Supporting Information for

Silver-Catalyzed Carbofluorination of Unactivated Alkenes with Ketones in Aqueous Solution

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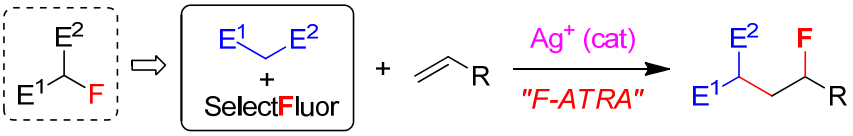

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1. Synthesis and Characterizations of Substrates.

All the ketones used were commercially available and directly used without further purification.

The following alkenes were commercially available and directly used without further purification.

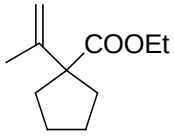
Allyl acetate (**A-1f**), 4-bromostyrene (**A-1g**), ethyl 4-methyl-4-pentenoate (**A-1p**), 4-penten-1-ol (**A-2b**), 5-bromo-1-penten (**A-2f**), 1-hexene (**A-2g**), allylacetone (**A-2h**), 4-pentenoic Acid (**A-2j**), ethyl 4-Pentenoate (**A-2k**), allylbenzene (**A-2m**), styrene (**A-2o**) and dimethyl *cis*-norbornene-*endo*-2,3-dicarboxylate (**A-5**).

The following alkenes were prepared according to literature methods. The references are given below.

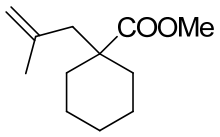
entry	reference	alkene
1	Whittaker, A. M; Lalic, G. *Org. Lett.* **2013**, *15*, 1112.	**A-1a, A-1b**
2	Zhang, C.; Li, Z.; Zhu, L.; Yu L.; Wang, Z.; Li, C. *J. Am. Chem. Soc.* **2013**, *135*, 14082.	**A-1c, A-1k, A-3e, A-10g**
3	Wang, L.; Prabhudas, B.; Clive, D. L. J. *J. Am. Chem. Soc.* **2009**, *131*, 6003.	**A-1d**
4	Shigehisa, H.; Aoki, T.; Yamaguchi, S.; Shimizu, N.; Hiroya, K. *J. Am. Chem. Soc.* **2013**, *135*, 10306.	**A-1e**
5	Cleary, P. A.; Woerpel, K. A. *Org. Lett*. **2005**, *7*, 5531.	**A-1h**
6	Blomquist, A. T.; Verdol, J. A. *J. Am. Chem. Soc*. **1955**, *77*, 78.	**A-1i**
7	Murphy, J. A.; Schoenebeck, F.; Findlay, N. J.; Thomson, D. W.; Zhou, S.; Garnier, J. *J. Am. Chem. Soc*. **2009**, *131*, 6475.	**A-1j**
8	Lee, E. E.; Batey, R. A. *J. Am. Chem. Soc.* **2005**, *127*, 14887.	**A-1l**

9	Li, Z.; Zhang, C.; Zhu, L.; Liu, C.; Li, C. *Org. Chem. Front*. **2014**, *1*, 100.	**A-2e, A-3b, A-4b, A-4c, A-10e, 22**
10	Waser, J.; Nambu, H.; Carreira, E. M. *J. Am. Chem. Soc.* **2005**, *127*, 8294.	**A-2i, A-3h, A-4a**
11	Henke, B. R.; Kouklis, A. J.; Heathcock, C. H. *J. Org. Chem*. **1992**, *57*, 7056.	**A-2l**
12	Sylvester, K. T.; Chirik, P. J. *J. Am. Chem. Soc.* **2009**, *131*, 8772.	**A-2n**
13	Larsen, C. R.; Grotjahn, D. B. *J. Am. Chem. Soc.* **2012**, *134*, 10357.	**A-3d**
14	Zheng, H.; Huo, X.; Zhao, C.; Jing, P.; Yang, J.; Fang, B.; She, X. *Org. Lett*. **2011**, *13*, 6448.	**A-3f**
15	Tsuji, J.; Sato, K.; Okumoto, H. *J. Org. Chem*. **1984**, *49*, 1341.	**A-3g**
16	Cren, S.; Schar, P.; Renaud, P.; Schenk, K. *J. Org. Chem*. **2009**, *74*, 2942.	**A-3l**
17	Barker, T. J.; Boger, D. L. *J. Am. Chem. Soc.* **2012**, *134*, 13588.	**6**
18	Forcellese, M. L.; Camerini, E.; Ruffini, B.; Mincione, E. *J. Org. Chem*. **1981**, *46*, 3326.	**8**
19	Weidner, K.; Giroult, A.; Panchaud, P.; Renaud, P. *J. Am. Chem. Soc.* **2010**, *132*, 17511.	**20**

The following two alkenes (**A-3i** and **A-3j**) are new compounds:

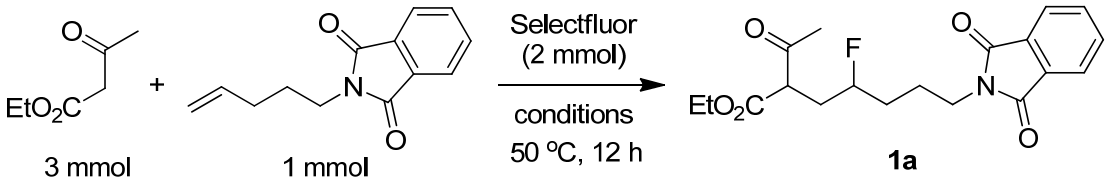


Ethyl 1-(prop-1-en-2-yl)cyclopentanecarboxylate (A-3i). This alkene was prepared by Wittig olefination of the corresponding ketone according to the conventional procedure. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.89 (s, 1H), 4.85-4.88 (m, 1H), 4.13 (q, *J* = 7.2 Hz, 2H), 2.20-2.28 (m, 2H), 1.75 (s, 3H), 1.57-1.74 (m, 6H), 1.23 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 175.8, 146.1, 110.7, 60.6, 60.3, 34.4, 23.7, 20.8, 14.1; IR (neat): ν (cm^{-1}) 3090, 2958, 2875, 1728, 1644, 1452, 1238, 1176, 1124, 1071, 1028, 894; ESI-MS: (*m/z*) 205 (M^{+}+Na); HRMS calcd for $C_{11}H_{18}NaO_2$ (M+Na): 205.1199, found 205.1196.



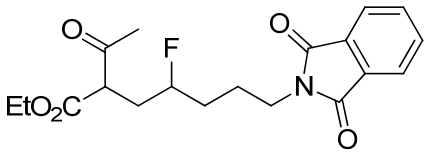
Methyl 1-(2-methylallyl)cyclohexanecarboxylate (A-3j). This compound was prepared from methyl cyclohexane-1-carboxylate by allylation with 2-methylallyl bromide according to the conventional method. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.78-4.81 (m, 1H), 4.63 (s, 1H), 3.67 (s, 3H), 2.26 (s, 2H), 2.03-2.11 (m, 2H), 1.66 (s, 3H), 1.50-1.62 (m, 3H), 1.18-1.40 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 177.1, 141.8, 114.2, 51.3, 48.5, 47.1, 34.6, 25.8, 23.7, 23.2; IR (neat): ν (cm^{-1}) 3059, 2926, 1775, 1716, 1439, 1396, 1363, 1267, 1052, 872, 738; EIMS: *m/z* (rel intensity) 196 (M^{+}, 29), 181 (4), 164 (14), 141 (59), 137 (75), 108 (16), 95 (20), 81 (100), 79 (25); HRMS calcd for $C_{12}H_{20}O_2$ (M): 196.1463, found 196.1464.

2. Table S1. Optimization of Conditions for the Synthesis of 1a.

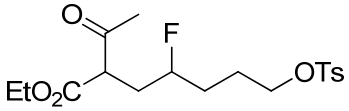


entry	conditions	yield (%)
1	$AgNO_3$ (0.2 mmol), H_2O (15 mL), CH_3CN (5 mL)	0
2	$AgNO_3$ (0.2 mmol), H_2O (15 mL), CH_2Cl_2 (5 mL)	50
3	AgOAc (0.2 mmol), H_2O (15 mL), CH_2Cl_2 (5 mL)	41
4	$AgNO_3$ (0.2 mmol), H_2O (12.5 mL), CH_2Cl_2 (2.5 mL)	50
5	$AgNO_3$ (0.2 mmol), H_2O (12.5 mL), CH_2Cl_2 (2.5 mL), HOAc (10 mmol)	72
6	$AgNO_3$ (0.2 mmol), H_2O (12.5 mL), CH_2Cl_2 (2.5 mL), TsOH (3 mmol)	31
7	$AgNO_3$ (0.2 mmol), H_2O (5 mL), CH_2Cl_2 (2.5 mL), HOAc (2.5 mL)	74
8	**$AgNO_3$ (0.2 mmol), H_2O (7.5 mL), CH_2Cl_2 (2.5 mL), HOAc (2.5 mL)**	**93**
9	H_2O (7.5 mL), CH_2Cl_2 (2.5 mL), HOAc (2.5 mL)	0

4. Synthesis and Characterizations of Products.

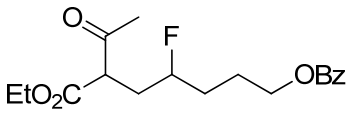


Ethyl 2-acetyl-7-(1,3-dioxoisoindolin-2-yl)-4-fluoroheptanoate (1a). *N*-(Pent-4-en-1-yl)phthalimide (**A-1a**, 215 mg, 1.0 mmol), $AgNO_3$ (34 mg, 0.20 mmol) and Selectfluor (706 mg, 2.0 mmol) were placed in a Schlenk tube under nitrogen atmosphere. Dichloromethane (2.5 mL), water (7.5 mL), acetic acid (2.5 mL) and ethyl acetoacetate (0.38 mL, 3.0 mmol) were added successively at room temperature. The reaction mixture was gently refluxed (at ~ 50 ^oC) with stirring for 12 h. The resulting mixture was cooled down to room temperature and extracted with CH_2Cl_2 (3 × 20 mL). The organic phases were combined and dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane/ethyl acetate (5:1, v:v) as the eluent to give the pure product **1a** as a colorless oil. Yield: 338 mg (93%). Ketone **1a** is in equilibrium with its enol form in $CDCl_3$ (in ~ 86:14 ratio at 20 ^oC), as indicated by ^1H NMR. ^1H NMR (400 MHz, $CDCl_3$) δ 7.82-7.84 (m, 2H), 7.71-7.73 (m, 2H), 4.40-4.61 (m, 1H), 4.17-4.27 (m, 2H), 3.66-3.75 (m, 3H), 2.00-2.52 (m, 5H), 1.59-1.89 (m, 4H), 1.24-1.30 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.3/202.2, 169.2/169.0, 168.2, 133.9, 131.9, 123.1, 91.6/91.5 (2d, J = 167.5 Hz), 61.5, 55.5/55.2 (2d, J = 2.3 Hz), 37.3, 33.3/33.1 (2d, J = 19.3 Hz), 32.5 (d, J = 20.5 Hz)/32.4 (2d, J = 20.0 Hz), 29.5/29.0, 24.2 (d, J = 1.5 Hz)/24.1 (d, J = 1.2 Hz), 13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -182.9/-183.5 (2m, 1F); IR (film): υ (cm^{-1}) 2938, 1772, 1713, 1397, 1362, 1048, 721; ESI-MS: (*m/z*) 386.1 (M^++Na); HRMS calcd for $C_{19}H_{22}FNNaO_5$ (M+Na): 386.1374, found: 386.1361.

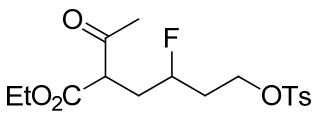


Ethyl 2-acetyl-4-fluoro-7-(tosyloxy)heptanoate (1b). Ketone **1b** is in equilibrium

with its enol form in $CDCl_3$ (in ~ 86:14 ratio at 20 ^oC), as indicated by ^1H NMR. Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 4.32-4.52 (m, 1H), 4.17-4.24 (m, 2H), 3.99-4.09 (m, 2H), 3.68-3.72 (m, 1H), 2.45 (s, 3H), 2.27/2.26 (2s, 3H), 1.95-2.20 (m, 2H), 1.57-1.84 (m, 4H), 1.25-1.30 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.3/202.2, 169.2/169.0, 144.8, 132.9, 129.9, 129.8, 127.8, 91.5 (d, *J* = 169.0 Hz)/91.4 (d, *J* = 168.2 Hz), 69.8, 61.6, 55.5/55.2, 33.2 (d, *J* = 20.4 Hz)/33.1 (d, *J* = 20.1 Hz), 31.3 (d, *J* = 21.0 Hz)/31.1 (d, *J* = 20.8 Hz), 29.6/29.2, 24.6 (d, *J* = 3.1 Hz), 21.6, 14.0/13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -183.2/-183.8 (2m, 1F); IR (neat): ν (cm^{-1}) 2927, 1742, 1721, 1598, 1444, 1359, 1176, 961, 815, 663; ESI-MS: (*m/z*) 411.1 (M^++Na); HRMS calcd for $C_{18}H_{25}FNaO_6S$ (M+Na): 411.1248, found 411.1254.

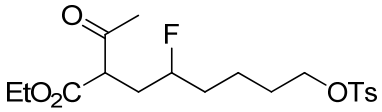


6-(Ethoxycarbonyl)-4-fluoro-7-oxooctyl benzoate (1c). Ketone **1c** is in equilibrium with its enol form in $CDCl_3$ (in ~ 86:14 ratio at 20 ^oC), as indicated by ^1H NMR. Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 8.03 (d, *J* = 8.0 Hz, 2H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 2H), 4.43-4.64 (m, 1H), 4.29-4.36 (m, 2H), 4.16-4.24 (m, 2H), 3.74-3.78 (m, 1H), 1.68-2.55 (m, 9H), 1.25-1.28 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.3, 169.2/169.1, 166.4, 132.9, 130.2, 129.5, 128.3, 91.8 (d, *J* = 168.5 Hz)/91.7 (d, *J* = 167.7 Hz), 64.4/64.3, 61.6, 55.6/55.3, 33.4 (d, *J* = 20.2 Hz)/33.2 (d, *J* = 19.8 Hz), 32.0 (d, *J* = 20.8 Hz)/31.9 (d, *J* = 20.2 Hz), 29.7/29.2, 24.4 (d, *J* = 3.8 Hz), 14.0/13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -182.9/-183.4 (2m, 1F); IR (neat): ν (cm^{-1}) 2960, 1742, 1721, 1452, 1276, 713; ESI-MS: (*m/z*) 361.1 (M^++Na); HRMS calcd for $C_{18}H_{23}FNaO_5$ (M+Na): 361.1422, found 361.1437.

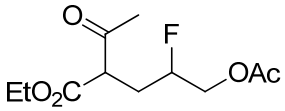


Ethyl 2-acetyl-4-fluoro-6-(tosyloxy)hexanoate (1d). Ketone **1d** is in equilibrium with its enol form in $CDCl_3$ (in ~ 94:6 ratio at 20 ^oC), as indicated by ^1H NMR.

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.0 Hz, 2H), 4.43-4.71 (m, 1H), 4.12-4.26 (m, 4H), 3.67-3.71 (m, 1H), 2.45 (s, 3H), 1.88-2.30 (m, 7H), 1.22-1.30 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.1/201.9, 169.1/168.8, 145.0, 132.7, 129.9, 127.8, 88.34/88.29 (2d, *J* = 168.6 Hz), 66.0 (d, *J* = 5.3 Hz), 61.7, 55.4 (d, *J* = 1.5 Hz)/55.2 (d, *J* = 3.1 Hz), 34.7/34.6 (2d, *J* = 20.5 Hz), 33.2/33.0 (2d, *J* = 19.0 Hz), 29.5/29.3, 21.6, 14.0/13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -186.0/-186.4 (2m, 1F); IR (neat): ν (cm^{-1}) 2981, 2933, 1740, 1716, 1598, 1362, 1249, 1190, 1178, 1097, 969, 816, 764, 665, 555; ESI-MS: (*m/z*) 397.2 (M^++Na); HRMS calcd for $C_{17}H_{24}FO_6S$ (M+H): 375.1272, found 375.1268.

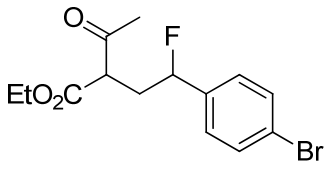


Ethyl 2-acetyl-4-fluoro-8-(tosyloxy)octanoate (1e). Ketone **1e** is in equilibrium with its enol form in $CDCl_3$ (in ~ 95:5 ratio at 20 ^{o}C), as indicated by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 4.28-4.55 (m, 1H), 4.17-4.26 (m, 2H), 4.02 (t, *J* = 6.4 Hz, 2H), 3.72 (dd, *J* = 7.6, 5.2 Hz, 1H), 2.45 (s, 3H), 2.25-2.31 (m, 3H), 1.94-2.25 (m, 2H), 1.33-1.73 (m, 6H), 1.23-1.32 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.4/202.3, 169.3/169.0, 144.8, 132.9, 129.8, 127.8, 91.9/91.8 (2d, *J* = 167.8 Hz), 70.1, 61.6, 55.6 (d, *J* = 2.2 Hz)/55.3 (d, *J* = 3.0 Hz), 34.4/34.3 (2d, *J* = 20.5 Hz), 33.3/33.1 (2d, *J* = 20.5 Hz), 29.6/29.2, 28.4, 21.5, 21.0/20.9, 14.0/13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -182.5/-183.1 (2m, 1F); IR (neat): ν (cm^{-1}) 2941, 1741, 1717, 1598, 1457, 1360, 1244, 1189, 1177, 1097, 1020, 932, 816, 664, 555; ESI-MS: (*m/z*) 425.1 (M^++Na); HRMS calcd for $C_{19}H_{27}FNaO_6S$ (M+Na): 425.1405, found 425.1386.

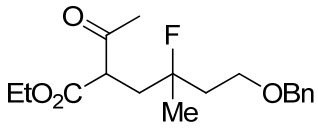


Ethyl 5-acetoxy-2-acetyl-4-fluoropentanoate (1f). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.53-4.72 (m, 1H), 4.03-4.21 (m, 4H), 2.68 (t, *J* = 7.2 Hz, 1H), 2.23 (s, 3H), 1.98-2.20 (m, 5H), 1.20-1.24 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.8,

170.5, 168.9/168.7, 89.2 (d, *J* = 172.7 Hz)/89.1 (d, *J* = 171.4 Hz), 65.24 (d, *J* = 22.2 Hz)/65.20 (d, *J* = 21.2 Hz), 61.8, 55.0 (d, *J* = 2.5 Hz)/54.7 (d, *J* = 3.0 Hz), 29.6 (*J* = 3.3 Hz)/29.4 (d, *J* = 3.0 Hz), 29.2, 20.6, 14.0/13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -190.1 (m, 1F); IR (neat): ν (cm^{-1}) 2984, 1747, 1647, 1448, 1369, 1327, 1152, 1096, 1047, 861; ESI-MS: (*m/z*) 271.0 (M^++Na); HRMS calcd for $C_{11}H_{17}FNaO_5$ (M+Na): 271.0952, found 271.0955.

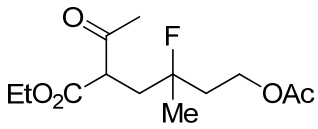


Ethyl 2-acetyl-4-(4-bromophenyl)-4-fluorobutanoate (1g). Ketone **1g** is in equilibrium with its enol form in $CDCl_3$ (in ~ 91:9 ratio at 20 °C), as indicated by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 7.6 Hz, 2H), 5.34-5.55 (m, 1H), 4.15-4.25 (m, 2H), 3.72-3.76 (m, 1H), 2.27-2.55 (m, 5H), 1.25-1.35 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.97/201.92, 169.0/168.9, 138.29/138.26 (2d, *J* = 19.8 Hz), 131.73/131.71, 127.02/126.95, 122.53 (d, *J* = 2.3 Hz)/122.50 (d, *J* = 3.0 Hz), 91.7 (d, *J* = 171.6 Hz)/91.6 (d, *J* = 171.3 Hz), 61.8, 55.5/55.2 (2d, *J* = 2.3 Hz), 35.3 (d, *J* = 23.6 Hz)/35.1 (d, *J* = 22.7 Hz), 29.7/29.3, 14.04/13.99; ^{19}F NMR (282 MHz, $CDCl_3$): δ -178.7/-179.2 (2m, 1F); IR (neat): ν (cm^{-1}) 2982, 2939, 1740, 1717, 1645, 1595, 1490, 1360, 1248, 1151, 1072, 1042, 1012, 824, 533; ESI-MS: (*m/z*) 353.0 (M^++Na); HRMS calcd for $C_{14}H_{16}BrFNaO_3$ (M+Na): 353.0159, found 353.0167.

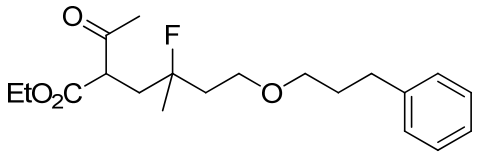


Ethyl 2-acetyl-6-(benzyloxy)-4-fluoro-4-methylhexanoate (1h). Ketone **1h** is in equilibrium with its enol form in $CDCl_3$ (in ~ 94:6 ratio at 20 °C), as indicated by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.36 (m, 5H), 4.48 (s, 2H), 4.15-4.22 (m, 2H), 3.72 (q, *J* = 6.8 Hz, 1H), 3.55-3.60 (m, 2H), 2.15-2.44 (m, 5H), 1.93-2.07 (m, 2H), 1.22-1.40 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.43/202.36,

169.7/169.6, 138.1, 128.4, 127.7/127.6, 127.65/127.62, 95.63/95.59 (2d, *J* = 167.8 Hz), 73.14/73.13, 65.6 (d, *J* = 7.6 Hz), 61.6, 55.0 (d, *J* = 3.0 Hz)/54.9 (d, *J* = 2.3 Hz), 39.7/39.4 (2d, *J* = 22.8 Hz), 37.6 (d, *J* = 21.3 Hz), 28.9/28.8 (2d, *J* = 1.6 Hz), 22.7/22.4 (2d, *J* = 24.3 Hz), 14.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ -143.7 (m, 1F); IR (neat): ν (cm^{-1}) 3064, 3030, 2982, 2938, 2871, 1744, 1717, 1644, 1496, 1454, 1367, 1247, 1145, 1115, 1027, 906, 864, 739, 699; ESI-MS: (*m/z*) 347.2 (M^++Na); HRMS calcd for $C_{18}H_{25}FNaO_4$ (M+Na): 347.1629, found 347.1634.

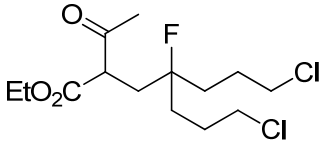


Ethyl 6-acetoxy-2-acetyl-4-fluoro-4-methylhexanoate (1i). Ketone **1i** is in equilibrium with its enol form in $CDCl_3$ (in ~ 91:9 ratio at 20 °C), as indicated by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.18-4.24 (m, 4H), 3.71 (q, *J* = 6.8 Hz, 1H), 2.14-2.45 (m, 5H), 1.87-2.05 (m, 5H), 1.23-1.40 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.1/202.0, 170.8, 169.6/169.5, 95.0 (d, *J* = 170.1 Hz)/94.9 (d, *J* = 169.3 Hz), 61.7, 59.8/59.7 (2d, *J* = 3.0 Hz), 54.8/54.7 (2d, *J* = 3.0 Hz), 38.5/38.1 (2d, *J* = 22.7 Hz), 37.53/37.51 (2d, *J* = 21.2 Hz), 28.9, 24.3/23.9 (2d, *J* = 24.3 Hz), 20.9, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -146.0 (m, 1F); IR (neat): ν (cm^{-1}) 2984, 2940, 1743, 1638, 1387, 1368, 1241, 1035, 861, 607; ESI-MS: (*m/z*) 299.1 (M^++Na); HRMS calcd for $C_{13}H_{21}FNaO_5$ (M+Na): 299.1265, found 299.1267.

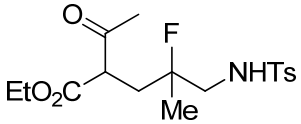


Ethyl 2-acetyl-4-fluoro-4-methyl-6-(3-phenylpropoxy)hexanoate (1j). Ketone **1j** is in equilibrium with its enol form in $CDCl_3$ (in ~ 81:19 ratio at 20 °C), as indicated by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 (t, *J* = 7.6 Hz, 2H), 7.07-7.10 (m, 3H), 4.07-4.14 (m, 2H), 3.63-3.67 (m, 1H), 3.40-3.49 (m, 2H), 3.30-3.36 (m, 2H), 2.04-2.62 (m, 7H), 1.75-1.88 (m, 4H), 1.15-1.30 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.4/202.3, 169.7, 141.9, 128.4, 128.3, 125.7, 95.7 (d, *J*

= 170.0 Hz), 70.2/70.1, 66.1/66.0, 61.5, 55.0 (d, *J* = 4.4 Hz)/54.9 (d, *J* = 4.0 Hz), 39.7/39.3 (2d, *J* = 22.9 Hz), 37.7/37.6 (2d, *J* = 21.1 Hz), 32.3, 31.3/31.2, 28.9/28.8, 24.7/24.3 (2d, *J* = 24.8 Hz), 13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -143.6 (m, 1F); IR (neat): ν (cm^{-1}) 3027, 2981, 2939, 2866, 1744, 1720, 1640, 1605, 1454, 1383, 1247, 1114, 747, 700; ESI-MS: (*m/z*) 375.3 (M^++Na); HRMS calcd for $C_{20}H_{29}FNaO_4$ (M+Na): 375.1942, found 375.1951.

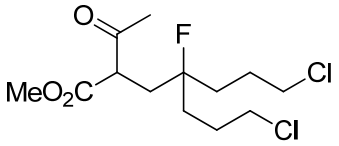


Ethyl 2-acetyl-7-chloro-4-(3-chloropropyl)-4-fluoroheptanoate (1k). Ketone **1k** is in equilibrium with its enol form in $CDCl_3$ (in ~ 86:14 ratio at 20 ^oC), as indicated by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.13-4.19 (m, 2H), 3.64 (t, *J* = 6.4 Hz, 1H), 3.45-3.55 (m, 4H), 2.16-2.32 (m, 5H), 1.65-1.84 (m, 8H), 1.24 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.0, 169.5, 97.2 (d, *J* = 172.4 Hz), 61.7, 54.4 (d, *J* = 3.1 Hz), 44.8, 34.9 (d, *J* = 21.3 Hz), 34.3 (d, *J* = 23.9 Hz), 34.0 (d, *J* = 24.0 Hz), 29.1, 26.5 (d, *J* = 3.1 Hz), 26.4 (d, *J* = 3.2 Hz), 13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -151.6 (m, 1F); IR (neat): ν (cm^{-1}) 2963, 1743, 1721, 1640, 1632, 1462, 1446, 1367, 1266, 1146, 1019, 928, 863, 737, 652; ESI-MS: (*m/z*) 327.0 (M-H); HRMS calcd for $C_{14}H_{22}Cl_2FO_3$ (M-H): 327.0936, found 327.0922.

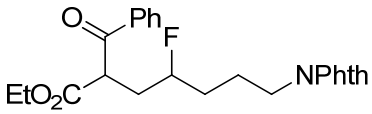


Ethyl 2-acetyl-4-fluoro-4-methyl-5-(4-methylphenylsulfonamido)pentanoate (1l). Ketone **1l** is in equilibrium with its enol form in $CDCl_3$ (in ~ 96:4 ratio at 20 ^oC), as indicated by ^{1}H NMR. Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.22-5.28 (m, 1H), 4.10-4.21 (m, 2H), 3.65-3.72 (m, 1H), 2.92-3.10 (m, 2H), 2.42 (s, 3H), 2.04-2.41 (m, 5H), 1.20-1.38 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.3/201.9, 169.5/169.3, 143.6, 136.7, 129.8, 127.0, 95.2 (d, *J* = 171.5 Hz), 61.8, 54.5/54.3 (2d, *J* = 3.1 Hz), 50.4/50.1 (2d, *J* = 25.1

Hz), 34.7/34.6 (2d, J = 20.5 Hz), 29.0/28.9, 22.4/22.2 (2d, J = 25.9 Hz), 21.5, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -151.9/-152.2 (2m, 1F); IR (neat): ν (cm^{-1}) 3293, 2984, 2938, 1740, 1717, 1598, 1449, 1362, 1336, 1162, 1092, 816, 664, 552; ESI-MS: (*m/z*) 396.1 (M^++Na); HRMS calcd for $C_{17}H_{24}FNNaO_5S$ (M+Na): 396.1251, found 396.1247.

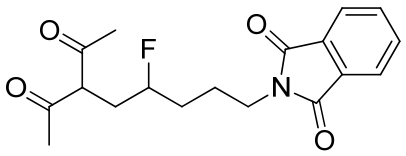


Methyl 2-acetyl-7-chloro-4-(3-chloropropyl)-4-fluoroheptanoate (1m). Ketone **1m** is in equilibrium with its enol form in $CDCl_3$ (in ~ 96:4 ratio at 20 ^oC), as indicated by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.76 (s, 3H), 3.72 (t, J = 6.4 Hz, 1H), 3.56 (t, J = 6.0 Hz, 4H), 2.16-2.45 (m, 5H), 1.68-1.88 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.9, 170.0, 97.2 (d, J = 172.3 Hz), 54.1 (d, J = 3.1 Hz), 52.8, 44.9, 35.1 (d, J = 21.3 Hz), 34.3 (d, J = 22.8 Hz), 34.0 (d, J = 23.5 Hz), 29.2, 26.5 (d, J = 4.6 Hz), 26.4 (d, J = 3.8 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -151.7 (m, 1F); IR (neat): ν (cm^{-1}) 2958, 2878, 1747, 1717, 1645, 1436, 1360, 1250, 1204, 1148, 1086, 915, 652; ESI-MS: (*m/z*) 337.1 (M^++Na); HRMS calcd for $C_{13}H_{21}Cl_2FNaO_3$ (M+Na): 337.0744, found 337.0743.

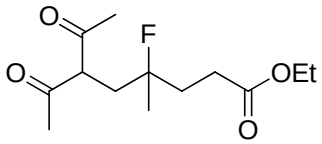


Ethyl 2-benzoyl-7-(1,3-dioxoisoindolin-2-yl)-4-fluoroheptanoate (1n). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (t, J = 7.6 Hz, 2H), 7.73-7.80 (m, 2H), 7.60-7.67 (m, 2H), 7.51 (t, J = 7.2 Hz, 1H), 7.40 (t, J = 7.6 Hz, 2H), 4.30-4.68 (m, 2H), 4.00-4.15 (m, 2H), 3.58-3.72 (m, 2H), 1.95-2.43 (m, 2H), 1.46-1.87 (m, 4H), 1.04-1.14 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.9/194.6, 169.5/169.4, 168.3, 136.2/135.5, 133.9, 133.7/133.6, 132.0, 128.80/128.75, 128.72, 123.2, 91.9 (d, J = 168.5 Hz)/91.6 (d, J = 168.5 Hz), 61.6, 50.0 (d, J = 2.3 Hz)/49.8 (d, J = 3.0 Hz), 37.5, 34.5 (d, J = 20.5 Hz)/34.3 (d, J = 19.7 Hz), 32.7 (d, J = 19.7 Hz), 24.3 (d, J = 3.7 Hz),

13.9; ^{19}F NMR (376 MHz, $CDCl_3$): δ -183.2 (m, 1F); IR (neat): ν (cm^{-1}) 2936, 1771.6, 1736, 1708, 1686, 1596, 1396, 1364, 1045, 720, 690; ESI-MS: (*m/z*) 448.1 (M^++Na); HRMS calcd for $C_{24}H_{24}FNNaO_5$ (M+Na): 448.1531, found 448.1578.

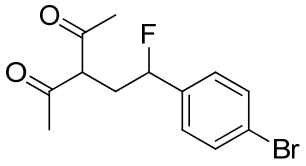


2-(6-Acetyl-4-fluoro-7-oxooctyl)isoindoline-1,3-dione (1o). Ketone **1o** is in equilibrium with its enol form in $CDCl_3$ (in ~ 50:50 ratio at 20 ^oC) as indicated by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 16.90 (s, 0.5H), 7.74-7.79 (m, 2H), 7.65-7.69 (m, 2H), 4.30-4.55 (m, 1H), 3.86 (dd, *J* = 8.0, 4.2 Hz, 0.5H), 3.59-3.73 (m, 2H), 2.33-2.58 (m, 1H), 2.15 (s, 3H), 2.07 (s, 3H), 1.49-2.05 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) (ketone + enol): δ 203.5, 203.2, 192.0, 168.4, 168.3, 134.0, 133.9, 131.9, 123.2, 106.0 (d, *J* = 2.7 Hz), 93.6 (d, *J* = 170.8 Hz), 91.7 (d, *J* = 168.4 Hz), 64.3 (d, *J* = 1.6 Hz), 37.32, 37.29, 33.3 (d, *J* = 20.9 Hz), 33.2 (d, *J* = 20.6 Hz), 32.4 (d, *J* = 20.1 Hz), 32.3 (d, *J* = 21.2 Hz), 29.6, 29.0, 24.3 (d, *J* = 3.8 Hz), 24.2 (d, *J* = 3.6 Hz), 23.34, 24.33; ^{19}F NMR (282 MHz, $CDCl_3$): δ -181.6/-182.3 (2m, 1F); IR (neat): ν (cm^{-1}) 3061, 2940, 2869, 1772, 1713, 1614, 1397, 1049, 1019, 720; ESI-MS: (*m/z*) 356.2 (M^++Na); HRMS calcd for $C_{18}H_{20}FNNaO_4$ (M+Na): 356.1269, found 356.1280.

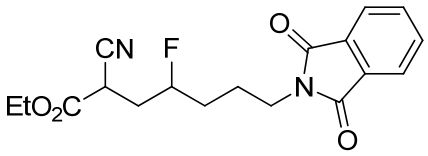


Ethyl 6-acetyl-4-fluoro-4-methyl-7-oxooctanoate (1p). Ketone **1p** is in equilibrium with its enol form in $CDCl_3$ (in ~ 45:55 ratio at 20 ^oC), as indicated by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 17.15 (s, 0.55H), 4.06-4.13 (m, 2H), 3.90 (t, *J* = 6.4 Hz, 0.45H), 1.79-2.71 (m, 12H), 1.19-1.24 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) (ketone + enol): δ 203.3, 203.1, 192.8, 173.1, 172.9, 105.3, 97.1 (d, *J* = 172.1 Hz), 95.4 (d, *J* = 170.6 Hz), 63.7, 60.6, 37.4 (d, *J* = 22.2 Hz), 37.3 (d, *J* = 21.2

Hz), 34.8 (d, *J* = 22.9 Hz), 34.6 (d, *J* = 23.7 Hz), 29.6, 29.0, 28.6 (d, *J* = 4.6 Hz), 28.5 (d, *J* = 4.2 Hz), 23.7 (d, *J* = 24.7 Hz), 23.0 (d, *J* = 25.5 Hz), 23.8, 23.7, 14.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ -148.3/-148.8 (2m, 1F); IR (neat): ν (cm^{-1}) 2984, 2939, 1732, 1702, 1597, 1360, 1188, 1103, 1024; ESI-MS: (*m/z*) 283.0 (M^++Na); HRMS calcd for $C_{13}H_{22}FO_4$ (M+H): 261.1497, found 261.1494.

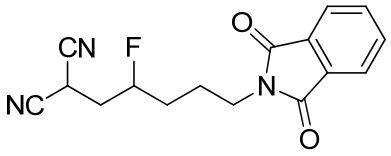


3-(2-(4-Bromophenyl)-2-fluoroethyl)pentane-2,4-dione (1q). Ketone **1q** is in equilibrium with its enol form in $CDCl_3$ (in ~ 45:55 ratio at 20 °C) as indicated by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 17.10 (s, 0.55H), 7.51-7.53 (m, 2H), 7.19 (t, *J* = 8.4 Hz, 2H), 5.30-5.49 (m, 1H), 3.95 (dd, *J* = 8.0, 5.6 Hz, 0.45H), 2.67-2.95 (m, 1.1H), 2.27-2.51 (m, 0.9H), 2.25/2.21 (2s, 2.7H), 2.02 (s, 3.3H); ^{13}C NMR (100 MHz, $CDCl_3$) (ketone + enol): δ 203.05, 202.96, 192.4, 138.4 (d, *J* = 26.6 Hz), 138.2 (d, *J* = 25.8 Hz), 131.79, 131.78, 127.0 (d, *J* = 6.8 Hz), 126.9 (d, *J* = 6.8 Hz), 122.6 (d, *J* = 2.3 Hz), 122.5 (d, *J* = 2.3 Hz), 104.8 (d, *J* = 4.6 Hz), 93.7 (d, *J* = 175.3 Hz), 91.8 (d, *J* = 171.6 Hz), 64.17, 64.16, 35.6 (d, *J* = 25.0 Hz), 35.4 (d, *J* = 22.8 Hz), 29.7, 29.1, 23.22, 23.20; ^{19}F NMR (282 MHz, $CDCl_3$): δ -176.4/-178.5 (2m, 1F); IR (neat): ν (cm^{-1}) 3005, 2937, 1730, 1703, 1595, 1489, 1408, 1360, 1153, 1072, 1011, 826, 741, 525; ESI-MS: (*m/z*) 323 (M^++Na); HRMS calcd for $C_{13}H_{14}BrFNaO_2$ (M+Na): 323.0053, found 323.0055.

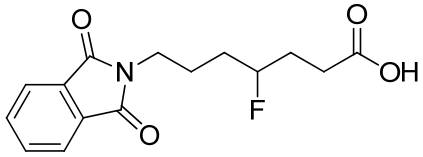


Ethyl 2-cyano-7-(1,3-dioxoisoindolin-2-yl)-4-fluoroheptanoate (1r). Compound **1r** was isolated as the 1:1 mixture of two stereoisomers. White solid, 80-82 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.82 (m, 2H), 7.68-7.70 (m, 2H), 4.60-4.80 (m, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 3.65-3.73 (m, 3H), 1.55-2.31 (m, 6H), 1.29 (t, *J* = 7.2 Hz, 3H);

^{13}C NMR (100 MHz, $CDCl_3$): δ 168.3, 165.5, 134.0, 132.0, 123.3, 116.1/115.8, 90.4/90.1 (2d, *J* = 171.1 Hz), 63.1, 37.3 (d, *J* = 5.9 Hz), 35.1/35.0 (2d, *J* = 20.8 Hz), 34.1 (d, *J* = 3.6 Hz)/33.4 (d, *J* = 3.9 Hz), 32.1 (d, *J* = 20.5 Hz)/32.1 (d, *J* = 20.3 Hz), 24.2, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -184.6 (m, 1F); IR (KBr): ν (cm^{-1}) 2932, 1773, 1739, 1719, 1397, 1368, 1276, 1248, 1049, 1024, 722; ESI-MS: (*m/z*) 369.1 (M^++Na); HRMS calcd for $C_{18}H_{19}FN_2NaO_4$ (M+Na): 369.1221, found 369.1232.

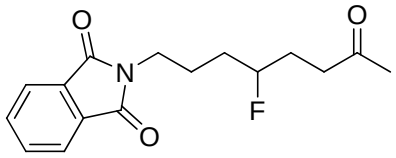


2-(5-(1,3-Dioxoisoindolin-2-yl)-2-fluoropentyl)malononitrile (1s). White solid. Mp: 116-118 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84-7.88 (m, 2H), 7.71-7.76 (m, 2H), 4.70-4.88 (m, 1H), 3.95-3.98 (m, 1H), 3.76 (t, *J* = 6.4 Hz, 2H), 2,19-2,35 (m, 2H), 1.65-1.97 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.4, 134.1, 131.9, 123.3, 112.3, 112.0, 89.4 (d, *J* = 171.3 Hz), 37.1, 36.0 (d, *J* = 20.2 Hz), 31.7 (d, *J* = 20.8 Hz), 24.0 (d, *J* = 4.3 Hz), 19.3 (d, *J* = 5.8 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -185.7 (m, 1F); IR (KBr): ν (cm^{-1}) 2924, 2854, 1771, 1710, 1439, 1398, 1363, 1049, 890, 864, 720, 530; ESI-MS: (*m/z*) 300.1 (M^++H); HRMS calcd for $C_{16}H_{15}FN_3O_2$ (M+Na): 300.1143, found 300.1138.

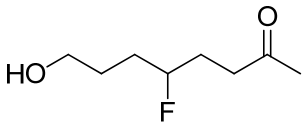


7-(1,3-Dioxoisoindolin-2-yl)-4-fluoroheptanoic acid. This compound was isolated in approximately 10% yield in the $AgNO_3$-catalyzed reaction of diethyl malonate with Selectfluor and *N*-(Pent-4-en-1-yl)phthalimide (**A-1a**) in CH_2Cl_2/H_2O/HOAc solution according to the typical procedure outlined in the synthesis of **1a**. White solid, 86-88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83-7.85 (m, 2H), 7.70-7.72 (m, 2H), 4.48-4.64 (m, 1H), 3.69-376 (m, 2H), 2.46-2.57 (m, 2H), 1.55-1.96 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.6, 168.4, 133.9, 132.0, 123.2, 92.4 (d, *J* = 169.0 Hz), 37.5, 32.2

(d, J = 20.6 Hz), 29.9 (d, J = 21.0 Hz), 29.5 (d, J = 4.3 Hz), 24.3 (d, J = 3.9 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -183.8 (m, 1F); IR (KBr): ν (cm^{-1}) 2942, 1772, 1719, 1713, 1707, 1440, 1400, 1367, 1051, 721; ESI-MS: (*m/z*) 316.1 (M^++Na); HRMS calcd for $C_{15}H_{16}FNNaO_4$ (M+Na): 316.0956, found 316.0966.

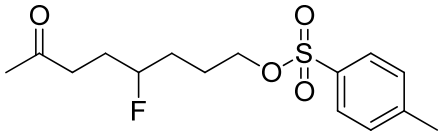


2-(4-Fluoro-7-oxooctyl)isoindoline-1,3-dione (2a). *N*-(Pent-4-en-1-yl)phthalimide (**A-1a**, 431 mg, 2.0 mmol), AgOAc (34 mg, 0.20 mmol), Selectfluor (1.41 g, 4.0 mmol) and sodium acetate (489 mg, 6.0 mmol) were placed in a Schlenk tube under nitrogen atmosphere. Water (20 mL) and acetone (20 mL) were then added successively at room temperature. The reaction mixture was then stirred at 50 ^{o}C for 12 h. The resulting mixture was cooled down to room temperature and extracted with CH_2Cl_2 (3 × 50 mL). The organic phases were combined and dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane/ethyl acetate (10:1, v:v) as the eluent to give the pure product **2a** as a white solid. Mp: 56–58 ^{o}C. Yield: 512 mg (88%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73-7.77 (m, 2H), 7.62-7.66 (m, 2H), 4.35-4.52 (m, 1H), 3.61-3.65 (m, 2H), 2.46-2.57 (m, 2H), 2.07 (s, 3H), 1.45-1.87 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.7, 168.3, 133.9, 132.0, 123.1, 92.8 (d, J = 167.0 Hz), 38.7 (d, J = 3.8 Hz), 37.4, 32.4 (d, J = 20.5 Hz), 29.9, 28.8 (d, J = 21.2 Hz), 24.3 (d, J = 3.8 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -183.7 (m, 1F); IR (KBr): υ (cm^{-1}) 2926, 1772, 1713, 1615, 1467, 1438, 1398, 1362, 1188, 1170, 1054, 721, 530; ESI-MS: (*m/z*) 314.1 (M^++Na); HRMS calcd for $C_{16}H_{18}FNNaO_3$ (M+Na): 314.1163, Found 314.1176.

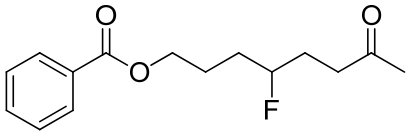


5-Fluoro-8-hydroxyoctan-2-one (2b). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ

4.39-4.56 (m, 1H), 3.61-3.64 (m, 2H), 2.52-2.62 (m, 2H), 2.13 (s, 3H), 2.09 (br s, 1H), 1.60-1.95 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.3, 93.4 (d, *J* = 167.0 Hz), 62.2, 38.8 (d, *J* = 3.8 Hz), 31.5 (d, *J* = 20.5 Hz), 30.0, 28.9 (d, *J* = 21.3 Hz), 28.2 (d, *J* = 3.8 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -182.5 (m, 1F); IR (neat): ν (cm^{-1}) 2950, 1715, 1435, 1361, 1166, 1059, 956; ESI-MS: (*m/z*) 185.2 (M^++Na); HRMS calcd for $C_8H_{15}FNaO_2$ (M+Na): 185.0948, found 185.0955.

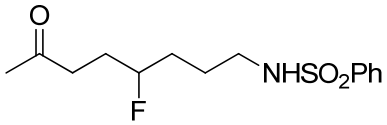


4-Fluoro-7-oxooctyl 4-methylbenzenesulfonate (2c). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 4.33-4.51 (m, 1H), 4.00-4.11 (m, 2H), 2.51-2.62 (m, 2H), 2.45 (s, 3H), 2.15 (s, 3H), 1.57-1.89 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.7, 144.8, 133.0, 129.9, 127.8, 92.7 (d, *J* = 167.6 Hz), 70.0, 38.7 (d, *J* = 3.0 Hz), 31.1 (d, *J* = 20.8 Hz), 29.9, 28.8 (d, *J* = 20.5 Hz), 24.7 (d, *J* = 4.3 Hz), 21.6; ^{19}F NMR (282 MHz, $CDCl_3$): δ -183.9 (m, 1F); IR (neat): ν (cm^{-1}) 2959, 2929, 1716, 1598, 1357, 1189, 1176, 1097, 947, 816, 664, 555; ESI-MS: (*m/z*) 339.0 (M^++Na); HRMS calcd for $C_{15}H_{21}FNaO_4S$ (M+Na): 339.1037, found 339.1036.

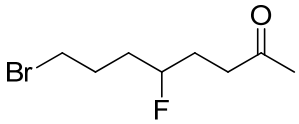


4-Fluoro-7-oxooctyl benzoate (2d). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 7.2 Hz, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 4.44-4.62 (m, 1H), 4.30-4.37 (m, 2H), 2.54-2.65 (m, 2H), 2.14 (s, 3H), 1.66-1.99 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.7, 166.5, 132.9, 130.2, 129.5, 128.3, 93.0 (d, *J* = 167.7 Hz), 64.4, 38.8 (d, *J* = 2.9 Hz), 31.8 (d, *J* = 21.4 Hz), 30.0, 28.9 (d, *J* = 20.9 Hz), 24.6 (d, *J* = 2.6 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -183.5 (m, 1F); IR (neat): ν (cm^{-1}) 2958, 1717, 1451, 1359, 1274, 1113, 951, 714; ESI-MS: (*m/z*) 289.1 (M^++Na); HRMS

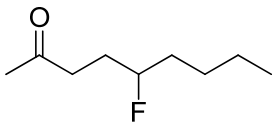
calcd for $C_{15}H_{19}FNaO_3$ (M+Na): 289.1210, found 289.1201.



***N*-(4-Fluoro-7-oxooctyl)benzenesulfonamide (2e).** Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, *J* = 7.2 Hz, 2H), 7.58 (t, *J* = 7.2 Hz, 1H), 7.51 (t, *J* = 7.2 Hz, 2H), 5.18 (br s, 1H), 4.33-4.50 (m, 1H), 2.95-2.98 (m, 2H), 2.50-2.62 (m, 2H), 2.15 (s, 3H), 1.54-1.90 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.2, 139.9, 132.6, 129.1, 126.9, 92.9 (d, *J* = 167.3 Hz), 42.8, 38.7 (d, *J* = 3.6 Hz), 31.9 (d, *J* = 21.3 Hz), 29.9, 28.8 (d, *J* = 20.9 Hz), 25.2 (d, *J* = 3.6 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -183.1 (m, 1F); IR (neat): ν (cm^{-1}) 3281, 2926, 1714, 1447, 1326, 1162, 1094, 757, 720, 691, 588; ESI-MS: (*m/z*) 324.1 (M^++Na); HRMS calcd for $C_{14}H_{20}FNNaO_3S$ (M+Na): 324.1040, found 314.1034.

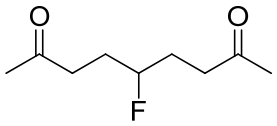


8-Bromo-5-fluorooctan-2-one (2f). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.39-4.57 (m, 1H), 3.39-3.46 (m, 2H), 2.54-2.64 (m, 2H), 2.14 (s, 3H), 1.65-2.10 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.8, 92.7 (d, *J* = 167.7 Hz), 38.7 (d, *J* = 3.8 Hz), 33.7 (d, *J* = 20.5 Hz), 33.4, 30.0, 28.9 (d, *J* = 20.5 Hz), 28.3 (d, *J* = 3.8 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -180.8 (m, 1F); IR (neat): ν (cm^{-1}) 2956, 1716, 1440, 1358, 1255, 1166, 862, 641, 561; ESI-MS: (*m/z*) 247.1 (M^++Na); HRMS calcd for $C_8H_{14}BrFNaO$ (M+Na): 247.0104, found 247.0107.

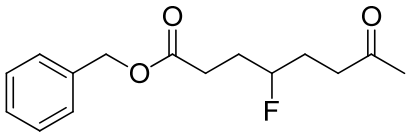


5-Fluorononan-2-one (2g). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.30-4.47 (m, 1H), 2.47-2.58 (m, 2H), 2.09 (s, 3H), 1.20-1.90 (m, 8H), 0.83 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.0, 93.5 (d, *J* = 166.3 Hz), 38.9 (d, *J* = 3.8 Hz), 34.8 (d, *J* = 20.4 Hz), 29.9, 28.9 (d, *J* = 20.8 Hz), 27.1 (d, *J* = 4.6 Hz), 22.4, 13.9; ^{19}F

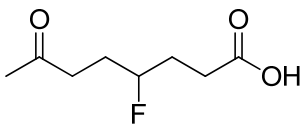
NMR (282 MHz, $CDCl_3$) δ -182.4 (m, 1F); IR (neat): ν (cm^{-1}) 2960, 2935, 2864, 1721, 1415, 1262, 1096, 1018, 800; EIMS: *m/z* (rel intensity) 145 (1), 97 (3), 59 (3), 58 (12), 55 (5), 46 (44), 45 (100), 43 (33), 42 (8), 41 (5); HRMS calcd for $C_9H_{17}FO$ (M): 160.1263, found 160.1265.



5-Fluorononane-2,8-dione (2h). White solid. Mp: 39-41 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 4.32-4.51 (m, 1H), 2.48-2.61 (m, 4H), 2.10 (s, 6H), 1.73-1.90 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.6, 92.6 (d, *J* = 167.0 Hz), 38.7 (d, *J* = 3.7 Hz), 29.9, 28.8 (d, *J* = 20.8 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -185.0 (m, 1F); IR (KBr): ν (cm^{-1}) 2968, 1711, 1705, 1415, 1367, 1255, 1159, 953, 843, 506; ESI-MS: (*m/z*) 197.1 (M^++Na); HRMS calcd for $C_9H_{15}FNaO_2$ (M+Na): 197.0948, found 197.0952.

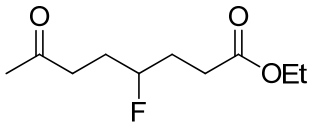


Benzyl 4-fluoro-7-oxooctanoate (2i). Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.29-7.37 (m, 5H), 5.11 (s, 2H), 4.41-4.58 (m, 1H), 2.43-2.63 (m, 4H), 2.14 (s, 3H), 1.78-1.98 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.7, 172.8, 135.9, 128.6, 128.3, 128.2, 92.4 (d, *J* = 167.8 Hz), 66.4, 38.7 (d, *J* = 3.8 Hz), 30.3 (d, *J* = 21.2 Hz), 30.0, 29.8 (d, *J* = 3.8 Hz), 28.8 (d, *J* = 20.5 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -185.6 (m, 1F); IR (neat): ν (cm^{-1}) 3066, 3034, 2934, 1730, 1717, 1498, 1358, 1166, 752, 699; ESI-MS: (*m/z*) 289.2 (M^++Na); HRMS calcd for $C_{15}H_{19}FNaO_3$ (M+Na): 289.1210, found 289.1216.

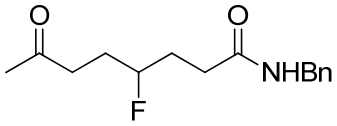


4-Fluoro-7-oxooctanoic acid (2j). Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 4.44-4.61 (m, 1H), 2.44-2.68 (m, 4H), 2.18 (s, 3H), 1.80-2.00 (m, 4H); ^{13}C NMR (100

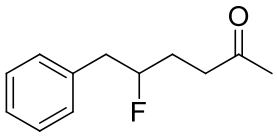
MHz, $CDCl_3$): δ 208.3, 178.6, 92.3 (d, *J* = 167.8 Hz), 38.7 (d, *J* = 3.8 Hz), 30.0 (d, *J* = 21.5 Hz), 29.8, 29.5 (d, *J* = 4.5 Hz), 28.7 (d, *J* = 20.9 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -185.3 (m, 1F); IR (neat): ν (cm^{-1}) 2924, 2852, 1716, 1420, 1362, 1168; ESI-MS: (*m/z*) 199.1 (M^++Na); HRMS calcd for $C_8H_{13}FNaO_3$ (M+Na): 199.0741, found 199.0743.



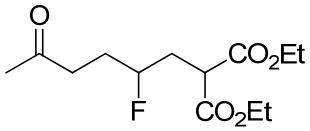
Ethyl 4-fluoro-7-oxooctanoate (2k). Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 4.42-4.60 (m, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 2.54-2.67 (m, 2H), 2.38-2.50 (m, 2H), 2.16 (s, 3H), 1.80-1.99 (m, 4H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.6, 172.8, 92.4 (d, *J* = 167.2 Hz), 60.3, 38.6 (d, *J* = 4.3 Hz), 30.2 (d, *J* = 20.8 Hz), 29.8, 29.7 (d, *J* = 5.1 Hz), 28.7 (d, *J* = 21.3 Hz), 14.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ -185.0 (m, 1F); IR (neat): ν (cm^{-1}) 2935, 1732, 1444, 1371, 1256, 1181, 1032, 934, 861, 749; ESI-MS: (*m/z*) 227.1 (M^++Na); HRMS calcd for $C_{10}H_{17}FNaO_3$ (M+Na): 227.1054, found 227.1058.



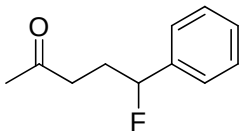
***N*-Benzyl-4-fluoro-7-oxooctanamide (2l).** White solid. Mp: 58-60 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 7.23-7.32 (m, 5H), 6.27 (br s, 1H), 4.38-4.56 (m, 3H), 2.50-2.61 (m, 2H), 2.25-2.40 (m, 2H), 2.13 (s, 3H), 1.78-2.05 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.9, 172.0, 138.3, 128.6, 127.7, 127.4, 92.8 (d, *J* = 167.0 Hz), 43.5, 38.8 (d, *J* = 3.9 Hz), 31.7 (d, *J* = 3.9 Hz), 30.8 (d, *J* = 20.5 Hz), 29.9, 28.7 (d, *J* = 20.3 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -184.8 (m, 1F); IR (KBr): ν (cm^{-1}) 3305, 3086, 3033, 2932, 1706, 1634, 1550, 1434, 1374, 1261, 1168, 1052, 754, 733, 698; ESI-MS: (*m/z*) 288.3 (M^++Na); HRMS calcd for $C_{15}H_{20}FNNaO_2$ (M+Na): 288.1370, found 288.1371.



5-Fluoro-6-phenylhexan-2-one (2m). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.20-7.31 (m, 5H), 4.58-4.77 (m, 1H), 2.81-3.02 (m, 2H), 2.51-2.67 (m, 2H), 2.13 (s, 3H), 1.78-2.01 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.8, 136.9 (d, J = 4.6 Hz), 129.3, 128.5, 126.7, 93.6 (d, J = 170.8 Hz), 41.7 (d, J = 21.2 Hz), 38.9 (d, J = 3.0 Hz), 30.0, 28.5 (d, J = 20.5 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -181.6 (m, 1F); IR (neat): ν (cm^{-1}) 3029, 2928, 1716, 1496, 1358, 1164, 741, 701; ESI-MS: (*m/z*) 217.0 (M^{+}+Na); HRMS calcd for $C_{12}H_{15}FNaO$ (M+Na): 217.0999, found 217.1003.

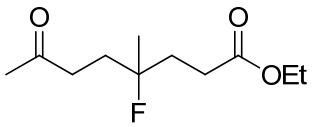


Diethyl 2-(2-fluoro-5-oxohexyl)malonate (2n). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.41-4.60 (m, 1H), 4.12-4.24 (m, 4H), 3.54 (t, J = 7.2 Hz, 1H), 2.51-2.62 (m, 2H), 2.09-2.24 (m, 5H), 1.79-1.96 (m, 2H), 1.20-1.26 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.4, 169.0, 168.8, 91.2 (d, J = 168.4 Hz), 61.6, 48.2 (d, J = 3.0 Hz), 38.5 (d, J = 3.7 Hz), 34.1 (d, J = 20.4 Hz), 29.9, 28.9 (d, J = 20.3 Hz), 14.0, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -185.0 (m, 1F); IR (neat): ν (cm^{-1}) 2983, 2939, 1732, 1467, 1446, 1370, 1154, 1026, 862; ESI-MS: (*m/z*) 299.2 (M^{+}+Na); HRMS calcd for $C_{13}H_{21}FNaO_5$ (M+Na): 299.1265, found 299.1273.

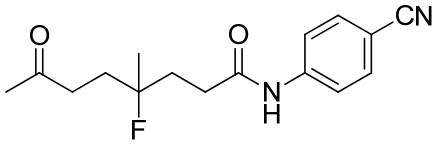


5-Fluoro-5-phenylpentan-2-one (2o). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.39 (m, 5H), 5.48 (dt, J = 48.4, 6.0 Hz, 1H), 2.52-2.67 (m, 2H), 2.11-2.22 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.6, 139.8 (d, J = 19.7 Hz), 128.5, 128.3 (d, J = 2.8 Hz), 125.3 (d, J = 6.7 Hz), 93.4 (d, J = 170.1 Hz), 38.6 (d, J = 3.9 Hz), 30.9 (d, J = 24.9 Hz), 30.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ -178.3 (m, 1F); IR (neat): ν (cm^{-1})

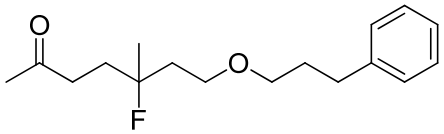
3065, 3034, 2932, 1716, 1496, 1454, 1361, 1163, 964, 762, 700; ESI-MS: (*m/z*) 203.1 (M^++Na); HRMS calcd for $C_{11}H_{13}FNaO$ (M+Na): 203.0843, found 203.0838.



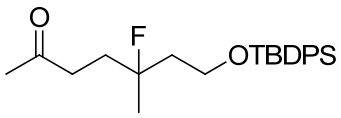
Ethyl 4-fluoro-4-methyl-7-oxooctanoate (3a). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.13 (q, *J* = 7.2 Hz, 2H), 2.57 (t, *J* = 8.0 Hz, 2H), 2.41 (t, *J* = 8.0 Hz, 2H), 2.17 (s, 3H), 1.81-2.07 (m, 4H), 1.29 (d, *J* = 22.0 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.7, 173.1, 95.5 (d, *J* = 169.2 Hz), 60.5, 37.5 (d, *J* = 4.9 Hz), 34.4 (d, *J* = 22.7 Hz), 32.9 (d, *J* = 22.8 Hz), 29.8, 28.6 (d, *J* = 5.3 Hz), 23.6 (d, *J* = 24.3 Hz), 14.1; ^{19}F NMR (282 MHz, $CDCl_3$): δ -149.6 (m, 1F); IR (neat): ν (cm^{-1}) 2983, 2938, 1735, 1447, 1384, 1164, 1104, 1027; ESI-MS: (*m/z*) 241.1 (M^++Na); HRMS calcd for $C_{11}H_{19}FNaO_3$ (M+Na): 241.1210, found 241.1207.



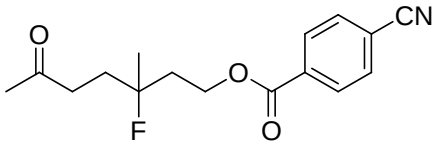
***N*-(4-Cyanophenyl)-4-fluoro-4-methyl-7-oxooctanamide (3b).** White solid. Mp: 79-81 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.54 (br s, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 8.8 Hz, 2H), 2.50-2.65 (m, 4H), 2.19 (s, 3H), 1.78-2.12 (m, 4H), 1.31 (d, *J* = 21.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.7, 171.6, 142.5, 133.2, 119.5, 119.0, 106.4, 95.9 (d, *J* = 169.4 Hz), 37.6 (d, *J* = 4.8 Hz), 34.6 (d, *J* = 22.7 Hz), 32.6 (d, *J* = 22.5 Hz), 31.6 (d, *J* = 5.9 Hz), 30.1, 23.9 (d, *J* = 23.6 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -148.8 (m, 1F); IR (KBr): ν (cm^{-1}) 3334, 3105, 2981, 2935, 2225, 1713, 1594, 1525, 1409, 1312, 1255, 1176, 841, 550; ESI-MS: (*m/z*) 313.1 (M^++Na); HRMS calcd for $C_{16}H_{19}FN_2NaO_2$ (M+Na): 313.1323, found 313.1315.



5-Fluoro-5-methyl-7-(3-phenylpropoxy)heptan-2-one (3c). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27 (t, *J* = 7.6 Hz, 2H), 7.17-7.19 (m, 3H), 3.51 (t, *J* = 6.8 Hz, 2H), 3.41 (t, *J* = 6.8 Hz, 2H), 2.67 (t, *J* = 7.6 Hz, 2H), 2.57 (t, *J* = 7.6 Hz, 2H), 2.16 (s, 3H), 1.85-1.96 (m, 6H), 1.33 (d, *J* = 21.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.0, 141.9, 128.4, 128.3, 125.8, 95.8 (d, *J* = 167.5 Hz), 70.2, 66.2 (d, *J* = 8.1 Hz), 39.3 (d, *J* = 22.7 Hz), 37.8 (d, *J* = 3.6 Hz), 33.4 (d, *J* = 22.9 Hz), 32.4, 31.2, 29.9, 24.5 (d, *J* = 25.6 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -145.3 (m, 1F); IR (neat): ν (cm^{-1}) 3027, 2940, 2865, 1718, 1455, 1381, 1357, 1161, 1113, 747, 700; ESI-MS: (*m/z*) 303.1 (M^++Na); HRMS calcd for $C_{17}H_{25}FNaO_2$ (M+Na): 303.1731, found 303.1736.

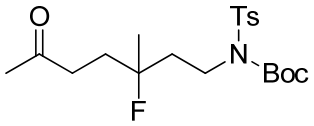


7-((*tert*-Butyldiphenylsilyl)oxy)-5-fluoro-5-methylheptan-2-one (3d). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65-7.67 (m, 4H), 7.35-7.46 (m, 6H), 3.78 (t, *J* = 6.6 Hz, 2H), 2.48-2.53 (m, 2H), 2.12 (s, 3H), 1.85-1.97 (m, 4H), 1.29 (d, *J* = 21.6 Hz, 3H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.0, 135.5, 133.5, 129.7, 127.7, 95.8 (d, *J* = 168.1 Hz), 59.6 (d, *J* = 8.3 Hz), 41.9 (d, *J* = 22.5 Hz), 37.7 (d, *J* = 4.4 Hz), 33.4 (d, *J* = 22.7 Hz), 29.9, 26.8, 24.6 (d, *J* = 25.2 Hz), 19.1; ^{19}F NMR (282 MHz, $CDCl_3$): δ -144.8 (m, 1F); IR (neat): ν (cm^{-1}) 3072, 2957, 2932, 2858, 1720, 1472, 1359, 1112, 823, 739, 703, 505; ESI-MS: (*m/z*) 423.2 (M^++Na); HRMS calcd for $C_{24}H_{33}FNaO_2Si$ (M+Na): 423.2126, found 423.2125.

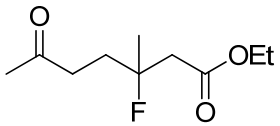


3-Fluoro-3-methyl-6-oxoheptyl 4-cyanobenzoate (3e). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, *J* = 8.0 Hz, 2H), 7.69 (d, *J* = 7.6 Hz, 2H), 4.45 (t, *J* = 6.8 Hz, 2H), 2.56 (t, *J* = 7.6 Hz, 2H), 1.83-2.14 (m, 7H), 1.34 (d, *J* = 22.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.5, 164.8, 133.9, 132.2, 130.0, 117.9, 116.4, 95.1 (d, *J* = 169.3 Hz), 61.3 (d, *J* = 5.4 Hz), 38.2 (d, *J* = 22.9 Hz), 37.5 (d, *J* = 5.1 Hz), 33.3 (d, *J*

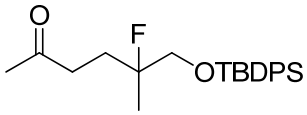
= 22.4 Hz), 29.9, 24.1 (d, *J* = 23.8 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -147.9 (m, 1F); IR (neat): ν (cm^{-1}) 2981, 2231, 1721, 1277, 1108, 1019, 862, 768, 692, 547; ESI-MS: (*m/z*) 314.0 (M^++Na); HRMS calcd for $C_{16}H_{18}FNNaO_3$ (M+Na): 314.1163, found 314.1168.



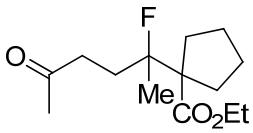
***tert*-Butyl (3-fluoro-3-methyl-6-oxoheptyl)(tosyl)carbamate (3f).** Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 3.92 (t, *J* = 8.0 Hz, 2H), 2.62 (t, *J* = 7.6 Hz, 2H), 2.44 (s, 3H), 2.19 (s, 3H), 1.85-2.16 (m, 4H), 1.38 (d, *J* = 24.0 Hz, 3H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.7, 150.7, 144.3, 137.2, 129.3, 127.7, 95.2 (d, *J* = 169.9 Hz), 84.4, 42.6 (d, *J* = 7.3 Hz), 39.4 (d, *J* = 22.7 Hz), 37.5 (d, *J* = 4.4 Hz), 33.0 (d, *J* = 22.8 Hz), 30.0, 27.8, 24.1 (d, *J* = 24.3 Hz), 21.6; ^{19}F NMR (282 MHz, $CDCl_3$): δ -148.2 (m, 1F); IR (neat): ν (cm^{-1}) 2981, 2934, 1721, 1598, 1356, 1157, 1088, 720, 676, 577, 547; ESI-MS: (*m/z*) 438.3 (M^++Na); HRMS calcd for $C_{20}H_{30}FNNaO_5S$ (M+Na): 438.1721, found 438.1724.



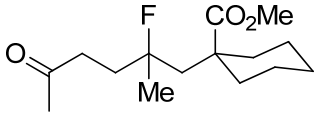
Ethyl 3-fluoro-3-methyl-6-oxoheptanoate (3g). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.09 (q, *J* = 7.2 Hz, 2H), 2.52-2.62 (m, 4H), 2.12 (s, 3H), 1.92-2.03 (m, 2H), 1.40 (d, *J* = 22.0 Hz, 3H), 1.21 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.5, 169.3 (d, *J* = 12.3 Hz), 94.3 (d, *J* = 170.6 Hz), 60.6, 44.4 (d, *J* = 26.3 Hz), 37.5 (d, *J* = 3.8 Hz), 32.9 (d, *J* = 22.0 Hz), 29.8, 24.5 (d, *J* = 24.2 Hz), 14.1; ^{19}F NMR (282 MHz, $CDCl_3$): δ -143.2 (m, 1F); IR (neat): ν (cm^{-1}) 2985, 2940, 1736, 1462, 1371, 1160, 1097, 1033; ESI-MS: (*m/z*) 227.0 (M^++Na); HRMS calcd for $C_{10}H_{17}FNaO_3$ (M+Na): 227.1054, found 227.1054.



6-((*tert*-Butyldiphenylsilyl)oxy)-5-fluoro-5-methylhexan-2-one (3h). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, *J* = 8.0 Hz, 4H), 7.27-7.37 (m, 6H), 3.51 (d, *J* = 16.0 Hz, 2H), 2.34-2.49 (m, 2H), 2.04 (s, 3H), 1.75-2.01 (m, 2H), 1.24 (d, *J* = 22.0 Hz, 3H), 0.99 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.9, 135.6, 133.1, 129.8, 127.7, 96.1 (d, *J* = 170.8 Hz), 68.5 (d, *J* = 28.8 Hz), 37.4 (d, *J* = 3.8 Hz), 30.0 (d, *J* = 22.0 Hz), 29.9, 26.8, 21.7 (d, *J* = 23.5 Hz), 19.3; ^{19}F NMR (282 MHz, $CDCl_3$): δ -154.0 (m, 1F); IR (neat): ν (cm^{-1}) 3072, 2958, 2932, 2858, 1720, 1589, 1428, 1112, 825, 741, 702; ESI-MS: (*m/z*) 409.2 (M^++Na); HRMS calcd for $C_{23}H_{31}FNaO_2Si$ (M+Na): 409.1970, found 409.1976.

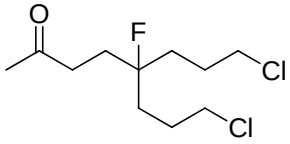


Ethyl 1-(2-fluoro-5-oxohexan-2-yl)cyclopentanecarboxylate (3i). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.15 (q, *J* = 7.2 Hz, 2H), 2.48-2.67 (m, 2H), 2.11-2.33 (m, 6H), 1.75-1.94 (m, 3H), 1.49-1.72 (m, 4H), 1.35 (d, *J* = 22.0 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.1, 174.9 (d, *J* = 9.9 Hz), 97.3 (d, *J* = 179.2 Hz), 63.4 (d, *J* = 22.8 Hz), 60.9, 37.8 (d, *J* = 3.8 Hz), 31.6 (d, *J* = 3.1 Hz), 30.8, 30.7 (d, *J* = 3.8 Hz), 30.5, 30.0, 24.7 (d, *J* = 19.0 Hz), 21.4 (d, *J* = 24.3 Hz), 14.0; ^{19}F NMR (376 MHz , $CDCl_3$): δ -156.5 (m, 1F); IR (neat): ν (cm^{-1}) 2961, 2876, 1721, 1454, 1429, 1385, 1358, 1299, 1261, 1177, 1098, 1025, 804, 733, 700; ESI-MS: (*m/z*) 281 (M^++Na); HRMS calcd for $C_{14}H_{23}FNaO_3$ (M+Na): 281.1523, found 281.1528.

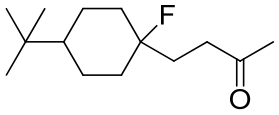


Methyl 1-(2-fluoro-2-methyl-5-oxohexyl)cyclohexanecarboxylate (3j). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.68 (s, 3H), 2.46-2.60 (m, 2H), 2.16 (s, 3H), 2.05-2.14 (m, 2H), 1.70-2.05 (m, 4H), 1.21-1.61 (m, 11H); ^{13}C NMR (100 MHz,

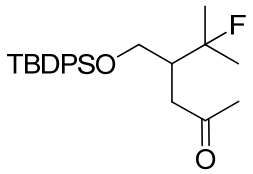
$CDCl_3$): δ 207.7, 177.2, 96.3 (d, *J* = 169.6 Hz), 51.5, 48.7 (d, *J* = 21.6 Hz), 45.0 (d, *J* = 1.1 Hz), 37.6 (d, *J* = 4.5 Hz), 35.9, 34.9 (d, *J* = 1.5 Hz), 34.7 (d, *J* = 23.0 Hz), 29.8, 25.6, 24.1 (d, *J* = 25.0 Hz), 22.64, 22.56; ^{19}F NMR (376 MHz , $CDCl_3$): δ -145.2 (m, 1F); IR (neat): ν (cm^{-1}) 2941, 2856, 1721, 1453, 1434, 1384, 1357, 1213, 1160, 1134, 1111, 1001; ESI-MS: (*m/z*) 295 (M^++Na); HRMS calcd for $C_{15}H_{25}FNaO_3$ (M+Na): 295.1680, found 295.1682.



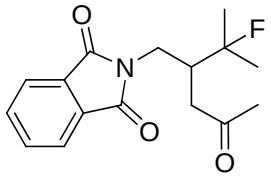
8-Chloro-5-(3-chloropropyl)-5-fluorooctan-2-one (3k). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.56 (t, *J* = 6.4 Hz, 4H), 2.55 (t, *J* = 8.0 Hz, 2H), 2.18 (s, 3H), 1.69-1.96 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.6, 97.3 (d, *J* = 171.6 Hz), 45.0, 37.2 (d, *J* = 5.0 Hz), 34.1 (d, *J* = 23.0 Hz), 30.4 (d, *J* = 22.3 Hz), 30.0, 26.5 (d, *J* = 5.9 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -152.9 (m, 1F); IR (neat): ν (cm^{-1}) 2961, 2852, 1718, 1446, 1357, 1318, 1164, 651; ESI-MS: (*m/z*) 279.1 (M^++Na); HRMS calcd for $C_{11}H_{19}Cl_2FNaO$ (M+Na): 279.0689, found 279.0692.



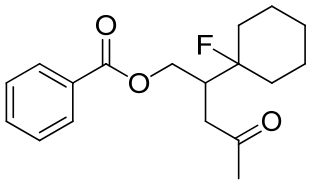
4-(4-(*tert*-Butyl)-1-fluorocyclohexyl)butan-2-one (3l). This compound was isolated as a 79:21 mixture of two stereoisomers determined by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.55-2.59 (m, 2H), 2.18/2.16 (2s, 3H), 1.78-1.95 (m, 4H), 1.54-1.62 (m, 2H), 0.93-1.38 (m, 5H), 0.86/0.85 (2s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.4/208.3, 96.6 (d, *J* = 169.7 Hz)/94.3 (d, *J* = 168.6 Hz), 47.3/47.2, 37.3 (d, *J* = 3.2 Hz)/37.2 (d, *J* = 2.9 Hz), 35.9 (d, *J* = 19.8 Hz)/35.4 (d, *J* = 21.9 Hz), 34.3 (d, *J* = 22.5 Hz)/28.6 (d, *J* = 23.2 Hz), 32.3/32.1, 29.9/29.8, 27.6/27.4, 24.5 (d, *J* = 11.9 Hz)/22.3; ^{19}F NMR (282 MHz, $CDCl_3$): δ -138.4/-162.9 (2m, 1F); IR (neat): ν (cm^{-1}) 2949, 2869, 1720, 1479, 1444, 1365, 1164, 1146, 821; ESI-MS: (*m/z*) 251.2 (M^++Na); HRMS calcd for $C_{14}H_{25}FNaO$ (M+Na): 251.1781, found 251.1787.



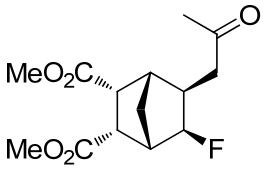
4-(((*tert*-Butyldiphenylsilyl)oxy)methyl)-5-fluoro-5-methylhexan-2-one (4a). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61-7.65 (m, 4H), 7.36-7.46 (m, 6H), 3.70 (dd, *J* = 10.4, 4.4 Hz, 1H), 3.61 (dd, *J* = 10.8, 6.0 Hz, 1H), 2.52-2.69 (m, 3H), 2.13 (s, 3H), 1.33 (d, *J* = 22.4 Hz, 3H), 1.30 (d, *J* = 22.0 Hz, 3H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.4, 135.63, 135.58, 133.2, 133.1, 129.81, 129.77, 127.7, 96.6 (d, *J* = 167.0 Hz), 63.0 (d, *J* = 7.9 Hz), 45.3 (d, *J* = 20.7 Hz), 40.9 (d, *J* = 4.6 Hz), 30.2, 26.9, 26.5 (d, *J* = 24.0 Hz), 24.3 (d, *J* = 24.8 Hz), 19.2; ^{19}F NMR (282 MHz, $CDCl_3$): δ -135.4 (m, 1F); IR (neat): ν (cm^{-1}) 3072, 3051, 2931, 2858, 1720, 1589, 1472, 1428, 1373, 1112, 824, 741, 702, 690, 505; ESI-MS: (*m/z*) 423.3 (M^++Na); HRMS calcd for $C_{24}H_{33}FNaO_2Si$ (M+Na): 423.2126, found 423.2136.



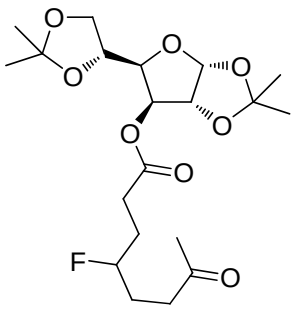
2-(2-(2-Fluoropropan-2-yl)-4-oxopentyl)isoindoline-1,3-dione (4b). White solid. Mp: 78-80 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.85 (m, 2H), 7.69-7.73 (m, 2H), 3.81 (dd, *J* = 13.6, 3.6 Hz 1H), 3.61 (dd, *J* = 13.6, 10.0 Hz, 1H), 2.83-2.91 (m, 1H), 2.72 (dd, *J* = 18.4, 4.0 Hz, 1H), 2.58 (dd, *J* = 18.0, 7.6 Hz, 1H), 2.05 (s, 3H), 1.48 (d, *J* = 22.0 Hz, 3H), 1.41 (d, *J* = 22.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.7, 168.5, 134.0, 131.9, 123.2, 96.0 (d, *J* = 168.2 Hz), 43.0 (d, *J* = 5.5 Hz), 41.8 (d, *J* = 21.1 Hz), 39.1 (d, *J* = 7.7 Hz), 29.8, 25.6 (d, *J* = 23.7 Hz), 24.0 (d, *J* = 24.9 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -138.8 (m, 1F); IR (KBr): ν (cm^{-1}) 2982, 1770, 1712, 1441, 1417, 1370, 1190, 1053, 906, 884, 724; ESI-MS: (*m/z*) 314.1 (M^++Na); HRMS calcd for $C_{16}H_{18}FNNaO_3$ (M+Na): 314.1163, found 314.1162.



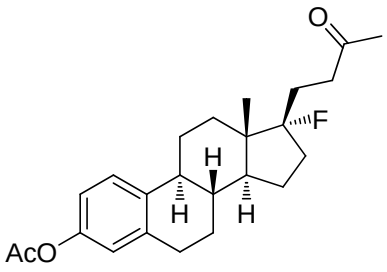
2-(1-Fluorocyclohexyl)-4-oxopentyl benzoate (4c). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 8.0, 2H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.40 (t, *J* = 8.0 Hz, 2H), 4.44 (dd, *J* = 12.0, 4.8 Hz, 1H), 4.21 (dd, *J* = 11.6, 6.8 Hz, 1H), 2.70-2.78 (m, 2H), 2.56 (dd, *J* = 18.4, 8.4 Hz, 1H), 2.13 (s, 3H), 1.77-1.89 (m, 2H), 1.35-1.64 (m, 7H), 1.10-1.22 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.8, 166.4, 133.1, 129.9, 129.5, 128.4, 96.3 (d, *J* = 173.4 Hz), 64.2 (d, *J* = 6.1 Hz), 41.7 (d, *J* = 21.9 Hz), 40.9 (d, *J* = 4.8 Hz), 33.9 (d, *J* = 22.9 Hz), 32.4 (d, *J* = 22.9 Hz), 25.1, 21.6 (d, *J* = 2.3 Hz), 21.5 (d, *J* = 2.4 Hz); ^{19}F NMR (282 MHz, $CDCl_3$): δ -160.8 (m, 1F); IR (neat): ν (cm^{-1}) 2937, 2865, 1720, 1450, 1273, 1117, 1070, 1026, 712; ESI-MS: (*m/z*) 329.2 (M^{+}+Na); HRMS calcd for $C_{18}H_{23}FNaO_3$ (M+Na): 329.1523, found 329.1523.



