Supporting Information

Visible-light-initiated external photocatalyst-free synthesis of α,α-difluoro-β-ketoamides from 4-aminocoumarins

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1. General information

Unless otherwise specified, all reagents and solvents were obtained from commercial suppliers and used without further purification. ^{1}H NMR spectra were recorded at 400 MHz and ^{13}C NMR spectra were recorded at 100 MHz by using a Bruker Avance 400 spectrometer in $CDCl_3$ with TMS as internal standard. The chemical shifts (δ) were expressed in ppm and J values were given in Hz. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. High-resolution mass spectral (HRMS) analysis was performed on a Bruker micr OTOF-Q II instrument using ESI techniques. TLC analysis was performed using precoated glass plates. Column chromatography was performed on silica gel (200-300 mesh). 4-aminocoumarins were prepared according to literature.[1-3]

The light source and the material of the irradiation vessel

Manufacturer: Beijing Rogertech Ltd.

Model: RLH-18

Broadband source: λ= 455 nm

Material of the irradiation vessel: quartz tube

Not use any filters

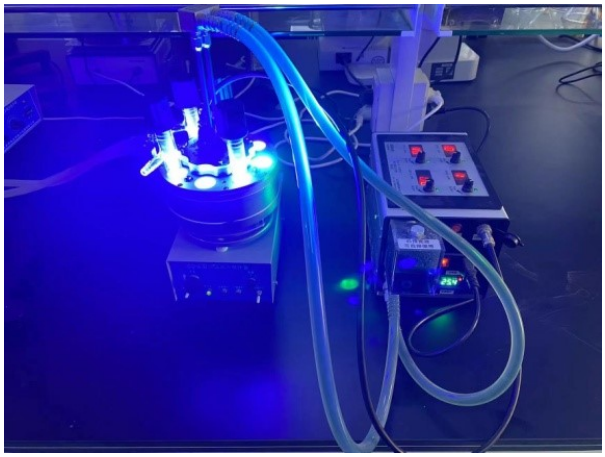


Figure S1 (Photographed by author Ningbo Li)

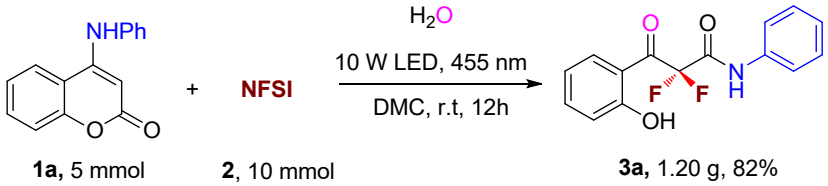
2. Experimental section

2.1 Typical procedure for the synthesis of α,α-difluoro-β-ketoamides 3

The mixture of 4-aminocoumarins **1** (1.0 equiv., 0.2 mmol), N-Fluorobenzenesulfonimide (2.0 equiv., 0.40 mmol), and H_2O (5.0 equiv., 1.0 mmol, about 1 drop) in dimethyl carbonate

(2.0 mL) was open to the air and stirred at room temperature under the irradiation of 10 W LED (455 nm) for about 12 h. After completion of the reaction, the resulting mixture was extracted with CH_2Cl_2 (5 mL × 3) and the organic phase was then removed under vacuum. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent (PE/EA = 6/1- 3/1) to give the desired products **3**.

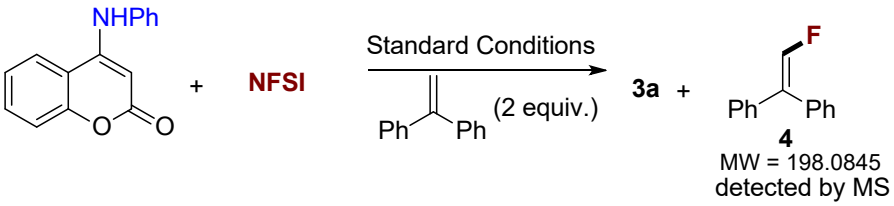
2.2 Procedure for gram-scale synthesis of 3a



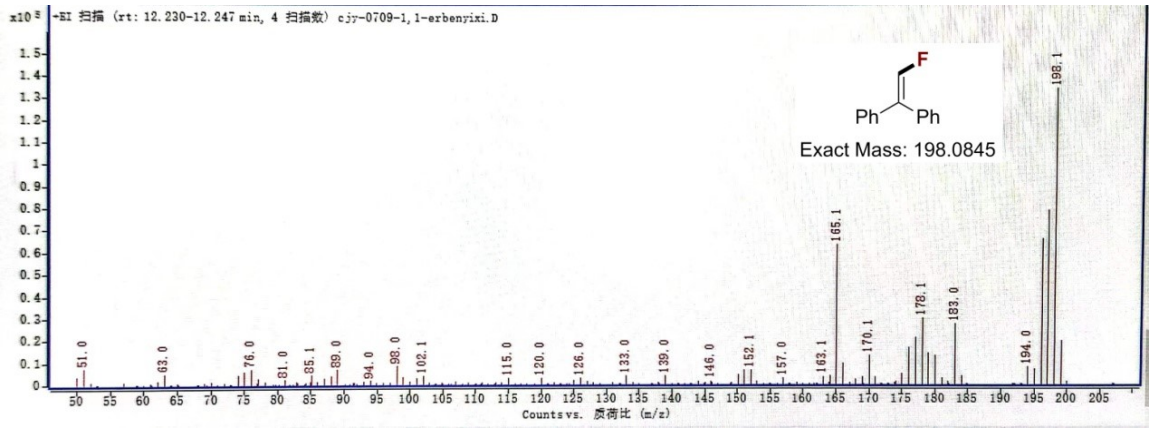
1a, 5 mmol **2**, 10 mmol **3a,** 1.20 g, 82%

The mixture of 4-aminocoumarin **1a** (5 mmol), N-Fluorobenzenesulfonimide (10 mmol), and H_2O (0.25 ml) in dimethyl carbonate (15 mL) was open to the air and stirred at room temperature under the irradiation of 10 W LED (455 nm) for about 12 h. After completion of the reaction, the resulting mixture was extracted with CH_2Cl_2 (30 mL × 3) and the organic phase was then removed under vacuum. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent (PE/EA = 5/1) to give the desired products **3a** (1.20 g, 82% yield).

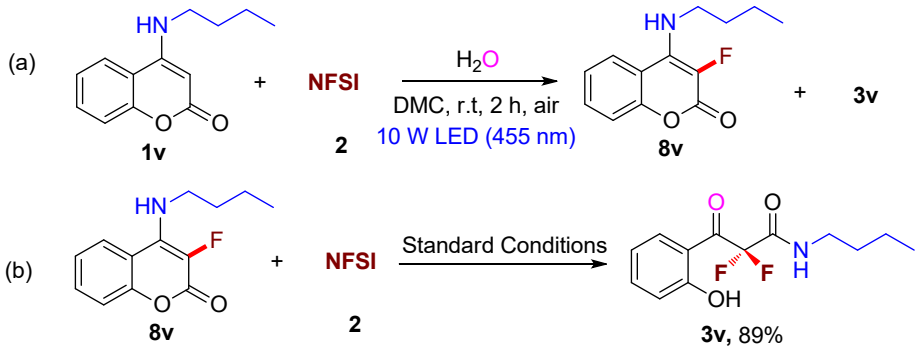
2.3 Active species trapping experiment



MS-analytical Results:

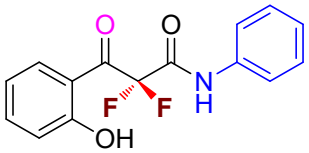


2.4 Control experiments

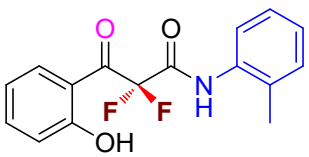


4-(butylamino)-2H-chromen-2-one (**1v**) was selected as the model reactant for the trapping experiment of the intermediate **8v**. Under standard conditions, the intermediate **8v** was successfully isolated and confirmed after 2 h. Furthermore, we found the intermediate **8v** can be further converted into the corresponding α,α-difluoro-β-ketoamide product **3v** under standard conditions.

3. Characterization data of products

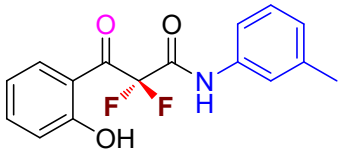


2,2-difluoro-3-(2-hydroxyphenyl)-3-oxo-N-phenylpropanamide **(3a):**[4] yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.24 (s, 1H), 8.18 (s, 1 H), 8.11 (d, J = 8.0 Hz, 1H), 7.56 (t, J = 6.8 Hz, 3H), 7.36 (t, J = 6.4 Hz, 2H), 7.21 (t, J = 6.4 Hz, 1H), 7.03 (t, J = 6.8 Hz, 1H), 6.97 (t, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.5 (t, J = 21.4 Hz), 164.3, 158.9 (t, J = 21.8 Hz), 138.7, 135.6, 131.8 (t, J = 4.6 Hz), 129.3, 126.1, 120.4, 119.8, 118.8, 115.4 (d, J =4.7 Hz), 110.5 (t, J = 214.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.57 ppm; HRMS (ESI) *m/z*: calcd for $C_{15}H_{12}F_2NO_3$ $[M+H]^+$ 292.0785, found 292.0791.

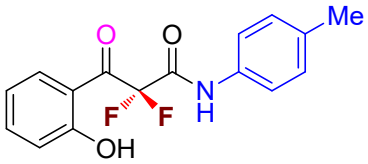


2,2-difluoro-3-(2-hydroxyphenyl)-3-oxo-N-(o-tolyl)propanamide **(3b):** yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.18 (s, 1H), 8.05 (d, J = 6.8 Hz, 1H), 7.86 (s, 1 H), 6.98 (d, J = 6.8 Hz, 1H), 7.50 (t, J = 5.6 Hz, 1H), 7.17-7.09 (m, 3H), 6.97 (d, J =

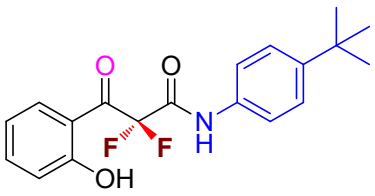
6.8 Hz, 1H), 6.90 (t, J = 6.2 Hz, 1H), 2.21 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.6 (t, J = 22.5 Hz), 163.3, 158.0 (t, J = 21.6 Hz), 137.6, 132.2, 130.8 (t, J = 4.7 Hz), 129.8, 128.8, 126.0, 125.8, 122.1, 118.7, 117.8, 114.4, 114.0, 109.7 (t, J = 213.2 Hz), 16.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.65 ppm; HRMS (ESI) *m/z*: calcd for $C_{16}H_{14}F_2NO_3$ $[M+H]^+$ 306.0942, found 306.0948.



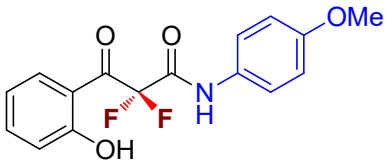
2,2-difluoro-3-(2-hydroxyphenyl)-3-oxo-N-(m-tolyl)propanamide **(3c):** [4] yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.21 (s, 1H), 8.05 (d, J = 7.6 Hz, 1H), 7.97 (s, 1 H), 7.52 (d, J = 6.8 Hz, 1H), 7.36 (s, 1H), 7.00-6.90 (m, 4H), 6.49 (d, J = 8.4 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.5 (t, J = 19.4 Hz), 163.3, 157.7 (t, J = 22.3 Hz), 137.6, 134.5, 130.8, 128.1, 125.9, 119.8, 118.8, 117.8 (d, J = 6.1 Hz), 116.3, 114.9, 110.5 (t, J = 215.5 Hz), 20.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.69 ppm; HRMS (ESI) *m/z*: calcd for $C_{16}H_{14}F_2NO_3$ $[M+H]^+$ 306.0942, found 306.0949.



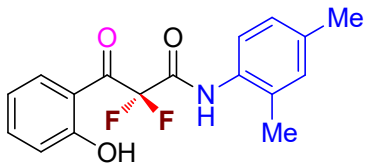
2,2-difluoro-3-(2-hydroxyphenyl)-3-oxo-N-(p-tolyl)propanamide **(3d):**[4] yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.18 (s, 1H), 8.02 (d, J = 7.6 Hz, 2H), 7.49 (t, J = 5.6 Hz, 1H), 7.36 (d, J = 6.8 Hz, 2H), 7.07 (d, J = 6.8 Hz, 2H), 6.94 (t, J = 6.4 Hz, 1H), 6.87 (d, J = 6.4 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.5 (t, J = 21.3 Hz), 164.3, 158.7 (t, J = 21.7 Hz), 138.6, 135.9, 133.0, 131.8 (t, J = 4.6 Hz), 129.8, 120.4, 119.8, 118.8, 115.4, 110.6 (t, J = 212.1 Hz), 21.0; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.59 ppm; HRMS (ESI) *m/z*: calcd for $C_{16}H_{14}F_2NO_3$ $[M+H]^+$ 306.0942, found 306.0950.



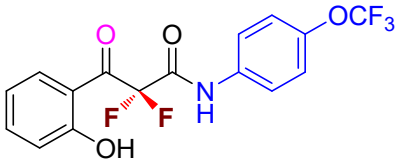
N-(4-(tert-butyl)phenyl)-2,2-difluoro-3-(2-hydroxyphenyl)-3-oxopropanamide **(3e):**[4] yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.18 (s, 1H), 8.03 (d, *J* = 7.6 Hz, 1H), 7.98 (s, 1 H), 7.50 (t, *J* = 6.6 Hz, 1H), 7.42 (d, *J* = 6.8 Hz, 2H), 7.30 (d, *J* = 6.8 Hz, 2H), 6.96 (d, *J* = 6.8 Hz, 1H), 6.90 (t, *J* = 6.2 Hz, 1H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.5 (t, *J* = 21.3 Hz), 163.3, 157.7 (t, *J* = 21.7 Hz), 148.3, 137.6, 131.9, 130.8, 125.1, 119.0, 118.7, 117.8, 114.4, 109.5 (t, *J* = 212.1 Hz), 33.5, 30.2; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.70 ppm; HRMS (ESI) *m/z*: calcd for $C_{19}H_{20}F_2NO_3$ $[M+H]^+$ 348.1411, found 348.1416.



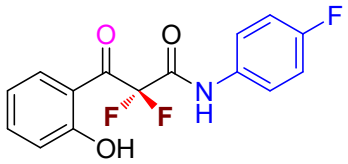
2,2-difluoro-3-(2-hydroxyphenyl)-N-(4-methoxyphenyl)-3-oxopropanamide **(3f):**[4] yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.18 (s, 1H), 8.03 (d, *J* = 7.6 Hz, 1H), 8.01 (s, 1 H), 7.50 (t, *J* = 6.2 Hz, 1H), 7.39 (d, *J* = 6.2 Hz, 2H), 6.95 (d, *J* = 6.8 Hz, 1H), 6.89 (t, *J* = 6.2 Hz, 1H), 6.79 (d, *J* = 6.8 Hz, 2H), 3.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.5 (t, *J* = 21.3 Hz), 163.2, 157.6 (t, *J* = 21.6 Hz), 156.6, 137.6, 130.8, 127.5, 121.1, 118.7, 117.8, 114.4, 113.4, 109.6 (t, *J* = 211.9 Hz), 54.5; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.58 ppm; HRMS (ESI) *m/z*: calcd for $C_{16}H_{14}F_2NO_4$ $[M+H]^+$ 322.0891, found 322.0896.



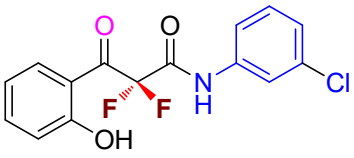
N-(2,4-dimethylphenyl)-2,2-difluoro-3-(2-hydroxyphenyl)-3-oxopropanamide **(3g):** yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.21 (s, 1H), 8.06 (d, *J* = 6.4 Hz, 1H), 7.76 (s, 1 H), 7.19-7.00 (m, 2H), 6.98-6.93 (m, 3H), 6.90 (d, *J* = 6.4 Hz, 1H), 2.23 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.7 (t, *J* = 21.5 Hz), 163.2, 157.9 (t, *J* = 21.4 Hz), 137.6, 135.7, 130.8, 130.5, 129.5, 128.8, 126.5, 122.2, 118.7, 117.8, 114.4, 109.7 (t, *J* = 212.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.72 ppm; HRMS: calcd for $C_{17}H_{16}F_2NO_3$ $[M+H]^+$ 320.1098, found 320.1093.



2,2-difluoro-3-(2-hydroxyphenyl)-3-oxo-N-(4-(trifluoromethoxy)phenyl) propanamide **(3h):** yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.13 (s, 1H), 8.16 (s, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.55-7.50 (m, 3H), 7.14 (d, *J* = 6.8 Hz, 2H), 6.95 (d, *J* = 6.8 Hz, 1H), 6.90 (t, *J* = 6.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.2 (t, *J* = 21.3 Hz), 163.3, 158.0 (t, *J* = 22.0 Hz), 145.6, 137.8, 133.1, 130.6 (t, *J* = 4.8 Hz), 120.9, 120.7, 118.8, 117.9, 114.4, 109.5 (t, *J* = 212.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.58 ppm; HRMS (ESI) *m/z*: calcd for $C_{16}H_{11}F_5NO_4$ $[M+H]^+$ 376.0608, found 376.0614.

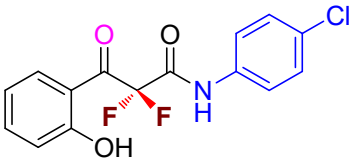


2,2-difluoro-N-(4-fluorophenyl)-3-(2-hydroxyphenyl)-3-oxopropanamide **(3i):**[4] yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.15 (s, 1H), 8.09 (s, 1H), 8.02 (d, *J* = 7.6 Hz, 1H), 7.51 (t, *J* = 8.8 Hz, 1H), 7.48-7.45 (m, 2H), 6.98 (t, *J* = 7.0 Hz, 3H), 6.90 (t, *J* = 6.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.4 (t, *J* = 21.4 Hz), 164.3, 160.4 (d, *J* = 159.8 Hz), 158.9 (t, *J* = 21.9 Hz), 138.8, 131.7 (t, *J* = 4.8 Hz), 131.6 (d, *J* = 2.4 Hz), 122.3 (d, *J* = 6.5 Hz), 119.8, 118.9, 116.1 (d, *J* =18.1 Hz), 115.4, 110.6 (t, *J* = 212.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.53, -115.13 ppm; HRMS (ESI) *m/z*: calcd for $C_{15}H_{11}F_3NO_3$ $[M+H]^+$ 310.0691, found 310.0695.

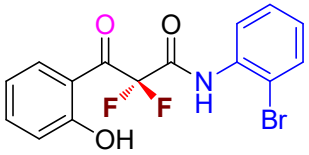


N-(3-chlorophenyl)-2,2-difluoro-3-(2-hydroxyphenyl)-3-oxopropanamide **(3j):**[4] yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.13 (s, 1H), 8.02 (d, *J* = 6.0 Hz, 2H), 7.63 (s, 1H), 7.52 (t, *J* = 6.2 Hz, 1H), 7.34 (d, *J* = 7.2 Hz, 1H), 7.22 (t, *J* = 6.4 Hz, 1H), 6.97 (d, *J* = 6.8 Hz, 1H), 6.97 (d, *J* = 6.8 Hz, 1H), 6.92 (t, *J* = 6.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.2 (t, *J* = 21.2 Hz), 163.4, 159.0 (t, *J* = 21.9 Hz), 138.8,

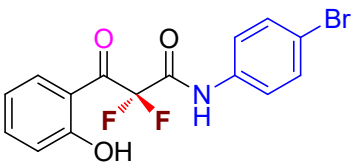
136.7, 135.1, 133.8, 130.3 (t, J = 4.8 Hz), 126.4, 120.6, 119.8, 118.9, 118.3, 115.4, 110.5 (t, J = 212.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.53 ppm; HRMS (ESI) *m/z*: calcd for $C_{15}H_{11}ClF_2NO_3$ $[M+H]^+$ 326.0396, found 326.0401.



N-(4-chlorophenyl)-2,2-difluoro-3-(2-hydroxyphenyl)-3-oxopropanamide **(3k):**[4] yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.14 (s, 1H), 8.07 (s, 1H), 8.02 (d, J = 6.4 Hz, 1H), 7.52 (t, J = 6.4 Hz, 1H), 7.45 (d, J = 7.2 Hz, 2H), 7.25 (d, J = 7.2 Hz, 2H), 6.97 (d, J = 6.8 Hz, 1H), 6.91 (d, J = 6.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.3 (t, J = 21.4 Hz), 163.3, 157.9 (t, J = 21.9 Hz), 137.8, 133.1, 130.6 (t, J = 4.8 Hz), 128.4, 120.6, 118.8, 117.9, 114.3, 109.5 (t, J = 212.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.50 ppm; HRMS (ESI) *m/z*: calcd for $C_{15}H_{11}ClF_2NO_3$ $[M+H]^+$ 326.0396, found 326.0399.

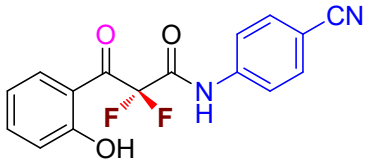


N-(2-bromophenyl)-2,2-difluoro-3-(2-hydroxyphenyl)-3-oxopropanamide **(3l):** yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.14 (s, 1H), 8.08 (s, 1H), 8.03 (d, J = 6.8 Hz, 1H), 7.65-7.46 (m, 4H), 7.26 (d, J = 6.8 Hz, 1H), 6.98 (d, J = 6.4 Hz, 1H), 6.91 (t, J = 6.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.3 (t, J = 20.9 Hz), 163.4, 157.8 (t, J = 22.0 Hz), 137.8, 133.2, 131.3, 130.7 (t, J = 4.8 Hz), 129.9, 128.3, 128.1, 120.6, 118.8, 117.9, 114.4, 109.5 (t, J = 212.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.53 ppm; HRMS (ESI) *m/z*: calcd for $C_{15}H_{11}BrF_2NO_3$ $[M+H]^+$ 369.9890, found 369.9895.

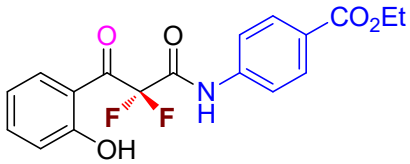


N-(4-bromophenyl)-2,2-difluoro-3-(2-hydroxyphenyl)-3-oxopropanamide **(3m):**[4] yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.14 (s, 1H), 8.06 (s, 1H), 8.02 (d, J

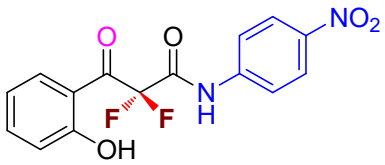
= 6.4 Hz, 1H), 7.52 (t, *J* = 6.2 Hz, 1H), 7.41 (s, 4H), 6.97 (d, *J* = 6.4 Hz, 1H), 6.91 (d, *J* = 6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.3 (t, *J* = 21.3 Hz), 163.3, 157.8 (t, *J* = 21.9 Hz), 137.8, 133.6, 131.3, 130.7 (t, *J* = 4.8 Hz), 128.3, 120.9, 118.8, 117.8, 114.3, 109.5 (t, *J* = 212.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.50 ppm; HRMS (ESI) *m/z*: calcd for $C_{15}H_{11}BrF_2NO_3$ $[M+H]^+$ 369.9890, found 369.9896.



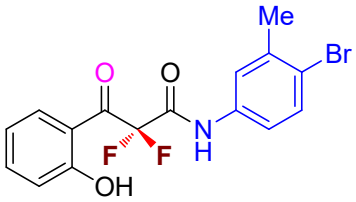
N-(4-cyanophenyl)-2,2-difluoro-3-(2-hydroxyphenyl)-3-oxopropanamide **(3n):** yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.44 (s, 1H), 9.10 (s, 1H), 8.71 (d, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 6.8 Hz, 2H), 7.62-7.53 (m, 3H), 7.00-6.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.7 (t, *J* = 21.2 Hz), 163.7, 157.4 (t, *J* = 21.4 Hz), 139.3, 138.0 (d, *J* = 5.5 Hz), 132.7 (d, *J* = 5.3 Hz), 132.5, 128.1, 126.7, 119.3, 119.1, 118.9, 117.8, 115.9, 109.5 (t, *J* = 212.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.36 ppm; HRMS (ESI) *m/z*: calcd for $C_{16}H_{11}F_2N_2O_3$ $[M+H]^+$ 317.0738, found 317.0746.



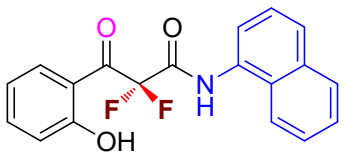
Ethyl 4-(2,2-difluoro-3-(2-hydroxyphenyl)-3-oxopropanamido)benzoate **(3o):** yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.10 (s, 1H), 8.42(s, 1H), 8.02-7.96 (m, 3H), 7.61 (d, *J* = 6.8 Hz, 2H), 7.51 (t, *J* = 6.2 Hz, 1H), 6.96 (d, *J* = 6.8 Hz, 1H), 6.90 (t, *J* = 6.2 Hz, 1H), 4.31-4.27 (m, 2H), 1.31 (t, *J* = 5.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.2 (t, *J* = 21.4 Hz), 164.8, 163.3, 158.1 (t, *J* = 22.2 Hz), 138.7, 137.8, 134.8, 132.7, 130.6 (t, *J* = 4.8 Hz), 130.5, 129.9, 128.0, 126.6 (d, *J* = 4.6 Hz), 118.8, 118.7, 117.9, 114.3, 113.3, 109.5 (t, *J* = 212.6 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.34 ppm; HRMS (ESI) *m/z*: calcd for $C_{18}H_{16}F_2NO_5$ $[M+H]^+$ 364.0997, found 364.1002.



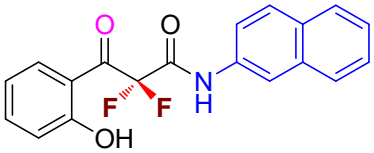
2,2-difluoro-3-(2-hydroxyphenyl)-N-(4-nitrophenyl)-3-oxopropanamide **(3p):** yellow solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.09 (s, 1H), 8.36 (s, 1H), 8.20 (d, *J* = 7.2 Hz, 2H), 7.74 (d, *J* = 7.2 Hz, 2H), 7.57-7.52 (m, 2H), 6.99 (d, *J* = 6.8 Hz, 1H), 6.55 (d, *J* = 7.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.9 (t, *J* = 20.5 Hz), 163.5, 158.3 (t, *J* = 22.3 Hz), 151.4, 143.9, 140.2, 138.1, 134.8, 130.6 (t, *J* = 4.8 Hz), 128.8, 128.5, 125.3, 124.2, 119.1, 118.0, 114.2, 109.5 (t, *J* = 212.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.34 ppm; HRMS (ESI) *m/z*: calcd for $C_{15}H_{11}F_2N_2O_5$ $[M+H]^+$ 337.0636, found 337.0640.



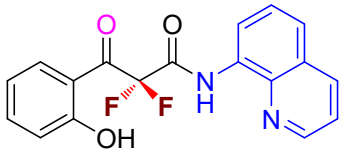
N-(4-bromo-3-methylphenyl)-2,2-difluoro-3-(2-hydroxyphenyl)-3-oxopropanamide **(3q):** yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.2 (s, 1H), 8.03 (d, *J* = 6.4 Hz, 1H), 7.90 (s, 1H), 7.52 (d, *J* = 6.0 Hz, 1H), 7.50-7.43 (m, 2H), 7.21-7.19 (m, 1H), 6.98 (d, *J* = 6.8 Hz, 1H), 6.92 (t, *J* = 6.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.3 (t, *J* = 20.1 Hz), 163.3, 158.3 (t, *J* = 22.5 Hz), 138.2, 137.8, 133.7, 132.0, 130.7, 121.4, 120.5, 118.8, 118.2, 117.9, 114.4, 109.5 (t, *J* = 212.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.56 ppm; HRMS (ESI) *m/z*: calcd for $C_{16}H_{13}BrF_2NO_3$ $[M+H]^+$ 384.0047, found 384.0053.



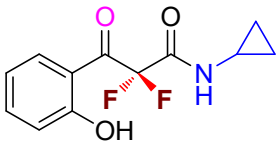
2,2-difluoro-3-(2-hydroxyphenyl)-N-(naphthalen-1-yl)-3-oxopropanamide **(3r):** yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.22 (s, 1H), 8.39 (s, 1H), 8.10 (d, *J* = 6.8 Hz, 1H), 7.82 (d, *J* = 5.6 Hz, 2H), 7.82-7.70 (m, 2H), 7.53-7.39 (m, 4H), 6.98 (d, *J* = 6.8 Hz, 1H), 6.91 (d, *J* = 6.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.6 (t, *J* = 21.3 Hz), 163.5, 158.6 (t, *J* = 21.6 Hz), 137.7, 133.0, 130.8, 128.7, 127.8 (d, *J* = 4.8 Hz), 126.5, 126.0, 125.5, 124.5, 120.4, 119.1, 118.8, 117.8, 114.4, 109.9 (t, *J* = 209.5 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.34 ppm; HRMS (ESI) *m/z*: calcd for $C_{19}H_{14}F_2NO_3$ $[M+H]^+$ 342.0942, found 342.0948.



2,2-difluoro-3-(2-hydroxyphenyl)-N-(naphthalen-2-yl)-3-oxopropanamide **(3s):** yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.21 (s, 1H), 8.18 (d, *J* = 6.8 Hz, 1H), 8.16 (s, 1H), 8.09 (d, *J* = 6.4 Hz, 1H), 7.79-7.73 (m, 3H), 7.54-7.43 (m, 4H), 7.41-6.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 184.4 (t, *J* = 21.3 Hz), 163.3, 158.3 (t, *J* = 21.7 Hz), 137.7, 132.4, 131.9, 130.8 (t, *J* = 4.7 Hz), 130.3, 128.3, 126.8, 126.6, 126.0, 125.0, 118.9, 118.3, 117.8, 116.8, 114.4, 109.5 (t, *J* = 204.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.52 ppm; HRMS (ESI) *m/z*: calcd for $C_{19}H_{14}F_2NO_3$ $[M+H]^+$ 342.0942, found 342.0947.

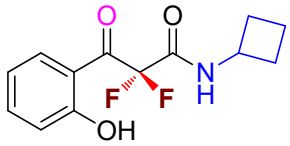


2,2-difluoro-3-(2-hydroxyphenyl)-3-oxo-N-(quinolin-8-yl)propanamide **(3t):** yellowish solid, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.25 (s, 1H), 10.83 (s, 1H), 8.81 (d, *J* = 4.8 Hz, 1H), 8.65 (d, *J* = 6.0 Hz, 1H), 8.15-8.08 (m, 2H), 7.58-7.44 (m, 4H), 6.98 (d, *J* = 7.2 Hz, 1H), 6.91 (t, *J* = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.5 (t, *J* = 21.7 Hz), 163.2, 158.3 (t, *J* = 19.8 Hz), 147.9, 137.4, 135.4, 134.2, 131.4, 130.5 (t, *J* = 4.8 Hz), 126.9, 126.0, 124.0, 122.6, 121.3, 120.3, 118.7, 117.8, 116.4, 115.0, 109.3 (t, *J* = 202.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.36 ppm; HRMS (ESI) *m/z*: calcd for $C_{18}H_{13}F_2N_2O_3$ $[M+H]^+$ 343.0894, found 343.0898.

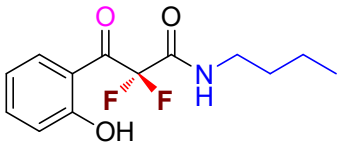


N-cyclopropyl-2,2-difluoro-3-(2-hydroxyphenyl)-3-oxopropanamide **(3u):** yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.18 (s, 1H), 7.99 (d, *J* = 6.8 Hz, 1H), 7.51 (t, *J* = 6.0 Hz, 1H), 6.98-6.90 (m, 2H), 6.49 (s, 1H), 2.78-2.72 (m, 1H), 0.82-0.78 (m, 1H), 0.59-0.56 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.6 (t, *J* = 21.3 Hz), 163.1, 161.2 (t, *J* = 21.6 Hz), 137.5, 130.9, 130.8 (t, *J* = 4.5 Hz), 129.9, 127.8, 118.6, 117.7, 114.4,

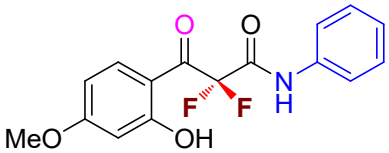
109.5 (t, J = 211.2 Hz), 21.9, 5.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -107.06 ppm; HRMS (ESI) *m/z*: calcd for $C_{12}H_{12}F_2NO_3$ $[M+H]^+$ 256.0785, found 256.0791.



N-cyclobutyl-2,2-difluoro-3-(2-hydroxyphenyl)-3-oxopropanamide **(3v):** yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.18 (s, 1H), 7.47 (d, J = 6.8 Hz, 1H), 7.43 (t, J = 6.2 Hz, 1H), 7.24 (t, J = 5.6 Hz, 2H), 6.19 (s, 1H), 4.45-4.38 (m, 1H), 2.43-2.00 (m, 2H), 1.99-1.95 (m, 2H), 1.80-1.69 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.9 (t, J = 21.3 Hz), 163.2, 160.1 (t, J = 21.4 Hz), 137.5, 130.9, 118.6, 117.8, 114.5, 109.6 (t, J = 210.9 Hz), 49.2, 31.4, 30.6, 13.4; ^{19}F NMR (376 MHz, $CDCl_3$) δ -107.03 ppm; HRMS (ESI) *m/z*: calcd for $C_{13}H_{14}F_2NO_3$ $[M+H]^+$ 270.0942, found 270.0948.

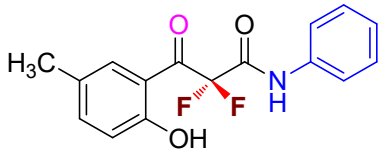


N-butyl-2,2-difluoro-3-(2-hydroxyphenyl)-3-oxopropanamide **(3w):** yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.12 (s, 1H), 7.99 (d, J = 6.8 Hz, 1H), 7.50 (t, J = 6.0 Hz, 1H), 6.95 (d, J = 6.8 Hz, 1H), 6.89 (t, J = 6.2 Hz, 1H), 6.42 (s, 1H), 3.31-3.27 (m, 2H), 1.52-1.46 (m, 2H), 1.31-1.27 (m, 2H), 0.86 (t, J = 5.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.8 (t, J = 20.5 Hz), 163.1, 160.1 (t, J = 21.5 Hz), 137.4, 130.8, 118.6, 117.7, 114.5, 109.5 (t, J = 211.0 Hz), 38.8, 30.1, 18.8, 12.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -107.06 ppm; HRMS (ESI) *m/z*: calcd for $C_{13}H_{16}F_2NO_3$ $[M+H]^+$ 272.1098, found 272.1103.

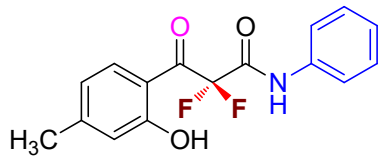


2,2-difluoro-3-(2-hydroxy-4-methoxyphenyl)-3-oxo-N-phenylpropanamide **(3x):**[4] yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 11.73 (s, 1H), 8.06 (s, 1H), 7.96 (d, J = 7.2 Hz, 1H), 7.48 (d, J = 6.4 Hz, 2H), 7.27 (d, J = 6.4 Hz, 2H), 7.11 (t, J = 5.8 Hz, 1H), 6.42 (d, J = 6.8 Hz, 1H), 6.42 (d, J = 2.0 Hz, 1H), 3.78 (s, 3H); ^{13}C NMR (100 MHz,

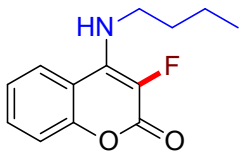
$CDCl_3$): δ 187.0 (t, *J* = 21.4 Hz), 166.7 (d, *J* = 26.5 Hz), 158.1 (t, *J* = 22.0 Hz), 134.7, 132.6, 128.2, 124.9, 111.9, 109.5 (t, *J* = 215.5 Hz), 108.6, 108.2, 107.6, 54.8; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.91 ppm; HRMS (ESI) *m/z*: calcd for $C_{16}H_{14}F_2NO_4$ $[M+H]^+$ 322.0891, found 322.0898.



2,2-difluoro-3-(2-hydroxy-5-methylphenyl)-3-oxo-N-phenylpropanamide **(3y):** yellowish solid, ^1H NMR (400 MHz, $CDCl_3$): δ 11.04 (s, 1H), 8.01 (s, 1H), 7.81 (s, 1H), 7.49 (d, *J* = 6.4 Hz, 2H), 7.34-7.28 (m, 2H), 7.14 (t, *J* = 5.8 Hz, 1H), 6.87 (d, *J* = 6.8 Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.3 (t, *J* = 21.4 Hz), 161.4, 157.9 (t, *J* = 22.2 Hz), 139.0, 134.6, 130.1 (d, *J* = 4.8 Hz), 128.3, 128.0, 125.1, 119.3, 117.5, 114.1, 109.6 (t, *J* = 212.1 Hz), 19.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.48 ppm; HRMS (ESI) *m/z*: calcd for $C_{16}H_{14}F_2NO_3$ $[M+H]^+$ 306.0942, found 306.0948.



2,2-difluoro-3-(2-hydroxy-4-methylphenyl)-3-oxo-N-phenylpropanamide **(3z):**[4] yellow solid, ^1H NMR (400 MHz, $CDCl_3$): δ 11.24 (s, 1H), 7.99 (s, 1H), 7.92 (d, *J* = 6.4 Hz, 1H), 7.49 (d, *J* = 6.8 Hz, 2H), 7.30 (t, *J* = 5.8 Hz, 2H), 7.14 (t, *J* = 5.8 Hz, 1H), 7.78 (s, 1H), 6.71 (d, *J* = 6.8 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 188.6 (t, *J* = 21.4 Hz), 163.5, 157.9 (t, *J* = 22.2 Hz), 150.1, 134.6, 130.6 (d, *J* = 4.8 Hz), 128.3, 125.0, 120.3, 119.3, 117.7, 112.3, 109.6 (t, *J* = 212.0 Hz), 21.3; ^{19}F NMR (376 MHz, $CDCl_3$) δ -106.82 ppm; HRMS (ESI) *m/z*: calcd for $C_{16}H_{14}F_2NO_3$ $[M+H]^+$ 306.0942, found 306.0947.



4-(butylamino)-3-fluoro-2H-chromen-2-one **(8v):** yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48-7.43 (m, 2H), 7.25 (t, *J* = 5.8 Hz, 2H), 4.89 (s, 1H), 3.62-3.58 (m, 2H), 1.65-1.62 (m, 2H), 1.40-1.37 (m, 2H), 0.90 (t, *J* = 5.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.3 (d, *J* = 19.1 Hz), 148.9, 136.1, 129.9, 128.6, 126.7, 123.2, 119.7 (d, *J* = 4.1 Hz), 114.2, 44.1, 31.7, 18.9, 12.7; ^{19}F NMR (376 MHz, $CDCl_3$) δ -169.3 ppm; HRMS (ESI) *m/z*: calcd for $C_{13}H_{15}FNO_2$ $[M+H]^+$ 236.1087, found 236.1092.

4. References

[1] Y. Y. Weng, H. Zhou, C. Sun, Y. Y. Xie, W. K. Su, J. Org. Chem., 2017, 82, 9047−9053.

[2] Y. Y. Weng, H. T. Chen, N. H. Li, L. Yang, L. Ackermann, Adv. Synth. Catal. 2021, 363, 1-6.

[3] C. Cheng, W.-W. Chen, B. Xu, M.-H. Xu, Org. Chem. Front. 2016, 3, 1111−1115.

[4] W. Q. Chen, H.-J. Li, M. Liu, P.-X. Gong, Y.-C. Wu, Org. Chem. Front. 2021, 8, 6636−6641.

