

Supporting Information

Electrochemical synthesis of β -difluoromethylamide compounds by *N*-benzenesulfonylacrylamide with difluorine reagents

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Table of Contents

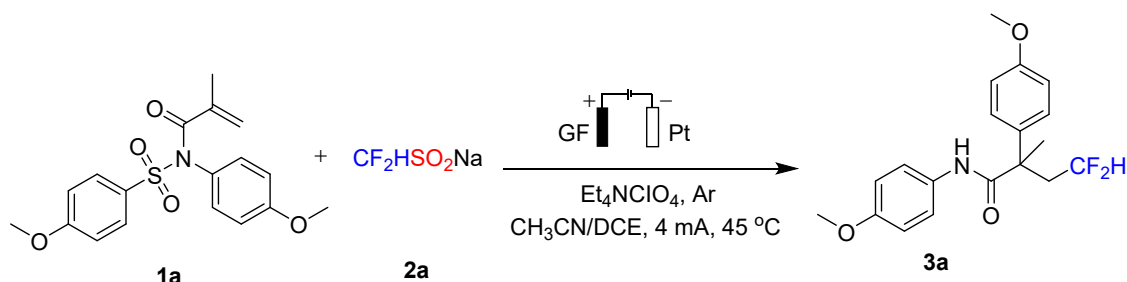
1. General methods.....	3
2. Supplementary experiments	4
3. Synthesis of Substrates.....	5
5. Control experiments	6
6. Electrochemical applications	7
7. Cyclic voltammetry studies.....	8
8. Characterization data for the products	9
9. Copies of the NMR spectra	19
10. References	48

1. General methods

Unless otherwise noted, all reagents and solvents were obtained commercially and used without further purification. Column chromatography on silica gel (300-400 mesh) was carried out using technical grade 60-90 °C petroleum ether and analytical grade EtOAc (without further purification). ^1H and ^{13}C and ^{19}F spectra were recorded on a 400 MHz or 600MHz spectrometer. Chemical shifts were reported in ppm. ^1H and ^{19}F NMR spectra were referenced to CDCl_3 (7.26 ppm) or DMSO (2.5 ppm) or MeOD (4.87 ppm), and ^{13}C -NMR spectra were referenced to CDCl_3 (77.0 ppm) or DMSO (39.5 ppm) or MeOD (49.0 ppm). Peak multiplicities were designated by the following abbreviations: s, singlet; d, doublet; t, triplet; m, multiplet; brs, broad singlet and J , coupling constant in Hz. The HRMS spectrum was measured by micromass QTOF₂ Quadrupole/Time of Flight Tandem mass spectrometer with electron spray ionization. Potentiostat was purchased from Shanghai Xinrui Company and the model is DJS-292B. Cyclic voltammograms were recorded on a CHI 660E potentiostat.

2. Supplementary experiments

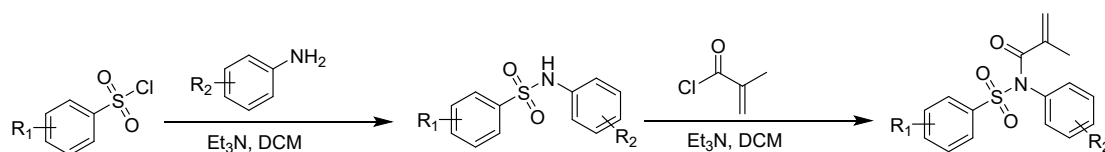
Table S1 Screening of reaction conditions^a



Entry	Electrode	Current (mA)	Electrolyte	T (°C)	Solvent	Yield (%) ^[b]
1	GF(+) Pt(-)	4	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	80
2	GF(+) Pt(-)	4	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	72 ^[c]
3	GF(+) Pt(-)	4	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	68 ^[d]
4	GF(+) Pt(-)	4	Et_4NClO_4	rt	$\text{CH}_3\text{CN}/\text{DCE}$	17
5	GF(+) Pt(-)	4	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	29
6	GF(+) Pt(-)	4	Et_4NClO_4	60	$\text{CH}_3\text{CN}/\text{DCE}$	72
7	GF(+) Pt(-)	4	Et_4NClO_4	35	$\text{CH}_3\text{CN}/\text{DCE}$	33
8	GF(+) Pt(-)	2	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	56 ^[e]
9	GF(+) Pt(-)	6	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	68 ^[f]
10	C(+) Pt(-)	4	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	60
11	C(+) Ni(-)	4	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	69
12	C(+) C(-)	4	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	54
13	RVC(+) RVC(-)	4	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	57
14	RVC(+) Pt(-)	4	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	60
15	Pt(+) Ni(-)	4	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	68
15	GF(+) Pt(-)	4	${}^n\text{Bu}_4\text{NClO}_4$	45	$\text{CH}_3\text{CN}/\text{DCE}$	45
16	GF(+) Pt(-)	4	${}^n\text{Bu}_4\text{NBF}_4$	45	$\text{CH}_3\text{CN}/\text{DCE}$	32
17	GF(+) Pt(-)	4	${}^n\text{Bu}_4\text{NBF}_6$	45	$\text{CH}_3\text{CN}/\text{DCE}$	29
18	GF(+) Pt(-)	4	${}^n\text{Bu}_4\text{NBr}$	45	$\text{CH}_3\text{CN}/\text{DCE}$	trace
19	GF(+) Pt(-)	4	LiClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	60
20	GF(+) Pt(-)	4	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	51
21	GF(+) Pt(-)	4	Et_4NClO_4	45	DCM/DCE	0
22	GF(+) Pt(-)	4	Et_4NClO_4	45	CH_3CN	45
23	GF(+) Pt(-)	4	Et_4NClO_4	45	DCE	0
24	GF(+) Pt(-)	4	Et_4NClO_4	45	CH_3OH	0
25	GF(+) Pt(-)	4	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCM}$	71
26	GF(+) Pt(-)	0	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	nr
26	GF(+) Pt(-)	4	Et_4NClO_4	45	$\text{CH}_3\text{CN}/\text{DCE}$	nr ^[g]

^[a] Reaction conditions: **1a** (0.1 mmol), **2a** (0.3 mmol), Et₄NClO₄ as electrolyte (0.4 mmol), MeCN and DCE (1:1) as solvent (4 mL), electrolysis at a constant current of 4 mA for 2 h in an undivided cell. ^[b] Isolated yields. ^[c] Et₄NClO₄ (0.05 M). ^[d] Et₄NClO₄ (0.125 M). ^[e] 2 mA, 4.5 h. ^[f] 6 mA, 1.5 h. ^[g] 4 mA, Air.

3. Synthesis of Substrates

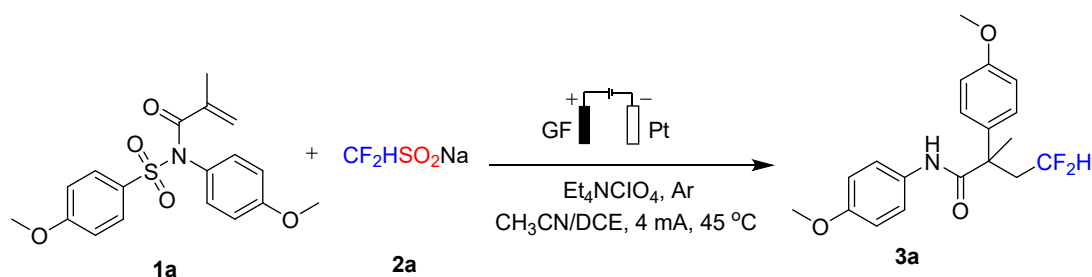


In a dry 100 mL round-bottom flask, a mixture of aniline (10 mmol) and Et₃N (20 mmol, 2 equiv) in 20 mL of DCM were stirred at room temperature^[1]. The benzene sulfochloride (11 mmol, 1.1 equiv) was added slowly by a dropping funnel. The reaction was monitored by TLC. After the reaction completed, the reaction mixture was washed with water and extracted with ethyl acetate (10 mL × 3). The combined organic layer was washed with brine, dried over Na₂SO₄, and the pure product was obtained by flash column chromatography on silica gel (hexane : ethyl acetate = 20 : 1 to 6 : 1).

Subsequently, in a dry 100 mL round-bottom flask, a mixture of *N*-phenylbenzenesulfonamide (10 mmol) and Et₃N (30 mmol) in 20 mL of DCM were stirred in ice bath. The methacryloyl chloride (12 mmol, 1.2 equiv) was added slowly by a dropping funnel. The reaction was monitored by TLC. After the reaction completed, the reaction mixture was washed with water and extracted with ethyl acetate (10 mL × 3). The combined organic layer was washed with brine, dried over Na₂SO₄, and the pure product was obtained by flash column chromatography on silica gel (hexane : ethyl acetate = 20 : 1 to 4 : 1).

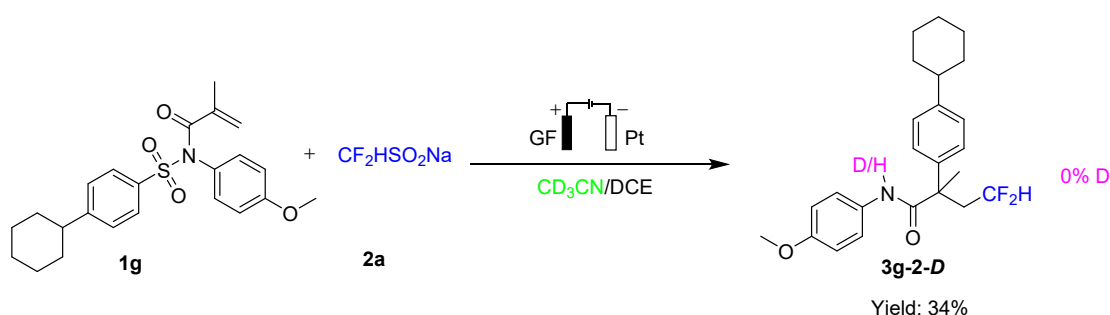
4. General procedure for the preparation of products

Electrochemical synthesis of β -difluoromethamide compounds **3a-3v**



N-phenylsulfonyl acrylamide **1a** (0.1 mmol) and sodium difluoromethanesulfonate **2a** (0.3 mmol) as substrates were added to the three-necked flask with Et₄NClO₄ (0.1 M). A total of 4 mL of solvent was added to the flask with CH₃CN (2 mL) and DCE (2 mL). The flask, equipped with carbon felt (GF) as anode and platinum sheet (Pt) as cathode, was electrolyzed at a constant current of 4 mA in an argon atmosphere until the substrate was completely consumed. The reaction solution was collected, concentrated under reduced pressure, and purified by gradient elution by silica gel column chromatography (hexane/ethyl acetate = 10:1/4:1 elution) to obtain β-difluoromethamide compounds..

Electrochemical synthesis of β-difluoromethamide compound **3g-2-D**



N-phenylsulfonyl acrylamide **1g** (0.1 mmol) and sodium difluoromethanesulfonate **2a** (0.3 mmol) as substrates were added to the three-necked flask with Et₄NClO₄ (0.1 M). A total of 4 mL of solvent was added to the flask with CD₃CN (2 mL) and DCE (2 mL). The flask, equipped with carbon felt (GF) as anode and platinum sheet (Pt) as cathode, was electrolyzed at a constant current of 4 mA in an argon atmosphere until the substrate was completely consumed. The reaction solution was collected, concentrated under reduced pressure, and purified by gradient elution by silica gel column chromatography (hexane/ethyl acetate = 10:1/4:1 elution) to obtain β-difluoromethamide compound.

5. Control experiments

5.1 TEMPO and BHT trapped experiment

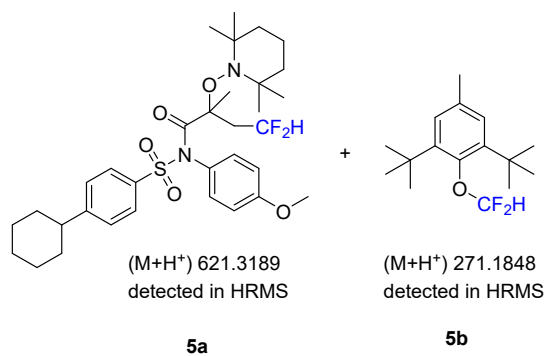
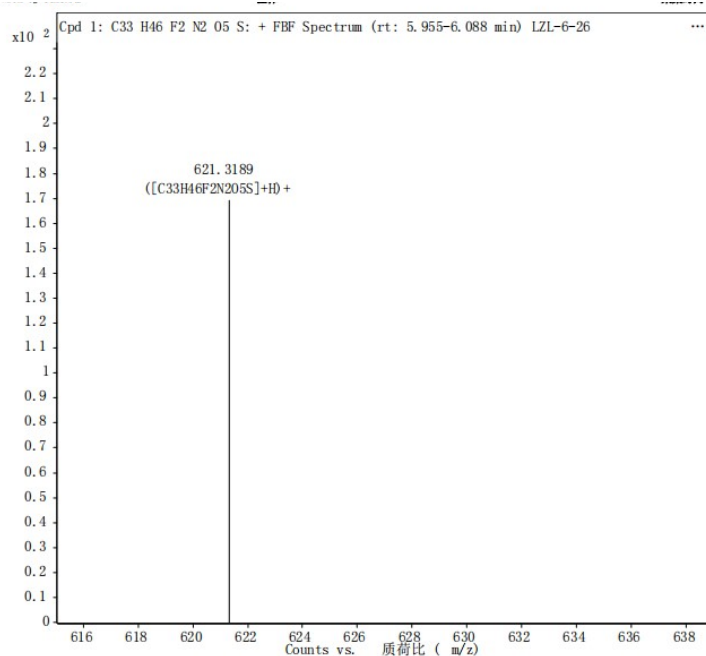
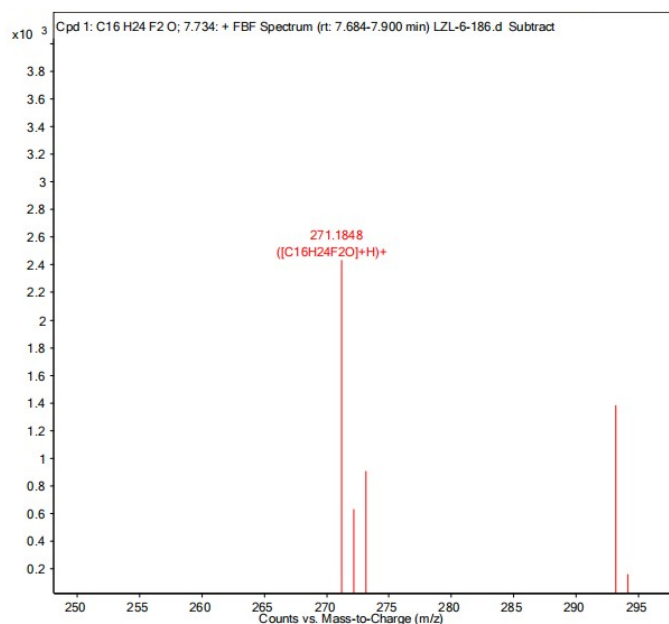
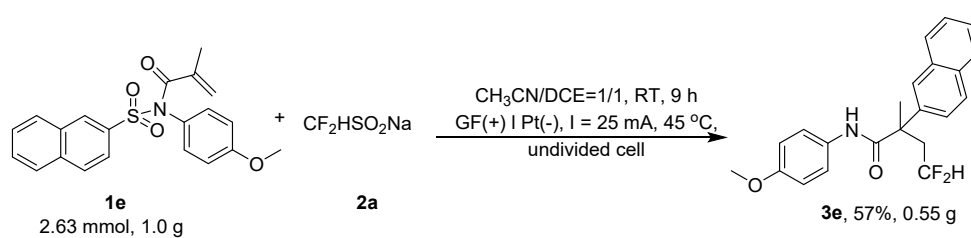


Fig. S1: Compound **5a** : HRMS (m/z) [ESI]: calculated for C₃₃H₄₇F₂N₂O₅S⁺ [M+H]⁺ : 621.3169, found 621.3189 . Compound **5b** : HRMS (m/z) [ESI]: calculated for C₁₆H₂₅F₂O⁺ [M+H]⁺ : 271.1868, found 271.1848 .





6. Electrochemical applications



1e (2.63 mmol, 1.0eq), Et_4NClO_4 (11.08 mmol, 4.0eq) and **2a** (13.85 mmol, 5.0eq) were added successively into a 400 ml round-bottomed flask. The battery was equipped with a carbon felt anode (6 cm x 6 cm) and a platinum plate cathode (6 cm x 6 cm). In an argon atmosphere, CH_3CN (50 mL) and DCE (50 mL) are injected into the reactor. electrolysis was carried out for the corresponding time at a constant current of 25 mA at 45 °C until the substrate was completely consumed. The reaction solution was collected, concentrated under reduced pressure, and purified by gradient elution by silica gel column chromatography (hexane/ethyl acetate = 10:1/4:1 elution) to obtain **2e**.

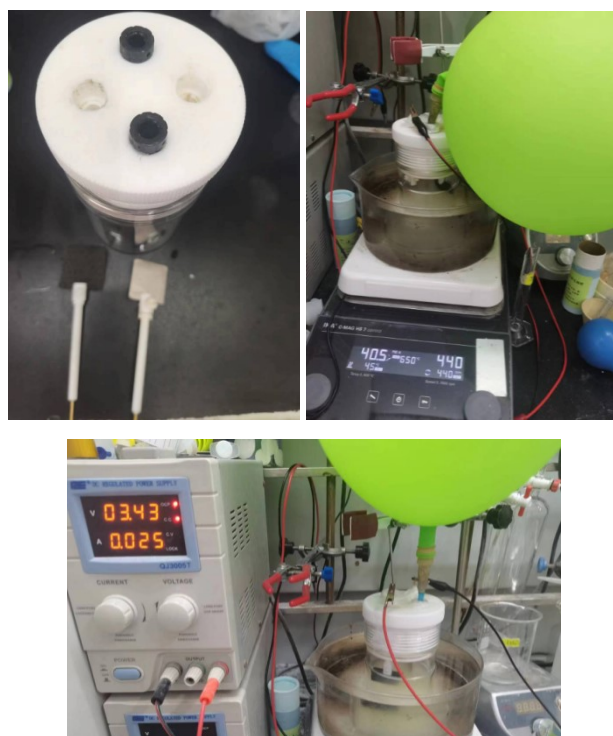


Fig. S2 Electrolysis setup

7. Cyclic voltammometry studies

The cyclic voltammograms were recorded in an electrolyte solution of LiClO_4 (0.1 M) in $\text{CH}_3\text{CN}/\text{H}_2\text{O}$ using a glassy carbon disk working electrode (diameter, 3 mm), a Pt wire auxiliary electrode and a Ag/AgCl reference electrode. The scan rate was 100 mV/s.

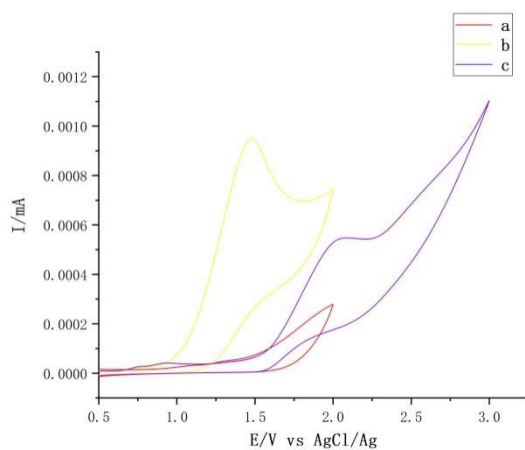


Fig. S3 Cyclic voltammograms in $\text{CH}_3\text{CN}/\text{H}_2\text{O} + 0.1 \text{ M LiClO}_4$. The scanning rate is set to 100 mV/s, $\text{CH}_3\text{CN}/\text{H}_2\text{O} + 0.1 \text{ M LiClO}_4$ cyclic voltammometry. a) Blank b) **2a** (0.3 mmol) c) **1a** (0.1 mmol). Charting with IUPAC. Init E (V)=0 V, Final E (V)=0 V, High E(V)= 3 V.

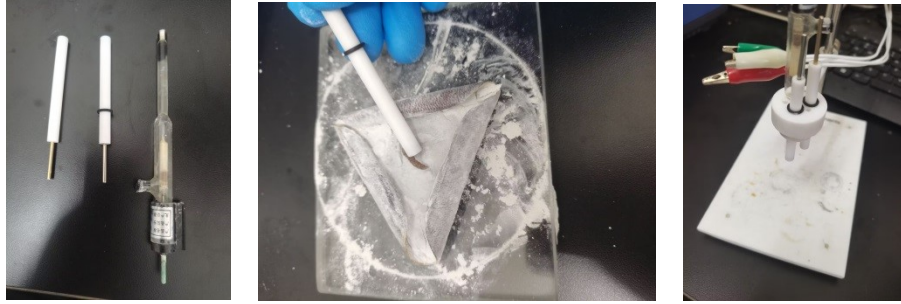
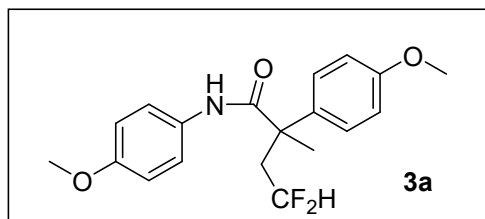
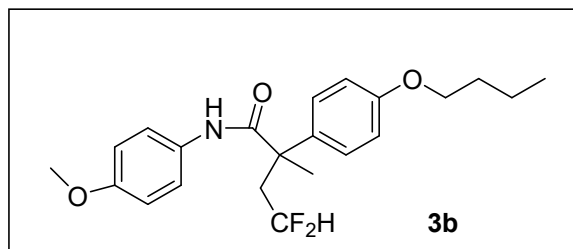


Fig. S4 Preparation for the CV test. Grinding material: aluminum powder. Grinding

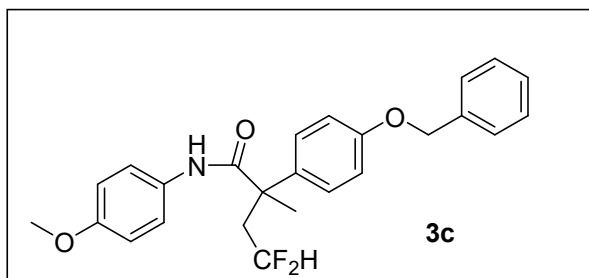
8. Characterization data for the products



4,4-difluoro-N,2-bis(4-methoxyphenyl)-2-methylbutanamide (3a). The title compound (27.2 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 78% yield. colourless liquid. ¹H NMR (400 MHz, CDCl₃) δ 7.32 (m, 2H), 7.23 (m, 2H), 6.95 (m, 2H), 6.81 (m, 2H), 6.72 (s, 1H), 5.84-5.53 (m, 1H), 3.83 (s, 3H), 3.76 (s, 3H), 2.71-2.65 (m, 1H), 2.49-2.45 (m, 1H), 1.75 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 174.3, 159.2, 156.6, 133.4, 130.6, 128.0, 121.9, 116.7 (t, *J* = 232.3 Hz), 114.6, 114.1, 55.5, 55.3, 48.0, 43.5 (t, *J* = 20.0 Hz), 23.7. ¹⁹F NMR (376 MHz, Chloroform-d) δ -110.85--111.01 (m, *J* = 71.4 Hz), -111.01--111.27 (m *J* = 97.8 Hz), 2F. HRMS(*m/z*)(ESI): calcd for C₁₉H₂₁F₂NNaO₃⁺ [*M*+Na]⁺ 372.1382, found 372.1380.

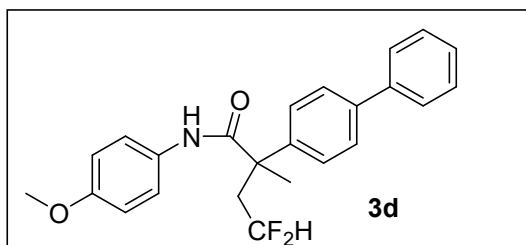


2-(4-butoxyphenyl)-4,4-difluoro-N-(4-methoxyphenyl)-2-methylbutanamide (3b). The title compound (30.9 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 79% yield. colourless liquid. ¹H NMR (400 MHz, CDCl₃) δ 7.30 (m 2H), 7.23 (m, 2H), 6.94 (m, 2H), 6.80 (m, 2H), 6.72 (s, 1H), 5.83-5.52 (m, 1H), 3.98 (t, *J* = 4.0 Hz, 2H), 3.76 (s, 3H), 2.70-2.61 (m, 1H), 2.49-2.44 (m, 1H), 1.80-1.77 (m, 2H), 1.75 (s, 3H), 1.54-1.48 (m, 2H), 0.99 (t, *J* = 8.0 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 174.4, 158.8, 156.6, 133.1, 130.6, 128.0, 121.8, 116.8 (t, *J* = 242.4 Hz), 115.1, 114.1, 67.8, 55.5, 48.0, 43.5 (t, *J* = 20.2 Hz), 31.3, 23.7, 19.3, 13.9. ¹⁹F NMR (376 MHz, CDCl₃) δ -111.05 (d, *J* = 3.8 Hz, 2F). HRMS(*m/z*)(ESI): calcd for C₂₂H₂₈F₂NO₃⁺ [*M*+H]⁺ 392.2032, found 392.2028.



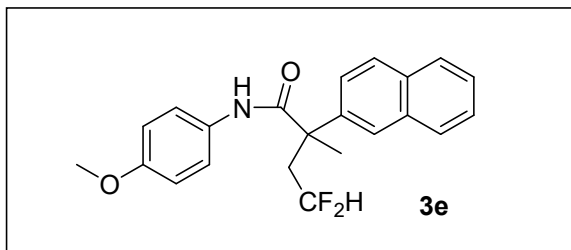
2-(4-(benzyloxy)phenyl)-4,4-difluoro-N-(4-methoxyphenyl)-2-methylbutanamide

(**3c**). The title compound (35.7 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 84% yield. colourless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.44 (m, 4H), 7.37-7.29 (m, 3H), 7.26-7.21 (m, 2H), 7.03 (m, 2H), 6.81 (m, 2H), 6.73 (s, 1H), 5.85-5.54 (m, 1H), 5.09 (s, 2H), 3.77 (s, 3H), 2.71-2.66 (m, 1H), 2.49-2.45 (m, 1H), 1.76 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 174.3, 158.4, 156.6, 136.6, 133.7 130.6, 128.7, 128.2, 128.0, 127.6, 121.9, 116.8 (t, $J = 242.4$ Hz), 115.5, 114.1, 70.1, 55.5, 48.0, 43.5 (t, $J = 20.2$ Hz), 23.7. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.02 (d, $J = 3.8$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{25}\text{H}_{26}\text{F}_2\text{NO}_3^+$ [$\text{M}+\text{H}$] $^+$ 426.1875, found 426.1874.



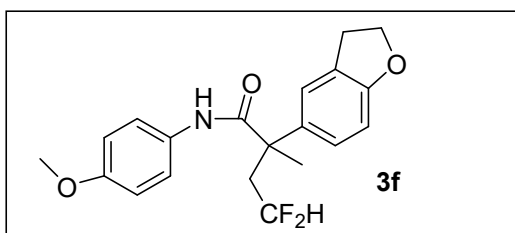
2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-N-(4-methoxyphenyl)-2-methylbutanamide

(**3d**). The title compound (35.2 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 89% yield. colourless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.65 (m, 2H), 7.60 (m, 2H), 7.46 (m, 4H), 7.37 (m, 1H), 7.25 (m, 2H), 6.81 (m, 2H), 6.77 (s, 1H), 5.92-5.61 (m, 1H), 3.75 (s, 3H), 2.76-2.71 (m, 1H), 2.54-2.0 (m, 1H), 1.82 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 173.9, 156.7, 140.9, 140.7, 140.0, 130.5, 129.0, 127.9, 127.8, 127.2, 122.0, 116.7 (t, $J = 232.3$ Hz), 114.1, 55.5, 43.6 (t, $J = 20.2$ Hz), 23.6. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -110.94 (d, $J = 3.8$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{24}\text{H}_{23}\text{F}_2\text{NaNO}_2^+$ [$\text{M}+\text{Na}$] $^+$ 418.1589, found 418.1578.



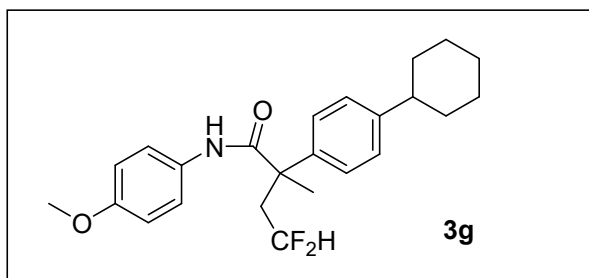
4,4-difluoro-N-(4-methoxyphenyl)-2-methyl-2-(naphthalen-2-yl)butanamide (3e).

