Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Photocatalytic Intramolecular Radical Cyclization involved Synergistic SET & HAT: Synthesis of 3,3-Difluoro-γ-Lactams

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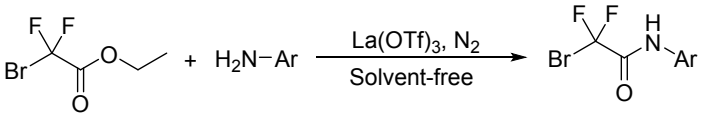
I. General Information

All reactions were run in a sealed tube with a Teflon plug valve under an ambient N_2 atmosphere. All commercially available reagent grade chemicals and solvents were used as received without further purification. ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz) and ^{19}F NMR (376 MHz) spectra are reported relative to chemical shift of tetramethylsilane (TMS). Chemical shifts (δ) are reported in ppm and coupling constants (*J*) in hertz (Hz). The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, q = quartet, m = multiplet. For HRMS (ESI) measurements, the mass analyzer is micrOTOF-Q.

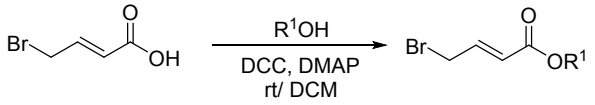
II. Preparation of substrates

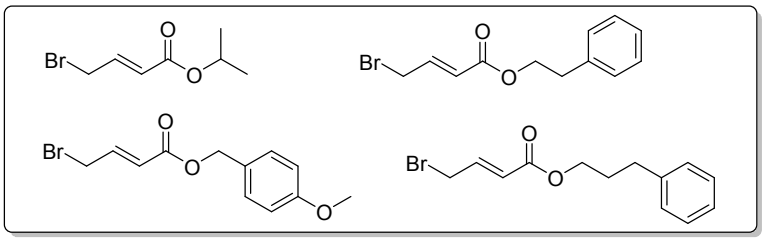
(1) Preparation of the *N*-substituted-2-bromo-2,2-difluoroacetamide [1]



A 10 mL Schlenk bomb was charged with lanthanum trifluoromethanesulfonate ($La(OTf)_3$, 0.25 mmol, 5 mol%), ethyl bromodifluoroaceate (6.0 mmol) and amine (5.0 mmol) in an atmosphere of N_2 at the room temperature. The mixture was monitored by TLC. After the amine was exhausted, purification by chromatography on silica gel afforded the target amides.

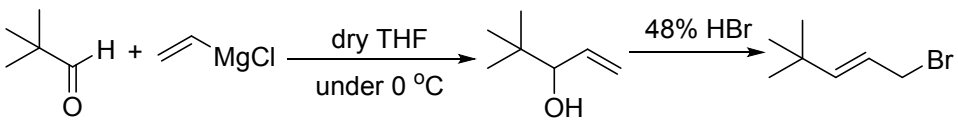
(2) Preparation of the 4-bromocrotonates [2]





To a solution of 4-bromocrotonic acid (1.0 equiv.) in DCM, alcohol (R^1OH, 1.0 equiv.) and DMAP (0.1 equiv.) was added. The reaction was stirred at 0 °C and DCC was added portionwise. Then, the reaction mixture was warmed to room temperature and stirred overnight. After the 4-bromocrotonic was exhausted, the mixture was filtered through short celite-pad and the residue was washed with DCM. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure, and the resulted residue was purified by silica gel column chromatography (petroleum ether/ ethyl acetate = 30: 1) to afford the desired 4-bromocrotonates as colorless oil.

(3) Preparation of the 1-bromo-4,4-dimethylpent-2-ene [3]

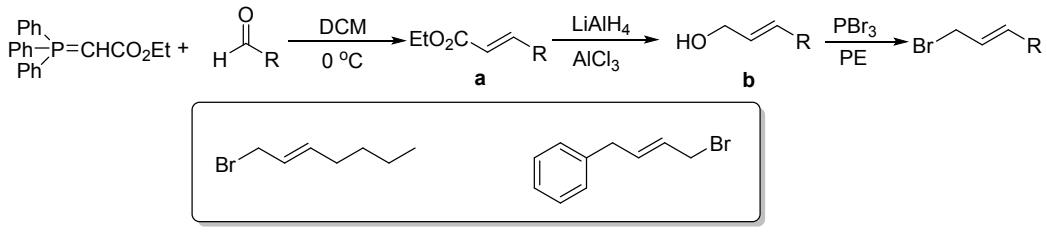


A 100 mL two necked round bottomed flask was charged with the appropriate aldehyde (20 mmol, 1.0 equiv.), which was dissolved in 35 mL of dry THF in an atmosphere of N_2 at 0 °C. The

vinyl magnesium chloride 2M solution in THF (30 mL, 30 mmol, 1.5 equiv.) was added dropwise and the mixture was stirred at room temperature for 2 h. After completion by TLC, the round bottomed flask was placed into an ice bath and 30 mL of saturated aqueous solution of ammonium chloride was added. Then 30 mL of ether was added and the aqueous phase was extracted two times. The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure to give the crude which was used in the next step without further purification.

The tertiary alcohol (1.0 equiv., 10 mmol) was diluted in a mixture of pentane: ether = 9:1 and HBr (48% aq., 5 mL) was added under vigorous stirring. After 10 min, the water phase was removed using a separation funnel. The organic phase was washed with saturated solution of sodium bicarbonate and then dried over anhydrous sodium sulfate. The solvent was evaporated and the desire product was afforded as colorless oil.

(4) Preparation of the 1-substituted-3-bromopropene [4-5]

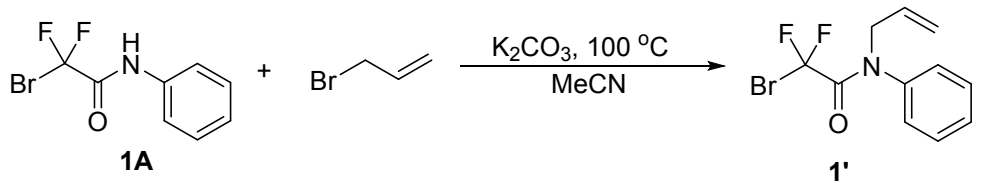


A 100 mL single necked round bottomed flask was charged with the [(ethoxycarbonyl)methylene]triphenylphosphorane (20 mmol, 1.0 equiv.) and DCM (20 mL) at 0 °C. The Pentanal or Phenylacetaldehyde (20 mmol, 1.0 equiv.) in DCM (20 mL) was added dropwise and the mixture was stirred overnight at room temperature. Then the solvent was removed by rotary evaporation, and petroleum ether (200 mL) was added into the residue. The resulting solid material was collected by filtration and washed with the same solvent. After the combined extract solution was concentrated, the residual oil was distilled to give desired crude **a** as colorless oil.

To an ice-cold, stirred suspension of $LiAlH_4$ (1.5 equiv.) in ether (20 mL) was added dropwise a solution of $AlCl_3$ (1.5 equiv.) in ether (10 mL). The mixture was stirred at room temperature for 30 min and ice-cooled again. To this cold mixture was added dropwise a solution of **a** (1.0 equiv.) in ether (20 mL), and the resulting mixture was stirred at 0 °C for 2 h. The reaction was quenched by addition of ether saturated with water followed by 10% NaOH. The mixture was filtered through Celite, and the ethereal solution was dried over $MgSO_4$. After evaporation of the solvent, the residue was distilled to give the desired crude **b** as colorless oil.

To a stirred solution of **b** (1.0 equiv.) in petroleum ether (30 mL) was added dropwise a solution of PBr_3 (1.7 equiv.) in the same solvent (20 mL) at -10 °C. After 2 h, the mixture was poured into ice-water (100 mL) and the organic phase was separated. The aqueous phase was extracted with ether, and the combined organic phase was washed with 5% $NaHCO_3$ and dried over $MgSO_4$. After evaporation of the solvent, the residue was distilled to give the desired crude 1-substituted-3-bromopropene.

(5) Preparation of *N*-allyl(but-3-en-1-yl/ propargyl)-2-bromo-2,2-difluoro-*N*-arylacetamide (1' as an example)[6]



To a solution of the 2-bromo-2,2-difluoro-*N*-phenylacetamide **1A** (1.25 g, 5.0 mmol) in CH_3CN (25 mL), K_2CO_3 (2.07 g, 15 mmol) and 3-bromopropene (1.21 g, 10 mmol) were added. The reaction mixture was stirred at 100 °C and monitored by TLC. After the amide was exhausted, the mixture was purified by silica gel column chromatography to give the desired product **1'**.

III. Reference

[1] C. P. Chen, R. S. Zeng, J. Y. Zhang, Y. S. Zhao, *Org. Lett.,* 2018, **20**, 888.

[2] A. D. G. Yamagata, S. Datta, K. E. Jackson, L. Stegbauer, R. S. Paton, D. J. Dixon, *Angew. Chem.*, 2015, **127**, 4981.

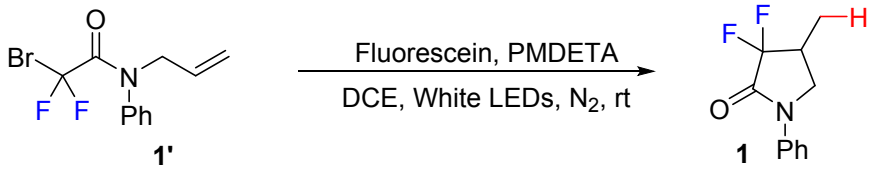
[3] D. Grassi, A. Alexakis, *Adv. Synth. Catal.,* 2015, **357**, 3171.

[4] Y. Watanabe, H. Iida, C. Kibayashi, *J. Org. Chem.*, 1989, **54**, 4088.

[5] N. B. Kondekar, S. R. V. Kandula, P. Kumar, *Tetrahedron Lett.*, 2004, **45**, 5477.

