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Supporting Information

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SUPPORTING INFORMATION

Synthesis of Di- and Trifluorinated Pyranones by Au^{I}-Catalyzed Alkoxyhalogenation of β-Hydroxy-α,α-Difluoro-Ynones

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Table of contents

General Information **S2**

A - PREPARATION OF THE β-HYDROXY-YNONES 1a-m **S3**

B - GOLD-CATALYZED CYCLIZATION OF β-HYDROXY-YNONES 1a-k **S16**

C - GOLD-CATALYZED ALKOXYHALOGENATIONS **S21**

C.1 - Gold-catalyzed alkoxyiodinations **S21**

C.2 - Gold-catalyzed alkoxybrominations **S24**

C.3 - Gold-catalyzed alkoxyfluorinations **S25**

D - FUNCTIONALIZATION OF VINYL IODIDE 3b VIA A STILLE COUPLING **S31**

E - CONTROL EXPERIMENTS **S31**

F - X-RAY DIFFRACTION **S35**

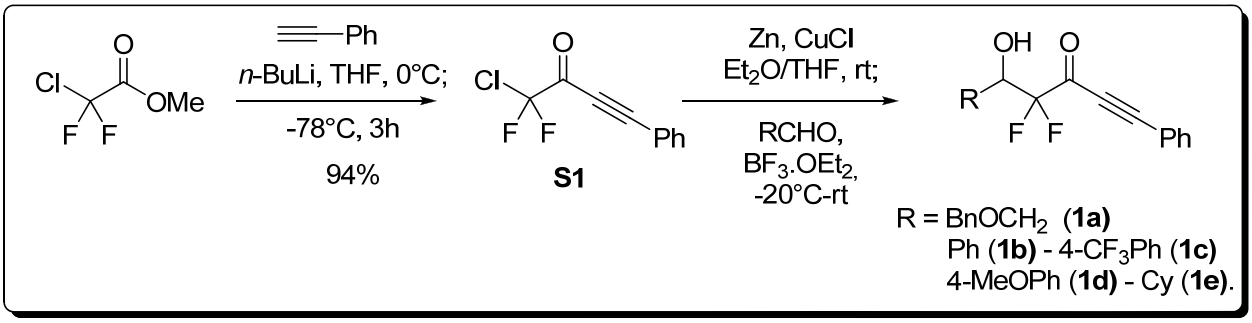
G - NMR SPECTRA **S62**

General Information

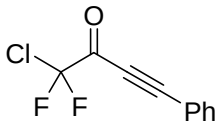
All reactions requiring anhydrous conditions were conducted in dried apparatus under an inert atmosphere of argon or nitrogen. THF, MeCN, DCM, Et_2O were dried prior to use according to procedures described by Pangborn and Grubbs.[1] Unless otherwise noted all commercial materials were used without purification. Gold (I) chloride (Alfa Aesar), Gold (III) chloride (ABCR), Chlorotriphenylphosphinegold (I) chloride (Aldrich) were purchased, stored under an inert atmosphere or argon and used as received. Zinc powder (Fischer Scientific) was thoroughly washed successively with 3M HCl, H_2O, MeOH and Et_2O, then dried *in vacuo* before using. Diisopropylamine was distilled from potassium hydroxide. All reactions were monitored by thin-layer chromatography (TLC) carried out on Merck Kiesegel 60 F_{254} plates, using U.V light (254 nm) as a visualizing agent and $KMnO_4$ stain and heat as developing agent. Column chromatography was carried out on Merck silica gel C60 (40-60 μm). ^1H NMR spectra were recorded in deuterated solvents using Bruker DPX200, DPX400, AV400 or AVC500 spectrometers, calibrated using residual undeuterated solvent as an internal reference. ^{13}C NMR spectra were recorded in deuterated solvents using Bruker DPX200, AV400 or AVC500 spectrometers. ^{19}F spectra were recorded on a Bruker AV400 spectrometer. Chemical shifts (δ) are quoted in parts per million (ppm) and coupling constants (*J*) are measured in hertz (Hz). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sext = sextet, br = broad, m = multiplet), coupling constants (Hz), integration. NMRs were processed in either MestRe-C or ACD/SpecManager. IUPAC names were obtained using the ACD/I-lab service. Mass spectra were recorded on Micromass GCT (CI^+), Autospec-oaTof and Bruker MicroTof (ESI^+) instruments. Optical rotations were determined on a Perkin Elmer 241 polarimeter in a 1dm cell. IR spectra were recorded on NaCl plates, neat or as thin films in solution in CH_2Cl_2 on a Bruker Tensor 27 FT-IR spectrometer. Absorptions are measured in wavenumbers and only peaks of interest are reported. Melting points are uncorrected.

[1] A. Pangborn, M. Giardello, R. Grubbs, *Organometallics* **1996**, *15*, 1518-1520.

A - Preparation of the β-hydroxy-ynones 1a-m



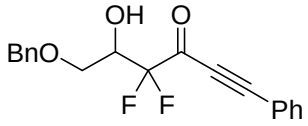
1-Chloro-1,1-difluoro-4-phenylbut-3-yn-2-one (S1)[2]



S1

To a solution of phenylacetylene (2.3 mL, 20.86 mmol, 1.1 eq.) in dry THF (95 mL) at 0°C was added *n*-BuLi (2.5M solution in hexane, 8.3 mL, 20.9 mmol, 1.1 eq.) dropwise. The reaction mixture was stirred at 0°C for 30 min and then cooled down to -78°C. A solution of methyl chlorodifluoroacetate (2.0 mL, 19.0 mmol, 1 eq.) in THF (10 mL) was then added slowly and the reaction mixture was stirred at -78°C for 3h. It was then quenched at -78°C by addition of a saturated aqueous solution of NH_4Cl. The layers were separated and the aqueous one was further extracted with Et_2O. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (hexane:EtOAc, 90:10) gave the product as an orange liquid (3.84 g, 17.9 mmol) in a 94% yield. $\mathbf{R_f}$ (hexane:EtOAc, 80:20) = 0.65. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.46 (dd, *J* = 8.1, 7.3 Hz, 2H), 7.58 (t, *J* = 7.6, 1H), 7.69 (dd, *J* = 8.6, 7.1 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 82.7, 100.5, 118.2, 119.0 (t, *J* = 302.8 Hz), 128.9, 132.4, 133.9, 168.1 (t, *J* = 35.7 Hz). **^{19}F NMR** (377 MHz, $CDCl_3$) δ: -66.37 (s). **IR** (neat) (ν, cm^{-1}): 3055, 2195, 1704, 1266, 740. **HRMS** (CI^+) calculated for $C_{10}H_9ClF_2NO$ ($[M+NH_4]^+$) 232.0341, found 232.0339.

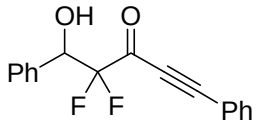
6-(Benzyloxy)-4,4-difluoro-5-hydroxy-1-phenylhex-1-yn-3-one (1a) [2]



1a

A suspension of acid-activated zinc powder (459 mg, 7.02 mmol, 3 eq.) and copper (I) chloride (69 mg, 0.702 mmol, 0.3 eq.) in dry Et_2O (9.4 mL) and THF (2.3 mL) was stirred at room temperature for 2h under argon. The reaction mixture was cooled down at 0°C, and **S1** (500 mg, 2.34 mmol, 1 eq.), benzyloxyacetaldehyde (0.4 mL, 2.57 mmol, 1.1 eq.) and boron trifluoride diethyl etherate (0.3 mL, 2.57 mmol, 1.1eq.) were added successively. The reaction mixture was stirred at room temperature for 5h, then filtered through a pad of Celite with Et_2O and the filtrate was concentrated *in vacuo*. Purification by column chromatography on silica gel (hexane:EtOAc, 90:10) gave the product as a yellow oil (479 mg, 1.45 mmol) in a 62% yield. $\mathbf{R_f}$ (hexane:EtOAc, 60:40) = 0.68. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 2.83 (d, *J* = 6.6 Hz, 1H), 3.74-3.81 (m, 2H), 4.36-4.46 (m, 1H), 4.59 (s, 2H), 7.29-7.64 (m, 10H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 67.8 (dd, *J* = 3.8, 2.9 Hz), 70.5 (dd, *J* = 26.7, 24.8 Hz), 73.7, 85.0, 98.6, 114.5 (dd, *J* = 258.0, 256.1 Hz), 118.9, 127.8, 128.0, 128.5, 128.8, 131.8, 133.7, 137.1, 176.5 (dd, *J* = 34.3, 32.4 Hz). **^{19}F NMR** (377 MHz, $CDCl_3$) δ: -120.05 (dd, *J* = 265.0, 13.8 Hz, 1F), -114.19 (dd, *J* = 265.1, 9.2 Hz, 1F). **IR** (neat) (ν, cm^{-1}): 3559, 3056, 2197, 1687, 1266, 1096, 738. **HRMS** (ESI^+) calculated for $C_{19}H_{16}F_2NaO_3$ ($[M + Na]^+$) 353.0965, found 353.0960.

4,4-difluoro-5-hydroxy-1,5-diphenylpent-1-yn-3-one (1b)[2]



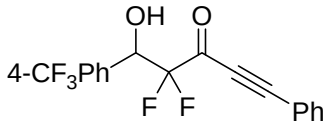
1b

The same procedure than for substrate **1a** was followed, employing 979 mg of acid-activated zinc powder (15.0 mmol, 3 eq.) and copper(I) chloride (149 mg, 1.5 mmol, 0.3 eq.) in THF:Et_2O (1:4, 25 mL). Then the ynone **S1** (1.07 g, 4.99 mmol, 1 eq.) in THF (2 mL), benzaldehyde (0.56 mL, 5.5 mmol, 1.1 eq.) and boron trifluoride diethyl etherate (0.68 mL, 5.5 mmol, 1.1 eq.) were added successively at -20°C. The mixture was stirred at -20°C for 2h and then at rt for a further 2h. Purification by column chromatography (Hexane:Et_2O, 8:2 to 7:3) yielded the product (850 mg, 60%) as an orange oil. $\mathbf{R_f}$ (Hexane:Et_2O, 7:3) = 0.23. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 2.64 (d, *J* = 5.2 Hz, 1H), 5.30 (ddd, *J* = 15.8, 7.6, 5.1 Hz, 1H), 7.36-7.55 (m, 8H), 7.56-7.62 (m, 2H). **^{13}C NMR** (126

[2] M. Kuroboshi, T. Ishihara, *Bull. Chem. Soc. Jpn.* **1990**, *63*, 428-437.

MHz, $CDCl_3$) δ: 73.2 (dd, *J* = 24.6, 24.2 Hz), 84.9, 99.4, 114.2 (dd, *J* = 255.7, 255.8 Hz), 118.7, 127.8, 128.4, 128.7, 129.2, 131.9, 133.7, 134.4, 177.3 (dd, *J* = 32.2, 32.1 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -111.7 (dd, *J* = 263.9, 7.5 Hz, 1F), -120.8 (dd, *J* = 263.9, 15.8 Hz, 1F). **IR** (neat) (ν, cm^{-1}): 3475, 3052, 2197, 1683, 1490, 1091, 759, 687. **HRMS** (CI^+) calculated for $C_{17}H_{16}NO_2F_2$ ($[M+NH_4]^+$) 304.1149, found 304.1139.

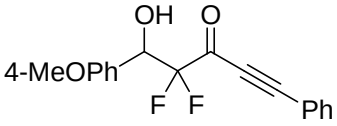
4,4-difluoro-5-hydroxy-1-phenyl-5-(4-(trifluoromethyl)phenyl)pent-1-yn-3-one (1c)



1c

The same procedure than for substrate **1a** was followed, employing 300 mg of **S1** (1.4 mmol, 1 eq.), 0.2mL of 4-trifluoromethylbenzaldehyde (1.54 mmol, 1.1 eq.) and boron trifluoride diethyl etherate (0.2 mL, 1.54 mmol, 1.1eq.) in THF:Et_2O (1:4, 7 mL). The mixture was left to warm to rt and was stirred at room temperature for 6h. Purification by column chromatography (hexane:Et_2O, 1:1) yielded the product (260 mg, 53%) as a pale yellow solid. **m.p.** = 94-96°C. **R_f** (hexane:Et_2O, 3:1) = 0.35. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 3.04 (d, *J* = 4.0 Hz, 1H), 5.36 (ddd, *J* = 15.3, 6.4, 3.2 Hz, 1H), 7.39-7.60 (m, 5H), 7.64 (d, *J* = 8.7 Hz, 2H), 7.67 (d, *J* = 8.7 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 72.6 (dd, *J* = 28.6, 24.8 Hz), 84.9, 100.1, 113.8 (dd, *J* = 261.8, 255.6 Hz), 118.5, 124.0 (q, *J* = 272.3 Hz), 125.3 (q, J_{C-F} = 3.8 Hz), 128.3, 128.3, 128.6, 128.6, 131.2 (q, *J* = 32.4 Hz), 132.1, 133.7, 133.7, 138.4, 176.9 (dd, *J* = 36.2, 32.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -62.7 (s, 3F), -110.8 (dd, *J* = 268.5, 6.9 Hz, 1F), -120.5 (dd, *J* = 268.5, 16.1 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 3444, 2946, 2195, 1680, 1141. **HRMS** (ESI^+) calculated for $C_{18}H_{11}F_5NaO_2$ ($[M+Na]^+$) 377.0577, found 377.0575.

4,4-difluoro-5-hydroxy-5-(4-methoxyphenyl)-1-phenylpent-1-yn-3-one (1d)

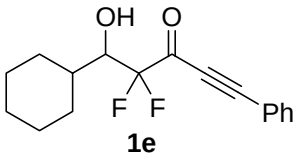


1d

The same procedure than for substrate **1a** was followed, employing 1.29 g of **S1** (6.0 mmol, 1 eq.), 0.802 mL of 4-methoxybenzaldehyde (6.6 mmol, 1.1 eq.) and boron trifluoride diethyl etherate (0.81 mL, 6.6 mmol, 1.1eq.) in THF:Et_2O (1:4, 30 mL). The mixture was left to warm to rt and was stirred at room temperature for 5h. Purification by column chromatography (hexane:Et_2O, 7:3) yielded the product (1.18 g, 60%) as a pale yellow solid. **m.p.** = 68 °C. **R_f** (hexane:Et_2O, 1:1) = 0.30. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 2.76 (br s, 1H), 3.79 (s, 3H), 5.23 (dd, *J* = 15.4, 8.0 Hz, 1H), 6.92 (d, *J* = 8.7 Hz, 2H), 7.42 (d, *J* = 8.9 Hz, 2H), 7.39-7.40 (m, 2H), 7.50-7.61 (m, 3H). **^{13}C NMR** (100

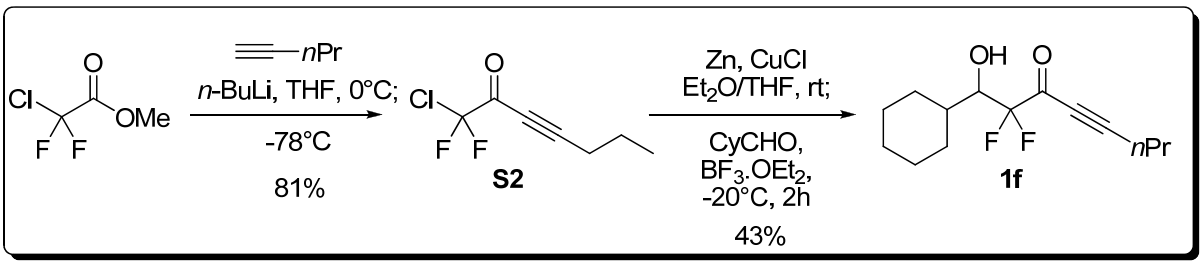
MHz, $CDCl_3$) δ: 55.2, 73.0 (dd, *J* = 28.4, 24.4 Hz), 85.2, 99.4, 113.9, 113.9, 114.5 (dd, *J* = 260.4, 254.8 Hz), 118.8, 126.8 (d, *J* = 1.6 Hz), 128.8, 128.8, 129.3, 129.3, 131.9, 133.7, 133.7, 160.2, 177.5 (dd, *J* = 35.6, 32.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -112.3 (dd, *J* = 261.6, 8.0 Hz, 1F), -120.5 (dd, *J* = 261.6, 16.0 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 3437, 2972, 2840, 2197, 1685, 1254, 1030. **HRMS** (ESI^+) calculated for $C_{18}H_{14}F_2NaO_3$ ($[M+Na]^+$) 339.0809, found 339.0803.

5-cyclohexyl-4,4-difluoro-5-hydroxy-1-phenylpent-1-yn-3-one (1e)

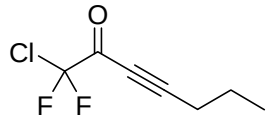


1e

The same procedure than for substrate **1a** was followed, employing 490 mg of acid-activated zinc powder (7.5 mmol, 3 eq.) and copper(I) chloride (74 mg, 0.75 mmol, 0.3 eq.) in THF:Et_2O (1:4, 12.5 mL). Then the ynone **S1** (533 mg, 2.5 mmol, 1 eq.) in THF (2 mL), cyclohexanecarbaldehyde (0.33 mL, 2.7 mmol, 1.1 eq.) and boron trifluoride diethyl etherate (0.33 mL, 2.7 mmol, 1.1eq.) were added successively at -20°C. The mixture was stirred at -20°C for 2h and then at rt for a further 2h. Purification by column chromatography (hexane:Et_2O, 8:2 to 7:3) yielded the product (279 mg, 38%) as an orange oil. **R_f** (hexane:Et_2O, 6:4) = 0.45. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.12-1.33 (m,5H), 1.65 (d, *J* = 12.4 Hz, 1H), 1.73-1.83 (m, 4H), 1.98 (d, *J* = 12.4 Hz, 1H), 2.38 (s br, 1H), 3.98 (m, 1H), 7.35-7.45 (m, 2H), 7.50 (t, *J* = 7.6 Hz, 1H), 7.60-7.70 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 25.8, 26.0, 26.1, 27.3, 29.8, 38.3, 74.6 (dd, *J* = 26.4, 23.6 Hz), 85.0, 98.7, 116.0 (dd, *J* = 259.6, 256.8 Hz), 118.9, 128.8, 131.9, 133.7, 177.7 (dd, *J* = 36.0, 32.8 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -110.4 (dd, *J* = 264.0, 8.0 Hz, 1F), -119.7 (dd, *J* = 264.0, 18.4 Hz, 1F). **IR** (neat) (ν, cm^{-1}): 3583, 3056, 2931, 2856, 2196, 1686, 1490, 1265, 739. **HRMS** (CI^+) calculated for $C_{17}H_{19}F_2O_2$ ($[M+H]^+$) 293.1353, found 293.1359.



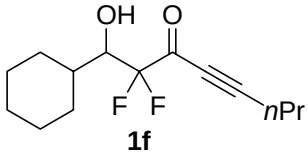
1-chloro-1,1-difluorohept-3-yn-2-one (S2)



S2

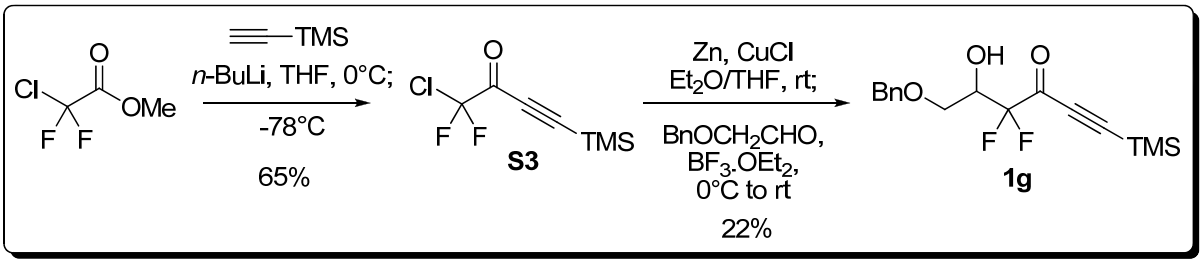
The same procedure than substrate **S1** was followed, employing 1.37 mL of methyl 2-chloro-2,2-difluoroacetate (15 mmol, 1 eq.), 1.63 mL of pentyne (16.5 mmol, 1.1 eq.), 7.2 mL of ^{n}BuLi (2.5M in hexanes, 18 mmol, 1.2 eq.) in dry THF (75 mL). Purification by column chromatography (hexane:Et_2O, 3:1) yielded the product (2.20 g, 81%) as a colourless oil. $\mathbf{R_f}$ (hexane:Et_2O, 1:1) = 0.65. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.06 (t, J = 7.3 Hz, 3H), 1.69 (sext, J = 7.2 Hz, 2H), 2.49 (t, J = 7.0 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 13.3, 20.8, 21.3, 75.4, 104.8, 118.8 (t, J = 302.8 Hz), 168.0 (t, J = 35.2 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -66.8 (s). **IR** (DCM) (ν, cm^{-1}): 2950, 1668, 960. **HRMS** (ESI^-) calculated for $C_7H_6ClF_2O$ ($[M-H]^-$) 179.0075, found 179.0069.

1-cyclohexyl-2,2-difluoro-1-hydroxyoct-4-yn-3-one (1f)

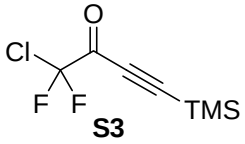


1f

The same procedure than substrate **1e** was followed, employing 0.98 g of **S2** (5.45 mmol, 1 eq.) and 726 µL of cyclohexanecarbaldehyde (6.0 mmol, 1.1 eq.) in THF:Et_2O (1:4, 24 mL). The reaction mixture was stirred at -20°C for 2h. Purification by column chromatography (hexane:Et_2O, 4:1) yielded the product (610 mg, 43%) as a pale yellow oil. $\mathbf{R_f}$ (hexane:Et_2O, 3:1) = 0.25. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.04 (t, J = 7.3 Hz, 3H), 1.10-1.30 (m, 6H), 1.66 (sext, J = 7.3 Hz, 2H), 1.67-1.97 (m, 5H), 2.23 (d, J = 7.1 Hz, 2H), 2.45 (t, J = 7.0 Hz, 2H), 3.82-3.96 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 13.4, 21.0, 21.3, 25.8, 26.0, 26.1, 27.2, 29.7, 38.2, 74.5 (dd, J = 26.4, 23.6 Hz), 77.8, 102.9, 115.8 (dd, J = 259.6, 257.2 Hz), 177.6 (dd, J = 35.6, 32.4 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -110.9 (dd, J = 263.9, 8.0 Hz, 1F), -120.1 (dd, J = 263.9, 17.2 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 3461, 2962, 2154, 1678, 980, 848. **HRMS** (ESI^+) calculated for $C_{14}H_{20}F_2NaO_2$ ($[M+Na]^+$) 281.1329, found 281.1325.

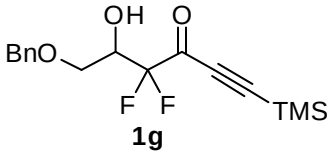


1-chloro-1,1-difluoro-4-(trimethylsilyl)but-3-yn-2-one (S3)

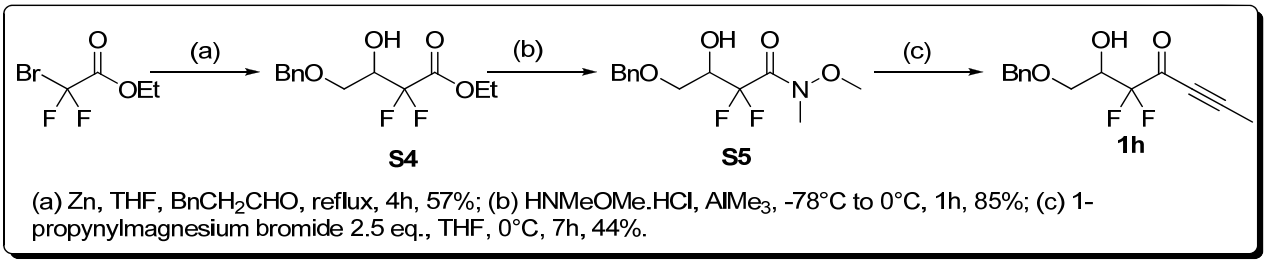


The same procedure than for substrate **S1** was followed, employing 2.0 mL of methyl 2-chloro-2,2-difluoroacetate (18.8 mmol, 1 eq.), 2.91 mL of trimethylsilylacetylene (20.7 mmol, 1.1 eq.), 9.0 mL of ^{n}BuLi (2.5M in hexanes, 18 mmol, 1.2 eq.) in dry THF (94 mL). Purification by column chromatography on silica gel (hexane:Et_2O, 3:1) yielded the product (1.45 g, 65%) as a colourless oil. $\mathbf{R_f}$ (hexane:Et_2O, 4:1) = 0.70. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 0.31 (s, 9H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: -1.3, 95.5, 110.0, 118.7 (t, J = 303.0 Hz), 167.5 (t, J = 35.6 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -66.9 (s). **IR** (DCM) (ν, cm^{-1}): 2967, 2161, 1716, 1076, 857. **HRMS** (ESI^-) calculated for $C_4ClF_2O_3$ ([M-$SiMe_3$-H]$^+$) 136.9606, found 136.9610.

6-(benzyloxy)-4,4-difluoro-5-hydroxy-1-(trimethylsilyl)hex-1-yn-3-one (1g)

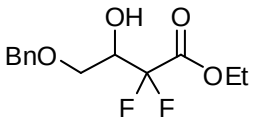


The same procedure than substrate **1a** was followed, employing 1.48 g of **S3** (7.0 mmol, 1 eq.) and 1.16 g of 2-(benzyloxy)acetaldehyde (7.7 mmol, 1.1 eq.) in THF:Et_2O (1:4, 40 mL). The mixture was left to warm to rt and was stirred at room temperature overnight. Purification by column chromatography on silica gel (hexane:Et_2O, 3:1) yielded the product (503 mg, 22%) as a colourless oil. $\mathbf{R_f}$ (hexane:Et_2O, 1:1) = 0.55. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 0.28 (s, 9H), 2.99 (d, J = 6.8 Hz, 1H), 3.71 (dd, J = 10.1, 6.8 Hz, 1H), 3.75 (dd, J = 10.1, 4.3 Hz, 1H), 4.30-4.40 (m, 1H), 4.55 (d, J = 11.9 Hz, 1H), 4.59 (d, J = 11.9 Hz, 1H), 7.30-7.40 (m, 5H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: -1.0, 67.6 (t, J = 3.2 Hz), 70.3 (dd, J = 27.2, 25.2 Hz), 73.7, 98.2, 107.2, 114.3 (dd, J = 258.4, 255.6 Hz), 127.8, 127.8,128.0, 128.5, 128.5, 137.1, 176.0 (dd, J = 34.8, 32.4 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -114.8 (dd, J = 265.0 Hz, 9.2 Hz, 1F), -120.4 (dd, J = 263.9, 12.6 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 3436, 2962, 2154, 1696, 1254, 1098, 851. **HRMS** (ESI^-) calculated for $C_{13}H_{11}F_2O_3$ ([M-$SiMe_3$-H]$^-$) 253.0676, found 253.0672.



(a) Zn, THF, $BnCH_2CHO$, reflux, 4h, 57%; (b) HNMeOMe.HCl, $AlMe_3$, -78°C to 0°C, 1h, 85%; (c) 1-propynylmagnesium bromide 2.5 eq., THF, 0°C, 7h, 44%.

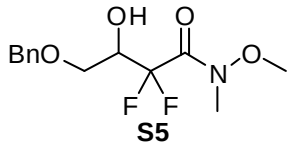
Ethyl 4-(benzyloxy)-2,2-difluoro-3-hydroxybutanoate (S4)[3]



S4

A suspension of acid-activated zinc powder (654 mg, 10.0 mmol, 2 eq.) in dry THF (12 mL) was stirred at reflux for 1h under argon. The bromodifluoroacetate (0.96 mL, 7.5 mmol, 1.5 eq.) and the benzyloxyacetaldehyde (0.7 mL, 5 mmol, 1 eq.) were added successively. The reaction mixture was stirred at reflux for 4h, then filtered through a pad of Celite with Et_2O and the filtrate was concentrated *in vacuo*. Purification by column chromatography on silica gel (hexane: Et_2O: 50:50) gave the product as a colourless oil (886 mg) in a 57% yield. $\mathbf{R_f}$ (hexane: Et_2O: 50:50) = 0.33; **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.3 (t, *J* = 7.2 Hz, 3H), 2.85 (d, *J* = 7.0 Hz, 1H), 3.72 (ddd, *J* = 10.2, 5.6, 1.0 Hz, 1H), 3.76 (ddd, *J* = 10.3, 4.2, 0.8 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.23-4.32 (m, 1H), 4.56 (s, 2 H), 7.39-7.39 (m, 5H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 13.8, 63.1, 67.7 (t, *J* = 3.6 Hz), 70.7 (dd, *J* = 26.8, 25.2 Hz), 73.8, 113.7 (dd, *J* = 256.4, 253.7 Hz), 127.9, 128.0, 128.5, 137.1, 163.2 (t, *J* = 31.6 Hz).**^{19}F NMR** (376 MHz, $CDCl_3$) δ: -115.18 (dd, *J* = 264.6, 8.7 Hz, 1F), -120.1 (dd, *J* = 264.6, 8.7 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 3469, 2875, 1760, 1497, 1096, 699. **HRMS** (ESI^+) calculated for $C_{13}H_{16}F_2NaO_4$ ($[M+Na]^+$) 297.0909, found 297.0908.

4-(benzyloxy)-2,2-difluoro-3-hydroxy-*N*-methoxy-*N*-methylbutanamide (S5)[4]



S5

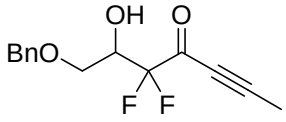
A suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (2.93 g, 30.0 mmol, 3.0 eq.) in tetrahydrofuran (40 mL. 0.2M) was cooled down to 0°C before slow addition of trimethylaluminium (15 mL, 2M in toluene, 30.0 mmol, 3.0 eq.,). The mixture was

[3] A. Otaka, J. Watanabe, A. Yukimasa, Y. Sasaki, H. Watanabe, T. Kinoshita, S. Oishi, H. Tamamura, N. Fujii, *J. Org. Chem.* **2004**, *69*, 1634-1645

[4] K. Iseki, D. Asada, Y. Kuroki, *J. Fluorine. Chem.* **1999**, *97*, 85-89.

allowed to reach rt till a transparent solution is obtained and then cooled down to -78°C. A solution of **S4** (0.10 mol, 2.74 g) in tetrahydrofuran (10 mL) was added. After 15 min at -78°C the solution was warmed up to 0°C and kept for 1h, before addition of 30 mL of a 1.5 M aqueous solution of hydrochloric acid. After separation of the phases and extraction of the aqueous one with ethyl acetate (3 × 30 mL), the combined organic layers were dried over magnesium sulphate and the solvents were evaporated. The crude product was purified by column chromatography on silica gel (hexane:EtOAc, 1:1) and yielded the expected product as a white solid (7.38 g, 85%). **m.p. =** 49 °C. $\mathbf{R_f}$ = 0.34. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 3.26-3.03 (bs, 3H), 3.74 (m, 2H), 3.74 (s, 3H), 4.37-4.50 (m, 1H), 4.56 (d, *J* = 11.8 Hz, 1H), 4.59 (d, *J* = 11.9 Hz, 1H), 7.33 (m, 5H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 33.1, 62.0, 63.3 (dd, *J* = 4.8, 2.4 Hz), 71.0 (dd, *J* = 26.0, 24.4 Hz), 73.6, 115.6, 127.8, 127.9, 128.4, 137.5, 163.1. **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -113.7 (d, *J* = 272.0 Hz, 1F), -117.3 (dd, *J* = 272.0, 13.1 Hz, 1F). **HRMS** (ESI^+) calculated for $C_{13}H_{17}F_2NNaO_4$ ($[M+Na]^+$) 312.1018, found 312.1017.

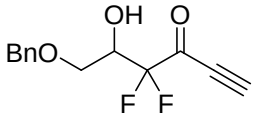
7-(benzyloxy)-5,5-difluoro-6-hydroxyhept-2-yn-4-one (1h)



1h

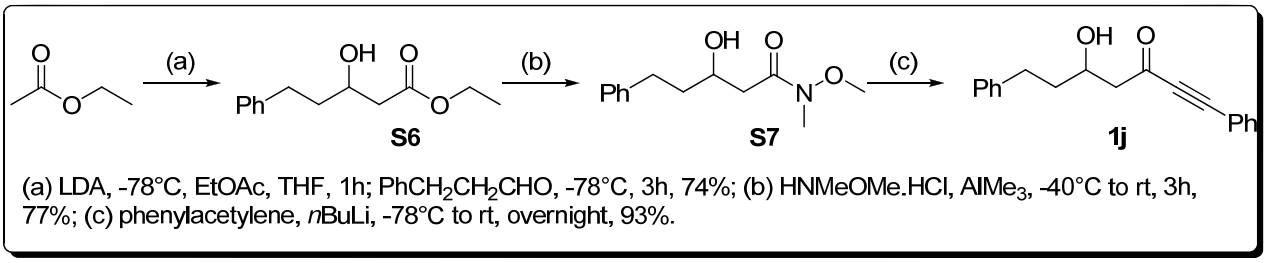
To a solution of 300 mg of **S5** (1.04 mmol, 1 eq.) in THF (2 mL) at 0°C, was added, 1-propynylmagnesium bromide (0.5 M in THF, 5.2 mL, 2.6 mmol, 2.5 eq.) under argon. The reaction mixture was then stirred at 0°C for 7h. After which, the reaction mixture was quenched at 0 °C by addition of a saturated aqueous solution of NH_4Cl. The aqueous layer was further extracted with Et_2O and the combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (hexane:EtOAc 7:3) yielded the product (122 mg, 44%) as a pale yellow oil. $\mathbf{R_f}$ (hexane:EtOAc, 6:4) = 0.57. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 2.12 (s, 3H), 2.90 (d, *J* = 6.3 Hz, 1H), 3.70 (dd, *J* = 10.1, 6.1 Hz, 1H), 3.75 (dd, *J* = 10.1, 4.3 Hz, 1H), 4.30-4.40 (m, 1H), 4.55 (d, *J* = 12.1 Hz, 1H), 4.58 (d, *J* = 11.9 Hz, 1H), 7.30-7.39 (m, 5H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 4.7, 67.7 (t, *J* = 3.0 Hz), 70.3 (dd, *J* = 27.6, 25.2 Hz), 73.7, 77.0, 98.7, 114.3 (dd, *J* = 258.0, 254.9 Hz), 127.8, 128.0, 128.5, 137.1, 176.4 (dd, *J* = 34.4, 31.6 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -114.3 (dd, *J* = 263.9 Hz, *J* = 8.0 Hz, 1F), -120.8 (dd, *J* = 263.9 Hz, *J* = 13.8 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 3442, 3033, 2874, 2218, 1694, 1096. **HRMS** (ESI^+) calculated for $C_{14}H_{14}F_2NaO_3$ ($[M+Na]^+$) 291.0809, found 291.0800.

6-(benzyloxy)-4,4-difluoro-5-hydroxyhex-1-yn-3-one (1i)

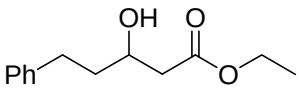


1i

The crude mixture resulting from the preparation of compound **1g** was used. To a solution of this crude (3 mmol) in methanol (30 mL) at rt was added a solution of sodium tetraborate in water (0.01M, 4.5 mL, 0.045 mmol, 1.5 mol%). After 20 min of stirring at rt, the brown reaction mixture was quenched by addition of cold HCl 1M (3.6 mL) and brine (15 mL). The yellowish solution was extracted with DCM (3*20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (hexane:EtOAc, 80:20) yielded the product (481 mg, 63%) as a colourless oil. $\mathbf{R_f}$ (hexane:Et_2O, 1:1) = 0.30. **^{1}H NMR** (400 MHz, C_6D_6) δ: 2.56 (s, 1H), 2.86 (br d, *J* = 4.7 Hz, 1H), 3.44-3.53 (m, 2H), 4.15-4.20 (m, 1H), 4.22-4.34 (m, 1H), 7.15-7.27 (m, 5H). **^{13}C NMR** (100 MHz, C_6D_6) δ: 67.8 (t, *J* = 3.2 Hz), 70.5 (dd, *J* = 26.8, 24.4 Hz), 73.5, 78.3, 85.5, 115.1 (dd, *J* = 257.6, 255.7 Hz), 127.9, 128.1, 128.6, 137.6, 176.4 (dd, *J* = 34.8, 33.2 Hz). **^{19}F NMR** (376 MHz, C_6D_6) δ: -115.5 (dd, *J* = 261.6 Hz, *J* = 9.2 Hz,1F), -120.4 (dd, *J* = 262.7 Hz, *J* = 13.8 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 3269, 2954, 2101, 1705, 1100. **HRMS** (ESI^-) calculated for $C_{13}H_{11}F_2O_3$ ($[M-H]^-$) 253.0676, found 253.0680.



Ethyl 3-hydroxy-5-phenylpentanoate (S6)[5]



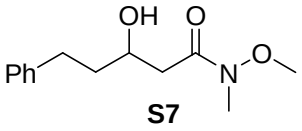
S6

To a precooled solution (0°C) of diisopropylamine (4.5 mL, 31.7 mmol, 1.7 eq.) in anhydrous THF (140 mL) was added *n*-butyl lithium (2.3 M in Hexane, 12.2 mL, 27.9 mmol, 1.5 eq.) under argon. The resulting reaction mixture was stirred for 30 min at this temperature, and then cooled down to -78°C, before adding distilled ethyl acetate (2.7 mL, 27.9 mmol, 1.5 eq.) in anhydrous THF. The resulting reaction mixture was stirred for

[5] I. Kuwajima, N. Minami, T. Sato, *Tetrahedron Lett.* **1976**, *17*, 2253-2256.

1h at -78°C before the 3-phenylproprionaldehyde (2.5 mL, 18.6 mmol, 1 eq.) in anhydrous THF. After 3 hours at -78°C, the reaction mixture was quenched by the addition of saturated ammonium chloride solution. The reaction mixture was left to warm up to room temperature and the obtained two layers were separated. The aqueous layer was extracted with ethyl acetate (3×50 ml) and the combined organic layers were then dried over $MgSO_4$, filtered and concentrated *in vacuo* to give a crude mixture that was purified by column chromatography on silica (1:4, EtOAc:hexane) and yielded **S6** as a colourless oil (3.06 g, 74 %). $\mathbf{R_f}$ (EtOAc:hexane, 1:4): 0.23. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.28 (t, *J* = 7.2 Hz, 3H), 1.76 (dddd, *J* = 20.5, 9.6, 6.8, 4.1 Hz, 1H), 1.87 (dddd, *J* = 13.7, 9.2, 8.9, 5.5 Hz, 1H), 2.46 (dd, *J* = 16.4, 8.5 Hz, 1H), 2.53 (dd, *J* = 16.4, 3.4 Hz, 1H) 2.73 (ddd, *J* = 13.7, 9.2, 6.8 Hz, 1H), 2.83 (ddd, *J* = 15.0, 9.9, 6.8 Hz, 1H), 3.02 (bs, 1H), 4.00 (m, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 7.13-7.31 (m, 5H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 14.6, 32.2, 38.5, 41.7, 61.1, 67.6, 126.3, 128.8, 128.9, 142.2, 173.4. **HRMS** (ESI^-) calculated for $C_{13}H_{19}O_3$ ($[M-H]^-$) 223.1334, found 223.1337.

3-hydroxy-*N*-methoxy-*N*-methyl-5-phenylpentanamide (S7)[6]



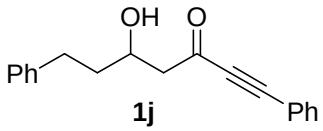
S7

A suspension of *N*,*O*-dimethylhydroxylamine hydrochloride (1.4 g, 14.4 mmol, 3.0 eq.) in tetrahydrofuran (50 mL) was cooled down to 0°C before slow addition of trimethylaluminum (7.2 ml, 2 M in toluene, 14.4 mmol). The mixture was allowed to reach rt till a transparent solution was obtained and then cooled down to -40°C. A solution of **S6** (1.07 g, 4.8 mmol) in tetrahydrofuran (10 mL) was then added. The reaction mixture was warmed to rt and stirred for 3h. It was then quenched cautiously at 0°C by addition of a 1.5 M aqueous solution of hydrochloric acid. After separation of the phases and extraction of the aqueous one with ethyl acetate (3 × 30 mL), the combined organic layers were dried over magnesium sulphate and the solvents were evaporated. The resulting residue was further purified by column chromatography on silica gel (EtOAc:hexane, 1:1) afforded **S7** as a pale yellow oil (872 mg, 77%). $\mathbf{R_f}$ (Et_2O:hexane, 1:1) = 0.21. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.75 (dddd, ^3J = 13.9, 9.8, 6.8, 4.0 Hz, 1H), 1.90 (dddd, ^3J = 13.9, 9.3, 8.6, 5.3 Hz, 1H), 2.49 (dd, ^3J = 16.6, 9.3 Hz, 1H), 2.67 (d, ^3J = 16.6, Hz, 1H), 2.73 (ddd, ^3J = 14.0, 9.6, 6.8 Hz, 1H), 2.86 (ddd, ^3J = 14.0, 9.8, 5.3 Hz, 1H), 3.20 (s, 3H), 3.68 (s, 3H), 3.92 (d, 1H), 4.07 (ddd, ^3J = 9.1, 9.1, 4.0, 2.3 Hz, 1H) and 7.18-7.30 (m, 5 H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 31.8, 38.2, 61.2, 67.2,

[6] F. Silva, M. Reiter, R. Mills-Webb, M., D. Klär, N. Bensel, A. Wagner, V. Gouverneur, *J. Org. Chem.* **2006**, *71*, 8390-8394.

125.8, 128.2, 129.0, 142.0, 173.8. **IR** (DCM) (ν, cm^{-1}): 3445, 1652. **HRMS** (ESI^+) calculated for $C_{13}H_{20}O_3N$ ($[M+H]^+$) 238.1443, found: 238.1443.

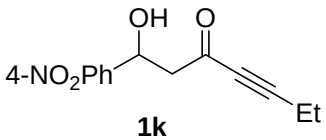
5-Hydroxy-1,7-diphenylhept-1-yn-3-one (1j)



1j

To a solution of phenylacetylene (450 µL, 4.1 mmol, 3 eq.) was added *n*BuLi (1.6 mL, 2.5M in hexanes, 4.1 mmol, 3 eq.) at 0 °C in THF (40 mL). After stirring for 30 min, the reaction mixture was cooled to -78 °C and a solution of the amide **S7** (350 mg, 1.5 mmol, 1 eq.) in THF was added dropwise. It was then warmed up to rt overnight until completion as judged by TLC and quenched at 0 °C by the addition of NH_4Cl. The reaction mixture was allowed to warm to rt and the two layers separated. The neutral aqueous layer was further extracted with EtOAc and the combined organic layers were then dried over $MgSO_4$, filtered and concentrated *in vacuo*. The residue was then purified by flash column chromatography on silica gel (hexane:EtOAc, 4:1) to yield the product (380 mg, 93%) as a pale yellow solid. **m.p. =** 45-50 °C. $\mathbf{R_f}$ (hexane:EtOAc, 9:1) = 0.28. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.79 (dddd, *J* = 16.6, 9.6, 7.0, 4.2 Hz, 1H), 1.90 (dddd, *J* = 17.2, 9.1, 8.4, 5.4 Hz, 1H), 2.71-2.86 (m, 2H), 2.88-2.93 (m, 2H), 4.24 (m, 1H), 7.15-7.66 (m, 10H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 31.7, 38.0, 52.0, 66.9, 87.8, 91.9, 119.6, 125.9, 128.4, 128.5, 128.7, 131.0, 133.2, 141.7, 187.6. **IR** (DCM) (ν, cm^{-1}): 3449, 3026, 2928, 2203, 1666, 1299. **HRMS** (ESI^+) calculated for $C_{19}H_{18}NaO_2$ ($[M+Na]^+$) 301.1204, found 301.1199.

1-hydroxy-1-(4-nitrophenyl)hept-4-yn-3-one (1k)[7]



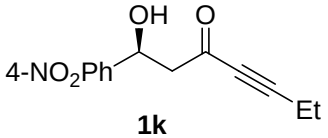
1k

To a precooled (0 °C) solution of diisopropylamine (210 µL, 1.5 mmol, 1.5 eq.) in anhydrous THF (25mL) was added *n*BuLi (0.6 mL, 2.5M in hexanes, 1.5 mmol, 1.5 eq.). The resulting solution was stirred at 0 °C for 30 min and then cooled down to -78 °C, before adding dropwise the hex-3-yn-2-one (300 µL, 1.3 mmol, 1.3 eq.). After 30 min of stirring at this temperature, the 4-nitrobenzaldehyde (151 mg, 1.0 mmol, 1 eq.) in anhydrous THF was added. The resulting reaction mixture was stirred at -78 °C for a further 30 mins and allowed to warm to rt. The reaction was quenched by addition of an aqueous saturated NH_4Cl solution. The obtained layers were separated and the aqueous

[7] F. Silva, M. Sawicki, V. Gouverneur, *Org. Lett.* **2006**, *8*, 5417-5419.

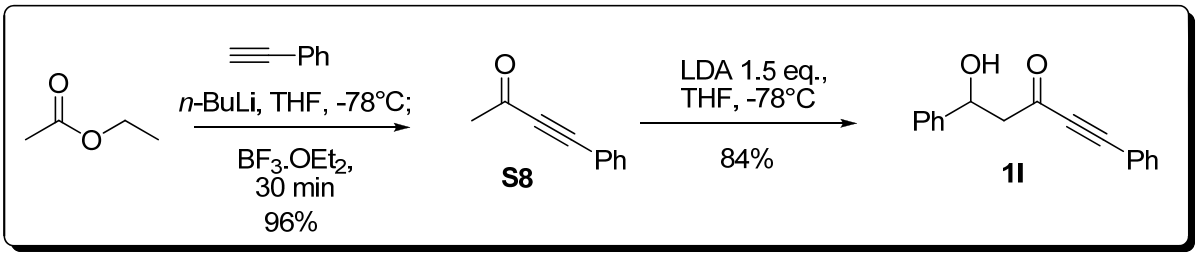
layer was further extracted with Et_2O (3 × 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo* to give a crude residue which was further purified by column chromatography (hexane:EtOAc, 9:1) yielded the product **1k** (90 mg, 68%) as a pale yellow oil. $\mathbf{R_f}$ (hexane:EtOAc, 3:2) = 0.55. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.22 (t, *J* = 7.5 Hz, 3H), 2.40 (q, *J* = 7.5 Hz, 2H), 2.99 (d, *J* = 6.3 Hz, 2H), 3.34 (d, *J* = 3.4 Hz, 1H), 5.33 (td, *J* = 6.1, 3.4 Hz, 1H), 7.56 (d, *J* = 8.8 Hz, 2H), 8.22 (d, *J* = 8.6 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 12.5, 12.8, 53.5, 68.6, 79.3, 97.8, 123.8, 126.4, 147.4, 149.5, 186.1. **IR** (neat) (ν, cm^{-1}): 3454, 2983, 2213, 1670, 1343. **HRMS** (ESI^-) calculated for $C_{13}H_{12}NO_4$ ($[M-H]^-$) 246.0766, found 246.0765.

(*R*)-1-hydroxy-1-(4-nitrophenyl)hept-4-yn-3-one ((*R*)-1k)[7]

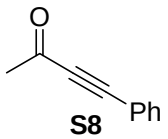


1k

The procedure already described by our group yielded the product (48 mg, 39%) as a pale yellow oil with 74% *ee*. HPLC (Chiralcel OJ, hexane:^{i}PrOH, 6:1, 1.0 $mL.min^{-1}$): t_R(maj) = 21.1 mins, t_R(min) = 22.6 mins. The analytical data agreed with that of the racemic product.



4-Phenylbut-3-yn-2-one (S8)[8]



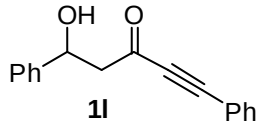
S8

To a solution of phenylacetylene (3.3 mL, 30 mmol, 2 eq.) in anhydrous THF (30 mL) at -78°C was added *n*-BuLi (2.5M solution in hexane, 12 mL, 30 mmol, 2 eq.) under argon. The reaction mixture was stirred for 30 min, then a solution of distilled ethyl acetate (1.5 mL, 15 mmol, 1 eq.) in THF (45 mL) and boron trifluoride diethyl etherate (4.4 mL, 36 mmol, 2.4 eq.) were added successively. After 30 min at -78°C, the reaction was quenched with a saturated solution of NH_4Cl and allowed to warm up to room

[8] a) M. Yamaguchi, K. Shibato, S. Fujiwara, I. Hirao, *Synthesis* **1986**, *5*, 421-422; b) P. Wessig, G. Müller, A. Kühn, R. Herre, H. Blumenthal, S. Troelenberg, *Synthesis* **2005**, *9*, 1445-1454.

temperature. The layers were separated and the aqueous layer was further extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. Purification by column chromatography on silica gel (hexane:EtOAc, 95:5) gave the product as a dark orange liquid (2.08 g, 14.4 mmol) in a 96% yield. $\mathbf{R_f}$ (hexane:EtOAc, 95:5) = 0.30. **^{1}H-NMR** (400 MHz, $CDCl_3$) δ: 2.46 (s, 3H), 7.37-7.60 (m, 5H). **^{13}C-NMR** (100 MHz, $CDCl_3$) δ: 32.8, 88.3, 90.3, 119.9, 128.6, 130.8, 133.1, 184.7. **HRMS** (CI^+) calculated for $C_{10}H_9O$ ($[M+H]^+$) 145.0653, found 145.0653.

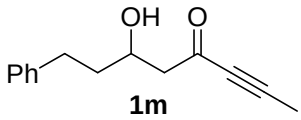
5-hydroxy-1,5-diphenylpent-1-yn-3-one (1l)



1l

The same procedure than substrate **1k** was followed employing the ynone **S8** (374 mg, 2.6 mmol, 1.3 eq.), diisopropylamine (460 µL, 3.0 mmol, 1.5 eq.), of ^{n}BuLi (1.2 mL, 2.5M in hexanes, 1.5 mmol, 1.5 eq.) and benzaldehyde (203 µL, 2.0 mmol, 1 eq.) in THF (7.5 mL). Purification by column chromatography (hexane:Et_2O, 3:2) yielded the product (420 mg, 84%) as a dark orange oil. $\mathbf{R_f}$ (hexane:Et_2O, 3:2) = 0.40. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 2.80 (br s, 1H), 3.09 (dd, *J* = 17.4, 3.4 Hz, 1H), 3.19 (dd, *J* = 17.4, 9.2 Hz, 1H), 5.33 (dd, *J* = 9.2, 3.4 Hz, 1H), 7.28-7.61 (m, 10H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 54.2, 69.9, 87.8, 92.3, 119.6, 125.8, 127.9, 128.6, 128.7, 131.1, 132.2, 142.4, 186.7. **IR** (DCM) (ν, cm^{-1}): 3429, 3062, 2204, 1666. **HRMS** (ESI^+) calculated for $C_{17}H_{14}NaO_2$ ($[M+Na]^+$) 273.0891, found 273.0891.

6-hydroxy-8-phenyloct-2-yn-4-one (1m)[6]



1m

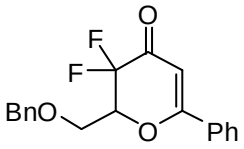
The same procedure than for substrate **1h** was followed employing 498 mg of **S7** (2.10 mmol, 1 eq.), 12.6 mL of 1-propynylmagnesium bromide (0.5 M in THF, 6.3 mmol, 3 eq.) in dry THF (20 mL). The reaction was quenched with NH_4Cl (30 mL) at 0 °C. Purification by column chromatography (hexane:EtOAc, 3:1) yielded the product (420 mg, 92%) as a pale yellow oil. $\mathbf{R_f}$ (hexane:EtOAc, 6:1) = 0.15. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.72 (dddd, *J* = 16.6, 9.8, 6.9, 4.0 Hz, 1H), 1.84 (dddd, *J* = 18.2, 9.2, 8.9, 5.5 Hz, 1H), 2.03 (s, 3H), 2.65-2.87 (m, 5H), 4.15 (dddd, *J* = 12.1, 8.4, 4.2, 3.9 Hz, 1H), 7.17-7.35 (m, 5H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 4.1, 31.7, 37.9, 52.1, 66.7, 80.3, 91.5, 125.9, 128.4, 128.5, 141.7, 187.6. **IR** (DCM) (ν, cm^{-1}): 3442, 3207, 2921, 2219, 1668, 1251. **HRMS** (ESI^+) calculated for $C_{14}H_{17}O_2$ ($[M+H]^+$) 217.1229, found 217.1232.

B- Gold-catalyzed cyclization of β-hydroxy-ynones 1a-k

General procedure A: Au^{I}-mediated cyclization

To a solution of the corresponding hydroxy-ynone **1a-k** (1 eq.) in DCM (0.1M) was added AuCl (5 mol%) at room temperature under Argon. After stirring overnight at room temperature, the mixture was filtered through a short silica pad. The filtrate was concentrated *in vacuo* and then purified by column chromatography on silica gel.

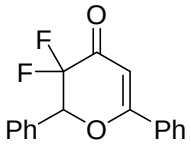
2-[(benzyloxy)methyl]-3,3-difluoro-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (2a)



2a

General procedure **A** was followed, employing 480 mg of **1a** (1.46 mmol, 1 eq.) and 17 mg of AuCl (0.073 mmol, 5 mol%) in DCM (15 mL). Purification by column chromatography (hexane:Et_20, 8:2) yielded the product (450 mg, 93%) as a pale yellow oil. $\mathbf{R_f}$ (hexane:Et_2O, 8:2) = 0.35. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 4.08 (dd, *J* = 11.4, 6.7 Hz, 1H), 4.12 (dd, *J* = 11.4, 3.3 Hz, 1H), 4.08 (s, 1H), 4.84 (dtd, *J* = 20.0, 6.8, 3.3 Hz, 1H), 6.17 (t, *J* = 2.4 Hz, 1H), 7.30-7.80 (m, 10H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 65.9 (t, *J* = 3.2 Hz), 73.2, 80.2 (dd, *J* = 28.4, 26.0 Hz), 100.0 (t, *J* = 1.6 Hz), 108.4 (t, *J* = 255.2 Hz), 127.1, 127.8, 128.1, 128.6, 129.0, 131.3, 132.9, 137.2, 171.1, 180.2 (t, *J* = 24.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -124.4 (d, *J* = 282.2 Hz, 1F), -123.3 (dd, *J* = 282.2, 19.5 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 2872, 1689, 1596, 909. **HRMS** (ESI^+) calculated for $C_{19}H_{16}F_2NaO_3$ ($[M+Na]^+$) 353.0965, found 353.0960.

3,3-difluoro-2,6-diphenyl-2,3-dihydro-4*H*-pyran-4-one (2b)

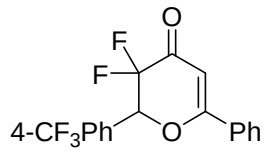


2b

General procedure **A** was followed, employing 391 mg of **1b** (1.37 mmol, 1 eq.) and 16 mg of AuCl (0.069 mmol, 5 mol%) in DCM (14 mL). Purification by column chromatography (hexane:Et_2O, 2:1) yielded the product (360 mg, 92%) as a pale yellow solid. **m.p.** = 91-93°C. $\mathbf{R_f}$ (hexane:Et_2O, 2:1) = 0.40. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.58 (dd, *J* = 26.4, 2.4 Hz, 1H), 6.27 (d, *J* = 4.3 Hz, 1H), 7.46-7.52 (m, 5H), 7.56-7.63 (m, 3H), 7.56-7.63 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 82.4 (dd, *J* = 31.2, 24.4 Hz), 100.1 (dd, *J* = 2.4, 1.2 Hz), 108.0 (dd, *J* = 257.2, 253.2 Hz), 127.2, 128.4, 128.7, 129.0, 129.7 (d, *J* = 0.8 Hz), 130.1, 131.2, 132.9, 171.9, 199.2 (t, *J* = 24.8 Hz). **^{19}F**

NMR (376 MHz, $CDCl_3$) δ: -121.0 (dd, *J* = 282.24, 26. Hz), -127.6 (d, *J* = 282.2 Hz). **IR** (DCM) (ν, cm^{-1}): 3039, 1689, 1613, 933. **HRMS** (ESI^+) calculated for $C_{17}H_{13}F_2O_2$ ($[M+H]^+$) 287.0884, found 287.0881.

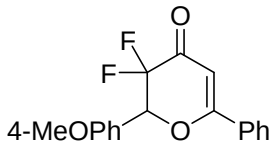
3,3-difluoro-6-phenyl-2-[4-(trifluoromethyl)phenyl]-2,3-dihydro-4*H*-pyran-4-one (2c)



2c

General procedure **A** was followed, employing 87 mg of **1c** (0.25 mmol, 1 eq.) and 3 mg of AuCl (0.013 mmol, 5 mol%) in DCM (2.5 mL). Purification by column chromatography (hexane:Et_2O, 3:1) yielded the product (82 mg, 94%) as a pale yellow oil. R_f (hexane:Et_2O, 3:1) = 0.20. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.66 (dd, *J* = 26.2, 1.9 Hz, 1H), 6.29 (d, *J* = 4.4 Hz, 1H), 7.47-7.54 (m, 2H), 7.57-7.63 (m, 1H), 7.74 (d, *J* = 8.7 Hz, 2H), 7.78 (d, *J* = 8.7 Hz, 2H), 7.80-7.84 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 81.6 (dd, *J* = 31.2, 24.4 Hz), 100.2 (d, *J* = 1.6 Hz), 107.7 (dd, *J* = 258.0, 254.5 Hz), 123.8 (q, J_F = 272.4 Hz), 125.7 (q, *J* = 3.6 Hz), 127.0, 128.7, 129.1, 130.9, 132.2 (q, *J* = 32.8 Hz), 133.1, 133.6, 171.6, 180.6 (t, *J* = 24.4 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -62.8 (s), -120.6 (dd, *J* = 282.2, 26.4 Hz), -127.9 (d, *J* = 282.2 Hz). **IR** (DCM) (ν, cm^{-1}): 2952, 1690, 1598, 1326, 1132. **HRMS** (ESI^+) calculated for $C_{18}H_{12}F_5O_2$ ($[M+H]^+$) 355.0757, found 355.0754

3,3-difluoro-2-(4-methoxyphenyl)-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (2d)

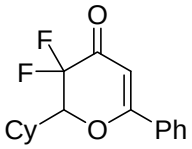


2d

General procedure **A** was followed, employing 81.5 mg of **1d** (0.26 mmol, 1 eq.) and 3 mg of AuCl (0.013 mmol, 5 mol%) in DCM (2.6 mL). Purification by column chromatography (hexane:Et_2O, 1:1) yielded the product (75 mg, 92%) as a white solid. **R_f** (hexane:Et_2O, 1:1) = 0.33. **m.p.** = 72°C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 3.87 (s, 3H), 5.52 (dd, *J* = 26.3, 2.3 Hz, 1H), 6.25 (d, *J* = 4.3 Hz, 1H), 7.02 (d, *J* = 8.6 Hz, 2H), 7.45-7.50 (m, 2H), 7.53 (d, *J* = 8.6 Hz, 2H), 7.55-7.59 (m, 1H), 7.81 (d, *J* = 7.8 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 55.4, 82.2 (dd, *J* = 31.5, 24.3 Hz), 100.0, 108.2 (dd, *J* = 256.1, 253.2 Hz), 114.1, 121.7, 127.0, 129.0, 129.9, 131.2, 132.9, 161.0, 172.0, 181.4 (t, *J* = 21.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -121.4 (dd, *J* = 282.2, 26.4 Hz), -127.6

(d, *J* = 281.1 Hz). **IR** (DCM) (ν, cm^{-1}): 2950, 1687, 1597, 1254, 1134. **HRMS** (ESI^+) calculated for $C_{18}H_{15}F_2O_3$ ($[M+H]^+$) 317.0989, found 317.0983.

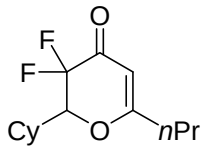
2-cyclohexyl-3,3-difluoro-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (2e)



2e

General procedure **A** was followed, employing 68 mg of **1e** (0.23 mmol, 1 eq.) and 3 mg of AuCl (0.012 mmol, 5 mol%) in DCM (2.3 mL). Purification by column chromatography (hexane:Et_2O, 3:1) yielded the product (64 mg, 94%) as an orange solid. **m.p** = 82°C. **R_f** (hexane:Et_2O, 3:1) = 0.35. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.18-2.30 (m, 11H), 4.31 (dt, *J* = 25.5, 5.1 Hz, 1H), 6.18 (d, *J* = 3.8 Hz, 1H), 7.45-7.50 (m, 2H), 7.52-7.58 (m, 1H), 7.74-7.78 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 25.8, 25.95, 25.97, 28.3, 29.8, 36.8, 84.1 (dd, *J* = 29.2, 25.2 Hz), 95.5, 109.8 (dd, *J* = 257.2, 253.3 Hz), 126.9, 129.0, 131.6, 132.7, 171.0, 181.3 (t, *J* = 24.8 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -121.6 (dd, *J* = 281.1, 25.2 Hz), -123.6 (d, *J* = 281.1 Hz). **IR** (DCM) (ν, cm^{-1}): 2931, 2856, 1688, 1607, 1132. **HRMS** (ESI^+) calculated for $C_{17}H_{19}F_2O_2$ ($[M+H]^+$) 293.1353, found 293.1347.

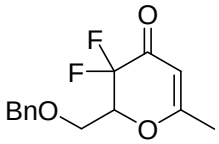
2-cyclohexyl-3,3-difluoro-6-propyl-2,3-dihydro-4*H*-pyran-4-one (2f)



2f

General procedure **A** was followed, employing 50 mg of **1f** (0.19 mmol, 1 eq.) and 2.3 mg of AuCl (0.01 mmol, 5 mol%) in DCM (2.0 mL). Purification by column chromatography (hexane:Et_2O, 3:1) yielded the product (45 mg, 90%) as a colourless oil. **R_f** (hexane:Et_2O, 3:1) = 0.25. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 0.96 (t, *J* = 7.3 Hz, 3H), 1.13-1.35 (m, 6H), 1.62 (sext, *J* = 7.5 Hz, 2H), 1.65-2.12 (m, 5H), 2.24-2.38 (m, 2H), 4.08 (dt, *J* = 26.7, 5.0 Hz, 1H), 5.43 (dd, *J* = 4.0, 1.3 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 13.4, 19.8, 25.8, 25.9, 26.0, 27.9, 29.5, 36.6, 36.8, 83.9 (dd, *J* = 29.6, 25.6 Hz), 101.9 (t, *J* = 1.6 Hz), 109.7 (dd, *J* = 257.2, 252.5 Hz), 179.5, 180.9 (t, *J* = 24.8 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -121.8 (dd, *J* = 279.9, 26.4 Hz), -124.0 (d, *J* = 279.9 Hz). **IR** (DCM) (ν, cm^{-1}): 2933, 1698, 1605, 1207, 1128. **HRMS** (ESI+) calculated for $C_{14}H_{21}F_2O_2$ ($[M+H]^+$) 259.1510, found 259.1504.

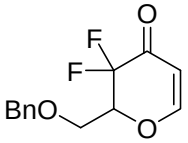
2-[(benzyloxy)methyl]-3,3-difluoro-6-methyl-2,3-dihydro-4*H*-pyran-4-one (2h)



2h

General procedure **A** was followed, employing 60 mg of **1h** (0.22 mmol, 1 eq.) and 2.5 mg of AuCl (0.011 mmol, 5 mol%) in MeCN (2.2 mL). Purification by column chromatography (hexane:Et_2O, 2:1) yielded the product (50 mg, 83%) as a colourless oil. $\mathbf{R_f}$ (hexane:Et_2O, 1:1) = 0.40. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 2.14 (s, 3H), 3.94 (dd, *J* = 11.4, 7.1 Hz, 1H), 4.00 (dd, *J* = 11.2, 2.7 Hz, 1H), 4.55-4.67 (m, 1H), 4.61 (d, *J* = 11.8 Hz, 1H), 4.65 (d, *J* = 11.8 Hz, 1H), 5.49 (br d, *J* = 3.3 Hz, 1H), 7.30-7.41 (m, 5H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 21.4, 65.9 (dd, *J* = 4.4, 2.0 Hz), 75.9, 80.1 (dd, *J* = 29.6, 25.7 Hz), 103.1 (t, *J* = 2.0 Hz), 108.1 (dd, *J* = 255.3, 253.3 Hz), 127.8, 128.1, 128.6, 137.1, 175.8, 179.5 (t, *J* = 24.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -123.1 (dd, *J* = 282.2, 23.0 Hz, 1F), -125.1 (d, *J* = 282.2 Hz, 1F). **IR** (neat) (ν, cm^{-1}): 2927, 1699, 1045. **HRMS** (ESI^+) calculated for $C_{14}H_{14}F_2NaO_3$ ($[M+Na]^+$) 291.0809, found 291.0803.

2-[(benzyloxy)methyl]-3,3-difluoro-2,3-dihydro-4*H*-pyran-4-one (2i)[9]



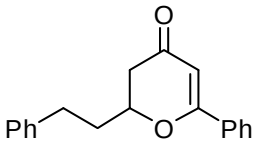
2i

To a solution of the corresponding hydroxynone **1i** (390 mg, 1.5 mmol, 1 eq.) in DCM (15 mL) was added $AuCl_3$ (46.4 mg, 0.15 mmol, 10 mol%), by portions of 11.6 mg (0.025 eq.) every 12 hours at room temperature under Argon. The reaction was monitored by ^{19}F NMR. After 2 days of stirring at room temperature, the mixture was filtered through a short silica pad. The filtrate was then concentrated *in vacuo.* Purification by column chromatography on silica gel (hexane:EtOAc, 80:20) yielded the product (300 mg, 75%) as a colourless oil. $\mathbf{R_f}$ (hexane:Et_2O, 3:2) = 0.34. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 3.96 (dd, *J* = 11.4, 6.8 Hz, 1H), 4.01 (dd, *J* = 11.4, 2.8 Hz, 1H), 4.61 (d, *J* = 12.1 Hz, 1H), 4.64 (d, *J* = 12.1 Hz, 1H), 4.65-4.74 (m, 1H), 5.61 (ddd, *J* = 5.8, 3.0, 2.9 Hz, 1H), 7.31-7.41 (m, 5H), 7.46 (d, *J* = 6.1 Hz, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 65.8 (t, *J* = 3.6 Hz), 73.9, 80.7 (t, *J* = 27.6 Hz), 104.9 (t, *J* = 1.6 Hz), 108.3 (t, *J* = 255.3 Hz), 127.8, 128.1, 128.6, 136.9, 163.6, 179.6 (t, *J* = 24.5 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -123.2 (ddd, *J* = 282.2, 13.8, 2.3 Hz, 1F), -122.4 (ddd, *J* = 282.2, 16.1,

[9] T. Taguchi, Y. Kodama, M. Kanazawa, *Carbohydr. Res.* **1993**, *249*, 243-252.

2.3 Hz, 1F). **IR** (neat) (ν, cm^{-1}): 2874, 1705, 1596, 1110. **HRMS** (ESI^+) calculated for $C_{13}H_{12}F_2NaO_3$ ($[M+Na]^+$) 277.0652, found 277.0647.

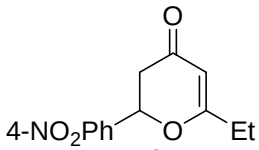
6-phenyl-2-(2-phenylethyl)-2,3-dihydro-4*H*-pyran-4-one (2j)



2j

General procedure **A** was followed, employing 56 mg of **1j** (0.20 mmol, 1 eq.) and 3 mg of AuCl (0.013 mmol, 6 mol%) in DCM (2 mL). Purification by column chromatography (hexane:EtOAc 7:3) yielded the product (50 mg, 89%) as a pale yellow oil. $\mathbf{R_f}$ (hexane:Et_2O, 6:4) = 0.26. **^{1}H NMR** (400 MHz, $CDCl_3$): 2.07 (ddd, *J* = 17.4, 9.1, 7.3, 4.3 Hz, 1H), 2.33 (ddd, *J* = 17.4, 14.4, 8.6, 5.8 Hz, 1H), 2.51 (dd, *J* = 16.7, 3.7 Hz, 1H), 2.62 (dd, *J* = 16.7, 13.4 Hz, 1H), 2.90 (ddd, *J* = 13.9, 8.6, 7.3 Hz, 1H), 2.99 (ddd, *J* = 13.9, 9.1, 5.8 Hz, 1H), 4.56 (m, J = 4.3, 3.7 Hz, 1H), 6.03 (s, 1H), 7.20-7.25 (m, 2.5H), 7.29-7.35 (m, 2H), 7.42-7.54 (m, 3.5 H), 7.73-7.77 (m, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 31.4, 36.2, 41.4, 78.5, 102.1, 126.3, 126.5, 128.4, 128.6, 128.7, 131.7, 132.8, 140.8, 170.1, 193.3. **IR** (neat) (ν, cm^{-1}): 3061, 3026, 2928, 1660, 1600, 1571, 1493, 1450, 1385, 1338, 1053, 773, 695. **HRMS** (ESI^+) calculated for $C_{19}H_{18}NaO_2$ ($[M+Na]^+$) 301.1199, found 301.1199.

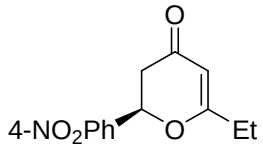
6-ethyl-3,3-difluoro-2-(4-nitrophenyl)-2,3-dihydro-4*H*-pyran-4-one (2k)



2k

General procedure **A** was followed, employing 83 mg of **1k** (0.33 mmol, 1 eq.) and 3.7 mg of AuCl (0.016 mmol, 5 mol%) in DCM (3.3 mL). Purification by column chromatography (hexane:Et_2O, 3:1) yielded the product (54 mg, 65%) as pale yellow oil. $\mathbf{R_f}$ (hexane:EtOAc, 3:2) = 0.55. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.20 (t, *J* = 7.3 Hz, 3H), 2.40 (q, *J* = 7.6 Hz, 2H), 2.67 (dd, *J* = 16.6, 6.3 Hz, 1H), 2.75 (dd, *J* = 16.6, 13.4 Hz, 1H), 5.49 (s, 1H), 5.50 (dd, *J* = 13.3, 4.3 Hz, 1H), 7.60 (d, *J* = 8.8 Hz, 2H), 8.29 (d, *J* = 8.6 Hz, 2H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ: 10.6, 27.9, 42.6, 79.4, 103.4, 123.8, 126.4, 147.4, 149.5, 168.2, 186.1. **IR** (neat) (ν, cm^{-1}): 2983, 1670, 1605, 1347. **HRMS** (ESI^-) calculated for $C_{13}H_{12}NO_4$ ($[M-H]^-$) 246.0766, found 246.0765.

(*R*)-6-ethyl-3,3-difluoro-2-(4-nitrophenyl)-2,3-dihydro-4*H*-pyran-4-one ((*R*)-2k)



2k

General procedure **A** was followed, employing 54 mg of (*R*)-**1k** (0.22 mmol, 1 eq.) and 2.5 mg of AuCl (0.011 mmol, 5 mol%) in DCM (2.2 mL). Purification by column chromatography (hexane:Et_2O, 3:1) yielded the product (35 mg, 65%) as a pale yellow oil with 74% *ee*. HPLC (Chiralcel OD, hexane:^{i}PrOH, 6:1, 0.7 mL.min^{-1}): t_R(min) = 31.1 mins, t_R(maj) = 43.1 mins. The analytical data agreed with that of the racemic product.

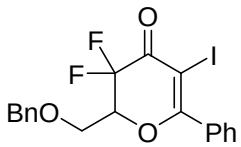
C - Gold-catalyzed alkoxyhalogenations

C.1 - GOLD-CATALYZED ALKOXYIODINATIONS

General procedure B: alkoxyiodination of difluorinated hydroxy-ynones 1a, 1b, 1d, 1e and 1f.