5. X-ray Crystallographic Data for 3z

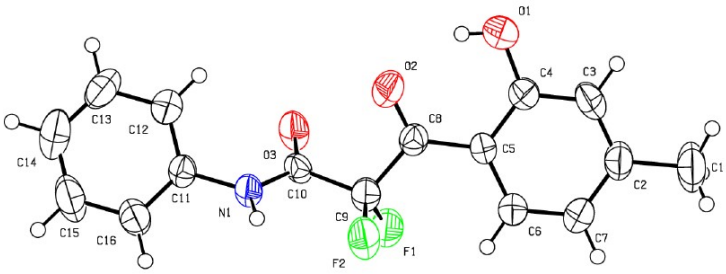


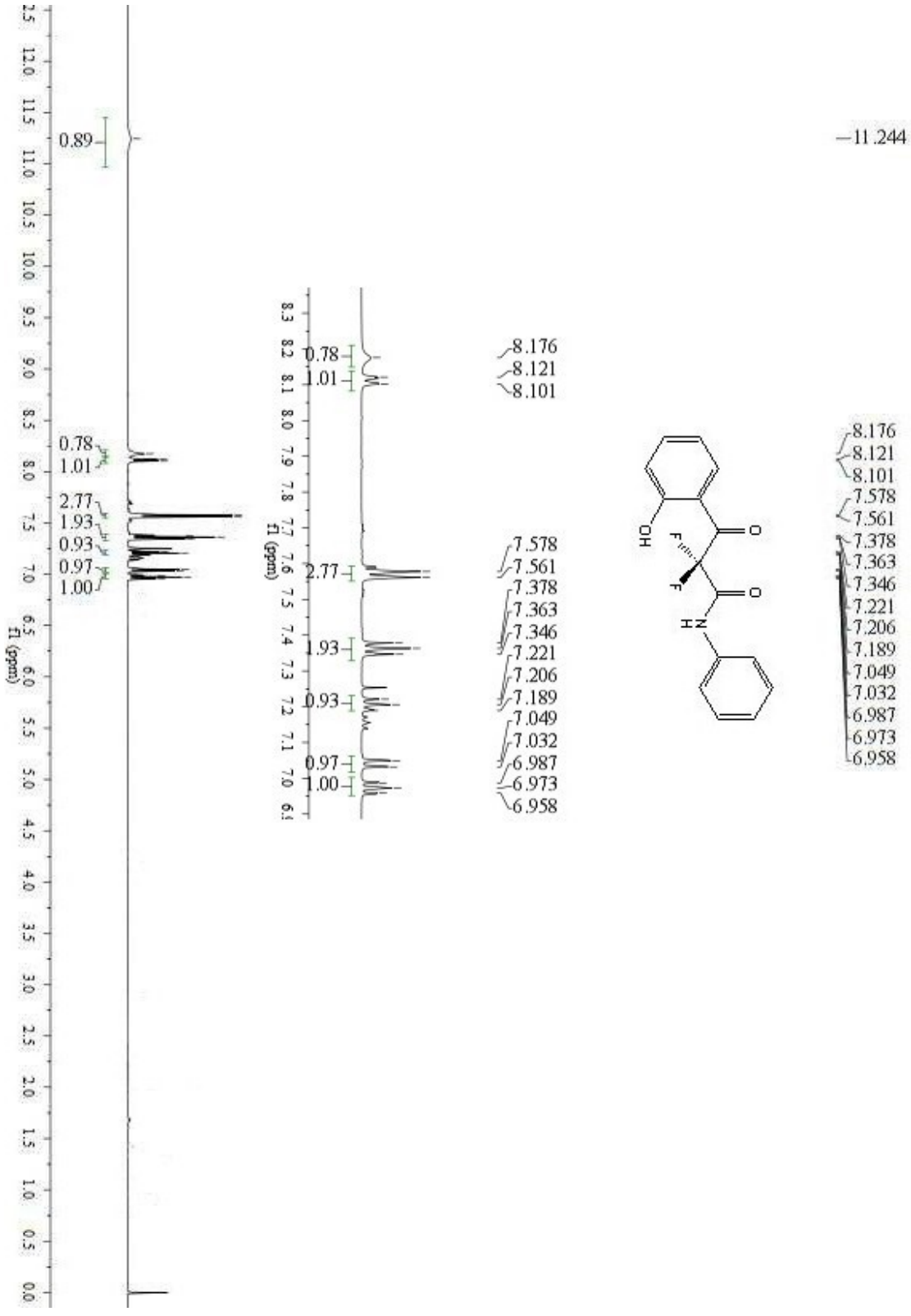
Figure S3. X-Ray crystal structure of **3z**

Table S1. Crystal data and structure refinement for **3z**

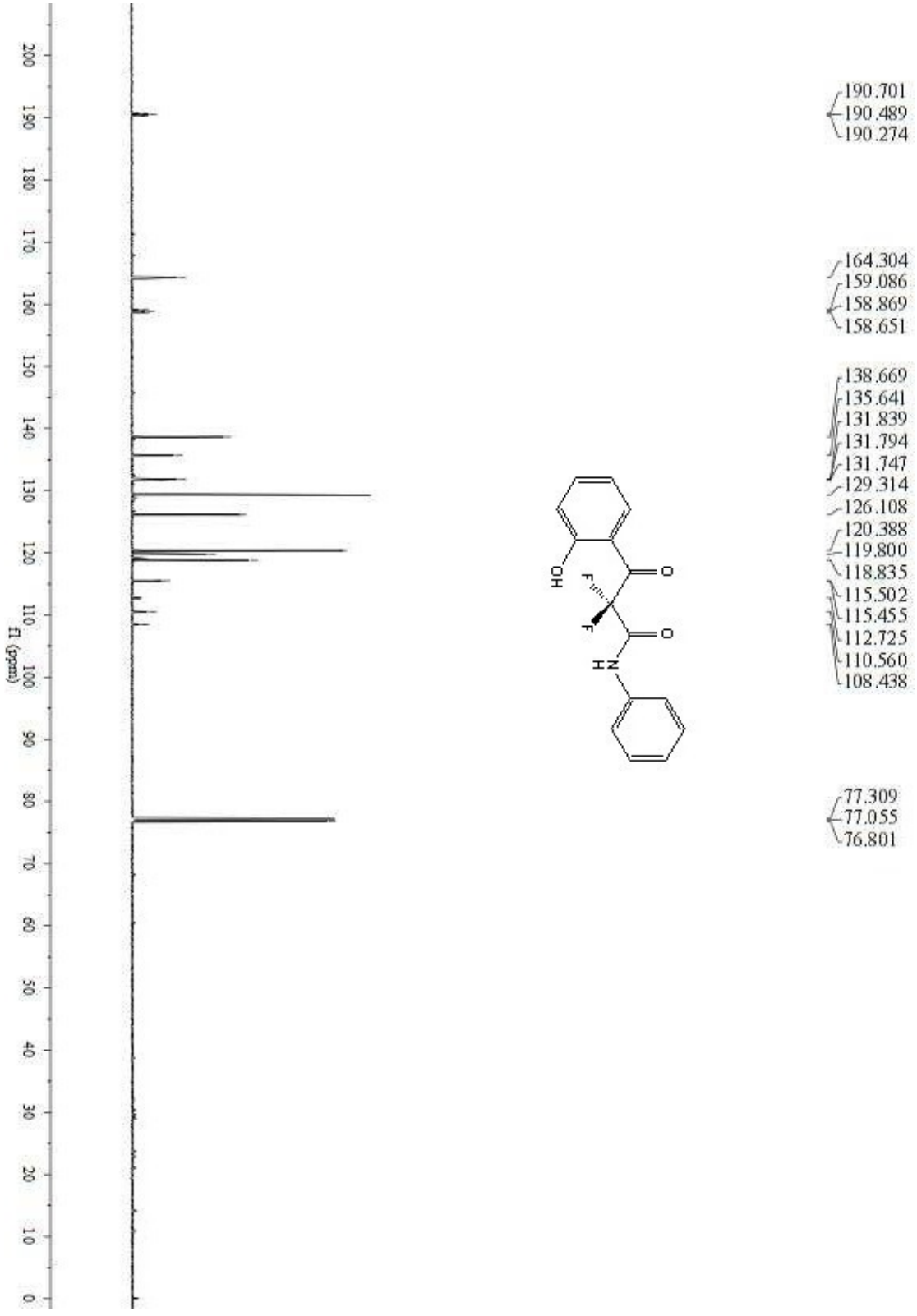
CCDC number	2175985
Empirical formula	$C_{16}H_{13}F_2NO_3$
Formula weight	305.27
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P 1 21/c 1
Unit cell dimensions	a = 5.0257(15) Å alpha = 90°. b = 17.525(5) Å beta = 92.944(10) °. c = 16.304(5) Å gamma = 90°.
Volume	1434.1(7) Å 3
Z	4
Calculated density	1.414 g/cm^3
Absorption coefficient	0.115 mm^{-1}
F(000)	632
Theta range for data collection	3.416 to 27.813°
Limiting indices	$-6 \le h \le 6$, $-22 \le k \le 22$, $-21 \le l \le 21$
Reflections collected	30190
Independent reflections	3368 [R_{int} = 0.1184]
Max. and min. transmission	0.7456 and 0.7017
Data / restraints / parameters	3368 / 0 / 201
Goodness-of-fit on F_2	1.007
Final R indices [I>=2σ (I)]	R_1 = 0.0630, wR_2 = 0.1172
R indices (all data)	R_1 = 0.1844, wR_2 = 0.1520
Largest diff. peak and hole	0.177 and -0.227 e Å^{-3}

CCDC-2175985 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

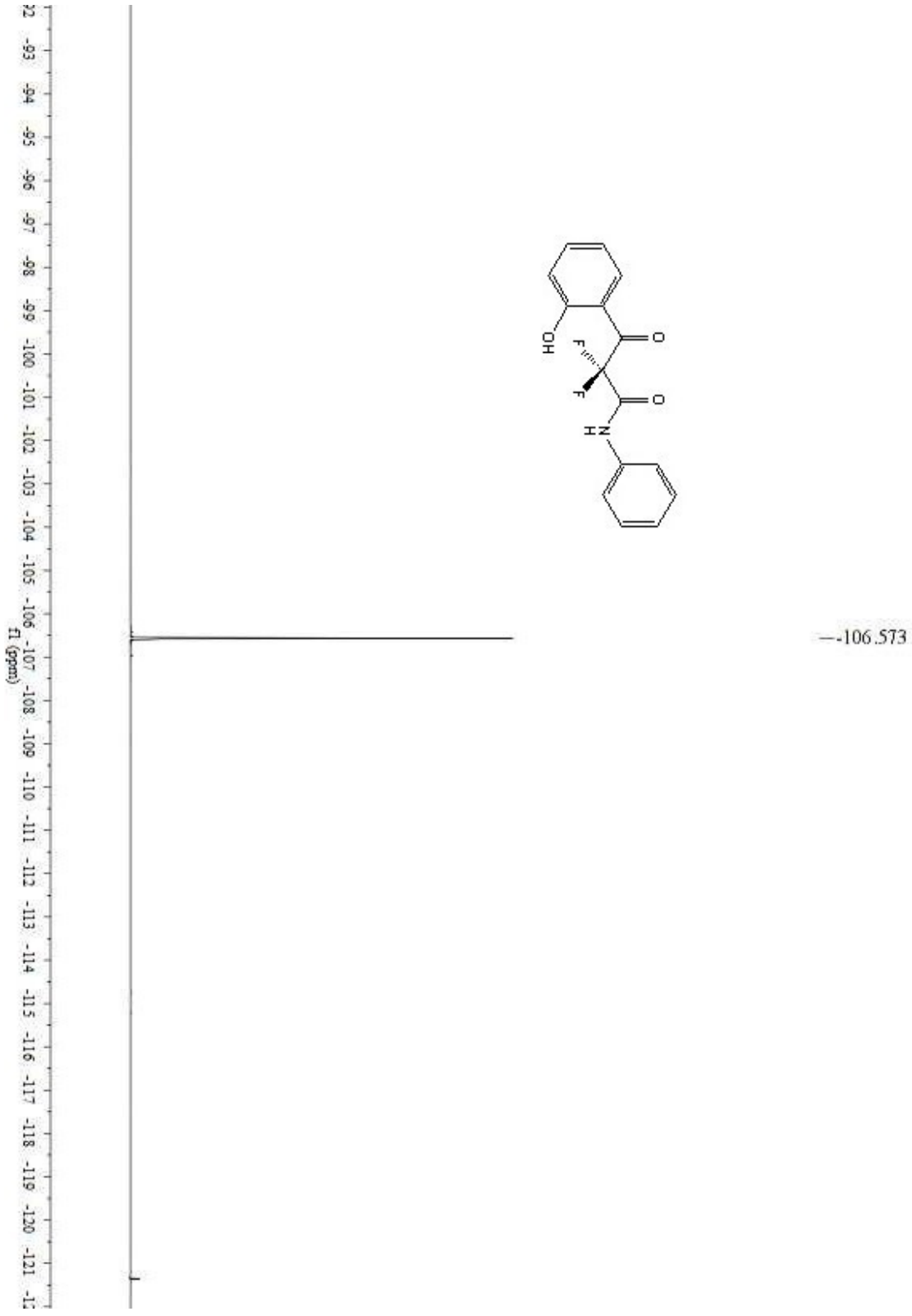
6. ^{1}H and ^{13}C NMR spectra of products



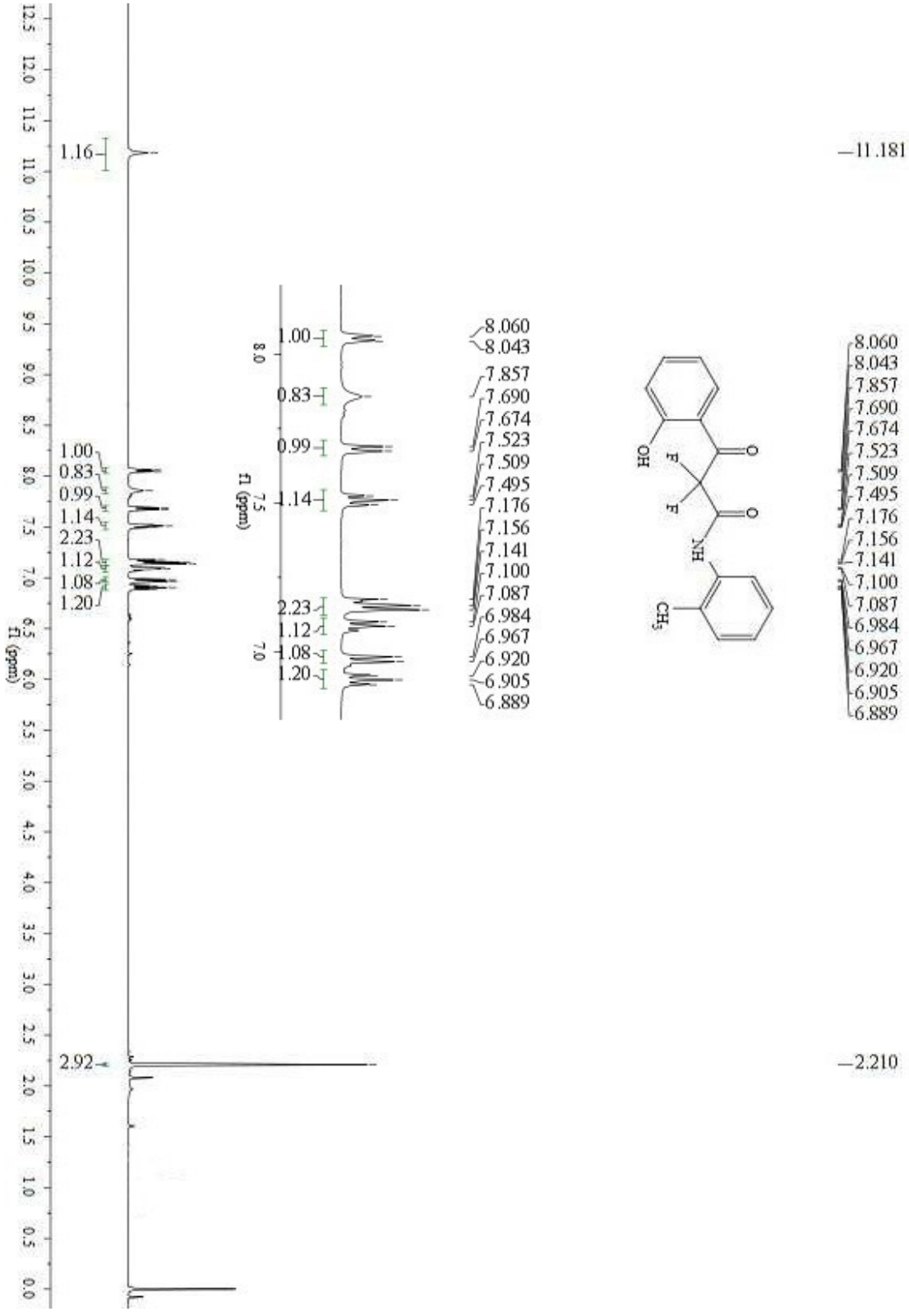
^{1}H NMR of **3a** in $CDCl_3$



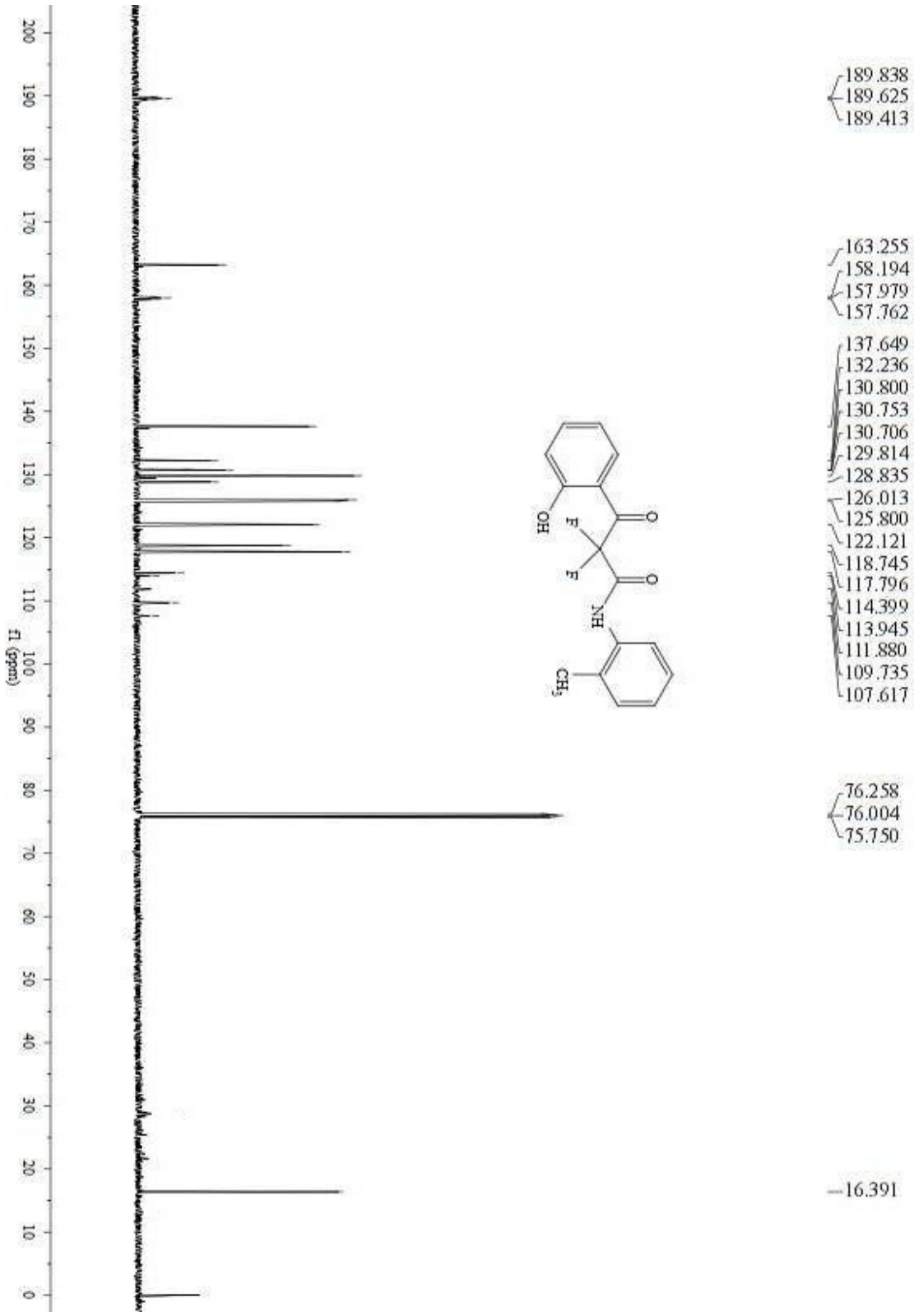
^{13}C NMR of **3a** in $CDCl_3$



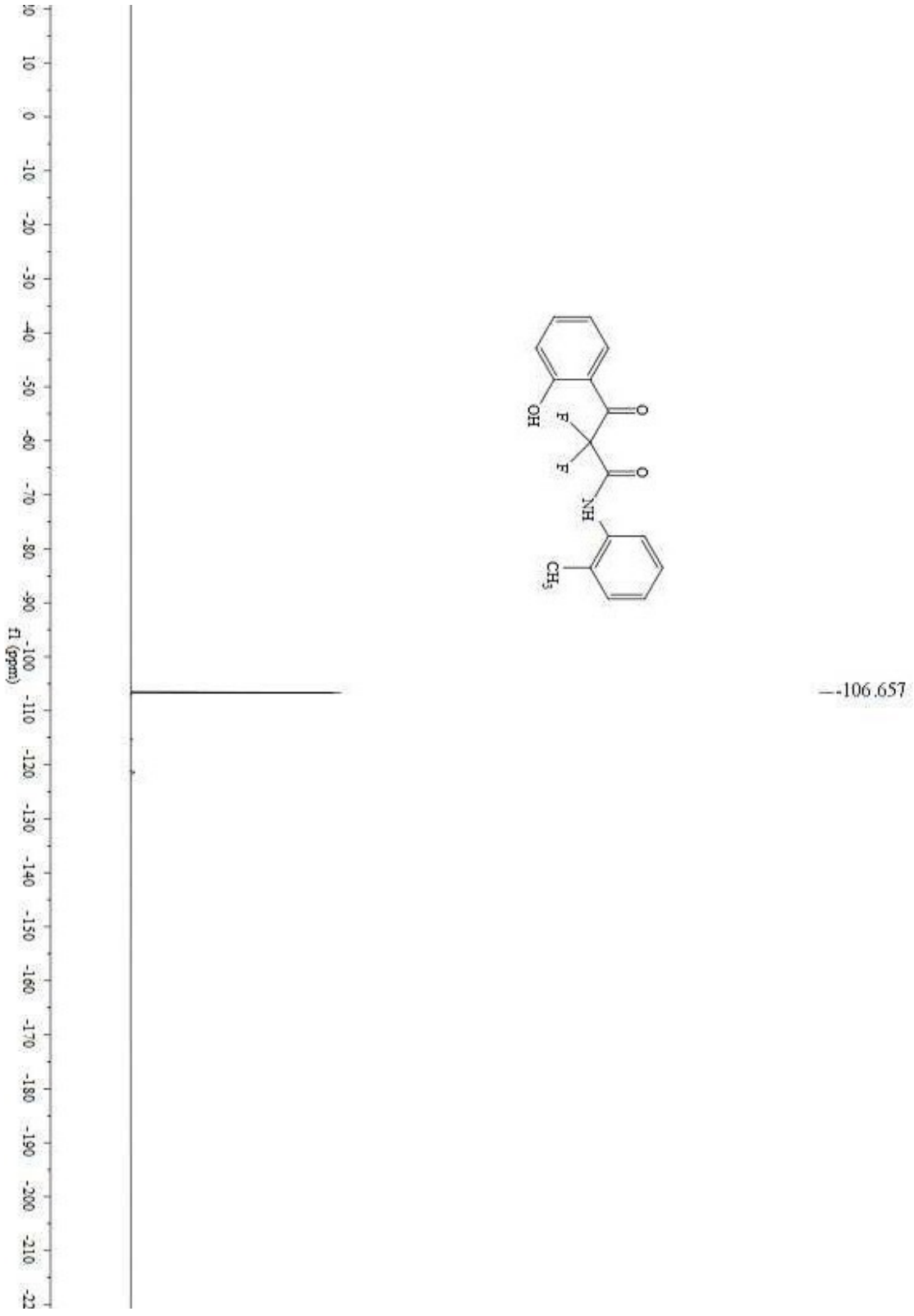
^{19}F NMR of **3a** in $CDCl_3$



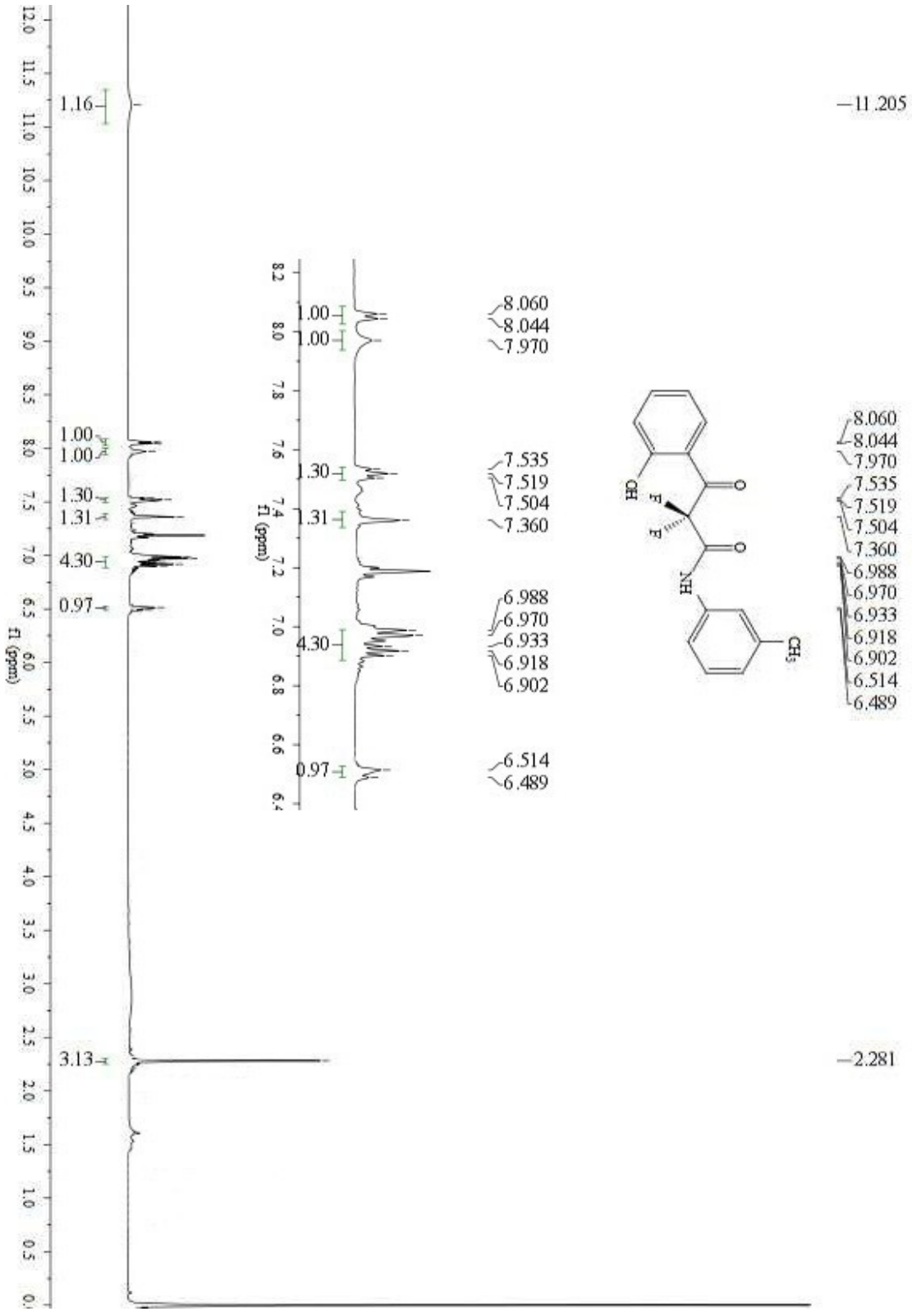
^{1}H NMR of **3b** in $CDCl_3$



^{13}C NMR of **3b** in $CDCl_3$



^{19}F NMR of **3b** in $CDCl_3$



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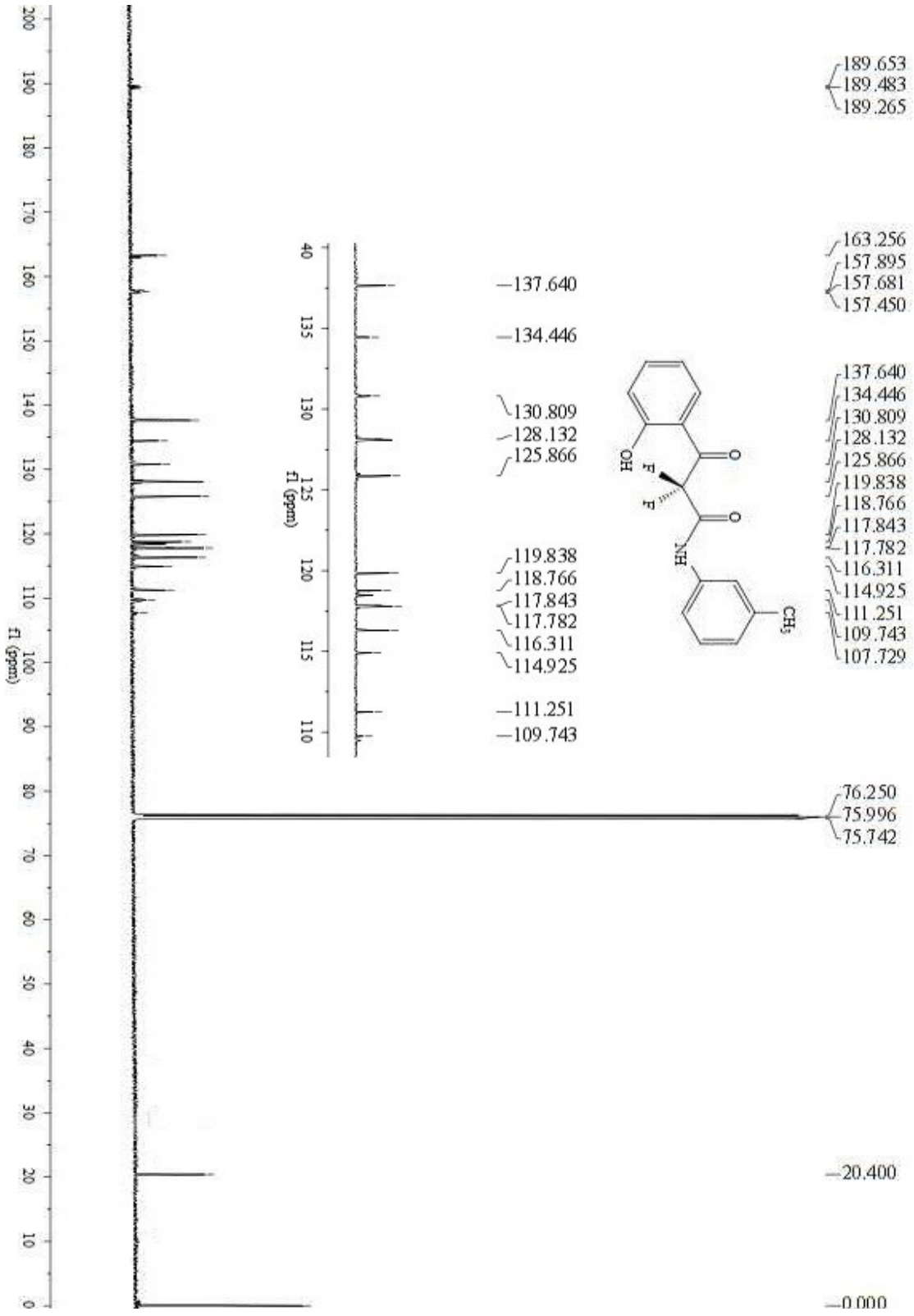
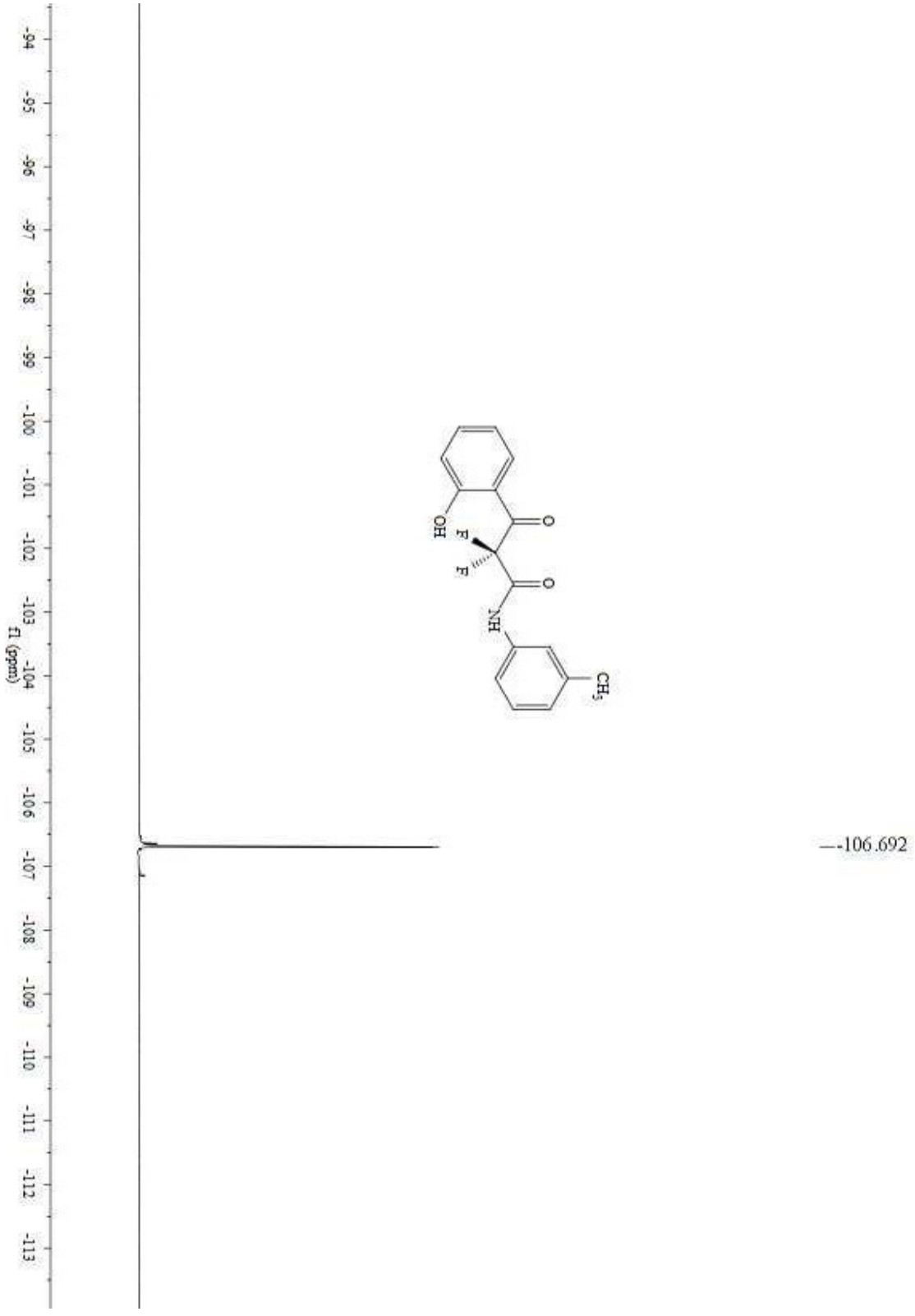
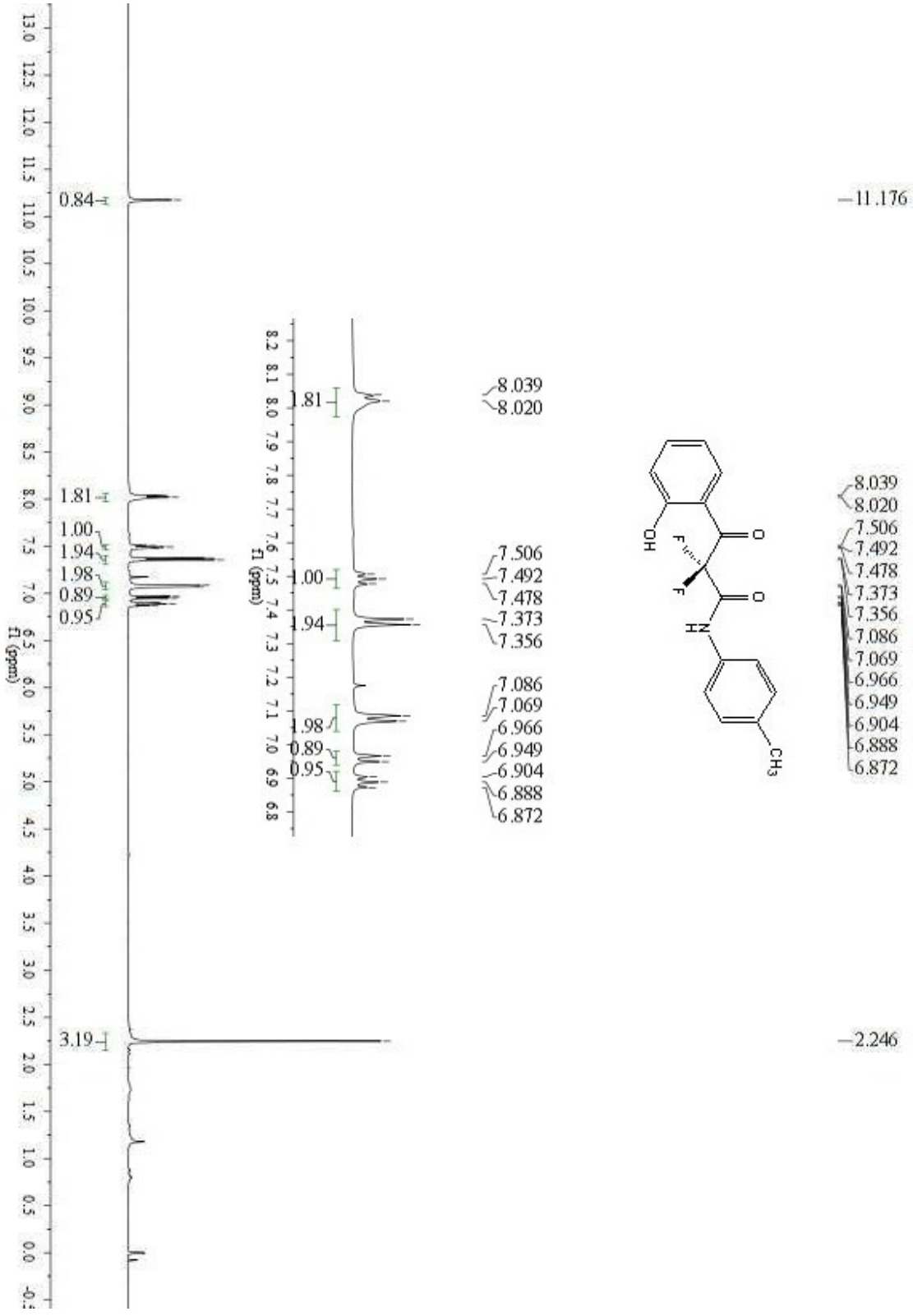


^{13}C NMR of **3c** in $CDCl_3$



^{19}F NMR of **3c** in $CDCl_3$



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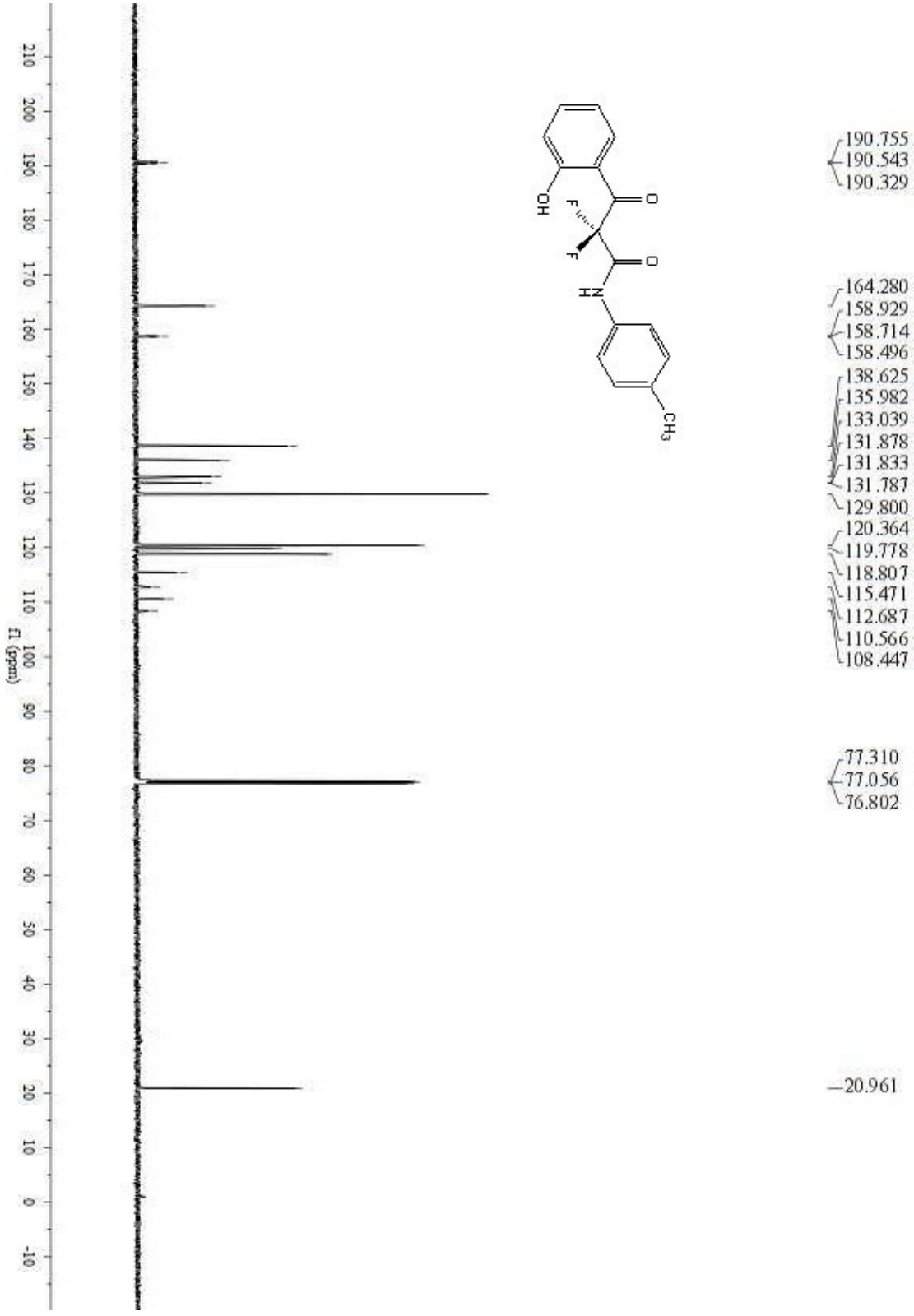
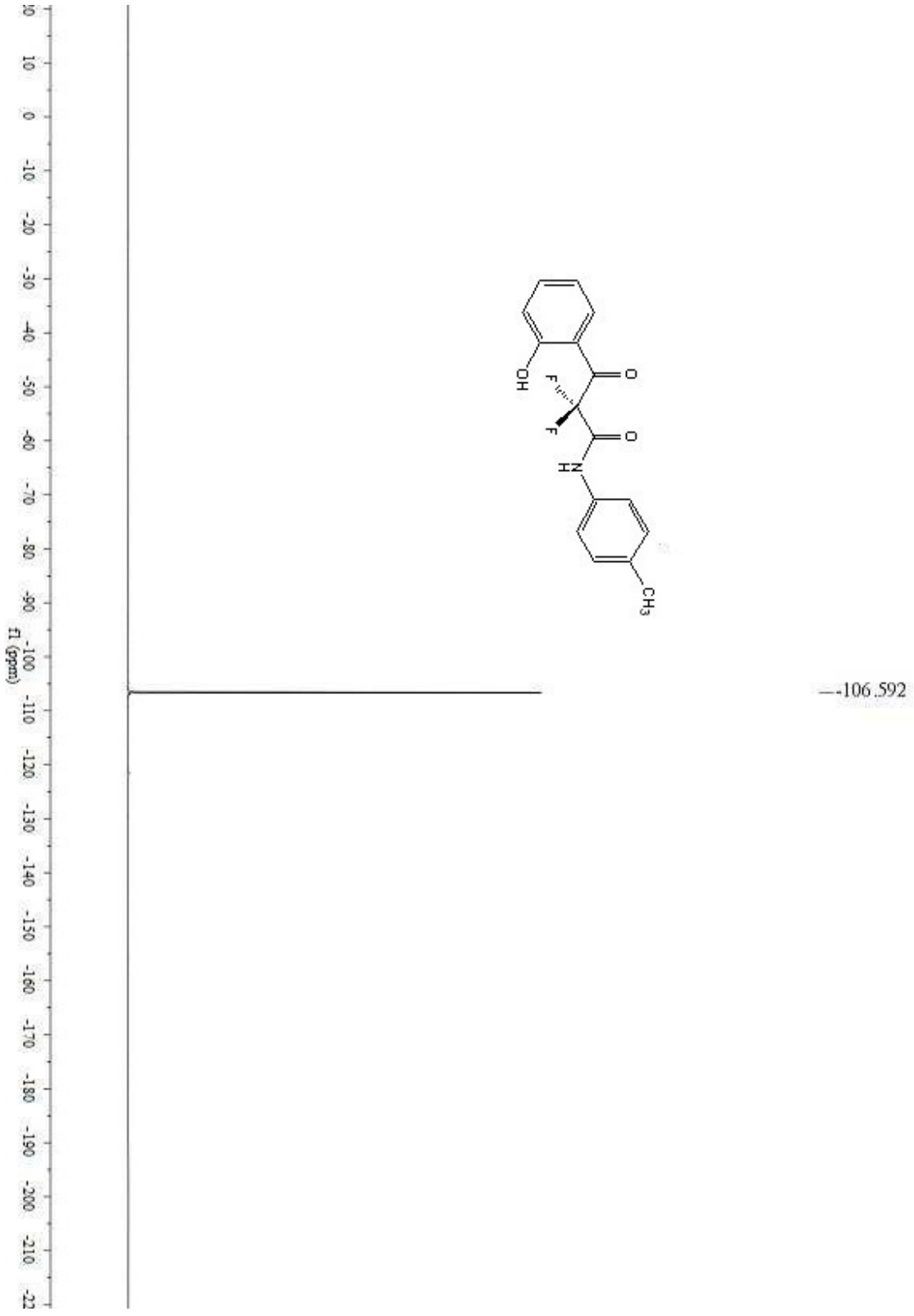
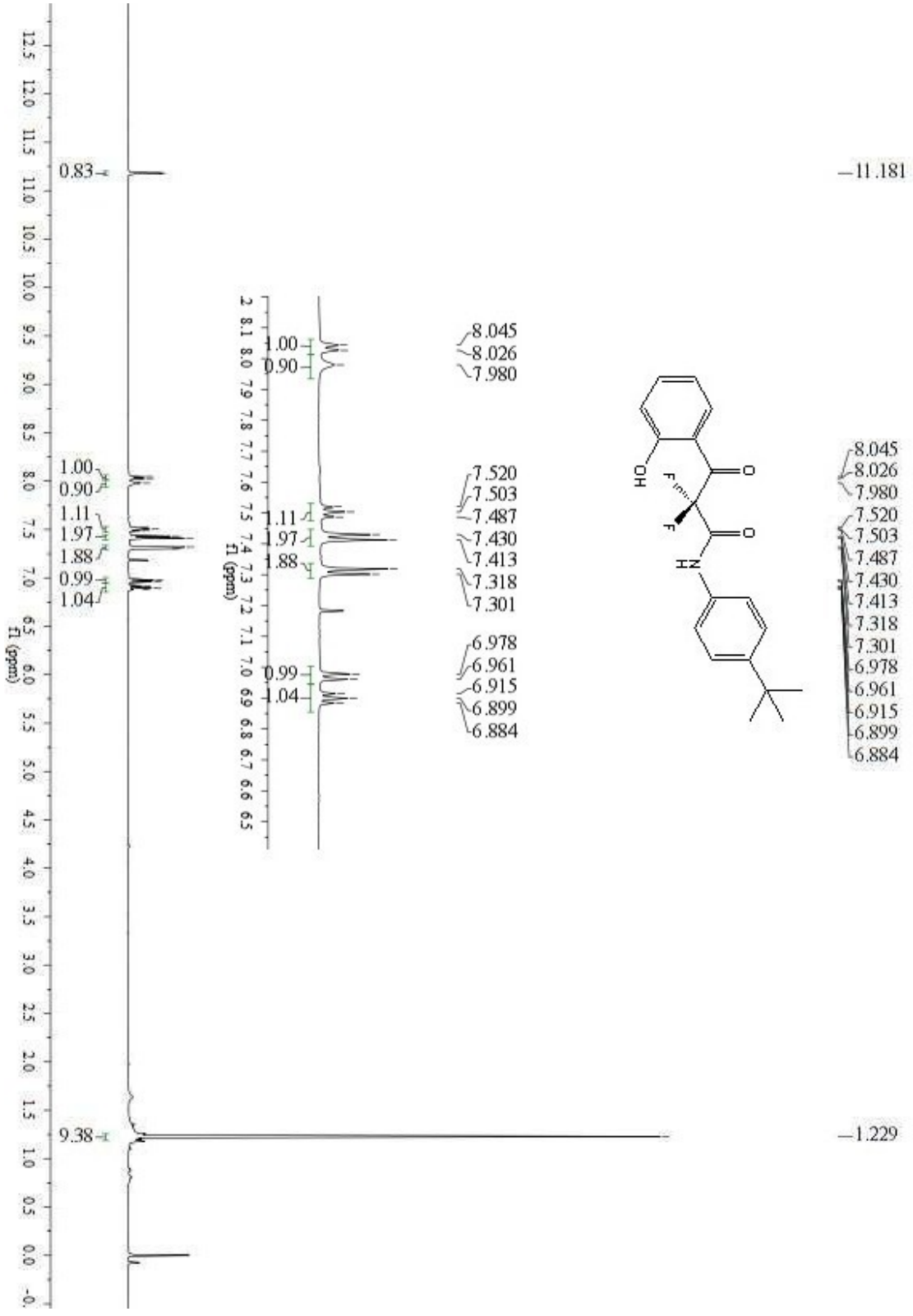


