Supporting Information

Copper Catalyzed One-Pot Difluoroalkylation and Lactonization of Unsaturated Carboxylic Acids

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1. General Information

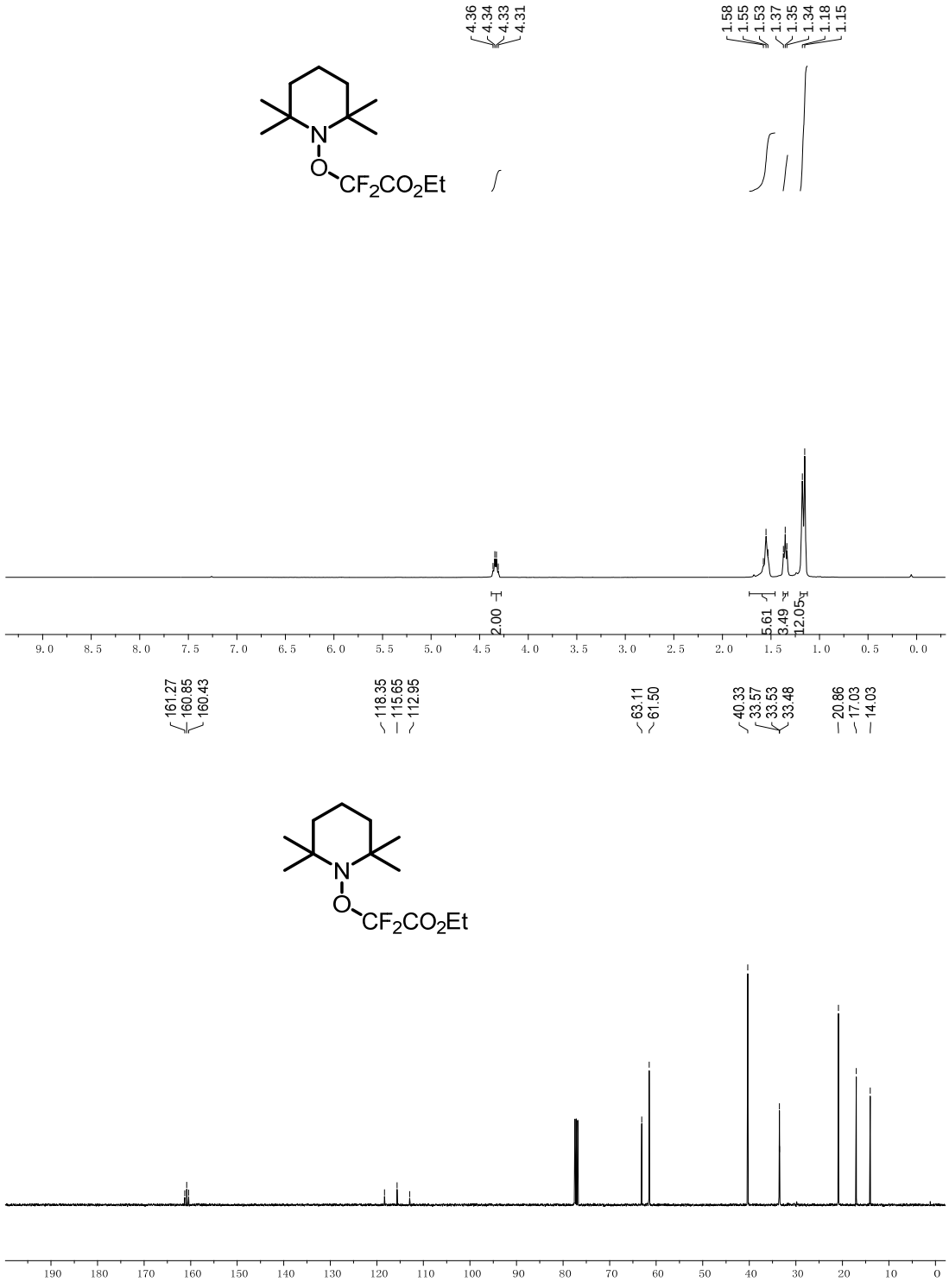
All experiments were conducted under argon atmosphere. Toluene, DMF, DMSO and acetonitrile were dried and distilled by the standard methods. Other commercially available reagents were purchased and used without further purification, unless otherwise stated. Flash chromatographic separations were carried out on 200-300 mesh silica gel. Reactions were monitored by TLC and GC analysis of reaction aliquots. GC analysis was performed on an Agilent 7890 Gas Chromatography using a HP-5 capillary column (30 m × 0.32 mm, 0.5 μm film). 1H, 13C and 19F NMR spectra were recorded in $CDCl_3$ on a Bruker AVANCE III spectrometer. Chemical shifts (δ) are reported in ppm, and coupling constants (J) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. High resolution spectra (HRMS) were recorded on a QTOF mass analyzer with electrospray ionization (ESI) through a Bruker Daltonics - micrOTOF-Q II.

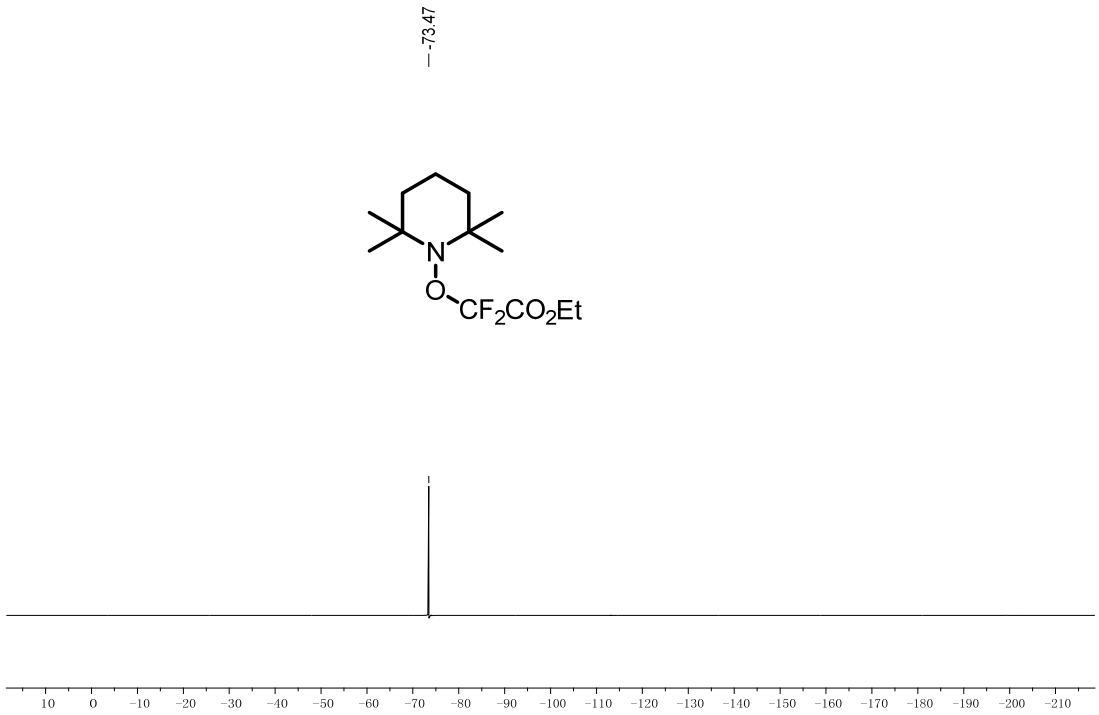
2. Preliminary Mechanistic Studies

To gain some mechanistic insight into the reaction, the radical scavenger 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO, 1.5 equiv) was added to the mixtures of **2a** and **1a** in standard reactions. The formation of **3aa** was inhibited and the yield of 13% of **2a**-TEMPO adduct was detected by GC.

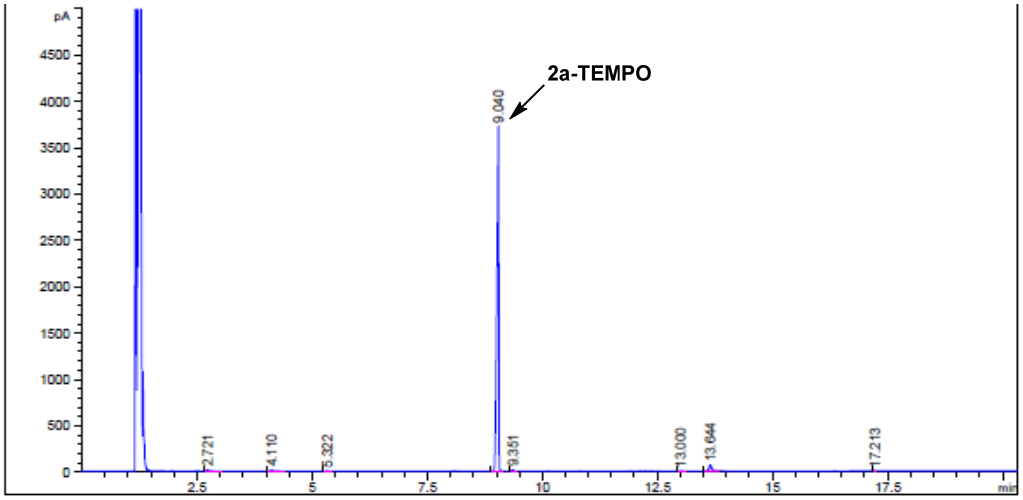
^{1}H, ^{13}C, and ^{19}F NMR spectra of **2a**-TEMPO

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.34 (q, *J* = 7.1 Hz, 2H), 1.58-1.53 (m, 6H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.18-1.15 (m, 12H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.85 (t, *J* = 42.6 Hz), 115.65 (t, *J* = 271.6 Hz), 63.11, 61.50, 40.33, 33.53 (t, *J* = 4.3 Hz), 20.86, 17.03, 14.03; ^{19}F NMR (376 MHz, $CDCl_3$) δ -73.47 (s, 2F).





The GC Spectrum of **2a**-TEMPO:

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Dilution              :      1.0000
Use Multiplier & Dilution Factor with ISTDs


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   2   4.110 BB    0.0720   50.48613   10.08369  0.46861
   3   5.322 BB    0.0467   11.05228    3.55684  0.10259
   4   9.040 BB    0.0397 1.03611e4  3721.44751 96.17119
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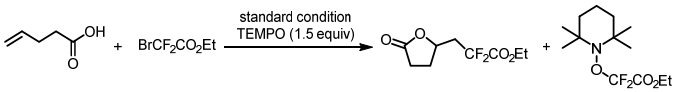
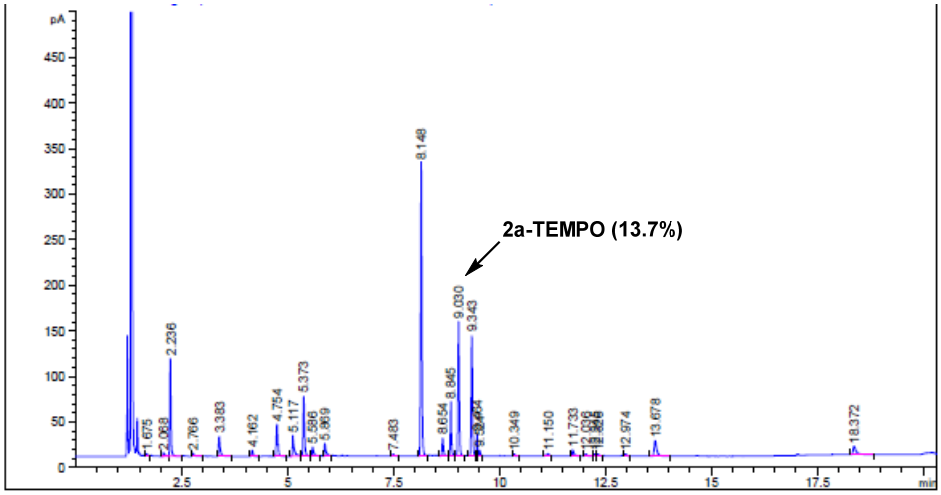
GC analysis of TEMPO Experiment:



1a **2a** **3aa**, trace **2a**-TEMPO, 13 %

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Signal 1: FID1 A, Front Signal

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   2   2.068 BV E  0.0428   12.21317    3.90987  0.51503
   3   2.236 VB R  0.0294  204.30287  107.55373  8.61555
   4   2.766 BB    0.0437    9.72368    3.25506  0.41005
   5   3.383 BB    0.0409   59.87366   21.79153  2.52490


   6   4.162 BB    0.0376   16.66769    6.75820  0.70288
   7   4.754 BB    0.0378   85.32107   35.32478  3.59803
   8   5.117 BV    0.0450   72.64551   22.92009  3.06349
   9   5.373 VV    0.0362  153.44002   65.31948  6.47064
  10   5.586 VB    0.0389   26.42059    9.71589  1.11417
  11   5.869 BB    0.0395   35.18233   13.04089  1.48366
  12   7.483 BB    0.0377    5.19851    2.04345  0.21922
  13   8.148 BB    0.0326  675.09662  320.15387 28.46914
  14   8.654 BB    0.0344   44.27967   19.60045  1.86729
  15   8.845 BB    0.0328  128.96809   58.66372  5.43864
  16   9.030 BB    0.0337  323.69095  146.92657 13.65020
  17   9.343 BV    0.0345  290.46576  131.70192 12.24908
  18   9.464 VV    0.0226   32.43692   23.42085  1.36788
  19   9.524 VB    0.0349   13.62048    6.07782  0.57438
  20  10.349 BB    0.0370    5.29939    2.12844  0.22348
  21  11.150 BB    0.0539   10.22838    2.69178  0.43134
  22  11.733 BB    0.0454   19.66507    6.40505  0.82929
  23  12.036 BB    0.0452    6.74620    2.16222  0.28449
  24  12.245 BV    0.0374    5.07095    2.12864  0.21384
  25  12.326 VB    0.0421    6.25859    2.19000  0.26393
  26  12.974 BB    0.0417    4.38724    1.59561  0.18501
  27  13.678 BB    0.0580   70.57849   17.02011  2.97633
  28  18.372 BB    0.0706   47.82541    8.91013  2.01682
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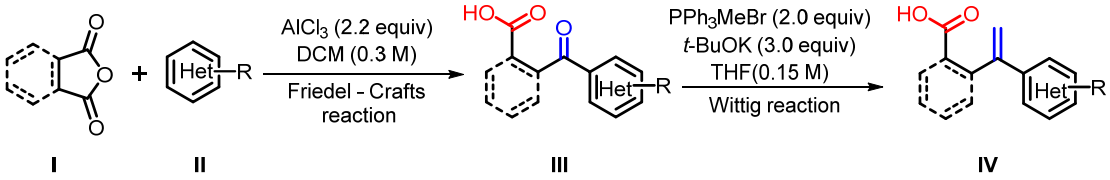
3. Experimental Procedures and NMR Data

General Procedure for the Preparation of Substrates



I II III IV

General Procedures for the preparation of compounds **III**:

Method A:[1]

To an oven dried 100mL round bottom flask containing succunic anhydride (1.0 g, 10 mmol) and arene (11 mmol, 1.1 equiv) in DCM (33 mL) was added $AlCl_3$ (22 mmol, 2.2 equiv) portion-wise at room temperature over 5 minutes and allowed to stir until completion. The reaction was poured over 1N HCl in ice, extracted with ether (66 mL) and washed with 1N HCl (3 x 15 mL). The organic layer was dried (Na_2SO_4) and concentrated to give the product as a solid that was subsequently washed with hexanes and vacuum filtered to afford the crude product **1g-1k**, **1m**, **1r**.

Method B:[2]

Into a solution of phthalic anhydride (1.48 g, 10 mmol) in toluene (6.4 mL), anhydrous $AlCl_3$ (2.67 g, 20 mmol) was added slowly. The reaction was stirred at 50 ℃ for 4 h, and then, it was diluted with 10 % sulfuric acid. The precipitate was collected by filtration to provide **1q** as a white solid.

Method C:[3]

To a flask equipped with a Dean-Stark trap, phthalic anhydride (1.48 g, 10 mmol) were charged and dissolved in chlorobenzene (6 mL). Aluminum chloride (4.0 g, 30 mmol) was added to the above solution under stirring in the presence of nitrogen protection. The reaction mixture was refluxed and stirred for 4 h at 75–80 °C. Upon cooling, the resulting mixture was poured into diluted HCl, agitated. At the beginning, white deposition was created, then the deposition dissolved and the resulting mixture became yellow and phase separation. 1.5 mL 40 % KOH was added in to the obtained organic layer. Moved the water layer and acidized it with a large amount of 10 % HCl water solution to precipitate the product **1o**.

Method D:[4]

To a two neck round-bottom flask equipped with a reflux condenser and addition funnel was added 1.2 mL (1.08 g, 10 mmol) anisole, 30 mL nitrobenzene (as a solvent) and 1.85 g (12.5 mmol) phthalic anhydride. To the additional funnel was added a solution of 3.33 g (25 mmol) of powdered anhydrous aluminum chloride and 8 mL nitrobenzene. This solution, at rt, was dropwise added to the flask during 10 m. The contents of the flask were stirred at rt for 5.5 h. After this time the reaction mixture was added to a solution of 150 mL HCl 20 % and 100 g ice and mixed throughly, extracted with ether. This phase was washed with H_2O, and extracted with saturated $NaHCO_3$. This solution was then washed with ether. The aqueous solution was transfer to a large beaker and acidified with HCl. The white percipitate formed and was collected by filtration through to give **1p**.

Method E:[5]

To a solution of Mg (6.0 mmol, 144 mg) in THF (3 mL) was added dropwise a solution of aryl bromide derivatives (6 mmol) and THF (8 mL) for 24 h. The mixture was then added to a solution of succinic anhydride (5 mmol) in THF (5 mL) at -90 °C. The mixture was stirred at room temperature over 6 h. After the reaction, the mixture was quenched with an aqueous solution of 1N HCl (5 mL). The aqueous layer was extracted with Et_2O and the organic phase was combined, dried with anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude product was purified by recrystallization (hexane/CH_2Cl_2 or toluene) to give **1l**.

General Procedure for the preparation of compounds **IV**[6]

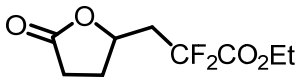
To a suspension of methyltriphenylphosphonium bromide (3.91 g, 11.0 mmol, 1.0 equiv) in THF (20 mL) was added sodium tert-butoxide (2.1 g, 22.0 mmol, 2.0 equiv) at 0 ºC. The mixture was then stirred for 30 min. Keto-acid III (8.5 mmol, 0.85 equiv) was then added to the reaction mixture at 0 ºC. The mixture was allowed to warm to room temperature and stirred for 16 h. The reaction mixture was concentrated under reduced pressure, and diluted with dichloromethane (50 mL) and NaOH (1 N, 50 mL). The aqueous layer was washed with CH_2Cl_2 (20 mL×2) and acidified with HCl (12 N) until it reached ca. pH 2. The aqueous layer was then extracted with CH_2Cl_2 (30 mL×3), dried ($MgSO_4$), and filtered. The resultant solution was concentrated under reduced

pressure and the crude product that was purified by flash column chromatography (Hexanes/EtOAc 1: 1) to give alkenoic acid **IV**.

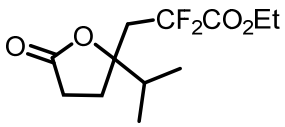
General Procedure for Copper Catalyzed One-Pot Difluoroalkylation and Lactonization of Unsaturated Carboxylic Acids

To a 25 mL of Schlenk tube was added CuBr (0.05 mmol, 10 mol %), $Na_2S_2O_5$ (0.1 mmol, 20 mol %), unsaturated carboxylic acids **1** (0.5 mmol, 1.0 equiv) under air and then evacuated and backfilled with Ar (3 times). DMSO (5 mL), PMDETA (1.0 mmol, 2.0 equiv) and ethyl bromodifluoroacetate (1.5 equiv) or perfluoroalkyl iodide (1.5 equiv) was added subsequently. The reaction mixture was heated to 85 ºC (oil bath). After stirring for 10 h, the reaction was cooled to room temperature. The reaction mixture was quenched with 50 ml of water and then extracted with ethyl acetate (3×60 ml). The combined organic extracts were washed with brine (50 mL) dried over anhydrous Na_2SO_4, filtered, and concentrated. The crude product was purified with silica gel chromatography to give the desired product.

^{1}H, ^{13}C, and ^{19}F NMR Spectra:

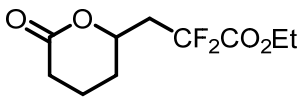


Ethyl 2,2-difluoro-3-(5-oxotetrahydrofuran-2-yl)propanoate (3aa). The product was purified by silica gel column chromatography (PE/EA = 5/1). Yield, 83%, 93.6 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.77-4.70 (m, 1H), 4.35 (q, *J* = 7.1 Hz, 2H), 2.69-2.33 (m, 5H), 2.03-1.93 (m, 1H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.01, 163.48 (t, *J* = 31.7 Hz, 1C), 114.36 (dd, *J* = 252.9, 250.1 Hz, 1C), 74.18 (dd, *J* = 6.5, 3.3 Hz, 1C), 63.54, 40.31(t, *J* = 23.3 Hz, 1C), 28.44, 28.38, 13.96; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.72 (dd, *J* = 1765.6, 265.8 Hz, 2F); HRMS (ESI): m/z calcd. for $C_9H_{12}F_2NaO_4^+$ [M + Na^+]: 245.0596, found: 245.0590.

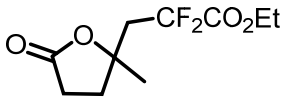


Ethyl 2,2-difluoro-3-(2-isopropyl-5-oxotetrahydrofuran-2-yl)propanoate (3ba). The product was purified by silica gel column chromatography (PE/EA = 5/1). Yield,

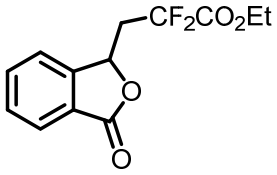
65%, 84.8 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.40-4.24 (m, 2H), 2.78-2,61 (m, 2H), 2.54-2.45 (m, 1H), 2.41-2.30 (m, 1H), 2.26-2.11 (m, 2H), 2.08-2.01 (m, 1H), 1.34 (t, *J* = 7.2 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H), 0.91 (d, *J* = 6.8 Hz, 3H) ; ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.87, 163.77 (t, *J* = 31.7 Hz, 1C), 115.45 (dd, *J* = 253.1, 249.4 Hz, 1C), 86.92 (dd, *J* = 5.9, 1.2 Hz, 1C), 63.54, 40.57 (dd, *J* = 23.6, 21.4 Hz, 1C), 37.07 (d, *J* =1.5Hz, 1C), 28.61, 27.24 (d, *J* = 3.4 Hz, 1C), 16.62, 16.39, 13.89; ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.98 (dd, *J* = 2165.7, 266.7 Hz, 2F); HRMS (ESI): m/z calcd. for $C_{12}H_{18}F_2NaO_4^+$ [M + Na^+]: 287.1065, found: 287.1064.



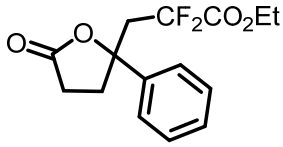
Ethyl 2,2-difluoro-3-(6-oxotetrahydro-2H-pyran-2-yl)propanoate (3ca). The product was purified by silica gel column chromatography (PE/EA = 3/1). Yield, 60%, 71.2 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.62-4.55 (m, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 2.67-2.53 (m, 2H), 2.48-2.28 (m, 2H), 2.03-1.82 (m, 3H), 1.69-1.59 (m, 1H), 1.36 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.03, 163.69 (t, *J* = 31.9 Hz, 1C), 114.45 (dd, *J* = 252.9, 242.9 Hz, 1C), 74.37 (dd, *J* = 7.0, 3.4 Hz, 1C), 63.47, 40.93 (t, *J* = 23.6 Hz, 1C), 29.26, 27.96, 18.43, 13.99; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.62 (dd, *J* = 2173.1, 263.3 Hz, 2F); HRMS (ESI): m/z calcd. for $C_{10}H_{14}F_2NaO_4^+$ [M + Na^+]: 259.0752, found:259.0759.



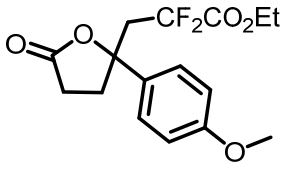
Ethyl 2,2-difluoro-3-(2-methyl-5-oxotetrahydrofuran-2-yl)propanoate (3da). The product was purified by silica gel column chromatography (PE/EA = 4/1). Yield, 67%, 79.7 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.39-4.26 (m, 2H), 2.63-2,48 (m, 4H), 2.35-2.27 (m, 1H), 2.11-2.04 (m, 1H), 1.50 (d, *J* = 1.1 Hz, 3H), 1.34 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.44, 163.66 (t, *J* = 31.7 Hz, 1C), 114.70 (dd, *J* = 252.5, 250.4 Hz, 1C), 82.56 (t, *J* = 3.3 Hz, 1C), 63.56, 44.28 (t, *J* = 22.8 Hz, 1C), 33.68 (d, *J* =2.1 Hz, 1C), 28.45, 26.81 (d, *J* = 2.7 Hz, 1C), 13.90; ^{19}F NMR (376 MHz, $CDCl_3$) δ -102.02 (q, *J* = 265.9 Hz, 2F); HRMS (ESI): m/z calcd. for $C_{10}H_{14}F_2NaO_4^+$ [M + Na^+]: 259.0752, found: 259.0750.



