Supporting Information

CuBr-Mediated Radical Cascade Difluoroacetamidation of Acrylamides Using *α,α*-Difluoro-*α*-(TMS)-acetamides

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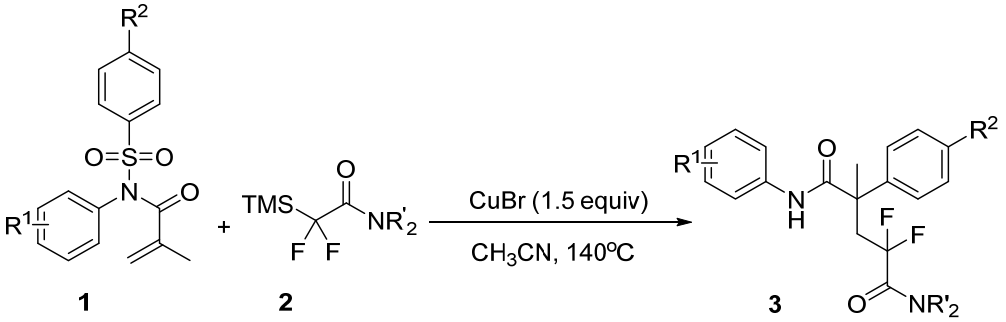
1. General information

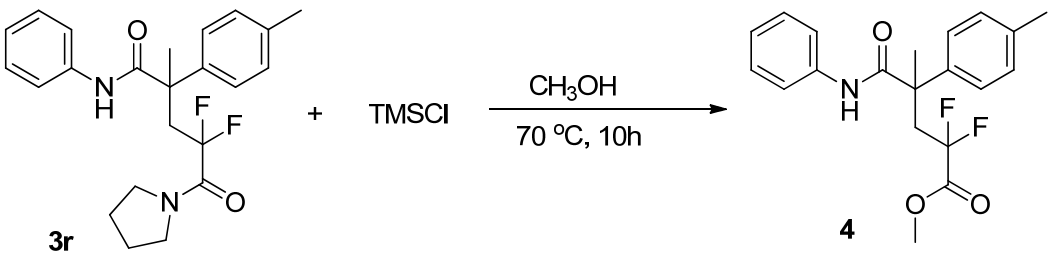
All manipulations were carried out in a sealed tube under a nitrogen atmosphere using standard Schlenk techniques. The solvents were distilled under nitrogen from sodium-benzophenone (THF, toluene, dioxane) or calcium hydride (DMF, MeCN, 1,2-DCE) before used. The *N*-(arylsulfonyl)acrylamides and *α*,*α*-difluoro-*α*-(TMS)-acetamide were prepared according to the literature methods (reference 5 and 19 in the manuscript). Other chemicals were obtained from commercial sources, and were used without further purification. Chemical shifs (δ, ppm) in the ^{1}H NMR spectra were recorded using TMS as internal standard. Chemical shifs in $^{13}C\{^{1}H\}$ NMR spectra were internally referenced to $CHCl_3$ (δ = 77.16 ppm).

2. General procedures for the reactions of *N*-(arylsulfonyl)acrylamides and *α*,*α*-difluoro-*α*-(TMS)-acetamides, 4 and 5.

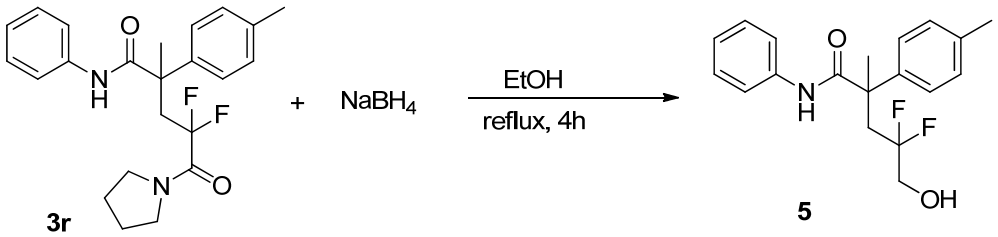


1 **2** **3**

1 (0.2 mmol), **2** (0.4 mmol), CuBr (42.9 mg, 0.3 mmol) and CH_3CN (2 mL) were mixed in an oven-dried sealed tube under N_2.The tube was sealed and heated at 140 ^{o}C for 6-9h. The resulting mixture was cooled to room temperature and the solvent was evaporated under vacuun. The crude product was purified by column chromatography on silica gel to afford the product **3**.

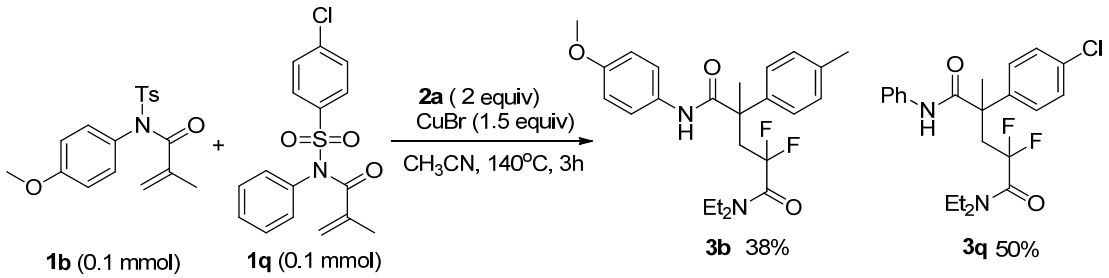


A 10 mL Schlenk tube was charged with **3r** (0.207 mmol, 83 mg), methanol (2 mL), and a magnetic stirring bar. At 0 °C, Me_3SiCl (5.17 mmol, 25 equiv) was added and the mixture was stirred at 70 °C for 10 h. The reaction was quenched with H_2O and extracted with diethyl ether. The organic phase was dried over sodium sulfate, concentrated in vacuo, and purified by column chromatography (PE:EA = 10:1) to afford the product **4** (68.0 mg, 91% yield) as a colorless oil.

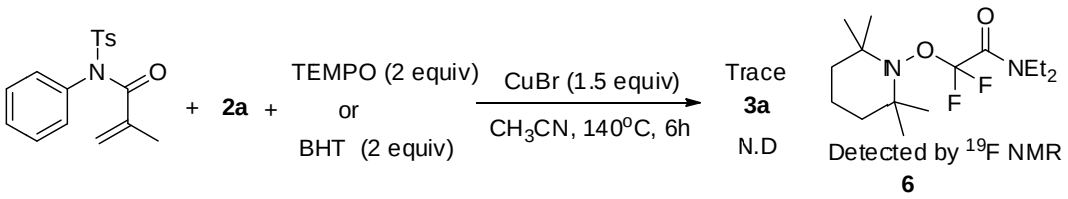


In a 25 mL round flask, difluoroamidated oxindole **3r** (0.227 mmol, 91 mg), sodium borohydride (3.41 mmol, 129.0 mg), a magnetic stirring bar, and ethanol (10 mL) were added under N_2. The resulting suspension was refluxed for 4 h. Then, the mixture was cooled to room temperature, quenched with aqueous HCl (1 M), and extracted with diethyl ether. The organic phase was concentrated in vacuo and purified by column chromatography (PE:EA = 3:1), affording the product **5** (64.4 mg, 85% yield) as a colorless oil.

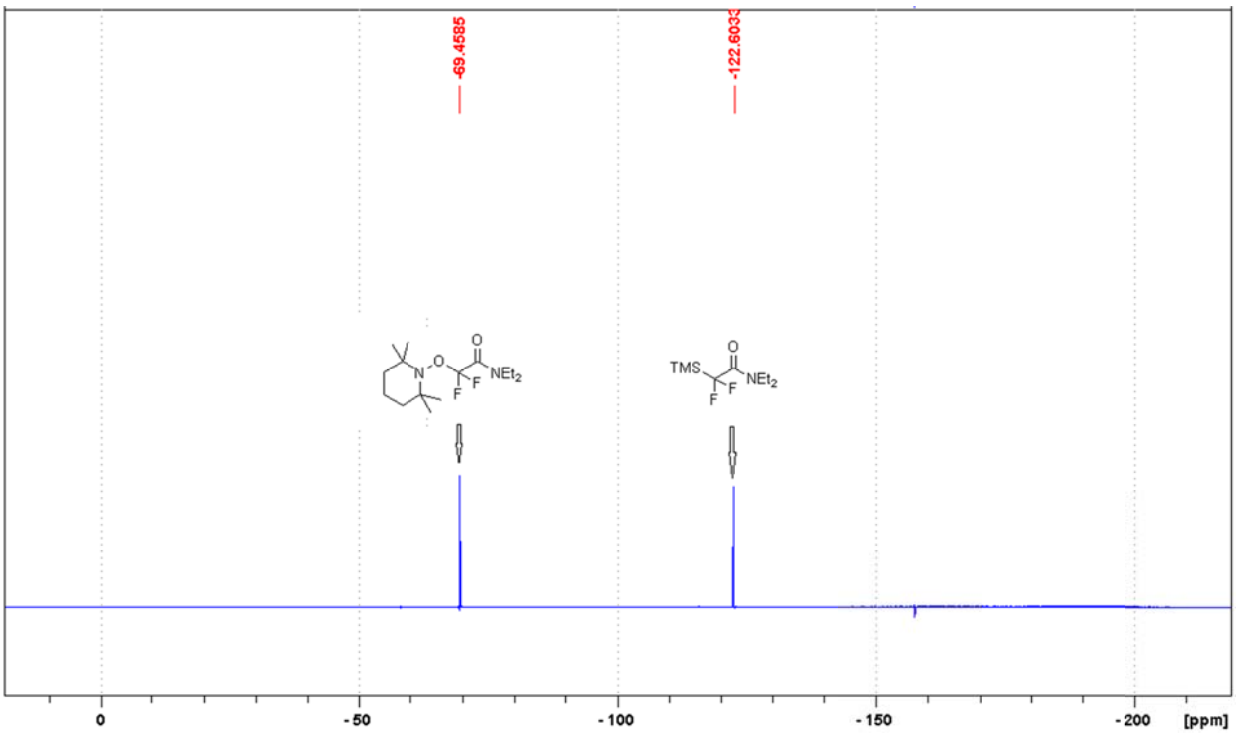
3. The mechanistic study.



1b (0.1 mmol), **1q** (0.1 mmol), **2a** (0.4 mmol), CuBr (42.9 mg, 0.3 mmol) and CH_3CN (2 mL) were mixed in an oven-dried sealed tube under N_2.The tube was sealed and heated at 140 ^oC for 3h. The resulting mixture was cooled to room temperature and the solvent was evaporated under vacuun. The crude product was purified by column chromatography on silica gel to afford the product **3b** (16.4 mg, 38%) and **3q** (21.1 mg, 50%).



The reactions were carried out according to the general procedures. When TEMPO (2 equiv) was added to the system, only trace target product **3a** was detected. The radical trapping product **6** was detected by the ^{19}F NMR. When BHT was added to the system, the reaction was completed hampered.



4. X-ray structure of 3p.

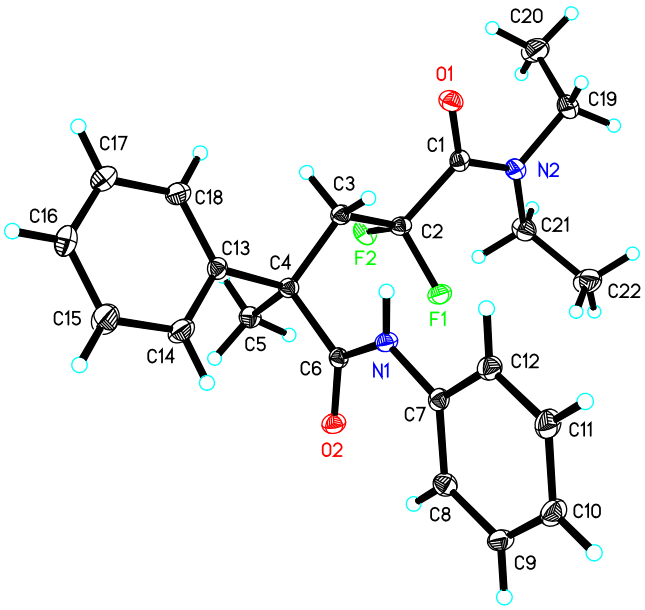


Table 1. Crystal data and structure refinement for **3p** (The ORTEP diagram of **3p** with ellipsoids shown at the 30% probability level).

Identification code	**3p**	
CCDC No.	1538133	
Empirical formula	$C_{22}\ H_{26}\ F_2\ N_2\ O_2$	
Formula weight	388.45	
Temperature	133(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 8.7598(9) Å	a= 90°.
	b = 25.852(3) Å	b= 96.431(2)°.
	c = 8.8958(9) Å	g = 90°.
Volume	2001.9(4) $Å^3$	
Z	4	

Density (calculated)	1.289 Mg/m^3
Absorption coefficient	0.095 mm^{-1}
F(000)	824
Crystal size	0.200 x 0.180 x 0.120 mm^3
Theta range for data collection	2.340 to 25.492°.
Index ranges	-10<=h<=9, -31<=k<=27, -10<=l<=10
Reflections collected	13847
Independent reflections	3727 [R(int) = 0.0376]
Completeness to theta = 25.242°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6811
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3727 / 0 / 261
Goodness-of-fit on F^2	1.010
Final R indices [I>2sigma(I)]	R1 = 0.0381, wR2 = 0.0827
R indices (all data)	R1 = 0.0599, wR2 = 0.0932
Extinction coefficient	0.0052(7)
Largest diff. peak and hole	0.242 and -0.192 $e.Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **3p**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
F(1)	2221(1)	5434(1)	7094(1)	28(1)
F(2)	4206(1)	5041(1)	8295(1)	28(1)
N(1)	475(2)	6317(1)	8652(2)	21(1)
N(2)	1832(2)	4346(1)	6909(2)	26(1)
O(1)	1174(1)	4460(1)	9285(1)	27(1)
O(2)	2665(1)	6616(1)	7807(1)	25(1)
C(1)	1818(2)	4613(1)	8195(2)	22(1)
C(2)	2659(2)	5138(1)	8354(2)	21(1)
C(3)	2430(2)	5429(1)	9780(2)	21(1)
C(4)	2983(2)	5999(1)	9844(2)	19(1)
C(5)	4682(2)	6045(1)	9569(2)	24(1)
C(6)	2029(2)	6336(1)	8649(2)	19(1)
C(7)	-651(2)	6604(1)	7729(2)	20(1)
C(8)	-303(2)	6968(1)	6660(2)	24(1)
C(9)	-1486(2)	7230(1)	5807(2)	27(1)
C(10)	-3001(2)	7135(1)	5993(2)	30(1)
C(11)	-3347(2)	6774(1)	7053(2)	31(1)
C(12)	-2180(2)	6509(1)	7911(2)	26(1)
C(13)	2875(2)	6241(1)	11415(2)	21(1)
C(14)	2709(2)	6770(1)	11547(2)	36(1)
C(15)	2800(2)	7012(1)	12944(2)	41(1)
C(16)	3045(2)	6725(1)	14248(2)	31(1)
C(17)	3209(2)	6199(1)	14145(2)	36(1)

C(18)	3135(2)	5959(1)	12743(2)	32(1)
C(19)	1045(2)	3842(1)	6810(2)	35(1)
C(20)	2048(3)	3417(1)	7563(2)	50(1)
C(21)	2697(2)	4465(1)	5623(2)	32(1)
C(22)	1690(3)	4662(1)	4242(2)	42(1)

Table 3.

Bond lengths [Å] and angles [°] for **3p**.

F(1)-C(2)	1.3753(18)
F(2)-C(2)	1.3850(18)
N(1)-C(6)	1.362(2)
N(1)-C(7)	1.420(2)
N(1)-H(1)	0.879(18)
N(2)-C(1)	1.337(2)
N(2)-C(19)	1.472(2)
N(2)-C(21)	1.474(2)
O(1)-C(1)	1.2401(19)
O(2)-C(6)	1.2201(18)
C(1)-C(2)	1.544(2)
C(2)-C(3)	1.507(2)
C(3)-C(4)	1.549(2)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(5)	1.540(2)
C(4)-C(13)	1.544(2)
C(4)-C(6)	1.546(2)
C(5)-H(5A)	0.9800
C(5)-H(5B)	0.9800
C(5)-H(5C)	0.9800

C(7)-C(12)	1.389(2)
C(7)-C(8)	1.395(2)
C(8)-C(9)	1.389(2)
C(8)-H(8)	0.9500
C(9)-C(10)	1.378(2)
C(9)-H(9)	0.9500
C(10)-C(11)	1.383(2)
C(10)-H(10)	0.9500
C(11)-C(12)	1.387(2)
C(11)-H(11)	0.9500
C(12)-H(12)	0.9500
C(13)-C(14)	1.382(2)
C(13)-C(18)	1.385(2)
C(14)-C(15)	1.385(2)
C(14)-H(14)	0.9500
C(15)-C(16)	1.374(3)
C(15)-H(15)	0.9500
C(16)-C(17)	1.370(3)
C(16)-H(16)	0.9500
C(17)-C(18)	1.388(2)
C(17)-H(17)	0.9500
C(18)-H(18)	0.9500
C(19)-C(20)	1.515(3)
C(19)-H(19A)	0.9900
C(19)-H(19B)	0.9900
C(20)-H(20A)	0.9800
C(20)-H(20B)	0.9800
C(20)-H(20C)	0.9800
C(21)-C(22)	1.519(3)

C(21)-H(21A)	0.9900
C(21)-H(21B)	0.9900
C(22)-H(22A)	0.9800
C(22)-H(22B)	0.9800
C(22)-H(22C)	0.9800

C(6)-N(1)-C(7)	127.52(14)
C(6)-N(1)-H(1)	119.2(12)
C(7)-N(1)-H(1)	113.2(12)
C(1)-N(2)-C(19)	117.29(14)
C(1)-N(2)-C(21)	127.67(14)
C(19)-N(2)-C(21)	114.62(14)
O(1)-C(1)-N(2)	123.56(15)
O(1)-C(1)-C(2)	117.62(14)
N(2)-C(1)-C(2)	118.82(14)
F(1)-C(2)-F(2)	104.75(11)
F(1)-C(2)-C(3)	110.91(13)
F(2)-C(2)-C(3)	110.21(13)
F(1)-C(2)-C(1)	109.10(13)
F(2)-C(2)-C(1)	107.25(12)
C(3)-C(2)-C(1)	114.14(13)
C(2)-C(3)-C(4)	115.77(12)
C(2)-C(3)-H(3A)	108.3
C(4)-C(3)-H(3A)	108.3
C(2)-C(3)-H(3B)	108.3
C(4)-C(3)-H(3B)	108.3
H(3A)-C(3)-H(3B)	107.4
C(5)-C(4)-C(13)	105.73(13)
C(5)-C(4)-C(6)	107.76(12)

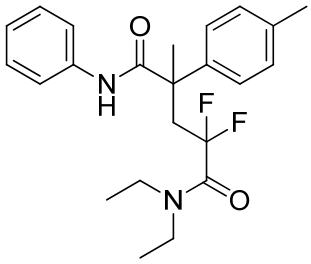
C(13)-C(4)-C(6)	108.05(12)
C(5)-C(4)-C(3)	111.81(13)
C(13)-C(4)-C(3)	111.60(12)
C(6)-C(4)-C(3)	111.60(13)
C(4)-C(5)-H(5A)	109.5
C(4)-C(5)-H(5B)	109.5
H(5A)-C(5)-H(5B)	109.5
C(4)-C(5)-H(5C)	109.5
H(5A)-C(5)-H(5C)	109.5
H(5B)-C(5)-H(5C)	109.5
O(2)-C(6)-N(1)	123.25(15)
O(2)-C(6)-C(4)	120.49(14)
N(1)-C(6)-C(4)	116.20(13)
C(12)-C(7)-C(8)	119.08(15)
C(12)-C(7)-N(1)	117.15(14)
C(8)-C(7)-N(1)	123.77(15)
C(9)-C(8)-C(7)	119.59(16)
C(9)-C(8)-H(8)	120.2
C(7)-C(8)-H(8)	120.2
C(10)-C(9)-C(8)	121.17(16)
C(10)-C(9)-H(9)	119.4
C(8)-C(9)-H(9)	119.4
C(9)-C(10)-C(11)	119.29(16)
C(9)-C(10)-H(10)	120.4
C(11)-C(10)-H(10)	120.4
C(10)-C(11)-C(12)	120.24(16)
C(10)-C(11)-H(11)	119.9
C(12)-C(11)-H(11)	119.9
C(11)-C(12)-C(7)	120.63(16)

C(11)-C(12)-H(12)	119.7
C(7)-C(12)-H(12)	119.7
C(14)-C(13)-C(18)	117.26(15)
C(14)-C(13)-C(4)	119.72(14)
C(18)-C(13)-C(4)	122.49(15)
C(13)-C(14)-C(15)	121.75(16)
C(13)-C(14)-H(14)	119.1
C(15)-C(14)-H(14)	119.1
C(16)-C(15)-C(14)	120.16(18)
C(16)-C(15)-H(15)	119.9
C(14)-C(15)-H(15)	119.9
C(17)-C(16)-C(15)	119.09(16)
C(17)-C(16)-H(16)	120.5
C(15)-C(16)-H(16)	120.5
C(16)-C(17)-C(18)	120.64(17)
C(16)-C(17)-H(17)	119.7
C(18)-C(17)-H(17)	119.7
C(13)-C(18)-C(17)	121.10(17)
C(13)-C(18)-H(18)	119.4
C(17)-C(18)-H(18)	119.4
N(2)-C(19)-C(20)	111.77(16)
N(2)-C(19)-H(19A)	109.3
C(20)-C(19)-H(19A)	109.3
N(2)-C(19)-H(19B)	109.3
C(20)-C(19)-H(19B)	109.3
H(19A)-C(19)-H(19B)	107.9
C(19)-C(20)-H(20A)	109.5
C(19)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5

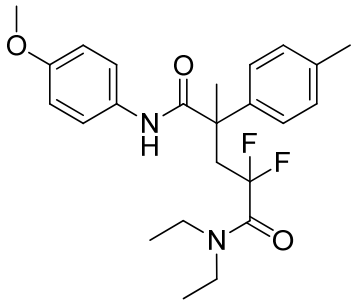
C(19)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
N(2)-C(21)-C(22)	113.28(16)
N(2)-C(21)-H(21A)	108.9
C(22)-C(21)-H(21A)	108.9
N(2)-C(21)-H(21B)	108.9
C(22)-C(21)-H(21B)	108.9
H(21A)-C(21)-H(21B)	107.7
C(21)-C(22)-H(22A)	109.5
C(21)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(21)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5

Symmetry transformations used to generate equivalent atoms:

5. Analytical data of products.

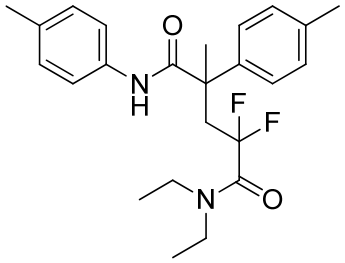


***N*^{1},*N*^{1}-diethyl-2,2-difluoro-4-methyl-*N*^{5}-phenyl-4-(*p*-tolyl)pentanediamide (3a).** The compound **3a** was obtained in 78% yield (62.7 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (3H, t, J = 7.1 Hz), 1.07 (3H, t, J = 7.1 Hz), 1.79 (3H, s), 2.27 (3H, s), 2.80 (1H, m), 3.16-3.40 (5H, m), 6.93 (1H, brs), 6.99 (1H, t, J = 7.32 Hz), 7.11 (2H, d, J = 8.0 Hz), 7.17-7.21 (2H, m), 7.25-7.31 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 21.1, 23.7, 41.9, 42.3 (t, J = 5.96 Hz), 42.4 (t, J = 21.4 Hz), 49.1, 119.2 (t, J = 254.0 Hz), 120.1, 124.4, 126.5, 128.9, 129.7, 137.4, 137.9, 139.9, 163.0 (t, J = 28.5 Hz), 173.8; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.6 (d, J = 270.8 Hz), -96.2 (d, J = 271.0 Hz); HRMS (EI, TOF) calcd for $C_{23}H_{28}F_2N_2O_2^+$ $[M]^+$: 402.2119, found: 402.2125.

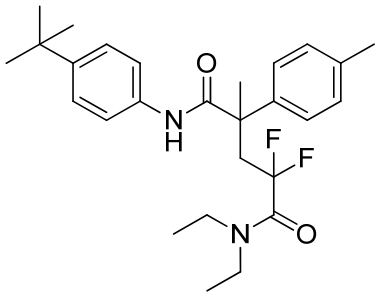


***N*^{1},*N*^{1}-diethyl-2,2-difluoro-*N*^{5}-(4-methoxyphenyl)-4-methyl-4-phenylpentanediamide (3b).** The compound **3b** was obtained in 82% yield (71.0 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (3H, t, J = 7.1 Hz), 1.07 (3H, t, J = 7.1 Hz), 1.79 (3H, s), 2.27 (3H, s), 2.79 (1H, m), 3.15-3.40 (5H, m), 3.69 (3H, s), 6.73 (2H,

dt, J = 3.4, 9.0 Hz), 6.83 (1H, brs), 7.10 (2H, d, J = 8.0 Hz), 7.18-7.20 (2H, m), 7.26 (2H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 21.1, 23.7, 41.9, 42.3 (t, J = 6.2 Hz), 42.5 (t, J = 21.4 Hz), 48.9, 55.6, 114.1, 119.2 (t, J = 256.8 Hz), 122.1, 126.5, 129.6, 130.9, 137.3, 140.1, 156.6, 163.1 (t, J = 28.4 Hz), 173.8; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.6 (d, J = 269.8 Hz), -96.3 (d, J = 270.1 Hz) ; HRMS (EI, TOF) calcd for $C_{24}H_{30}F_2N_2O_3^+$ $[M]^+$: 432.2224, found: 432.2235.

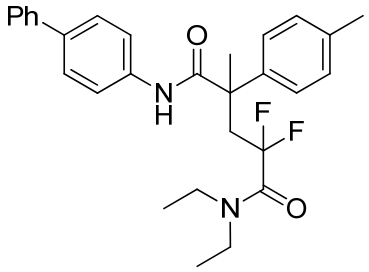


***N*^{1},*N*^{1}-diethyl-2,2-difluoro-4-methyl-*N*^{5,4}-di-*p*-tolylpentanediamide (3c).** The compound **3c** was obtained in 83% yield (69.2 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (3H, t, J = 7.1 Hz), 1.06 (3H, t, J = 7.0 Hz), 1.78 (3H, s), 2.20 (3H,s), 2.26 (3H, s), 2.78 (1H, m), 3.15-3.41 (5H, m), 6.87 (1H, brs), 6.99 (2H, d, J = 8.2 Hz), 7.10 (2H, d, J = 8.0Hz), 7.17 (2H, d, J = 8.2 Hz), 7.25 (2H, d, J = 8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 20.9, 21.0, 41.9, 42.3 (t, J = 6.2 Hz), 42.5 (t, J = 21.5 Hz), 49.0, 119.2 (t, J = 253.7 Hz), 120.2, 126.5, 129.4, 129.6, 134.0, 135.3, 137.3, 140.1, 163.1 (t, J = 28.6 Hz), 173.7; ^{19}F NMR ($CDCl_3$, 376 MHz) δ –94.6 (d, J = 270.5 Hz), -96.2 (d, J = 270.6 Hz); HRMS (EI, TOF) calcd for $C_{24}H_{30}F_2N_2O_2^+$ $[M]^+$: 416.2275, found:416.2279.



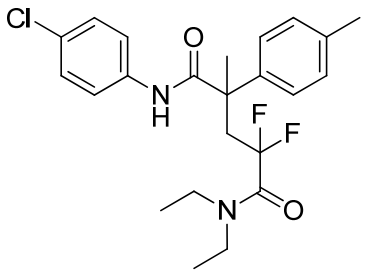
N^1-(4-(*tert*-butyl)phenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3d).

The compound **3d** was obtained in 81% yield (74.4 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (3H, t, J = 7.1 Hz), 1.07 (3H, t, J = 7.0 Hz), 1.20 (9H, s), 1.79 (3H, s), 2.27 (3H, s), 2.72-2.86 (1H, m), 3.15-3.26 (5H, m), 6.80 (1H, brs), 7.09 (2H, d, J = 8.0 Hz), 7.22-7.26 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 21.0, 23.7, 31.4, 34.4, 41.9, 42.3 (t, J = 5.8 Hz), 42.4 (t, J = 21.5 Hz), 48.9, 119.2 (t , J = 253.7 Hz), 119.8, 125.8, 126.5, 129.6, 135.3, 137.3, 140.1, 163.1 (t, J = 28.7 Hz), 173.7; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.6 (d, J = 270.3 Hz), -96.3 (d, J = 270.6 Hz); HRMS (EI, TOF) calcd for $C_{27}H_{36}F_2N_2O_2^+$ $[M]^+$: 458.2745, found: 458.2747.

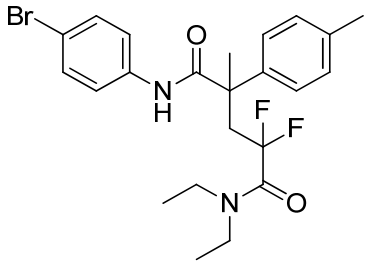


N^1-([1,1'-biphenyl]-4-yl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3e).

The compound **3e** was obtained in 77% yield (73.7 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (3H, t, J = 7.1 Hz), 1.08 (3H, t, J = 7.0 Hz), 1.81 (3H, s), 2.28 (3H, s), 2.75-2.89 (1H, m), 3.18-3.25 (5H, m), 6.98 (1H, brs), 7.12 (2H, d, J = 8.0 Hz), 7.21-7.28 (3H, m), 7.31-7.39 (3H, m), 7.7.42-7.48 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 21.0, 23.7, 41.9, 42.3 (t, J = 5.8 Hz), 42.4 (t, J = 21.4 Hz), 49.1, 119.2 (t, J = 253.8 Hz), 120.3, 126.4, 126.9, 127.2, 127.6, 128.8, 129.7, 137.2, 137.4, 139.7, 140.6, 163.0 (t, J = 28.5 Hz), 173.9; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.5 (d, J = 271.0 Hz), -96.2 (d, J = 270.9 Hz); HRMS (EI, TOF) calcd for $C_{29}H_{32}F_2N_2O_2^+$ $[M]^+$: 478.2432, found: 478.2433.

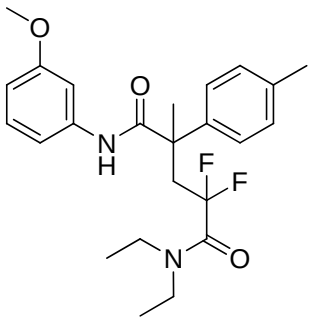


N^1-(4-chlorophenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3f). The compound **3f** was obtained in 84% yield (73.4 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (3H, t, J = 7.1 Hz), 1.07 (3H, t, J = 7.0 Hz), 1.78 (3H, s), 2.27 (3H, s), 2.72-2.85 (1H, m), 3.01-3.39 (5H, m), 6.96 (1H, brs), 7.10-7.16 (4H, m), 7.23-7.26 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.3, 21.1, 23.8, 42.3 (t, J = 6.2 Hz), 42.4 (t, J = 21.6 Hz), 49.1, 119.2 (t, J = 254.8 Hz), 121.3, 126.5, 128.9, 129.4, 129.8, 136.5, 137.5, 139.8, 163.0 (t, J = 28.6 Hz), 173.9; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.4 (d, J = 272.1 Hz), -96.2 (d, J = 272.7 Hz); HRMS (EI, TOF) calcd for $C_{23}H_{27}ClF_2N_2O_2^+$ $[M]^+$: 436.1729, found: 436.1745

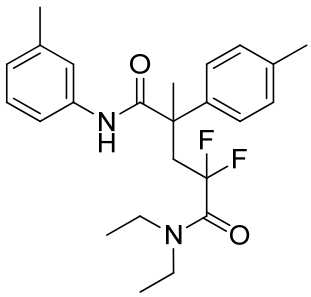


N^1-(4-bromophenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3g). The compound **3g** was obtained in 85% yield (81.8 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (3H, t, J = 7.1 Hz), 1.06 (3H, t, J = 7.0 Hz), 1.78 (3H, s), 2.27 (3H, s), 2.71-2.85 (1H, m), 3.16-3.35 (5H, m), 6.96 (1H, brs), 7.10 (2H, d, J = 8.0 Hz), 7.18-7.30 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 21.0, 23.7, 41.9, 42.3 (t, J = 6.1 Hz), 42.4 (t, J = 21.7 Hz), 49.1, 116.9, 119.1 (t, J = 254.2 Hz), 121.7, 126.4,

129.4, 131.9, 137.0, 137.5, 139.8, 162.9 (t, J = 28.5 Hz), 173.9; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.4 (d, J = 272.2 Hz), -96.2 (d, J = 272.1 Hz); HRMS (EI, TOF) calcd for $C_{23}H_{27}BrF_2N_2O_2^+$ $[M]^+$: 480.1224, found: 480.1226.

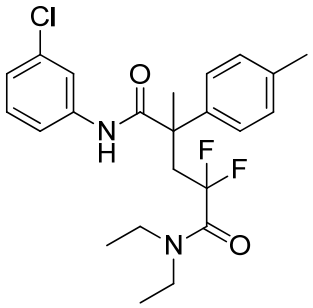


***N*^{1},*N*^{1}-diethyl-2,2-difluoro-*N*^{5}-(3-methoxyphenyl)-4-methyl-4-(*p*-tolyl)pentanediamide (3h).** The compound **3h** was obtained in 79% yield (68.4 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (3H, t, J = 7.1 Hz), 1.07 (3H, t, J = 7.0 Hz), 1.79 (3H, s), 2.27 (3H, s), 2.72-2.85 (1H, m), 3.15-3.43 (5H, m), 3.69 (3H, s), 6.71-6.75 (2H, m), 6.83 (1H, brs), 7.10 (2H, d, J = 8.0 Hz), 7.18-7.20 (2H, m), 7.26 (2H, d, J = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 21.1, 23.7, 41.9, 42.3 (t, J = 5.7 Hz), 42.5 (t, J = 21.4 Hz), 48.9, 55.6, 114.1, 119.2 (t, J = 253.7 Hz), 122.1, 126.5, 129.6, 130.9, 137.3, 140.1, 156.6, 163.1 (t, J = 28.4 Hz); ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.7 (d, J = 269.4 Hz), -96.3 (d, J = 269.5 Hz); HRMS (EI, TOF) calcd for $C_{24}H_{30}F_2N_2O_3^+$ $[M]^+$: 432.2224, found: 432.2233.

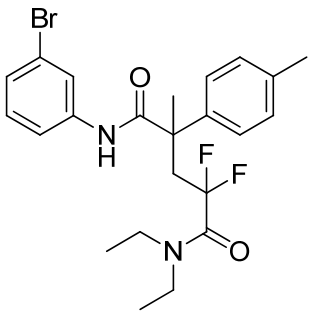


***N*^{1},*N*^{1}-diethyl-2,2-difluoro-4-methyl-*N*^{5}-(*m*-tolyl)-4-(*p*-tolyl)pentanediamide (3i).** The compound **3i** was obtained in 82% yield (68.4 mg) as colorless liquid after column

chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (3H, t, J = 7.1 Hz), 1.07 (3H, t, J = 7.0 Hz), 1.78 (3H, s), 2.22 (3H, s), 2.27 (3H, s), 2.73-2.87 (1H, m), 3.16-3.40 (5H, m), 6.80-6.82 (1H, m), 6.87 (1H, brs), 7.06-7.08 (2H, m), 7.10 (2H, d, J = 8.1 Hz), 7.17 (1H, s), 7.25 (2H, d, J = 8.2 Hz) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 21.1, 23.7, 41.9, 42.2 (t, J = 5.9 Hz), 42.4 (t, J = 21.4 Hz), 49.1, 117.1, 119.2 (t, J = 253.9 Hz), 120.7, 125.2, 126.5, 128.8, 129.7, 137.4, 137.8, 138.9, 139.9, 163.0 (t, J = 28.7 Hz), 173.8; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.7 (d, J = 270.9 Hz), -96.2 (d, J = 271.3 Hz); HRMS (EI, TOF) calcd for $C_{24}H_{30}F_2N_2O_2^+$ $[M]^+$: 416.2275, found: 416.2281.

