Supplementary Material (ESI) for Chemical Communications

SUPPORTING INFORMATION

Domino gold catalyzed rearrangement and fluorination of propargyl acetates

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1. General information.

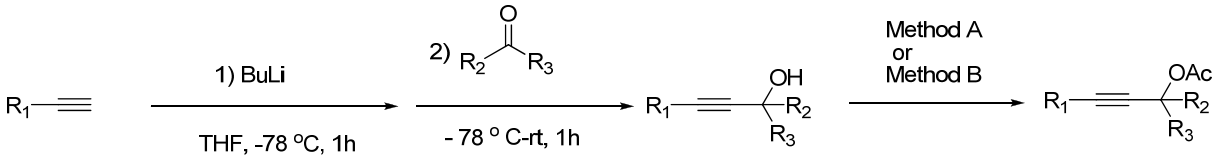
NMR spectra were recorded on AV2 400 or AV2 500 MHz Bruker spectrometers. Chemical shifts are given in ppm. The spectra are calibrated to the residual ^{1}H and ^{13}C signals of the solvents. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), doublet-doublet (dd), quintet (quint), septet (sept), multiplet (m), and broad (br). Infrared spectra were recorded on a JASCO FT/IR-4100 spectrometer. High-resolution electrospray ionization and electronic impact mass spectrometry was performed on a Finnigan MAT 900 (Thermo Finnigan, San Jose, CA; USA) doublefocusing magnetic sector mass spectrometer. Ten spectra were acquired. A mass accuracy ≤ 2 ppm was obtained in the peak matching acquisition mode by using a solution containing 2 <l PEG200, 2 <l PPG450, and 1.5 mg NaOAc (all obtained from Sigma-Aldrich, CH-Buchs) dissolved in 100ml MeOH (HPLC Supra grade, Scharlau, E-Barcelona) as internal standard. GC-MS analysis was done on a Finnigan Voyager GC8000 Top.

Materials and Methods: Unless otherwise stated, starting materials were purchased from Aldrich and/or Fluka. All reagents were used as received. $IPrAuNTf_2$ was prepared according to previously reported procedures.[1] Solvents were purchased in HPLC quality, degassed by purging thoroughly with nitrogen and dried over activated molecular sieves of appropriate size. Alternatively, they were purged with argon and passed through alumina columns in a solvent purification system (Innovative Technology). Unless otherwise stated, reactions were not run under inert atmosphere. Conversion was monitored by thin layer chromatography (TLC) using Merck TLC silica gel 60 F_{254}. Flash column chromatography was performed over silica gel (230-400 mesh). The determination of the E/Z ratios for the α-fluoroenones derived of secondary acetates was done by ^{1}H-NMR of the crude reaction mixtures.

[1] L. Ricard, F. Gagosz, *Organometallics* 2007, **26**, 4704.

2. Preparation and characterization of starting materials

2.1. General procedures



Scheme 1

A solution of the corresponding alkyne (1.0 equiv.) in anhydrous THF (0.3 M) was treated with *n*BuLi (1.05 equiv.) at -78°C for 1 h. The corresponding aldehyde or ketone was added dropwise. The resulting reaction mixture was stirred at -78ºC for 30 min and then warmed up to rt for another 30 min. It was quenched with saturated NH_4Cl (aq. sol.) and extracted with ether. The combined organic layers were dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. The residue was purified by column chromatography if needed. The propargylic alcohols were transformed into the corresponding propargylic acetates using two different reaction conditions.

Method A:

Propargylic alcohol (1 equiv.) was dissolved in CH_2Cl_2 (0.1 M). DMAP (0.05 equiv.), Et_3N (2 equiv.) and Ac_2O (1.5 equiv.) were sequentially added. The resulting mixture was stirred overnight. The solvent was evaporated and the residue was purified by column chromatography on silica gel.

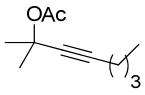
Method B:

Propargylic alcohol (1 equiv.) was stirred with Ac_2O (1.5 equiv.) neat at rt for 30 min in the presence of $Mg(ClO_4)_2$ (0.01 equiv.). The reaction mixture was diluted with water and extracted with CH_2Cl_2. The organic layer was dried with Na_2SO_4 and the organic solvent was concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (Hexane:EtOAc 40:1).[2]

[2] A. K. Chakraborti, L. Sharma, R. Gulhane, R. *Tetrahedron* 2003, **59**, 7661.

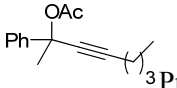
2.2. Characterizations of Starting materials

2-Methyloct-3-yn-2-yl acetate (1a)[3]



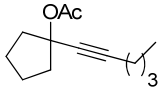
Propargyl acetate **1a** was obtained according to Method B. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.19 (t, J = 6.8 Hz, 2H), 2.0 (s, 3H), 1.63 (s, 6H), 1.50-1.42 (m, 2H), 1.41-1.33 (m, 2H), 0.89 (t, J = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.4, 84.6, 81.3, 72.6, 30.6, 29.3, 22.1, 21.9, 18.4, 13.6.

1-(Hex-1-ynyl)cycloheptyl acetate (1b)[4]



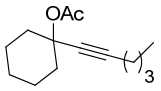
Propargyl acetate **1b** was obtained according to Method A. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.49-7.46 (m, 2H), 7.27-7.23 (m, 2H), 7.19-7.16 (m, 1H), 2.23 (t, J = 6.9 Hz, 2H), 1.96 (s, 3H), 1.77 (s, 3H), 1.51–1.45 (m, 2H), 1.41–1.33 (m, 2H), 0.85 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.2, 143.9, 128.8, 128.2, 125.6, 88.7, 80.2, 76.7, 33.0, 31.2, 22.6, 22.5, 19.2, 14.2.

1-(Hex-1-ynyl)cyclopentyl acetate (1c)[3]



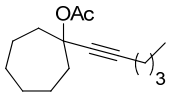
Propargyl acetate **1c** was obtained according to Method B. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.22–2.15 (m, 4H), 2.12–2.04 (m, 2H), 2.02 (s, 3H), 1.74–1.70 (m, 4H), 1.50–1.44 (m, 2H), 1.43–1.35 (m, 2H), 0.90 (t, J = 7.6 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2, 85.8, 81.6, 81.2, 41.1, 31.3, 23.7, 22.5, 22.4, 19.0, 14.2

1-(Hex-1-ynyl)cyclohexyl acetate (1d)[3]



Propargyl acetate **1d** was obtained according to Method B. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.2 (t, J = 7.2 Hz, 2H), 2.11–2.06 (m, 2H), 2.03 (s, 3H), 1.84–1.77 (m, 2H), 1.63–1.29 (m, 10H), 0.91 (t, J = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.8, 87.4, 80.7, 76.7, 37.9, 31.4, 25.8, 23.4, 22.7, 22.5, 19.1, 14.2.

1-(Hex-1-ynyl)cycloheptyl acetate (1e)[3]



Propargyl acetate **1e** was obtained according to Method A. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.24–2.17 (m, 4H), 2.06–2.04 (m, 2H), 2.01 (s, 3H), 1.57–1.37 (m, 12H), 0.90 (t, J = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.1, 86.9, 82.1, 80.2, 41.1, 31.4, 28.8, 22.9, 22.8, 22.5, 19.1, 14.2.

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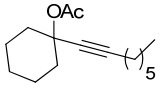
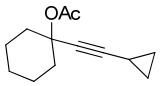
[3] M.Yu, G. Zhang, L. Zhang, *Org. Lett*. 2007, **9**, 2147.
[4] I. Matsuda, K.-I. Komori, K. Itoh, *J. Am. Chem. Soc.* 2002, **124**, 9072.

1-(Oct-1-ynyl)cyclohexyl acetate (1f)



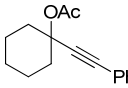
Propargyl acetate **1f** was obtained according Method A. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.13 (t, *J* = 7.1 Hz, 2H), 2.00-1.97 (m, 2H), 1.93 (s, 3H), 1.70 (m, 2H), 1.53-1.48 (m, 4H), 1.44-1.39 (m, 3H), 1.30-1.18 (m, 7H), 0.79 (t, *J* = 6.9 Hz, 3H) . ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8, 87.5, 80.7, 76.7, 38.0, 31.9, 29.3, 29.1, 25.9, 23.4, 23.1, 22.7, 19.4, 14.6. IR (film): $\tilde{\upsilon}$ = 2932, 2858, 1744, 1447, 1365, 1300, 1263, 1227, 1184, 1130, 1019, 957, 914, 840 cm^{-1}. HRMS (ESI): *m/z*: calcd for $C_{16}H_{26}O_2Na$: 273.1825. Found: 273.1825.

1-(Cyclopropylethynyl)cyclohexyl acetate (1g)



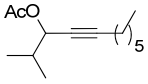
Propargyl acetate **1g** was obtained according to Method A. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.97-1.94 (m, 2H), 1.92 (s, 3H), 1.72 (m, 2H), 1.52-1.36 (m, 5H), 1.20-1.17 (m, 2H), 0.69-0.65 (m, 2H), 0.60-0.57 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.8, 90.6, 76.6, 75.8, 37.9, 25.8, 23.3, 22.7, 9.0, 0.2. IR (film): $\tilde{\upsilon}$ = 2935, 2859, 2359, 2239, 1741, 1447, 1365, 1298, 1264, 1225, 1175, 1132, 1020, 963, 913, 888 cm^{-1}. HRMS (ESI): *m/z*: calcd for $C_{13}H_{18}O_2Na$: 229.1199. Found: 229.1198

1-(2-Phenylethynyl)cyclohexyl acetate (1h)[3]



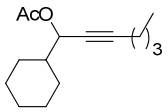
Propargyl acetate **1h** was obtained according to Method B. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46 -7.44 (m, 2H), 7.29 -7.28 (m, 3H), 2.24 -2.19 (m, 2H), 2.07 (s, 3H), 1.93 -1.88 (m, 2H), 1.70 -1.65 (m, 4H), 1.59 – 1.53 (m, 1H), 1.39 -1.33 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.8, 132.4, 128.8, 128.7, 123.4, 89.8, 86.8, 76.5, 37.8, 25.8, 23.3, 22.6.

2-Methylundec-4-yn-3-yl acetate (5a)



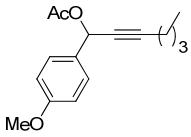
Propargyl acetate **5a** was obtained according to Method A. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.24 (dt, *J* = 5.6, 2.0 Hz, 1H), 2.24 (td, *J* = 5.6, 2.0 Hz, 2H), 2.10 (s, 3H), 2.02 (m, 1H), 1.60-1.27 (m, 8H), 1.03 (d, *J* = 6.7 Hz, 3H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.92 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.2, 86.8, 76.1, 69.5, 32.5, 31.3, 28.5 (2 x C), 22.5, 21.1, 18.7, 18.3, 17.5, 14.0. IR (film): $\tilde{\upsilon}$ = 2961, 2931, 2858, 1741, 1466, 1370, 1231, 1157, 1018, 980 cm^{-1}. HRMS (ESI): *m/z*: calcd for $C_{14}H_{24}O_2Na$: 247.1668. Found: 247.1668.

1-Cyclohexylhept-2-ynyl acetate (5b)[3]



Propargyl acetate **5b** was obtained according to Method A. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.20 (d, J = 6.0 Hz, 1H), 2.21 (t, J = 7.0 Hz ,2H), 2.07 (s, 3H), 1.84 - 1.58 (m, 5H), 1.49 (quint, J = 7.2 Hz, 2H), 1.39 (Sext, J = 7.2 Hz, 2H), 1.27 – 1.03 (m, 6H), 0.90 (t, J = 7.2 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.8, 87.3, 77.0, 69.4, 42.6, 31.2, 29.2, 28.7, 26.9, 26.4, 26.3, 22.5, 21.7, 19.0, 14.1.

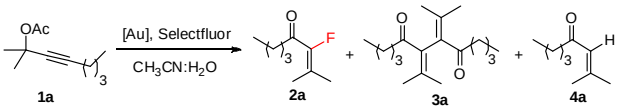
1-(4-Methoxyphenyl)hept-2-ynyl acetate (5c)[3]



Propargyl acetate **5c** was obtained according to Method A. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (d, J = 8.5 Hz, 2H), 6.89 (d, J = 8.5 Hz, 2H), 6.42 (s, 1H), 3.81 (s, 3H), 2.27 (t, J = 7.0 Hz, 2H), 2.07 (s, 3H), 1.52 (quint, J = 7.2 Hz, 2H), 1.41 (sext, J = 7.2 Hz, 2H), 0.91 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.0, 159.9, 129.9, 129.3, 113.8, 88.1, 76.8, 65.8, 55.3, 30.5, 21.9, 21.2, 18.5, 13.6.

3. General procedures for gold catalyzed rearrangement and fluorination of propargyl acetates.

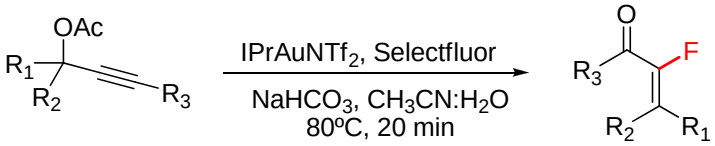
Optimization Experiments



1a **2a** **3a** **4a**

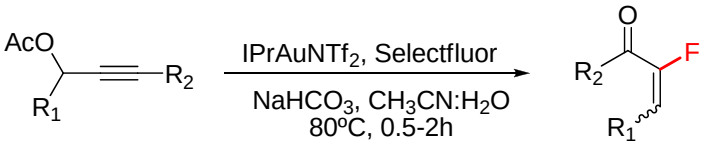
Entry	Catalyst	Additives	Conversion	Ratio [b]
1	$Ph_3PAuNTf_2$	-	100	54:45:1
2	$Ph_3PAuNTf_2$	MgO (1 eq.)	55	77:12:11
3	$Ph_3PAuNTf_2$	$NaHCO_3$ (1 eq.)	100	75:13:12
4	$(PhO)_3PAuSbF_6$	$NaHCO_3$ (1 eq.)	61	0:0:100
5	$Ph_3PAuNTf_2$	$NaHCO_3$ (1 eq.), 60ºC	60	92:0:8
6	**$IPrAuNTf_2$**	**$NaHCO_3$ (1 eq.)**	**100**	**99:<1:<1**

3.1 General procedure for tertiary acetates.



The corresponding propargyl acetate (1 equiv.), followed by $IPrAuNTf_2$ (0.05 equiv.) were added to a solution of Selectfluor (2 equiv.) and $NaHCO_3$ (1 equiv.,) in $MeCN:H_2O$ (20:1, 0.02 M), The reaction was stirred for 15-30 min at 80 ^oC and monotorized by TLC. Upon reaction completion, the mixture was diluted with DCM (5 ml) and an aqueous solution of $Na_2S_2O_3$ (5% v/v) (2 ml) was added. The mixture was extracted with DCM (3 x 5 mL) and the combined organic phases were dried over $MgSO_4$. The solvent was evaporated under reduced pressure and the residue was purified by silica gel flash column chromatography (Pentane/diethyl ether = 100/1) to yield the desired α-fluoroenones **2**.

