Three-Component Difluoroalkylamination of Alkenes Mediated by Photoredox and Iron Cooperative Catalysis

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1. General Information

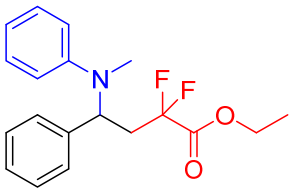
All chemical reagents are obtained from commercial suppliers and used without further purification. All known compounds are characterized by ^{1}H NMR, ^{13}C NMR and ^{19}F NMR and compared with previously reported data. All experiments were conducted with a schlenk tube. Analytical thin-layer chromatography are performed on glass plates precoated with silica gel impregnated with a fluorescent indicator (254 nm), and the plates are visualized by exposure to ultraviolet light. Mass spectra are taken on a Waters UPLC H-class LC-MS instrument in the electrospray ionization (ESI) mode. Only molecular ions (M + 1) are given for the ESI-MS analysis. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra are recorded on an AVANCE 500 Bruker spectrometer operating at 500 MHz, 126 MHz and 470 MHz in $CDCl_3$, respectively. Chemical shifts in ppm from tetramethylsilane as an internal standard in $CDCl_3$, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet-doublet, m = multiplet, br = broad), coupling constants (Hz), and assignment. ^{19}F NMR chemical shifts were determined relative to $CFCl_3$ as inter standard.

2. Experimental Procedure

A 10 mL reaction vessel with a magnetic stirring bar was equipped with *fac*-$Ir(ppy)_3$ (1.3 mg, 0.002 mmol, 0.01 equiv), $FeCl_2$ (5.1 mg, 0.04 mmol, 0.2 equiv) and K_2CO_3 (83.0 mg, 0.6 mmol, 3 equiv). The tube was then evacuated and back-filled with argon (Ar) for 3 times. Subsequently, 1,2-dichloroethane (2 mL) was added followed by alkene **1** (0.2 mmol, 1.0 equiv), N-methyl anilines **2** (0.3 mmol, 1.5 equiv) and $BrCF_2COOEt$ **3** (0.5 mmol, 2.5 equiv) via syringe under Ar. Once added, the Schlenk tube was sealed at atmospheric pressure of Ar (1 atm). The reaction was stirred and irradiated with a 5 W blue LED lamp at r.t. for 18 h. The resulting mixture was diluted with 3 mL EtOAc. The reaction mixture was extracted by EtOAc with three times and the combined organic phases were concentrated *in vacuo*. The residue was purified by silica gel flash column chromatography (petroleum ether/EtOAc = 98/2~98/5) to give the pure desired product.

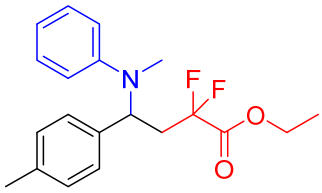
3. Characterization Data

Ethyl 2,2-difluoro-4-(methyl(phenyl)amino)-4-phenylbutanoate (4a)



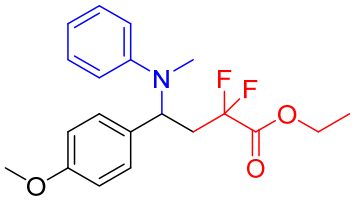
Following the general procedure, the title compound was obtained (61.9 mg, 93% yield, colorless oil).**^{1}H NMR (500 MHz, $CDCl_3$)** δ7.26 (d, J = 6.0 Hz, 5H), 7.08 (d, J = 5.5 Hz, 2H), 6.97 – 6.79 (m, 3H), 5.32 (d, J = 10.6 Hz, 1H), 4.04 – 3.96 (m, 1H), 3.90 – 3.81 (m, 1H), 3.26 – 3.14 (m, 1H), 2.63 (d, J = 11.3 Hz, 1H), 2.38 (s, 3H), 0.99 (t, J = 7.1 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ163.62 (t, J^{C-F} = 31.5 Hz), 150.06 (s), 137.67 (s), 129.11 (s), 128.49 (s), 127.80 (s), 126.88 (s), 118.76 (s), 116.25 (dd, J^{C-F} = 231.84, 258.3 Hz), 115.50 (s), 62.75 (s), 58.04 (dd, J^{C-F} = 12.6, 5.04 Hz), 36.04 (t, J^{C-F} = 23.94 Hz), 31.95 (s), 13.51 (s); **^{19}F NMR (470 MHz, $CDCl_3$)** -99.82 (d, J= 263.2 Hz, 1F), -109.21 (dd, J = 263.2, 28.2 Hz, 1F); **ESI-MS** m/z: 334.1540 $[M+1]^+$.

Ethyl 2,2-difluoro-4-(methyl(phenyl)amino)-4-(p-tolyl)butanoate (4b)



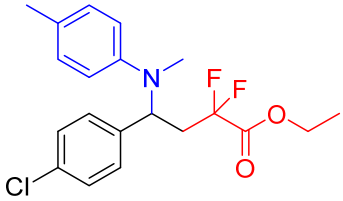
Following the general procedure, the title compound was obtained (62.5 mg, 90% yield, colorless oil).**^{1}H NMR (500 MHz, $CDCl_3$)** δ7.25 (d, J = 4.9 Hz, 2H), 7.07 (d, J = 7.7 Hz, 2H), 6.96 (d, J = 6.5 Hz, 2H), 6.87 (d, J = 5.8 Hz, 2H), 6.82 (s, 1H), 5.28 (d, J = 9.4 Hz, 1H), 3.99 (dd, J = 10.7, 7.1 Hz, 1H), 3.85 (dd, J = 10.7, 7.1 Hz, 1H), 3.25 – 3.11 (m, 1H), 2.60 (d, J = 10.2 Hz, 1H), 2.37 (s, 3H), 2.30 (s, 3H), 0.99 (t, J = 7.1 Hz, 3H); **^{13}C NMR (126MHz, $CDCl_3$)** δ163.62 (t, J^{C-F} = 31.5 Hz), 150.15 (s), 137.50 (s), 134.62 (s), 129.14 (s), 129.09 (s), 126.82 (s), 118.66 (s), 115.65 (dd, J^{C-F} = 243.18, 15.12 Hz),115.50 (s), 62.73 (s), 57.79 (dd, J^{C-F} = 7.56, 3.78 Hz), 36.13 (t, J^{C-F} = 23.94 Hz), 31.88 (s), 21.05 (s), 13.50 (s); **^{19}F NMR (470 MHz, $CDCl_3$)** δ-99.78 (d, J = 6.8 Hz), -109.26 (d, J = 28.0 Hz,1F); **ESI-MS** m/z: 348.4058 $[M+1]^+$.

Ethyl 2,2-difluoro-4-(4-methoxyphenyl)-4-(methyl(p-tolyl)amino)butanoate (4c)[1]



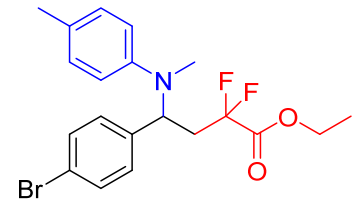
Following the general procedure, the title compound was obtained (64.6 mg, 89% yield, colorless oil).**^{1}H NMR (500 MHz, $CDCl_3$)** δ7.24 (dd, J = 7.9, 6.4 Hz, 2H), 6.98 (d, J = 8.6 Hz, 2H), 6.87 (d, J = 8.1 Hz, 2H), 6.81 (dd, J = 17.4, 8.0 Hz, 3H), 5.27 (d, J = 8.3 Hz, 1H), 3.99 (dd, J = 10.7, 7.2 Hz, 1H), 3.86 (dd, J = 10.7, 7.2 Hz, 1H), 3.77 (s, 3H), 3.23 – 3.11 (m, 1H), 2.58 (dd, J = 17.6, 3.6 Hz, 1H), 2.35 (s, 3H), 0.99 (t, J = 7.2 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ163.65 (t, J^{C-F} = 31.5 Hz), 159.07 (s), 150.19 (s), 129.77 (s), 129.06 (s), 128.02 (s), 118.71 (s), 116.26 (dd, J^{C-F} = 257.04, 245.7 Hz), 115.61 (s), 113.74 (s), 62.71 (s), 57.63 (dd, J = 9.1, 2.0 Hz), 55.25 (s), 36.19 (t, J^{C-F} = 23.94 Hz), 31.71 (s), 13.50 (s); **^{19}F NMR (470 MHz, $CDCl_3$)** δ-99.79 (d, J = 12.0 Hz, 1F), -109.24 (d, J = 27.8 Hz, 1F); **ESI-MS** m/z: 364.4048 $[M+1]^+$.

Ethyl 4-(4-chlorophenyl)-2,2-difluoro-4-(methyl(phenyl)amino)butanoate (4d)



Following the general procedure, the title compound was obtained (62.4 mg, 85% yield, colorless oil).**^{1}H NMR (500 MHz, $CDCl_3$)** δ7.28 – 7.24 (m, 4H), 7.00 (d, J = 8.0 Hz, 2H), 6.92 – 6.81 (m, 3H), 5.27 (d, J = 11.1 Hz, 1H), 4.01 (dd, J = 10.7, 7.1 Hz, 1H), 3.89 (dd, J = 10.7, 7.2 Hz, 1H), 3.17 (dd, J = 26.6, 20.0 Hz, 1H), 2.58 (dd, J = 23.4, 10.4 Hz, 1H), 2.36 (s, 3H), 1.01 (t, J = 7.1 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ163.62 (t, J= 63 Hz), 150.06 (s), 137.67 (s), 129.18 (s), 128.66 (s), 128.20 (s), 125.56(s), 118.76 (s), 116.26 (dd, J= 244.44, 231.84 Hz), 115.50 (s), 62.75 (s), 58.04 (dd, J= 12.6, 7.56 Hz), 36.04 (t, J= 23.94 Hz), 31.95 (s), 13.51 (s); **^{19}F NMR (470 MHz, $CDCl_3$)** δ-99.87 (d, J=258.5 Hz), -109.31 (dd, J = 263.2, 23.5 Hz); **ESI-MS** m/z: 368.8208 $[M+1]^+$.

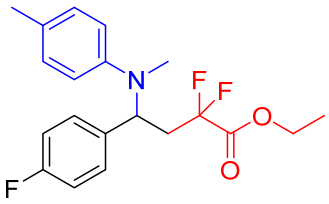
Ethyl 4-(4-bromophenyl)-2,2-difluoro-4-(methyl(phenyl)amino)butanoate (4e)



Following the general procedure, the title compound was obtained (72.3 mg, 88% yield, colorless oil).**^{1}H NMR (500 MHz, $CDCl_3$)** δ7.39 (d, J = 8.3 Hz, 2H), 7.25 (d, J = 9.0 Hz, 2H), 6.94 (d, J = 8.0 Hz, 2H), 6.90 – 6.81 (m, 3H), 5.25 (d, J = 9.6 Hz, 1H), 4.01 (dd, J = 10.7, 7.2 Hz, 1H), 3.89 (dd, J = 10.7, 7.1 Hz, 1H), 3.22 – 3.10 (m, 1H), 2.58 (dd, J = 23.3, 10.6 Hz, 1H), 2.37 (s, 3H),

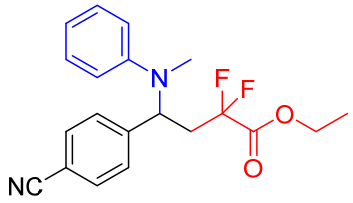
1.01 (t, J = 7.1 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ163.53 (t, J= 63 Hz), 149.83 (s), 136.56 (s), 131.62 (s), 129.20 (s), 128.57 (s), 121.81 (s), 119.16 (s), 116.99 (dd, J= 246.96, 246.33 Hz), 115.71 (s), 62.84 (s), 57.86 (dd, J = 8.3, 4.0 Hz), 35.90 (t, J= 47.88 Hz), 31.93 (s), 13.53 (s); **^{19}F NMR (470 MHz, $CDCl_3$)** δ-99.87 (d, J= 263.2 Hz, 1F), -109.29 (dd, J = 258.5, 23.5 Hz, 1F); **ESI-MS** m/z: 426.0802 $[M+1]^+$.

Ethyl 2,2-difluoro-4-(4-fluorophenyl)-4-(methyl(phenyl)amino)butanoate (4f)



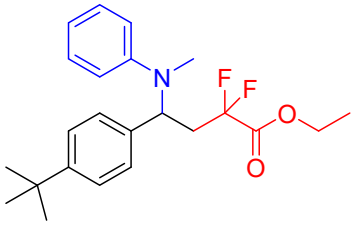
Following the general procedure, the title compound was obtained (64.2 mg, 88% yield, colorless oil).**^{1}H NMR (500 MHz, $CDCl_3$)** δ7.27 (d, J = 6.9 Hz, 2H), 7.06 – 7.01 (m, 2H), 6.95 (t, J = 8.7 Hz, 2H), 6.85 (dd, J = 17.7, 7.8 Hz, 3H), 5.28 (d, J = 9.9 Hz, 1H), 4.01 (dd, J = 10.7, 7.1 Hz, 1H), 3.88 (dd, J = 10.7, 7.2 Hz, 1H), 3.18 (dd, J = 26.7, 20.4 Hz, 1H), 2.59 (dd, J = 23.2, 10.3 Hz, 1H), 2.36 (s, 3H), 1.00 (t, J = 7.2 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ163.56 (t, J= 64.26 Hz), 162.24 (d, J= 246.96 Hz), 149.95 (s), 134.48 (d, J= 278.46 Hz), 129.17 (s), 128.50 (d, J = 8.0 Hz), 119.06 (s), 115.70 (s), 115.59 (dd, J= 257.04, 126 Hz), 115.43 (s), 115.26 (s), 62.80 (s), 57.70 (dd, J = 6.8, 3.0 Hz), 36.32 (s), 36.13 (s), 35.94 (s), 31.77 (s), 13.52 (s); **^{19}F NMR (470 MHz, $CDCl_3$)** δ-99.85 (d, J = 264.0 Hz, 1F), -109.33 (dd, J = 261.1, 26.8 Hz, 1F), -114.42 (s, 1F); **ESI-MS** m/z: 366.3962 $[M+1]^+$.

Ethyl 4-(4-cyanophenyl)-2,2-difluoro-4-(methyl(phenyl)amino)butanoate (4g)



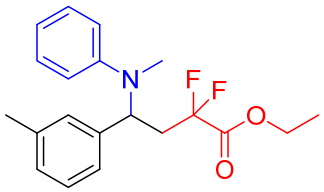
Following the general procedure, the title compound was obtained (55.1 mg, 77% yield, colorless oil).**^{1}H NMR (500 MHz, $CDCl_3$)** δ7.58 (d, J = 8.2 Hz, 2H), 7.29 (s, 1H), 7.25 (s, 1H), 7.19 (d, J = 8.2 Hz, 2H), 6.85 (d, J = 8.4 Hz, 3H), 5.33 (d, J = 14.8 Hz, 1H), 4.03 (dd, J = 10.7, 7.2 Hz, 1H), 3.91 (dd, J = 10.7, 7.2 Hz, 1H), 3.19 (dd, J = 26.1, 19.1 Hz, 1H), 2.62 (dd, J = 26.5, 14.5 Hz, 1H), 2.39 (s, 3H), 1.02 (t, J = 7.2 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ163.43 (t, J= 32.13 Hz), 149.48 (s), 143.02 (s), 132.35 (s), 129.32 (s), 127.58 (s), 119.48 (s), 118.44 (s), 115.61 (s), 115.48 (dd, J= 250.4, 243.18 Hz), 111.84 (s), 60.41 (s), 58.09 (dd, J = 8.8, 2.1 Hz), 35.71 (t, J= 24.57 Hz), 32.15 (s), 14.22 (s); **^{19}F NMR (470 MHz, $CDCl_3$)** δ-99.99 (d, J= 263.2 Hz, 1F), -109.22 (dd, J = 26.4, 10.7 Hz,1F) **ESI-MS** m/z: 359.3888 $[M+1]^+$.

Ethyl 4-(4-(tert-butyl)phenyl)-2,2-difluoro-4-(methyl(phenyl)amino) butanoate (4h)



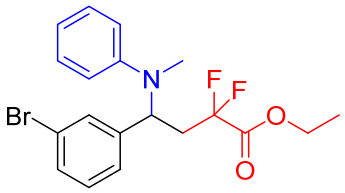
Following the general procedure, the title compound was obtained (73.9 mg, 95% yield, colorless oil).**^{1}H NMR (500 MHz, CDCl$_3$)** δ7.28 (d, J = 8.4 Hz, 2H), 7.24 (d, J = 8.5 Hz, 2H), 7.01 (d, J = 8.3 Hz, 2H), 6.87 (d, J = 8.2 Hz, 2H), 6.81 (t, J = 7.3 Hz, 1H), 5.31 (d, J = 8.6 Hz, 1H), 3.98 (dd, J = 10.7, 7.2 Hz, 1H), 3.84 (dd, J = 10.7, 7.2 Hz, 1H), 3.18 (dd, J = 26.7, 20.7 Hz, 1H), 2.62 (dd, J = 23.8, 10.1 Hz, 1H), 2.40 (s, 3H), 1.28 (s, 9H), 0.98 (t, J = 7.2 Hz, 3H); **^{13}C NMR (126 MHz, CDCl$_3$)** δ163.67 (t, J= 31.5 Hz), 150.66 (s), 150.14 (s), 134.76 (s), 129.06 (s), 126.54 (s), 125.34 (s), 118.50 (s), 116.27 (dd, J= 257.04, 244.44 Hz), 115.27 (s), 62.72 (s), 57.45 (dd, J = 15.12, 6.3 Hz), 36.15 (t, J= 23.94 Hz), 34.50 (s), 31.95 (s), 31.30 (s), 13.48 (s); **^{19}F NMR (470 MHz, CDCl$_3$)** δ-99.86 (dd, J = 12.9, 5.9 Hz, 1F), -109.11 (dd, J = 27.8, 9.9 Hz, 1F); **ESI-MS** m/z: 390.4868 $[M+1]^+$.

Ethyl 2,2-difluoro-4-(methyl(phenyl)amino)-4-(m-tolyl)butanoate (4i)



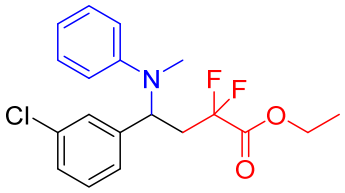
Following the general procedure, the title compound was obtained (59.7 mg, 86% yield, colorless oil).**^{1}H NMR (500 MHz, CDCl$_3$)** δ7.26 (t, J = 3.7 Hz, 2H), 7.15 (t, J = 7.6 Hz, 1H), 7.06 (d, J = 7.5 Hz, 1H), 6.90 – 6.83 (m, 4H), 6.81 (t, J = 7.2 Hz, 1H), 5.29 (d, J = 8.9 Hz, 1H), 3.99 (dd, J = 10.7, 7.2 Hz, 1H), 3.85 (dd, J = 10.7, 7.1 Hz, 1H), 3.18 (dd, J = 27.1, 19.9 Hz, 1H), 2.65 – 2.58 (m, 1H), 2.40 (s, 3H), 2.29 (s, 3H), 1.00 (t, J = 7.1 Hz, 3H); **^{13}C NMR (126 MHz, CDCl$_3$)** δ163.64 (t, J= 31.5 Hz), 150.08 (s), 138.13 (s), 137.73 (s), 129.07 (s), 128.43 (d, J = 18.6 Hz), 127.50 (s), 124.03 (s), 118.57 (s), 116.25 (dd, J = 255.78, 244.44 Hz), 115.34 (s), 62.74 (s), 57.77 (dd, J = 14.2, 6.9 Hz), 36.12 (t, J= 23.94 Hz), 31.96 (s), 21.58 (s), 13.51 (s); **^{19}F NMR (470 MHz, CDCl$_3$)** δ-99.87 (d, J= 263.2 Hz，1F), -109.04 (dd, J = 258.5, 9.4 Hz, 1F); **ESI-MS** m/z: 348.4058 $[M+1]^+$.

Ethyl 4-(3-bromophenyl)-2,2-difluoro-4-(methyl(phenyl)amino)butanoate (4j)



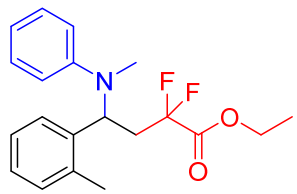
Following the general procedure, the title compound was obtained (67.4 mg, 82% yield, colorless oil).**^{1}H NMR (500 MHz, $CDCl_3$)** δ7.40 (d, J = 7.9 Hz, 1H), 7.28 (d, J = 11.0 Hz, 3H), 7.14 (t, J = 7.8 Hz, 1H), 7.01 (s, 1H), 6.88 (s, 3H), 5.25 (d, J = 9.0 Hz, 1H), 4.02 (dd, J = 10.7, 7.1 Hz, 1H), 3.89 (dd, J = 10.7, 7.2 Hz, 1H), 3.16 (dd, J = 19.4, 11.2 Hz, 1H), 2.62 (dd, J = 19.4, 9.7 Hz, 1H), 2.43 (s, 3H), 1.03 (t, J = 7.1 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ163.49 (t, J= 32.13 Hz), 149.72 (s), 140.16 (s), 130.94 (s), 130.09 (s), 129.73 (s), 129.20 (s), 125.73 (s), 122.69 (s), 119.24 (dd, J= 254.3, 248.5 Hz), 119.10 (s), 115.51 (s), 60.43 (s), 57.72 (dd, J = 10.4, 2.8 Hz), 35.93 (t, J= 23.94 Hz), 32.03 (s), 13.53 (s); **^{19}F NMR (470 MHz, $CDCl_3$)** δ-100.06 (dd, J= 12.3, 6.7 Hz, 1F), -108.94 (dd, J = 26.6, 10.2 Hz, 1F); **ESI-MS** m/z: 412.0645 $[M+1]^+$.