Ethyl 2,2-difluoro-3-(3-oxo-1,3-dihydroisobenzofuran-1-yl)propanoate (3ea).[7] The product was purified by silica gel column chromatography (PE/EA = 4/1). Yield, 55%, 74.1 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.7 Hz, 1H), 7.72 (t, *J* = 7.5 Hz, 1H), 7.58 (t, *J* = 7.5 Hz, 1H), 7.51 (d, *J* = 7.7 Hz, 1H), 5.69 (dd, *J* = 9.0, 3.1 Hz, 1H), 4.45-4.34 (m, 2H), 2.84-2.72 (m, 1H), 2.65-2.51 (m, 1H), 1.38 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 169.40, 163.42 (t, *J* = 31.6 Hz, 1C), 148.19, 134.58, 129.95, 126.16, 125.80, 122.10, 114.28 (dd, *J* = 253.8, 251.2 Hz, 1C), 74.84 (dd, *J* = 7.1, 3.6 Hz, 1C), 63.66, 40.42 (t, *J* = 23.8 Hz, 1C), 13.99; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.21 (dd, *J* = 1740.5, 265.9 Hz, 2F).

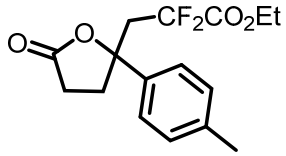


Ethyl 2,2-difluoro-3-(5-oxo-2-phenyltetrahydrofuran-2-yl)propanoate (3fa).[7] The product was purified by silica gel column chromatography (PE/EA = 4/1). Yield, 76%, 112.9 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.30 (m, 5H), 4.27-4.11 (m, 2H), 2.95-2.34 (m, 6H), 1.30 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.28, 163.47 (t, *J* = 31.6 Hz, 1C), 141.79, 128.81 (2C), 128.39, 124.70 (2C), 114.33 (t, *J* = 252.0 Hz, 1C), 84.73 (t, *J* = 4.4 Hz, 1C), 63.44, 45.66 (t, *J* = 23.1 Hz, 1C), 34.56, 28.03, 13.86; ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.08 (t, *J* = 14.5 Hz, 2F).

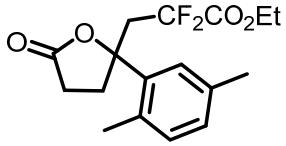


Ethyl 2,2-difluoro-3-(2-(4-methoxyphenyl)-5-oxotetrahydrofuran-2-yl)propanoate (3ga).[7] The product was purified by silica gel column chromatography (PE/EA = 4/1). Yield, 90%, 146.9 mg, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 7.8 Hz, 2H), 6.86 (d, *J* = 7.8 Hz, 2H), 4.23-4.08 (m, 2H), 3.77 (s, 3H), 2.85-2.76 (m,

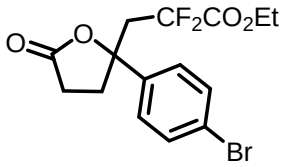
2H), 2.66-2.47 (m, 3H), 2.41-2.34 (m, 1H),1.27 (t, J = 7.0 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.38, 163.50 (t, J = 31.9 Hz, 1C), 159.58, 133.50, 126.18 (2C), 114.36 (t, J = 252.0 Hz, 1C), 114.09 (2C), 84.74 (t, J = 4.2 Hz, 1C), 63.43, 55.45, 45.90 (t, J = 22.6 Hz, 1C), 34.45, 28.18, 13.89; ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.12 (t, J = 14.7 Hz, 2F).



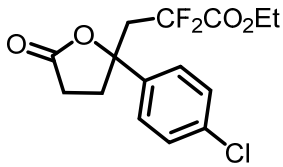
Ethyl 2,2-difluoro-3-(5-oxo-2-(*p*-tolyl)tetrahydrofuran-2-yl)propanoate (3ha).[7] The product was purified by silica gel column chromatography (PE/EA = 4/1). Yield, 85%, 133.1 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 8.3 Hz, 2H), 7.17 (d, J = 8.3 Hz, 2H), 4.26-4.09 (m, 2H), 2.93-2.76 (m, 2H), 2.73-2.65 (m, 1H), 2.61-2.48 (m, 2H), 2.43-2.36 (m, 1H), 2.33 (s, 3H),1.30 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.39, 163.45 (t, J = 31.5 Hz, 1C), 138.79, 138.27, 129.47 (2C), 124.70 (2C), 114.38 (t, J = 252.0 Hz, 1C), 84.83 (t, J = 4.4 Hz, 1C), 63.43, 45.78 (t, J = 23.1Hz, 1C), 34.49, 28.13, 21.12, 13.89; ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.02 (t, J = 14.6 Hz, 2F).



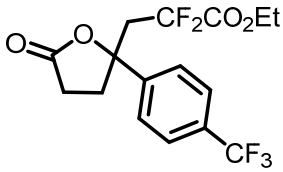
Ethyl 3-(2-(2,5-dimethylphenyl)-5-oxotetrahydrofuran-2-yl)-2,2difluoropropanoate (3ia). The product was purified by silica gel column chromatography (PE/EA = 4/1). Yield, 86%, 139.8 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (s, 1H), 6.98 (dd, J = 17.8, 7.5 Hz, 2H), 4.21-4.05 (m, 2H), 2.93-2.68 (m, 3H), 2.62-2.47 (m, 2H), 2.42-2.35 (m, 1H), 2.31 (s, 3H), 2.23 (s, 3H), 1.24 (t, J = 6.9 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.28, 163.50 (t, J = 31.6 Hz, 1C), 139.86, 135.85, 132.70, 130.19, 129.05,125.76, 114.62 (t, J = 251.9 Hz, 1C), 85.40 (t, J = 4.3 Hz, 1C), 63.40, 43.83 (t, J = 22.9 Hz, 1C), 33.59, 27.95, 21.17, 21.02, 13.83; ^{19}F NMR (376 MHz, $CDCl_3$) δ -100.42-102.91 (m, 2F); HRMS (ESI): m/z calcd. for $C_{17}H_{20}F_2NaO_4^+$ [M + Na^+]: 349.1222, found: 349.1219.



Ethyl 3-(2-(4-bromophenyl)-5-oxotetrahydrofuran-2-yl)-2,2-difluoropropanoate (3ja).[7] The product was purified by silica gel column chromatography (PE/EA = 4/1). Yield, 69%, 129.3 mg, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.6 Hz, 2H), 7.23 (d, *J* = 8.6 Hz, 2H), 4.31-4.16 (m, 2H), 2.87-2.80 (m, 2H), 2.75-2.59 (m, 2H), 2.52-2.37 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.84, 163.44 (t, *J* = 31.7 Hz, 1C), 140.92, 132.02 (2C), 126.57 (2C), 122.61, 114.20 (t, *J* = 252.3 Hz, 1C), 84.29 (t, *J* = 4.4 Hz, 1C), 63.61, 45.56 (t, *J* = 23.1 Hz, 1C), 34.73, 27.94, 13.92; ^{19}F NMR (376 MHz, $CDCl_3$) δ -100.39-102.04 (m, 2F).

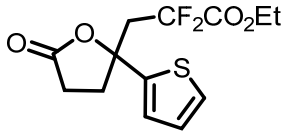


Ethyl 3-(2-(4-chlorophenyl)-5-oxotetrahydrofuran-2-yl)-2,2-difluoropropanoate (3ka).[7] The product was purified by silica gel column chromatography (PE/EA = 4/1). Yield, 72%, 118.7 mg, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.7 Hz, 2H), 7.29 (d, *J* = 8.7 Hz, 2H), 4.31-4.16 (m, 2H), 2.88-2.80 (m, 2H), 2.76-2.59 (m, 2H), 2.52-2.37 (m, 2H), 1.32 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.88, 163.42 (t, *J* = 31.5 Hz, 1C), 140.34, 134.43, 129.01 (2C), 126.25 (2C), 114.20 (t, *J* = 252.2 Hz, 1C), 84.26 (t, *J* = 4.2 Hz, 1C), 63.56, 45.56 (t, *J* = 23.1 Hz, 1C), 34.77, 27.91, 13.88; ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.22 (q, *J* = 267.6 Hz, 2F).

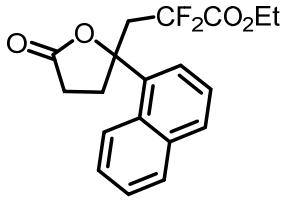


Ethyl 2,2-difluoro-3-(5-oxo-2-(4-(trifluoromethyl)phenyl)tetrahydrofuran-2-yl)-propanoate (3la). The product was purified by silica gel column chromatography (PE/EA = 4/1). Yield, 66%, 119.6 mg, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66

(d, J = 8.2 Hz, 2H), 7.49 (d, J = 8.2 Hz, 2H), 4.32-4.16 (m, 2H), 2.91-2.84(m, 2H), 2.79-2.61 (m, 2H), 2.54-2.39 (m, 2H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.65, 163.41 (t, J = 31.1 Hz, 1C), 145.93, 131.10 (dd, J = 62.8, 29.9 Hz, 1C), 125.92 (dd, J = 7.5, 3.8 Hz, 1C), 125.27 (2C), 122.55, 114.16 (t, J = 252.5 Hz, 1C), 84.18 (t, J = 4.1 Hz, 1C), 63.65, 45.47 (t, J = 23.3 Hz, 1C), 34.94, 27.82, 13.89; ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.78 (d, J = 13.2 Hz, 3F), -101.27 (q, J = 269.1 Hz, 2F); HRMS (ESI): m/z calcd. for $C_{16}H_{15}F_5NaO_4^+$ [M + Na^+]: 389.0783, found: 389.0782.

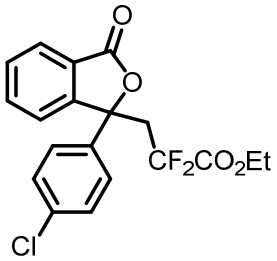


Ethyl 2,2-difluoro-3-(5-oxo-2-(thiophen-2-yl)tetrahydrofuran-2-yl)propanoate (3ma). The product was purified by silica gel column chromatography (PE/EA = 4/1). Yield, 50%, 76.4 mg, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (dd, J = 5.0, 1.3 Hz, 1H), 7.01 (dd, J = 3.6, 1.3 Hz, 1H), 6.97 (dd, J = 5.0, 3.6 Hz, 1H), 4.29-4.13 (m, 2H), 3.03-2.86 (m, 2H), 2.80-2.72 (m, 1H), 2.67-2.51 (m, 3H), 1.31 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 174.84, 163.34 (t, J = 31.6 Hz, 1C), 145.22, 127.23, 126.08, 124.85, 114.15 (t, J = 251.9 Hz, 1C), 83.37 (t, J = 4.5 Hz, 1C), 63.56, 46.21 (t, J = 23.2 Hz, 1C), 34.83, 28.54, 13.90; ^{19}F NMR (376 MHz, $CDCl_3$) δ -100.53-102.03 (m, 2F); HRMS (ESI): m/z calcd. for $C_{13}H_{14}F_2NaO_4S^+$ [M + Na^+]: 327.0473, found: 327.0476.

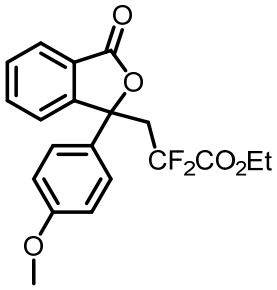


Ethyl 2,2-difluoro-3-(2-(naphthalen-1-yl)-5-oxotetrahydrofuran-2-yl)propanoate (3na). The product was purified by silica gel column chromatography (PE/EA = 4/1). Yield, 61%, 107.6 mg, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88-7.82 (m, 4H), 7.52-7.51 (m, 2H), 7.41-7.39 (m, 1H), 4.19-4.01 (m, 2H), 3.05-2.88 (m, 2H), 2.82-2.75 (m, 1H), 2.66-2.60 (m, 2H), 2.48-2.38 (m, 1H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.37, 163.49 (t, J = 31.6 Hz, 1C), 138.80, 132.91, 132.89,128.92, 128.43, 127.67, 126.93, 126.88, 123.75, 122.50, 114.38 (t, J = 252.1 Hz, 1C), 84.85 (t,

J = 4.3 Hz, 1C), 63.14, 45.52 (t, J = 23.3 Hz, 1C), 34.47, 28.01, 13.76; ^{19}F NMR (376 MHz, $CDCl_3$) δ -100.15-101.74 (m, 2F); HRMS (ESI): m/z calcd. for $C_{19}H_{18}F_2NaO_4^+$ [M + Na^+]: 371.1065, found: 371.1062.

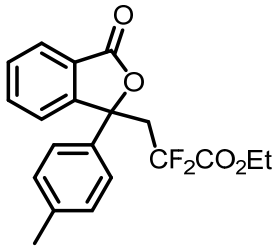


Ethyl 3-(1-(4-chlorophenyl)-3-oxo-1,3-dihydroisobenzofuran-1-yl)-2,2-difluoro-propanoate (3oa).[7] The product was purified by silica gel column chromatography (PE/EA = 5/1). Yield, 87%, 165.8 mg, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, J = 7.6 Hz, 1H), 7.73-7.69 (m, 1H), 7.60-7.54 (m, 2H), 7.46-7.43 (m, 2H), 7.35-7.33 (m, 2H), 4.33-4.21 (m, 2H), 3.45-3.34 (m, 1H), 3.18-3.08 (m, 1H), 1.33 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.52, 163.43 (t, J = 31.3 Hz, 1C), 150.82, 138.38, 134.95, 134.67, 130.02, 129.25 (2C), 126.41, 126.26 (2C), 124.96, 122.69, 113.91 (dd, J = 254.9, 251.9 Hz, 1C), 84.73 (dd, J = 6.3, 3.5 Hz, 1C), 63.67, 44.04 (t, J = 23.6 Hz, 1C), 13.90; ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.31 (dd, J = 1045.9, 268.5 Hz, 2F).

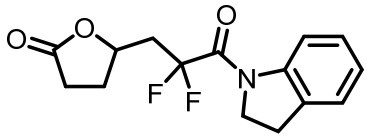


Ethyl 2,2-difluoro-3-(1-(4-methoxyphenyl)-3-oxo-1,3-dihydroisobenzofuran-1-yl) propanoate (3pa). The product was purified by silica gel column chromatography (PE/EA = 5/1). Yield, 85%, 161.2 mg, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 7.6 Hz, 1H), 7.69 (t, J = 7.5 Hz, 1H), 7.59-7.52 (m, 2H), 7.40-7.36 (m, 2H), 6.89-6.85 (m, 2H), 4.32-4.19 (m, 2H), 3.78 (s, 3H), 3.48-3.37 (m, 1H), 3.19-3.09 (m, 1H), 1.33 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.90, 163.53 (t, J = 31.4 Hz, 1C), 159.87, 151.23, 134.38, 131.74, 129.70, 126.28 (2C), 126.18, 125.24, 122.89, 114.30 (2C), 114.03 (dd, J = 254.9, 251.0 Hz, 1C), 85.25 (dd, J = 6.7, 2.9 Hz, 1C),

63.56, 55.44, 44.08 (t, J = 23.6 Hz, 1C), 13.87; ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.29 (dd, J = 1298.9, 267.7 Hz, 2F); HRMS (ESI): m/z calcd. for $C_{20}H_{18}F_2NaO_5^+$ [M + Na^+]: 399.1015, found: 399.1012.

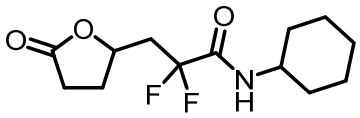


Ethyl 2,2-difluoro-3-(3-oxo-1-(p-tolyl)-1,3-dihydroisobenzofuran-1-yl)propanoate (3qa).[7] The product was purified by silica gel column chromatography (PE/EA = 5/1). Yield, 94%, 169.7 mg, colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, J = 7.6 Hz, 1H), 7.70-7.66 (m, 1H), 7.60 (d, J = 7.8 Hz, 1H), 7.52 (t, J = 7.5 Hz, 1H), 7.37 (d, J = 8.1 Hz, 2H), 7.17 (d, J = 8.1 Hz, 2H), 4.32-4.19 (m, 2H), 3.49-3.38 (m, 1H), 3.22-3.12 (m, 1H), 2.31 (s, 3H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 168.93, 163.50 (t, J = 31.5 Hz, 1C), 151.28, 138.72, 136.88, 134.43, 129.66 (3C), 126.11, 125.03, 124.61 (2C), 122.81, 114.03 (dd, J = 255.2, 251.7 Hz, 1C), 85.25 (dd, J = 6.5, 3.3 Hz, 1C), 63.53, 43.97 (t, J = 23.6 Hz, 1C), 21.05, 13.84; ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.22 (dd, J = 1218.8, 267.8 Hz, 2F).

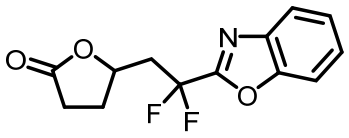


5-(2,2-difluoro-3-(indolin-1-yl)-3-oxopropyl)dihydrofuran-2(3H)-one (3ab). The product was purified by silica gel column chromatography (PE/EA = 3/1). Yield, 83%, 122.3 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16 (d, J = 8.0 Hz, 1H), 7.25-7.21 (m, 2H), 7.13-7.09 (m, 1H),4.92-4.86 (m, 1H), 4,34 (t, J = 8.3 Hz, 2H), 3.20 (t, J = 8.3 Hz, 2H), 2.80-2.46 (m, 5H), 2.07-1.98 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.50, 160.55 (t, J = 29.6 Hz, 1C), 142.45, 131.90, 127.61, 125.43, 124.87, 117.95 (t, J = 256.6 Hz, 1C), 117.88, 74.96 (t, J = 4.2 Hz, 1C), 47.85 (t, J = 7.6 Hz, 1C), 39.92 (t, J = 22.9 Hz, 1C), 29.02, 28.67, 28.58; ^{19}F NMR (376 MHz, $CDCl_3$) δ -101.50 (q, J = 288.7 Hz, 2F). HRMS (ESI): m/z calcd. for $C_{15}H_{15}F_2NNaO_3^+$ [M + Na^+]: 318.0912, found: 318.0917.

2,2-difluoro-3-(5-oxotetrahydrofuran-2-yl)-N-phenylpropanamide (3ac). The product was purified by silica gel column chromatography (PE/EA = 3/1). Yield, 80%, 108.9 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.57 (d, J = 7.9 Hz, 2H), 7.37 (t, J = 7.9 Hz, 2H), 7.21 (t, J = 7.4 Hz, 1H), 4.84-4.77 (m, 1H), 2.74-2.44 (m, 5H), 2.06-1.95 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.43, 161.40 (t, J = 27.7 Hz, 1C), 135.92, 129.32 (2C), 125.92, 120.63 (2C), 116.41 (t, J = 255.4 Hz, 1C), 74.44 (t, J = 3.7 Hz, 1C), 39.51 (t, J = 23.3 Hz, 1C), 28.59, 28.35; ^{19}F NMR (376 MHz, $CDCl_3$) δ -102.82-104.48 (m, 2F); HRMS (ESI): m/z calcd. for $C_{13}H_{13}F_2NNaO_3^+$ [M + Na^+]: 292.0756, found: 292.0761.

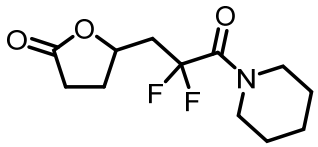


N-cyclohexyl-2,2-difluoro-3-(5-oxotetrahydrofuran-2-yl)propanamide (3ad). The product was purified by silica gel column chromatography (PE/EA = 3/1). Yield, 75%, 103.7 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.40 (s, 1H), 4.74-4.67 (m, 1H), 3.77-3.70 (m, 1H), 2.61-2.38 (m, 5H), 2.00-1.90 (m, 3H), 1.72-1.69 (m, 2H), 1.62-1.58 (m, 1H), 1.38-1.29 (m, 2H), 1.24-1.13 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.28, 162.49 (t, J = 27.8 Hz, 1C), 116.29 (t, J = 253.9 Hz, 1C), 74.49 (t, J = 4.6 Hz, 1C), 48.83, 39.52 (t, J = 23.5 Hz, 1C), 32.59, 32.47, 28.52, 28.30, 25.32, 24.75 (2C); ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.58 (q, J = 258.9 Hz, 2F); HRMS (ESI): m/z calcd. for $C_{13}H_{19}F_2NNaO_3^+$ [M + Na^+]: 298.1225, found: 298.1231.

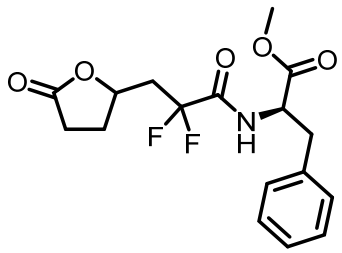


5-(3-(benzo[d]oxazol-2-yl)-2,2-difluoro-3-oxopropyl)dihydrofuran-2(3H)-one (3-ae). The product was purified by silica gel column chromatography (PE/EA = 3/1). Yield, 84%, 112.7 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83-7.81 (m, 1H), 7.65-7.63 (m, 1H), 7.51-7.42 (m, 2H), 4.98-4.91 (m, 1H), 3.13-2.99 (m, 1H), 2.87-

2.74 (m, 1H), 2.63-2.49 (m, 3H), 2.13-2.03 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.05, 157.17 (t, *J* = 32.8 Hz, 1C), 150.81, 139.92, 127.33, 125.64, 121.49, 115.14 (t, *J* = 242.2 Hz, 1C), 111.67, 74.44 (t, *J* = 3.9 Hz, 1C), 41.48 (t, *J* = 23.3 Hz, 1C), 28.94, 28.55; ^{19}F NMR (376 MHz, $CDCl_3$) δ -96.63 (dd, *J* = 1016.5, 281.7 Hz, 2F); HRMS (ESI): m/z calcd. for $C_{13}H_{11}F_2NNaO_3^+$ [M + Na^+]: 290.0599, found: 290.0603.



5-(2,2-difluoro-3-oxo-3-(piperidin-1-yl)propyl)dihydrofuran-2(3H)-one (3af). The product was purified by silica gel column chromatography (PE/EA = 3/1). Yield, 79%, 102.7 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.86-4.80 (m, 1H), 3.64-3.61 (m, 2H), 3.56-3.53 (m, 2H), 2.71-2.41 (m, 5H), 2.04-1.93 (m, 1H), 1.70-1.56 (m, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.57, 161.07 (t, *J* = 28.1 Hz, 1C), 118.32 (t, *J* = 256.7 Hz, 1C), 75.20 (t, *J* = 4.4 Hz, 1C), 46.92 (t, *J* = 6.5 Hz, 1C), 44.60, 40.62 (t, *J* = 23.1 Hz, 1C), 29.11, 28.65, 26.55, 25.67, 24.46; ^{19}F NMR (376 MHz, $CDCl_3$) δ -97.87 (dd, *J* = 670.3, 285.7 Hz, 2F); HRMS (ESI): m/z calcd. for $C_{12}H_{17}F_2NNaO_3^+$ [M + Na^+]: 284.1069, found: 284.1067.



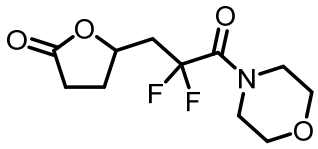
Methyl (2,2-difluoro-3-(5-oxotetrahydrofuran-2-yl)propanoyl)-D-phenylalanina-Te (*dr* = 1:1.8) (3ag). The product was purified by silica gel column chromatography (PE/EA = 3/1). Yield, 78%, 137.9 mg, light yellow oil.

Major isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.16 (m, 3H), 7.07-7.05 (m, 2H), 6.90-6.85 (m, 1H), 4.86-4.78 (m, 1H), 4.39-4.32 (m, 1H), 3.70 (s, 3H), 3.21-2.98 (m, 2H), 2.55-2.20 (m, 5H), 1.90-1.76 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.21, 170.91, 163.05 (t, *J* = 28.6 Hz, 1C), 135.34, 129.31 (2C), 128.78 (2C), 127.41, 116.07 (t, *J* = 254.1 Hz, 1C), 74.31-74.14 (m, 1C), 53.19, 52.79, 39.49 (t, *J* = 23.3 Hz, 1C),

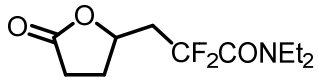
37.68, 28.50, 28.35; ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.50 (dd, *J* = 322.3, 227.4 Hz, 2F).

Minor isomer: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25-7.16 (m, 3H), 7.07-7.05 (m, 2H), 6.90-6.85 (m, 1H), 4.86-4.78 (m, 1H), 4.63-4.56 (m, 1H), 3.68 (s, 3H), 3.21-2.98 (m, 2H), 2.55-2.20 (m, 5H), 1.90-1.76 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.17, 170.91, 163.05 (t, *J* = 28.6 Hz, 1C), 135.22, 129.27 (2C), 128.82 (2C), 127.48, 116.04 (t, *J* = 254.4 Hz, 1C), 74.31-74.14 (m, 1C), 53.25, 52.73, 39.40 (t, *J* = 23.2 Hz, 1C), 37.52, 28.50, 28.35; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.04 (dd, *J* = 317.3, 147.5 Hz, 2F).

HRMS (ESI): m/z calcd. for $C_{17}H_{19}F_2NNaO_5^+$ [M + Na^+]: 378.1124, found: 378.1120.

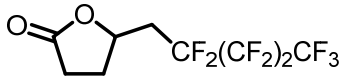


5-(2,2-difluoro-3-morpholino-3-oxopropyl)dihydrofuran-2(3H)-one (3ah). The product was purified by silica gel column chromatography (PE/EA = 3/1). Yield, 75%, 98.4 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.87-4.80 (m, 1H), 3.74-3.62 (m, 8H), 2.72-2.42 (m, 5H), 2.06-1.94 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.44, 161.37 (t, *J* = 28.7 Hz, 1C), 118.18 (t, *J* = 256.5 Hz, 1C), 74.90 (t, *J* = 4.3 Hz, 1C), 66.82, 66.75, 46.57 (t, *J* = 6.2 Hz, 1C), 43.55, 40.41 (t, *J* = 22.8 Hz, 1C), 29.06, 28.59; ^{19}F NMR (376 MHz, $CDCl_3$) δ -97.79 (q, *J* = 288.3 Hz, 2F); HRMS (ESI): m/z calcd. for $C_{11}H_{15}F_2NNaO_4^+$ [M + Na^+]: 286.0861, found: 286.0863.