^{13}C NMR of **3d** in $CDCl_3$



^{19}F NMR of **3d** in $CDCl_3$



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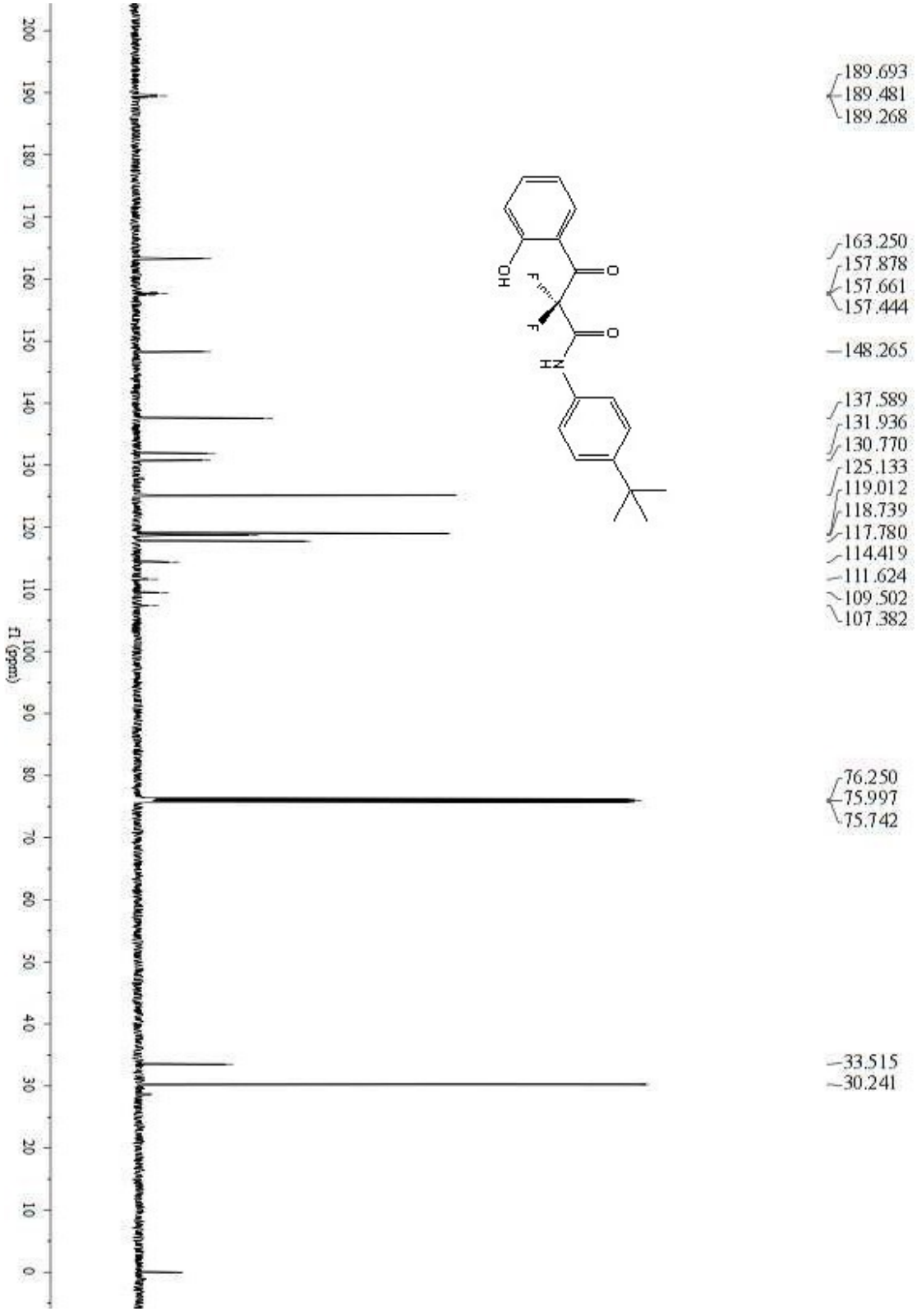
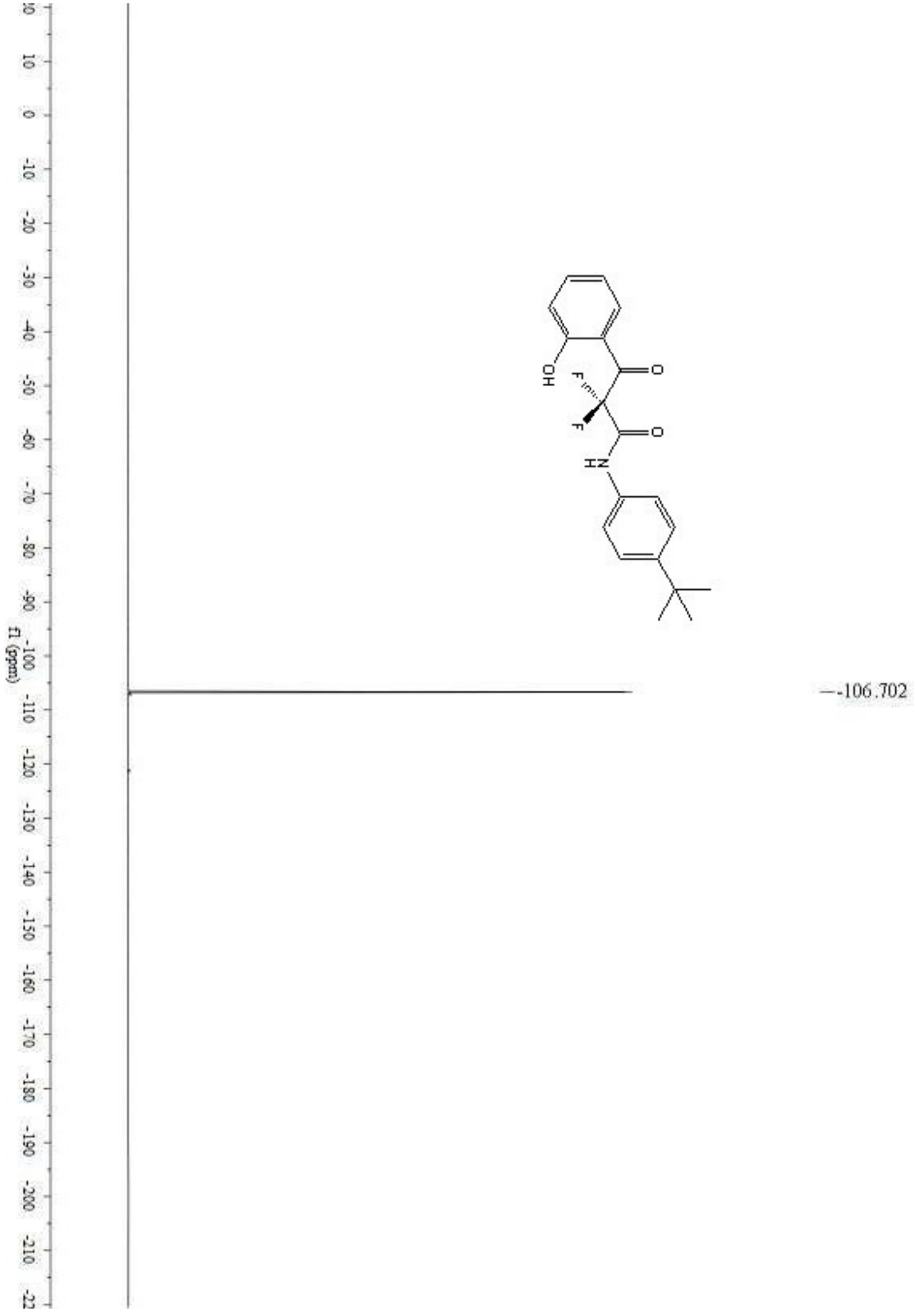
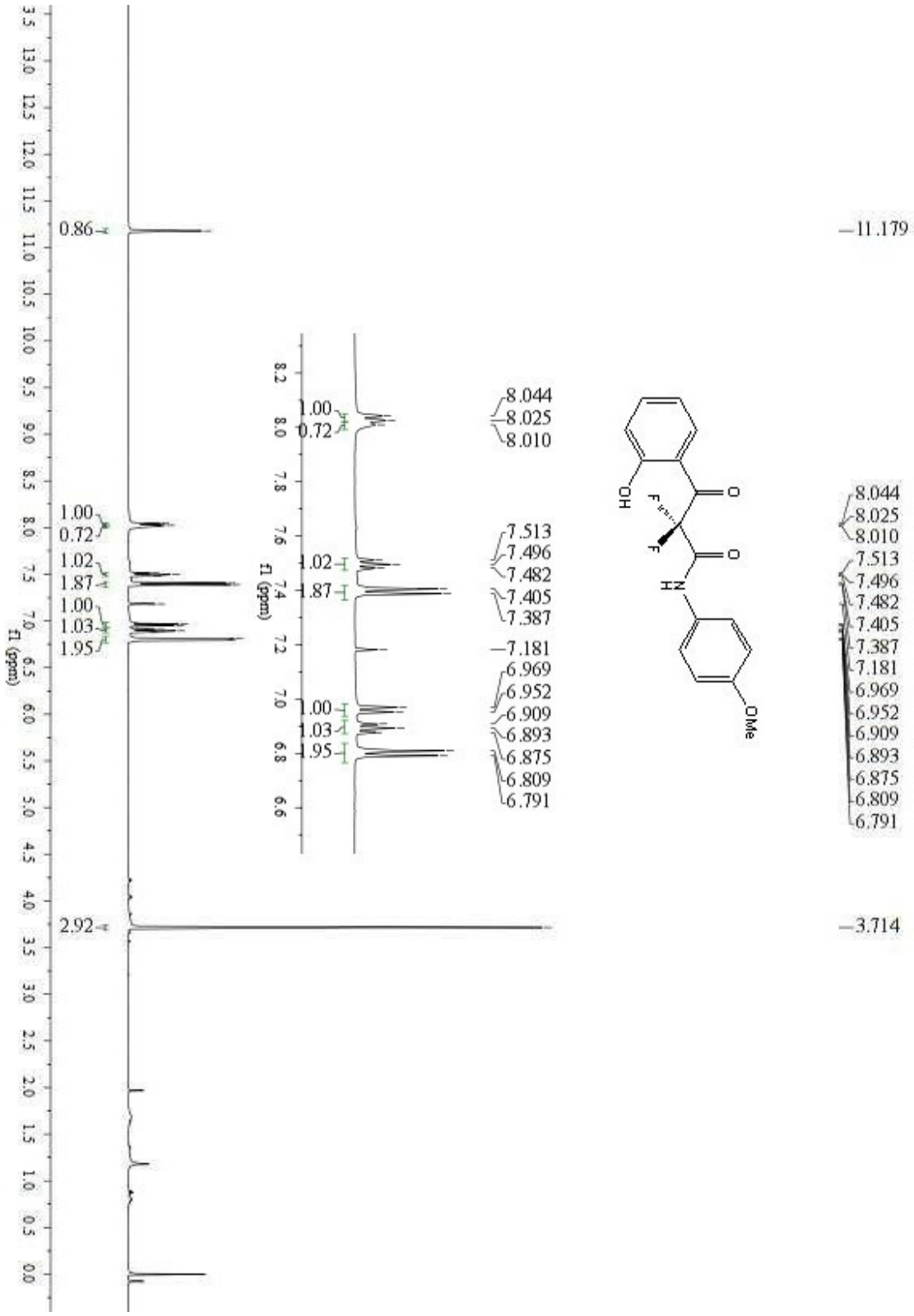


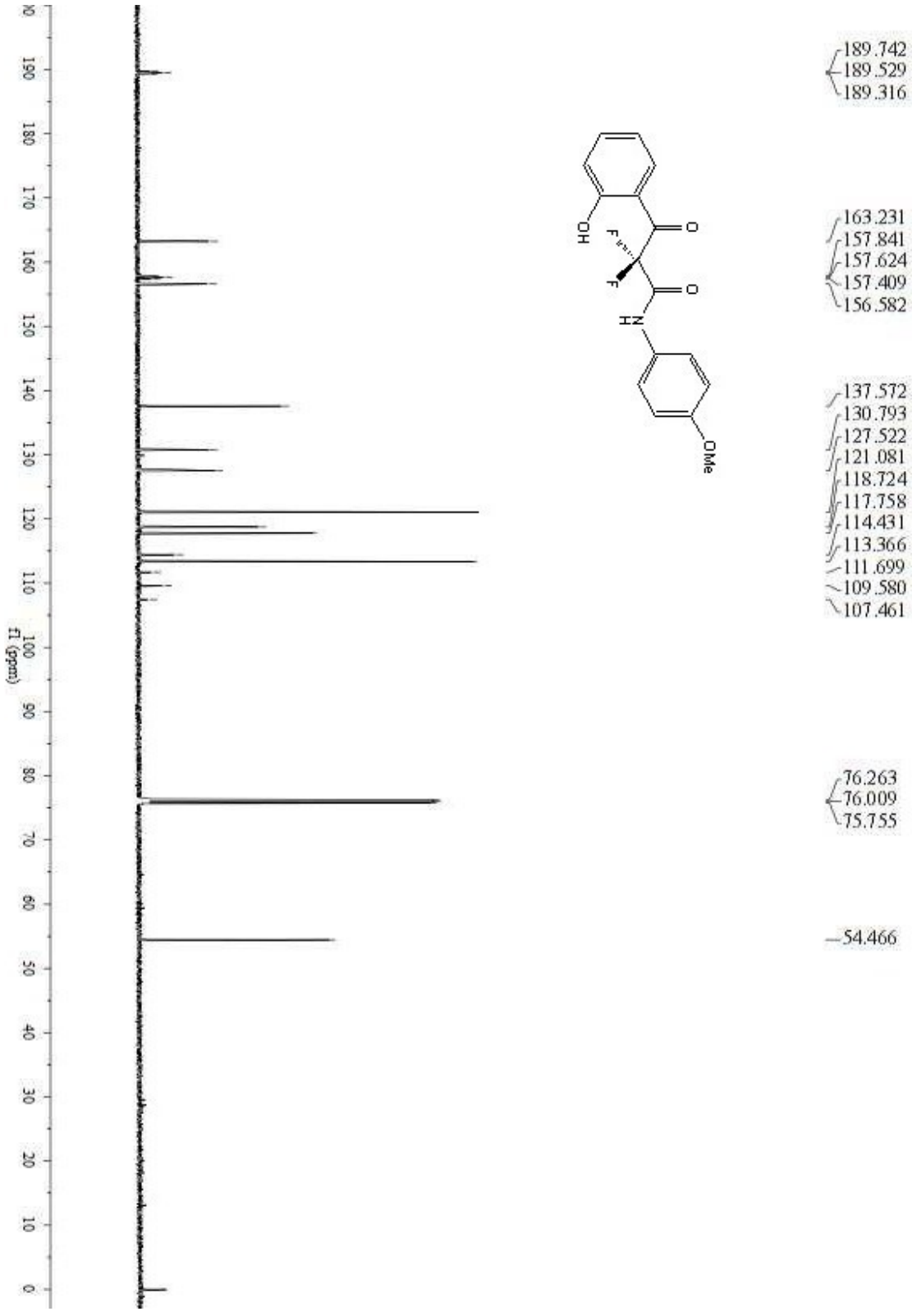
^{13}C NMR of **3e** in $CDCl_3$



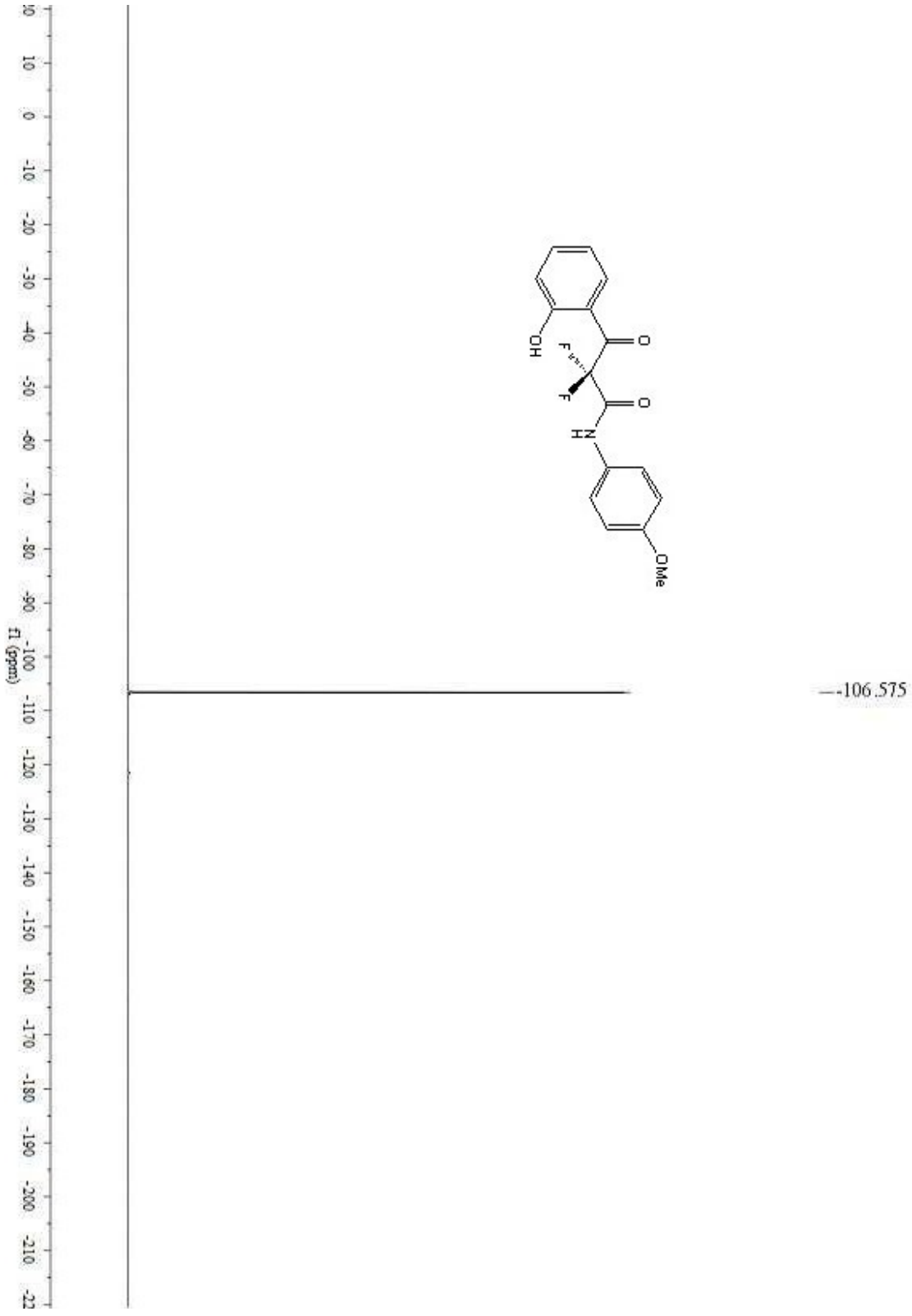
^{19}F NMR of **3e** in $CDCl_3$



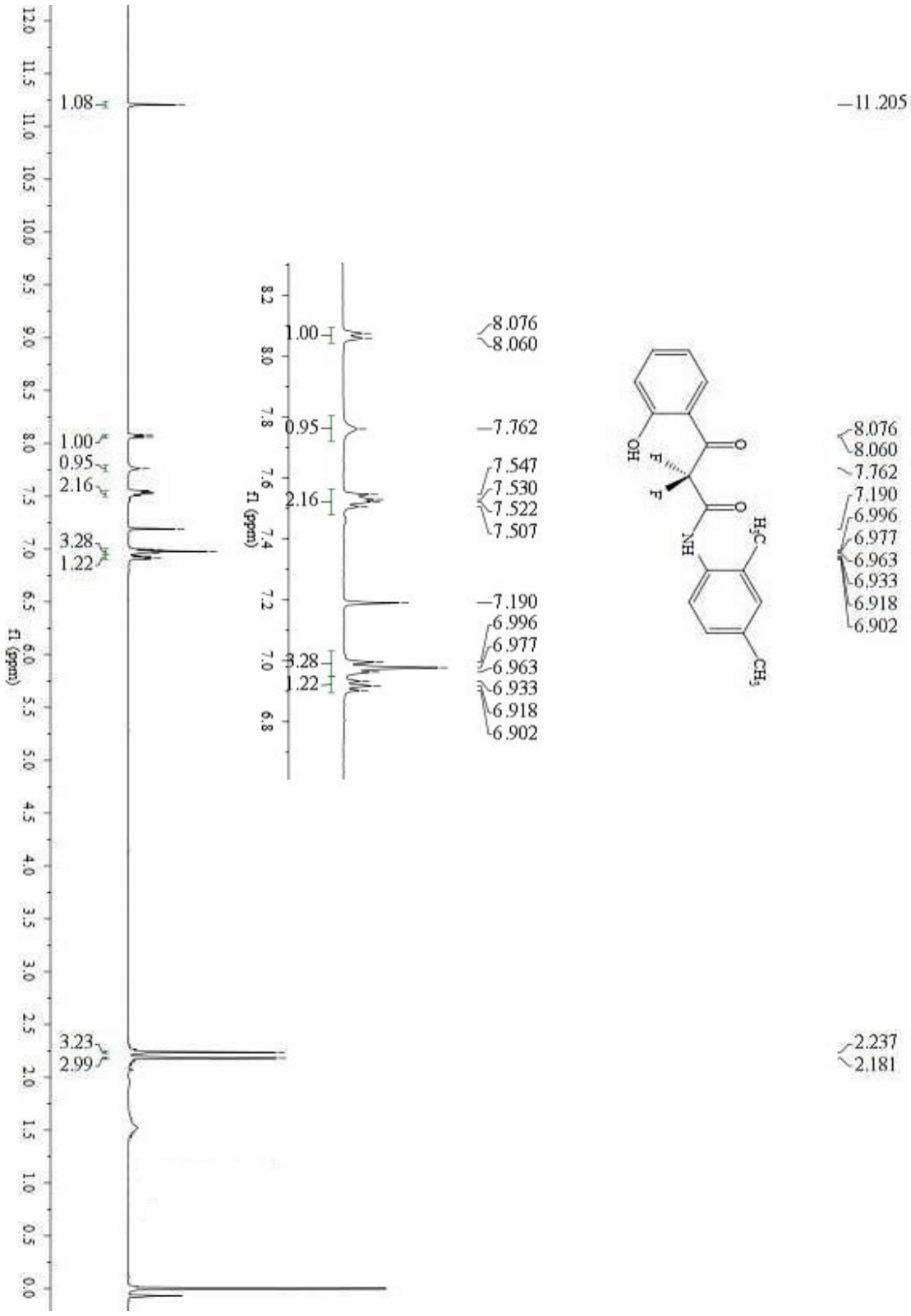
^{1}H NMR of **3f** in $CDCl_3$



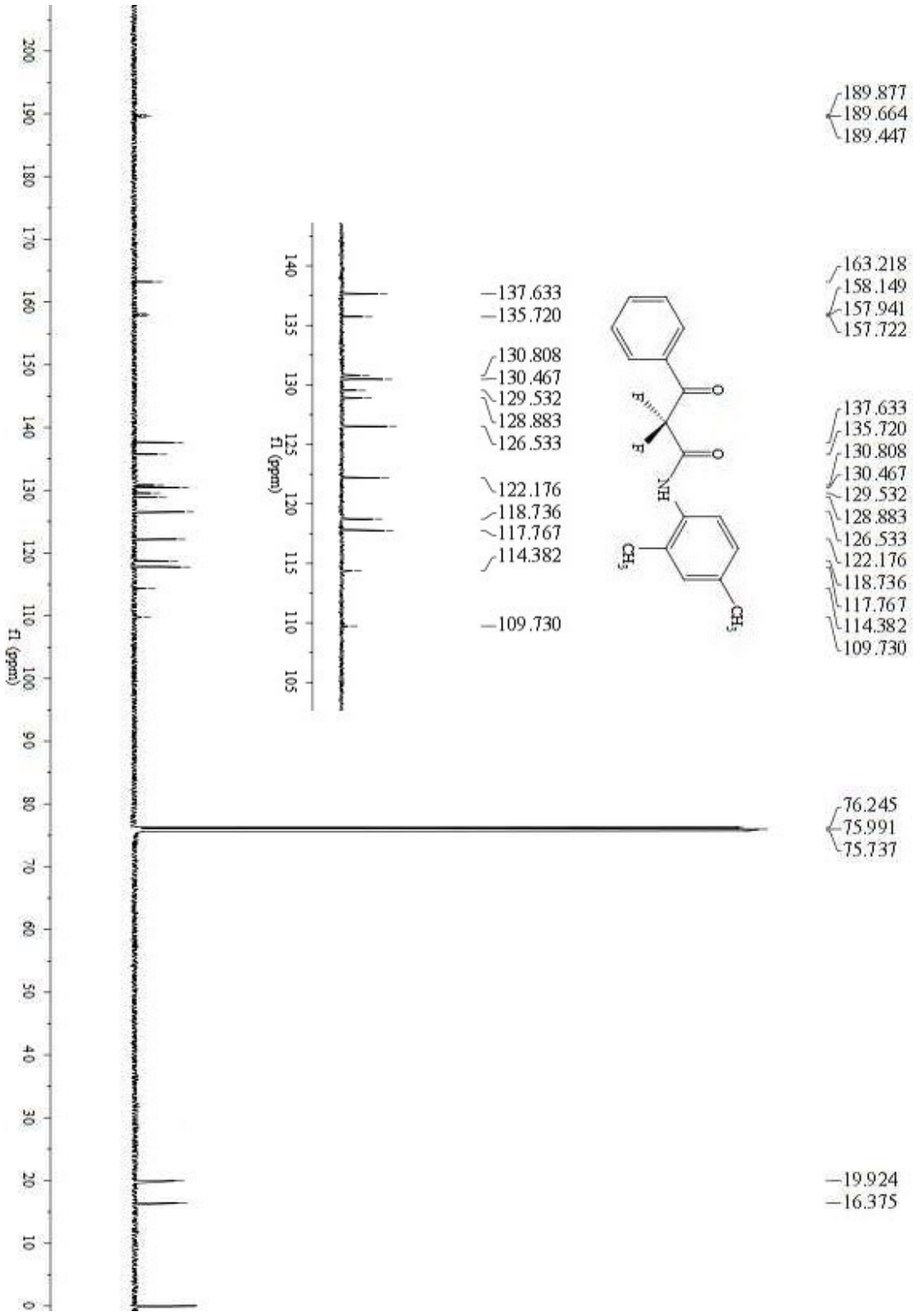
^{13}C NMR of **3f** in $CDCl_3$



^{19}F NMR of **3f** in $CDCl_3$



^{1}H NMR of **3g** in $CDCl_3$



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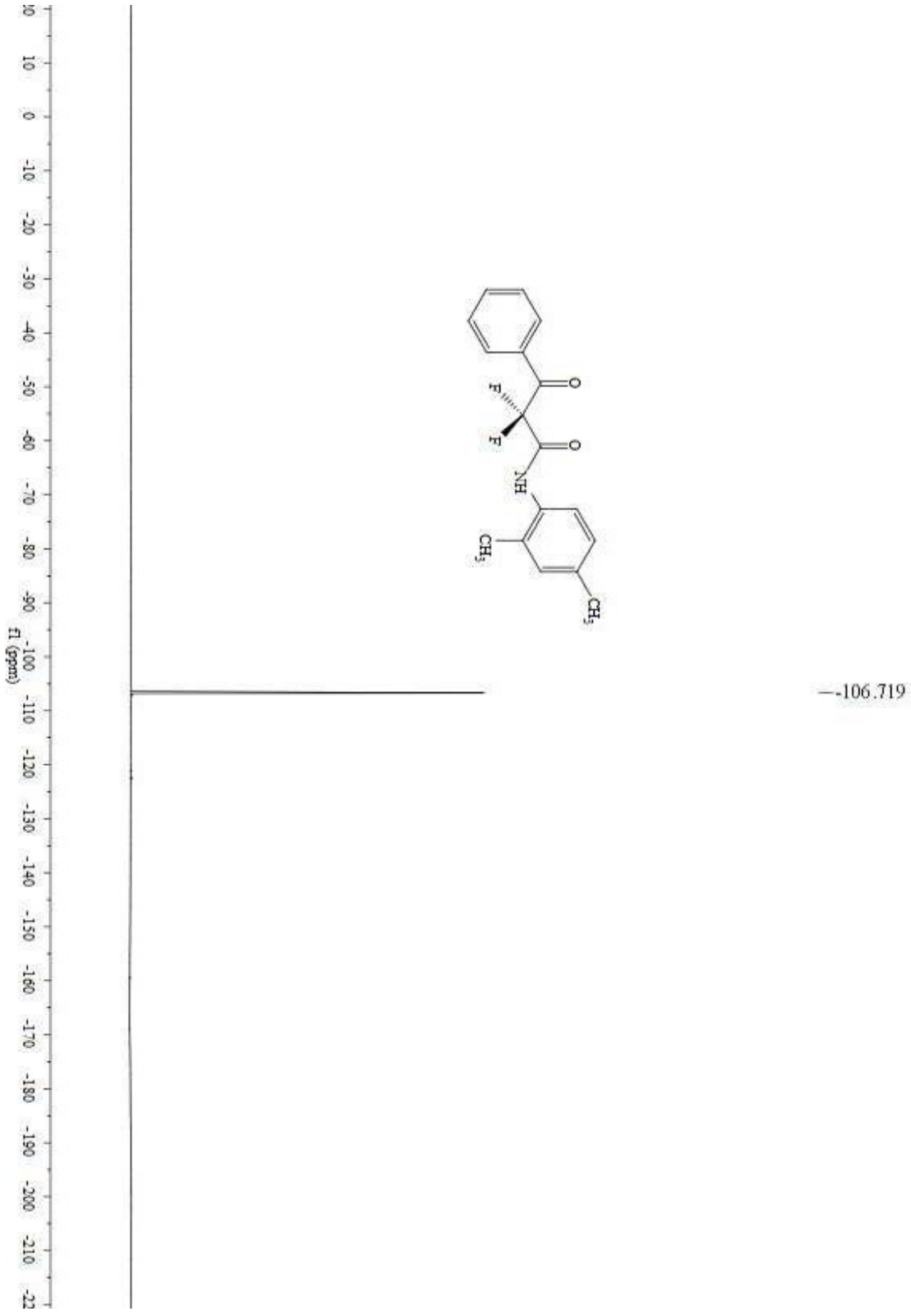
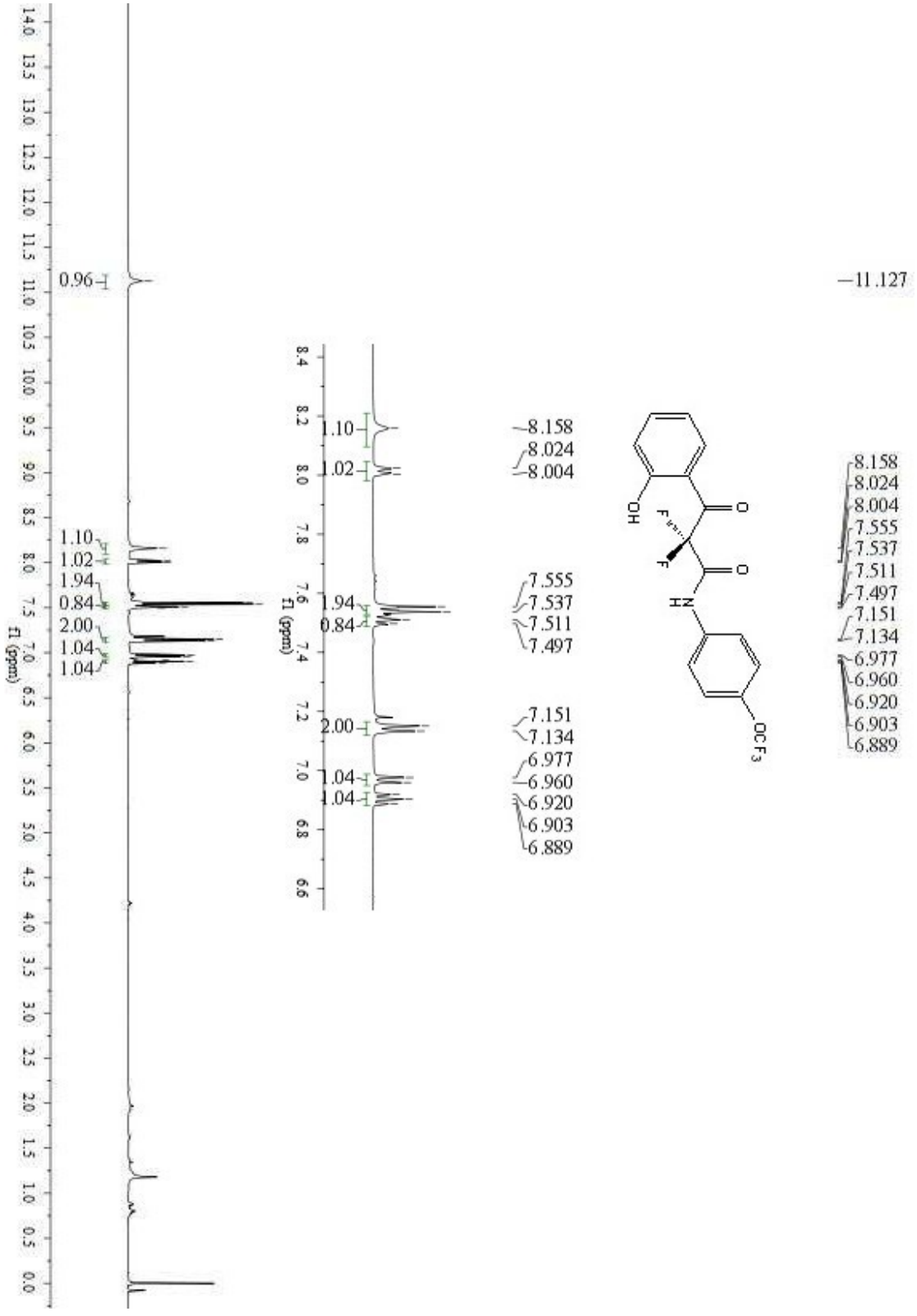
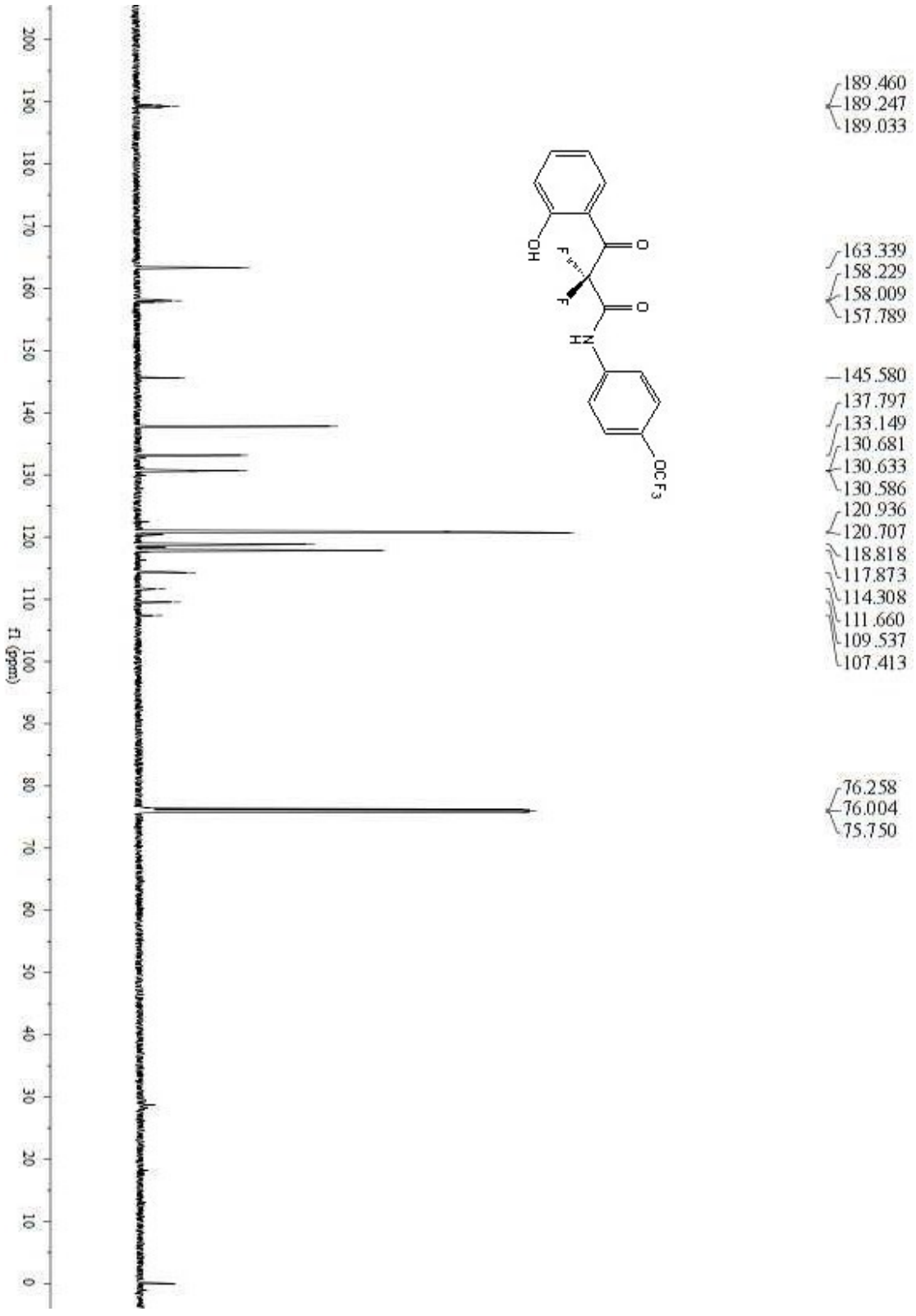