Ethyl 4-(3-chlorophenyl)-2,2-difluoro-4-(methyl(phenyl)amino)butanoate (4k)



Following the general procedure, the title compound was obtained (63.9 mg, 87% yield, colorless oil).**^{1}H NMR (500 MHz, $CDCl_3$)** δ7.26 (t, J = 7.8 Hz, 3H), 7.20 (t, J = 7.7 Hz, 1H), 7.09 (s, 1H), 6.95 (d, J = 5.8 Hz, 1H), 6.86 (dd, J = 13.9, 6.9 Hz, 3H), 5.27 (d, J = 9.7 Hz, 1H), 4.01 (dd, J = 10.8, 7.2 Hz, 1H), 3.89 (dd, J = 10.7, 7.2 Hz, 1H), 3.16 (dd, J = 33.1, 25.9 Hz, 1H), 2.61 (dd, J = 21.4, 13.5 Hz, 1H), 2.42 (s, 3H), 1.02 (t, J = 7.1 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ163.49 (d, J = 31.5 Hz), 149.67 (s), 139.82 (s), 134.50 (s), 129.82 (s), 129.22 (s), 128.04 (s), 126.92 (s), 125.28 (s), 119.16 (s), 115.91 (dd, J= 257.04, 248.22 Hz), 115.59 (s), 62.86 (s), 57.85 (dd, J = 7.4, 4.5 Hz), 35.96 (t, J = 23.94 Hz), 32.14 (s), 13.53 (s); **^{19}F NMR (470 MHz, $CDCl_3$)** δ -100.02 (d, J= 258.5 Hz, 1F), -109.04 (dd, J = 272.6, 18.8 Hz, 1F); **ESI-MS** m/z: 368.1151 $[M+1]^+$.

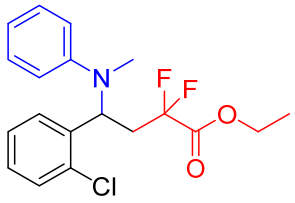
Ethyl 2,2-difluoro-4-(methyl(phenyl)amino)-4-(o-tolyl)butanoate (4l)



Following the general procedure, the title compound was obtained (59.0 mg, 85% yield, colorless oil).**^{1}H NMR (500 MHz, $CDCl_3$)** δ7.29 (s, 1H), 7.24 (d, J = 7.8 Hz, 2H), 7.19 (dd, J = 14.2, 7.4 Hz, 2H), 7.13 (d, J = 7.0 Hz, 1H), 6.89 (d, J = 6.9 Hz, 2H), 6.80 (s, 1H), 5.41 – 5.34 (m, 1H), 3.95 (dd, J = 10.7, 7.2

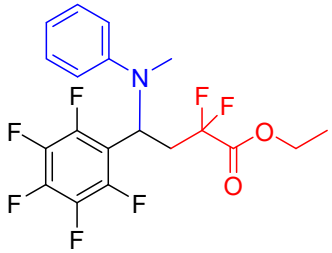
Hz, 1H), 3.88 (dd, J = 10.7, 7.2 Hz, 1H), 3.06 (dd, J = 33.2, 23.3 Hz, 1H), 2.65 (dd, J = 30.8, 22.0 Hz, 1H), 2.48 (s, 3H), 1.07 (t, J = 7.2 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ163.71 (t, J= 28.98 Hz), 149.68 (s), 137.72 (s), 136.14 (s), 131.18 (s), 129.13 (s), 127.71 (s), 126.92 (s), 125.47 (s), 114.96 (s), 112.38 (dd, J= 256.2, 243.6 Hz), 60.43 (s), 54.31 (dd, J = 10.4, 5.1 Hz), 35.90 (t, J = 21.1 Hz), 31.94 (s), 21.09 (s), 14.23 (s);**^{19}F NMR (470 MHz, $CDCl_3$)** δ-100.84 (d, J = 263.2 Hz, 1F), -107.02 (dd, J= 263.2, 4.7 Hz, 1F); **ESI-MS** m/z: 348.1697 $[M+1]^+$.

Ethyl 4-(2-chlorophenyl)-2,2-difluoro-4-(methyl(phenyl)amino) butanoate (4m)



Following the general procedure, the title compound was obtained (60.9 mg, 83% yield, colorless oil). **^{1}H NMR (500 MHz, $CDCl_3$)** δ 7.37 (dd, J = 7.6, 1.4 Hz, 1H), 7.32 (d, J = 7.3 Hz, 1H), 7.23 (d, J = 7.3 Hz, 3H), 6.87 (d, J = 8.2 Hz, 2H), 6.79 (t, J = 7.2 Hz, 1H), 6.74 – 6.59 (m, 1H), 5.62 (dd, J = 9.4, 5.1 Hz, 1H), 4.03 (dd, J = 10.7, 7.1 Hz, 1H), 3.93 (dd, J = 10.7, 7.2 Hz, 1H), 3.03 (dd, J = 25.6, 10.8 Hz, 1H), 2.83 (dd, J = 30.8, 22.0 Hz, 1H), 2.66 (s, 3H), 1.08 (t, J = 7.2 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ163.70 (t, J = 25.83 Hz), 149.81 (s), 136.19 (s), 134.49 (s), 130.45 (s), 128.97 (s), 128.8 (s), 128.41 (s), 126.53 (s), 115.09 (s), 114.86 (dd, J= 256.9, 245.7 Hz), 62.96 (s), 54.58 (dd, J = 7.1, 2.5 Hz), 36.18 (t, J= 24.57 Hz), 30.92 (s), 13.59 (s); **^{19}F NMR (470 MHz, $CDCl_3$)** δ-101.30 (d, J=263.2 Hz, 1F), -107.16 (dd, J = 21.4, 13.3 Hz, 1F); **ESI-MS** m/z: 368.1151 $[M+1]^+$.

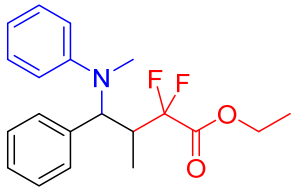
Ethyl 2,2-difluoro-4-(methyl(phenyl)amino)-4-(perfluorophenyl) butanoate (4n)



Following the general procedure, the title compound was obtained (74.4 mg, 88% yield, colorless oil).**^{1}H NMR (500 MHz, $CDCl_3$)** δ7.08 (d, J = 5.3 Hz, 2H), 6.88 (d, J = 7.2 Hz, 2H), 6.85 – 6.81 (m, 1H), 5.32 (d, J = 10.3 Hz, 1H), 4.00 (dd, J = 10.6, 7.2 Hz, 1H), 3.86 (dd, J = 10.6, 7.2 Hz, 1H), 3.21 (dd, J = 31.1, 16.1 Hz, 1H), 2.85 (s, 3H), 2.63 (dd, J = 23.6, 11.8 Hz, 1H), 1.00 (t, J = 7.1 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ163.42 (t, J= 32.13 Hz), 148.97 (s), 144.35 (m), 138.59 (m), 129.39 (m), 129.04 (s), 128.86 (s), 120.92 (s), 117.35 (s), 115.41 (dd, J= 240.66, 175.14 Hz), 63.07 (s), 52.51 (dd, J = 10.0, 3.6 Hz), 36.20 (t, J= 10.71 Hz), 32.07 (s), 13.67 (s);

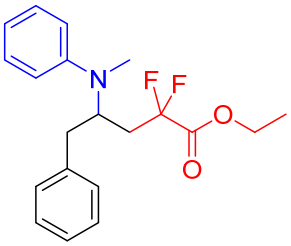
^{19}F NMR (470 MHz, $CDCl_3$) δ-101.22 (d,J= 263.2 Hz, 1F), -110.51 (d, J= 253.8 Hz, 1F), -137.82 (d, J = 21.5 Hz, 2F), -153.10 (s, 1F), -160.54 (dd, J = 37.6, 23.5 Hz, 2F); **ESI-MS** m/z: 424.3308 $[M+1]^+$.

Ethyl 2,2-difluoro-3-methyl-4-(methyl(phenyl)amino)-4-phenylbutanoate (4p)



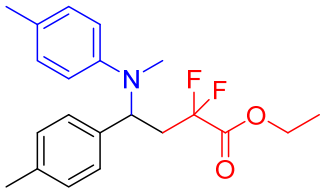
Following the general procedure, the title compound was obtained (56.2 mg, 81% yield, colorless oil).**^{1}H NMR (500 MHz, $CDCl_3$)** δ7.23 (t, J = 8.6 Hz, 5H), 7.18 (d, J = 7.6 Hz, 2H), 6.84 (d, J = 8.2 Hz, 2H), 6.75 (t, J = 7.3 Hz, 1H), 5.12 (d, J = 10.6 Hz, 1H), 3.82 (dd, J = 10.7, 7.2 Hz, 1H), 3.73 (dd, J = 10.7, 7.2 Hz, 1H), 3.35 (dd, J = 17.1, 6.9 Hz, 1H), 2.57 (s, 3H), 2.04 (s, 3H), 1.17 (t, J = 7.2 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ164.09 (t, J= 32.13 Hz), 150.18 (s), 136.91 (s), 129.22 (s), 128.15 (s), 128.00 (s), 127.71 (s), 118.42 (dd, J= 257.4, 249.8 Hz), 117.73 (s), 114.23 (s), 62.69 (s), 60.44 (s), 39.16 (t, J = 21.42 Hz), 32.07 (s), 14.24 (s), 10.61 (s); **^{19}F NMR (470 MHz, $CDCl_3$)** δ-106.22 (dd, J = 253.8, 9.4 Hz, 1F), -112.44 (dd, J = 253.8, 14.1 Hz,1F); **ESI-MS** m/z: 348.4058 $[M+1]^+$.

Ethyl 2,2-difluoro-4-(methyl(phenyl)amino)-5-phenylpentanoate (4q)



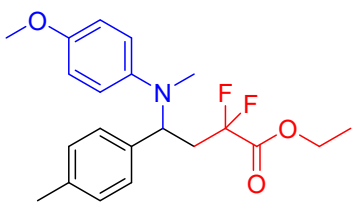
Following the general procedure, the title compound was obtained (50.7 mg, 73% yield, colorless oil).**^{1}H NMR (500 MHz, $CDCl_3$)** δ7.25 – 7.23 (m, 3H), 7.10 (d, J = 7.0 Hz, 2H), 6.99 (dd, J = 14.8, 7.2 Hz, 2H), 6.81 (d, J = 8.1 Hz, 2H), 6.77 (t, J = 7.3 Hz, 1H), 3.99 (dd, J = 10.7, 7.2 Hz, 1H), 3.85 (dd, J = 10.7, 7.2 Hz, 1H), 2.98 (s, 1H), 2.82 (d, J = 14.7 Hz, 2H), 2.66 (s, 3H), 2.15 (dd, J = 23.4, 11.4 Hz, 2H), 0.98 (t, J = 7.2 Hz, 3H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ163.57 (t, J = 22.68 Hz), 149.93 (s), 135.26 (s), 129.15 (s), 127.89 (s), 125.11 (s), 121.60 (s), 118.89 (s), 115.83 (dd, J= 253.2, 245.7Hz), 115.51 (s), 60.45 (s), 57.59 (dd, J= 10.08, 2.52 Hz), 39.53 (s), 36.13 (t, J= 23.94 Hz), 31.91 (s), 14.23 (s); **^{19}F NMR (470 MHz, $CDCl_3$)** δ-100.20 (dd, J = 249.1, 103.4 Hz, 1F), -109.22 (d, J = 258.5 Hz,1F); **ESI-MS** m/z: 348.1697 $[M+1]^+$.

Ethyl 2,2-difluoro-4-(methyl(p-tolyl)amino)-4-(p-tolyl)butanoate (4s)



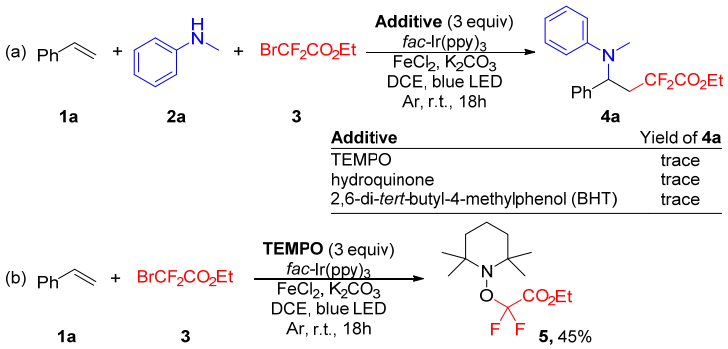
Following the general procedure, the title compound was obtained (54.9 mg, 76% yield, colorless oil).**^{1}H NMR (500 MHz, CDCl$_3$)** δ7.26 (d, J = 4.9 Hz, 2H), 7.08 (d, J = 7.7 Hz, 2H), 6.97 (d, J = 6.5 Hz, 2H), 6.88 (d, J = 5.8 Hz, 2H), 5.29 (d, J = 9.4 Hz, 1H), 4.00 (dd, J = 10.7, 7.2 Hz, 1H), 3.86 (dd, J = 10.7, 7.2 Hz, 1H), 3.20 (dd, J = 39.4, 14.2 Hz, 1H), 2.61 (dd, J = 24.0, 13.8 Hz, 1H), 2.38 (s, 3H), 2.31 (s, 3H), 2.06 (s, 3H), 1.00 (t, J = 7.1 Hz, 3H); **^{13}C NMR (126 MHz, CDCl$_3$)** δ163.67 (t, J = 31.2 Hz), 150.20 (s), 137.55 (s), 134.67 (s), 129.19 (s), 129.14 (s), 126.87 (s), 118.71 (s), 115.55 (s), 113.79 (dd, J= 255.4, 243.9 Hz), 62.78 (s), 57.85 (dd, J = 7.6, 4.2 Hz), 36.18 (t, J = 23.8 Hz), 31.93 (s), 21.10 (s), 13.55 (s); **^{19}F NMR (471 MHz, CDCl$_3$)** δ-99.91 (d, J = 263.2 Hz, 1F), -109.19 (dd, J = 258.5, 28.2 Hz,1F); **ESI-MS** m/z: 361.1853 $[M+1]^+$.

Ethyl 2,2-difluoro-4-((4-methoxyphenyl)(methyl)amino)-4-(p-tolyl)butanoate (4t)[1]



Following the general procedure, the title compound was obtained (61.8 mg, 82% yield, colorless oil).**^{1}H NMR (500 MHz, CDCl$_3$)** δ7.24 (dd, J = 7.9, 6.4 Hz, 2H), 6.98 (d, J = 8.6 Hz, 2H), 6.86 (d, J = 8.1 Hz, 2H), 6.82 – 6.78 (m, 2H), 5.27 (d, J = 8.3 Hz, 1H), 3.99 (dd, J = 10.7, 7.2 Hz, 1H), 3.85 (dd, J = 10.7, 7.2 Hz, 1H), 3.76 (s, 3H), 3.16 (dd, J = 27.0, 20.9 Hz, 1H), 2.57 (dd, J = 23.7, 9.8 Hz, 1H), 2.48 (s, 3H), 2.34 (s, 3H), 0.99 (t, J = 7.2 Hz, 3H).; **^{13}C NMR (126 MHz, CDCl$_3$)** δ164.26 (t, J= 31.5 Hz), 153.33 (s), 145.88 (s), 138.82 (s), 130.37 (s), 129.67 (s), 128.62 (s), 116.21 (s), 115.90 (dd, J= 257.1, 245.9 Hz), 114.35 (s), 63.32 (s), 58.23 (dd, J = 9.1, 2.0 Hz), 36.79 (t, J= 23.94 Hz), 32.31 (s), 23.33 (s), 14.10 (s); **^{19}F NMR (471 MHz, CDCl$_3$)** δ-99.83 (tt, J = 263.2 Hz, 1F), -105.69 (dd, J = 258.5, 28.2 Hz,1F); **ESI-MS** m/z: 378.1803 $[M+1]^+$.

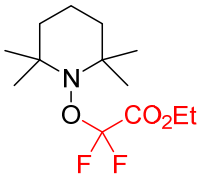
4. Control experiments



Reaction (a): A 10 mL reaction vessel with a magnetic stirring bar was equipped with *fac*-Ir(ppy)$_3$ (1.3 mg, 0.002mmol, 0.01 equiv), $FeCl_2$ (5.1 mg, 0.04 mmol, 0.2 equiv), K_2CO_3 (82.9 mg, 0.6 mmol, 3.0 equiv) and TEMPO/BHT/hydroquinone (0.6 mmol, 3.0 equiv). The tube was then evacuated and back-filled with argon (Ar) for 3 times. Subsequently, DCE (2 mL) was added followed by styrene **1a** (20.8mg, 0.2 mmol, 1.0 equiv), N-Me aniline **2a** (32.1mg, 0.3 mmol, 1.5 equiv) and $BrCF_2CO_2Et$ **3** (101.6mg, 0.5 mmol, 2.5 equiv) via syringe under Ar. Once added, the Schlenk tube was sealed at atmospheric pressure of Ar (1 atm). The reaction was stirred and irradiated with a 5 W blue LED lamp at r.t. for 18 h. No desired product **4a** was detected.

Reaction (b): A 10 mL reaction vessel with a magnetic stirring bar was equipped with *fac*-Ir(ppy)$_3$ (1.3 mg, 0.002mmol, 0.01 equiv), $FeCl_2$ (5.1 mg, 0.04 mmol, 0.2 equiv) K_2CO_3 (82.9 mg, 0.6 mmol, 3.0 equiv) and TEMPO (93.8 mg, 0.6 mmol, 3.0 equiv). The tube was then evacuated and back-filled with argon (Ar) for 3 times. Subsequently, DCE (2 mL) was added followed by styrene **1a** (20.8mg, 0.2 mmol, 1.0 equiv) and $BrCF_2CO_2Et$ **3** (101.6mg, 0.5 mmol, 2.5 equiv) via syringe under Ar. Once added, the Schlenk tube was sealed at atmospheric pressure of Ar (1 atm). The reaction was stirred and irradiated with a 5 W blue LED lamp at r.t. for 18 h. Then, the solvent was removed in vacuum and the crude product was purified by silica gel flash column chromatography (silica: 200-300 mesh, petroleum ether/ethyl acetate99/1~98/2) to give the radical coupling adduct **5** (TEMPO-CF_2COOEt) as colorless oil in 45% yield.

Ethyl 2,2-difluoro-2-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)acetate[2]



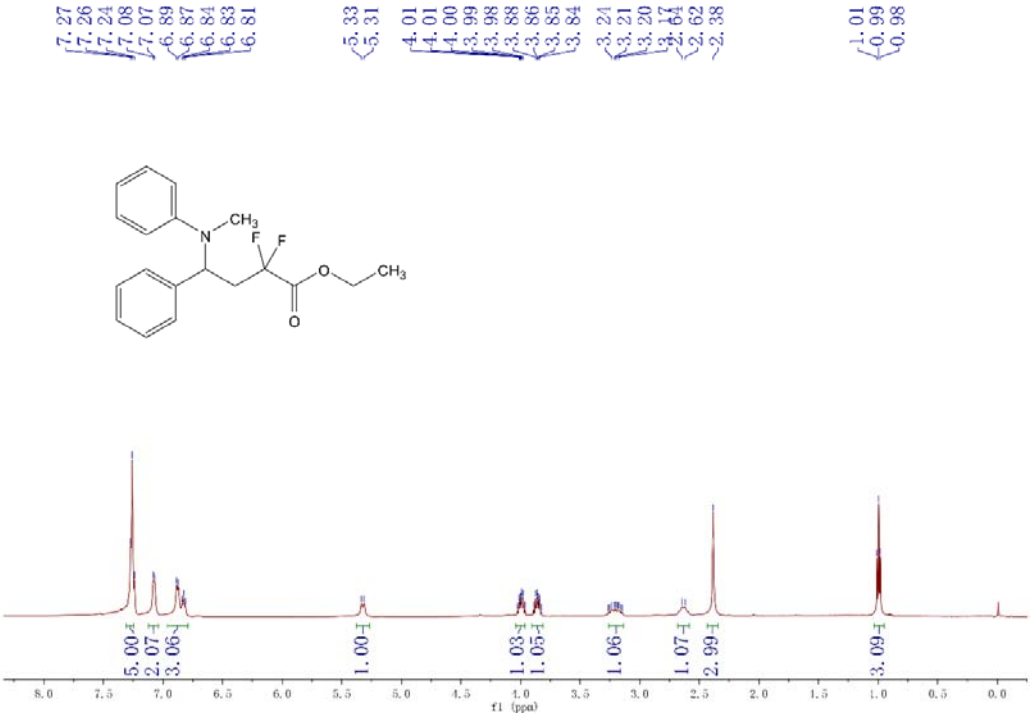
^{1}H NMR (500 MHz, $CDCl_3$) δ 4.30 (q, J = 7.1 Hz, 2H), 1.58-1.55 (m, 6H), 1.36 (t, J = 12.5 Hz, 3H), 1.20 (d, J = 25 Hz, 12H); **^{13}C NMR (126 MHz, $CDCl_3$)** δ 163.58 (t, J = 32.13 Hz), 114.93 (t, J = 252 Hz), 62.86 (s), 61.34 (s), 40.12 (s), 33.23 (s), 21.18 (s), 16.97 (s), 13.10 (s); **^{19}F NMR (470 MHz, $CDCl_3$)** δ -73.44 (s). **ESI-MS** m/z: 280.3278 $[M+1]^+$.

References:

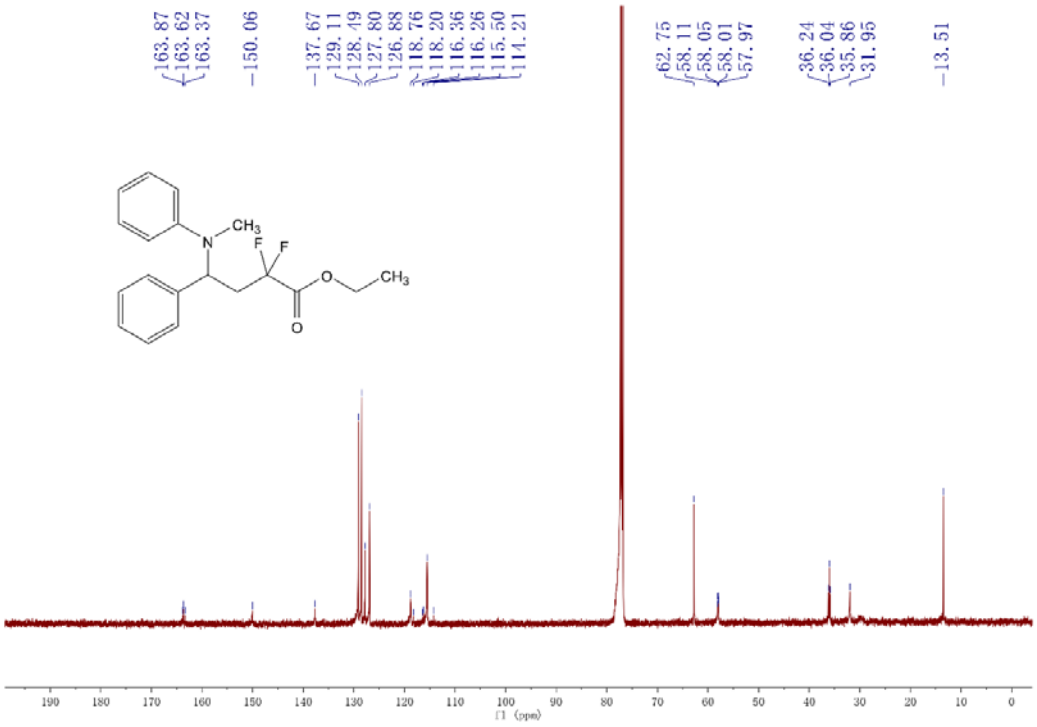
[1] S. N. Gockel, T. L. Buchanan, K. L. Hull, *J. Am. Chem. Soc.*2018, **140**, 58.