The title compound (28.0 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 6 : 1) in 76% yield. colourless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.91-7.86 (m, 4H), 7.57-7.55 (m, 2H), 7.45-7.43 (m, 1H), 7.22-7.19 (m, 2H), 6.80-6.78 (m, 2H), 6.71 (s, 1H), 5.86-5.55 (m, 1H), 3.75 (s, 3H), 2.83-2.77 (m, 1H), 2.63-2.58 (m, 1H), 1.90 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 173.9, 156.7, 138.9, 133.3, 132.7, 130.5, 129.4, 128.2, 127.7, 126.9, 125.4, 124.9, 122.0, 116.7 (t, $J = 232.3$ Hz), 114.1, 55.5, 48.8, 43.2 (t, $J = 20.2$ Hz), 23.5. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -110.96 (s, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{22}\text{H}_{22}\text{F}_2\text{NO}_2^+$ $[\text{M}+\text{H}]^+$ 370.1613, found 370.1614.



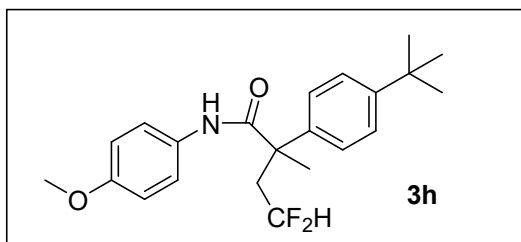
2-(2,3-dihydrobenzofuran-5-yl)-4,4-difluoro-N-(4-methoxyphenyl)-2-

methylbutanamide (3f). The title compound (29.2 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 81% yield. White solid. m.p. 105.2-107.5 °C. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.26-7.22 (m, 3H), 7.14-7.12 (m, 1H), 6.82-6.80 (m, 3H), 6.76 (s, 1H), 5.83-5.53 (m, 1H), 4.61 (t, $J = 8.0$ Hz, 2H), 3.77 (s, 3H), 3.23 (t, $J = 12.0$ Hz, 2H), 2.69-2.64 (m, 1H), 2.48-2.44 (m, 1H), 1.74 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 174.5, 159.9, 156.6, 133.4, 130.6, 128.4, 126.5, 123.5, 121.8, 116.8 (t, $J = 242.4$ Hz), 114.1, 109.7, 71.6, 55.5, 48.2, 43.7 (t, $J = 20.2$ Hz), 29.7, 23.8. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.01 (d, $J = 7.5$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{20}\text{H}_{22}\text{F}_2\text{NO}_3^+$ $[\text{M}+\text{H}]^+$ 362.1562, found 362.1562.



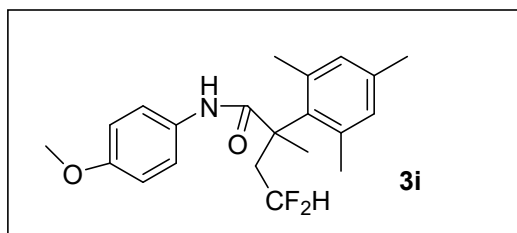
2-(4-cyclohexylphenyl)-4,4-difluoro-N-(4-methoxyphenyl)-2-methylbutanamide

(**3g**). The title compound (32.1 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 80% yield. colourless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.32-7.29 (m, 2H), 7.26-7.22 (m, 4H), 6.82-6.79 (m, 2H), 6.72 (s, 1H), 5.84-5.54 (m, 1H), 3.76 (s, 3H), 2.71-2.66 (m, 1H), 2.53 -2.44 (m, 2H), 1.89-1.85 (m, 5H), 1.76 (s, 3H), 1.43-1.38 (m, 5H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 174.3, 156.6, 148.0, 138.9, 130.6, 127.7, 126.6, 122.0, 116.7 (t, $J = 232.3$ Hz), 114.1, 55.5, 48.3, 44.1, 43.6 (t, $J = 20.2$ Hz), 34.3 (d, $J = 10.1$ Hz), 26.8, 26.1, 23.6. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -110.97 (d, $J = 7.5$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{24}\text{H}_{30}\text{F}_2\text{NO}_2^+$ [$\text{M}+\text{H}$] $^+$ 402.2239, found 402.2238.

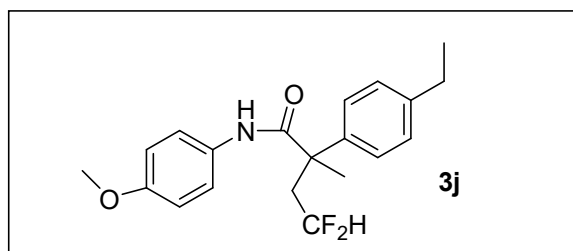


2-(4-(tert-butyl)phenyl)-4,4-difluoro-N-(4-methoxyphenyl)-2-methylbutanamide

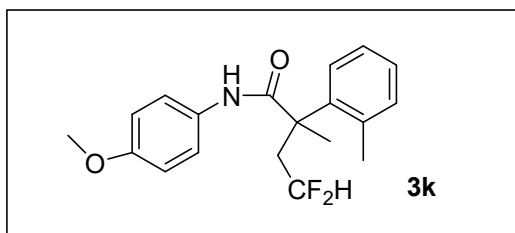
(**3h**). The title compound (25.5 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 68% yield. colourless liquid. $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.44-7.42 (m, 2H), 7.33-7.31 (m, 2H), 7.25-7.23 (m, 2H), 6.83-6.81 (m, 2H), 6.70 (s, 1H), 5.82-5.59 (m, 1H), 3.77 (s, 3H), 2.71-2.67 (m, 1H), 2.52-2.46 (m, 1H), 1.77 (s, 3H), 1.33 (s, 9H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 174.2, 156.6, 151.1, 138.5, 130.6, 126.4, 126.3, 122.0, 116.8 (t, $J = 237.5$ Hz), 114.1, 55.5, 48.3, 43.6 (t, $J = 25.0$ Hz), 31.4, 31.3, 23.6. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.00 (d, $J = 11.3$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{22}\text{H}_{28}\text{F}_2\text{NO}_2^+$ [$\text{M}+\text{H}$] $^+$ 376.2083, found 376.2083.



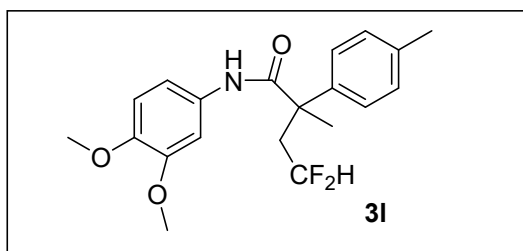
4,4-difluoro-2-mesityl-N-(4-methoxyphenyl)-2-methylbutanamide (3i). The title compound (26.0 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 72% yield. colourless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.25-7.23 (m, 2H), 6.87 (s, 2H), 6.84-6.82 (m, 3H), 5.92-5.64 (m, 1H), 3.77 (s, 3H), 2.67-2.57 (m, 2H), 2.40 (s, 6H), 2.26 (s, 3H), 1.96 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 177.0, 156.6, 138.5, 137.2, 134.2, 132.7, 130.9, 121.9, 117.3 (t, $J = 232.3$ Hz), 114.2, 55.5, 51.1, 41.7 (t, $J = 20.2$ Hz), 29.0, 23.6, 20.4. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.35 (d, $J = 63.9$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{21}\text{H}_{25}\text{F}_2\text{NNaO}_2^+$ $[\text{M}+\text{Na}]^+$ 384.1746, found 384.1737.



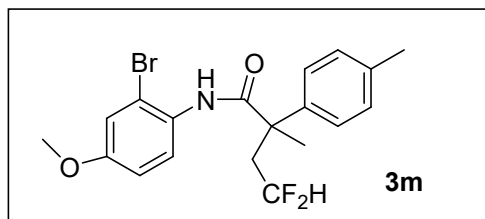
2-(4-ethylphenyl)-4,4-difluoro-N-(4-methoxyphenyl)-2-methylbutanamide (3j). The title compound (27.5 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 74% yield. white solid. m.p. 99.2-99.8 °C. $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.32-7.30 (m, 2H), 7.26-7.25 (m, 2H), 7.24-7.23 (m, 2H), 6.82-6.80 (m, 2H), 6.69 (s, 1H), 5.82-5.57 (m, 1H), 3.77 (s, 3H), 2.73-2.64 (m, 3H), 2.54-2.46 (m, 1H), 1.77 (s, 3H), 1.26 (t, $J = 8.0$ Hz, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 174.2, 156.6, 144.2, 138.8, 130.6, 128.8, 126.7, 121.9, 116.8 (t, $J = 237.5$ Hz), 114.1, 55.5, 43.5 (t, $J = 12.6$ Hz), 28.4, 23.6, 15.3. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.02 (d, $J = 3.8$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{20}\text{H}_{24}\text{F}_2\text{NO}_2^+$ $[\text{M}+\text{H}]^+$ 348.1770, found 348.1763.



4,4-difluoro-N-(4-methoxyphenyl)-2-methyl-2-(o-tolyl)butanamide (3k). The title compound (24.3 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 73% yield. colourless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.48-7.46 (m, 1H), 7.31-7.30 (m, 2H), 7.26-7.24 (m, 1H), 7.23-7.20 (m, 2H), 6.82-6.80 (m, 2H), 6.73 (s, 1H), 5.67-5.37 (m, 1H), 3.76 (s, 3H), 2.69-2.64 (m, 2H), 2.31 (s, 3H), 1.82 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 175.0, 156.7, 138.5, 137.3, 132.9, 130.5, 128.5, 127.2, 126.8, 122.0, 116.7 (t, $J = 232.3$ Hz), 114.2, 55.5, 48.3, 43.5 (t, $J = 20.2$ Hz), 25.9, 20.5. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.16 (s, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{19}\text{H}_{21}\text{F}_2\text{NNaO}_2^+$ [$\text{M}+\text{Na}$] $^+$ 356.1433, found 356.1420.

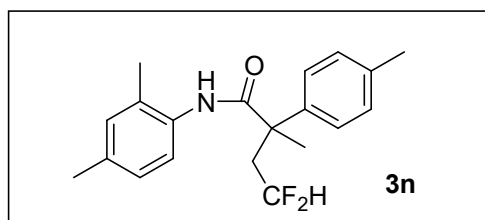


N-(3,4-dimethoxyphenyl)-4,4-difluoro-2-methyl-2-(p-tolyl)butanamide (3l). The title compound (31.9 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 88% yield. colourless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.30-7.28 (m, 2H), 7.26-7.23 (m, 3H), 6.73-6.72 (m, 2H), 6.64-6.61 (m, 1H), 5.83-5.52 (m, 1H), 3.86 (s, 3H), 3.83 (s, 3H), 2.71-2.66 (m, 1H), 2.52-2.38 (m, 1H), 2.38 (s, 3H), 1.77 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 174.2, 149.0, 146.0, 138.4, 138.0, 131.2, 130.1, 126.6, 116.7 (t, $J = 232.3$ Hz), 111.8, 111.1, 104.8, 56.1, 55.9, 48.4, 43.5 (t, $J = 20.2$ Hz), 23.6, 21.0. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.07 (d, $J = 3.8$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{20}\text{H}_{24}\text{F}_2\text{NO}_3^+$ [$\text{M}+\text{H}$] $^+$ 364.1719, found 364.1717.



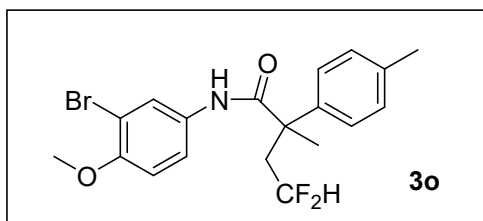
***N*-(2-bromo-4-methoxyphenyl)-4,4-difluoro-2-methyl-2-(*p*-tolyl)butanamide (3m).**

The title compound (22.2 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 54% yield. colourless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.50-7.49 (m, 1H), 7.32-7.30 (m, 1H), 7.30-7.25 (m, 4H), 6.81-6.79 (m, 1H), 6.66 (s, 1H), 5.82-5.52 (m, 1H), 3.85 (s, 3H), 2.70-2.65 (m, 1H), 2.54-2.38 (m, 1H), 2.38 (s, 3H), 1.76 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 174.3, 153.0, 138.2, 138.1, 131.3, 130.1, 126.6, 125.5, 120.6, 119.0, 116.6 (t, $J = 242.4$ Hz), 111.9, 111.5, 56.5, 48.4, 43.4 (t, $J = 20.2$ Hz), 23.5, 21.0. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.10 (d, $J = 2.2$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{19}\text{H}_{21}\text{BrF}_2\text{NO}_2^+$ [$\text{M}+\text{H}$] $^+$ 412.0718, found 412.0708.



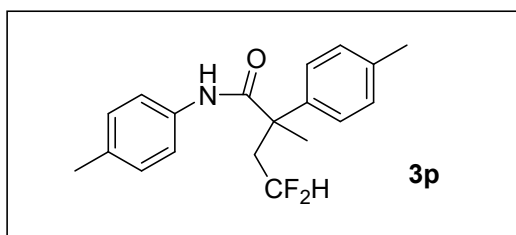
***N*-(2,4-dimethylphenyl)-4,4-difluoro-2-methyl-2-(*p*-tolyl)butanamide (3n).**

The title compound (19.9 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 60% yield. colourless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.55 (m, 1H), 7.33 (m, 2H), 7.25 (m, 2H), 6.98 (m, 1H), 6.90 (s, 1H), 6.61 (s, 1H), 5.86-5.56 (m, 1H), 2.38 (s, 3H), 2.25 (s, 3H), 1.83 (s, 3H), 1.79 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 174.4, 138.6, 138.0, 134.9, 132.8, 131.1, 130.0, 129.1, 127.3, 126.7, 122.7, 116.8 (t, $J = 242.4$ Hz), 48.4, 43.2 (t, $J = 20.2$ Hz), 23.6, 21.0, 20.8, 17.1. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -110.94 (s, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{20}\text{H}_{24}\text{F}_2\text{NO}_2^+$ [$\text{M}+\text{H}$] $^+$ 332.1821, found 332.1825.

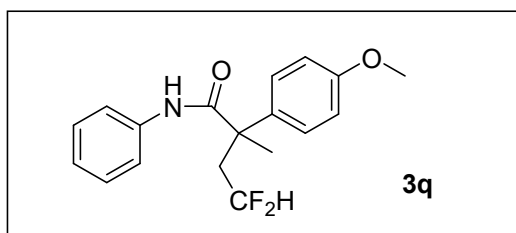


***N*-(3-bromo-4-methoxyphenyl)-4,4-difluoro-2-methyl-2-(*p*-tolyl)butanamide (3o).**

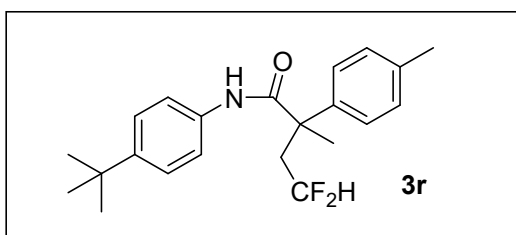
The title compound (31.2 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 76% yield. colourless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.53 (m, 1H), 7.36-7.34 (m, 1H), 7.32-7.27 (m, 4H), 6.85-6.83 (m, 1H), 6.70 (s, 1H), 5.82-5.58 (m, 1H), 3.89 (s, 3H), 2.73-2.69 (m, 1H), 2.54-2.42 (m, 1H), 2.42 (s, 3H), 1.79 (s, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 174.4, 153.0, 138.2, 131.3, 130.2, 126.6, 125.5, 120.6, 116.7 (t, $J = 239.4$ Hz), 111.8, 111.4, 56.5, 48.4, 43.4 (t, $J = 25.2$ Hz), 23.5, 21.1. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.11 (d, $J = 3.8$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{19}\text{H}_{20}\text{BrF}_2\text{NaNO}_3^+$ $[\text{M}+\text{Na}]^+$ 450.0487, found 450.0480.



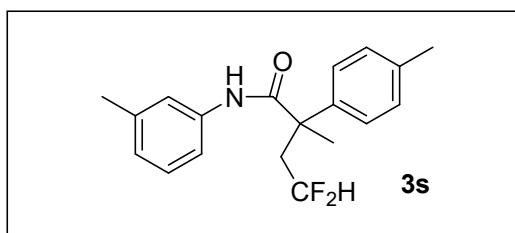
4,4-difluoro-2-methyl-*N*,2-di-*p*-tolylbutanamide (3p). The title compound (25.4 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 80% yield. white solid. m.p. 92.2-93.0 °C. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.29-7.26 (m, 2H), 7.24-7.20 (m, 4H), 7.08-7.06 (m, 2H), 6.72 (s, 1H), 5.83- 5.53(m, 1H), 2.75-2.62 (m, 1H), 2.54-2.41 (m, 1H), 2.37 (s, 3H), 2.28 (s, 3H), 1.76 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 174.2, 138.5, 137.9, 135.0, 134.2, 130.0, 129.4, 126.6, 120.0, 116.7 (t, $J = 232.3$ Hz), 48.4, 43.5 (t, $J = 20.2$ Hz), 23.5, 21.0, 20.8. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.03 (d, $J = 3.8$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{19}\text{H}_{22}\text{F}_2\text{NO}^+$ $[\text{M}+\text{H}]^+$ 318.1664, found 318.1660.



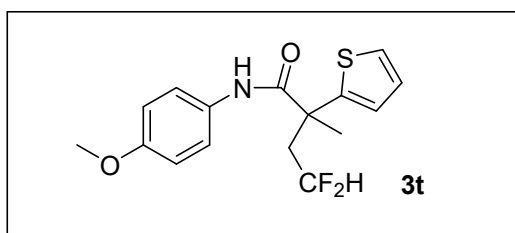
4,4-difluoro-2-(4-methoxyphenyl)-2-methyl-N-phenylbutanamide (3q). The title compound (21.7 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 68% yield. colourless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.35-7.31 (m, 4H), 7.29-7.26 (m, 2H), 7.10-7.06 (m, 1H), 6.97-6.95 (m, 2H), 6.78 (s, 1H), 5.83-5.52 (m, 1H), 3.84 (s, 3H), 2.71-2.64 (m, 1H), 2.55-2.46 (m, 1H), 1.77 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 174.4, 159.2, 137.5, 133.1, 129.0, 128.0, 124.5, 119.8, 116.7 (t, $J = 242.4$ Hz), 114.7, 55.4, 48.2, 43.5 (t, $J = 20.2$ Hz), 23.7. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.11 (d, $J = 3.1$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{18}\text{H}_{19}\text{F}_2\text{NaNO}_2^+$ [$\text{M}+\text{H}$] $^+$ 342.1276, found 342.1266.



N-(4-(tert-butyl)phenyl)-4,4-difluoro-2-methyl-2-(p-tolyl)butanamide (3r). The title compound (27.3 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 76% yield. Yellow liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.28-7.22 (m, 8H), 6.73 (s, 1H), 5.82-5.52 (m, 1H), 2.70-2.61(m, 1H), 2.54-2.44 (m, 1H), 2.36 (s, 3H), 1.75 (s, 3H), 1.26 (s, 9H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 174.2, 147.6, 138.5, 137.9, 134.9, 130.0, 126.6, 125.8, 119.6, 116.7 (t, $J = 242.4$ Hz), 48.4, 43.5 (t, $J = 20.2$ Hz), 34.4, 31.3, 23.5, 21.0. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.04 (d, $J = 3.2$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{22}\text{H}_{28}\text{F}_2\text{NO}_2^+$ [$\text{M}+\text{H}$] $^+$ 360.2133, found 360.2140.

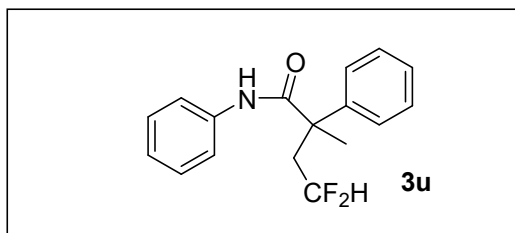


4,4-difluoro-2-methyl-N-(m-tolyl)-2-(p-tolyl)butanamide (3s). The title compound (22.8 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 72% yield. colourless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.29-7.20 (m, 5H), 7.17-7.08 (m, 2H), 6.90-6.89 (m, 1H), 6.74 (s, 1H), 5.84-5.53 (m, 1H), 2.71-2.65 (m, 1H), 2.51-2.45 (m, 1H), 2.37 (s, 3H), 2.29 (s, 3H), 1.76 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 174.3, 139.0, 138.4, 138.0, 137.5, 130.1, 128.8, 126.6, 125.3, 120.5, 116.9, 116.6 (t, $J = 232.3$ Hz), 48.5, 43.5 (t, $J = 20.2$ Hz), 23.5, 21.4, 21.0. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.03 (d, $J = 2.3$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{19}\text{H}_{21}\text{F}_2\text{NONa}^+$ $[\text{M}+\text{Na}]^+$ 340.1489, found 340.1489.

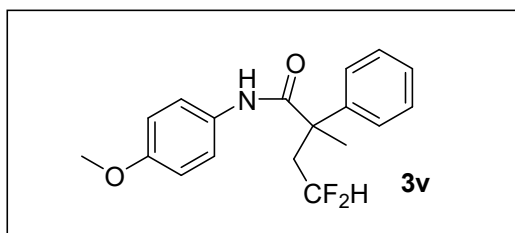


4,4-difluoro-N-(4-methoxyphenyl)-2-methyl-2-(thiophen-2-yl)butanamide(3t).

The title compound (23.1 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 71% yield. colourless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.38-7.37 (m, 1H), 7.26-7.24 (m, 2H), 7.12-7.08 (m, 2H), 7.06 (s, 1H), 6.83-6.81 (m, 2H), 6.00-5.70 (m, 1H), 3.77 (s, 3H), 2.85-2.74 (m, 1H), 2.60-2.50 (m, 1H), 1.84 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 172.4, 156.8, 146.4, 130.3, 127.6, 126.2, 125.9, 122.0, 116.3 (t, $J = 242.2$ Hz), 114.1, 55.5, 47.0, 44.1 (t, $J = 20.2$ Hz), 25.1. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.07. (d, $J = 2.3$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{16}\text{H}_{18}\text{F}_2\text{NOS}^+$ $[\text{M}+\text{H}]^+$ 326.1021, found 326.1029.



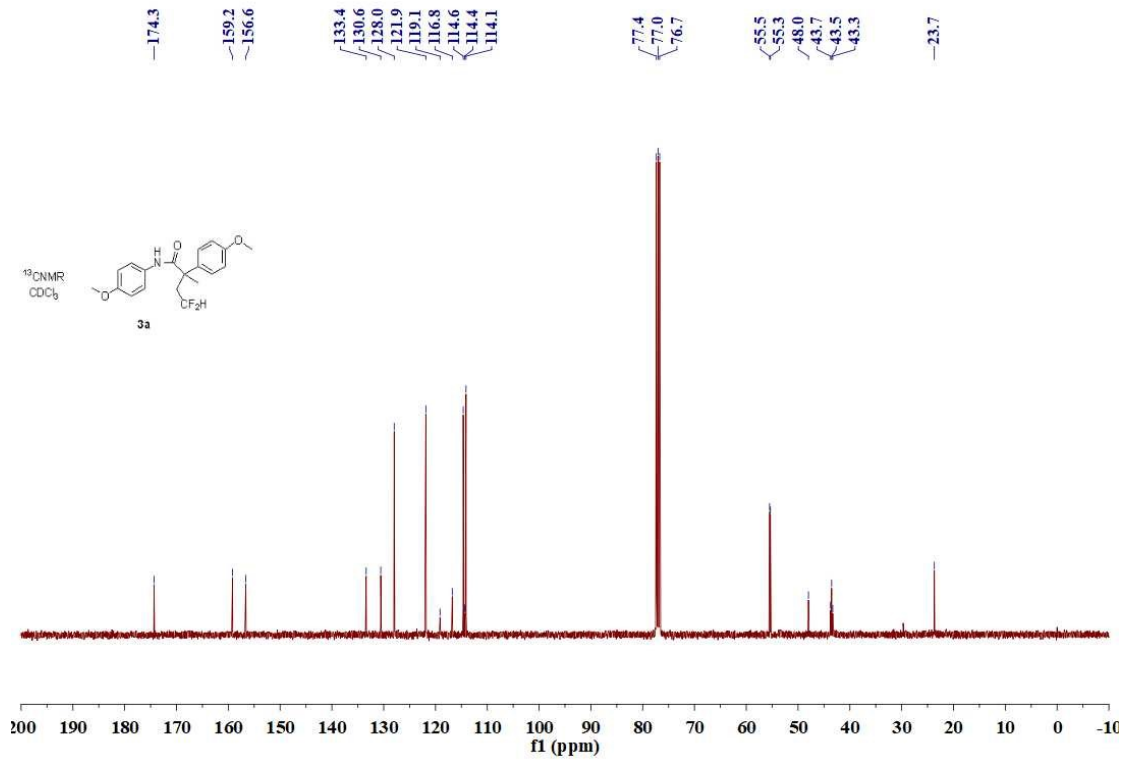
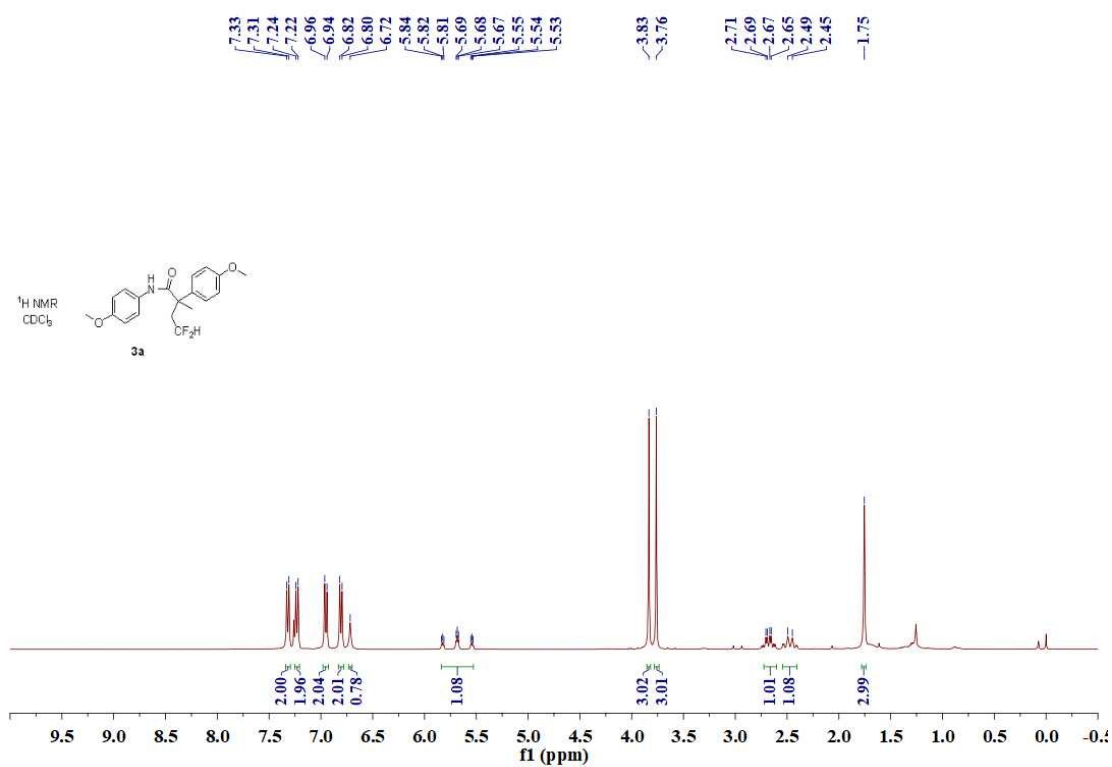
4,4-difluoro-2-methyl-N,2-diphenylbutanamide (3u). The title compound (12.4 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 43% yield. Yellow liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.47-7.42 (m, 5H), 7.35-7.27 (m, 5H), 6.74 (s, 1H), 5.86-5.56 (m, 1H), 2.80-2.65 (m, 1H), 2.54-2.44 (m, 1H), 1.80 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 174.0, 141.5, 137.5, 129.4, 129.0, 128.2, 126.7, 124.6, 119.9, 116.6 (t, $J = 232.3$ Hz), 48.8, 43.5 (t, $J = 20.2$ Hz), 23.4. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.08 (s). (d, $J = 2.3$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{17}\text{H}_{18}\text{F}_2\text{NO}^+$ [$\text{M}+\text{H}$] $^+$ 290.1351, found 290.1350.

