Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information for

Halogen-Bond-Promoted Direct Cross-Coupling of Ethyl 3-bromo-3-alkyl-2,2-difluoropropanoate with Coumarins/Quinolinones

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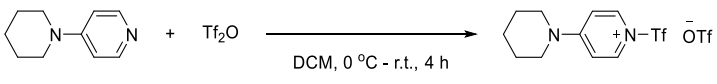
1. General information

^{1}H NMR and ^{13}C NMR spectra were recorded on an Agilent MR400 spectrometer. ^{19}F NMR was recorded on an Agilent MR400 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. NMR yield was determined by ^{19}F NMR using fluorobenzene as an internal standard before working up the reaction. High-resolution mass spectra were recorded on a Thermo Scientific Q Exactive HF with Fourier-transform (orbitrap) mass spectrometer and Agilent Technologies 7250 GCQTOF in laboratory of mass spectrometry analysis at Shanghai Institute of Organic Chemistry. Melting points were taken on a SGW X-4 Melting Point Apparatus. The optical absorption spectra were determined by the Puxi T6 ultraviolet-visible Spectrophotometer.

Materials: All reagents were used as received from commercial sources, unless specified otherwise, or prepared as described in the literature. All reagents were weighed and handled in air at room temperature. LED (390-395 nm, 410-415 nm, 440-445 nm) were purchased from WATTCAS^{TM}, and relevant experiments were performed in a WP-TEC-1020SL parallel reactor from WATTCAS^{TM}.

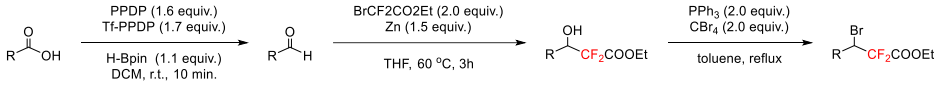
2. General procedure for the synthesis of Ethyl 3-bromo-3-alkyl-2,2-difluoropropanoate



Tf - PPDP

General procedure for the synthesis of Tf - PPDP (**step 1**)[1]. $(CF_3SO_2)_2O$ (16.1 mL, 96.0 mmol, 1.2 equiv.) was added into a solution of 4-piperidin-1-ylpyridine

(13.0 g, 80.0 mmol, 1.0 equiv.) in DCM (120.0 mL) at 0 ºC. After addition is completed, the mixture was warmed to room temperature and stirred for 4 h. Upon completion, 80 mL of n-hexane was added and the crude product then precipitated out of the solution. The solid was filtered and washed with hexane (100 mL × 2), then the pure product was obtained as a white powder after dried under reduced pressure (28.8 g, 81%).



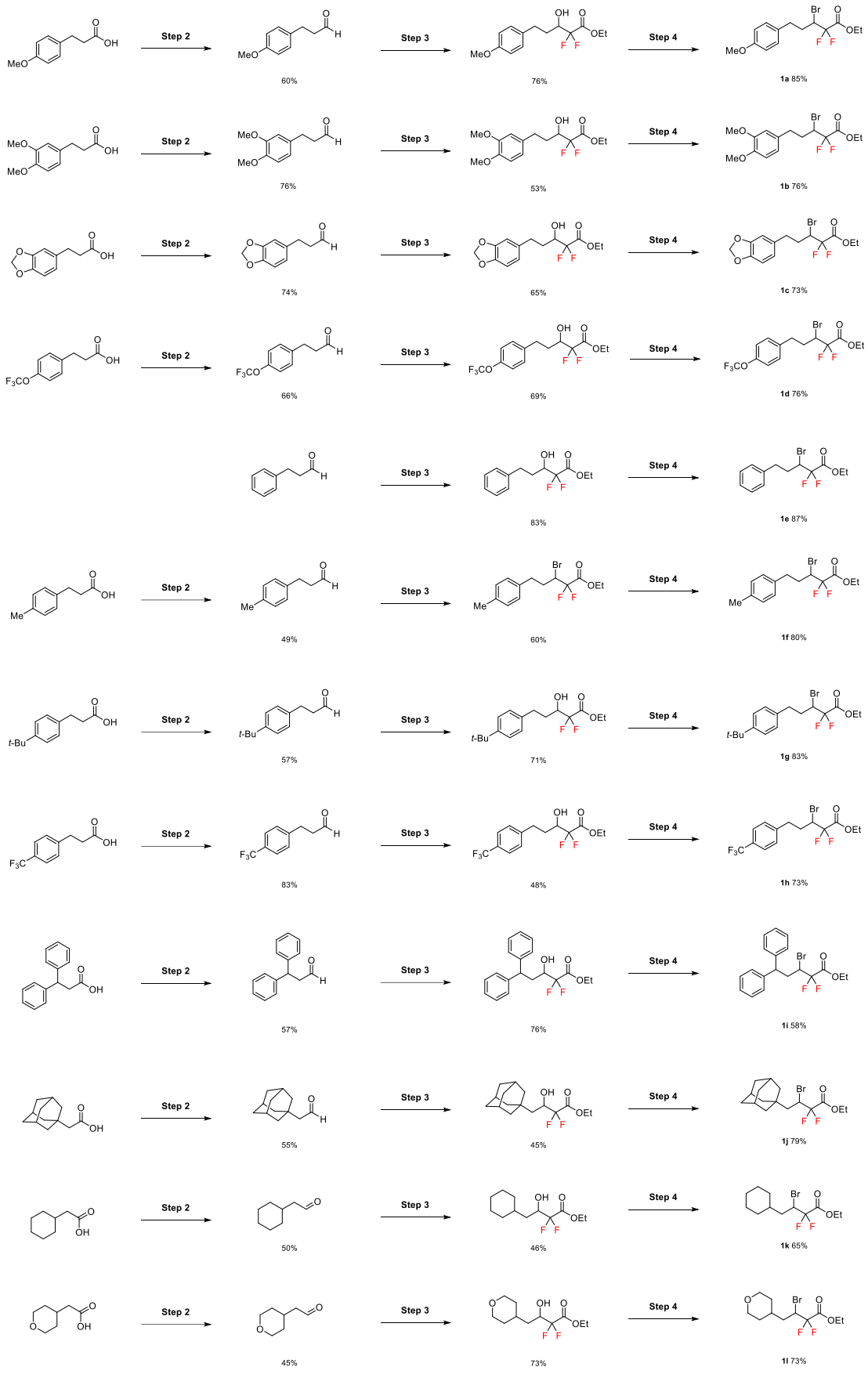
Alkyl carboxylic acids | Alkyl aldehydes | Ethyl 3-alkyl-3-hydroxyl-2,2-difluoro-propanoate | Ethyl 3-bromo-3-alkyl-2,2-difluoropropanoate

General procedure for the synthesis of alkyl aldehydes (**step 2**) [1]. To a 100 mL schlenk tube equipped with a magnetic stirring bar, alkyl carboxylic acid (4.0 mmol, 1.0 equiv.), PPDP (6.4 mmol, 1.6 equiv.) and DCM (50.0 mL) were added in air, followed by Tf-PPDP (6.8 mmol, 1.7 equiv.) and HBpin (4.4 mmol, 1.1 equiv.). After the reaction was stirred for 10 min, the crude mixture was quenched by H_2O and extracted by DCM (3 x 20.0 mL). The combined organic layers were dried over anhydrous Na_2SO_4. After the solvent was removed under reduced pressure, the resulting residue was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate to afford the desired alkyl aldehydes.

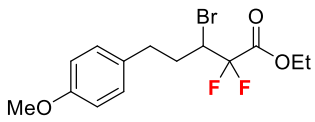
General procedure for the synthesis of ethyl 3-alkyl-3-hydroxyl-2,2-difluoro-propanoate (**step 3**) [2]. Ethyl bromodifluoroacetate (5 mmol, 2.0 equiv) was added to a mixture of zinc dust (3.75 mmol, 1.5 equiv) in THF (7 mL) at room temperature under an argon atmosphere. After stirred for 5 min, alkyl aldehydes (2.5 mmol, 1.0 equiv) was added subsequently and the mixtures were refluxed for 3 h. After cooling down to room temperature, the reaction was quenched with sat. NH_4Cl solution (7 mL). The aqueous layer was extracted with Et_2O (15 mL × 3). The combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After the solvent was removed under reduced pressure, the

resulting residue was purified by flash column chromatography on silica gel and eluted with petroleum ether/ethyl acetate to afford the pure product.

General procedure for the synthesis of ethyl 3-bromo-3-alkyl-2,2-difluoropropanoate (**step 4**) [3]. To a solution of ethyl ethyl 3-alkyl-3-hydroxyl-2,2-difluoro-propanoate (1.0 mmol, 1.0 equiv) and PPh_3 (2.0 mmol, 2.0 equiv) in toluene (10.0 mL), tetrabromomethane (2.0 mmol, 2.0 equiv) was added in one portion. The mixture was refluxed at 110 °C for 3 h. After cooling down to room temperature, the reaction was quenched with H_2O (30 mL). The mixtures was extracted with EtOAc (20 mL × 3). The combined organic layers were washed with brine (30 mL), dried over anhydrous Na_2SO_4 and concentrated. The pure product was obtained by flash chromatography on silica gel.

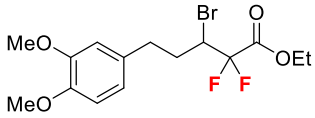

Step 2
Step 3
Step 4
60%
76%
1a 85%
76%
53%
1b 76%
74%
65%
1c 73%
66%
69%
1d 76%
83%
1e 87%
49%
60%
1f 80%
57%
71%
1g 83%
83%
48%
1h 73%
57%
76%
1i 58%
55%
45%
1j 79%
50%
46%
1k 65%
45%
73%
1l 73%

ethyl 3-bromo-2,2-difluoro-5-(4-methoxyphenyl)pentanoate (1a)



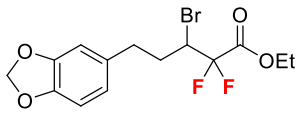
Obtained in 85% yield as a yellow oily liquid (298.5 mg, eluent: PE/EA = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.13 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.0 Hz, 2H), 4.34 (q, J = 7.1 Hz, 2H), 4.21 – 4.11 (m, 1H), 3.80 (s, 3H), 2.99 – 2.93 (m, 1H), 2.73 – 2.65 (m, 1H), 2.31 – 2.23 (m, 1H), 2.20 – 2.10 (m, 1H), 1.34 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.4 (t, J = 32.4 Hz), 158.3, 131.6, 129.5, 114.1, 113.6 (dd, J = 259.1 Hz, J = 254.3 Hz), 63.5, 55.3, 49.3 (dd, J = 28.1 Hz, J = 25.3 Hz), 32.1, 31.8, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.75 (dd, J = 255.3 Hz, J = 9.0 Hz, 1F), -114.95 (dd, J = 254.9 Hz, J = 13.2 Hz, 1F). **HRMS (ESI)**: calculated for $C_{14}H_{17}O_3BrF_2Na$ ([M+Na]$^+$): 373.0221; Found: 373.0220.

ethyl 3-bromo-5-(3,4-dimethoxyphenyl)-2,2-difluoropentanoate (1b)



Obtained in 76% yield as a yellow oily liquid (289.7 mg, eluent: PE/EA = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.80 (d, J = 8.4 Hz, 1H), 6.75 – 6.71 (m, 2H), 4.32 (q, J = 7.2 Hz, 2H), 4.20 – 4.10 (m, 1H), 3.87 (s, 3H), 3.85 (s, 3H), 2.98 – 2.92 (m, 1H), 2.71 – 2.64 (m, 1H), 2.31 – 2.23 (m, 1H), 2.19 – 2.09 (m, 1H), 1.32 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2 (t, J = 32.4 Hz), 149.0, 147.6, 132.0, 120.4, 113.5 (dd, J = 259.1 Hz, J = 254.3 Hz), 111.6, 111.3, 63.4, 55.8 (d, J = 5.5 Hz), 55.7 (d, J = 6.0 Hz), 49.5 – 49.0 (m), 32.2, 31.9, 13.8 (d, J = 1.7 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -104.61 (d, J = 254.9 Hz, 1F), -114.08 (d, J = 254.2 Hz, 1F). **HRMS (ESI)**: calculated for $C_{15}H_{20}O_4BrF_2$ ([M+H]$^+$): 381.0508; Found: 381.0505.

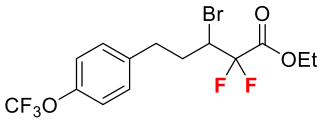
ethyl 5-(benzo[*d*][1,3]dioxol-5-yl)-3-bromo-2,2-difluoropentanoate (1c)



Obtained in 73% yield as a yellow oily liquid (266.6 mg, eluent: PE/EA = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.74 (d, J = 7.6 Hz, 1H), 6.68 – 6.65 (m, 2H), 5.92 (s 2H), 4.34 (q, J = 7.2 Hz, 2H),

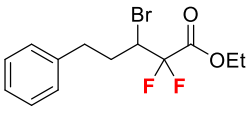
4.21 – 4.12 (m, 1H), 2.95 – 2.89 (m, 1H), 2.69 – 2.62 (m, 1H), 2.29 – 2.20 (m, 1H), 2.17 – 2.08 (m, 1H), 1.33 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 162.2 (t, *J* = 32.4 Hz), 147.9, 146.2, 133.2, 121.4, 113.6 (dd, *J* = 258.9 Hz, *J* = 254.2 Hz), 108.8, 108.4, 100.9, 63.4, 49.5 – 48.9 (m), 32.4, 32.0, 13.8 (d, *J* = 2.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -104.93 (d, *J* = 255.3 Hz, 1F), -113.82 (d, *J* = 255.7 Hz, 1F). **HRMS (ESI)**: calculated for $C_{14}H_{16}O_4BrF_2$ ($[M+H]^+$): 365.0195; Found: 365.0191.

ethyl 3-bromo-2,2-difluoro-5-(4-(trifluoromethoxy)phenyl)pentanoate (1d)



Obtained in 76% yield as a yellow oily liquid (307.9 mg, eluent: PE/EA = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.25 (d, *J* = 8.8 Hz, 2H), 7.17 (d, *J* = 8.4 Hz, 2H), 4.35 (q, *J* = 7.2 Hz, 2H), 4.25 – 4.15 (m, 1H), 3.06 – 3.00 (m, 1H), 2.81 – 2.73 (m, 1H), 2.36 – 2.27 (m, 1H), 2.23 – 2.13 (m, 1H), 1.33 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 162.3 (t, *J* = 32.4 Hz), 148.0 (q, *J* = 3.7 Hz), 138.6, 129.9, 121.3, 120.6 (q, *J* = 257.5 Hz), 113.6 (dd, *J* = 259.2 Hz, *J* = 254.2 Hz), 63.5, 49.4 – 48.8 (m), 32.2, 31.9, 13.7 (d, *J* = 2.2 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -57.96 - -58.06 (m, 3F), -105.06 (d, *J* = 256.1 Hz, 1F), -114.26 (d, *J* = 256.4 Hz, 1F). **HRMS (ESI)**: calculated for $C_{14}H_{15}O_3BrF_5$ ($[M+H]^+$): 405.0119; Found: 405.0119.

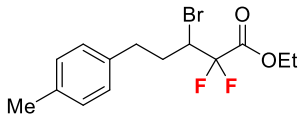
ethyl 3-bromo-2,2-difluoro-5-phenylpentanoate (1e)



This compound is known[4].Obtained in 87% yield as a yellow oily liquid (279.4 mg, eluent: PE/EA = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.37 – 7.33 (m, 2H), 7.29 – 7.24 (m, 3H), 4.36 (q, *J* = 7.2 Hz, 2H), 4.28 – 4.18 (m, 1H), 3.09 – 3.02 (m, 1H), 2.82 – 2.74 (m, 1H), 2.40 – 2.31 (m, 1H), 2.27 – 2.17 (m, 1H), 1.35 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 162.3 (t, *J* = 32.4 Hz), 139.7, 128.8 - 128.7 (m), 128.5, 126.7 - 126.5 (m), 113.6 (dd, *J* = 259.2 Hz, *J* = 254.1 Hz), 63.5, 49.7 – 49.0 (m), 32.8, 31.9,

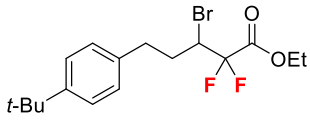
13.9 (d, *J* = 7.2 Hz).

ethyl 3-bromo-2,2-difluoro-5-(*p*-tolyl)pentanoate (1f)



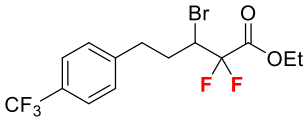
Obtained in 80% yield as a yellow oily liquid (268.2 mg, eluent: PE/EA = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.19 (dd, *J* = 10.4 Hz, *J* = 8.4 Hz, 4H), 4.39 (q, *J* = 7.2 Hz, 2H), 4.32 – 4.23 (m, 1H), 3.09 – 3.02 (m, 1H), 2.82 – 2.75 (m, 1H), 2.41 – 2.33 (m, 4H), 2.29 – 2.20 (m, 1H), 1.39 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 162.2 (t, *J* = 32.5 Hz), 136.5, 136.0, 129.4, 128.4, 113.6 (dd, *J* = 258.9 Hz, *J* = 254.2 Hz), 63.4, 49.7 – 49.1 (m), 32.2, 31.0, 20.9 (d, *J* = 3.2 Hz), 13.8 (d, *J* = 2.6 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -106.30 (dd, *J* = 255.3 Hz, *J* = 9.8 Hz, 1F), -113.11 (dd, *J* = 255.3 Hz, *J* = 13.9 Hz, 1F). **HRMS (ESI)**: calculated for $C_{14}H_{17}BrO_2BrF_2Na$ ([M+Na]$^+$): 357.0272; Found: 357.0269.

ethyl 3-bromo-5-(4-(*tert*-butyl)phenyl)-2,2-difluoropentanoate (1g)



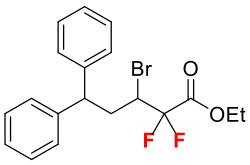
Obtained in 83% yield as a yellow oily liquid (313.13 mg, eluent: PE/EA = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.44 (d, *J* = 8.0 Hz, 2H), 7.25 (d, *J* = 8.0 Hz, 2H), 4.41 (q, *J* = 7.2 Hz, 2H), 4.38 – 4.28 (m, 1H), 3.12 – 3.05 (m, 1H), 2.86 – 2.78 (m, 1H), 2.45 – 2.37 (m, 1H), 2.33 – 2.23 (m, 1H), 1.43 (s, 9H), 1.40 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 162.2 (t, *J* = 32.4 Hz), 149.3, 136.5, 128.2, 125.6, 113.6 (dd, *J* = 259.1 Hz, *J* = 254.4 Hz), 63.3, 49.5 (t, *J* = 26.3 Hz), 34.4, 32.2, 32.0, 30.4, 13.8 (d, *J* = 2.4 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -106.49 (dd, *J* = 257.9 Hz, *J* = 10.5 Hz, 1F), -112.85 (dd, *J* = 255.3 Hz, *J* = 13.2 Hz, 1F). **HRMS (ESI)**: calculated for $C_{17}H_{23}BrO_2BrF_2Na$ ([M+Na]$^+$): 399.0742; Found: 399.0741.

ethyl 3-bromo-2,2-difluoro-5-(4-(trifluoromethyl)phenyl)pentanoate (1h)



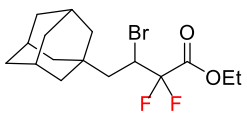
Obtained in 73% yield as a yellow oily liquid (284.1 mg, eluent: PE/EA = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (d, J = 8.0 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 4.35 (q, J = 7.2 Hz, 2H), 4.24 – 4.14 (m, 1H), 3.11 – 3.04 (m, 1H), 2.86 – 2.78 (m, 1H), 2.39 – 2.30 (m, 1H), 2.25 – 2.15 (m, 1H), 1.33 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2 (t, J = 32.3 Hz), 143.9, 129.0 (d, J = 5.1 Hz), 128.9 (q, J = 35.9 Hz), 125.7, 124.4 (q, J = 273.1 Hz), 113.6 (dd, J = 259.4 Hz, J = 254.4 Hz), 63.6, 49.0 (td, J = 26.6 Hz, J = 6.8 Hz), 32.7, 31.7 13.8 (d, J = 3.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -62.29 - -62.38 (m, 3H), -104.83 (dd, J = 256.8 Hz, J = 7.5 Hz, 1F), -114.31 (d, J = 255.7 Hz, 1F). **HRMS (ESI)**: calculated for $C_{14}H_{18}BrO_2NBrF_5$ ($[M+NH_4]^+$): 406.0436; Found: 406.0437.

ethyl 3-bromo-2,2-difluoro-5,5-diphenylpentanoate (1i)



Obtained in 58% yield as a yellow oily liquid (230.4 mg, eluent: PE/EA = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.45 – 7.26 (m, 10H), 4.46 (dd, J = 12.0 Hz, J = 3.6 Hz, 1H), 4.38 (q, J = 7.2 Hz, 2H), 4.21 – 4.11 (m, 1H), 2.95 – 2.88 (m, 1H), 2.67 – 2.59 (m, 1H), 1.36 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2 (t, J = 32.4 Hz), 143.7, 141.4, 129.1, 128.7, 128.2, 127.6, 127.2, 126.7, 113.6 (dd, J = 259.3 Hz, J = 254.5 Hz), 63.5, 49.0 – 48.4 (m), 48.0, 36.1, 13.8 (d, J = 2.4 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -106.88 (dd, J = 255.7 Hz, J = 10.9 Hz, 1F), -111.87 (dd, J = 256.1 Hz, J = 14.3 Hz, 1F). **HRMS (ESI)**: calculated for $C_{19}H_{19}O_2BrF_2Na$ ($[M+Na]^+$): 419.0429; Found: 419.0425.

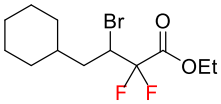
ethyl 4-((3*r*,5*r*,7*r*)-adamantan-1-yl)-3-bromo-2,2-difluorobutanoate (1j)



Obtained in 79% yield as a yellow oily liquid (288.5 mg, eluent: PE/EA = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.33 (q, J = 7.1 Hz, 2H), 4.29 – 4.22 (m, 1H), 1.96 – 1.89 (m, 4H), 1.81 – 1.75 (m, 1H), 1.71 – 1.60 (m, 7H), 1.55 (s, 5H), 1.34 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz,

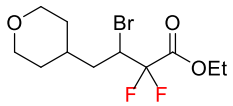
$CDCl_3$) δ 162.5 (t, J = 32.5 Hz), 114.0 (dd, J = 258.9 Hz, J = 254.0 Hz), 63.4, 44.9, 43.4 – 42.8 (m), 42.3, 36.8, 32.3, 28.5, 13.9 (d, J = 3.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.46 (d, J = 254.2 Hz, 1F), -113.99 (dd, J = 253.8 Hz, J = 10.1 Hz, 1F). **HRMS (ESI)**: calculated for $C_{16}H_{23}O_2BrF_2Na$ ([M+Na]$^+$): 387.0742; Found: 387.0740.

ethyl 3-bromo-4-cyclohexyl-2,2-difluorobutanoate (1k)



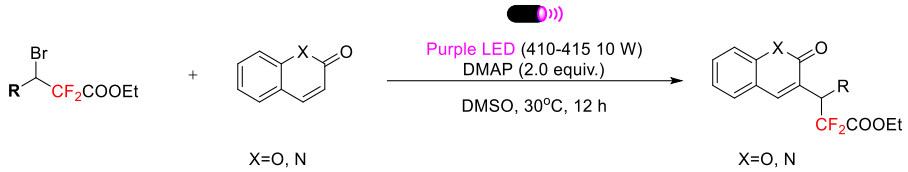
Obtained in 65% yield as a yellow oily liquid (206.8 mg, eluent: PE/EA = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.33 (q, J = 7.1 Hz, 2H), 4.30 – 4.26 (m, 1H), 1.84 – 1.53 (m, 8H), 1.33 (t, J = 7.0 Hz, 3H), 1.28 – 0.96 (m, 4H), 0.79 (qd, J = 11.9 Hz, J = 2.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.4 (t, J = 32.5 Hz), 113.7 (dd, J = 258.8 Hz, J = 253.9 Hz), 63.4, 48.2 – 47.6 (m), 37.3, 34.6, 33.9, 31.1, 26.4, 26.2, 25.8, 13.9 (d, J = 3.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -106.01 (d, J = 254.5 Hz, 1F), -115.68 (dd, J = 254.5 Hz, J = 14.3 Hz, 1F). **HRMS (ESI)**: calculated for $C_{12}H_{20}O_2BrF_2$([M+H]$^+$): 313.0609; Found: 313.0606.

ethyl 3-bromo-2,2-difluoro-4-(tetrahydro-2*H*-pyran-4-yl)butanoate (1l)



Obtained in 73% yield as a yellow oily liquid (230.1 mg, eluent: PE/EA = 40:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.30 (q, J = 7.2 Hz, 2H), 4.27 – 4.22 (m, 1H), 3.93 – 3.87 (m, 2H), 3.38 – 3.29 (m, 2H), 1.88 – 1.68 (m, 3H), 1.62 – 1.53 (m, 2H), 1.40 – 1.32 (m, 1H), 1.30 (t, J = 7.2 Hz, 3H), 1.14 (qd, J = 13.5 Hz, J = 4.4 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 162.2 (t, J = 32.3 Hz), 113.5 (dd, J = 259.2 Hz, J = 254.2 Hz), 67.7 (d, J = 6.8 Hz), 67.4 (d, J = 6.8 Hz), 63.4, 47.2 – 46.7 (m), 36.7, 33.3, 32.2, 31.1, 13.8 (d, J = 2.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -105.00 (d, J = 254.6 Hz, 1F), -115.00 (d, J = 255.7 Hz, 1F). **HRMS (ESI)**: calculated for $C_{11}H_{18}O_3BrF_2$ ([M+H]$^+$): 315.0402; Found: 315.0398.

3. General procedure for cross-coupling of Ethyl 3-bromo-3-alkyl-2,2-difluoropropanoate with coumarins/quinolinones



A 25 mL oven-dried Schlenk tube equipped with a magnetic stirrer bar was charged with the heterocycles (1.6 mmol, 8.0 equiv), DMAP (0.4 mmol, 2.0 equiv). The tube was evacuated and backfilled with argon for three times, followed by the addition of dry DMSO (1.0 mL) and Ethyl 3-bromo-3-alkyl-2,2-difluoropropanoate (0.2 mmol, 1.0 equiv). The tube was screw capped and heated to 30°C (heat was produced by LED) under irradiation of purple LED (410-415 nm, the set-up is detailed in Figure S1). After stirring for 12 h, the reaction mixture was then quenched with saturated NaCl solution and diluted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The product was purified with silica gel chromatography.

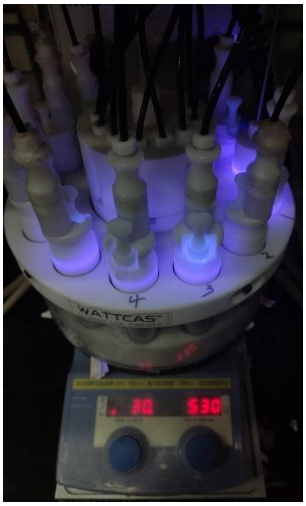
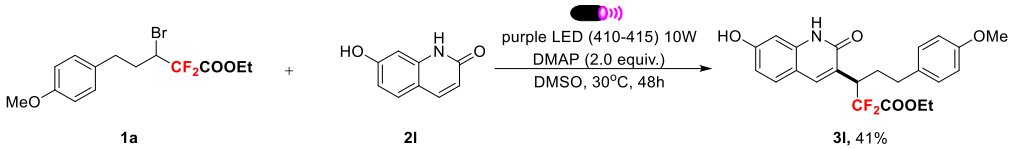


Figure S1. experiment set-up

4.Detailed procedure for the gram scale synthesis



A 50 mL oven-dried Schlenk tube equipped with a magnetic stirrer bar was charged with **2l** (40 mmol, 8.0 equiv), DMAP (10 mmol, 2.0 equiv). The tube was evacuated and backfilled with argon for three times, followed by the addition of dry DMSO (25 mL) and **1a** (5 mmol, 1.0 equiv). The tube was screw capped and heated to 30°C (heat was produced by LEDs) under irradiation of purple LEDs (410-415 nm, the set-up is detailed in Figure S2). After stirring for 48h, the reaction mixture was then quenched with saturated NaCl solution and diluted with ethyl acetate. The organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The product (884.4 mg, 41% yield) was purified with silica gel chromatography to give corresponding pure product. recovery ratio of coumarin: 81% (5.21 g).

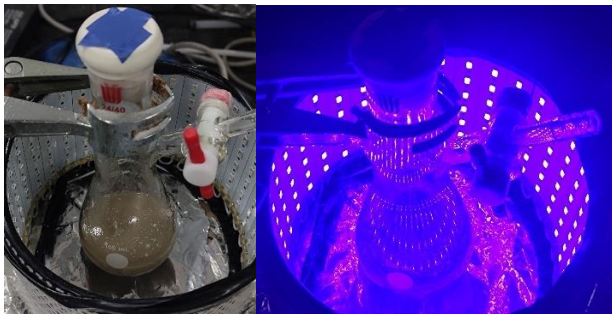
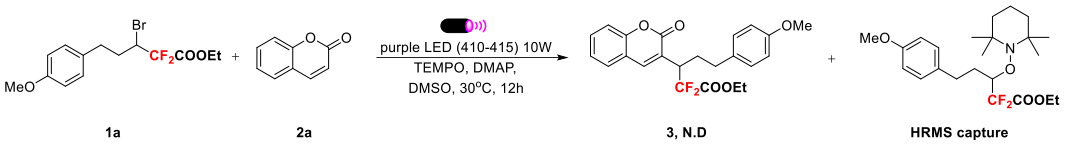


Figure S2. experiment set-up

5. Mechanism studies

5.1 Addition of radical and SET inhibitors



1a 2a 3, N.D HRMS capture

A 25 mL oven-dried Schlenk tube equipped with a magnetic stirrer bar was charged with the **2a** (0.8 mmol, 8.0 equiv), DMAP (0.2 mmol, 2.0 equiv), TEMPO (0.2 mmol, 2.0 equiv). The tube was evacuated and backfilled with argon for three times, followed by the addition of dry DMSO (0.5 mL) and **1a** (0.1 mmol, 1.0 equiv). The tube was screw capped and heated to 30°C (heat was produced by LED) under irradiation of purple LED (410-415 nm). After stirring for 12 h, the reaction mixture was cooled to room temperature, the reaction solution was diluted with 2 mL ethyl acetate, pretreatment and monitored by TLC, F-NMR and sent to HRMS. The results indicated that the reaction was totally suppressed by the addition of a radical scavenger TEMPO, which suggests that the involvement of radical intermediates is likely during the reaction.

High resolution ESI-MS and MS/MS experiments for detecting TEMPO complex

High resolution ESI-MS and MS/MS spectra were recorded on a Q Exactive HF Orbitrap mass spectrometer (Thermo Fisher Scientific Inc.) equipped with ESI ion source. The ESI conditions were: spray voltage 3500 V; capillary temperature, 275°C; sheath gas flow rate 35 arb. units. Data acquisition and analysis were done with the Thermo Xcalibur (version 4.2.47) software package. The elemental composition analysis of the ion at *m/z* 428.2602 by HRMS (Figure S3 and S4) supported the proposed structure of TEMPO complex.

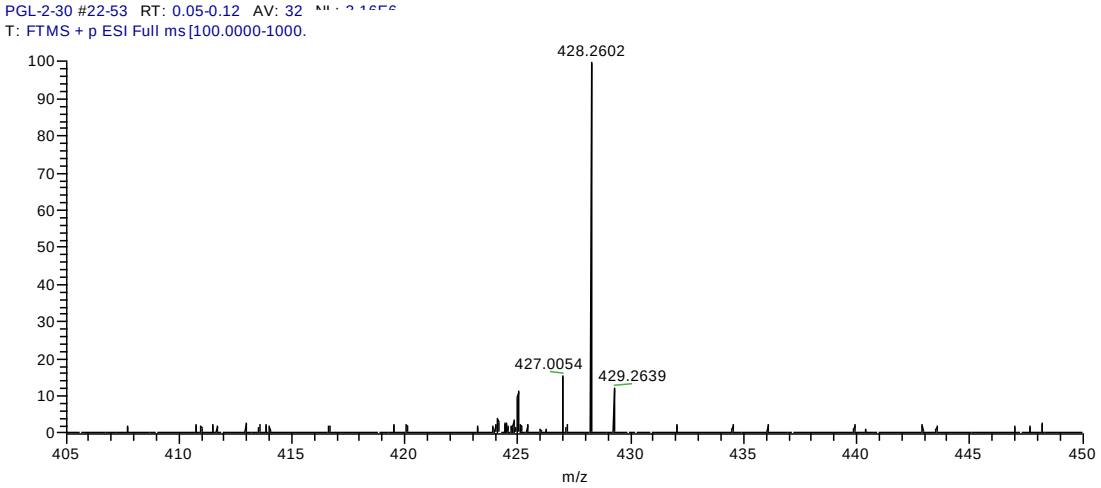


Figure S3. High resolution ESI-MS spectrum of TEMPO complex calculated for $C_{23}H_{36}O_4NF_2$ ([M+H]$^+$): 428.2607; Found: 428.2602.

Elemental composition search on mass 428.2602

m/z= 423.2602-433.2602

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
428.2602	428.2607	-1.24	5.5	$C_{23}H_{36}O_4NF_2$

Figure S4. Elemental composition analysis of the ion at *m/z* 428.2602

5.2. UV-vis experiments

1a (0.1 mmol)

Figure S5. Optical absorption spectra studies.

A λ/nm	**1a**	DMAP	**1a** + DMAP
330	0.097	0.025	0.305
340	0.078	0.013	0.214
350	0.060	0.010	0.159
360	0.044	0.009	0.122
370	0.033	0.007	0.101
380	0.026	0.007	0.087
390	0.022	0.006	0.075
400	0.019	0.005	0.065
410	0.017	0.005	0.057
420	0.016	0.005	0.051
430	0.015	0.005	0.045
440	0.015	0.004	0.041
450	0.014	0.004	0.037
460	0.014	0.004	0.032
470	0.013	0.004	0.029
480	0.012	0.004	0.026
490	0.011	0.004	0.022
500	0.011	0.004	0.020
510	0.010	0.004	0.019
520	0.010	0.004	0.017
530	0.010	0.005	0.017
540	0.010	0.005	0.016
550	0.010	0.004	0.015
560	0.010	0.004	0.015
570	0.009	0.005	0.014
580	0.008	0.004	0.013
590	0.009	0.004	0.012
600	0.008	0.004	0.012

6. Materials and methods of tumor cell growth inhibition test

6.1 Cell lines and culture condition

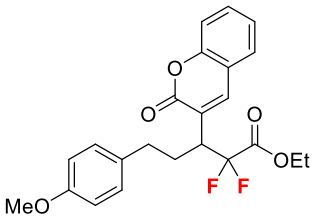
Huh-7 cells and A549 cells were purchased from Servicebio Technology Co., Ltd., (catalog numbers STCC10102G and STCC10201 G, Wuhan, China), the complete medium consisted of DMEM medium and Ham's F-12K medium (Servicebio Technology Co., Ltd., catalog numbers G4202-500 and G4560-500, Wuhan, China), 1% penicillin and streptomycin (Cellcook Biotech Co., Ltd., catalog numbers CM1005-005, Guangzhou, China), and 10% FBS (Procell Life Science&Technology Co., Ltd., catalog numbers 164210-50, Wuhan, China) , respectively. The incubation environment was 37°C and 5 per cent CO2.

6.2 Tumour cell growth inhibition assay

In vitro experiments were conducted using Huh-7 and A549 cells in the logarithmic growth phase. Huh7 and A549 cells were seeded into 96-well plates at a density of 5 × 103 cells per well. A series of concentrations of the compound (0, 2, 4, 8, 16, 32 and 64μM) were used to evaluate the proliferative effect on Huh7 and A549 cells. After incubation for 48 hours, 100 μl of CCK-8 containing solution (ratio of culture medium to CCK-8 was 9:1) (APExBIO, catalog numbers K1018, USA) was added, and incubated at 37°C for 1.5 hours. The corresponding absorbance was detected at a wavelength of 450nm. Absorbance values were converted to cell viability (%) by Microsoft Excel, and cell growth curves and IC50 were generated by GraphPad Prism 10 software analysis.

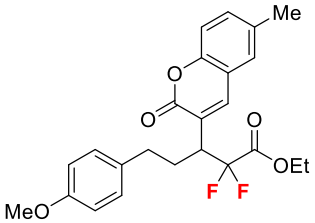
7. Characterization data for the products

ethyl 2,2-difluoro-5-(4-methoxyphenyl)-3-(2-oxo-2*H*-chromen-3-yl) pentanoate (3a)



Obtained in 77% yield as a white solid (64.1 mg, eluent: PE/EA = 12:1), mp: 88 – 90°C, recovery ratio of coumarin: 71% (166.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.56 – 7.52 (m, 1H), 7.49 (dd, J = 8.0 Hz, J = 1.6 Hz, 1H), 7.34 – 7.28 (m, 2H), 7.03 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.8 Hz, 2H), 4.24 (q, J = 7.2 Hz, 2H), 4.02 – 3.90 (m, 1H), 3.72 (s, 3H), 2.59 (t, J = 7.8 Hz, 2H), 2.32 – 2.24 (m, 1H), 2.15 – 2.04 (m, 1H), 1.25 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.4 (t, J = 32.9 Hz), 161.4, 158.0, 153.2, 141.8, 132.7, 132.0, 129.2, 128.1, 124.6, 123.6 (d, J = 5.6 Hz),118.9, 116.5, 115.7 (t, J = 256.3 Hz), 113.9, 63.2, 55.2, 42.0 (t, J = 22.9 Hz), 32.1, 29.8, 13.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -108.27 (dd, J = 253.8 Hz, J = 13.9 Hz, 1F), -111.21 (dd, J = 253.8 Hz, J = 18.4 Hz, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{23}O_5F_2$ ($[M+H]^+$): 417.1508; Found: 417.1506.

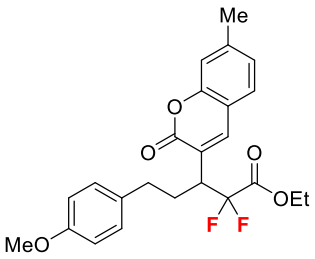
ethyl 2,2-difluoro-5-(4-methoxyphenyl)-3-(6-methyl-2-oxo-2*H*-chromen-3-yl)pentanoate (3b)



Obtained in 77% yield as a white solid (66.3 mg, eluent: PE/EA = 12:1), mp: 70 – 72°C, recovery ratio of coumarin: 76% (194.8 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 7.35 (dd, J = 8.4 Hz, J = 2.0 Hz, 1H), 7.29 (s, 1H), 7.23 (d, J = 8.4 Hz, 1H), 7.03 (d, J = 8.4 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 4.24 (q, J = 7.2 Hz, 2H), 4.01 – 3.89 (m, 1H), 3.74 (s, 3H), 2.57 (t, J = 7.8 Hz,2H), 2.41 (s, 3H), 2.31 – 2.23 (m, 1H), 2.13 – 2.03 (m, 1H), 1.25 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.5 (t, J = 32.8 Hz), 161.7, 158.1, 151.4, 141.9, 134.5, 133.1, 132.8, 129.3, 128.0, 123.5 (d, J = 5.4 Hz), 118.7, 116.4, 115.8 (t, J = 256.0 Hz), 114.0, 63.3, 55.3, 42.1 (t, J = 22.9 Hz), 32.2, 30.0,

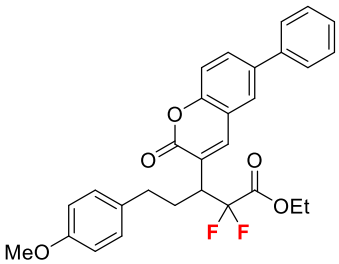
20.9, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -108.17 (dd, J = 253.8 Hz, J = 13.5 Hz, 1F), -111.35 (dd, J = 253.8 Hz, J = 18.4 Hz, 1F). **HRMS (ESI)**: calculated for $C_{24}H_{25}O_5F_2$ ([M+H]$^+$): 431.1665; Found: 431.1664.

ethyl 2,2-difluoro-5-(4-methoxyphenyl)-3-(7-methyl-2-oxo-2*H*-chromen-3-yl)pentanoate (3c)



Obtained in 67% yield as a white solid (57.7 mg, eluent: PE/EA = 12:1), mp: 69 – 71°C, recovery ratio of coumarin: 82% (210.1 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.13 - 7.10 (m, 2H), 7.03 (d, J = 8.8 Hz, 2H), 6.77 (d, J = 8.4 Hz, 2H), 4.23 (q, J = 7.2 Hz, 2H), 4.00 – 3.88 (m, 1H), 3.73 (s, 3H), 2.58 (t, J = 7.8 Hz, 2H), 2.46 (s, 3H), 2.31 – 2.22 (m, 1H), 2.13 – 2.03 (m, 1H), 1.24 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.5 (t, J = 32.4 Hz), 161.8, 158.1, 153.4, 143.5, 141.9, 132.9, 129.3, 127.9, 125.9, 122.3 (d, J = 5.8 Hz), 116.7 (d, J = 2.4 Hz), 116.6, 115.9 (t, J = 255.9 Hz), 114.0, 63.2, 55.3 (d, J = 4.0 Hz), 42.0 (t, J = 22.8 Hz), 32.2, 29.9, 21.9, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -108.08 (dd, J = 253.4 Hz, J = 13.9 Hz, 1F), -111.45 (dd, J = 253.4 Hz, J = 19.2 Hz, 1F). **HRMS (ESI)**: calculated for $C_{24}H_{25}O_5F_2$ ([M+H]$^+$): 431.1665; Found: 431.1666.

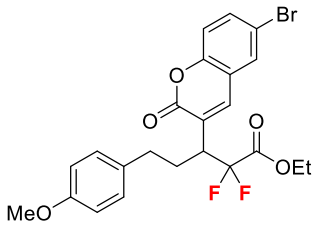
ethyl 2,2-difluoro-5-(4-methoxyphenyl)-3-(2-oxo-6-phenyl-2*H*-chromen-3-yl)pentanoate (3d)



Obtained in 79% yield as a colorless liquid (77.8 mg, eluent: PE/EA = 12:1), recovery ratio of coumarin: 87% (309.3 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.76 (dd, J = 8.8 Hz, J = 2.4 Hz, 1H), 7.68 (d, J = 2.0 Hz, 1H), 7.59 (d, J = 7.6 Hz, 2H), 7.49 (t, J = 7.6 Hz, 2H), 7.42 – 7.39 (m, 2H), 7.05 (d, J = 8.4 Hz, 2H), 6.78 (d, J = 8.8 Hz, 2H), 4.27 (q, J = 7.2 Hz, 2H), 4.07 – 3.95 (m, 1H), 3.72 (s, 3H), 2.62 (t, J = 7.8 Hz, 2H),

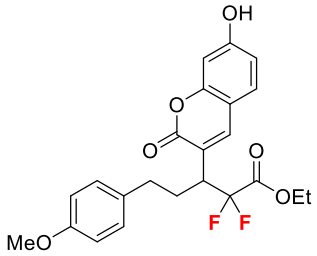
2.36 – 2.28 (m, 1H), 2.20 – 2.10 (m, 1H), 1.28 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 163.4 (t, *J* = 32.8 Hz), 161.4, 158.1, 152.6, 141.9, 139.4, 138.0, 132.7, 130.9, 129.3 (d, *J* = 12.6 Hz), 129.2 – 129.1 (m), 128.0 – 127.8 (m), 127.1 (d, *J* = 3.2 Hz), 126.4 (d, *J* = 6.1 Hz), 124.0 (d, *J* = 5.3 Hz), 119.1, 116.9 (d, *J* = 11.1 Hz), 115.8 (t, *J* = 256.2 Hz), 113.9 (d, *J* = 5.2 Hz), 63.3, 55.3 (d, *J* = 12.6 Hz), 42.4 – 41.8 (m), 32.2, 29.9, 13.9(d, *J* = 6.2 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -107.97 (d, *J* = 252.3 Hz, 1F), -110.87 (d, *J* = 253.0 Hz, 1F). **HRMS (ESI)**: calculated for $C_{29}H_{27}O_5F_2$ ($[M+H]^+$): 493.1821; Found: 493.1819.

ethyl 3-(6-bromo-2-oxo-2*H*-chromen-3-yl)-2,2-difluoro-5-(4-methoxyphenyl)pentanoate (3e)



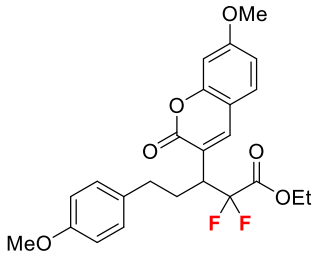
Obtained in 54% yield as a white solid (53.5 mg, eluent: PE/EA = 15:1), mp: 103 – 105°C, recovery ratio of coumarin: 67% (241.3 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.63 – 7.61 (m, 3H), 7.21 (d, *J* = 9.2 Hz, 1H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.76(d, *J* = 8.8 Hz, 2H), 4.24 (q, *J* = 7.2 Hz, 2H), 4.00 – 3.88 (m, 1H), 3.72 (s, 3H), 2.63 – 2.52 (m, 2H), 2.31 – 2.23 (m, 1H), 2.13 – 2.03 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 163.3 (t, *J* = 32.8 Hz), 160.9, 158.2, 152.1, 140.5, 134.7, 132.6, 130.5, 129.3, 125.1(d, *J* = 5.1 Hz), 120.5, 118.4, 117.3, 115.6 (t, *J* = 257.0 Hz), 114.0, 63.4, 55.3 (d, *J* = 3.8 Hz), 42.2 (t, *J* = 24.3 Hz), 32.2, 29.9, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -109.20 (d, *J* = 254.5 Hz, 1F), -111.39 (d, *J* = 257.2 Hz, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{22}O_5BrF_2$ ($[M+H]^+$): 495.0613; Found: 495.0612.

ethyl 2,2-difluoro-3-(7-hydroxy-2-oxo-2*H*-chromen-3-yl)-5-(4-methoxyphenyl)pentanoate (3g)



Obtained in 81% yield as a white solid (70.0 mg, eluent: PE/EA = 5:1), mp: 134 – 136°C, recovery ratio of coumarin: 78% (202.3 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 8.29 (s, 1H), 7.73 (s, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 2.4 Hz, 1H), 6.84 (dd, *J* = 8.4 Hz, *J* = 2.4 Hz, 1H), 6.77(d, *J* = 8.4 Hz, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.96 – 3.83 (m, 1H), 3.72 (s, 3H), 2.61- 2.56 (m, 2H), 2.33 – 2.24 (m, 1H), 2.17 – 2.06 (m, 1H), 1.27 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 164.1 (t, *J* = 32.8 Hz), 163.1, 160.9 (d, *J* = 2.7 Hz)), 158.0, 154.8, 143.2, 132.8, 129.6 (d, *J* = 4.9 Hz), 129.3 (d, *J* = 14.2 Hz), 118.4 (d, *J* = 4.7 Hz), 115.9 (t, *J* = 255.8 Hz), 114.1, 114.0 (d, *J* = 6.5 Hz), 112.3, 102.8 (d, *J* = 14.3 Hz), 63.5, 55.3 (d, *J* = 13.8 Hz), 42.2 – 41.6 (m), 32.1, 29.5, 13.8 (d, *J* = 7.0 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -108.22(dd, *J* = 251.9 Hz, *J* = 12.8 Hz, 1F), -111.89 (dd, *J* = 251.9 Hz, *J* = 19.6 Hz, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{23}O_6F_2$ ($[M+H]^+$): 433.1457; Found: 433.1456.

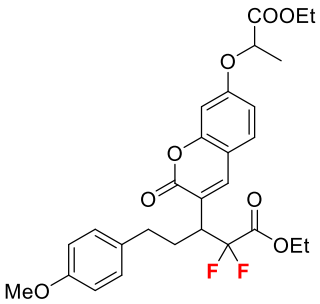
ethyl 2,2-difluoro-3-(7-methoxy-2-oxo-2*H*-chromen-3-yl)-5-(4-methoxyphenyl)pentanoate (3h)



Obtained in 67% yield as a light-yellow oily liquid (59.8 mg, eluent: PE/EA = 10:1), recovery ratio of coumarin: 63% (177.6 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.68 (s, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.86 (dd, *J* = 8.4 Hz, *J* = 2.4 Hz, 1H), 6.81 (d, *J* = 2.4 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.97 – 3.85 (m, 4H), 3.74 (s, 3H), 2.57 (t, *J* = 7.8 Hz, 2H)., 2.29 – 2.21 (m, 1H), 2.12 – 2.02 (m, 1H), 1.25 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 163.5 (t, *J* = 33.0 Hz), 163.1, 161.9, 158.1, 155.2, 142.0, 132.9, 129.3, 129.2, 119.7 (d, *J* = 5.7 Hz), 115.9 (t, *J* = 256.0 Hz), 113.9, 112.9, 112.7, 100.6, 63.2, 55.9 (d, *J* = 4.3 Hz), 55.3 (d, *J* = 4.0 Hz), 42.0 (t, *J* = 22.7 Hz), 32.2, 29.9, 14.0. **^{19}F NMR** (376 MHz,

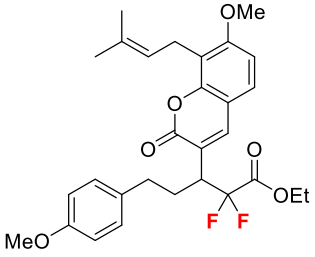
$CDCl_3$) δ -108.11(dd, J = 252.7 Hz, J = 12.8 Hz, 1F), -111.58 (dd, J = 253.0 Hz, J = 18.4 Hz, 1F). **HRMS (ESI)**: calculated for $C_{24}H_{25}O_6F_2$ ([M+H]$^+$): 447.1614; Found: 447.1613.

ethyl 3-(7-((1-ethoxy-1-oxopropan-2-yl)oxy)-2-oxo-2*H*-chromen-3-yl)-2,2-difluoro-5-(4-methoxyphenyl)pentanoate (3i)



Obtained in 86% yield as a light-yellow oily liquid (91.6 mg, eluent: PE/EA = 10:1), recovery ratio of coumarin: 65% (272.7 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.67 (s, 1H), 7.39 (d, J = 8.4 Hz, 1H), 7.02 (d, J = 8.4 Hz, 2H), 6.86 (dt, J = 8.8 Hz, J = 2.8 Hz, 1H), 6.76 (d, J = 8.0 Hz, 2H), 6.72 (t, J = 3.2 Hz, 1H), 4.79 (q, J = 6.8 Hz, 1H), 4.23 (qd, J = 7.1 Hz, J = 2.8 Hz, 4H), 3.94 – 3.84 (m, 1H), 3.73 (s, 3H), 2.55 (t, J = 7.8 Hz, 2H), 2.28 – 2.19 (m, 1H), 2.11 – 2.01 (m, 1H), 1.66 (d, J = 7.2 Hz, 3H),1.30 – 1.22 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 171.2 (d, J = 1.4 Hz), 163.4 (t, J = 32.9 Hz), 161.7 (d, J = 2.7 Hz), 160.8, 158.0, 154.8, 141.8, 132.8, 129.4, 129.3, 120.1 (d, J = 5.4 Hz), 115.8 (t, J = 260.0 Hz), 113.9, 113.3 (d, J = 11.7 Hz), 113.2 (d, J = 1.5 Hz), 101.5 (d, J = 12.1 Hz), 72.8 (d, J = 2.9 Hz), 63.2, 61.8, 55.2, 42.2 – 41.6 (m), 32.0 (d, J = 3.3 Hz), 29.8, 18.4, 14.3, 13.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -108.79 (ddd, J = 253.4 Hz, J = 45.1 Hz, J = 13.9 Hz, 1F), -112.01 (dm, J = 252.7 Hz, 1F). **HRMS (ESI)**: calculated for $C_{28}H_{31}O_8F_2$ ([M+H]$^+$): 533.1982; Found: 533.1978.