[2] Nie, X.; Cheng, C.; Zhu, G. *Angew. Chem., Int. Ed.* 2017, **56**, 1898.

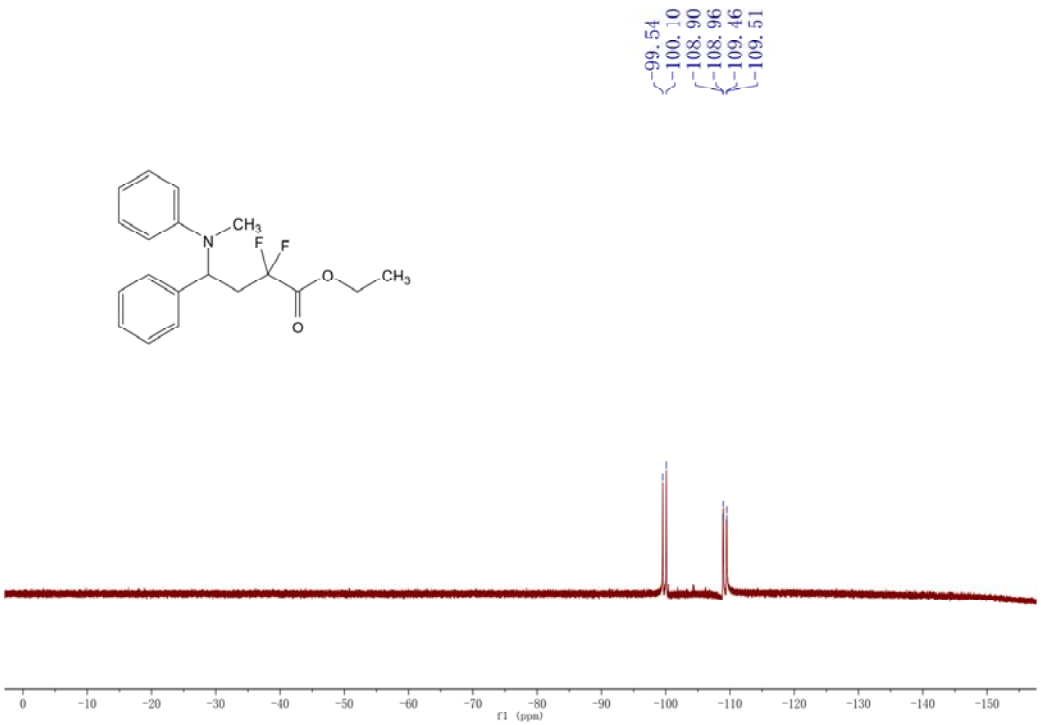
5. NMR Spectra



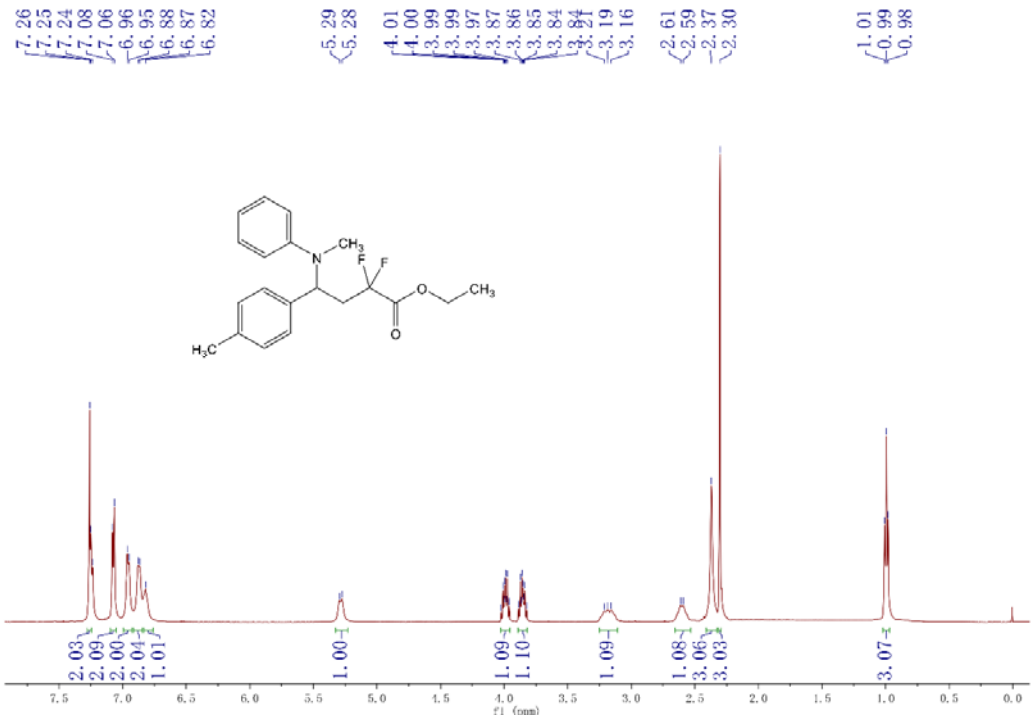
^{1}H NMR of **4a**



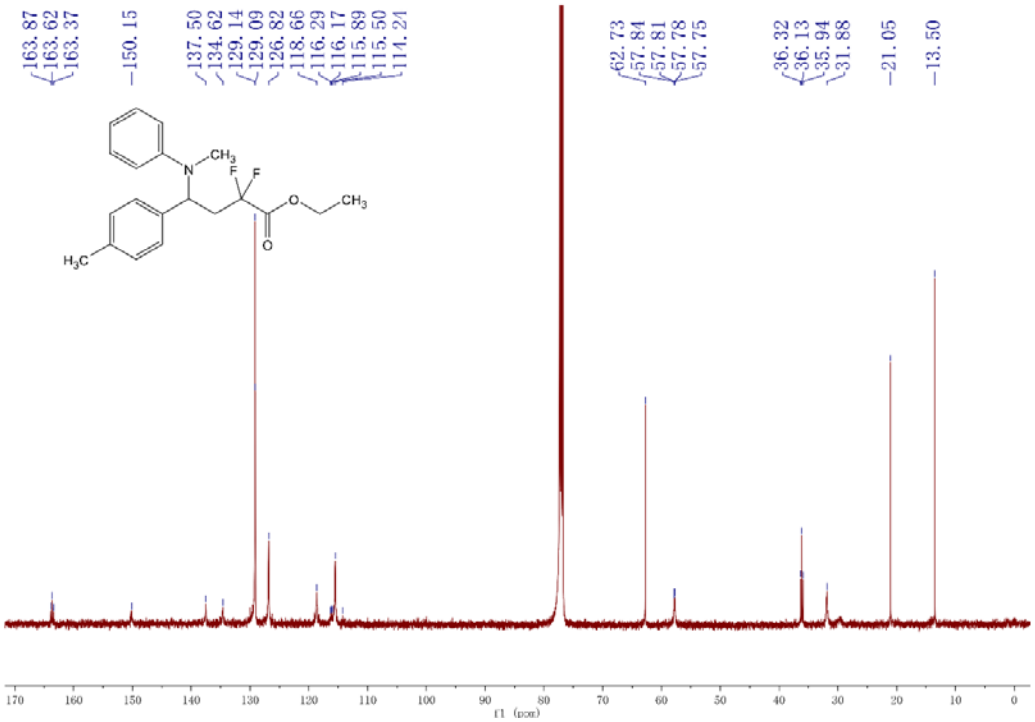
^{13}C NMR of **4a**



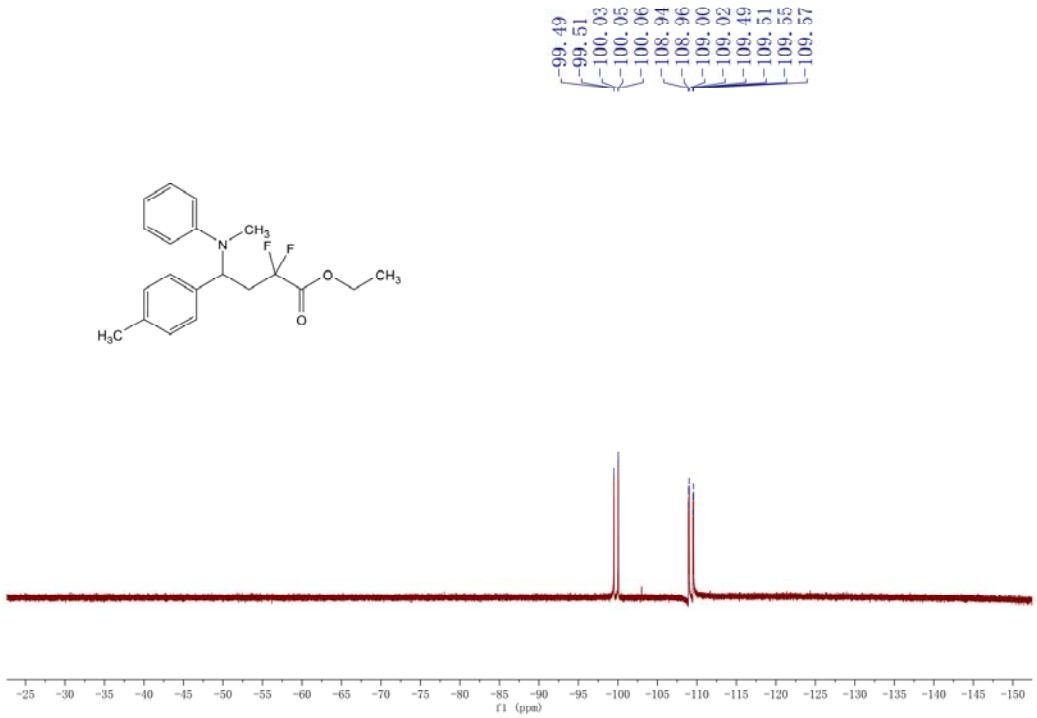
^{19}F NMR of **4a**



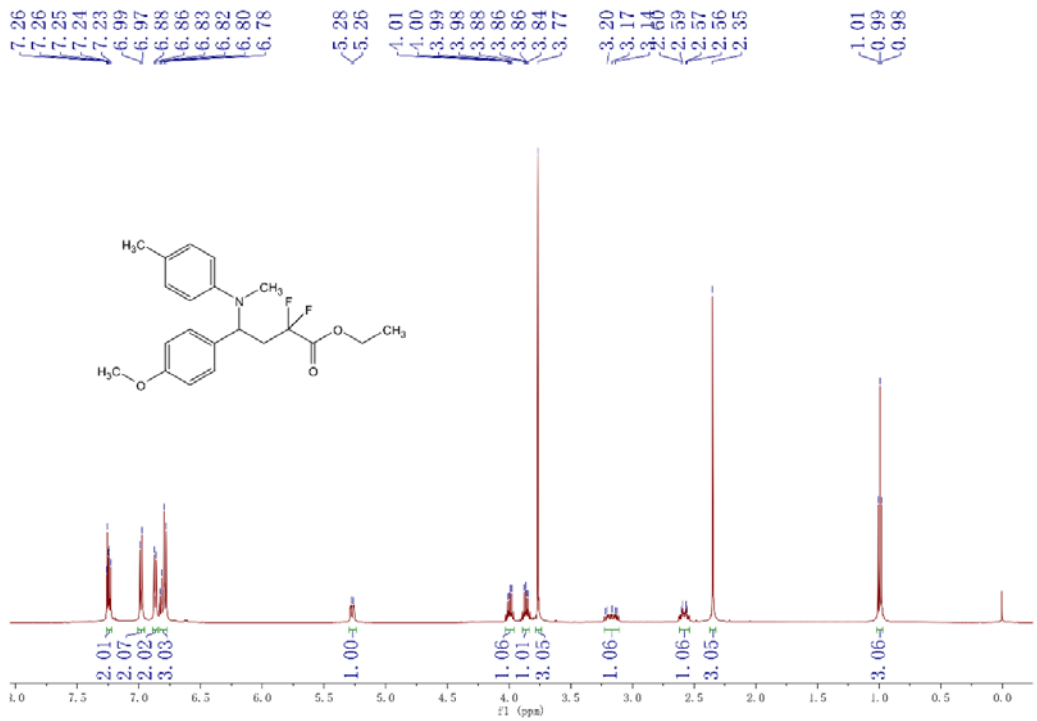
^{1}H NMR of **4b**



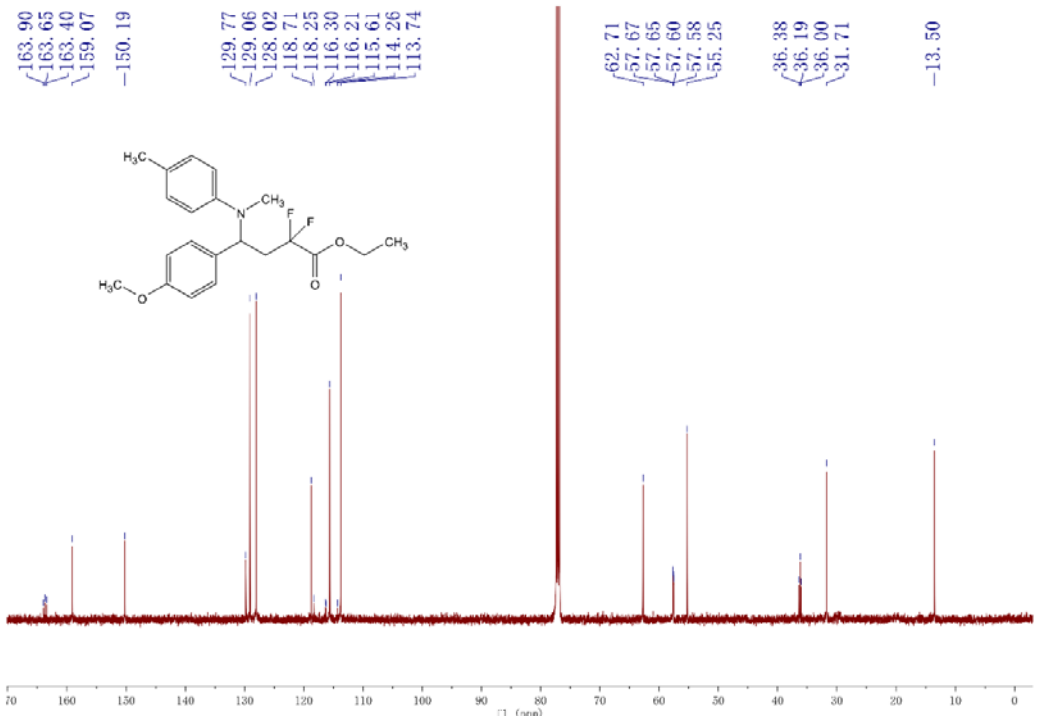
^{13}C NMR of **4b**



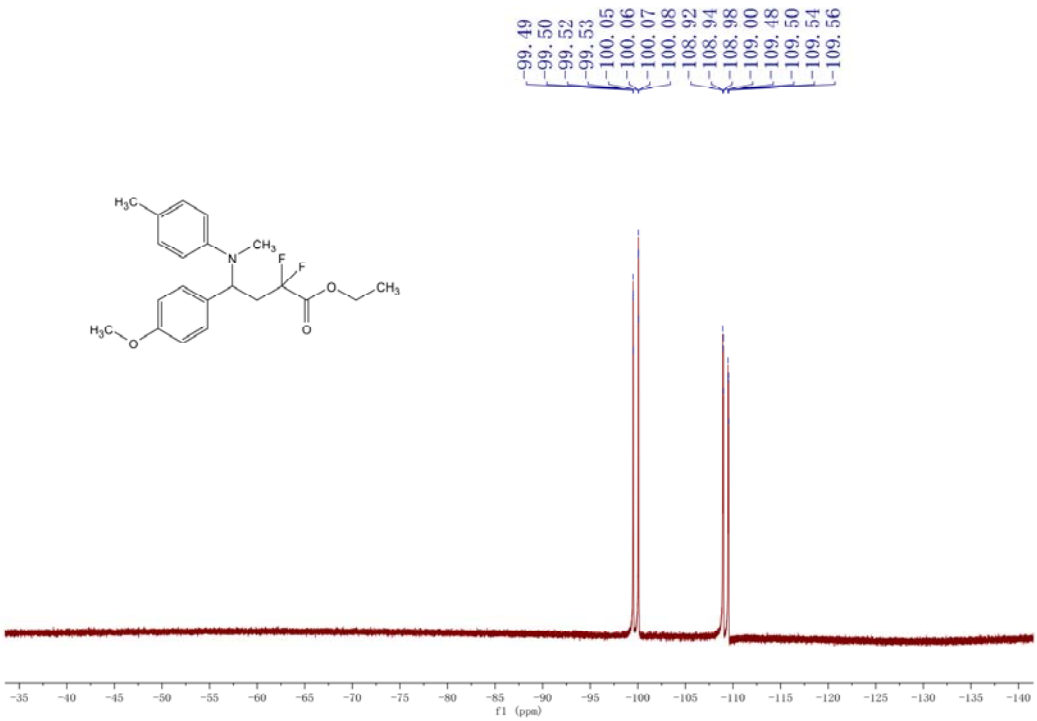
^{19}F NMR of **4b**



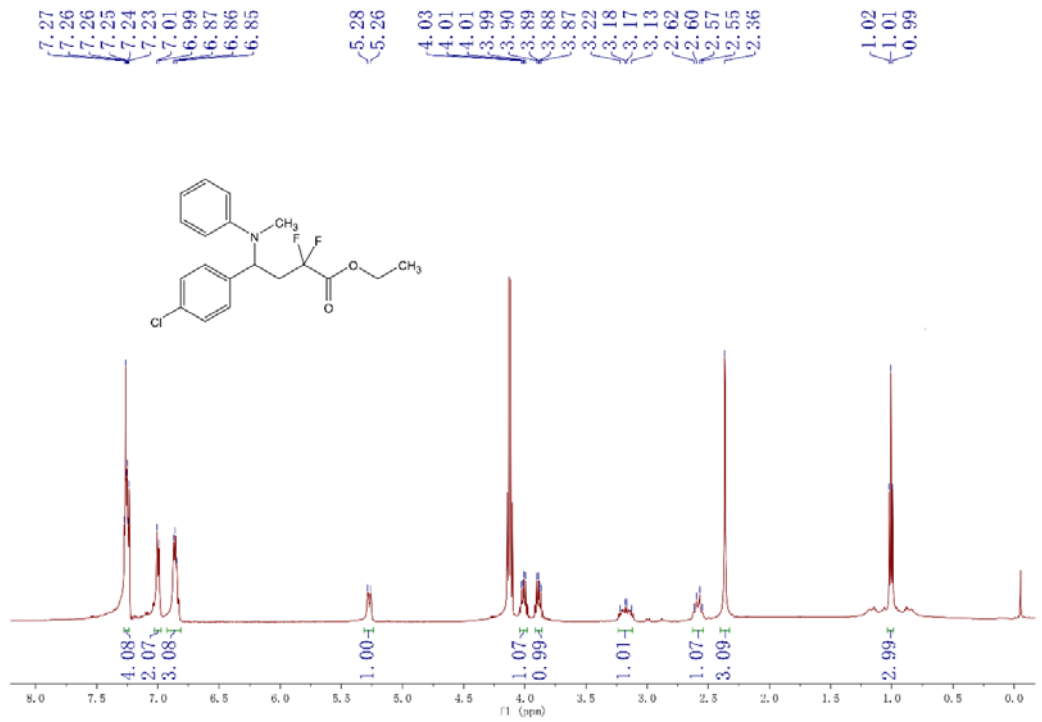
^{1}H NMR of **4c**



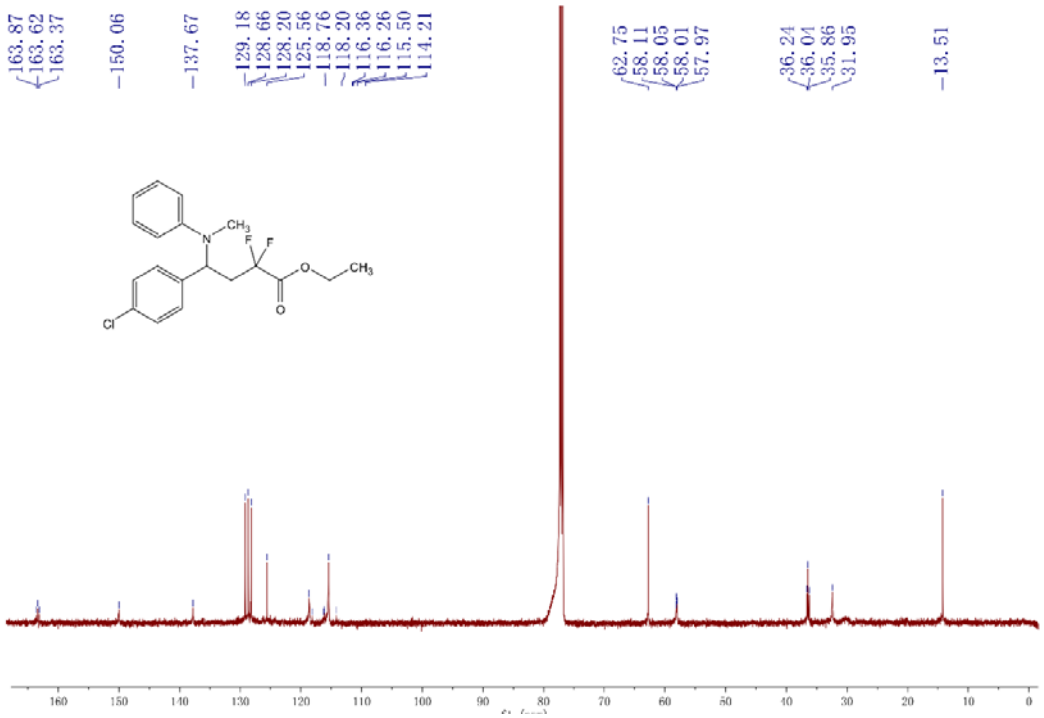
^{13}C NMR of **4c**



