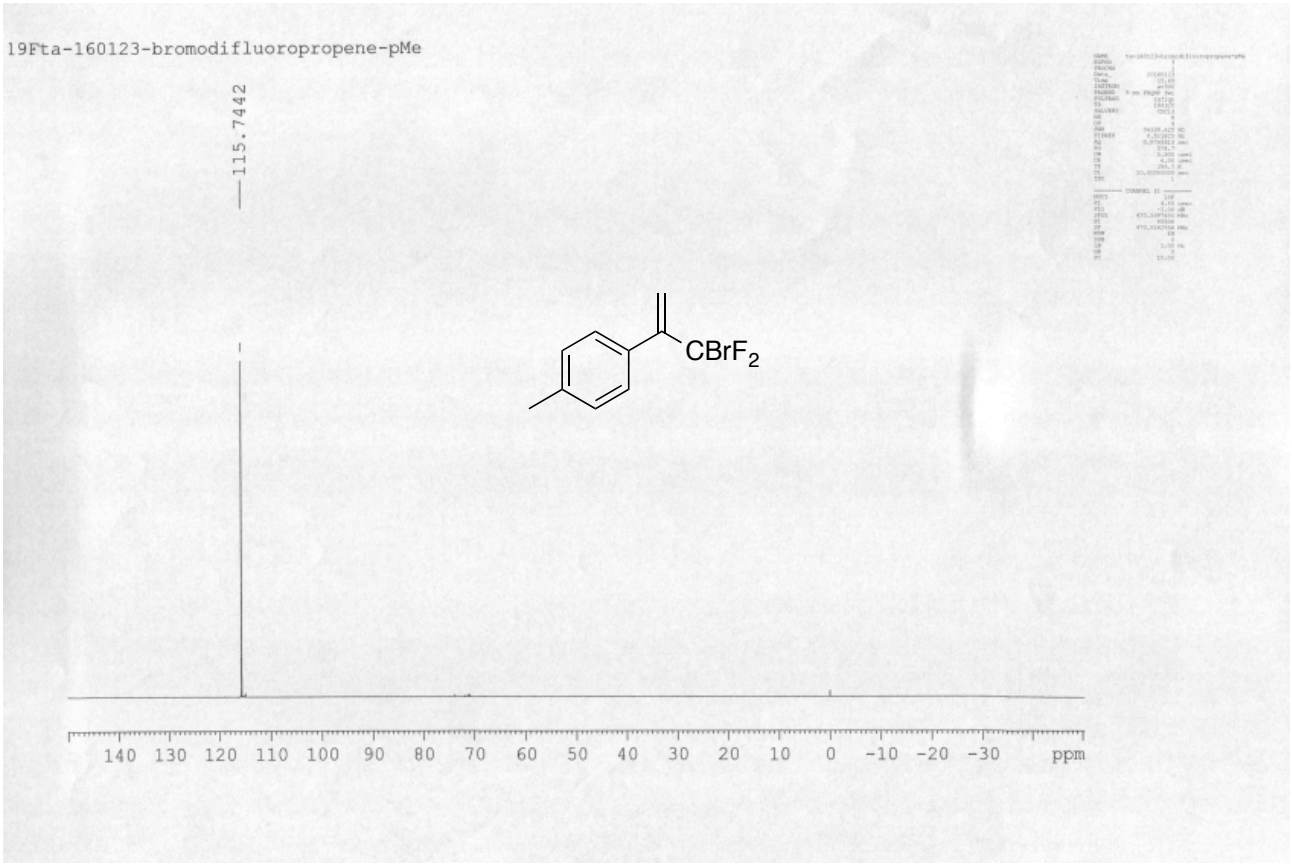
(1) T. Nihei, N. Iwai, T. Matsuda and T. Kitazume, *J. Org. Chem.*, 2005, **70**, 5912–5915.
(2) G. K. S. Prakash, J. Hu, M. M. Alauddin, P. S. Conti and G. A. Olar, *J. Fluorine Chem.*, 2003, **121**, 239–243.
(3) J. P. John and D. A. Colby, *J. Org. Chem.*, 2011, **76**, 9163–9168.
(4) Q.-Q. Min, Z. Yin, Z. Feng, W.-H. Guo and X. Zhang, *J. Am. Chem. Soc.*, 2014, **136**, 1230–1233.
(5) S. Sasaki, T. Suzuki, T. Uchiya, S. Toyota, A. Hirano, M. Tanemura, H. Teramoto, T. Yamauchi and K. Higashiyama, *J. Fluorine Chem.*, 2016, **192**, 78–85.

8. ^{1}H, ^{13}C and ^{19}F NMR charts

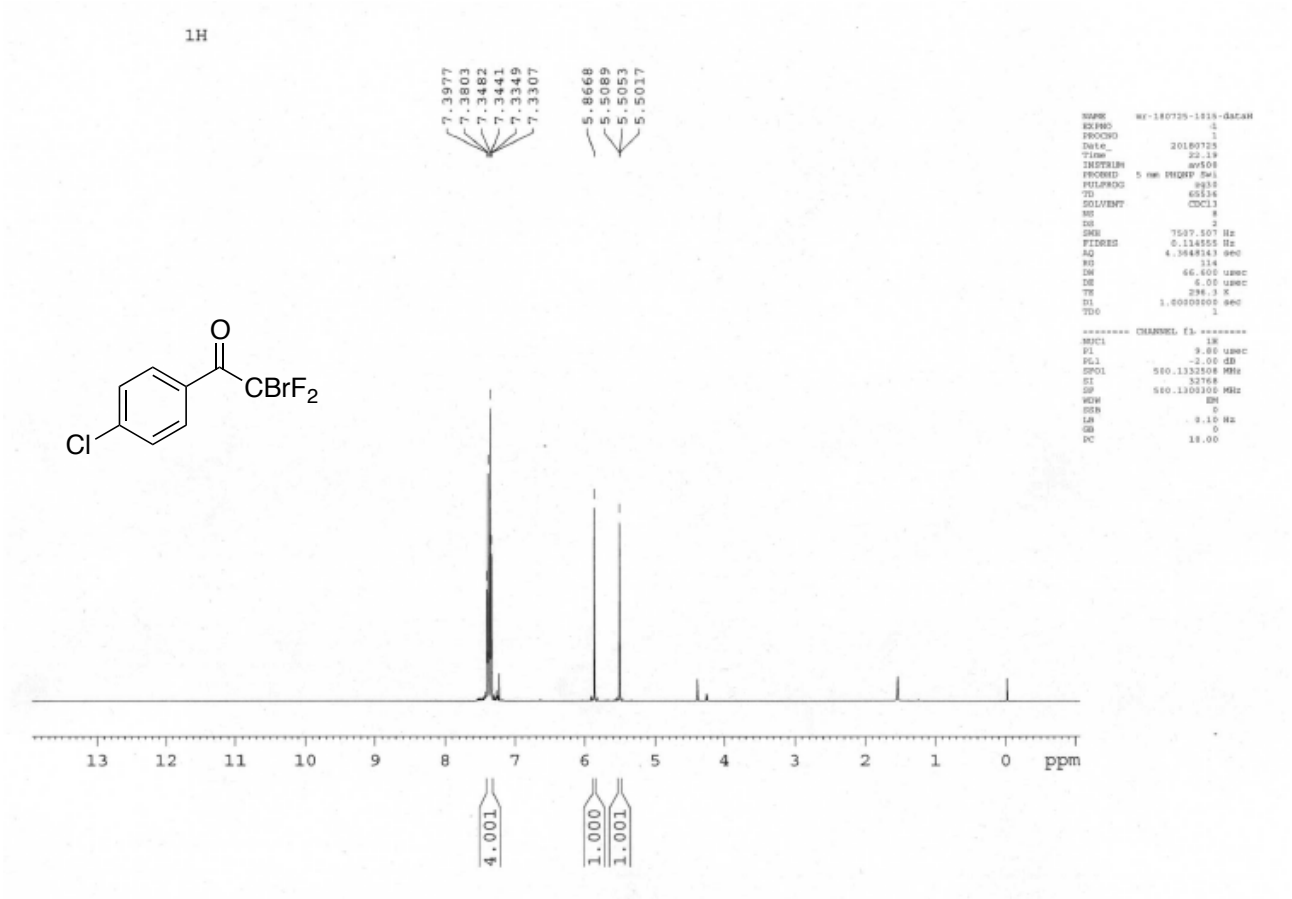
1-(3-Bromo-3,3-difluoroprop-1-en-2-yl)-4-methylbenzene (3b)

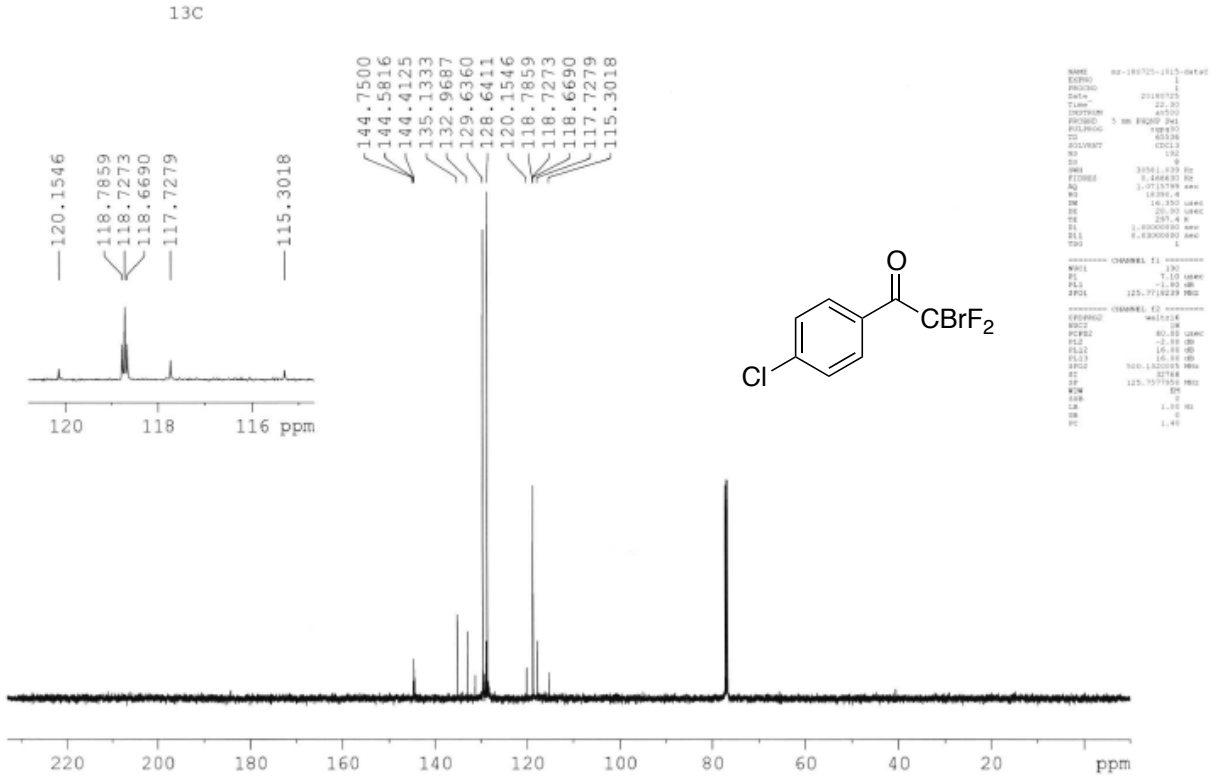






1-(3-Bromo-3,3-difluoroprop-1-en-2-yl)-4-chlorobenzene (3c)

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117.7279
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O
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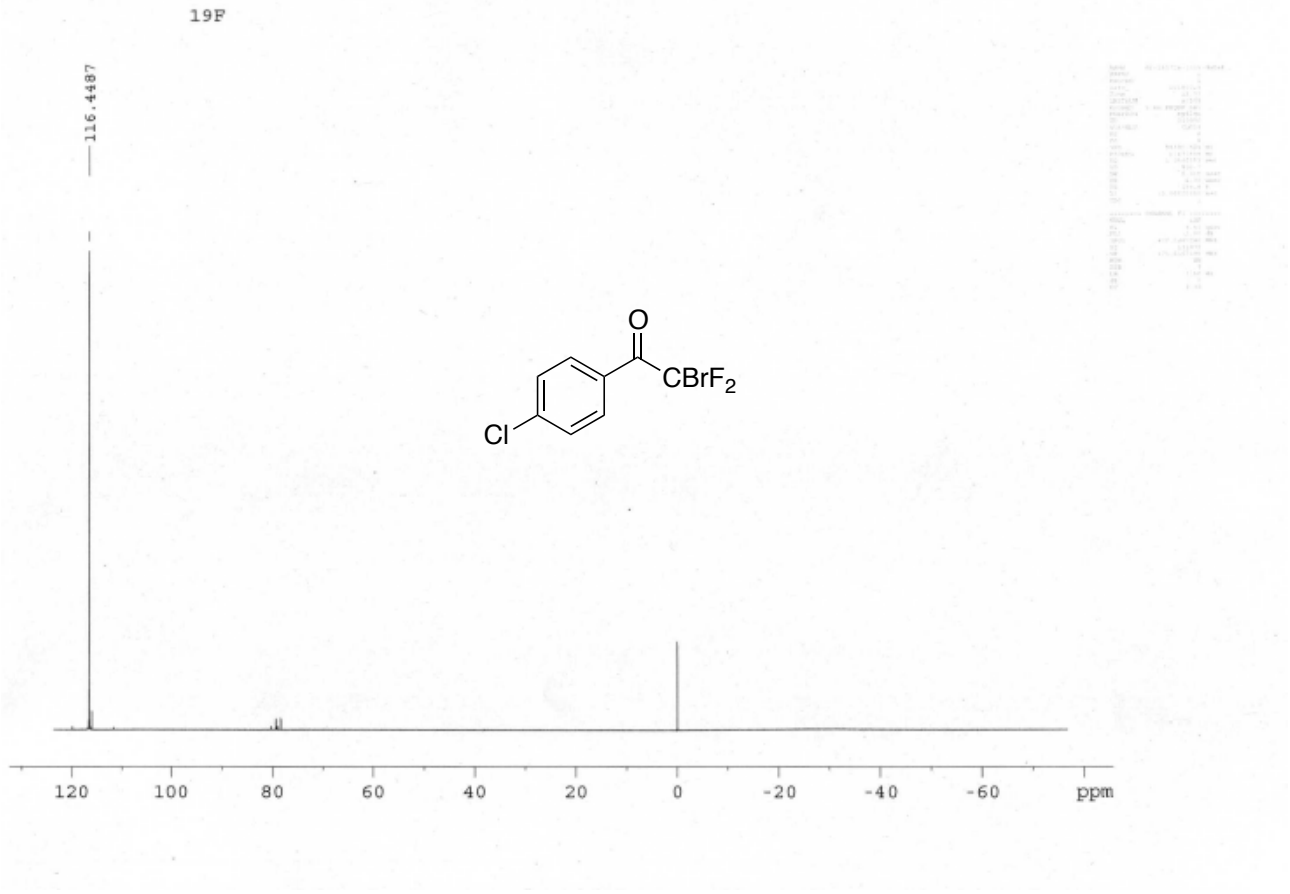
20
ppm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Cl
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100
80
60
40
20
0
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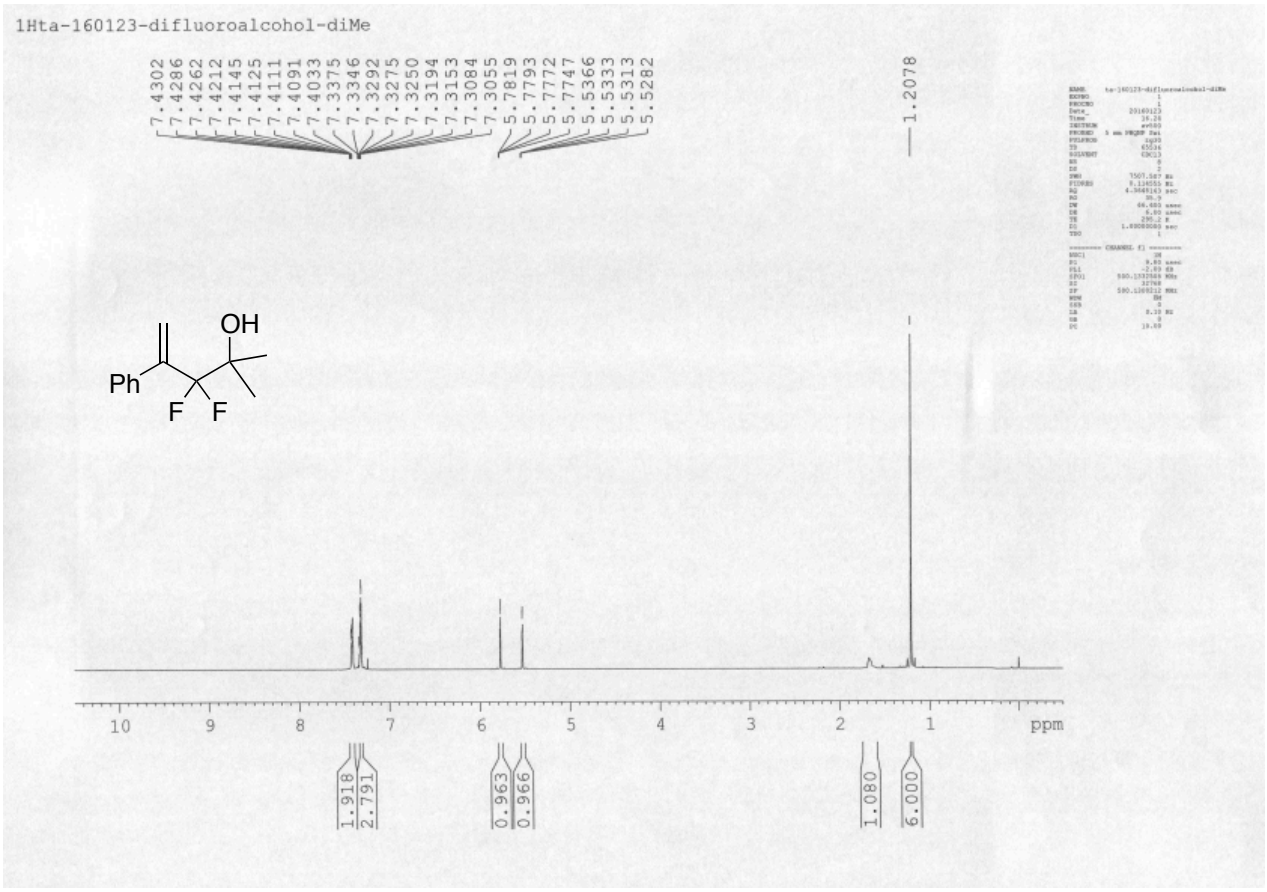
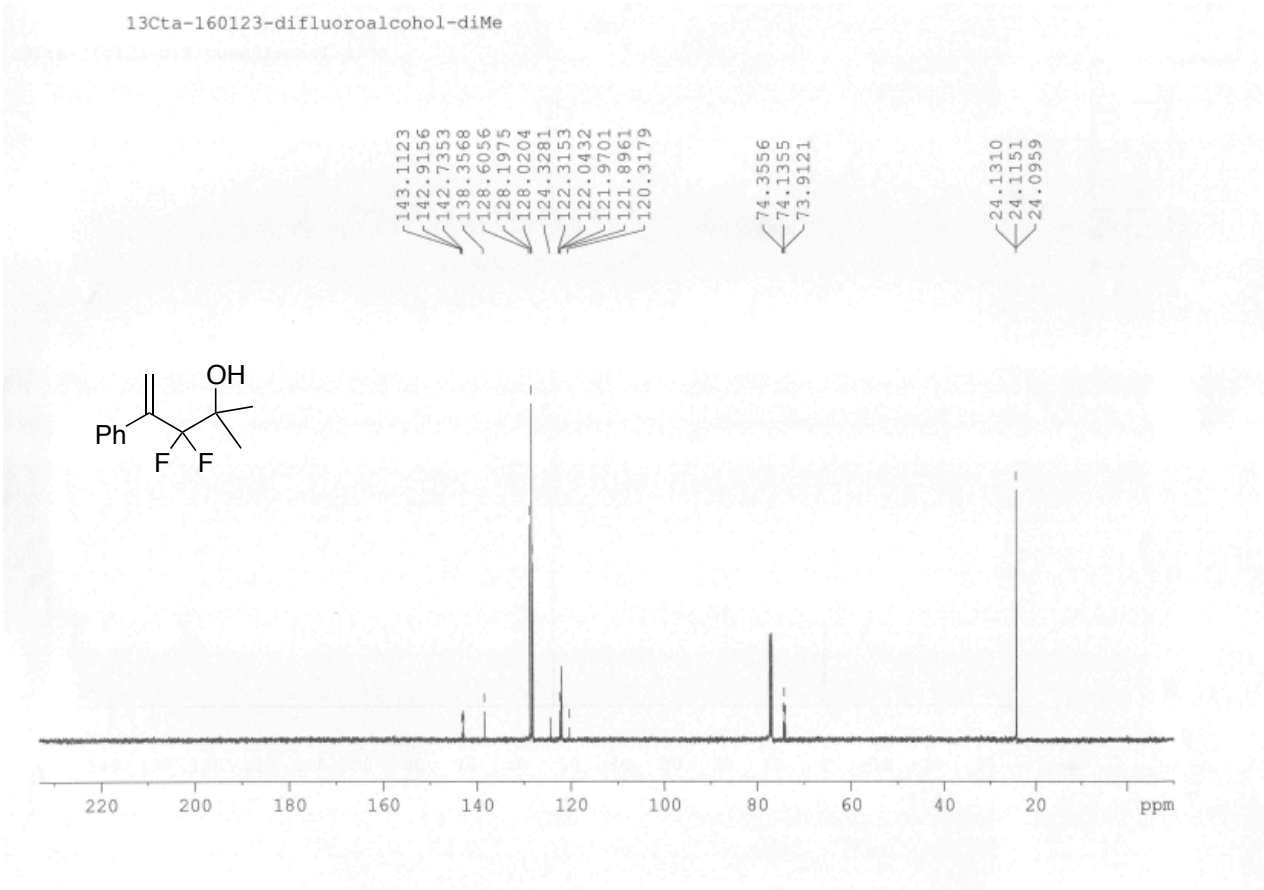
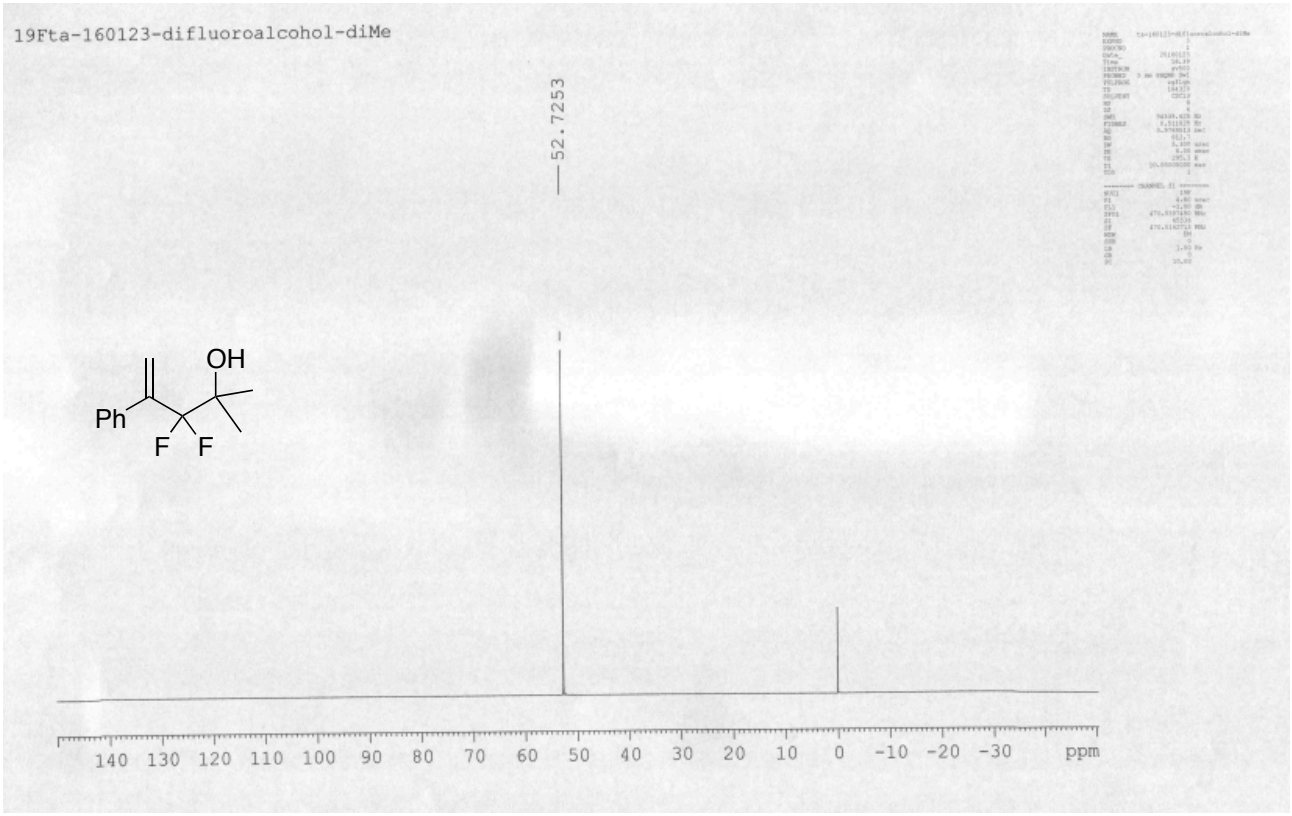
-40
-60
ppm

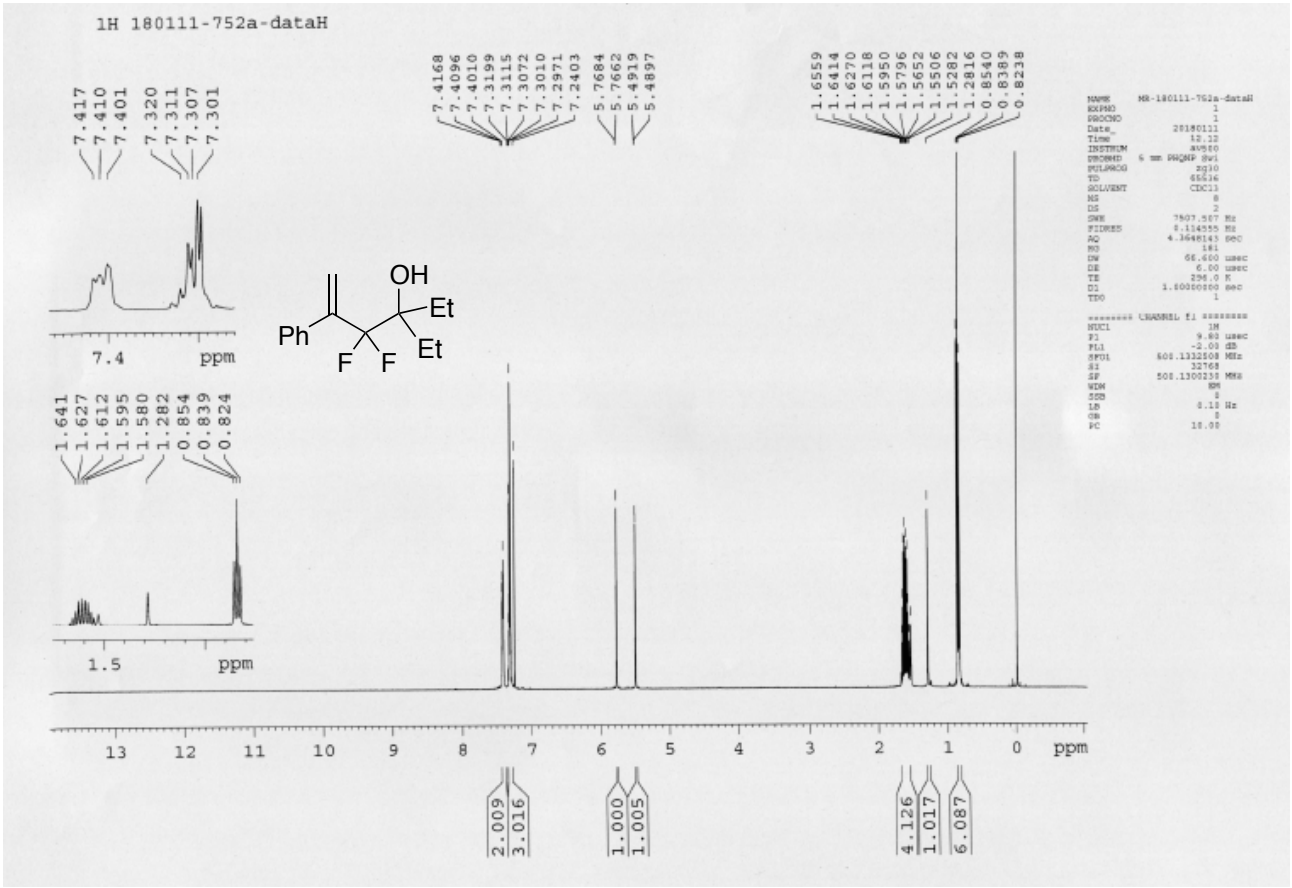
3,3-Difluoro-2-methyl-4-phenylpent-4-en-2-ol (1a)

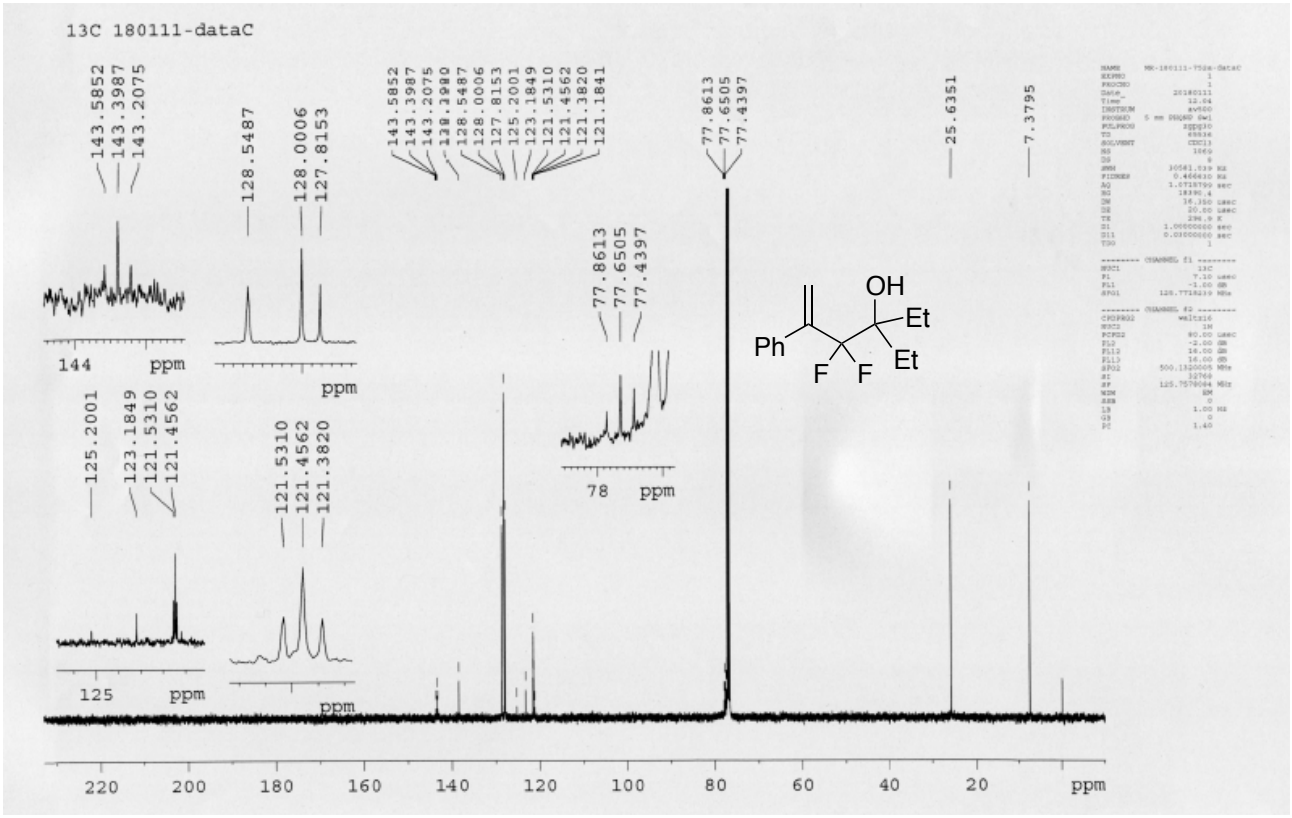






3-Ethyl-4,4-difluoro-5-phenylhex-5-en-3-ol (1b)