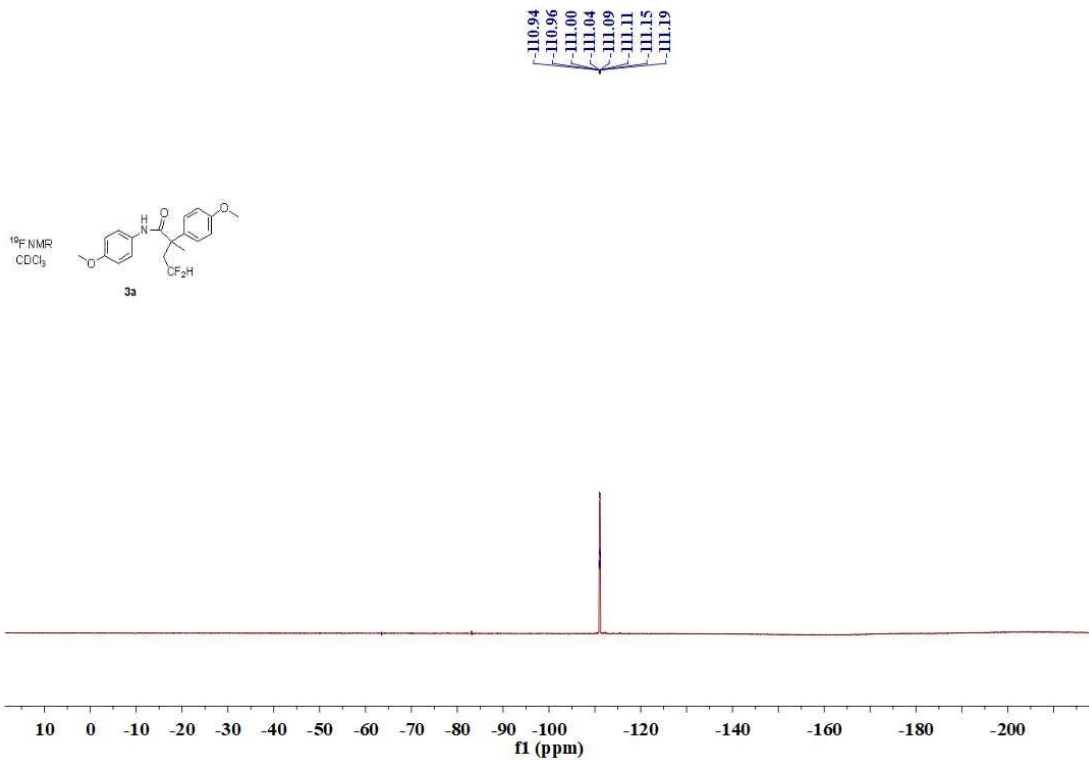


4,4-difluoro-N-(4-methoxyphenyl)-2-methyl-2-phenylbutanamide (3v). The title compound (15.0 mg) was isolated by flash chromatography (hexane : ethyl acetate = 20 : 1 to 4 : 1) in 47% yield. Colorless liquid. $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.46-7.36 (m, 5H), 7.24-7.22 (m, 2H), 6.82-6.80 (m, 2H), 6.70 (s, 1H), 5.86-5.56 (m, 1H), 3.76 (s, 3H), 2.73-2.68 (m, 1H), 2.52- 2.47 (m, 1H), 1.79 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 174.0, 156.7, 141.7, 130.5, 129.4, 128.1, 126.7, 122.0, 116.7 (t, $J = 242.4$ Hz), 114.1, 55.5, 48.6, 43.5 (t, $J = 20.2$ Hz), 23.5. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -111.02 (d, $J = 2.4$ Hz, 2F). HRMS(m/z)(ESI): calcd for $\text{C}_{18}\text{H}_{20}\text{F}_2\text{NO}^+$ [$\text{M}+\text{H}$] $^+$ 320.1457, found 320.1460.

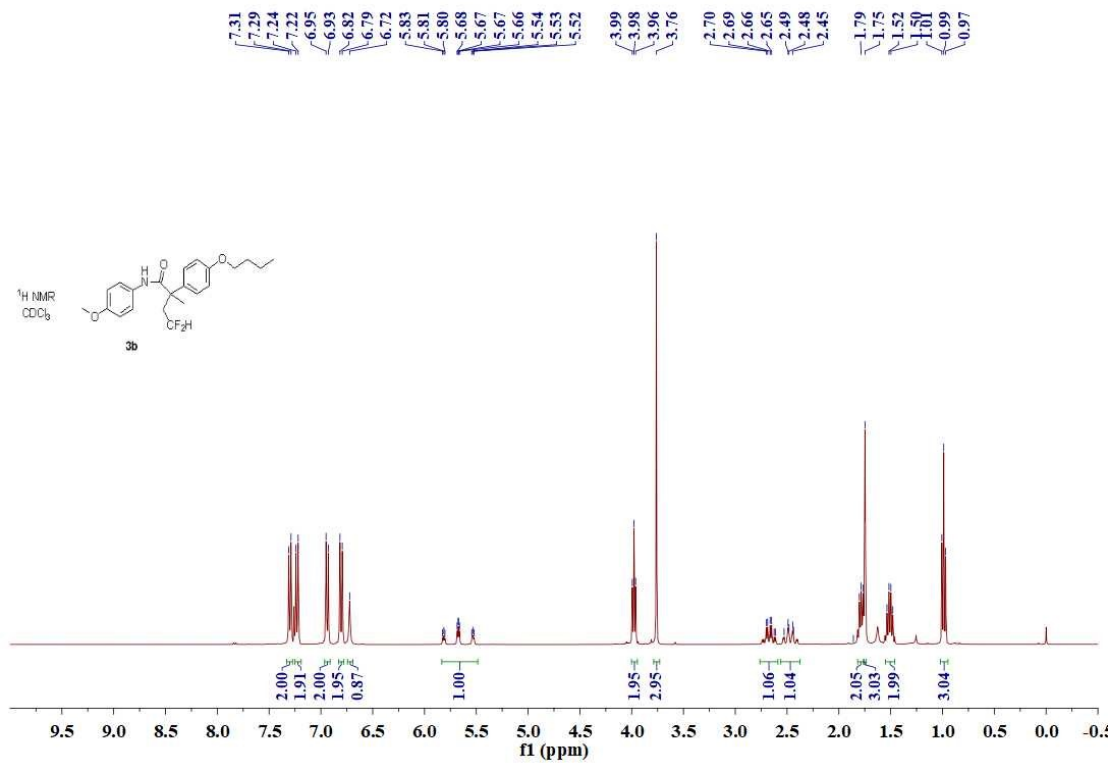
9. Copies of the NMR spectra

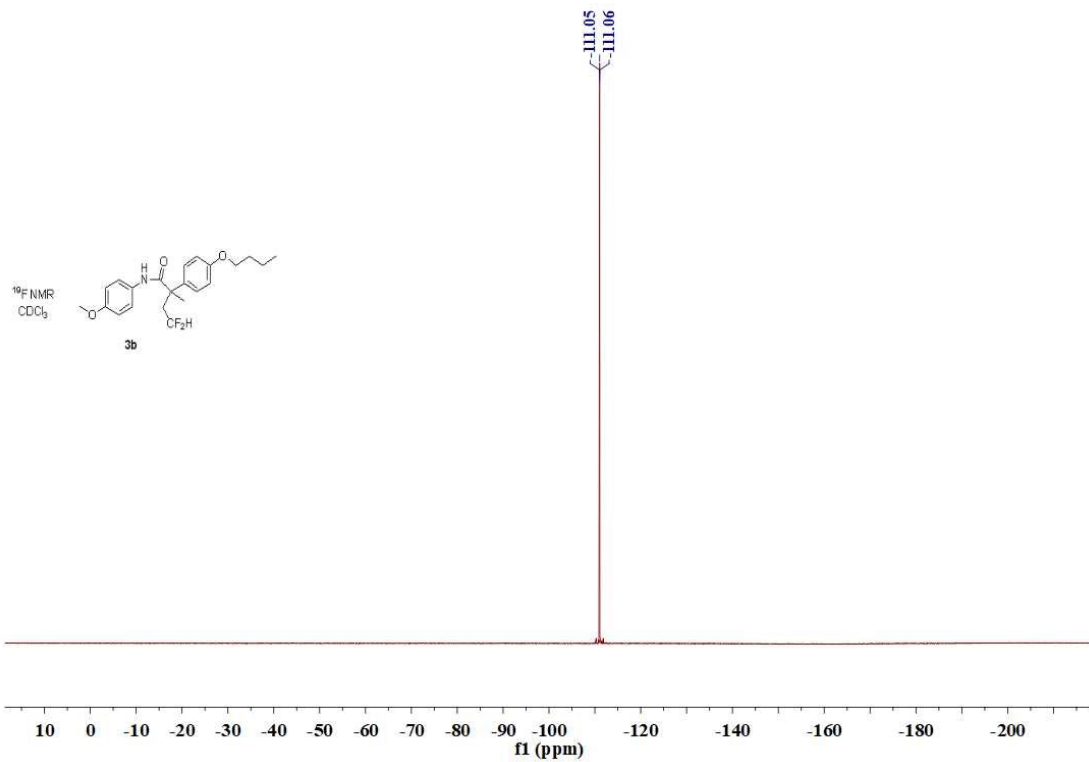
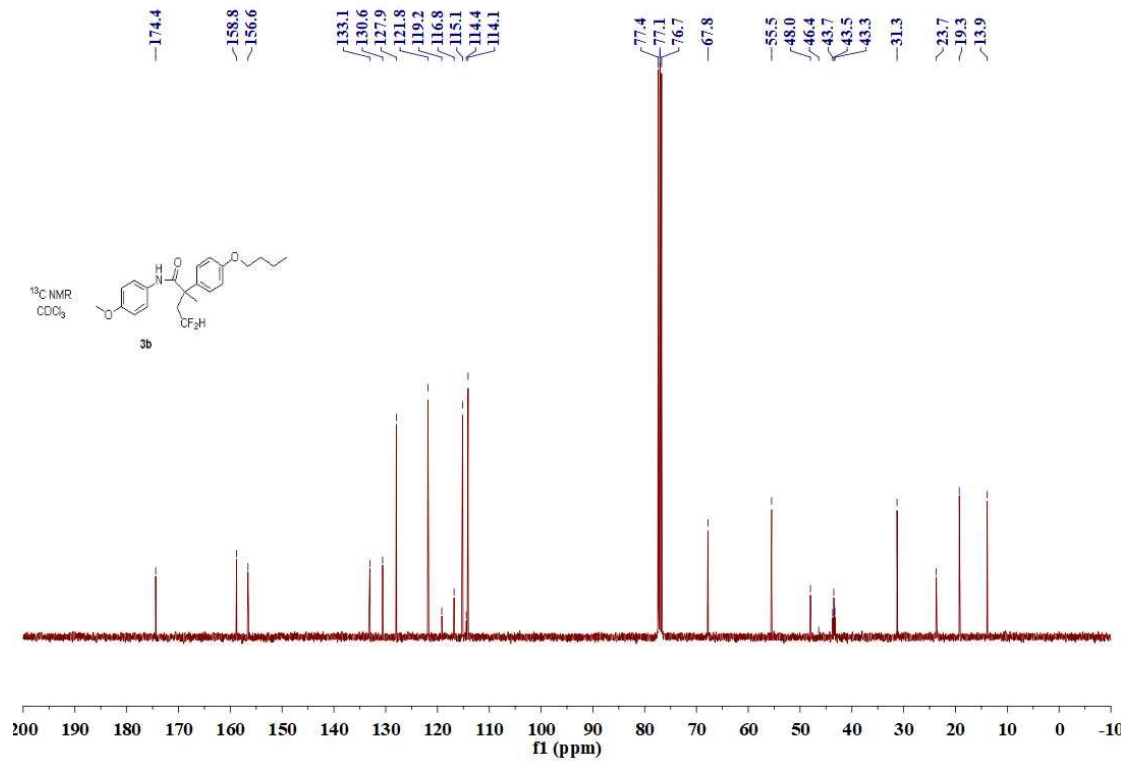
4,4-difluoro-*N*,2-bis(4-methoxyphenyl)-2-methylbutanamide (3a).



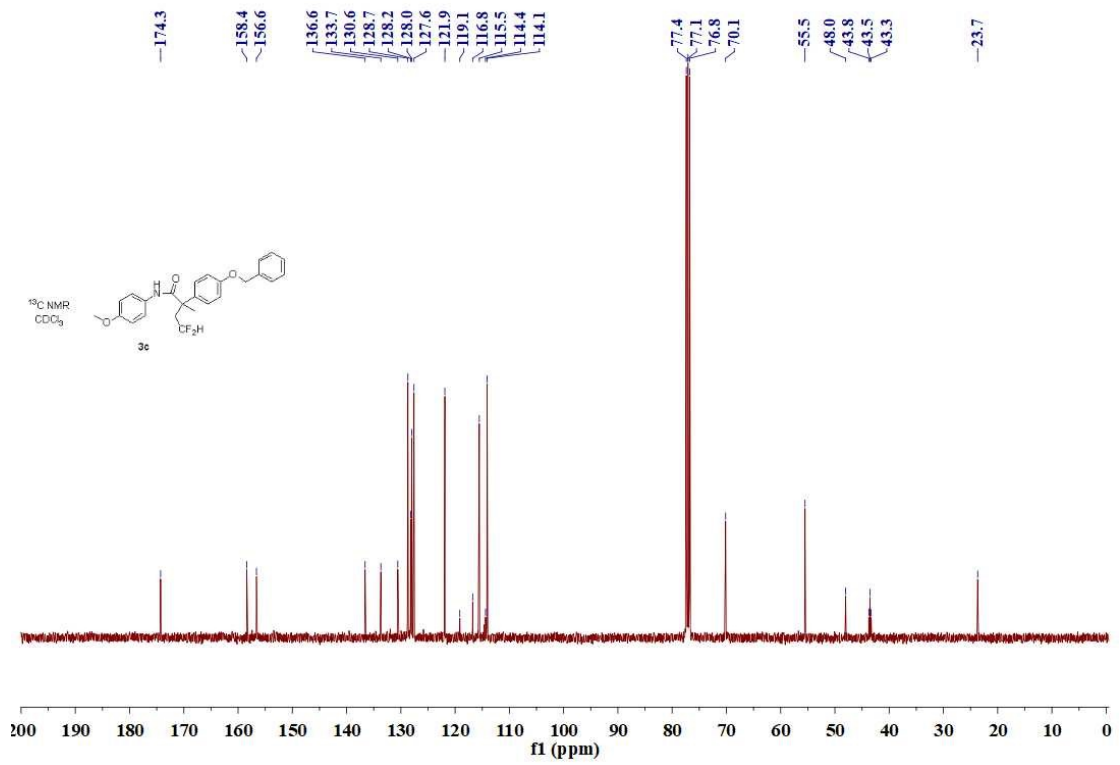
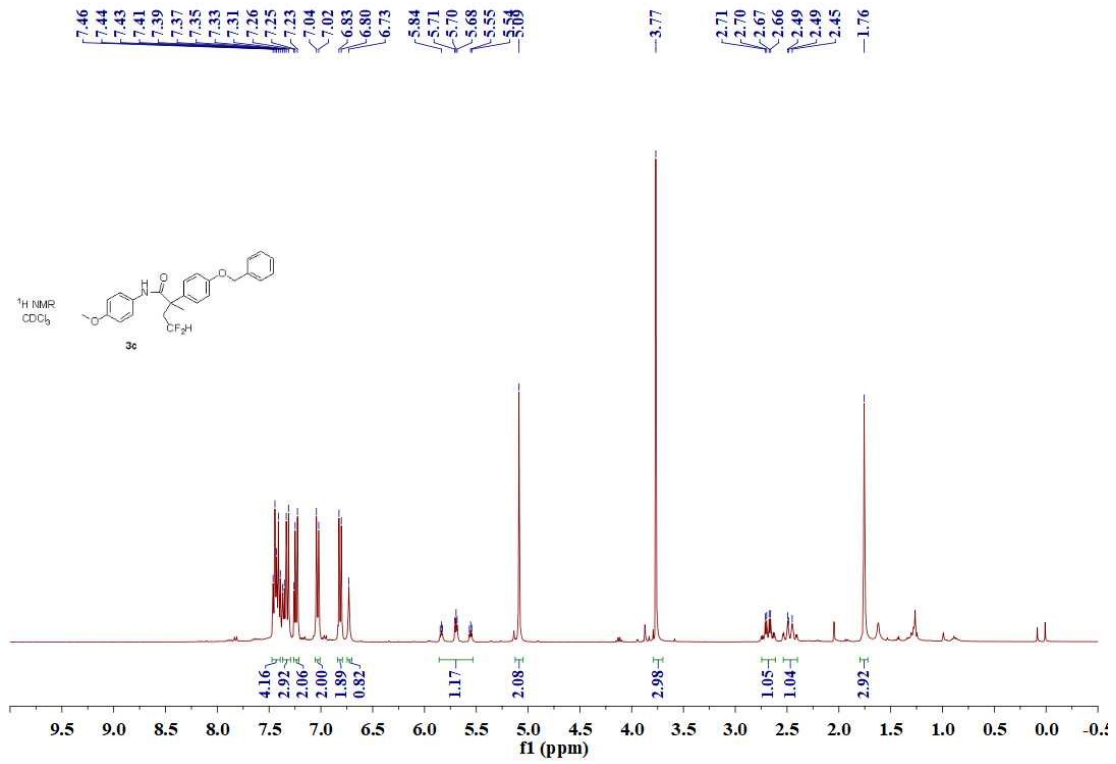


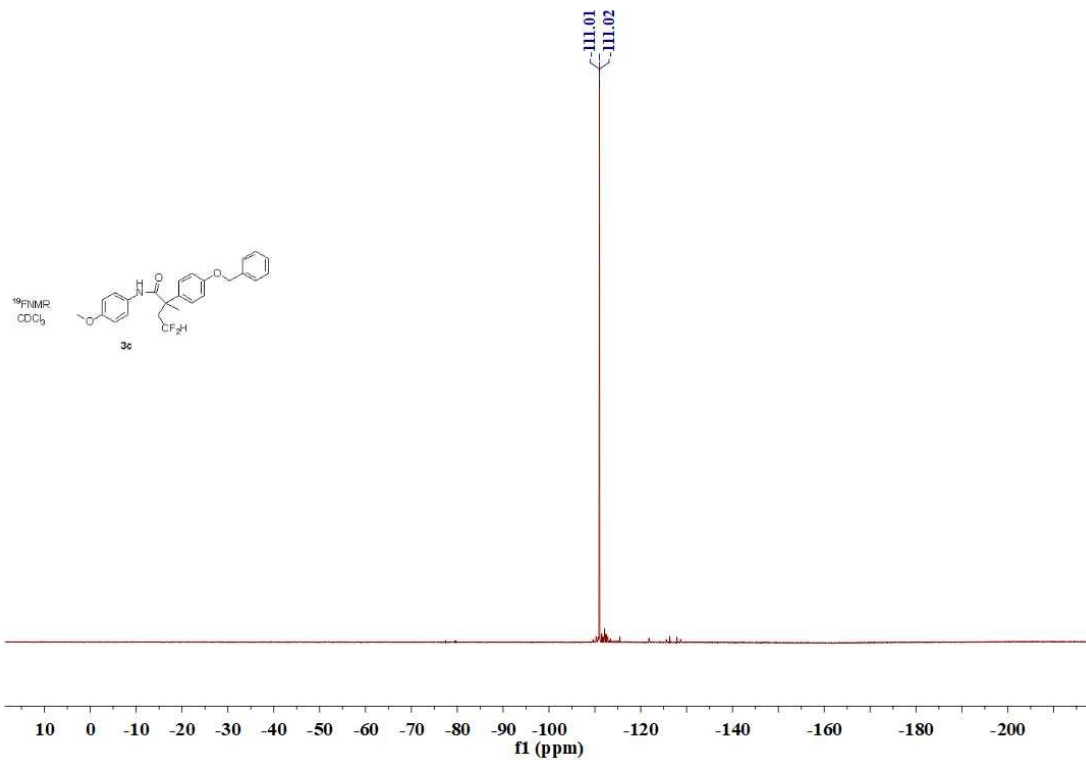
2-(4-butoxyphenyl)-4,4-difluoro-N-(4-methoxyphenyl)-2-methylbutanamide (3b).



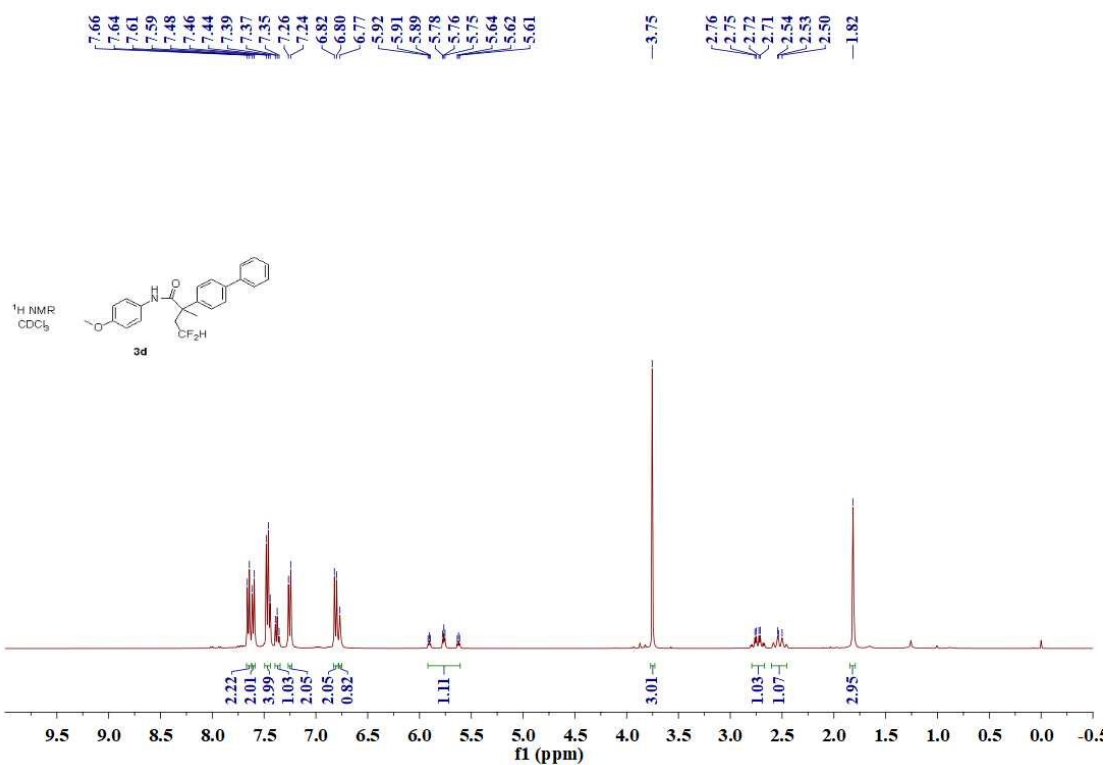


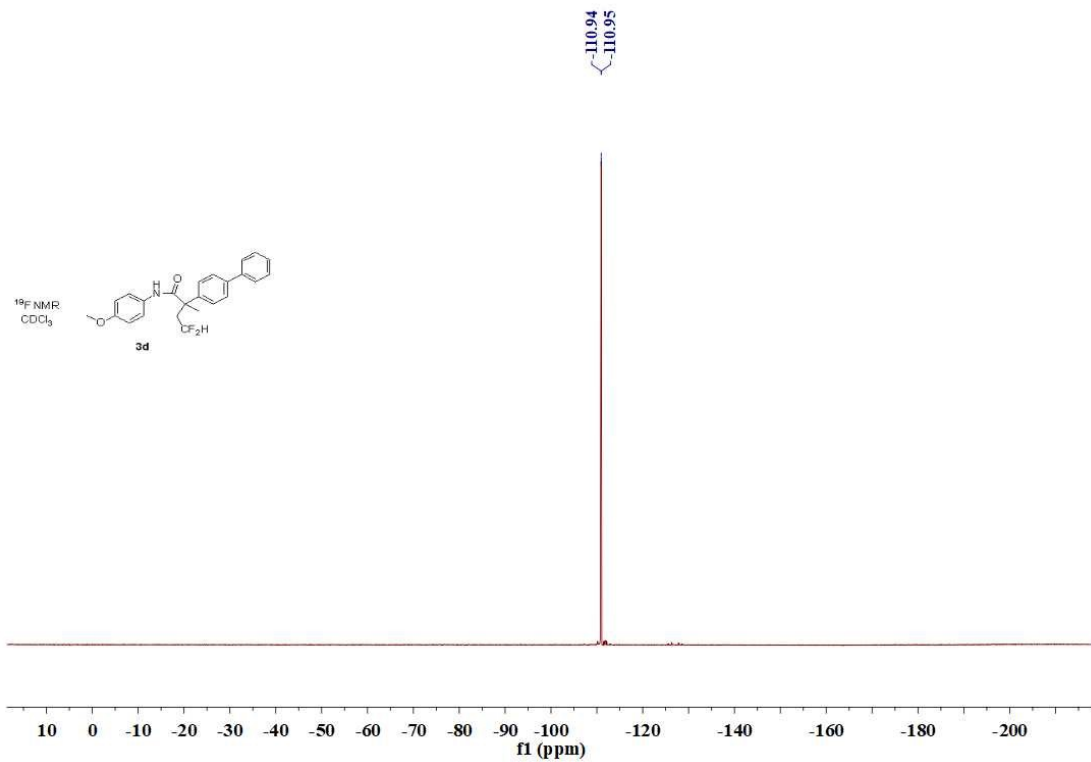
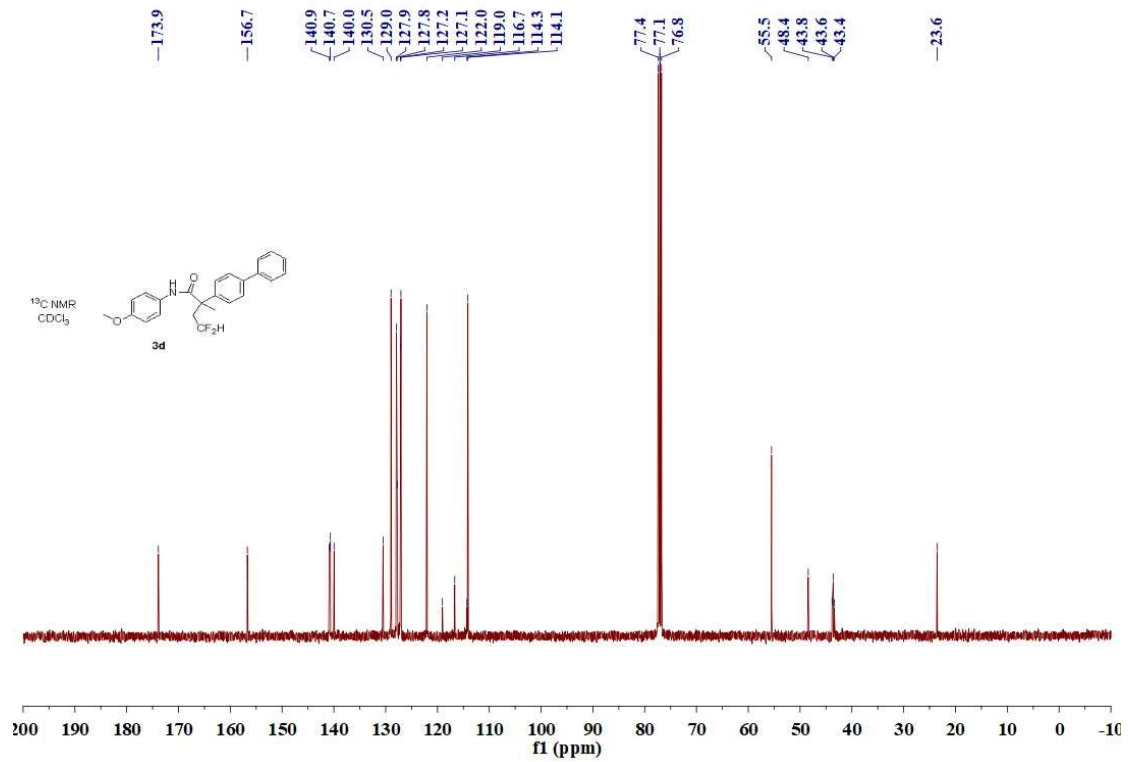
2-(4-(benzyloxy)phenyl)-4,4-difluoro-N-(4-methoxyphenyl)-2-methylbutanamide (3c).