[6] K. Sun, S. N. Wang, R. R. Feng, Y. X. Zhang, X. Wang, Z. G. Zhang, B. Zhang, *Org. Lett.*, 2019, **21**, 2052.

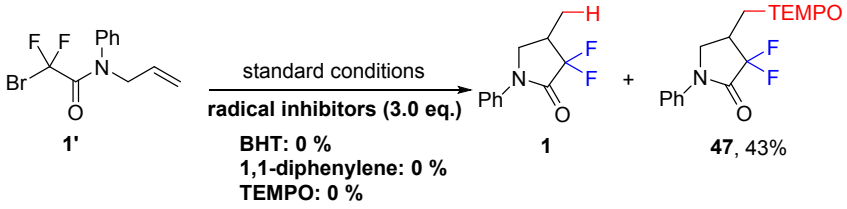
IV. General procedure for the synthesis of intramolecular cyclization product (1 as an example)



A 10mL Schlenk bomb was charged with Fluorescein (8.3 mg, 10 mol%), **1'** (0.25 mmol, 1.0 equiv.) and PMDETA (87.0 mg, 2.0 equiv.) in DCE (2 mL). Then the reaction was stirred under N_2 atmosphere upon irradiation of 3W white LEDs at room temperature for 10 h. The reaction was monitored by TLC. After completed, the mixture was quenched with water (15 mL) and extracted with CH_2Cl_2 (20 mL × 3). The combined organic phase was dried over anhydrous $MgSO_4$ and evaporated to leave a residue, which was purified by column chromatography on silica gel using petroleum ether / ethyl acetate (60:1) as an eluent to give pure products **1** as a white solid.

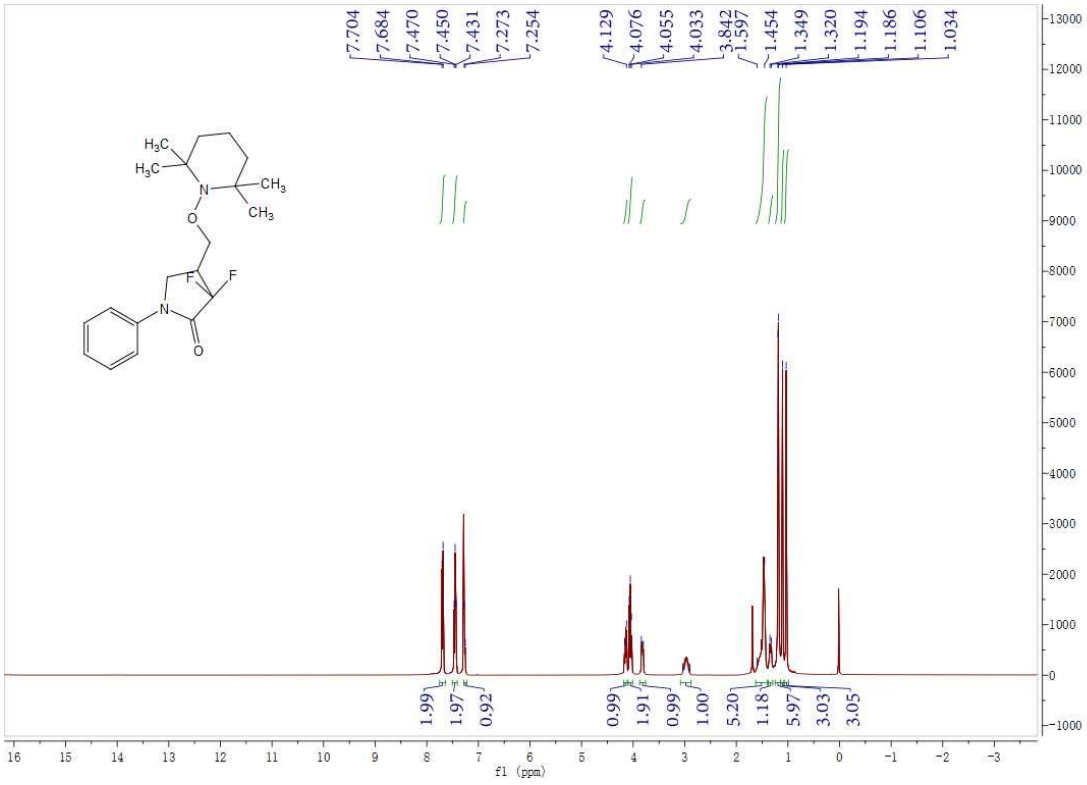
V. Control experiment

(1) Radical trapping



The radical trapping experiment were conduct with *N*-allyl-2-bromo-2,2-difluoro-*N*-phenylacetamide **1'** under the standard conditions with three different trapping agents to capture the radical intermediates expected in our system. After the reaction was completed, no desired product **1** was

detected by TLC, indicating that the reaction was completely inhibited. Meanwhile, it was found that TEMPO, the most common trapping agent, captured alkyl radical and the adduct **47** was isolated in a yield of 43%, the structure of which was confirmed by NMR (Figure S1). White solid, m. p. 123.4-124.5 °C, 43% (39 mg);^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.69 (d, J = 8.0 Hz, 2H), 7.45 (t, J = 8.0 Hz, 2H), 7.27 (t, J = 7.6 Hz, 1H), 4.16-4.12 (m, 1H), 4.05 (t, J = 8.4 Hz, 2H), 3.84-3.80 (m, 1H), 3.03-2.90 (m, 1H), 1.59-1.45 (m, 5H), 1.33 (d, J = 11.6 Hz, 1H), 1.19 (d, J = 3.2 Hz, 6H), 1.10 (s, 3H), 1.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.22 (t, J_{F-C} = 30.8 Hz) 138.03, 129.17, 126.10, 119.96, 117.17 (t, J_{F-C} = 250.1 Hz), 71.65, 60.10, 46.62 (d, J_{F-C} = 4.1 Hz), 39.67, 39.25 (t, J_{F-C} = 21.7 Hz), 33.07, 19.97 (d, J_{F-C} = 10.9 Hz), 16.97. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -106.25 (d, J = 255.6 Hz), -117.80 (d, J = 269.2 Hz). HRMS: $C_{20}H_{29}F_2N_2O_2$ $[M + H]^+$, found: 367.2191, calculated: 367.2192.



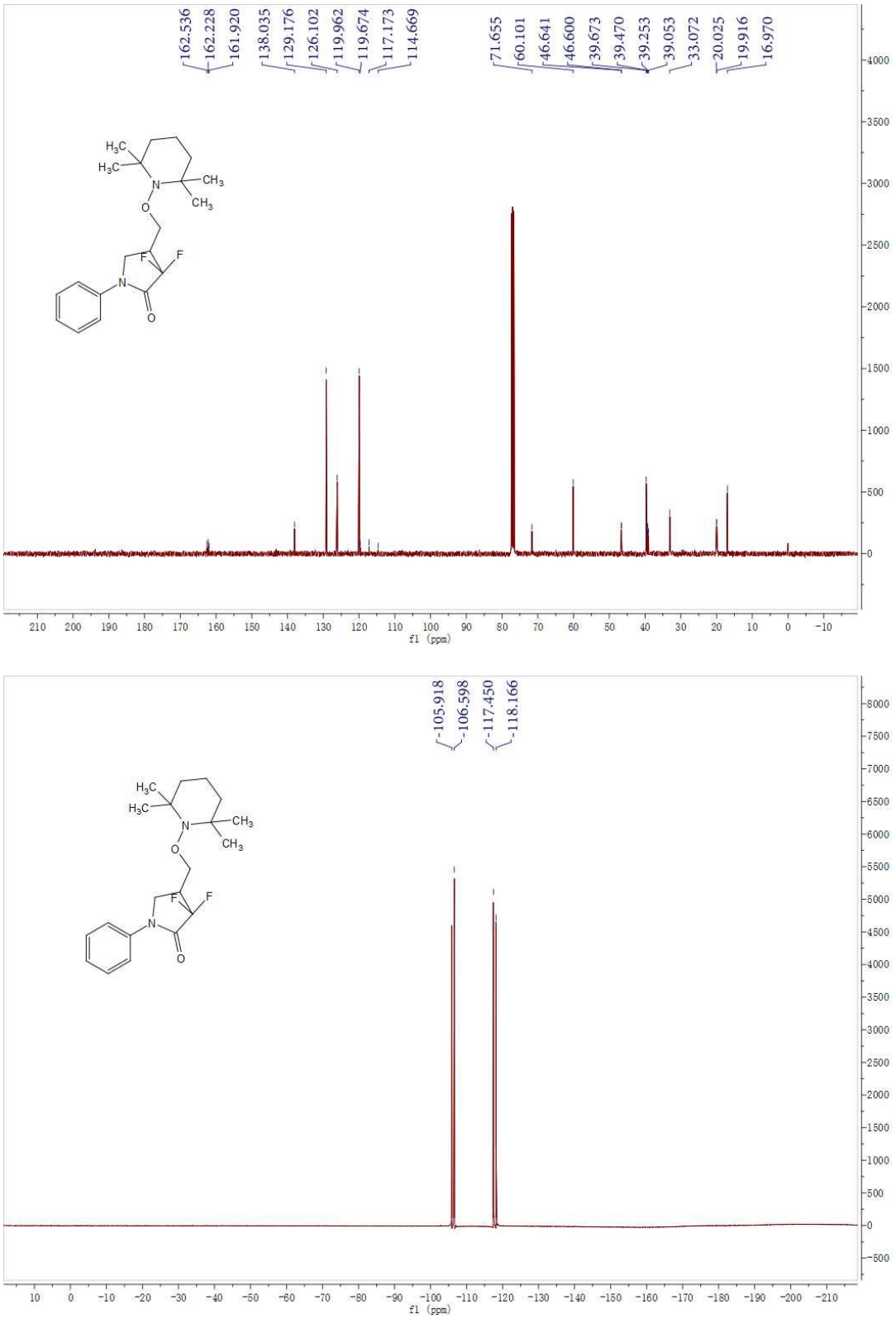


Figure S1: NMR of the adduct **47** of functionalized alkyl radical with TEMPO

(2) Luminescence quenching screening studies

All Fluorescein solution were irradiated 410 nm approximately and the emission intensity from 350 nm to 650 nm was recorded by F-7000 FL Spectrophotometer. A 4 mL solution of Fluorescein in MeCN (0.001 mmol/mL) was added **1'** (0.04 mmol, 0.08 mmol, 0.16 mmol, 0.32 mmol in turn)

or PMDETA (0.020 μmol, 0.040 μmol, 0.060 μmol, 0.080 μmol in turn). Then the emission intensity was collected and the results were presented in Figure S2-S3.