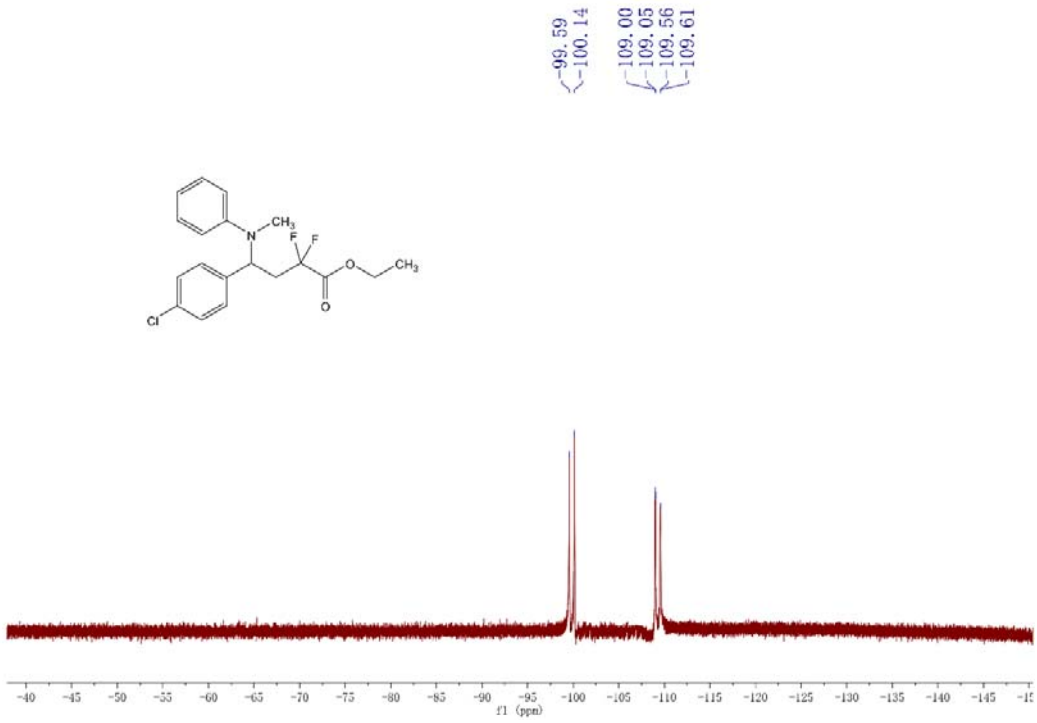
^{19}F NMR of **4c**



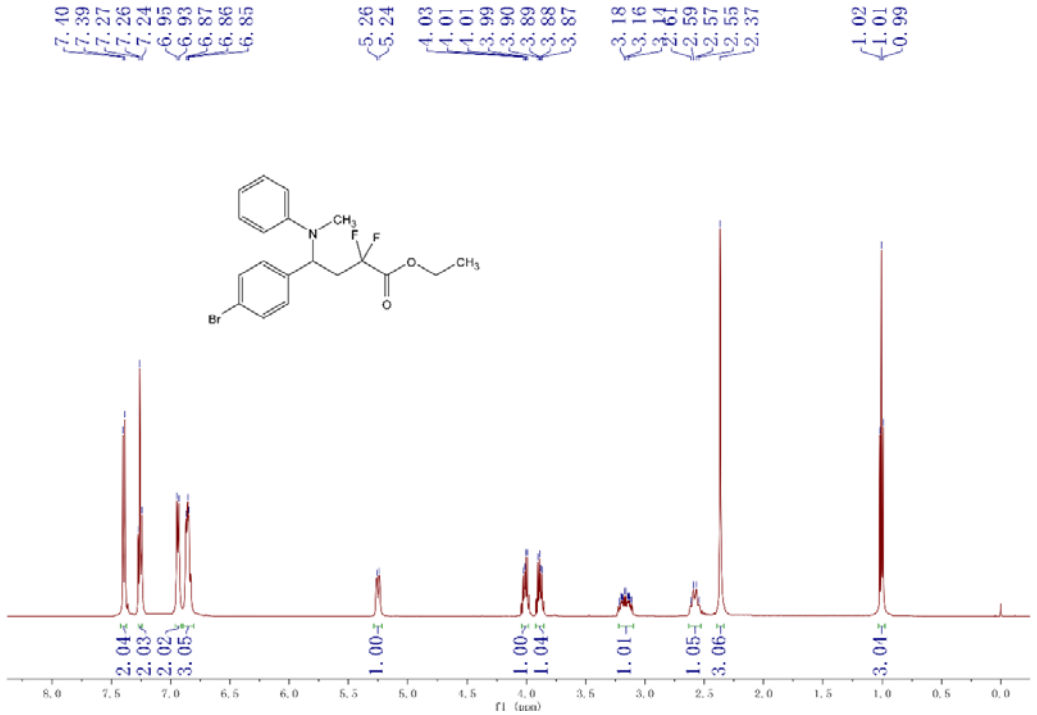
^{1}H NMR of **4d**



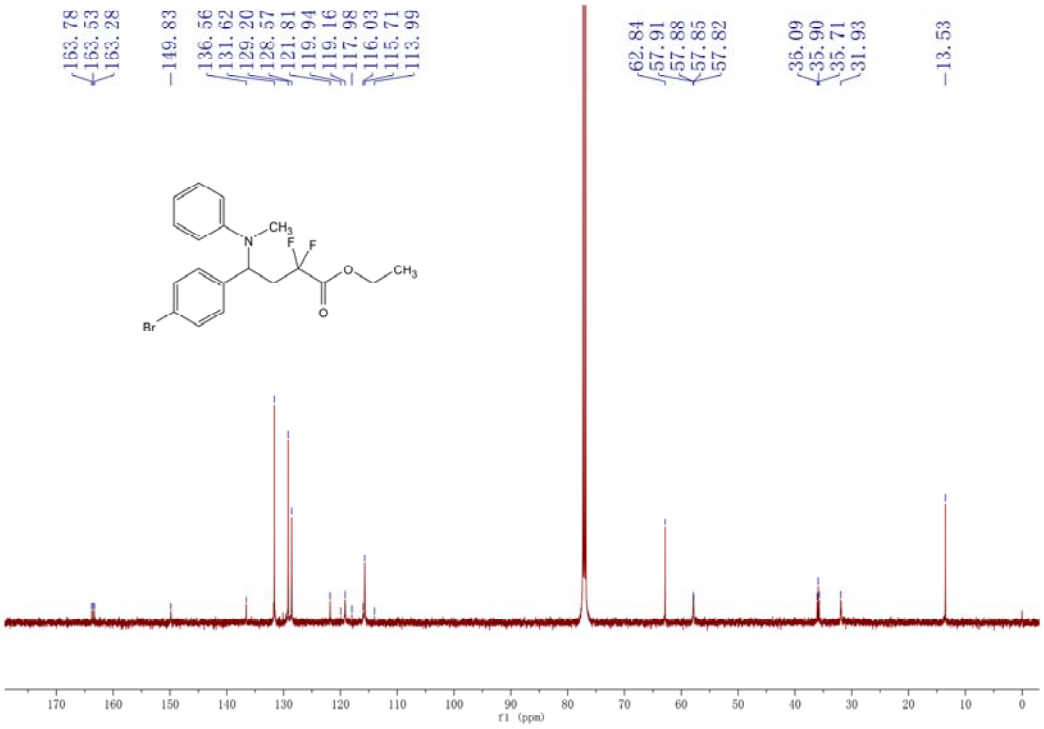
^{13}C NMR of **4d**



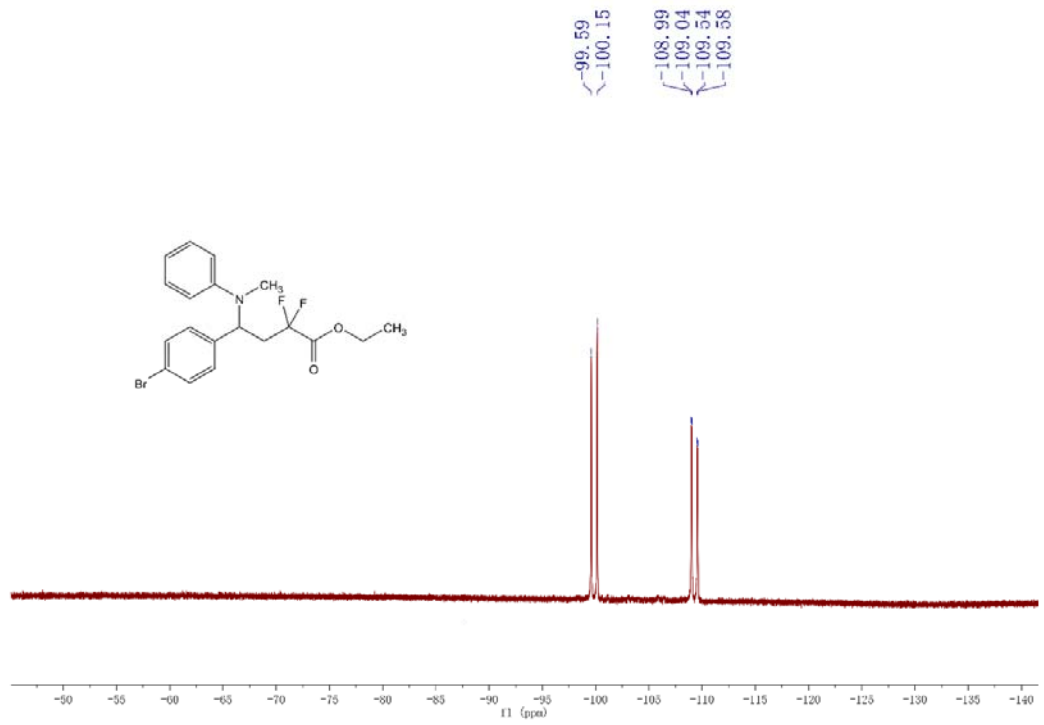
^{19}F NMR of **4d**



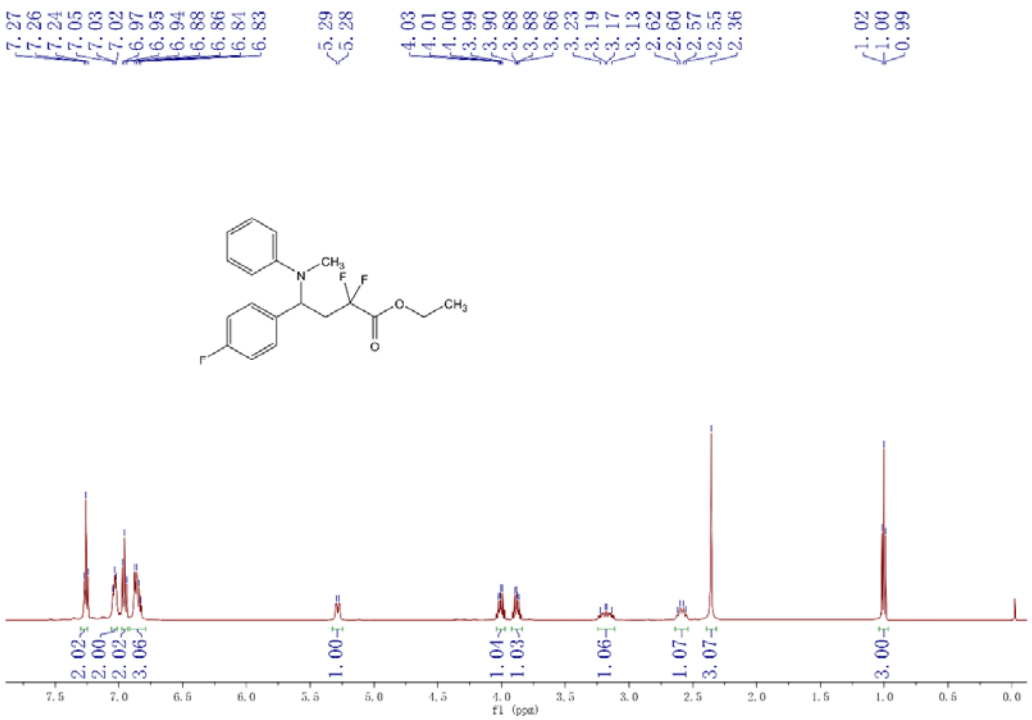
^{1}H NMR of **4e**



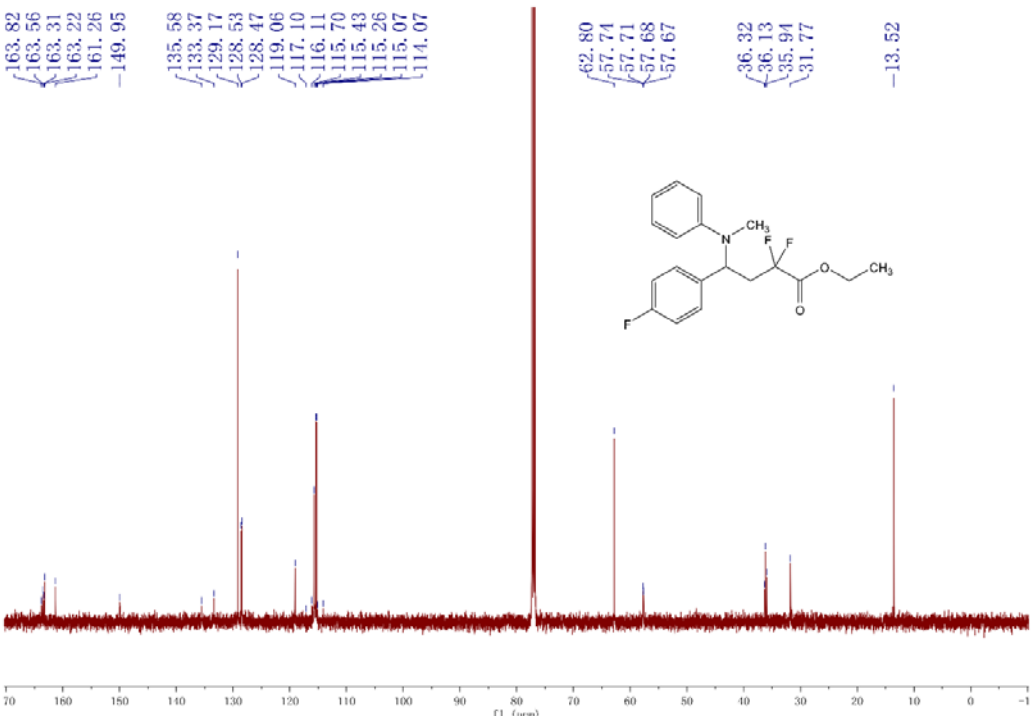
^{13}C NMR of **4e**



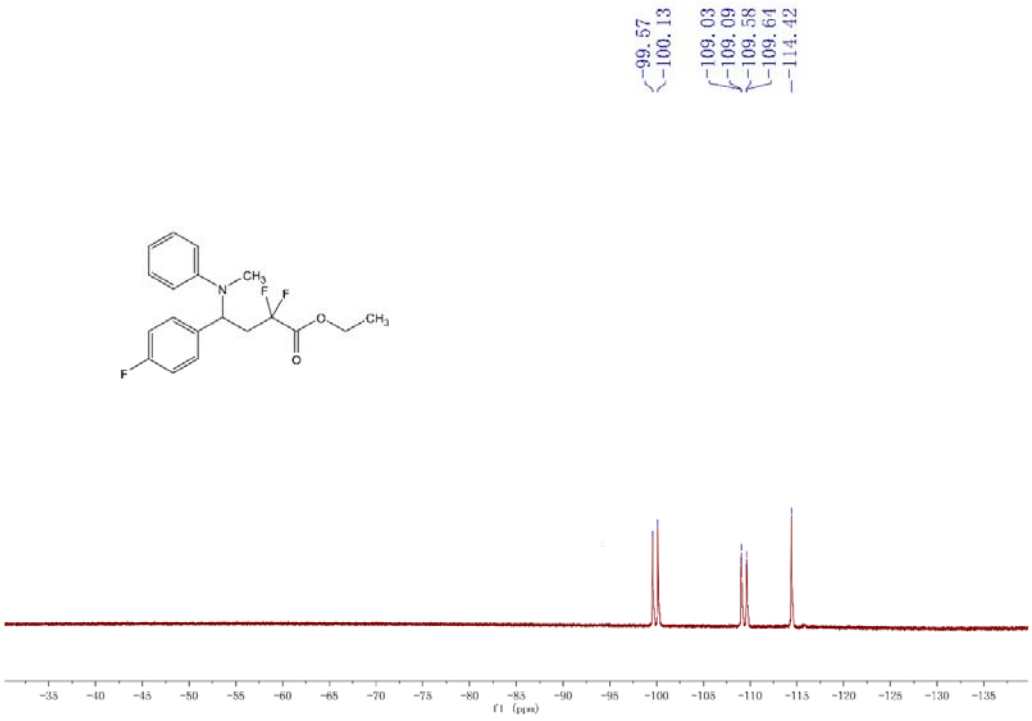
^{19}F NMR of **4e**



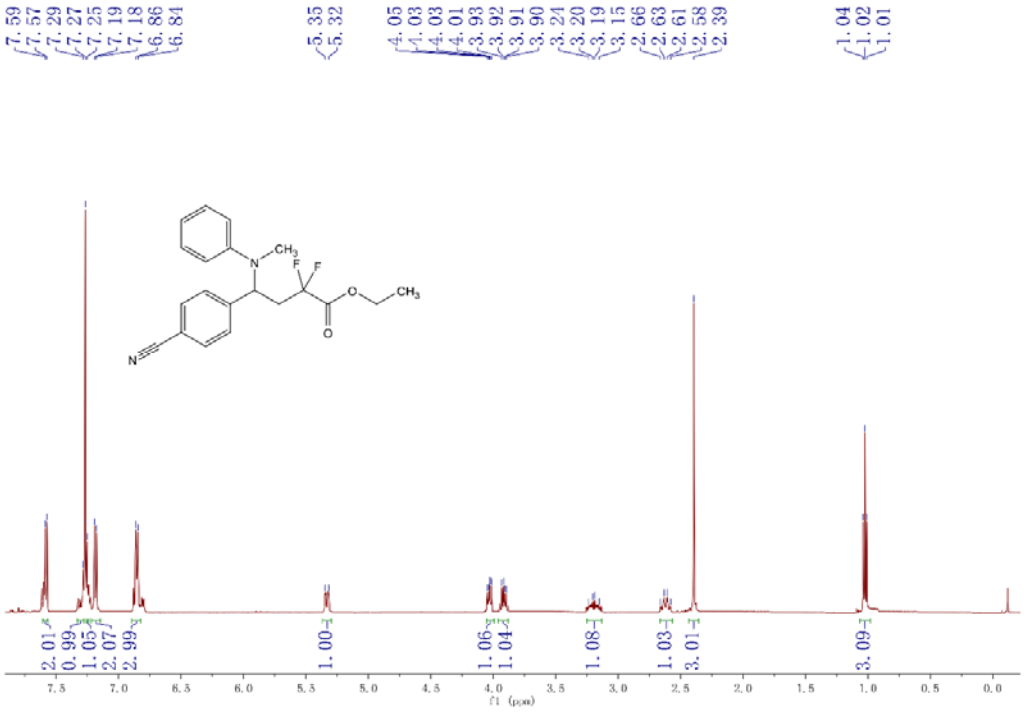
^{1}H NMR of **4f**



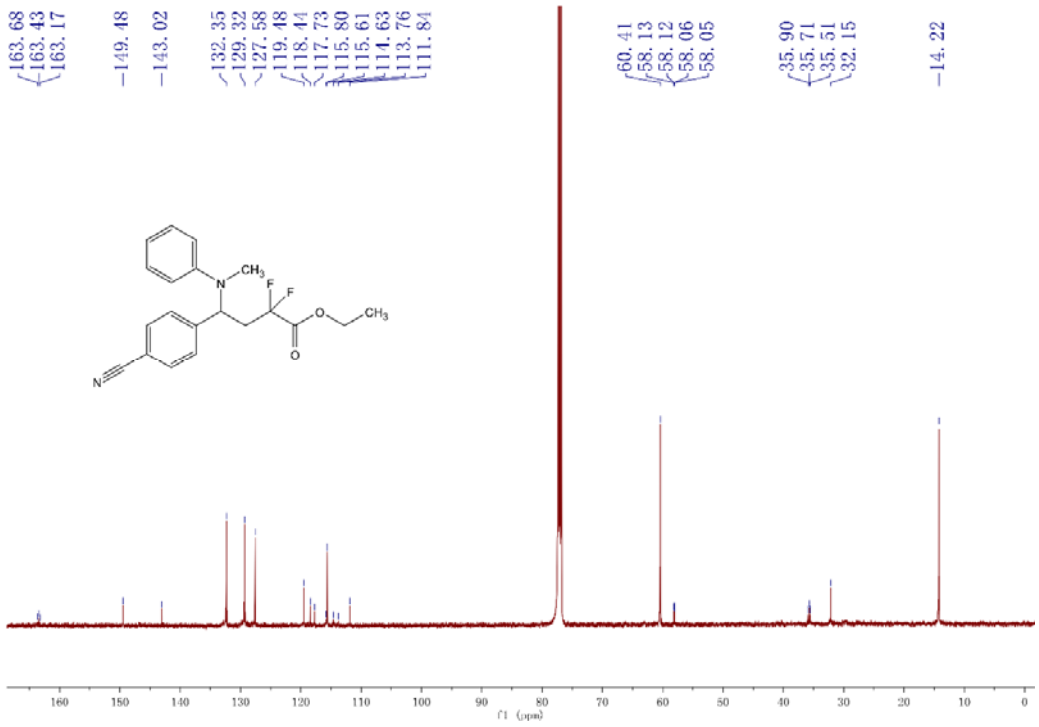
^{13}C NMR of **4f**



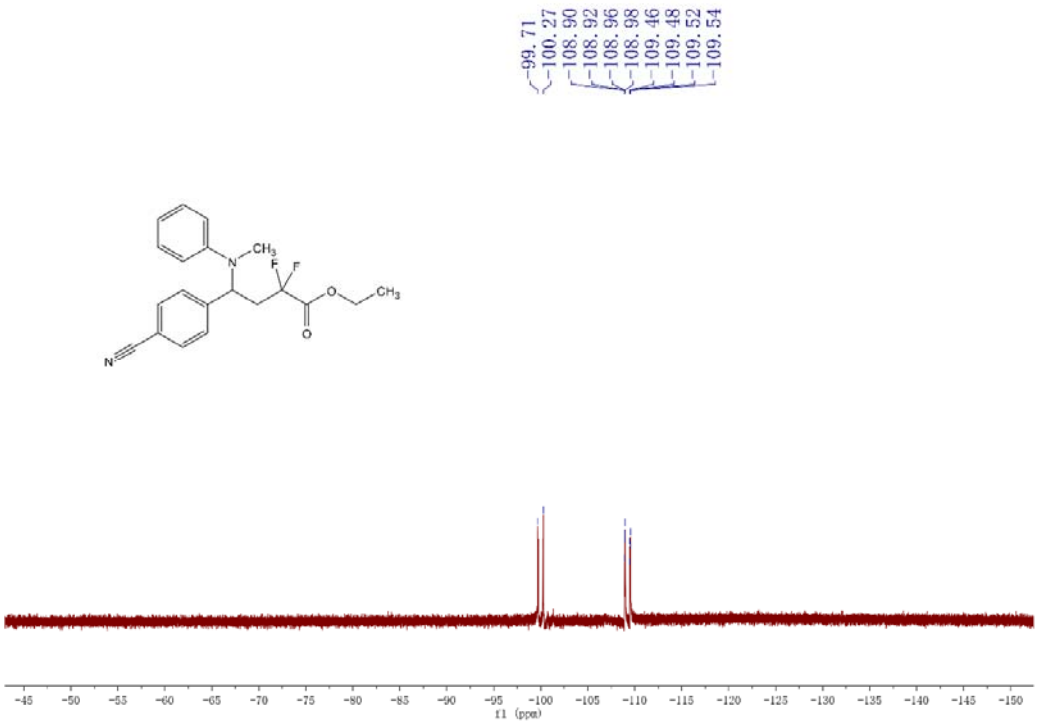
^{19}F NMR of **4f**