To a solution of the corresponding hydroxy-ynone **1** (1 eq.) in acetone (0.1M) was added NIS (1.2 eq.), followed by AuCl (5 mol%) at room temperature under Argon. The reaction mixture was stirred at room temperature until completion as monitored by TLC. The mixture was then quenched with a saturated aqueous solution of $Na_2S_2O_3$. The mixture was then partitioned and the aqueous layer was extracted three times with Et_2O. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo.* The crude product was then purified by column chromatography on silica gel.

2-[(benzyloxy)methyl]-3,3-difluoro-5-iodo-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (3a)

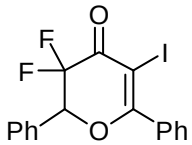


3a

General procedure B was followed, using the ynone **1a** (101 mg, 0.31 mmol, 1 eq.), NIS (83 mg, 0.37 mmol, 1.2 eq.) and AuCl (3.6 mg, 0.055 mmol, 5 mol%) in acetone (3 mL) for 17h. Purification by column chromatography (hexane:Et_2O 8/2) gave the product as a yellow oil (92 mg, 65%). $\mathbf{R_f}$ (hexane:Et_2O 6:4) = 0.47. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 4.01 (dd, *J* = 5.2, 9.2 Hz, 1H), 4.08 (dd, *J* = 2.0, 9.2 Hz, 1H), 4.61 (d, *J* = 24.0 Hz, 1H),

4.63 (d, *J* = 24.0 Hz, 1H), 4.88 (dtd, *J* = 2.0, 5.2, 15.6 Hz, 1H), 7.28-7.38 (m, 5H), 7.44-7.56 (m, 3H), 7.70-7.74 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 65.9, 72.8, 73.9, 80.2 (dd, *J* = 25.2, 26.5 Hz), 107.0 (t, *J* = 256 Hz), 127.7, 128.1, 128.2, 128.6, 129.8, 132.1, 134.3, 137.0, 172.5, 177.0 (t, *J* = 25.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -118.30 (dd, *J* = 5.2, 278.7 Hz, 1F), -121.9 (d, *J* = 15.6, 278.7 Hz, 1F). **IR** (neat) (ν, cm^{-1}): 3086, 3052, 1697, 1542, 1487, 1163, 1092, 696. **HRMS** (CI^+) calculated for $C_{19}H_{16}O_3F_2I$ ($[M+H]^+$) 457.0096, found 457.0112.

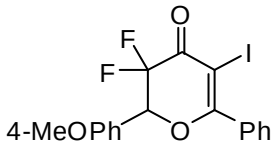
3,3-difluoro-5-iodo-2,6-diphenyl-2,3-dihydro-4*H*-pyran-4-one (3b)



3b

General procedure B was followed, using the ynone **1b** (100 mg, 0.35 mmol, 1 eq.), NIS (94 mg, 0.42 mmol, 1.2 eq.) and AuCl (4 mg, 0.018 mmol, 5 mol%) in acetone (3.5 mL) for 24h. Purification by column chromatography (Hexane:Et_2O, 8:2) gave the product as a yellow solid (109 mg, 76%). **m.p.** = 137°C. **R_f** (Hexane:Et_2O, 7:3) = 0.47. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.65 (dd, *J* = 2.0, 26.4 Hz, 1H), 7.40-7.58 (m, 8H), 7.76-7.81 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 73.1, 82.3 (dd, *J* = 24.0, 24.2 Hz), 106.6 (t, *J* = 257 Hz), 128.2, 128.3, 128.7, 128.9, 129.9, 130.3, 132.3, 134.1, 173.4, 178.1 (t, *J* = 25.2 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -119.7 (dd, *J* = 26.3, 277.0 Hz, 1F), -122.9 (d, *J* = 277 Hz, 1F). **IR** (CH_2Cl_2) (ν, cm^{-1}): 1695, 1540, 1486, 1152, 1111, 929, 696. **HRMS** (CI^+) calculated for $C_{17}H_{12}O_2F_2I$ ($[M+H]^+$) 412.9850, found 412.9864.

3,3-difluoro-5-iodo-2-(4-methoxyphenyl)-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (3d)

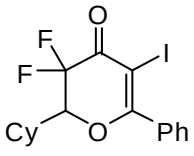


3d

General procedure **B** was followed, employing 63 mg of **1d** (0.2 mmol, 1 eq.) and 3.0 mg of AuCl (0.013 mmol, 6 mol%) in acetone (2 mL). Purification by column chromatography (hexane:Et_2O, 5:5) yielded the product (81 mg, 92%) as a pale yellow solid. **m.p** = 162°C.**R_f** (hexane:Et_2O 1:1) = 0.55. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 3.85 (s, 3H), 5.60 (dd, *J* = 25.8, 2.3 Hz, 1H), 6.98 (d, *J* = 9.1 Hz, 2H), 7.46 (d, *J* = 9.1 Hz, 2H), 7.47-7.51 (m, 2H), 7.52-7.57 (m, 1H), 7.76-7.80 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 55.4, 73.1, 82.2 (dd, *J* = 31.5, 23.8 Hz), 106.8 (dd, *J* = 259.4, 255.6 Hz), 114.1, 120.7, 128.1, 129.9, 130.0, 132.3, 134.1, 161.1, 173.7, 178.3 (t, *J* = 25.0 Hz). **^{19}F NMR** (376

MHz, $CDCl_3$) δ: -120.1 (dd, *J* = 276.5, 26.4 Hz, 1F), -122.7 (d, *J* = 276.5 Hz, 1F). **IR** (CH_2Cl_2) (ν, cm^{-1}): 2864, 1698, 1612, 995, 530. **HRMS** (ESI^+) calculated for $C_{18}H_{13}F_2INaO_3$ ($[M+Na]^+$) 464.9770, found 464.9769.

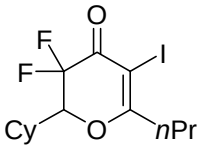
2-cyclohexyl-3,3-difluoro-5-iodo-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (3e)



3e

General procedure B was followed, using the ynone **1e** (100 mg, 0.34 mmol, 1 eq.), NIS (92 mg, 0.41 mmol, 1.2 eq.) and AuCl (4 mg, 0.017 mmol, 5 mol%) in acetone (3 mL) for 14h. Purification by column chromatography (hexane:Et_2O 8/2) gave the product as a yellow solid (92 mg, 65%). **m.p.** = 77°C.**R_f** (hexane:Et_2O 6:4) = 0.60. **^{1}H NMR** (400 MHZ, $CDCl_3$): 1.15-1.47 (m, 6H), 1.66-2.24 (m, 5H), 4.39 (ddd, *J* = 6.0, 6.8, 22.8 Hz, 1H), 7.45-7.57 (m, 3H), 7.70-7.75 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$): 25.7, 25.8, 25.9, 28.1, 29.4, 36.5, 72.3, 84.1 (t, *J* = 27 Hz), 108.4 (t, *J* = 258 Hz), 128.2, 129.7, 132.1, 134.3, 173.2, 178.2 (t, *J* = 25.7 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$): -119.3 (dd, *J* = 22.8, 276.0 Hz, 1F), -120.3 (dd, *J* = 6.8, 276.0 Hz, 1F). **IR** (CH_2Cl_2) (ν, cm^{-1}): 2931, 2855, 1694, 1543, 1488, 1446, 1160, 1111, 1029, 739, 696. **HRMS** (CI^+) calculated for $C_{17}H_{18}O_2F_2I$ ($[M+H]^+$) 419.0302, found 419.0320.

2-cyclohexyl-3,3-difluoro-5-iodo-6-propyl-2,3-dihydro-4*H*-pyran-4-one (3f)



3f

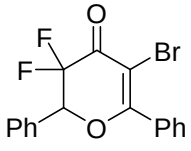
General procedure B was followed, using the ynone **1f** (100 mg, 0.39 mmol, 1 eq.), NIS (105 mg, 0.47 mmol, 1.2 eq.) and AuCl (5 mg, 0.022 mmol, 5 mol%) in acetone (4 mL) for 20h. Purification by column chromatography (hexane:Et_2O 8/2) gave the product as an orange oil (101 mg, 68%). **R_f** (hexane:Et_2O, 6:4) = 0.50. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.02 (t, *J* = 7.4 Hz, 3H), 1.16-1.41 (m, 5H), 1.65-1.88 (m, 6H), 1.96-2.16 (m, 2H) 2.76 (t, *J* = 7.4 Hz, 2H), 4.14 (dt, *J* = 5.2, 5.6, 25.5 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 13.6, 20.0, 25.7, 25.8, 25.9, 27.9 (d, *J* = 1.5 Hz), 29.4 (d, *J* = 2.1 Hz), 36.4, 40.6, 73.6, 83.8 (dd, *J* = 25.3, 25.6 Hz), 108.0 (dd, *J* = 256.3, 256.7 Hz), 177.1 (t, *J* = 25.6 Hz), 179.1. **^{19}F NMR** (376 MHz, $CDCl_3$) δ:-118.7 (dd, *J* = 25.5, 275.6 Hz, 1F), -120.1 (dd, *J* = 5.2, 275.6 Hz, 1F). **IR** (neat) (ν, cm^{-1}): 2931, 2856, 1699, 1555, 1452, 1359, 1126, 814. **HRMS** (CI^+) calculated for $C_{14}H_{20}F_2IO_2$ ($[M+H]^+$) 385.0476, found 385.0460.

C.2 - GOLD-CATALYZED ALKOXYBROMINATIONS

General procedure C: alkoxybromination of difluorinated hydroxy-ynones 1b and 1d.

To a solution of the corresponding hydroxynone **1b** or **1d** (1 eq.) in DCM (0.1M) was added NBS (1.2 eq.) followed by AuCl (5 mol%) at room temperature under Argon. The reaction mixture was stirred at room temperature until completion as monitored by TLC. The mixture was then quenched with a saturated aqueous solution of $Na_2S_2O_3$ and then partitioned. The aqueous layer was extracted three times with DCM. The combined organic extracts were washed with brine, dried over $MgSO_4$ and concentrated *in vacuo.* The crude product was then purified by column chromatography on silica gel.

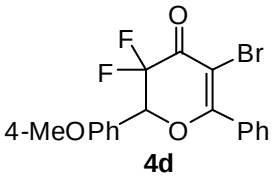
5-bromo-3,3-difluoro-2,6-diphenyl-2,3-dihydro-4*H*-pyran-4-one (4b)



4b

General procedure C was followed, using the ynone **1b** (102 mg, 0.36 mmol, 1 eq.), NBS (77 mg, 0.43 mmol, 1.2 eq.) and AuCl (4 mg, 0.017 mmol, 5 mol%) in acetone (4 mL) for 17h. Purification by column chromatography (hexane:Et_2O 8/2) gave the product as a white solid (108 mg, 82%). **m.p.** = 140-142°C.**R_f** (hexane:Et_2O 6:4) = 0.56. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.58 (dd, *J* = 2.0, 26.0 Hz, 1H), 7.41-7.60 (m, 8H), 7.84 (d, *J* = 7.2 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 82.4 (t, *J* = 24.1 Hz), 98.0, 107.8 (dd, *J* = 255.5, 256.0 Hz), 128.2, 128.3, 128.7, 128.9, 129.8, 130.3, 132.1, 132.4, 170.8, 176.5 (t, *J* = 25.8 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -120.0 (dd, *J* = 26.3, 278.3 Hz, 1F), -123.2 (d, *J* = 278.3 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 1702, 1548, 1489, 1193, 1155, 1115, 932, 695. **HRMS** (CI^+) calculated for $C_{17}H_{12}O_2F_2Br$ ($[M+H]^+$) 364.9989, found 364.9998.

5-bromo-3,3-difluoro-2-(4-methoxyphenyl)-6-phenyl-2,3-dihydro-4H-pyran-4-one (4d)



4d

General procedure C was followed, using the ynone **1d** (100 mg, 0.32 mmol, 1 eq.), NBS (68 mg, 0.38 mmol, 1.2 eq.) and AuCl (4 mg, 0.017 mmol, 5 mol%) in acetone (3 mL) for 20h. Purification by column chromatography (hexane:Et_2O 7/3) gave the product as a pale orange solid (88 mg, 70%). **m.p.** = 118-122°C.**R_f** (hexane:Et_2O 6:4) = 0.38. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 3.84 (s, 3H), 5.57 (dd, *J* = 2.0, 26.0 Hz, 1H), 6.98 (d, *J* = 8.5

Hz, 2H), 7.44-7.49 (m, 4H), 7.53-7.57 (m, 1H), 7.82 (d, *J* = 8.5 Hz, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 55.3, 82.2 (t, *J* = 24 Hz), 97.9, 108.0 (t, *J* = 255.0 Hz), 114.2, 120.8, 128.2, 129.8, 129.9, 132.2, 132.4, 161.1, 171.0, 176.7 (t, *J* = 25.8 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -120.3 (dd, *J* = 26.0, 277.3 Hz, 1F), -123.0 (d, *J* = 277.3 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 1701, 1548, 1517, 1488, 1254, 1154, 1115, 932, 819, 738, 695. **HRMS** (CI^+) calculated for $C_{18}H_{14}O_3F_2Br$ ($[M+H]^+$) 395.0094, found 395.0090.

C.3 - GOLD-CATALYZED ALKOXYFLUORINATIONS

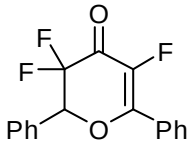
General procedure D: alkoxyfluorination of difluorinated hydroxy-ynones 1b, 1d-f, 1h.

To a solution of the corresponding hydroxy-ynone **1** (1 eq.) in acetonitrile (0.1M) was added Selectfluor® (2.5 eq.) and AuCl (10 mol%) at room temperature under Argon. The reaction mixture was stirred at room temperature until completion as monitored by ^{19}F NMR. It was then diluted with DCM, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude mixture was then directly purified by column chromatography on silica gel.

General procedure E: alkoxyfluorination of non-fluorinated hydroxy-ynones 1j, 1l, 1m.

To a solution of the corresponding hydroxy-ynone **1** (1 eq.) in acetonitrile/water (1:1) (0.05M) was added Selectfluor® (2.5 eq.) followed by AuCl (5 mol%) at room temperature. The reaction mixture was stirred at room temperature until completion as monitored by TLC. The mixture was then quenched with water and extracted three times with diethyl ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. The crude mixture was then purified by silica gel chromatography.

3,3,5-trifluoro-2,6-diphenyl-2,3-dihydro-4*H*-pyran-4-one (6b)



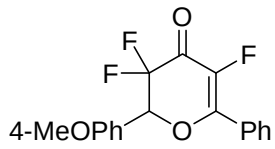
6b

General procedure **D** was followed, starting from **1b** (100 mg, 0.35 mmol, 1 eq.), AuCl (8 mg, 0.035 mmol, 10 mol%) and Selectfluor® (308 mg, 0.87 mmol, 2.5 eq.) in acetonitrile (3.5 mL). The reaction mixture was stirred at rt for 4 days. Purification by silica gel column chromatography (hexane:Et_2O, 3:1) yielded the product (22 mg, 20%) as a pale yellow solid, along with product **2b** (33 mg, 33%).

(6b) m.p. = 88-90°C. **R_f** (hexane:Et_2O, 3:1) = 0.40. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 5.51 (dd, *J* = 26.6, 1.7 Hz, 1H), 7.48-7.61 (m, 8H), 7.94 (d, *J* = 7.7 Hz, 2H). **^{13}C NMR** (126

MHz, $CDCl_3$) δ: 82.5 (dd, *J* = 30.5, 23.8 Hz), 108.5 (ddd, *J* = 262.7, 254.2 Hz, *J* = 9.1 Hz), 128.3, 128.6 (d, *J* = 5.7 Hz), 128.7, 128.8 (d, *J* = 8.6 Hz), 128.9, 129.1, 130.3, 132.9, 140.6 (ddd, *J* = 248.0 Hz, *J* = 4.8, 2.9 Hz), 159.0 (d, *J* = 19.6 Hz), 174.1 (td, *J* = 26.7, 17.6 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -119.8 (ddd, *J* = 282.2, 26.4 Hz, 2.3 Hz, 1F), -124.5 (dd, *J* = 283.4, 12.6 Hz, 2.3 Hz, 1F), -167.1 (dd, *J* = 12.6, 3.4 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 2871, 1730, 1605, 1043. **HRMS** (ESI^-) calculated for $C_{17}H_{11}F_3NaO_2$ ($[M+Na]^-$) 327.0602, found 327.0603.

3,3,5-trifluoro-2-(4-methoxyphenyl)-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (6d)

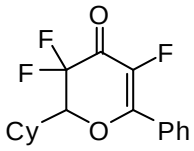


6d

General procedure **D** was followed, employing 100 mg of **1d** (0.316 mmol, 1 eq.), 7.4 mg of AuCl (0.032 mmol, 10 mol%) and 280.0 mg of Selectfluor® (0.79 mmol, 2.5 eq.) in MeCN (3.2 mL). The reaction mixture was stirred at rt for 4 days. Purification by silica gel column chromatography (hexane:Et_2O, 3:1) yielded the product **6d** (27 mg, 26%) as a white solid, along with the product **2d** (33 mg, 33%).

(**6d) m.p.** = 81°C. **R_f** (hexane:Et_2O, 3:1) = 0.25. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 3.87 (s, 1H), 5.44 (dd, *J* = 26.5, 2.3 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 2H), 7.48-7.53 (m, 4H), 7.55-7.60 (m, 1H), 7.91-7.94 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 55.4, 82.3 (dd, *J* = 31.5, 23.8 Hz), 108.5 (ddd, *J* = 262.5, 253.7, 8.6 Hz), 114.1, 121.0, 128.6 (d, *J* = 5.7 Hz), 128.8 (d, *J* = 8.1 Hz), 128.9, 129.9, 132.9, 140.6 (ddd, *J* = 247.0, 4.8, 2.9 Hz), 159.1 (d, *J* = 19.1 Hz), 161.1, 174.3 (td, *J* = 26.7, 17.2 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -120.2 (dd, *J* = 282.2, 27.5 Hz, 1F), -124.3 (dd, *J* = 282.2, 11.5 Hz, 1F), -167.3 (dd, *J* = 11.5, 2.3 Hz). **IR** (DCM) (ν, cm^{-1}): 2864, 1720, 1612, 1065. **HRMS** (ESI^+) calculated for $C_{18}H_{14}F_3O_3$ ($[M+H]^+$) 355.0895, found 355.0889.

2-cyclohexyl-3,3,5-trifluoro-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (6e)

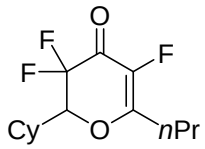


6e

General procedure **D** was followed, starting from **1e** (100 mg, 0.34 mmol, 1 eq.), AuCl (8 mg, 0.03 mmol, 10 mol%) and Selectfluor® (303 mg, 0.86 mmol, 2.5 eq.) in acetonitrile (3.5 mL). The reaction mixture was stirred at rt for 3 days and a half (87h). Purification by column chromatography on silica gel (hexane:Et_2O, 9:1) yielded the product (22 mg, 20%) as a pale yellow solid along with product **2e** (15 mg, 15%).

(6e) m.p. = 108°C.**R_f** (hexane:Et_2O, 4:1) = 0.35. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 1.18-2.27 (m, 11H), 4.25 (ddd, *J* = 26.8, 5.8, 3.8 Hz, 1H), 7.50-7.60 (m, 3H), 7.89 (d, *J* = 7.7 Hz, 2H,). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 25.7, 25.9, 25.9, 28.3, 29.6, 36.7, 84.3 (dd, *J* = 28.6, 25.3 Hz), 110.3 (ddd, *J* = 262.7, 254.2 Hz, $^3J_{C\text{-}F}$ = 8.1 Hz), 128.6 (d, $J_{C\text{-}F}$ = 8.1 Hz), 128.9, 129.3, 132.7, 140.4 (dt, *J* = 247.4, 3.8 Hz), 158.6 (d, *J* = 18.6 Hz), 174.1 (td, *J* = 26.7, 16.7 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -119.9 (ddd, *J* = 281.1, 26.4, 3.4 Hz), -121.7 (dd, *J* = 282.2, 10.3 Hz), -168.2 (dd, *J* = 11.6, 3.5 Hz). **IR** (DCM) (ν, cm^{-1}): 2854, 1718, 1620, 1041. **HRMS** (ESI^+) calculated for $C_{17}H_{18}F_3O_2$ ($[M+H]^+$) 311.1259, found 311.1262.

2-cyclohexyl-3,3,5-trifluoro-6-propyl-2,3-dihydro-4*H*-pyran-4-one (6f)

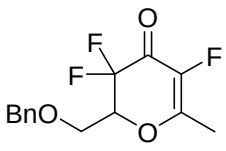


6f

General procedure **D** was followed, employing 100 mg of **1f** (0.397 mmol, 1 eq.), 9 mg of AuCl (0.039 mmol, 10 mol%) and 343 mg of Selectfluor® (0.97 mmol ,2.5 eq.) in MeCN (4.0 mL). The reaction mixture was stirred at rt for 3 days. Purification by column chromatography (hexane:Et_2O, 3:1) yielded the product **6f** (29 mg, 27%) as a colourless oil and the product **2f** (37 mg, 37%).

(6f) R_f (hexane:Et_2O, 3:1) = 0.35. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 1.00 (t, *J* = 7.4 Hz, 3H), 1.23-1.38 (m, 6H), 1.65-2.12 (m, 7H), 2.52 (dddd, *J* = 11.2, 7.3, 3.9, 1.6 Hz, 2H), 4.03 (ddd, *J* = 28.2, 5.7, 3.8 Hz, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 13.5, 19.3, 25.7, 25.8, 25.9, 27.9, 29.4, 30.9, 36.5, 84.3 (dd, *J* = 29.1, 25.3 Hz), 110.3 (ddd, *J* = 263.7, 254.2, 9.5 Hz), 140.2 (ddd, *J* = 238.4, 5.7, 3.3 Hz), 167.0 (d, *J* = 25.8 Hz), 172.6 (td, *J* = 26.7, 15.7 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ:-119.8 (ddd, *J* = 282.2, 26.4, 2.3 Hz, 1H), -124.5 (dd, *J* = 283.4, 12.6 Hz, 1F), -167.1 (dd, *J* = 12.6, 3.4 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 2884, 1730, 1622, 1052. **HRMS** (ESI^-) calculated for $C_{14}H_{19}F_3NaO_2$ ($[M\text{-}Na]^-$) 299.1224, found 299.1229.

2-[(benzyloxy)methyl]-3,3,5-trifluoro-6-methyl-2,3-dihydro-4*H*-pyran-4-one (6h)



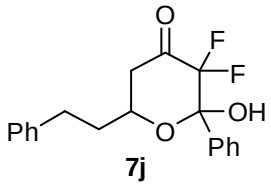
6h

General procedure **D** was followed, using 75 mg of **1h** (0.28 mmol, 1 eq.), Selectfluor® (248 mg, 0.69 mmol, 2.5 eq.) and AuCl (3 mg, 0.013 mmol, 5 mol%) in acetonitrile (3 mL). The reaction mixture was stirred at rt for 62h and then quenched by addition of

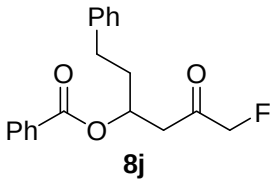
water. The aqueous layer was extracted three times with diethyl ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent removed *in vacuo*. Purification by column chromatography on silica gel (Hexane:Et_2O, 8:2) yielded the product (19.6 mg, 24%) as a pale yellow oil, along with product **2h** (32.6 mg, 43%).

(6h) $\mathbf{R_f}$ (hexane:Et_2O, 5:5) = 0.50. $^{\mathbf{1}}$**H NMR** (400 MHz, $CDCl_3$) δ: 2.22 (d, *J* = 4 Hz, 3H), 3.92 (dd, *J* = 6.8, 11.4 Hz, 1H), 3.98 (dd, *J* = 2.8, 11.4 Hz, 1H), 4.51-4.66 (m, 1H), 4.61 (d, *J* = 4 Hz, 2H), 7.30-7.41 (m, 5H). $^{\mathbf{13}}$**C NMR** (126 MHz, $CDCl_3$) δ: 15.6, 65.7 (dt, *J* = 11.3, 2.5 Hz), 73.9, 80.3 (dd, *J* = 54.2, 24.8 Hz), 109.0 (td, J = 256.0, 9.5 Hz), 127.8, 128.2, 128.6, 136.8, 140.5 (td, *J* = 240.4, 4.2 Hz), 163.5 (d, *J* = 27.2 Hz), 171.3 (td, *J* = 25.8, 16.2 Hz). $^{\mathbf{19}}$**F NMR** (376 MHz, $CDCl_3$) δ: -120.9 (ddd, *J* = 6.8, 7.1, 283.7 Hz, 1F), -121.8 (dt, *J* = 9.8, 283.7 Hz, 1F), -169.9 (ddq, *J* = 4.0, 6.9, 10.3 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 3069, 2913, 1708, 1453, 1266, 1112, 738. **HRMS** (CI^+) calculated for $C_{14}H_{17}NO_3F_3$ ($[M+NH_4]^+$) 304.1161, found 304.1169.

3,3-difluoro-2-hydroxy-2-phenyl-6-(2-phenylethyl)tetrahydro-4*H*-pyran-4-one (7j) and 4-fluoro-3-oxo-1-(2-phenylethyl)butyl benzoate (8j)



7j



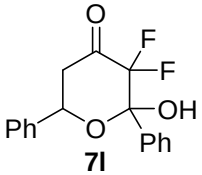
8j

General procedure **E** was followed, starting from **1j** (100 mg, 0.36 mmol, 1 eq.), Selectfluor® (318 mg, 0.9 mmol, 2.5 eq.) and 4.2 mg of AuCl (0.018 mmol, 5 mol%) in acetonitrile (3 mL) and water (3 mL). The reaction mixture was stirred at rt for 18 h. Purification by column chromatography (Hexane:EtOAc, 7:3) yielded the desired product (67 mg, 56%) along with product **8j** (45 mg, 39%).

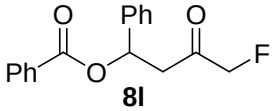
(**7j**) white solid. **m.p.** = 82°C.$\mathbf{R_f}$ (Hexane:EtOAc, 6:4) = 0.44. $^{\mathbf{1}}$**H NMR** (400 MHz, $CDCl_3$) δ: 1. 98-2.08 (m, 1H), 2.13-2.24 (m, 1H), 2.71 (dt, *J* = 13.9, 3.05, 3.03 Hz, 1H), 2.79 (ddd, *J* = 13.9, 6.8, 1.8 Hz, 1H), 2.85-2.95 (m, *J* = 13.9 Hz, 1H), 2.98 (ddd, *J* = 13.9, 11.4, 5.1 Hz, 1H), 3.02 (d, *J* = 4.0 Hz, 1H), 4.42-4.50 (m, 1H), 7.18-7.24 (m, 3H), 7.28-7.33 (m, 2H). $^{\mathbf{13}}$**C NMR** (126 MHz, $CDCl_3$) δ: 31.5, 36.9, 45.6, 68.9, 98.6 (t, *J* = 24.0 Hz), 110.8 (t, *J* = 248.5 Hz), 126.2, 127.2, 128.3, 128.4, 128.5, 130.0, 135.9, 140.9, 193.8 (t, *J* = 26.3 Hz). $^{\mathbf{19}}$**F NMR** (376 MHz, $CDCl_3$) δ: -113.2 (dt, *J* = 256.0, 3.8 Hz, 1F), -113.9 (dd, *J* = 256.0, 3.8 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 3420, 3062, 3028, 2932, 1757, 1452, 1087, 737, 701. **HRMS** (ESI^-) calculated for $C_{19}H_{17}F_2O_3$ ($[M-H]^-$) 331.1154, found 331.1151.

(**8j**) colourless oil. $\mathbf{R_f}$ (Hexane:EtOAc, 6:4) = 0.85. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 2.05-2.20 (m, 2H), 2.71-2.80 (m, 2H), 2.92 (ddd, *J* = 16.6, 5.4, 3.0 Hz, 1H), 3.03 (ddd, *J* = 16.6, 6.8, 3.0 Hz, 1H), 4.80 (dd, *J* = 47.4, 5.8 Hz, 1H), 4.80 (dd, *J* = 47.6, 38.0 Hz, 1H), 5.55 (dt, *J* = 12.4, 6.6, 5.8 Hz, 1H), 7.15-7.21 (m, 3H), 7.27-7.33 (m, 2H), 7.42-7.50 (m, 2H), 7.55-7.60 (m, 1H), 7.99-8.03 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 31.6, 36.0, 43.1, 70.0 (d, *J* = 1.4 Hz), 84.7 (d, *J* = 128.6 Hz), 126.1, 128.3, 128.5, 129.6, 130.0, 133.2, 140.9, 166.0, 204.1 (d, *J* = 21 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -226.8 (tt, *J* = 47.7, 3.0 Hz). **IR** (DCM) (ν, cm^{-1}): 2913, 1717, 1272, 1112, 737, 701. **HRMS** (ESI^+) calculated for $C_{19}H_{19}FNaO_3$ ($[M+Na]^+$) 337.1203, found 337.1210.

3,3-difluoro-2-hydroxy-2,6-diphenyltetrahydro-4*H*-pyran-4-one (7l) and 4-fluoro-3-oxo-1-phenylbutyl benzoate (8l)



7l



8l

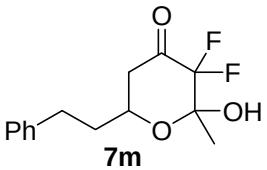
General procedure **E** was followed, starting from 101 mg of **1l** (0.4 mmol, 1 eq.), AuCl (4.6 mg, 0.02 mmol, 5 mol%) and Selectfluor® (351 mg, 0.99 mmol, 2.5 eq.) in acetonitrile (3 mL) and water (3 mL). The reaction mixture was stirred at rt for 20h. Purification by silica gel column chromatography (Hexane:Et_2O, 8:2 to 5:5) yielded the product (60.5 mg, 50%) along with product **8l** (15 mg, 13%).

(**7l**) white solid. **m.p.** = 96°C. $\mathbf{R_f}$ (Hexane:EtOAc, 6:4) = 0.45. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 2.96 (dt, *J* = 14.4, 3.2, 3.0 Hz, 1H), 3.14 (d, *J* = 4 Hz, 1H), 3.26 (ddd, *J* = 14.4, 11.4, 5.3 Hz, 1H), 5.53 (d br, *J* = 11.2 Hz, 1H), 7.36-7.55 (m, 8H), 7.76-7.82 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 48.0, 71.8, 99.0 (dd, *J* = 24.0, 24.0 Hz), 110.9 (dd, *J* = 248.2, 248.2 Hz), 126.1, 127.2, 128.3, 128.7, 128.9, 130.1, 135.6, 139.1, 193.3 (dd, *J* = 22.7, 22.7 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -113.6 (d, *J* = 256.4 Hz, 1F), -137.0 (dd, *J* = 256.1, 3.0 Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 3396, 3065, 2928, 1758, 1451, 1072n 758n 729, 699. **HRMS** (ESI^-) calculated for $C_{17}H_{13}F_2O_3$ ($[M-H]^-$) 303.0843, found 303.0838.

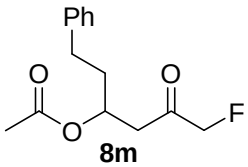
(8l) pale yellow solid. **m.p. =** 61°C. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 3.13 (ddd, *J* = 17.0, 5.0, 2.5 Hz, 1H), 3.42 (ddd, *J* = 17.0, 8.5, 3.1 Hz, 1H), 4.76 (dd, *J* = 21.1, 16.1, 1H), 4.86 (dd, *J* = 21.1, 16.4 Hz, 1H), 6.49 (dd, *J* = 8.5, 5.0 Hz, 1H), 7.3–7.6 (m, 8H), 8.04 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 45.3, 71.6, 85.1 (d, *J* = 185.0 Hz), 126.4, 128.4, 128.5, 128.8, 129.7, 129.8, 133.2, 139.3, 165.4, 203.4 (d, *J* = 21.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -227.2 (dddd, *J* = 16.4, 16.1, 3.1, 2.5 Hz, 1F). **IR** (CH_2Cl_2) (ν, cm^{-1}):

3064, 3034, 2926, 1721, 1602, 1495, 1452, 1270, 1110, 713. **HRMS** (ESI^+) calculated for $C_{17}H_{15}FNaO_3$ ($[M+Na]^+$) 309.0897, found 309.0897.

3,3-difluoro-2-hydroxy-2-methyl-6-(2-phenylethyl)tetrahydro-4*H*-pyran-4-one (7m) and 4-fluoro-3-oxo-1-(2-phenylethyl)butyl acetate (8m)



7m



8m

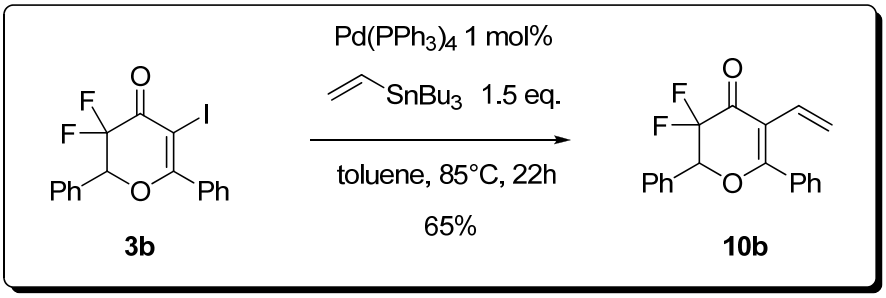
General procedure **E** was followed, using ynone **1m** (104 mg, 0.48 mmol, 1 eq.), AuCl (5.6 mg, 0.02 mmol, 5 mol%) and Selectfluor® (426 mg, 1.2 mmol, 2.5 eq.) in acetonitrile (2.5 mL and water (2.5 mL). The reaction mixture was stirred at rt for 13h. Purification by column silica gel chromatography (Hexane:Et_2O, 6:4 to 5:5) yielded **7m** (53 mg, 41%) along with product **8m** (39 mg, 32%).

(**7m**) white solid. **m.p.** = 70-74°C.**R_f** (Hexane:EtOAc, 6:4) = 0.33. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 1.63 (d, *J* = 1.2 Hz, 3H), 1.81-1.92 (m, 1H), 1.96-2.08 (m, 1H), 2.58 (s, 1H), 2.59 (dt, *J* = 14.2, 3.2 Hz, 1H), 2.68 (ddd, *J* = 13.9, 9.2, 7.0 Hz, 1H), 2.72-2.85 (m, 2H), 4.22-4.30 (m, 1H), 7.17-7.23 (m, 3H), 7.27-7.32 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 20.9, 31.4, 36.9, 45.7, 69.1, 98.3 (dd, *J* = 26.0, 25.8 Hz), 111.0 (dd, *J* = 250.3, 250.5 Hz), 126.2, 128.4, 128.5, 141.0, 194.1 (t, *J* = 22.9 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -115.8 (d, *J* = 256.4 Hz, 1F), -138.4 (dd, *J* = 256.1, 3.1Hz, 1F). **IR** (DCM) (ν, cm^{-1}): 3064, 3034, 2930, 1737, 1602, 1495, 1451, 1110, 1070, 1027, 714. **HRMS** (ESI^-) calculated for $C_{14}H_{15}F_2O_3$ ($[M-H]^-$) 269.0993, found 269.0995.

(**8j**) colourless oil. **R_f** (Hexane:EtOAc, 6:4) = 0.69. **^{1}H NMR** (500 MHz, $CDCl_3$) δ: 1. 93-1.99 (m, 2H), 2.02 (s, 3H), 2.62-2.71 (m, 2H), 2.80-2.85 (m, 2H), 4.78 (dd, *J* = 47.5, 5.5 Hz, 1H), 4.78 (dd, *J* = 47.5, 37.5 Hz, 1H), 5.27-5.33 (m, 1H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 21.0, 31.5, 35.8, 43.0, 69.3 (d, *J* = 1.4 Hz), 85.1 (d, *J* = 185.2 Hz), 126.1, 128.3, 128.5, 140.9, 170.5, 204.2 (d, *J* = 20.3 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -226.9 (tdd, *J* = 48.0, 3.4, 2.5 Hz). **IR** (neat) (ν, cm^{-1}): 2931, 1737, 1633, 1374, 1420, 1043. **HRMS** (ESI^+) calculated for $C_{14}H_{17}FNaO_3$ ($[M+Na]^+$) 275.1057, found 275.1054.

D – FUNCTIONALIZATION OF VINYL IODIDE 3b VIA A STILLE COUPLING

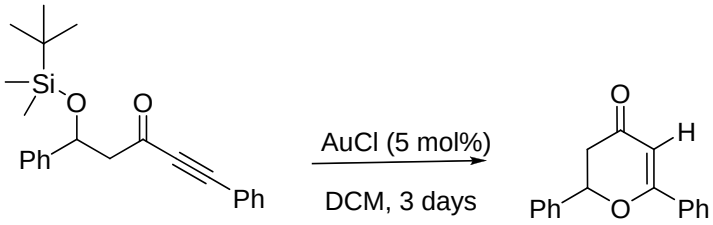
3,3-difluoro-2,6-diphenyl-5-vinyl-2,3-dihydro-4*H*-pyran-4-one (10b)

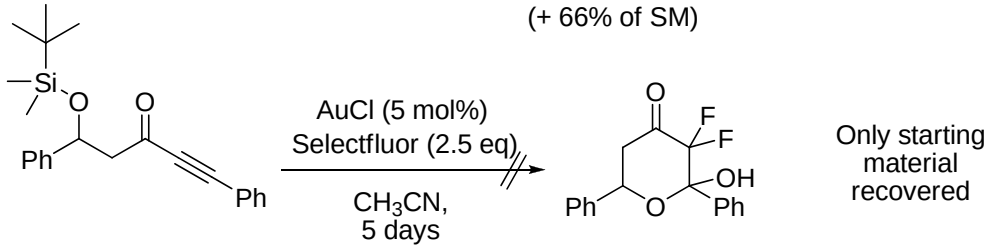


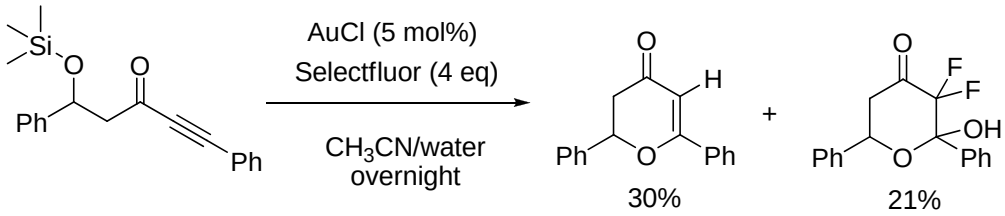
The iododihydropyranone **3b** (80.6 mg, 0.20 mmol, 1 eq.) was dissolved in anhydrous toluene (2 mL) and stirred at room temperature. $Pd(PPh_3)_4$ (2.2 mg, 0.02 mmol, 1 mol%), tributylvinylstannane (85 µL, 0.3 mmol, 1.5 eq.) were then added and the mixture heated at 85°C for 22h. After completion, the reaction mixture was allowed to cool to ambient temperature and partitioned between a saturated solution of aqueous potassium fluoride and Et_2O. The aqueous layer was extracted three times with Et_2O then the combined organic phases were washed with a saturated solution of aqueous potassium fluoride and brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford the crude product. Purification by column chromatography on silica gel (hexane:Et_2O, 9:1) furnished the desired product as a yellow solid (40 mg, 65%). **m.p.** = 112-114°C. $\mathbf{R_f}$ (Hexane:Et_2O, 8:2) = 0.47. **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 5.37 (dd, *J* = 10.8, 2.8 Hz, 1H), 5.60 (dd, *J* = 26.4, 2.4 Hz, 1H), 6.12-6.26 (m, 2H), 7.42-7.58 (m, 8H), 7.62-7.68 (m, 2H). **^{13}C NMR** (126 MHz, $CDCl_3$) δ: 81.5 (dd, *J* = 24.1, 23.9 Hz), 107.1 (dd, *J* = 252.5, 252.4 Hz), 119.9, 127.4, 128.3, 128.4, 128.6, 129.7, 130.0, 130.1, 131.8, 132.4, 171.5, 180.6 (t, *J* = 24.7 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ: -122.8 (dd, *J* = 26.3, 278.3 Hz, 1F), -126.1 (d, *J* = 278.3 Hz, 1F). **IR** (CH_2Cl_2) (ν, cm^{-1}): 3054, 2987, 1421, 1265, 738. **HRMS** (CI^+) calculated for $C_{19}H_{15}O_2F_2$ ($[M+H]^+$) 313.1040, found 313.1028.

E - CONTROL EXPERIMENTS

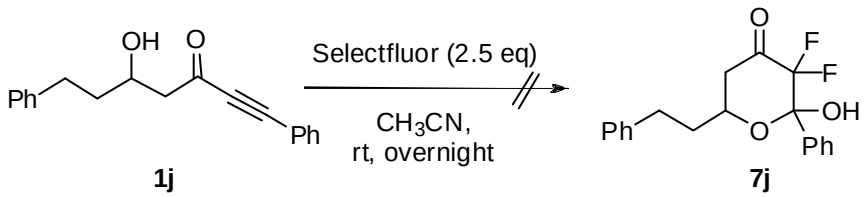
Cyclizations of O-silylated hydroxy-ynones

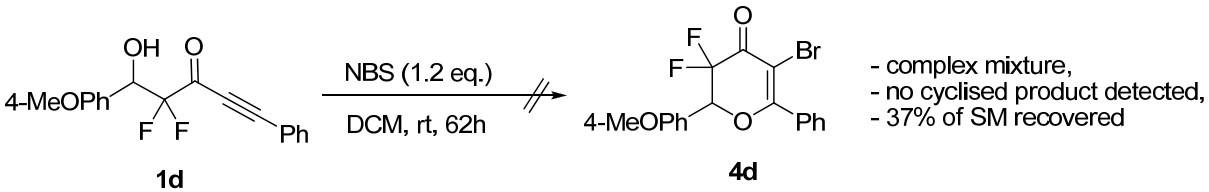


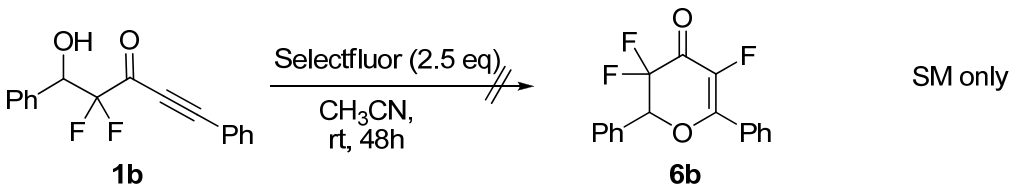


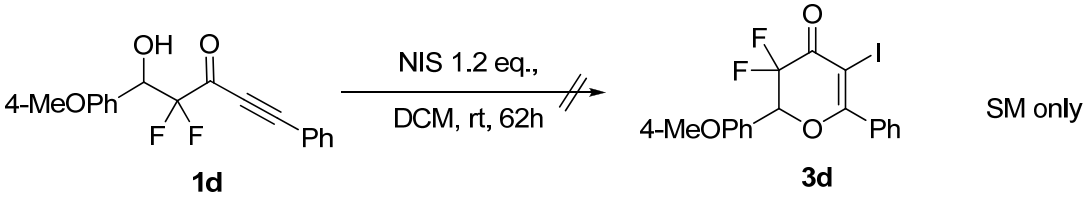


Cyclizations in the absence of gold catalyst

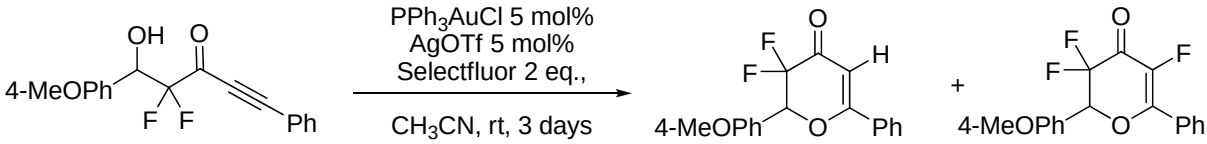








Alkoxyfluorination with a different source of gold

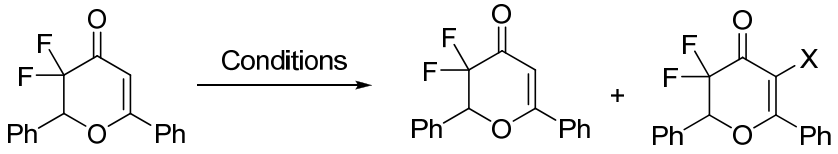


1d **2d** **6d**

crude ratio 2:1

Investigation of the mechanism of the alkoxyhalogenation

1 - Starting from gemdifluorinated β-hydroxy-ynones



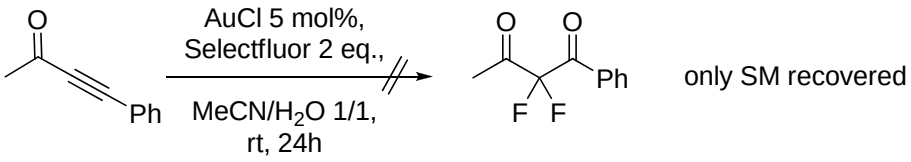
2b **2b** **3b, 4b or 6b**

X = I, Br or F

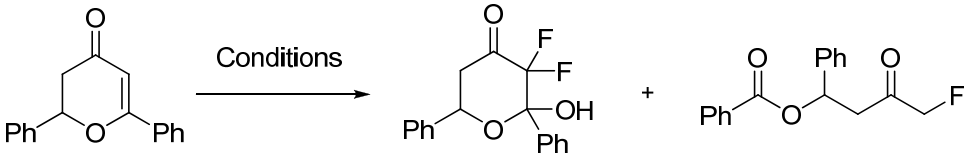
Entry	Conditions	Results
1	NIS (1.2 eq.), acetone, rt, 39h	no reaction (**2b** only) **3b** not observed
2	AuCl (5 mol%), NIS (1.2 eq.), acetone, rt, 27h	no reaction (**2b** only) **3b** not observed
3	NBS (1.2 eq.), DCM, rt, 62h	37% of **2b** recovered traces of **4b** seen by ^{19}F NMR[a]
4	AuCl (5 mol%), NBS (1.2 eq.), DCM, rt, 48h	no reaction (**2b** only) **4b** not observed
5	Selectfluor® (2.5 eq.), CH_3CN, rt, 64h	no reaction (**2b** only) **6b** not observed
6	AuCl (5 mol%), Selectfluor® (2.5 eq.), CH_3CN, rt, 51h	no reaction (**2b** only) **6b** not observed

[a] less than 10% of **4b** seen by ^{19}F NMR, didn't increase with the time and could'nt be isolated after purification.

2 - Starting from 4-phenylbut-3-yn-2-one[10]



3 - Starting from β-hydroxy-ynones

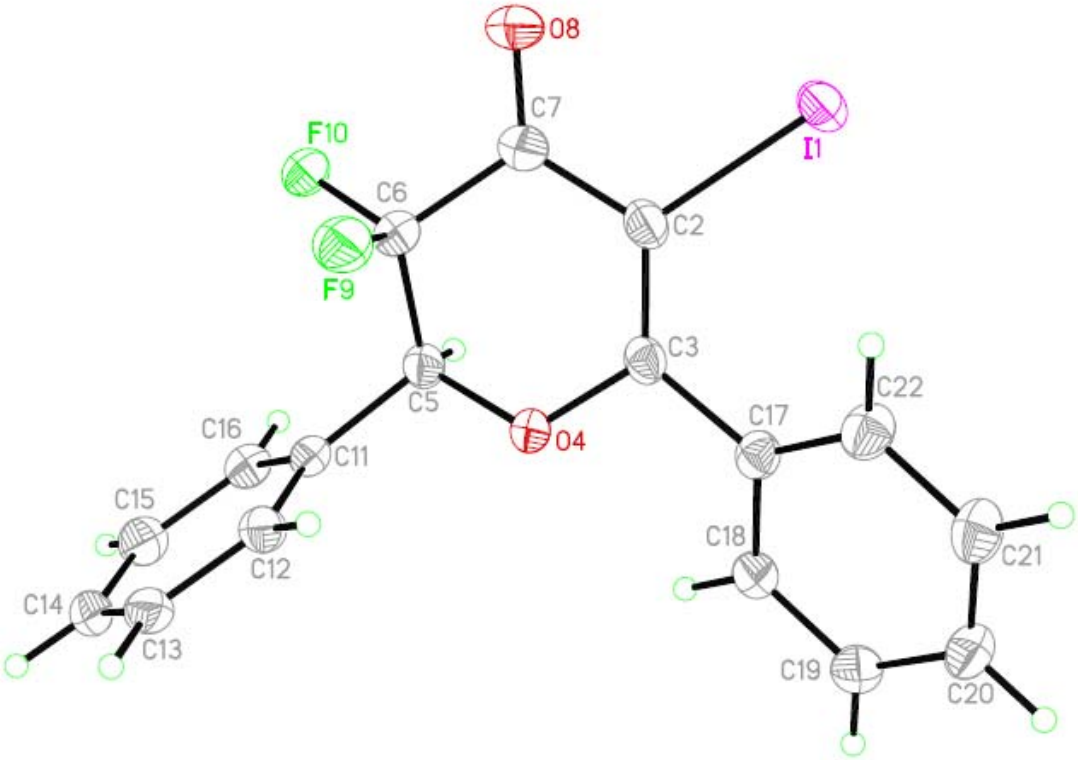


Entry	Conditions	7l	8l
1	Selectfluor® (4 eq.), CH_3CN, rt	37%	50%
2	AuCl (5 mol%), Selectfluor® (4 eq.), CH_3CN, rt	29%	46%
3	Selectfluor® (4 eq.), water/CH_3CN, rt	43%	15%
4	AuCl (5 mol%), Selectfluor® (4 eq.), water/CH_3CN, rt	62%	38%

[10] A. Monney, Master Thesis, University of Fribourg (Switzerland), **2008**.

F - X-RAY DIFFRACTION

Single-crystal X-ray diffraction report for 3,3-difluoro-5-iodo-2,6-diphenyl-2,3-dihydro-4*H*-pyran-4-one (3b)



Crystals of ethyl 3,3-difluoro-5-iodo-2,6-diphenyl-2,3-dihydro-4*H*-pyran-4-one were grown by slow diffusion (hexane/ether). A polycrystalline aggregate was cut to give a fragment having dimensions approximately 0.30x0.19x0.15 mm. This was mounted on a glass fibre using perfluoropolyether oil and cooled rapidly to 150K in a stream of cold N_2 using an Oxford Cryosystems CRYOSTREAM unit. Single crystal X-ray diffraction data were collected using graphite monochromated Mo Kα radiation (λ = 0.71073 Å) on an Enraf-Nonius KappaCCD S39 diffractometer. The diffractometer was equipped with a Cryostream N_2 open-flow cooling device, and the data were collected at 150K.[11] Series of ω-scans were performed in such a way as to cover a sphere of data to a maximum resolution of 0.77Å. Cell parameters and intensity data were processed using the DENZO-SMN package.[12] The structure was solved by direct methods[13] and refined by full-matrix

[11] J. Cosier, A. M. Glazer, *J. Appl. Cryst.* **1986**, *19*, 105.
[12] Z. Otwinowski, W. Minor, Processing of X-ray Diffraction Data Collected in Oscillation Mode, Methods Enzymol, **1997**, 276. Eds C. W. Carter, R. M. Sweet, Academic Press.

least squares on F using the CRYSTALS suite.[14] Intensities were corrected for absorption effects by the multi-scan method, based on multiple scans of identical and Laue equivalent reflections.[12] A 3-term Chebychev polynomial weighting scheme was applied.[15] All non-hydrogen atoms were refined with anisotropic displacement parameters, except where there was disorder present and the atoms were too close together to resolve the electron density fully. In this case, the overlapping atoms were refined with isotropic displacement parameters. Hydrogen atoms were positioned geometrically and refined using a riding model. The Flack parameter refined to a value of 0.45(16) (2733 Friedel-pairs) so the Friedel-pairs were merged for the final refinement. Thermal ellipsoid plots (at 50% probability) are shown above. A summary of crystallographic data is given below, as are full list of atomic coordinates, anisotropic thermal parameters and those bond lengths and angles.

[13] A. Altomare, G. Cascarano, G. Giacovazzo, A. Guagliardi ,M. C. Burla, G. Polidori, M. Camalli, *J. Appl. Cryst.* **1994,** *27*, 435.
[14] Betteridge, P.W., Carruthers, J.R., Cooper, R.I., Prout, K. & Watkin, D.J., *J. Appl. Cryst.* **2003**, *36*, 1487.
[15] a) Prince, E. Mathematical Techniques in Crystallography and Materials Science, Springer-Verlag, New York, **1982**; b) D.J. Watkin, *Acta Cryst.* **1994**, *A50*, 411-437.

Table 1: Crystal data and refinement details

Identification code	5713	
Empirical formula	C17 H11 F2 I1 O2	
Formula weight	412.17	
Temperature	150 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 9.7334(3) Å	α= 90°.
	b = 15.8229(5) Å	β= 112.1971(14)°.
	c = 10.4611(4) Å	γ = 90°.
Volume	1491.72(9) $Å^3$	
Z	4	
Density (calculated)	1.835 Mg/m^3	
Absorption coefficient	2.172 mm^{-1}	
F(000)	800	
Crystal size	0.30 x 0.19 x 0.15 mm^3	
Theta range for data collection	5.154 to 27.439°.	
Index ranges	-12<=h<=12, -20<=k<=20, -13<=l<=13	
Reflections collected	16951	
Independent reflections	3370 [R(int) = 0.030]	
Completeness to theta = 25.244°	98.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.72 and 0.63	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3370 / 0 / 199	
Goodness-of-fit on F^2	1.0056	
Final R indices [I>2sigma(I)]	R1 = 0.0283, wR2 = 0.0645	
R indices (all data)	R1 = 0.0359, wR2 = 0.0676	
Largest diff. peak and hole	0.85 and -0.80 $e.Å^{-3}$	

Table 2: Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2x10^3$). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
I(1)	1810(1)	4578(1)	2791(1)	30
C(2)	2338(3)	5624(2)	1833(3)	25
C(3)	2732(3)	6392(2)	2444(3)	21
O(4)	2898(2)	7076(1)	1717(2)	23
C(5)	2242(3)	7053(2)	228(2)	22
C(6)	2667(3)	6226(2)	-250(3)	26
C(7)	2258(3)	5462(2)	439(3)	29
O(8)	1951(3)	4794(1)	-168(2)	48
F(9)	4161(2)	6191(1)	52(2)	35
F(10)	1993(2)	6168(1)	-1640(2)	35
C(11)	2734(3)	7825(2)	-311(2)	21
C(12)	4217(3)	8088(2)	226(3)	23
C(13)	4657(3)	8781(2)	-335(3)	27
C(14)	3621(3)	9220(2)	-1429(3)	29
C(15)	2156(3)	8967(2)	-1958(3)	30
C(16)	1712(3)	8272(2)	-1399(3)	25
C(17)	3055(3)	6644(2)	3883(3)	22
C(18)	2656(3)	7457(2)	4144(3)	27
C(19)	2983(3)	7726(2)	5484(3)	33
C(20)	3726(3)	7195(2)	6587(3)	32
C(21)	4149(3)	6399(2)	6341(3)	33
C(22)	3826(3)	6124(2)	4999(3)	29

Table 3: Hydrogen bonds [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(19)-H(191)...O(8)#1	0.94	2.52	3.292(4)	140

Symmetry transformations used to generate equivalent atoms:

#1 -x+1/2,y+1/2,-z+1/2

Table 4: Bond lengths (Å) and angles (°C)

I(1)-C(2)	2.097(2)	C(22)-H(221)	0.941
C(2)-C(3)	1.358(3)		
C(2)-C(7)	1.453(4)	I(1)-C(2)-C(3)	123.87(19)
C(3)-O(4)	1.367(3)	I(1)-C(2)-C(7)	114.20(18)
C(3)-C(17)	1.472(4)	C(3)-C(2)-C(7)	121.9(2)
O(4)-C(5)	1.444(3)	C(2)-C(3)-O(4)	121.2(2)
C(5)-C(6)	1.513(3)	C(2)-C(3)-C(17)	129.6(2)
C(5)-C(11)	1.498(3)	O(4)-C(3)-C(17)	109.2(2)
C(5)-H(51)	0.986	C(3)-O(4)-C(5)	118.92(18)
C(6)-C(7)	1.535(4)	O(4)-C(5)-C(6)	108.24(19)
C(6)-F(9)	1.367(3)	O(4)-C(5)-C(11)	108.19(19)
C(6)-F(10)	1.354(3)	C(6)-C(5)-C(11)	114.5(2)
C(7)-O(8)	1.210(3)	O(4)-C(5)-H(51)	108.0
C(11)-C(12)	1.400(3)	C(6)-C(5)-H(51)	108.0
C(11)-C(16)	1.389(4)	C(11)-C(5)-H(51)	109.8
C(12)-C(13)	1.385(4)	C(5)-C(6)-C(7)	112.0(2)
C(12)-H(121)	0.949	C(5)-C(6)-F(9)	111.0(2)
C(13)-C(14)	1.391(4)	C(7)-C(6)-F(9)	107.5(2)
C(13)-H(131)	0.954	C(5)-C(6)-F(10)	109.4(2)
C(14)-C(15)	1.380(4)	C(7)-C(6)-F(10)	110.1(2)
C(14)-H(141)	0.948	F(9)-C(6)-F(10)	106.7(2)
C(15)-C(16)	1.389(4)	C(6)-C(7)-C(2)	114.0(2)
C(15)-H(151)	0.945	C(6)-C(7)-O(8)	119.9(3)
C(16)-H(161)	0.948	C(2)-C(7)-O(8)	126.1(3)
C(17)-C(18)	1.400(4)	C(5)-C(11)-C(12)	121.3(2)
C(17)-C(22)	1.393(4)	C(5)-C(11)-C(16)	119.4(2)
C(18)-C(19)	1.383(4)	C(12)-C(11)-C(16)	119.2(2)
C(18)-H(181)	0.940	C(11)-C(12)-C(13)	120.1(2)
C(19)-C(20)	1.389(4)	C(11)-C(12)-H(121)	119.5
C(19)-H(191)	0.941	C(13)-C(12)-H(121)	120.3
C(20)-C(21)	1.379(4)	C(12)-C(13)-C(14)	120.0(2)
C(20)-H(201)	0.949	C(12)-C(13)-H(131)	119.5
C(21)-C(22)	1.387(4)	C(14)-C(13)-H(131)	120.5
C(21)-H(211)	0.940	C(13)-C(14)-C(15)	120.2(2)

C(13)-C(14)-H(141)	120.0	C(19)-C(18)-H(181)	120.6
C(15)-C(14)-H(141)	119.8	C(18)-C(19)-C(20)	120.3(3)
C(14)-C(15)-C(16)	120.0(2)	C(18)-C(19)-H(191)	119.2
C(14)-C(15)-H(151)	119.8	C(20)-C(19)-H(191)	120.5
C(16)-C(15)-H(151)	120.2	C(19)-C(20)-C(21)	119.7(3)
C(15)-C(16)-C(11)	120.5(2)	C(19)-C(20)-H(201)	120.0
C(15)-C(16)-H(161)	120.4	C(21)-C(20)-H(201)	120.3
C(11)-C(16)-H(161)	119.1	C(20)-C(21)-C(22)	120.4(3)
C(3)-C(17)-C(18)	118.7(2)	C(20)-C(21)-H(211)	119.8
C(3)-C(17)-C(22)	122.4(2)	C(22)-C(21)-H(211)	119.8
C(18)-C(17)-C(22)	118.7(2)	C(17)-C(22)-C(21)	120.5(2)
C(17)-C(18)-C(19)	120.4(2)	C(17)-C(22)-H(221)	119.5
C(17)-C(18)-H(181)	119.0	C(21)-C(22)-H(221)	120.1

Symmetry transformations used to generate equivalent atoms:

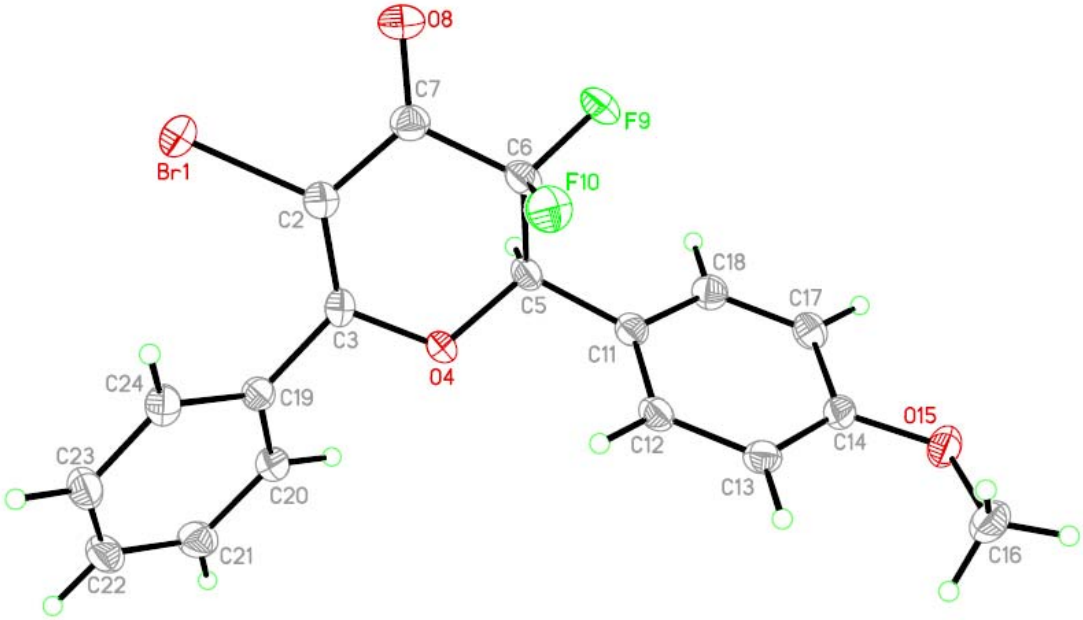
Table 5: Hydrogen coordinates ($x10^4$) and isotropic displacement parameters ($Å^2 x\ 10^3$)

	x	y	z	U(eq)
H(51)	1155	7061	-53	26
H(121)	4921	7783	965	28
H(131)	5670	8955	37	33
H(141)	3924	9691	-1818	35
H(151)	1458	9267	-2702	36
H(161)	709	8092	-1762	29
H(181)	2177	7819	3394	34
H(191)	2682	8269	5639	40
H(201)	3943	7381	7505	40
H(211)	4661	6041	7087	39
H(221)	4131	5584	4837	33

Table 6: Anisotropic displacement parameters ($Å^2x10^3$). The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
I(1)	38(1)	22(1)	35(1)	4(1)	19(1)	-1(1)
C(2)	27(1)	22(1)	27(1)	4(1)	13(1)	-2(1)
C(3)	21(1)	22(1)	25(1)	2(1)	13(1)	0(1)
O(4)	32(1)	22(1)	18(1)	-1(1)	11(1)	-4(1)
C(5)	24(1)	23(1)	20(1)	0(1)	8(1)	-2(1)
C(6)	32(1)	25(1)	22(1)	-4(1)	12(1)	-4(1)
C(7)	39(2)	22(1)	28(1)	-1(1)	13(1)	-2(1)
O(8)	88(2)	23(1)	36(1)	-8(1)	28(1)	-10(1)
F(9)	36(1)	30(1)	44(1)	-3(1)	22(1)	2(1)
F(10)	54(1)	32(1)	19(1)	-7(1)	14(1)	-12(1)
C(11)	24(1)	21(1)	20(1)	-3(1)	11(1)	-2(1)
C(12)	24(1)	22(1)	23(1)	0(1)	8(1)	0(1)
C(13)	27(1)	27(1)	29(1)	-6(1)	13(1)	-6(1)
C(14)	45(2)	21(1)	26(1)	0(1)	19(1)	-3(1)
C(15)	36(1)	26(1)	25(1)	3(1)	9(1)	5(1)
C(16)	25(1)	26(1)	22(1)	-2(1)	8(1)	1(1)
C(17)	22(1)	24(1)	23(1)	0(1)	12(1)	1(1)
C(18)	36(1)	22(1)	27(1)	1(1)	15(1)	-1(1)
C(19)	48(2)	23(1)	33(2)	-3(1)	21(1)	-2(1)
C(20)	40(2)	36(2)	24(1)	-5(1)	17(1)	-5(1)
C(21)	35(2)	39(2)	23(1)	5(1)	9(1)	4(1)
C(22)	31(1)	29(1)	26(1)	1(1)	11(1)	8(1)

Single-crystal X-ray diffraction report for 5-bromo-3,3-difluoro-2-(4-methoxyphenyl)-6-phenyl-2,3-dihydro-4H-pyran-4-one (4d)



Crystals of 5-bromo-3,3-difluoro-2-(4-methoxyphenyl)-6-phenyl-2,3-dihydro-4H-pyran-4-one were grown by slow diffusion (hexane/ether). A polycrystalline aggregate was cut to give a fragment having dimensions approximately 0.33x0.15x0.14 mm. This was mounted on a glass fibre using perfluoropolyether oil and cooled rapidly to 150K in a stream of cold N_2 using an Oxford Cryosystems CRYOSTREAM unit. Single crystal X-ray diffraction data were collected using graphite monochromated Mo Kα radiation (λ = 0.71073 Å) on an Enraf-Nonius KappaCCD S39 diffractometer. The diffractometer was equipped with a Cryostream N_2 open-flow cooling device, and the data were collected at 150K.[11] Series of ω-scans were performed in such a way as to cover a sphere of data to a maximum resolution of 0.77Å. Cell parameters and intensity data were processed using the DENZO-SMN package.[12] The structure was solved by direct methods[13] and refined by full-matrix least squares on F using the CRYSTALS suite.[14] Intensities were corrected for absorption effects by the multi-scan method, based on multiple scans of identical and Laue equivalent reflections.[12] A 3-term Chebychev polynomial weighting scheme was applied.[15] All non-hydrogen atoms were refined with anisotropic displacement parameters, except where there was disorder present and the atoms were too close together to resolve the electron density fully. In this case, the overlapping atoms were refined with isotropic displacement parameters. Hydrogen atoms were positioned geometrically and refined using a riding model. The Flack parameter refined to a value of 0.45(16) (2733 Friedel-pairs) so the Friedel-pairs were merged for the final refinement. Thermal ellipsoid plots (at 50% probability) are shown above. A summary of crystallographic data is given below, as are full list of atomic coordinates, anisotropic thermal parameters and those bond lengths and angles

Table 1: Crystal data and refinement details

Identification code	5791	
Empirical formula	C18 H13 Br1 F2 O3	
Formula weight	395.20	
Temperature	150 K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 7.5812(1) Å	α= 90°.
	b = 13.6990(1) Å	β= 90°.
	c = 15.1450(2) Å	γ = 90°.
Volume	1572.88(3) $Å^3$	
Z	4	
Density (calculated)	1.669 Mg/m^3	
Absorption coefficient	2.649 mm^{-1}	
F(000)	792	
Crystal size	0.33 x 0.15 x 0.14 mm^3	
Theta range for data collection	5.212 to 27.477°.	
Index ranges	-9<=h<=9, -17<=k<=17, -19<=l<=19	
Reflections collected	26706	
Independent reflections	3566 [R(int) = 0.055]	
Completeness to theta = 27.477°	99.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.69 and 0.61	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3547 / 0 / 218	
Goodness-of-fit on F^2	1.0000	
Final R indices [I>2sigma(I)]	R1 = 0.0233, wR2 = 0.0515	
R indices (all data)	R1 = 0.0264, wR2 = 0.0529	
Absolute structure parameter	0.001(6)	
Largest diff. peak and hole	0.37 and -0.68 $e.Å^{-3}$	

Table 2: Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2x10^3$). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	11891(1)	6085(1)	6456(1)	30
C(2)	10552(2)	4929(1)	6375(1)	21
C(3)	8856(2)	4903(1)	6077(1)	18
O(4)	7997(2)	4045(1)	5917(1)	20
C(5)	9007(2)	3158(1)	5851(1)	19
C(6)	10348(3)	3139(1)	6597(1)	22
C(7)	11499(2)	4055(2)	6622(1)	23
O(8)	13031(2)	4005(1)	6861(1)	33
F(9)	11372(2)	2333(1)	6512(1)	30
F(10)	9533(2)	3075(1)	7401(1)	28
C(11)	7803(2)	2293(1)	5892(1)	19
C(12)	6285(2)	2294(1)	6409(1)	20
C(13)	5310(2)	1445(1)	6531(1)	21
C(14)	5861(3)	578(1)	6140(1)	20
O(15)	5017(2)	-297(1)	6229(1)	26
C(16)	3689(3)	-363(2)	6893(2)	29
C(17)	7363(3)	573(1)	5601(1)	22
C(18)	8310(3)	1425(1)	5477(1)	21
C(19)	7712(2)	5744(1)	5872(1)	19
C(20)	6643(3)	5720(1)	5125(1)	22
C(21)	5605(3)	6521(2)	4907(1)	28
C(22)	5581(3)	7333(2)	5450(2)	29
C(23)	6588(3)	7351(2)	6214(1)	27
C(24)	7664(3)	6566(1)	6422(1)	23

Table 3: Hydrogen bonds [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(16)-H(163)...O(8)#1	0.97	2.59	3.240(3)	124

Symmetry transformations used to generate equivalent atoms:

#1 -x+2,y-1/2,-z+3/2

Table 4: Hydrogen coordinates ($x10^4$) and isotropic displacement parameters ($Å^2 x\ 10^3$)

	x	y	z	U(eq)
H(51)	9658	3155	5279	22
H(121)	5931	2882	6686	24
H(131)	4280	1450	6884	24
H(161)	3260	-1030	6920	43
H(163)	4187	-189	7463	43
H(162)	2714	74	6761	43
H(171)	7713	-25	5317	28
H(181)	9320	1416	5104	27
H(201)	6651	5162	4764	27
H(211)	4919	6511	4389	32
H(221)	4886	7879	5294	33
H(231)	6545	7900	6591	32
H(241)	8368	6584	6941	29

Br(1)-C(2)	1.8847(19)	C(22)-C(23)	1.387(3)
C(2)-C(3)	1.363(3)	C(22)-H(221)	0.944
C(2)-C(7)	1.446(3)	C(23)-C(24)	1.386(3)
C(3)-O(4)	1.366(2)	C(23)-H(231)	0.945
C(3)-C(19)	1.475(3)	C(24)-H(241)	0.951
O(4)-C(5)	1.441(2)		
C(5)-C(6)	1.520(3)	Br(1)-C(2)-C(3)	123.48(15)
C(5)-C(11)	1.497(3)	Br(1)-C(2)-C(7)	114.28(13)
C(5)-H(51)	0.997	C(3)-C(2)-C(7)	122.19(17)
C(6)-C(7)	1.528(3)	C(2)-C(3)-O(4)	122.09(17)
C(6)-F(9)	1.357(2)	C(2)-C(3)-C(19)	127.14(17)
C(6)-F(10)	1.368(2)	O(4)-C(3)-C(19)	110.77(15)
C(7)-O(8)	1.219(2)	C(3)-O(4)-C(5)	119.02(14)
C(11)-C(12)	1.392(3)	O(4)-C(5)-C(6)	108.57(15)
C(11)-C(18)	1.399(3)	O(4)-C(5)-C(11)	109.94(15)
C(12)-C(13)	1.389(3)	C(6)-C(5)-C(11)	111.38(16)
C(12)-H(121)	0.947	O(4)-C(5)-H(51)	109.1
C(13)-C(14)	1.392(3)	C(6)-C(5)-H(51)	108.3
C(13)-H(131)	0.947	C(11)-C(5)-H(51)	109.5
C(14)-O(15)	1.366(2)	C(5)-C(6)-C(7)	112.75(16)
C(14)-C(17)	1.401(3)	C(5)-C(6)-F(9)	108.98(16)
O(15)-C(16)	1.425(2)	C(7)-C(6)-F(9)	110.12(15)
C(16)-H(161)	0.971	C(5)-C(6)-F(10)	111.09(16)
C(16)-H(163)	0.973	C(7)-C(6)-F(10)	106.84(15)
C(16)-H(162)	0.972	F(9)-C(6)-F(10)	106.89(15)
C(17)-C(18)	1.383(3)	C(6)-C(7)-C(2)	112.94(15)
C(17)-H(171)	0.962	C(6)-C(7)-O(8)	120.35(18)
C(18)-H(181)	0.951	C(2)-C(7)-O(8)	126.66(19)
C(19)-C(20)	1.393(3)	C(5)-C(11)-C(12)	121.78(17)
C(19)-C(24)	1.401(3)	C(5)-C(11)-C(18)	119.14(17)
C(20)-C(21)	1.390(3)	C(12)-C(11)-C(18)	118.71(18)
C(20)-H(201)	0.940	C(11)-C(12)-C(13)	120.94(18)
C(21)-C(22)	1.383(3)	C(11)-C(12)-H(121)	119.0
C(21)-H(211)	0.942	C(13)-C(12)-H(121)	120.1