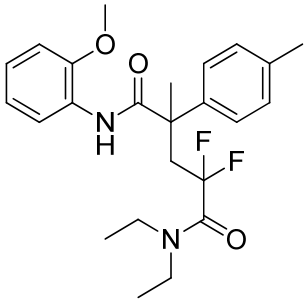


***N*^{1}-(3-chlorophenyl)-*N*^{5},*N*^{5}-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3j).** The compound **3j** was obtained in 85% yield (74.3 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (3H, t, J = 7.1 Hz), 1.07 (3H, t, J = 7.0 Hz), 1.78 (3H, s), 2.28 (3H, s), 2.72-2.85 (1H, m), 3.16-3.41 (5H, m), 6.95-6.98 (2H, m), 7.10-7.14 (4H, m), 7.24 (2H, d, J = 8.3 Hz), 7.45 (t, J = 1.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 21.0, 23.8, 41.9, 42.3 (t, J = 6.0 Hz), 42.4 (t, J = 21.5 Hz), 49.2, 117.9, 119.2 (t, J = 254.0 Hz), 120.1, 124.4, 126.5, 129.8, 129.9, 134.7, 137.6, 139.0, 139.7, 163.0 (t, J = 28.5 Hz), 173.9; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.4 (d, J = 272.2 Hz), -96.2 (d, J = 272.2 Hz); HRMS (EI, TOF) calcd for $C_{23}H_{27}ClF_2N_2O_2^+$ $[M]^+$: 436.1729, found: 436.1734.



***N*^{1}-(3-bromophenyl)-*N*^{5},*N*^{5}-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3k).**

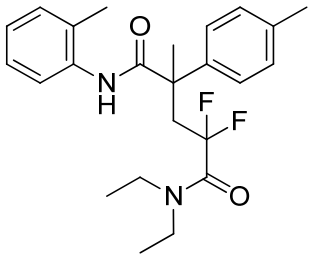
The compound **3k** was obtained in 88% yield (84.7 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (3H, t, J = 7.1 Hz), 1.07 (3H, t, J = 7.0 Hz), 1.78 (3H, s), 2.27 (3H, s), 2.78 (1H, td, J = 13.4, 24.5 Hz), 3.16-3.41 (5H, m), 6.94-6.97 (1H, d, J = 9.6 Hz), 7.04 (1H, t, J = 8.0 Hz), 7.10-7.12 (3H, m), 7.18-7.22 (3H, m), 7.58 (1H, t, J = 1.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 21.0, 23.7, 41.9, 42.2 (t, J = 6.1 Hz), 42.3 (t, J = 21.6 Hz), 49.1, 118.5, 119.1 (t, J = 254.1 Hz), 122.6, 122.9, 126.4, 127.3, 129.8, 130.2, 137.5, 139.2, 139.7, 162.9 (t, J = 28.6 Hz), 173.9; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.4 (d, J = 272.5 Hz), -96.1 (d, J = 272.5 Hz); HRMS (EI, TOF) calcd for $C_{23}H_{27}BrF_2N_2O_2^+$ $[M]^+$: 480.1224, found: 480.1226.



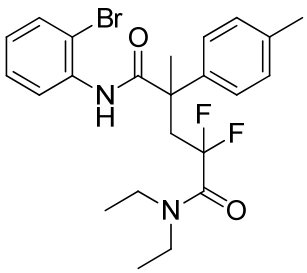
***N*^{1},*N*^{1}-diethyl-2,2-difluoro-*N*^{5}-(2-methoxyphenyl)-4-methyl-4-(*p*-tolyl)pentanediamide (3l).**

The compound **3l** was obtained in 80% yield (69.3 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (3H, t, J = 7.1 Hz), 1.07 (3H, t, J = 7.0 Hz), 1.79 (3H, s), 2.27 (3H, s), 2.74-2.88 (1H, m), 3.16-3.41 (5H, m), 3.71 (3H, s), 6.55

(1H, ddd, J = 0.7, 2.4, 8.2 Hz), 6.71 (1H, dd, J = 1.2, 8.0 Hz), 6.90 (1H, brs), 7.05-7.13 (4H, m), 7.25 (2H, d, J = 8.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 41.9, 42.2 (t, J = 5.8 Hz), 42.4 (t, J = 21.5 Hz), 49.1, 55.4, 105.6, 110.3, 112.1, 119.1 (t, J = 253.9 Hz), 126.5, 129.6, 129.7, 137.4, 139.2, 139.9, 160.2, 163.0 (t, J = 28.7 Hz), 173.8; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.6 (d, J = 271.0 Hz), -96.2 (d, J = 271.2 Hz); HRMS (EI, TOF) calcd for $C_{24}H_{30}F_2N_2O_3^+$ $[M]^+$: 432.2224, found: 432.2225.

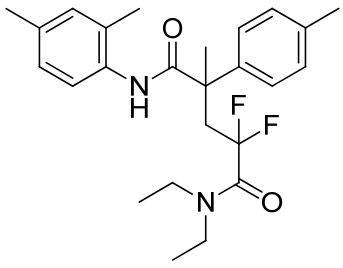


***N*^{1},*N*^{1}-diethyl-2,2-difluoro-4-methyl-*N*^{5}-(*o*-tolyl)-4-(*p*-tolyl)pentanediamide (3m).** The compound **3m** was obtained in 78% yield (65.1 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (3H, t, J = 7.1 Hz), 1.07 (3H, t, J = 7.0 Hz), 1.80 (3H, s), 1.83 (3H, s), 2.27 (3H, s), 2.80-2.94 (1H, m), 3.16-3.23 (5H, m), 6.75 (1H, m), 6.93 (1H, dt, J = 1.0, 7.4 Hz), 7.00 (1H, d, J = 7.0 Hz), 7.07-7.14 (3H, m), 7.30 (2H, d, J = 8.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 17.2, 21.0, 23.5, 41.8, 42.1 (t, J = 21.7 Hz), 42.2 (t, J = 6.2 Hz), 49.2, 119.2 (t, J = 253.7 Hz), 122.5, 125.0, 126.7, 126.8, 128.9, 129.7, 130.4, 135.8, 137.4, 139.9, 163.0 (t, J = 28.5 Hz), 173.9; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.9 (d, J = 269.4 Hz), -96.9 (d, J = 269.6 Hz); HRMS (EI, TOF) calcd for $C_{24}H_{30}F_2N_2O_2^+$ $[M]^+$: 416.2275, found: 416.2281.



***N*^{1}-(2-bromophenyl)-*N*^{5},*N*^{5}-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3n).**

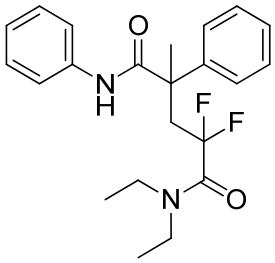
The compound **3n** was obtained in 83% yield (79.8 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (3H, t, J = 7.1 Hz), 1.06 (3H, t, J = 7.0 Hz), 1.85 (3H, s), 2.26 (3H, s), 2.80-2.93 (1H, m), 3.18-3.27 (5H, m), 6.84 (1H, dt, J = 1.5, 8.0 Hz), 7.12 (2H, d, J = 8.0 Hz), 7.18-7.23 (1H, m), 7.29 (2H, d, J = 8.0 Hz), 7.36 (1H, dt, J = 1.4, 8.0 Hz), 7.54 (1H, brs); ^{13}C NMR (100 MHz, CDCl3) δ 12.4, 14.4, 21.0, 23.3, 41.9, 42.1 (t, J = 21.3 Hz), 42.2 (t, J = 6.2 Hz), 49.4, 113.7, 119.2 (t, J = 253.9 Hz), 121.6, 125.1, 126.6, 128.3, 129.7, 132.2, 135.8, 137.5, 139.4, 162.9 (t, J = 28.5 Hz), 174.0; ^{19}F NMR (CDCl3, 376 MHz) δ -95.1 (d, J = 271.5 Hz), -95.9 (d, J = 271.8 Hz); HRMS (EI, TOF) calcd for $C_{23}H_{27}BrF_2N_2O_2^+$ $[M]^+$: 480.1224, found: 480.1219.



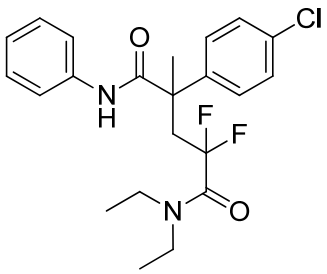
***N*^{1}-(2,4-dimethylphenyl)-*N*^{5},*N*^{5}-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3o).**

The compound **3o** was obtained in 81% yield (69.8 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (3H, t, J = 7.1 Hz), 1.06 (3H, t, J = 7.0 Hz), 1.79 (3H, s), 1.82 (3H, s), 2.17 (3H, s), 2.27 (3H, s), 2.78-2.92 (1H, m), 3.15-3.39 (5H, m), 6.68 (1H, brs), 6.83 (1H, s), 6.90 (1H, d, J = 8.2 Hz), 7.12 (2H, d, J = 8.0 Hz), 7.30 (2H,

d, J = 8.0 Hz), 7.49 (1H, d, J = 8.1 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 17.2, 20.9, 21.0, 23.5, 41.9, 42.2 (t, J = 21.4 Hz), 42.3 (t, J = 6.0 Hz), 49.1, 119.2 (t, J = 253.8 Hz), 122.9, 126.7, 127.3, 129.3, 129.6, 131.1, 133.1, 134.8, 137.4, 140.1, 163.1 (t, J = 28.4 Hz), 174.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.9 (d, J = 269.2 Hz), -95.9 (d, J = 269.3 Hz); HRMS (EI, TOF) calcd for $C_{25}H_{33}F_2N_2O_2^+$ $[M]^+$: 430.2432, found: 430.2442.

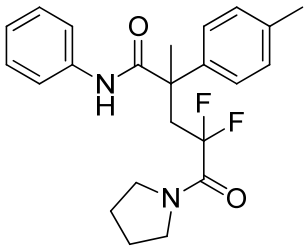


***N*^{1},*N*^{1}-diethyl-2,2-difluoro-4-methyl-*N*^{5},4-diphenylpentanediamide (3p).** The compound **3** was obtained in 77% yield (59.8 mg) as white solid after column chromatography (PE/EA=15:1). Melting point: 96.0 - 97.1 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (3H, t, J = 7.1 Hz), 1.07 (3H, t, J = 7.0 Hz), 1.83 (3H, s), 2.75-2.88 (1H, m), 3.16-3.26 (5H, m), 6.91 (1H, brs), 7.00 (1H, t, J = 7.4 Hz), 7.18-7.25 (3H, m), 7.29-7.33 (4H, m), 7.37-7.40 (2H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 23.6, 41.9, 42.2 (t, J = 5.8 Hz), 42.5 (t, J = 21.4 Hz), 49.4, 119.1 (t, J = 253.7 Hz), 120.1, 124.5, 126.6, 127.7, 129.9, 137.8, 143.0, 163.0 (t, J = 28.5 Hz), 173.6; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.5 (d, J = 270.9 Hz), -96.2 (d, J = 271.0 Hz); HRMS (EI, TOF) calcd for $C_{22}H_{26}F_2N_2O_2^+$ $[M]^+$: 388.1962, found: 388.1964.

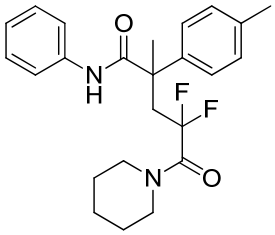


2-(4-chlorophenyl)-*N*^{5},*N*^{5}-diethyl-4,4-difluoro-2-methyl-*N*^{1}-phenylpentanediamide (3q). The

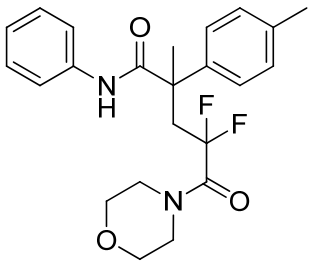
compound **3q** was obtained in 86% yield (72.8 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (3H, t, J = 7.1 Hz), 1.08 (3H, t, J = 7.0 Hz), 1.80 (3H, s), 2.71-2.84 (1H, m), 3.17-3.40 (5H, m), 6.94 (1H, brs), 7.00-7.03 (1H, m), 7.18-7.23 (2H, m), 7.26-7.33 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.4, 14.4, 23.6, 41.9, 42.3 (t, J = 6.1 Hz), 42.4 (t, J = 21.6 Hz), 48.9, 119.1 (t, J = 254.3 Hz), 120.2, 124.6, 128.1, 129.0, 129.1, 133.6, 137.7, 141.6, 162.9 (t, J = 28.5 Hz), 173.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.4 (d, J = 272.7 Hz), -96.4 (d, J = 272.5 Hz); HRMS (EI, TOF) calcd for $C_{22}H_{25}ClF_2N_2O_2^+$ $[M]^+$: 422.1573, found: 422.1574



4,4-difluoro-2-methyl-5-oxo-*N*-phenyl-5-(pyrrolidin-1-yl)-2-(*p*-tolyl)pentanamide (3r). The compound **3r** was obtained in 81% yield (64.8 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.61-1.69 (2H, m), 1.75-1.82 (5H, m), 2.27 (3H, s), 2.71-2.85 (1H, m), 3.04 (3H, s), 3.12-3.30 (3H, m), 3.47 (2H, t, J = 6.4 Hz), 6.90 (1H, brs), 6.97-7.02 (1H, m), 7.11 (2H, d, J = 8.04 Hz), 7.17-7.21 (2H, m), 7.24-7.30 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 23.3, 23.6, 26.6, 42.2 (t, J = 22.1 Hz), 46.8 (t, J = 6.2 Hz), 47.6, 48.9, 119.6 (t, J = 251.8 Hz), 120.0, 124.5, 126.7, 128.9, 129.7, 137.5, 137.9, 139.5, 162.2 (t, J = 29.3 Hz), 173.9; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -96.8, -96.9; HRMS (EI, TOF) calcd for $C_{23}H_{26}F_2N_2O_2^+$ $[M]^+$: 400.1962, found: 400.1967.

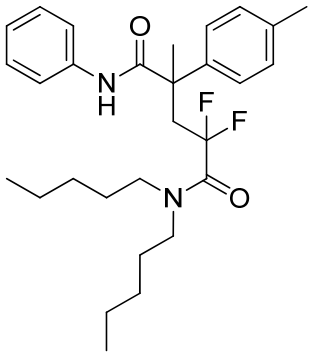


4,4-difluoro-2-methyl-5-oxo-*N*-phenyl-5-(piperidin-1-yl)-2-(*p*-tolyl)pentanamide (3s). The compound **3s** was obtained in 87% yield (72.0 mg) as colorless liquid after column chromatography (PE/EA=15:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44-1.55 (6H, m), 1.79 (3H, s), 2.27 (3H, s), 2.76 (1H, td, J = 14.5, 24.1 Hz), 3.17-3.30 (2H, m), 3.30-3.47 (3H, m), 6.90 (1H, brs), 6.99 (1H, t, J = 7.3 Hz), 7.11 (2H, d, J = 8.2 Hz), 7.18 (2H, dd, J = 7.5, 9.7 Hz), 7.24-7.29 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 23.5, 24.5, 25.6, 26.5, 42.5 (t, J = 21.6 Hz), 44.6, 47.1 (t, J = 6.3 Hz), 49.1, 119.1 (t, J = 253.3 Hz), 120.1, 124.5, 126.6, 129.0, 129.7, 137.5, 137.9, 139.8, 161.9 (t, J = 28.3 Hz), 173.9; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -93.9 (d, J = 270.2 Hz), -95.0 (d, J = 270.5 Hz); HRMS (EI, TOF) calcd for $C_{24}H_{28}F_2N_2O_2^+$ $[M]^+$: 414.2119, found: 414.2115.

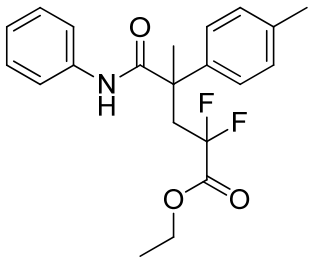


4,4-difluoro-2-methyl-5-morpholino-5-oxo-*N*-phenyl-2-(*p*-tolyl)pentanamide (3t). The compound **3t** was obtained in 80% yield (66.6 mg) as colorless liquid after column chromatography (PE/EA=7:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.80 (3H, m), 2.29 (3H, m), 2.74 (1H, td, J =15.2, 23.3 Hz), 3.16-3.38 (2H, m), 3.45-3.60 (7H, m), 6.86 (1H, brs), 7.01 (t, J = 7.3 Hz), 7.12 (d, J = 8.0 Hz), 7.19-7.23 (2H, m), 7.26-7.30 (4H, m); ^{13}C NMR (100

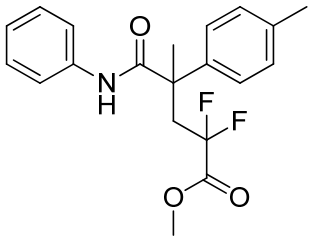
MHz, $CDCl_3$) δ 21.1, 23.3, 42.6 (t, J = 21.2 Hz), 43.5, 46.7 (t, J = 6.4 Hz), 49.0, 66.7, 118.9 (t, J = 253.0 Hz), 120.1, 124.5, 126.6, 129.0, 129.7, 137.6, 137.8, 139.6, 162.2 (t, J = 28.7 Hz), 173.8; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -93.6 (d, J = 272.0 Hz), -94.6 (d, J = 272.1 Hz); HRMS (EI, TOF) calcd for $C_{23}H_{26}F_2N_2O_3^+$ $[M]^+$: 416.1911, found: 416.1919.



2,2-difluoro-4-methyl-*N*^{1},*N*^{1}-dipentyl-*N*^{5}-phenyl-4-(*p*-tolyl)pentanediamide (3u). The compound **3u** was obtained in 68% yield (66.2 mg) as colorless liquid after column chromatography (PE/EA=20:1). ^{1}H NMR (400 MHz, CDCl3) δ 0.77-0.82 (6H, m), 1.11-1.25 (8H, m), 1.39-1.50 (4H, m), 1.79 (3H, s), 2.27 (3H, s), 2.70-2.83 (1H, m), 3.10-3.29 (5H, m), 6.94 (1H, brs), 6.99 (1H, t, J = 7.4 Hz), 7.10 (2H, d, J = 8.1 Hz), 7.19 (2H, t, J = 7.6 Hz), 7.25-7.31 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 14.1, 21.0, 22.4, 22.5, 23.6, 26.7, 28.8, 28.9, 29.2, 42.6 (t, J = 21.6 Hz), 47.7, 48.1 (t, J = 5.6 Hz), 49.1, 119.2 (t, J = 253.5 Hz), 120.1, 124.4, 126.5, 128.9, 129.7, 137.4, 137.9, 140.1, 163.3 (t, J = 28.5 Hz), 173.8; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -94.7 (d, J = 268.9 Hz), -96.2 (d, J = 270.0 Hz); HRMS (EI, TOF) calcd for $C_{29}H_{40}F_2N_2O_2^+$ $[M]^+$: 486.3058, found: 486.3054.

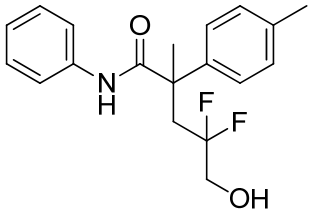


Ethyl 2,2-difluoro-4-methyl-5-oxo-5-(phenylamino)-4-(*p*-tolyl)pentanoate (3v). The compound was obtained in 25% (18.8 mg) yield as colorless liquid after column chromatography (PE/EA=10:1). ^{1}H NMR (400 MHz, CDCl3) δ 1.14 (3H, t, J = 7.2 Hz), 1.79 (3H, s), 2.29 (2H, s), 2.76 (1H, td, J = 15.4, 20.7 Hz), 3.07 (1H, q, J = 15.5 Hz), 3.85 (2H, m), 6.69 (1H, brs), 6.98-7.047.02 (1H, m), 7.13 (2H, d, J = 8.1 Hz), 7.17-7.26 (6H, m); ^{13}C NMR (125.8 MHz, $CDCl_3$) δ 12.8, 20.1, 22.2, 41.7 (t, J = 22.7 Hz), 48.0 (d, J = 3.7 Hz), 61.8, 115.06 (t, J = 250.2 Hz), 118.9, 123.6, 126.3, 128.0, 128.8, 136.7, 136.96, 137.0, 162.9 (t, J = 33.6 Hz), 173.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -97.1 (d, J = 262.4 Hz), -100.7 (d, J = 261.9 Hz); HRMS (ESI, TOF) calcd for $C_{21}H_{23}F_2NNaO_3^+$ [M + Na^+]: 398.1538, found: 398.1543.



Methyl 2,2-difluoro-4-methyl-5-oxo-5-(phenylamino)-4-(*p*-tolyl)pentanoate (4). The compound **4** was obtained in 91% yield as colorless liquid after column chromatography (PE/EA=10:1). ^{1}H NMR (400 MHz, CDCl3) δ 1.78 (3H, s), 2.28 (3H, s), 2.75 (1H, td, J = 14.7, 21.6 Hz), 3.07 (1H, q, J = 15.4 Hz), 3.43 (3H, s), 6.68 (1H, brs), 6.98-7.02 (1H, m), 7.12-7.16 (2H, m), 7.17-7.25 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 23.0, 42.8 (dd,

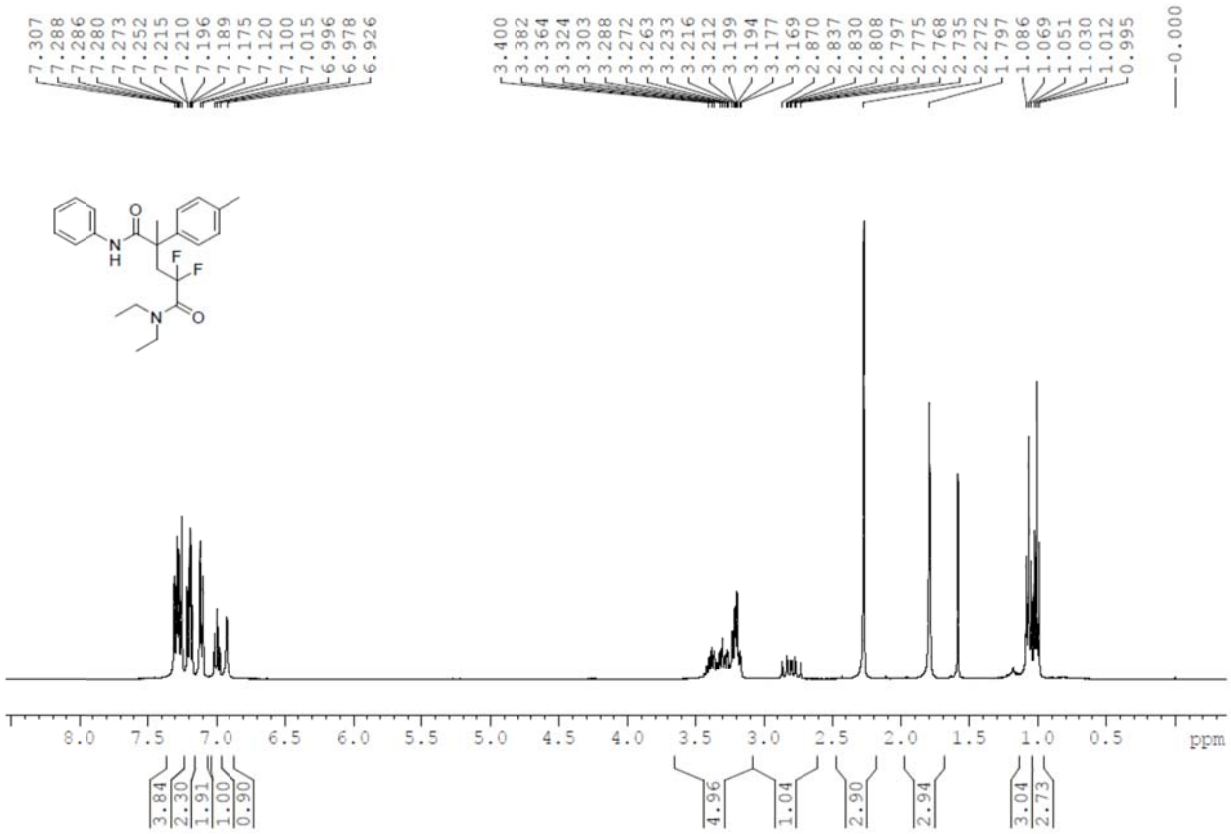
J = 22.2, 23.7 Hz), 48.9 (d, J = 4.2 Hz), 53.2, 116.08 (dd, J = 247.8, 250.7 Hz), 119.9, 124.6, 127.3, 129.1, 129.8, 137.6, 137.7, 138.1, 164.3 (t, J = 32.2 Hz), 173.9; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -96.6 (d, J = 261.8 Hz), -100.5 (d, J = 261.8 Hz); HRMS (EI, TOF) calcd for $C_{20}H_{21}F_2NO_3^+$ $[M]^+$: 361.1489, found: 361.1487.



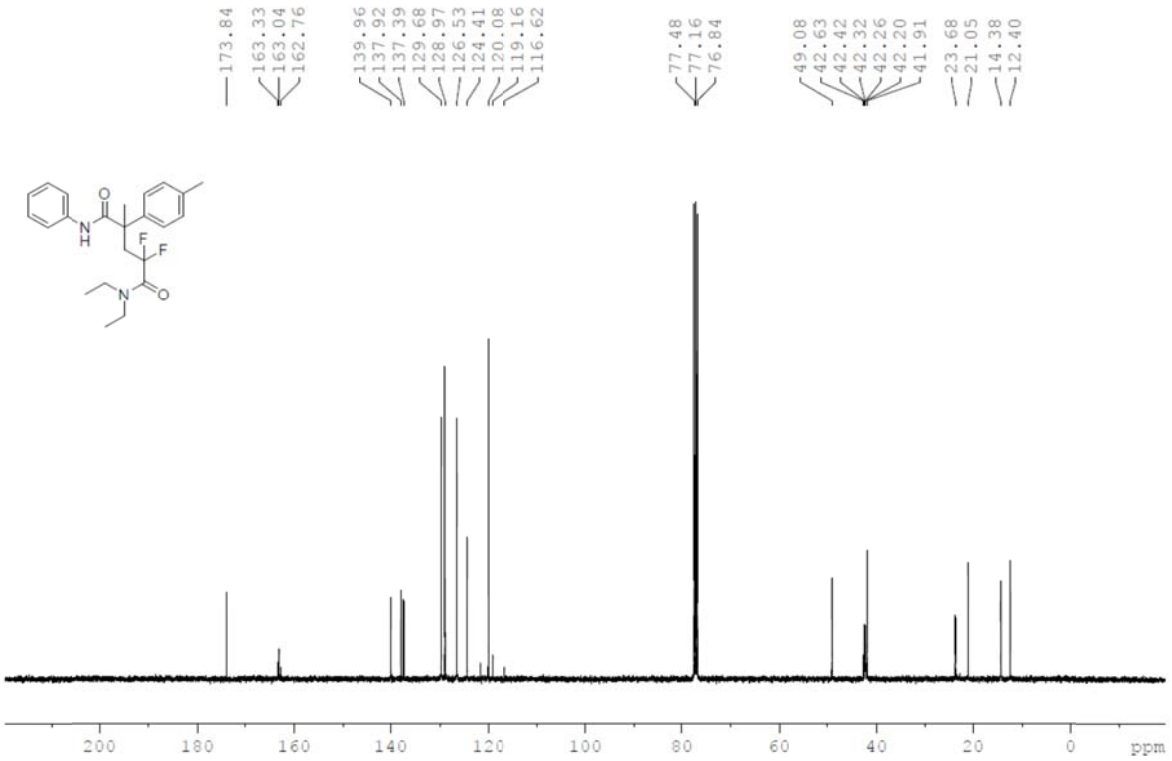
4,4-difluoro-5-hydroxy-2-methyl-N-phenyl-2-(*p*-tolyl)pentanamide (5). The compound **5** was obtained in 85% yield as colorless liquid after column chromatography (PE/EA=3:1). ^{1}H NMR (400 MHz, CDCl3) δ 1.79 (3H, s), 2.27 (3H, s), 2.37 (1H, td, J = 14.0, 19.2 Hz), 2.88-3.01 (1H, m), 3.09 (1H, brs), 3.41-3.56 (2H, m), 6.95 (1H, brs), 7.00-7.04 (1H, m), 7.12 (2H, d, J = 8.1 Hz), 7.17-7.29 (6H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 23.4, 41.8 (t, J = 23.2 Hz), 49.1, 64.5 (t, J = 31.1 Hz), 120.4, 123.2 (t, J = 242.9 Hz), 124.9, 126.3, 129.1, 129.9, 137.5, 137.7, 139.9, 174.9; ^{19}F NMR ($CDCl_3$, 376 MHz) δ -99.2 (d, J = 256.0 Hz), -101.1 (d, J = 255.6 Hz); HRMS (EI, TOF) calcd for $C_{19}H_{21}F_2NO_2^+$ $[M]^+$: 333.1540, found: 333.1541.

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

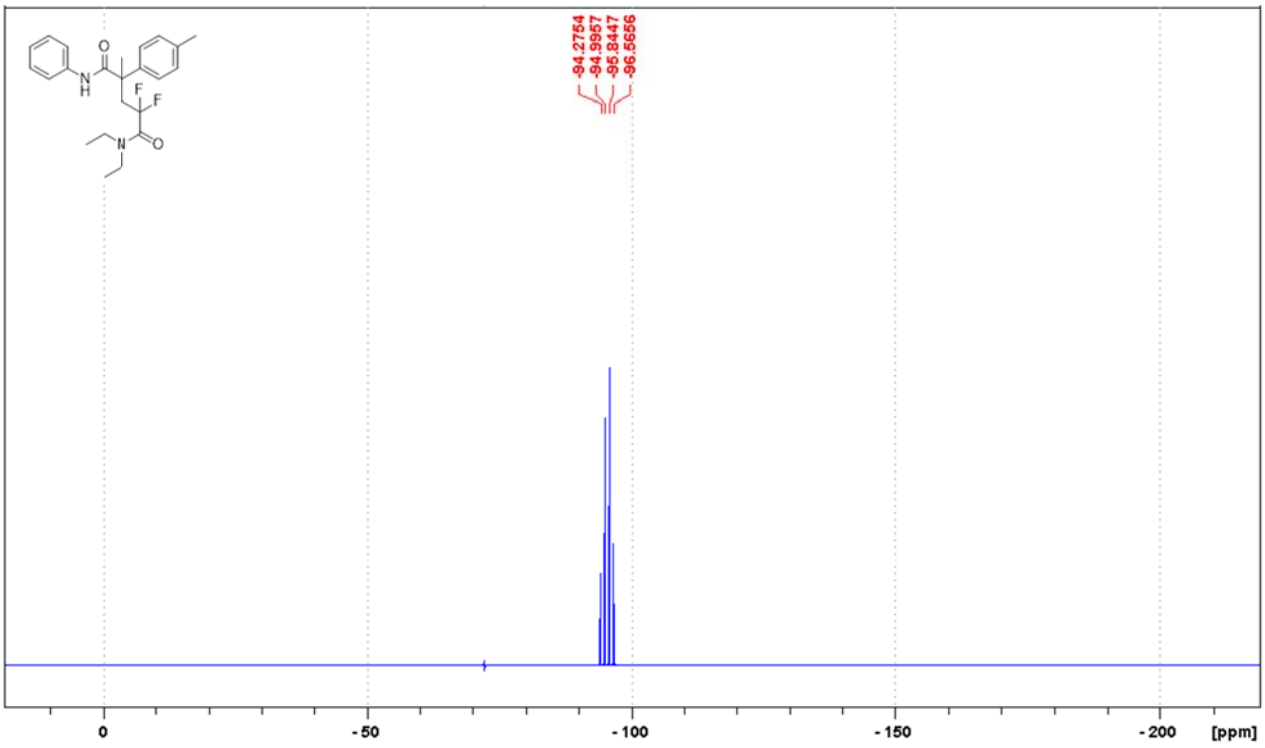
^{1}H NMR of N^{1},N^{1}-diethyl-2,2-difluoro-4-methyl-N^{5}-phenyl-4-(*p*-tolyl) pentanediamide (3a).



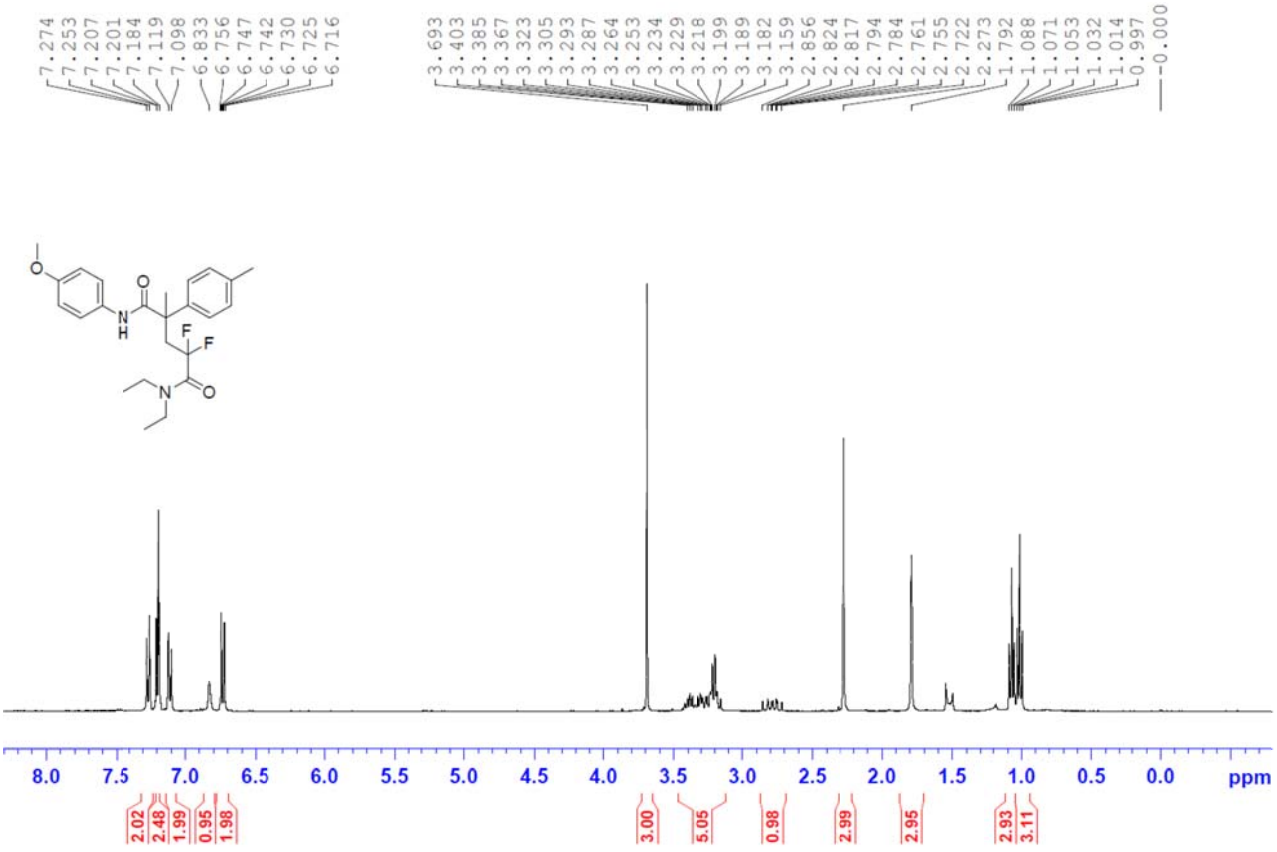
^{13}C NMR of N^{1},N^{1}-diethyl-2,2-difluoro-4-methyl-N^{5}-phenyl-4-(*p*-tolyl) pentanediamide (3a).