(1*R,2*R**,3*R**,4*S**,5*R**,6*R**)-Dimethyl 5-fluoro-6-(2-oxopropyl)bicyclo[2.2.1]-heptane-2,3-dicarboxylate (5).** Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.00 (dd, *J* = 54.4, 6.4 Hz, 1H), 3.61 (s, 3H), 3.59 (s, 3H), 3.05-3.10 (m, 1H), 2.83-2.92 (m, 2H), 2.68 (t, *J* = 6.8 Hz, 1H), 2.60 (dd, *J* = 16.8, 8.4 Hz, 1H), 2.28-2.36 (m, 1H), 2.20 (br s, 1H), 2.11 (s, 3H), 1.82 (d, *J* = 10.8 Hz, 1H), 1.24 (d, *J* = 10.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.3, 171.83, 171.77, 93.0 (d, *J* = 183.3 Hz), 51.7, 51.5, 46.5, 46.1 (d, *J* = 22.7 Hz), 43.6, 43.1 (d, *J* = 9.7 Hz), 41.8 (d, *J* = 17.4 Hz), 37.5 (d, *J* = 17.9 Hz), 34.0, 29.5; ^{19}F NMR (282 MHz, $CDCl_3$): δ -190.8 (m, 1F); IR (neat): ν (cm^{-1}) 2955, 1740, 1436, 1358, 1267, 1202, 1171, 1051, 995; ESI-MS: (*m/z*) 309.0 (M^{+}+Na); HRMS calcd for $C_{14}H_{19}FNaO_5$ (M+Na): 309.1109, found 309.1107. The stereochemistry was confirmed by 2D NOESY experiments.

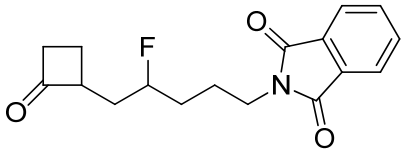


(3a*R*,5*R*,6*S*,6a*R*)-5-((*R*)-2,2-Dimethyl-1,3-dioxolan-4-yl)-2,2-dimethyltetrahydro-furo[2,3-*d*][1,3]dioxol-6-yl 4-fluoro-7-oxooctanoate (7). This compound was isolated as a 1:1 mixture of two stereoisomers determined by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.82 (t, *J* = 3.2 Hz, 1H), 5.22 (d, *J* = 2.4 Hz, 1H), 4.38-4.56 (m, 2H), 4.12-4.16 (m, 2H), 3.95-4.12 (m, 2H), 2.39-2.62 (m, 4H), 2.11 (s, 3H), 1.74-1.94 (m, 4H), 1.47 (s, 3H), 1.35 (s, 3H), 1.27 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.5, 171.6/171.5, 112.2, 109.3, 105.02/105.01, 92.3 (d, *J* = 167.7 Hz)/92.2 (d, *J* = 167.6 Hz), 83.23/83.21, 79.75/79.71, 76.1, 72.4/72.3, 67.24/67.20, 38.7 (d, *J* = 3.8 Hz)/38.6 (d, *J* = 2.0 Hz), 30.2 (d, *J* = 20.7 Hz)/30.1 (d, *J* = 21.8 Hz), 29.9 (d, *J* = 17.5 Hz)/29.8 (d, *J* = 22.6 Hz), 28.8 (d, *J* = 3.7 Hz)/28.6 (d, *J* = 3.5 Hz), 26.8/26.7, 26.1, 25.21/25.18.; ^{19}F NMR (282 MHz, $CDCl_3$): δ -185.2 (m, 1F); IR (neat): ν (cm^{-1}) 2988, 2937, 1747, 1717, 1374, 1254, 1217, 1162, 1076, 1023, 846; ESI-MS: (*m/z*) 441.2 (M^{+}+Na); HRMS calcd for $C_{20}H_{31}FNaO_8$ (M+Na): 441.1895, found 441.1889.



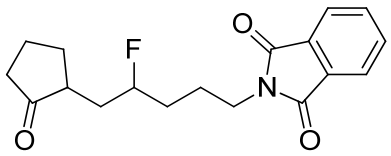
(8*R*,9*S*,13*S*,14*S*,17*S*)-17-Fluoro-13-methyl-17-(3-oxobutyl)-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl acetate (9). White solid. Mp: 129-131 ^{o}C; $[\alpha]_D^{26}$ = 38.5 (c 0.28, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 (d, *J* = 8.0 Hz, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 6.72 (s, 1H), 2.79 (br s, 2H), 2.60-2.68 (m, 1H), 2.45-2.53 (m, 1H), 2.15-2.30 (m, 5H), 2.11 (s, 3H), 1.20-1.98 (m, 13H), 0.66 (s,

3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.7, 169.9, 148.4, 138.2, 137.9, 126.4, 121.5, 118.5, 107.5 (d, *J* = 177.7 Hz), 49.2, 47.2 (d, *J* = 19.2 Hz), 43.8, 38.4, 38.2 (d, *J* = 4.1 Hz), 34.1 (d, *J* = 22.6 Hz), 30.1 (d, *J* = 4.4 Hz), 30.0, 29.5, 27.5, 27.2 (d, *J* = 23.3 Hz), 25.8, 23.3, 21.1, 15.0 (d, *J* = 6.5 Hz); ^{19}F NMR (282 MHz , $CDCl_3$): δ -154.5 (m, 1F); IR (KBr): ν (cm^{-1}) 2958, 2932, 2908, 2876, 2852, 1752, 1704, 1496, 1437, 1367, 1225. ESI-MS: (*m/z*) 409.2 (M^++Na); HRMS calcd for $C_{24}H_{31}FNaO_3$ (M+Na): 409.2149, found 409.2150. The stereochemistry was confirmed by 2D NOESY experiments.

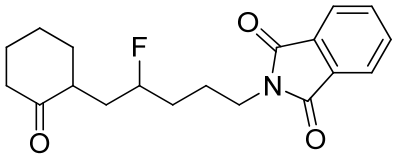


2-(4-Fluoro-5-(2-oxocyclobutyl)pentyl)isoindoline-1,3-dione (10a). *N*-(Pent-4-en-1-yl)phthalimide (**A-1a**, 43 mg, 0.2 mmol), AgOAc (6.7 mg, 0.04 mmol), Selectfluor (141 mg, 0.4 mmol) and potassium acetate (58.9 mg, 0.6 mmol) were placed in a Schlenk tube under nitrogen atmosphere. Water (1.0 mL), acetic acid (0.4 mL) and cyclobutanone (150 μl, 2 mmol) were then added successively at room temperature. The reaction mixture was heated to 50 ^{o}C and stirred for 12 h. The resulting mixture was cooled down to room temperature and extracted with dichloromethane (15 mL × 3). The combined organic phases were dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane/ethyl acetate (5:1, v:v) as the eluent to give the pure product **10a** as a white solid. Mp: 53-54 ^{o}C. Yield: 25.5 mg (42%). This compound was isolated as the 1:1 mixture of two diastereoisomers determined by ^{1}H NMR. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.92 (m, 2H), 7.68-7.79 (m, 2H), 4.49-4.81 (m, 1H), 3.66-3.80 (m, 2H), 3.41-3.56 (m, 1H), 3.04-3.14 (m, 1H), 2.88-2.96 (m, 1H), 2.22-2.32 (m, 1H), 1.49-2.12 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.5/210.4, 168.3, 133.93/133.91, 132.0, 123.2, 92.3 (d, *J* = 168.6 Hz)/91.1 (d, *J* = 169.3 Hz), 56.7 (d, *J* = 2.2 Hz)/56.3 (d, *J* = 3.0 Hz), 45.0/44.7, 37.5/37.4, 34.9 (d, *J* = 21.2 Hz)/34.4 (d, *J* = 21.2 Hz), 32.5 (d, *J* = 21.3 Hz)/32.2 (d, *J* = 21.3 Hz), 24.31 (d, *J* = 4.5 Hz)/24.29 (d, *J* = 3.8 Hz), 17.5/17.0; ^{19}F NMR (282

MHz , $CDCl_3$): δ -182.3 (m, 1F); IR (KBr): ν (cm^{-1}) 3075, 2934, 2855, 1732, 1645, 1454, 1434, 1375, 1195, 1131, 1077, 999, 893; ESI-MS: (*m/z*) 326 (M^++Na); HRMS calcd for $C_{17}H_{19}NFO_3$ (M+H): 304.1343, found 304.1340.

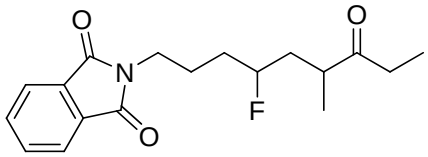


2-(4-Fluoro-5-(2-oxocyclopentyl)pentyl)isoindoline-1,3-dione (10b). This compound was isolated as the ~1:1.1 mixture of two stereoisomers determined by ^1H NMR. White solid, 66-68 ^oC; ^1H NMR (400 MHz, $CDCl_3$): δ 7.80-7.91 (m, 2H), 7.67-7.78 (m, 2H), 4.50-4.82 (m, 1H), 3.63-3.81 (m, 2H), 1.31-2.42 (m, 13H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 220.5/220.4, 168.4, 134.0/133.9, 132.0, 123.2, 93.0 (d, *J* = 167.8 Hz)/91.6 (d, *J* = 168.5 Hz), 46.6 (d, *J* = 2.3 Hz)/45.7 (d, *J* = 2.2 Hz), 37.7/37.5, 37.4, 35.2 (d, *J* = 21.3 Hz)/34.9 (d, *J* = 20.5 Hz), 32.8 (d, *J* = 21.2 Hz)/32.5 (d, *J* = 21.3 Hz), 30.5/29.6, 24.4 (d, *J* = 4.5 Hz)/24.3 (d, *J* = 3.8 Hz), 20.8/20.6; ^{19}F NMR (282 MHz , $CDCl_3$): δ -181.5/-183.4 (2m, 1F); IR (KBr): ν (cm^{-1}) 2953, 2876, 1772, 1736, 1713, 1467, 1438, 1397, 1363, 1157, 1040, 872, 721, 530; ESI-MS: (*m/z*) 340 (M^++Na); HRMS calcd for $C_{18}H_{21}FNO_3$ (M+H): 318.1500, found 318.1498.

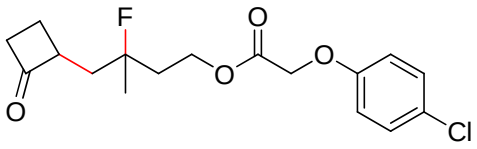


2-(4-Fluoro-5-(2-oxocyclohexyl)pentyl)isoindoline-1,3-dione (10c). This compound was isolated as the ~1:1 mixture of two diastereoisomers determined by ^{19}F NMR. Colorless oil; ^1H NMR (400 MHz, $CDCl_3$): δ 7.80-7.93 (m, 2H), 7.67-7.79 (m, 2H), 4.47-4.74 (m, 1H), 3.63-3.82 (m, 2H), 2.47-2.66 (m, 1H), 1.28-2.45 (m, 14H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 212.7/212.4, 168.3, 133.91/133.87, 132.08/132.05, 123.2, 93.0 (d, *J* = 165.6 Hz)/90.9 (d, *J* = 167.0 Hz), 46.9 (d, *J* = 2.3 Hz)/46.4 (d, *J* = 3.0 Hz), 42.3/42.0, 37.7/37.5, 35.6 (d, *J* = 20.5 Hz)/34.4 (d, *J* = 20.5 Hz), 35.5/33.3, 33.1 (d, *J* = 21.3 Hz)/32.7 (d, *J* = 20.5 Hz), 28.2/27.9, 25.3/25.1, 24.41 (d, *J* = 5.3 Hz)/24.36 (d,

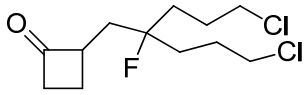
J = 4.6 Hz); ^{19}F NMR (282 MHz , $CDCl_3$): δ -182.5/-183.1 (2m, 1F); IR (neat): ν (cm^{-1}) 2936, 2862, 1773, 1717, 1615, 1467, 1438, 1399, 1128, 1054, 881, 857, 797, 721, 530; ESI-MS: (*m/z*) 354 (M^++Na); HRMS calcd for $C_{19}H_{22}FNNaO_3$ (M+Na): 354.1476, found 354.1483.



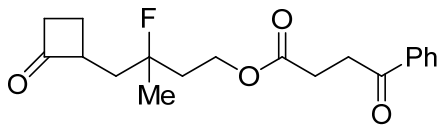
2-(4-Fluoro-6-methyl-7-oxononyl)isoindoline-1,3-dione (10d). This compound was obtained as the 1:1 mixture of two stereoisomers. The two isomers were separated by column chromatography on silica gel. **One isomer**: White solid. Mp: 34-36 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75-7.78 (m, 2H), 7.63-7.65 (m, 2H), 4.41-4.59 (m, 1H), 3.60-3.68 (m, 2H), 2.65-2.71 (m, 1H), 2.35-2.47 (m, 2H), 1.31-1.98 (m, 6H), 1.04 (d, J = 6.8 Hz, 3H), 0.96 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 214.7, 168.3, 133.9, 132.0, 123.2, 92.2 (d, J = 166.1 Hz), 41.7, 38.3 (d, J = 20.3 Hz), 37.6, 34.9, 32.8 (d, J = 20.0 Hz), 24.3 (d, J = 4.4 Hz), 17.9, 7.7; ^{19}F NMR (282 MHz, $CDCl_3$): δ -183.0 (m, 1F); IR (KBr): ν (cm^{-1}) 2937, 1771, 1709, 1399, 1376, 1049, 877, 722, 529; ESI-MS: (*m/z*) 342.1 (M^++Na); HRMS calcd for $C_{14}H_{22}FNNaO_3$ (M+Na): 342.1476, found 342.1468. **The other isomer**: Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75-7.77 (m, 2H), 7.63-7.65 (m, 2H), 4.22-4.40 (m, 1H), 3.61-3.66 (m, 2H), 2.75-2.80 (m, 1H), 2.32-2.52 (m, 2H), 1.44-1.95 (m, 6H), 1.03 (d, J = 7.2 Hz, 3H), 0.96 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 214.4, 168.4, 133.9, 132.0, 123.2, 91.7 (d, J = 167.7 Hz), 42.1, 38.0 (d, J = 20.6 Hz), 37.5, 34.2, 32.7 (d, J = 21.8 Hz), 24.3 (d, J = 4.4 Hz), 16.3, 7.7; ^{19}F NMR (282 MHz, $CDCl_3$): δ -182.6 (m, 1F); IR (neat): ν (cm^{-1}) 2938, 1773, 1713, 1437, 1397, 1047, 721; ESI-MS: (*m/z*) 342.1 (M^++Na); HRMS calcd for $C_{14}H_{22}FNNaO_3$ (M+Na): 342.1476, found 342.1468.



3-Fluoro-3-methyl-4-(2-oxocyclobutyl)butyl 2-(4-chlorophenoxy)acetate (10e). This compound was isolated as the 1:1 mixture of two stereoisomers. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22-7.26 (m, 2H), 6.81-6.85 (m, 2H), 4.60 (s, 2H), 4.32-4.37 (m, 2H), 3.42-3.54 (m, 1H), 3.08-3,18 (m, 1H), 2.88-2.97 (m, 1H), 2.28-2.36 (m, 1H), 1.69-2.16 (m, 5H), 1.34 (d, *J* = 21.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.2, 168.5, 156.3, 129.4, 126.6, 115.9, 95.1 (d, *J* = 169.2 Hz)/94.9 (d, *J* = 170.1 Hz), 65.4, 60.9 (d, *J* = 6.6 Hz)/60.8 (d, *J* = 6.3 Hz), 55.6 (d, *J* = 4.0 Hz)/55.5 (d, *J* = 3.8 Hz), 45.3/45.2, 39.4 (d, *J* = 22.7 Hz)/39.1 (d, *J* = 22.8 Hz), 38.4 (d, *J* = 23.1 Hz)/37.8 (d, *J* = 22.8 Hz), 24.7 (d, *J* = 24.3 Hz)/24.0 (d, *J* = 23.8 Hz), 19.0/18.6; ^{19}F NMR (282 MHz, $CDCl_3$): δ -146.6 (m, 1F); IR (neat): ν (cm^{-1}) 2980, 2930, 1778, 1594, 1583, 1492, 1442, 1293, 1197, 1080, 1006, 826, 642; ESI-MS: (*m/z*) 365.1 (M^++Na); HRMS calcd for $C_{17}H_{24}O_4NClF$ (M+NH_4): 360.1372, found 360.1370.

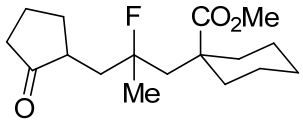


2-(5-Chloro-2-(3-chloropropyl)-2-fluoropentyl)cyclobutanone (10f). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.40-3.58 (m, 5H), 3.06-3.16 (m, 1H), 2.86-2.95 (m, 1H), 2.27-2.36 (m, 1H), 2.01-2.13 (m, 1H), 1.67-1.85 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.1, 97.3 (d, *J* = 172.8 Hz), 55.3 (d, *J* = 2.9 Hz), 45.3, 45.0, 36.5 (d, *J* = 22.5 Hz), 34.8 (d, *J* = 23.1 Hz), 34.0 (d, *J* = 23.0 Hz), 26.6 (d, *J* = 6.9 Hz), 26.4 (d, *J* = 6.2 Hz), 18.8; ^{19}F NMR (282 MHz, $CDCl_3$): δ -151.3 (m, 1F); IR (neat): ν (cm^{-1}) 2960, 2875, 1778, 1446, 1395, 1318, 1200, 1087, 934, 790, 715, 651; ESI-MS: (*m/z*) 291.1 (M^++Na); HRMS calcd for $C_{12}H_{19}Cl_2FNaO$ (M+Na): 291.0689, found 291.0697.

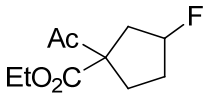


3-Fluoro-3-methyl-4-(2-oxocyclobutyl)butyl 4-oxo-4-phenylbutanoate (10g). This compound was isolated as the 1:1 mixture of two stereoisomers determined by ^{1}H

NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.97 (d, *J* = 7.2 Hz, 2H), 7.56 (t, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 7.6 Hz, 2H), 4.21-4.26 (m, 2H), 3.45-3.52 (m, 1H), 3.30 (t, *J* = 6.8 Hz, 2H), 3.05-3.15 (m, 1H), 2.86-2.95 (m, 1H), 2.74 (t, *J* = 6.8 Hz, 2H), 1.68-2.35 (m, 6H), 1.36 (d, *J* = 22.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.2, 198.0, 172.7, 136.4, 133.2, 128.6, 128.0, 95.4 (d, *J* = 167.9 Hz)/95.1 (d, *J* = 169.0 Hz), 60.1 (d, *J* = 6.8 Hz)/60.0 (d, *J* = 6.2 Hz), 55.7 (d, *J* = 1.5 Hz), 45.3/45.2, 39.4 (d, *J* = 22.7 Hz)/39.1 (d, *J* = 23.3 Hz), 38.6 (d, *J* = 22.7 Hz)/37.9 (d, *J* = 22.8 Hz), 33.3, 28.2, 24.8 (d, *J* = 22.3 Hz)/24.1 (d, *J* = 24.8 Hz), 19.0/18.6; ^{19}F NMR (282 MHz, $CDCl_3$): δ -145.2/-145.5 (2m, 1F); IR (neat): ν (cm^{-1}) 2980, 2929, 1778, 1734, 1686, 1596, 1449, 1361, 1216, 1163, 749, 691; ESI-MS: (*m/z*) 357.1 (M^++Na); HRMS calcd for $C_{19}H_{24}FO_4$ (M+H): 335.1653, found 335.1651.

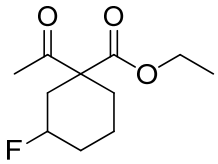


Methyl 1-(2-fluoro-2-methyl-3-(2-oxocyclopentyl)propyl)cyclohexanecarboxylate (10h). This compound was isolated as the 1:1 mixture of two diastereoisomers determined by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.68 (s, 3H), 1.70-2.46 (m, 11H), 1.23-1.46 (m, 13H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 220.8/220.6, 177.5/177.4, 97.1 (d, *J* = 170.9 Hz)/96.7 (d, *J* = 170.8 Hz), 51.6, 50.1/47.7, 45.84/45.83, 45.6 (d, *J* = 3.0 Hz)/45.1 (d, *J* = 3.8 Hz), 42.3 (d, *J* = 22.7 Hz)/40.8 (d, *J* = 22.0 Hz), 37.3/37.2, 36.2/36.0, 35.0/34.7, 31.7 (d, *J* = 24.3 Hz)/31.7 (d, *J* = 25.0 Hz), 25.7, 25.5 (d, *J* = 25.1 Hz)/23.6 (d, *J* = 25.0 Hz), 22.74/22.70, 22.6, 20.78/20.75; ^{19}F NMR (282 MHz , $CDCl_3$): δ -143.8 (m, 1F); IR (neat): ν (cm^{-1}) 2939, 2857, 1736, 1452, 1384, 1268, 1212, 1157, 1138, 1002, 921, 894, 828, 766; ESI-MS: (*m/z*) 321 (M^++Na); HRMS calcd for $C_{17}H_{27}FNaO_3$ (M+Na): 312.1836, found 321.1843.



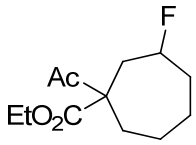
Ethyl 1-acetyl-3-fluorocyclopentanecarboxylate (11). The solution of **1d** (150 mg, 0.4 mmol) in THF (1 mL) was slowly added to a solution of NaH (17.6 mg, 60%

dispersion in mineral oil, 0.44 mmol) in THF (7 mL) at 0 ^{o}C. The reaction mixture was stirring at room temperature for 3 h. Water (10 mL) was added and the phases were separated. The aqueous phase was extracted with Et_2O (3 × 20 mL). The combined organic phases were dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane/ethyl acetate (20:1, v:v) as the eluent to give the pure product **11** as a colorless oil. Yield: 64.7 mg (80%). This compound was isolated as the mixture of two diastereoisomers in 74:26 ratio determined by ^{19}F NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.01-5.28 (m, 1H), 4.16-4.28 (m, 2H), 2.35-2.62 (m, 3H), 1.64-2.21 (m, 6H), 1.20-1.32 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 202.7/202.4, 172.6/172.3, 95.4 (d, *J* = 172.3 Hz)/95.3 (d, *J* = 173.1 Hz), 65.8/65.7, 61.71/61.74, 39.7 (d, *J* = 22.8 Hz)/39.5 (d, *J* = 22.0 Hz), 33.0 (d, *J* = 21.3 Hz)/32.7 (d, *J* = 22.1 Hz), 30.4/30.2, 26.3/25.9, 13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -170.7/-171.2 (2m, 1F); IR (neat): ν (cm^{-1}) 2981, 1716, 1432, 1358, 1300, 1260, 1192, 1154, 1098, 1079, 1035, 942, 862; ESI-MS: (*m/z*) 203 (M^{+}+H); HRMS calcd for $C_{10}H_{16}O_3F$ (M+H): 203.1078, found 203.1077.

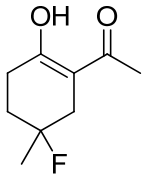


Ethyl 1-acetyl-3-fluorocyclohexanecarboxylate (12). This compound was isolated as the mixture of two stereoisomers in 82:18 ratio determined by ^{19}F NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.60-4.85 (m, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 2.15-2.52 (m, 1H), 2.11/2.09 (2s, 3H), 1.31-1.95 (m, 7H), 1.20 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 203.4, 171.5/171.4, 89.1 (d, *J* = 169.3 Hz)/88.5 (d, *J* = 168.5 Hz), 61.6/61.4, 60.8/60.7, 35.7 (d, *J* = 21.3 Hz)/34.8 (d, *J* = 20.6 Hz), 31.1 (d, *J* = 19.4 Hz)/30.5 (d, *J* = 19.9 Hz), 29.6/29.5 (d, *J* = 1.5 Hz), 25.7 (d, *J* = 1.4 Hz)/25.3, 19.1 (d, *J* = 9.1 Hz)/18.1 (d, *J* = 6.1 Hz), 13.9/13.8; ^{19}F NMR (282 MHz, $CDCl_3$): δ -173.9/-177.1 (2m, 1F); IR (neat): ν (cm^{-1}) 2951, 1737, 1713, 1468, 1450, 1358, 1224, 1141; ESI-MS: (*m/z*) 239.1 (M^{+}+Na); HRMS calcd for $C_{11}H_{17}FNaO_3$ (M+Na):

239.1054, found 239.1046.

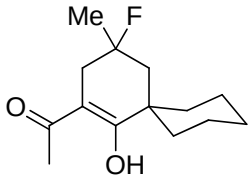


Ethyl 1-acetyl-3-fluorocycloheptanecarboxylate (13). This compound was isolated as the mixture of two stereoisomers in 63:37 ratio determined by ^{19}F NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.57-4.92 (m, 1H), 4.17-4.25 (m, 2H), 2.51-2.67 (m, 1H), 2.22-2.35 (m, 1H), 1.90-2.21 (m, 6H), 1.34-1.84 (m, 5H), 1.23-1.32 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 204.0/203.7, 172.6/172.5, 91.2 (d, *J* = 165.6 Hz)/91.0 (d, *J* = 166.2 Hz), 61.61/61.57, 60.2 (d, *J* = 10.6 Hz)/60.1 (d, *J* = 9.1 Hz), 38.2 (d, *J* = 25.0 Hz)/37.9 (d, *J* = 25.1 Hz), 35.7 (d, *J* = 21.3 Hz)/35.5 (d, *J* = 21.3 Hz), 32.5/32.4, 25.8/25.6, 24.3 (d, *J* = 12.2 Hz)/23.5 (d, *J* = 12.2 Hz), 23.4/23.1, 14.0/13.9; ^{19}F NMR (282 MHz, $CDCl_3$): δ -162.8/-164.1 (2m, 1F); IR (neat): ν (cm^{-1}) 2932, 2865, 1763, 1712, 1472, 1456, 1362, 1335, 1251, 1203, 1179, 1151, 1120, 1076, 1051, 1003, 962, 933, 600; ESI-MS: (*m/z*) 253 (M^++Na); HRMS calcd for $C_{12}H_{19}FNaO_3$ (M+Na): 253.1210, found 253.1210.

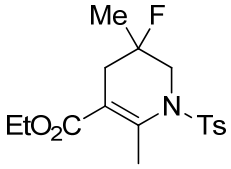


1-(5-Fluoro-2-hydroxy-5-methylcyclohex-1-en-1-yl)ethanone (14). The solution of **3a** (43.6 mg, 0.2 mmol) in THF (4 mL) was added slowly into the solution of potassium *tert*-butoxide (56.1 mg, 0.5 mmol) in THF (6 mL) at 0 ^{o}C. The resulting mixture was allowed to warm up to room temperature and stirred for 12 h. The reaction was quenched by slow addition of 2 mL of 1 N aqueous HCl. The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane/ethyl acetate (50:1, v:v) as the eluent to give the pure product **14** as a colorless

oil. Yield: 23.4 mg (68%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 15.93 (br s, 1H), 2.59-2.69 (m, 2H), 2.30-2.53 (m, 2H), 2.11 (s, 3H), 2.00-2.08 (m, 1H), 1.66-1.83 (m, 1H), 1.49 (d, *J* = 20.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.4, 181.1, 103.5, 92.2 (d, *J* = 167.9 Hz), 36.1 (d, *J* = 24.2 Hz), 31.9 (d, *J* = 22.7 Hz), 27.6 (d, *J* = 5.9 Hz), 26.6 (d, *J* = 24.1 Hz), 24.8; ^{19}F NMR (282 MHz, $CDCl_3$): δ -147.9 (m, 1F); IR (neat): ν (cm^{-1}) 2979, 2936, 1612, 1417, 1381, 1309, 1249, 1209, 1097, 946, 907, 866, 837, 756; ESI-MS: (*m/z*) 195.1 (M^++Na); HRMS calcd for $C_9H_{13}FNaO_2$ (M+Na): 195.0792, found 195.0794.

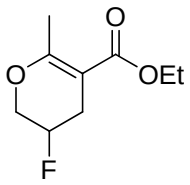


1-(4-Fluoro-1-hydroxy-4-methylspiro[5.5]undec-1-en-2-yl)ethanone (15). Compound **15** is in equilibrium with its ketone form in about 90:10 ratio in $CDCl_3$ at room temperature determined by ^{1}H NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 16.67 (s, 1H), 2.62-2.75 (m, 1H), 2.32-2.56 (m, 2H), 2.14 (s, 3H), 1.91-2.01 (m, 1H), 1.59-1.86 (m, 5H), 1.23-1.55 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 188.8, 102.1 (d, *J* = 1.5 Hz), 92.5 (d, *J* = 167.8 Hz), 40.7, 40.4 (d, *J* = 20.5 Hz), 36.5 (d, *J* = 24.3 Hz), 36.3, 32.8 (d, *J* = 4.5 Hz), 27.9 (d, *J* = 25.1 Hz), 25.4, 24.8, 21.1, 21.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ -145.7 (m, 1F); IR (neat): ν (cm^{-1}) 2926, 2859, 1761, 1730, 1699, 1664, 1596, 1498, 1452, 1378, 1248, 1149, 1124, 954, 870; ESI-MS: (*m/z*) 241 (M^++H); HRMS calcd for $C_{14}H_{21}FNaO_2$ (M+Na): 263.1418, found 263.1419.



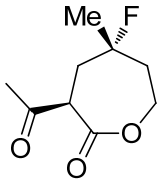
Ethyl 5-fluoro-2,5-dimethyl-1-tosyl-1,4,5,6-tetrahydropyridine-3-carboxylate (16). A round-bottom flask was charged with **1l** (46.5 mg, 0.12 mmol), followed by the addition of toluene (2 mL), *p*-toluenesulfonic acid monohydrate (2.4 mg, 0.1 equiv)

and 3Å molecular sieves. The reaction mixture was then refluxed (~ 120 ^{o}C) with stirring for 12 h. Water (5 mL) was added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane/ethyl acetate (8:1, v:v) as the eluent to give the pure product **16** as a white solid. Mp: 88-89 ^{o}C. Yield: 34.6 mg (81%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J* = 8.4 Hz, 2H), 7.30 (t, *J* = 8.4 Hz, 2H), 4.35 (ddd, *J* = 13.2, 7.6, 1.6 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.33 (dd, *J* = 28.0, 13.6 Hz, 1H), 2.67 (t, *J* = 18.4 Hz, 1H), 2.31-2.50 (m, 7H), 1.50 (d, *J* = 20.4 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.5, 145.5, 144.0, 138.4, 129.7, 127.1 (d, *J* = 2.2 Hz), 110.1, 89.7 (d, *J* = 172.3 Hz), 60.4, 53.3 (d, *J* = 24.3 Hz), 36.8 (d, *J* = 24.3 Hz), 24.2 (d, *J* = 24.3 Hz), 21.5, 18.6, 14.2; ^{19}F NMR (282 MHz, $CDCl_3$): δ -145.3 (m, 1F); IR (KBr): ν (cm^{-1}) 2981, 2936, 1705, 1612, 1447, 1384, 1346, 1258, 1219, 1163, 1090, 941, 844, 814, 730, 712, 654; ESI-MS: (*m/z*) 356 (M^{+}+H); HRMS calcd for $C_{17}H_{23}FNO_4S$ (M+H): 356.1326, found 356.1324.



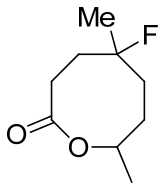
Ethyl 3-fluoro-6-methyl-3,4-dihydro-2*H*-pyran-5-carboxylate (17). At 0 ^{o}C a round-bottom flask was charged with **1f** (49.7 mg, 0.2 mmol), potassium carbonate (138 mg, 1 mmol) and methanol (10 mL). The reaction temperature was maintained at 0 ^{o}C while the heterogeneous mixture was stirred for 1 h. Water (10 mL) was added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phase was dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the residue was added to a solution of *p*-toluenesulfonic acid monohydrate (40 mg, 0.2 mmol) in toluene (20 mL). The reaction mixture was then refluxed with stirring for 2 h. Water was added and the

phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane/ethyl acetate (10:1, v:v) as the eluent to give the pure product **17** as a colorless oil. Yield: 24.8 mg (66%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.93-5.06 (m, 1H), 4.20-4.27 (m, 1H), 4.17 (q, *J* = 6.8 Hz, 2H), 3.85-3.97 (m, 1H), 2.47-2.74 (m, 2H), 2.28 (s, 3H), 1.28 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.8, 164.4, 98.1, 83.2 (d, *J* = 172.2 Hz), 66.9 (d, *J* = 21.4 Hz), 59.9, 27.3 (d, *J* = 22.5 Hz), 19.8, 14.3; ^{19}F NMR (282 MHz, $CDCl_3$): δ -182.9 (m, 1F); IR (neat): ν (cm^{-1}) 2959, 2929, 1733, 1715, 1646, 1287, 1256, 1102, 1059, 1028, 799; EIMS: *m/z* (rel intensity) 188 (M^+, 35), 159 (29), 149 (30), 143 (100), 139 (11), 116 (20), 97 (27), 55 (20), 43 (51); HRMS calcd for $C_9H_{13}FO_3$ (M): 188.0849, found 188.0853.



(3*R,5*S**)-3-Acetyl-5-fluoro-5-methyloxepan-2-one (18).** A round-bottom flask was charged with **1h** (300 mg, 0.92 mmol), Pd/C (218 mg, 0.09 mmol) and methanol (8 mL). A hydrogen atmosphere (1 atm) was applied under which the reaction mixture was stirred for 6 h. The resulting heterogeneous mixture was filtered and the precipitate was washed with CH_2Cl_2. The combined organic phases were washed with brine and dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was added to a solution of *p*-toluenesulfonic acid monohydrate (18.4 mg, 0.09 mmol) in CH_2Cl_2 (36 mL). The reaction mixture was then refluxed with stirring for 7 h. Water (20 mL) was added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was purified by column chromatography on silica

gel with hexane/ethyl acetate (10:1, v:v) as the eluent to give the pure product **18** as a white solid. Mp: 116-117 ^{o}C. Yield: 93.5 mg (54%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.59 (dd, *J* = 13.6, 11.6 Hz, 1H), 4.23 (dq, *J* = 13.6, 2.4 Hz, 1H), 4.07 (d, *J* = 12.0 Hz, 1H), 2.42-2.48 (m, 1H), 2.30 (s, 3H), 2.09-2.20 (m, 1H), 1.76-2.05 (m, 2H), 1.48 (d, *J* = 21.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 201.4, 172.5, 92.9 (d, *J* = 169.7 Hz), 63.5, 49.3 (d, *J* = 2.6 Hz), 39.7 (d, *J* = 22.4 Hz), 35.5 (d, *J* = 22.4 Hz), 29.5, 28.1 (d, *J* = 23.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ -150.8 (m, 1F); IR (KBr): ν (cm^{-1}) 2992, 2948, 2927, 1729, 1711, 1485, 1334, 1288, 1153, 1120, 1080, 1056, 973, 856, 776, 741, 603; ESI-MS: (*m/z*) 211 (M^{+}+Na); HRMS calcd for $C_9H_{13}FNaO_3$ (M+Na): 211.0741, found 211.0743. The stereochemistry was confirmed by 2D NOESY experiments.



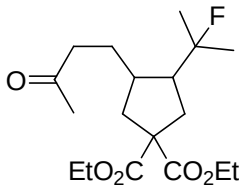
5-Fluoro-5,8-dimethyloxocan-2-one (19). At -10 ^{o}C a round-bottom flask was charged with sodium borohydride (45.5 mg, 1.2 mmol), H_2O (4 mL) and THF (12 mL), followed by very slow addition of a solution of **3a** (440 mg, 2.0 mmol) in THF (8 mL). The reaction mixture was stirred for 1 h at this temperature. Water was added and the phases were separated. The aqueous phase was extracted with CH_2Cl_2. The removal of solvent under reduced pressure gave the crude reduction product.

The crude reduction product was added to a solution of 1 M aqueous sodium hydroxide (4 mL, 4.0 mmol) and methanol (20 mL). The reaction mixture was stirred at room temperature for 6 h. The reaction was quenched by slow addition of 10 mL of 1 N aquous HCl. The aqueous phase was extracted with CH_2Cl_2. The combined organic phase was dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with methylene chloride/methanol (30:1, v:v) as the eluent to give 4-fluoro-7-hydroxy-4-methyloctanoic acid as a colorless oil. Yield: 334 mg (87%). ^{1}H

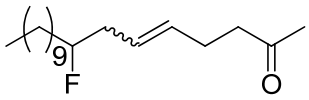
NMR (400 MHz, $CDCl_3$): δ 6.91 (br s, 2H), 3.74-3.82 (m, 1H), 2.40-2.45 (m, 2H), 1.45-2.02 (m, 6H), 1.28/1.27 (2d, *J* = 21.6 Hz, 3H), 1.18/1.17 (2d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.3, 96.3 (d, *J* = 169.0 Hz)/96.2 (d, *J* = 167.3 Hz), 68.20/68.18, 35.6/35.3, 34.2 (d, *J* = 22.4 Hz)/33.9 (d, *J* = 23.1 Hz), 32.7 (d, *J* = 5.2 Hz)/32.6 (d, *J* = 5.3 Hz), 28.4 (d, *J* = 5.3 Hz)/28.3 (d, *J* = 5.7 Hz), 23.9 (d, *J* = 20.4 Hz)/23.7 (d, *J* = 20.7 Hz), 23.2/23.1; ^{19}F NMR (282 MHz, $CDCl_3$): δ -147.0 (m, 1F); IR (neat): ν (cm^{-1}) 2973, 1713, 1452, 1417, 1384, 1294, 936, 885; ESI-MS: (*m/z*) 215.1 (M^++Na); HRMS calcd for $C_9H_{17}FNaO_3$ (M+Na): 215.1054, found 215.1052.

To the solution of the above hydroxy acid (96 mg, 0.5 mmol) in THF (3 mL) was added triethylamine (43 μl, 0.6 mmol) and 2,4,6-trichlorobenzoyl chloride (86 μl, 0.6 mmol). The resulting solution was stirred at room temperature for 2 h and then diluted with toluene (20 mL). This mixture was added dropwise via a syringe pump to the solution of DMAP (110 mg, 0.9 mmol) in toluene (50 mL) over a period of 12 h. After the addition was complete, the resulting solution was heated at reflux for 12 h. The mixture was then cooled down to room temperature and concentrated in vacuo. The residue was diluted with ethyl acetate, then washed successively with 1 N aqueous HCl, saturated aqueous $NaHCO_3$ and brine, and then dried over anhydrous Na_2SO_4. After the removal of solvent under reduced pressure, the crude product was purified by column chromatography on silica gel with hexane/ethyl acetate (40:1, v:v) as the eluent to give the pure product **19** as a colorless oil. Yield: 67.9 mg (78%). Compound **19** was isolated as the 1:1 mixture of two stereoisomers determined by ^1H NMR. ^1H NMR (400 MHz, $CDCl_3$): δ 4.71-4.84 (m, 1H), 2.87 (dt, *J* = 13.2, 3.6 Hz, 0.5H), 2.35-2.60 (m, 2H), 2.10-2.25 (m, 0.5H), 1.55-2.05 (m, 5H), 1.43/1.38 (2d, *J* = 16.8 Hz, 3H), 1.35 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.5/176.2, 97.0 (d, *J* = 177.0 Hz)/95.3 (d, *J* = 182.1 Hz), 76.2/75.0 (d, *J* = 2.4 Hz), 39.2 (d, *J* = 23.2 Hz)/35.2 (d, *J* = 25.2 Hz), 37.3 (d, *J* = 28.1 Hz)/30.1 (d, *J* = 25.0 Hz), 33.4/28.0 (d, *J* = 2.3 Hz), 33.2 (d, *J* = 13.4 Hz)/29.7 (d, *J* = 11.8 Hz), 32.4/32.3, 25.9 (d, *J* = 23.5 Hz)/21.3 (d, *J* = 21.1 Hz); ^{19}F NMR (282 MHz, $CDCl_3$) δ -127.2/-154.3 (2m, 1F); IR (neat): ν (cm^{-1}) 2980, 2937, 1729, 1458, 1379, 1343, 1282, 1260, 1132, 1072, 975, 871; ESI-MS: (*m/z*) 197.1 (M^++Na); HRMS calcd for $C_9H_{15}FNaO_2$ (M+Na):

197.0948, found 197.0952.



Diethyl 3-(2-fluoropropan-2-yl)-4-(3-oxobutyl)cyclopentane-1,1-dicarboxylate (21). This compound was isolated as the mixture of two stereoisomers in 81:19 ratio determined by ^{19}F NMR. Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.08-4.18 (m, 4H), 2.12-2.54 (m, 4H), 1.79-2.19 (m, 8H), 1.41 (d, *J* = 20.8 Hz, 3H), 1.33 (d, *J* = 22.0 Hz, 3H), 1.16-1.30 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.9/208.5, 172.9/172.2, 172.6/171.9, 95.3 (d, *J* = 170.7 Hz)/96.7 (d, *J* = 166.3 Hz), 61.5, 57.5/58.7, 52.1 (d, *J* = 20.7 Hz)/53.3 (d, *J* = 22.0 Hz), 41.8/42.0, 39.7/39.5, 37.3/39.3, 32.4 (d, *J* = 2.7 Hz)/36.1 (d, *J* = 8.6 Hz), 29.8/29.2, 27.7 (d, *J* = 25.7 Hz)/26.7 (d, *J* = 24.8 Hz), 26.2 (d, *J* = 24.4 Hz)/23.7 (d, *J* = 23.9 Hz), 22.3, 13.8; ^{19}F NMR (282 MHz, $CDCl_3$): δ -139.5/-148.4 (2m, 1F); IR (neat): ν (cm^{-1}) 2982, 2935, 1731, 1447, 1388, 1367, 1252, 1179, 1098, 1033, 863; ESI-MS: (*m/z*) 367.1 (M^++Na); HRMS calcd for $C_{18}H_{29}FNaO_5$ (M+Na): 367.1891, found 367.1900.

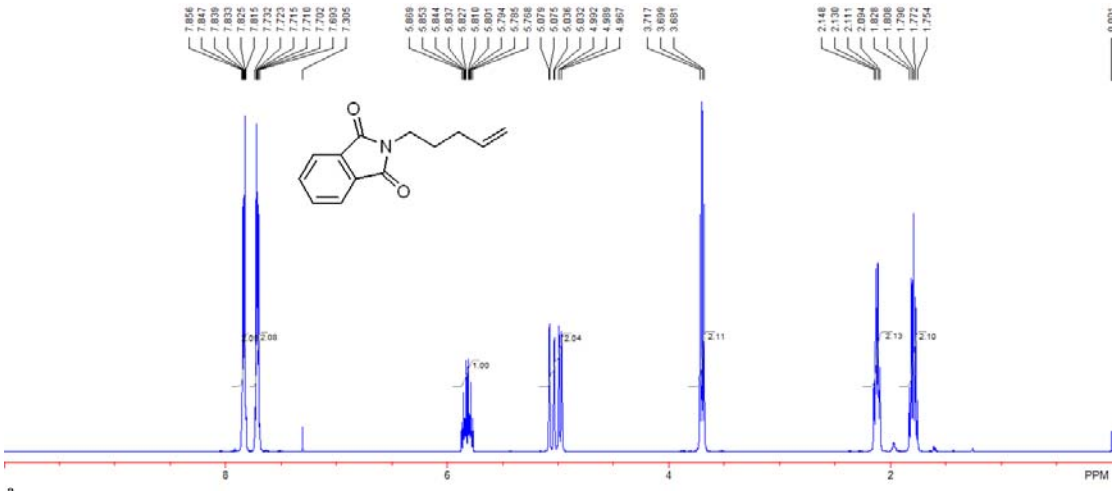


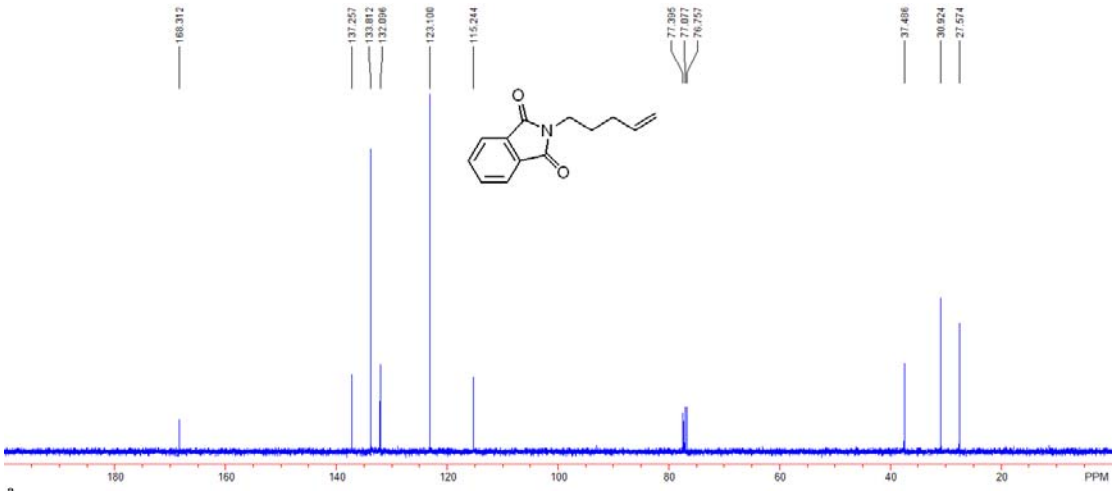
8-Fluorooctadec-5-en-2-one (23). This compound was isolated as the mixture of two stereoisomers in about 10:1 ratio determined by HPLC. White solid, 45-47 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.41-5.54 (m, 2H), 4.35-4.53 (m, 1H), 2.47-2.52 (m, 2H), 2.19-2.40 (m, 4H), 2.13 (s, 3H), 1.26-1.66 (m, 18H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.2, 131.6/130.5, 125.7 (d, *J* = 5.7 Hz)/125.2 (d, *J* = 5.0 Hz), 93.8 (d, *J* = 168.3 Hz), 43.2, 38.2 (d, *J* = 22.0 Hz)/32.9 (d, *J* = 21.8 Hz), 34.7 (d, *J* = 18.0 Hz)/34.5 (d, *J* = 20.3 Hz), 31.8, 30.0/29.9, 29.55, 29.52, 29.47, 29.41, 29.3, 26.7, 25.0 (2d, *J* = 3.4 Hz), 22.6/21.6, 14.0; ^{19}F NMR (282 MHz, $CDCl_3$): δ -180.0 (m, 1F); IR (KBr): ν (cm^{-1}) 2955, 2922, 2850, 1714, 1464, 1262, 1090, 1027,

968, 803; ESI-MS: (*m/z*) 307.3 (M^++Na); HRMS calcd for $C_{18}H_{33}FNaO$ (M+Na): 307.2408, found 307.2404.

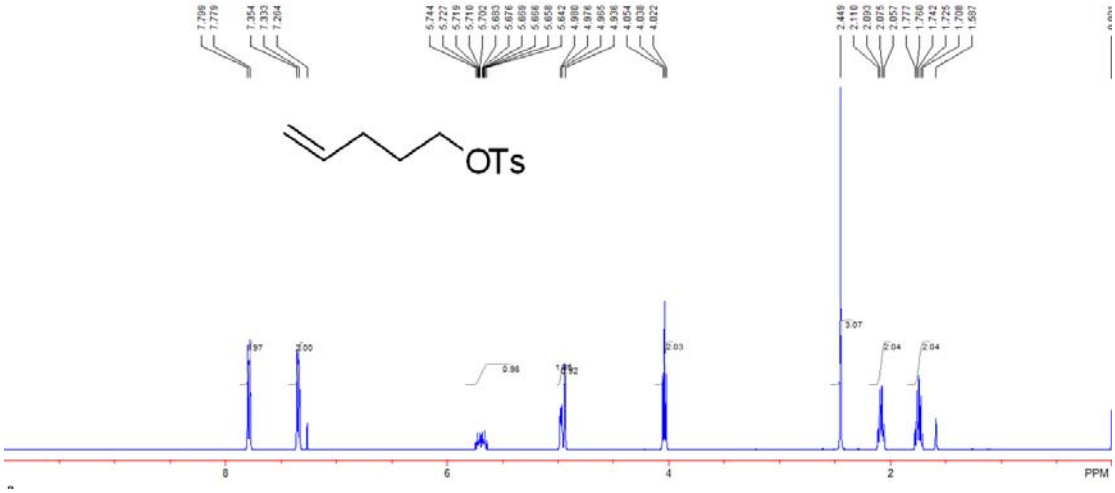
5. ^{1}H and ^{13}C NMR Spectra of Substrates.