Table 5: Bond lengths (Å) and angles (°C)

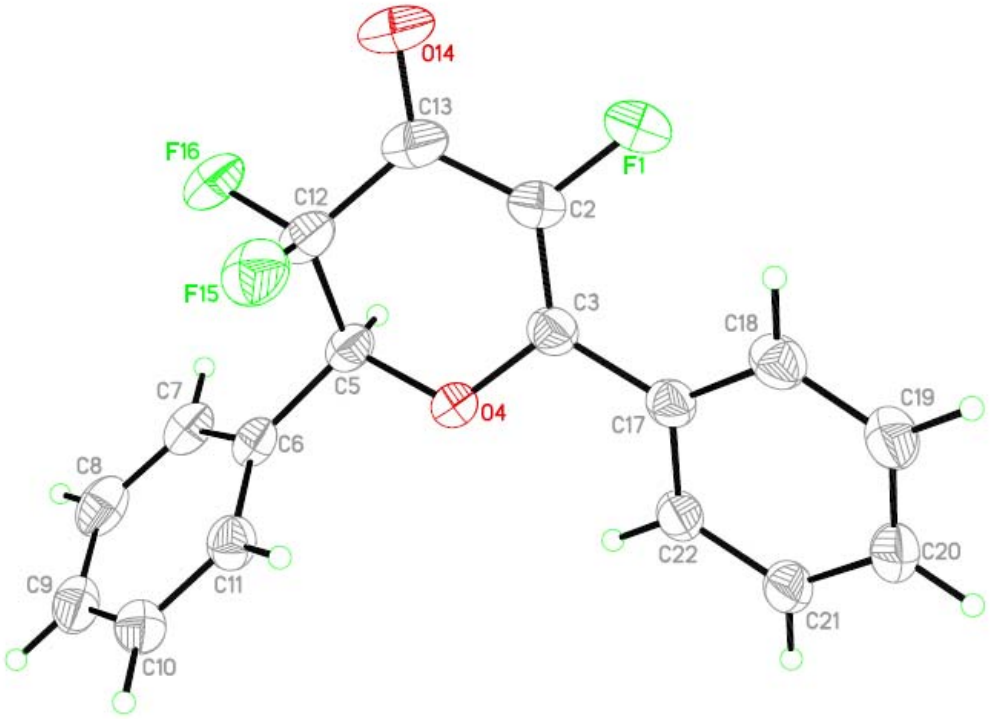
C(12)-C(13)-C(14)	119.83(17)	C(3)-C(19)-C(20)	119.63(17)
C(12)-C(13)-H(131)	120.6	C(3)-C(19)-C(24)	121.21(17)
C(14)-C(13)-H(131)	119.6	C(20)-C(19)-C(24)	119.16(18)
C(13)-C(14)-O(15)	124.50(17)	C(19)-C(20)-C(21)	120.22(18)
C(13)-C(14)-C(17)	119.78(17)	C(19)-C(20)-H(201)	119.2
O(15)-C(14)-C(17)	115.71(17)	C(21)-C(20)-H(201)	120.6
C(14)-O(15)-C(16)	117.14(16)	C(20)-C(21)-C(22)	120.12(19)
O(15)-C(16)-H(161)	109.0	C(20)-C(21)-H(211)	119.9
O(15)-C(16)-H(163)	109.7	C(22)-C(21)-H(211)	120.0
H(161)-C(16)-H(163)	108.9	C(21)-C(22)-C(23)	120.18(19)
O(15)-C(16)-H(162)	110.7	C(21)-C(22)-H(221)	119.7
H(161)-C(16)-H(162)	109.5	C(23)-C(22)-H(221)	120.2
H(163)-C(16)-H(162)	109.1	C(22)-C(23)-C(24)	119.99(19)
C(14)-C(17)-C(18)	119.77(18)	C(22)-C(23)-H(231)	119.9
C(14)-C(17)-H(171)	119.3	C(24)-C(23)-H(231)	120.1
C(18)-C(17)-H(171)	120.9	C(19)-C(24)-C(23)	120.25(19)
C(11)-C(18)-C(17)	120.92(17)	C(19)-C(24)-H(241)	119.9
C(11)-C(18)-H(181)	119.9	C(23)-C(24)-H(241)	119.9
C(17)-C(18)-H(181)	119.2		

Symmetry transformations used to generate equivalent atoms:

Table 6: Anisotropic displacement parameters ($Å^2x10^3$). The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	26(1)	23(1)	42(1)	-4(1)	-5(1)	-5(1)
C(2)	21(1)	20(1)	24(1)	-1(1)	-1(1)	0(1)
C(3)	22(1)	14(1)	18(1)	-1(1)	1(1)	-2(1)
O(4)	18(1)	14(1)	29(1)	1(1)	-2(1)	3(1)
C(5)	20(1)	15(1)	22(1)	0(1)	0(1)	4(1)
C(6)	22(1)	20(1)	23(1)	4(1)	-2(1)	5(1)
C(7)	21(1)	24(1)	23(1)	-1(1)	-3(1)	1(1)
O(8)	22(1)	33(1)	43(1)	1(1)	-10(1)	1(1)
F(9)	25(1)	21(1)	45(1)	1(1)	-5(1)	9(1)
F(10)	31(1)	32(1)	22(1)	6(1)	0(1)	-1(1)
C(11)	19(1)	18(1)	20(1)	2(1)	0(1)	2(1)
C(12)	20(1)	17(1)	23(1)	-1(1)	-1(1)	4(1)
C(13)	17(1)	23(1)	23(1)	0(1)	1(1)	2(1)
C(14)	19(1)	18(1)	22(1)	3(1)	-3(1)	-1(1)
O(15)	26(1)	20(1)	33(1)	1(1)	4(1)	-5(1)
C(16)	24(1)	31(1)	32(1)	6(1)	3(1)	-7(1)
C(17)	25(1)	18(1)	23(1)	-3(1)	1(1)	3(1)
C(18)	21(1)	21(1)	22(1)	-2(1)	3(1)	2(1)
C(19)	18(1)	18(1)	21(1)	3(1)	3(1)	0(1)
C(20)	21(1)	20(1)	26(1)	2(1)	-2(1)	0(1)
C(21)	23(1)	28(1)	32(1)	7(1)	-3(1)	2(1)
C(22)	24(1)	21(1)	40(1)	8(1)	5(1)	4(1)
C(23)	27(1)	18(1)	35(1)	-1(1)	6(1)	2(1)
C(24)	25(1)	20(1)	24(1)	-1(1)	2(1)	-1(1)

Single-crystal X-ray diffraction report for 3,3,5-trifluoro-2,6-diphenyl-2,3-dihydro-4*H*-pyran-4-one (6b)



Crystals of 3,3,5-trifluoro-2,6-diphenyl-2,3-dihydro-4*H*-pyran-4-one were grown by slow diffusion (hexane/ether). A polycrystalline aggregate was cut to give a fragment having dimensions approximately 0.14x0.10x0.10 mm. This was mounted on a glass fibre using perfluoropolyether oil and cooled rapidly to 150K in a stream of cold N_2 using an Oxford Cryosystems CRYOSTREAM unit. Single crystal X-ray diffraction data were collected using graphite monochromated Mo Kα radiation (λ = 0.71073 Å) on an Enraf-Nonius KappaCCD S39 diffractometer. The diffractometer was equipped with a Cryostream N_2 open-flow cooling device, and the data were collected at 150K.[11] Series of ω-scans were performed in such a way as to cover a sphere of data to a maximum resolution of 0.77Å. Cell parameters and intensity data were processed using the DENZO-SMN package.[12] The structure was solved by direct methods[13] and refined by full-matrix least squares on F using the CRYSTALS suite.[14] Intensities were corrected for absorption effects by the multi-scan method, based on multiple scans of identical and Laue equivalent reflections.[12] A 3-term Chebychev polynomial weighting scheme was applied.[15] All non-hydrogen atoms were refined with anisotropic displacement parameters, except where there was disorder present and the atoms were too close together to resolve the electron density fully. In this case, the overlapping atoms were refined with isotropic displacement parameters. Hydrogen atoms were positioned geometrically and refined using a riding model. The Flack parameter refined to a value of 0.45(16) (2733 Friedel-pairs) so the Friedel-pairs were merged for the final refinement. Thermal ellipsoid plots (at 50% probability) are shown above. A summary of crystallographic data is given below, as are full list of atomic coordinates, anisotropic thermal parameters and those bond lengths and angles

Table 1: Crystal data and refinement details

Identification code	5770	
Empirical formula	C17 H11 F3 O2	
Formula weight	304.27	
Temperature	150 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 9.2979(2) Å	α= 90°.
	b = 14.9993(3) Å	β= 108.9089(8)°.
	c = 10.4756(2) Å	γ = 90°.
Volume	1382.11(5) $Å^3$	
Z	4	
Density (calculated)	1.462 Mg/m^3	
Absorption coefficient	0.122 mm^{-1}	
F(000)	624	
Crystal size	0.14 x 0.10 x 0.10 mm^3	
Theta range for data collection	5.105 to 27.491°.	
Index ranges	-12<=h<=12, -19<=k<=19, -13<=l<=13	
Reflections collected	21605	
Independent reflections	3147 [R(int) = 0.040]	
Completeness to theta = 27.491°	99.3 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.99 and 0.95	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3147 / 0 / 199	
Goodness-of-fit on F^2	0.9532	
Final R indices [I>2sigma(I)]	R1 = 0.0425, wR2 = 0.0988	
R indices (all data)	R1 = 0.0648, wR2 = 0.1078	
Largest diff. peak and hole	0.29 and -0.33 $e.Å^{-3}$	

Table 2: Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2x10^3$). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
F(1)	3187(1)	4654(1)	2159(1)	58
C(2)	2859(2)	5323(1)	2878(2)	39
C(3)	2331(2)	6112(1)	2283(1)	31
O(4)	2112(1)	6810(1)	3031(1)	30
C(5)	2868(2)	6788(1)	4468(1)	30
C(6)	2349(2)	7578(1)	5088(1)	29
C(7)	3368(2)	7965(1)	6230(1)	34
C(8)	2915(2)	8667(1)	6862(2)	41
C(9)	1457(2)	9008(1)	6345(2)	39
C(10)	446(2)	8634(1)	5194(2)	37
C(11)	884(2)	7915(1)	4577(1)	32
C(12)	2581(2)	5892(1)	5001(2)	37
C(13)	3053(2)	5122(1)	4264(2)	43
O(14)	3510(2)	4415(1)	4825(1)	60
F(15)	1069(1)	5787(1)	4851(1)	48
F(16)	3335(1)	5841(1)	6340(1)	51
C(17)	1914(2)	6336(1)	844(1)	30
C(18)	1453(2)	5685(1)	-162(2)	35
C(19)	1014(2)	5927(1)	-1507(2)	39
C(20)	1039(2)	6813(1)	-1871(2)	39
C(21)	1507(2)	7459(1)	-883(2)	36
C(22)	1931(2)	7230(1)	467(1)	32

Table 3: Hydrogen bonds [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(21)-H(211)...O(14)#1	0.95	2.45	3.139(2)	130

Symmetry transformations used to generate equivalent atoms:

#1 -x+1/2,y+1/2,-z+1/2

Table 4: Bond lengths (Å) and angles (°C)

F(1)-C(2)	1.3468(18)	C(22)-H(221)	0.951
C(2)-C(3)	1.354(2)		
C(2)-C(13)	1.436(2)	F(1)-C(2)-C(3)	120.49(14)
C(3)-O(4)	1.3611(16)	F(1)-C(2)-C(13)	115.59(13)
C(3)-C(17)	1.4681(19)	C(3)-C(2)-C(13)	123.87(14)
O(4)-C(5)	1.4402(16)	C(2)-C(3)-O(4)	120.42(13)
C(5)-C(6)	1.504(2)	C(2)-C(3)-C(17)	127.43(13)
C(5)-C(12)	1.5117(19)	O(4)-C(3)-C(17)	112.15(11)
C(5)-H(51)	0.986	C(3)-O(4)-C(5)	118.11(10)
C(6)-C(7)	1.3893(19)	O(4)-C(5)-C(6)	108.54(10)
C(6)-C(11)	1.3878(19)	O(4)-C(5)-C(12)	108.73(11)
C(7)-C(8)	1.381(2)	C(6)-C(5)-C(12)	114.85(12)
C(7)-H(71)	0.941	O(4)-C(5)-H(51)	108.2
C(8)-C(9)	1.384(2)	C(6)-C(5)-H(51)	110.1
C(8)-H(81)	0.968	C(12)-C(5)-H(51)	106.2
C(9)-C(10)	1.385(2)	C(5)-C(6)-C(7)	118.47(13)
C(9)-H(91)	0.949	C(5)-C(6)-C(11)	122.16(12)
C(10)-C(11)	1.384(2)	C(7)-C(6)-C(11)	119.35(14)
C(10)-H(101)	0.953	C(6)-C(7)-C(8)	120.19(14)
C(11)-H(111)	0.943	C(6)-C(7)-H(71)	119.8
C(12)-C(13)	1.532(2)	C(8)-C(7)-H(71)	120.0
C(12)-F(15)	1.3719(18)	C(7)-C(8)-C(9)	120.41(14)
C(12)-F(16)	1.3520(17)	C(7)-C(8)-H(81)	119.7
C(13)-O(14)	1.2192(18)	C(9)-C(8)-H(81)	119.9
C(17)-C(18)	1.398(2)	C(8)-C(9)-C(10)	119.56(14)
C(17)-C(22)	1.3995(19)	C(8)-C(9)-H(91)	120.9
C(18)-C(19)	1.383(2)	C(10)-C(9)-H(91)	119.6
C(18)-H(181)	0.954	C(9)-C(10)-C(11)	120.18(14)
C(19)-C(20)	1.384(2)	C(9)-C(10)-H(101)	120.4
C(19)-H(191)	0.955	C(11)-C(10)-H(101)	119.4
C(20)-C(21)	1.381(2)	C(6)-C(11)-C(10)	120.28(13)
C(20)-H(201)	0.959	C(6)-C(11)-H(111)	120.5
C(21)-C(22)	1.382(2)	C(10)-C(11)-H(111)	119.2
C(21)-H(211)	0.946	C(5)-C(12)-C(13)	111.74(12)

C(5)-C(12)-F(15)	110.92(12)	C(19)-C(18)-H(181)	120.3
C(13)-C(12)-F(15)	107.85(13)	C(18)-C(19)-C(20)	120.45(14)
C(5)-C(12)-F(16)	109.85(12)	C(18)-C(19)-H(191)	119.2
C(13)-C(12)-F(16)	110.06(12)	C(20)-C(19)-H(191)	120.4
F(15)-C(12)-F(16)	106.25(12)	C(19)-C(20)-C(21)	119.75(14)
C(12)-C(13)-C(2)	112.86(12)	C(19)-C(20)-H(201)	121.0
C(12)-C(13)-O(14)	121.66(15)	C(21)-C(20)-H(201)	119.3
C(2)-C(13)-O(14)	125.46(16)	C(20)-C(21)-C(22)	120.57(14)
C(3)-C(17)-C(18)	121.96(13)	C(20)-C(21)-H(211)	119.9
C(3)-C(17)-C(22)	119.02(12)	C(22)-C(21)-H(211)	119.5
C(18)-C(17)-C(22)	118.99(13)	C(17)-C(22)-C(21)	120.08(13)
C(17)-C(18)-C(19)	120.15(14)	C(17)-C(22)-H(221)	119.6
C(17)-C(18)-H(181)	119.6	C(21)-C(22)-H(221)	120.4

Symmetry transformations used to generate equivalent atoms:

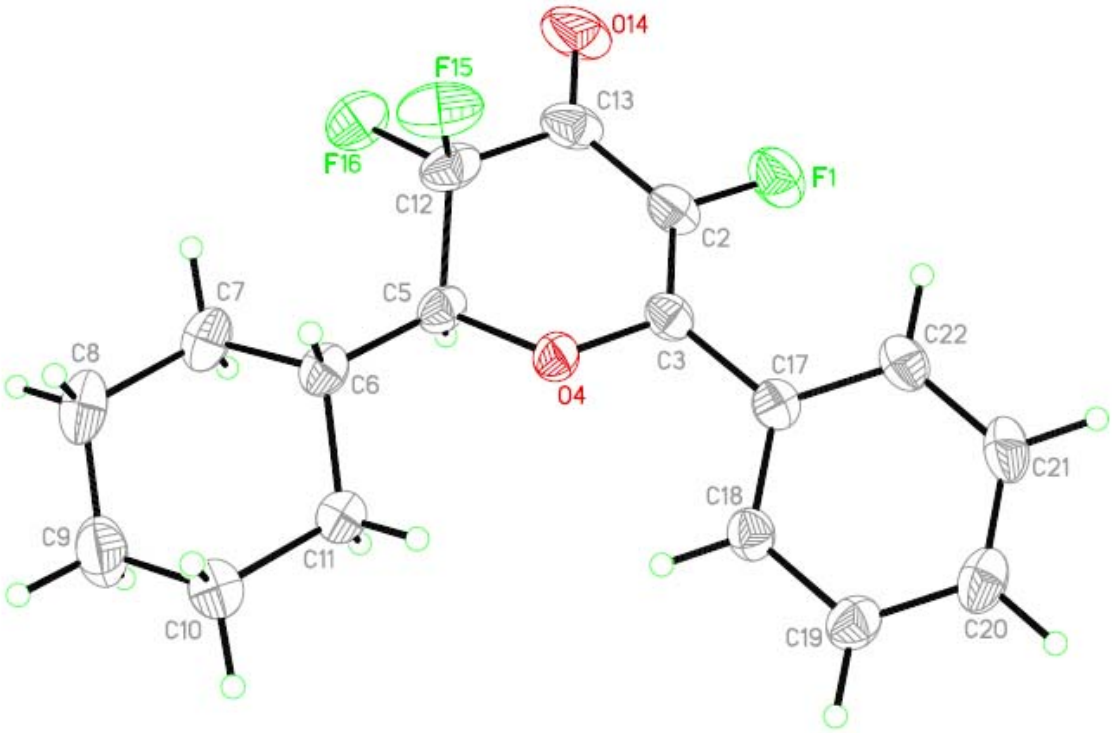
Table 5: Hydrogen coordinates (x10^4) and isotropic displacement parameters (Å^{2}x 10^3)

	x	y	z	U(eq)
H(51)	3973	6822	4636	35
H(71)	4367	7745	6576	40
H(81)	3622	8923	7672	50
H(91)	1143	9496	6767	47
H(101)	-556	8867	4819	44
H(111)	179	7662	3801	39
H(181)	1445	5073	85	44
H(191)	692	5476	-2184	46
H(201)	752	6985	-2801	47
H(211)	1525	8064	-1128	46
H(221)	2245	7677	1145	39

Table 6: Anisotropic displacement parameters ($Å^2x10^3$). The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
F(1)	83(1)	36(1)	58(1)	3(1)	28(1)	21(1)
C(2)	49(1)	29(1)	43(1)	5(1)	18(1)	8(1)
C(3)	32(1)	28(1)	35(1)	2(1)	15(1)	3(1)
O(4)	36(1)	28(1)	26(1)	4(1)	11(1)	5(1)
C(5)	27(1)	36(1)	25(1)	6(1)	6(1)	2(1)
C(6)	30(1)	34(1)	23(1)	5(1)	9(1)	-2(1)
C(7)	32(1)	41(1)	27(1)	6(1)	6(1)	-6(1)
C(8)	50(1)	41(1)	28(1)	0(1)	8(1)	-16(1)
C(9)	55(1)	33(1)	33(1)	-2(1)	21(1)	-6(1)
C(10)	37(1)	40(1)	34(1)	2(1)	14(1)	3(1)
C(11)	30(1)	39(1)	27(1)	-2(1)	7(1)	-2(1)
C(12)	37(1)	41(1)	33(1)	13(1)	10(1)	2(1)
C(13)	49(1)	33(1)	47(1)	12(1)	14(1)	5(1)
O(14)	84(1)	36(1)	61(1)	22(1)	23(1)	14(1)
F(15)	47(1)	47(1)	56(1)	10(1)	25(1)	-7(1)
F(16)	65(1)	52(1)	33(1)	18(1)	11(1)	9(1)
C(17)	32(1)	28(1)	34(1)	2(1)	17(1)	3(1)
C(18)	40(1)	28(1)	42(1)	-2(1)	19(1)	-2(1)
C(19)	45(1)	37(1)	37(1)	-8(1)	16(1)	-2(1)
C(20)	49(1)	41(1)	32(1)	0(1)	19(1)	3(1)
C(21)	50(1)	30(1)	35(1)	3(1)	23(1)	3(1)
C(22)	41(1)	27(1)	32(1)	-1(1)	18(1)	1(1)

Single-crystal X-ray diffraction report for 2-cyclohexyl-3,3,5-trifluoro-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (6e)



Crystals of 2-cyclohexyl-3,3,5-trifluoro-6-phenyl-2,3-dihydro-4*H*-pyran-4-one were grown by slow diffusion (hexane/ether). A polycrystalline aggregate was cut to give a fragment having dimensions approximately 0.45x0.35x0.21 mm. This was mounted on a glass fibre using perfluoropolyether oil and cooled rapidly to 150K in a stream of cold N_2 using an Oxford Cryosystems CRYOSTREAM unit. Single crystal X-ray diffraction data were collected using graphite monochromated Mo Kα radiation (λ = 0.71073 Å) on an Enraf-Nonius KappaCCD S39 diffractometer. The diffractometer was equipped with a Cryostream N_2 open-flow cooling device, and the data were collected at 150K.[11] Series of ω-scans were performed in such a way as to cover a sphere of data to a maximum resolution of 0.77Å. Cell parameters and intensity data were processed using the DENZO-SMN package.[12] The structure was solved by direct methods[13] and refined by full-matrix least squares on F using the CRYSTALS suite.[14] Intensities were corrected for absorption effects by the multi-scan method, based on multiple scans of identical and Laue equivalent reflections.[12] A 3-term Chebychev polynomial weighting scheme was applied.[15] All non-hydrogen atoms were refined with anisotropic displacement parameters, except where there was disorder present and the atoms were too close together to resolve the electron density fully. In this case, the overlapping atoms were refined with isotropic displacement parameters. Hydrogen atoms were positioned geometrically and refined using a riding model. The Flack parameter refined to a value of 0.45(16) (2733 Friedel-pairs) so the Friedel-pairs were merged for the final refinement. Thermal ellipsoid plots (at 50% probability) are shown above. A summary of crystallographic data is given below, as are full list of atomic coordinates, anisotropic thermal parameters and those bond lengths and angles

Table 1: Crystal data and refinement details

Identification code	5792	
Empirical formula	C17 H17 F3 O2	
Formula weight	310.31	
Temperature	150 K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 1 21/c 1	
Unit cell dimensions	a = 8.7380(2) Å	α= 90°.
	b = 20.0767(4) Å	β= 102.6480(7)°.
	c = 8.5989(2) Å	γ = 90°.
Volume	1471.90(6) $Å^3$	
Z	4	
Density (calculated)	1.400 Mg/m^3	
Absorption coefficient	0.116 mm^{-1}	
F(000)	648	
Crystal size	0.45 x 0.35 x 0.21 mm^3	
Theta range for data collection	5.196 to 27.487°.	
Index ranges	-11<=h<=11, -24<=k<=26, -11<=l<=11	
Reflections collected	19174	
Independent reflections	3344 [R(int) = 0.038]	
Completeness to theta = 26.937°	99.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.98 and 0.94	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3344 / 0 / 199	
Goodness-of-fit on F^2	1.0000	
Final R indices [I>2sigma(I)]	R1 = 0.0396, wR2 = 0.0857	
R indices (all data)	R1 = 0.0685, wR2 = 0.0961	
Largest diff. peak and hole	0.36 and -0.38 $e.Å^{-3}$	

Table 2: Atomic coordinates ($x10^4$) and equivalent isotropic displacement parameters ($Å^2x10^3$). U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
F(1)	5621(1)	5123(1)	8536(1)	45
C(2)	4264(2)	5342(1)	7535(2)	32
C(3)	3481(2)	4954(1)	6337(2)	26
O(4)	2235(1)	5206(1)	5270(1)	28
C(5)	2145(2)	5925(1)	5052(2)	27
C(6)	669(2)	6076(1)	3792(2)	29
C(7)	606(2)	6815(1)	3312(2)	39
C(8)	-797(2)	6972(1)	1964(2)	44
C(9)	-840(2)	6534(1)	524(2)	51
C(10)	-815(2)	5802(1)	982(2)	46
C(11)	607(2)	5638(1)	2316(2)	37
C(12)	2286(2)	6233(1)	6687(2)	36
C(13)	3759(2)	5997(1)	7863(2)	37
O(14)	4411(2)	6350(1)	8967(1)	56
F(15)	1011(1)	6076(1)	7298(1)	55
F(16)	2340(1)	6906(1)	6612(1)	54
C(17)	3806(2)	4255(1)	6021(2)	26
C(18)	3260(2)	3994(1)	4492(2)	28
C(19)	3548(2)	3335(1)	4172(2)	33
C(20)	4368(2)	2927(1)	5368(2)	37
C(21)	4904(2)	3180(1)	6888(2)	36
C(22)	4626(2)	3837(1)	7225(2)	31

Table 3: Bond lengths (Å) and angles (°C)

F(1)-C(2)	1.3763(17)	C(19)-C(20)	1.385(2)
C(2)-C(3)	1.3526(19)	C(19)-H(191)	0.968
C(2)-C(13)	1.434(2)	C(20)-C(21)	1.384(2)
C(3)-O(4)	1.3580(16)	C(20)-H(201)	0.958
C(3)-C(17)	1.4691(19)	C(21)-C(22)	1.383(2)
O(4)-C(5)	1.4569(16)	C(21)-H(211)	0.982
C(5)-C(6)	1.5223(19)	C(22)-H(221)	0.961
C(5)-C(12)	1.5154(19)		
C(5)-H(51)	1.003	F(1)-C(2)-C(3)	120.96(13)
C(6)-C(7)	1.538(2)	F(1)-C(2)-C(13)	115.49(12)
C(6)-C(11)	1.5347(19)	C(3)-C(2)-C(13)	123.54(13)
C(6)-H(61)	1.001	C(2)-C(3)-O(4)	119.76(13)
C(7)-C(8)	1.524(2)	C(2)-C(3)-C(17)	127.30(13)
C(7)-H(71)	0.985	O(4)-C(3)-C(17)	112.94(11)
C(7)-H(72)	0.993	C(3)-O(4)-C(5)	118.00(10)
C(8)-C(9)	1.512(2)	O(4)-C(5)-C(6)	107.61(10)
C(8)-H(81)	0.994	O(4)-C(5)-C(12)	107.04(11)
C(8)-H(82)	0.999	C(6)-C(5)-C(12)	117.60(12)
C(9)-C(10)	1.521(2)	O(4)-C(5)-H(51)	108.7
C(9)-H(91)	0.990	C(6)-C(5)-H(51)	109.5
C(9)-H(92)	0.995	C(12)-C(5)-H(51)	106.1
C(10)-C(11)	1.531(2)	C(5)-C(6)-C(7)	110.96(11)
C(10)-H(101)	1.005	C(5)-C(6)-C(11)	110.21(11)
C(10)-H(102)	1.001	C(7)-C(6)-C(11)	109.77(12)
C(11)-H(111)	0.985	C(5)-C(6)-H(61)	108.6
C(11)-H(112)	0.990	C(7)-C(6)-H(61)	109.0
C(12)-C(13)	1.528(2)	C(11)-C(6)-H(61)	108.2
C(12)-F(15)	1.3688(17)	C(6)-C(7)-C(8)	112.22(13)
C(12)-F(16)	1.3553(17)	C(6)-C(7)-H(71)	109.5
C(13)-O(14)	1.2202(17)	C(8)-C(7)-H(71)	108.8
C(17)-C(18)	1.3985(19)	C(6)-C(7)-H(72)	107.4
C(17)-C(22)	1.4011(19)	C(8)-C(7)-H(72)	109.0
C(18)-C(19)	1.386(2)	H(71)-C(7)-H(72)	109.9
C(18)-H(181)	0.973	C(7)-C(8)-C(9)	112.02(13)

C(7)-C(8)-H(81)	108.3	C(13)-C(12)-F(15)	108.24(12)
C(9)-C(8)-H(81)	110.2	C(5)-C(12)-F(16)	111.04(12)
C(7)-C(8)-H(82)	108.7	C(13)-C(12)-F(16)	107.89(12)
C(9)-C(8)-H(82)	107.1	F(15)-C(12)-F(16)	106.72(12)
H(81)-C(8)-H(82)	110.5	C(12)-C(13)-C(2)	113.85(12)
C(8)-C(9)-C(10)	110.67(14)	C(12)-C(13)-O(14)	121.17(15)
C(8)-C(9)-H(91)	109.1	C(2)-C(13)-O(14)	124.98(15)
C(10)-C(9)-H(91)	109.2	C(3)-C(17)-C(18)	119.43(12)
C(8)-C(9)-H(92)	108.5	C(3)-C(17)-C(22)	121.56(12)
C(10)-C(9)-H(92)	108.5	C(18)-C(17)-C(22)	119.00(13)
H(91)-C(9)-H(92)	110.9	C(17)-C(18)-C(19)	120.30(13)
C(9)-C(10)-C(11)	111.39(14)	C(17)-C(18)-H(181)	120.2
C(9)-C(10)-H(101)	108.0	C(19)-C(18)-H(181)	119.5
C(11)-C(10)-H(101)	109.1	C(18)-C(19)-C(20)	120.24(14)
C(9)-C(10)-H(102)	110.3	C(18)-C(19)-H(191)	119.7
C(11)-C(10)-H(102)	107.6	C(20)-C(19)-H(191)	120.1
H(101)-C(10)-H(102)	110.4	C(19)-C(20)-C(21)	119.84(14)
C(6)-C(11)-C(10)	111.89(12)	C(19)-C(20)-H(201)	119.4
C(6)-C(11)-H(111)	107.5	C(21)-C(20)-H(201)	120.8
C(10)-C(11)-H(111)	109.2	C(20)-C(21)-C(22)	120.59(14)
C(6)-C(11)-H(112)	108.8	C(20)-C(21)-H(211)	120.6
C(10)-C(11)-H(112)	109.5	C(22)-C(21)-H(211)	118.8
H(111)-C(11)-H(112)	109.9	C(17)-C(22)-C(21)	120.03(14)
C(5)-C(12)-C(13)	111.95(12)	C(17)-C(22)-H(221)	119.9
C(5)-C(12)-F(15)	110.79(12)	C(21)-C(22)-H(221)	120.0

Symmetry transformations used to generate equivalent atoms:

Table 4: Hydrogen bonds [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(20)-H(201)...O(14)#1	0.96	2.49	3.352(2)	150
C(22)-H(221)...O(14)#2	0.96	2.41	3.220(2)	141

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y-1/2,-z+3/2 #2 -x+1,-y+1,-z+2

Table 5: Hydrogen coordinates ($x10^4$) and isotropic displacement parameters ($Å^2 x\ 10^3$)

	x	y	z	U(eq)
H(51)	3090	6078	4666	33
H(61)	-267	5969	4241	34
H(71)	543	7093	4241	46
H(72)	1585	6917	2954	47
H(81)	-740	7448	1671	52
H(82)	-1781	6882	2343	53
H(91)	-1811	6628	-285	61
H(92)	106	6630	95	61
H(101)	-1800	5703	1362	53
H(102)	-754	5515	45	53
H(111)	1574	5721	1935	45
H(112)	562	5165	2628	44
H(181)	2674	4274	3644	35
H(191)	3169	3159	3108	41
H(201)	4550	2472	5133	47
H(211)	5491	2897	7744	43
H(221)	4988	4007	8288	39

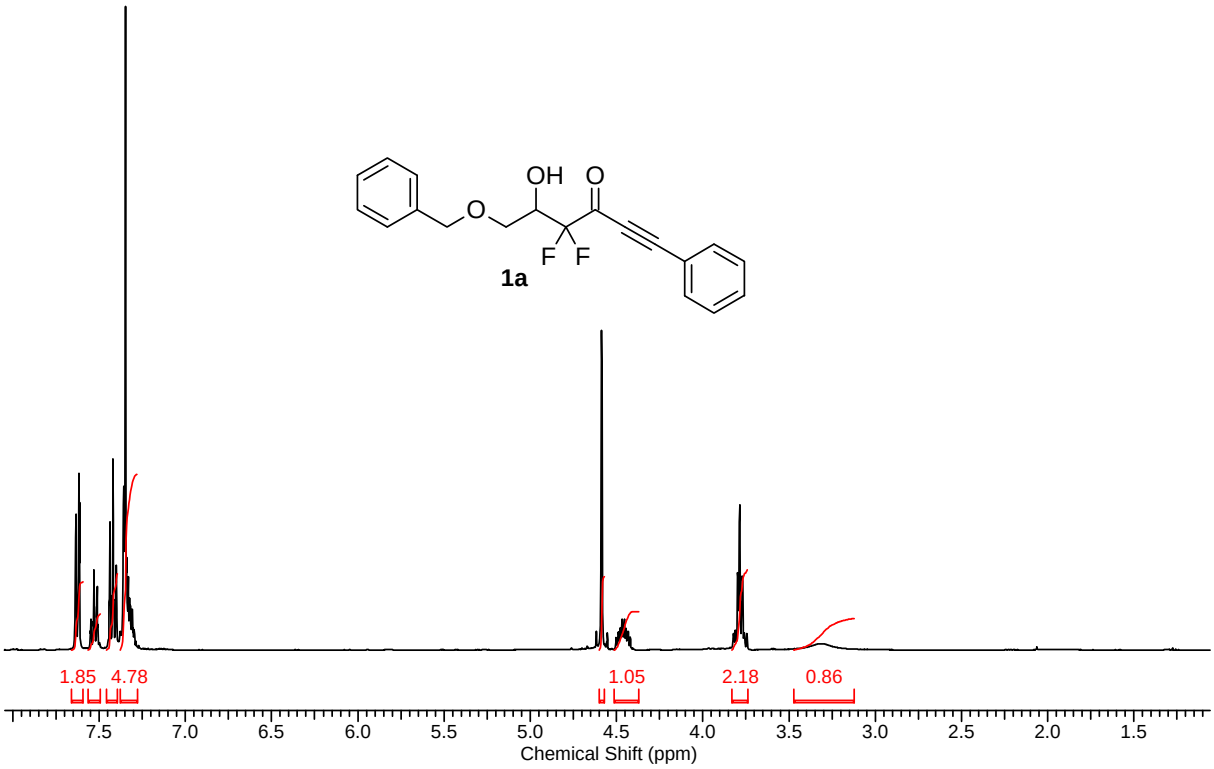
Table 6: Anisotropic displacement parameters ($Å^2x10^3$). The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

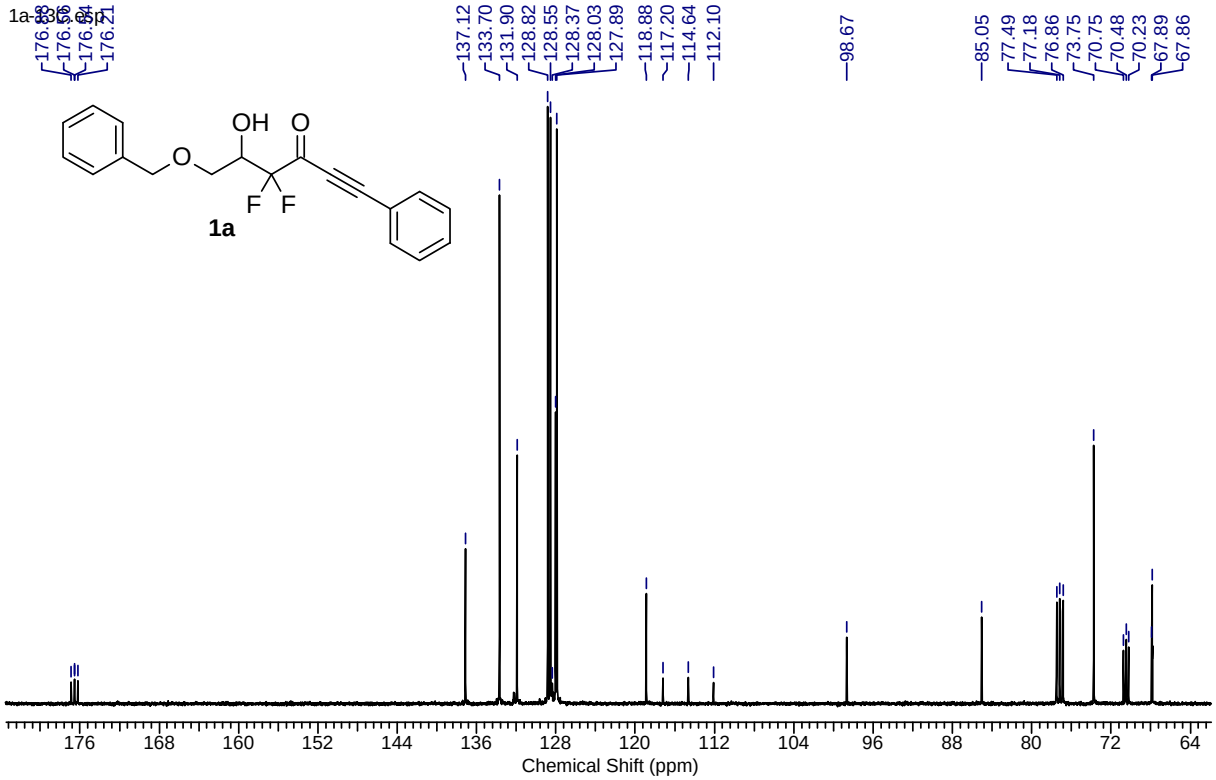
	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
F(1)	48(1)	45(1)	35(1)	4(1)	-5(1)	-6(1)
C(2)	37(1)	34(1)	25(1)	2(1)	2(1)	-7(1)
C(3)	28(1)	28(1)	23(1)	3(1)	6(1)	-3(1)
O(4)	32(1)	20(1)	29(1)	-1(1)	2(1)	-1(1)
C(5)	33(1)	18(1)	32(1)	-2(1)	11(1)	-3(1)
C(6)	29(1)	25(1)	34(1)	1(1)	10(1)	0(1)
C(7)	40(1)	26(1)	52(1)	3(1)	11(1)	4(1)
C(8)	40(1)	34(1)	59(1)	12(1)	11(1)	11(1)
C(9)	52(1)	54(1)	45(1)	13(1)	6(1)	17(1)
C(10)	50(1)	44(1)	38(1)	-2(1)	-1(1)	12(1)
C(11)	42(1)	32(1)	34(1)	-3(1)	3(1)	8(1)
C(12)	48(1)	25(1)	39(1)	-8(1)	17(1)	-6(1)
C(13)	56(1)	31(1)	25(1)	-3(1)	9(1)	-15(1)
O(14)	92(1)	40(1)	30(1)	-9(1)	0(1)	-19(1)
F(15)	58(1)	66(1)	48(1)	-16(1)	29(1)	-7(1)
F(16)	77(1)	26(1)	53(1)	-13(1)	5(1)	1(1)
C(17)	24(1)	26(1)	27(1)	3(1)	7(1)	-3(1)
C(18)	28(1)	26(1)	29(1)	3(1)	4(1)	-2(1)
C(19)	37(1)	26(1)	37(1)	-2(1)	9(1)	-3(1)
C(20)	39(1)	25(1)	49(1)	6(1)	18(1)	2(1)
C(21)	36(1)	35(1)	39(1)	16(1)	13(1)	6(1)
C(22)	31(1)	36(1)	28(1)	8(1)	8(1)	0(1)

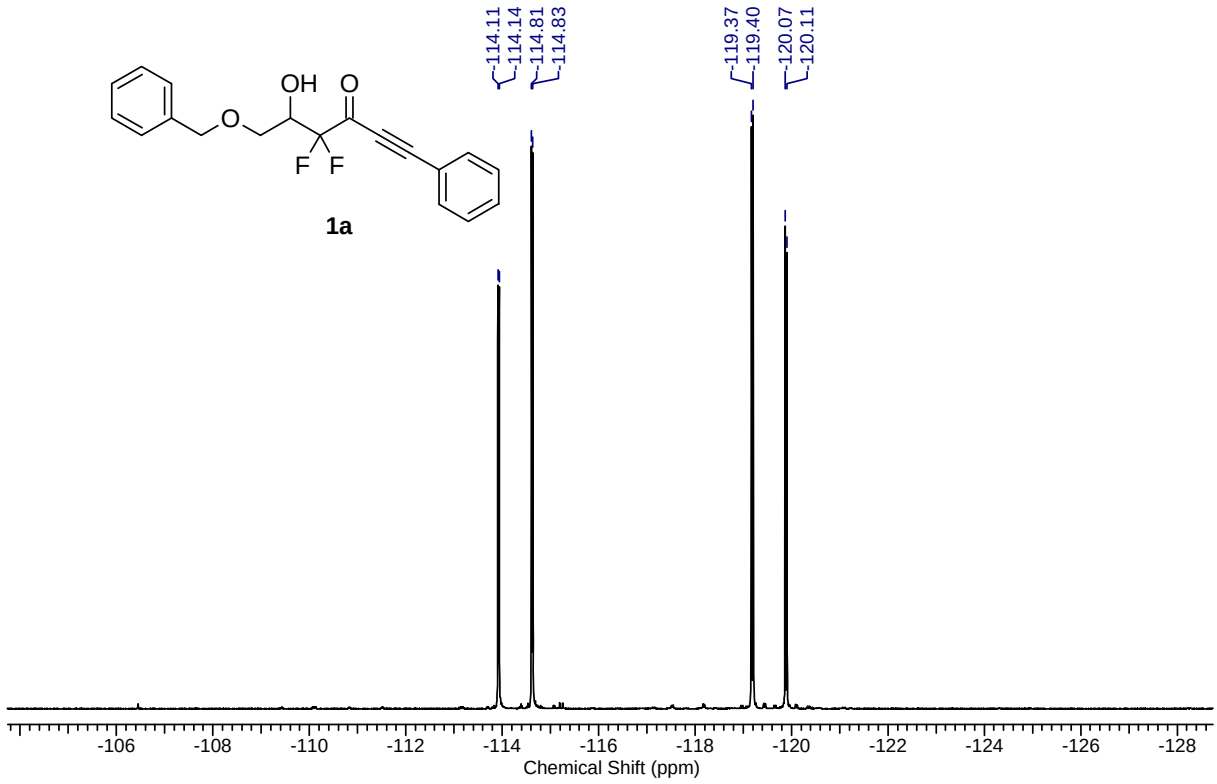
G - NMR SPECTRA

G.1 – Starting Materials

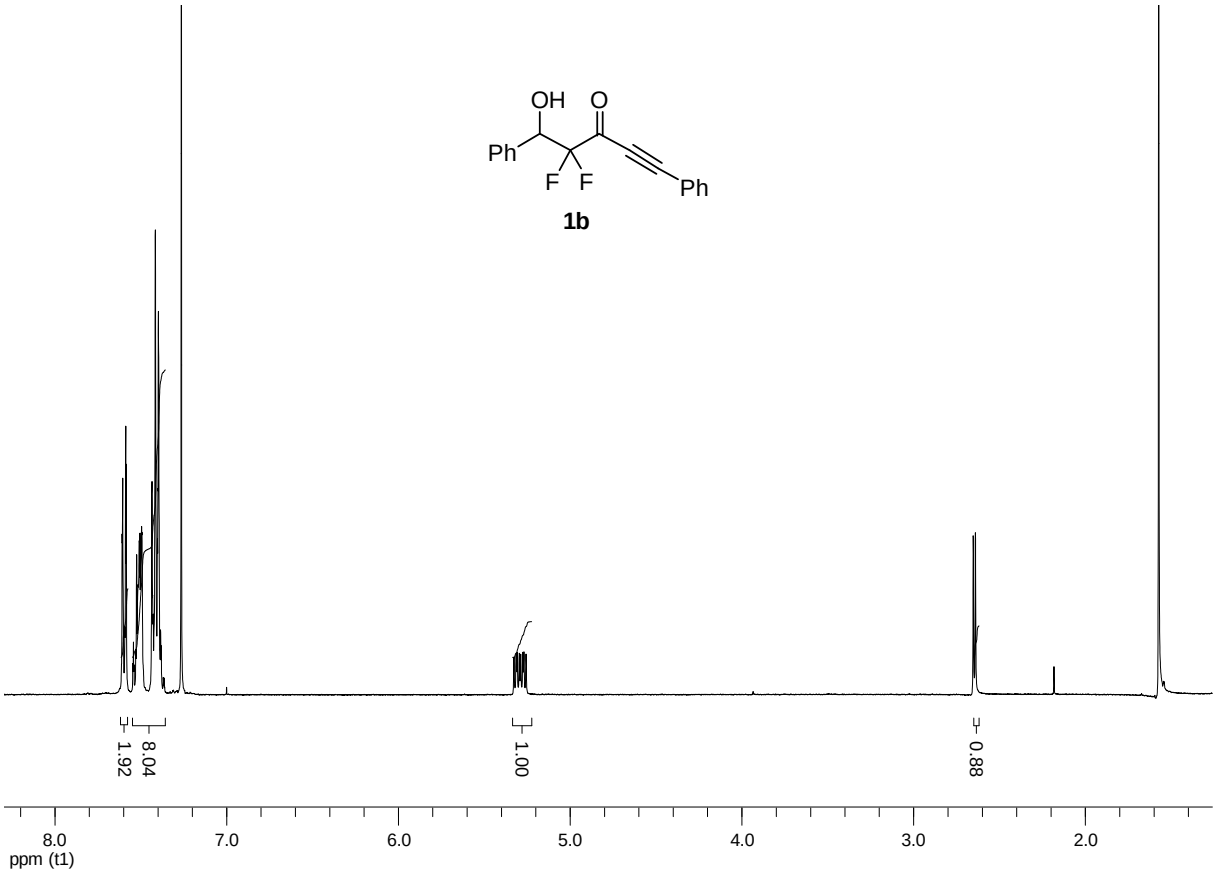
6-(Benzyloxy)-4,4-difluoro-5-hydroxy-1-phenylhex-1-yn-3-one (1a)

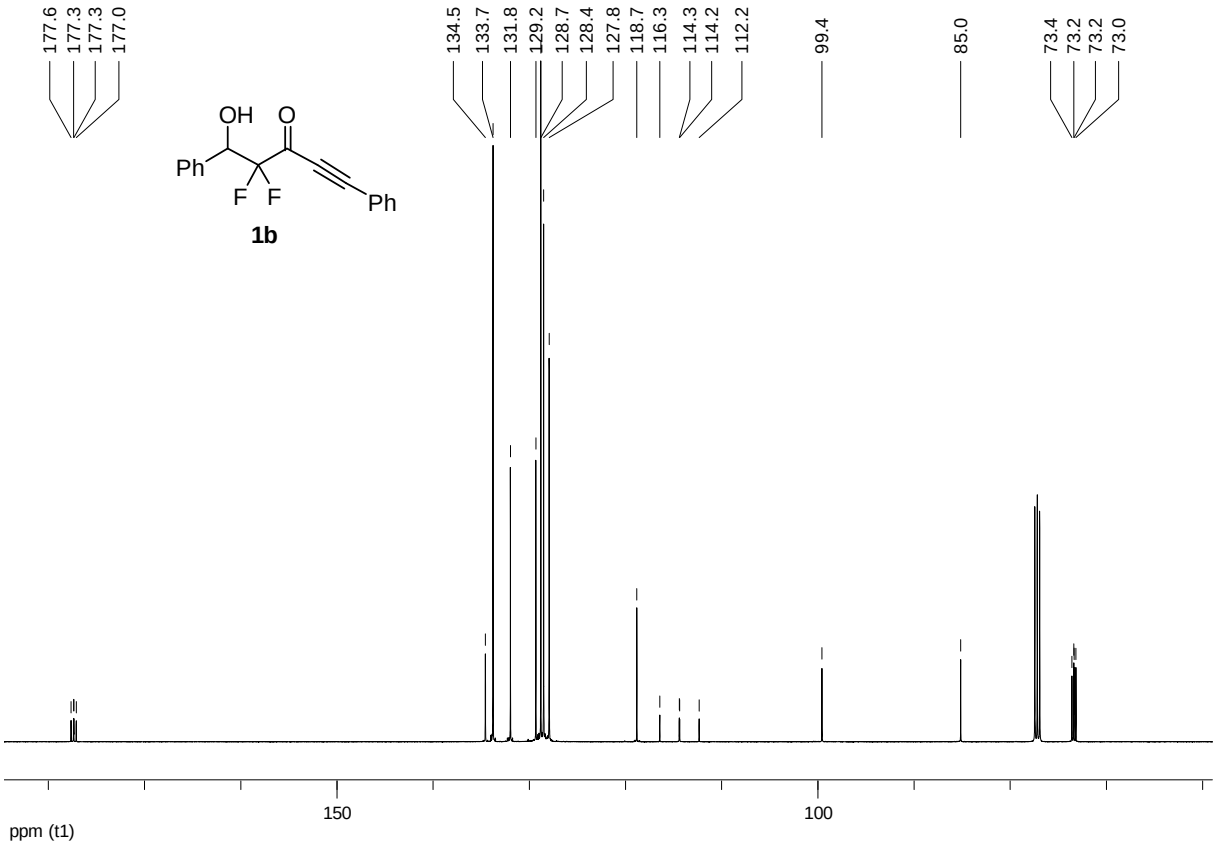






4,4-difluoro-5-hydroxy-1,5-diphenylpent-1-yn-3-one (1b)

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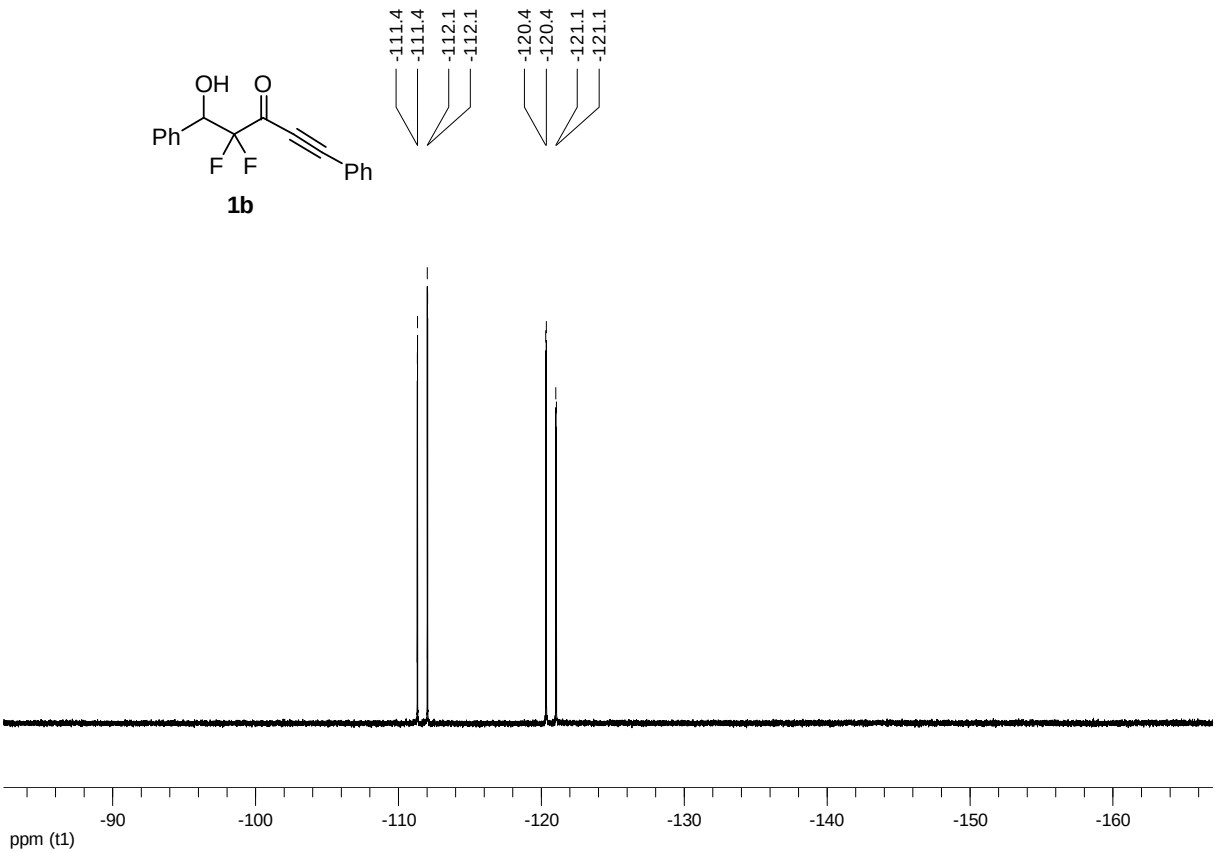
ppm (t1)

1b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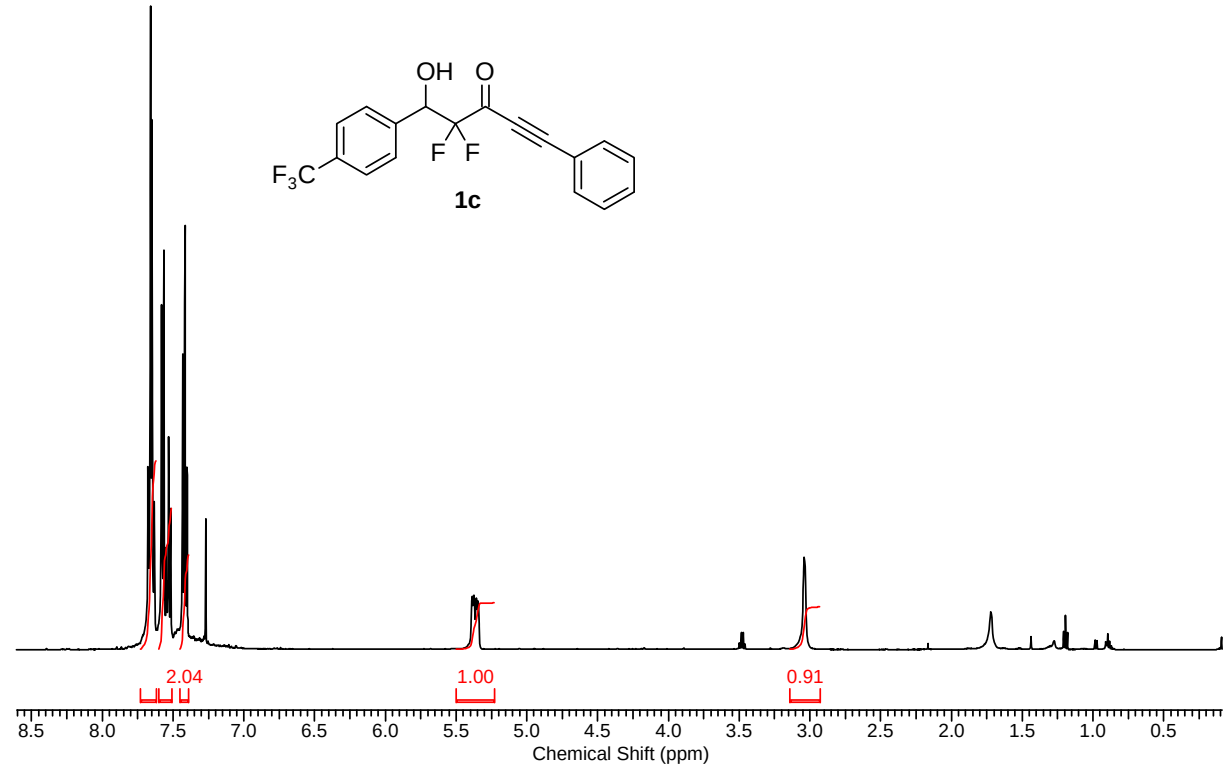
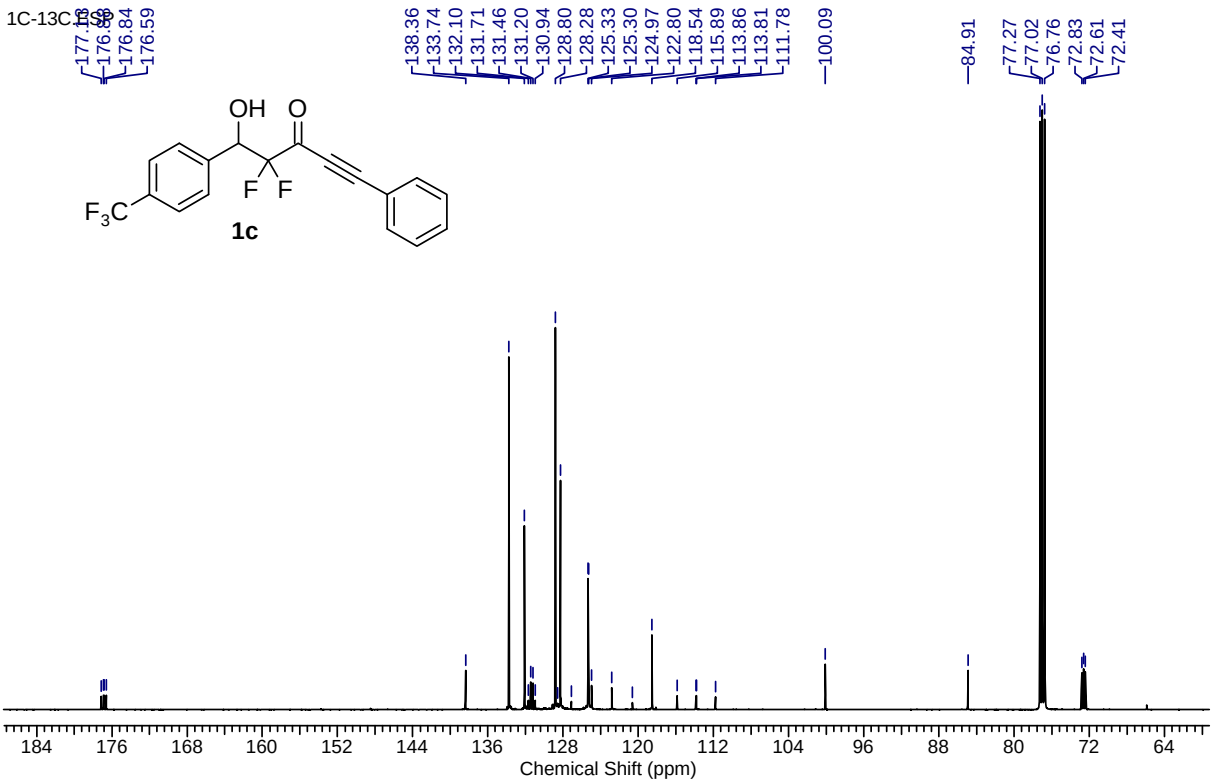
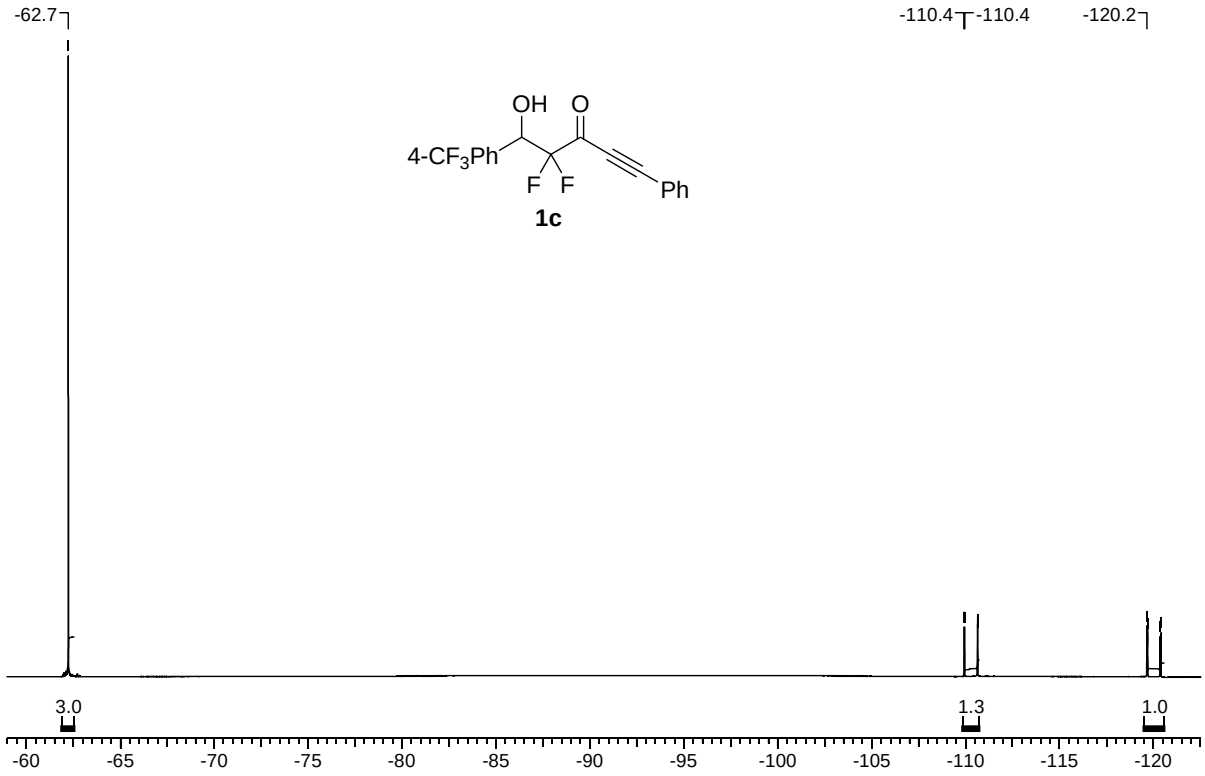
1b

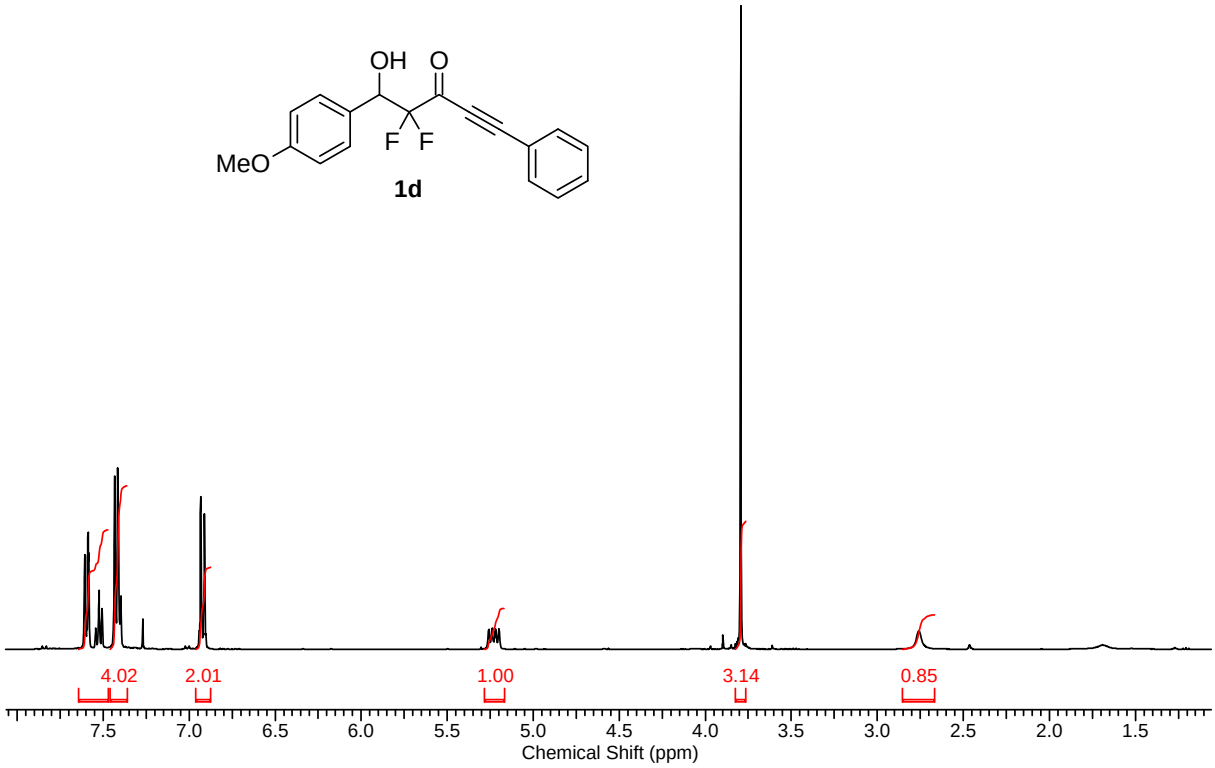
4,4-difluoro-5-hydroxy-1-phenyl-5-(4-(trifluoromethyl)phenyl)pent-1-yn-3-one (1c)

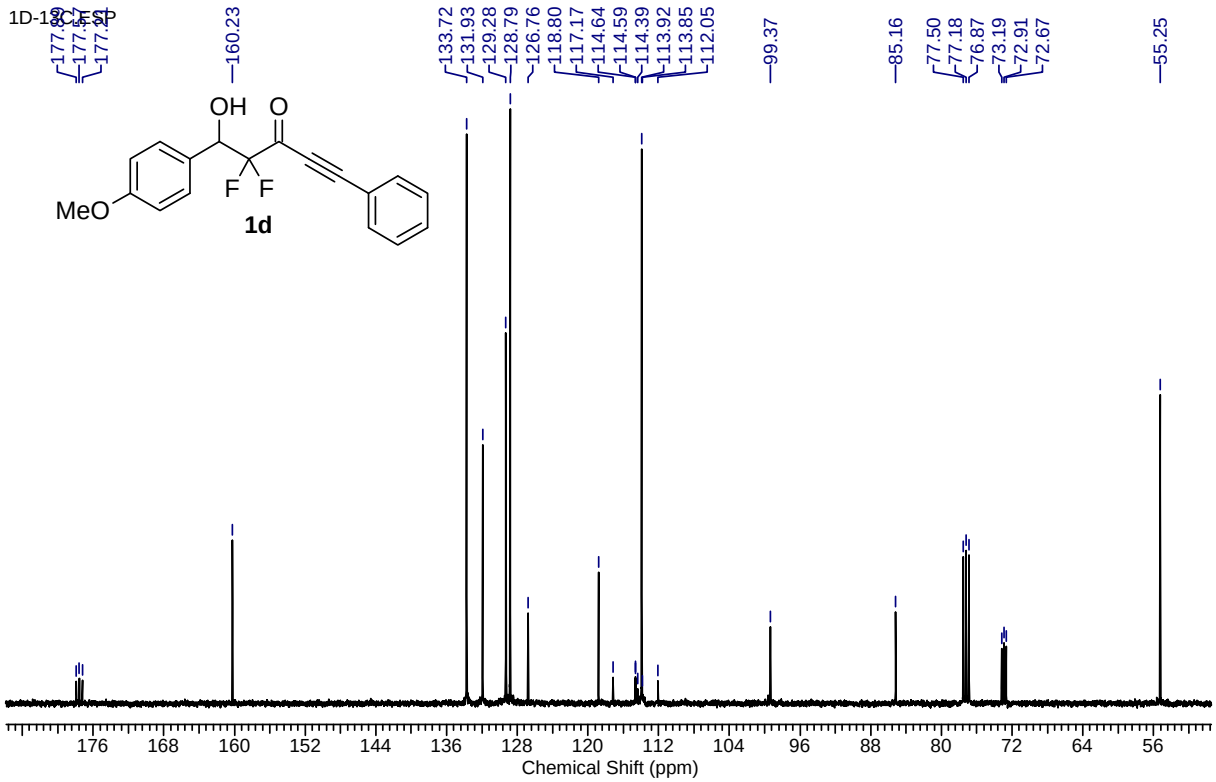






4,4-difluoro-5-hydroxy-5-(4-methoxyphenyl)-1-phenylpent-1-yn-3-one (1d)