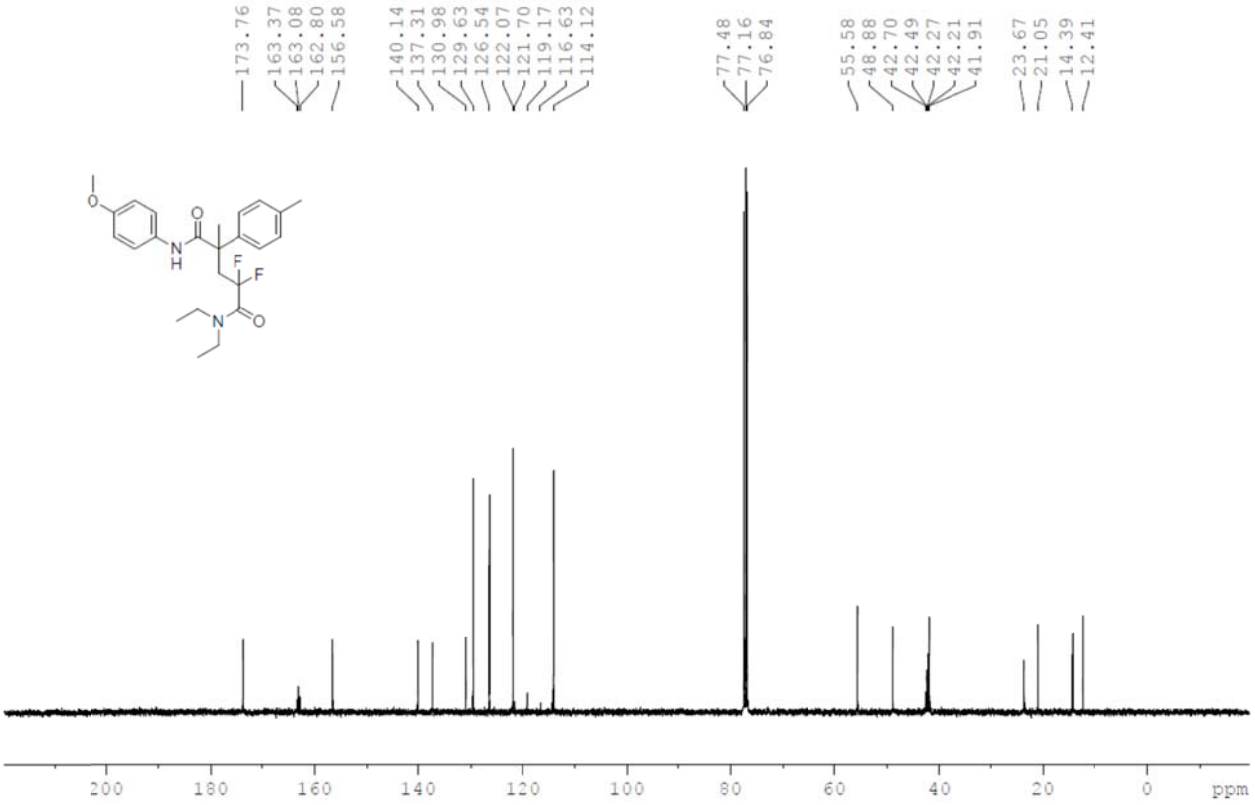
^{19}F NMR of N^1,N^1-diethyl-2,2-difluoro-4-methyl-N^5-phenyl-4-(*p*-tolyl) pentanediamide (3a).



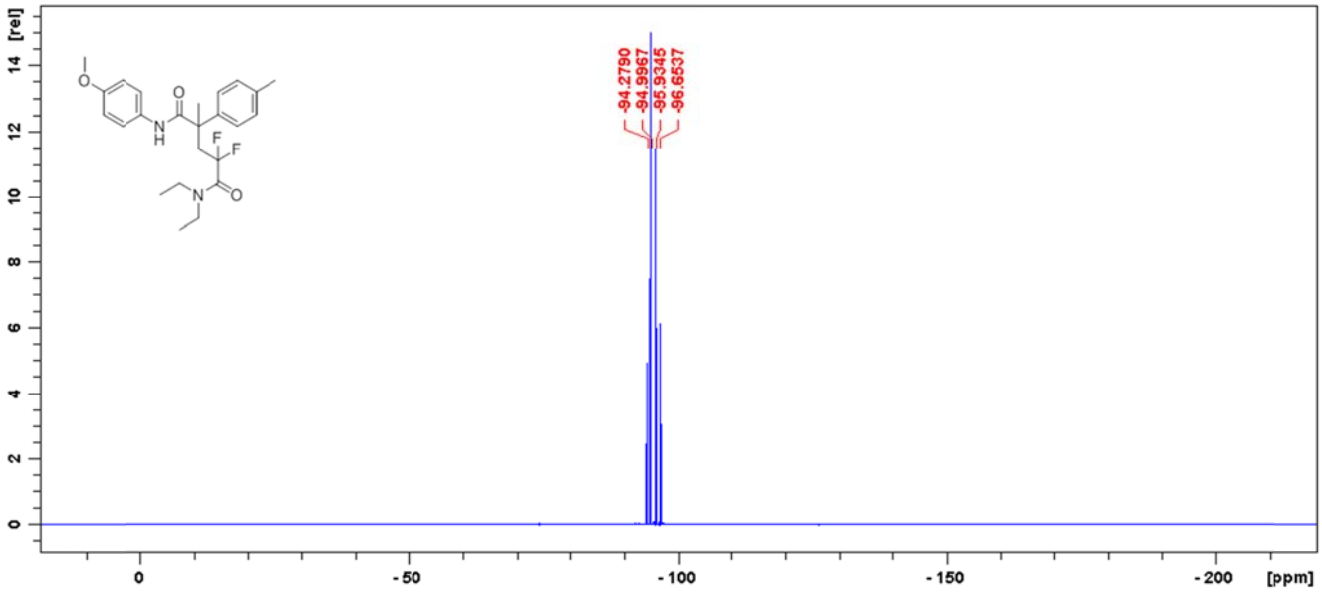
^{1}H NMR of N^1,N^1-diethyl-2,2-difluoro-N^5-(4-methoxyphenyl)-4-methyl-4- phenylpentanediamide (3b)



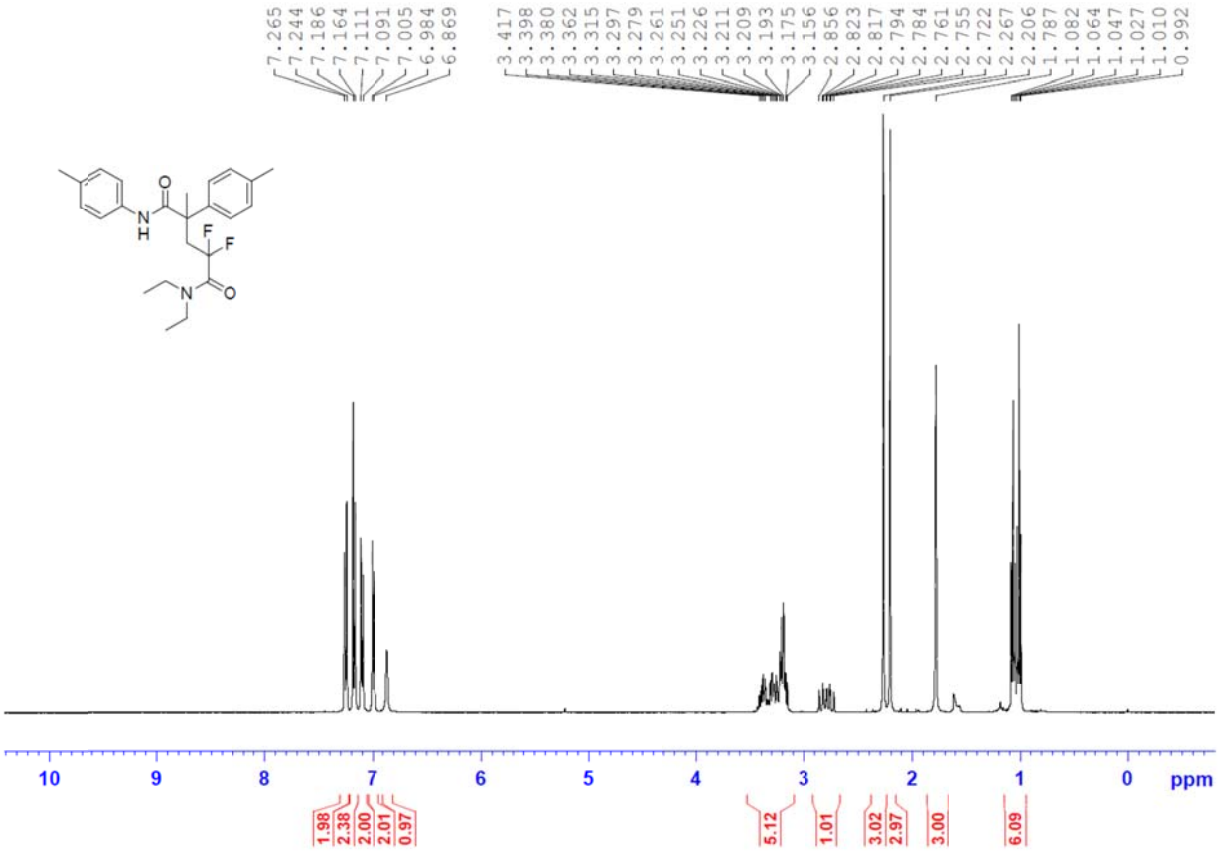
^{13}C NMR of N^1,N^1-diethyl-2,2-difluoro-N^5-(4-methoxyphenyl)-4-methyl-4- phenylpentanediamide (3b)



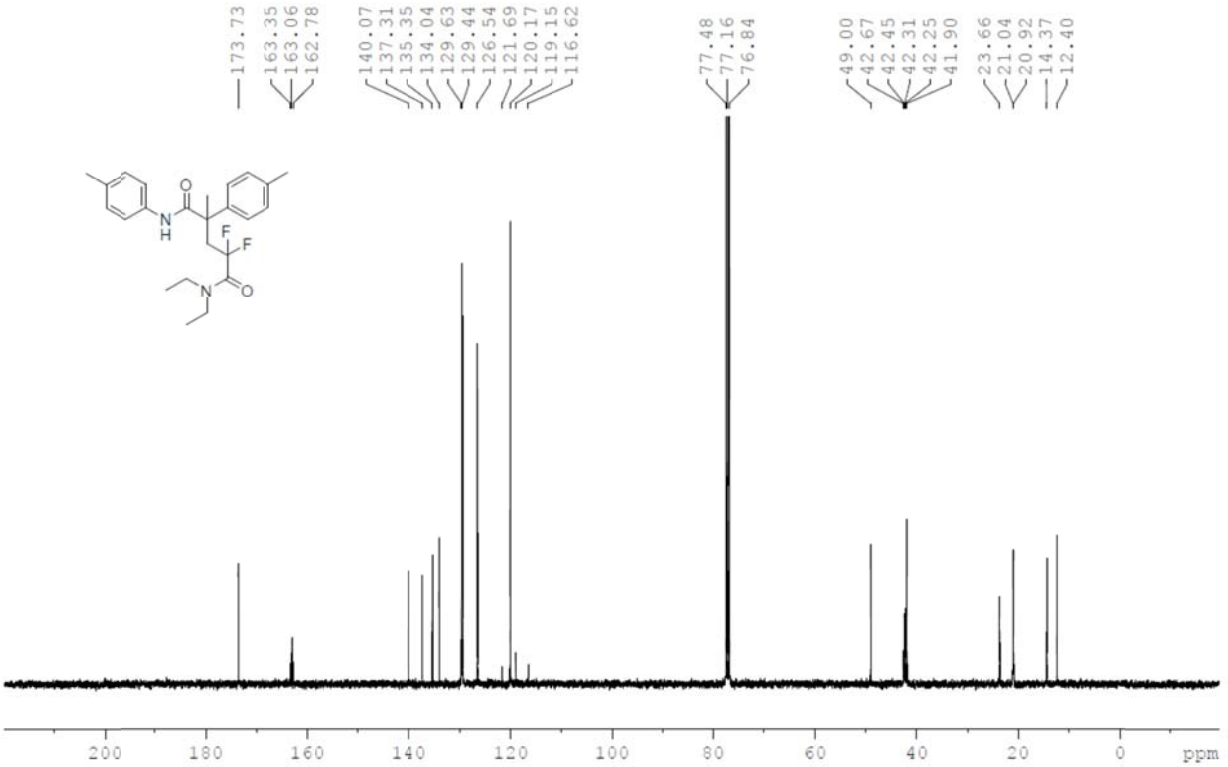
^{19}F NMR of N^1,N^1-diethyl-2,2-difluoro-N^5-(4-methoxyphenyl)-4-methyl-4- phenylpentanediamide (3b)



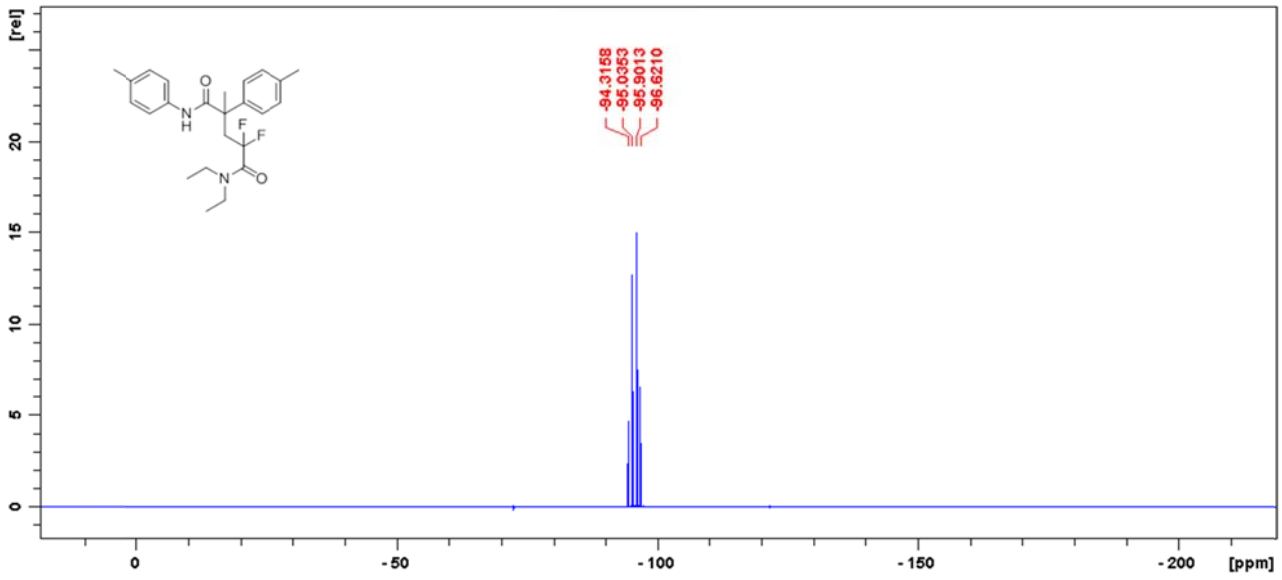
^{1}H NMR of N^{1},N^{1}-diethyl-2,2-difluoro-4-methyl-$N^{5,4}$-di-*p*-tolylpentanediamide (3c)



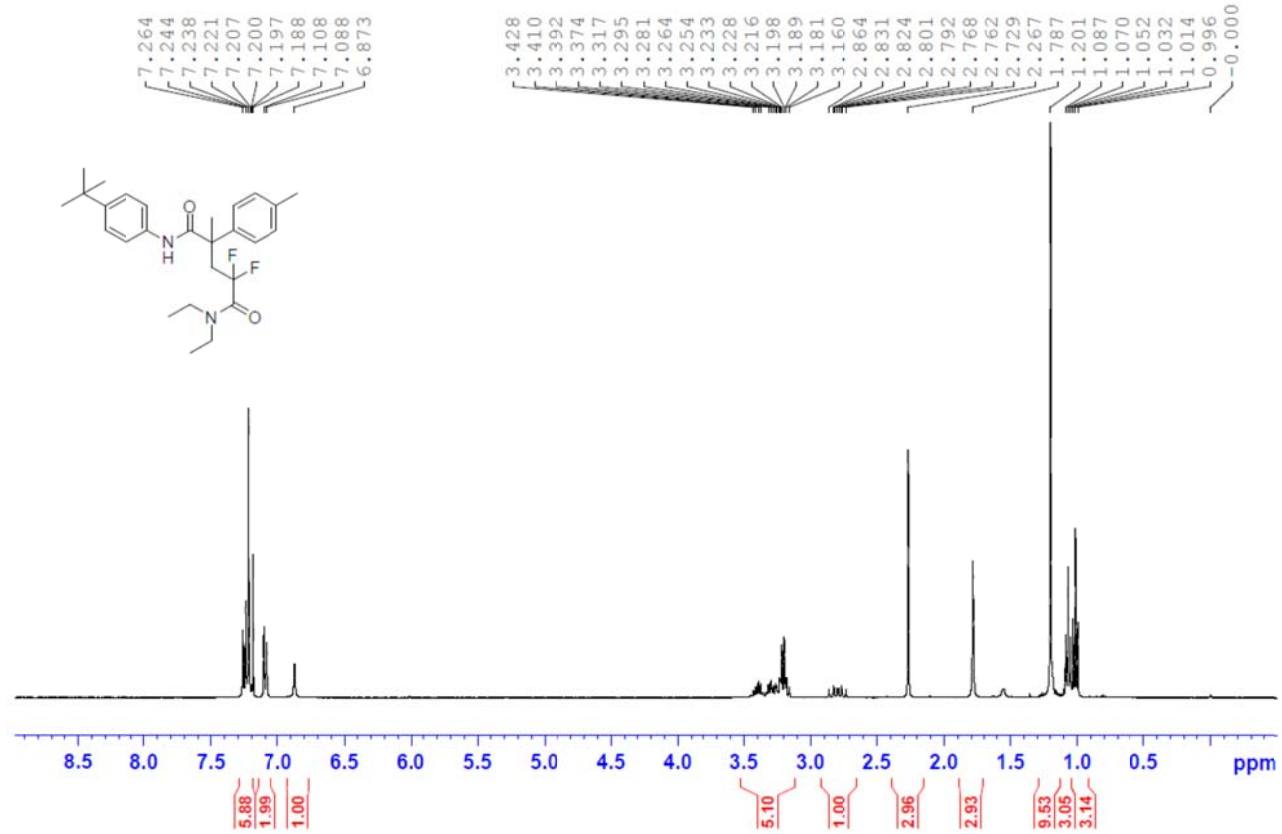
^{13}C NMR of N^{1},N^{1}-diethyl-2,2-difluoro-4-methyl-$N^{5,4}$-di-*p*-tolylpentanediamide (3c)



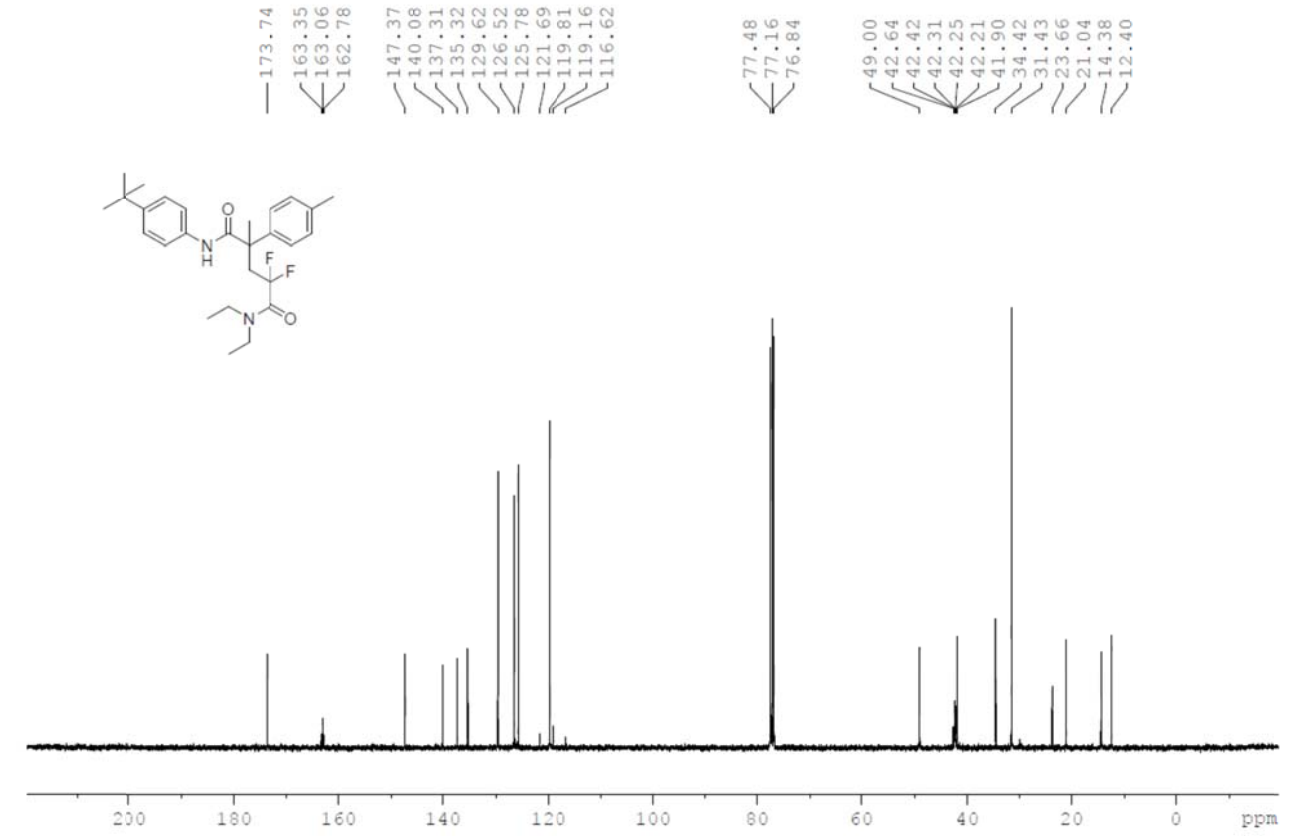
^{19}F NMR of N^1,N^1-diethyl-2,2-difluoro-4-methyl-$N^{5,4}$-di-*p*-tolylpentanediamide (3c)



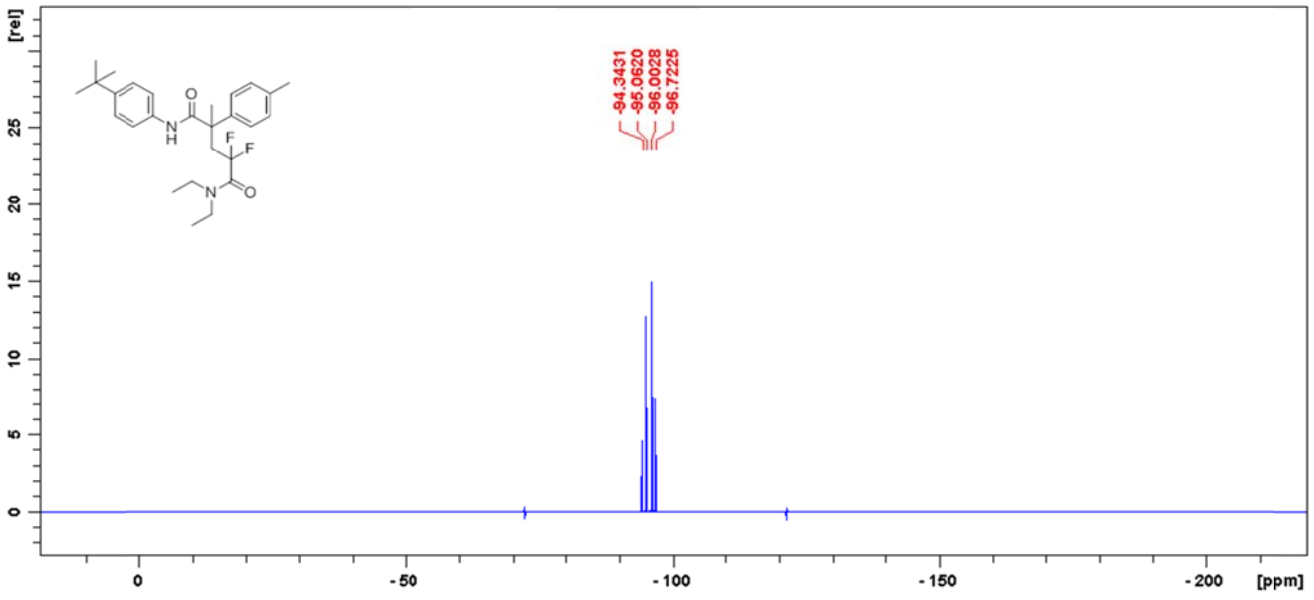
^{1}H NMR of N^1-(4-(*tert*-butyl)phenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3d)



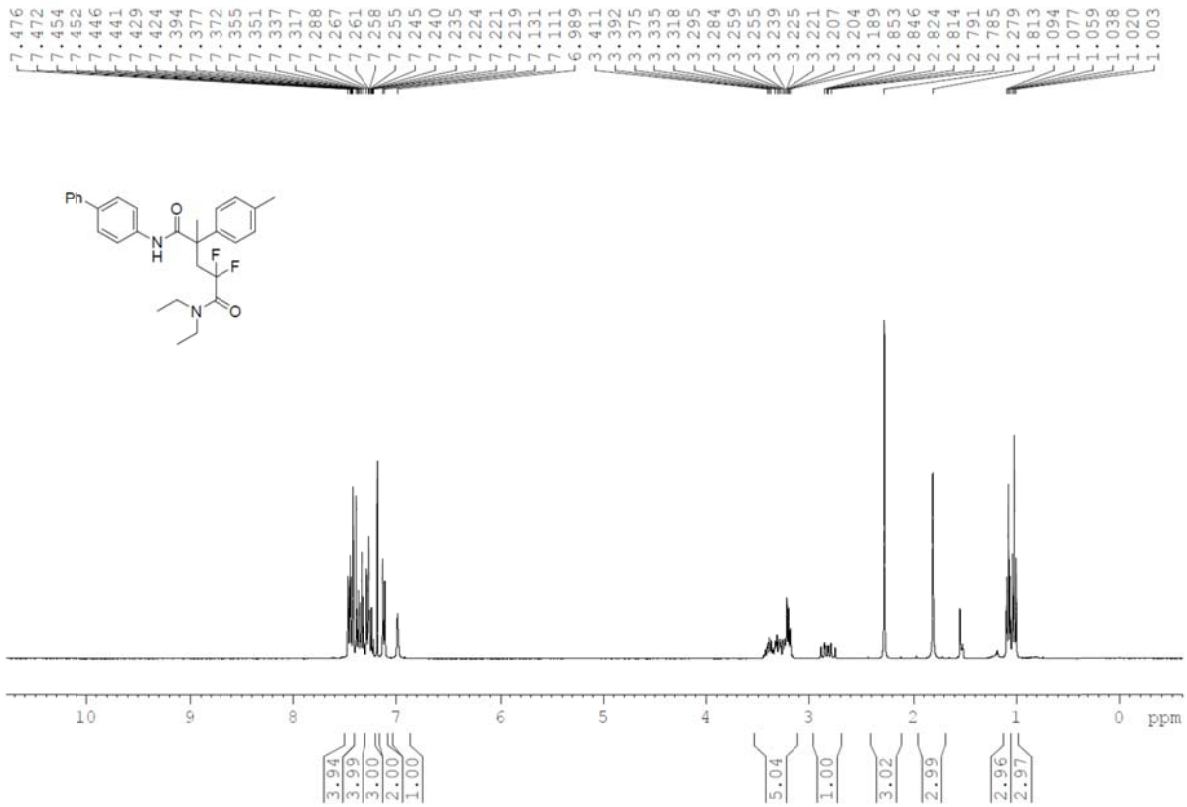
^{13}C NMR of N^1-(4-(*tert*-butyl)phenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3d)



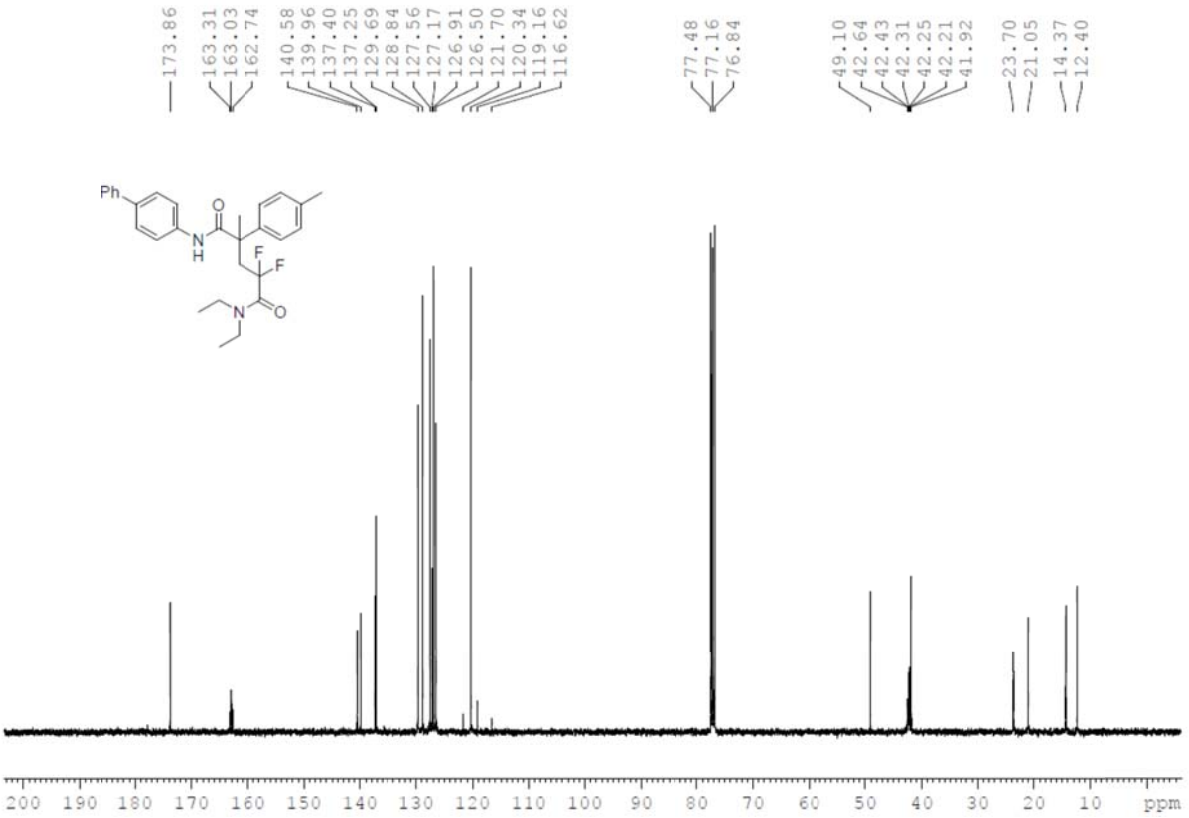
^{19}F NMR of N^1-(4-(*tert*-butyl)phenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3d)



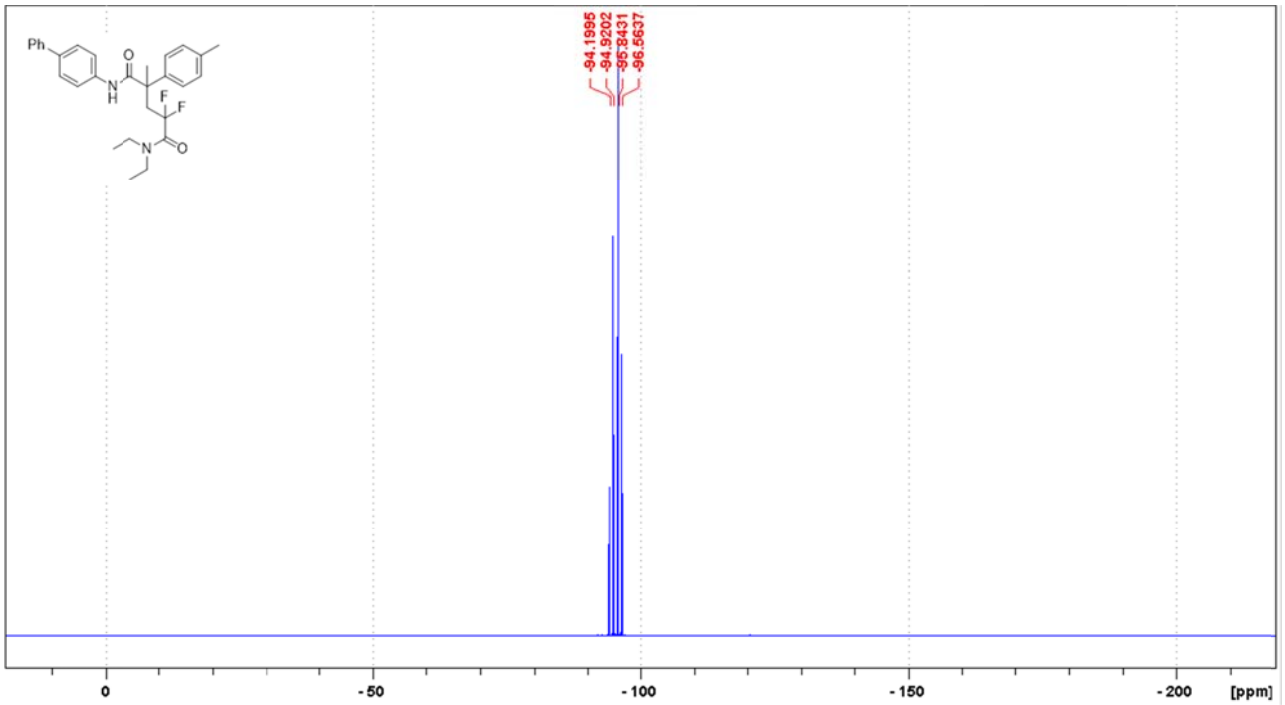
^{1}H NMR of N^{1}-([1,1'-biphenyl]-4-yl)-N^{5},N^{5}-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3e)