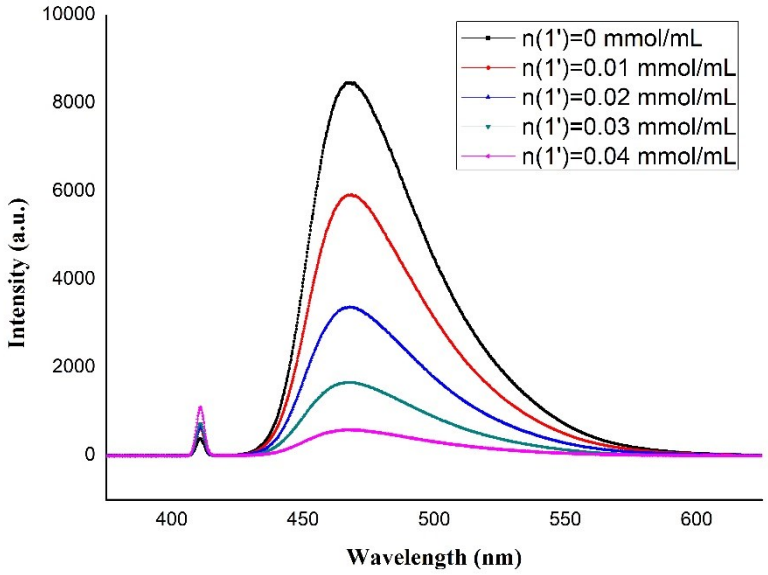


Figure S2: Fluorescence quenching of Fluorescein by **1'**

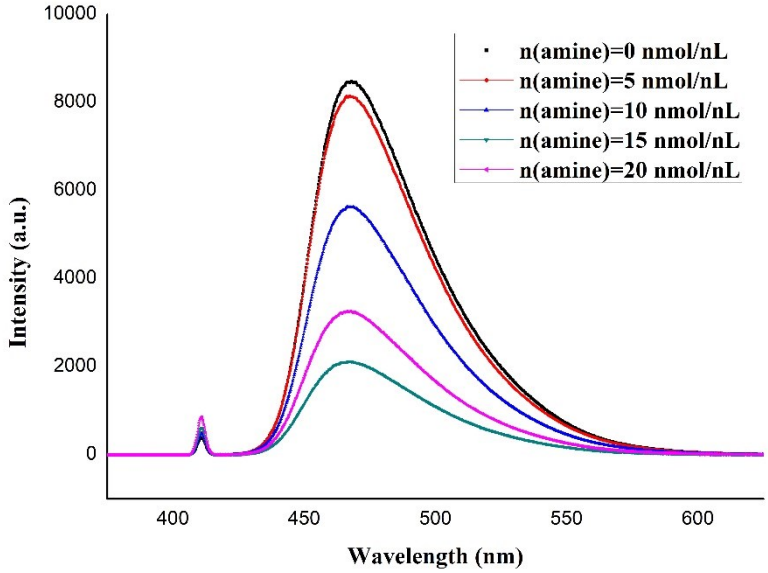


Figure S3: Fluorescence quenching of Fluorescein by PMDETA

An indeed fluorescence quenching phenomenon of fluorescein under various concentrations of **1'** or PMDETA was demonstrated in a curve of $[I_0/I]$ vs $[C/C_0]$, as shown in Figure S4-S5.

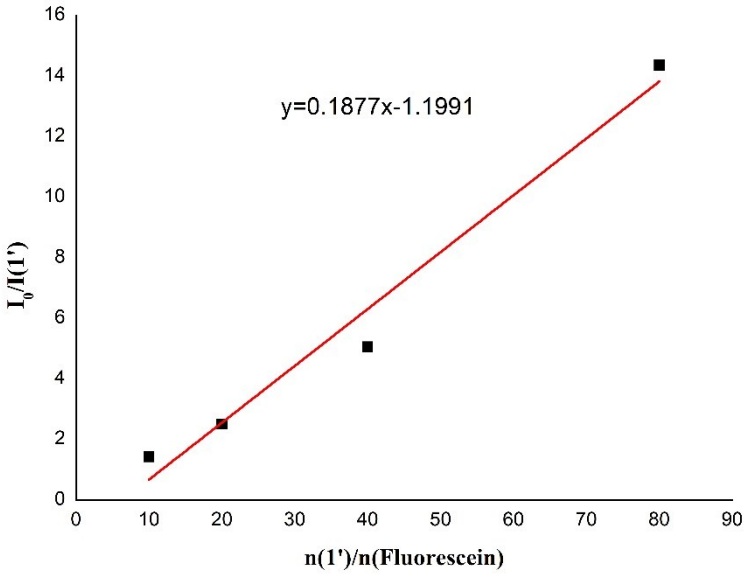


Figure S4: Stern-Volmer plot of Fluorescein by **1'**

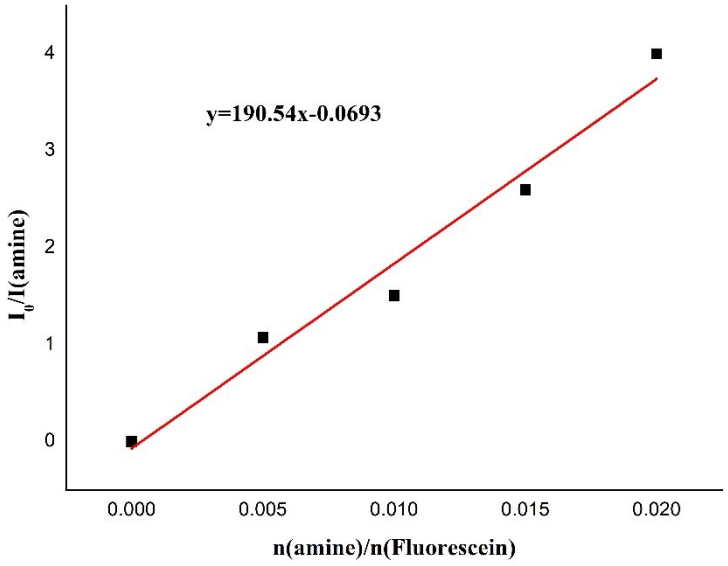
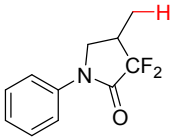


Figure S5: Stern-Volmer plot of Fluorescein by PMDETA

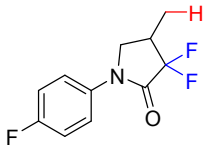
VI. Characterization data for the products (reactions was conducted at 0.25 mmol scale).

3,3-difluoro-4-methyl-1-phenylpyrrolidin-2-one (1)



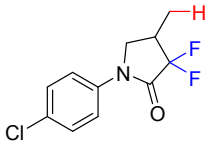
White solid, m. p. 93.2-95.4 ℃, 80% (43 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.69 (d, J = 8.0 Hz, 2H), 7.46 (t, J = 8.0 Hz, 2H), 7.29 (t, J = 7.6 Hz, 1H), 3.99 (t, J = 8.8 Hz, 1H), 3.54 (t, J = 8.4 Hz, 1H), 2.85-2.72 (m, 1H), 1.36 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.56 (t, $J_{F\text{-}C}$ = 31.3 Hz) 138.04, 129.18, 126.08, 119.88, 117.70 (t, $J_{F\text{-}C}$ = 250.8 Hz), 49.87 (d, $J_{F\text{-}C}$ = 6.1 Hz), 34.75 (t, $J_{F\text{-}C}$ = 21.7 Hz), 10.02 (d, $J_{F\text{-}C}$ = 8.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -111.03 (d, J = 265.8 Hz), -119.51 (d, J = 265.8 Hz). HRMS: $C_{11}H_{12}F_2NO$ $[M + H]^+$, found: 212.0866, calculated: 212.0881.

3,3-difluoro-1-(4-fluorophenyl)-4-methylpyrrolidin-2-one (2)



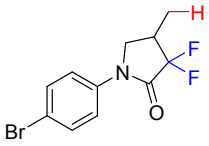
White solid, m. p. 73.5-75.5 °C, 79% (45mg); ^{1}H NMR（400 MHz, $CDCl_3$）δ: 7.66-7.61 (m, 2H), 7.16-7.10 (m, 2H), 3.95 (t, J = 9.2 Hz, 1H), 3.50 (t, J = 8.8 Hz, 1H), 2.83-2.70 (m, 1H), 1.34 (dd, J = 6.8 Hz, J = 1.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.49 (t, $J_{F\text{-}C}$ = 31.5 Hz), 160.33 (d, $J_{F\text{-}C}$ = 245.0 Hz), 134.11 (d, $J_{F\text{-}C}$ = 2.8 Hz), 121.72 (d, $J_{F\text{-}C}$ = 8.1 Hz), 117.59 (t, $J_{F\text{-}C}$ = 249.1 Hz), 116.01 (d, $J_{F\text{-}C}$ = 22.5 Hz), 50.10 (d, $J_{F\text{-}C}$ = 6.2 Hz), 34.77 (t, $J_{F\text{-}C}$ = 21.7 Hz), 10.01 (d, $J_{F\text{-}C}$ = 8.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -111.04 (d, J = 266.2 Hz), -115.21, -119.45 (d, J = 266.2 Hz). HRMS: $C_{11}H_{11}F_3NO$ $[M + H]^+$, found: 230.0782, calculated: 230.0787.