^{19}F NMR of **3g** in $CDCl_3$



^{1}H NMR of **3h** in $CDCl_3$



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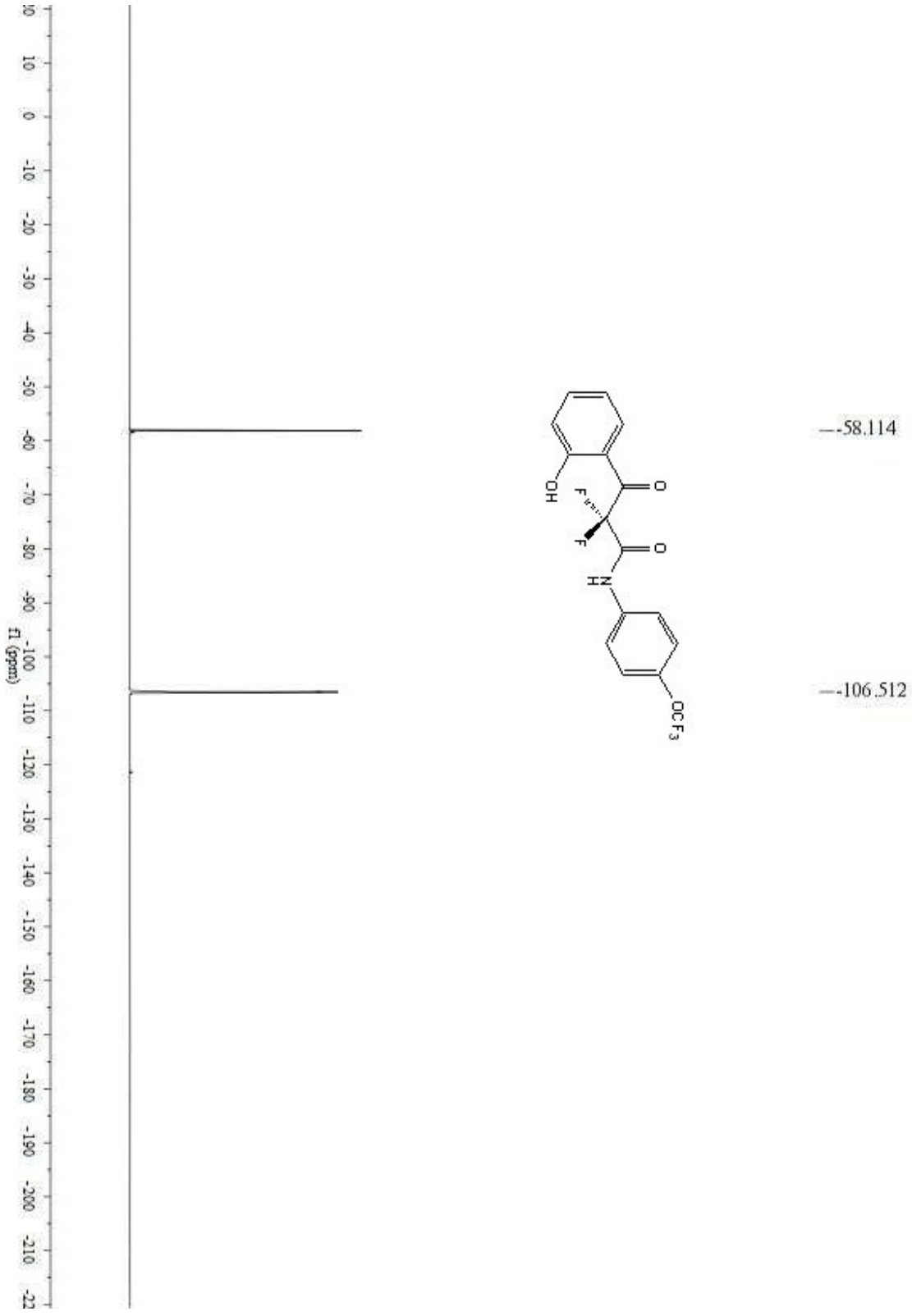

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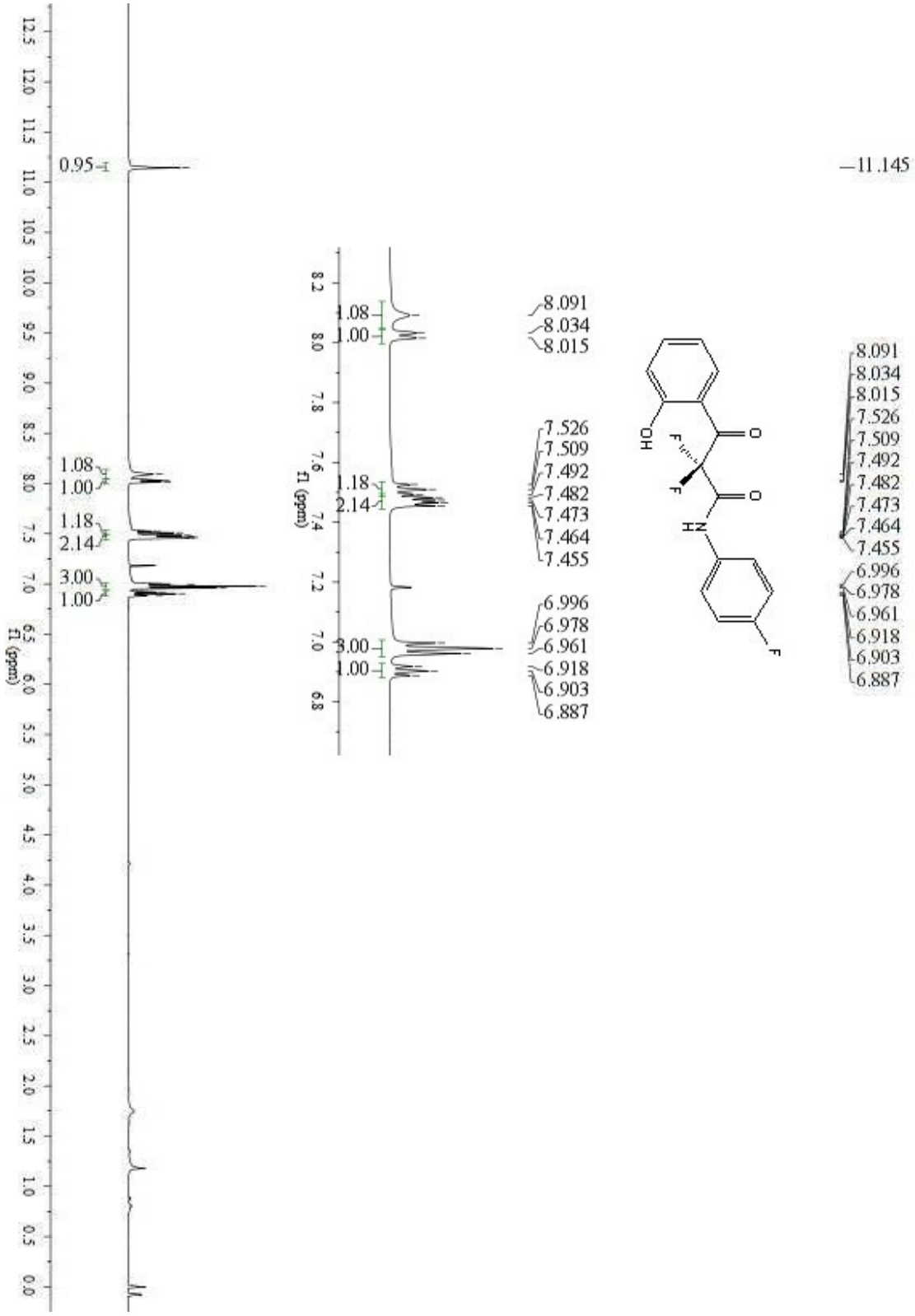
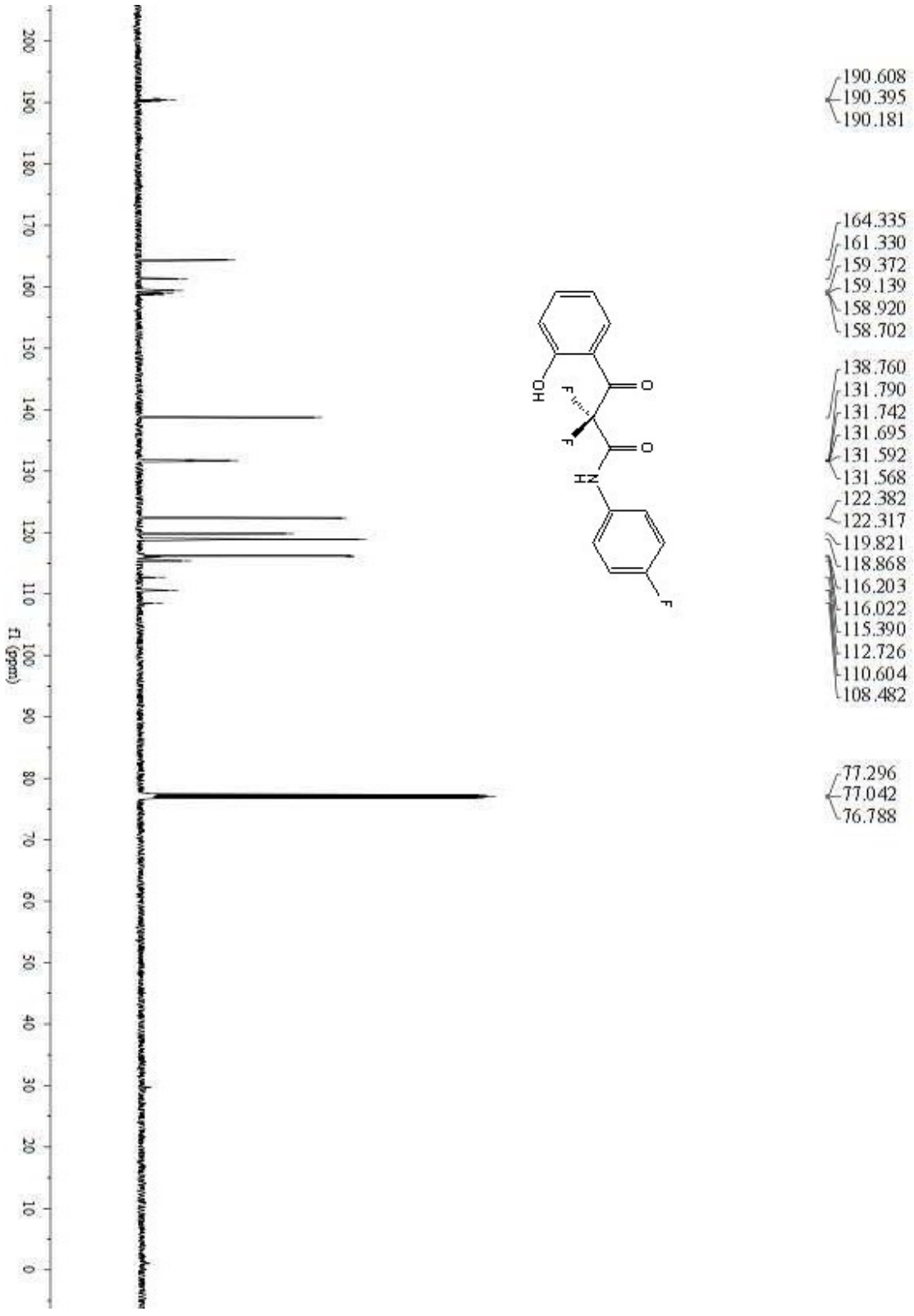


^{1}H NMR of **3i** in $CDCl_3$



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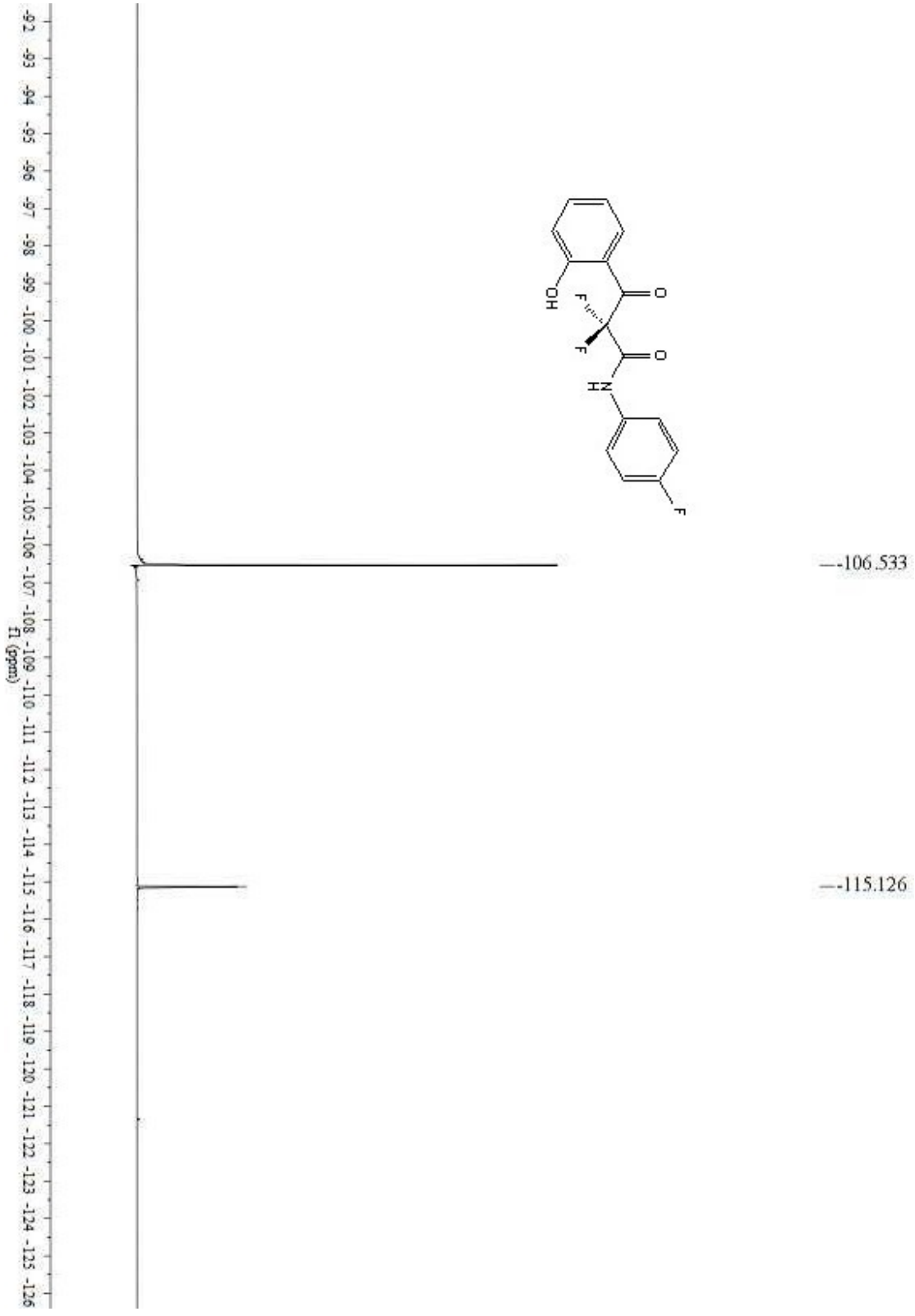

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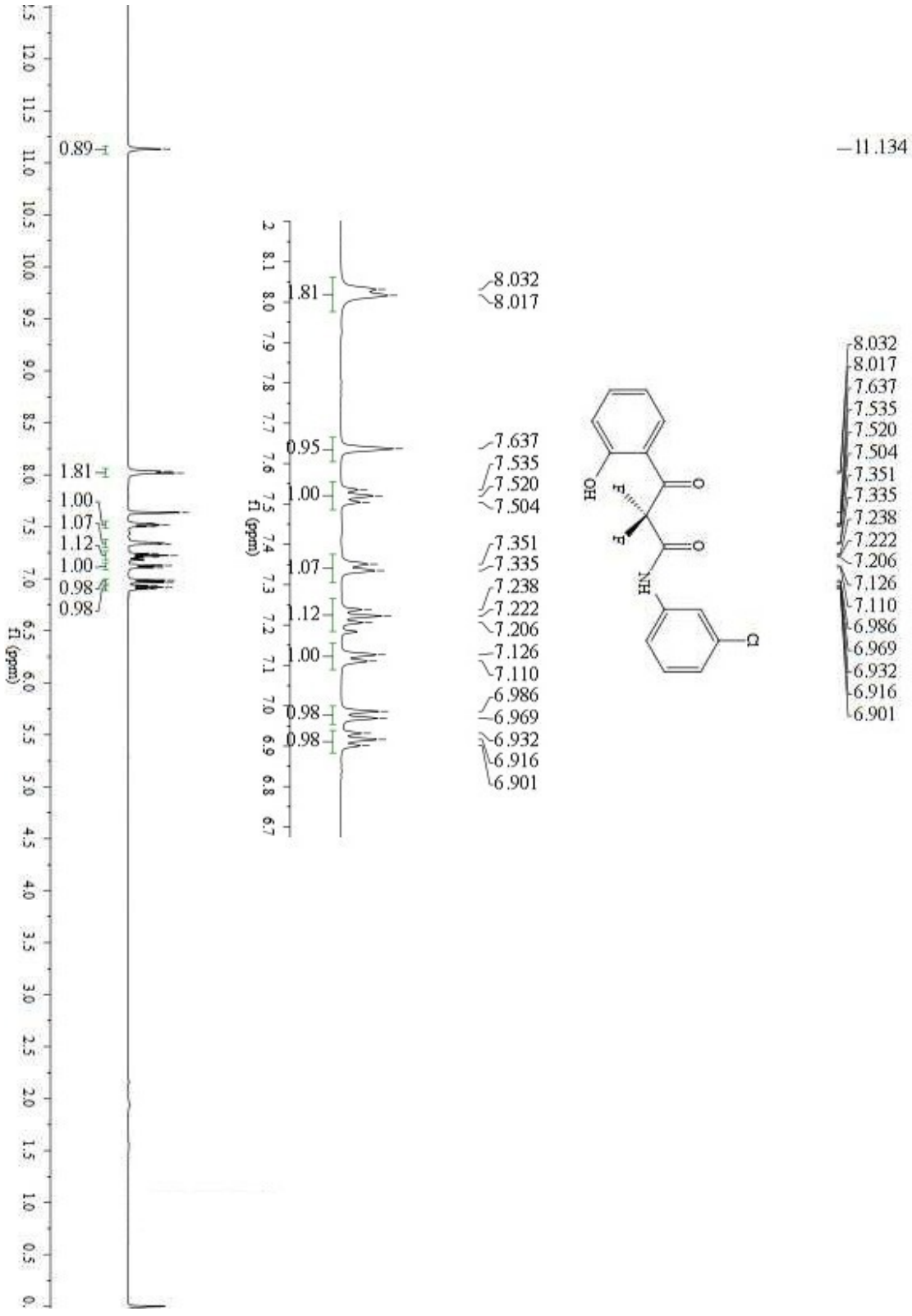

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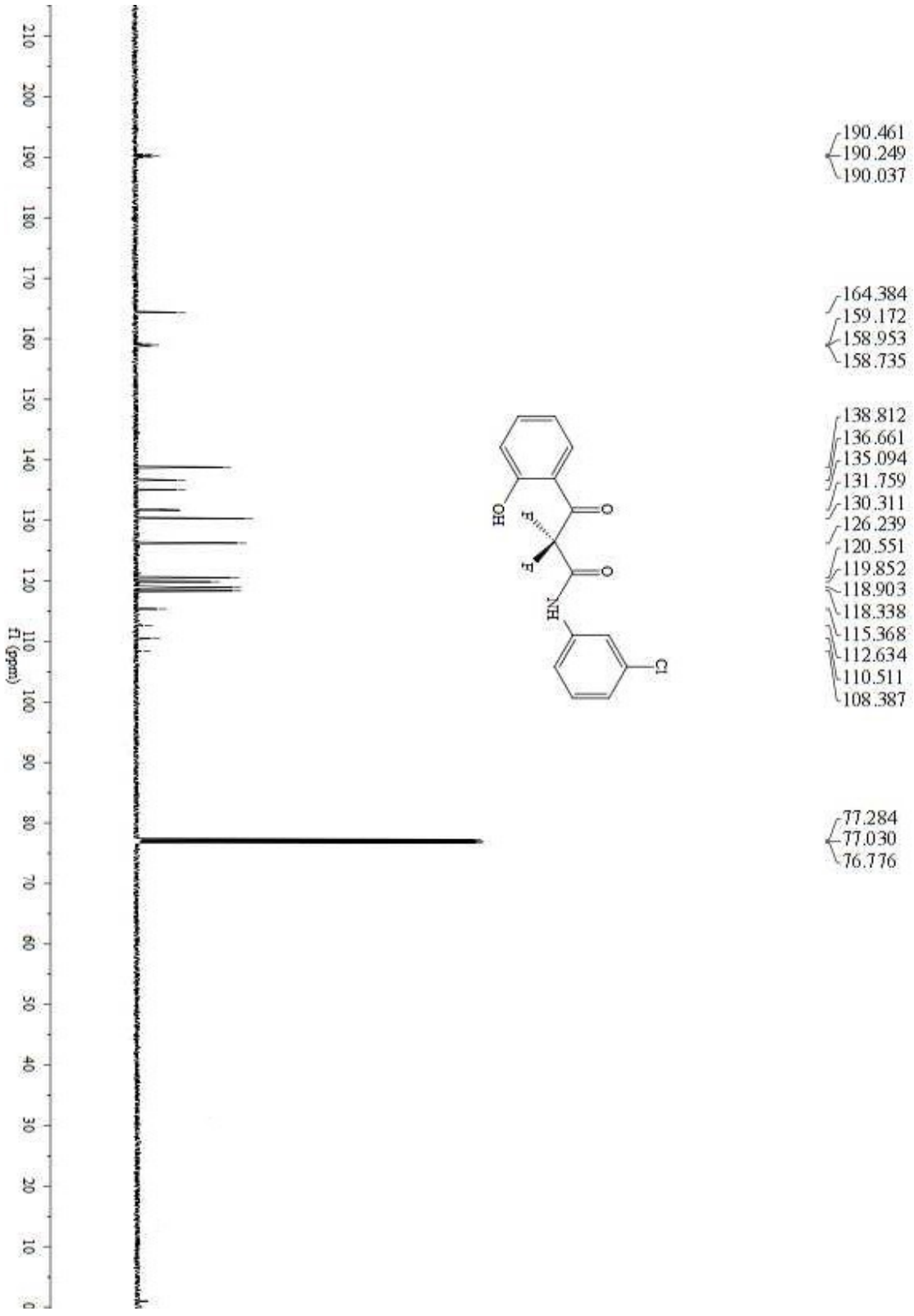

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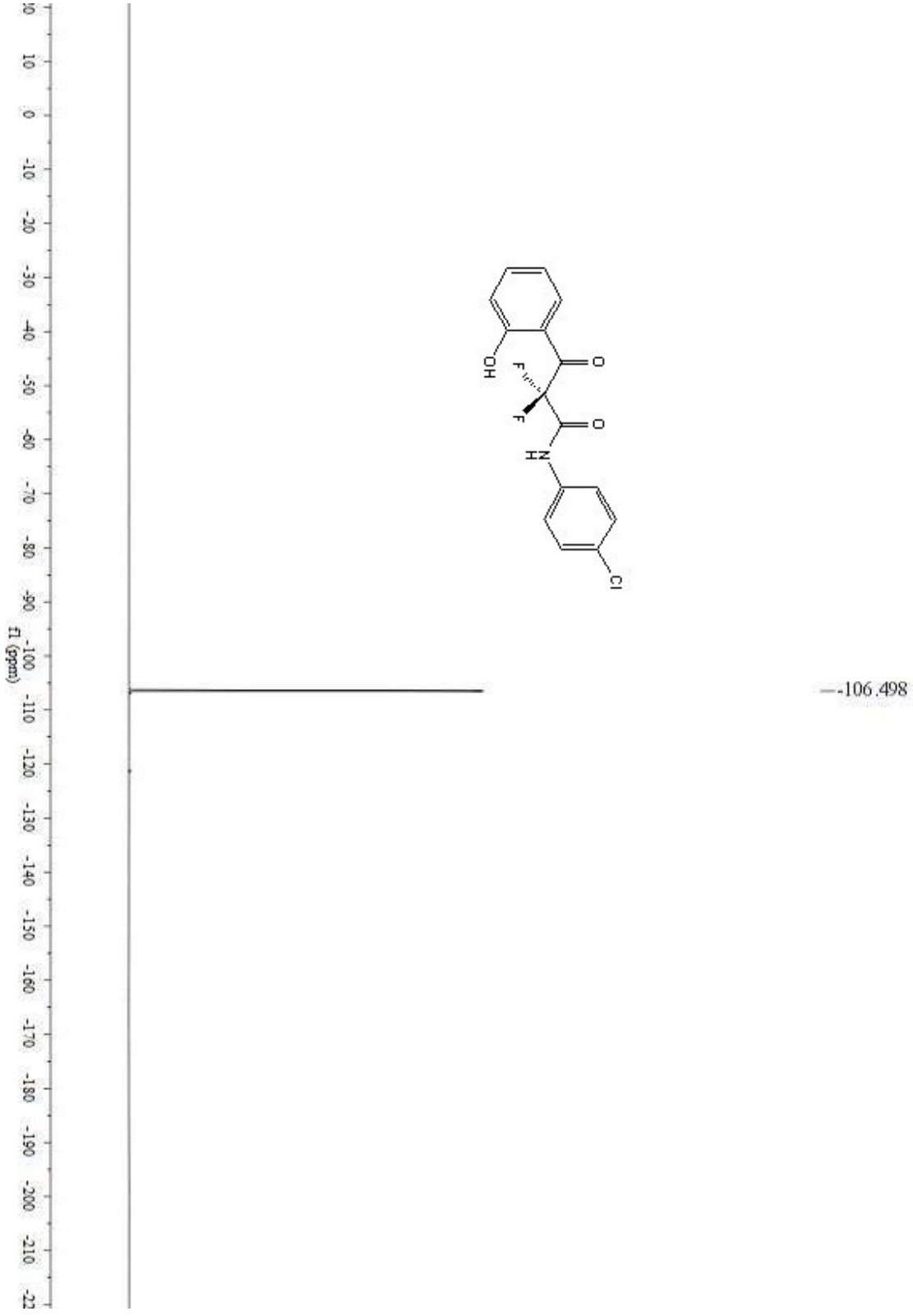

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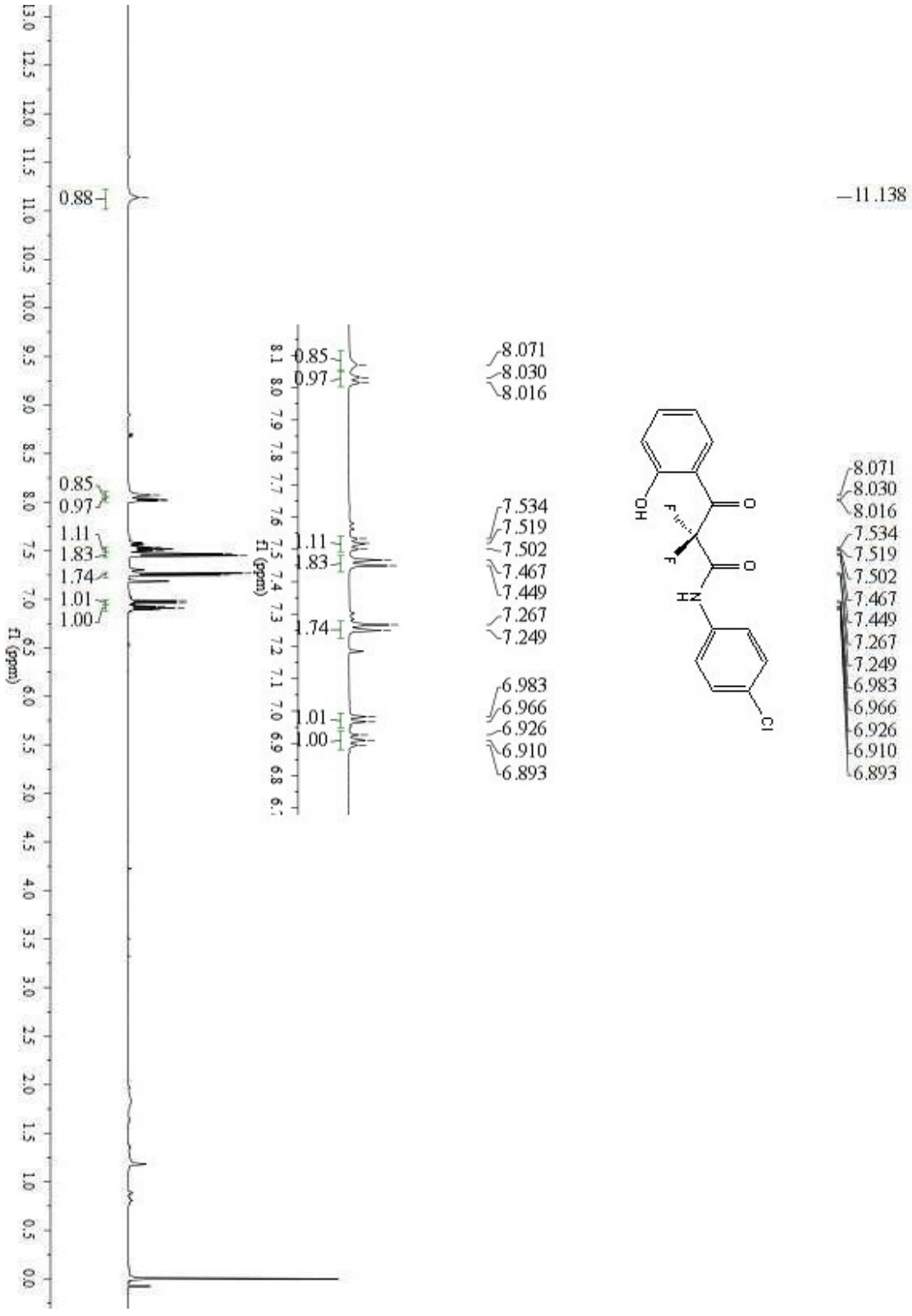
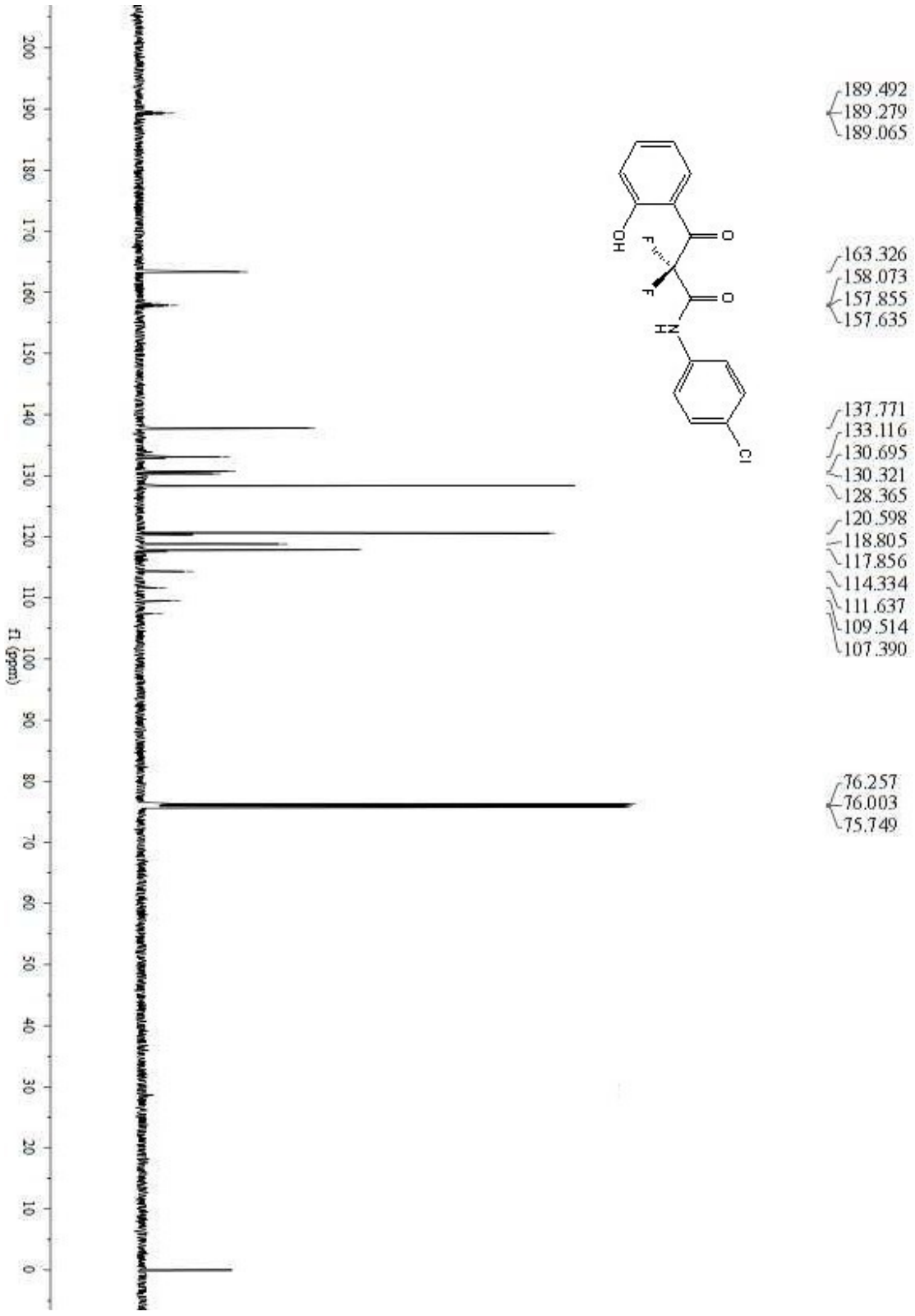
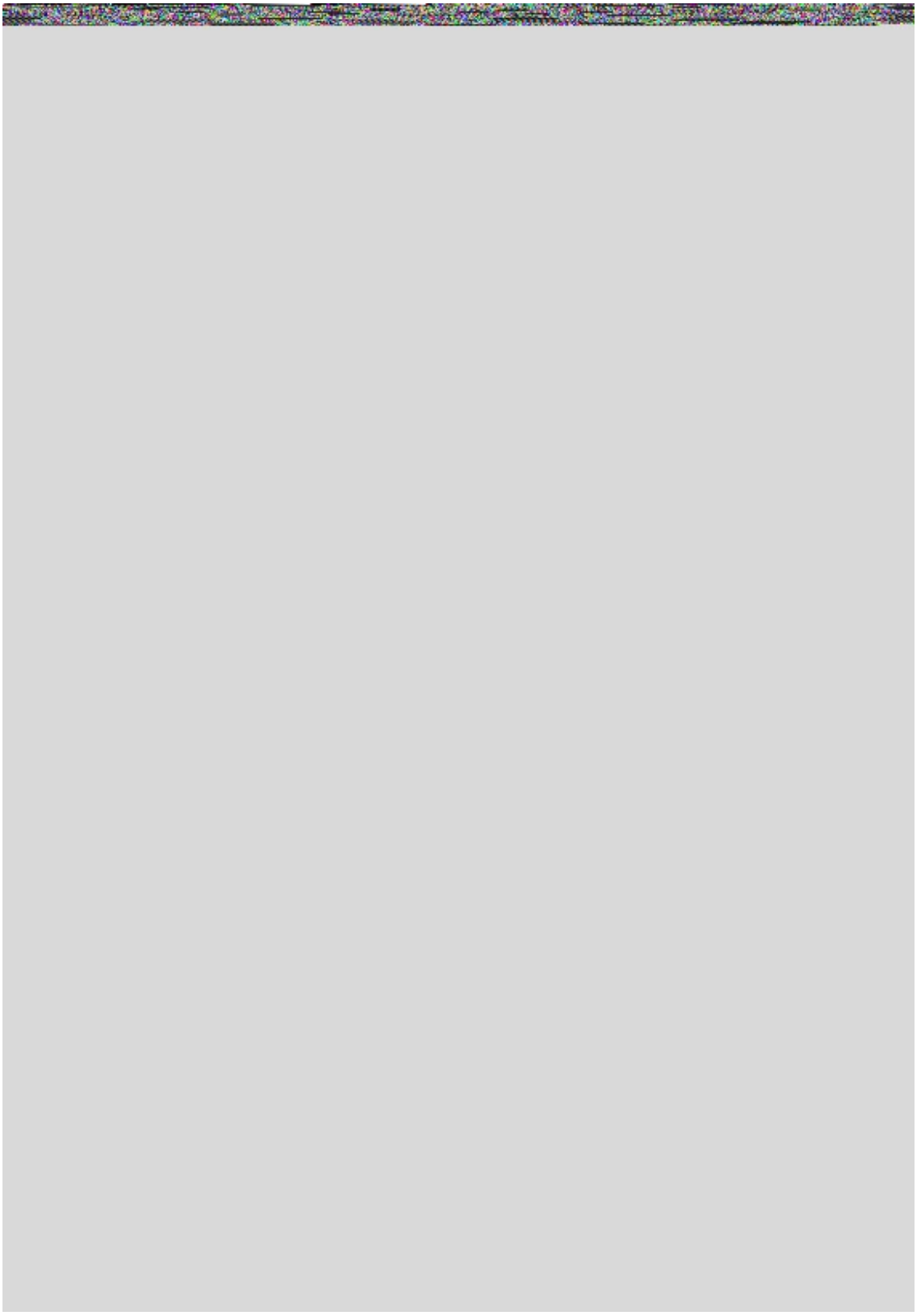


^{1}H NMR of **3k** in $CDCl_3$



^{13}C NMR of **3k** in $CDCl_3$



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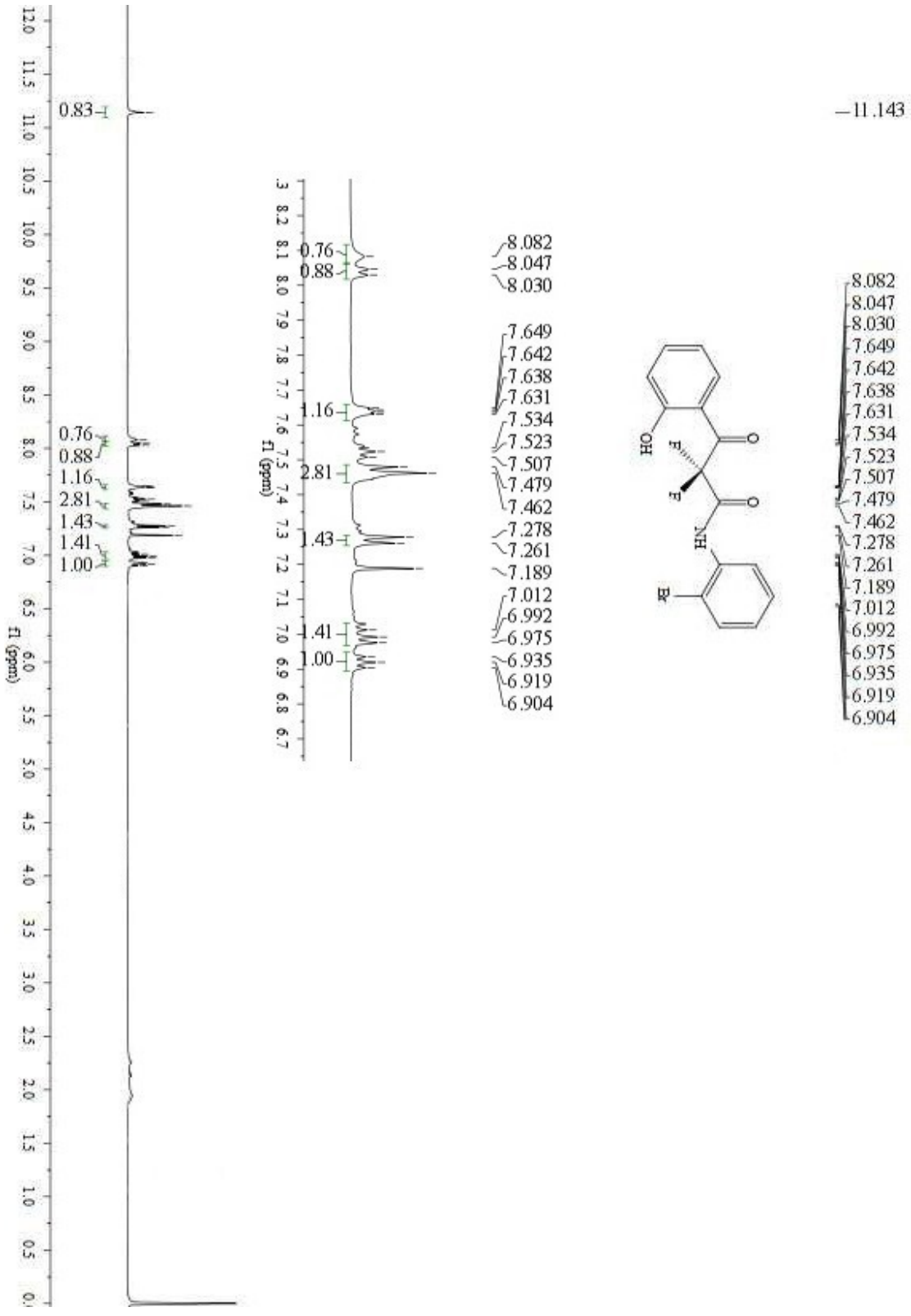

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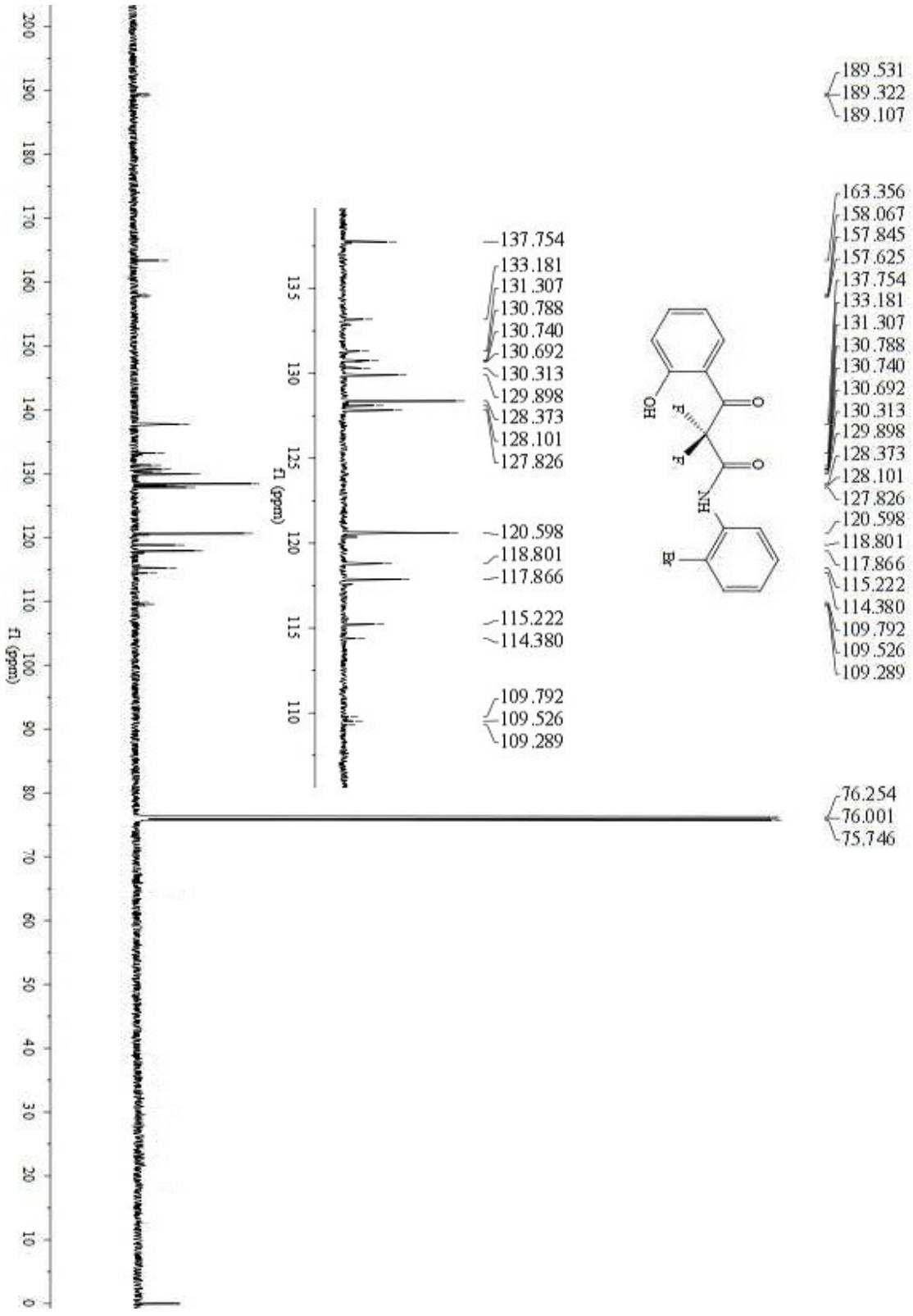