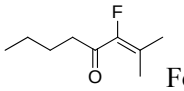
3.2 general procedures for secondary acetates.



The corresponding propargyl acetate (1 equiv.) followed by $IPrAuNTf_2$ (0.05 equiv.) were added to a solution of Selectfluor (2 equiv.) and $NaHCO_3$ (1 equiv.) in $MeCN:H_2O$ (20:1, 0.1 M). The reaction was stirred for 0.5-2h at 80 ^oC and was monotorized by TLC. When the reaction was finished, the mixture was diluted with DCM (5 ml) and an aqueous solution of $Na_2S_2O_3$ (5% v/v) (2 ml) was added. The mixture was extracted with DCM (3 x 5 mL) and the combined organic phases were dried over $MgSO_4$. The solvent was evaporated under reduced pressure and the residue was purified through silica gel flash column chromatography (Pentane/diethyl ether = 100/1) to yield the desired α-fluoroenones **6**.

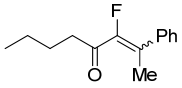
3.3 Characterization of products

3-fluoro-2-methyloct-2-en-4-one (2a)



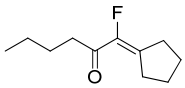
Following the general procedure, compound **2a** was isolated in 77% yield; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.57 (dt, J = 7.4, 3.8 Hz, 2H), 2.08 (d, J = 3.4 Hz, 3H), 1.83 (d, J = 4.1 Hz, 3H), 1.58 (quint, J = 7.2 Hz, 2H), 1.33 (quint, J = 7.2 Hz, 2H), 0.91 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.0 (d, $J_{C\text{-}F}$ = 38.2 Hz), 151.5 (d, $J_{C\text{-}F}$ = 247.4 Hz), 127.9 (d, $J_{C\text{-}F}$ = 14.9 Hz), 39.9 (d, $J_{C\text{-}F}$ = 2.4 Hz), 25.9 (d, $J_{C\text{-}F}$ = 2.4 Hz), 22.8, 19.0 (d, $J_{C\text{-}F}$ = 23.8 Hz), 18.9 (d, $J_{C\text{-}F}$ = 16.7 Hz), 14.3. IR (film): $\tilde{\upsilon}$ = 2960, 1699, 1638, 1373, 1261, 1183, 1138, 1019, 911, 808, 730 cm^{-1}; HRMS (EI): *m/z*: calcd for $C_9H_{15}FO$: 158.1107, found: 158.1106.

3-fluoro-2-phenyloct-2-en-4-one (2b)



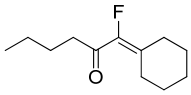
Following the general procedure, compound **2b** was isolated in 84% yield as an unseparable *E:Z* mixture of olefins in a ratio 1.5:1. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.40-7.32 (m, 8H, major and minor), 7.17-7.16 (m, 2H, major and minor), 2.68 (dt, *J* = 7.3, 3.9 Hz, 2H, minor), 2.43 (d, *J* = 3.6 Hz, 3H, minor), 2.42 (dt, *J* = 7.7, 3.3 Hz, 2H, major), 2.13 (d, *J* = 3.5 Hz, 3H, major), 1.65 (quint, *J* = 7.2 Hz, 2H, minor), 1.46 (quint, *J* = 7.2 Hz, 2H, major), 1.32 (quint, *J* = 7.2 Hz, 2H, minor), 1.22 (quint, *J* = 7.2 Hz, 2H, major), 0.94 (t, *J* = 7.2 Hz, 3H, minor), 0.84 (t, *J* = 7.2 Hz, 3H, major). ^{13} C NMR (100 MHz, $CDCl_3$): δ = 197.8 (d, $J_{C\text{-}F}$ = 38.1 Hz), 195.1 (d, $J_{C\text{-}F}$ = 34.6 Hz), 151.4 (d, $J_{C\text{-}F}$ = 256.3 Hz), 150.4 (d, $J_{C\text{-}F}$ = 253.9 Hz), 138.9 (d, $J_{C\text{-}F}$ = 5.9 Hz), 138.4 (d, $J_{C\text{-}F}$ = 1.8 Hz), 129.7 (d, $J_{C\text{-}F}$ = 18.4 Hz), 128.9, 128.7, 128.6 (d, $J_{C\text{-}F}$ = 4.2 Hz), 128.4, 128.1(d, $J_{C\text{-}F}$ = 2.9 Hz), 40.3, 26.0 (d, $J_{C\text{-}F}$ = 2.4 Hz), 25.9 (d, $J_{C\text{-}F}$ = 1.8 Hz), 22.8, 22.7, 20.0 (d, $J_{C\text{-}F}$ = 7.7 Hz), 18.4 (d, $J_{C\text{-}F}$ = 1.5 Hz), 14.3, 14.2. (Of the two sets of signals expected for the two isomers three carbon signals are missing due to overlapping). IR (film): $\tilde{\upsilon}$ = 2959, 2933, 2872, 1698, 1622, 1492, 1442, 1404, 1376, 1258, 1197, 1120, 1376, 1258, 1197, 1120, 1068, 1026, 911, 761, 732, 696 cm^{-1}; HRMS (EI): *m/z*: calcd for $C_{14}H_{17}FO$: 220.1263, found: 220.1253.

1-Cyclopentylidene-1-fluorohexan-2-one (2c)[5]



Following the general procedure, compound **2c** was isolated in 82% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.71-2.67 (m, 2H), 2.58 (dt, *J* = 7.4, 3.3 Hz, 2H), 2.50-2.46 (m, 2H), 1.74 (quint, *J* = 7.2 Hz, 2H), 1.67 (quint, *J* = 6.6 Hz, 2H), 1.58 (quint, *J* = 7.2 Hz, 2H), 1.35 (sext, *J* = 7.4 Hz, 2H), 0.91 (t, J = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 196.3 (d, $J_{C\text{-}F}$ = 35.2 Hz), 149.7 (d, $J_{C\text{-}F}$ = 249.1 Hz), 140.0 (d, $J_{C\text{-}F}$ = 14.3 Hz), 39.3 (d, $J_{C\text{-}F}$ = 2.9 Hz), 31.7 (d, $J_{C\text{-}F}$ = 1.7 Hz), 31.0 (d, $J_{C\text{-}F}$ = 3.6 Hz), 27.6, 26.0, 25.9 (d, $J_{C\text{-}F}$ = 2.3 Hz), 22.9, 14.4.

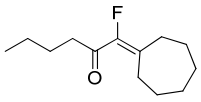
1-cyclohexylidene-1-fluorohexan-2-one (2d)



Following the general procedure, compound **2d** was isolated in 71% yield; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.74-2.71 (m, 2H), 2.59 (dt, *J* = 7.6, 3.9 Hz, 2H), 2.30-2.28 (m, 2H), 1.63-1.54 (m, 8H), 1.34 (sext, *J* = 6.9 Hz, 2H), 0.91 (t, J = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 197.8 (d, $J_{C\text{-}F}$ = 38.7 Hz), 148.9 (d, $J_{C\text{-}F}$ = 247.3 Hz), 134.9 (d, $J_{C\text{-}F}$ = 12.5 Hz), 40.5, 28.2 (d, $J_{C\text{-}F}$ = 1.7 Hz), 27.9 (d, $J_{C\text{-}F}$ = 10.1 Hz), 27.8 (d, $J_{C\text{-}F}$ = 1.7 Hz), 27.7 (d, $J_{C\text{-}F}$ = 2.3 Hz), 26.6, 26.0 (d, $J_{C\text{-}F}$ = 2.3 Hz), 22.9, 14.4. IR (film): $\tilde{\upsilon}$ = 2933, 2858, 1698, 1633, 1450, 1405, 1351, 1256, 1179, 1117, 1048, 908, 855, 807, 732, 647 cm^{-1}; HRMS (EI): *m/z*: calcd for $C_{12}H_{19}FO$: 198.1420, found: 198.1419.

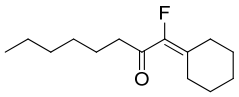
[5] L.Cui, G. Zhang, L. Zhang, *Bioorg. Med. Chem. Lett.* 2009, **19**, 3884

1-Cycloheptylidene-1-fluorohexan-2-one (2e)



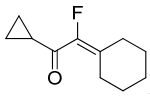
Following the general procedure, compound **2e** was isolated in 87% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.74-2.71 (m, 2H), 2.58 (dt, J = 7.5, 4.0 Hz, 2H), 2.44-2.40 (m, 2H), 1.65-1.49 (m, 10H), 1.33 (sext, J = 6.9 Hz, 2H), 0.90 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5 (d, $J_{C\text{-}F}$ = 40.7 Hz), 150.7 (d, $J_{C\text{-}F}$ = 248.7 Hz), 137.5 (d, $J_{C\text{-}F}$ = 11.3 Hz), 39.6 (d, $J_{C\text{-}F}$ = 2.2 Hz), 29.4, 29.4 (d, $J_{C\text{-}F}$ = 9.7 Hz), 29.2 (d, $J_{C\text{-}F}$ = 2.2 Hz), 29.1, 27.2 (d, $J_{C\text{-}F}$ = 2.5 Hz), 26.5 (d, $J_{C\text{-}F}$ = 1.5 Hz), 25.4 (d, $J_{C\text{-}F}$ = 2.5 Hz), 22.3, 13.9. IR (film): $\tilde{\upsilon}$ = 2928, 2857, 1696, 1620, 1455, 1261, 1168, 1104, 1041, 911, 808, 733 cm^{-1}; HRMS (EI): *m/z*: calcd for $C_{13}H_{21}FO$: 212.1577, found: 212.1577.

1-Cyclohexylidene-1-fluorooctan-2-one (2f)



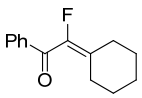
Following the general procedure, compound **2f** was isolated in 79% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.75-2.72 (m, 2H), 2.58 (dt, J = 7.4, 3.7 Hz, 2H), 2.31-2.28 (m, 2H), 1.64-1.55 (m, 8H), 1.33-1.27 (m, 6H), 0.88 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.3 (d, $J_{C\text{-}F}$ = 41.4 Hz), 148.3 (d, $J_{C\text{-}F}$ = 247.9 Hz), 134.3 (d, $J_{C\text{-}F}$ = 11.4 Hz), 40.2 (d, $J_{C\text{-}F}$ = 2.2 Hz), 31.6, 28.9, 27.6 (d, $J_{C\text{-}F}$ = 2.2 Hz), 27.3 (d, $J_{C\text{-}F}$ = 9.9 Hz), 27.2 (d, $J_{C\text{-}F}$ = 1.8 Hz), 27.1 (d, $J_{C\text{-}F}$ = 2.9 Hz), 26.0, 23.3 (d, $J_{C\text{-}F}$ = 2.2 Hz), 22.5, 14.0. IR (film): $\tilde{\upsilon}$ = 2930, 2857, 1699, 1634, 1450, 1404, 1352, 1254, 1175, 1117, 1051, 978, 773 cm^{-1}; HRMS (EI): *m/z*: calcd for $C_{14}H_{23}FO$: 226.1733, found: 226.1733.

2-Cyclohexylidene-1-cyclopropyl-2-fluoroethanone (2g)



Following the general procedure, compound **2g** was isolated in 57% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.72-2.70 (m, 2H), 2.47-2.42 (m, 1H), 2.35-2.31 (m, 2H), 1.66-1.56 (m, 6H), 1.11-1.06 (m, 2H), 0.96-0.92 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5 (d, $J_{C\text{-}F}$ = 39.6 Hz), 148.3 (d, $J_{C\text{-}F}$ = 247.2 Hz), 133.7 (d, $J_{C\text{-}F}$ = 13.2 Hz), 27.5 (d, $J_{C\text{-}F}$ = 2.2 Hz), 27.4 (d, $J_{C\text{-}F}$ = 9.5 Hz), 27.3 (d, $J_{C\text{-}F}$ = 2.6 Hz), 27.2 (d, $J_{C\text{-}F}$ = 1.8 Hz), 26.0, 17.8, 17.7. IR (film): $\tilde{\upsilon}$ = 2933, 2857, 1683, 1632, 1449, 1382, 1253, 12001177, 1050, 979, 731 cm^{-1}; HRMS (EI): *m/z*: calcd for $C_{11}H_{15}FO$: 182.1107, Found: 182.1107.

2-Cyclohexylidene-2-fluoro-1-phenylethanone (2h)[6]

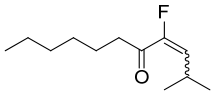


Following the general procedure, compound **2h** was isolated in 81% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88-7.85 (m, 2H), 7.56 (tt, J = 6.6, 1.3 Hz, 1H), 7.47-7.43 (m, 2H), 2.50-2.48 (m, 2H),

[6] H.Hata, T. Kobayashi, H. Amii, K. Uneyama, J. T. Welch, *Tetrahedron Lett*. 2002, **43**, 6099.

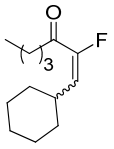
2.49-2.41 (m, 2H), 1.72-1.60 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.7 (d, $J_{C\text{-}F}$ = 34.8 Hz), 147.9 (d, $J_{C\text{-}F}$ = 249.4 Hz), 137.1 (d, $J_{C\text{-}F}$ = 3.6 Hz), 133.7 (d, $J_{C\text{-}F}$ = 11.3 Hz), 133.0, 129.4(d, $J_{C\text{-}F}$ = 4.4 Hz), 128.3, 28.0 (d, $J_{C\text{-}F}$ = 2.9 Hz), 27.6 (d, $J_{C\text{-}F}$ = 2.6 Hz), 27.2 (d, $J_{C\text{-}F}$ = 1.4 Hz), 27.1 (d, $J_{C\text{-}F}$ = 8.8 Hz), 26.1. IR (film): $\tilde{\upsilon}$ = 2934, 2857, 1671, 1597, 1448, 1289, 1226, 1182, 1149, 1127, 960, 908, 731 cm^{-1}; HRMS (EI): *m/z*: calcd for $C_{14}H_{15}FO$: 218.1, found: 218.1.