^{1}H NMR of **4g**



^{13}C NMR of **4g**



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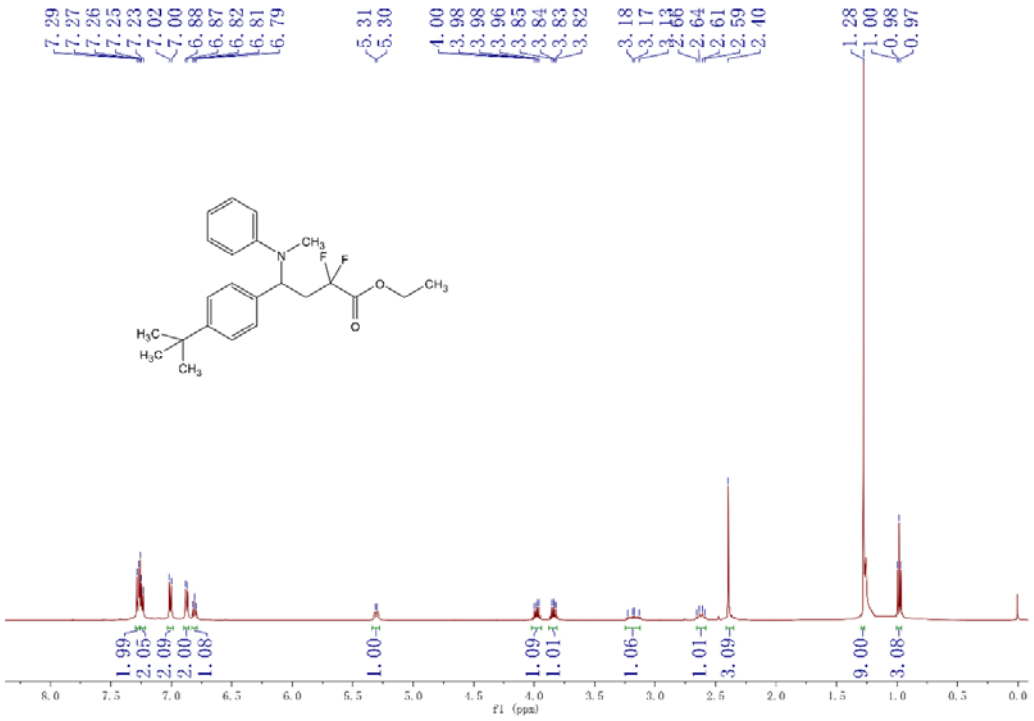

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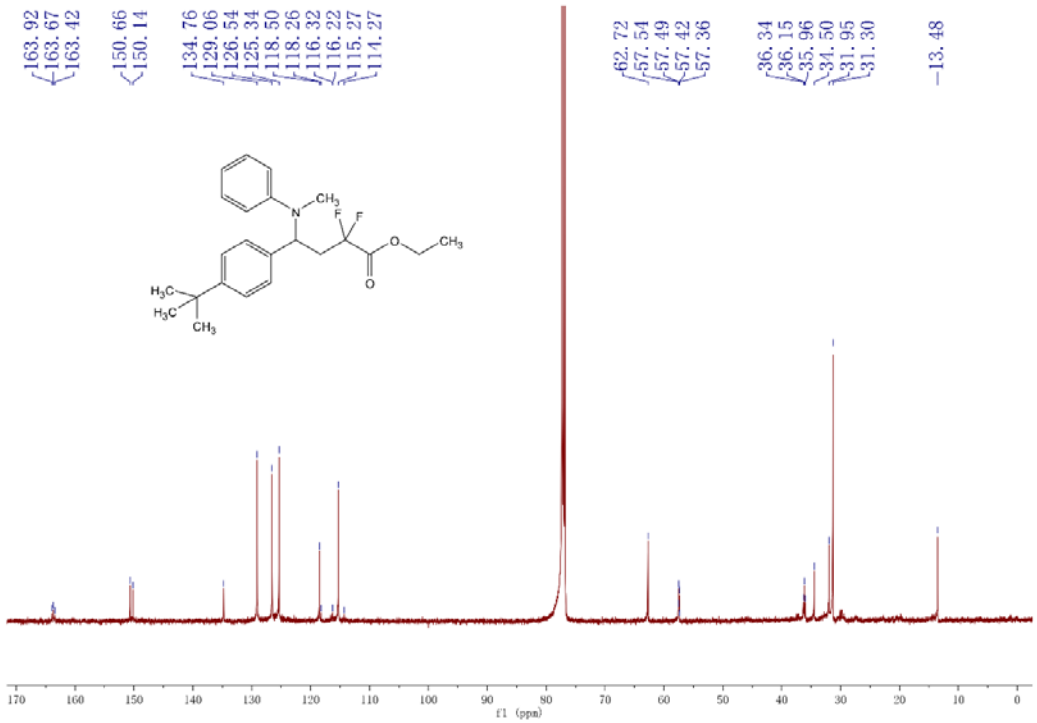
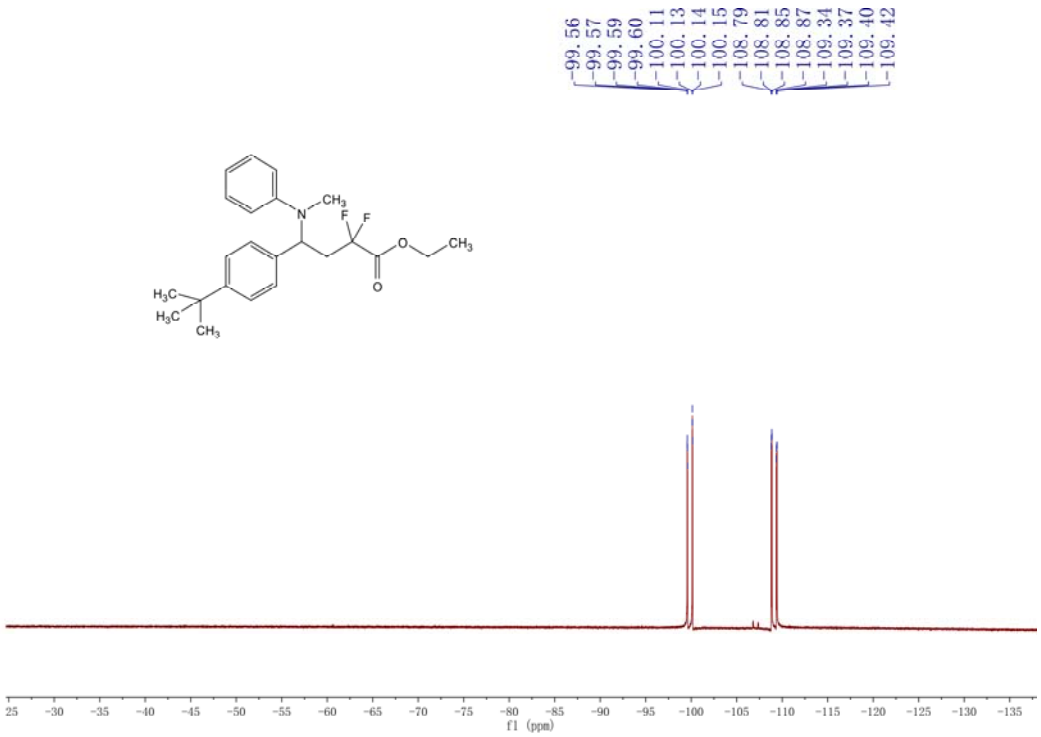


^{13}C NMR of **4h**



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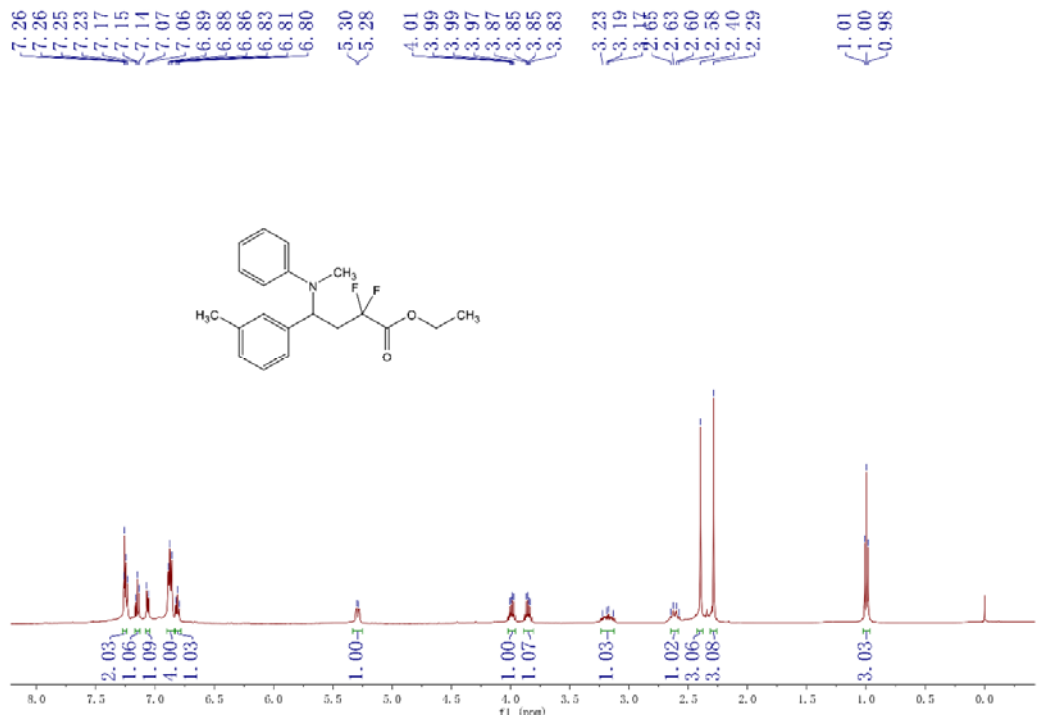
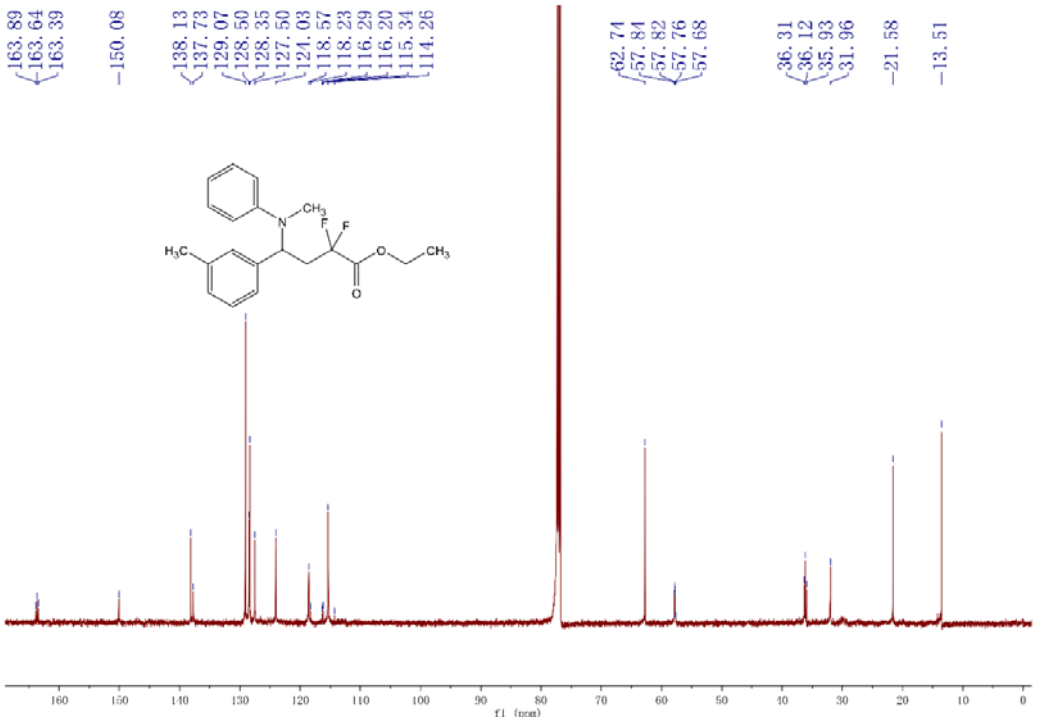
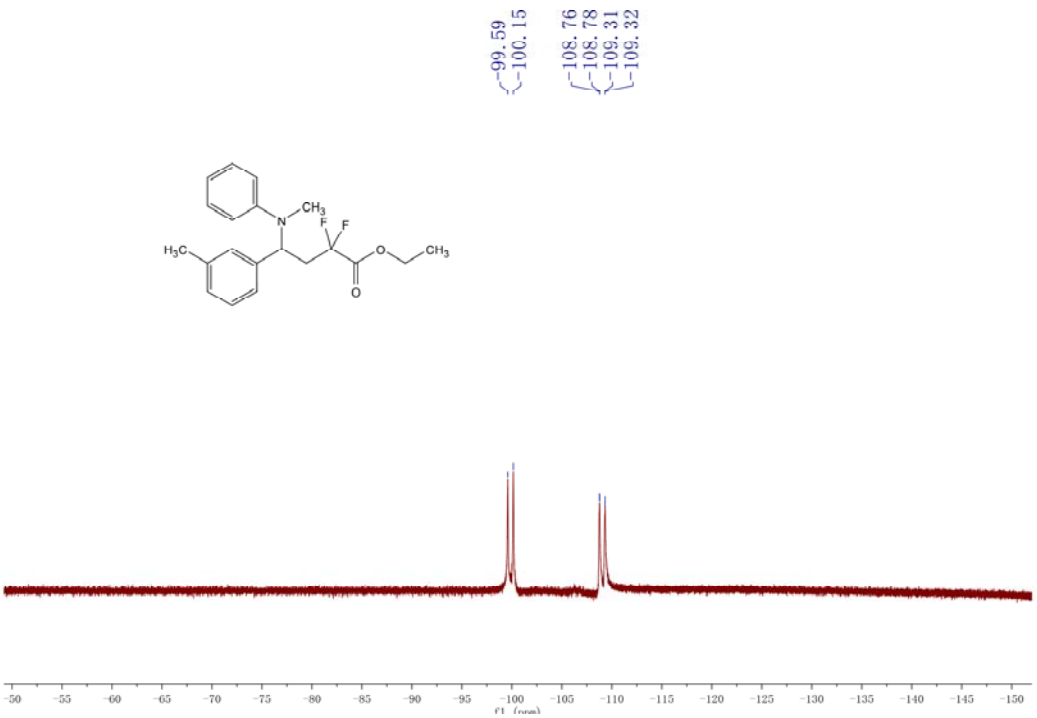


^{1}H NMR of **4i**



^{13}C NMR of **4i**



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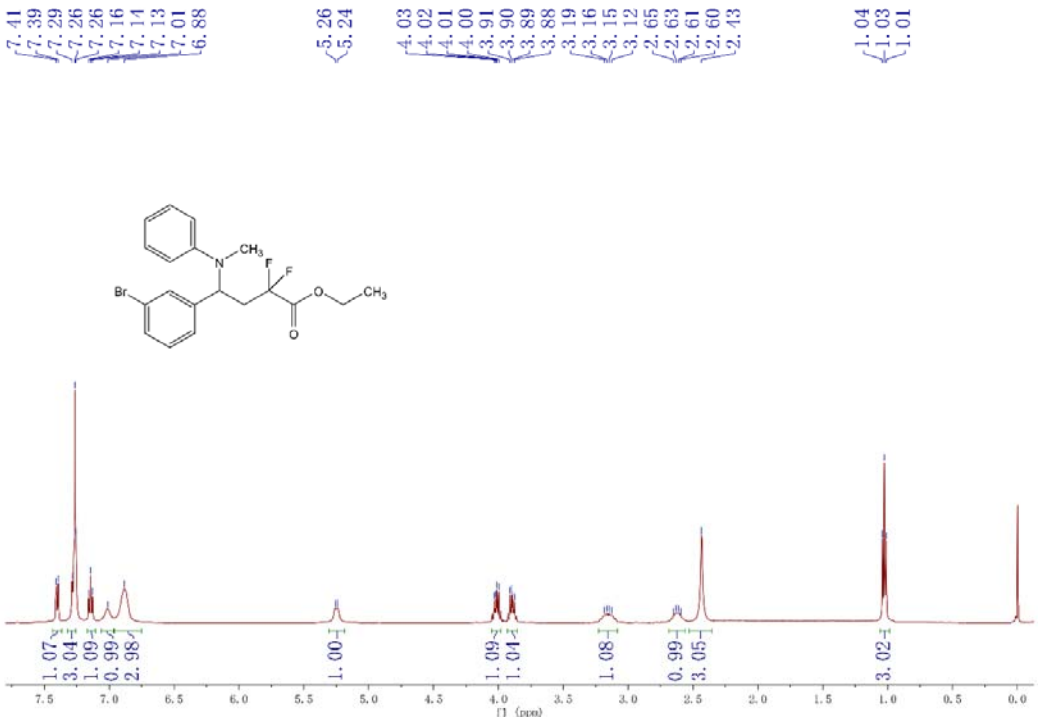
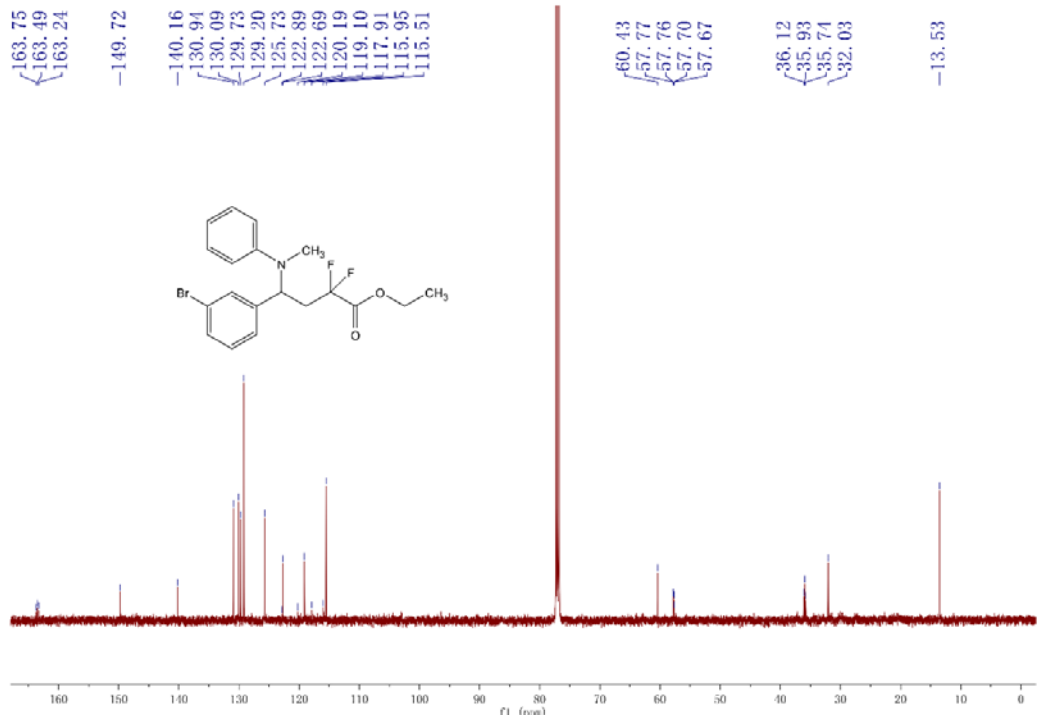