3,3-difluoro-1-(4-cholrophenyl)-4-methylpyrrolidin-2-one (3)



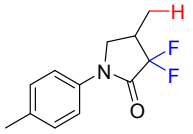
White solid, m. p. 97.4-98.9 °C, 70% (43 mg); ^{1}H NMR（400 MHz, $CDCl_3$）δ: 7.63 (d, J = 8.8 Hz, 2H), 7.40 (d, J = 8.8 Hz, 2H), 3.94 (t, J = 8.8 Hz, 1H), 3.49 (t, J = 8.4 Hz, 1H), 2.85-2.68 (m, 1H), 1.33 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.55 (t, $J_{F\text{-}C}$ = 31.6 Hz), 136.58, 131.37, 129.25, 120.95, 117.46 (t, $J_{F\text{-}C}$ = 251.2 Hz), 49.78 (d, $J_{F\text{-}C}$ = 6.2 Hz), 34.69 (t, $J_{F\text{-}C}$ = 21.7 Hz), 9.97 (d, $J_{F\text{-}C}$ = 8.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -111.08 (d, J = 266.6 Hz), -119.41 (d, J = 266.2 Hz). HRMS: $C_{11}H_{10}ClF_2NNaO$ $[M + Na]^+$, found: 268.0315, calculated: 268.0311.

3,3-difluoro-1-(4-bromophenyl)-4-methylpyrrolidin-2-one (4)



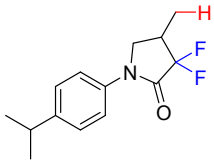
White solid, m. p. 111.9-113.5 °C, 73% (53 mg);. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59-7.54 (m, 4H), 3.94 (t, J = 8.8 Hz, 1H), 3.49 (t, J = 8.4 Hz, 1H), 2.85-2.68 (m, 1H), 1.33 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.57 (t, $J_{F\text{-}C}$ = 31.8 Hz), 137.07, 132.22, 121.22, 119.13, 117.47 (t, $J_{F\text{-}C}$ = 249.8 Hz), 49.70 (d, $J_{F\text{-}C}$ = 6.2 Hz), 34.66 (t, $J_{F\text{-}C}$ = 21.8 Hz), 9.97 (d, $J_{F\text{-}C}$ = 8.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -111.11 (d, J = 266.2 Hz), -119.38 (d, J = 266.2 Hz). HRMS: $C_{11}H_{10}BrF_2NNaO$ $[M + Na]^+$; found: 311.9808, calculated: 311.9806.

3,3-difluoro-1-(4-methylphenyl)-4-methylpyrrolidin-2-one (5)



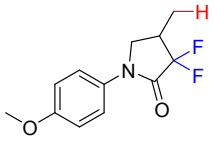
White soild, m. p. 72.8-74.4 °C, 77% (43 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53 (d, J = 8.4 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 3.94 (t, J = 8.8 Hz, 1H), 3.48 (t, J = 8.4 Hz, 1H), 2.81-2.68 (m, 1H), 2.37 (s, 3H), 1.32 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.39 (t, $J_{F\text{-}C}$ = 31.5 Hz), 135.95, 135.54, 129.69, 119.88, 117.76 (t, $J_{F\text{-}C}$ = 248.9 Hz), 49.98 (d, $J_{F\text{-}C}$ = 6.2 Hz), 34.77 (t, $J_{F\text{-}C}$ = 21.6 Hz), 20.93, 10.05 (d, $J_{F\text{-}C}$ = 8.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -110.88 (d, J = 265.4 Hz), -119.43 (d, J = 265.4 Hz). HRMS: $C_{12}H_{14}F_2NO$ $[M + H]^+$; found: 226.1034, calculated: 226.1038.

3,3-difluoro-1-(4-isopropylphenyl)-4-methylpyrrolidin-2-one (6)



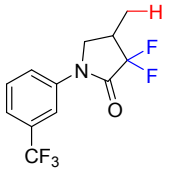
White solid, m. p. 116.5-118.3 °C, 65% (41 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (d, J = 8.8 Hz, 2H), 7.29 (d, J = 8.8 Hz, 2H), 3.95 (t, J = 8.4 Hz, 1H), 3.50 (t, J = 8.4 Hz, 1H), 2.97-2.90 (m, 1H), 2.82-2.69 (m, 1H), 1.32 (d, J = 6.8 Hz, 3H), 1.27 (d, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.42 (t, $J_{F\text{-}C}$ = 31.1 Hz), 146.97, 135.74, 127.12, 120.01, 117.78 (t, $J_{F\text{-}C}$ = 250.3 Hz), 50.00 (d, $J_{F\text{-}C}$ = 6.1 Hz), 34.80 (t, $J_{F\text{-}C}$ = 21.7 Hz), 33.69, 23.93, 10.09 (d, $J_{F\text{-}C}$ = 8.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -110.90 (d, J = 265.4 Hz), -119.51 (d, J = 265.4 Hz). HRMS: $C_{14}H_{17}F_2NNaO$ $[M + Na]^+$; found: 276.1168, calculated: 276.1170.

3,3-difluoro-1-(4-methoxyphenyl)-4-methylpyrrolidin-2-one (7)



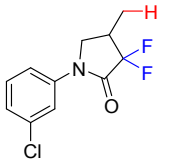
White solid, m. p. 112.0-113.7 °C, 75% (45 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.58-7.54 (m, 2H), 6.97-6.93 (m, 2H), 3.92 (t, J = 9.2 Hz, 1H), 3.83 (s, 3H), 3.47 (t, J = 8.4 Hz, 1H), 2.82-2.69 (m, 1H), 1.32 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.25 (t, $J_{F\text{-}C}$ = 31.3 Hz), 157.62, 131.14, 121.61, 117.79 (t, $J_{F\text{-}C}$ = 250.6 Hz), 114.43, 55.50, 50.26 (d, $J_{F\text{-}C}$ = 6.2 Hz), 34.82 (t, $J_{F\text{-}C}$ = 21.7 Hz), 10.88 (d, $J_{F\text{-}C}$ = 8.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -110.78 (d, J = 265.8 Hz), -119.37 (d, J = 265.4 Hz). HRMS: $C_{12}H_{14}F_2NO_2$ $[M + H]^+$; found: 242.0981, calculated: 242.0987.

3,3-difluoro-4-methyl-1-(3-(trifluoromethyl)phenyl)pyrrolidin-2-one (8)



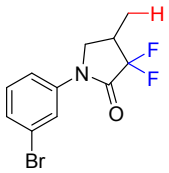
White solid, m. p. 71.2-73.8 °C, 81% (56 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98 (d, J = 8.0 Hz, 1H), 7.88 (s, 1H), 7.59-7.51 (m, 2H), 4.01 (t, J = 8.8 Hz, 1H), 3.56 (t, J = 8.8 Hz, 1H), 2.88-2.71 (m, 1H), 1.36 (dd, J = 6.8 Hz, J = 1.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.82 (t, $J_{F\text{-}C}$ = 32.0 Hz), 138.55, 131.65 (q, $J_{F\text{-}C}$ = 32.6 Hz), 129.86, 123.63 (q, $J_{F\text{-}C}$ = 270.8 Hz), 122.93, 122.55 (q, $J_{F\text{-}C}$ = 3.7 Hz), 117.35 (t, $J_{F\text{-}C}$ = 249.4 Hz), 116.20 (q, $J_{F\text{-}C}$ = 3.8 Hz), 49.68 (d, $J_{F\text{-}C}$ = 6.1 Hz), 34.73 (t, $J_{F\text{-}C}$ = 21.7 Hz), 9.93 (d, $J_{F\text{-}C}$ = 8.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -62.76, -111.32 (d, J = 266.5 Hz), -119.50 (d, J = 266.9 Hz). HRMS: $C_{12}H_{10}F_5NNaO$ $[M + Na]^+$; found: 302.0568, calculated: 302.0575.

3,3-difluoro-4-methyl-1-(3-chlorophenyl)pyrrolidin-2-one (9)



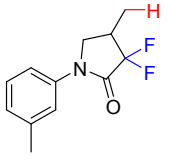
White solid, m. p. 79.9-81.4 °C, 83% (51 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70 (t, J = 2.0 Hz, 1H), 7.60 (d, J = 8.4 Hz, 1H), 7.36 (t, J = 8.0 Hz, 1H), 7.24 (d, J = 8.0 Hz, 1H), 3.95 (t, J = 8.4 Hz, 1H), 3.50 (t, J = 8.0 Hz, 1H), 2.83-2.70 (m, 1H), 1.33 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.66 (t, $J_{F\text{-}C}$ = 31.7 Hz), 139.10, 134.96, 130.21, 126.08, 119.84, 117.73, 117.43 (t, $J_{F\text{-}C}$ = 251.1 Hz), 49.73 (d, $J_{F\text{-}C}$ = 6.1 Hz), 34.69 (t, $J_{F\text{-}C}$ = 21.7 Hz), 9.96 (d, $J_{F\text{-}C}$ = 8.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -111.19 (d, J = 266.5 Hz), -119.47 (d, J = 266.5 Hz). HRMS: $C_{11}H_{10}ClF_2NNaO$ $[M + Na]^+$; found: 268.0307, calculated: 268.0311.