***N*,*N*-diethyl-2,2-difluoro-3-(5-oxotetrahydrofuran-2-yl)propanamide (3ai).** The product was purified by silica gel column chromatography (PE/EA = 3/1). Yield, 63%, 80.1 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.87-4.80 (m, 1H), 3.52 (q, *J* = 7.0 Hz, 2H), 3.38 (q, *J* = 7.1 Hz, 2H), 2.72-2.42 (m, 5H), 2.05-1.94 (m, 1H), 1.21 (t, *J* = 7.0 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 176.57, 162.16 (t, *J* = 28.2 Hz, 1C), 118.30 (t, *J* = 256.6 Hz, 1C), 75.22 (t, *J* = 4.4 Hz, 1C), 41.95 (t, *J* = 6.2 Hz, 1C), 41.72, 40.63 (t, *J* = 23.2 Hz, 1C), 29.13, 28.61, 14.35, 12.39; ^{19}F NMR

(376 MHz, $CDCl_3$) δ -98.44 (dd, J = 677.2, 285.5 Hz, 2F); HRMS (ESI): m/z calcd. for $C_{11}H_{17}F_2NNaO_3^+$ [M + Na^+]: 272.1069, found: 272.1065.



5-(2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptyl)dihydrofuran-2(3H)-one (3aj). The product was purified by silica gel column chromatography (PE/EA = 3/1). Yield, 41%, 64.9 mg, light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.89-4.83 (m, 1H), 2.74-2.32 (m, 5H), 2.08-1.98 (m, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 175.77, 73.22, 36.68 (t, J = 21.2 Hz, 1C), 29.03, 28.41; ^{19}F NMR (376 MHz, $CDCl_3$) δ -81.02 (tt, J = 9.3, 2.9 Hz, 3F), -112.90-113.02 (m, 2F), -124.49 (dt, J = 12.8, 9.1 Hz, 2F), -125.92-126.02 (m, 2F). HRMS (ESI): m/z calcd. for $C_9H_7F_9NaO_2^+$ [M + Na^+]: 341.0195, found: 341.0193.

References.

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[2] T.-J. Zhang, S.-Y. Li, W.-Y. Yuan, Q.-X. Wu, L. Wang, S. Yang, Q. Sun and F.-H. Meng, *Bioorg. Med. Chem. Lett.*, 2017, **27**, 729.
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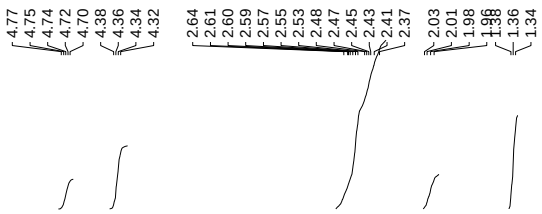
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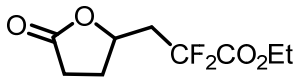
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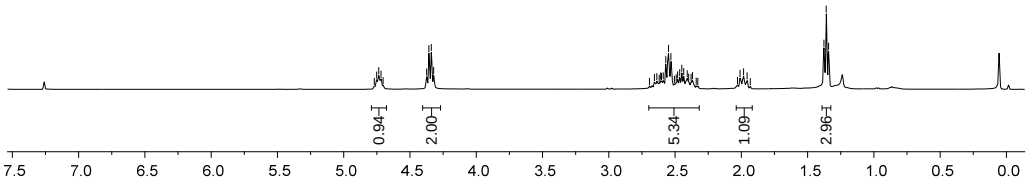
3aa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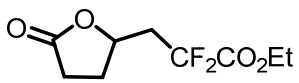
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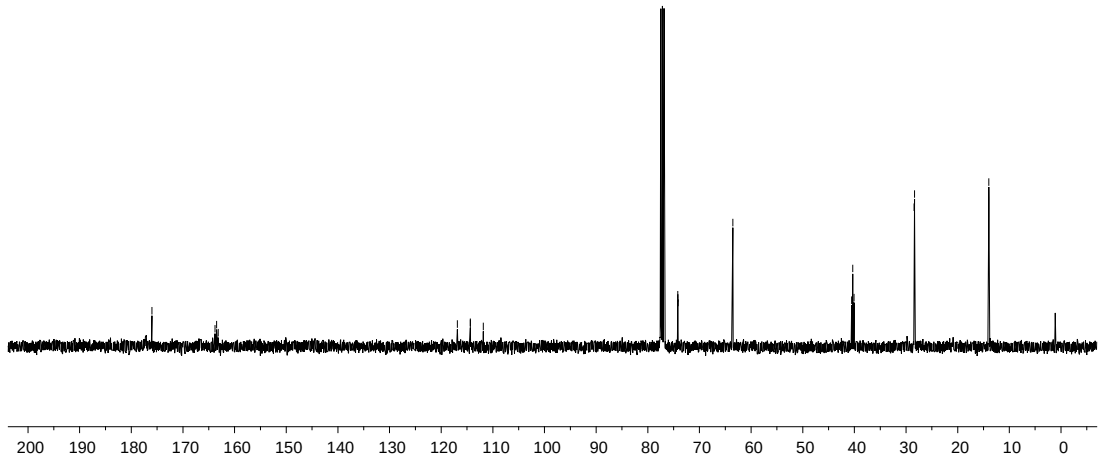
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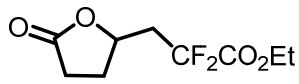

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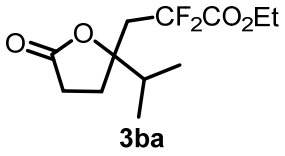