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Et
Ph
F
F
144 ppm
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125 ppm
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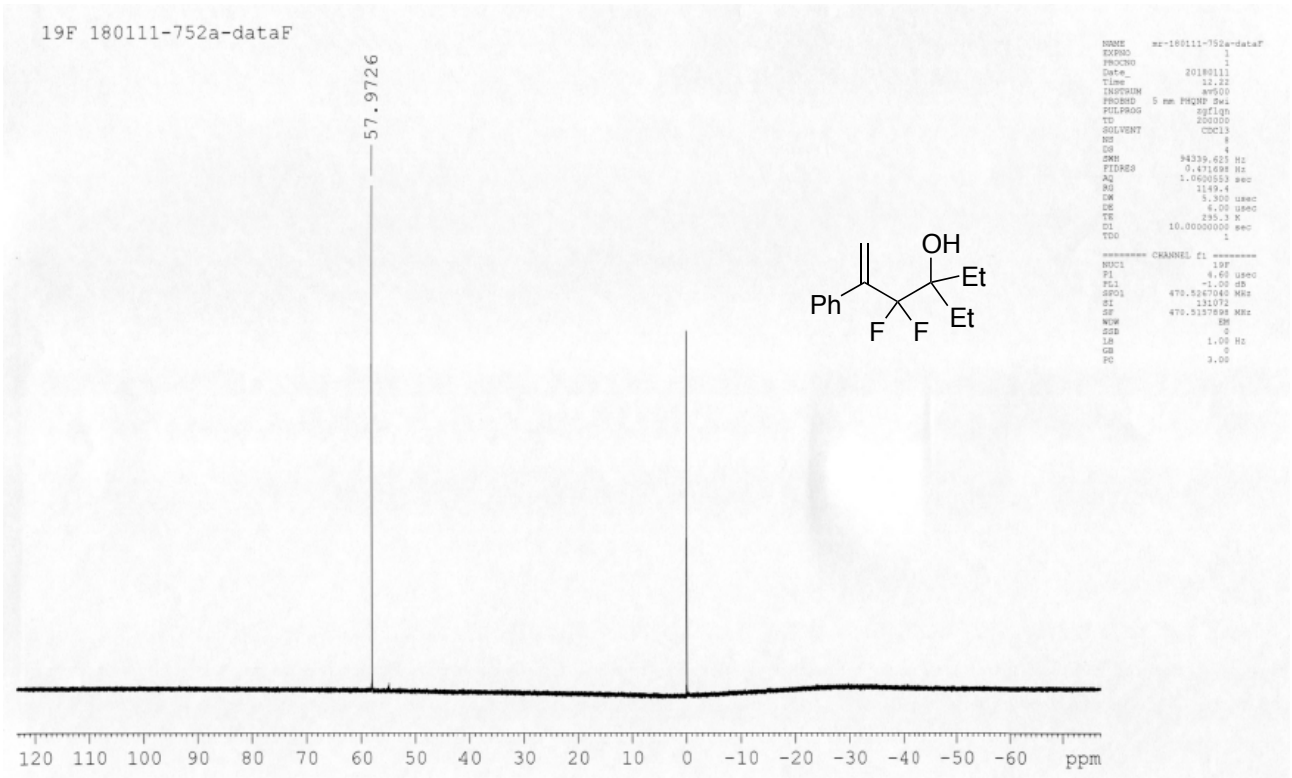
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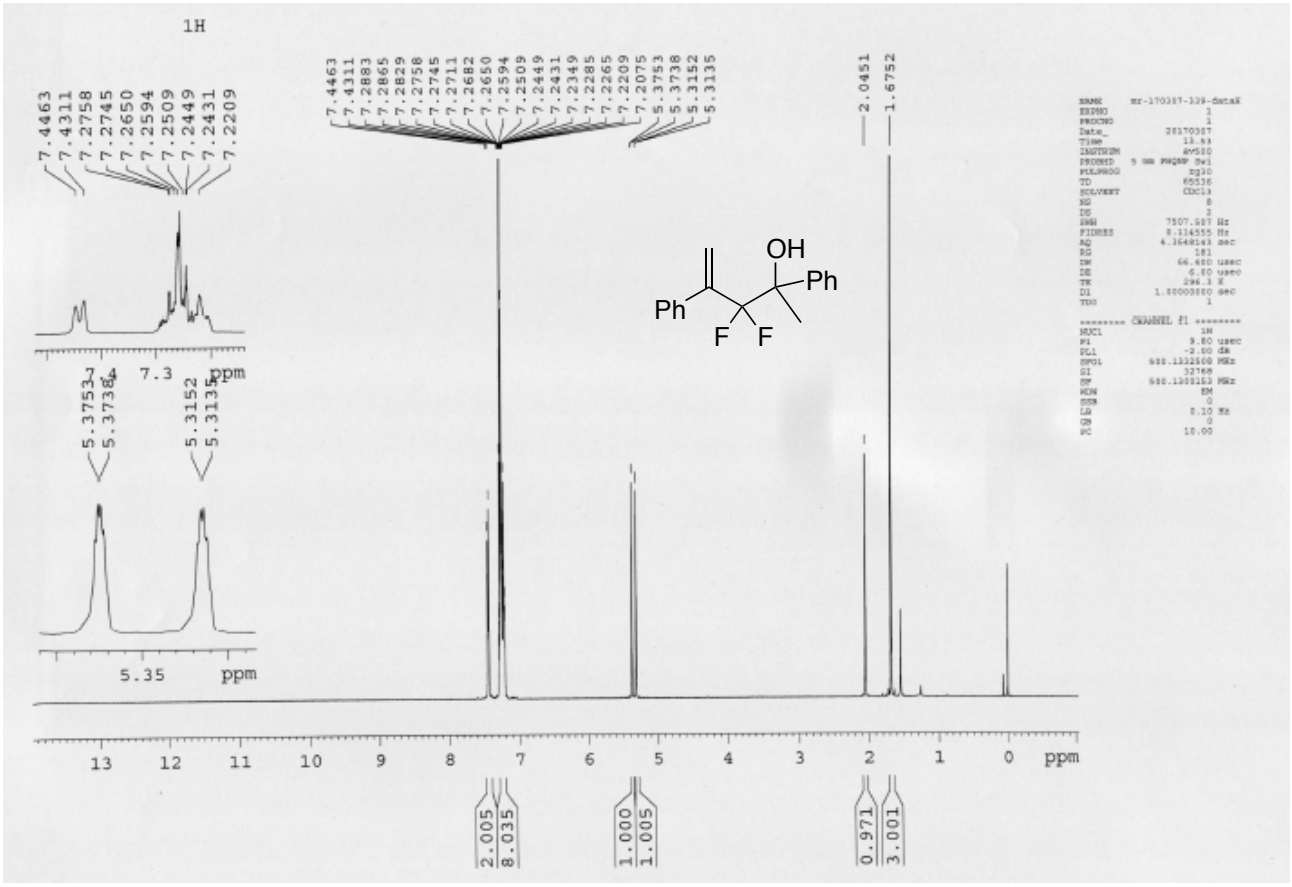
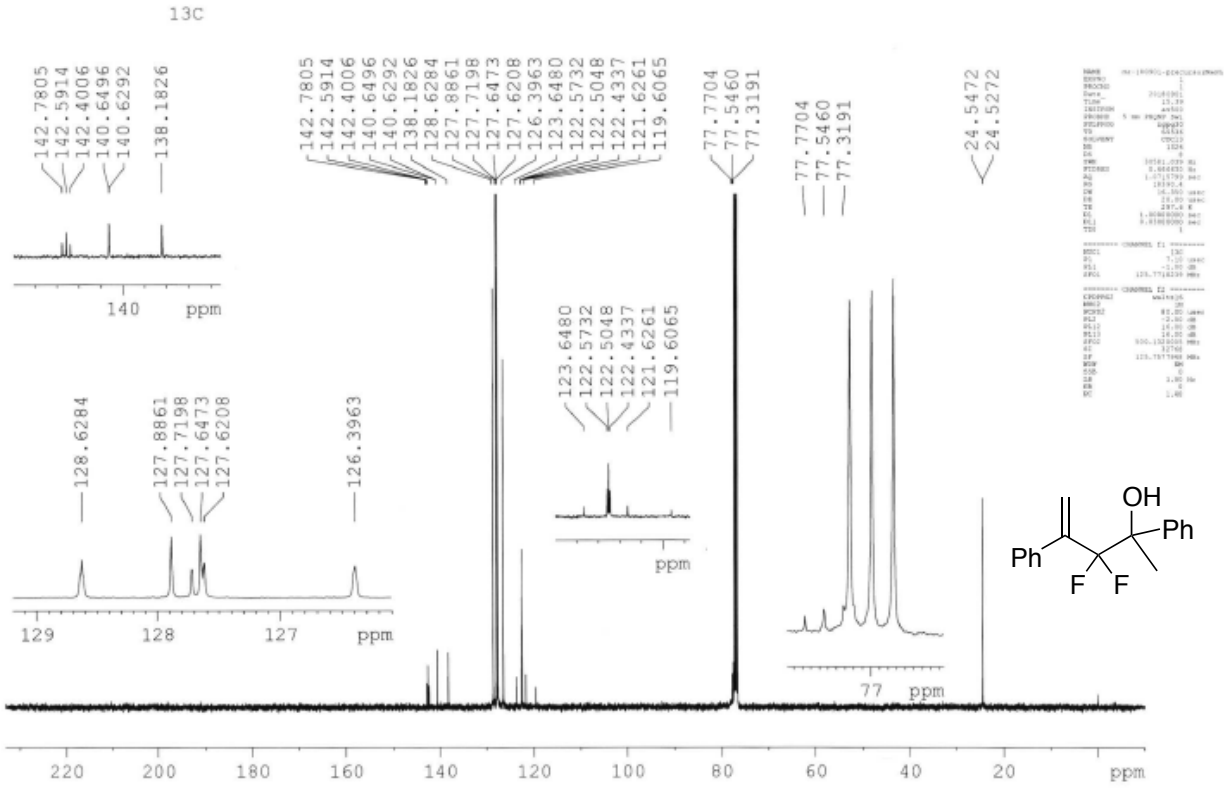
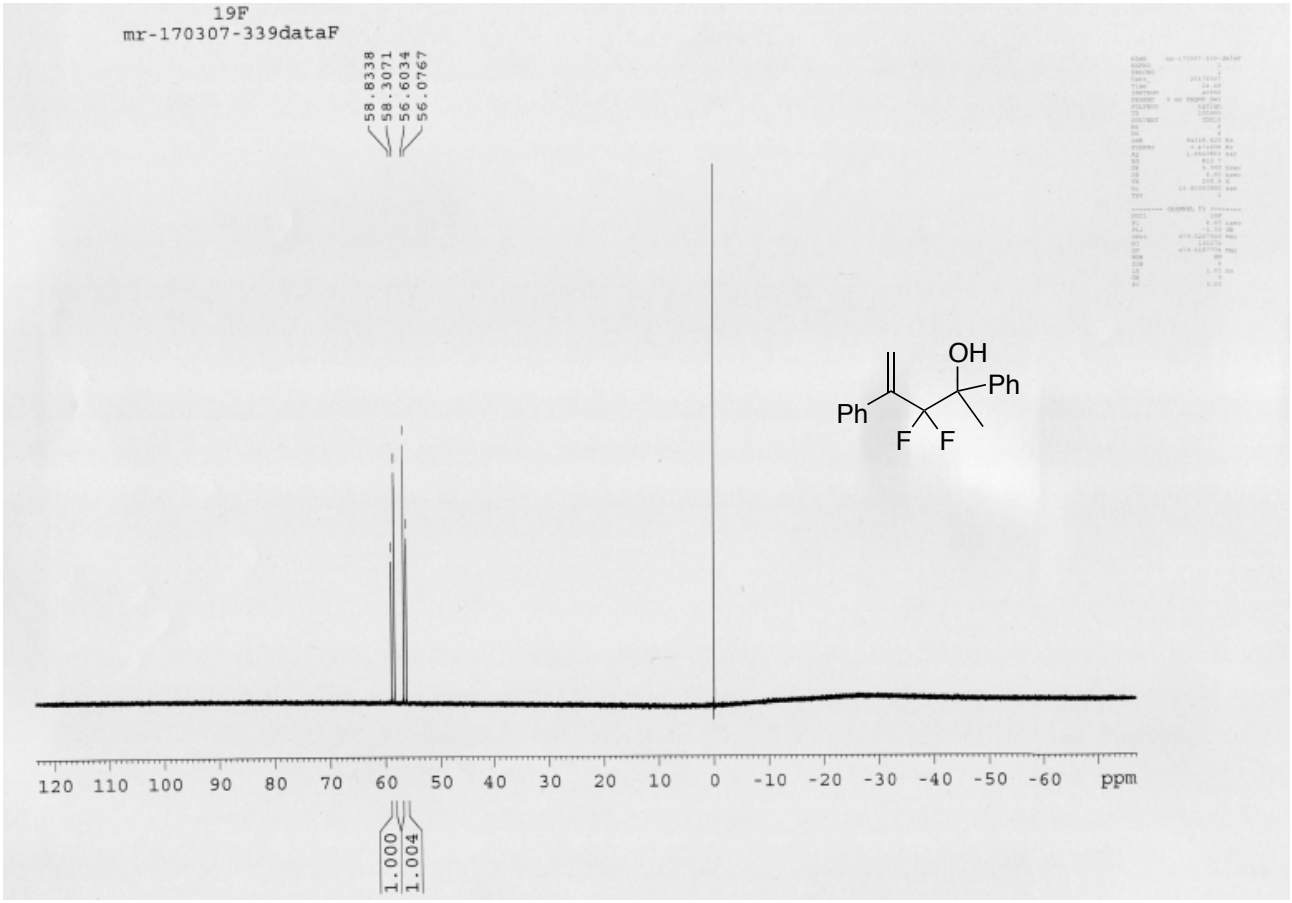
OH
Et
Et
Ph
F
F
120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 ppm

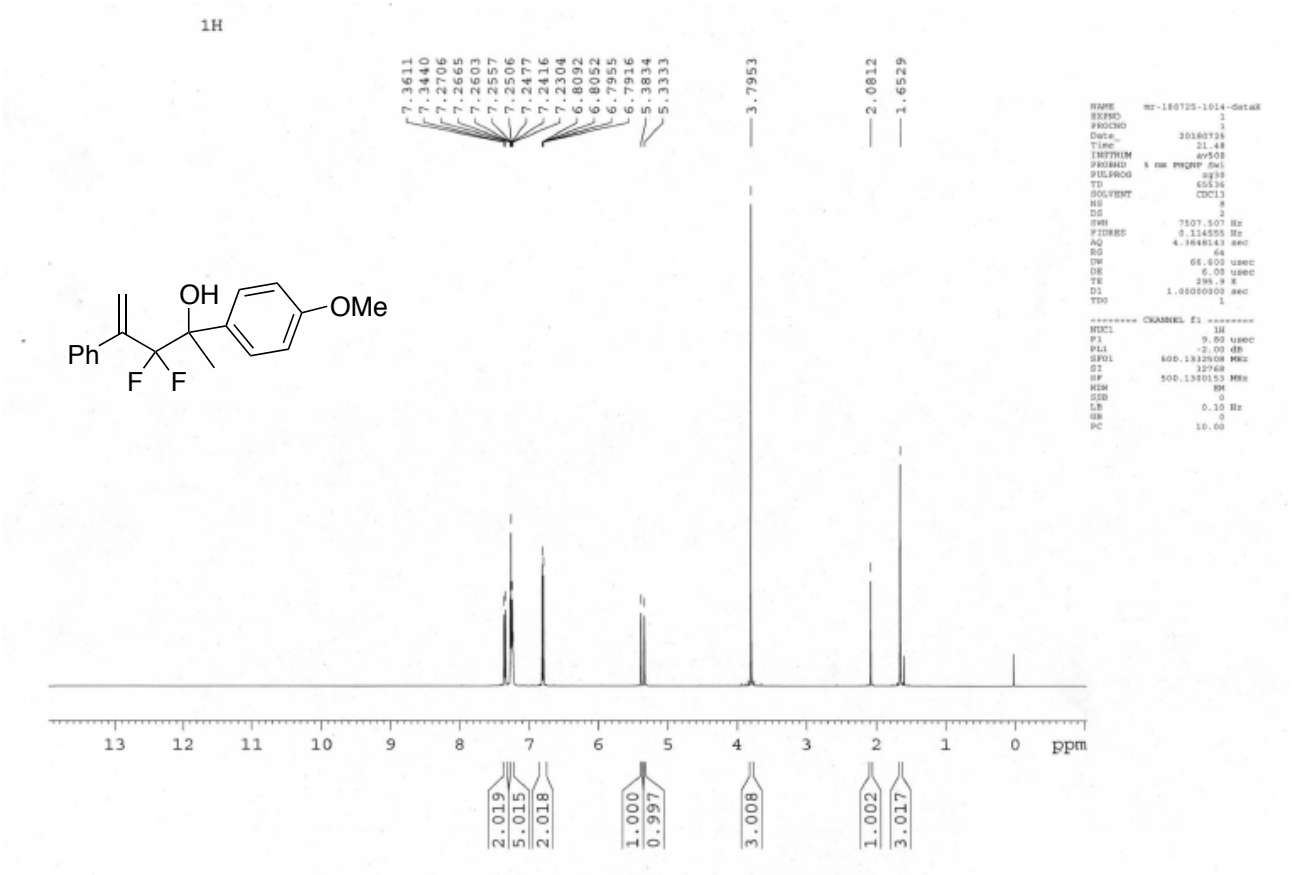
3,3-Difluoro-2,4-diphenylpent-4-en-2-ol (1c)

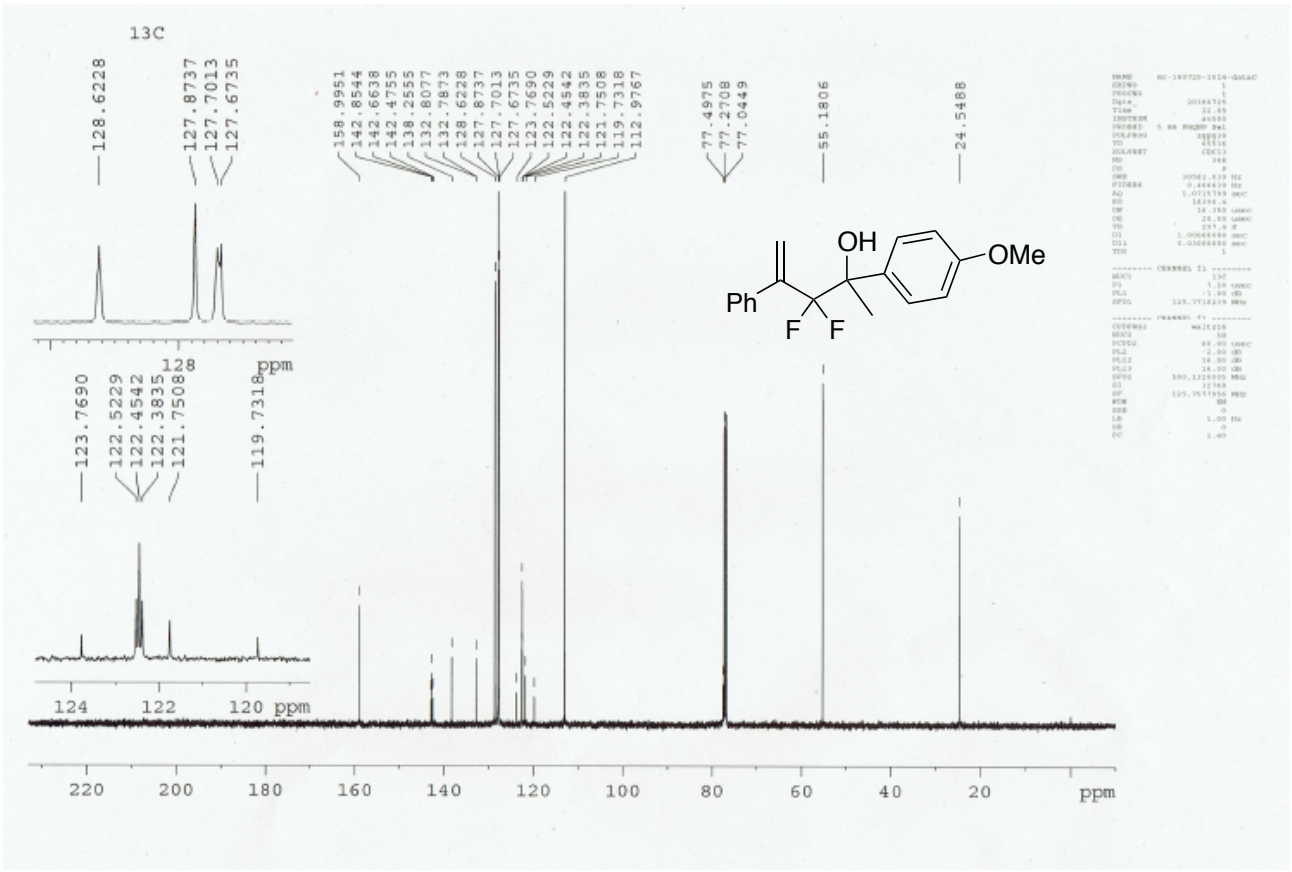


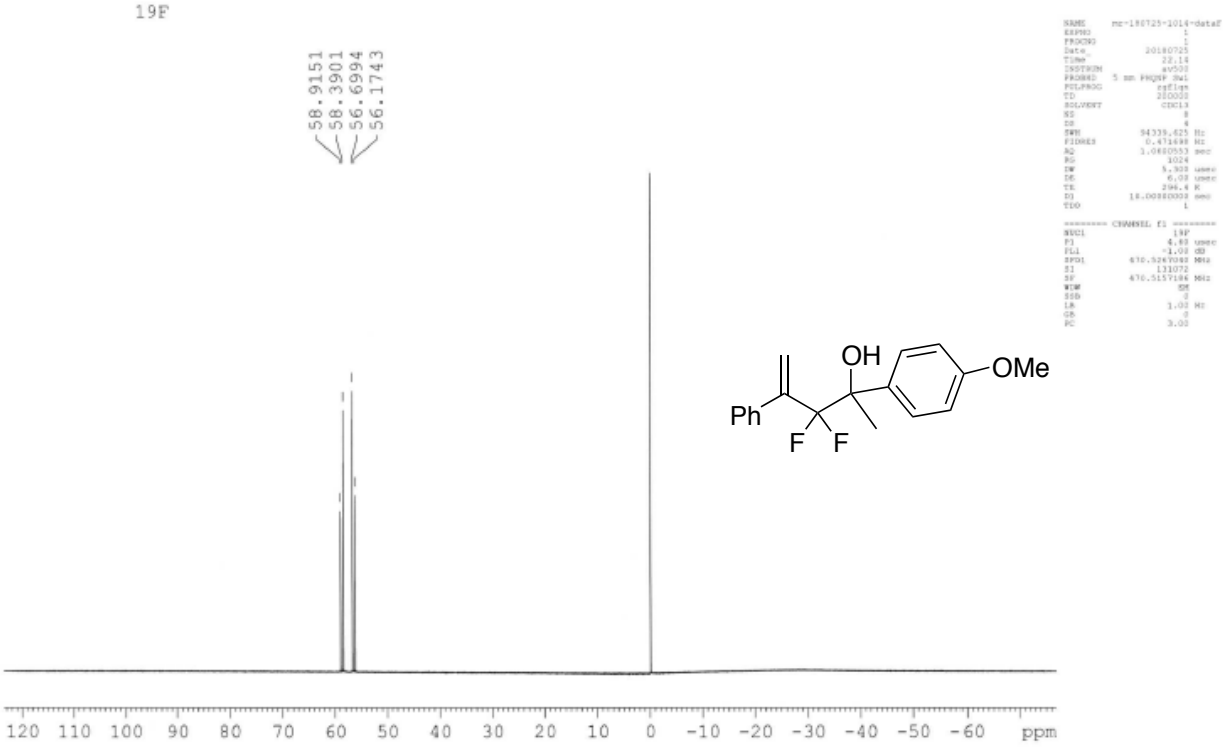




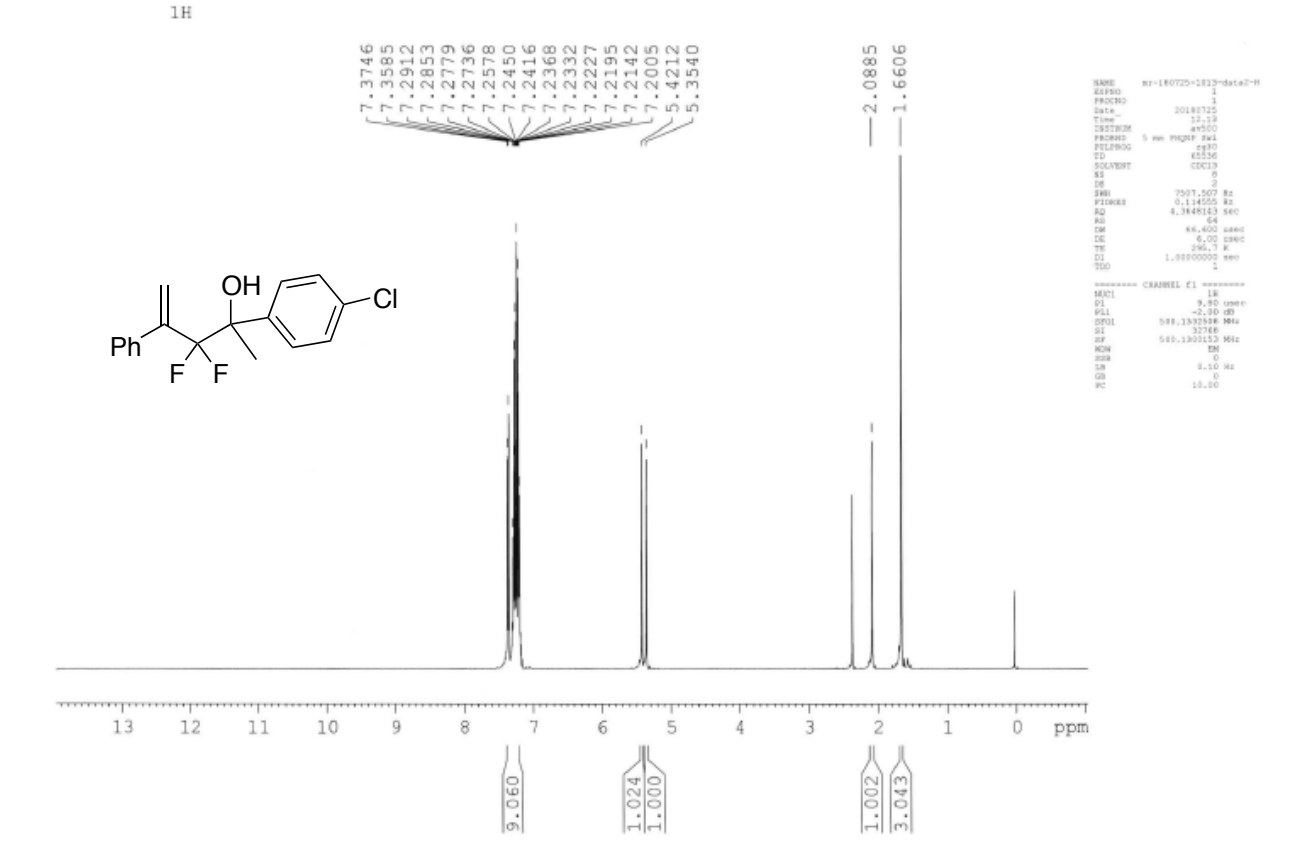
3,3-Difluoro-2-(4-methoxyphenyl)-4-phenylpent-4-en-2-ol (1d)

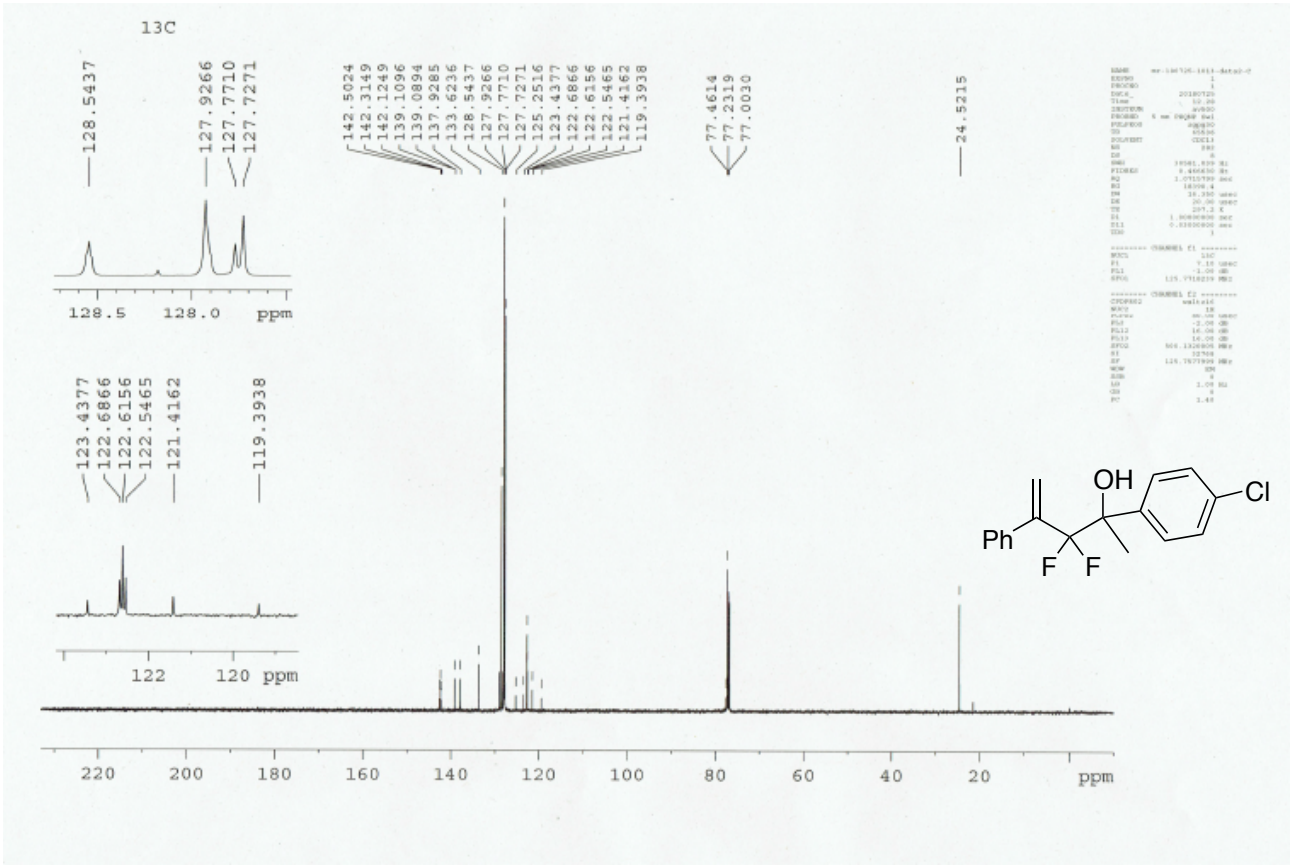


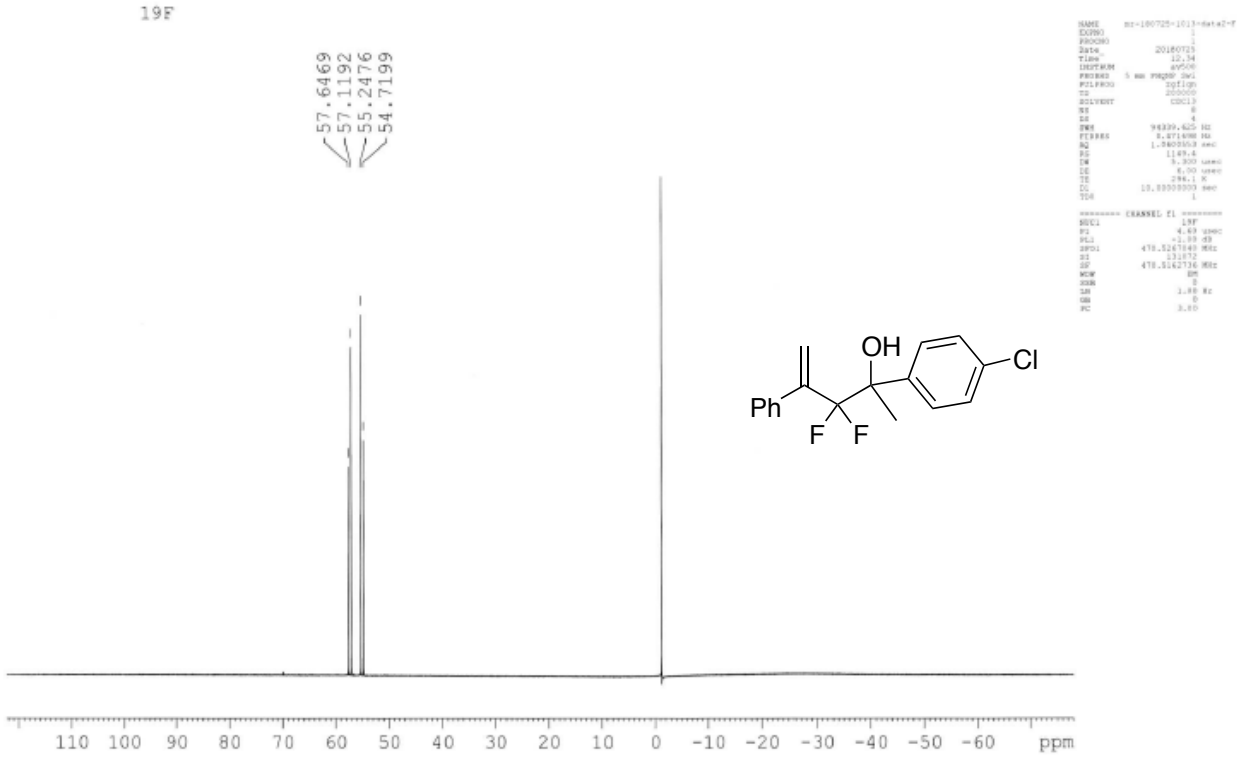

13C
128.6228
127.8737
127.7013
127.6735
158.9951
142.8544
142.6638
142.4755
138.2555
132.8077
132.7873
128.6228
127.8737
127.7013
127.6735
123.7690
122.5229
122.4542
122.3835
121.7508
119.7318
112.9767
77.4975
77.2708
77.0449
55.1806
24.5488
OH
OMe
Ph
F F
ppm
220 200 180 160 140 120 100 80 60 40 20 ppm


19F
58.9151
58.3901
56.6994
56.1743
OH
OMe
Ph
F F
120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 ppm

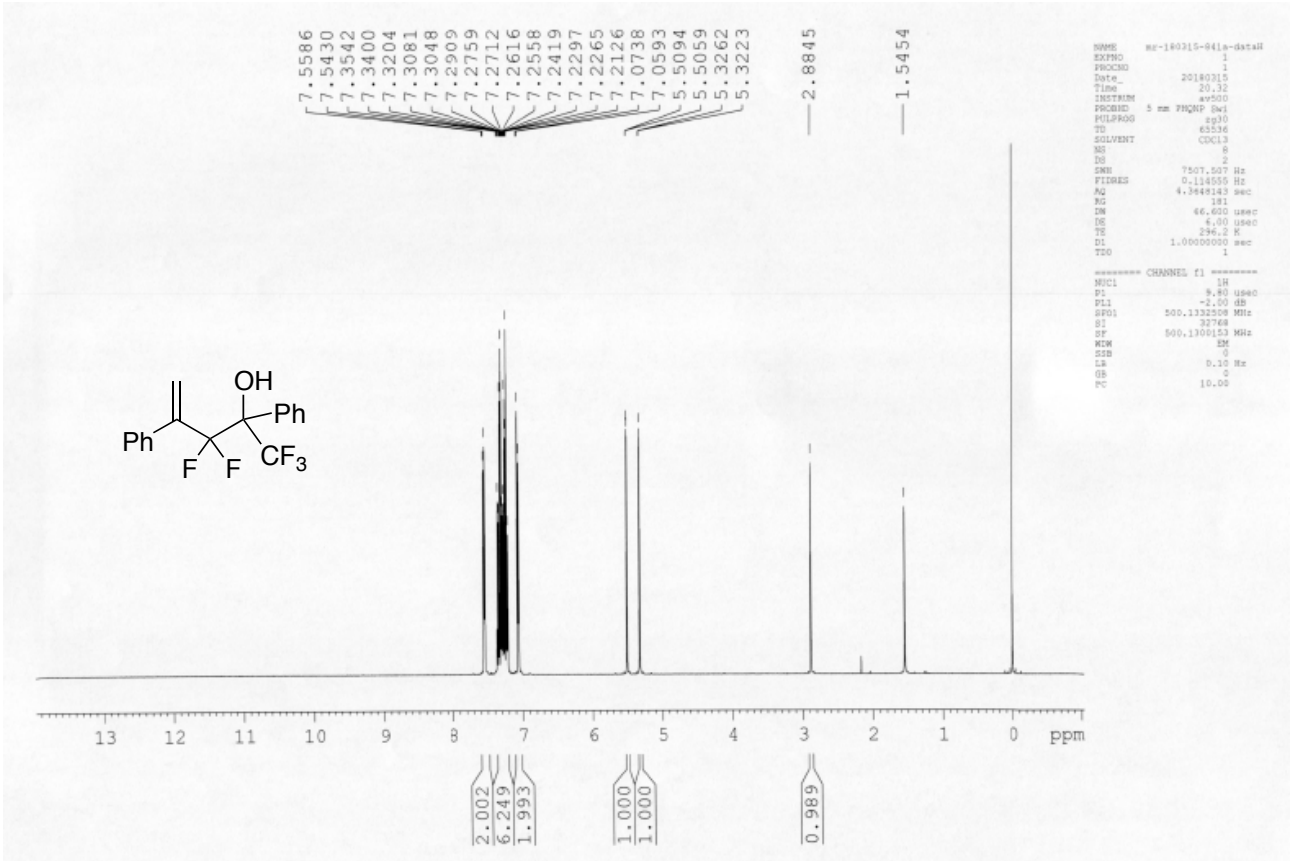
2-(4-Chlorophenyl)-3,3-difluoro-4-phenylpent-4-en-2-ol (1e)