3,3-difluoro-4-methyl-1-(3-bromophenyl)pyrrolidin-2-one (10)



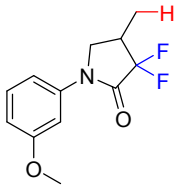
White solid, m. p. 82.6-84.7 °C, 82% (59 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.83 (t, J = 2.0 Hz, 1H), 7.68 (d, J = 8.8 Hz, 1H), 7.40 (d, J = 8.8 Hz, 1H), 7.31 (d, J = 8.4 Hz, 1H), 3.95 (t, J = 8.8 Hz, 1H), 3.50 (t, J = 8.4 Hz, 1H), 2.83-2.70 (m, 1H), 1.34 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.64 (t, $J_{F\text{-}C}$ = 31.6 Hz), 139.23, 130.48, 129.03, 122.86, 122.63, 118.28 117.39 (t, $J_{F\text{-}C}$ = 250.6 Hz), 49.73 (d, $J_{F\text{-}C}$ = 6.2 Hz), 34.70 (t, $J_{F\text{-}C}$ = 21.8 Hz), 9.98 (d, $J_{F\text{-}C}$ = 8.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -111.19 (d, J = 266.5 Hz), -119.46 (d, J = 266.5 Hz). HRMS: $C_{11}H_{11}BrF_2NO$ $[M + H]^+$; found: 289.9978, calculated: 289.9987.

3,3-difluoro-4-methyl-1-(3-methylphenyl)pyrrolidin-2-one (11)



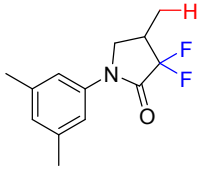
White solid, M. P. 63.8-65.5 °C, 64% (36 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50 (s, 1H), 7.44 (d, J = 8.0 Hz, 1H), 7.31 (t, J = 8.0 Hz, 1H), 7.08 (d, J = 7.6 Hz, 1H), 3.95 (t, J = 8.8 Hz, 1H), 3.50 (t, J = 8.8 Hz, 1H), 2.81-2.68 (m, 1H), 2.40 (s, 3H), 1.33 (dd, J = 6.8 Hz, J = 1.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.52 (t, $J_{F\text{-}C}$ = 31.2 Hz), 139.19, 137.97, 128.98, 126.92, 120.66, 117.73 (t, $J_{F\text{-}C}$ = 249.1 Hz), 117.03, 50.00 (d, $J_{F\text{-}C}$ = 6.1 Hz), 34.78 (t, $J_{F\text{-}C}$ = 21.6 Hz), 21.57, 10.04 (d, $J_{F\text{-}C}$ = 8.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -110.96 (d, J = 265.4 Hz), -119.56 (d, J = 265.4 Hz). HRMS: $C_{12}H_{14}F_2NO$ $[M + H]^+$; found: 226.1030, calculated: 226.1038.

3,3-difluoro-4-methyl-1-(3-methoxyphenyl)pyrrolidin-2-one (12)



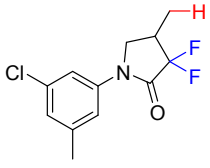
White solid, m. p. 55.1-56.5 °C, 52% (31 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39 (s, 1H), 7.33 (t, J = 8.4 Hz, 1H), 7.14 (d, J = 9.6 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 3.95 (t, J = 8.8 Hz, 1H), 3.84 (s, 3H), 3.49 (t, J = 8.0 Hz, 1H), 2.82-2.68 (m, 1H), 1.33 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.62 (t, $J_{F\text{-}C}$ = 31.3 Hz), 160.15, 139.21, 129.87, 117.69(t, $J_{F\text{-}C}$ = 249.4 Hz), 111.77, 111.71, 106.01, 55.43, 49.96 (d, $J_{F\text{-}C}$ = 6.2 Hz), 34.69 (t, $J_{F\text{-}C}$ = 21.6 Hz), 10.01 (d, $J_{F\text{-}C}$ = 8.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -111.01 (d, J = 265.4 Hz), -119.48 (d, J = 265.4 Hz). HRMS: $C_{12}H_{14}F_2NO_2$ $[M + H]^+$; found: 242.0984, calculated: 242.0987.

3,3-difluoro-4-methyl-1-(3,5-dimethylphenyl)pyrrolidin-2-one (13)



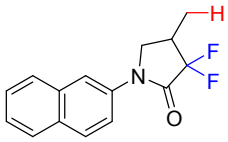
White solid, m. p. 55.5-57.0 °C, 69% (33 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.27 (s, 2H), 6.90 (s, 1H), 3.93 (t, J = 8.8 Hz, 1H), 3.49 (t, J = 8.8 Hz, 1H), 2.80-2.67 (m, 1H), 2.36 (s, 6H), 1.32 (dd, J = 7.2 Hz, J = 1.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.49 (t, $J_{F\text{-}C}$ = 31.2 Hz), 138.94, 137.91, 127.87, 117.87, 117.77 (t, $J_{F\text{-}C}$ = 249.1 Hz), 50.14 (d, $J_{F\text{-}C}$ = 6.1 Hz), 34.79 (t, $J_{F\text{-}C}$ = 21.7 Hz), 21.45, 10.04 (d, $J_{F\text{-}C}$ = 8.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -110.92 (d, J = 265.4 Hz), -119.59 (d, J = 266.0 Hz). HRMS: $C_{13}H_{16}F_2NO$ $[M + H]^+$; found: 240.1190, calculated: 240.1194.

3,3-difluoro-4-methyl-1-(3-chloro-5-dimethylphenyl)pyrrolidin-2-one (14)



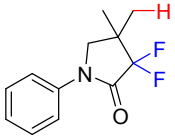
White solid, m. p. 52.5-54.1 °C, 80% (52 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.47 (s, 1H), 7.43 (s, 1H), 7.06 (s, 1H), 3.93 (t, J = 8.8 Hz, 1H), 3.48 (t, J = 8.4 Hz, 1H), 2.81-2.68 (m, 1H), 2.38 (s, 3H), 1.33 (dd, J = 6.8 Hz, J = 1.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.62 (t, $J_{F\text{-}C}$ = 31.3 Hz), 140.73, 138.87, 134.56, 126.79, 118.63, 117.46 (t, $J_{F\text{-}C}$ = 251.0 Hz), 117.01, 49.85 (d, $J_{F\text{-}C}$ = 6.2 Hz), 34.69 (t, $J_{F\text{-}C}$ = 21.7 Hz), 21.46, 9.96 (d, $J_{F\text{-}C}$ = 8.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -111.14 (d, J = 266.5 Hz), -119.50 (d, J = 266.5 Hz). HRMS: $C_{12}H_{12}ClF_2NNaO$ $[M + Na]^+$; found: 282.0464, calculated: 282.0468.

3,3-difluoro-4-methyl-1-(naphthalen-2-yl)pyrrolidin-2-one (15)



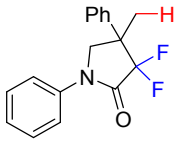
White soild, m. p. 157.9-159.7 °C, 82% (54mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97-7.83 (m, 5H), 7.55-7.48 (m, 2H), 4.08 (t, J = 8.4 Hz, 1H), 3.63 (t, J = 8.4 Hz, 1H), 2.87-2.74 (m, 1H), 1.37 (d, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.73 (t, $J_{F\text{-}C}$ = 31.5 Hz) 135.68, 133.29, 131.37, 129.10, 127.86, 127.63, 126.84, 126.04, 118.99, 117.71 (t, $J_{F\text{-}C}$ = 250.4 Hz), 117.50, 50.15 (d, $J_{F\text{-}C}$ = 6.1 Hz), 34.84 (t, $J_{F\text{-}C}$ = 21.6 Hz), 10.42 (d, $J_{F\text{-}C}$ = 8.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -110.83 (d, J = 265.8 Hz), -119.35 (d, J = 265.8 Hz). HRMS: $C_{15}H_{14}F_2NO$ $[M + H]^+$ found:262,1043, calculated: 262.1038.

3,3-difluoro-4,4-dimethyl-1-phenylpyrrolidin-2-one (16)



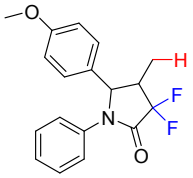
White solid, m. p. 51.4-53.6 °C, 71% (40 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65 (d, J = 8.4 Hz, 2H), 7.44 (t, J = 7.2 Hz, 2H), 7.26 (t, J = 7.6 Hz, 1H), 3.61 (s, 2H), 1.31 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.58 (t, $J_{F\text{-}C}$ = 31.4 Hz), 138.24, 129.19, 125.97, 119.79, 118.50 (t, $J_{F\text{-}C}$ = 253.3 Hz), 56.68 (t, $J_{F\text{-}C}$ = 1.9 Hz), 38.38 (t, $J_{F\text{-}C}$ = 19.8 Hz), 19.74 (t, $J_{F\text{-}C}$ = 4.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -120.69 (t, J = 2.3 Hz). HRMS: $C_{12}H_{14}F_2NO$ $[M + H]^+$; found: 226.1033, calculated: 226.1038.

3,3-difluoro-4-methyl-1,4-diphenylpyrrolidin-2-one (17)



Colorless oil, 45% (32 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.75-7.73 (m, 2H), 7.51-7.36 (m, 7H), 7.31 (t, J = 7.2 Hz, 1H), 4.40 (d, J = 9.6 Hz, 1H), 3.93 (dd, J = 9.6 Hz, J = 2.4 Hz, 1H), 1.63 (d, J = 2.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.29 (t, $J_{F\text{-}C}$ = 32.8 Hz), 138.07, 137.94 (d, $J_{F\text{-}C}$ = 2.7 Hz), 129.34, 128.96, 127.91, 126.24, 126.20, 120.01, 118.03 (t, $J_{F\text{-}C}$ = 259.4 Hz), 54.74 (t, $J_{F\text{-}C}$ = 3.9 Hz), 46.09 (t, $J_{F\text{-}C}$ = 18.5 Hz), 24.06 (t, $J_{F\text{-}C}$ = 5.9 Hz, $J_{F\text{-}C}$ = 2.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -110.79 (d, J = 261.6 Hz), -120.58 (d, J = 262.0 Hz). HRMS: $C_{17}H_{16}F_2NO$ $[M + H]^+$; found: 288.1185, calculated: 288.1194.