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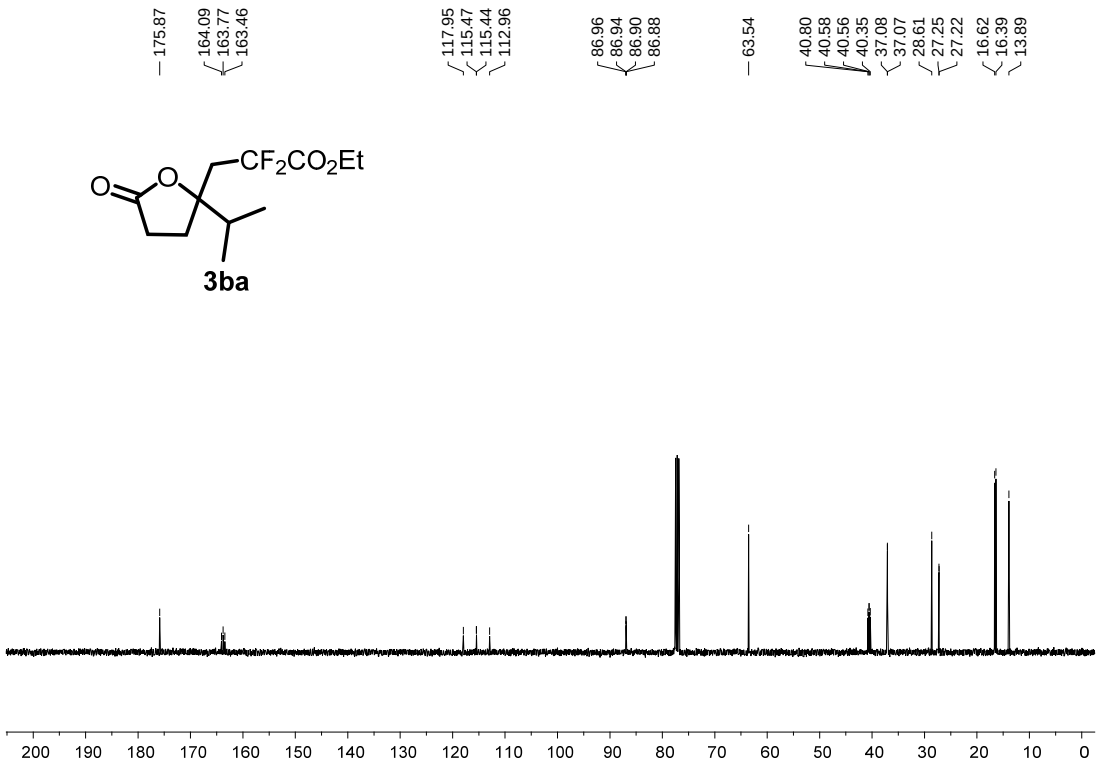
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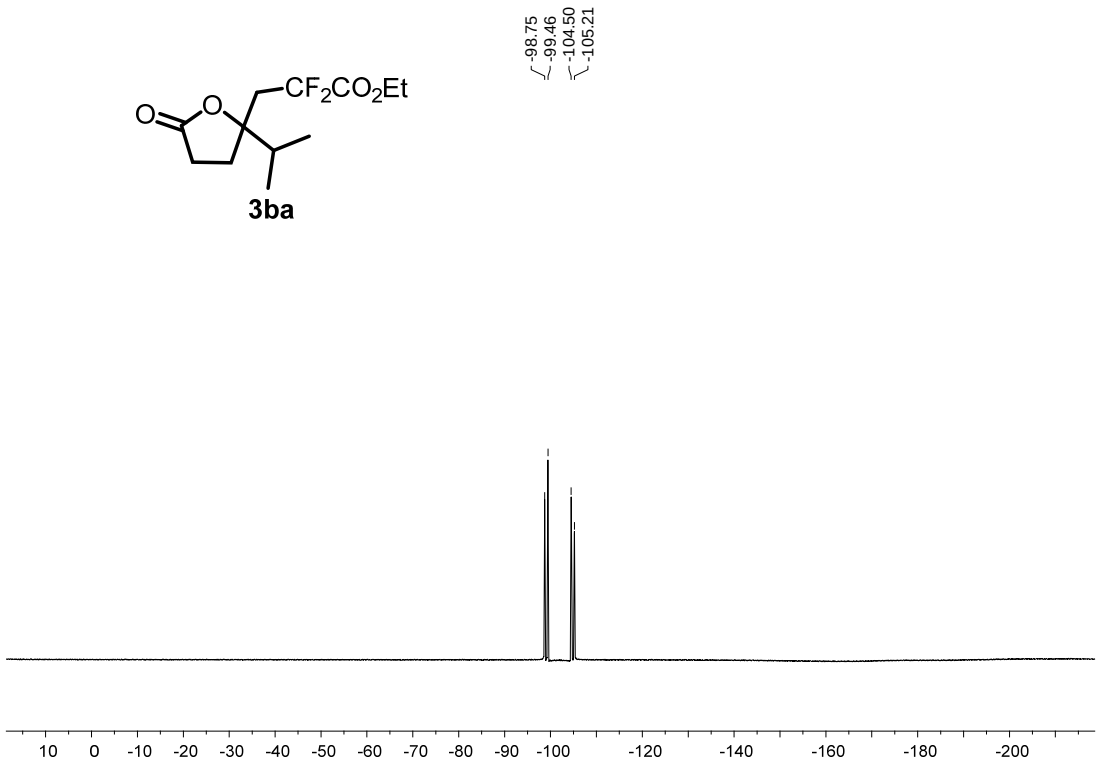
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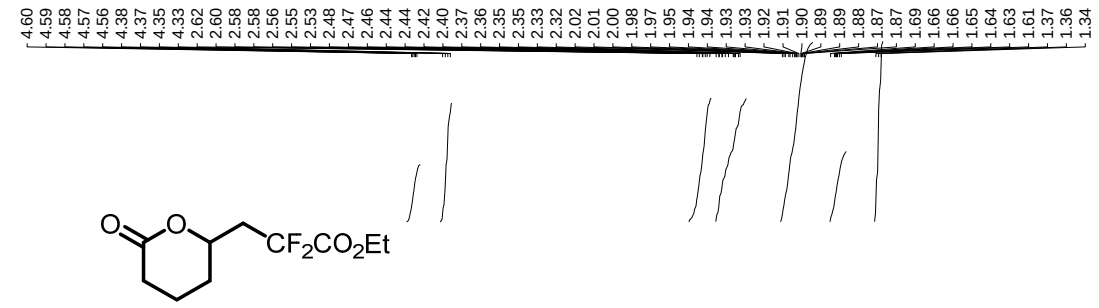
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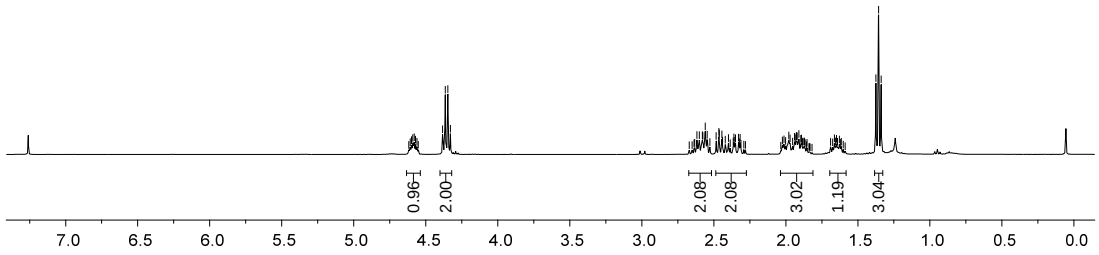
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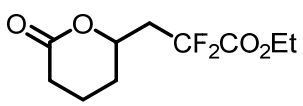
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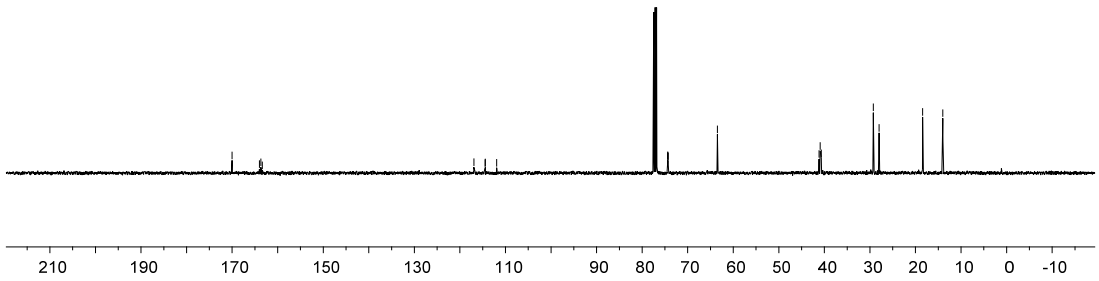
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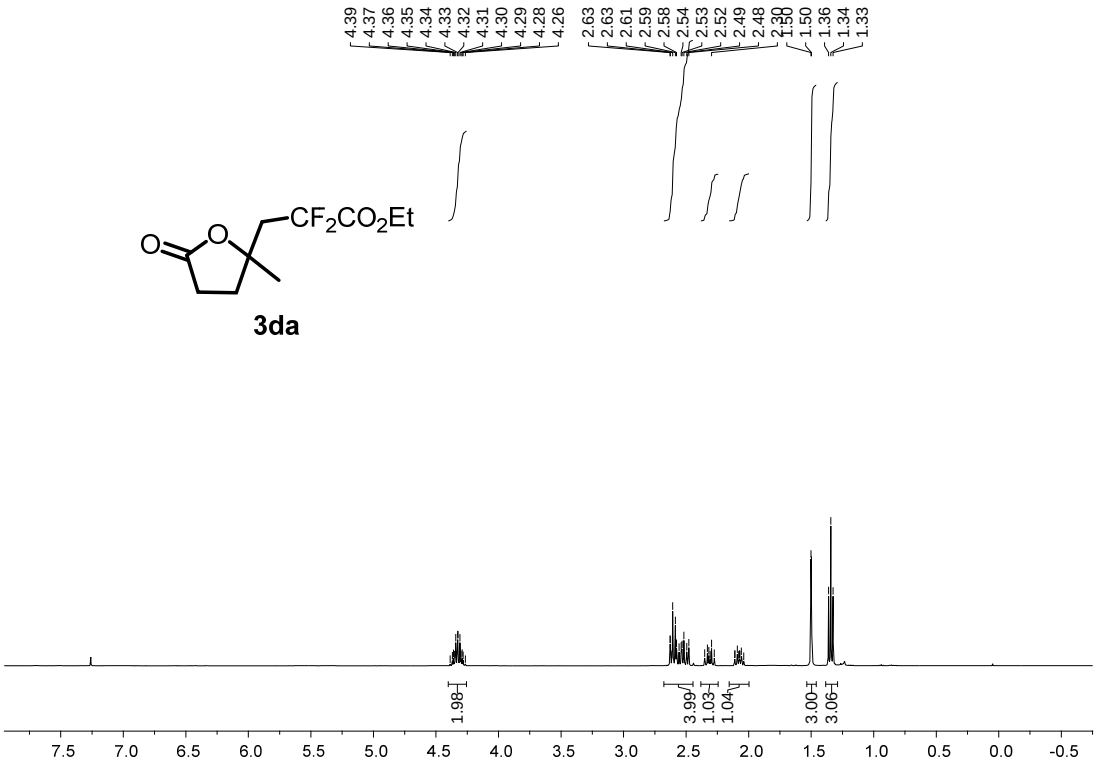
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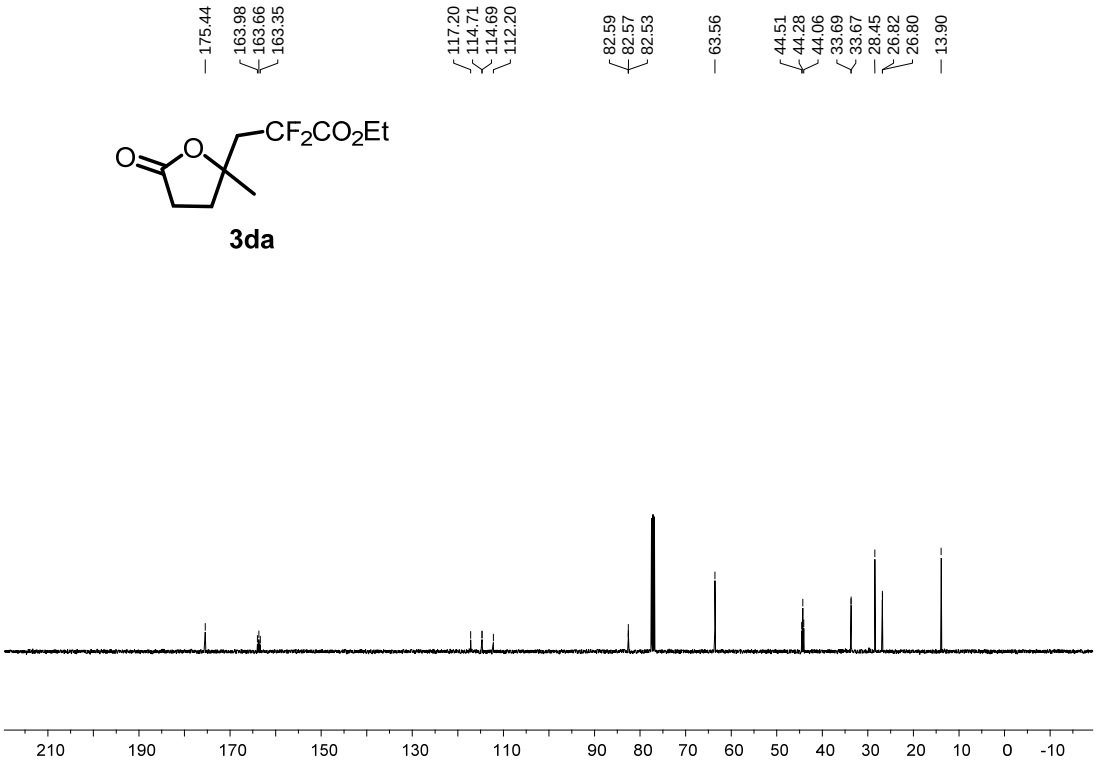
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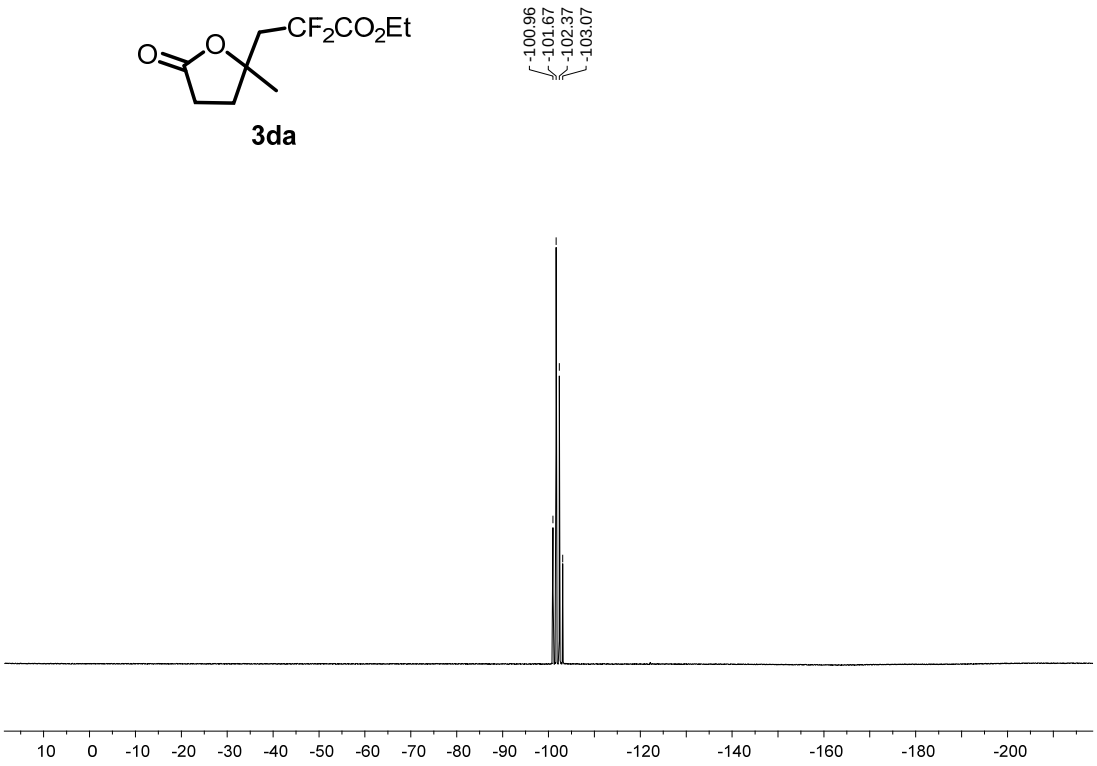
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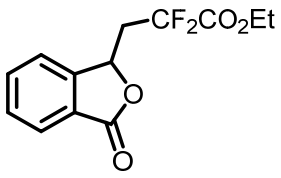
3ea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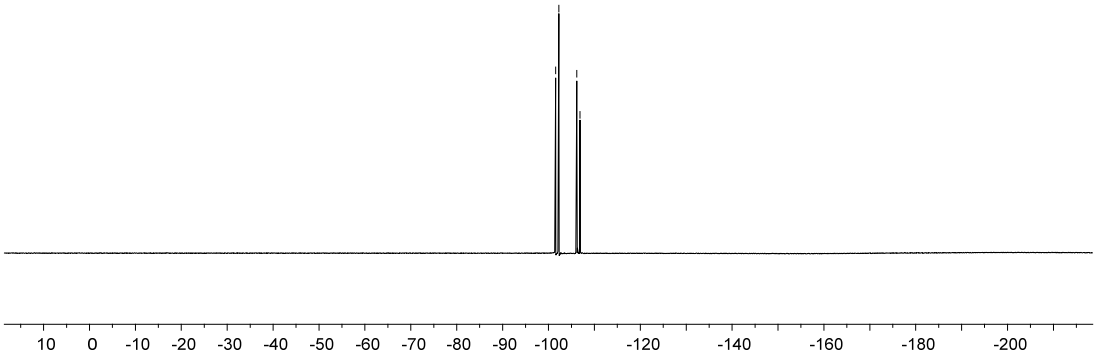
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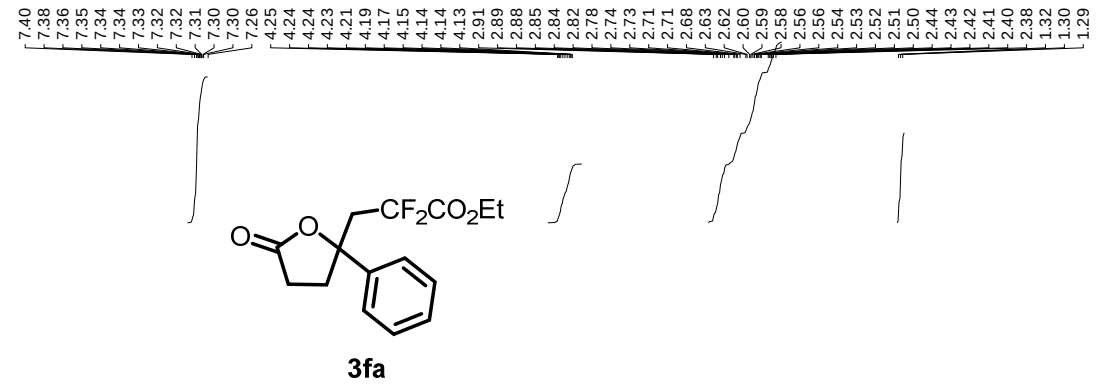
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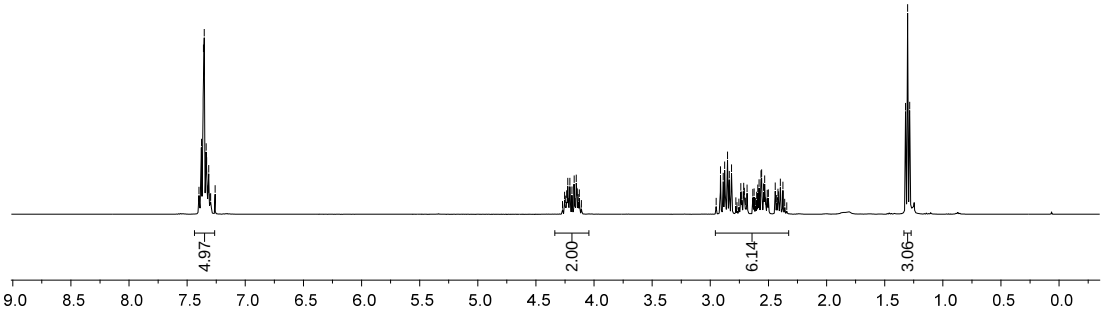
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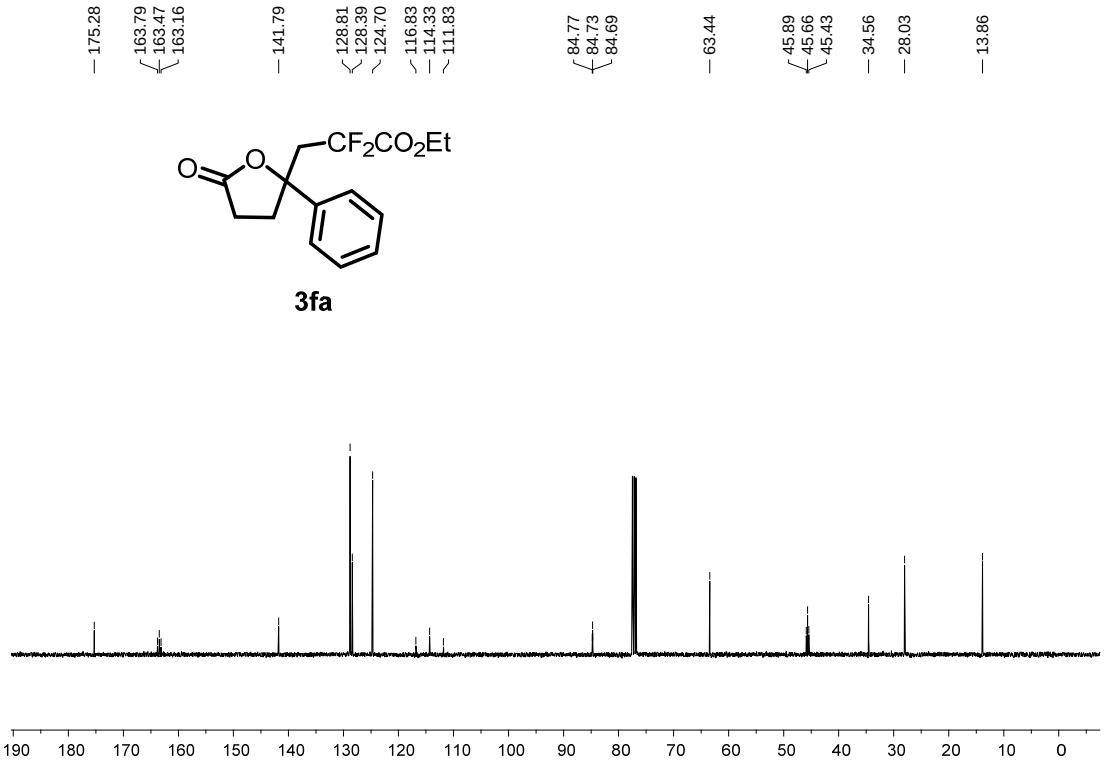
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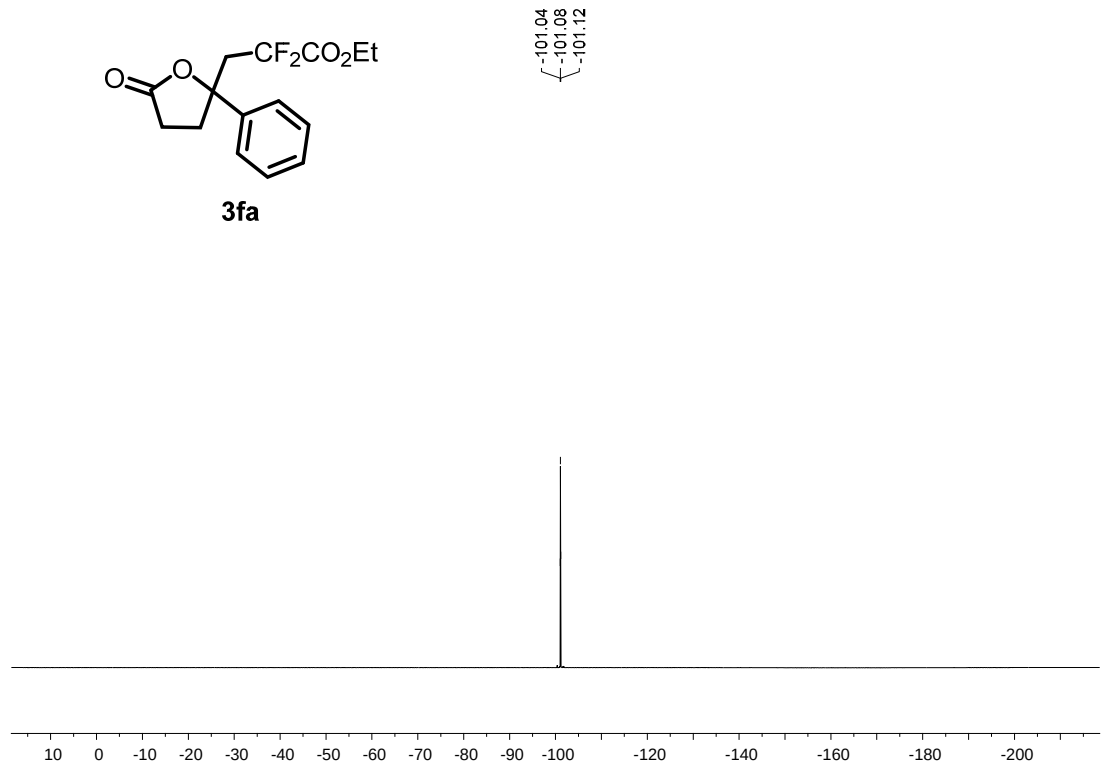
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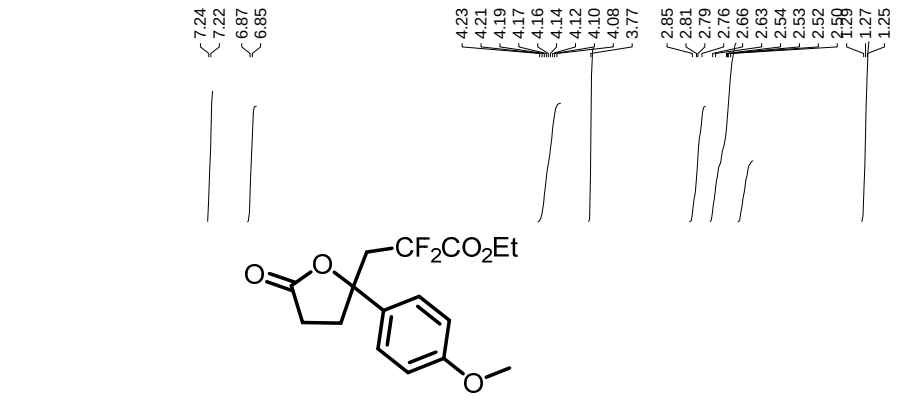
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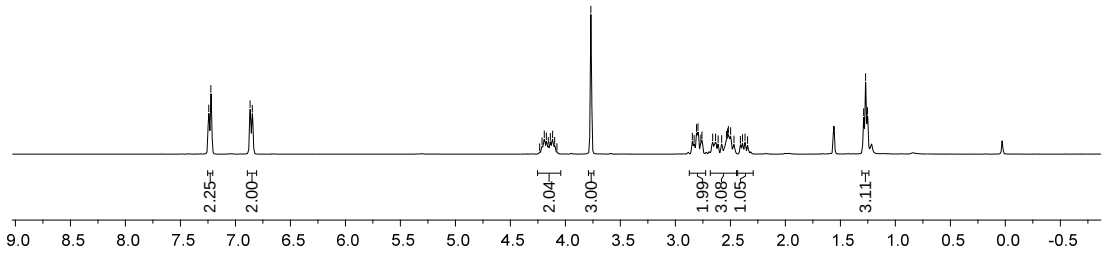
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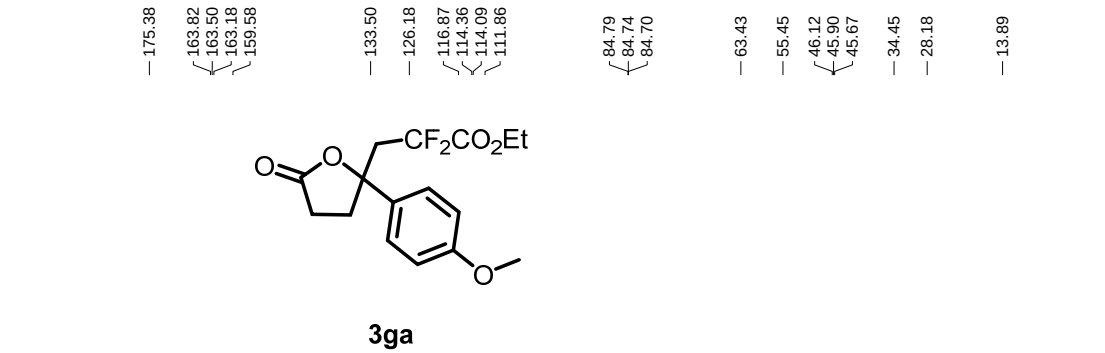
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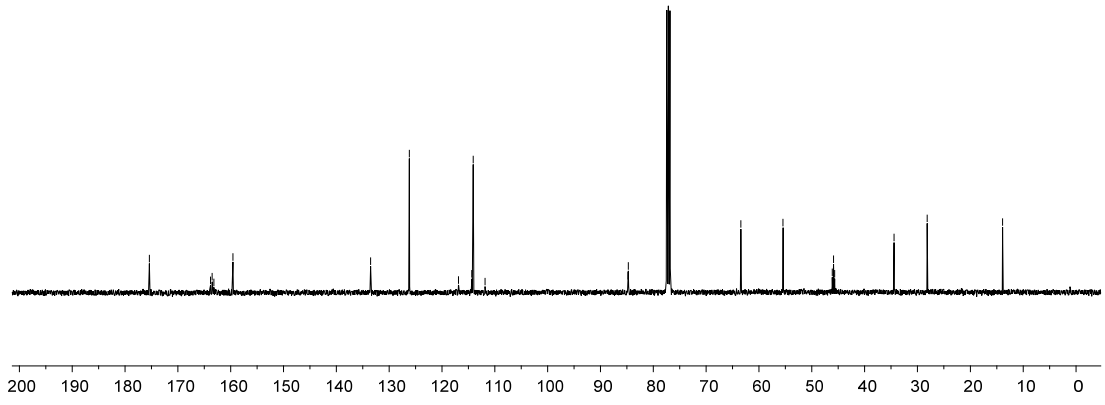
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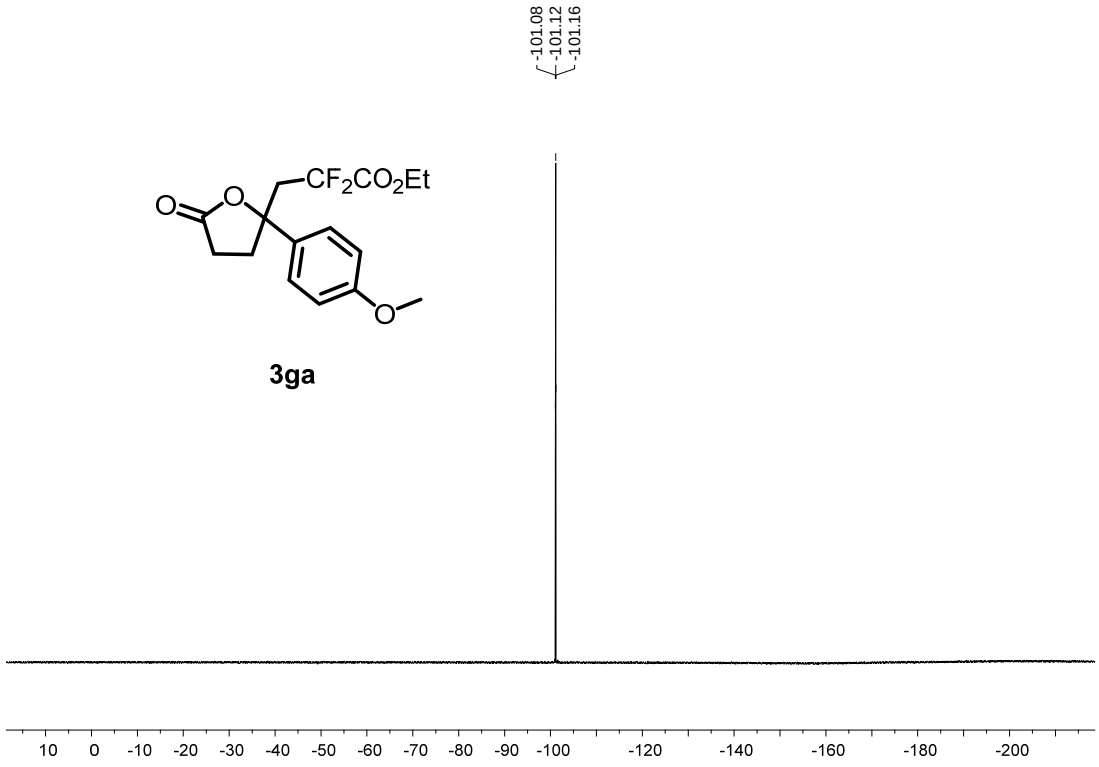
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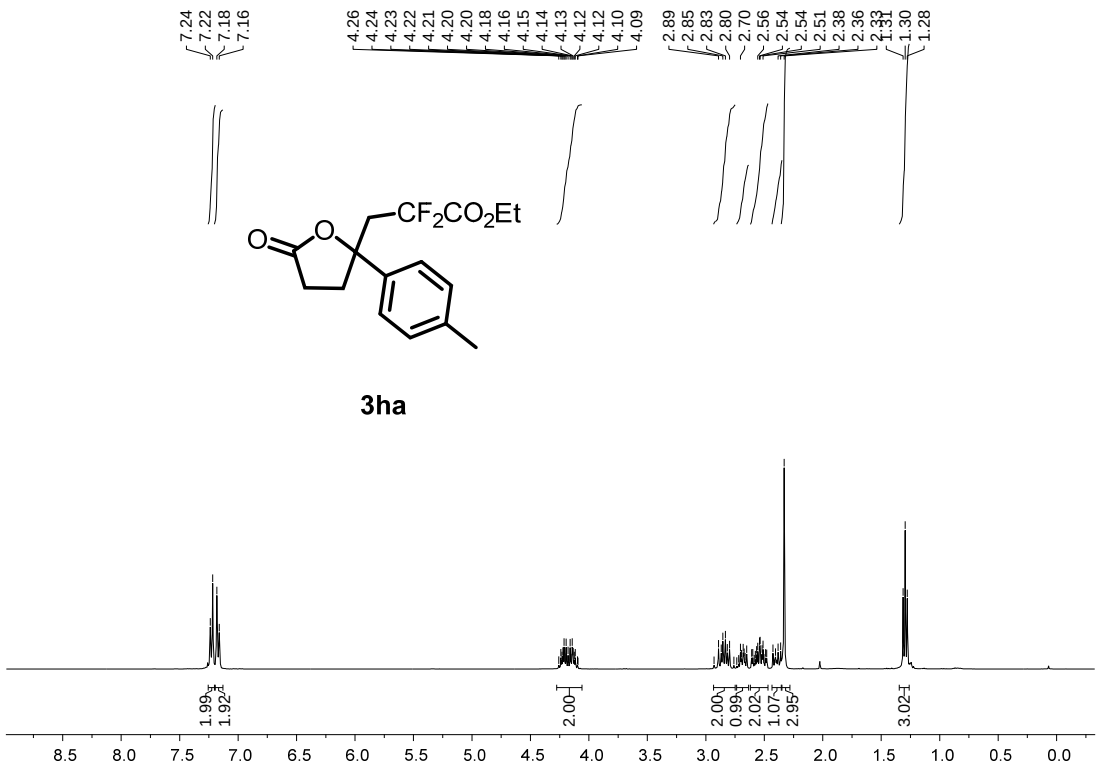
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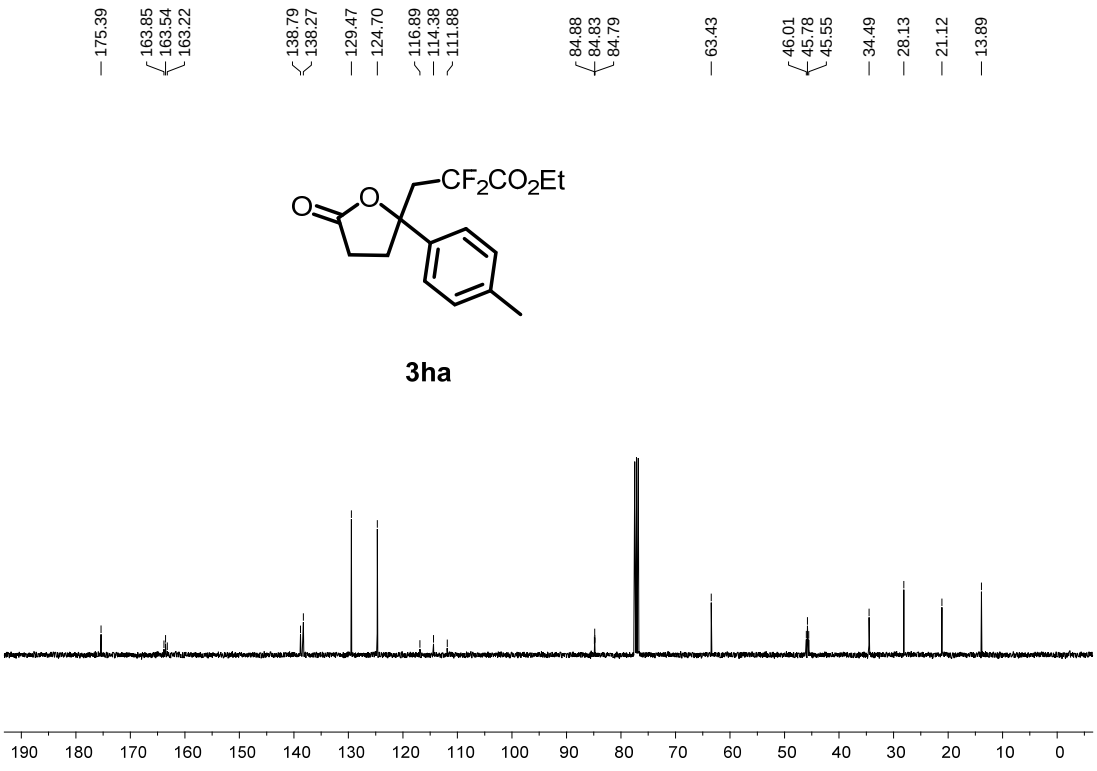
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45.55
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O
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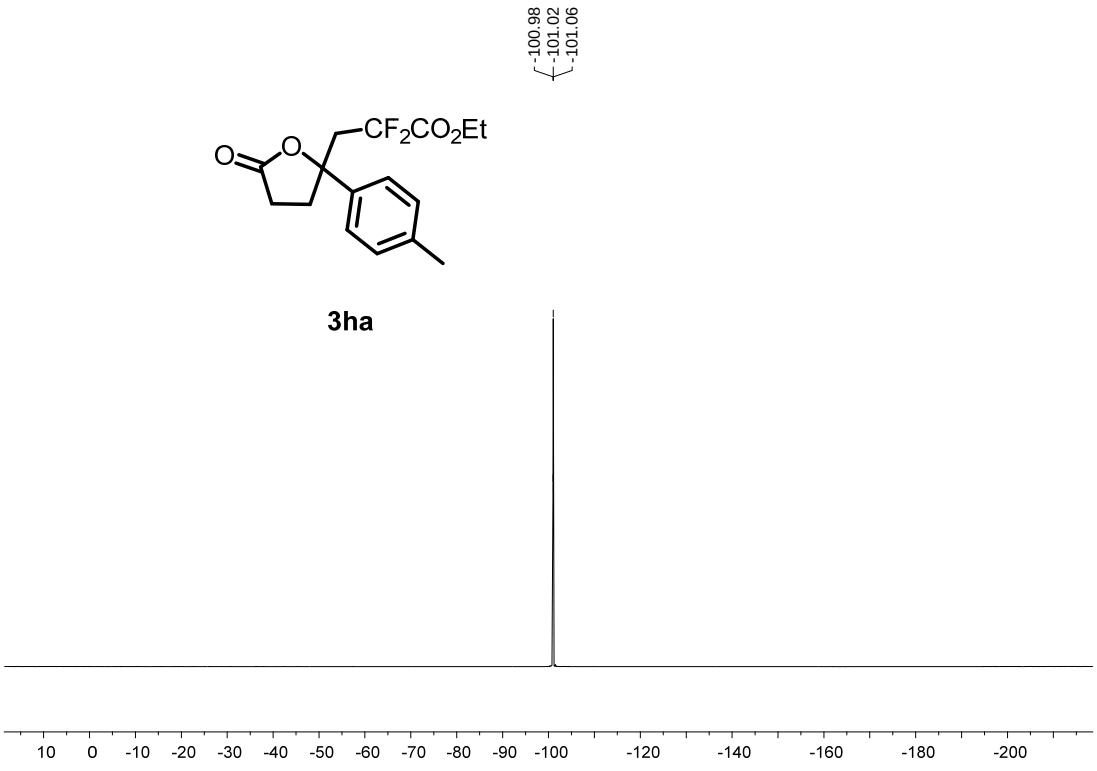
3ha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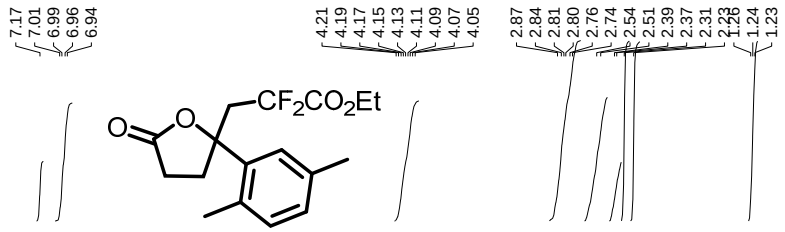
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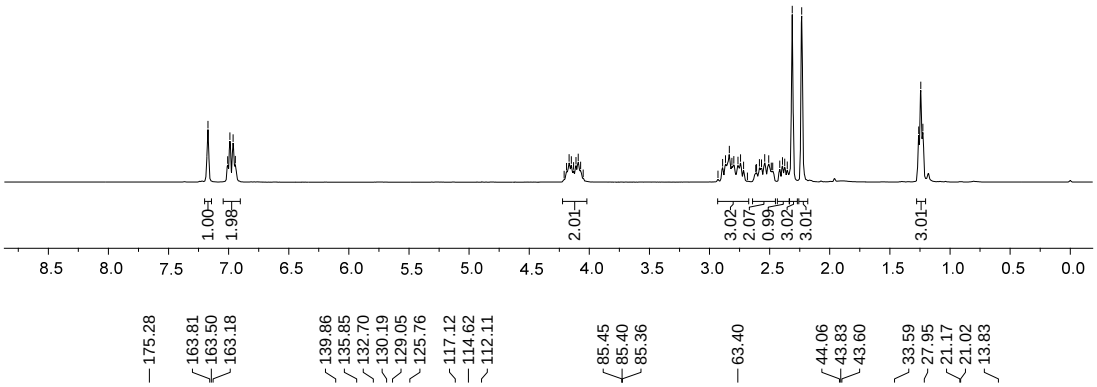
3ia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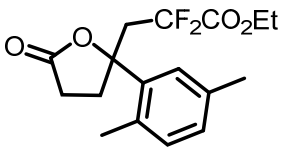
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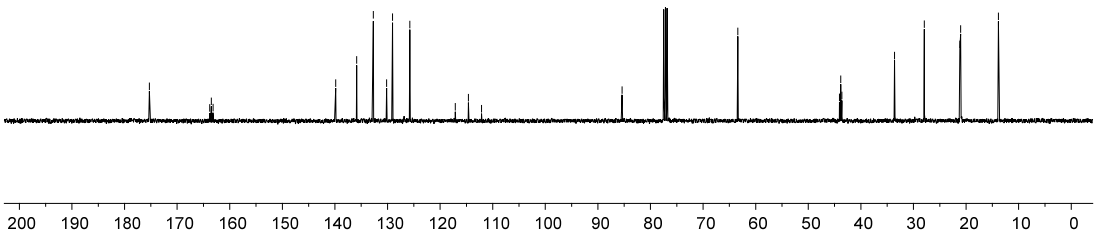
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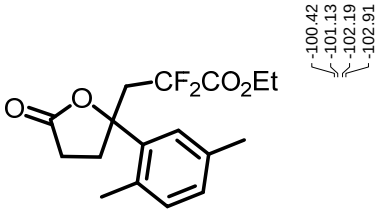
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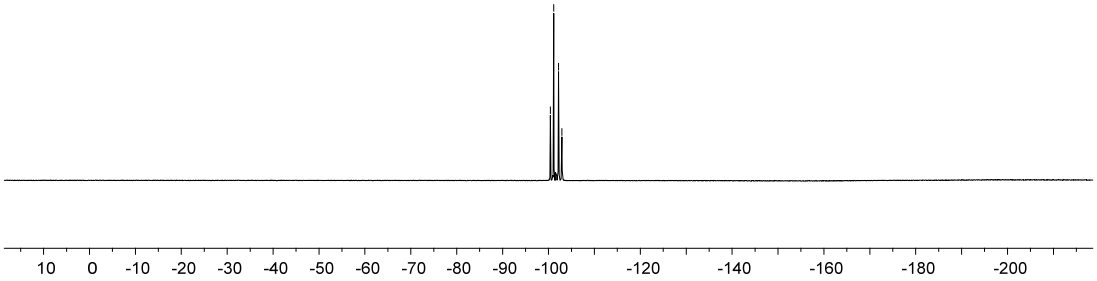
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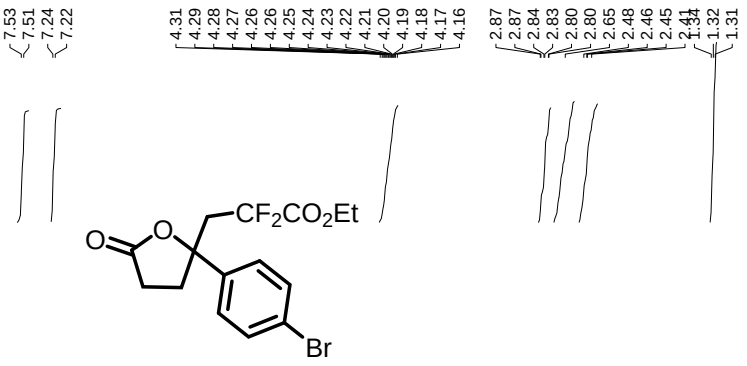
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Br