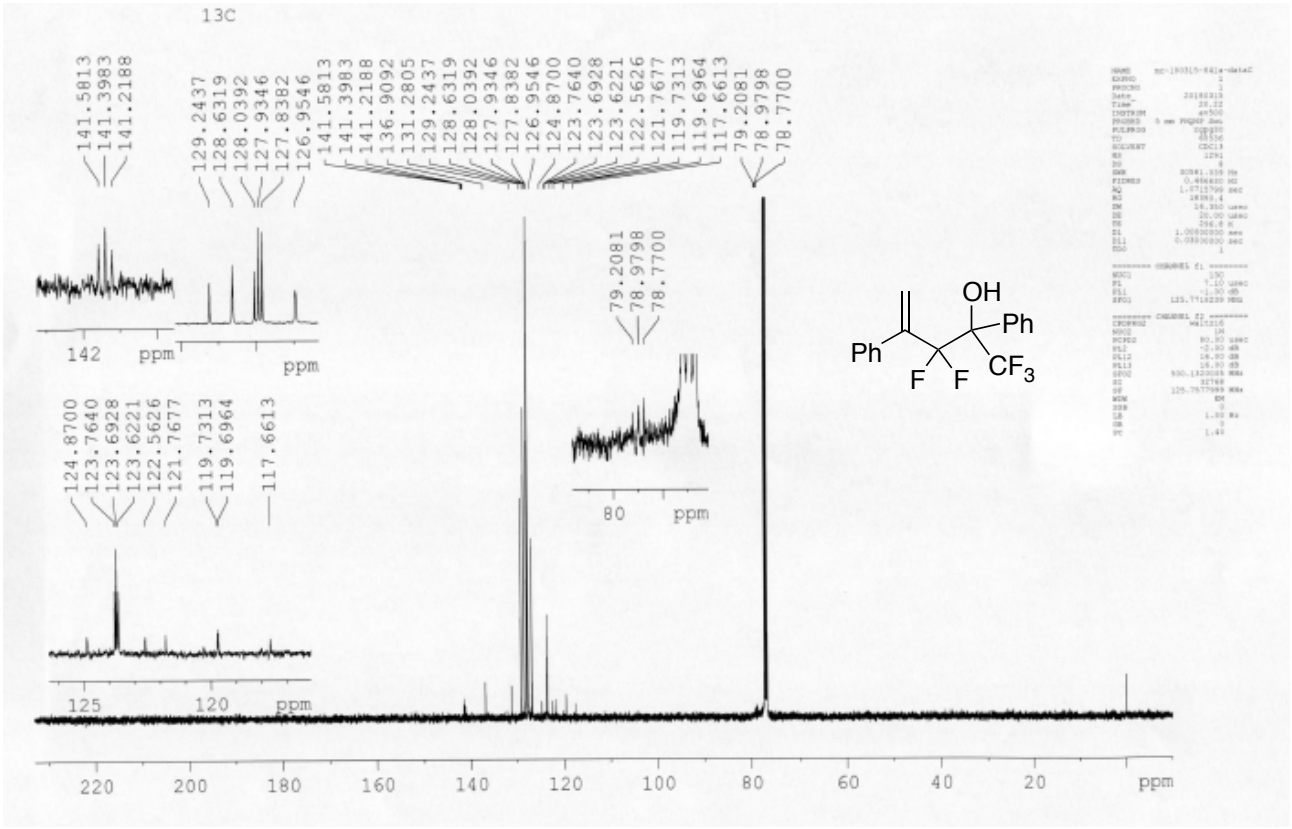


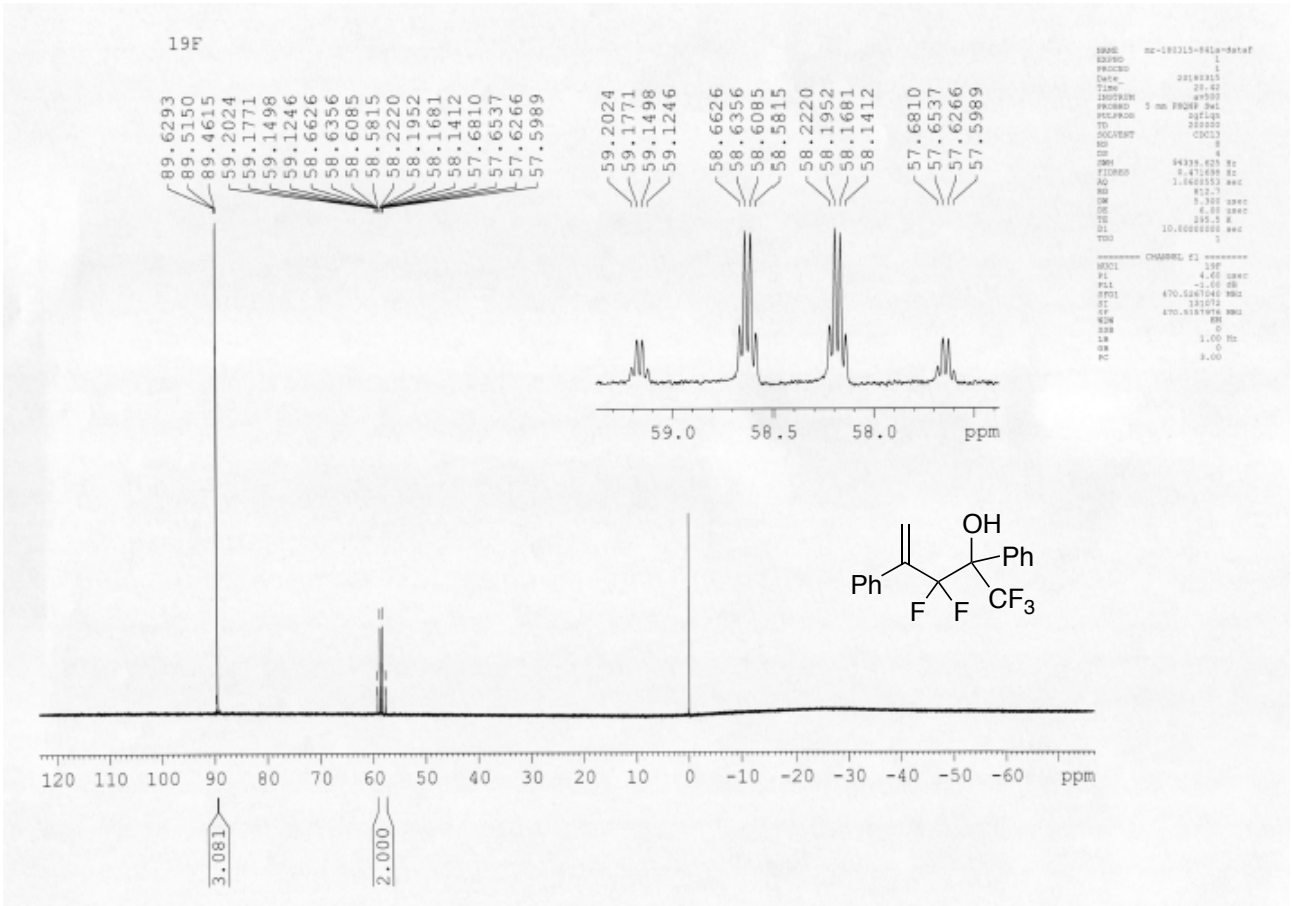




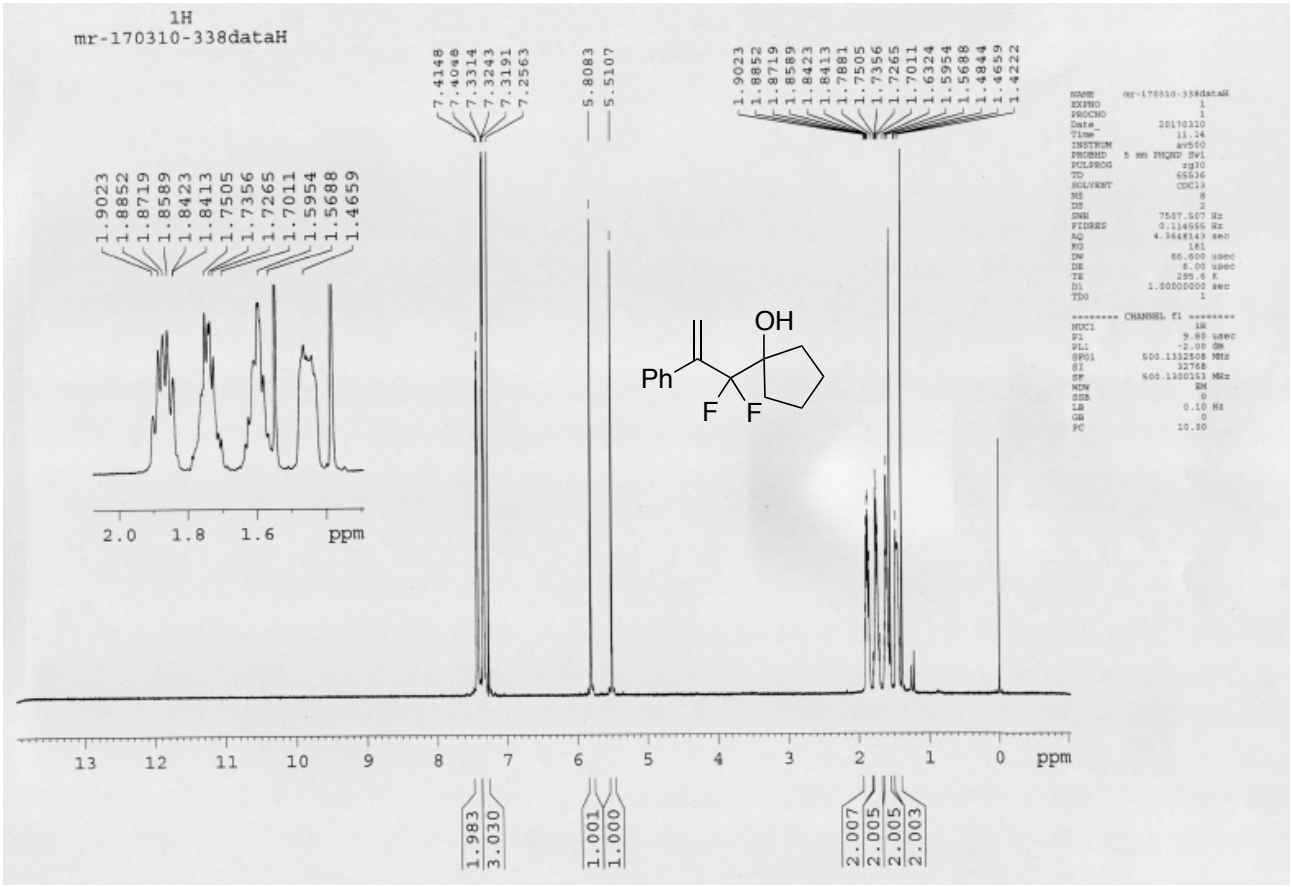
1,1,1,3,3-Pentafluoro-2,4-diphenylpent-4-en-2-ol (1f)

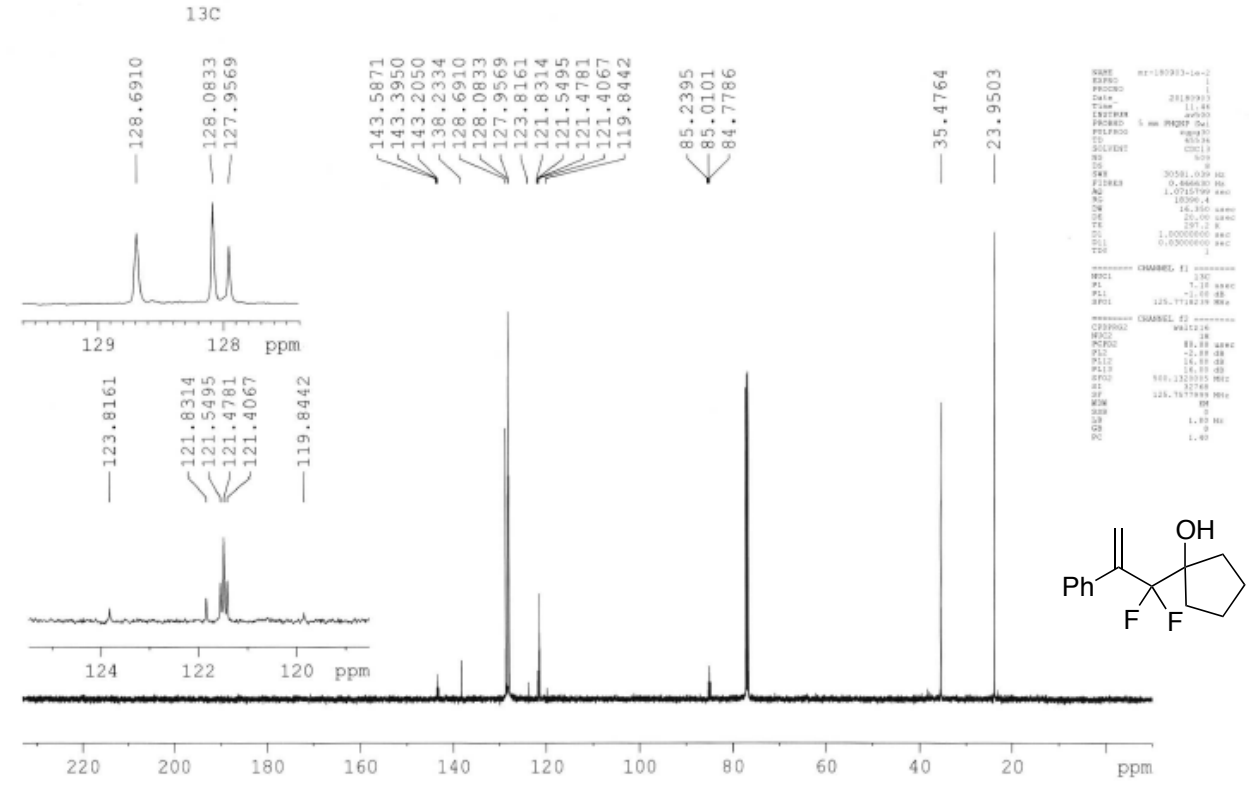


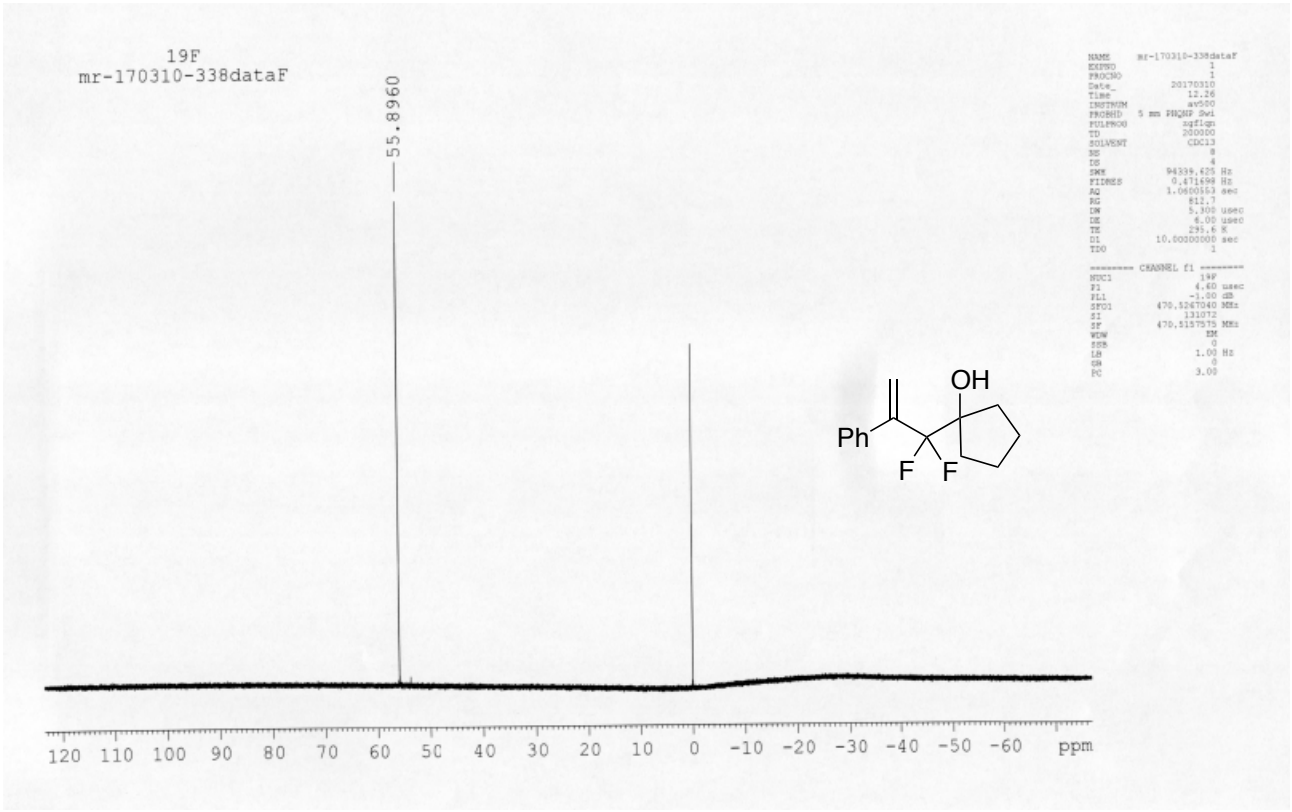

13C
141.5813
141.3983
141.2188
129.2437
128.6319
128.0392
127.9346
127.8382
126.9546
124.8700
123.7640
123.6928
123.6221
122.5626
121.7677
119.7313
119.6964
117.6613
79.2081
78.9798
78.7700
OH
Ph
Ph
F
F
CF3
ppm


19F
89.6293
89.5150
89.4615
59.2024
59.1771
59.1498
59.1246
58.6626
58.6356
58.6085
58.5815
58.2220
58.1952
58.1681
58.1412
57.6810
57.6537
57.6266
57.5989
OH
Ph
Ph
F
F
CF3
3.081
2.000
ppm

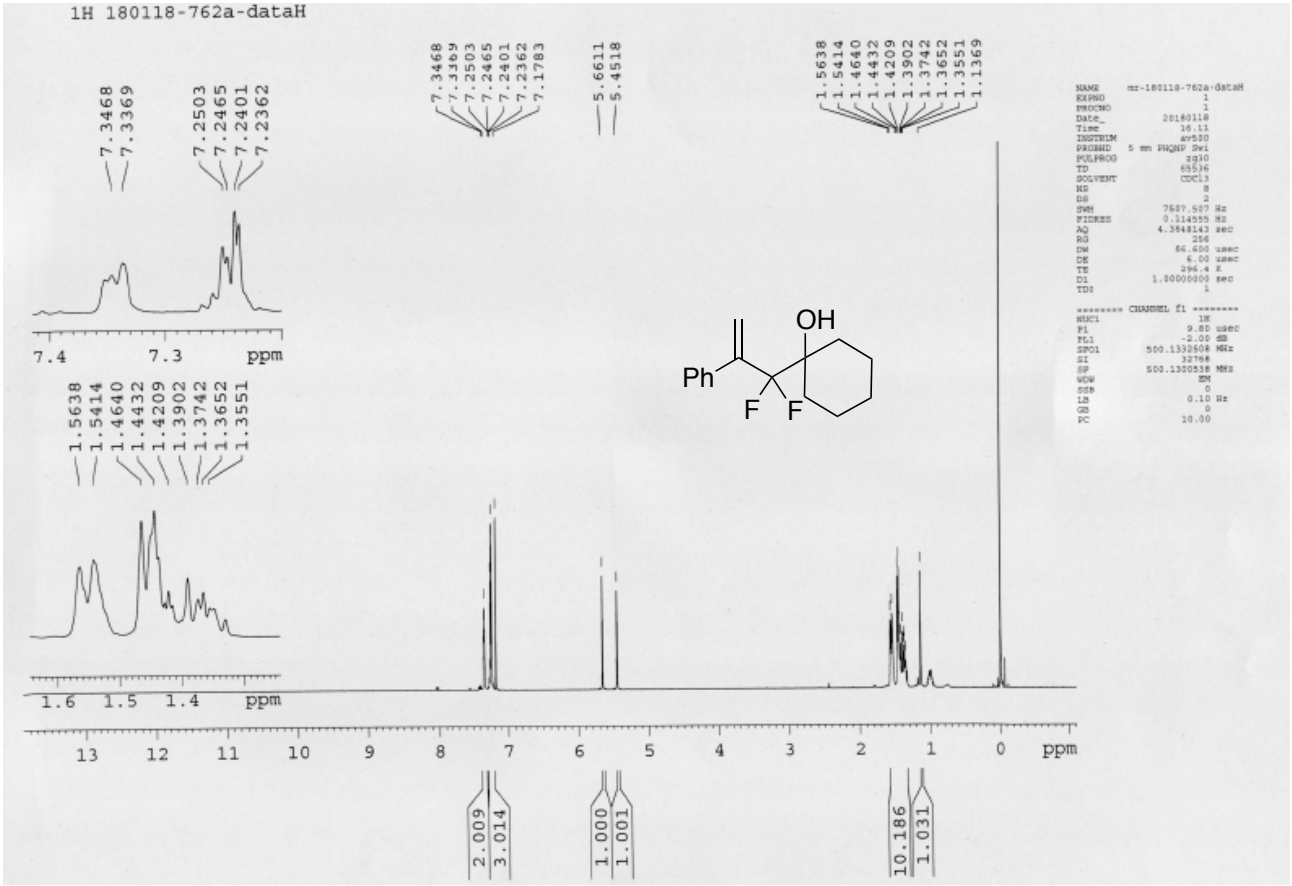
1-(1,1-Difluoro-2-phenylallyl)cyclopentan-1-ol (1g)

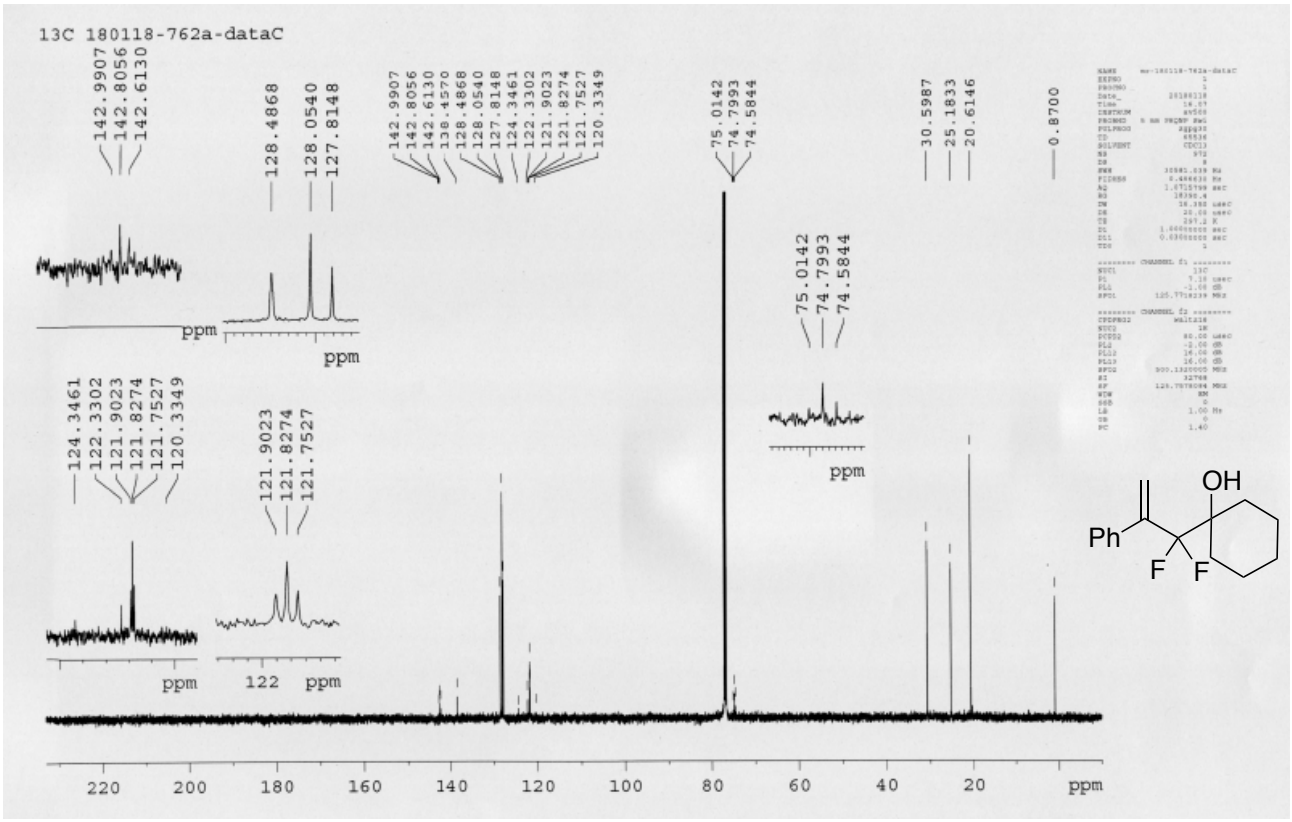


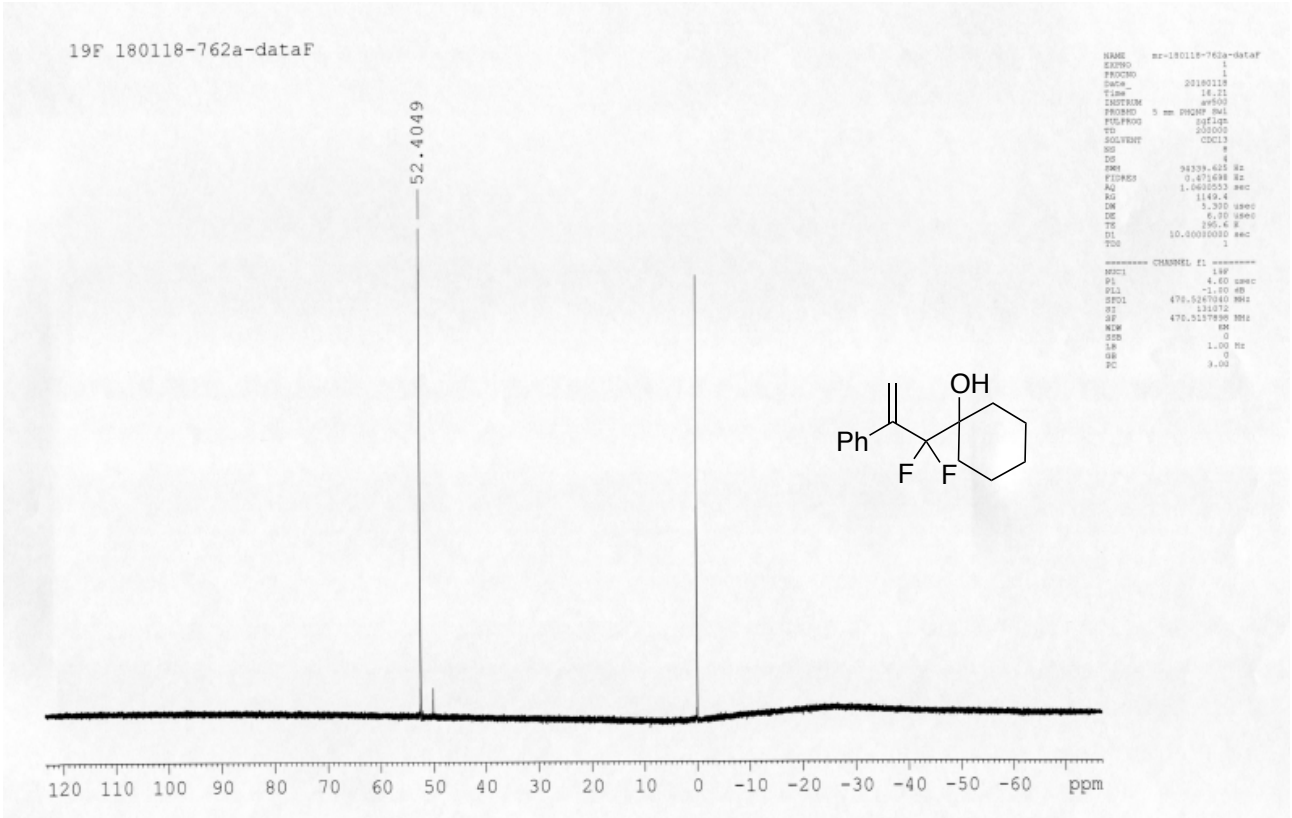




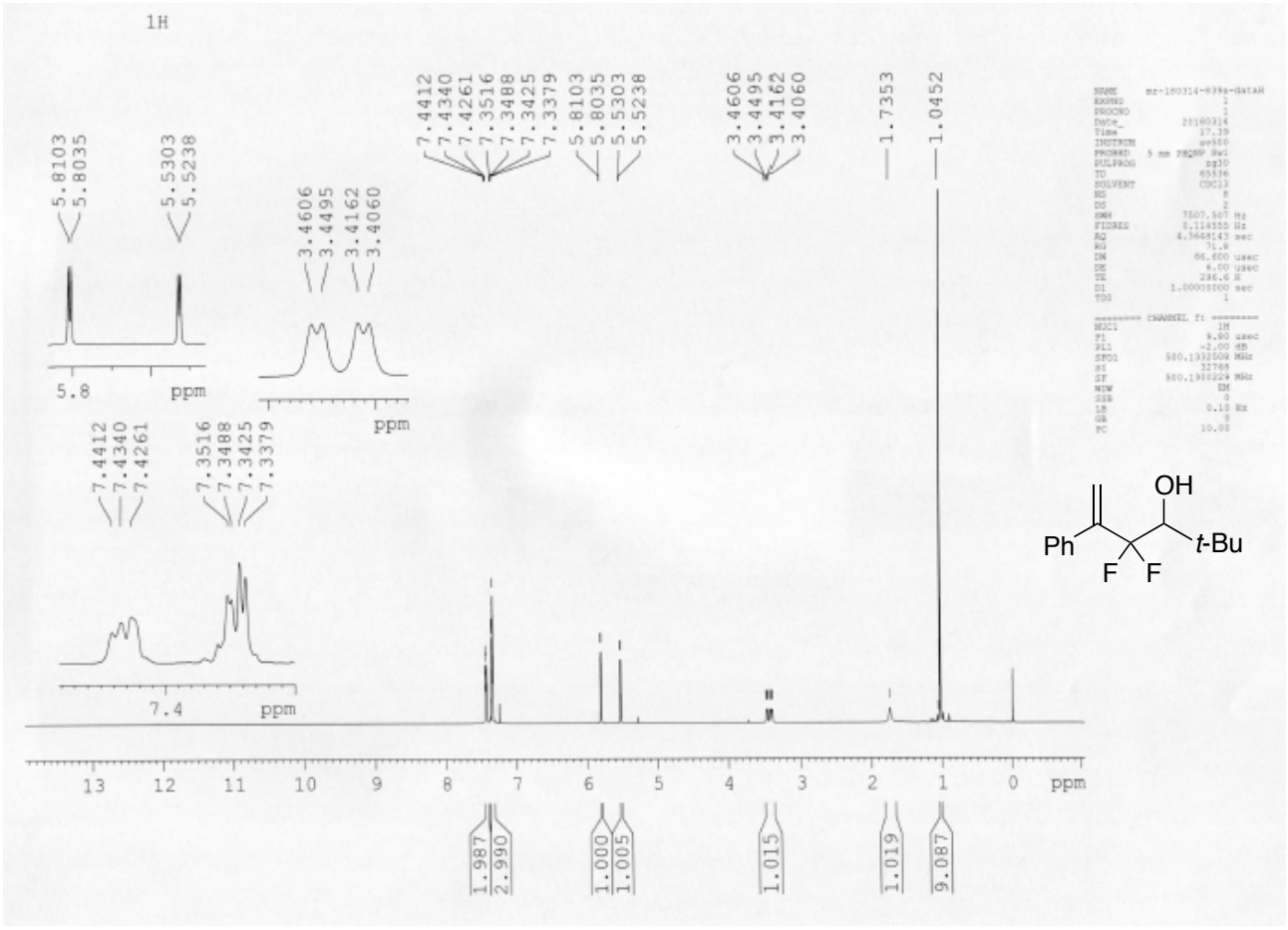
1-(1,1-Difluoro-2-phenylallyl)cyclohexan-1-ol (1h)

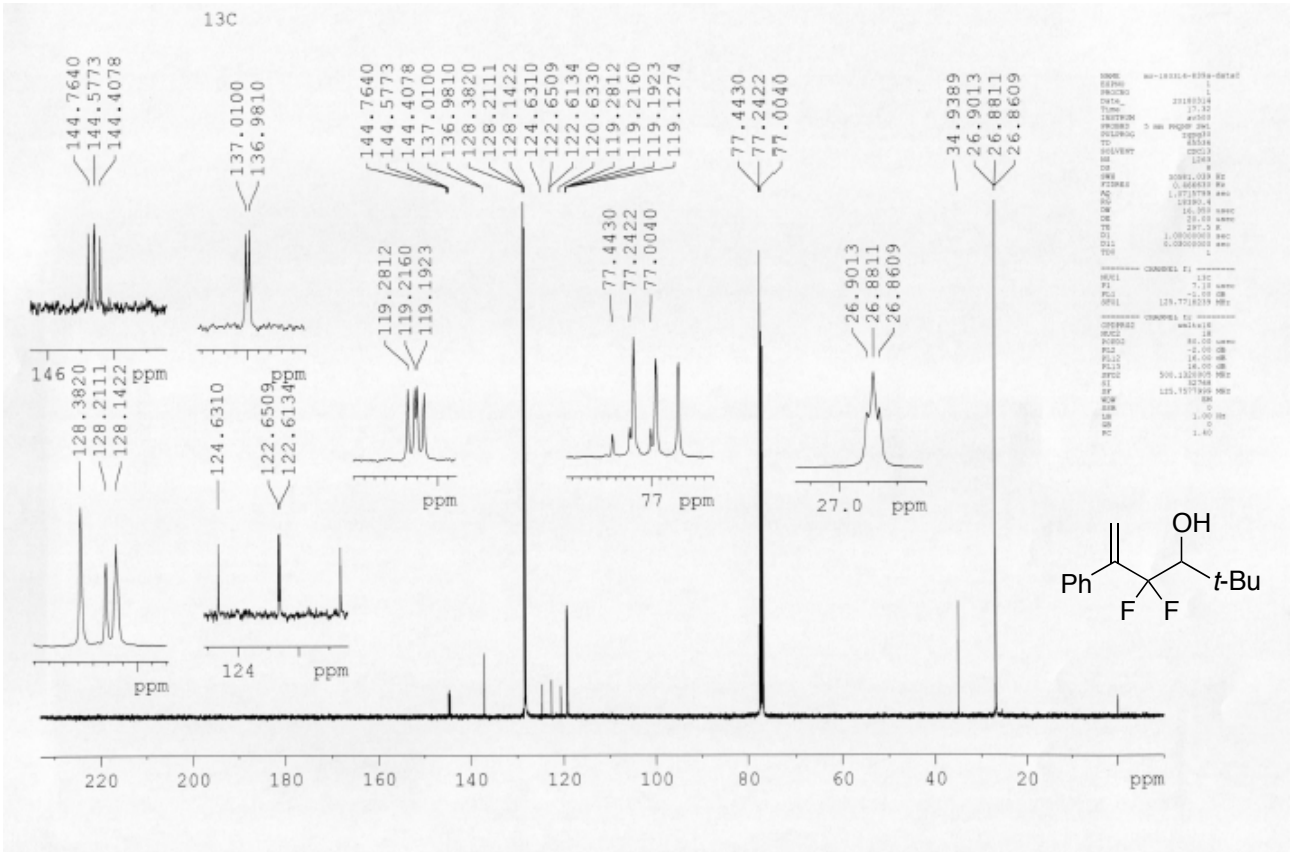


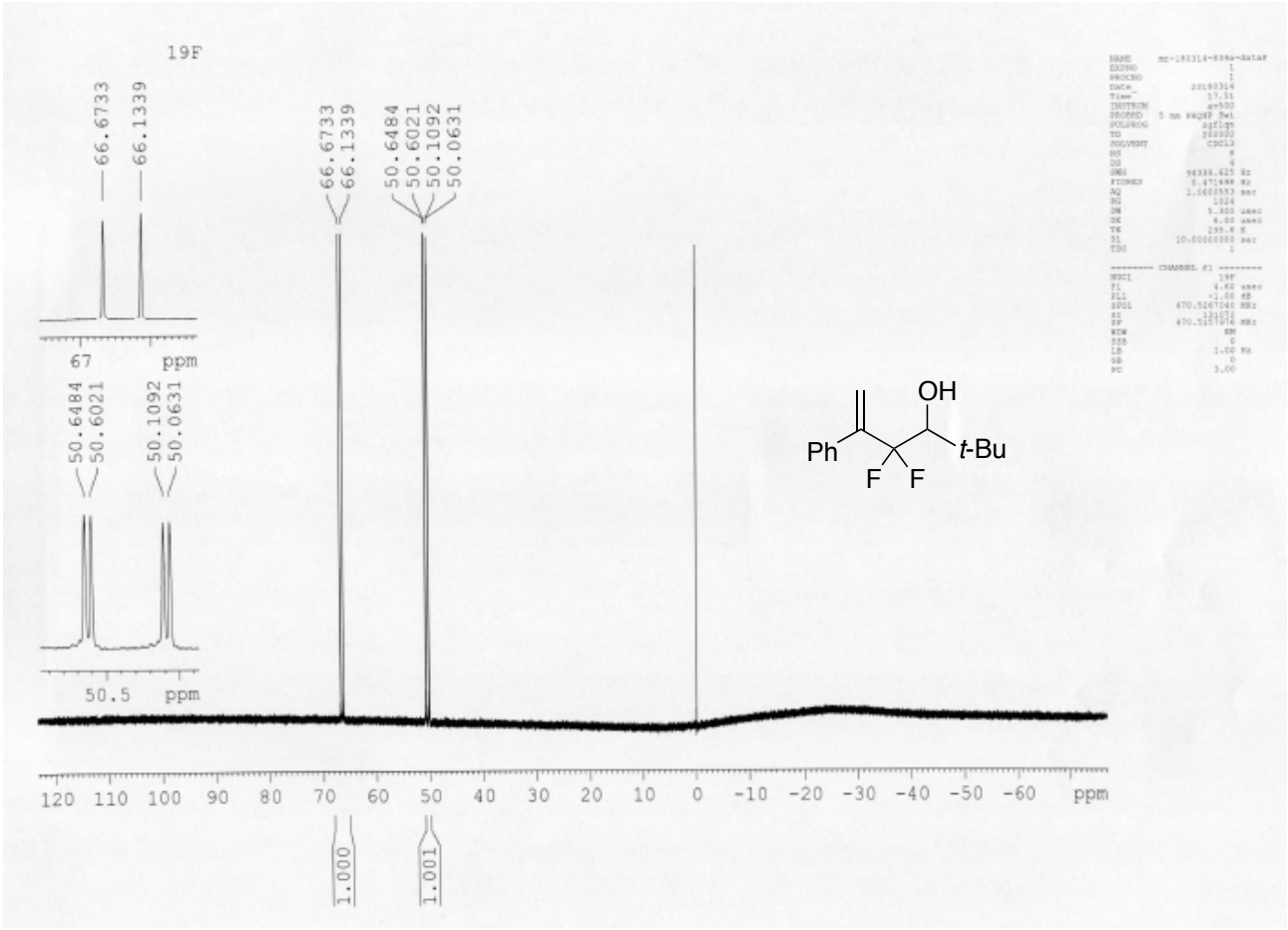

13C 180118-762a-dataC
142.9907
142.8056
142.6130
128.4868
128.0540
127.8148
124.3461
122.3302
121.9023
121.8274
121.7527
120.3349
75.0142
74.7993
74.5844
30.5987
25.1833
20.6146
0.8700
ppm
OH
Ph
F
F


19F 180118-762a-dataF
52.4049
OH
Ph
F
F

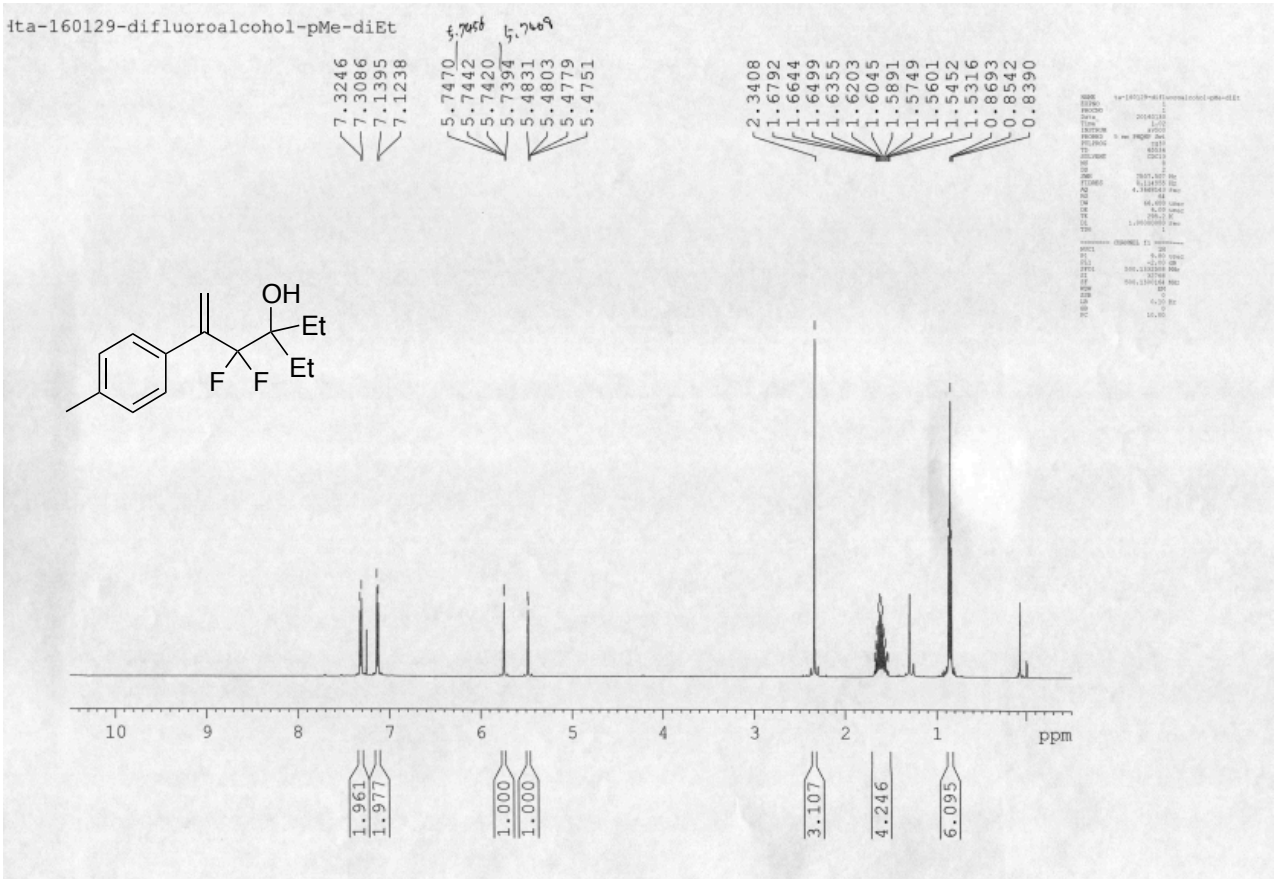
4,4-Difluoro-2,2-dimethyl-5-phenylhex-5-en-3-ol (1i)