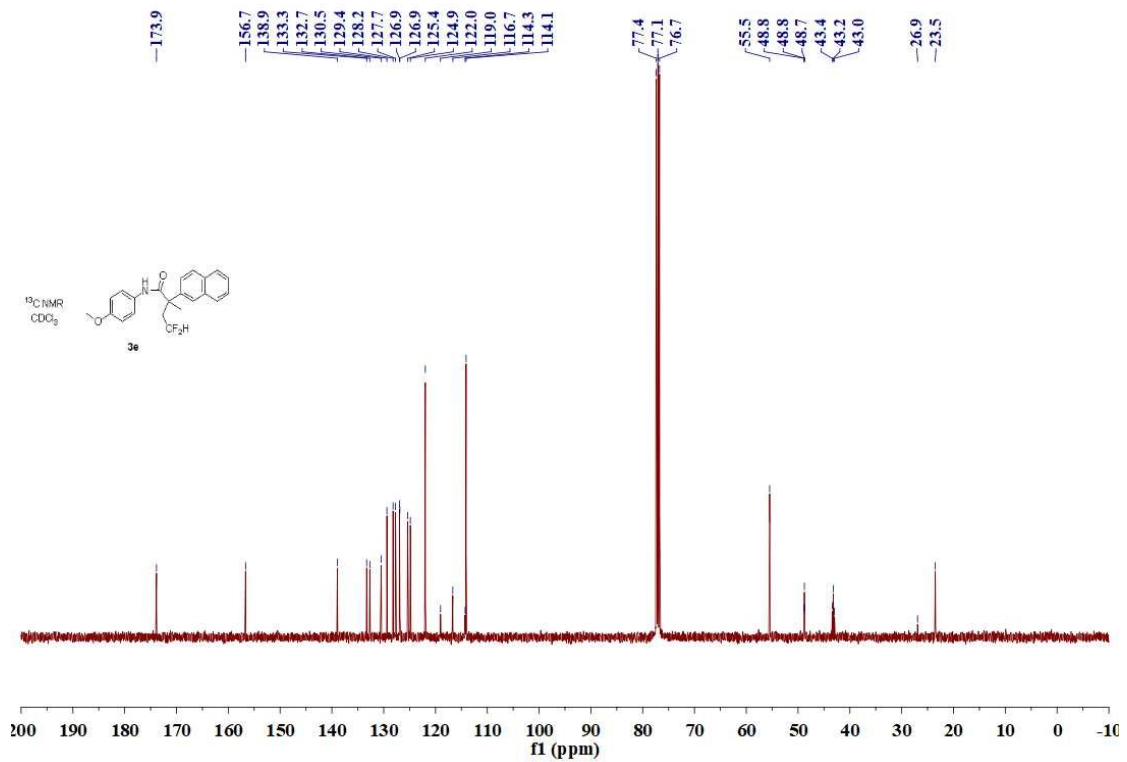
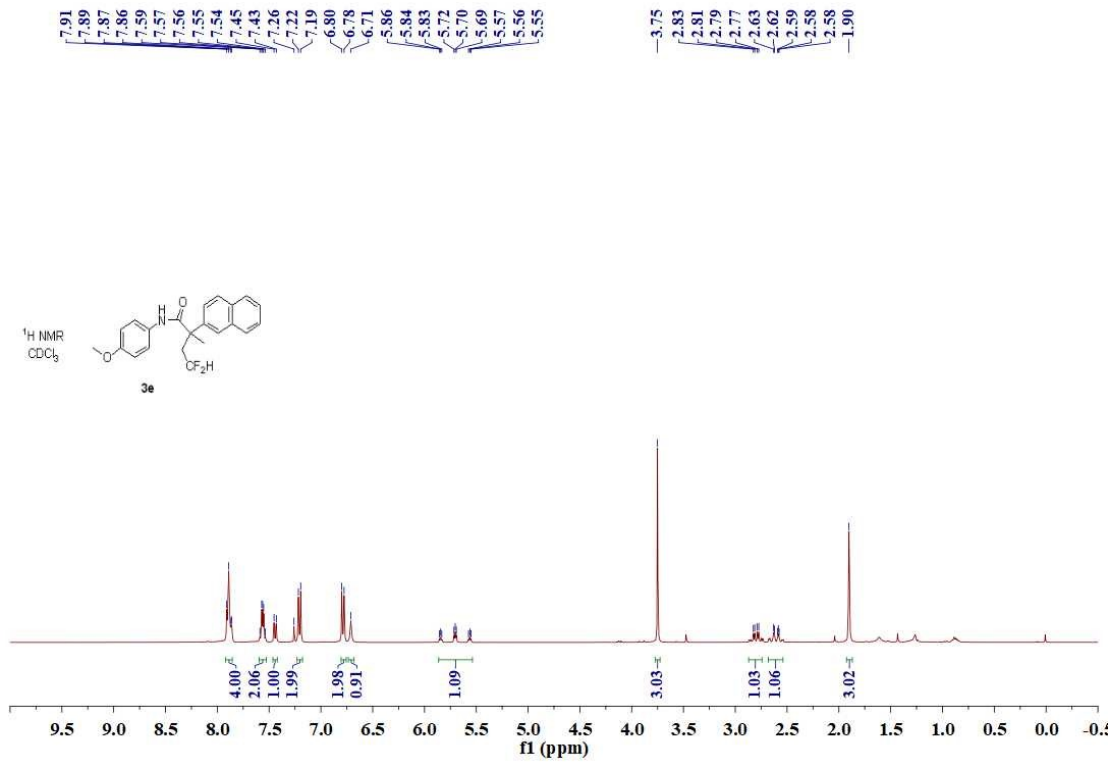


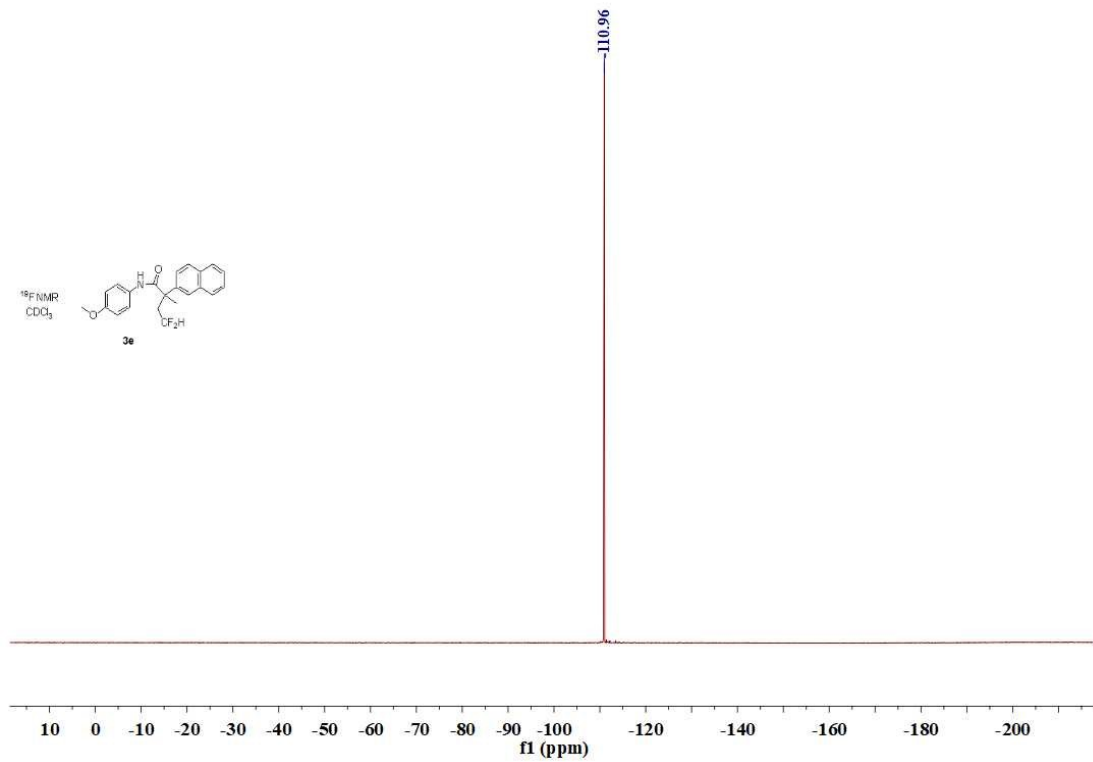
2-([1,1'-biphenyl]-4-yl)-4,4-difluoro-N-(4-methoxyphenyl)-2-methylbutanamide (3d).



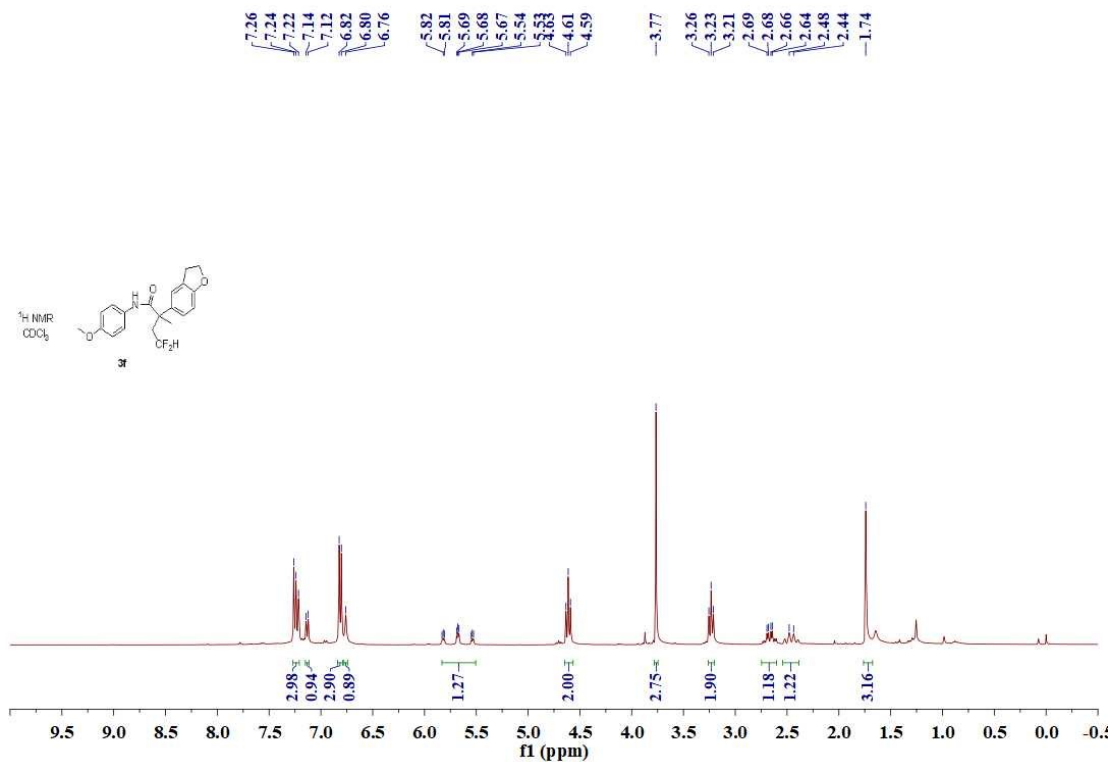


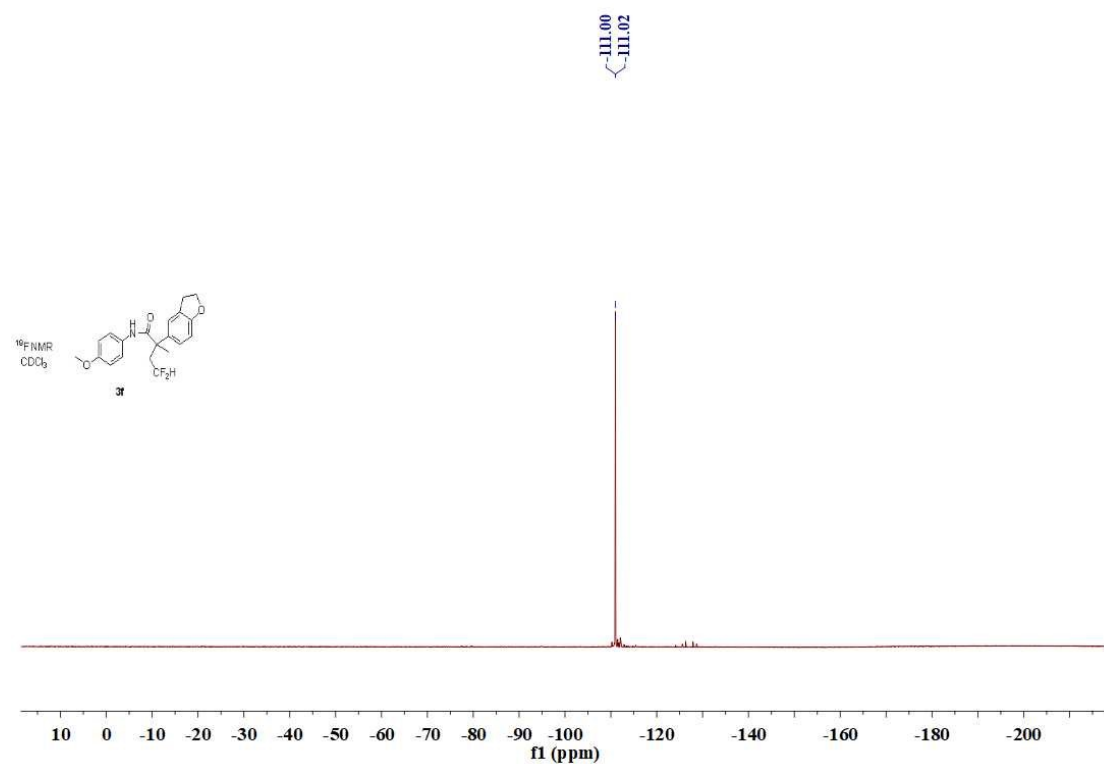
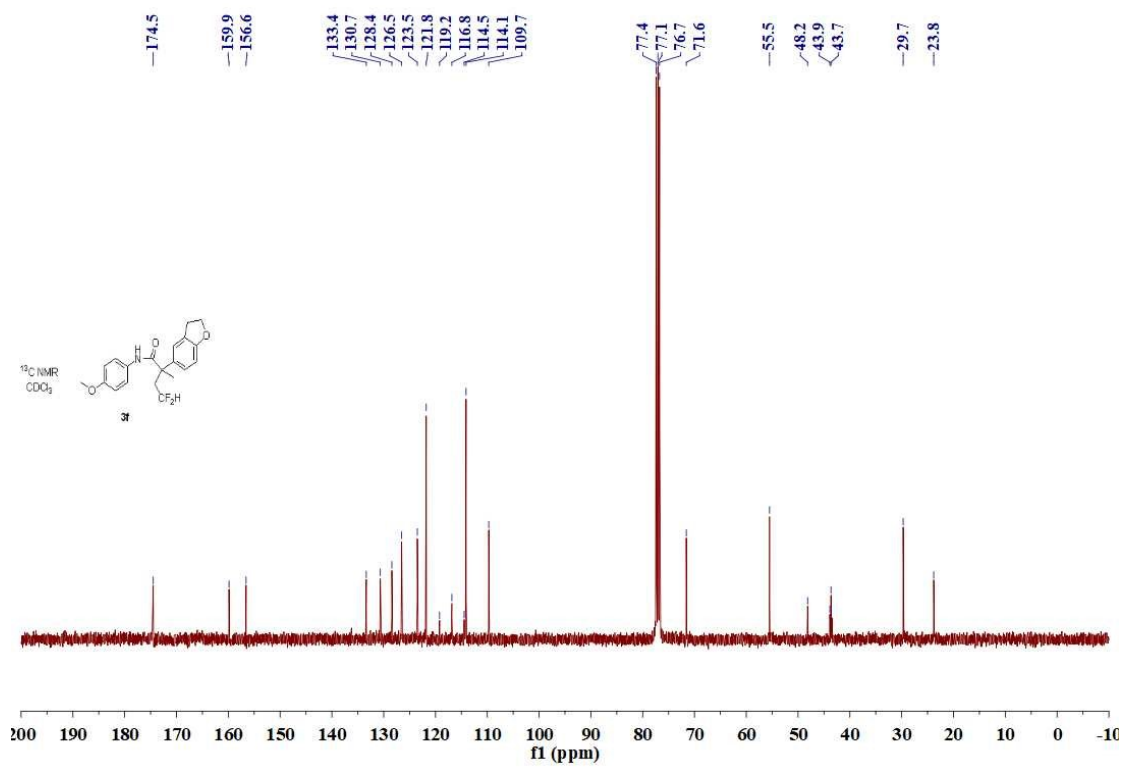
4,4-difluoro-*N*-(4-methoxyphenyl)-2-methyl-2-(naphthalen-2-yl)butanamide (3e).



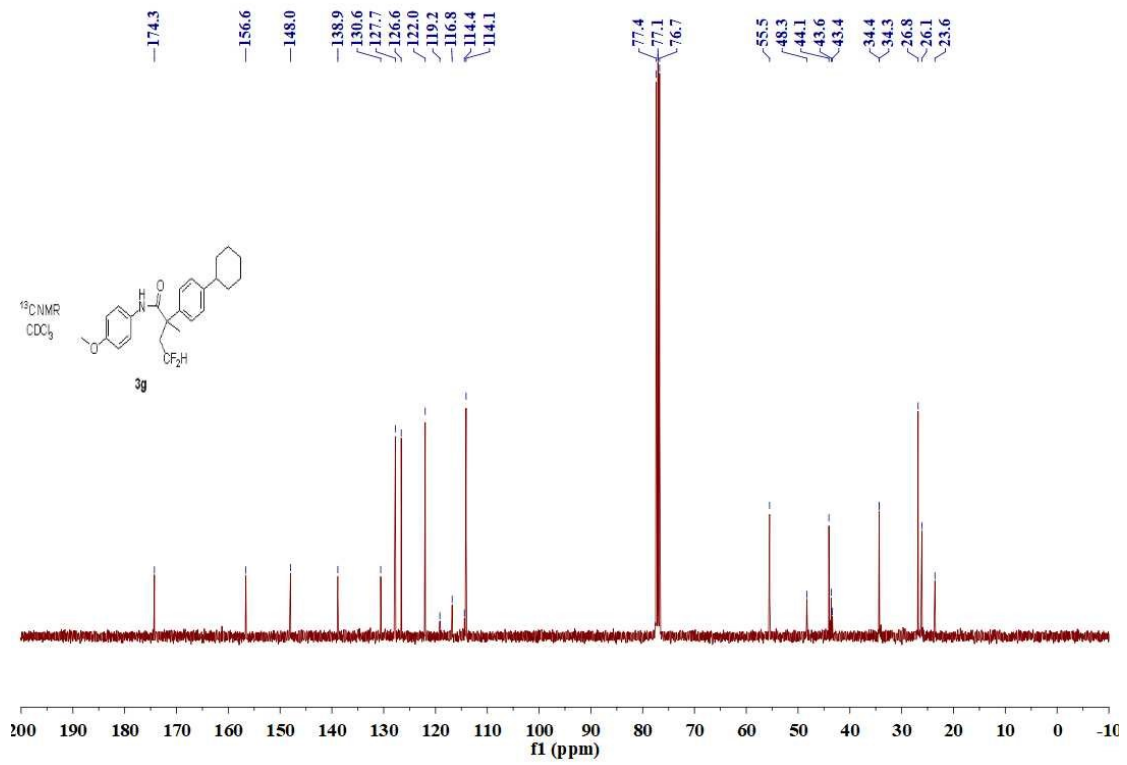
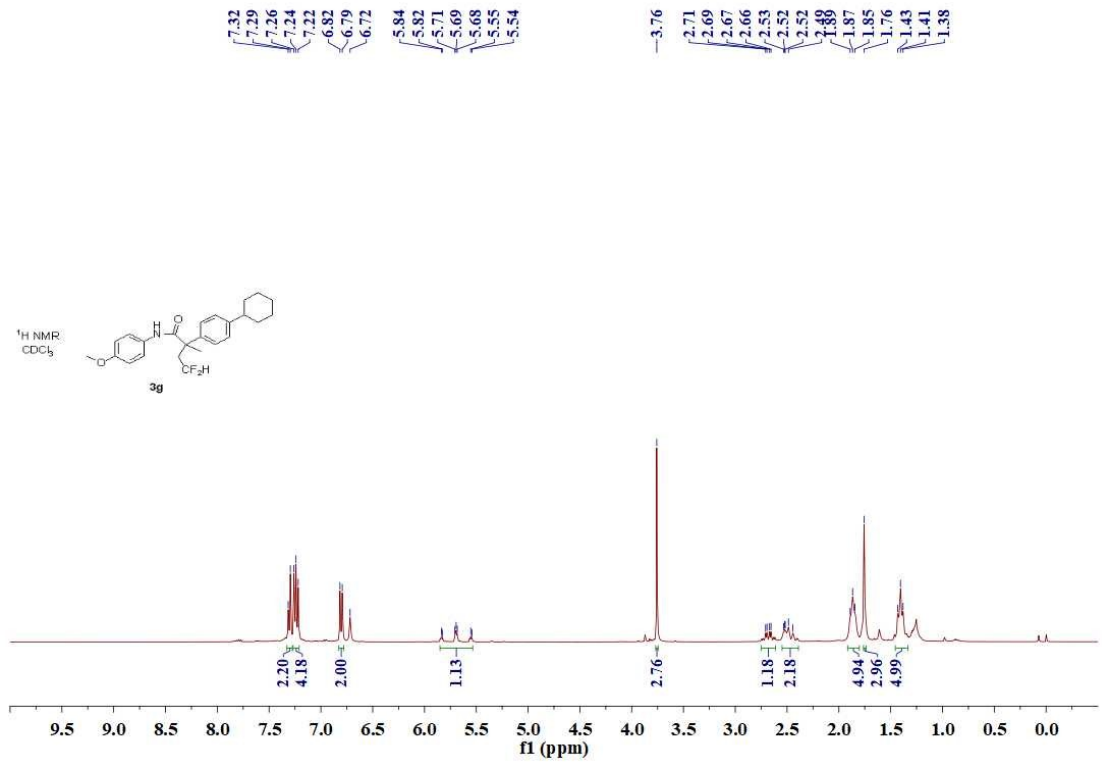


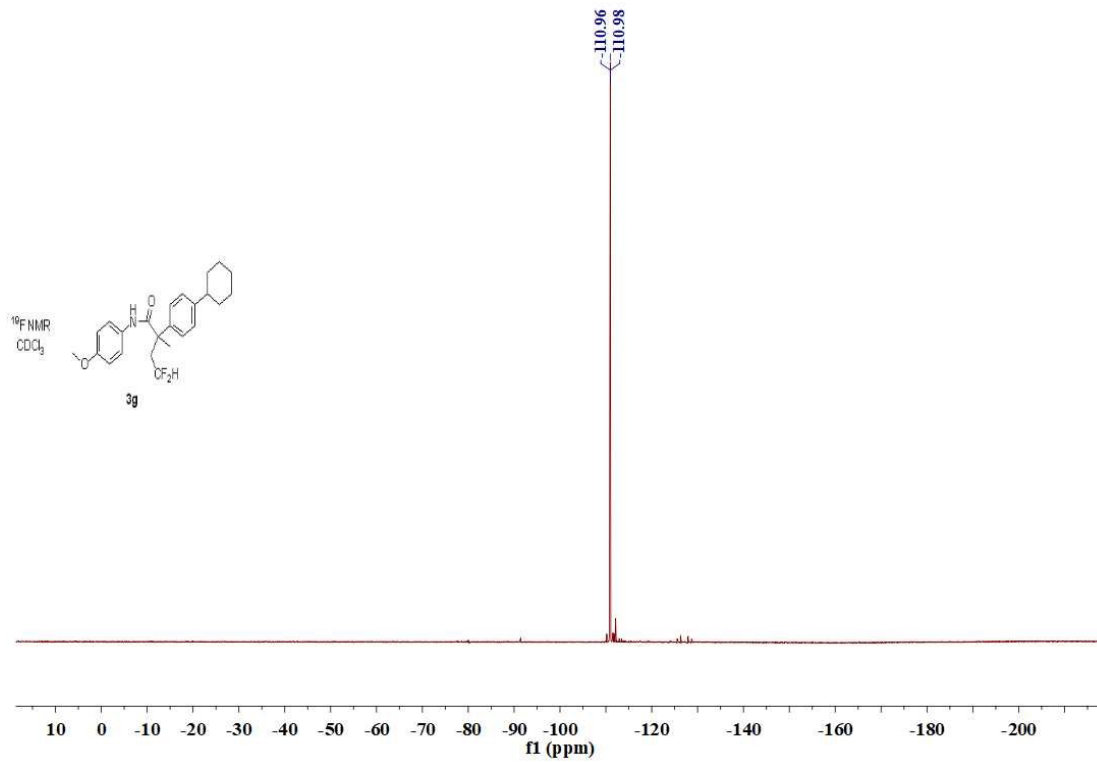
2-(2,3-dihydrobenzofuran-5-yl)-4,4-difluoro-*N*-(4-methoxyphenyl)-2-methylbutanamide (3f).



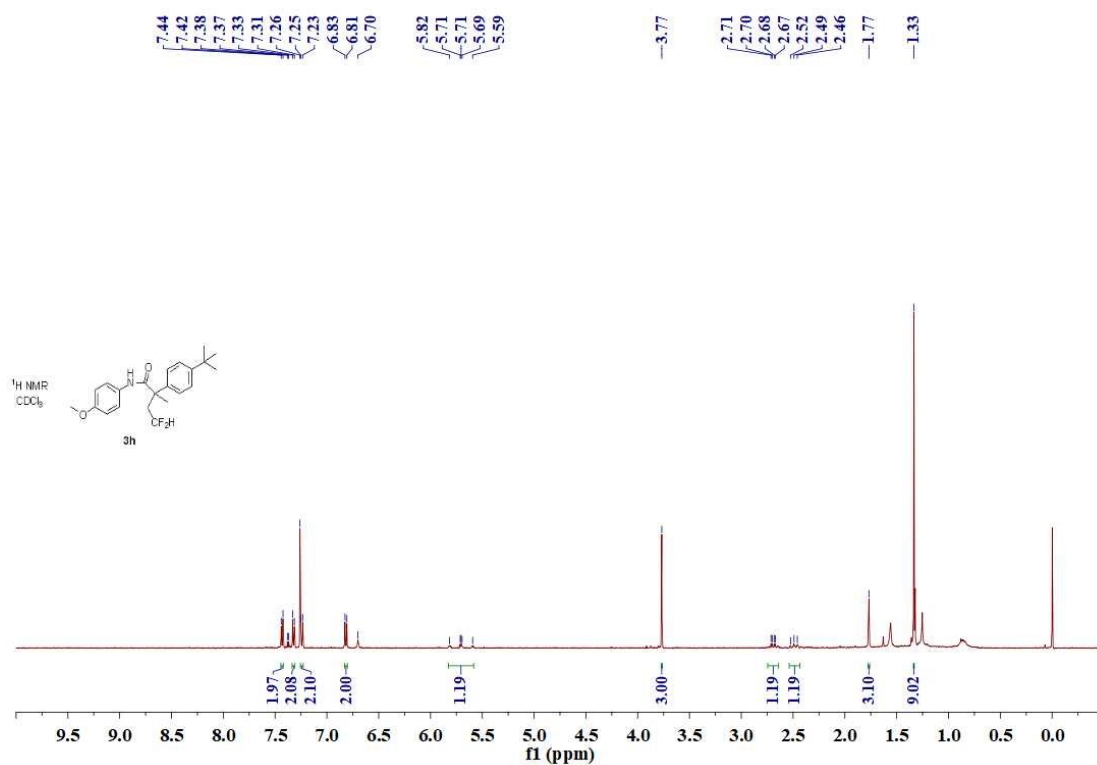


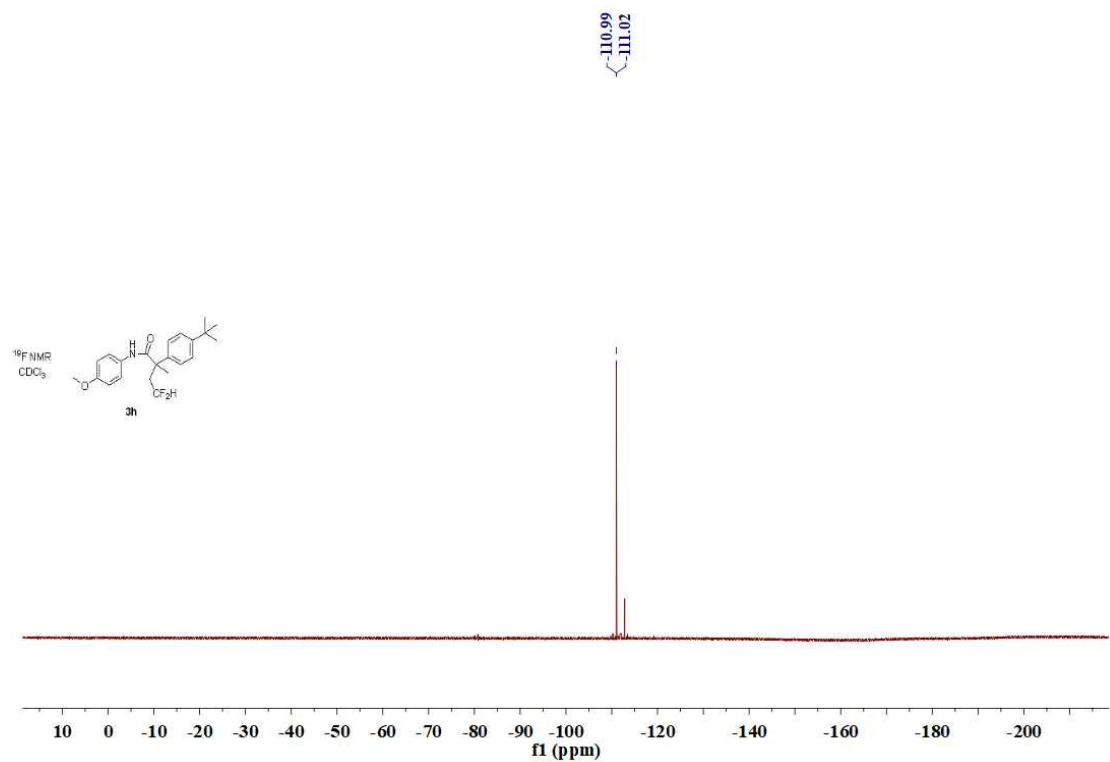
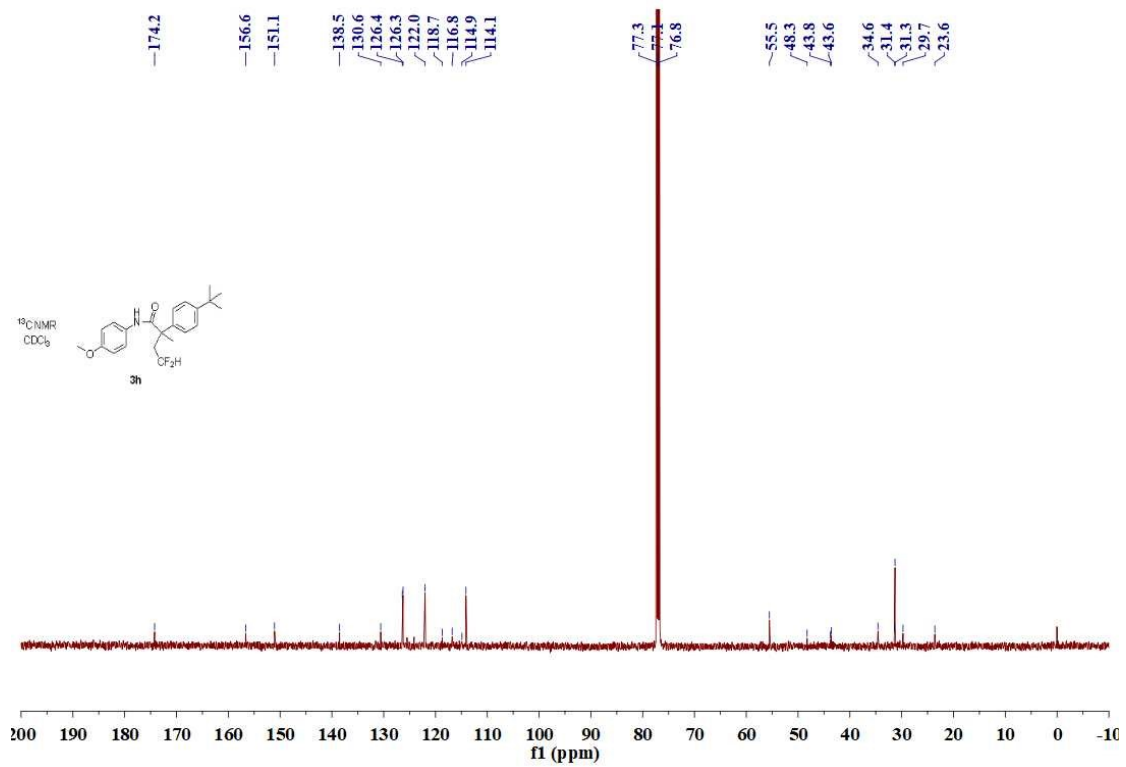
2-(4-cyclohexylphenyl)-4,4-difluoro-N-(4-methoxyphenyl)-2-methylbutanamide (3g).