4-Fluoro-2-methylundec-3-en-5-one (6a)



Following the general procedure, compound **6a** was isolated in 71% yield as an unseparable *E:Z* mixture of olefins in a ratio 4:1. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.87 (dd, $J_{H\text{-}F}$ = 35.0 Hz, J = 9.2 Hz, 1H, minor isomer), 5.51 (dd, $J_{H\text{-}F}$ = 23.7 Hz, J = 10.7 Hz, 1H, major isomer), 3.42-2.32 (m, 1H, major isomer), 2.86-2.78 (m, 1H, minor isomer), 2.61-2.56 (m, 4H, major and minor isomer), 1.62-1.56 (m, 4H, major and minor isomers), 1.33-1.25 (m, 12H, major and minor isomers), 1.07 (d, J = 6.8 Hz, 6H, minor isomer), 1.02 (dd, J = 6.7, 0.9 Hz, 6H, major isomer), 0.90-0.86 (m, 6H, minor and major isomers). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.6 (d, $J_{C\text{-}F}$ = 39.9 Hz), 195.2 (d, $J_{C\text{-}F}$ = 35.7 Hz), 154.2 (d, $J_{C\text{-}F}$ = 261.0 Hz), 152.7 (d, $J_{C\text{-}F}$ = 253.9 Hz), 128.5 (d, $J_{C\text{-}F}$ = 15.5 Hz), 125.6 (d, $J_{C\text{-}F}$ = 11.3 Hz), 40.3 (d, $J_{C\text{-}F}$ = 3.5 Hz), 38.3, 32.1, 32.0, 29.4, 29.3, 25.3 (d, $J_{C\text{-}F}$ = 5.9 Hz), 25.1 (d, $J_{C\text{-}F}$ = 2.9 Hz), 24.1, 23.5 (d, $J_{C\text{-}F}$ = 1.8 Hz), 23.2 (d, $J_{C\text{-}F}$ = 2.4 Hz), 23.0, 22.6 (d, $J_{C\text{-}F}$ = 1.2 Hz), 14.5. (Of the two sets of signals expected for the two isomers two carbon signals are missing due to overlapping). IR (film): $\tilde{\upsilon}$ = 2931, 1706, 1641, 1466, 1373, 1260, 1098, 904, 808, 725 cm^{-1}; HRMS (EI): *m/z*: calcd for $C_{12}H_{21}FO$: 200.1576, found: 200.1577.

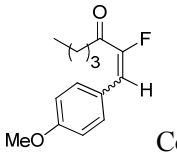
1-Cyclohexyl-2-fluorohept-1-en-3-one (6b)



Following the general procedure, compound **6b** was obtained in 72% yield as a *E:Z* mixture of olefins in a ratio 4.5:1. Major isomer: ^{1}H NMR (400 MHz, TMSCl + $CDCl_3$): δ = 5.47 (dd, $J_{H\text{-}F}$ = 23.2 Hz, J = 10.2 Hz, 1H), 3.02-2.99 (m, 1H), 2.54 (dt, $J_{H\text{-}F}$ = 3.5 Hz, J = 7.3 Hz, 2H), 1.32-1.23 (m, 6H), 1.03-1.00 (m, 8H), 0.86 (t, J = 7.3 Hz, 3H) . ^{13}C NMR (100 MHz, TMSCl + $CDCl_3$): δ = 197.5 (d, $J_{C\text{-}F}$ = 38 Hz), 153.3 (d, $J_{C\text{-}F}$ = 250 Hz), 127.1 (d, $J_{C\text{-}F}$ = 15.3 Hz), 40.0 (d, $J_{C\text{-}F}$ = 2.9 Hz), 34.6 (d, $J_{C\text{-}F}$ = 5.2 Hz), 33.3 (d, $J_{C\text{-}F}$ = 2.2 Hz), 26.3, 25.9, 25.6, 22.8, 14.4. Minor isomer: ^{1}H NMR (400 MHz, TMSCl + $CDCl_3$): δ = 5.91 (dd, $J_{H\text{-}F}$ = 35.3 Hz, J = 9.7 Hz, 1H), 3.02-2.99 (m, 1H), 2.54 (dt, $J_{H\text{-}F}$ = 3.5 Hz, J = 7.3 Hz, 2H), 1.32-1.23 (m, 6H), 1.03-1.00 (m, 8H), 0.86 (t, J = 7.3 Hz, 3H) . ^{13}C NMR (100 MHz, TMSCl + $CDCl_3$): δ = 194.7 (d, $J_{C\text{-}F}$ = 31 Hz), 153.9 (d, $J_{C\text{-}F}$ = 259 Hz), 123.7 (d, $J_{C\text{-}F}$ = 12.1 Hz), 37.5, 33.9 (d, $J_{C\text{-}F}$ = 2.2 Hz), 32.1 (d, $J_{C\text{-}F}$ = 1.8 Hz), 25.8, 25.1, 22.3, 22.2, 14.0. IR (film): $\tilde{\upsilon}$ = 2928, 2853, 1706, 1638, 1449,

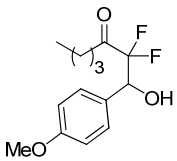
1374, 1293, 1260, 1164, 1099, 1042, 803 cm^{-1}; HRMS (EI): *m/z*: calcd for $C_{13}H_{21}FO$: 212.1576. Found: 212.1574.

2-Fuoro-1-(4-methoxyphenyl)hept-1-en-3-one (6c)



Compound **6c** was obtained in 50% yield as an unseparable *Z:E* mixture of olefins in a ratio 2:1. Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 8.9 Hz, 2H), 6.96 (d, *J* = 8.9 Hz, 2H), 6.82 (d, $J_{H\text{-}F}$ = 37.3 Hz, 1H), 3.87 (s, 3H), 2.74 (td, *J* = 7.3, 2.2 Hz, 2H), 1.73-1.63 (m, 2H), 1.45-1.34 (m, 2H), 0.98 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.0 (d, $J_{C\text{-}F}$ = 31.6 Hz), 160.8 (d, $J_{C\text{-}F}$ = 3.4 Hz), 153.1 (d, $J_{C\text{-}F}$ = 269 Hz), 132.4 (d, $J_{C\text{-}F}$ = 8.5 Hz), 123.9 (d, $J_{C\text{-}F}$ = 4.0 Hz), 115.0 (d, $J_{C\text{-}F}$ = 5.9 Hz), 114.4, 55.3, 37.6 (d, $J_{C\text{-}F}$ = 0.8 Hz), 25.9 (d, $J_{C\text{-}F}$ = 1.4 Hz), 22.4, 13.9. Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 8.9 Hz, 2H), 6.91 (d, *J* = 8.9 Hz, 2H), 6.64 (d, $J_{H\text{-}F}$ = 26.7 Hz, 1H), 3.86 (s, 3H), 2.69 (td, *J* = 7.5, 3.7 Hz, 2H), 1.73-1.63 (m, 2H), 1.45-1.34 (m, 2H), 0.95 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.6 (d, $J_{C\text{-}F}$ = 30.8 Hz), 160.6 (d, $J_{C\text{-}F}$ = 1.6 Hz), 152.0 (d, $J_{C\text{-}F}$ = 253 Hz), 132.2 (d, $J_{C\text{-}F}$ = 2.8 Hz), 123.2 (d, $J_{C\text{-}F}$ = 10.4 Hz), 120.2 (d, $J_{C\text{-}F}$ = 28.8 Hz), 113.6, 55.3, 39.9 (d, $J_{C\text{-}F}$ = 2.1 Hz), 25.9 (d, $J_{C\text{-}F}$ = 2.1 Hz), 22.3, 13.9. IR (film): $\tilde{\upsilon}$ = 2958, 2933, 2872, 1700, 1682, 1601, 1509, 1301, 1252, 1160, 1030, 888, 828, 769, 731, 598, 534 cm^{-1}. HRMS (EI): *m/z*: calcd for $C_{14}H_{17}FO_2$: 236.1213. Found: 236.1213.

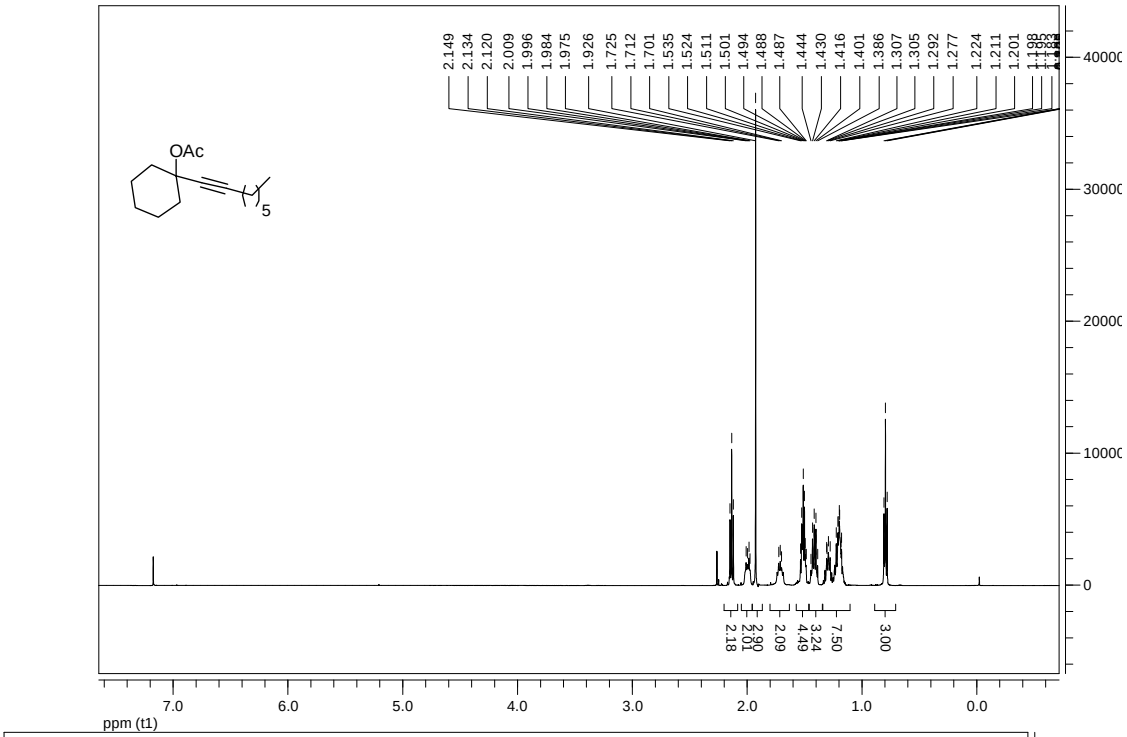
2,2-Difluoro-1-hydroxy-1-(4-methoxyphenyl)heptan-3-one (7)

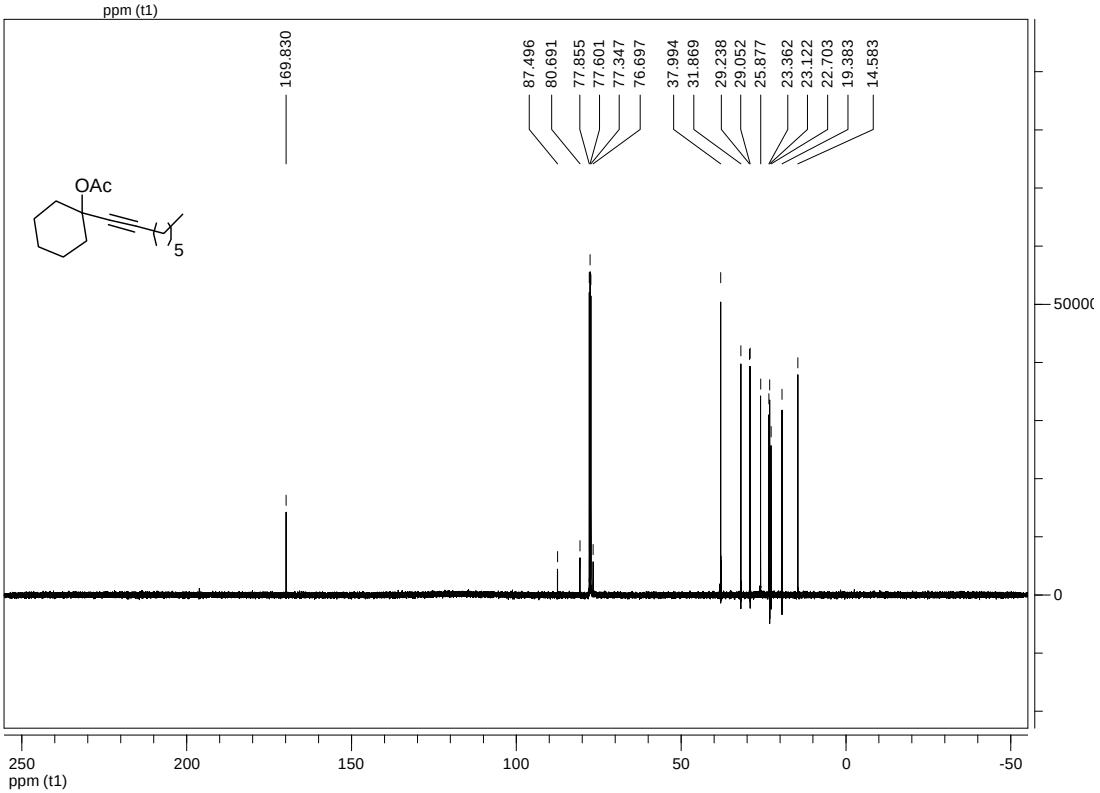


Compound **7** was obtained in 26% yield ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (d, *J* = 8.6 Hz, 2H), 6.95 (d, *J* = 8.6 Hz, 2H), 5.13 (dd, $J_{H\text{-}F}$ = 16.4, 7.8 Hz, 1H), 3.85 (s, 3H), 2.64-2.58 (m, 2H), 1.62-1.54 (m, 2H), 1.32 (sext, *J* = 7.4 Hz, 2H), 0.92 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.7 (dd, $J_{C\text{-}F}$ = 31.0, 28.0 Hz), 160.3, 129.1 (t, $J_{C\text{-}F}$ = 2.0 Hz), 126.8, 114.8 (dd, $J_{C\text{-}F}$ = 260, 254 Hz), 113.9, 72.8 (dd, $J_{C\text{-}F}$ = 29, 24 Hz), 55.3, 37.7, 24.4 21.9, 13.7; . IR (film): $\tilde{\upsilon}$ = 2960, 2934, 2873, 1737, 1612, 1513, 1464, 1401, 1249, 1175, 1069, 1030, 840, 794, 732, 580, 544 cm^{-1}; HRMS (EI):: *m/z*: calcd for $C_{14}H_{18}F_2O_3$: 272.1224. Found: 272.1225.