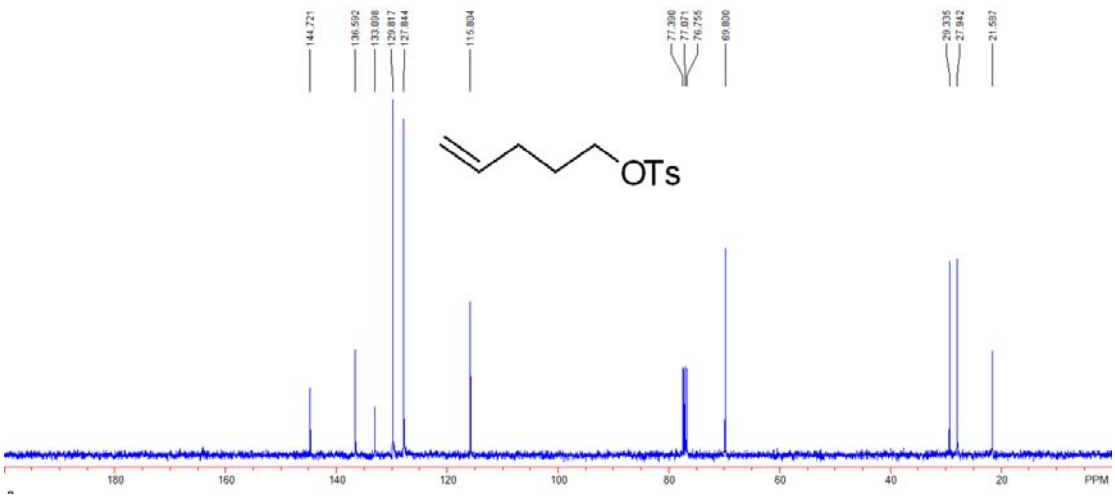
Compound **A-1a**



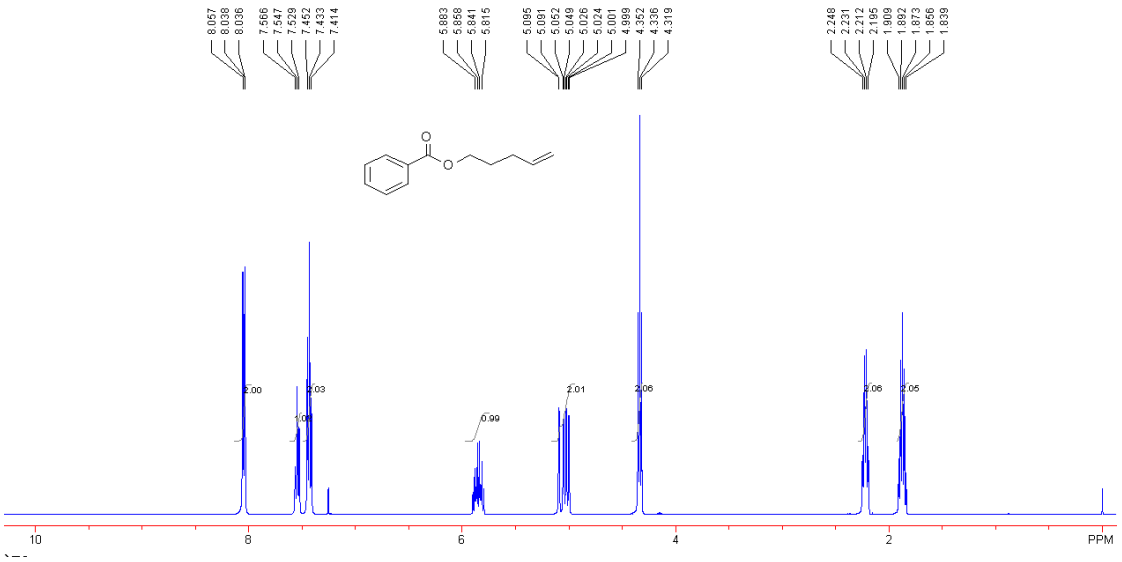


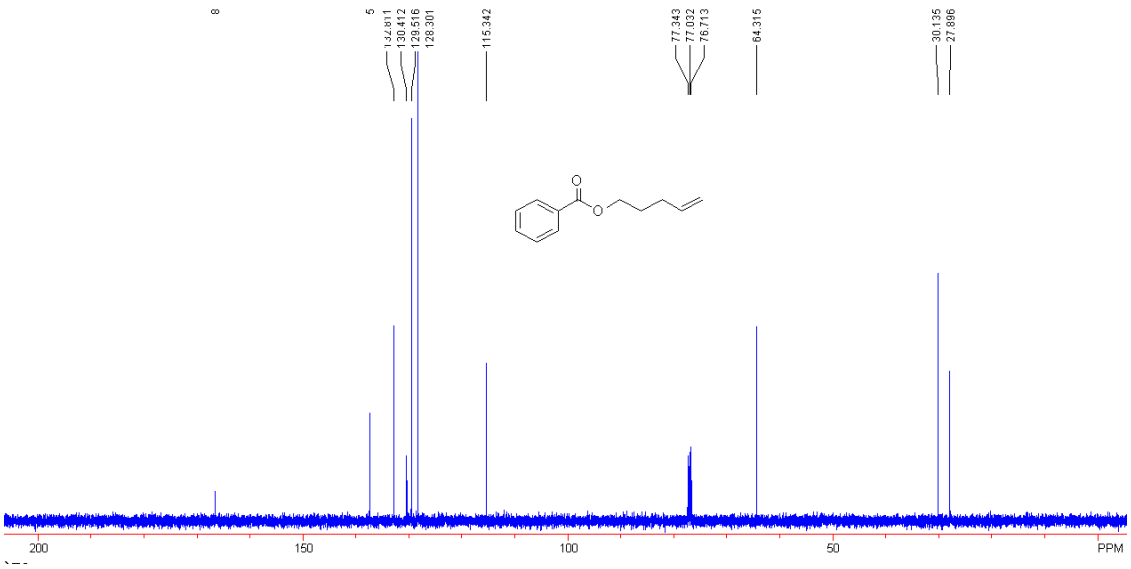
Compound **A-1b**



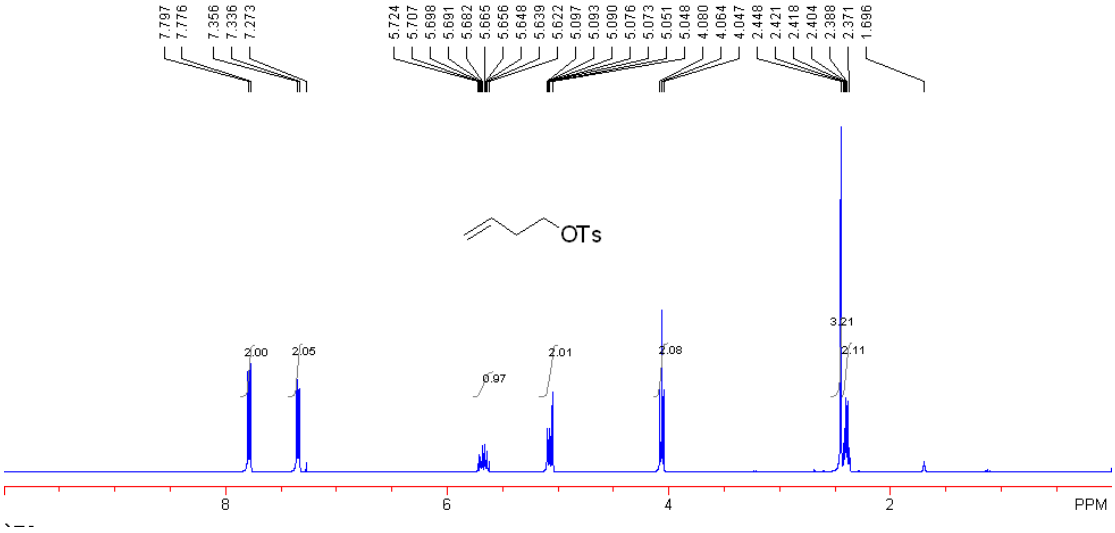


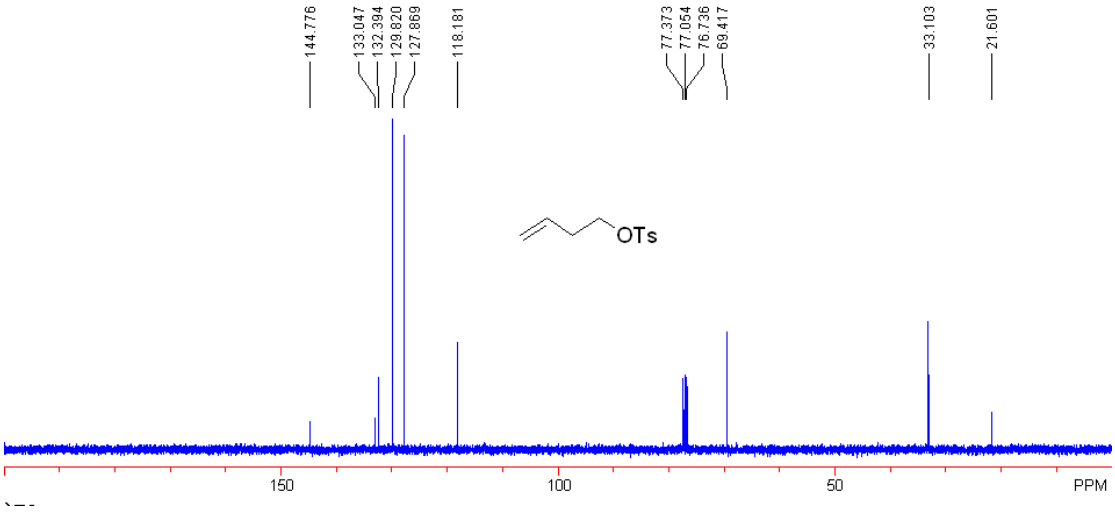
Compound **A-1c**



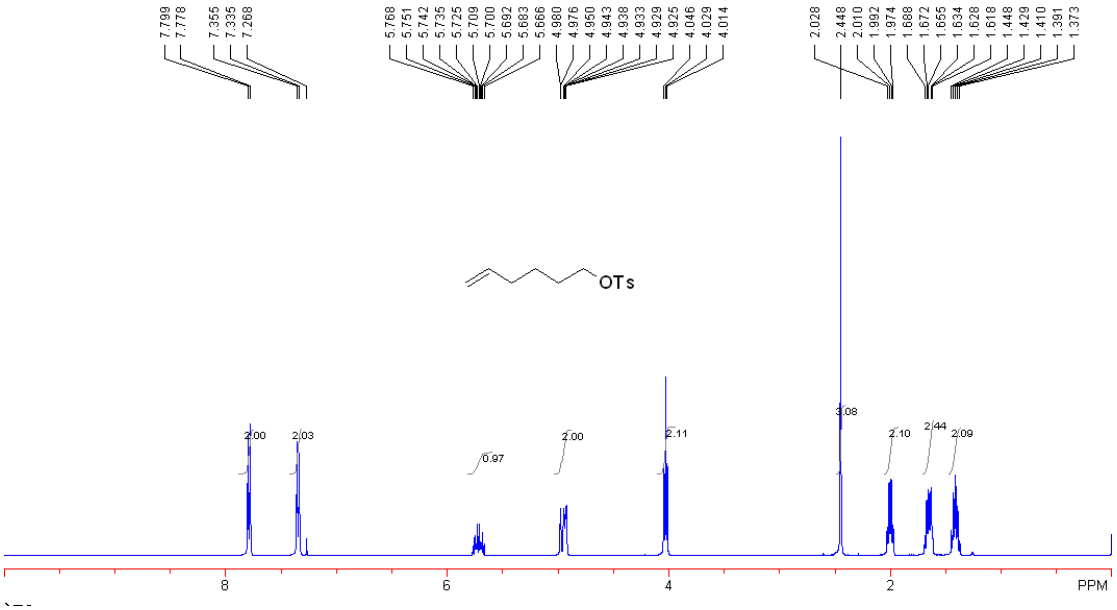


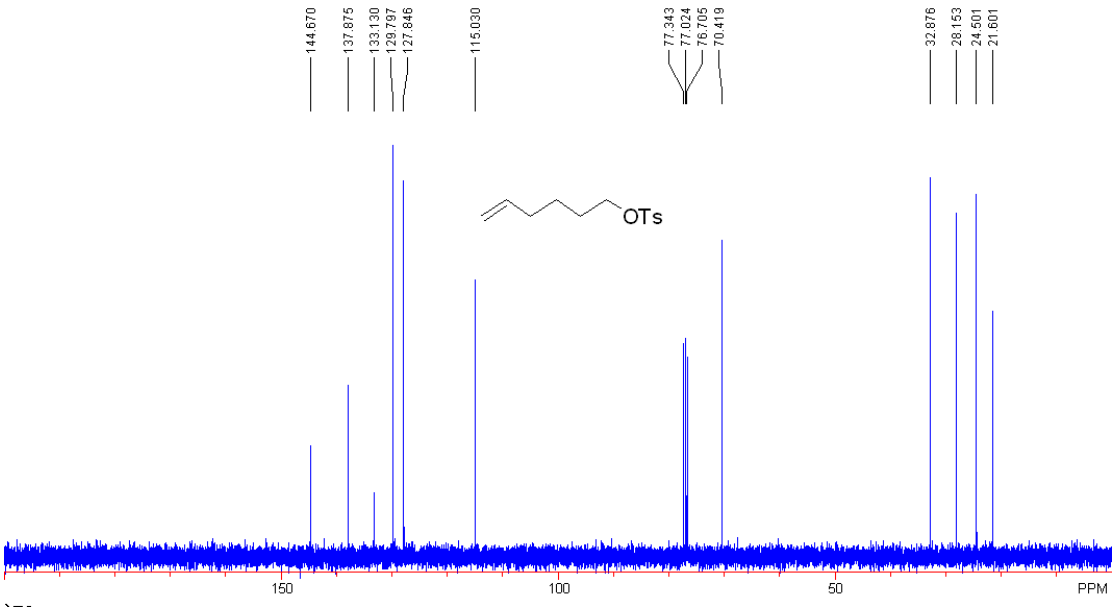
Compound **A-1d**



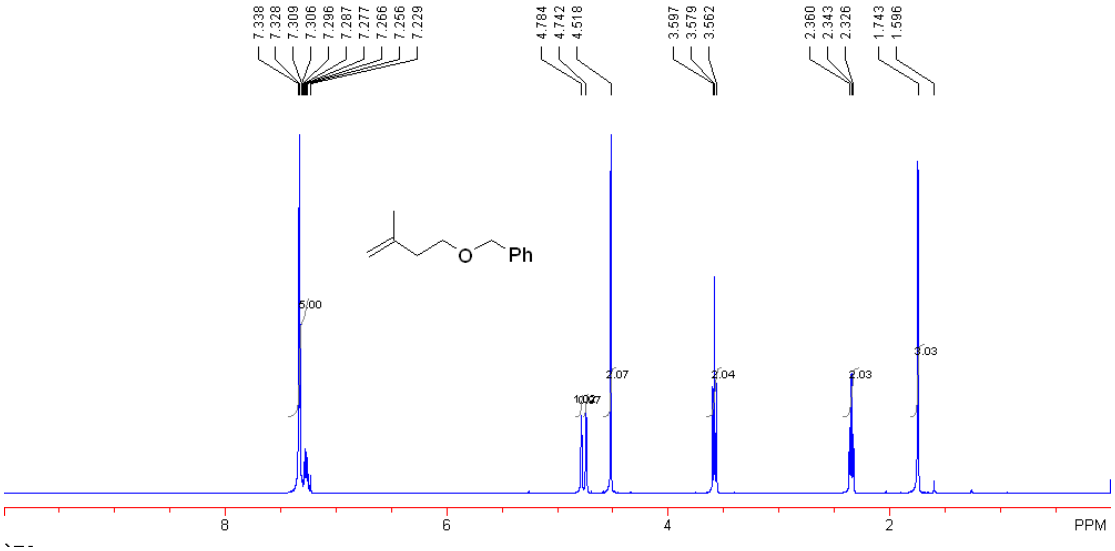


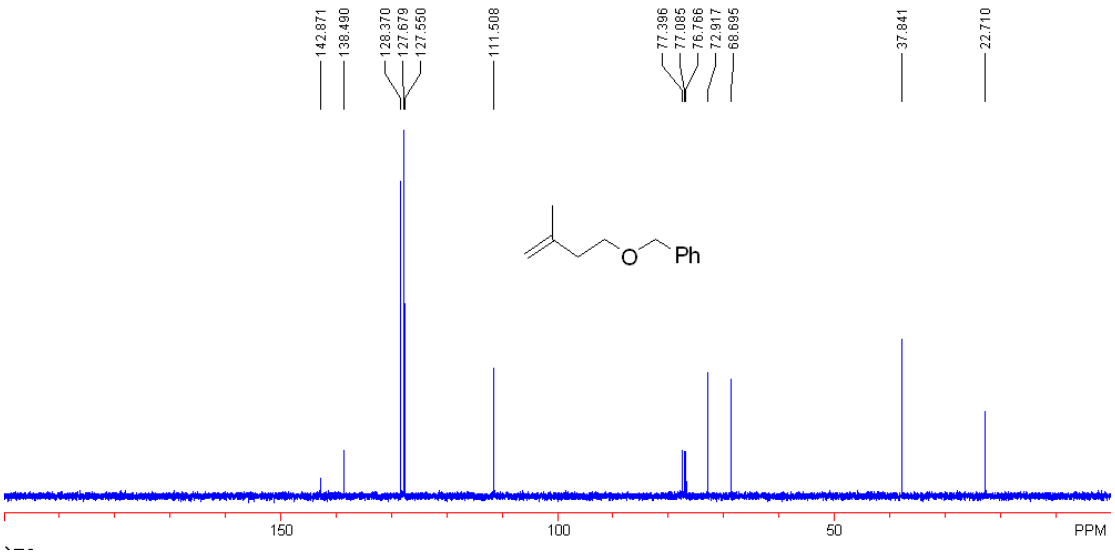
Compound **A-1e**



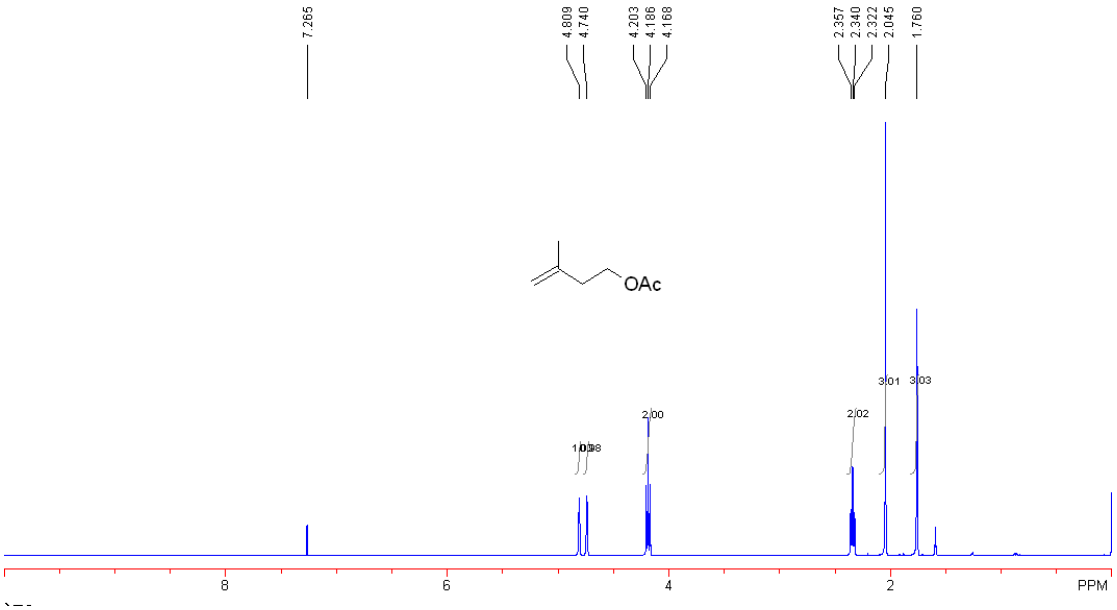


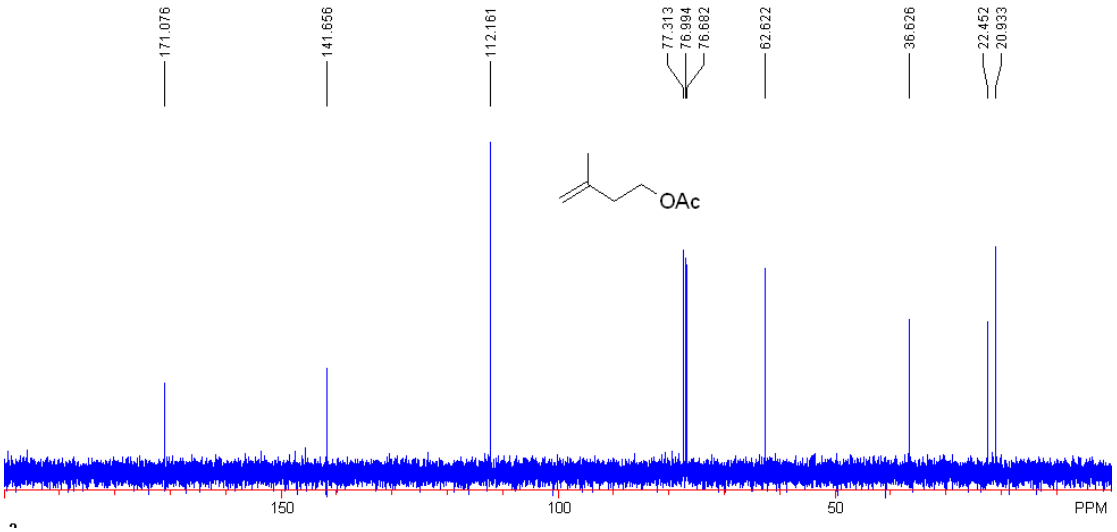
Compound **A-1h**



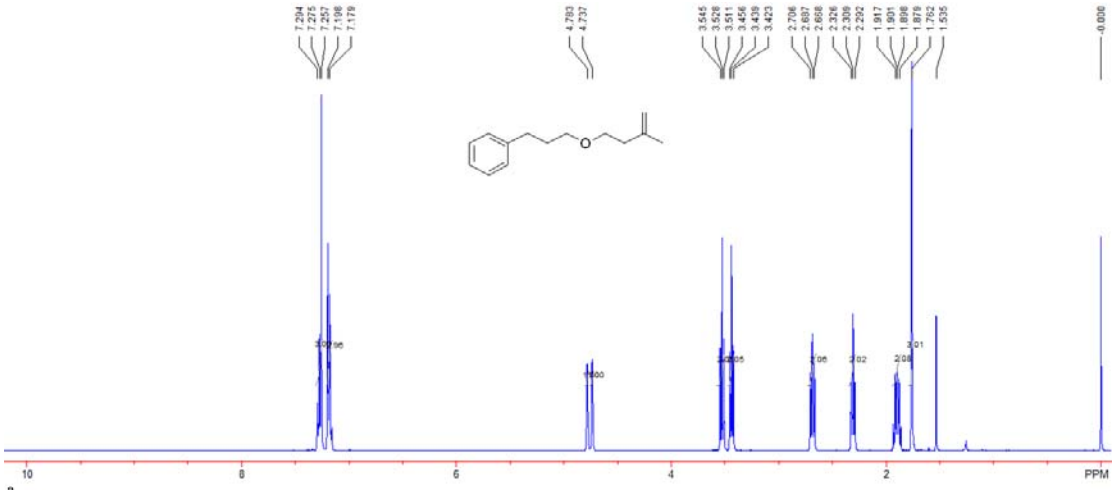


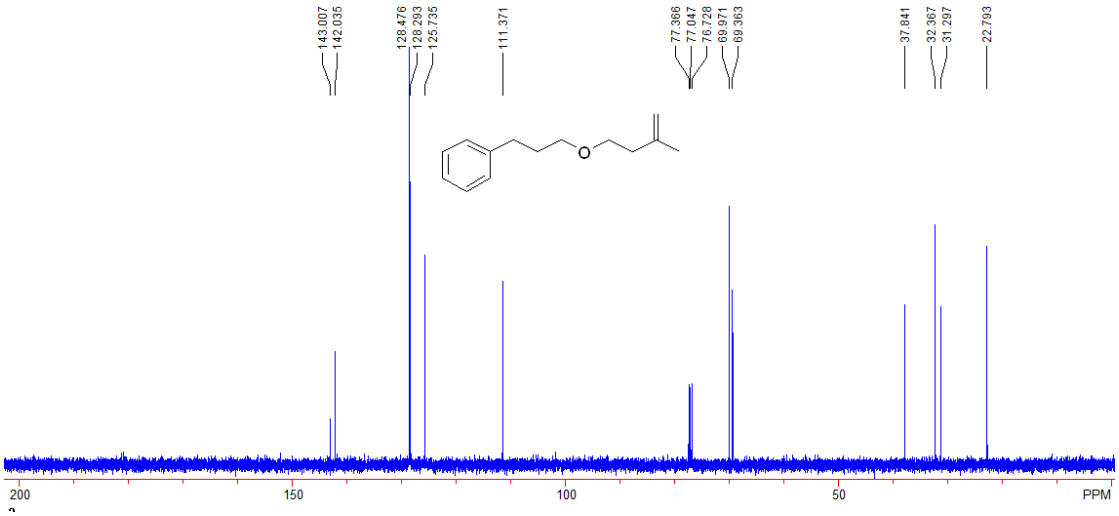
Compound **A-1i**



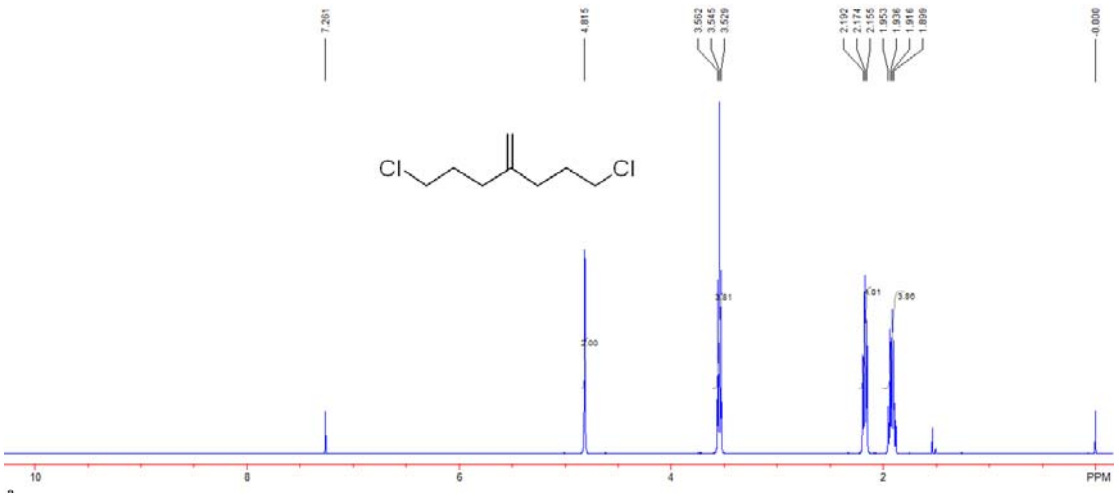


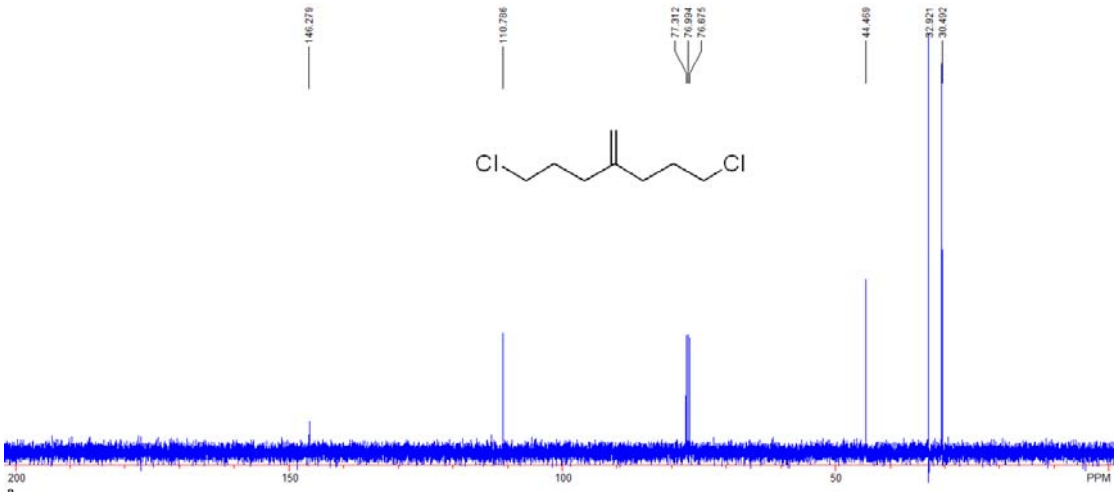
Compound **A-1j**



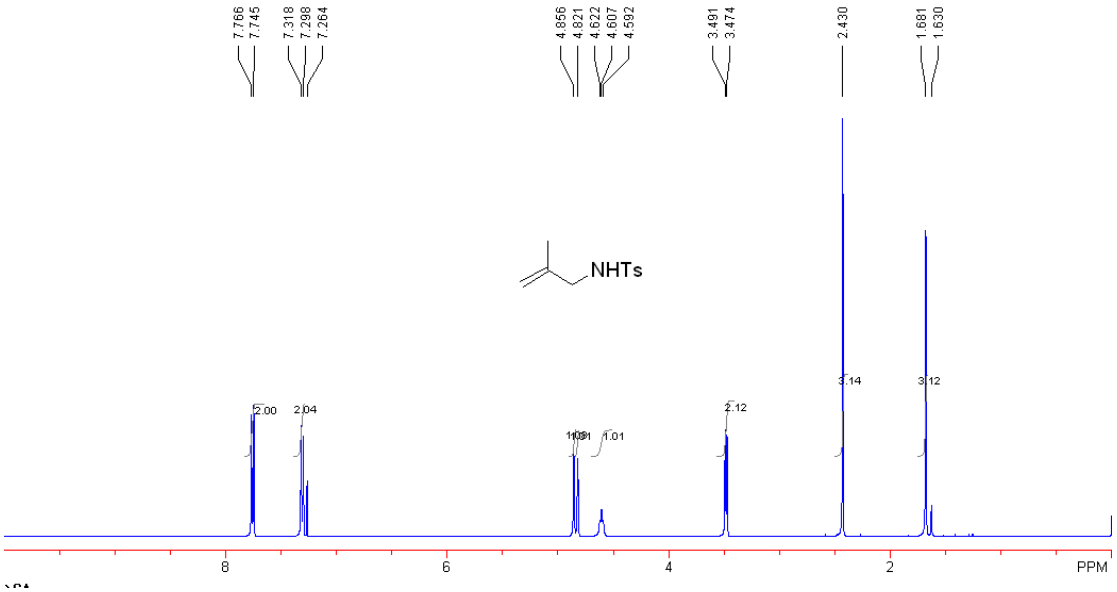


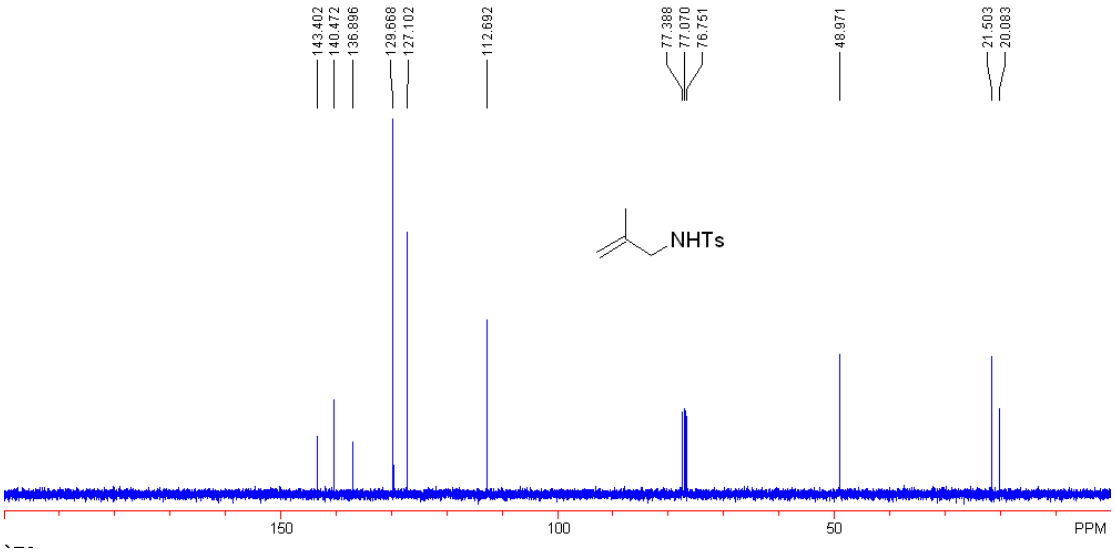
Compound **A-1k**



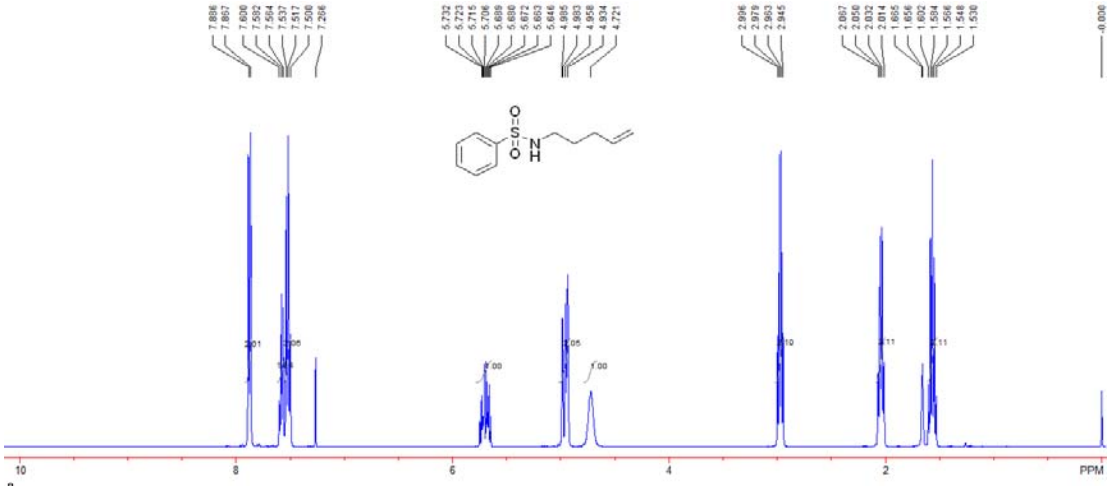


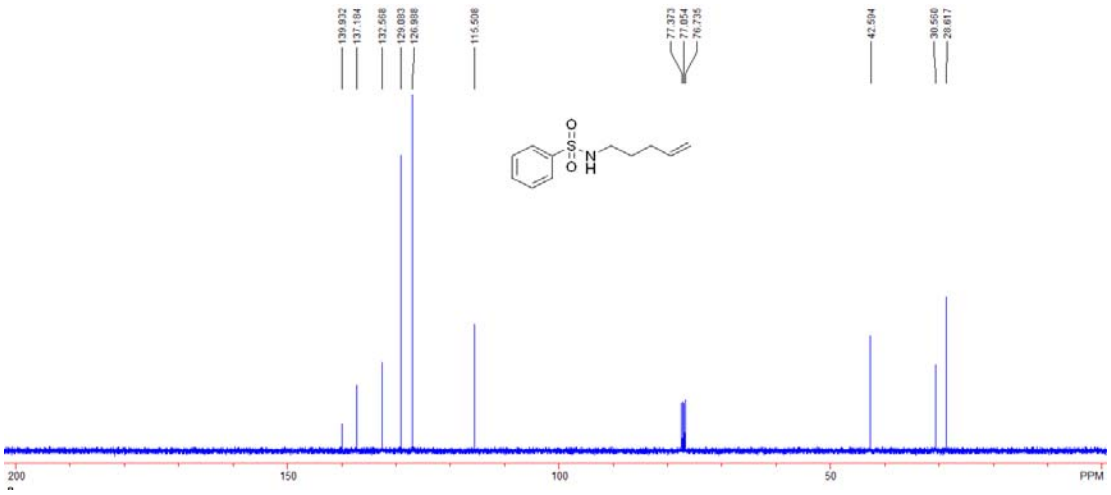
Compound **A-1l**



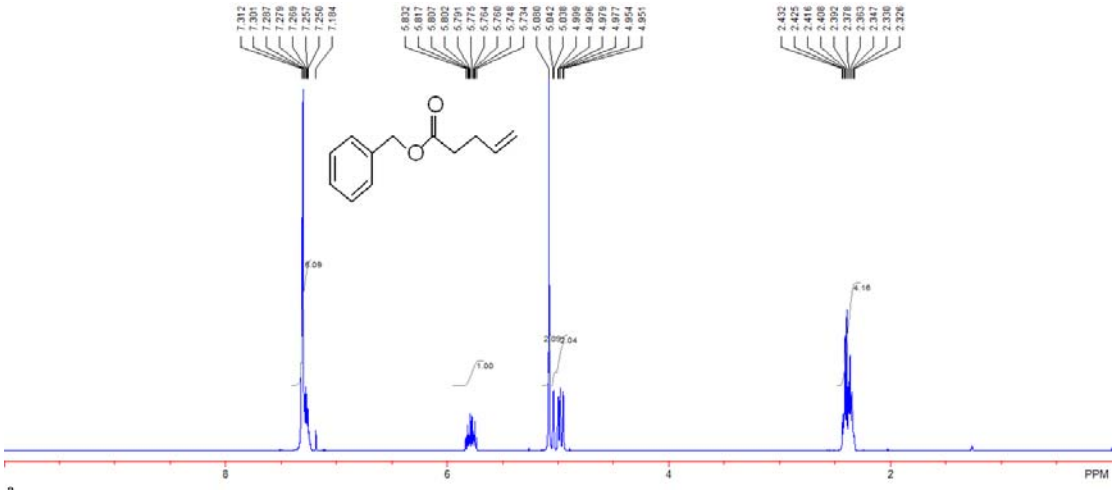


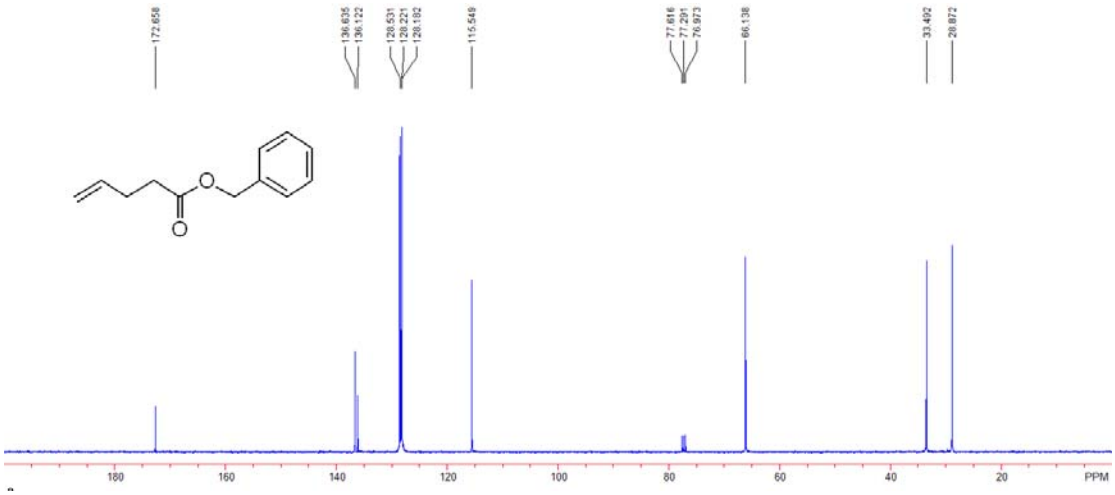
Compound **A-2e**





Compound **A-2i**





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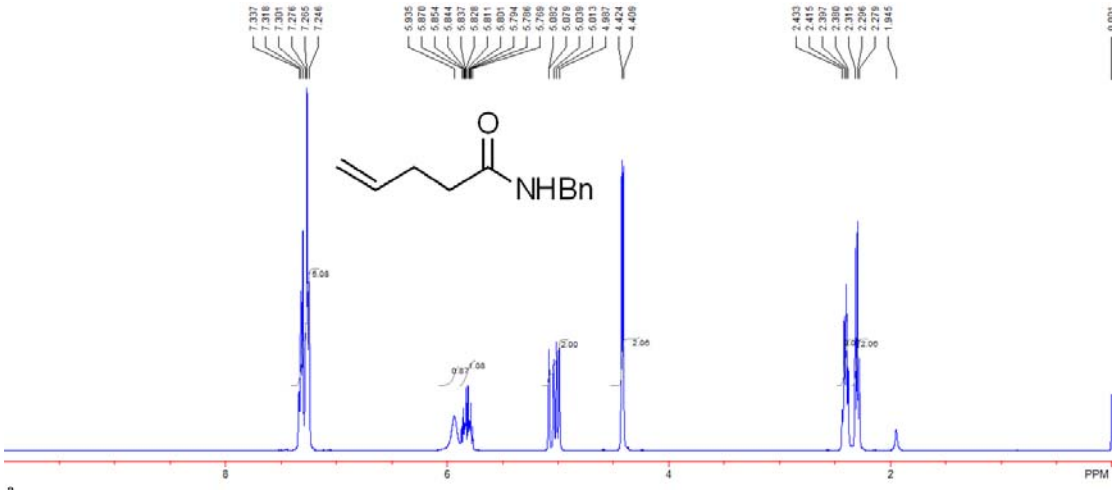
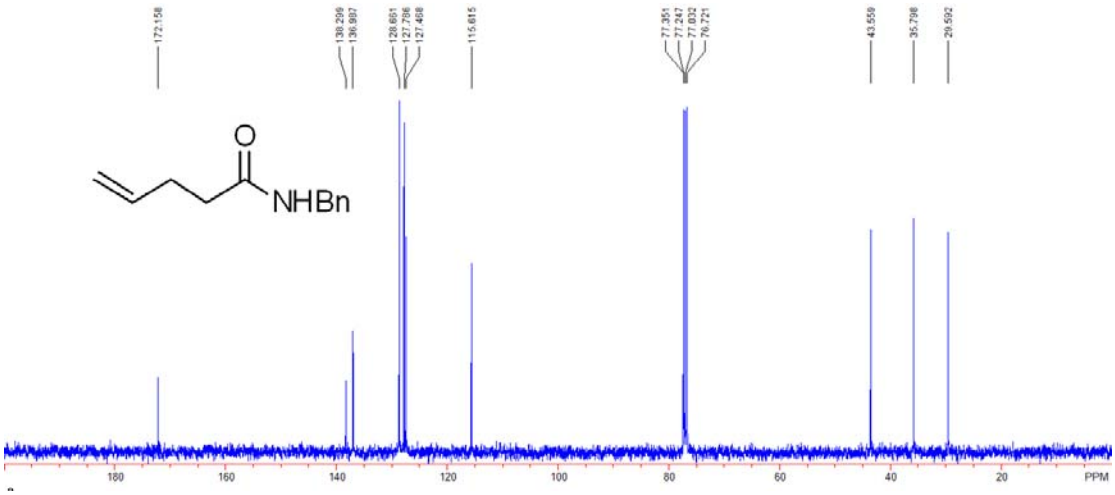
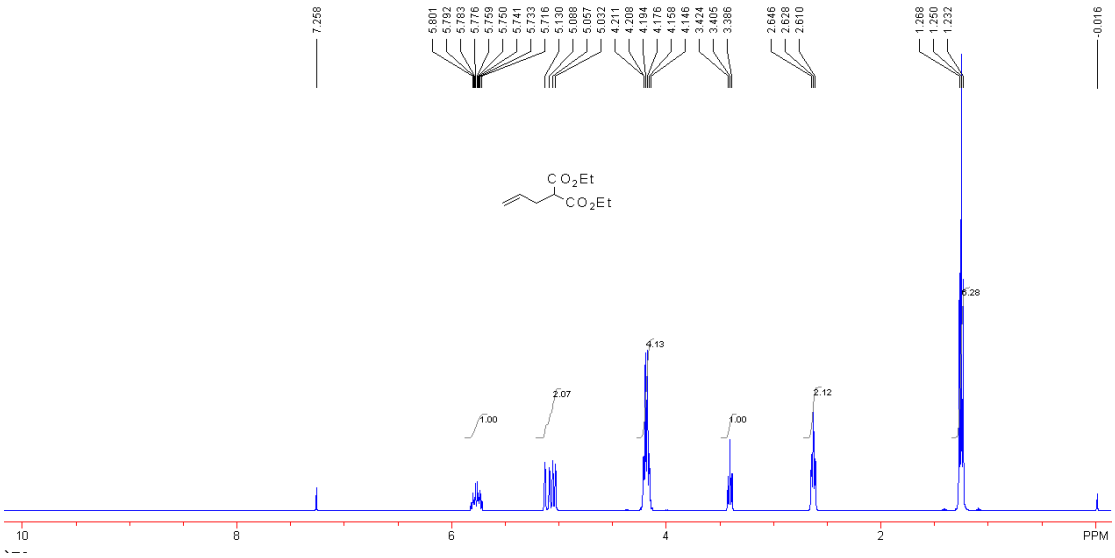
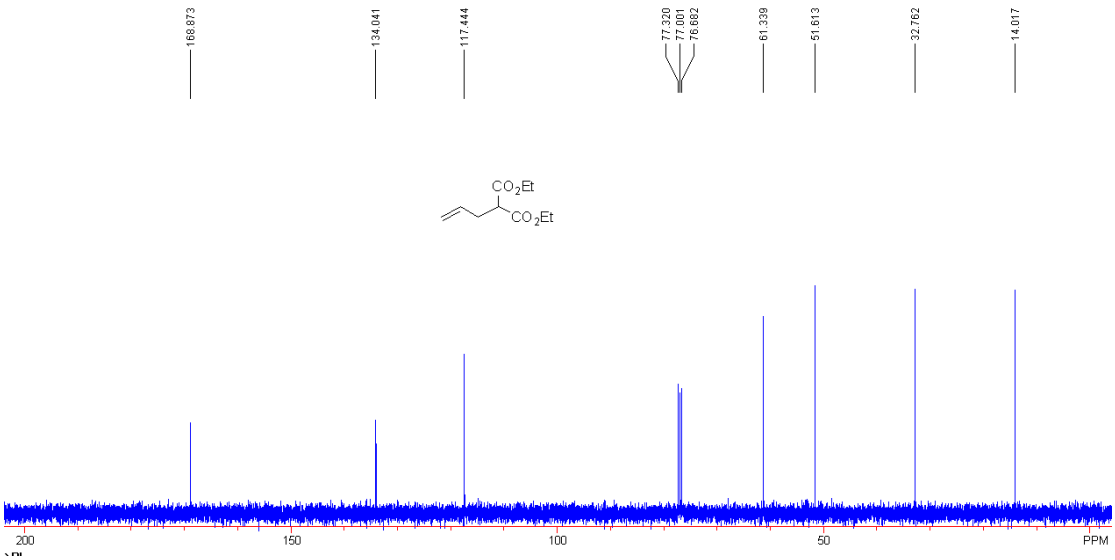


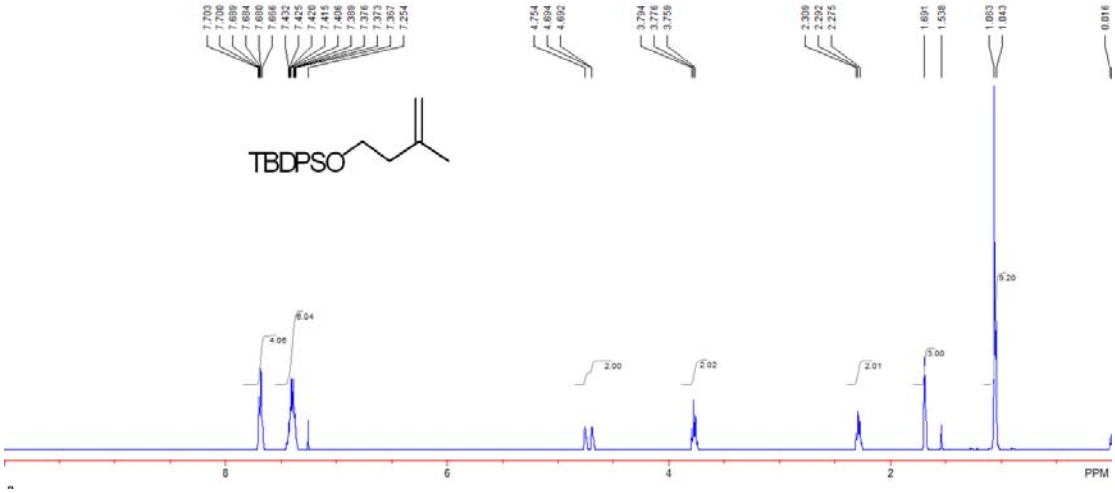


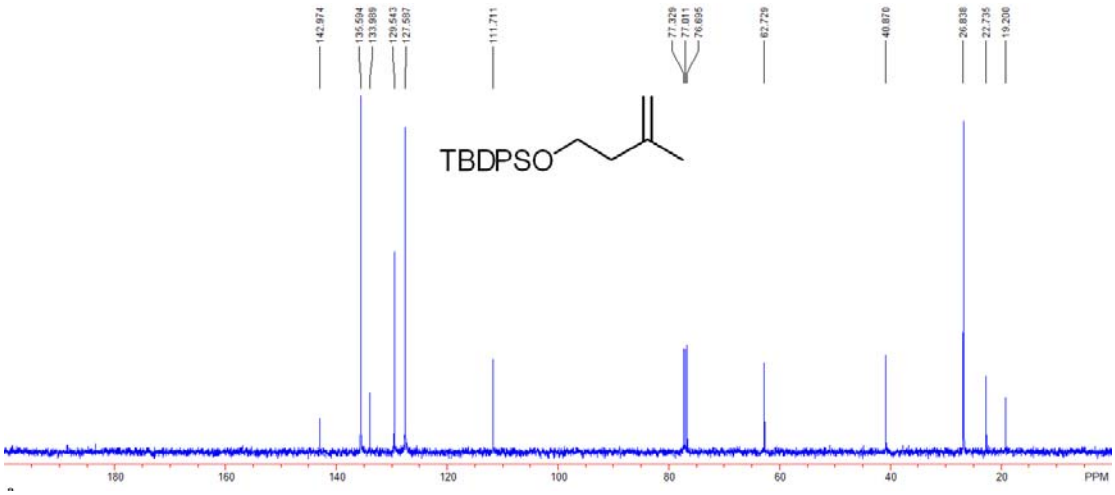
Compound **A-2n**



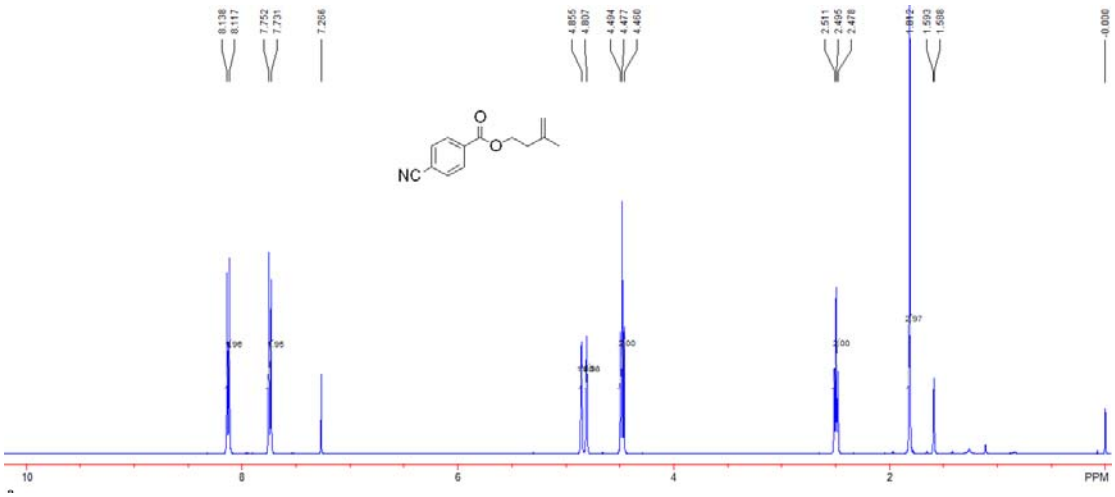


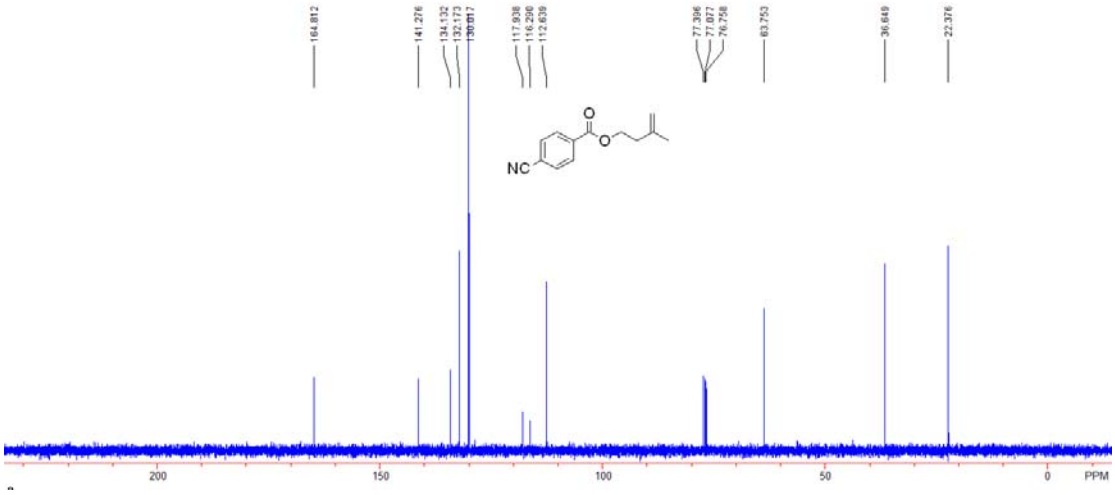
Compound **A-3d**



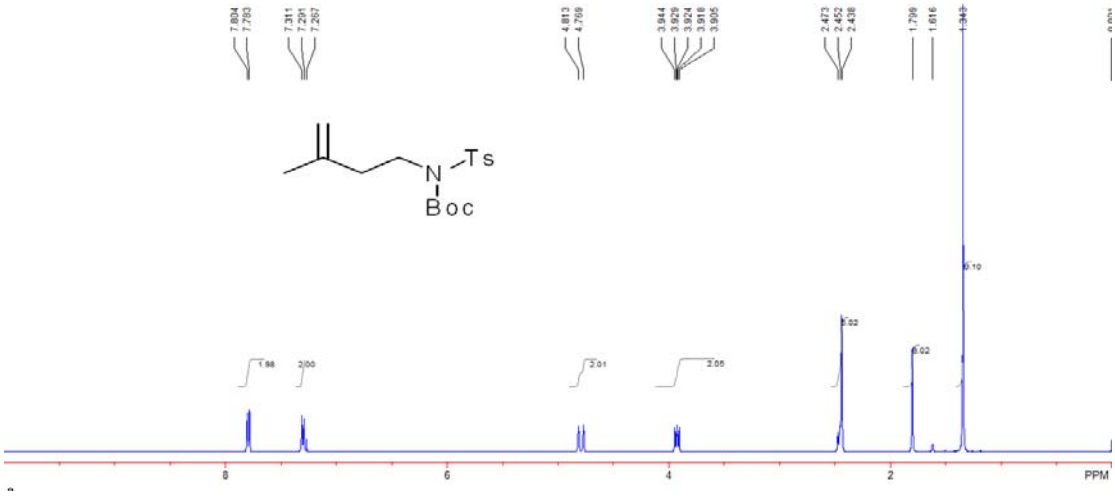


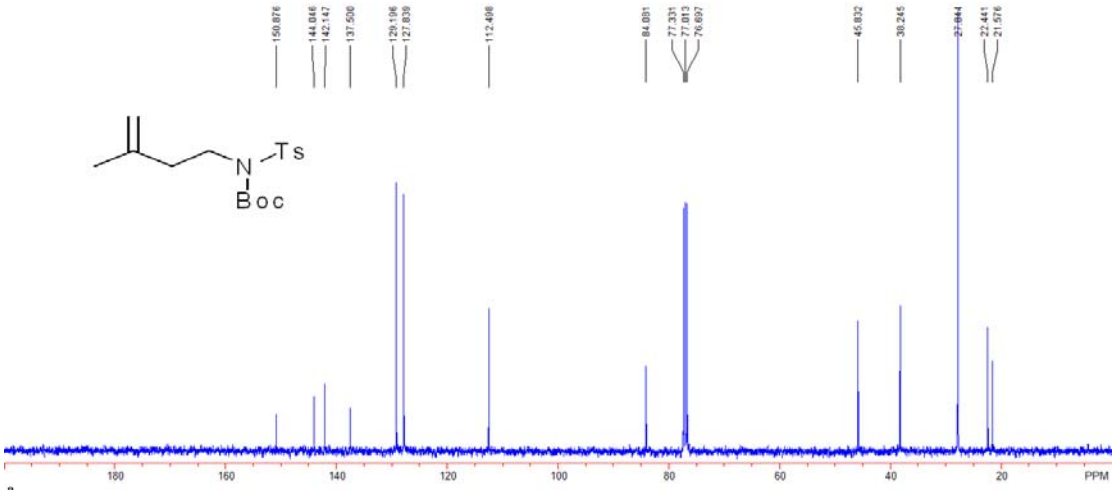
Compound **A-3e**



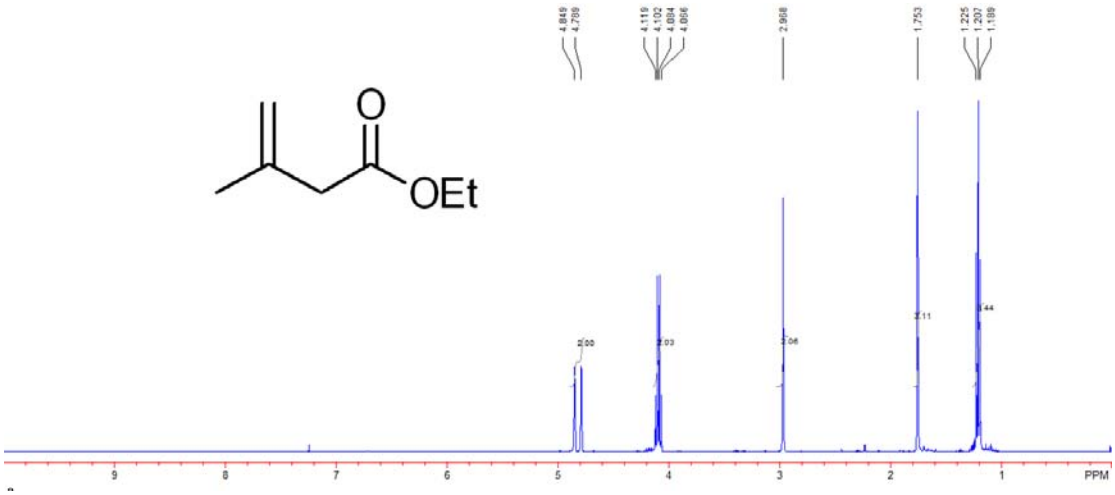


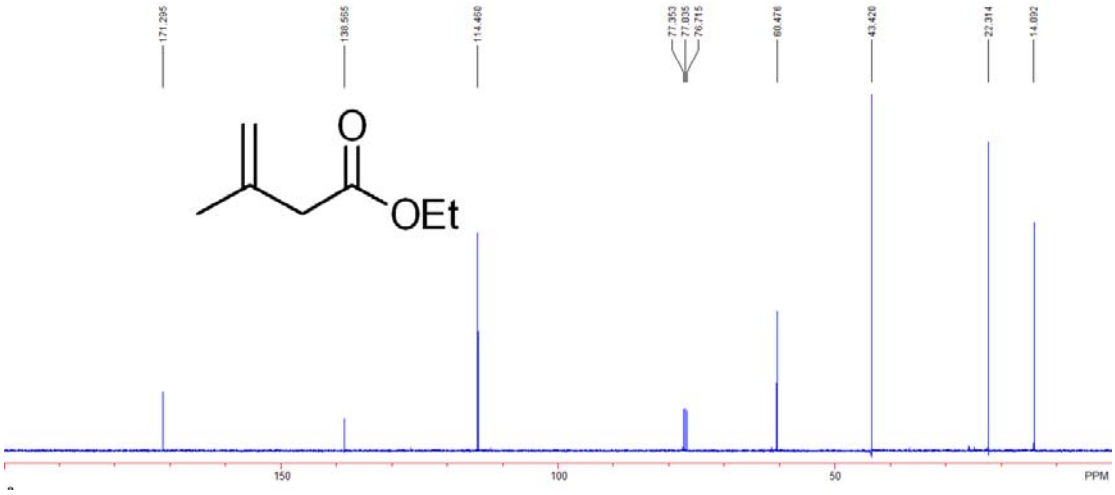
Compound **A-3f**



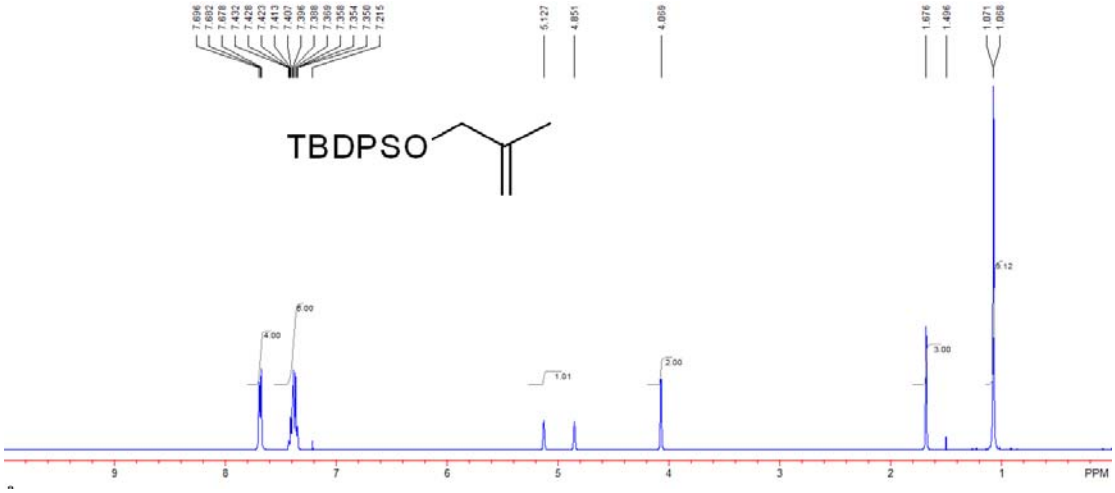


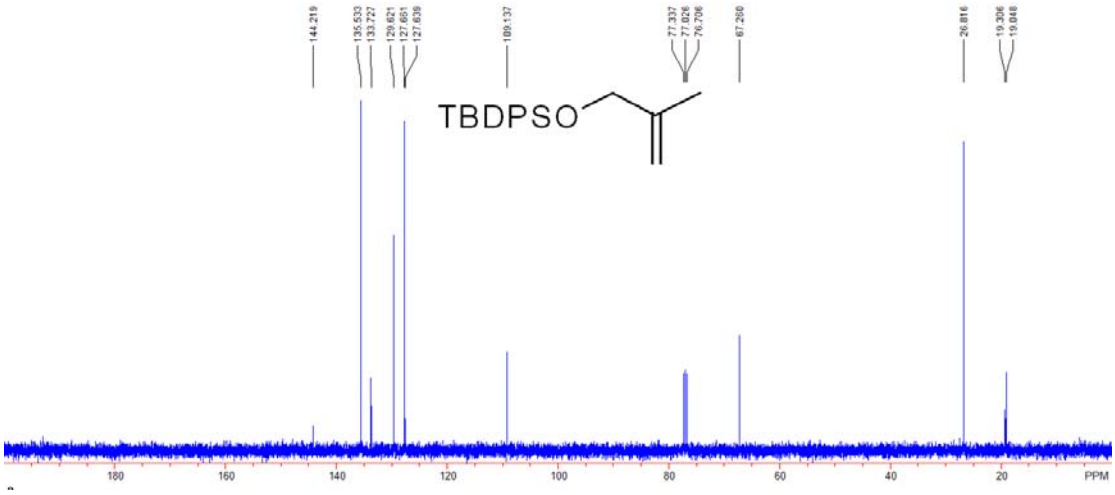
Compound **A-3g**



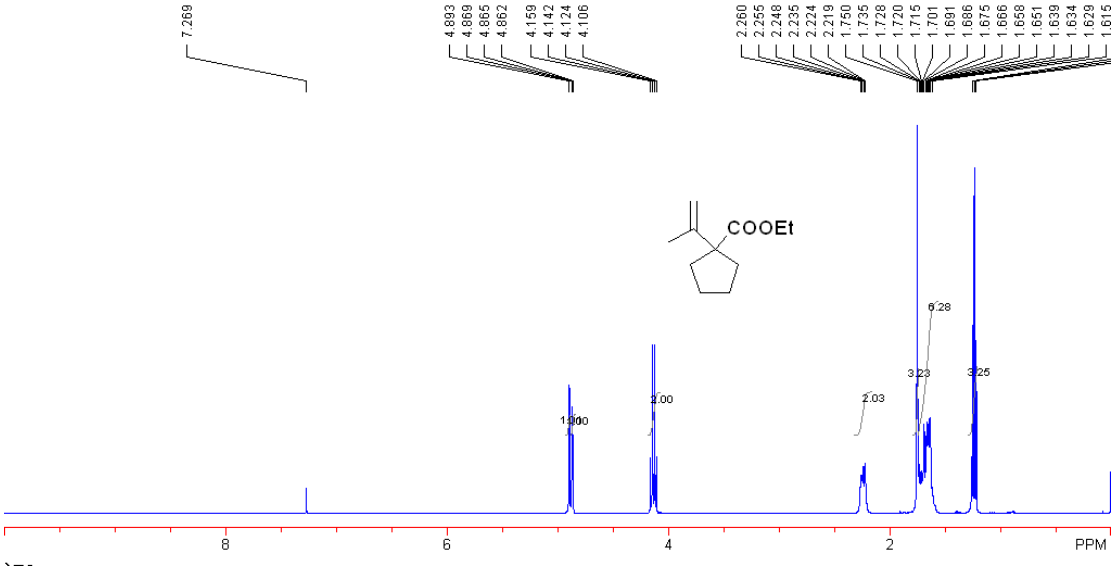


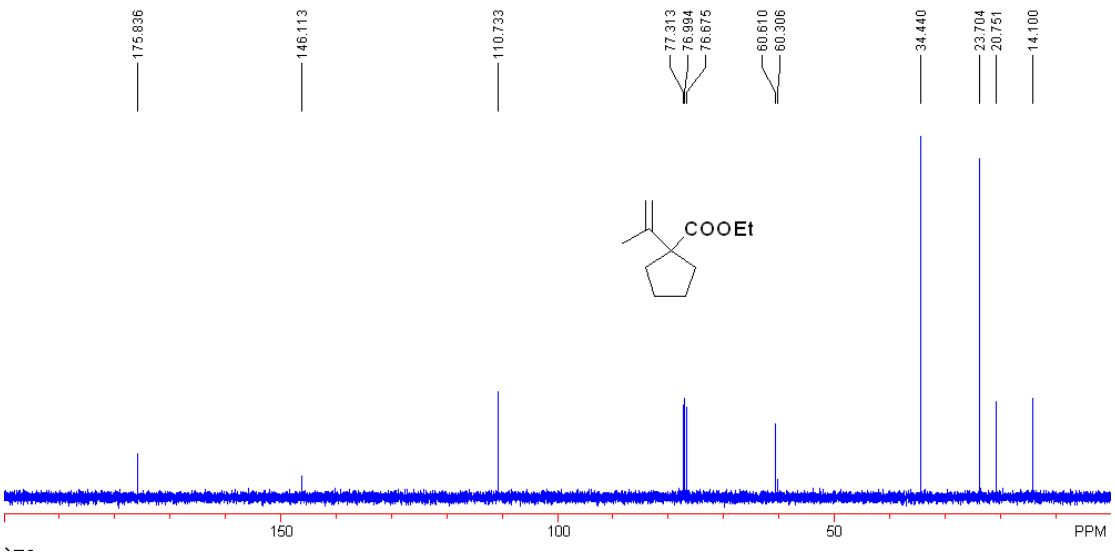
Compound **A-3h**



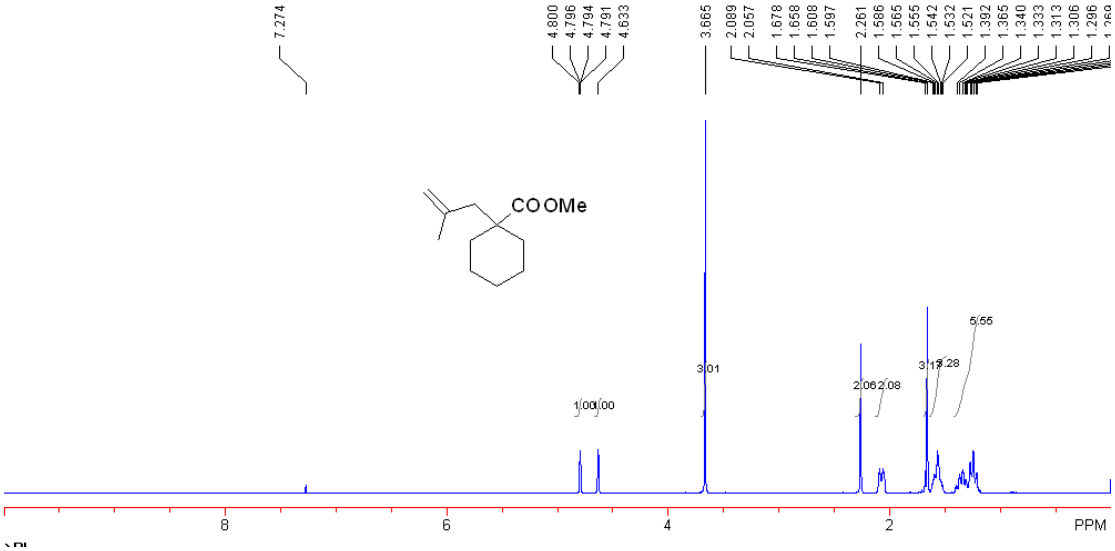


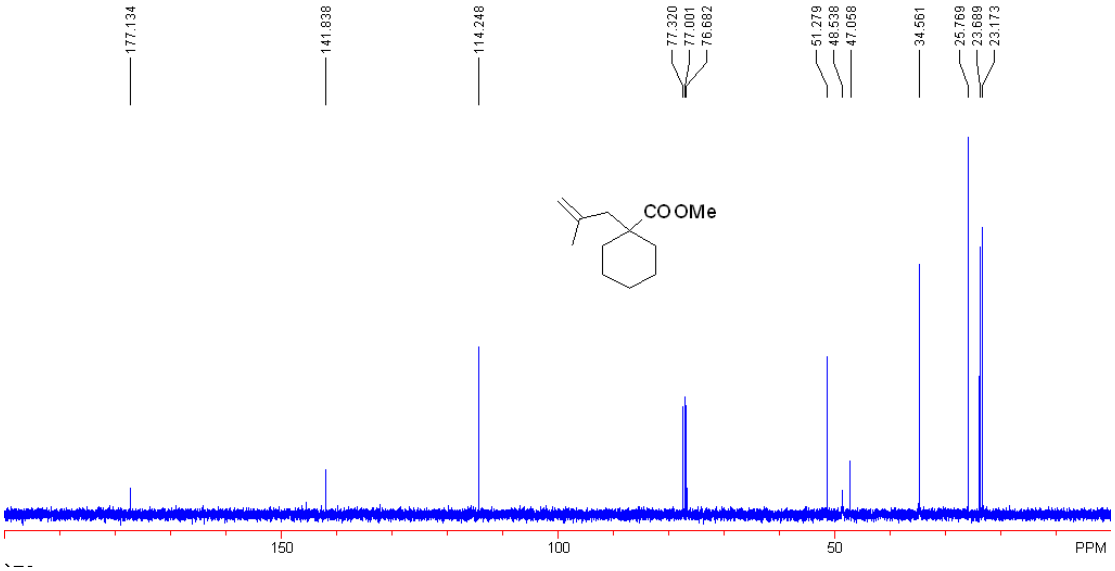
Compound **A-3i**



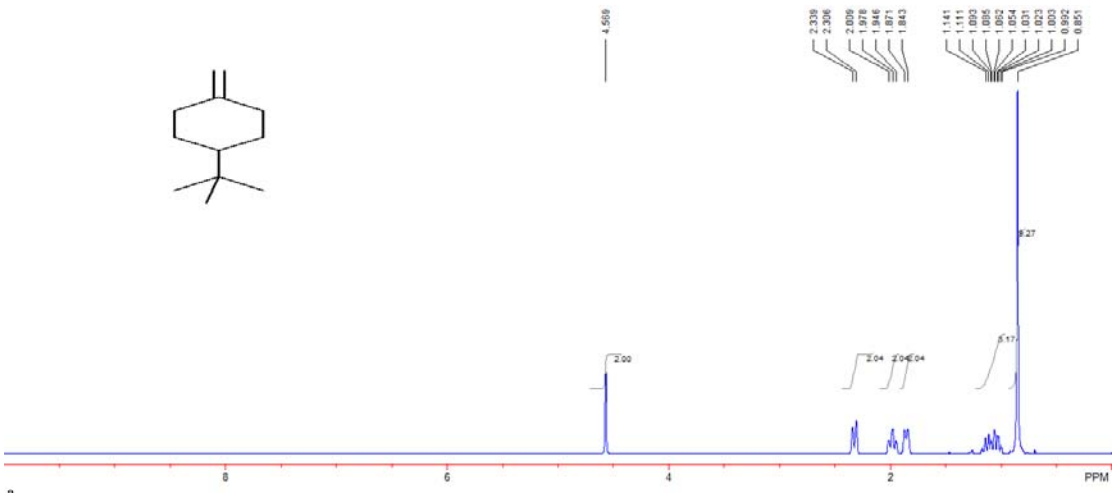


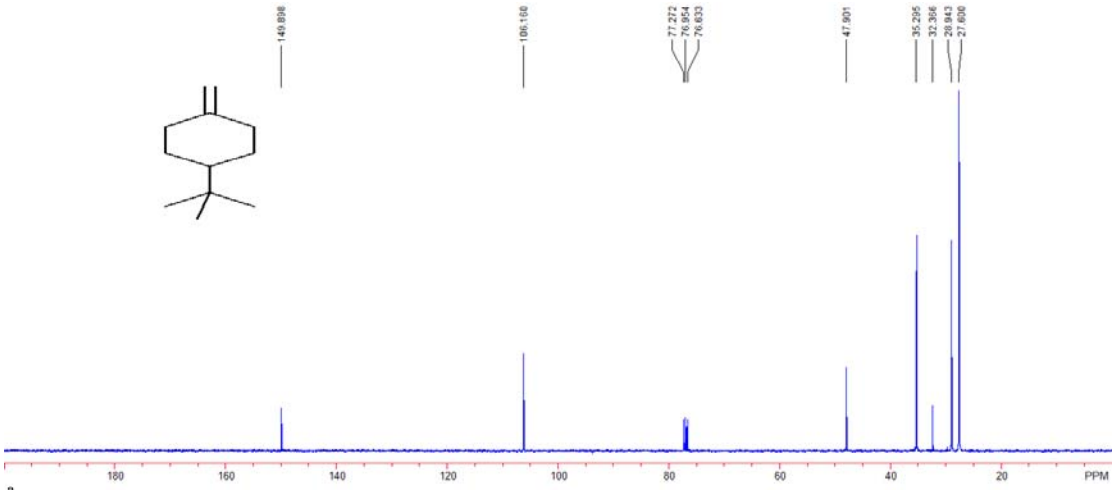
Compound **A-3j**



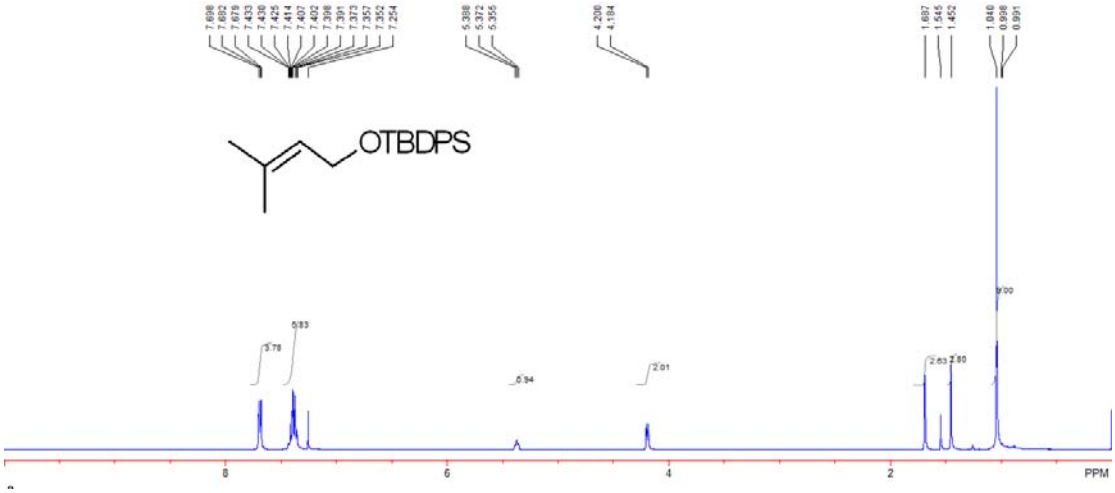


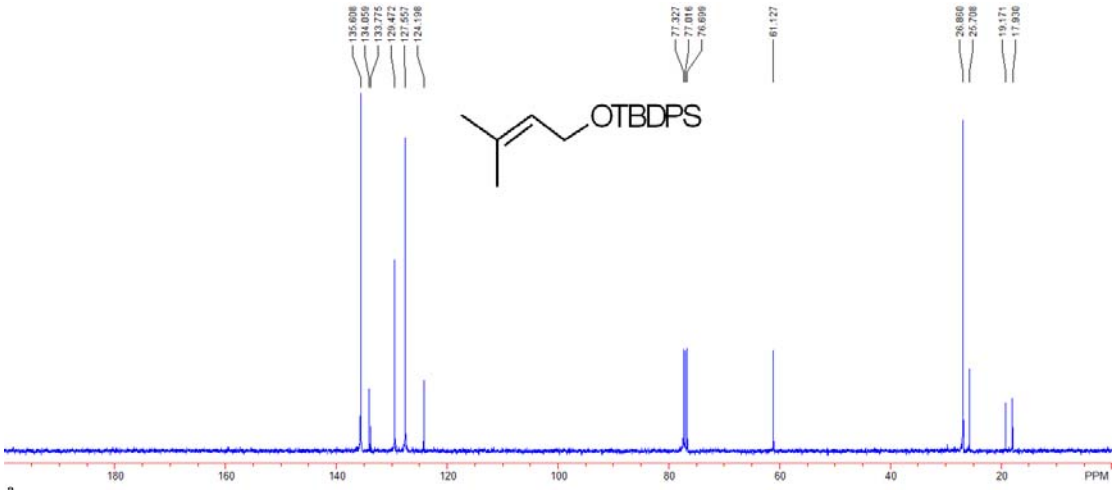
Compound **A-3l**



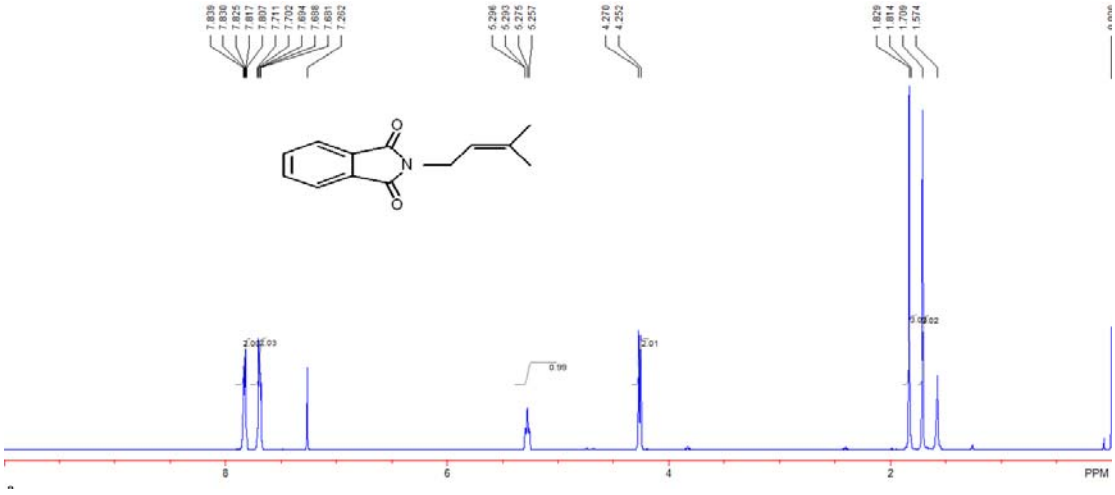


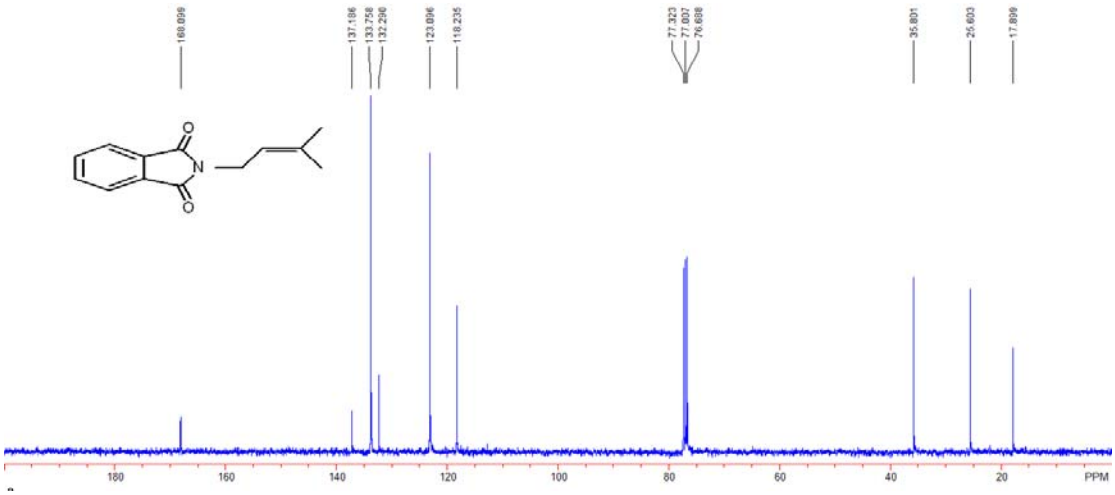
Compound **A-4a**



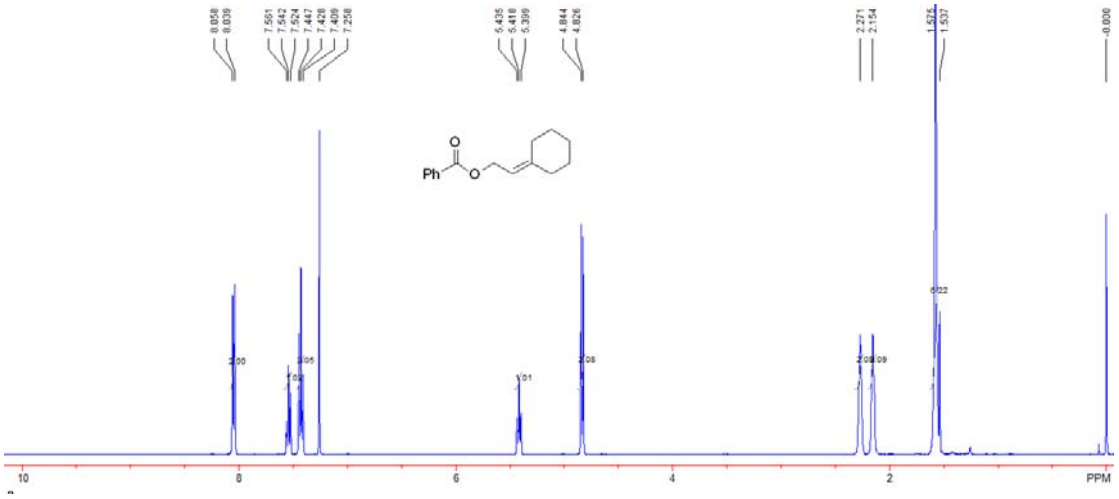


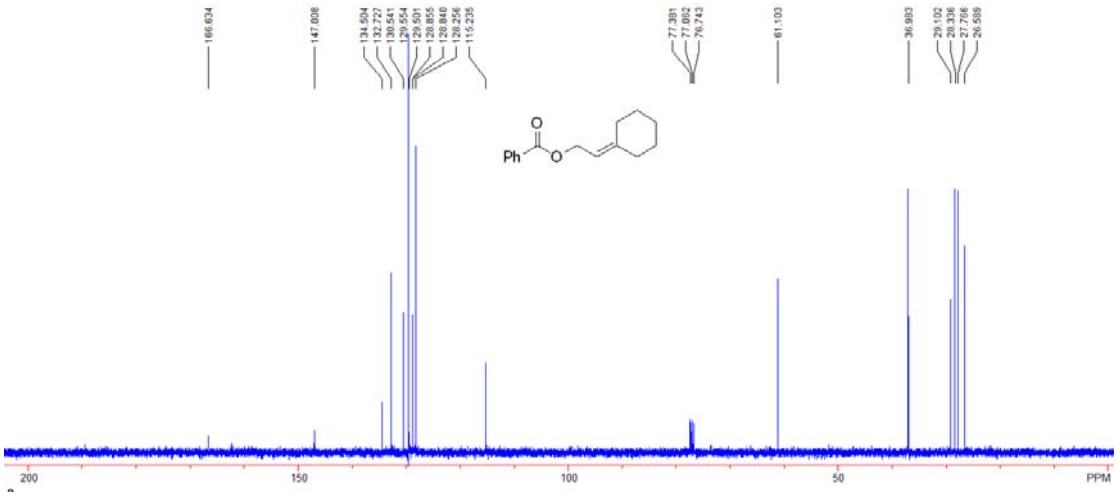
Compound **A-4b**



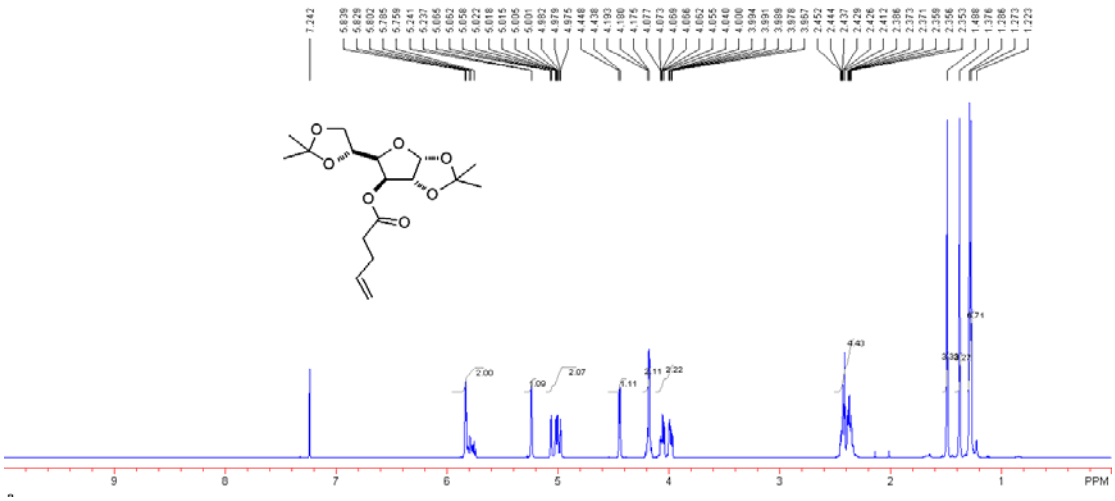


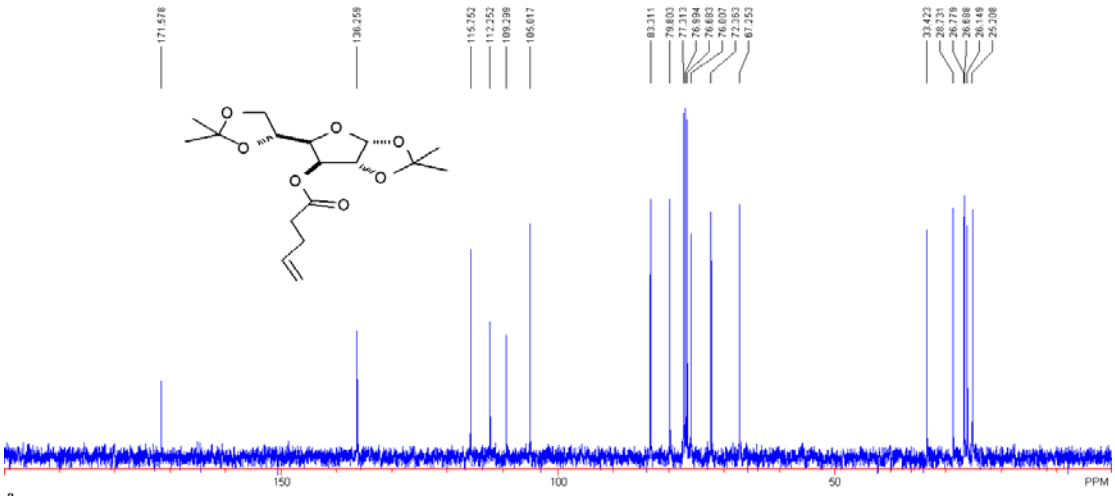
Compound **A-4c**



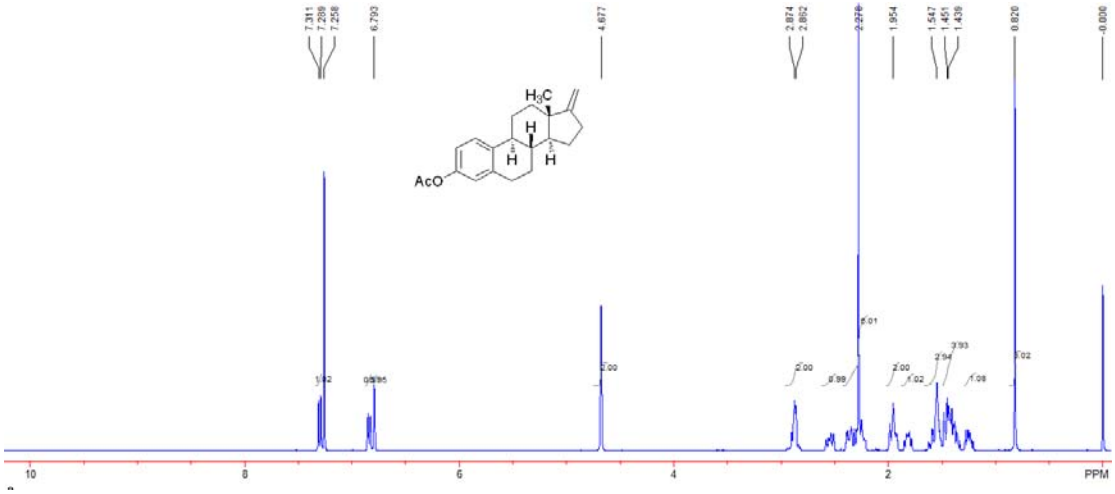


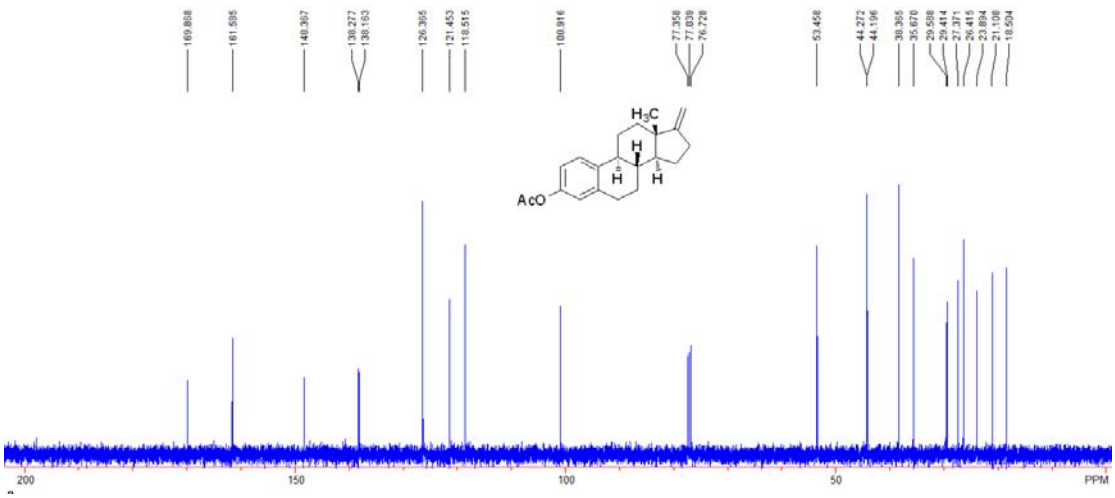
Compound **6**



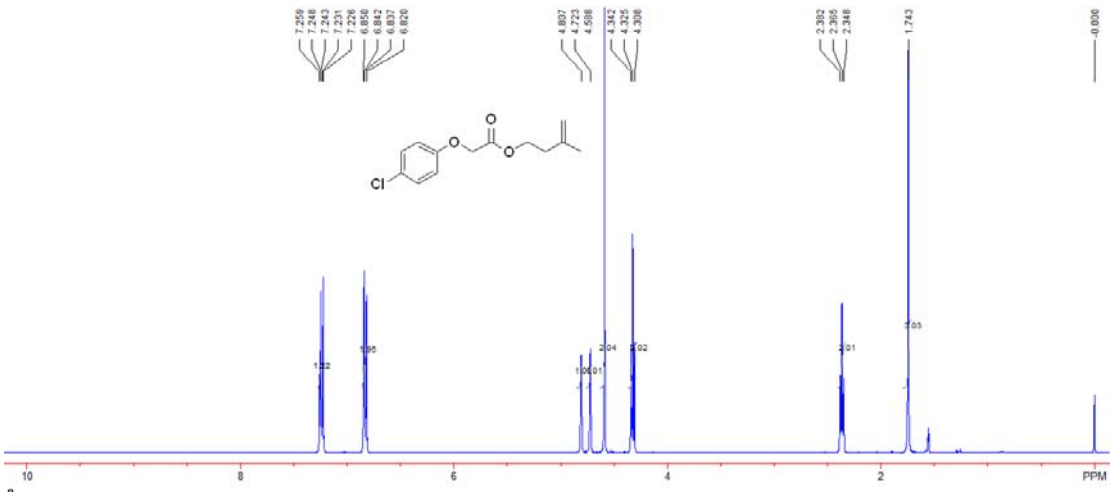


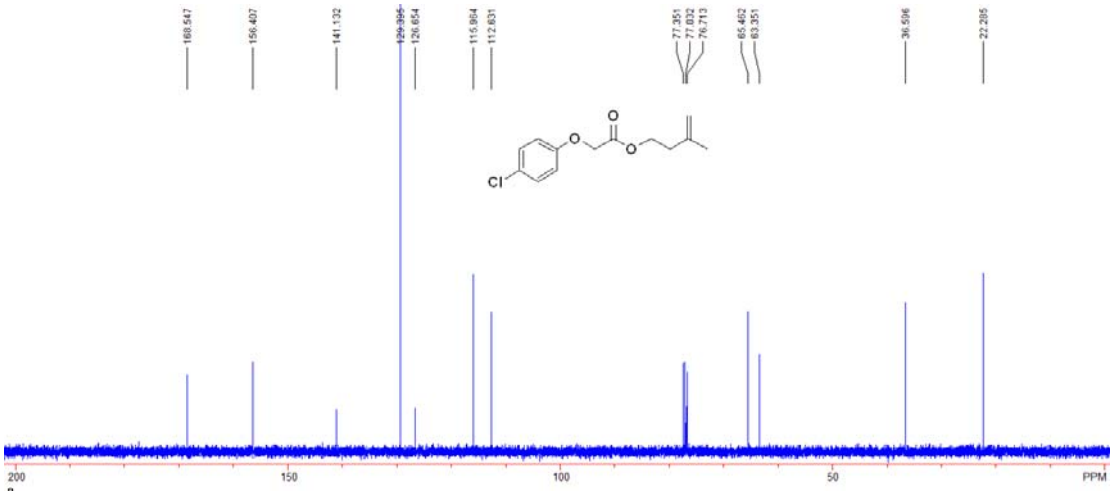
Compound **8**


7.311
7.289
7.258
6.793
4.677
2.874
2.862
2.276
1.954
1.547
1.451
1.438
0.820
-0.000
H3C
H
H
H
AcO
1.00
2.00
5.01
2.00
1.02
2.94
3.93
1.08
3.02
10
8
6
4
2
PPM

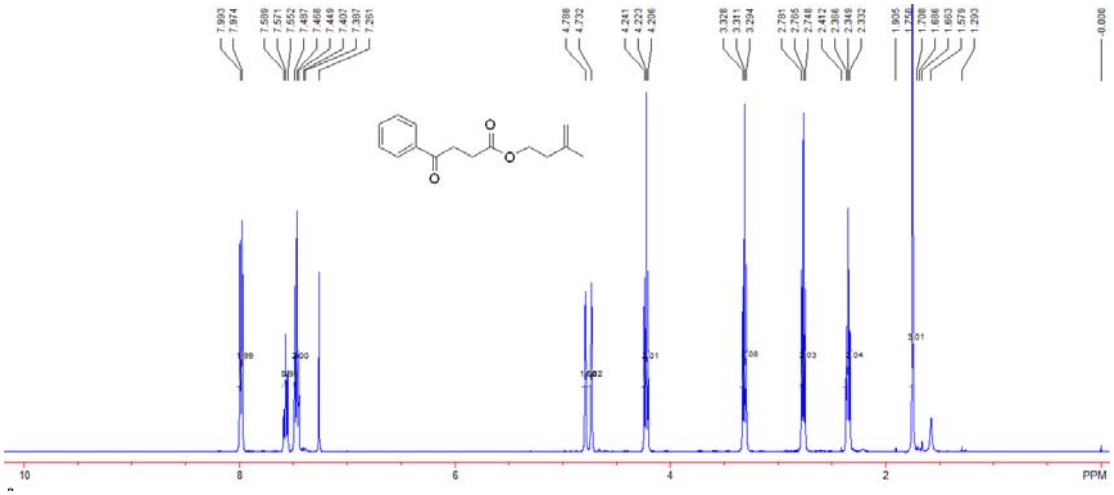

169.868
161.585
140.397
138.277
136.163
126.305
121.453
118.515
100.916
77.358
77.039
76.720
53.458
44.272
44.196
39.305
35.670
29.588
29.414
27.371
26.415
23.894
21.598
15.504
H3C
H
H
H
AcO
200
150
100
50
PPM

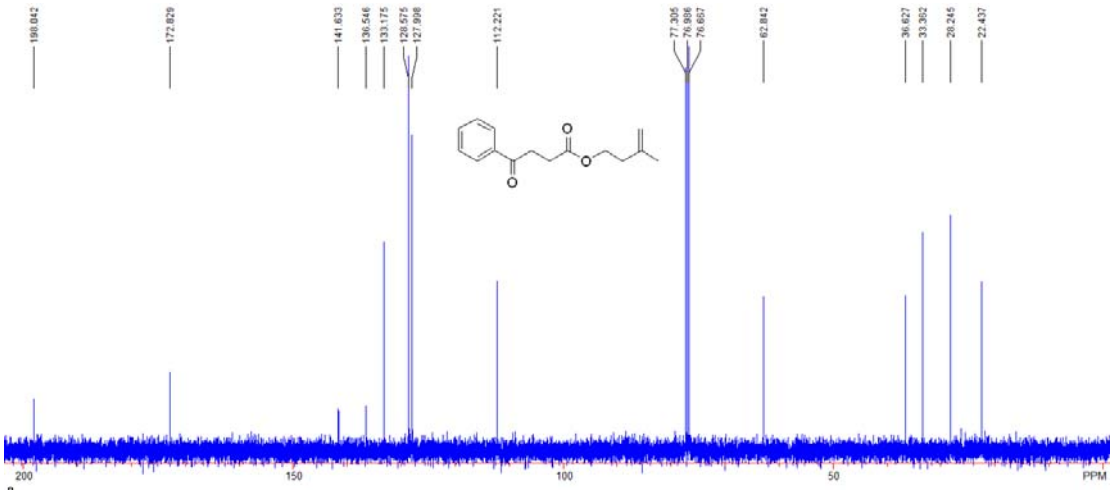
Compound **A-10e**



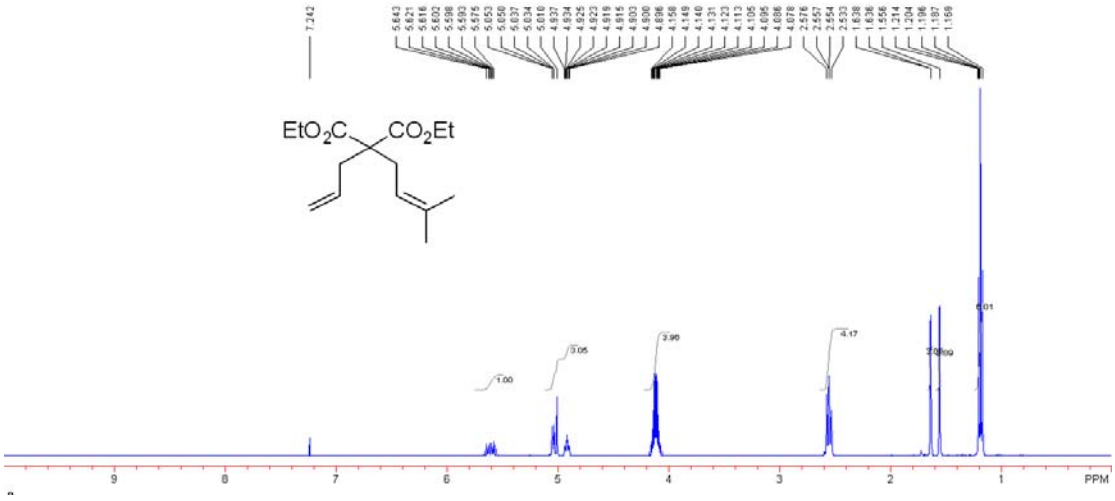


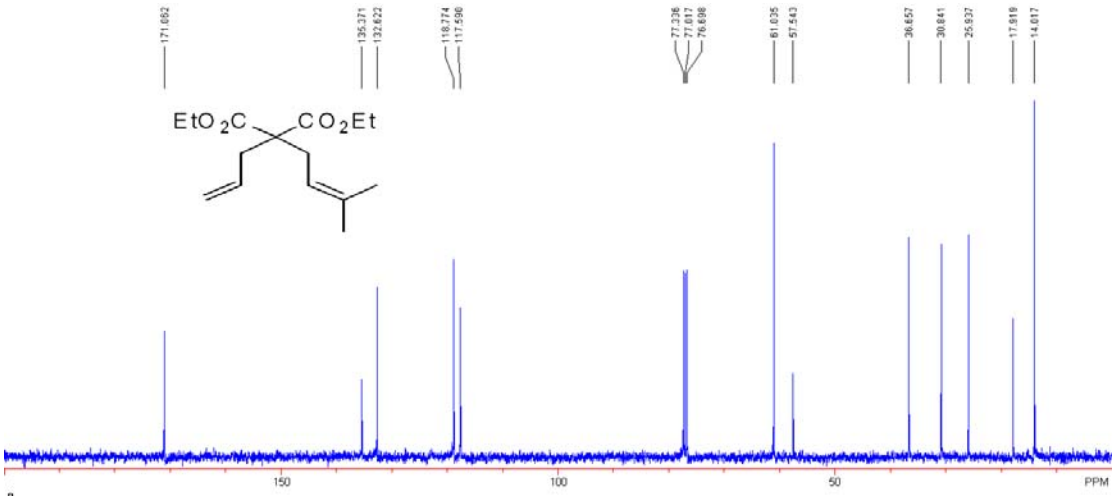
Compound **A-10g**



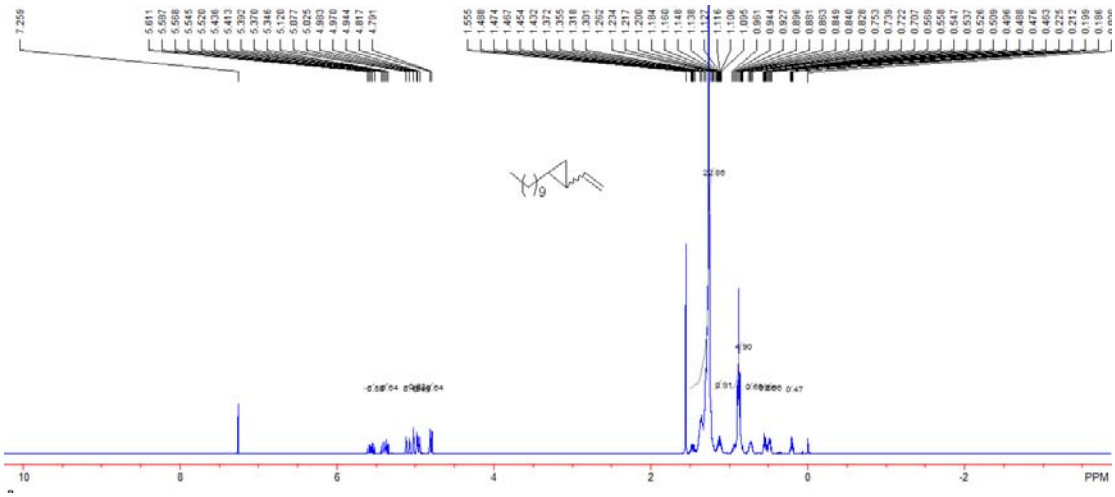


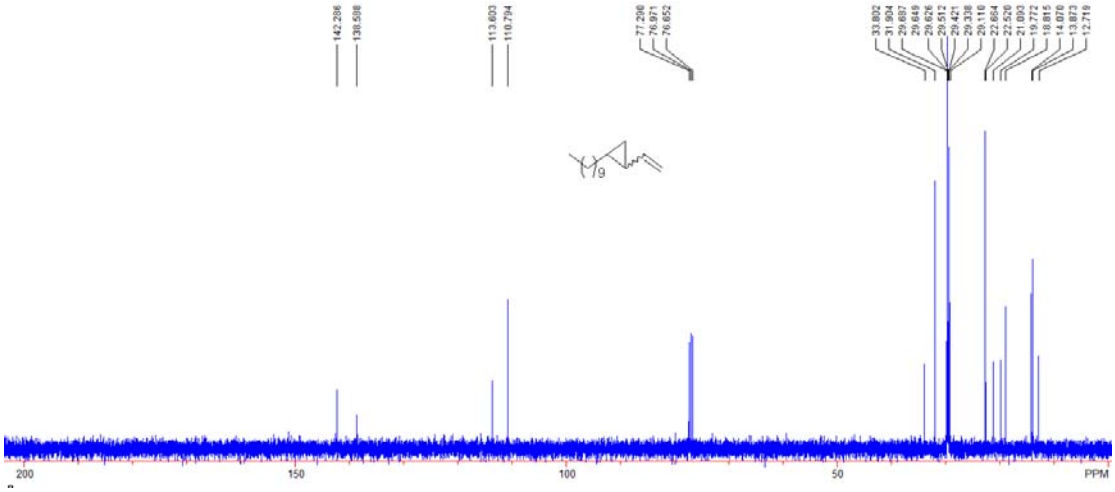
Compound **20**





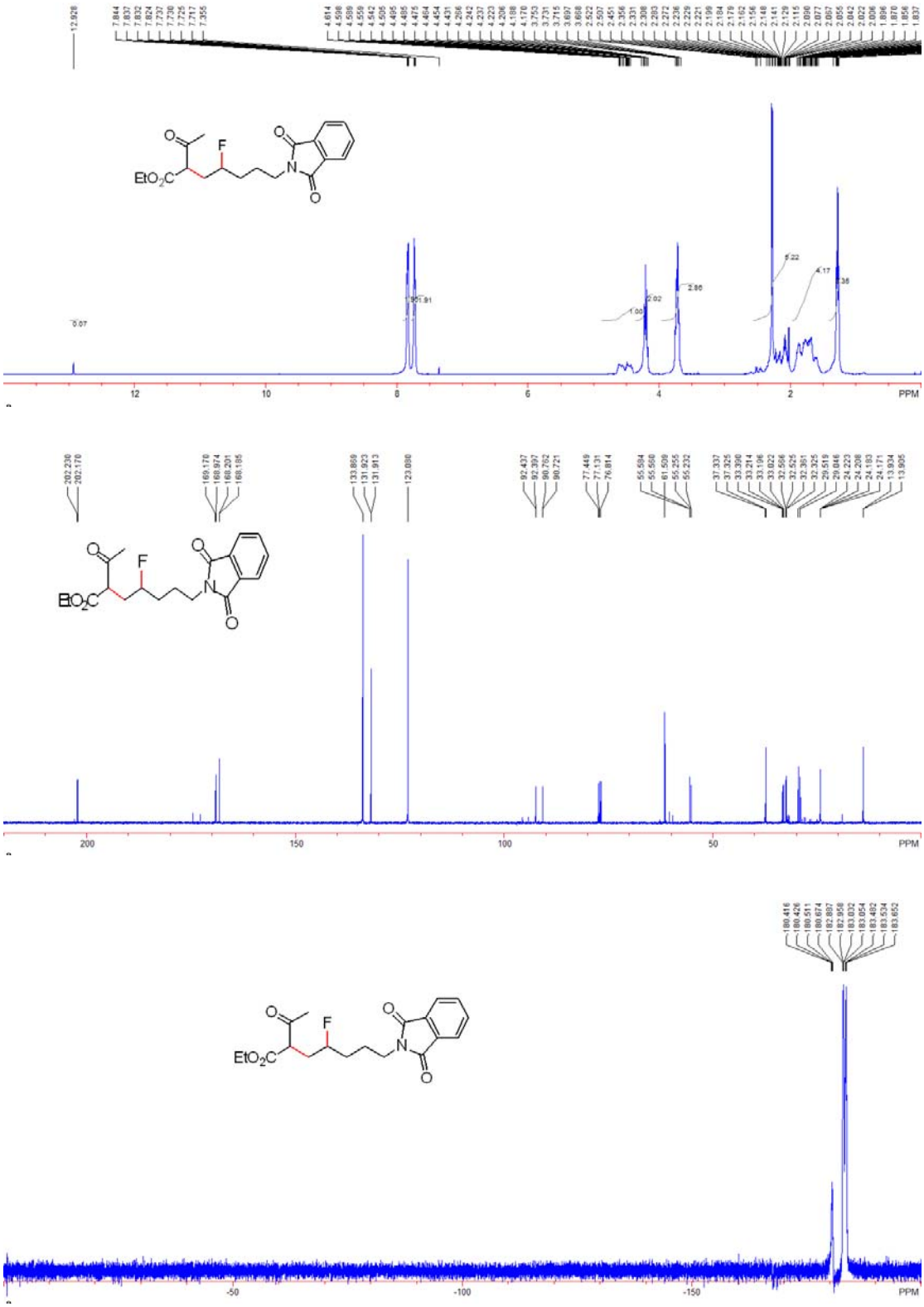
Compound **22**



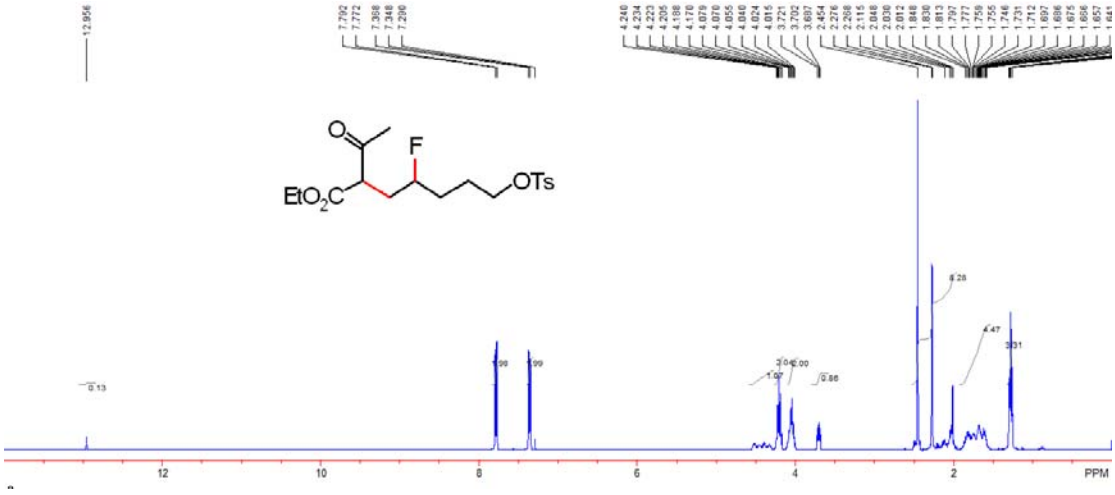


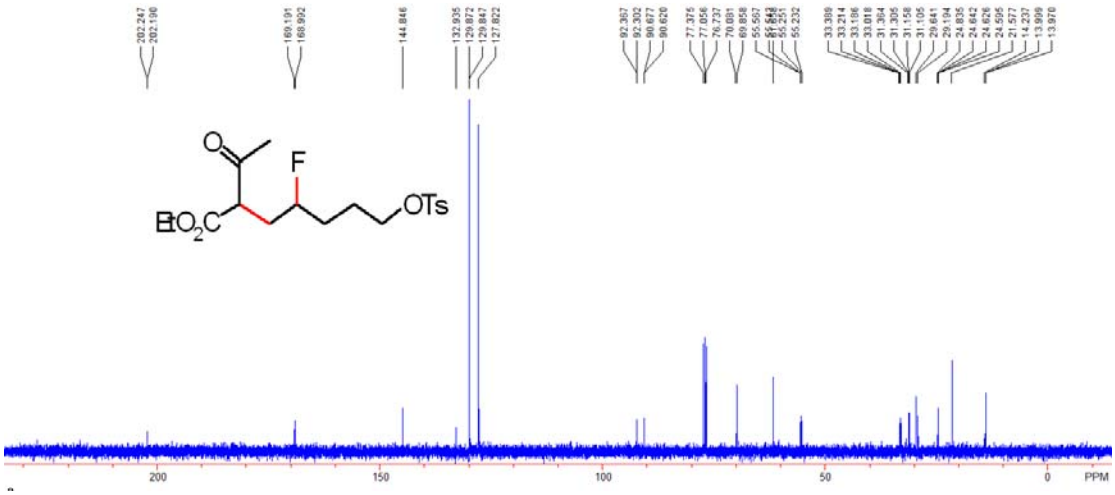
6. ^{1}H, ^{13}C and ^{19}F NMR Spectra of Products.