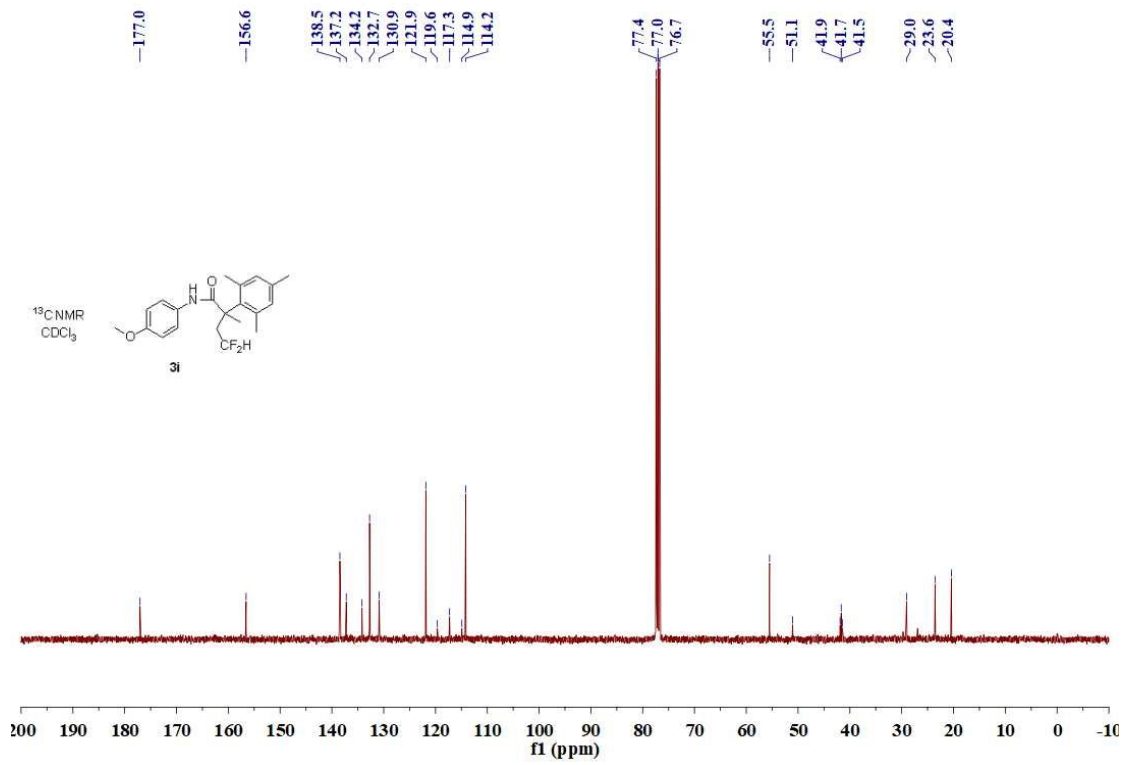
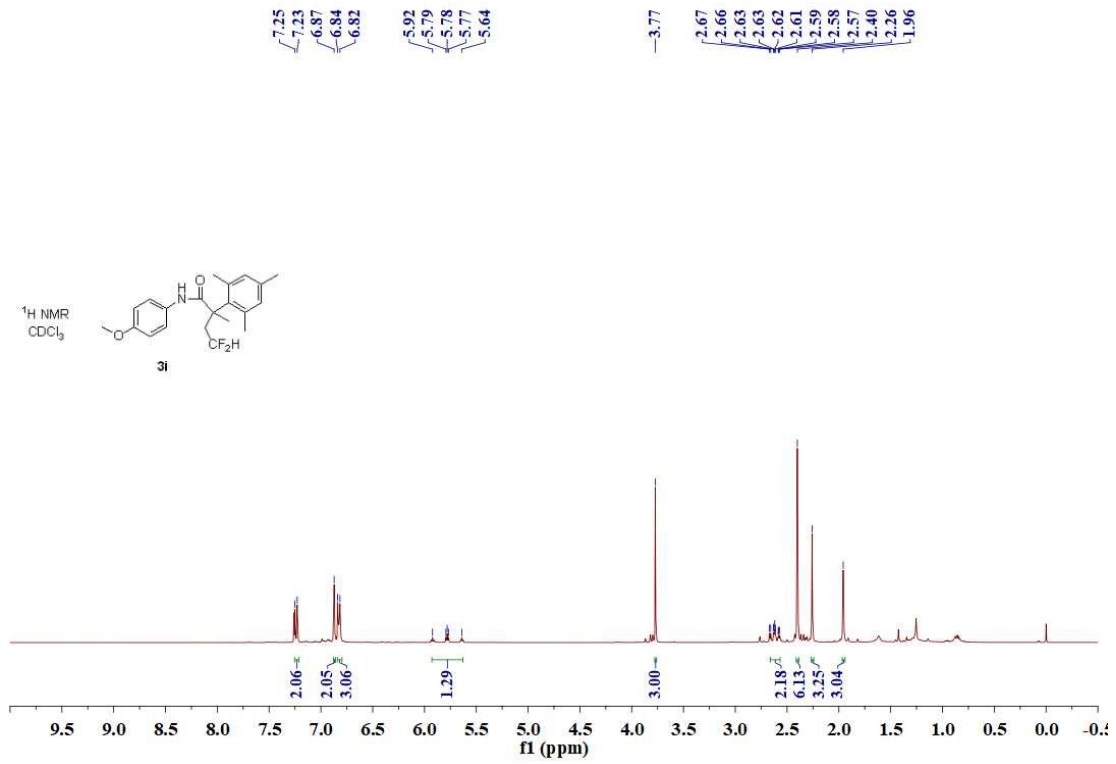


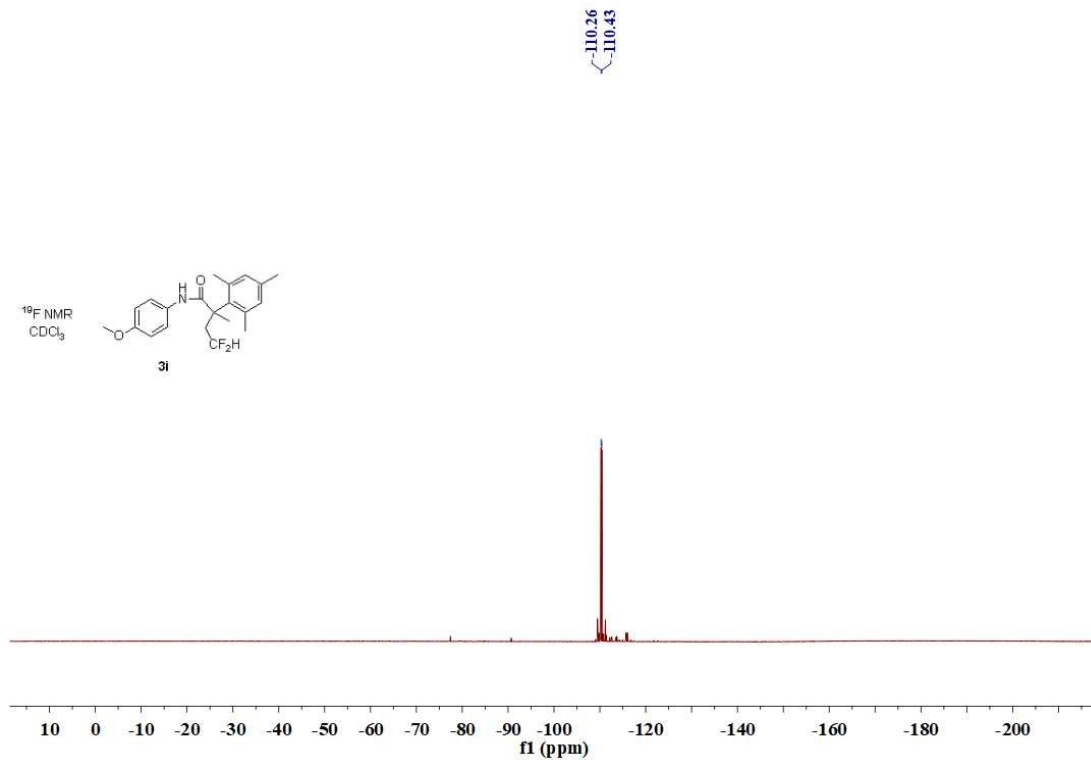
2-(4-(tert-butyl)phenyl)-4,4-difluoro-N-(4-methoxyphenyl)-2-methylbutanamide (3h).



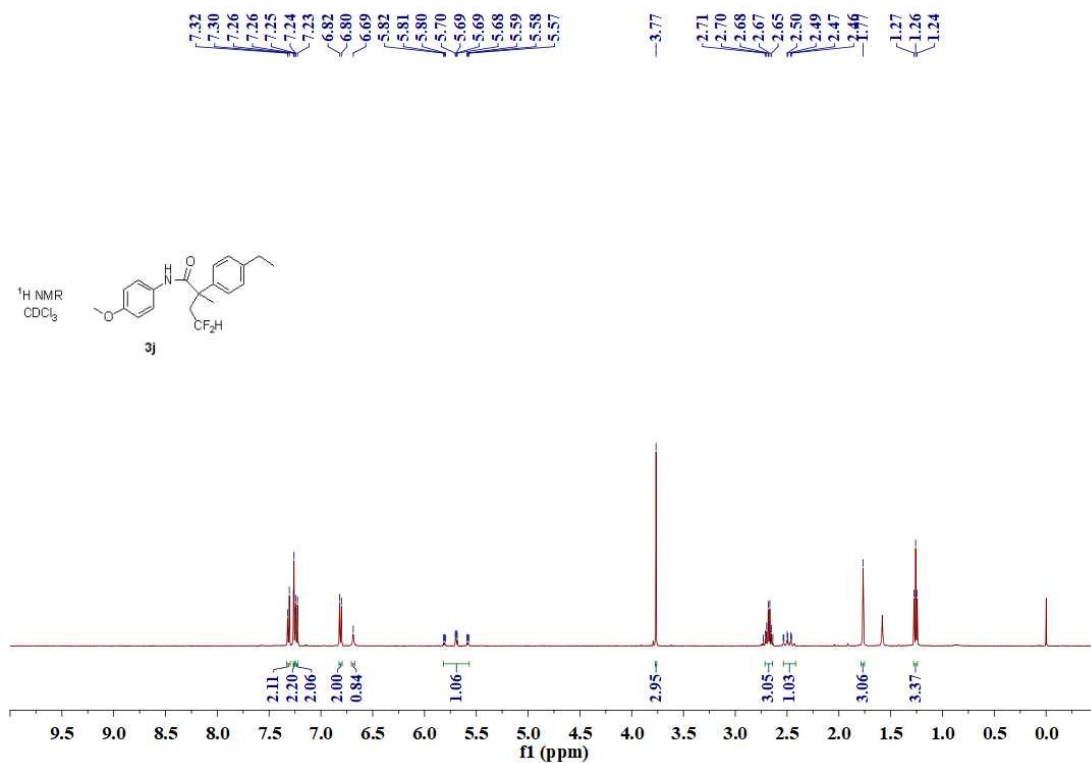


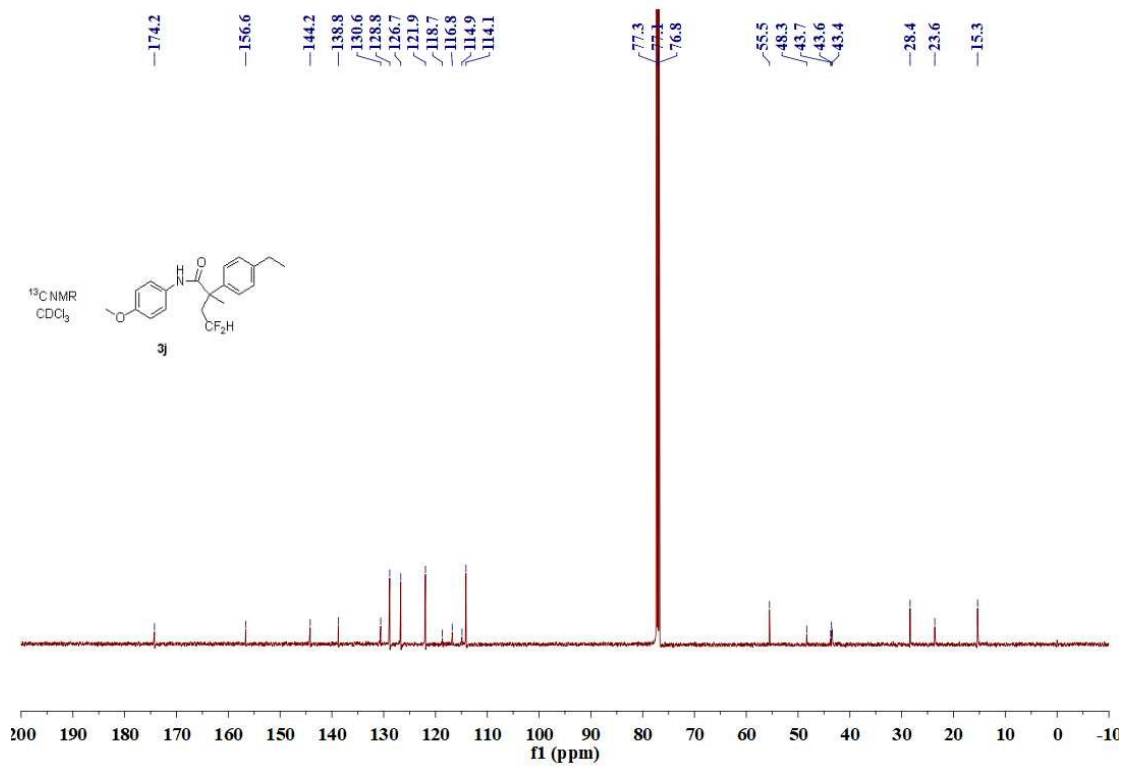
4,4-difluoro-2-mesityl-*N*-(4-methoxyphenyl)-2-methylbutanamide (3i).



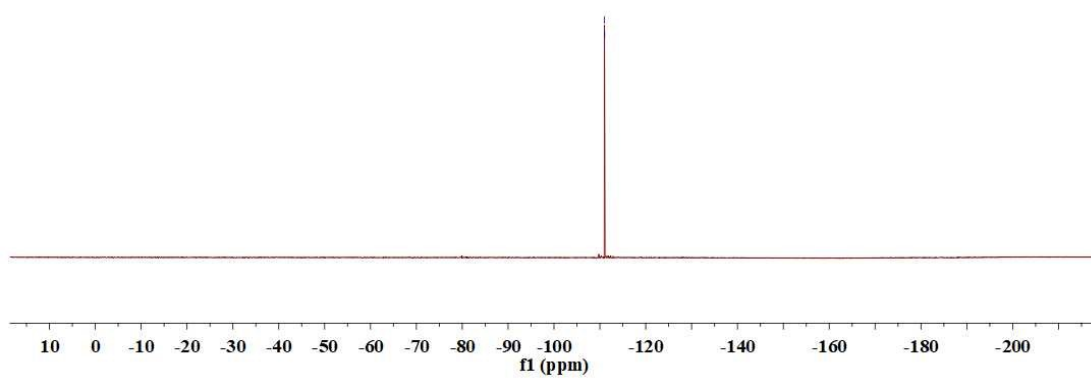


2-(4-ethylphenyl)-4,4-difluoro-N-(4-methoxyphenyl)-2-methylbutanamide (3j).

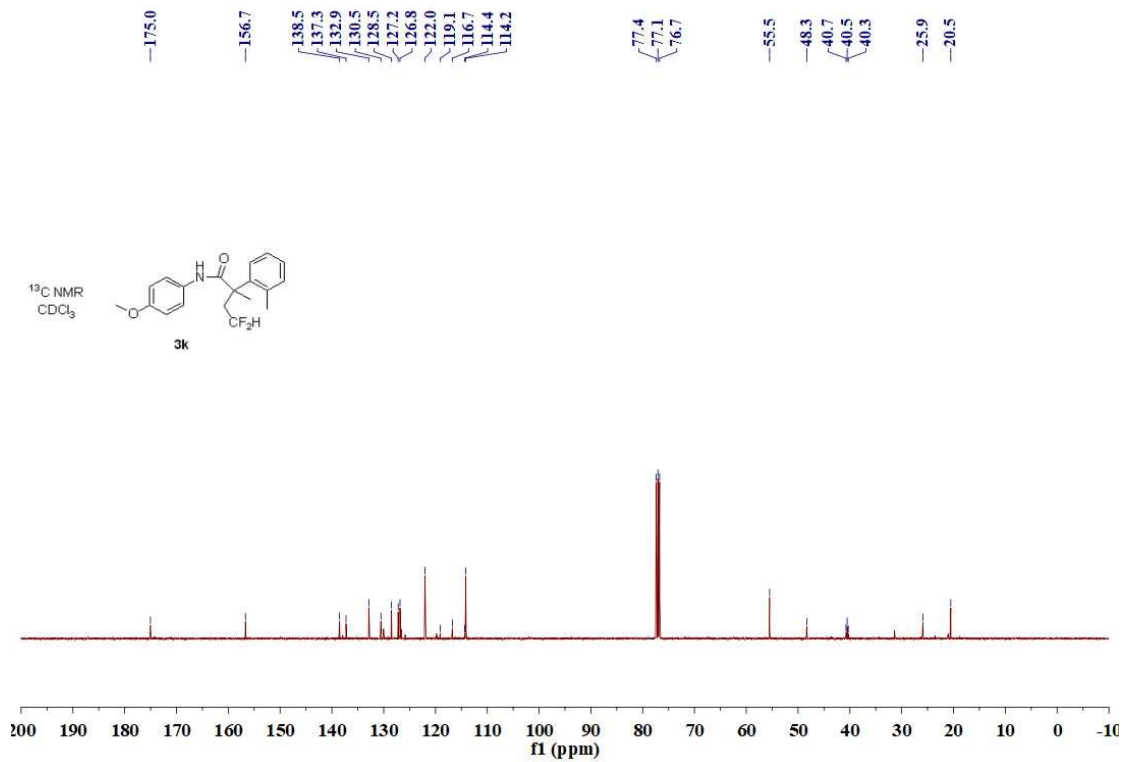
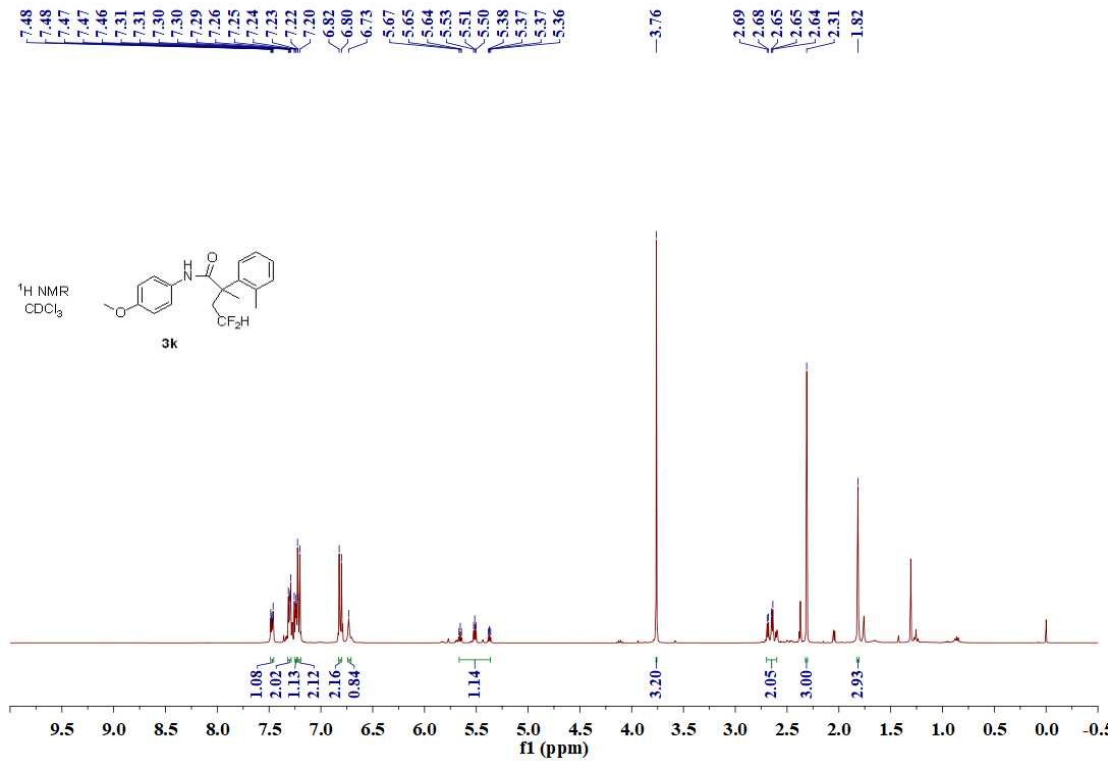