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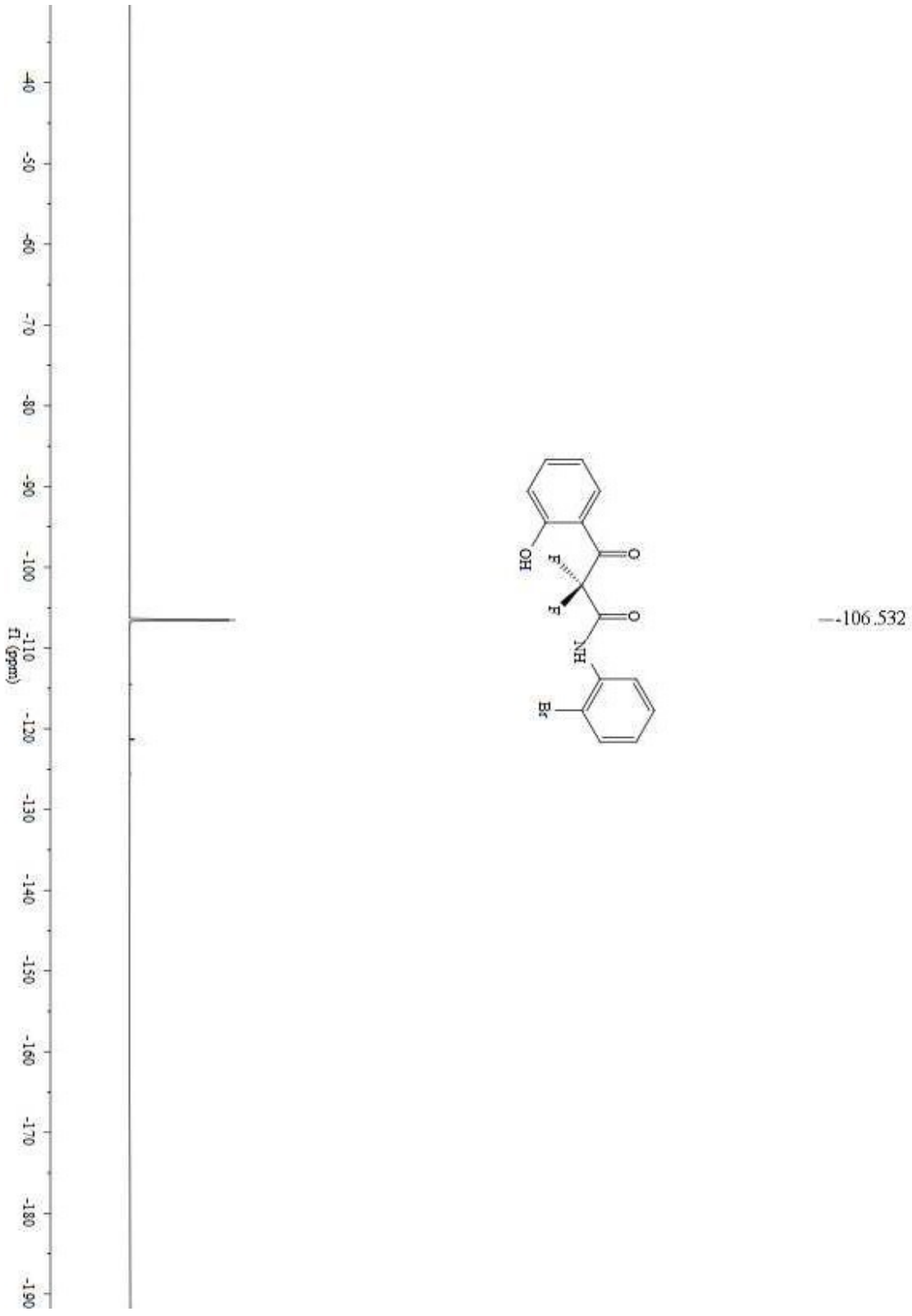

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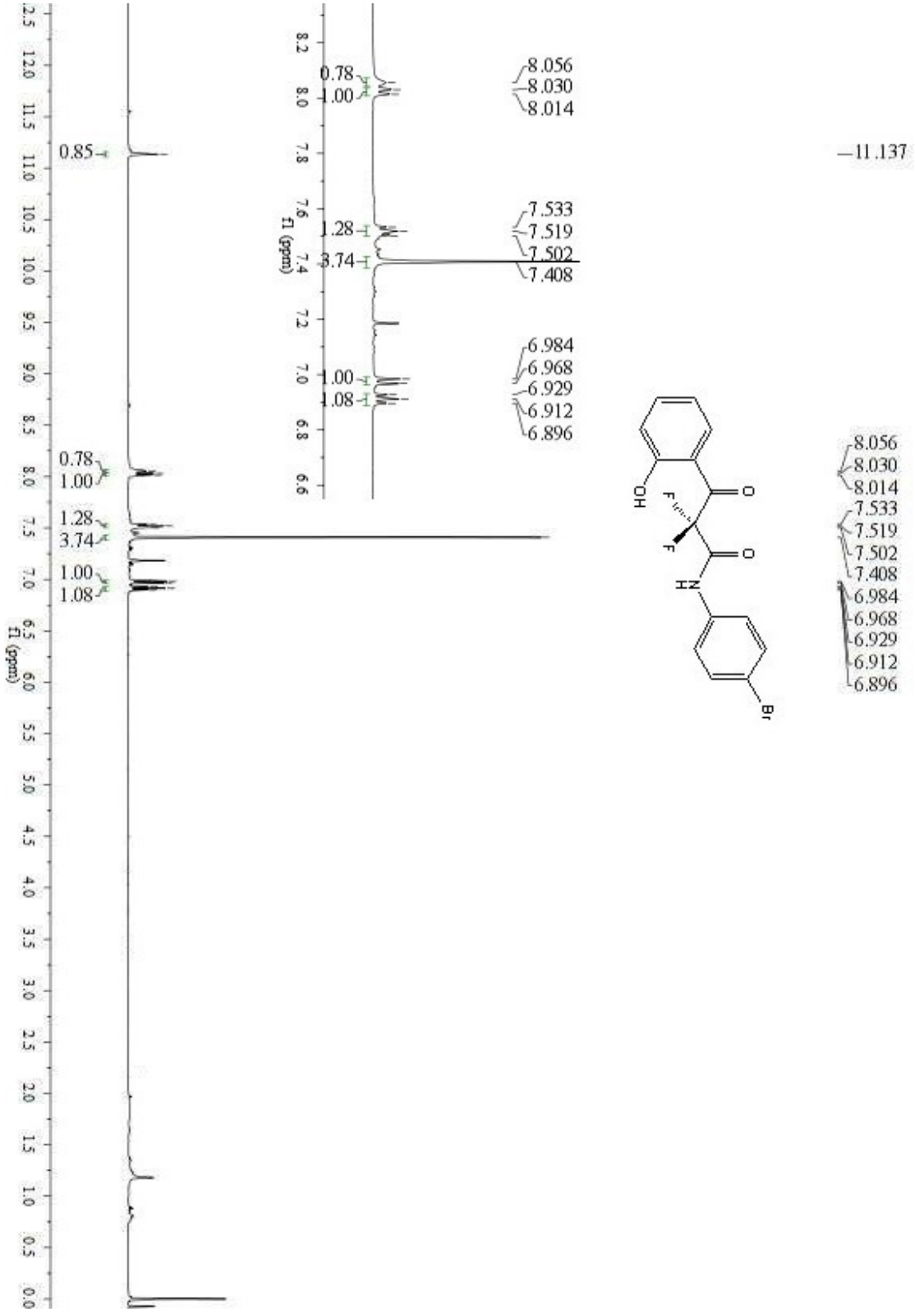

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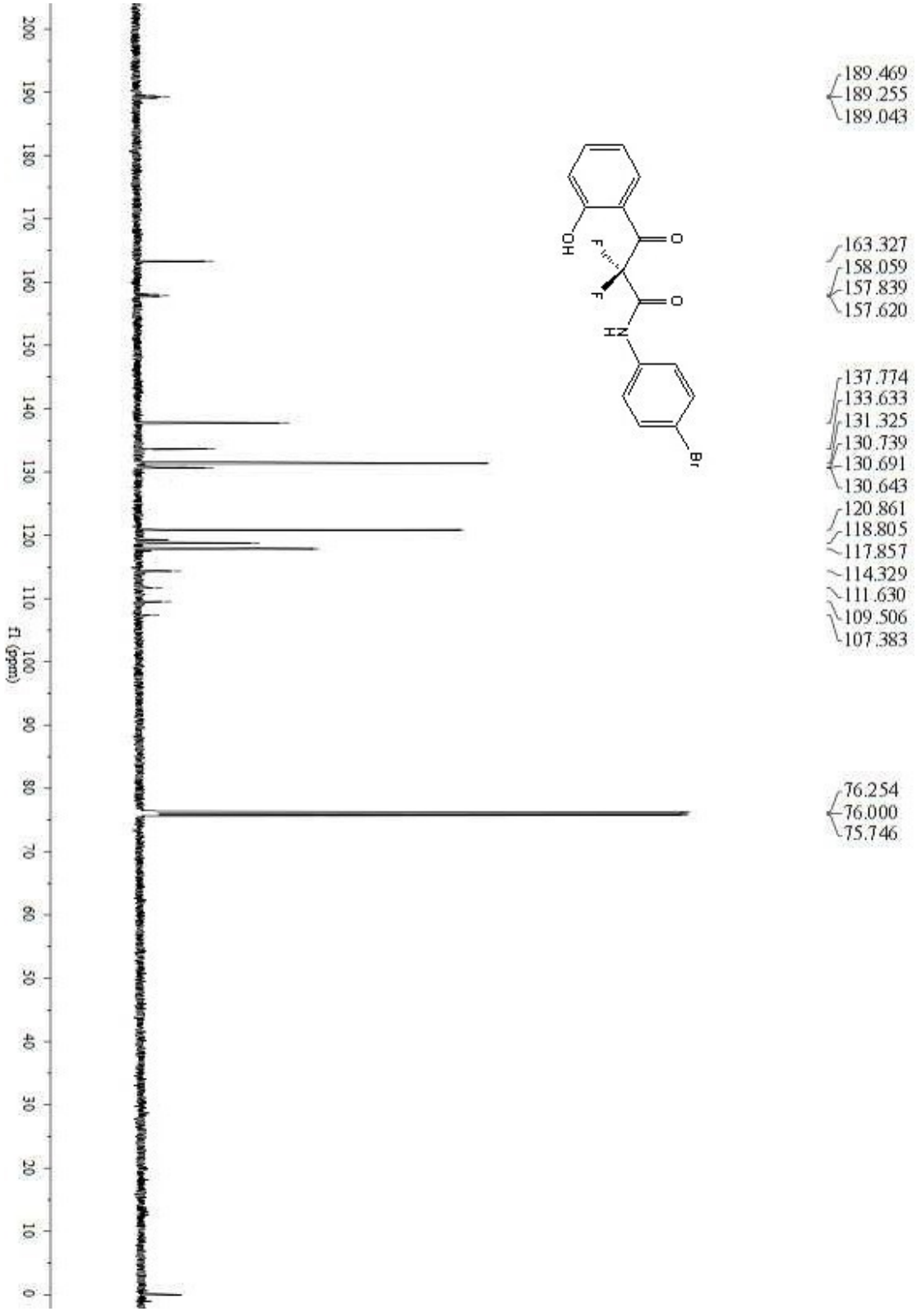
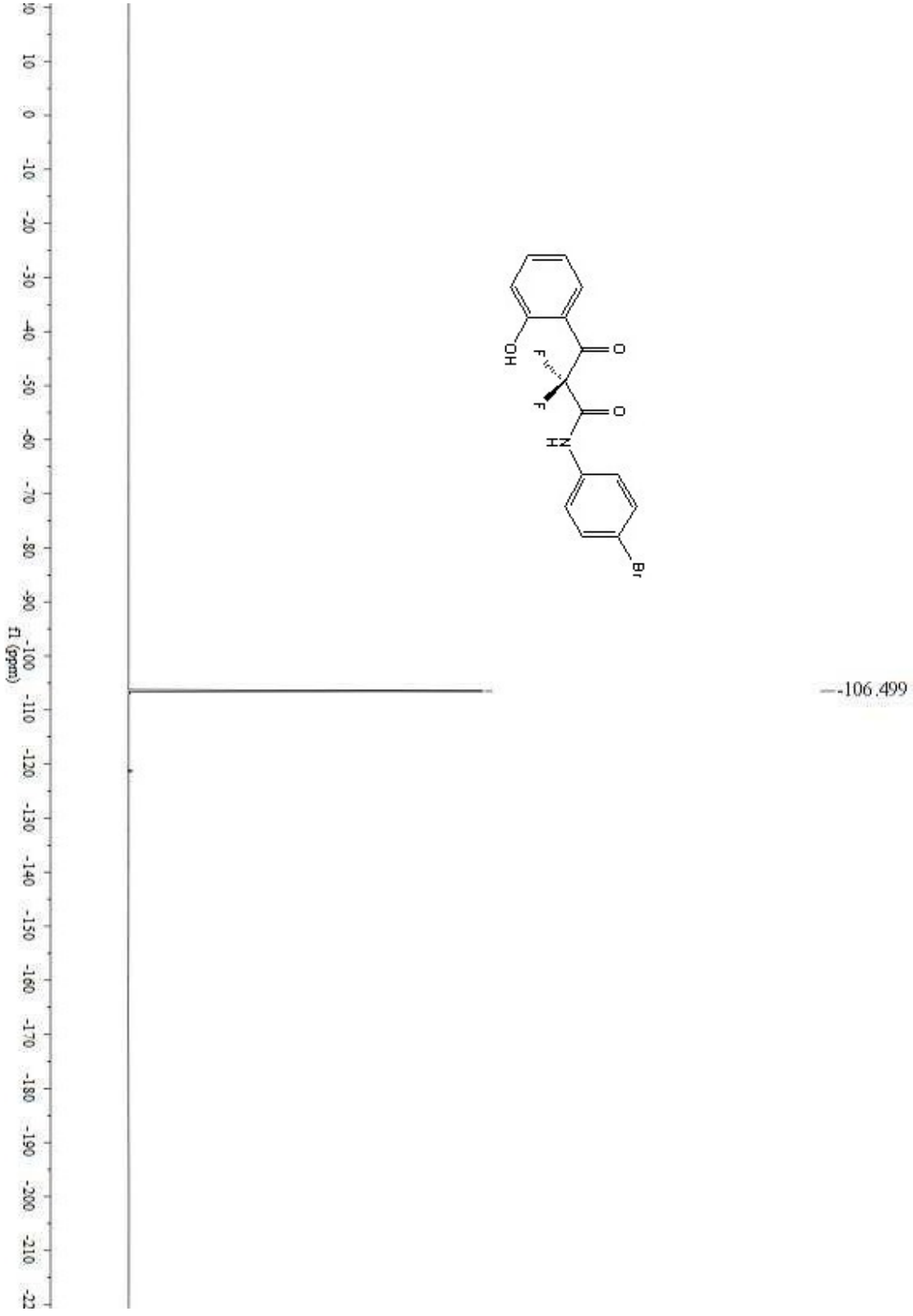
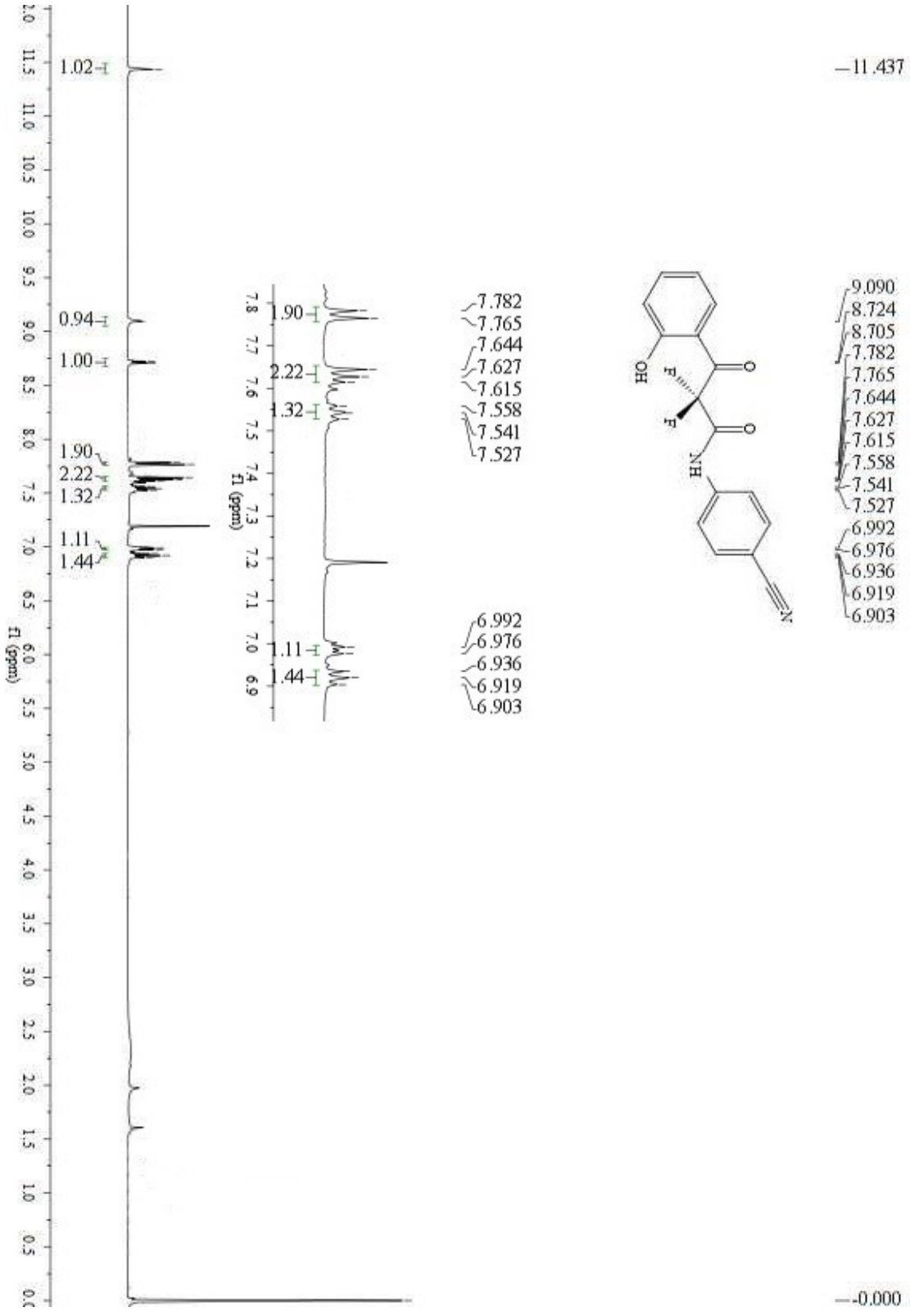


^{13}C NMR of **3m** in $CDCl_3$



^{19}F NMR of **3m** in $CDCl_3$



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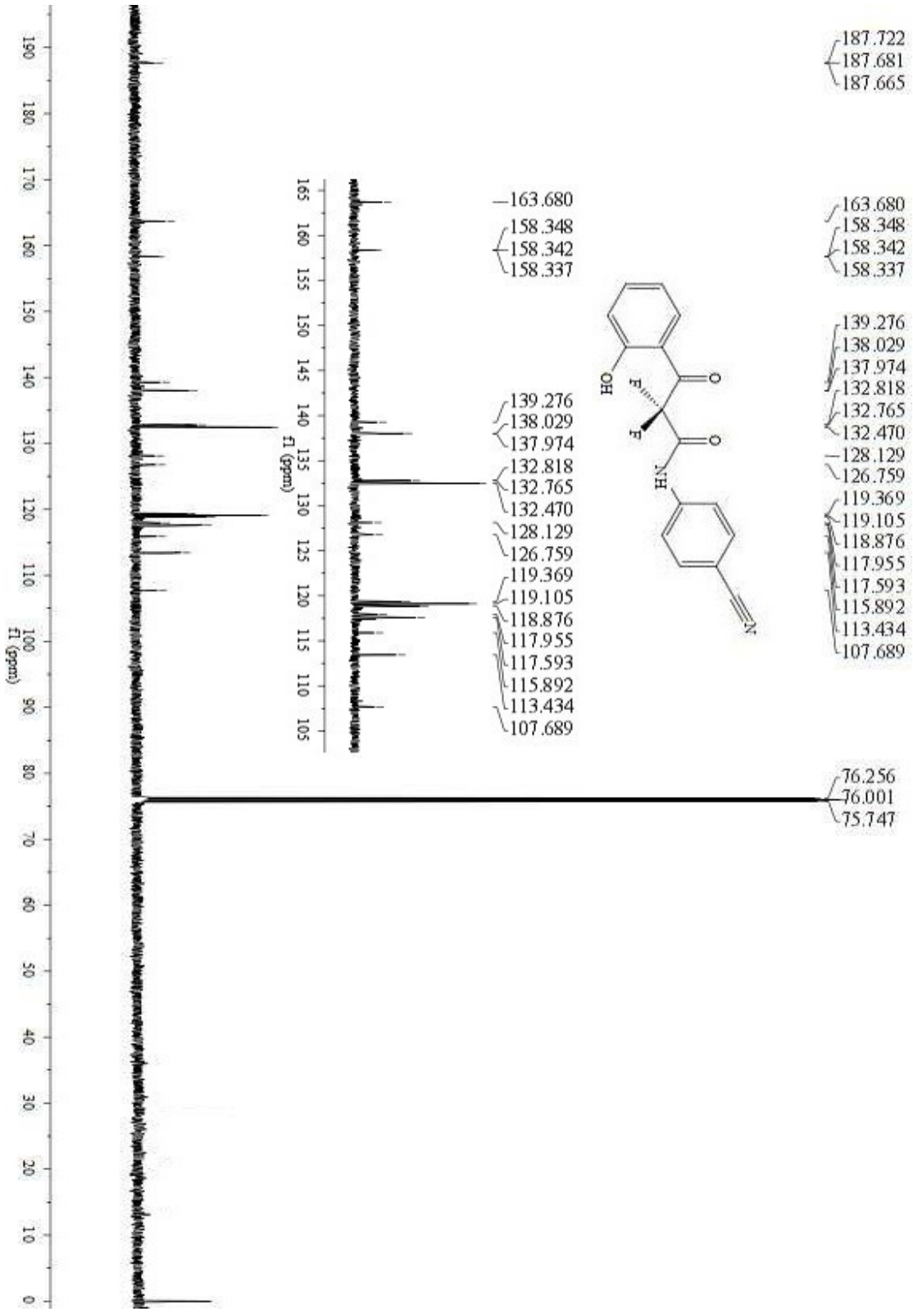

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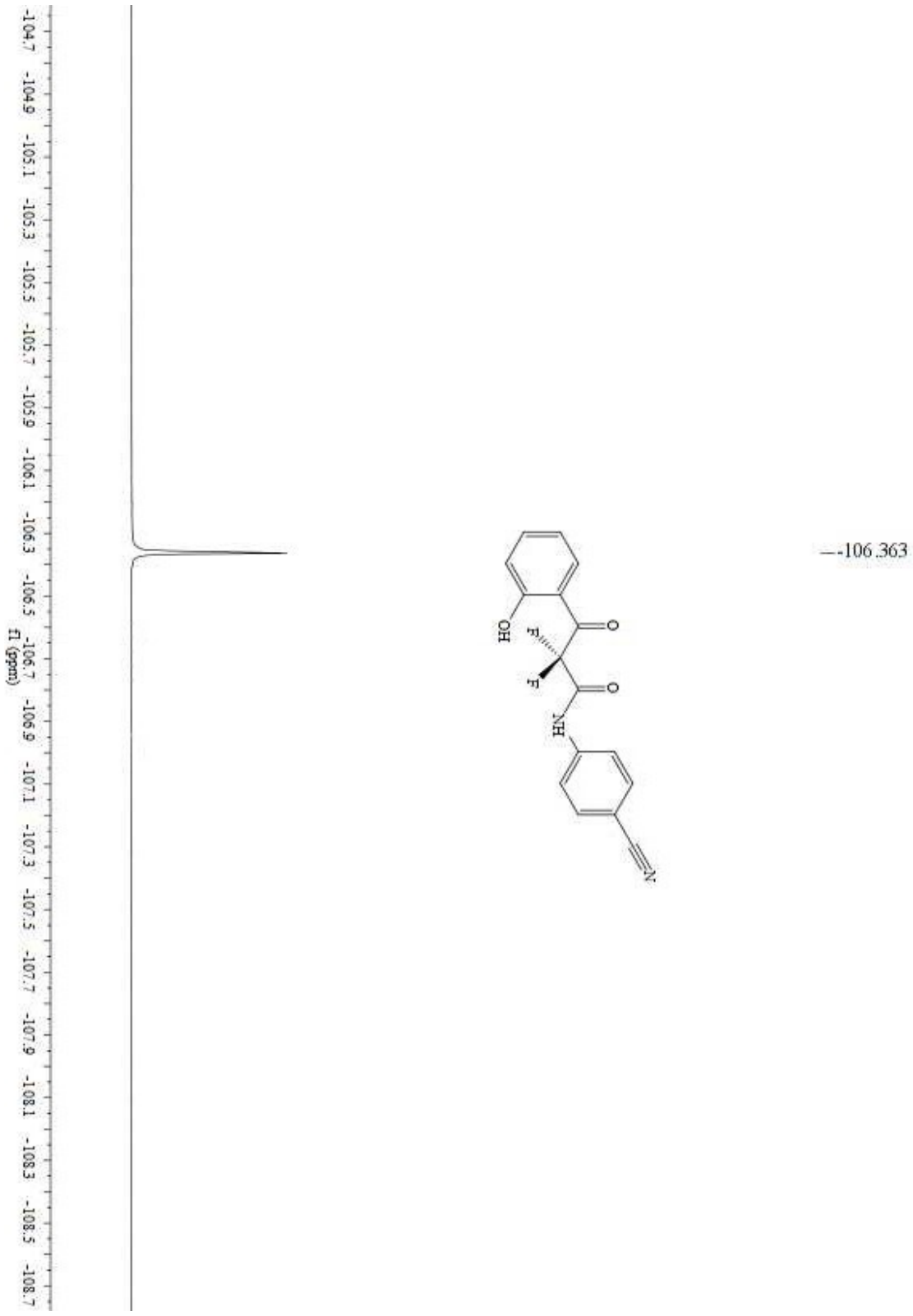

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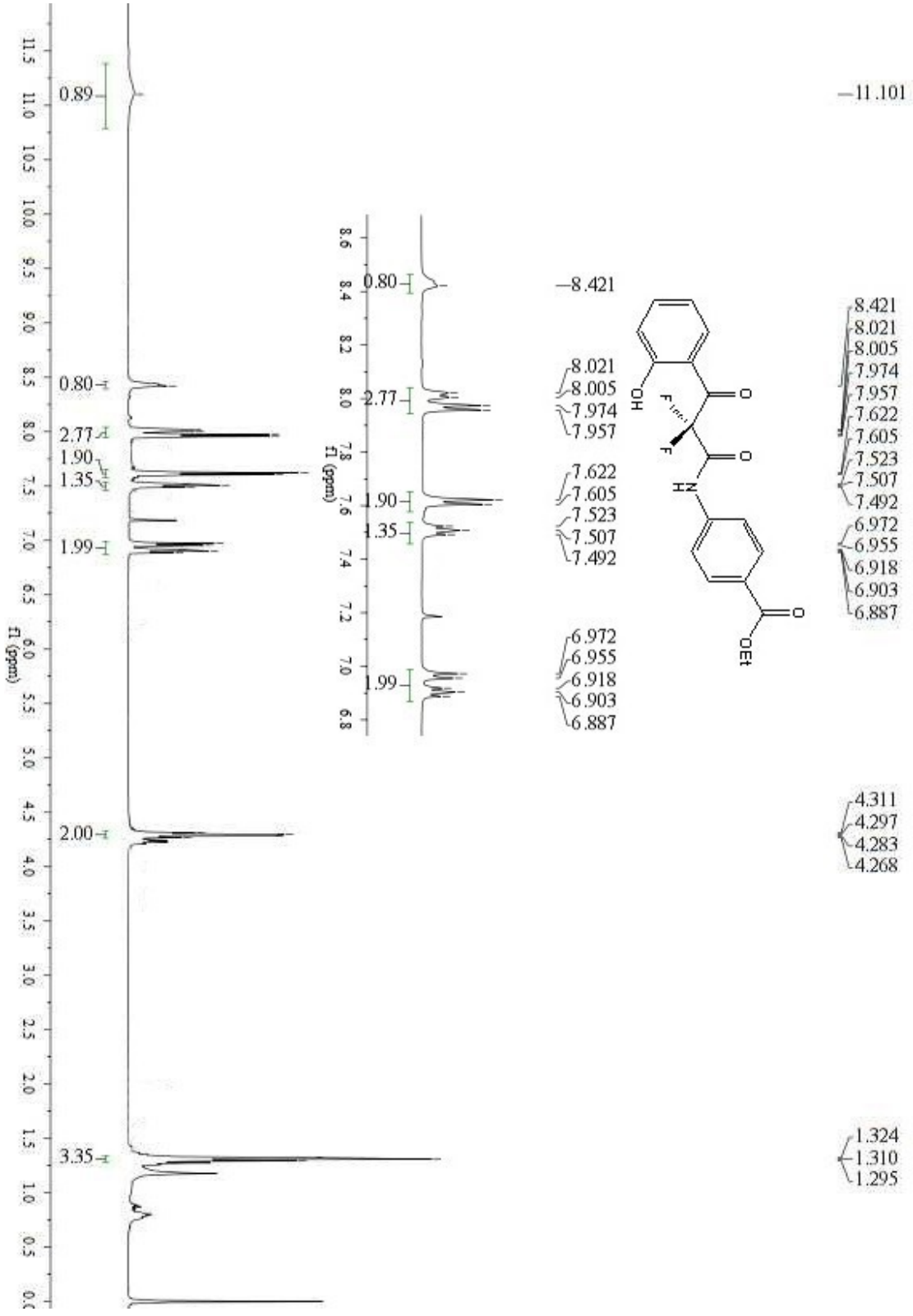

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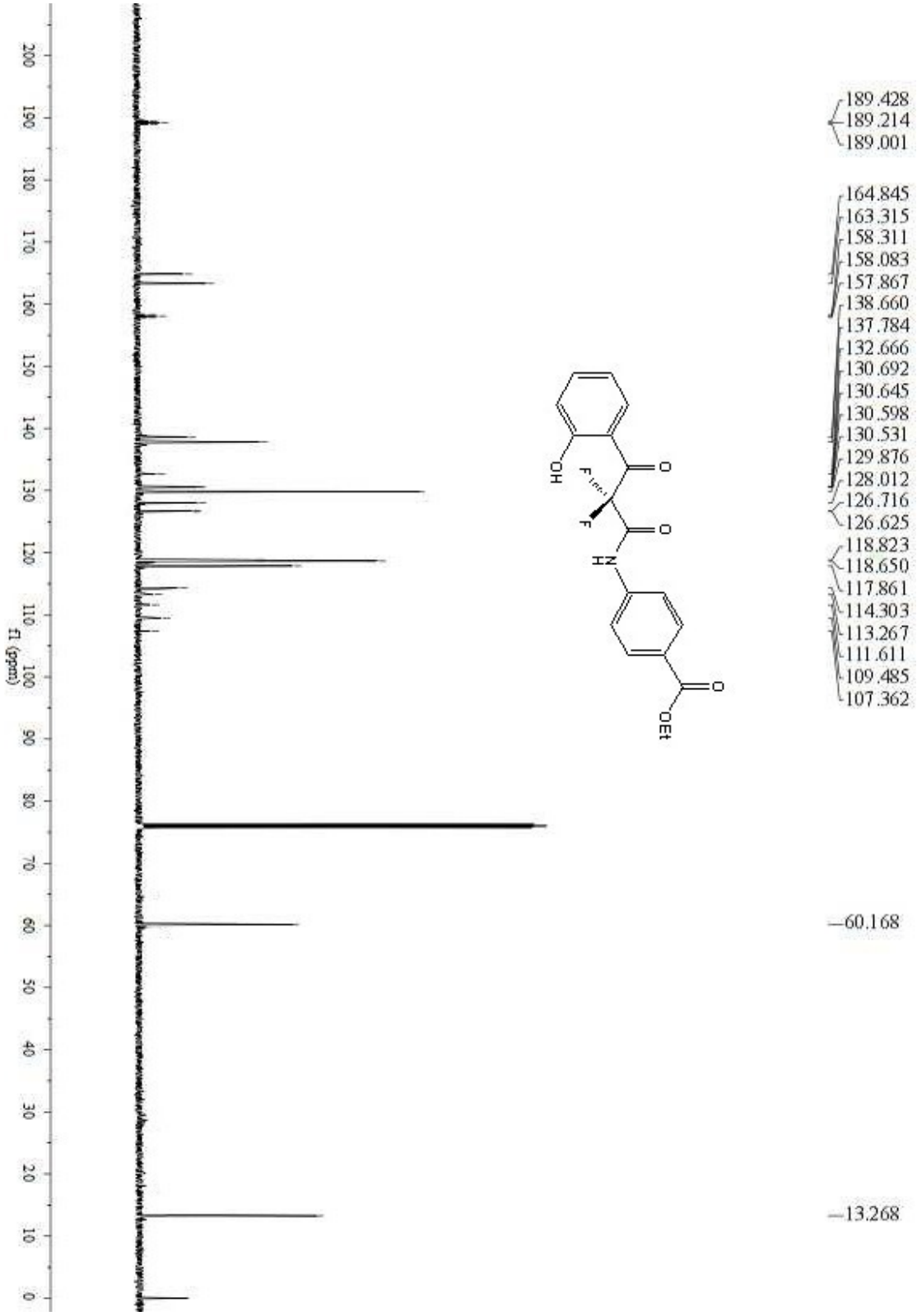

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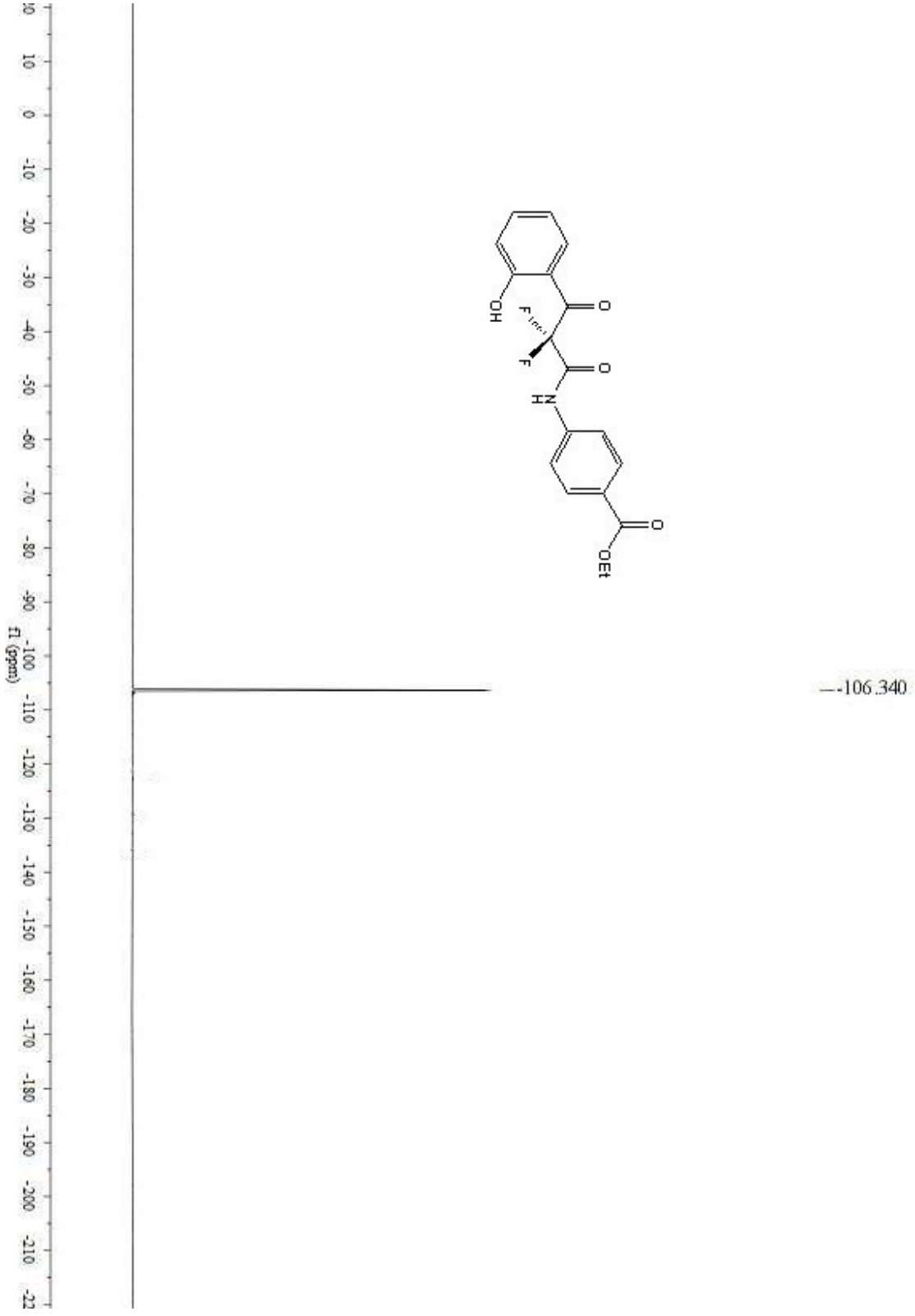

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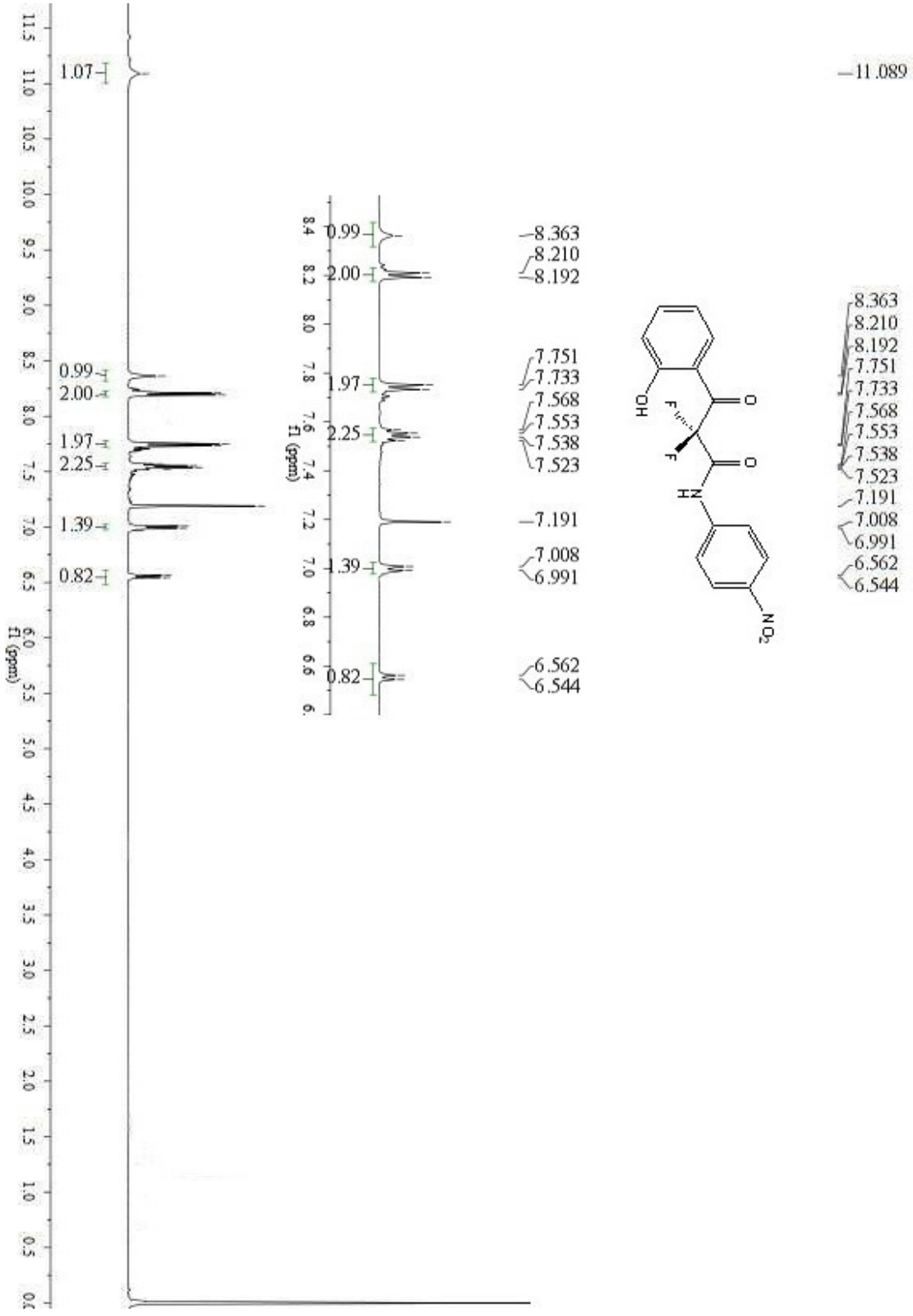