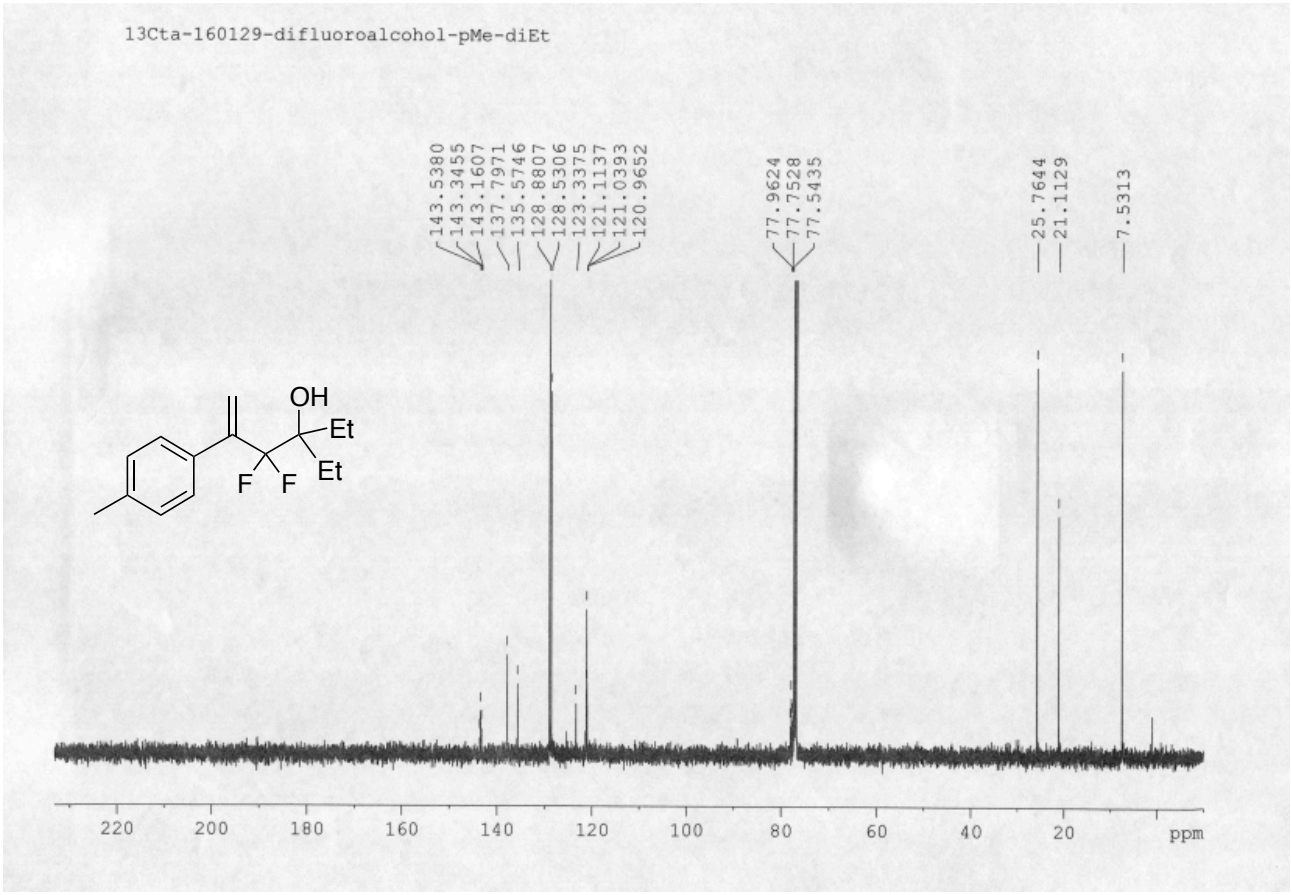


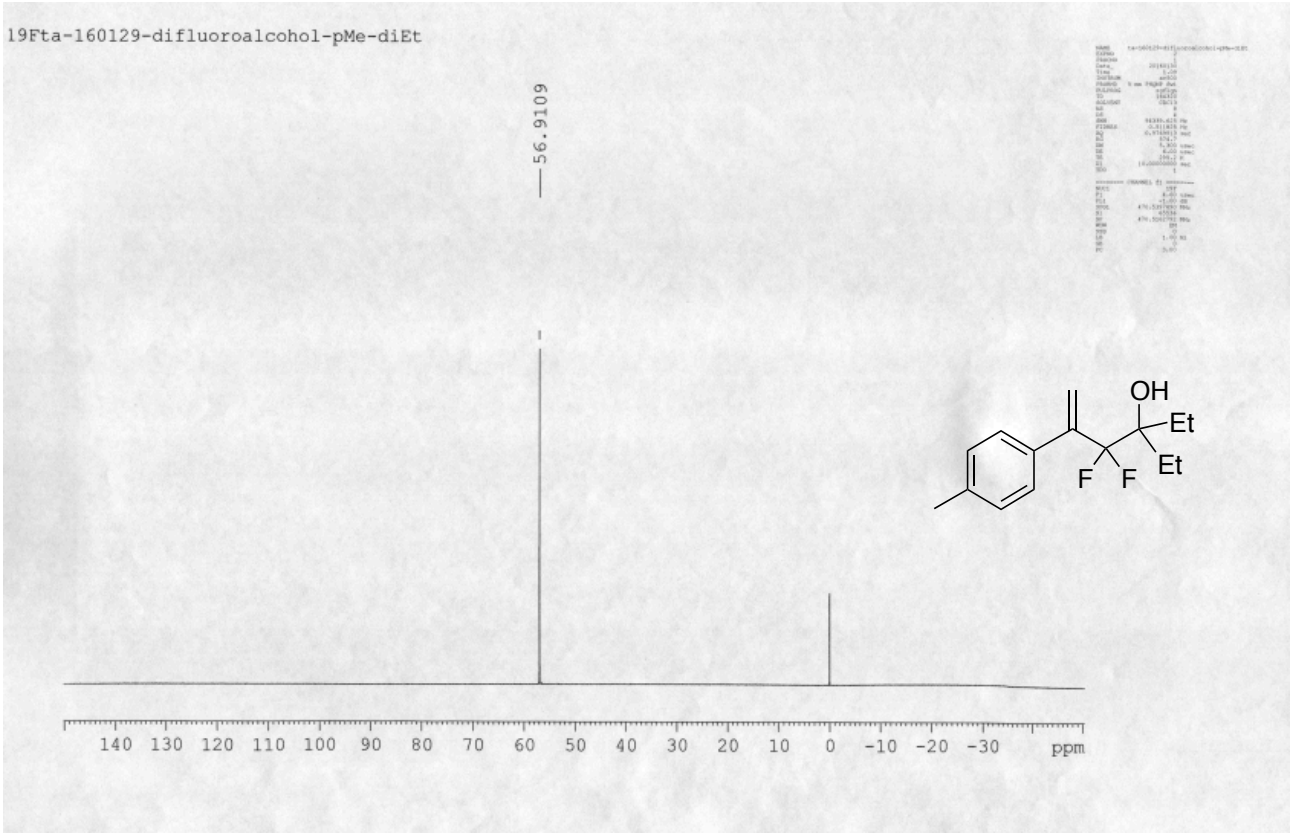




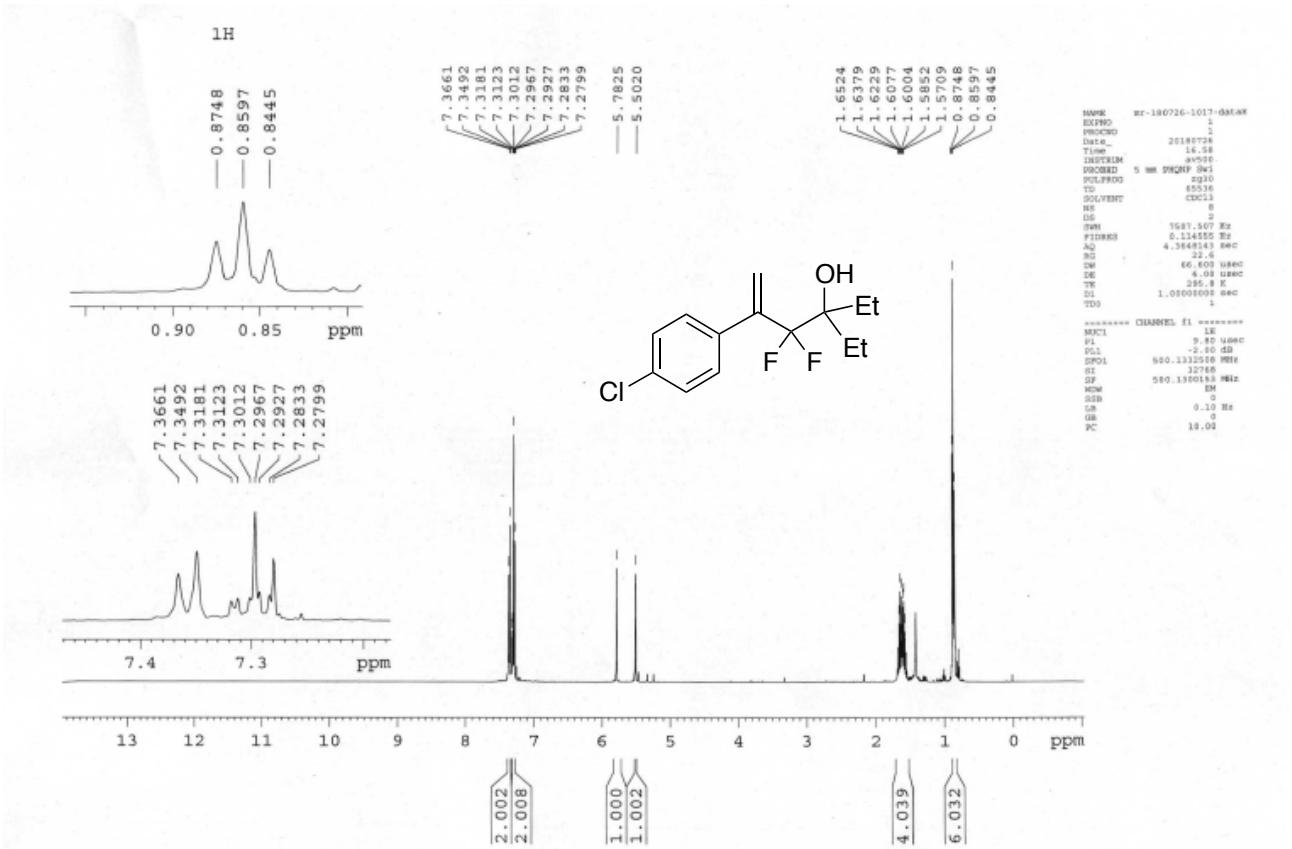
3-Ethyl-4,4-difluoro-5-(4-methylphenyl)hex-5-en-3-ol (1j)

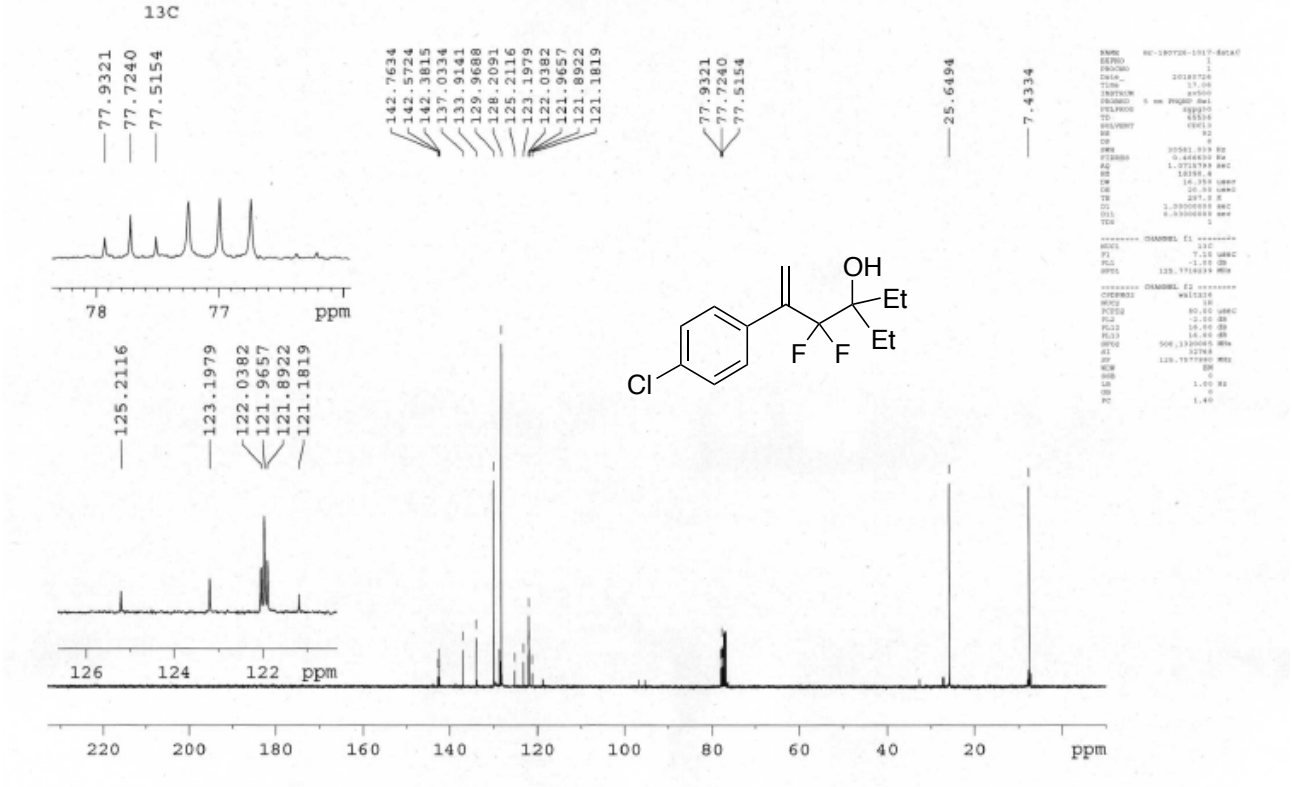


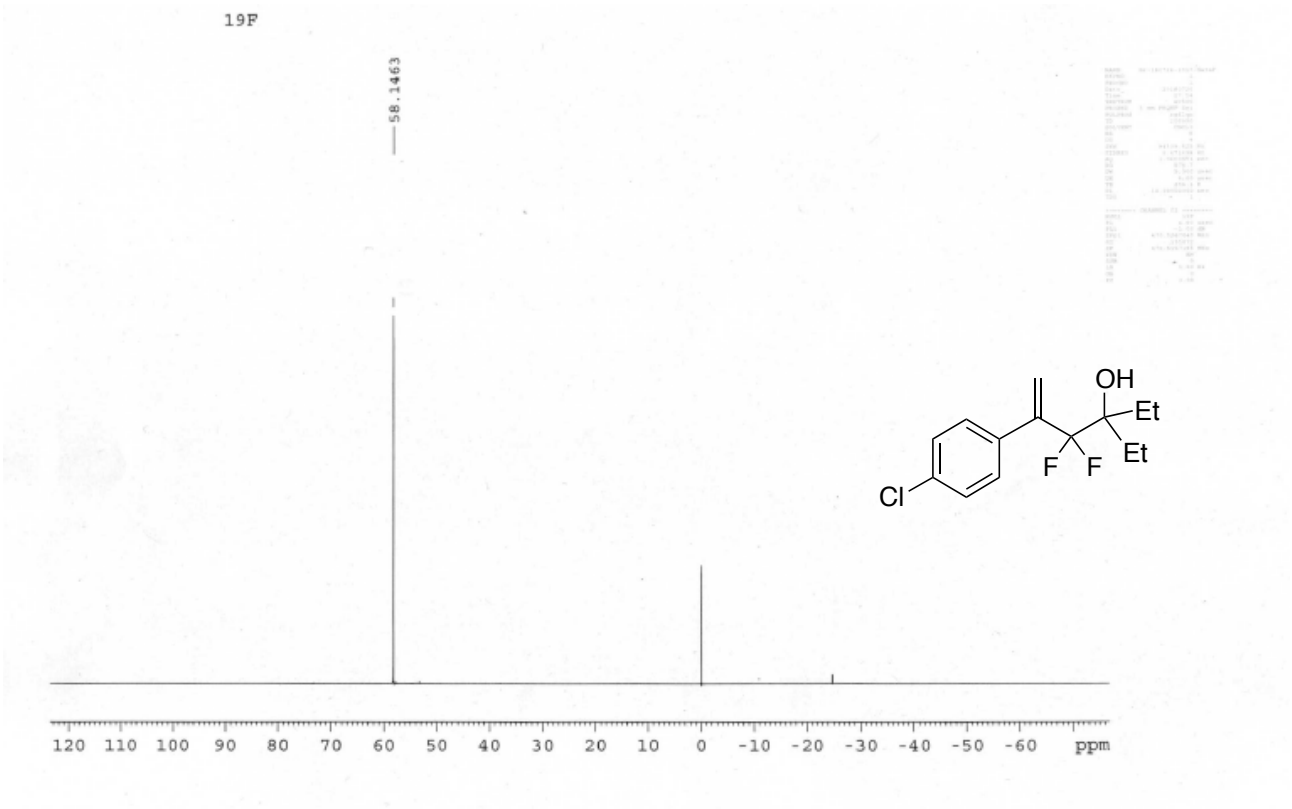

13Cta-160129-difluoroalcohol-pMe-diEt
143.5380
143.3455
143.1607
137.7971
135.5746
128.8807
128.5306
123.3375
121.1137
121.0393
120.9652
77.9624
77.7528
77.5435
25.7644
21.1129
7.5313
OH
Et
Et
F
F
220
200
180
160
140
120
100
80
60
40
20
ppm


19Fta-160129-difluoroalcohol-pMe-diEt
56.9109
OH
Et
Et
F
F
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
ppm

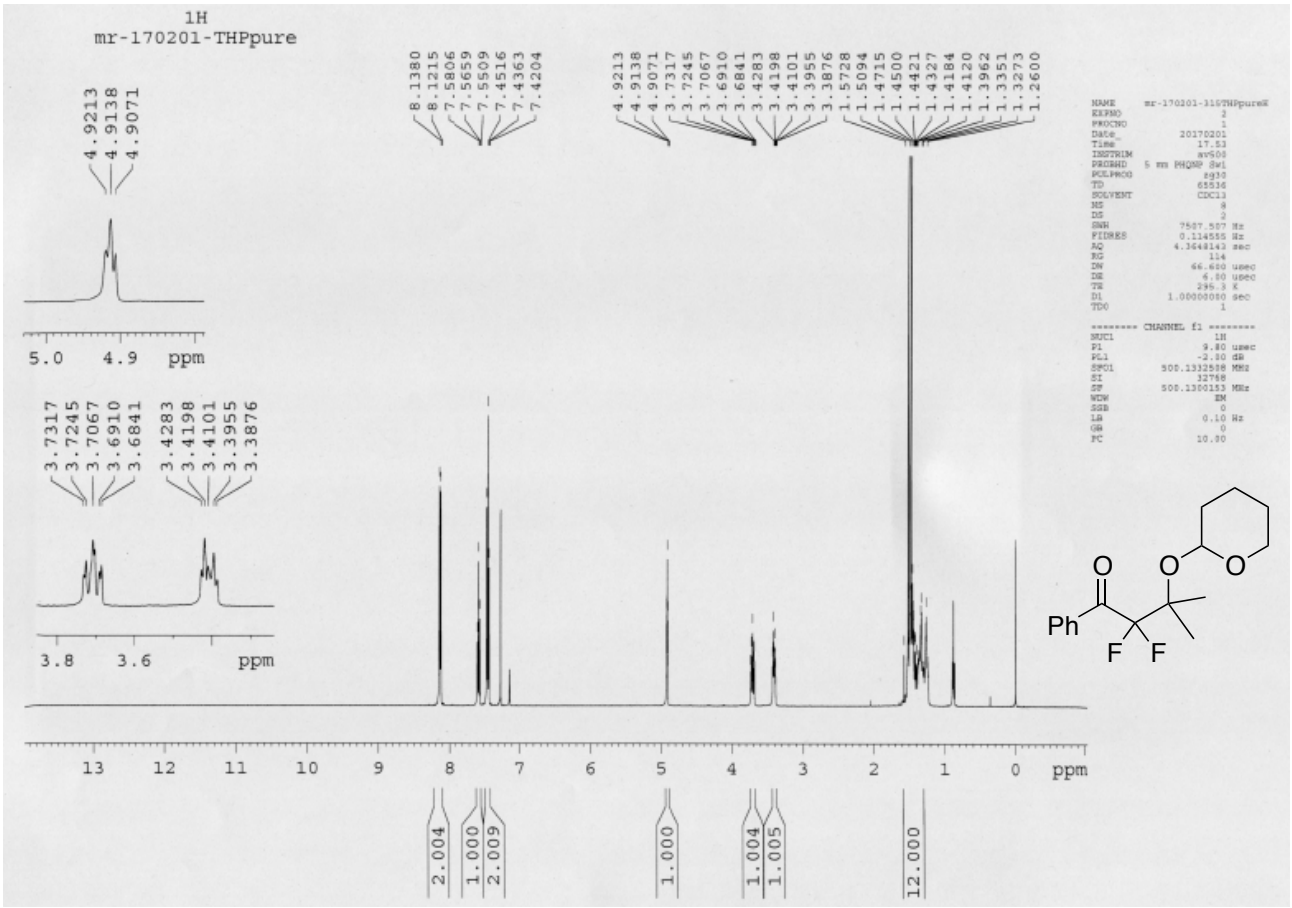
5-(4-Chlorophenyl)-3-ethyl-4,4-difluorohex-5-en-3-ol (1k)

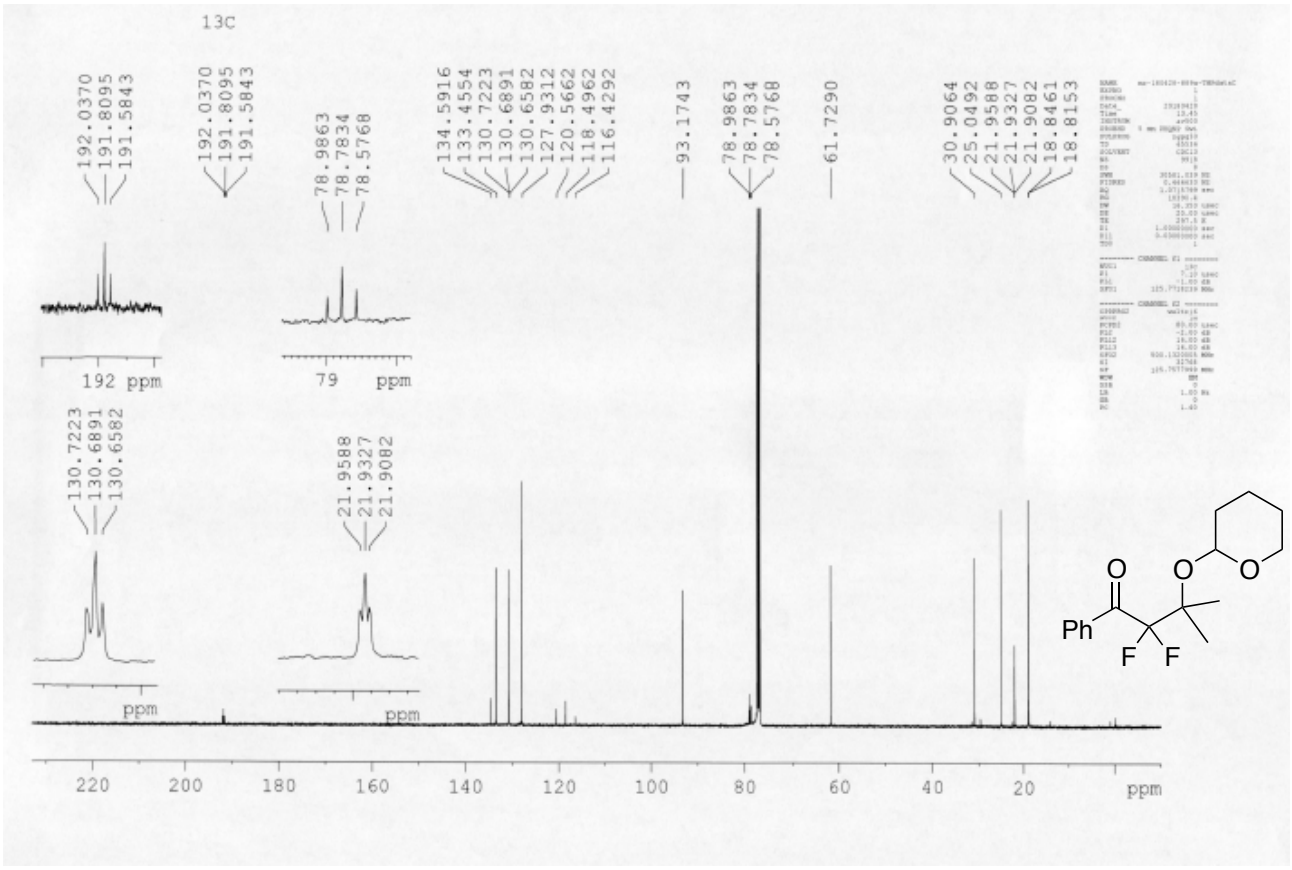


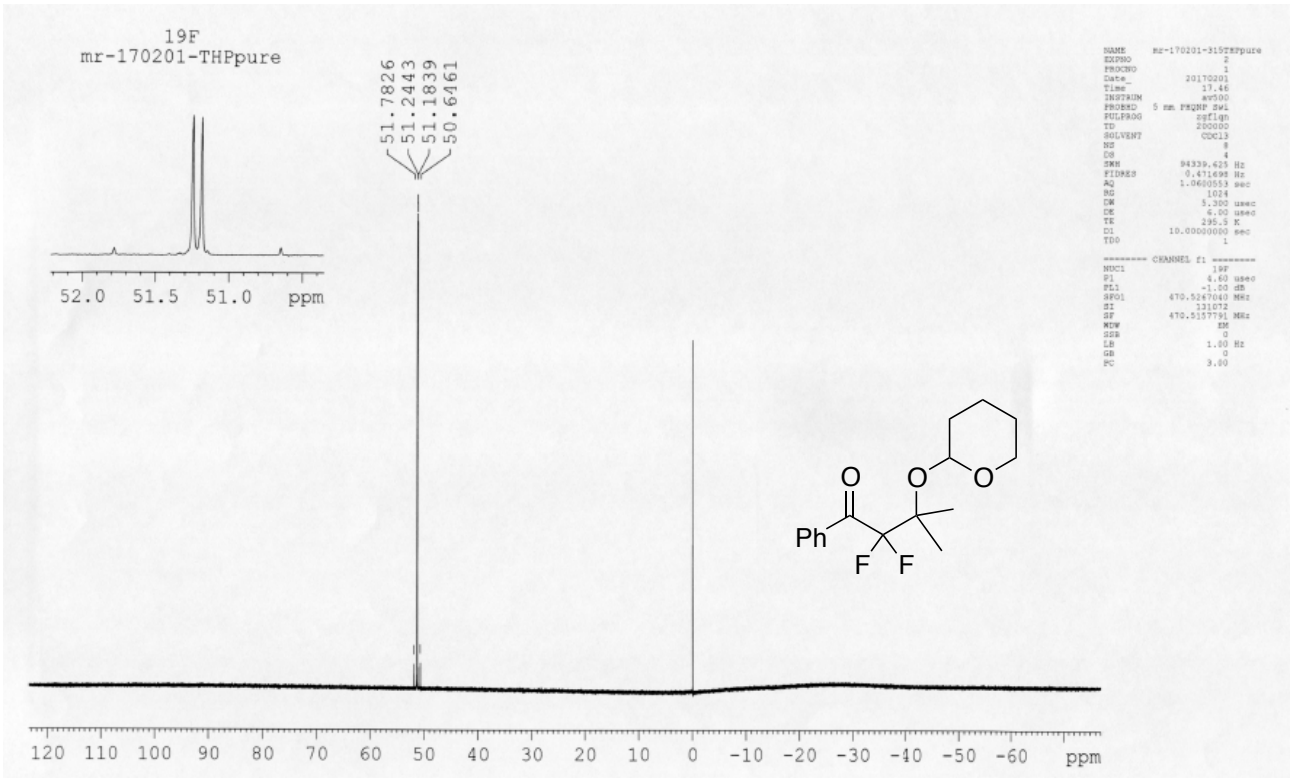




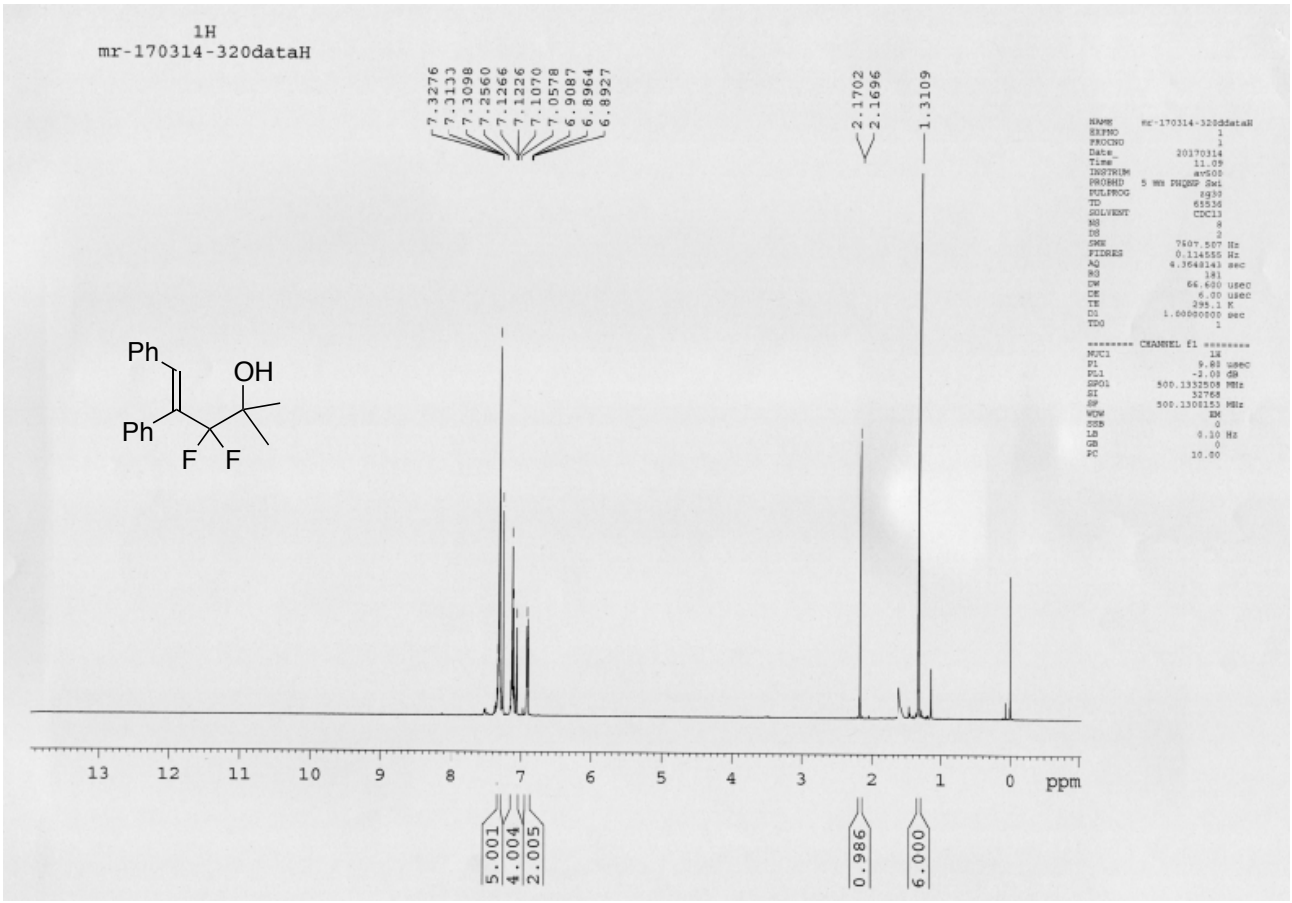
2,2-Difluoro-3-methyl-1-phenyl-3-[(tetrahydro-2*H*-pyran-2-yl)oxy]butan-1-one

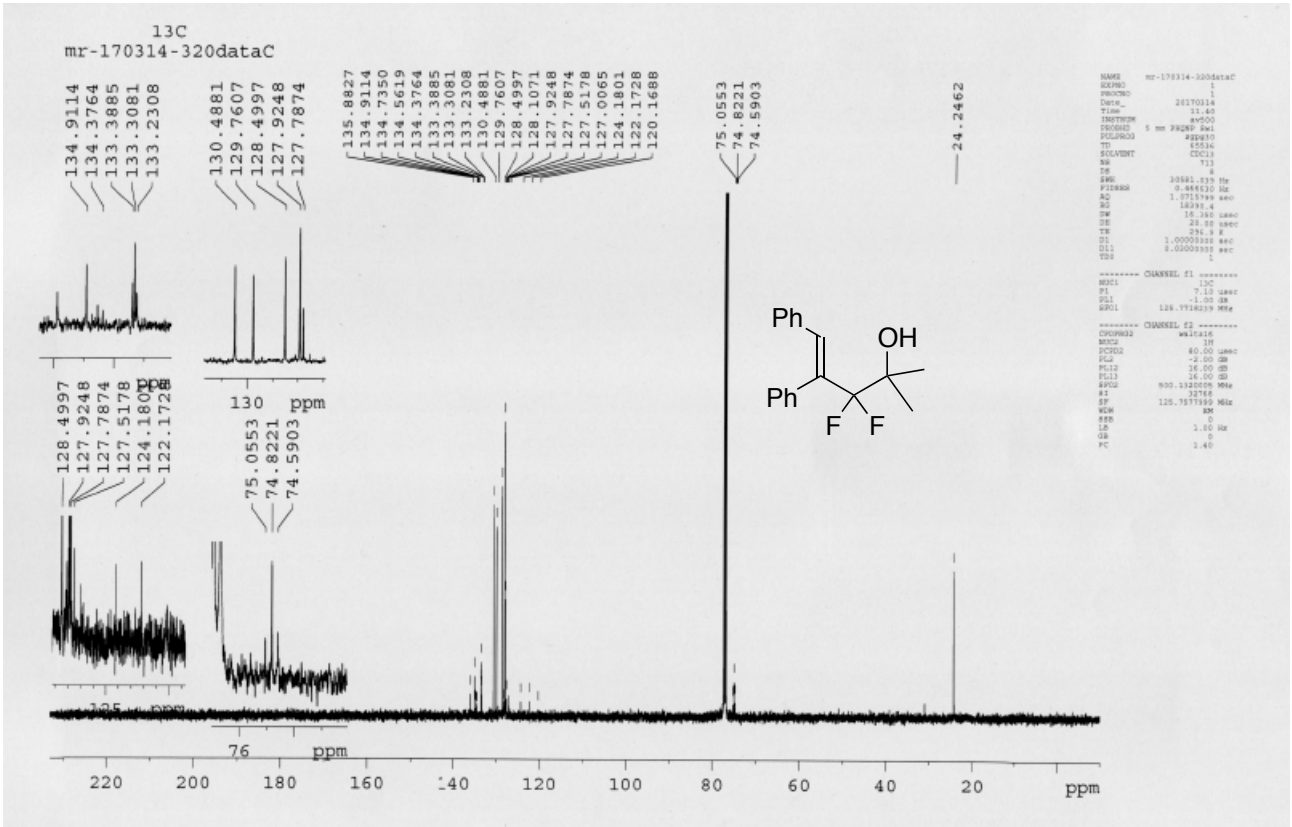


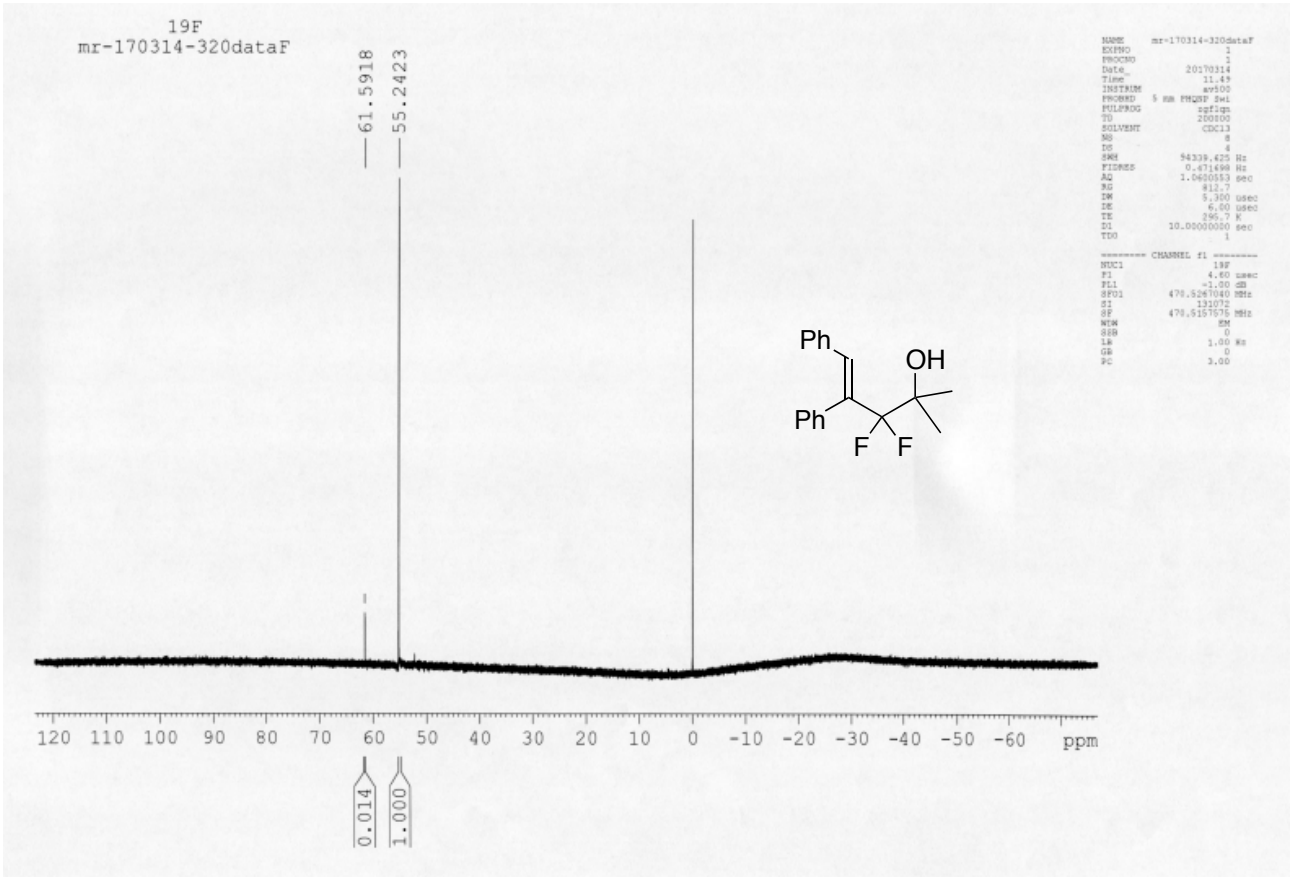

13C
192.0370
191.8095
191.5843
134.5916
133.4554
130.7223
130.6891
130.6582
127.9312
120.5662
118.4962
116.4292
93.1743
78.9863
78.7834
78.5768
61.7290
30.9064
25.0492
21.9588
21.9327
21.9082
18.8461
18.8153
192 ppm
79 ppm
ppm
220 200 180 160 140 120 100 80 60 40 20 ppm
O
O
O
Ph
F
F