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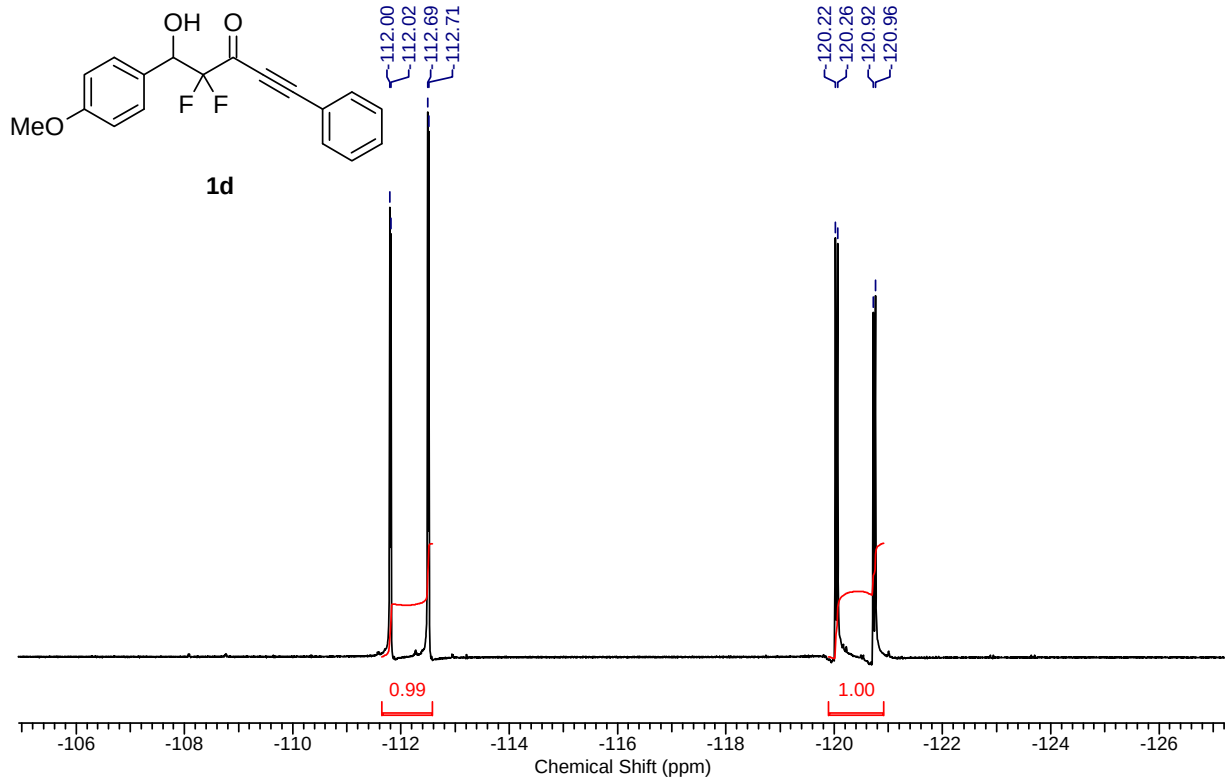
Chemical Shift (ppm)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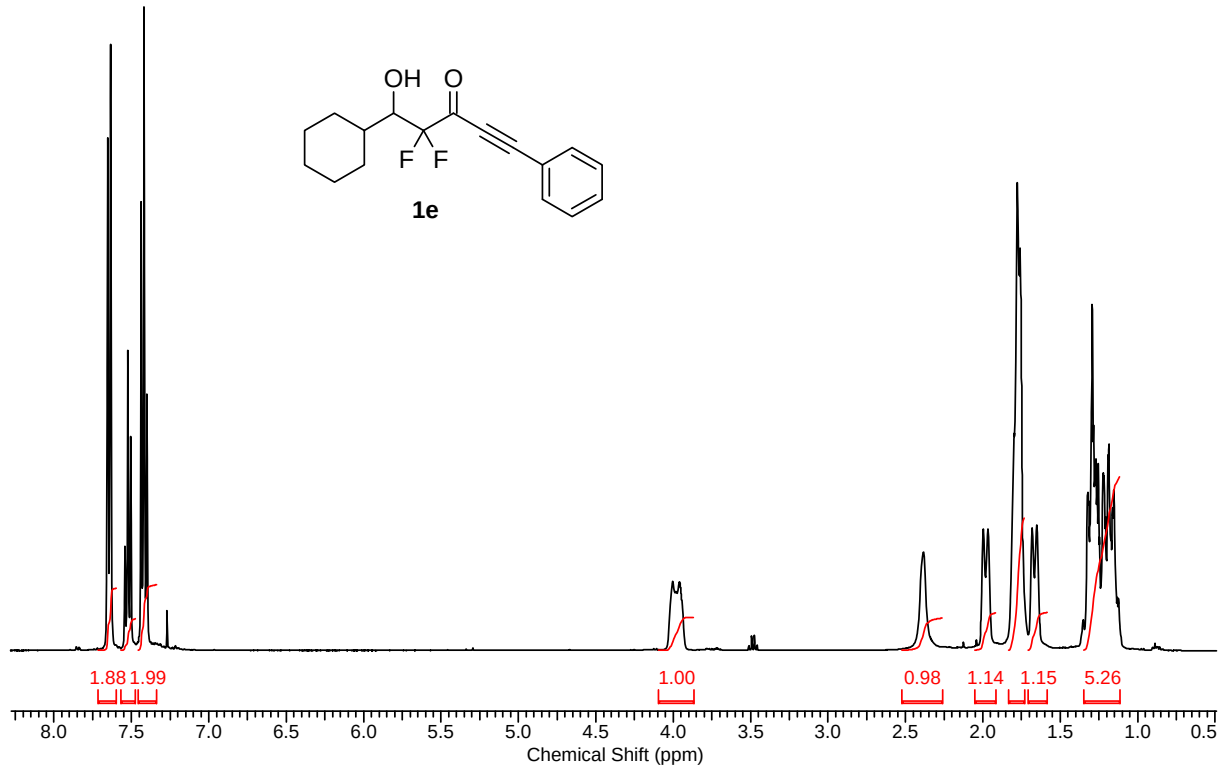
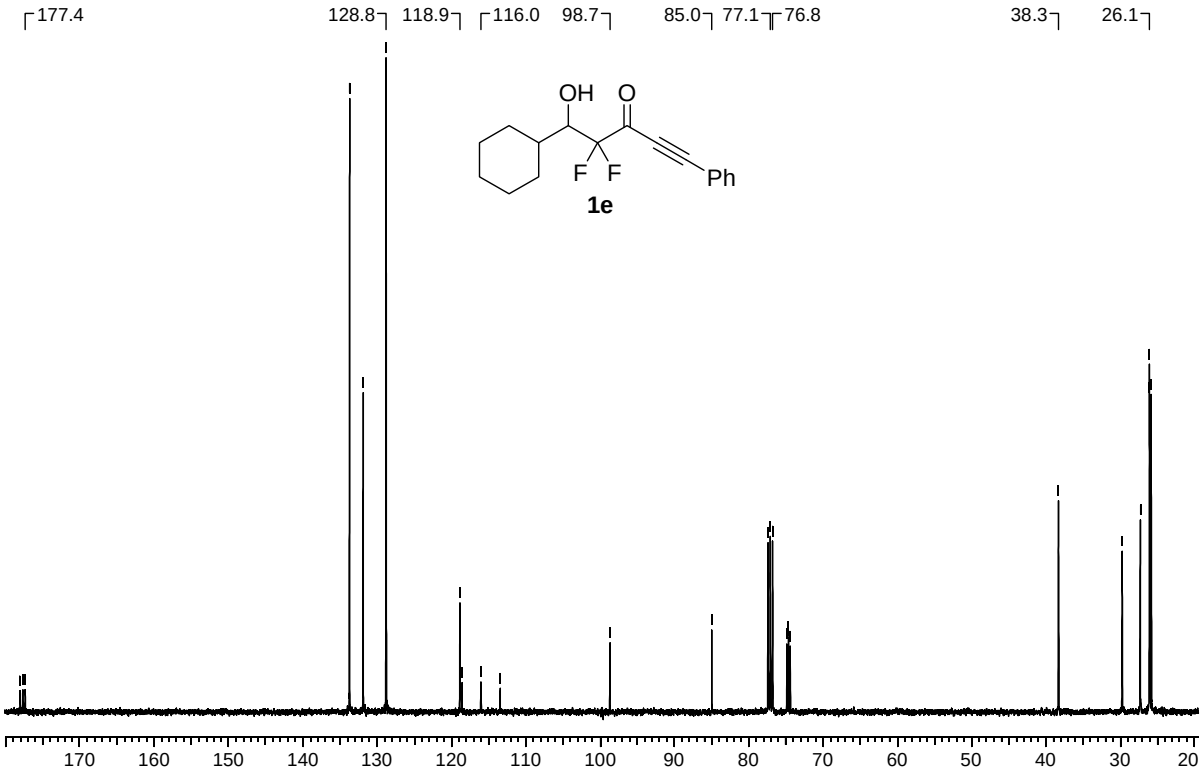
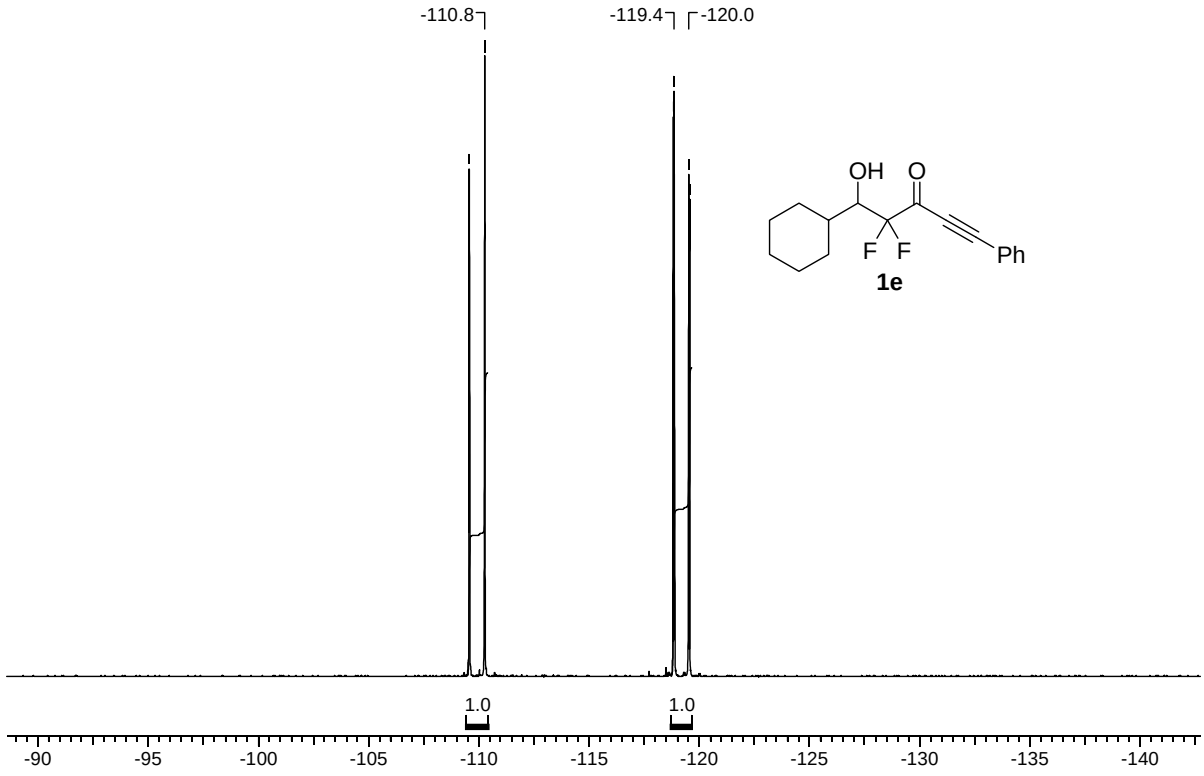
-106
-108
-110
-112
-114
-116
-118
-120
-122
-124
-126
Chemical Shift (ppm)

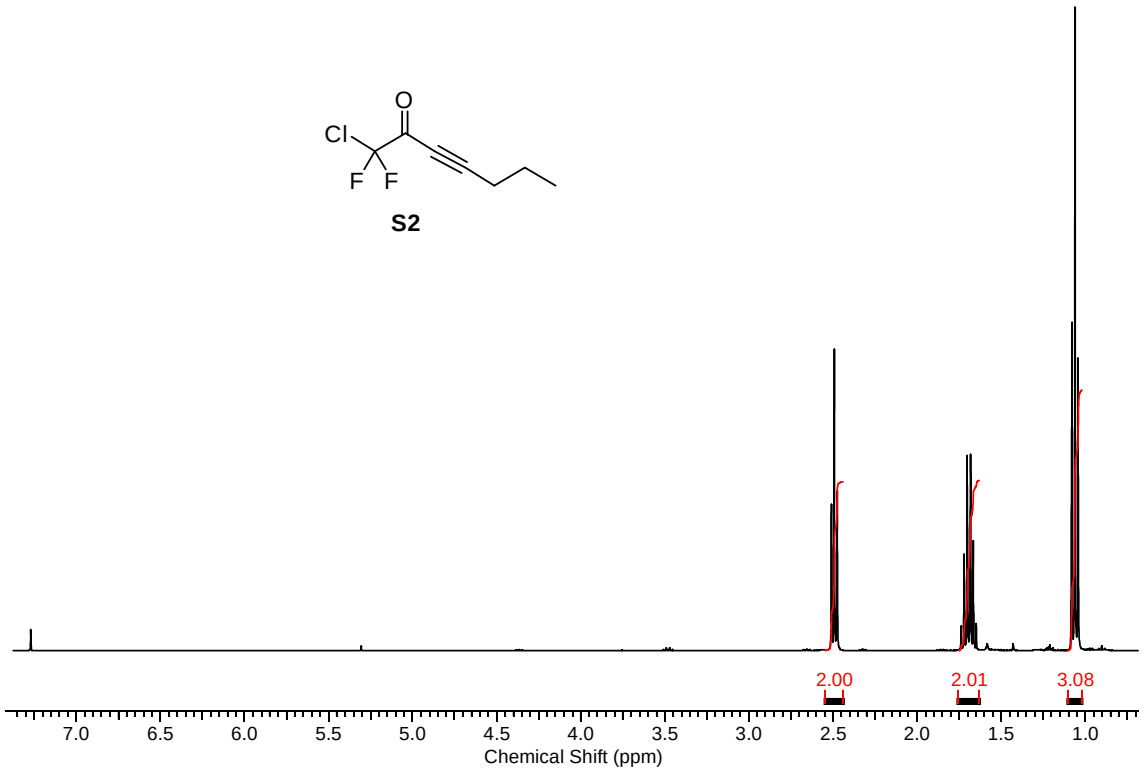
5-cyclohexyl-4,4-difluoro-5-hydroxy-1-phenylpent-1-yn-3-one (1e)

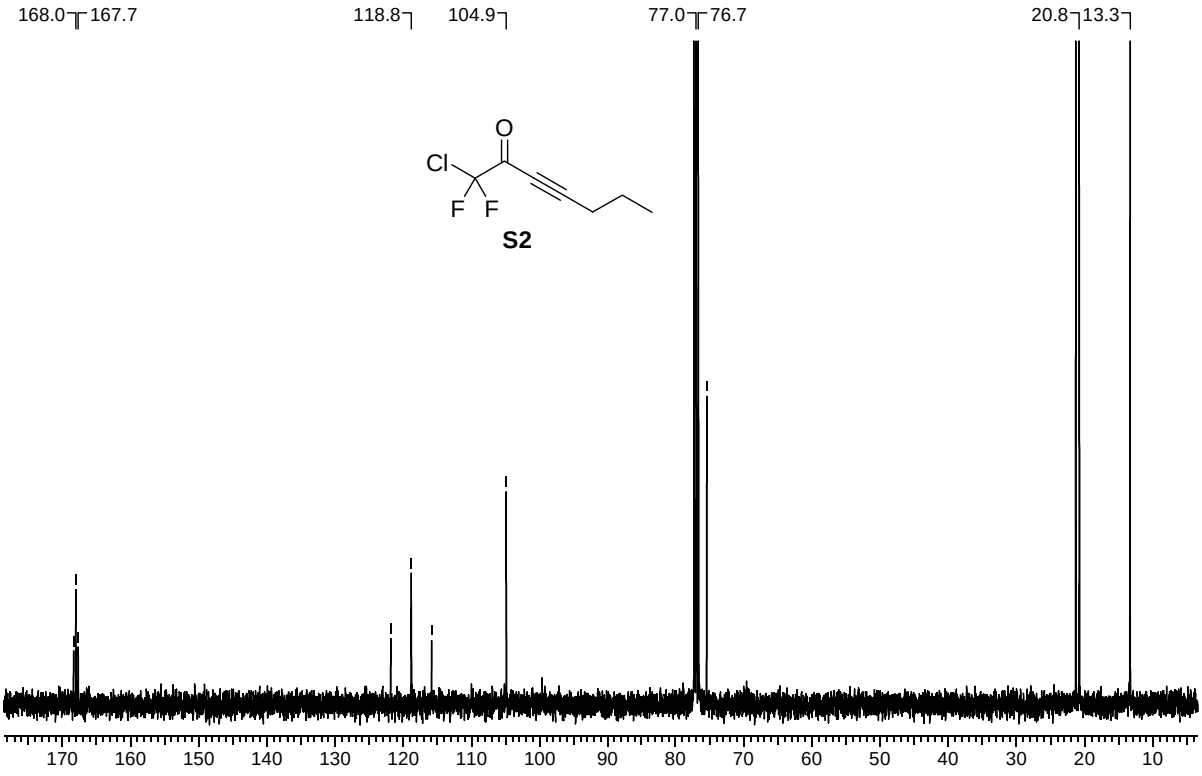


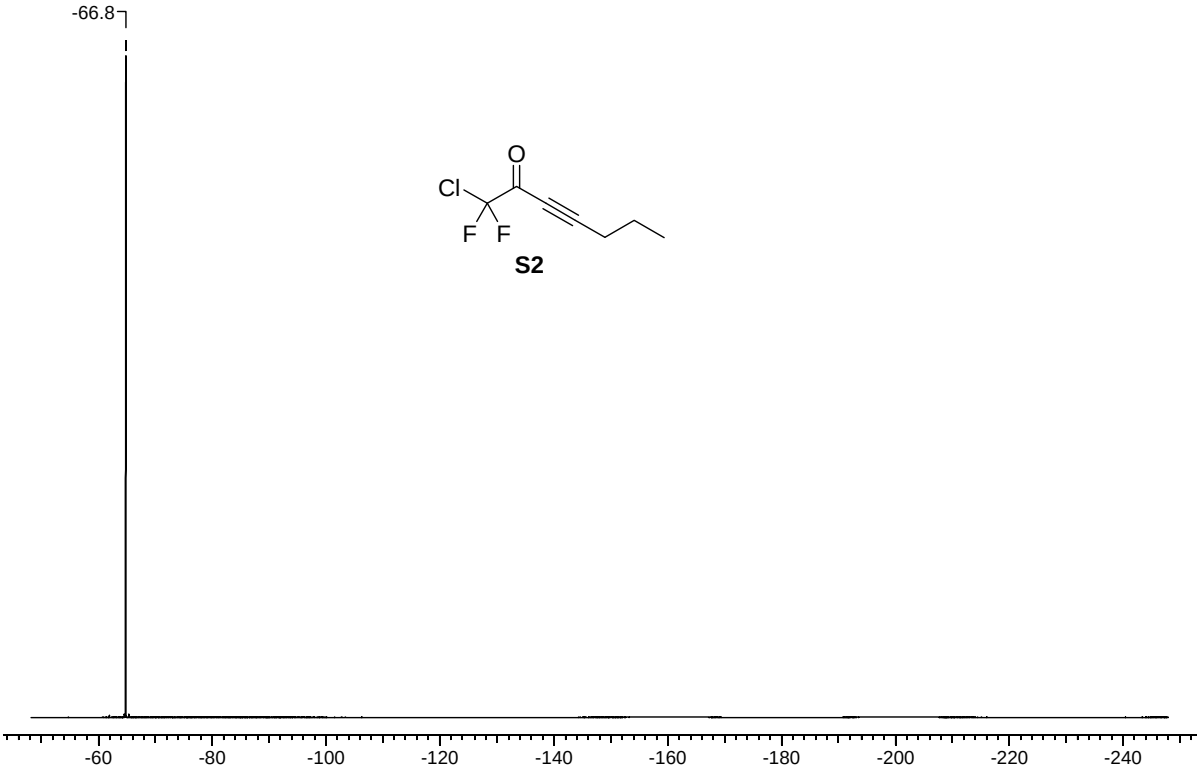




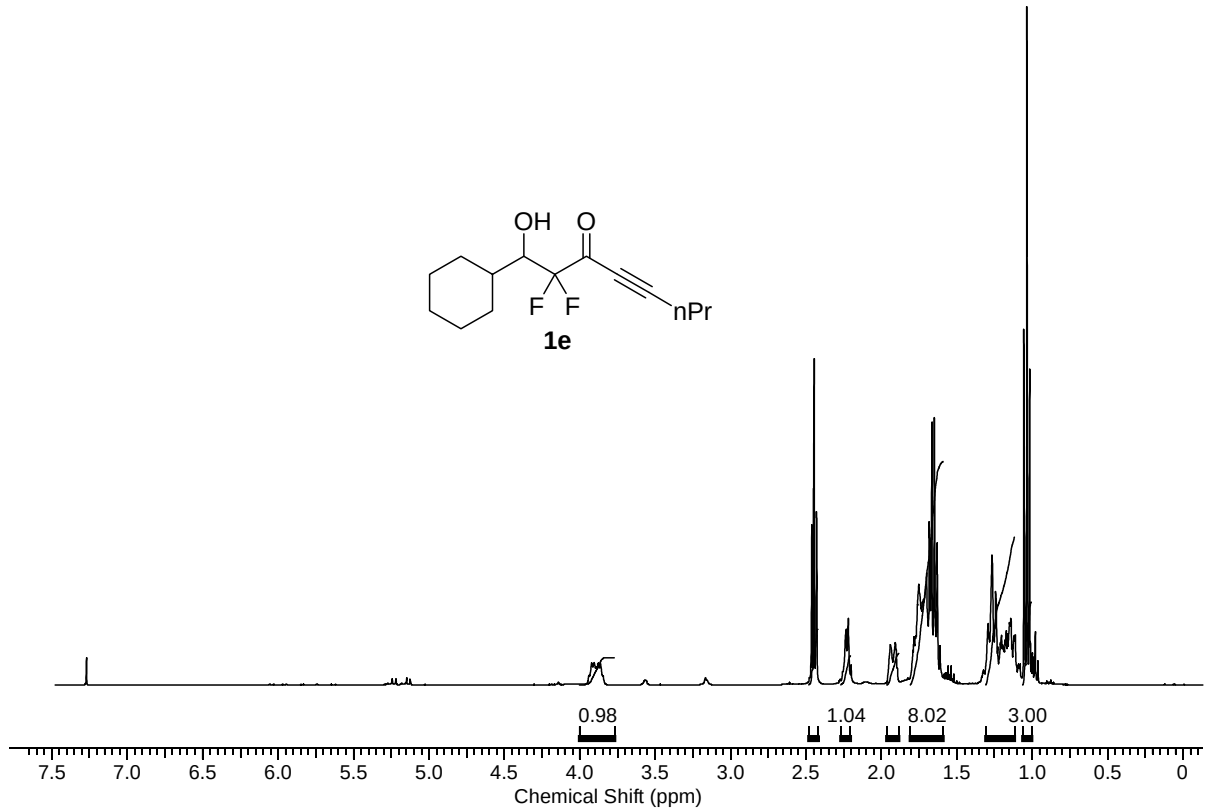
1-chloro-1,1-difluorohept-3-yn-2-one (S2)

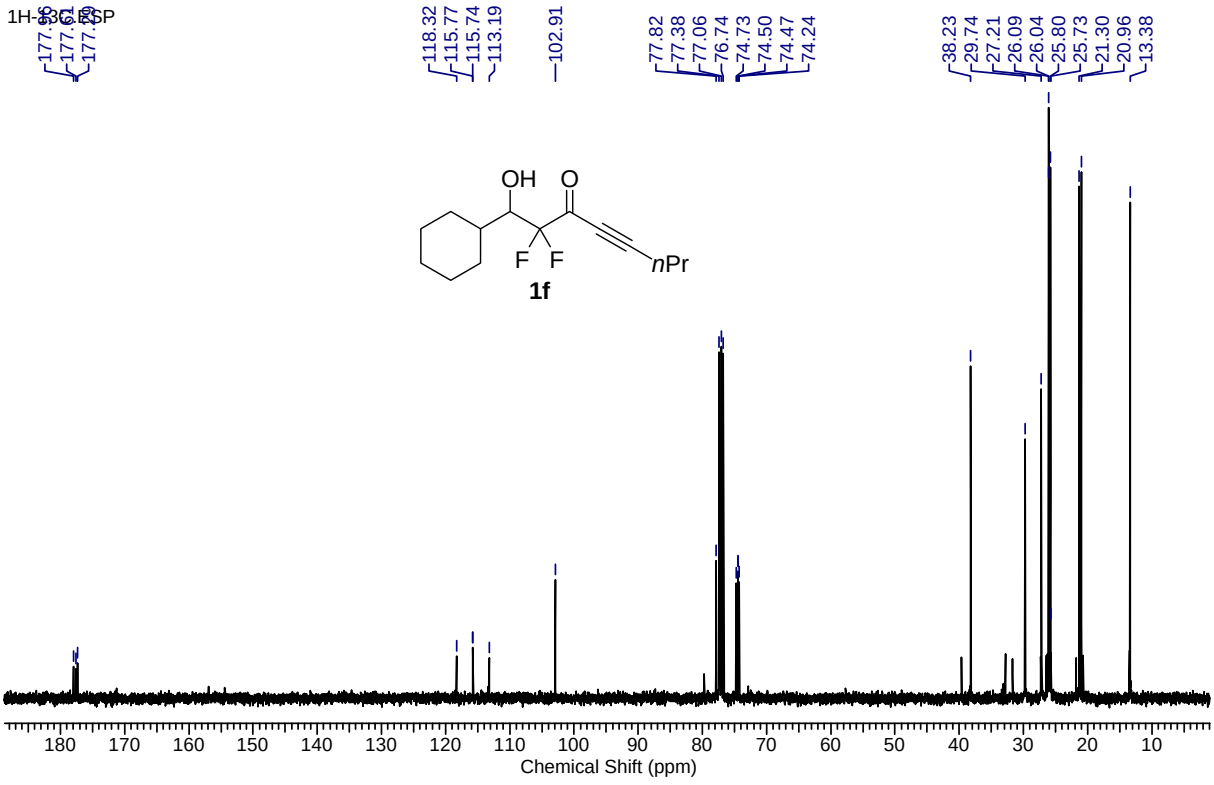


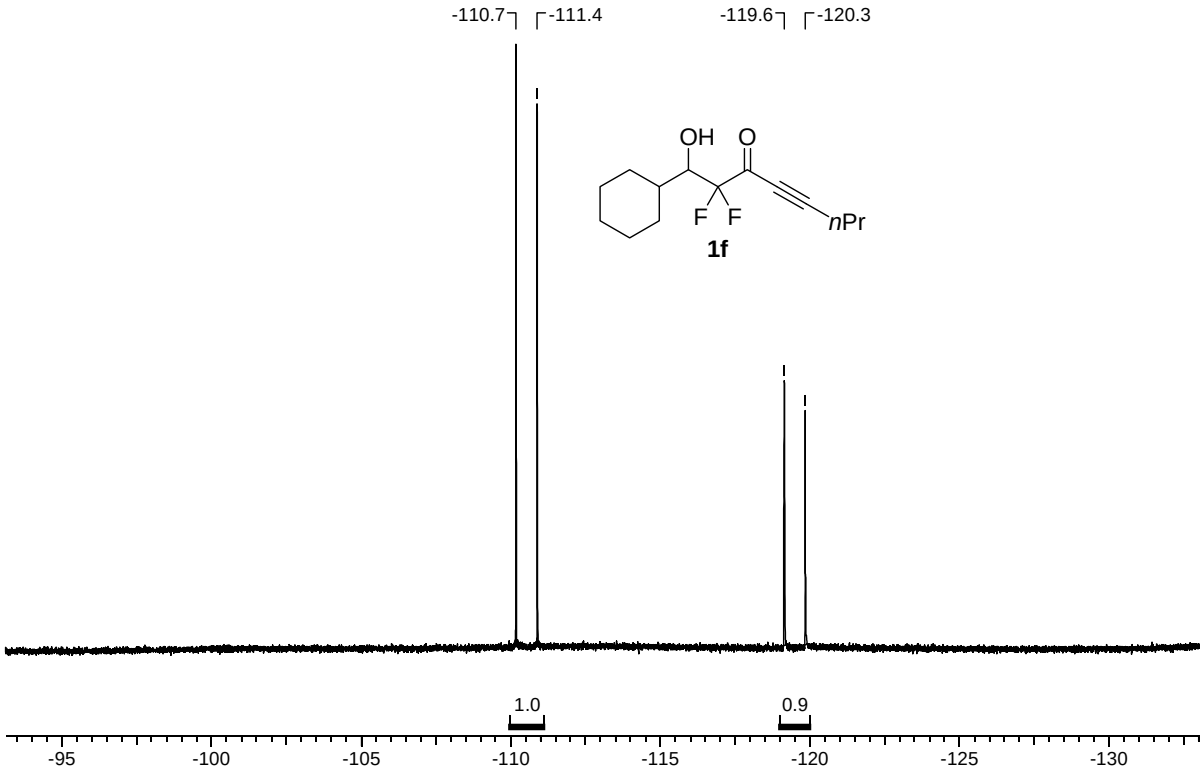

168.0
167.7
118.8
104.9
77.0
76.7
20.8
13.3
O
Cl
F F
S2
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10


-66.8
O
Cl
F F
S2
-60 -80 -100 -120 -140 -160 -180 -200 -220 -240

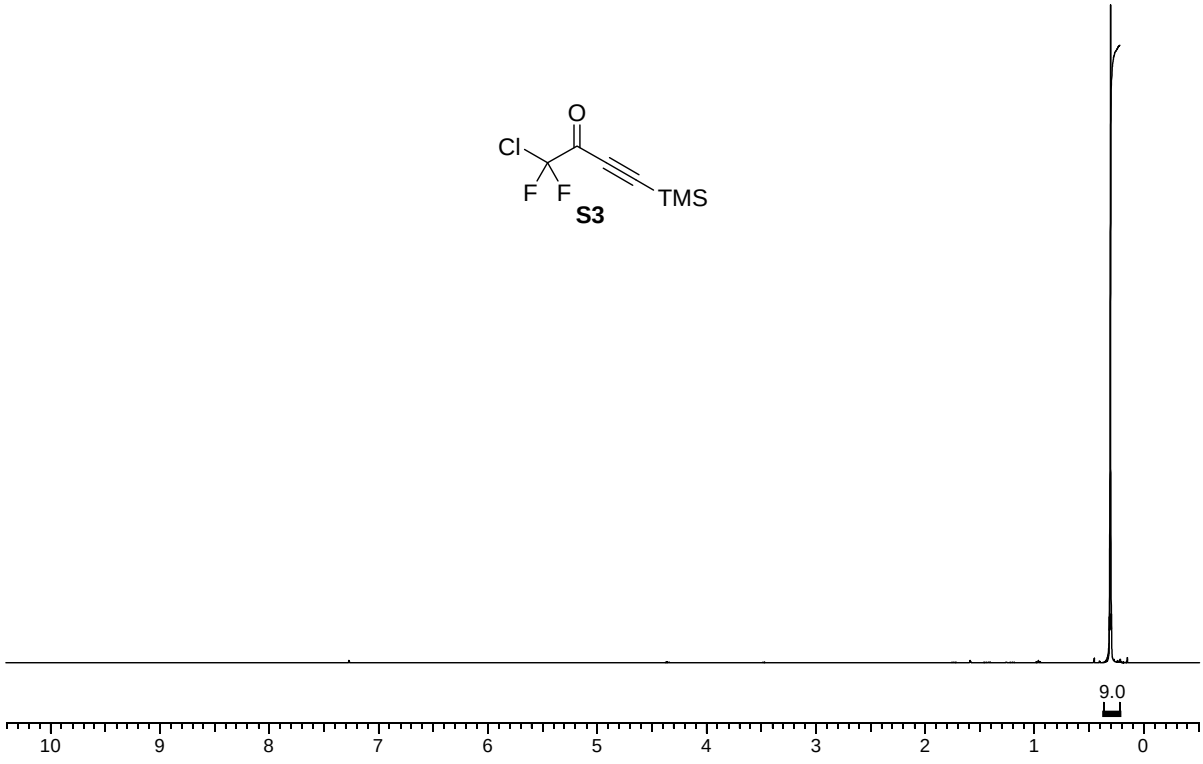
1-cyclohexyl-2,2-difluoro-1-hydroxyoct-4-yn-3-one (1f)

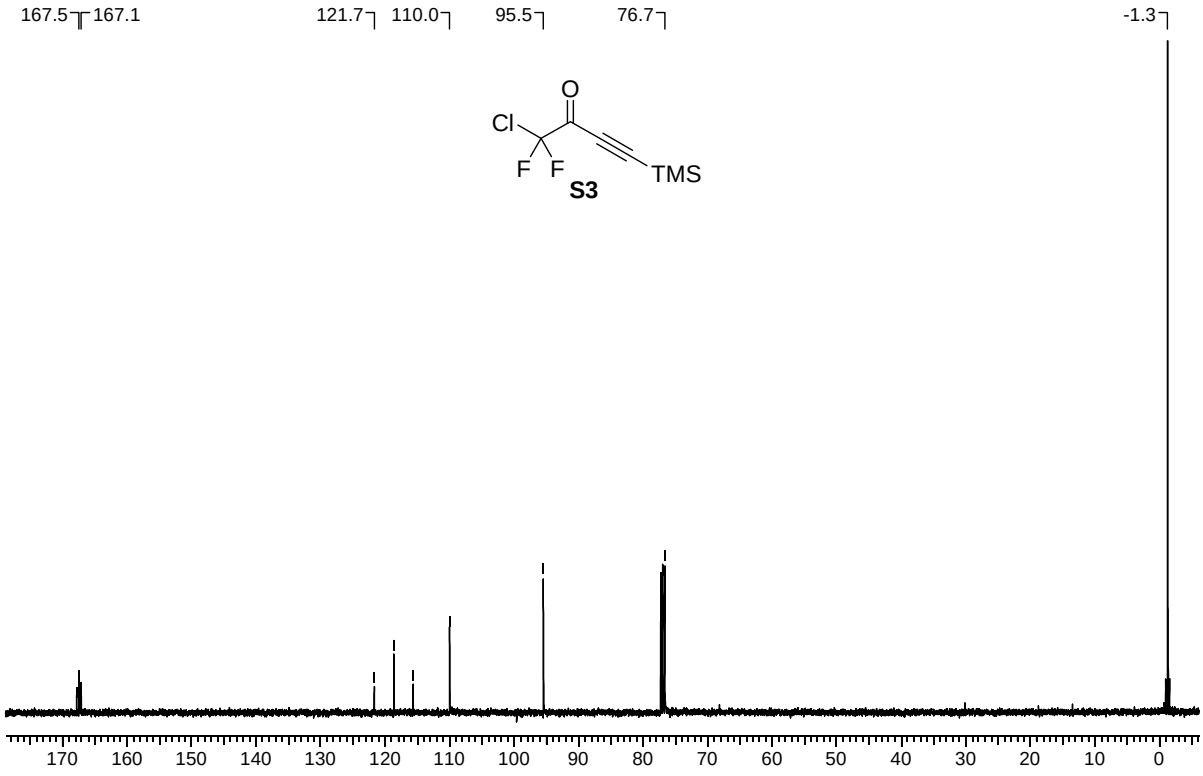


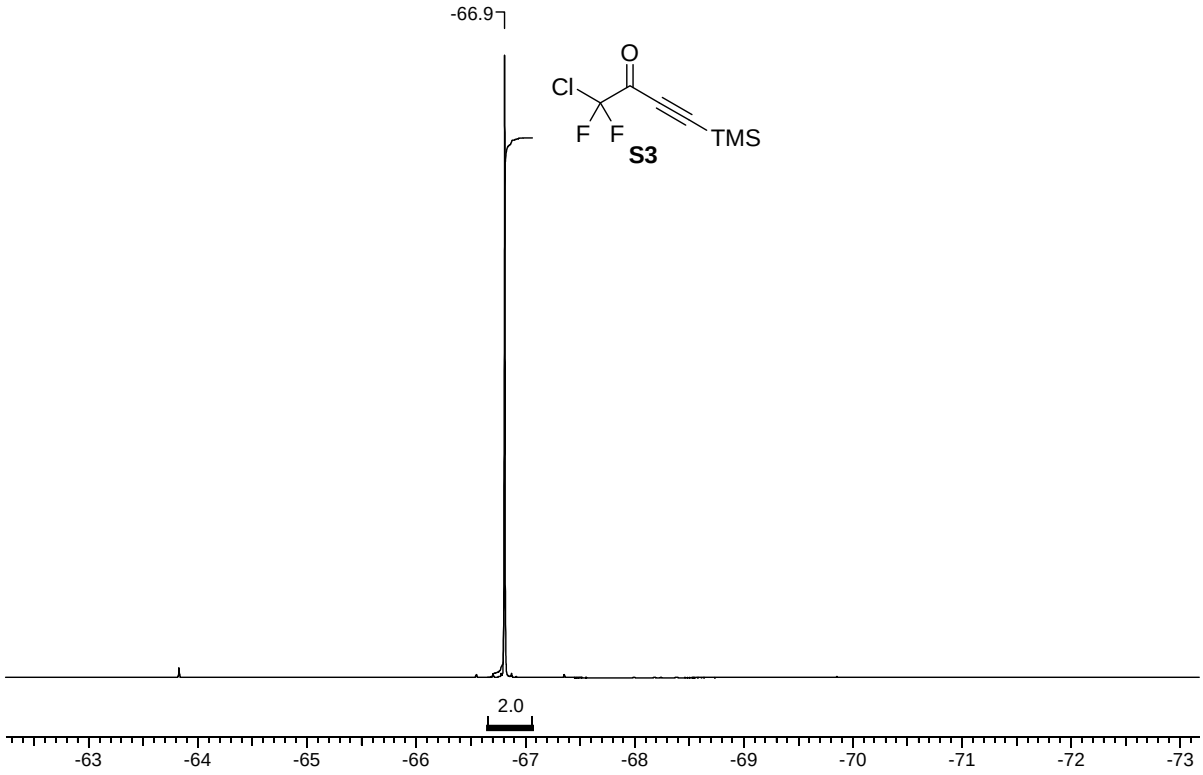




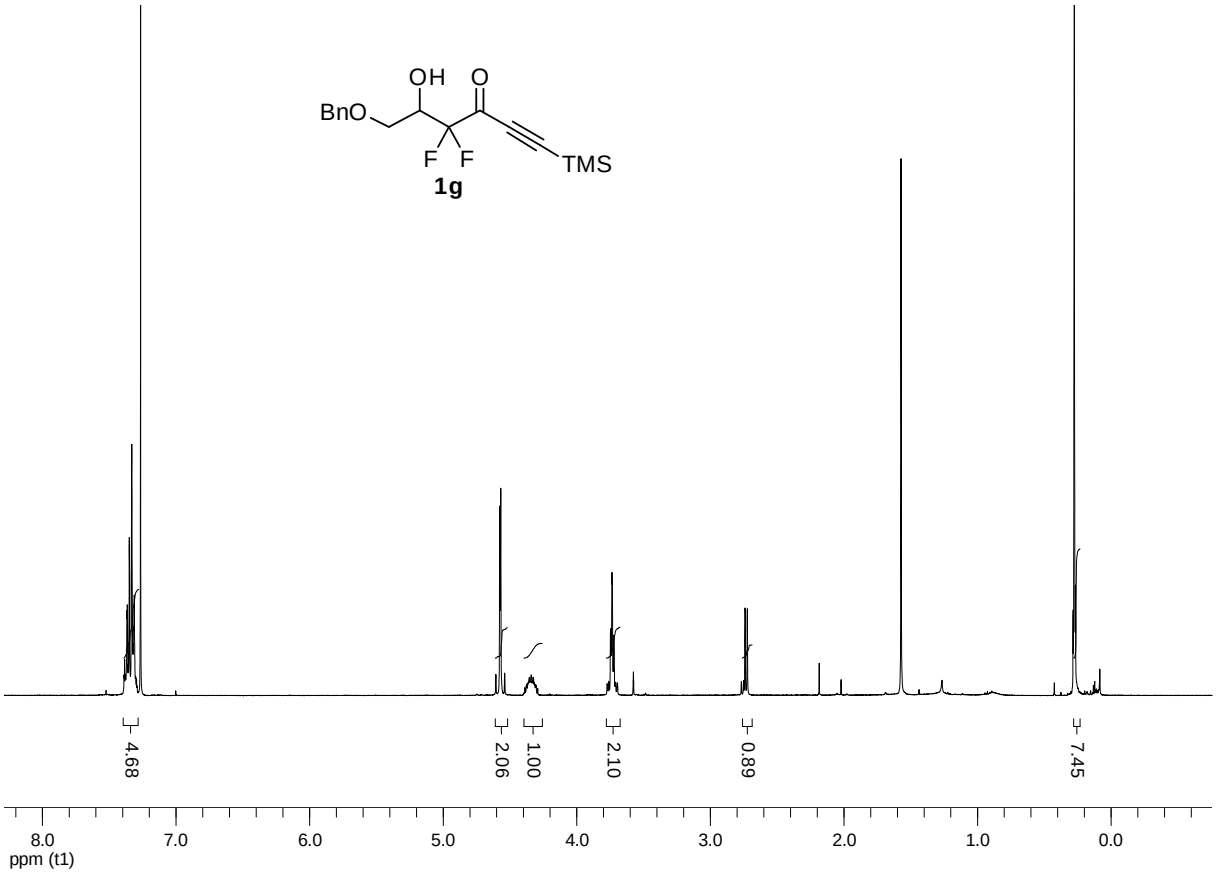
1-chloro-1,1-difluoro-4-(trimethylsilyl)but-3-yn-2-one (S3)

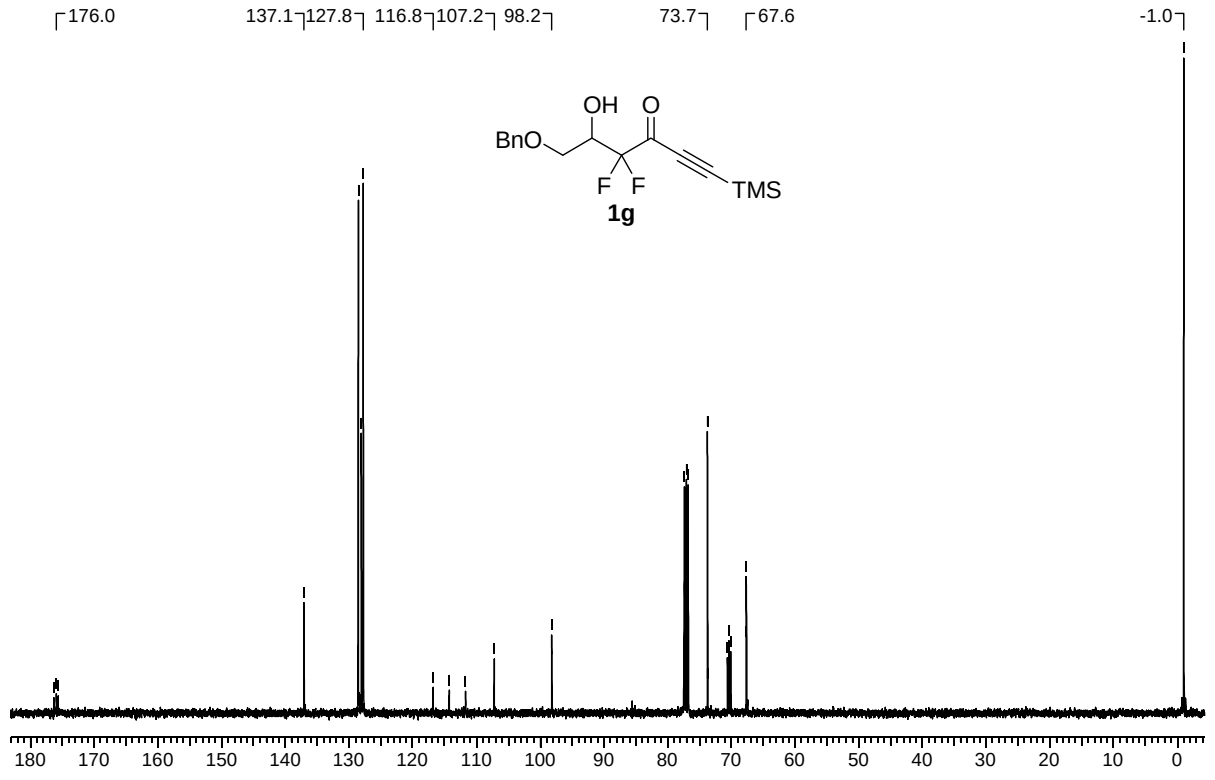


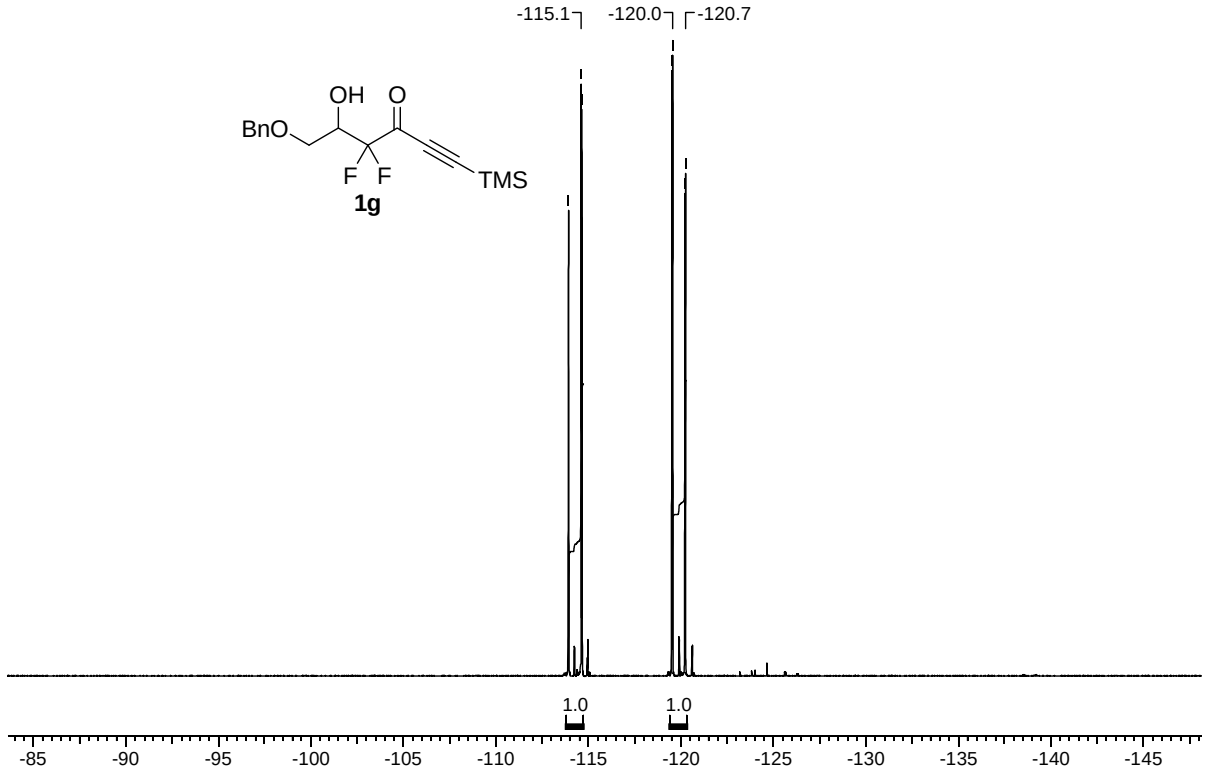

167.5
167.1
121.7
110.0
95.5
76.7
-1.3
O
Cl
F
F
TMS
S3
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


-66.9
O
Cl
F
F
TMS
S3
2.0
-63
-64
-65
-66
-67
-68
-69
-70
-71
-72
-73

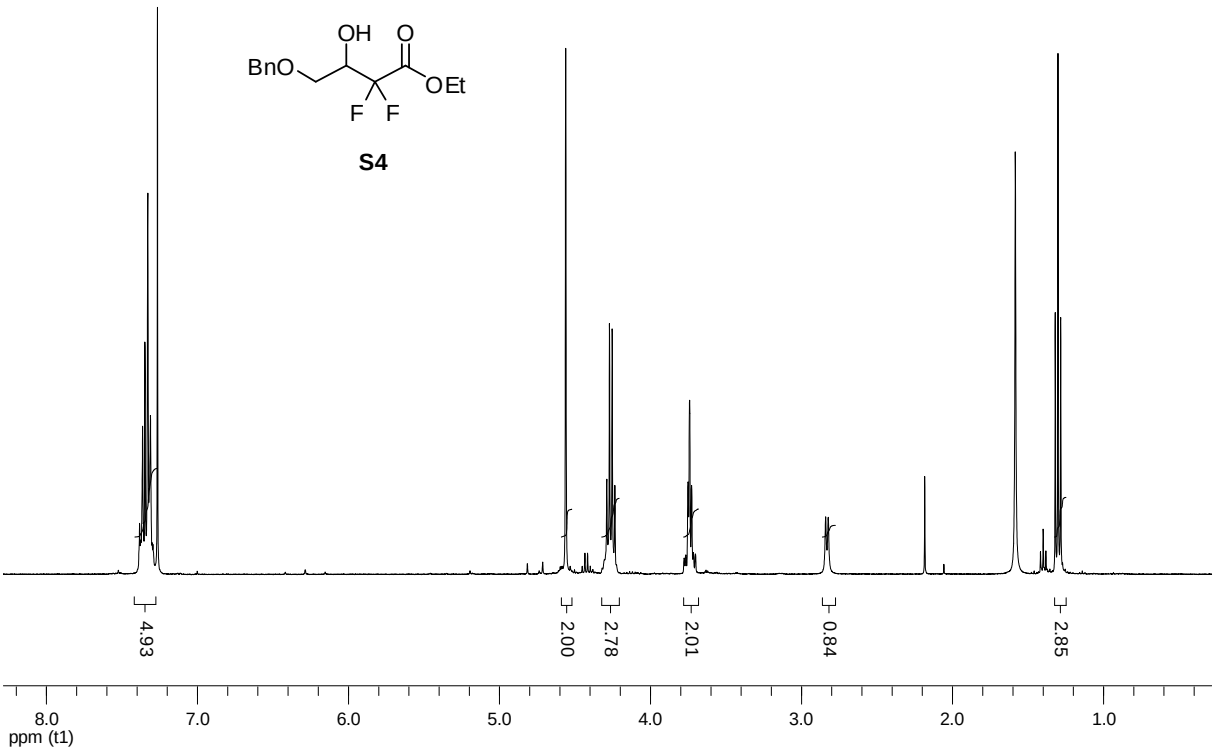
6-(benzyloxy)-4,4-difluoro-5-hydroxy-1-(trimethylsilyl)hex-1-yn-3-one (1g)

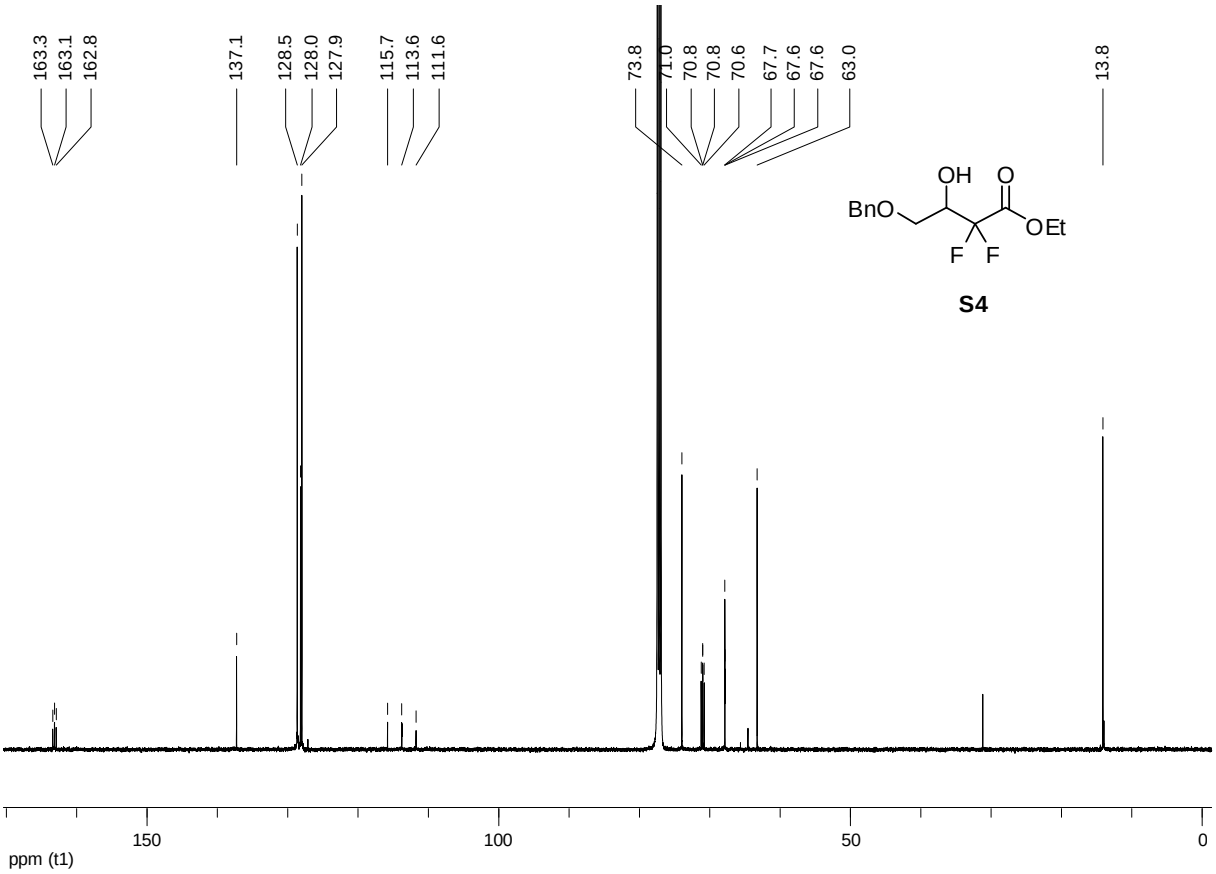




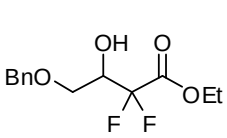


Ethyl 4-(benzyloxy)-2,2-difluoro-3-hydroxybutanoate (S4)

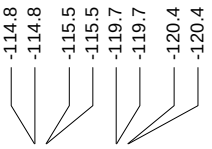


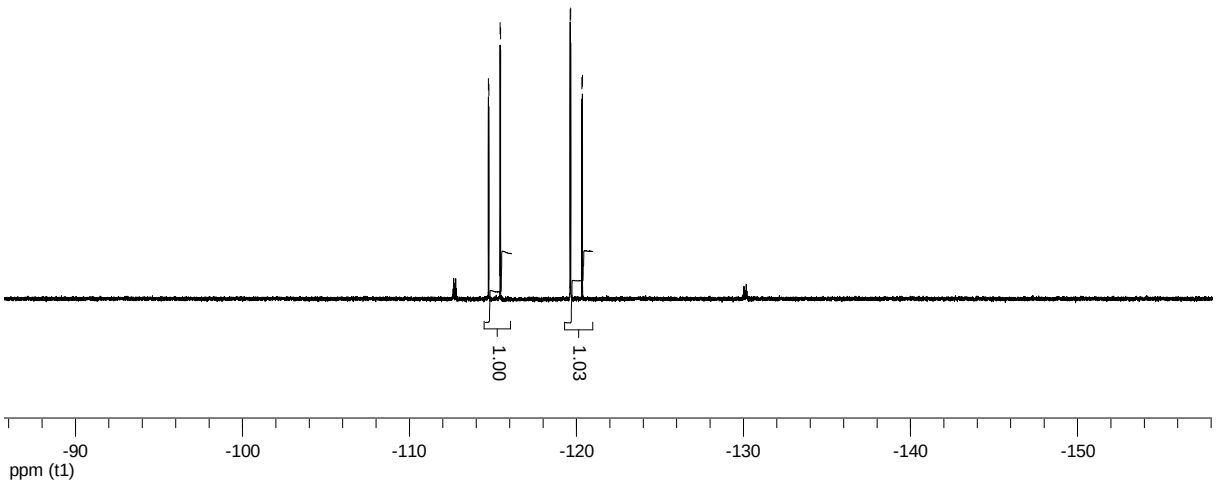

163.3
163.1
162.8
137.1
128.5
128.0
127.9
115.7
113.6
111.6
73.8
71.0
70.8
70.8
70.6
67.7
67.6
67.6
63.0
13.8
OH
O
BnO
OEt
F F
150
100
50
0
ppm (t1)

S4

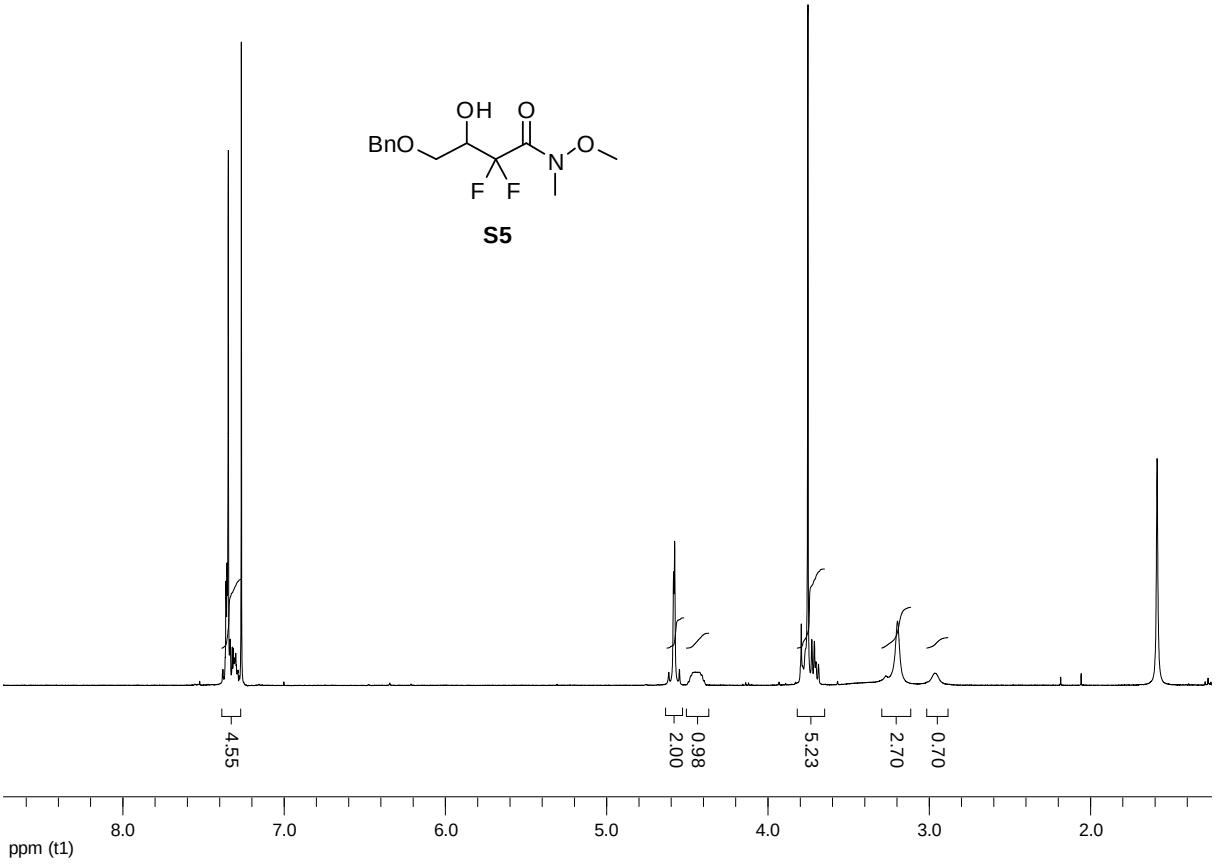

OH
O
BnO
OEt
F F

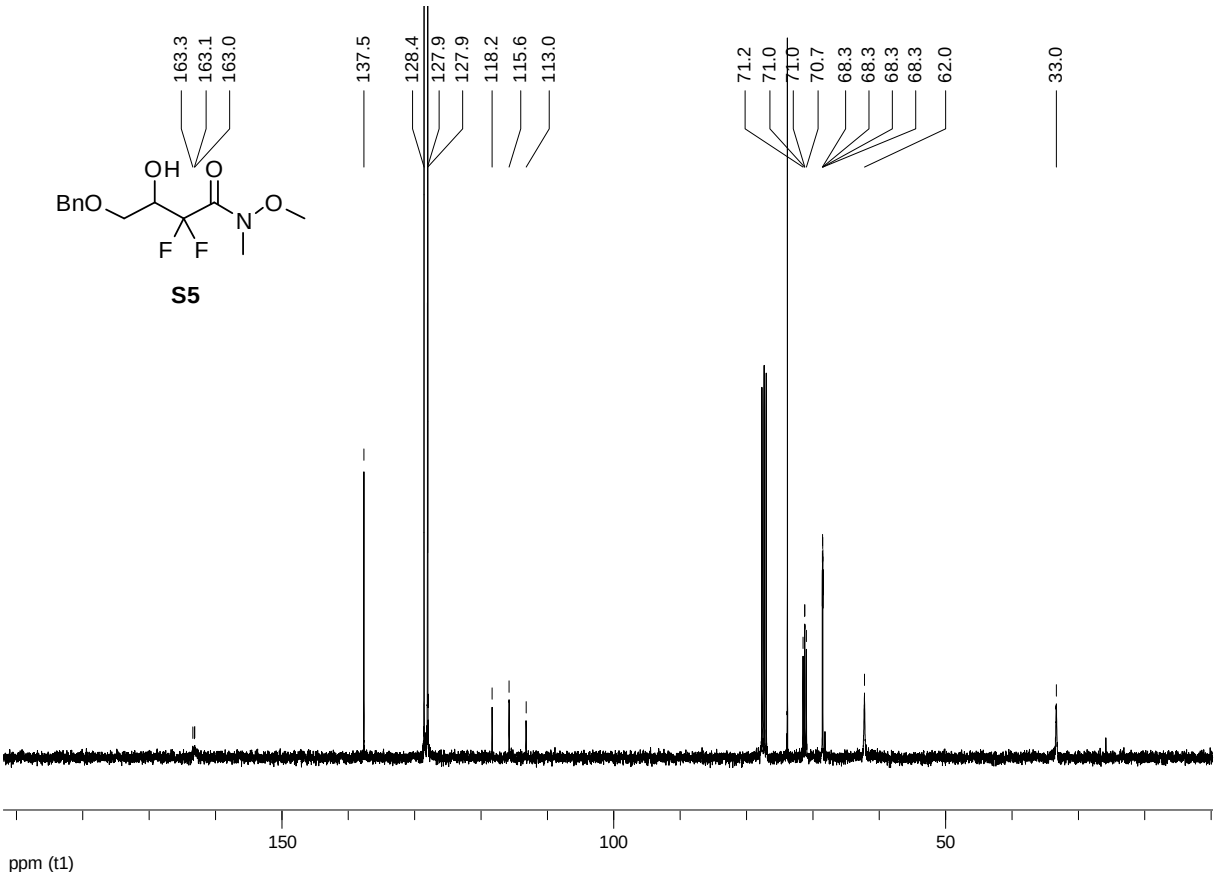
S4

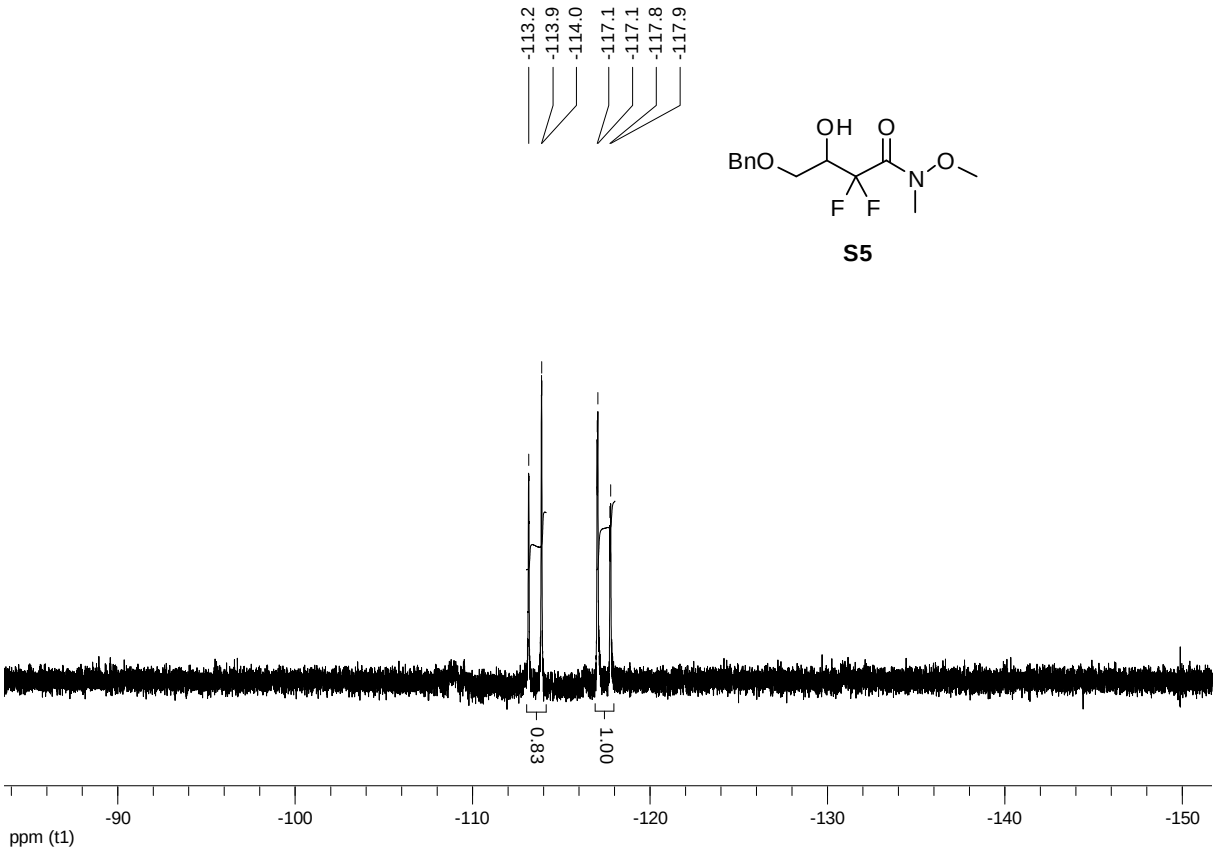

-114.8
-114.8
-115.5
-115.5
-119.7
-119.7
-120.4
-120.4


1.00
1.03
-90
-100
-110
-120
-130
-140
-150
ppm (t1)

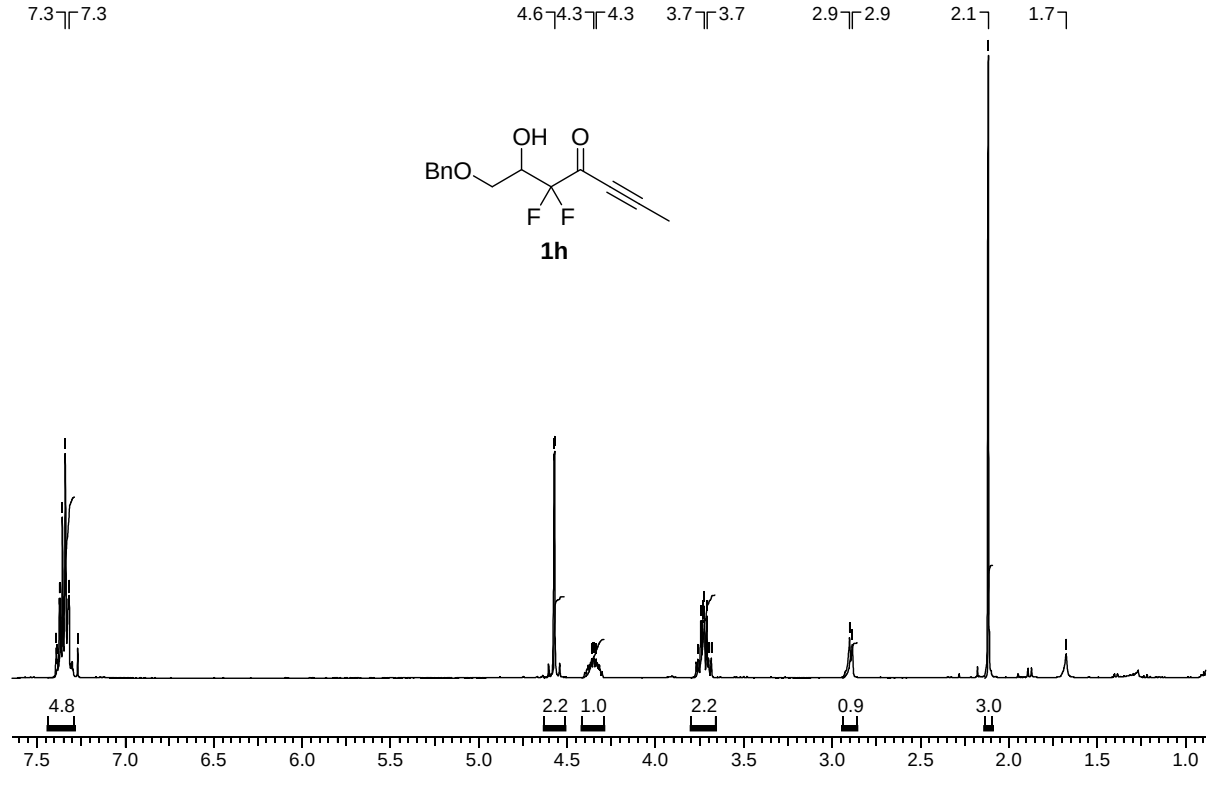
4-(benzyloxy)-2,2-difluoro-3-hydroxy-*N*-methoxy-*N*-methylbutanamide (S5)

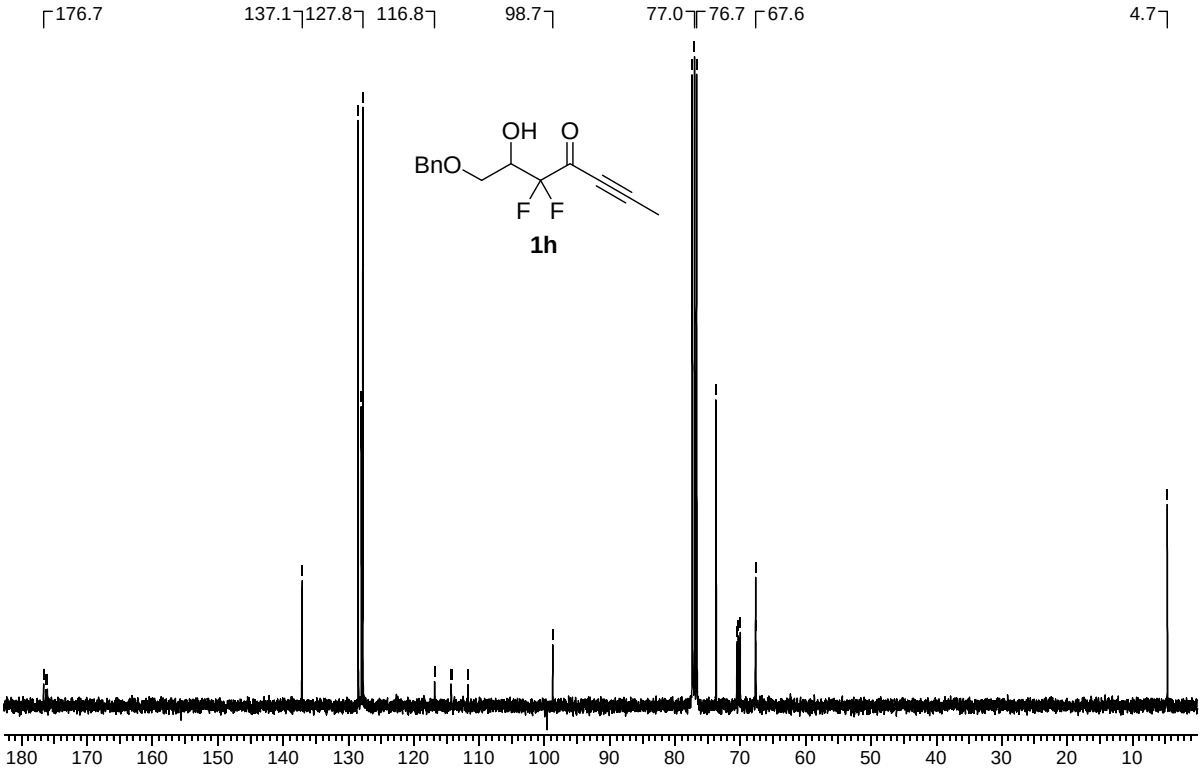


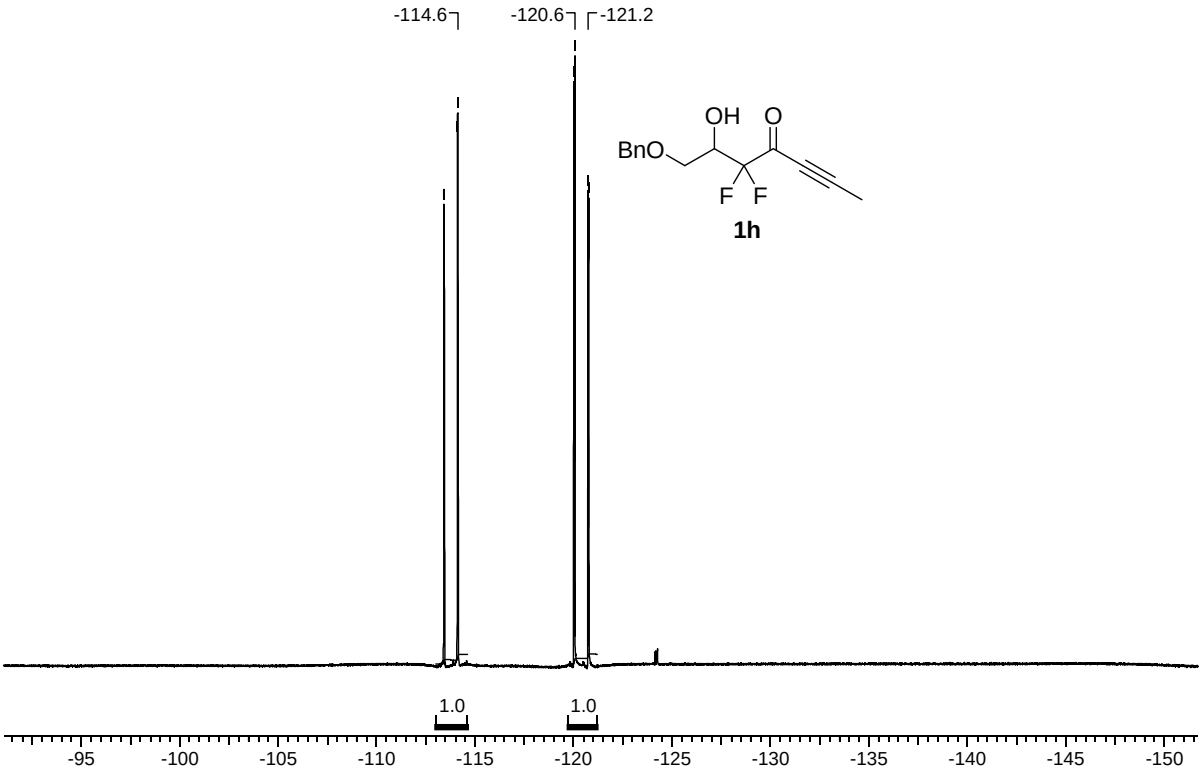




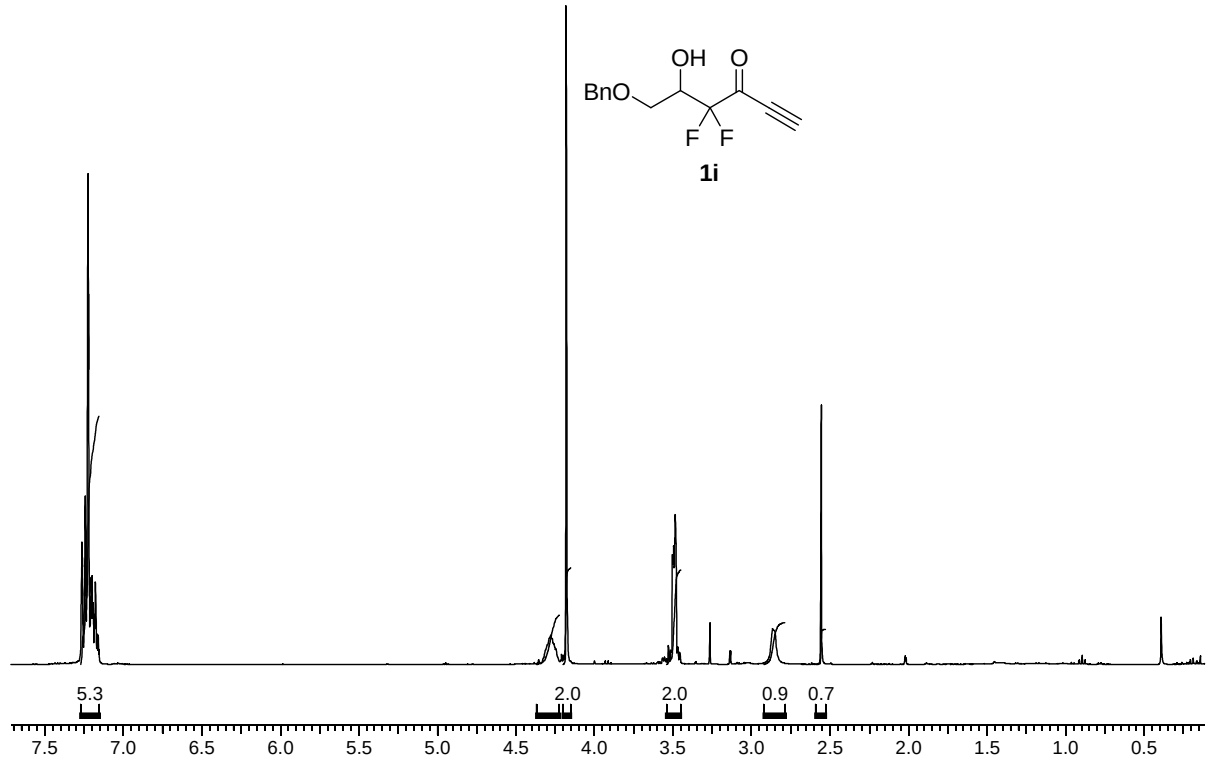
7-(benzyloxy)-5,5-difluoro-6-hydroxyhept-2-yn-4-one (1h)