^{1}H NMR of **4j**



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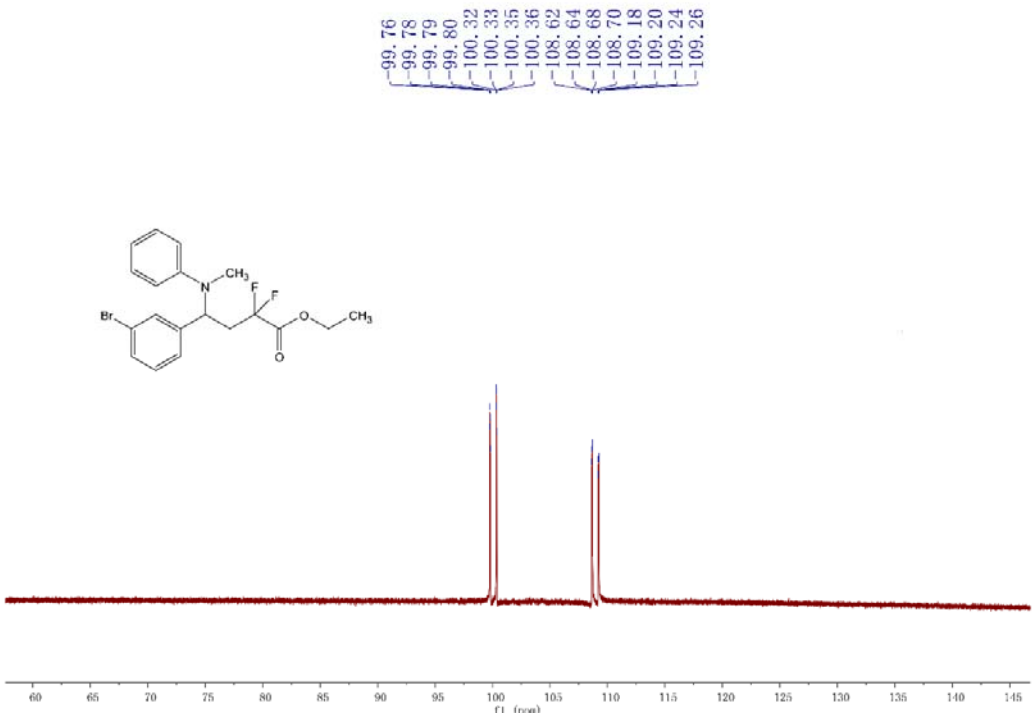

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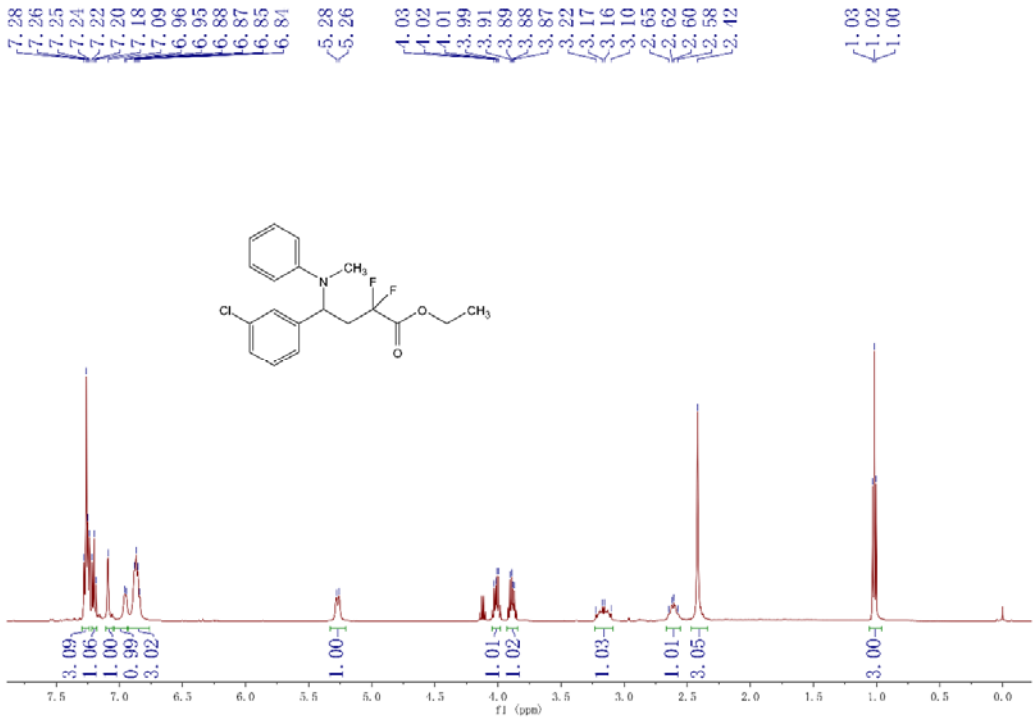

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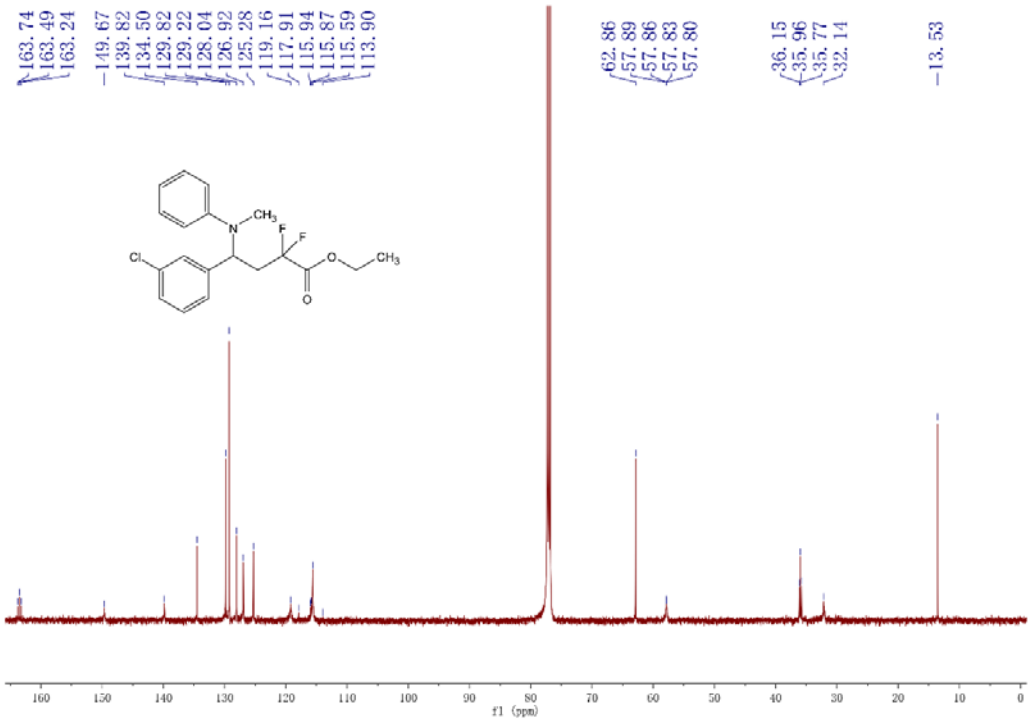
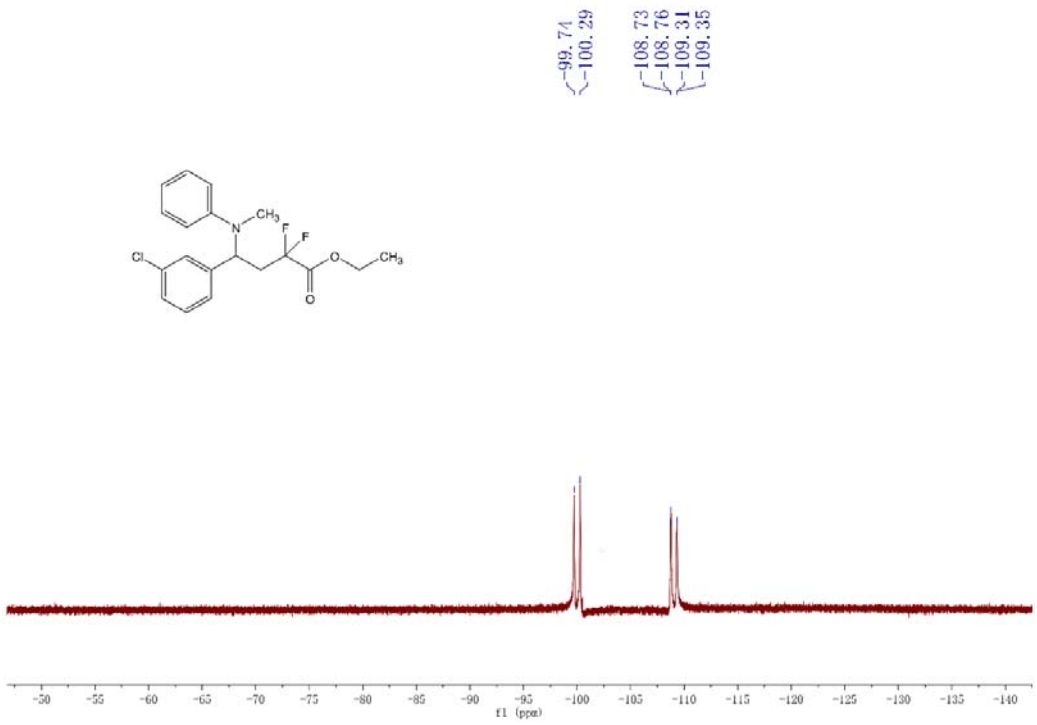


^{13}C NMR of **4k**



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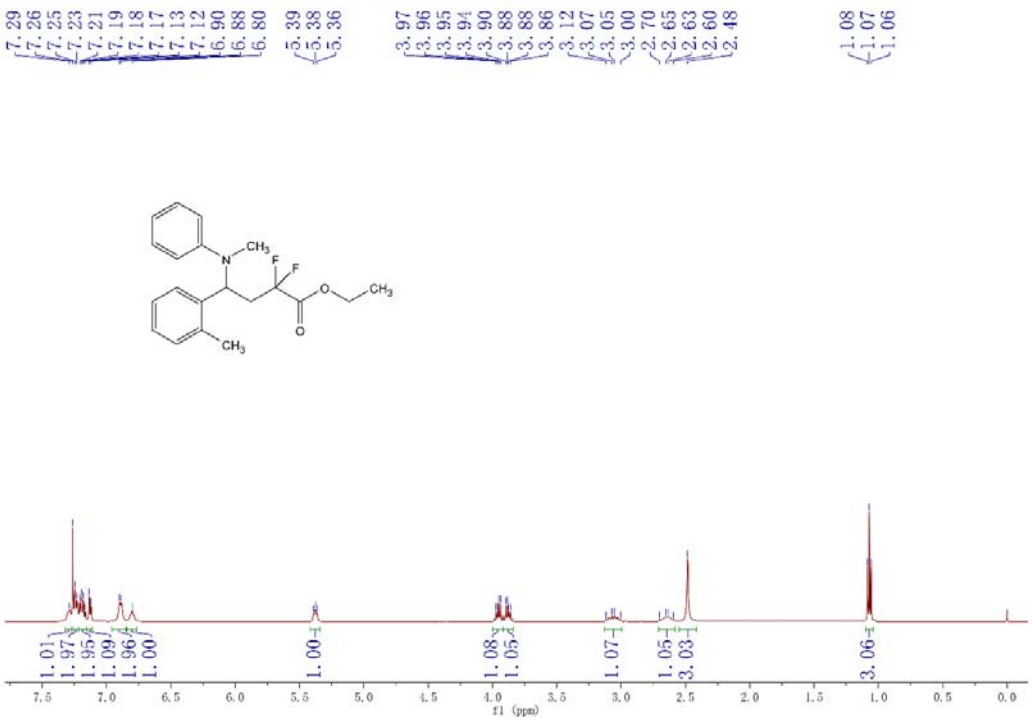
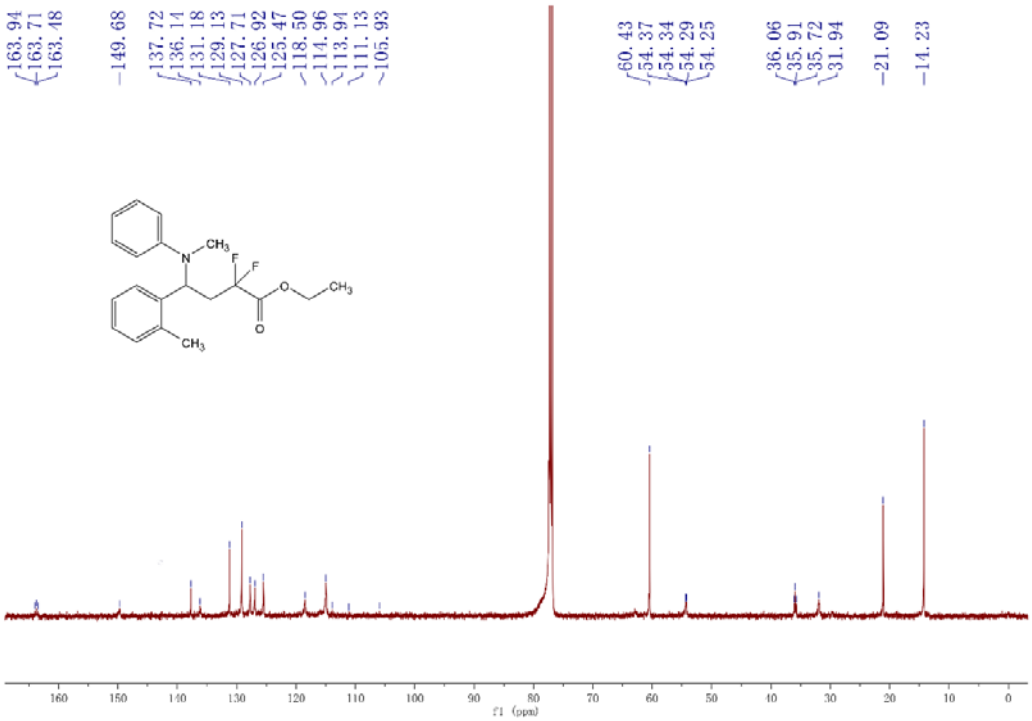
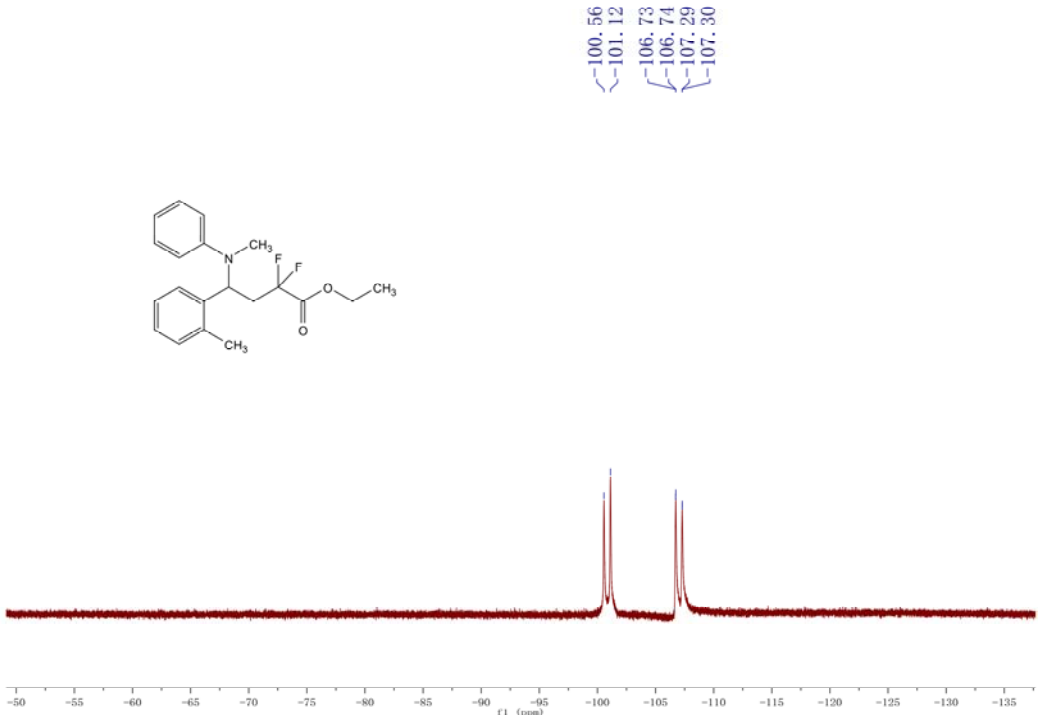