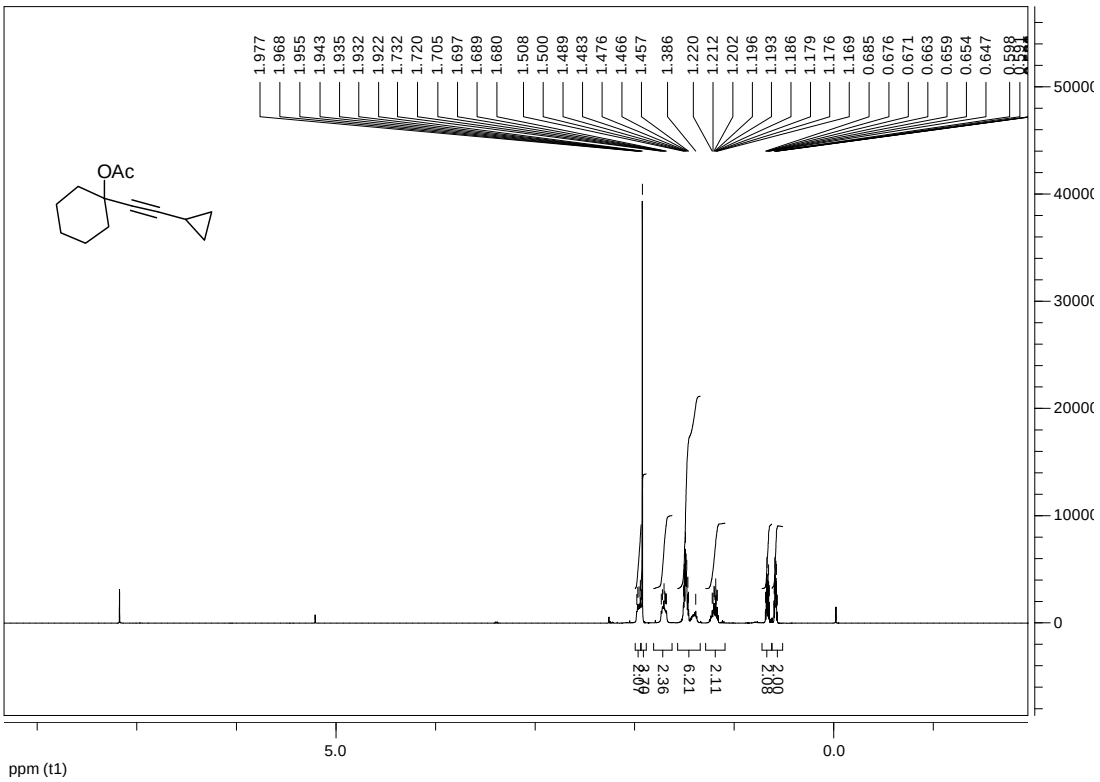
4. ^{1}H and ^{13}C charts of starting materials and products

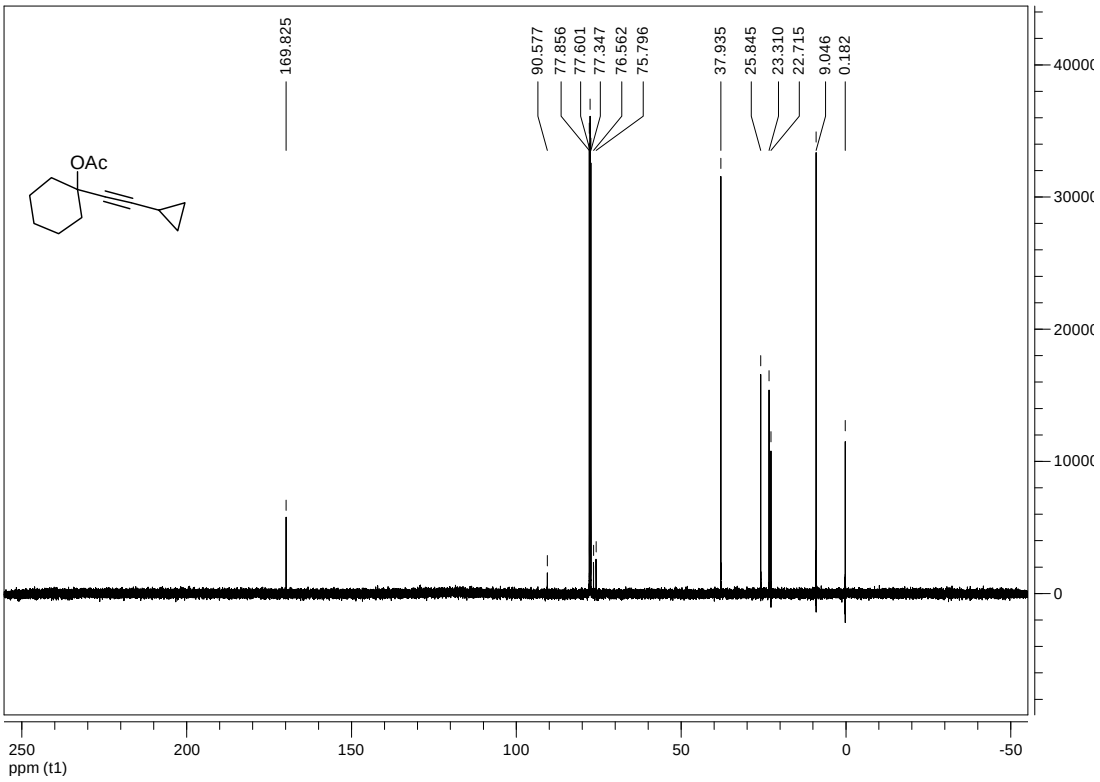
1-(Oct-1-ynyl)cyclohexyl acetate (1f)



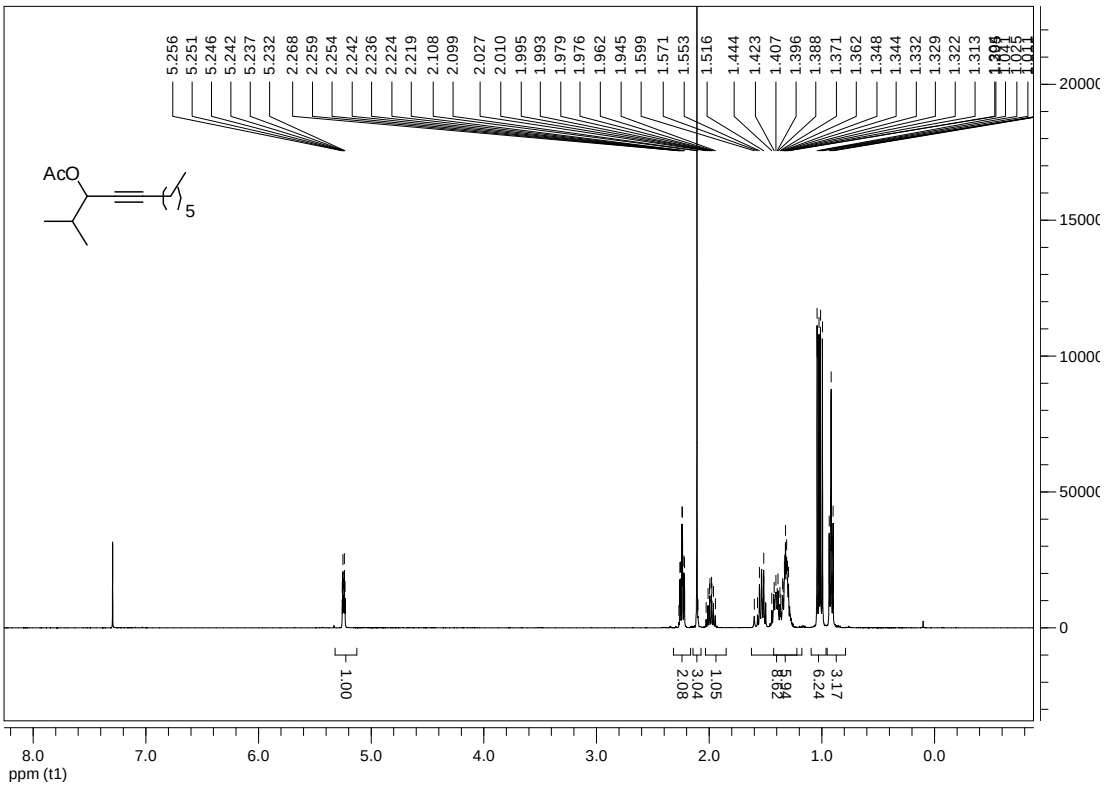


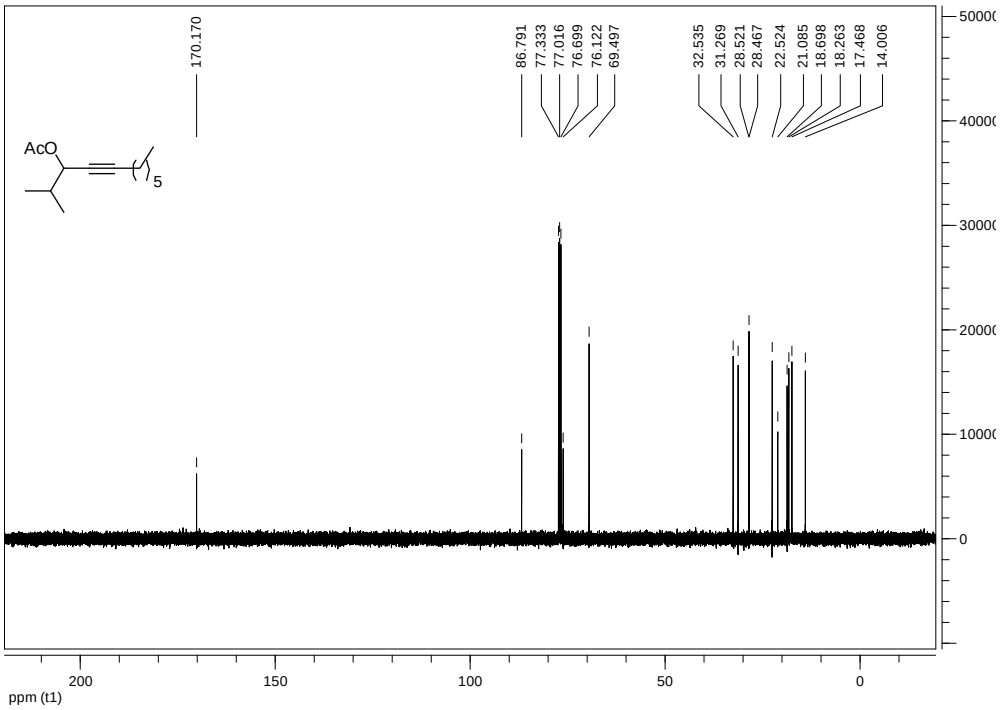
1-(Cyclopropylethynyl)cyclohexyl acetate (1g)



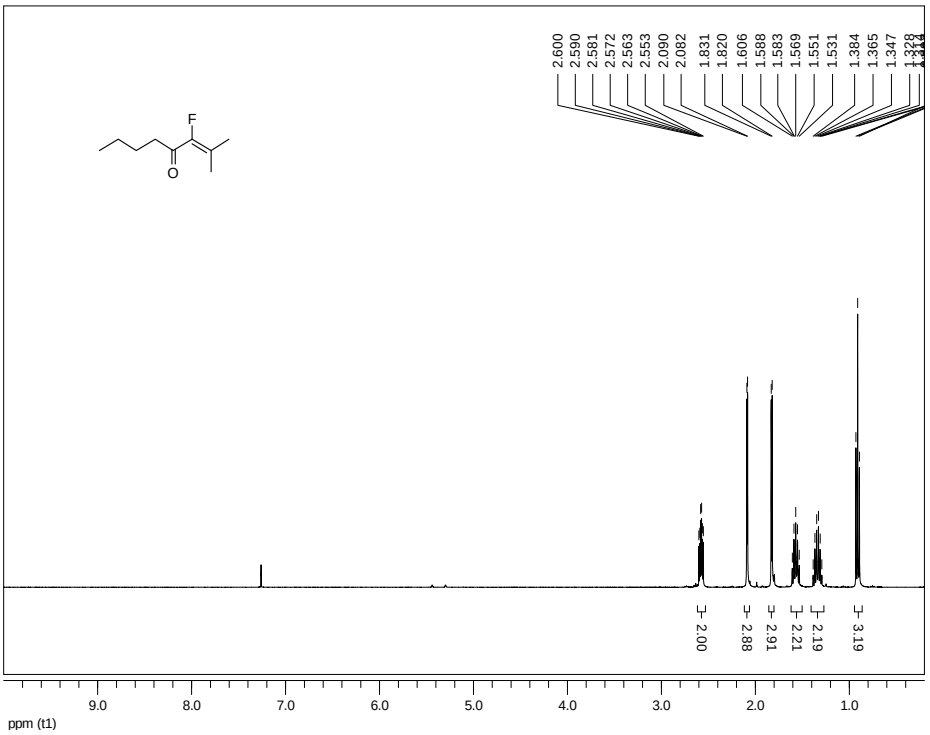


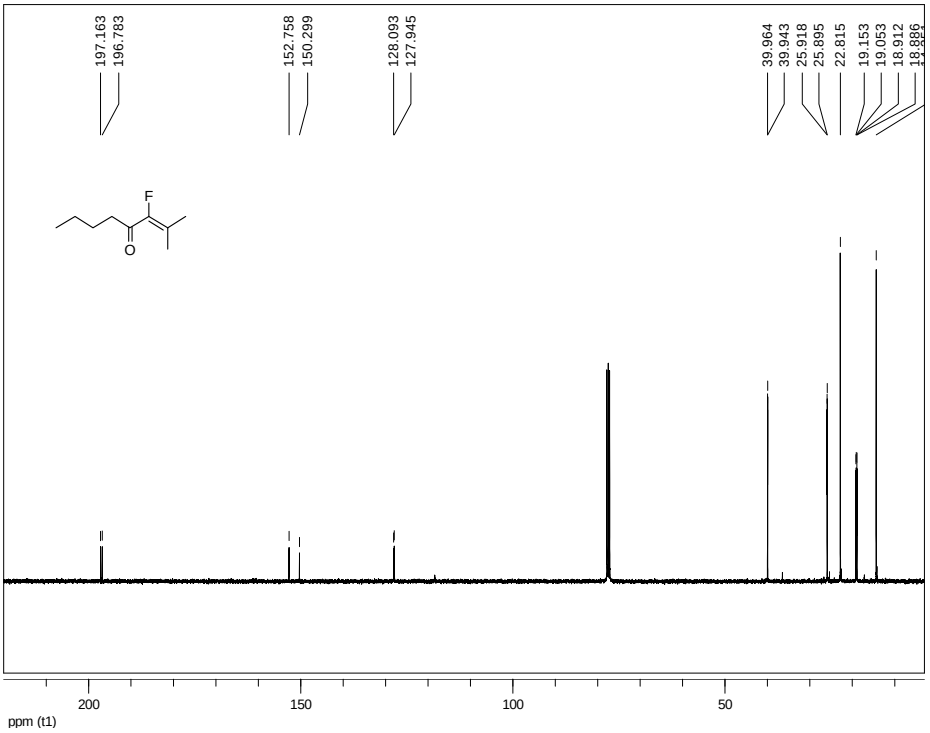
2-Methylundec-4-yn-3-yl acetate (5a)