19F
mr-170201-THPpure
51.7826
51.2443
51.1839
50.6461
52.0 51.5 51.0 ppm
120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 ppm
O
O
O
Ph
F
F

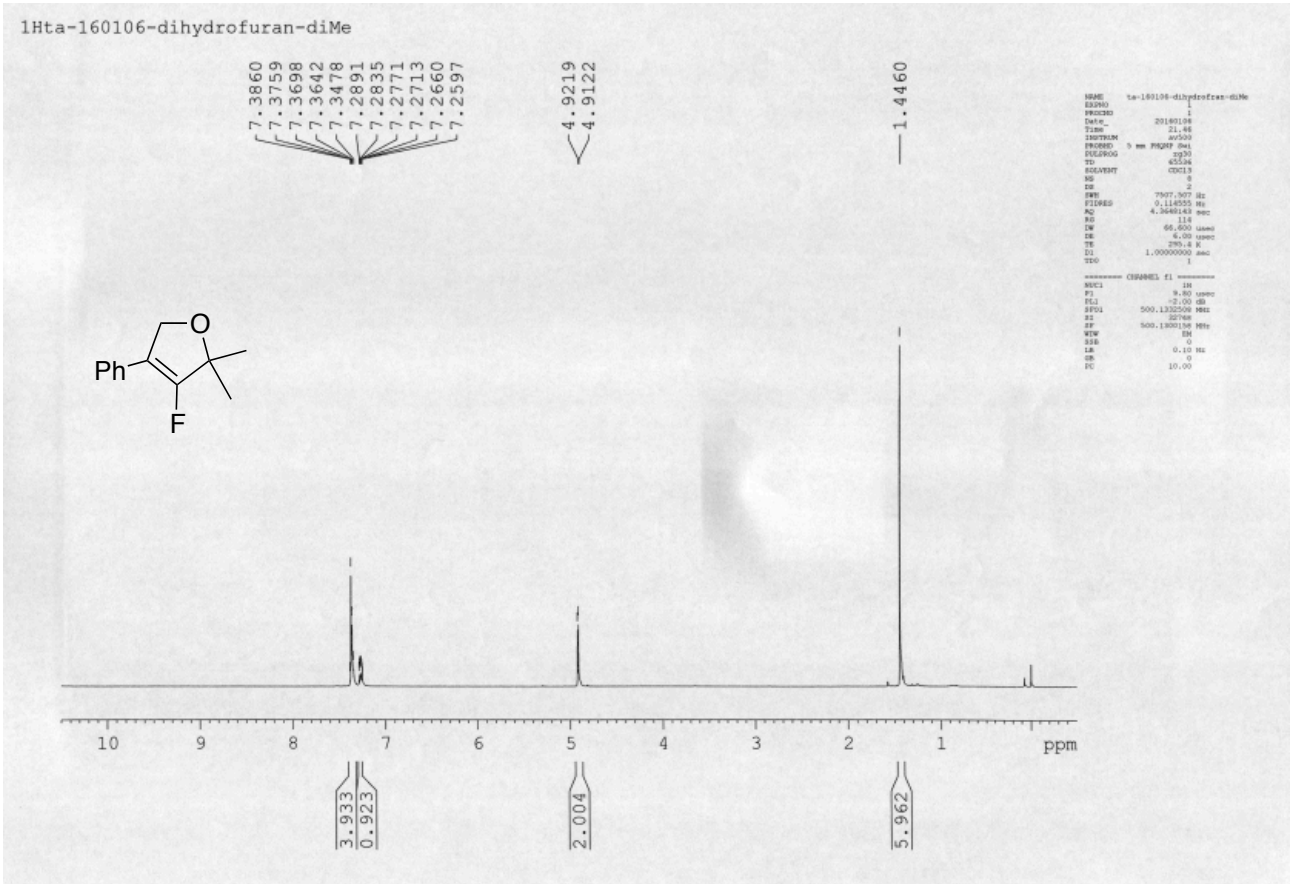
3,3-Difluoro-2-methyl-4,5-diphenylpent-4-en-2-ol (1l)

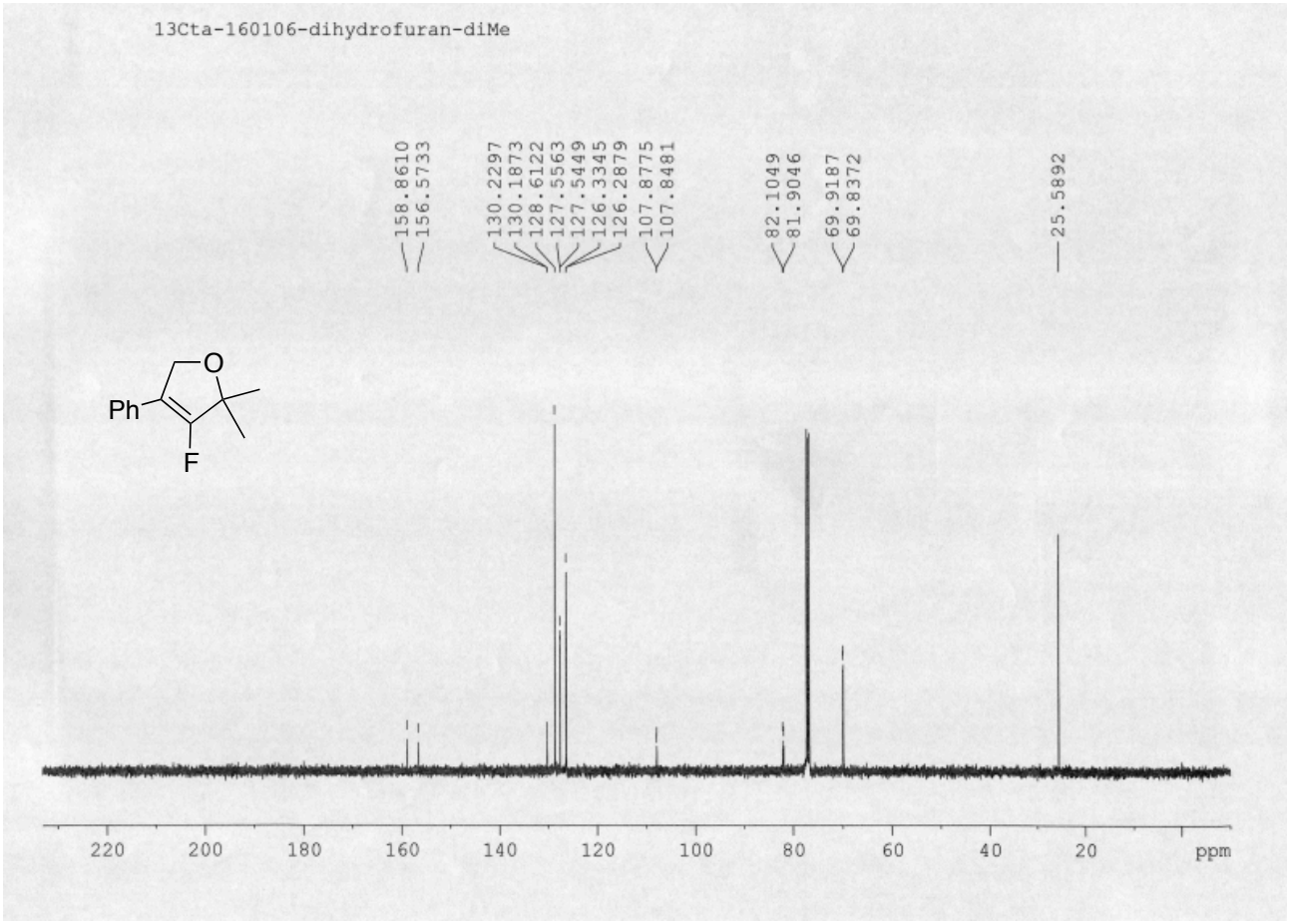


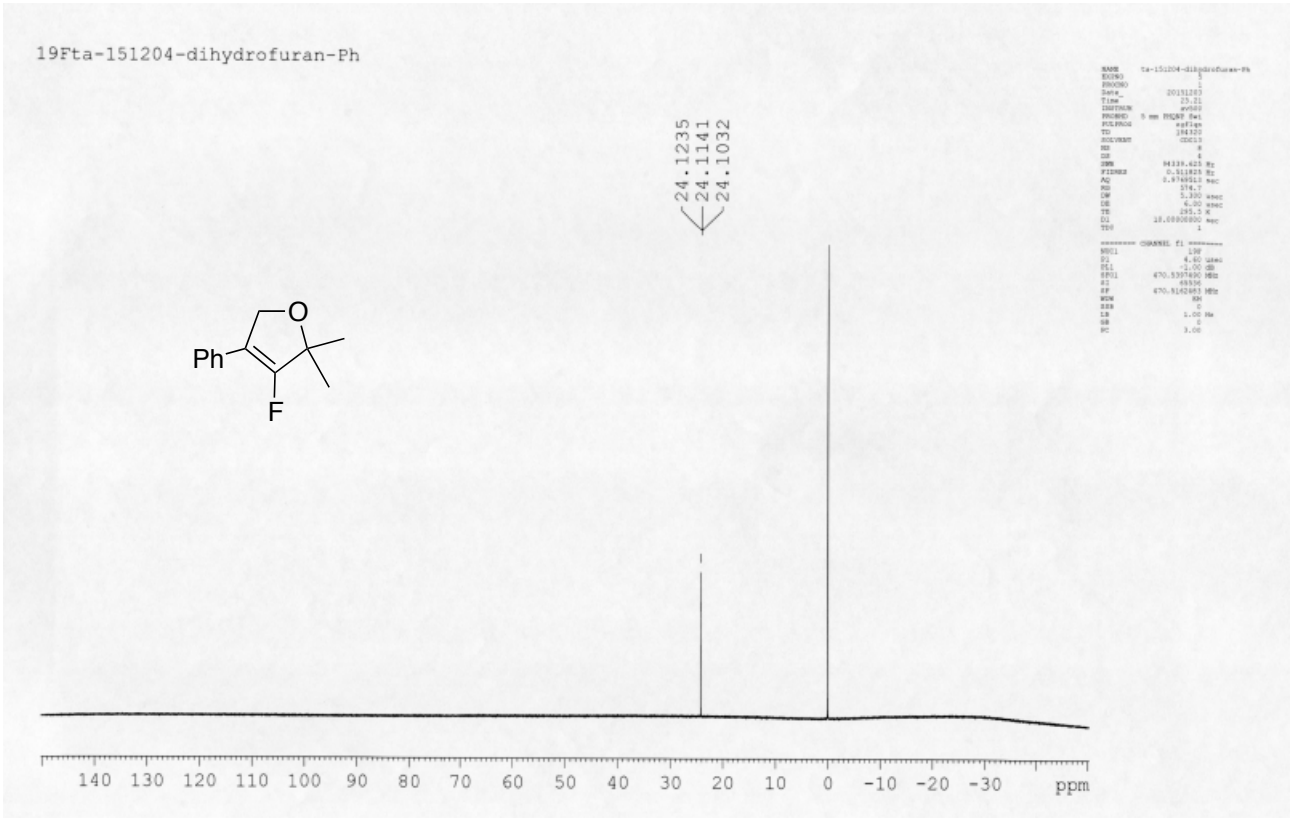




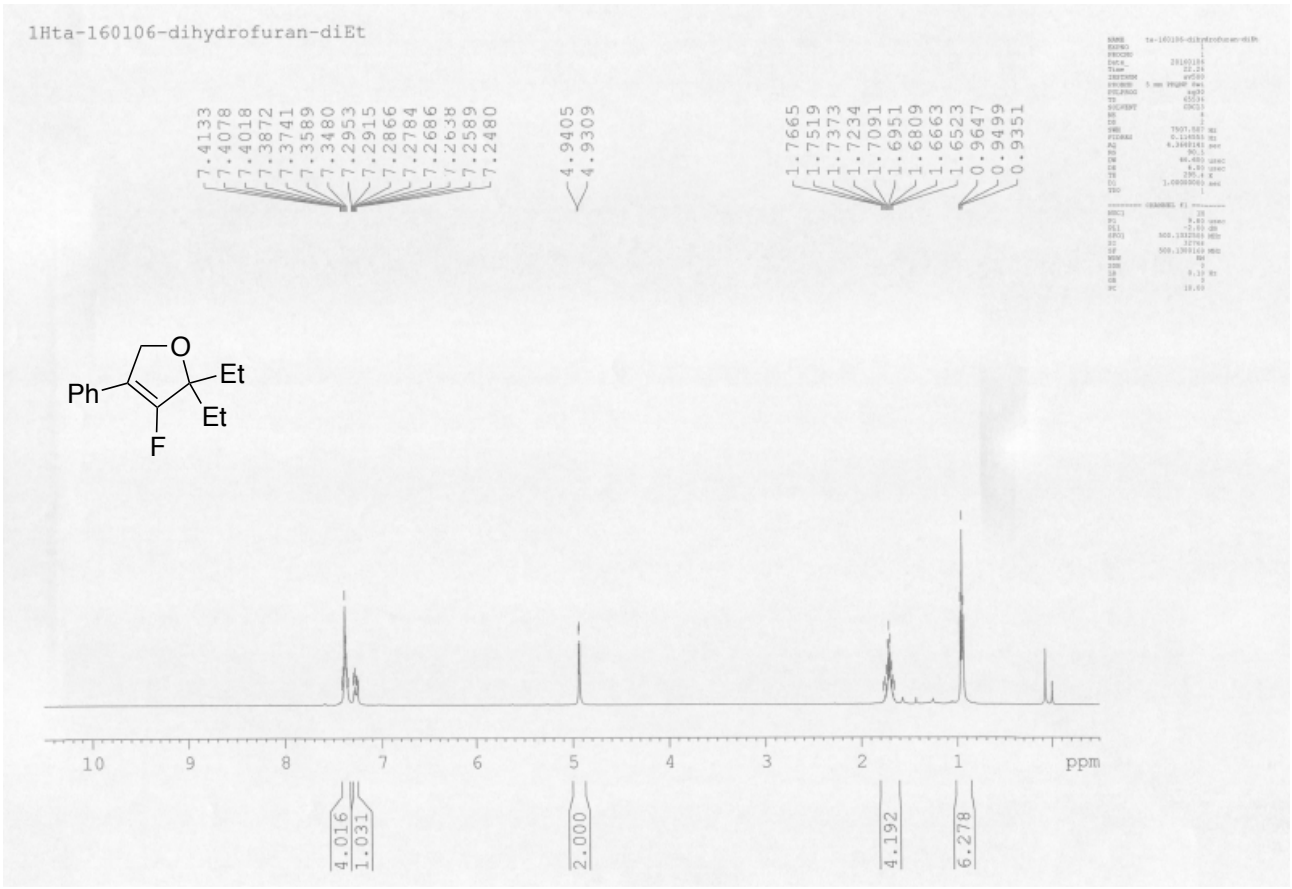
3-Fluoro-2,2-dimethyl-4-phenyl-2,5-dihydrofuran (4a)

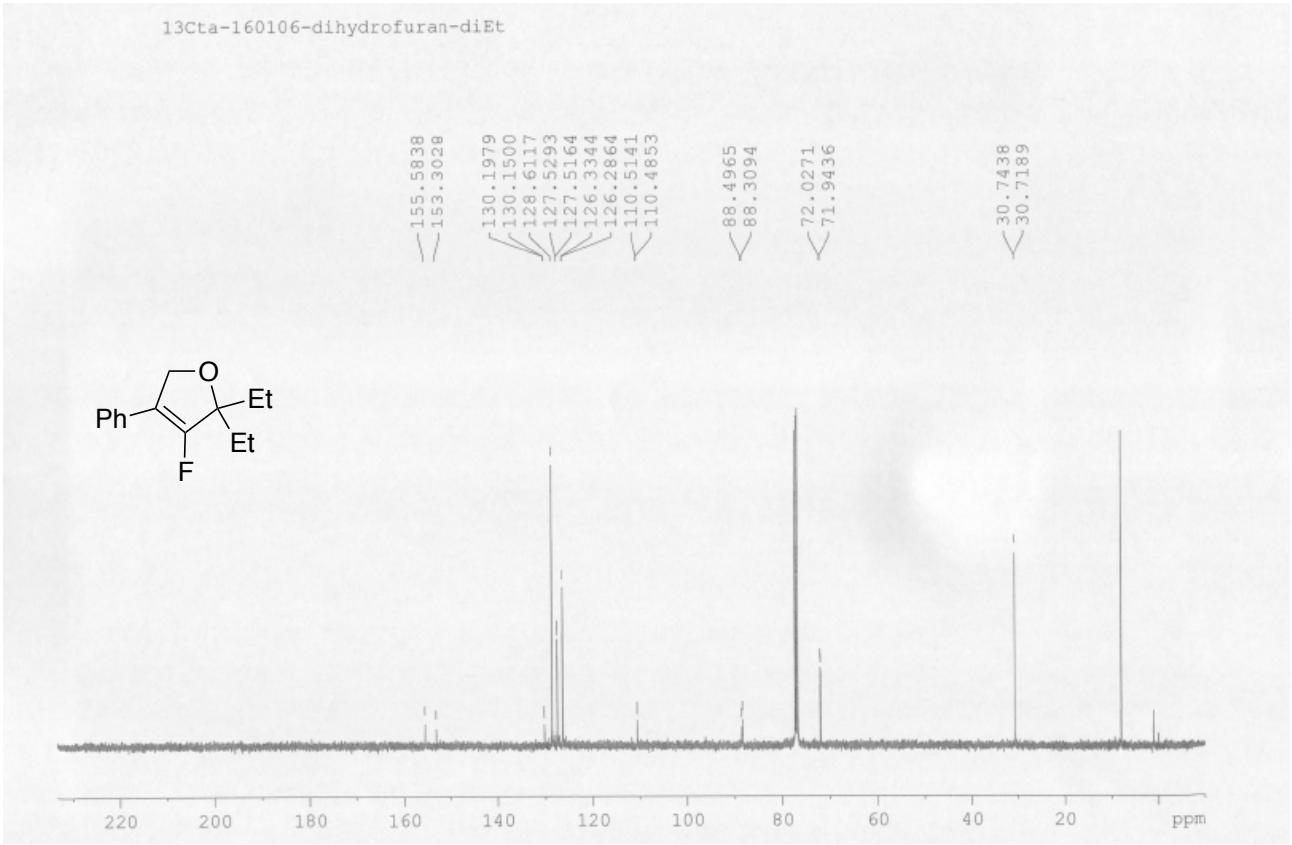


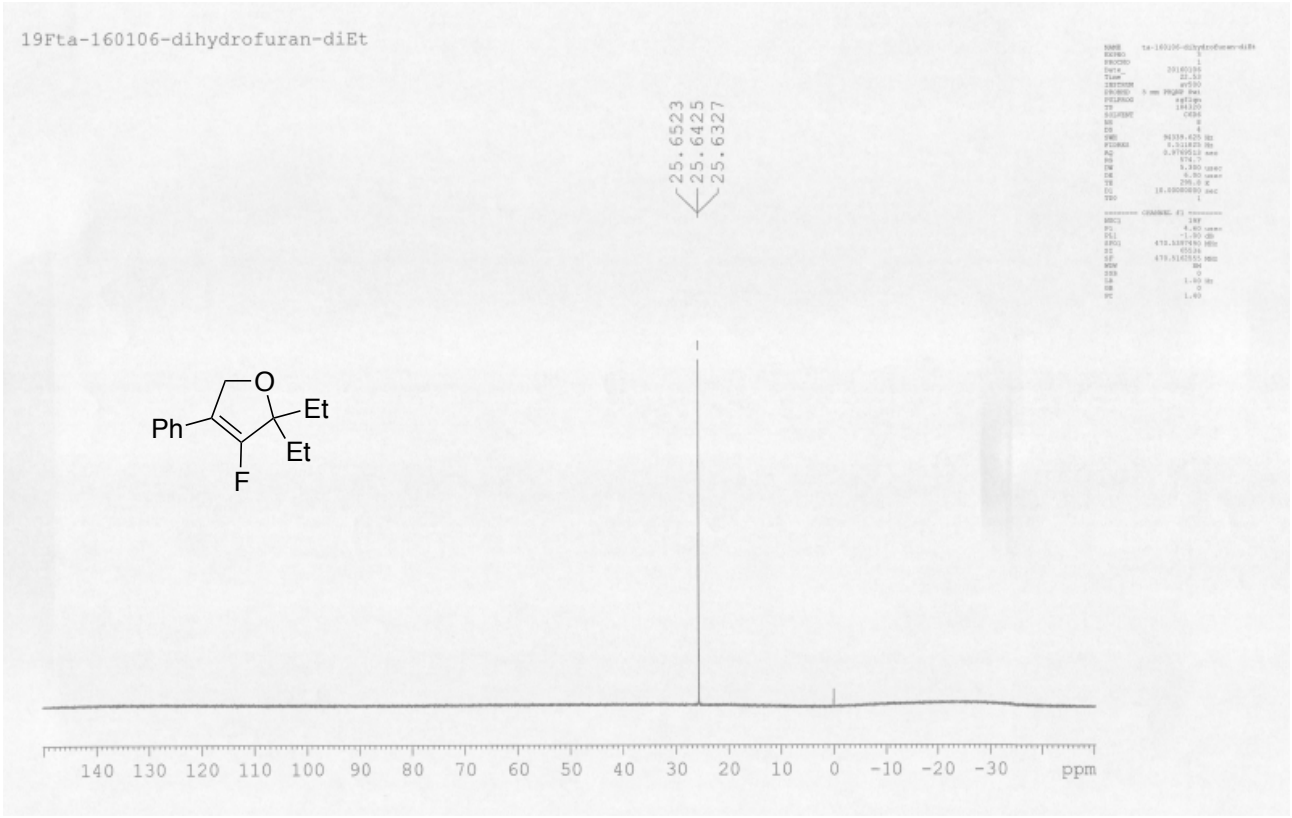

13Cta-160106-dihydrofuran-diMe
158.8610
156.5733
130.2297
130.1873
128.6122
127.5563
127.5449
126.3345
126.2879
107.8775
107.8481
82.1049
81.9046
69.9187
69.8372
25.5892
O
Ph
F
220
200
180
160
140
120
100
80
60
40
20
ppm


19Fta-151204-dihydrofuran-Ph
24.1235
24.1141
24.1032
O
Ph
F
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
ppm

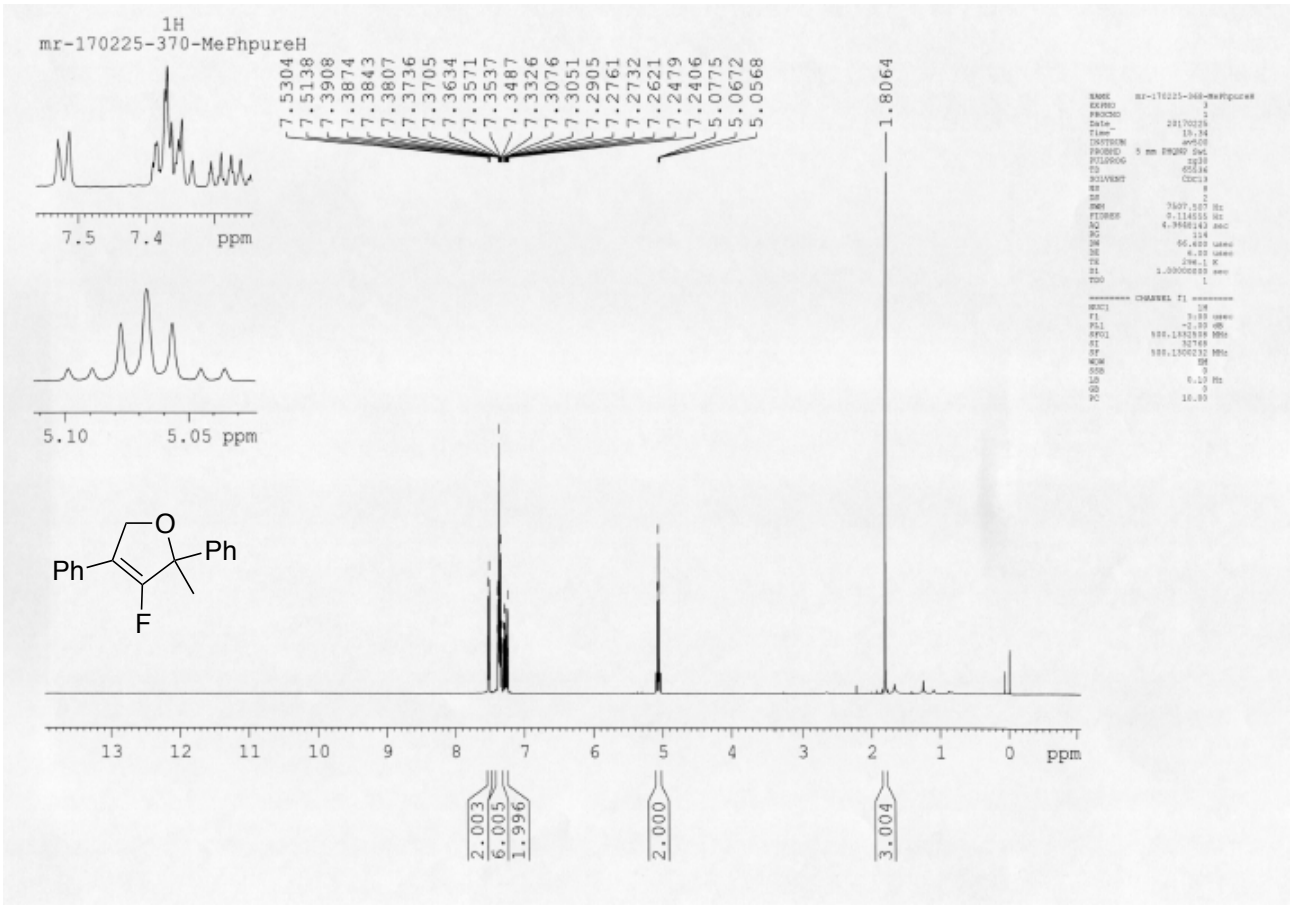
2,2-Diethyl-3-fluoro-4-phenyl-2,5-dihydrofuran (4b)

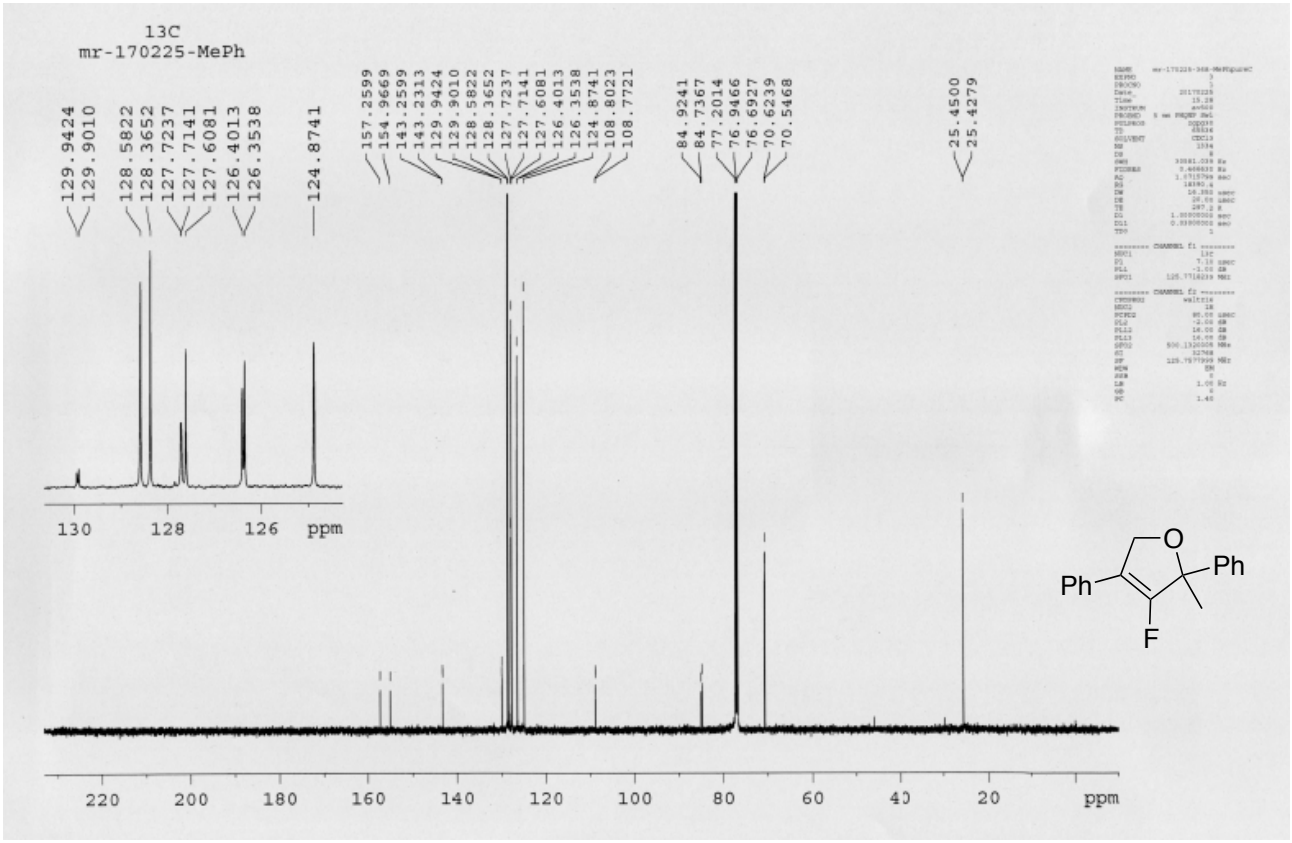


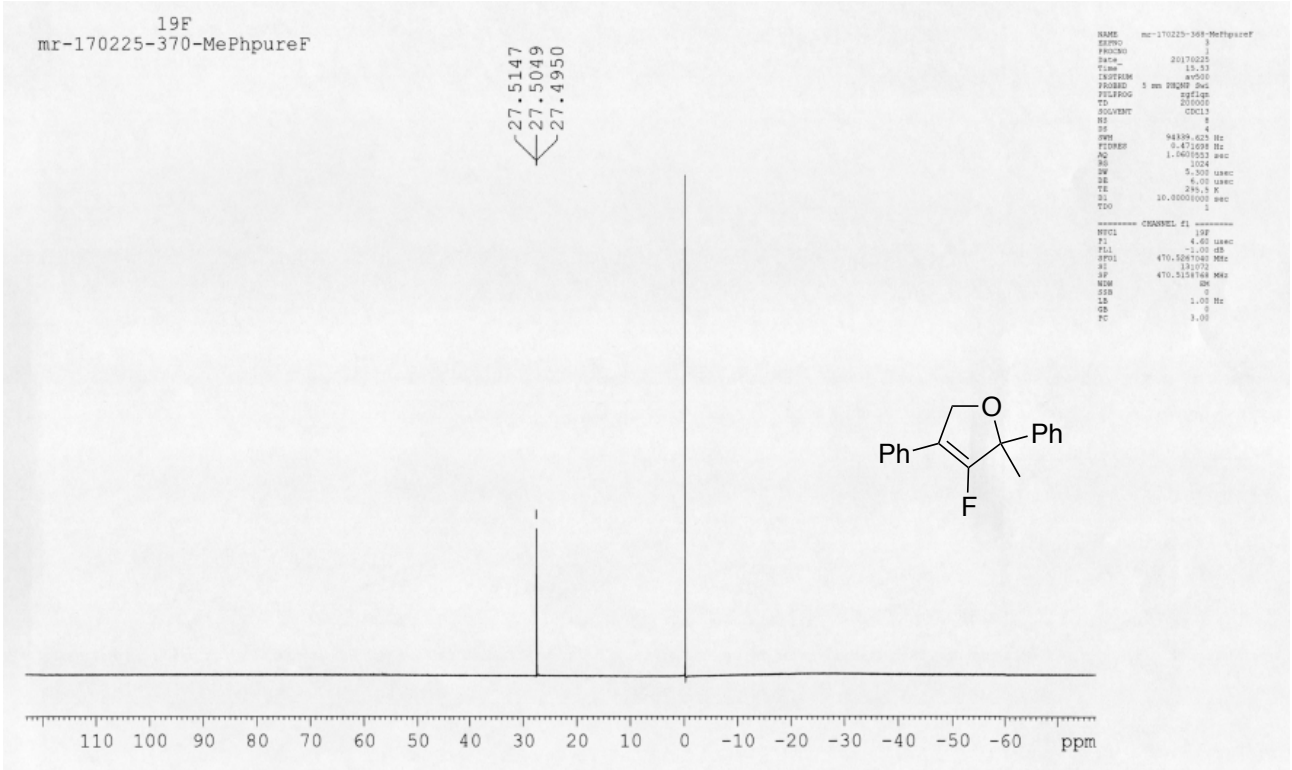




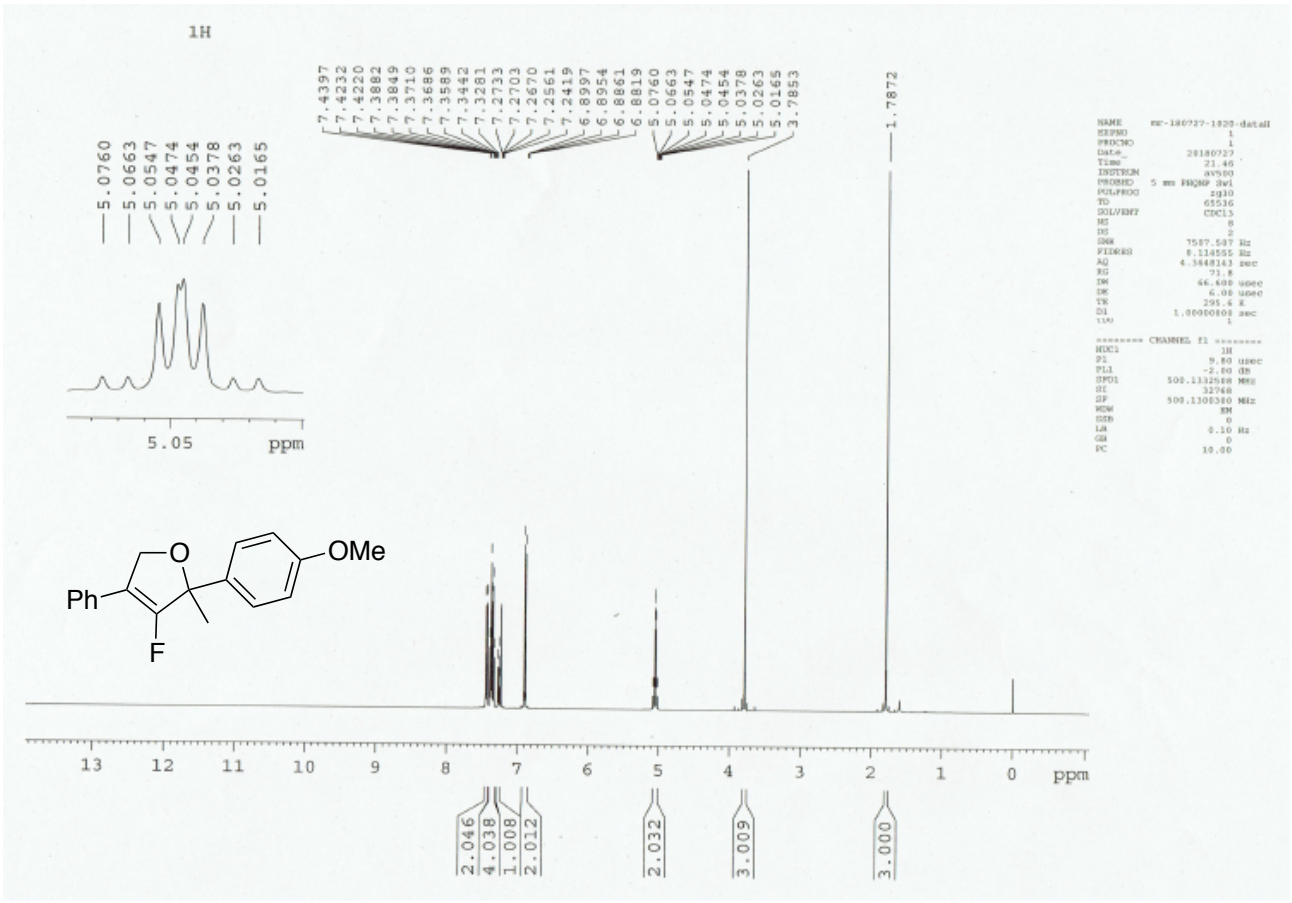
3-Fluoro-2-methyl-2,4-diphenyl-2,5-dihydrofuran (4c)