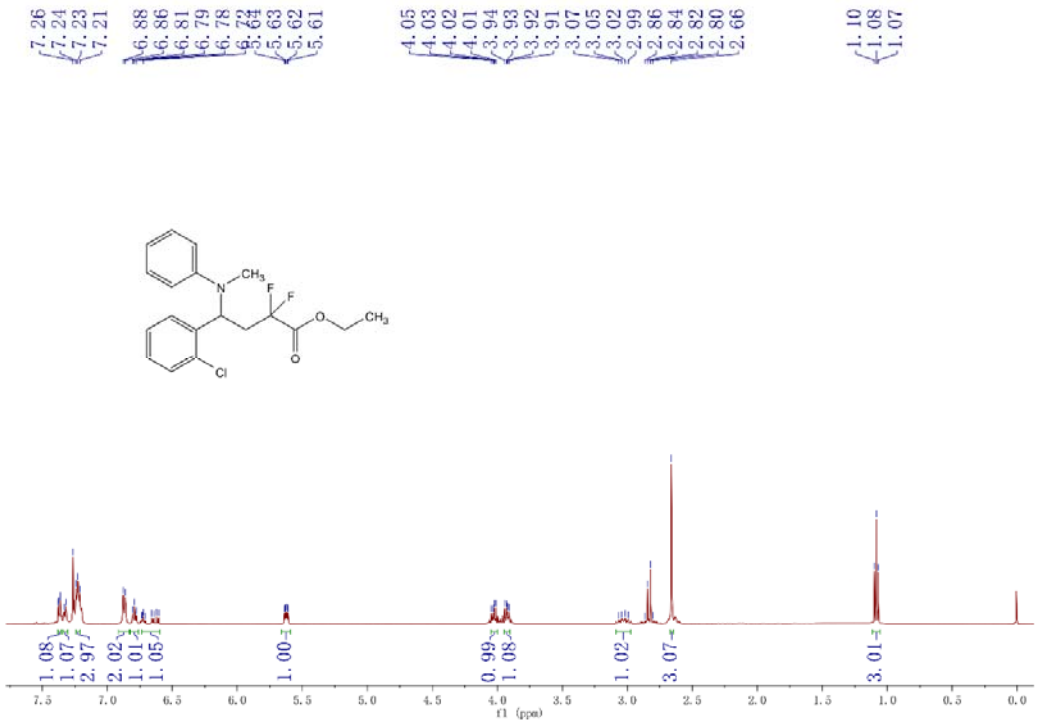
^{1}H NMR of **4l**



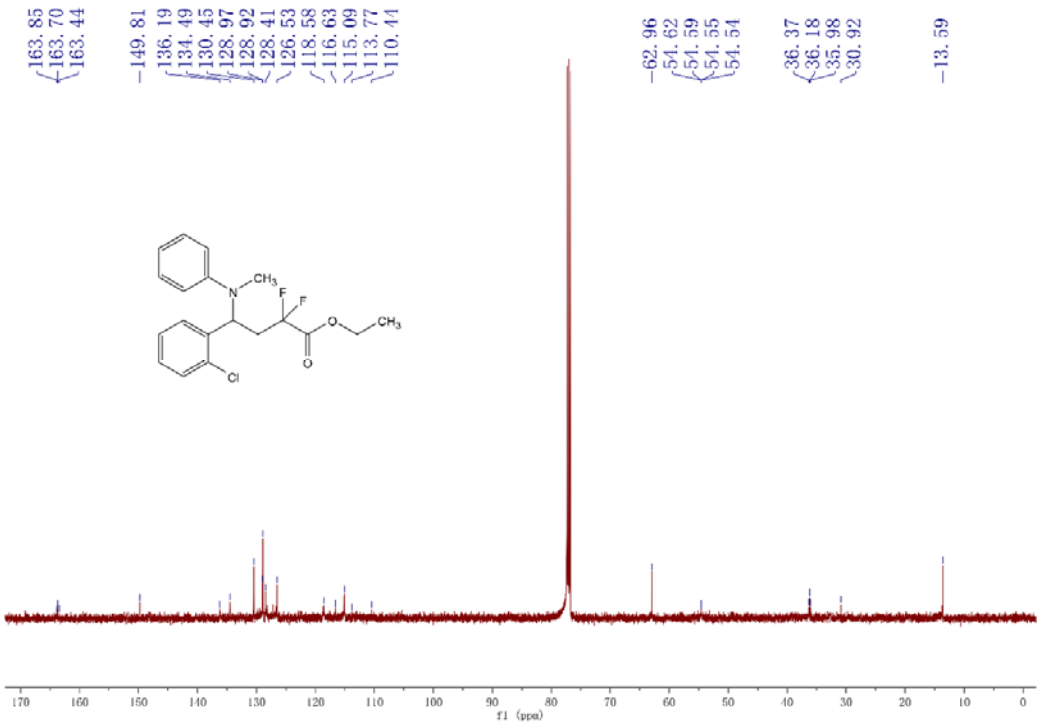
^{13}C NMR of **4l**



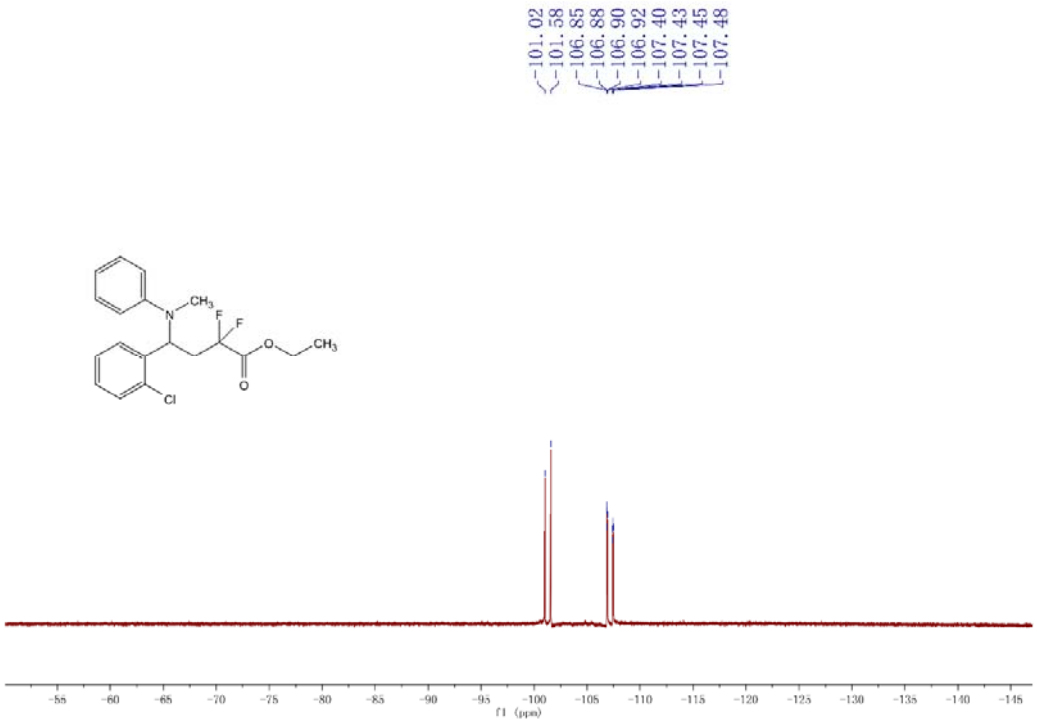
^{19}F NMR of **4l**



^{1}H NMR of **4m**



^{13}C NMR of **4m**



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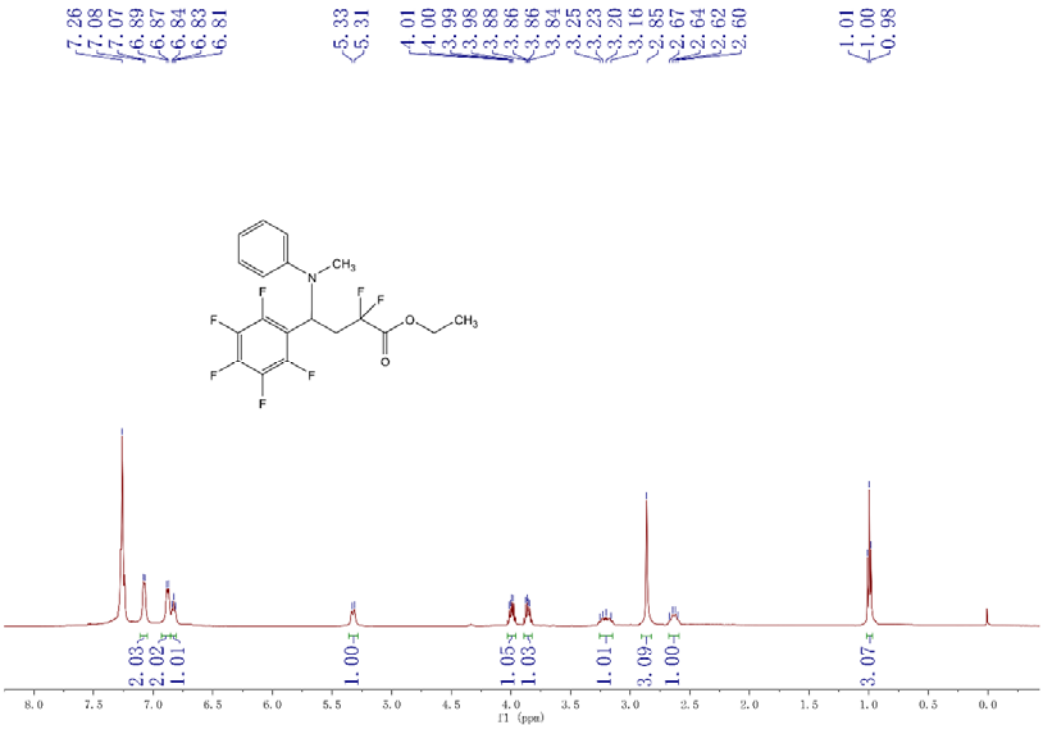
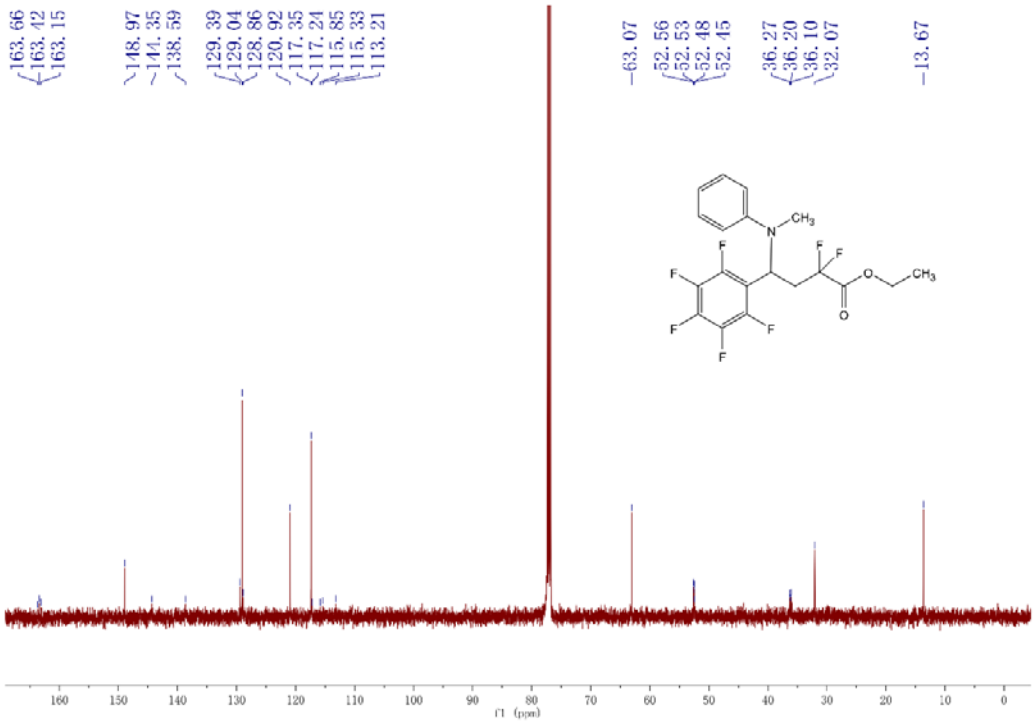
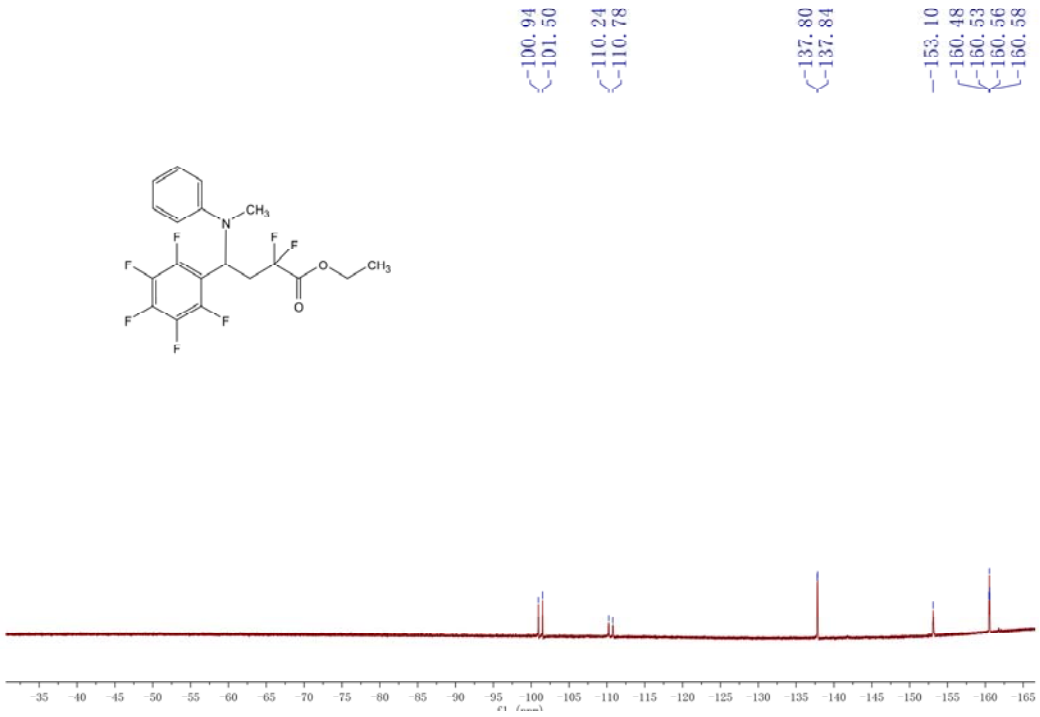


^{1}H NMR of **4n**



^{13}C NMR of **4n**



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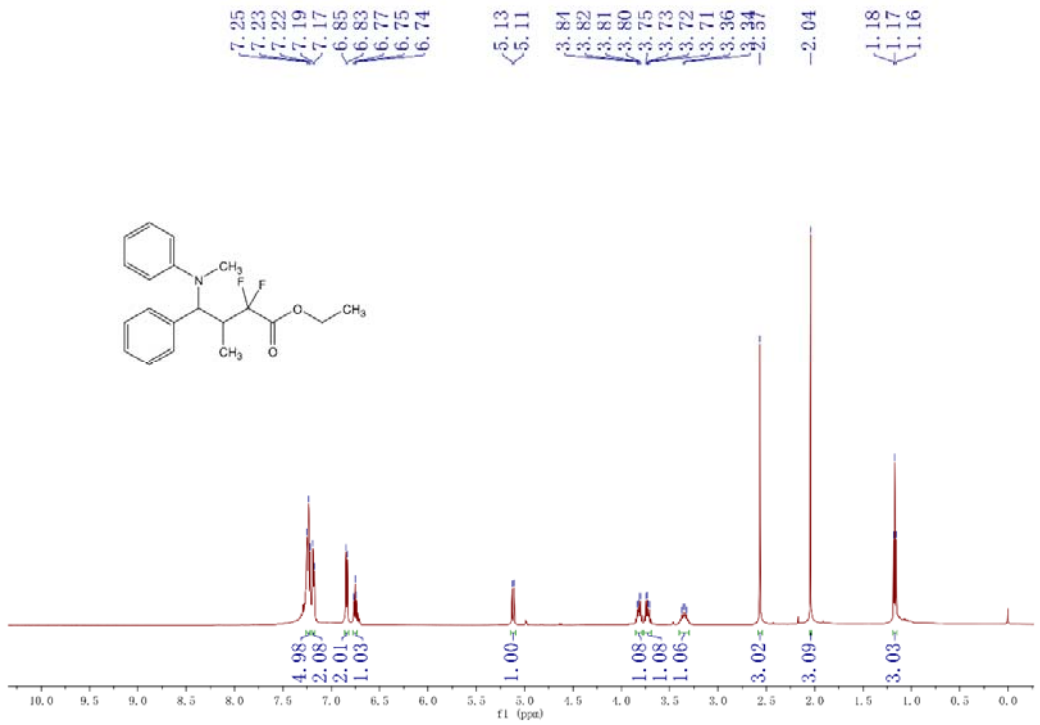

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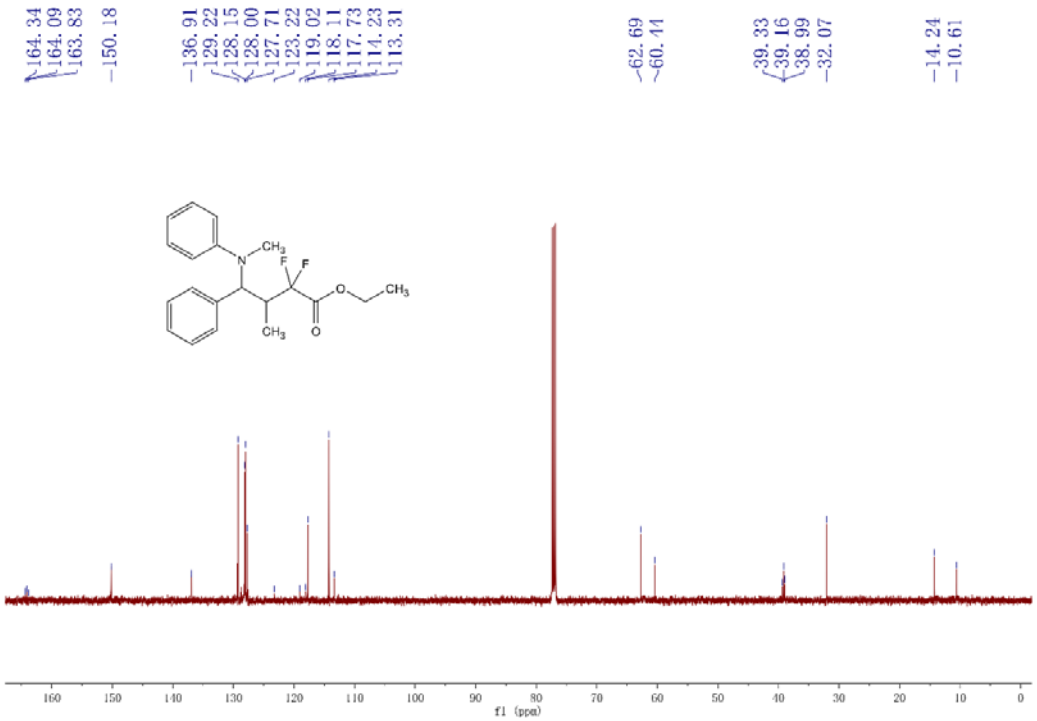

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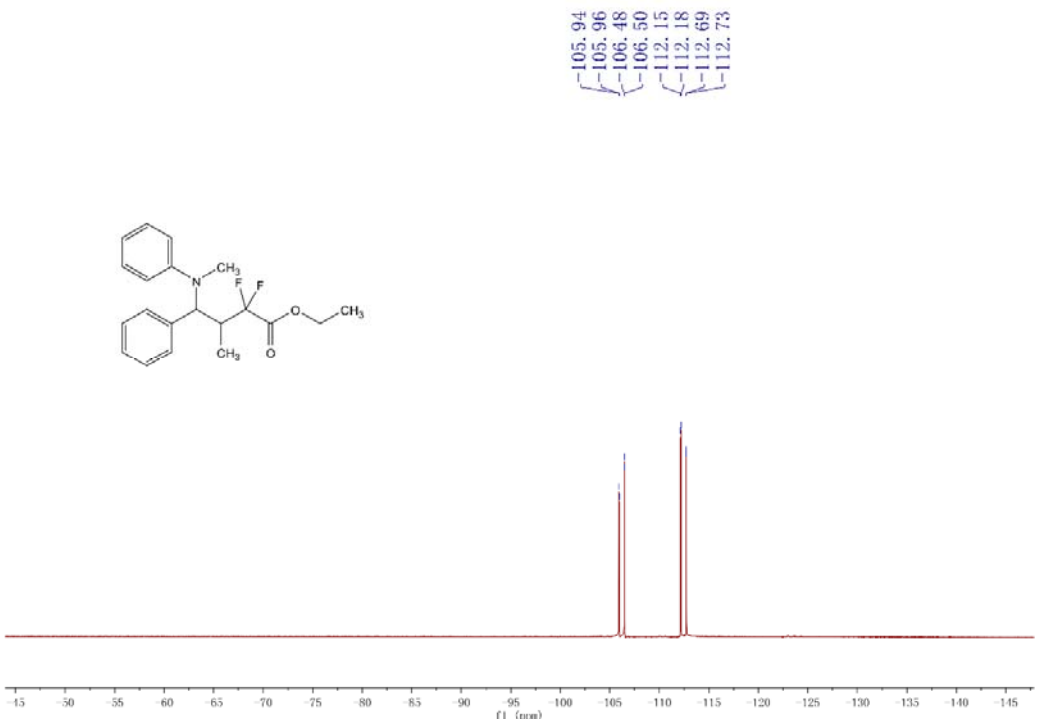
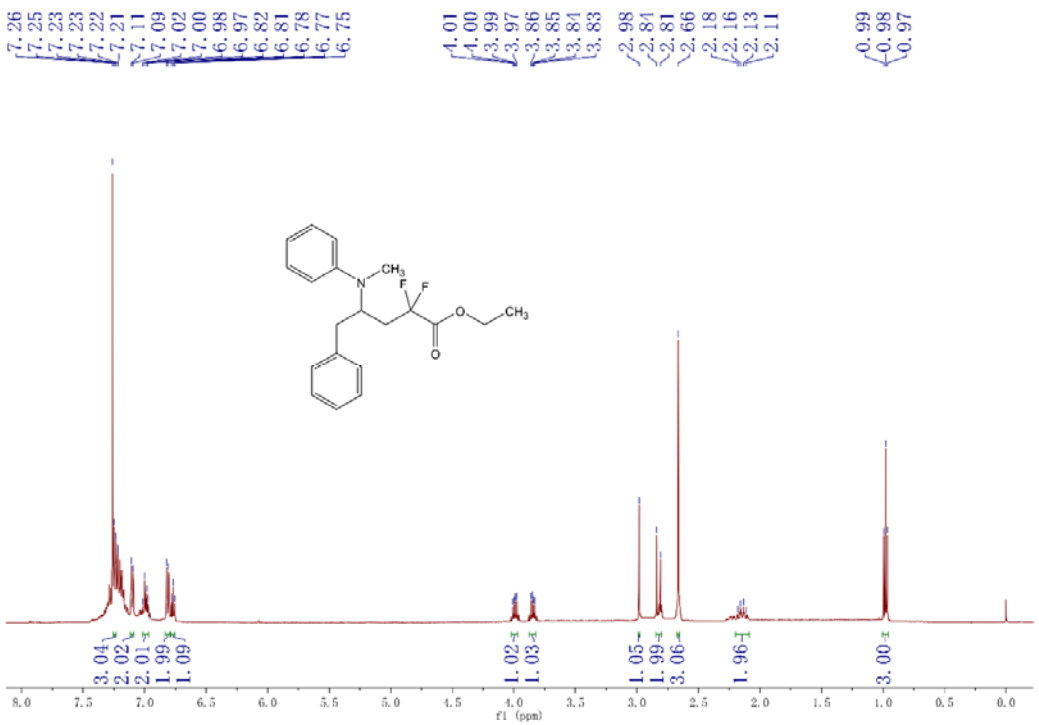
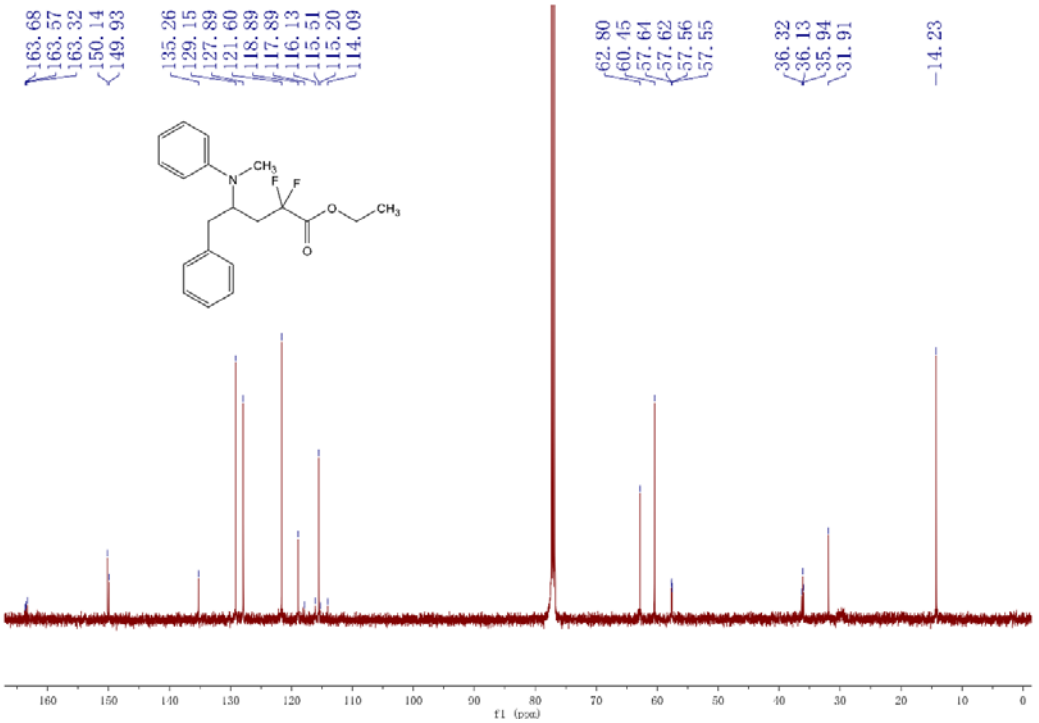


^{19}F NMR of **4p**



^{1}H NMR of **4q**



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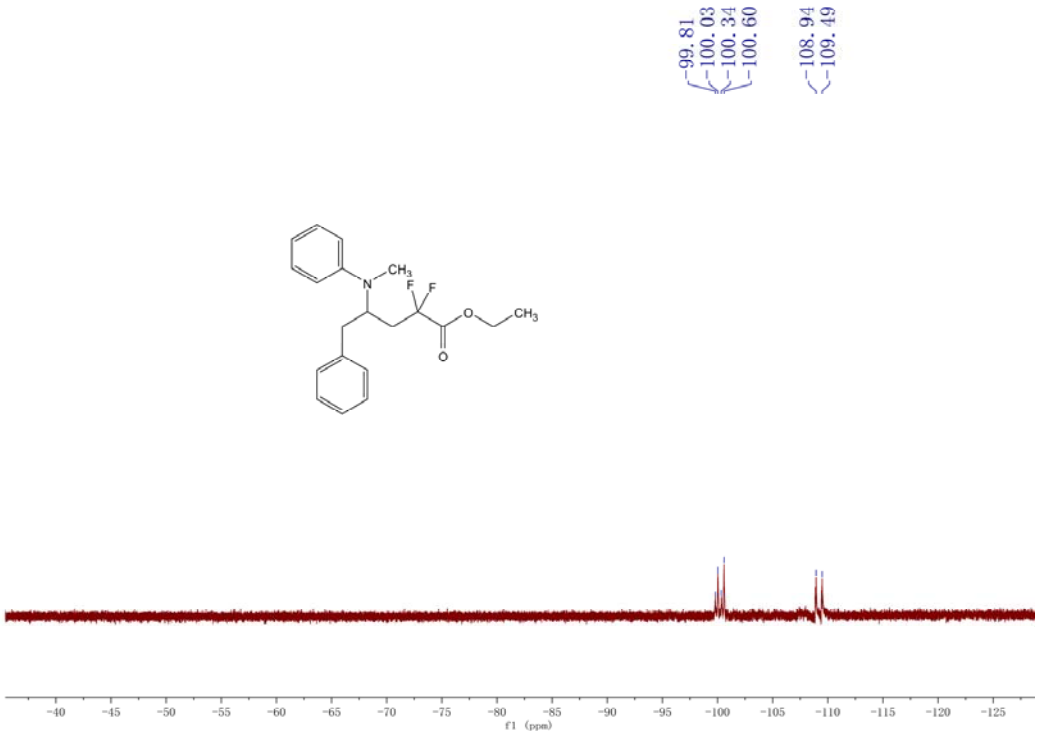