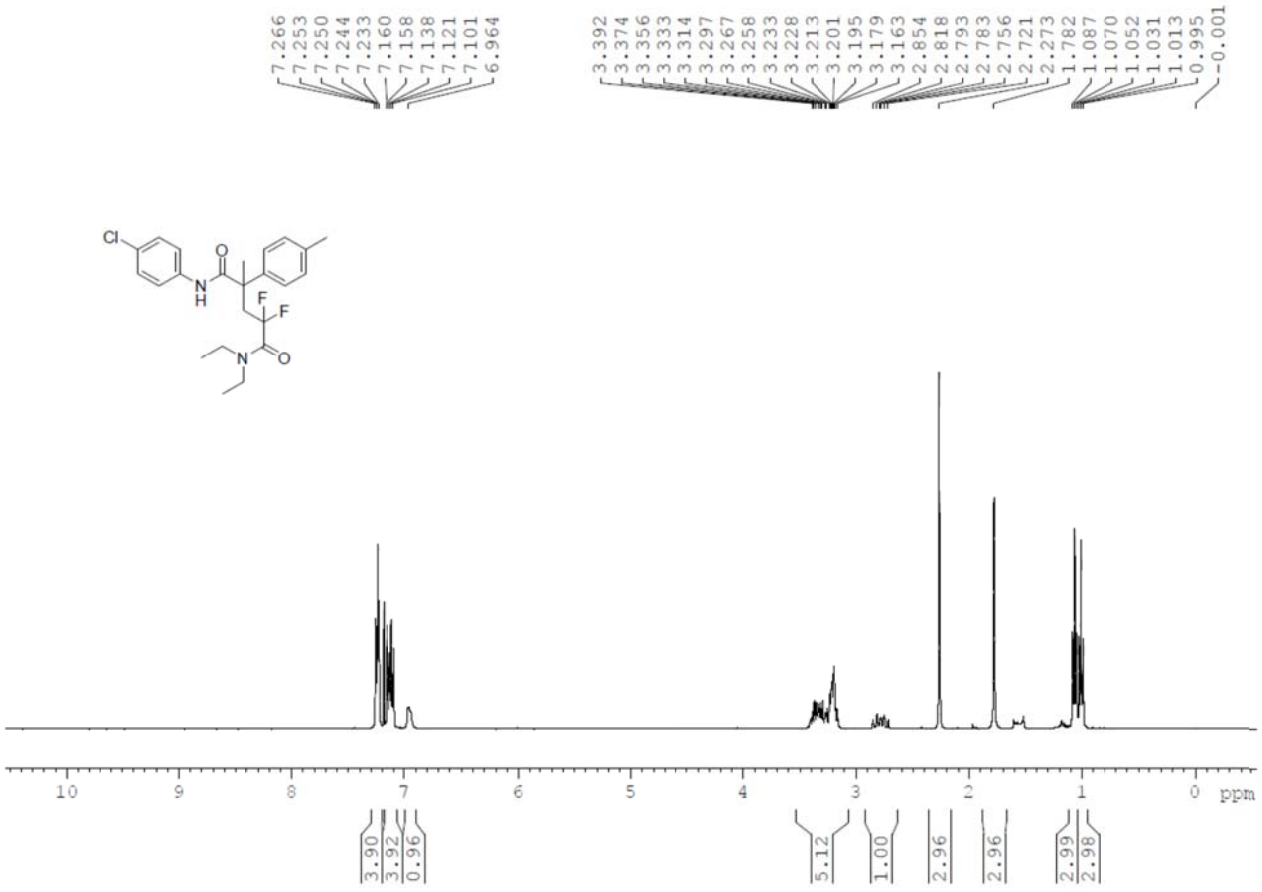
^{13}C NMR of N^{1}-([1,1'-biphenyl]-4-yl)-N^{5},N^{5}-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3e)



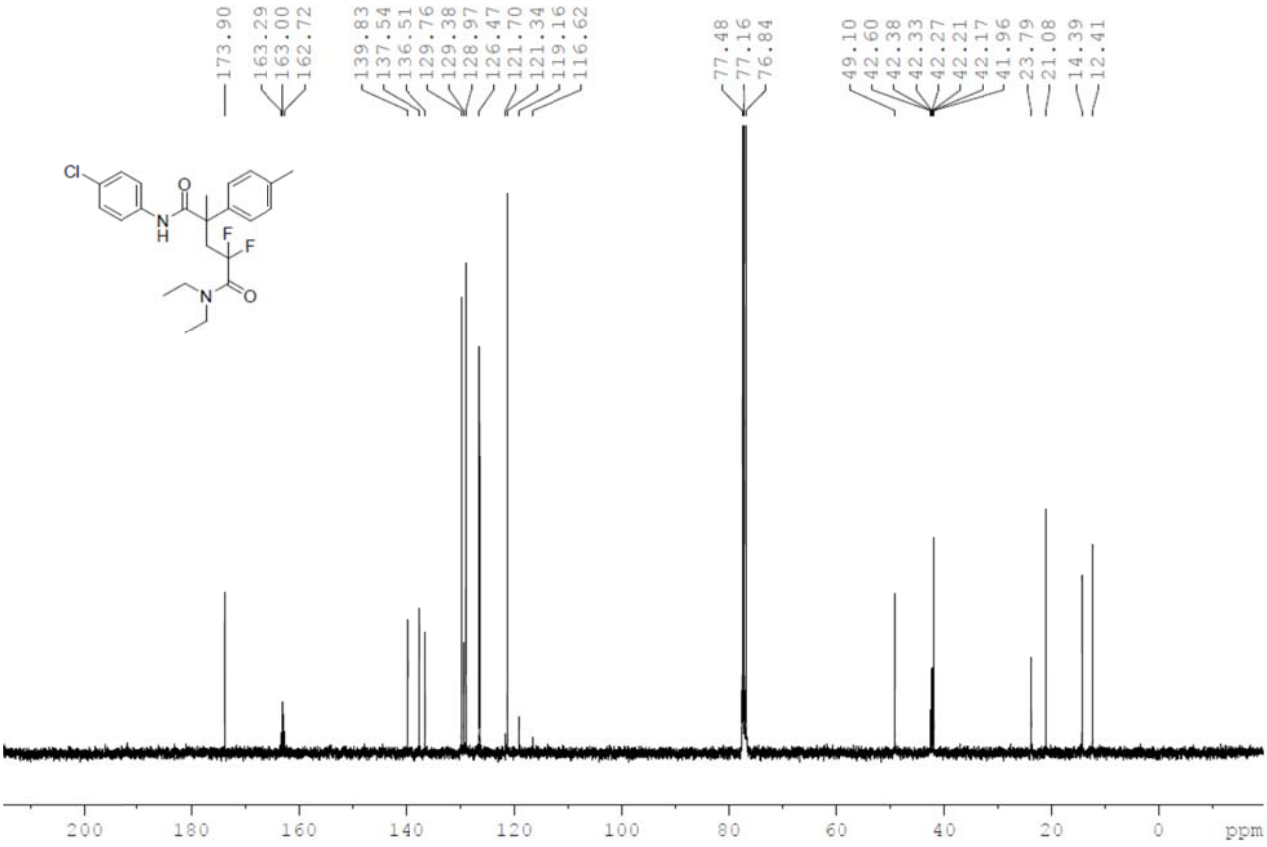
^{19}F NMR of N^1-([1,1'-biphenyl]-4-yl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3e)



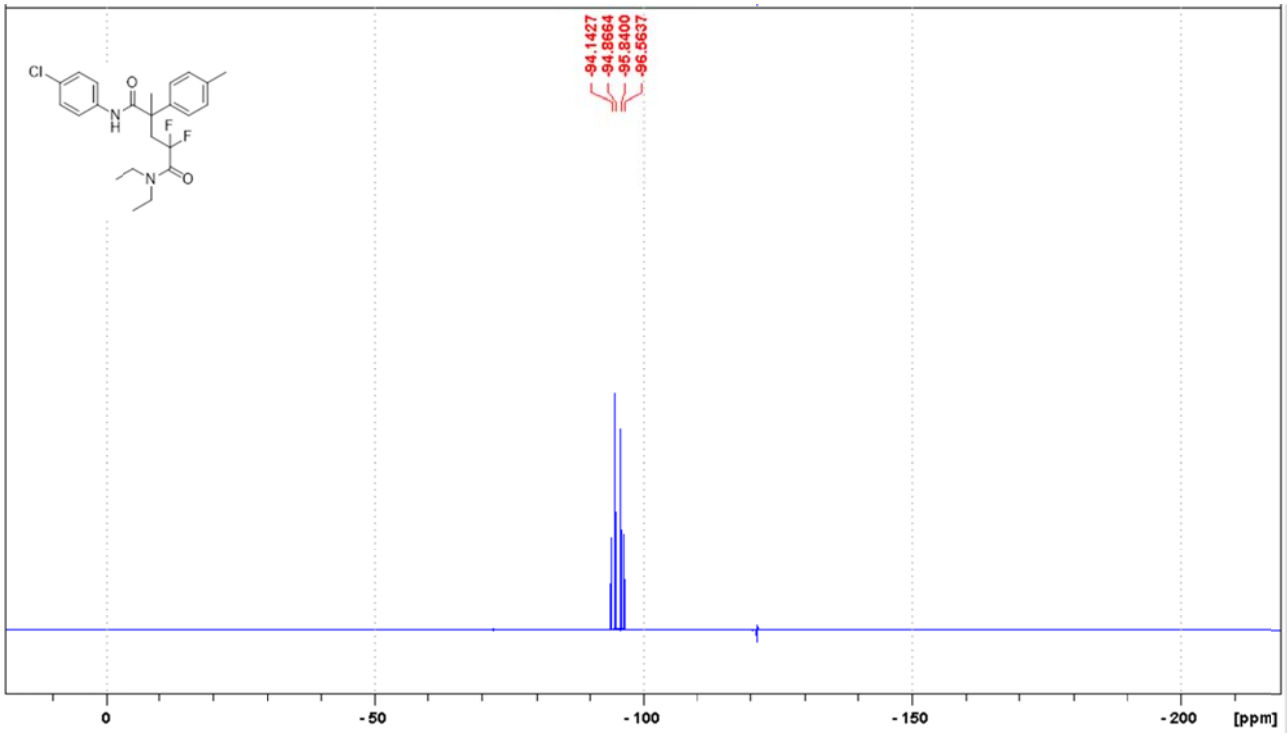
^{1}H NMR of N^1-(4-chlorophenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3f)



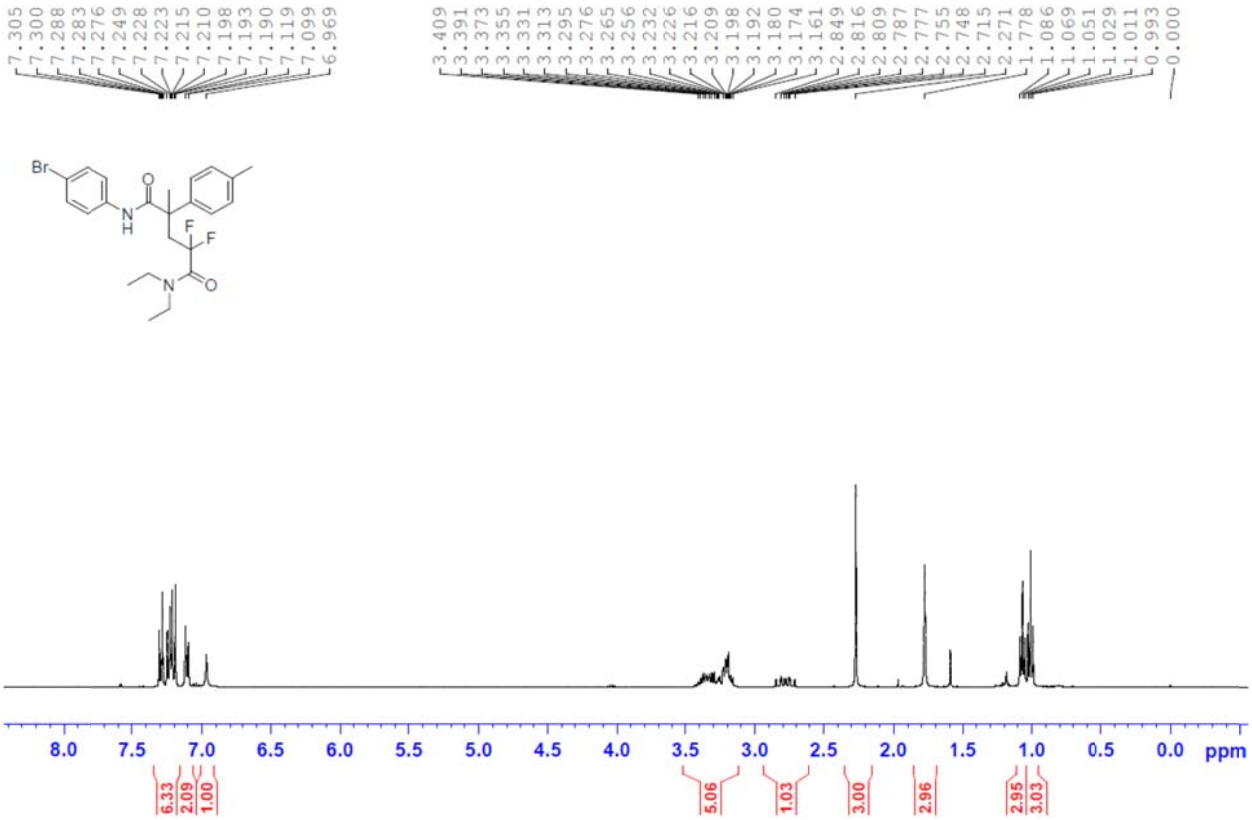
^{13}C NMR of N^1-(4-chlorophenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3f)



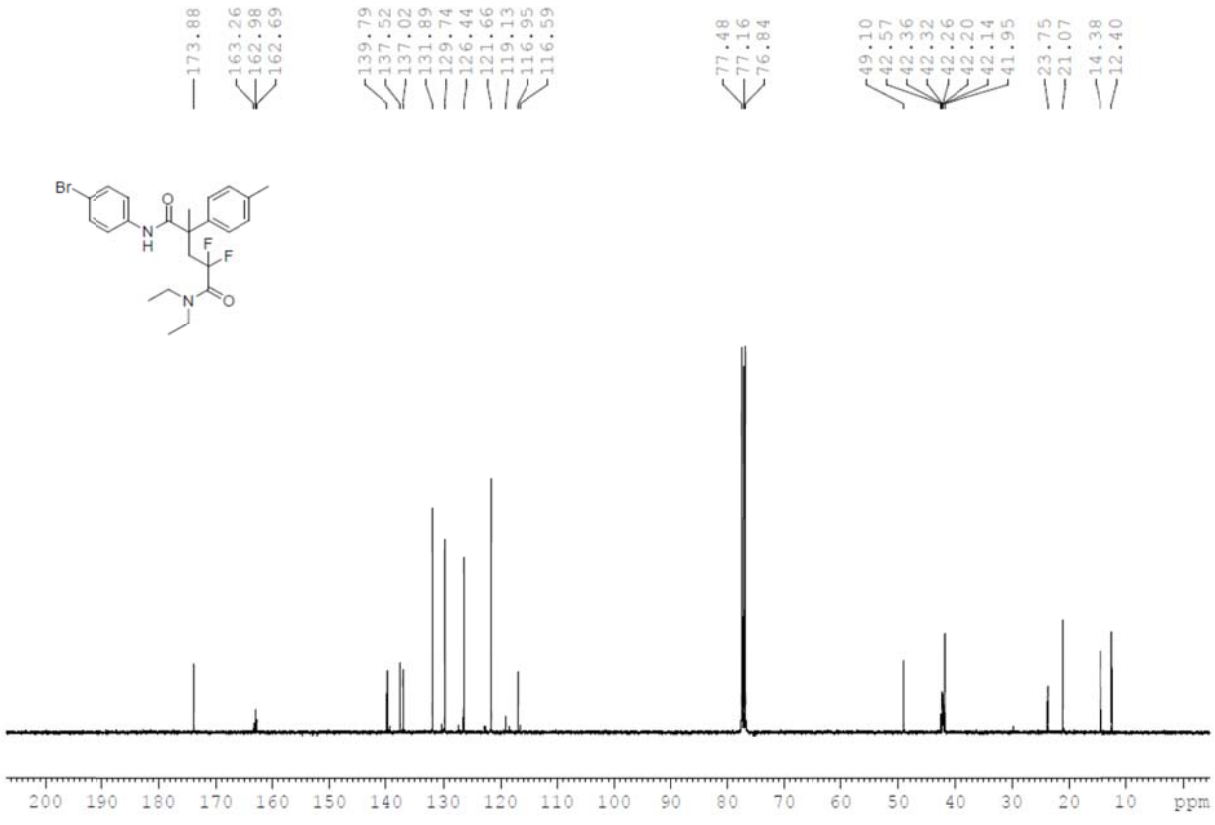
^{19}F NMR of N^1-(4-chlorophenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3f)



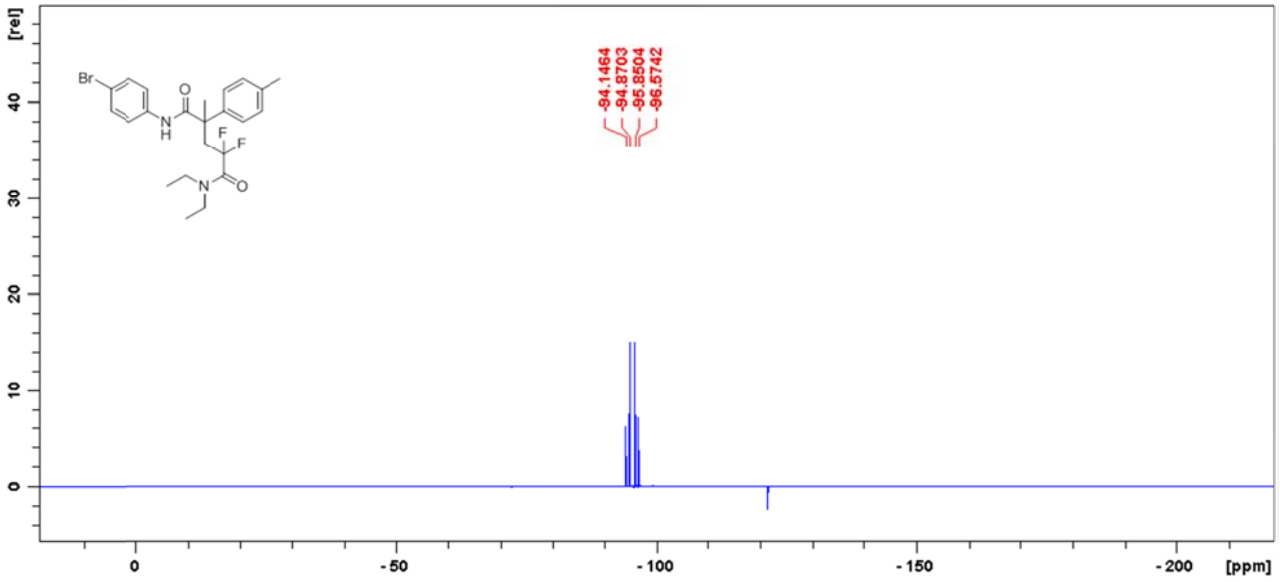
^{1}H NMR of N^{1}-(4-bromophenyl)-N^{5},N^{5}-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3g)



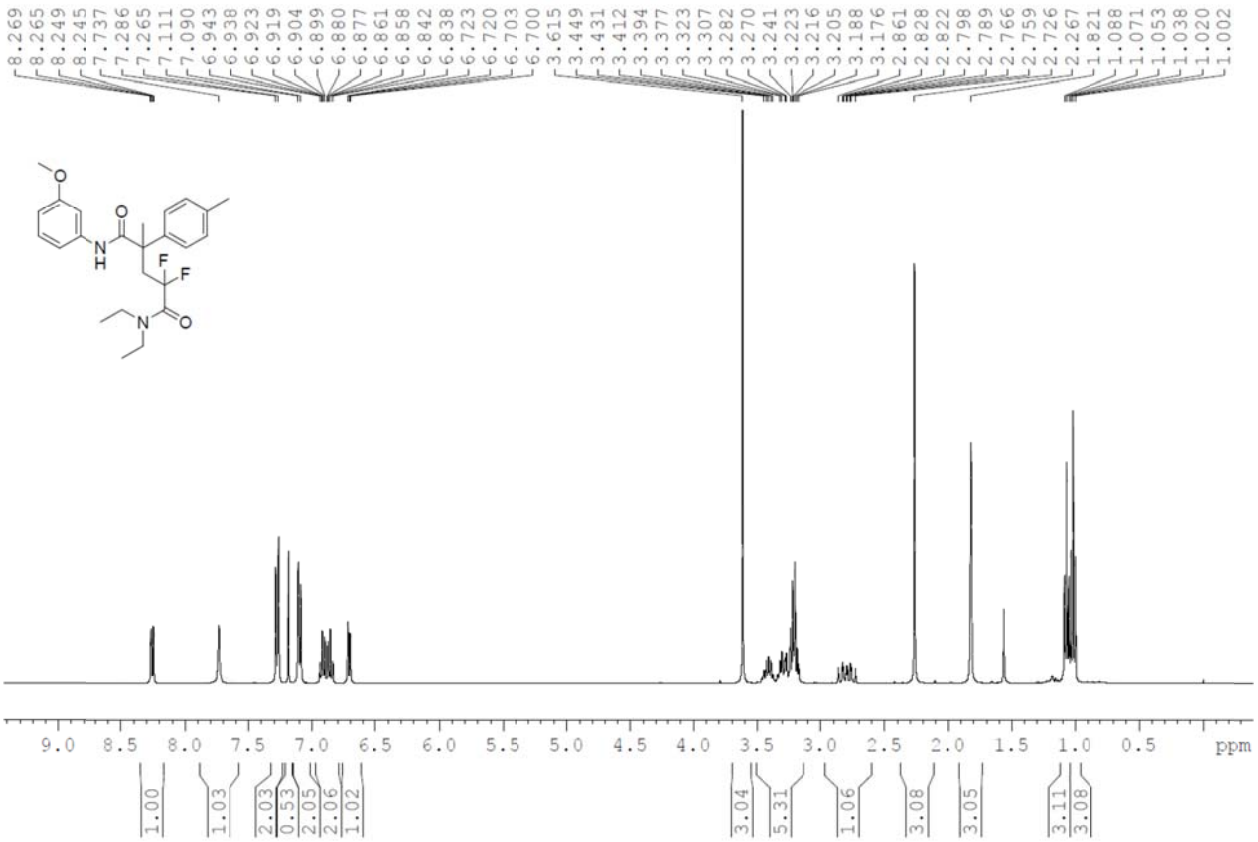
^{13}C NMR of N^{1}-(4-bromophenyl)-N^{5},N^{5}-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3g)



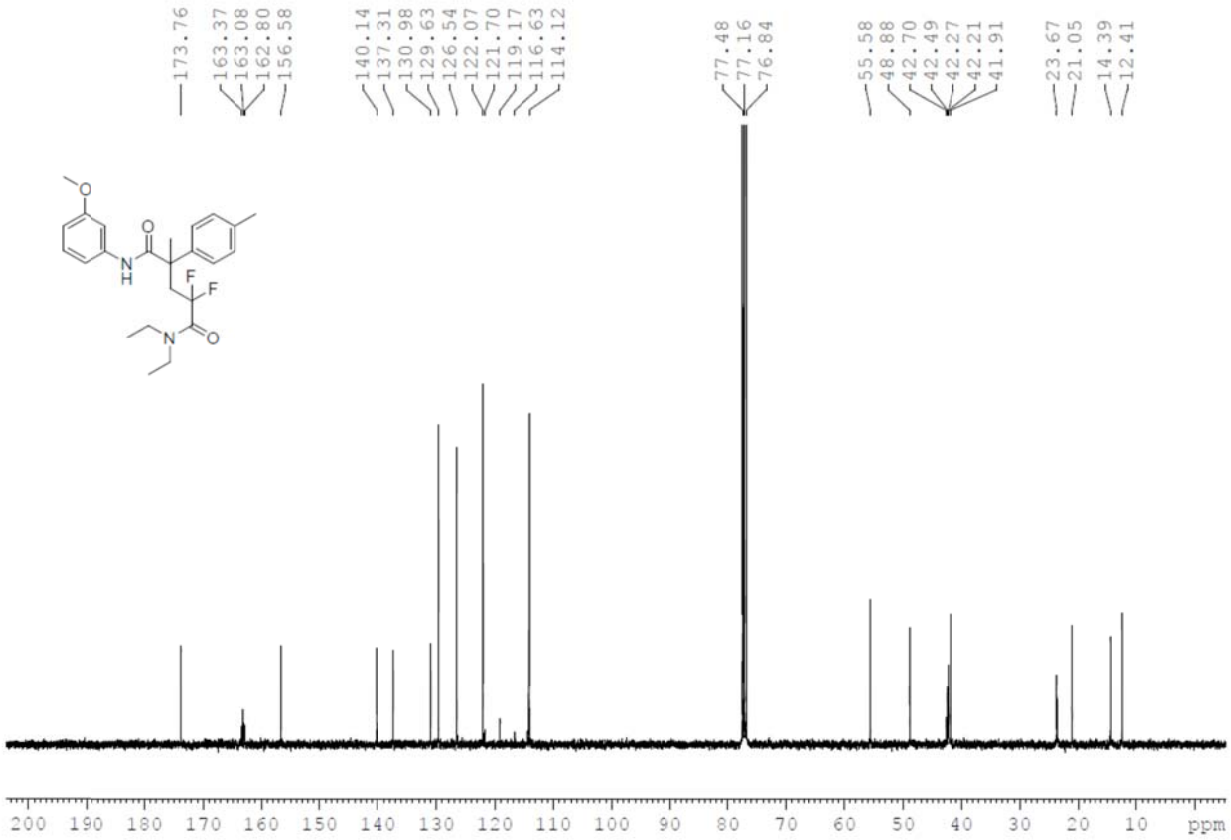
^{19}F NMR of N^1-(4-bromophenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl)pentanediamide (3g)



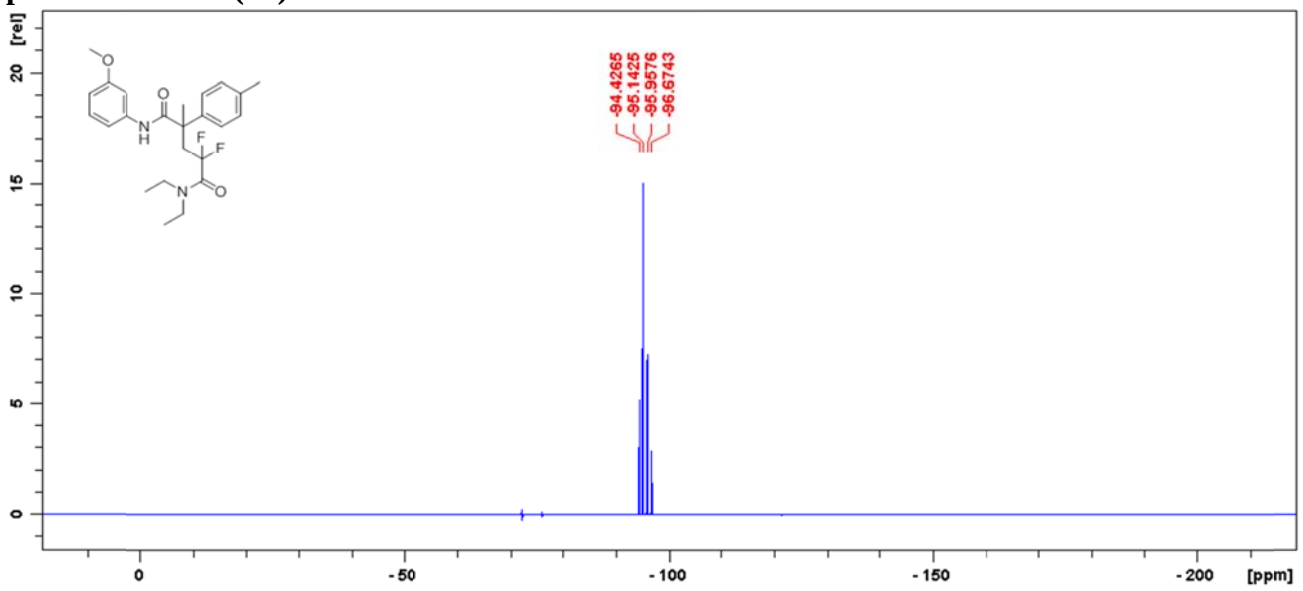
^{1}H NMR of N^1,N^1-diethyl-2,2-difluoro-N^5-(3-methoxyphenyl)-4-methyl-4-(*p*-tolyl)pentanediamide (3h)



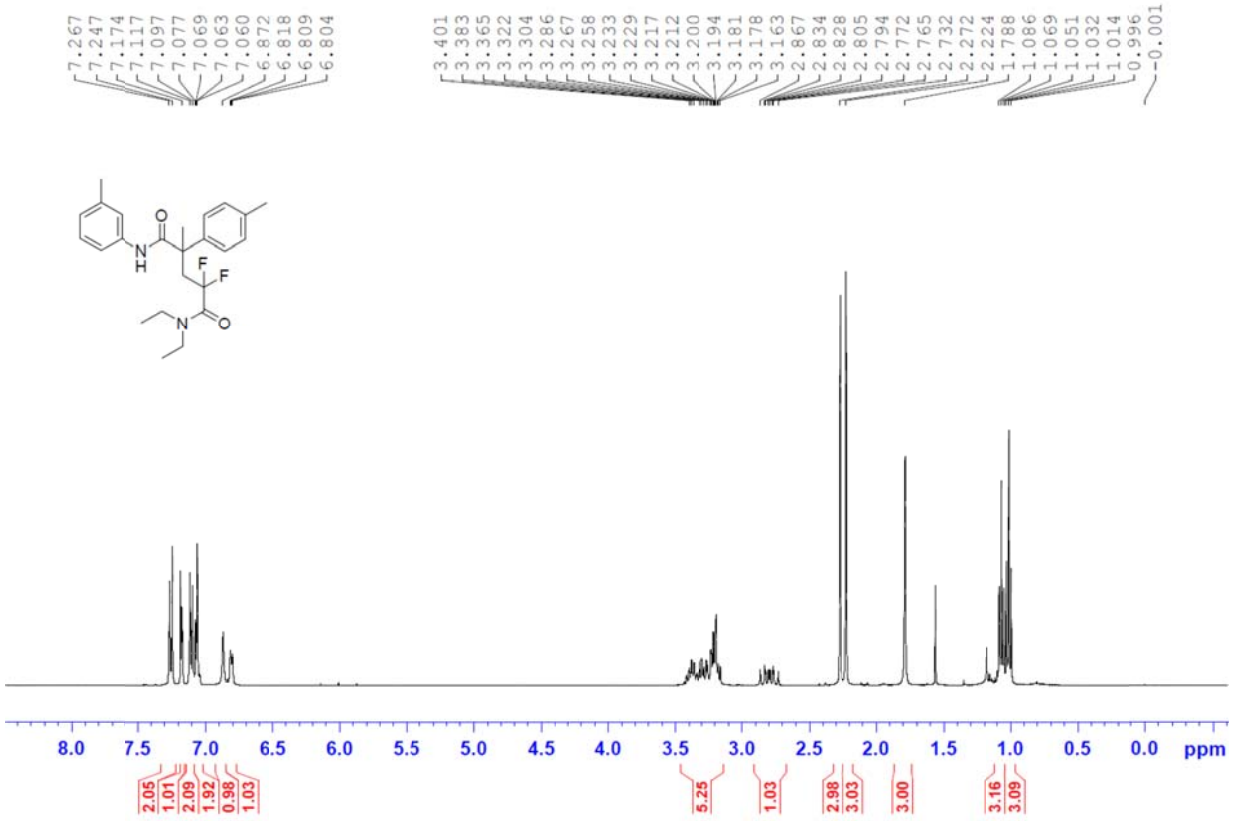
^{13}C NMR of N^1,N^1-diethyl-2,2-difluoro-N^5-(3-methoxyphenyl)-4-methyl-4-(*p*-tolyl)pentanediamide (3h)



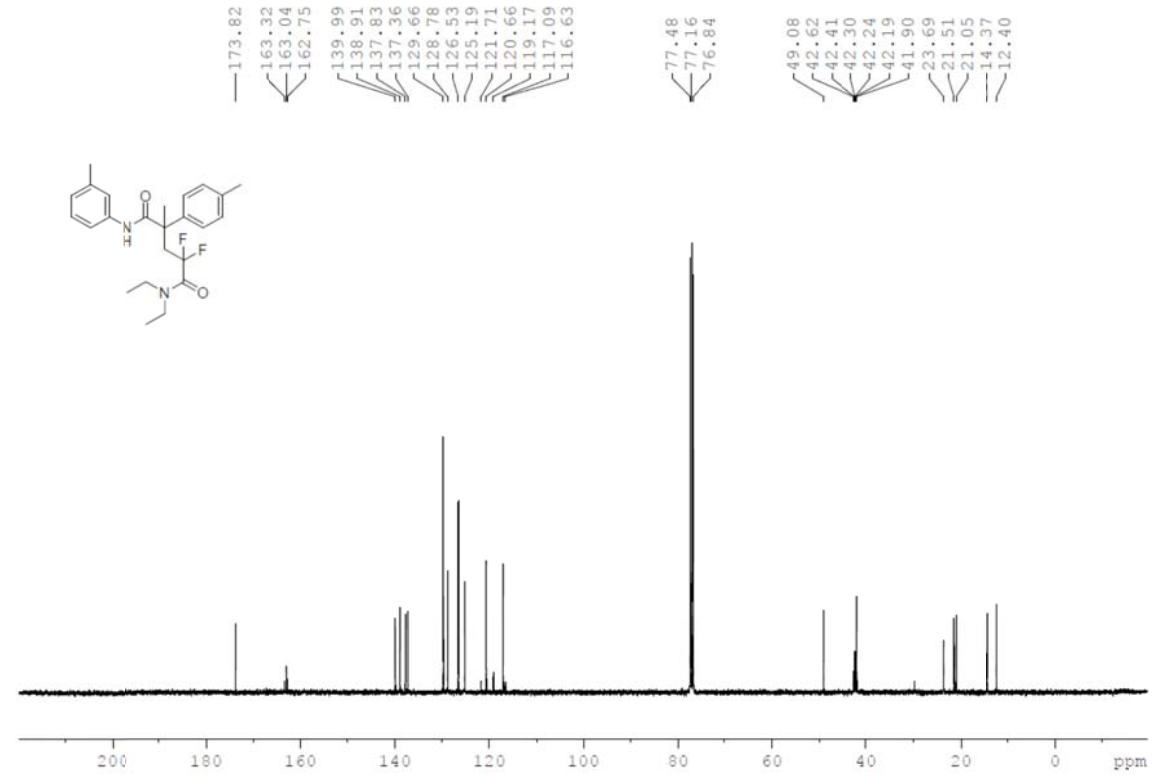
^{19}F NMR of N^1,N^1-diethyl-2,2-difluoro-N^5-(3-methoxyphenyl)-4-methyl-4-(*p*-tolyl) pentanediamide (3h)



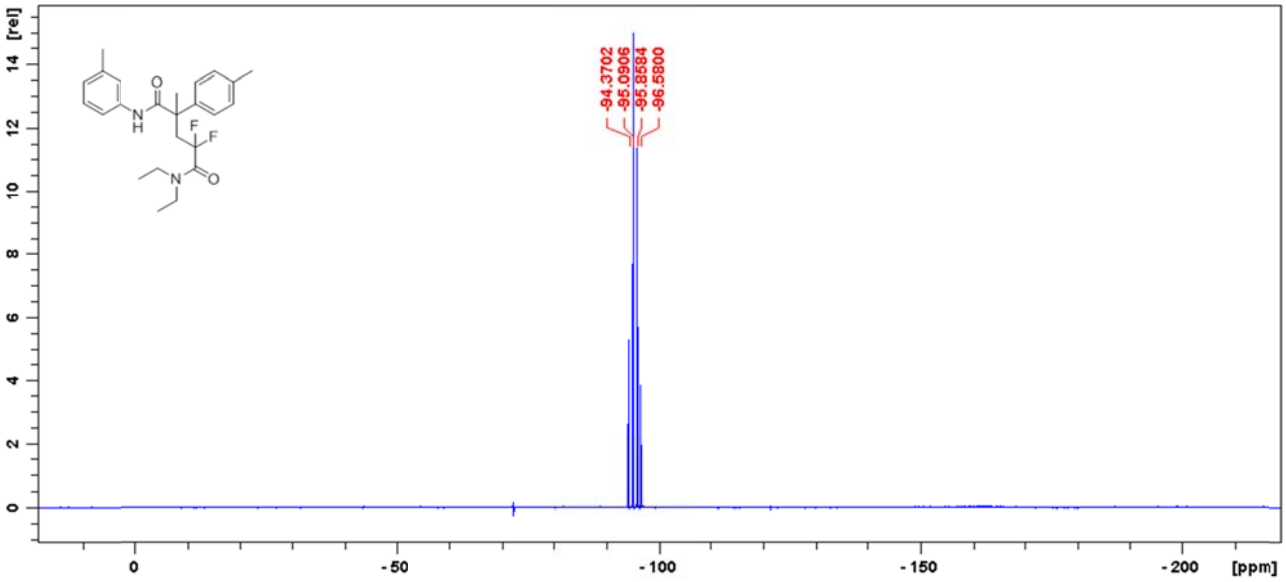
^{1}H NMR of N^{1},N^{1}-diethyl-2,2-difluoro-4-methyl-N^{5}-(*m*-tolyl)-4-(*p*-tolyl) pentanediamide (3i)