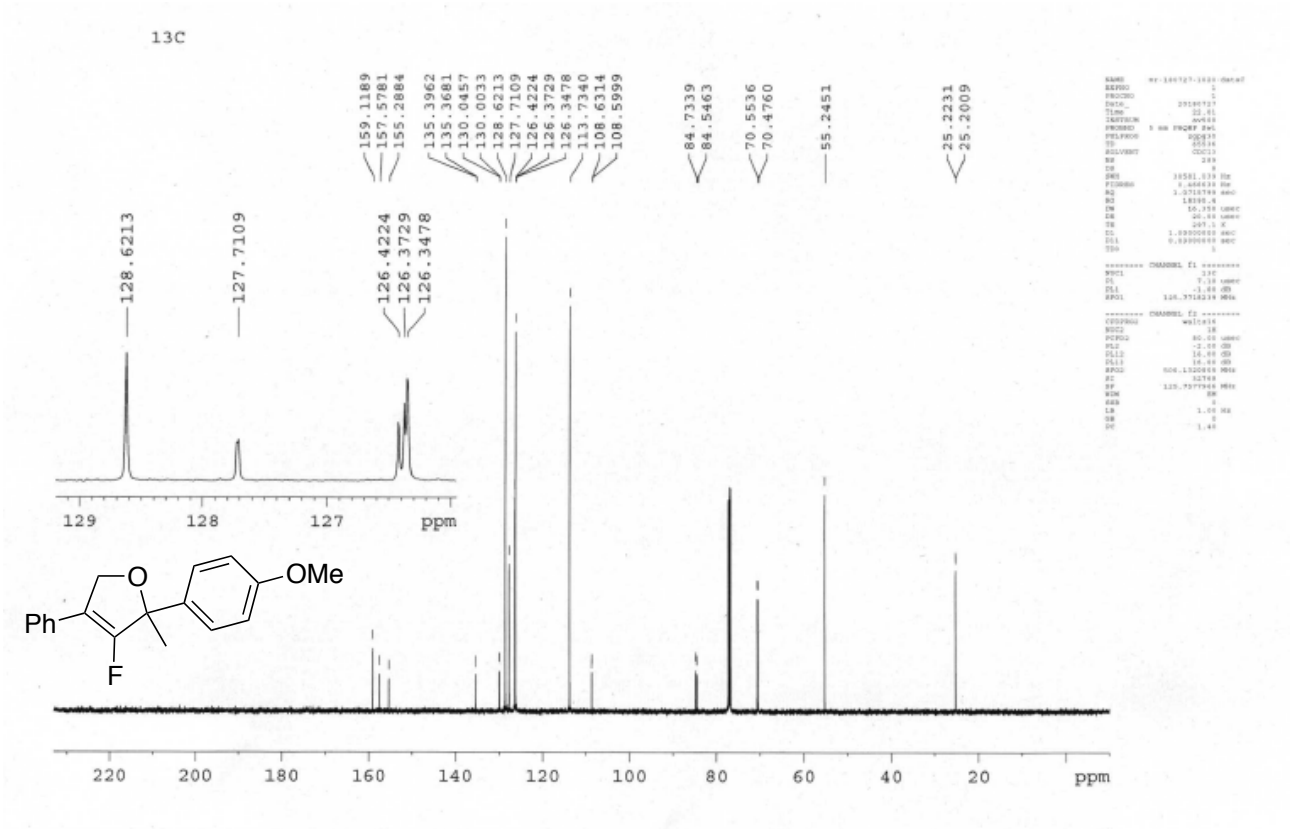


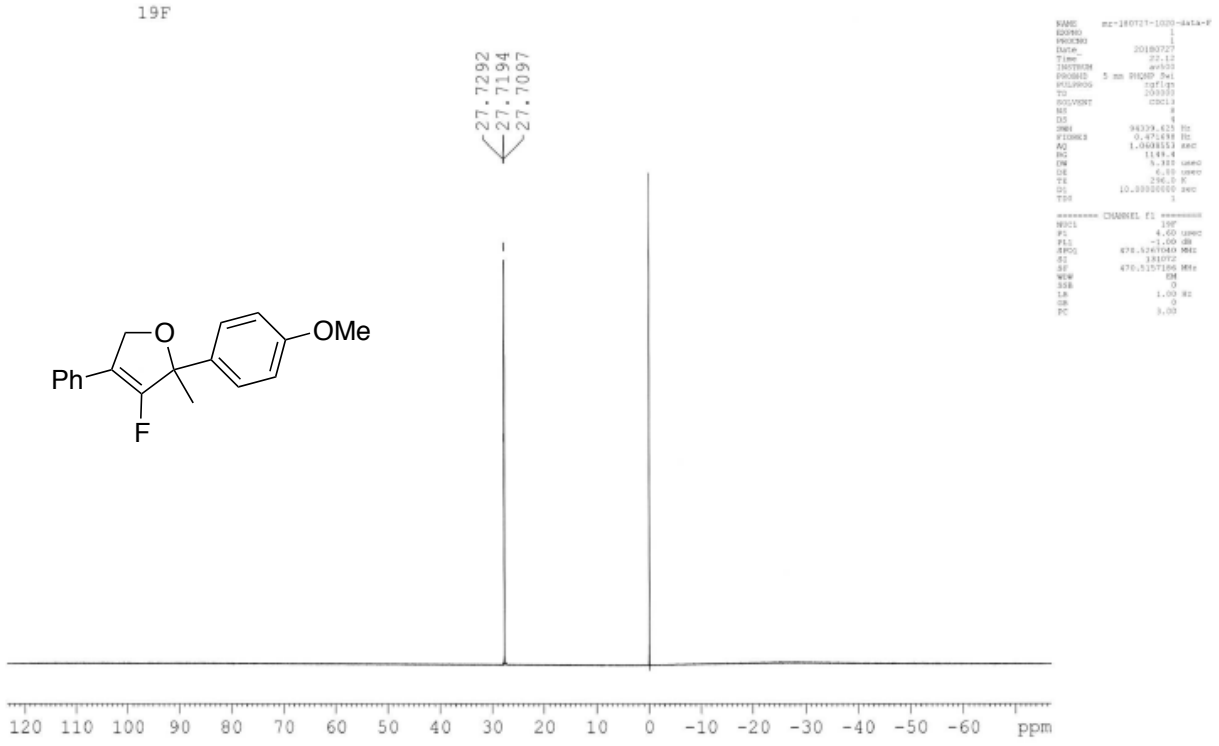

13C
mr-170225-MePh
129.9424
129.9010
128.5822
128.3652
127.7237
127.7141
127.6081
126.4013
126.3538
124.8741
157.2599
154.9669
143.2599
143.2313
129.9424
129.9010
128.5822
128.3652
127.7237
127.7141
127.6081
126.4013
126.3538
124.8741
108.8023
108.7721
84.9241
84.7367
77.2014
76.9466
76.6927
70.6239
70.5468
25.4500
25.4279
130
128
126
ppm
220
200
180
160
140
120
100
80
60
40
20
ppm
Ph
Ph
O
F


19F
mr-170225-370-MePhpureF
27.5147
27.5049
27.4950
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
ppm
Ph
Ph
O
F

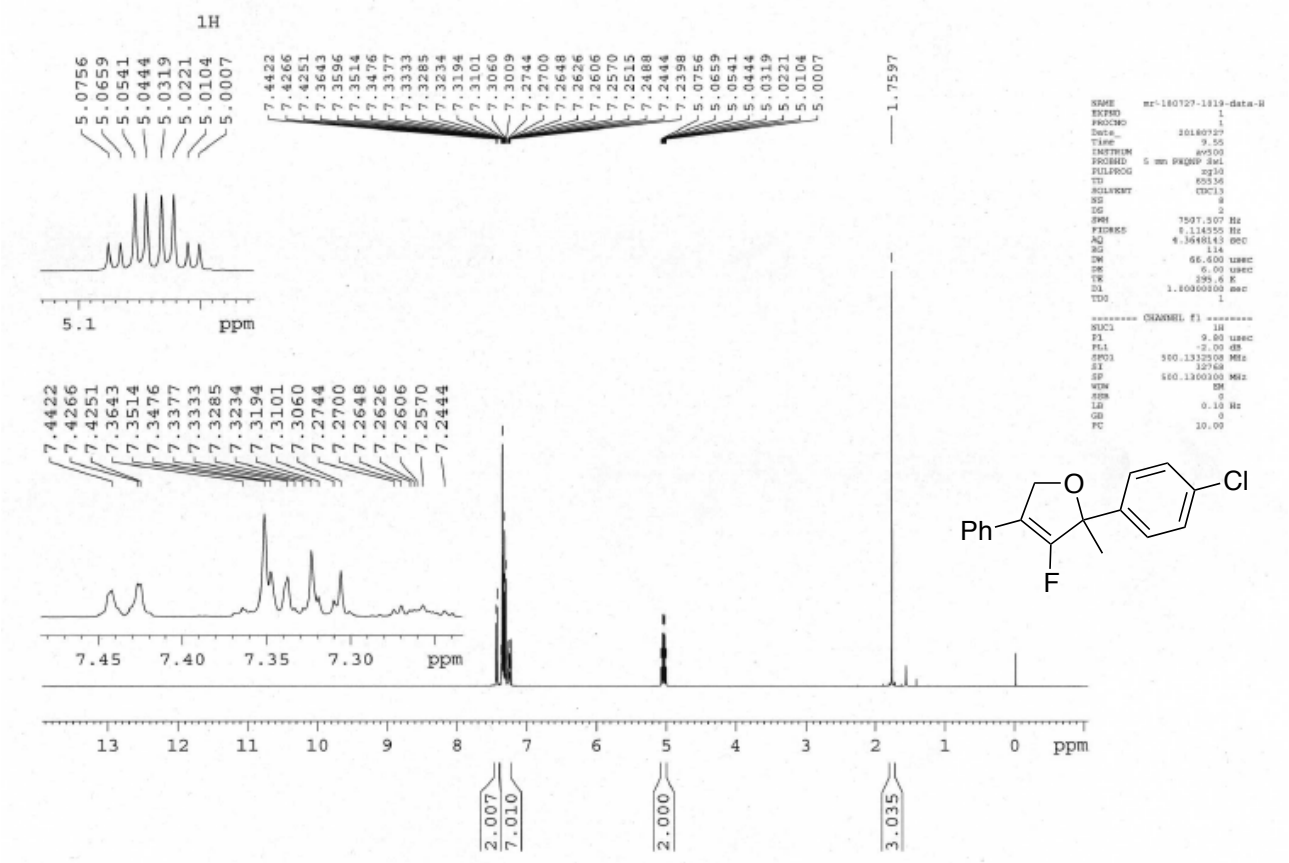
3-Fluoro-2-(4-methoxyphenyl)-2-methyl-4-phenyl-2,5-dihydrofuran (4d)

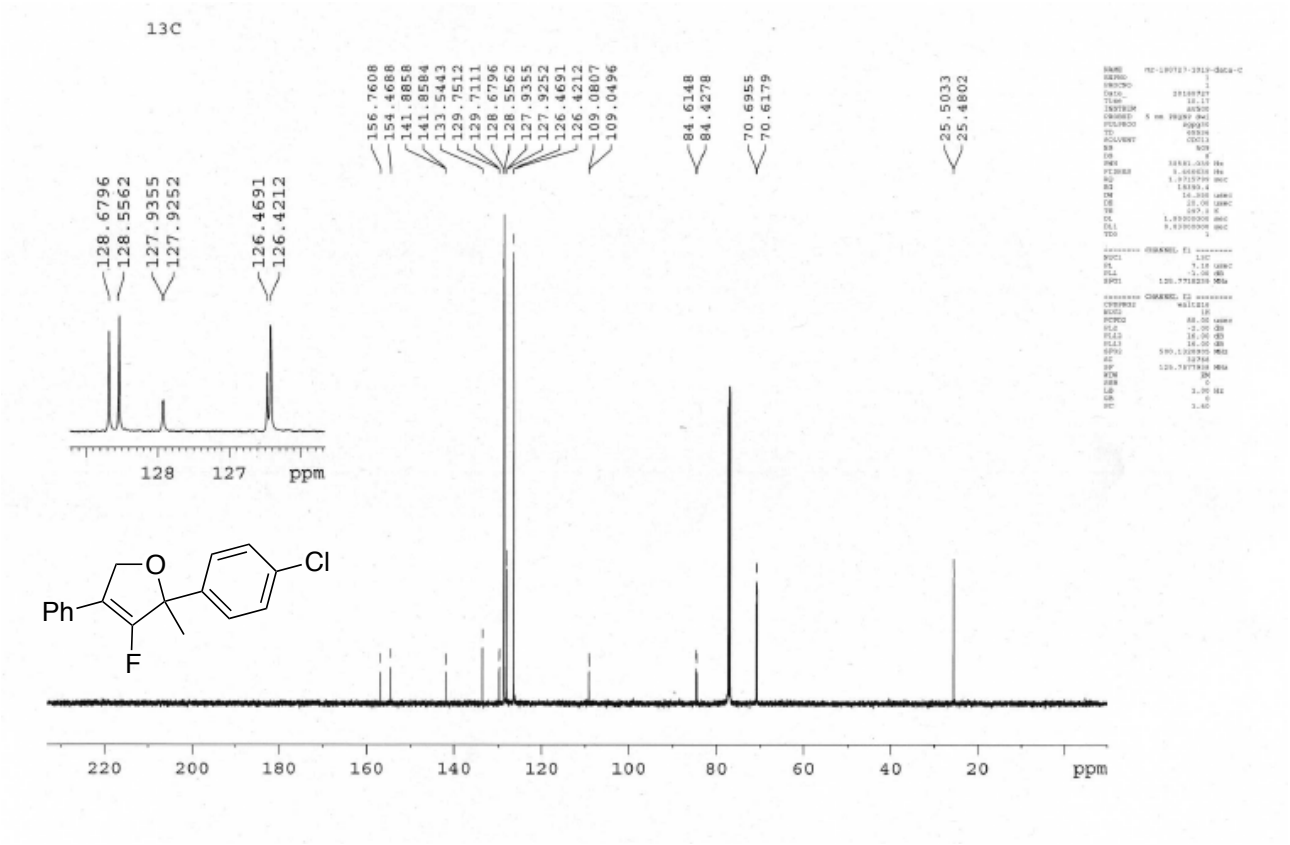


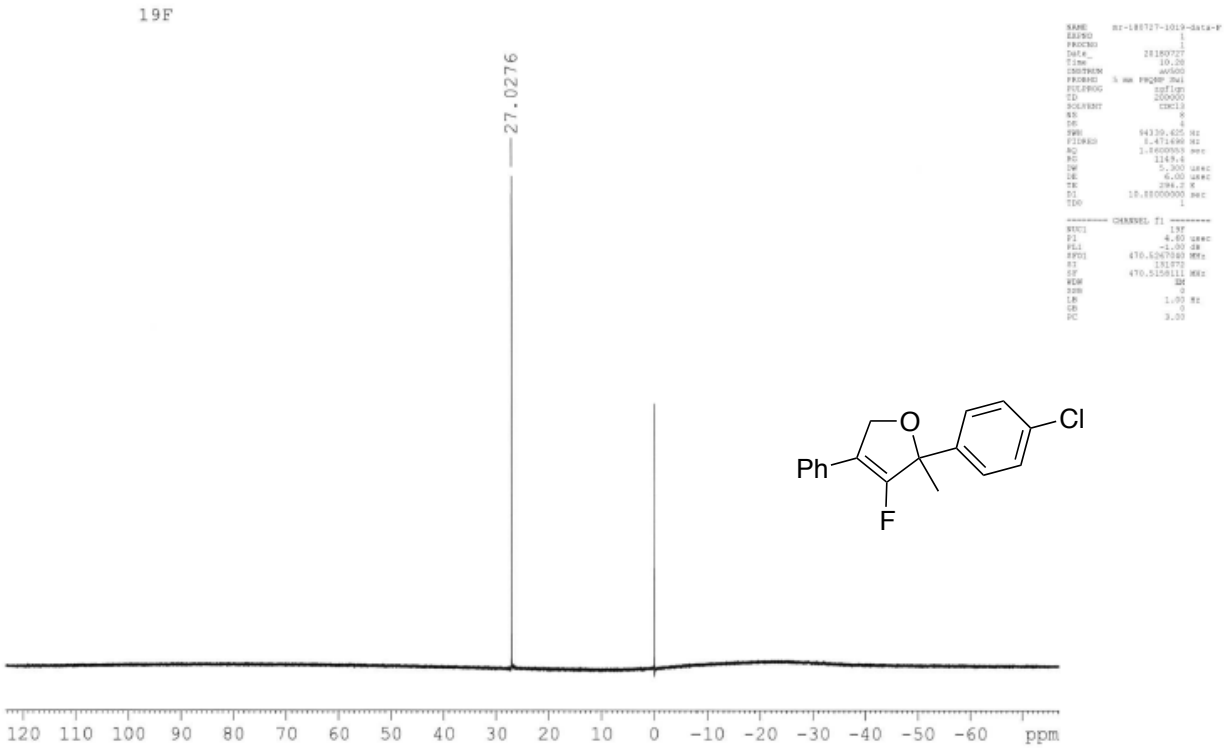




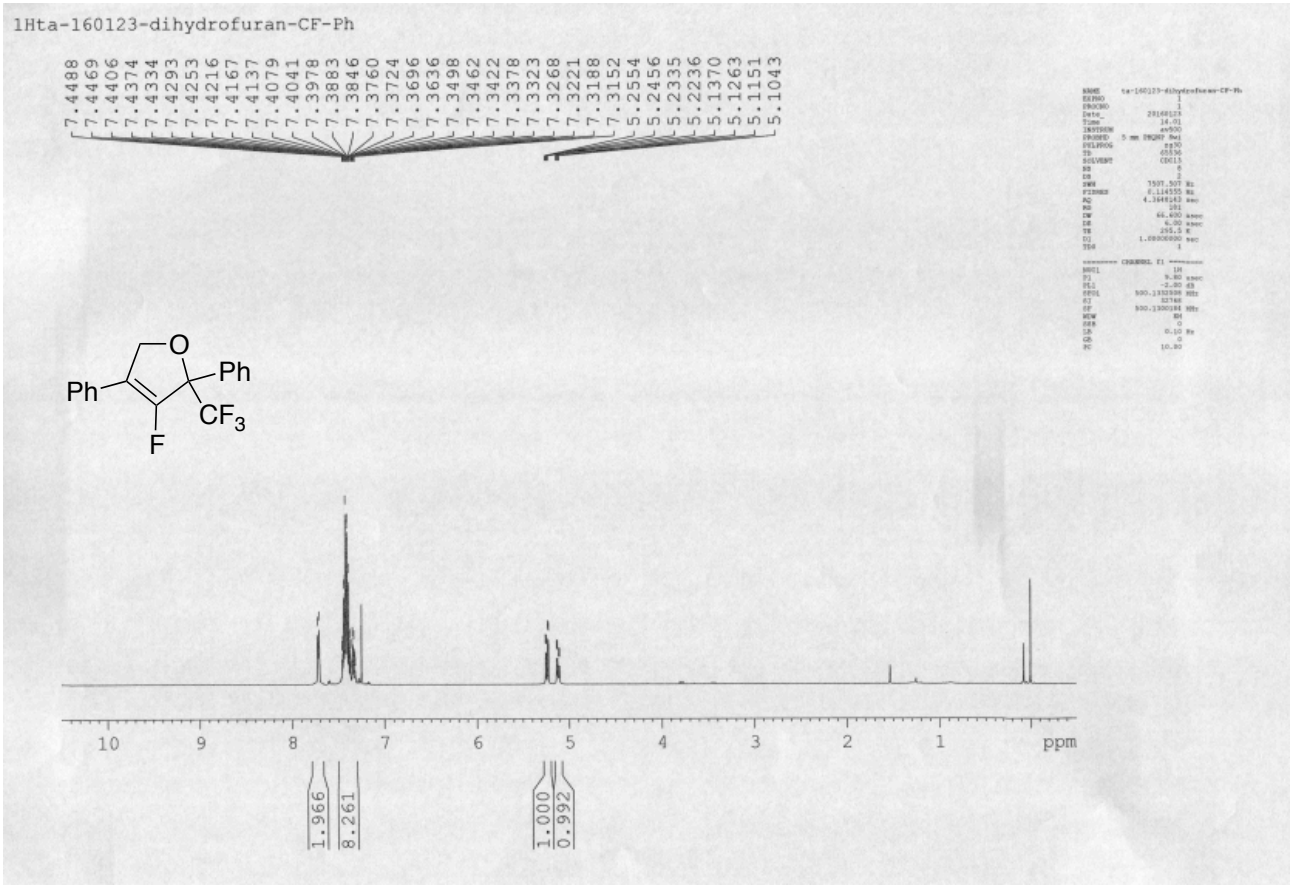
2-(4-Chlorophenyl)-3-fluoro-2-methyl-4-phenyl-2,5-dihydrofuran (4e)

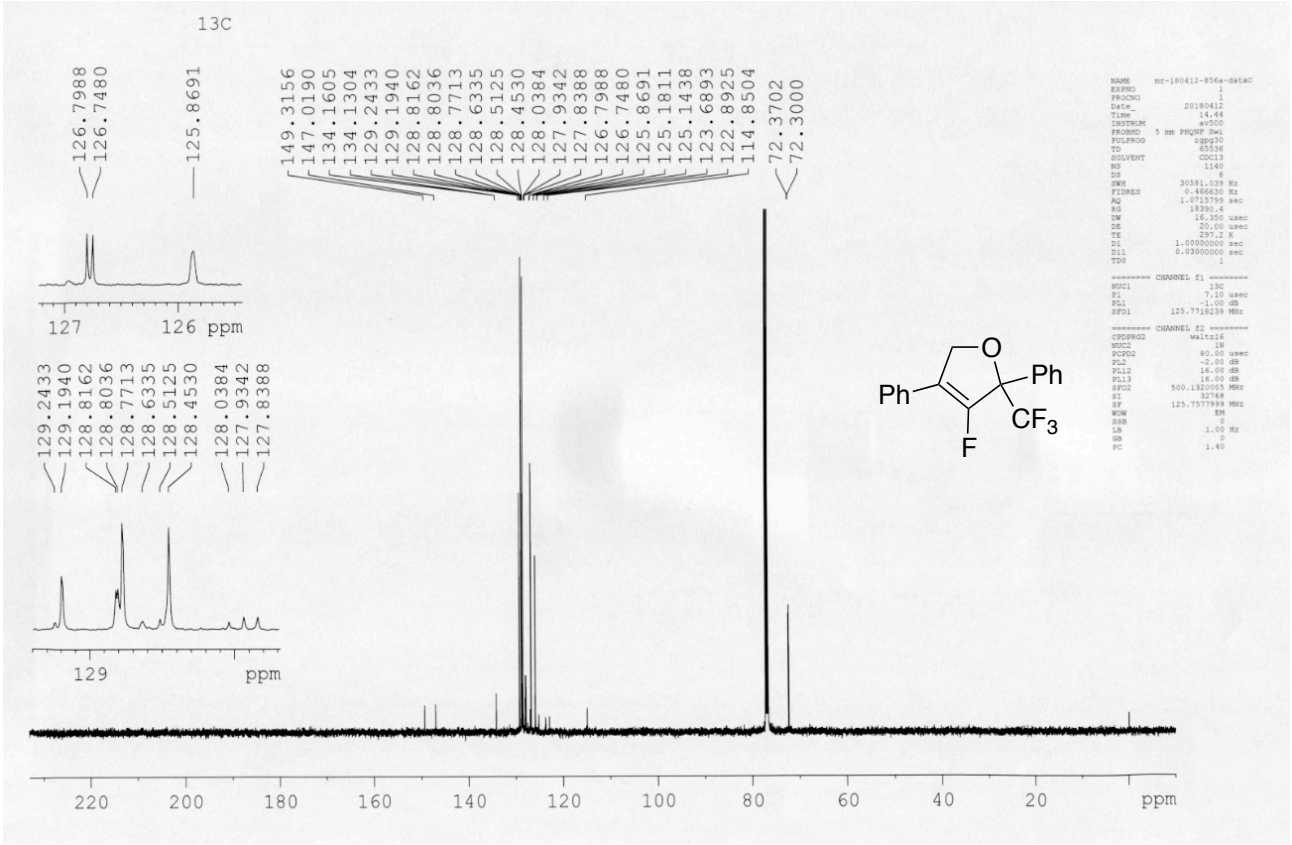


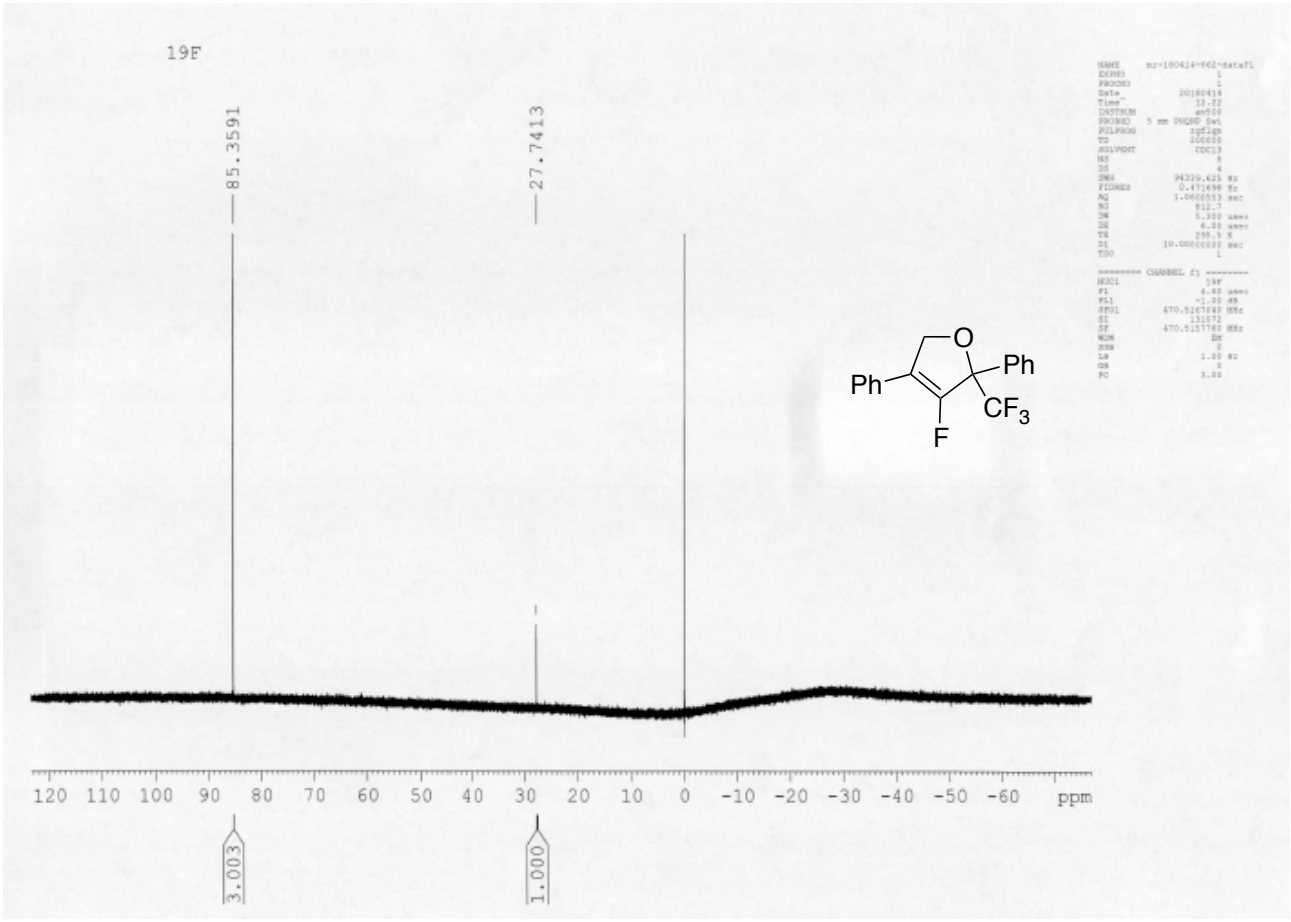

13C
156.7608
154.4688
141.8858
141.8504
133.5443
129.7512
129.7111
128.6796
128.5562
127.9355
127.9252
126.4691
126.4212
109.0807
109.0496
84.6148
84.4278
70.6955
70.6179
25.5033
25.4802
128.6796
128.5562
127.9355
127.9252
126.4691
126.4212
128
127
ppm
O
Cl
Ph
F
220
200
180
160
140
120
100
80
60
40
20
ppm


19F
27.0276
O
Cl
Ph
F
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
ppm

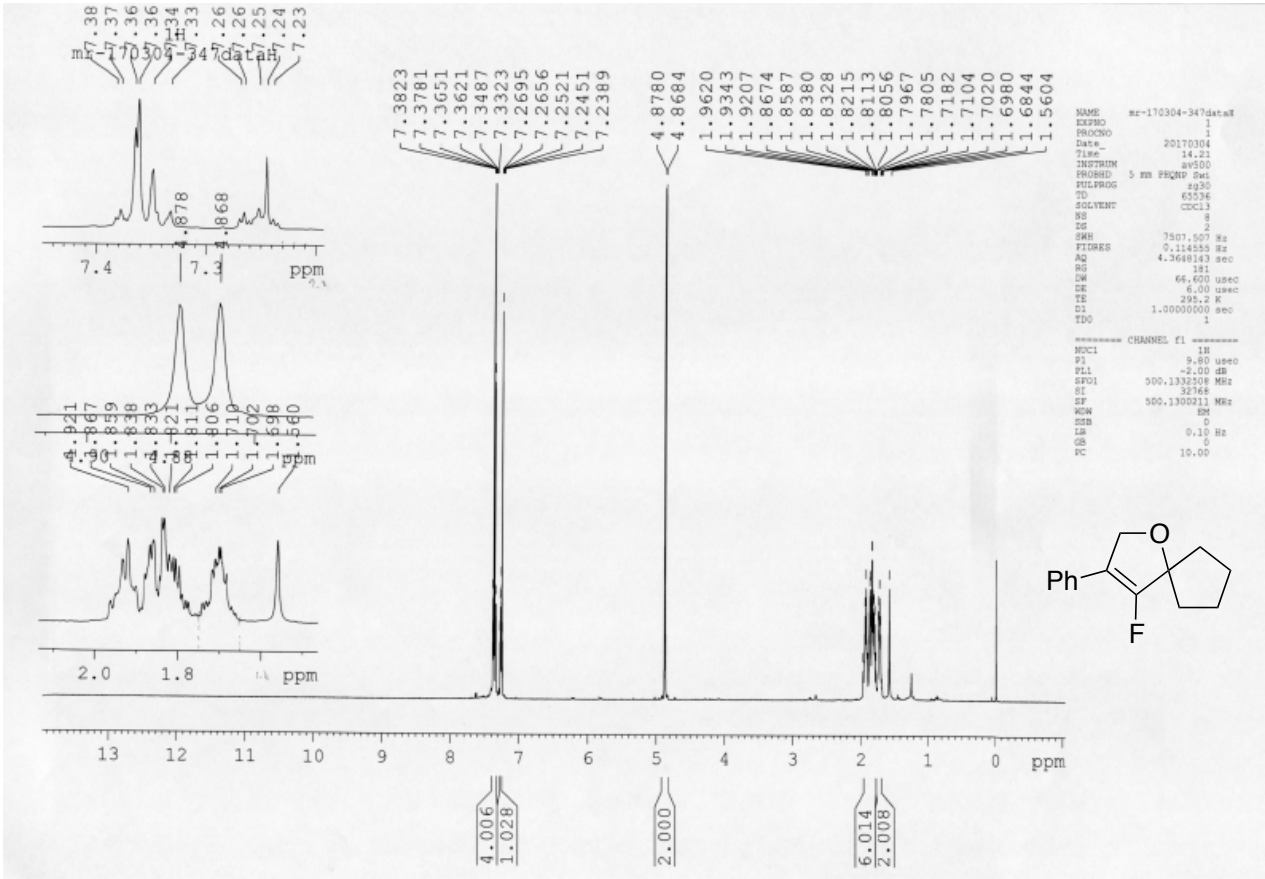
3-Fluoro-2,4-diphenyl-2-(trifluoromethyl)-2,5-dihydrofuran (4f)

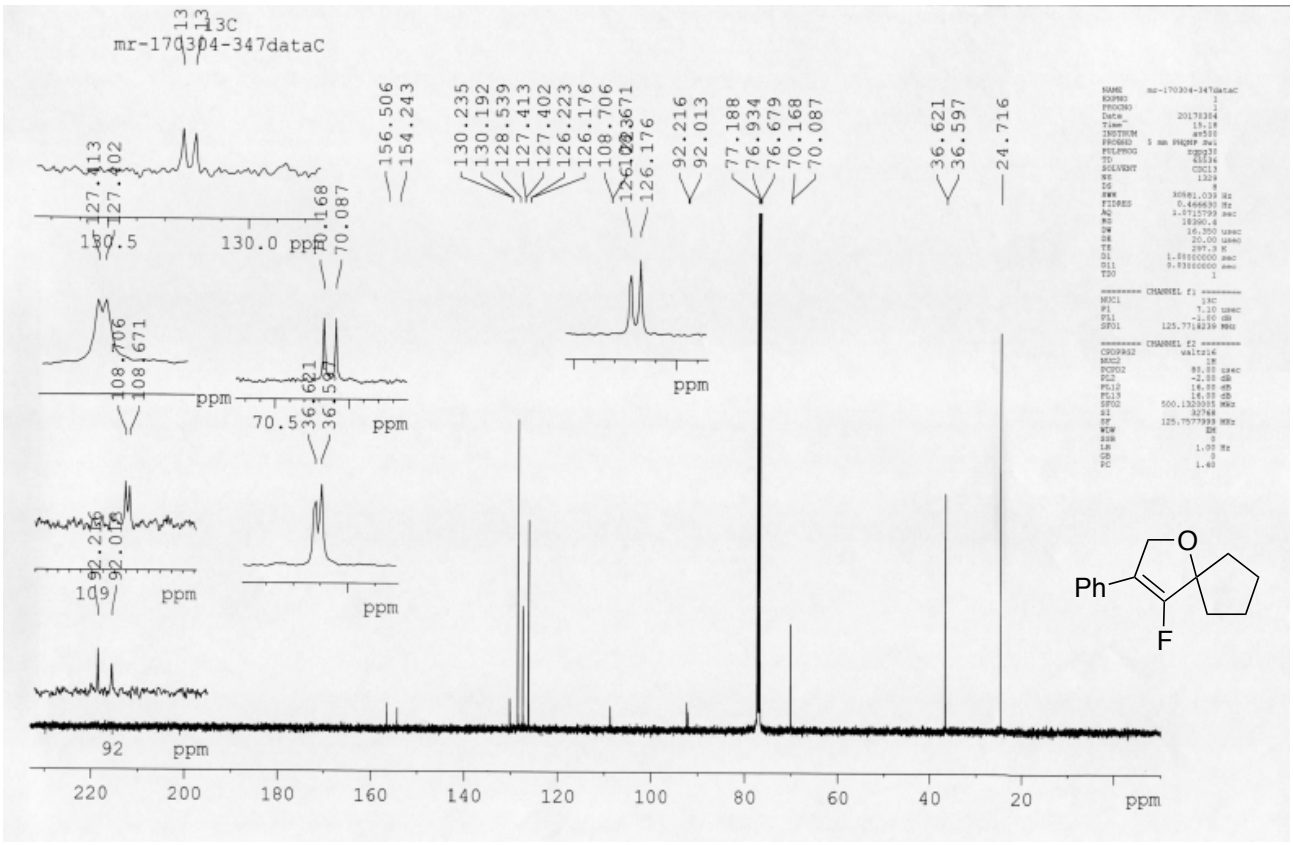


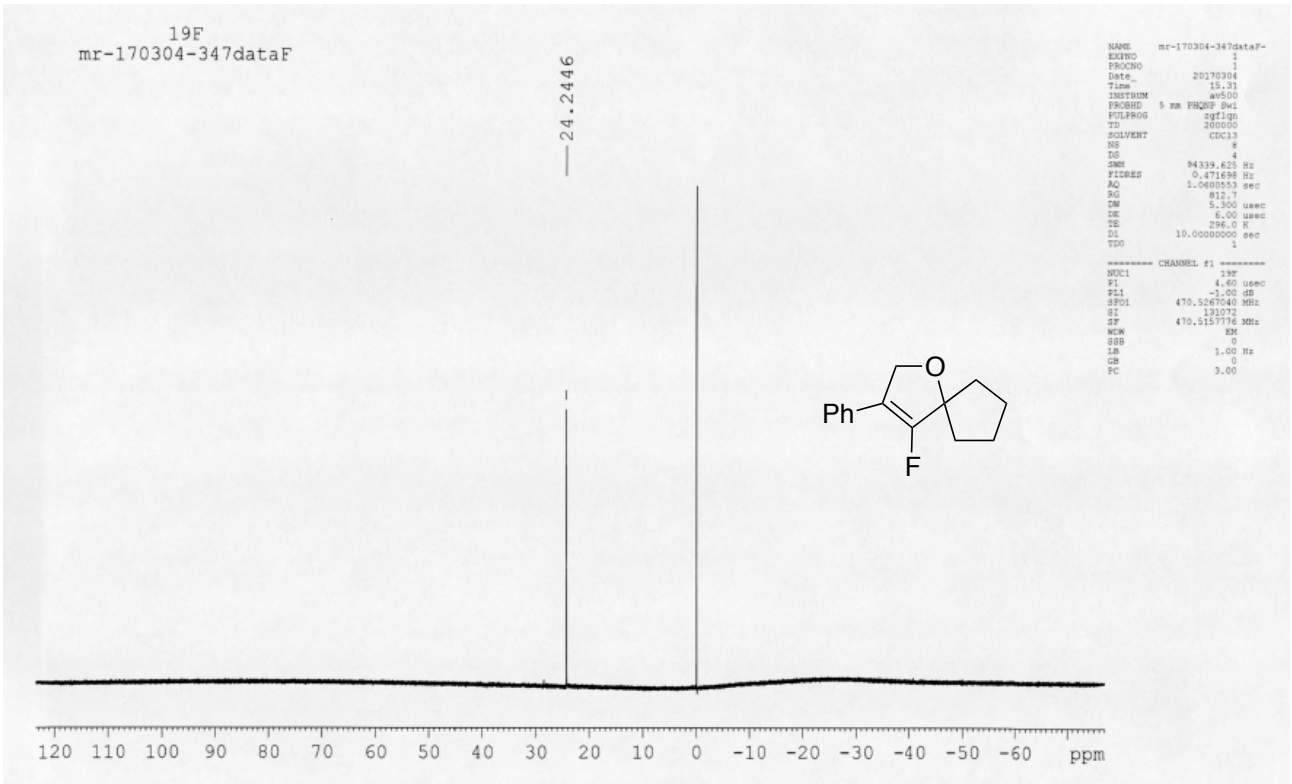




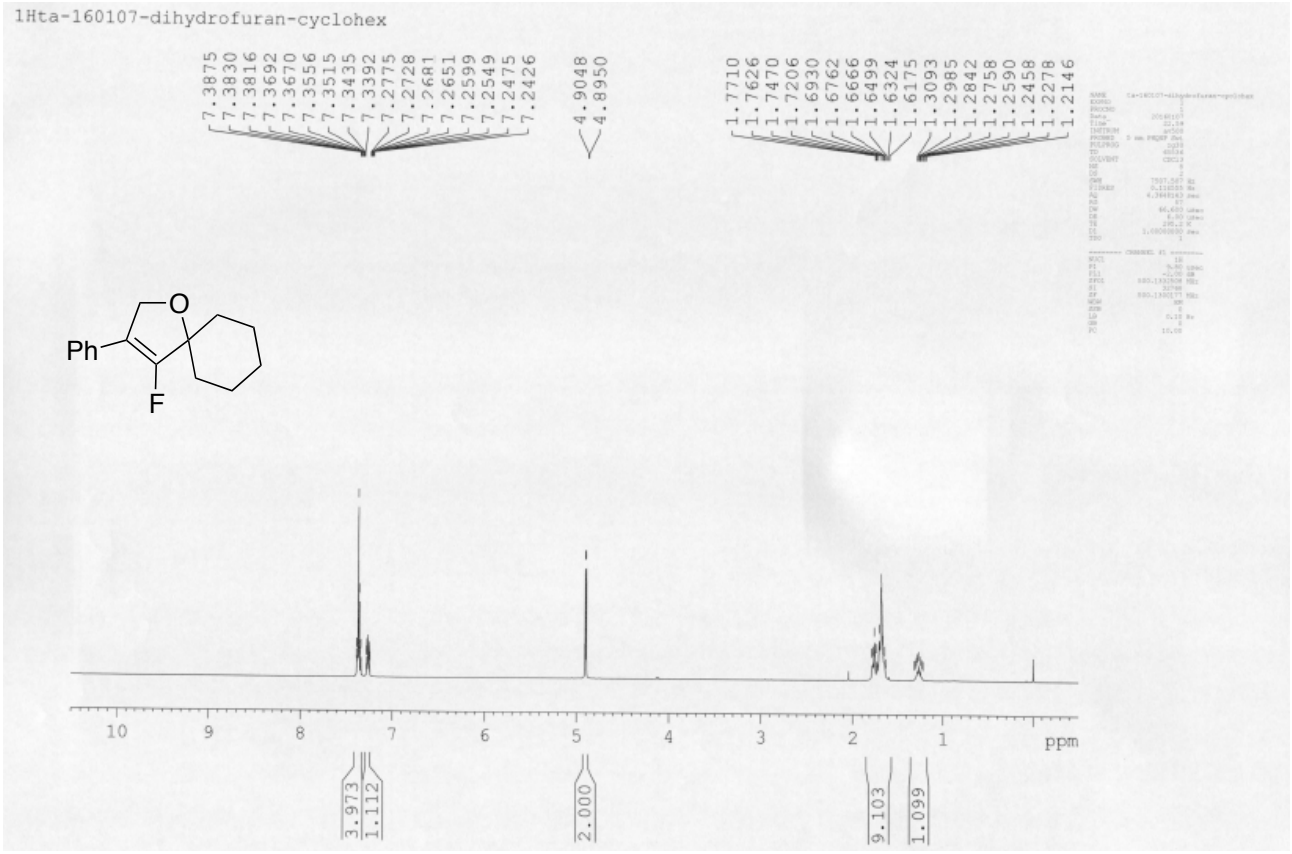
4-Fluoro-3-phenyl-1-oxaspiro[4.4]non-3-ene (4g)