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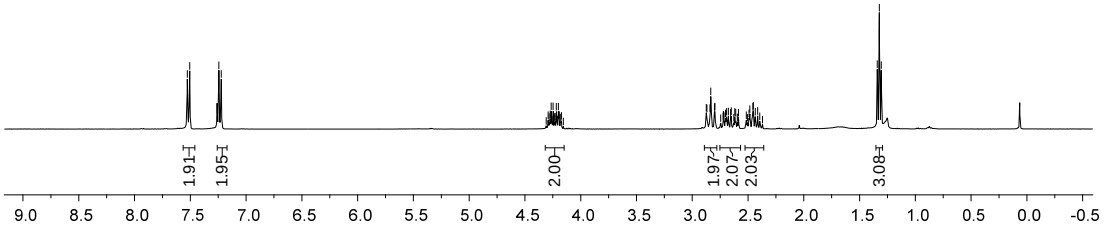
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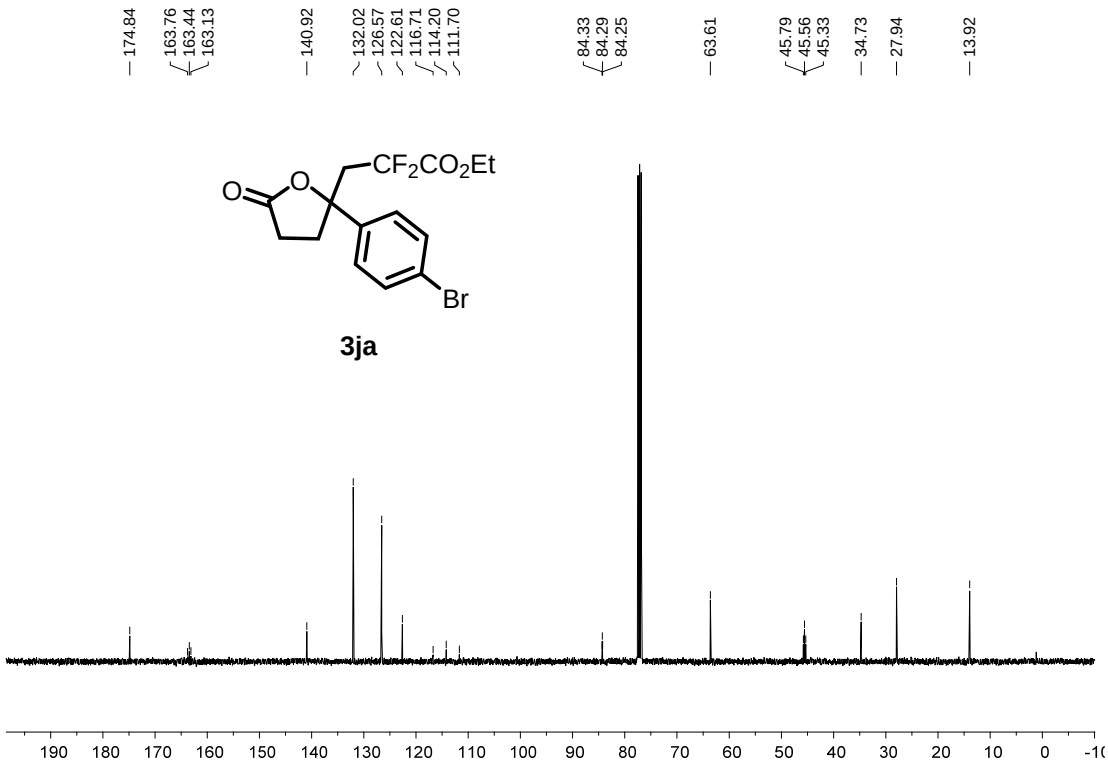
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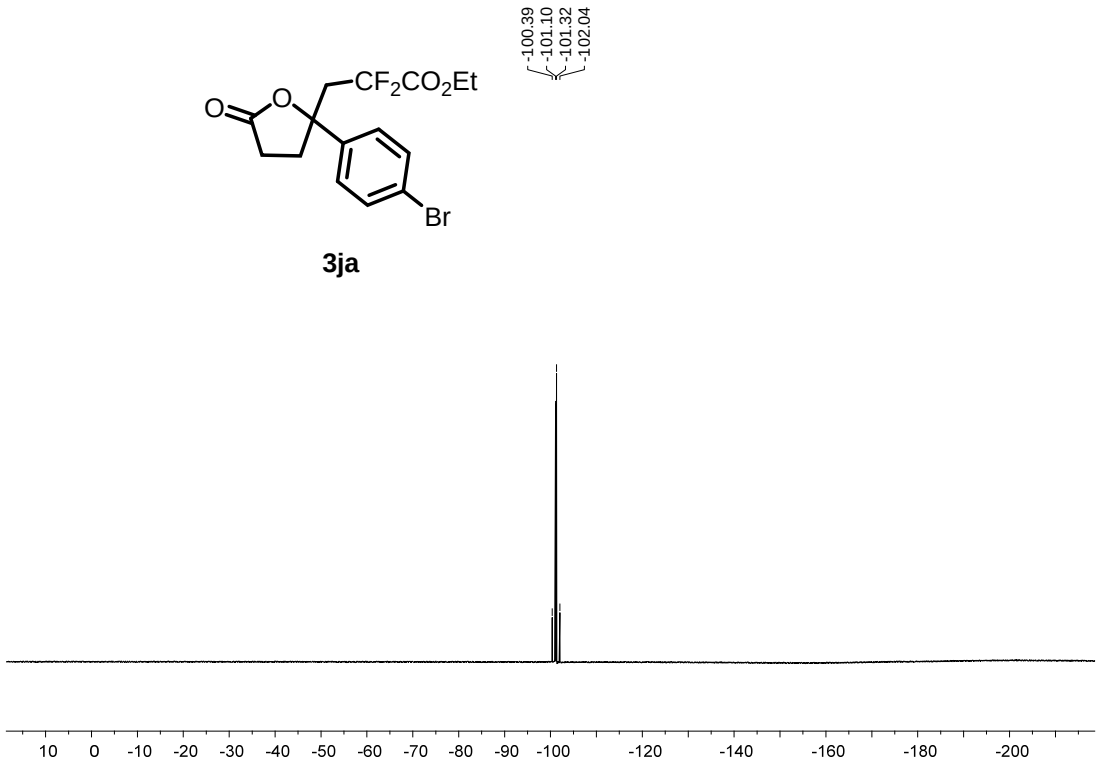
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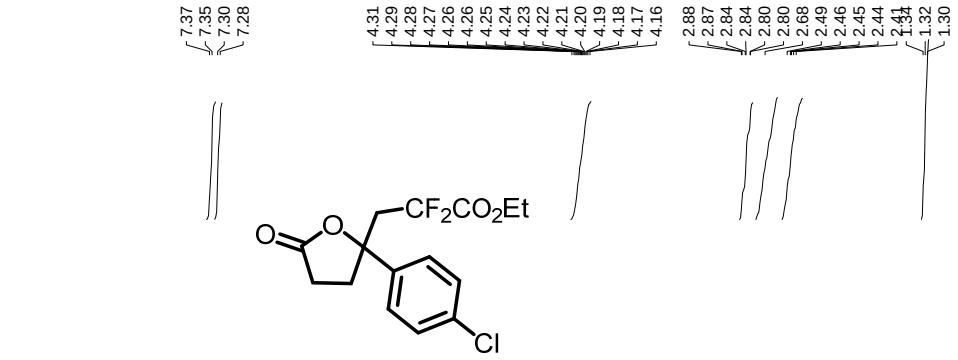
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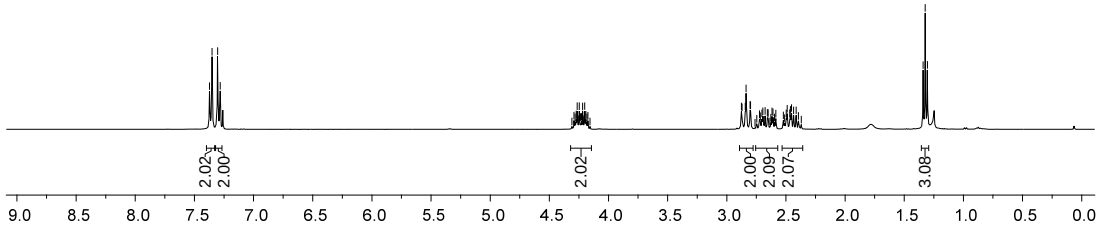
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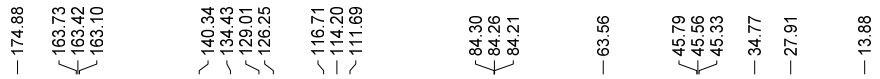
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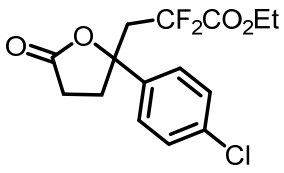
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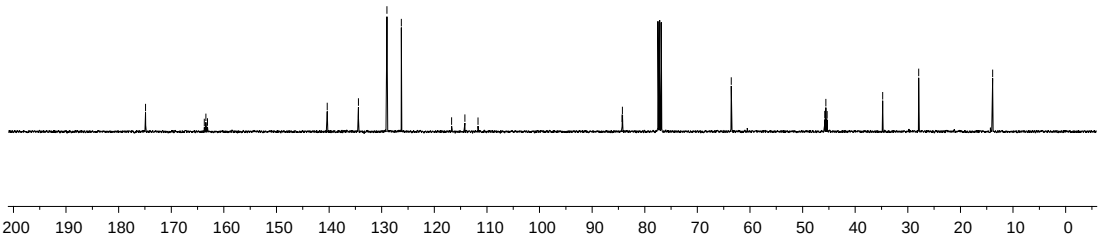
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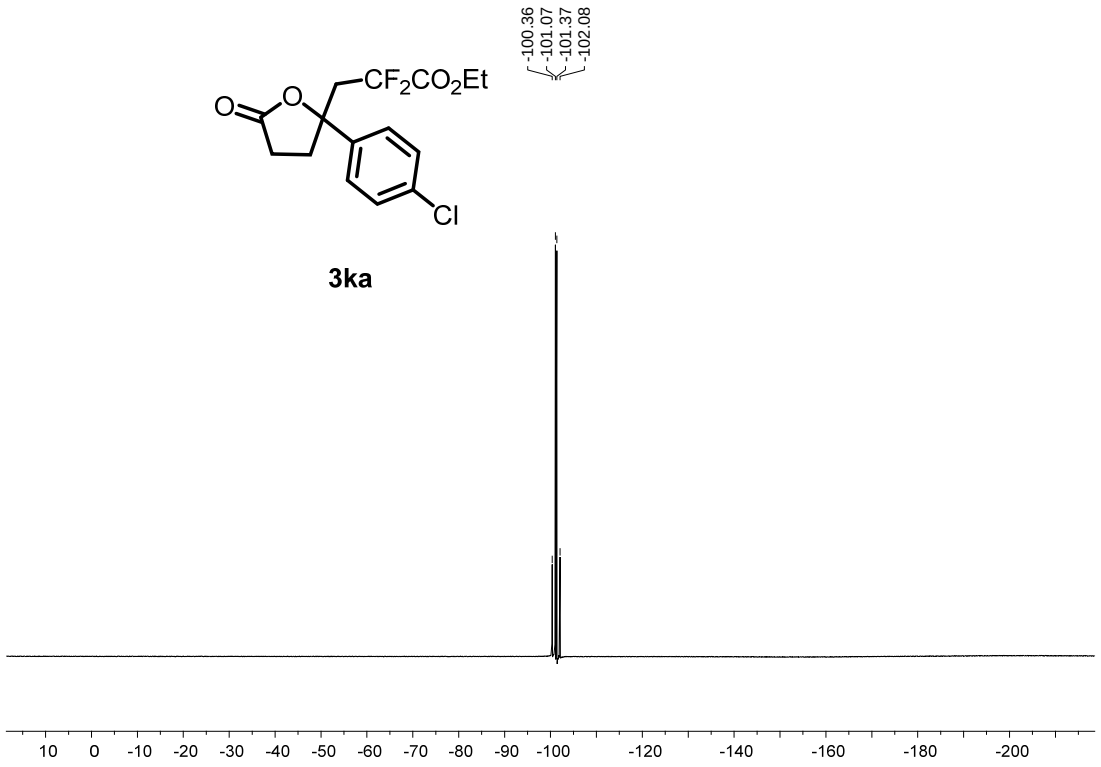
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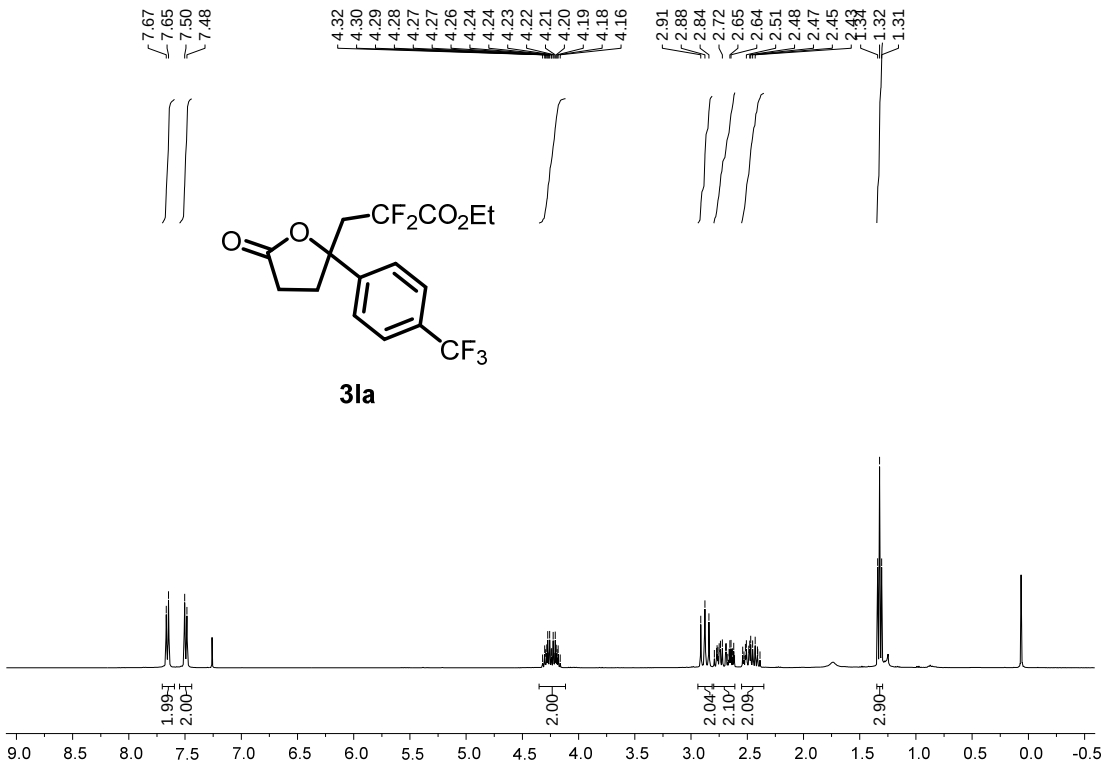
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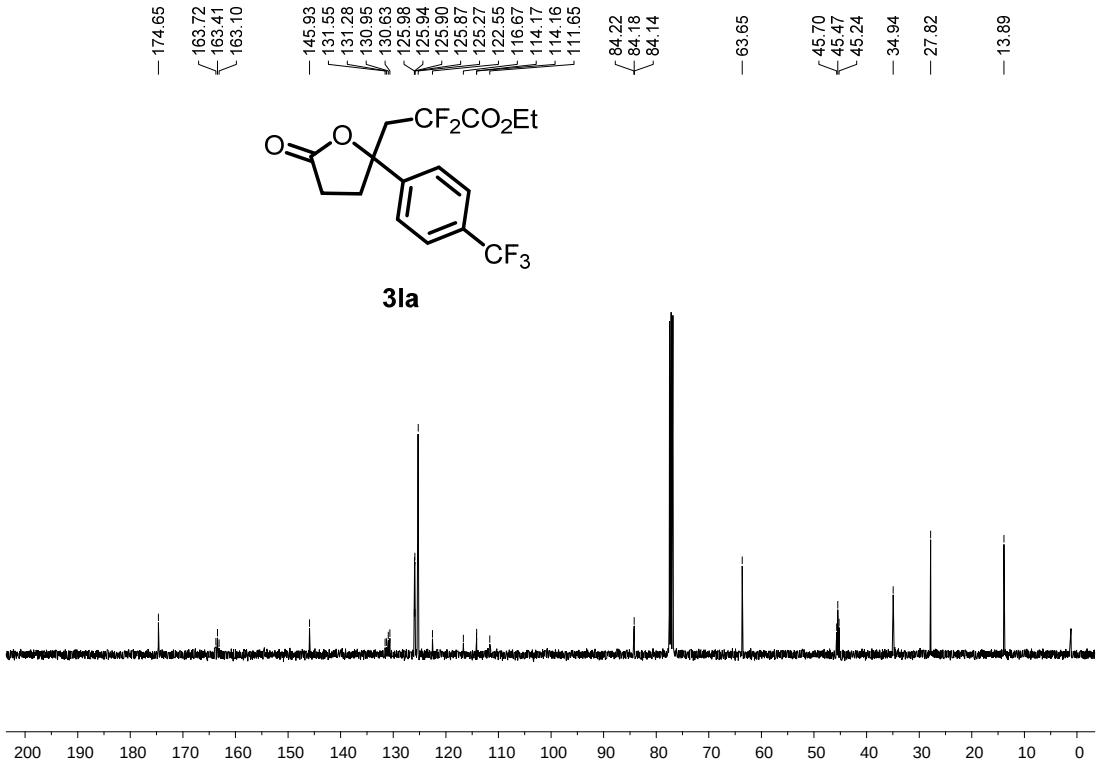
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45.24
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13.89
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O
O
CF3
3la
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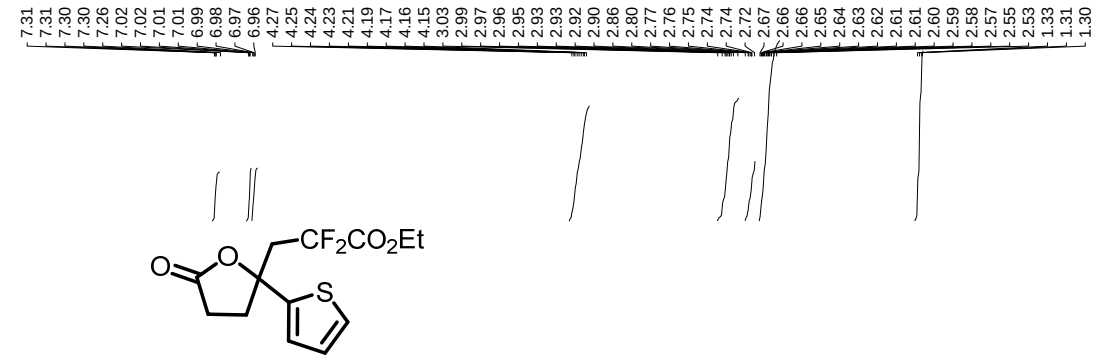
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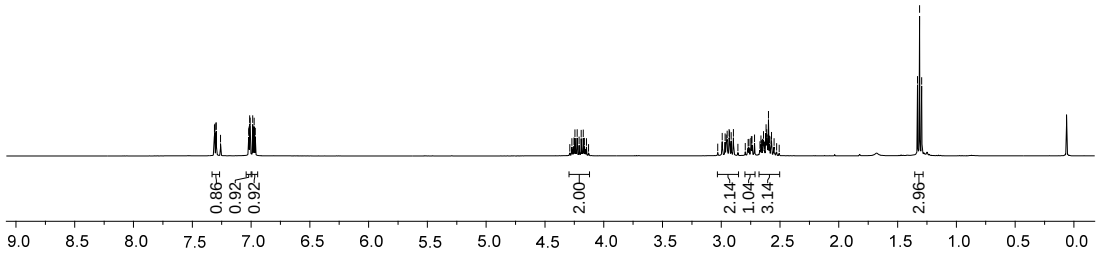
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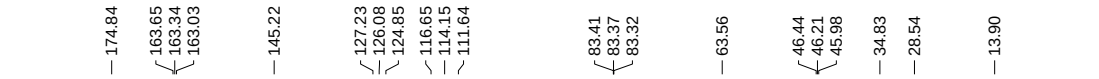
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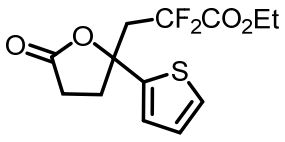
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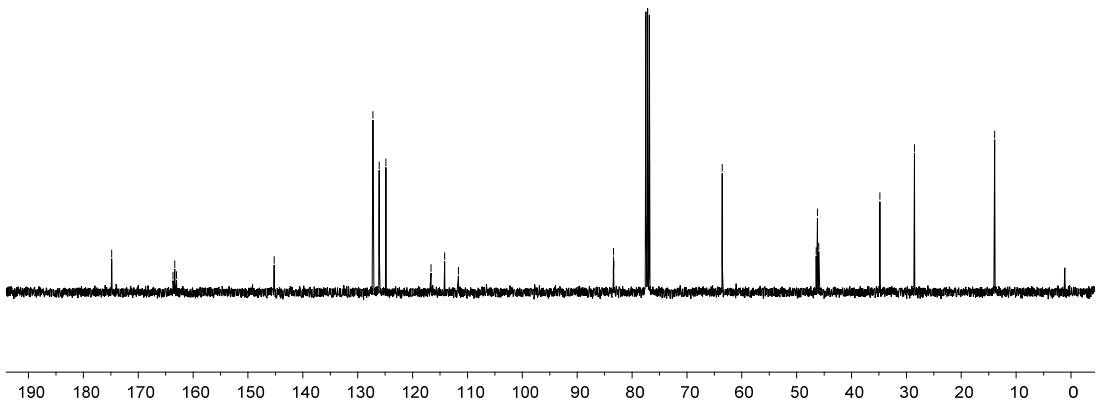