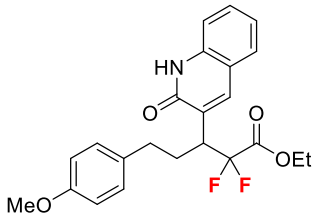
ethyl 2,2-difluoro-3-(7-methoxy-8-(3-methylbut-2-en-1-yl)-2-oxo-2*H*-chromen-3-yl)-5-(4-methoxyphenyl)pentanoate (3j)



Obtained in 45% yield as a light-yellow oily liquid (46.3 mg, eluent: PE/EA = 13:1), recovery ratio of coumarin: 73% (356.7 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.30 (d, J = 8.8 Hz, 1H), 7.04 (d, J = 8.8 Hz, 2H),

6.85 (d, *J* = 8.8 Hz, 1H), 6.78 (d, *J* = 8.8 Hz, 2H), 5.24 – 5.21 (m, 1H), 4.23 (q, *J* = 8.2 Hz, 2H), 3.98 – 3.87 (m, 4H), 3.74 (s, 3H), 3.53 (d, *J* = 7.2 Hz, 2H), 2.57 (t, *J* = 7.8 Hz, 2H)., 2.29 – 2.21 (m, 1H), 2.12 – 2.00 (m, 1H), 1.84 (s, 3H), 1.68 (s, 3H), 1.23 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 163.6 (t, *J* = 33.0 Hz), 161.9, 160.4,158.0, 152.1, 142.3 (d, *J* = 6.8 Hz), 133.0, 132.8, 129.3 (d, *J* = 12.9 Hz), 126.7 (d, *J* = 13.7 Hz), 121.1 (d, *J* = 16.7 Hz), 119.5 (d, *J* = 5.8 Hz), 117.3, 116.0 (t, *J* = 255.9 Hz), 113.9 (d, *J* = 5.1 Hz), 113,1, 107.7 (d, *J* = 9.5 Hz), 63.1, 56.2 (d, *J* = 16.1 Hz), 55.2 (d, *J* = 13.5 Hz), 42.3 – 41.7 (m), 32.1, 29.9, 25.9 (d, *J* = 8.4 Hz), 22.1 – 22.0 (m), 18.0 (d, *J* = 5.9 Hz), 13.8 (d, *J* = 5.9 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -107.36 (d, *J* = 253.0 Hz, 1F), -111.36 (d, *J* = 252.7 Hz, 1F). **HRMS (ESI)**: calculated for $C_{29}H_{33}O_6F_2$ ($[M+H]^+$): 515.2240; Found: 515.2236.

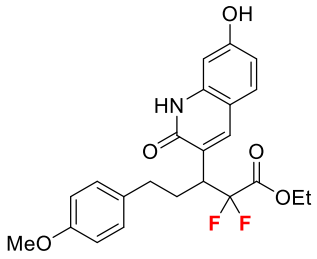
ethyl 2,2-difluoro-5-(4-methoxyphenyl)-3-(2-oxo-1,2-dihydroquinolin-3-yl) pentanoate (3k)



Obtained in 67% yield as a light-yellow oily liquid (55.7 mg, eluent: PE/EA = 3:1), recovery ratio of coumarin: 78% (181.2 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 13.0 (s, 1H), 7.94 (s, 1H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.59 – 7.56 (m, 1H), 7.49 (d, *J* = 8.4 Hz, 1H), 7.27 (t, *J* = 7.0 Hz, 1H), 7.09 (d, *J* = 8.8 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 2H), 4.39 - 4.28 (m, 1H), 4.20 (q, *J* = 7.2 Hz, 2H), 3.74 (s, 3H), 2.62 (t, *J* = 7.8 Hz, 2H), 2.42 – 2.34 (m, 1H), 2.26 – 2.16 (m, 1H), 1.18 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 164.3, 163.9 (t, *J* = 32.9 Hz), 158.0, 139.6, 138.0, 133.3, 130.9 (d, *J* = 5.2 Hz), 129.4 (d, *J* = 12.7 Hz), 128.1 (d, *J* = 6.9 Hz), 127.6 (d, *J* = 5.0 Hz), 122.9 (d, *J* = 12.5 Hz), 119.8, 116.4 (t, *J* = 255.4 Hz), 116.0 (d, *J* = 8.7 Hz), 113.8 (d, *J* = 5.8 Hz), 62.9, 55.3 (d, *J* = 13.4 Hz), 41.0 – 40.5 (m), 32.1, 30.2, 13.8 (d, *J* = 4.7 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -107.10 (dd, *J* = 251.5 Hz, *J* = 12.4 Hz, 1F), -111.89 (dd, *J* = 251.9 Hz, *J* = 19.6 Hz, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{24}O_4NF_2$ ($[M+H]^+$): 416.1668;

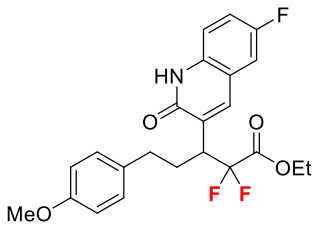
Found: 416.1667.

ethyl 2,2-difluoro-3-(7-hydroxy-2-oxo-1,2-dihydroquinolin-3-yl)-5-(4-methoxyphenyl)pentanoate (3l)



Obtained in 45% yield as a white solid (38.8 mg, eluent: PE/EA = 1:2), mp: 188 – 190°C, recovery ratio of coumarin: 85% (219.2 mg). **^{1}H NMR** (400 MHz, DMSO-d_6) δ 11.7 (s, 1H), 10.2 (s, 1H), 7.87 (s, 1H), 7.54 (d, J = 8.4 Hz, 1H), 7.04 (d, J = 8.4 Hz, 2H), 6.78 (d, J = 8.8 Hz, 2H), 6.73 (d, J = 2.0 Hz, 1H), 6.67 (dd, J = 8.0 Hz, J = 2.4 Hz, 1H), 4.15 (q, J = 6.5 Hz, 2H), 3.97 – 3.86 (m, 1H), 3.68 (s, 3H), 2.50 – 2.44 (m, 1H), 2.38 – 2.30 (m, 1H), 2.16 – 2.02 (m, 2H), 1.10 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, DMSO-d_6) δ 163.3 (t, J = 32.9 Hz), 162.3, 160.0, 157.6, 140.2, 138.7, 132.9, 129.8, 129.4, 122.1 (d, J = 4.6 Hz), 116.5 (t, J = 254.3 Hz), 113.7, 112.5, 112.0, 99.6, 62.8, 55.0, 31.4, 39.0, 13.6. **^{19}F NMR** (376 MHz, DMSO-d_6) δ -108.26 (d, J = 247.8 Hz, 1F), -112.43 (d, J = 250.0 Hz, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{24}O_5NF_2$ ([M+H]$^+$): 432.1617; Found: 432.1618.

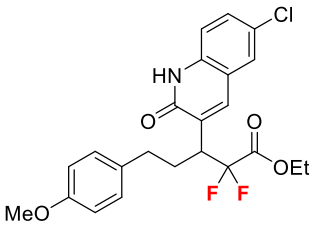
ethyl 2,2-difluoro-3-(6-fluoro-2-oxo-1,2-dihydroquinolin-3-yl)-5-(4-methoxyphenyl)pentanoate (3m)



Obtained in 49% yield as a light-yellow oily liquid (42.5 mg, eluent: PE/EA = 3:1), recovery ratio of coumarin: 72% (187.94 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 13.21 (s, 1H), 7.88 (s, 1H), 7.47 – 7.44 (m, 1H), 7.35 – 7.29 (m, 2H), 7.07 (d, J = 8.4 Hz, 2H), 6.78 (d, J = 8.4 Hz, 2H), 4.37 – 4.25 (m, 1H), 4.20 (q, J = 7.2 Hz, 2H), 3.74 (s, 3H), 2.60 (t, J = 7.8 Hz, 2H), 2.41 – 2.32 (m, 1H), 2.23 – 2.13 (m, 1H), 1.19 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 164.0, 163.8 (t, J = 32.9 Hz), 159.5, 158.0, 157.1, 138.8, 134.5, 133.1, 129.4 (d, J = 15.9 Hz), 120.4 (d, J = 9.0 Hz), 119.5 – 119.1 (m), 117.9 – 117.5 (m),

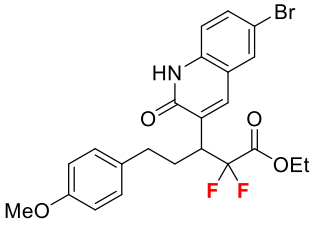
116.2 (t, *J* = 256.1 Hz), 113.9 (d, *J* = 7.1 Hz), 113.0 – 112.6 (m), 63.0, 55.2 (d, *J* = 14.6 Hz), 41.0 – 40.4 (m), 32.1, 30.1, 13.8 (d, *J* = 6.2 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -107.92 (dd, *J* = 252.7 Hz, *J* = 13.2 Hz, 1F), -111.96 (dd, *J* = 252.3 Hz, *J* = 19.5 Hz, 1F), -119.78 - -119.84 (m, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{23}O_4NF_3$ ($[M+H]^+$): 434.1574; Found: 434.1569.

ethyl 3-(6-chloro-2-oxo-1,2-dihydroquinolin-3-yl)-2,2-difluoro-5-(4-methoxyphenyl)pentanoate (3n)



Obtained in 41% yield as a white solid (36.9 mg, eluent: PE/EA = 3:1), mp: 137 – 139°C, recovery ratio of coumarin: 83% (238.5 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 13.12 (s, 1H), 7.85 (s, 1H), 7.60 (d, *J* = 2.4 Hz, 1H), 7.50 (dd, *J* = 8.8 Hz, *J* = 2.4 Hz, 1H), 7.40 (d, *J* = 8.8 Hz, 1H), 7.06 (d, *J* = 8.4 Hz, 2H), 6.77 (d, *J* = 8.4 Hz, 2H), 4.35 – 4.27 (m, 1H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.74 (s, 3H), 2.59 (t, *J* = 7.8 Hz, 2H), 2.40 – 2.31 (m, 1H), 2.22 – 2.12 (m, 1H), 1.19 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 164.1, 163.8 (t, *J* = 33.0 Hz), 158.0, 138.5, 136.4, 133.0, 131.1, 129.4, 129.0, 128.2, 127.2, 120.7, 117.5, 116.2 (t, *J* = 256.1 Hz), 113.9, 63.0, 55.3 (d, *J* = 3.1 Hz), 40.7 (t, *J* = 22.4 Hz), 32.1, 30.1, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -108.11 (d, *J* = 251.9 Hz, 1F), -111.92 (d, *J* = 253.4 Hz, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{23}O_4NClF_2$ ($[M+H]^+$): 450.1278; Found: 450.1276.

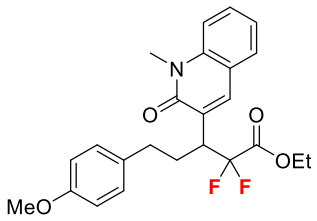
ethyl 3-(6-bromo-2-oxo-1,2-dihydroquinolin-3-yl)-2,2-difluoro-5-(4-methoxyphenyl)pentanoate (3o)



Obtained in 48% yield as a white solid (47.4 mg, eluent: PE/EA = 2:1), mp: 139 – 141°C, recovery ratio of coumarin: 80% (286.8 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 13.14 (s, 1H), 7.84 (s, 1H), 7.76 (d, *J* = 2.4 Hz, 1H), 7.63 (dd, *J* = 8.8 Hz, *J* = 2.4 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.05 (d, *J* = 8.4

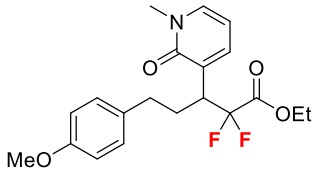
Hz, 2H), 6.77 (d, *J* = 8.4 Hz, 2H), 4.34 – 4.27 (m, 1H), 4.20 (q, *J* = 7.8 Hz, 2H), 3.74 (s, 3H), 2.59 (t, *J* = 7.6 Hz, 2H), 2.40 – 2.31 (m, 1H), 2.21 – 2.12 (m, 1H), 1.19 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 164.1, 163.7 (t, *J* = 32.6 Hz), 158.1, 138.4, 136.7, 133.8, 133.0, 130.3, 129.4, 129.0 (d, *J* = 5.1 Hz), 121.2,117.7, 116.2 (t, *J* = 256.3 Hz), 115.5, 113.9, 63.0, 55.3 (d, *J* = 5.8 Hz), 40.7 (t, *J* = 22.2 Hz), 32.1, 30.1, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -107.46 (dd, *J* = 252.7 Hz, *J* = 13.2 Hz, 1F), -111.26 (dd, *J* = 252.3 Hz, *J* = 19.2 Hz, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{23}O_4NBrF_2$ ($[M+H]^+$): 494.0773; Found: 494.0771.

ethyl 2,2-difluoro-5-(4-methoxyphenyl)-3-(1-methyl-2-oxo-1,2-dihydroquinolin-3-yl)pentanoate (3p)



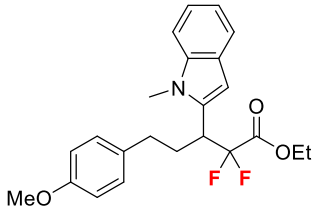
Obtained in 52% yield as a white solid (44.7 mg, eluent: PE/EA = 4:1), mp: 75 – 77°C, recovery ratio of coumarin: 65% (165.5 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.78(s, 1H), 7.60 – 7.57 (m, 2H), 7.35 (d, *J* = 8.8 Hz, 1H), 7.26 (t, *J* = 7.6 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.77 (d, *J* = 8.8 Hz, 2H), 4.36 – 4.27 (m, 1H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.76 (s, 3H), 3.74 (s, 3H), 2.62 – 2.48 (m, 2H), 2.32 – 2.24 (m, 1H), 2.15 – 2.07 (m, 1H), 1.21 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 163.8 (t, *J* = 32.8 Hz), 162.2, 157.9, 139.4, 137.8, 133.4, 130.9, 129.3, 129.2, 127.7 (d, *J* = 5.2 Hz), 122.4, 120.2, 116.3 (t, *J* = 251.0 Hz), 114.1, 113.8, 62.9, 55.3, 41.6 (t, *J* = 22.5 Hz), 32.3, 30.4, 30.3, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -107.85 (dd, *J* = 252.7 Hz, *J* = 9.0 Hz, 1F), -111.09 (dd, *J* = 252.3 Hz, *J* = 19.2 Hz, 1F). **HRMS (ESI)**: calculated for $C_{24}H_{26}O_4NF_2$ ($[M+H]^+$): 430.1824; Found: 430.1826.

ethyl 2,2-difluoro-5-(4-methoxyphenyl)-3-(1-methyl-2-oxo-1,2-dihydropyridin-3-yl)pentanoate (3q)



Obtained in 61% yield as a light-yellow oily liquid (46.3 mg, eluent: PE/EA = 1:2), recovery ratio of coumarin: 64% (111.7 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (d, J = 6.8 Hz, 1H), 7.27 – 7.24 (m, 1H), 7.04 (d, J = 8.4 Hz, 2H), 6.79 (d, J = 8.8 Hz, 2H), 6.19 (t, J = 7.0 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 4.17 – 4.01 (m, 1H), 3.76 (s, 3H), 3.56 (s, 3H), 2.56 – 2.42 (m, 2H), 2.22 – 2.13 (m, 1H), 2.02 – 1.92 (m, 1H), 1.22 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.9 (t, J = 33.1 Hz), 162.9, 157.9, 138.1, 137.7, 133.5, 129.3, 126.9 (d, J = 5.4 Hz), 116.4 (t, J = 249.7 Hz), 113.8, 105.6, 62.8, 55.3, 41.2 (t, J = 22.4 Hz), 38.4, 32.2, 30.3, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -108.16 (d, J = 251.2 Hz, 1F), -111.49 (dd, J = 251.5 Hz, J = 19.2 Hz, 1F). **HRMS (ESI)**: calculated for $C_{20}H_{24}O_4NF_2$ ([M+H]$^+$): 380.1668; Found: 380.1667.

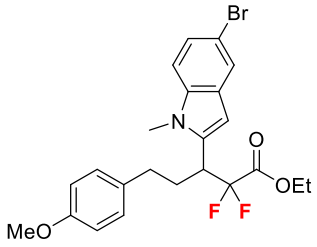
ethyl 2,2-difluoro-5-(4-methoxyphenyl)-3-(1-methyl-1H-indol-2-yl)pentanoate (3r)



Obtained in 48% yield as a yellow oily liquid liquid (38.5 mg, eluent: PE/EA = 18:1). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62 (d, J = 8.0 Hz, 1H), 7.33 (d, J = 8.0 Hz, 1H), 7.24 (t, J = 7.4 Hz, 1H), 7.13 (t, J = 7.4 Hz, 1H), 6.98 (d, J = 8.4 Hz, 2H), 6.82 (d, J = 8.4 Hz, 2H), 6.57 (s, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.80 (s, 3H), 3.71 – 3.62 (m, 1H), 3.59 (s, 3H), 2.70 – 2.63 (m, 1H), 2.49 – 2.42 (m, 1H), 2.37 – 2.21 (m, 2H), 1.10 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.9 (t, J = 32.8 Hz), 158.2, 137.5, 134.1 (d, J = 5.7 Hz), 132.6, 129.4, 127.8, 121.7, 120.7, 119.7, 116.0 (t, J = 256.9 Hz), 114.0, 109.5, 101.9, 63.0, 55.4, 40.5 (t, J = 24.0 Hz), 31.7, 30.3, 29.8, 13.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -106.79 (d, J = 252.3 Hz, 1F), -110.49 (dd, J = 256.1 Hz, J = 15.4 Hz, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{26}O_3NF_2$ ([M+H]$^+$): 402.1875; Found: 402.1876.

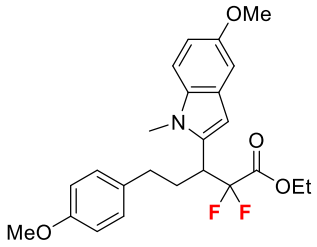
ethyl 3-(5-bromo-1-methyl-1*H*-indol-2-yl)-2,2-difluoro-5-(4-methoxypheny

l)pentanoate (3s)



Obtained in 35% yield as a light-yellow oily liquid (33.6 mg, eluent: PE/EA = 18:1), recovery ratio of coumarin: 75% (315.1 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, J = 1.6 Hz, 1H), 7.72 (dd, J = 8.4 Hz, J = 1.6 Hz, 1H), 7.18 (d, J = 8.8 Hz, 1H), 6.95 (d, J = 8.4 Hz, 2H), 6.81 (d, J = 8.8 Hz, 2H), 6.49 (s, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.79 (s, 3H), 3.67 – 3.56 (m, 1H), 3.54 (s, 3H), 2.68 – 2.62 (m, 1H), 2.47 – 2.39 (m, 1H), 2.36 – 2.18 (m, 2H), 1.11 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.8 (t, J = 32.7 Hz), 158.2, 136.2, 135.4 (d, J = 5.8 Hz), 132.3, 129.4, 129.3, 124.6 - 124.5 (m), 123.0 (d, J = 3.2 Hz), 115.8 (t, J = 256.9 Hz), 114.0, 113.0, 111.0 - 110.9 (m), 101.4, 63.0, 55.4 (d, J = 10.0 Hz), 40.7 - 40.3 (m), 31.6, 30.0 (d, J = 3.0 Hz), 29.9 (d, J = 4.5 Hz), 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -107.02 (dd, J = 256.8 Hz, J = 11.3 Hz, 1F), -110.25 (dd, J = 256.8 Hz, J = 15.0 Hz, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{25}O_3NBrF_2$ ($[M+H]^+$): 480.0980; Found: 480.0979.

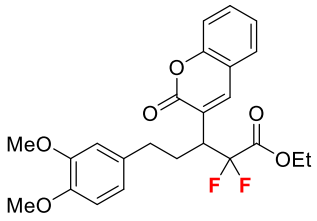
ethyl 2,2-difluoro-3-(5-methoxy-1-methyl-1H-indol-2-yl)-5-(4-methoxyphenyl)pentanoate (3t)



Obtained in 37% yield as a yellow oily liquid (31.9 mg, eluent: PE/EA = 18:1), recovery ratio of coumarin: 77% (198.6 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.22 (m, 1H), 7.10 (d, J = 2.0 Hz, 1H), 6.99 (d, J = 8.0 Hz, 2H), 6.92 (dd, J = 8.8 Hz, J = 2.4 Hz, 1H), 6.84 (d, J = 8.8 Hz, 2H), 6.51 (s, 1H), 4.16 (q, J = 6.9 Hz, 2H), 3.88 (s, 3H), 3.81 (s, 3H), 3.74 – 3.61 (m, 1H), 3.56 (s, 3H), 2.71 – 2.65 (m, 1H), 2.50 – 2.43 (m, 1H), 2.37 – 2.22 (m, 2H), 1.11 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.9 (t, J = 32.8 Hz), 158.1, 154.2, 134.4 (d, J = 5.8 Hz), 132.9, 132.1, 129.4, 128.0, 115.9 (t, J = 256.6 Hz), 114.0, 112.0, 110.2, 102.1, 101.4, 62.9, 55.9 (d, J = 4.8 Hz), 55.3 (d, J = 4.8 Hz), 40.5 (t, J = 22.7 Hz), 31.7, 30.2, 29.9, 13.8. **^{19}F NMR**

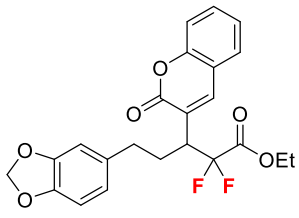
(376 MHz, $CDCl_3$) δ -106.60 (dd, J = 254.9 Hz, J = 13.9 Hz, 1F), -111.39 (dd, J = 254.5 Hz, J = 16.5 Hz, 1F). **HRMS (ESI)**: calculated for $C_{24}H_{28}O_4NF_2$ ($[M+H]^+$): 432.1981; Found: 432.1983.

ethyl 5-(3,4-dimethoxyphenyl)-2,2-difluoro-3-(2-oxo-2*H*-chromen-3-yl)pentanoate (4a)



Obtained in 78% yield as a white solid (69.6 mg, eluent: PE/EA = 8:1), mp: 83 – 85°C, recovery ratio of coumarin: 81% (189.4 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.53 (t, J = 8.6 Hz, 1H), 7.47 (d, J = 7.6 Hz, 1H), 7.33 – 7.26 (m, 2H), 6.70 (d, J = 8.4 Hz, 1H), 6.64 (d, J = 6.8 Hz, 2H), 4.22 (q, J = 7.2 Hz, 2H), 4.02 – 3.91 (m, 1H), 3.84 (s, 3H), 3.77 (s, 3H), 2.59 (t, J = 7.6 Hz, 2H), 2.32 – 2.24 (m, 1H), 2.17 – 2.08 (m, 1H), 1.23 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.4 (t, J = 32.9 Hz), 161.5, 153.2, 148.8, 147.4, 141.9, 133.2, 132.1, 128.1, 124.7, 123.6 (d, J = 5.5 Hz), 120.2, 118.9, 116.6, 115.7 (t, J = 256.1 Hz), 111.6, 111.2, 77.4, 63.2, 55.9, 41.9 (t, J = 23.0 Hz), 32.6, 29.8, 13.8. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -108.17 (dm, J = 253.4 Hz, 1F), -111.33 (dt, J = 253.4 Hz, J = 10.5 Hz, 1F). **HRMS (ESI)**: calculated for $C_{24}H_{25}O_6F_2$ ($[M+H]^+$): 447.1614; Found: 447.1613.

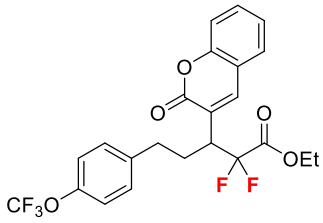
ethyl 5-(benzo[*d*][1,3]dioxol-5-yl)-2,2-difluoro-3-(2-oxo-2*H*-chromen-3-yl)pentanoate (4b)



Obtained in 72% yield as a white solid (62.0 mg, eluent: PE/EA = 11:1), mp: 73 – 75°C, recovery ratio of coumarin: 77% (180.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.57 – 7.53 (m, 1H), 7.50 (dd, J = 7.6 Hz, J = 1.6 Hz, 1H), 7.34 – 7.28 (m, 2H), 6.66 (d, J = 8.0 Hz, 1H), 6.60 (d, J = 1.6 Hz, 1H), 6.55 (dd, J = 8.0 Hz, J = 1.6 Hz, 1H), 5.84 (dd, J = 7.2 Hz, J = 1.6 Hz, 2H), 4.25 (q, J = 7.1 Hz, 2H), 4.01 – 3.89 (m, 1H), 2.62 – 2.51 (m, 2H), 2.31 –

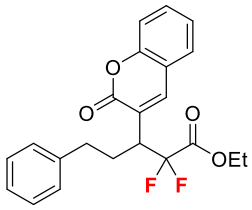
2.23 (m, 1H), 2.13 – 2.03 (m, 1H), 1.26 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 163.4 (t, *J* = 32.8 Hz), 161.5, 153.3, 147.8, 146.0, 141.9, 134.5, 132.1, 128.2, 124.7, 123.6 (d, *J* = 5.1 Hz), 121.3, 118.9, 116.7, 115.7 (t, *J* = 255.8 Hz), 108.7, 108.4, 100.9, 63.3, 42.0 (t, *J* = 22.9 Hz), 32.9, 29.9, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -108.72 (dd, *J* = 253.8 Hz, *J* = 13.2 Hz, 1F), -111.99 (dd, *J* = 253.4 Hz, *J* = 18.8 Hz, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{21}O_6F_2$ ([M+H]$^+$): 431.1301; Found: 431.1298.

ethyl 2,2-difluoro-3-(2-oxo-2*H*-chromen-3-yl)-5-(4-(trifluoromethoxy)phenyl)pentanoate (4c)



Obtained in 72% yield as a white solid (67.7 mg, eluent: PE/EA = 15:1), mp: 62 – 64°C, recovery ratio of coumarin: 78% (182.4 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.77 (s, 1H), 7.57 – 7.53 (m, 1H), 7.50 (dd, *J* = 7.6 Hz, *J* = 1.6 Hz, 1H), 7.35 – 7.29 (m, 2H), 7.15 (d, *J* = 8.4 Hz, 2H), 7.08 (d, *J* = 8.4 Hz, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 4.04 – 3.92 (m, 1H), 2.65 (t, *J* = 7.8 Hz, 2H), 2.35 – 2.27 (m, 1H), 2.17 – 2.07 (m, 1H), 1.24 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 163.3 (t, *J* = 32.7 Hz), 161.5, 153.3, 147.7 (q, *J* =1.9 Hz), 142.0, 139.5, 132.3, 129.7, 128.3, 124.8, 123.6 (d, *J* = 5.5 Hz), 121.2, 120.5 (q, *J* = 260.9 Hz), 118.9, 116.7, 115.7 (t, *J* = 256.3 Hz), 63.4, 42.1 (t, *J* = 23.0 Hz), 32.4, 29.8 (t, *J* = 2.9 Hz), 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -58.02 (d, *J* = 7.4 Hz, 3F), -107.76 (dm, *J* = 254.9 Hz, 1F), -111.45 (dm, *J* = 254.9 Hz, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{20}O_5F_5$ ([M+H]$^+$): 471.1225; Found: 471.1224.

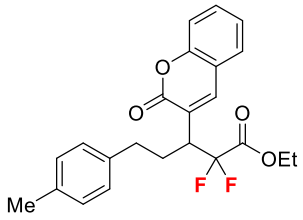
ethyl 2,2-difluoro-3-(2-oxo-2*H*-chromen-3-yl)-5-phenylpentanoate (4d)



Obtained in 74% yield as a white solid (57.2 mg, eluent: PE/EA = 15:1), mp: 100 – 102°C, recovery ratio of coumarin: 76% (177.7 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.76 (s, 1H), 7.54 (t, *J* = 8.6 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.34 – 7.22

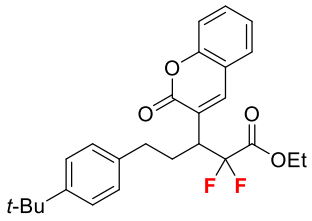
(m, 4H), 7.16 – 7.12 (m, 3H), 4.24 (q, *J* = 7.2 Hz, 2H), 4.05 – 3.93 (m, 1H), 2.64 (t, *J* = 8.0 Hz, 2H), 2.36 – 2.27 (m, 1H), 2.19 – 2.09 (m, 1H), 1.25 (t, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 163.4 (t, *J* = 32.9 Hz), 161.5, 153.3, 141.9, 140.8, 132.1, 128.6, 128.4, 128.2, 126.3, 124.7, 123.7 (d, *J* = 5.7 Hz), 119.0, 116.7, 115.8 (t, *J* = 256.2 Hz), 63.3, 42.2 (t, *J* = 22.9 Hz), 33.1, 29.7, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -108.15 (dd, *J* = 254.2 Hz, *J* = 13.2 Hz, 1F), -111.18 (dd, *J* = 254.2 Hz, *J* = 18.4 Hz, 1F). **HRMS (ESI)**: calculated for $C_{22}H_{21}O_4F_2$ ($[M+H]^+$): 387.1402; Found: 387.1403.

ethyl 2,2-difluoro-3-(2-oxo-2*H*-chromen-3-yl)-5-(*p*-tolyl)pentanoate (4e)



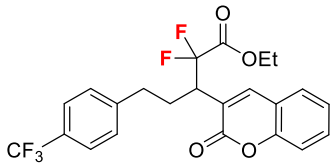
Obtained in 73% yield as a white solid (58.5 mg, eluent: PE/EA = 14:1), mp: 70 – 72°C, recovery ratio of coumarin: 78% (182.4 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) *δ* 7.74 (s, 1H), 7.54 (t, *J* = 8.6 Hz, 1H), 7.49 (dd, *J* = 7.6 Hz, *J* = 1.6 Hz, 1H), 7.34 – 7.26 (m, 2H), 7.03 (q, *J* = 7.1 Hz, 4H), 4.25 (q, *J* = 7.2 Hz, 2H), 4.04 – 3.92 (m, 1H), 2.62 (t, *J* = 8.6 Hz, 2H), 2.36 – 2.26 (m, 1H), 2.24 (s, 3H), 2.18 – 2.09 (m, 1H), 1.26 (t, *J* = 7.2 Hz,3H). **^{13}C NMR** (101 MHz, $CDCl_3$) *δ* 163.4 (t, *J* = 32.8 Hz), 161.5, 153.3, 141.9, 137.7, 135.9, 132.0, 129.3, 128.2, 128.2, 124.7, 123.7 (d, *J* = 5.6 Hz), 119.0, 116.6, 115.8 (t, *J* = 256.1 Hz), 63.3, 42.2 (t, *J* = 22.8 Hz), 32.7, 29.7, 21.0, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) *δ* -108.15 (dd, *J* = 254.2 Hz, *J* = 13.2 Hz, 1F), -111.18 (dd, *J* = 254.2 Hz, *J* = 18.4 Hz, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{23}O_4F_2$ ($[M+H]^+$): 401.1559; Found: 401.1558.

ethyl 5-(4-(*tert*-butyl)phenyl)-2,2-difluoro-3-(2-oxo-2*H*-chromen-3-yl)pentanoate (4f)



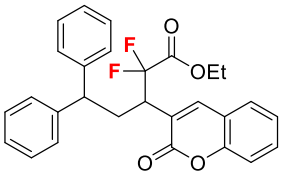
Obtained in 67% yield as a colorless liquid (59.3 mg, eluent: PE/EA = 14:1), recovery ratio of coumarin: 83% (194.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.56 – 7.52 (m, 1H), 7.49 (dd, J = 9.2 Hz, J = 1.6 Hz, 1H), 7.34 – 7.25 (m, 4H), 7.07 (d, J = 8.0 Hz, 2H), 4.25 (q, J = 7.2 Hz, 2H), 4.07 – 3.96 (m, 1H), 2.71 – 2.57 (m, 2H), 2.37 – 2.29 (m, 1H), 2.19 – 2.09 (m, 1H), 1.28 – 1.25 (m, 12H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.4 (t, J = 32.9 Hz), 161.5, 153.3, 149.1, 141.8, 137.7, 132.0, 128.2, 128.0, 125.5, 124.7, 123.7 (d, J = 5.2 Hz), 118.9, 116.6, 115.8 (t, J = 256.2 Hz), 63.3, 42.2 (t, J = 22.9 Hz), 34.4, 32.6, 31.4, 29.6 (t, J = 3.1 Hz), 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -108.42 (dm, J = 254.2 Hz, 1F), -111.16 (dm, J = 253.4 Hz, 1F). **HRMS (ESI)**: calculated for $C_{26}H_{29}O_4F_2$ ($[M+H]^+$): 443.2028; Found: 443.2027.

ethyl 2,2-difluoro-3-(2-oxo-2*H*-chromen-3-yl)-5-(4-(trifluoromethyl)phenyl) pentanoate (4g)



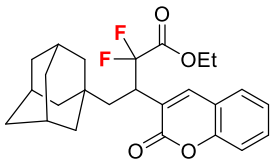
Obtained in 75% yield as a colorless liquid (68.2 mg, eluent: PE/EA = 10:1), mp: 64 – 66°C, recovery ratio of coumarin: 77% (180.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.58 – 7.53 (m, 1H), 7.50 – 7.47 (m, 3H), 7.34 – 7.29 (m, 2H), 7.25 (d, J = 8.4 Hz, 2H), 4.24 (q, J = 7.2 Hz, 2H), 4.04 – 3.93 (m, 1H), 2.74 – 2.69 (m, 2H), 2.38 – 2.30 (m, 1H), 2.20 – 2.10 (m, 1H), 1.24 (t, J = 7.2 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.3 (t, J = 32.8 Hz), 161.5, 153.3, 144.9, 142.0, 132.3, 128.8, 128.7 (q, J = 32.6 Hz), 128.2, 125.5 (q, J = 3.8 Hz), 124.8, 124.3 (q, J = 260.5 Hz), 123.5 (d, J = 5.8 Hz), 118.8, 116.7, 115.7 (t, J = 256.4 Hz), 63.4, 42.1 (t, J = 23.0 Hz), 33.0, 29.6, 13.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ – 63.04 (s, 3F), -108.13 (dd, J = 254.9 Hz, J = 13.2 Hz, 1F), -112.13 (dd, J = 255.3 Hz, J = 18.8 Hz, 1F). **HRMS (ESI)**: calculated for $C_{23}H_{20}O_4F_5$ ($[M+H]^+$): 455.1276; Found: 455.1272.

ethyl 2,2-difluoro-3-(2-oxo-2*H*-chromen-3-yl)-5,5-diphenylpentanoate (4h)



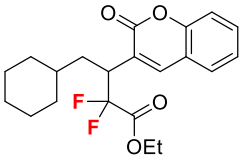
Obtained in 80% yield as a colorless liquid (74.0 mg, eluent: PE/EA = 10:1), recovery ratio of coumarin: 85% (198.7 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 (s, 1H), 7.56 – 7.52 (m, 1H), 7.44 (dd, J = 7.6 Hz, J = 1.6 Hz, 1H), 7.33 – 7.28 (m, 4H), 7.24 – 7.18 (m, 7H), 7.08 – 7.03 (m, 1H), 4.21 (qd, J = 7.2 Hz, J = 2.0 Hz, 2H), 3.89 – 3.78 (m, 2H), 2.82 – 2.75 (m, 1H), 2.69 – 2.61 (m, 1H), 1.21 (t, J = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.3 (t, J = 32.8 Hz), 161.1, 153.4, 144.1, 142.9, 142.4 (d, J = 2.9 Hz), 132.1, 128.8 (d, J = 2.7 Hz), 128.6 (d, J = 1.7 Hz), 128.2 (m), 128.0, 127.6, 126.9, 126.5, 124.6 (d, J = 1.8 Hz), 123.2 (d, J = 4.3 Hz), 118.9, 116.6, 115.8 (t, J = 256.2 Hz), 63.3, 48.6 (m), 41.8 (t, J = 23.4 Hz), 33.6, 13.8 (d, J = 1.7 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -108.01 (d, J = 253.0 Hz, 1F), -109.67 (d, J = 252.3 Hz, 1F). **HRMS (ESI)**: calculated for $C_{28}H_{25}O_4F_2$ ($[M+H]^+$): 463.1715; Found: 463.1711.

ethyl 4-((3*r*,5*r*,7*r*)-adamantan-1-yl)-2,2-difluoro-3-(2-oxo-2*H*-chromen-3-yl) butanoate (4i)



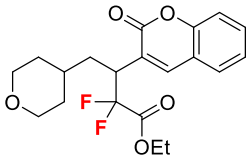
Obtained in 60% yield as a white solid (51.6 mg, eluent: PE/EA = 10:1), mp: 122 – 124°C, recovery ratio of coumarin: 68% (159.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.55 – 7.51 (m, 2H), 7.34 – 7.27 (m, 2H), 4.28 (q, J = 7.2 Hz, 2H), 4.14 – 4.03 (m, 1H), 1.89 (s, 3H), 1.72 (d, J = 14.4 Hz, 1H), 1.66 – 1.54 (m, 7H), 1.48 (d, J = 11.6 Hz, 3H), 1.35 – 1.29 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.6 (t, J = 33.1 Hz), 161.5, 153.3, 141.8, 131.9, 128.2, 126.1, 124.6, 119.1, 116.7, 116.3 (t, J = 256.0 Hz), 63.3, 43.1, 42.6, 36.8, 36.7 (t, J = 24.0 Hz), 32.8, 28.5, 14.0. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -110.12 (m, 2F). **HRMS (ESI)**: calculated for $C_{25}H_{29}O_4F_2$ ($[M+H]^+$): 431.2028; Found: 431.2025.

ethyl 4-cyclohexyl-2,2-difluoro-3-(2-oxo-2*H*-chromen-3-yl)butanoate (4j)



Obtained in 77% yield as a white solid (58.3 mg, eluent: PE/EA = 8:1), mp: 102 – 104°C, recovery ratio of coumarin: 80% (187.0 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.55 – 7.50 (m, 2H), 7.32 – 7.26 (m, 2H), 4.33 – 4.21 (m, 2H), 4.13 – 4.01 (m, 1H), 1.84 (d, *J* = 12.4 Hz, 1H), 1.79 – 1.57 (m, 6H), 1.28 (t, *J* = 7.2 Hz, 3H),1.20 – 1.05 (m, 4H), 1.00 – 0.90 (m, 1H), 0.88 – 0.78 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.6 (t, *J* = 33.0 Hz), 161.5, 153.2, 141.8, 131.9 (d, *J* = 2.7 Hz), 128.2, 124.7 – 124.6 (m), 124.1 (d, *J* = 4.9 Hz), 119.0, 116.7 – 116.5 (m), 116.0 (t, *J* = 256.0 Hz), 63.2, 39.6 – 39.0 (m), 35.4, 34.5, 34.3, 32.0, 26.4, 26.2, 25.9, 13.9 (d, *J* = 3.4 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -109.71 (dd, *J* = 253.0 Hz, *J* = 14.7 Hz, 1F), -111.02 (dd, *J* = 252.7 Hz, *J* = 17.7 Hz, 1F). **HRMS (ESI)**: calculated for $C_{21}H_{24}O_4F_2$ ($[M]^+$): 378.1637; Found: 378.1633.

ethyl 2,2-difluoro-3-(2-oxo-2*H*-chromen-3-yl)-4-(tetrahydro-2H-pyran-4-yl) butanoate (4k)



Obtained in 82% yield as a white solid (62.4 mg, eluent: PE/EA = 8:1), mp: 113 – 115°C, recovery ratio of coumarin: 87% (203.4 mg). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.57 – 7.51 (m, 2H), 7.34 – 7.29 (m, 2H), 4.31 – 4.23 (m, 2H), 4.14 – 4.02 (m, 1H), 3.94 – 3.86 (m, 2H), 3.26 (m, 2H), 1.84 – 1.76 (m, 3H), 1.51 – 1.17 (m, 7H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.4 (t, *J* = 32.9 Hz), 161.5, 153.2, 142.0, 132.2, 128.3, 124.8, 123.9 (d, *J* = 5.6 Hz), 118.9, 116.7, 115.9 (t, *J* = 256.1 Hz), 67.7 (d, *J* = 2.9 Hz), 63.3, 38.8 (t, *J* = 22.6 Hz), 35.3, 33.8, 32.0 (d, *J* = 6.6 Hz), 14.0. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -108.82 (dd, *J* = 254.2 Hz, *J* = 13.5 Hz, 1F), -111.59 (dd, *J* = 254.2 Hz, *J* = 18.0 Hz, 1F). **HRMS (ESI)**: calculated for $C_{20}H_{23}O_5F_2$ ($[M+H]^+$): 381.1508; Found: 381.1504.

8. Reference

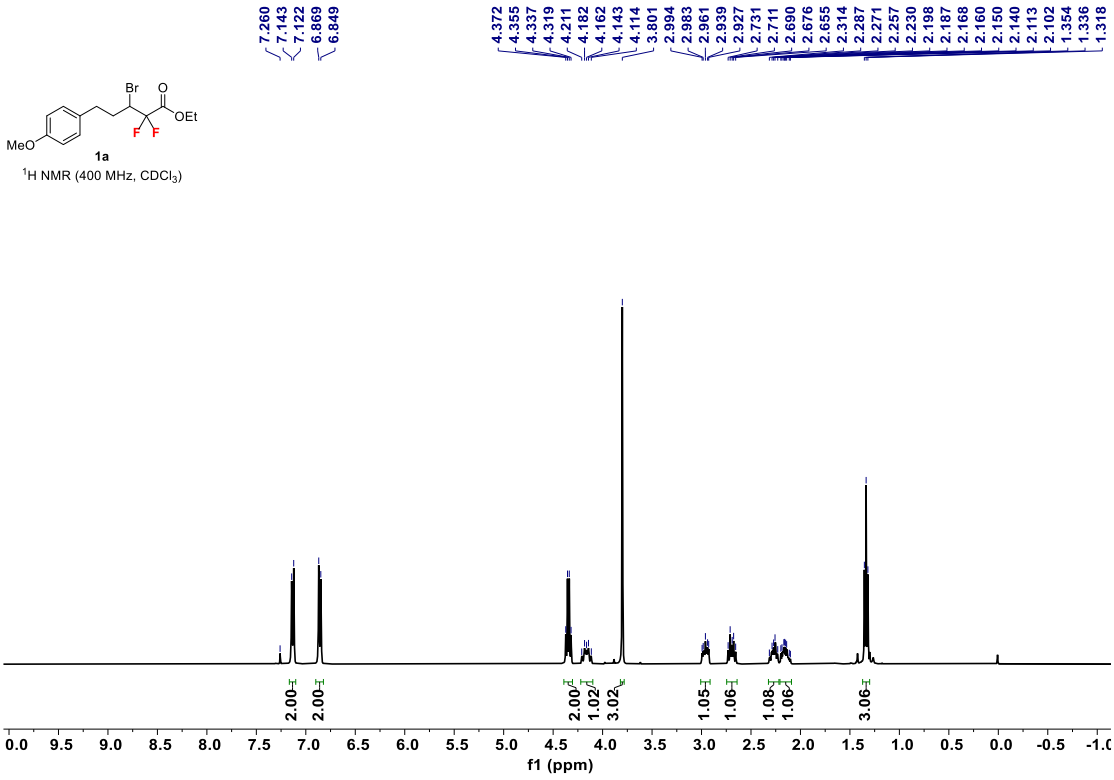
[1] D. Chen, L. Xu, Y. Yu, Q. Mo, X. Qi and C. Liu, Triflylpyridinium Enables Rapid and Scalable Controlled Reduction of Carboxylic Acids to Aldehydes using Pinacolborane, *Angew. Chem. Int. Ed. Engl.,* 2023, **62**, e202215168.

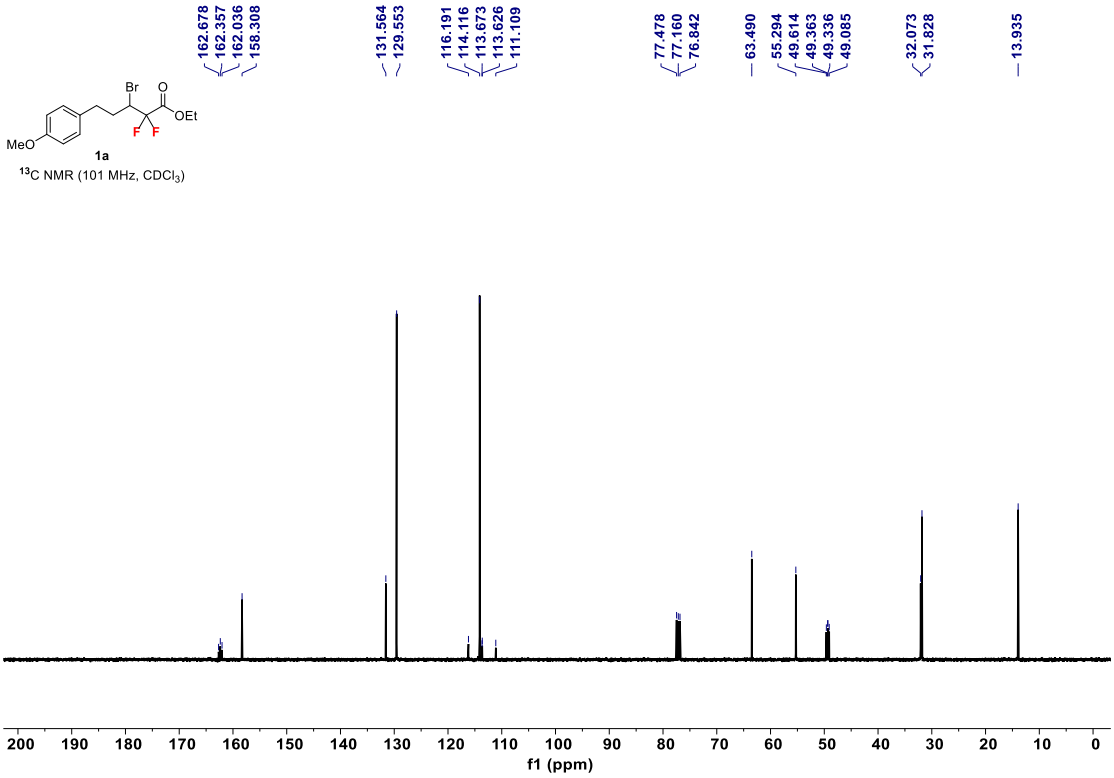
[2] F. Friese, C. Mück-Lichtenfeld and A. Studer, Remote C-H functionalization using radical translocating arylating groups, *Nat. Commun.*, 2018, *9*, 2808.

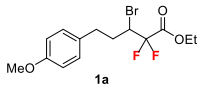
[3] X. Lin, F. Zheng and F-J. Qing, Iron-Catalyzed Cross-Coupling Reactions between Arylzinc Reagents and Alkyl Halides Bearing β-Fluorines, *Organometallics*, 2012, **31**, 1578–1582.

[4] X. Li, Z. Feng, Z.-X. Jiang and X. Zhang, Nickel-catalyzed reductive cross-coupling of (hetero)aryl iodides with fluorinated secondary alkyl bromides, *Org. Lett.*, 2015, **17**, 5570.