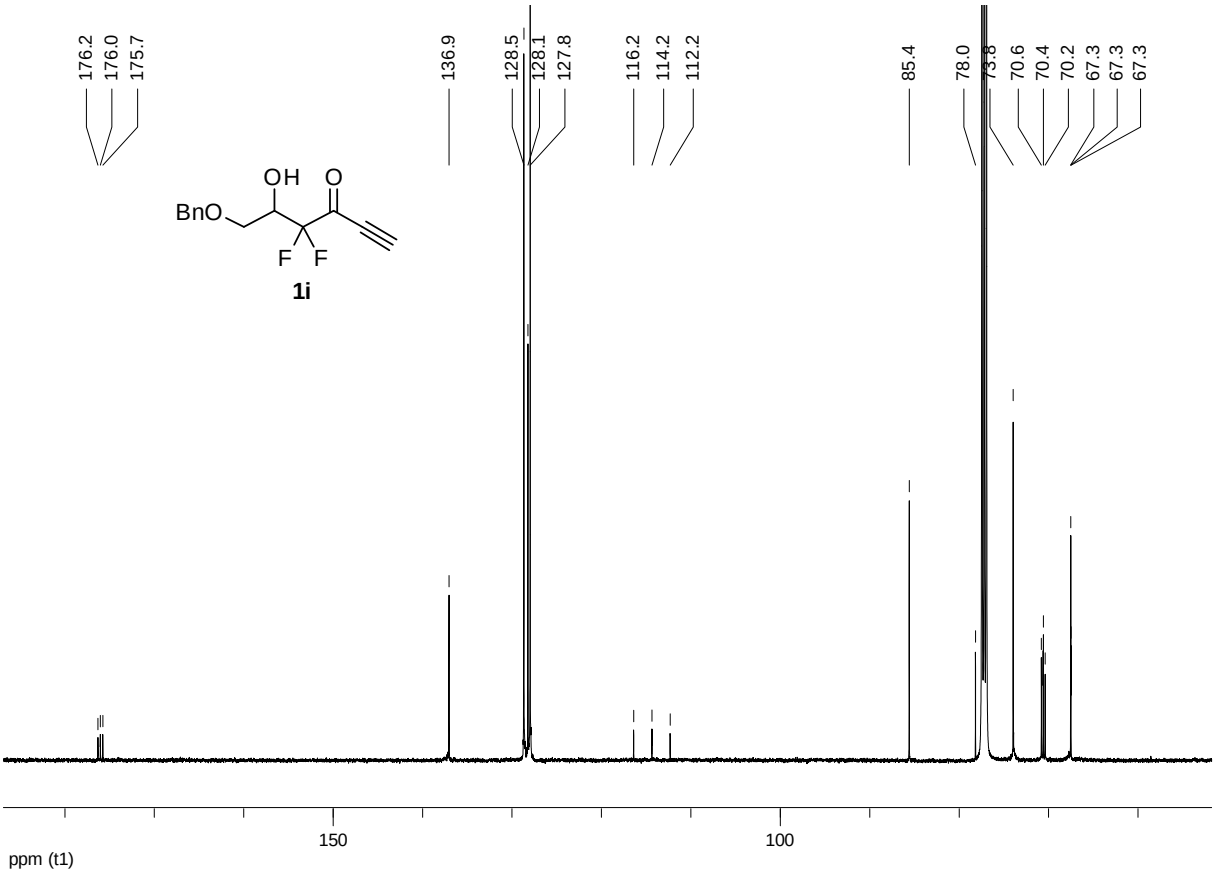


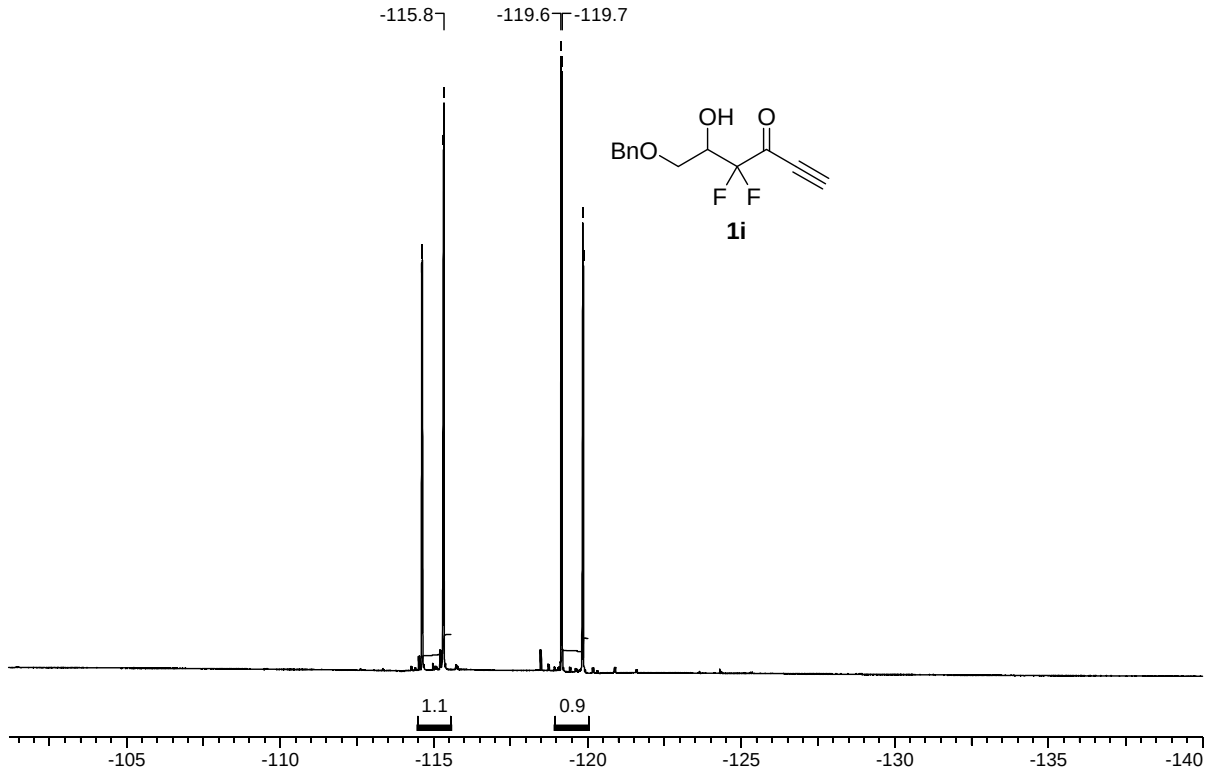

176.7
137.1
127.8
116.8
98.7
77.0
76.7
67.6
4.7
OH
O
BnO
F
F
1h
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


-114.6
-120.6
-121.2
OH
O
BnO
F
F
1h
1.0
1.0
-95
-100
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150

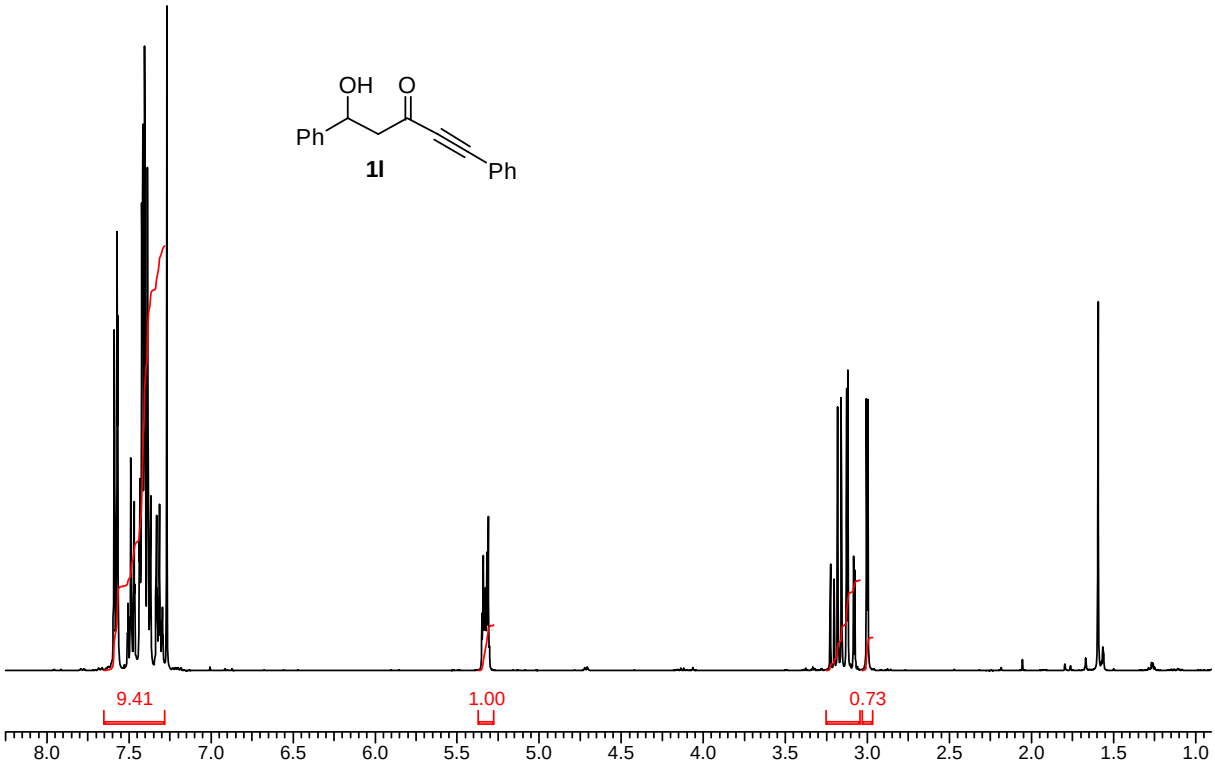
6-(benzyloxy)-4,4-difluoro-5-hydroxyhex-1-yn-3-one (1i)

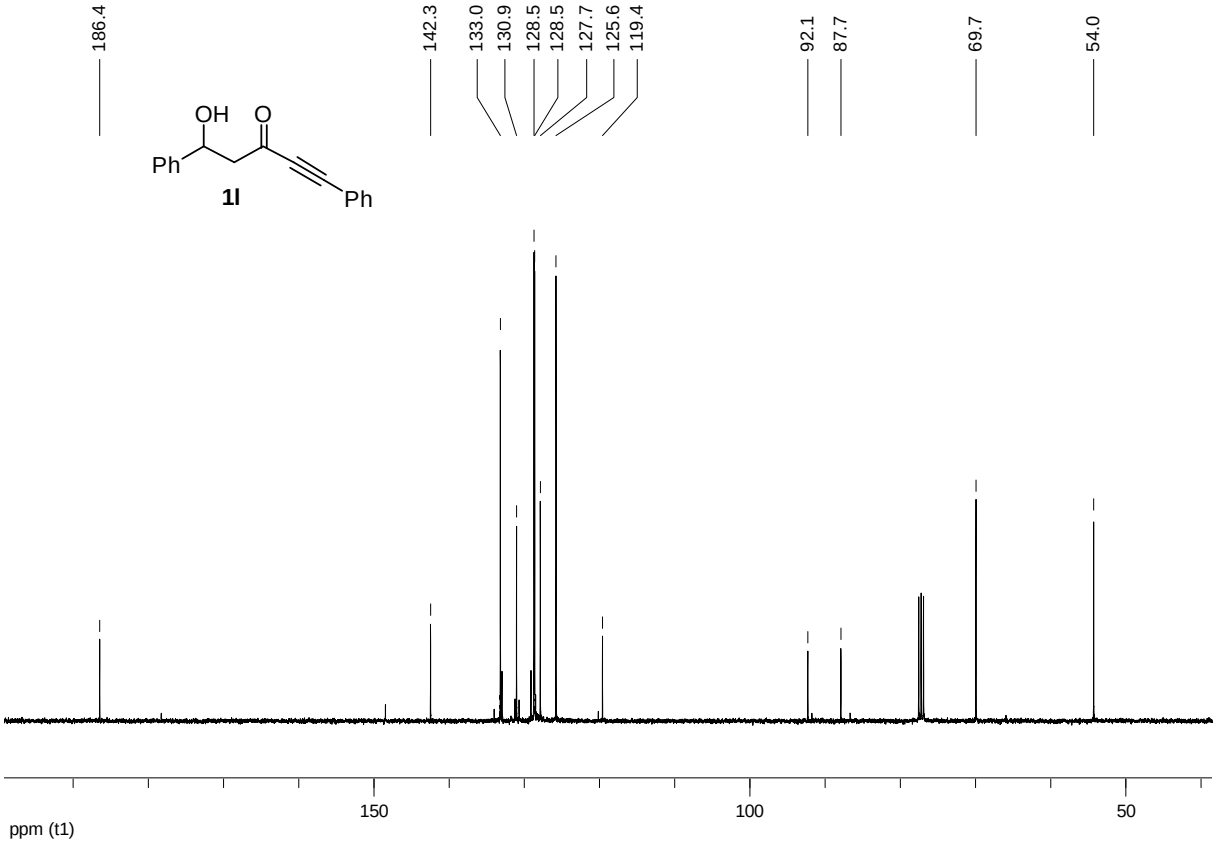






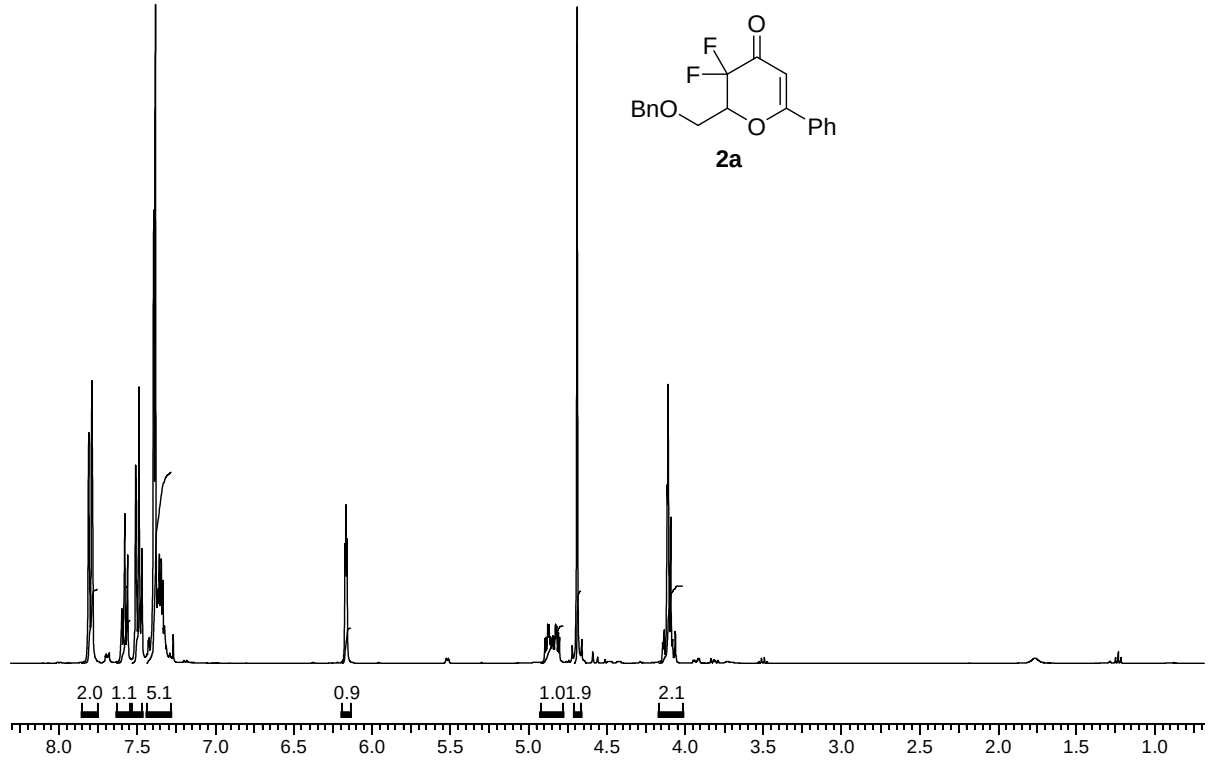
5-hydroxy-1,5-diphenylpent-1-yn-3-one(1l)

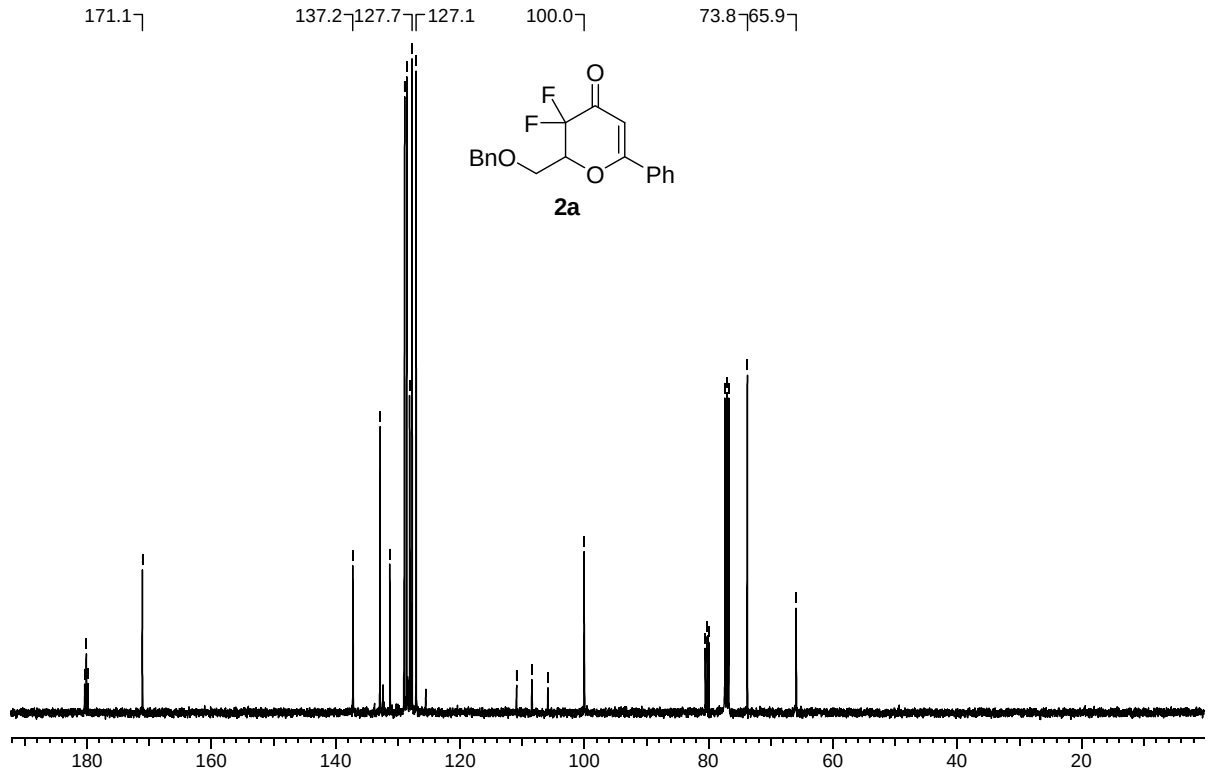


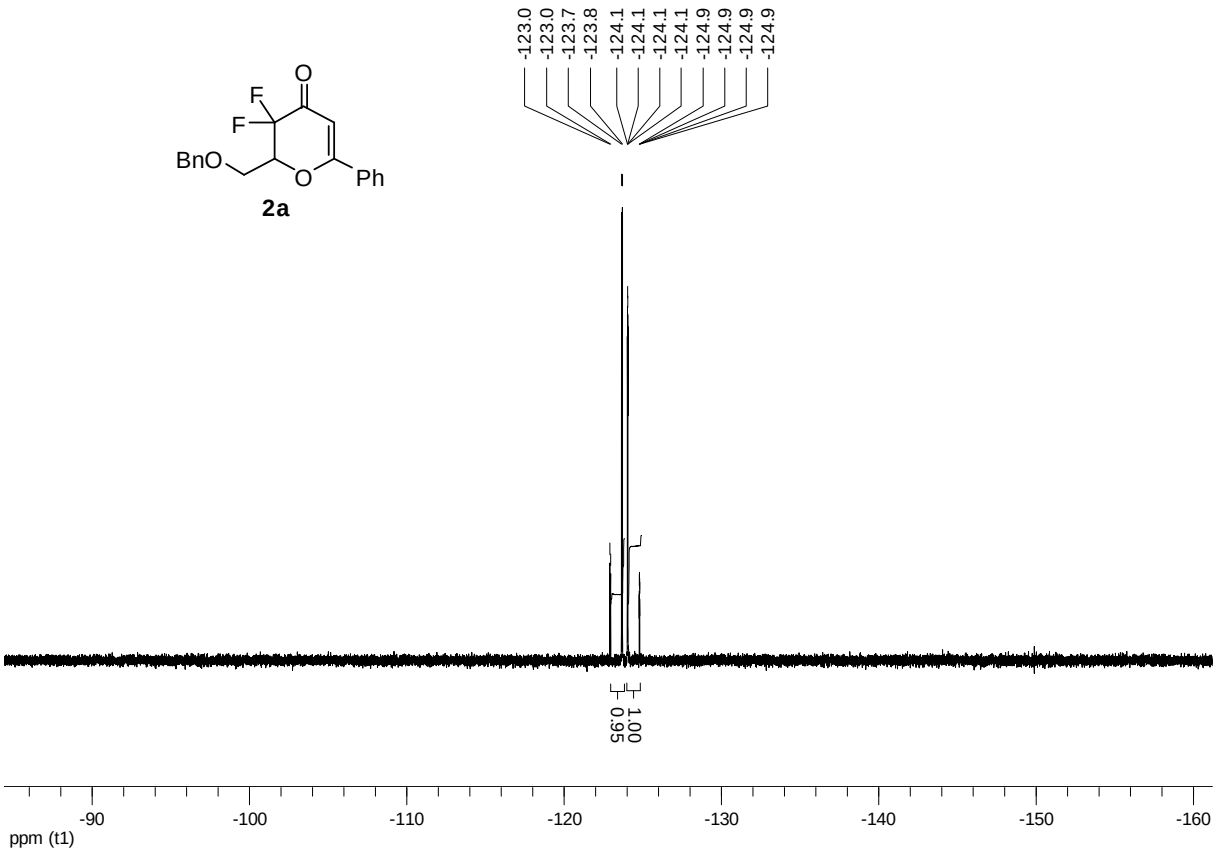


G.2 – Cyclized products 2a-2k

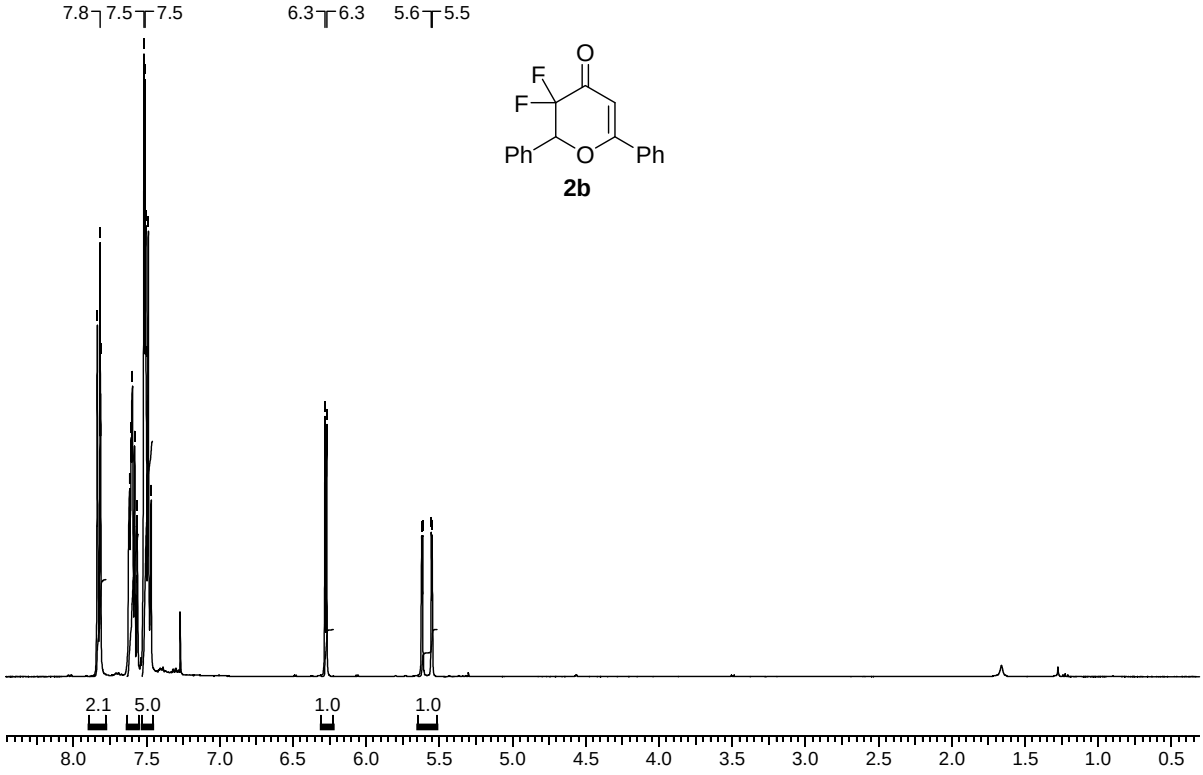
2-[(benzyloxy)methyl]-3,3-difluoro-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (2a)

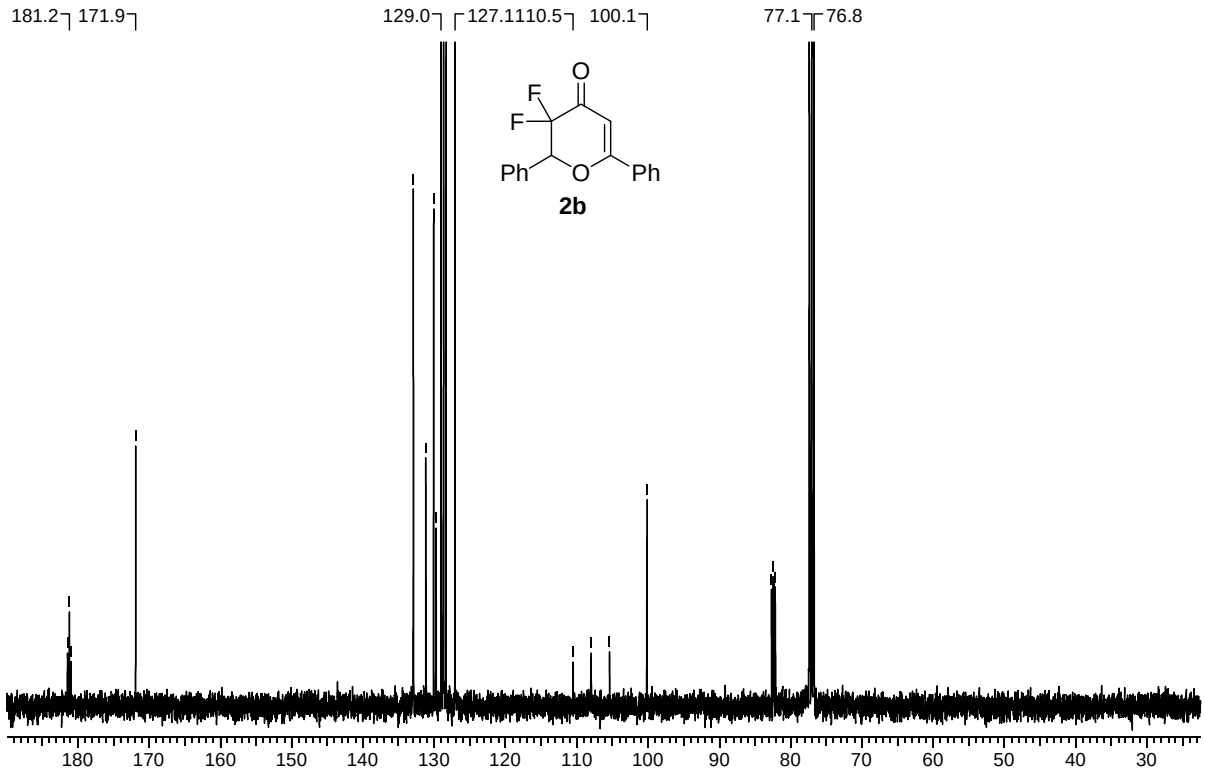


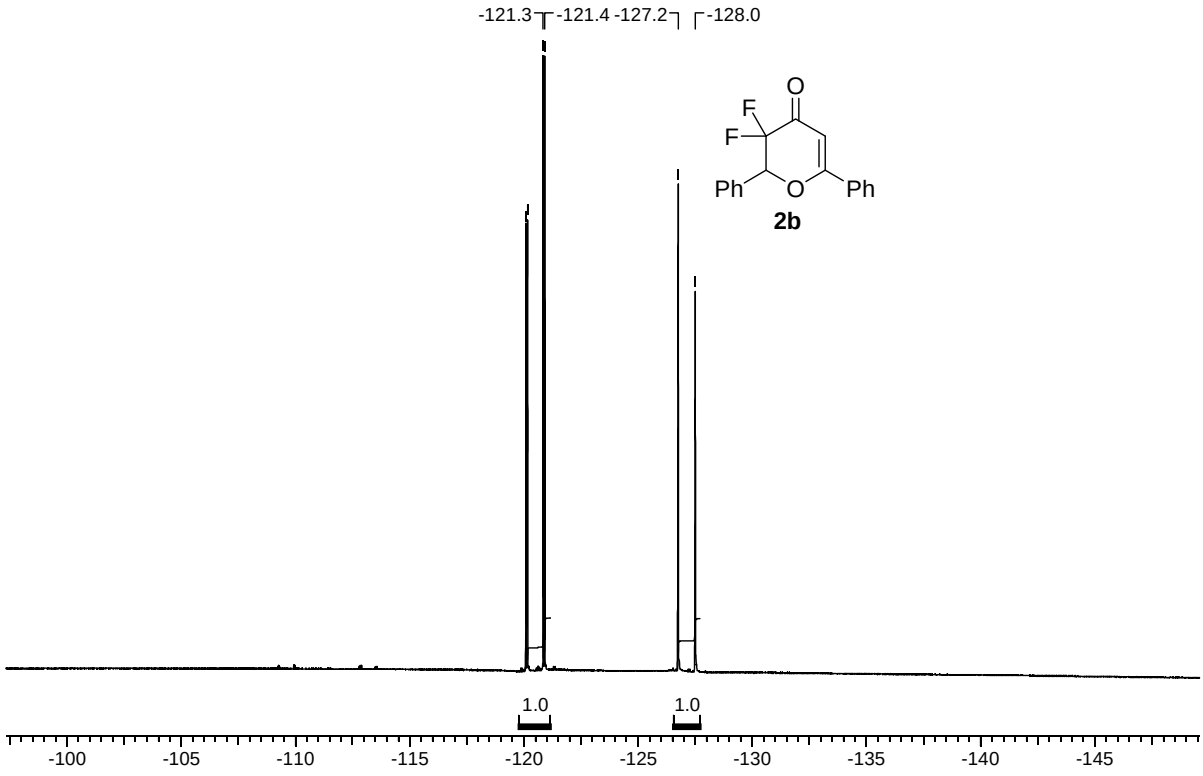

171.1
137.2
127.7
127.1
100.0
73.8
65.9
F
F
O
BnO
O
Ph
2a
180
160
140
120
100
80
60
40
20


-123.0
-123.0
-123.7
-123.8
-124.1
-124.1
-124.1
-124.1
-124.9
-124.9
-124.9
-124.9
F
F
O
BnO
O
Ph
2a
0.95
1.00
-90
-100
-110
-120
-130
-140
-150
-160
ppm (t1)

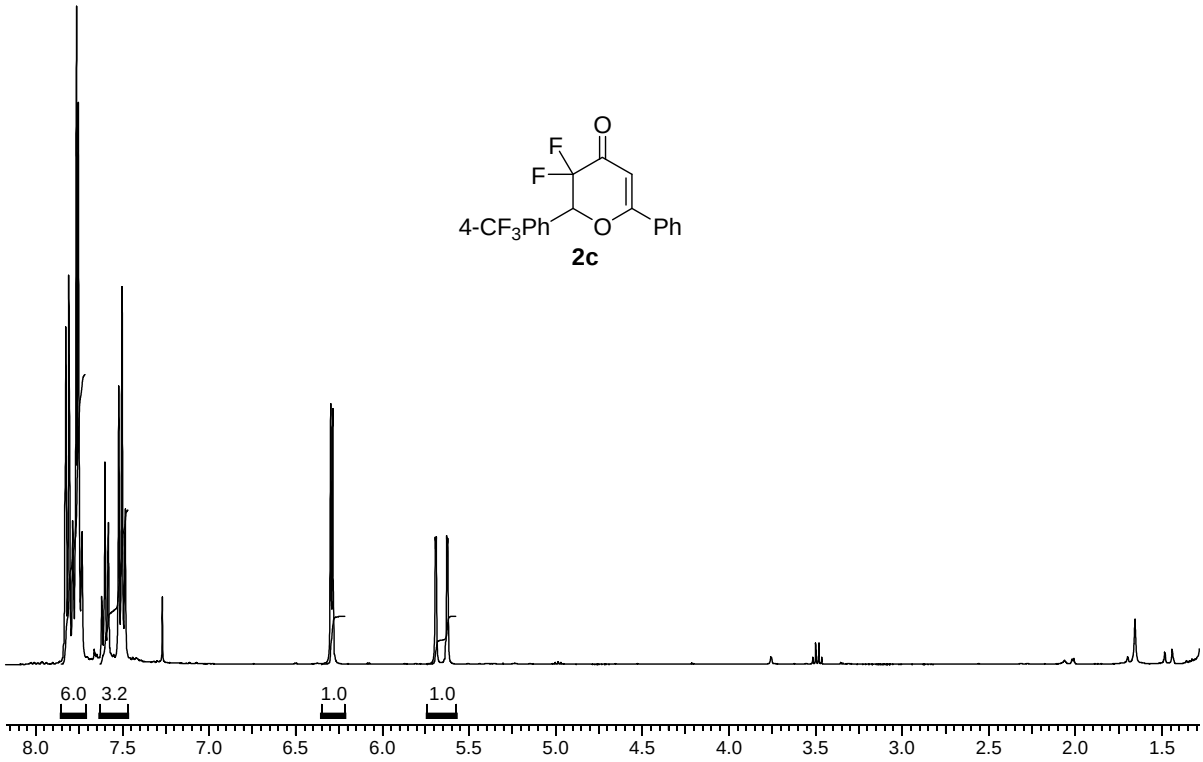
3,3-difluoro-2,6-diphenyl-2,3-dihydro-4*H*-pyran-4-one (2b)

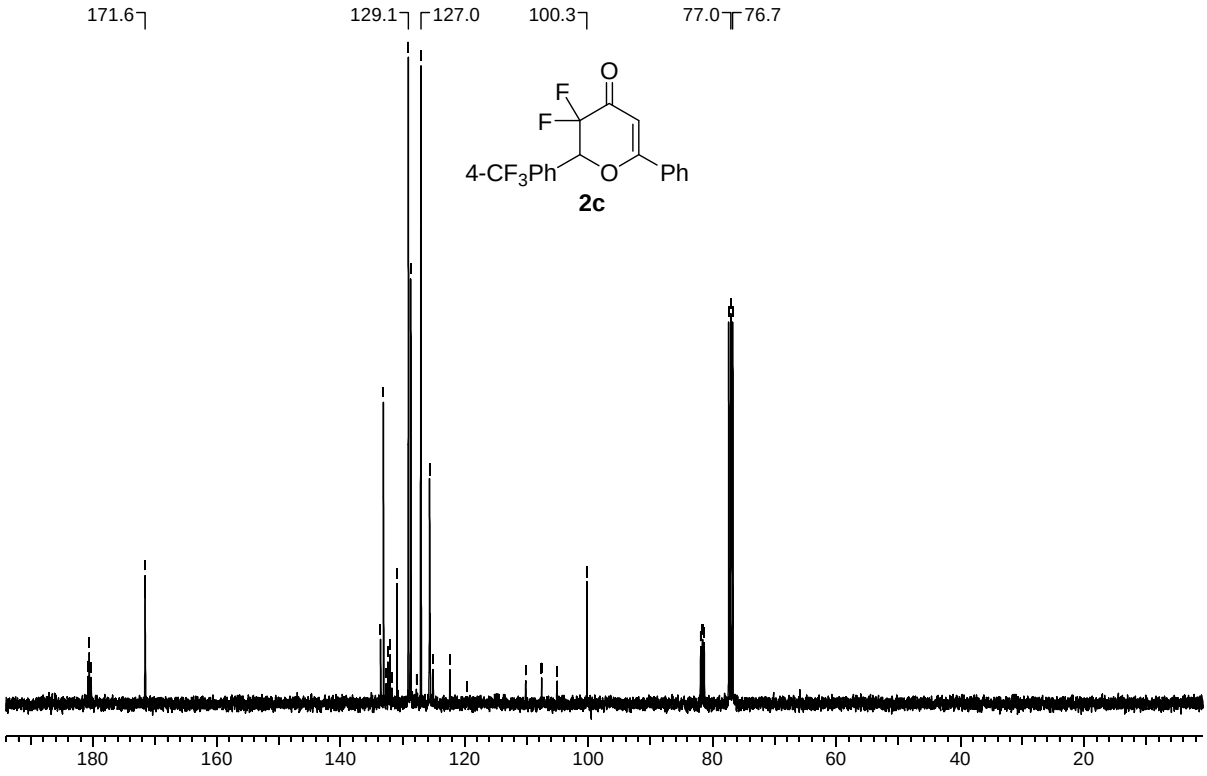


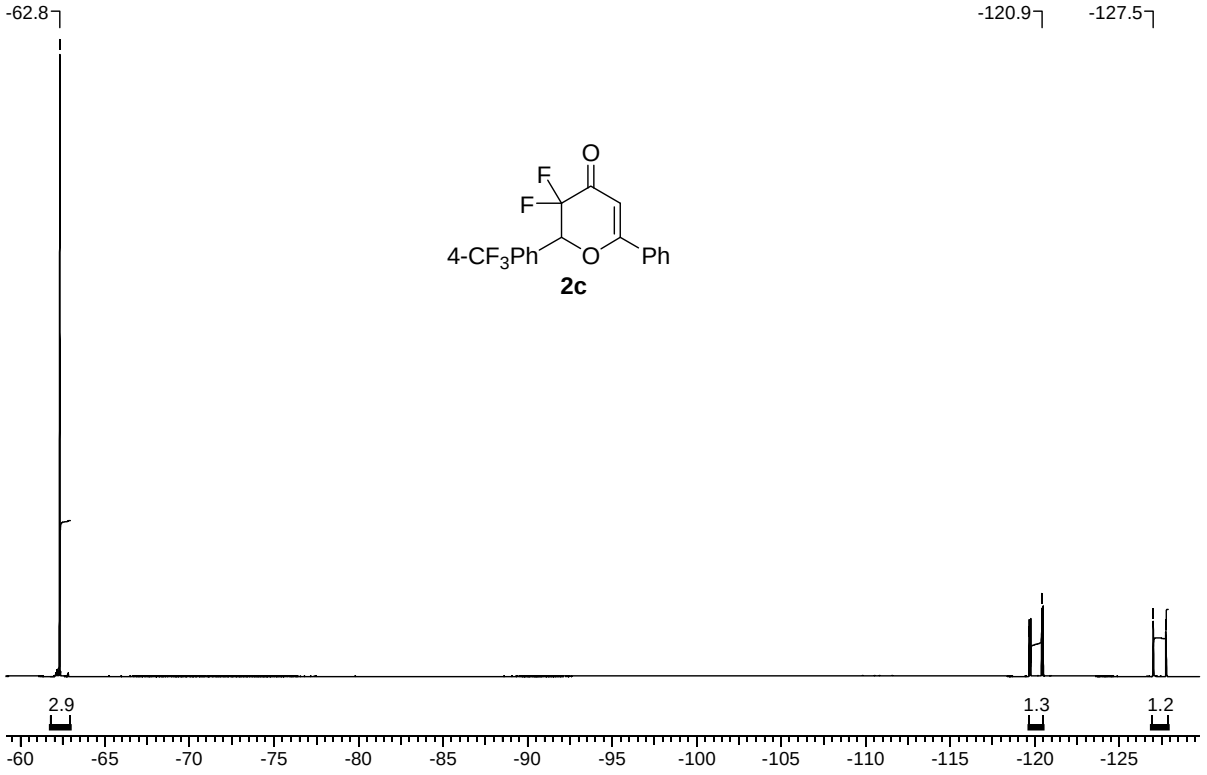




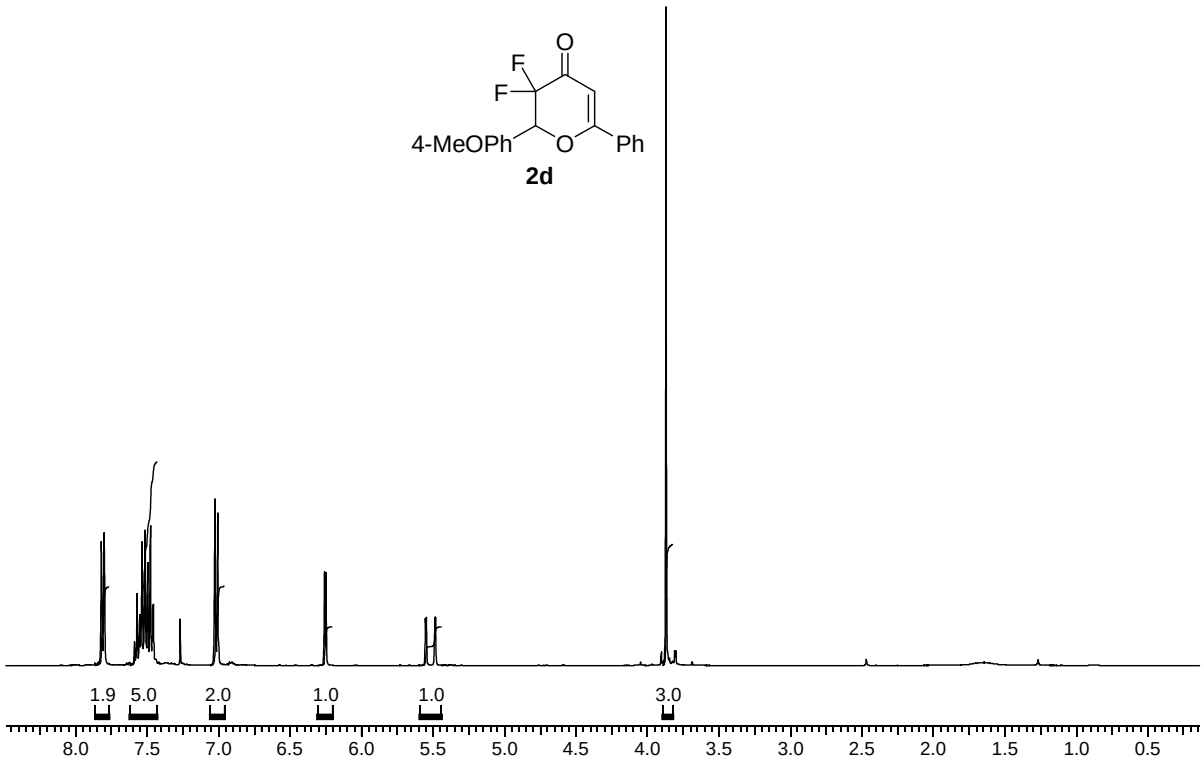
3,3-difluoro-6-phenyl-2-[4-(trifluoromethyl)phenyl]-2,3-dihydro-4*H*-pyran-4-one (2c)

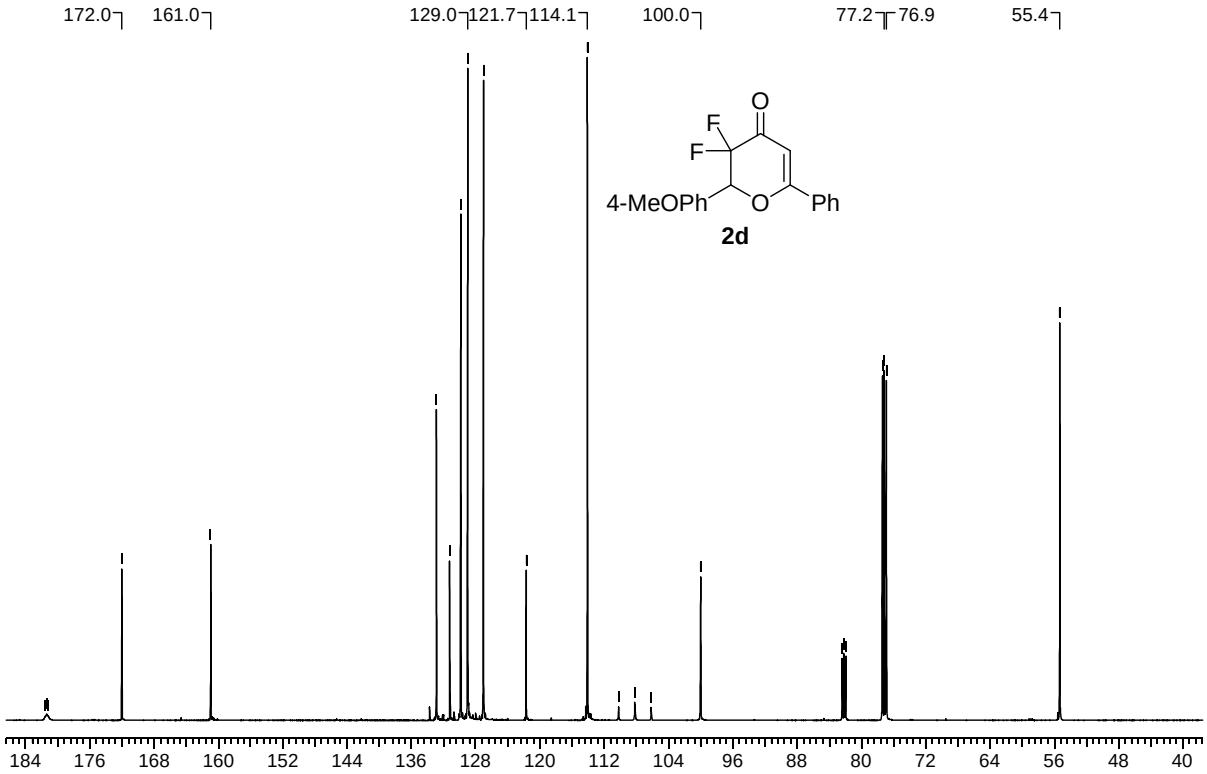


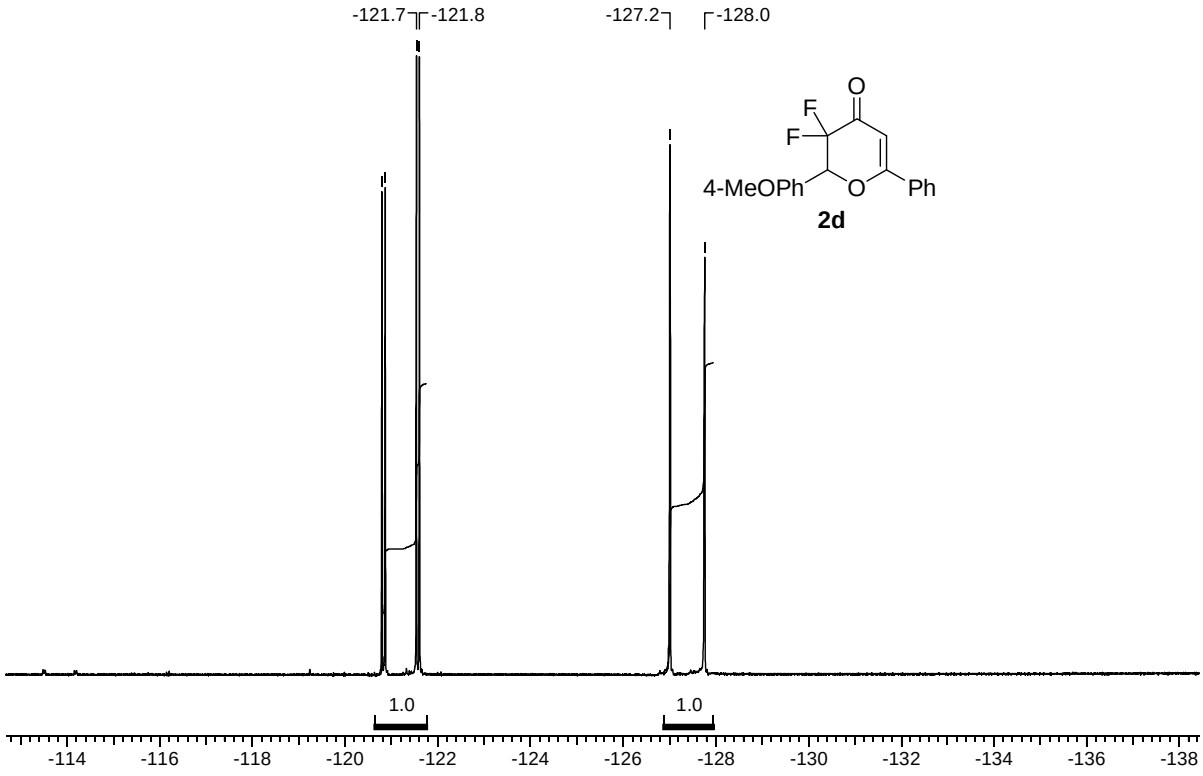

171.6
129.1
127.0
100.3
77.0
76.7
O
F
F
4-CF3Ph
O
Ph
2c
180
160
140
120
100
80
60
40
20


-62.8
-120.9
-127.5
O
F
F
4-CF3Ph
O
Ph
2c
2.9
1.3
1.2
-60
-65
-70
-75
-80
-85
-90
-95
-100
-105
-110
-115
-120
-125

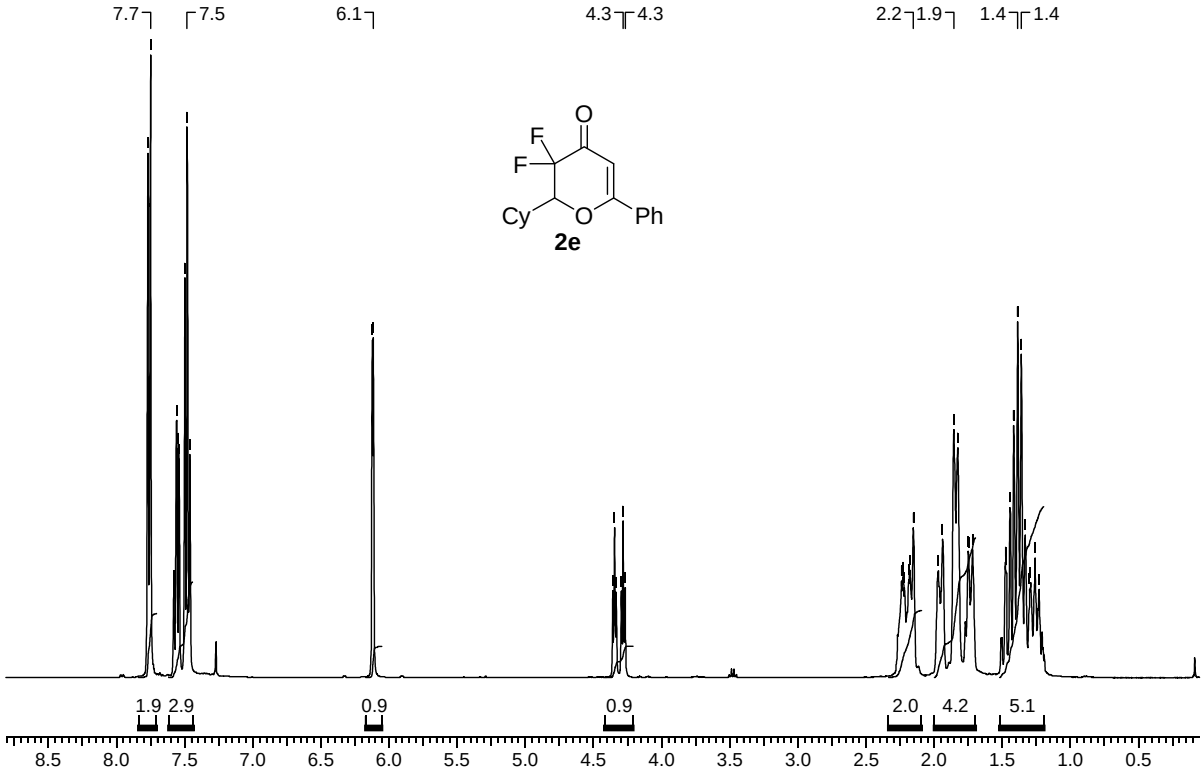
3,3-difluoro-2-(4-methoxyphenyl)-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (2d)

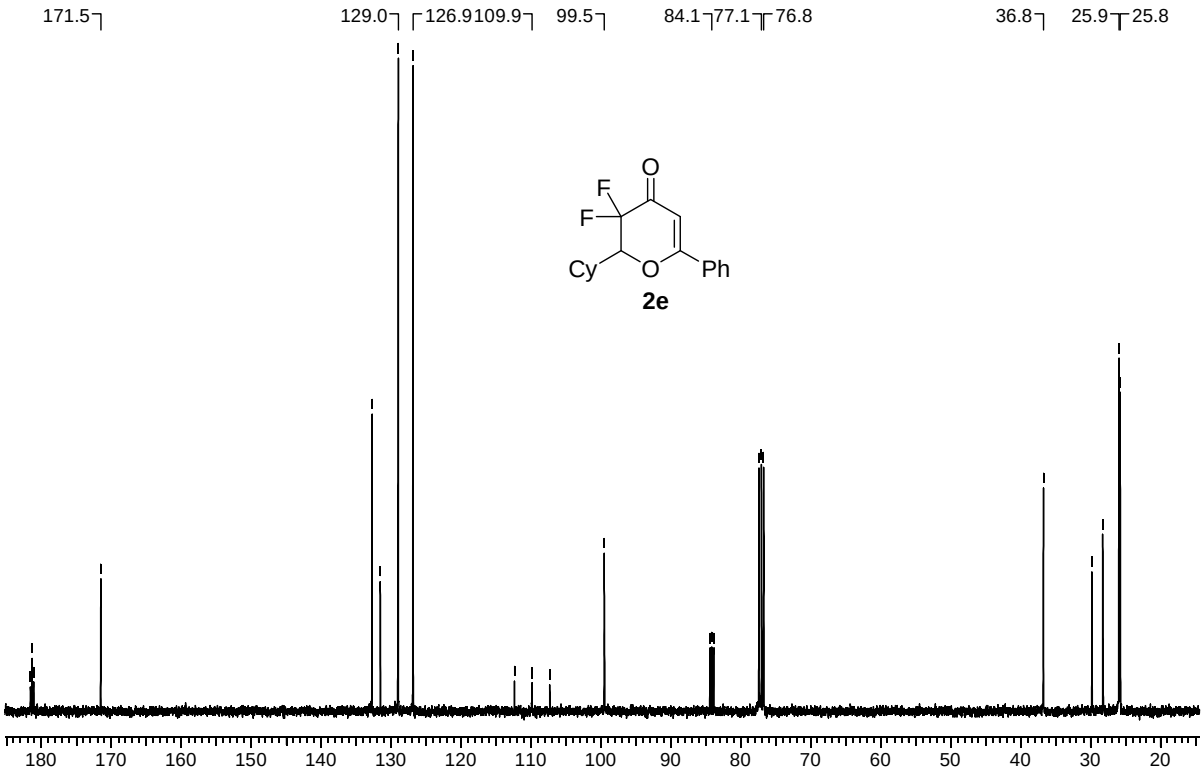


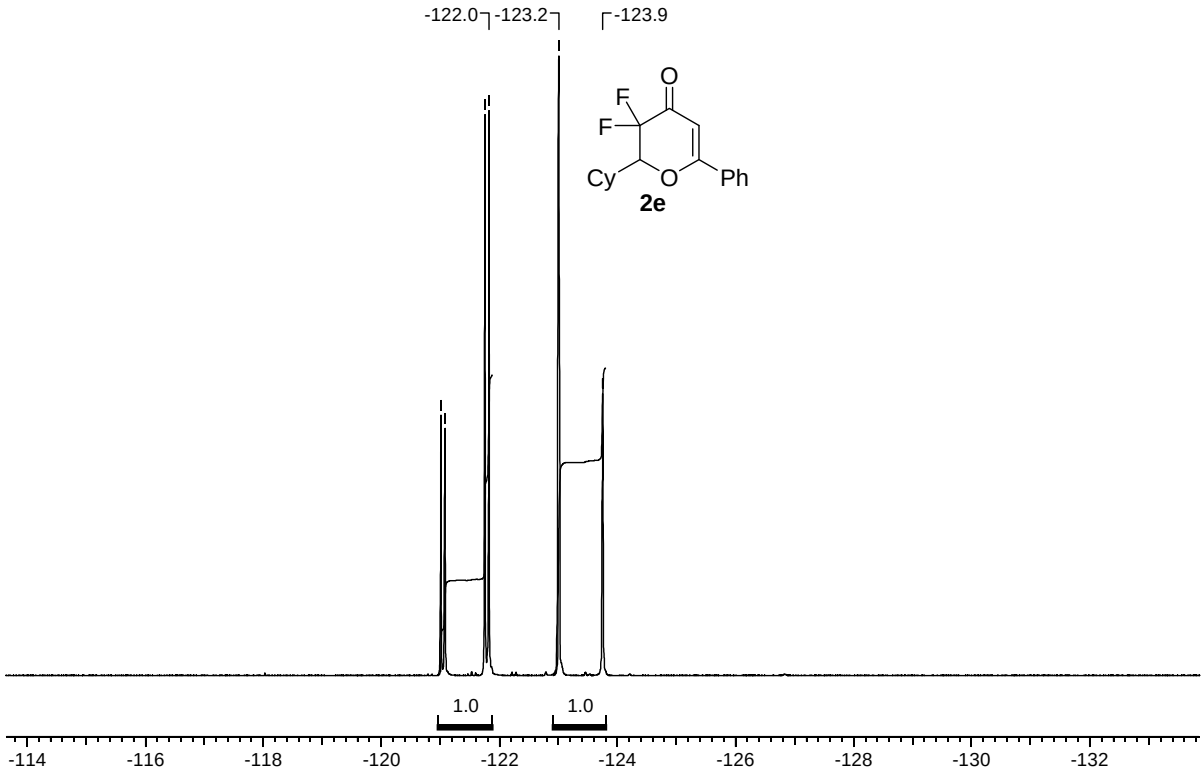




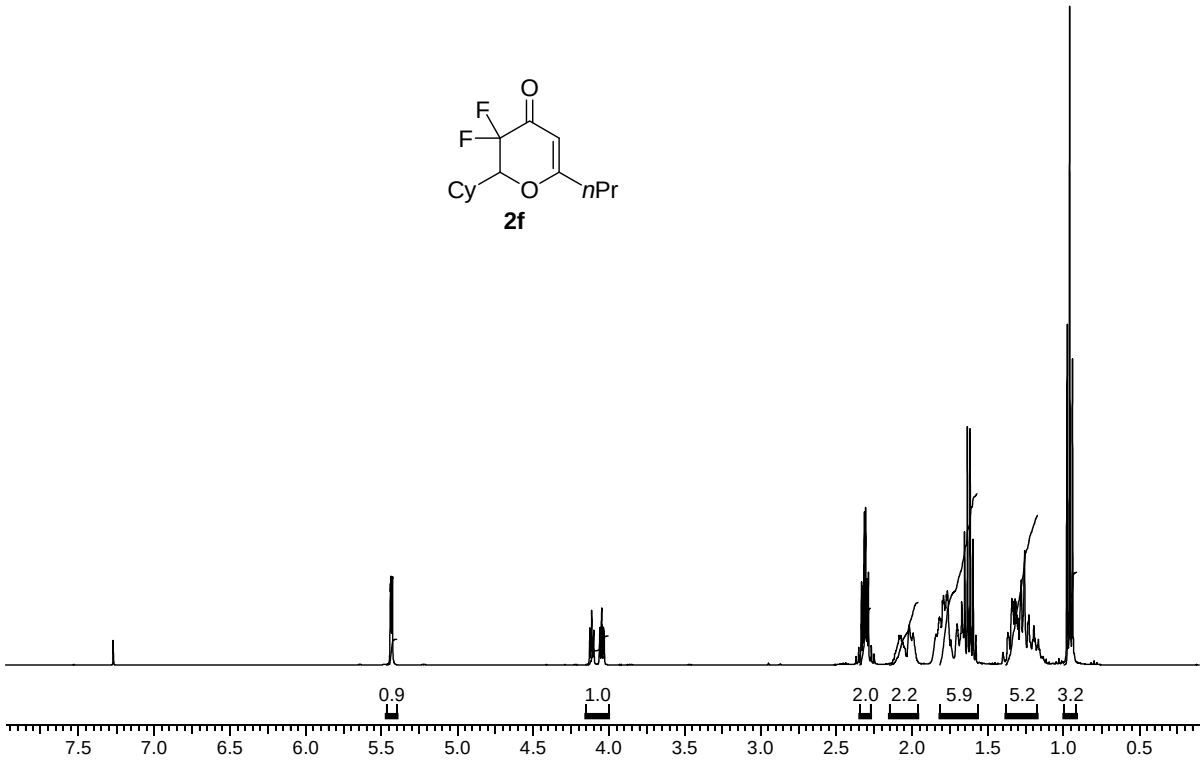
2-cyclohexyl-3,3-difluoro-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (2e)

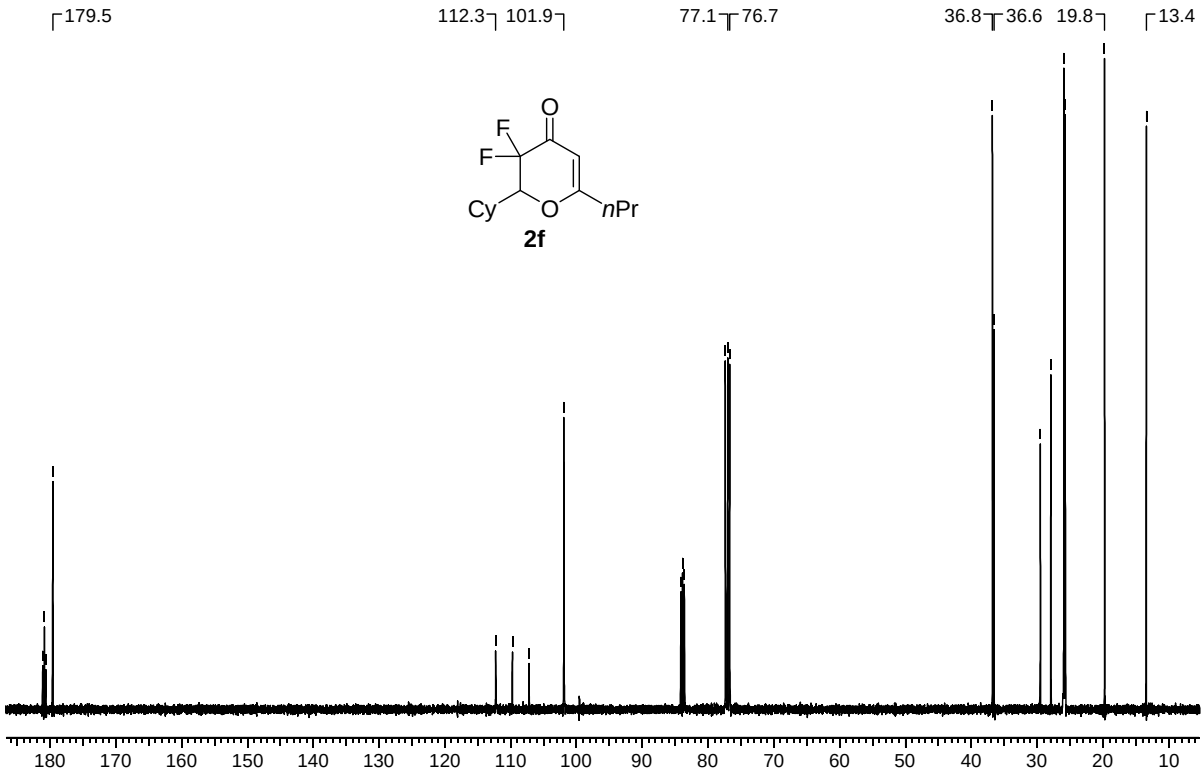


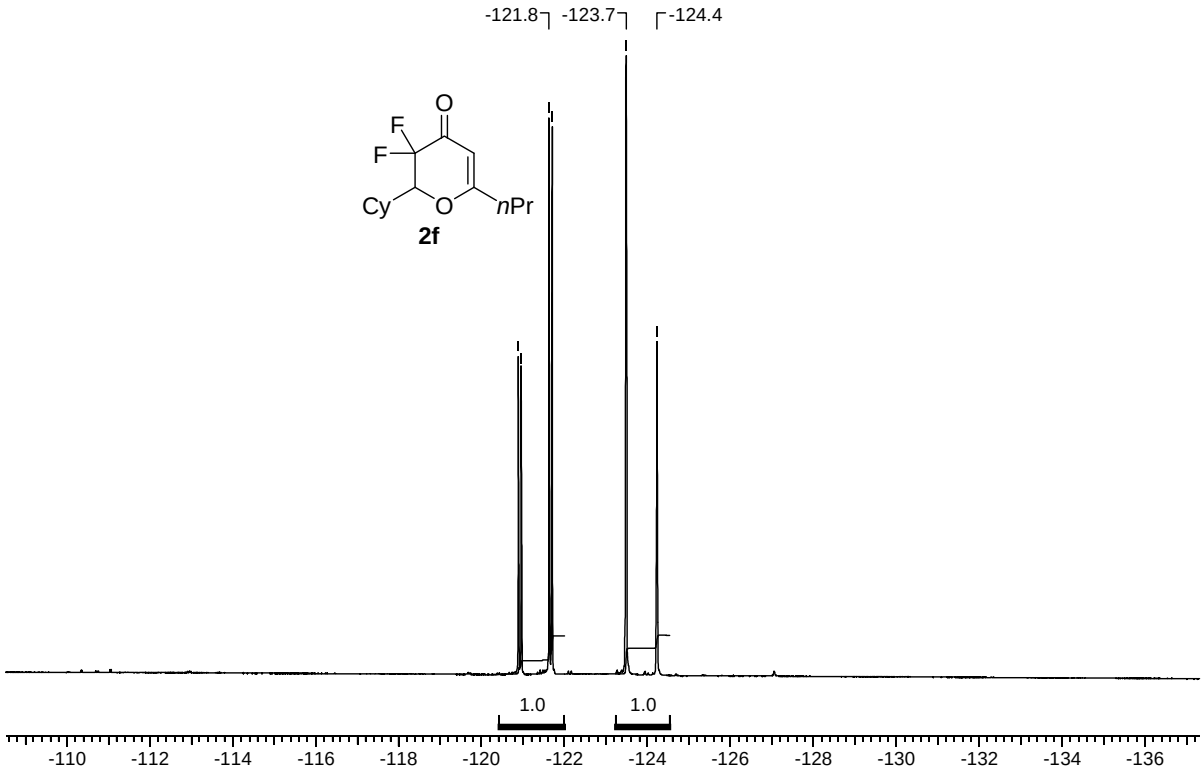

171.5
129.0
126.9
109.9
99.5
84.1
77.1
76.8
36.8
25.9
25.8
O
F
F
Cy
O
Ph
2e
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20


-122.0
-123.2
-123.9
O
F
F
Cy
O
Ph
2e
1.0
1.0
-114
-116
-118
-120
-122
-124
-126
-128
-130
-132