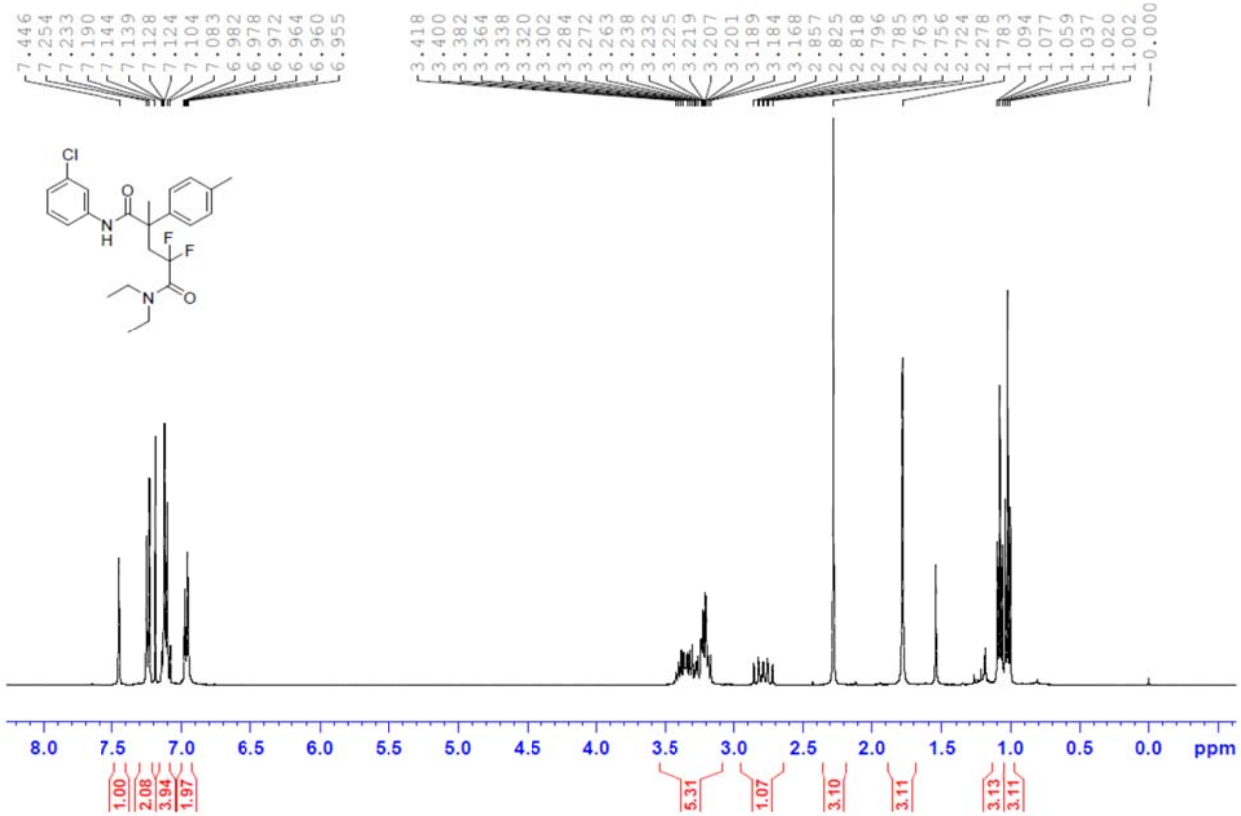
^{13}C NMR of N^{1},N^{1}-diethyl-2,2-difluoro-4-methyl-N^{5}-(*m*-tolyl)-4-(*p*-tolyl) pentanediamide (3i)



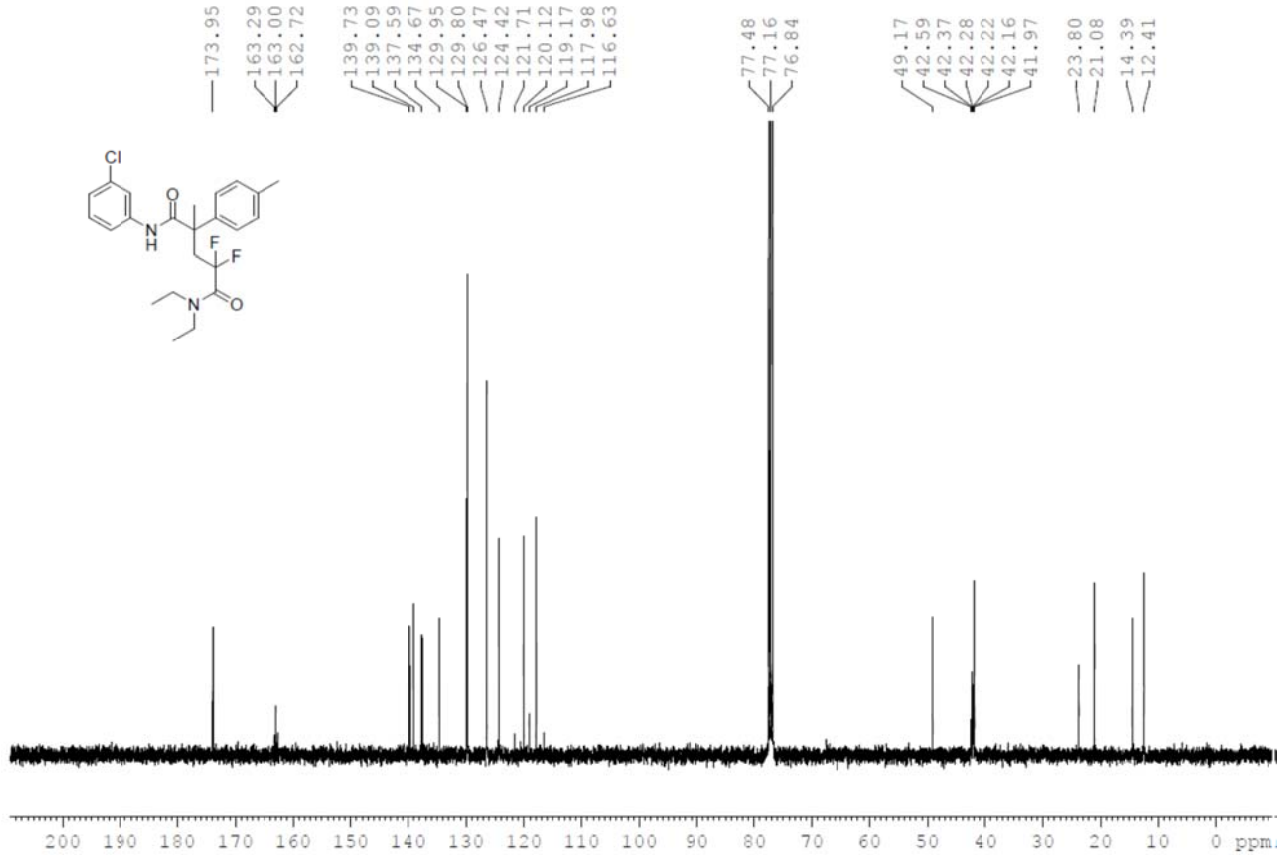
^{19}F NMR of N^1,N^1-diethyl-2,2-difluoro-4-methyl-N^5-(*m*-tolyl)-4-(*p*-tolyl) pentanediamide (3i)



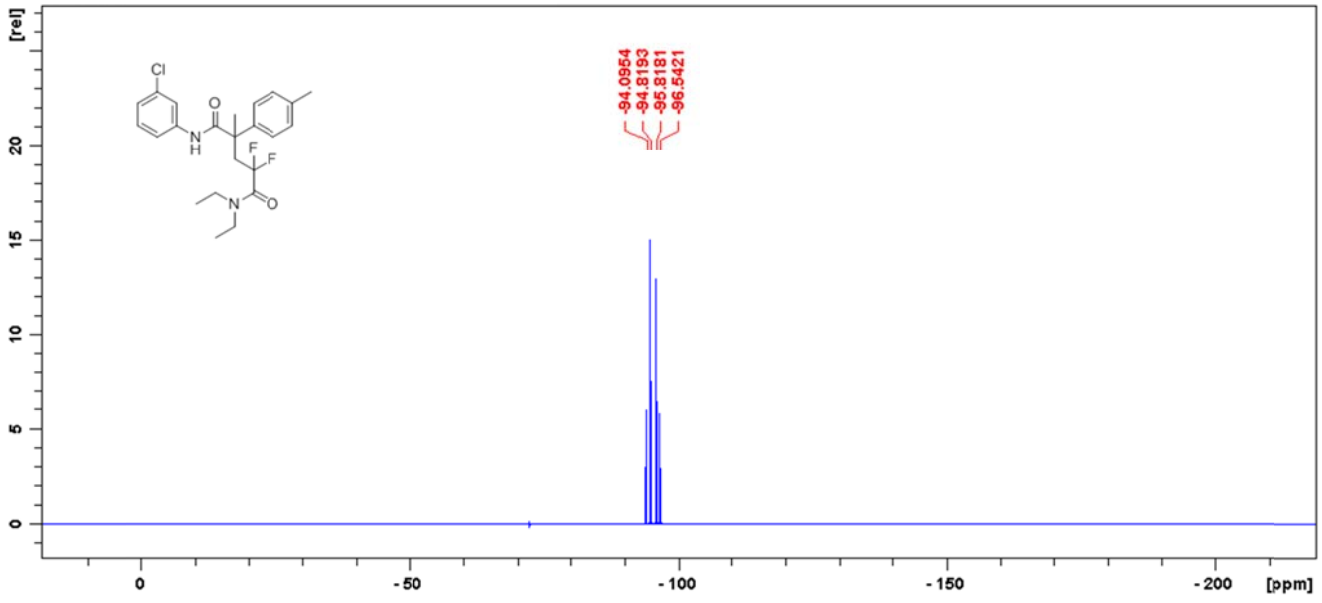
^{1}H NMR of N^1-(3-chlorophenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl) pentanediamide (3)



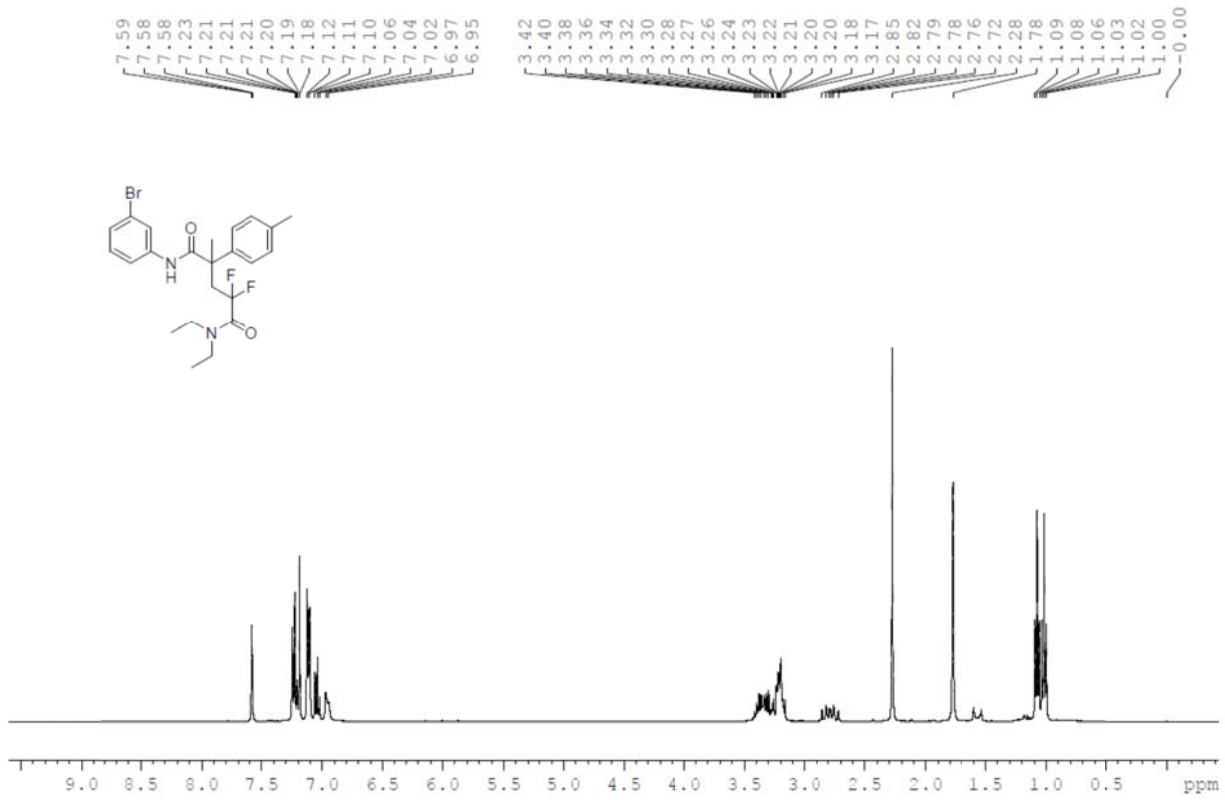
^{13}C NMR of N^1-(3-chlorophenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl) pentanediamide (3)



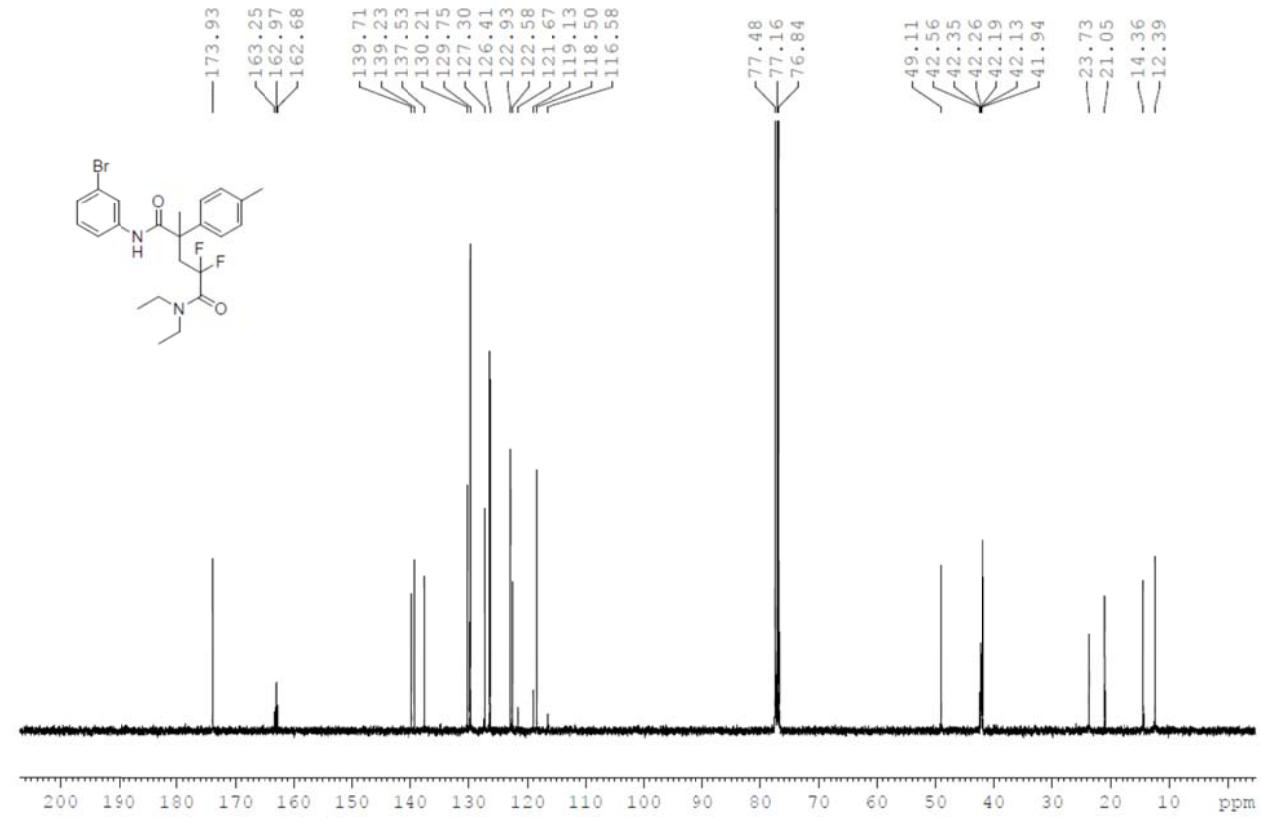
^{19}F NMR of N^1-(3-chlorophenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl) pentanediamide (3)



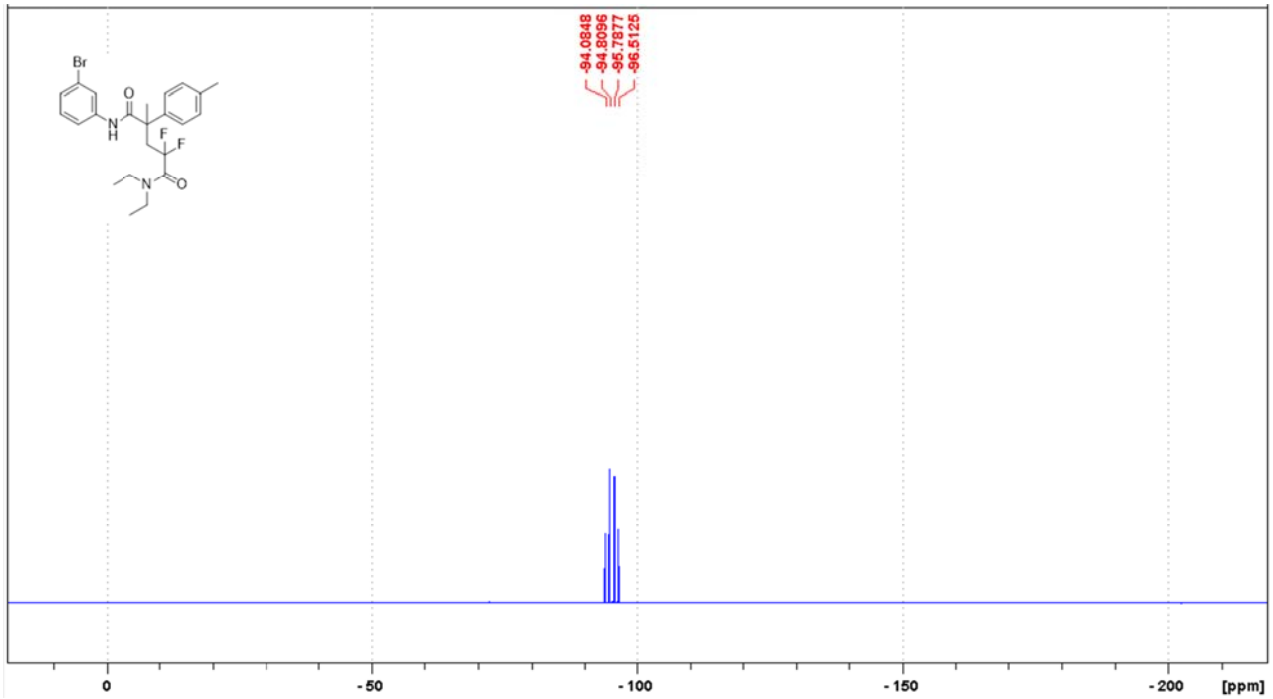
^{1}H NMR of N^{1}-(3-bromophenyl)-N^{5},N^{5}-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl) pentanediamide (3j)



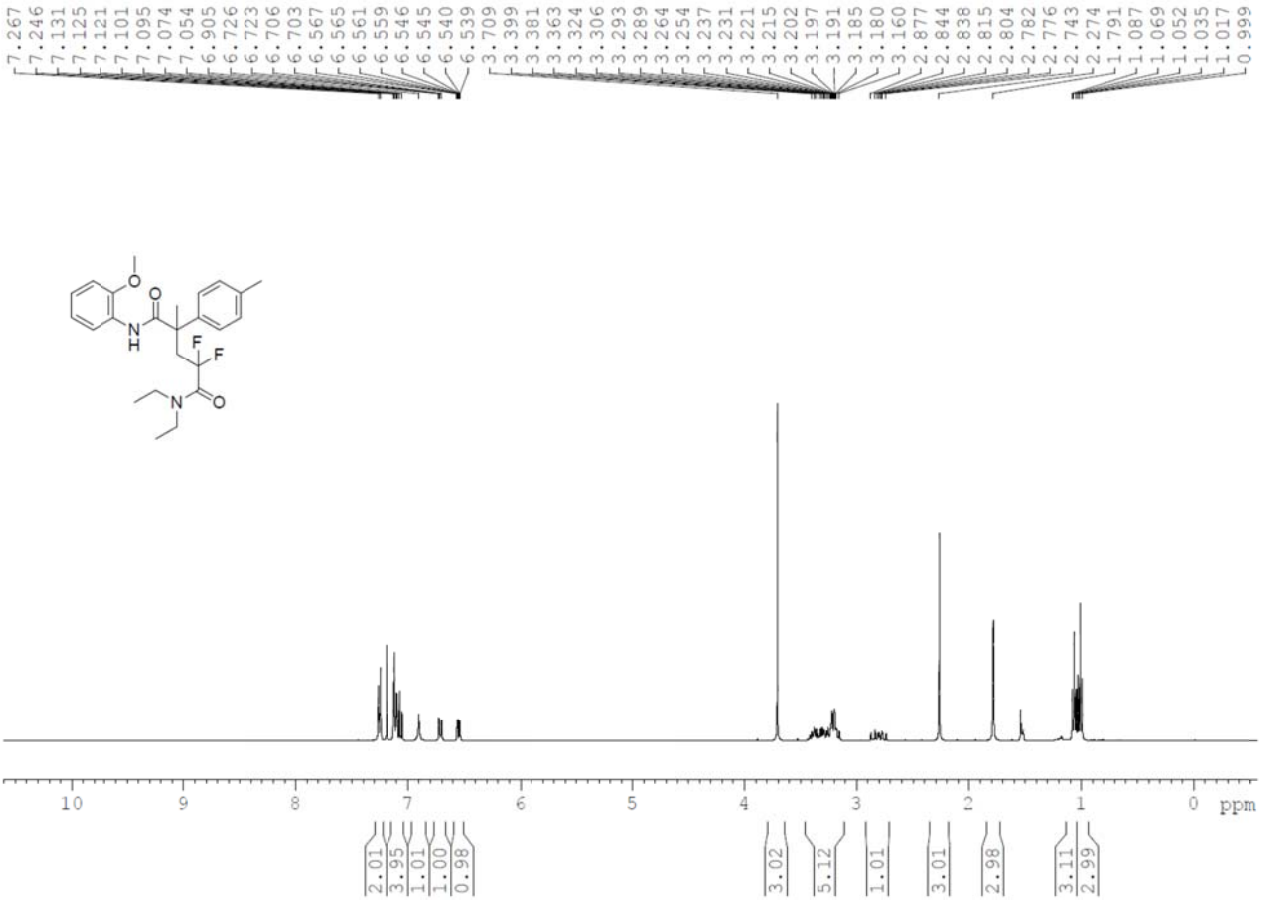
^{13}C NMR of N^{1}-(3-bromophenyl)-N^{5},N^{5}-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl) pentanediamide (3j)



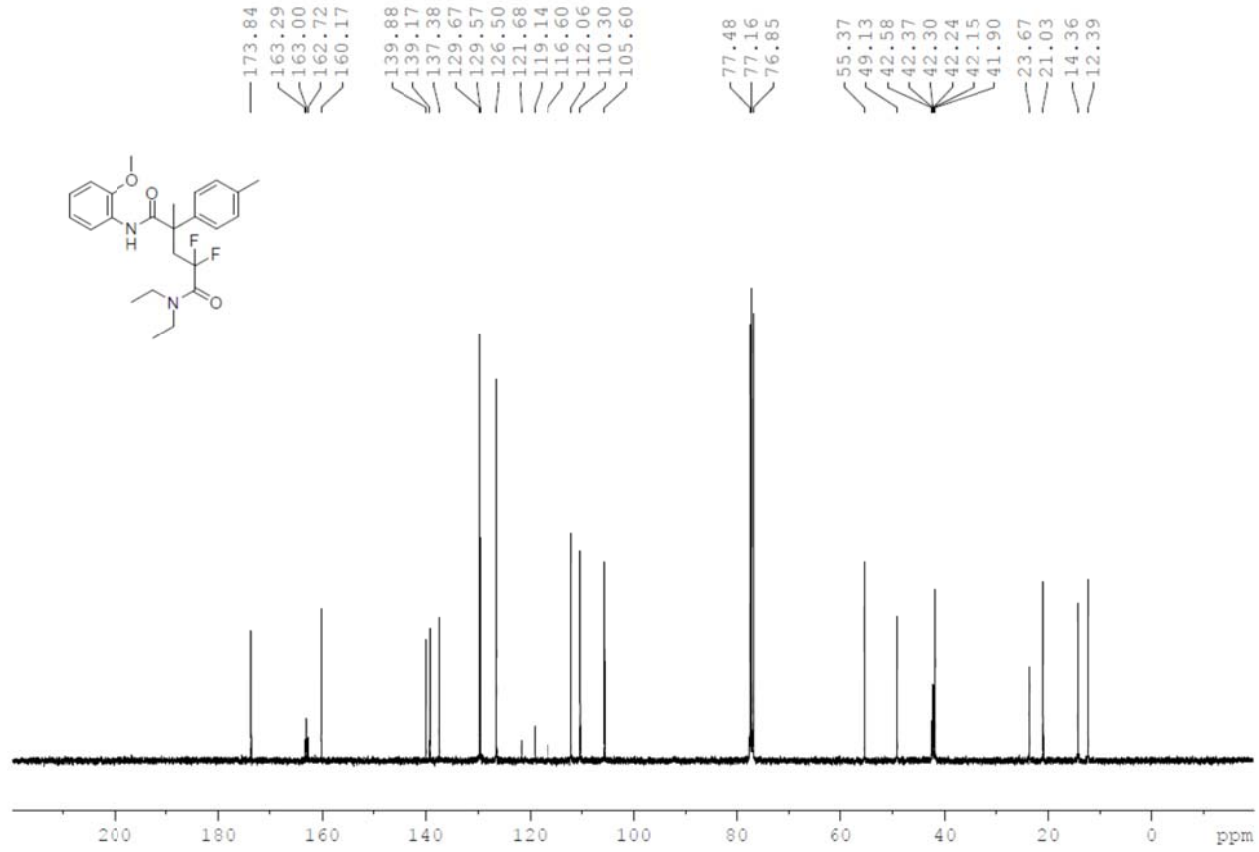
^{19}F NMR of N^1-(3-bromophenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl) pentanediamide (3j)



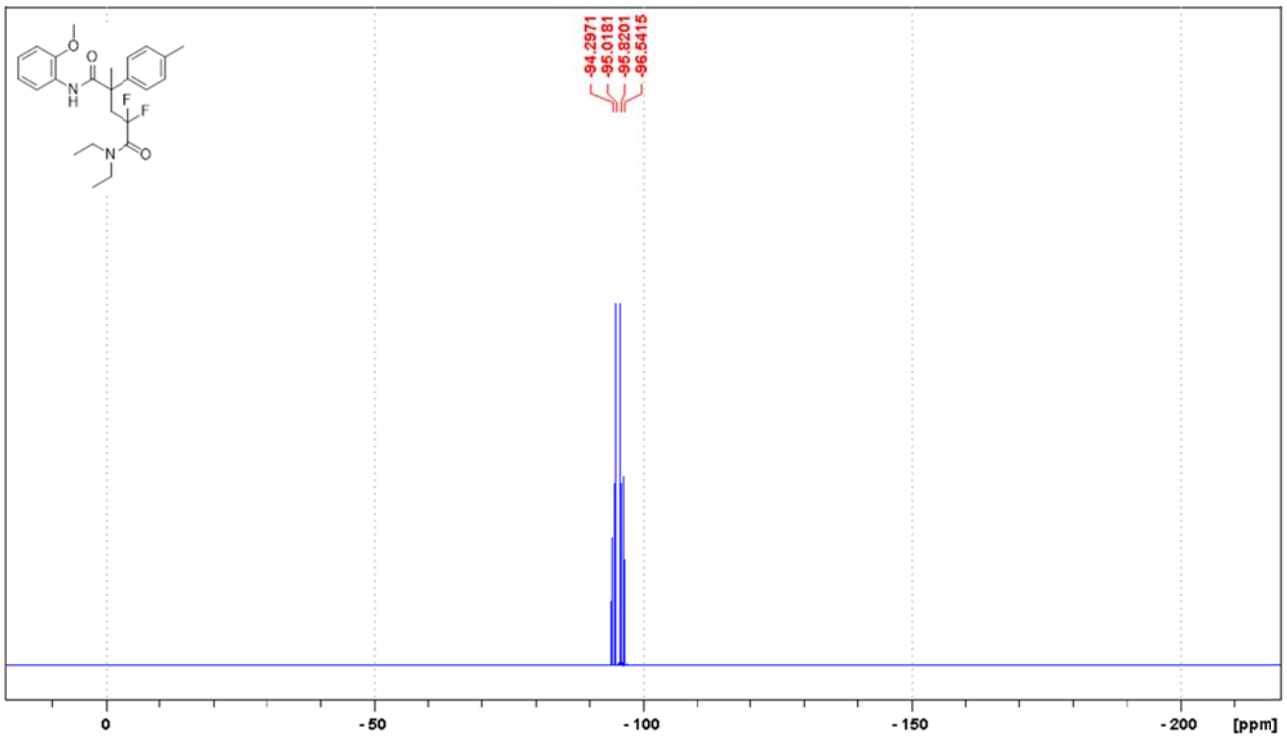
^{1}H NMR of N^1,N^1-diethyl-2,2-difluoro-N^5-(2-methoxyphenyl)-4-methyl-4-(*p*-tolyl) pentanediamide (3k)



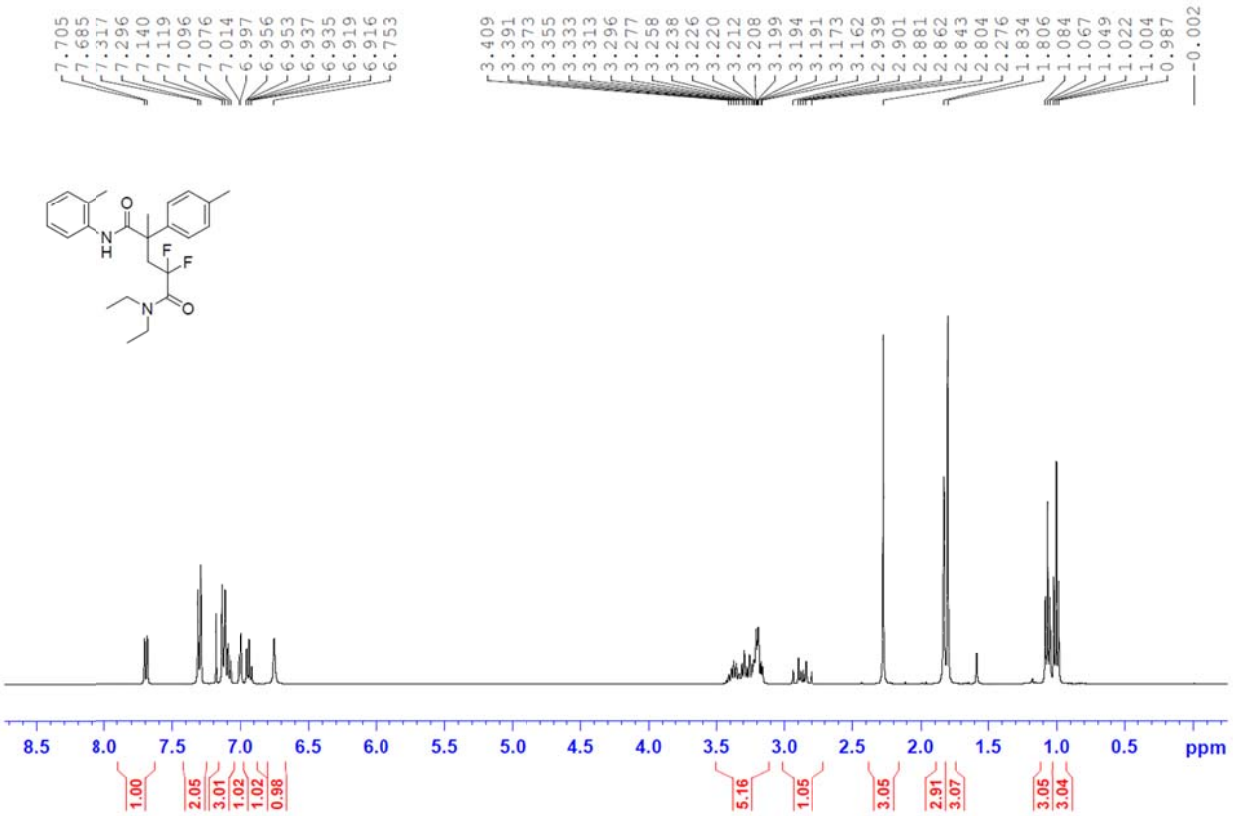
^{13}C NMR of N^1,N^1-diethyl-2,2-difluoro-N^5-(2-methoxyphenyl)-4-methyl-4-(*p*-tolyl) pentanediamide (3k)