9. Copies of ^{1}H NMR, ^{19}F NMR and ^{13}C NMR charts of the Products

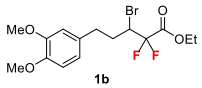






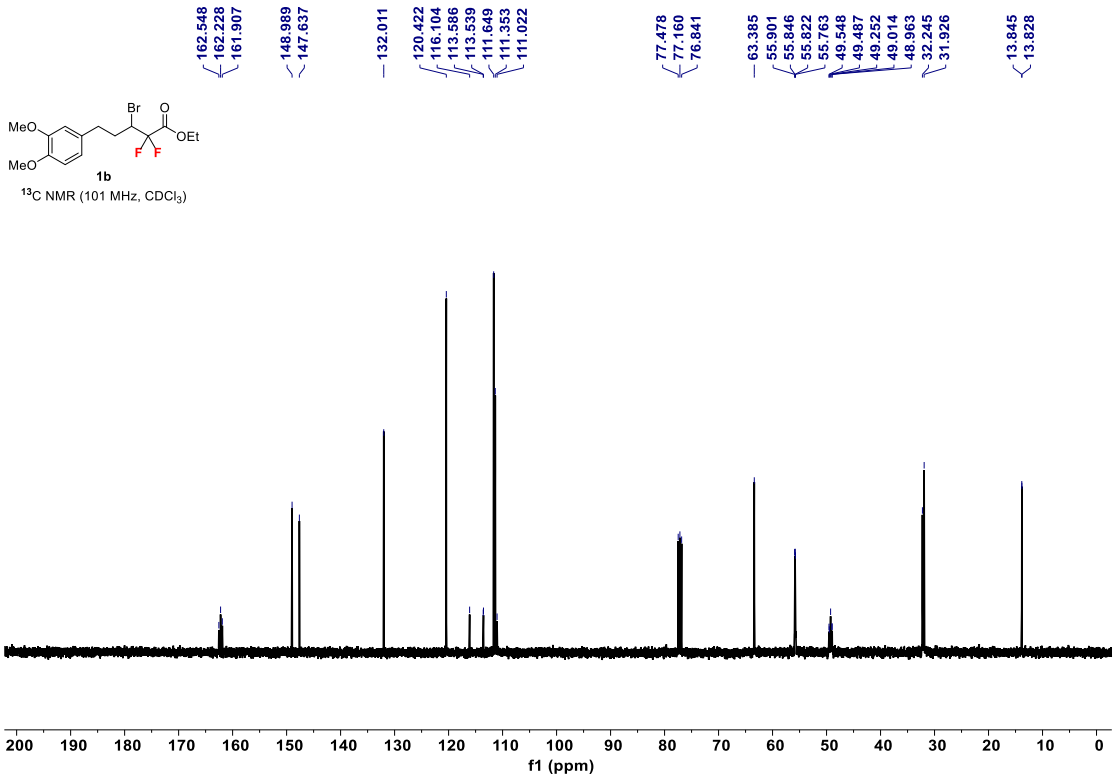
1a

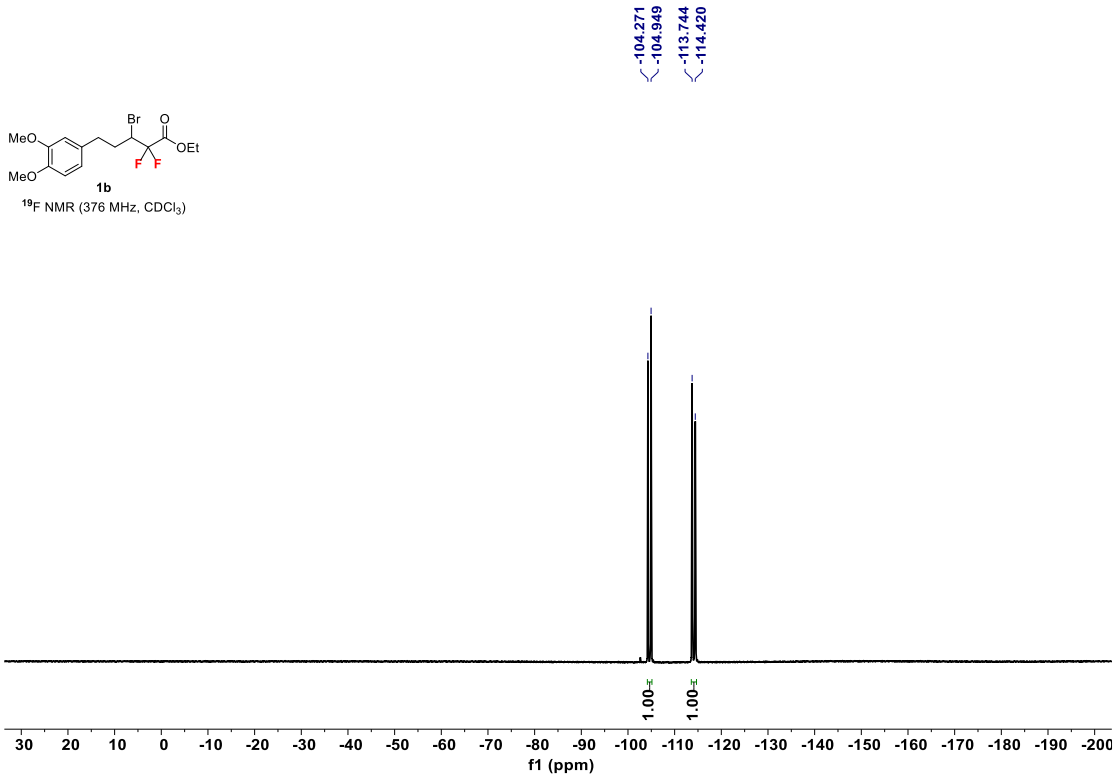
^{19}F NMR (376 MHz, $CDCl_3$)

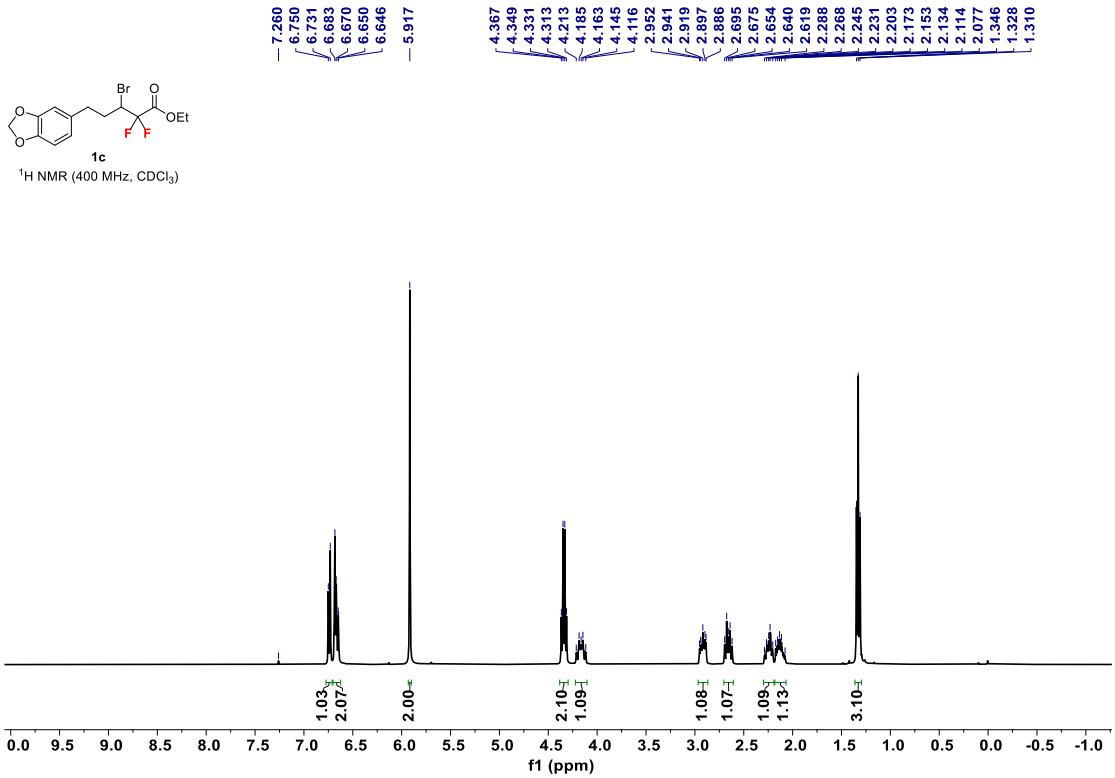


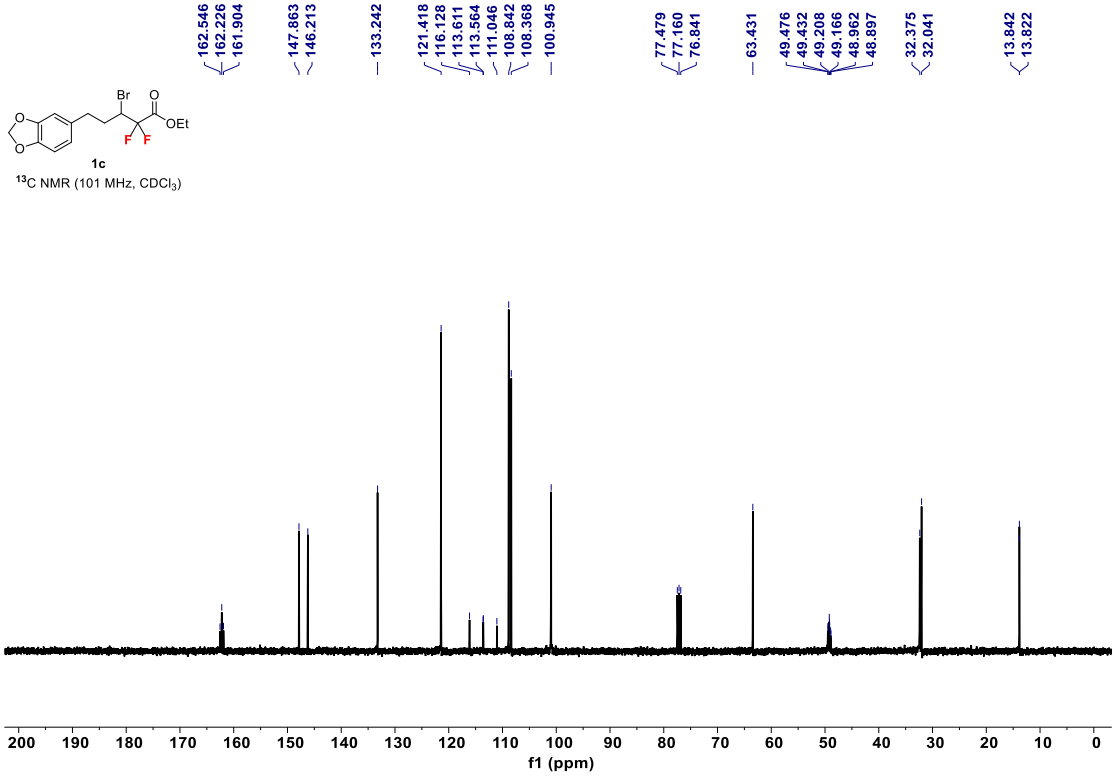
1b

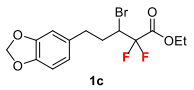
^{1}H NMR (400 MHz, $CDCl_3$)


162.548
162.228
161.907
148.989
147.637
132.011
120.422
116.104
113.586
113.539
111.649
111.353
111.022
77.478
77.160
76.841
63.385
55.901
55.846
55.822
55.763
49.548
49.487
49.252
49.014
48.963
32.245
31.926
13.845
13.828
Br
O
OEt
MeO
MeO
F F
1b
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-104.271
-104.949
-113.744
-114.420
Br
O
OEt
MeO
MeO
F F
1b
19F NMR (376 MHz, CDCl3)
1.00
1.00
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

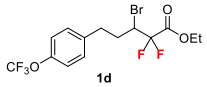

7.260
6.750
6.731
6.683
6.670
6.650
6.646
5.917
4.367
4.349
4.331
4.313
4.213
4.185
4.163
4.145
4.116
2.952
2.941
2.919
2.897
2.886
2.695
2.675
2.654
2.640
2.619
2.288
2.268
2.245
2.231
2.203
2.173
2.153
2.134
2.114
2.077
1.346
1.328
1.310
Br
O
OEt
F F
1c
1H NMR (400 MHz, CDCl3)
1.03
2.07
2.00
2.10
1.09
1.08
1.07
1.09
1.13
3.10
f1 (ppm)


162.546
162.226
161.904
147.863
146.213
133.242
121.418
116.128
113.611
113.564
111.046
108.842
108.368
100.945
77.479
77.160
76.841
63.431
49.476
49.432
49.208
49.166
48.962
48.897
32.375
32.041
13.842
13.822
Br
O
OEt
F F
1c
13C NMR (101 MHz, CDCl3)
f1 (ppm)



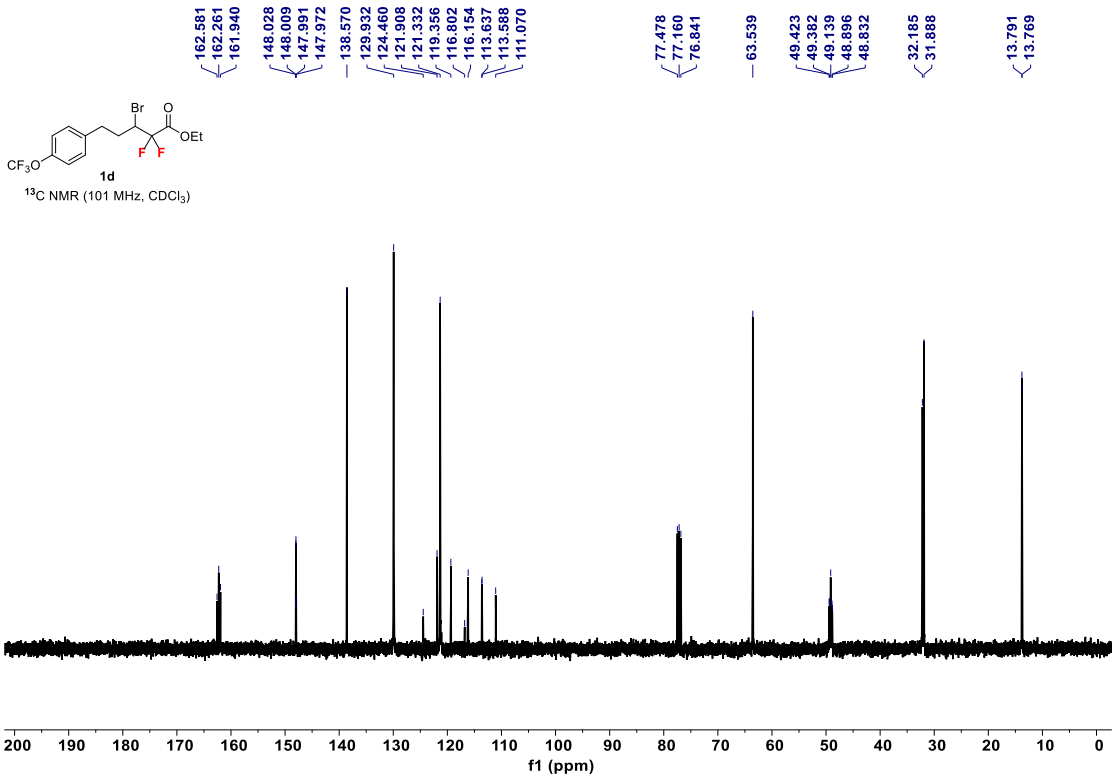
1c

^{19}F NMR (376 MHz, $CDCl_3$)



1d

^{1}H NMR (400 MHz, $CDCl_3$)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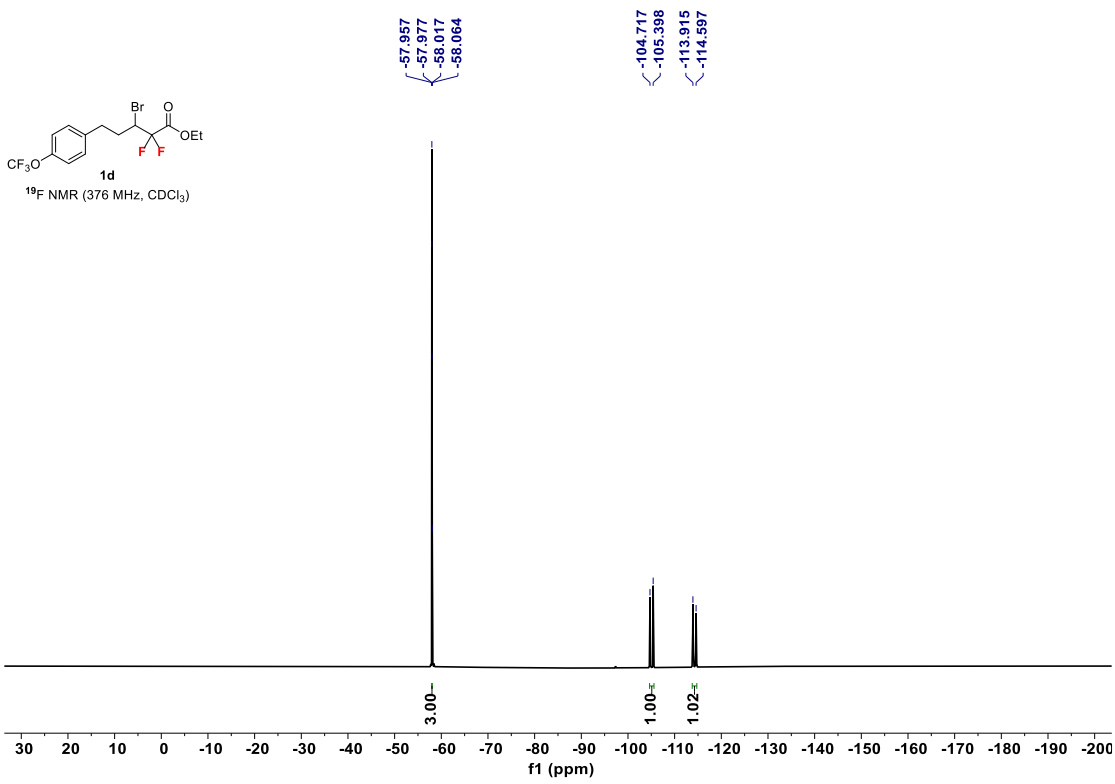
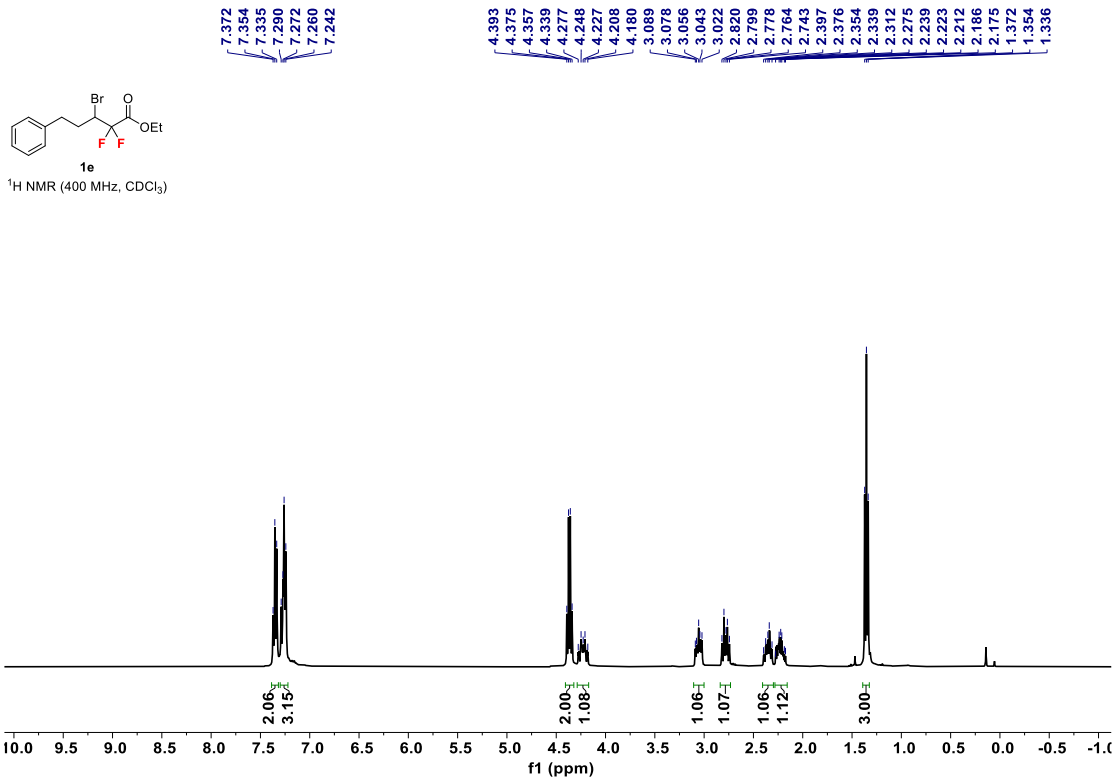
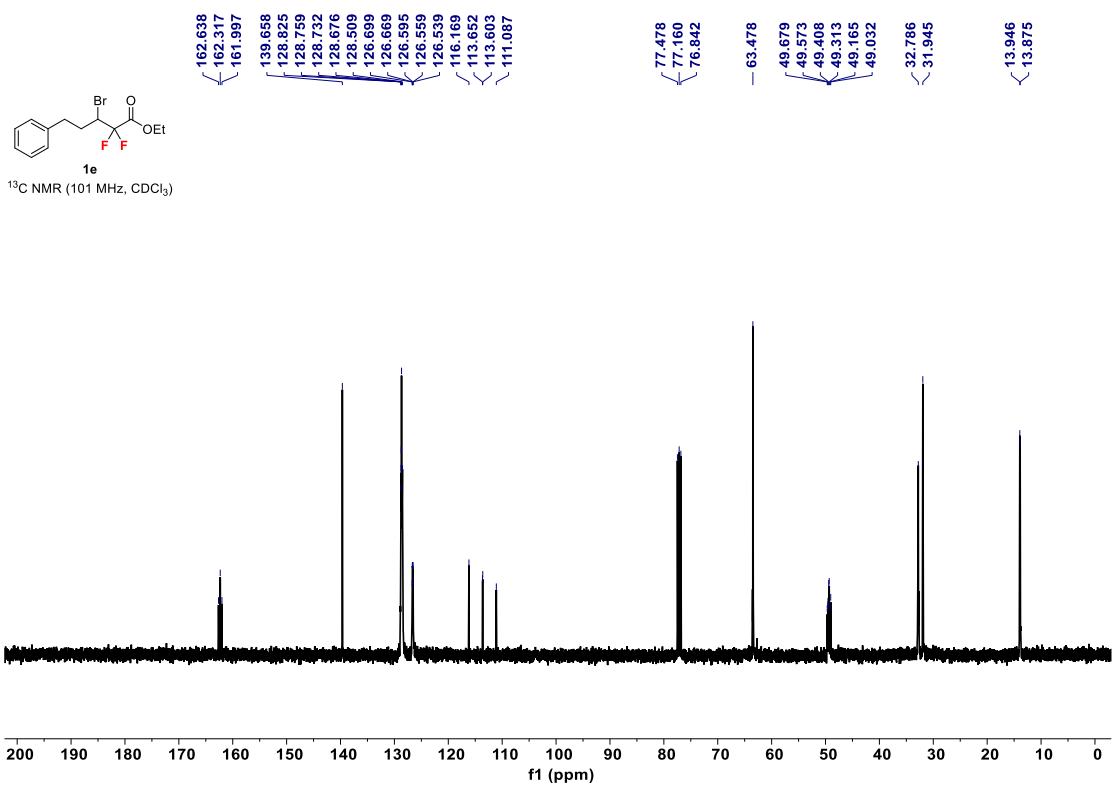
162.261
161.940
148.028
148.009
147.991
147.972
138.570
129.932
124.460
121.908
121.332
119.356
116.802
116.154
113.637
113.588
111.070
77.478
77.160
76.841
63.539
49.423
49.382
49.139
48.896
48.832
32.185
31.888
13.791
13.769
Br
O
OEt
F F
CF3O
1d
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-57.957
-57.977
-58.017
-58.064
-104.717
-105.398
-113.915
-114.597
Br
O
OEt
F F
CF3O
1d
19F NMR (376 MHz, CDCl3)
3.00
1.00
1.02
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)



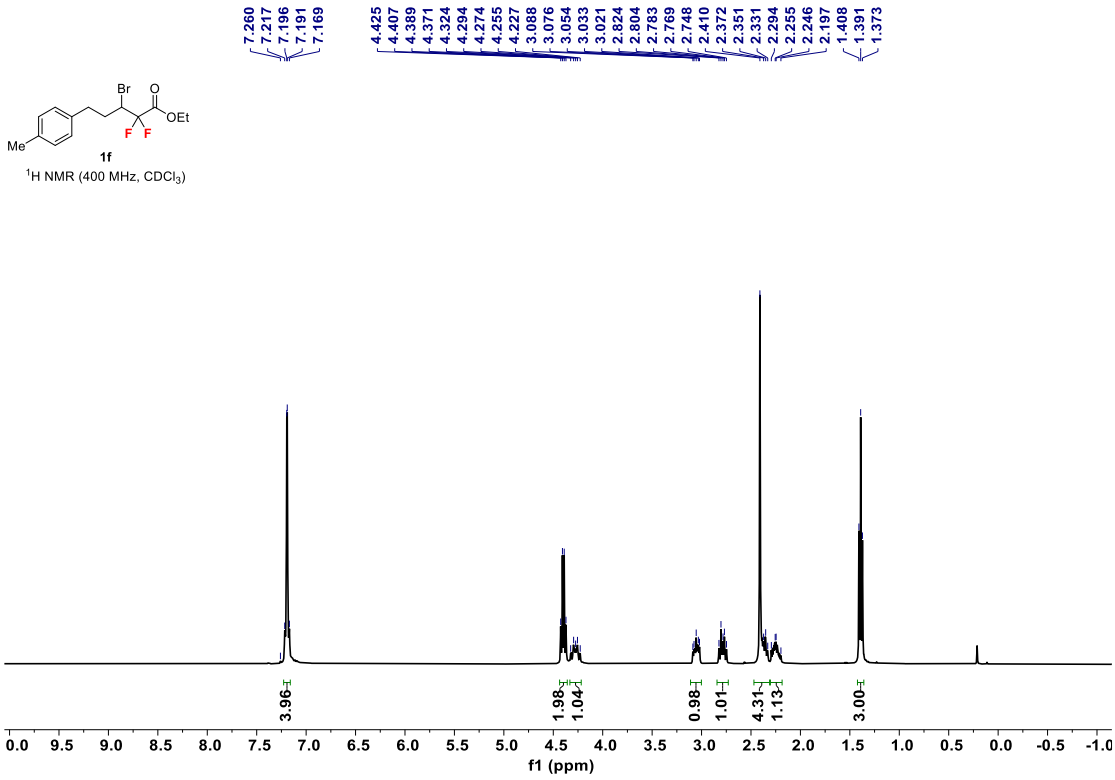
1e

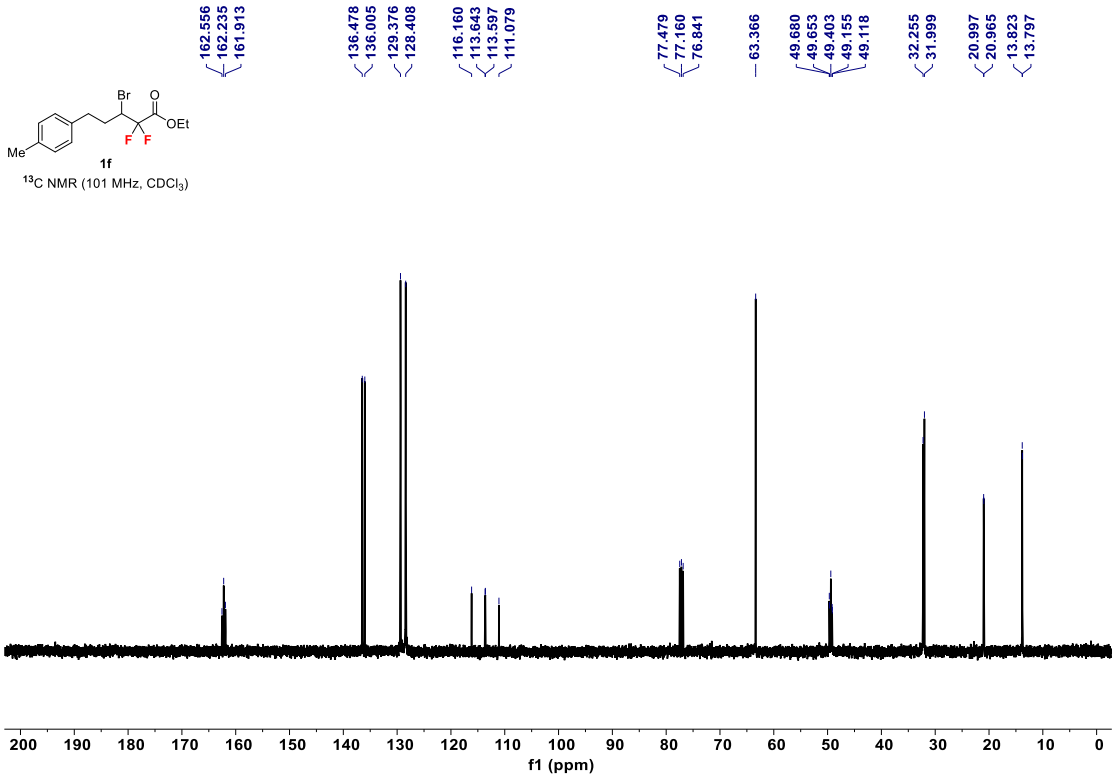
^{1}H NMR (400 MHz, $CDCl_3$)

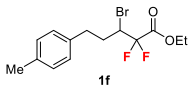


1e

^{13}C NMR (101 MHz, $CDCl_3$)

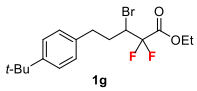

7.260
7.217
7.196
7.191
7.169
4.425
4.407
4.389
4.371
4.324
4.294
4.274
4.255
4.227
3.088
3.076
3.054
3.033
3.021
2.824
2.804
2.783
2.769
2.748
2.410
2.372
2.351
2.331
2.294
2.255
2.246
2.197
1.408
1.391
1.373
Br
O
OEt
F F
Me
1f
^{1}H NMR (400 MHz, CDCl$_3$)
3.96
1.98
1.04
0.98
1.01
4.31
1.13
3.00
f1 (ppm)


162.556
162.235
161.913
136.478
136.005
129.376
128.408
116.160
113.643
113.597
111.079
77.479
77.160
76.841
63.366
49.680
49.653
49.403
49.155
49.118
32.255
31.999
20.997
20.965
13.823
13.797
Br
O
OEt
F F
Me
1f
^{13}C NMR (101 MHz, CDCl$_3$)
f1 (ppm)



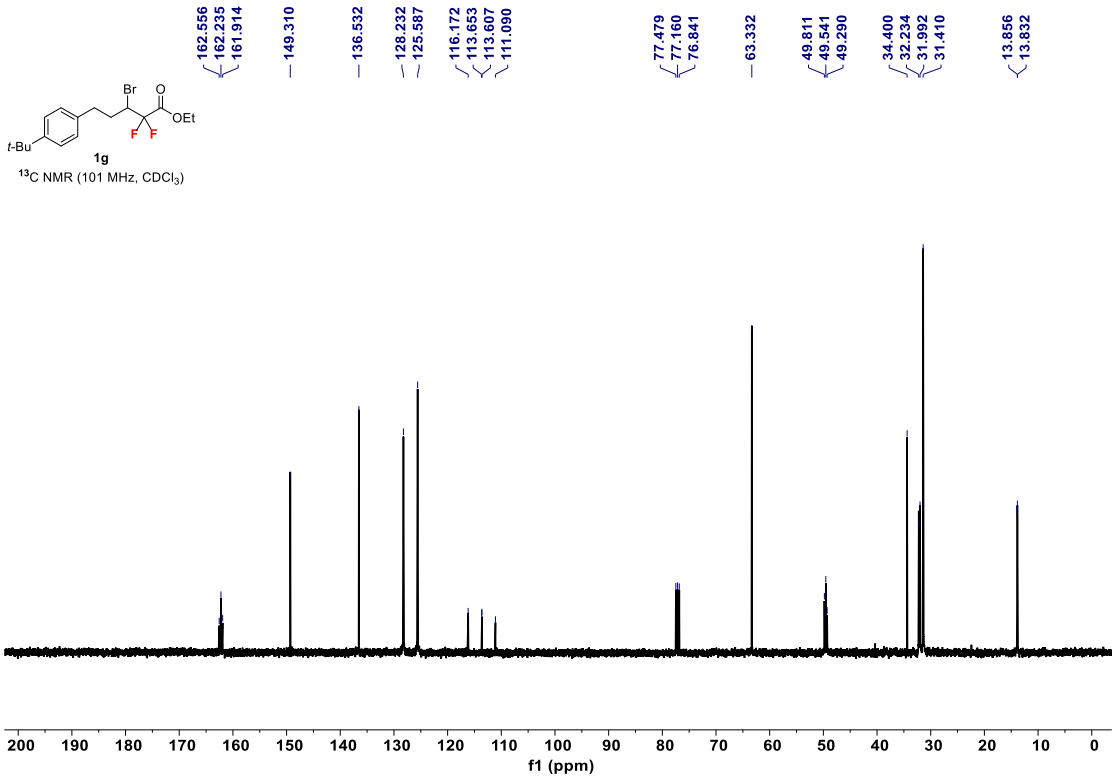
1f

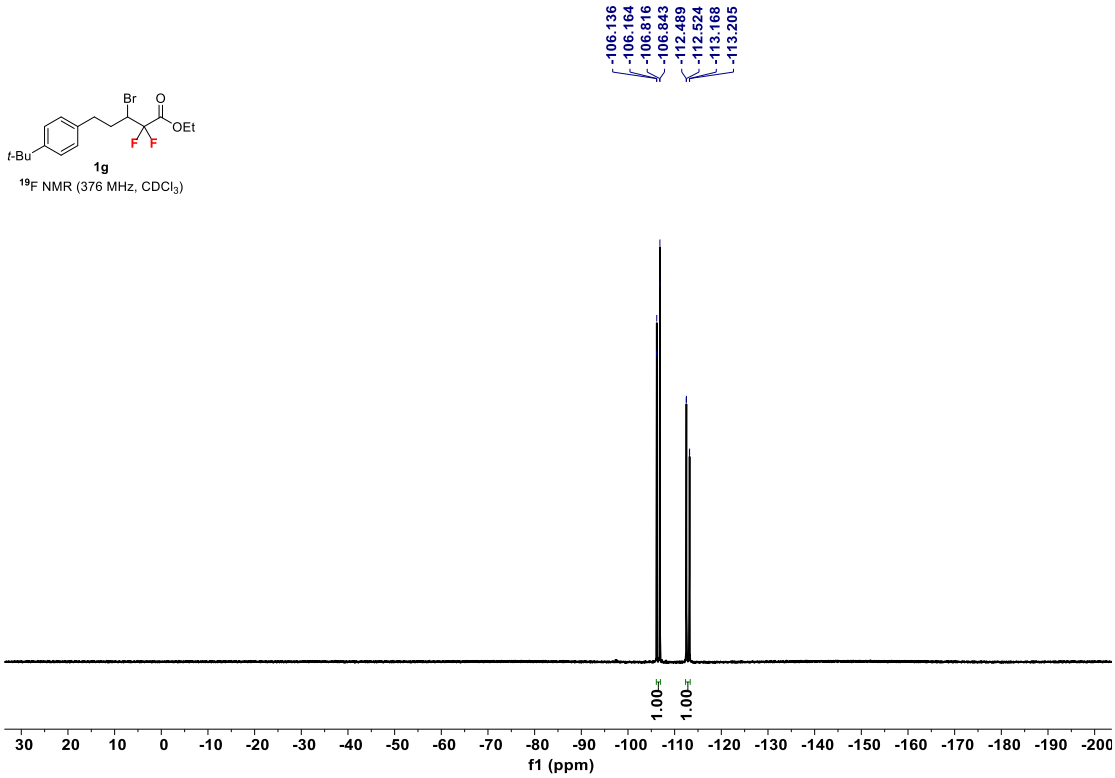
^{19}F NMR (376 MHz, $CDCl_3$)

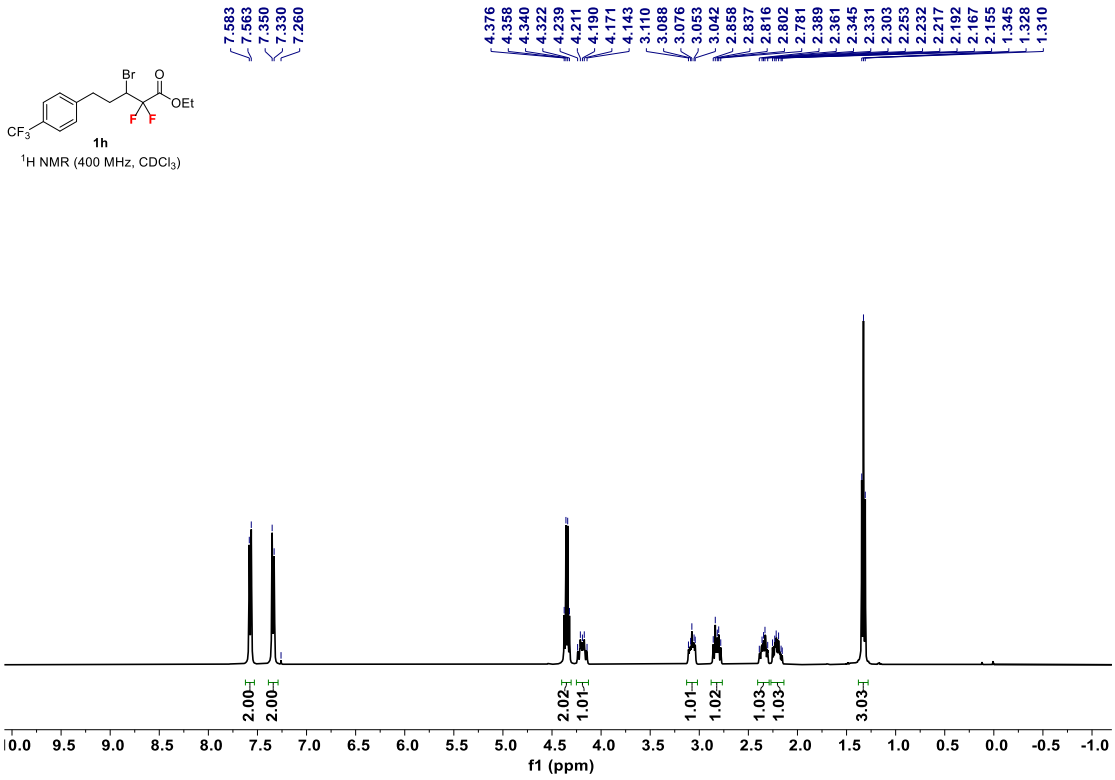


1g

^{1}H NMR (400 MHz, $CDCl_3$)


162.556
162.235
161.914
149.310
136.532
128.232
125.587
116.172
113.653
113.607
111.090
77.479
77.160
76.841
63.332
49.811
49.541
49.290
34.400
32.234
31.992
31.410
13.856
13.832
Br
O
OEt
F
F
t-Bu
1g
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-106.136
-106.164
-106.816
-106.843
-112.489
-112.524
-113.168
-113.205
Br
O
OEt
F
F
t-Bu
1g
19F NMR (376 MHz, CDCl3)
1.00
1.00
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)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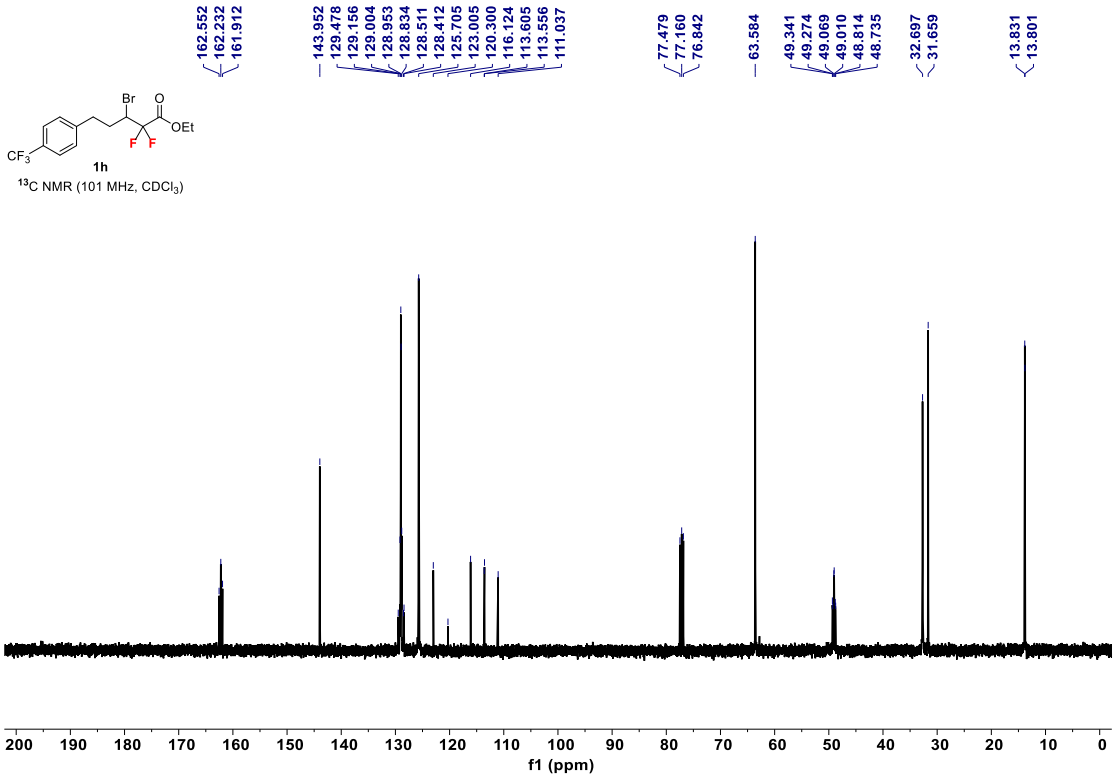
7.563
7.350
7.330
7.260
4.376
4.358
4.340
4.322
4.239
4.211
4.190
4.171
4.143
3.110
3.088
3.076
3.053
3.042
2.858
2.837
2.816
2.802
2.781
2.389
2.361
2.345
2.331
2.303
2.253
2.232
2.217
2.192
2.167
2.155
1.345
1.328
1.310
Br
O
OEt
F
F
CF3
1h
1H NMR (400 MHz, CDCl3)
2.00
2.00
2.02
1.01
1.01
1.02
1.03
1.03
3.03
f1 (ppm)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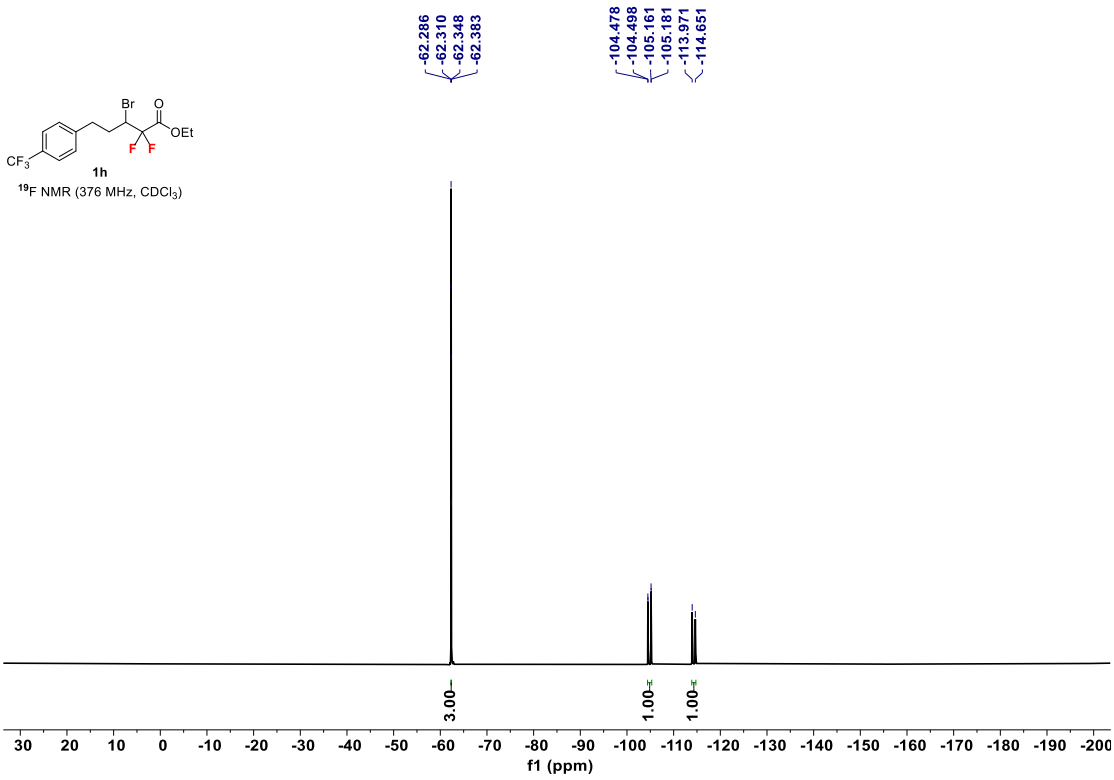
162.232
161.912
143.952
129.478
129.156
129.004
128.953
128.834
128.511
128.412
125.705
123.005
120.300
116.124
113.605
113.556
111.037
77.479
77.160
76.842
63.584
49.341
49.274
49.069
49.010
48.814
48.735
32.697
31.659
13.831
13.801
Br
O
OEt
F
F
CF3
1h
13C NMR (101 MHz, CDCl3)
f1 (ppm)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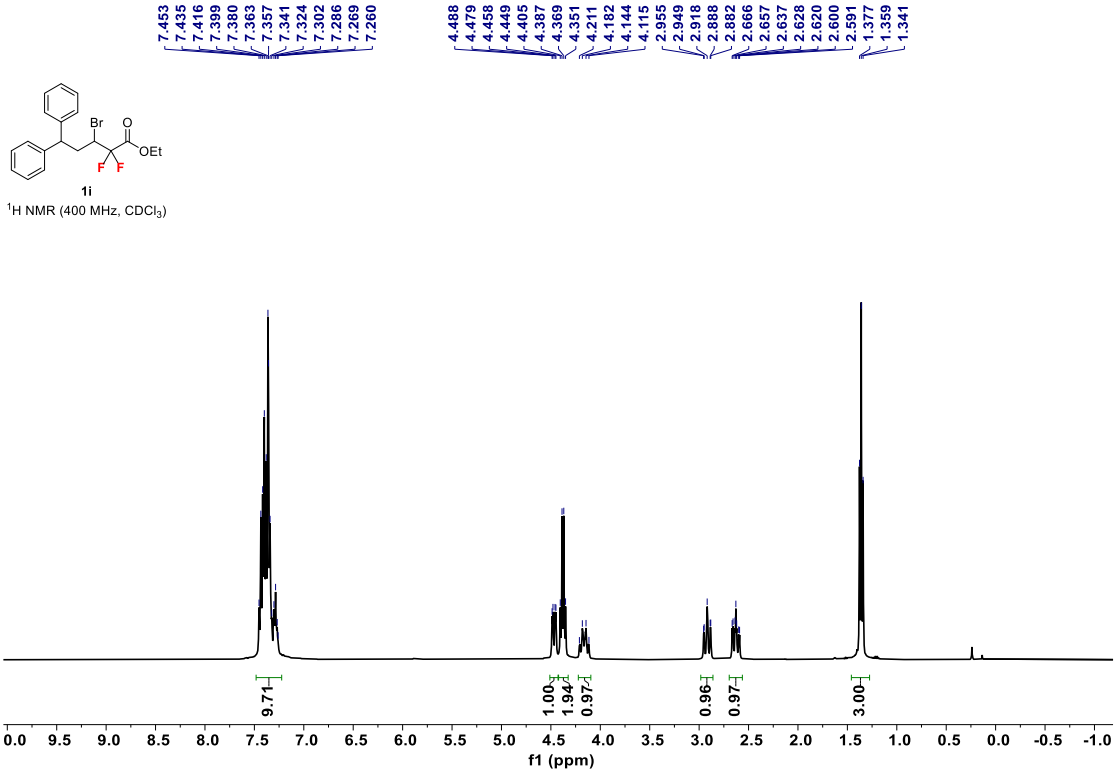
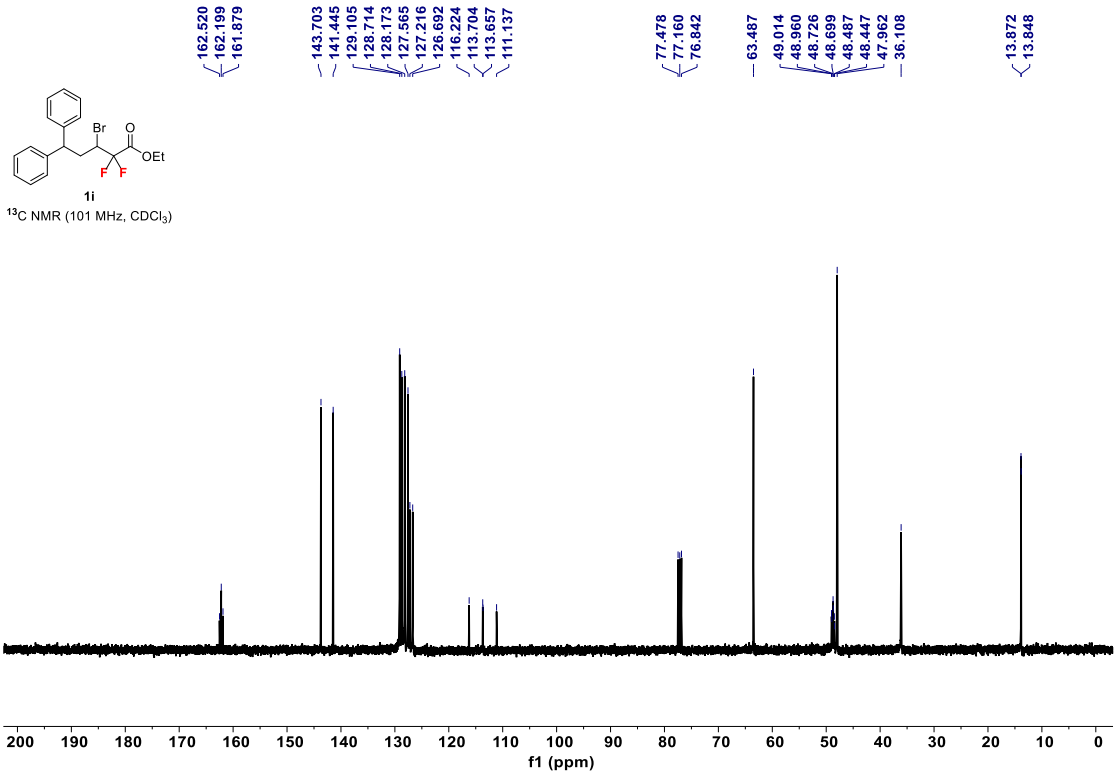
-62.310
-62.348
-62.383
-104.478
-104.498
-105.161
-105.181
-113.971
-114.651
Br
O
OEt
F F
CF3
1h
19F NMR (376 MHz, CDCl3)
3.00
1.00
1.00
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)


7.453
7.435
7.416
7.399
7.380
7.363
7.357
7.341
7.324
7.302
7.286
7.269
7.260
4.488
4.479
4.458
4.449
4.405
4.387
4.369
4.351
4.211
4.182
4.144
4.115
2.955
2.949
2.918
2.888
2.882
2.666
2.657
2.637
2.628
2.620
2.600
2.591
1.377
1.359
1.341
Br
O
OEt
F F
1i
1H NMR (400 MHz, CDCl3)
9.71
1.00
1.94
0.97
0.96
0.97
3.00
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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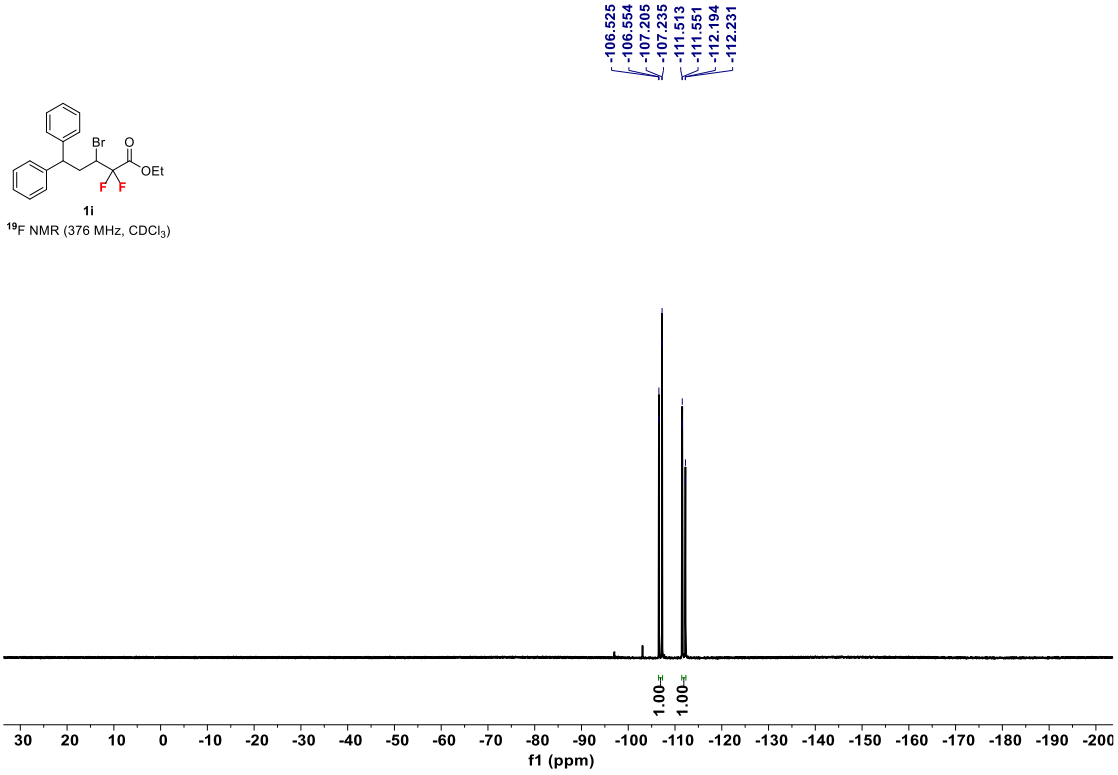
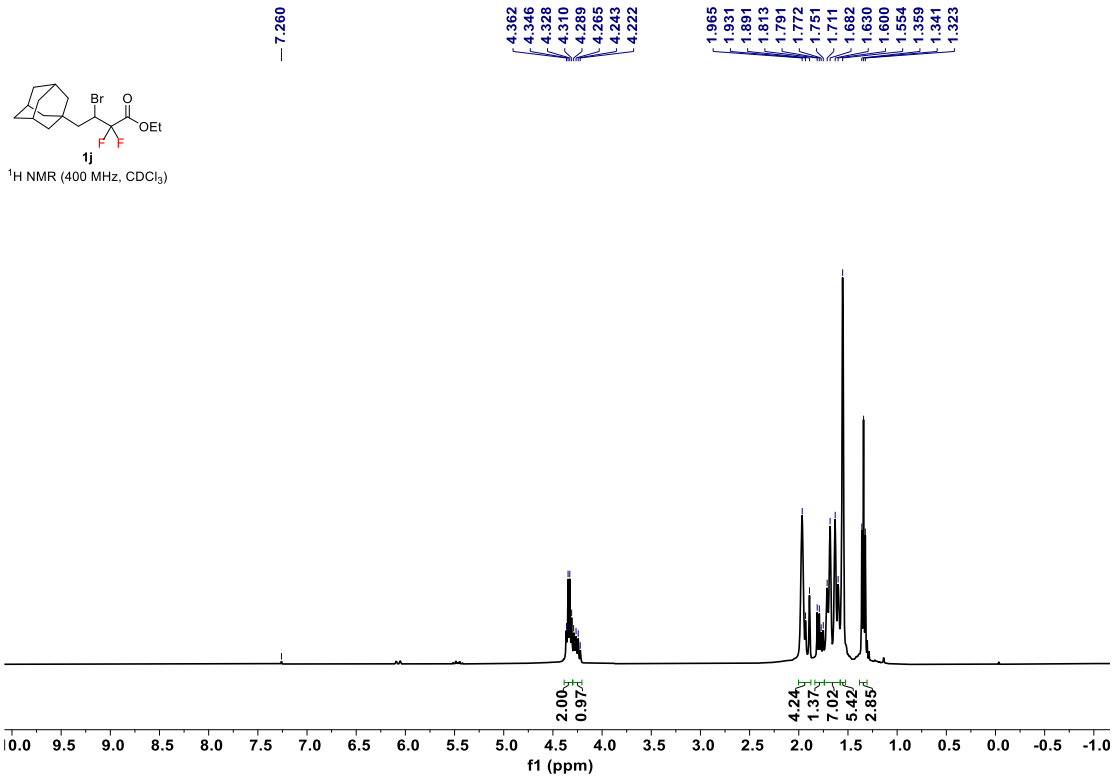
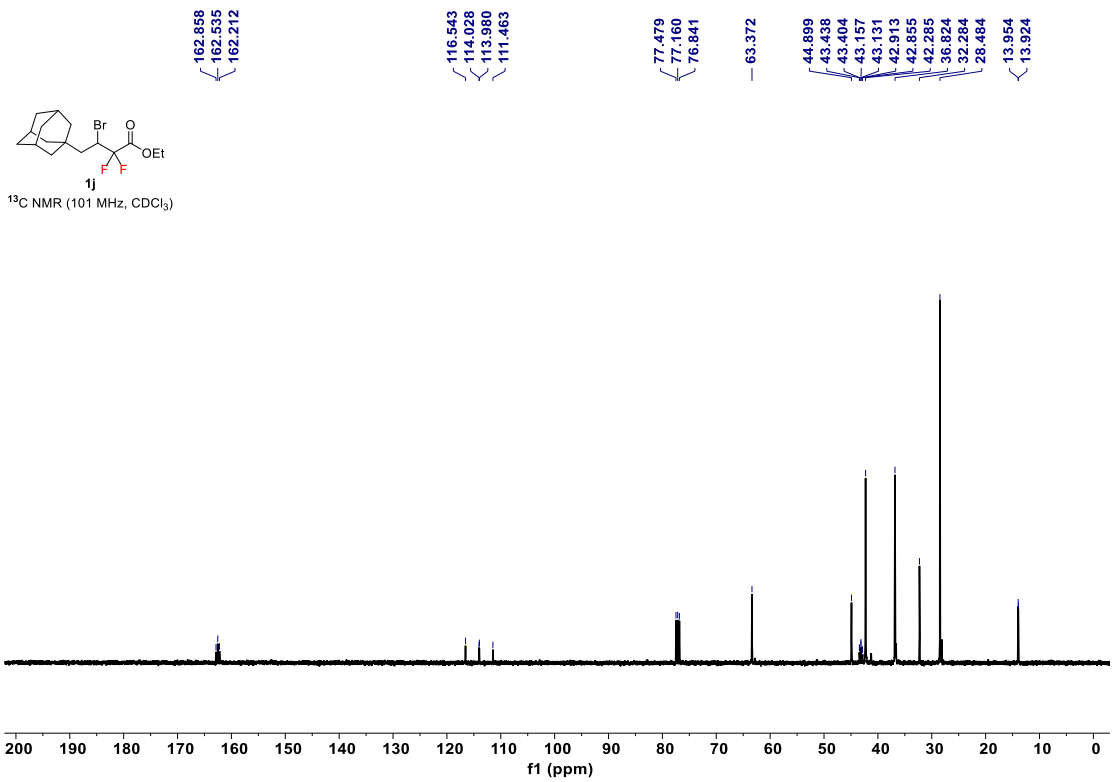
162.199
161.879
143.703
141.445
129.105
128.714
128.173
127.565
127.216
126.692
116.224
113.704
113.657
111.137
77.478
77.160
76.842
63.487
49.014
48.960
48.726
48.699
48.487
48.447
47.962
36.108
13.872
13.848
Br
O
OEt
F
F
1i
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-106.525
-106.554
-107.205
-107.235
-111.513
-111.551
-112.194
-112.231
Br
O
OEt
F
F
1i
19F NMR (376 MHz, CDCl3)
1.00
1.00
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)