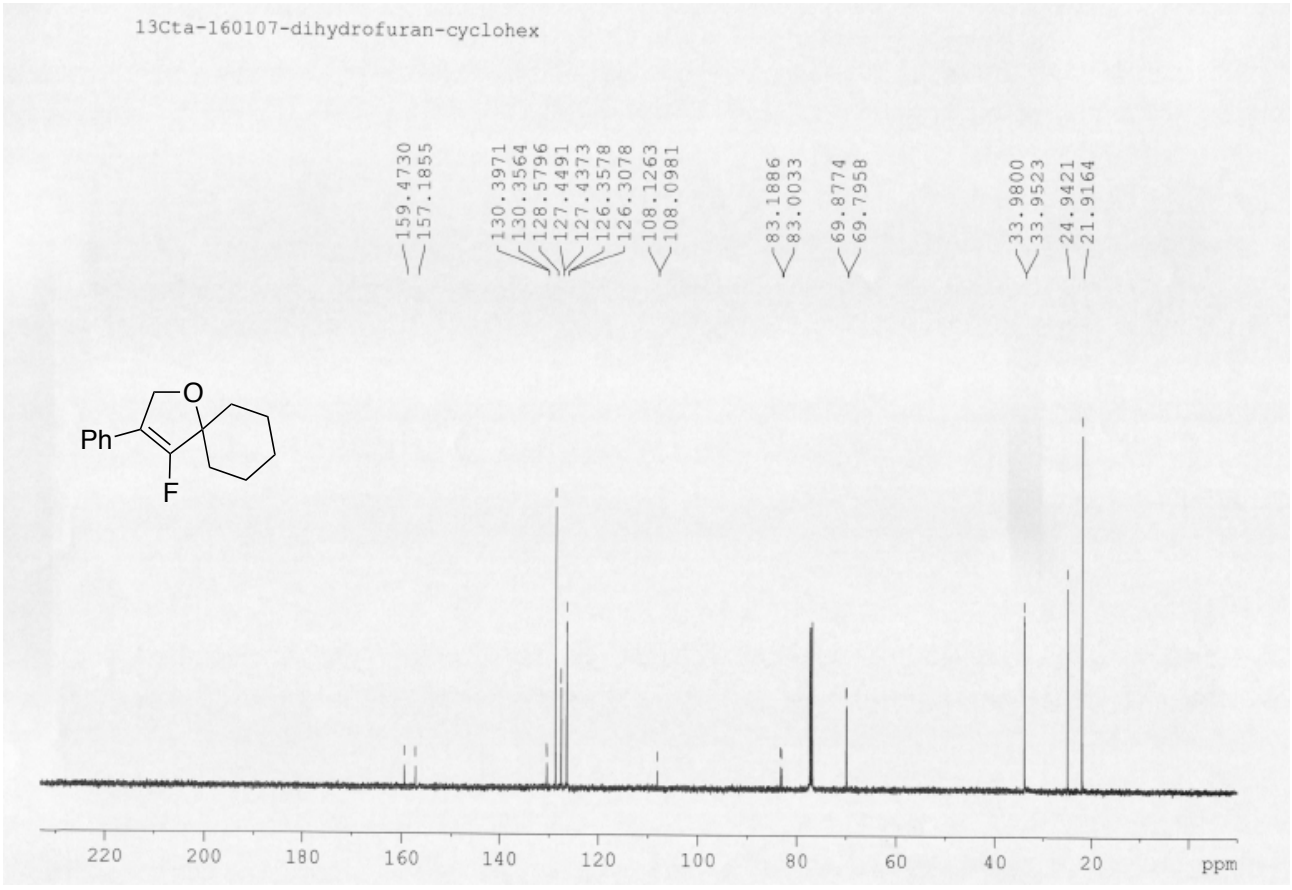


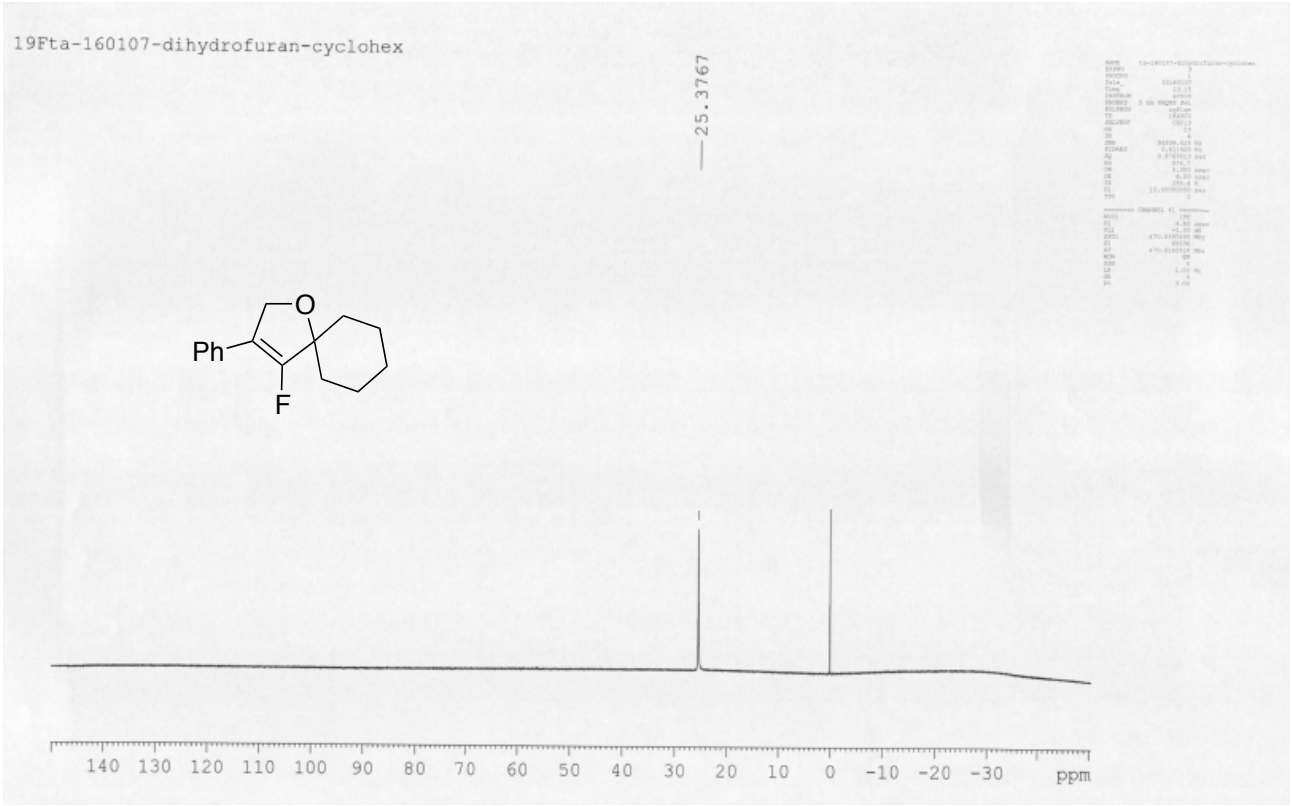

13C
mr-170304-347dataC
156.506
154.243
130.235
130.192
128.539
127.413
127.402
126.223
126.176
92.216
92.013
77.188
76.934
76.679
70.168
70.087
36.621
36.597
24.716
Ph
O
F
ppm


19F
mr-170304-347dataF
24.2446
Ph
O
F
ppm

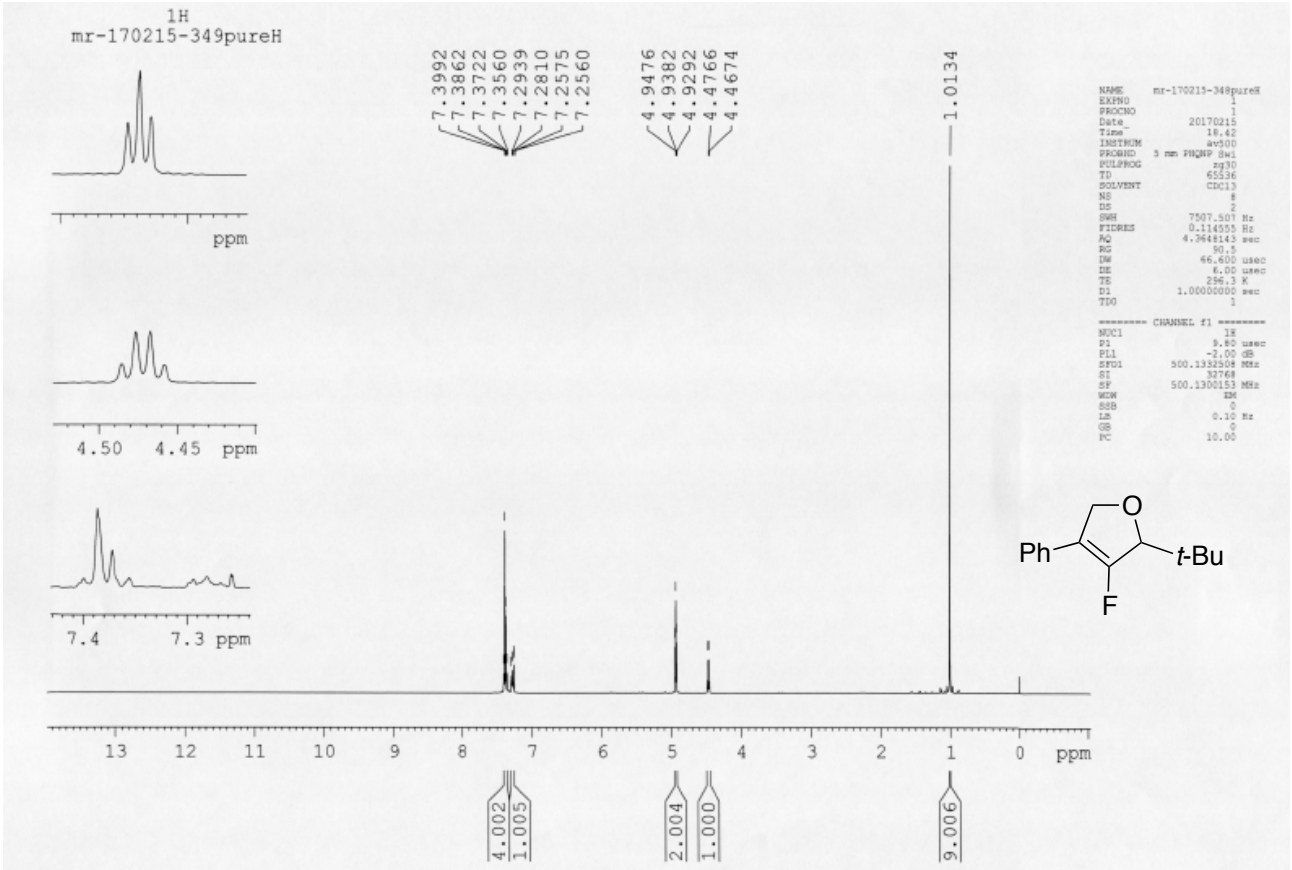
4-Fluoro-3-phenyl-1-oxaspiro[4.5]dec-3-ene (4h)

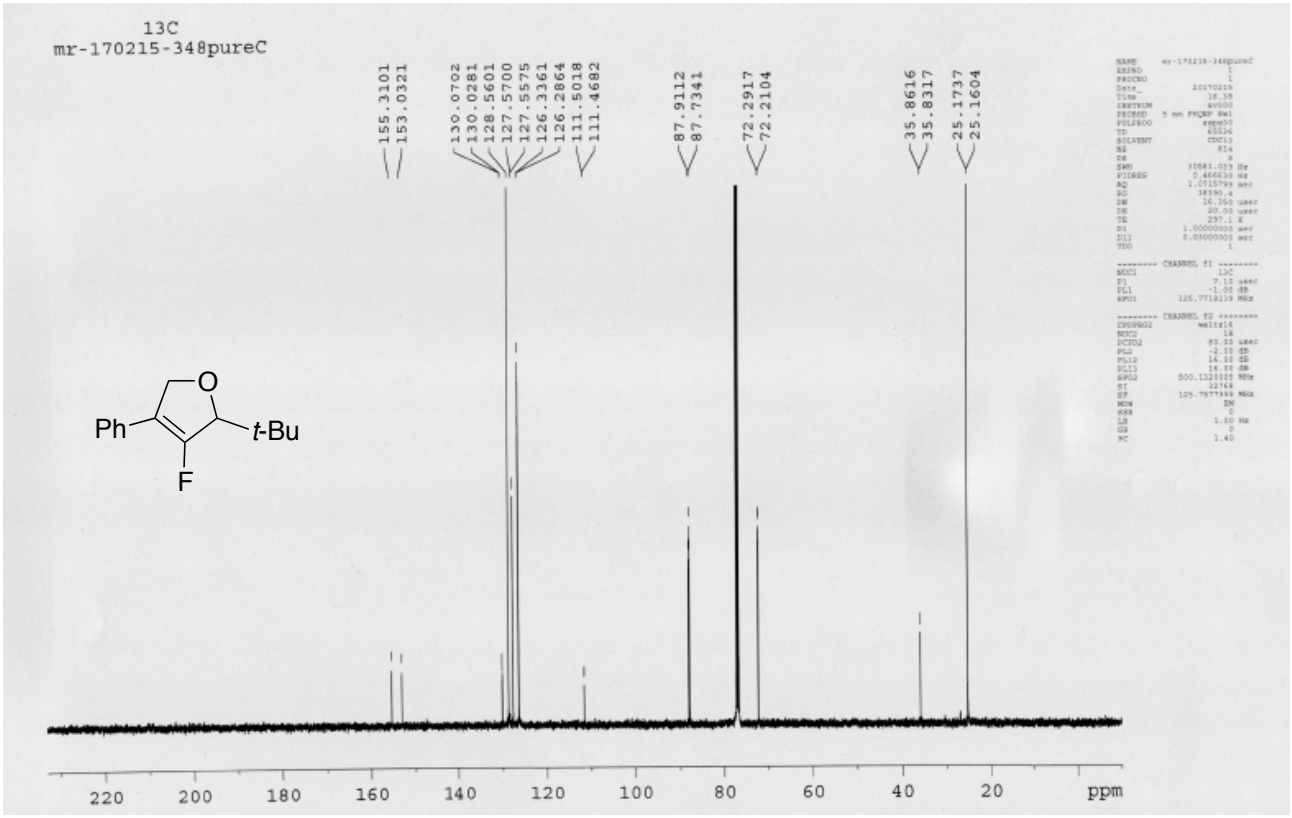


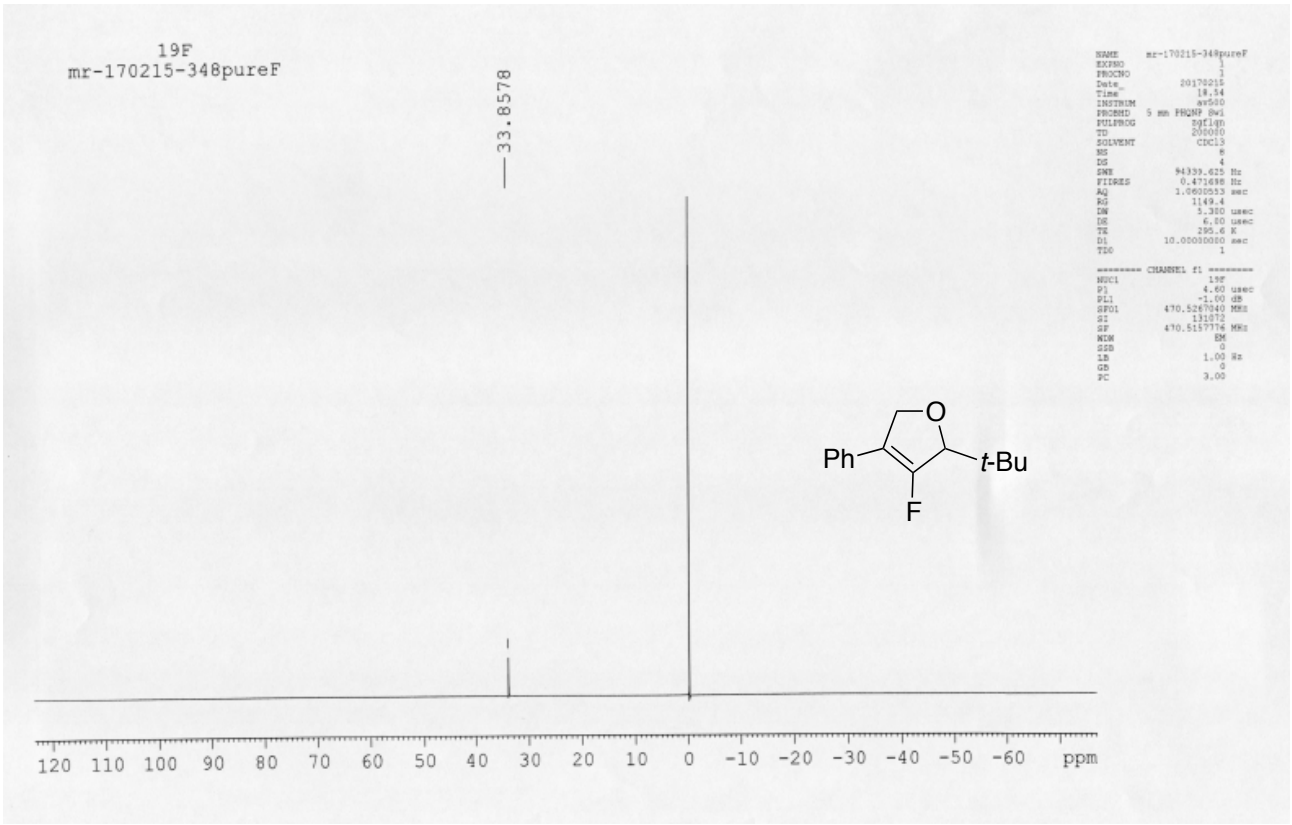




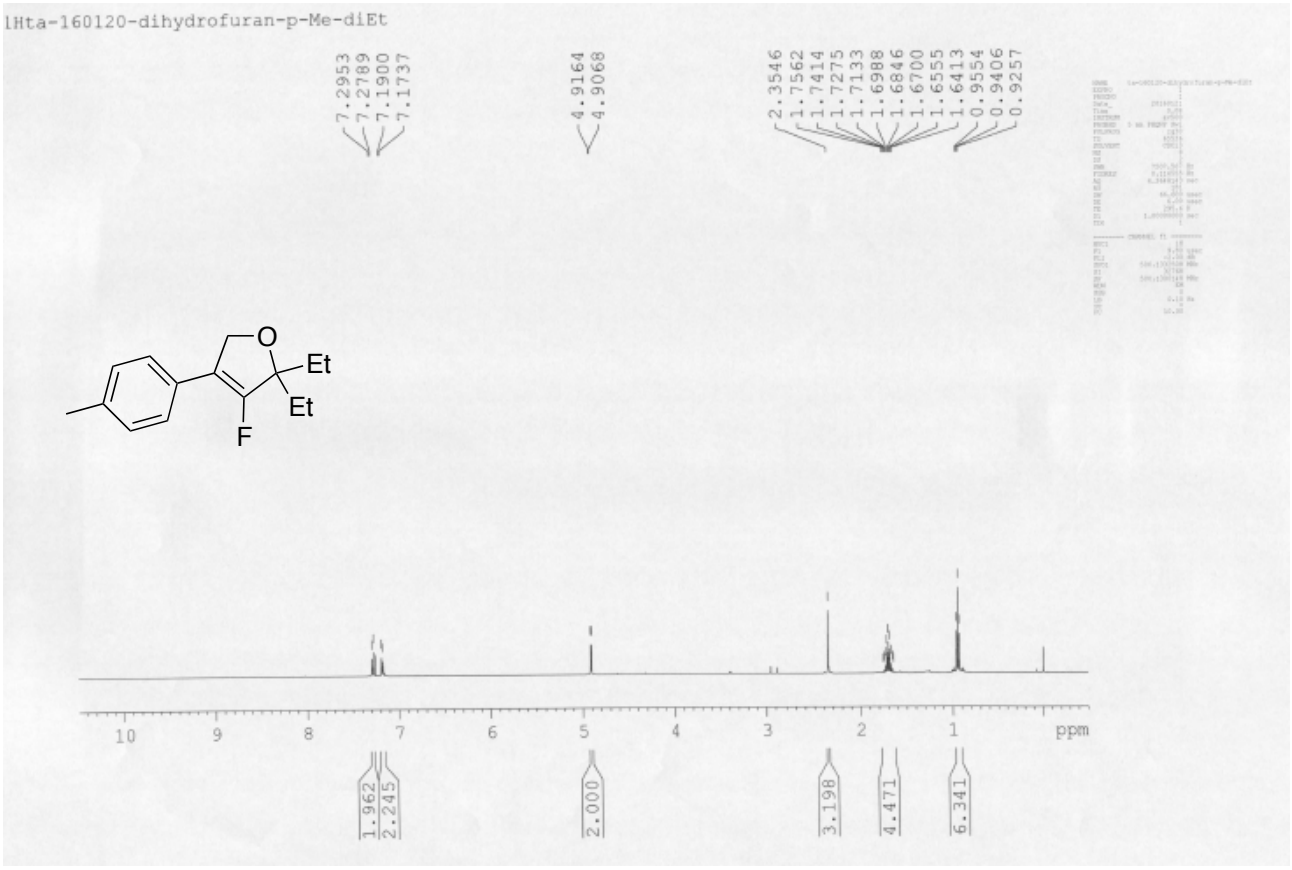
2-(*tert*-Butyl)-3-fluoro-4-phenyl-2,5-dihydrofuran (4i)

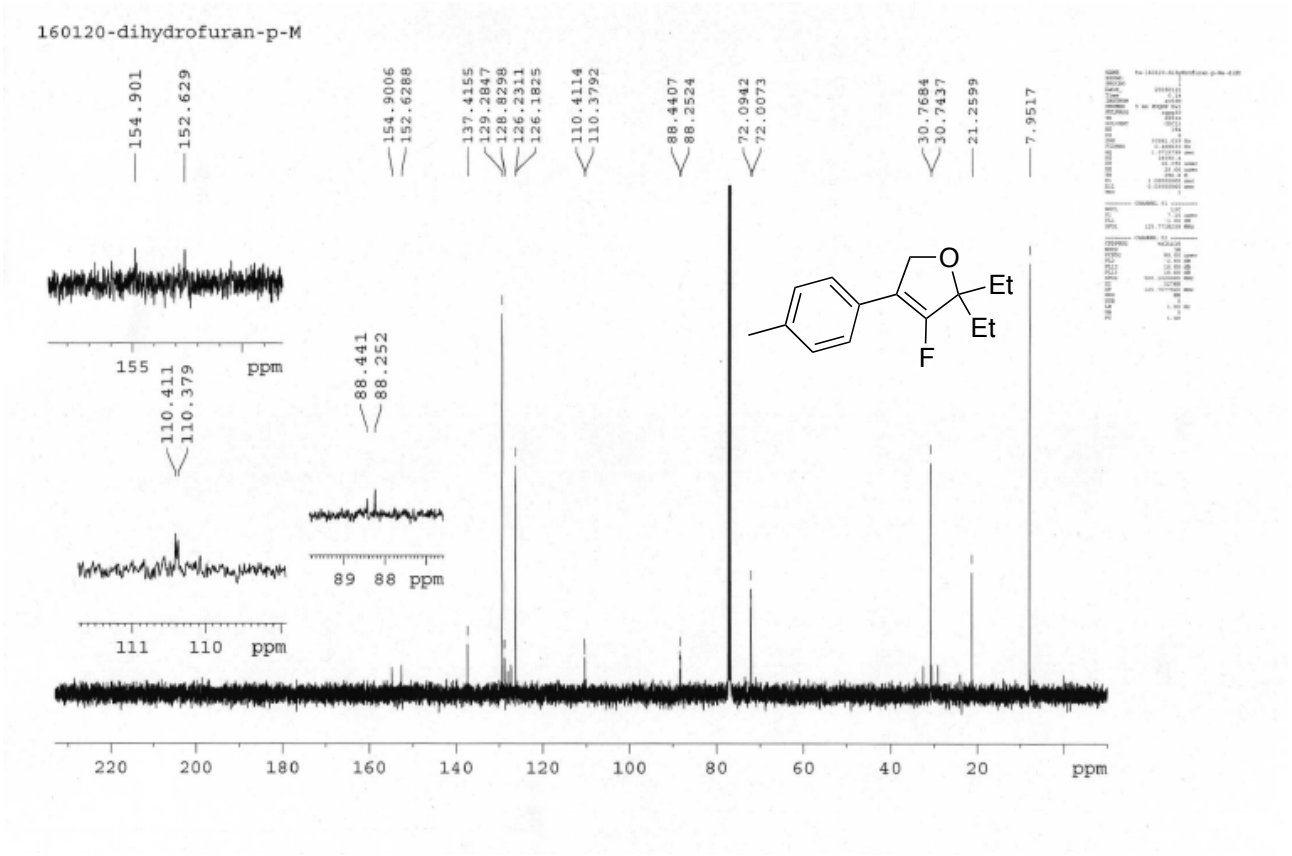


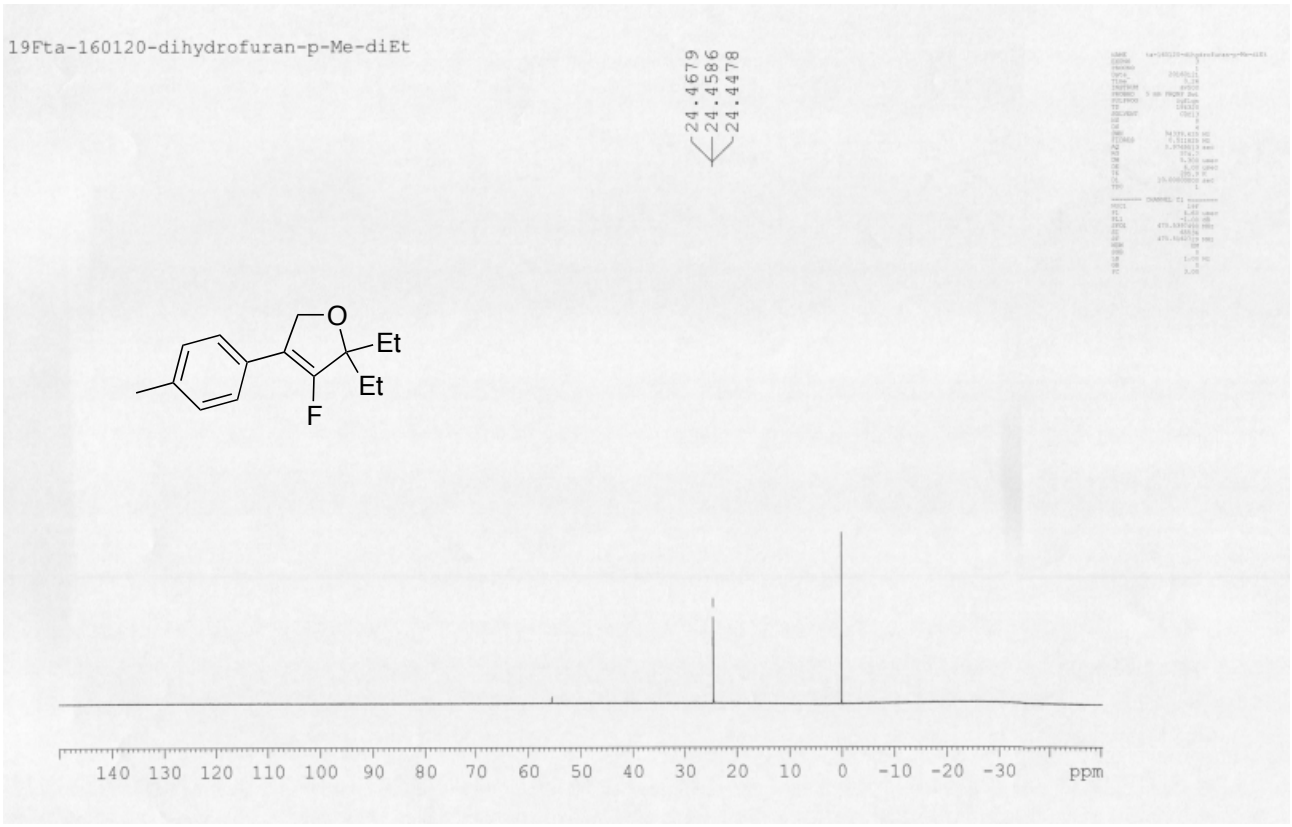

13C
mr-170215-348pureC
155.3101
153.0321
130.0702
130.0281
128.5601
127.5700
127.5575
126.3361
126.2864
111.5018
111.4682
87.9112
87.7341
72.2917
72.2104
35.8616
35.8317
25.1737
25.1604
Ph
t-Bu
F
220
200
180
160
140
120
100
80
60
40
20
ppm


19F
mr-170215-348pureF
33.8578
Ph
t-Bu
F
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
ppm

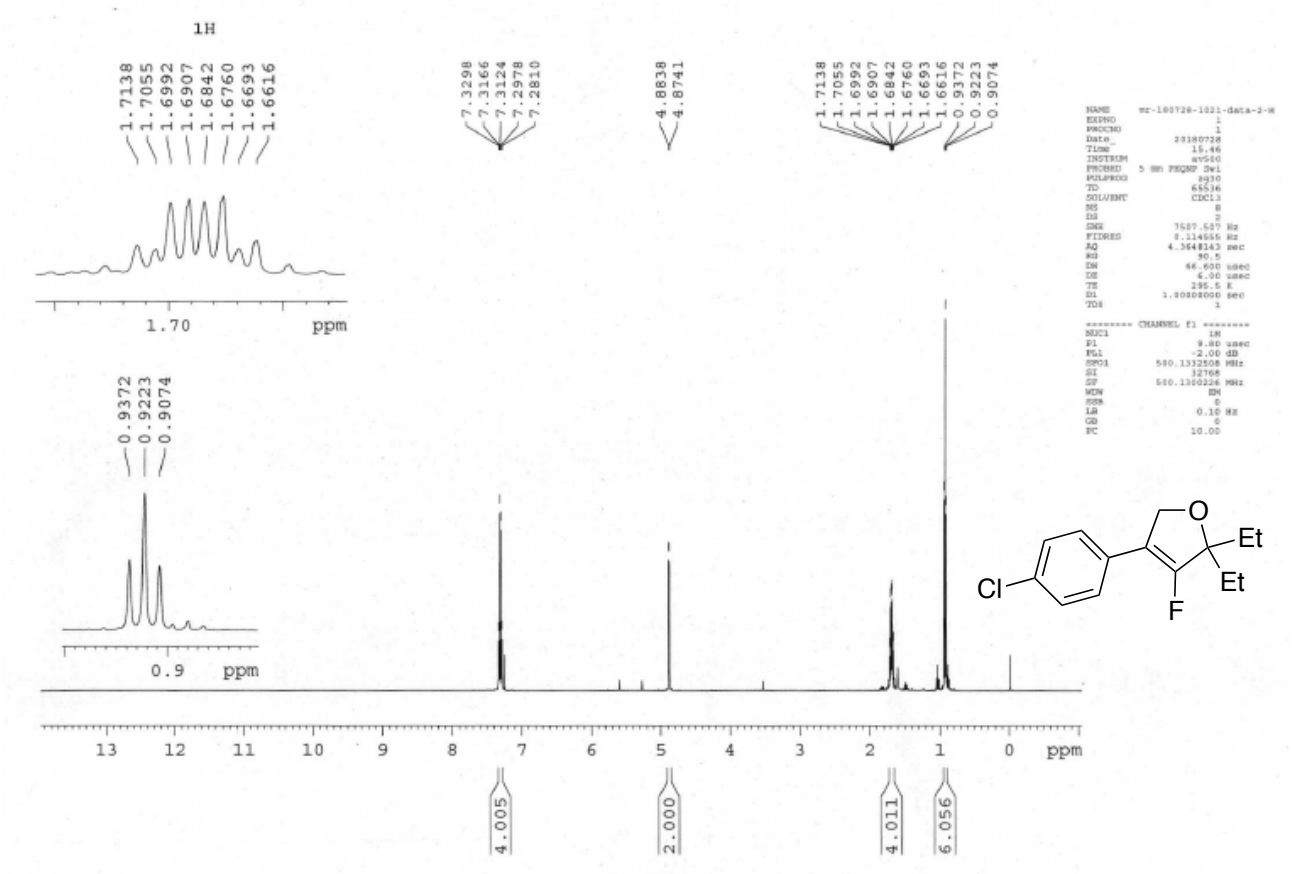
2,2-Diethyl-3-fluoro-4-(4-methylphenyl)-2,5-dihydrofuran (4j)