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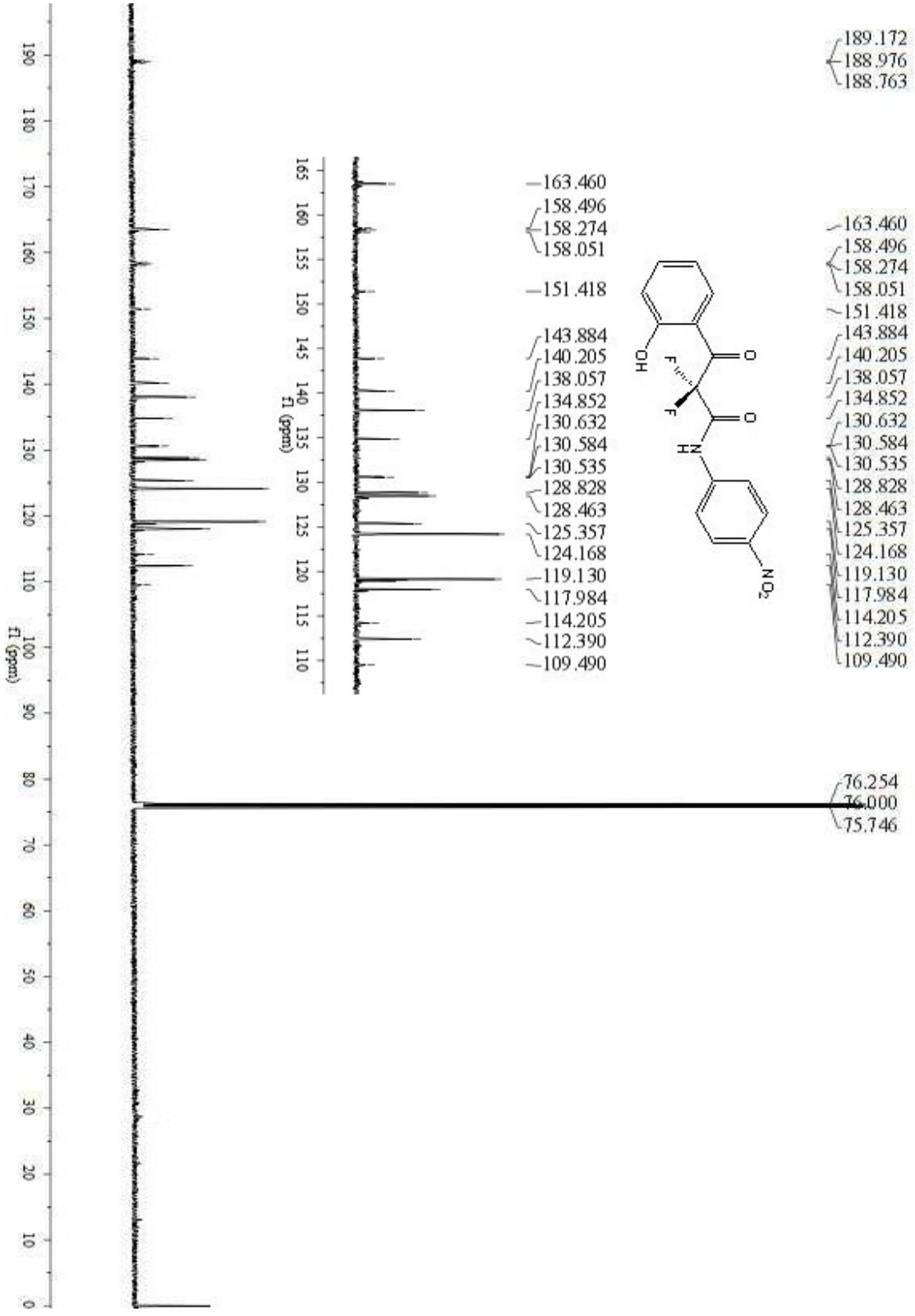
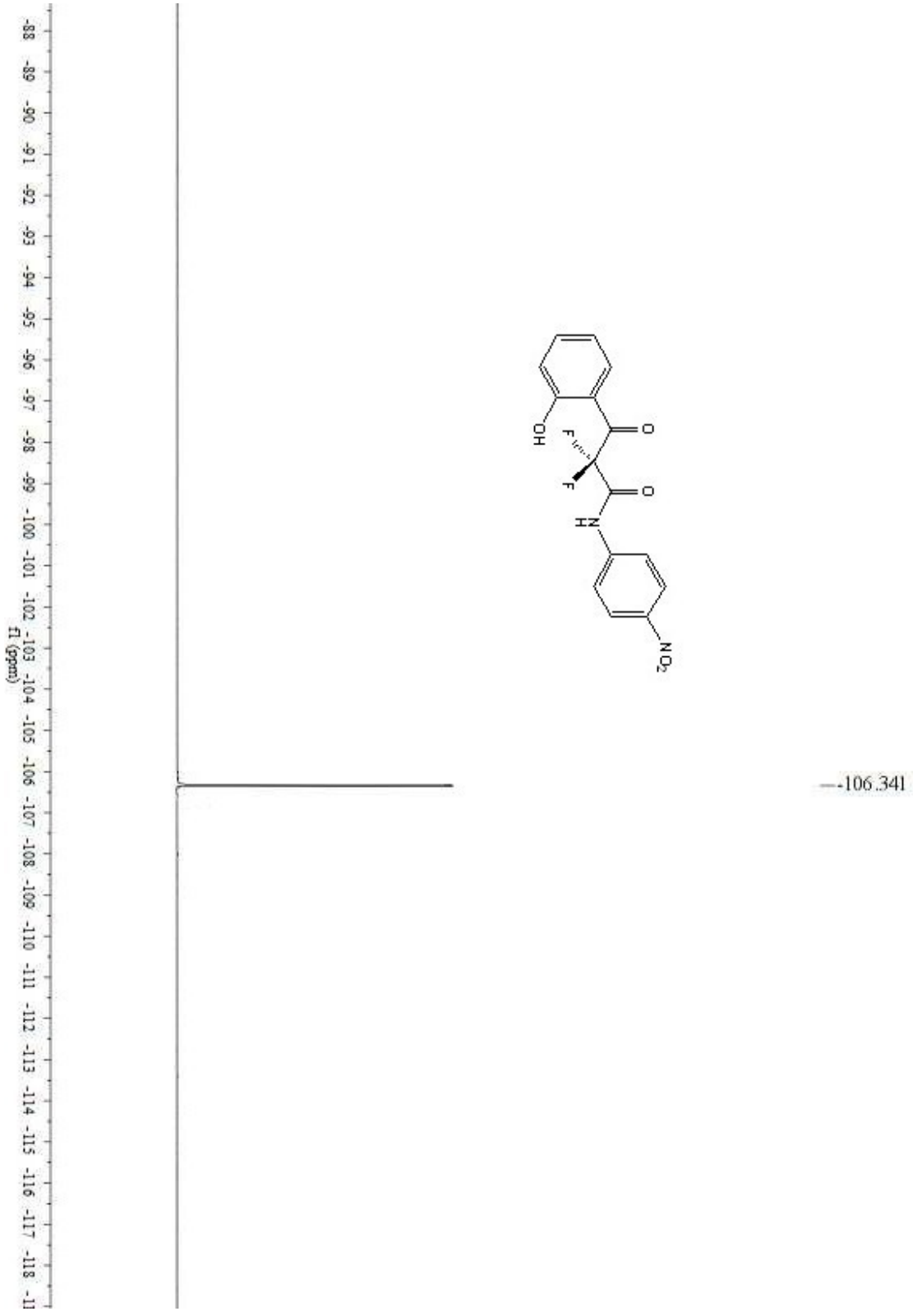
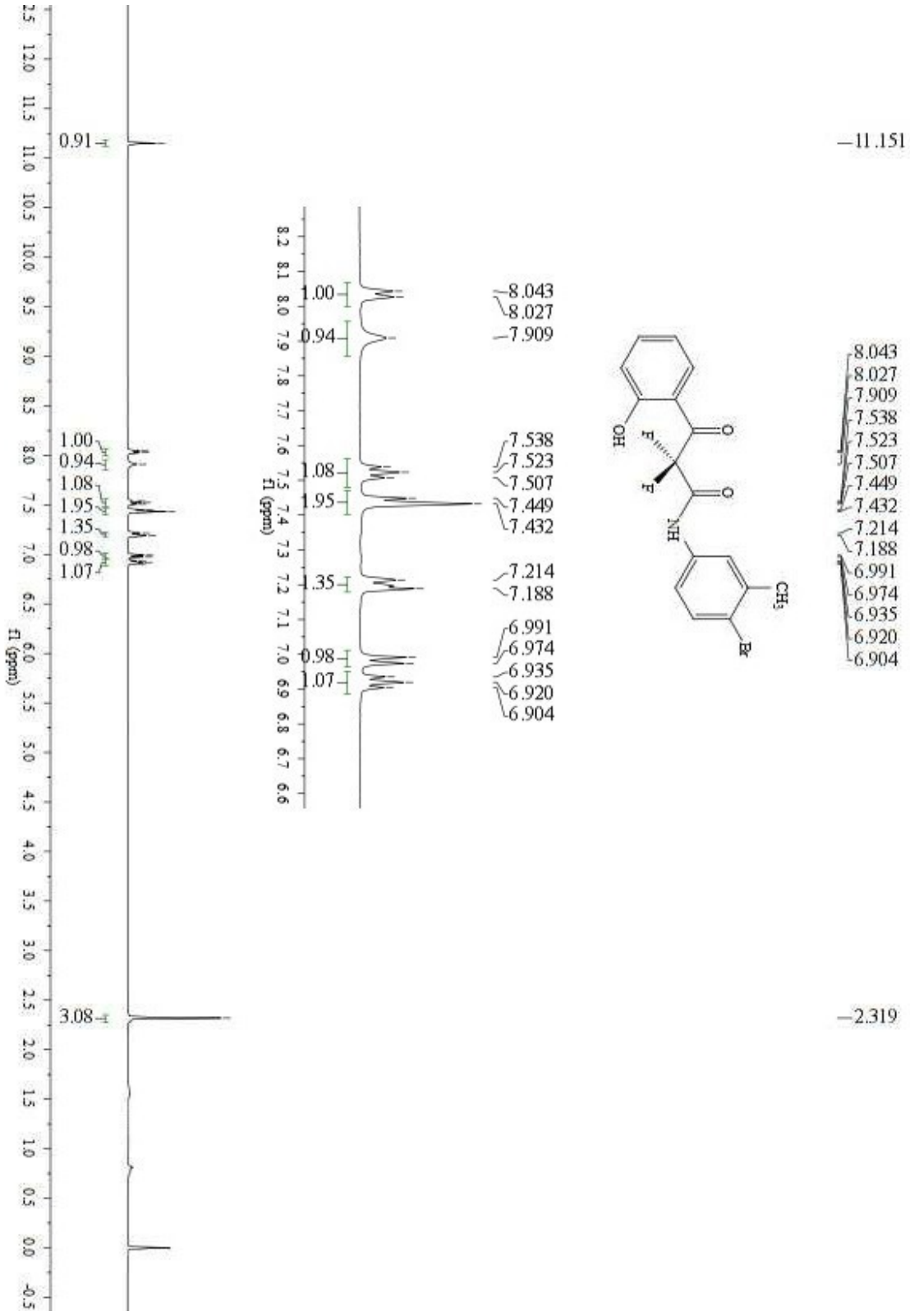


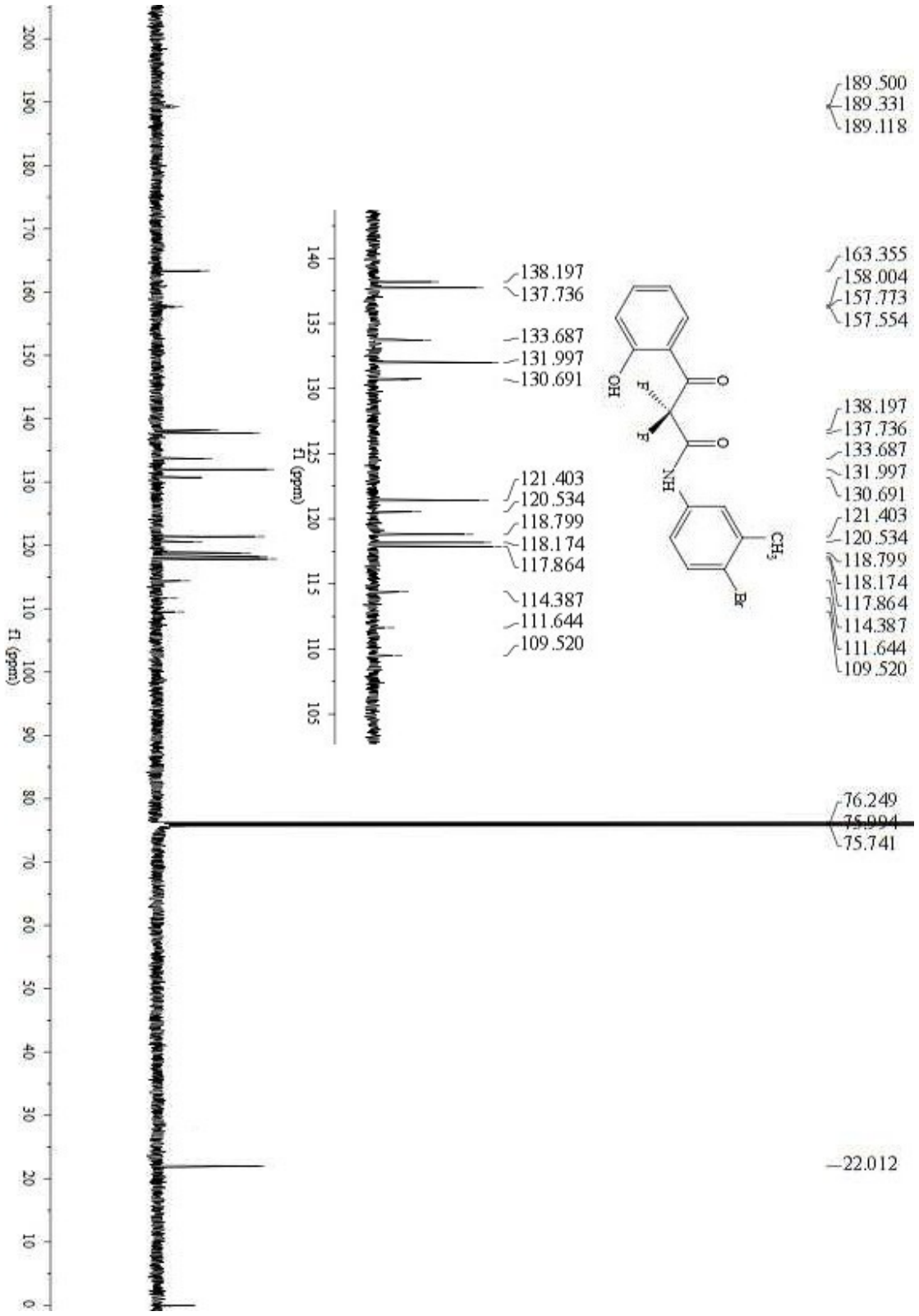
^{13}C NMR of **3p** in $CDCl_3$



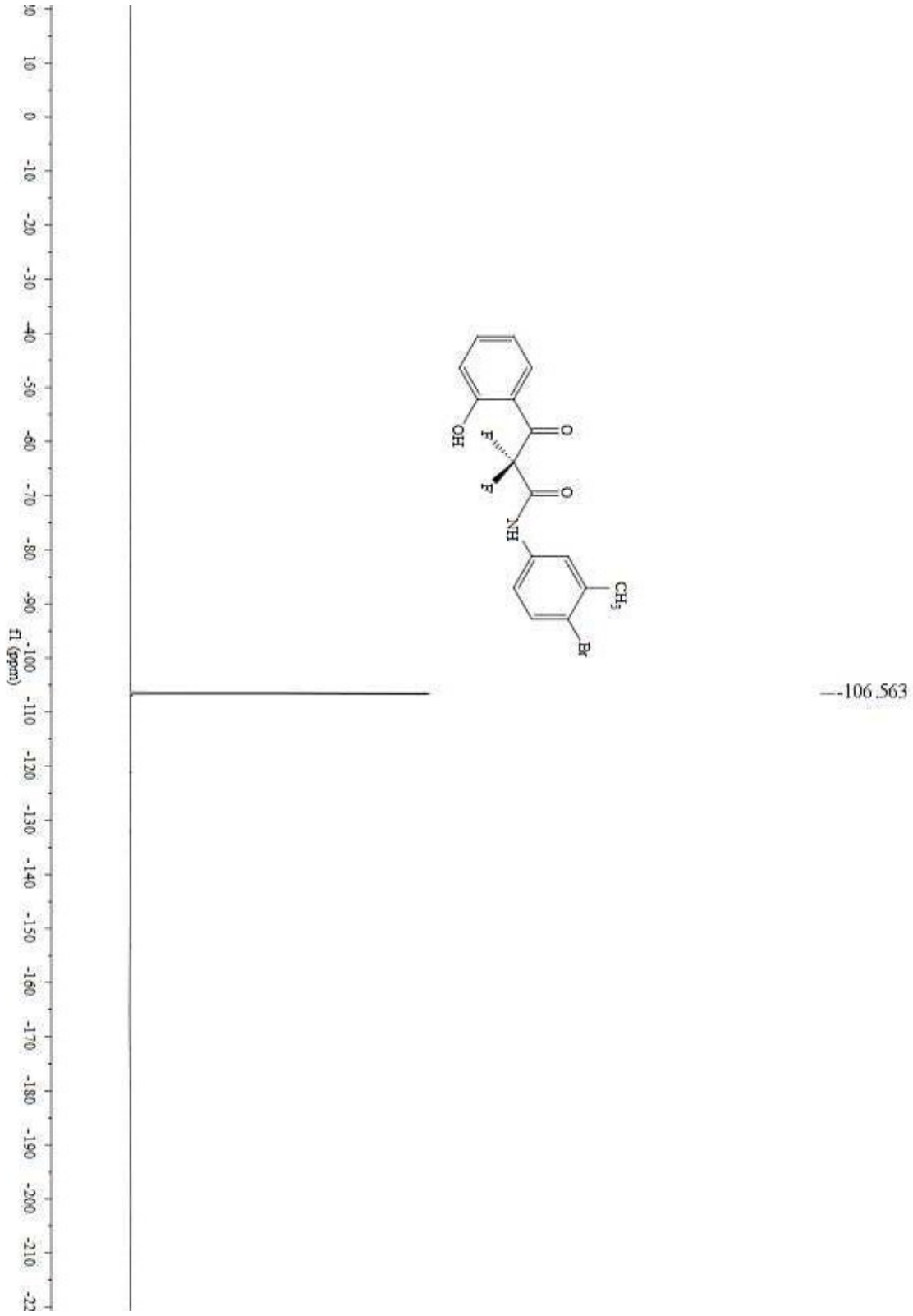
^{19}F NMR of **3p** in $CDCl_3$



^{1}H NMR of **3q** in $CDCl_3$



^{13}C NMR of **3q** in $CDCl_3$



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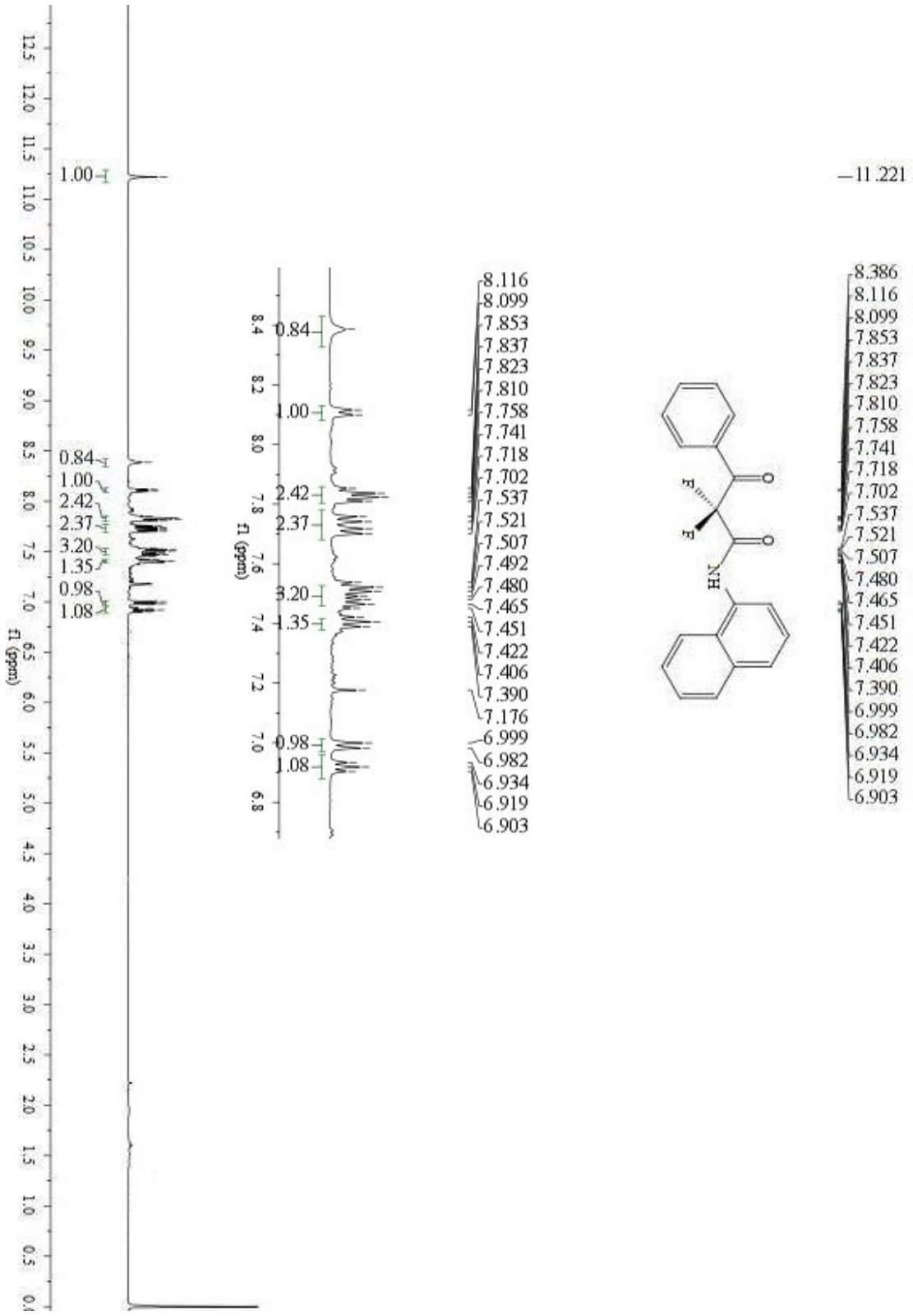

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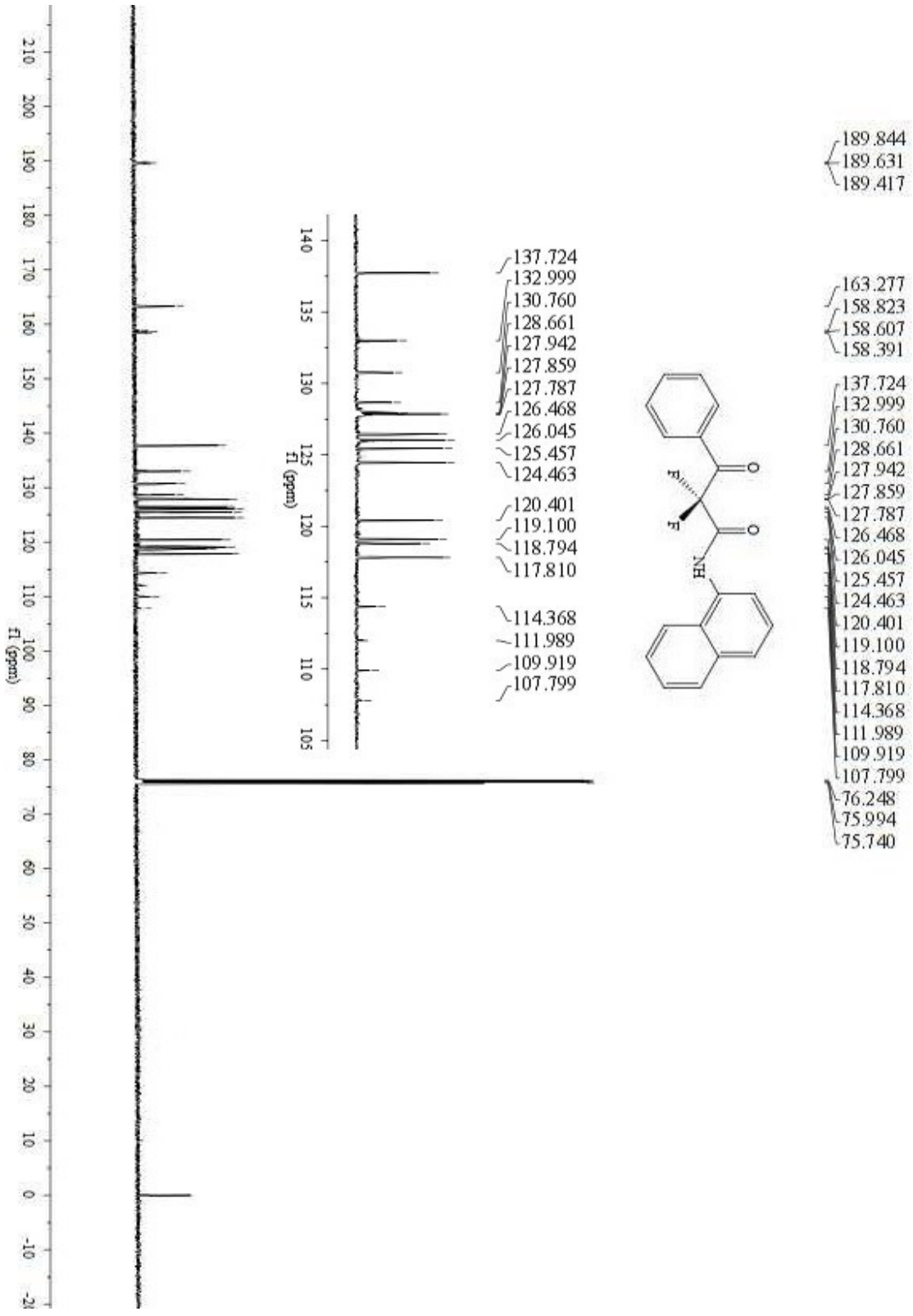
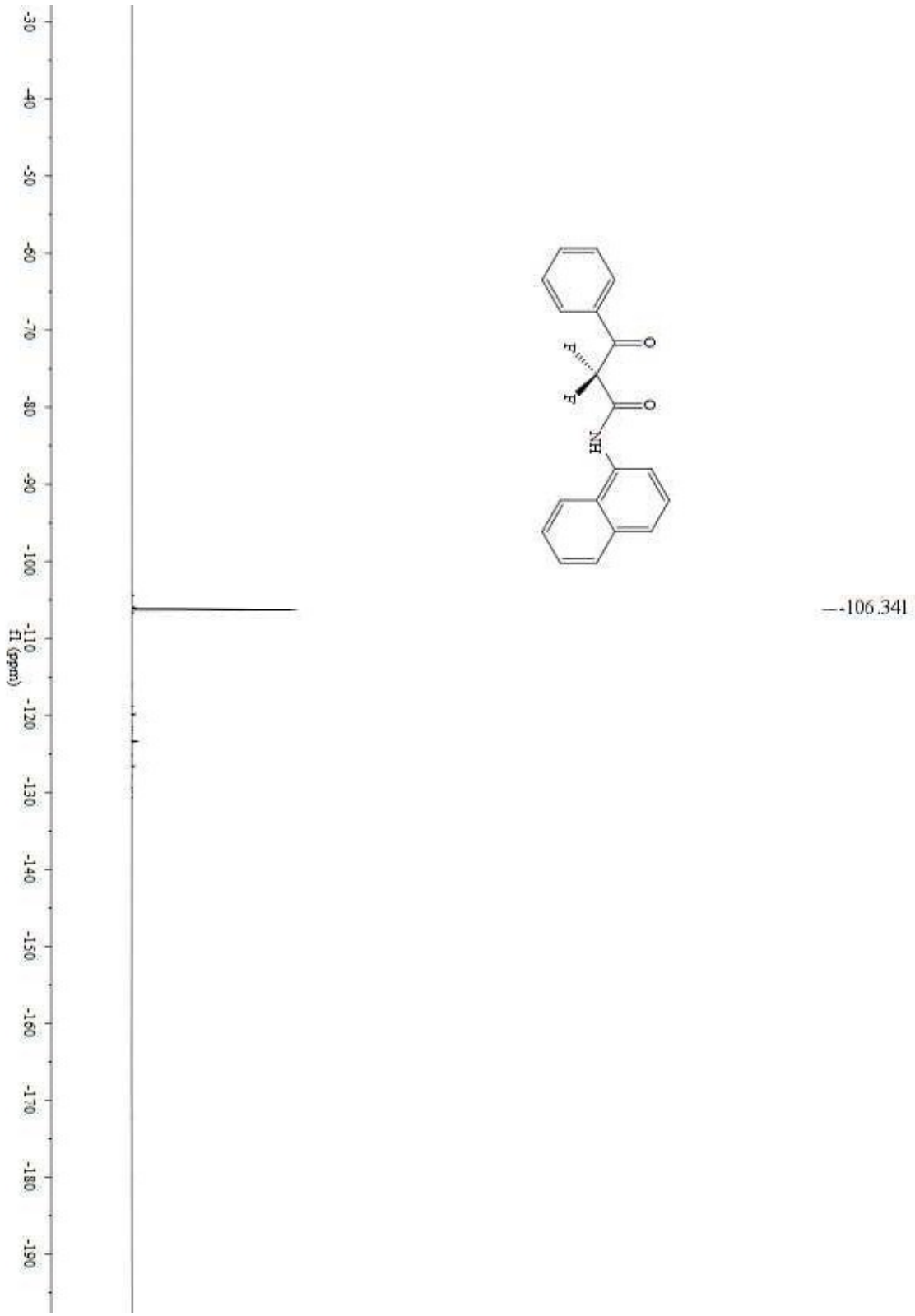
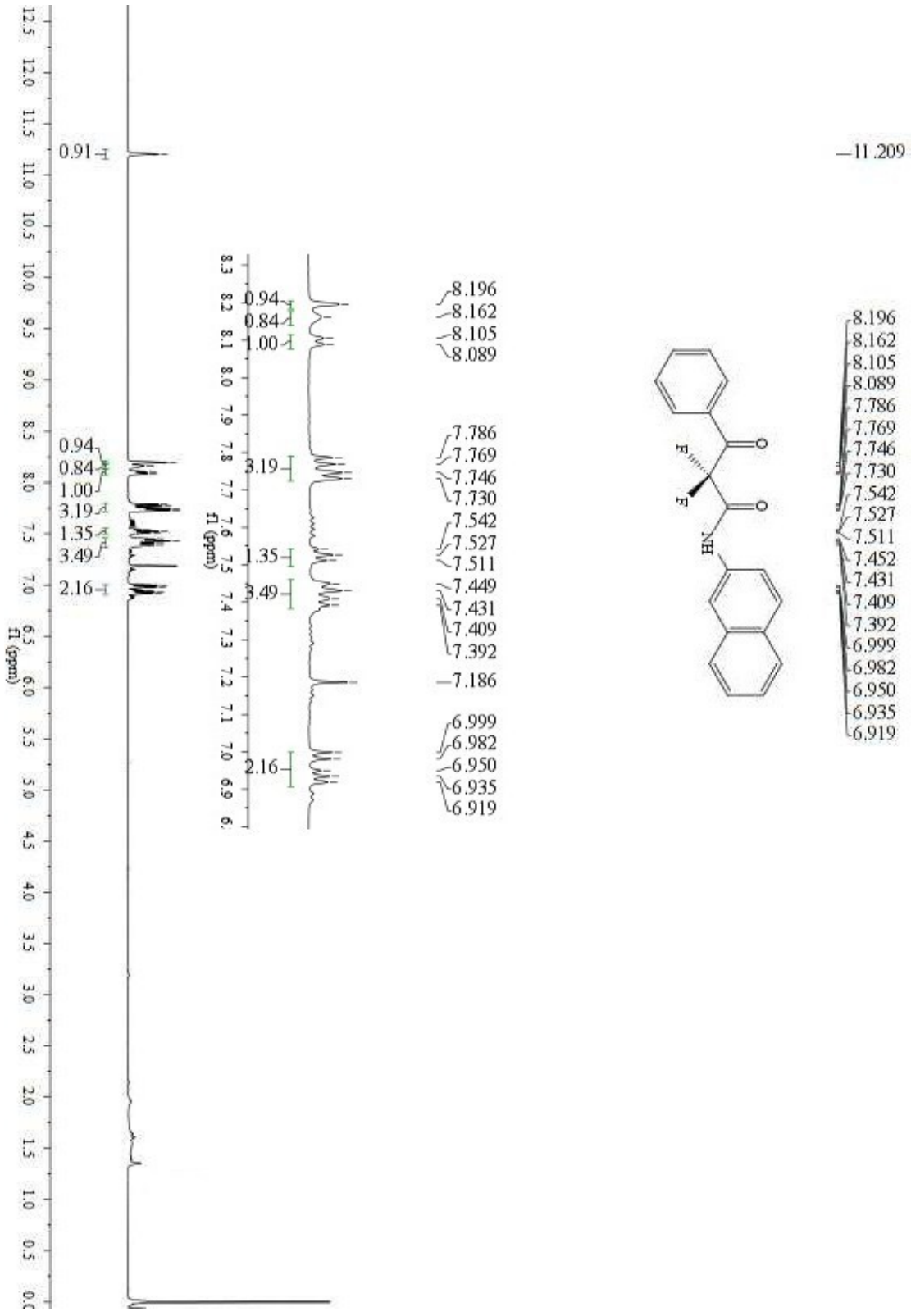