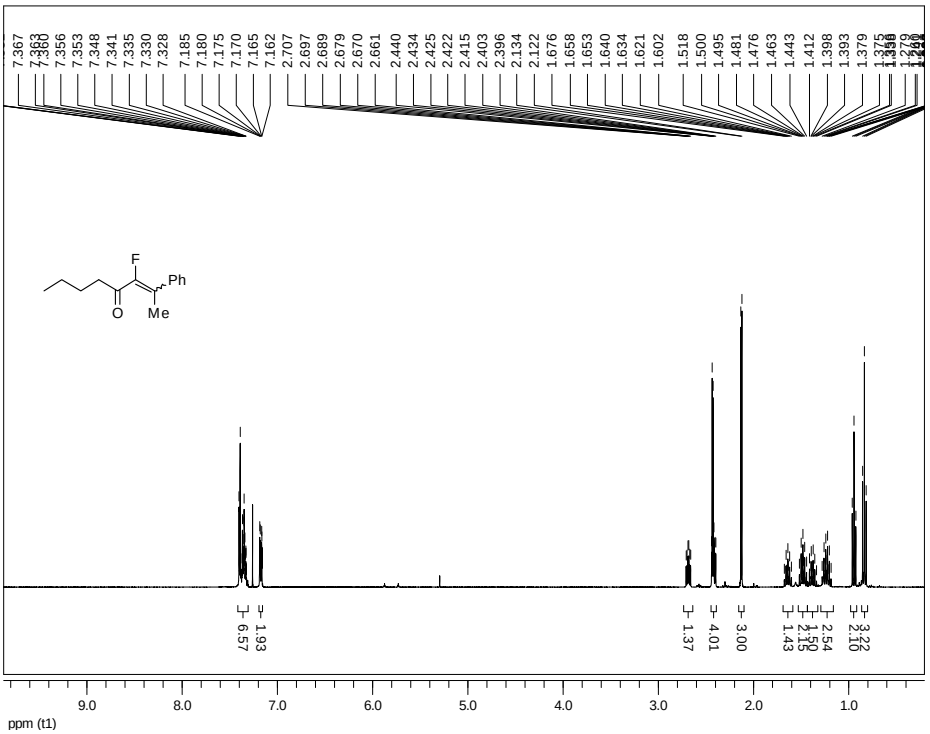


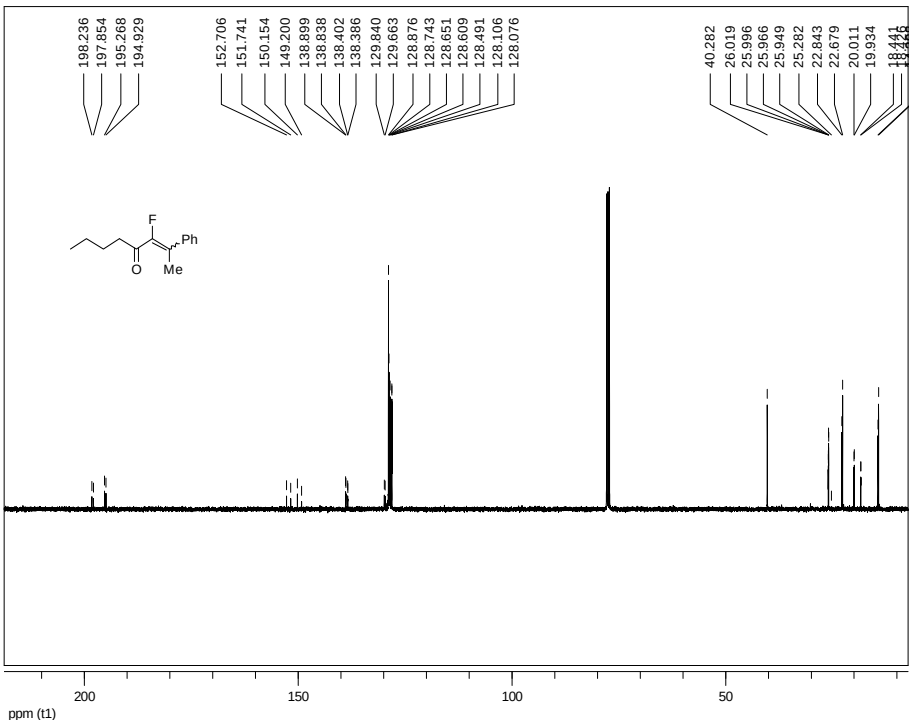
3-Fluoro-2-methyloct-2-en-4-one (2a)

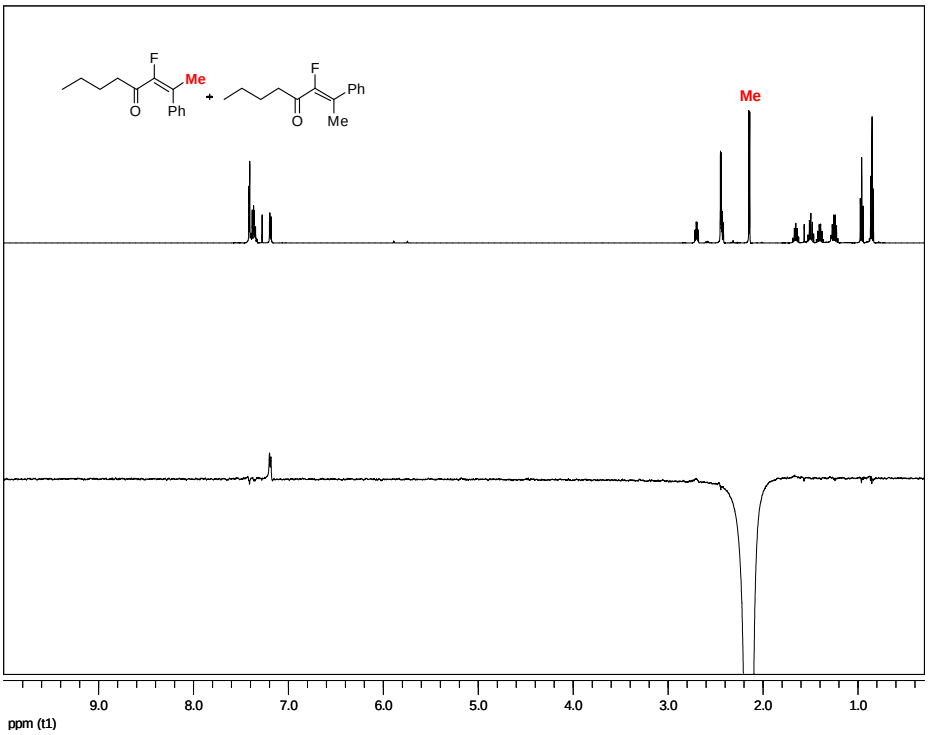




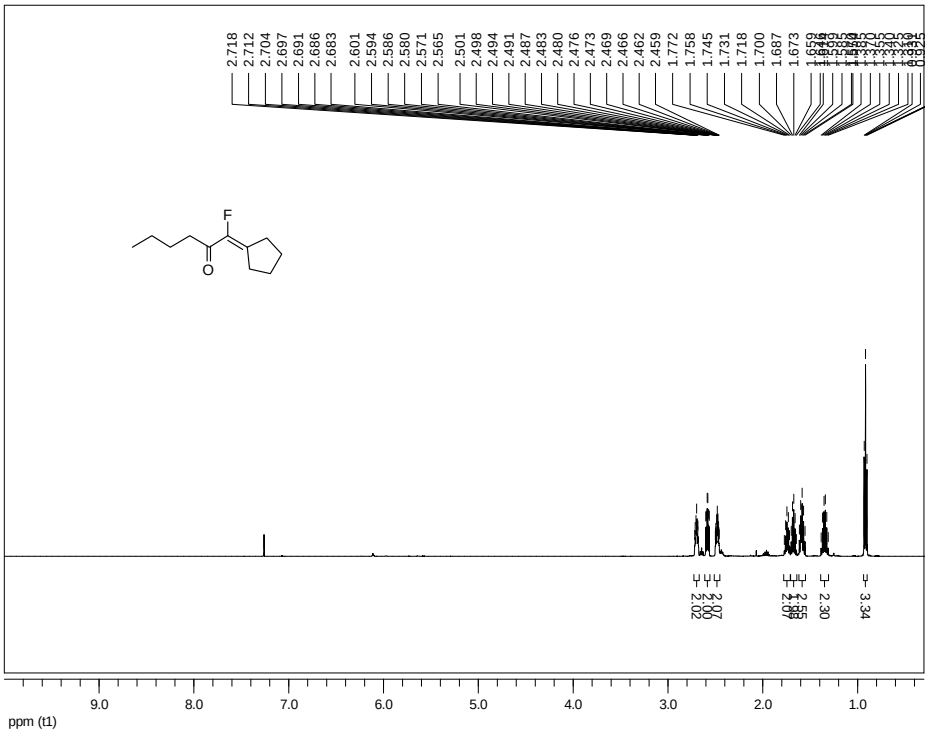
3-Fluoro-2-phenyloct-2-en-4-one (2b)

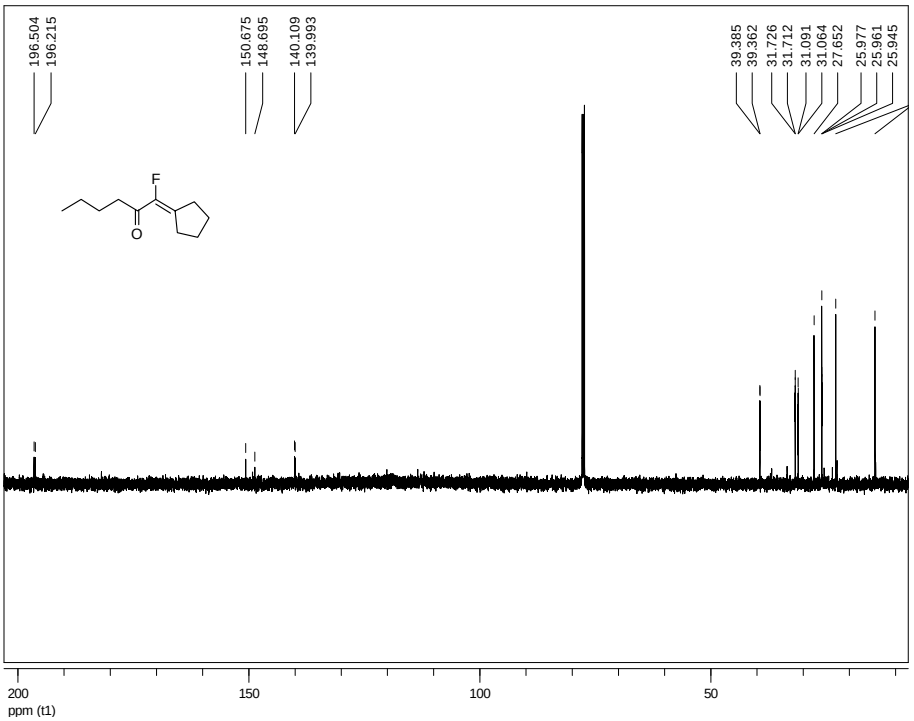

F
Ph
O
Me
6.57
1.93
1.37
4.01
3.00
1.43
2.54
3.22
2.10
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)


198.236
197.854
195.268
194.929
152.706
151.741
150.154
149.200
138.899
138.838
138.402
138.386
129.840
129.663
128.876
128.743
128.651
128.609
128.491
128.106
128.076
40.282
26.019
25.996
25.966
25.949
25.282
22.843
22.679
20.011
19.934
F
Ph
O
Me
200
150
100
50
ppm (t1)

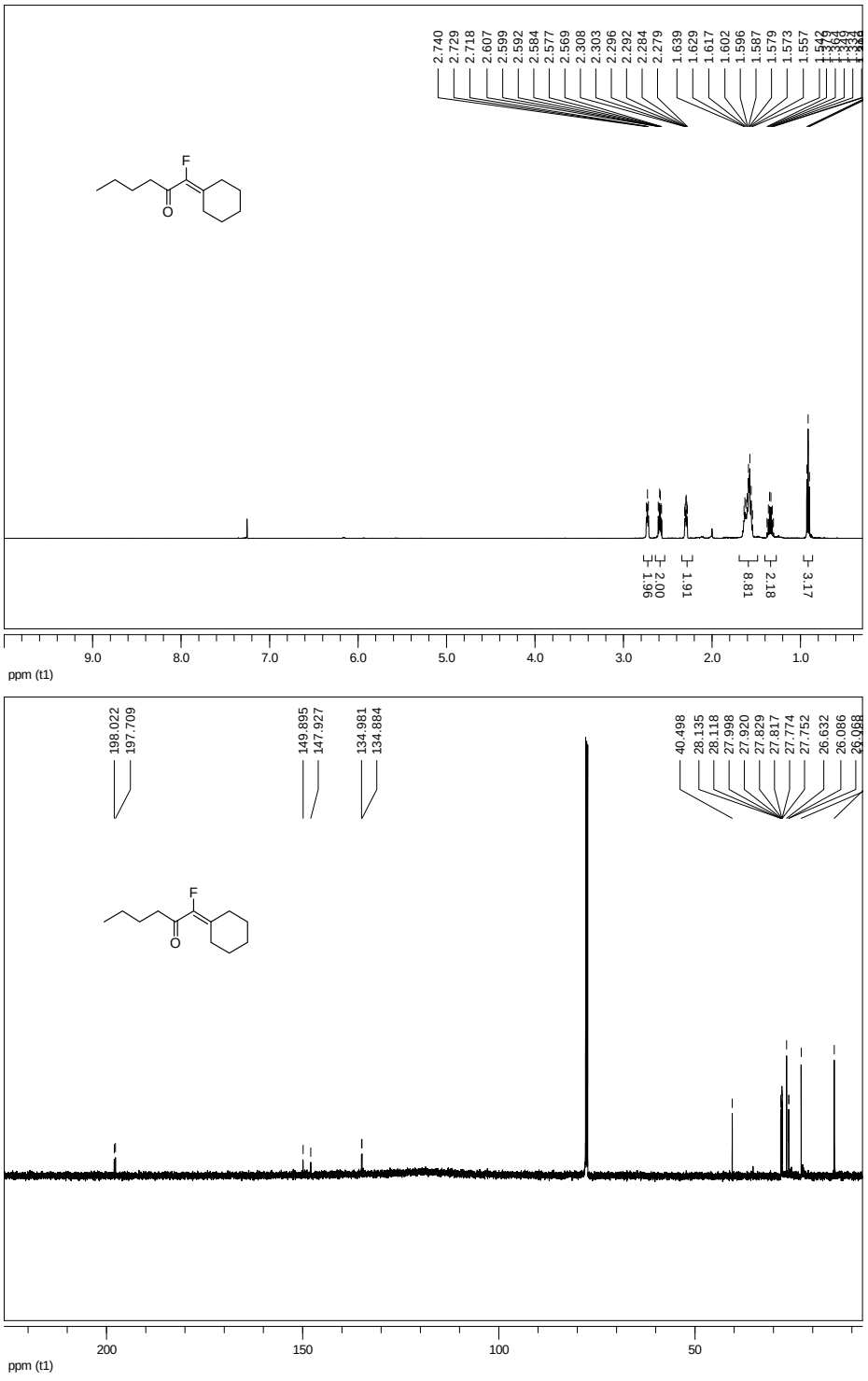


1-Cyclopentylidene-1-fluorohexan-2-one (2c)