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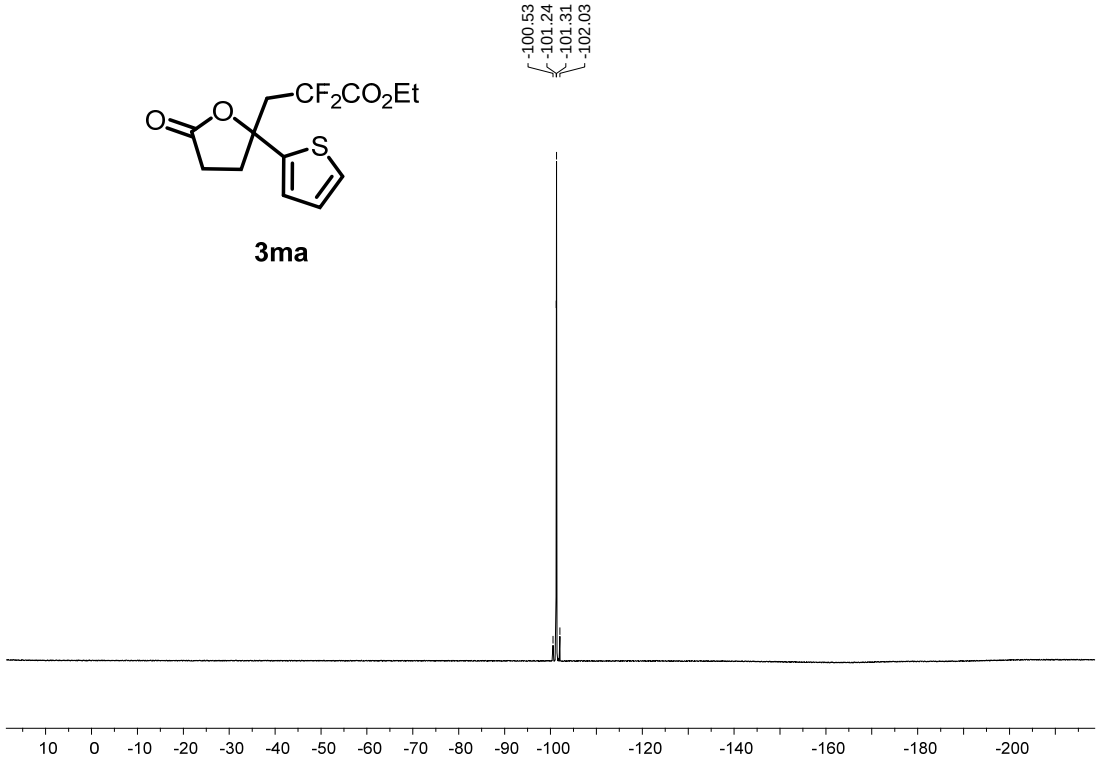
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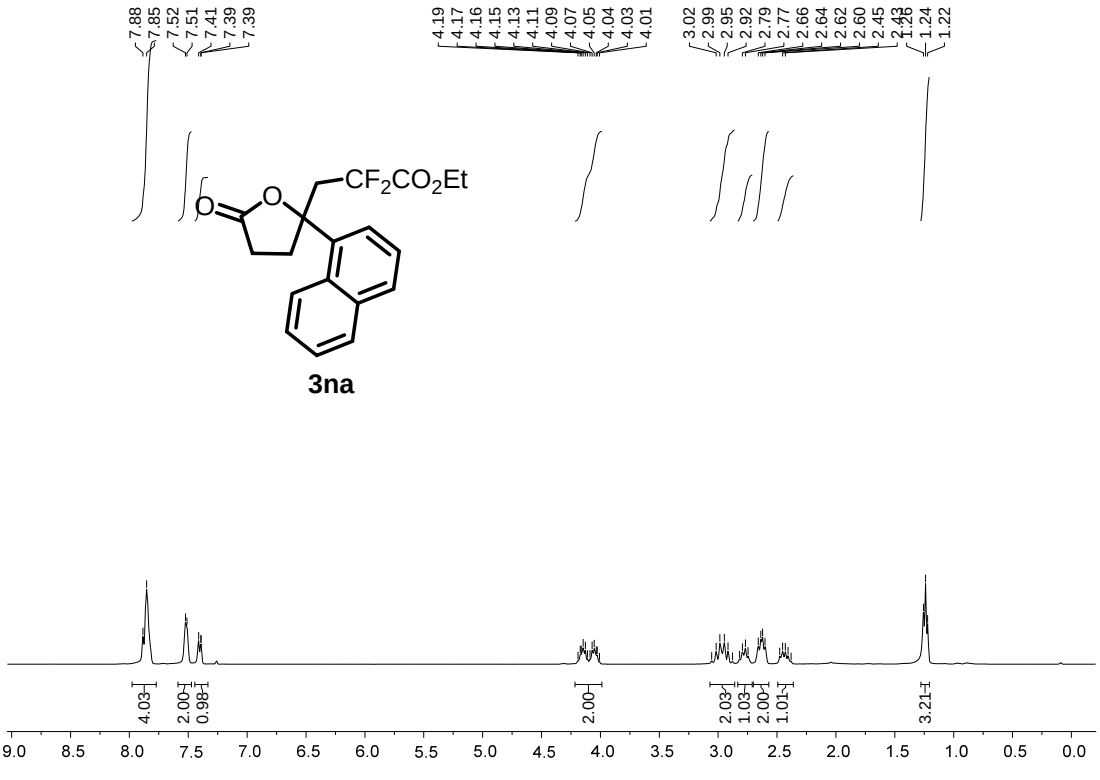
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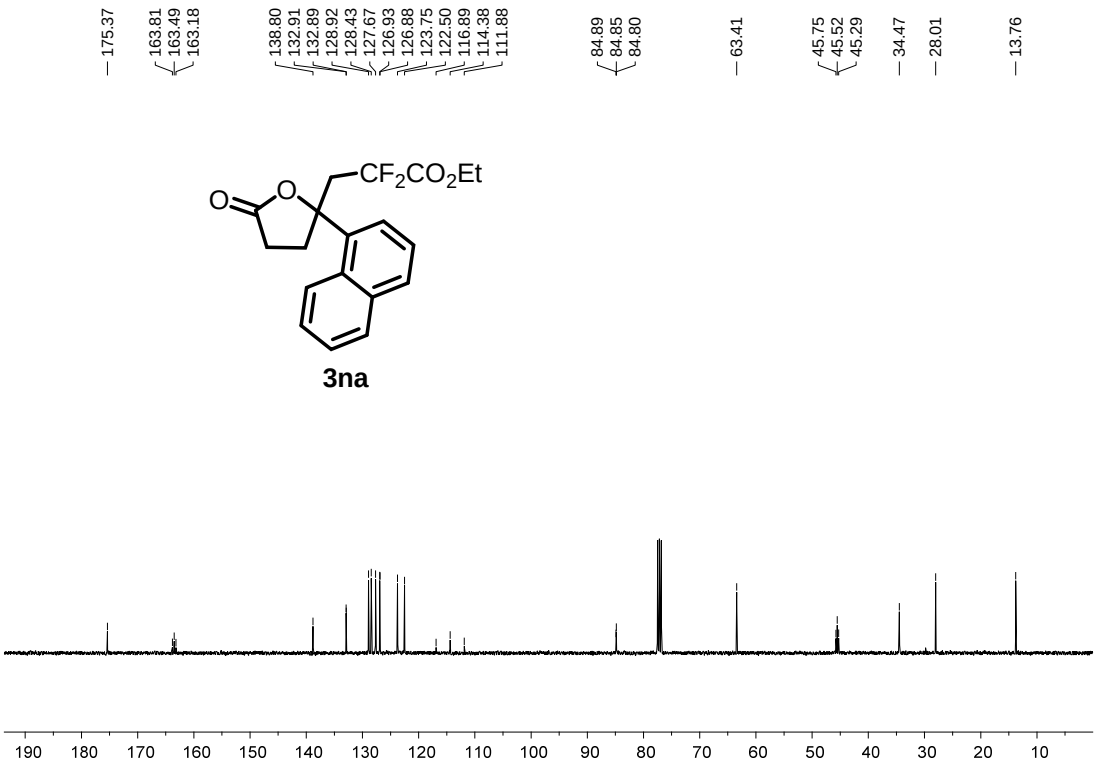
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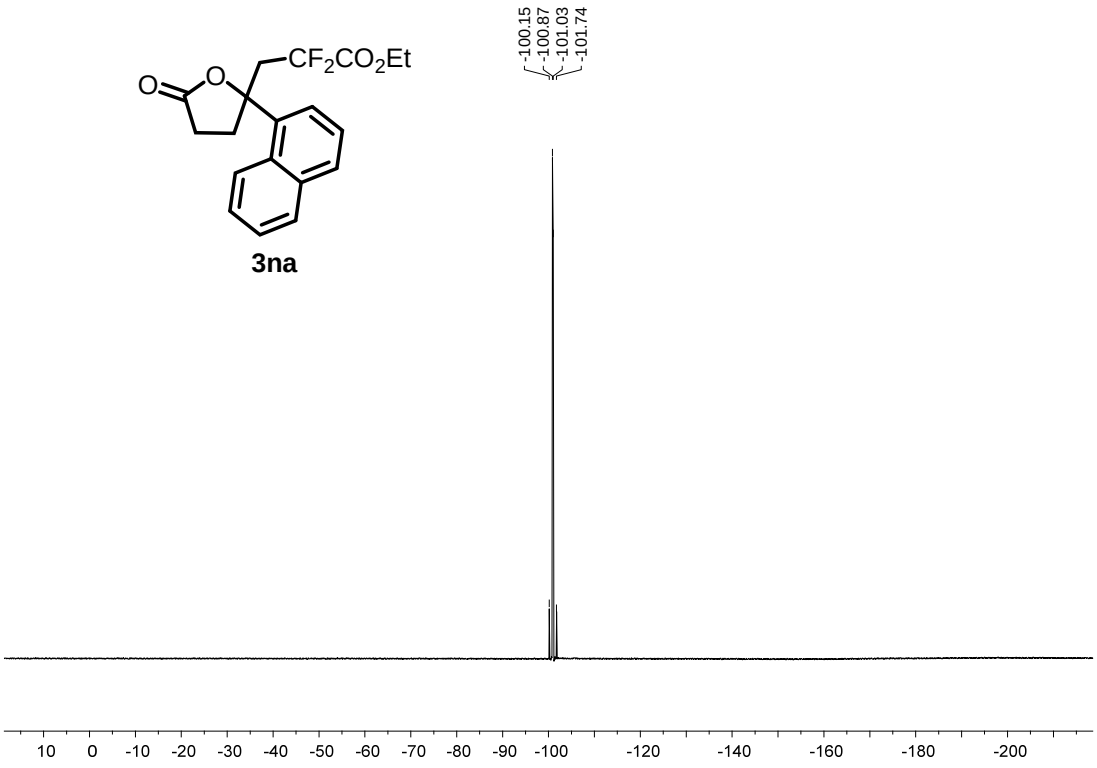
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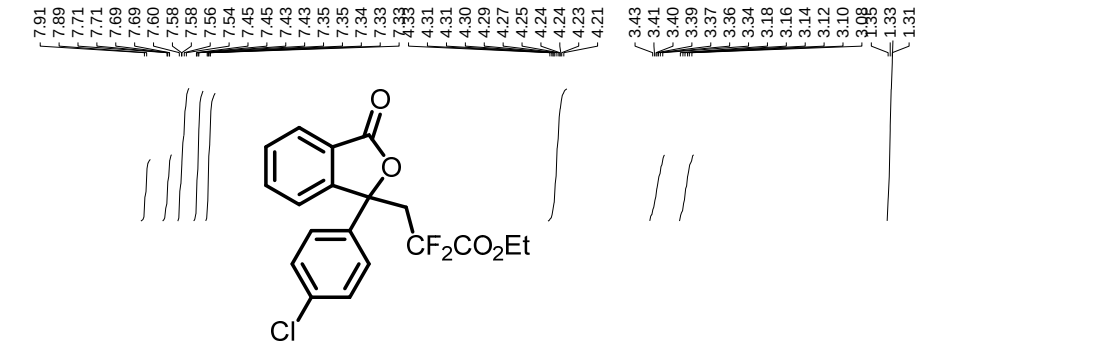
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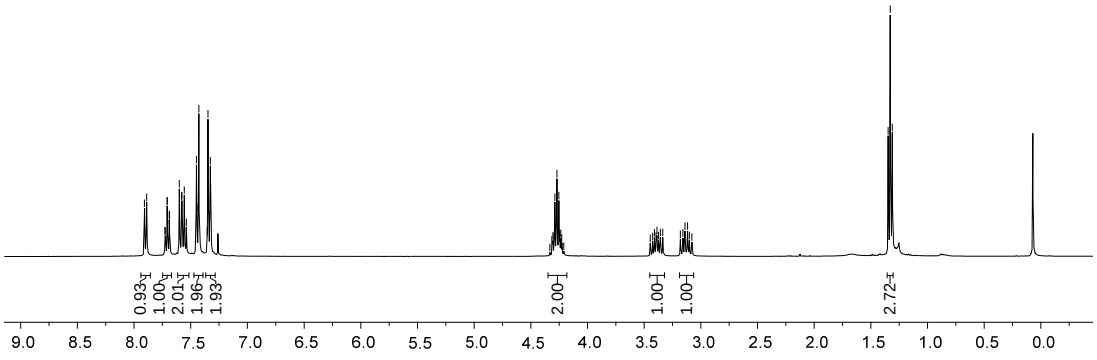
3oa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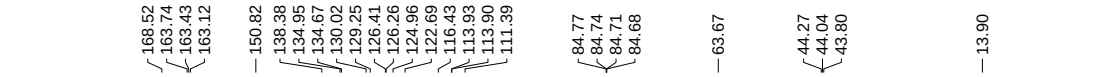
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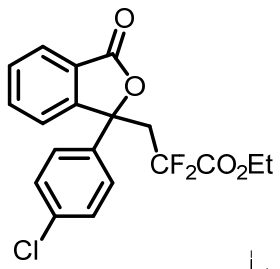
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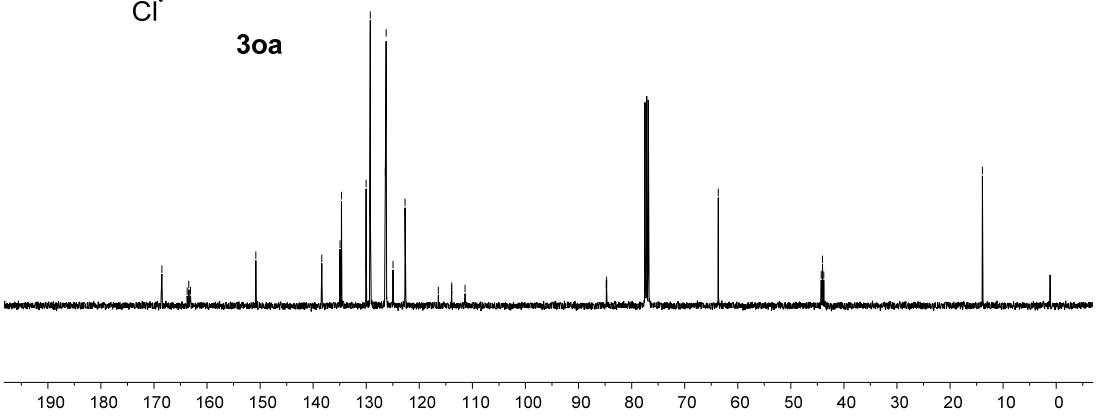
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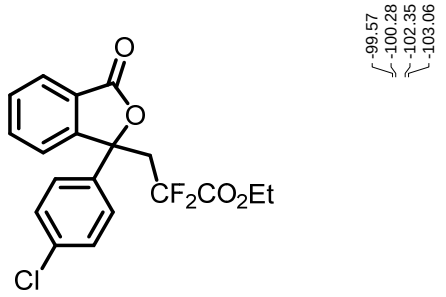
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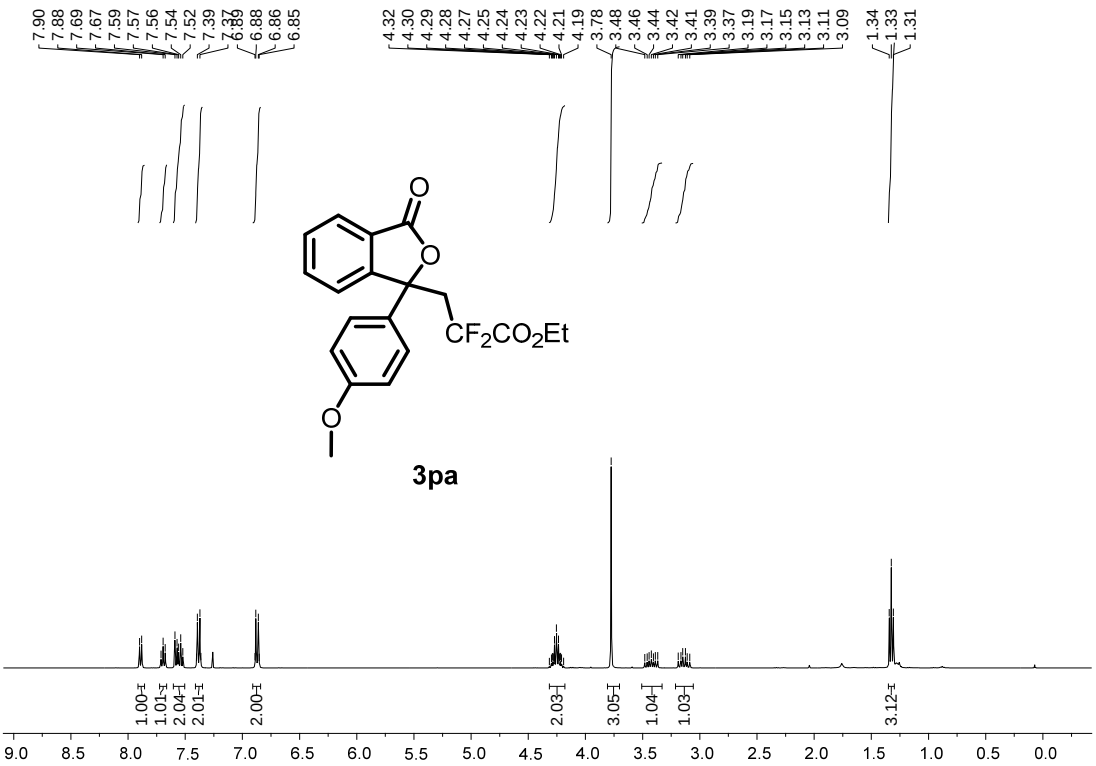
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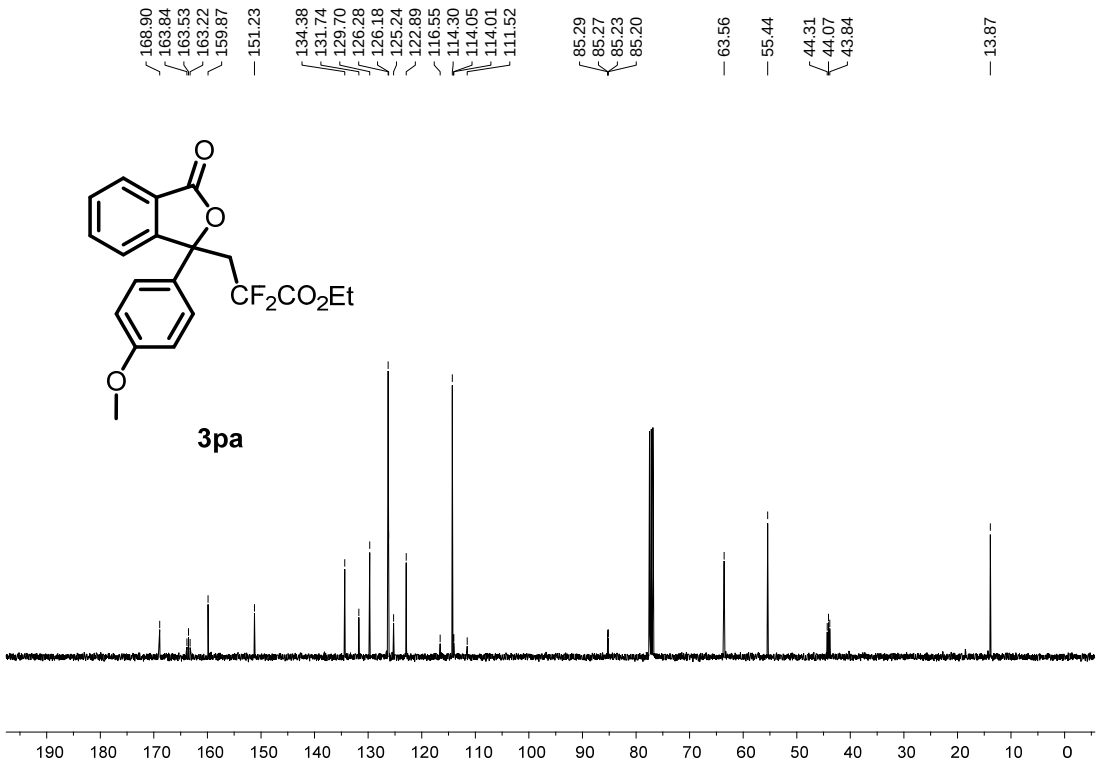
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44.31
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O
CF2CO2Et
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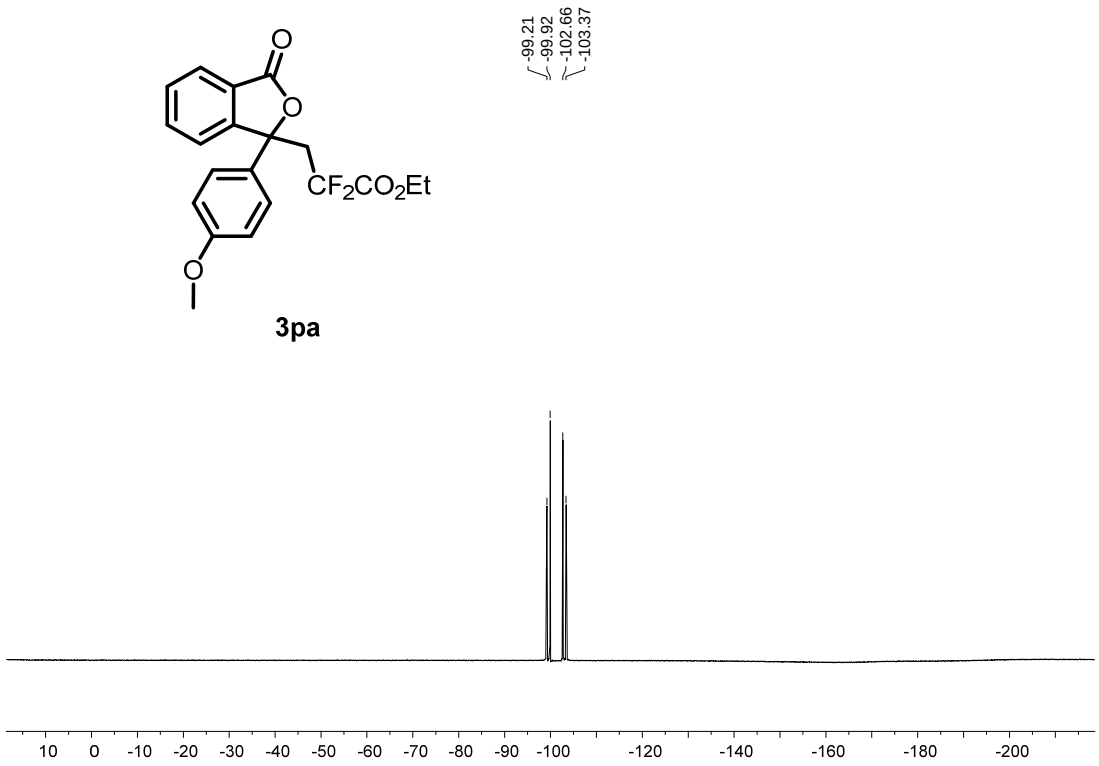
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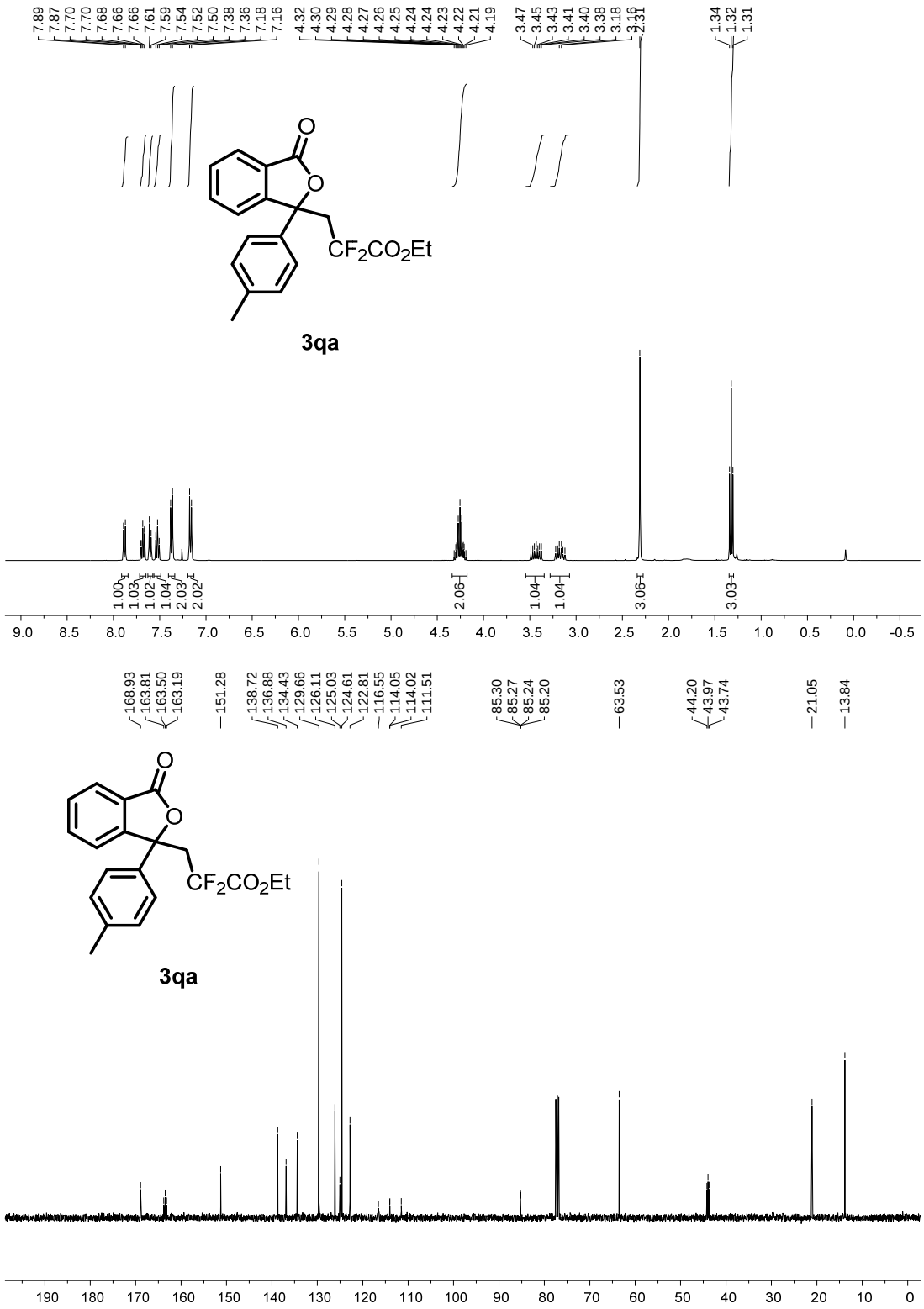
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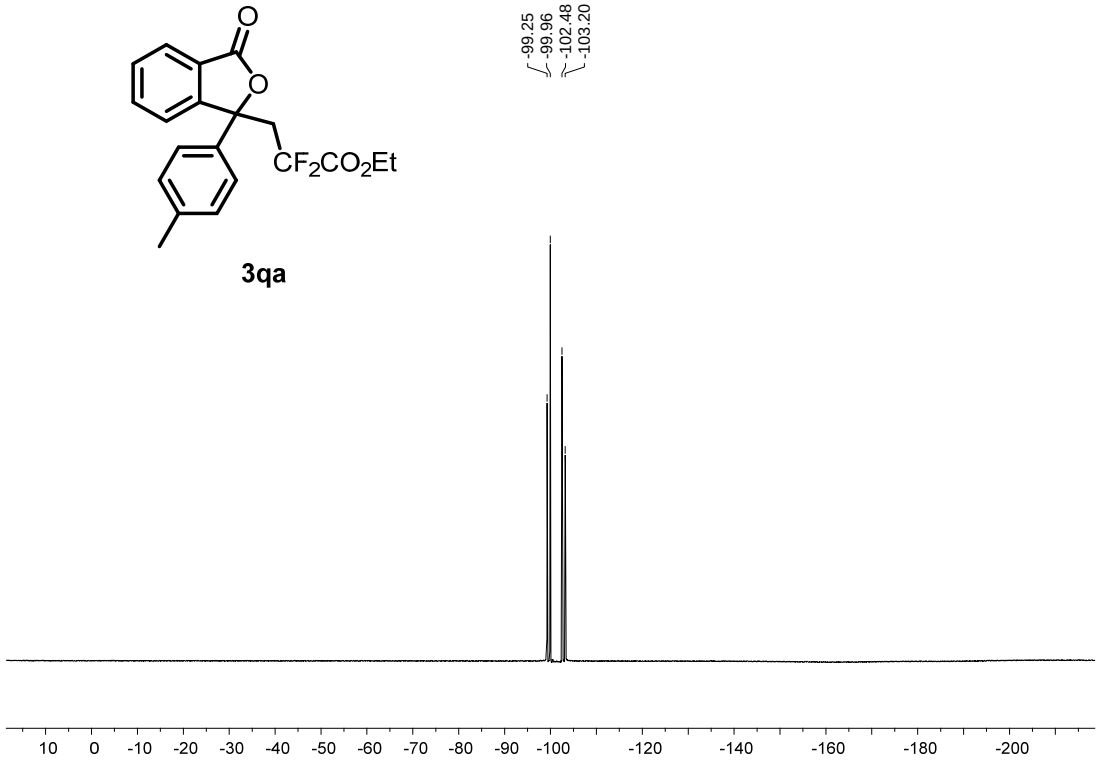
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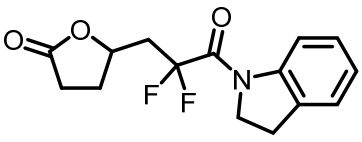