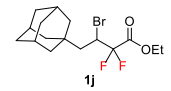
1j

^{1}H NMR (400 MHz, $CDCl_3$)



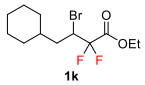
1j

^{13}C NMR (101 MHz, $CDCl_3$)



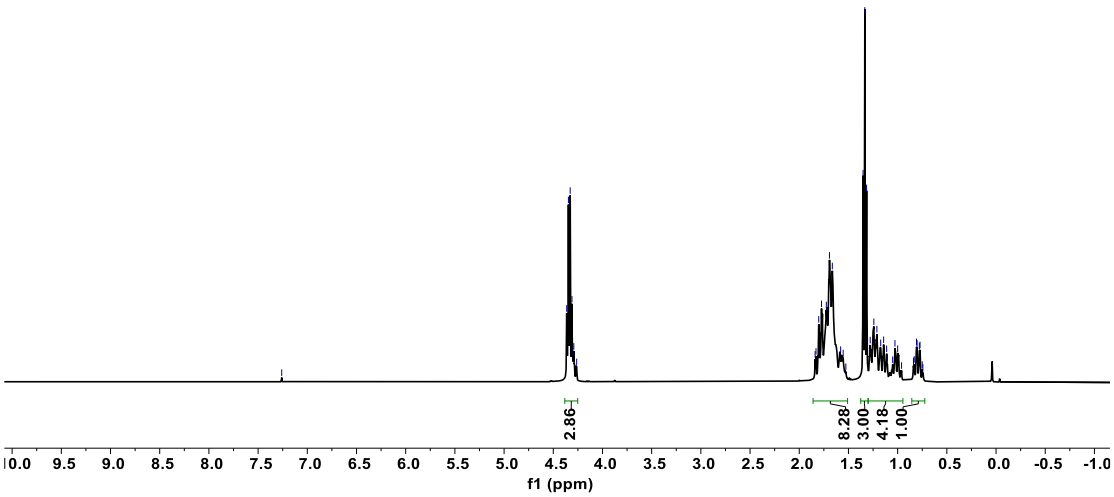
1j

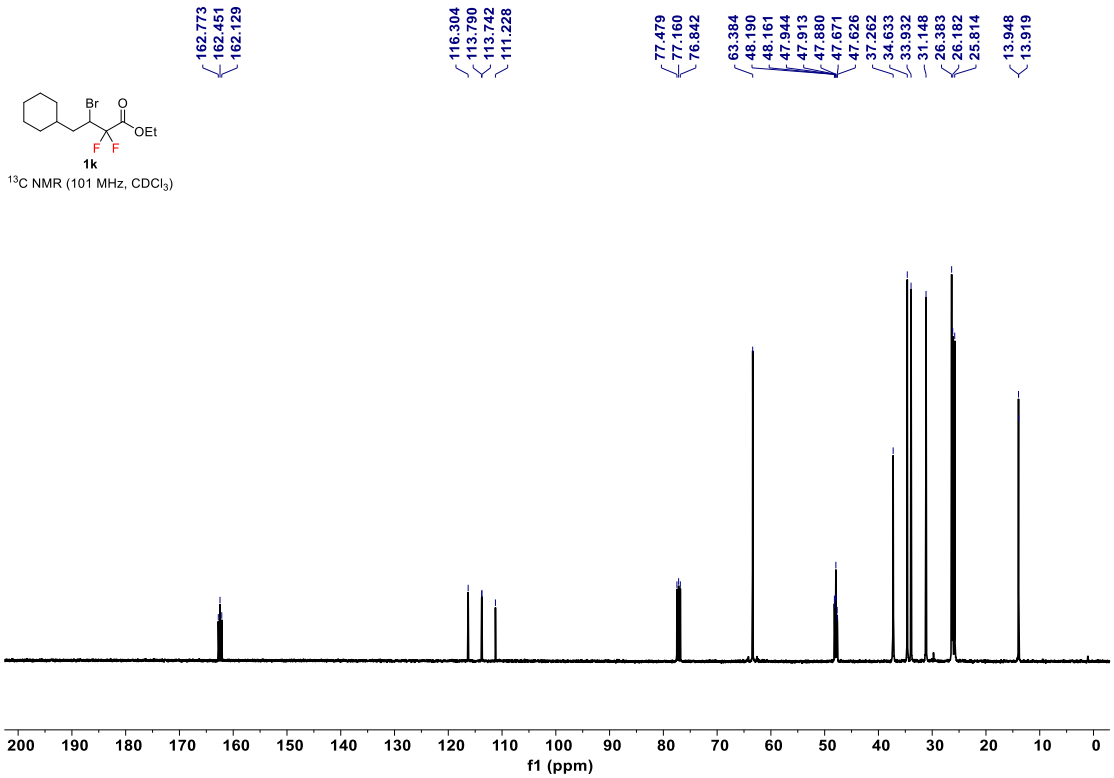
^{19}F NMR (376 MHz, $CDCl_3$)



1k

^{1}H NMR (400 MHz, $CDCl_3$)

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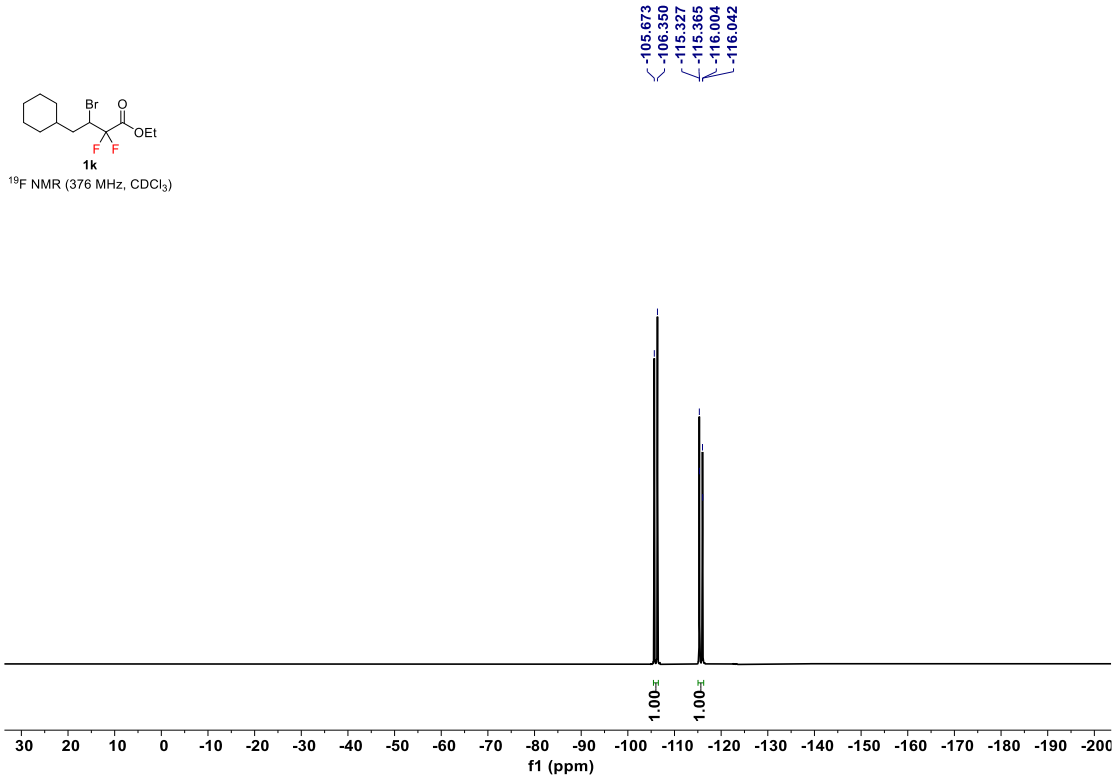
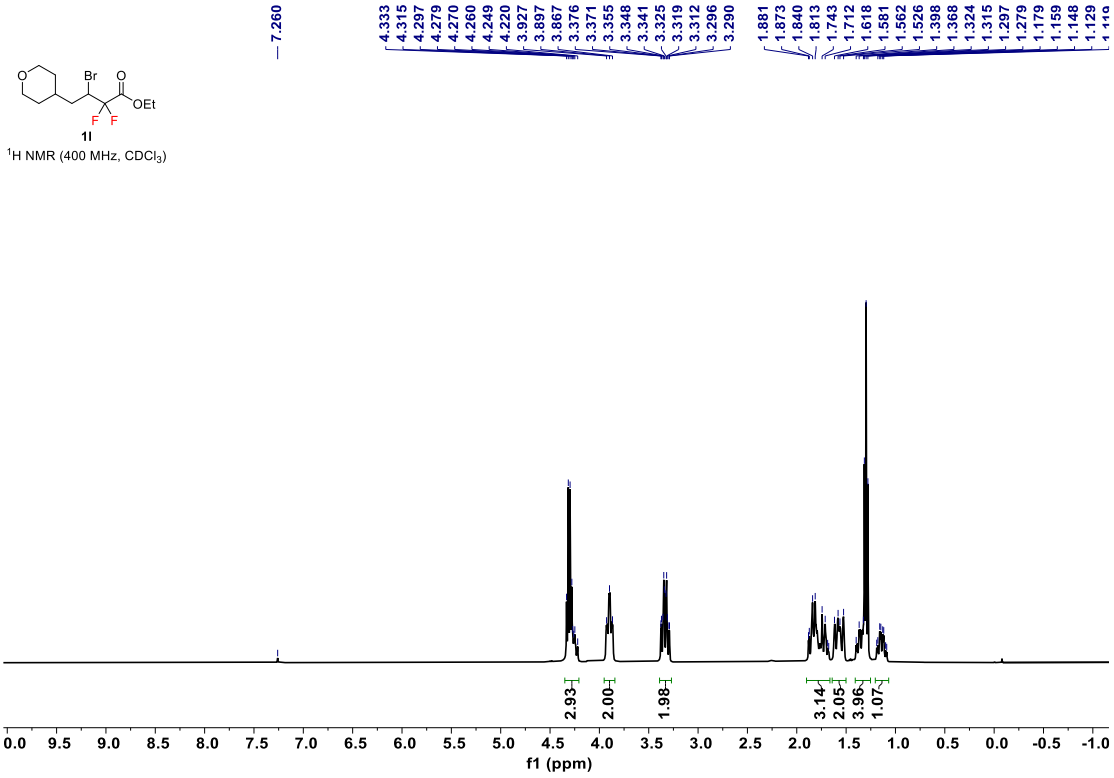
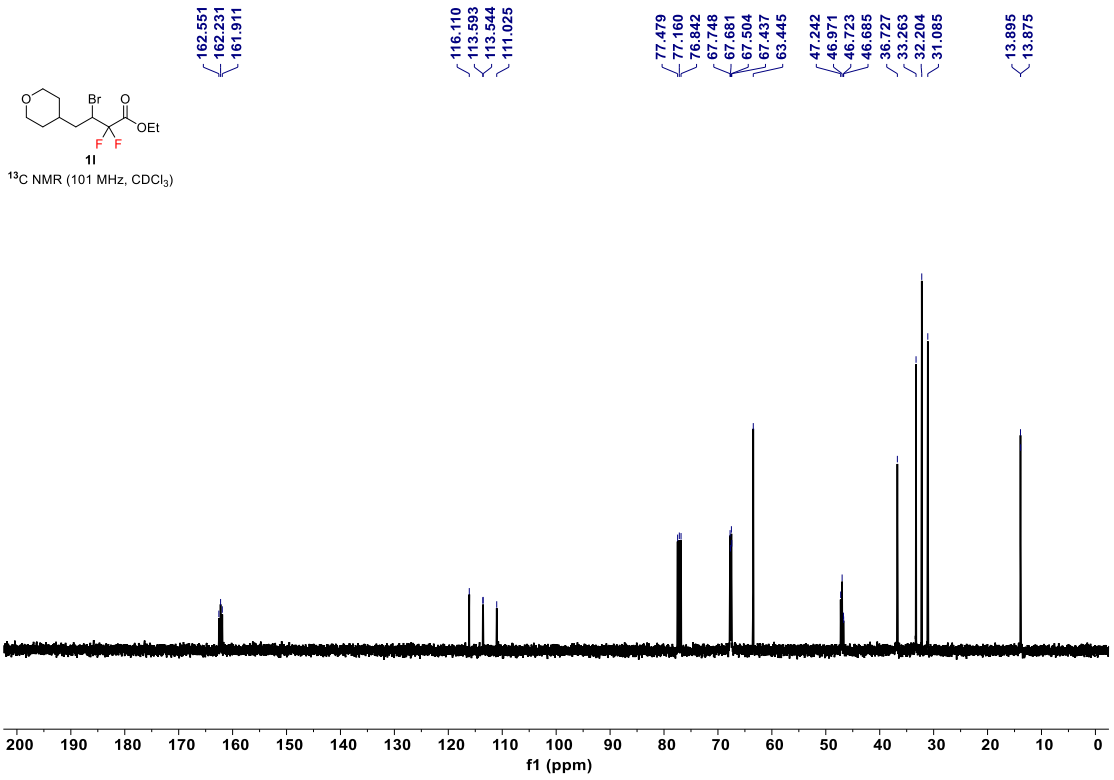
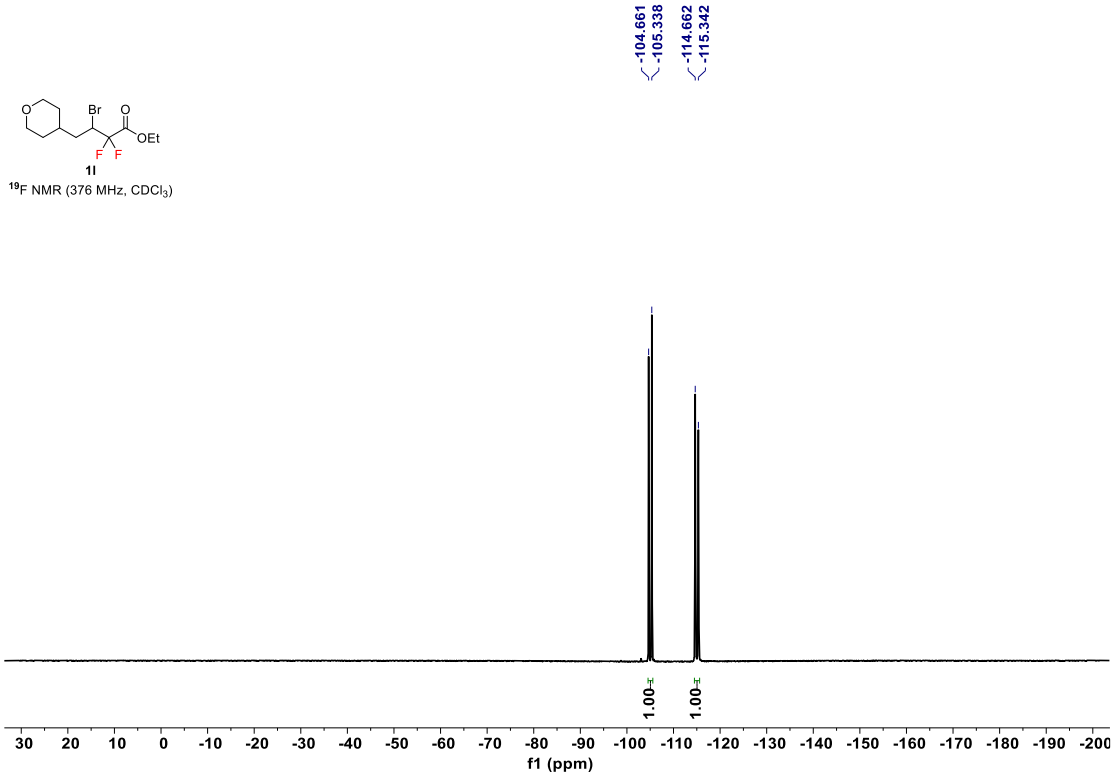
162.451
162.129
116.304
113.790
113.742
111.228
77.479
77.160
76.842
63.384
48.190
48.161
47.944
47.913
47.880
47.671
47.626
37.262
34.633
33.932
31.148
26.383
26.182
25.814
13.948
13.919
Br
O
OEt
F F
1k
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-105.673
-106.350
-115.327
-115.365
-116.004
-116.042
Br
O
OEt
F F
1k
19F NMR (376 MHz, CDCl3)
1.00
1.00
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

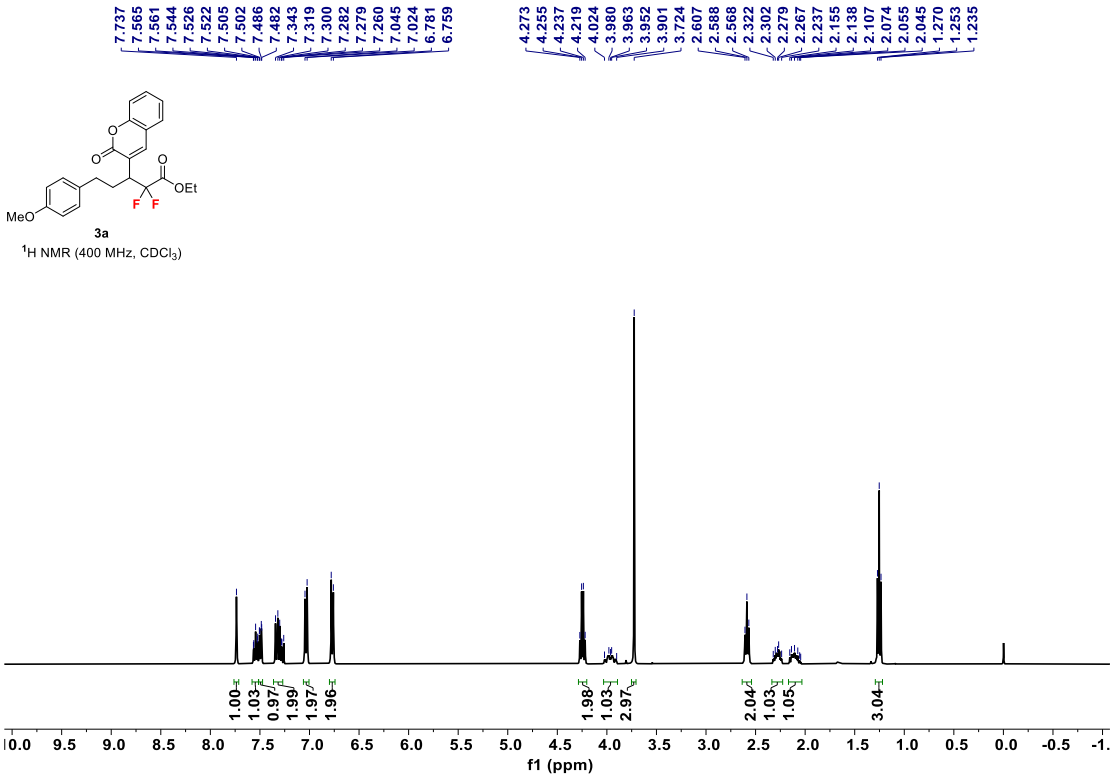

7.260
4.333
4.315
4.297
4.279
4.270
4.260
4.249
4.220
3.927
3.897
3.867
3.376
3.371
3.355
3.348
3.341
3.325
3.319
3.312
3.296
3.290
1.881
1.873
1.840
1.813
1.743
1.712
1.618
1.581
1.562
1.526
1.398
1.368
1.324
1.315
1.297
1.279
1.179
1.159
1.148
1.129
Br
O
O
OEt
F
F
1l
^{1}H NMR (400 MHz, CDCl$_3$)
2.93
2.00
1.98
3.14
2.05
3.96
1.07
f1 (ppm)


162.551
162.231
161.911
116.110
113.593
113.544
111.025
77.479
77.160
76.842
67.748
67.681
67.504
67.437
63.445
47.242
46.971
46.723
46.685
36.727
33.263
32.204
31.085
13.895
13.875
Br
O
O
OEt
F
F
1l
^{13}C NMR (101 MHz, CDCl$_3$)
f1 (ppm)



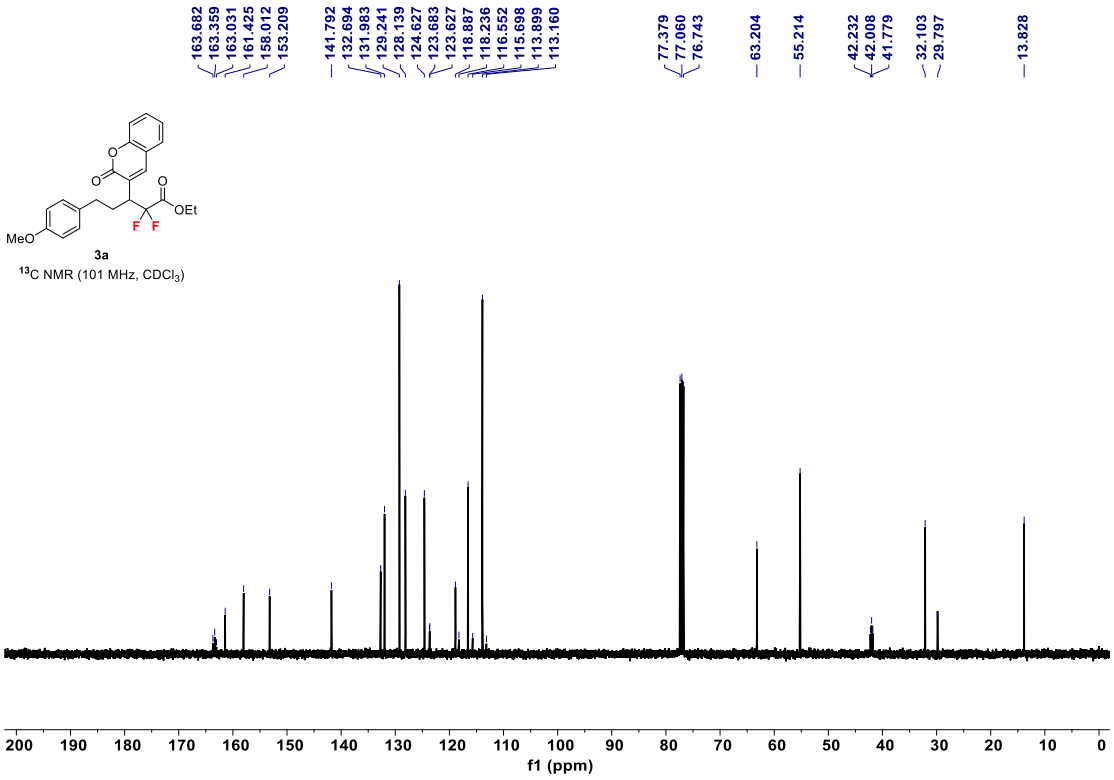
1l

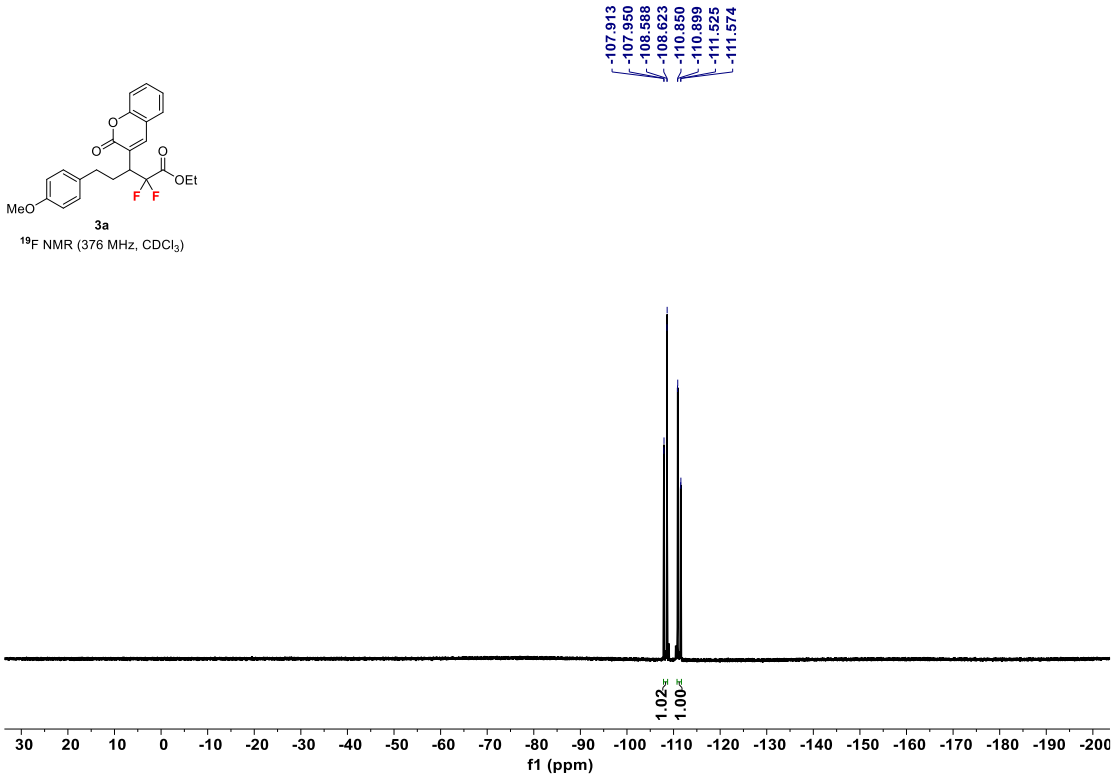
^{19}F NMR (376 MHz, $CDCl_3$)

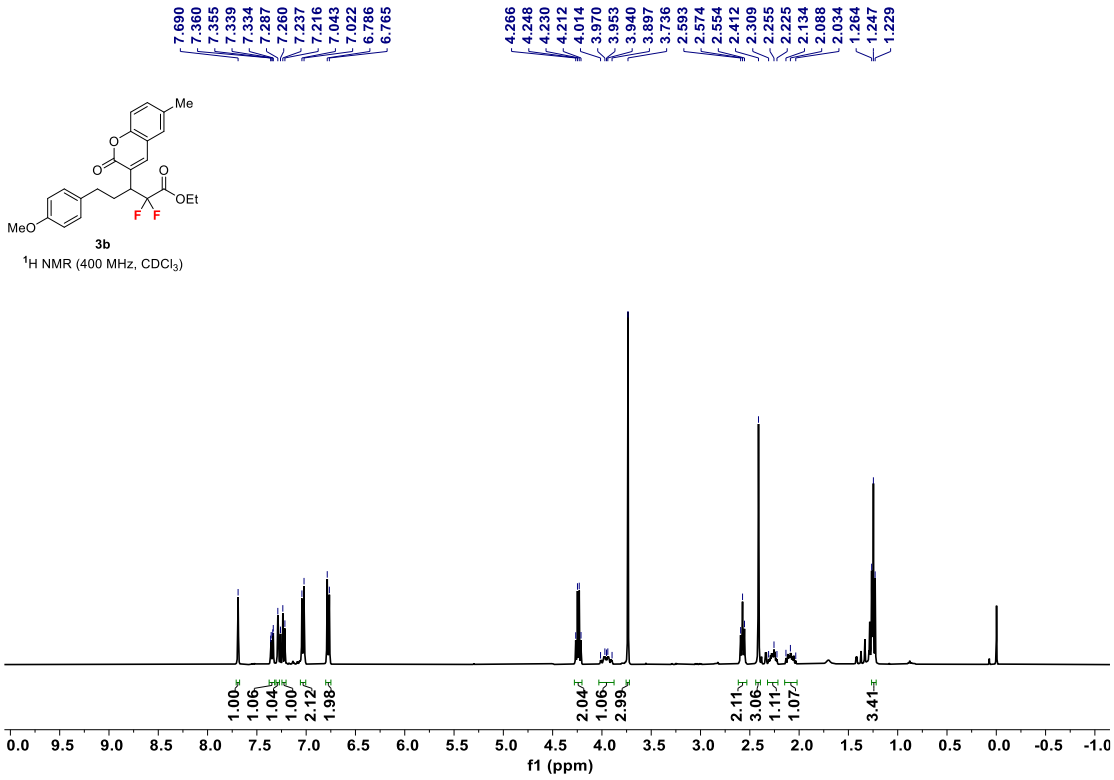


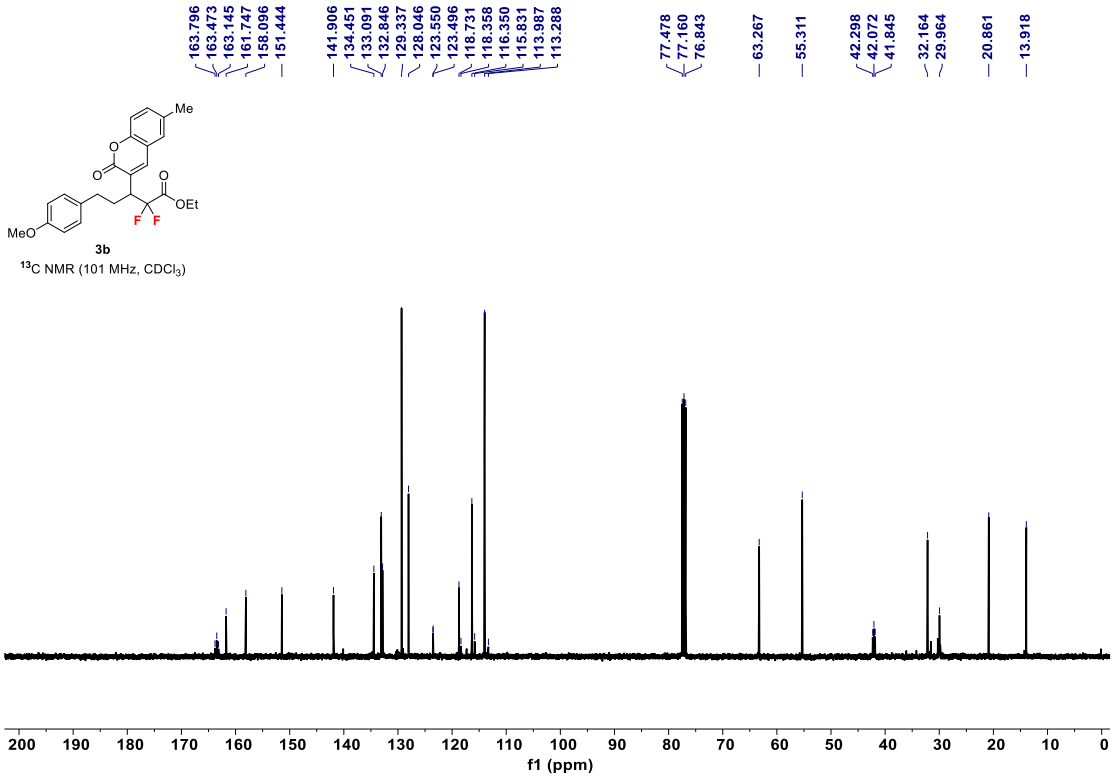
3a

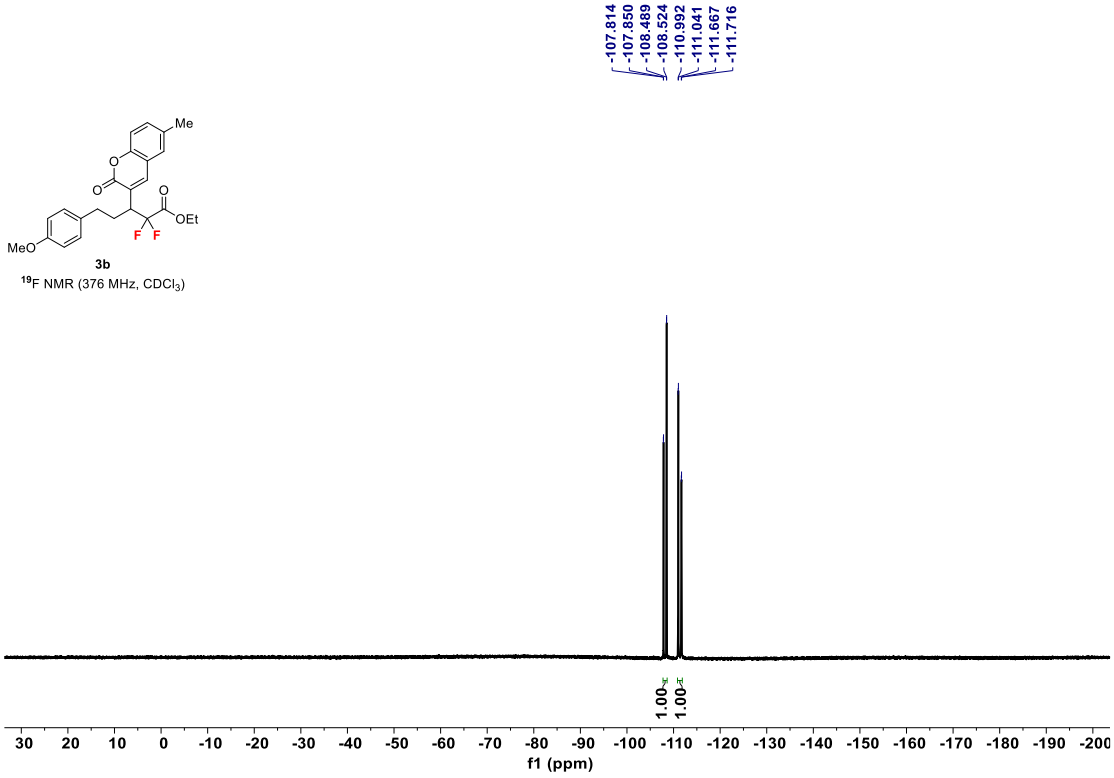
^{1}H NMR (400 MHz, $CDCl_3$)


163.682
163.359
163.031
161.425
158.012
153.209
141.792
132.694
131.983
129.241
128.139
124.627
123.683
123.627
118.887
118.236
116.552
115.698
113.899
113.160
77.379
77.060
76.743
63.204
55.214
42.232
42.008
41.779
32.103
29.797
13.828
MeO
O
O
O
OEt
F F
3a
13C NMR (101 MHz, CDCl3)
f1 (ppm)


-107.913
-107.950
-108.588
-108.623
-110.850
-110.899
-111.525
-111.574
1.02
1.00
MeO
O
O
O
OEt
F F
3a
19F NMR (376 MHz, CDCl3)
f1 (ppm)

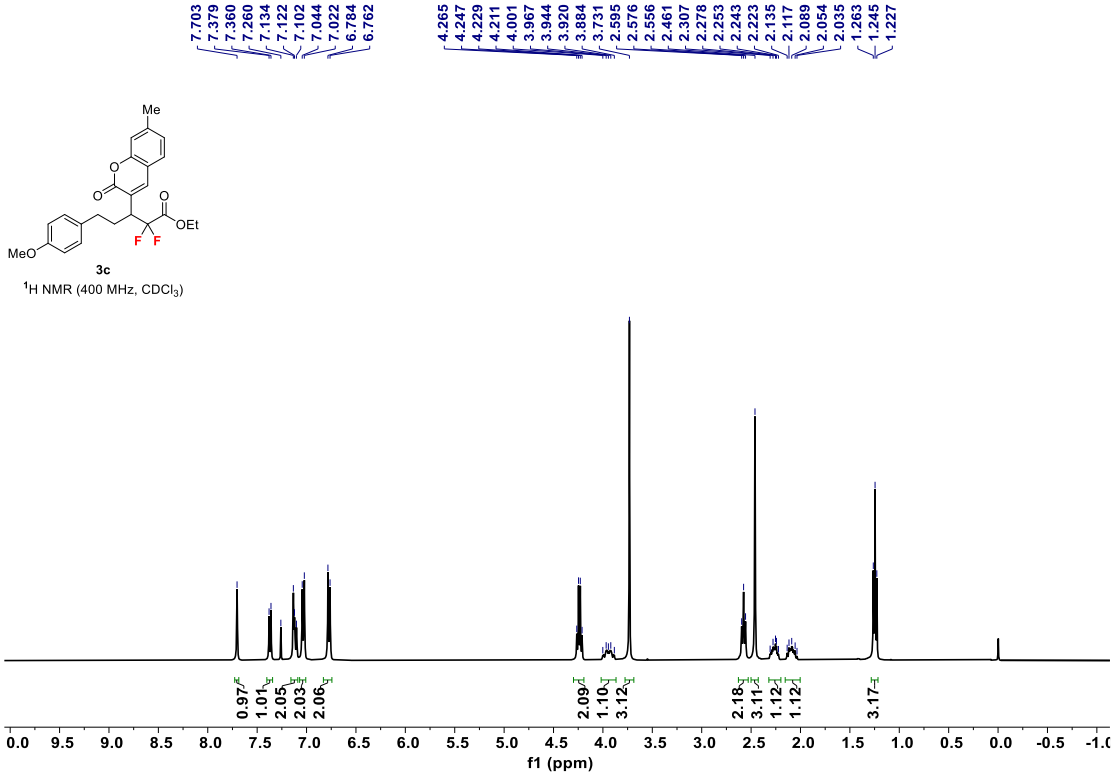

7.690
7.360
7.355
7.339
7.334
7.287
7.260
7.237
7.216
7.043
7.022
6.786
6.765
4.266
4.248
4.230
4.212
4.014
3.970
3.953
3.940
3.897
3.736
2.593
2.574
2.554
2.412
2.309
2.255
2.225
2.134
2.088
2.034
1.264
1.247
1.229
Me
O
O
O
OEt
F F
MeO
3b
1H NMR (400 MHz, CDCl3)
1.00
1.06
1.04
1.00
2.12
1.98
2.04
1.06
2.99
2.11
3.06
1.11
1.07
3.41
f1 (ppm)


163.796
163.473
163.145
161.747
158.096
151.444
141.906
134.451
133.091
132.846
129.337
128.046
123.550
123.496
118.731
118.358
116.350
115.831
113.987
113.288
77.478
77.160
76.843
63.267
55.311
42.298
42.072
41.845
32.164
29.964
20.861
13.918
Me
O
O
O
OEt
F F
MeO
3b
13C NMR (101 MHz, CDCl3)
f1 (ppm)



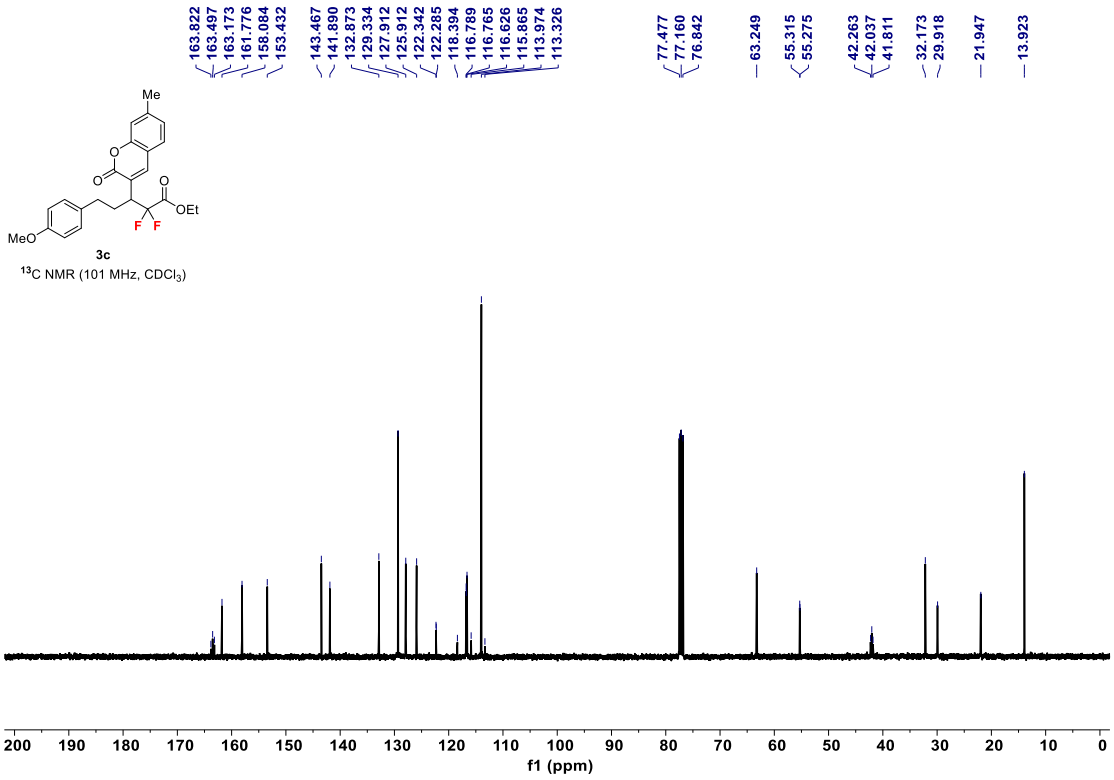
3b

^{19}F NMR (376 MHz, $CDCl_3$)



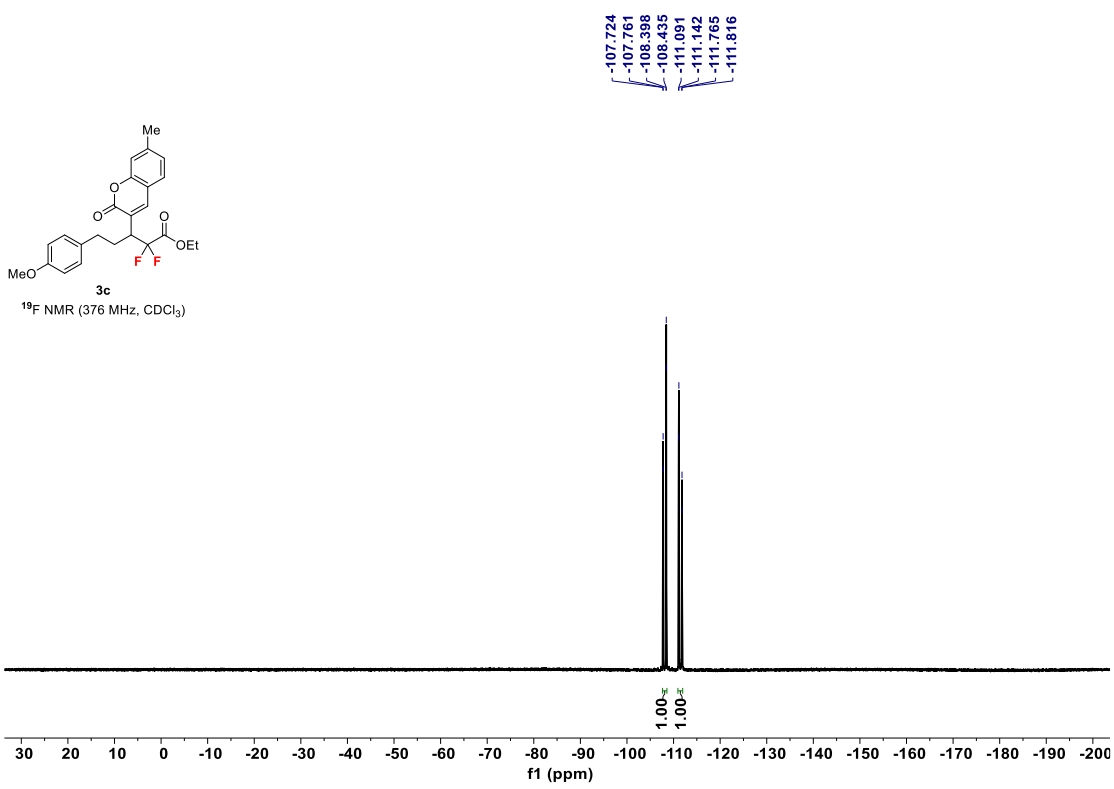
3c

^{1}H NMR (400 MHz, $CDCl_3$)



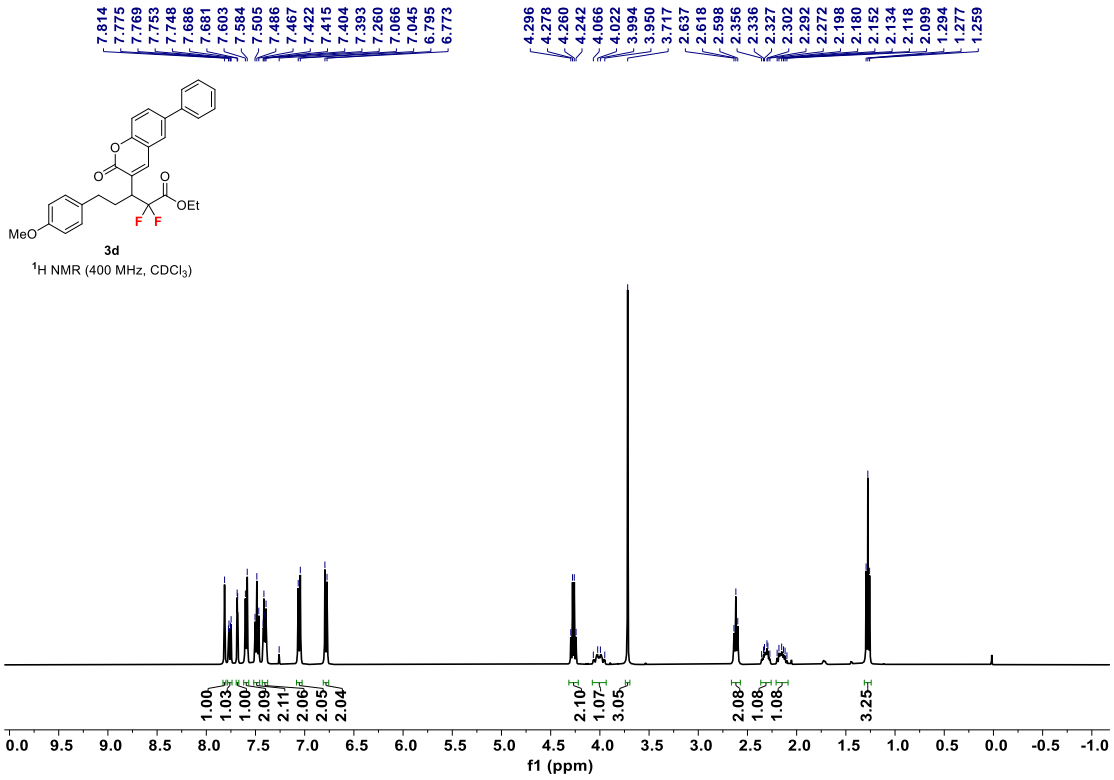
3c

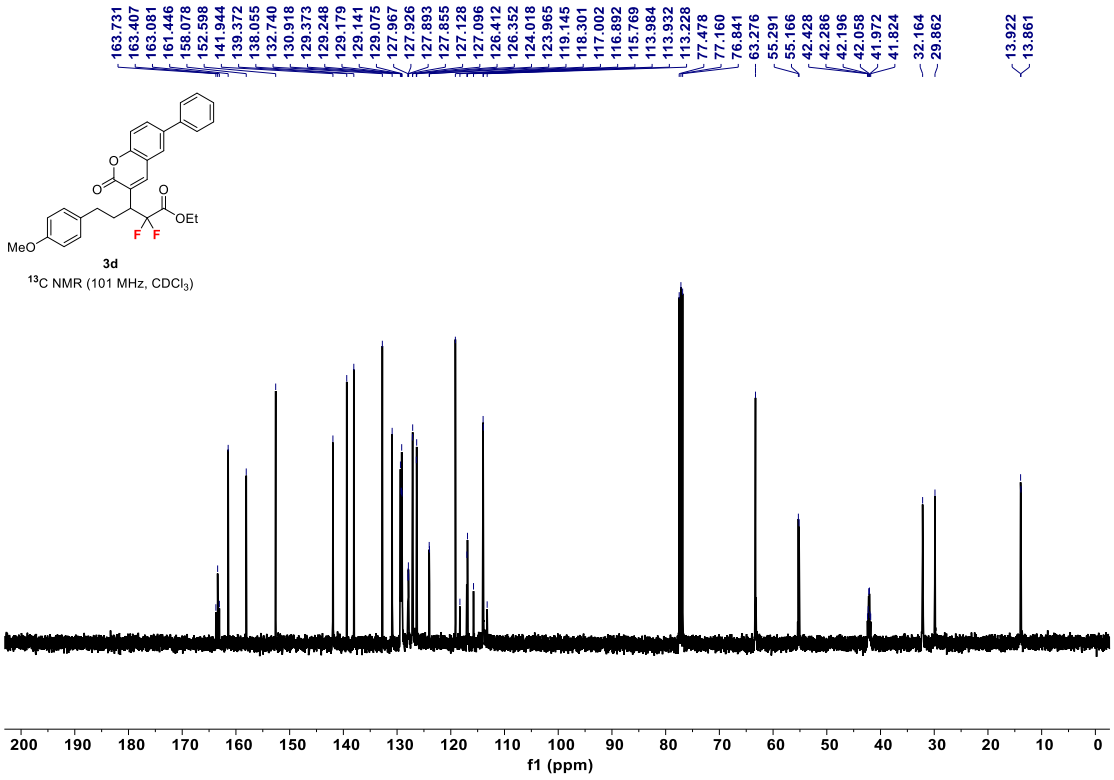
^{13}C NMR (101 MHz, $CDCl_3$)

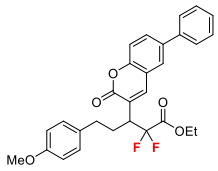


3c

^{19}F NMR (376 MHz, $CDCl_3$)

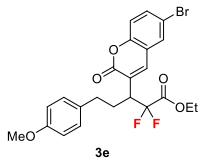

7.814
7.775
7.769
7.753
7.748
7.686
7.681
7.603
7.584
7.505
7.486
7.467
7.422
7.415
7.404
7.393
7.260
7.066
7.045
6.795
6.773
4.296
4.278
4.260
4.242
4.066
4.022
3.994
3.950
3.717
2.637
2.618
2.598
2.356
2.336
2.327
2.302
2.292
2.272
2.198
2.180
2.152
2.134
2.118
2.099
1.294
1.277
1.259
MeO
O
O
O
OEt
F F
3d
1H NMR (400 MHz, CDCl3)
1.00
1.03
1.00
2.09
2.11
2.06
2.05
2.04
2.10
1.07
3.05
2.08
1.08
1.08
3.25
f1 (ppm)


163.731
163.407
163.081
161.446
158.078
152.598
141.944
139.372
138.055
132.740
130.918
129.373
129.248
129.179
129.141
129.075
127.967
127.926
127.893
127.855
127.128
127.096
126.412
126.352
124.018
123.965
119.145
118.301
117.002
116.892
115.769
113.984
113.932
113.228
77.478
77.160
76.841
63.276
55.291
55.166
42.428
42.286
42.196
42.058
41.972
41.824
32.164
29.862
13.922
13.861
MeO
O
O
O
OEt
F F
3d
13C NMR (101 MHz, CDCl3)
f1 (ppm)