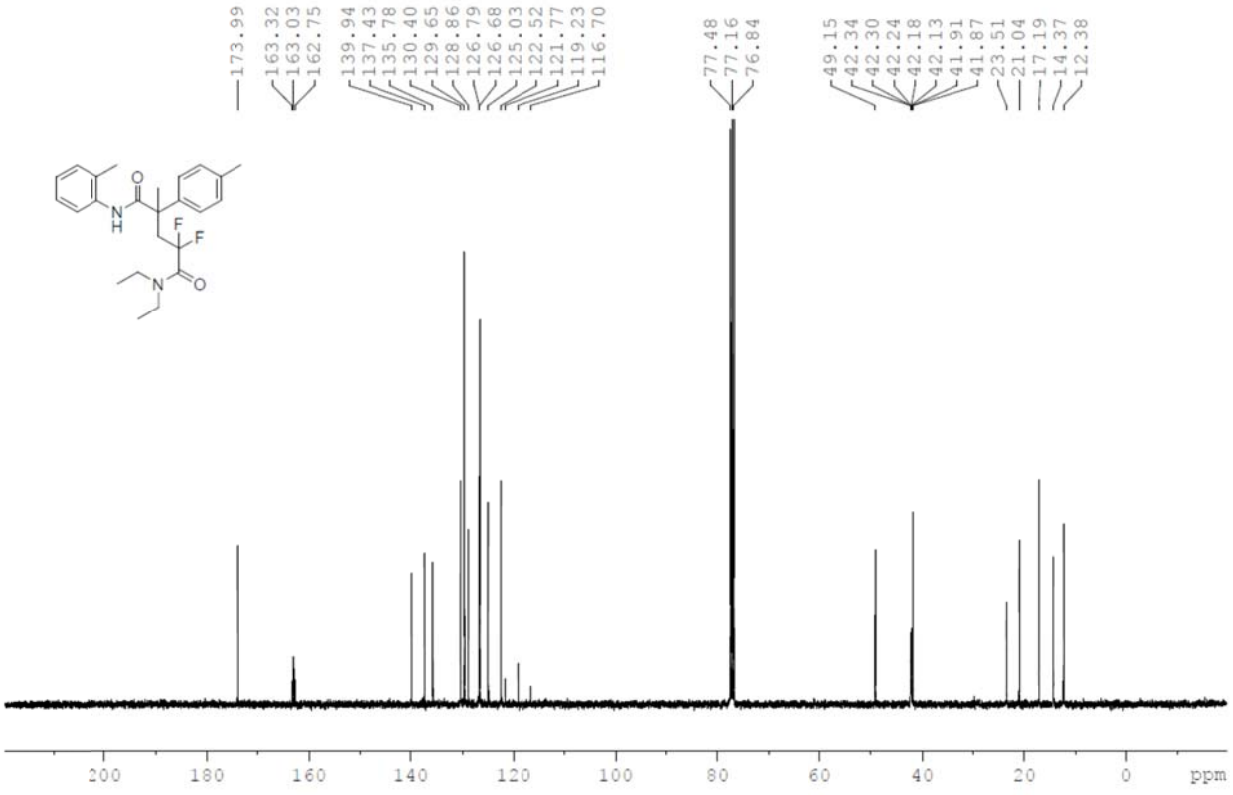
^{19}F NMR of N^1,N^1-diethyl-2,2-difluoro-N^5-(2-methoxyphenyl)-4-methyl-4-(*p*-tolyl) pentanediamide (3k)



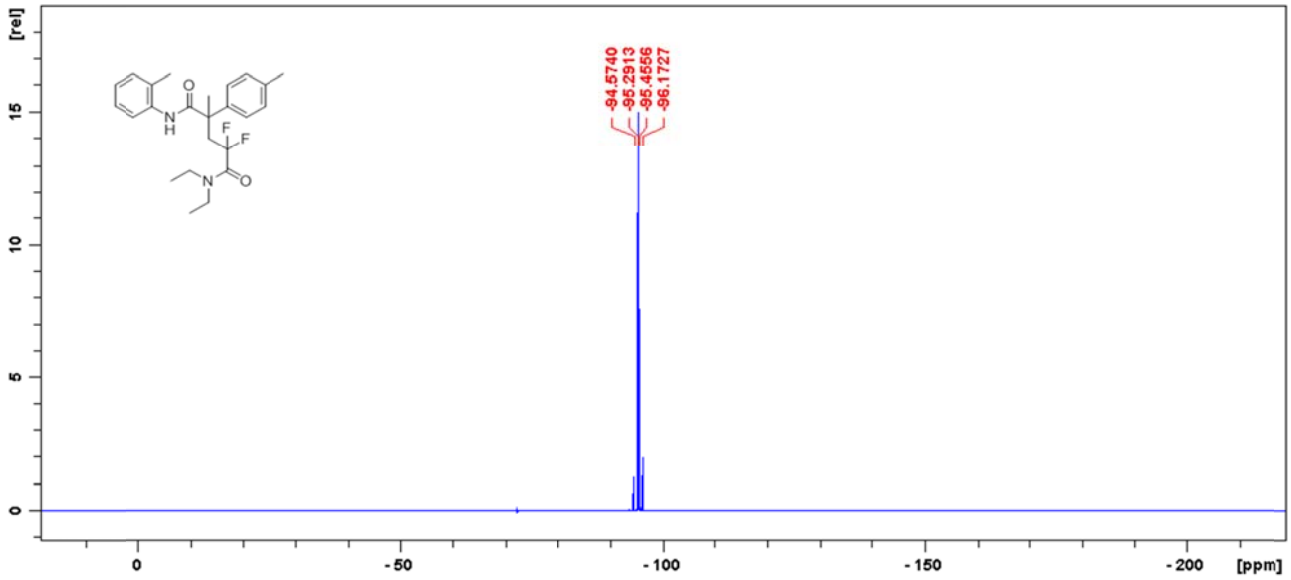
^{1}H NMR of N^{1},N^{1}-diethyl-2,2-difluoro-4-methyl-N^{5}-(*o*-tolyl)-4-(*p*-tolyl) pentanediamide (3l)



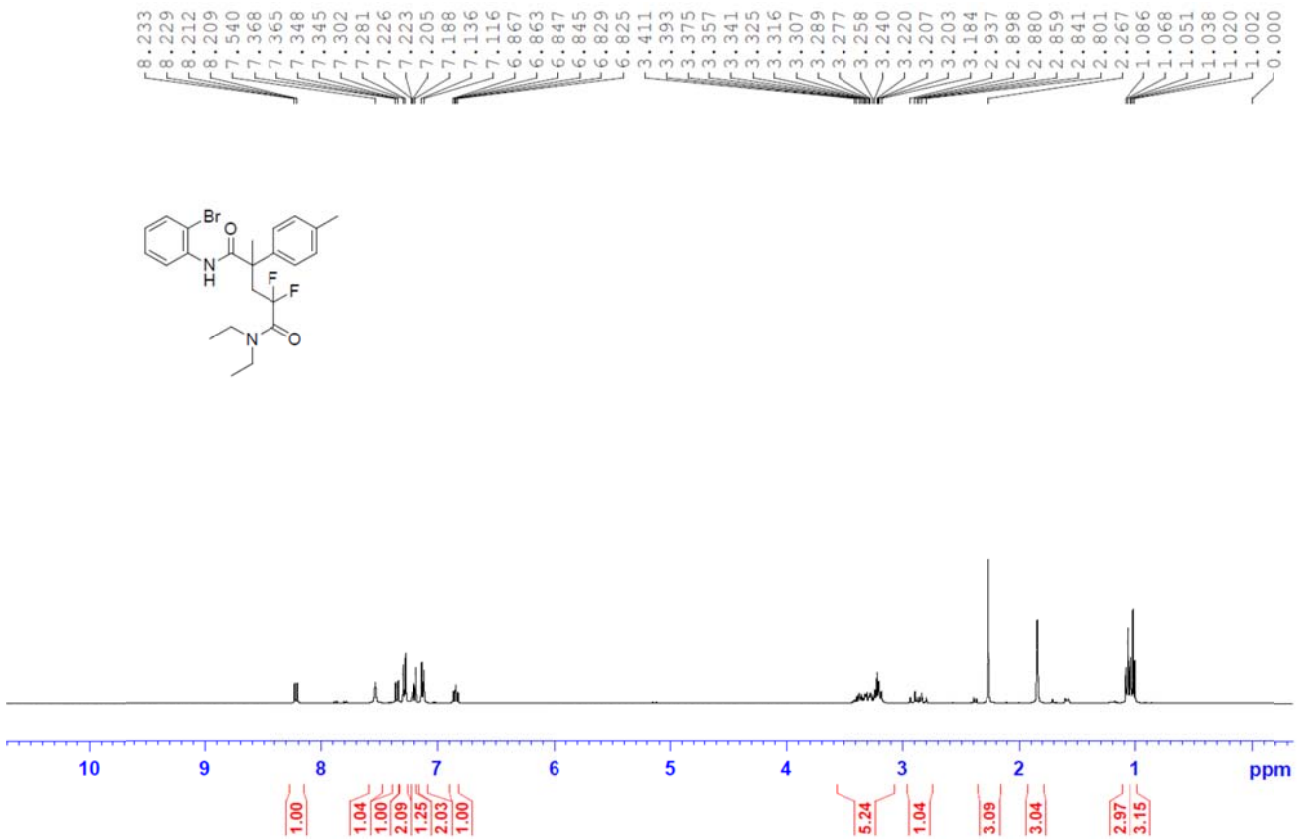
^{13}C NMR of N^{1},N^{1}-diethyl-2,2-difluoro-4-methyl-N^{5}-(*o*-tolyl)-4-(*p*-tolyl) pentanediamide (3l)



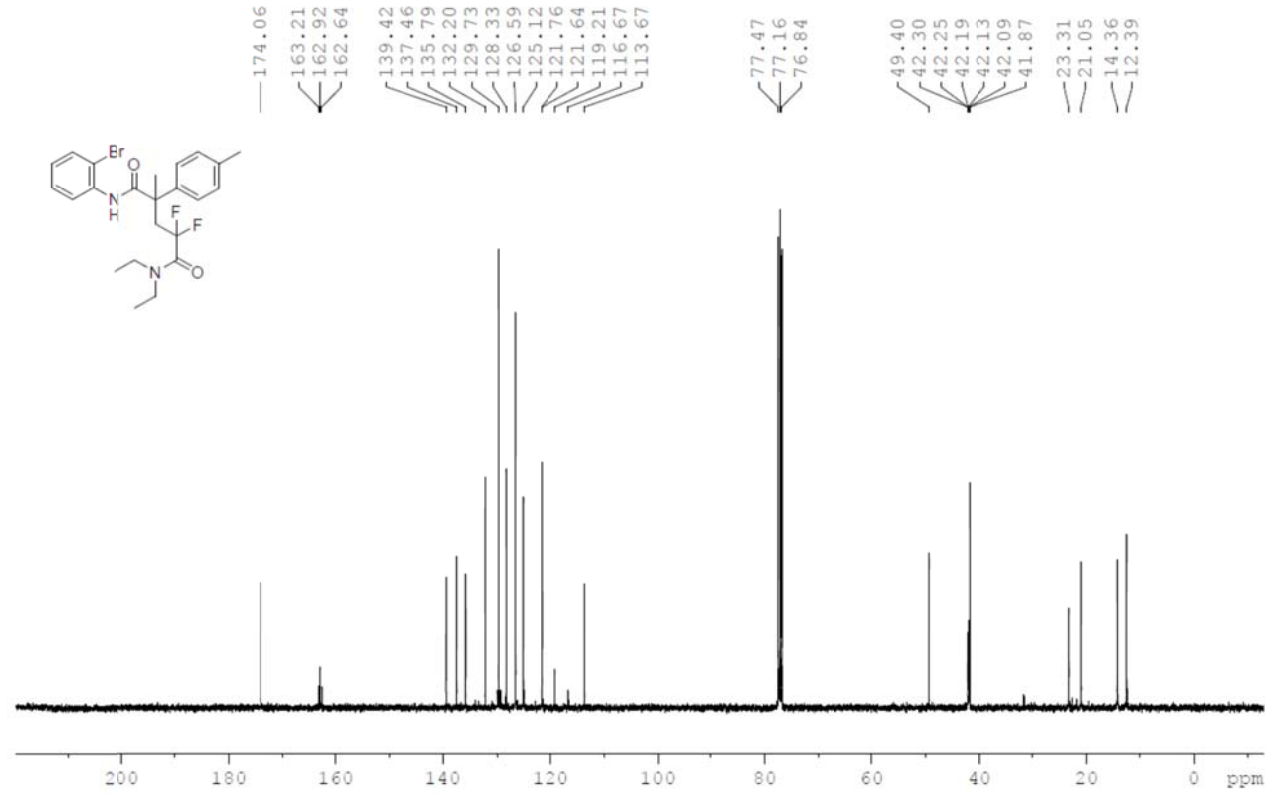
^{19}F NMR of N^1,N^1-diethyl-2,2-difluoro-4-methyl-N^5-(*o*-tolyl)-4-(*p*-tolyl) pentanediamide (3l)



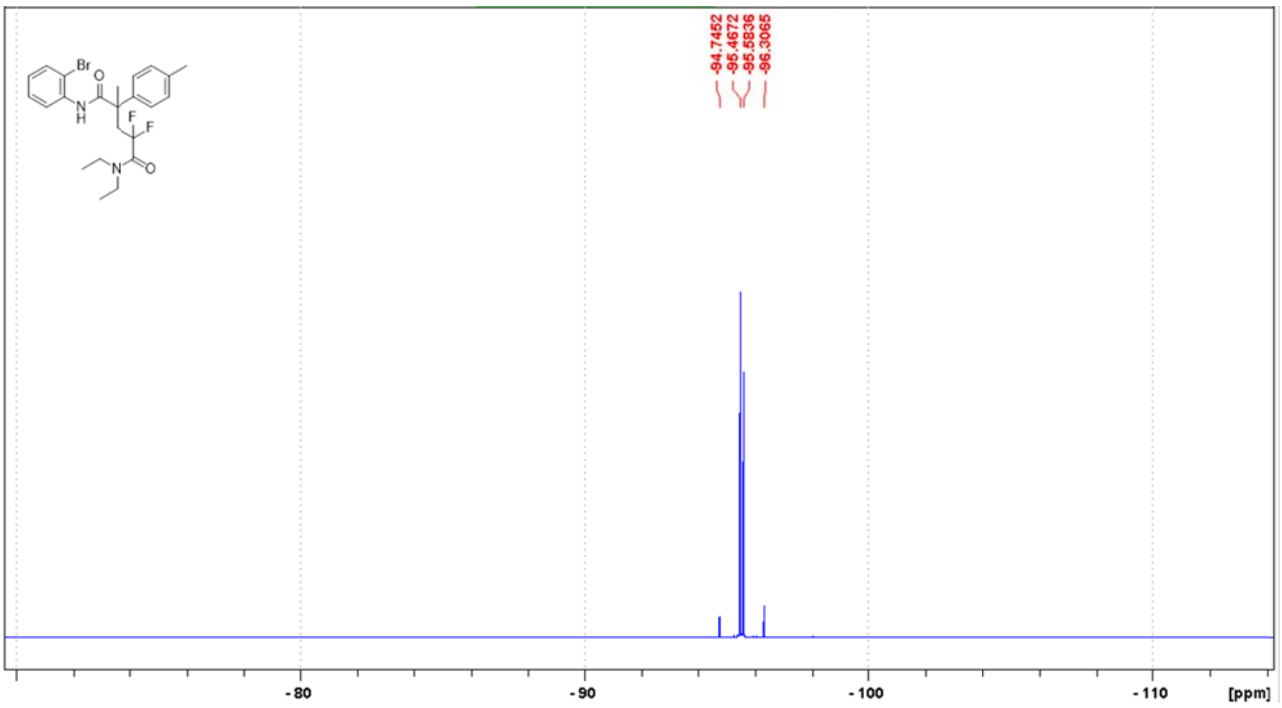
^{1}H NMR of N^1-(2-bromophenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl) pentanediamide (3m)



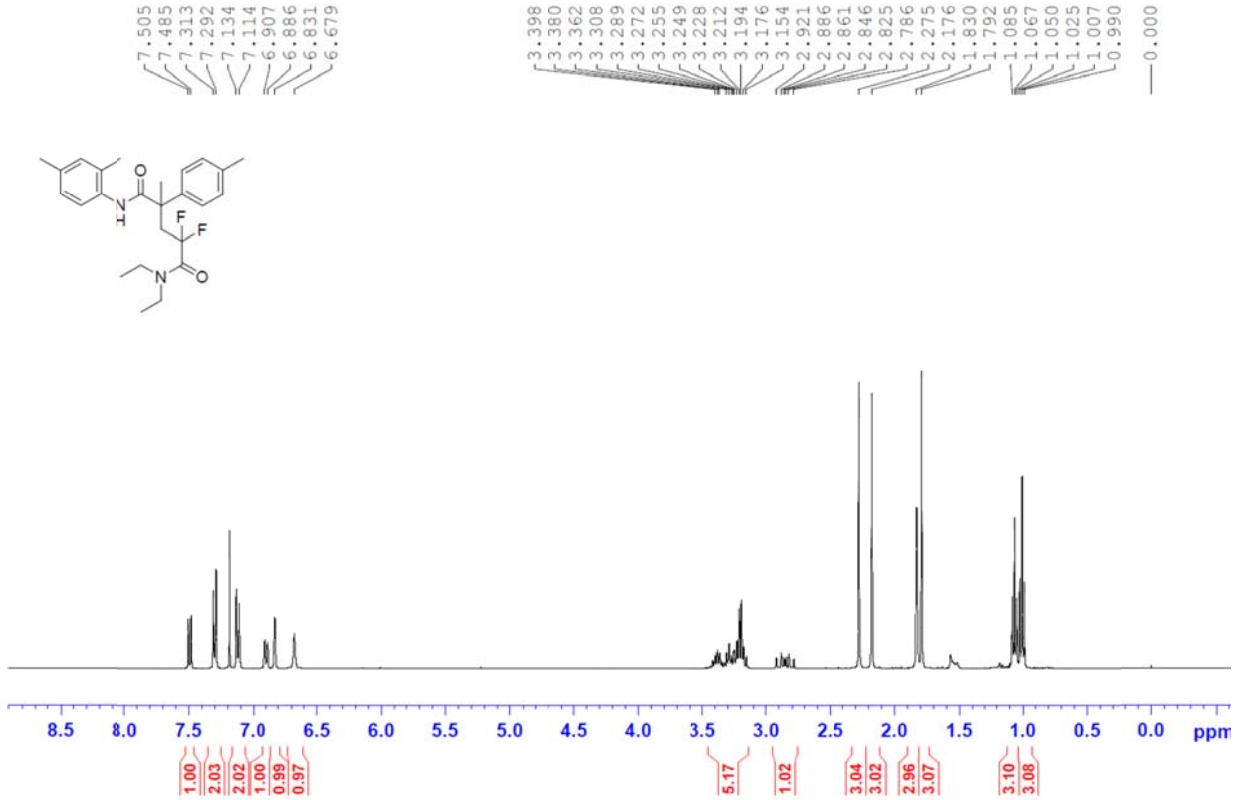
^{13}C NMR of N^1-(2-bromophenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl) pentanediamide (3m)



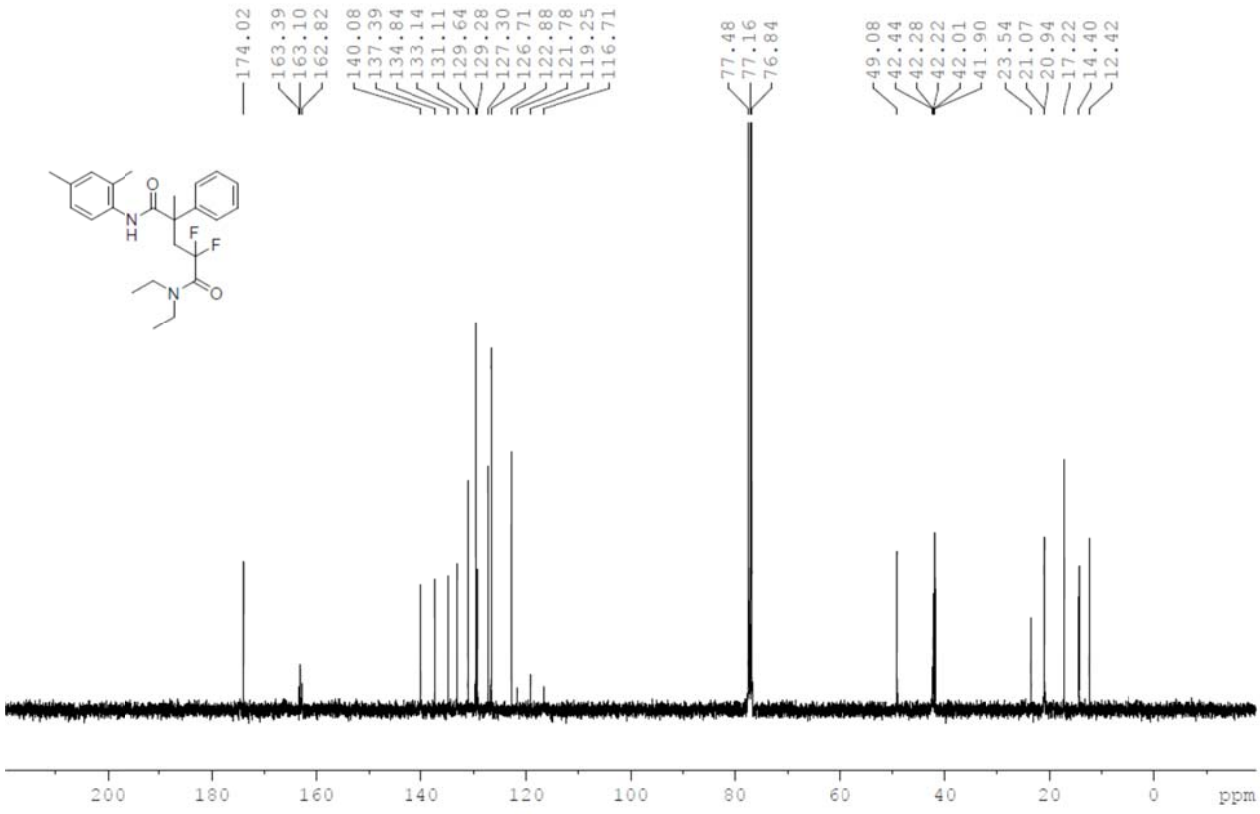
^{19}F NMR of N^1-(2-bromophenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl) pentanediamide (3m)



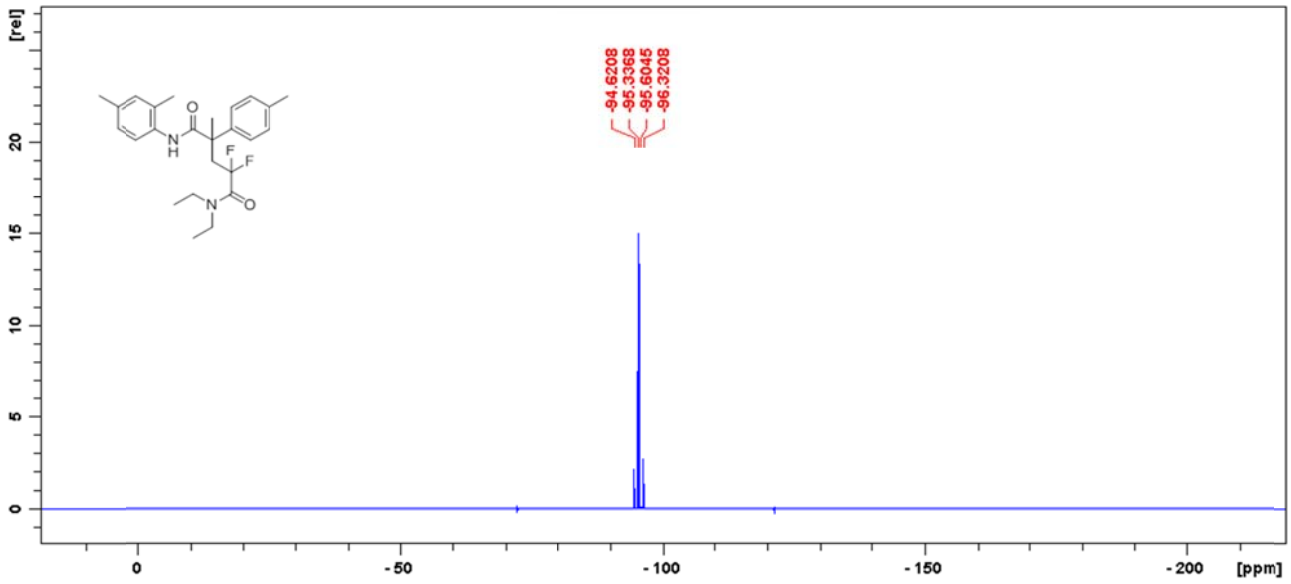
^{1}H NMR of N^{1}-(2,4-dimethylphenyl)-N^{5},N^{5}-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl) pentanediamide (3o)



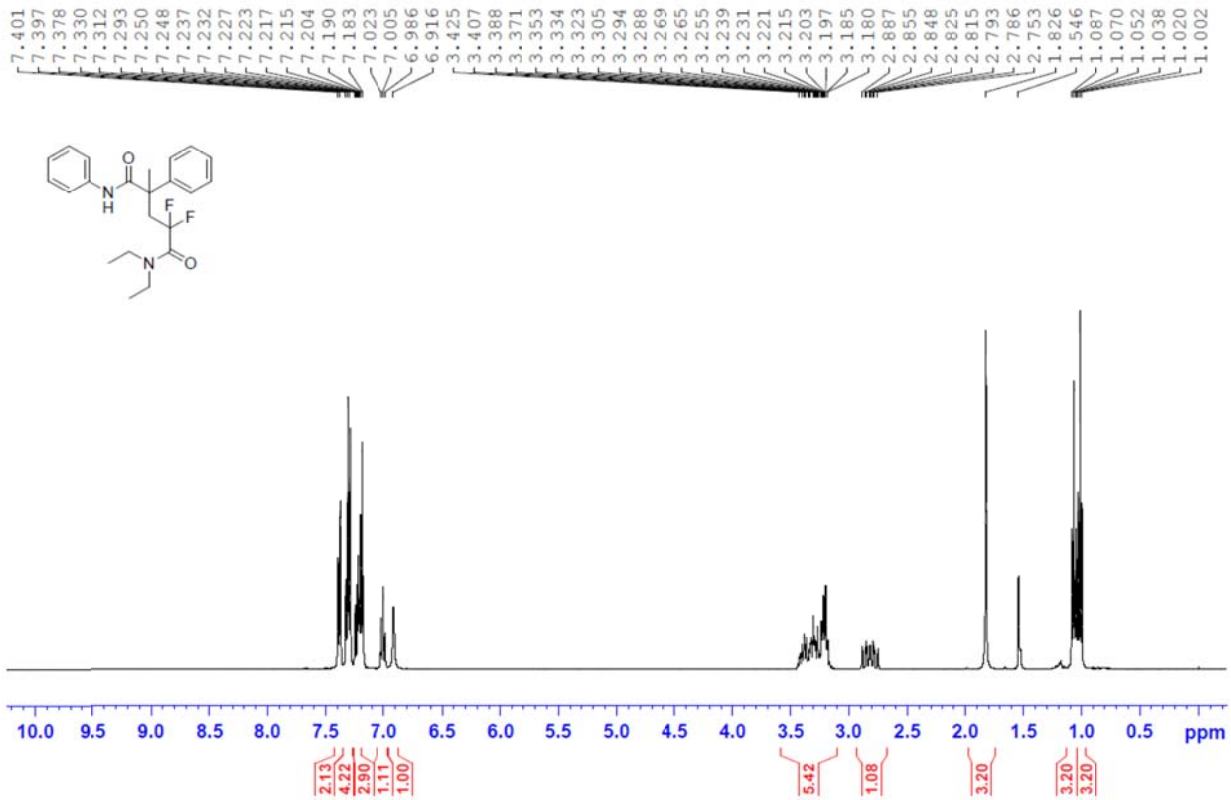
^{13}C NMR of N^{1}-(2,4-dimethylphenyl)-N^{5},N^{5}-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl) pentanediamide (3o)



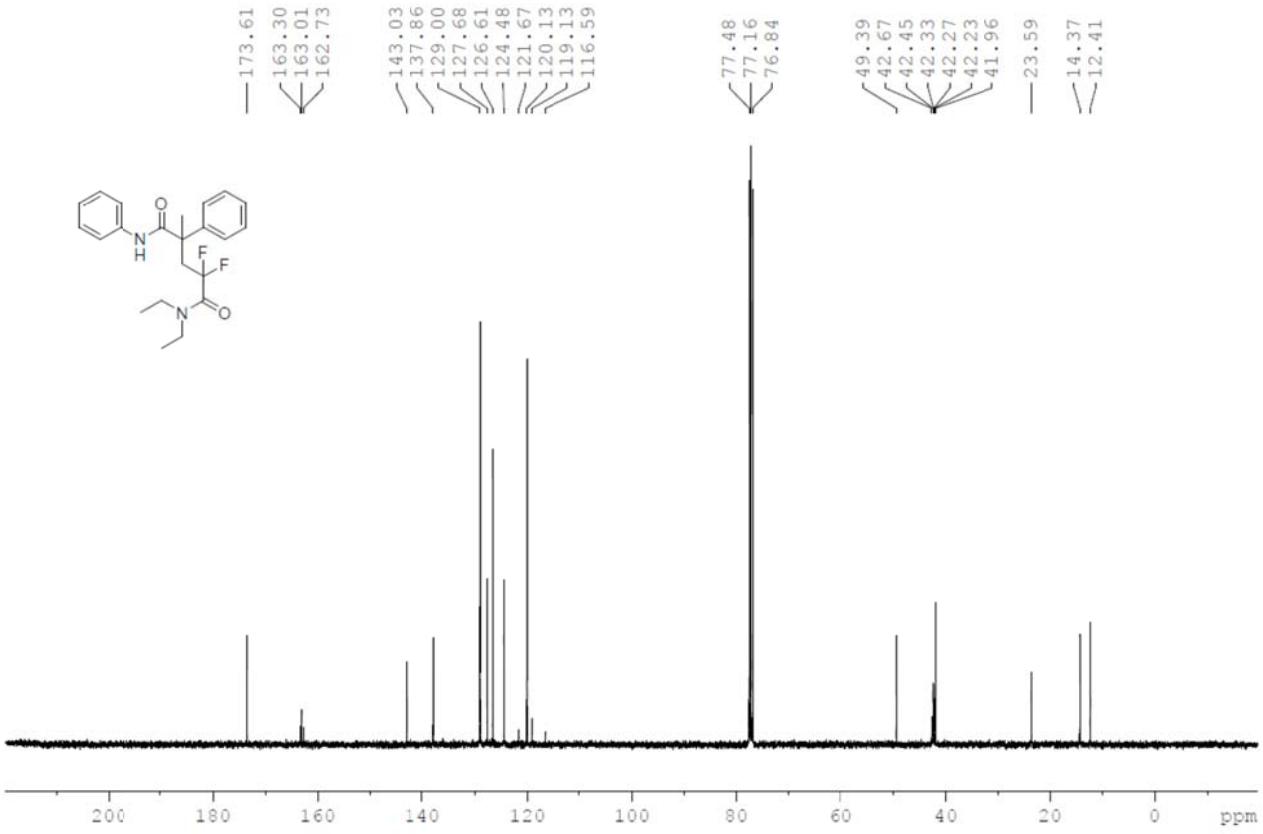
^{19}F NMR of N^1-(2,4-dimethylphenyl)-N^5,N^5-diethyl-4,4-difluoro-2-methyl-2-(*p*-tolyl) pentanediamide (3o)



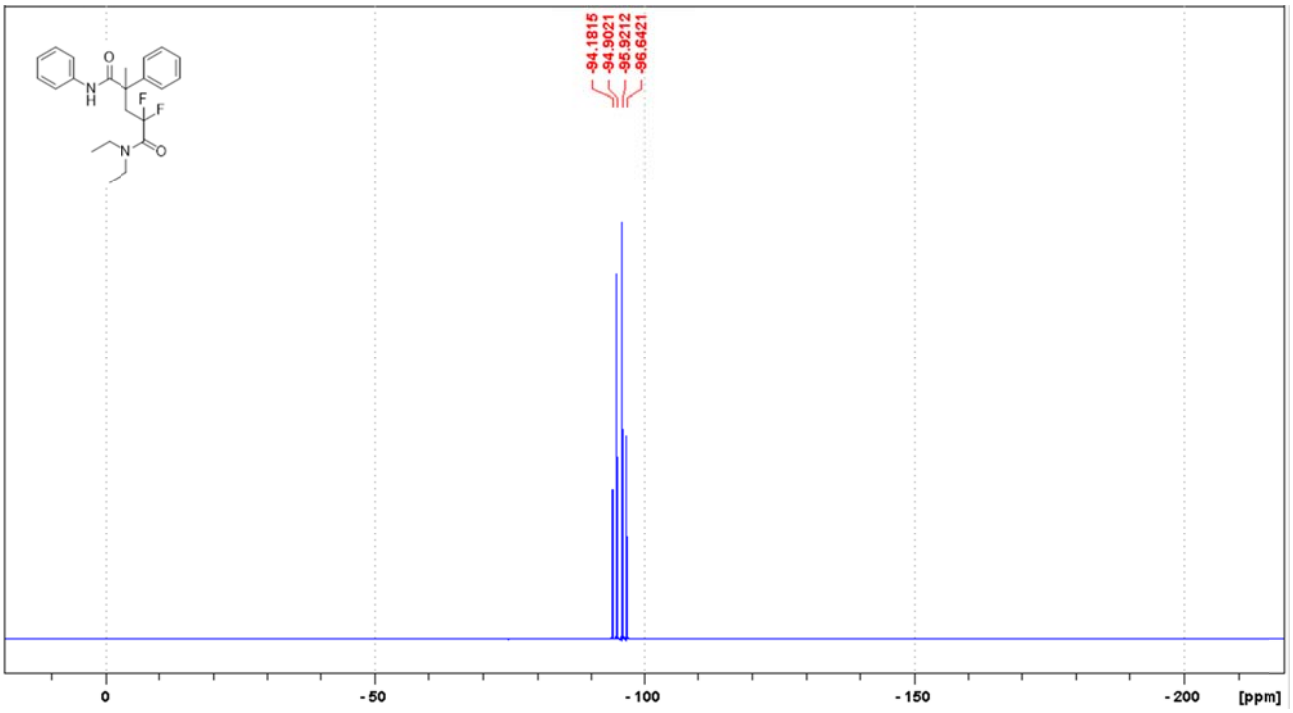
^{1}H NMR of N^1,N^1-diethyl-2,2-difluoro-4-methyl-N^5,4-diphenylpentanediamide (3p)



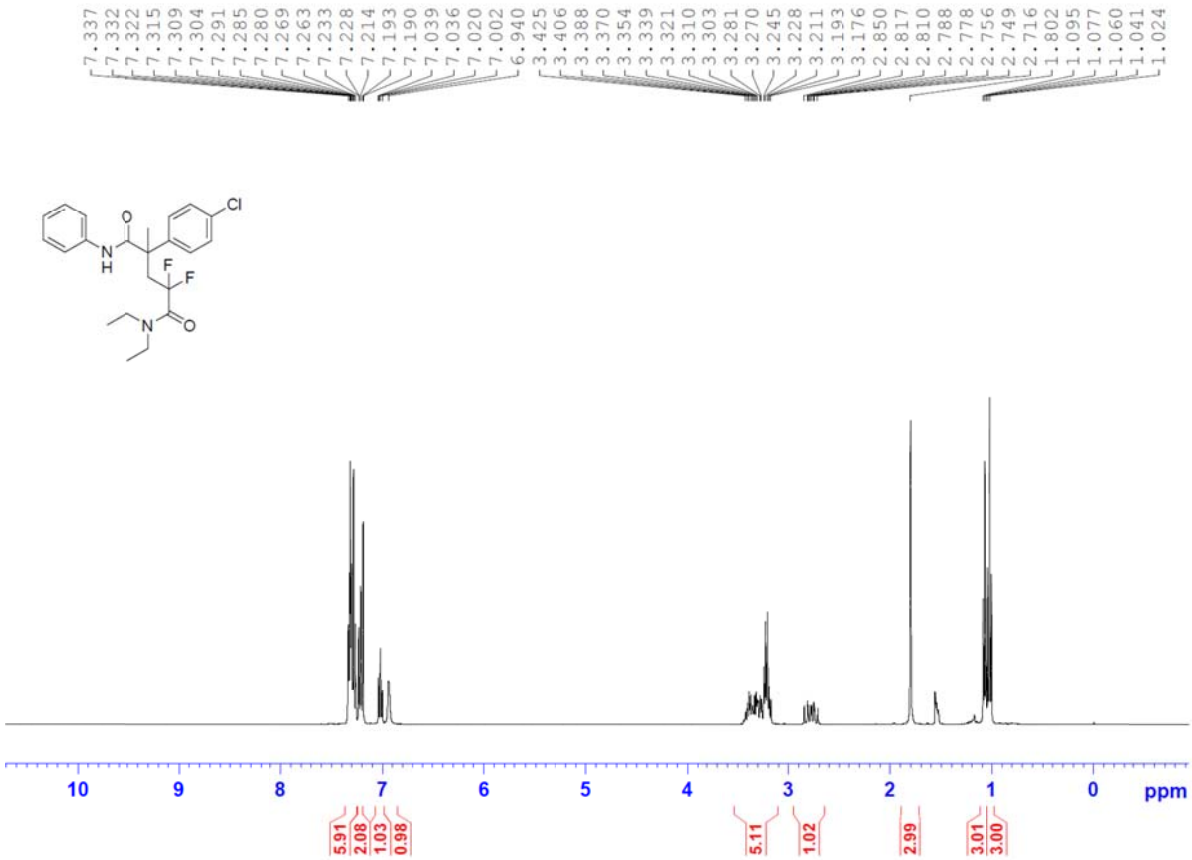
^{13}C NMR of N^1,N^1-diethyl-2,2-difluoro-4-methyl-N^5,4-diphenylpentanediamide (3p)