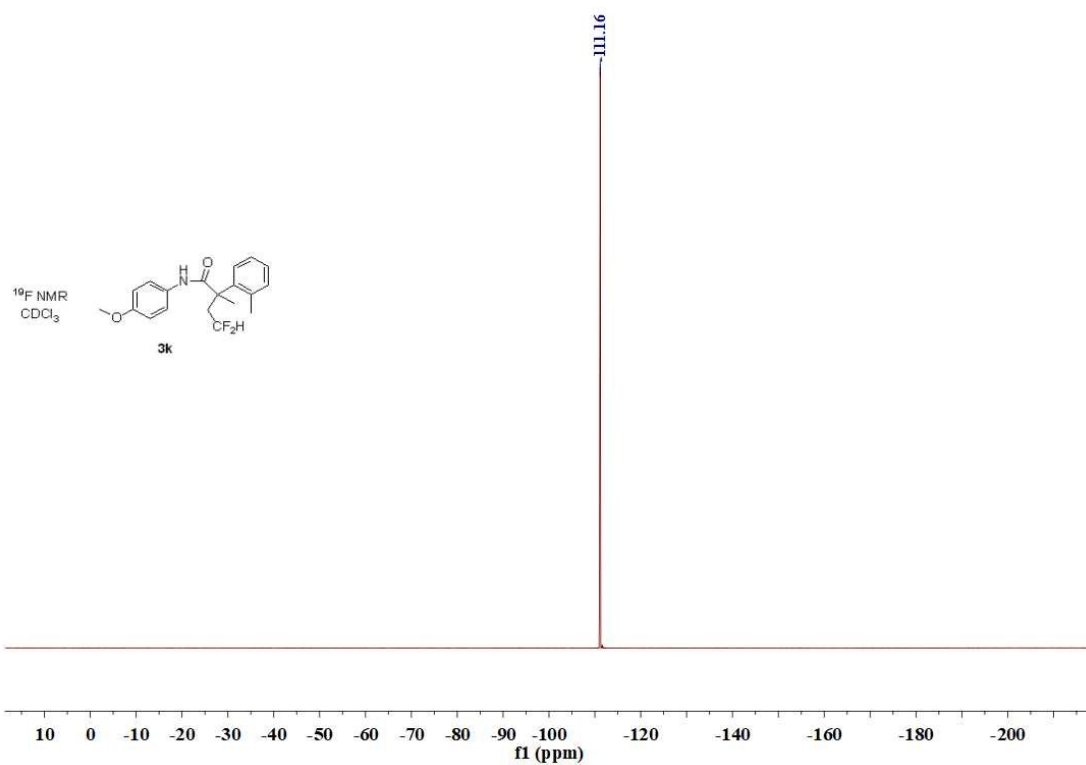


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111.03

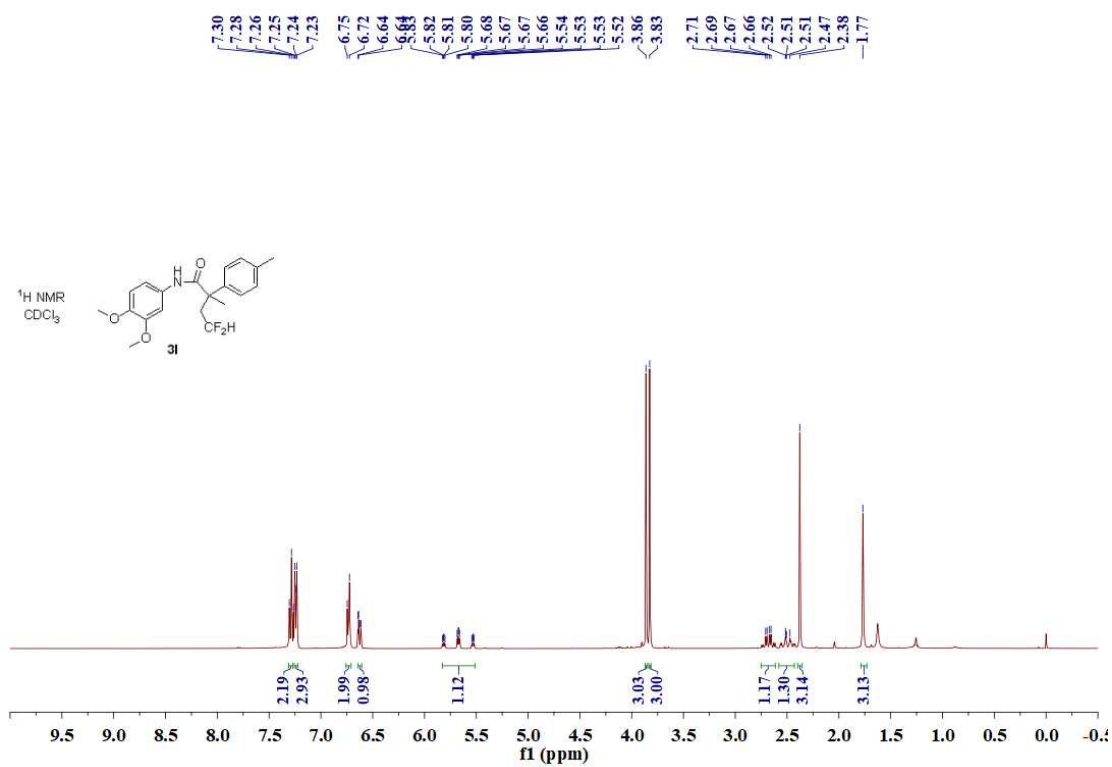


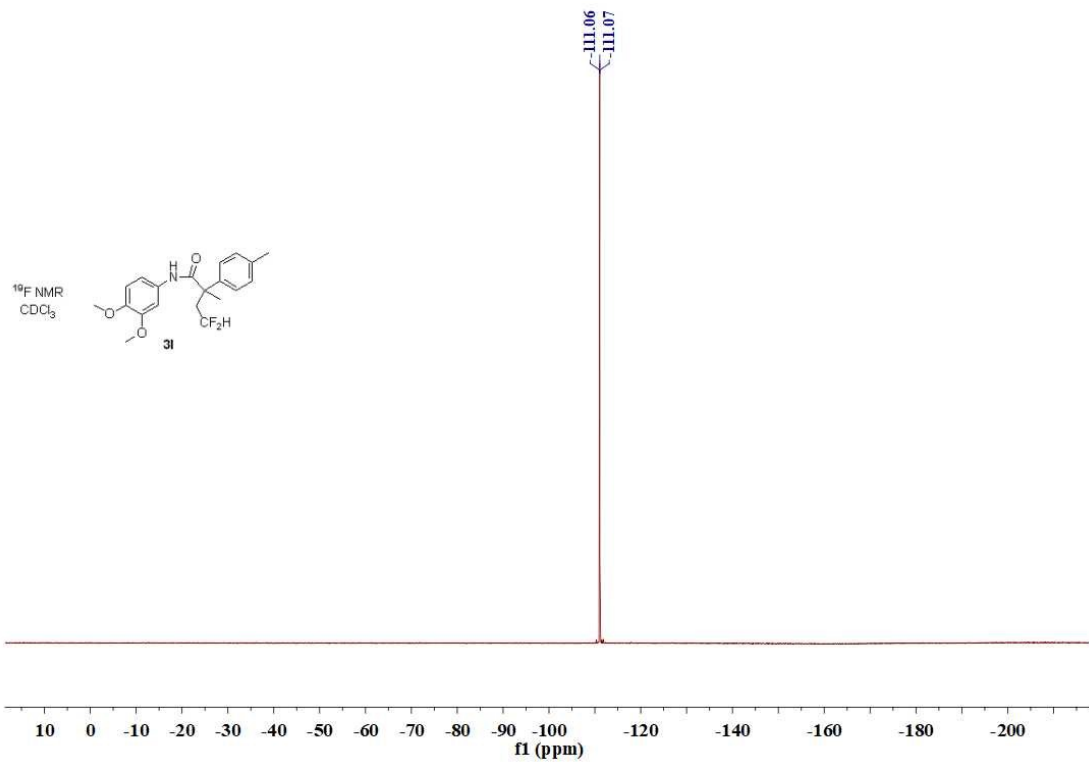
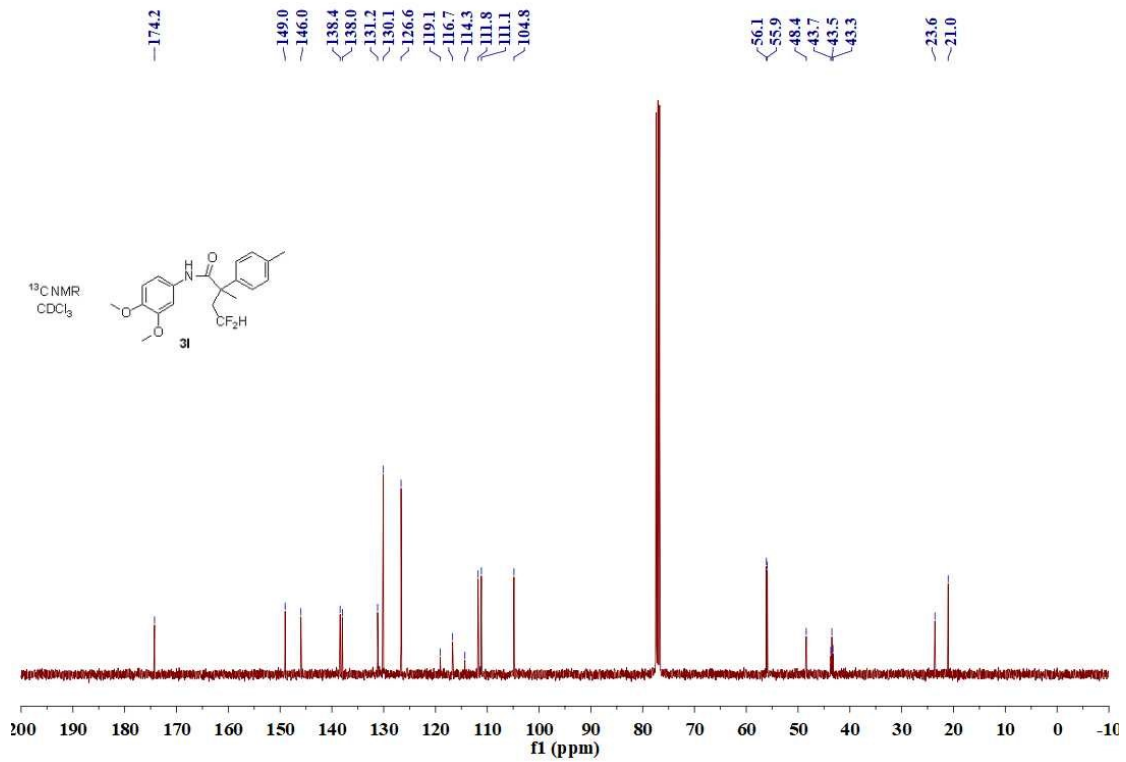
4,4-difluoro-*N*-(4-methoxyphenyl)-2-methyl-2-(*o*-tolyl)butanamide (3k).



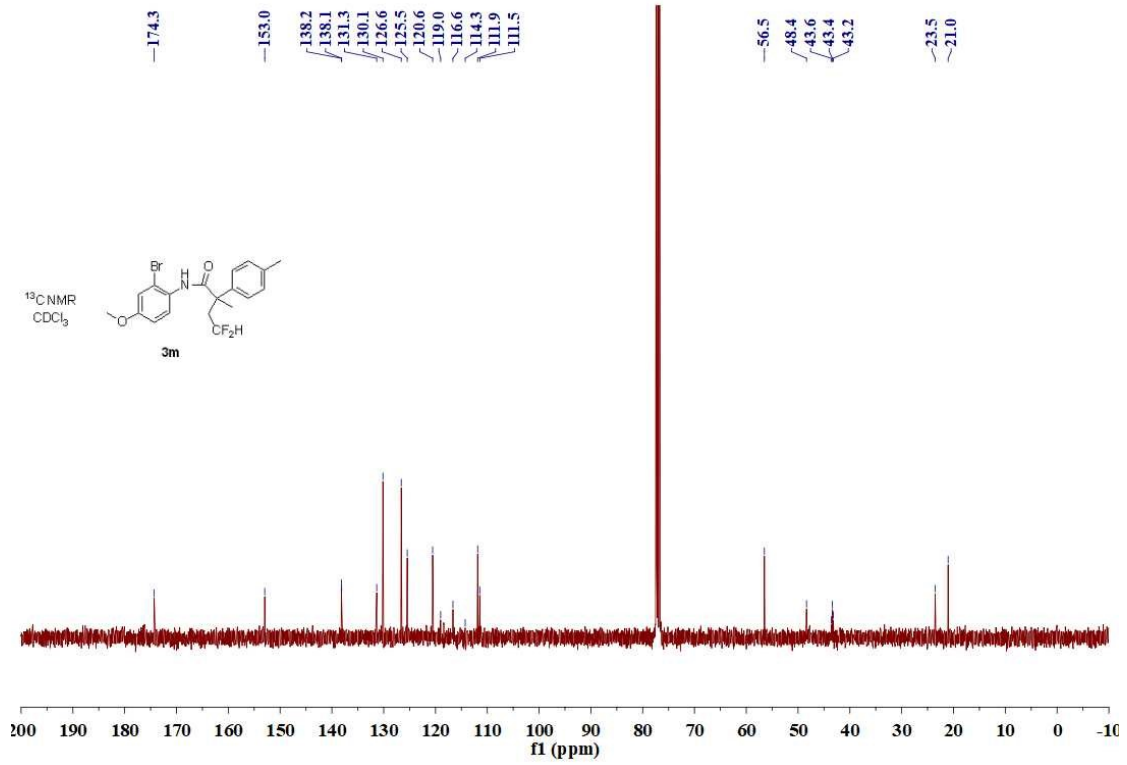
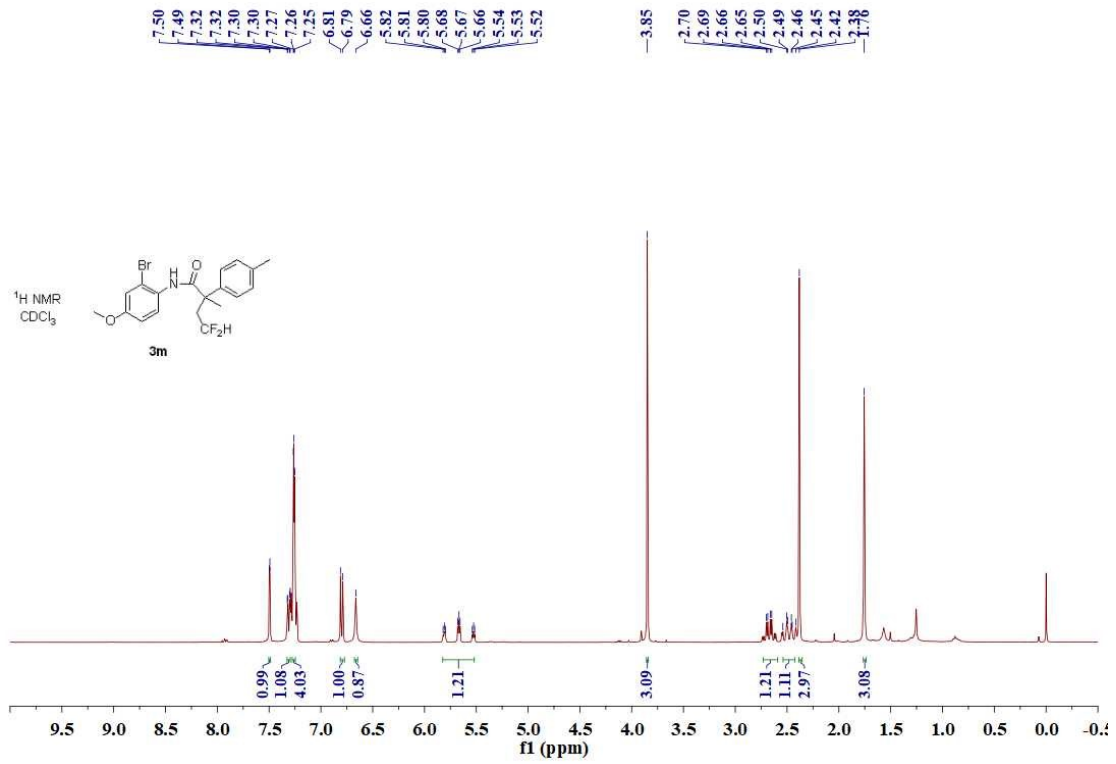


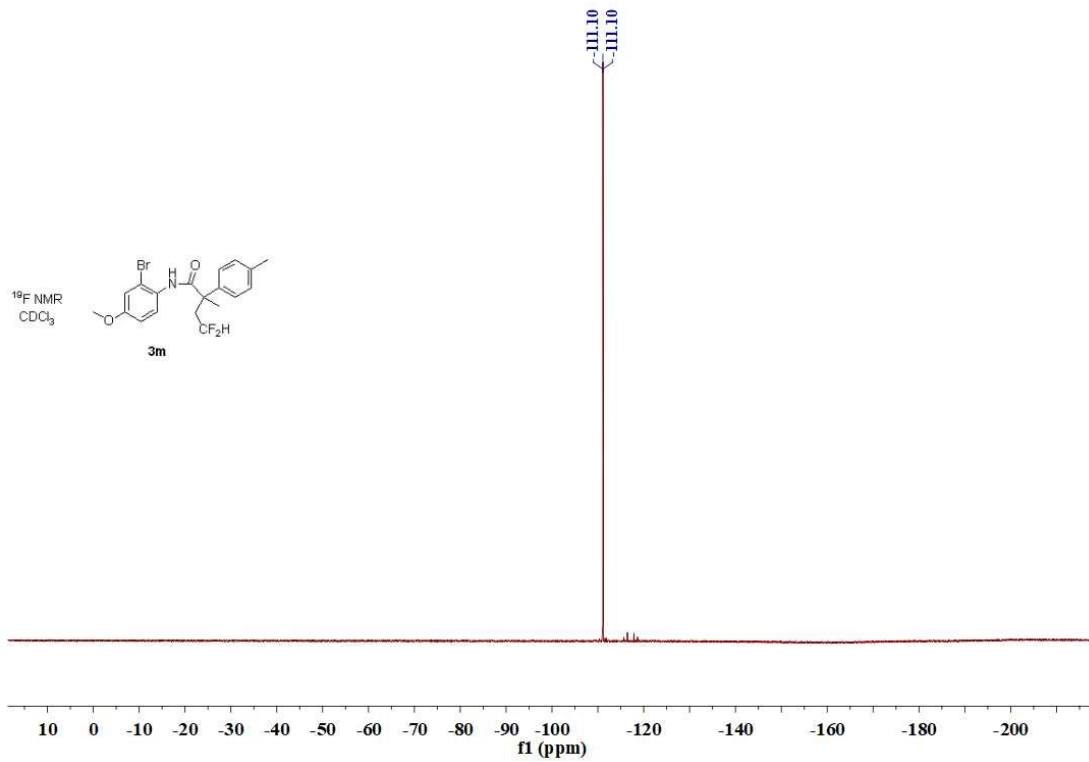
N-(3,4-dimethoxyphenyl)-4,4-difluoro-2-methyl-2-(*p*-tolyl)butanamide (**3l**).



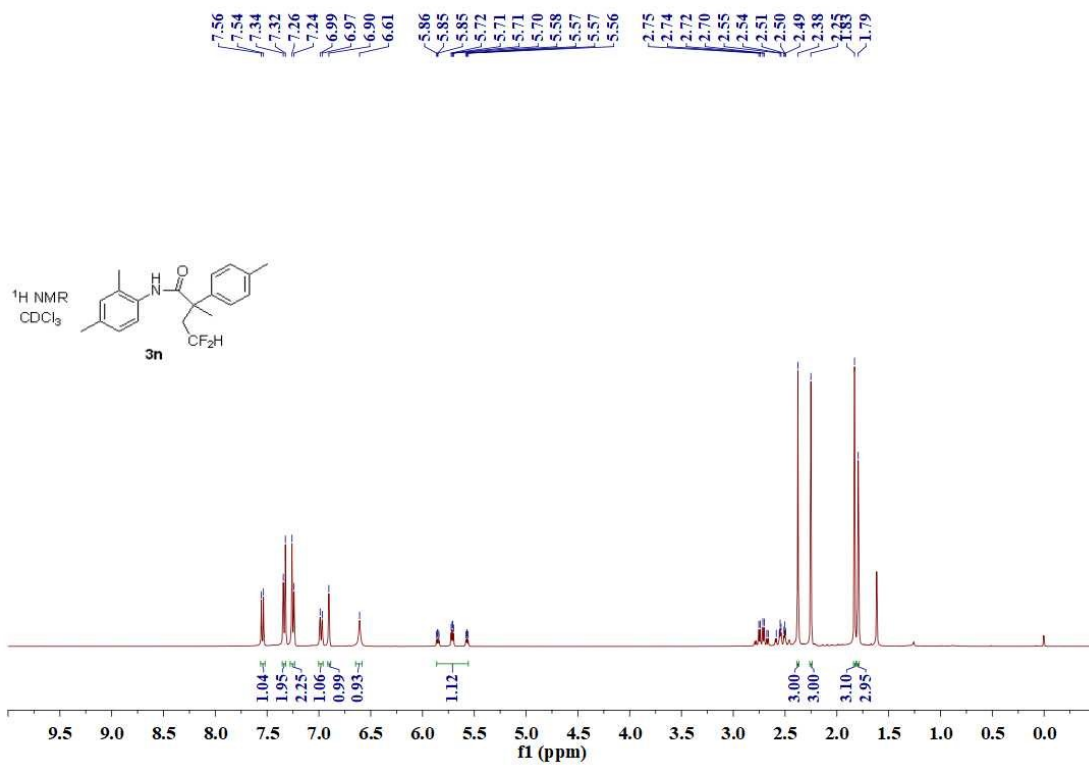


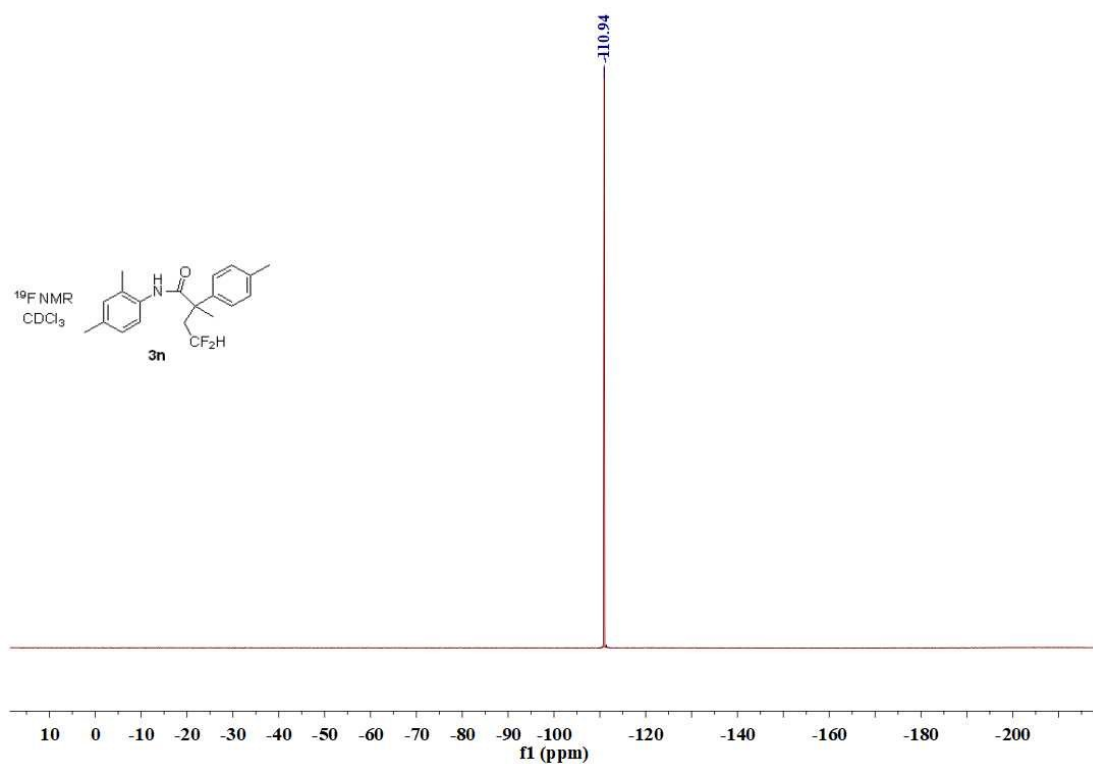
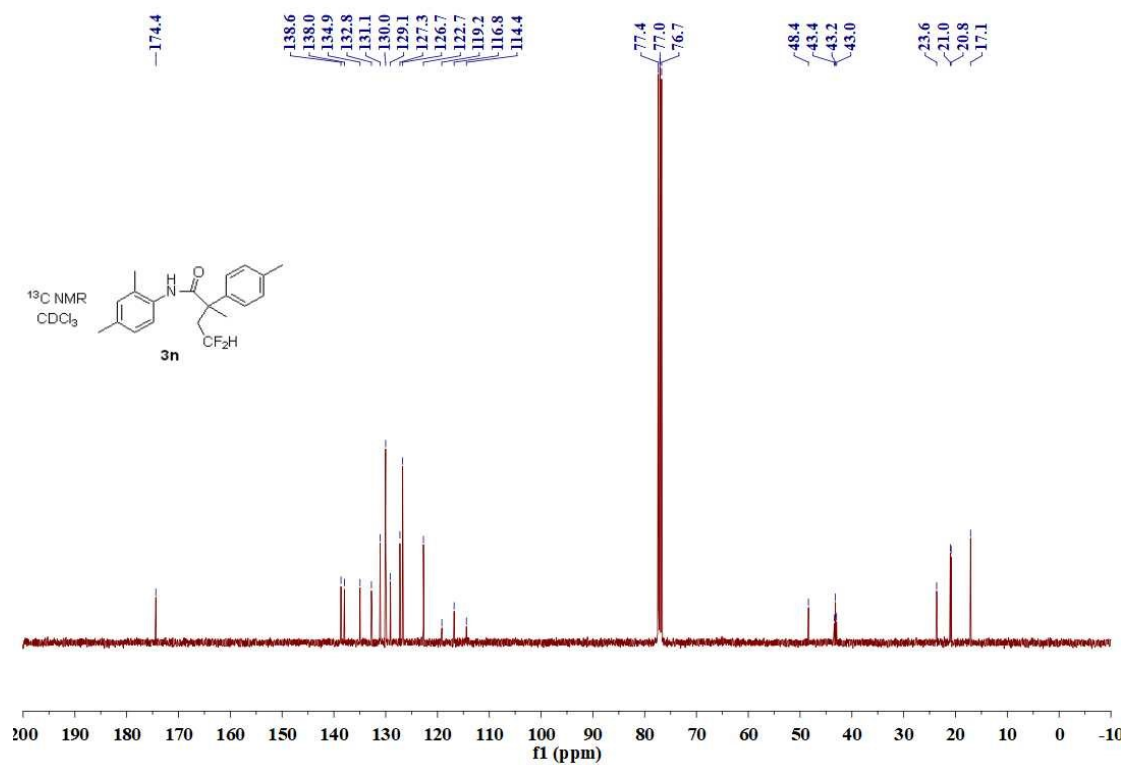
***N*-(2-bromo-4-methoxyphenyl)-4,4-difluoro-2-methyl-2-(*p*-tolyl)butanamide (3m).**



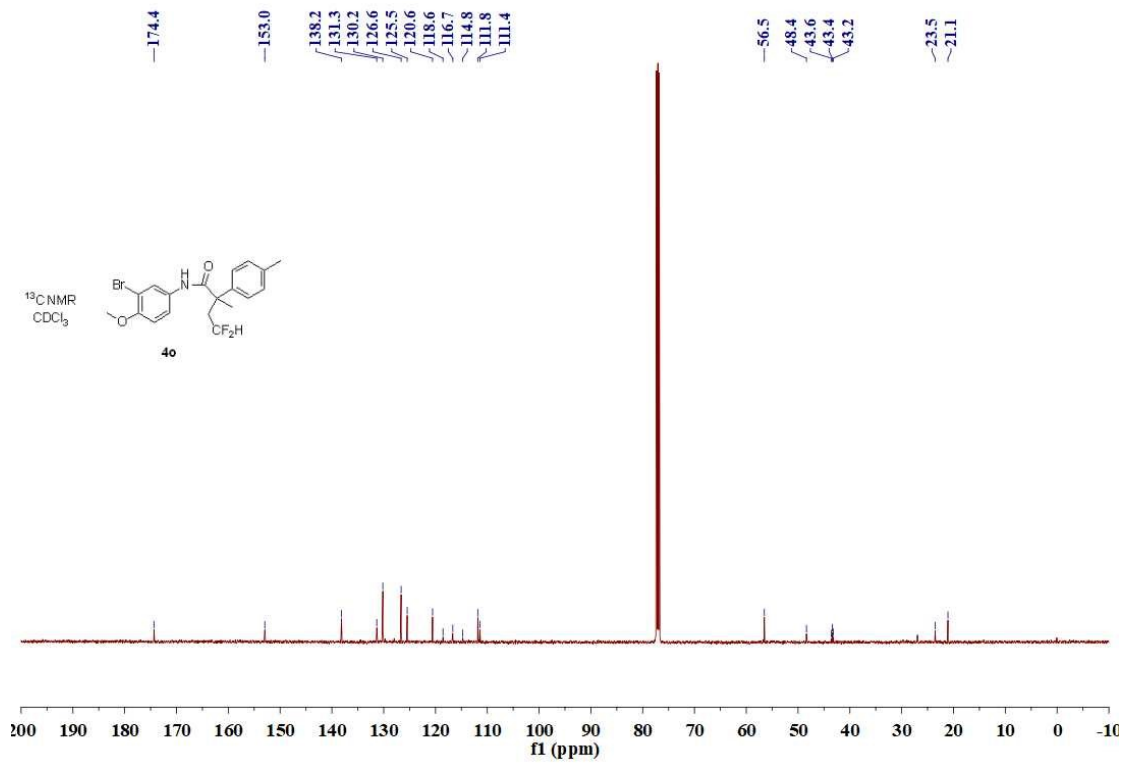
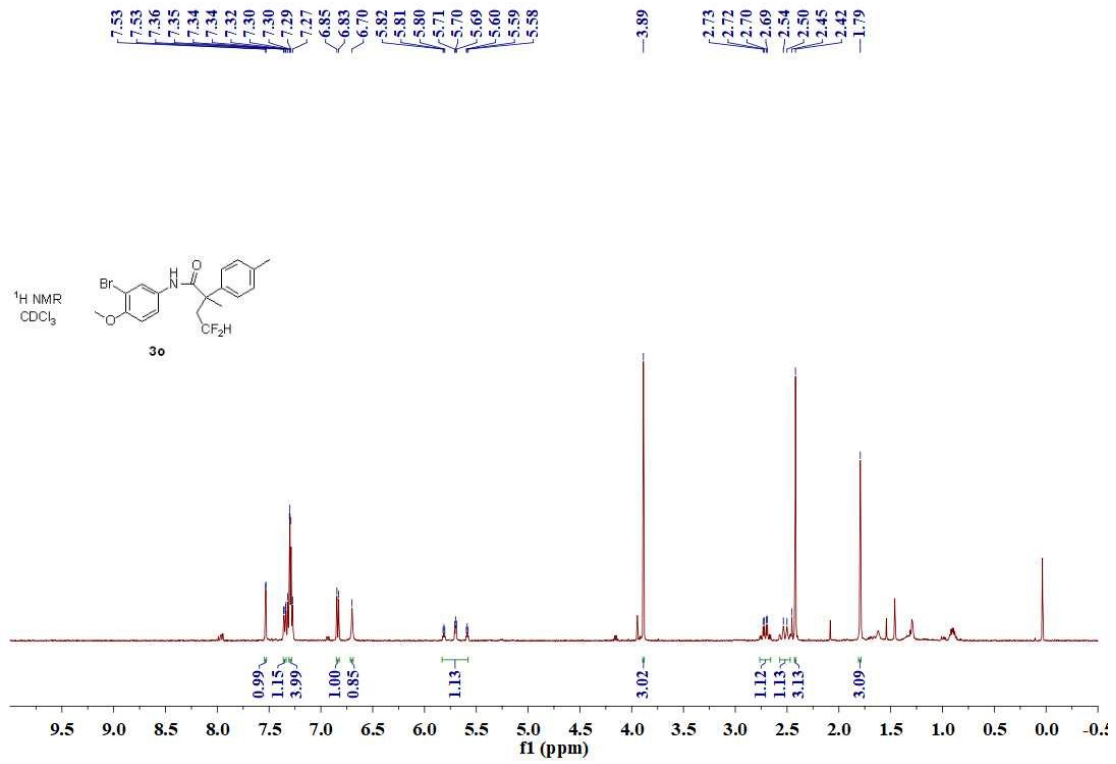


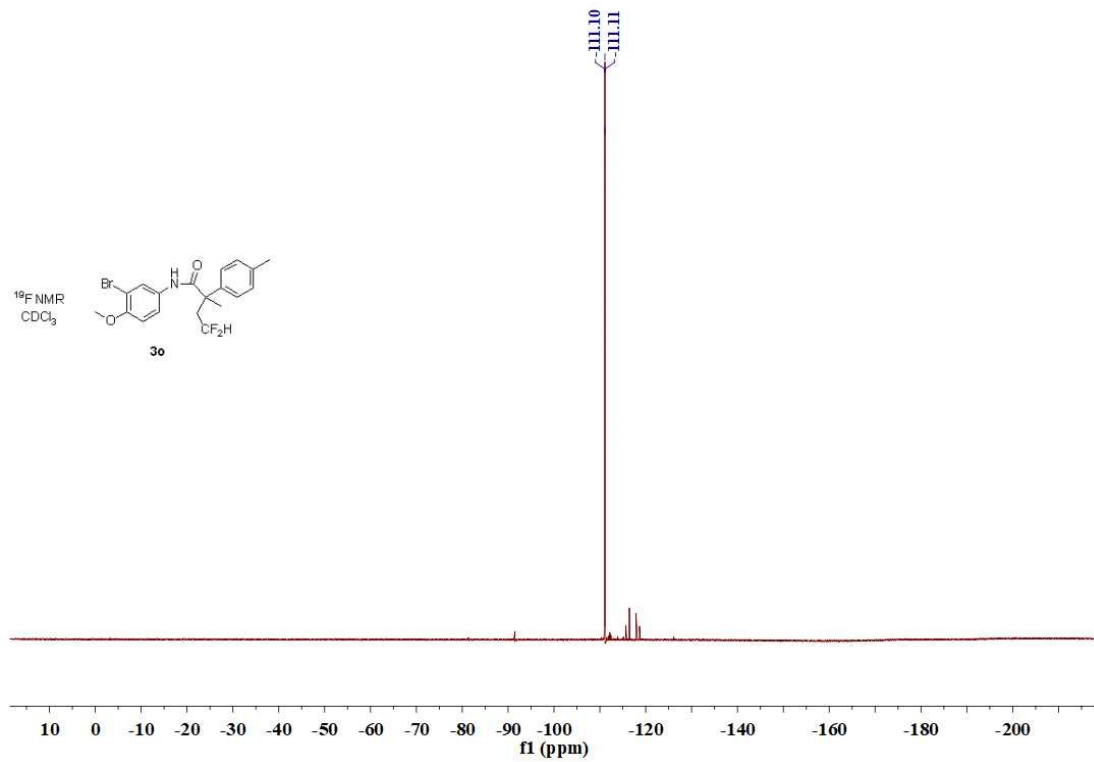
N-(2,4-dimethylphenyl)-4,4-difluoro-2-methyl-2-(*p*-tolyl)butanamide (**3n**).