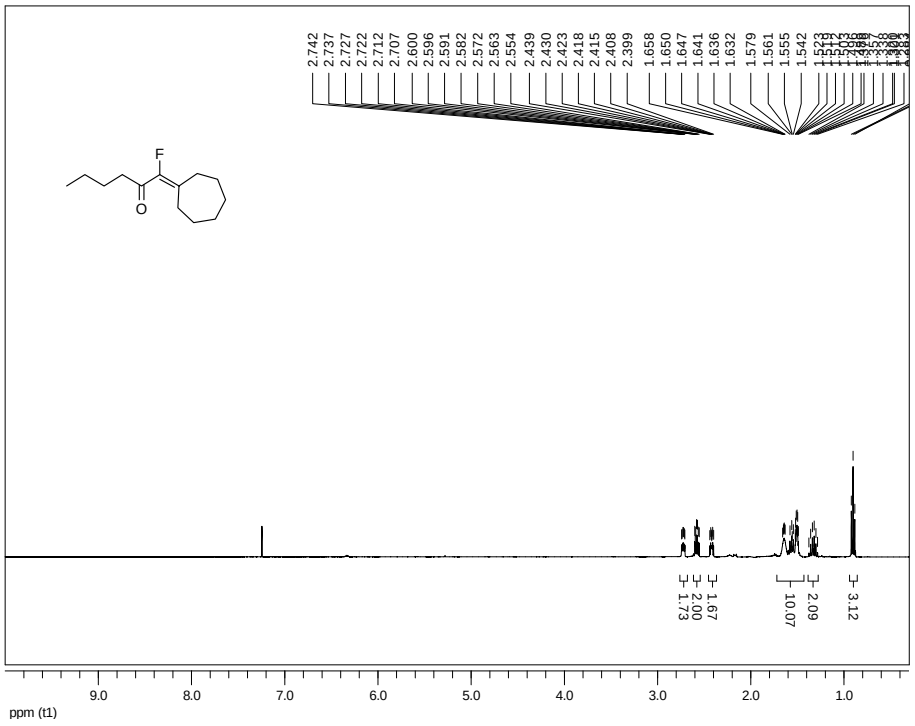

2.718
2.712
2.704
2.697
2.691
2.686
2.683
2.601
2.594
2.586
2.580
2.571
2.565
2.501
2.498
2.494
2.491
2.487
2.483
2.480
2.476
2.473
2.469
2.466
2.462
2.459
1.772
1.758
1.745
1.731
1.718
1.700
1.687
1.673
F
O
2.02
2.07
2.30
3.34
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

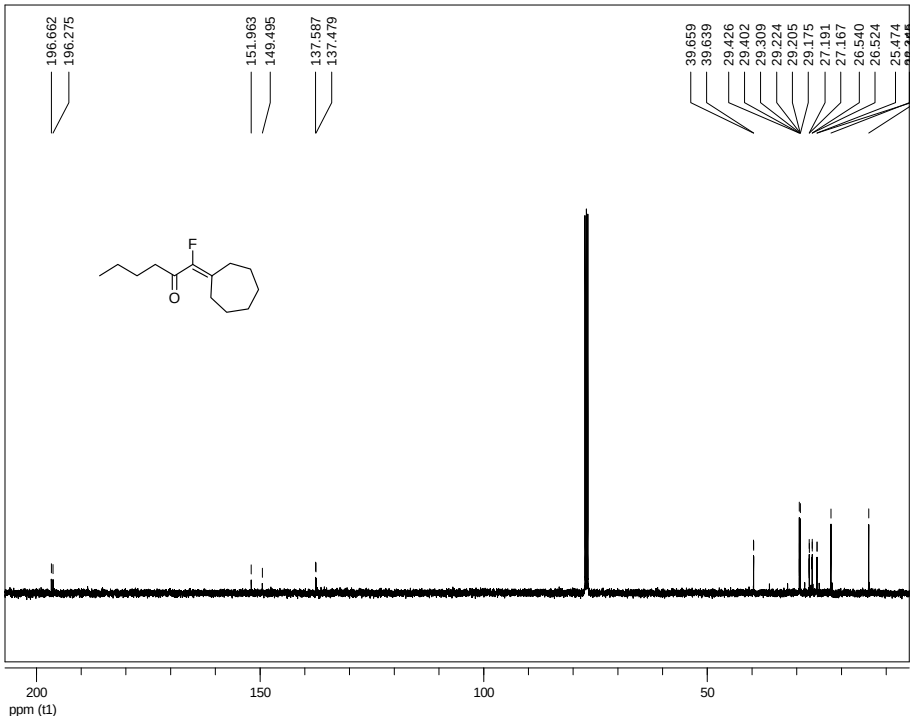

196.504
196.215
150.675
148.695
140.109
139.993
39.385
39.362
31.726
31.712
31.091
31.064
27.652
25.977
25.961
25.945
F
O
200
150
100
50
ppm (t1)

1-Cyclohexylidene-1-fluorohexan-2-one (2d)

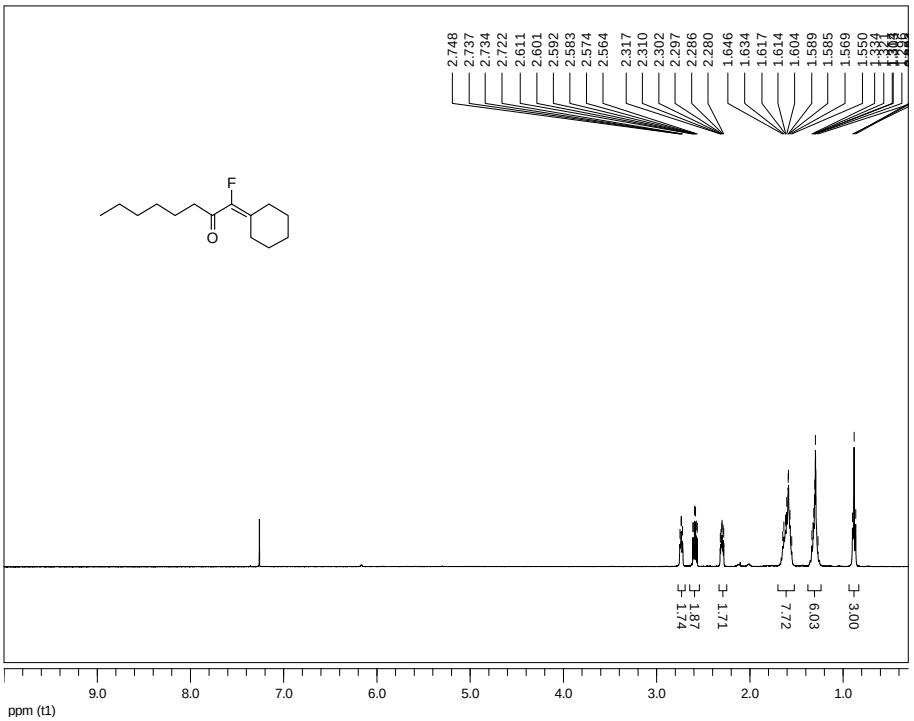


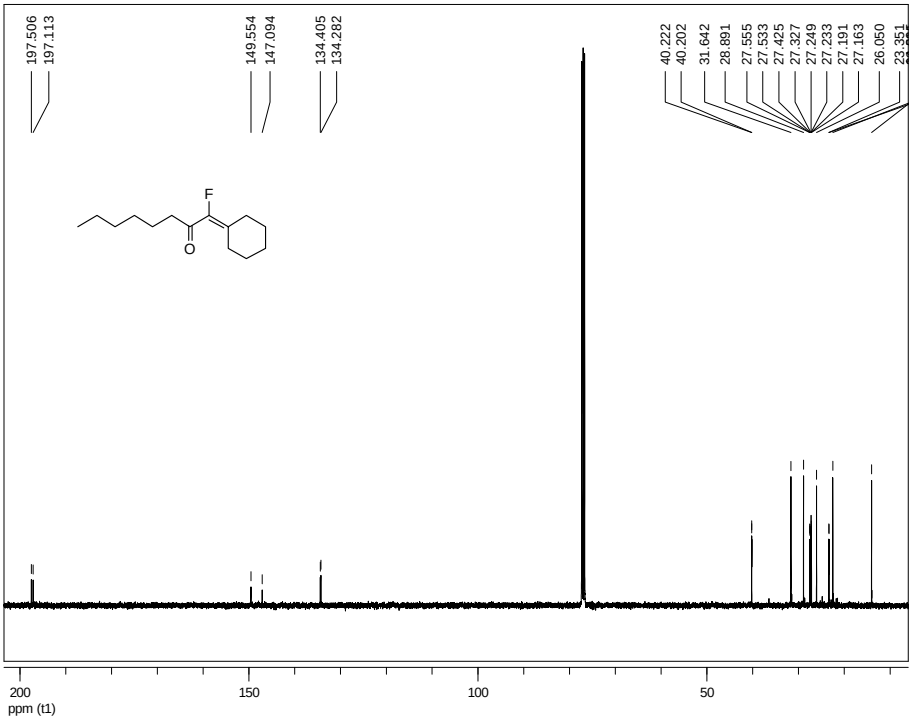
1-Cycloheptylidene-1-fluorohexan-2-one (2e)



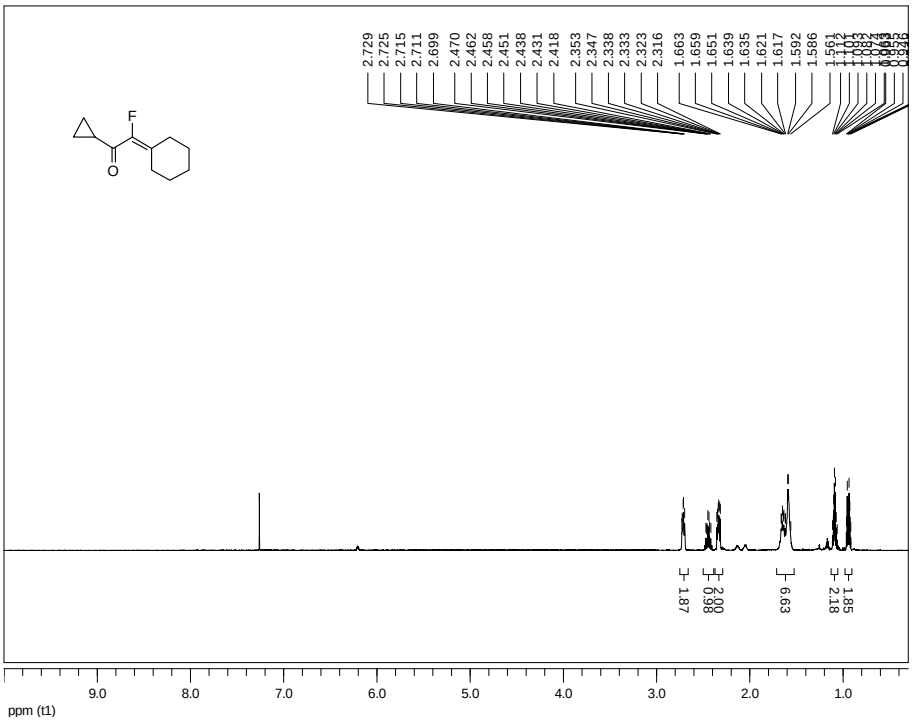


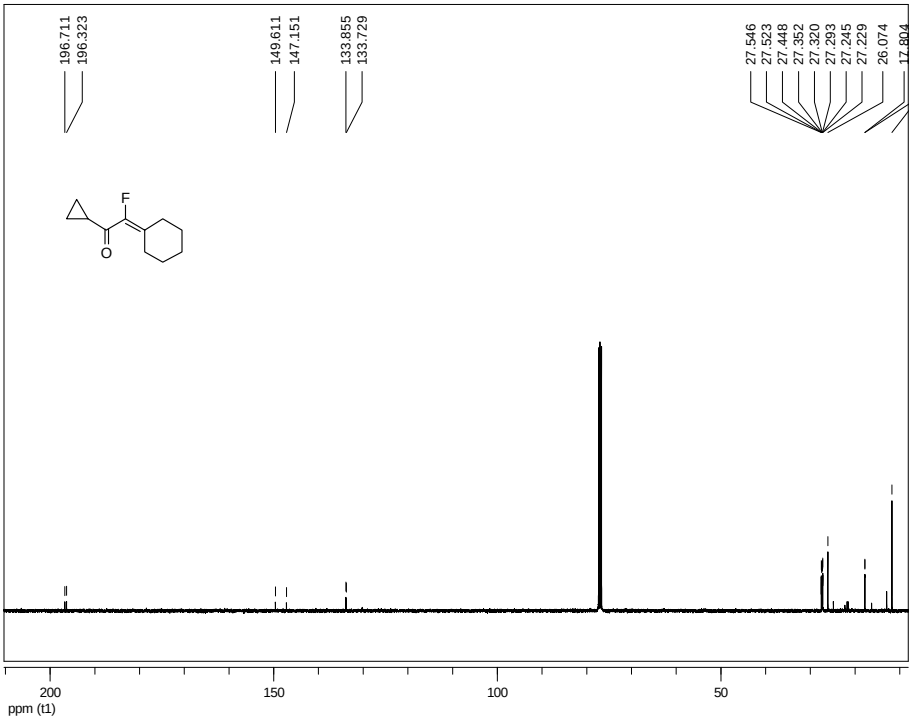
1-Cyclohexylidene-1-fluorooctan-2-one (2f)