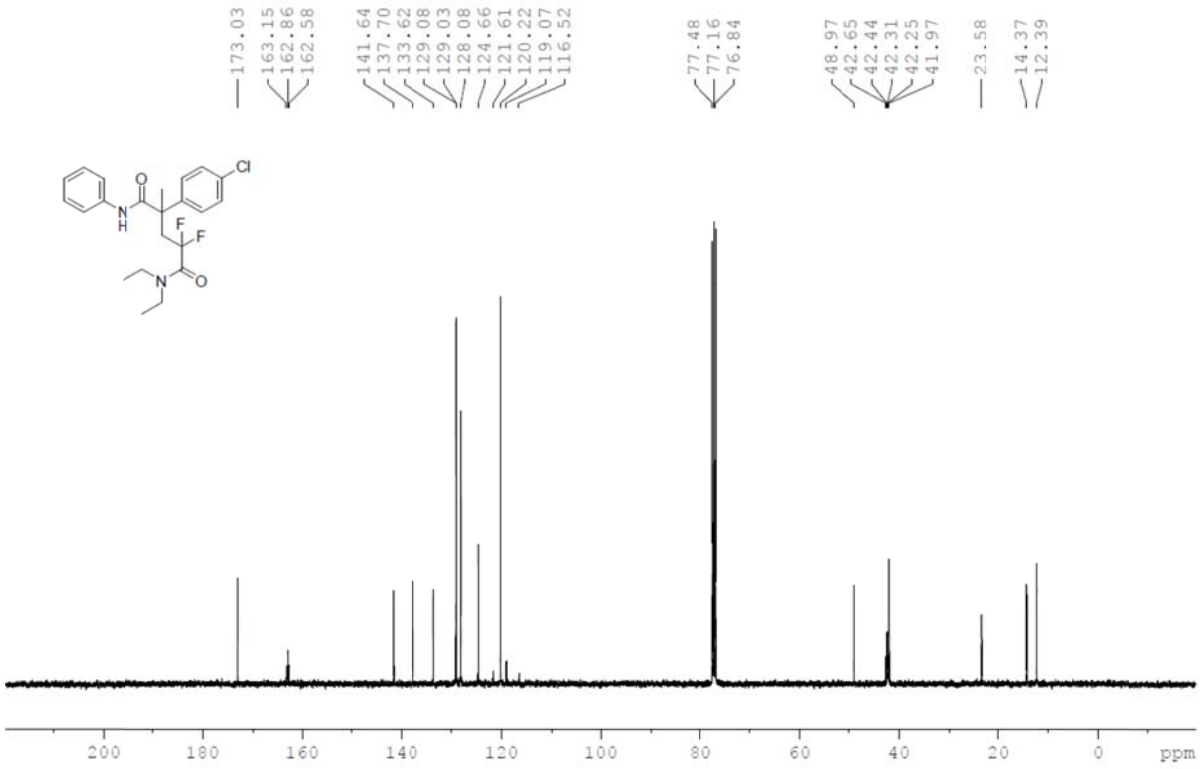
^{19}F NMR of N^1,N^1-diethyl-2,2-difluoro-4-methyl-N^5,4-diphenylpentanediamide (3p)



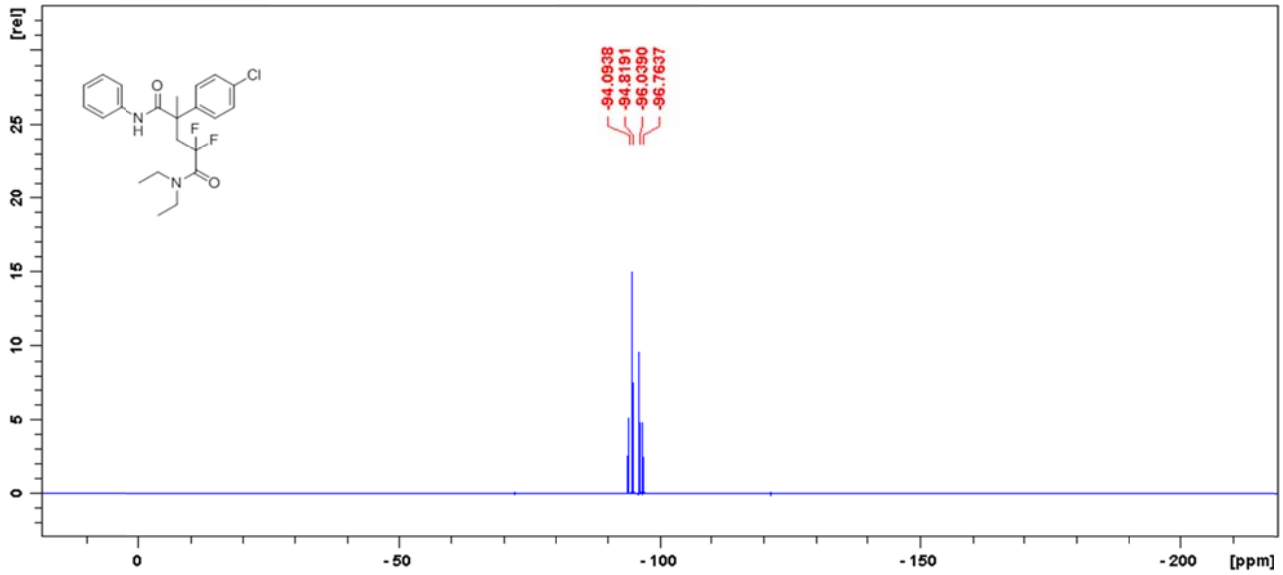
^{1}H NMR of 2-(4-chlorophenyl)-*N*^{5},*N*^{5}-diethyl-4,4-difluoro-2-methyl-*N*^{1}-phenylpentanediamide (3q)



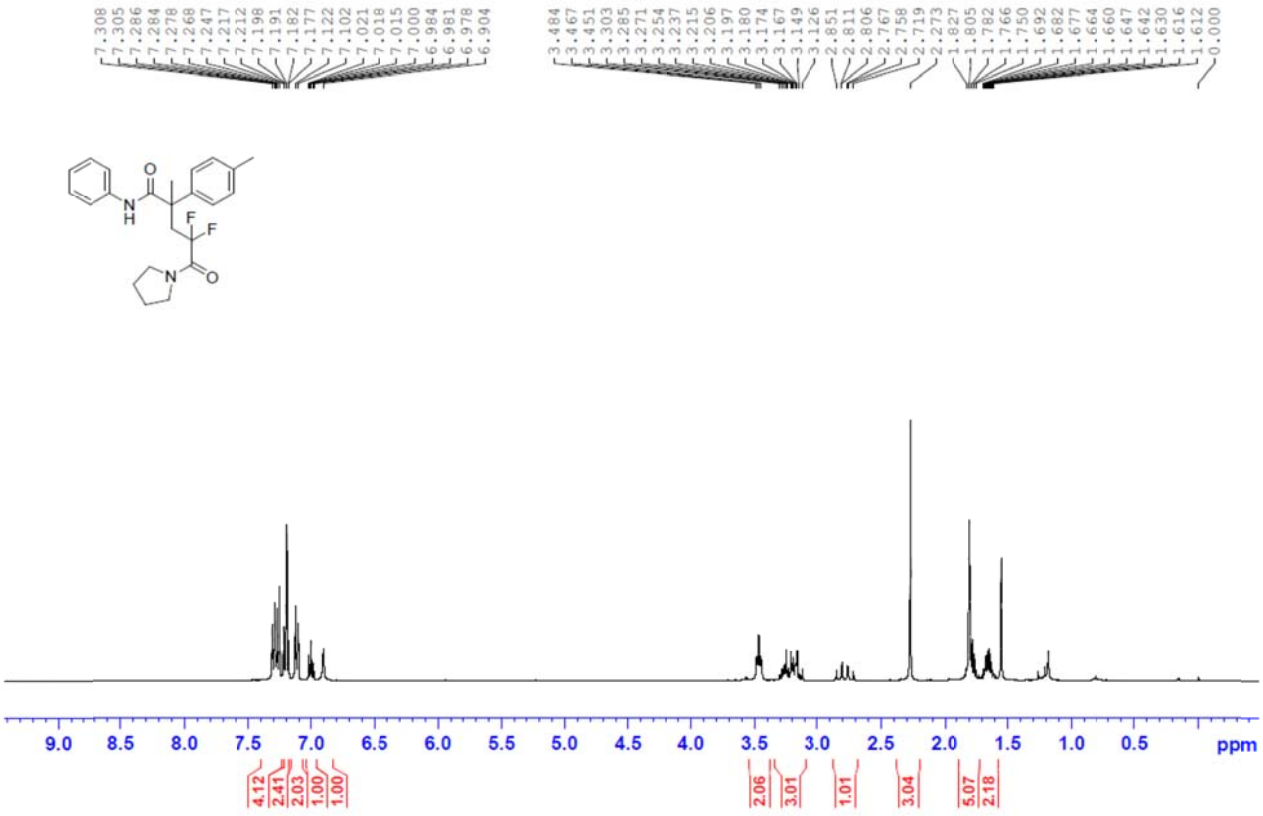
^{13}C NMR of 2-(4-chlorophenyl)-*N*^{5},*N*^{5}-diethyl-4,4-difluoro-2-methyl-*N*^{1}-phenylpentanediamide (3q)



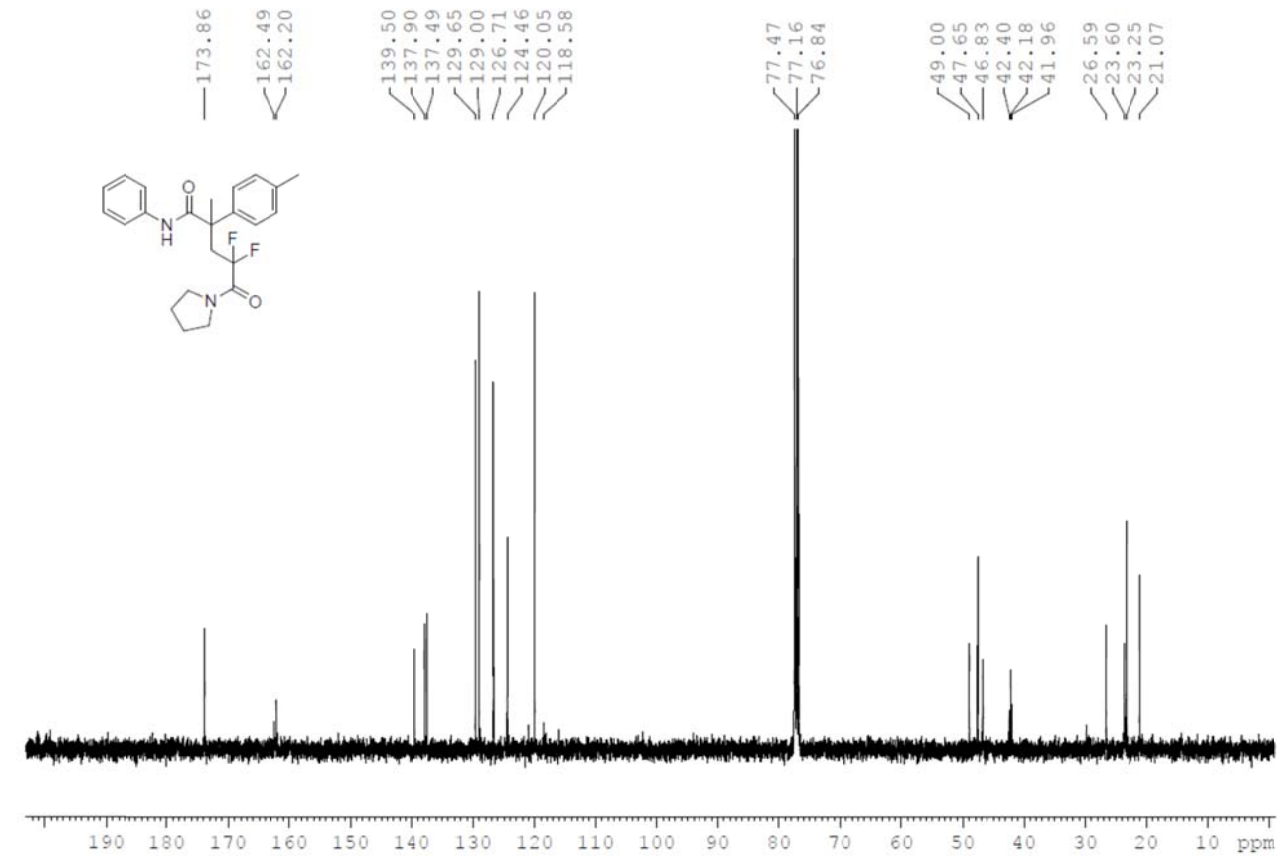
^{19}F NMR of 2-(4-chlorophenyl)-*N*^{5},*N*^{5}-diethyl-4,4-difluoro-2-methyl-*N*^{1}-phenylpentanediamide (3q)



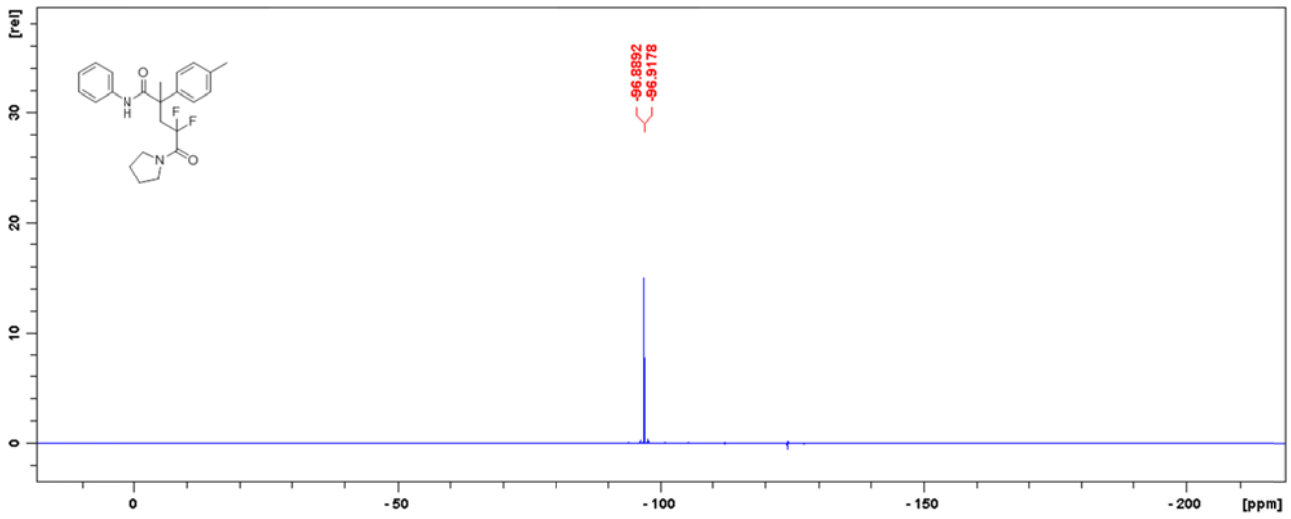
^{1}H NMR of 4,4-difluoro-2-methyl-5-oxo-*N*-phenyl-5-(pyrrolidin-1-yl)-2-(*p*-tolyl) pentanamide (3r)



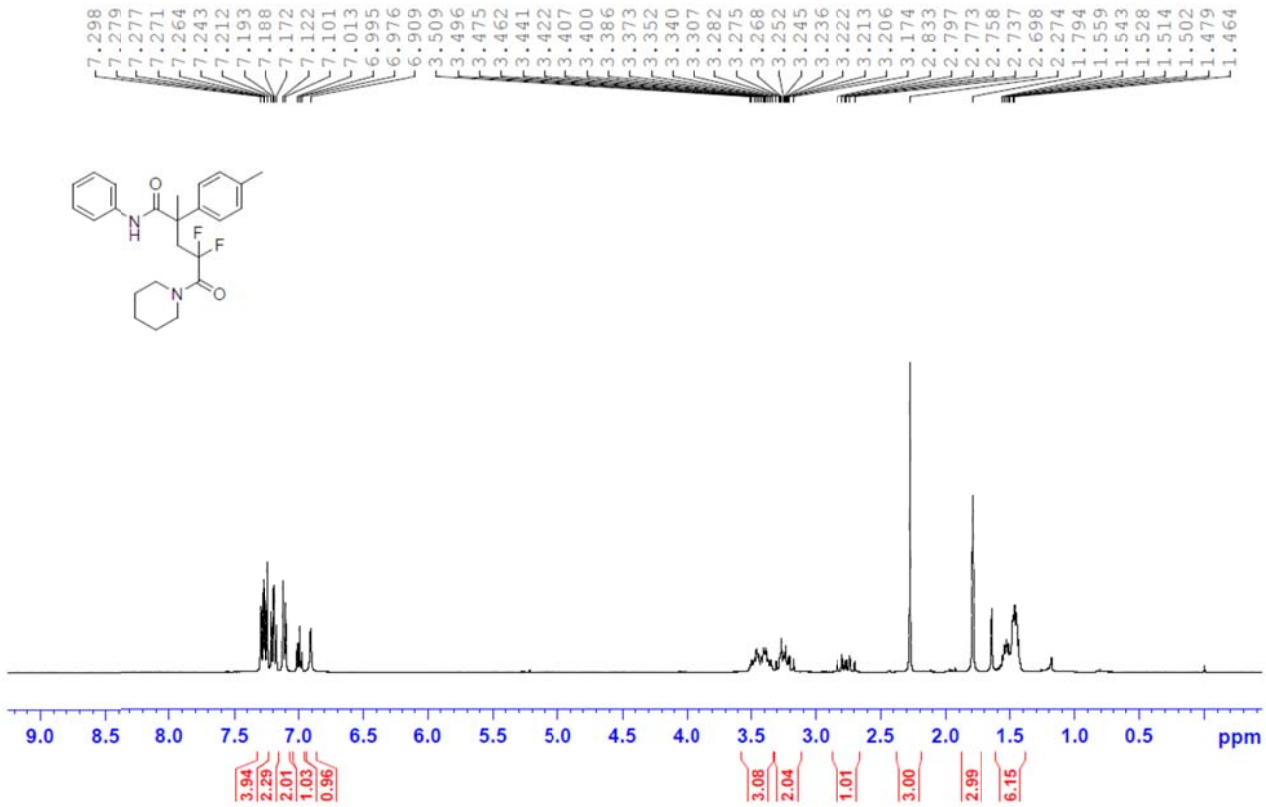
^{13}C NMR of 4,4-difluoro-2-methyl-5-oxo-*N*-phenyl-5-(pyrrolidin-1-yl)-2-(*p*-tolyl) pentanamide (3r)



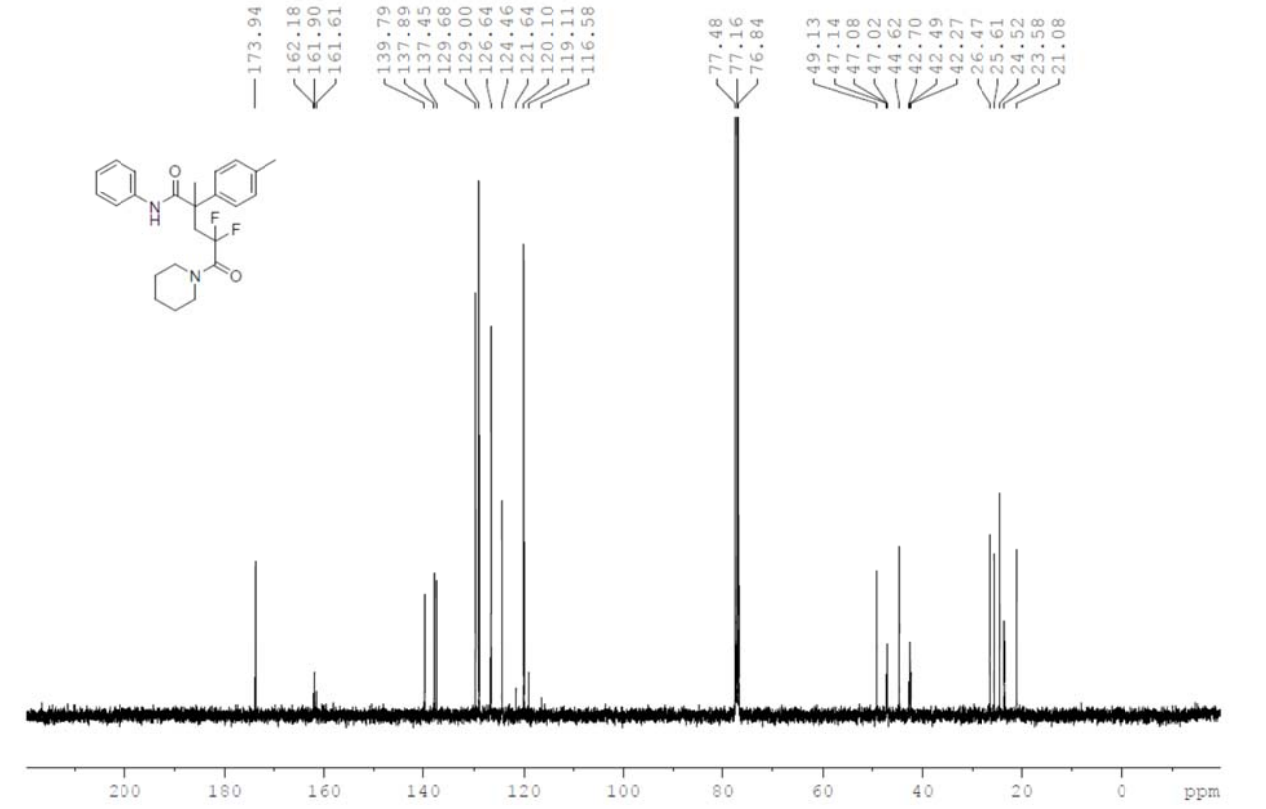
^{19}F NMR of 4,4-difluoro-2-methyl-5-oxo-*N*-phenyl-5-(pyrrolidin-1-yl)-2-(*p*-tolyl) pentanamide (3r)



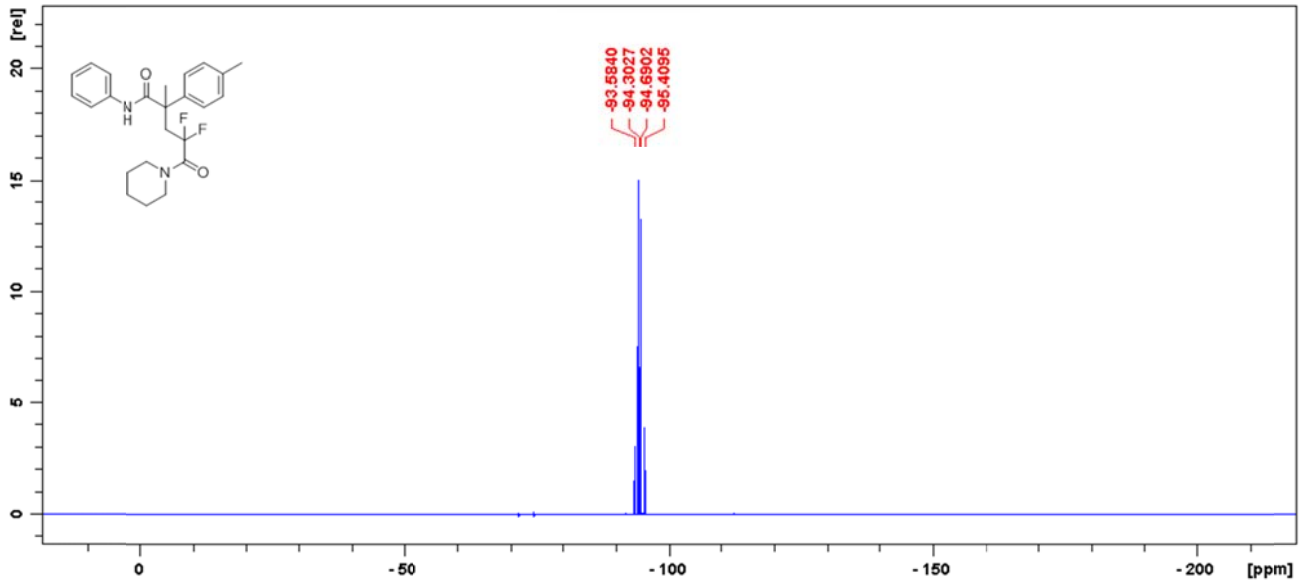
^{1}H NMR of 4,4-difluoro-2-methyl-5-oxo-*N*-phenyl-5-(piperidin-1-yl)-2-(*p*-tolyl) pentanamide (3s)



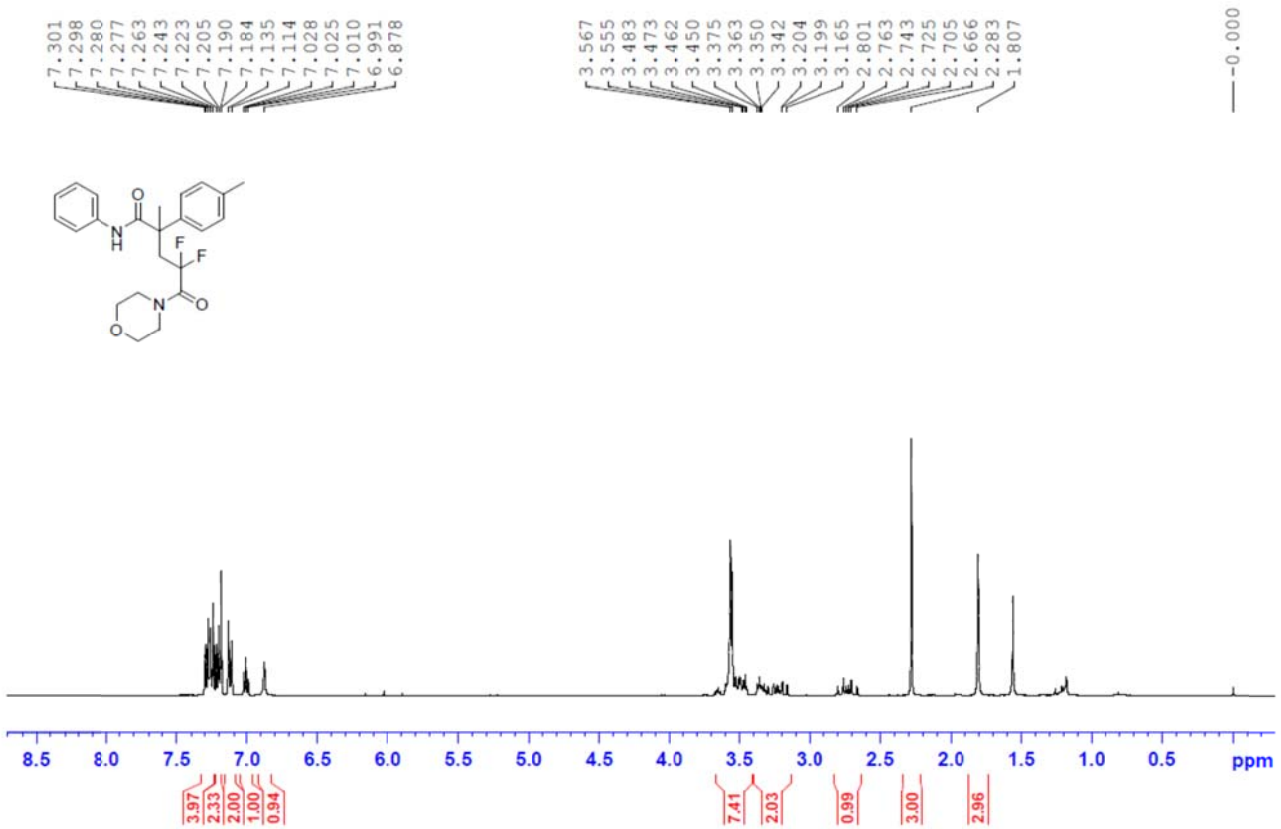
^{13}C NMR of 4,4-difluoro-2-methyl-5-oxo-*N*-phenyl-5-(piperidin-1-yl)-2-(*p*-tolyl) pentanamide (3s)



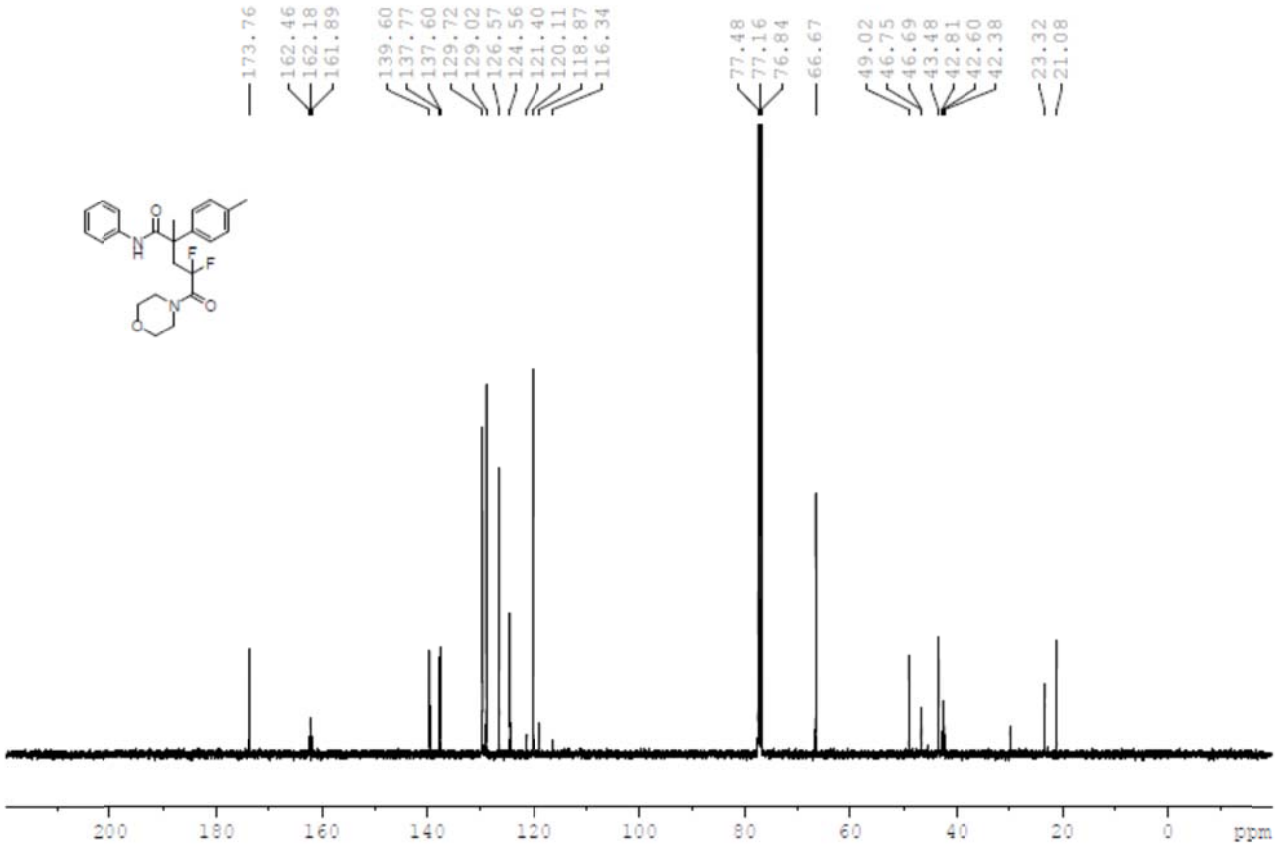
^{19}F NMR of 4,4-difluoro-2-methyl-5-oxo-*N*-phenyl-5-(piperidin-1-yl)-2-(*p*-tolyl) pentanamide (3s)



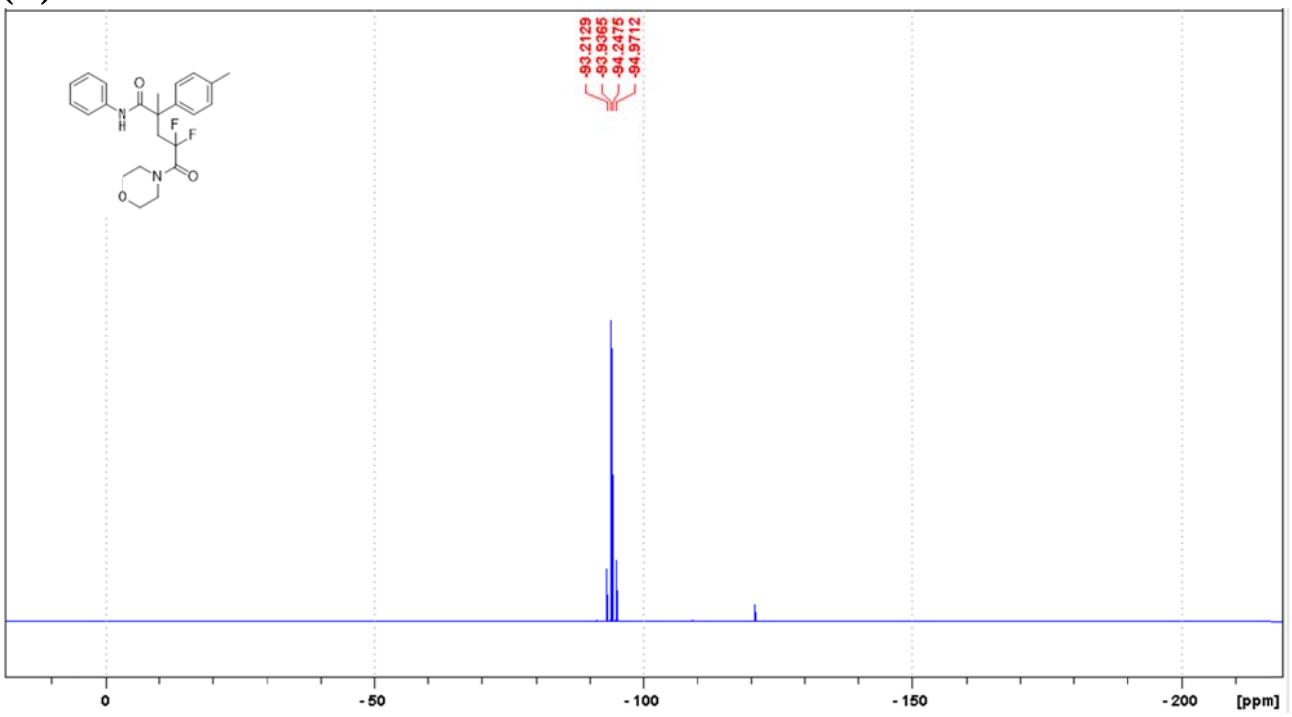
^{1}H NMR of 4,4-difluoro-2-methyl-5-morpholino-5-oxo-*N*-phenyl-2-(*p*-tolyl) pentanamide (3t)