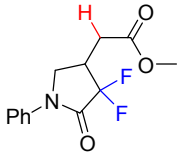
3,3-difluoro-5-(4-methoxyphenyl)-4-methyl-1-phenylpyrrolidin-2-one (18)



White solid, m. p. 84.2-86.6 °C, 40% (32 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.33-7.25 (m, 4H), 7.15-7.11 (m, 3H), 6.83-6.81 (m,2H), 4.73 (dd, J = 7.6 Hz, J = 1.6 Hz, 1H), 3.76 (s, 3H), 2.58-2.43 (m, 1H), 1.29 (d, J = 8.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 163.42 (t, $J_{F\text{-}C}$ = 30.8 Hz), 159.68, 135.85, 128.81, 128.29, 126.44, 123.48, 117.33 (t, $J_{F\text{-}C}$ = 237.14 Hz), 114.45, 65.18 (t, $J_{F\text{-}C}$ = 7.0 Hz), 55.25, 45.51 (t, $J_{F\text{-}C}$ = 20.9 Hz), 8.27 (d, $J_{F\text{-}C}$ = 8.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -111.78 (d, J = 266.9

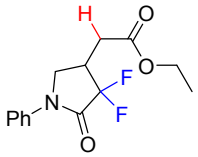
Hz), -119.00 (d, J = 266.5 Hz). HRMS: $C_{18}H_{18}F_2NO$ $[M + H]^+$; found: 318.1299, calculated: 318.1300.

methyl 2-(4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)acetate (19)



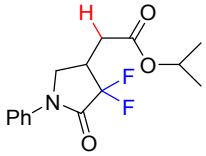
White solid, m. p. 75.7-77.6 ℃, 72% (48mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (d, J = 8.0 Hz, 2H), 7.44 (t, J = 8.0 Hz, 2H), 7.27 (t, J = 7.6 Hz, 1H), 4.20 (t, J = 8.8 Hz, 1H), 3.77 (s, 3H), 3.63 (t, J = 9.6 Hz, 1H), 3.21-3.06 (m, 1H), 2.96 (dd, J = 17.2 Hz, J = 4.4 Hz, 1H), 2.66 (dd, J = 17.2 Hz, J = 10.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.00, 161.71 (t, $J_{F\text{-}C}$ = 31.4 Hz), 137.77, 129.22, 126.29, 119.97, 117.01 (t, $J_{F\text{-}C}$ = 248.4 Hz), 52.30, 48.54 (d, $J_{F\text{-}C}$ = 5.9 Hz), 36.32 (t, $J_{F\text{-}C}$ = 20.0 Hz), 30.38 (d, $J_{F\text{-}C}$ = 7.5 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.99 (d, J = 267.7 Hz), -116.75 (d, J = 267.7 Hz). HRMS: $C_{13}H_{13}F_2NNaO_3$ $[M + Na]^+$; found: 292.0752, calculated: 292.0756.

ethyl 2-(4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)acetate (20)



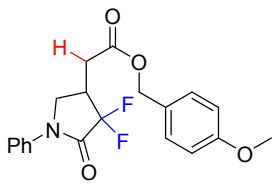
White solid, m. p. 66.1-67.6 ℃, 77% (54mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (d, J = 8.0 Hz, 2H), 7.44 (t, J = 8.0 Hz, 2H), 7.27 (t, J = 7.2 Hz, 1H), 4.25-4.18 (m, 3H), 3.64 (t, J = 8.0 Hz, 1H), 3.21-3.06 (m, 1H), 2.94 (dd, J = 17.2 Hz, J = 4.0 Hz, 1H), 2.65 (dd, J = 17.2 Hz, J = 10.8 Hz, 1H), 1.32 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.52, 161.77 (t, $J_{F\text{-}C}$ = 30.4 Hz), 137.81, 129.21, 126.27, 119.97, 117.05 (t, $J_{F\text{-}C}$ = 248.5 Hz), 61.36, 48.55 (d, $J_{F\text{-}C}$ = 5.8 Hz), 36.33 (t, $J_{F\text{-}C}$ = 20.0 Hz), 30.67 (d, $J_{F\text{-}C}$ = 7.3 Hz), 14.15. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.89 (d, J = 270.7 Hz), -116.74 (d, J = 268.0 Hz). HRMS: $C_{14}H_{15}F_2NNaO_3$ $[M + Na]^+$; found: 306.0898, calculated: 306.0912.

isopropyl 2-(4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)acetate (21)



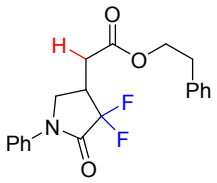
White solid, m.p. 80.5-82.3 ℃, 60% (45mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (d, J = 8.4 Hz, 2H), 7.44 (t, J = 8.4 Hz, 2H), 7.27 (t, J = 7.6 Hz, 1H), 5.11-5.05 (m, 1H), 4.20 (t, J = 8.4 Hz, 1H), 3.64 (t, J = 8.4 Hz, 1H), 3.21-3.05 (m, 1H), 2.92 (dd, J = 17.2 Hz, J = 4.4 Hz, 1H), 2.62 (dd, J = 17.2 Hz, J = 10.8 Hz, 1H), 1.29 (d, J = 6.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 169.97, 161.79 (t, $J_{F\text{-}C}$ = 31.5 Hz), 137.85, 129.19, 126.24, 119.98, 117.06 (t, $J_{F\text{-}C}$ = 249.6 Hz), 69.01, 48.55 (d, $J_{F\text{-}C}$ = 5.9 Hz), 36.38 (t, $J_{F\text{-}C}$ = 20.1 Hz), 31.03 (d, $J_{F\text{-}C}$ = 7.2 Hz), 21.75. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.85 (d, J = 254.1 Hz), -116.67 (d, J = 267.7 Hz). HRMS: $C_{15}H_{17}F_2NNaO_3$ $[M + Na]^+$; found: 320.1060, calculated: 320.1069.

4-methoxybenzyl 2-(4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)acetate (22)



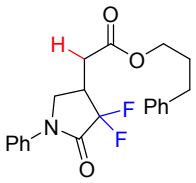
White solid, m. p. 86.9-88.2 ℃, 55% (52mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.64 (d, J = 7.6 Hz, 2H), 7.44 (t, J = 7.6 Hz, 2H), 7.33 (d, J = 8.8 Hz, 2H), 7.27 (t, J = 7.2 Hz, 1H), 6.93 (d, J = 8.4 Hz, 2H), 5.14 (s, 2H), 4.15 (t, J = 9.2 Hz, 1H), 3.83 (s, 3H), 3.61 (t, J = 9.2 Hz, 1H), 3.20-3.05 (m, 1H), 2.97 (dd, J = 17.2 Hz, J = 4.0 Hz, 1H), 2.67 (dd, J = 17.2 Hz, J = 10.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.44, 161.73 (t, $J_{F\text{-}C}$ = 31.6 Hz), 159.90, 137.75, 130.38, 129.22, 127.30, 126.28, 119.92, 117.01 (t, $J_{F\text{-}C}$ = 248.5 Hz), 114.07, 67.02, 55.33, 48.44 (d, $J_{F\text{-}C}$ = 5.9 Hz), 36.32 (t, $J_{F\text{-}C}$ = 20.1 Hz), 30.70 (d, $J_{F\text{-}C}$ = 7.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -109.93 (d, J = 267.3 Hz), -116.59 (d, J = 267.3 Hz). HRMS: $C_{20}H_{19}F_2NNaO_4$ $[M + Na]^+$; found: 398.1168, calculated: 398.1174.

2-(4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)acetate (23)



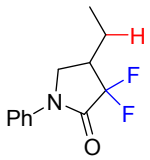
White solid, m. p. 77.7-79.3 °C, 73% (66mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63 (d, J = 7.6 Hz, 2H), 7.44 (t, J = 7.6 Hz, 2H), 7.34-7.21 (m, 6H), 4.41 (t, J = 6.8 Hz, 2H), 4.00 (t, J = 8.4 Hz, 1H), 3.51 (t, J = 8.4 Hz, 1H), 3.12-2.98 (m, 3H), 2.92 (dd, J = 16.0 Hz, J = 4.4 Hz, 1H), 2.61 (dd, J = 17.2 Hz, J = 10.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.38, 161.73 (t, $J_{F\text{-}C}$ = 30.6 Hz), 137.74, 137.46, 129.19, 128.88, 128.62, 126.78, 126.28, 119.99, 117.02 (t, $J_{F\text{-}C}$ = 252.5 Hz), 65.63, 48.40 (d, $J_{F\text{-}C}$ = 5.8 Hz), 36.26 (t, $J_{F\text{-}C}$ = 20.9 Hz), 34.97, 30.62 (d, $J_{F\text{-}C}$ = 7.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -110.06 (d, J = 267.7 Hz), -116.76 (d, J = 267.3 Hz). HRMS: $C_{20}H_{19}F_2NNaO_3$ $[M + Na]^+$; found: 382.1216, calculated: 382.1225.

3-phenylpropyl 2-(4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)acetate (24)



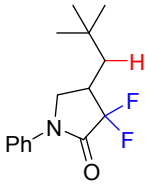
Colorless oil, 69% (65mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68 (d, J = 8.4 Hz, 2H), 7.44 (t, J = 8.4 Hz, 2H), 7.34-7.21 (m, 6H), 4.22-4.15 (m, 3H), 3.62 (t, J = 8.0 Hz, 1H), 3.17-3.02 (m, 1H), 2.92 (dd, J = 17.2 Hz, J = 4.4 Hz, 1H), 2.74 (t, J = 7.2 Hz, 2H), 2.63 (dd, J = 17.2 Hz, J = 10.4 Hz, 1H), 2.07-2.00 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.57, 161.77 (t, $J_{F\text{-}C}$ = 30.6 Hz), 140.95, 137.80, 129.24, 128.53, 128.40, 126.29, 126.16, 119.95, 117.10 (t, $J_{F\text{-}C}$ = 248.6 Hz), 64.83, 48.53 (d, $J_{F\text{-}C}$ = 5.8 Hz), 36.22 (t, $J_{F\text{-}C}$ = 21.8 Hz), 32.23, 30.59 (d, $J_{F\text{-}C}$ = 7.4 Hz), 30.00. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -110.09 (d, J = 267.3 Hz), -116.71 (d, J = 267.3 Hz). HRMS: $C_{21}H_{21}F_2NNaO_3$ $[M + Na]^+$; found: 396.1378, calculated: 396.1382.