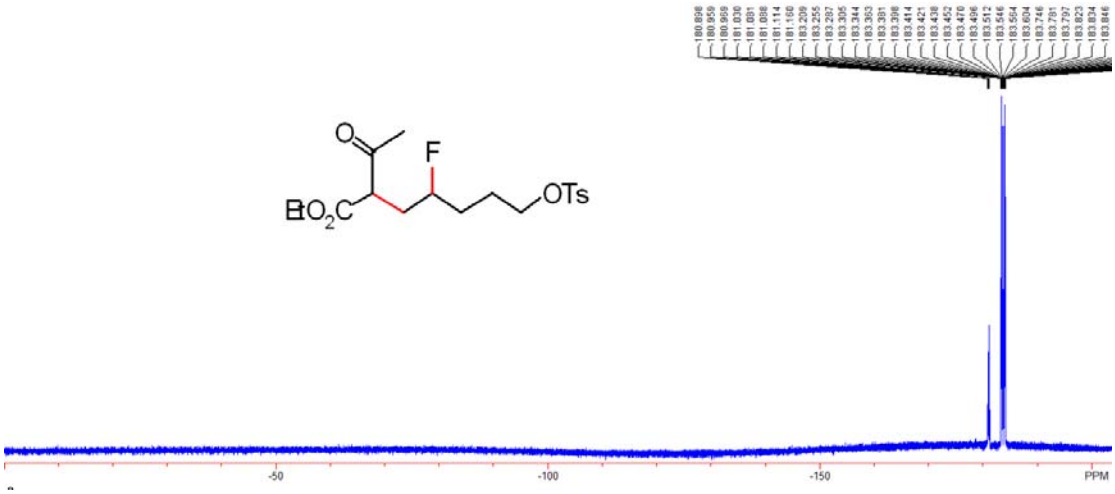
Compound **1a**



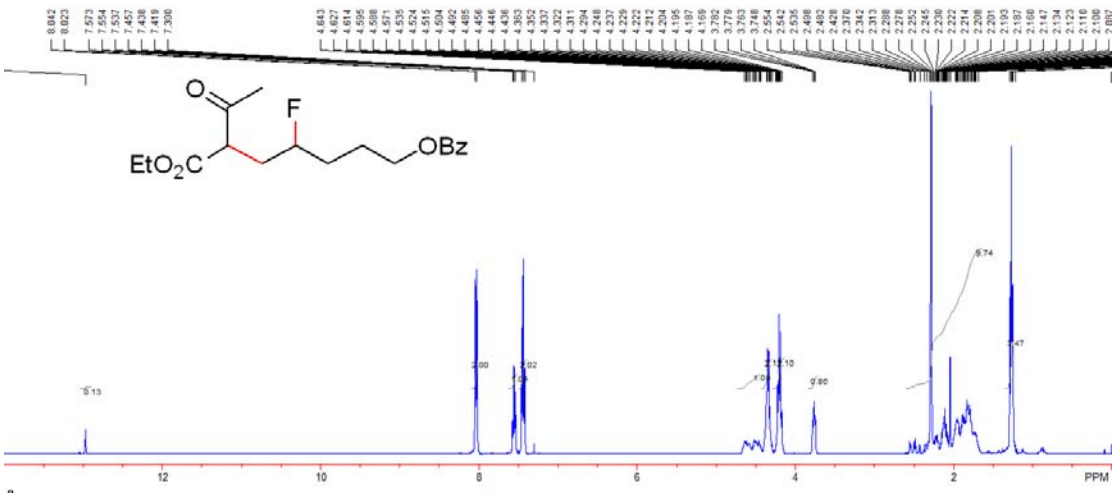
Compound **1b**

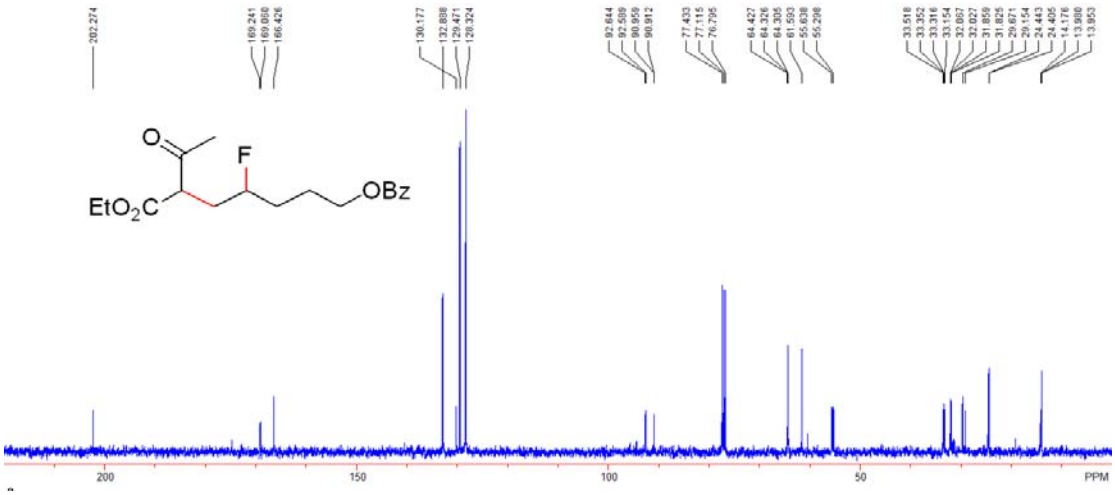


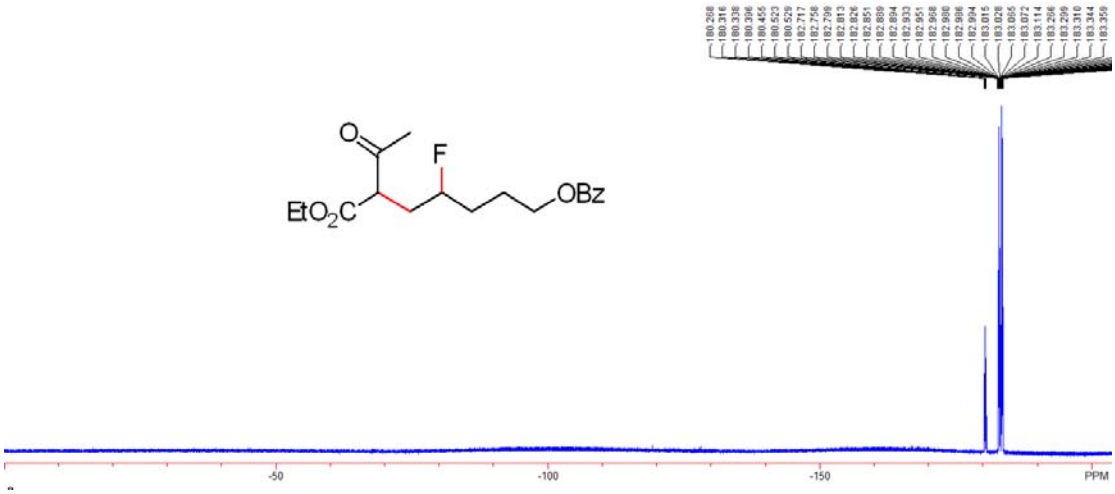




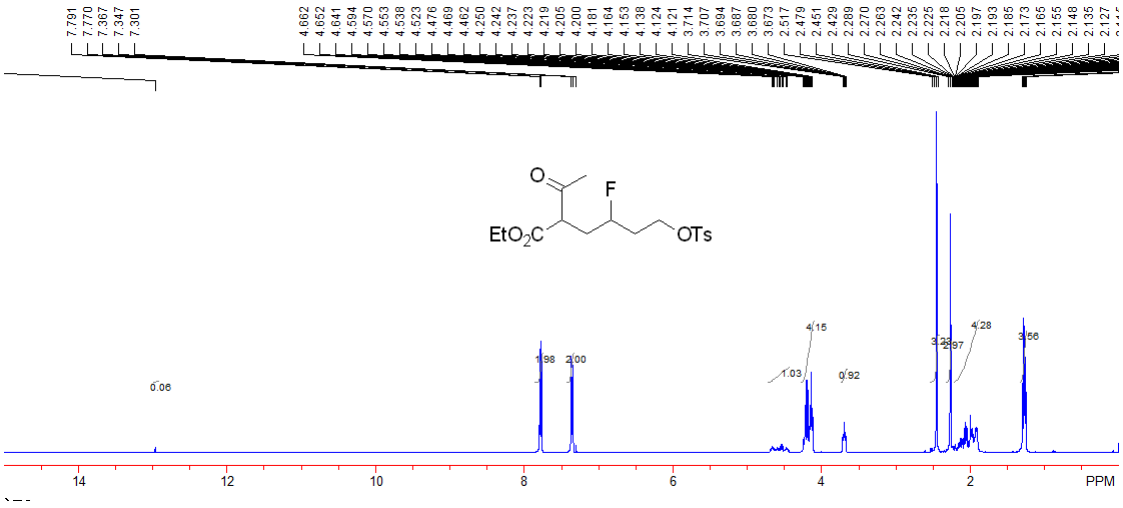
Compound **1c**

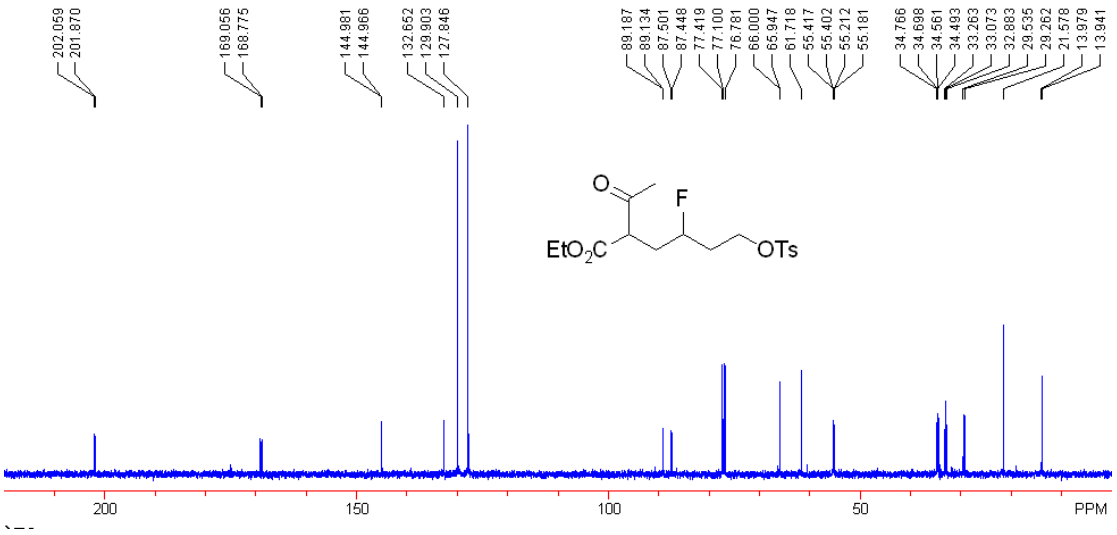


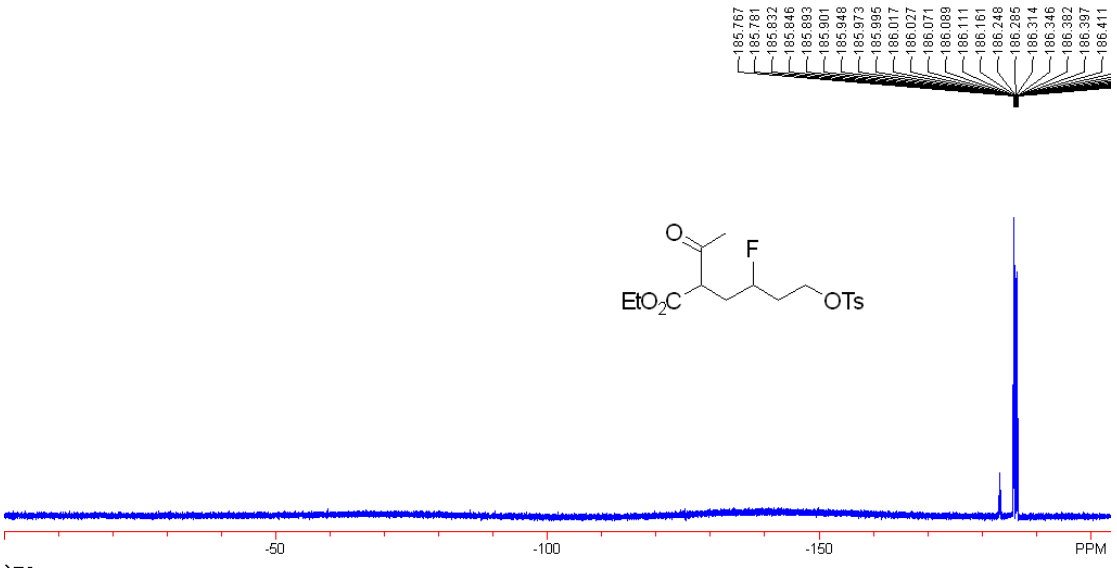




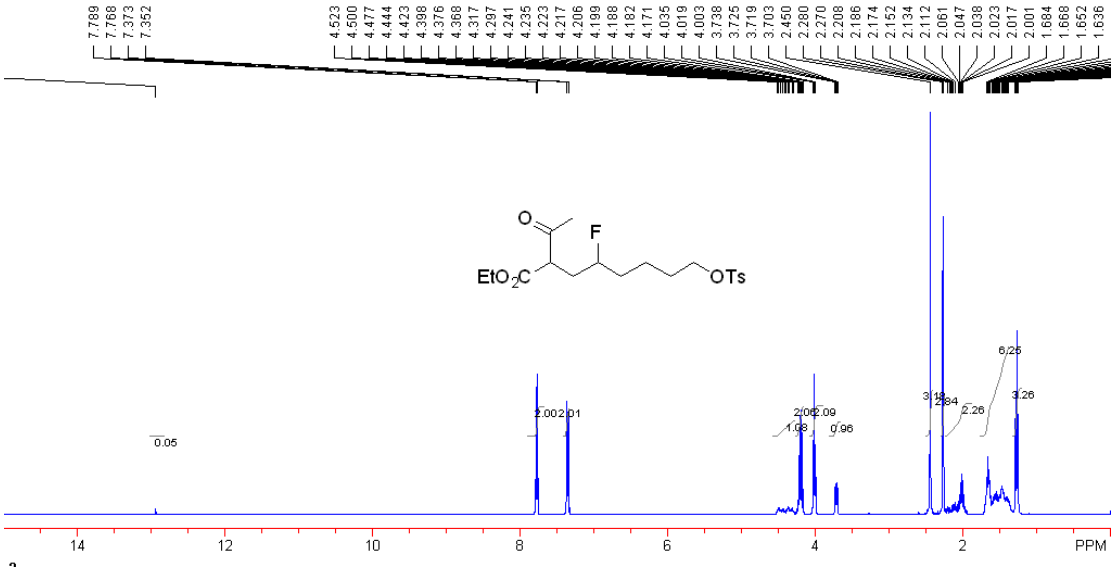
Compound **1d**

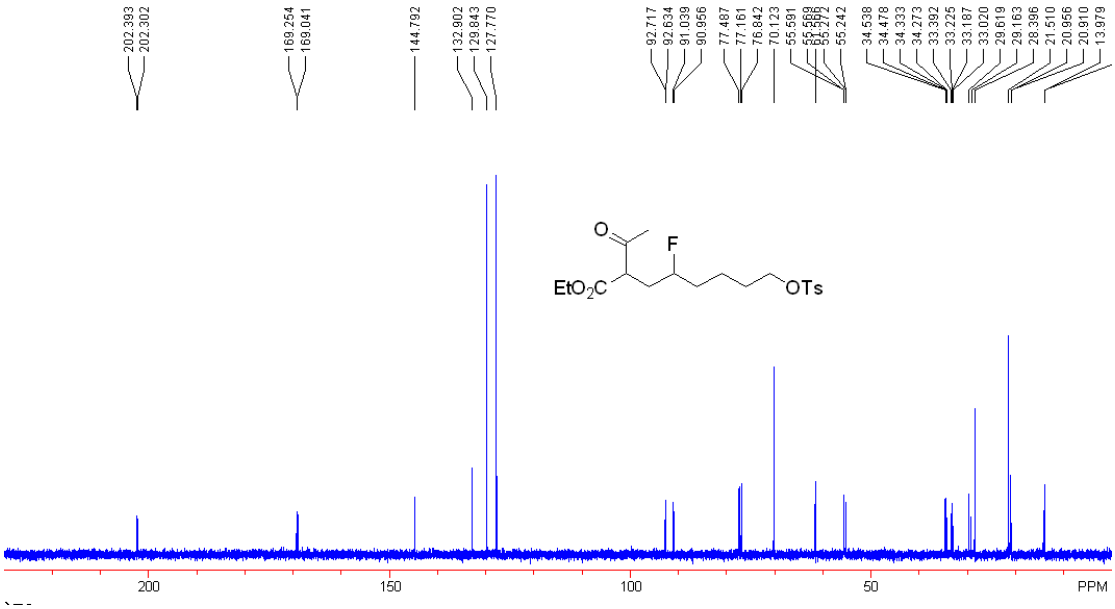

7.791
7.770
7.367
7.347
7.301
4.662
4.652
4.641
4.594
4.570
4.553
4.538
4.523
4.476
4.469
4.462
4.250
4.242
4.237
4.223
4.219
4.205
4.200
4.181
4.164
4.153
4.138
4.124
4.121
3.714
3.707
3.694
3.687
3.680
3.673
2.517
2.479
2.451
2.429
2.289
2.270
2.263
2.242
2.235
2.225
2.218
2.205
2.197
2.193
2.185
2.173
2.165
2.155
2.148
2.135
2.127
O
F
EtO2C
OTs
0.06
1.98
2.00
1.03
4.15
0.92
3.28
2.97
4.28
3.56
14
12
10
8
6
4
2
PPM

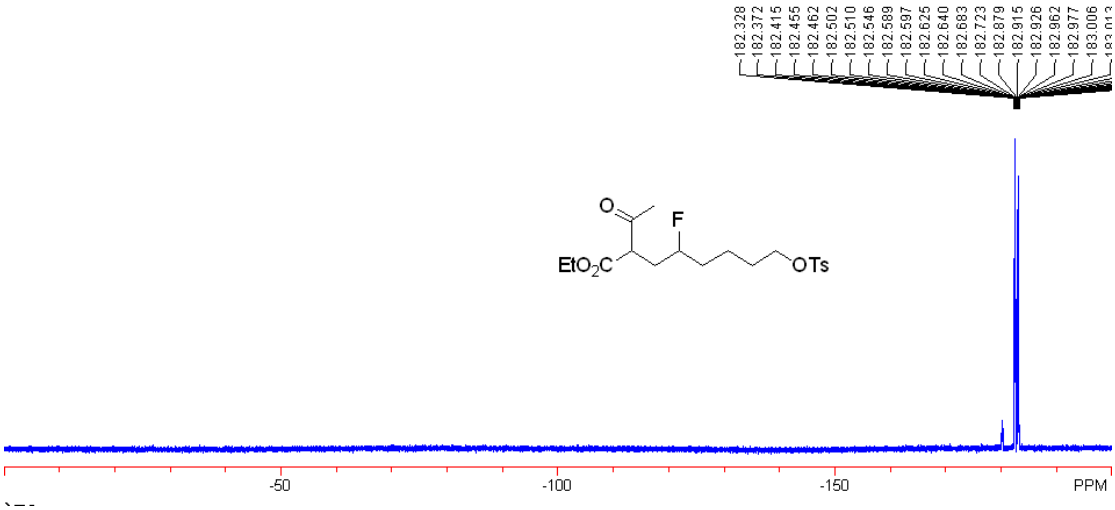

202.059
201.870
169.056
168.775
144.981
144.966
132.652
129.903
127.846
89.187
89.134
87.501
87.448
77.419
77.100
76.781
66.000
65.947
61.718
55.417
55.402
55.212
55.181
34.766
34.698
34.561
34.493
33.263
33.073
32.883
29.535
29.262
21.578
13.979
13.941
O
F
EtO2C
OTs
200
150
100
50
PPM


185.767
185.781
185.832
185.846
185.893
185.901
185.948
185.973
185.995
186.017
186.027
186.071
186.089
186.111
186.161
186.248
186.285
186.314
186.346
186.382
186.397
186.411
O
F
EtO2C
OTs
-50
-100
-150
PPM

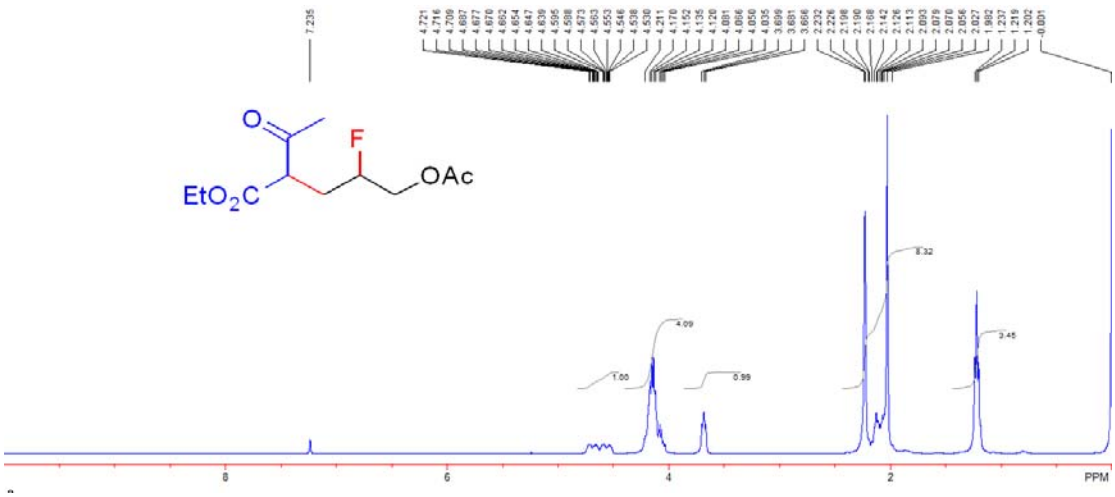
Compound **1e**

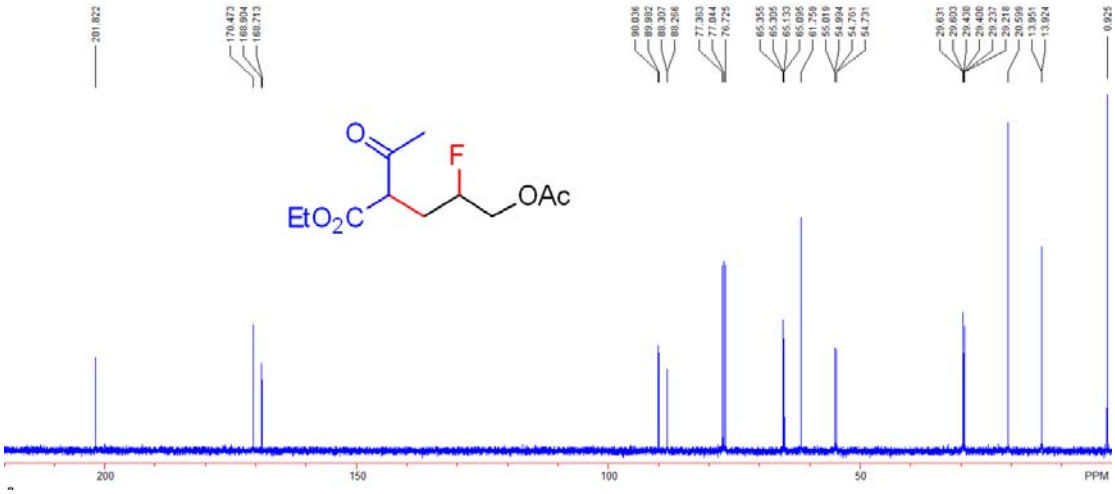

7.789
7.768
7.373
7.352
4.523
4.500
4.477
4.444
4.423
4.398
4.376
4.368
4.317
4.297
4.241
4.235
4.223
4.217
4.206
4.199
4.188
4.182
4.171
4.035
4.019
4.003
3.738
3.725
3.719
3.703
2.450
2.280
2.270
2.208
2.186
2.174
2.152
2.134
2.112
2.061
2.047
2.038
2.023
2.017
2.001
1.684
1.668
1.652
1.636
O
F
EtO2C
OTs
6.25
3.26
2.84
2.26
2.00
2.01
2.09
1.08
0.96
0.05
14
12
10
8
6
4
2
PPM

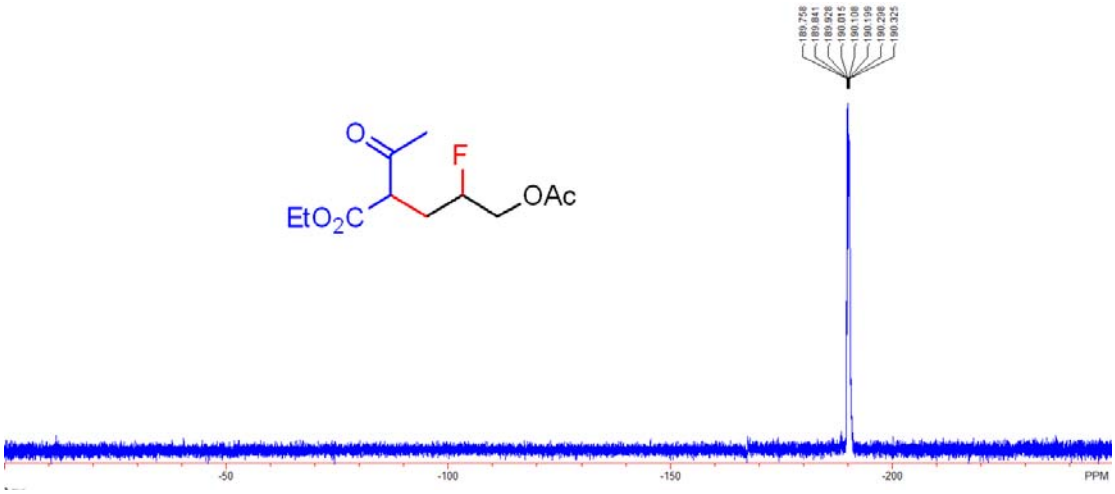

202.393
202.302
169.254
169.041
144.792
132.902
129.843
127.770
92.717
92.634
91.039
90.956
77.487
77.161
76.842
70.123
55.591
55.242
34.538
34.478
34.333
34.273
33.392
33.225
33.187
33.020
29.619
29.163
28.396
21.510
20.956
20.910
13.979
O
F
EtO2C
OTs
200
150
100
50
PPM


182.328
182.372
182.415
182.455
182.462
182.502
182.510
182.546
182.589
182.597
182.625
182.640
182.683
182.723
182.879
182.915
182.926
182.962
182.977
183.006
O
F
EtO2C
OTs
-50
-100
-150
PPM

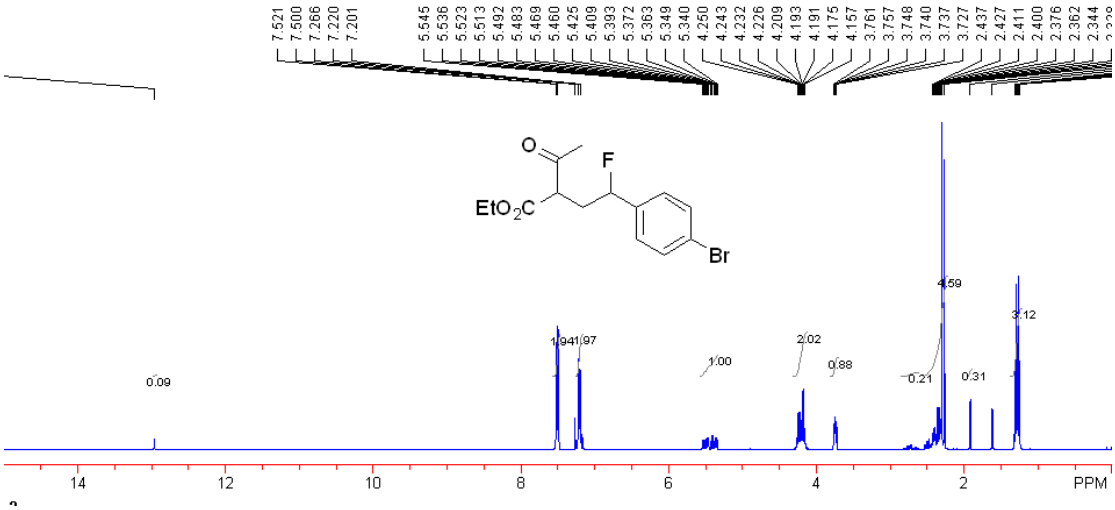
Compound **1f**







Compound **1g**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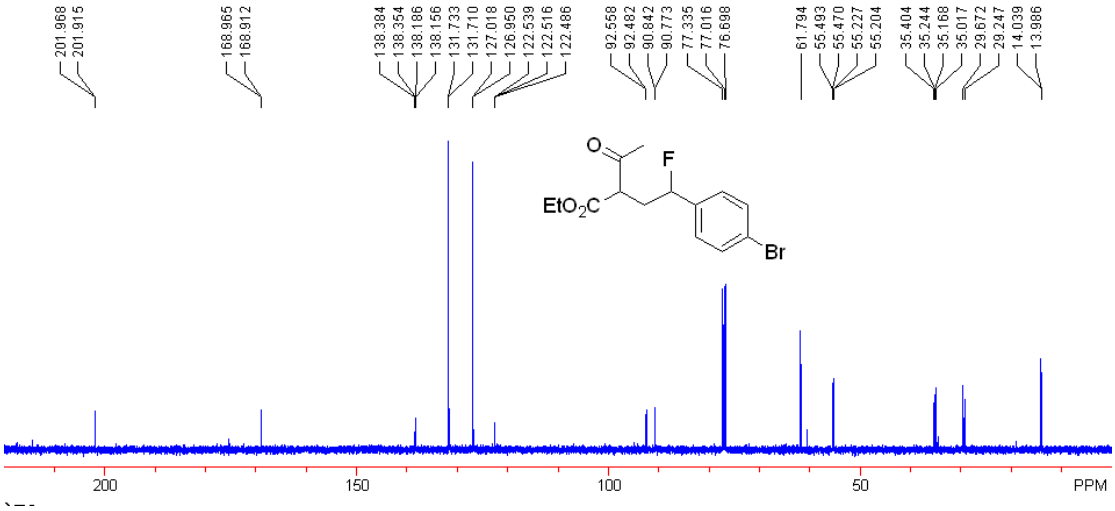
5.536
5.523
5.513
5.492
5.483
5.469
5.460
5.425
5.409
5.393
5.372
5.363
5.349
5.340
4.250
4.243
4.232
4.226
4.209
4.193
4.191
4.175
4.157
3.761
3.757
3.748
3.740
3.737
3.727
2.437
2.427
2.411
2.400
2.376
2.362
2.344
O
F
EtO2C
Br
4.59
3.12
1.94
1.97
2.02
1.00
0.88
0.21
0.31
0.09
14
12
10
8
6
4
2
PPM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168.912
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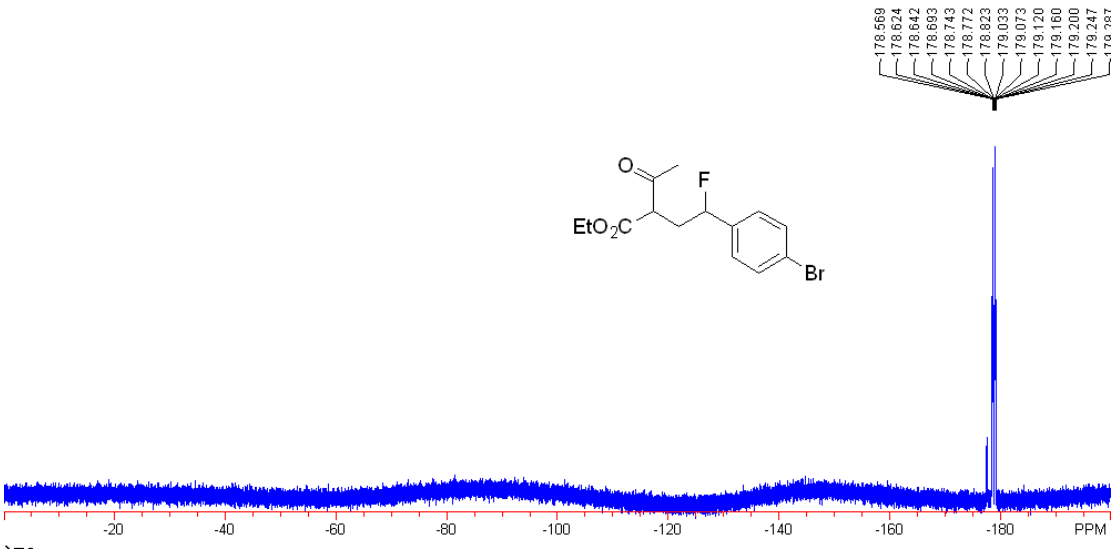
138.354
138.186
138.156
131.733
131.710
127.018
126.950
122.539
122.516
122.486
92.558
92.482
90.842
90.773
77.335
77.016
76.698
61.794
55.493
55.470
55.227
55.204
35.404
35.244
35.168
35.017
29.672
29.247
14.039
13.986
O
F
EtO2C
Br
200
150
100
50
PPM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178.642
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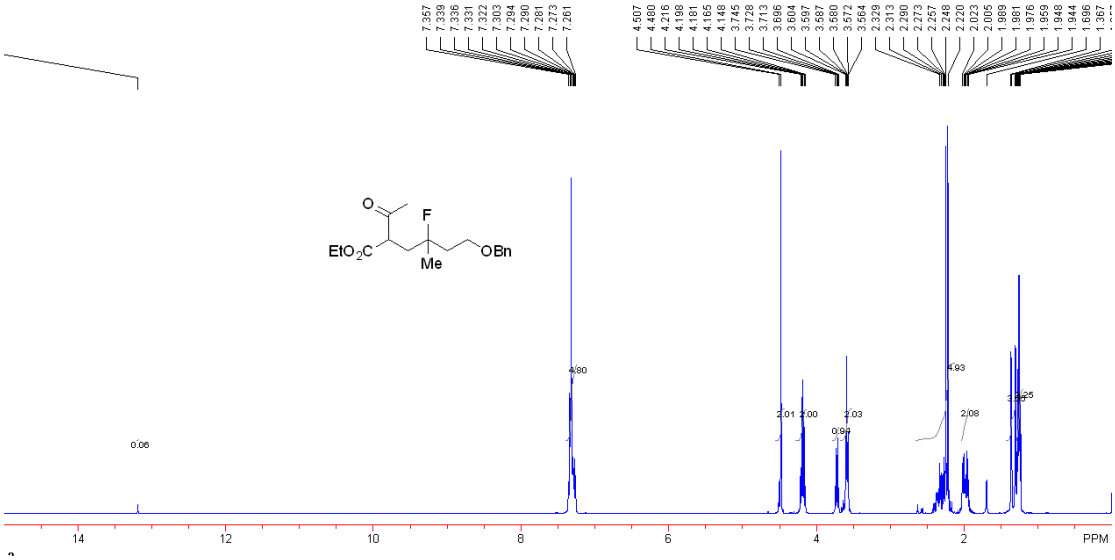
178.772
178.823
179.033
179.073
179.120
179.160
179.200
179.247
O
F
EtO2C
Br
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

Compound **1h**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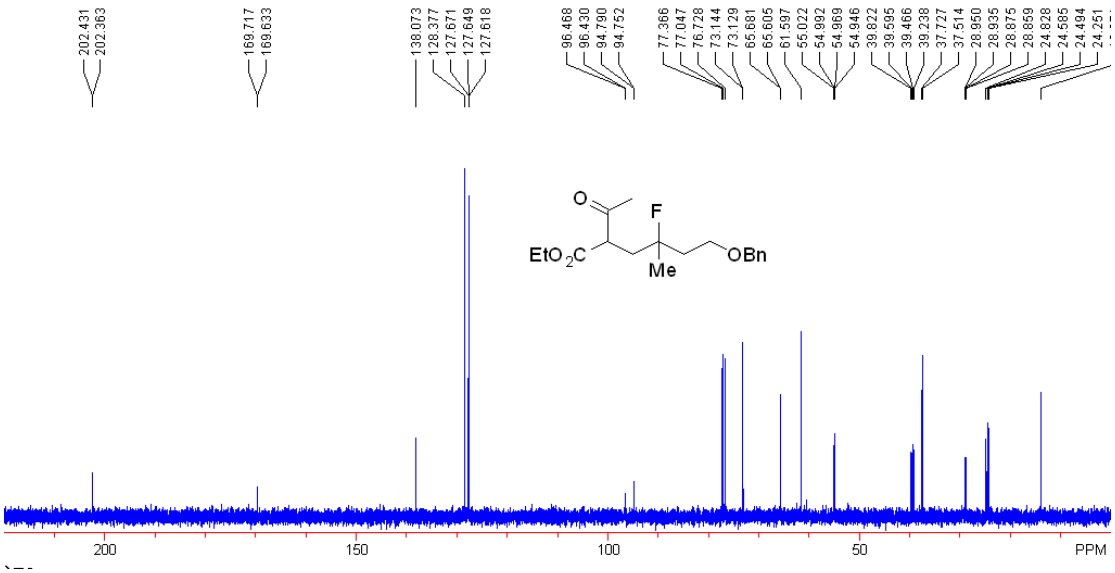
7.339
7.336
7.331
7.322
7.303
7.294
7.290
7.281
7.273
7.261
4.507
4.480
4.216
4.198
4.181
4.165
4.148
3.745
3.728
3.713
3.696
3.604
3.597
3.587
3.580
3.572
3.564
2.329
2.313
2.290
2.273
2.257
2.248
2.220
2.023
2.005
1.989
1.981
1.976
1.959
1.948
1.944
1.696
1.367
O
F
EtO2C
Me
OBn
0.06
4.80
2.01
2.00
2.03
0.93
4.93
2.08
3.25
14
12
10
8
6
4
2
PPM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138.073
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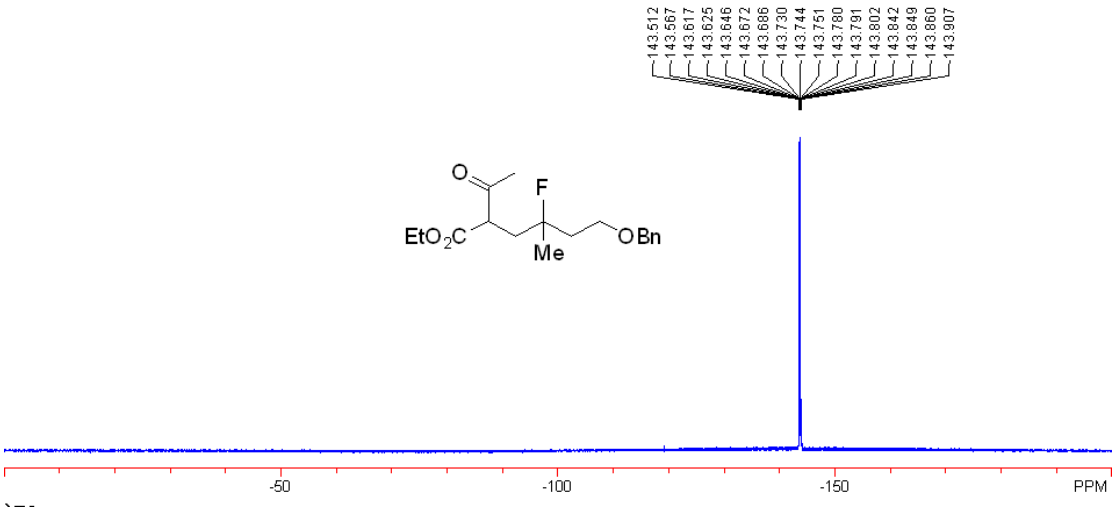
127.671
127.649
127.618
96.468
96.430
94.790
94.752
77.366
77.047
76.728
73.144
73.129
65.681
65.605
61.597
55.022
54.992
54.969
54.946
39.822
39.595
39.466
39.238
37.727
37.514
28.950
28.935
28.875
28.859
24.828
24.585
24.494
24.251
O
F
EtO2C
Me
OBn
200
150
100
50
PPM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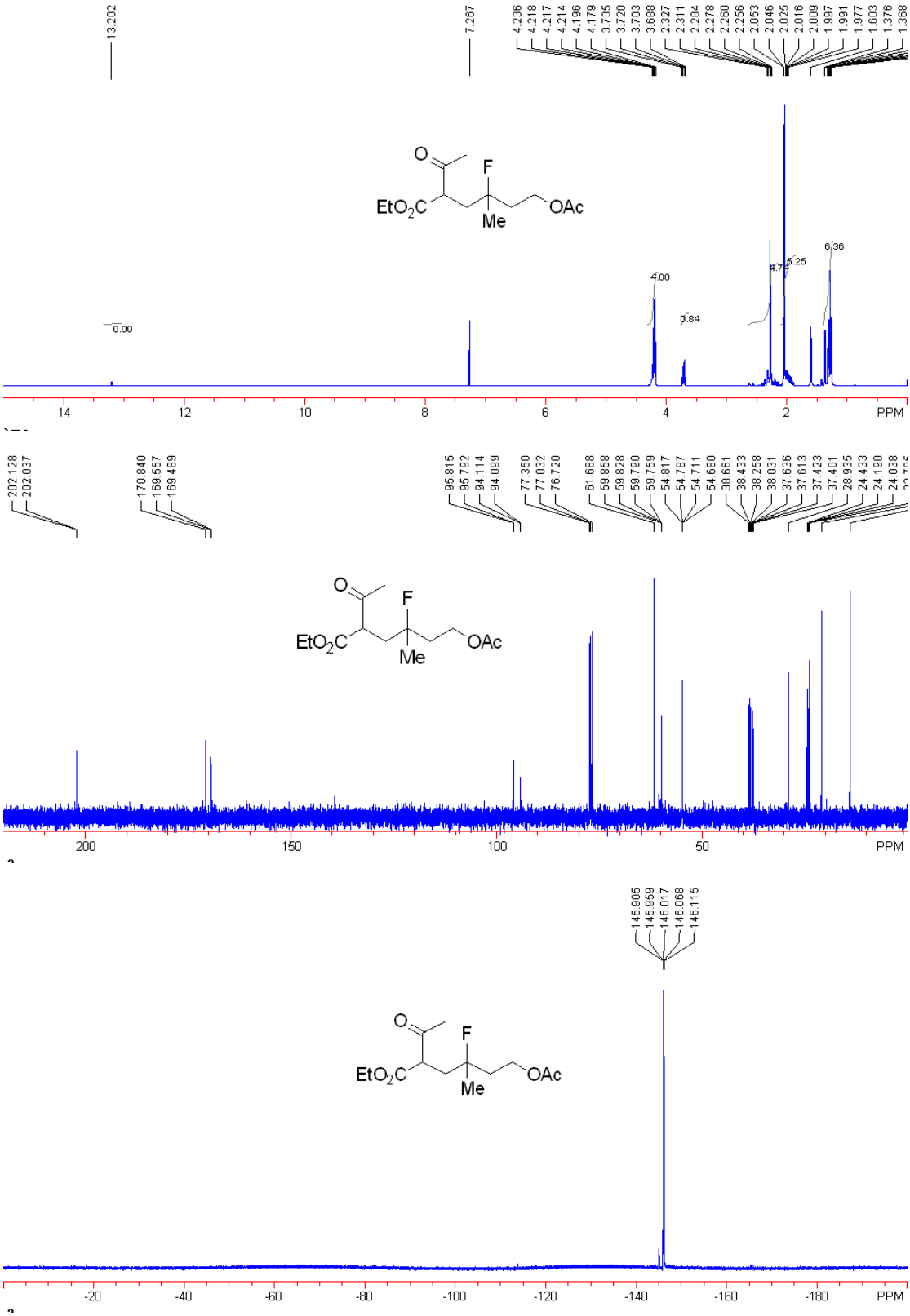
143.617
143.625
143.646
143.672
143.686
143.730
143.744
143.751
143.780
143.791
143.802
143.842
143.849
143.860
143.907
O
F
EtO2C
Me
OBn
-50
-100
-150
PPM

Compound **1i**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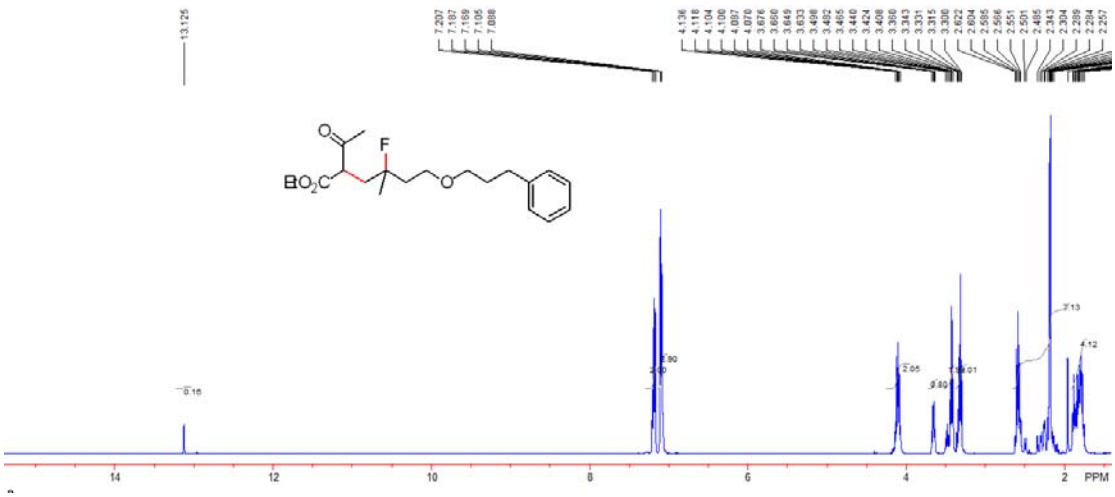
7.267
4.236
4.218
4.217
4.214
4.196
4.179
3.735
3.720
3.703
3.688
2.327
2.311
2.284
2.278
2.260
2.256
2.053
2.046
2.025
2.016
2.009
1.997
1.991
1.977
1.603
1.376
1.368
O
F
EtO2C
Me
OAc
6.36
5.25
4.77
4.00
0.84
0.09
14
12
10
8
6
4
2
PPM
202.128
202.037
170.840
169.557
169.489
95.815
95.792
94.114
94.099
77.350
77.032
76.720
61.688
59.858
59.828
59.790
59.759
54.817
54.787
54.711
54.680
38.661
38.433
38.258
38.031
37.636
37.613
37.423
37.401
28.935
24.433
24.190
24.038
200
150
100
50
PPM
145.905
145.959
146.017
146.068
146.115
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

Compound **1j**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7.197
7.169
7.105
7.088
4.136
4.118
4.104
4.100
4.097
4.070
3.676
3.666
3.649
3.633
3.498
3.465
3.440
3.424
3.408
3.380
3.343
3.331
3.315
3.300
2.622
2.604
2.595
2.566
2.551
2.535
2.496
2.343
2.304
2.289
2.284
2.257
F
O
BtO2C
0.16
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2.05
9.80
9.01
7.13
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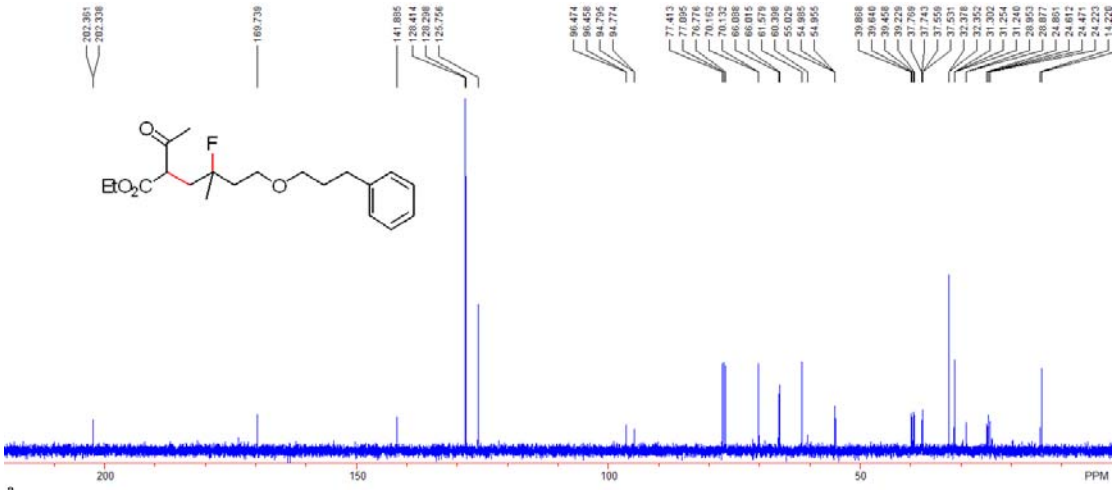
14
12
10
8
6
4
2
PPM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125.756
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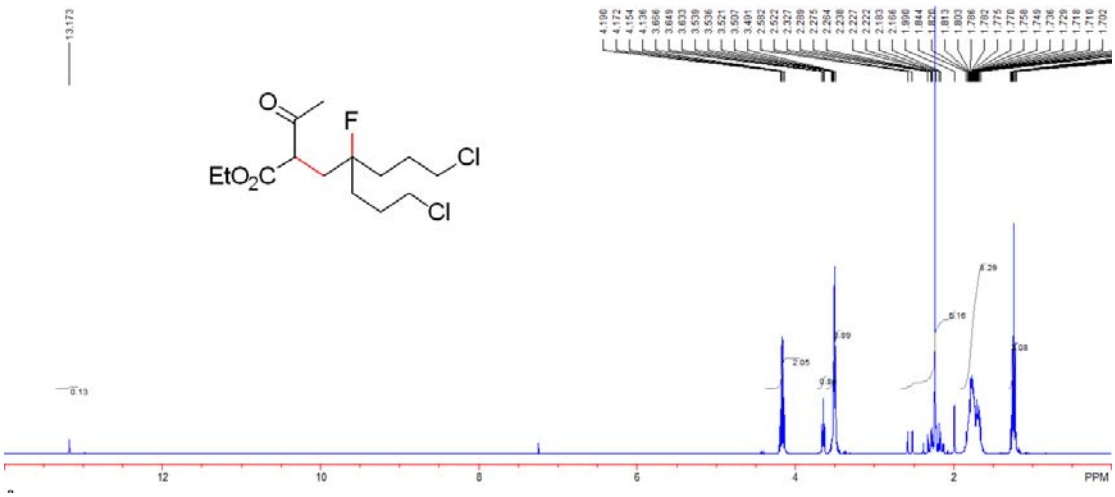
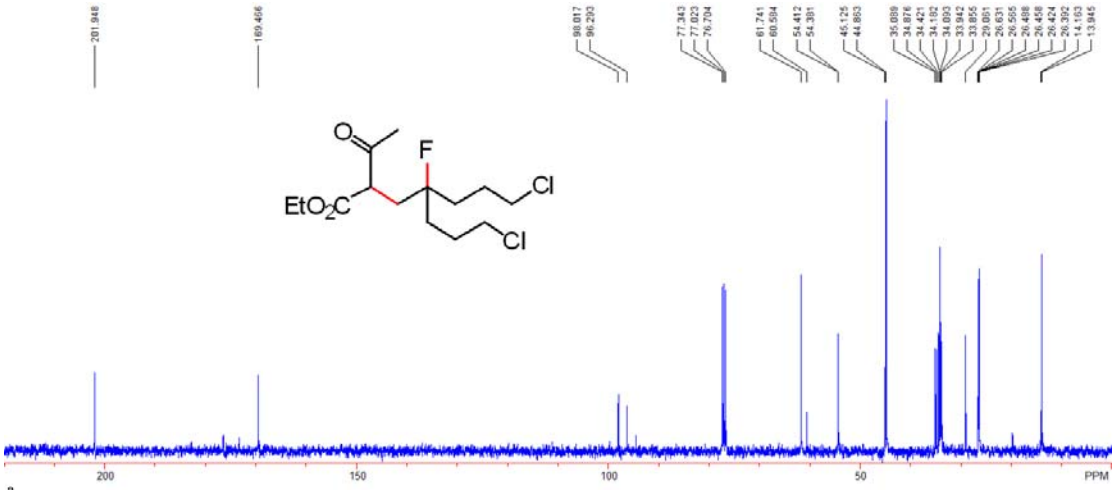
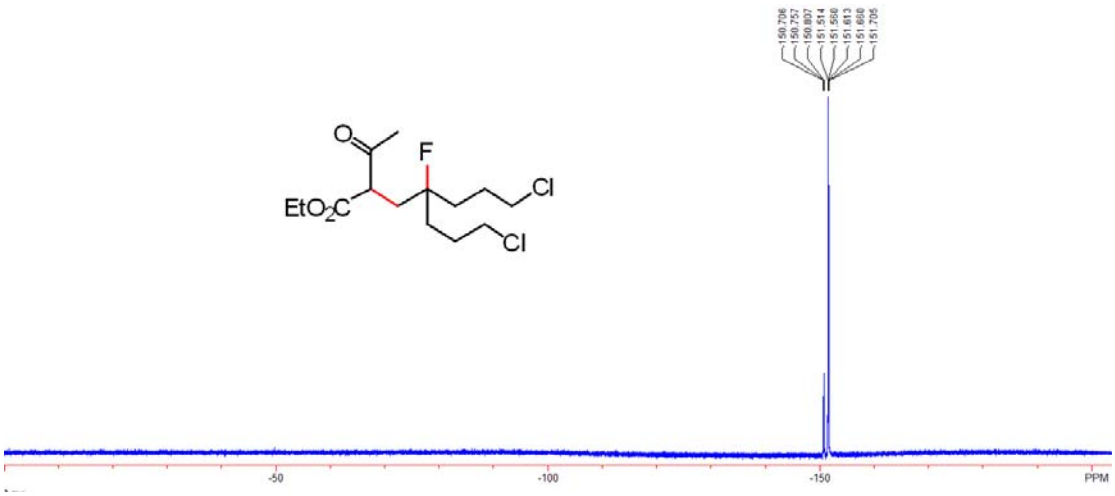
96.458
94.795
94.774
77.413
77.095
76.776
70.162
70.132
66.688
66.615
61.579
60.398
55.029
54.985
54.955
39.808
39.646
39.458
39.229
38.999
37.743
37.559
37.531
32.378
32.352
31.302
31.254
31.246
28.953
28.877
24.851
24.612
24.471
24.223
14.226
F
O
BtO2C
200
150
100
50
PPM


143.351
143.401
143.457
143.507
143.514
143.553
143.573
143.594
143.624
143.635
143.646
143.686
143.692
F
O
BtO2C
-50
-100
-150
PPM

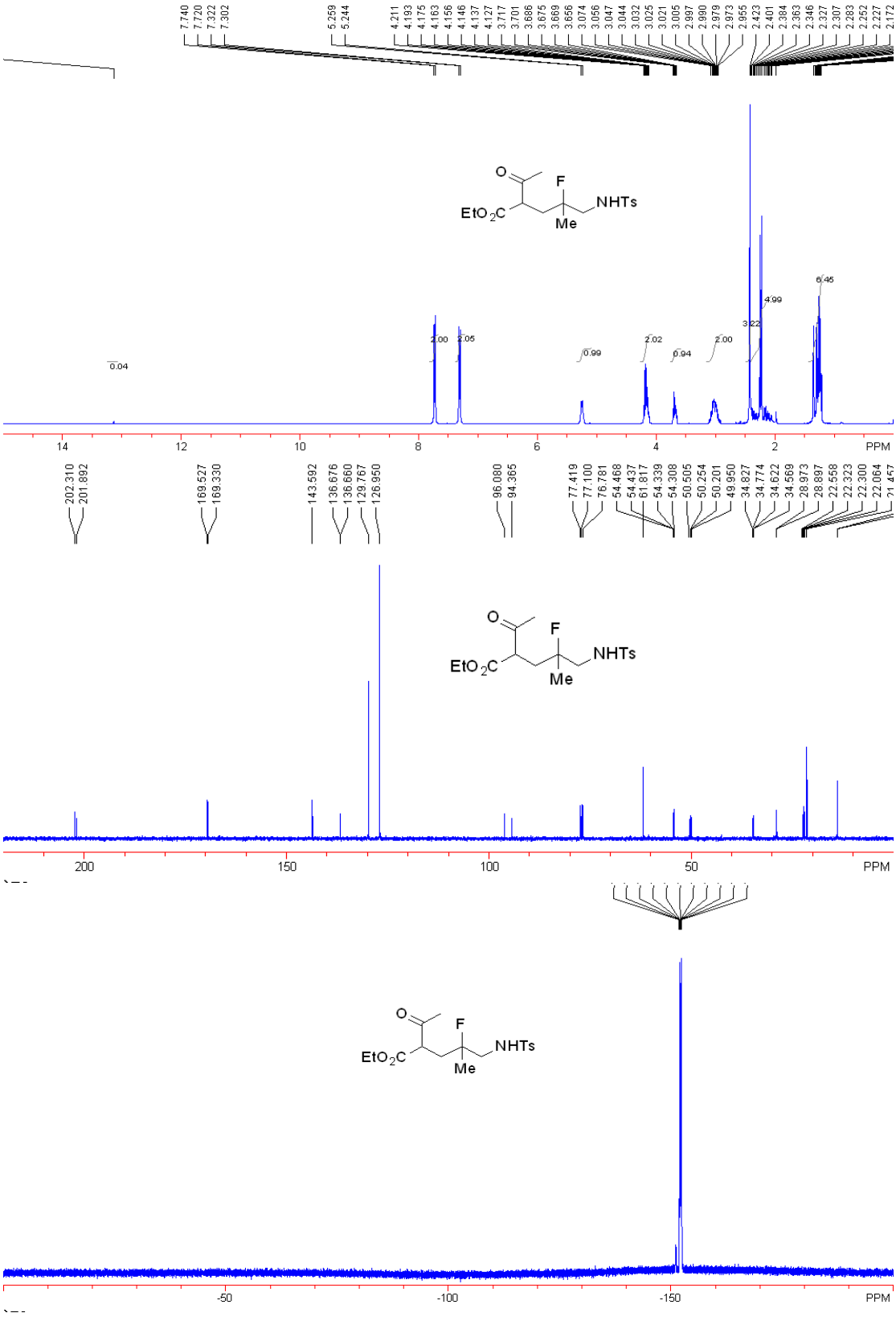
Compound **1k**







Compound **1l**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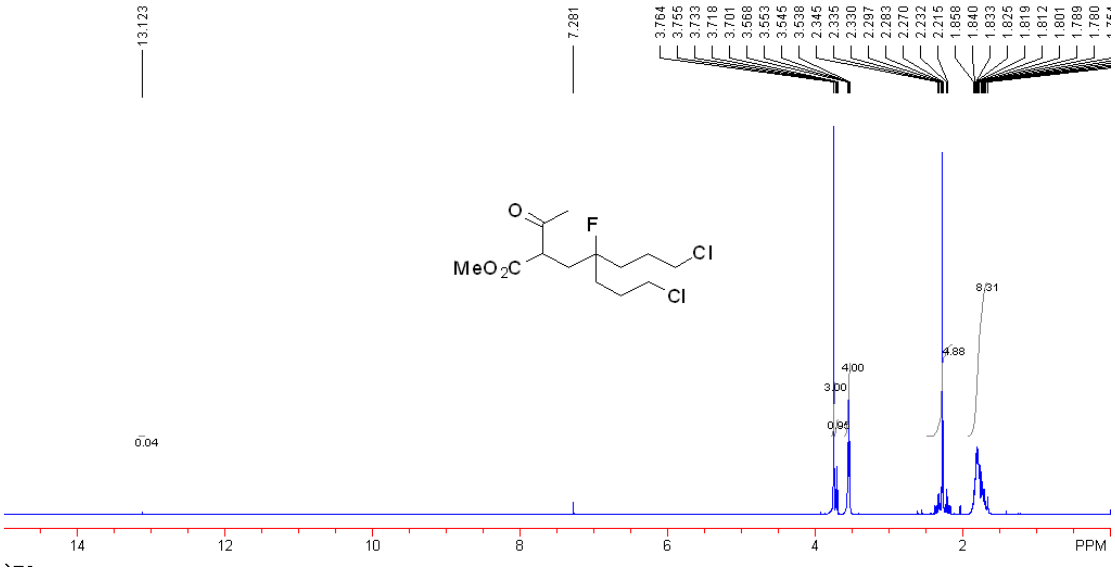
7.302
5.259
5.244
4.211
4.193
4.175
4.163
4.156
4.146
4.137
4.127
3.717
3.701
3.686
3.675
3.669
3.656
3.074
3.056
3.047
3.044
3.032
3.025
3.021
3.005
2.987
2.990
2.979
2.973
2.955
2.423
2.401
2.384
2.363
2.346
2.327
2.307
2.283
2.252
2.227
2.172
O
F
NHTs
EtO2C
Me
0.04
2.00
2.05
0.99
2.02
0.94
2.00
3.22
4.99
6.46
14
12
10
8
6
4
2
PPM
202.310
201.892
169.527
169.330
143.592
136.676
136.660
129.767
126.950
96.080
94.365
77.419
77.100
76.781
54.468
54.437
61.817
54.339
54.308
50.505
50.254
50.201
49.950
34.827
34.774
34.622
34.569
28.973
28.897
22.558
22.323
22.300
22.064
200
150
100
50
PPM
-50
-100
-150
PPM

Compound **1m**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3.764
3.755
3.733
3.718
3.701
3.568
3.553
3.545
3.538
2.345
2.335
2.330
2.297
2.283
2.270
2.232
2.215
1.858
1.840
1.833
1.825
1.819
1.812
1.801
1.789
1.780
O
F
MeO2C
Cl
Cl
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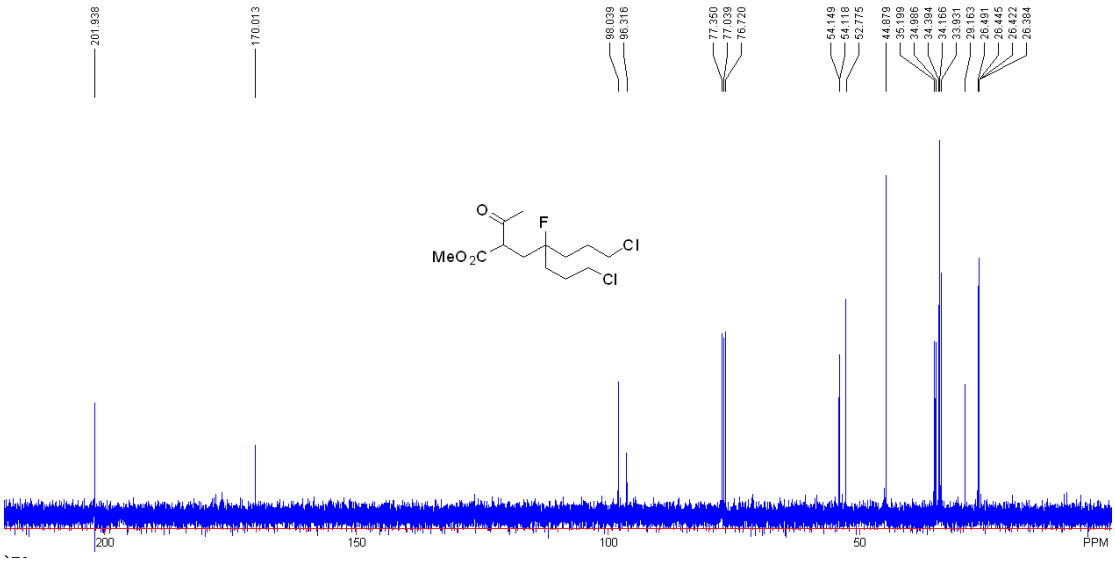
4.88
4.00
3.00
0.95
0.04
14
12
10
8
6
4
2
PPM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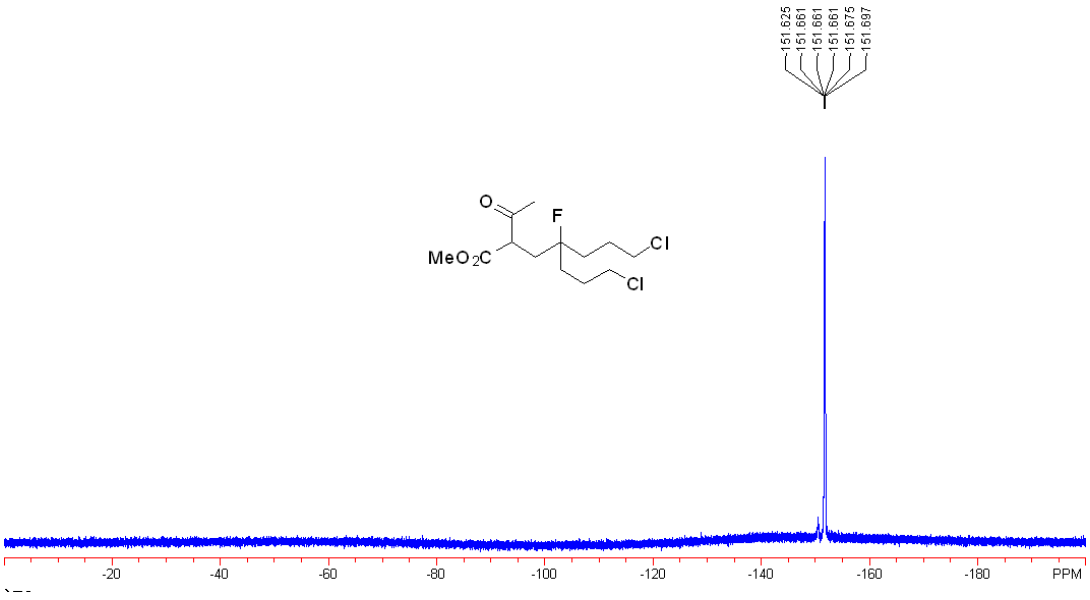
98.039
96.316
77.350
77.039
76.720
54.149
54.118
52.775
44.879
35.199
34.986
34.394
34.166
33.931
29.163
26.491
26.445
26.422
26.384
O
F
MeO2C
Cl
Cl
200
150
100
50
PPM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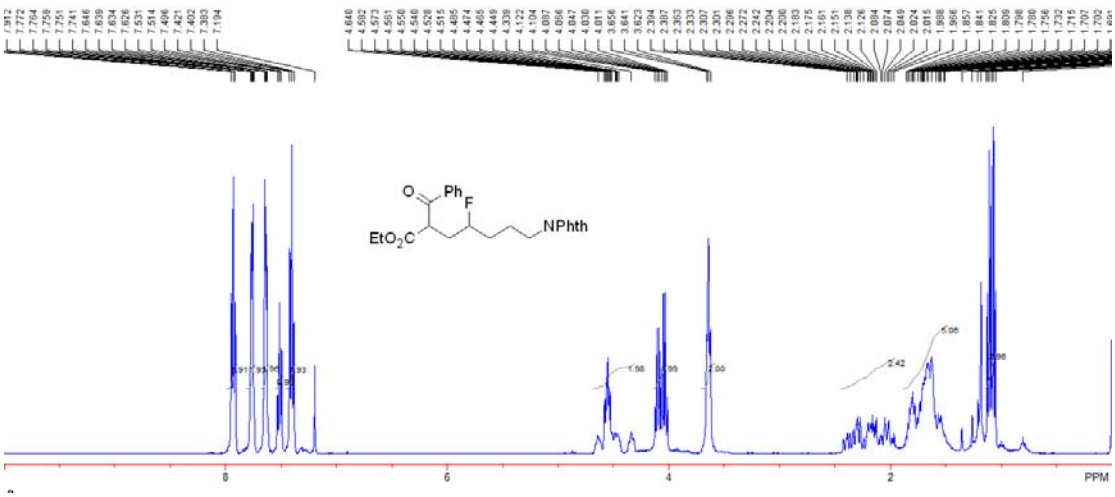
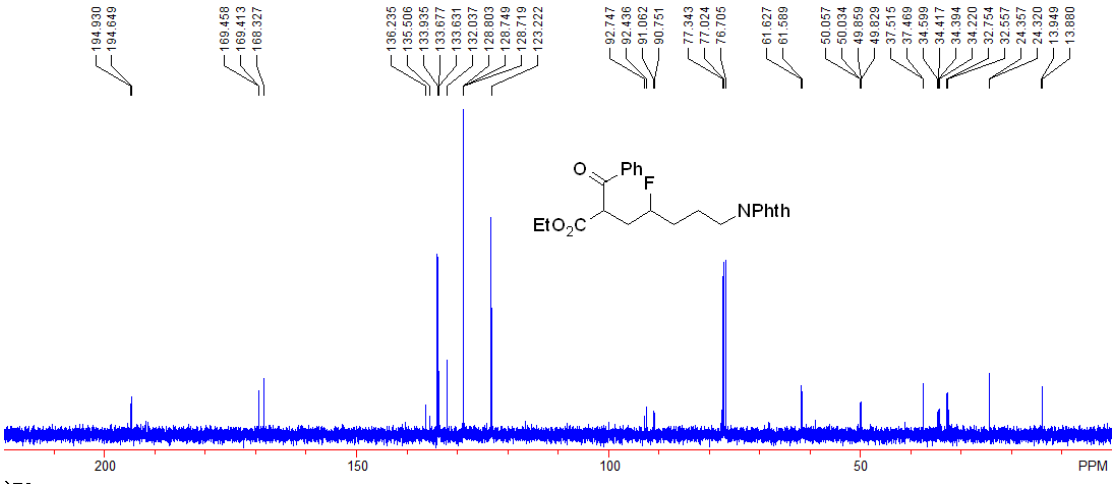
151.661
151.661
151.661
151.675
151.697
O
F
MeO2C
Cl
Cl
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

Compound **1n**


O
Ph
F
EtO2C
NPhth
PPM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194.649
169.458
169.413
168.327
136.235
135.506
133.935
133.677
133.631
132.037
128.803
128.749
128.719
123.222
92.747
92.436
91.062
90.751
77.343
77.024
76.705
61.627
61.589
50.057
50.034
49.859
49.829
37.515
37.469
34.599
34.417
34.394
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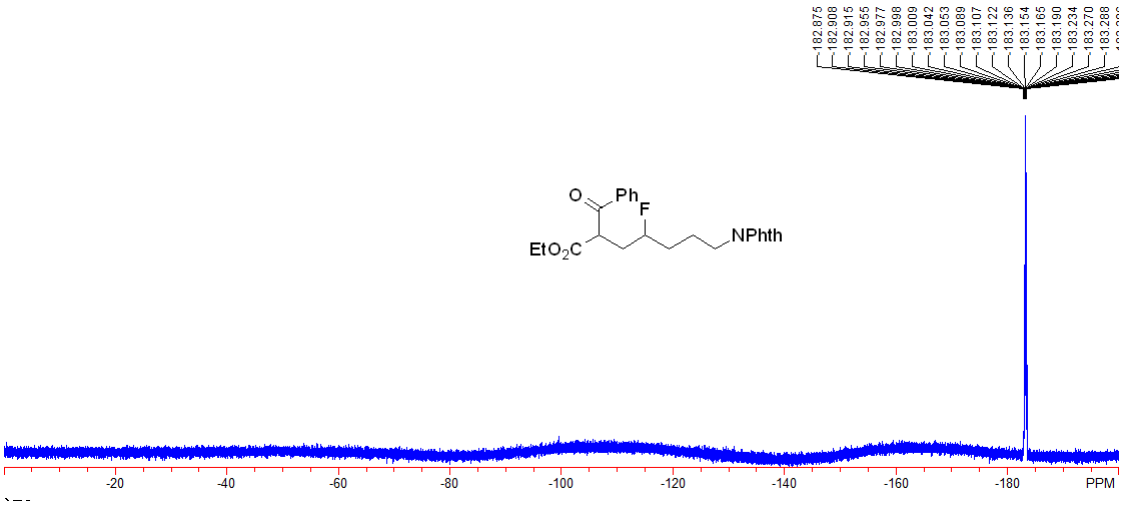
32.557
24.357
24.320
13.949
13.880
O
Ph
F
EtO2C
NPhth
PPM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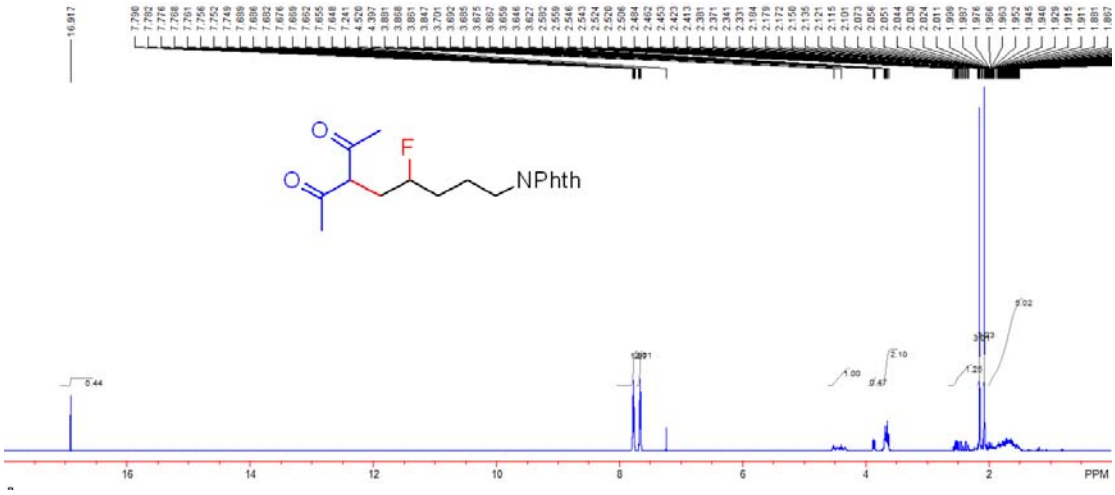
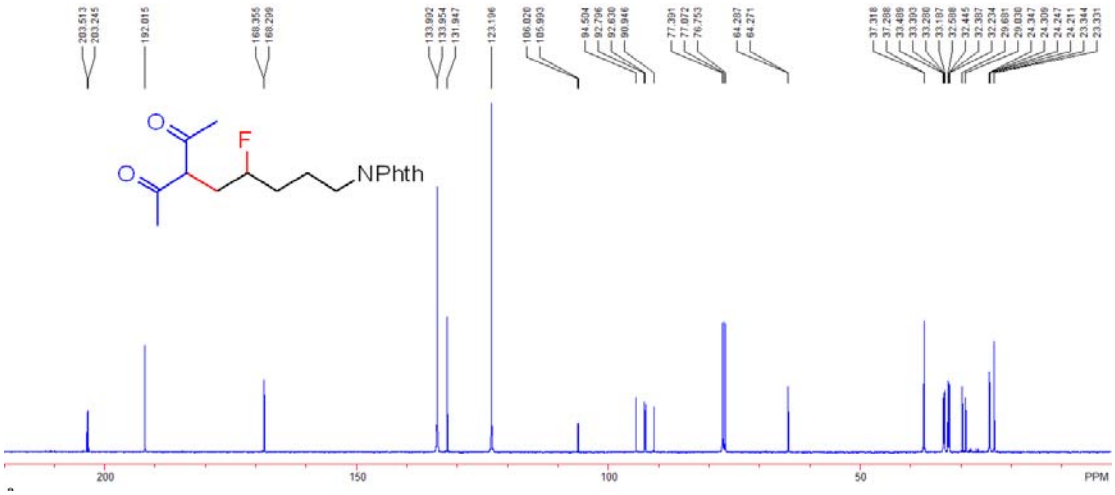
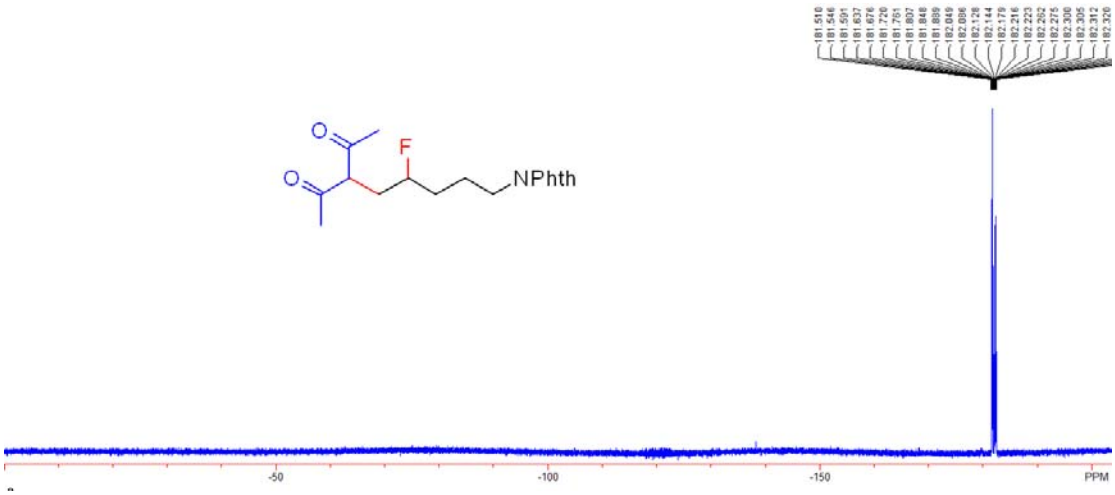
183.009
183.042
183.053
183.089
183.107
183.122
183.136
183.154
183.165
183.190
183.234
183.270
183.288
O
Ph
F
EtO2C
NPhth
PPM