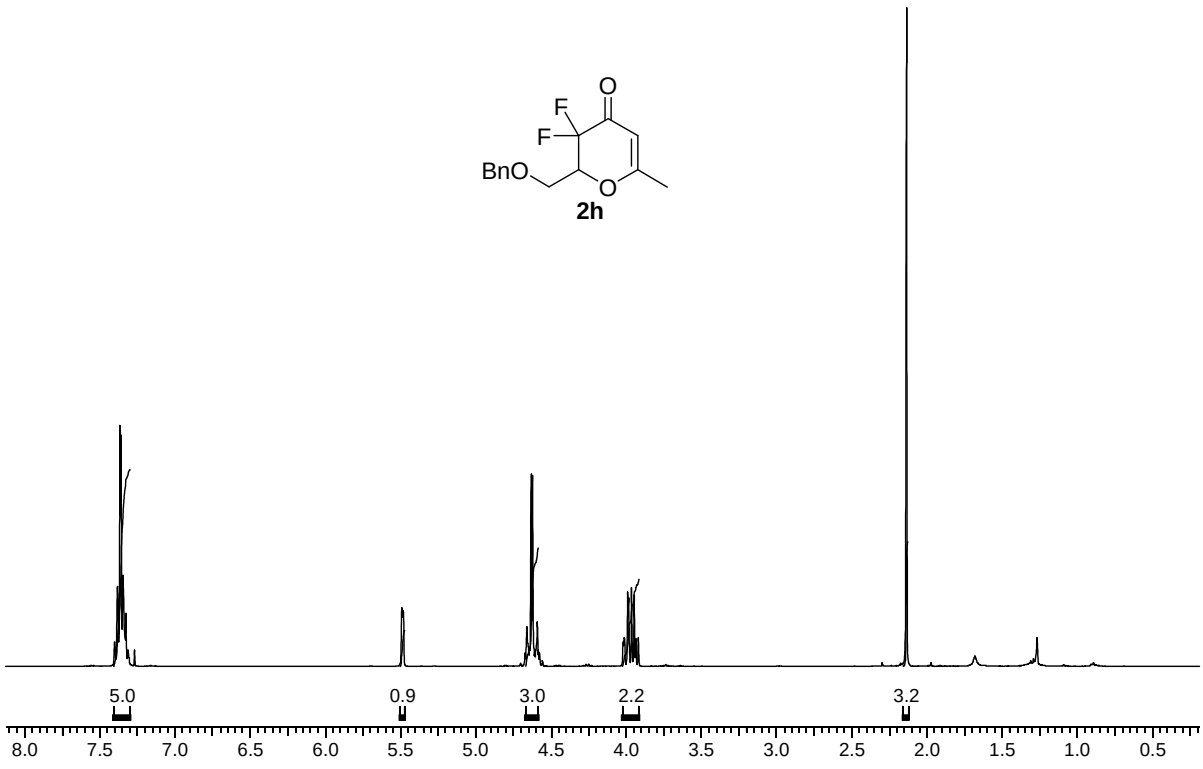
2-cyclohexyl-3,3-difluoro-6-propyl-2,3-dihydro-4*H*-pyran-4-one (2f)

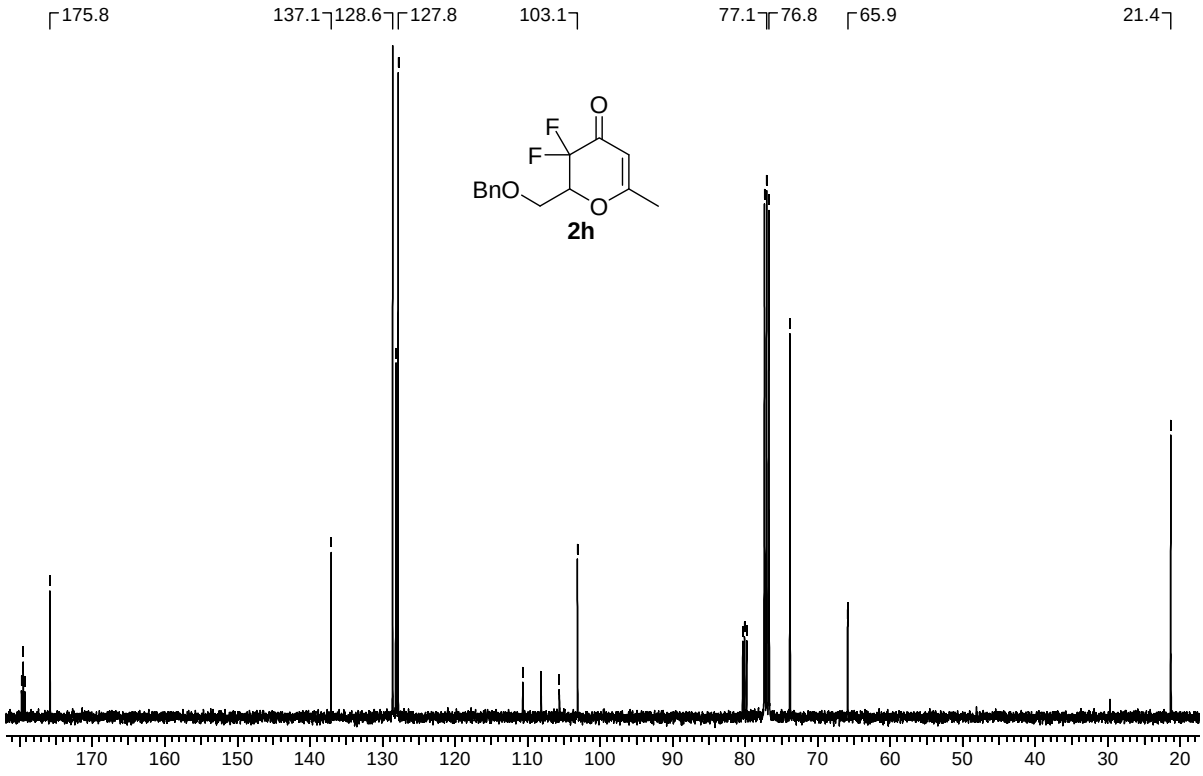


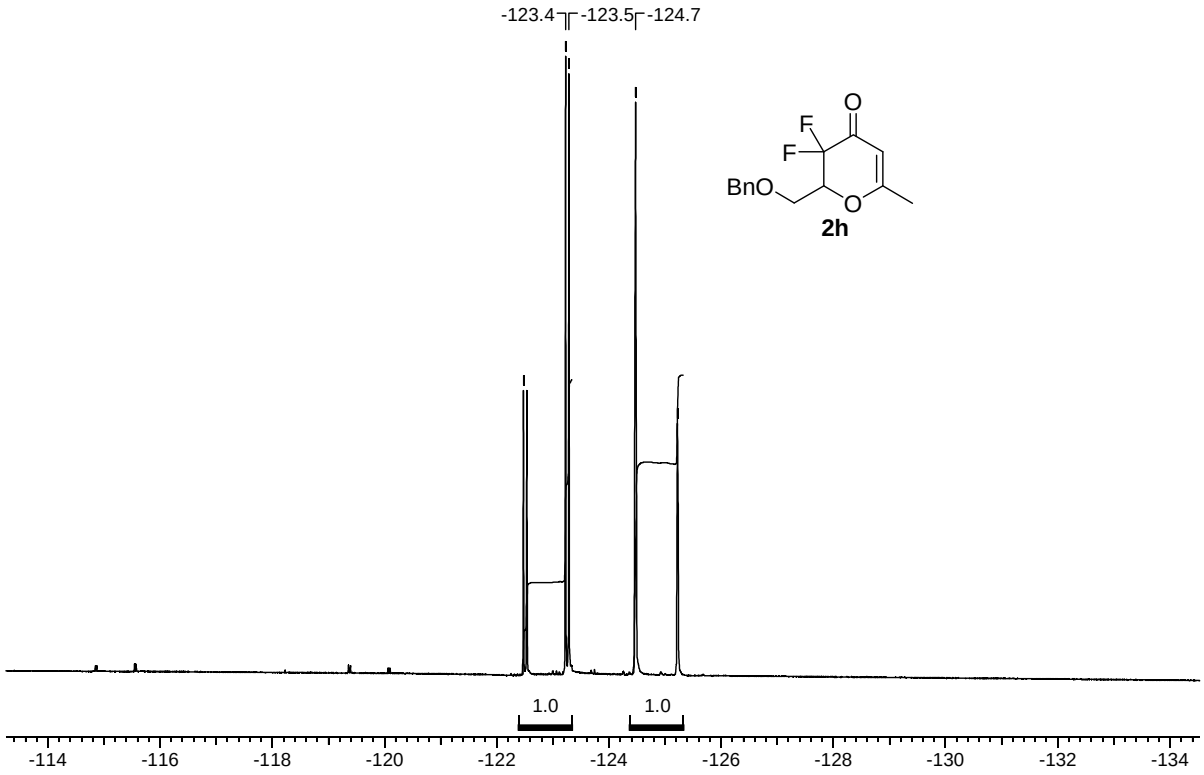




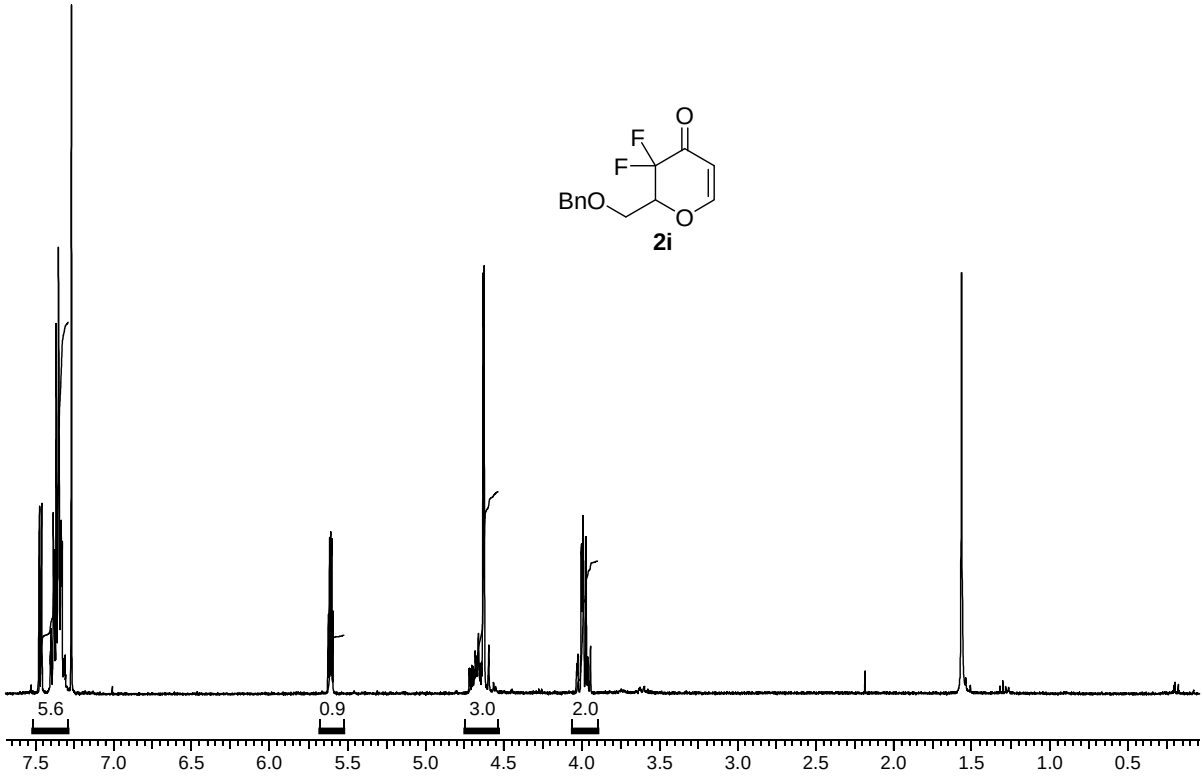
2-[(benzyloxy)methyl]-3,3-difluoro-6-methyl-2,3-dihydro-4*H*-pyran-4-one (2h)

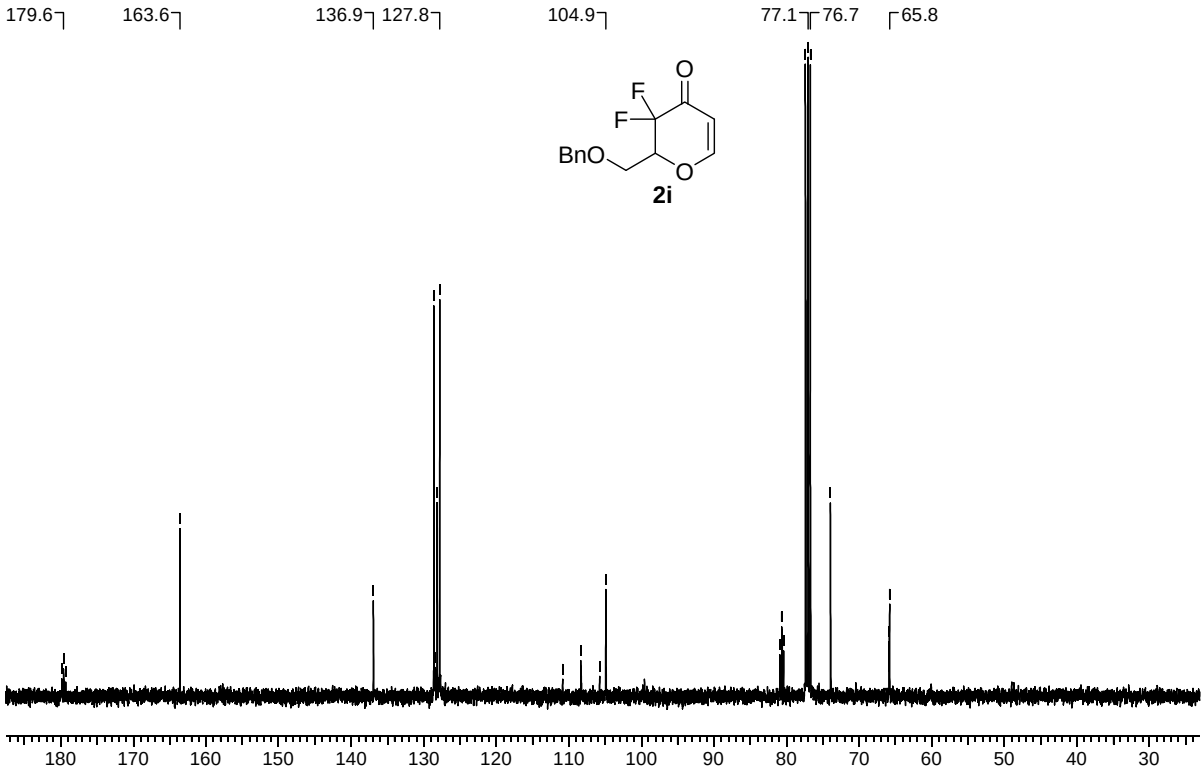


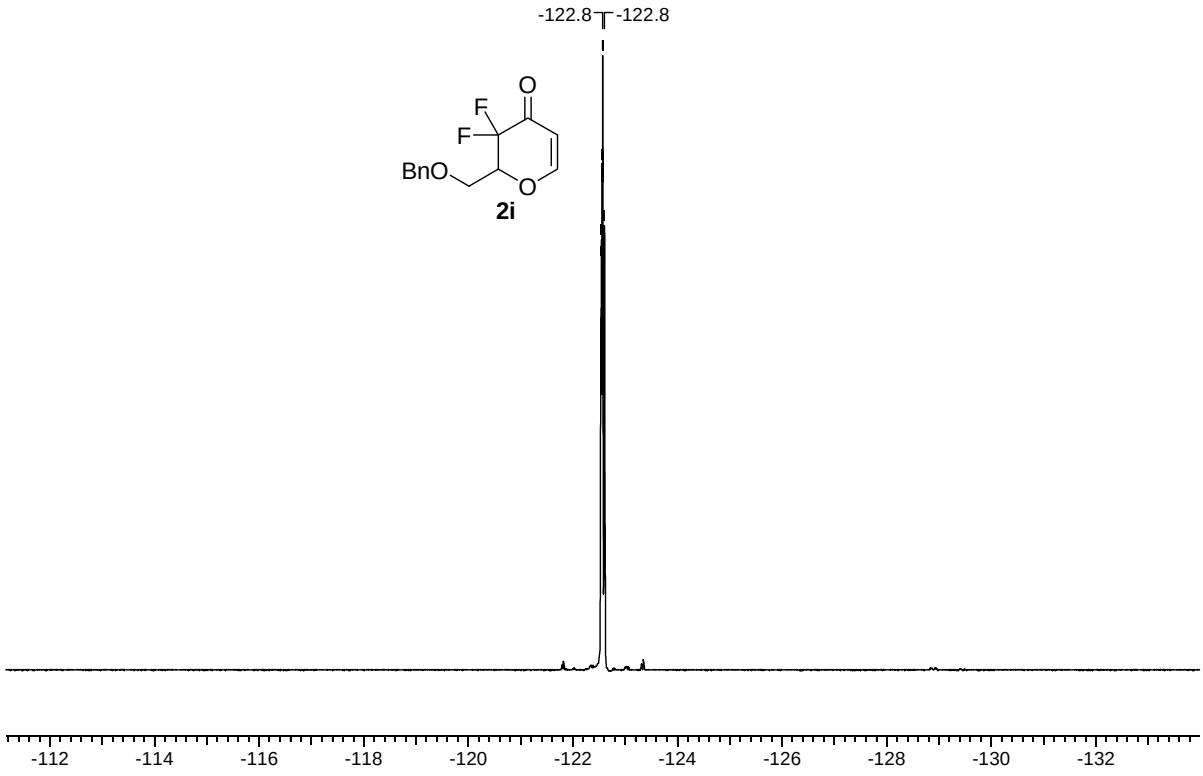

175.8
137.1
128.6
127.8
103.1
77.1
76.8
65.9
21.4
F
F
O
BnO
O
2h
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20


-123.4
-123.5
-124.7
F
F
O
BnO
O
2h
1.0
1.0
-114
-116
-118
-120
-122
-124
-126
-128
-130
-132
-134

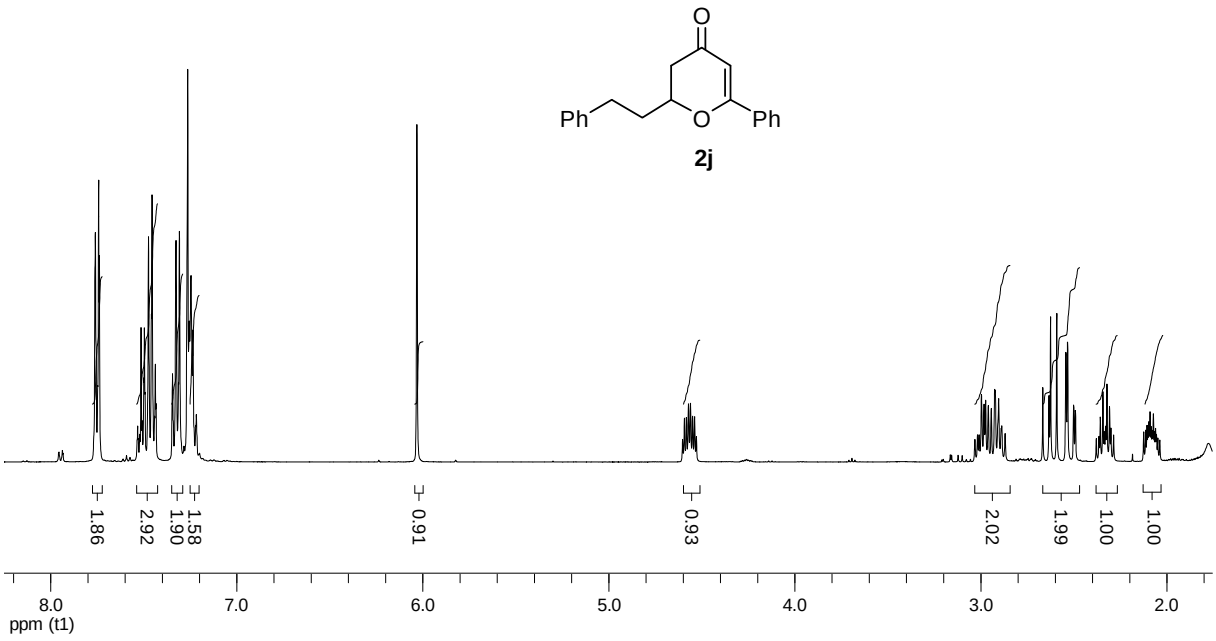
2-[(benzyloxy)methyl]-3,3-difluoro-2,3-dihydro-4*H*-pyran-4-one (2i)

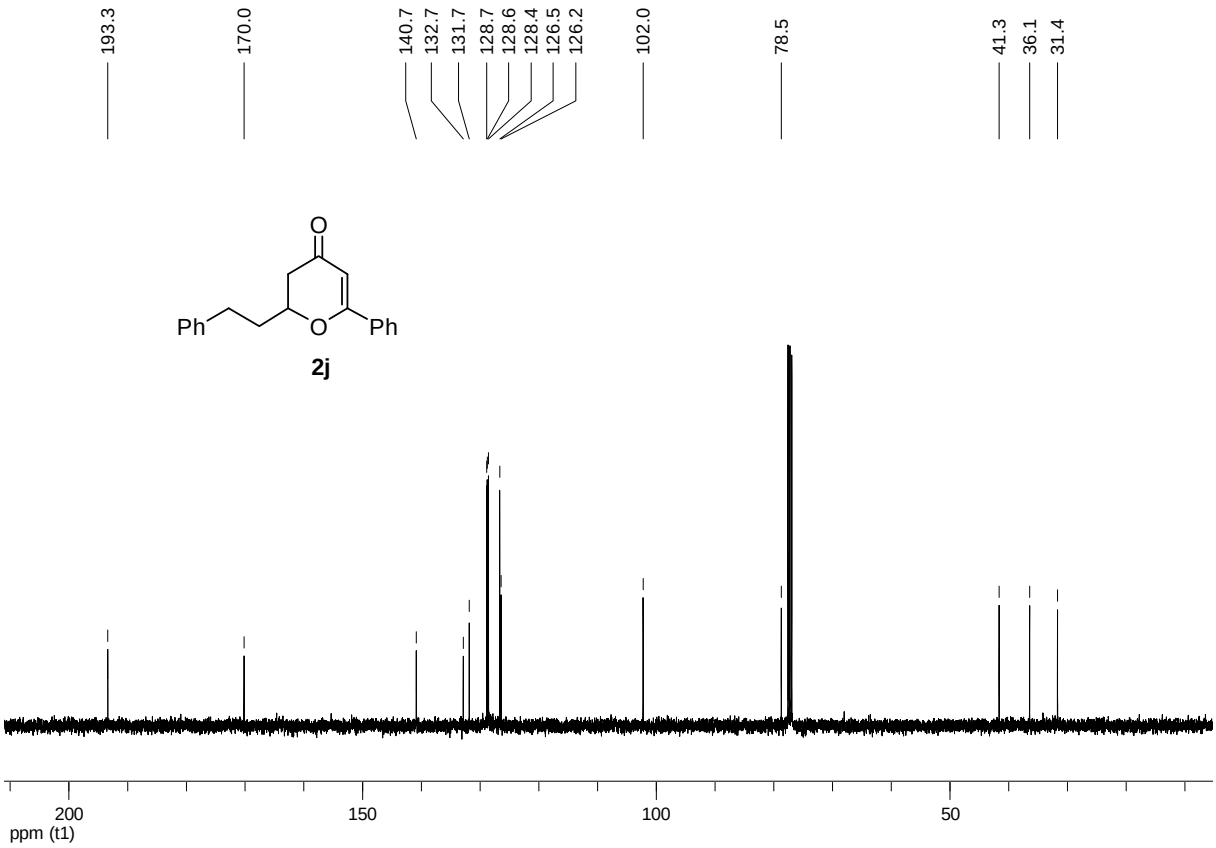






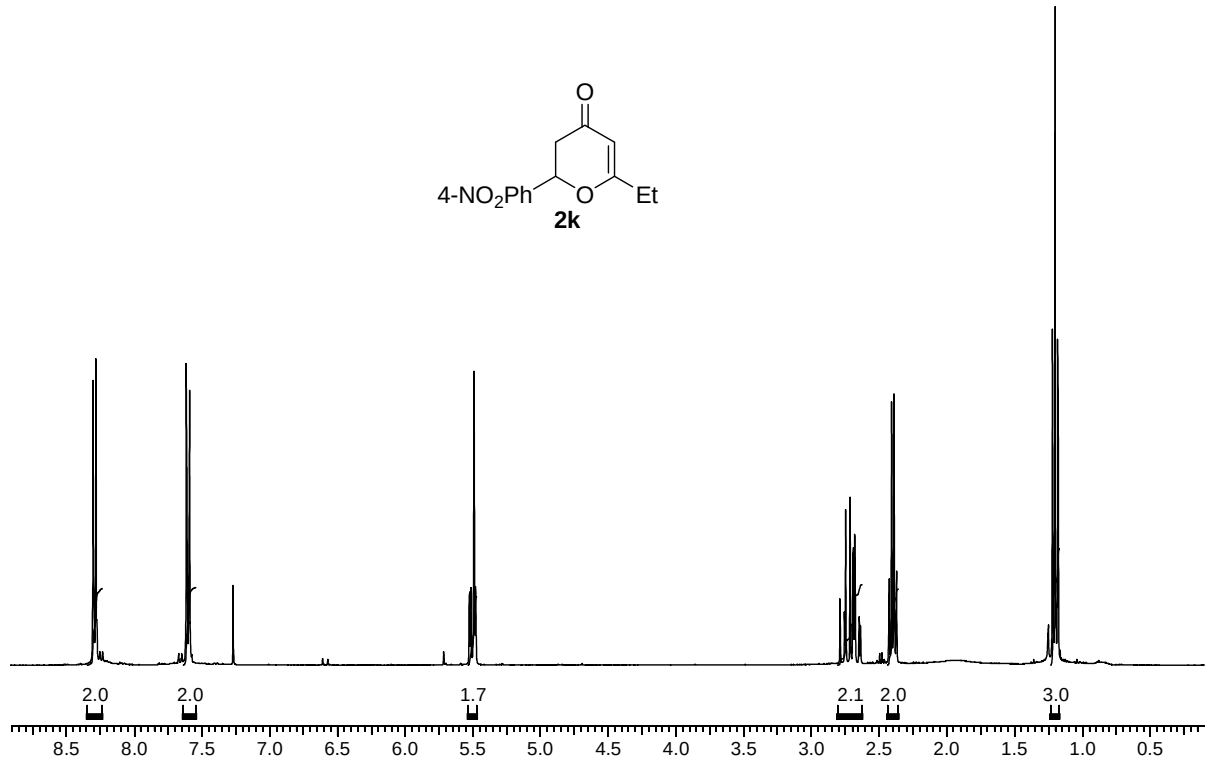
6-phenyl-2-(2-phenylethyl)-2,3-dihydro-4*H*-pyran-4-one (2j)



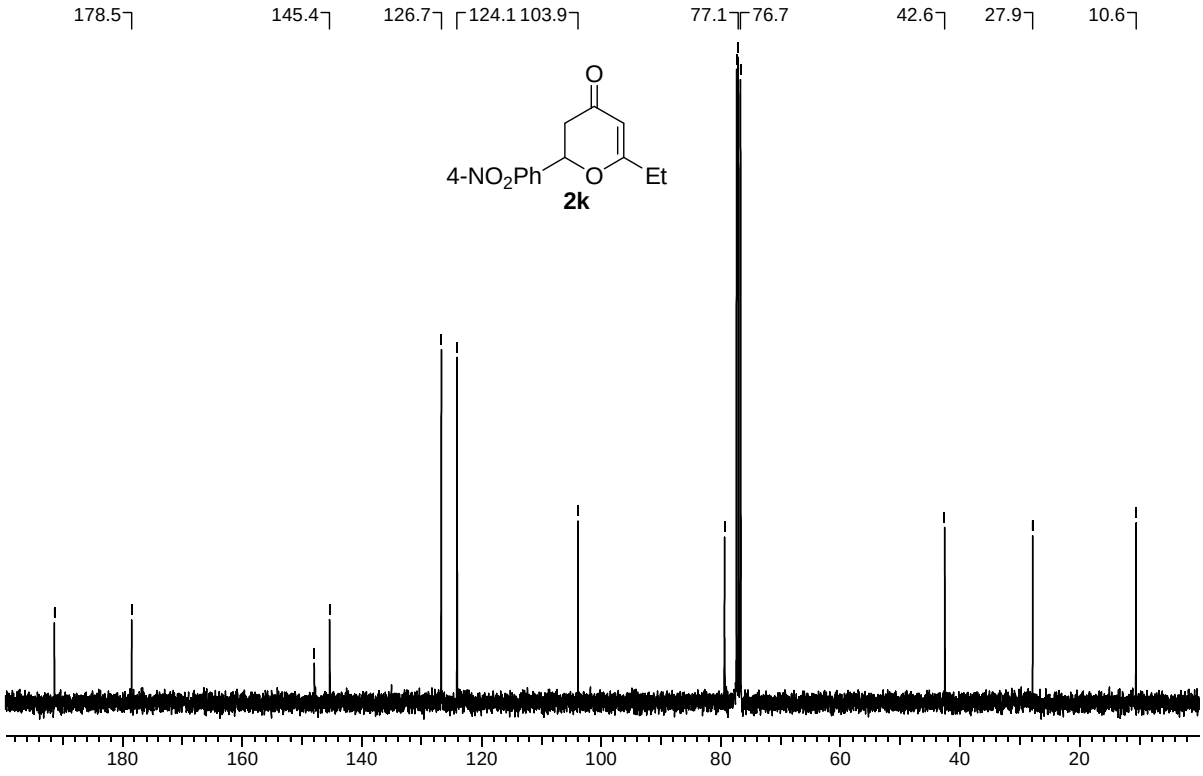


2j

(*R*)-6-ethyl-3,3-difluoro-2-(4-nitrophenyl)-2,3-dihydro-4*H*-pyran-4-one ((*R*)-2k)

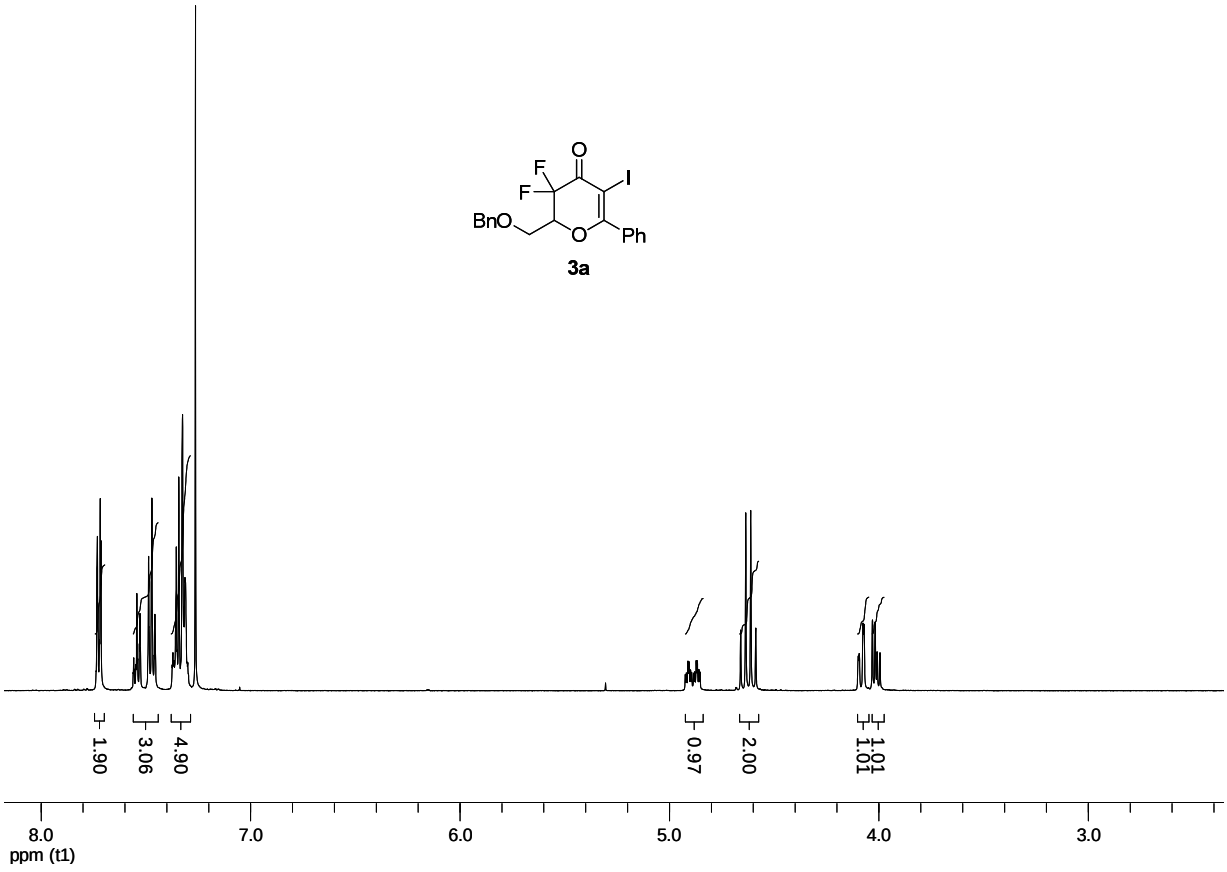


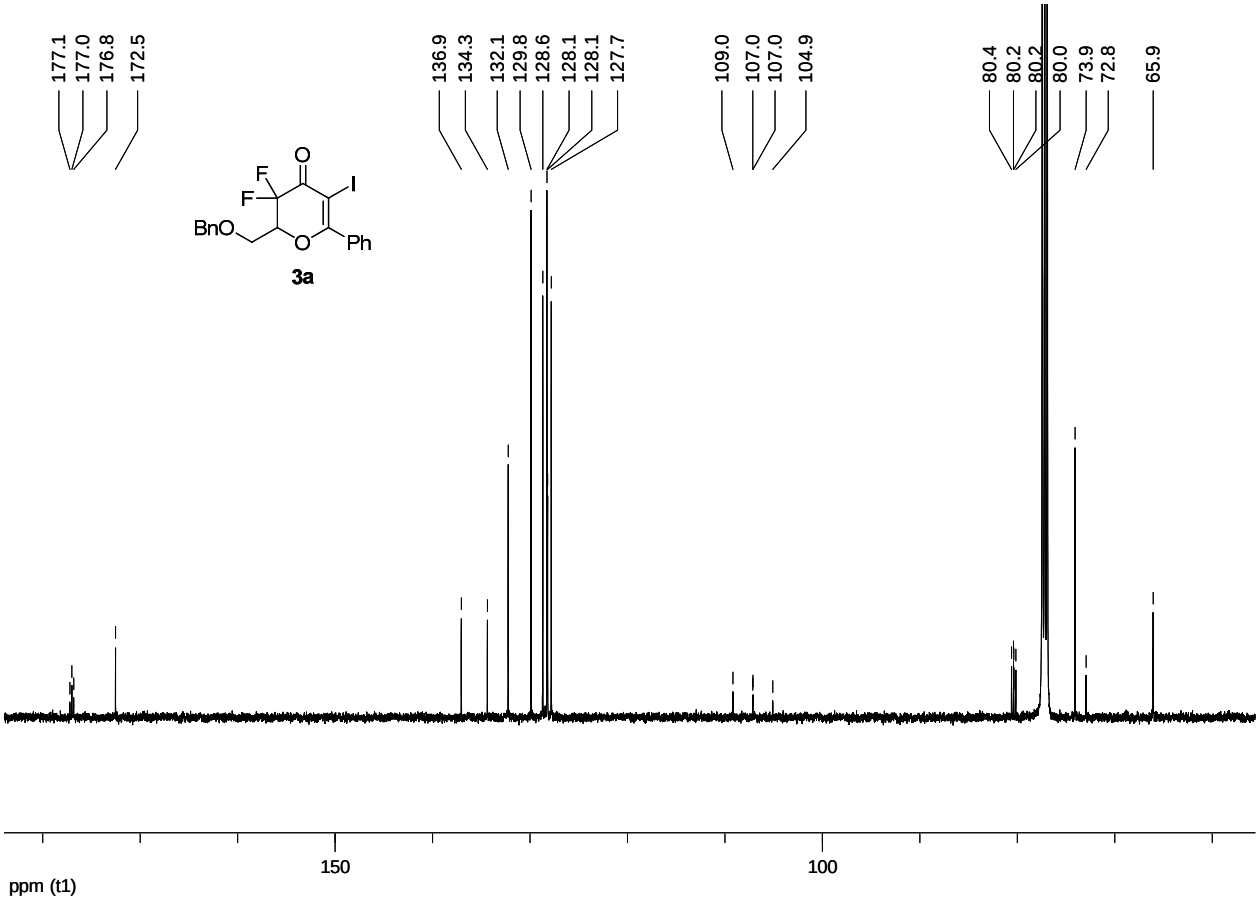
2k

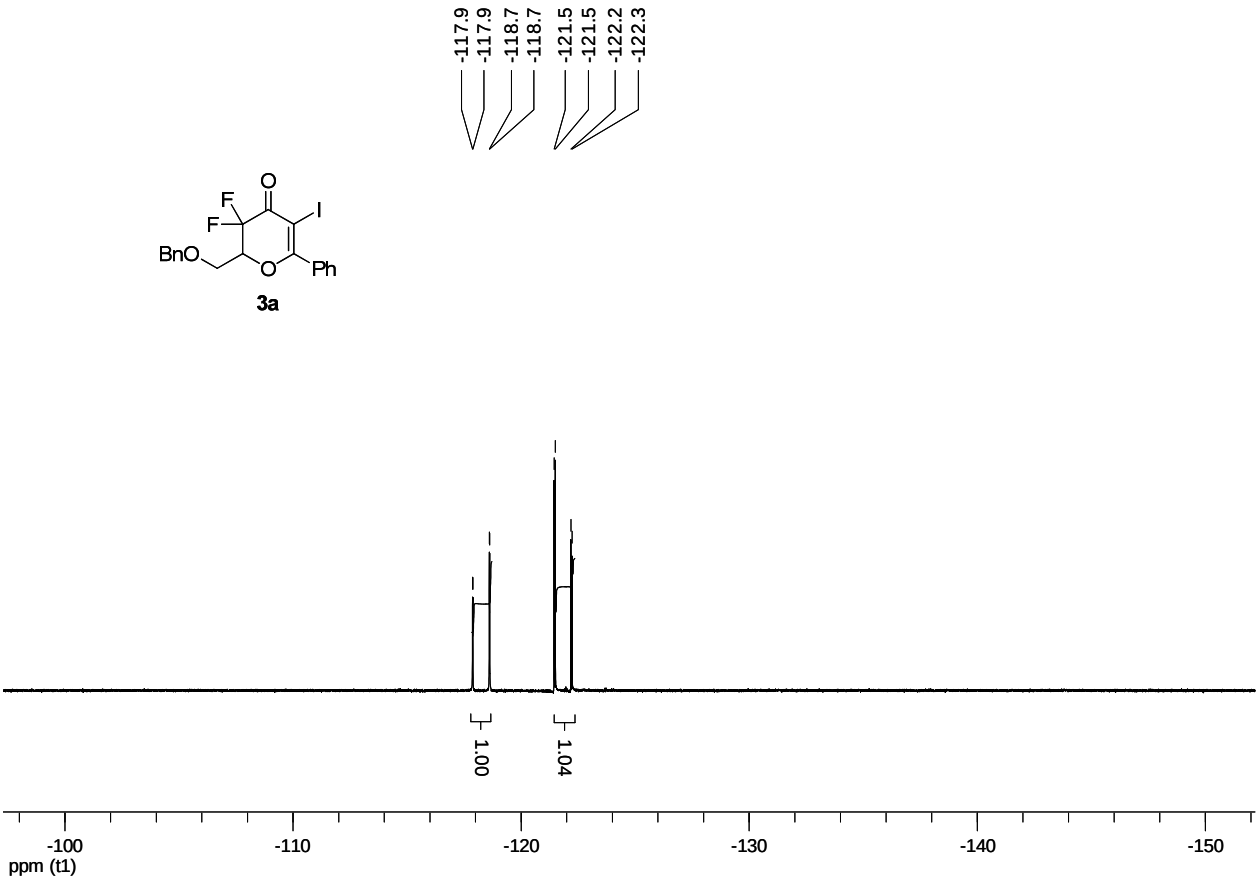


G.2 – Iododifluorodihydropyranones 3a, 3b and 3d-f

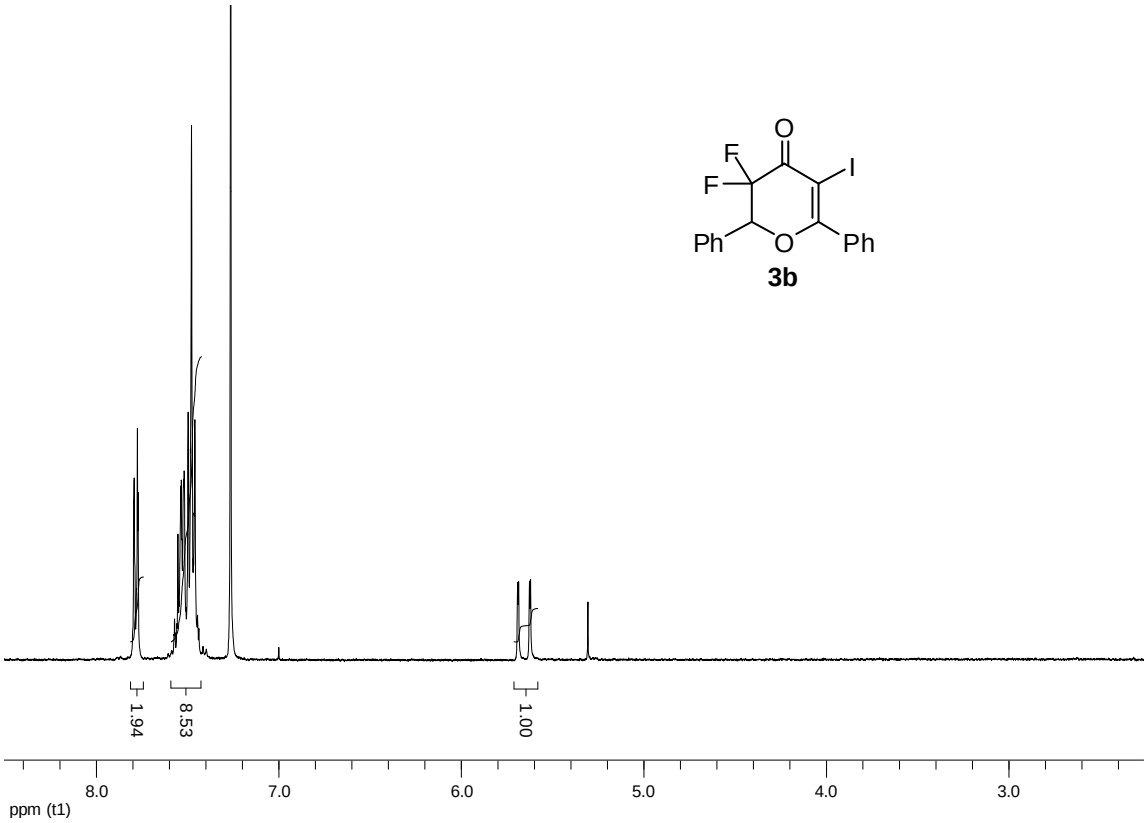
2-[(benzyloxy)methyl]-3,3-difluoro-5-iodo-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (3a)

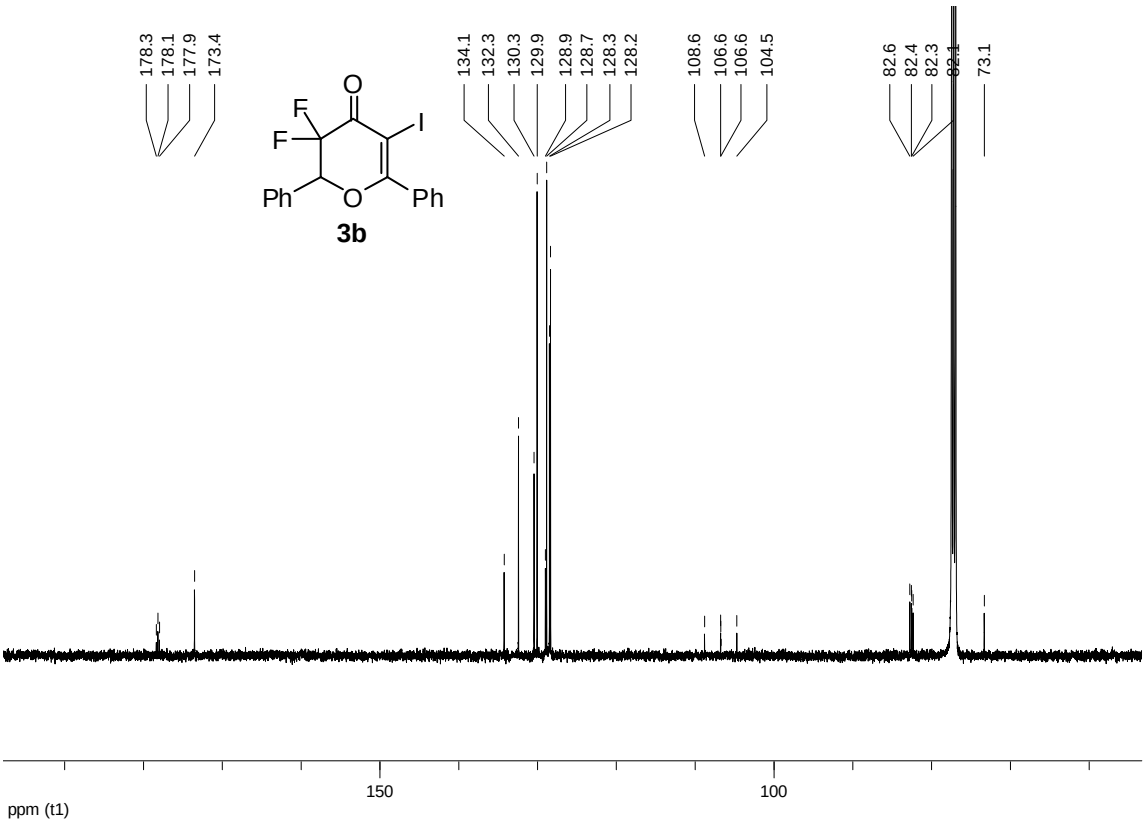


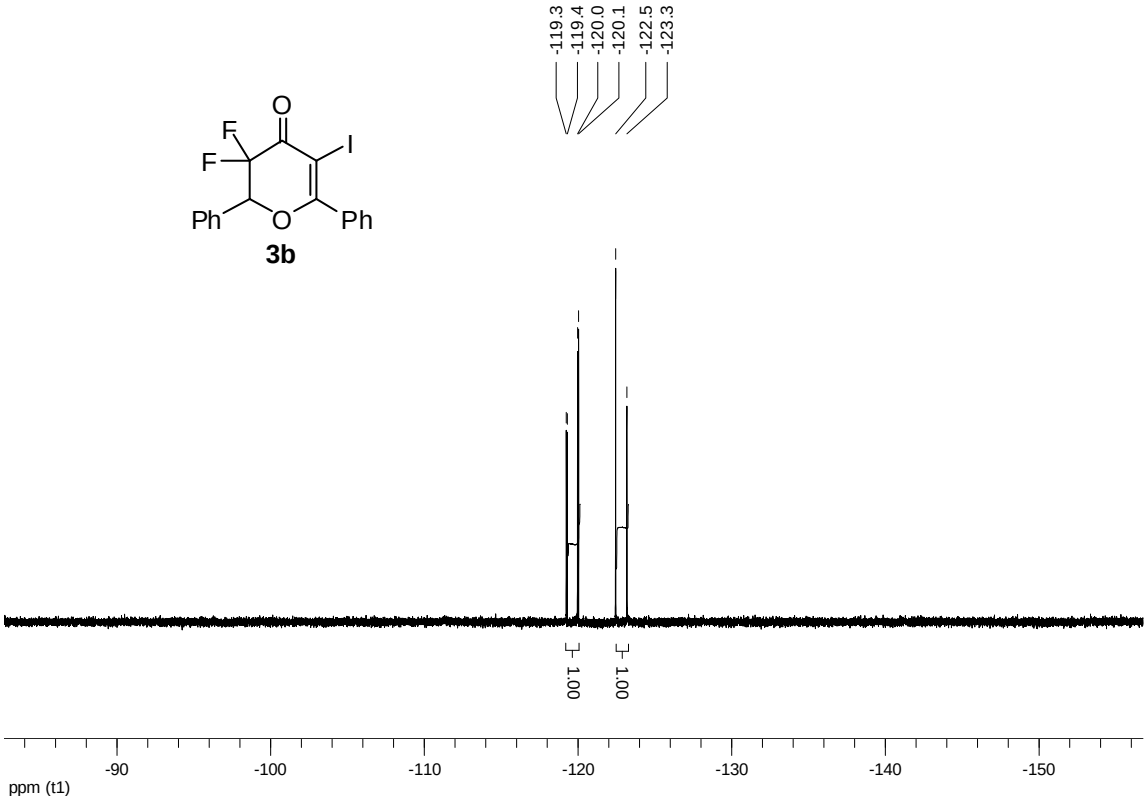

177.1
177.0
176.8
172.5
136.9
134.3
132.1
129.8
128.6
128.1
128.1
127.7
109.0
107.0
107.0
104.9
80.4
80.2
80.2
80.0
73.9
72.8
65.9
F
F
O
I
BnO
O
Ph
3a
150
100
ppm (t1)


-117.9
-117.9
-118.7
-118.7
-121.5
-121.5
-122.2
-122.3
F
F
O
I
BnO
O
Ph
3a
1.00
1.04
-100
-110
-120
-130
-140
-150
ppm (t1)

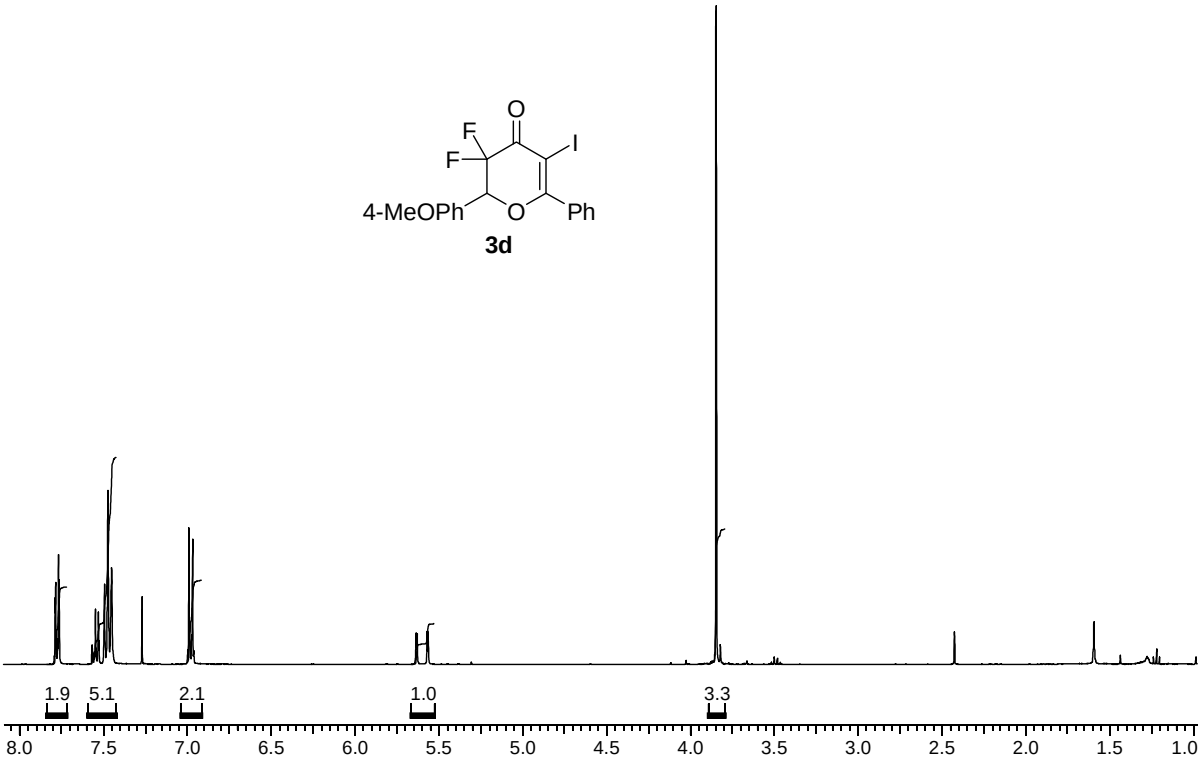
3,3-difluoro-5-iodo-2,6-diphenyl-2,3-dihydro-4*H*-pyran-4-one (3b)

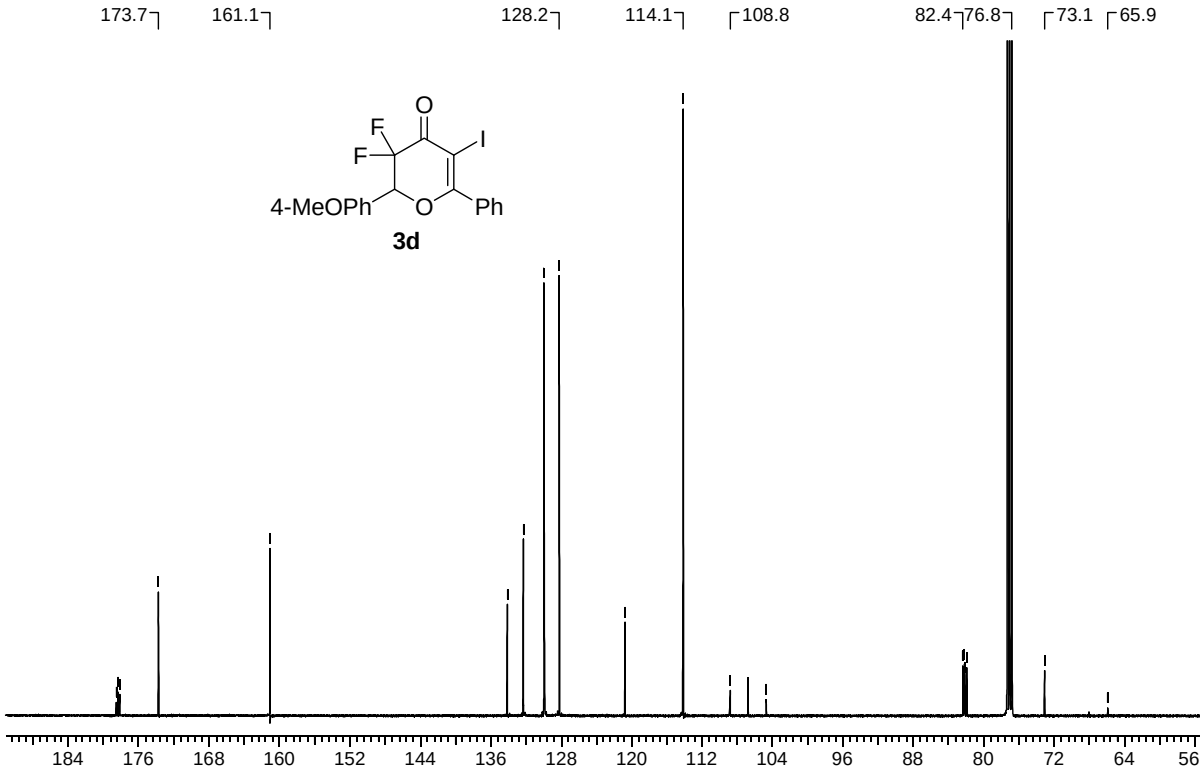


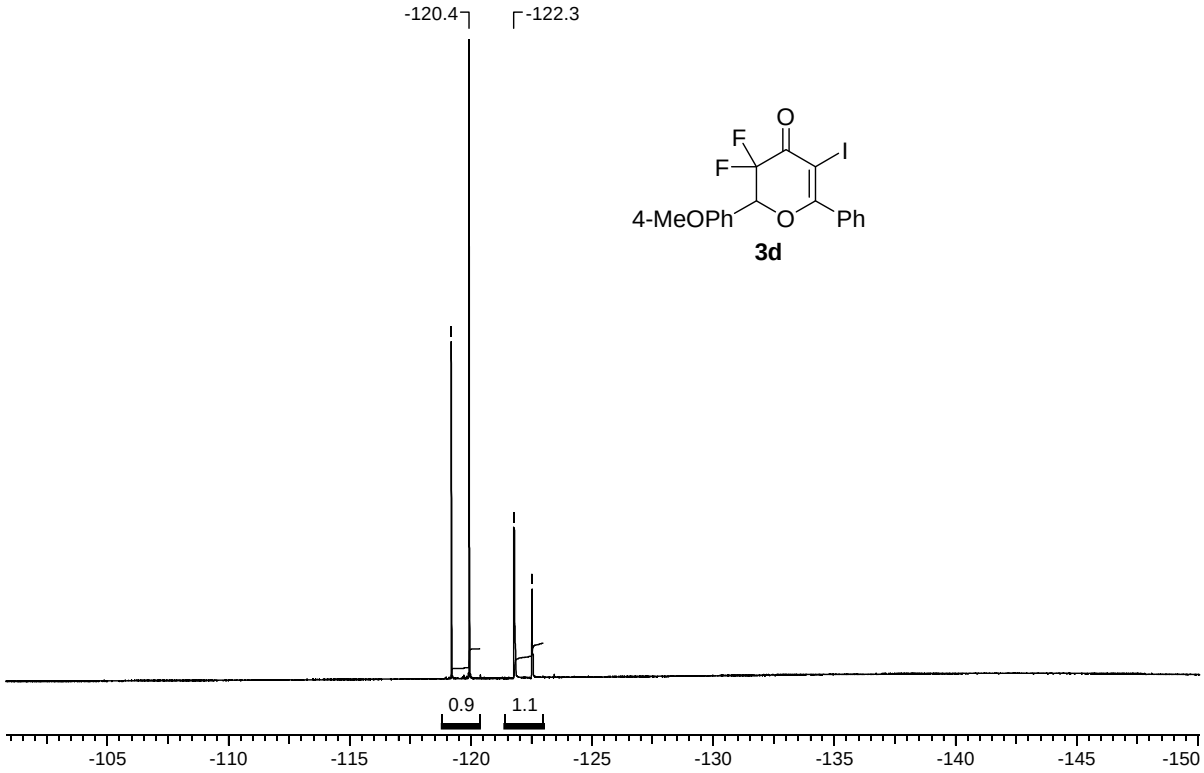




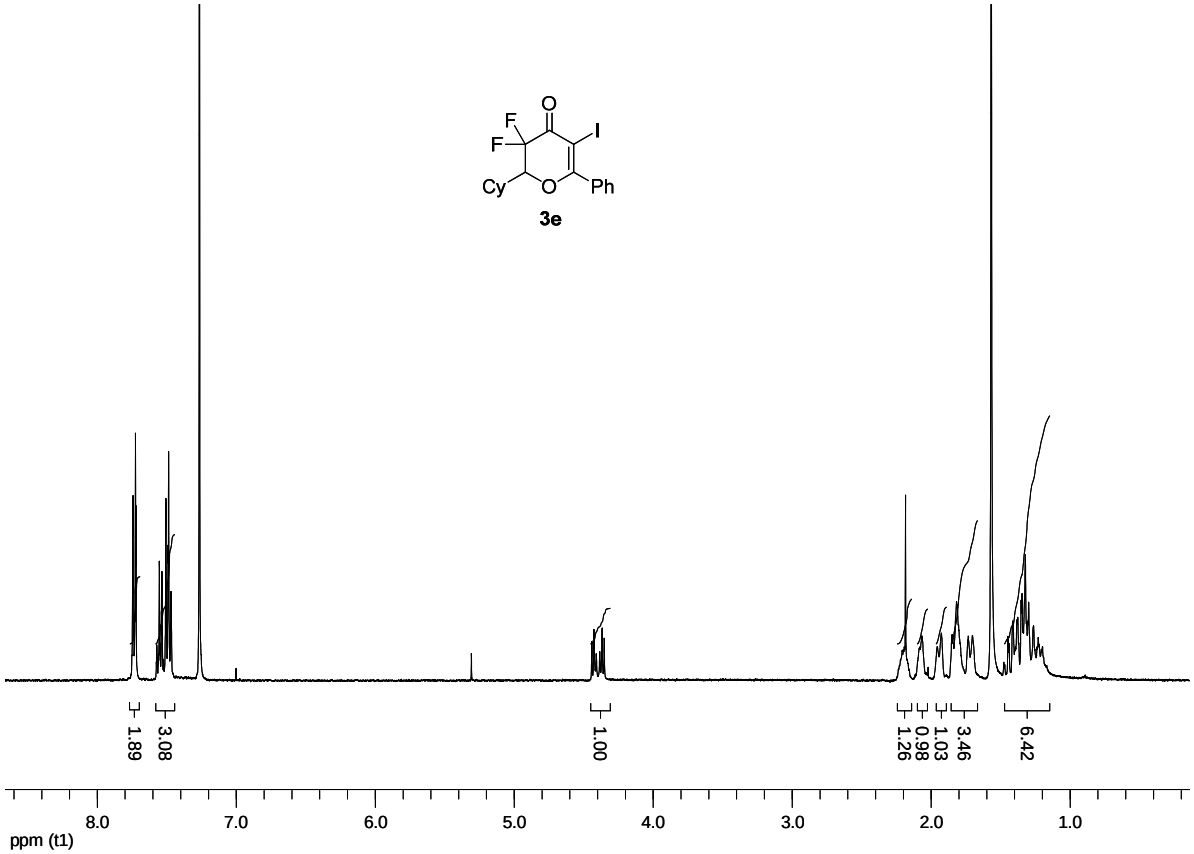
3,3-difluoro-5-iodo-2-(4-methoxyphenyl)-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (3d)

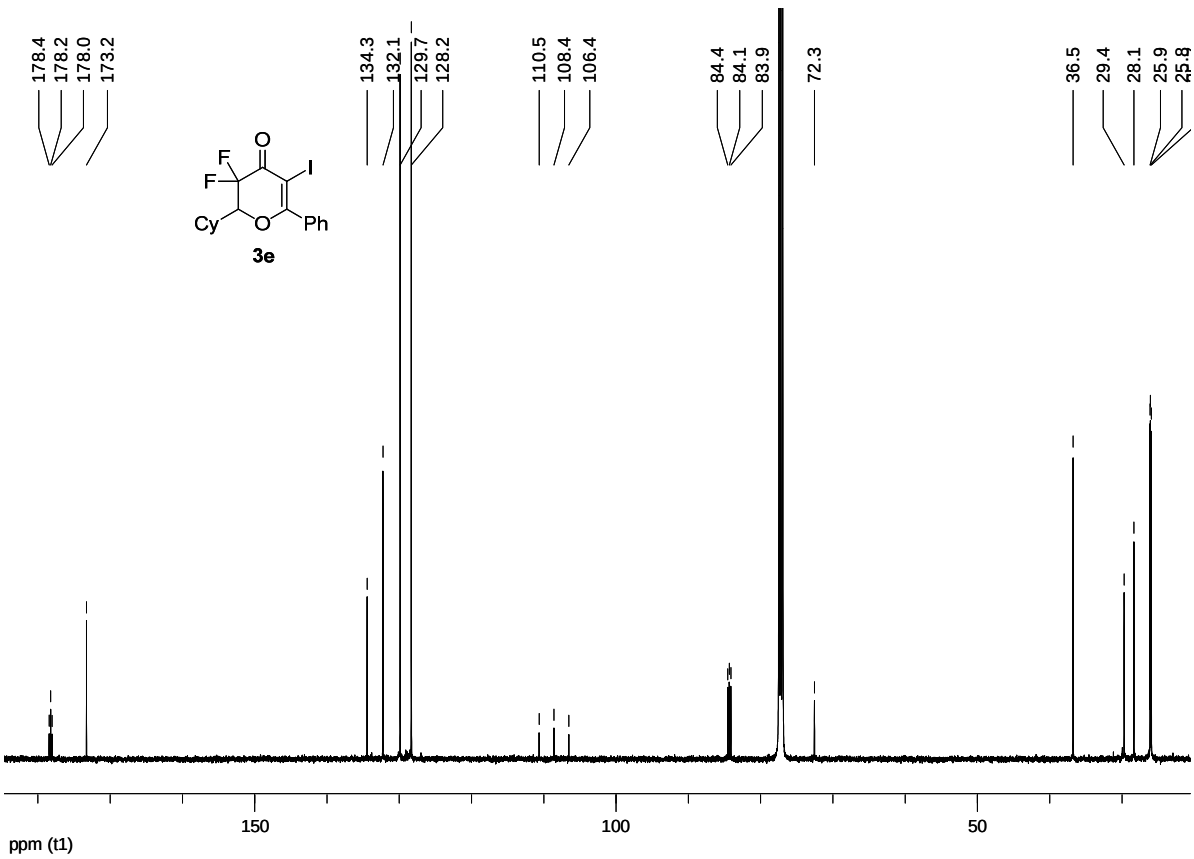


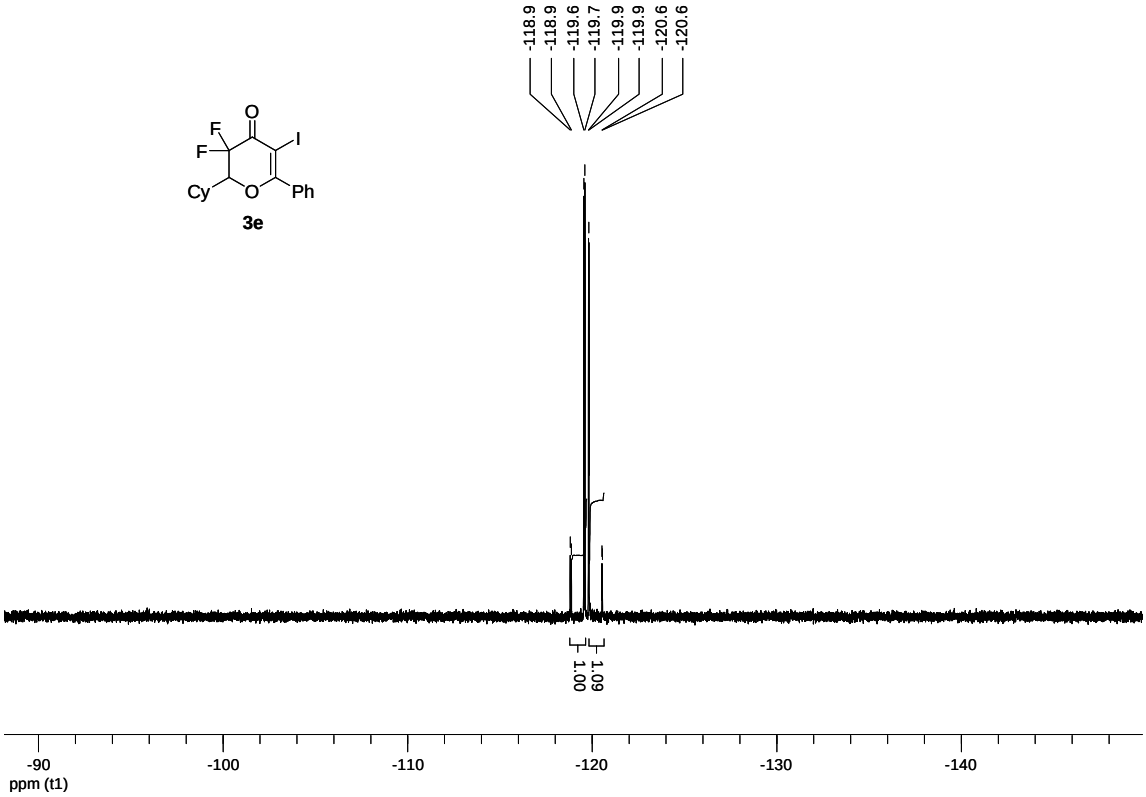

173.7
161.1
128.2
114.1
108.8
82.4
76.8
73.1
65.9
O
F
F
I
4-MeOPh
O
Ph
3d
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56


-120.4
-122.3
O
F
F
I
4-MeOPh
O
Ph
3d
0.9
1.1
-105
-110
-115
-120
-125
-130
-135
-140
-145
-150

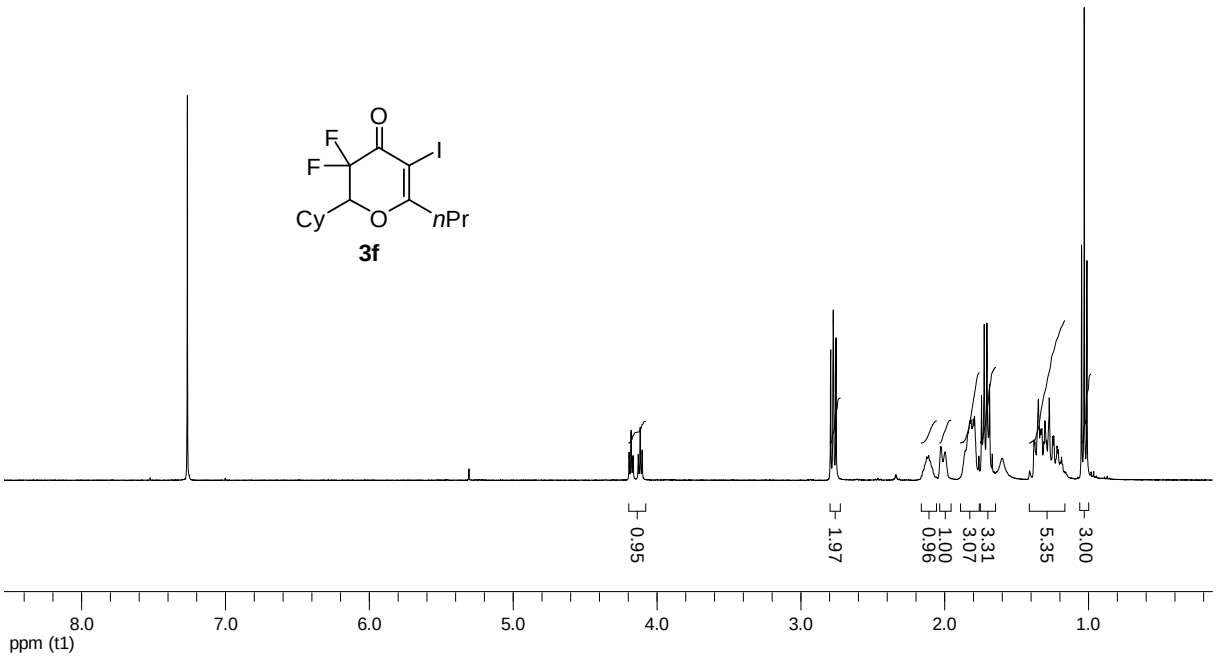
2-cyclohexyl-3,3-difluoro-5-iodo-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (3e)