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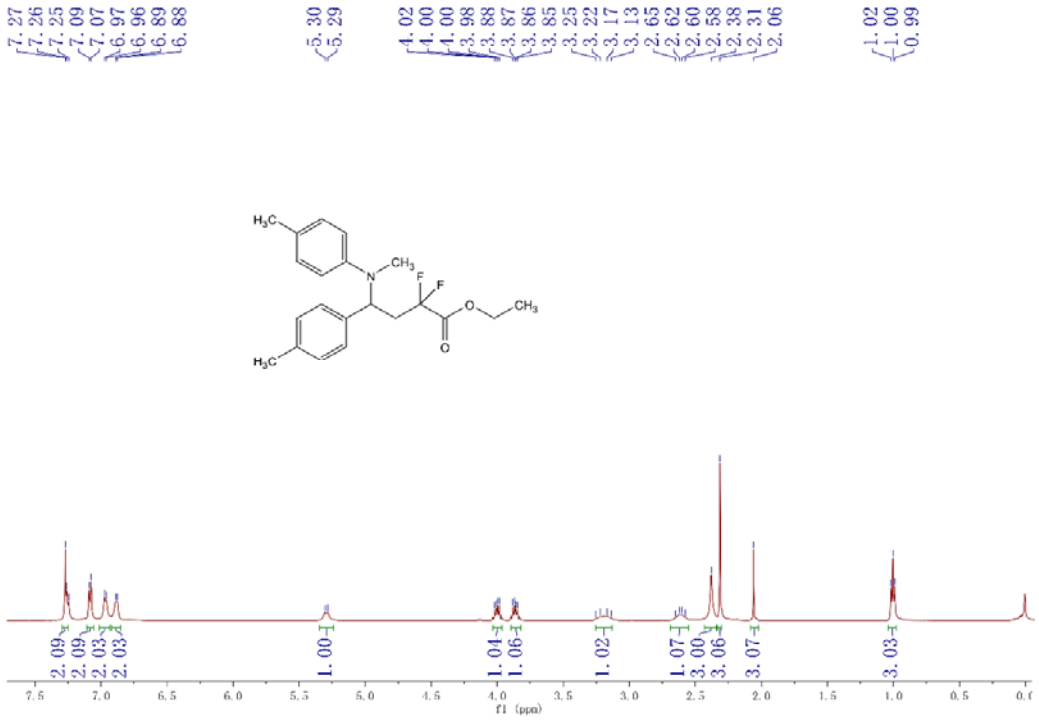

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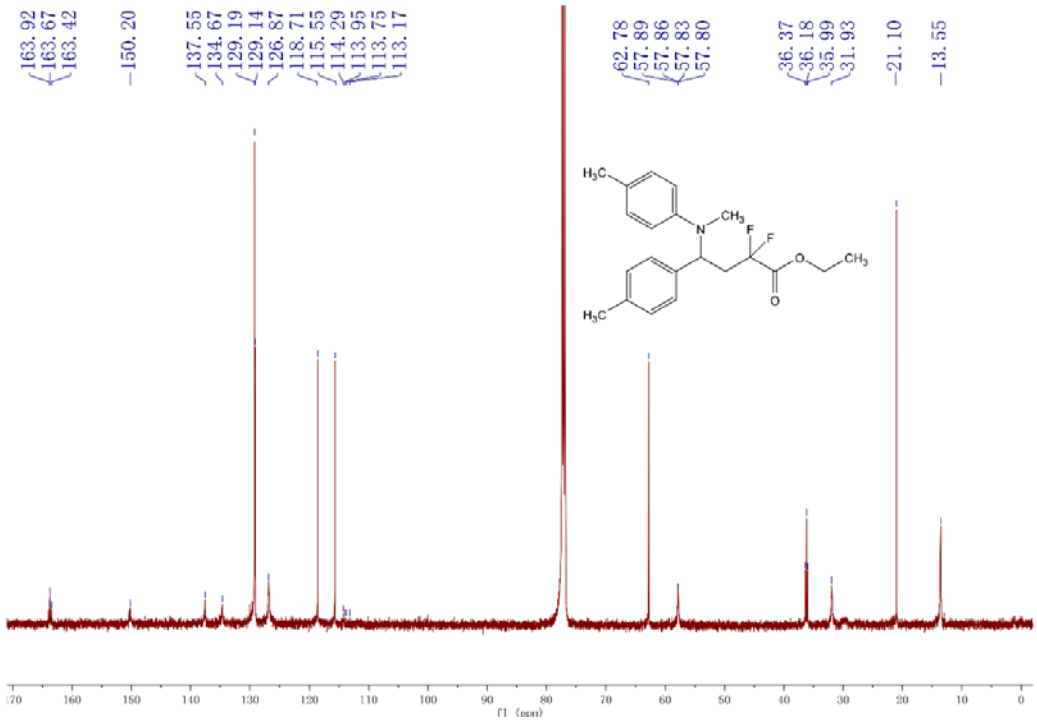
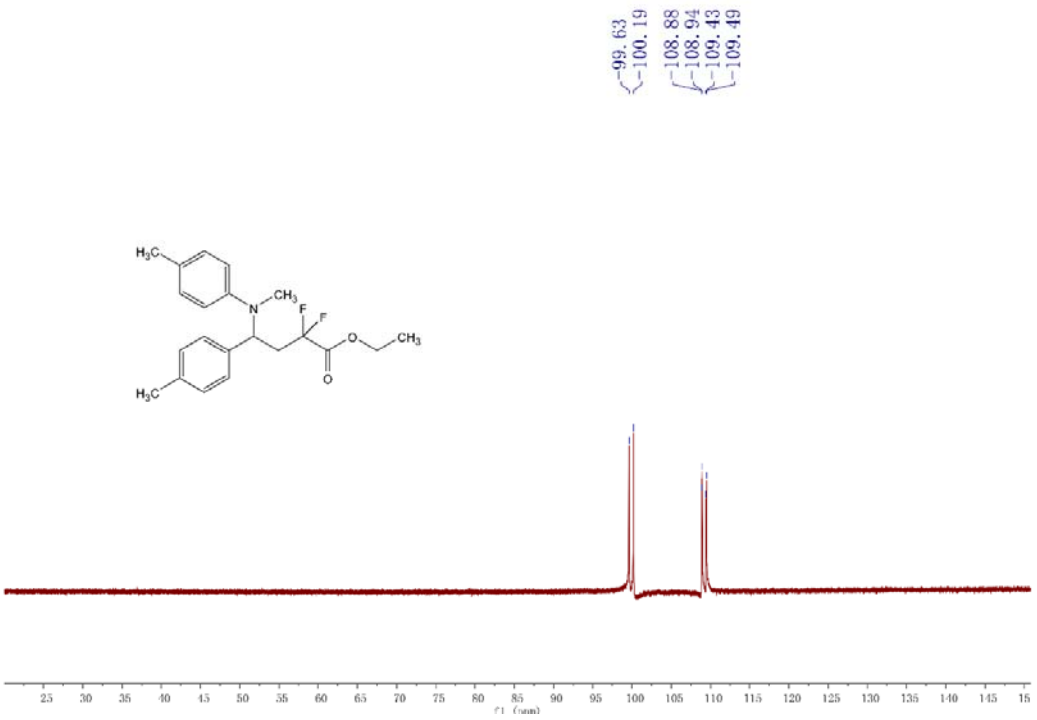


^{13}C NMR of **4s**



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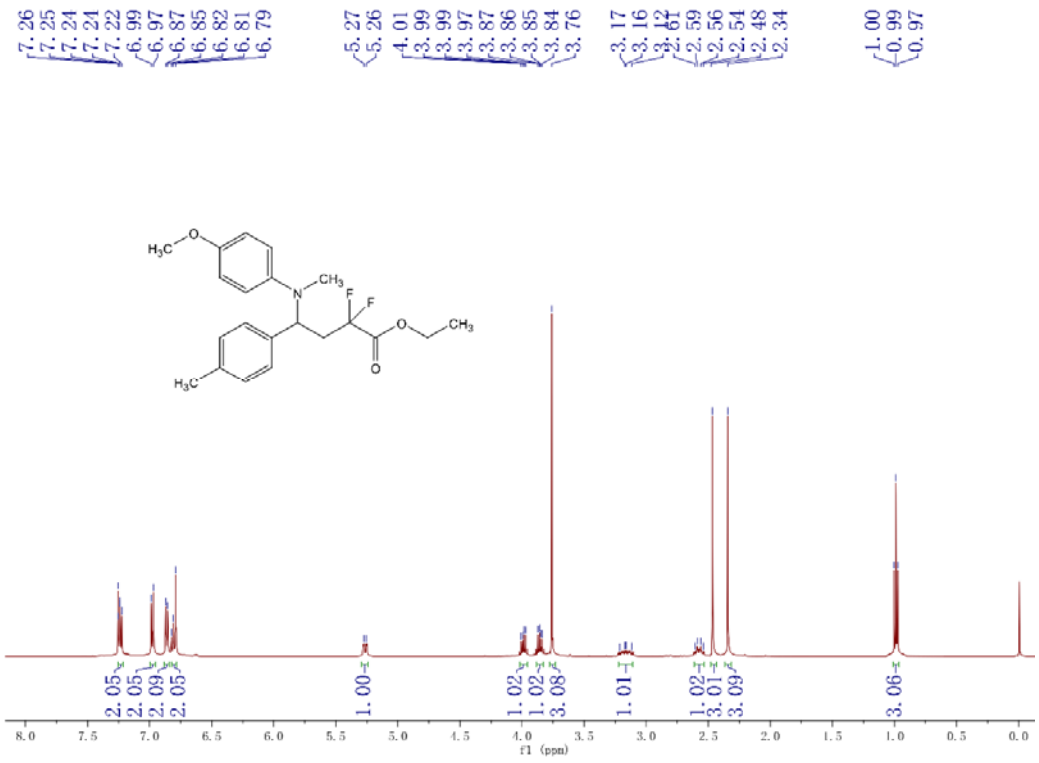

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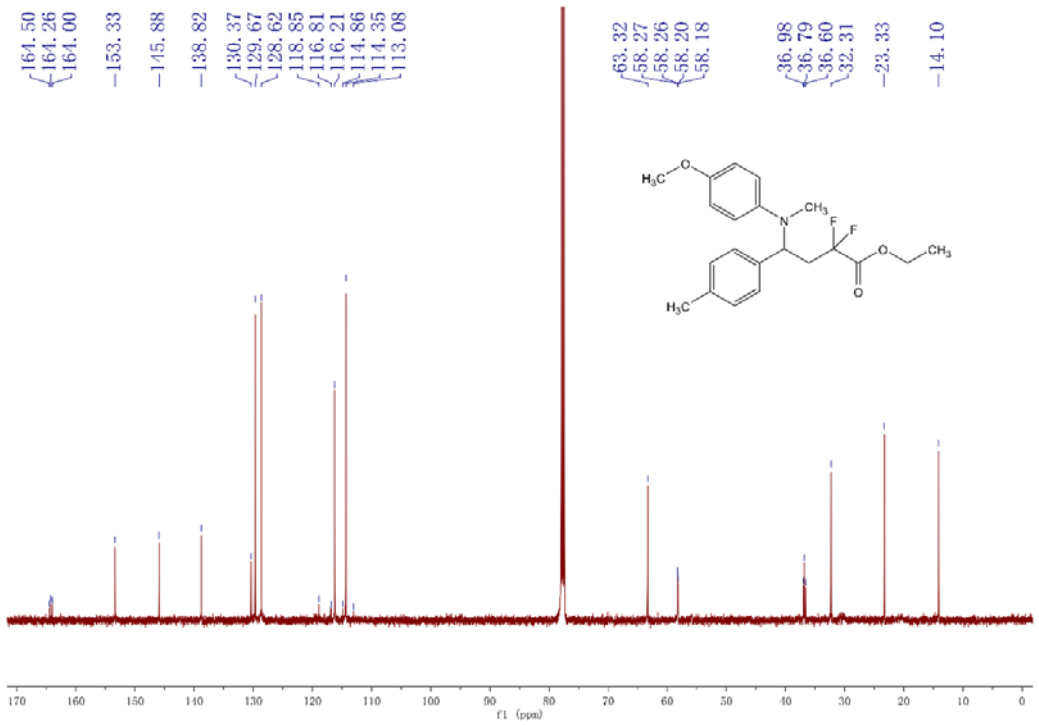

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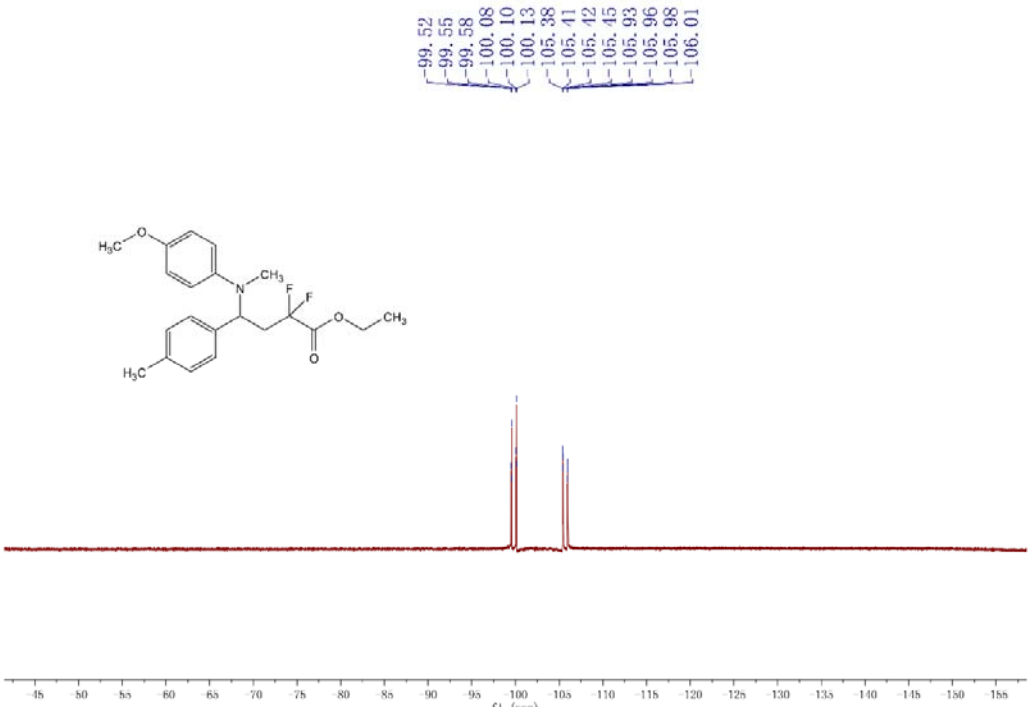

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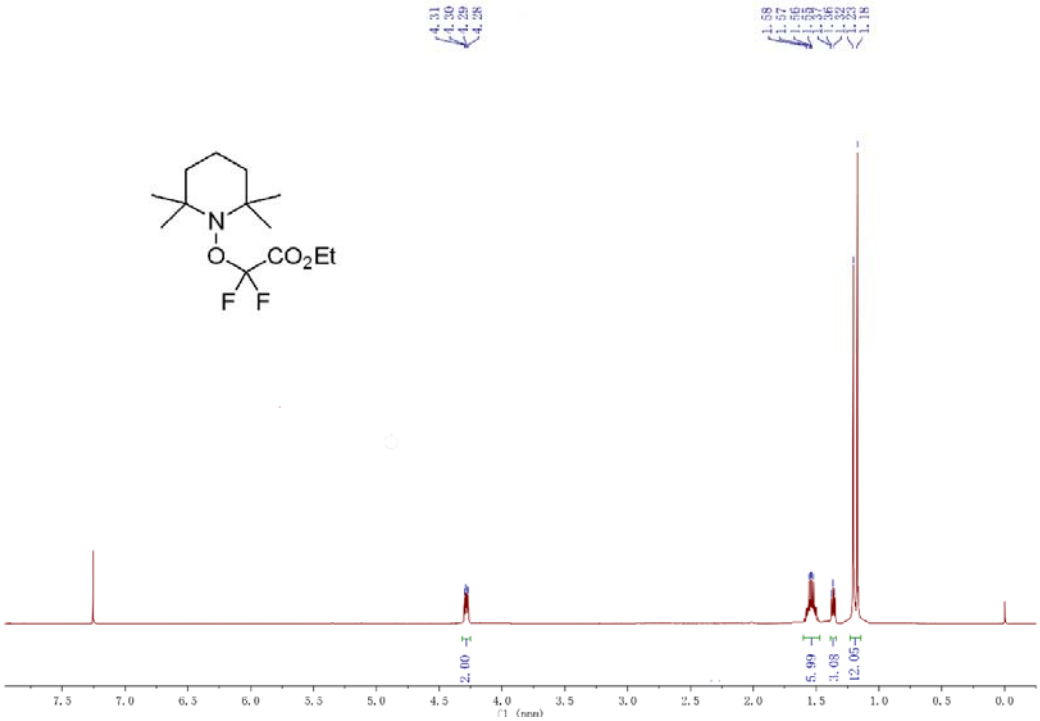
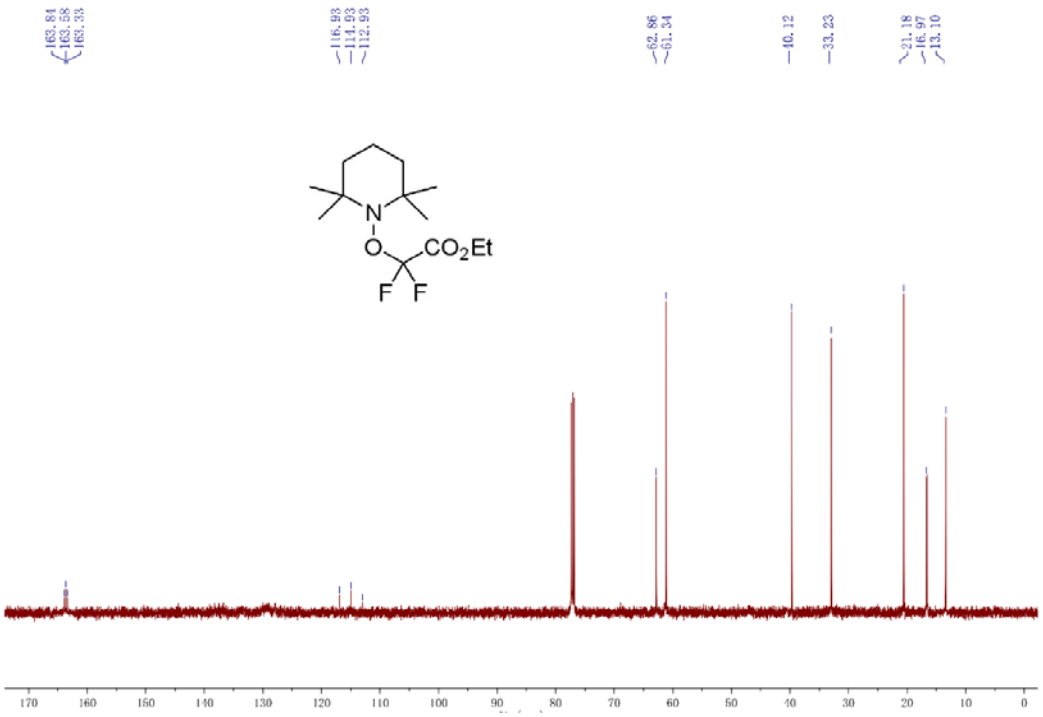


^{1}H NMR of **5**



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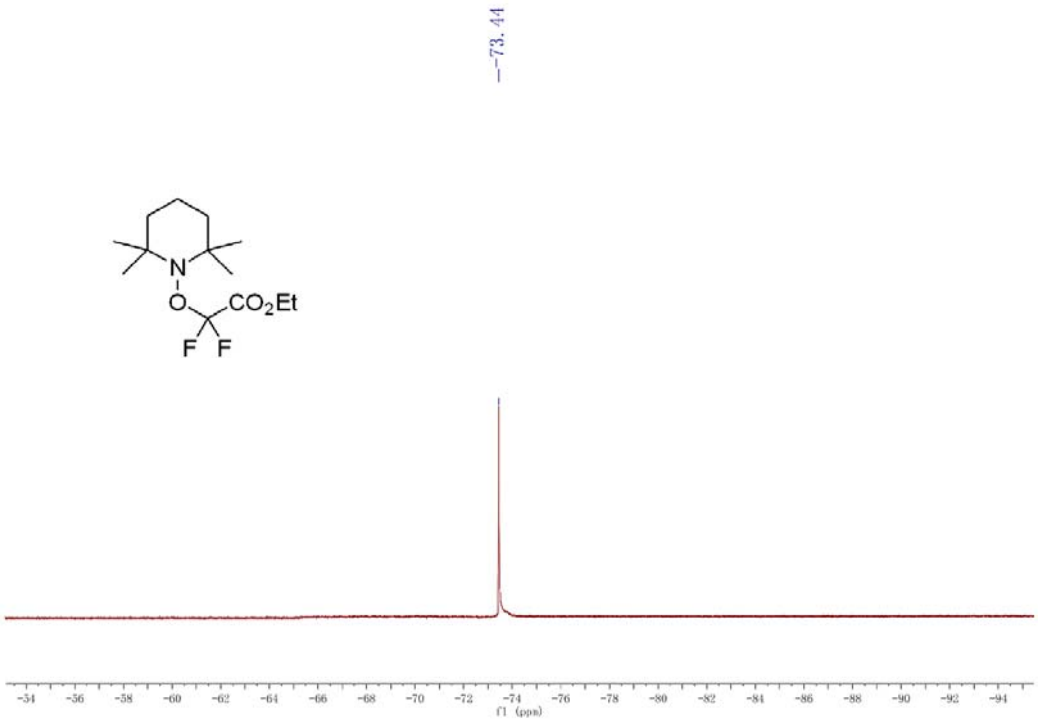

^{19}F NMR of **5**