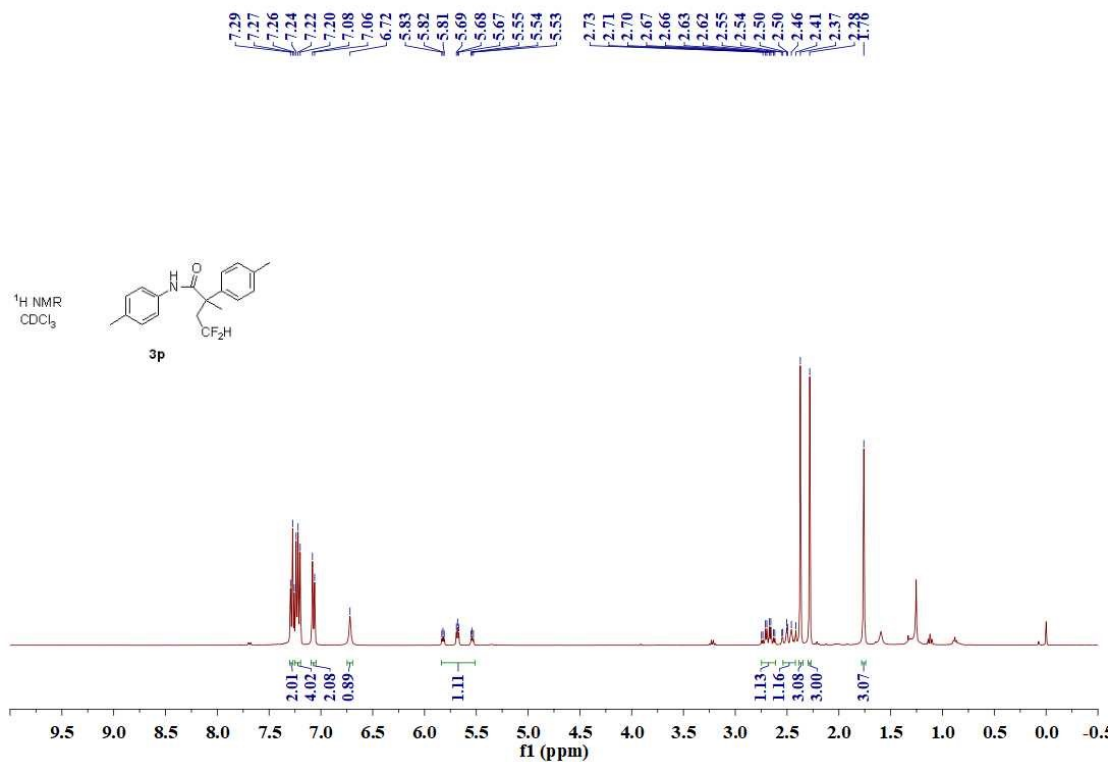


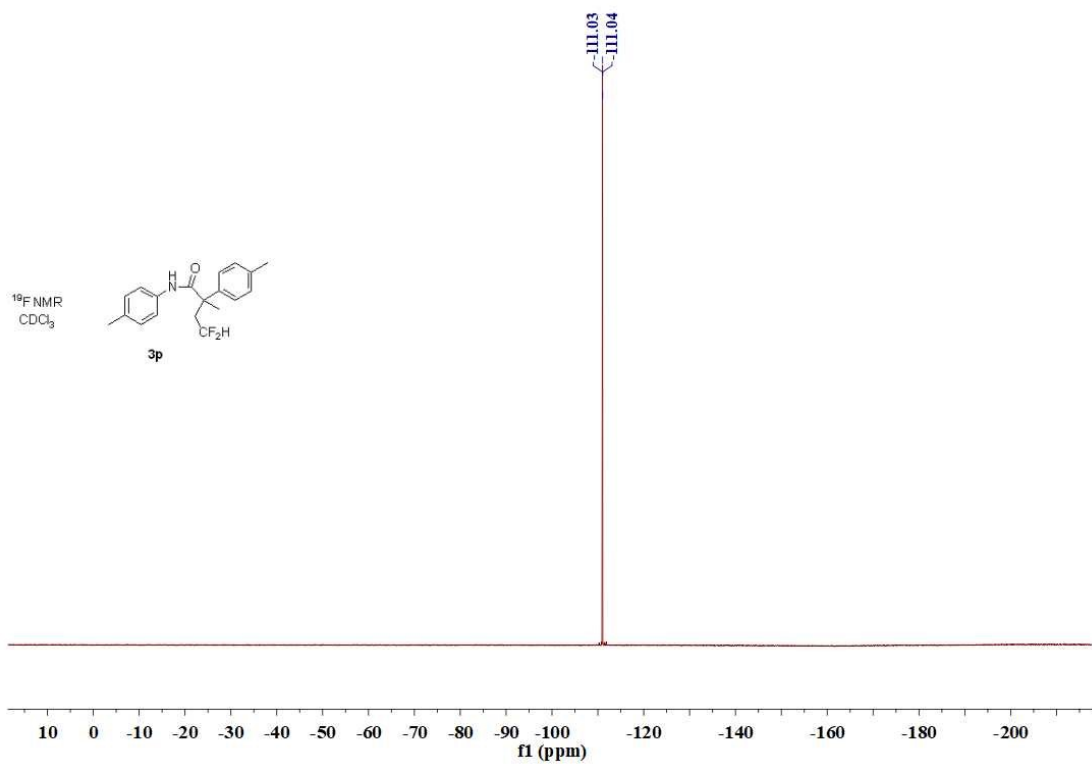
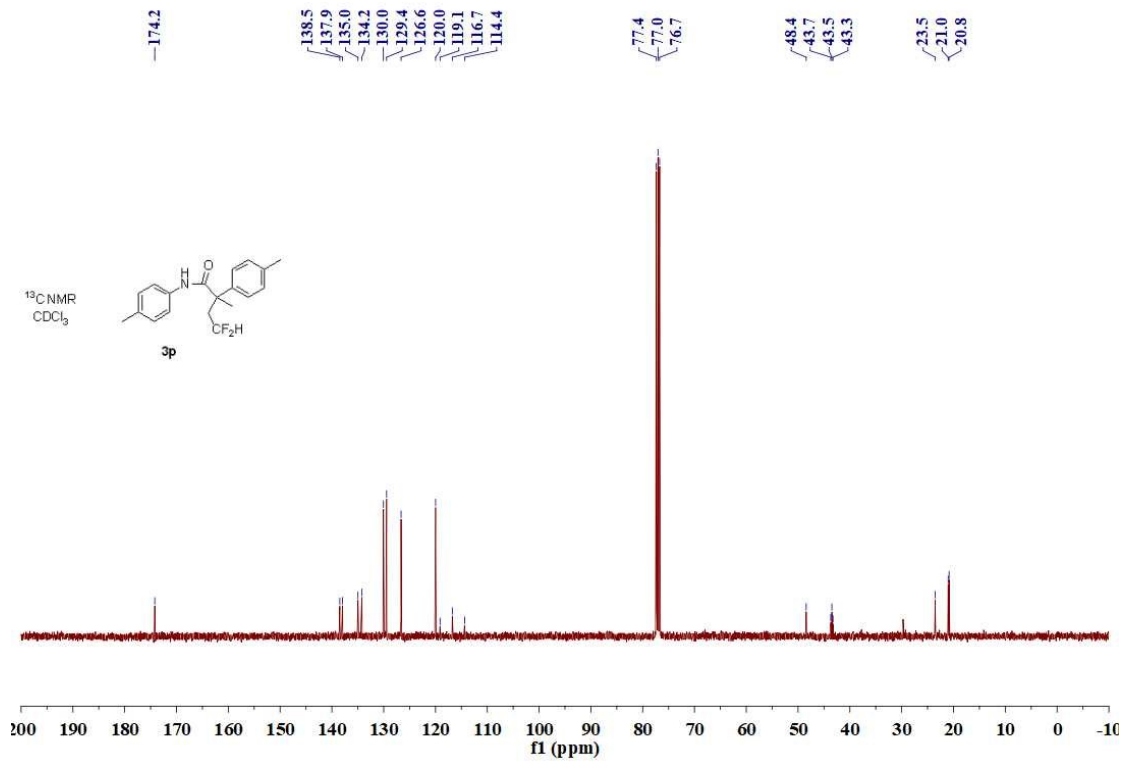
***N*-(3-bromo-4-methoxyphenyl)-4,4-difluoro-2-methyl-2-(*p*-tolyl)butanamide (3o).**



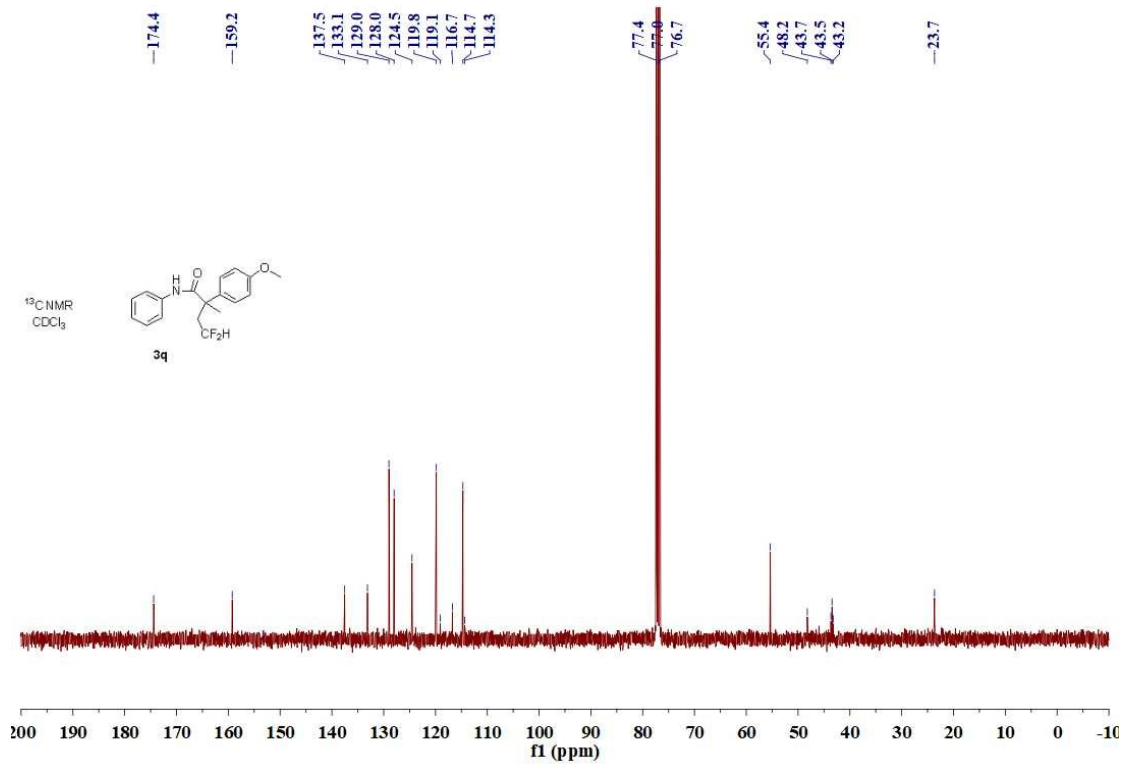
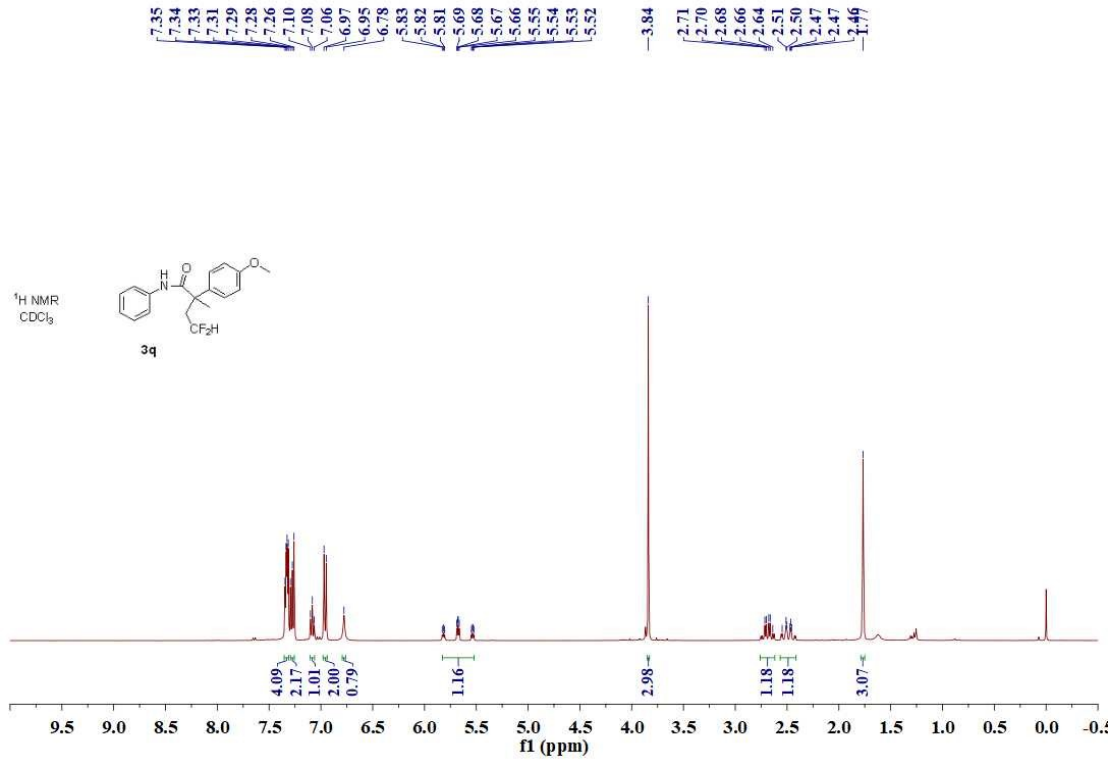


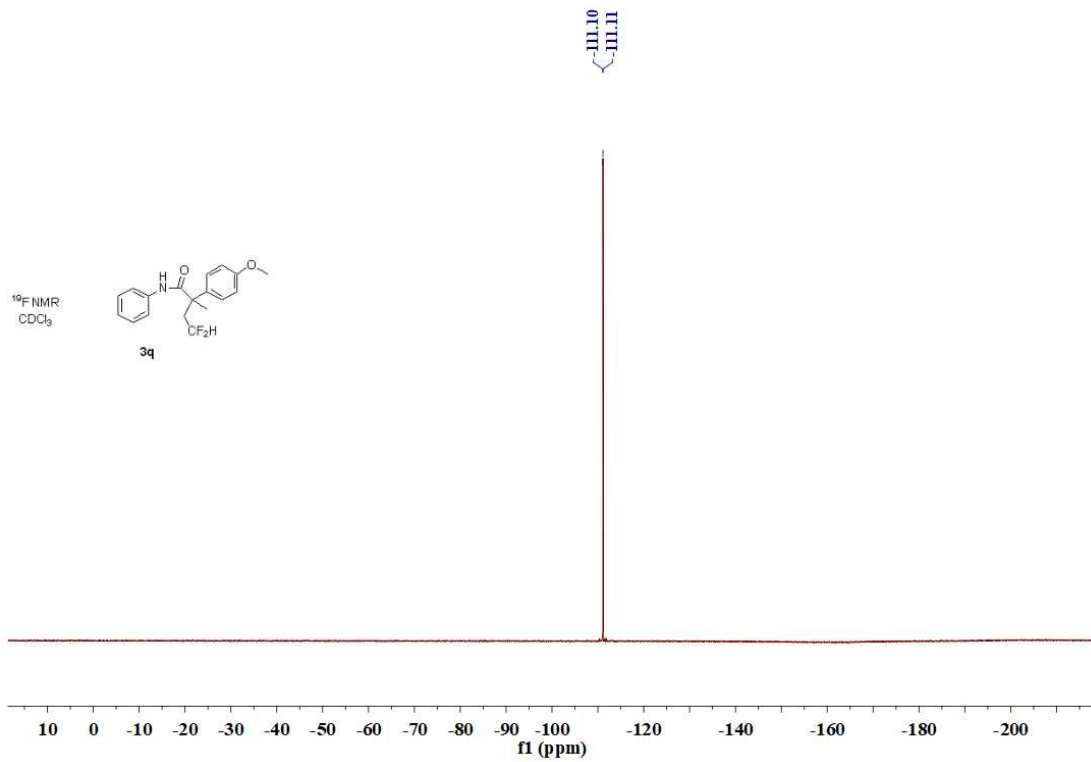
4,4-difluoro-2-methyl-N,2-di-p-tolylbutanamide (3p).



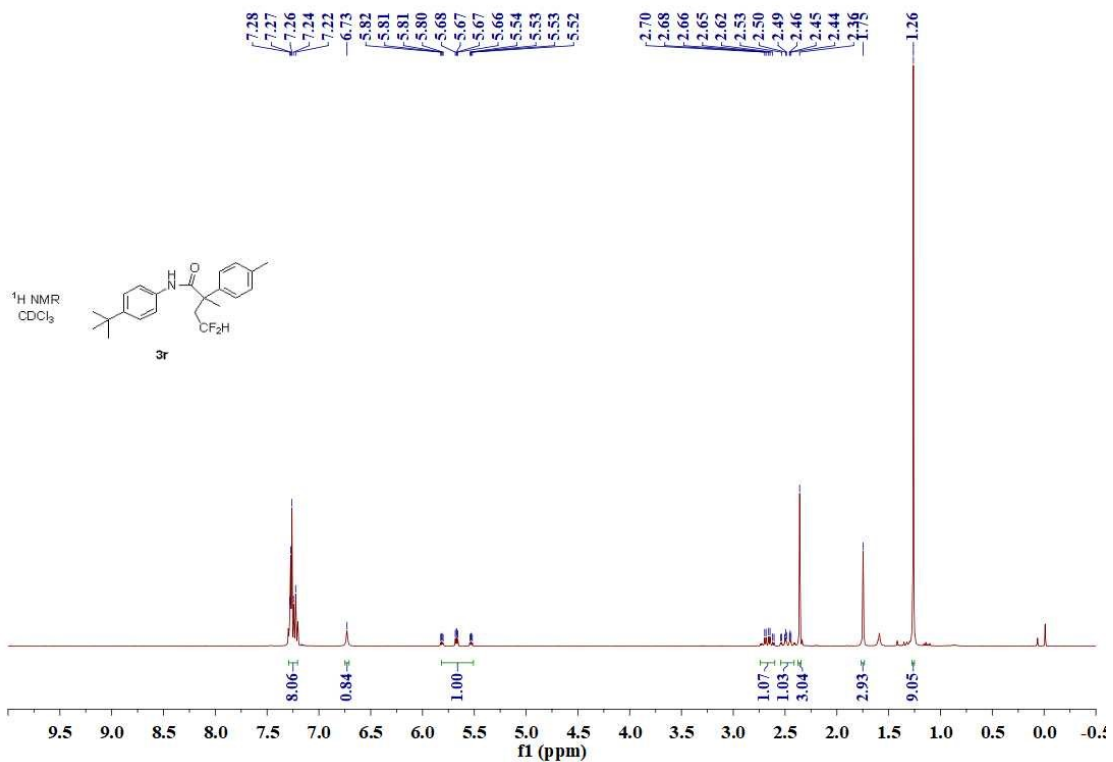


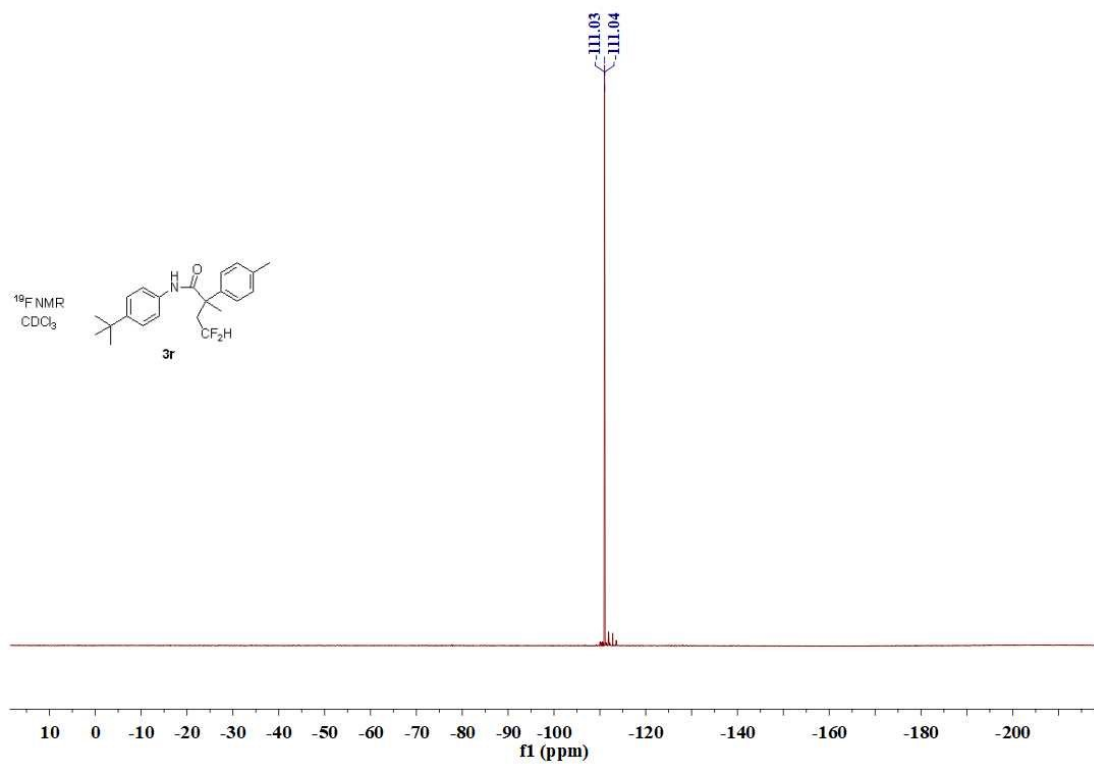
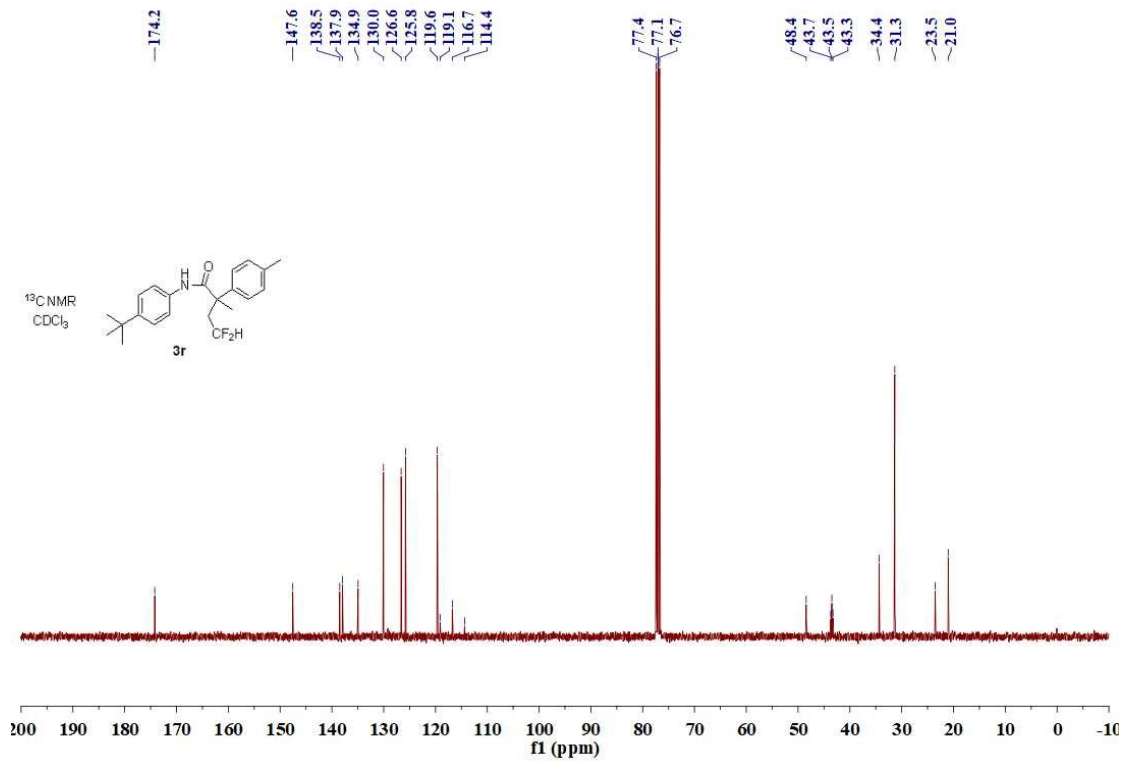
4,4-difluoro-2-(4-methoxyphenyl)-2-methyl-N-phenylbutanamide (3q).