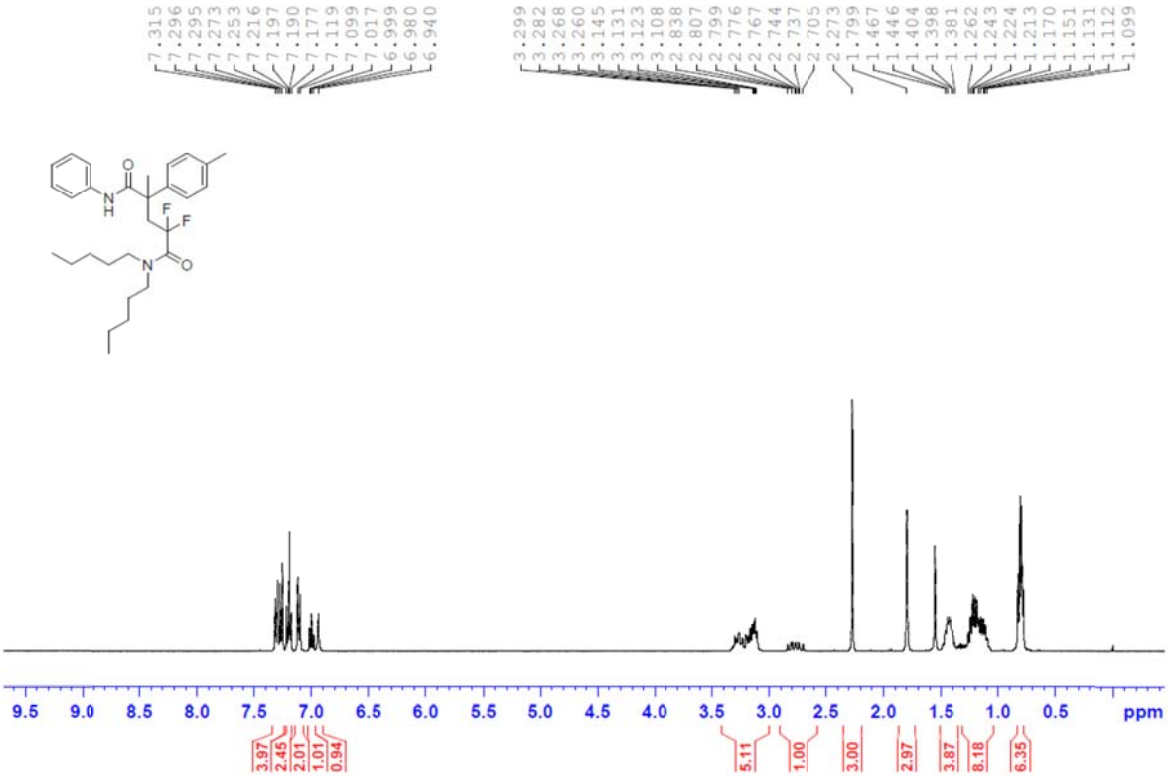
^{13}C NMR of 4,4-difluoro-2-methyl-5-morpholino-5-oxo-*N*-phenyl-2-(*p*-tolyl) pentanamide (3t)



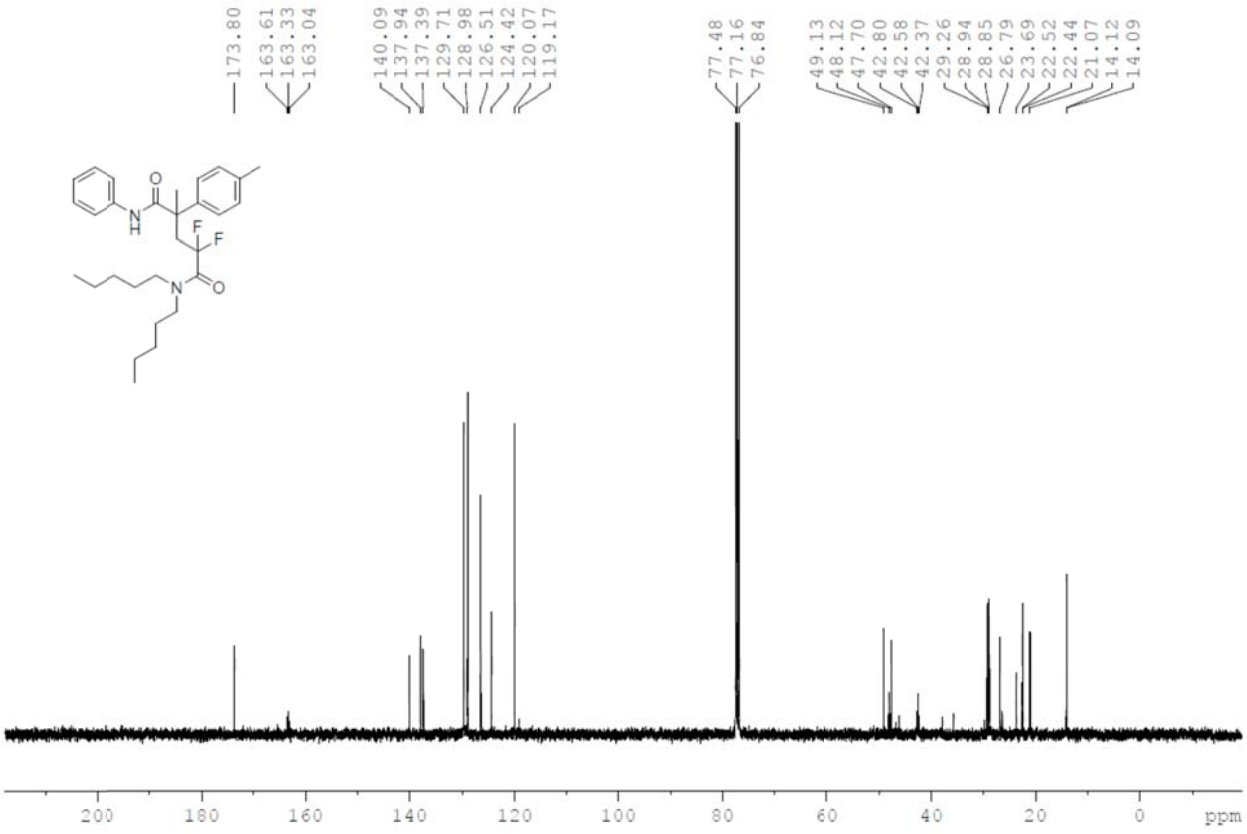
^{19}H NMR of 4,4-difluoro-2-methyl-5-morpholino-5-oxo-*N*-phenyl-2-(*p*-tolyl) pentanamide (3t)



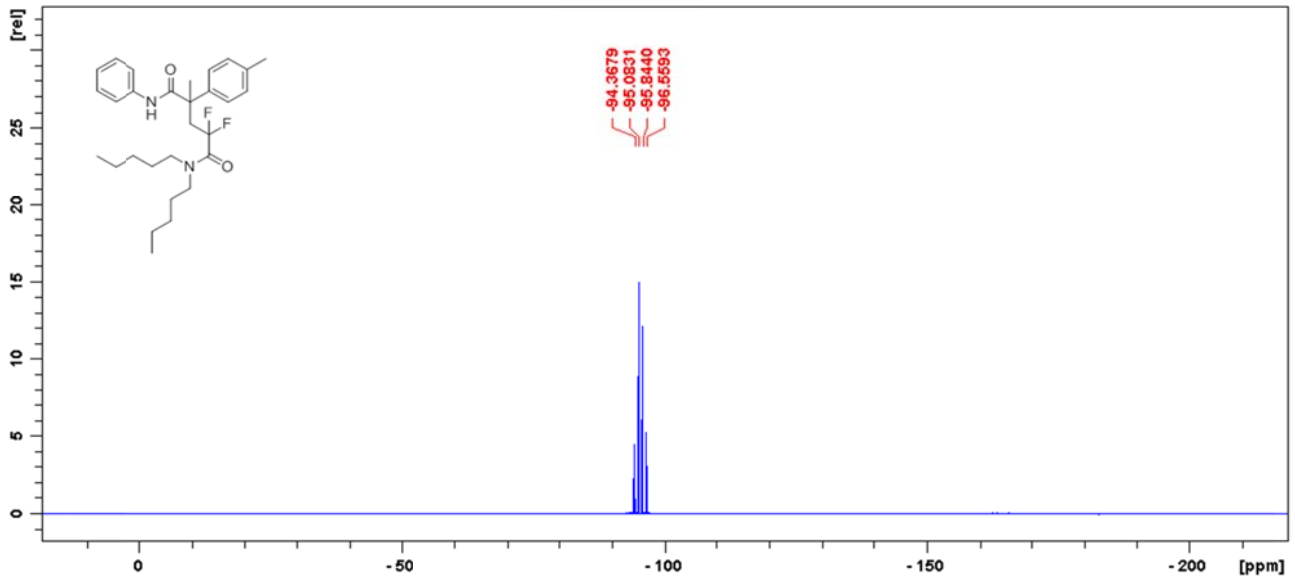
^{1}H NMR of 2,2-difluoro-4-methyl-*N*^{1},*N*^{1}-dipentyl-*N*^{5}-phenyl-4-(*p*-tolyl) pentanediamide (3u)



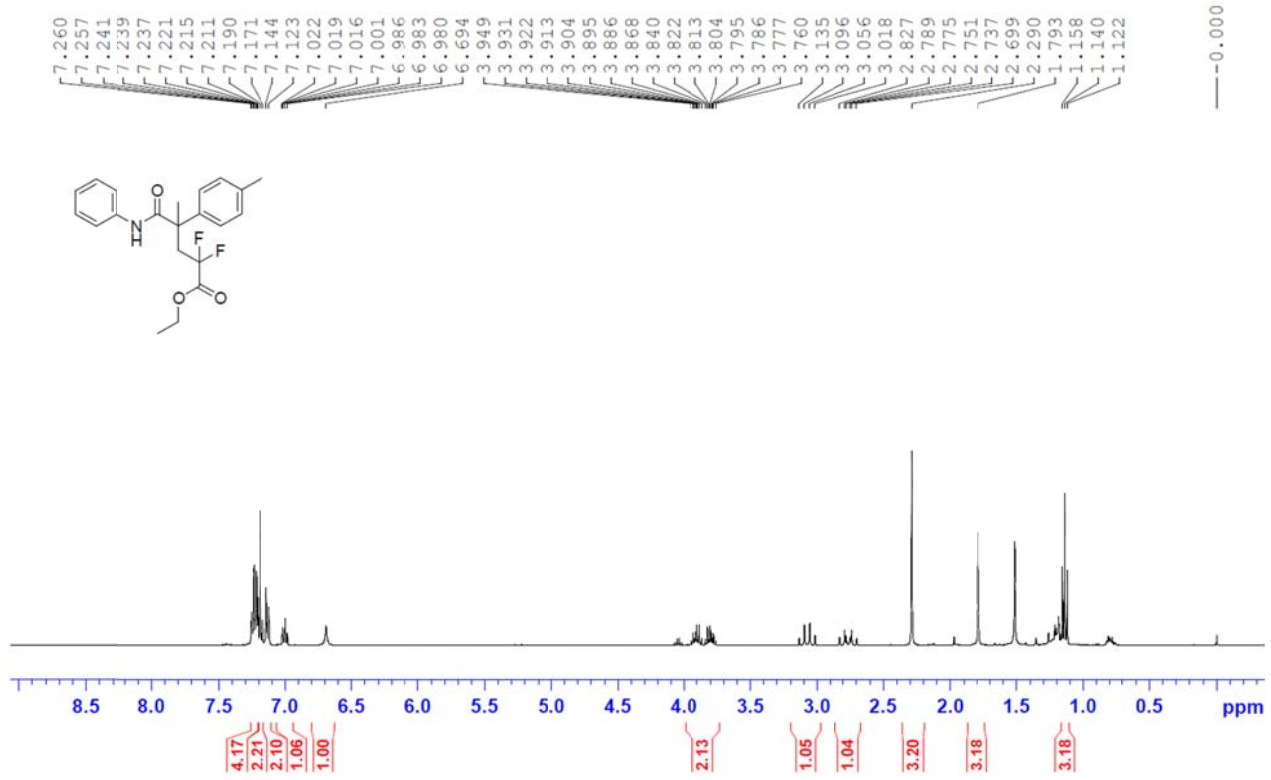
^{13}C NMR of 2,2-difluoro-4-methyl-*N*^{1},*N*^{1}-dipentyl-*N*^{5}-phenyl-4-(*p*-tolyl) pentanediamide (3u)



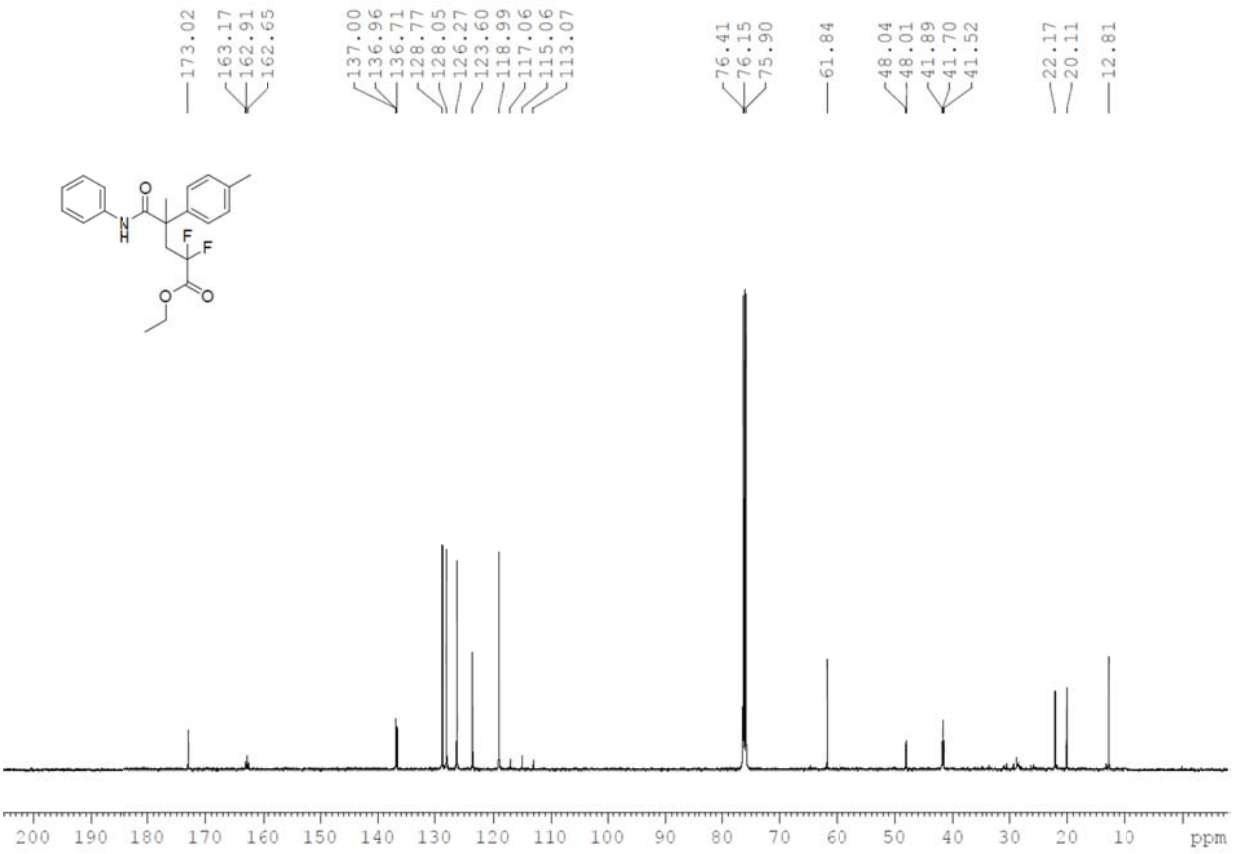
^{19}F NMR of 2,2-difluoro-4-methyl-N^1,N^1-dipentyl-N^5-phenyl-4-(*p*-tolyl) pentanediamide (3u)



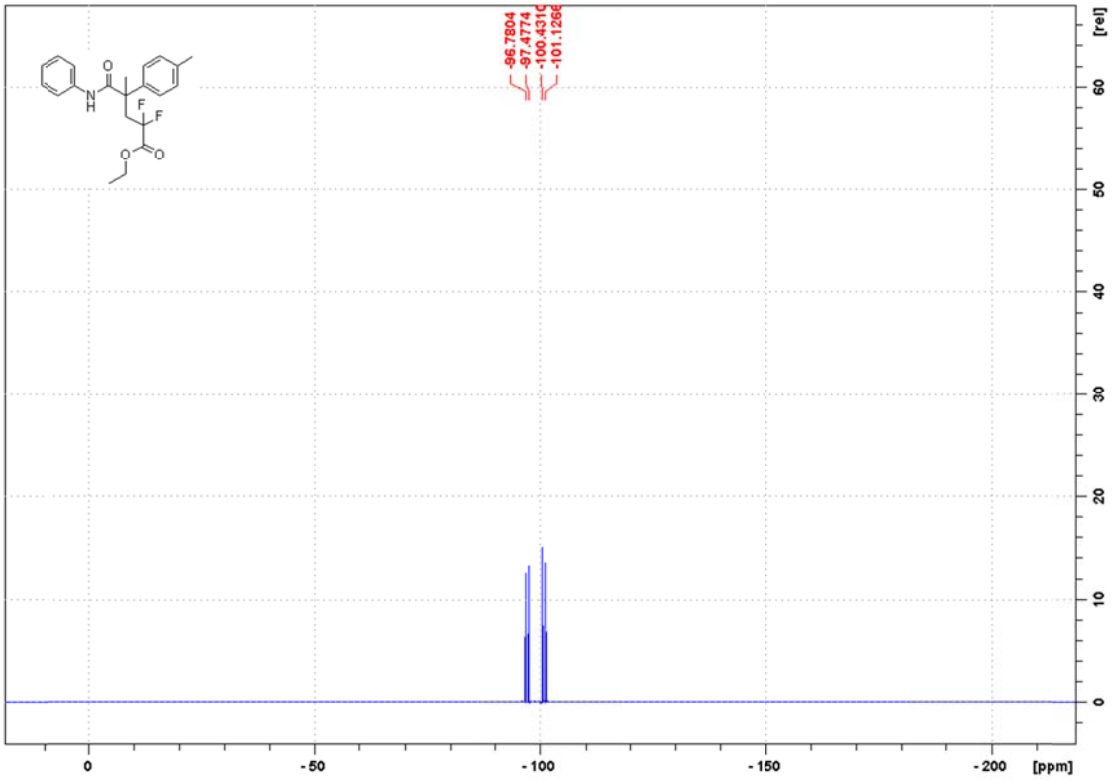
^{1}H NMR of ethyl 2,2-difluoro-4-methyl-5-oxo-5-(phenylamino)-4-(*p*-tolyl) pentanoate (3v)



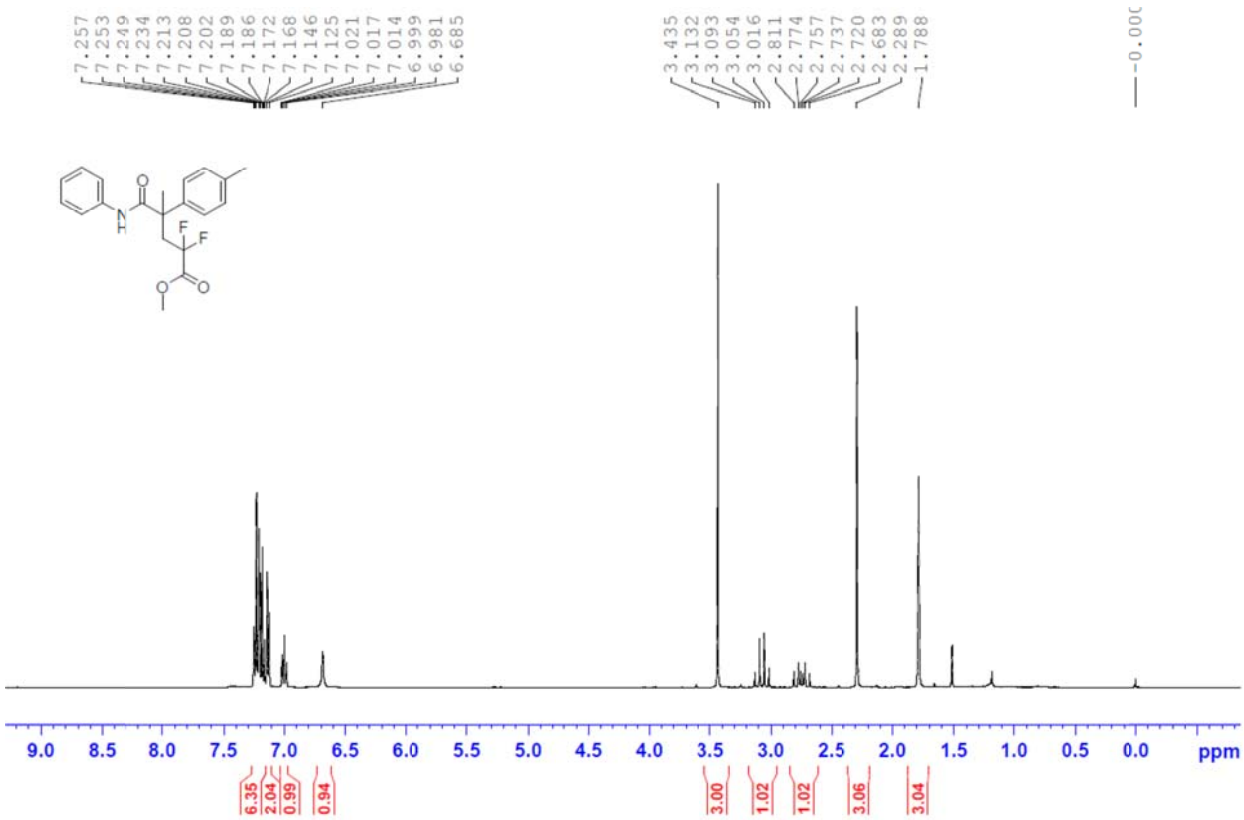
^{13}C NMR of ethyl 2,2-difluoro-4-methyl-5-oxo-5-(phenylamino)-4-(*p*-tolyl) pentanoate (3v)



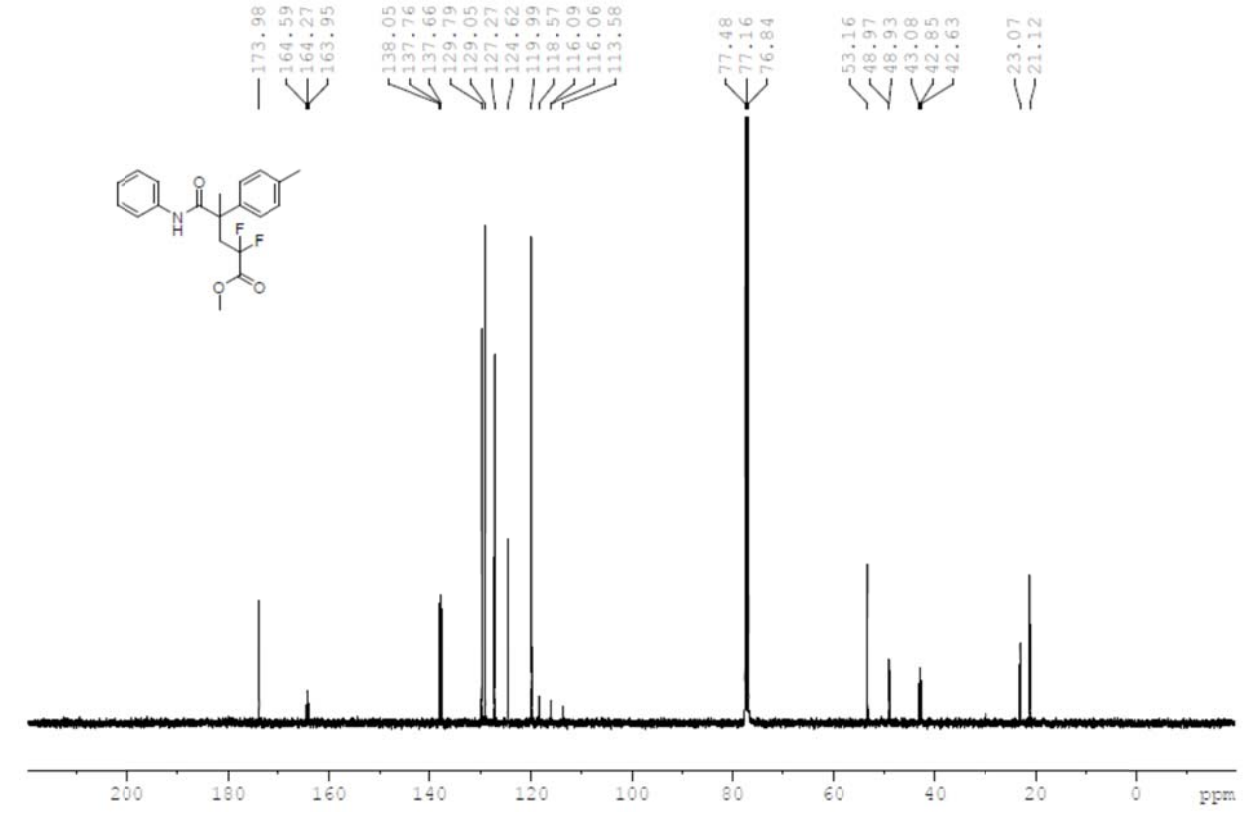
^{19}F NMR of ethyl 2,2-difluoro-4-methyl-5-oxo-5-(phenylamino)-4-(*p*-tolyl) pentanoate (3v)



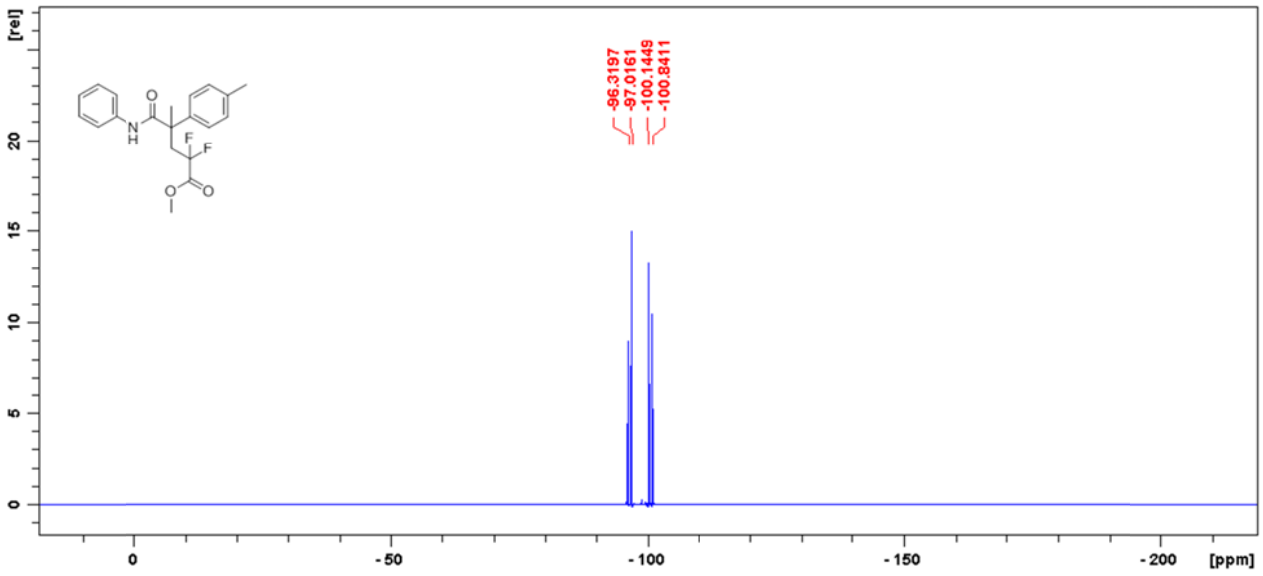
^{1}H NMR of Methyl 2,2-difluoro-4-methyl-5-oxo-5-(phenylamino)-4-(*p*-tolyl) pentanoate (4)



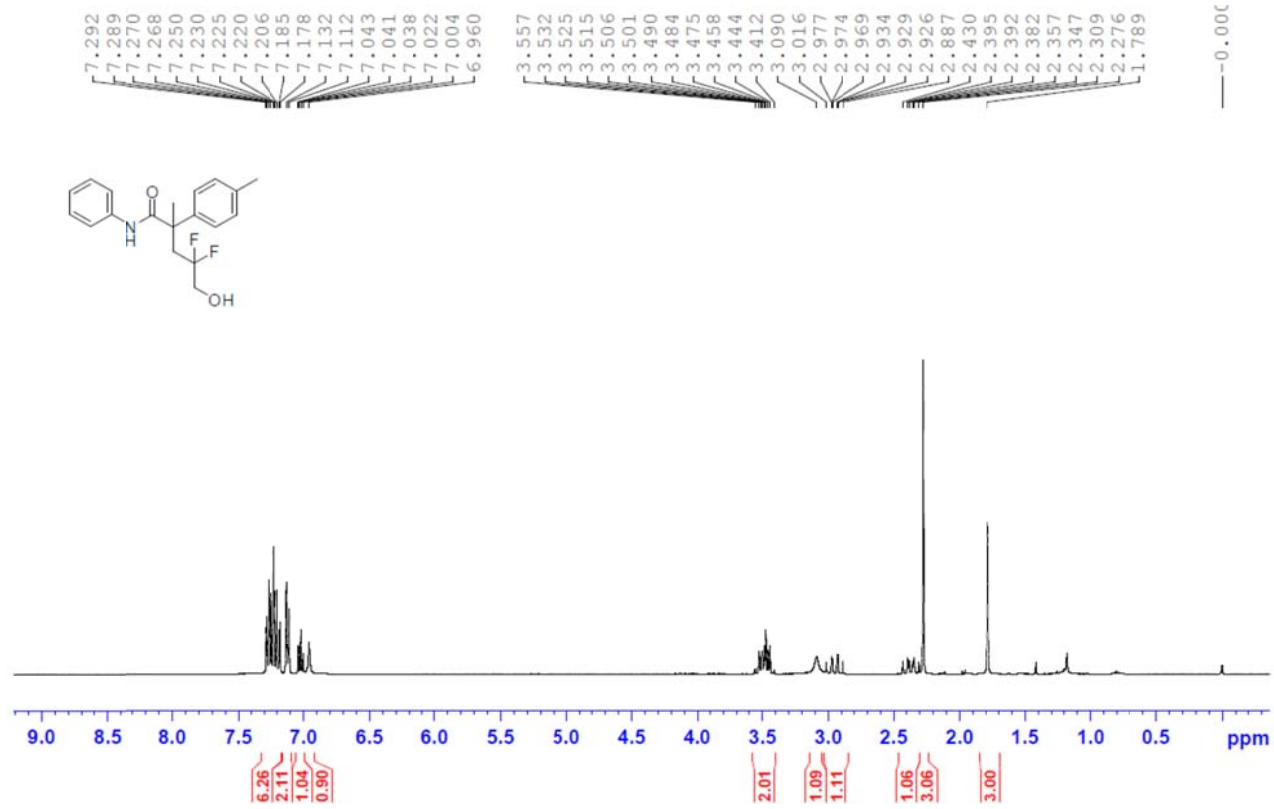
^{13}C NMR of Methyl 2,2-difluoro-4-methyl-5-oxo-5-(phenylamino)-4-(*p*-tolyl) pentanoate (4)



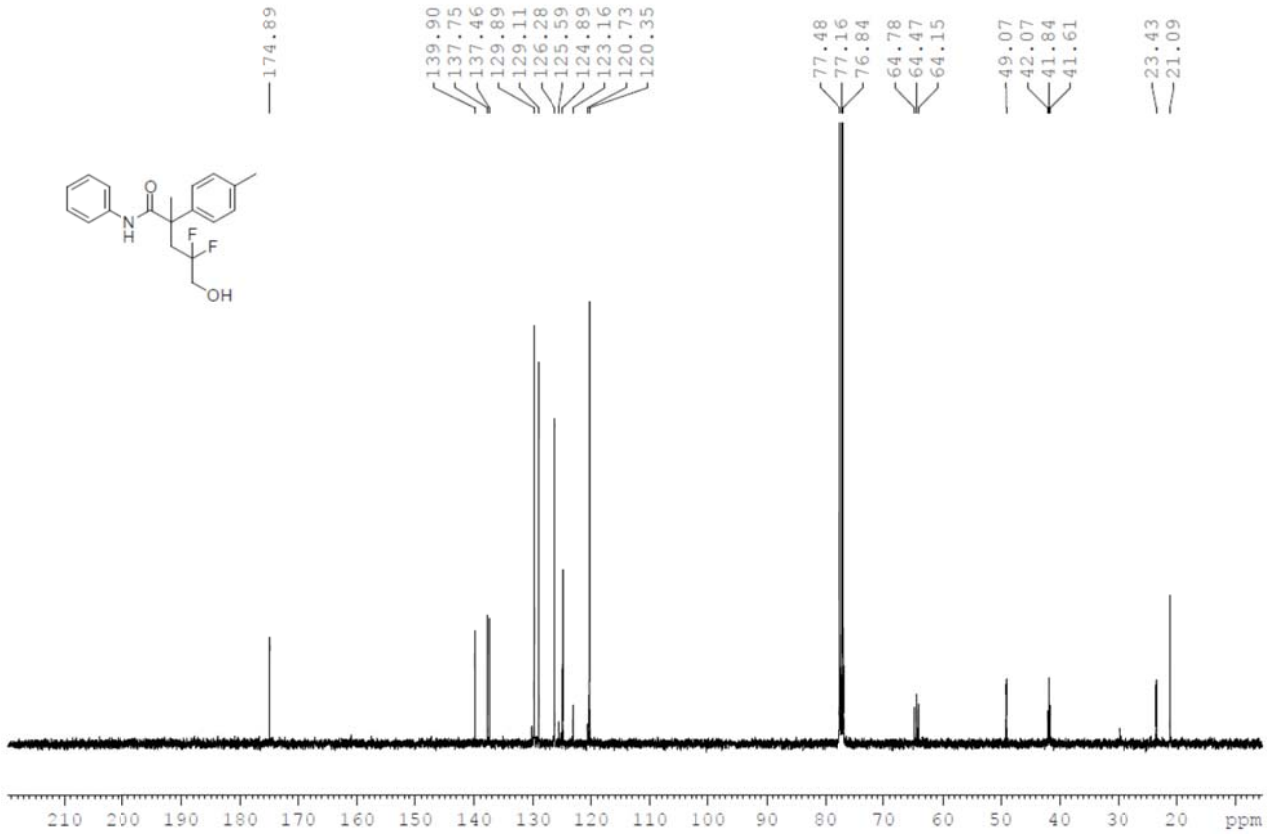
^{19}F NMR of Methyl 2,2-difluoro-4-methyl-5-oxo-5-(phenylamino)-4-(*p*-tolyl) pentanoate (4)



^{1}H NMR of 4,4-difluoro-5-hydroxy-2-methyl-N-phenyl-2-(*p*-tolyl)pentanamide (5)



^{13}C NMR of 4,4-difluoro-5-hydroxy-2-methyl-N-phenyl-2-(*p*-tolyl)pentanamide (5)



^{19}F NMR of 4,4-difluoro-5-hydroxy-2-methyl-N-phenyl-2-(*p*-tolyl)pentanamide (5)