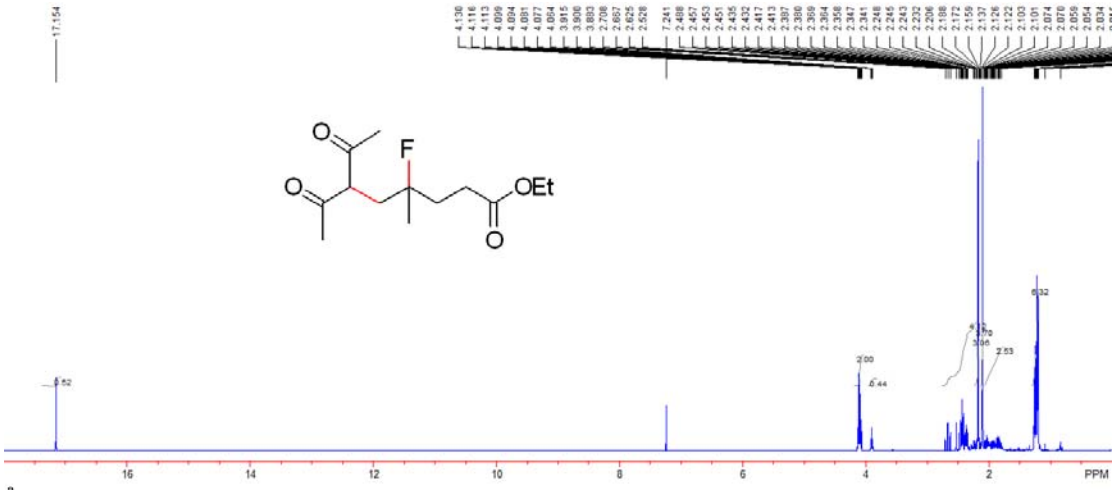
Compound **1o**

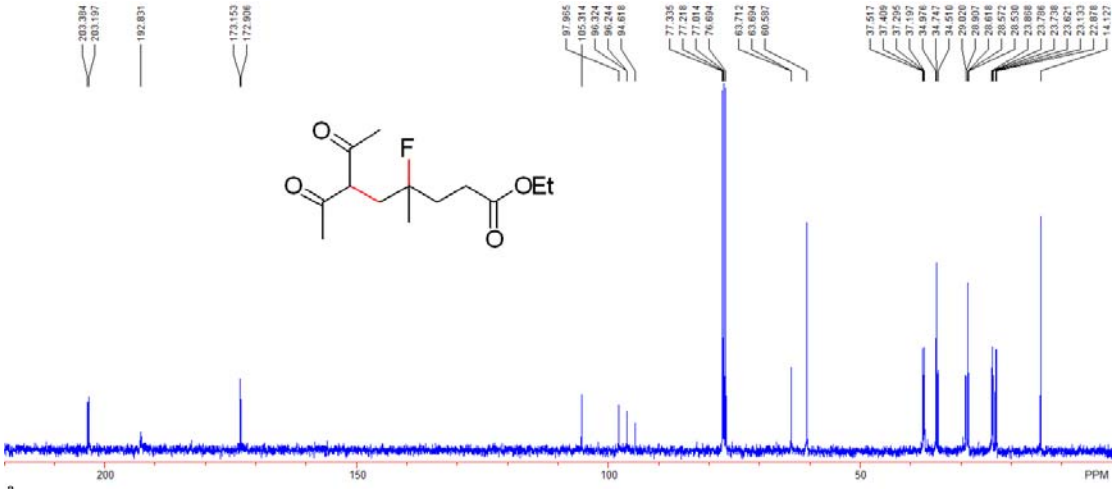


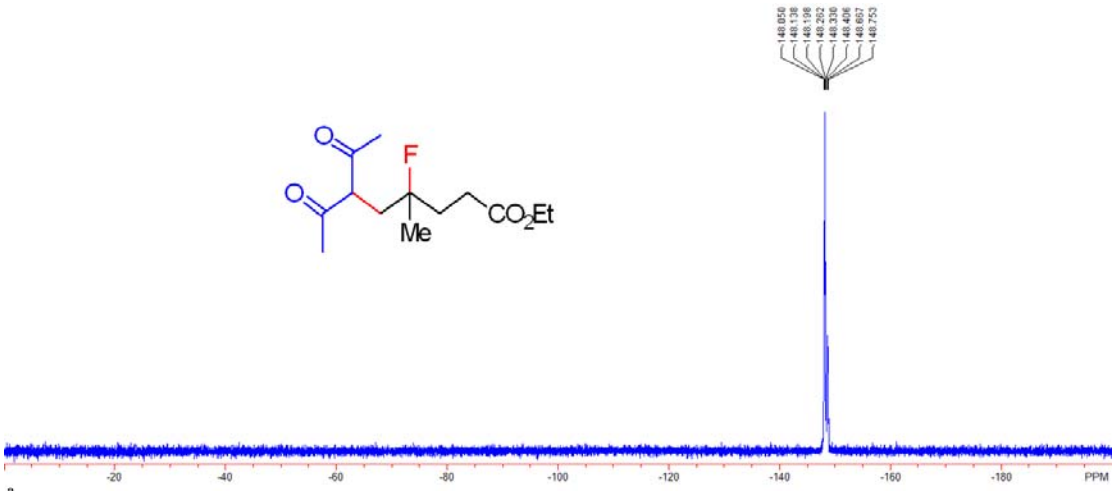




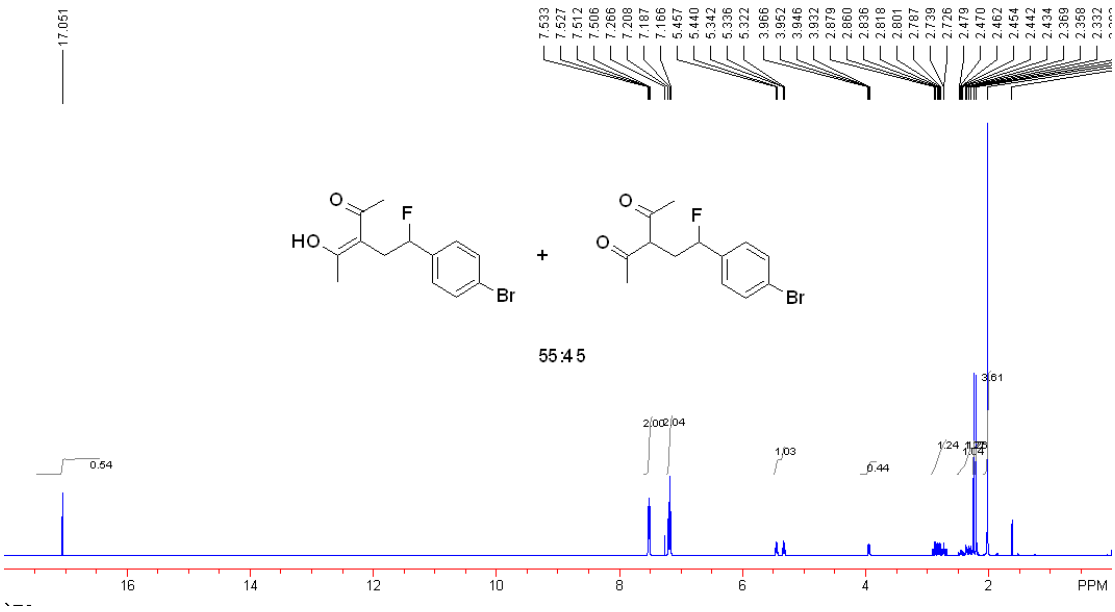
Compound **1p**

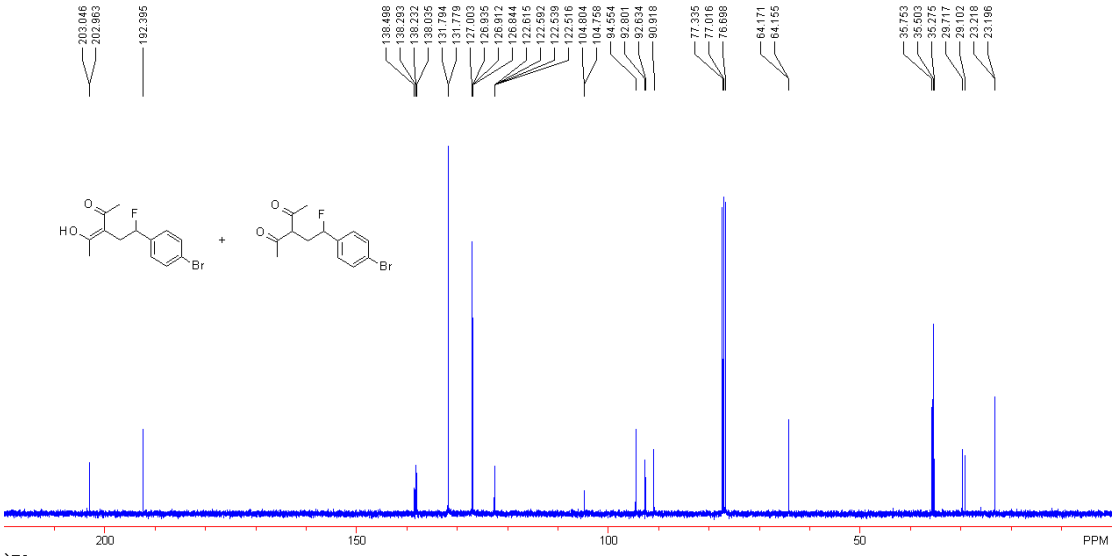


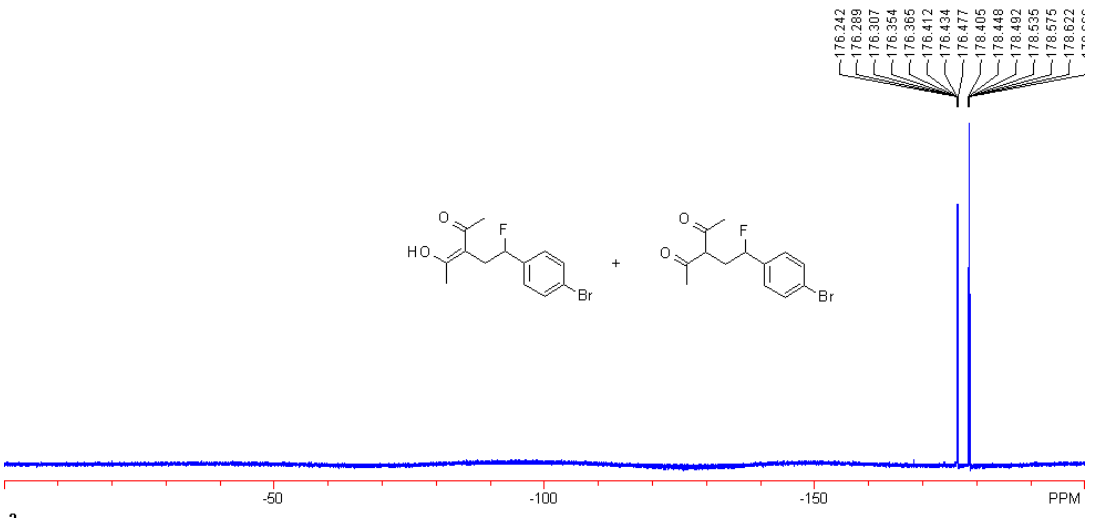




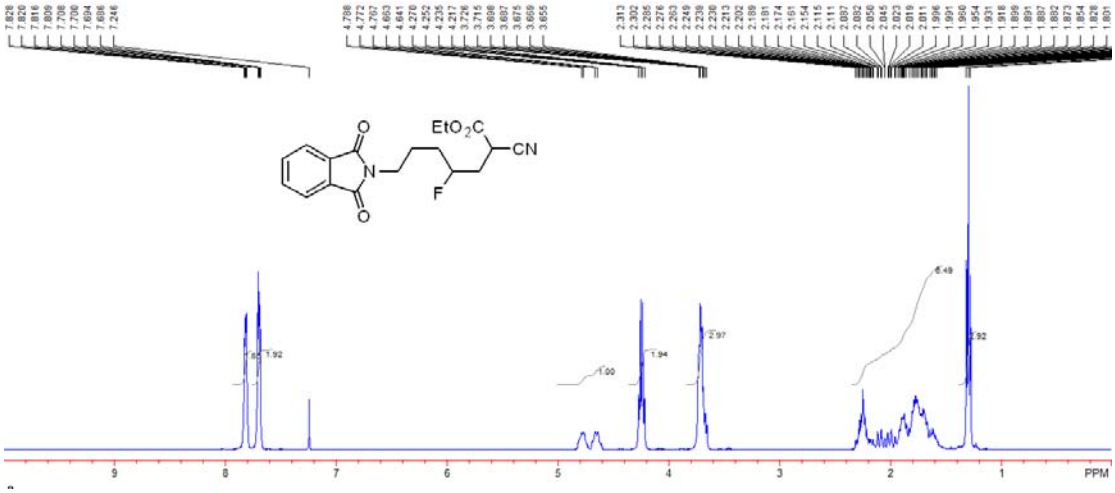
Compound **1q**

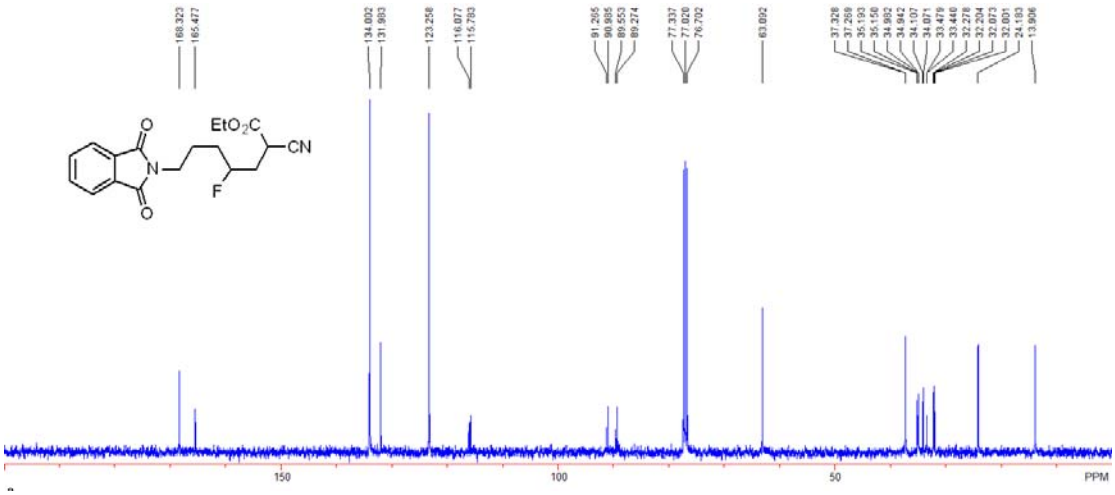


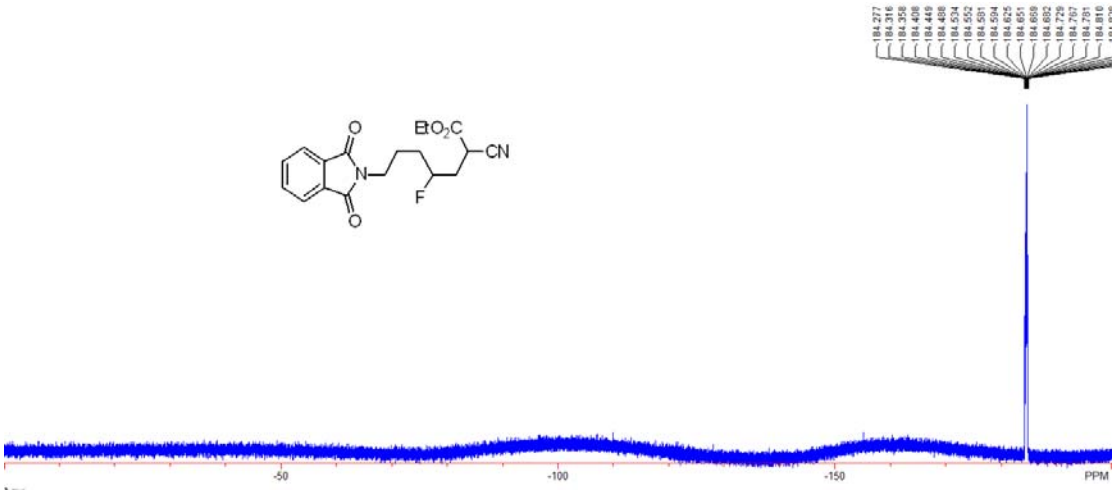




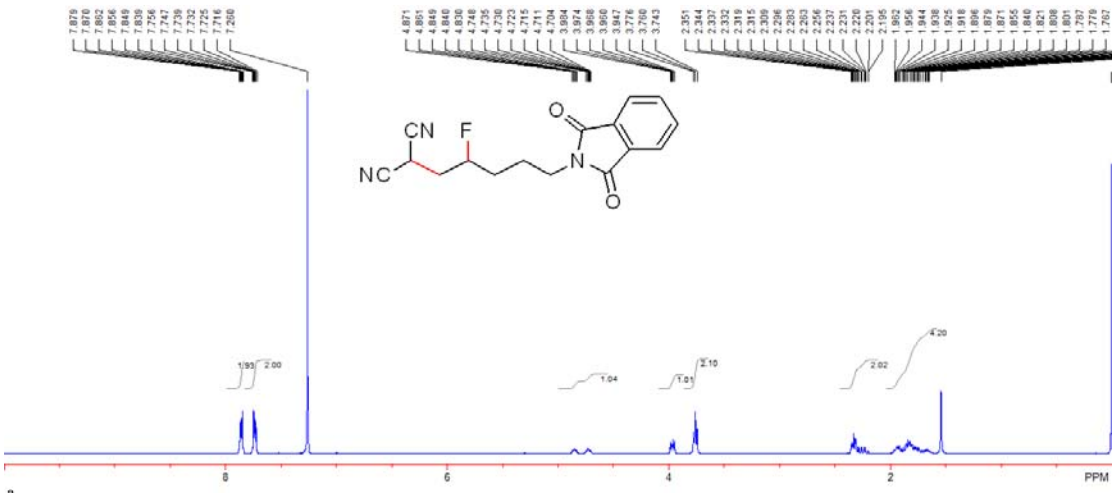
Compound **1r**

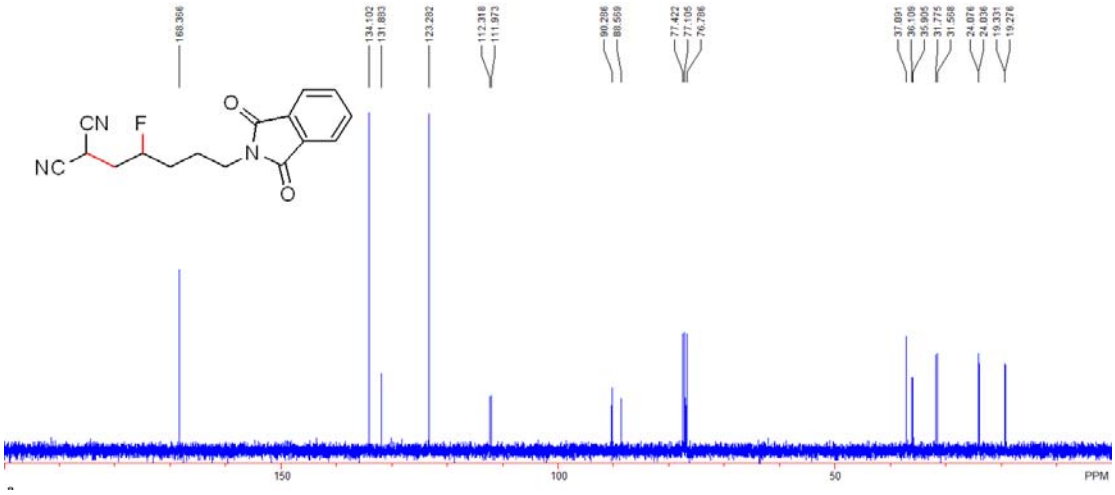

EtO2C
CN
F
O
N
O
1.92
1.00
1.94
2.97
6.49
2.92
PPM

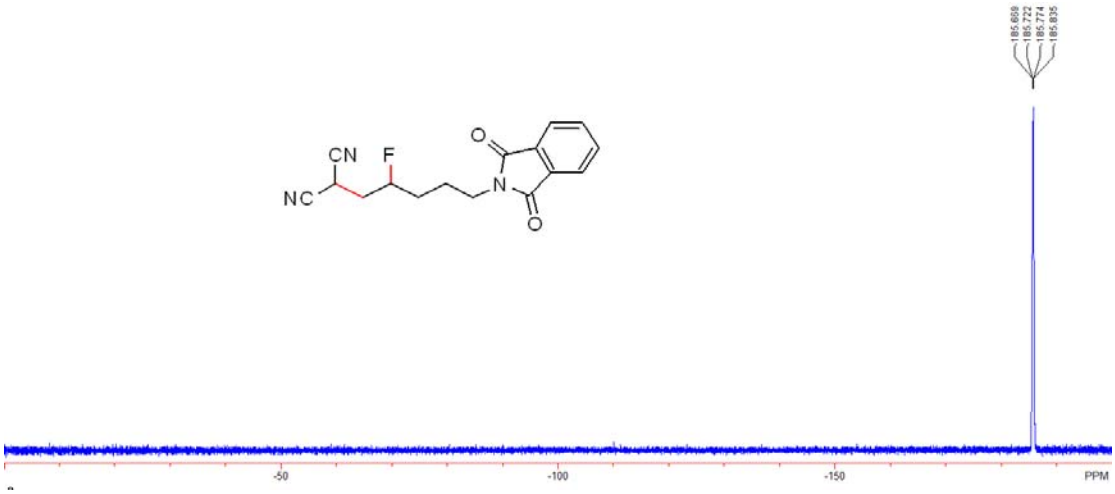

EtO2C
CN
F
O
N
O
168.323
165.477
134.602
131.803
123.258
116.877
115.793
91.265
90.805
89.553
89.274
77.337
77.026
76.702
63.602
37.326
37.269
35.193
35.156
34.892
34.842
34.107
34.071
33.478
33.446
32.376
32.334
32.073
32.001
24.193
13.906
150
100
50
PPM


EtO2C
CN
F
O
N
O
184.277
184.316
184.358
184.408
184.449
184.488
184.534
184.552
184.591
184.594
184.625
184.651
184.659
184.682
184.729
184.767
184.791
-50
-100
-150
PPM

Compound **1s**

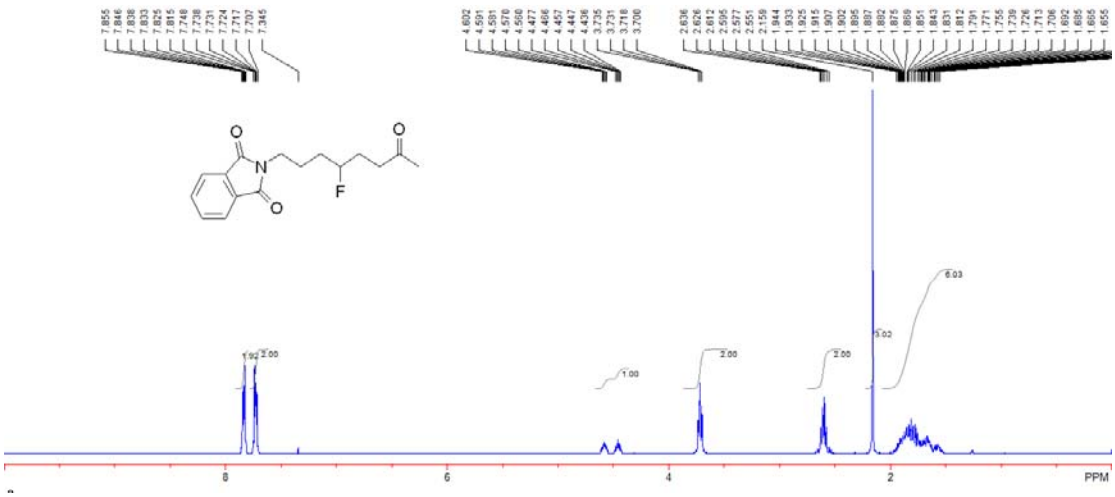


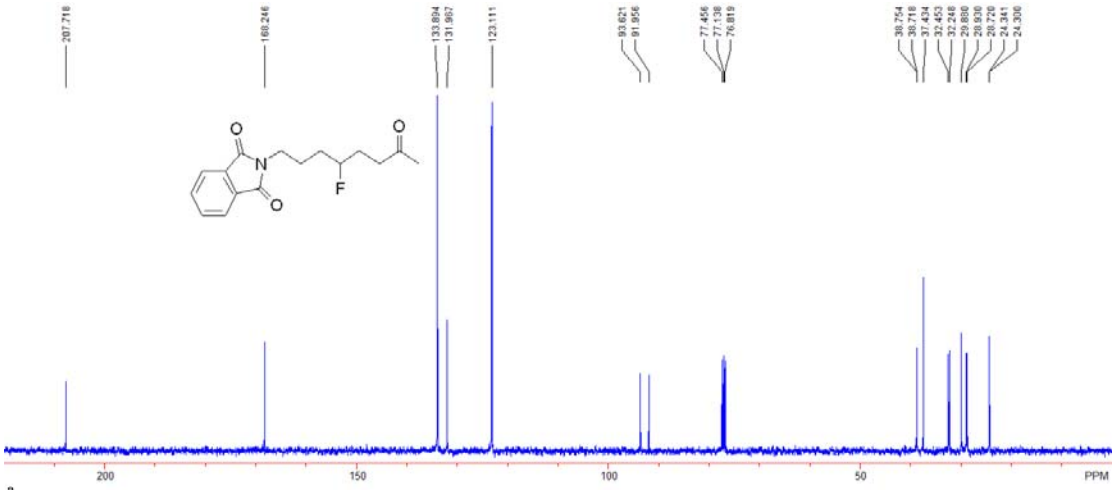


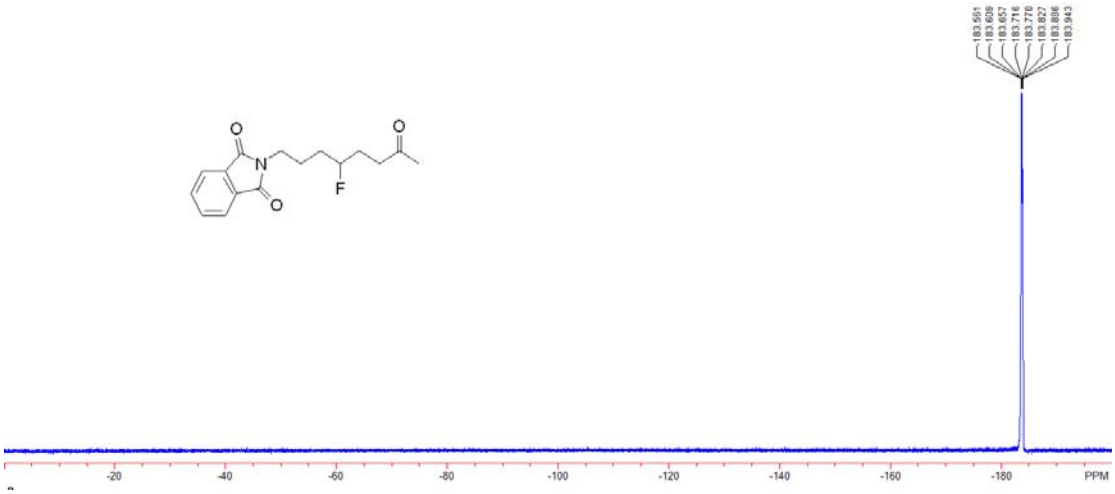


.

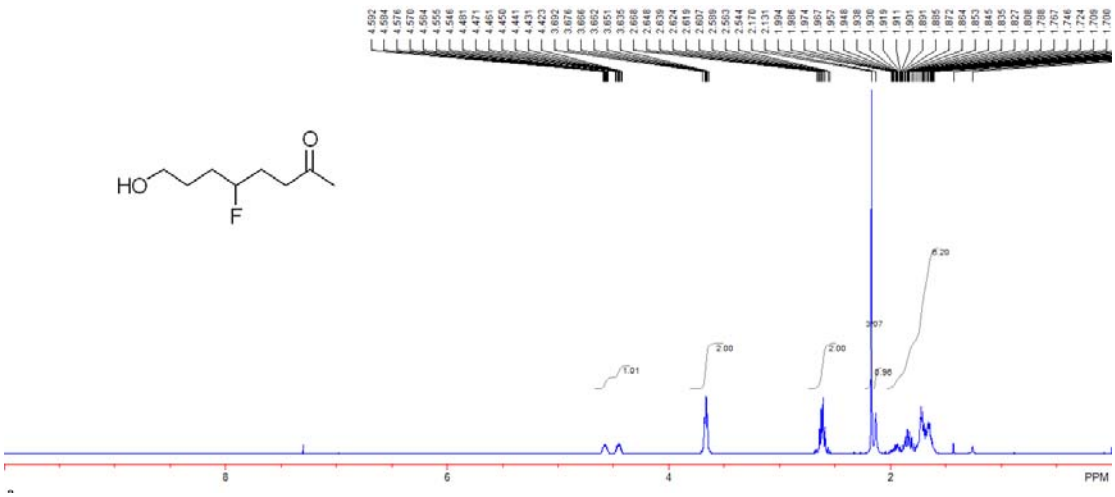
Compound **2a**

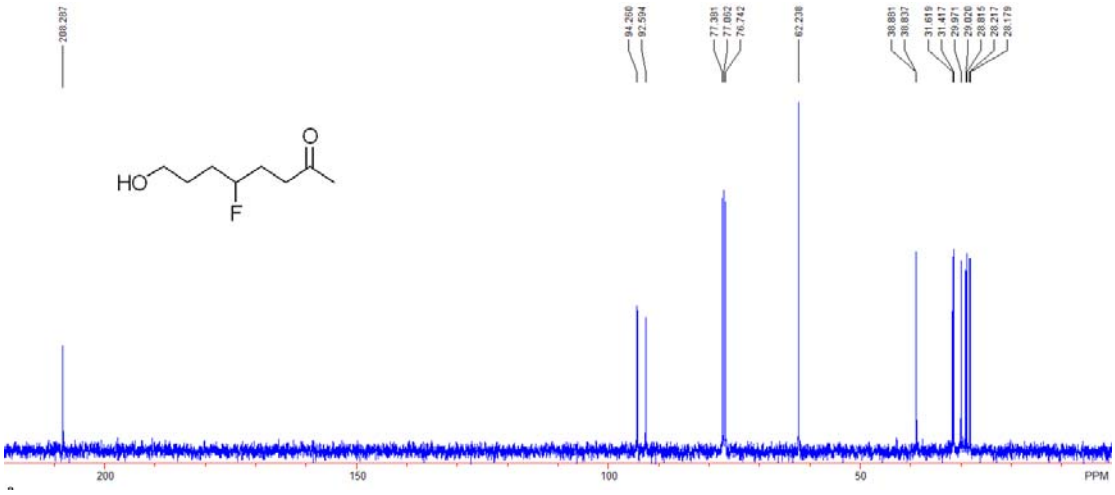

7.855
7.846
7.838
7.833
7.825
7.815
7.746
7.738
7.731
7.724
7.717
7.707
7.345
4.602
4.591
4.581
4.570
4.560
4.477
4.466
4.457
4.447
4.436
3.735
3.731
3.718
3.700
2.636
2.626
2.612
2.595
2.577
2.551
2.159
1.944
1.933
1.925
1.915
1.907
1.902
1.895
1.892
1.892
1.875
1.869
1.851
1.843
1.831
1.812
1.791
1.771
1.755
1.739
1.724
1.713
1.706
1.692
1.685
1.655
O
N
O
O
F
O
1.92
2.00
1.00
2.00
2.00
5.02
6.03
8
6
4
2
PPM

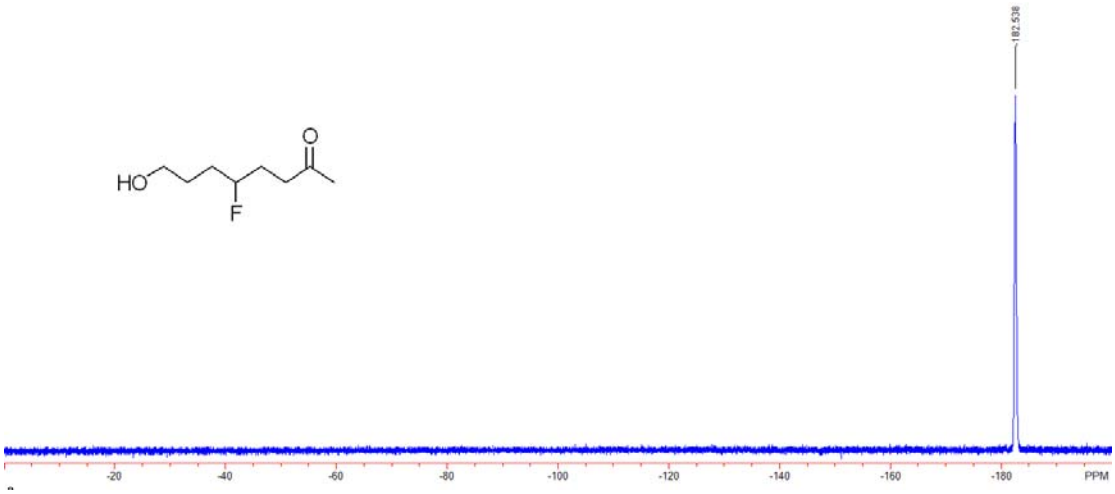

207.716
160.246
133.894
131.987
123.111
93.621
91.956
77.456
77.138
76.819
30.754
30.716
30.434
32.453
32.248
29.880
28.930
28.720
24.341
24.300
O
N
O
O
F
O
200
150
100
50
PPM


183.561
183.609
183.657
183.716
183.770
183.827
183.886
183.943
O
N
O
O
F
O
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

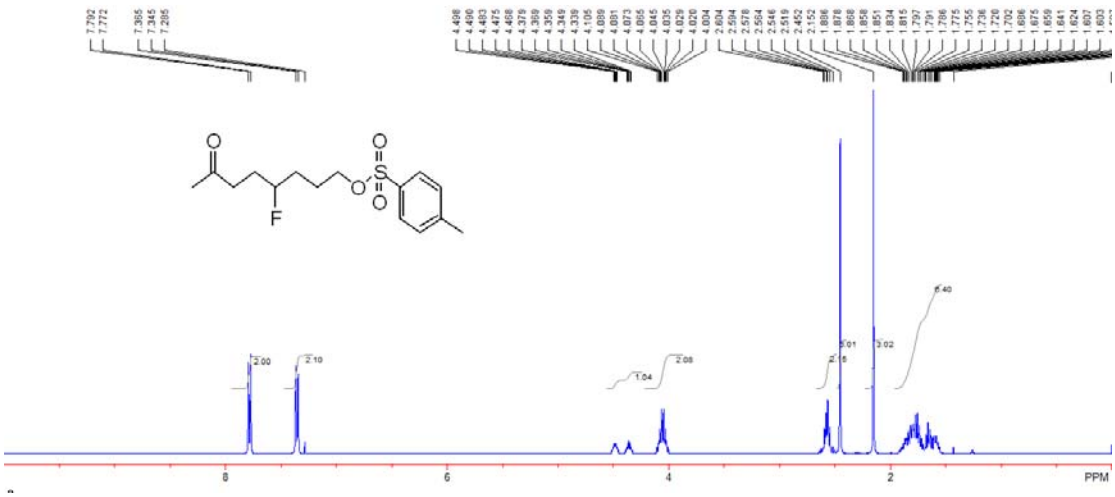
Compound **2b**

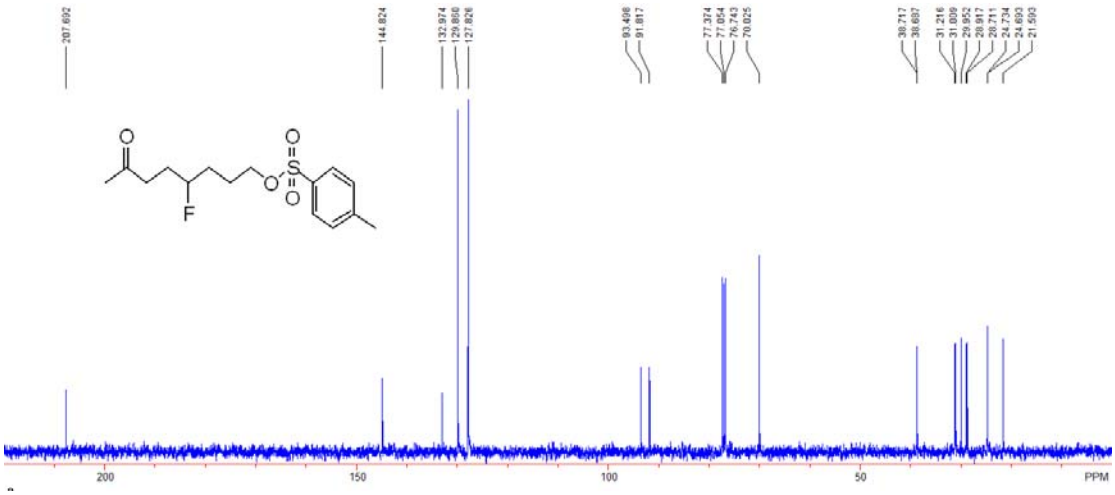

HO
F
O
1.01
2.00
2.00
3.07
5.96
6.29
8
6
4
2
PPM

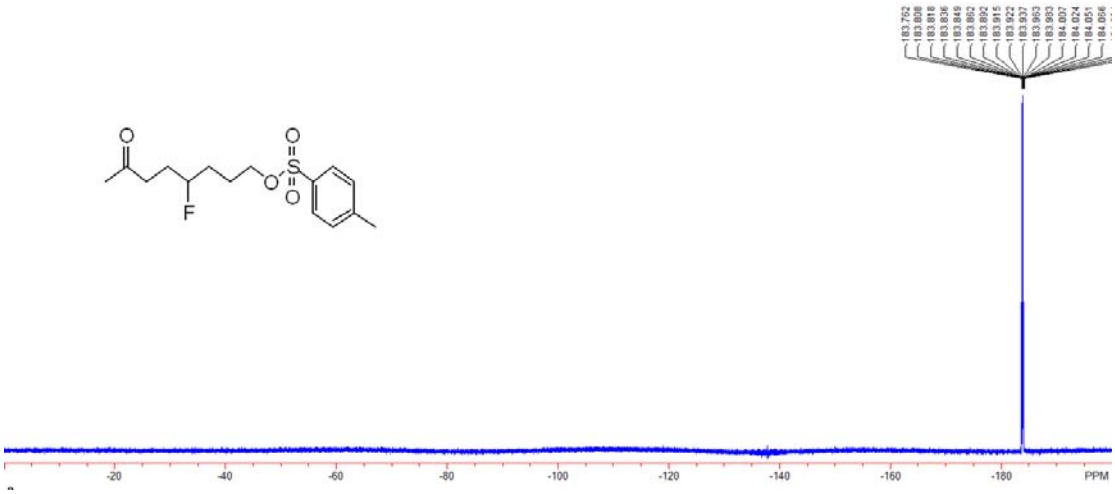

HO
F
O
200
150
100
50
PPM


HO
F
O
-182.538
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

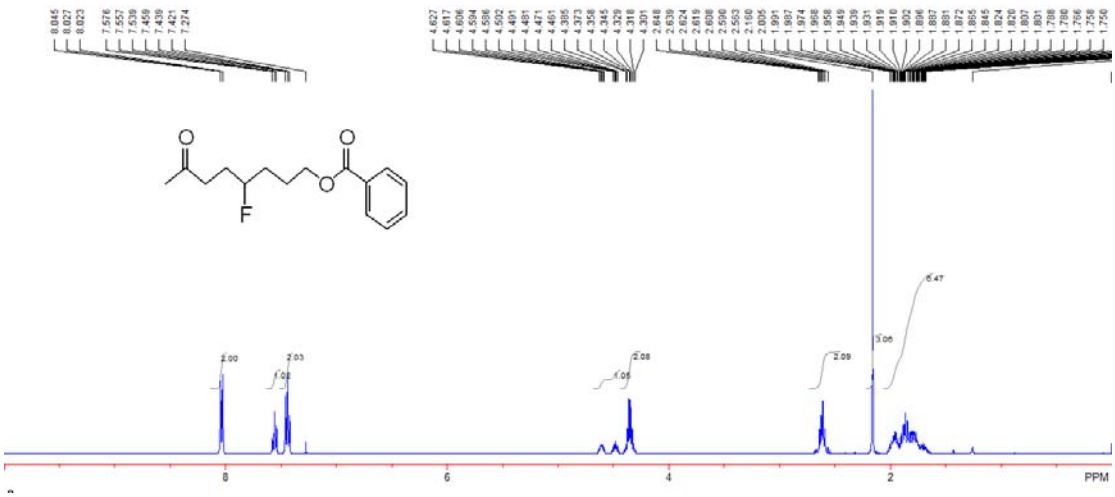
Compound **2c**

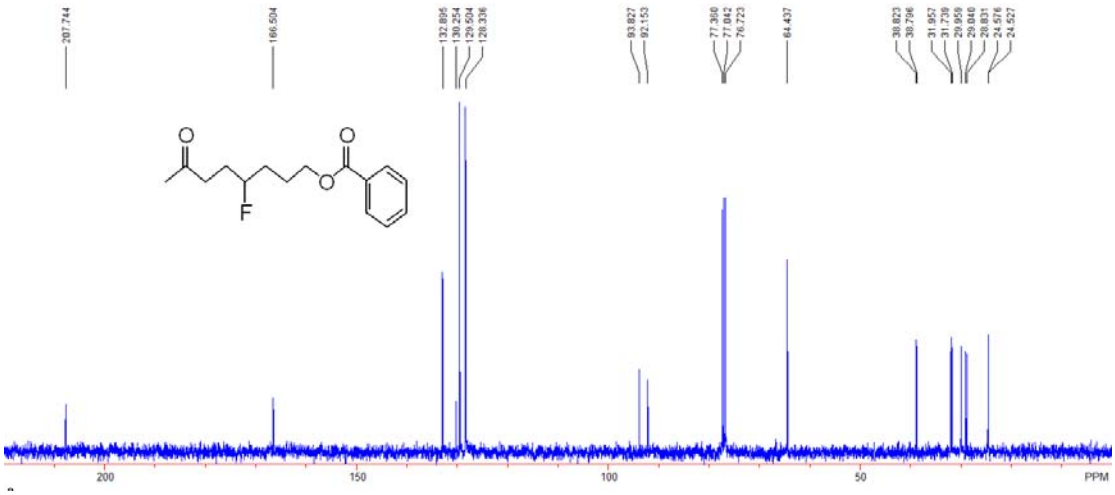


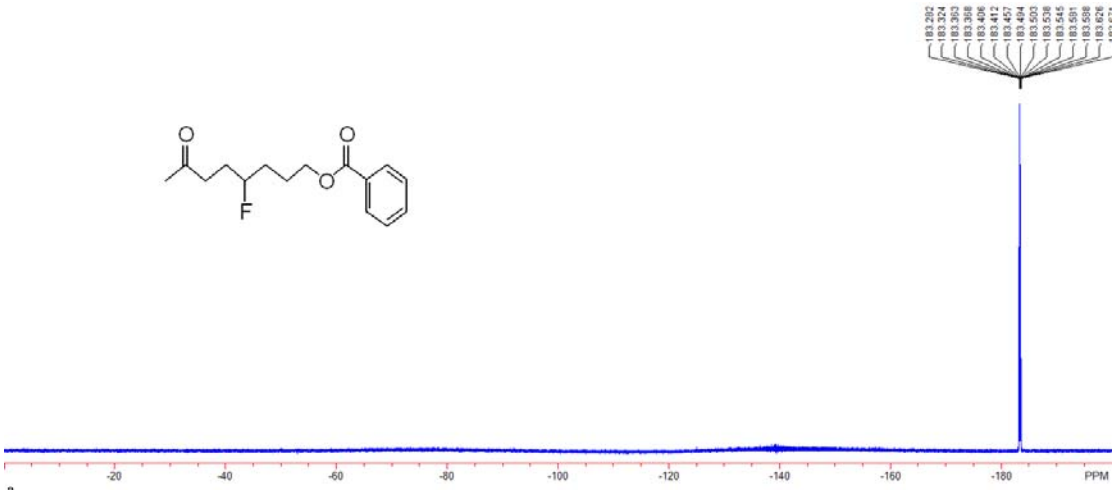




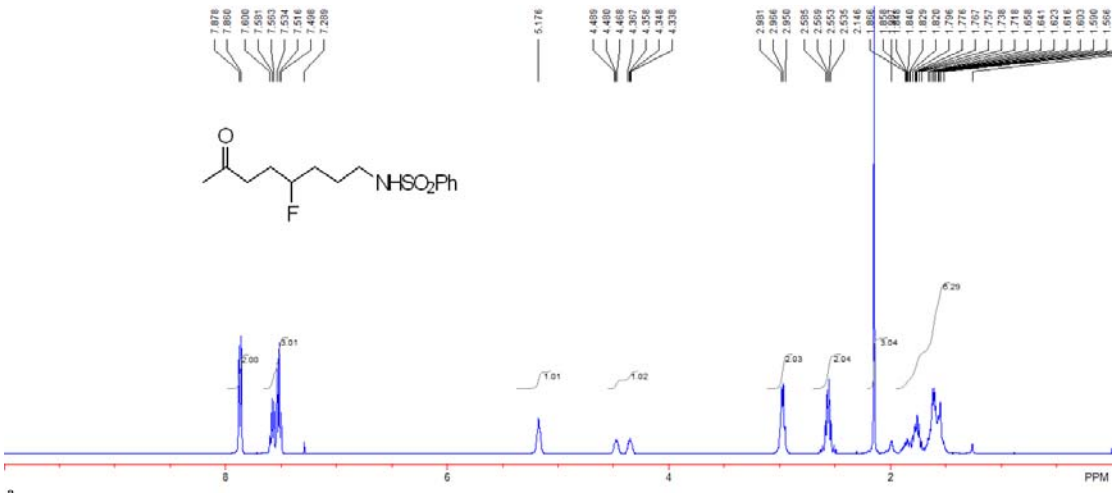
Compound **2d**

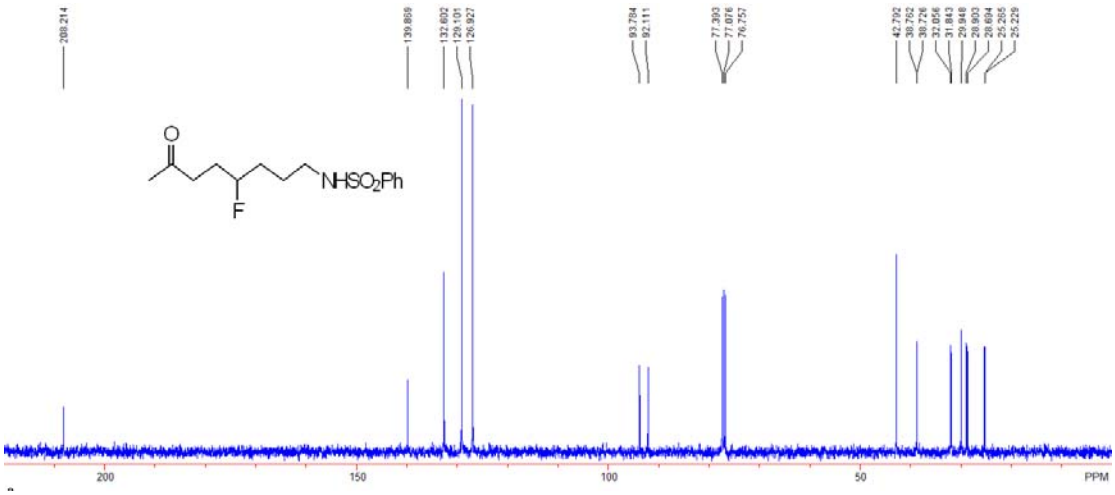

8.045
8.027
8.023
7.576
7.557
7.539
7.459
7.439
7.421
7.274
4.627
4.617
4.606
4.594
4.586
4.502
4.491
4.481
4.471
4.461
4.395
4.373
4.358
4.345
4.329
4.316
4.301
2.648
2.639
2.624
2.619
2.608
2.596
2.583
2.160
2.005
1.991
1.987
1.974
1.958
1.956
1.946
1.939
1.931
1.919
1.910
1.902
1.896
1.887
1.881
1.872
1.855
1.845
1.824
1.820
1.807
1.803
1.798
1.798
1.756
1.758
1.750
O
O
O
F
2.00
2.03
1.02
2.08
1.05
2.09
3.06
5.47
8
6
4
2
PPM

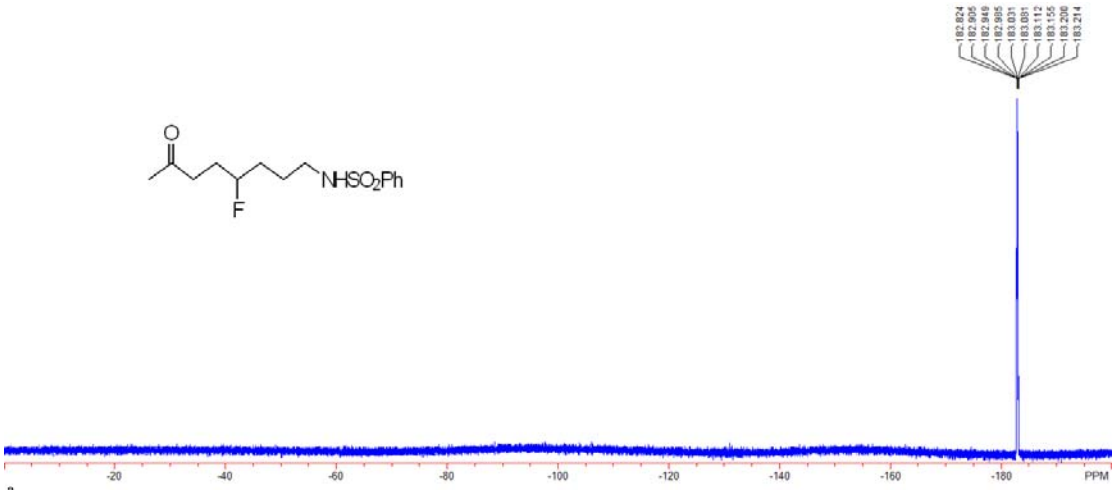

207.744
166.504
132.895
130.254
129.504
128.336
83.827
82.153
77.386
77.042
76.723
64.437
38.823
30.796
31.957
31.739
29.959
29.848
28.831
24.976
24.527
O
O
O
F
200
150
100
50
PPM


183.282
183.324
183.363
183.388
183.409
183.412
183.457
183.494
183.503
183.538
183.545
183.591
183.598
183.626
O
O
O
F
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

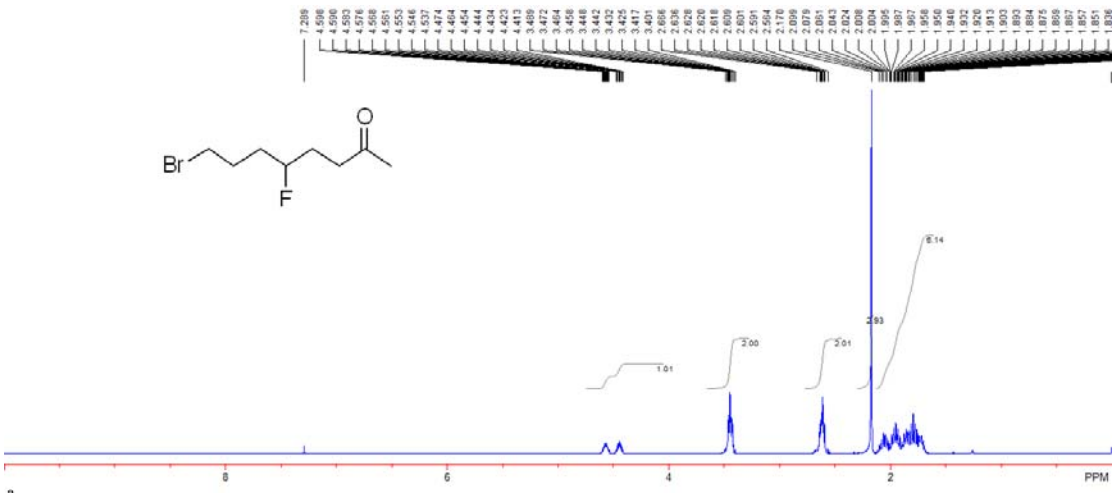
Compound **2e**

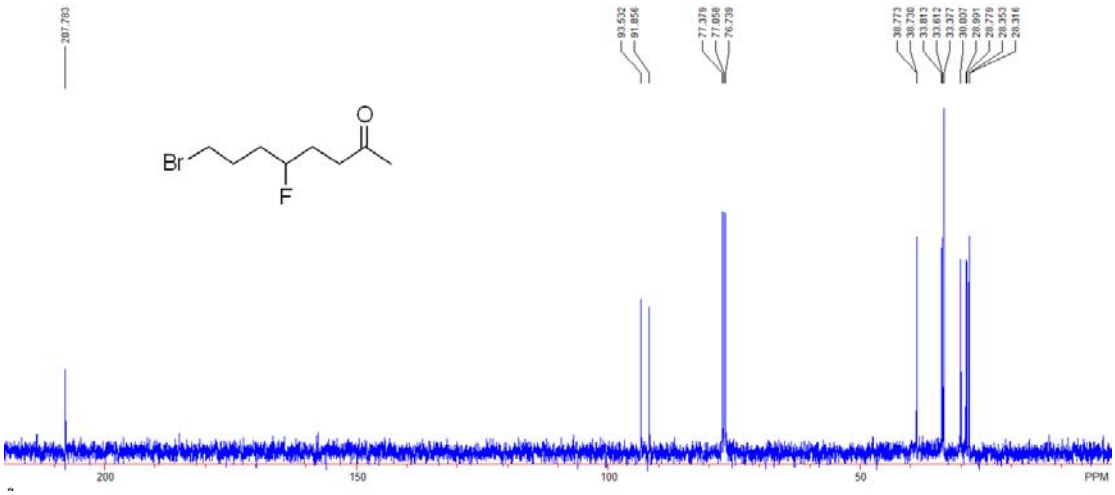


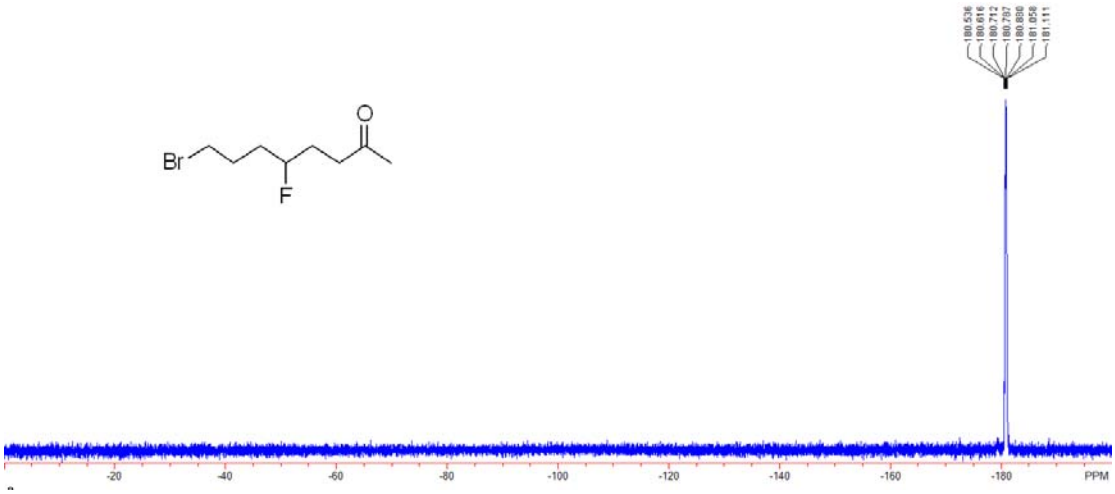




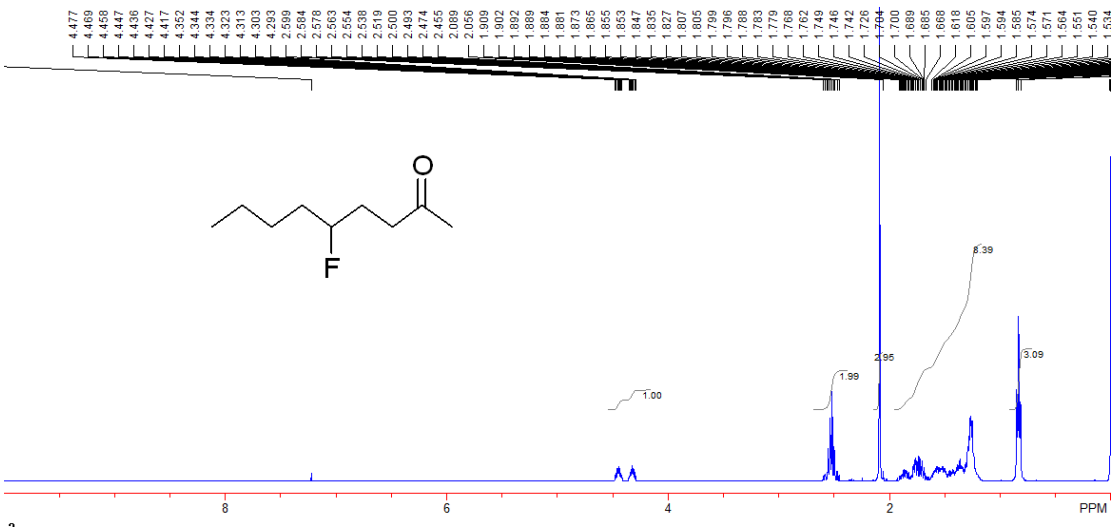
Compound **2f**

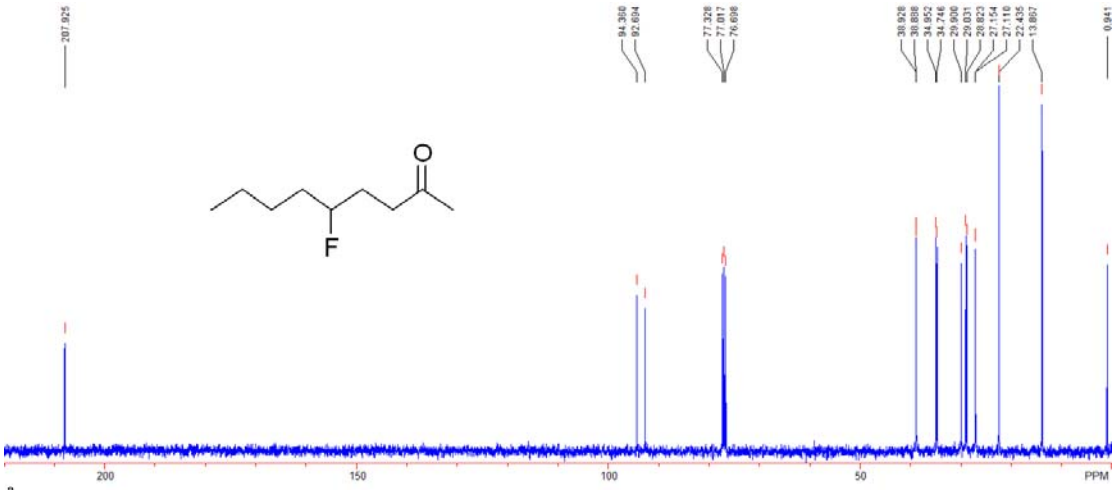

Br
F
O
1.01
2.00
2.01
2.93
6.14
8
6
4
2
PPM

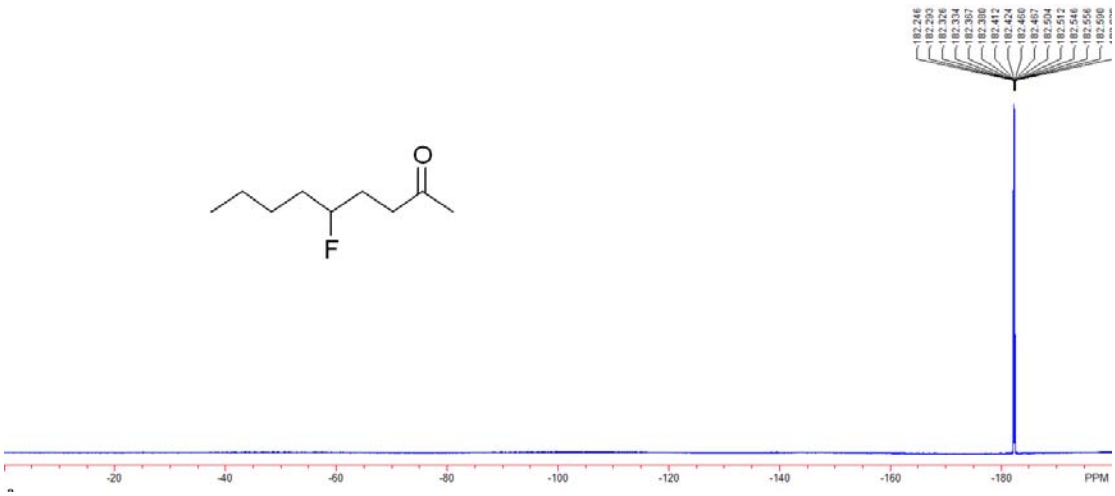

Br
F
O
207.783
200
150
100
50
PPM


Br
F
O
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

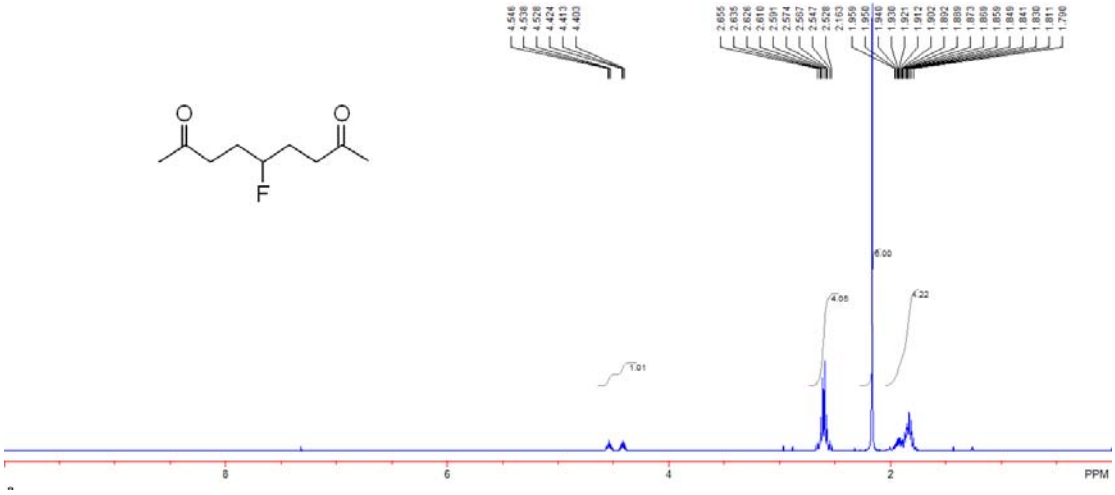
Compound **2g**

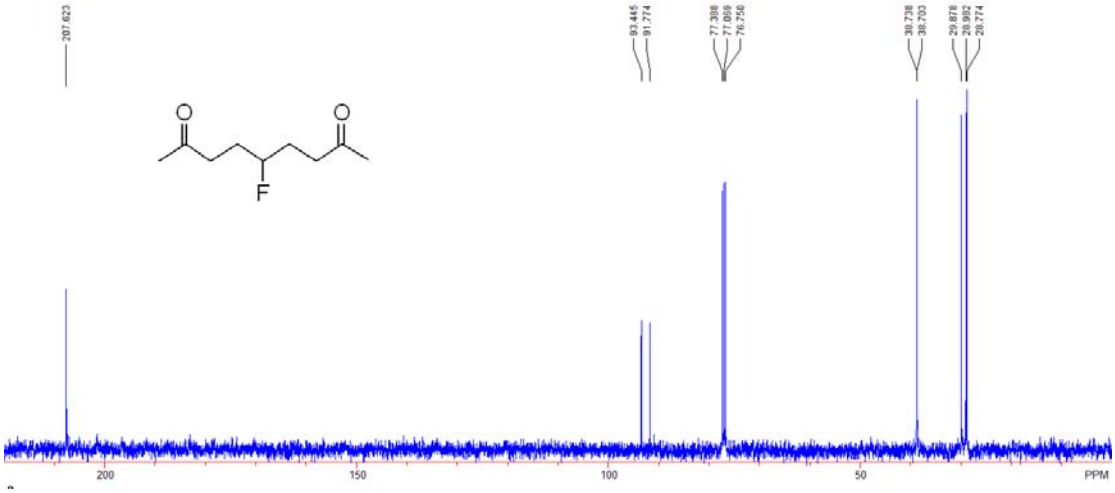

O
F
1.00
1.99
2.95
8.39
3.09
8
6
4
2
PPM

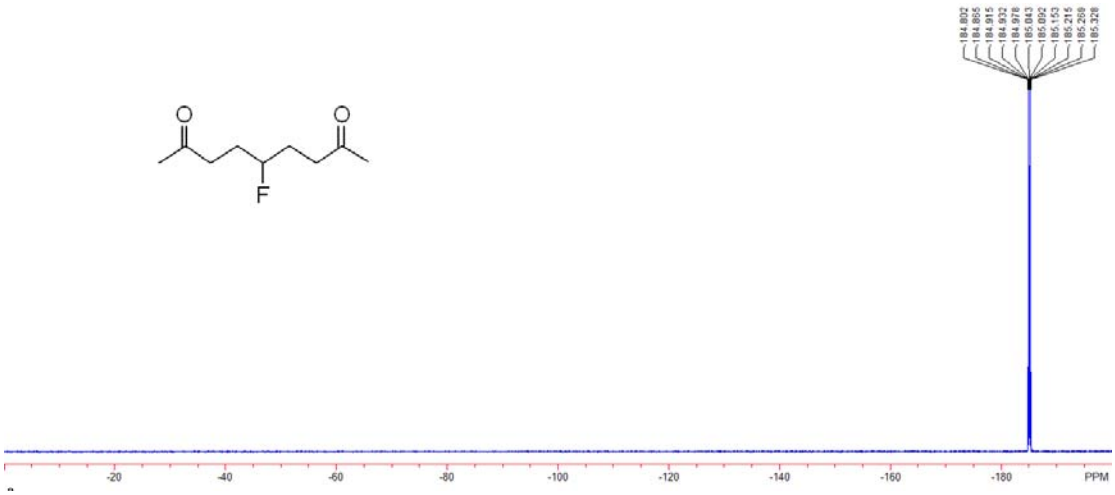

O
F
200
150
100
50
PPM


O
F
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

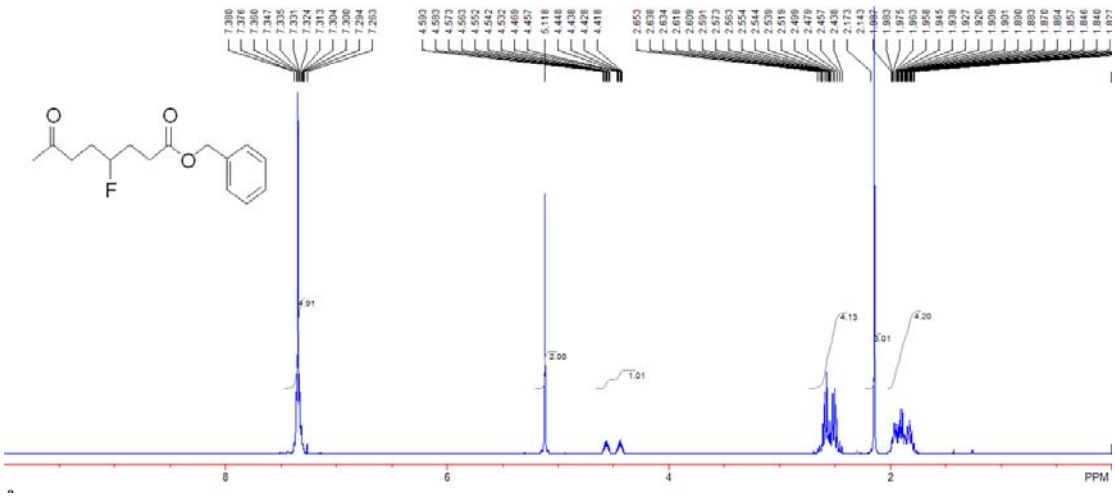
Compound **2h**

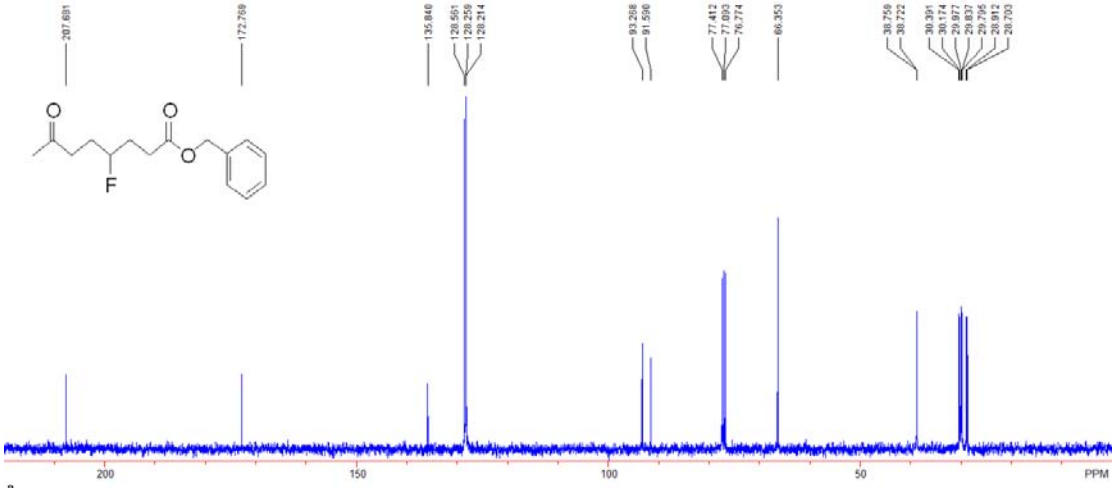

4.546
4.538
4.528
4.424
4.413
4.403
2.655
2.635
2.626
2.610
2.591
2.574
2.557
2.541
2.528
2.163
1.959
1.950
1.940
1.930
1.921
1.912
1.902
1.892
1.888
1.873
1.869
1.859
1.849
1.841
1.836
1.811
1.796
6.00
4.05
4.22
1.01
F
8
6
4
2
PPM

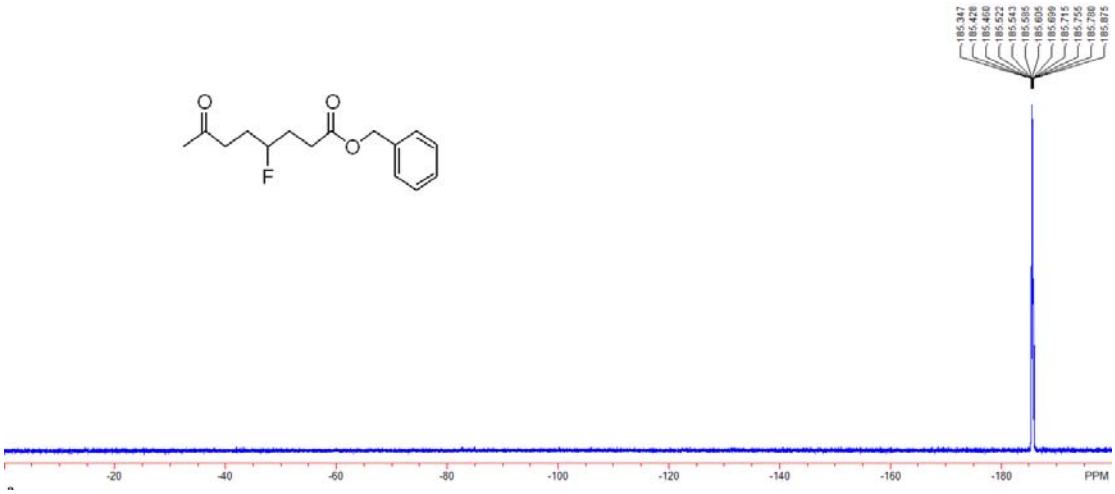

207.623
93.445
91.774
77.398
77.069
76.750
38.738
38.703
29.878
29.982
28.774
F
200
150
100
50
PPM


184.802
184.865
184.915
184.932
184.978
185.043
185.092
185.153
185.215
185.269
185.328
F
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

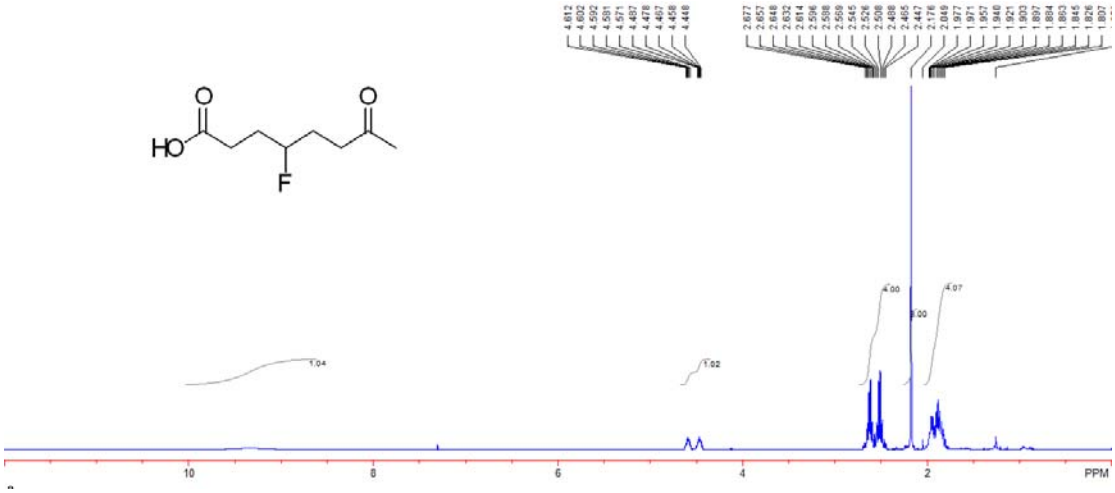
Compound **2i**

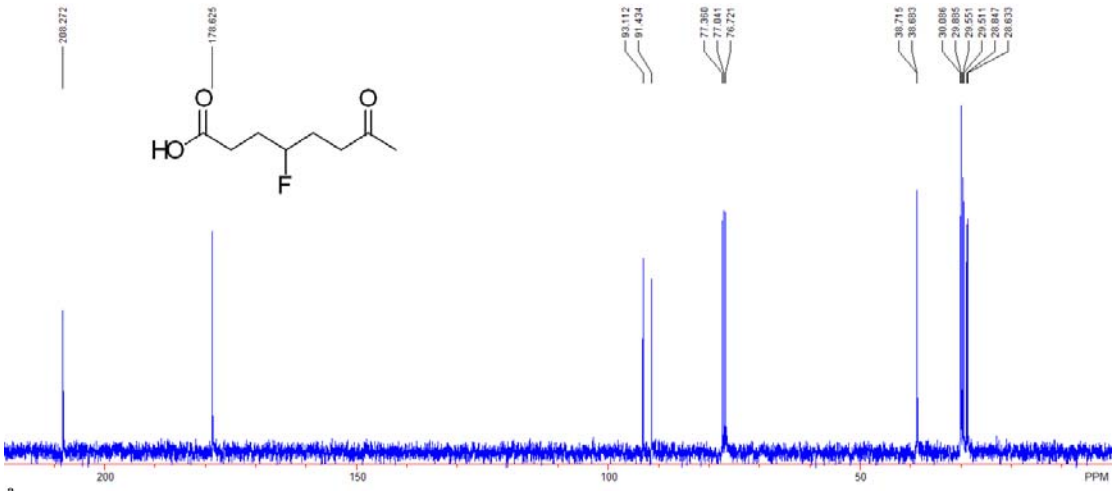

4.91
2.00
1.01
4.13
3.01
4.20
8
6
4
2
PPM

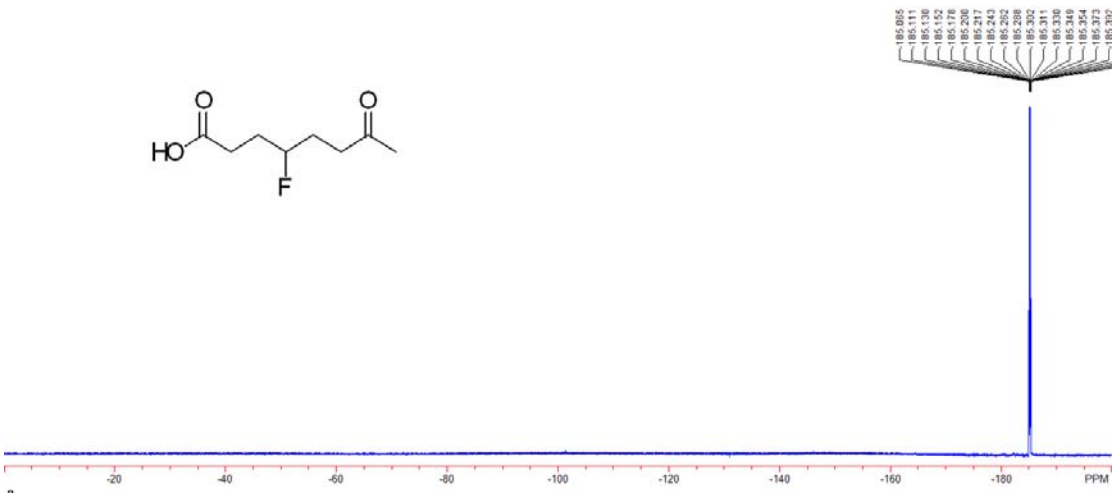

207.691
172.769
135.846
128.591
128.259
128.214
93.258
91.596
77.412
77.093
76.774
66.353
38.759
38.722
30.391
30.174
29.977
29.837
29.695
28.972
28.703
200
150
100
50
PPM


185.347
185.428
185.460
185.522
185.543
185.585
185.605
185.669
185.711
185.755
185.790
185.875
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