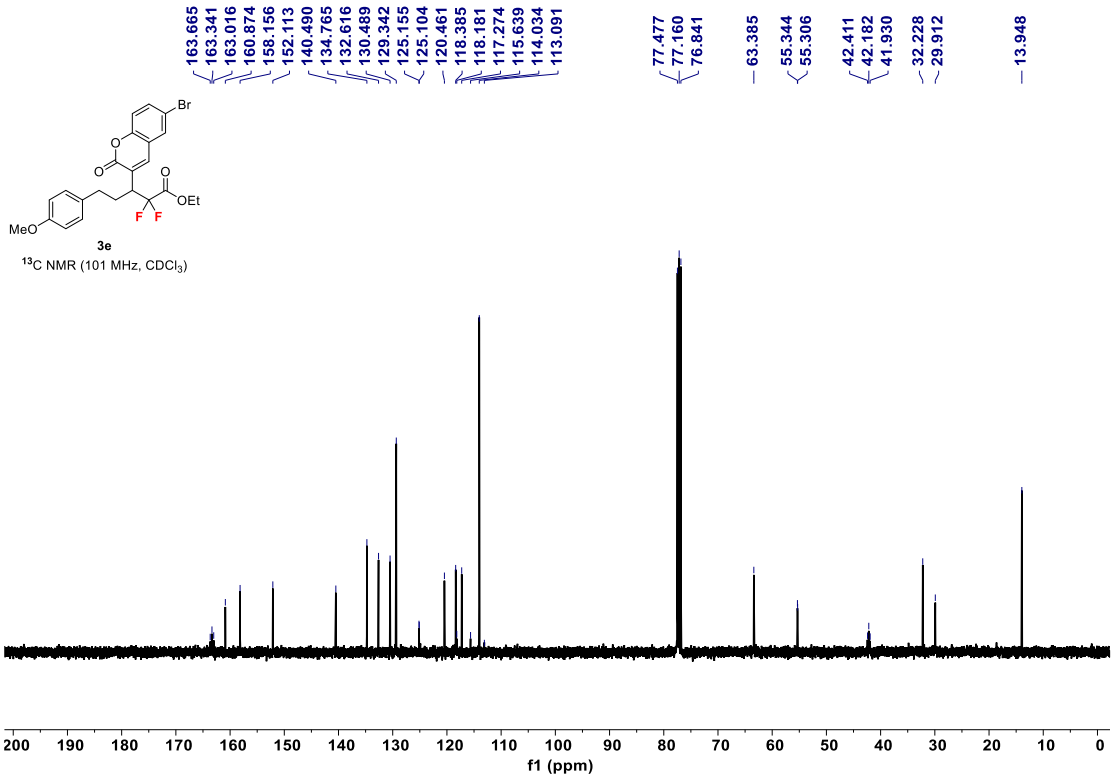
3d

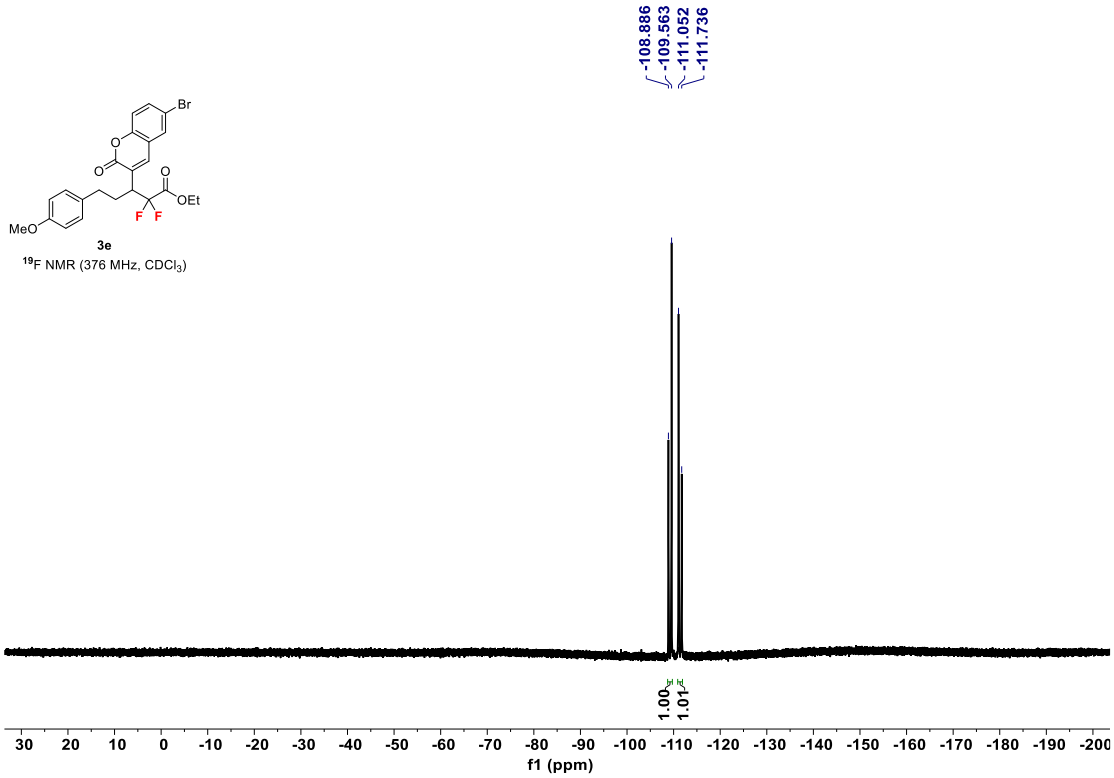
^{19}F NMR (376 MHz, $CDCl_3$)

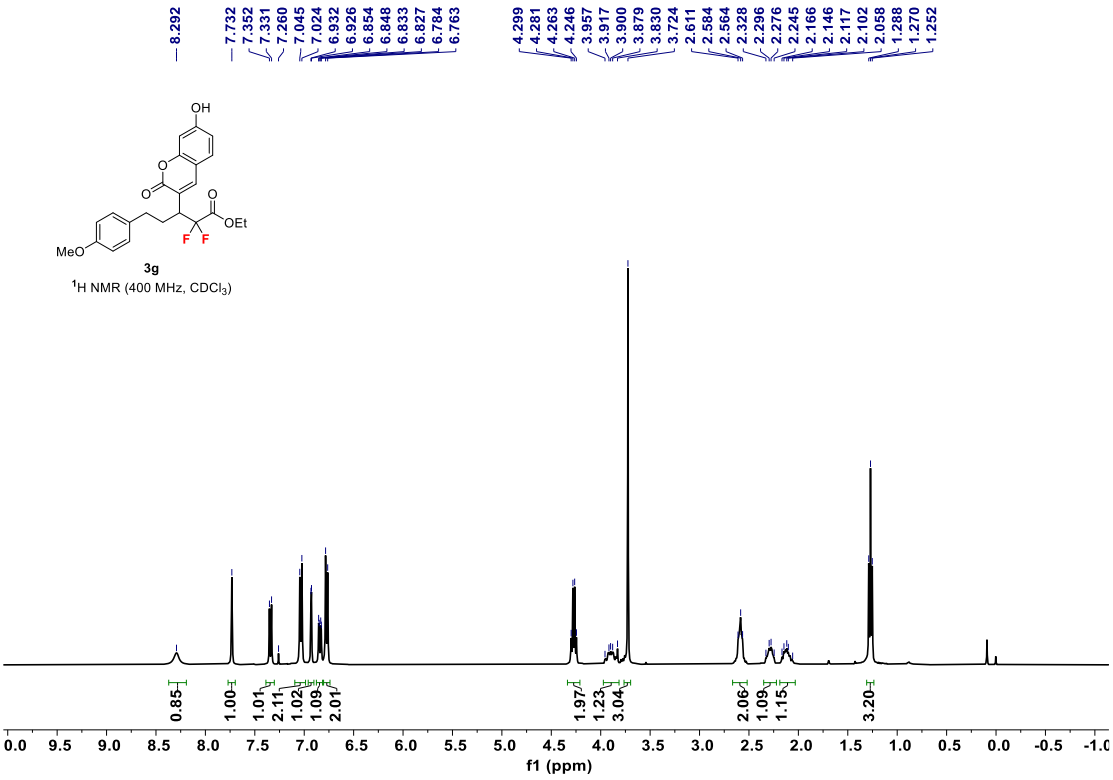


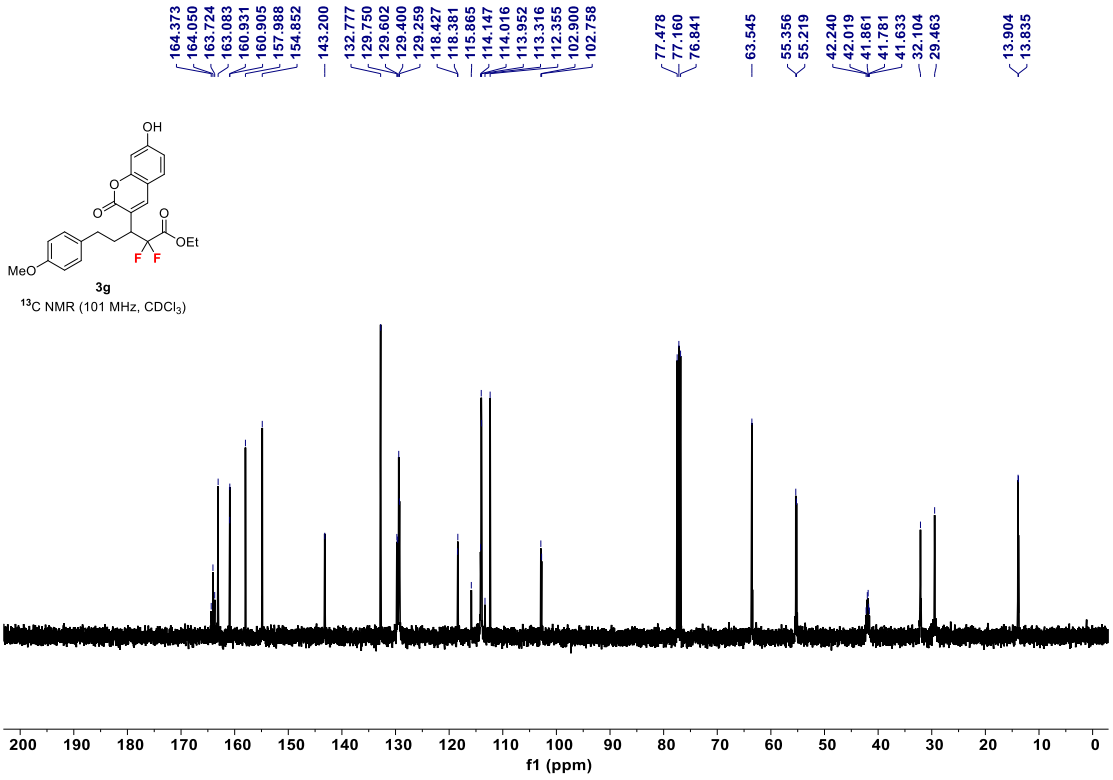
3e

^{1}H NMR (400 MHz, $CDCl_3$)


163.665
163.341
163.016
160.874
158.156
152.113
140.490
134.765
132.616
130.489
129.342
125.155
125.104
120.461
118.385
118.181
117.274
115.639
114.034
113.091
77.477
77.160
76.841
63.385
55.344
55.306
42.411
42.182
41.930
32.228
29.912
13.948
Br
O
O
O
OEt
F F
MeO
3e
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-108.886
-109.563
-111.052
-111.736
Br
O
O
O
OEt
F F
MeO
3e
19F NMR (376 MHz, CDCl3)
1.00
1.01
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)


8.292
7.732
7.352
7.331
7.260
7.045
7.024
6.932
6.926
6.854
6.848
6.833
6.827
6.784
6.763
4.299
4.281
4.263
4.246
3.957
3.917
3.900
3.879
3.830
3.724
2.611
2.584
2.564
2.328
2.296
2.276
2.245
2.166
2.146
2.117
2.102
2.058
1.288
1.270
1.252
OH
O
O
O
OEt
F F
MeO
3g
1H NMR (400 MHz, CDCl3)
0.85
1.00
1.01
2.11
1.02
1.09
2.01
1.97
1.23
3.04
2.06
1.09
1.15
3.20
f1 (ppm)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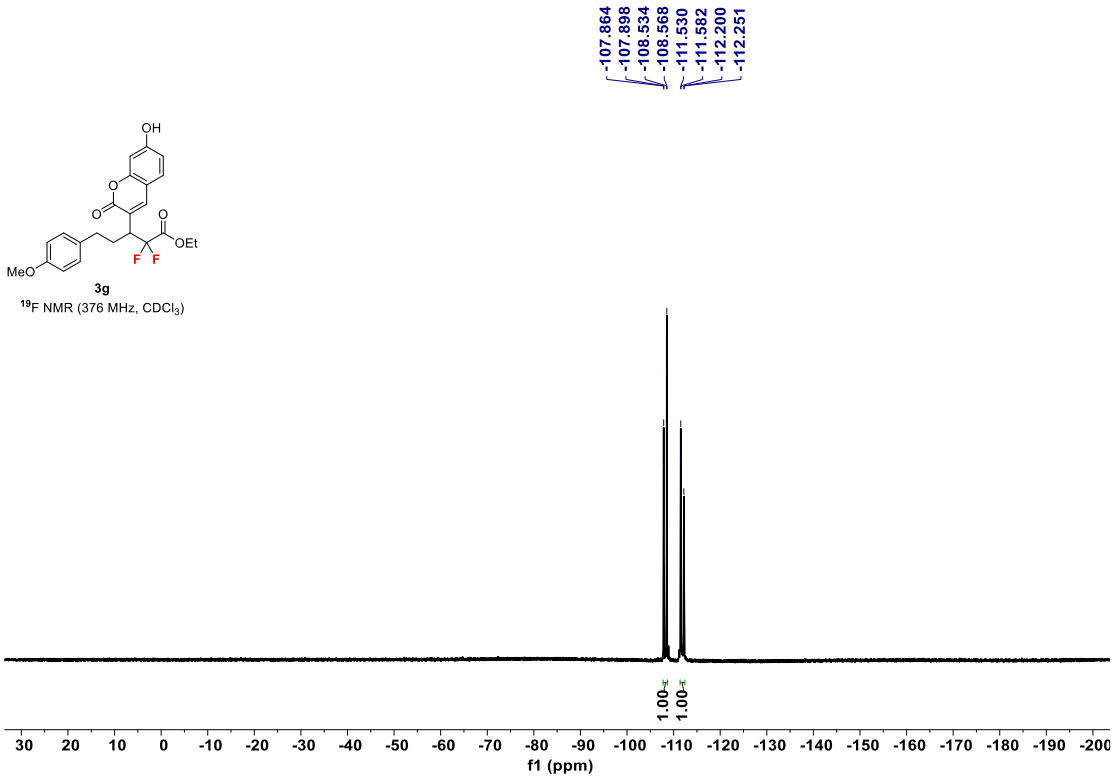
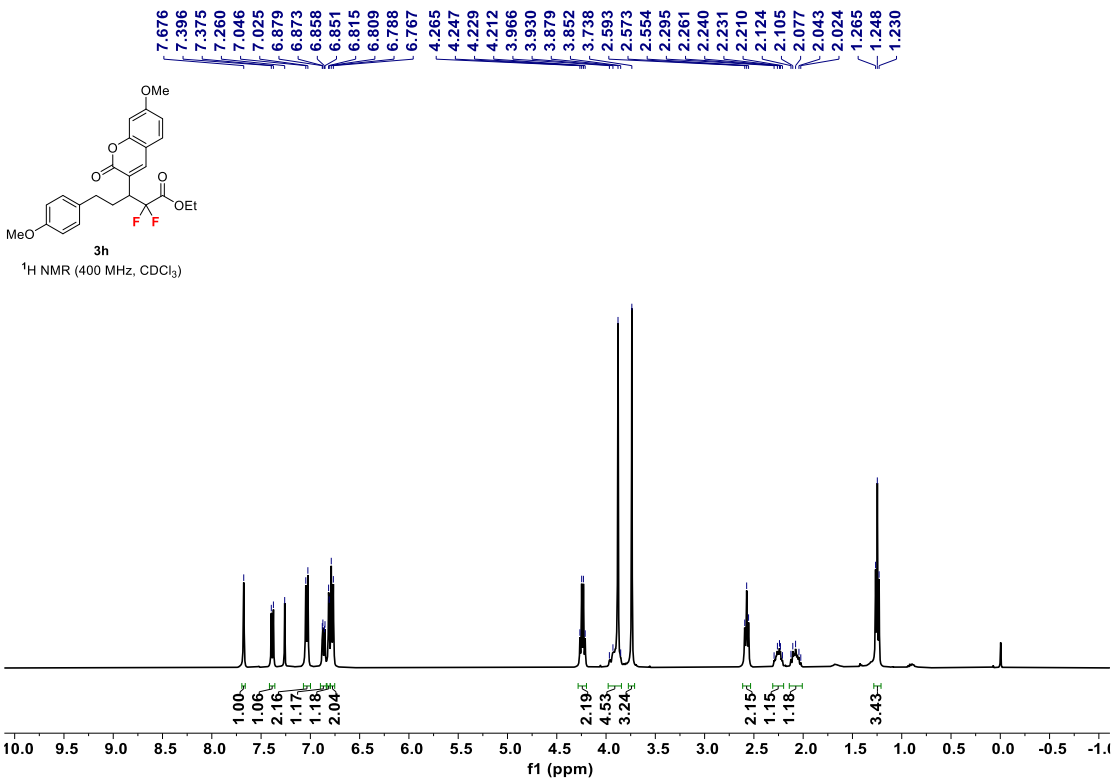
164.050
163.724
163.083
160.931
160.905
157.988
154.852
143.200
132.777
129.750
129.602
129.400
129.259
118.427
118.381
115.865
114.147
114.016
113.952
113.316
112.355
102.900
102.758
77.478
77.160
76.841
63.545
55.356
55.219
42.240
42.019
41.861
41.781
41.633
32.104
29.463
13.904
13.835
OH
O
O
O
OEt
F F
MeO
3g
13C NMR (101 MHz, CDCl3)
f1 (ppm)



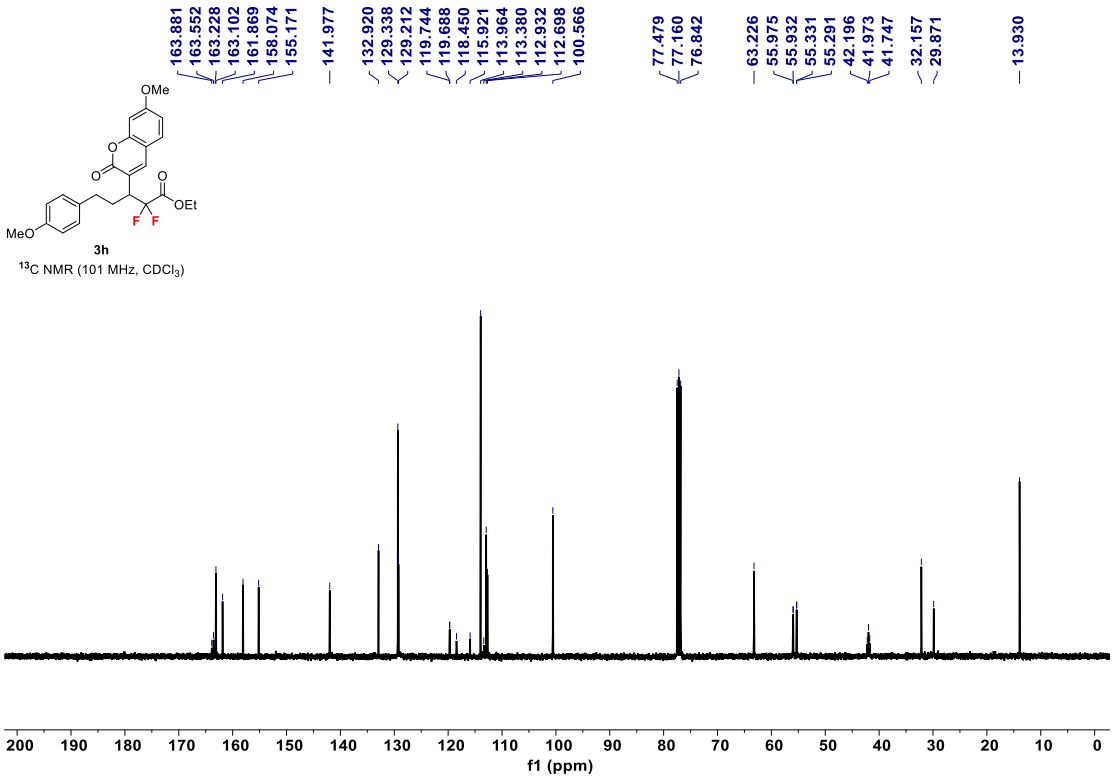
3g

^{19}F NMR (376 MHz, $CDCl_3$)



3h

^{1}H NMR (400 MHz, $CDCl_3$)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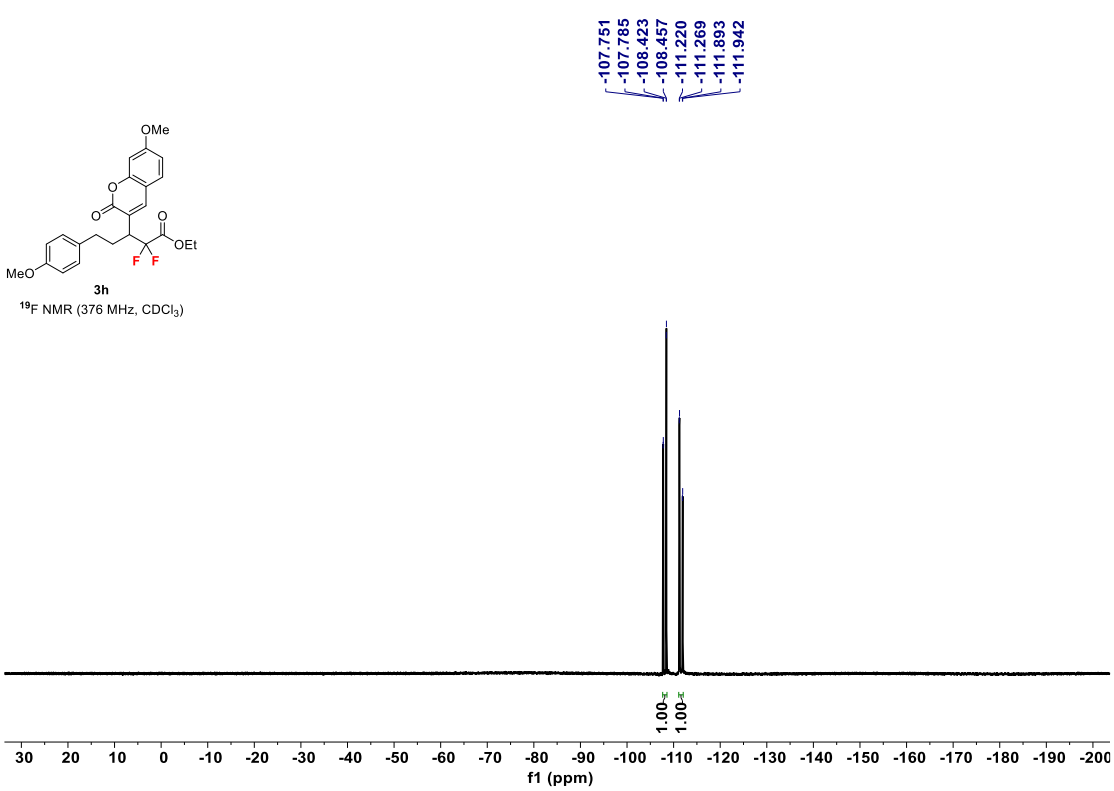
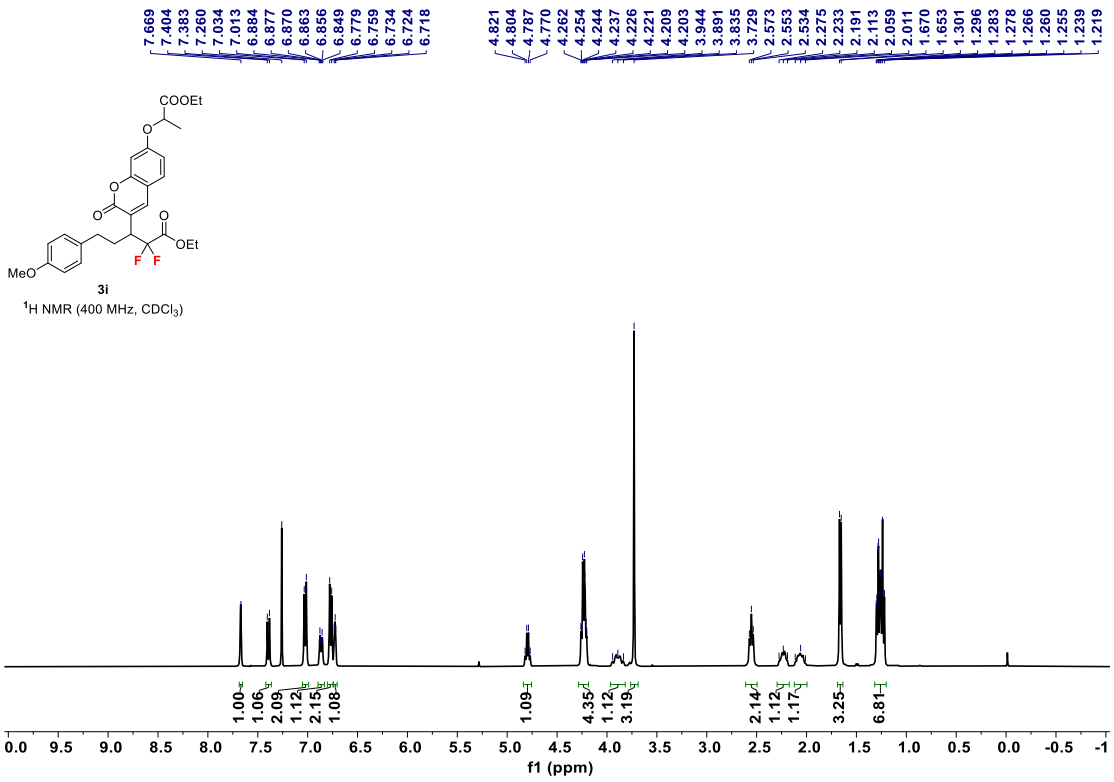
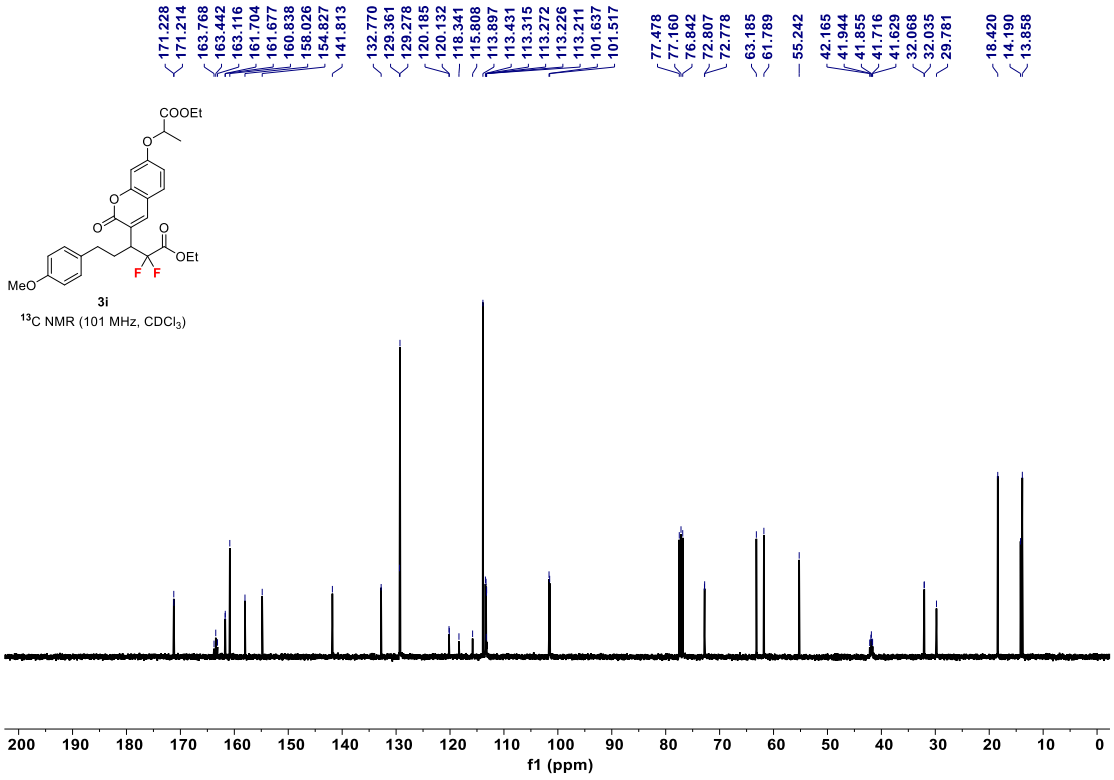
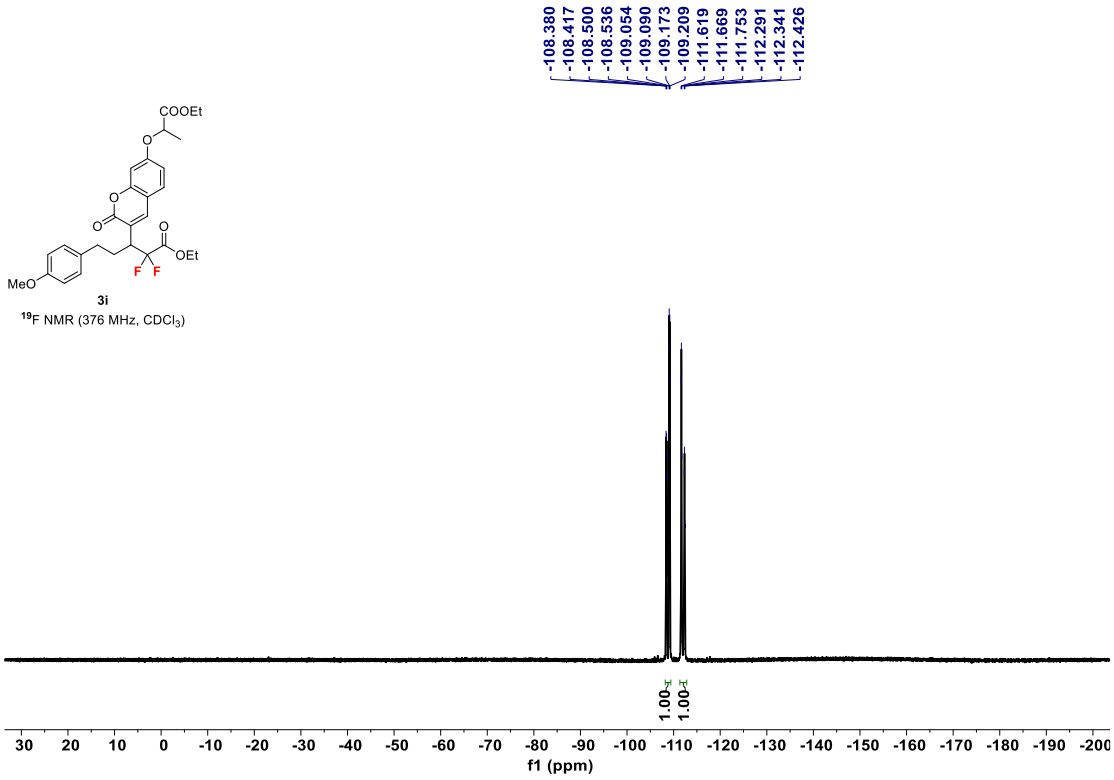
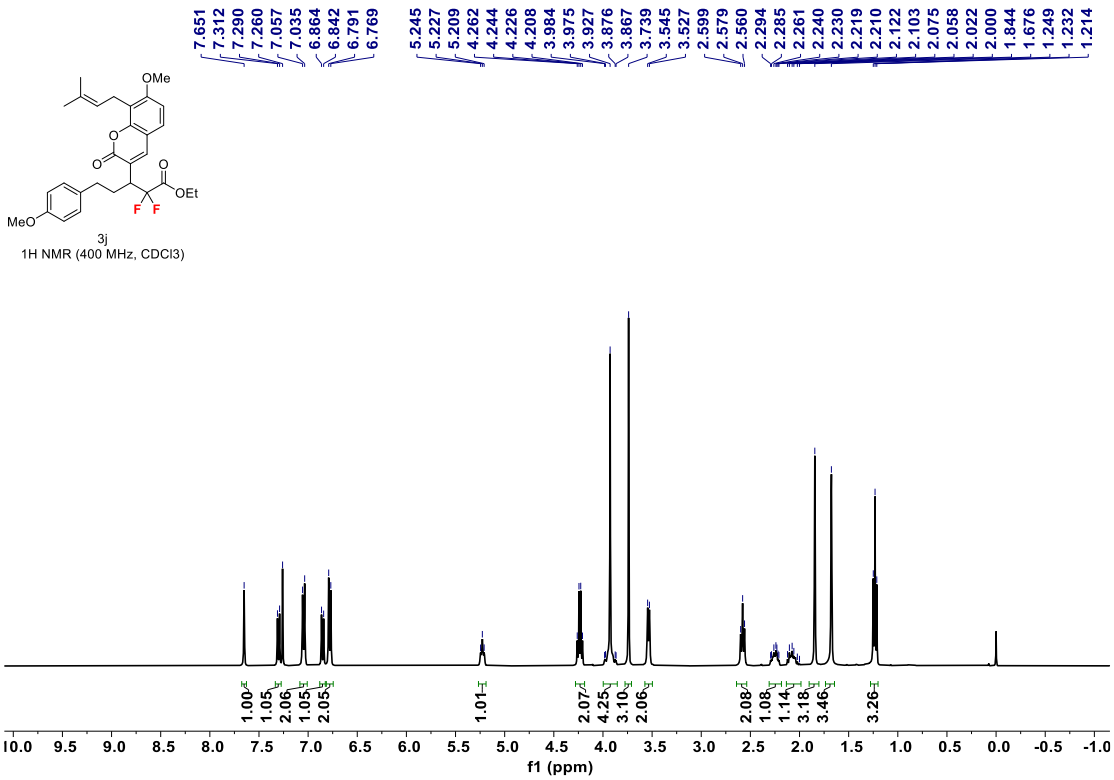
163.552
163.228
163.102
161.869
158.074
155.171
141.977
132.920
129.338
129.212
119.744
119.688
118.450
115.921
113.964
113.380
112.932
112.698
100.566
77.479
77.160
76.842
63.226
55.975
55.932
55.331
55.291
42.196
41.973
41.747
32.157
29.871
13.930
OMe
O
O
O
OEt
F F
MeO
3h
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

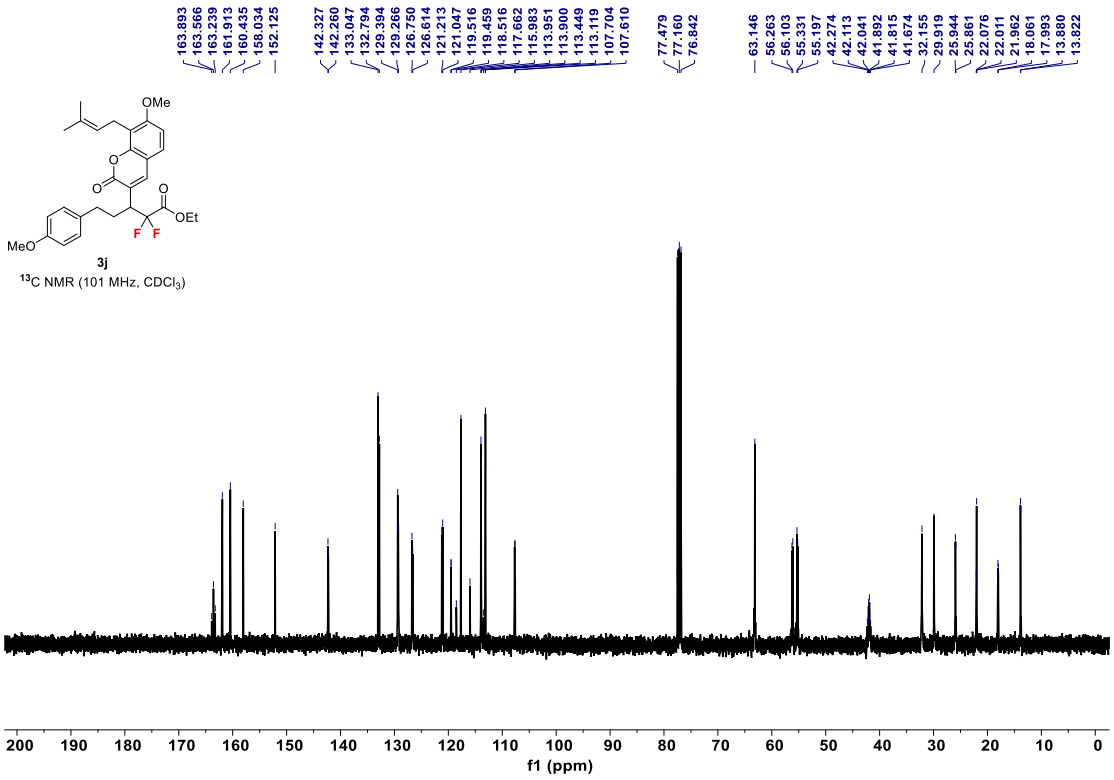

-107.751
-107.785
-108.423
-108.457
-111.220
-111.269
-111.893
-111.942
OMe
O
O
O
OEt
F F
MeO
3h
19F NMR (376 MHz, CDCl3)
1.00
1.00
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

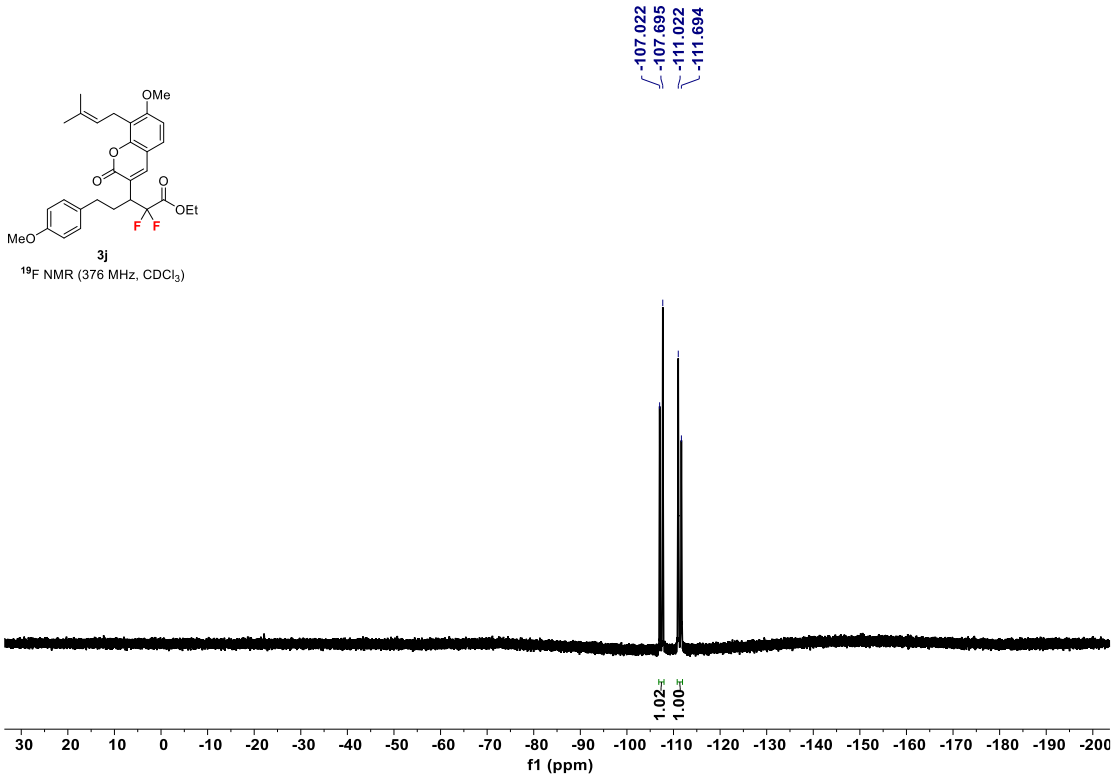

7.669
7.404
7.383
7.260
7.034
7.013
6.884
6.877
6.870
6.863
6.856
6.849
6.779
6.759
6.734
6.724
6.718
4.821
4.804
4.787
4.770
4.262
4.254
4.244
4.237
4.226
4.221
4.209
4.203
3.944
3.891
3.835
3.729
2.573
2.553
2.534
2.275
2.233
2.191
2.113
2.059
2.011
1.670
1.653
1.301
1.296
1.283
1.278
1.266
1.260
1.255
1.239
1.219
COOEt
O
O
O
O
OEt
F F
MeO
3i
1H NMR (400 MHz, CDCl3)
1.00
1.06
2.09
1.12
2.15
1.08
1.09
4.35
1.12
3.19
2.14
1.12
1.17
3.25
6.81
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)

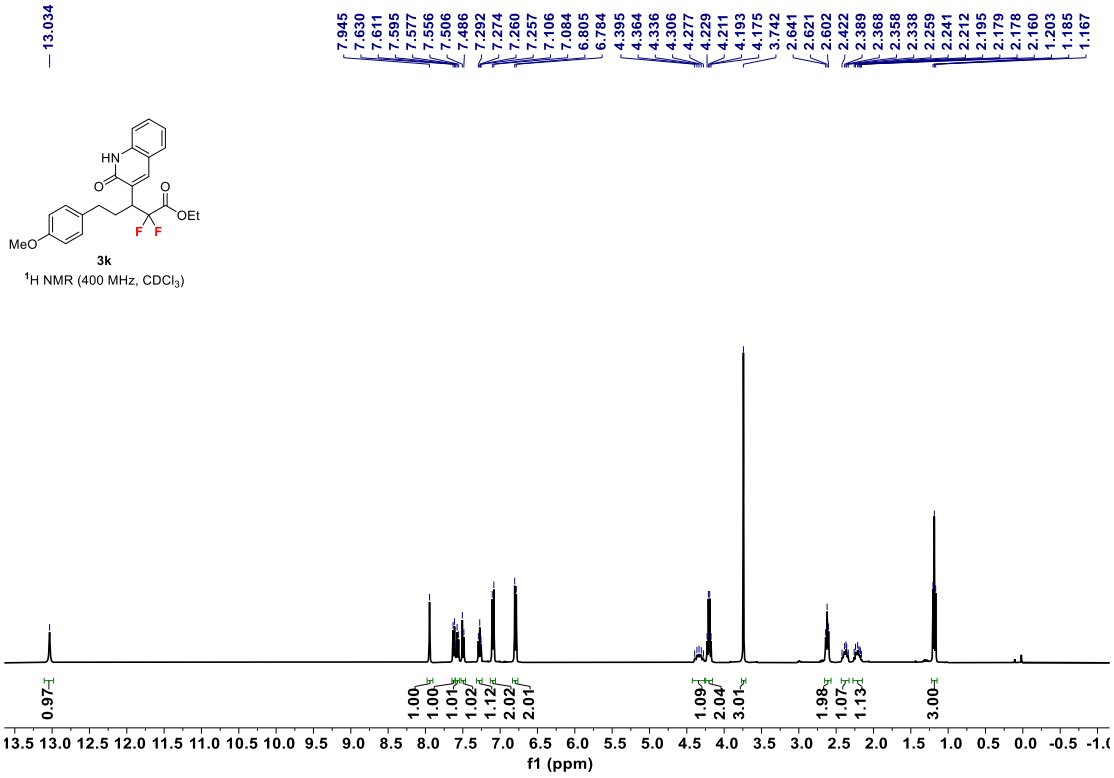

171.228
171.214
163.768
163.442
163.116
161.704
161.677
160.838
158.026
154.827
141.813
132.770
129.361
129.278
120.185
120.132
118.341
115.808
113.897
113.431
113.315
113.272
113.226
113.211
101.637
101.517
77.478
77.160
76.842
72.807
72.778
63.185
61.789
55.242
42.165
41.944
41.855
41.716
41.629
32.068
32.035
29.781
18.420
14.190
13.858
COOEt
O
O
O
O
OEt
F F
MeO
3i
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

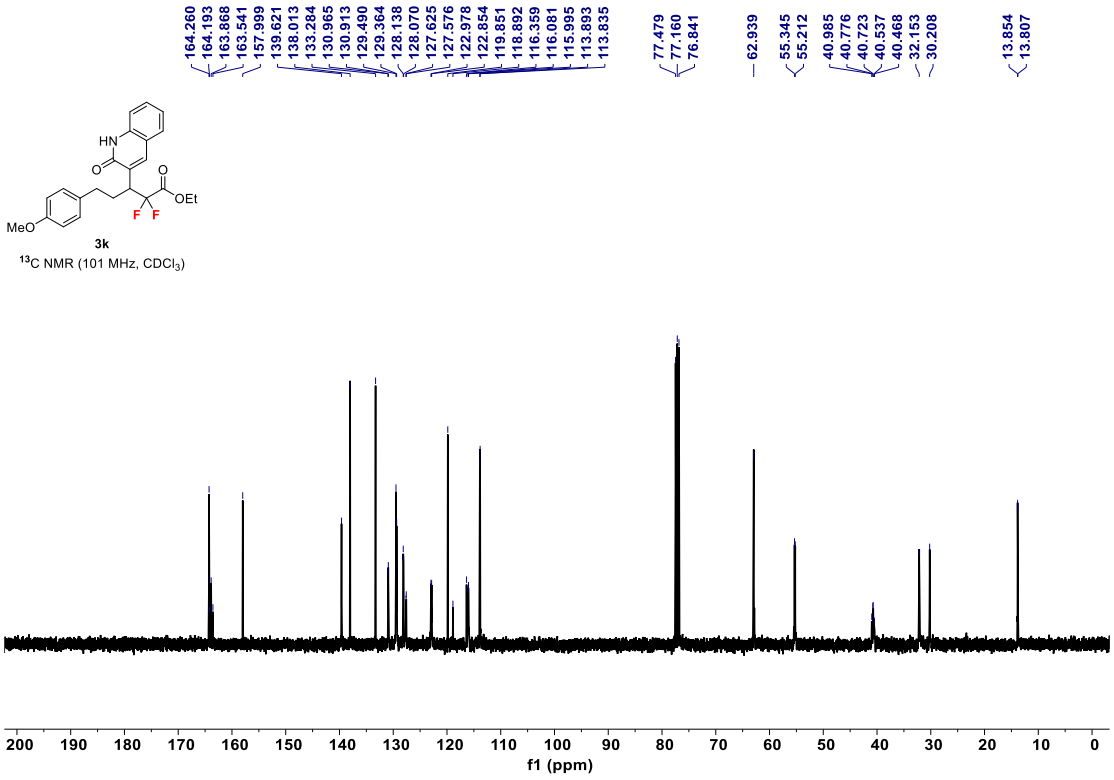

-108.380
-108.417
-108.500
-108.536
-109.054
-109.090
-109.173
-109.209
-111.619
-111.669
-111.753
-112.291
-112.341
-112.426
COOEt
OEt
F F
MeO
3i
19F NMR (376 MHz, CDCl3)
1.00
1.00
f1 (ppm)

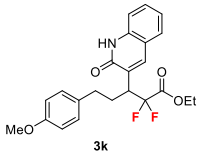

7.651
7.312
7.290
7.260
7.057
7.035
6.864
6.842
6.791
6.769
5.245
5.227
5.209
4.262
4.244
4.226
4.208
3.984
3.975
3.927
3.876
3.867
3.739
3.545
3.527
2.599
2.579
2.560
2.294
2.285
2.261
2.240
2.230
2.219
2.210
2.122
2.103
2.075
2.058
2.022
2.000
1.844
1.676
1.249
1.232
1.214
OMe
OEt
F F
MeO
3j
1H NMR (400 MHz, CDCl3)
1.00
1.05
2.06
1.05
2.05
1.01
2.07
4.25
3.10
2.06
2.08
1.08
1.14
3.18
3.46
3.26
f1 (ppm)


163.893
163.566
163.239
161.913
160.435
158.034
152.125
142.327
142.260
133.047
132.794
129.394
129.266
126.750
126.614
121.213
121.047
119.516
119.459
118.516
117.662
115.983
113.951
113.900
113.449
113.119
107.704
107.610
77.479
77.160
76.842
63.146
56.263
56.103
55.331
55.197
42.274
42.113
42.041
41.892
41.815
41.674
32.155
29.919
25.944
25.861
22.076
22.011
21.962
18.061
17.993
13.880
13.822
OMe
O
O
O
OEt
F F
MeO
3j
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-107.022
-107.695
-111.022
-111.694
OMe
O
O
O
OEt
F F
MeO
3j
19F NMR (376 MHz, CDCl3)
1.02
1.00
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

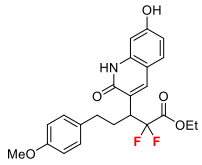

13.034
7.945
7.630
7.611
7.595
7.577
7.556
7.506
7.486
7.292
7.274
7.260
7.257
7.106
7.084
6.805
6.784
4.395
4.364
4.336
4.306
4.277
4.229
4.211
4.193
4.175
3.742
2.641
2.621
2.602
2.422
2.389
2.368
2.358
2.338
2.259
2.241
2.212
2.195
2.179
2.178
2.160
1.203
1.185
1.167
HN
O
O
OEt
F F
MeO
3k
1H NMR (400 MHz, CDCl3)
0.97
1.00
1.00
1.01
1.02
1.12
2.02
2.01
1.09
2.04
3.01
1.98
1.07
1.13
3.00
f1 (ppm)


164.260
164.193
163.868
163.541
157.999
139.621
138.013
133.284
130.965
130.913
129.490
129.364
128.138
128.070
127.625
127.576
122.978
122.854
119.851
118.892
116.359
116.081
115.995
113.893
113.835
77.479
77.160
76.841
62.939
55.345
55.212
40.985
40.776
40.723
40.537
40.468
32.153
30.208
13.854
13.807
HN
O
O
OEt
F F
MeO
3k
13C NMR (101 MHz, CDCl3)
f1 (ppm)



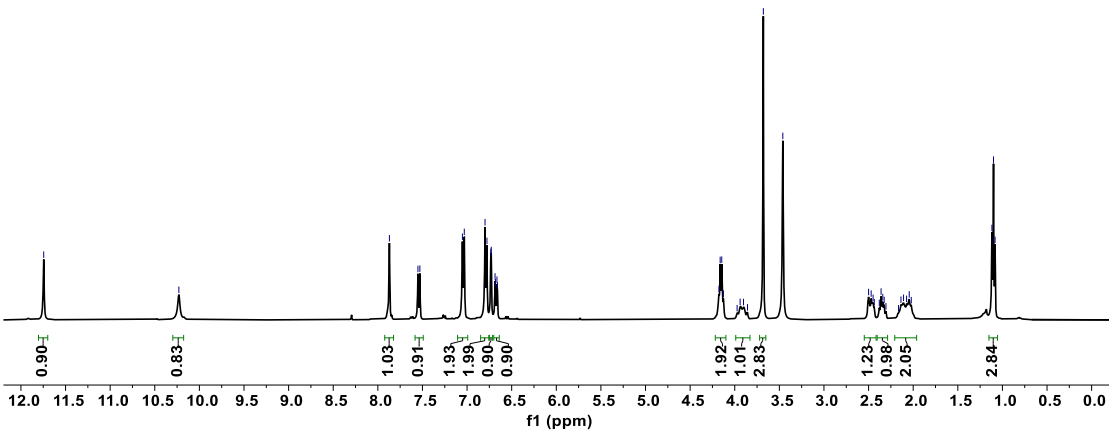
3k

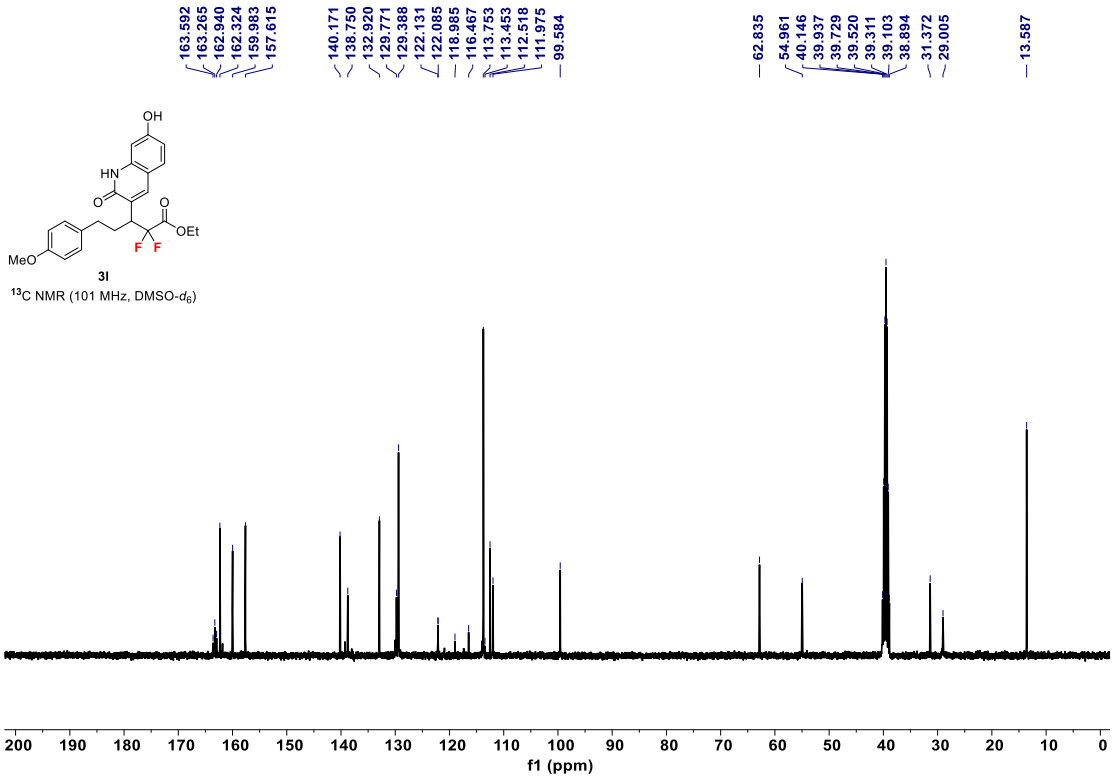
^{19}F NMR (376 MHz, $CDCl_3$)