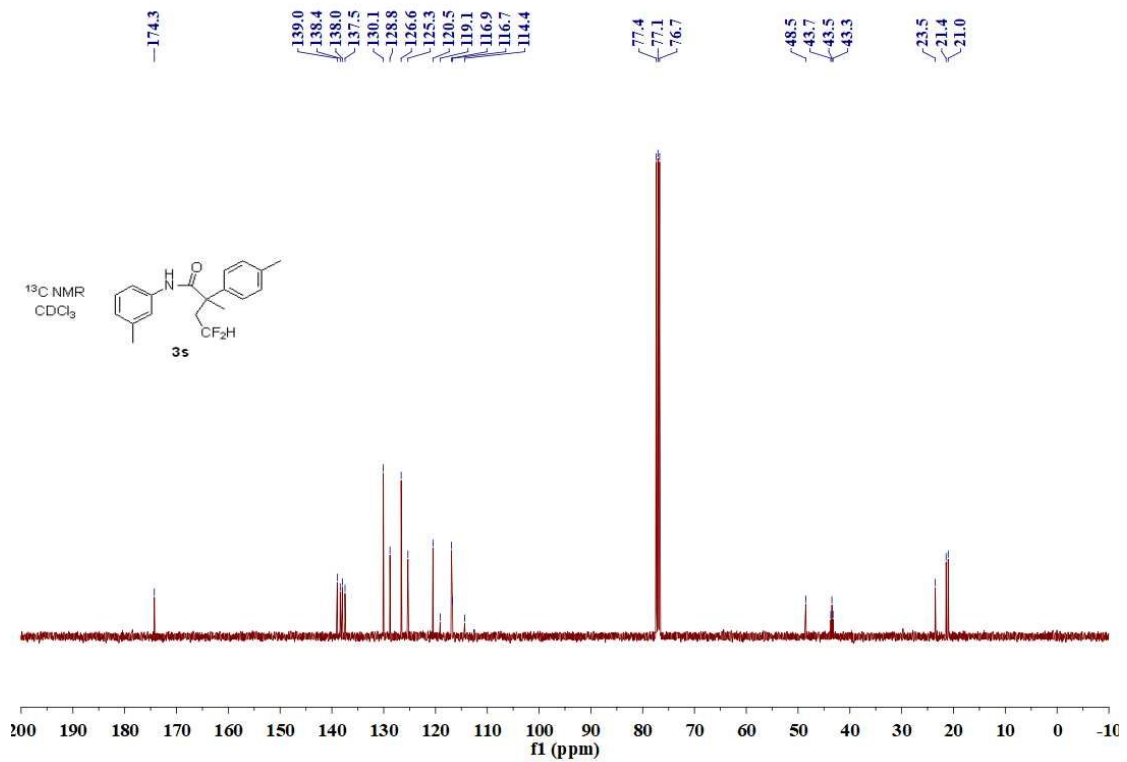
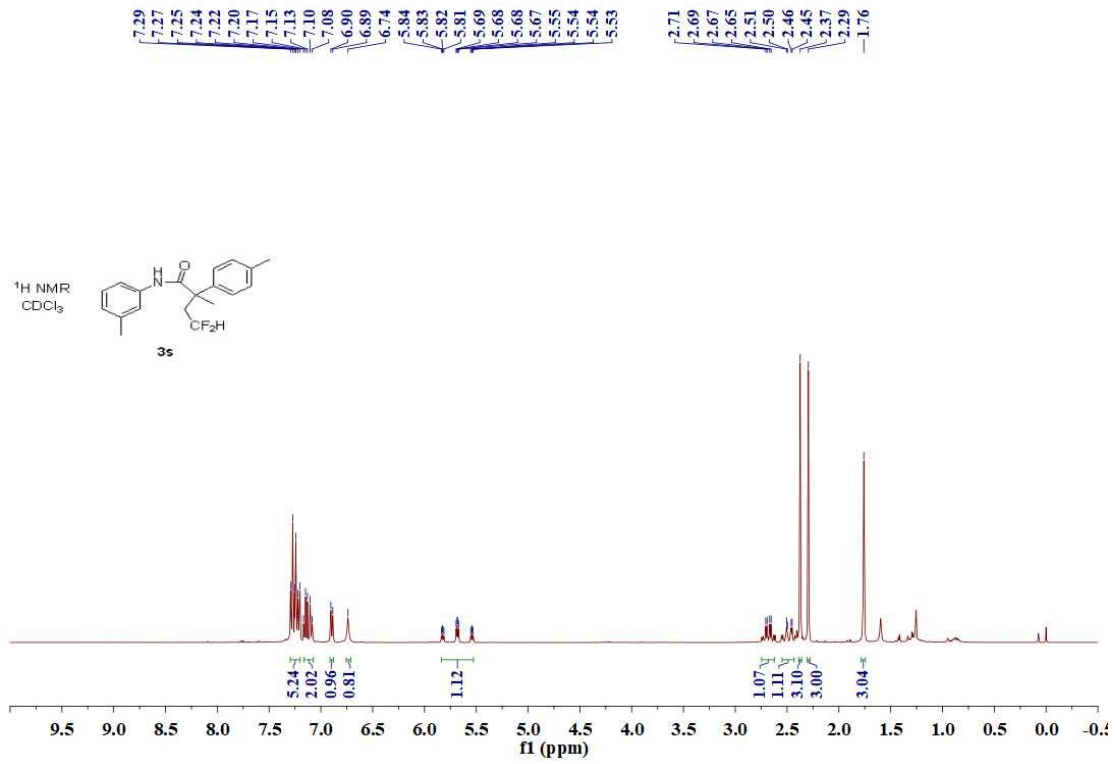


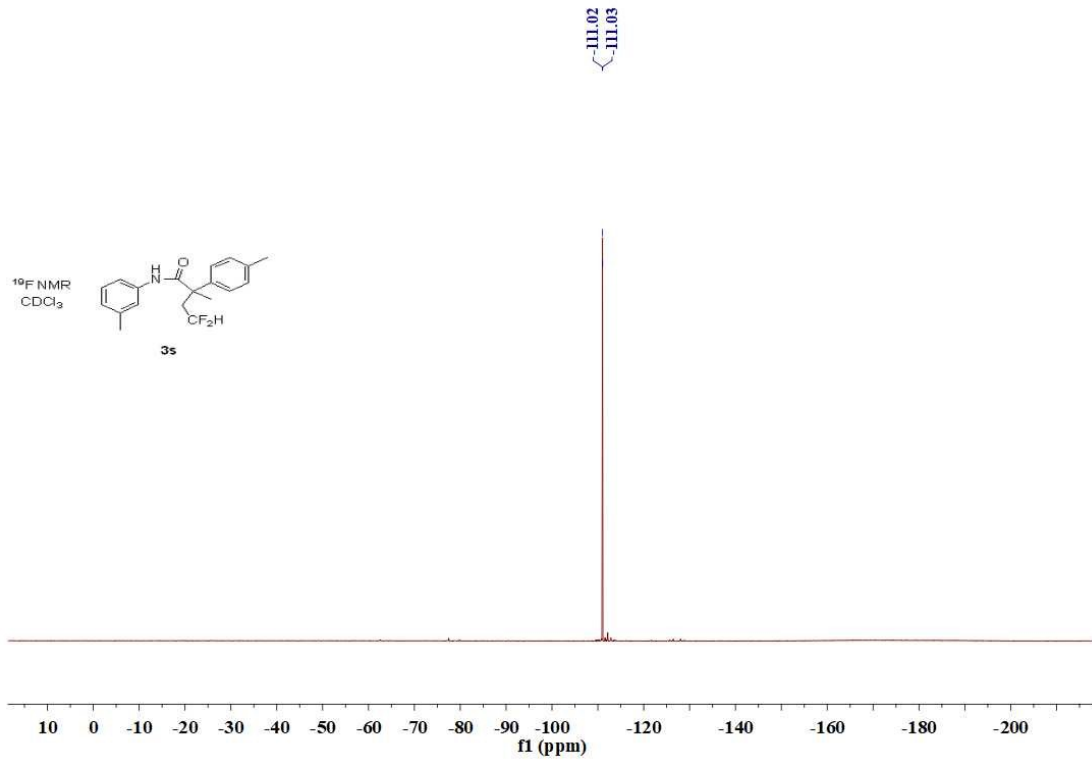
***N*-(4-(tert-butyl)phenyl)-4,4-difluoro-2-methyl-2-(p-tolyl)butanamide (3r).**



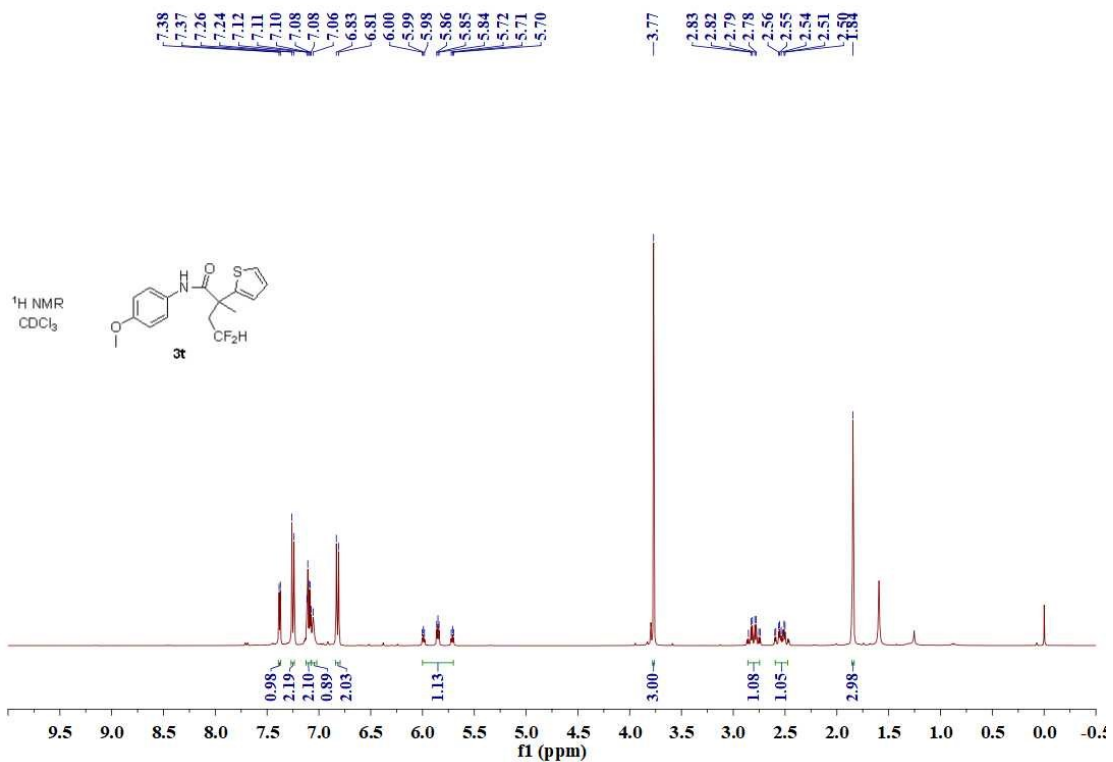


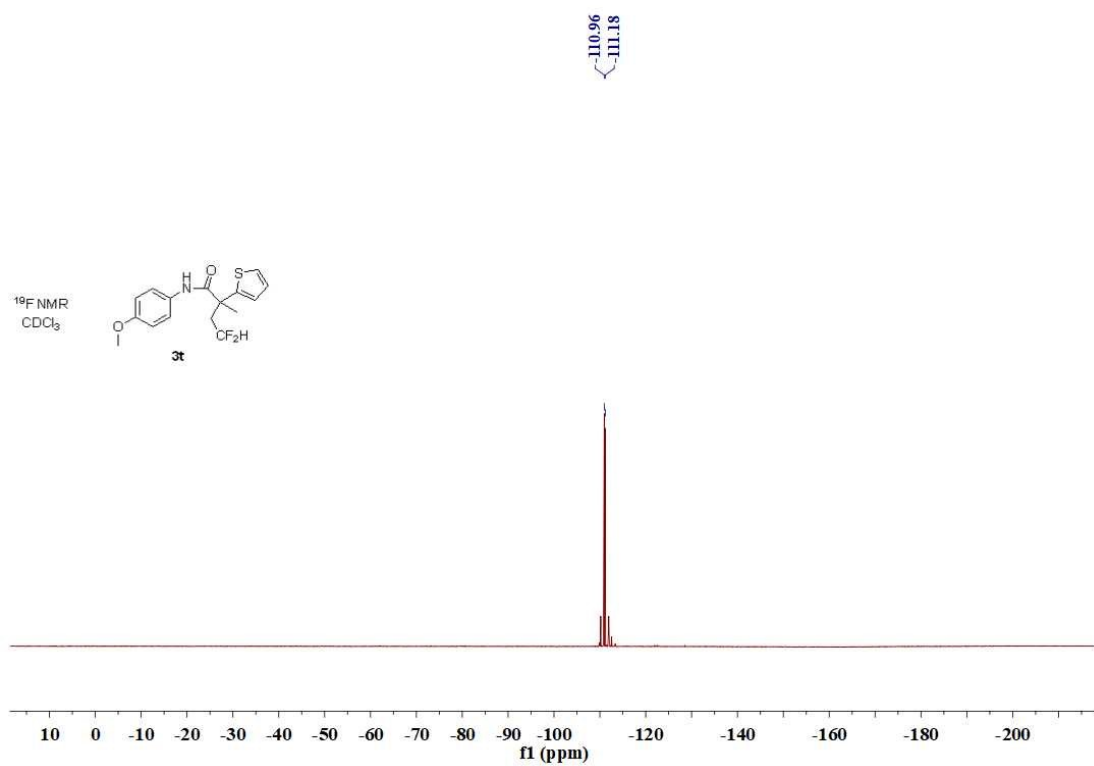
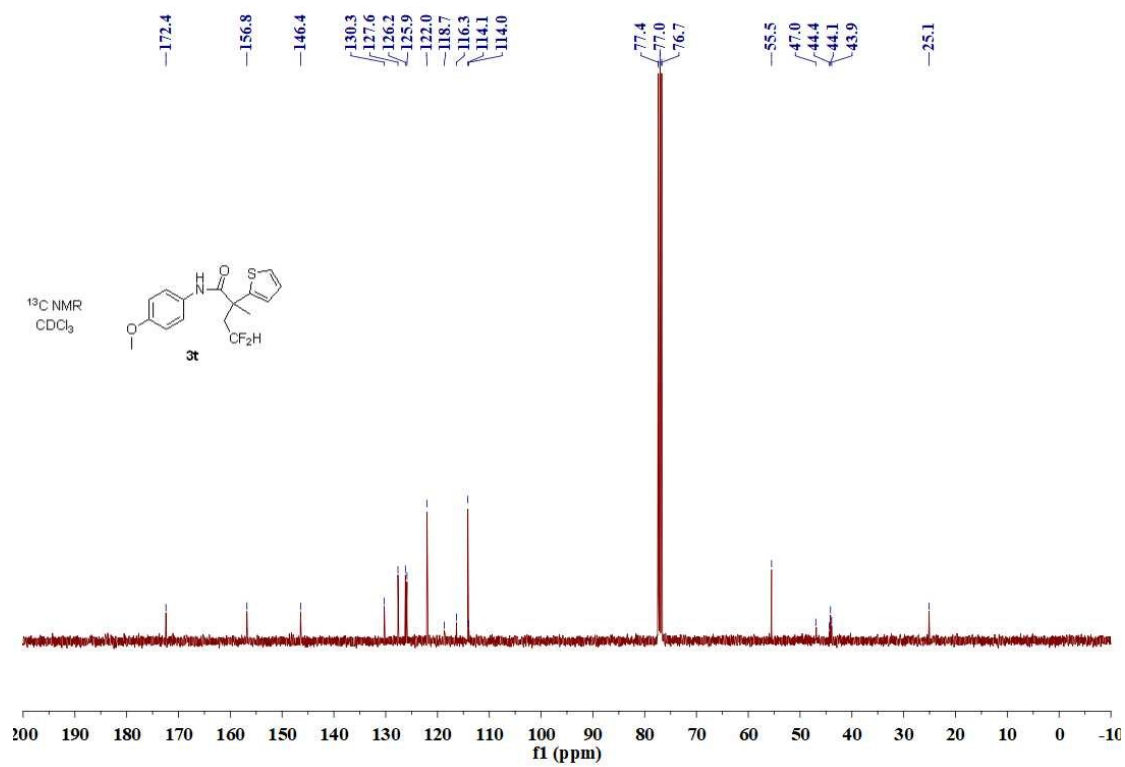
4,4-difluoro-2-methyl-N-(m-tolyl)-2-(p-tolyl)butanamide (3s).



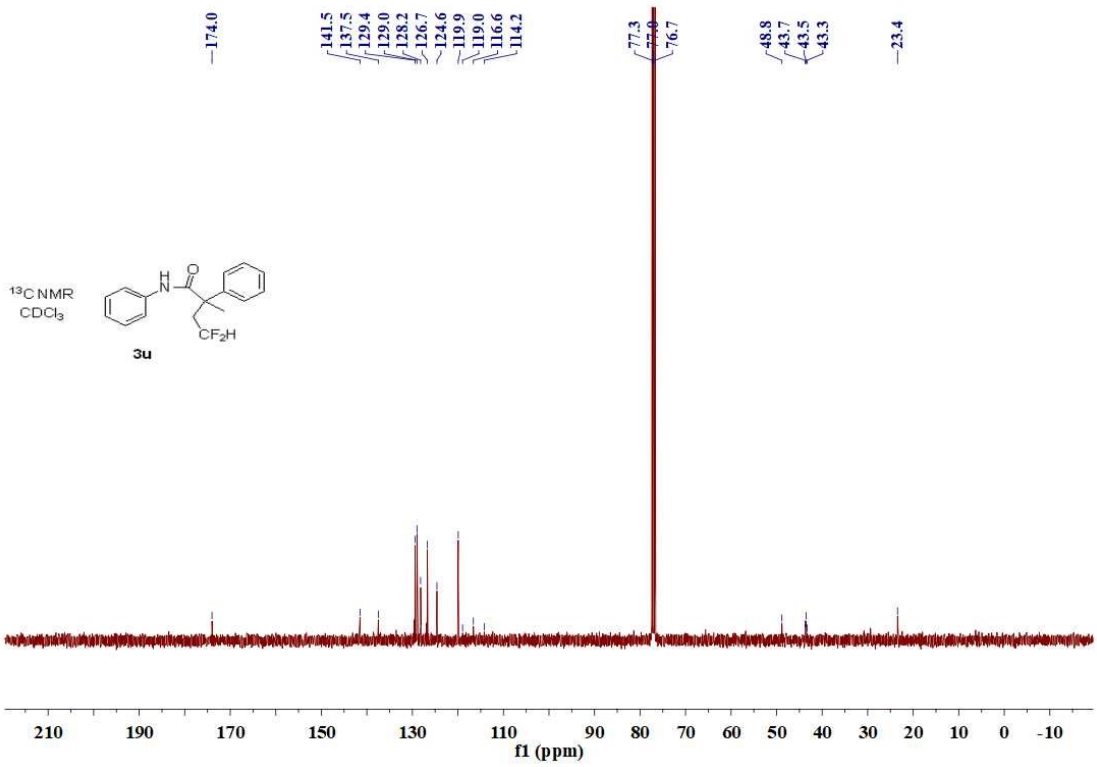
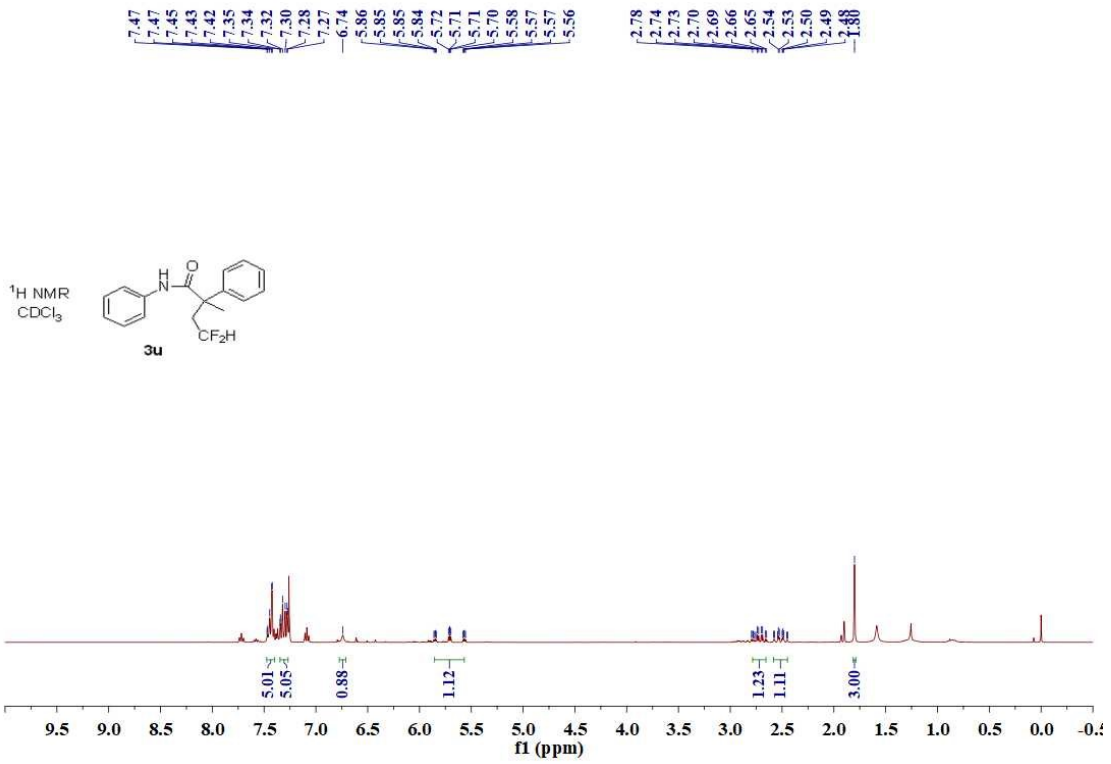


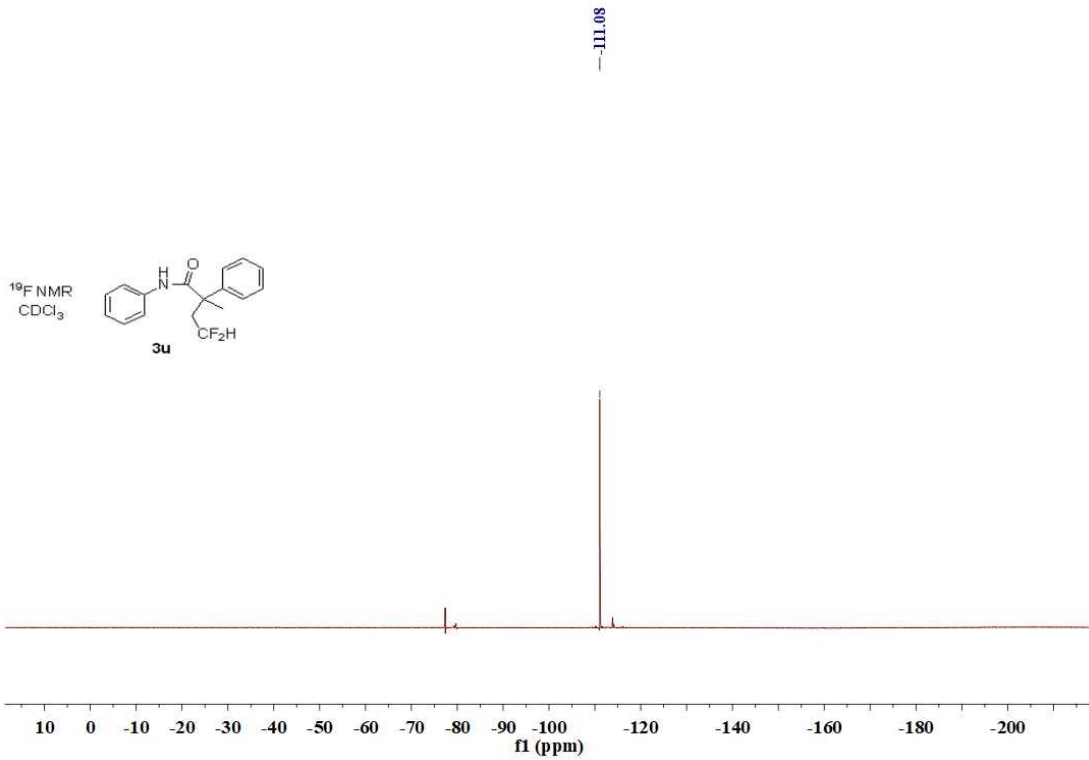
4,4-difluoro-*N*-(4-methoxyphenyl)-2-methyl-2-(thiophen-2-yl)butanamide (3t).



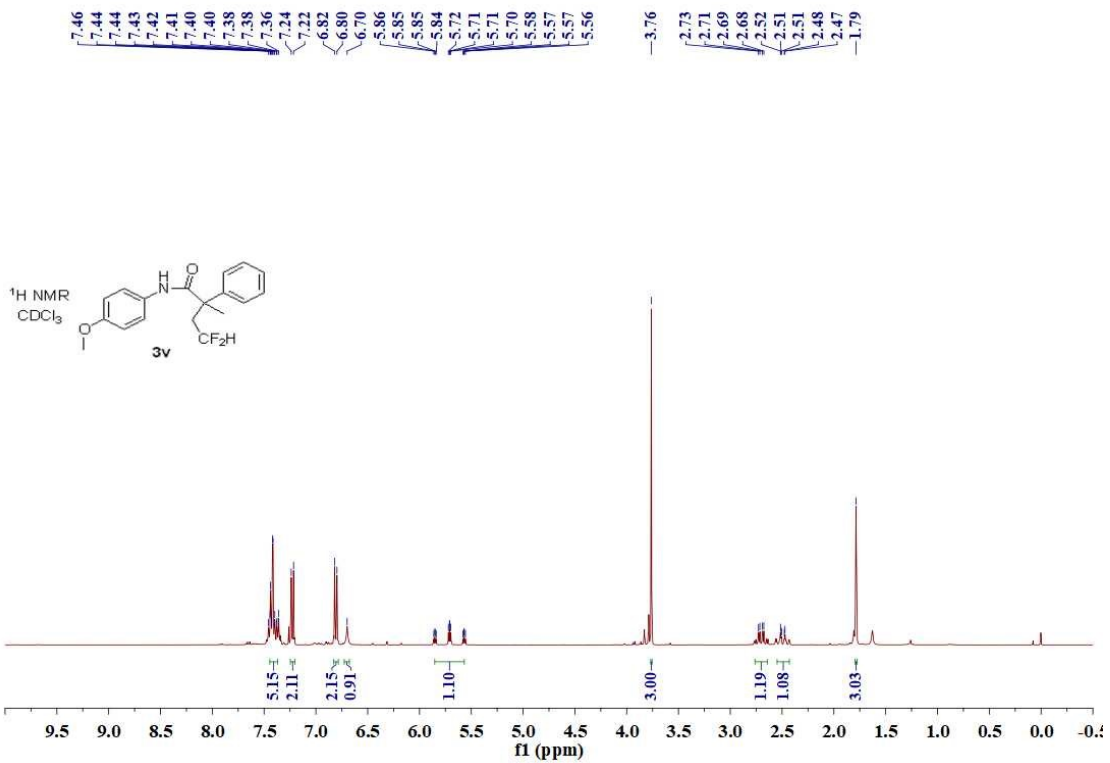


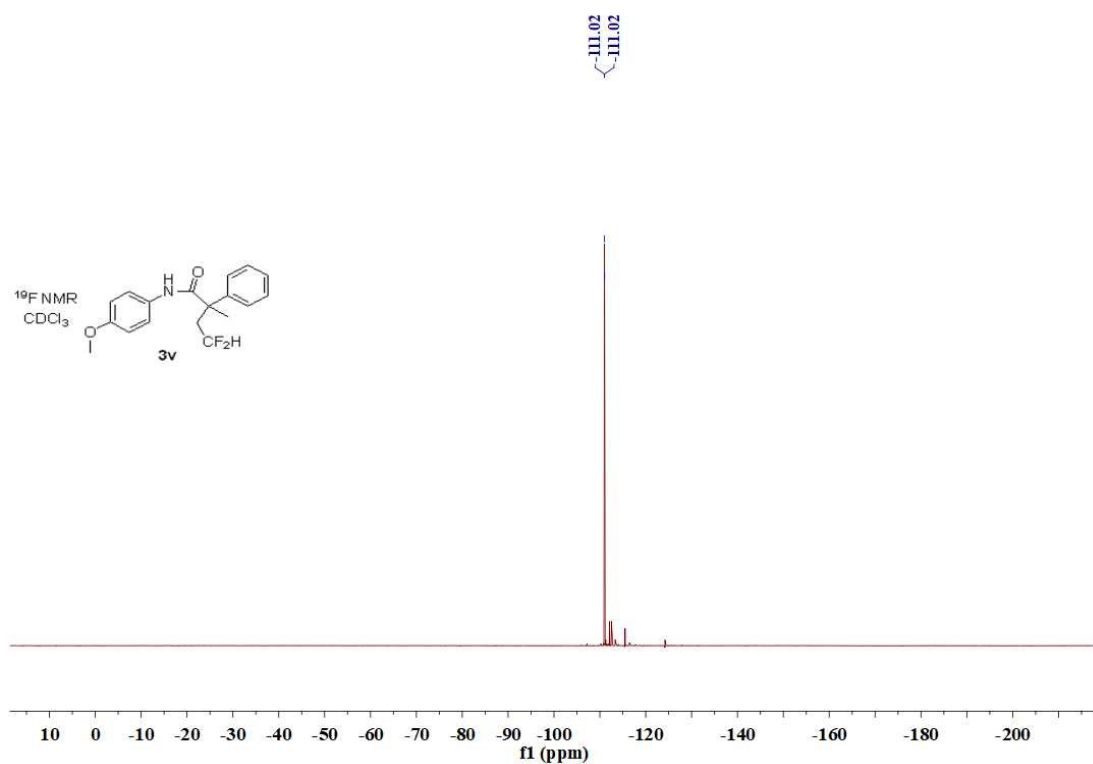
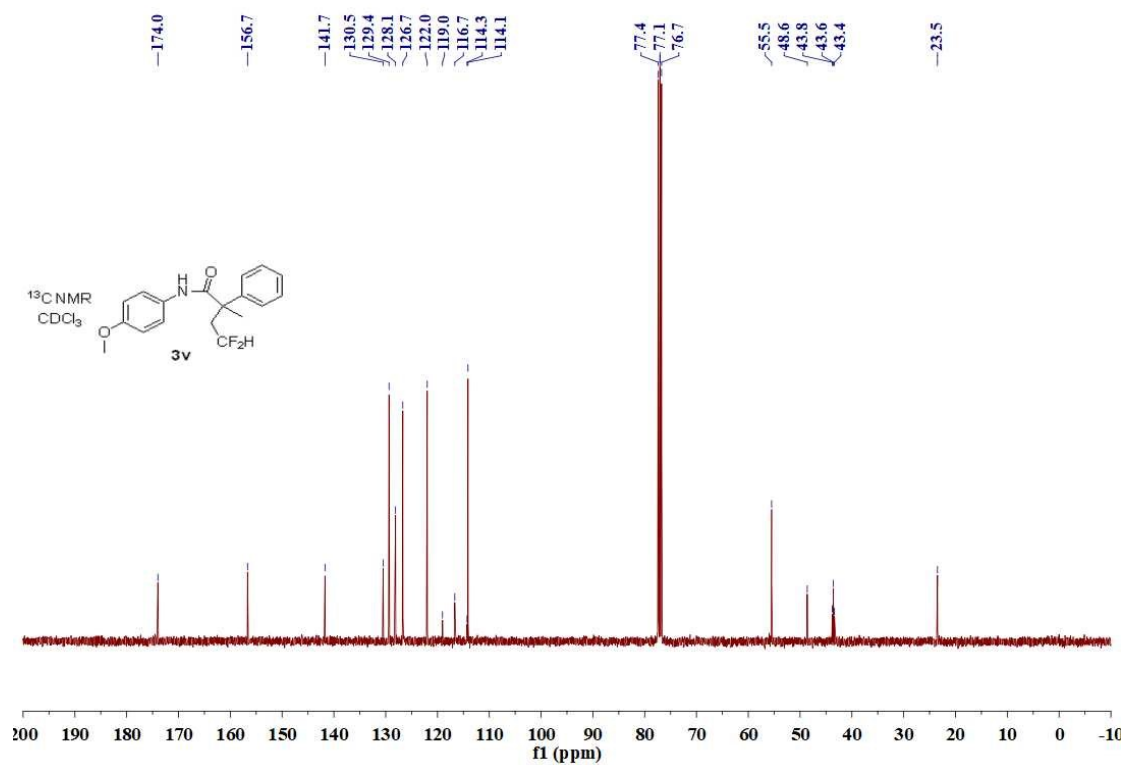
4,4-difluoro-2-methyl-N,2-diphenylbutanamide (3u).





4,4-difluoro-N-(4-methoxyphenyl)-2-methyl-2-phenylbutanamide (3v).





10. References

- 1 J. Wang, M. Liu, J. Zou, W. Sun, X. Liu, *Org. Lett.* 2022, **24**, 309-313