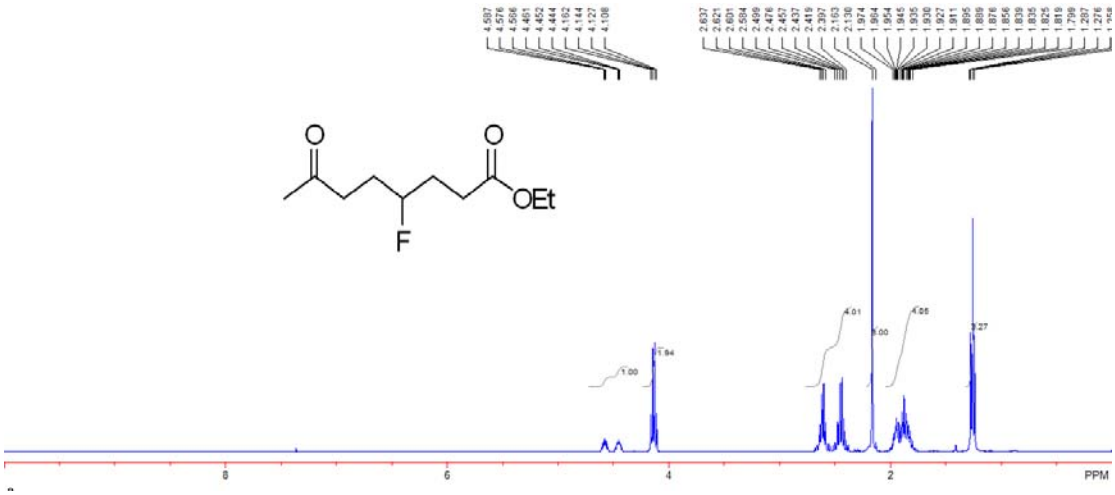
Compound **2j**

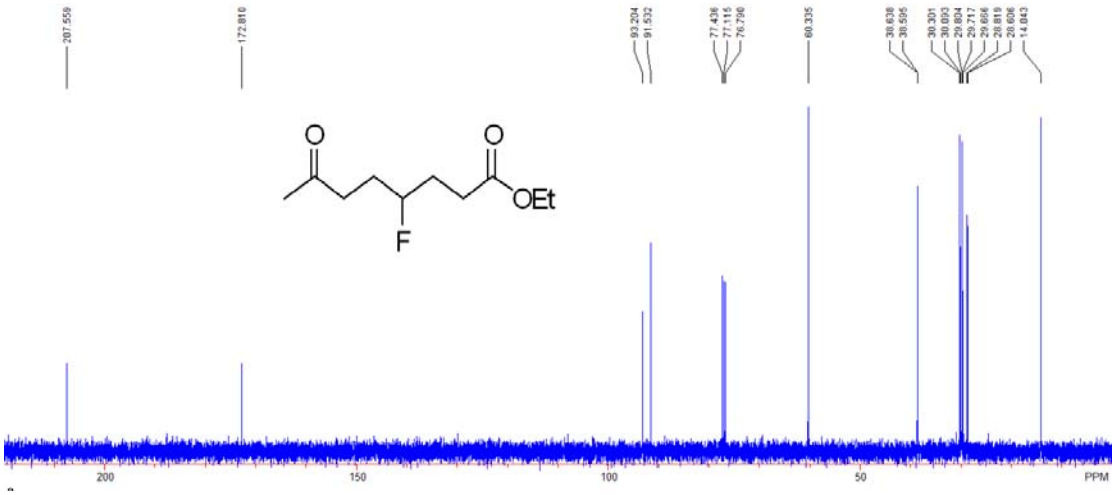


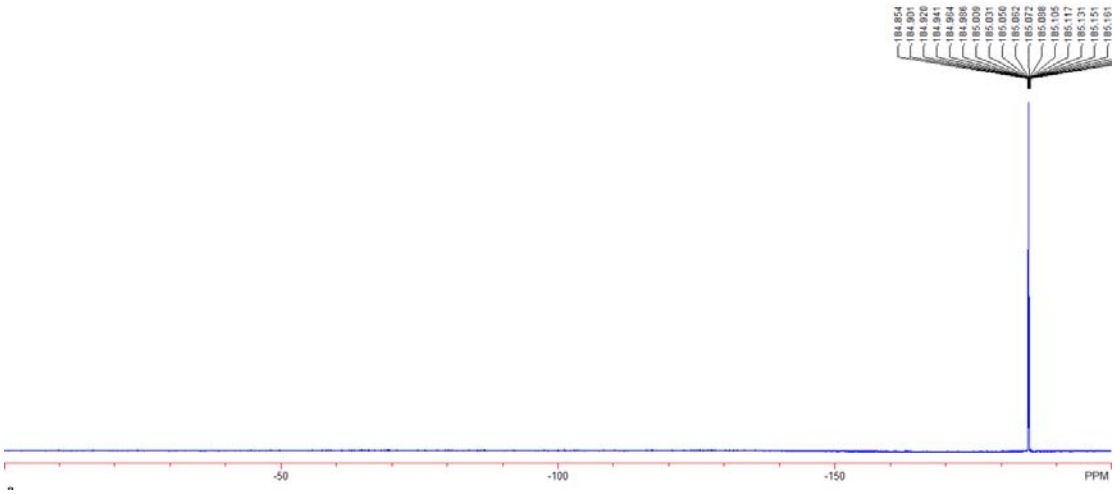




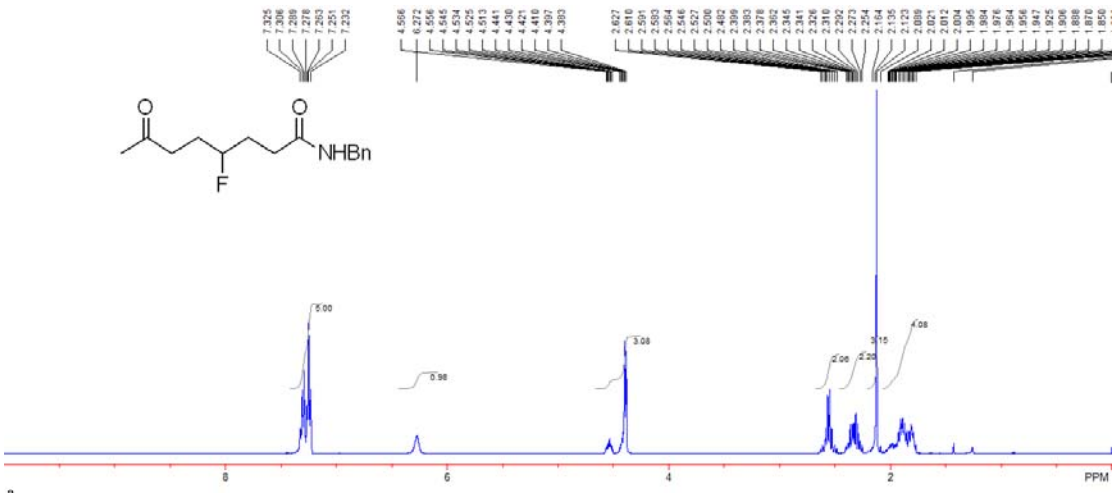
Compound **2k**

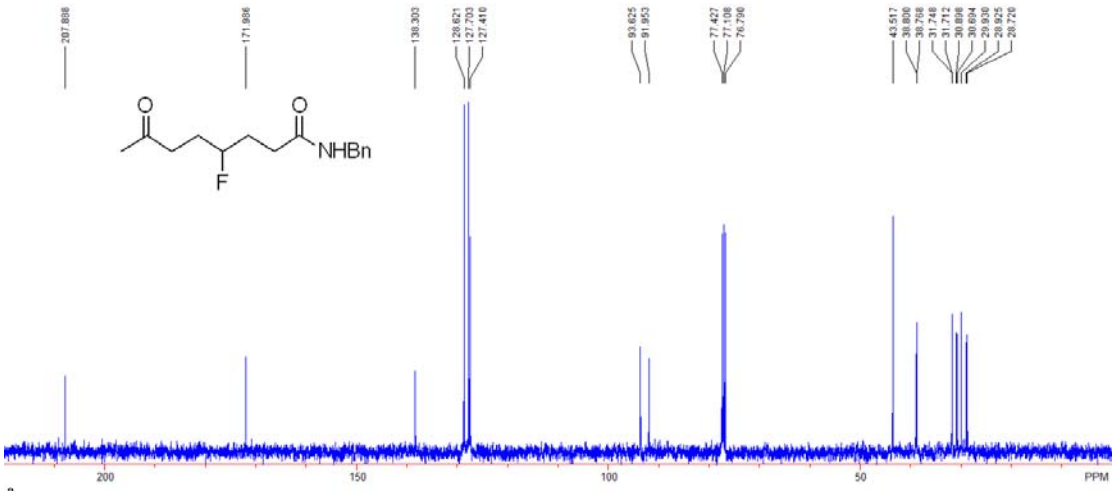


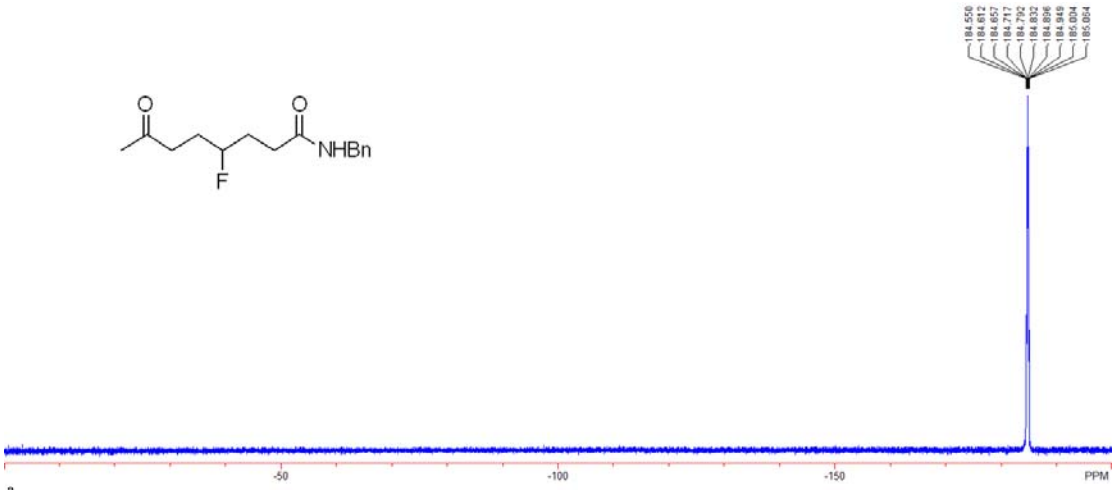




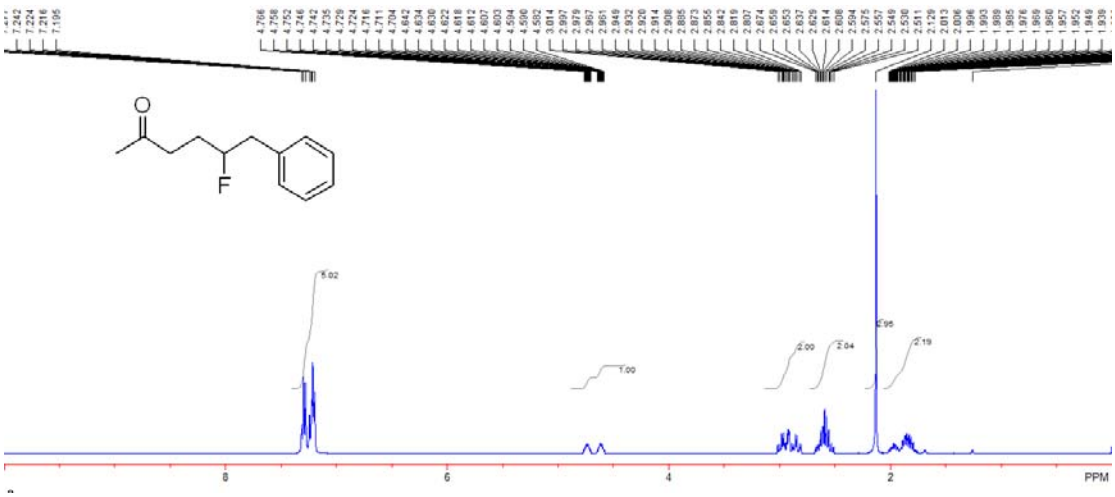
Compound **2l**

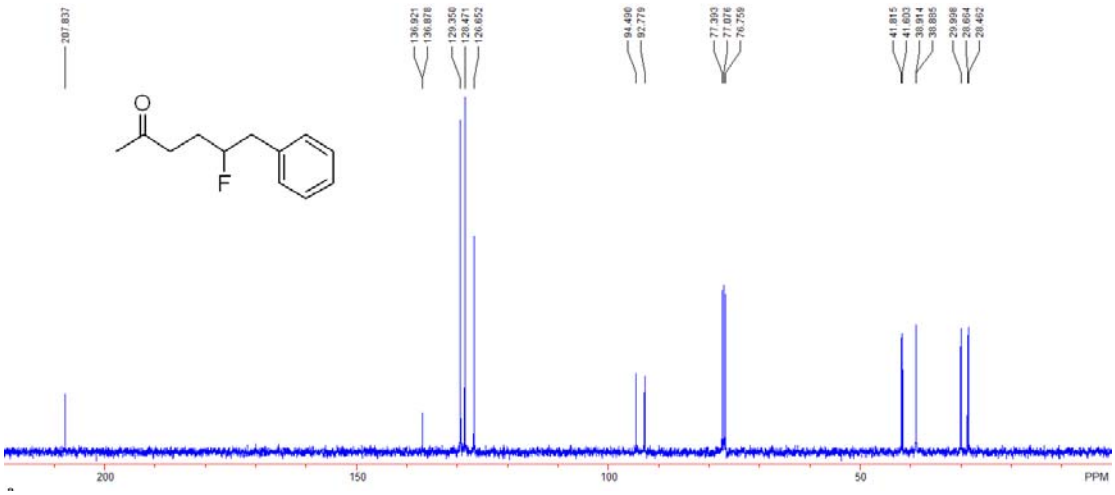






Compound **2m**


5.02
1.00
2.00
2.04
2.95
2.19
8
6
4
2
PPM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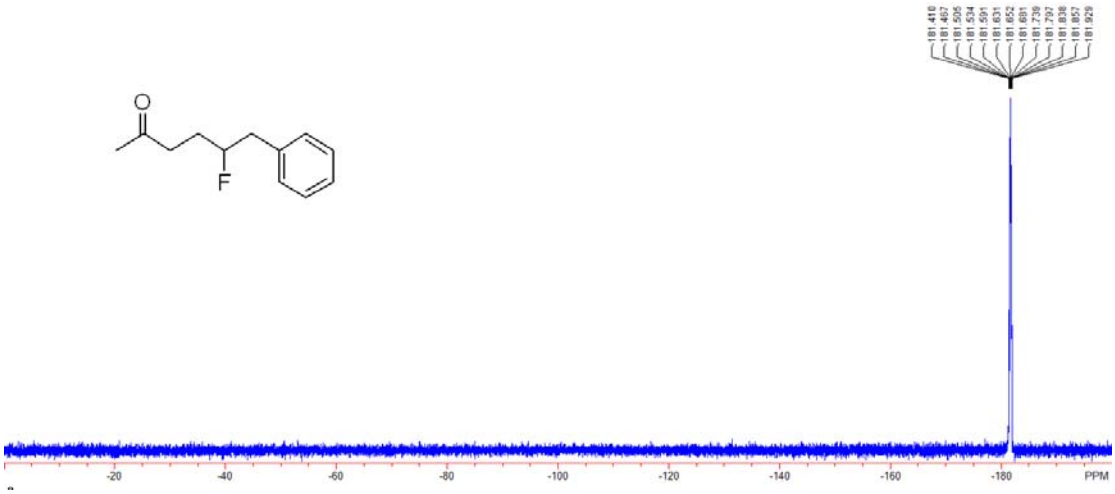
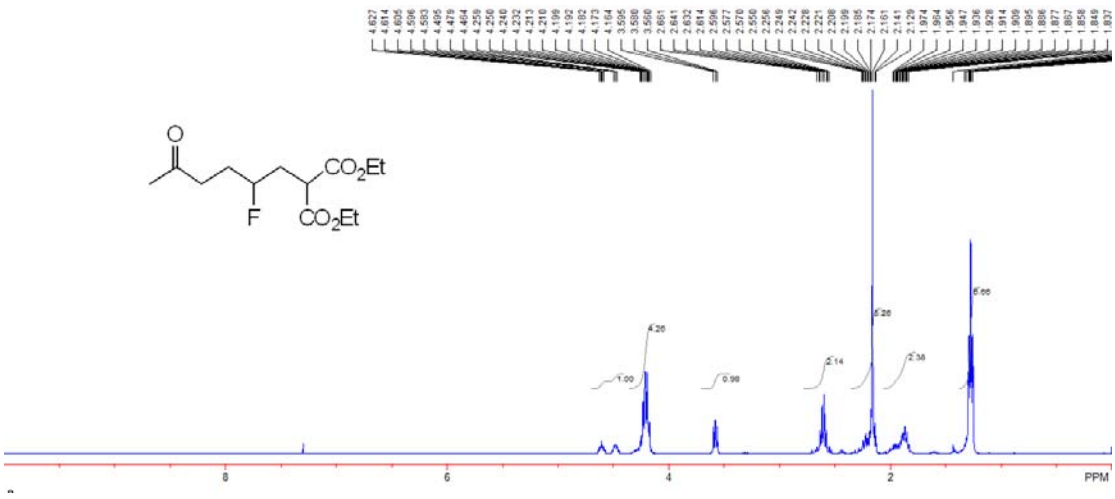
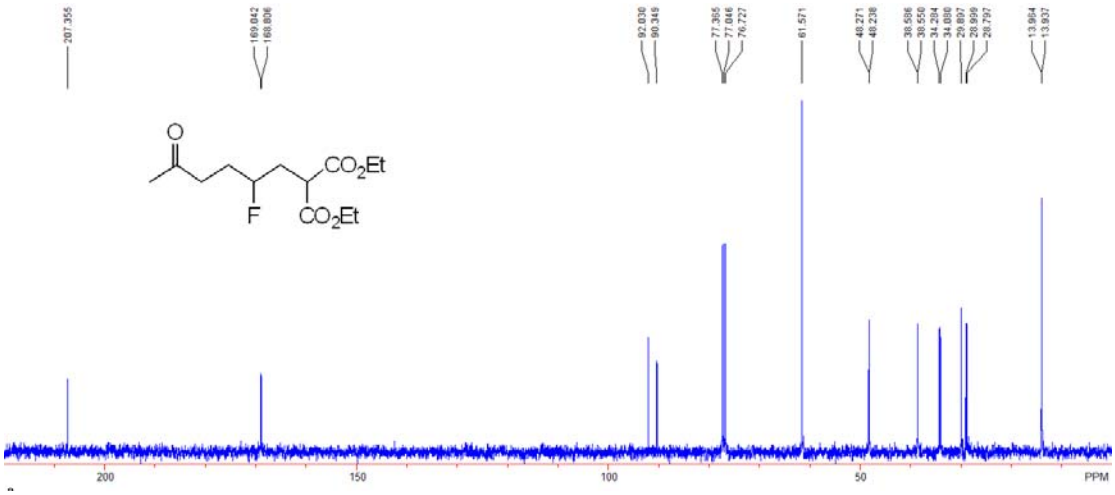
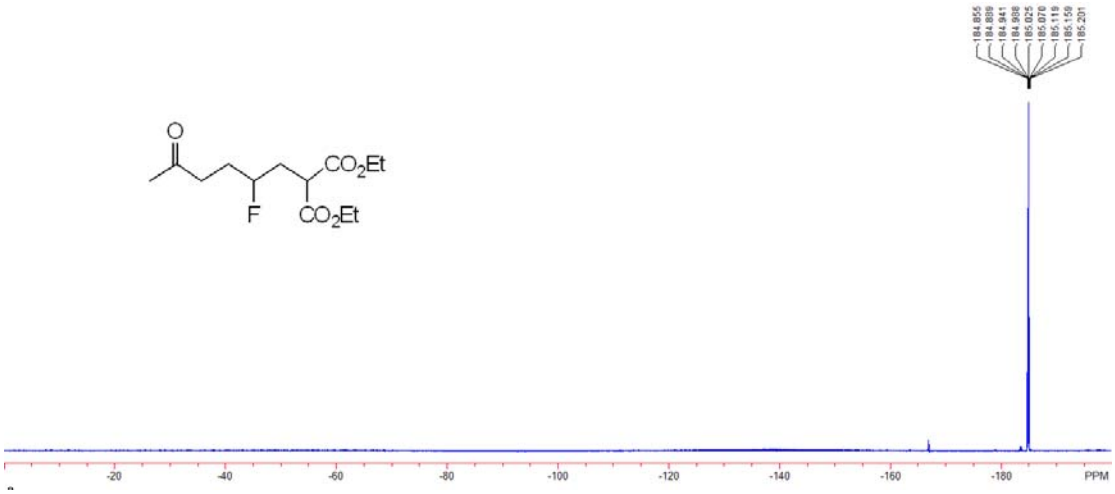
136.878
129.356
128.471
126.652
94.496
92.779
77.393
77.076
76.759
41.815
41.603
30.814
30.695
29.906
28.664
28.462
200
150
100
50
PPM


181.410
181.467
181.505
181.534
181.591
181.631
181.652
181.691
181.739
181.797
181.838
181.857
181.929
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

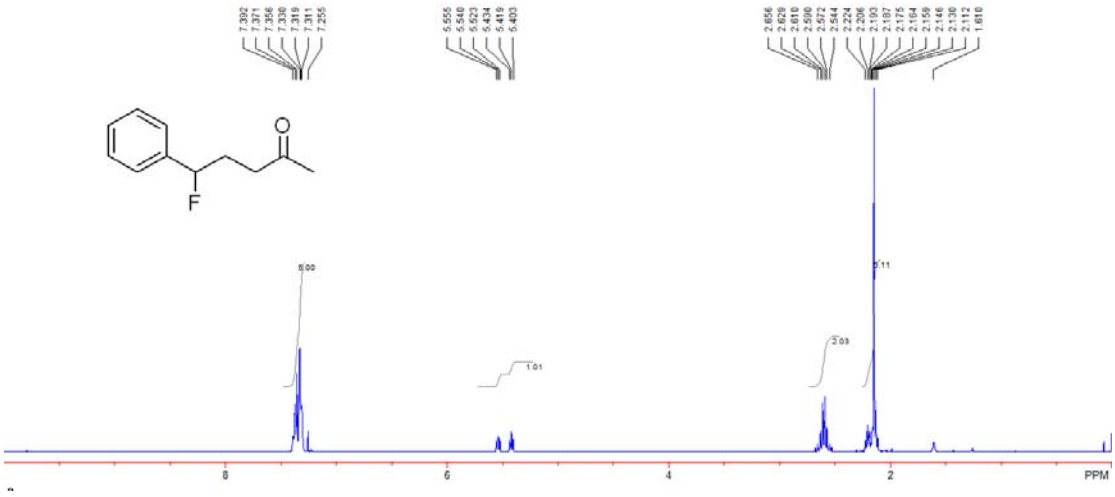
Compound **2n**

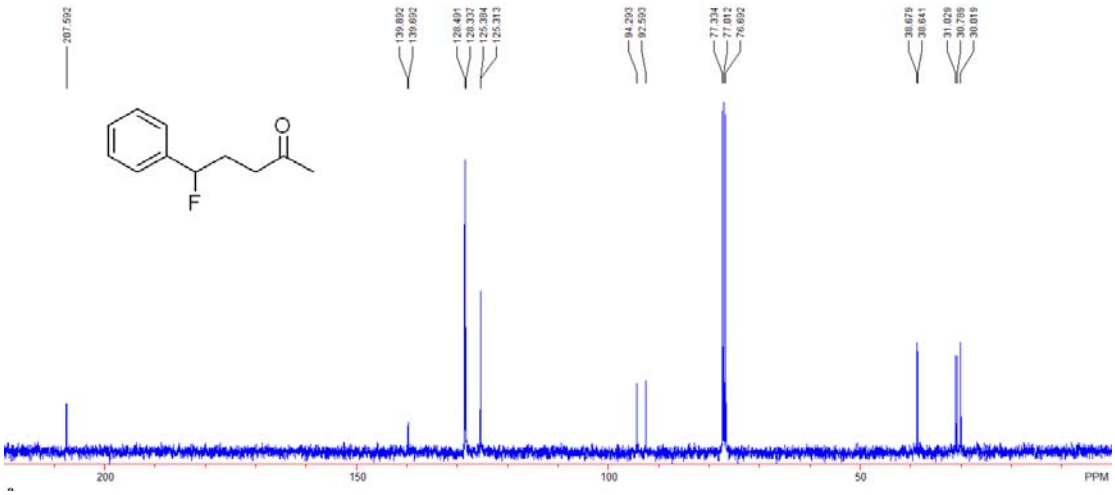

O
CO2Et
F
CO2Et
1.00
4.26
0.98
2.14
5.26
2.38
5.66
8
6
4
2
PPM

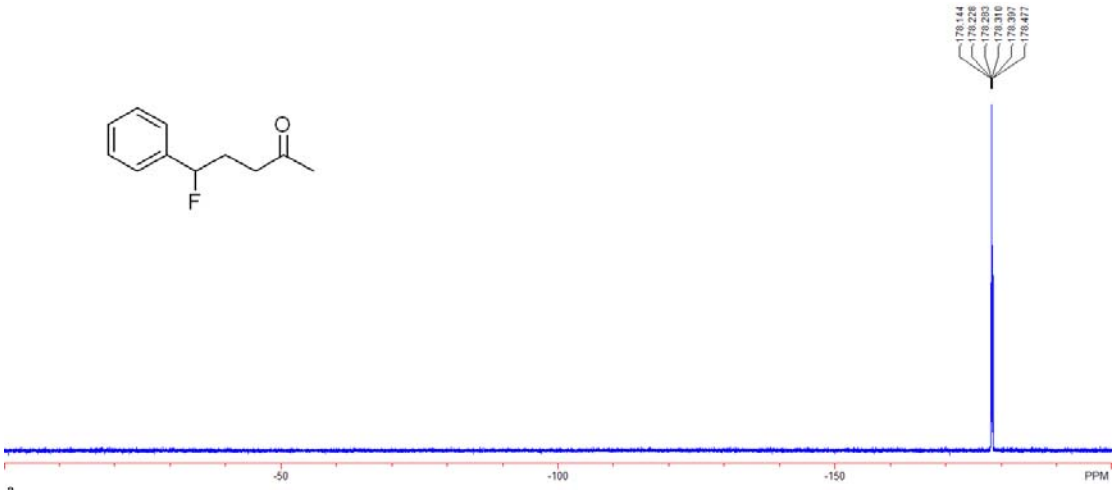

207.355
169.842
168.806
92.636
90.349
77.365
77.046
76.727
61.571
40.271
40.236
38.596
38.556
34.394
34.886
29.897
28.999
28.797
13.964
13.937
O
CO2Et
F
CO2Et
200
150
100
50
PPM


184.855
184.839
184.941
184.908
185.025
185.070
185.119
185.159
185.201
O
CO2Et
F
CO2Et
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

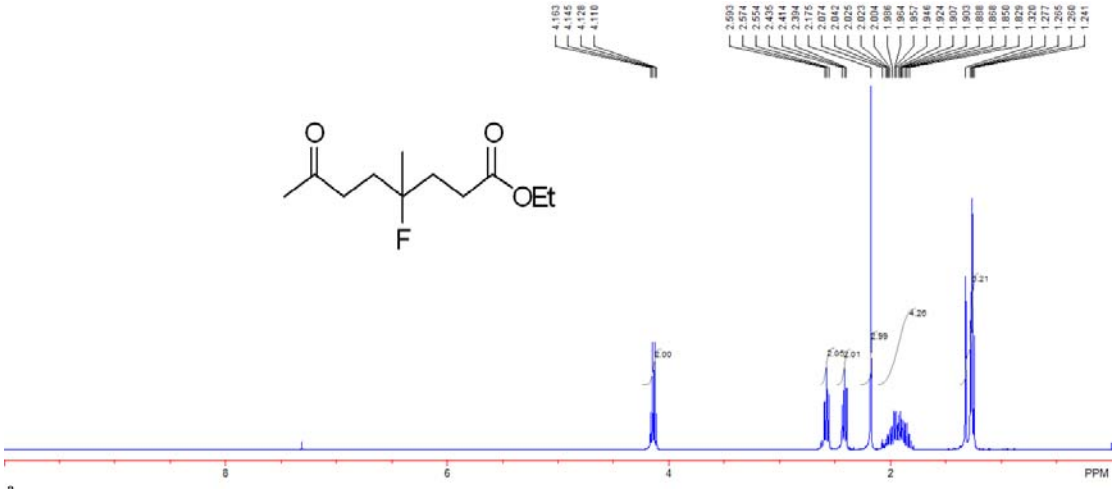
Compound **2o**

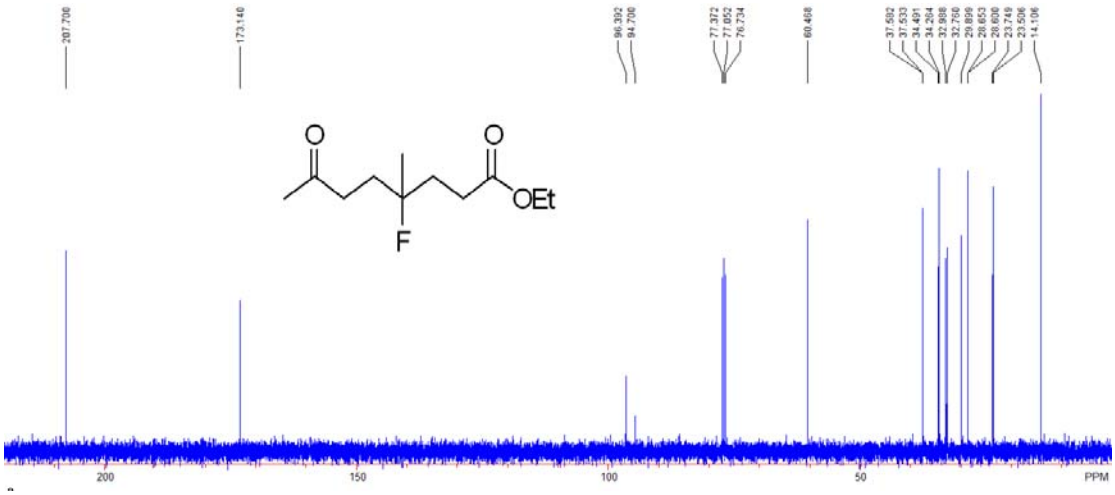

7.392
7.371
7.356
7.330
7.319
7.311
7.255
5.555
5.540
5.523
5.434
5.419
5.403
2.656
2.629
2.610
2.590
2.572
2.544
2.224
2.206
2.193
2.187
2.175
2.164
2.156
2.146
2.130
2.112
1.610
F
5.00
1.01
2.03
3.11
8
6
4
2
PPM

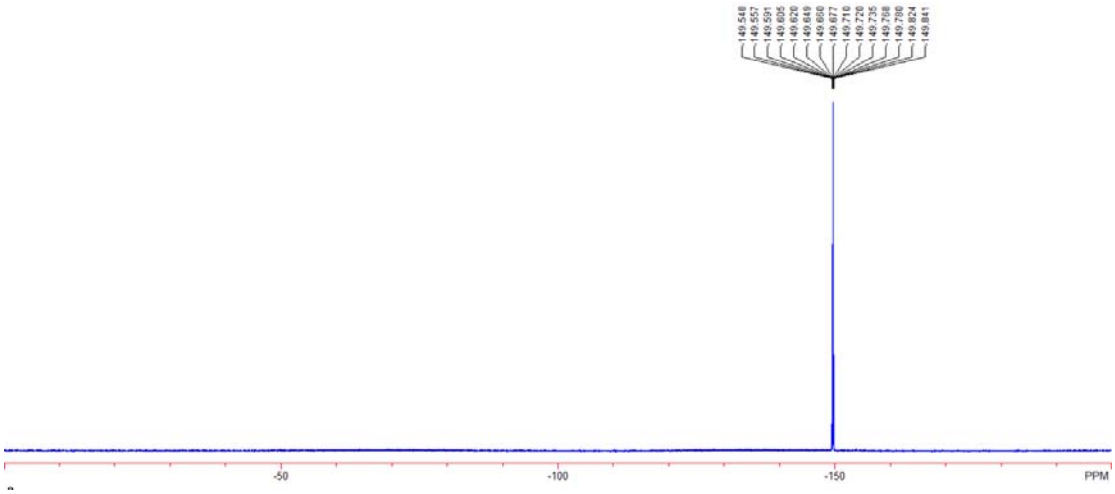

207.592
139.802
139.692
128.491
128.337
125.394
125.313
94.293
92.593
77.324
77.012
76.692
39.679
39.641
31.029
30.799
30.619
F
200
150
100
50
PPM


170.144
170.226
170.293
170.310
170.397
170.477
F
-50
-100
-150
PPM

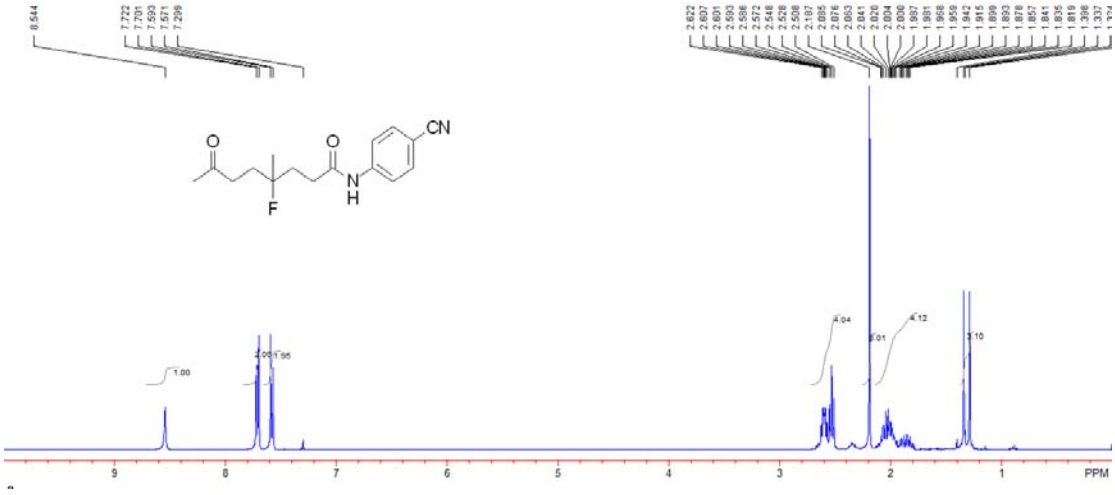
Compound **3a**

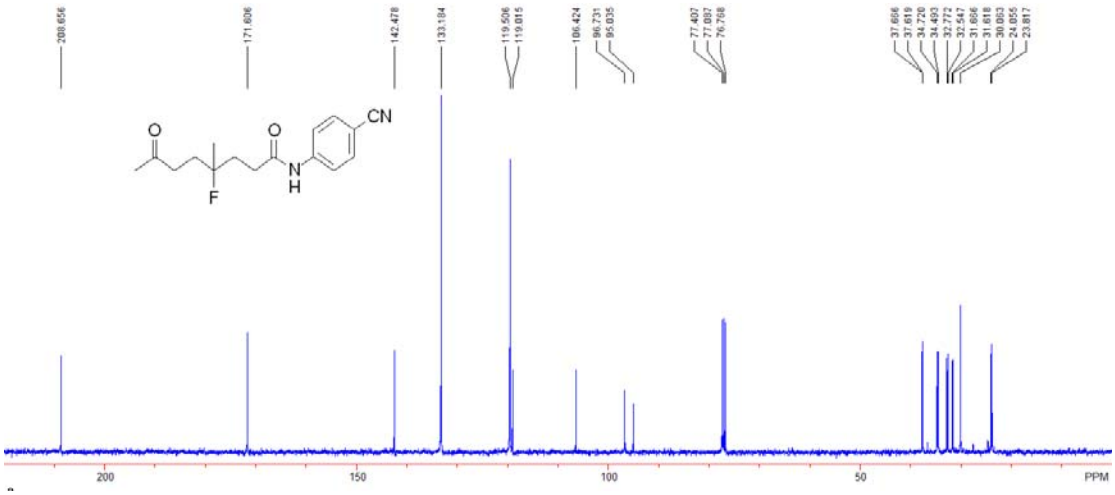

4.163
4.145
4.128
4.110
3.593
3.574
3.554
3.435
2.414
2.394
2.175
2.074
2.042
2.025
2.023
2.004
1.998
1.984
1.957
1.946
1.924
1.903
1.898
1.858
1.850
1.829
1.326
1.277
1.265
1.241
O
O
OEt
F
E.00
2.01
2.99
4.26
3.21
8
6
4
2
PPM

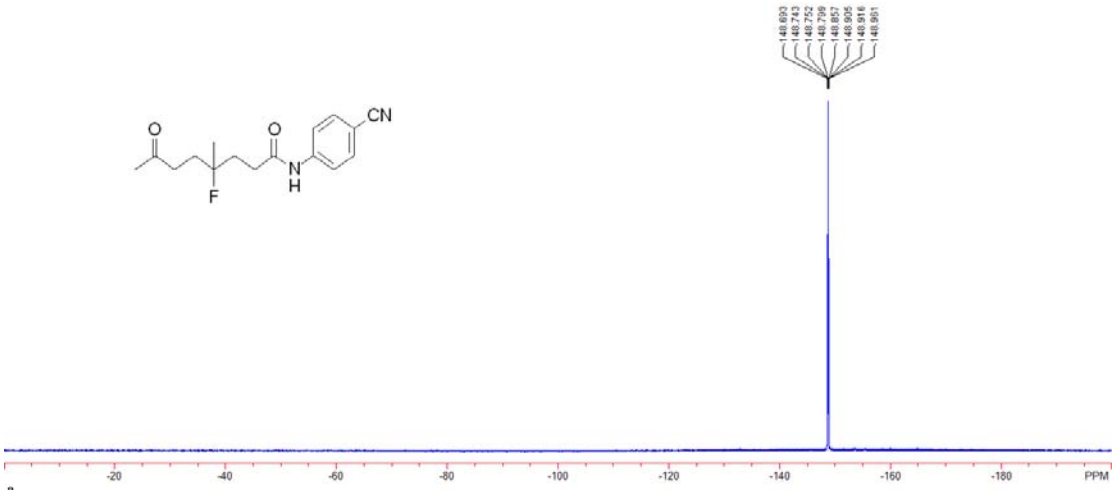

207.706
173.146
96.392
94.706
77.372
77.052
76.734
60.468
37.592
37.533
34.491
34.264
32.908
32.766
29.899
29.653
28.605
28.458
23.749
23.506
14.106
O
O
OEt
F
200
150
100
50
PPM


149.548
149.557
149.591
149.605
149.620
149.649
149.660
149.677
149.710
149.720
149.735
149.768
149.780
149.824
149.841
-50
-100
-150
PPM

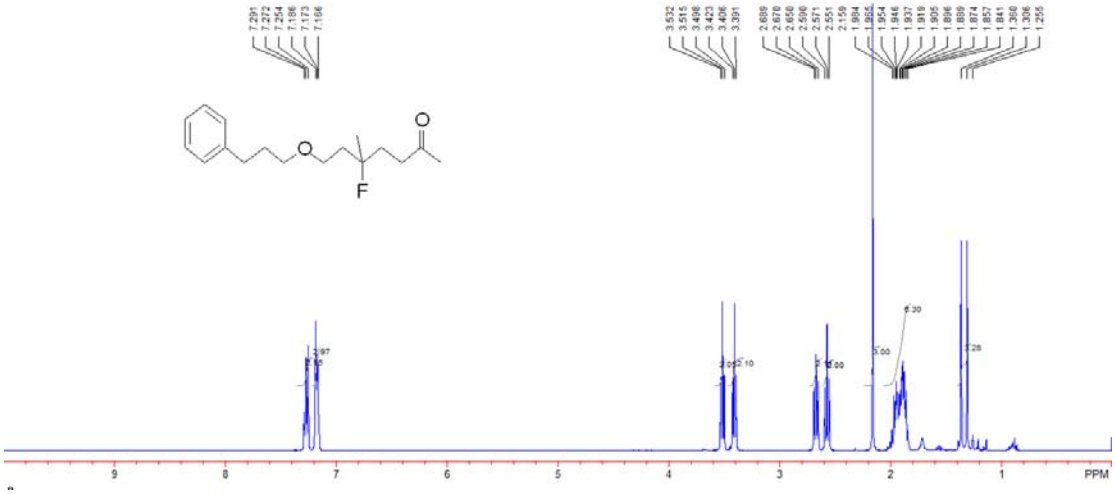
Compound **3b**







Compound **3c**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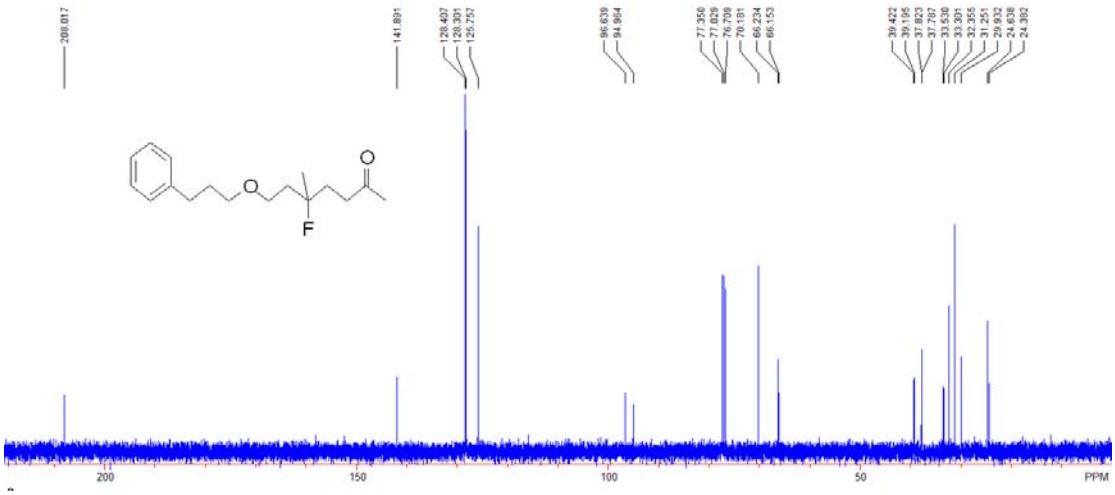
7.254
7.196
7.173
7.166
3.532
3.515
3.498
3.423
3.406
3.391
2.689
2.670
2.650
2.590
2.571
2.551
2.159
2.139
1.954
1.946
1.937
1.919
1.905
1.896
1.889
1.874
1.857
1.841
1.380
1.306
1.255
O
O
F
PPM


209.017
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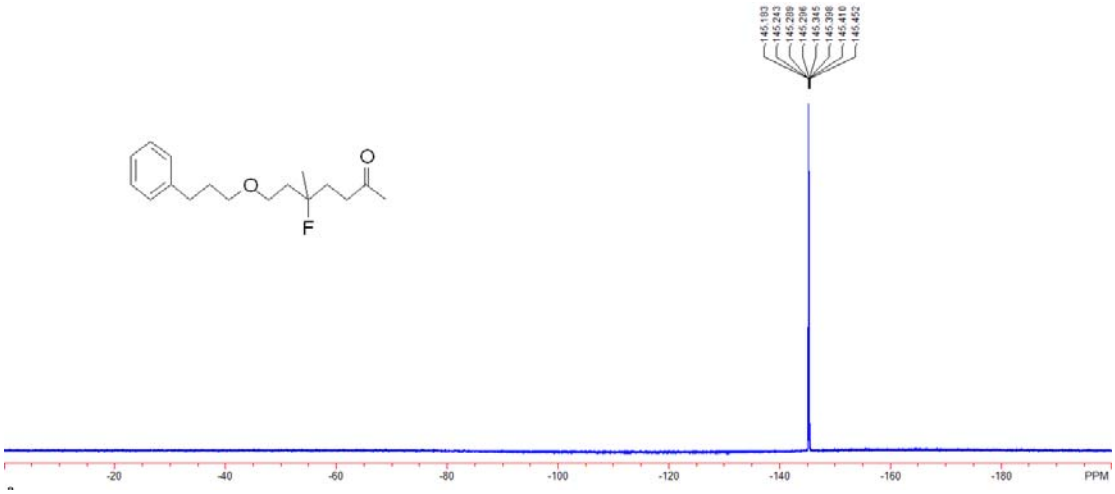
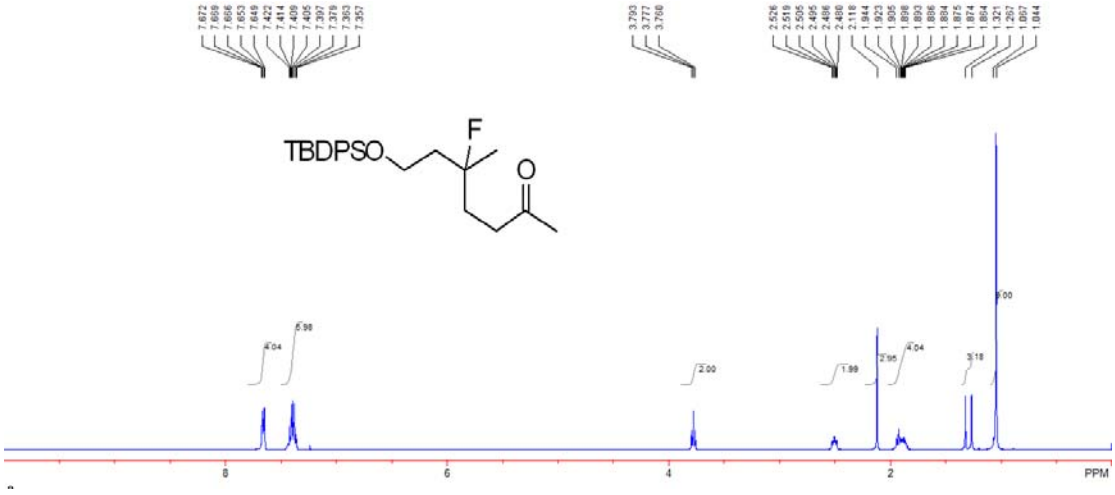
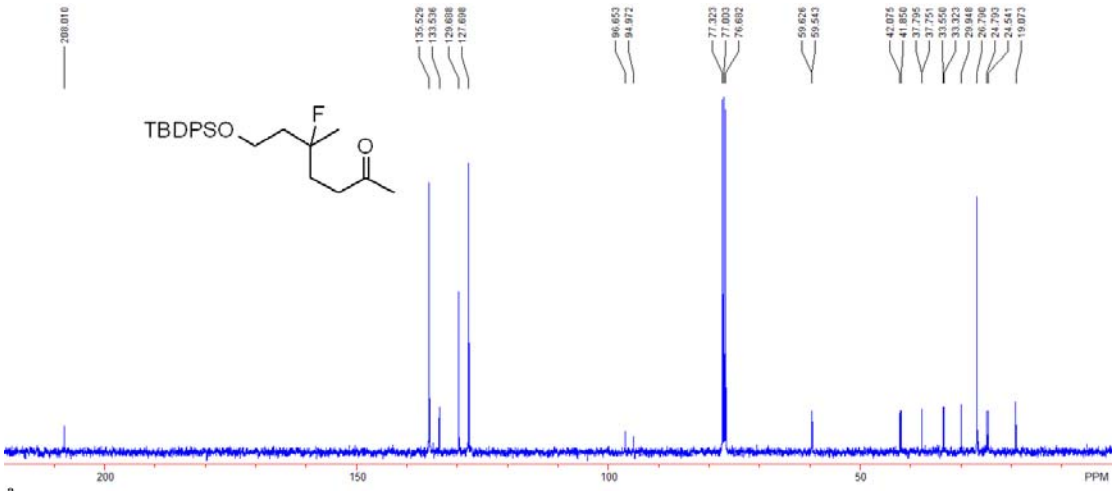
128.407
128.301
125.757
96.639
94.864
77.356
77.029
76.709
70.181
66.234
66.153
39.422
39.195
37.823
37.787
33.538
33.301
32.355
31.251
29.932
24.638
24.392
O
O
F
PPM

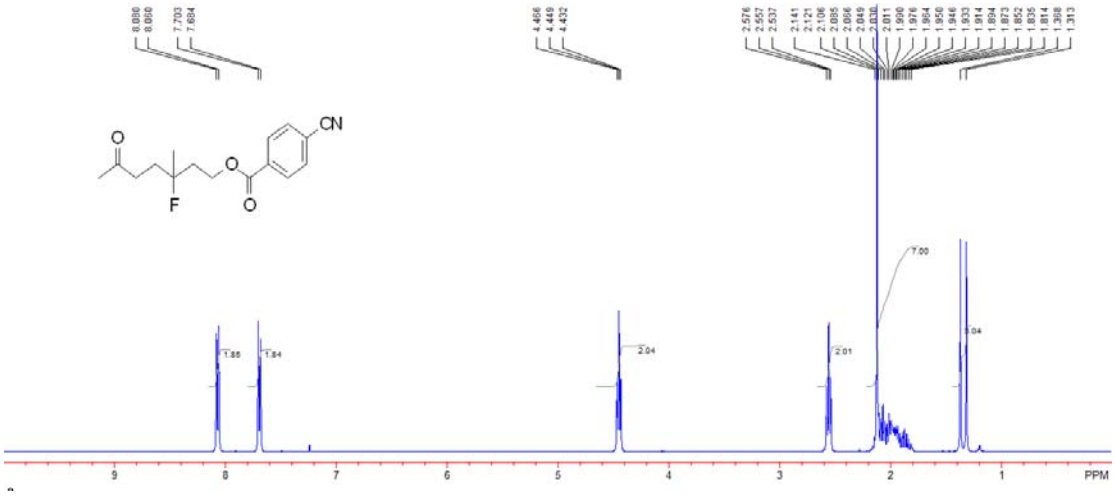

145.193
145.243
145.289
145.296
145.345
145.398
145.410
145.452
O
O
F
PPM

Compound **3d**





Compound **3e**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8.080
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7.694
4.456
4.446
4.432
2.576
2.557
2.537
2.141
2.121
2.106
2.085
2.066
2.049
2.030
2.011
1.990
1.976
1.964
1.956
1.946
1.933
1.914
1.894
1.873
1.852
1.835
1.814
1.388
1.313
CN
O
O
O
F
O
1.85
1.84
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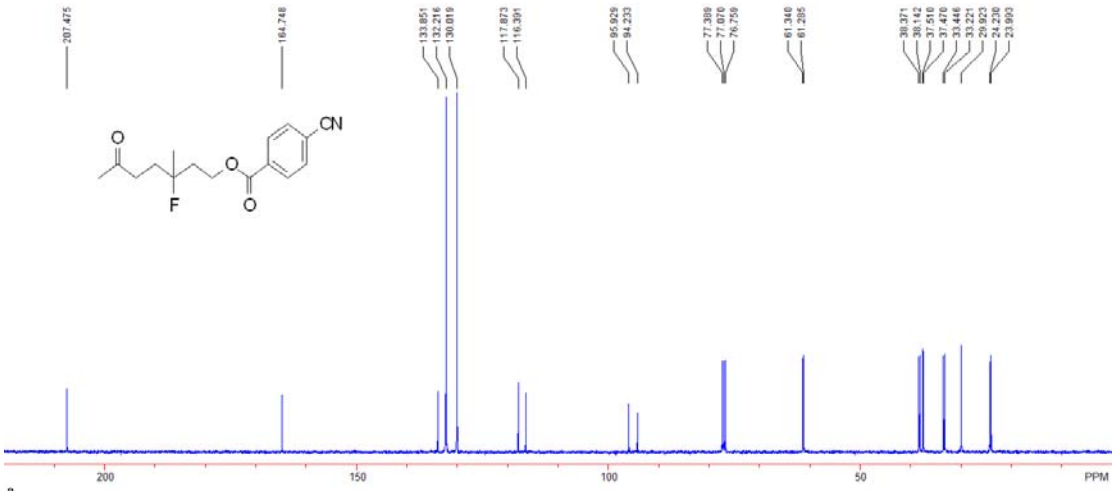
2.01
7.00
4.04
9
8
7
6
5
4
3
2
1
PPM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133.851
132.216
130.819
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116.391
95.929
94.233
77.399
77.076
76.759
61.348
61.285
30.371
30.142
37.510
37.478
33.446
33.221
29.923
24.308
23.899
CN
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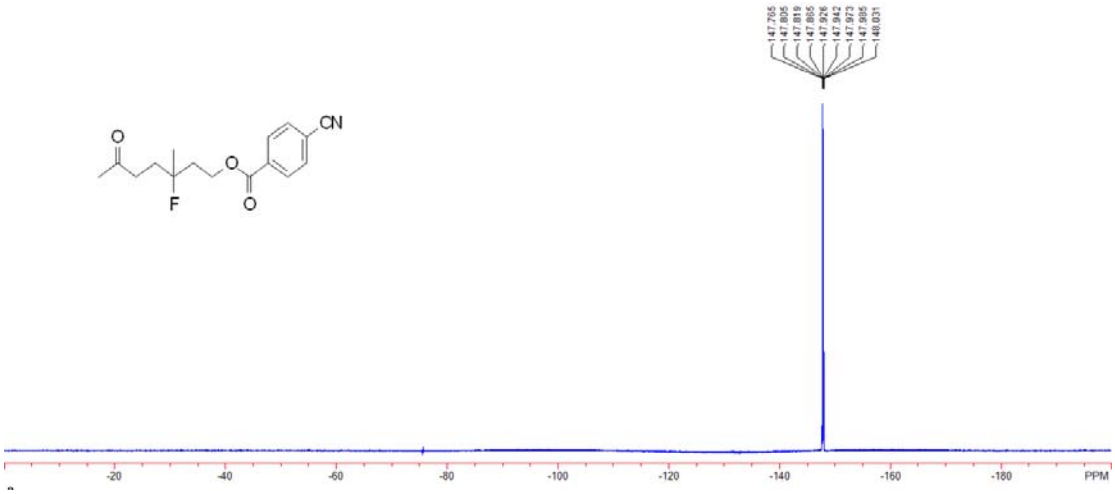
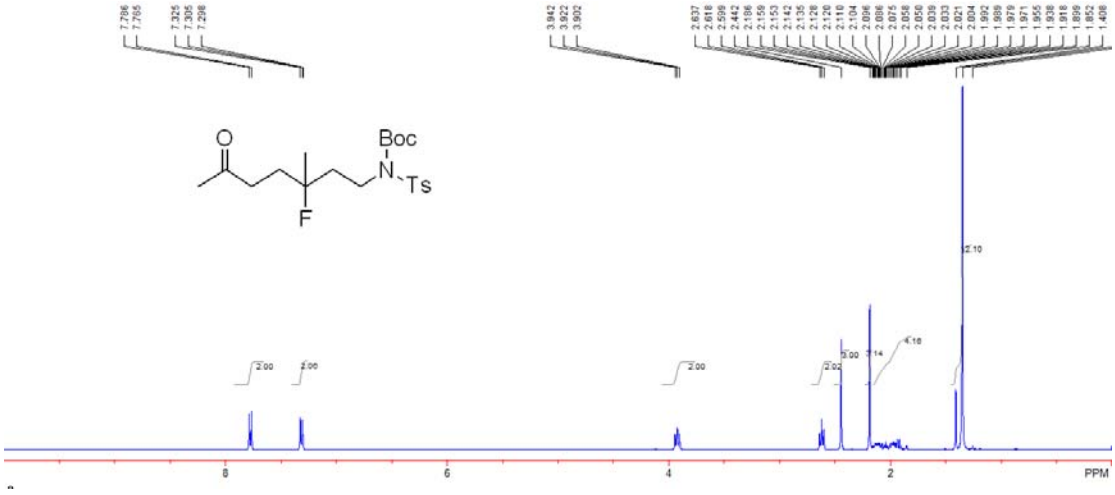
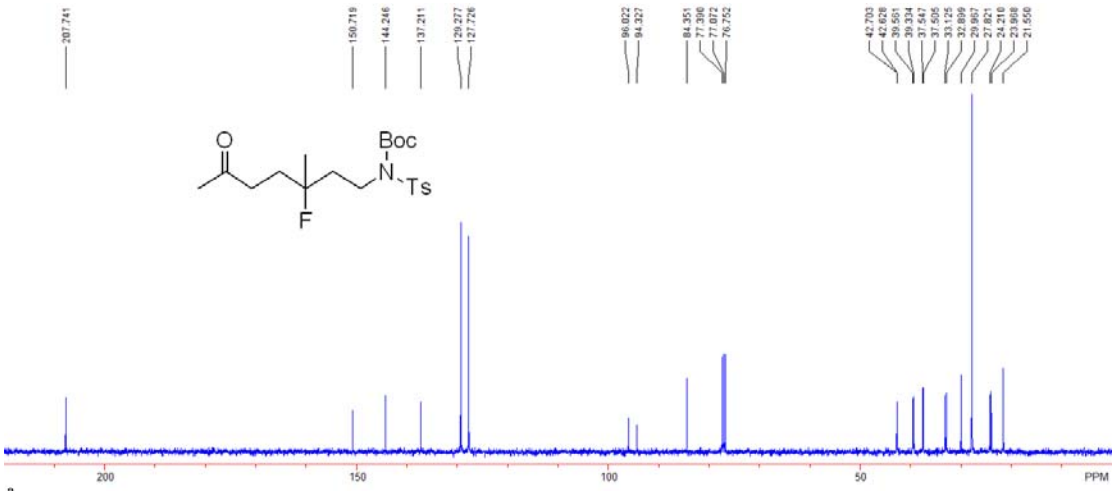
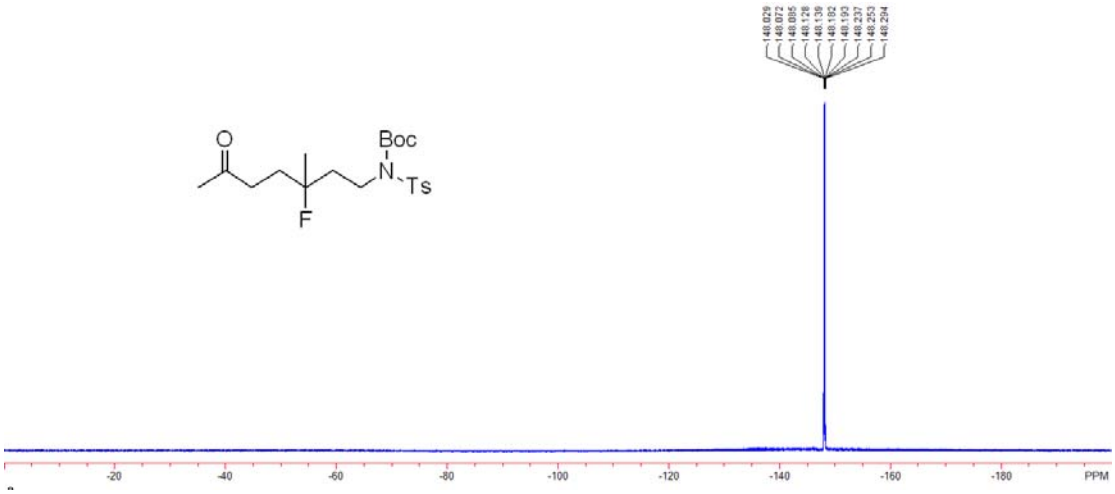
O
O
F
O
200
150
100
50
PPM


147.765
147.805
147.819
147.885
147.926
147.942
147.973
147.995
148.031
CN
O
O
O
F
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

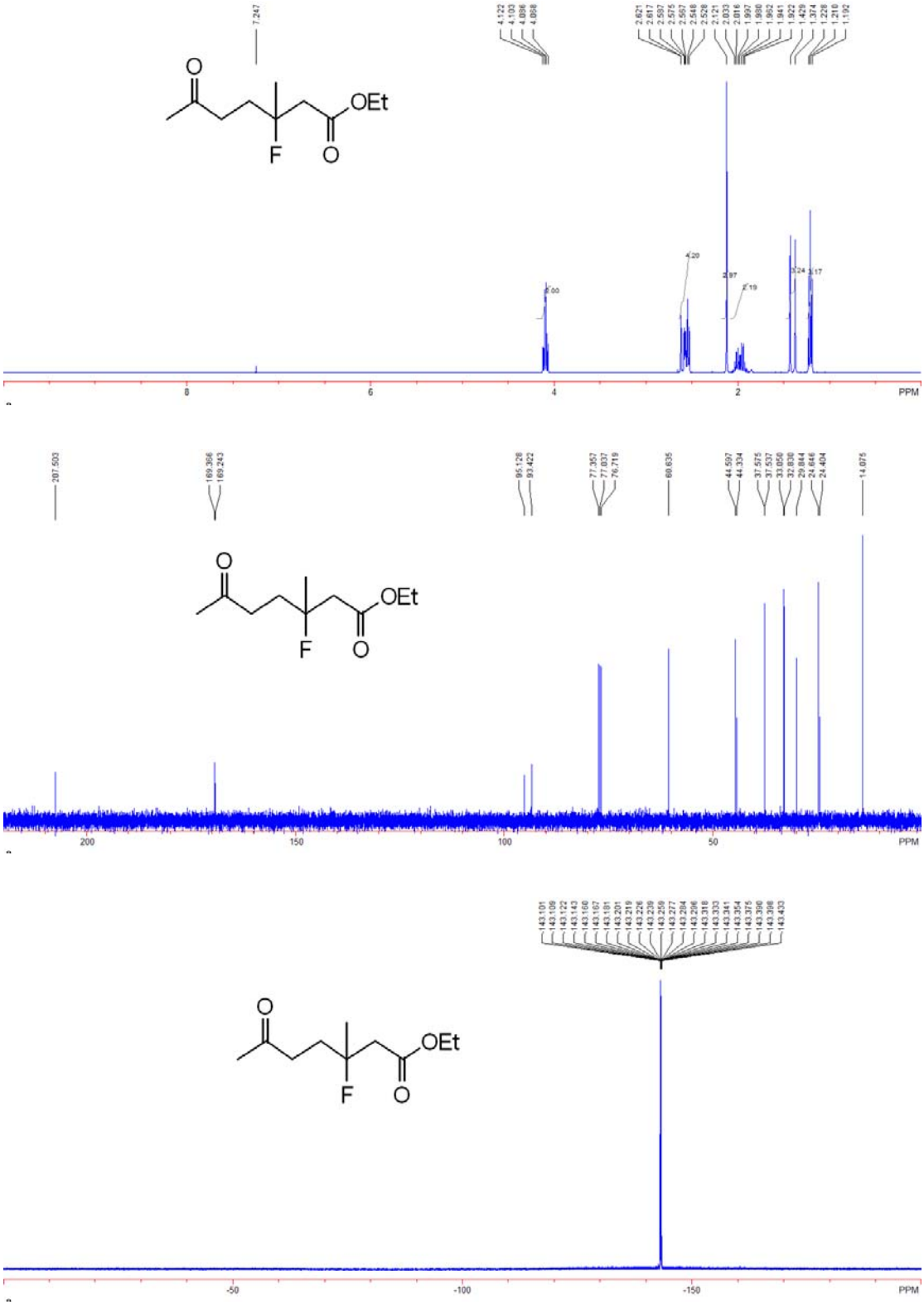
Compound **3f**



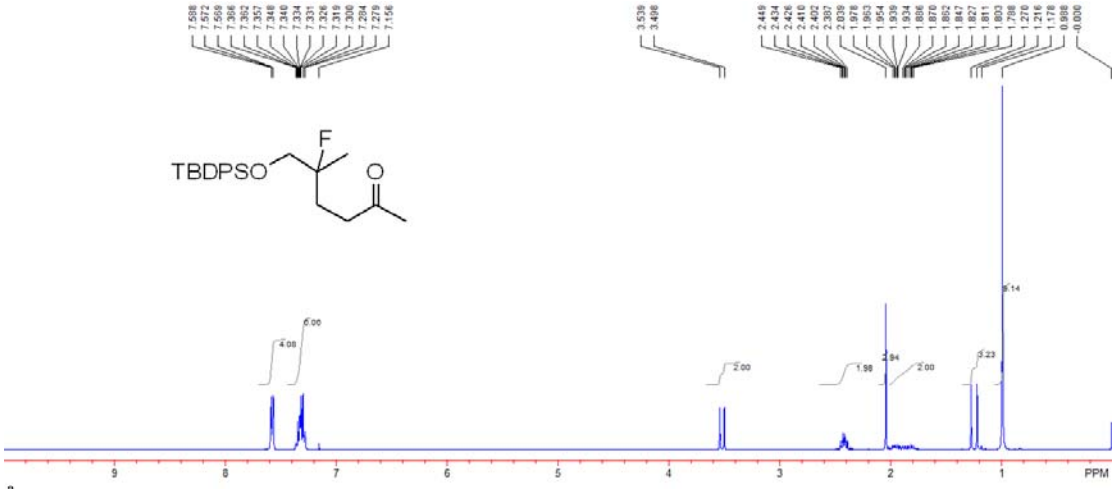


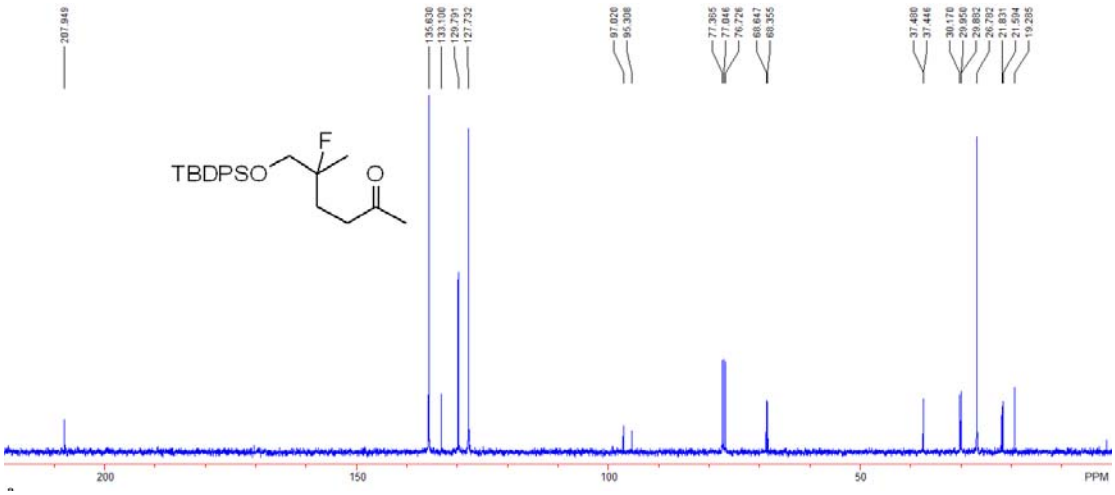


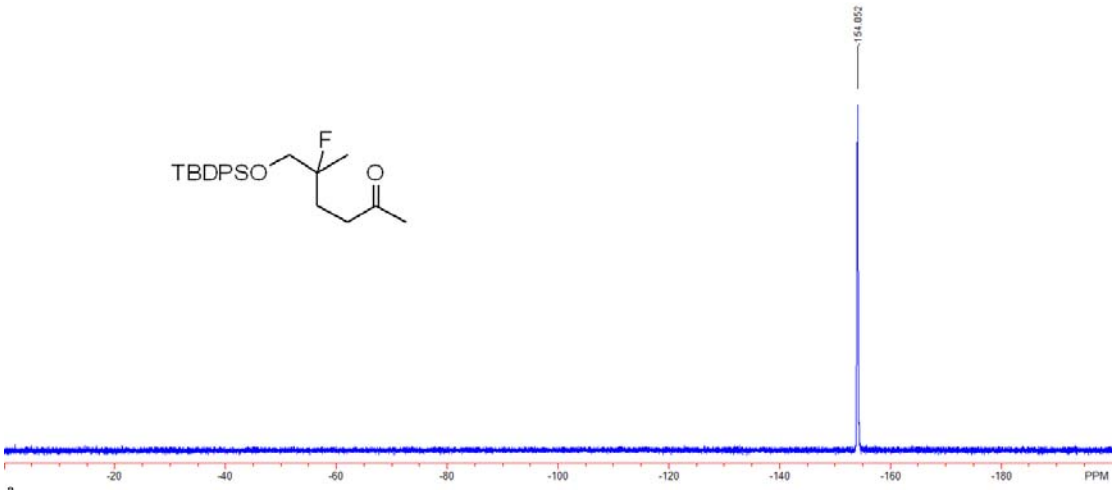
Compound **3g**



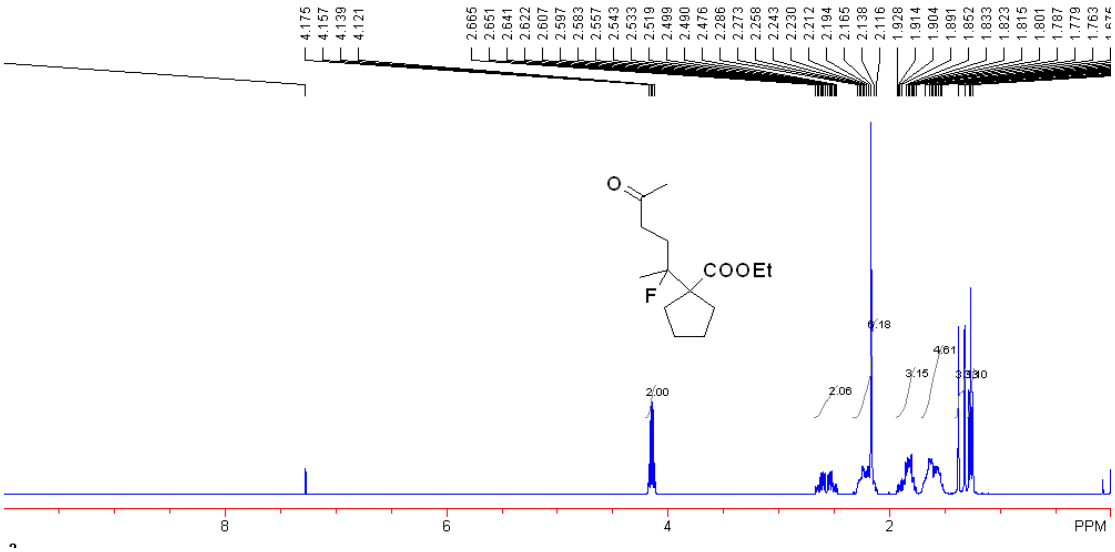
Compound **3h**







Compound **3i**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4.139
4.121
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2.651
2.641
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2.607
2.597
2.583
2.557
2.543
2.533
2.519
2.499
2.490
2.476
2.286
2.273
2.258
2.243
2.230
2.212
2.194
2.165
2.138
2.116
1.928
1.914
1.904
1.891
1.852
1.833
1.823
1.815
1.801
1.787
1.779
1.763
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COOEt
F
6.18
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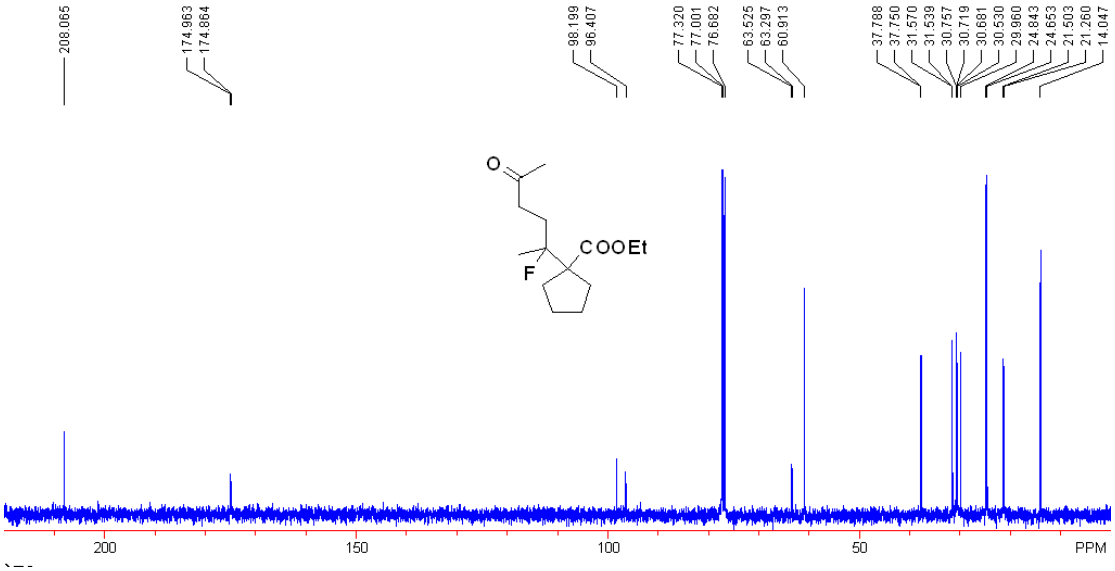
3.15
3.30
2.00
2.06
8
6
4
2
PPM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77.320
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76.682
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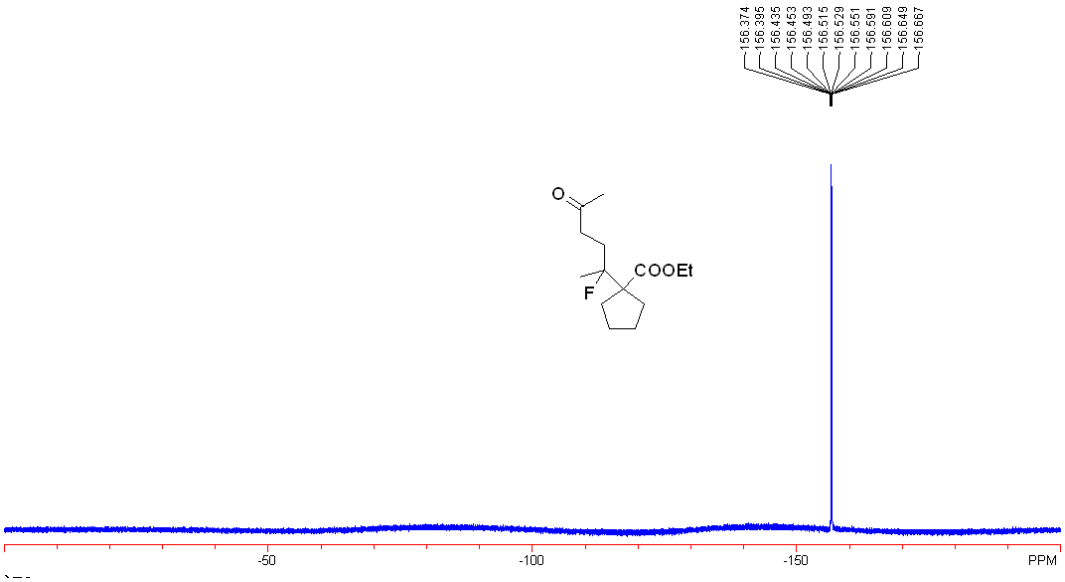
63.297
60.913
37.788
37.750
31.570
31.539
30.757
30.719
30.681
30.530
29.960
24.843
24.653
21.503
21.260
14.047
O
COOEt
F
200
150
100
50
PPM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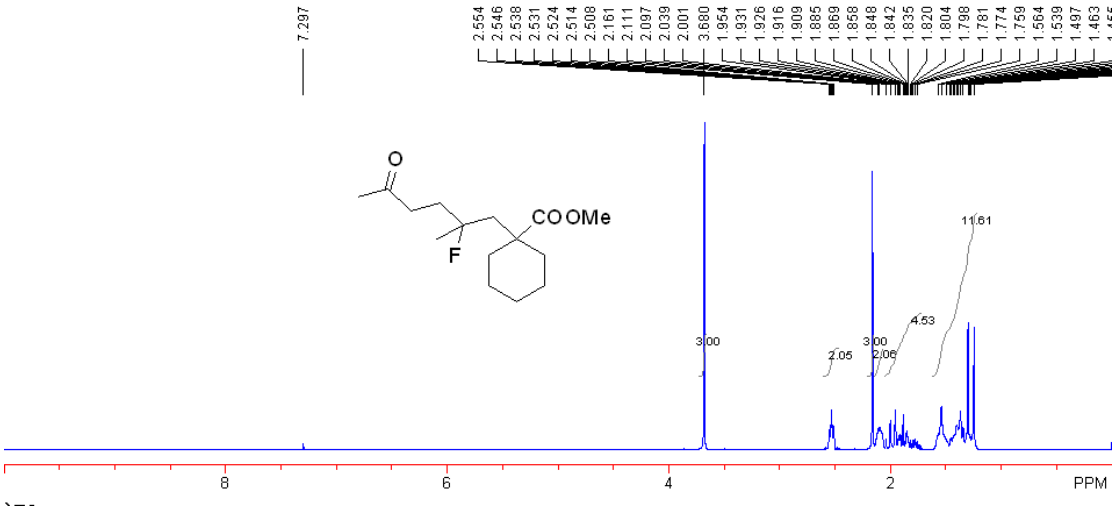
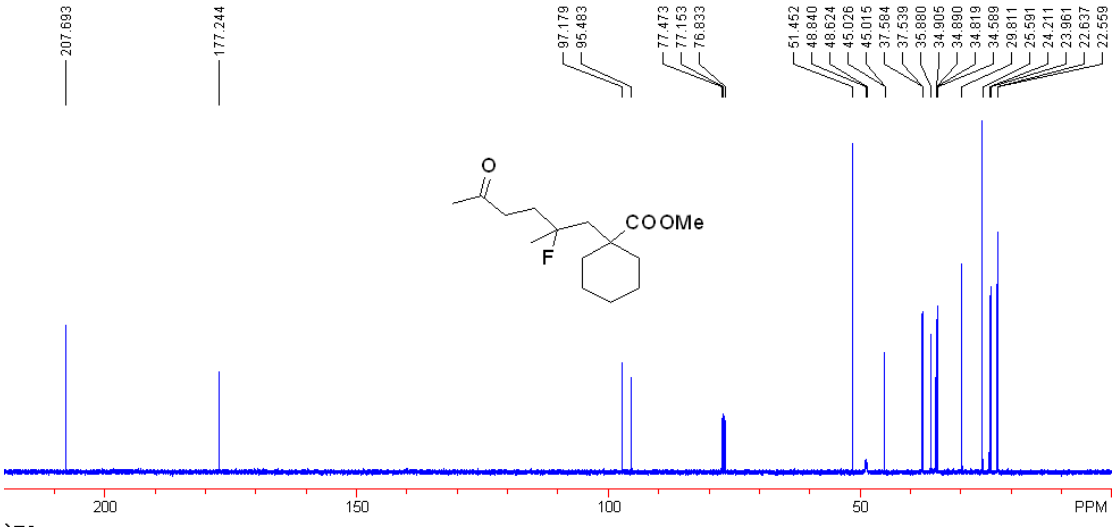
156.435
156.453
156.493
156.515
156.529
156.551
156.591
156.609
156.649
156.667
O
COOEt
F
-50
-100
-150
PPM