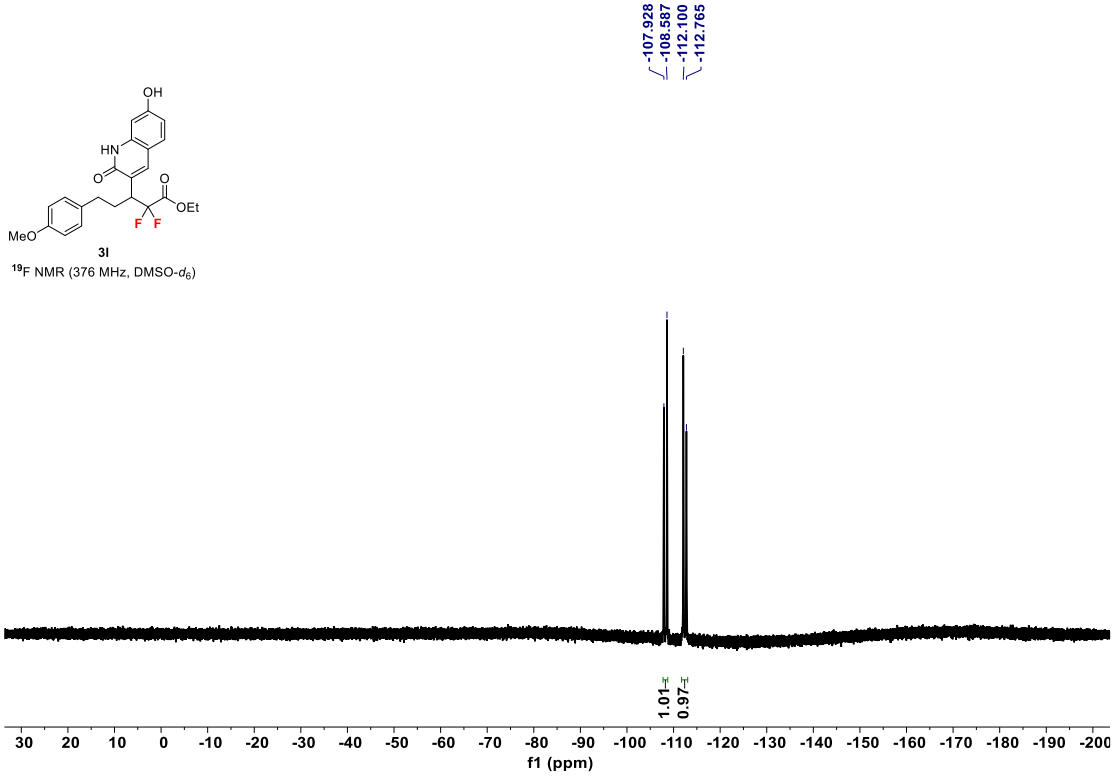


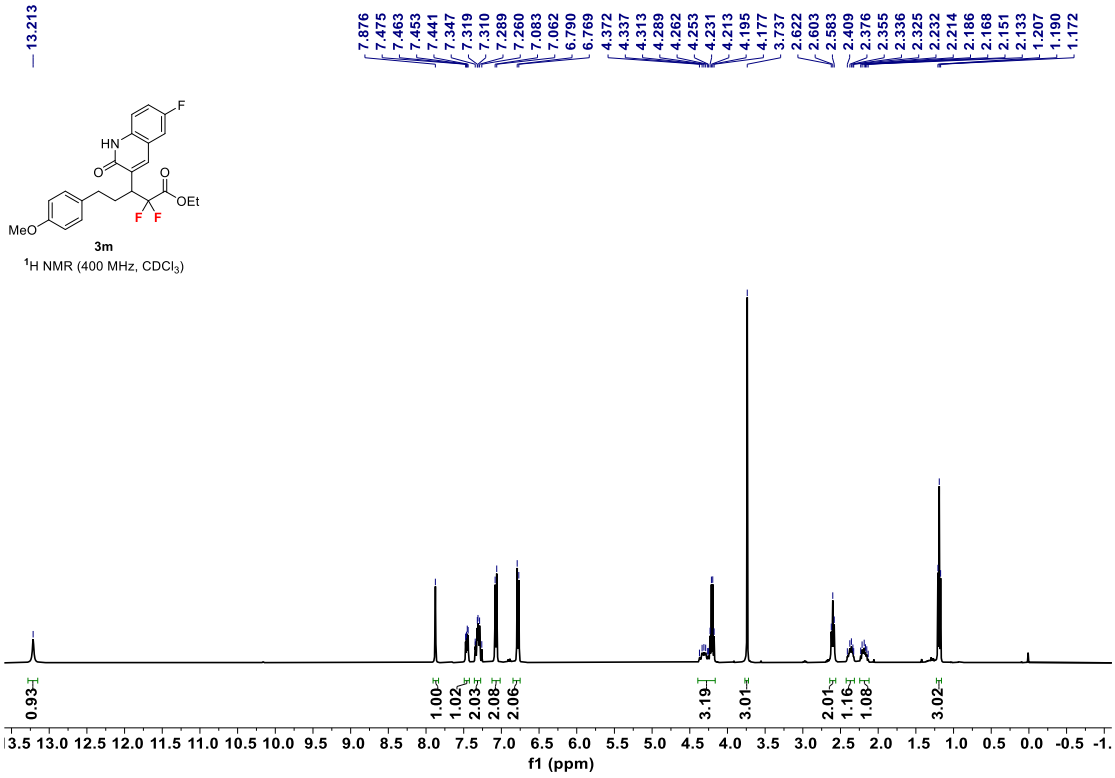
3l

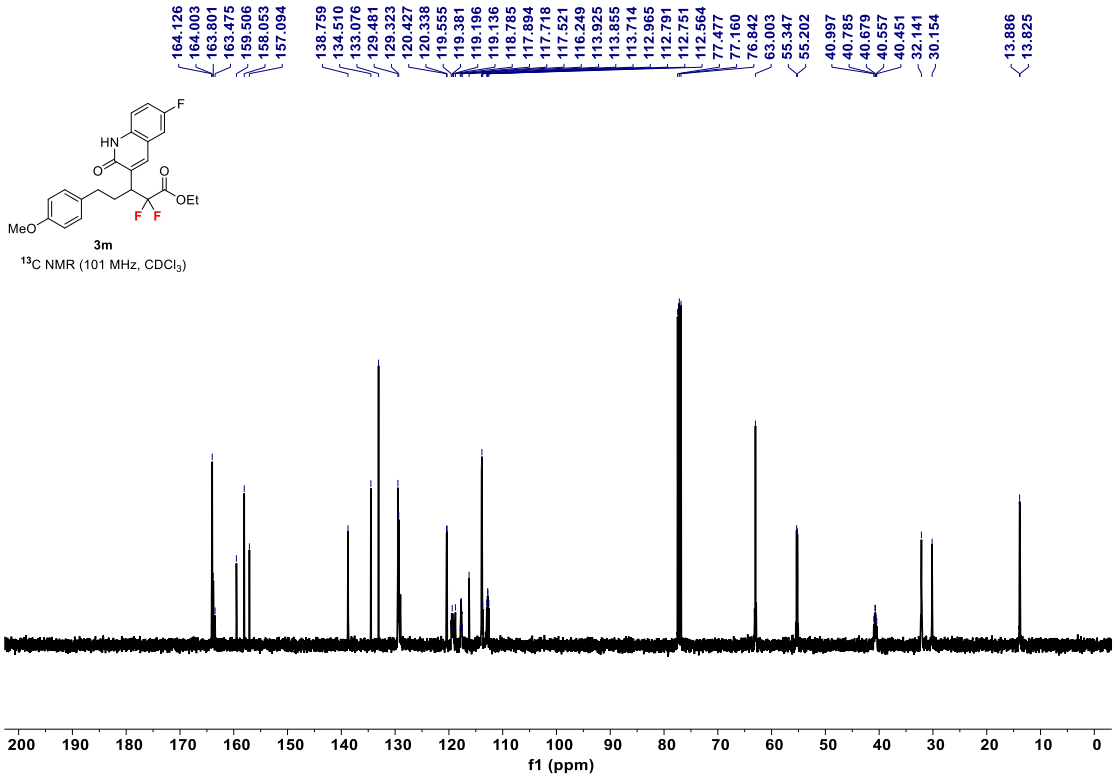
^{1}H NMR (400 MHz, DMSO-d_6)

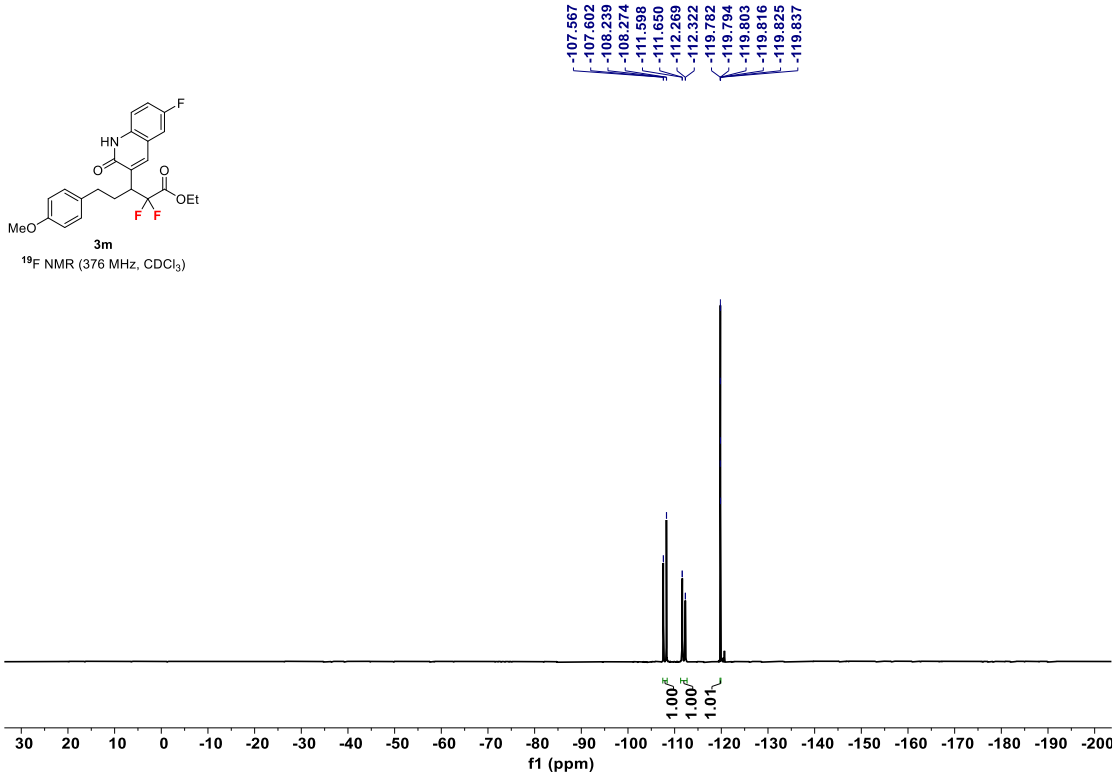



163.592
163.265
162.940
162.324
159.983
157.615
140.171
138.750
132.920
129.771
129.388
122.131
122.085
118.985
116.467
113.753
113.453
112.518
111.975
99.584
62.835
54.961
40.146
39.937
39.729
39.520
39.311
39.103
38.894
31.372
29.005
13.587
OH
HN
O
O
OEt
F F
MeO
3l
13C NMR (101 MHz, DMSO-d6)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-107.928
-108.587
-112.100
-112.765
OH
HN
O
O
OEt
F F
MeO
3l
19F NMR (376 MHz, DMSO-d6)
1.01
0.97
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

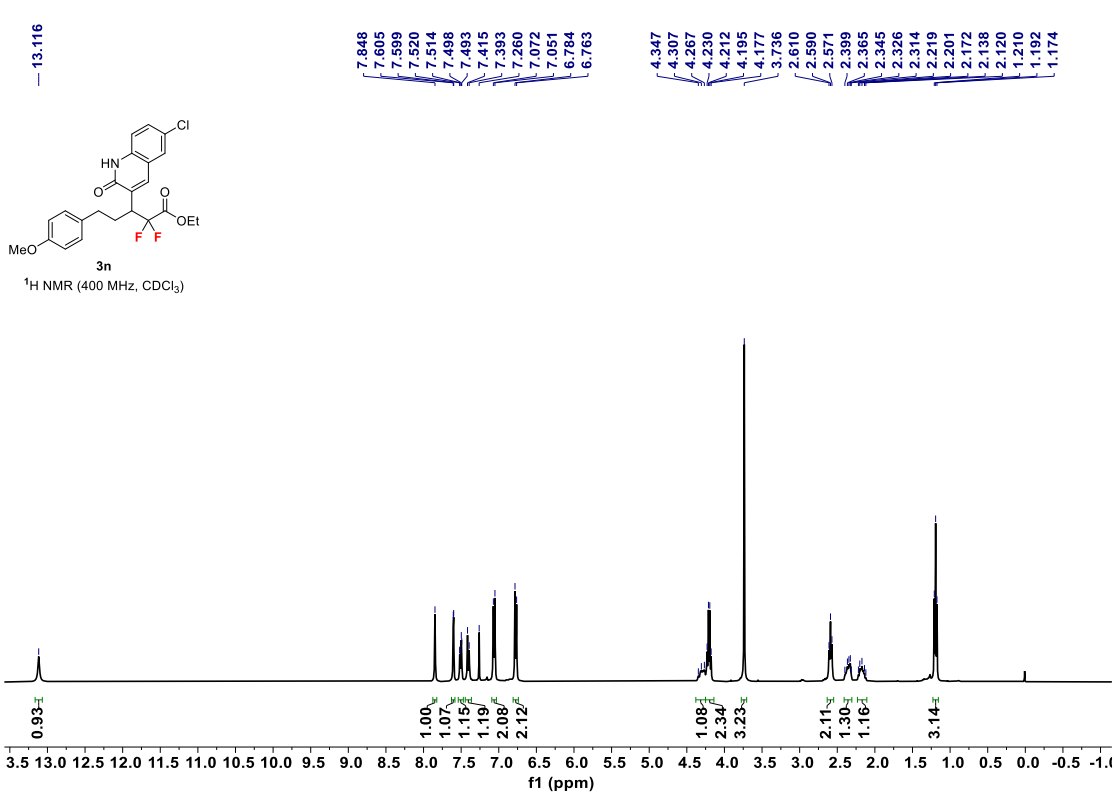

13.213
7.876
7.475
7.463
7.453
7.441
7.347
7.319
7.310
7.289
7.260
7.083
7.062
6.790
6.769
4.372
4.337
4.313
4.289
4.262
4.253
4.231
4.213
4.195
4.177
3.737
2.622
2.603
2.583
2.409
2.376
2.355
2.336
2.325
2.232
2.214
2.186
2.168
2.151
2.133
1.207
1.190
1.172
F
HN
O
O
OEt
F F
MeO
3m
1H NMR (400 MHz, CDCl3)
0.93
1.00
1.02
2.03
2.08
2.06
3.19
3.01
2.01
1.16
1.08
3.02
f1 (ppm)


164.126
164.003
163.801
163.475
159.506
158.053
157.094
138.759
134.510
133.076
129.481
129.323
120.427
120.338
119.555
119.381
119.196
119.136
118.785
117.894
117.718
117.521
116.249
113.925
113.855
113.714
112.965
112.791
112.751
112.564
77.477
77.160
76.842
63.003
55.347
55.202
40.997
40.785
40.679
40.557
40.451
32.141
30.154
13.886
13.825
F
HN
O
O
OEt
F F
MeO
3m
13C NMR (101 MHz, CDCl3)
f1 (ppm)



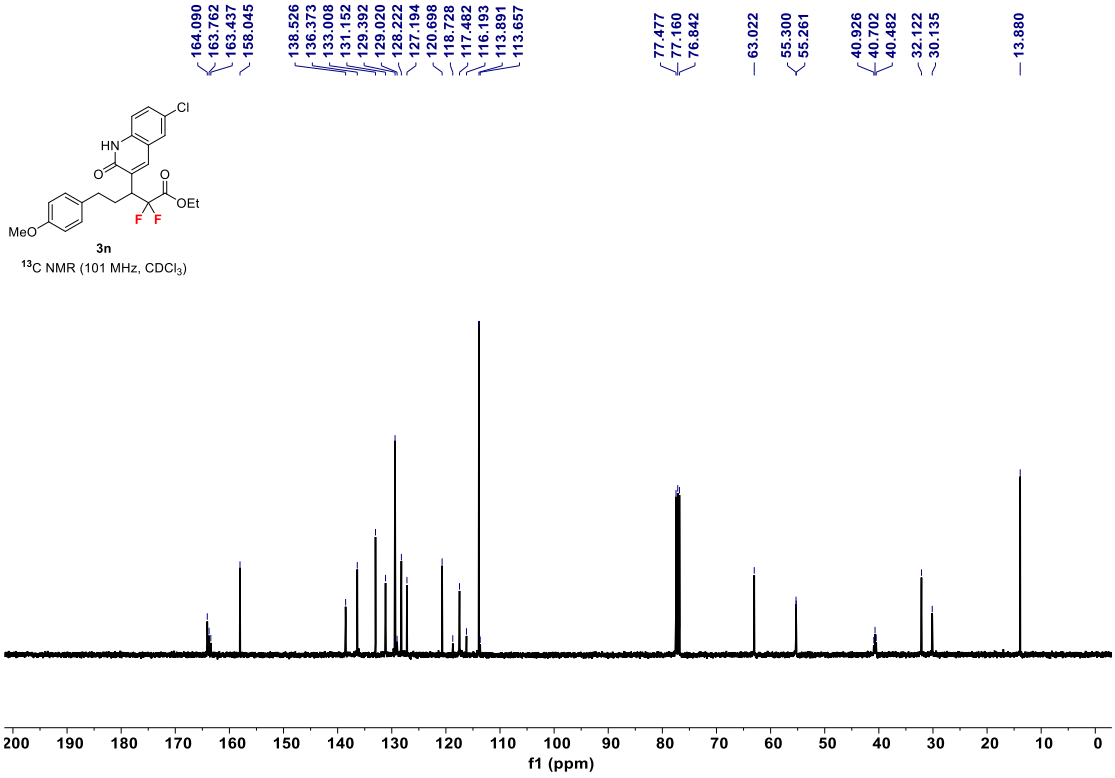
3m

^{19}F NMR (376 MHz, $CDCl_3$)



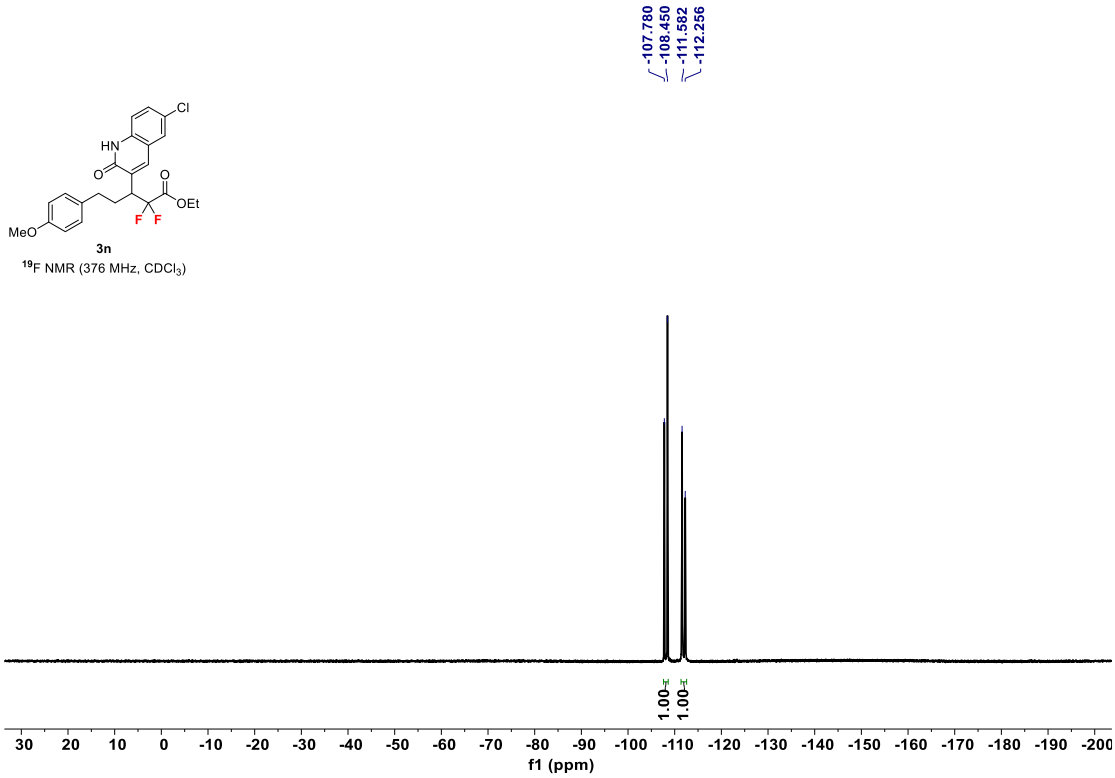
3n

^{1}H NMR (400 MHz, $CDCl_3$)



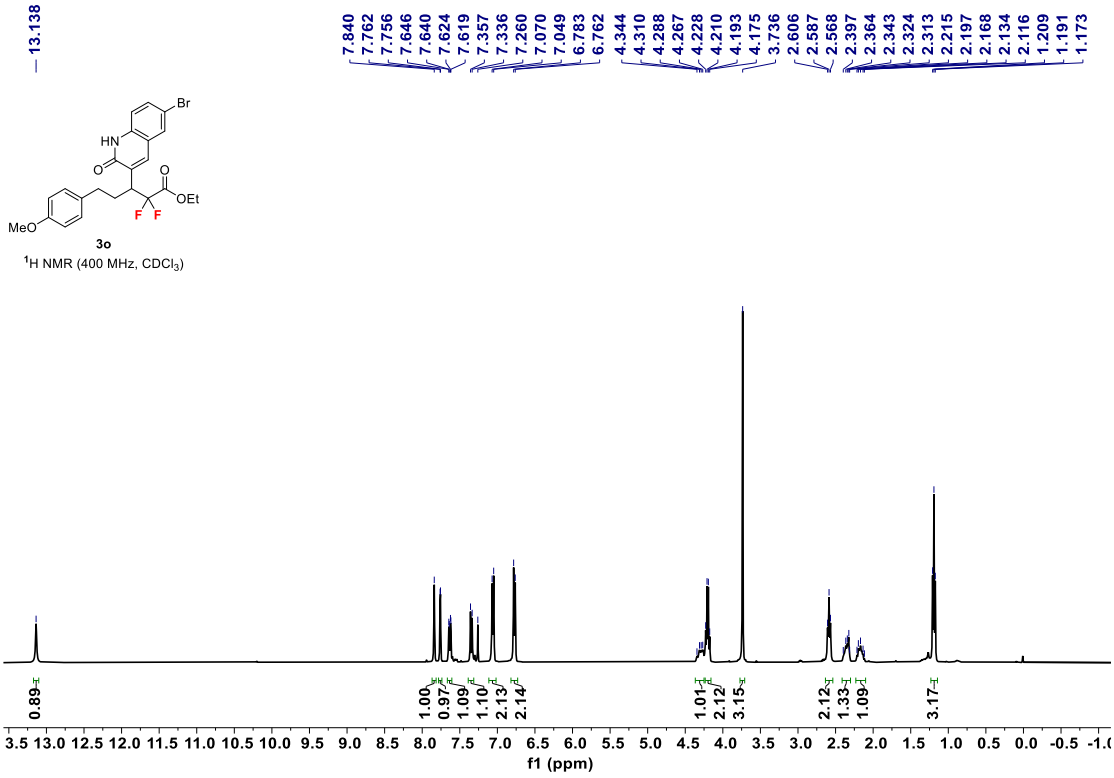
3n

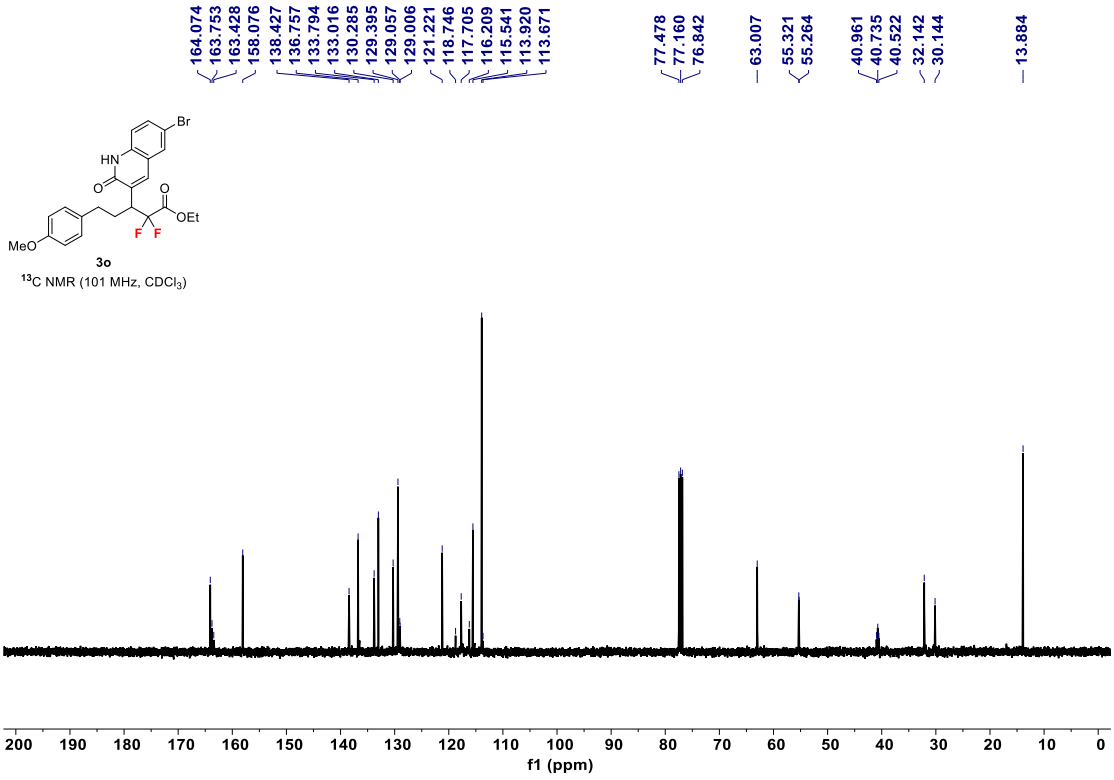
^{13}C NMR (101 MHz, $CDCl_3$)

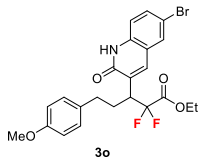


3n

^{19}F NMR (376 MHz, $CDCl_3$)

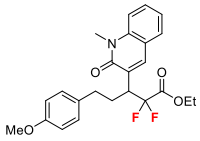

13.138
7.840
7.762
7.756
7.646
7.640
7.624
7.619
7.357
7.336
7.260
7.070
7.049
6.783
6.762
4.344
4.310
4.288
4.267
4.228
4.210
4.193
4.175
3.736
2.606
2.587
2.568
2.397
2.364
2.343
2.324
2.313
2.215
2.197
2.168
2.134
2.116
1.209
1.191
1.173
Br
HN
O
O
OEt
F F
MeO
3o
1H NMR (400 MHz, CDCl3)
0.89
1.00
0.97
1.09
1.10
2.13
2.14
1.01
2.12
3.15
2.12
1.33
1.09
3.17
f1 (ppm)


164.074
163.753
163.428
158.076
138.427
136.757
133.794
133.016
130.285
129.395
129.057
129.006
121.221
118.746
117.705
116.209
115.541
113.920
113.671
77.478
77.160
76.842
63.007
55.321
55.264
40.961
40.735
40.522
32.142
30.144
13.884
Br
HN
O
O
OEt
F F
MeO
3o
13C NMR (101 MHz, CDCl3)
f1 (ppm)



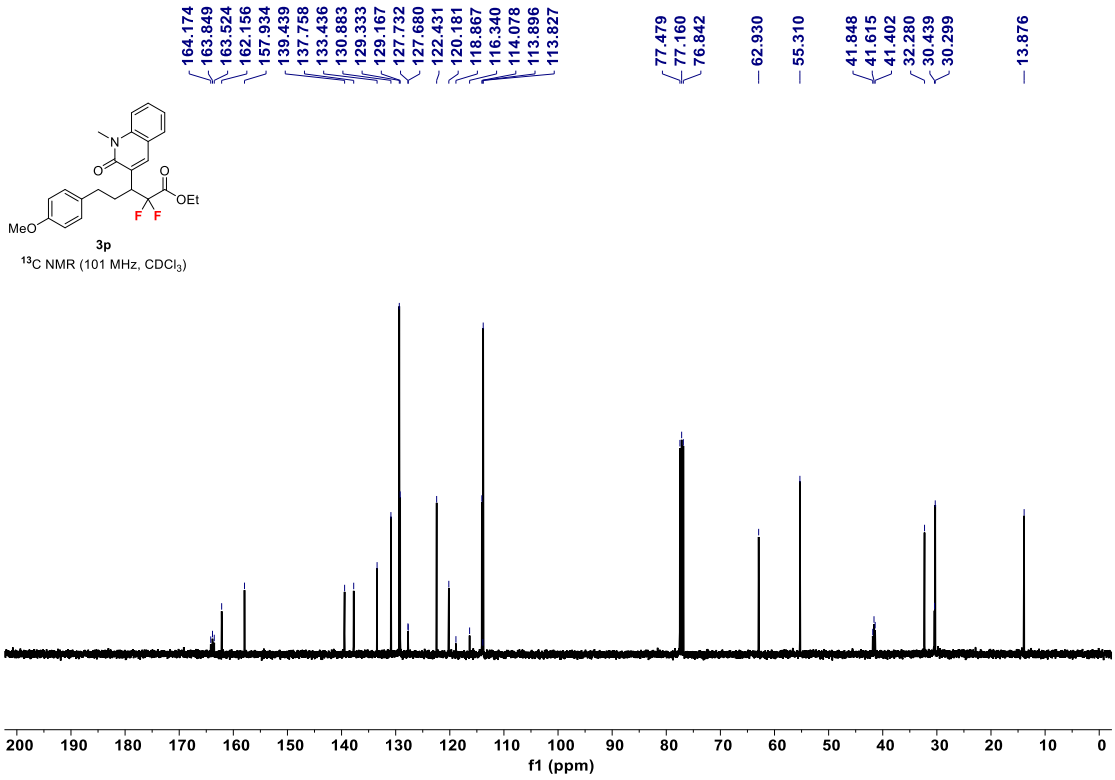
3o

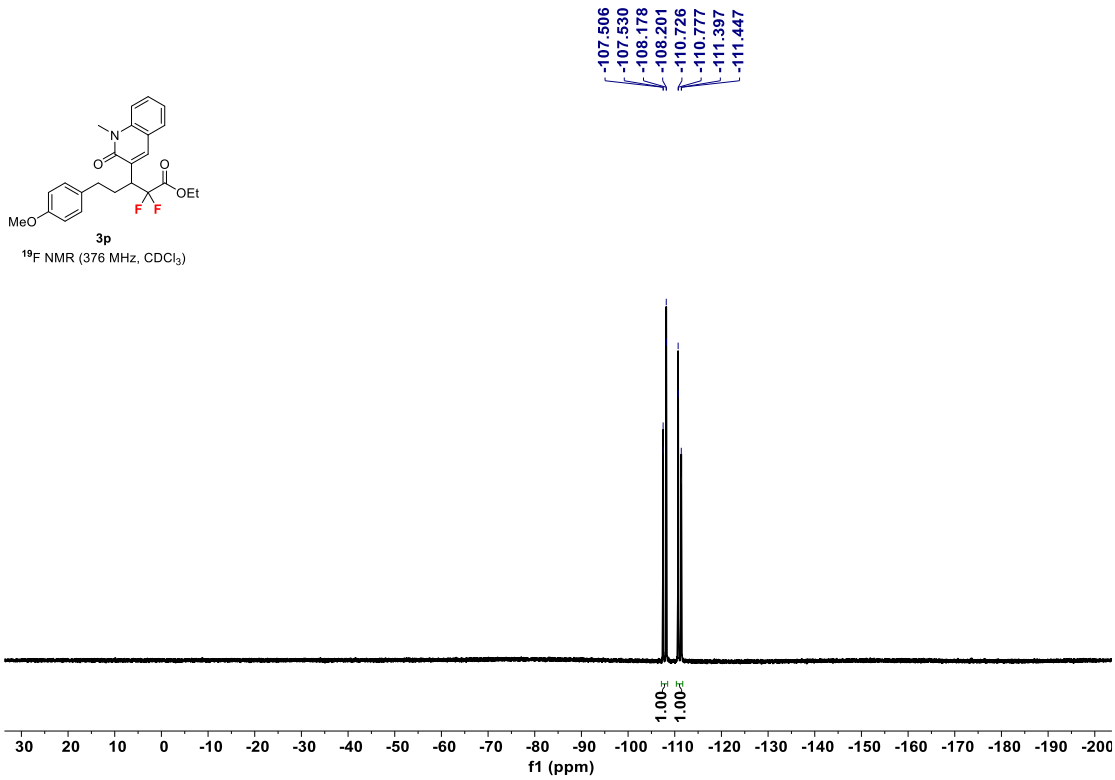
^{19}F NMR (376 MHz, $CDCl_3$)

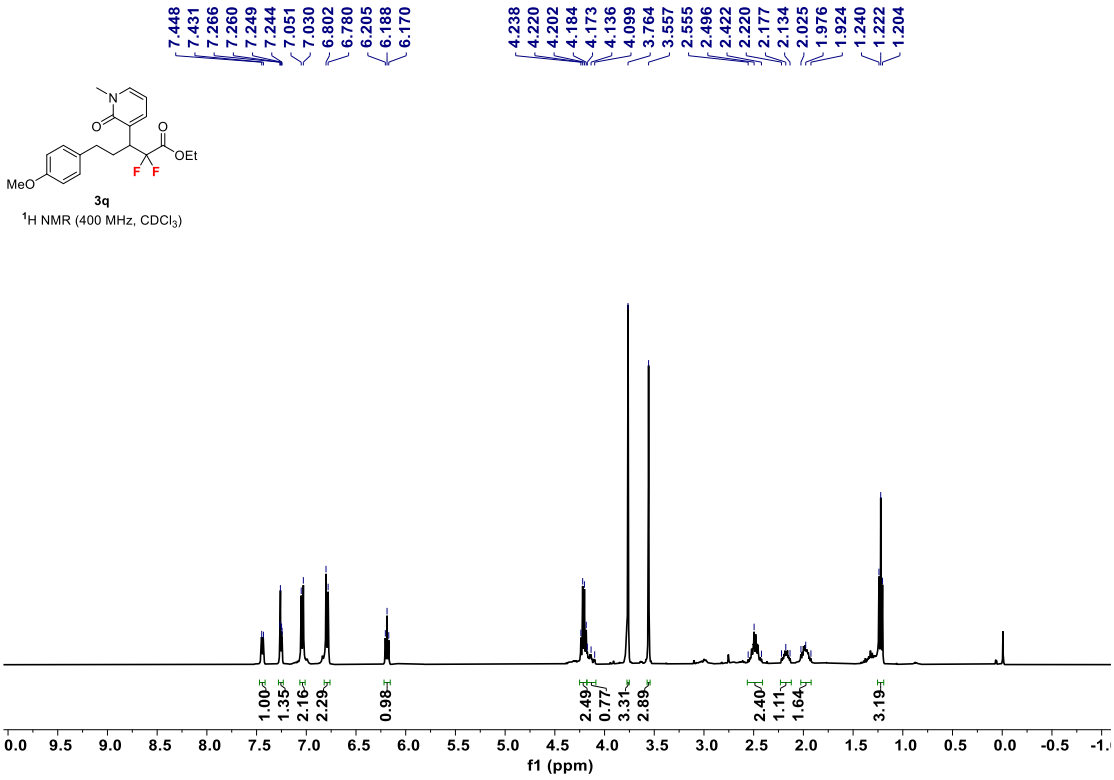


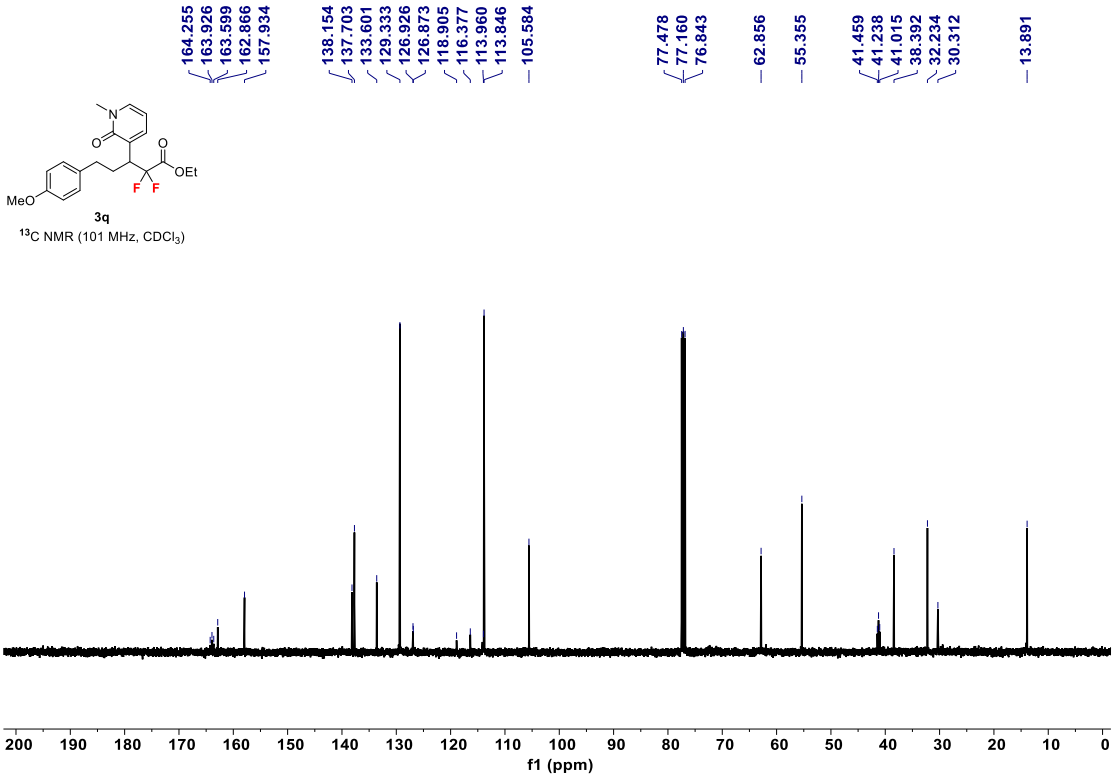
3p

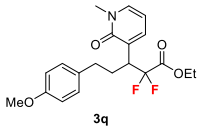
^{1}H NMR (400 MHz, $CDCl_3$)


164.174
163.849
163.524
162.156
157.934
139.439
137.758
133.436
130.883
129.333
129.167
127.732
127.680
122.431
120.181
118.867
116.340
114.078
113.896
113.827
77.479
77.160
76.842
62.930
55.310
41.848
41.615
41.402
32.280
30.439
30.299
13.876
MeO
OEt
F F
3p
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-107.506
-107.530
-108.178
-108.201
-110.726
-110.777
-111.397
-111.447
MeO
OEt
F F
3p
19F NMR (376 MHz, CDCl3)
1.00
1.00
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

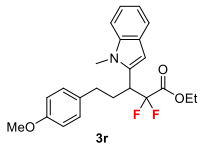

7.448
7.431
7.266
7.260
7.249
7.244
7.051
7.030
6.802
6.780
6.205
6.188
6.170
4.238
4.220
4.202
4.184
4.173
4.136
4.099
3.764
3.557
2.555
2.496
2.422
2.220
2.177
2.134
2.025
1.976
1.924
1.240
1.222
1.204
MeO
OEt
F F
3q
1H NMR (400 MHz, CDCl3)
1.00
1.35
2.16
2.29
0.98
2.49
0.77
3.31
2.89
2.40
1.11
1.64
3.19
f1 (ppm)


164.255
163.926
163.599
162.866
157.934
138.154
137.703
133.601
129.333
126.926
126.873
118.905
116.377
113.960
113.846
105.584
77.478
77.160
76.843
62.856
55.355
41.459
41.238
41.015
38.392
32.234
30.312
13.891
MeO
OEt
F F
3q
13C NMR (101 MHz, CDCl3)
f1 (ppm)



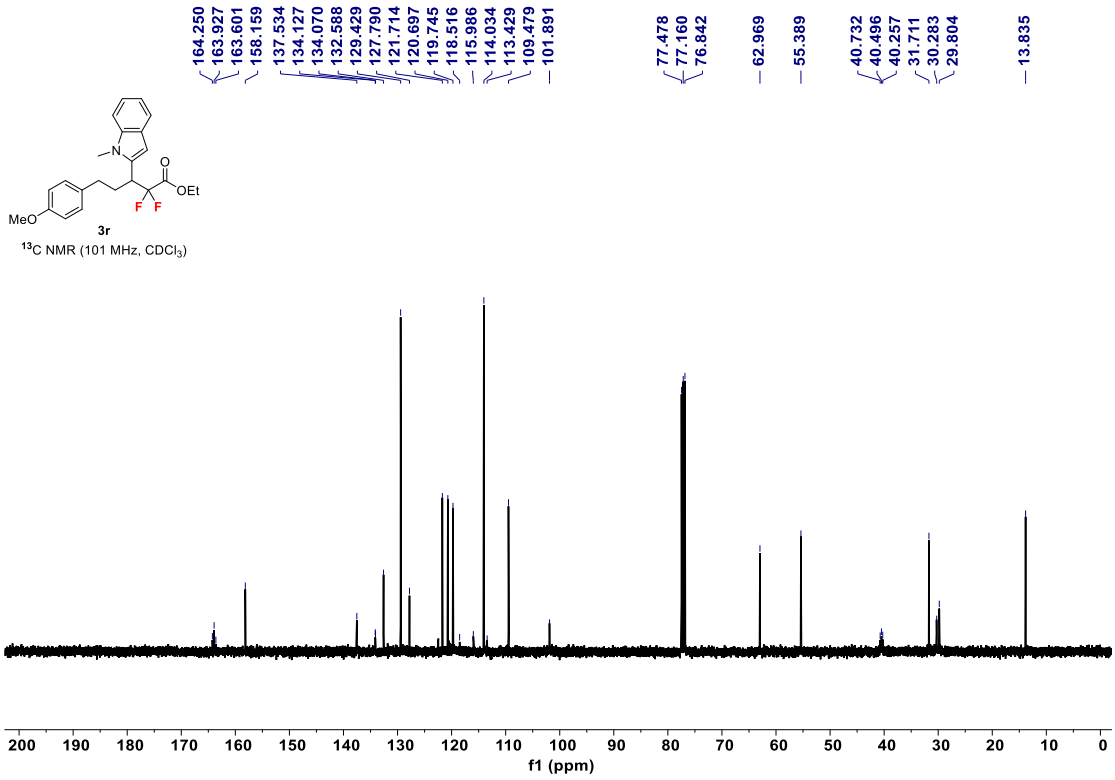
3q

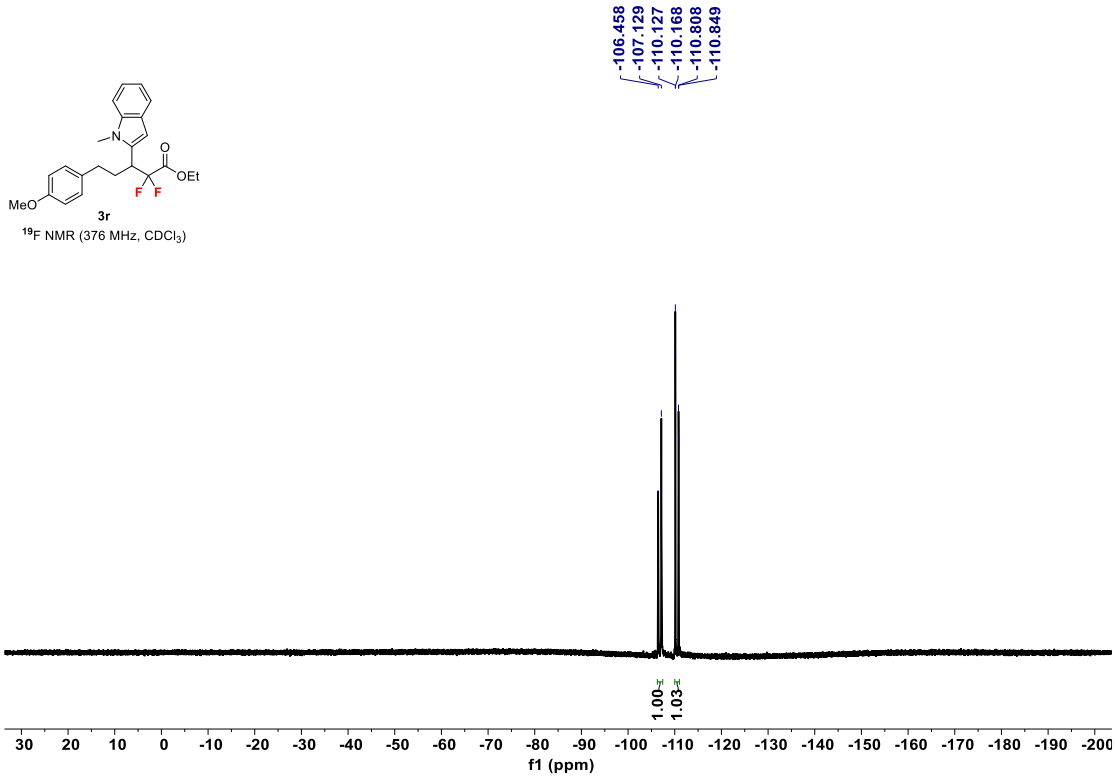
^{19}F NMR (376 MHz, $CDCl_3$)

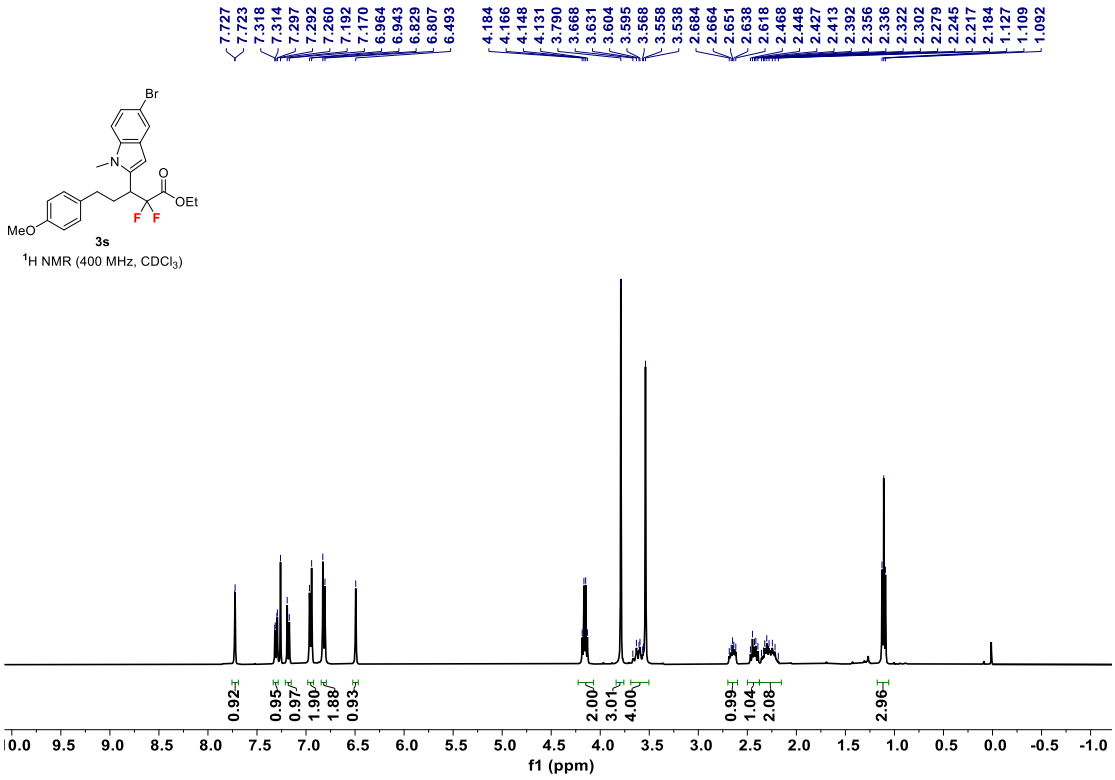


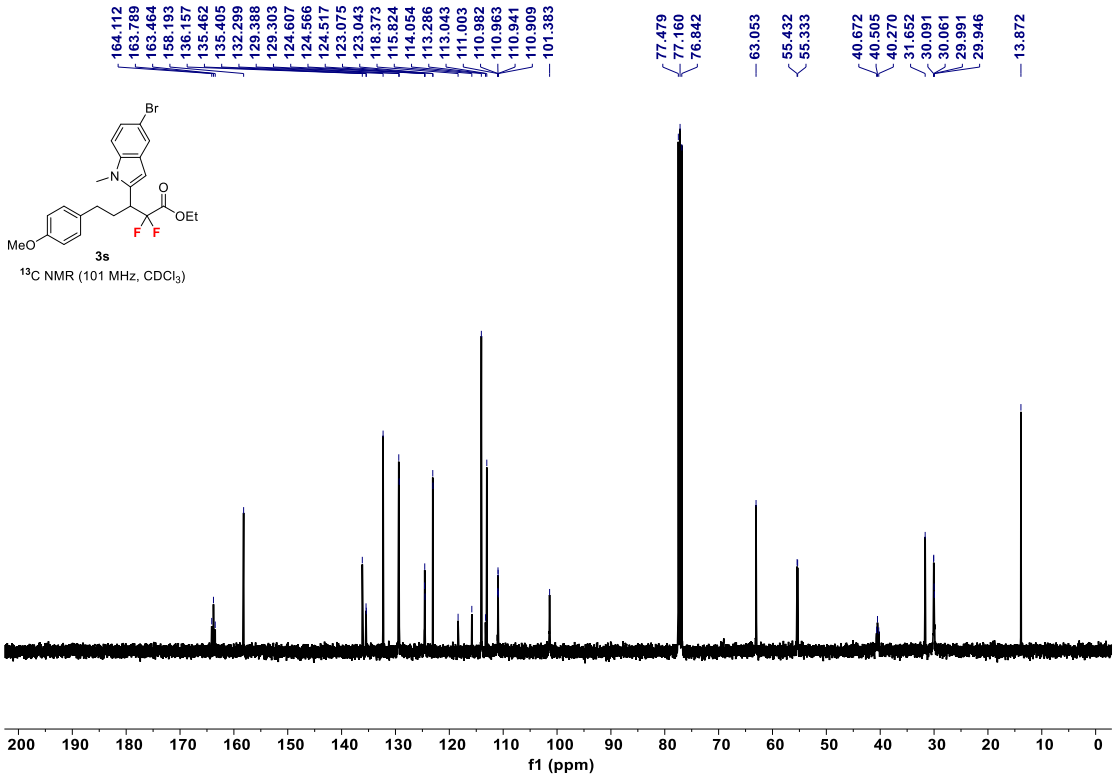
3r

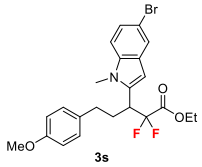
^{1}H NMR (400 MHz, $CDCl_3$)