3,3-difluoro-4-ethyl-1-phenylpyrrolidin-2-one (25)



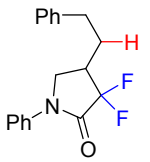
White solid, m. p. 72.7-74.5 ℃, 48% (27 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (d, J = 8.0 Hz, 2H), 7.44 (t, J = 7.6 Hz, 2H), 7.26 (t, J = 7.2 Hz, 1H), 3.95 (t, J = 8.4 Hz, 1H), 3.55 (t, J = 8.0 Hz, 1H), 2.64-2.52 (m, 1H), 1.98-1.88 (m, 1H), 1.72-1.62 (m, 1H), 1.13 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.77 (t, $J_{F\text{-}C}$ = 30.9 Hz), 138.04, 129.18, 126.09, 119.93, 117.75 (t, $J_{F\text{-}C}$ = 248.2 Hz), 48.46 (d, $J_{F\text{-}C}$ = 6.9 Hz), 41.25 (t, $J_{F\text{-}C}$ = 21.0 Hz), 18.94 (d, $J_{F\text{-}C}$ = 7.2 Hz), 11.35. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -108.27 (d, J = 267.7 Hz), -118.75 (d, J = 267.7 Hz). HRMS: $C_{12}H_{13}F_2NNaO$ $[M + Na]^+$; found: 248.0858, calculated: 248.0857.

3,3-difluoro-4-neopentyl-1-phenylpyrrolidin-2-one (26)



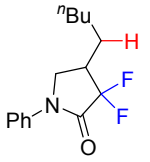
White solid, m. p. 110.8-112.7℃, 50% (28 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66 (d, J = 7.6 Hz, 2H), 7.44 (t, J = 7.6 Hz, 2H), 7.27 (t, J = 7.6 Hz, 1H), 3.98 (t, J = 9.2 Hz, 1H), 3.60 (t, J = 9.6 Hz, 1H), 2.73-2.60 (m, 1H), 1.93 (dd, J = 14.8 Hz, J = 4.0 Hz, 1H), 1.47 (dd, J = 14.4 Hz, J = 8.0 Hz, 1H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.54 (t, $J_{F\text{-}C}$ = 30.5 Hz), 137.93, 129.21, 126.14, 119.94, 117.74 (t, $J_{F\text{-}C}$ = 253.1 Hz), 50.46 (d, $J_{F\text{-}C}$ = 7.6 Hz), 39.06 (d, $J_{F\text{-}C}$ = 5.3 Hz), 36.99 (t, $J_{F\text{-}C}$ = 21.0 Hz), 30.22, 29.73. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -110.79 (d, J = 265.4 Hz), -116.90 (d, J = 233.8 Hz). HRMS: $C_{15}H_{19}F_2NNaO$ $[M + Na]^+$; found: 290.1345, calculated: 290.1327.

3,3-difluoro-4-phenethyl-1-phenylpyrrolidin-2-one (27)



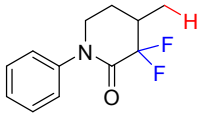
White solid, m. p. 83.2-84.8 ℃, 42% (32 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.64 (d, J = 7.6 Hz, 2H), 7.43 (t, J = 7.6 Hz, 2H), 7.37-7.33 (m, 2H), 7.27-7.25 (m, 4H), 3.86 (t, J = 9.2 Hz, 1H), 3.54 (t, J = 9.2 Hz, 1H), 2.92-2.78 (m, 2H), 2.71-2.59 (m, 1H), 2.31-2.22 (m, 1H), 1.98-1.89 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.53 (t, $J_{F\text{-}C}$ = 30.5 Hz), 140.41, 137.96, 129.18, 128.69, 128.40, 126.48, 126.12, 119.90, 117.77 (t, $J_{F\text{-}C}$ = 248.1 Hz), 48.51 (d, $J_{F\text{-}C}$ = 7.1 Hz), 38.92 (t, $J_{F\text{-}C}$ = 20.9 Hz), 32.88, 27.28 (d, $J_{F\text{-}C}$ = 5.6 Hz), 29.73. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -108.43 (d, J = 266.9 Hz), -117.99 (d, J = 266.9 Hz). HRMS: $C_{18}H_{17}F_2NO$ $[M + H]^+$; found: 302.1352, calculated: 302.1351.

3,3-difluoro-4-pentyl-1-phenylpyrrolidin-2-one (28)



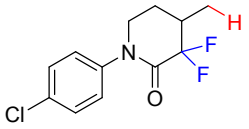
White solid, m. p. 52.7-54.9 ℃, 39% (26 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (d, J = 7.6 Hz, 2H), 7.44 (t, J = 7.6 Hz, 2H), 7.26 (t, J = 7.2 Hz, 1H), 3.94 (t, J = 9.2 Hz, 1H), 3.56 (t, J = 8.0 Hz, 1H), 2.70-2.58 (m, 1H), 1.92-1.83 (m, 1H), 1.62-1.36 (m, 7H), 0.94 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.80 (t, $J_{F\text{-}C}$ = 32.2 Hz), 137.99, 129.21, 126.12, 119.89, 117.77 (t, $J_{F\text{-}C}$ = 247.9 Hz), 48.65 (d, $J_{F\text{-}C}$ = 7.1 Hz), 39.75 (t, $J_{F\text{-}C}$ = 21.0 Hz), 31.71, 26.51, 25.45 (d, $J_{F\text{-}C}$ = 6.5 Hz), 22.45, 14.05. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -108.77 (d, J = 266.9 Hz), -118.50 (d, J = 266.9 Hz). HRMS: $C_{15}H_{19}F_2NNaO$ [M + Na]$^+$; found: 290.1321, calculated: 290.1327.

3,3-difluoro-4-methyl-1-phenylpiperidin-2-one (29)



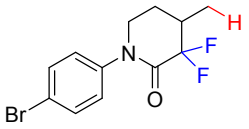
White solid, m. p. 98.7-101.1 ℃, 75% (42 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44 (t, J = 7.6 Hz, 2H), 7.35-7.30 (m, 3H), 3.84-3.76 (m, 1H), 3.70-3.64 (m, 1H), 2.55-2.41 (m, 1H), 2.09-2.03 (m, 2H), 1.28 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.71 (t, $J_{F\text{-}C}$ = 30.2 Hz), 141.29, 129.39, 127.62, 125.62, 113.77 (t, $J_{F\text{-}C}$ = 245.6 Hz), 49.78, 36.27 (t, $J_{F\text{-}C}$ = 21.9 Hz), 26.70 (d, $J_{F\text{-}C}$ = 7.4 Hz), 11.88 (dd, $J_{F\text{-}C}$ = 6.1 Hz, $J_{F\text{-}C}$ = 2.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -108.85 (d, J = 278.2 Hz), -113.28 (d, J = 277.8 Hz). HRMS: $C_{12}H_{13}F_2NNaO$ [M + Na]$^+$; found: 248.0857, calculated: 248.0857.

3,3-difluoro-4-methyl-1-(4-chlorophenyl)-piperidin-2-one (30)



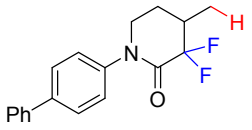
White solid, m. p. 121.6-123.3 ℃, 68% (44 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41 (d, J = 8.8 Hz, 2H), 7.25 (d, J = 8.8 Hz, 2H), 3.82-3.74 (m, 1H), 3.68-3.62 (m, 1H), 2.53-2.40 (m, 1H), 2.12-2.02 (m, 2H), 1.28 (d, J = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.76 (t, $J_{F\text{-}C}$ = 30.4 Hz), 139.69, 133.21, 129.51, 126.96, 113.64 (t, $J_{F\text{-}C}$ = 245.0 Hz), 49.62, 36.26 (t, $J_{F\text{-}C}$ = 21.8 Hz), 26.66 (dd, $J_{F\text{-}C}$ = 7.3 Hz, $J_{F\text{-}C}$ = 1.4 Hz), 11.82 (dd, $J_{F\text{-}C}$ = 6.3 Hz, $J_{F\text{-}C}$ = 2.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -108.80 (d, J = 278.6 Hz), -113.27 (d, J = 278.6 Hz). HRMS: $C_{12}H_{12}ClF_2NNaO$ [M + Na]$^+$; found: 282.0472, calculated: 282.0468.

3,3-difluoro-4-methyl-1-(4-chlorophenyl)-piperidin-2-one (31)



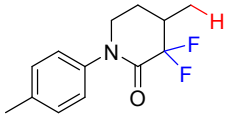
White solid, m. p. 138.9-140.6 ℃, 64% (49 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57-7.54 (m, 2H), 7.20-7.18 (m, 2H), 3.81-3.75 (m, 1H), 3.66-3.63 (m, 1H), 2.52-2.38 (m, 1H), 2.12-1.99 (m, 2H), 1.27 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.71 (t, $J_{F\text{-}C}$ = 30.4 Hz), 140.22, 132.48, 127.28, 121.13 (d, $J_{F\text{-}C}$ = 1.8 Hz), 113.64 (t, $J_{F\text{-}C}$ = 246.2 Hz), 49.55, 36.24 (t, $J_{F\text{-}C}$ = 21.8 Hz), 26.65 (d, $J_{F\text{-}C}$ = 7.2 Hz), 11.82 (dd, $J_{F\text{-}C}$ = 6.2 Hz, $J_{F\text{-}C}$ = 1.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -108.84 (d, J = 278.6 Hz), -113.21 (d, J = 278.6 Hz). HRMS: $C_{12}H_{13}BrF_2NO$ [M + H]$^+$; found: 304.0151, calculated: 304.0143.