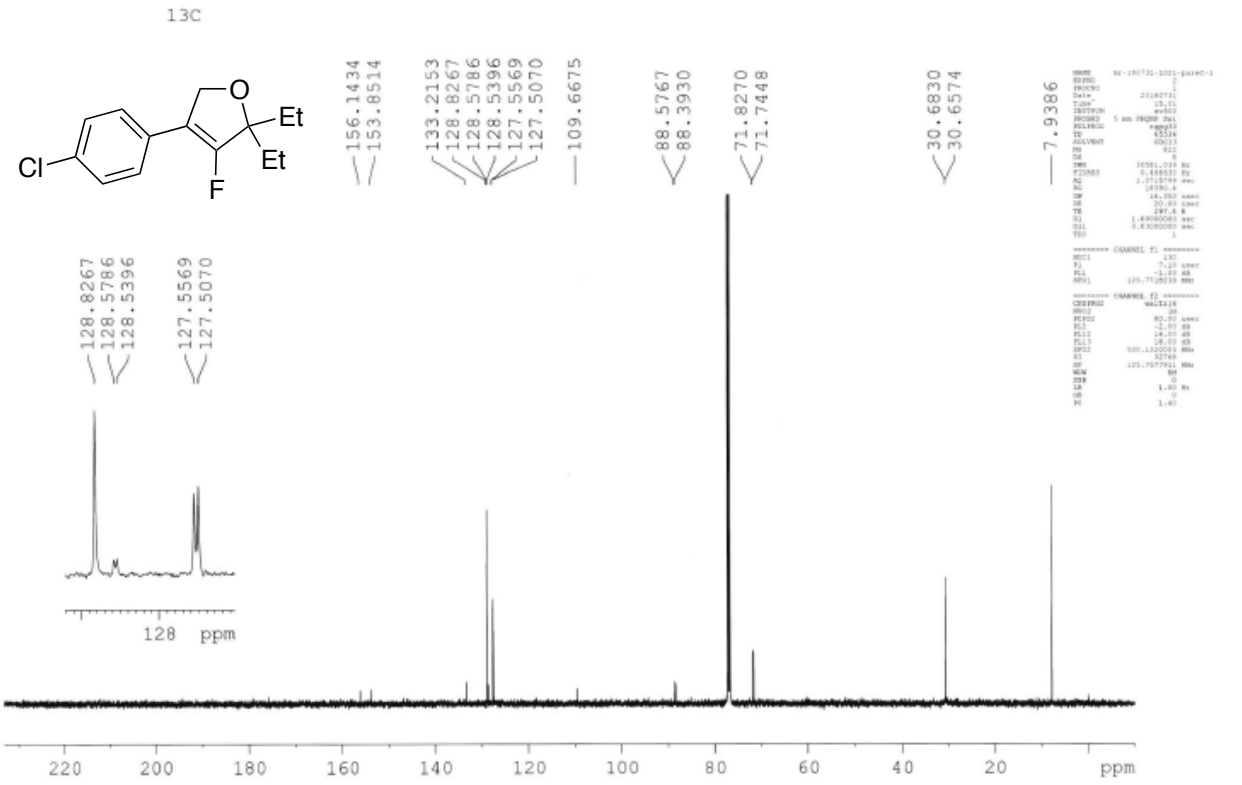


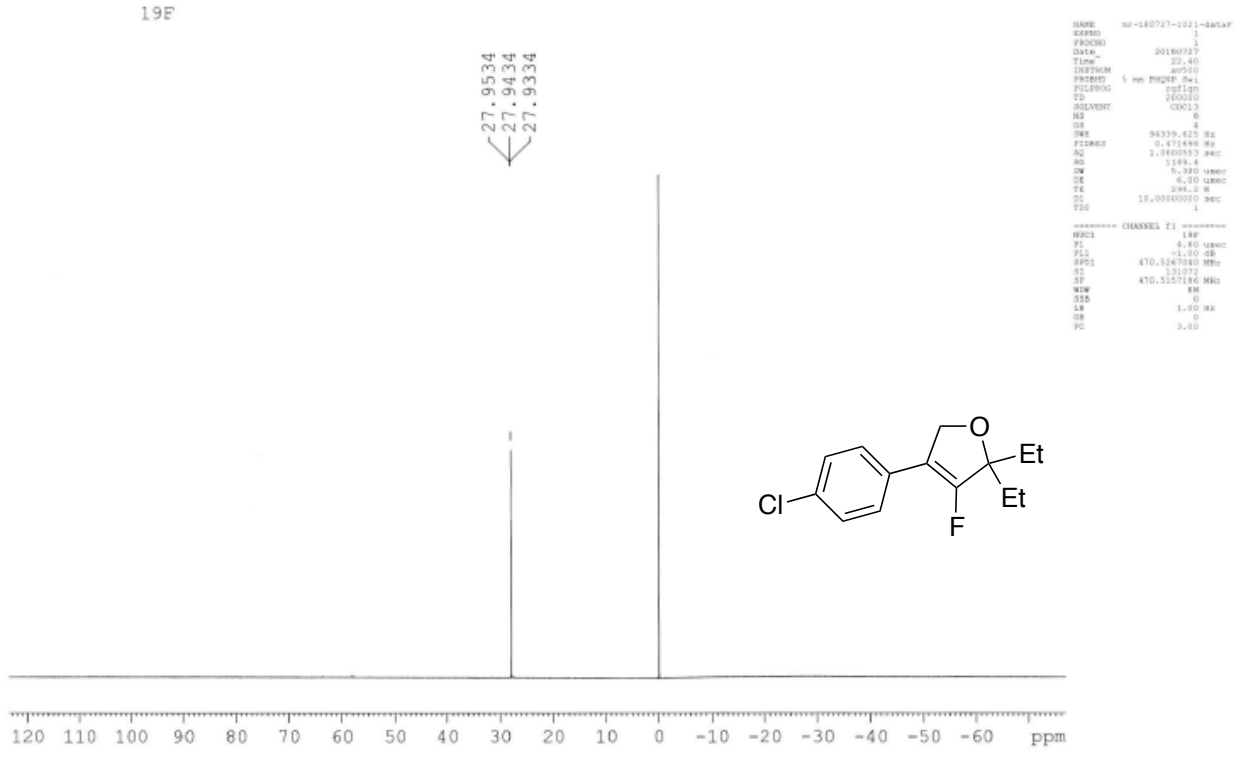




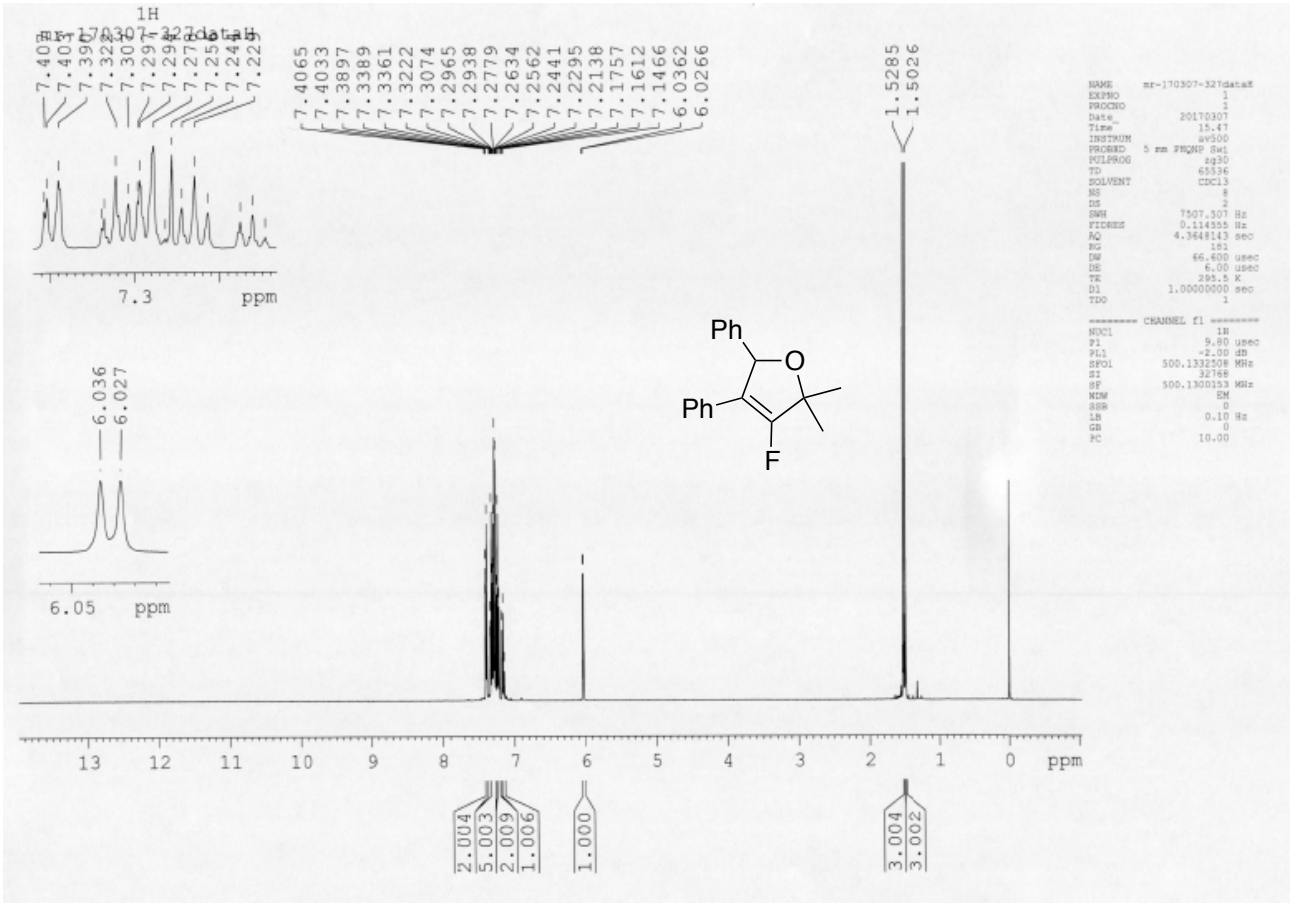
4-(4-Chlorophenyl)-2,2-diethyl-3-fluoro-2,5-dihydrofuran (4k)

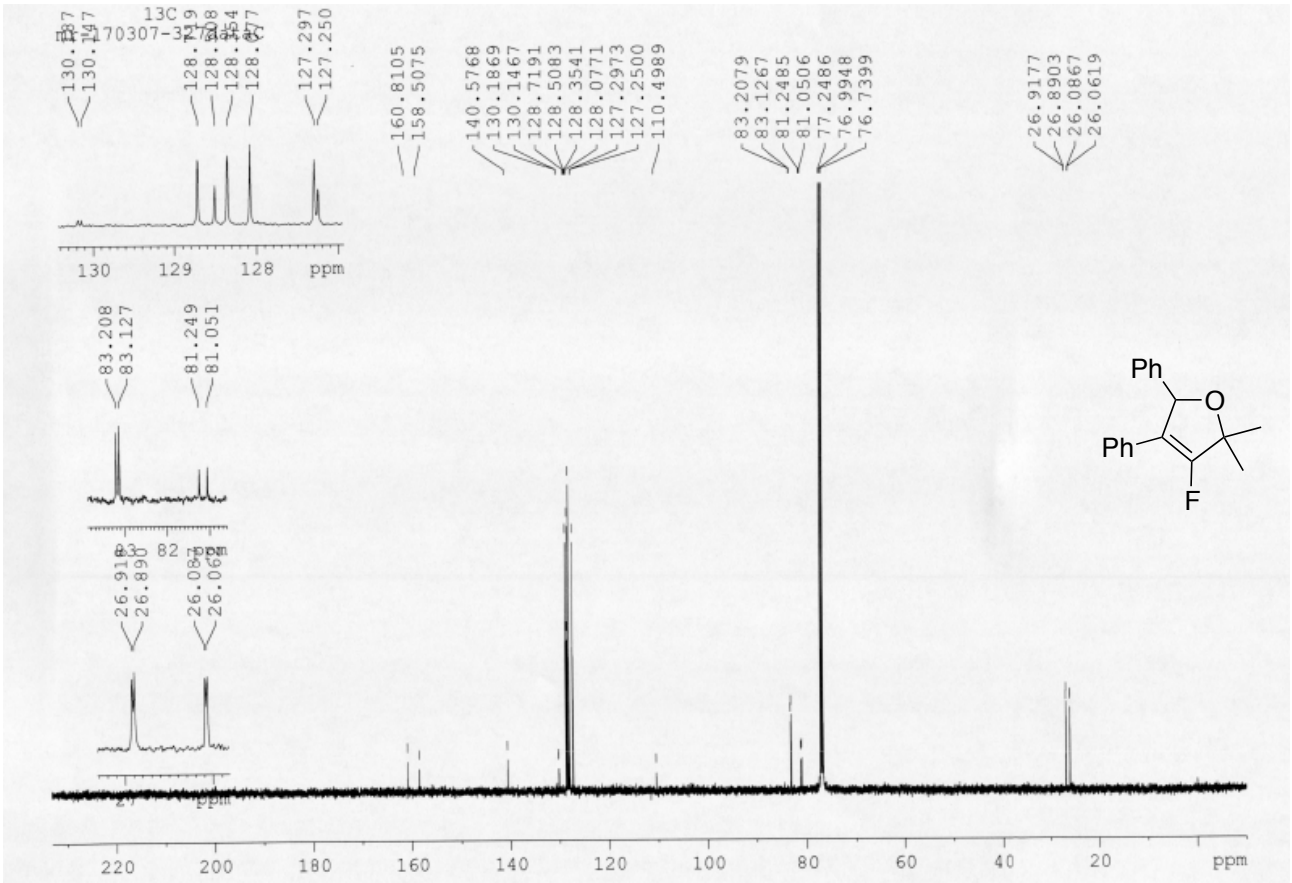


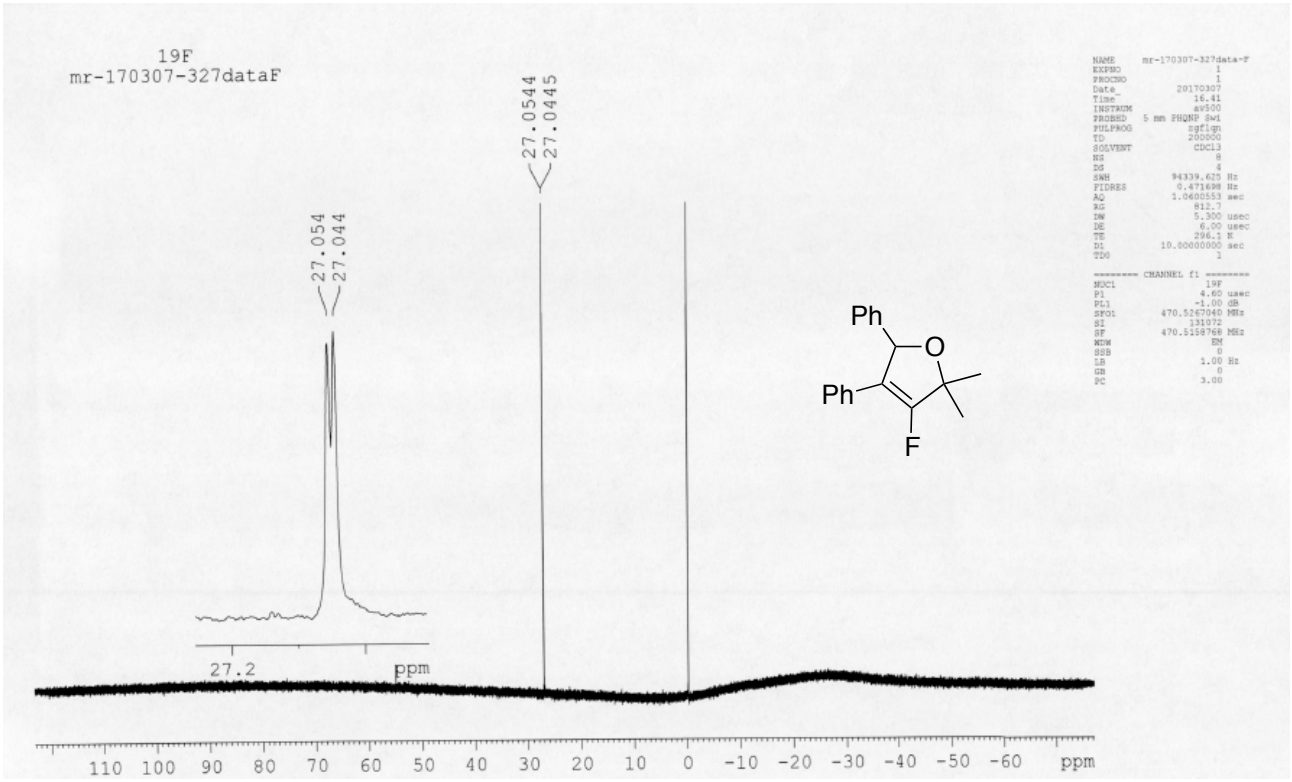

13C
Cl
O
Et
Et
F
156.1434
153.8514
133.2153
128.8267
128.5786
128.5396
127.5569
127.5070
109.6675
88.5767
88.3930
71.8270
71.7448
30.6830
30.6574
7.9386
128.8267
128.5786
128.5396
127.5569
127.5070
128 ppm
220 200 180 160 140 120 100 80 60 40 20 ppm


19F
27.9534
27.9434
27.9334
Cl
O
Et
Et
F
120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 ppm

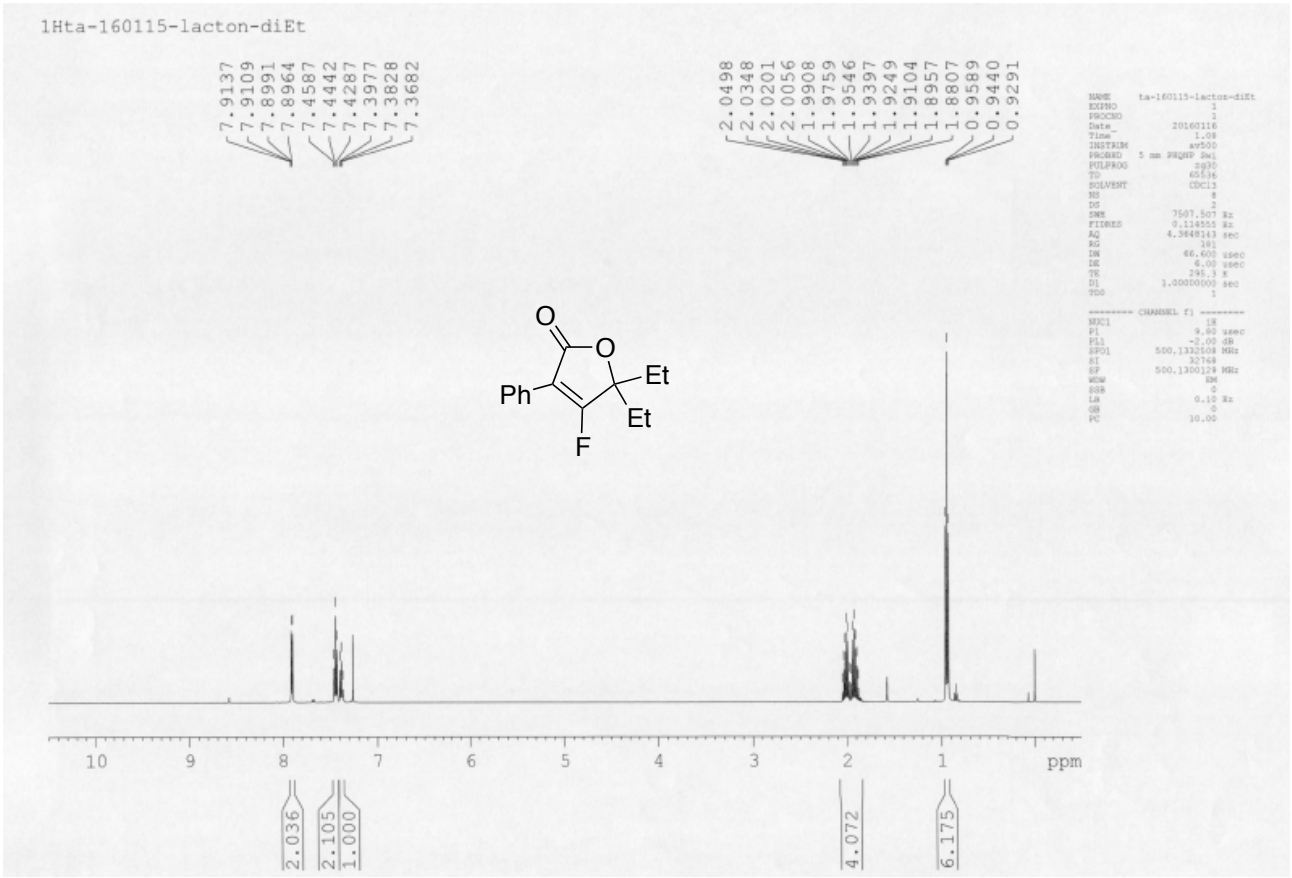
3-Fluoro-2,2-dimethyl-4,5-diphenyl-2,5-dihydrofuran (4l)

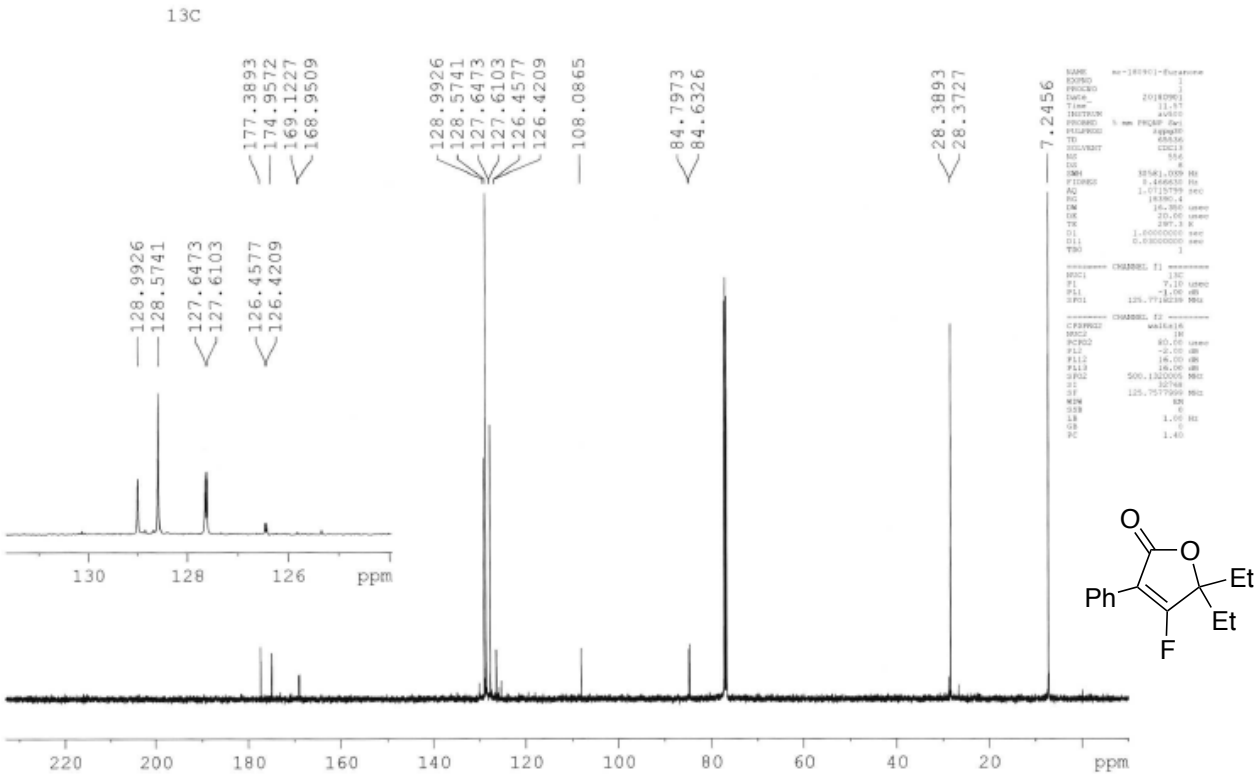


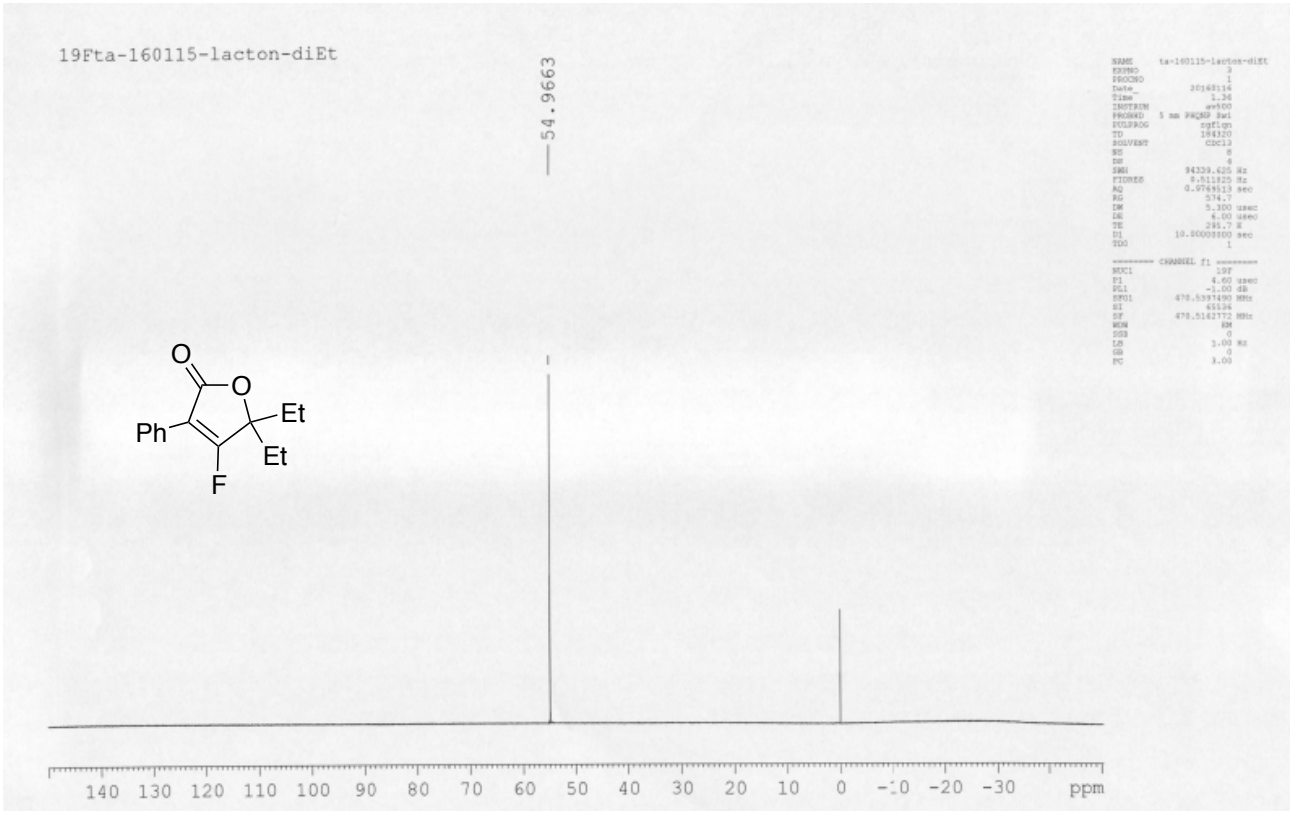




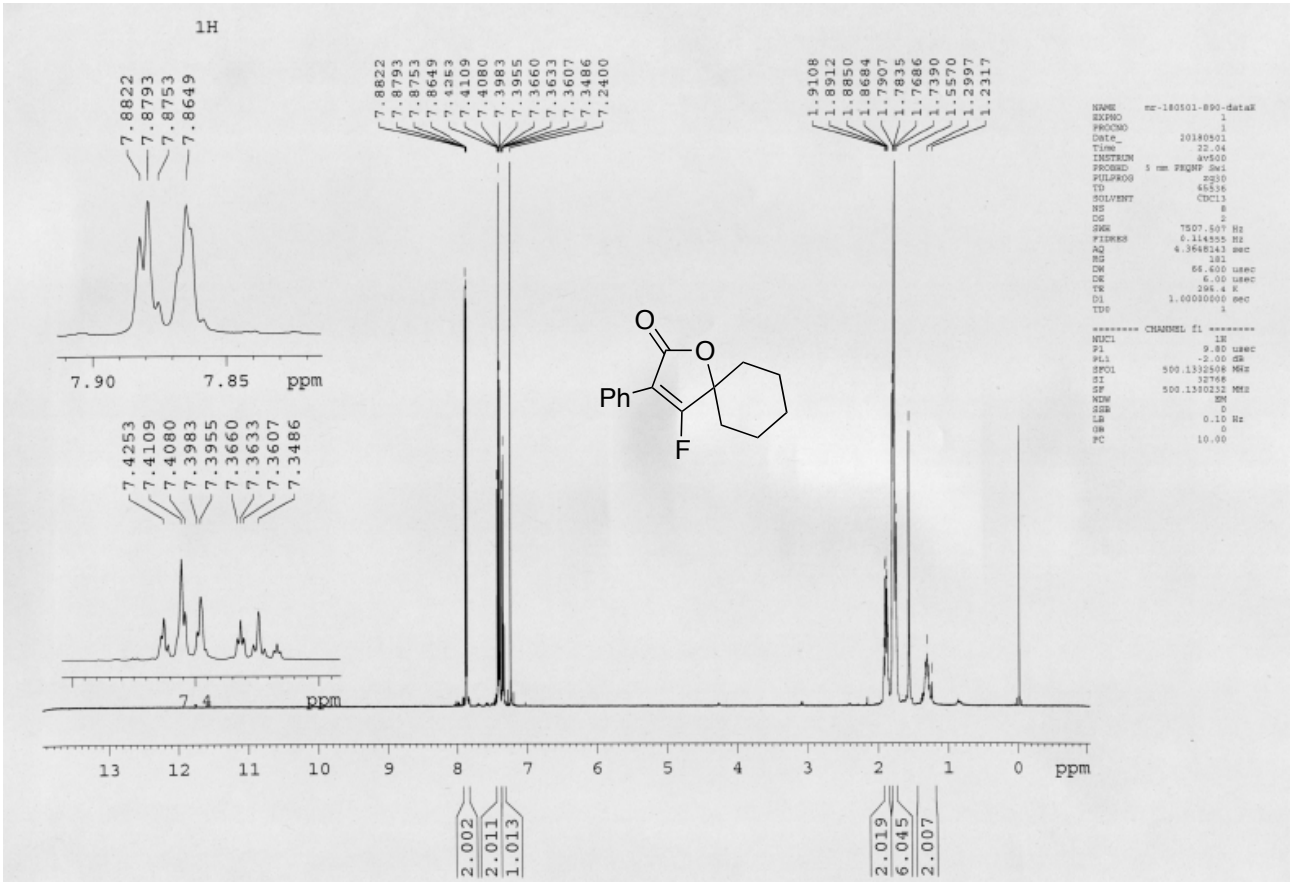
5,5-Diethyl-4-fluoro-3-phenylfuran-2(5*H*)-one (5b)

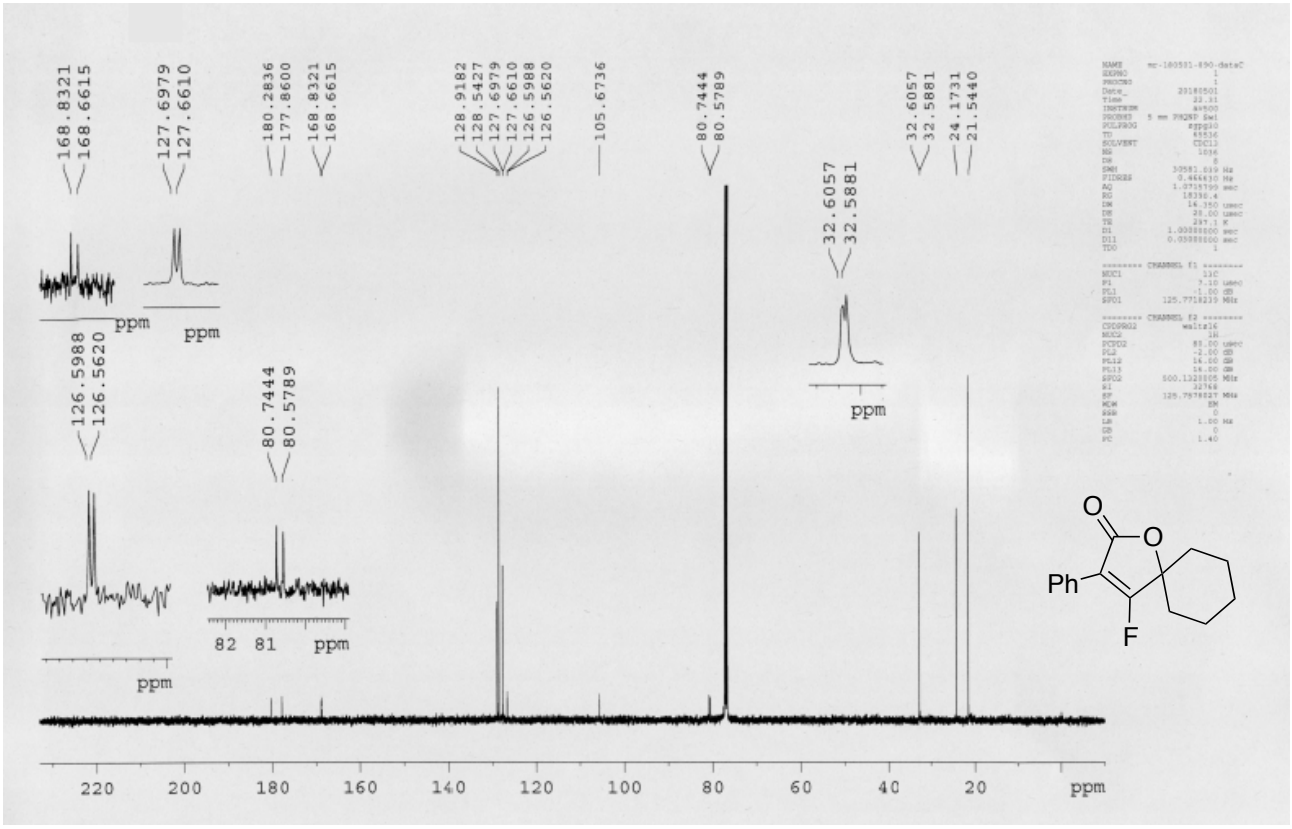


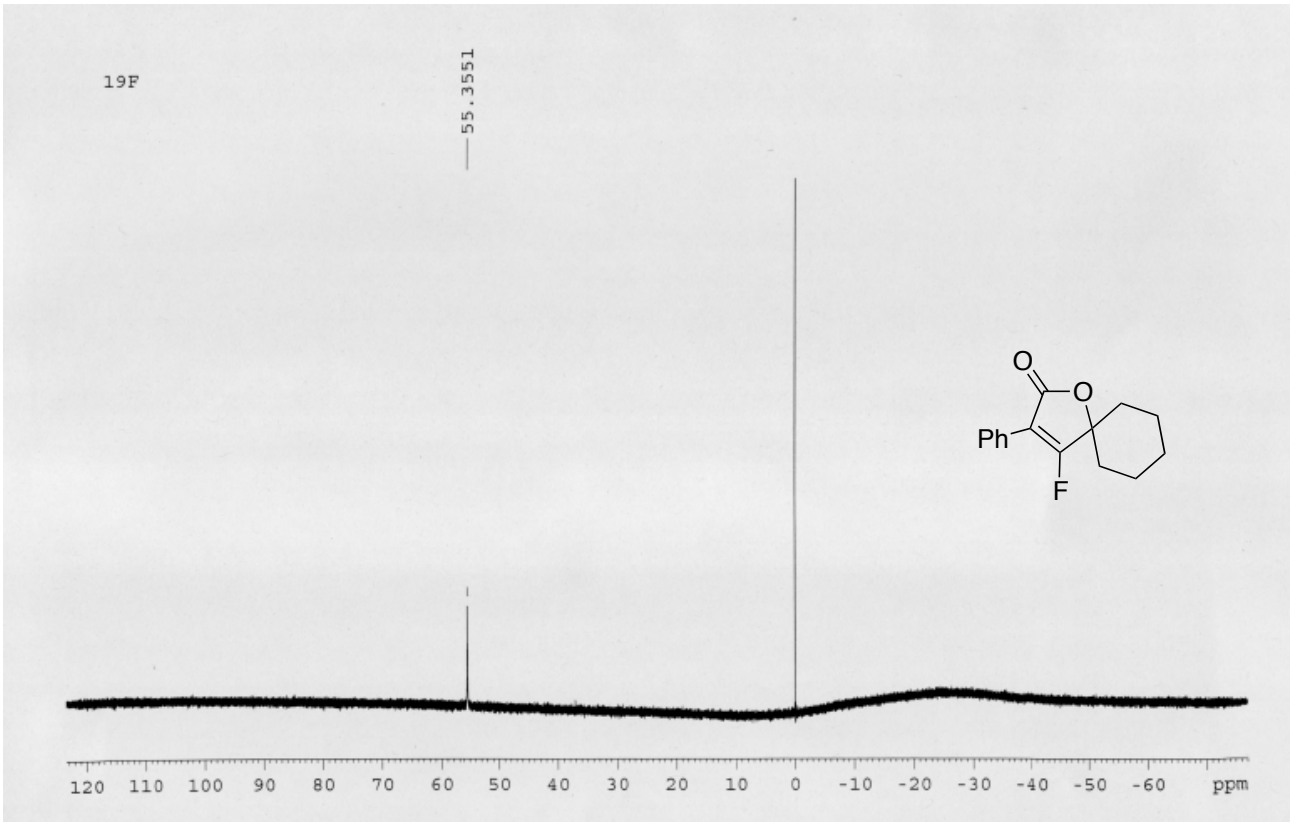

13C
177.3893
174.9572
169.1227
168.9509
128.9926
128.5741
127.6473
127.6103
126.4577
126.4209
108.0865
84.7973
84.6326
28.3893
28.3727
7.2456
130
128
126
ppm
220
200
180
160
140
120
100
80
60
40
20
ppm
O
O
Et
Ph
Et
F


19Fta-160115-lacton-diEt
54.9663
O
O
Et
Ph
Et
F
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30
ppm

4-Fluoro-3-phenyl-1-oxaspiro[4.5]dec-3-ene-2-one (5h)






19F
55.3551
O
O
Ph
F
120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 ppm