Compound **3j**


7.297
2.554
2.546
2.538
2.531
2.524
2.514
2.508
2.161
2.111
2.097
2.039
2.001
3.680
1.954
1.931
1.926
1.916
1.909
1.885
1.869
1.858
1.848
1.842
1.835
1.820
1.804
1.798
1.781
1.774
1.759
1.564
1.539
1.497
1.463
O
COOMe
F
11.61
4.53
3.00
3.00
2.05
2.06
8
6
4
2
PPM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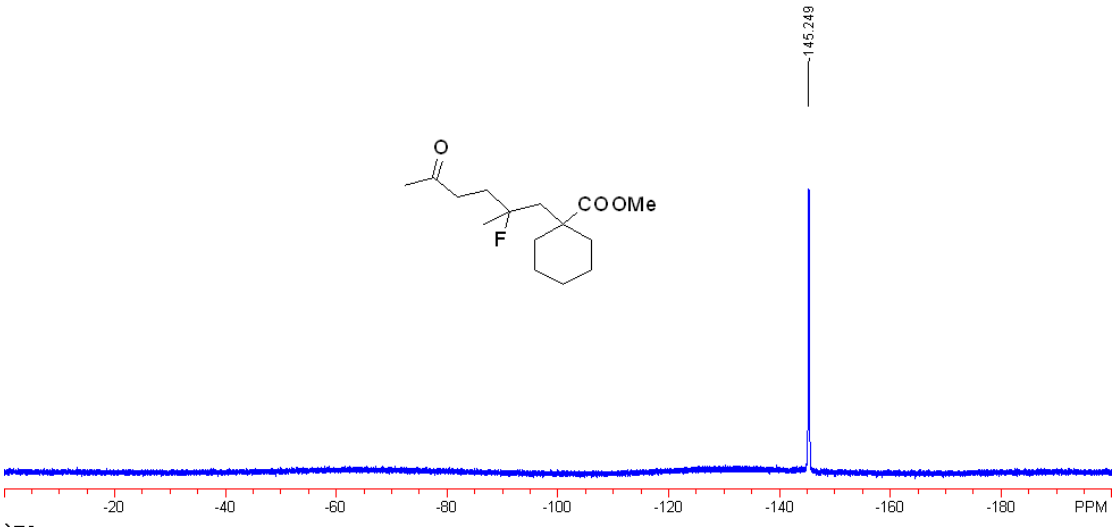
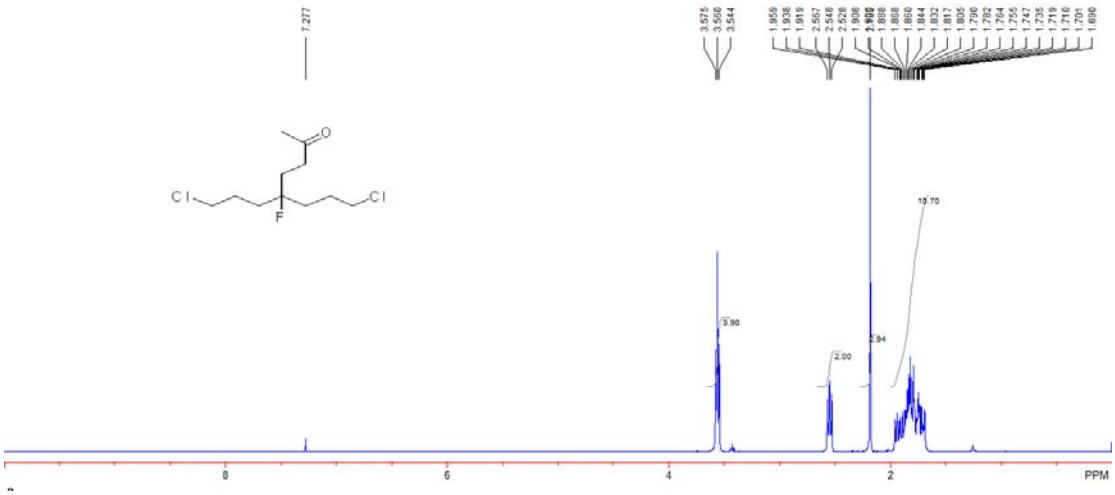
97.179
95.483
77.473
77.153
76.833
51.452
48.840
48.624
45.026
45.015
37.584
37.539
35.880
34.905
34.890
34.819
34.589
29.811
25.591
24.211
23.961
22.637
22.559
O
COOMe
F
200
150
100
50
PPM


145.249
O
COOMe
F
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

Compound **3k**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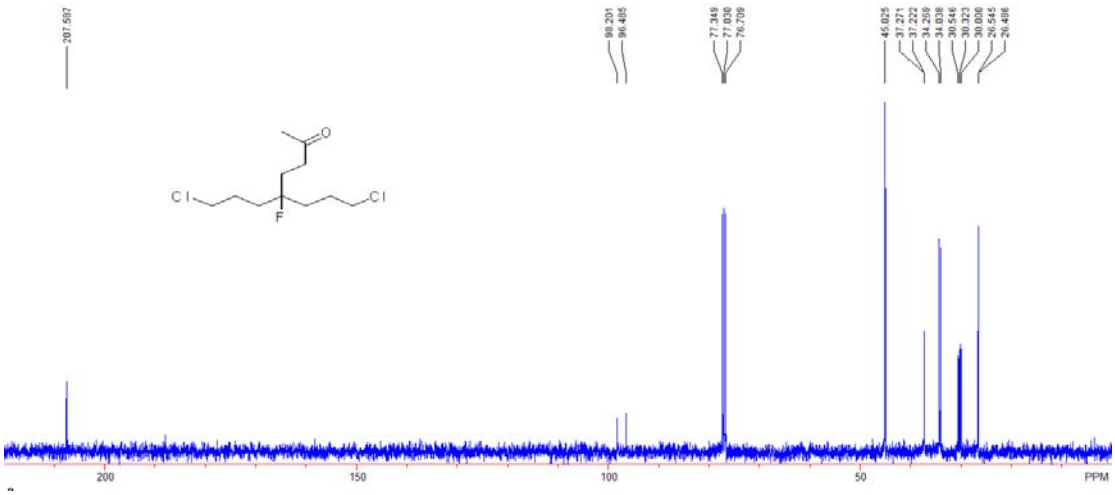
3.575
3.560
3.544
1.959
1.938
1.919
1.915
2.567
2.548
2.528
1.908
1.898
1.888
1.858
1.850
1.844
1.832
1.817
1.805
1.796
1.792
1.784
1.755
1.747
1.735
1.719
1.716
1.701
1.690
Cl
O
F
Cl
15.70
3.90
2.94
2.00
8
6
4
2
PPM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96.486
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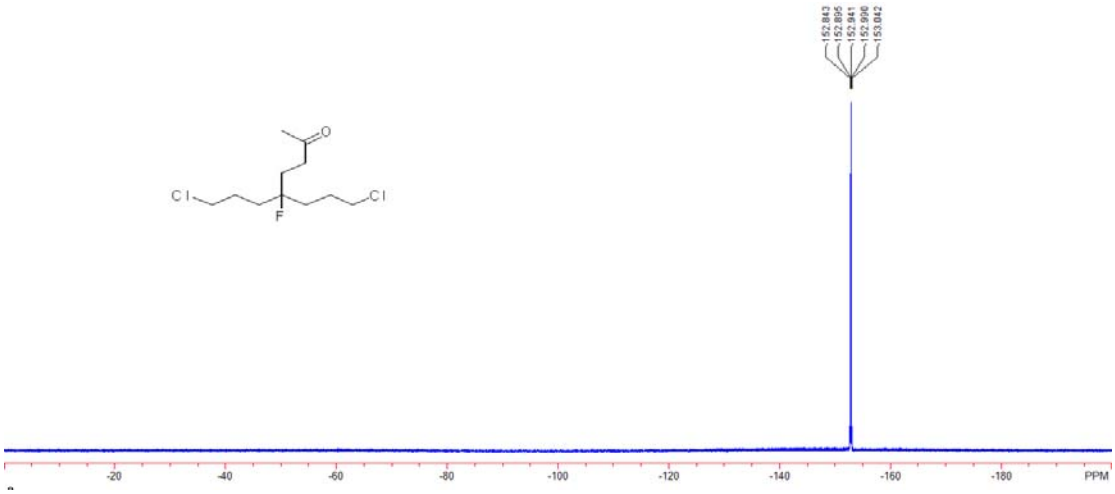
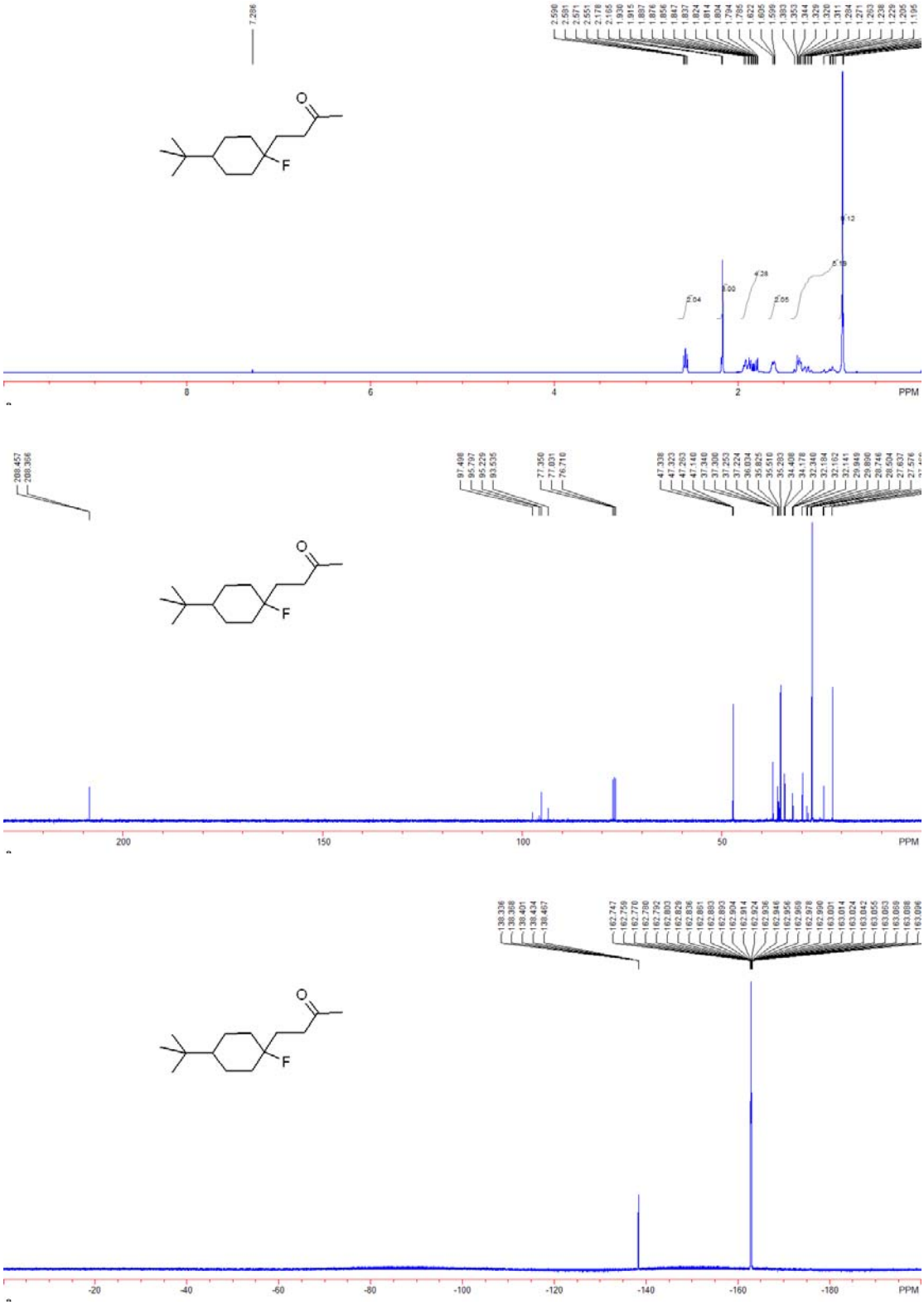
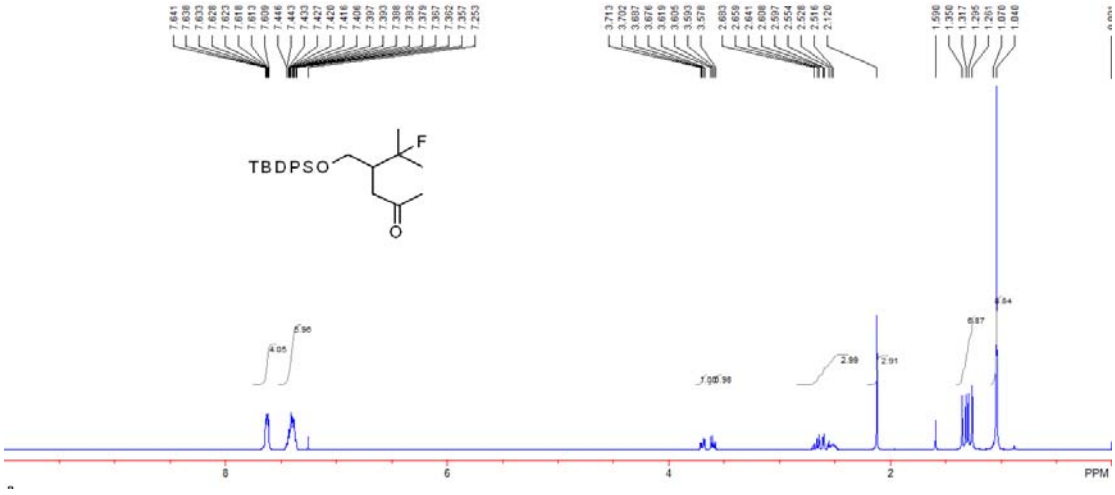
76.706
45.825
37.271
37.222
34.639
34.599
30.546
30.323
30.006
25.545
26.486
Cl
O
F
Cl
200
150
100
50
PPM

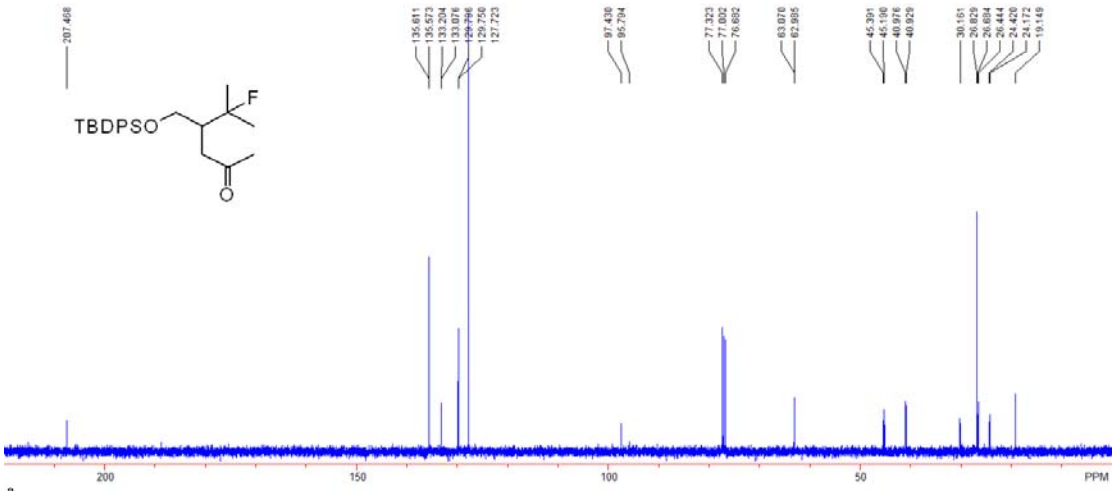

152.843
152.895
152.941
152.990
153.042
Cl
O
F
Cl
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

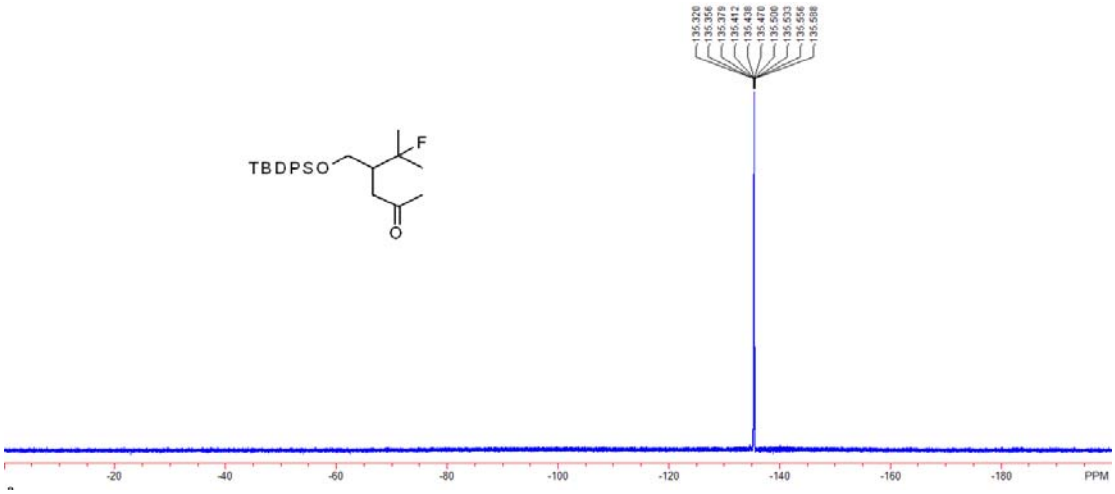
Compound **3l**



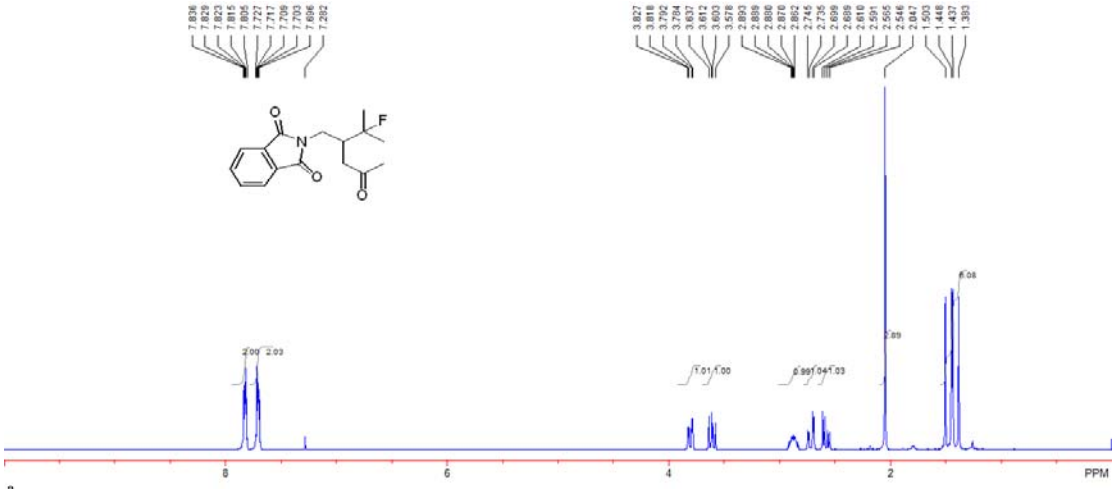
Compound **4a**







Compound **4b**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7.805
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7.717
7.709
7.703
7.696
7.202
3.827
3.818
3.792
3.784
3.637
3.612
3.603
3.578
2.893
2.889
2.886
2.876
2.862
2.745
2.735
2.699
2.689
2.610
2.591
2.565
2.546
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1.432
1.393
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0.99
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1.03
2.00
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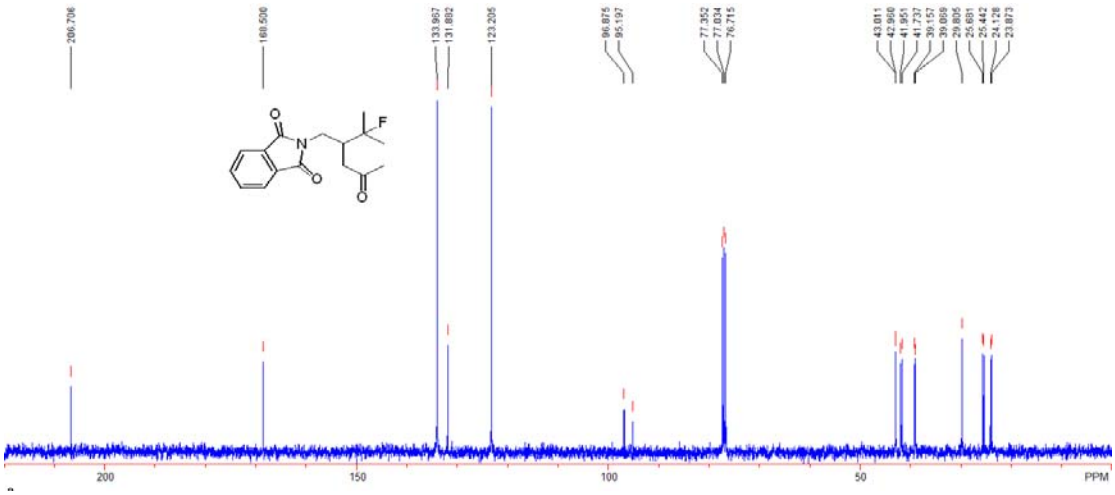
6
4
2
PPM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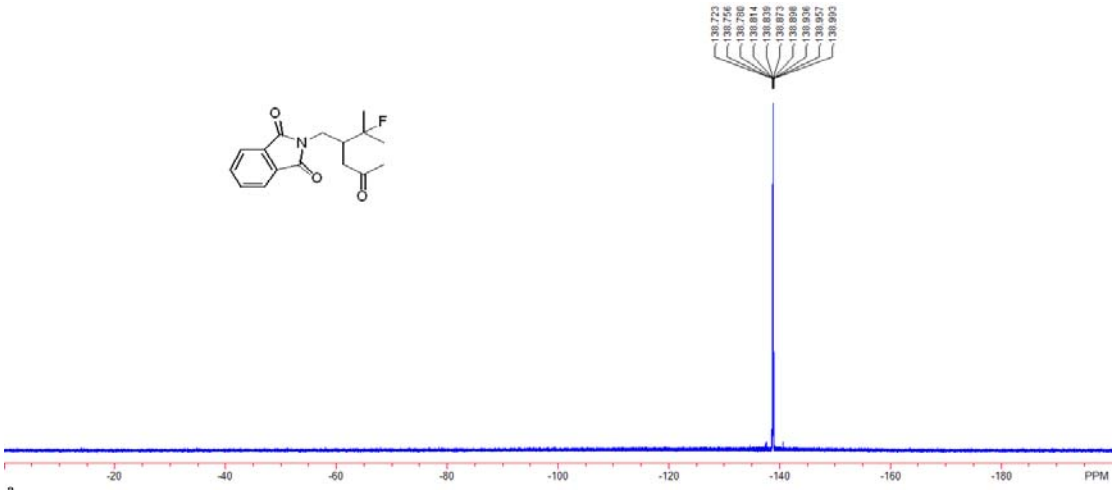
131.892
123.206
86.875
85.197
77.352
77.034
76.715
43.811
42.906
41.951
41.737
39.157
39.808
29.805
25.691
25.442
24.178
23.879
200
150
100
50
PPM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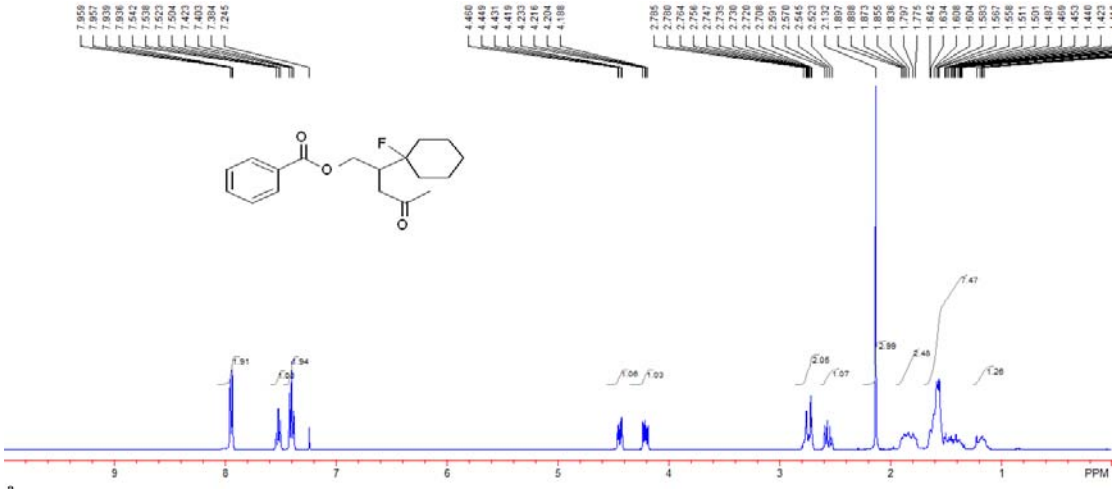
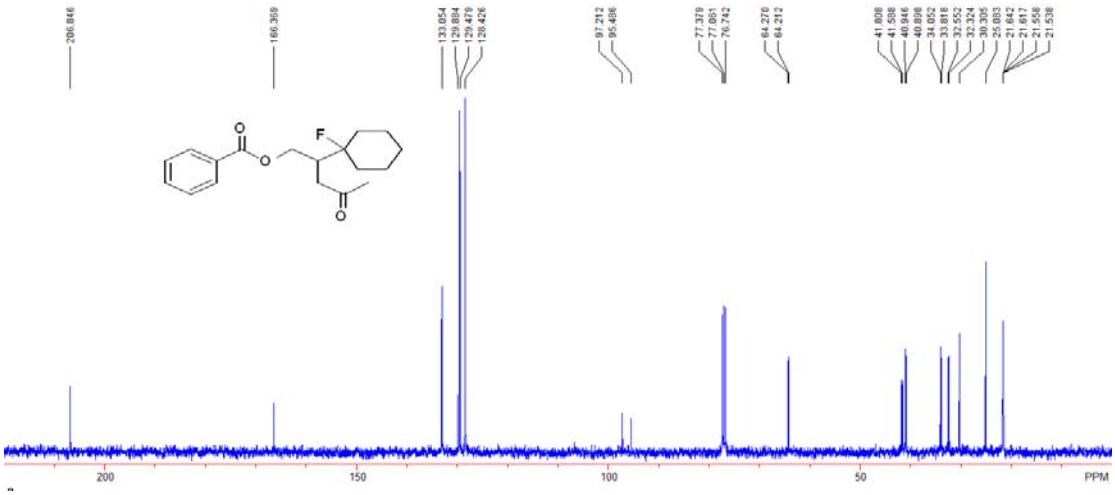
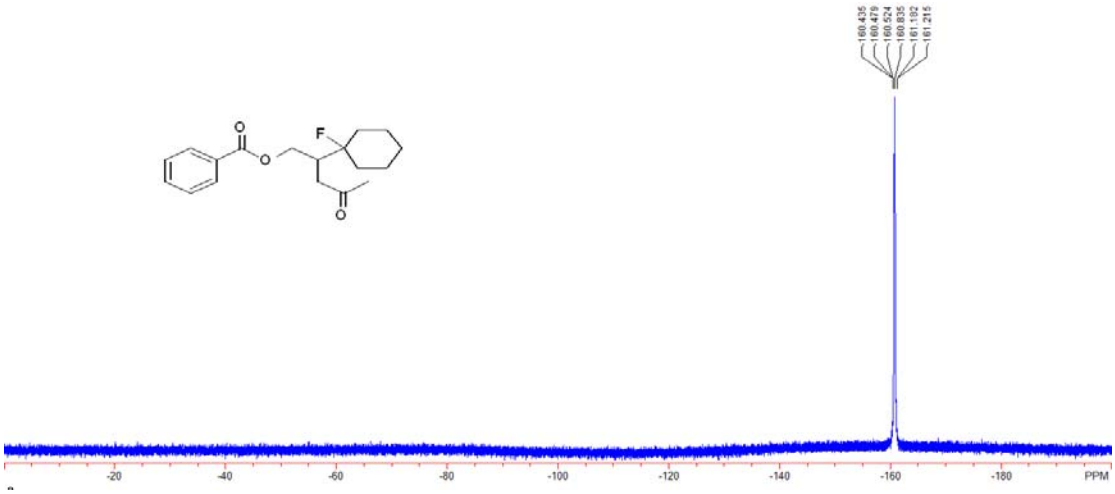
138.756
138.790
138.814
138.839
138.873
138.898
138.936
138.957
138.993
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