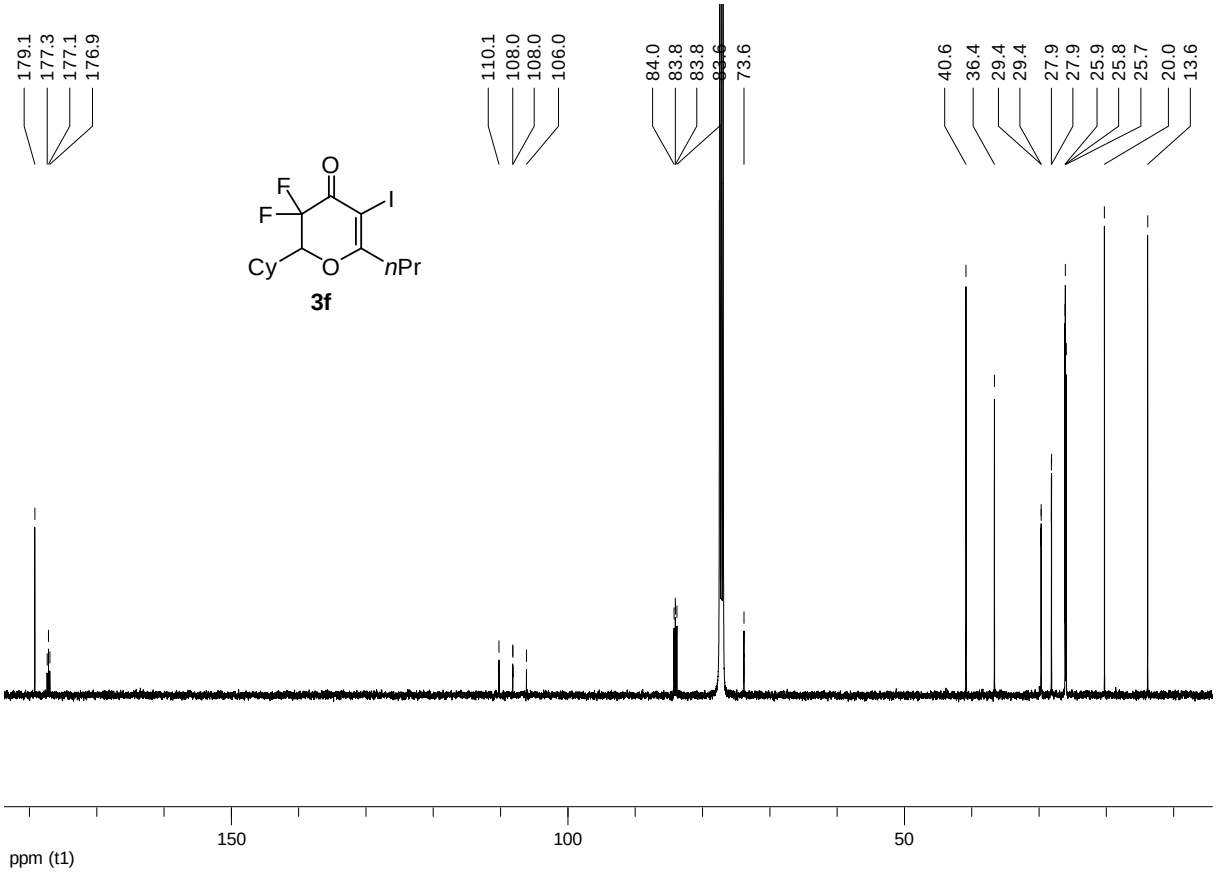




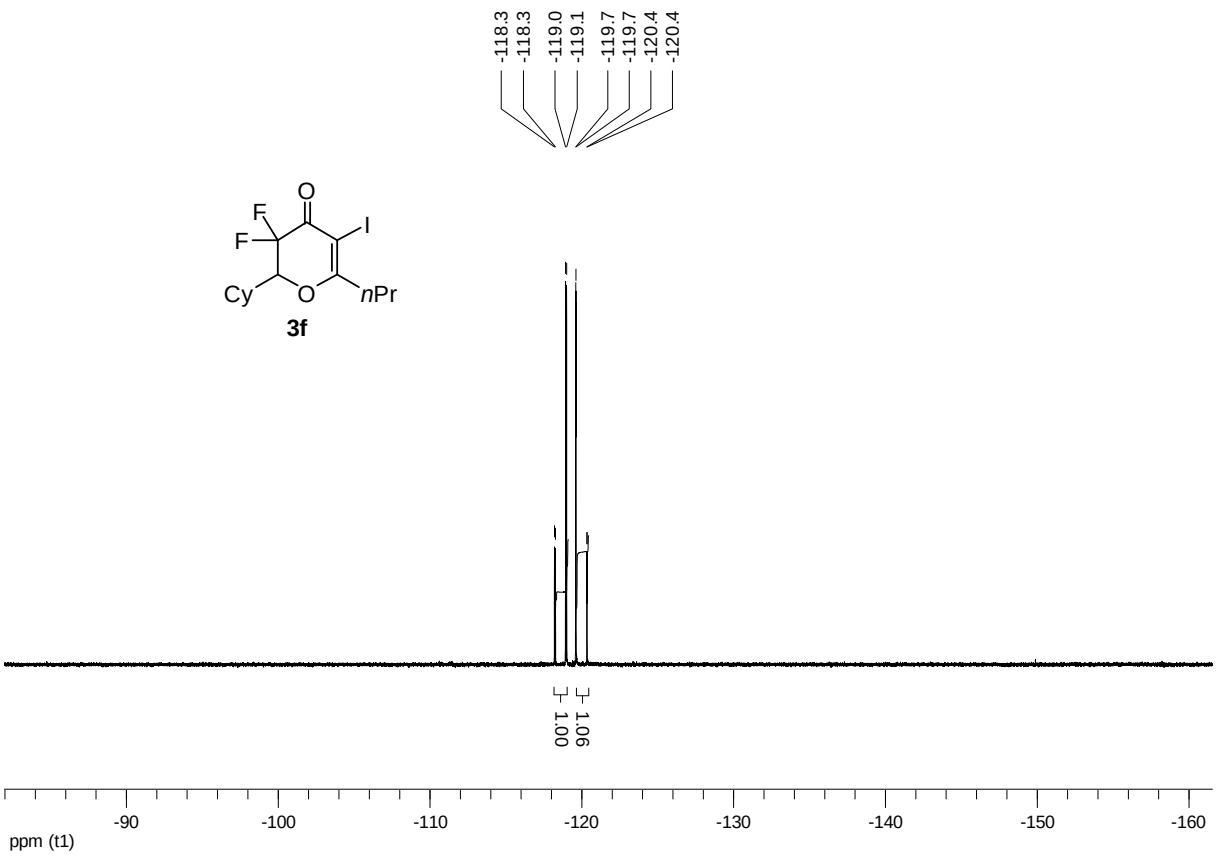


2-cyclohexyl-3,3-difluoro-5-iodo-6-propyl-2,3-dihydro-4*H*-pyran-4-one (3f)




179.1
177.3
177.1
176.9
110.1
108.0
108.0
106.0
84.0
83.8
83.8
73.6
40.6
36.4
29.4
29.4
27.9
27.9
25.9
25.8
25.7
20.0
13.6
O
F
F
I
Cy
O
nPr
150
100
50
ppm (t1)

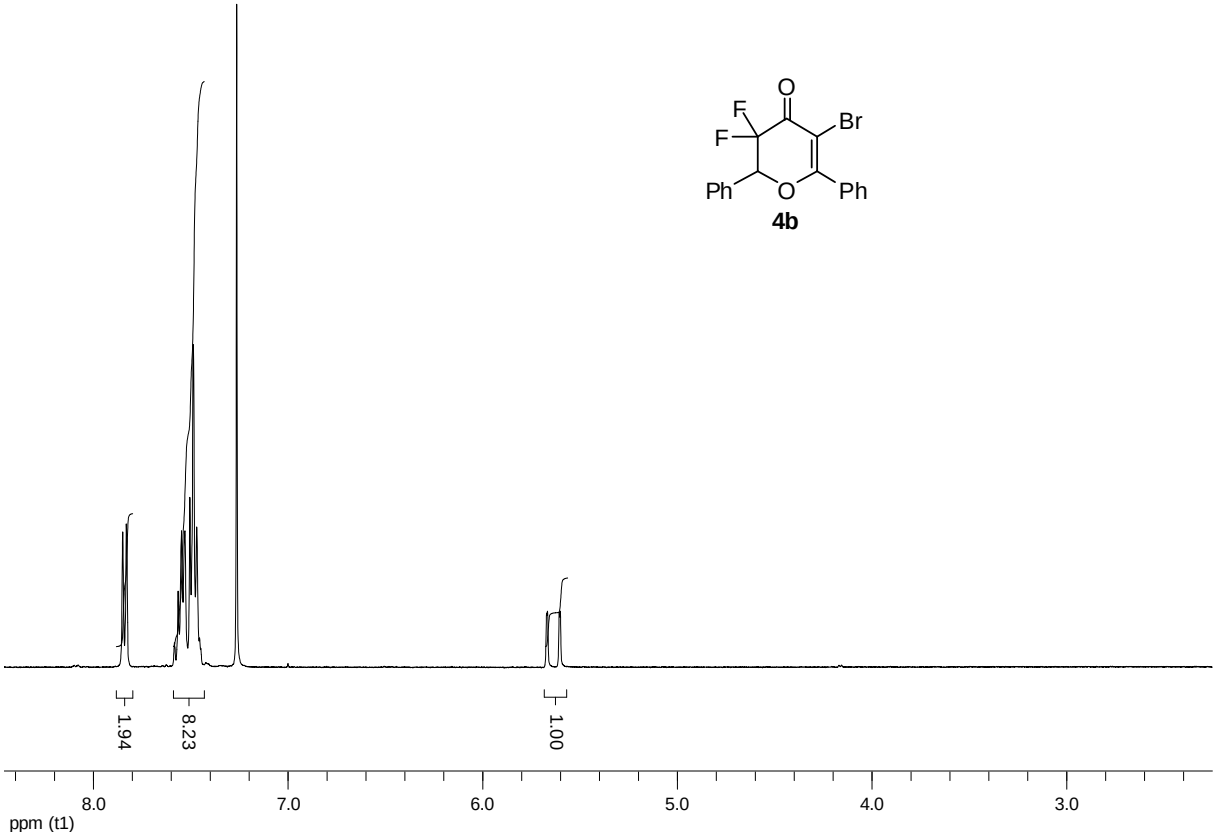
3f

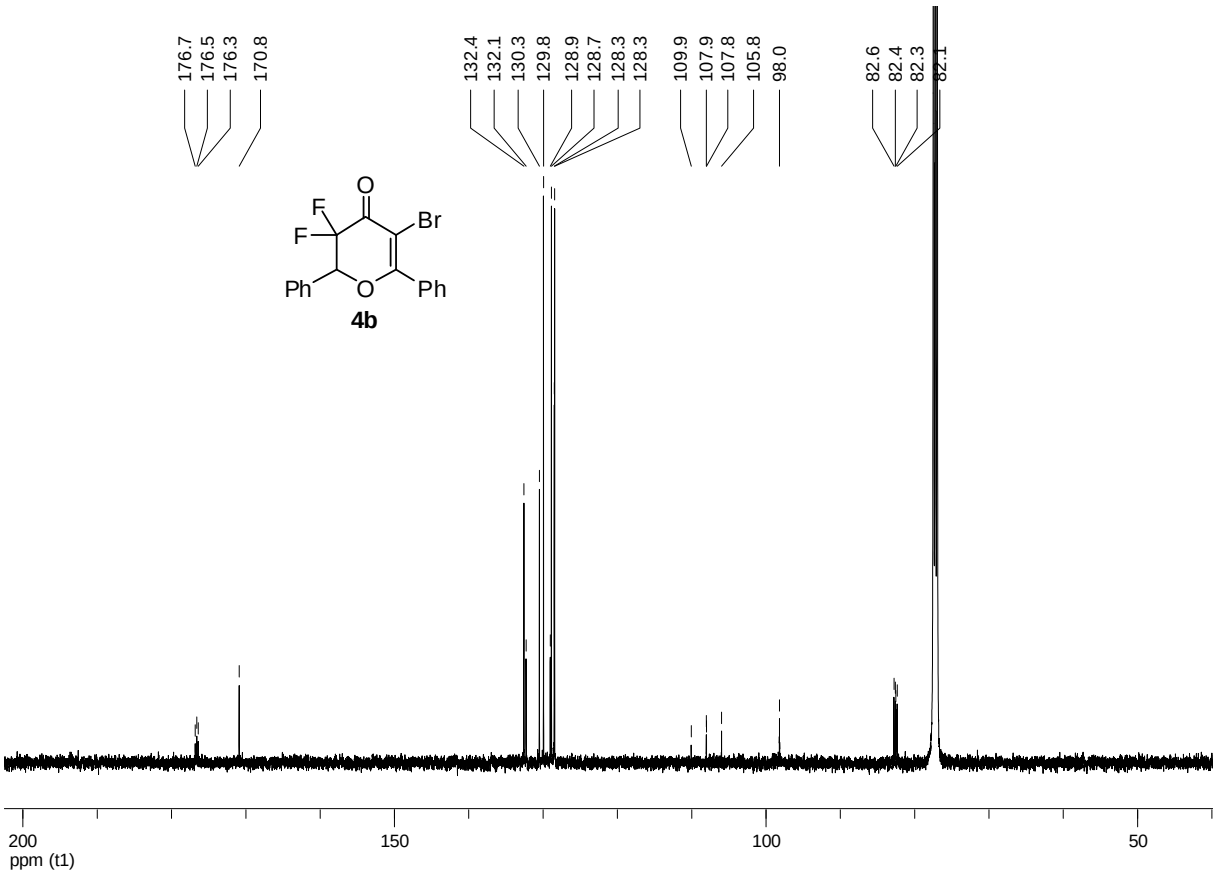

-118.3
-118.3
-119.0
-119.1
-119.7
-119.7
-120.4
-120.4
O
F
F
I
Cy
O
nPr
1.00
1.06
-90
-100
-110
-120
-130
-140
-150
-160
ppm (t1)

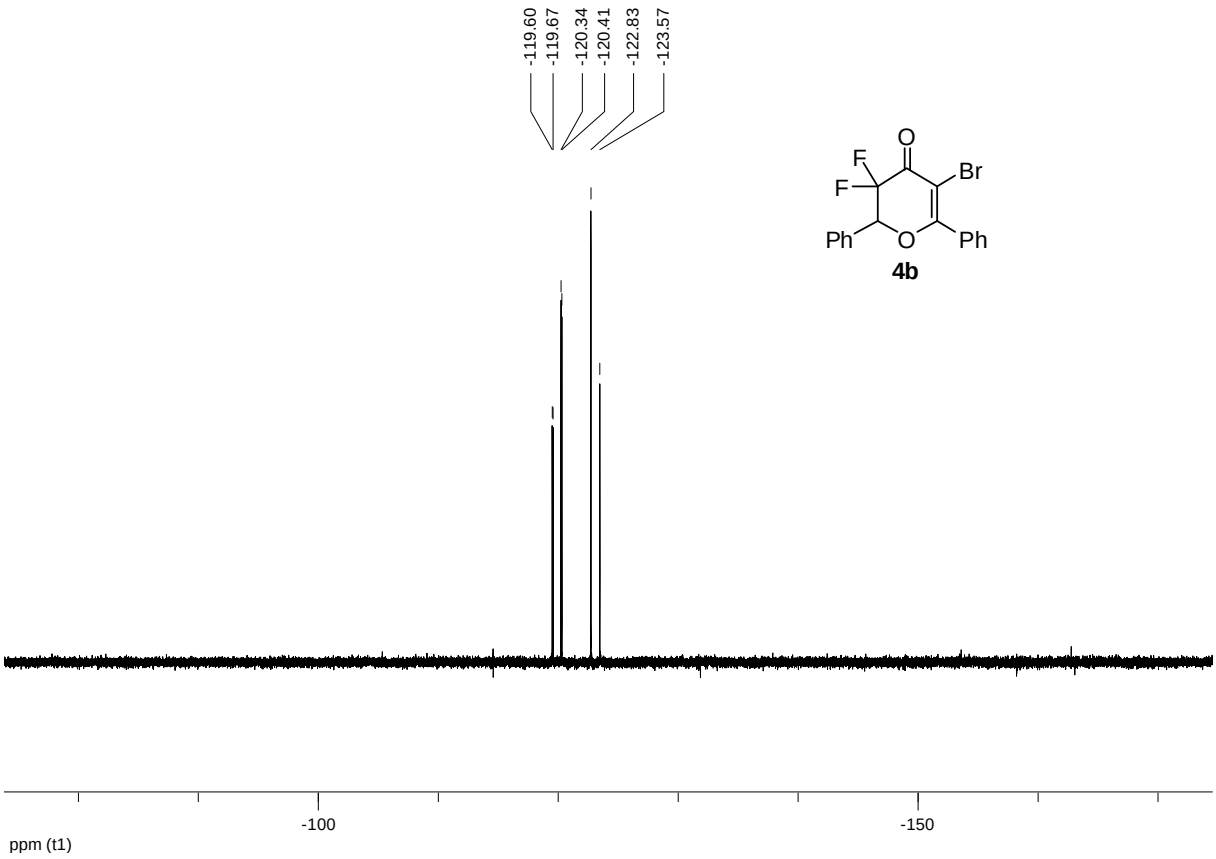
3f

G.4 – Bromodifluorodihydropyranones 4b and 4d

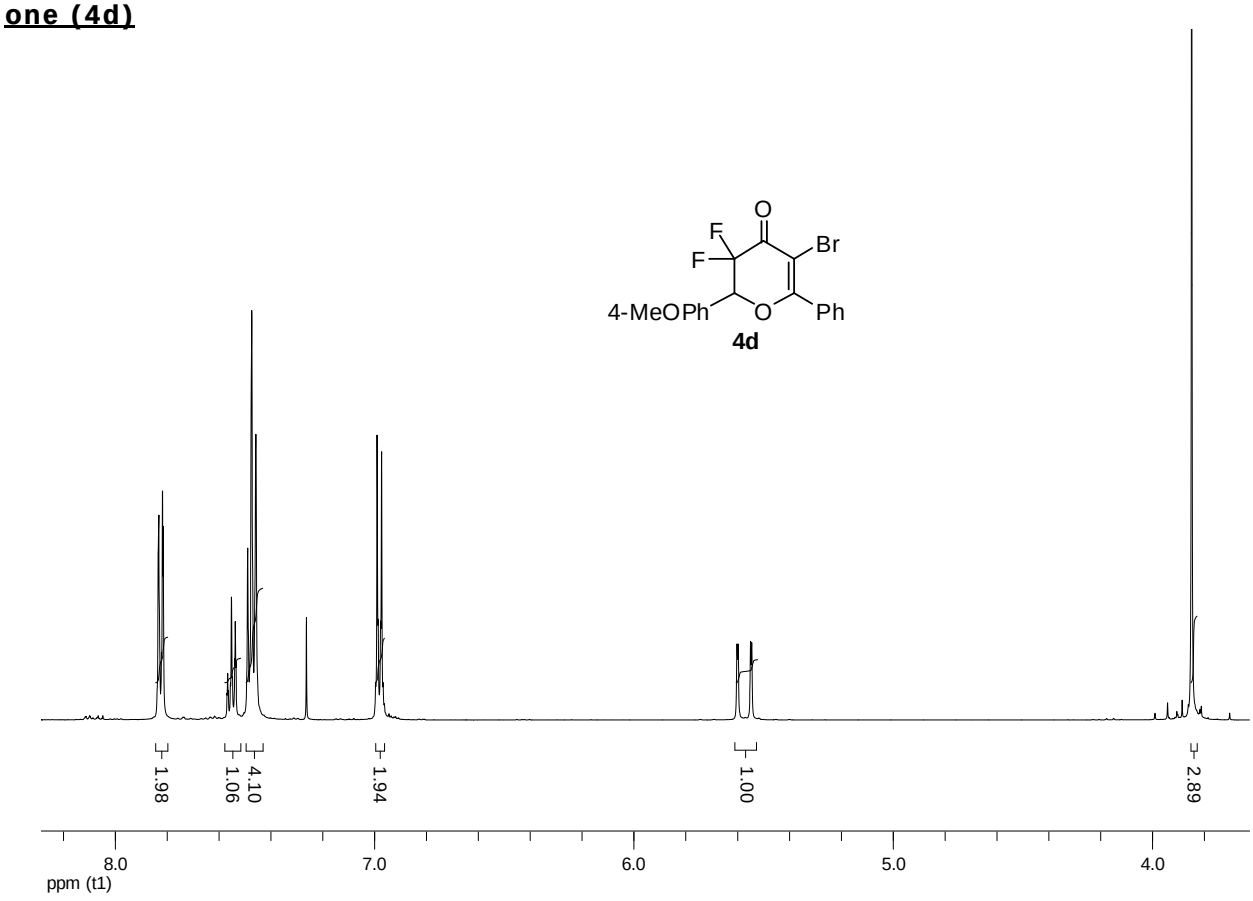
5-bromo-3,3-difluoro-2,6-diphenyl-2,3-dihydro-4*H*-pyran-4-one (4b)

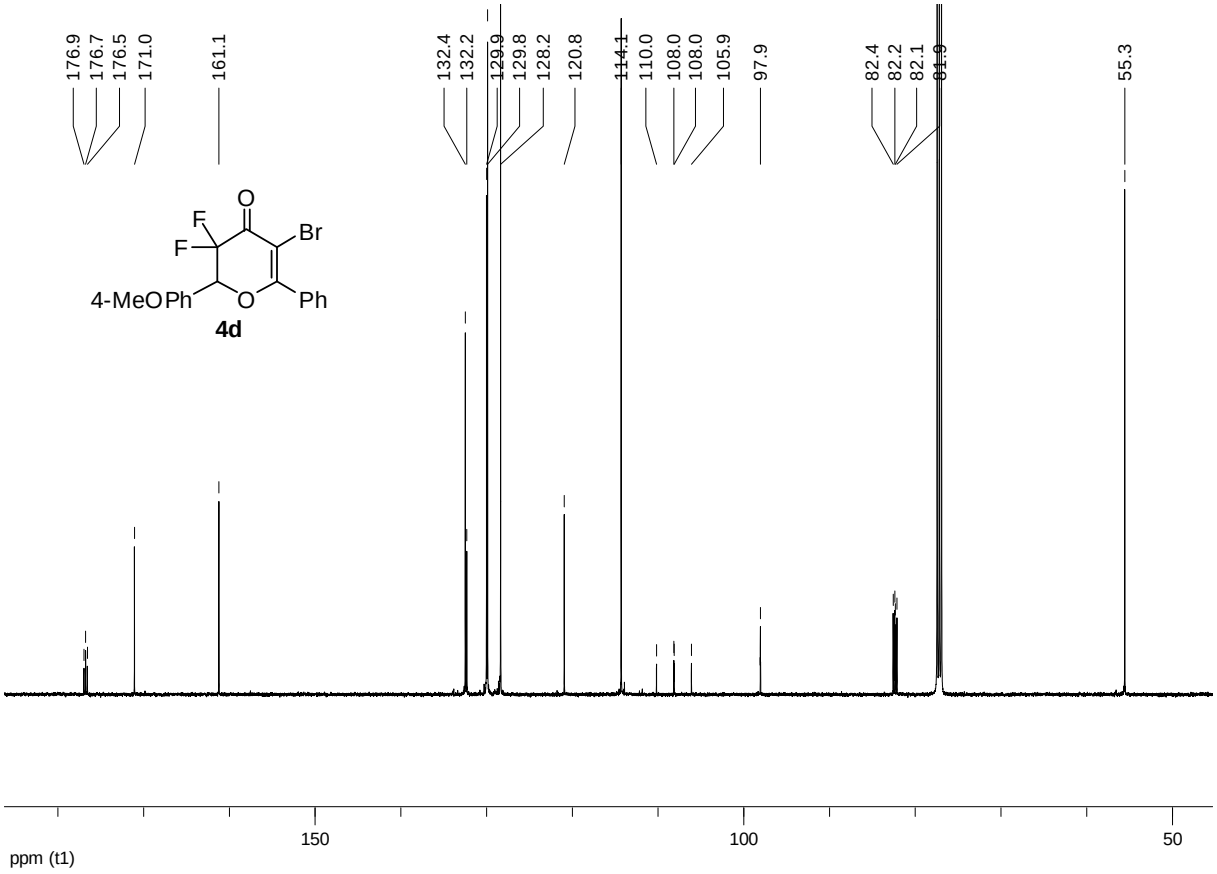


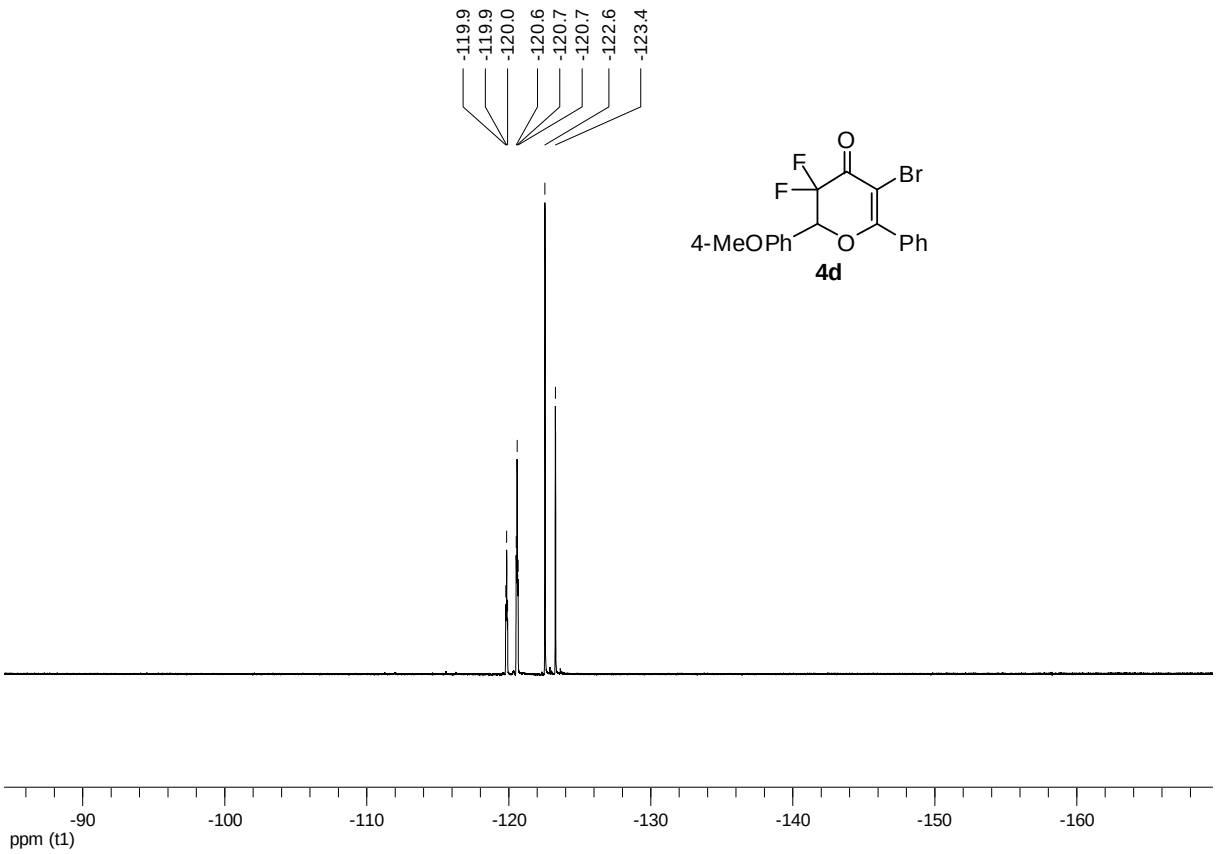




5-bromo-3,3-difluoro-2-(4-methoxyphenyl)-6-phenyl-2,3-dihydro-4H-pyran-4-one (4d)

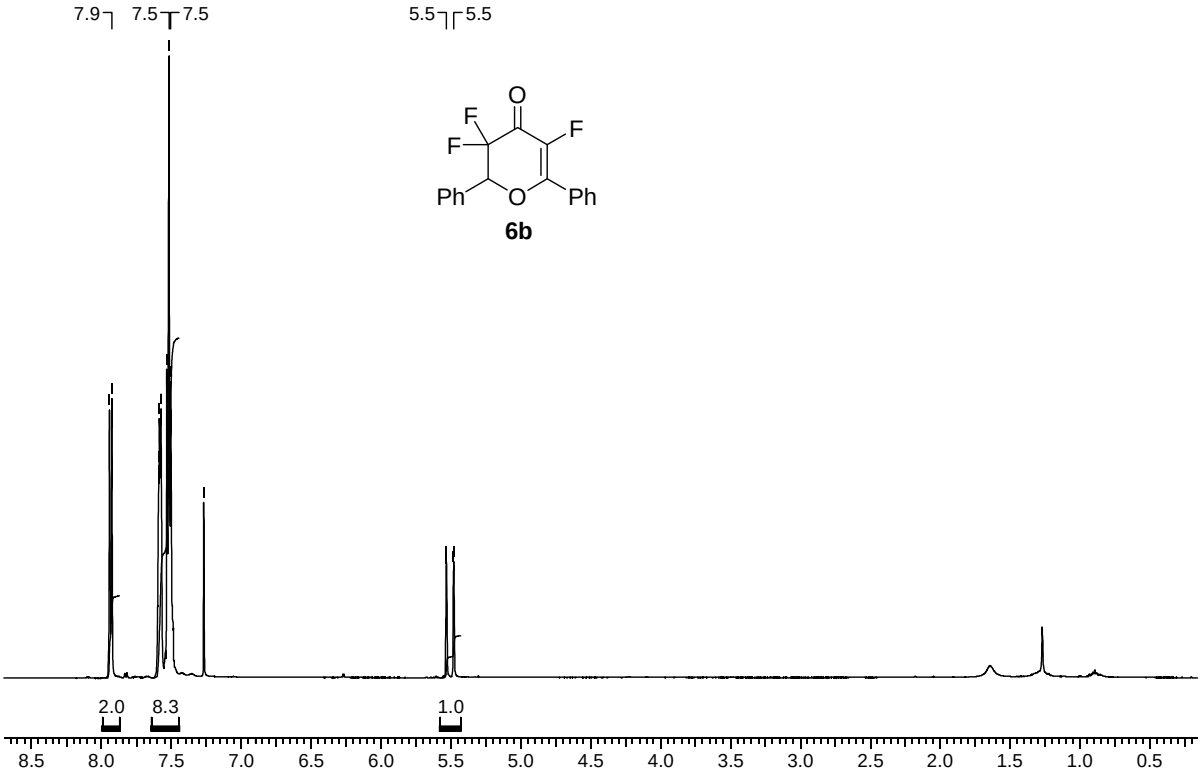



176.9
176.7
176.5
171.0
161.1
132.4
132.2
129.9
129.8
128.2
120.8
114.1
110.0
108.0
108.0
105.9
97.9
82.4
82.2
82.1
81.9
55.3
O
F
F
Br
4-MeOPh
O
Ph
4d
150
100
50
ppm (t1)

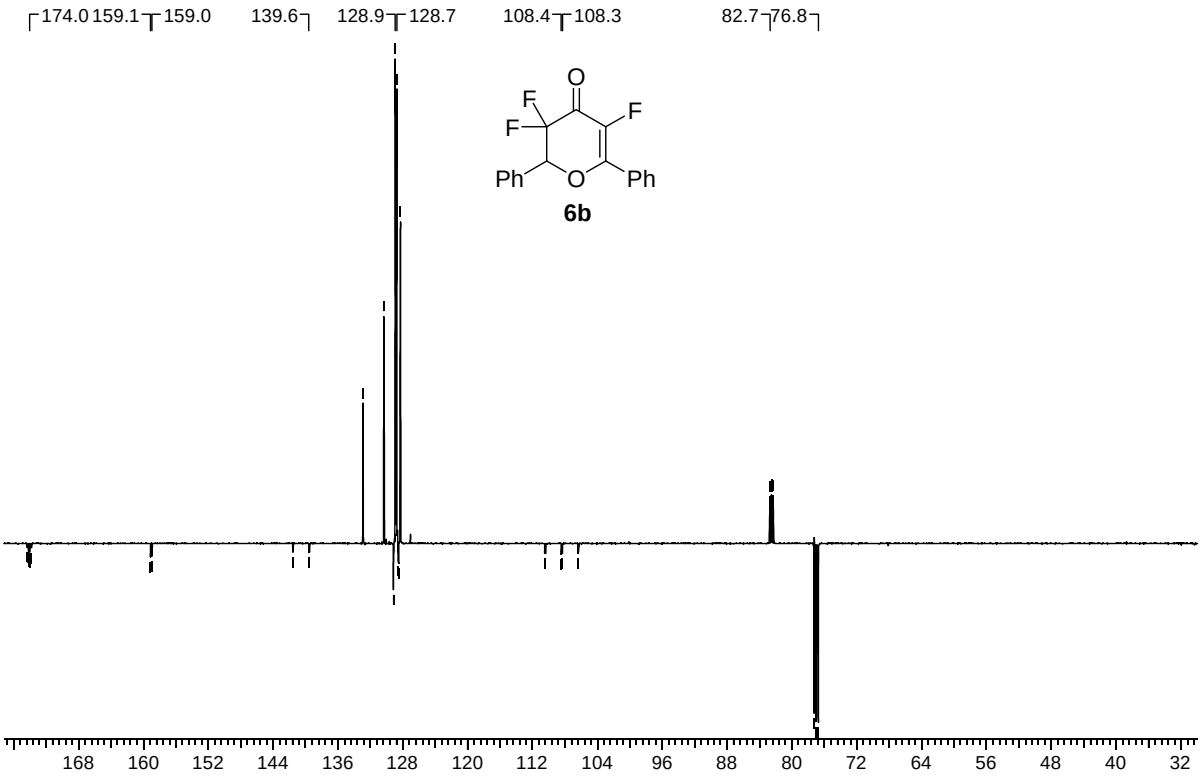

-119.9
-119.9
-120.0
-120.6
-120.7
-120.7
-122.6
-123.4
O
F
F
Br
4-MeOPh
O
Ph
4d
-90
-100
-110
-120
-130
-140
-150
-160
ppm (t1)

G.5 – Trifluorodihydropyranones 6b, 6d, 6e, 6f, 6h

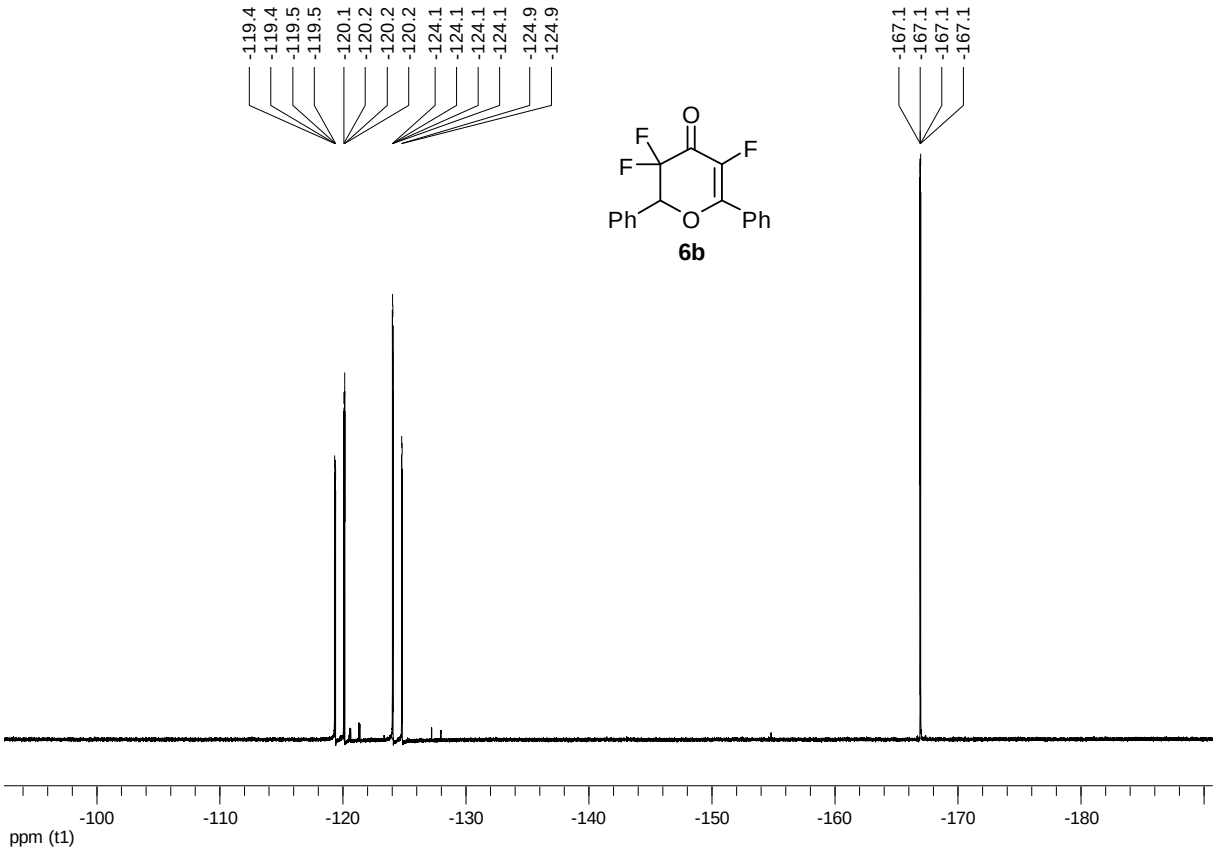
3,3,5-trifluoro-2,6-diphenyl-2,3-dihydro-4*H*-pyran-4-one (6b)



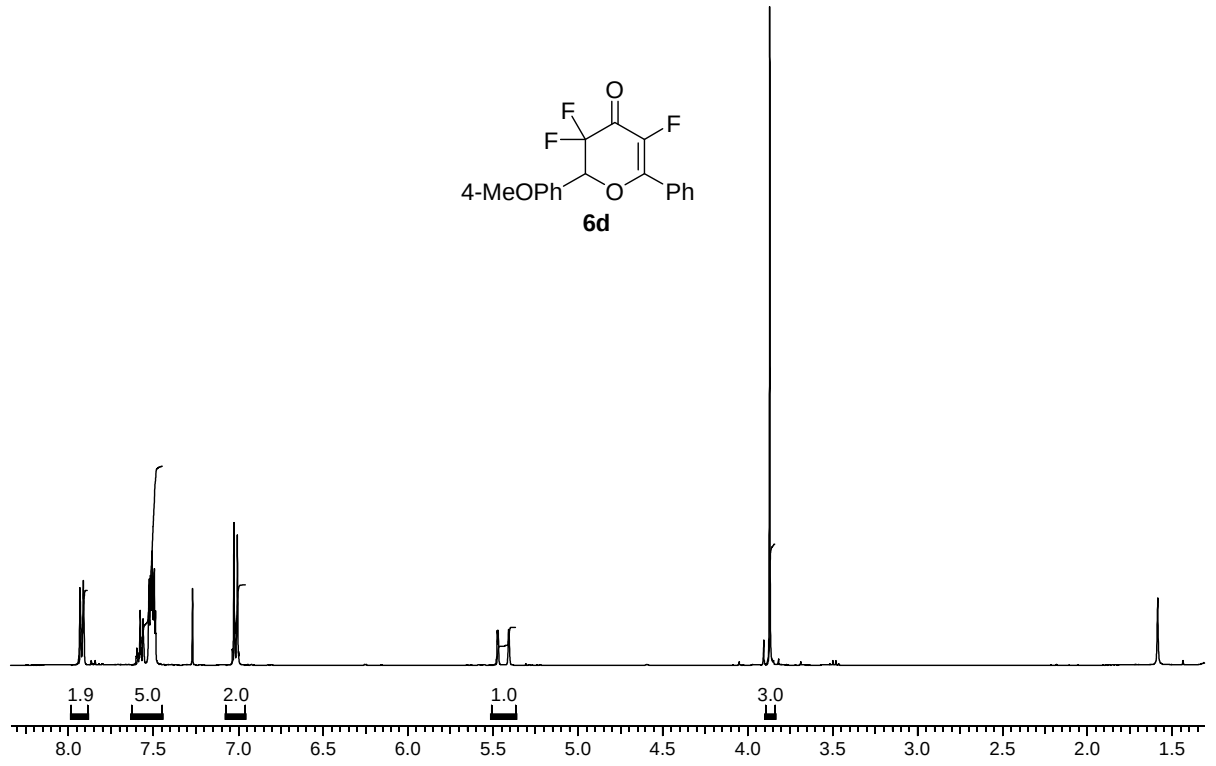
6b

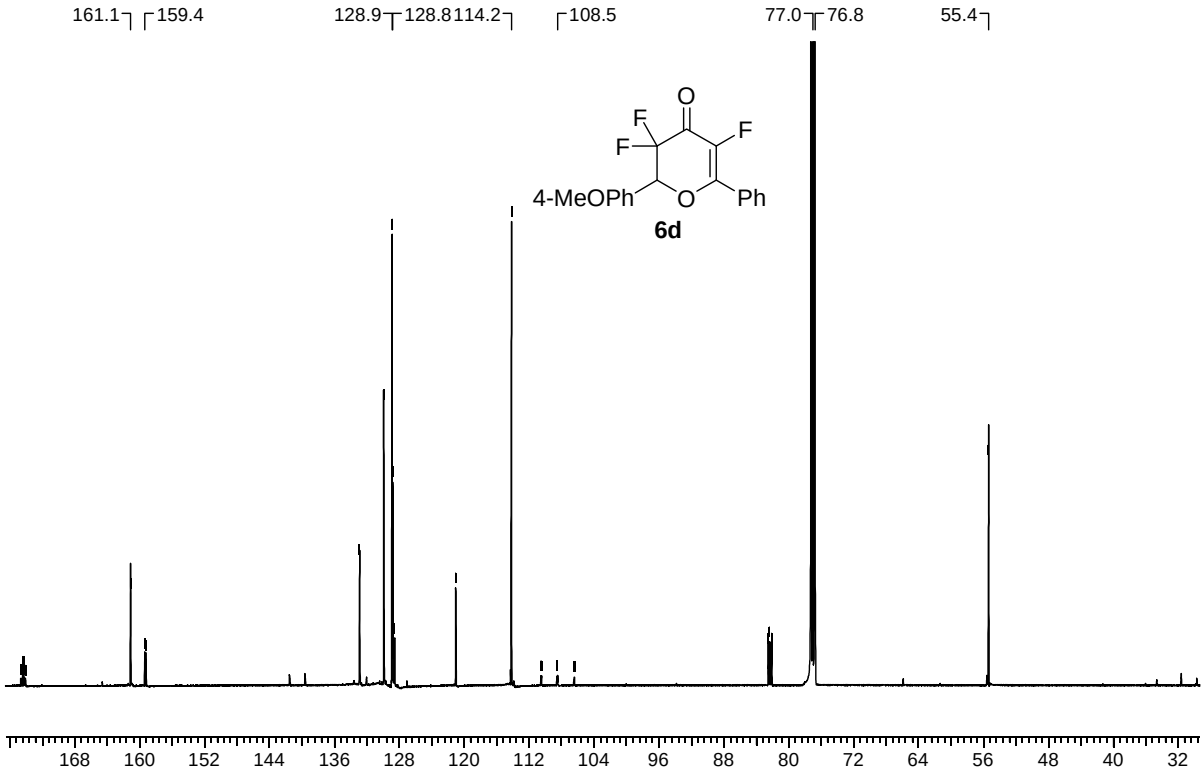


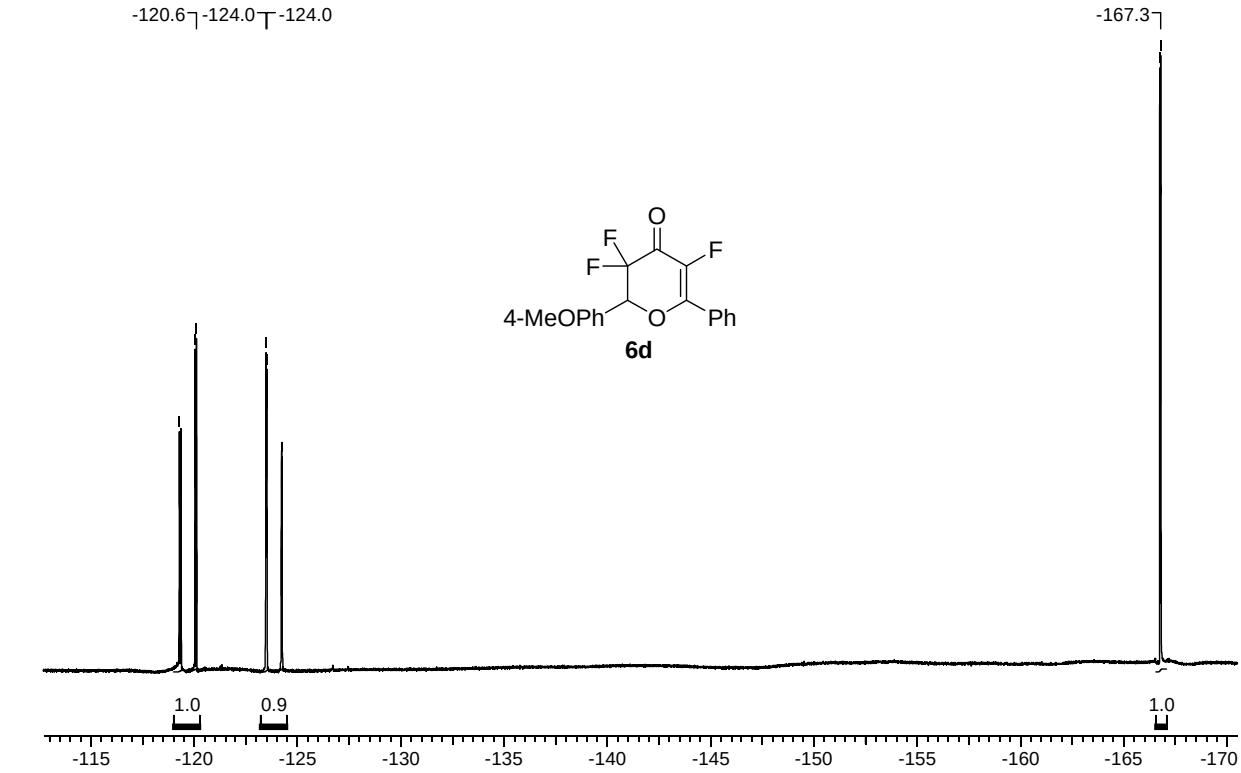
6b



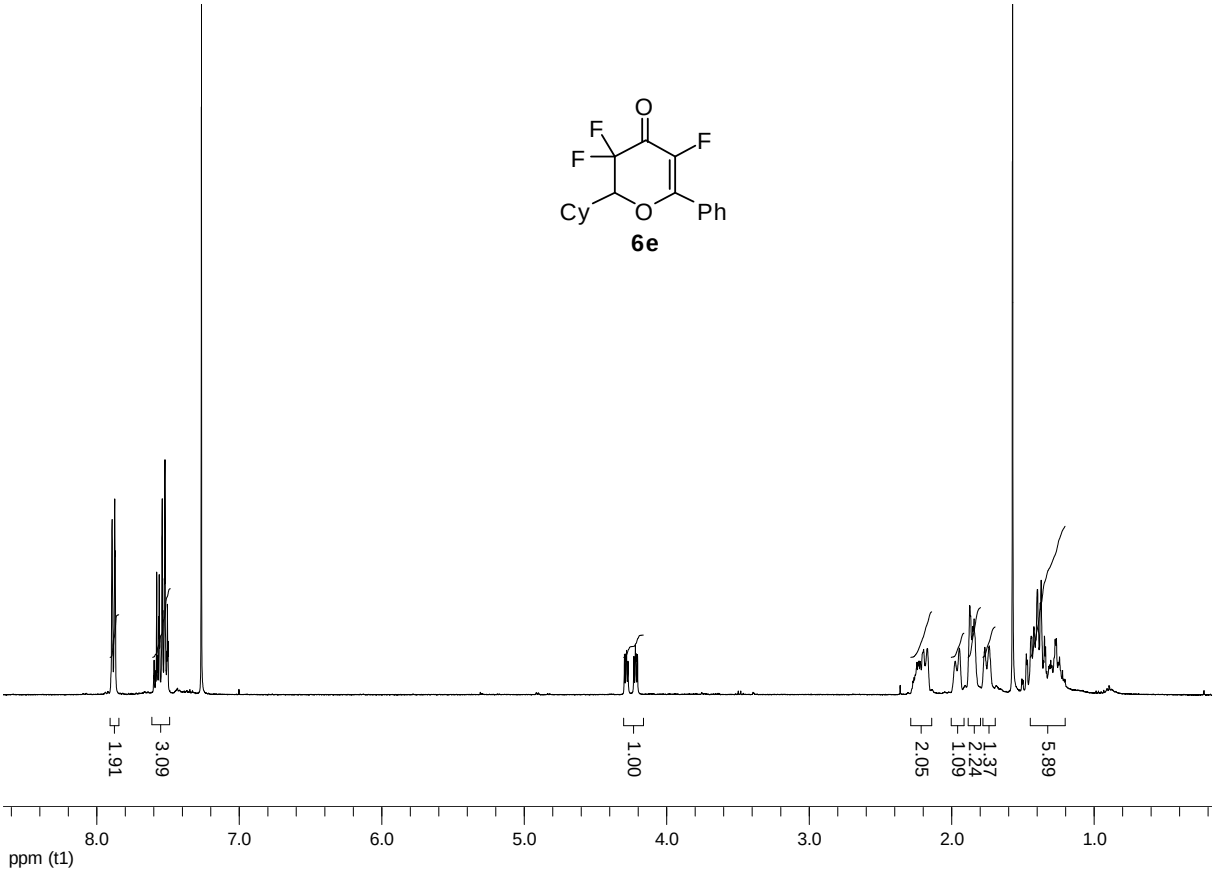
3,3,5-trifluoro-2-(4-methoxyphenyl)-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (6d)

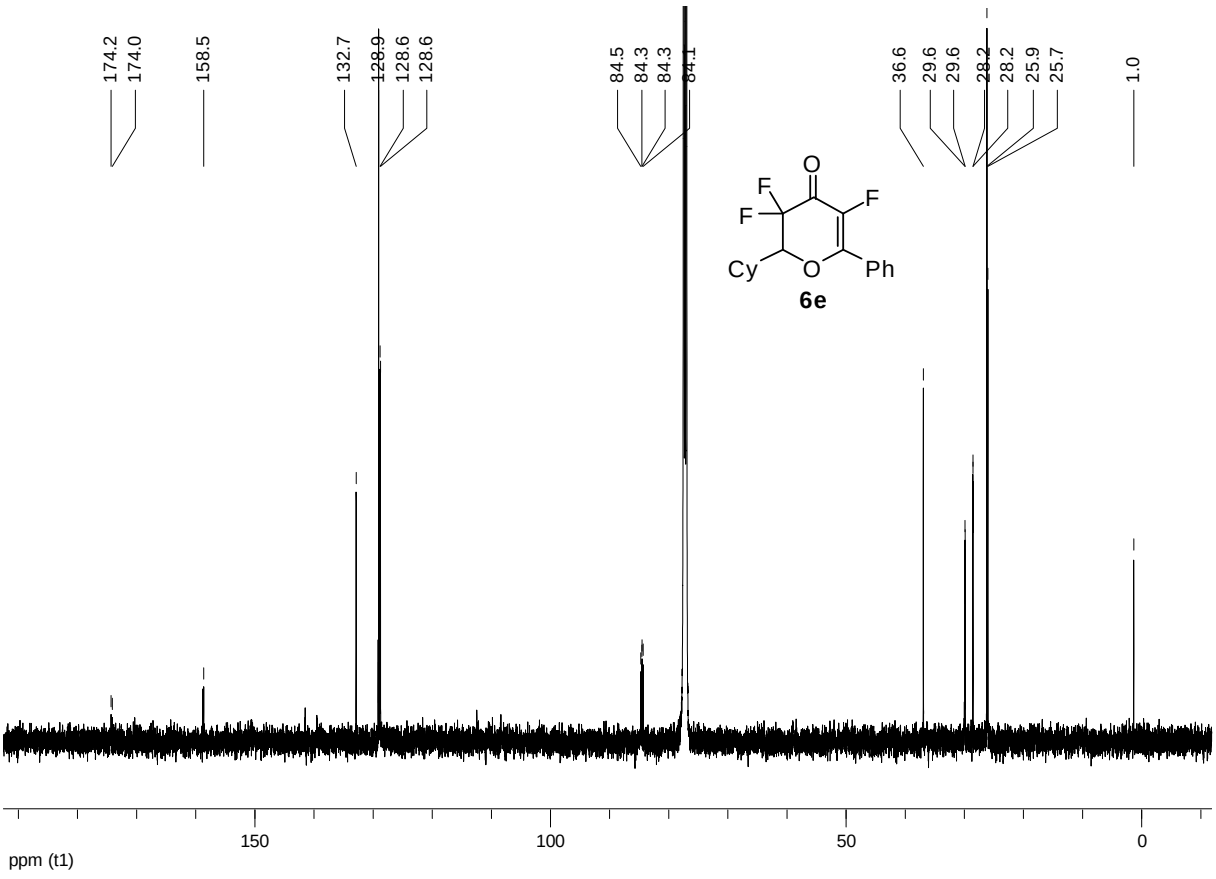


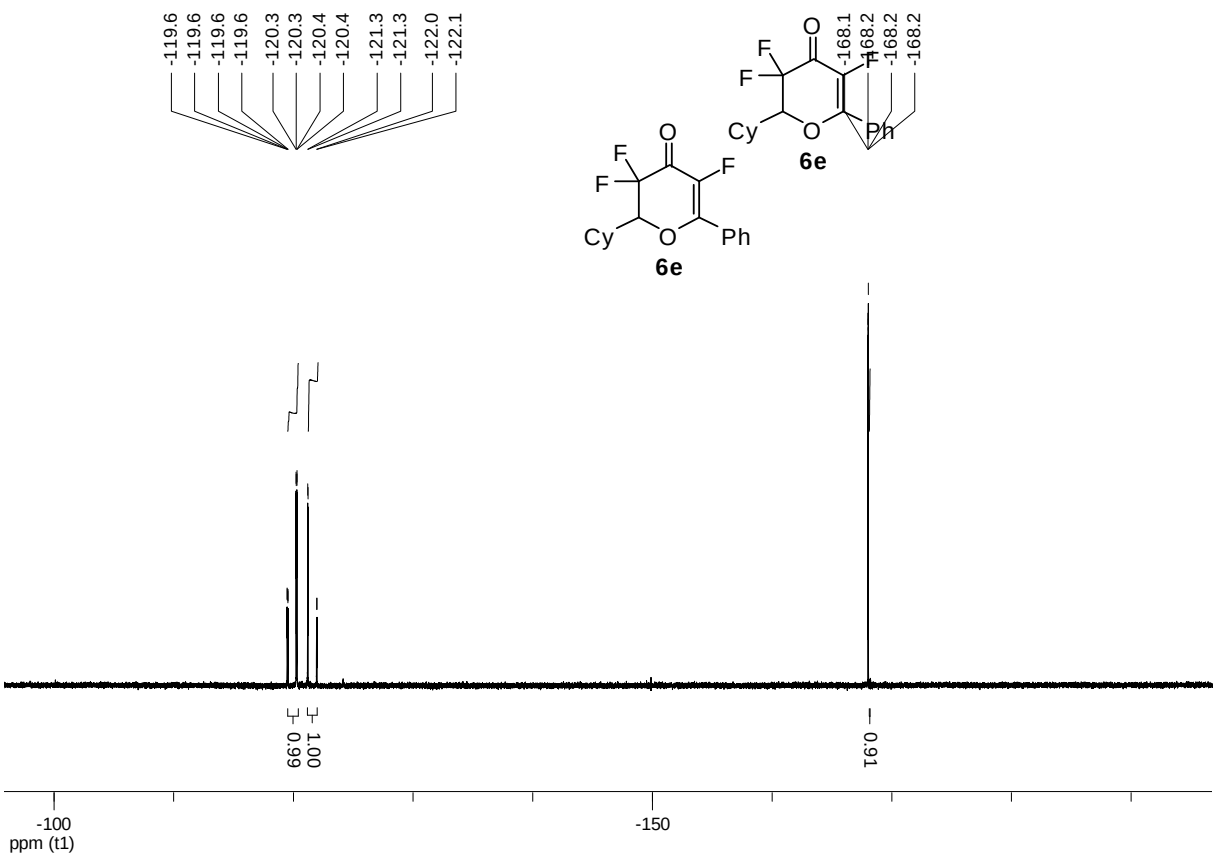

161.1
159.4
128.9
128.8
114.2
108.5
77.0
76.8
55.4
O
F
F
F
4-MeOPh
O
Ph
6d
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32


-120.6
-124.0
-124.0
-167.3
O
F
F
F
4-MeOPh
O
Ph
6d
1.0
0.9
1.0
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
-165
-170

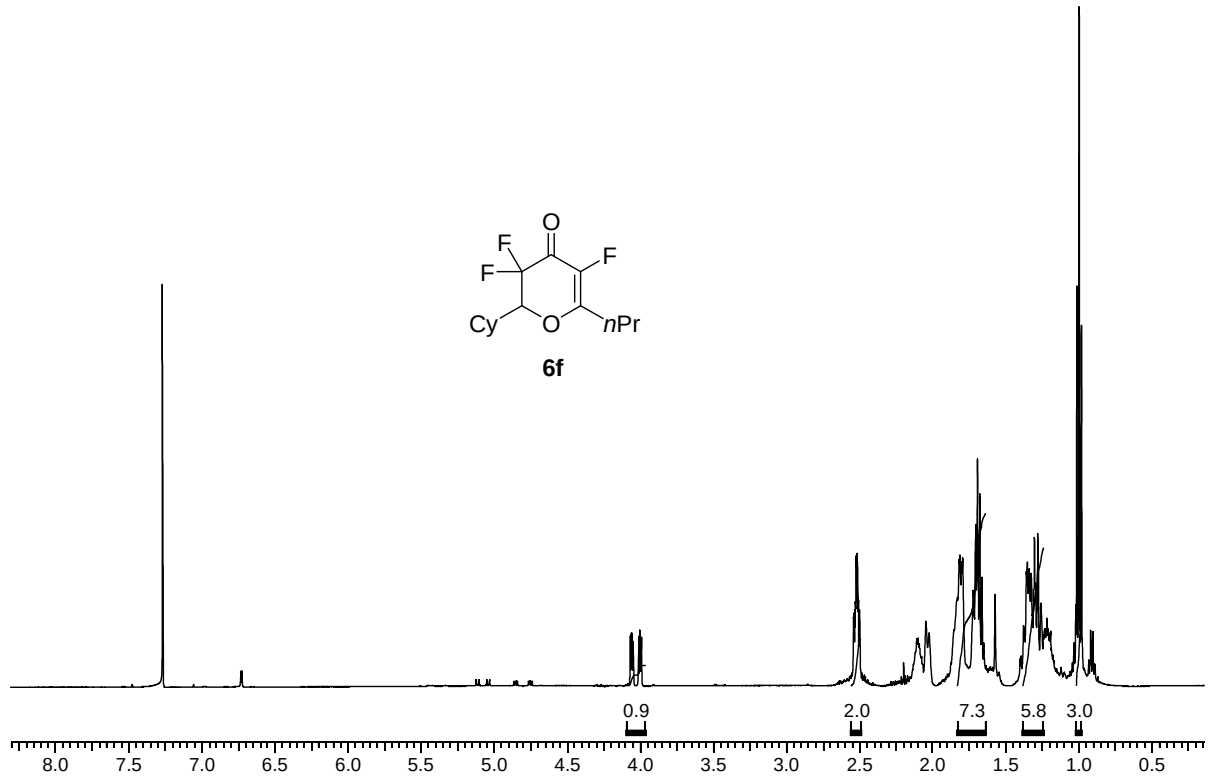
2-cyclohexyl-3,3,5-trifluoro-6-phenyl-2,3-dihydro-4*H*-pyran-4-one (6e)

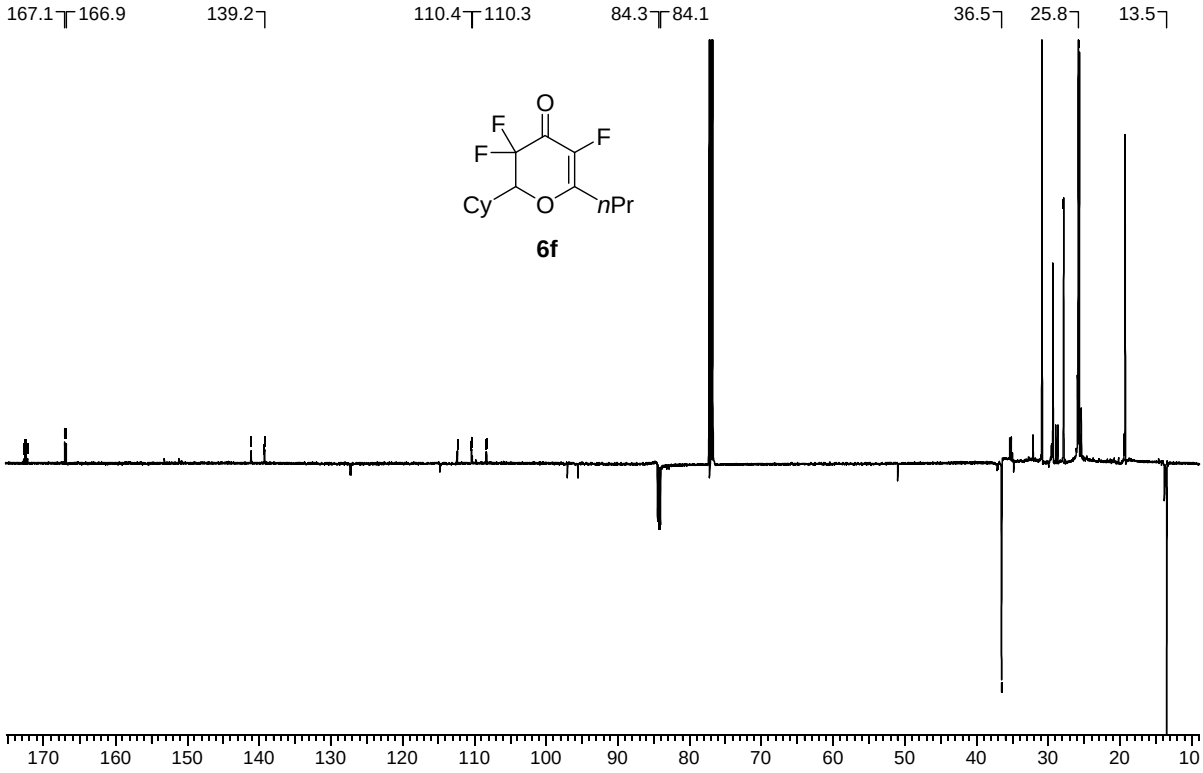


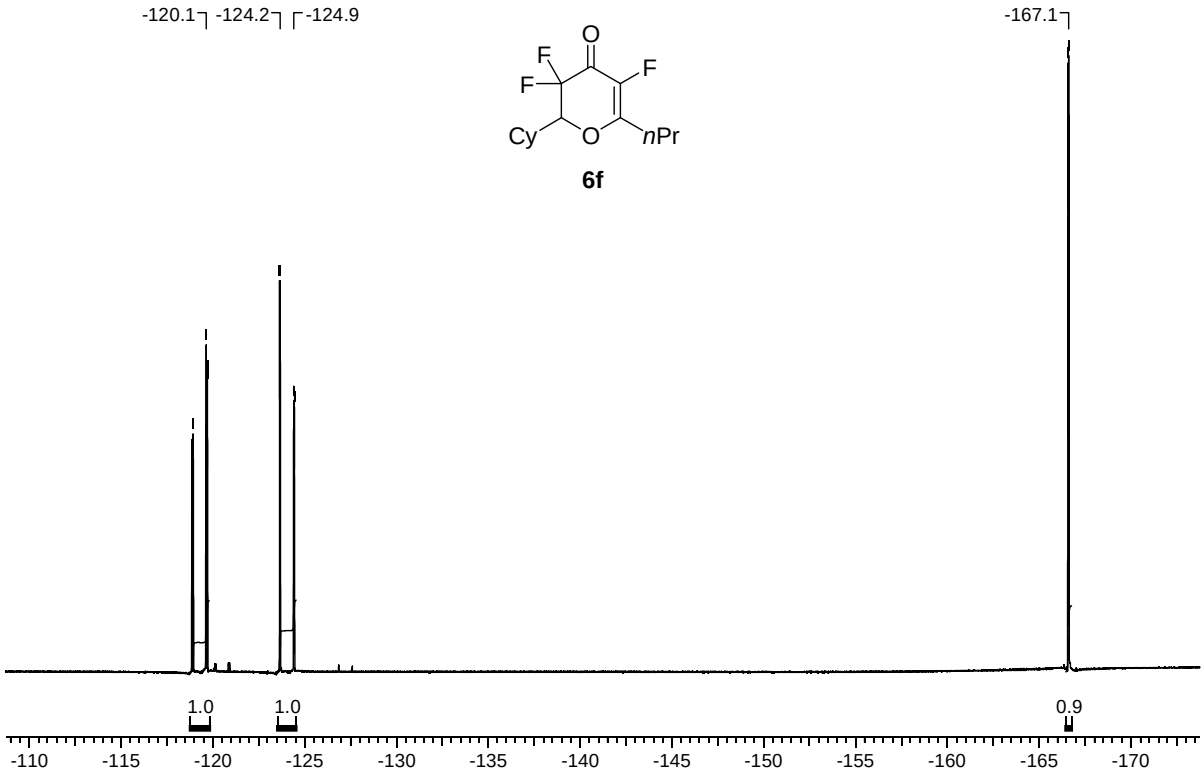




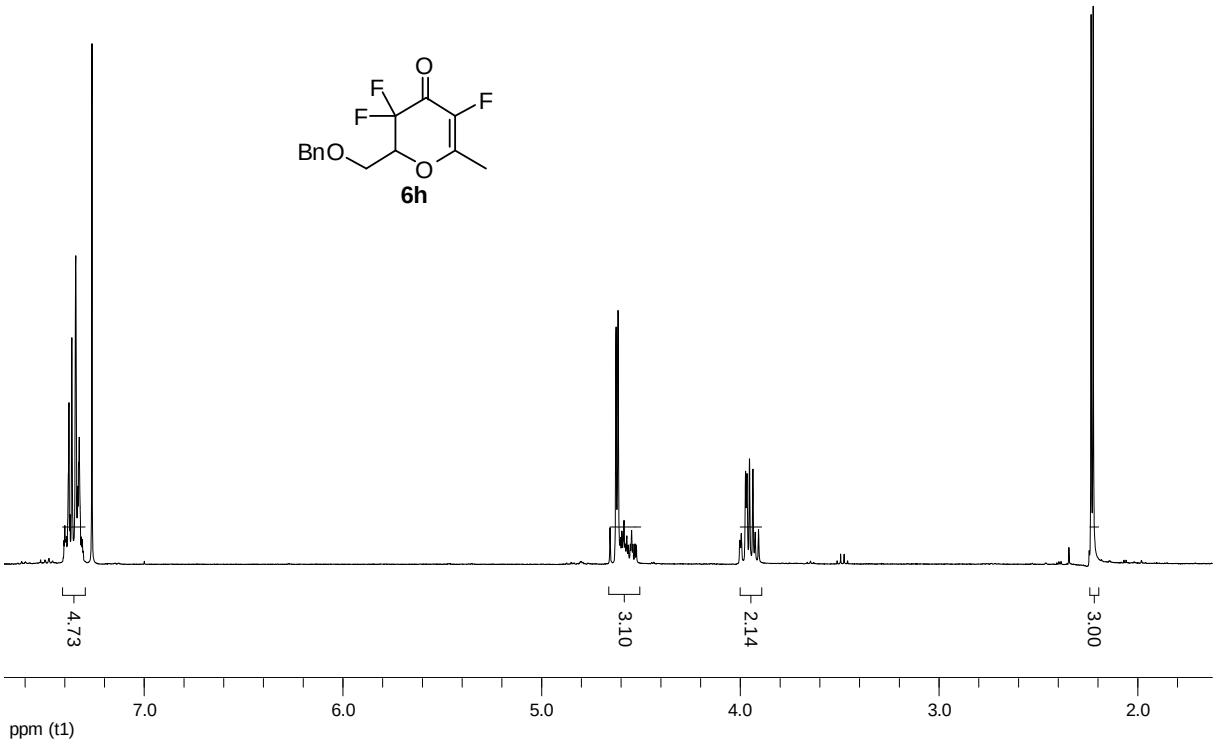
2-cyclohexyl-3,3,5-trifluoro-6-propyl-2,3-dihydro-4*H*-pyran-4-one (6f)

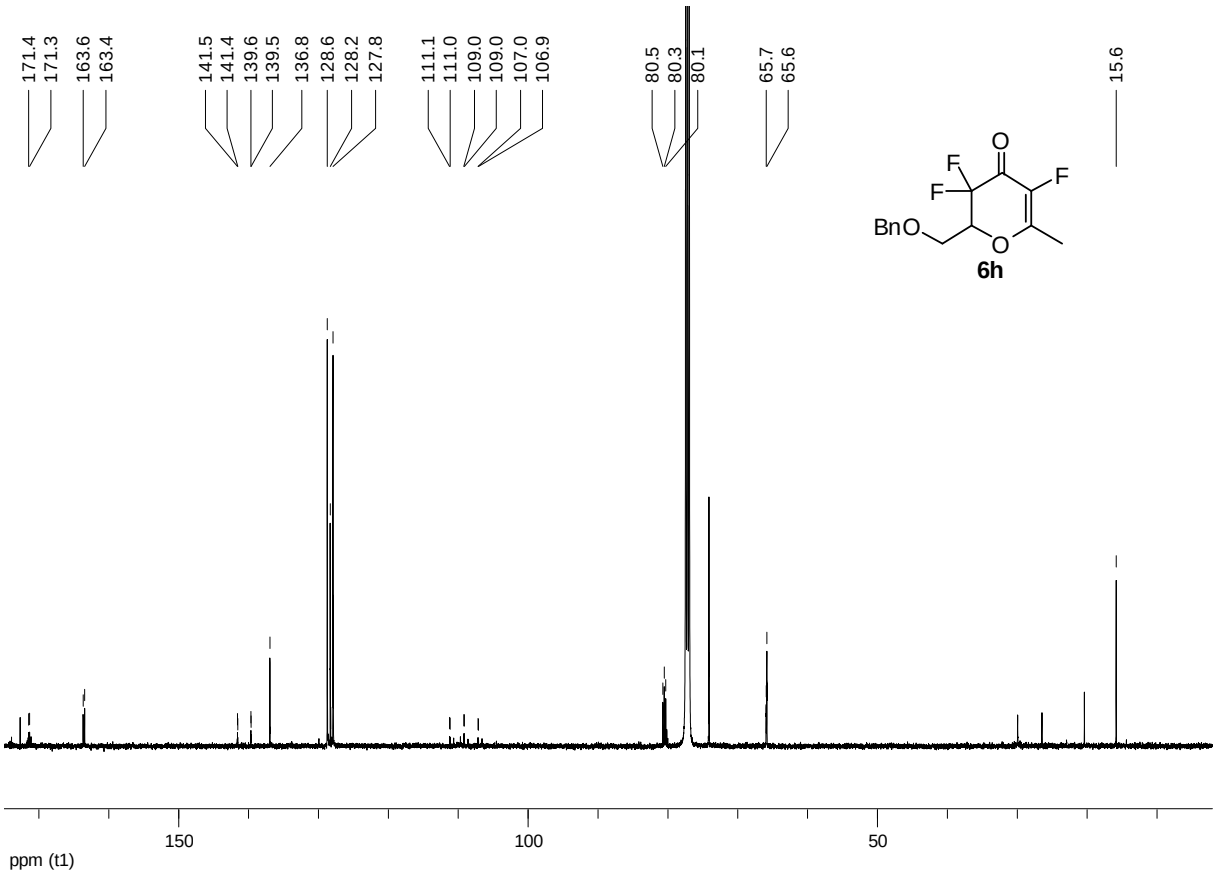


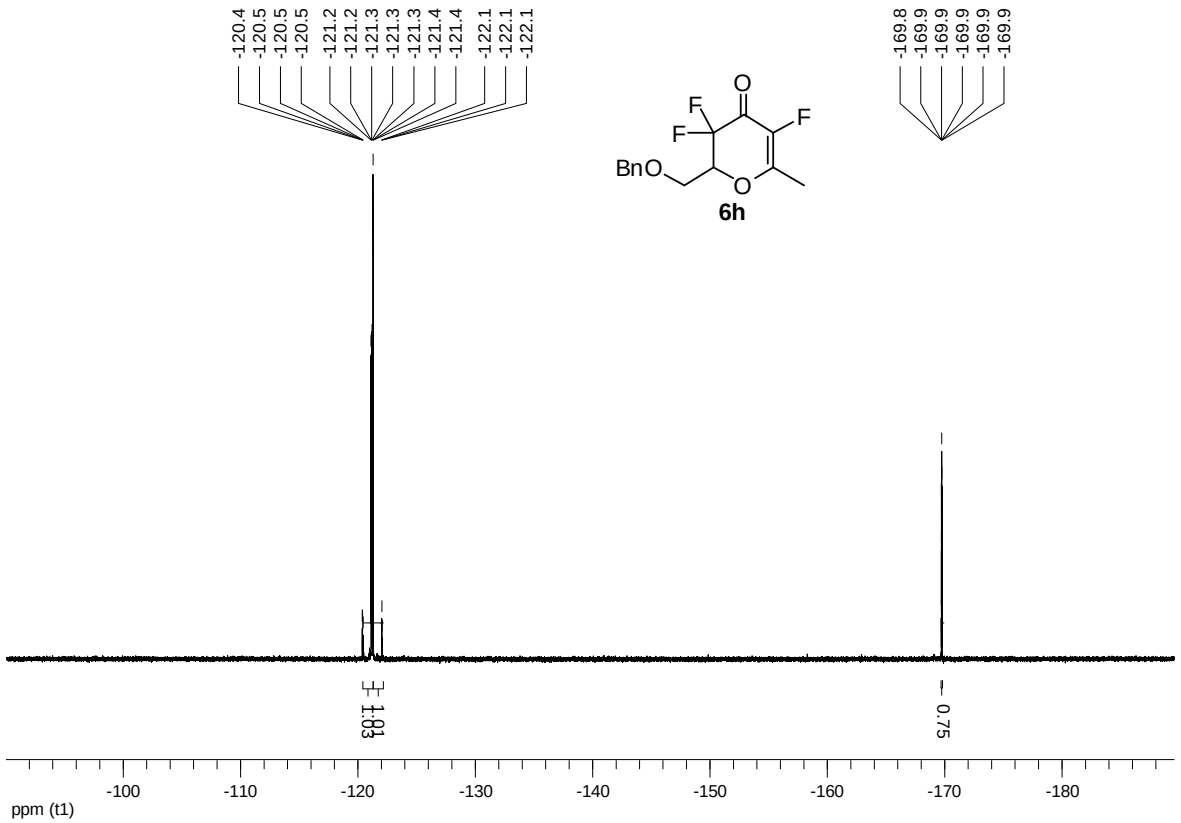

167.1
166.9
139.2
110.4
110.3
84.3
84.1
36.5
25.8
13.5
O
F
F
F
Cy
O
nPr
6f
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