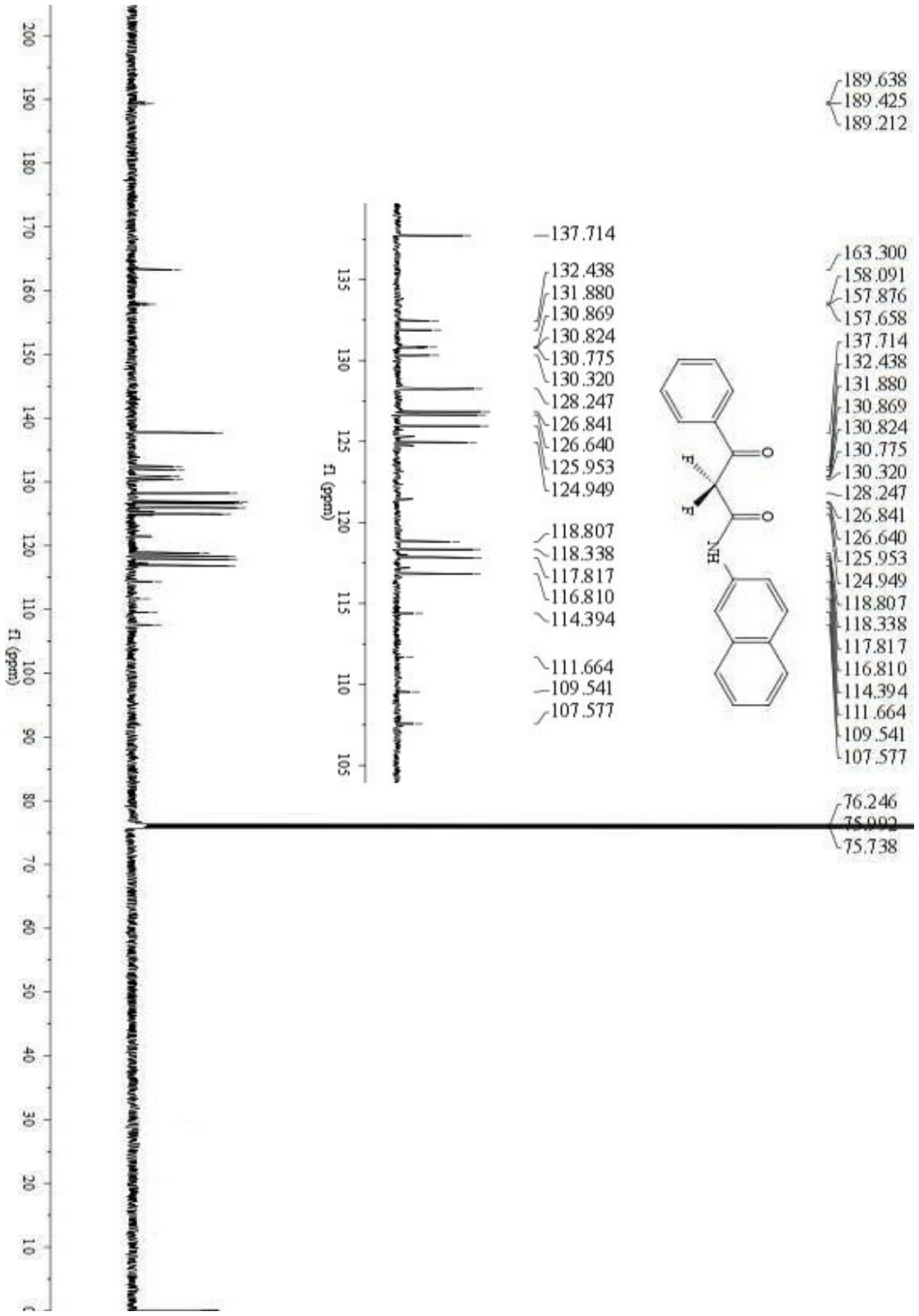
^{13}C NMR of **3r** in $CDCl_3$



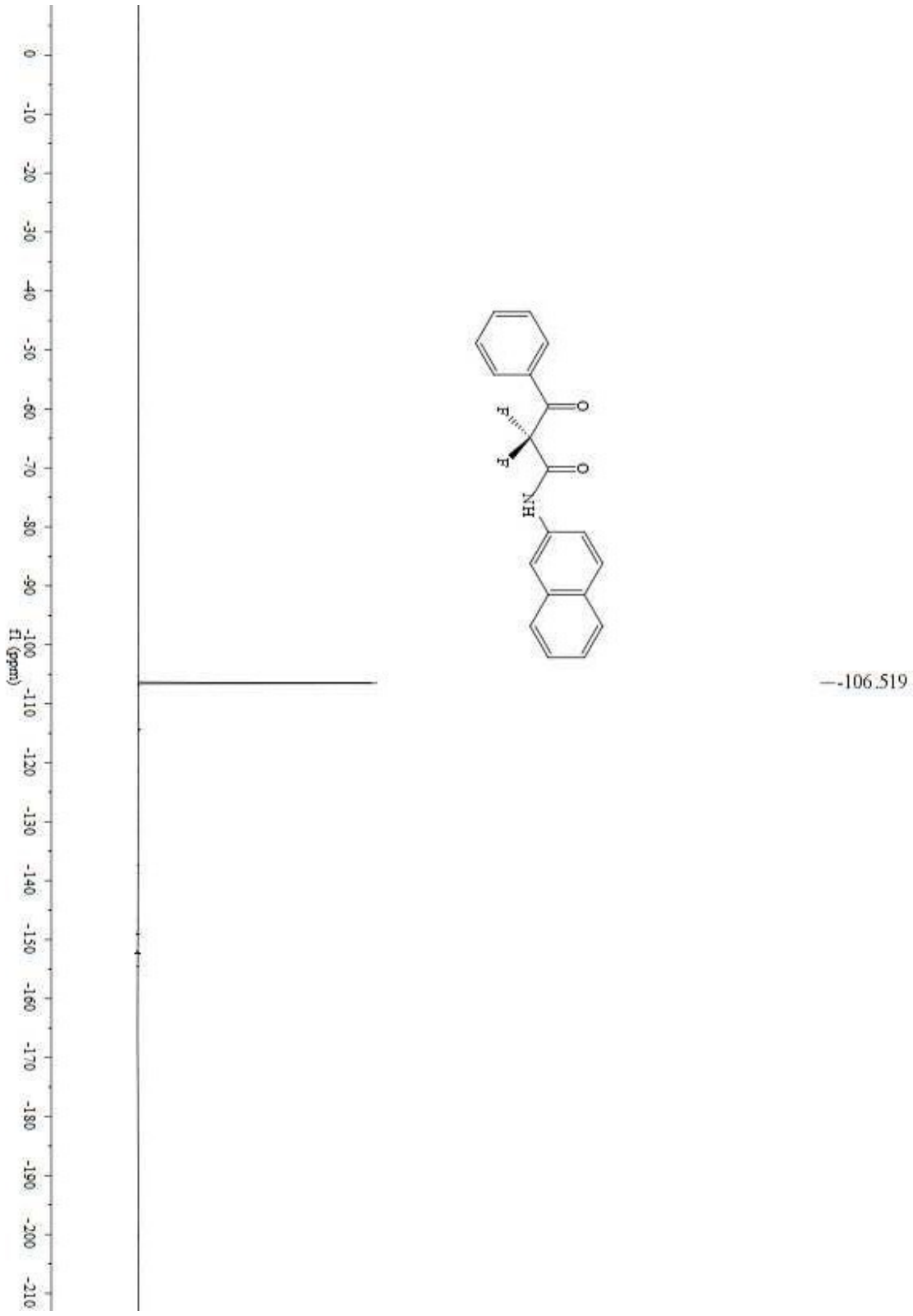
^{19}F NMR of **3r** in $CDCl_3$



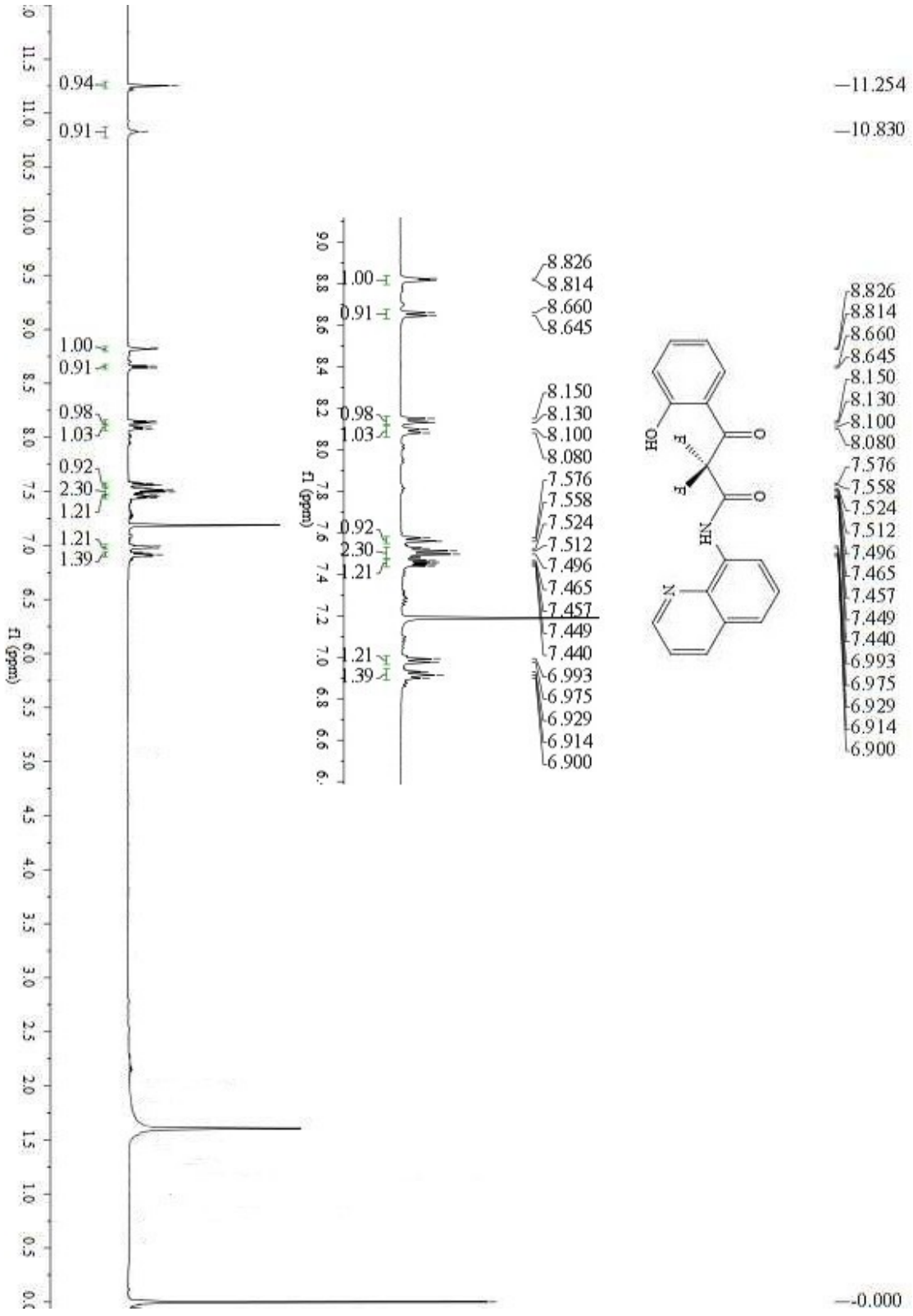
^{1}H NMR of **3s** in $CDCl_3$



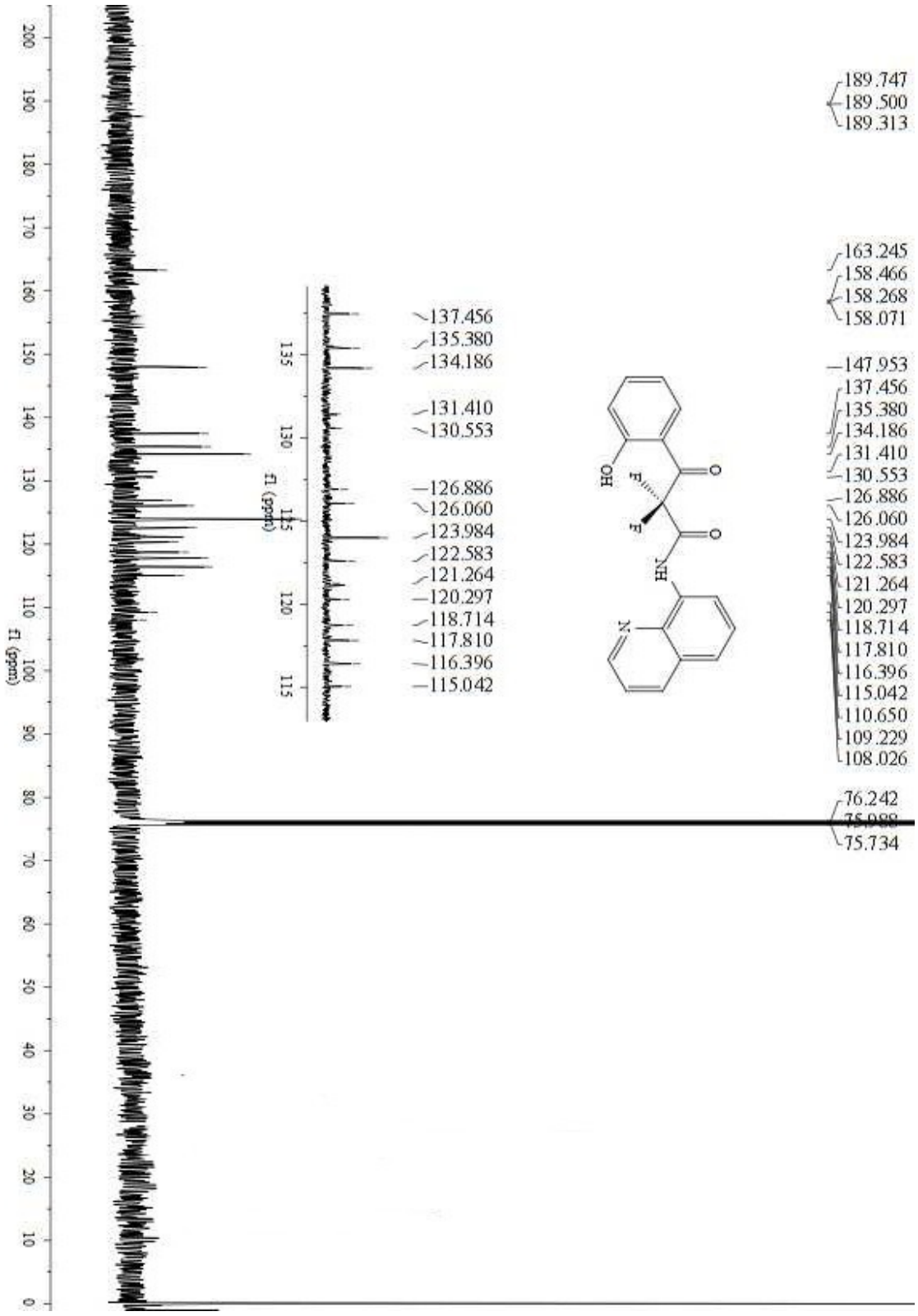
^{13}C NMR of **3s** in $CDCl_3$



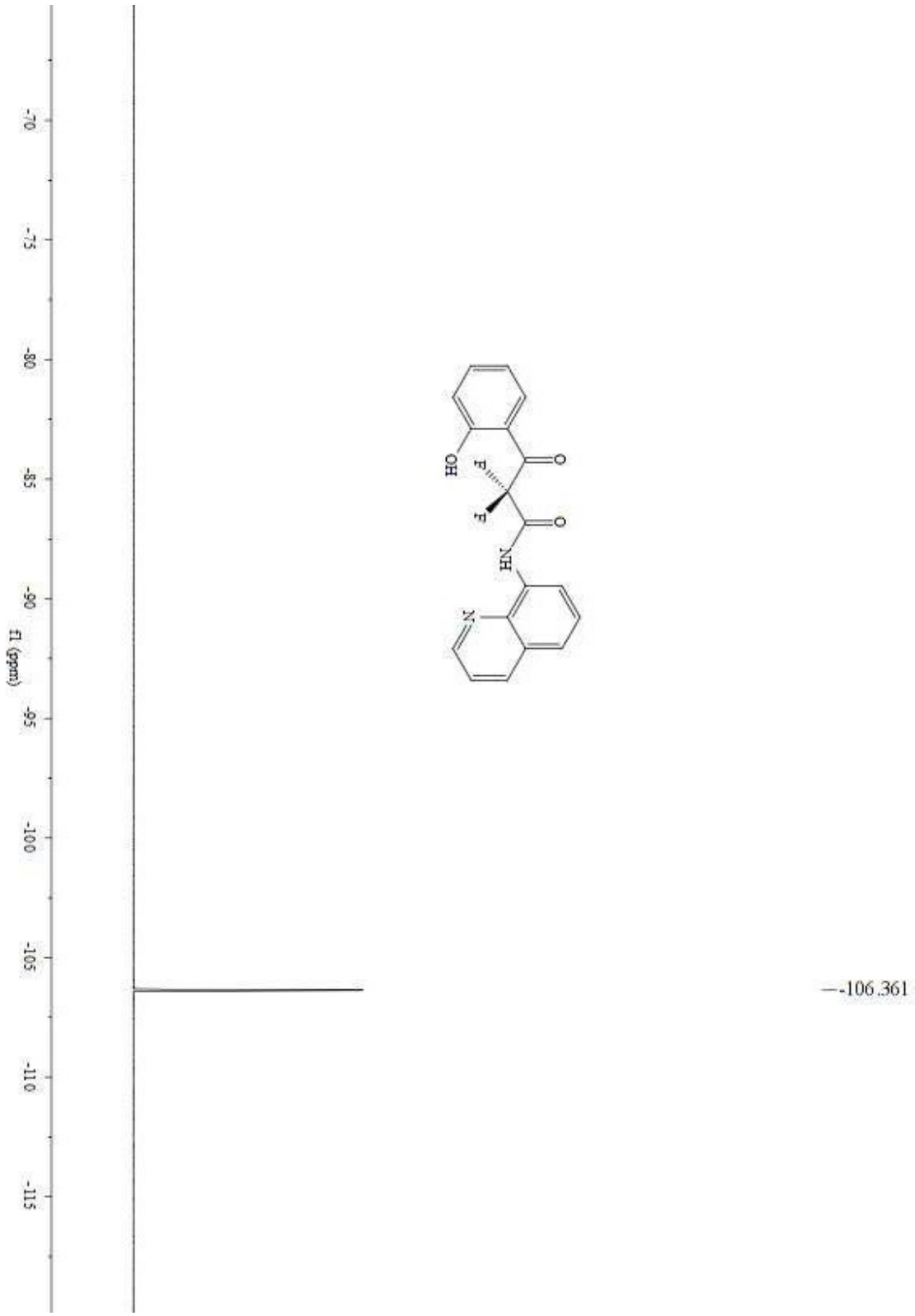
^{19}F NMR of **3s** in $CDCl_3$



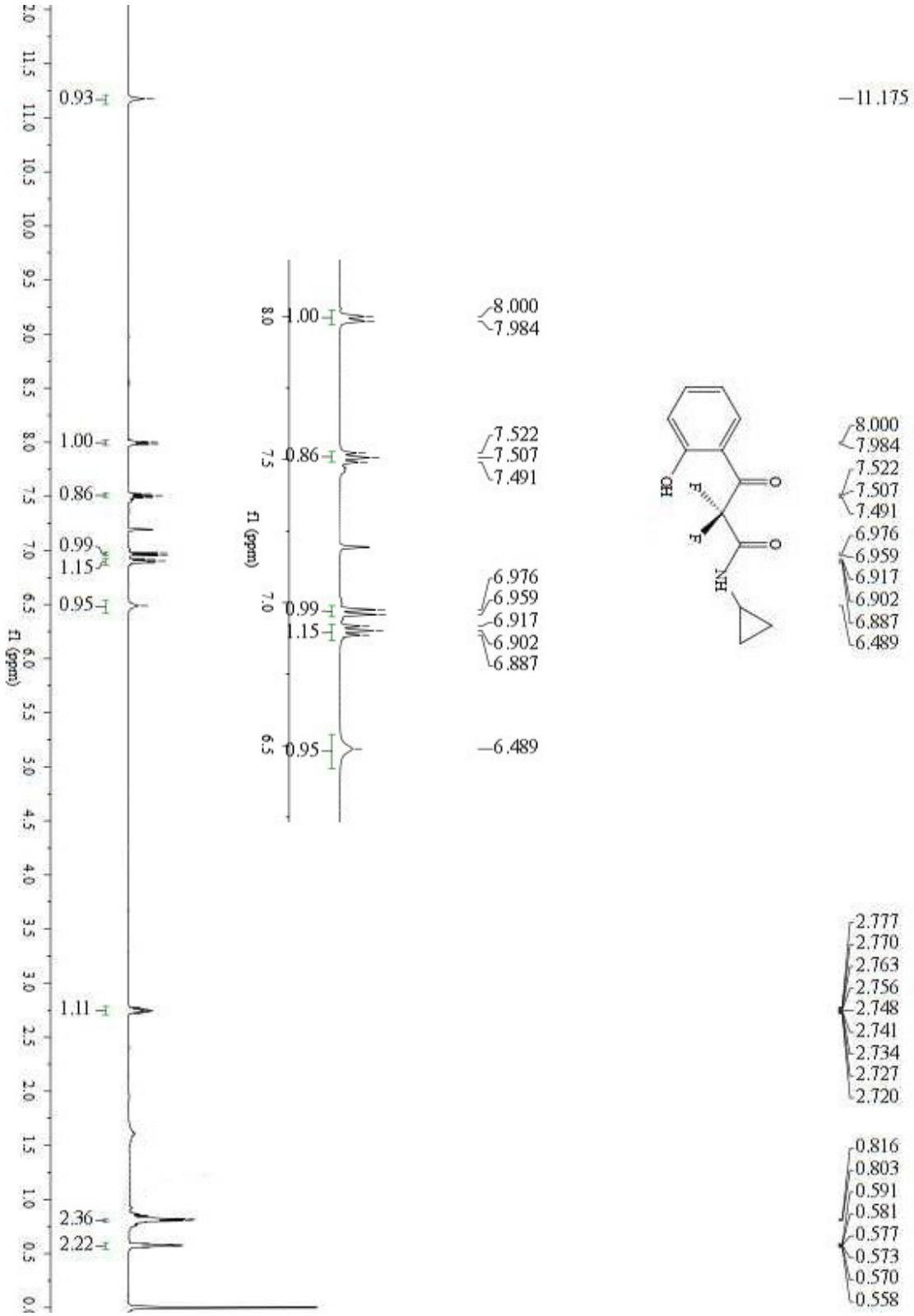
^{1}H NMR of **3t** in $CDCl_3$



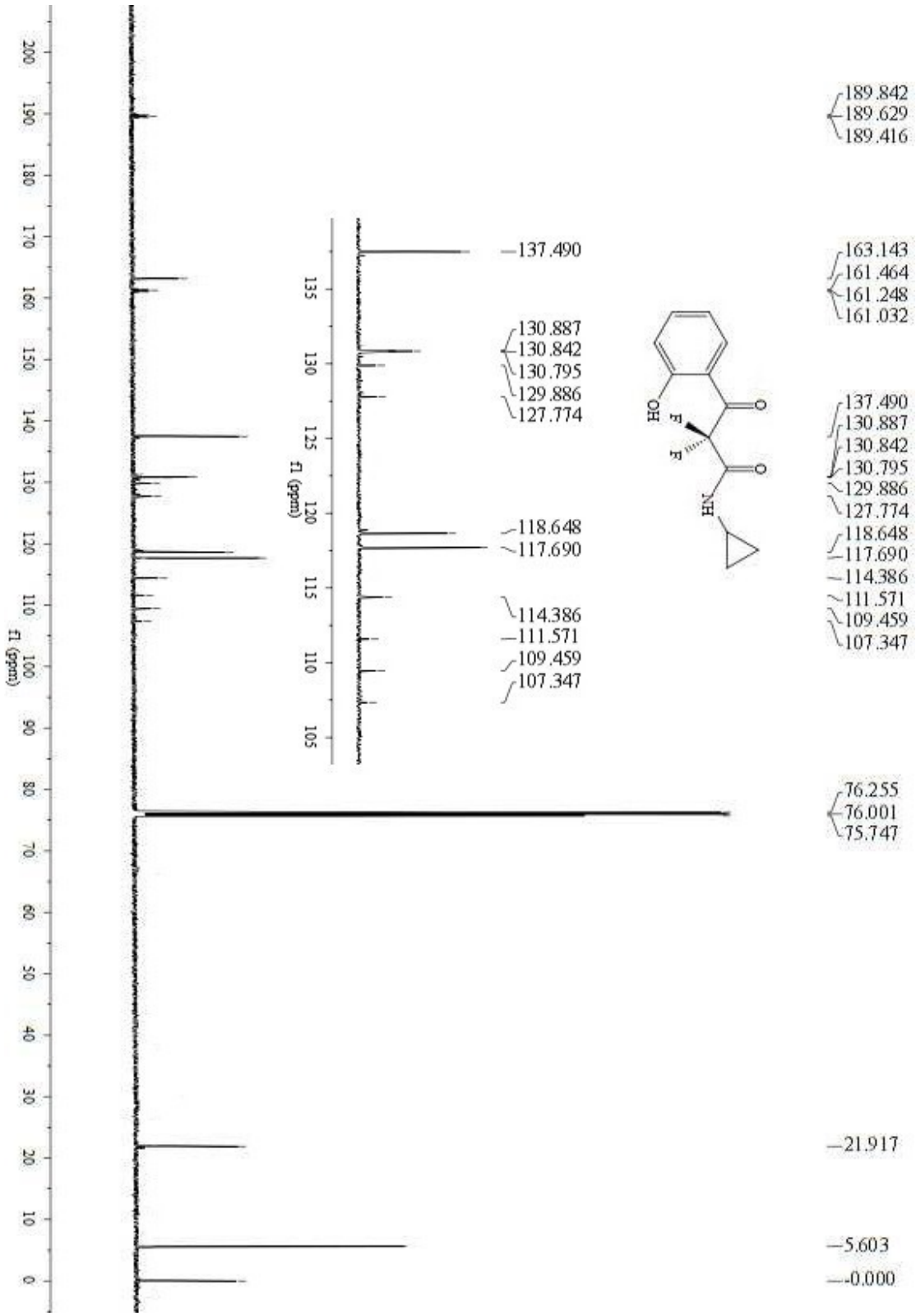
^{13}C NMR of **3t** in $CDCl_3$



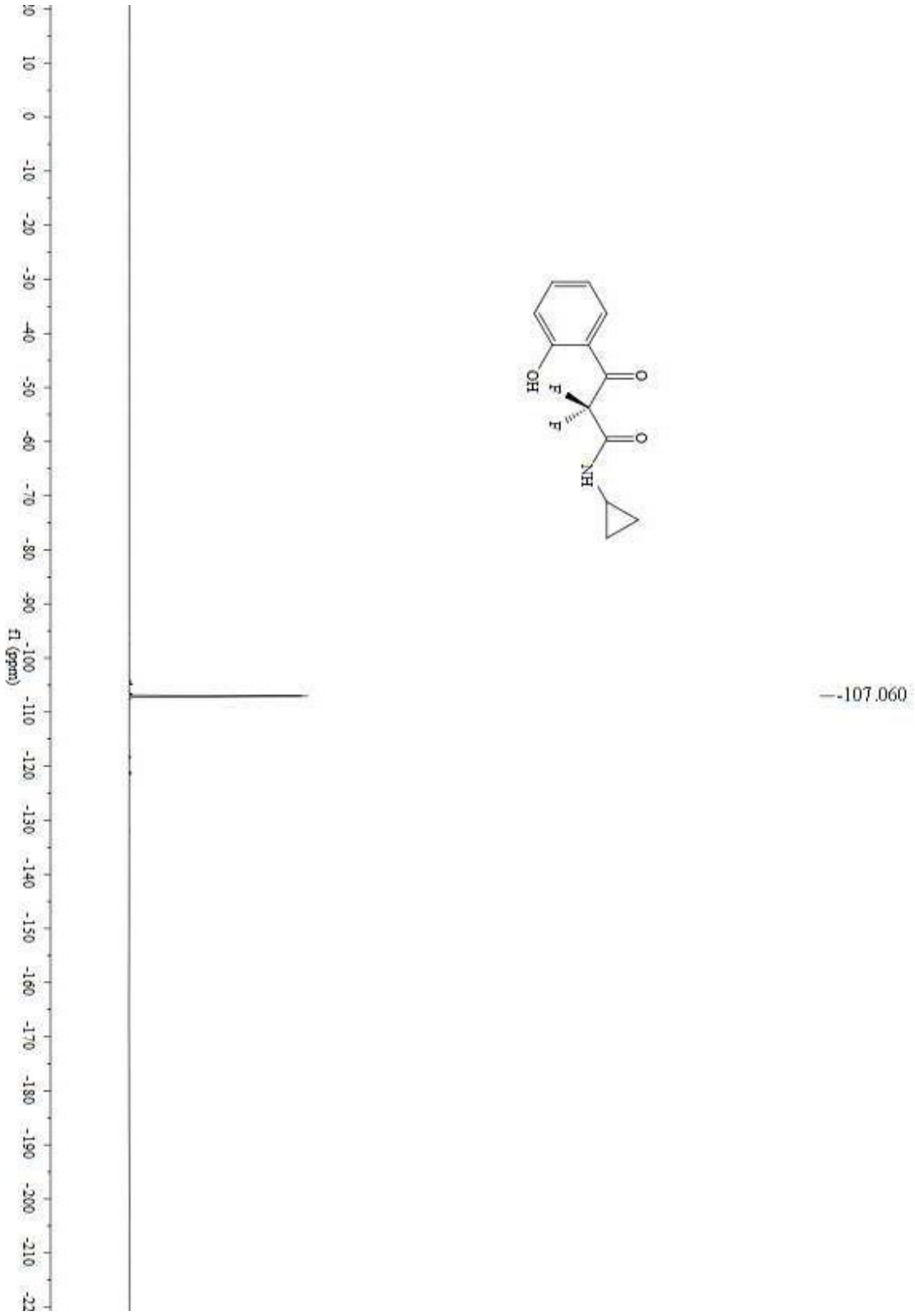
^{19}F NMR of **3t** in $CDCl_3$



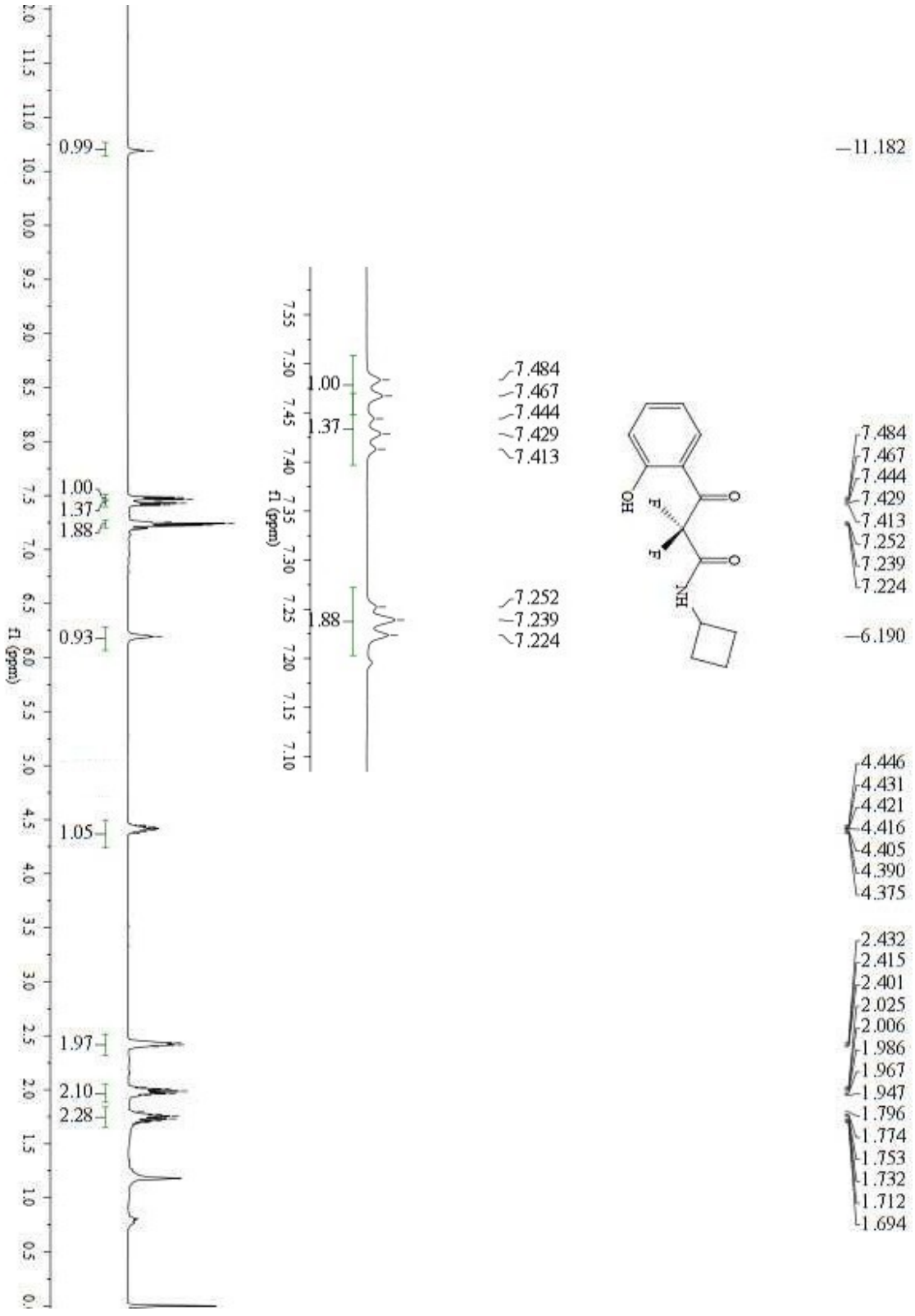
^{1}H NMR of **3u** in $CDCl_3$



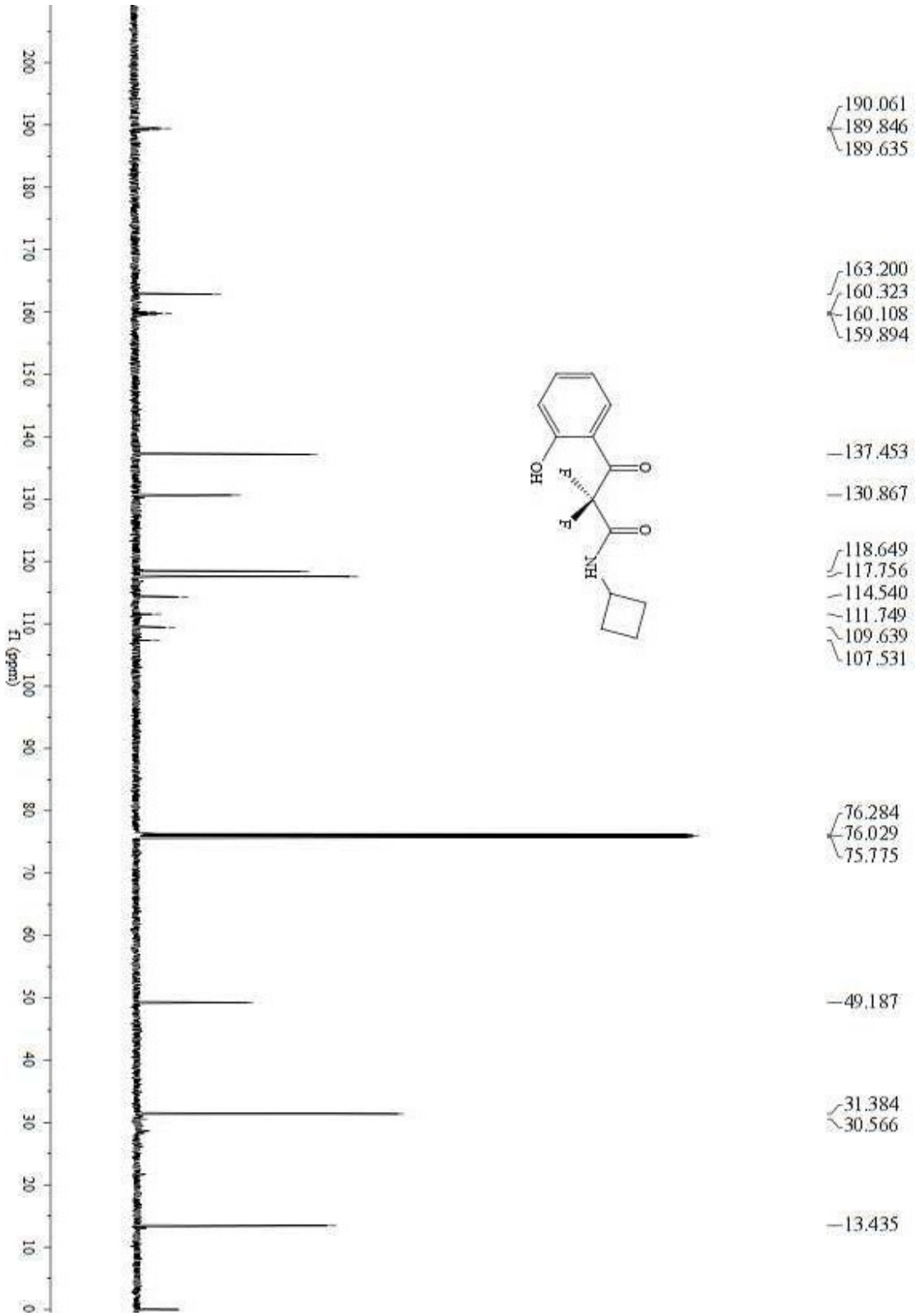
^{13}C NMR of **3u** in $CDCl_3$



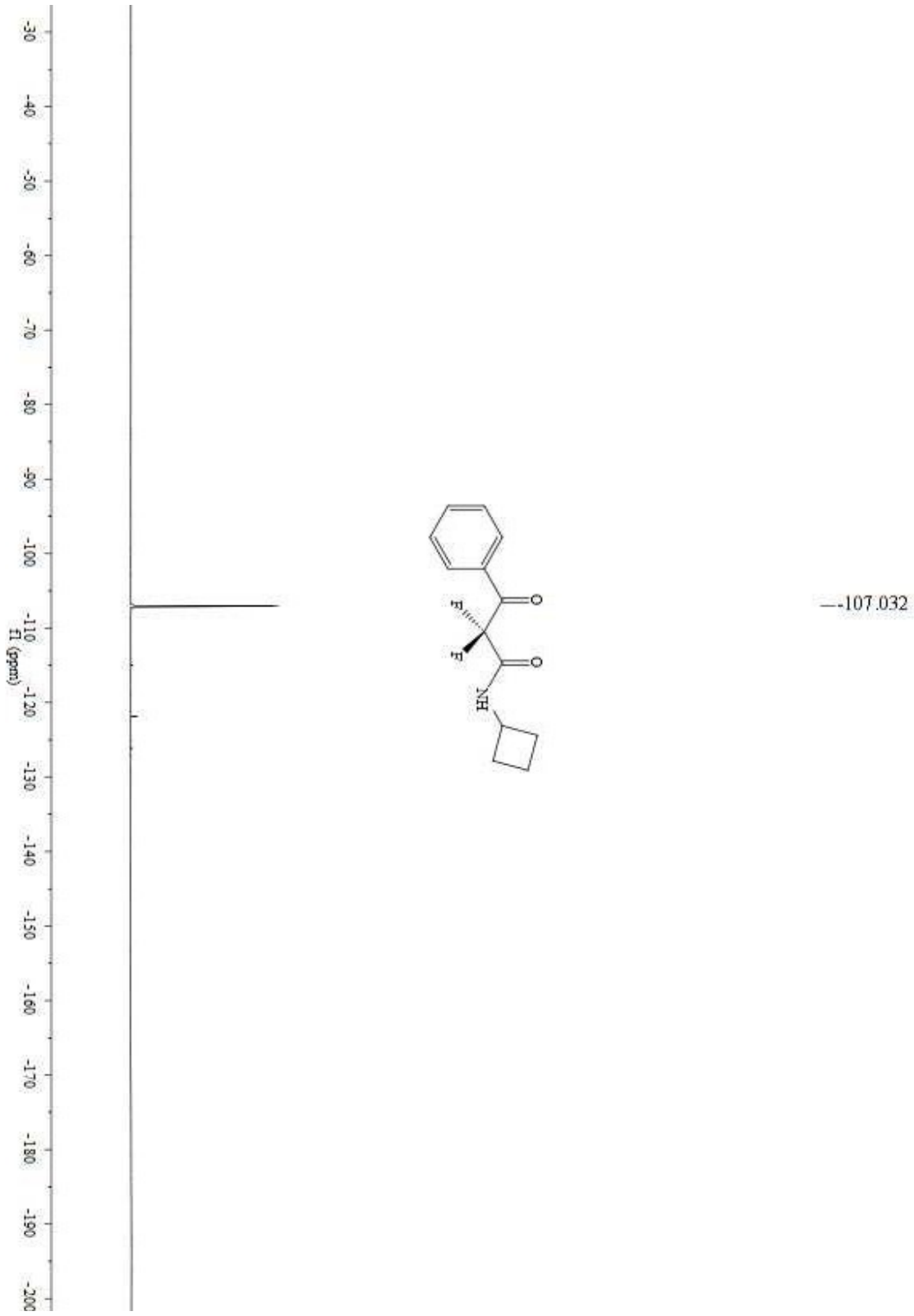
^{19}F NMR of **3u** in $CDCl_3$



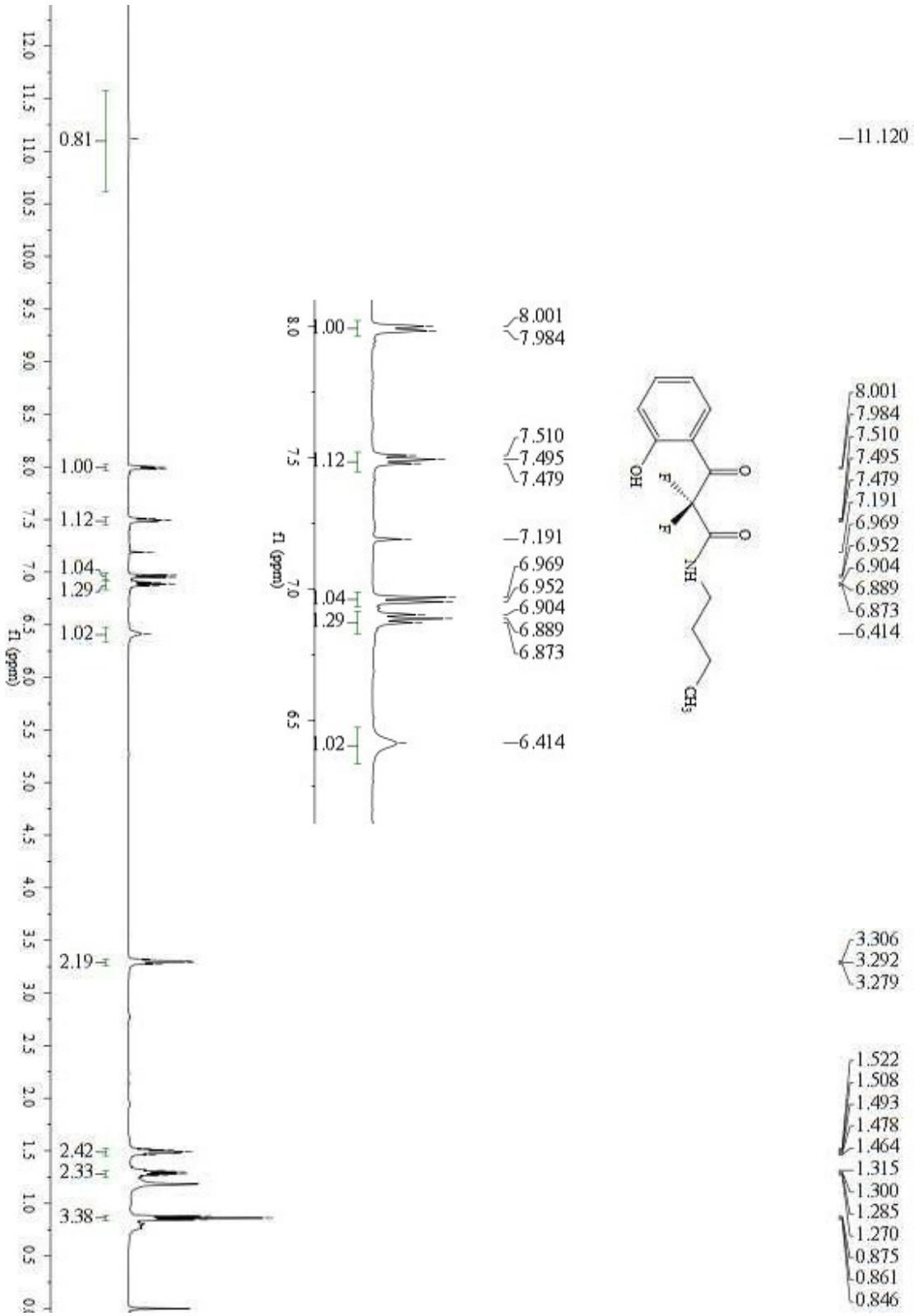
^{1}H NMR of **3v** in $CDCl_3$



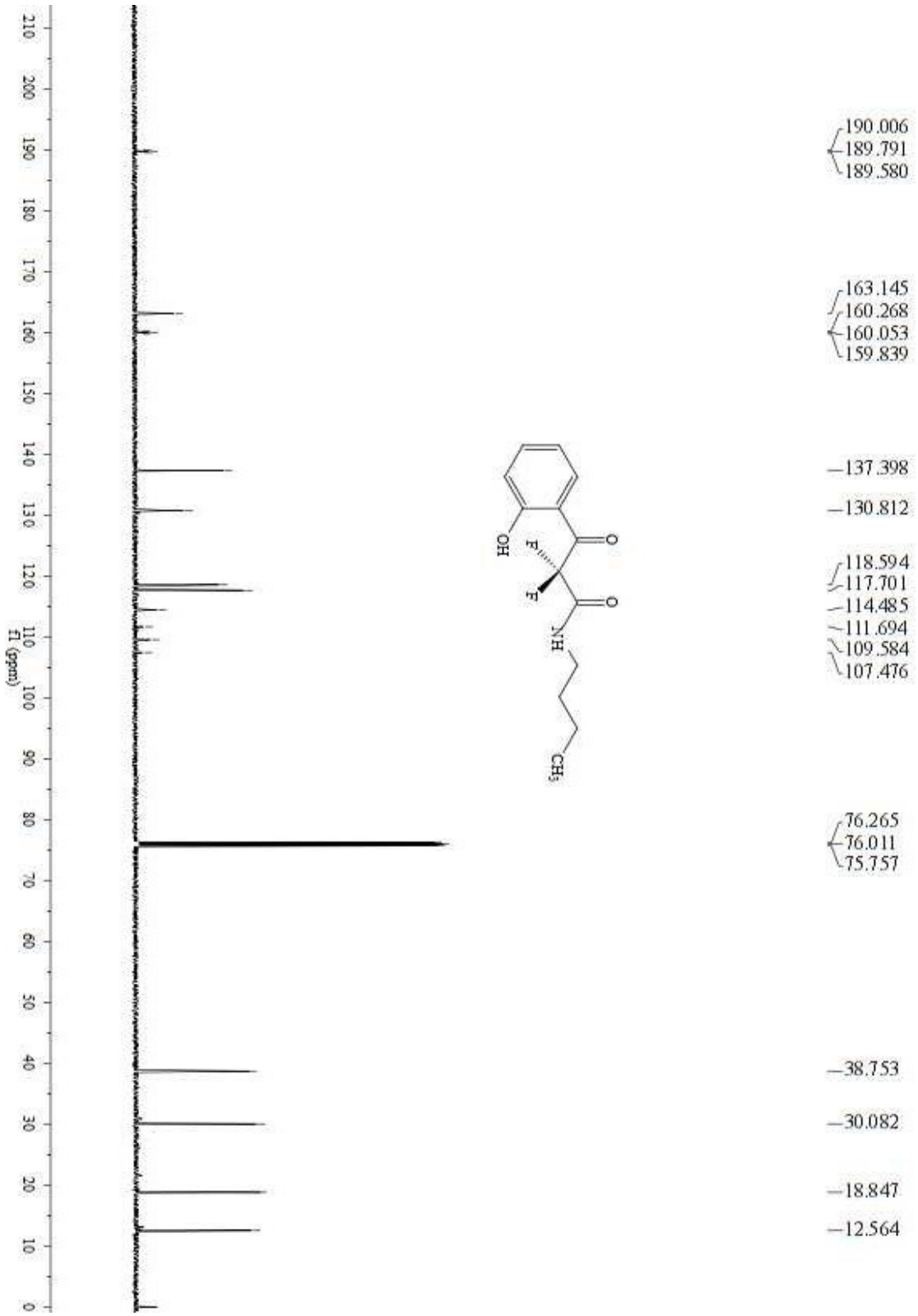
^{13}C NMR of **3v** in $CDCl_3$



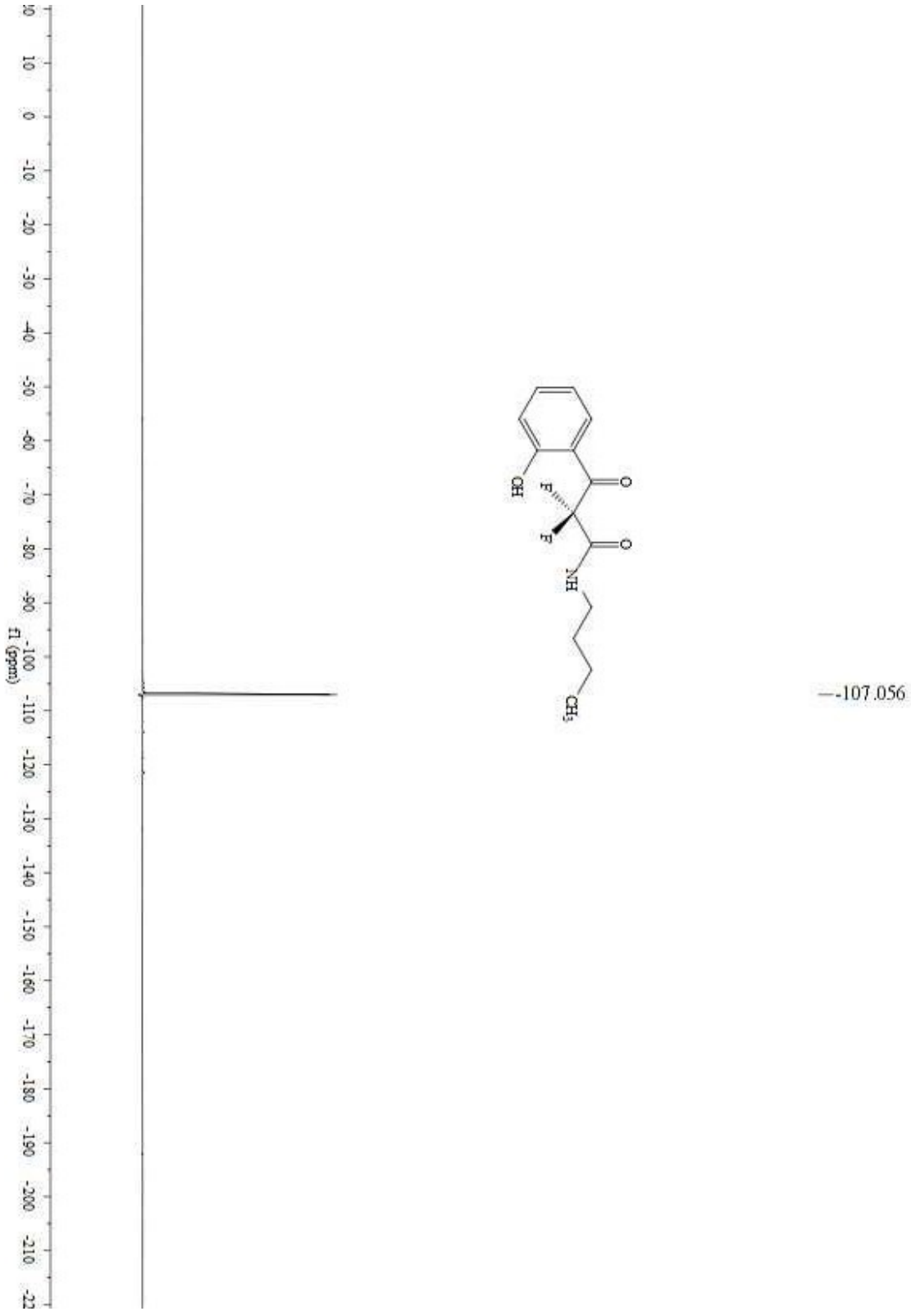