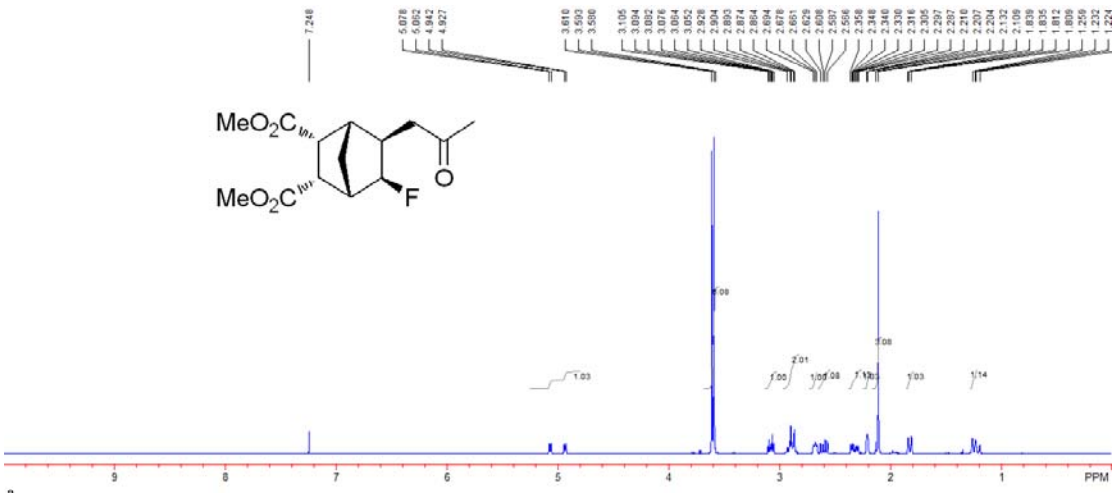
Compound **4c**

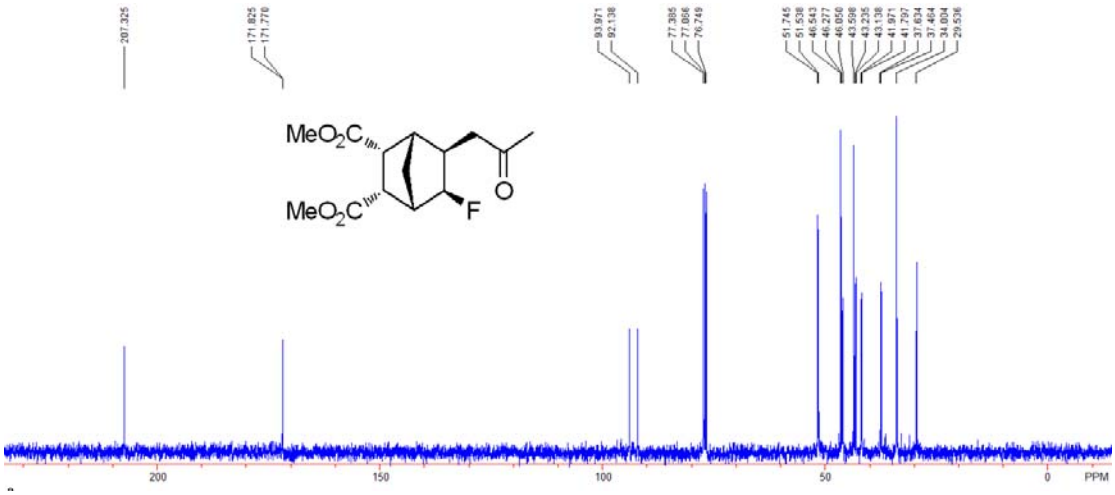


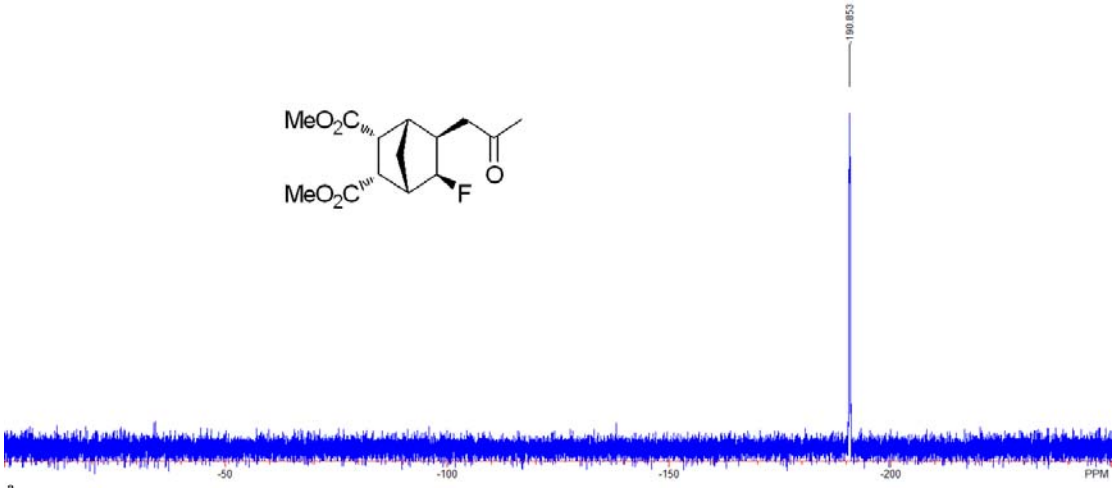




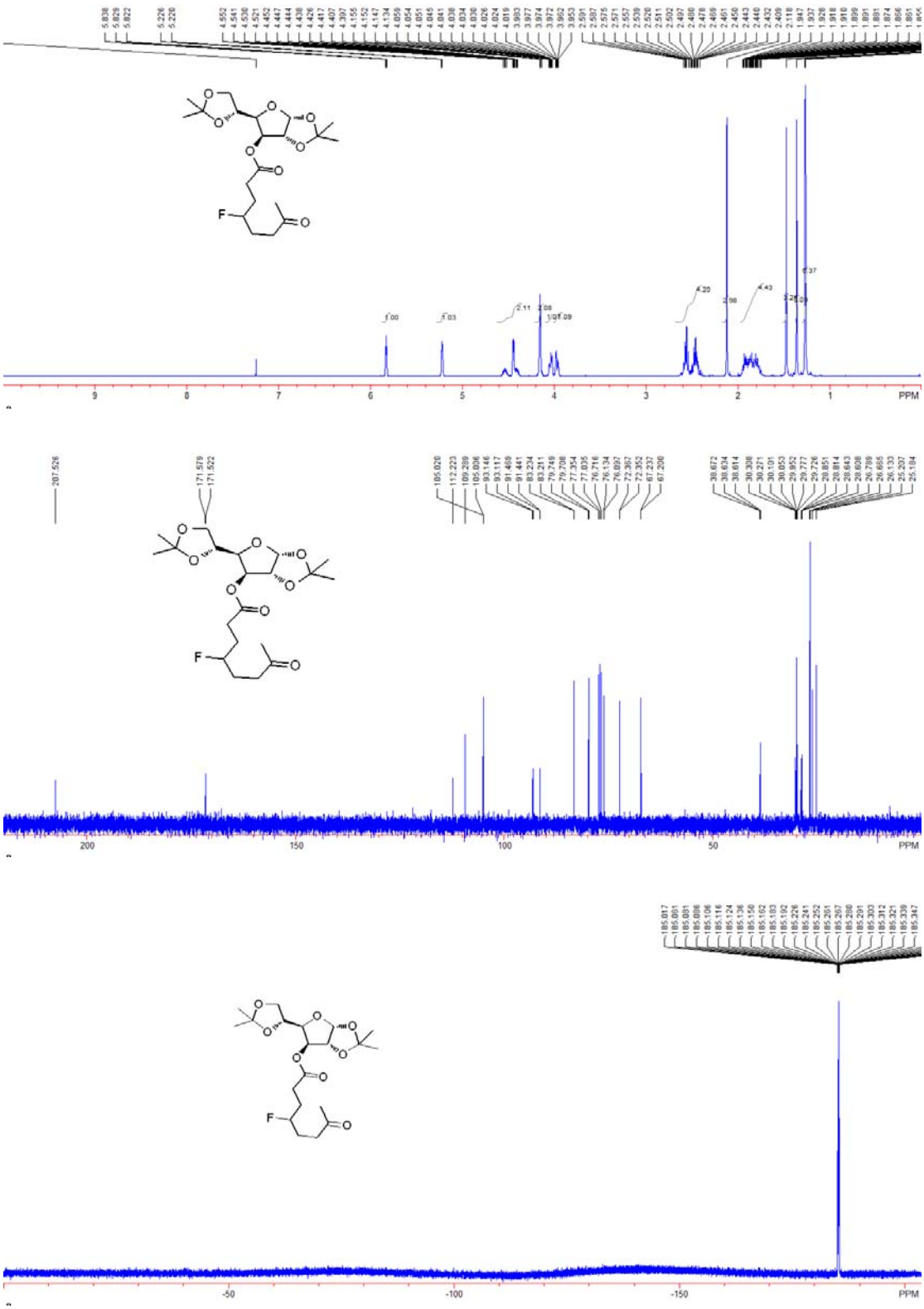
Compound **5**



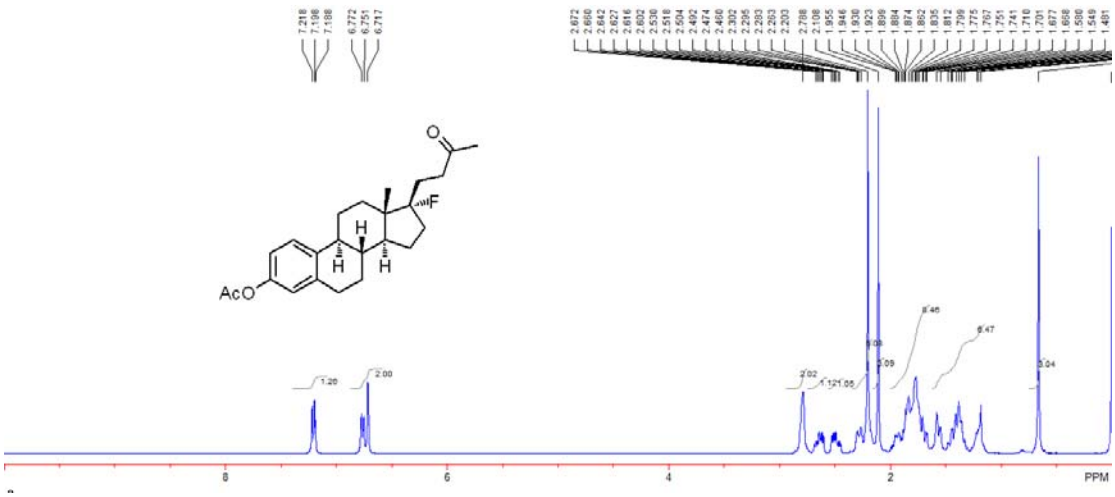


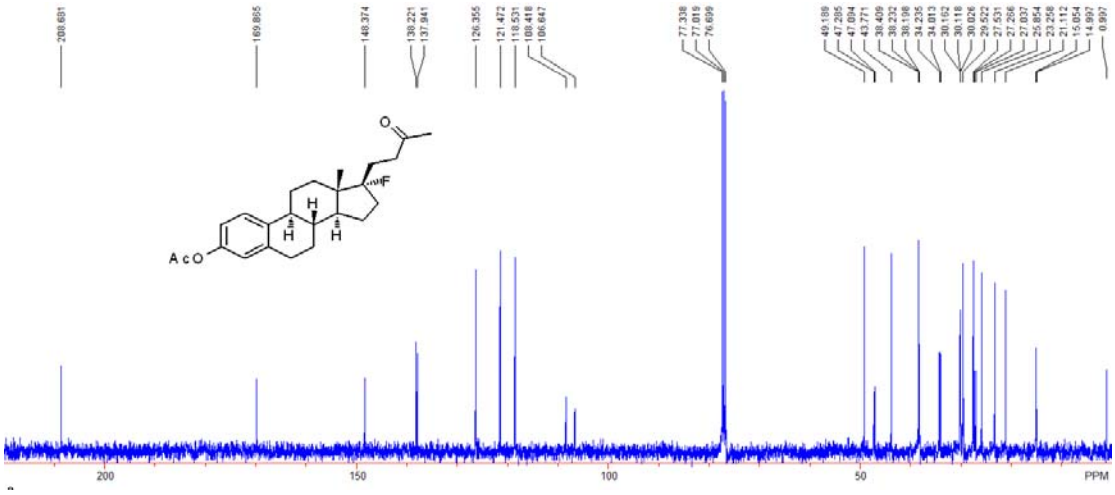


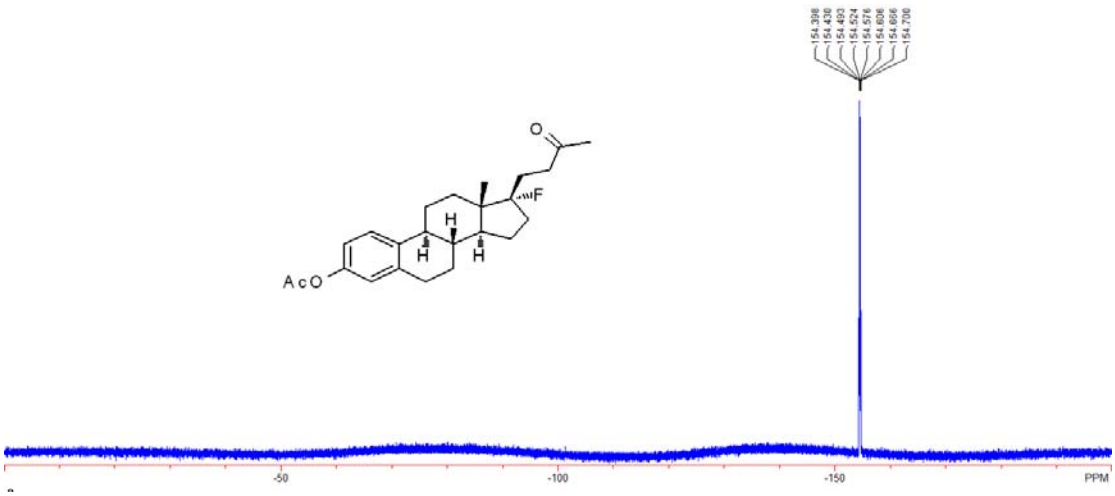
Compound **7**



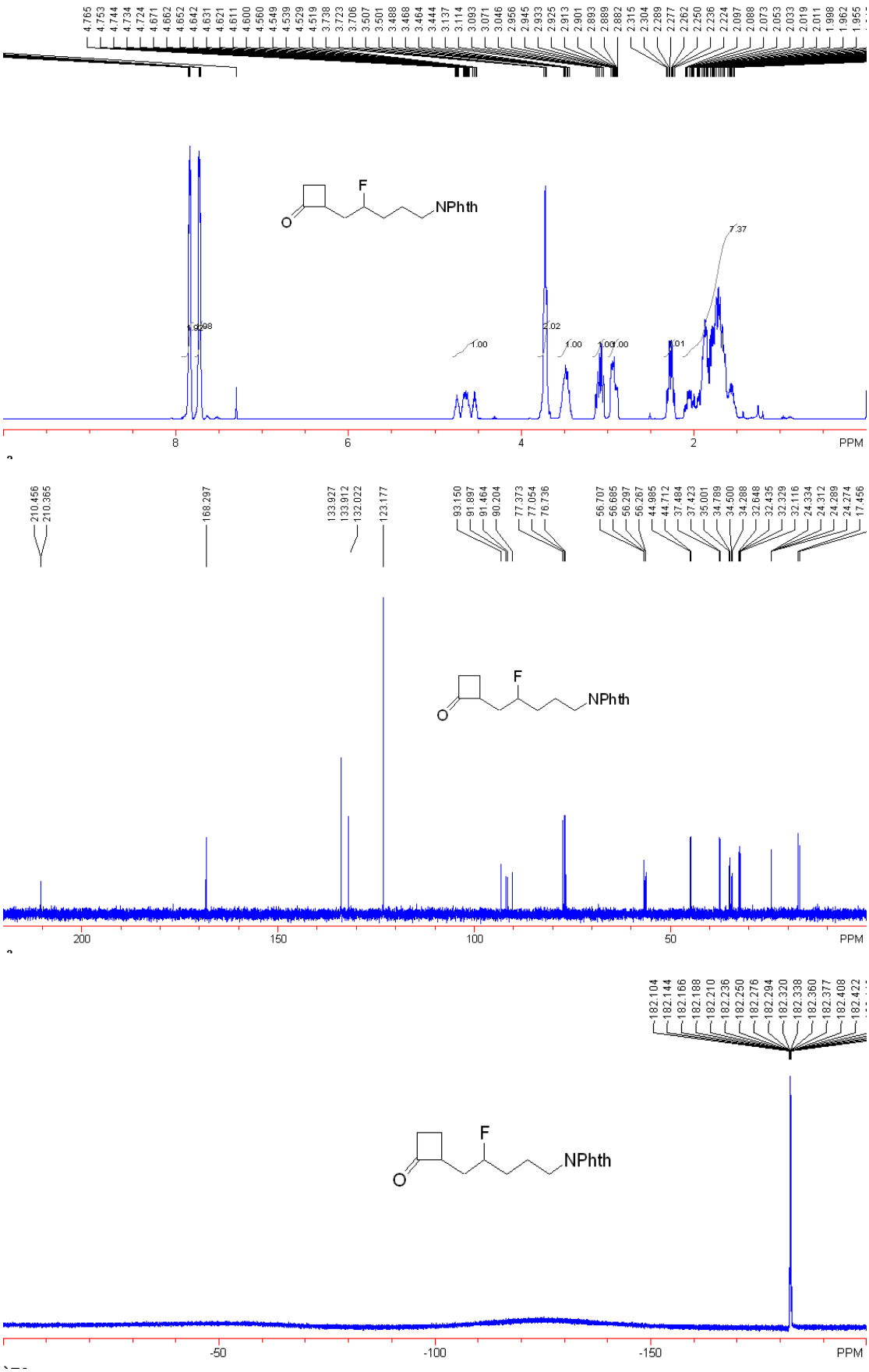
Compound **9**



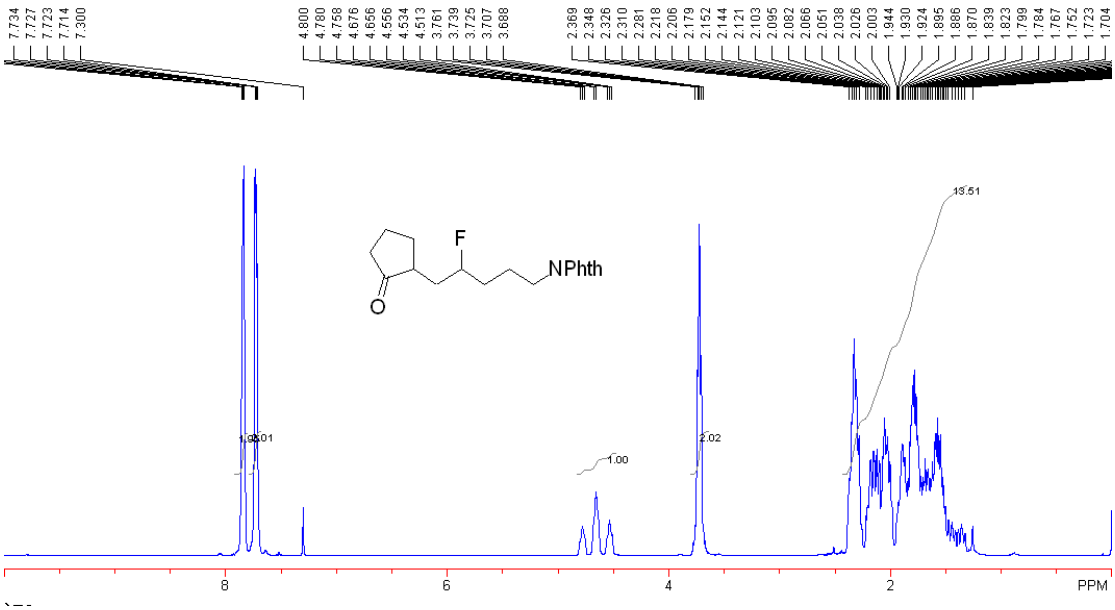


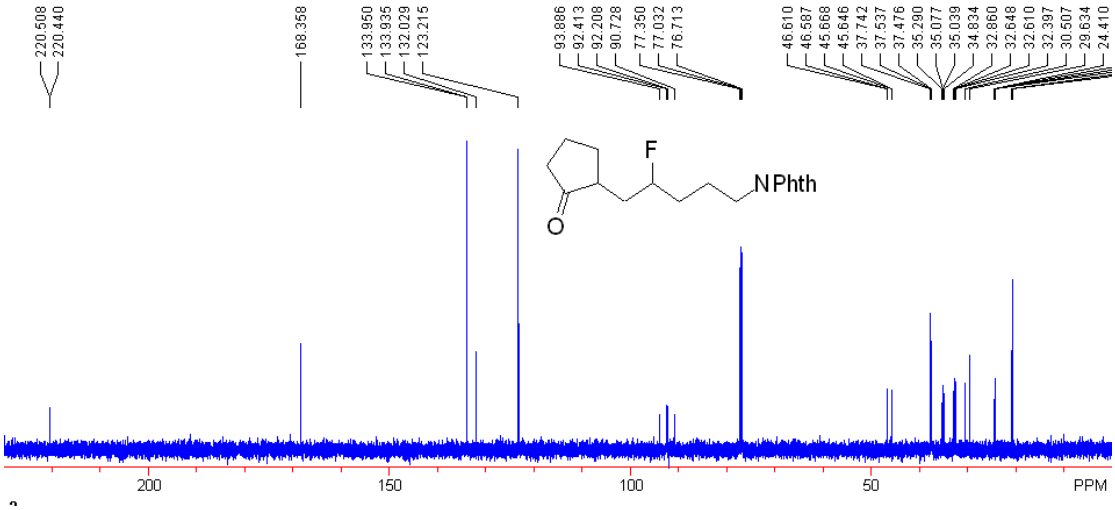


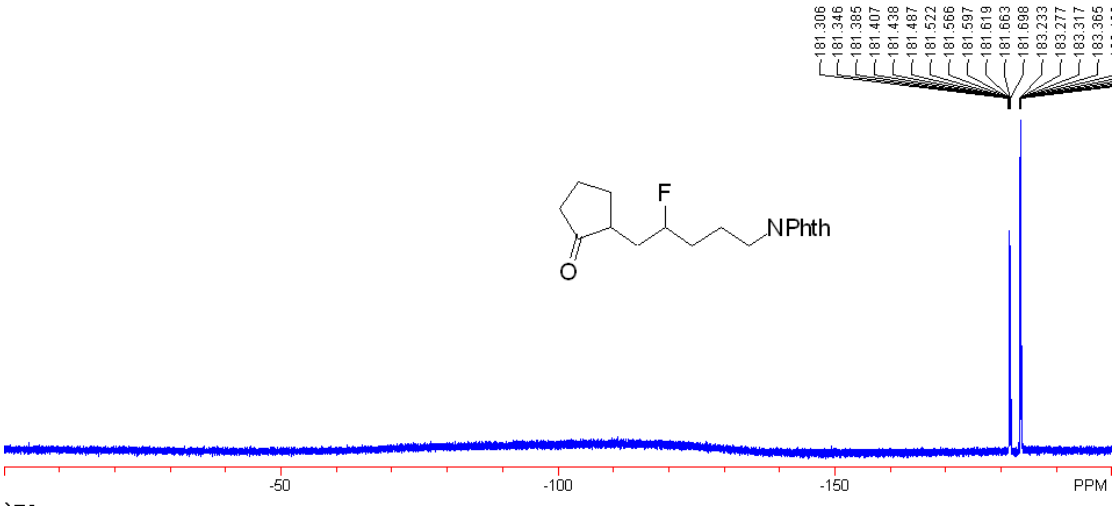
Compound **10a**



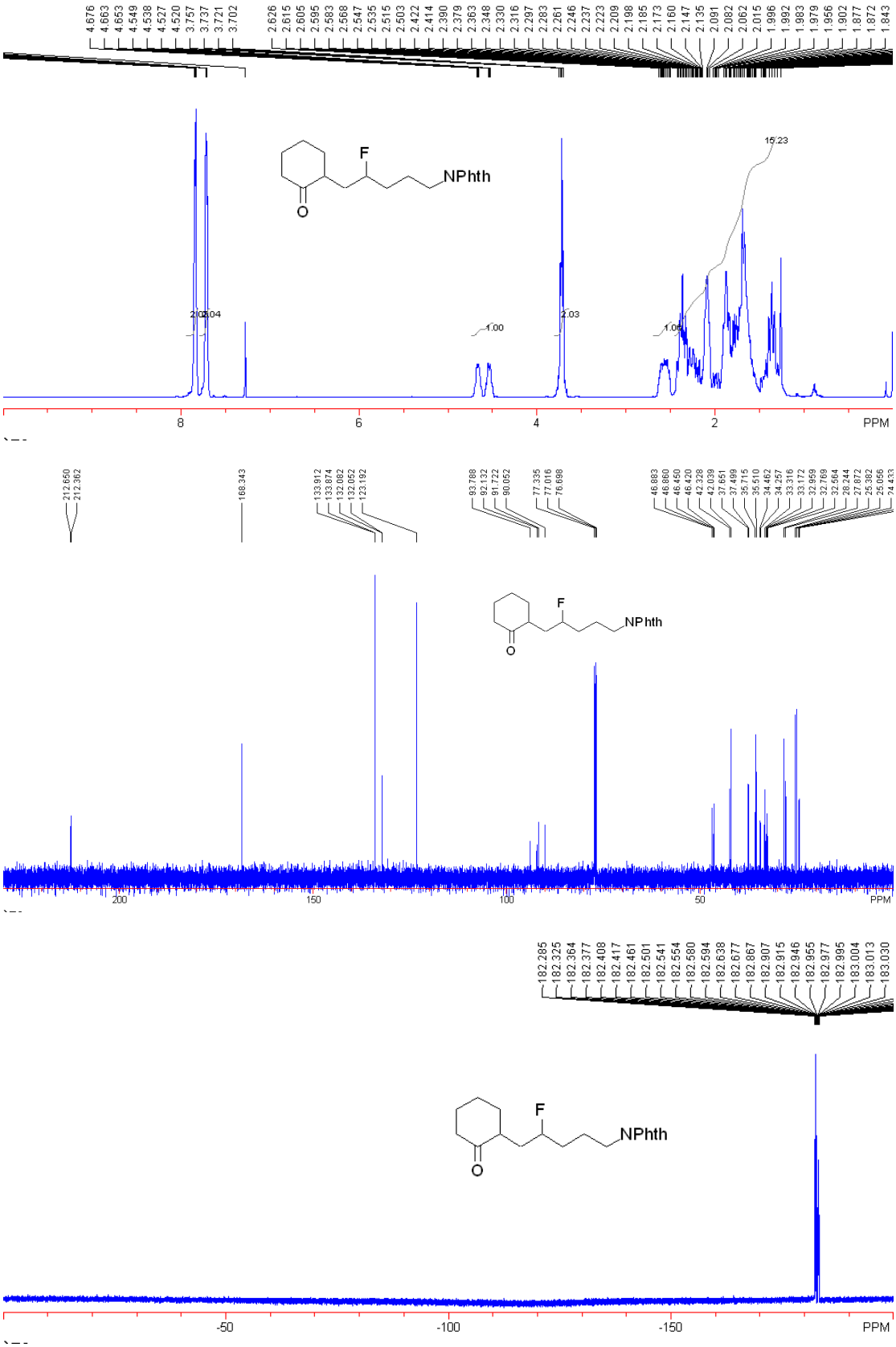
Compound **10b**



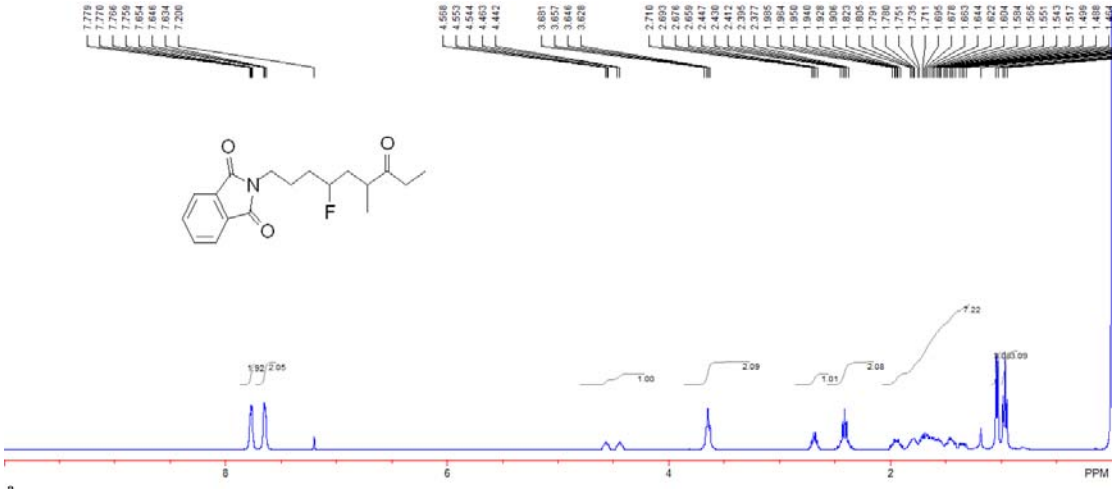


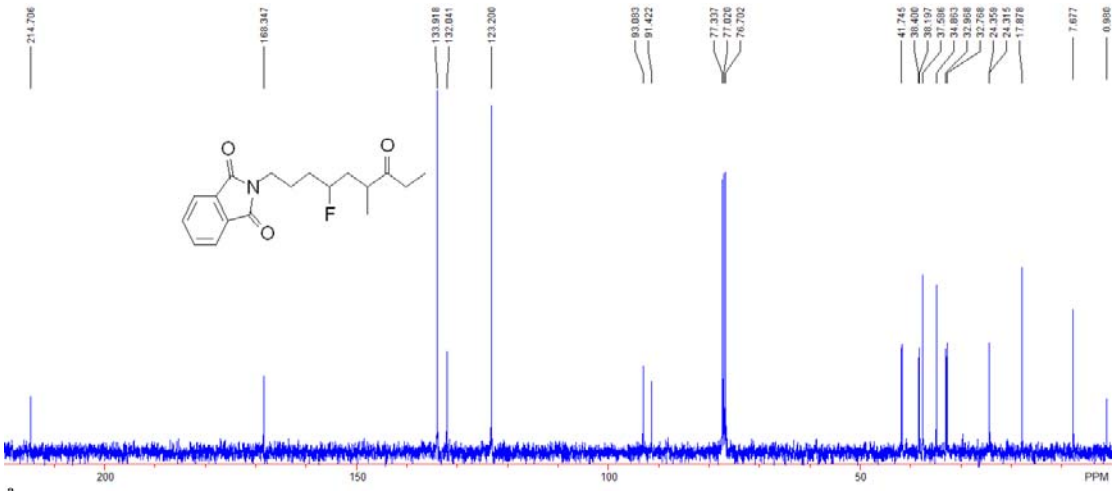


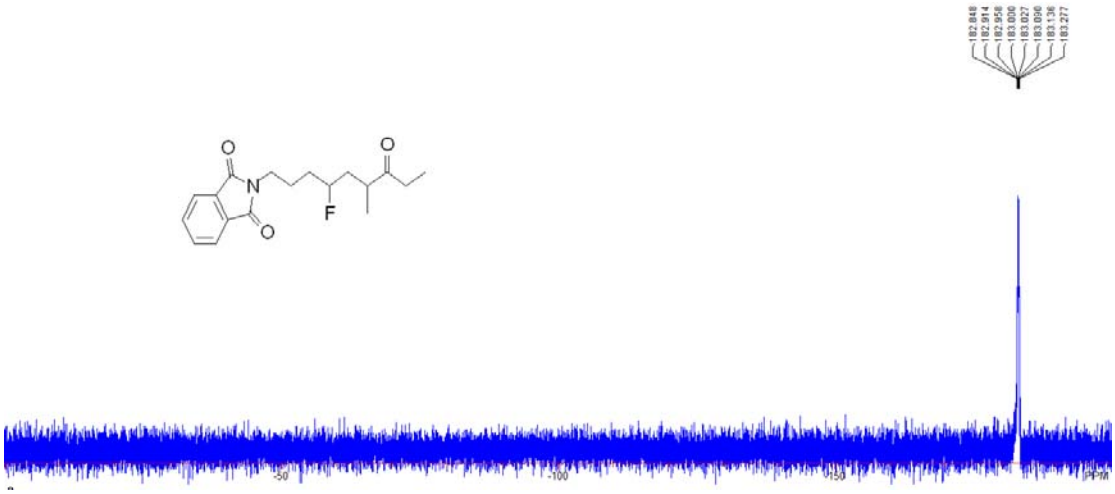
Compound **10c**



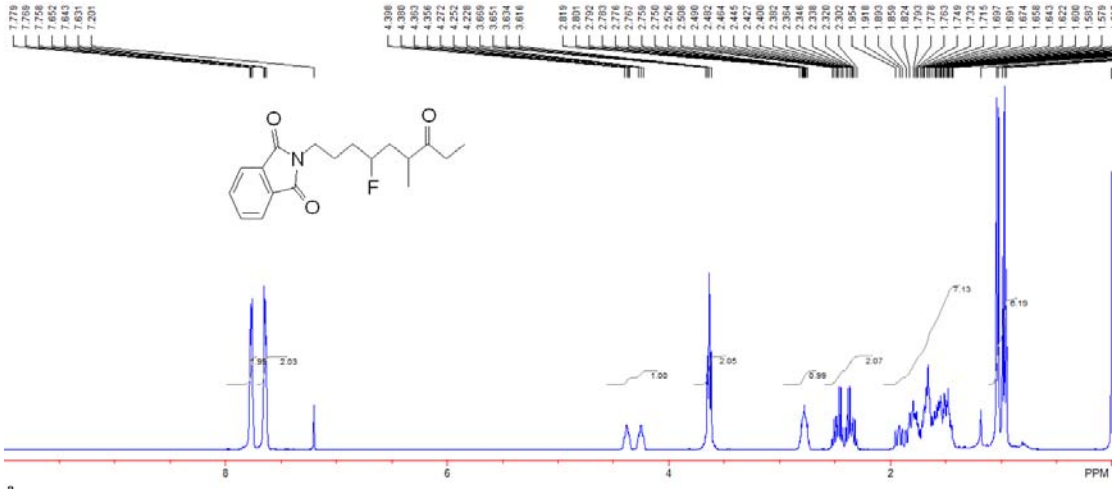
Compound **10d (stereoisomer 1)**

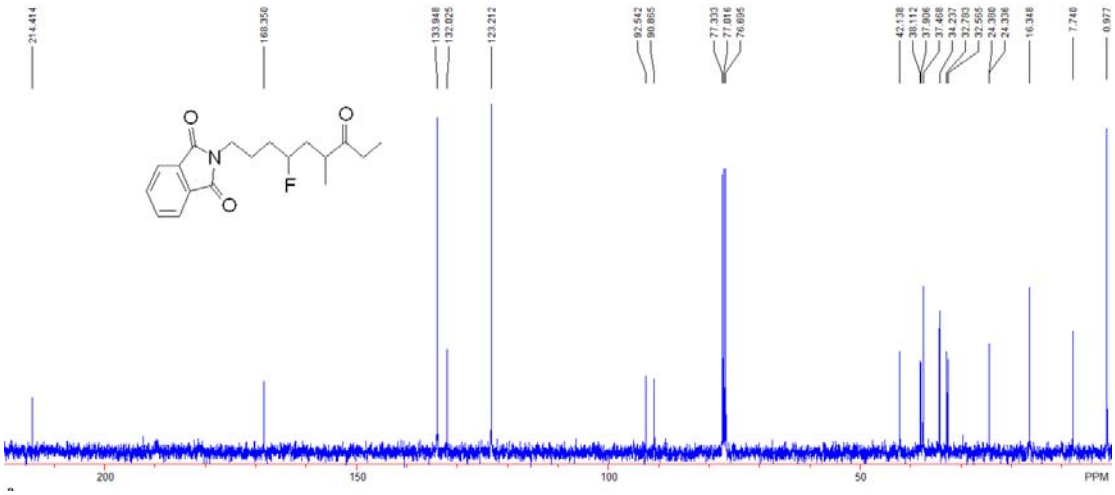


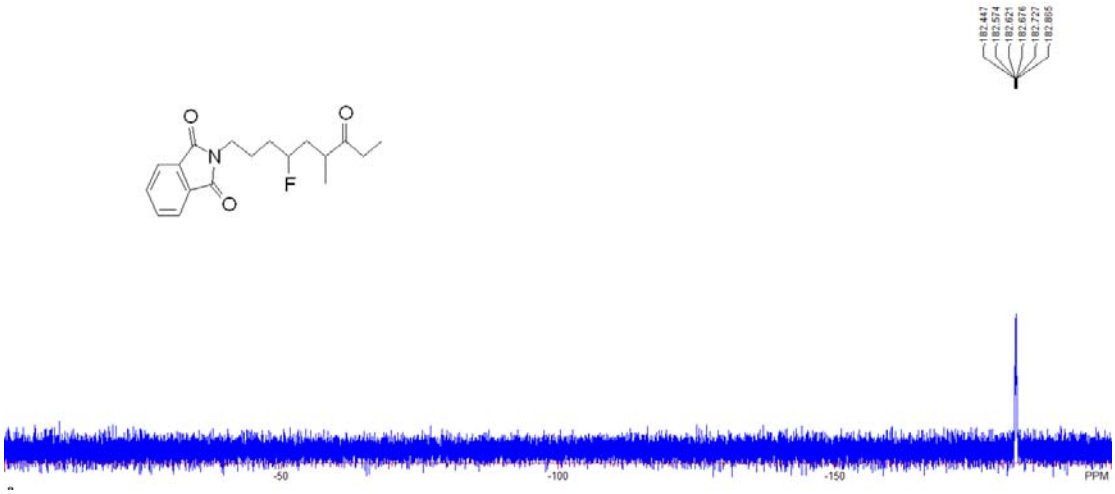




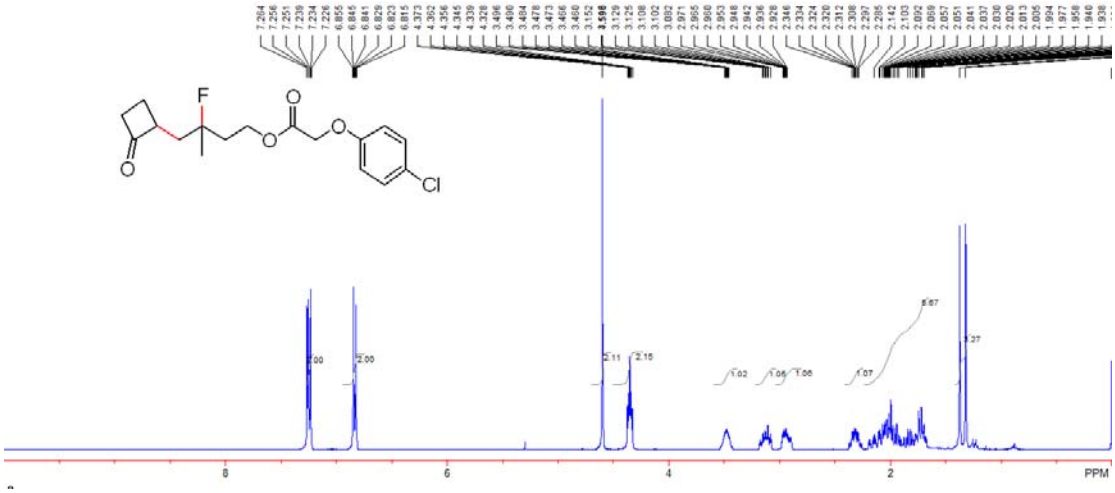
Compound **10d (stereoisomer 2)**

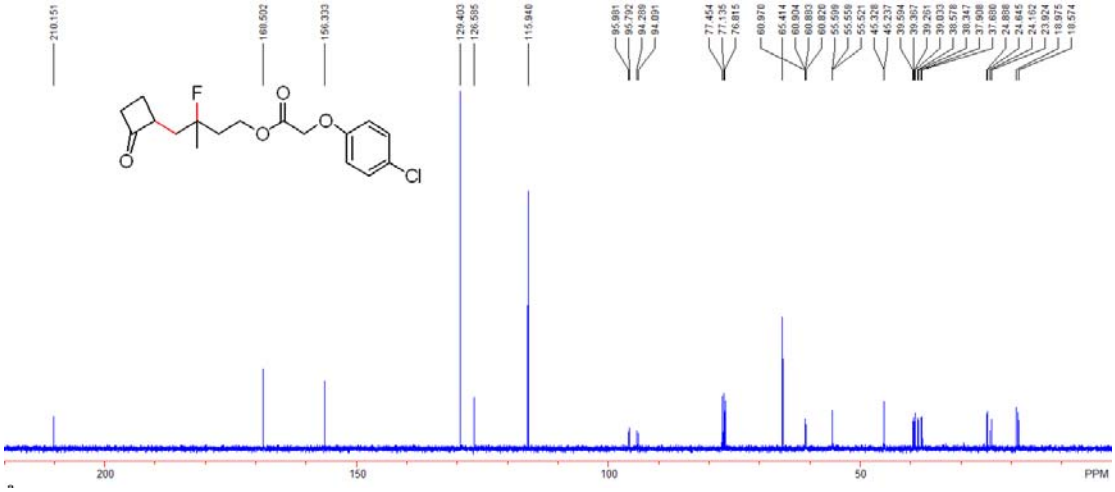


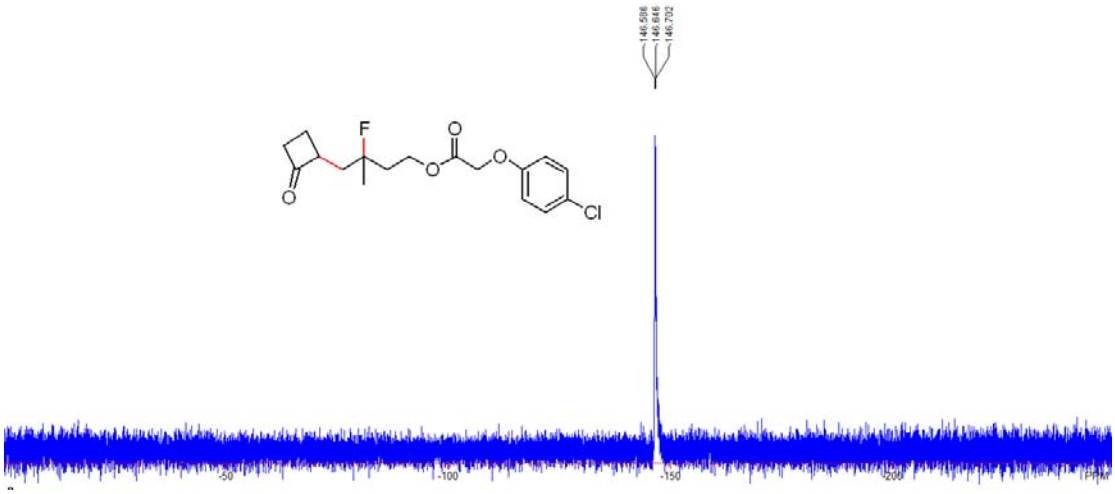




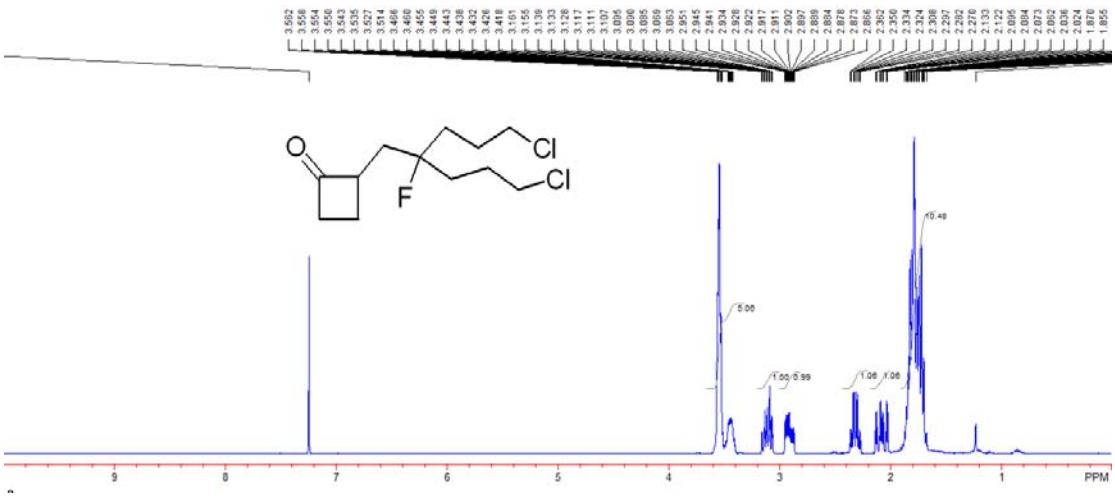
Compound **10e**

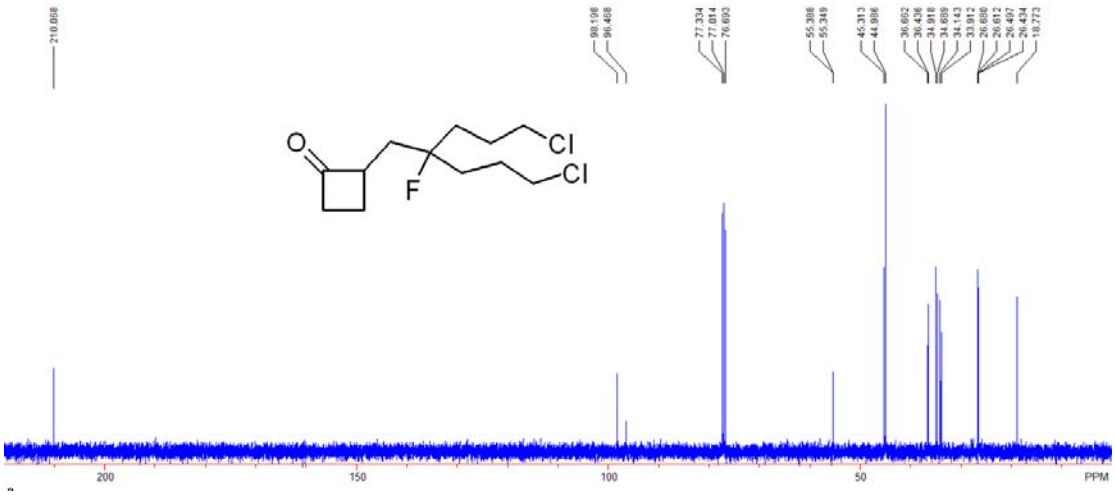


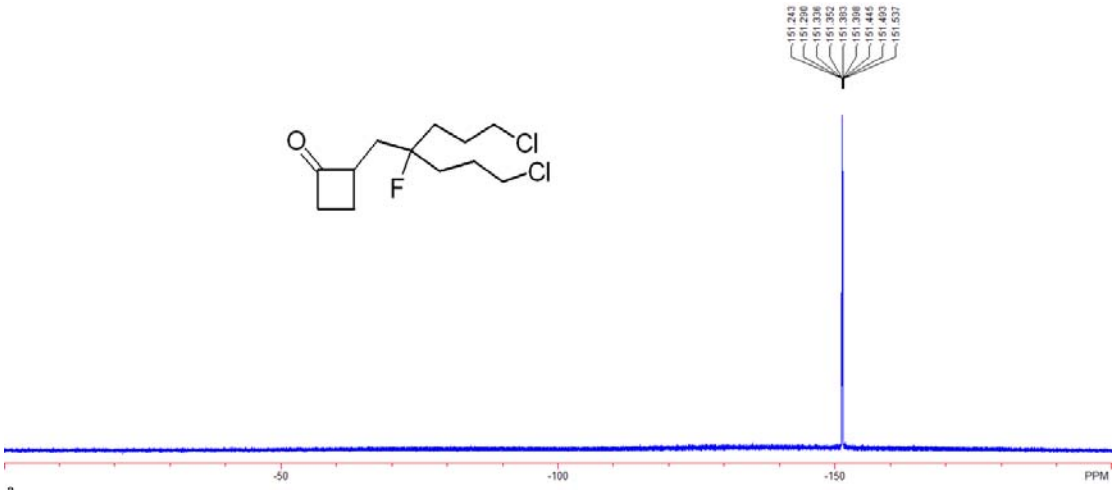




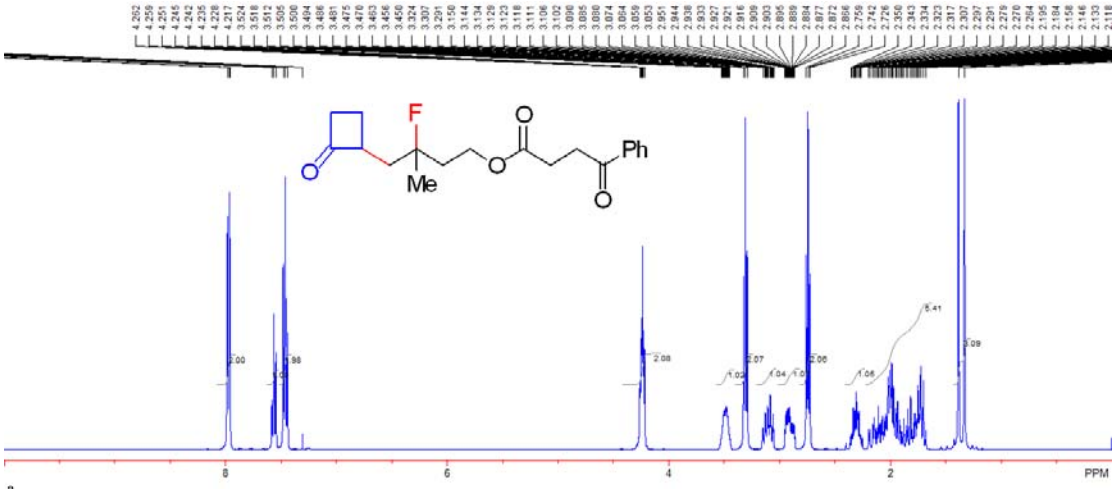
Compound **10f**

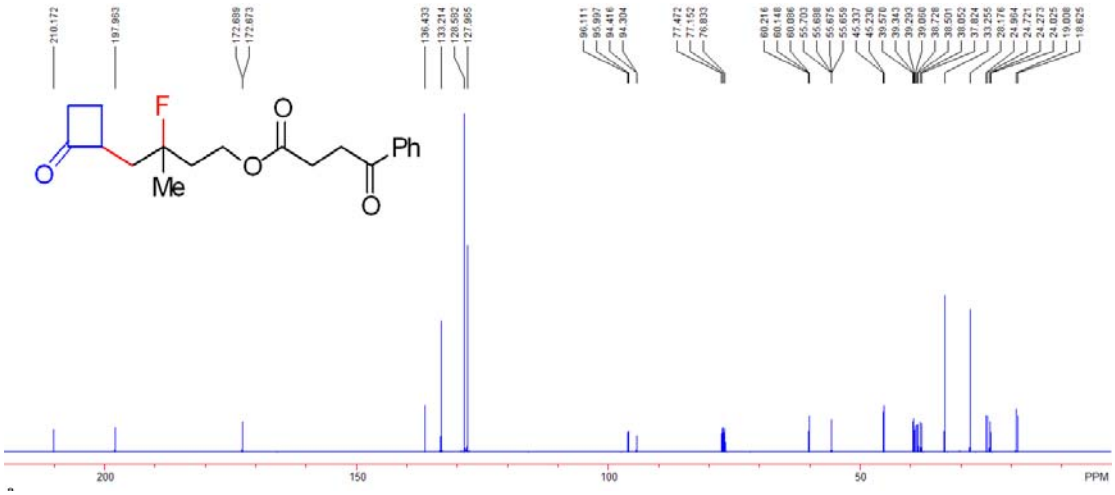


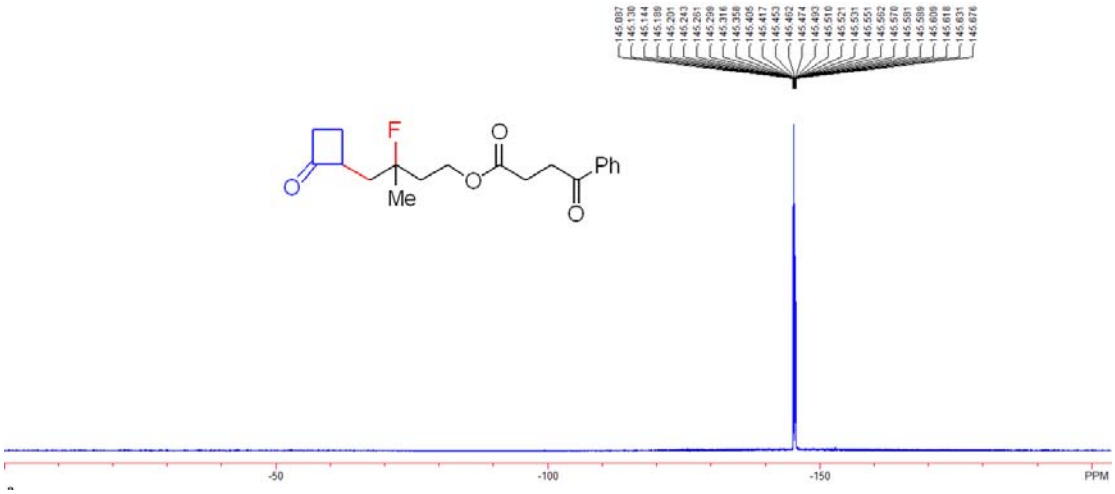




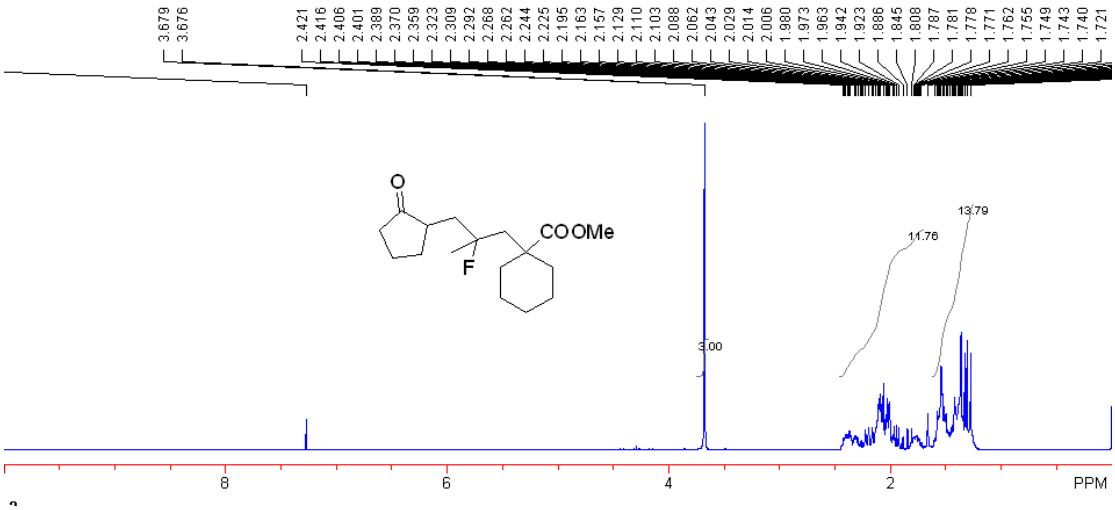
Compound **10g**

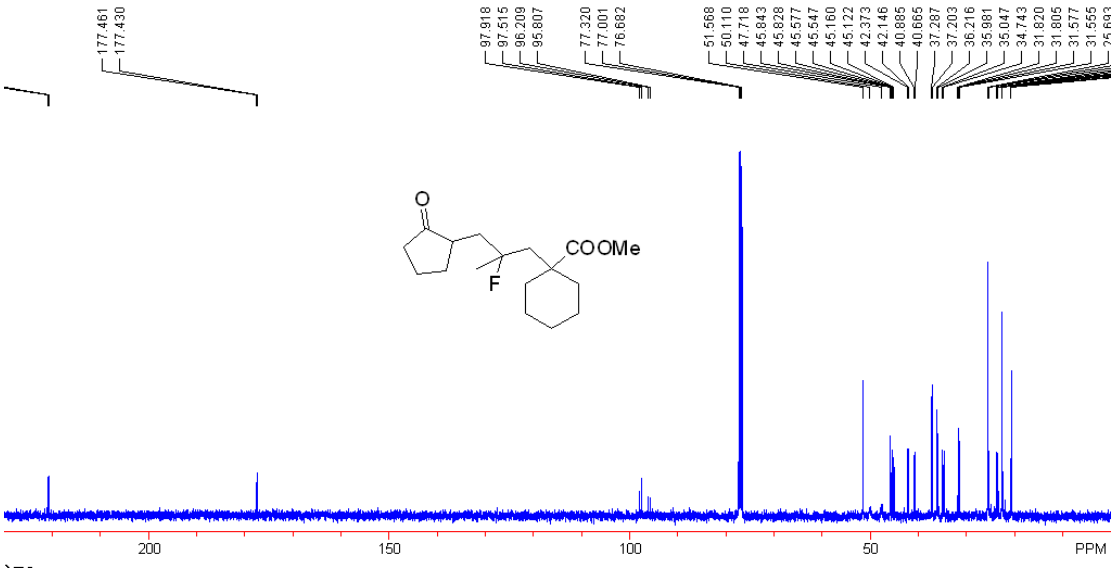


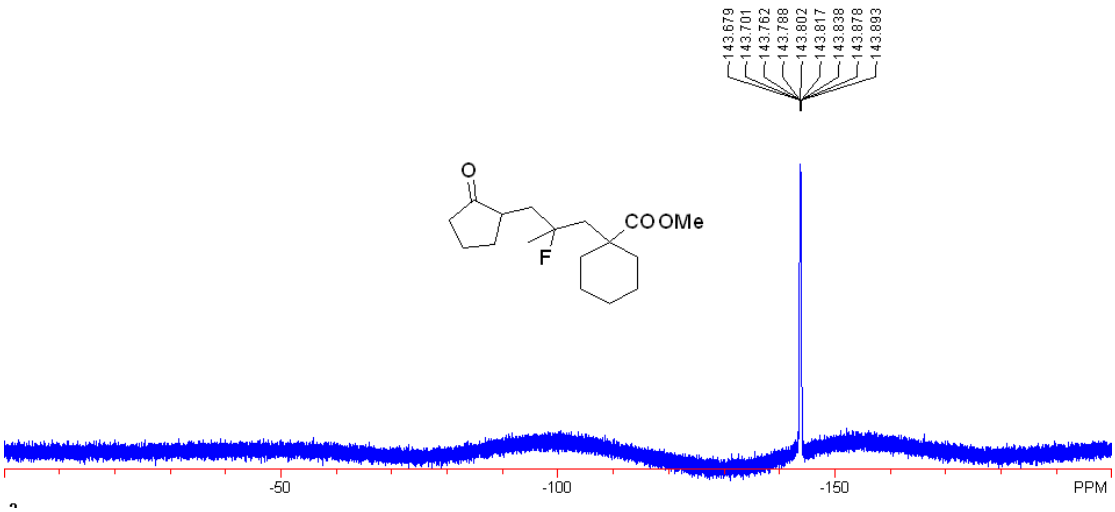




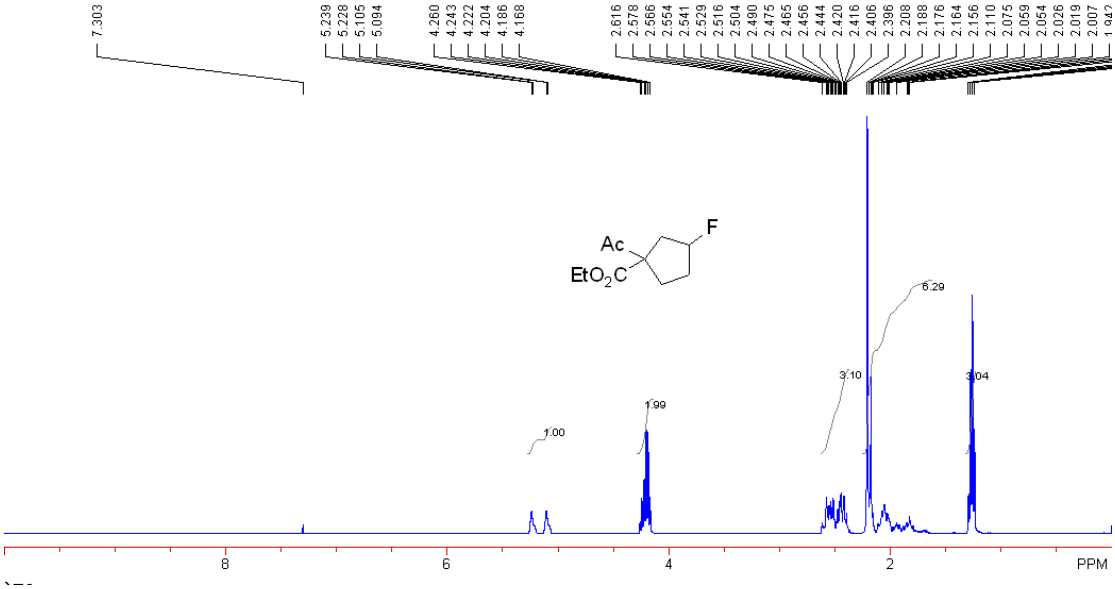
Compound **10h**







Compound **11**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2.529
2.516
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2.420
2.416
2.406
2.396
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2.188
2.176
2.164
2.156
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2.054
2.026
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EtO2C
F
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1.99
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3.04
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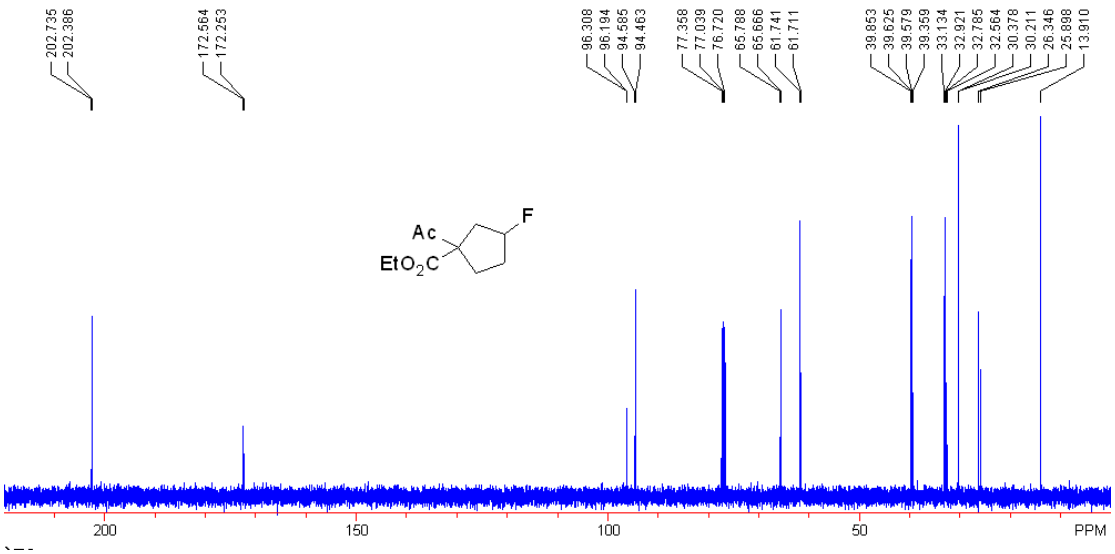
2
PPM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76.720
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65.666
61.741
61.711
39.853
39.625
39.579
39.359
33.134
32.921
32.785
32.564
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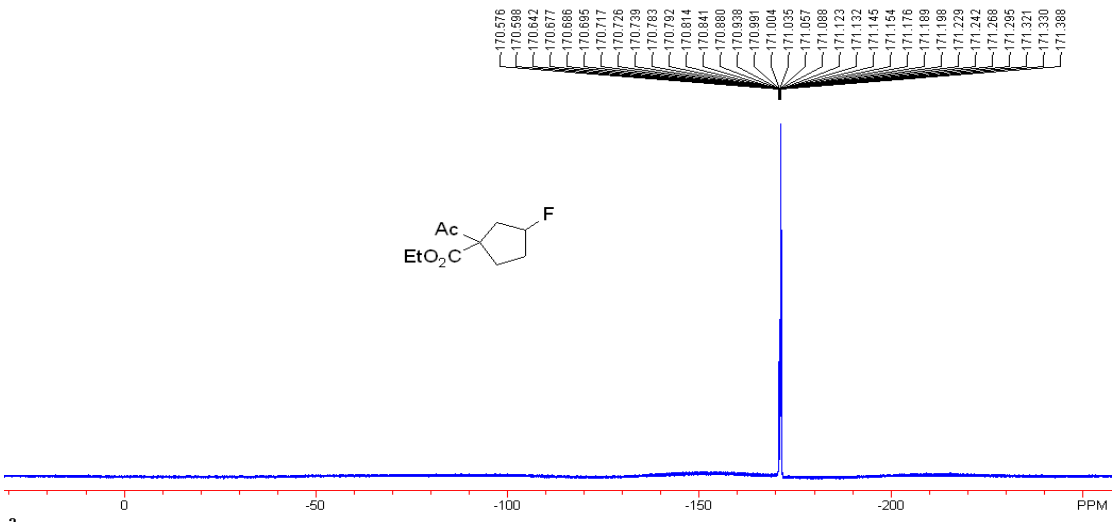
30.211
26.346
25.898
13.910
Ac
EtO2C
F
200
150
100
50
PPM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171.242
171.268
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171.388
Ac
EtO2C
F
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-50
-100
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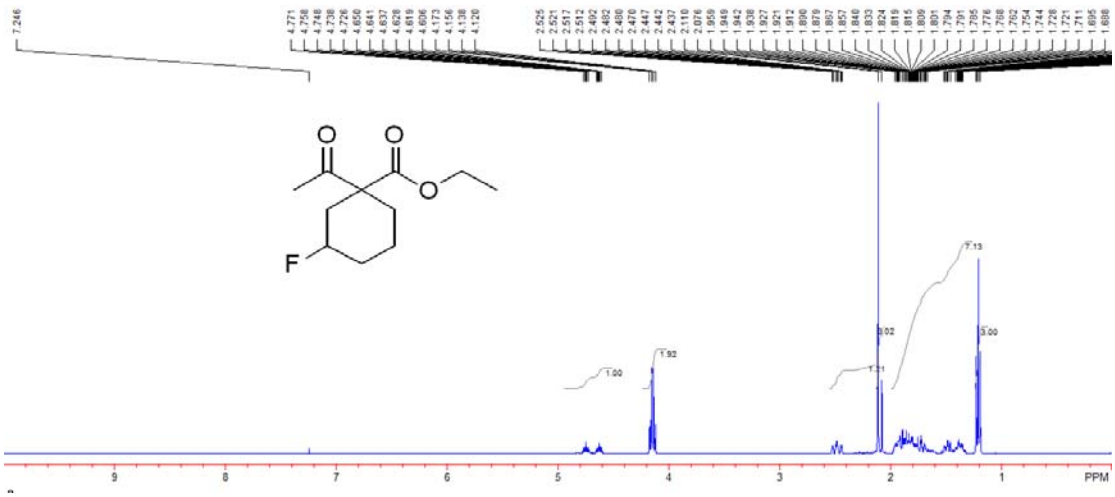
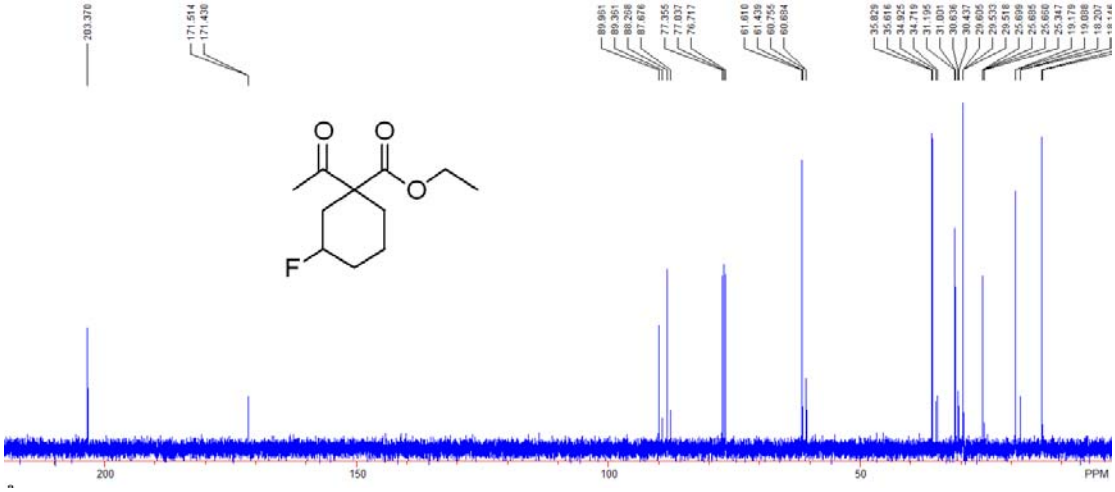
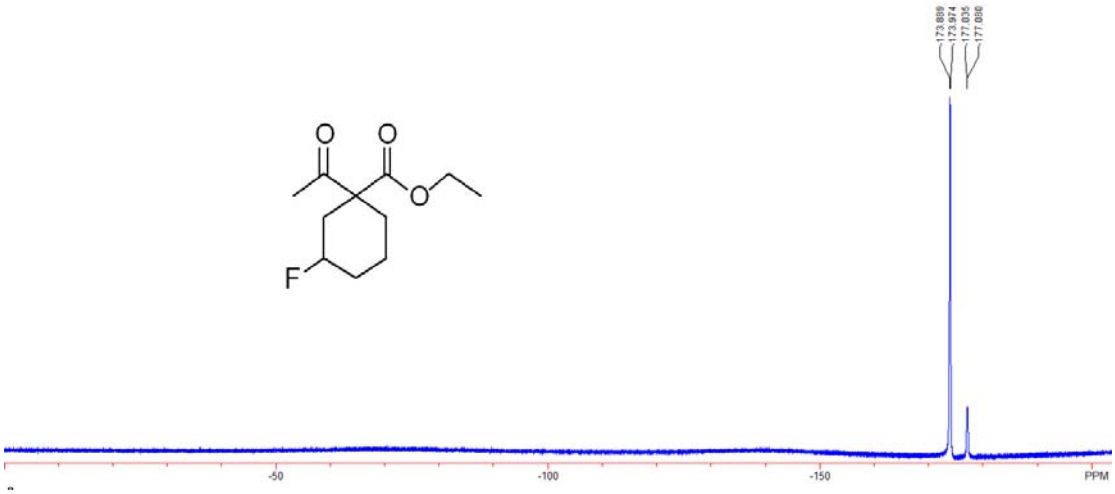
-200
PPM

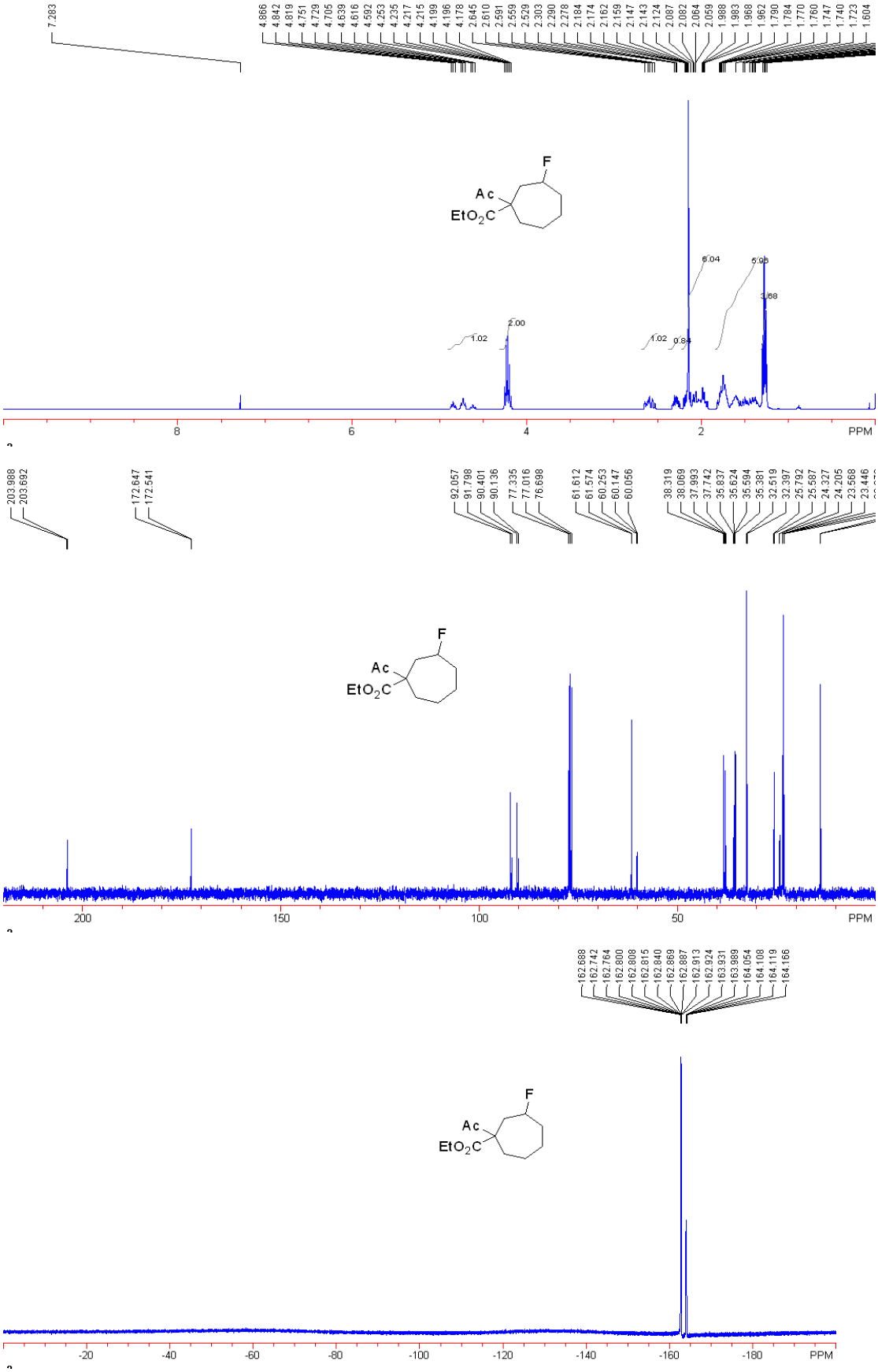
Compound **12**



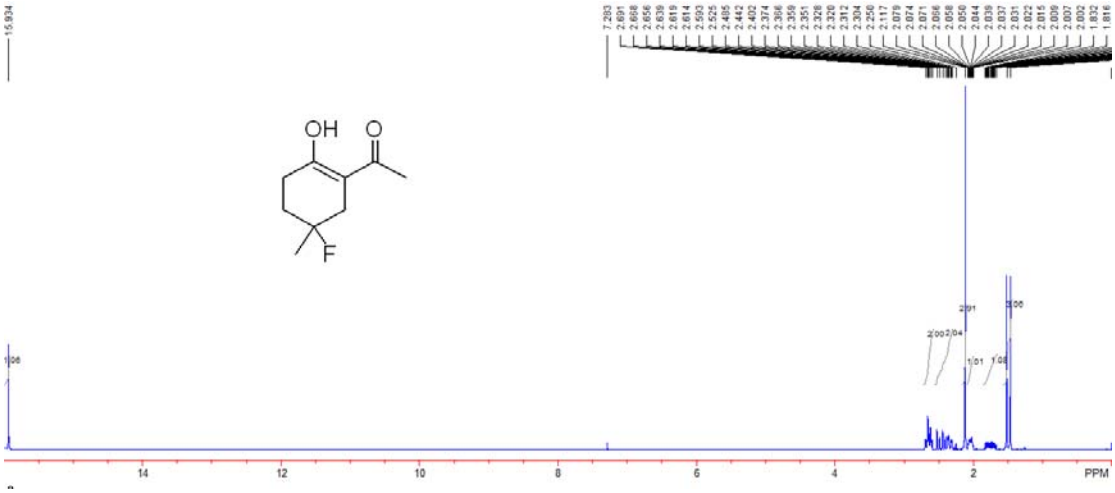


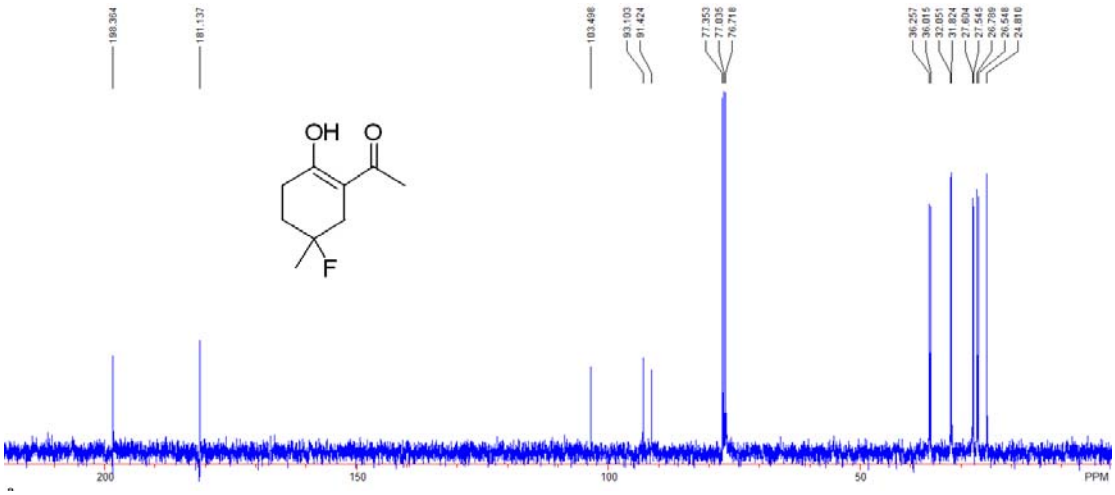


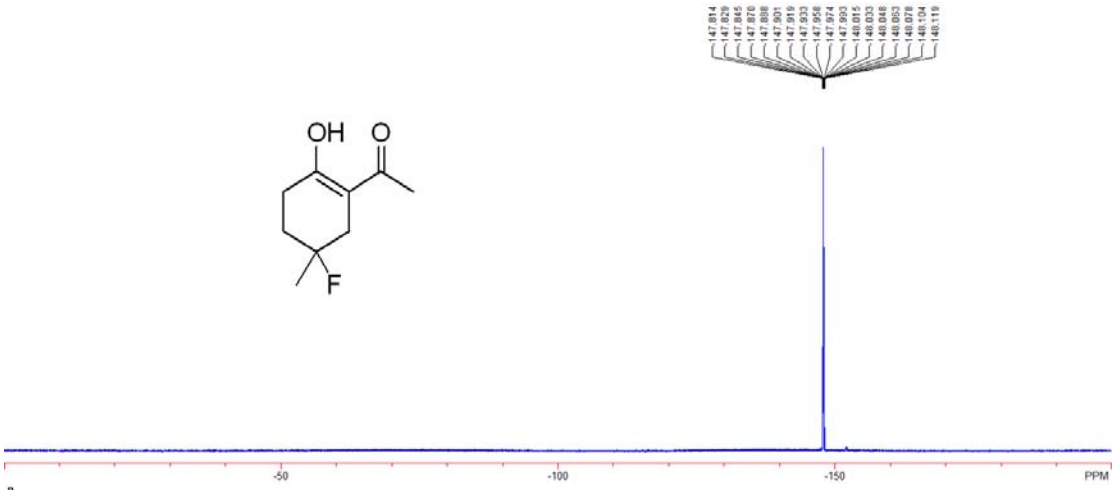
Compound **13**



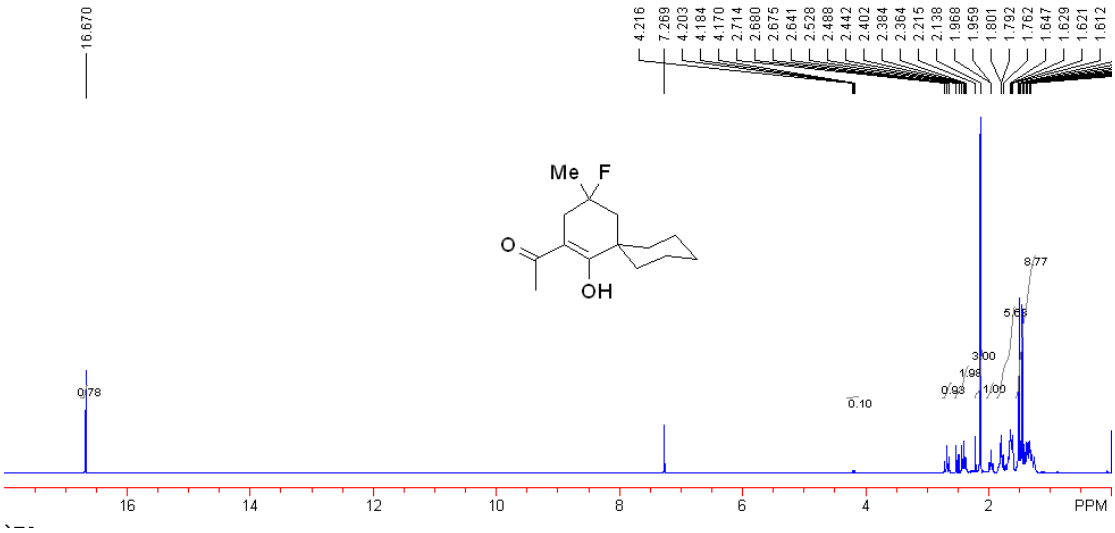
Compound **14**







Compound **15**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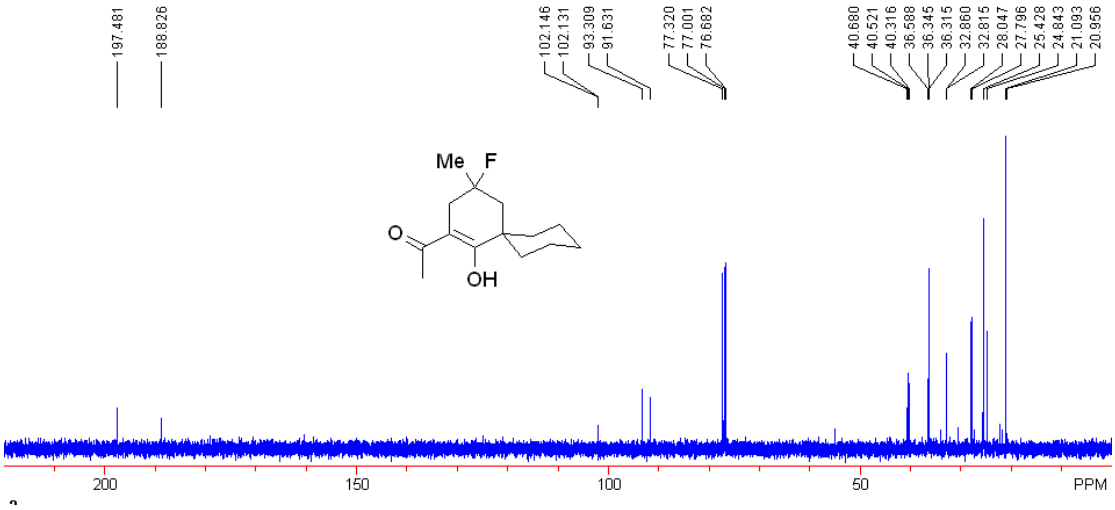
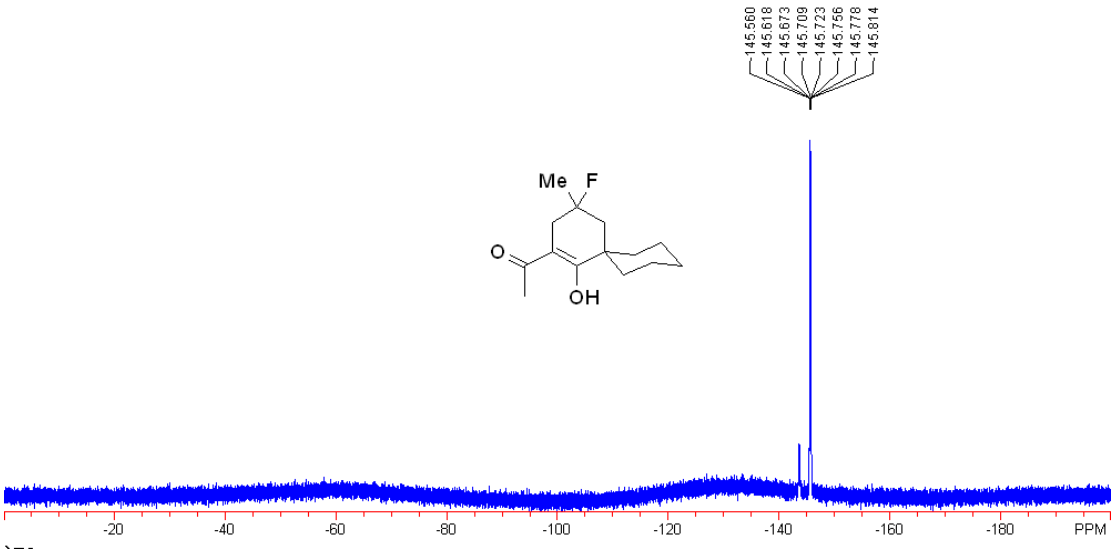
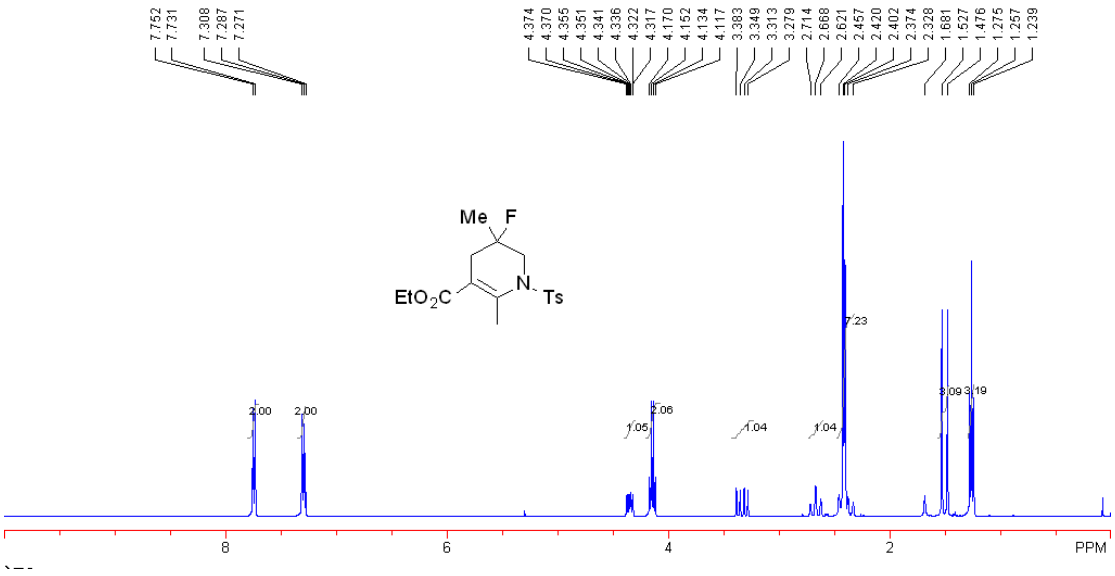
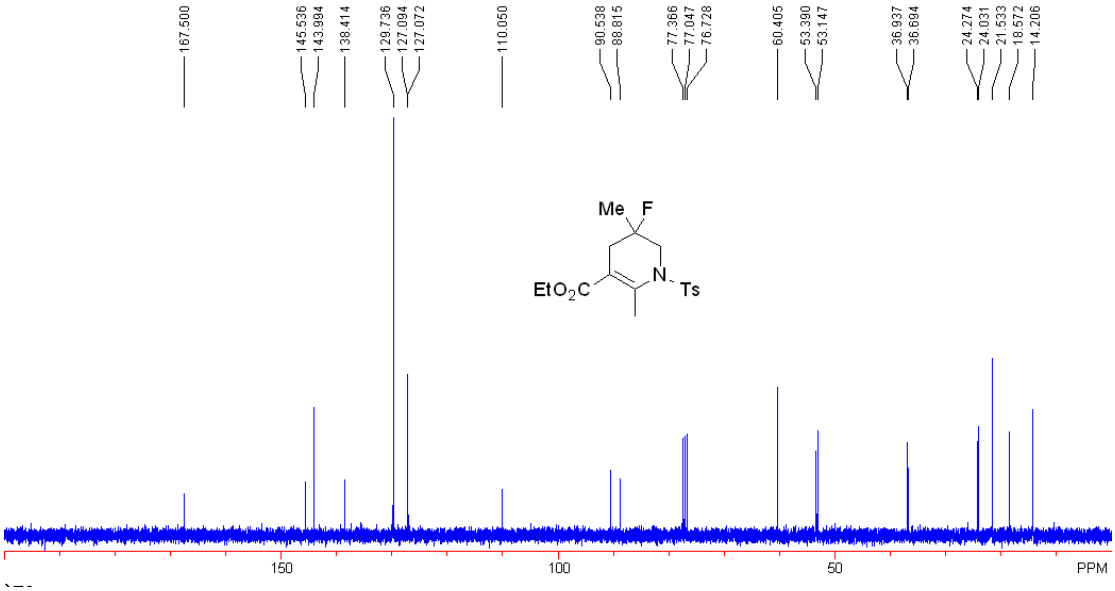
4.216
7.269
4.203
4.184
4.170
2.714
2.680
2.675
2.641
2.528
2.488
2.442
2.402
2.384
2.364
2.215
2.138
1.968
1.959
1.801
1.792
1.762
1.647
1.629
1.621
1.612
Me F
O
OH
8.77
5.68
3.00
1.98
0.93
1.00
0.78
0.10
16
14
12
10
8
6
4
2
PPM

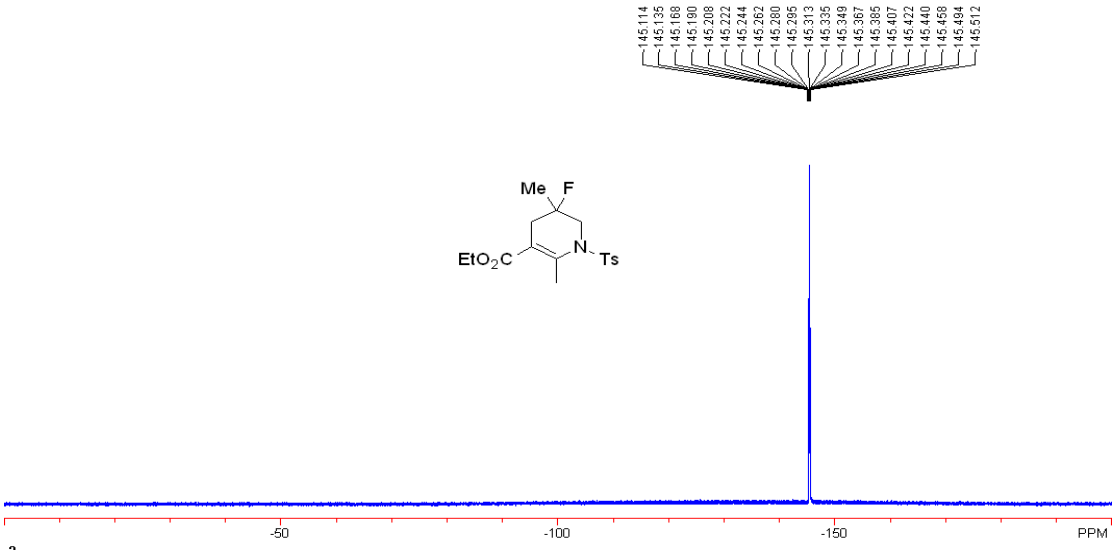

197.481
188.826
102.146
102.131
93.309
91.631
77.320
77.001
76.682
40.680
40.521
40.316
36.588
36.345
36.315
32.860
32.815
28.047
27.796
25.428
24.843
21.093
20.956
Me F
O
OH
200
150
100
50
PPM


145.560
145.618
145.673
145.709
145.723
145.756
145.778
145.814
Me F
O
OH
-20
-40
-60
-80
-100
-120
-140
-160
-180
PPM

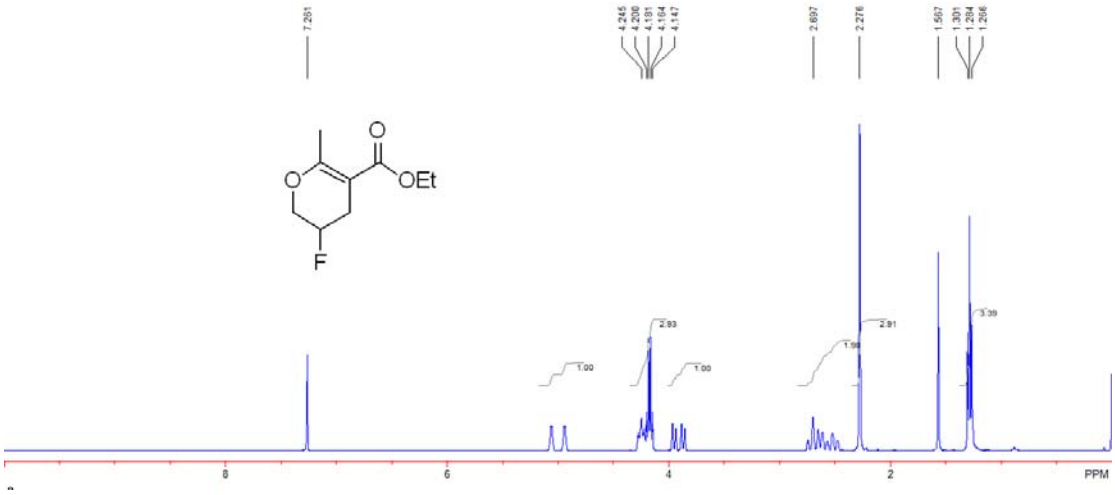
Compound **16**

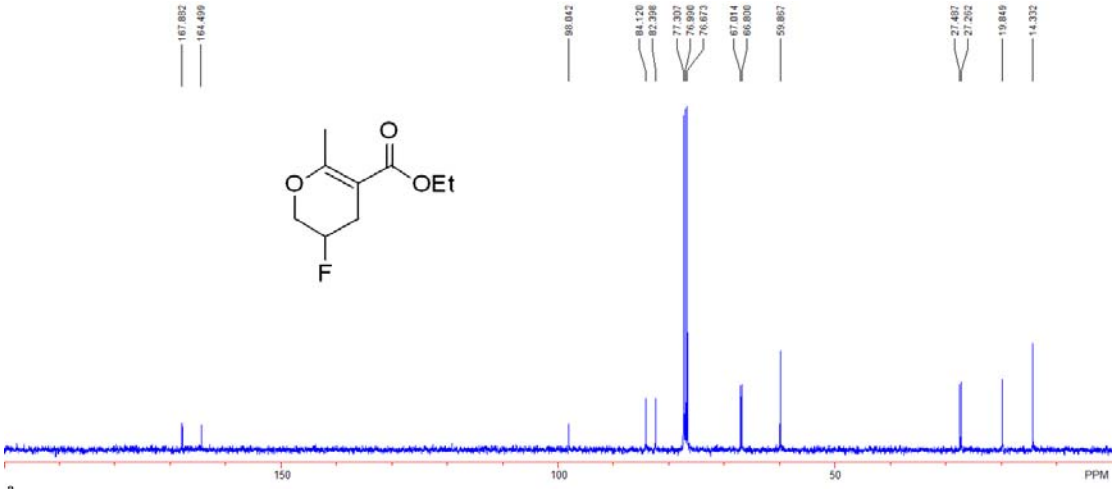

7.752
7.731
7.308
7.287
7.271
4.374
4.370
4.355
4.351
4.341
4.336
4.322
4.317
4.170
4.152
4.134
4.117
3.383
3.349
3.313
3.279
2.714
2.668
2.621
2.457
2.420
2.402
2.374
2.328
1.681
1.527
1.476
1.275
1.257
1.239
Me F
EtO2C
N
Ts
2.00
2.00
1.05
2.06
1.04
1.04
7.23
3.09
3.19
8
6
4
2
PPM

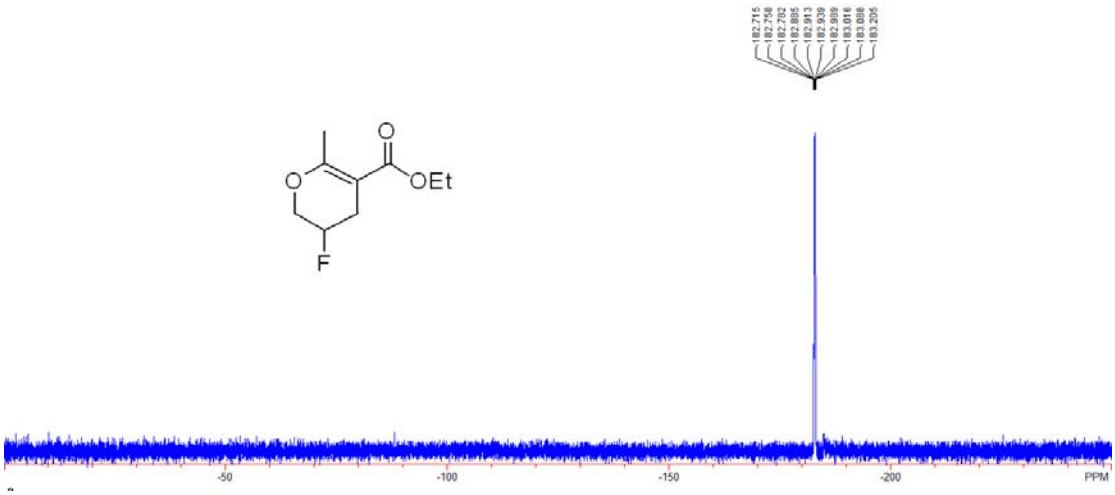

167.500
145.536
143.994
138.414
129.736
127.094
127.072
110.050
90.538
88.815
77.366
77.047
76.728
60.405
53.390
53.147
36.937
36.694
24.274
24.031
21.533
18.572
14.206
Me F
EtO2C
N
Ts
150
100
50
PPM


145.114
145.135
145.168
145.190
145.208
145.222
145.244
145.262
145.280
145.295
145.313
145.335
145.349
145.367
145.385
145.407
145.422
145.440
145.458
145.494
145.512
Me F
EtO2C
N
Ts
-50
-100
-150
PPM

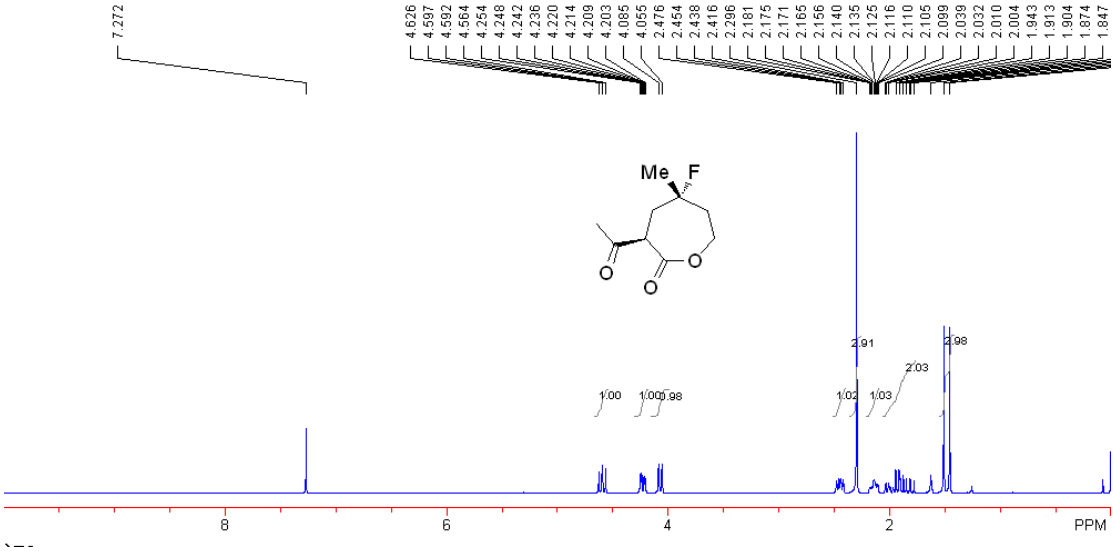
Compound **17**

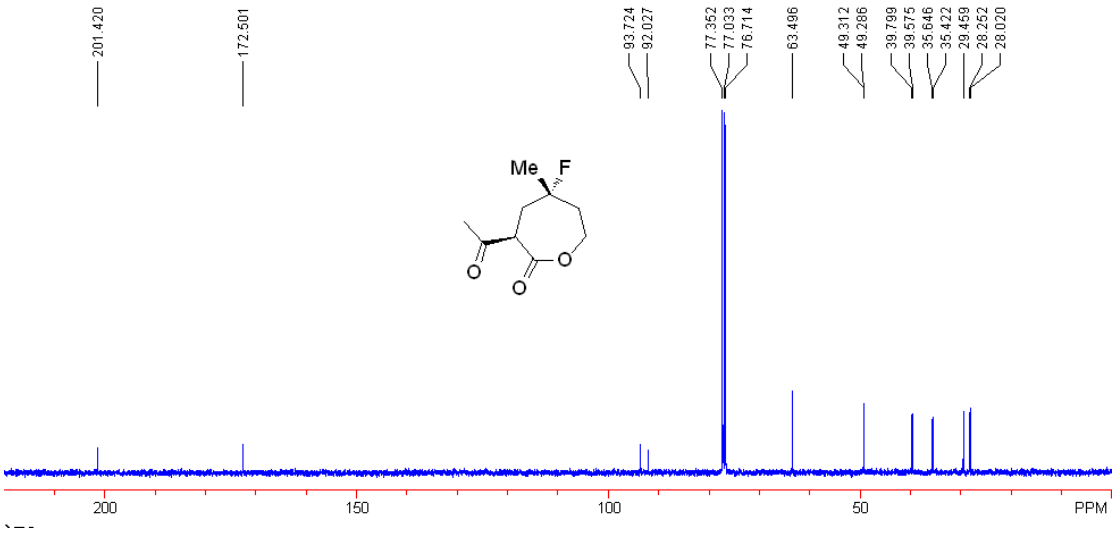

7.261
4.245
4.206
4.191
4.164
4.147
2.697
2.276
1.567
1.301
1.284
1.266
O
OEt
O
F
1.00
2.93
1.00
1.98
2.91
3.39
8
6
4
2
PPM

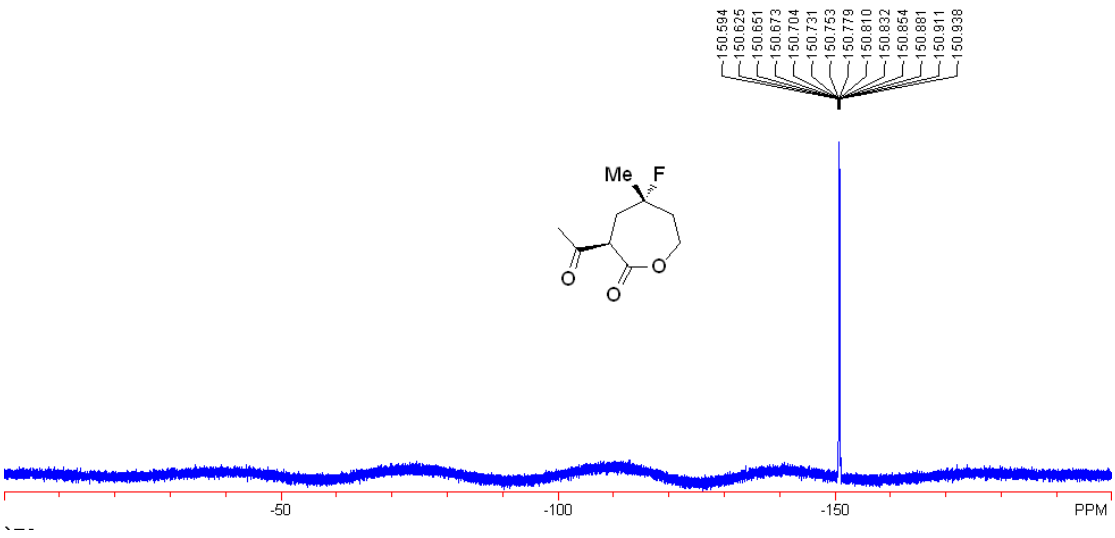

167.882
164.499
98.042
84.120
82.398
77.307
76.990
76.673
67.014
66.800
59.857
27.487
27.292
19.849
14.332
O
OEt
O
F
150
100
50
PPM


182.715
182.758
182.792
182.885
182.913
182.939
182.989
183.016
183.088
183.206
O
OEt
O
F
-50
-100
-150
-200
PPM

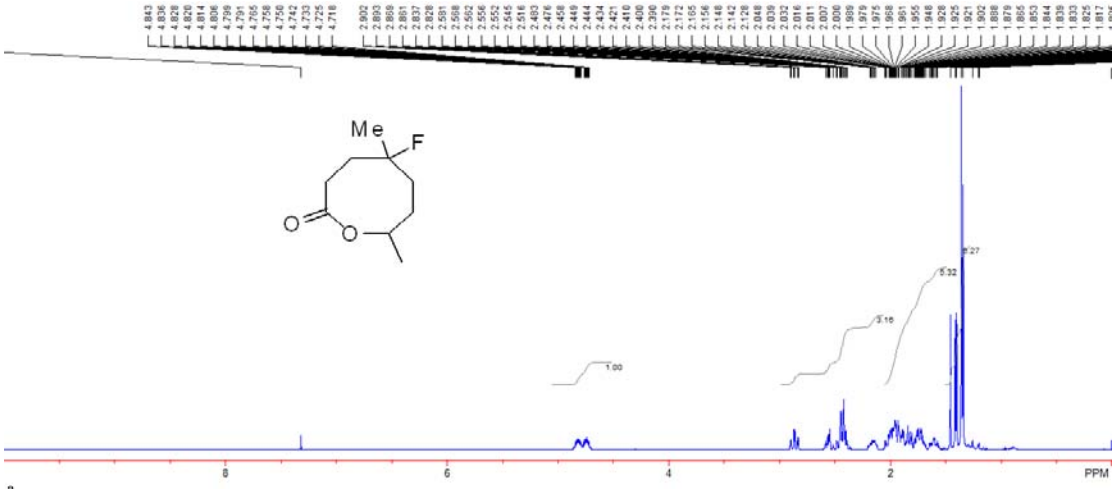
Compound **18**

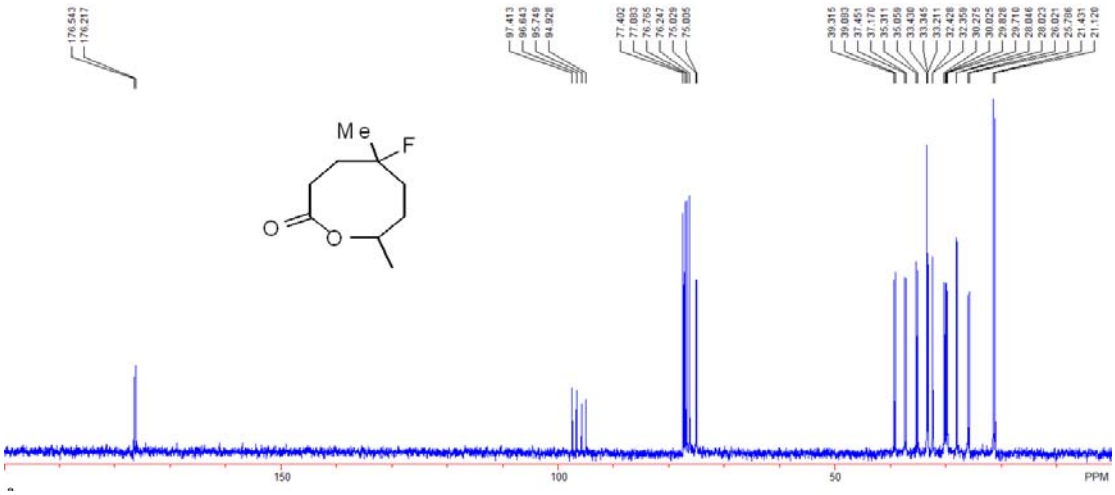

7.272
4.626
4.597
4.592
4.564
4.254
4.248
4.242
4.236
4.220
4.214
4.209
4.203
4.085
4.055
2.476
2.454
2.438
2.416
2.296
2.181
2.175
2.171
2.165
2.156
2.140
2.135
2.125
2.116
2.110
2.105
2.099
2.039
2.032
2.010
2.004
1.943
1.913
1.904
1.874
1.847
Me
F
O
O
2.91
2.98
2.03
1.00
1.00
0.98
1.02
1.03
8
6
4
2
PPM

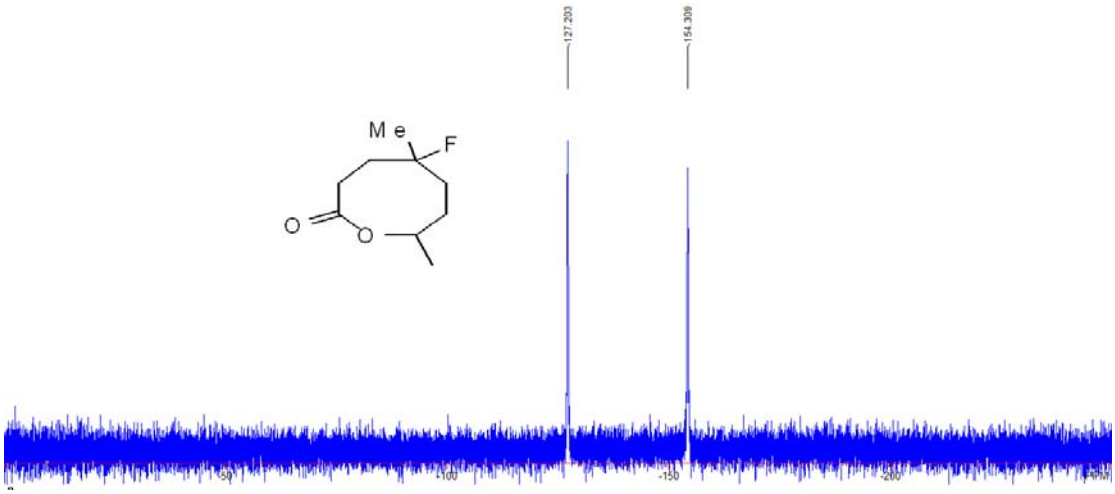

201.420
172.501
93.724
92.027
77.352
77.033
76.714
63.496
49.312
49.286
39.799
39.575
35.646
35.422
29.459
28.252
28.020
Me
F
O
O
200
150
100
50
PPM


150.594
150.625
150.651
150.673
150.704
150.731
150.753
150.779
150.810
150.832
150.854
150.881
150.911
150.938
Me
F
O
O
-50
-100
-150
PPM

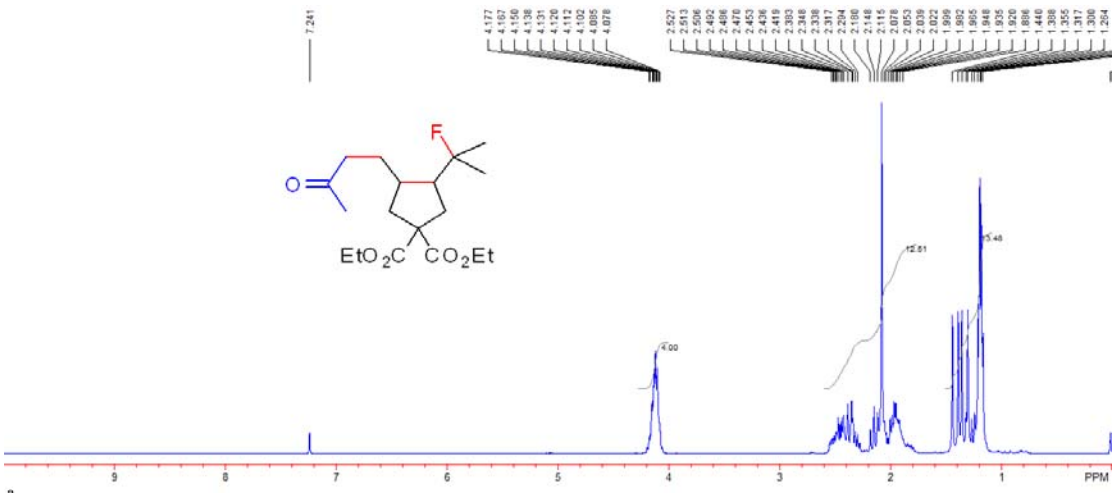
Compound **19**

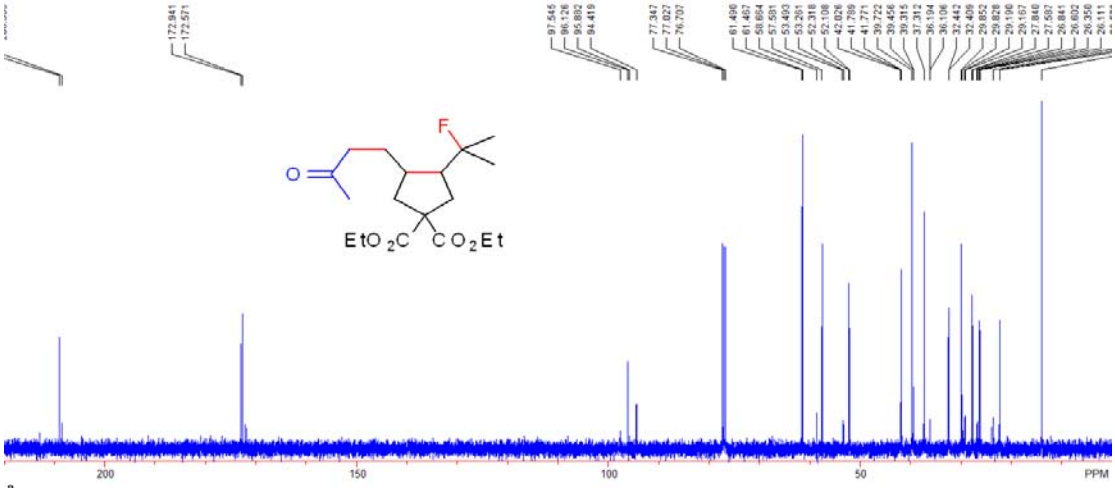

Me
F
O
O
1.00
3.16
5.32
8.27
8
6
4
2
PPM

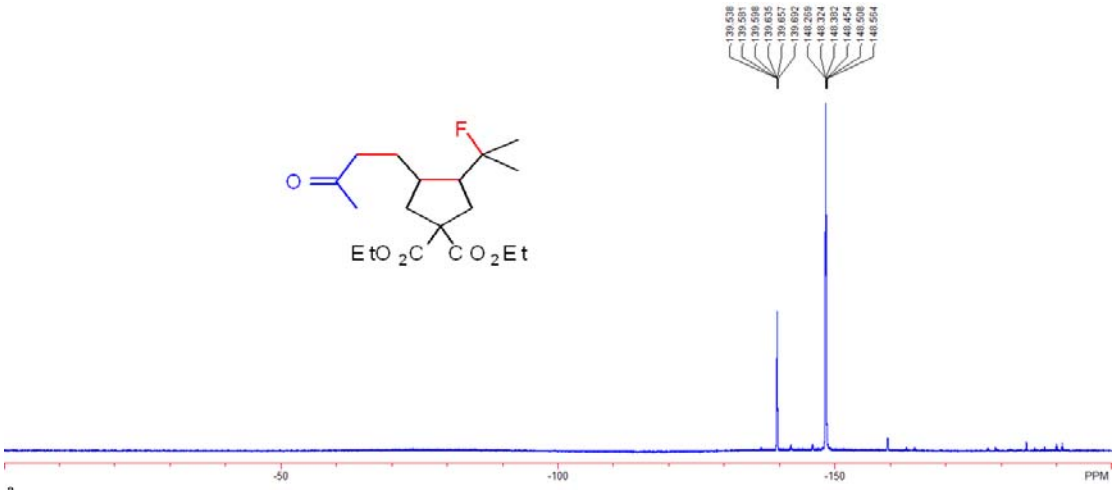

Me
F
O
O
150
100
50
PPM


127.203
154.309
Me
F
O
O
-50
-100
-150
-200

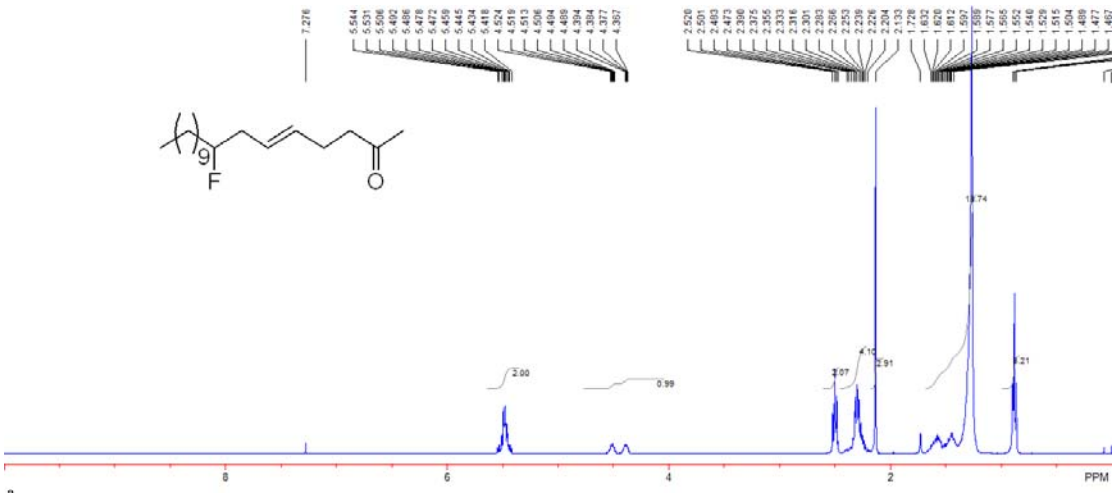
Compound **21**

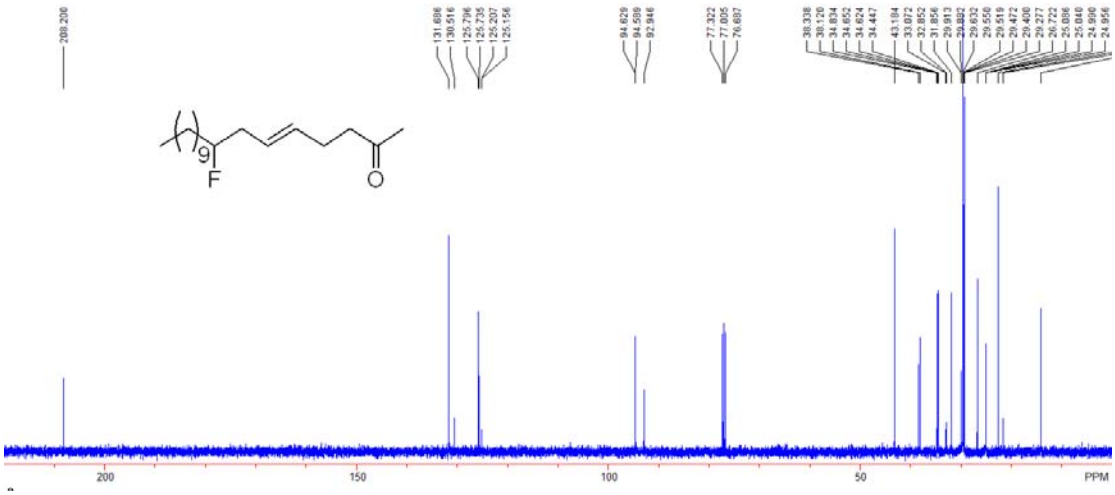

F
O
EtO2C
CO2Et
4.00
12.61
15.48
PPM

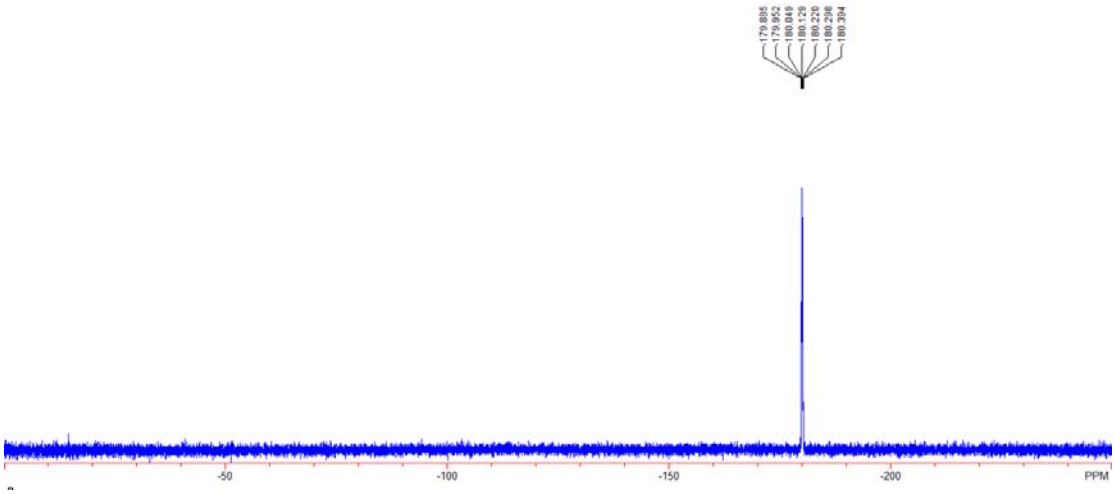

F
O
EtO2C
CO2Et
PPM


F
O
EtO2C
CO2Et
PPM

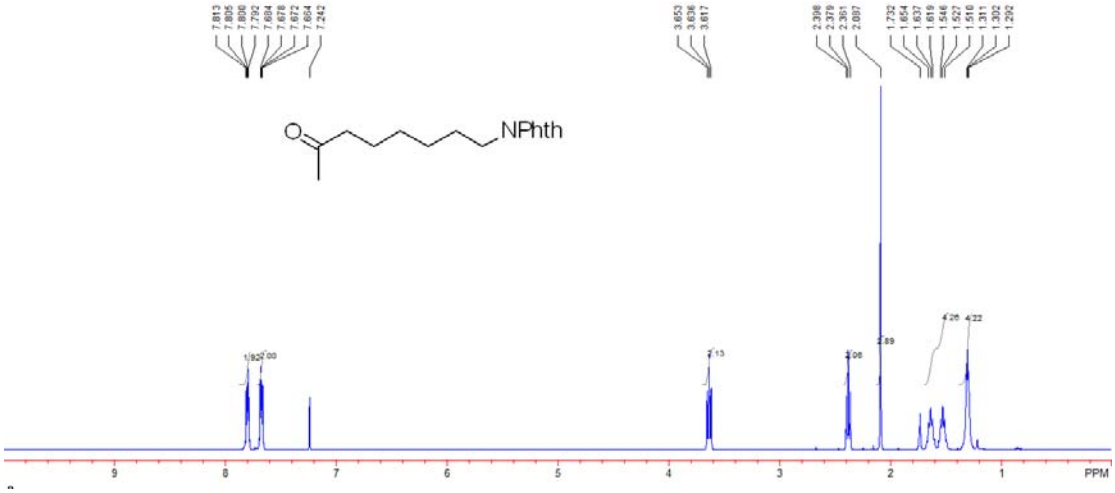
Compound **23**

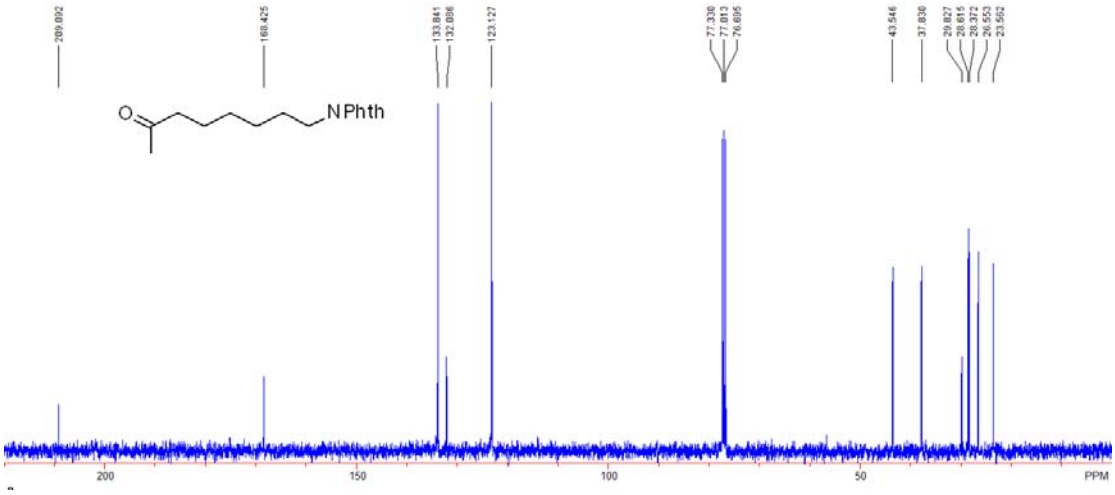

F
O
2.00
0.99
3.07
4.10
2.91
19.74
4.21
8
6
4
2
PPM

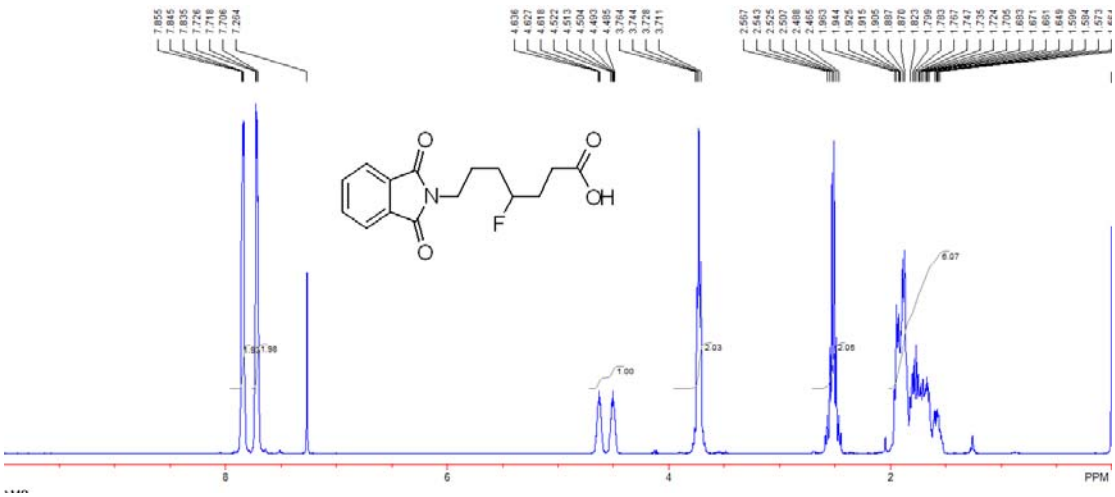

F
O
200
150
100
50
PPM


-50
-100
-150
-200
PPM

Compound **24** (Reference: Li, L.; Herzon, S. B. *Nat. Chem*. **2014**, *6*, 22.)



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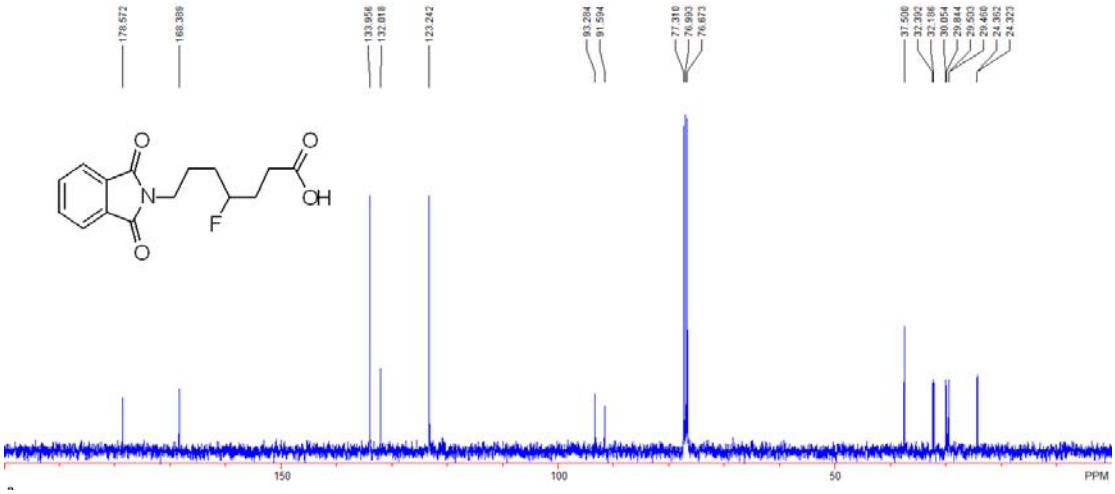
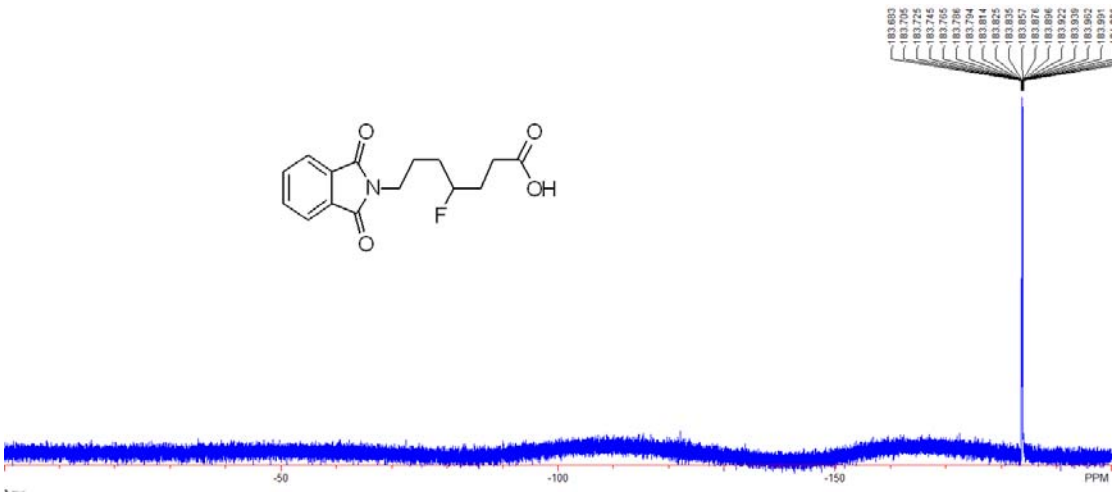
7.726
7.718
7.706
7.264
4.636
4.627
4.618
4.522
4.513
4.504
4.493
4.485
3.764
3.744
3.728
3.711
2.567
2.543
2.525
2.503
2.488
2.465
1.963
1.944
1.925
1.915
1.905
1.897
1.870
1.823
1.799
1.783
1.767
1.747
1.735
1.724
1.705
1.693
1.671
1.651
1.649
1.599
1.584
1.573
O
O
N
F
OH
O
1.98
1.00
2.03
2.08
6.07
8
6
4
2
PPM


176.572
168.389
133.956
132.618
123.242
93.284
91.594
77.316
76.993
76.673
37.506
32.392
32.186
30.654
29.844
29.503
29.400
24.352
24.223
O
O
N
F
OH
O
150
100
50
PPM


183.683
183.705
183.725
183.745
183.765
183.786
183.794
183.814
183.825
183.835
183.857
183.876
183.896
183.922
183.939
183.962
183.991
O
O
N
F
OH
O
-50
-100
-150
PPM