164.250
163.927
163.601
158.159
137.534
134.127
134.070
132.588
129.429
127.790
121.714
120.697
119.745
118.516
115.986
114.034
113.429
109.479
101.891
77.478
77.160
76.842
62.969
55.389
40.732
40.496
40.257
31.711
30.283
29.804
13.835
MeO
O
OEt
F F
3r
13C NMR (101 MHz, CDCl3)
f1 (ppm)


-106.458
-107.129
-110.127
-110.168
-110.808
-110.849
MeO
O
OEt
F F
3r
19F NMR (376 MHz, CDCl3)
1.00
1.03
f1 (ppm)

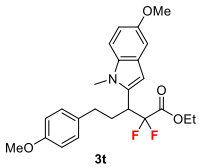

7.727
7.723
7.318
7.314
7.297
7.292
7.260
7.192
7.170
6.964
6.943
6.829
6.807
6.493
4.184
4.166
4.148
4.131
3.790
3.668
3.631
3.604
3.595
3.568
3.558
3.538
2.684
2.664
2.651
2.638
2.618
2.468
2.448
2.427
2.413
2.392
2.356
2.336
2.322
2.302
2.279
2.245
2.217
2.184
1.127
1.109
1.092
Br
N
O
OEt
F F
MeO
3s
^{1}H NMR (400 MHz, CDCl$_3$)
0.92
0.95
0.97
1.90
1.88
0.93
2.00
3.01
4.00
0.99
1.04
2.08
2.96
f1 (ppm)


164.112
163.789
163.464
158.193
136.157
135.462
135.405
132.299
129.388
129.303
124.607
124.566
124.517
123.075
123.043
118.373
115.824
114.054
113.286
113.043
111.003
110.982
110.963
110.941
110.909
101.383
77.479
77.160
76.842
63.053
55.432
55.333
40.672
40.505
40.270
31.652
30.091
30.061
29.991
29.946
13.872
Br
N
O
OEt
F F
MeO
3s
^{13}C NMR (101 MHz, CDCl$_3$)
f1 (ppm)



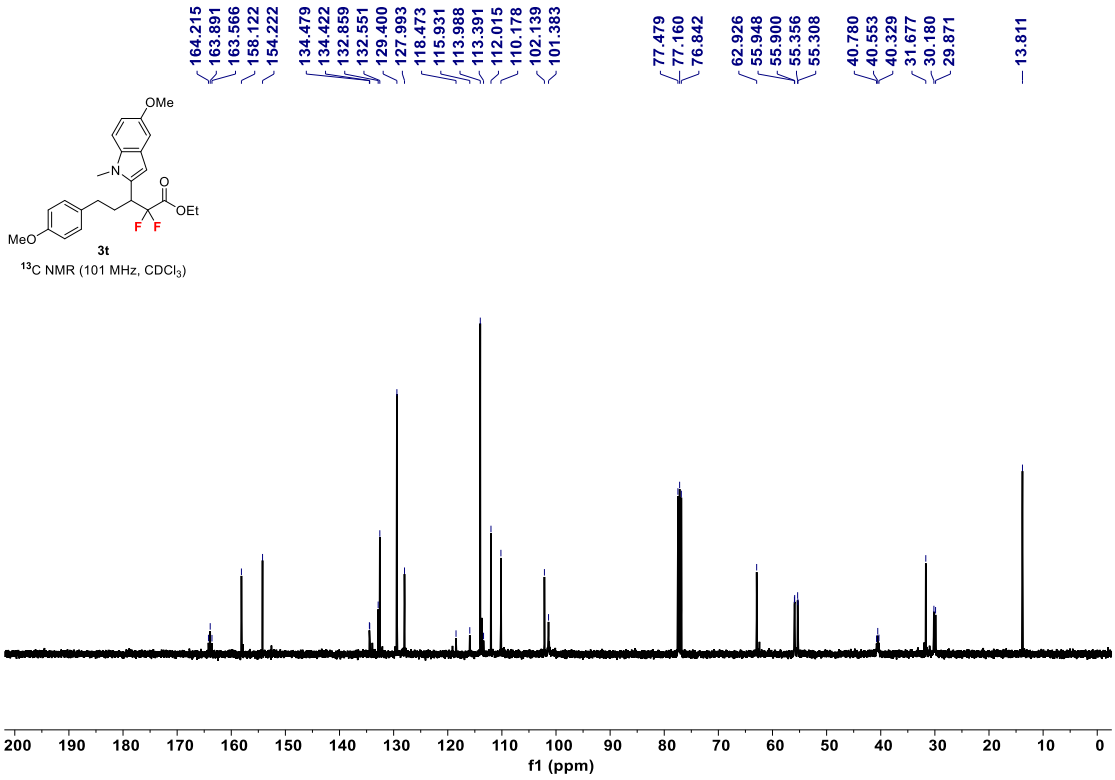
3s

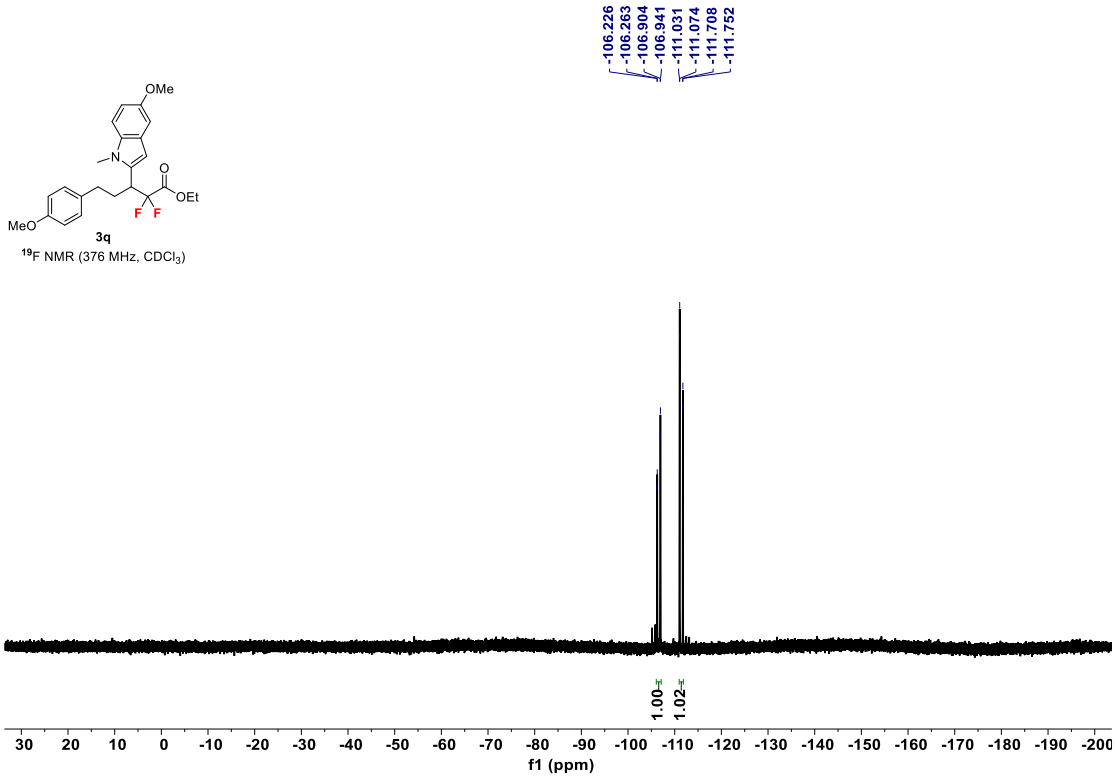
^{19}F NMR (376 MHz, $CDCl_3$)

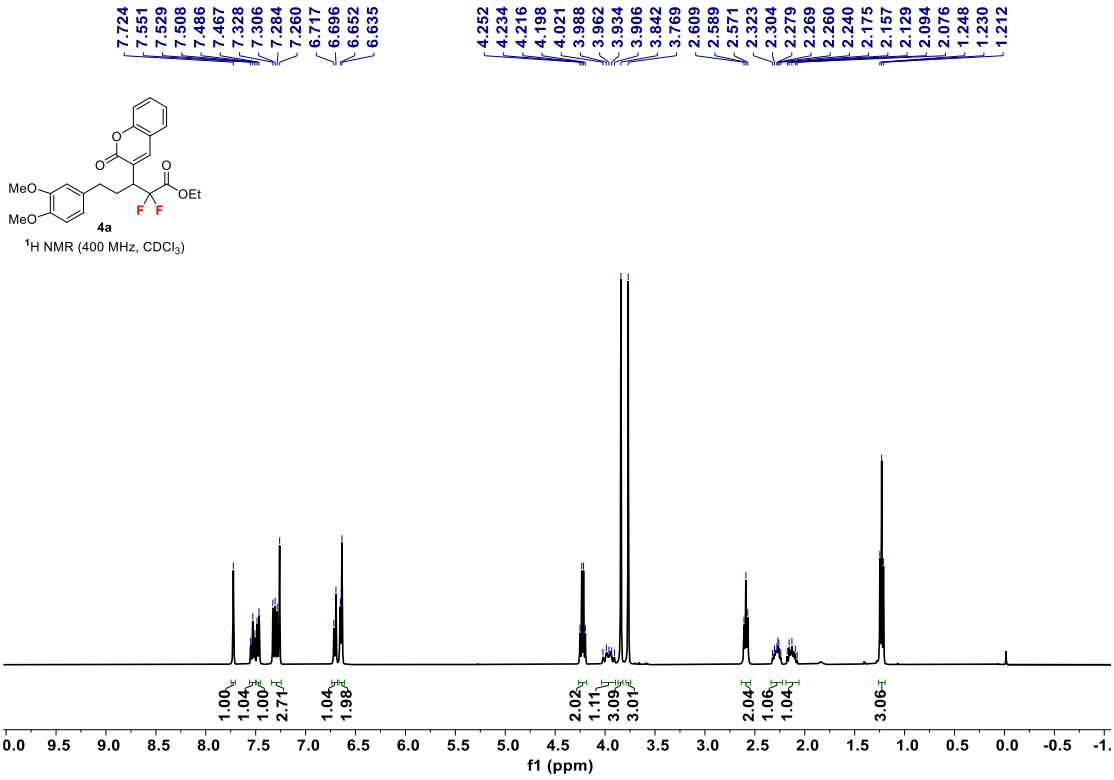


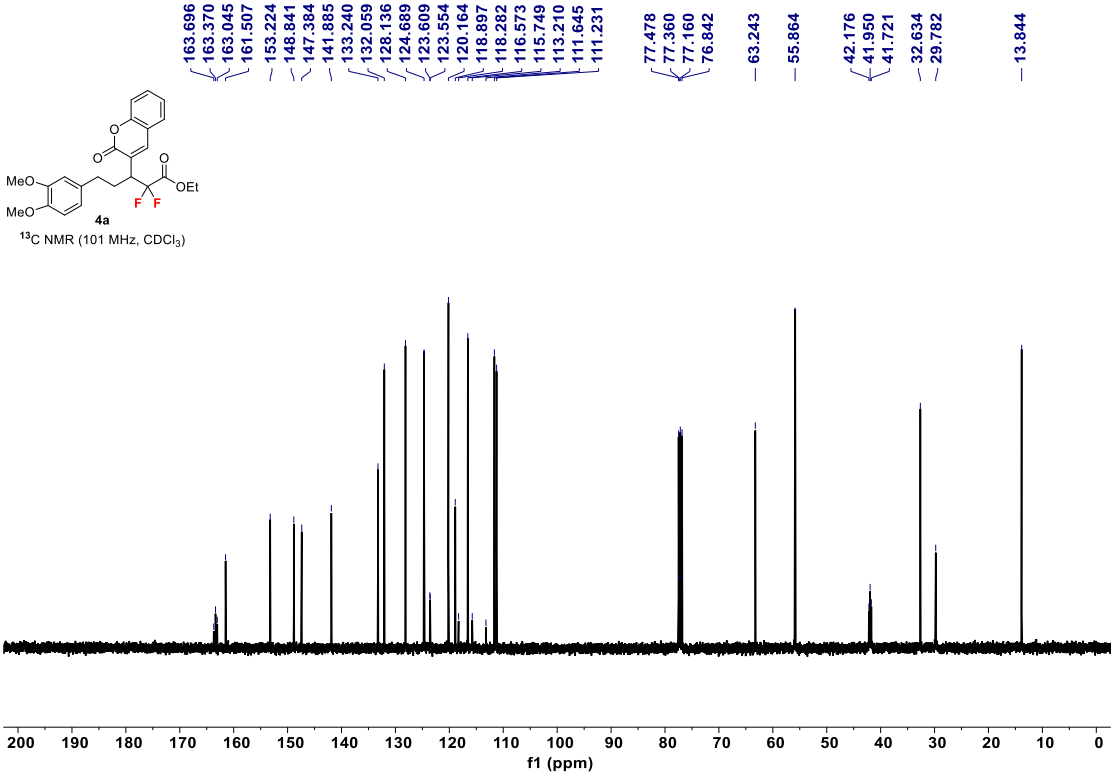
3t

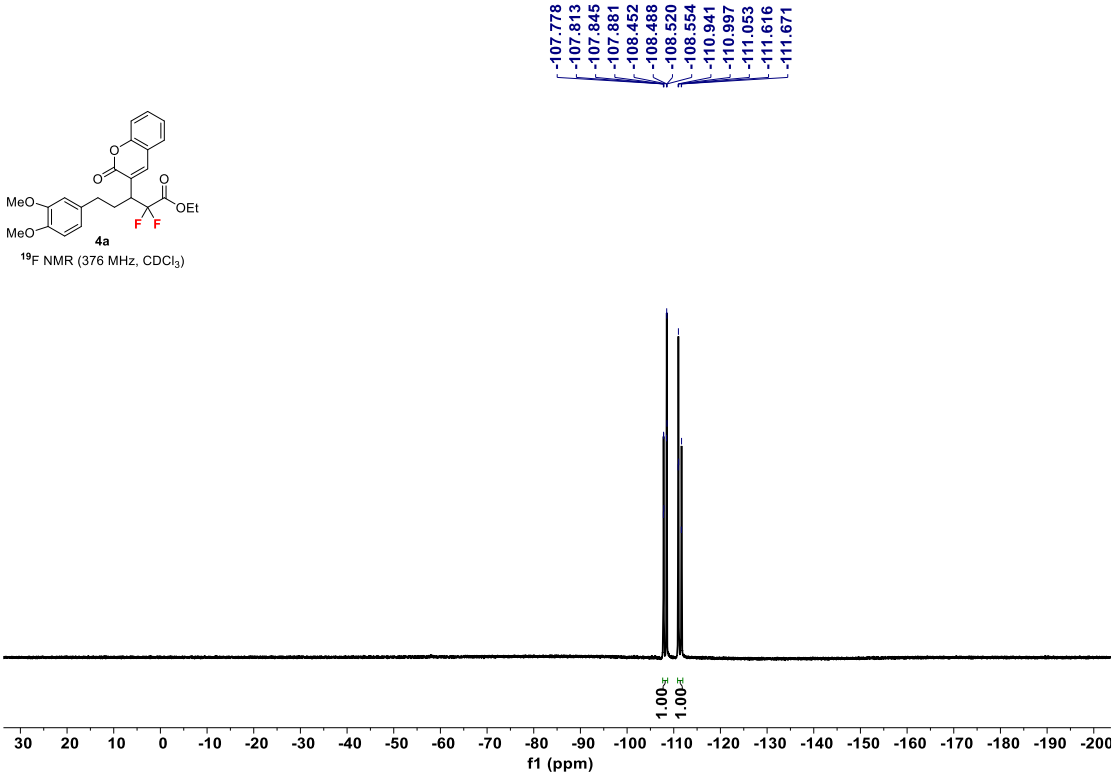
^{1}H NMR (400 MHz, $CDCl_3$)

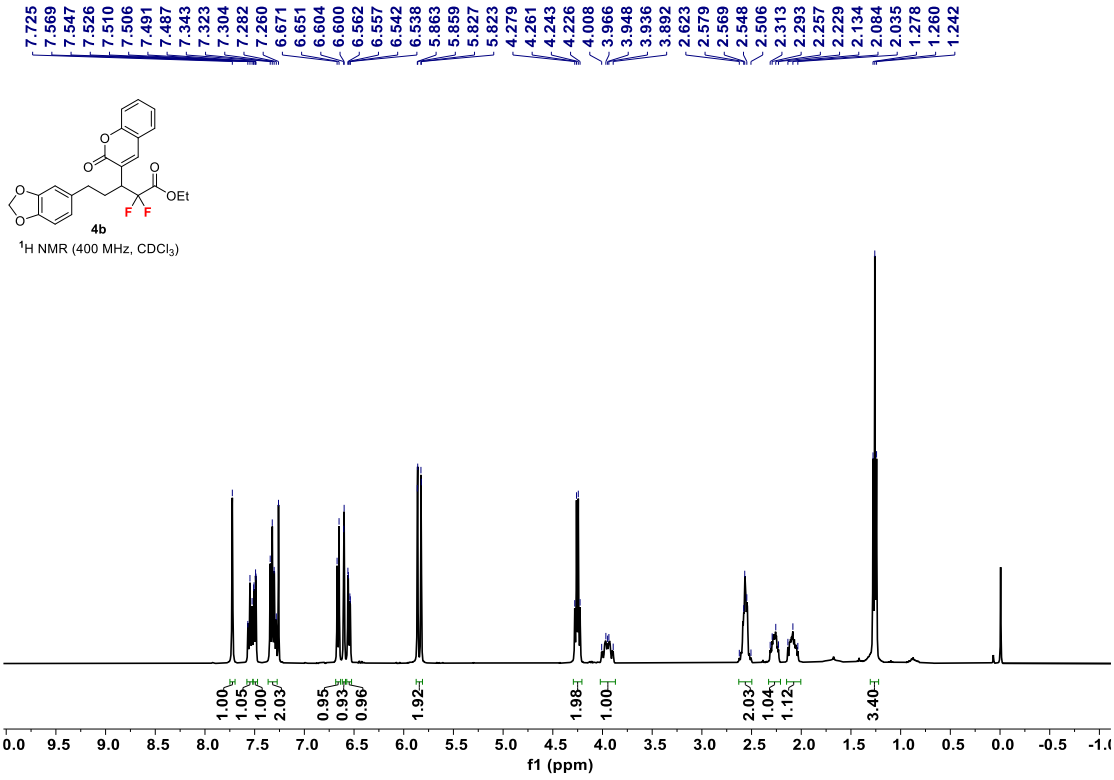

164.215
163.891
163.566
158.122
154.222
134.479
134.422
132.859
132.551
129.400
127.993
118.473
115.931
113.988
113.391
112.015
110.178
102.139
101.383
77.479
77.160
76.842
62.926
55.948
55.900
55.356
55.308
40.780
40.553
40.329
31.677
30.180
29.871
13.811
OMe
N
O
OEt
F F
MeO
3t
^{13}C NMR (101 MHz, CDCl$_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

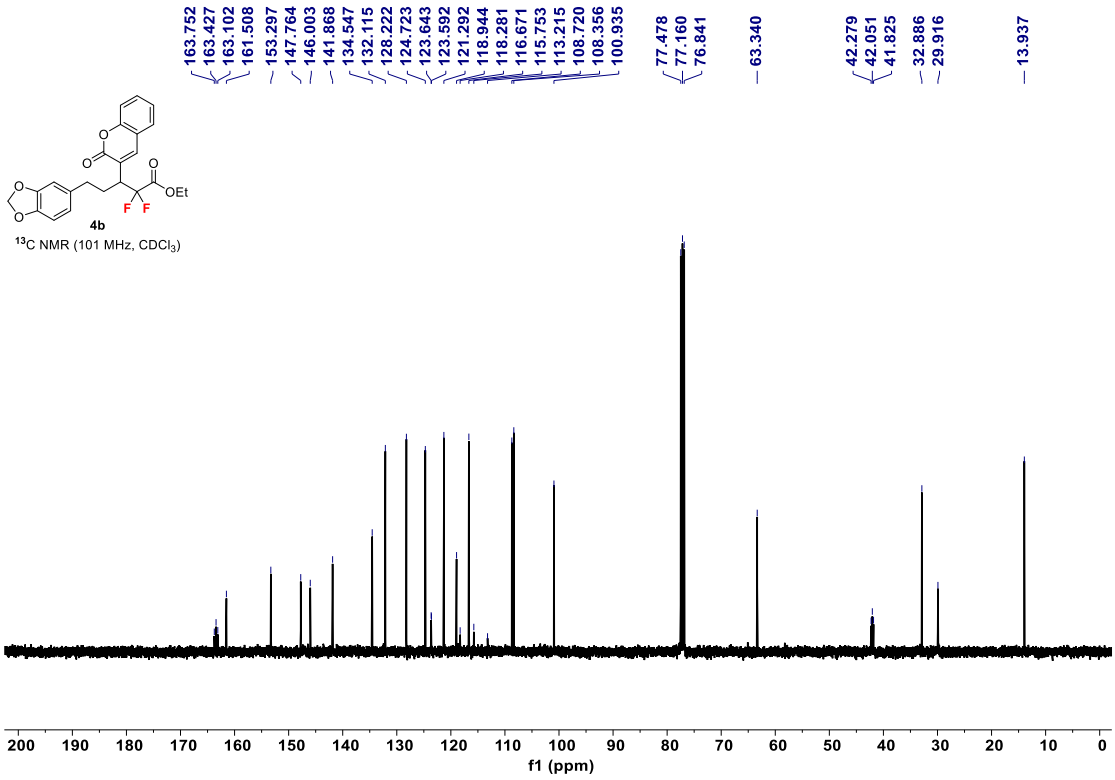

-106.226
-106.263
-106.904
-106.941
-111.031
-111.074
-111.708
-111.752
OMe
N
O
OEt
F F
MeO
3q
^{19}F NMR (376 MHz, CDCl$_3$)
1.00
1.02
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

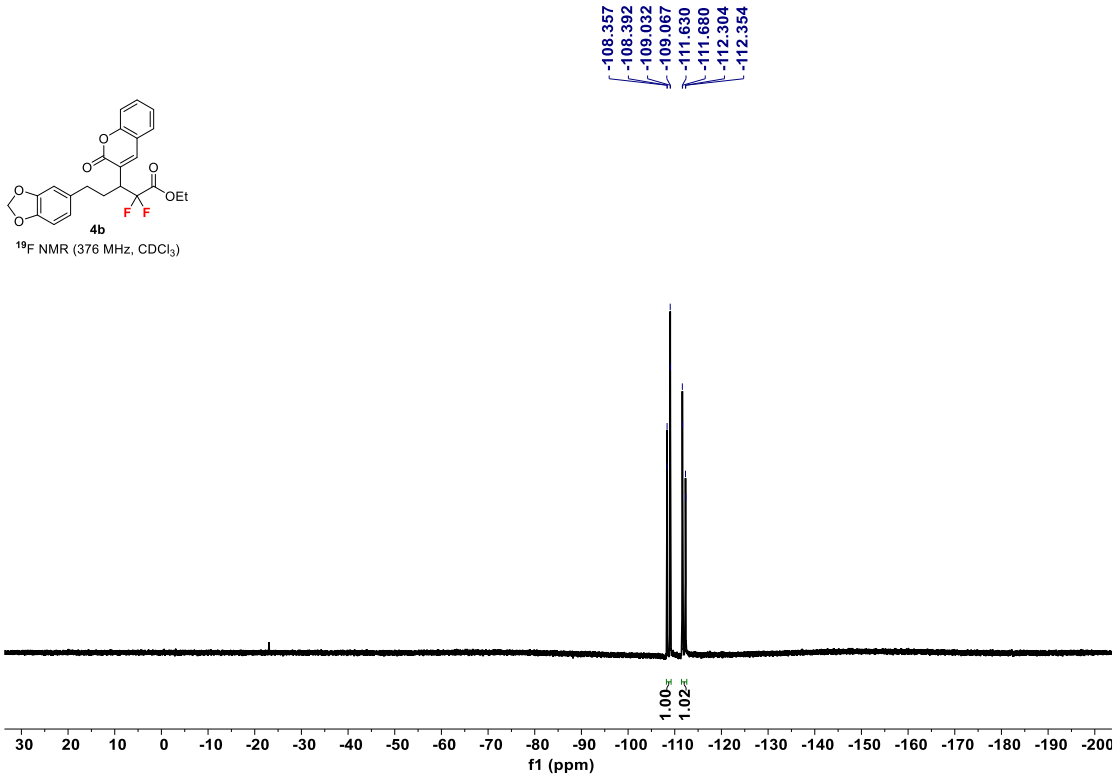

7.724
7.551
7.529
7.508
7.486
7.467
7.328
7.306
7.284
7.260
6.717
6.696
6.652
6.635
4.252
4.234
4.216
4.198
4.021
3.988
3.962
3.934
3.906
3.842
3.769
2.609
2.589
2.571
2.323
2.304
2.279
2.269
2.260
2.240
2.175
2.157
2.129
2.094
2.076
1.248
1.230
1.212
MeO
MeO
O
O
O
OEt
F F
4a
1H NMR (400 MHz, CDCl3)
1.00
1.04
1.00
2.71
1.04
1.98
2.02
1.11
3.09
3.01
2.04
1.06
1.04
3.06
f1 (ppm)

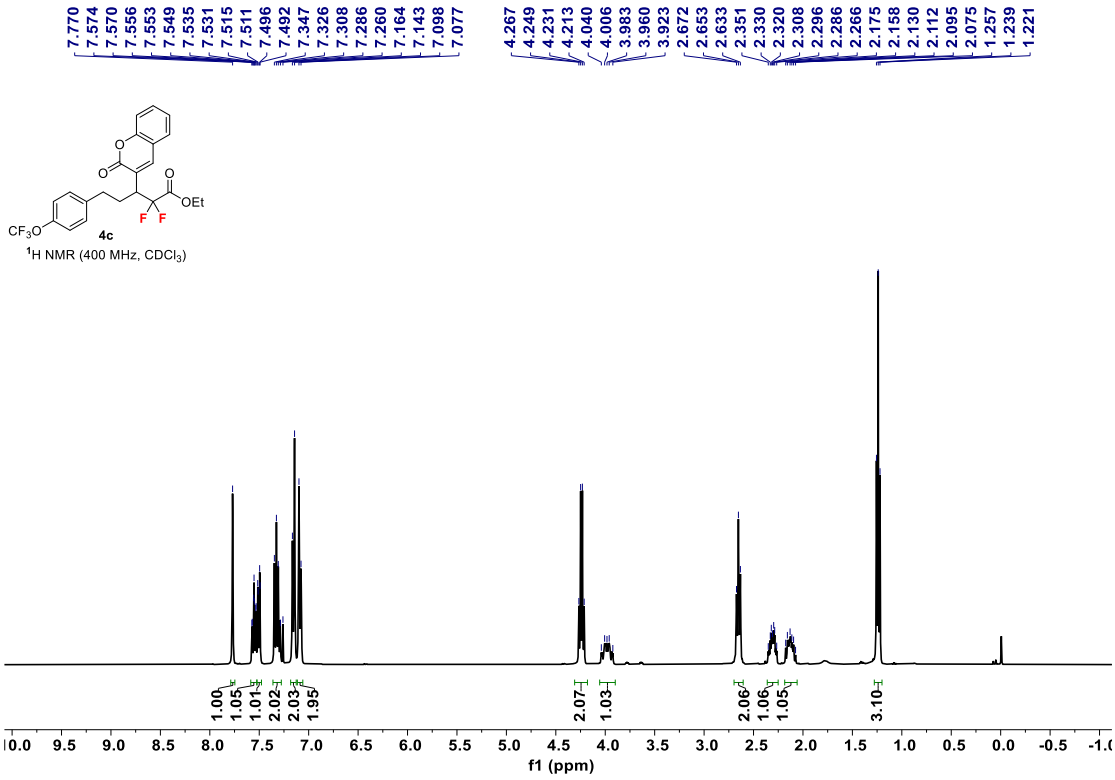

163.696
163.370
163.045
161.507
153.224
148.841
147.384
141.885
133.240
132.059
128.136
124.689
123.609
123.554
120.164
118.897
118.282
116.573
115.749
113.210
111.645
111.231
77.478
77.360
77.160
76.842
63.243
55.864
42.176
41.950
41.721
32.634
29.782
13.844
MeO
MeO
O
O
O
OEt
F F
4a
13C NMR (101 MHz, CDCl3)
f1 (ppm)

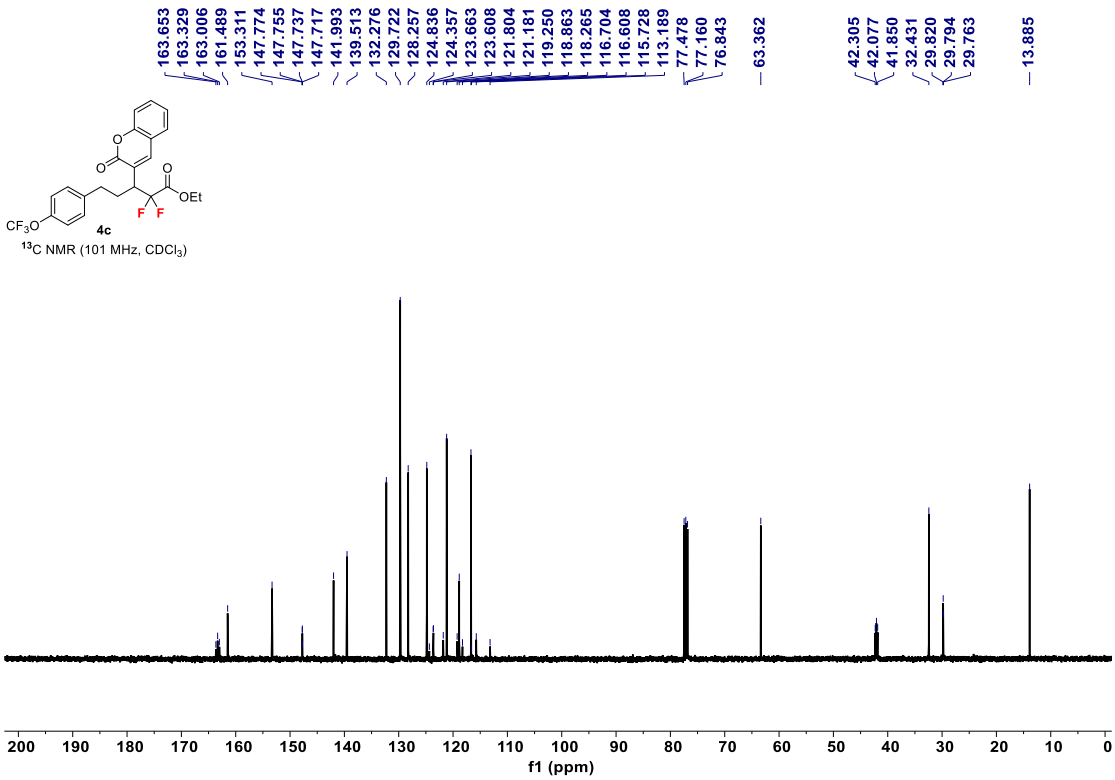

-107.778
-107.813
-107.845
-107.881
-108.452
-108.488
-108.520
-108.554
-110.941
-110.997
-111.053
-111.616
-111.671
MeO
MeO
O
O
O
OEt
F F
4a
19F NMR (376 MHz, CDCl3)
1.00
1.00
f1 (ppm)

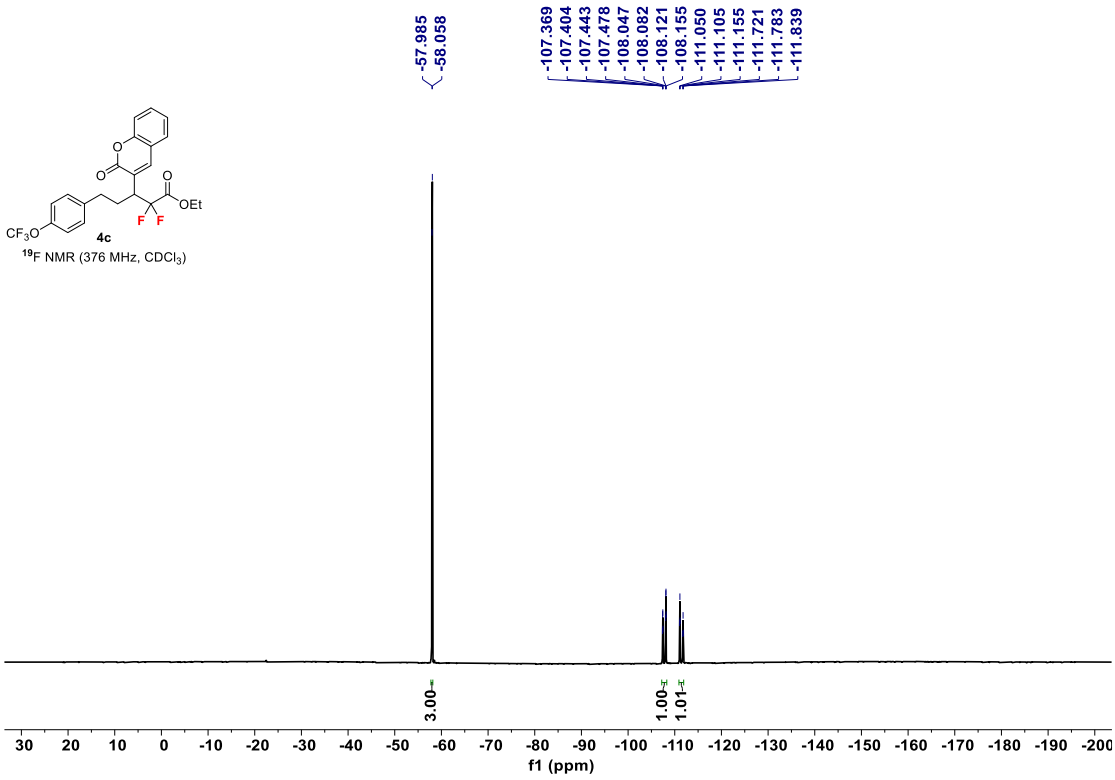

7.725
7.569
7.547
7.526
7.510
7.506
7.491
7.487
7.343
7.323
7.304
7.282
7.260
6.671
6.651
6.604
6.600
6.562
6.557
6.542
6.538
5.863
5.859
5.827
5.823
4.279
4.261
4.243
4.226
4.008
3.966
3.948
3.936
3.892
2.623
2.579
2.569
2.548
2.506
2.313
2.293
2.257
2.229
2.134
2.084
2.035
1.278
1.260
1.242
O
O
O
O
O
OEt
F F
4b
1H NMR (400 MHz, CDCl3)
1.00
1.05
1.00
2.03
0.95
0.93
0.96
1.92
1.98
1.00
2.03
1.04
1.12
3.40
f1 (ppm)


163.752
163.427
163.102
161.508
153.297
147.764
146.003
141.868
134.547
132.115
128.222
124.723
123.643
123.592
121.292
118.944
118.281
116.671
115.753
113.215
108.720
108.356
100.935
77.478
77.160
76.841
63.340
42.279
42.051
41.825
32.886
29.916
13.937
O
O
O
O
OEt
F F
4b
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-108.357
-108.392
-109.032
-109.067
-111.630
-111.680
-112.304
-112.354
O
O
O
O
OEt
F F
4b
19F NMR (376 MHz, CDCl3)
1.00
1.02
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

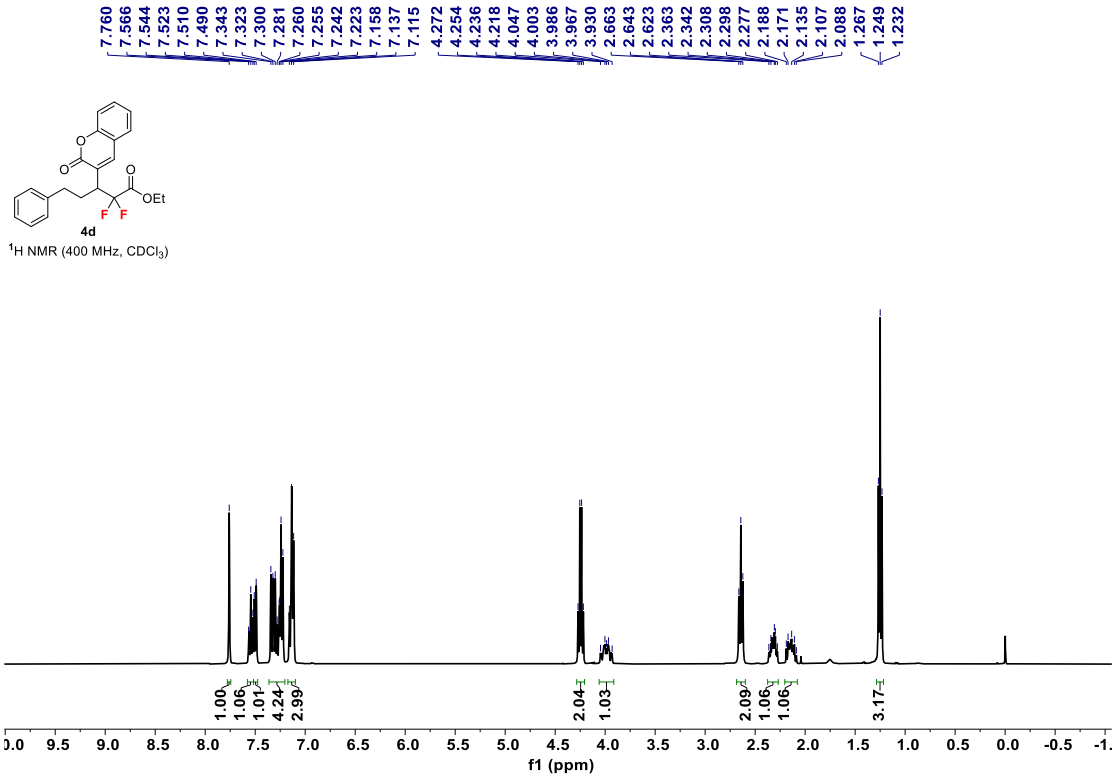

7.770
7.574
7.570
7.556
7.553
7.549
7.535
7.531
7.515
7.511
7.496
7.492
7.347
7.326
7.308
7.286
7.260
7.164
7.143
7.098
7.077
4.267
4.249
4.231
4.213
4.040
4.006
3.983
3.960
3.923
2.672
2.653
2.633
2.351
2.330
2.320
2.308
2.296
2.286
2.266
2.175
2.158
2.130
2.112
2.095
2.075
1.257
1.239
1.221
O
O
O
OEt
F F
CF3O
4c
1H NMR (400 MHz, CDCl3)
1.00
1.05
1.01
2.02
2.03
1.95
2.07
1.03
2.06
1.06
1.05
3.10
f1 (ppm)


163.653
163.329
163.006
161.489
153.311
147.774
147.755
147.737
147.717
141.993
139.513
132.276
129.722
128.257
124.836
124.357
123.663
123.608
121.804
121.181
119.250
118.863
118.265
116.704
116.608
115.728
113.189
77.478
77.160
76.843
63.362
42.305
42.077
41.850
32.431
29.820
29.794
29.763
13.885
O
O
O
OEt
F F
CF3O
4c
13C NMR (101 MHz, CDCl3)
f1 (ppm)



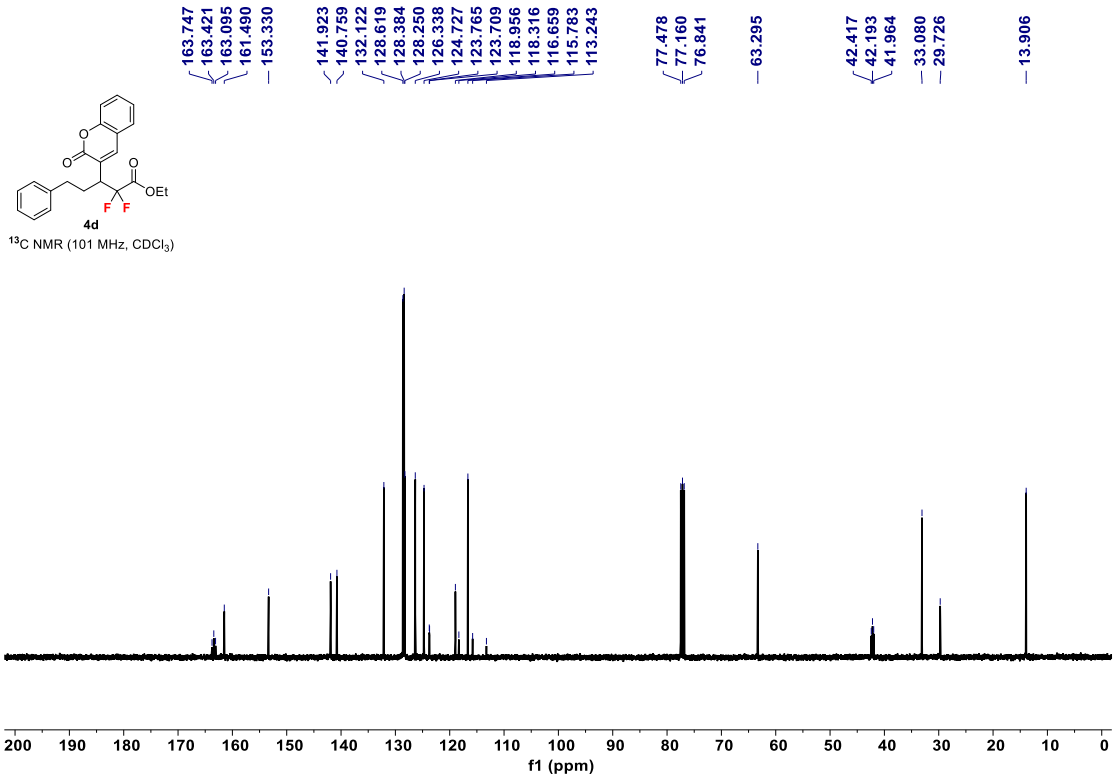
4c

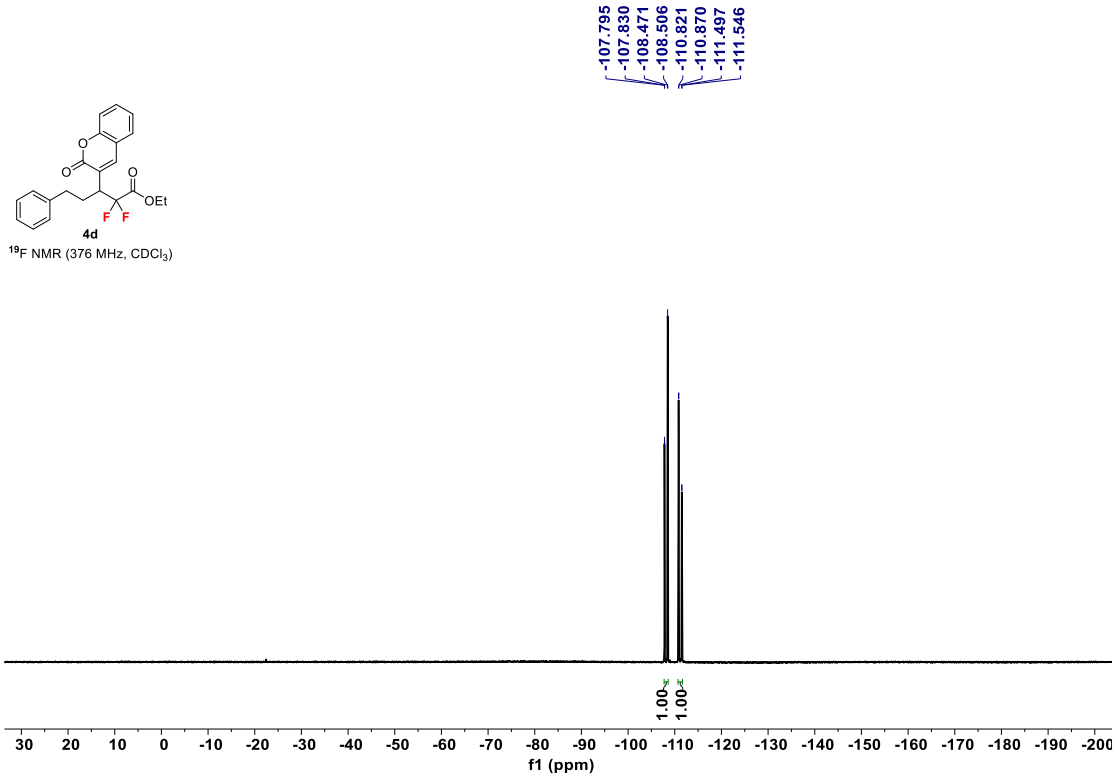
^{19}F NMR (376 MHz, $CDCl_3$)

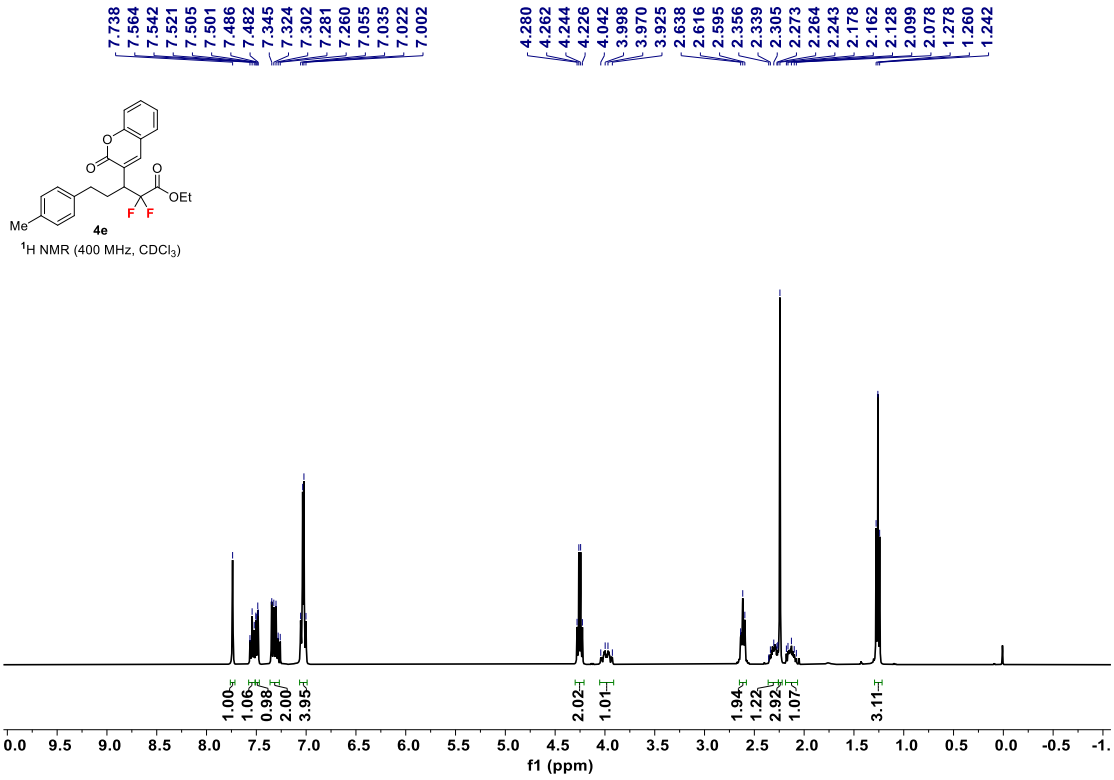


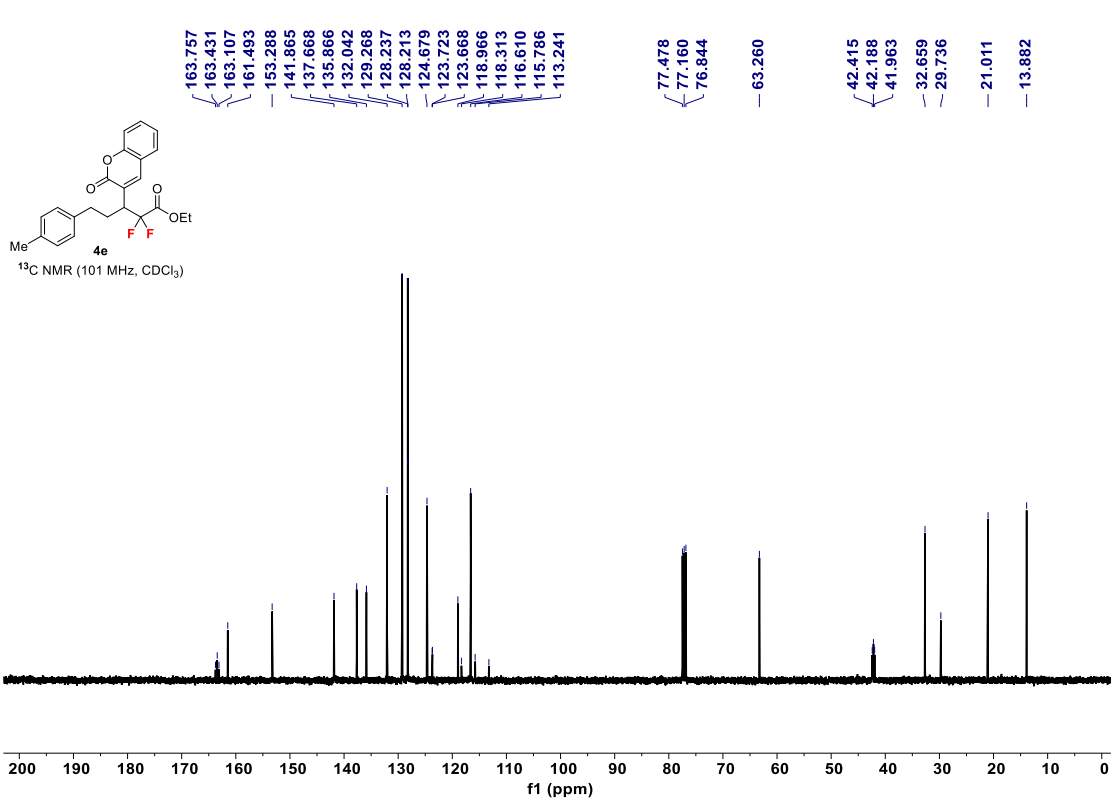
4d

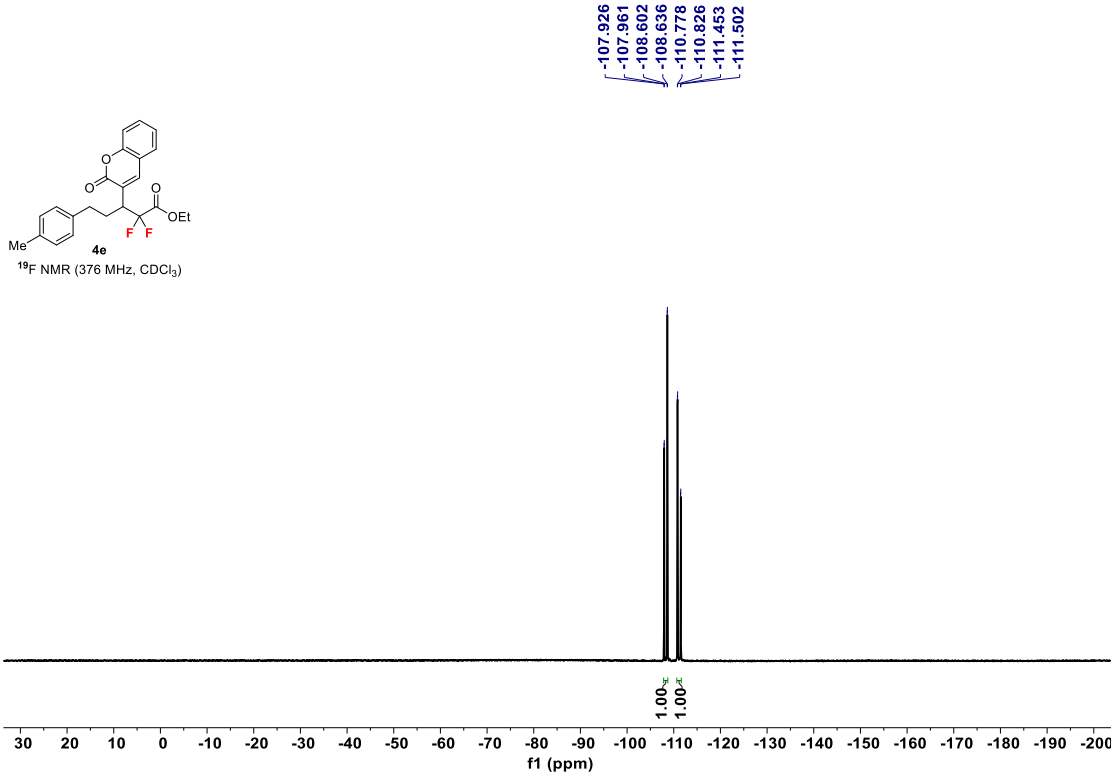
^{1}H NMR (400 MHz, $CDCl_3$)