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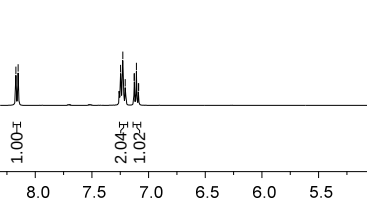

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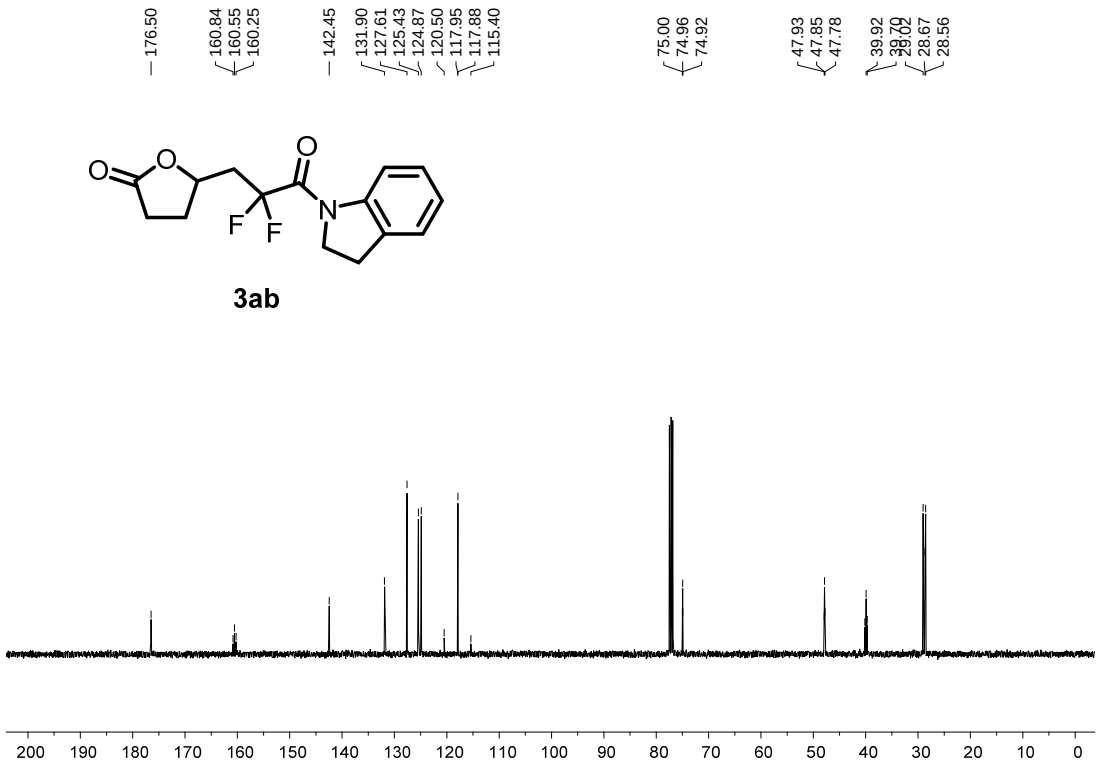
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O
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F
N
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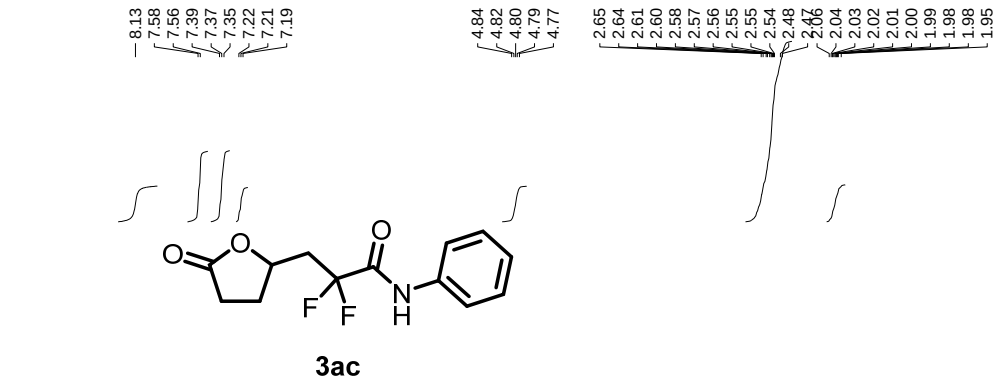
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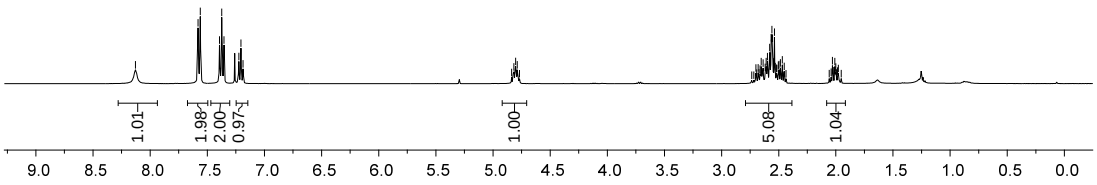
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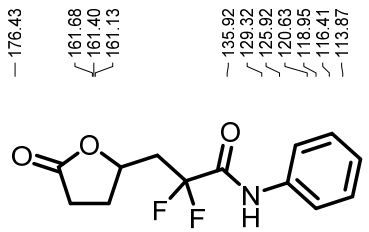
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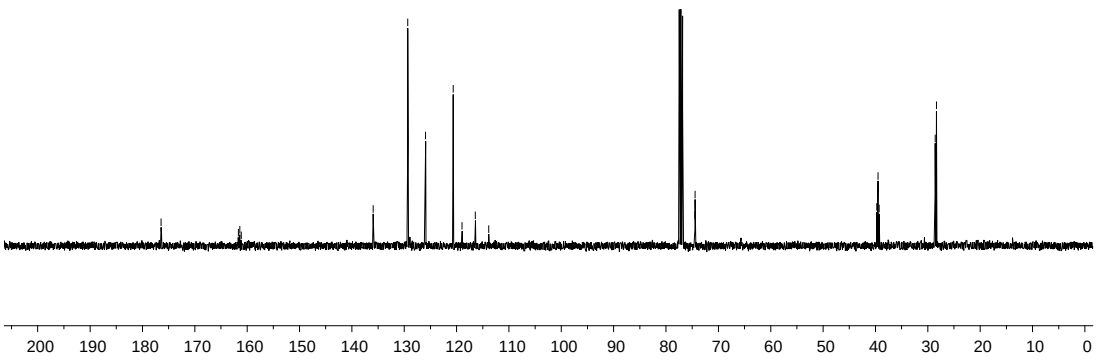
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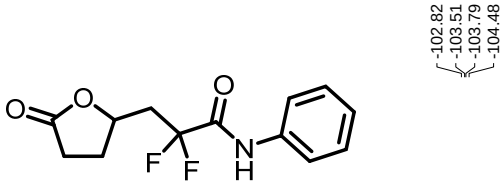
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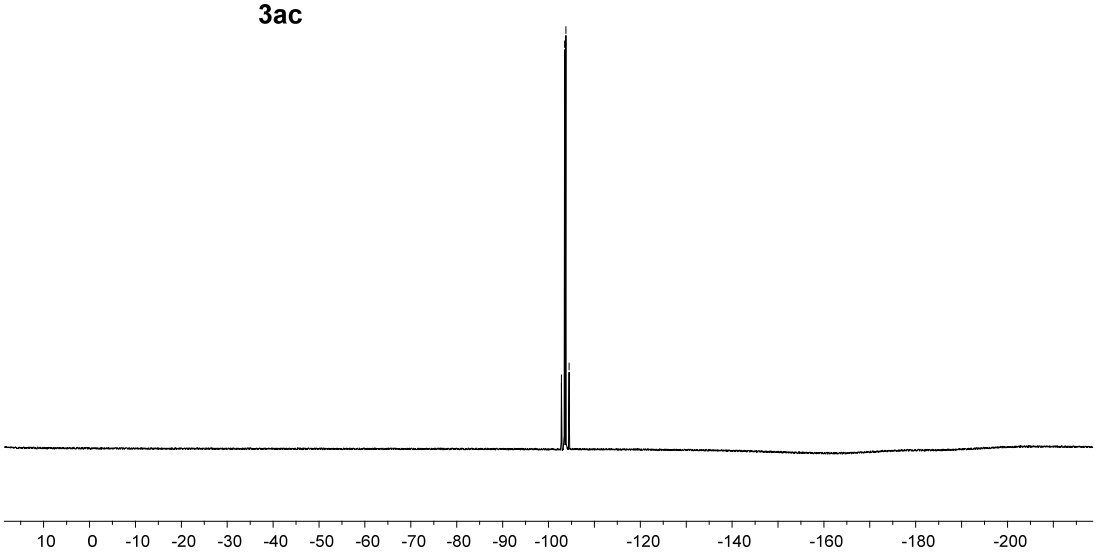
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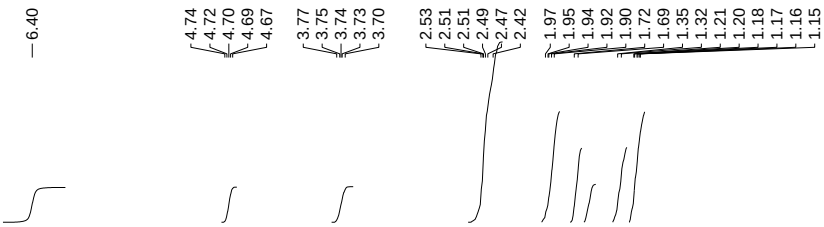
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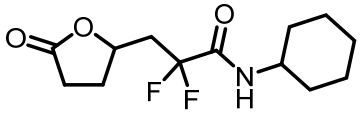
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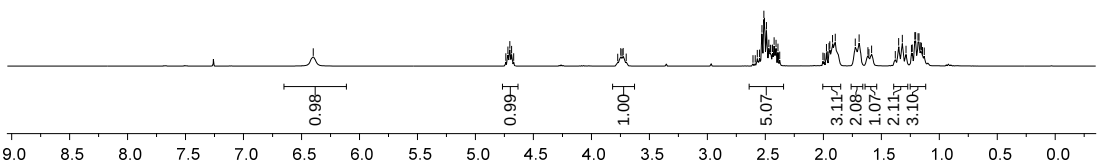
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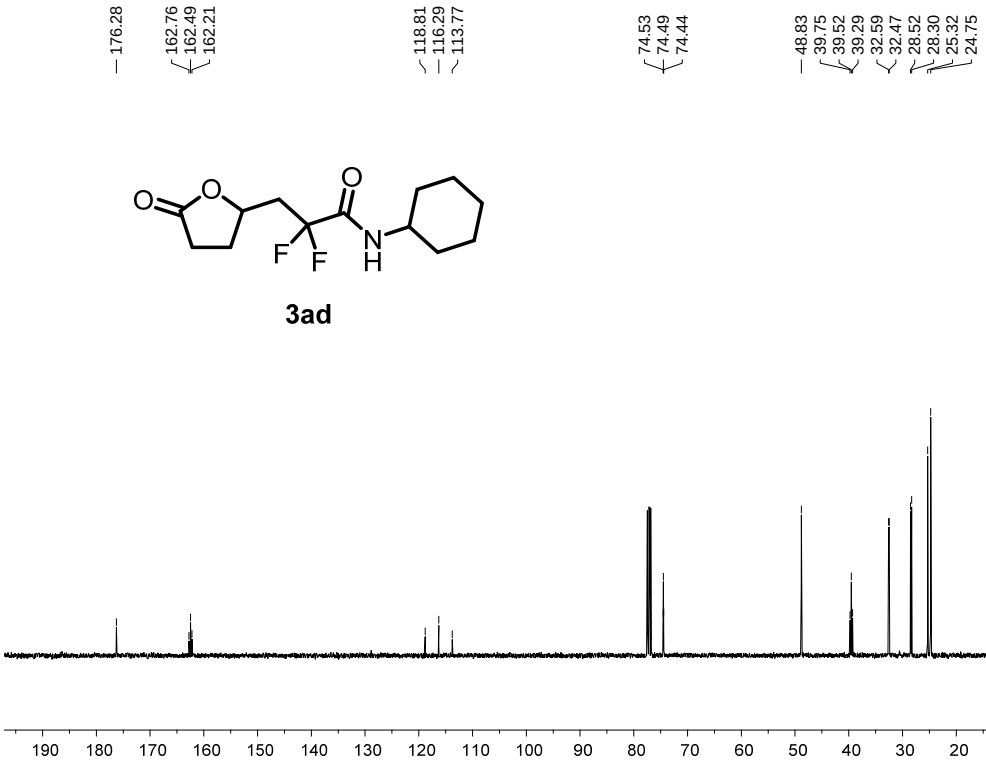
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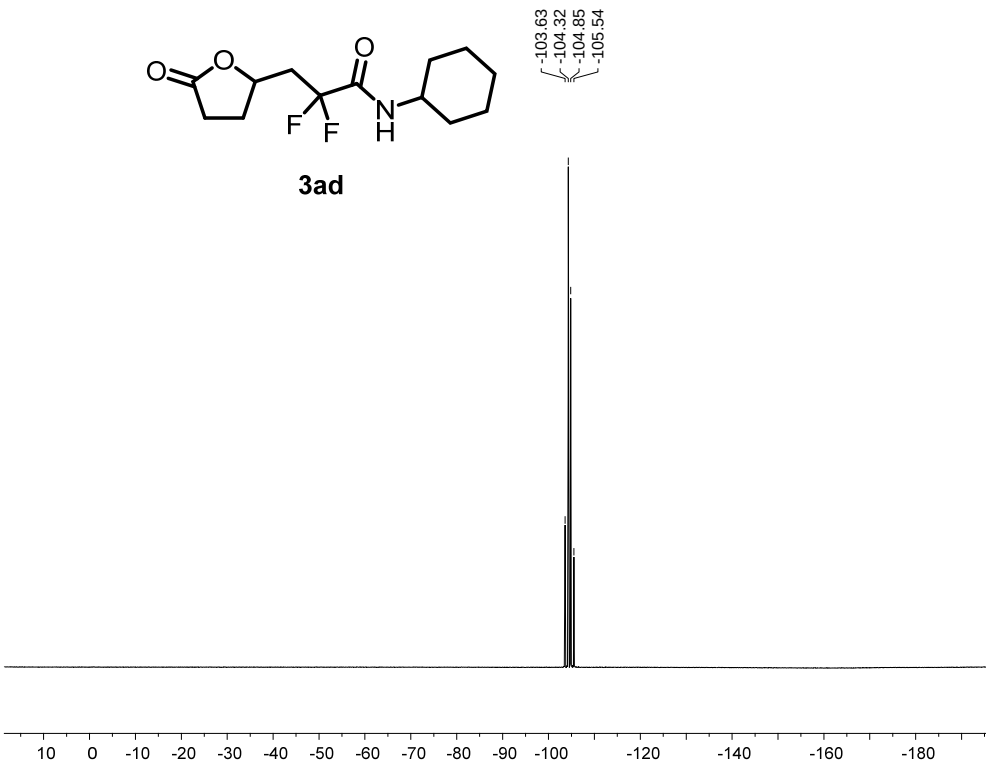
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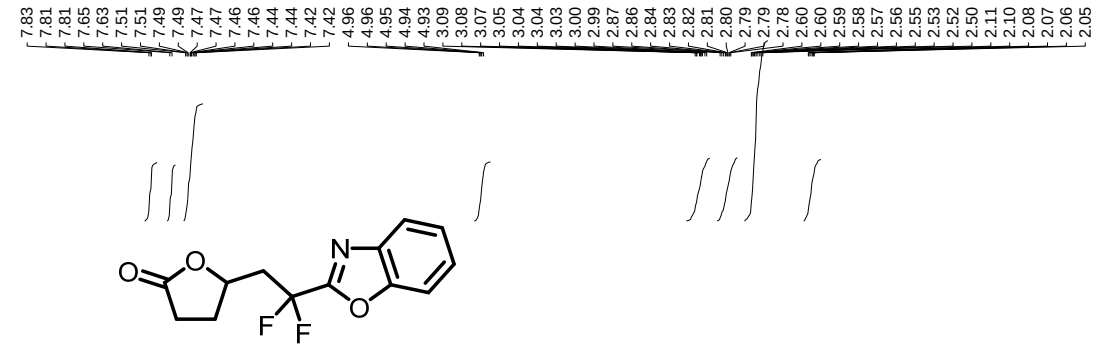
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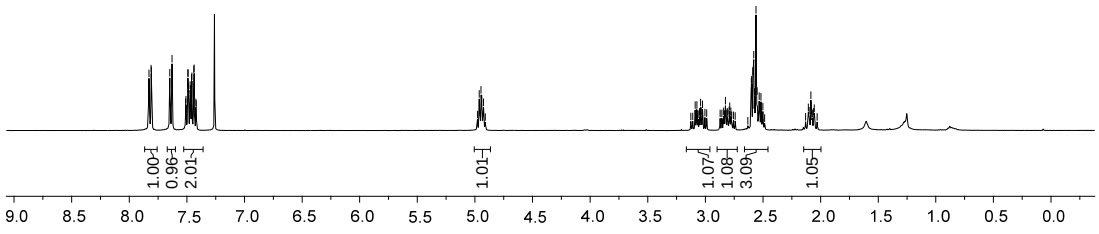
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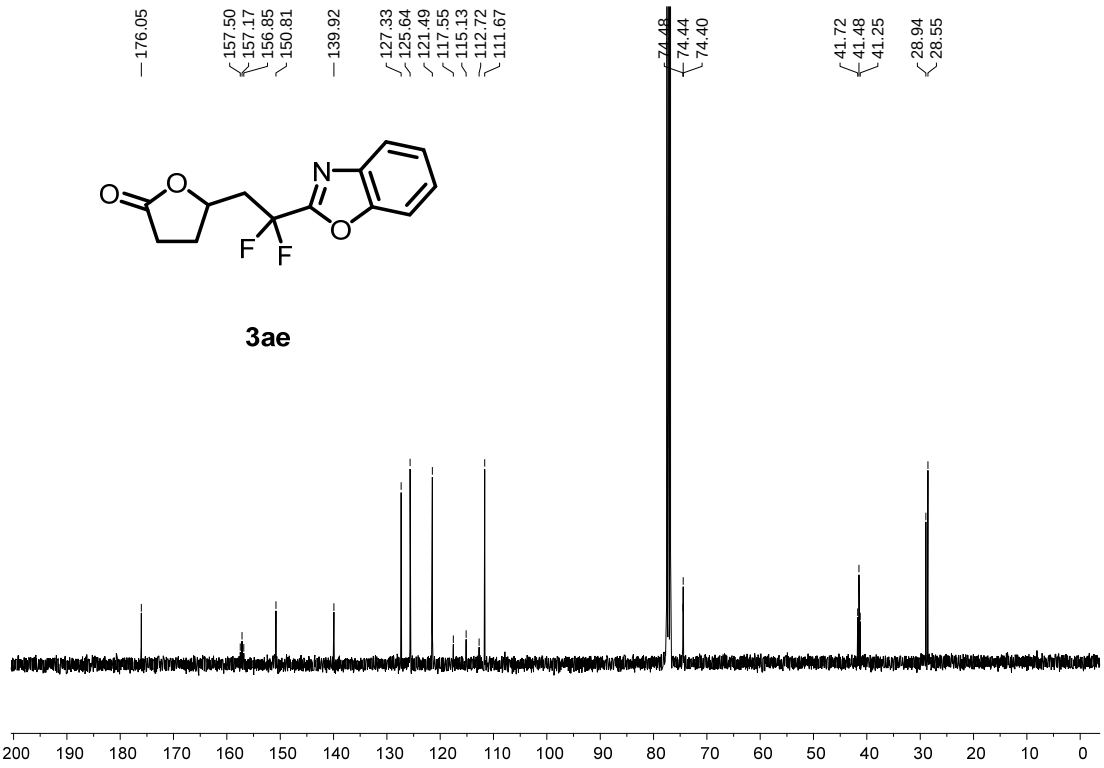
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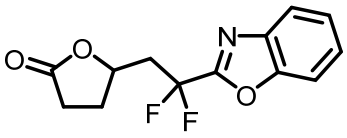
3ae



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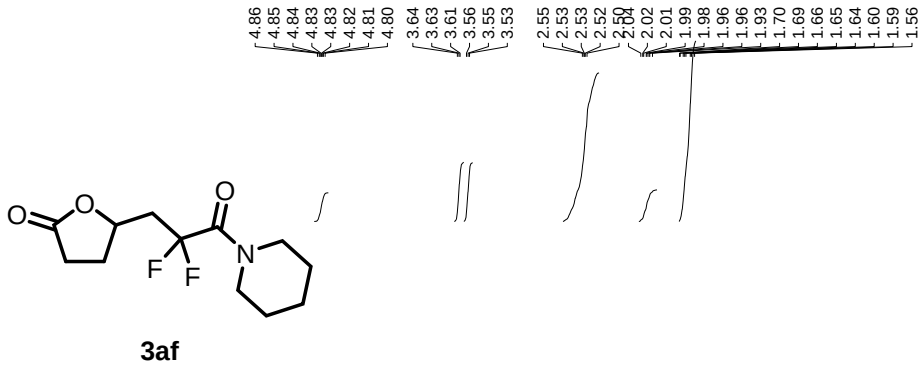

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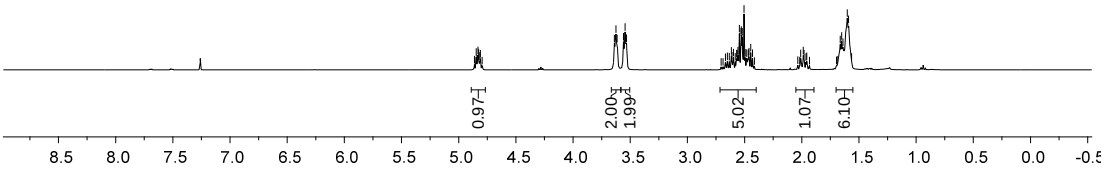