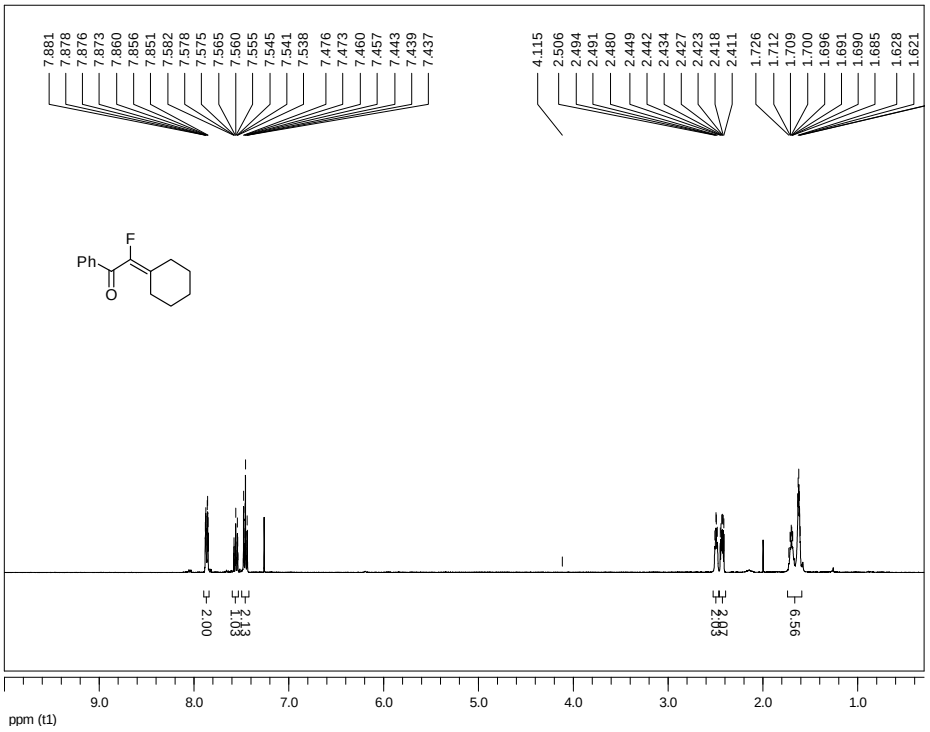


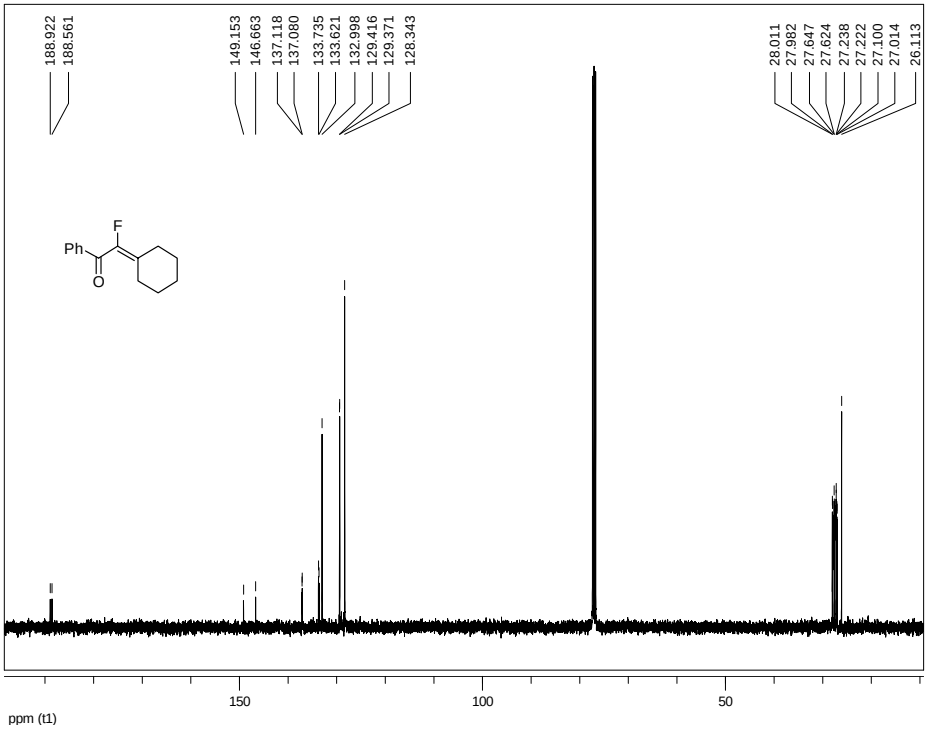
2-Cyclohexylidene-1-cyclopropyl-2-fluoroethanone (2g)



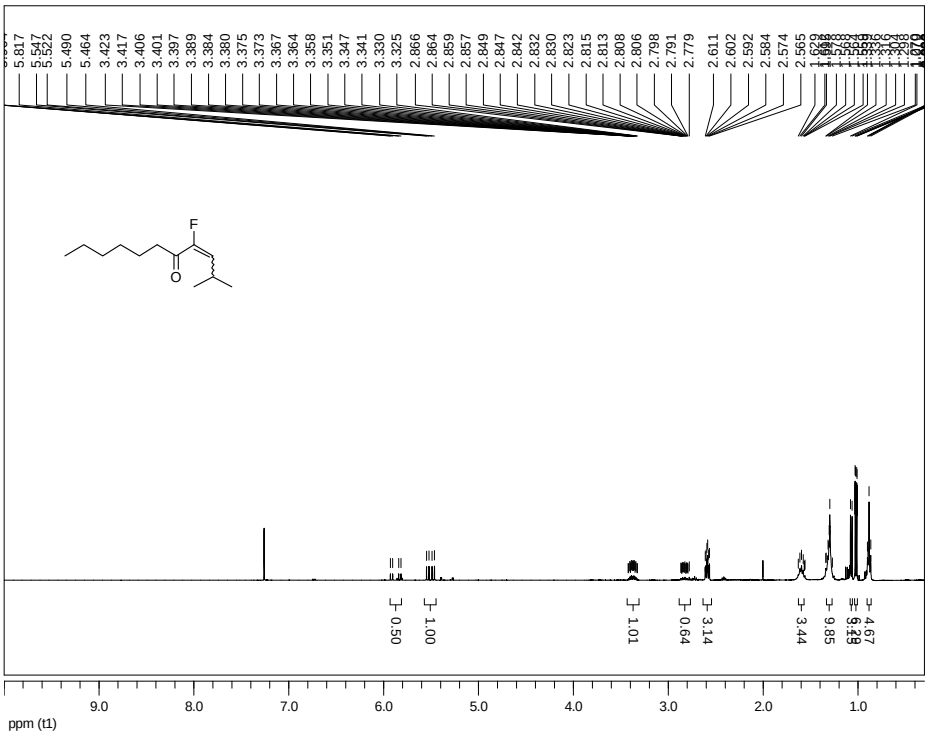


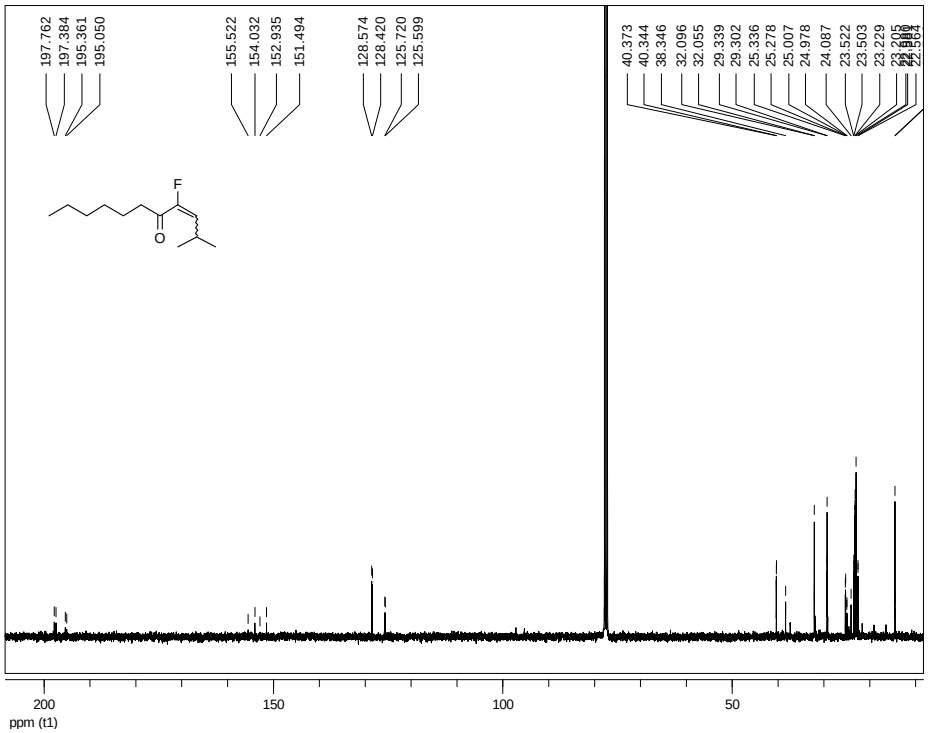
2-Cyclohexylidene-2-fluoro-1-phenylethanone (2h)



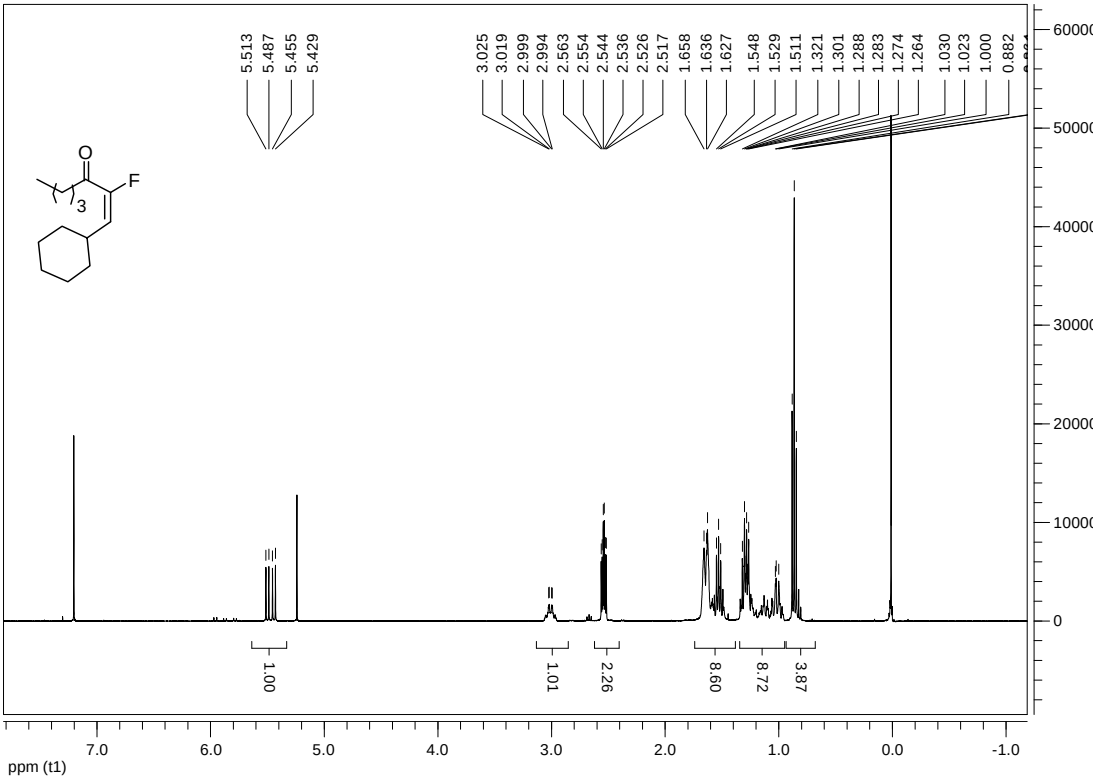


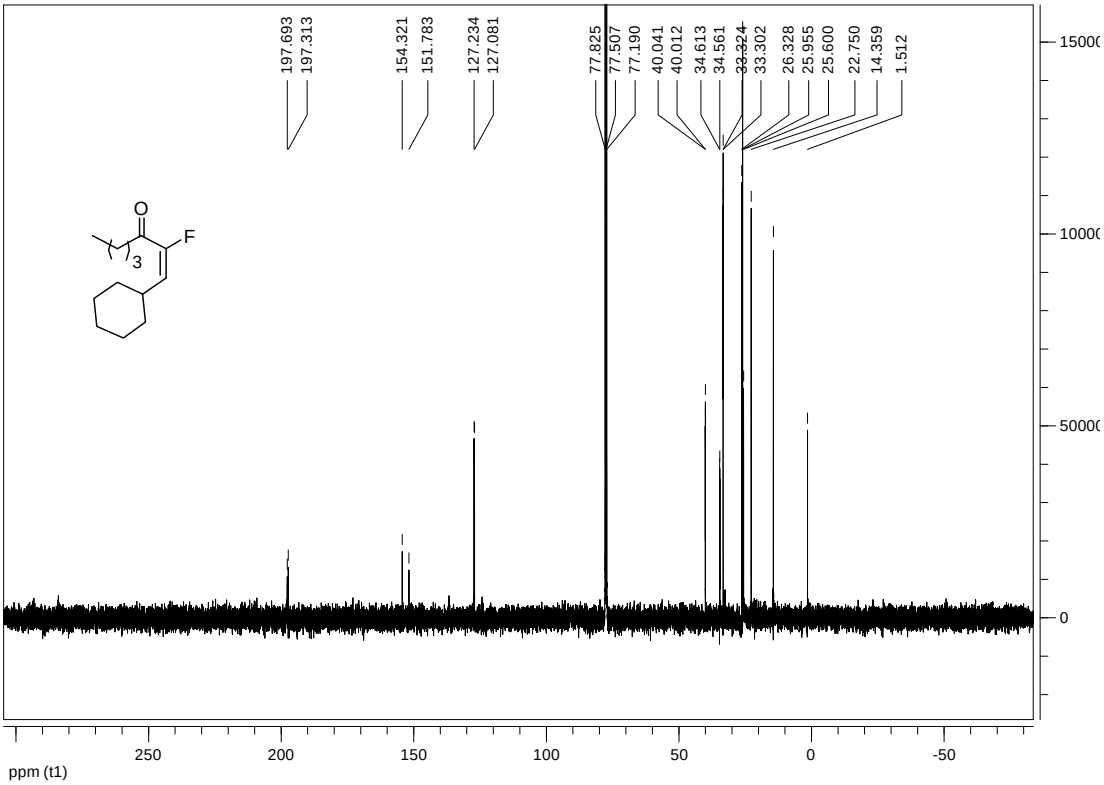
4-Fluoro-2-methylundec-3-en-5-one (6a)