-120.1
-124.2
-124.9
-167.1
O
F
F
F
Cy
O
nPr
6f
1.0
1.0
0.9
-110
-115
-120
-125
-130
-135
-140
-145
-150
-155
-160
-165
-170

2-[(benzyloxy)methyl]-3,3,5-trifluoro-6-methyl-2,3-dihydro-4*H*-pyran-4-one (6h)

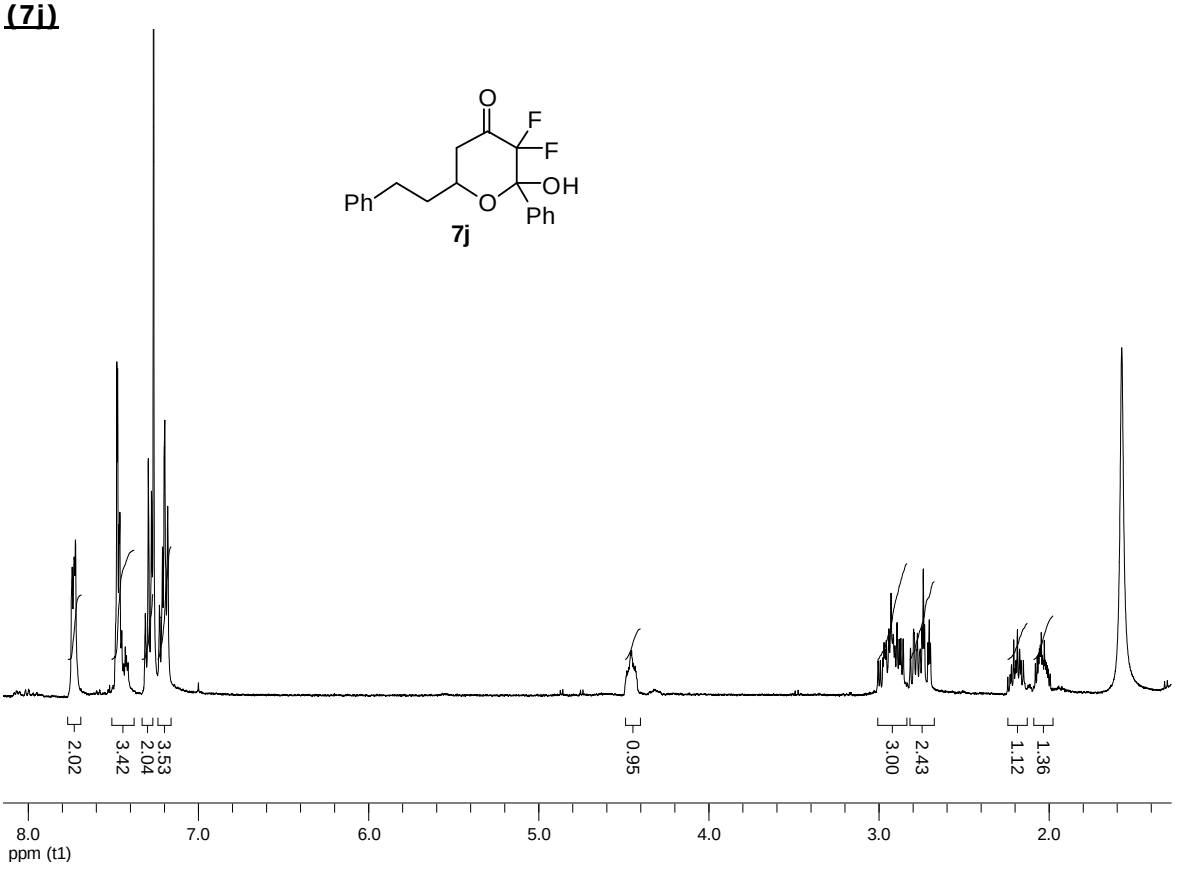


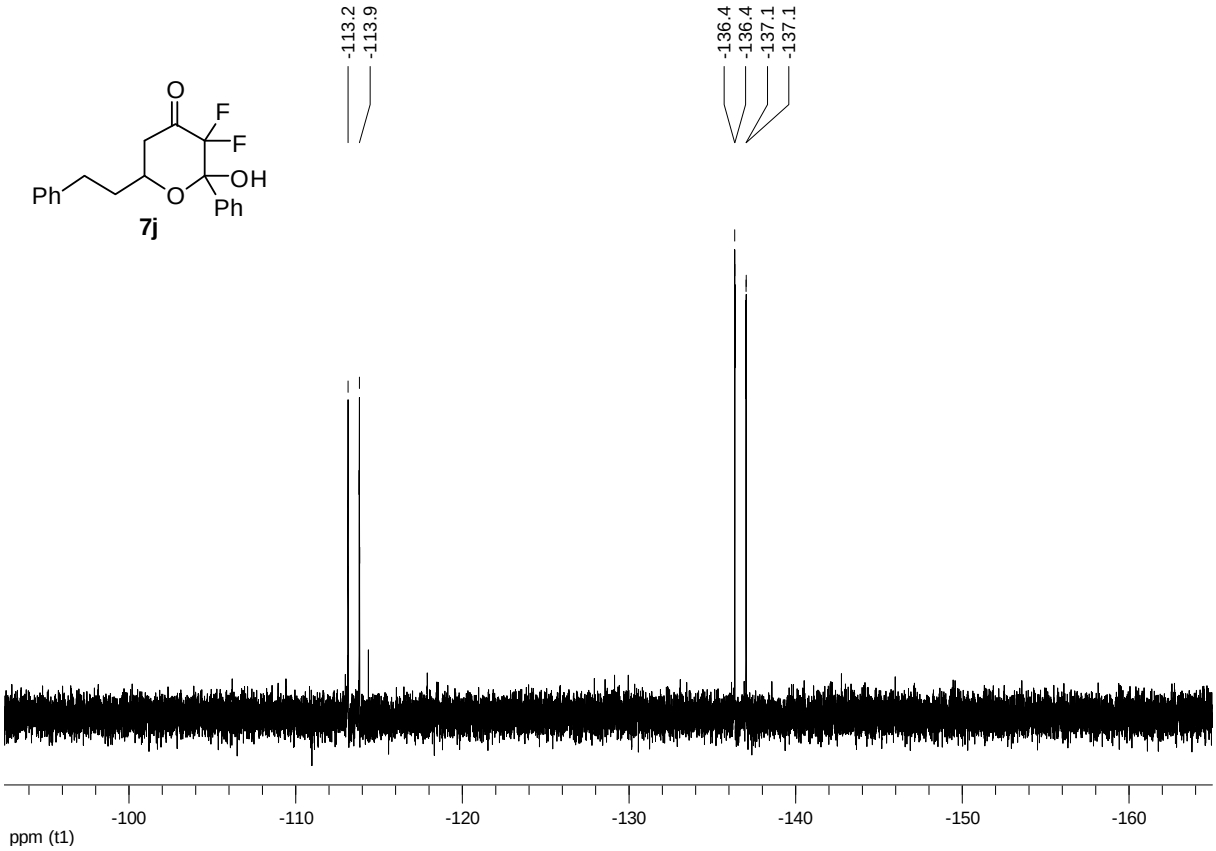


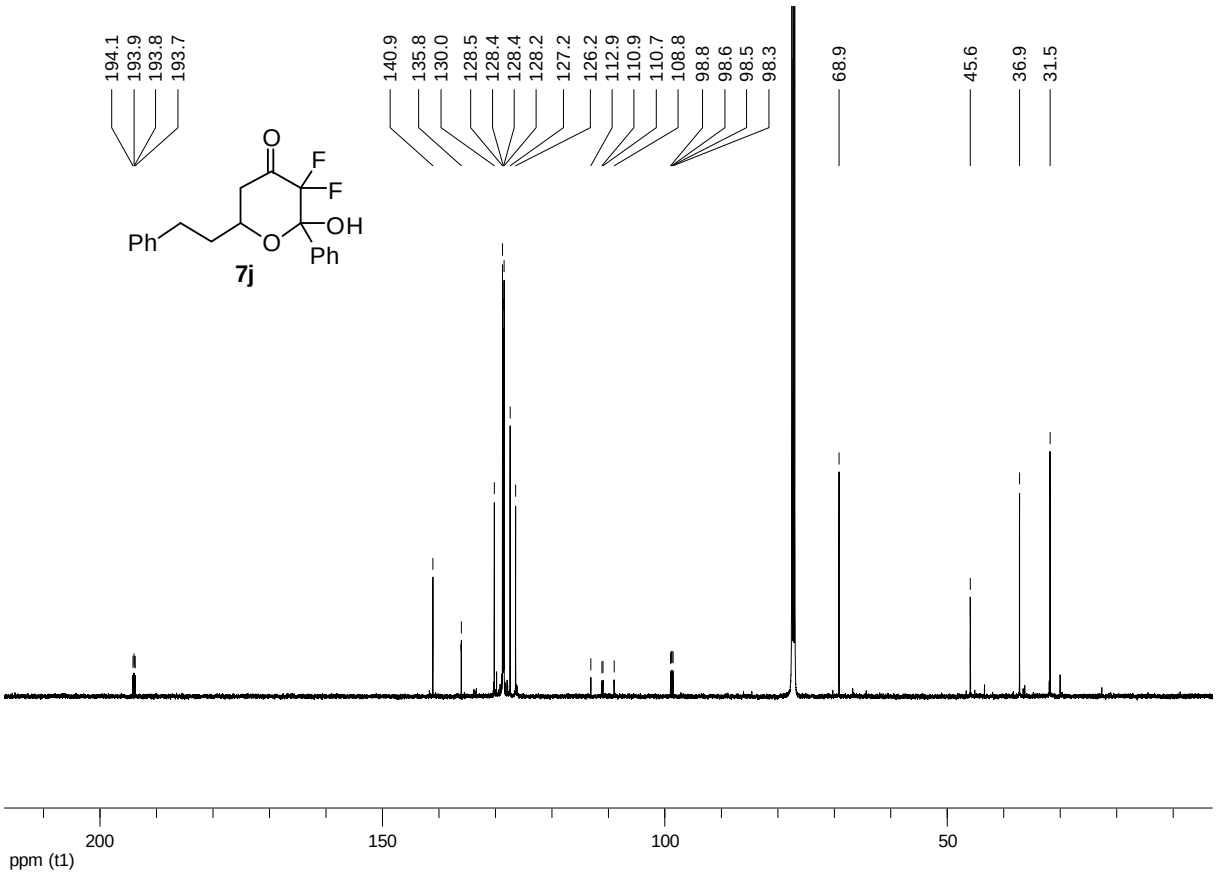


G.6 – Difluorotetrahydropyranones 7j, 7l, 7m and monofluorinated ketones 8j, 8l, 8m

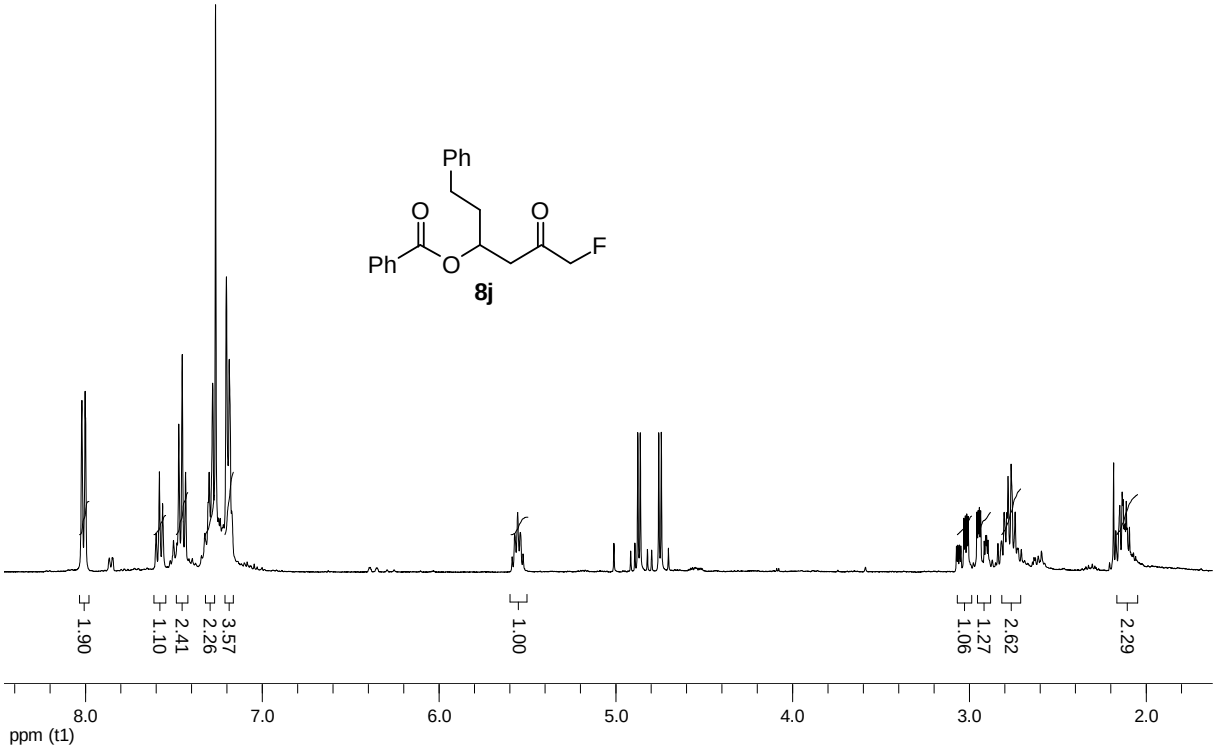
3,3-difluoro-2-hydroxy-2-phenyl-6-(2-phenylethyl)tetrahydro-4*H*-pyran-4-one (7j)

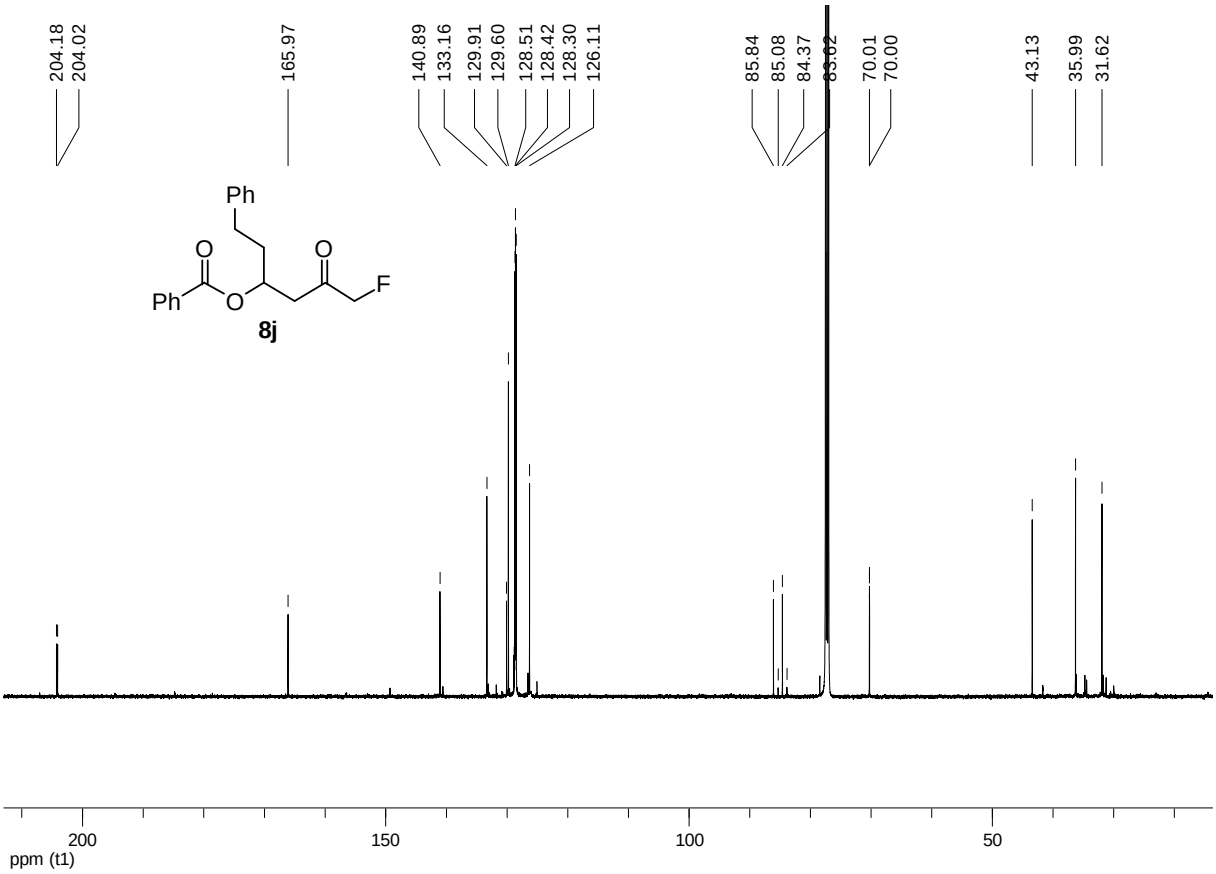


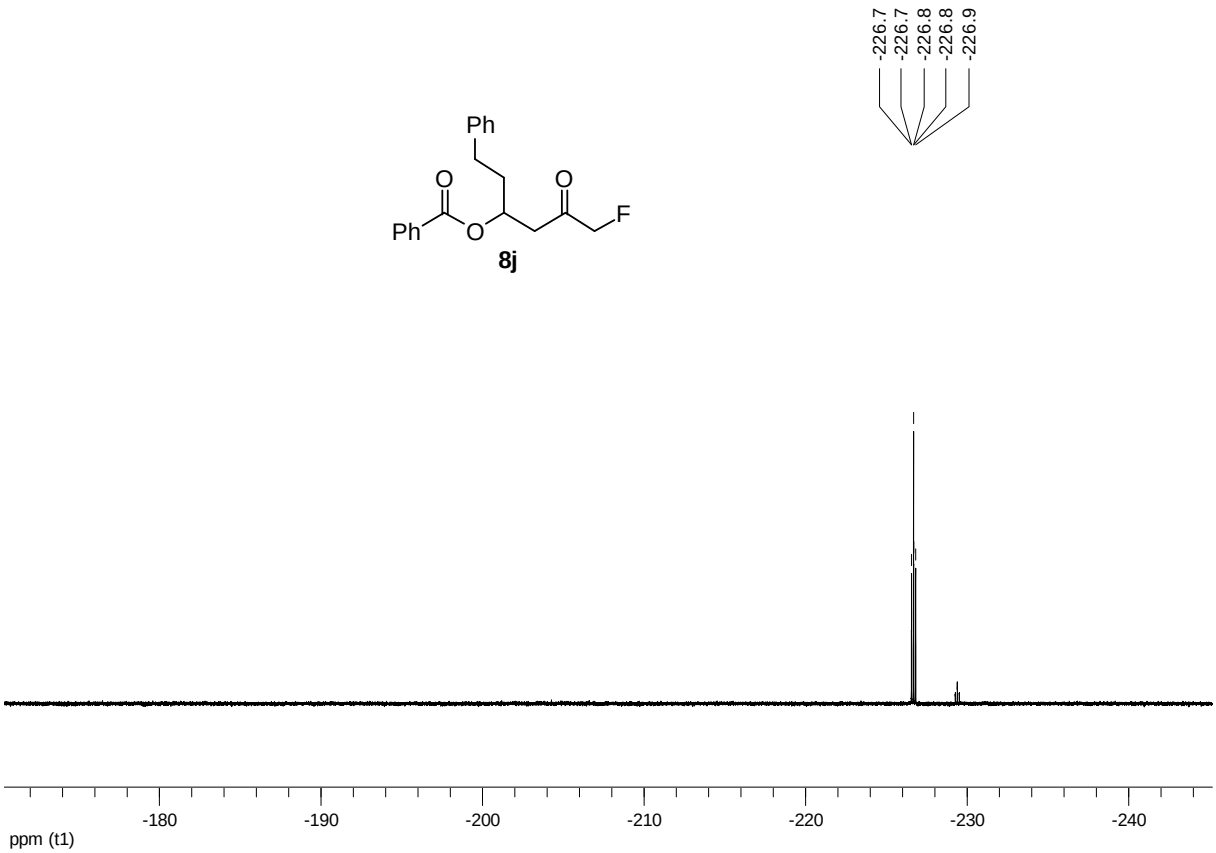

-113.2
-113.9
-136.4
-136.4
-137.1
-137.1
O
F
F
OH
Ph
O
Ph
7j
-100
-110
-120
-130
-140
-150
-160
ppm (t1)


194.1
193.9
193.8
193.7
140.9
135.8
130.0
128.5
128.4
128.4
128.2
127.2
126.2
112.9
110.9
110.7
108.8
98.8
98.6
98.5
98.3
68.9
45.6
36.9
31.5
O
F
F
OH
Ph
O
Ph
7j
200
150
100
50
ppm (t1)

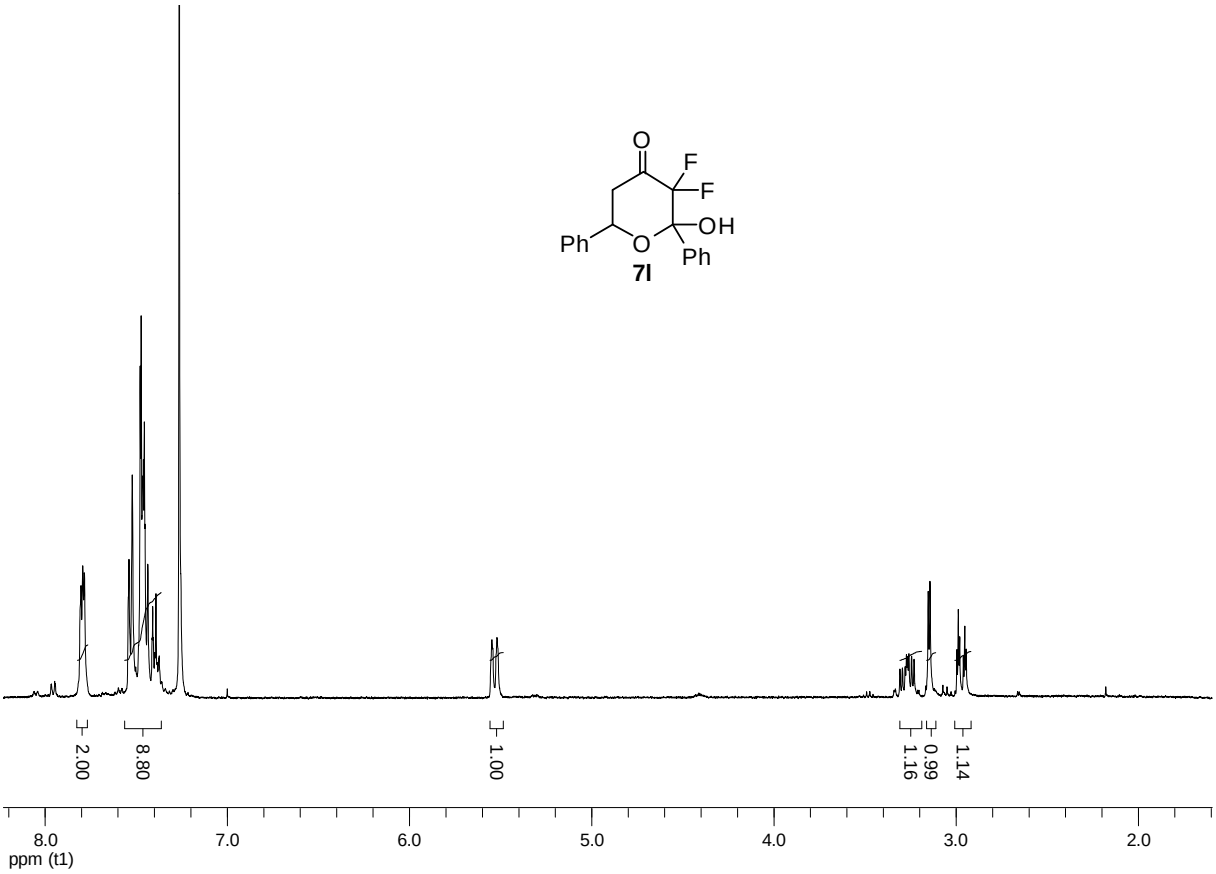
4-fluoro-3-oxo-1-(2-phenylethyl)butyl benzoate (8j)

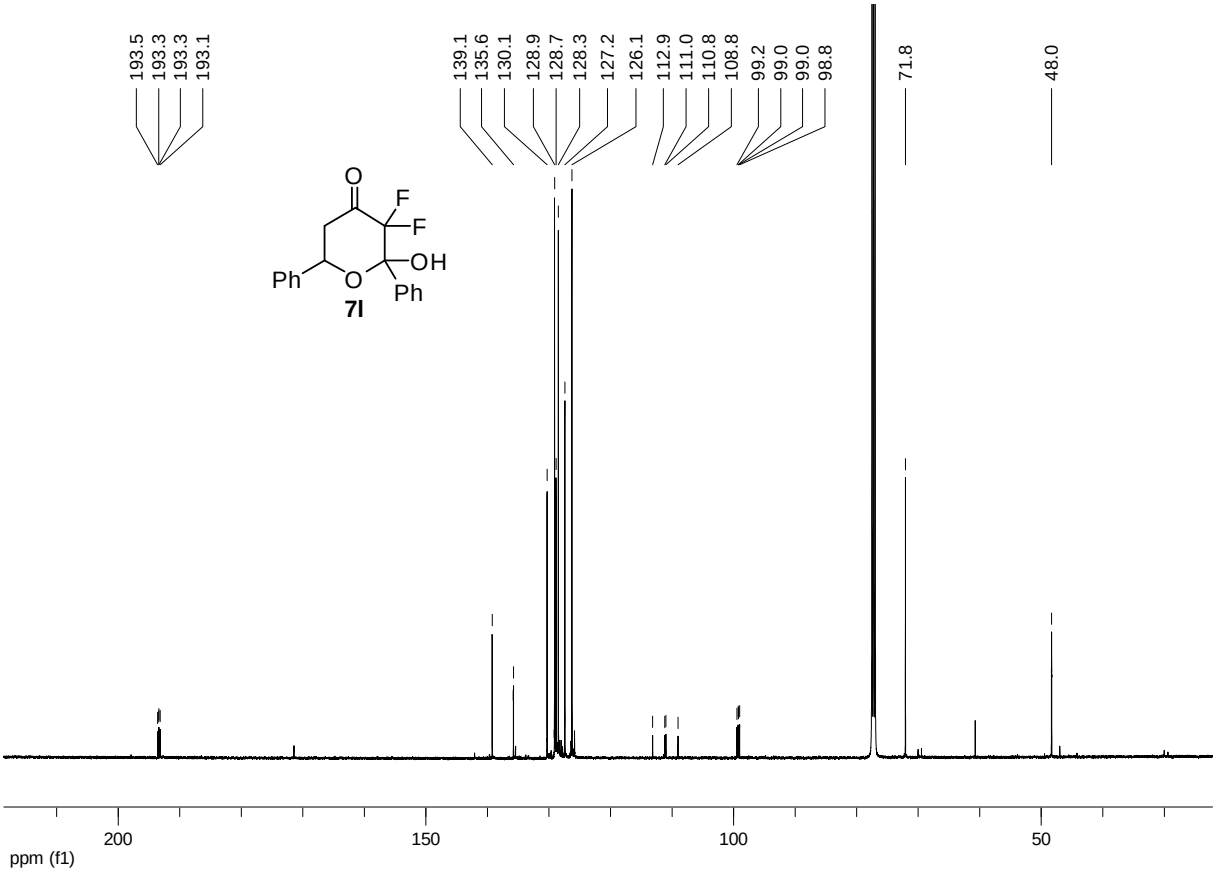


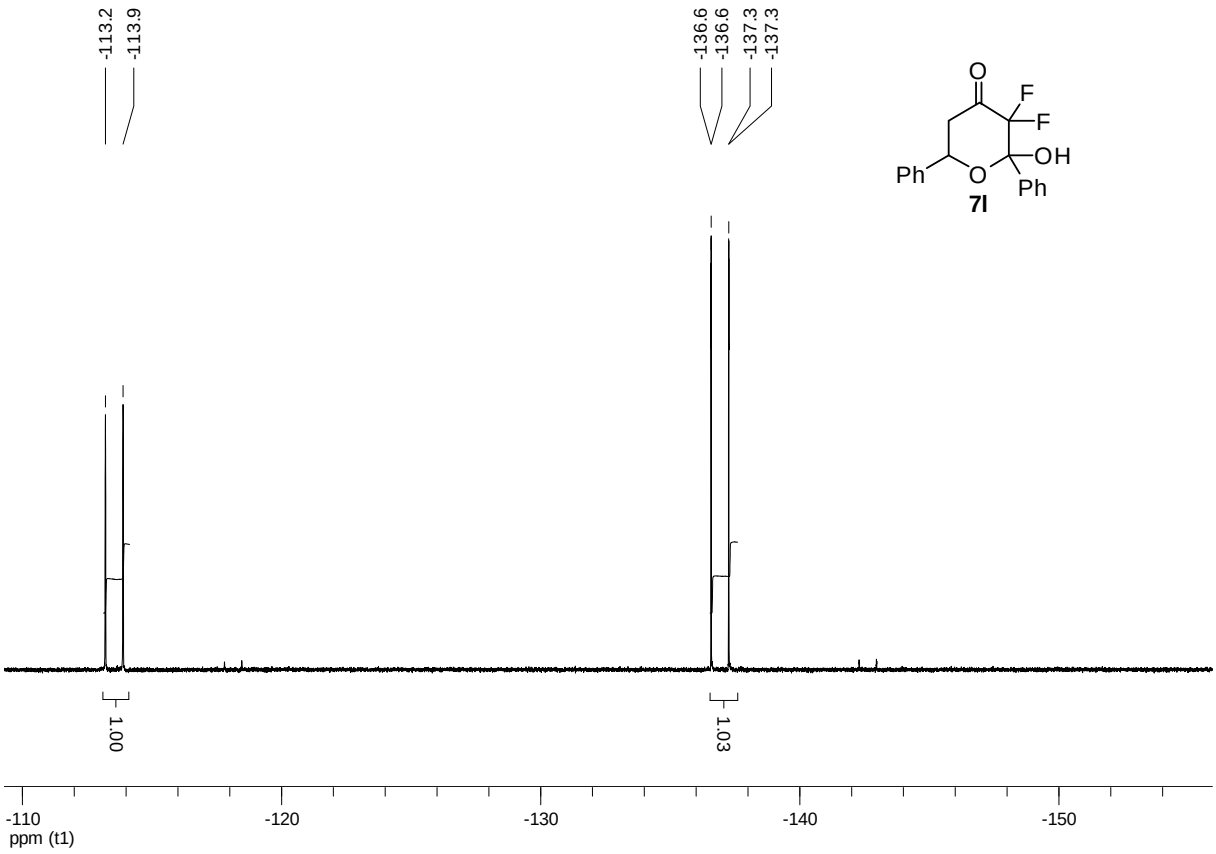




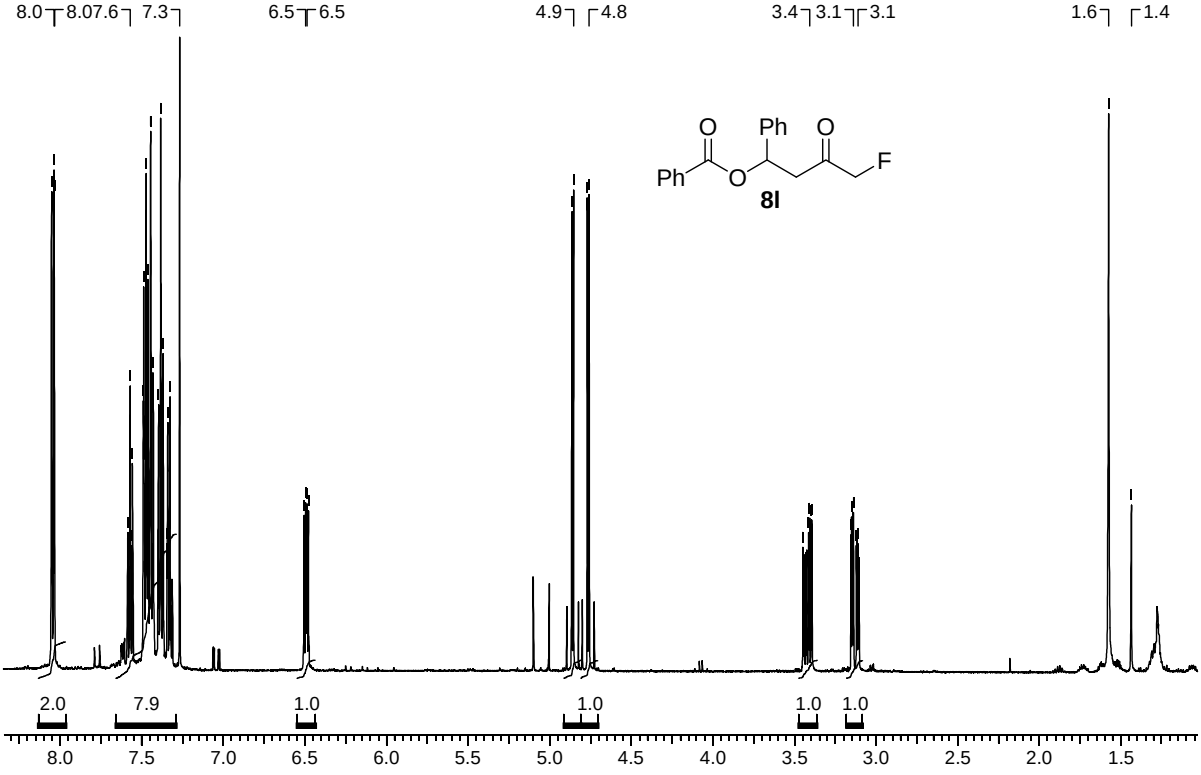
3,3-difluoro-2-hydroxy-2,6-diphenyltetrahydro-4*H*-pyran-4-one (7l)

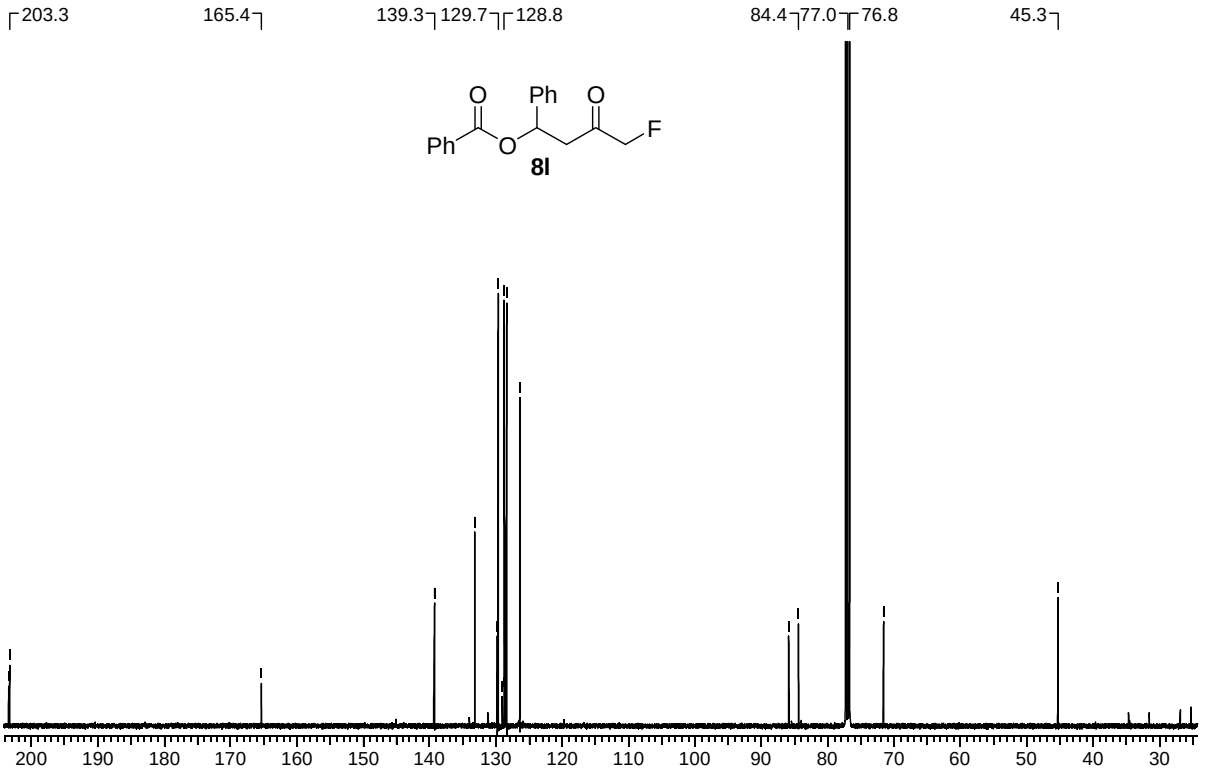


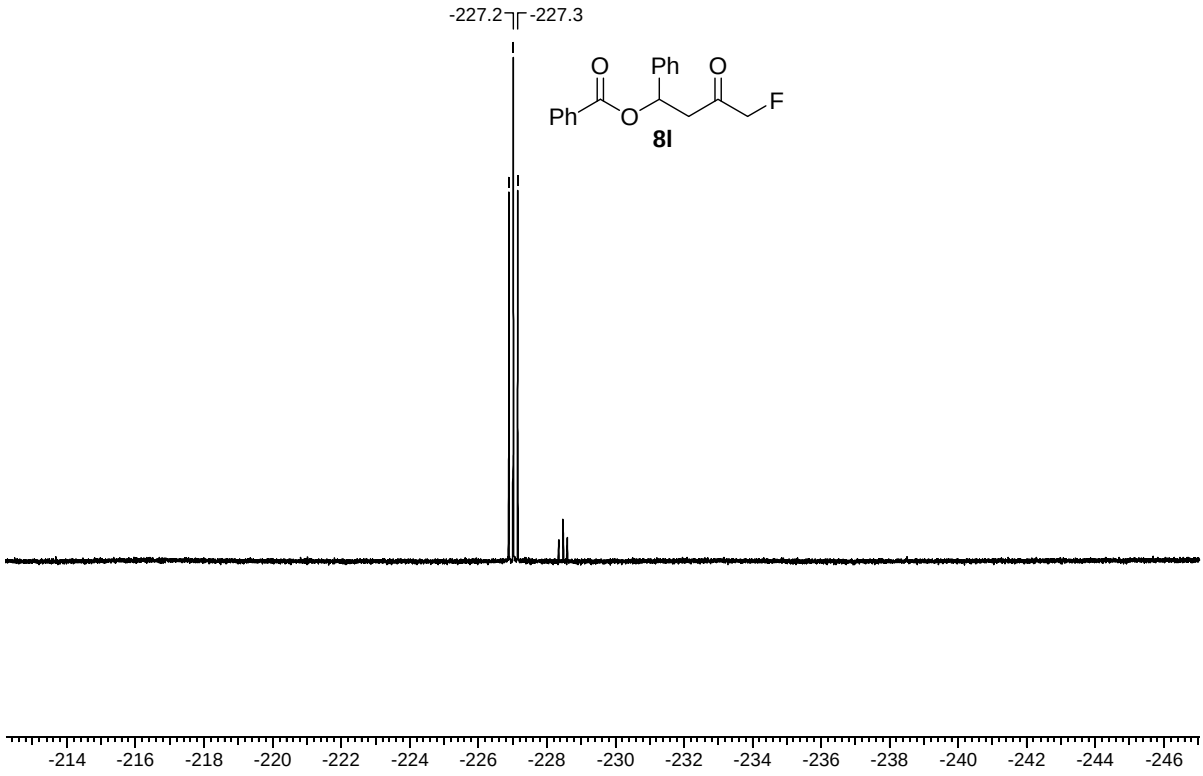

193.5
193.3
193.3
193.1
139.1
135.6
130.1
128.9
128.7
128.3
127.2
126.1
112.9
111.0
110.8
108.8
99.2
99.0
99.0
98.8
71.8
48.0
O
F
F
OH
Ph
O
Ph
7l
200
150
100
50
ppm (f1)


-113.2
-113.9
-136.6
-136.6
-137.3
-137.3
O
F
F
OH
Ph
O
Ph
7l
1.00
1.03
-110
-120
-130
-140
-150
ppm (t1)

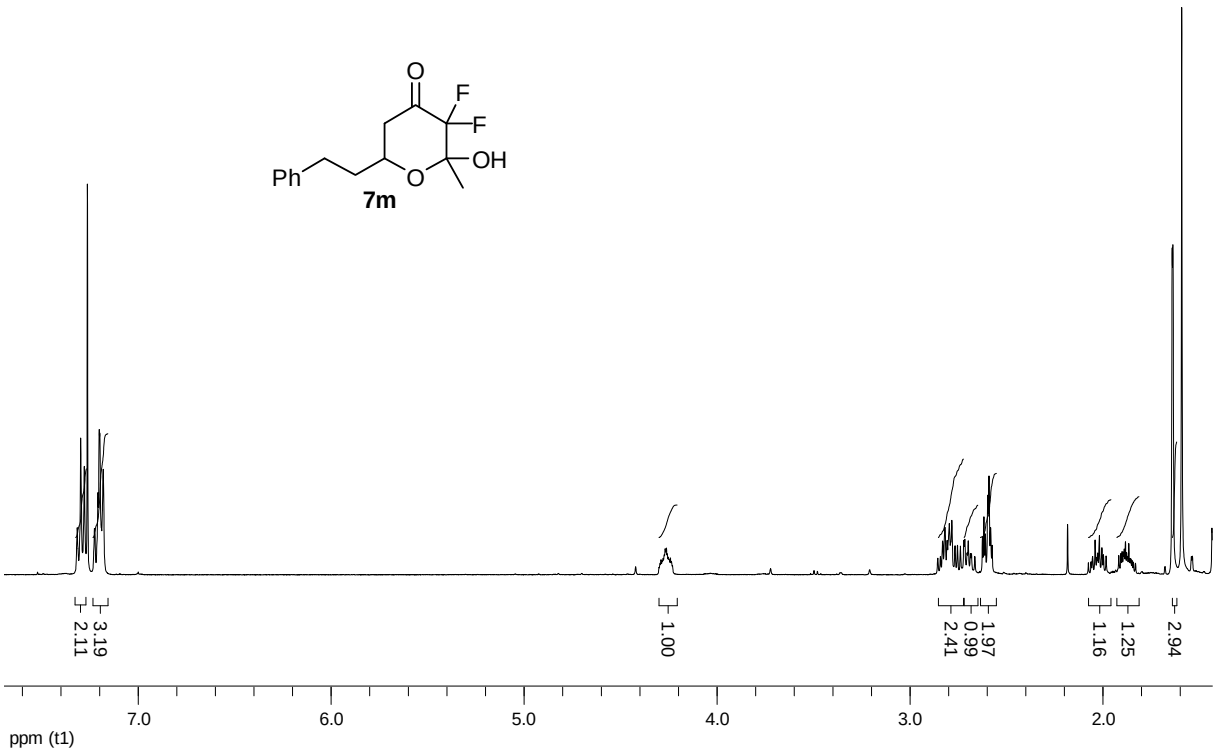
4-fluoro-3-oxo-1-phenylbutylbenzoate (8l)

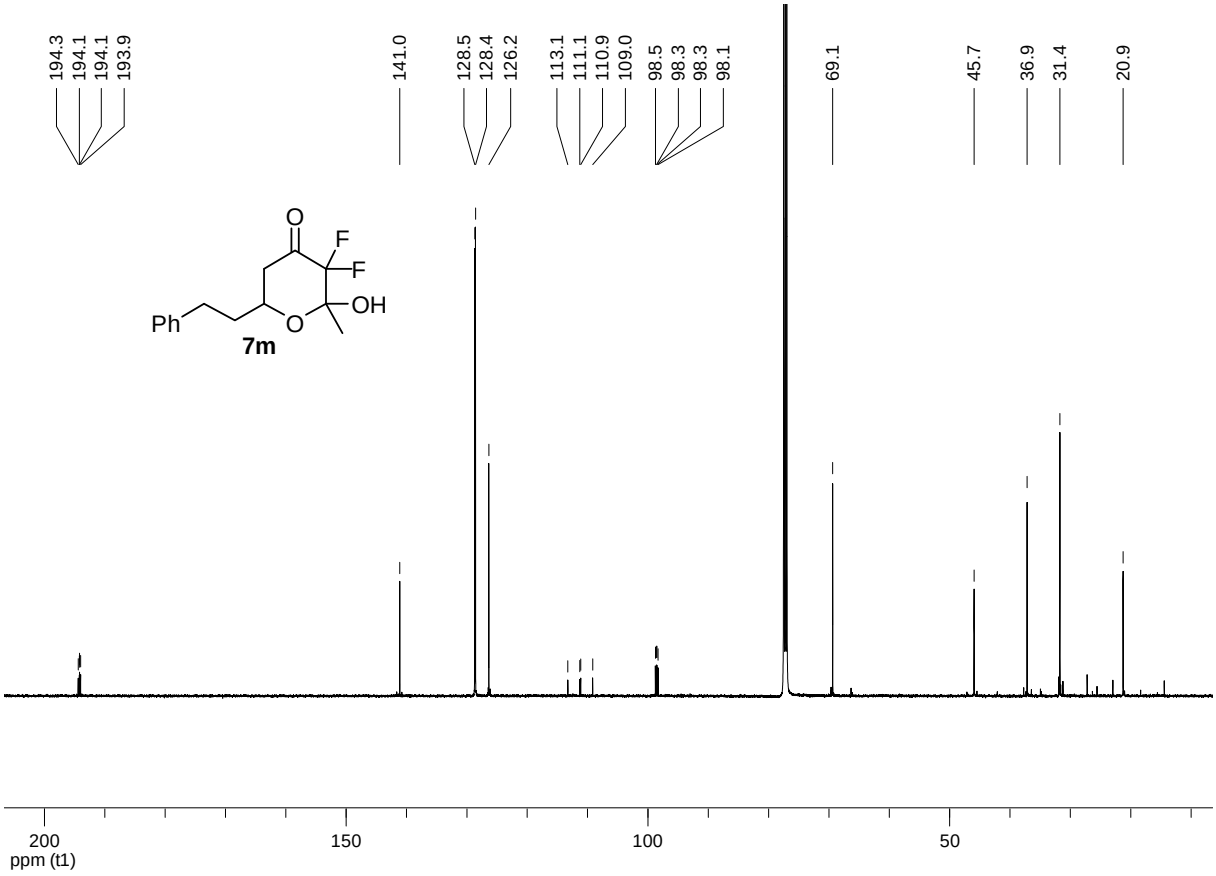


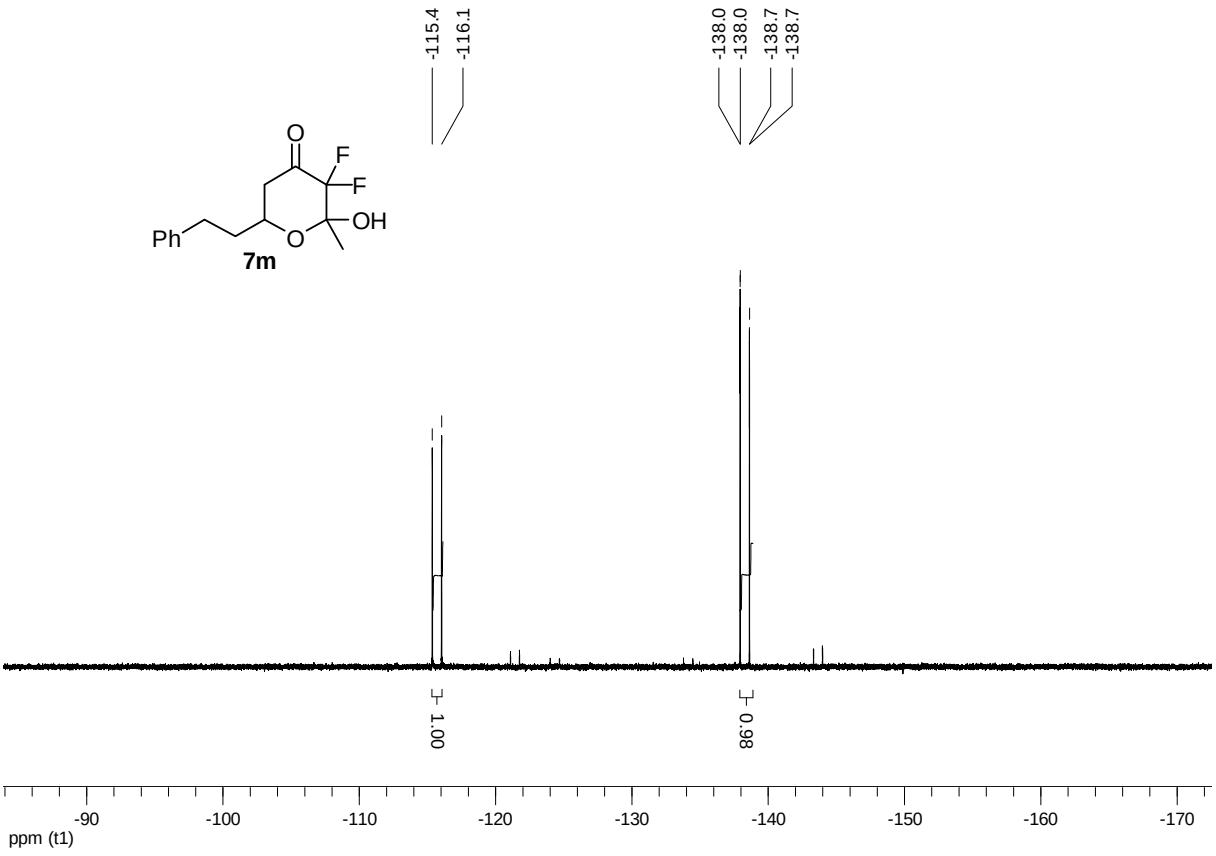




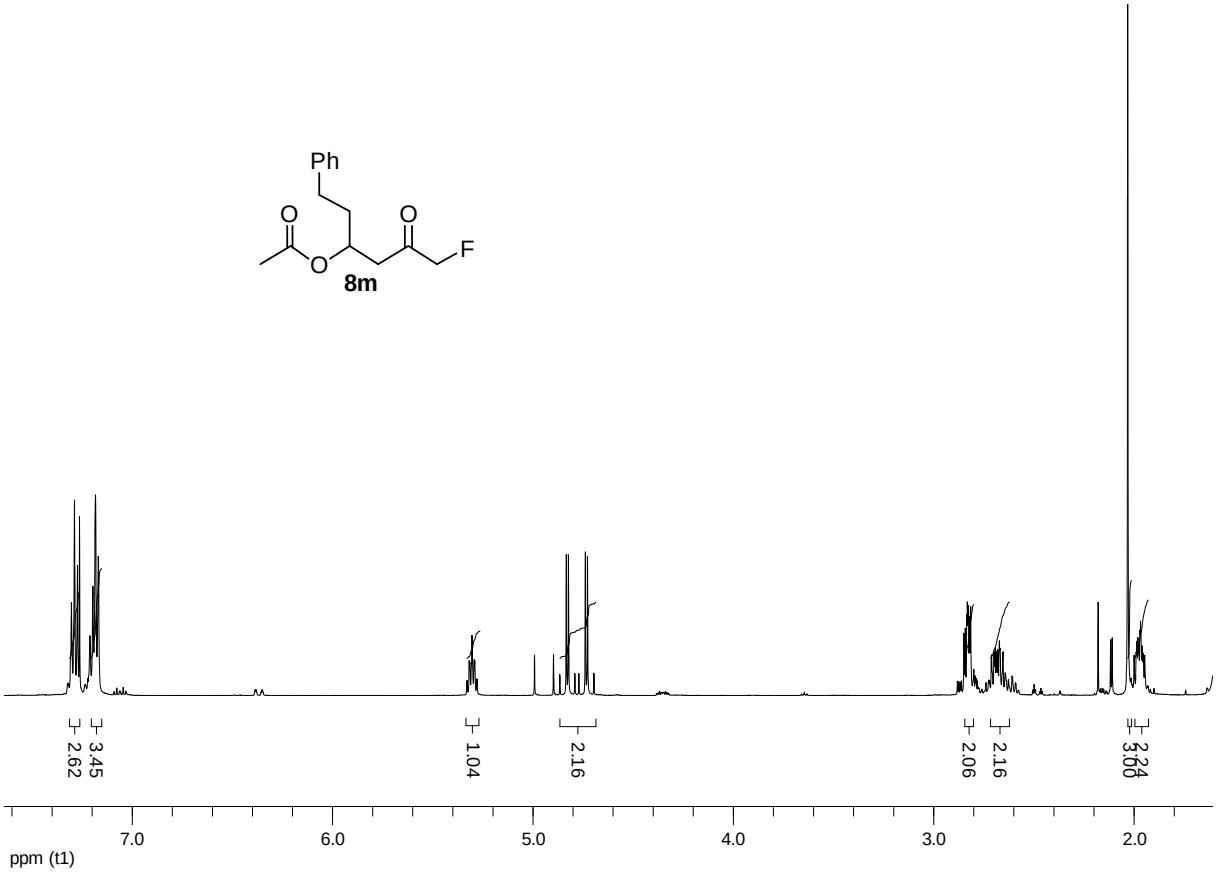
3,3-difluoro-2-hydroxy-2-methyl-6-(2-phenylethyl)tetrahydro-4*H*-pyran-4-one (7m)

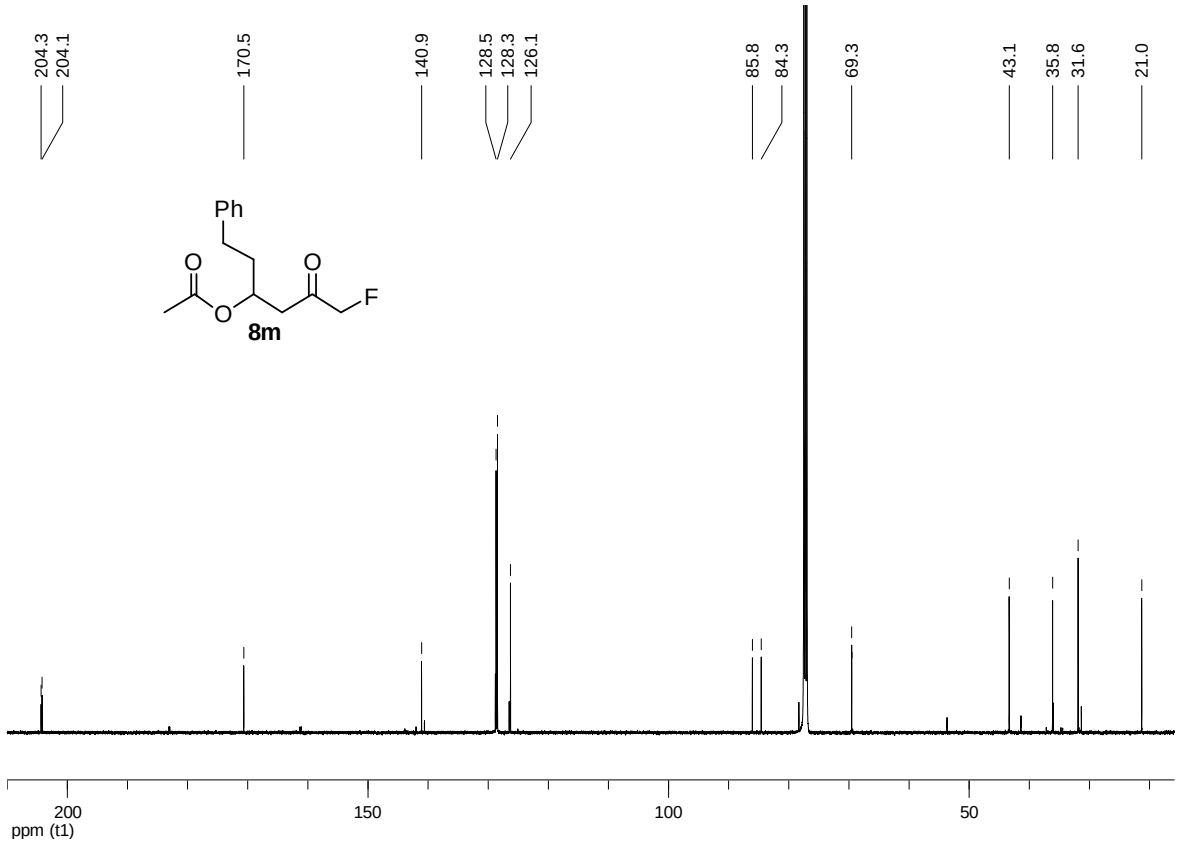


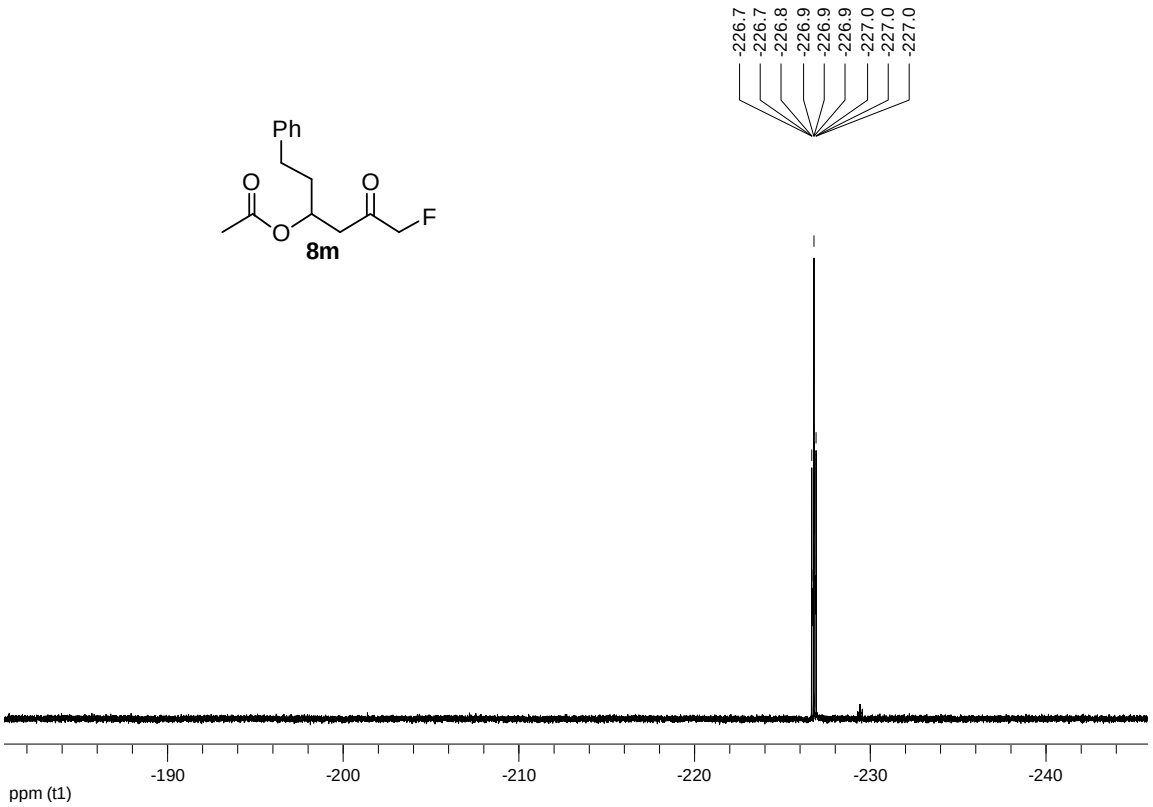

194.3
194.1
194.1
193.9
141.0
128.5
128.4
126.2
113.1
111.1
110.9
109.0
98.5
98.3
98.3
98.1
69.1
45.7
36.9
31.4
20.9
O
F
F
OH
Ph
O
7m
200
150
100
50
ppm (t1)


-115.4
-116.1
-138.0
-138.0
-138.7
-138.7
O
F
F
OH
Ph
O
7m
1.00
0.98
-90
-100
-110
-120
-130
-140
-150
-160
-170
ppm (t1)

4-fluoro-3-oxo-1-(2-phenylethyl)butyl acetate (8m)

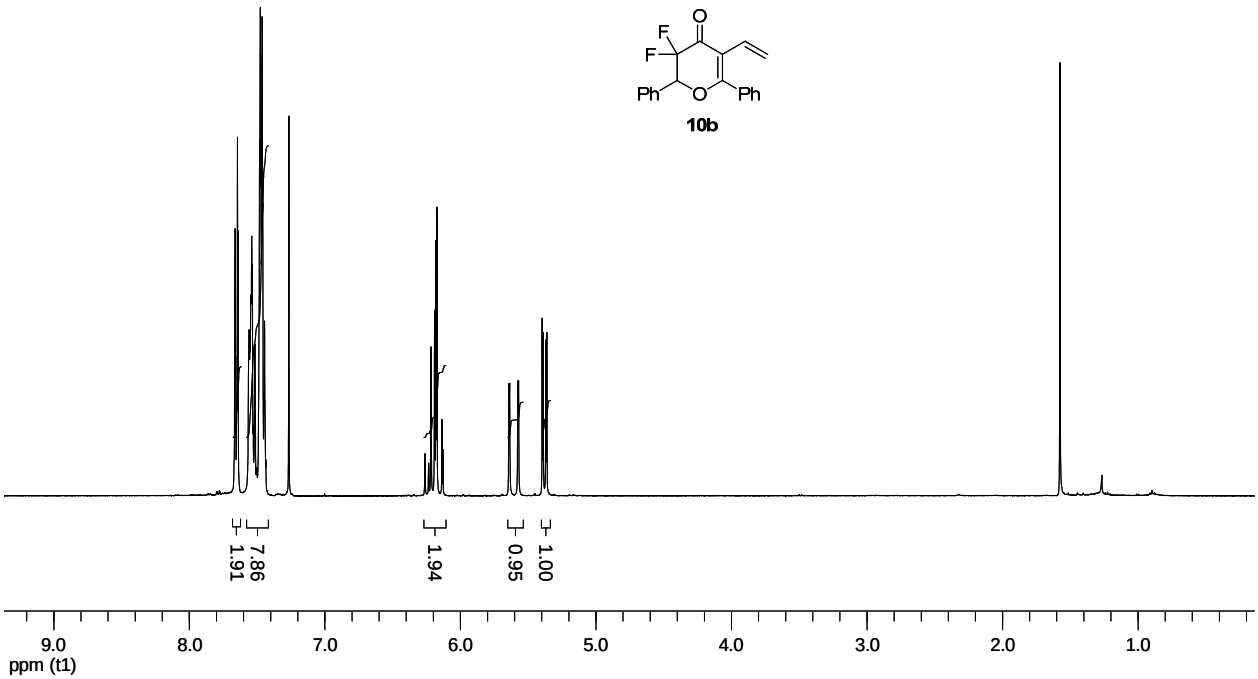


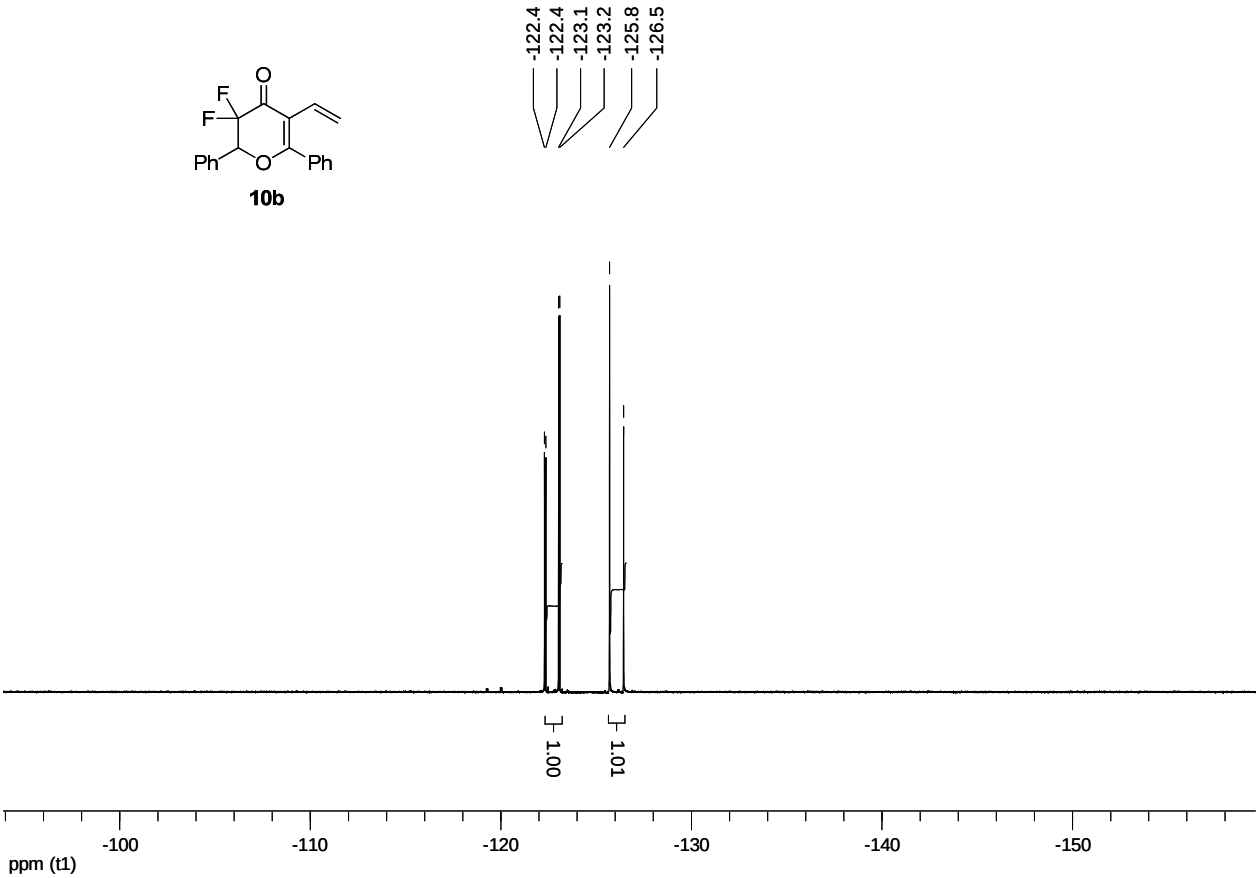


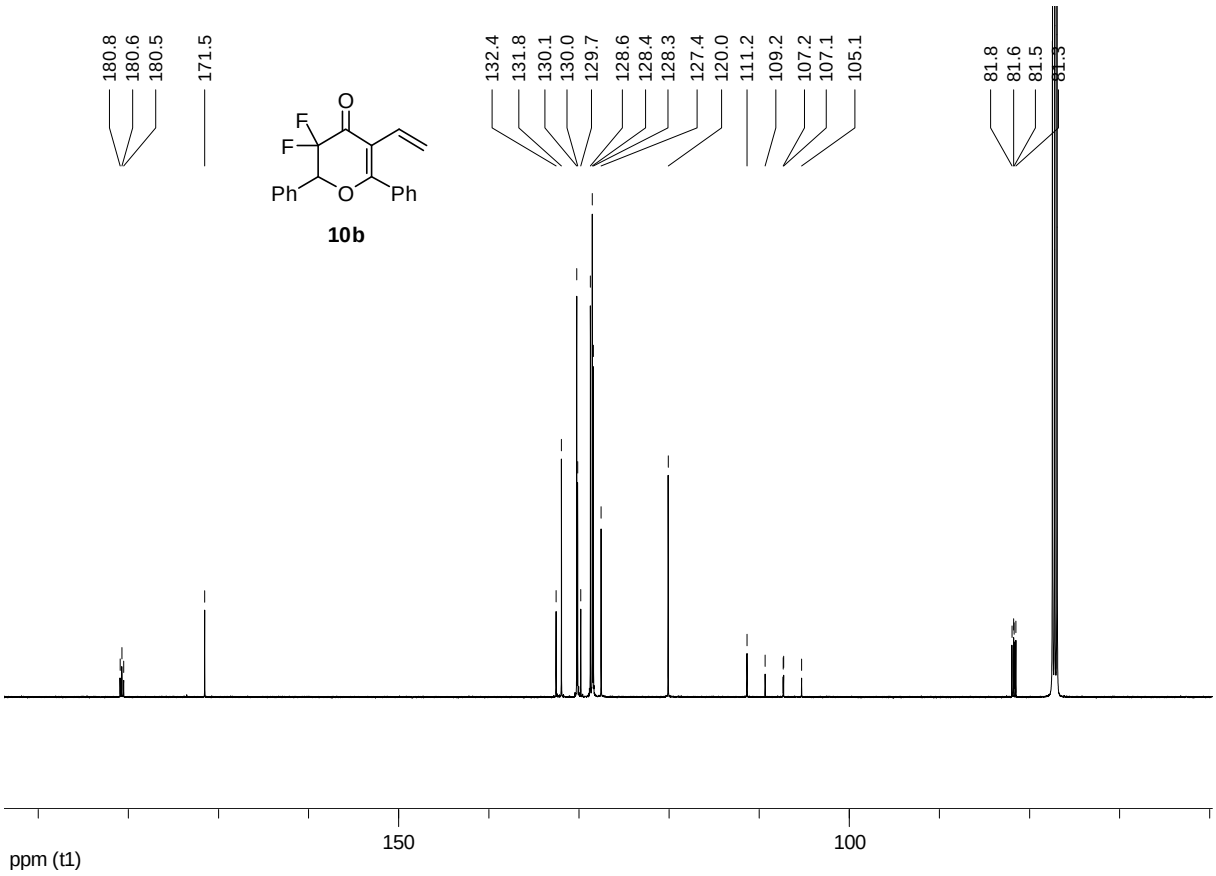


G.7 – NMR Spectra of compound 10b

3,3-difluoro-2,6-diphenyl-5-vinyl-2,3-dihydro-4*H*-pyran-4-one (10b)




-122.4
-122.4
-123.1
-123.2
-125.8
-126.5
F
F
O
Ph
O
Ph
10b
1.00
1.01
-100
-110
-120
-130
-140
-150
ppm (t1)


180.8
180.6
180.5
171.5
132.4
131.8
130.1
130.0
129.7
128.6
128.4
128.3
127.4
120.0
111.2
109.2
107.2
107.1
105.1
81.8
81.6
81.5
81.3
F
F
O
Ph
O
Ph
10b
150
100
ppm (t1)