^{19}F NMR of **3v** in $CDCl_3$



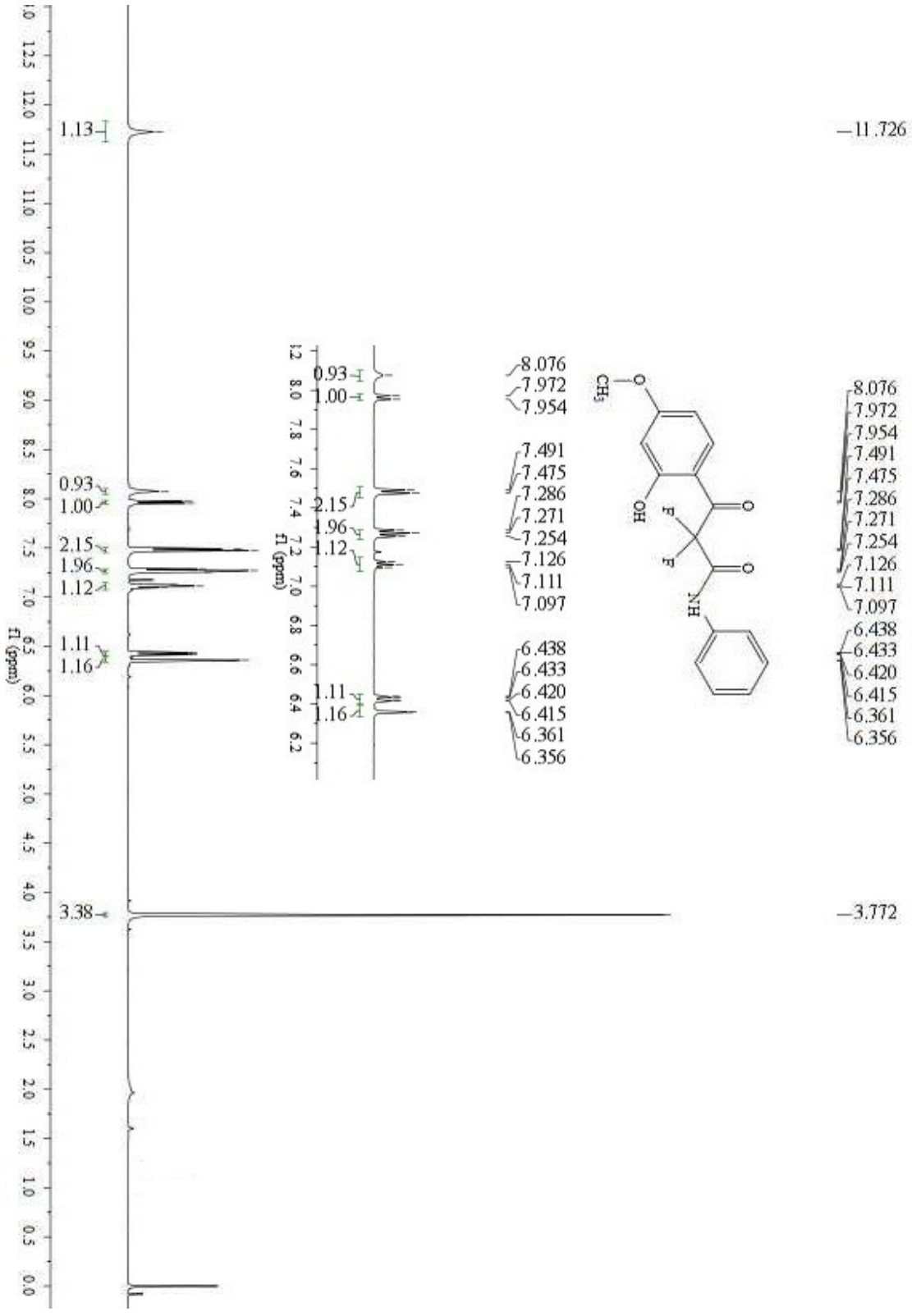
^{1}H NMR of **3w** in $CDCl_3$



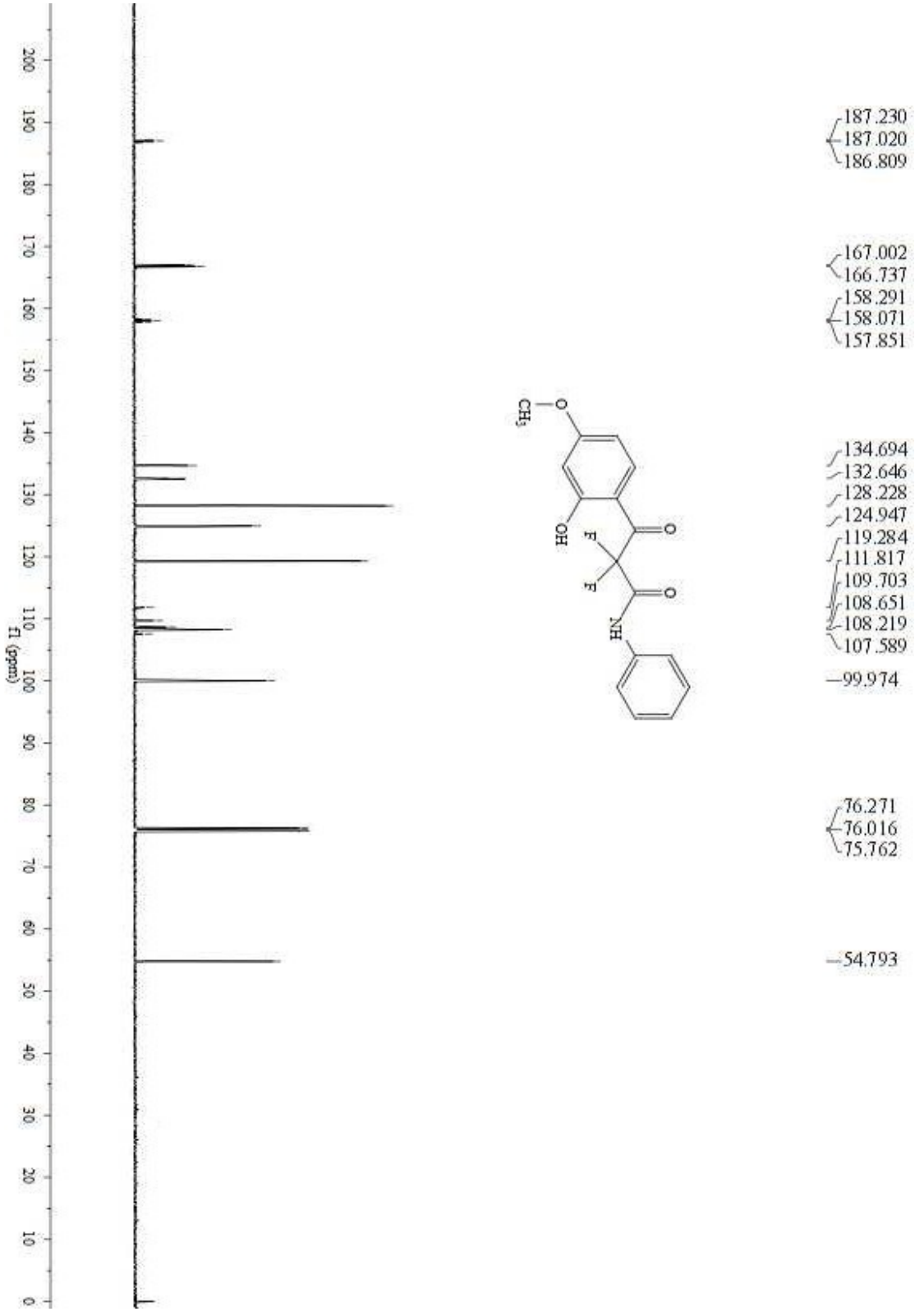
^{13}C NMR of **3w** in $CDCl_3$



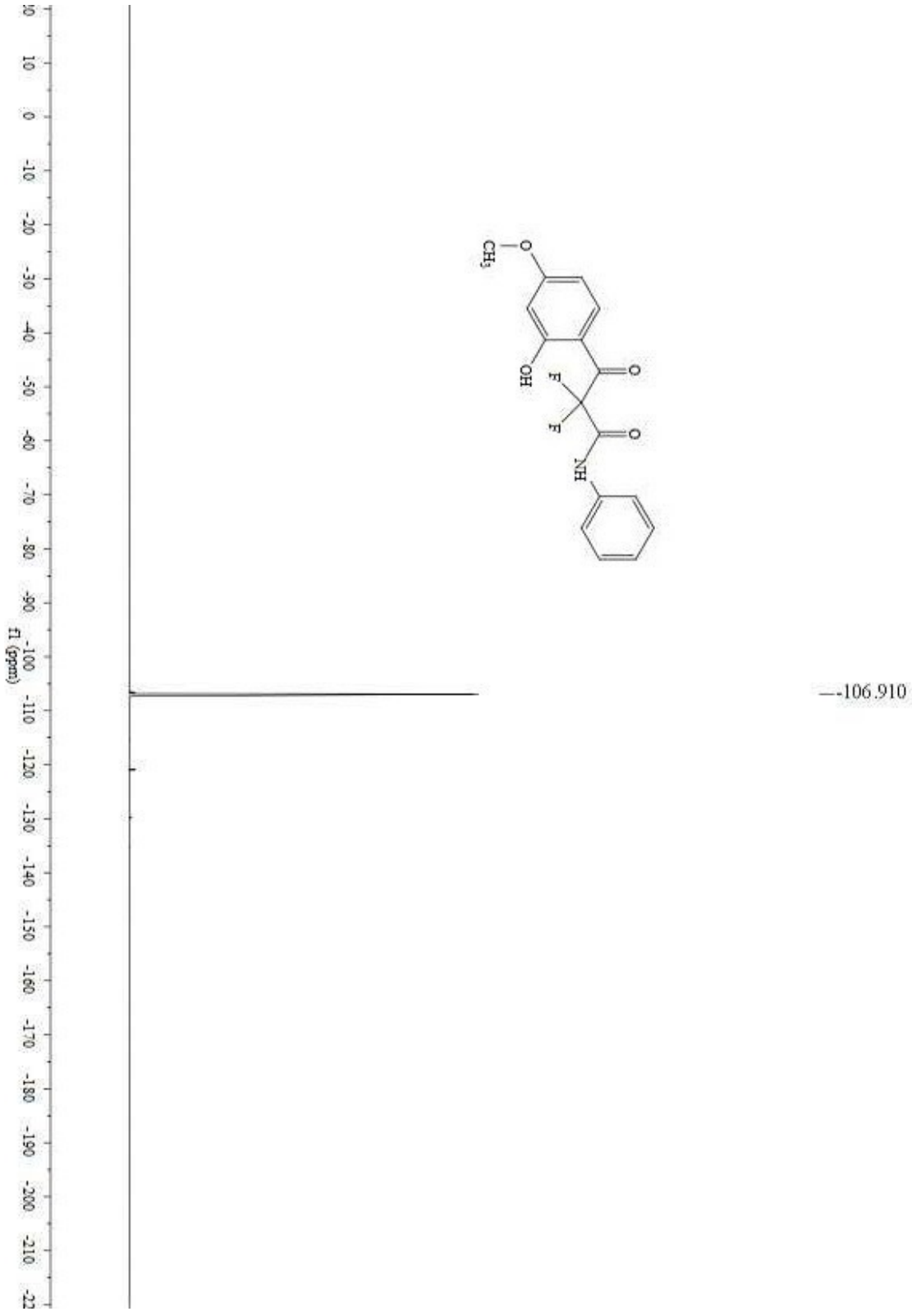
^{19}F NMR of **3w** in $CDCl_3$



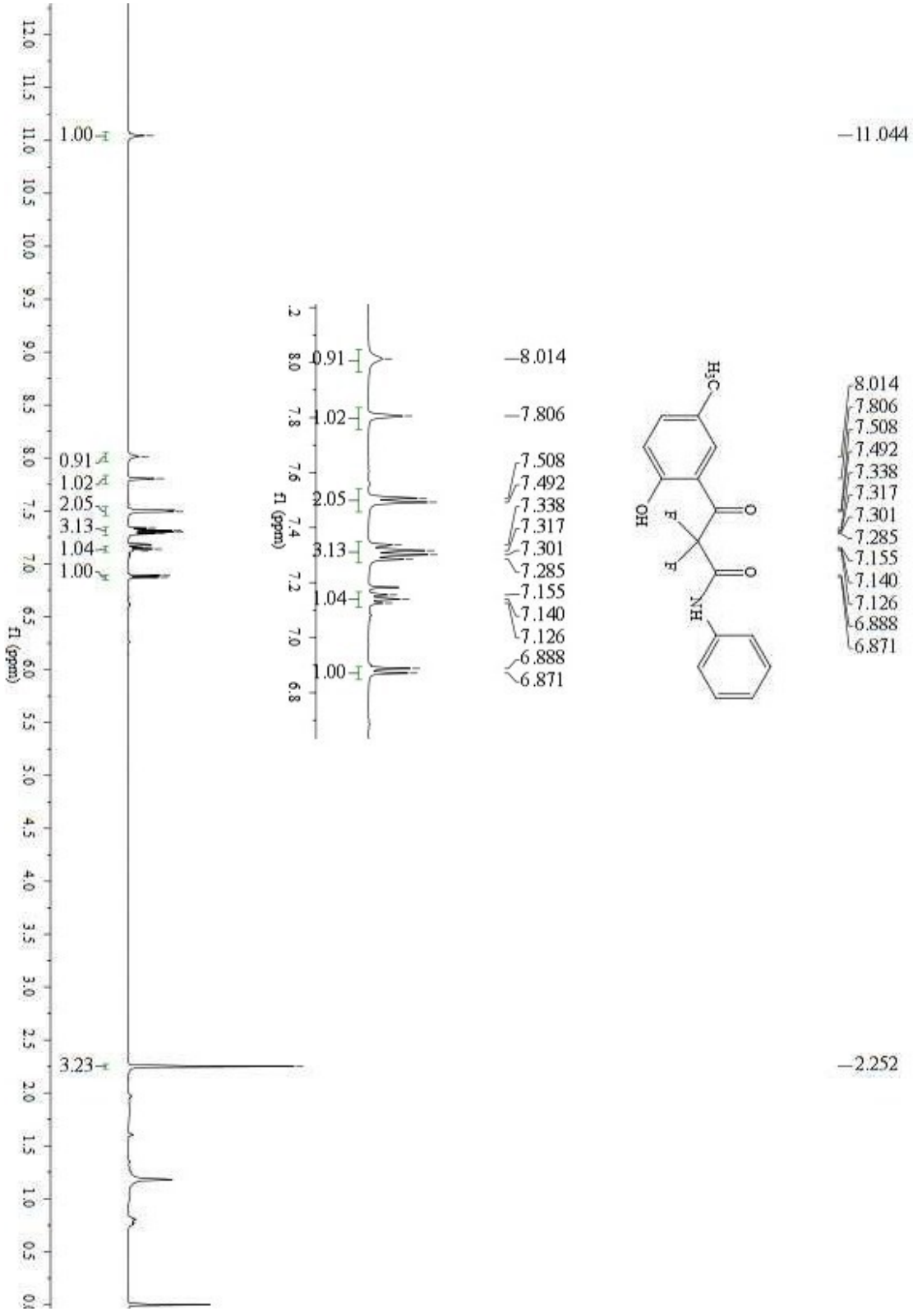
^{1}H NMR of **3x** in $CDCl_3$



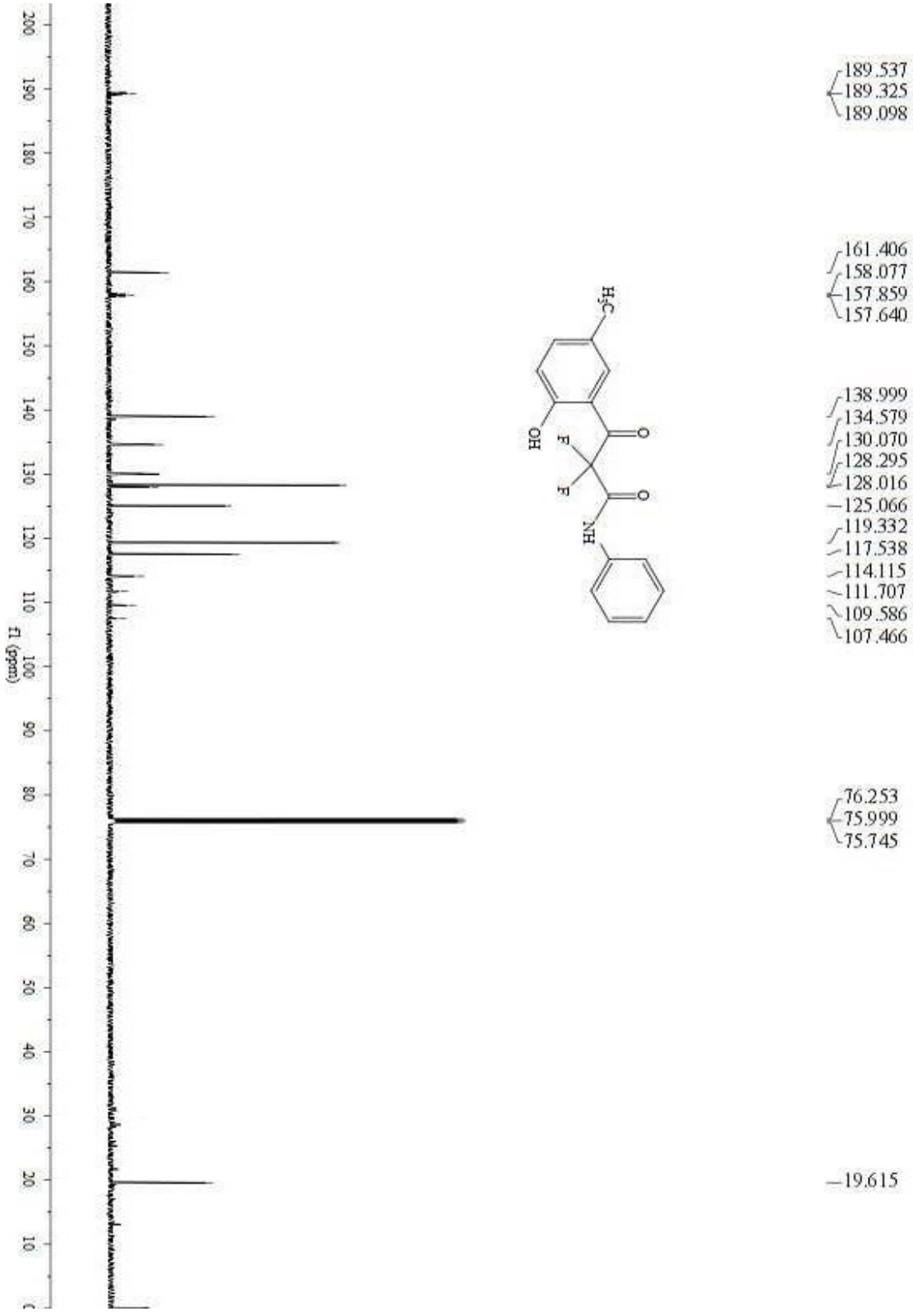
^{13}C NMR of **3x** in $CDCl_3$



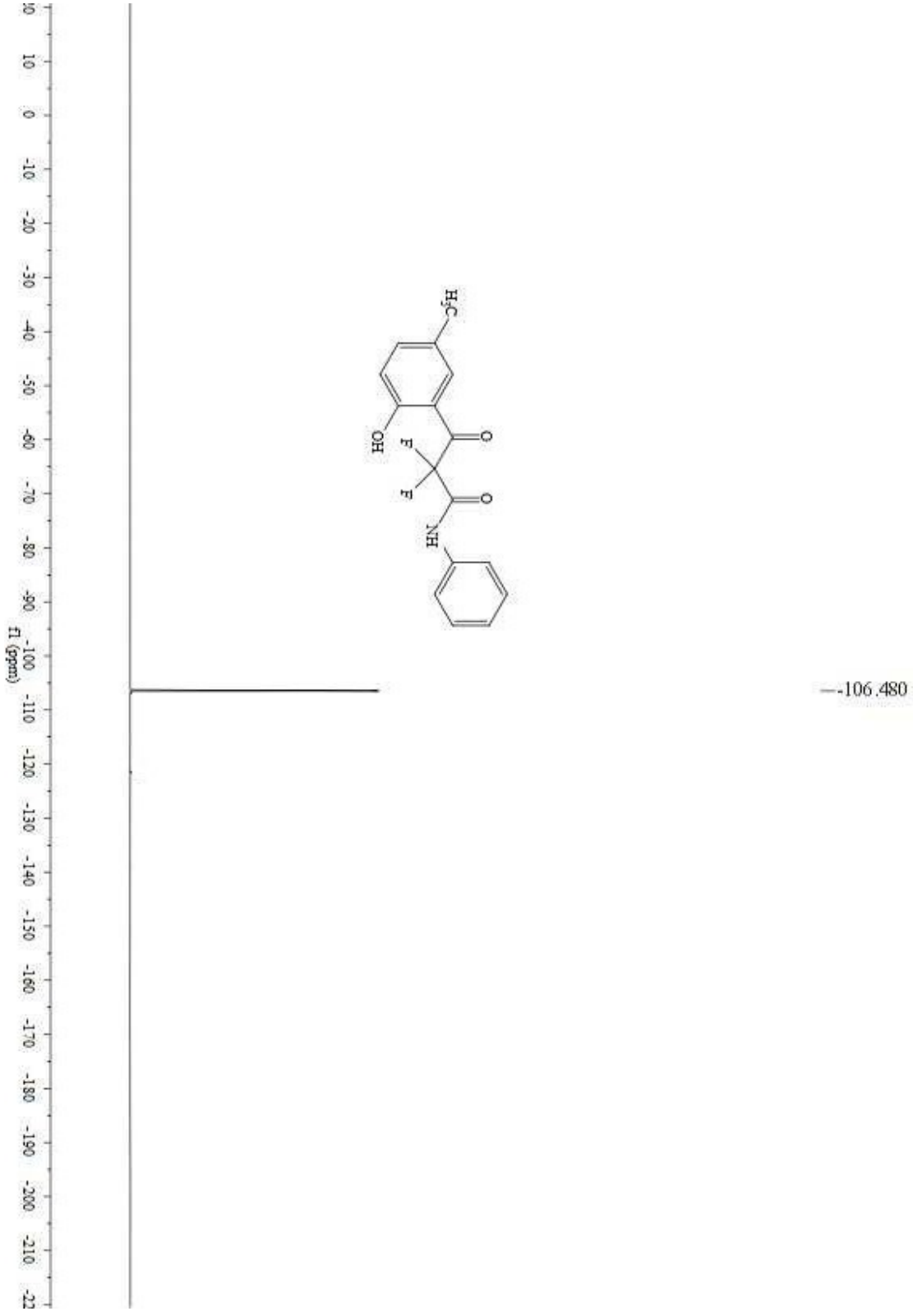
^{19}F NMR of **3x** in $CDCl_3$



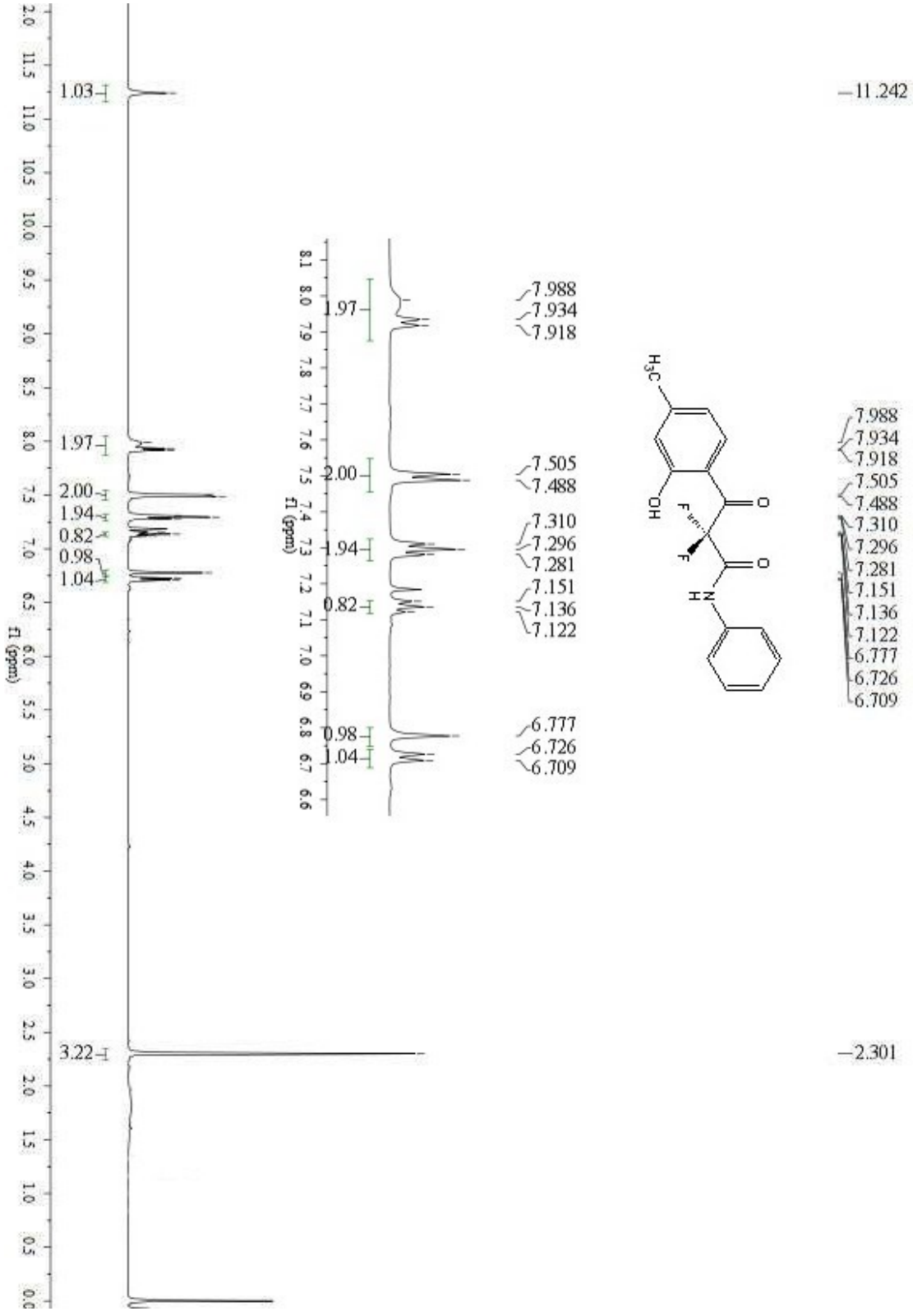
^{1}H NMR of **3y** in $CDCl_3$



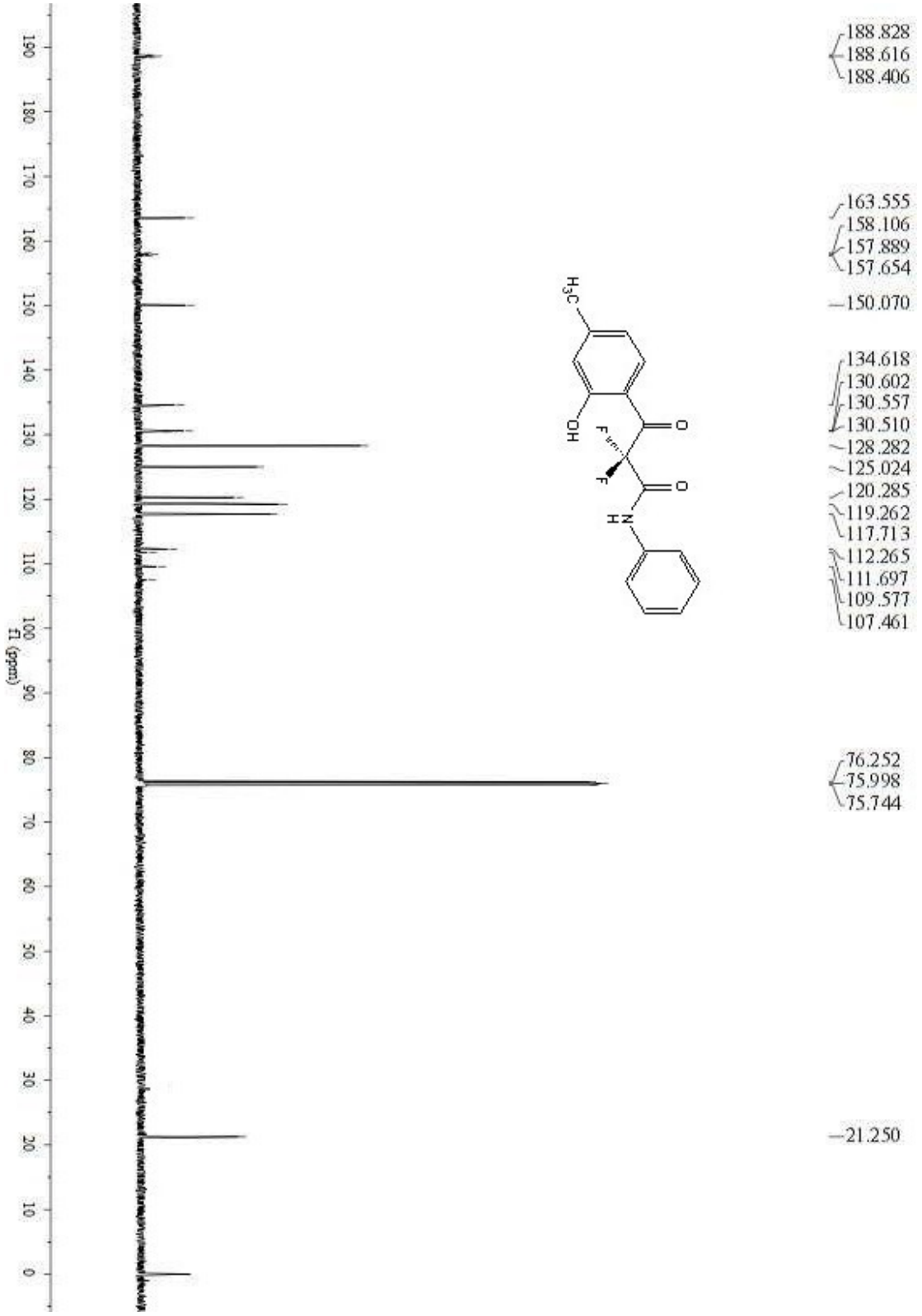
^{13}C NMR of **3y** in $CDCl_3$



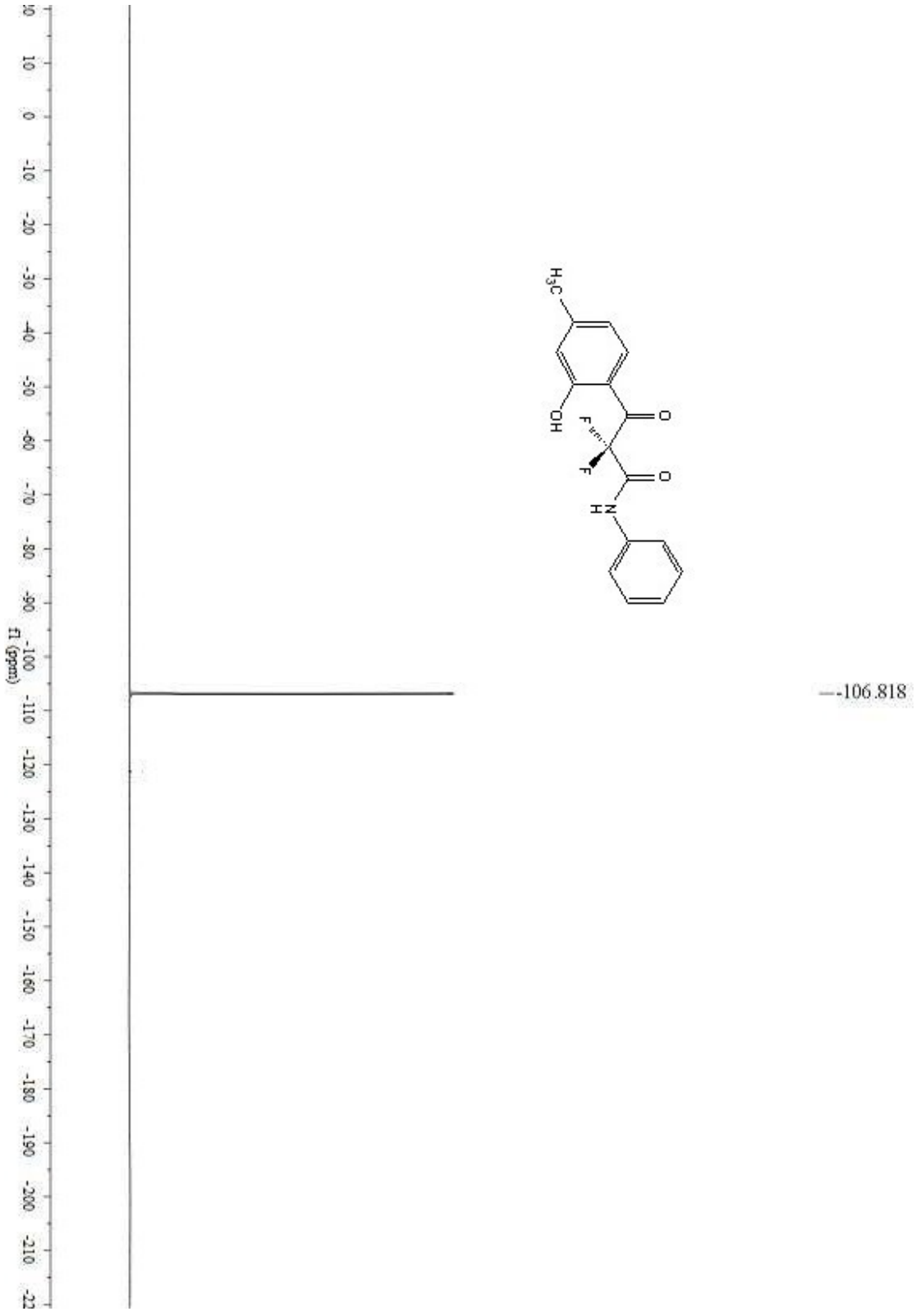
^{19}F NMR of **3y** in $CDCl_3$



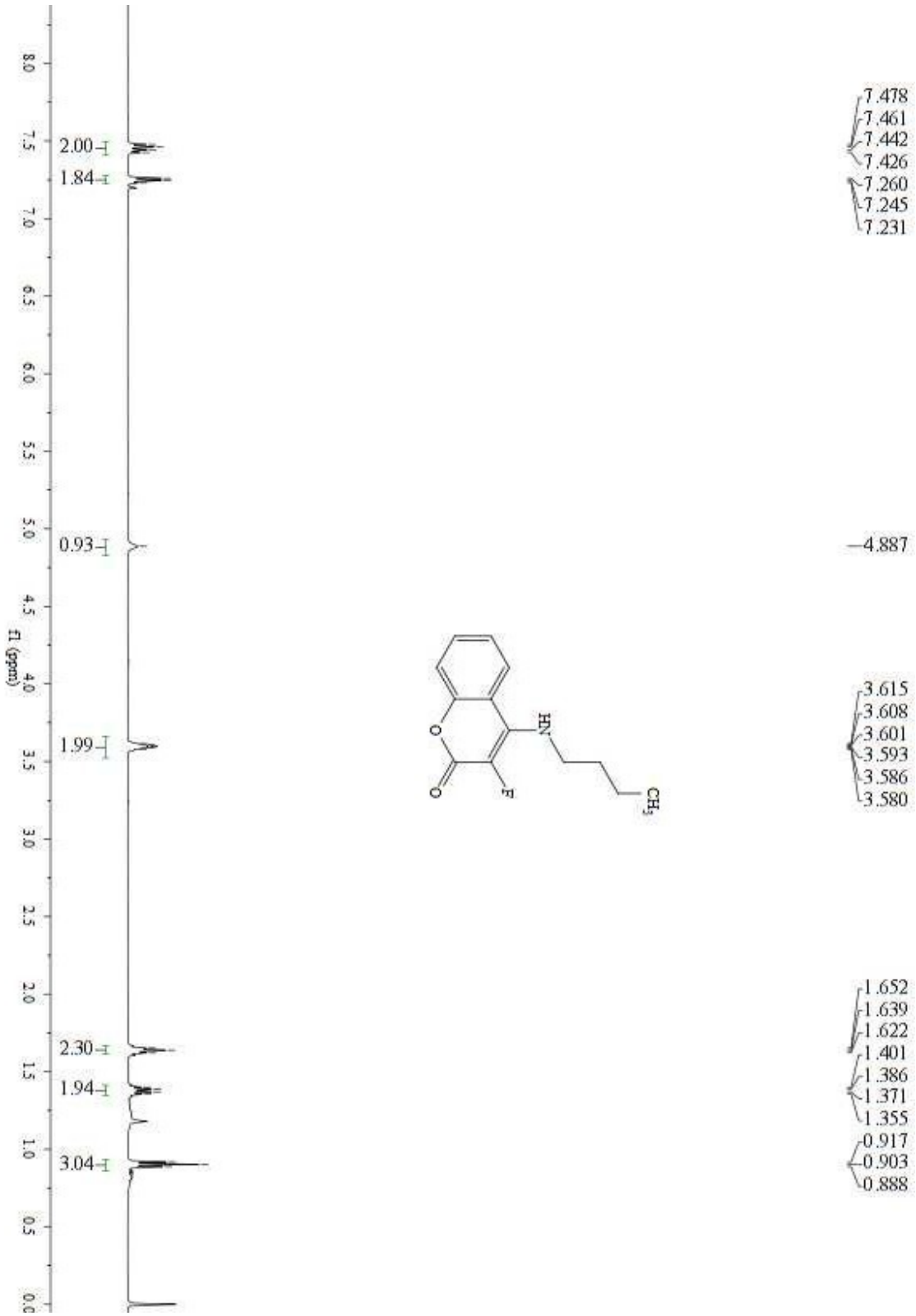
^{1}H NMR of **3z** in $CDCl_3$



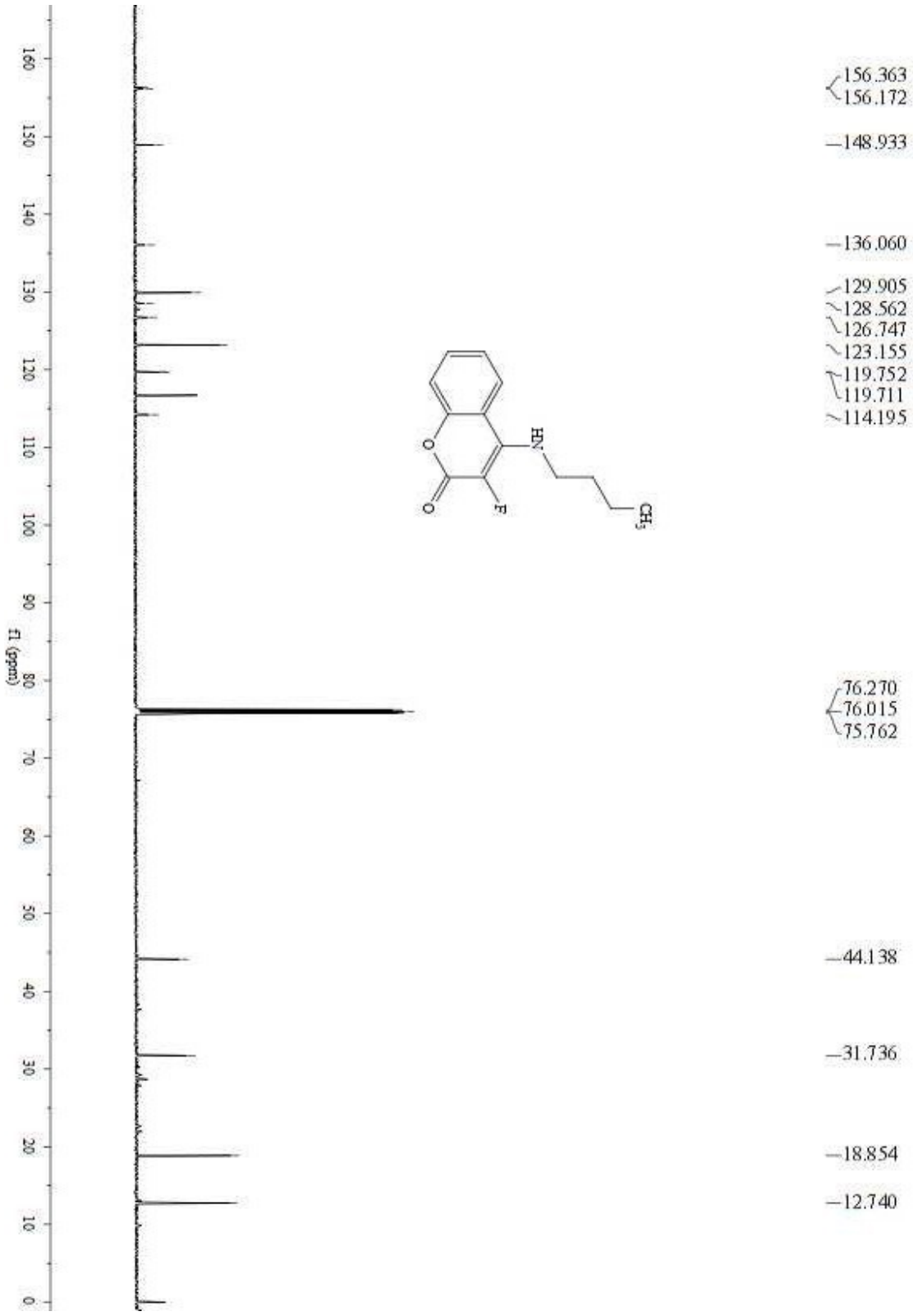
^{13}C NMR of **3z** in $CDCl_3$



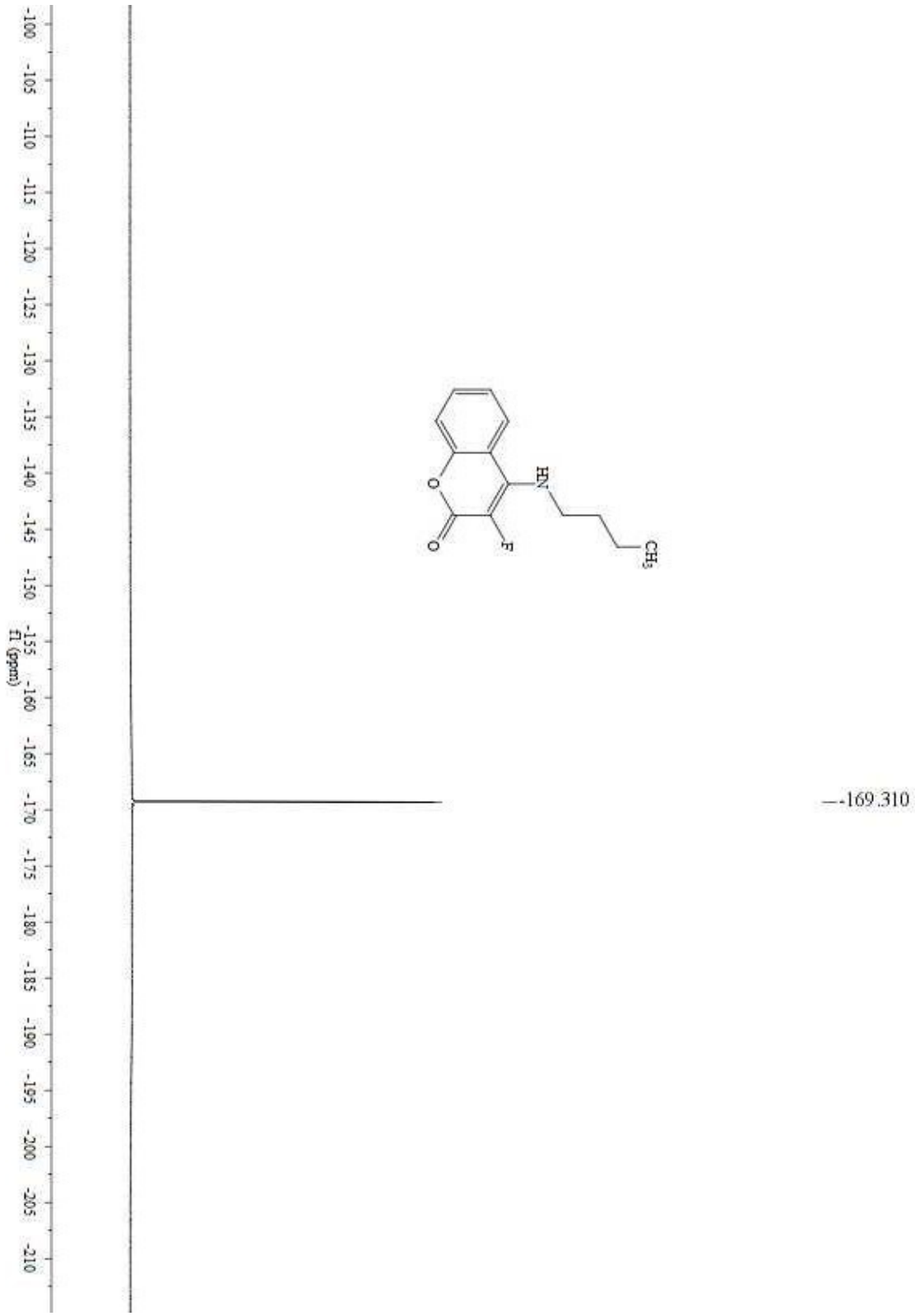
^{19}F NMR of **3z** in $CDCl_3$



^{1}H NMR of **8v** in $CDCl_3$



^{13}C NMR of **8v** in $CDCl_3$



^{19}F NMR of **8v** in $CDCl_3$