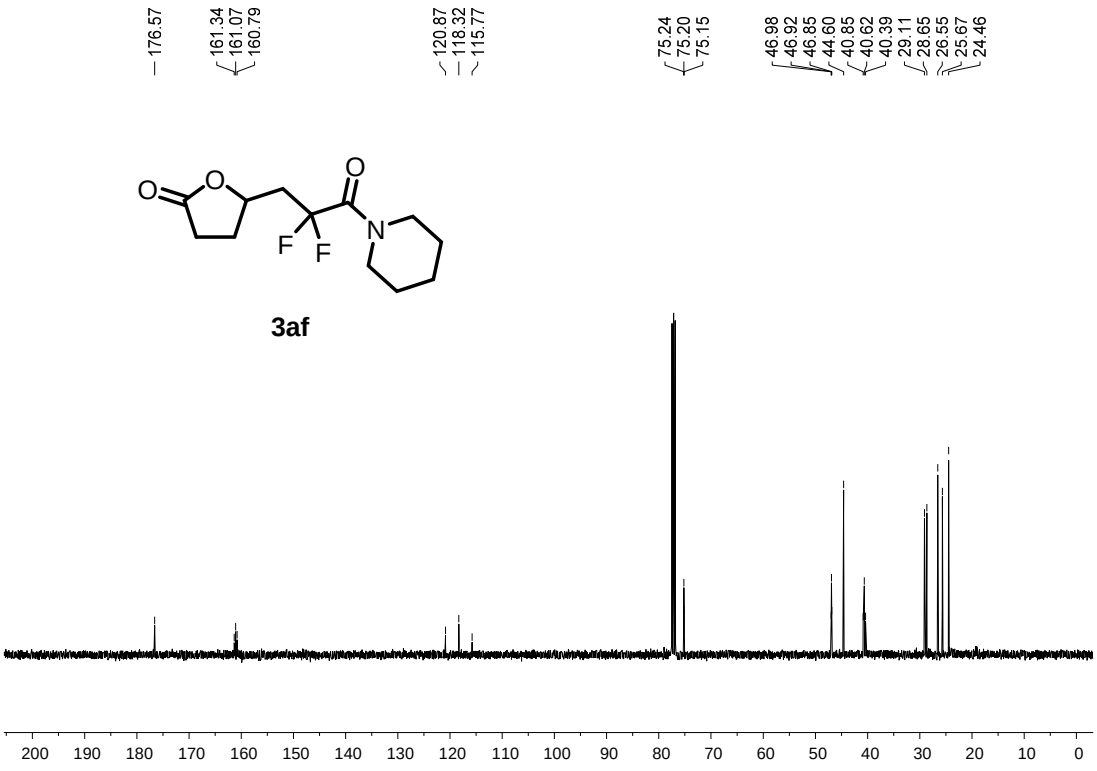
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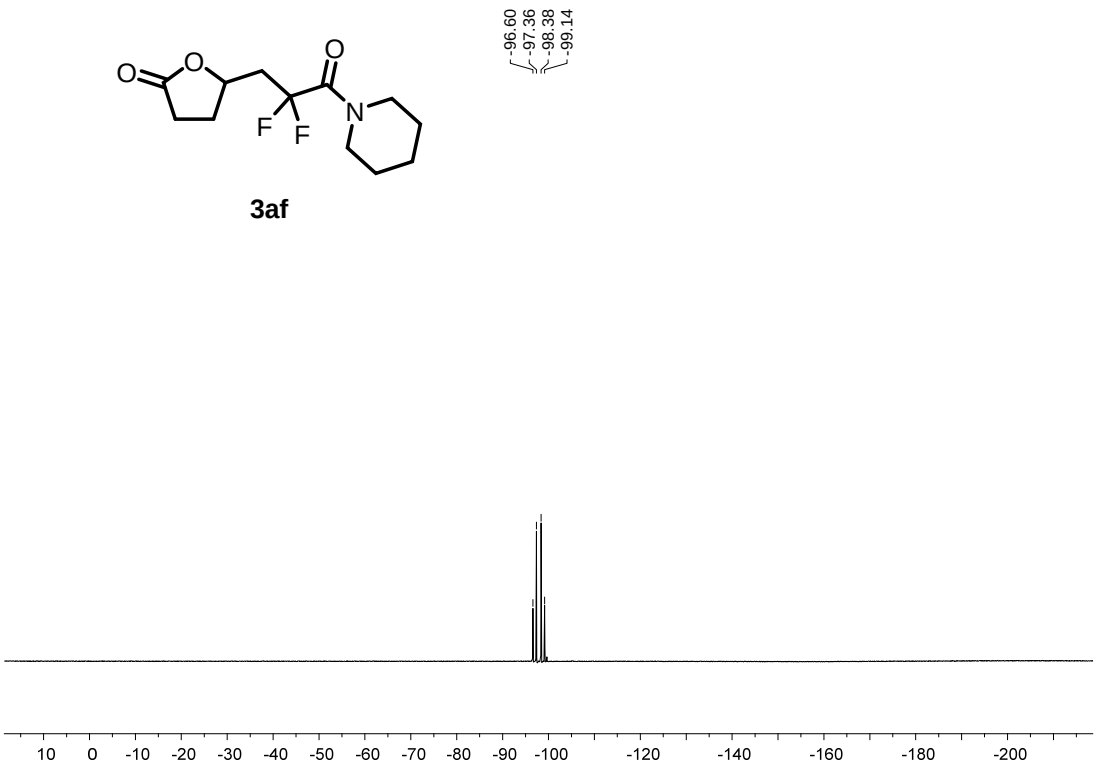
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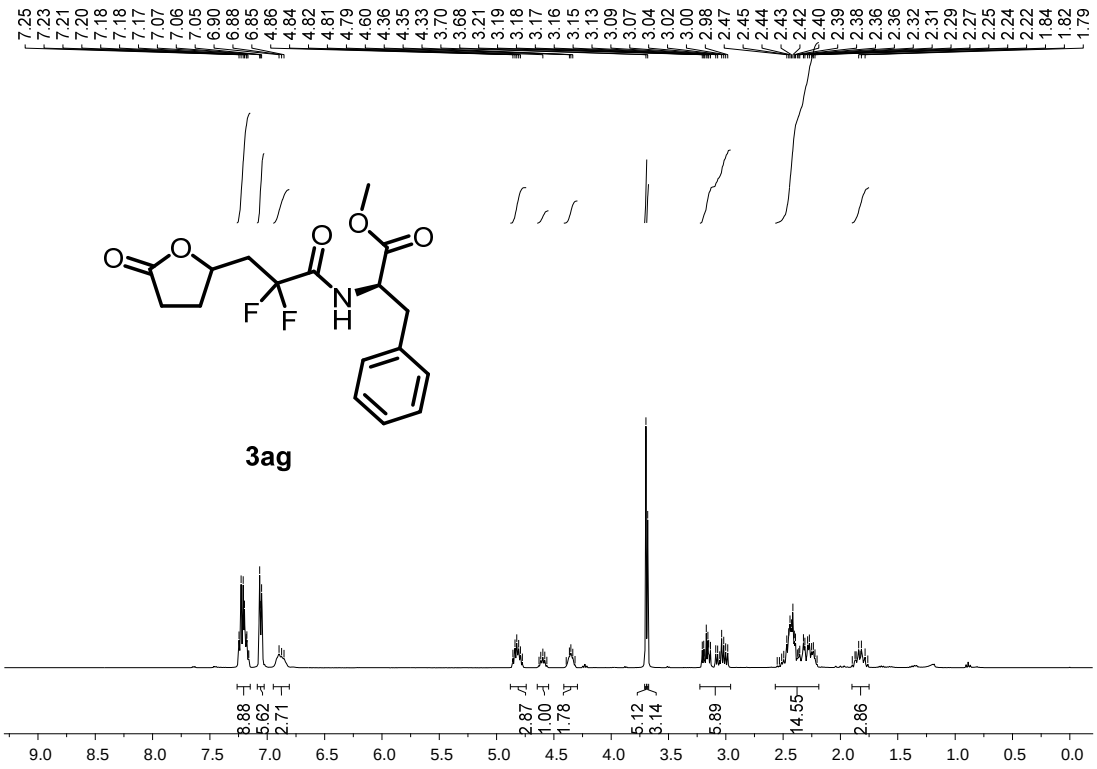
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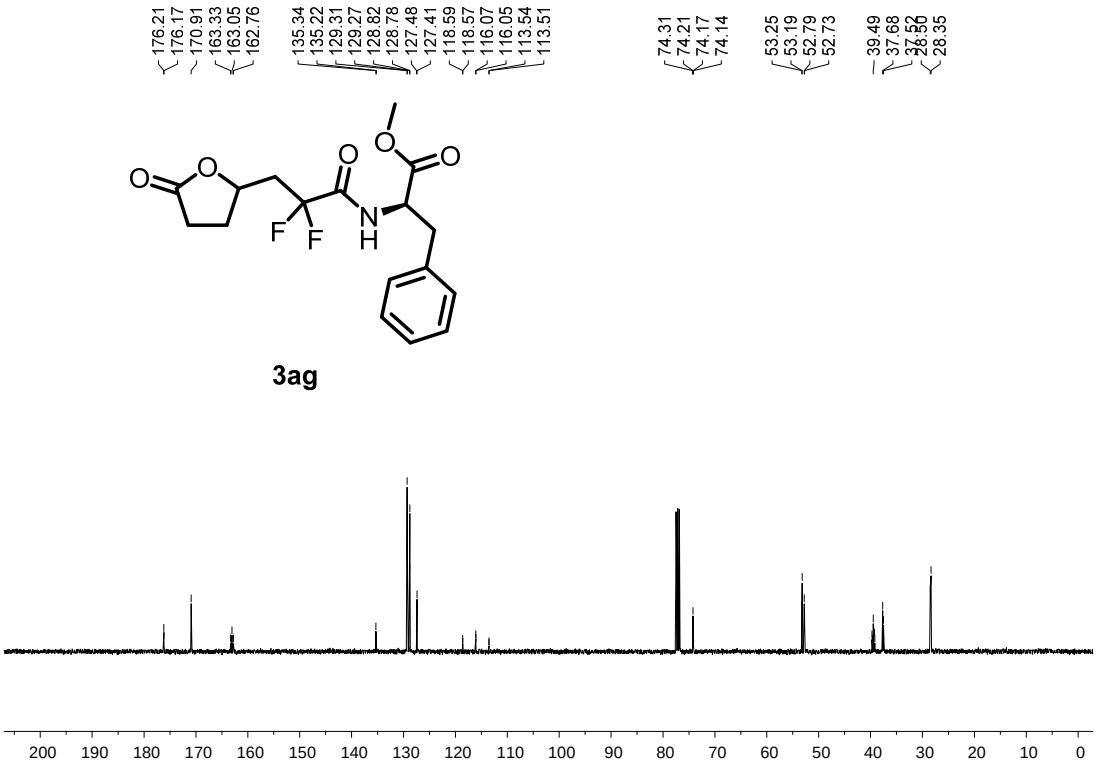
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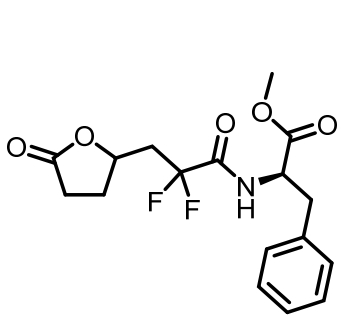

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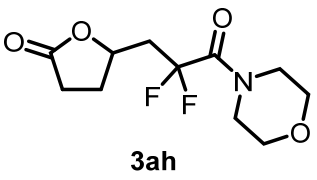

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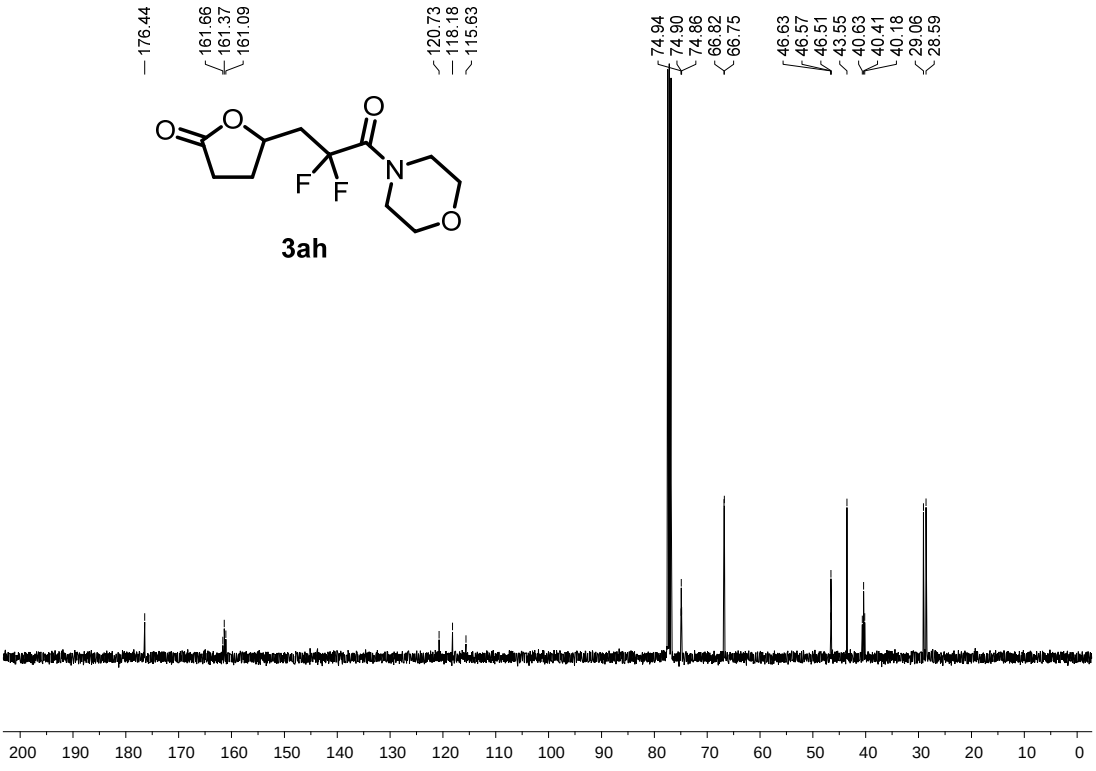
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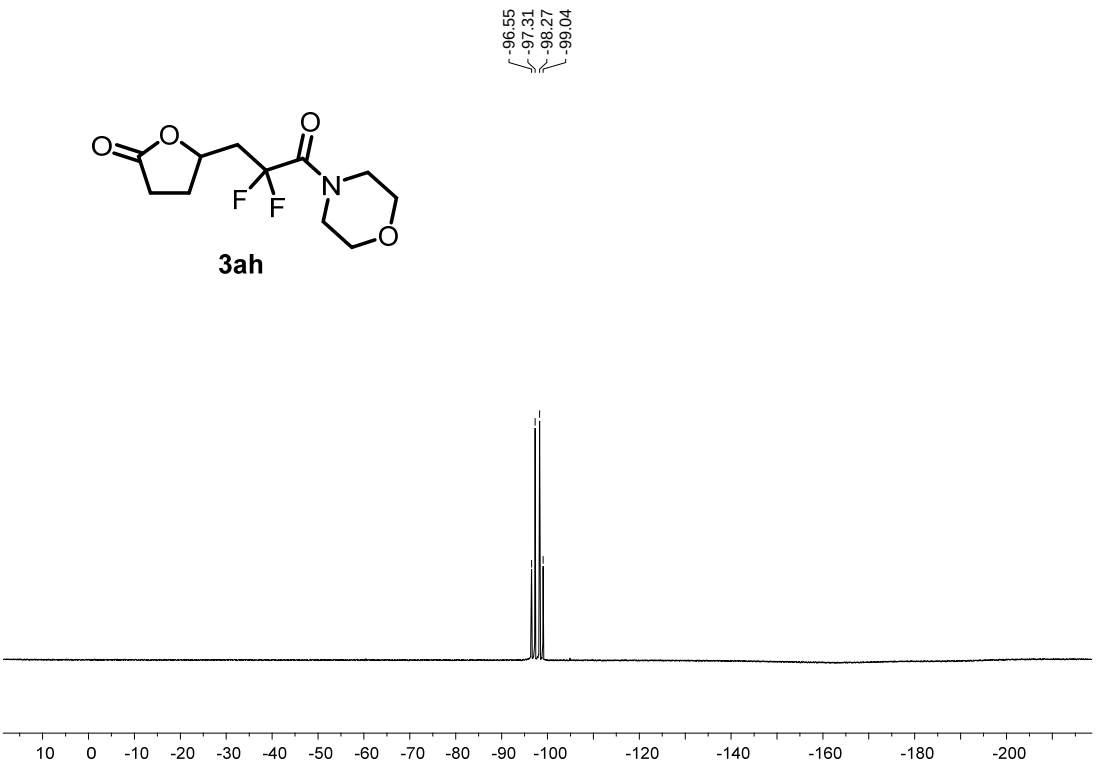
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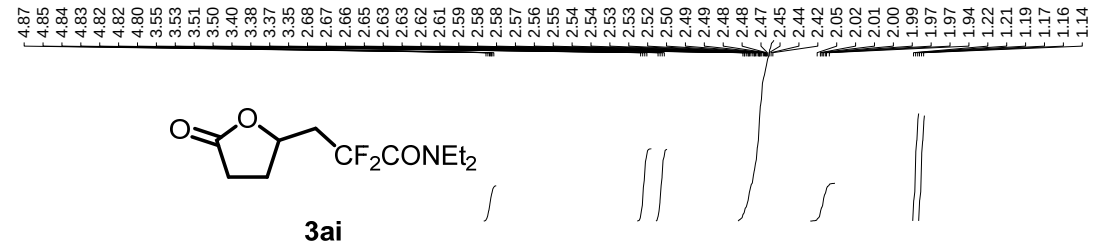
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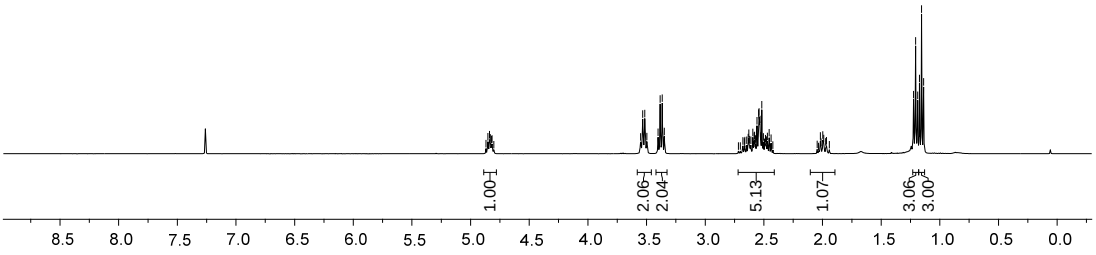
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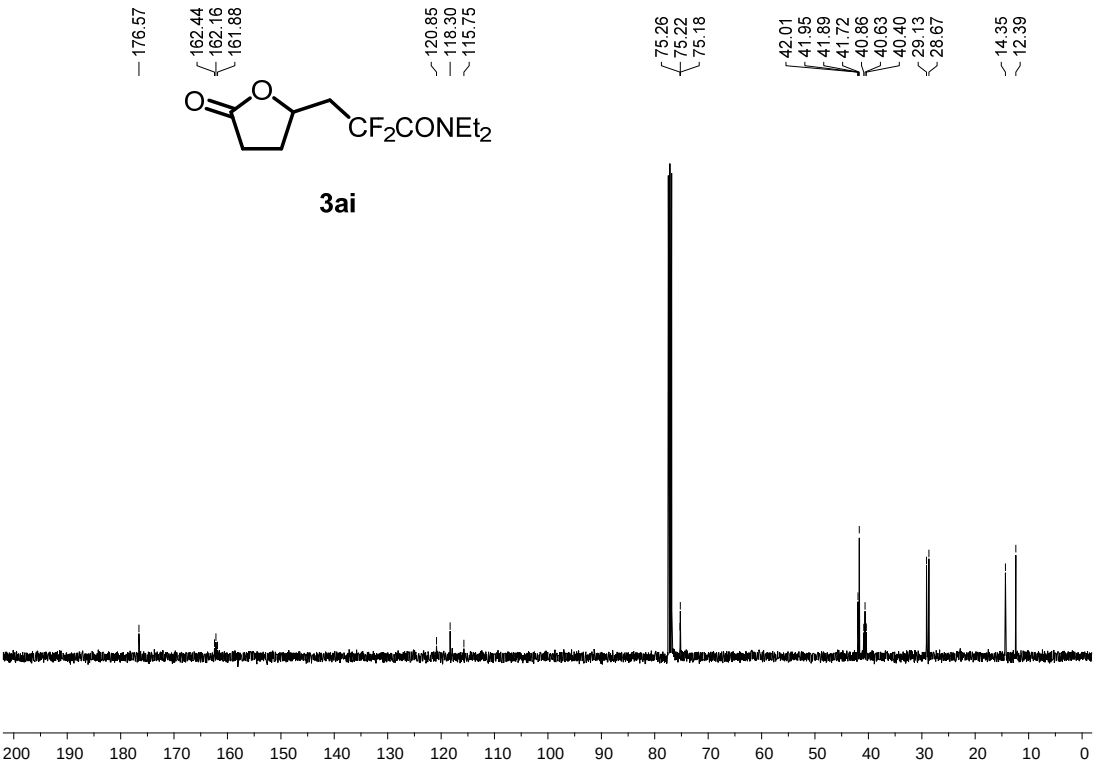
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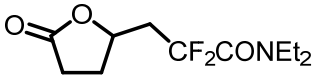
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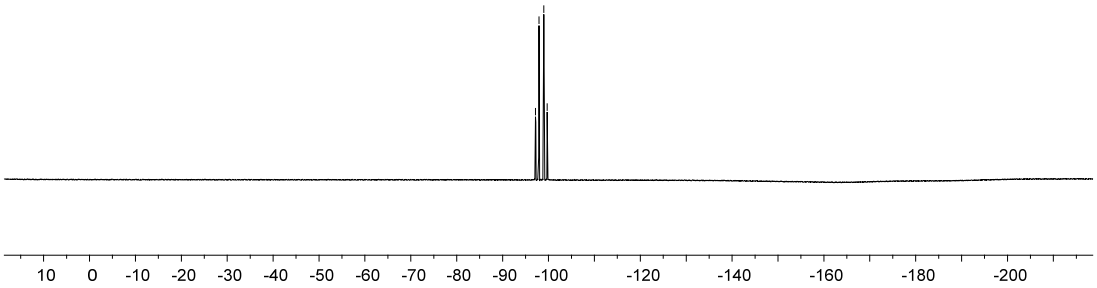
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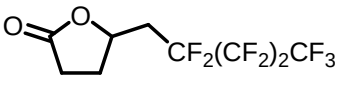
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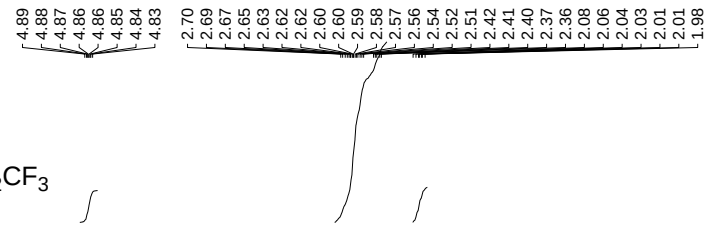
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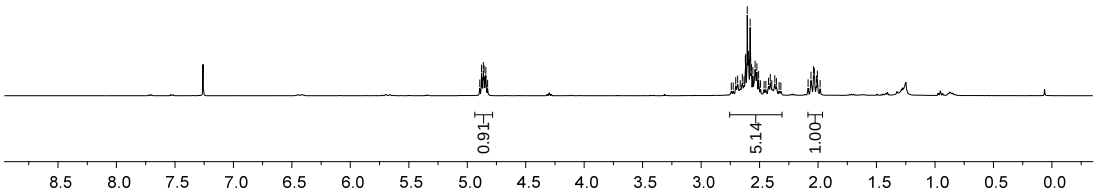
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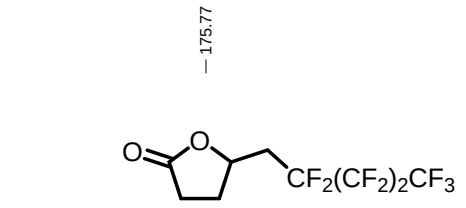
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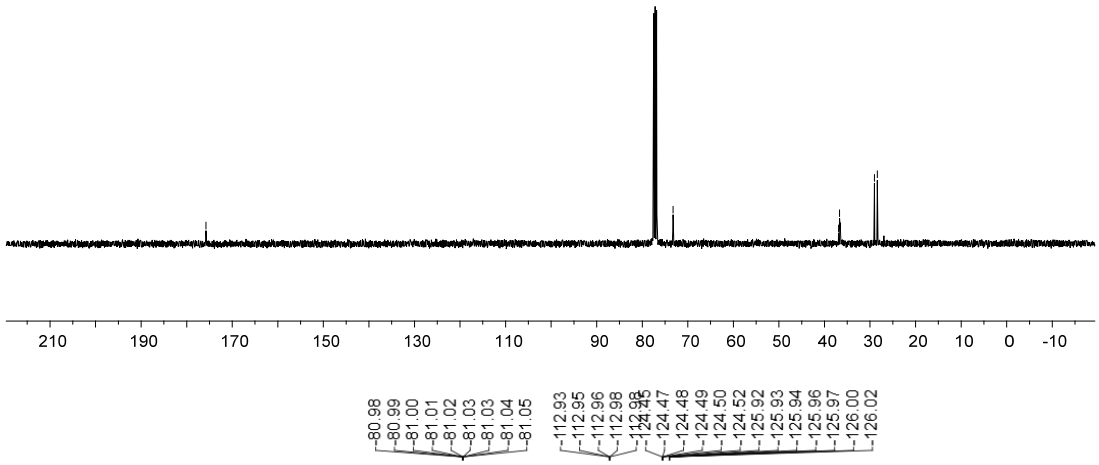
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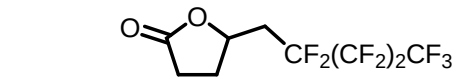
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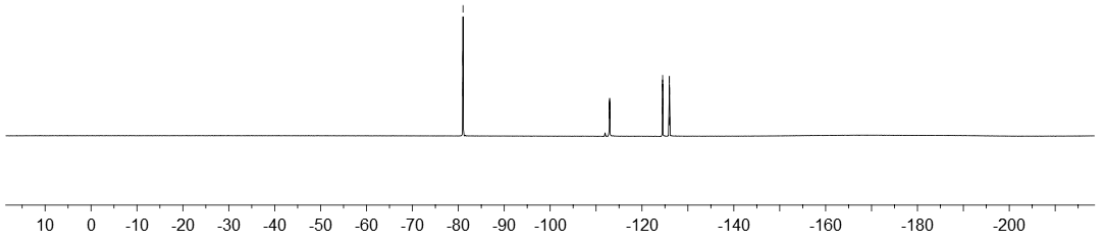
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