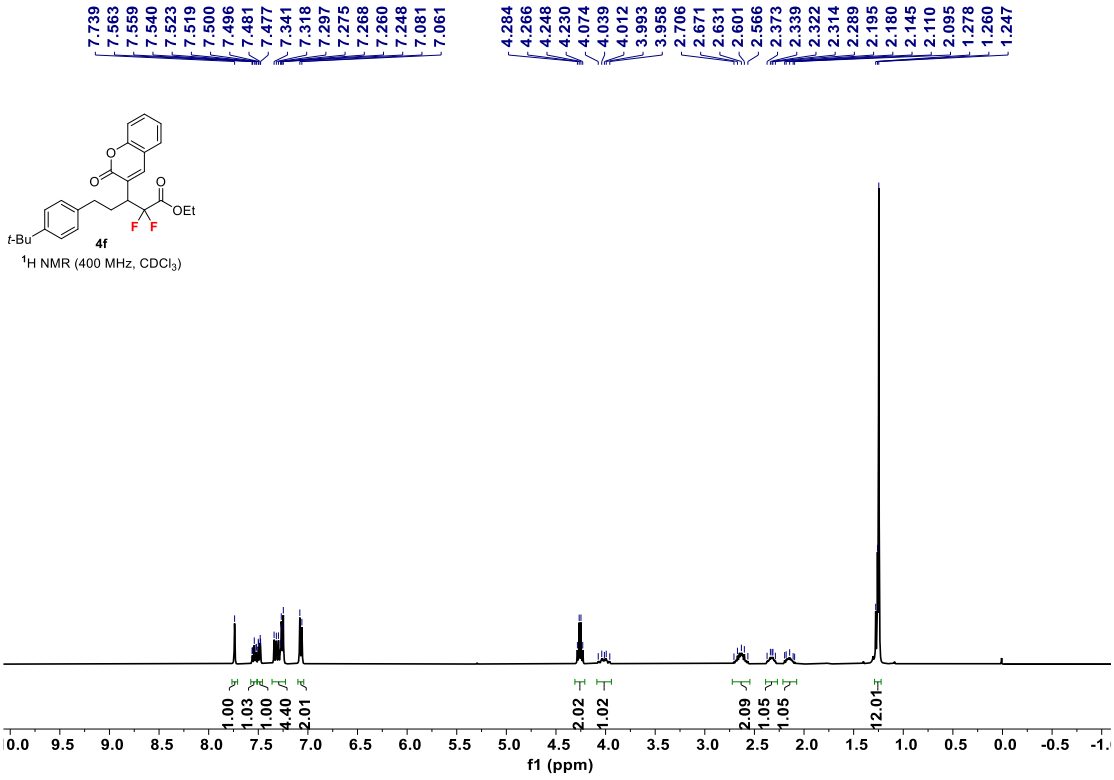

163.747
163.421
163.095
161.490
153.330
141.923
140.759
132.122
128.619
128.384
128.250
126.338
124.727
123.765
123.709
118.956
118.316
116.659
115.783
113.243
77.478
77.160
76.841
63.295
42.417
42.193
41.964
33.080
29.726
13.906
O
O
O
OEt
F F
4d
^{13}C NMR (101 MHz, CDCl$_3$)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

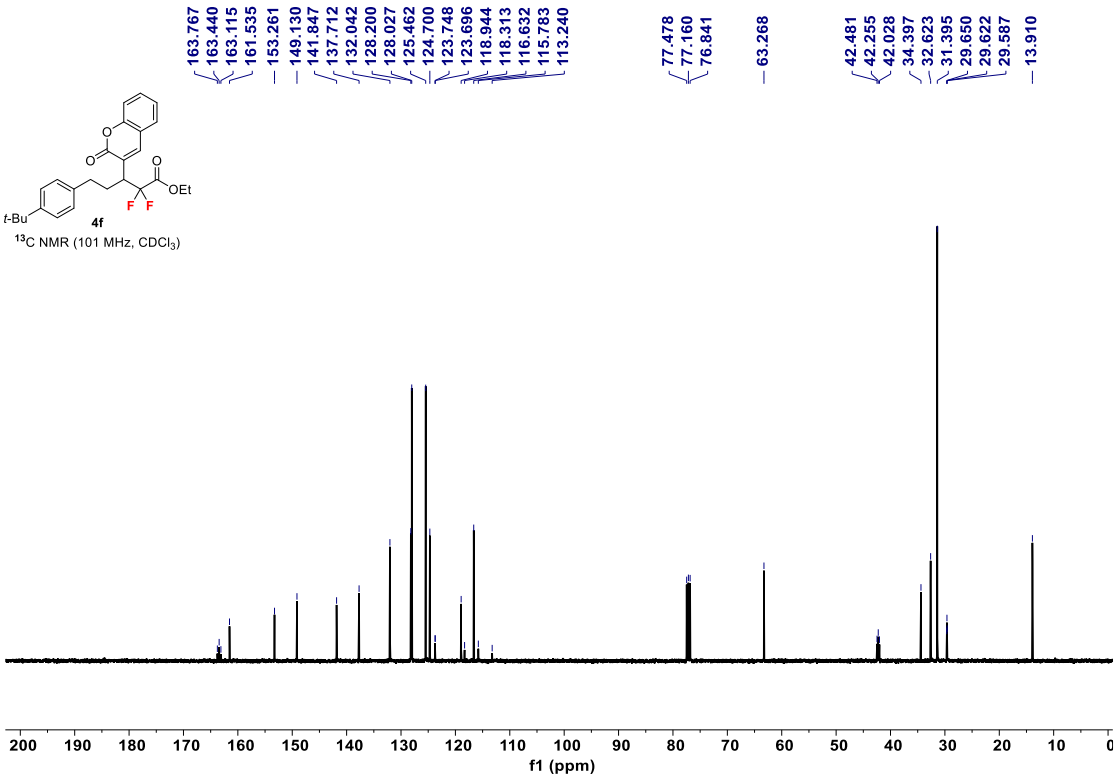

-107.795
-107.830
-108.471
-108.506
-110.821
-110.870
-111.497
-111.546
O
O
O
OEt
F F
4d
^{19}F NMR (376 MHz, CDCl$_3$)
1.00
1.00
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

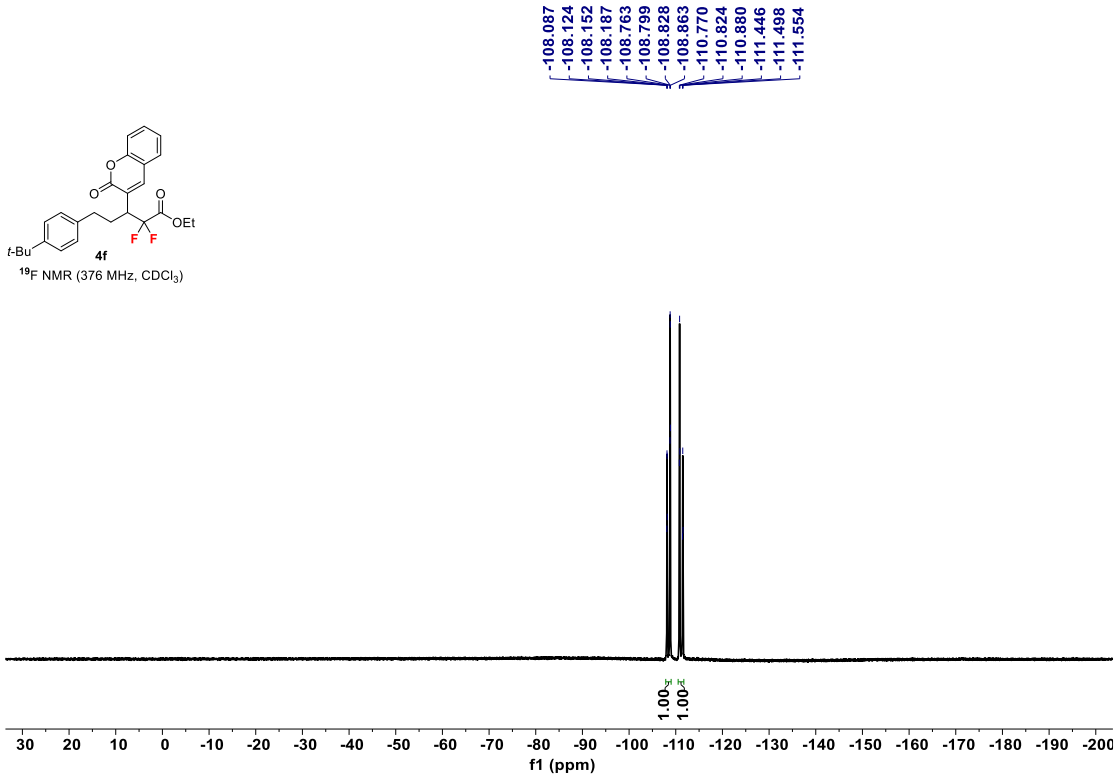

7.738
7.564
7.542
7.521
7.505
7.501
7.486
7.482
7.345
7.324
7.302
7.281
7.260
7.055
7.035
7.022
7.002
4.280
4.262
4.244
4.226
4.042
3.998
3.970
3.925
2.638
2.616
2.595
2.356
2.339
2.305
2.273
2.264
2.243
2.178
2.162
2.128
2.099
2.078
1.278
1.260
1.242
O
O
O
OEt
F F
Me
4e
1H NMR (400 MHz, CDCl3)
1.00
1.06
0.98
2.00
3.95
2.02
1.01
1.94
1.22
2.92
1.07
3.11
f1 (ppm)

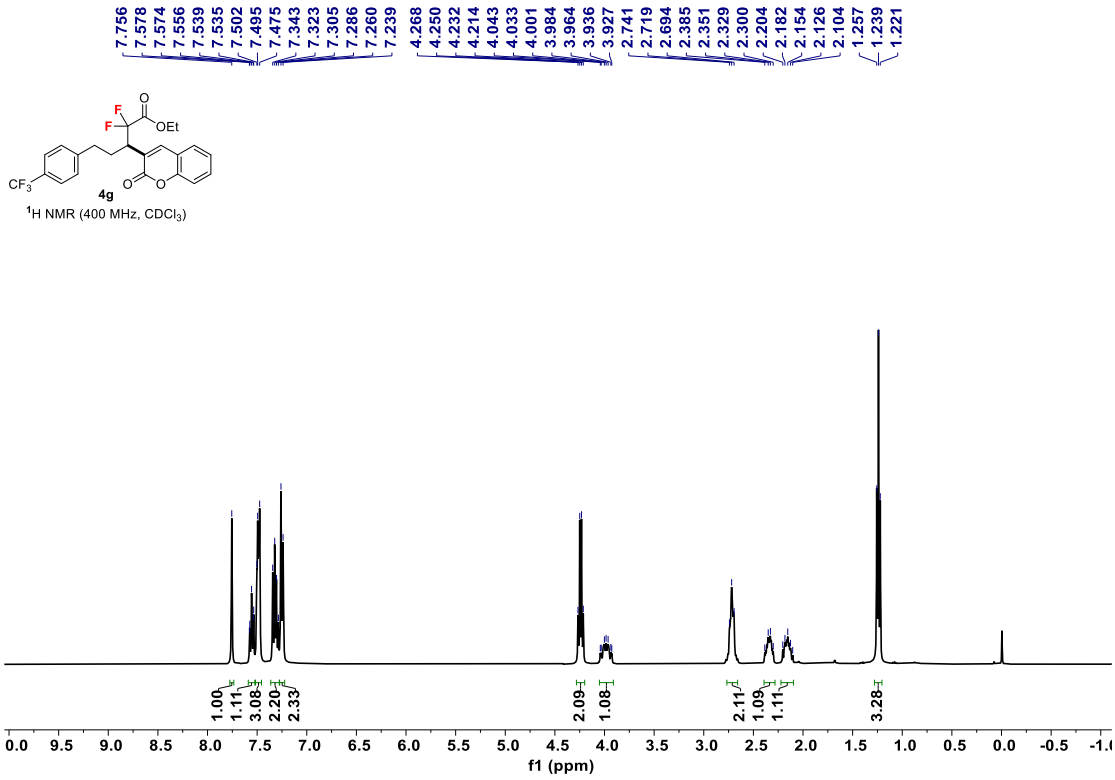

163.757
163.431
163.107
161.493
153.288
141.865
137.668
135.866
132.042
129.268
128.237
128.213
124.679
123.723
123.668
118.966
118.313
116.610
115.786
113.241
77.478
77.160
76.844
63.260
42.415
42.188
41.963
32.659
29.736
21.011
13.882
O
O
O
OEt
F F
Me
4e
13C NMR (101 MHz, CDCl3)
f1 (ppm)

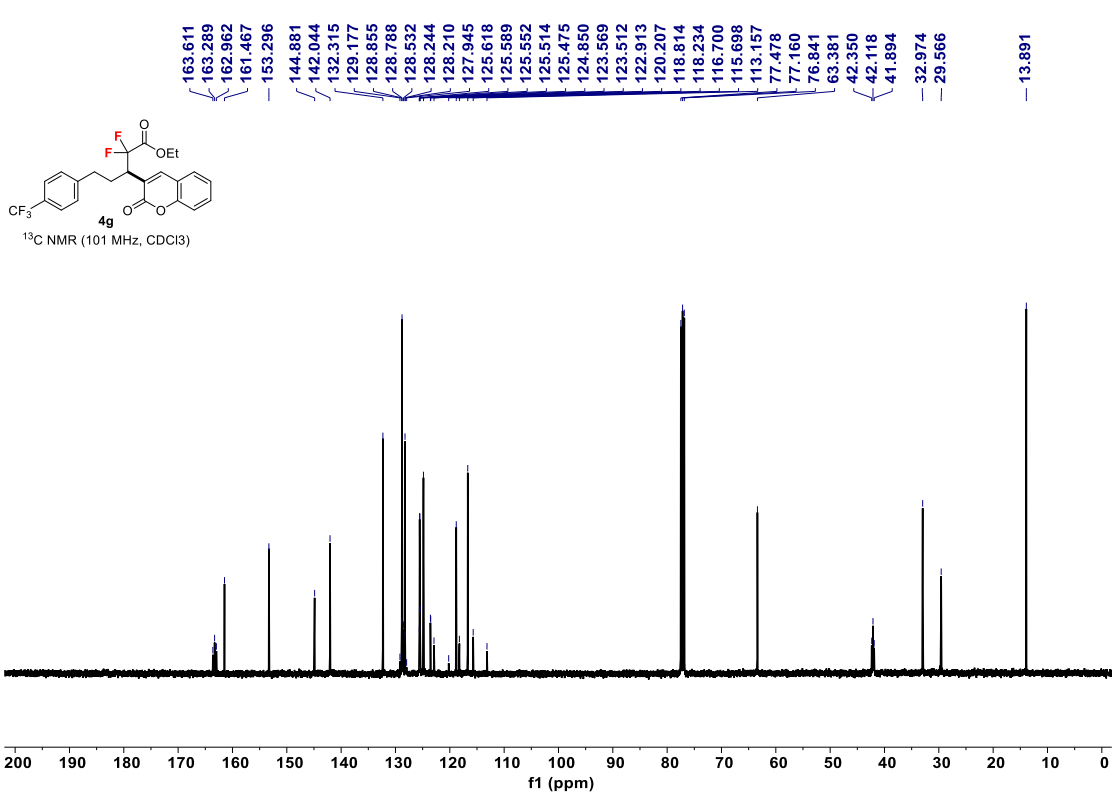

-107.926
-107.961
-108.602
-108.636
-110.778
-110.826
-111.453
-111.502
O
O
O
OEt
F F
Me
4e
19F NMR (376 MHz, CDCl3)
1.00
1.00
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)

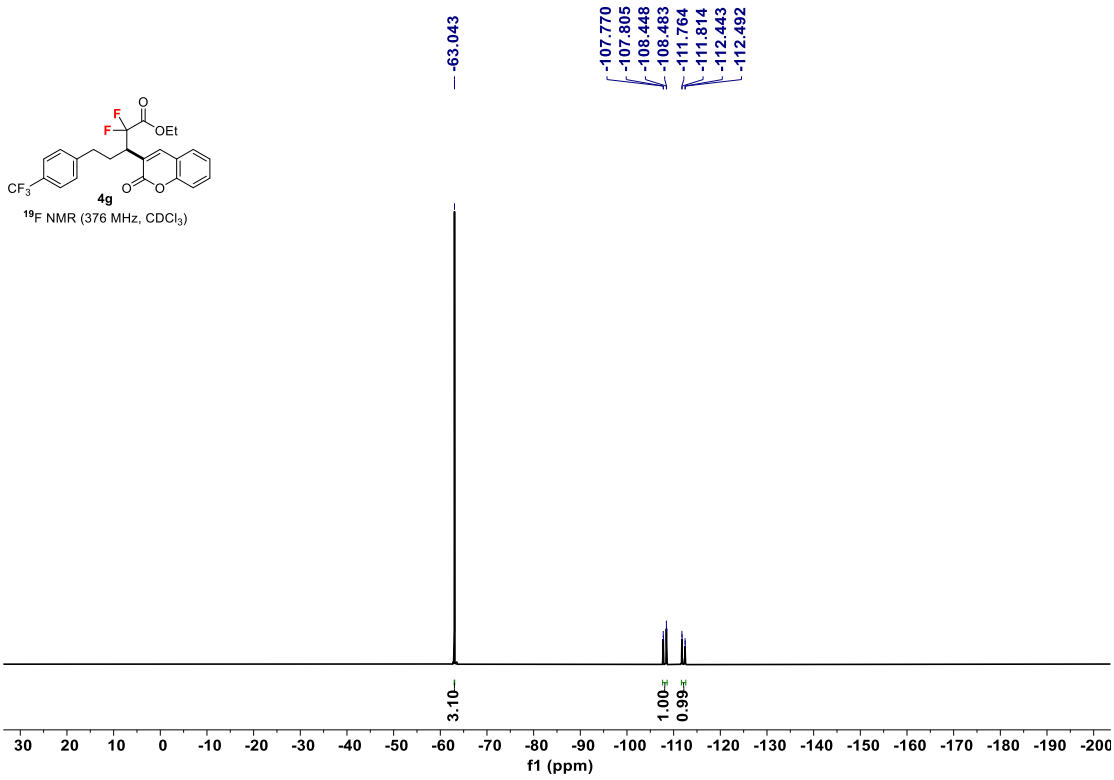

7.739
7.563
7.559
7.540
7.523
7.519
7.500
7.496
7.481
7.477
7.341
7.318
7.297
7.275
7.268
7.260
7.248
7.081
7.061
4.284
4.266
4.248
4.230
4.074
4.039
4.012
3.993
3.958
2.706
2.671
2.631
2.601
2.566
2.373
2.339
2.322
2.314
2.289
2.195
2.180
2.145
2.110
2.095
1.278
1.260
1.247
O
O
O
OEt
F F
t-Bu
4f
1H NMR (400 MHz, CDCl3)
1.00
1.03
1.00
4.40
2.01
2.02
1.02
2.09
1.05
1.05
12.01
0.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

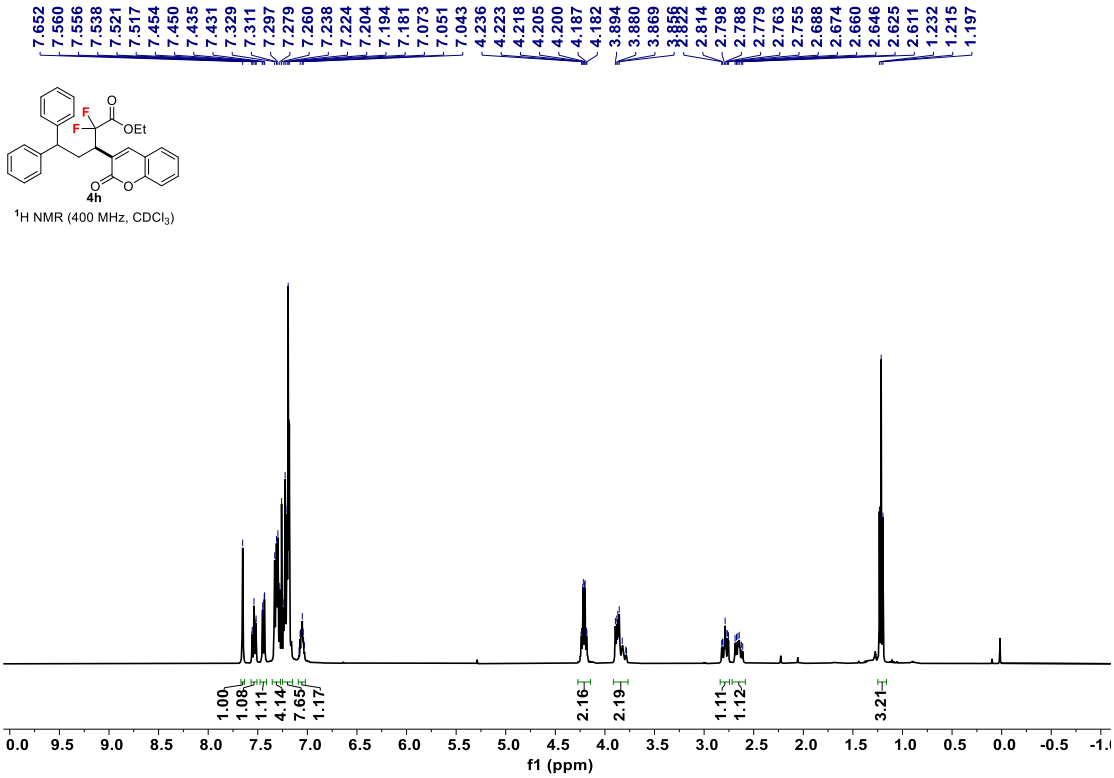

163.767
163.440
163.115
161.535
153.261
149.130
141.847
137.712
132.042
128.200
128.027
125.462
124.700
123.748
123.696
118.944
118.313
116.632
115.783
113.240
77.478
77.160
76.841
63.268
42.481
42.255
42.028
34.397
32.623
31.395
29.650
29.622
29.587
13.910
O
O
O
OEt
F F
t-Bu
4f
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

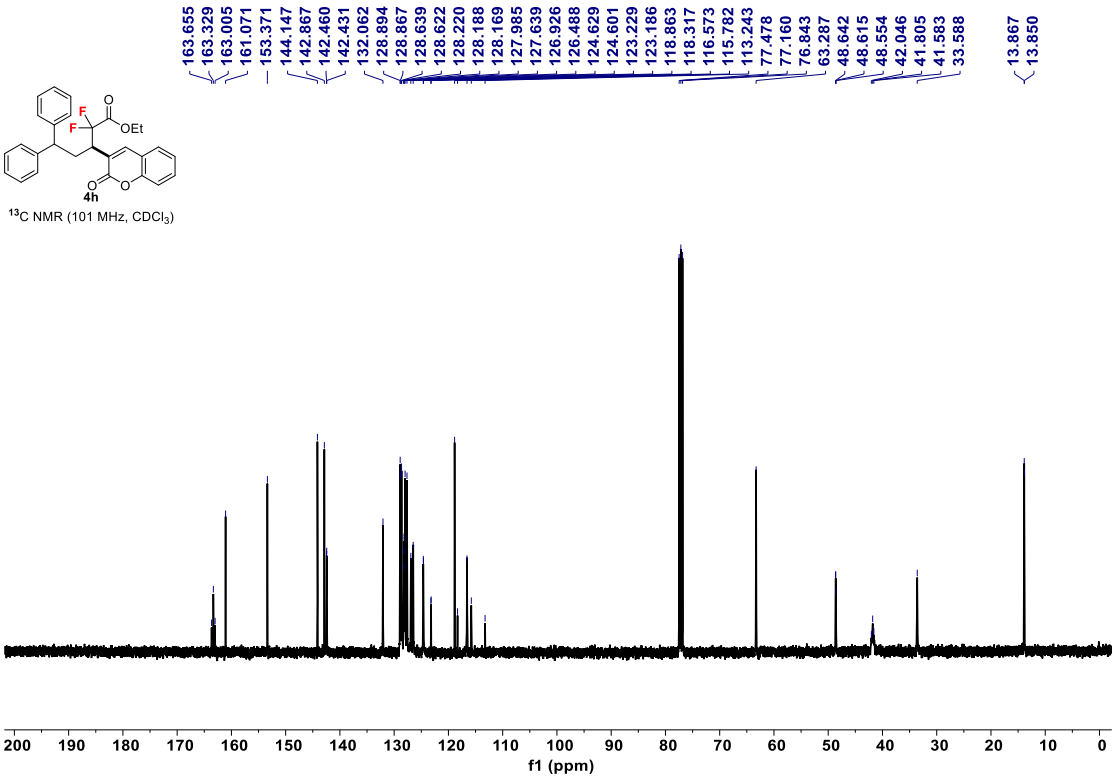

-108.087
-108.124
-108.152
-108.187
-108.763
-108.799
-108.828
-108.863
-110.770
-110.824
-110.880
-111.446
-111.498
-111.554
O
O
O
OEt
F F
t-Bu
4f
19F NMR (376 MHz, CDCl3)
1.00
1.00
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)


7.756
7.578
7.574
7.556
7.539
7.535
7.502
7.495
7.475
7.343
7.323
7.305
7.286
7.260
7.239
4.268
4.250
4.232
4.214
4.043
4.033
4.001
3.984
3.964
3.936
3.927
2.741
2.719
2.694
2.385
2.351
2.329
2.300
2.204
2.182
2.154
2.126
2.104
1.257
1.239
1.221
F
F
O
OEt
CF3
O
O
4g
1H NMR (400 MHz, CDCl3)
1.00
1.11
3.08
2.20
2.33
2.09
1.08
2.11
1.09
1.11
3.28
f1 (ppm)

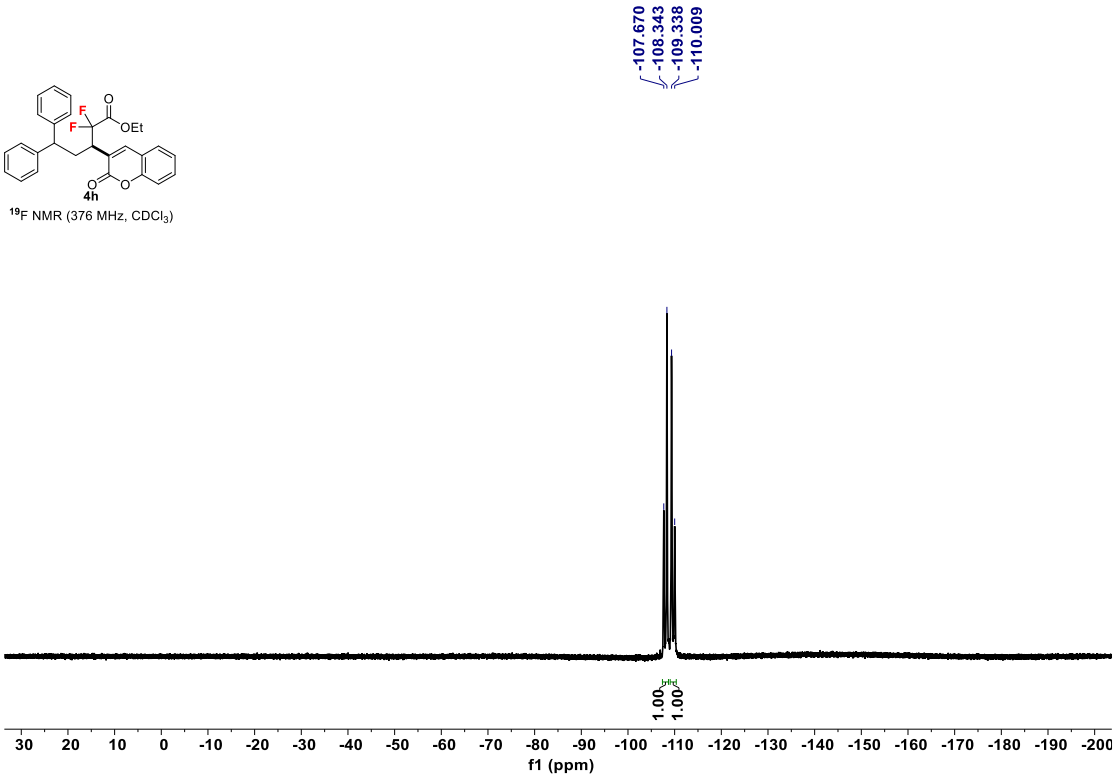

163.611
163.289
162.962
161.467
153.296
144.881
142.044
132.315
129.177
128.855
128.788
128.532
128.244
128.210
127.945
125.618
125.589
125.552
125.514
125.475
124.850
123.569
123.512
122.913
120.207
118.814
118.234
116.700
115.698
113.157
77.478
77.160
76.841
63.381
42.350
42.118
41.894
32.974
29.566
13.891
F
F
O
OEt
CF3
O
O
4g
13C NMR (101 MHz, CDCl3)
f1 (ppm)


-63.043
-107.770
-107.805
-108.448
-108.483
-111.764
-111.814
-112.443
-112.492
4g
19F NMR (376 MHz, CDCl3)
3.10
1.00
0.99
f1 (ppm)

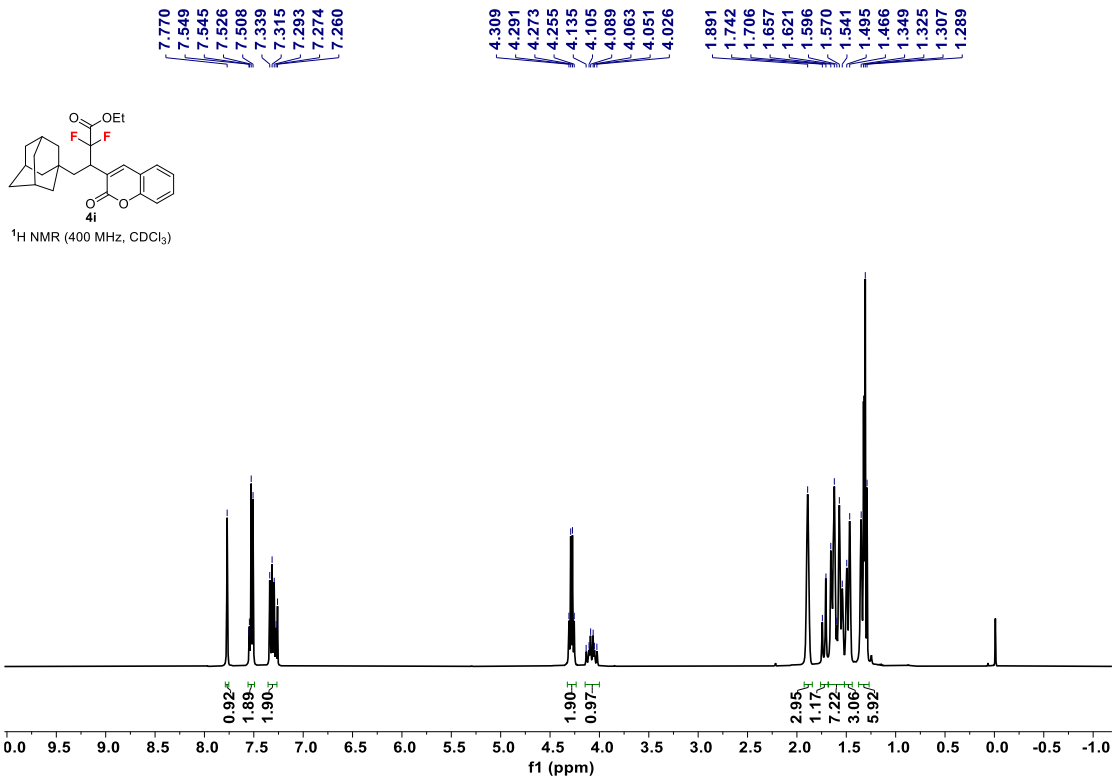

4h
1H NMR (400 MHz, CDCl3)
1.00
1.08
1.11
4.14
7.65
1.17
2.16
2.19
1.11
1.12
3.21
f1 (ppm)

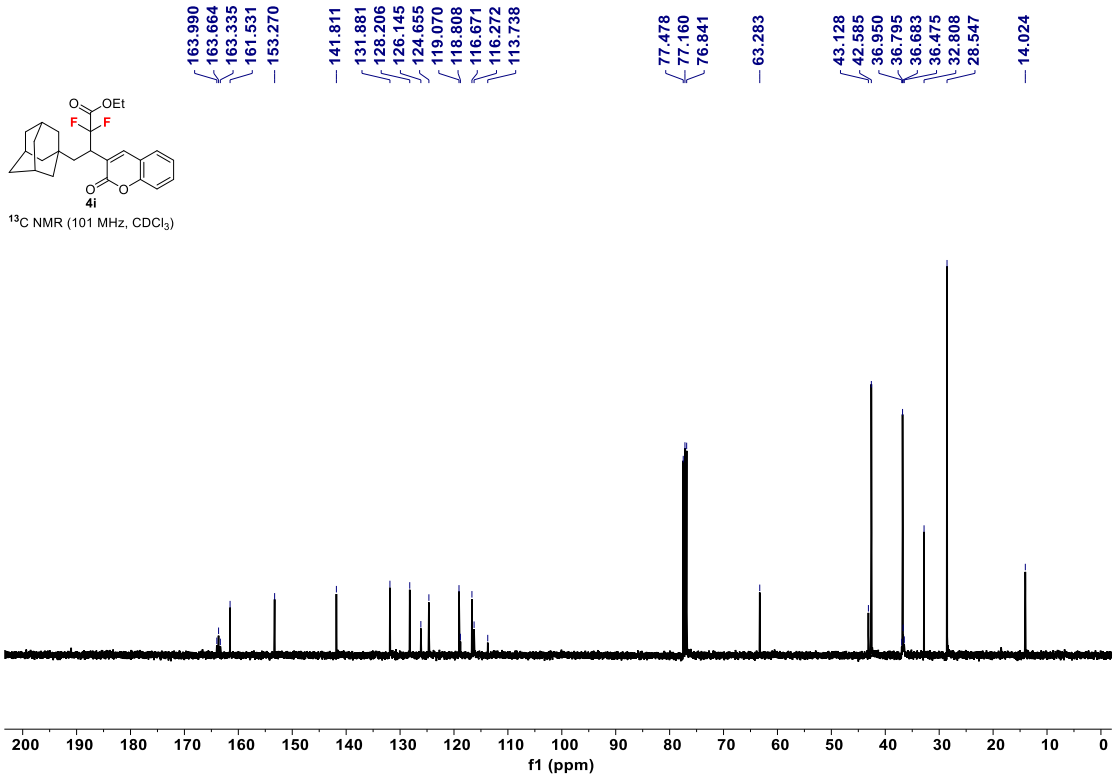


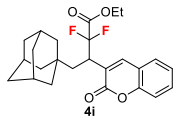
^{13}C NMR (101 MHz, $CDCl_3$)



^{19}F NMR (376 MHz, $CDCl_3$)


7.770
7.549
7.545
7.526
7.508
7.339
7.315
7.293
7.274
7.260
4.309
4.291
4.273
4.255
4.135
4.105
4.089
4.063
4.051
4.026
1.891
1.742
1.706
1.657
1.621
1.596
1.570
1.541
1.495
1.466
1.349
1.325
1.307
1.289
O
OEt
F
F
O
O
4i
1H NMR (400 MHz, CDCl3)
0.92
1.89
1.90
1.90
0.97
2.95
1.17
7.22
3.06
5.92
f1 (ppm)


163.990
163.664
163.335
161.531
153.270
141.811
131.881
128.206
126.145
124.655
119.070
118.808
116.671
116.272
113.738
77.478
77.160
76.841
63.283
43.128
42.585
36.950
36.795
36.683
36.475
32.808
28.547
14.024
O
OEt
F
F
O
O
4i
13C NMR (101 MHz, CDCl3)
f1 (ppm)

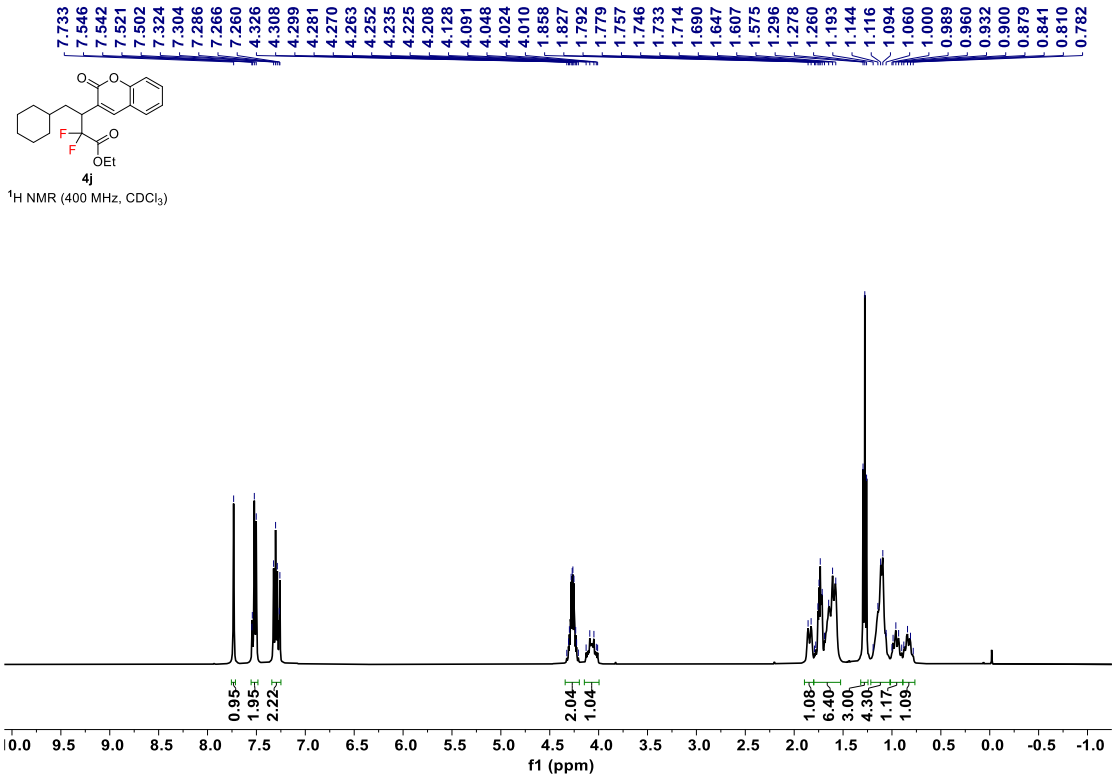


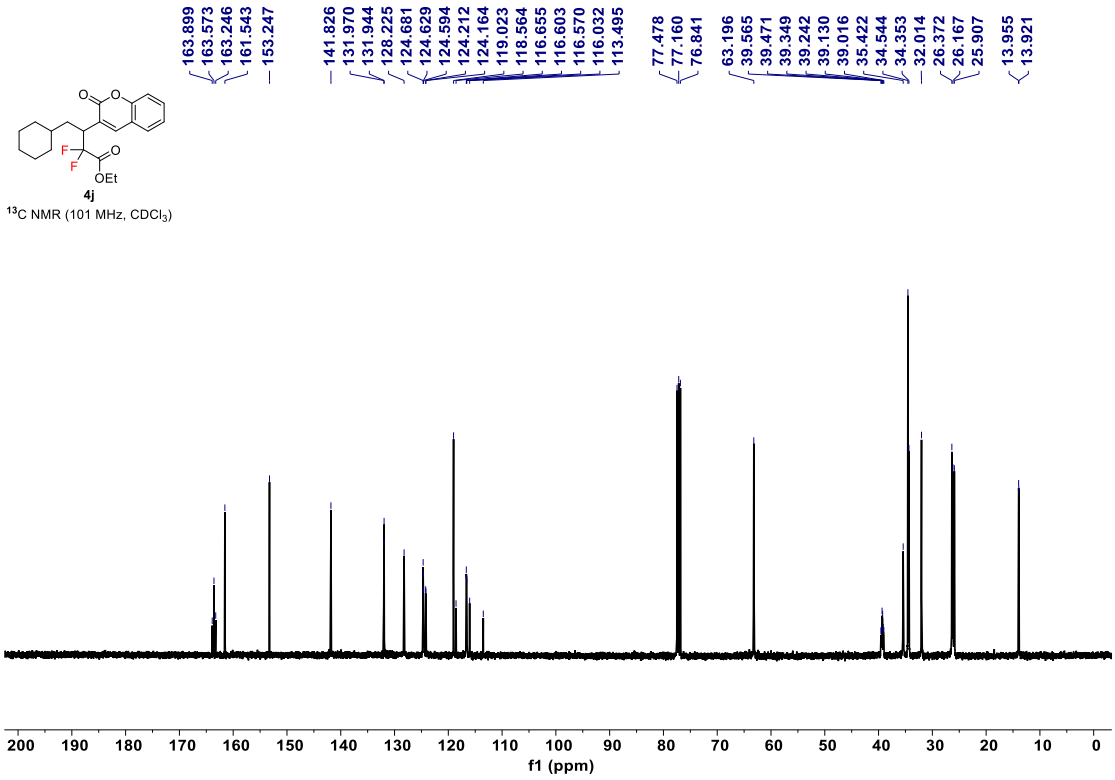
4i

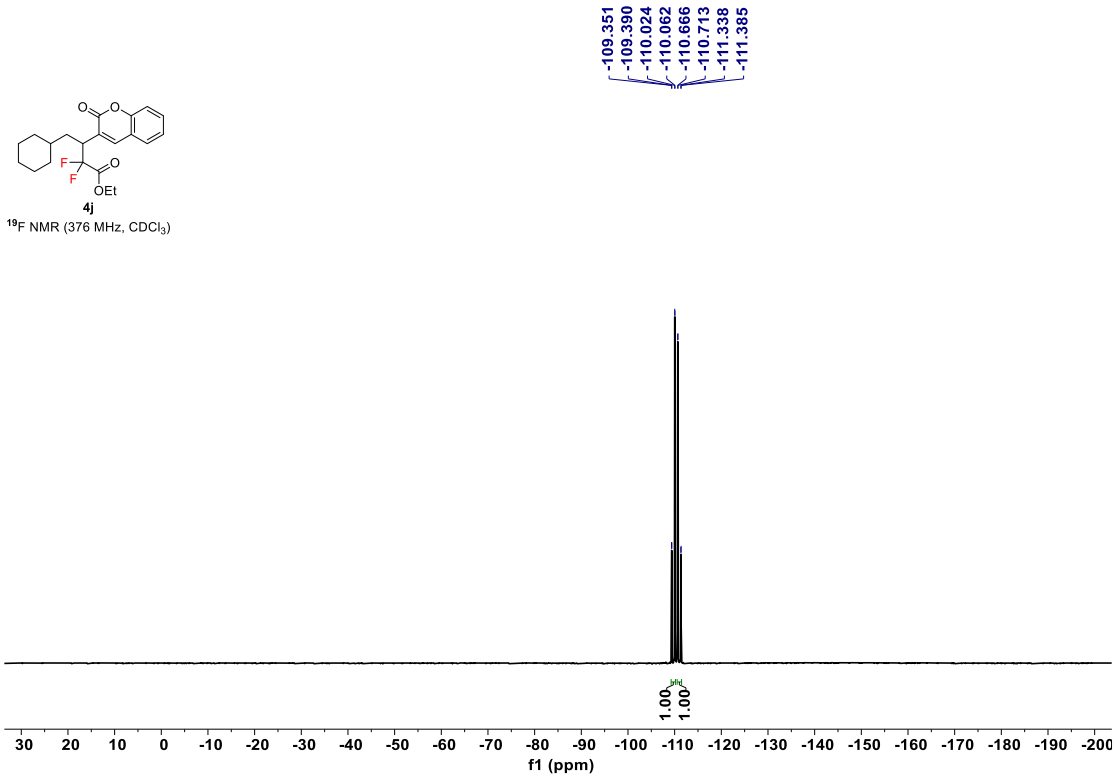
^{19}F NMR (376 MHz, $CDCl_3$)

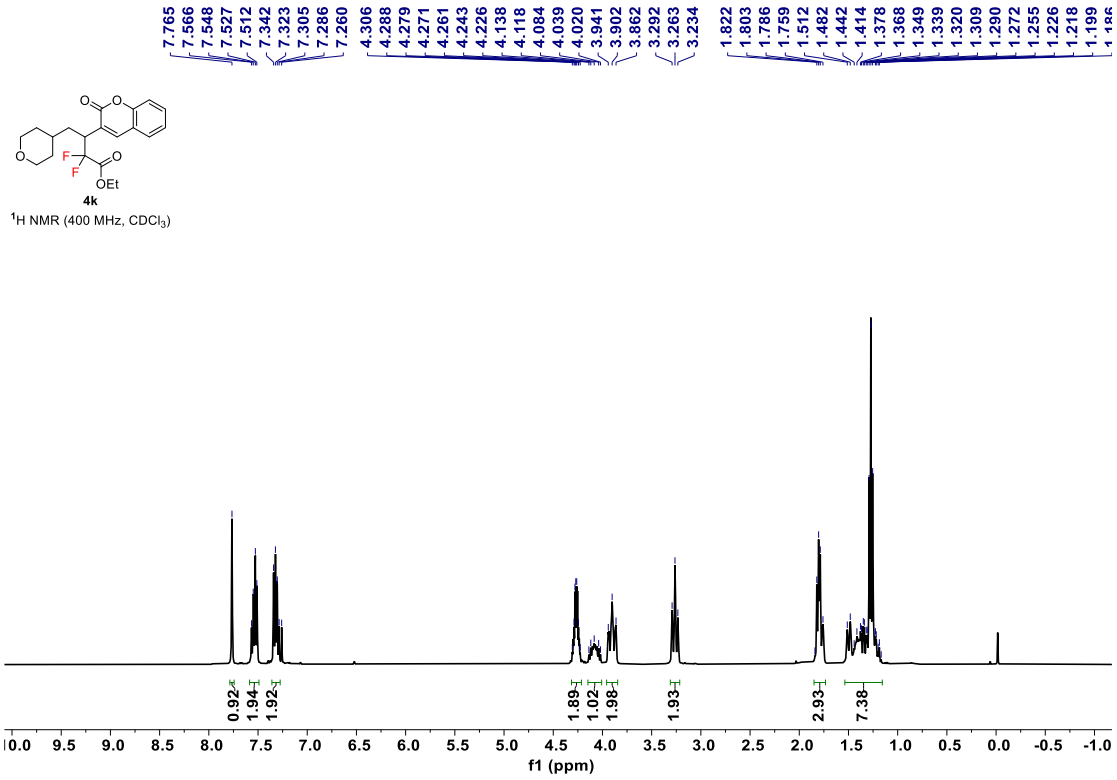
4j

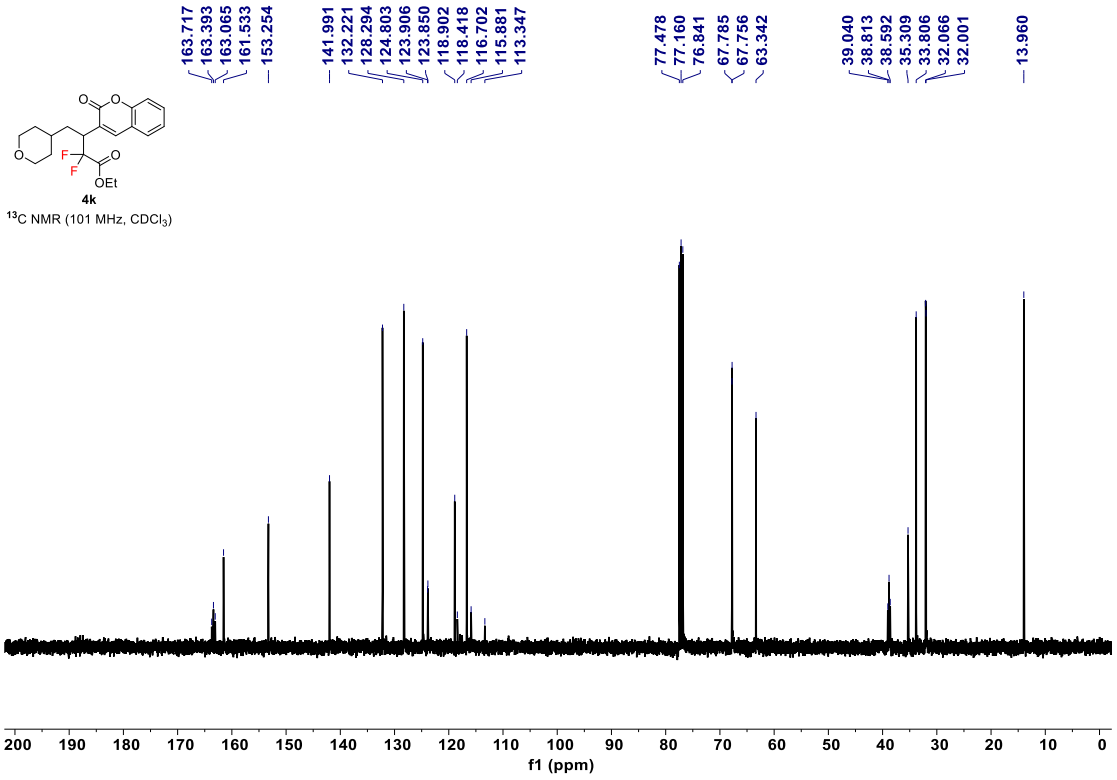
^{1}H NMR (400 MHz, $CDCl_3$)

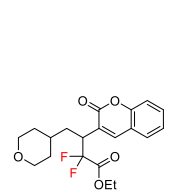



163.899
163.573
163.246
161.543
153.247
141.826
131.970
131.944
128.225
124.681
124.629
124.594
124.212
124.164
119.023
118.564
116.655
116.603
116.570
116.032
113.495
77.478
77.160
76.841
63.196
39.565
39.471
39.349
39.242
39.130
39.016
35.422
34.544
34.353
32.014
26.372
26.167
25.907
13.955
13.921
O
O
F
F
O
OEt
4j
13C NMR (101 MHz, CDCl3)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


-109.351
-109.390
-110.024
-110.062
-110.666
-110.713
-111.338
-111.385
O
O
F
F
O
OEt
4j
19F NMR (376 MHz, CDCl3)
1.00
1.00
30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200
f1 (ppm)


7.765
7.566
7.548
7.527
7.512
7.342
7.323
7.305
7.286
7.260
4.306
4.288
4.279
4.271
4.261
4.243
4.226
4.138
4.118
4.084
4.039
4.020
3.941
3.902
3.862
3.292
3.263
3.234
1.822
1.803
1.786
1.759
1.512
1.482
1.442
1.414
1.378
1.368
1.349
1.339
1.320
1.309
1.290
1.272
1.255
1.226
1.218
1.199
O
O
O
F
F
O
OEt
4k
1H NMR (400 MHz, CDCl3)
0.92
1.94
1.92
1.89
1.02
1.98
1.93
2.93
7.38
f1 (ppm)


163.717
163.393
163.065
161.533
153.254
141.991
132.221
128.294
124.803
123.906
123.850
118.902
118.418
116.702
115.881
113.347
77.478
77.160
76.841
67.785
67.756
63.342
39.040
38.813
38.592
35.309
33.806
32.066
32.001
13.960
O
O
O
F
F
O
OEt
4k
13C NMR (101 MHz, CDCl3)
f1 (ppm)



4k

^{19}F NMR (376 MHz, $CDCl_3$)