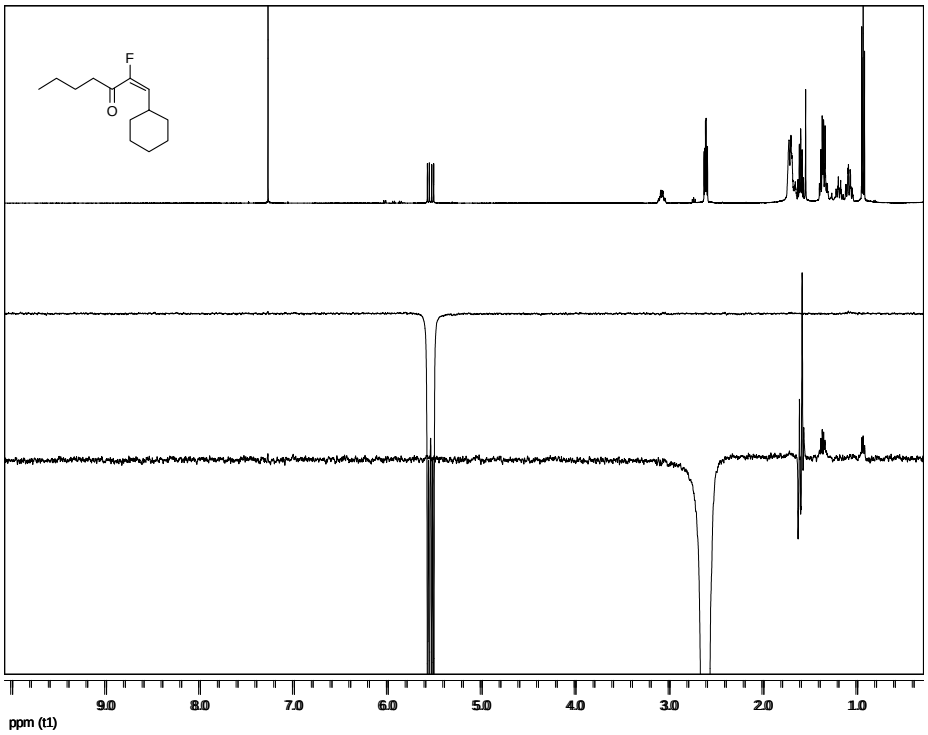




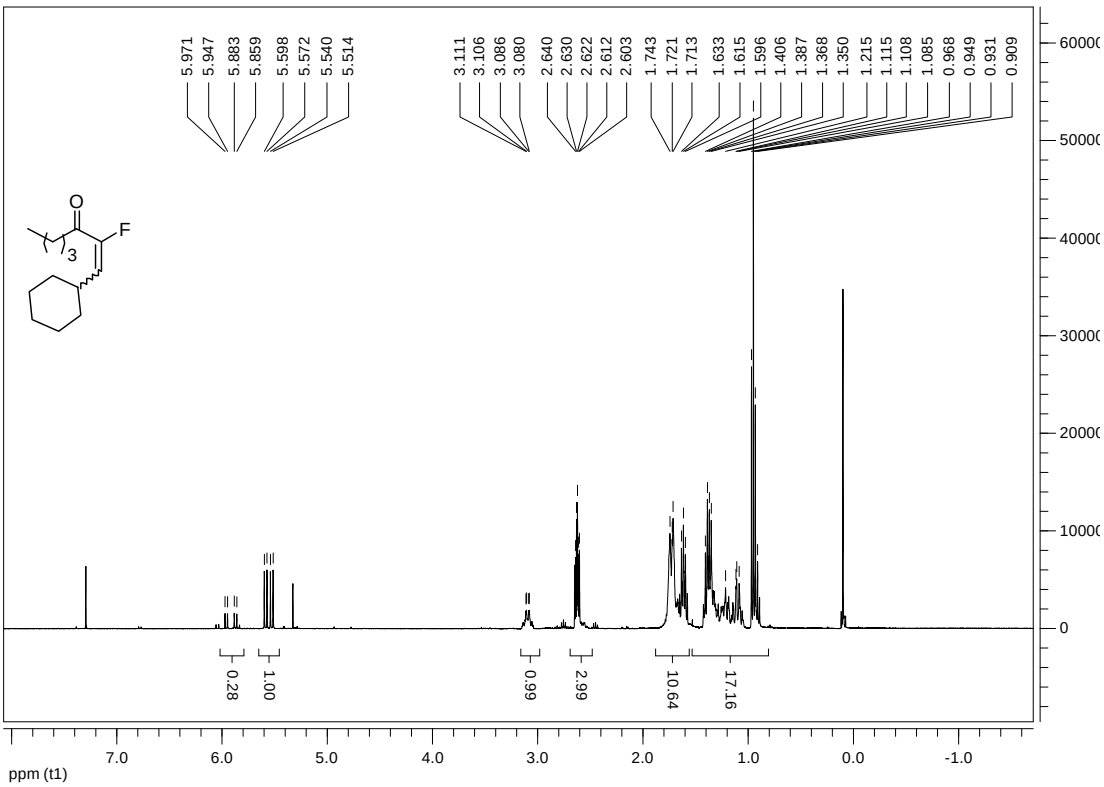
1-(*E*)-Cyclohexyl-2-fluorohept-1-en-3-one (6b)

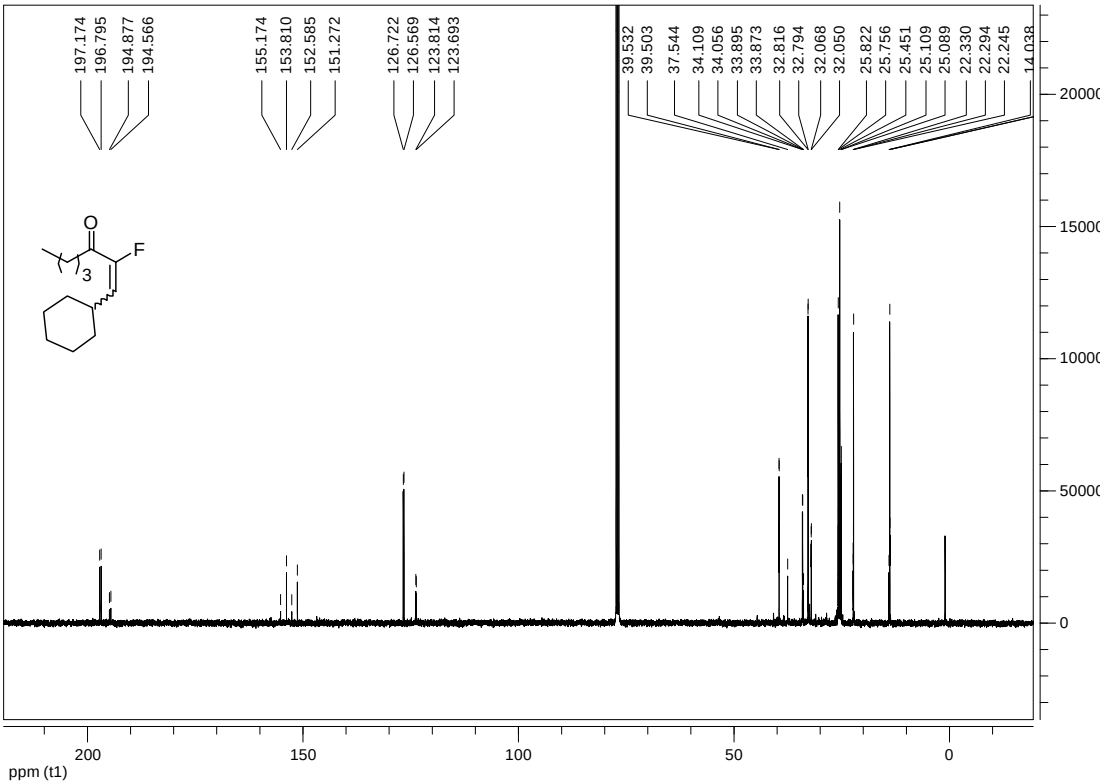

5.513
5.487
5.455
5.429
3.025
3.019
2.999
2.994
2.563
2.554
2.544
2.536
2.526
2.517
1.658
1.636
1.627
1.548
1.529
1.511
1.321
1.301
1.288
1.283
1.274
1.264
1.030
1.023
1.000
0.882
O
F
3
1.00
1.01
2.26
8.60
8.72
3.87
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
-1.0
ppm (t1)


197.693
197.313
154.321
151.783
127.234
127.081
77.825
77.507
77.190
40.041
40.012
34.613
34.561
33.324
33.302
26.328
25.955
25.600
22.750
14.359
1.512
O
F
3
250
200
150
100
50
0
-50
ppm (t1)

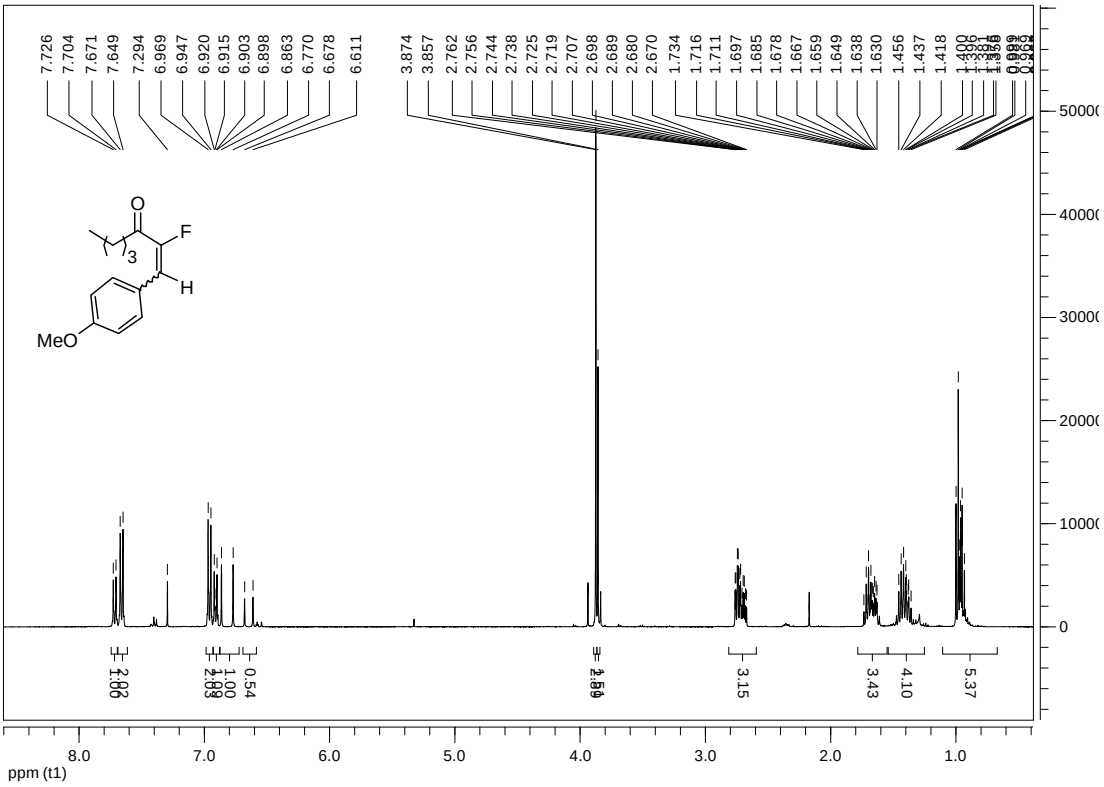

F
O
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

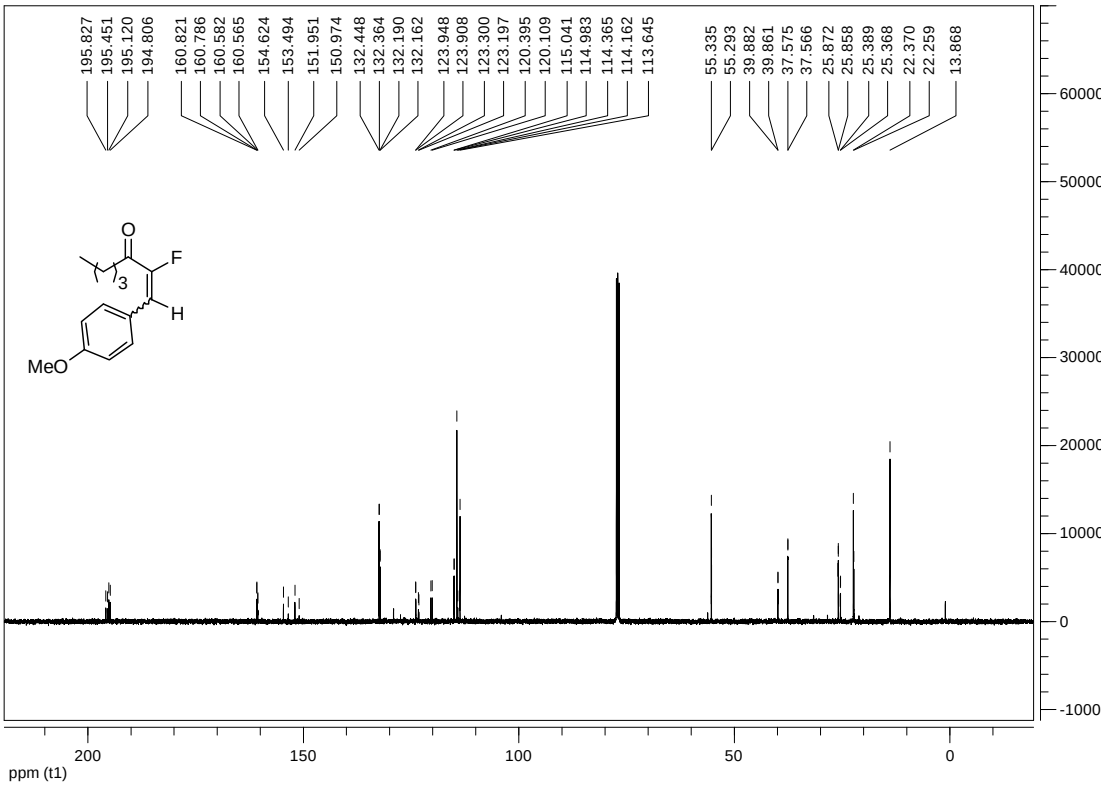
1-(*E/Z*)-Cyclohexyl-2-fluorohept-1-en-3-one (6b)





2-Fuoro-1-(4-methoxyphenyl)hept-1-en-3-one (6c)





2,2-Difluoro-1-hydroxy-1-(4-methoxyphenyl)heptan-3-one (7)