3,3-difluoro-4-methyl-1-(4-chlorophenyl)-piperidin-2-one (32)



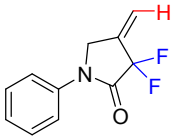
White solid, m. p. 182.8-184.4 ℃, 62% (47 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66-7.59 (m, 4H), 7.47 (t, J = 7.2 Hz, 2H), 7.40-7.37 (m, 3H), 3.88-3.81 (m, 1H), 3.75-3.69 (m, 1H), 2.56-2.43 (m, 1H), 2.12-2.04 (m, 2H), 1.30 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.79 (t, $J_{F\text{-}C}$ = 30.6 Hz), 140.57, 140.39, 140.21, 128.83, 128.05, 127.58, 127.13, 125.86, 113.78 (t, $J_{F\text{-}C}$ = 245.5 Hz), 49.69, 36.29 (t, $J_{F\text{-}C}$ = 21.8 Hz), 26.75 (d, $J_{F\text{-}C}$ = 7.2 Hz), 11.88 (dd, $J_{F\text{-}C}$ = 6.1 Hz, $J_{F\text{-}C}$ = 2.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -108.69 (d, J = 278.2 Hz), -113.21 (d, J = 278.2 Hz). HRMS: $C_{18}H_{18}F_2NO$ $[M + H]^+$; found: 302.1351, calculated: 302.1351.

3,3-difluoro-4-methyl-1-(4-chlorophenyl)-piperidin-2-one (33)



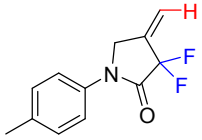
White solid, m. p. 121.6-123.3 ℃, 61% (36 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.24 (d, J = 8.4 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 3.81-3.73 (m, 1H), 3.68-3.62 (m, 1H), 2.53-2.40 (m, 1H), 2.38 (s, 3H), 2.08-2.02 (m, 2H), 1.28 (d, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.76 (t, $J_{F\text{-}C}$ = 30.2 Hz), 138.63, 137.60, 130.04, 125.48, 113.77 (t, $J_{F\text{-}C}$ = 245.7 Hz), 49.92, 36.26 (t, $J_{F\text{-}C}$ = 21.8 Hz), 26.69 (dd, $J_{F\text{-}C}$ = 7.4 Hz, $J_{F\text{-}C}$ = 1.3 Hz), 21.12, 11.90 (dd, $J_{F\text{-}C}$ = 6.1 Hz, $J_{F\text{-}C}$ = 2.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -108.75 (d, J = 277.8 Hz), -113.38 (d, J = 277.8 Hz). HRMS $C_{13}H_{15}F_2NNaO$ $[M + Na]^+$; found: 262.1013, calculated: 262.1014.

3,3-difluoro-4-methylene-1-phenylpyrrolidin-2-one (34)



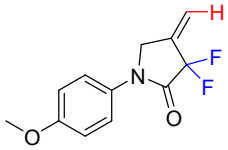
White solid, m. p. 114.1-115.6 °C, 75% (39 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (d, J = 8.0 Hz, 2H), 7.46 (t, J = 8.0 Hz, 2H), 7.29 (t, J = 7.6 Hz, 1H), 6.08 (s, 1H), 5.78 (s, 1H), 4.52 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.96 (t, $J_{F\text{-}C}$ = 30.5 Hz), 137.57, 132.68 (t, $J_{F\text{-}C}$ = 19.8 Hz), 129.30, 126.43, 120.10, 118.30 (t, $J_{F\text{-}C}$ = 2.7 Hz), 110.84 (t, $J_{F\text{-}C}$ = 244.9 Hz), 48.39 (t, $J_{F\text{-}C}$ = 2.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -102.90. HRMS: $C_{11}H_{10}F_2NO$ $[M + H]^+$, found: 210.0720, calculated: 210.0725.

3,3-difluoro-4-methylene-1-(*p*-tolyl)pyrrolidin-2-one (35)



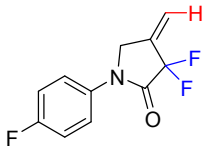
White solid, m. p. 132.5-134.2 °C, 70% (39 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59 (d, J = 8.8 Hz, 2H), 7.25 (d, J = 8.8 Hz, 2H), 6.07 (s, 1H), 5.77 (s, 1H), 4.48 (s, 2H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.78 (t, $J_{F\text{-}C}$ = 30.6 Hz), 136.36, 135.05, 132.80 (t, $J_{F\text{-}C}$ = 19.8 Hz), 129.81, 120.08, 118.17 (t, $J_{F\text{-}C}$ = 2.7 Hz), 110.90 (t, $J_{F\text{-}C}$ = 244.8 Hz), 48.48 (t, $J_{F\text{-}C}$ = 2.2 Hz), 20.97. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -102.79. HRMS: $C_{12}H_{12}F_2NO$ $[M + H]^+$, found: 224.0874, calculated: 224.0881.

3,3-difluoro-1-(4-methoxyphenyl)-4-methylenepyrrolidin-2-one (36)



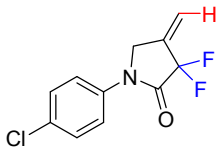
White solid, m. p. 125.3-126.9 °C, 66% (39 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.63 (d, J = 9.2 Hz, 2H), 6.97 (d, J = 9.2 Hz, 2H), 6.07 (s, 1H), 5.76 (s, 1H), 4.48 (t, J = 2.0 Hz, 2H), 3.84 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.64 (t, J_{F-C} = 30.3 Hz), 157.84, 132.86 (t, J_{F-C} = 19.9 Hz), 130.60, 121.87, 118.09 (t, J_{F-C} = 2.7 Hz), 114.43, 110.91 (t, J_{F-C} = 244.7 Hz), 55.52, 48.75 (t, J_{F-C} = 2.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -102.76. HRMS: $C_{12}H_{12}F_2NO_2$ $[M + H]^+$, found: 240.0828, calculated: 240.0831.

3,3-difluoro-1-(4-fluorophenyl)-4-methylenepyrrolidin-2-one (37)



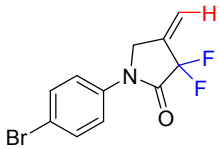
White solid, m. p. 115.7-117.8 °C, 42% (24 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73-7.68 (m, 2H), 7.18-7.12 (m, 2H), 6.09 (s, 1H), 5.79 (s, 1H), 4.50 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.89 (t, J_{F-C} = 31.7 Hz), 161.66 (d, J_{F-C} = 245.6 Hz), 133.63 (d, J_{F-C} = 2.6 Hz), 132.42 (t, J_{F-C} = 20.0 Hz), 122.02 (d, J_{F-C} = 8.2 Hz), 118.52 (t, J_{F-C} = 2.7 Hz), 116.15 (d, J_{F-C} = 22.5 Hz), 110.74 (t, J_{F-C} = 245.0 Hz), 48.62 (t, J_{F-C} = 2.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -102.83, -114.59. HRMS: $C_{11}H_9F_3NO$ $[M + H]^+$; found: 228.0621, calculated: 228.0631.

3,3-difluoro-1-(4-cholrophenyl)-4-methylenepyrrolidin-2-one (38)



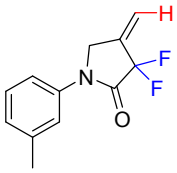
White solid, m. p. 143.8-145 °C, 44% (27 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70 (d, J = 8.8 Hz, 2H), 7.42 (d, J = 9.2 Hz, 2H), 6.10 (s, 1H), 5.80 (s, 1H), 4.50 (t, J = 2.0 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.96 (t, J_{F-C} = 31.1 Hz), 136.12, 132.24 (t, J_{F-C} = 19.8 Hz), 131.74, 129.38, 121.16, 118.65 (t, J_{F-C} = 2.7 Hz), 110.64 (t, J_{F-C} = 245.0 Hz), 48.32 (t, J_{F-C} = 2.2 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -102.81. HRMS: $C_{11}H_9ClF_2NO$ $[M + H]^+$; found: 244.0325, calculated:244.0335.

3,3-difluoro-1-(4-bromophenyl)-4-methylenepyrrolidin-2-one (39)



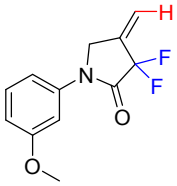
White solid, m. p. 149.1-150.5 °C, 43% (31 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66-7,56 (m, 4H), 6.10 (s, 1H), 5.80 (s, 1H), 4.49 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.97 (t, J_{F-C} = 31.0 Hz), 136.63, 132.34, 121.41, 119.53, 118.68, 110.63 (t, J_{F-C} = 245.3 Hz), 99.99, 48.25 (t, J_{F-C} = 2.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -102.79. HRMS: $C_{11}H_9BrF_2NO$ $[M+H]^+$; found: 287.9822, calculated: 287.9830.

3,3-difluoro-4-methylene-1-(*m*-tolyl)pyrrolidin-2-one (40)



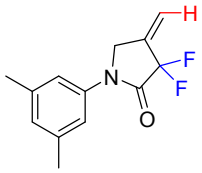
White solid, m. p. 97.7-99.6 °C, 58% (32 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.56 (s, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 8.0 Hz, 1H), 7.10 (d, J = 7.6 Hz, 1H), 6.08 (s, 1H), 5.77 (s, 1H), 4.50 (s, 2H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.92 (t, J_{F-C} = 30.6 Hz), 139.33, 137.49, 132.79 (t, J_{F-C} = 19.8 Hz), 129.09, 127.28, 120.09, 118.17 (t, J_{F-C} = 2.7 Hz), 117.26, 110.86 (t, J_{F-C} = 244.8 Hz), 48.53 (t, J_{F-C} = 2.2 Hz), 21.59. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -102.92. HRMS: $C_{12}H_{12}F_2NO$ $[M + H]^+$; found: 224.0878, calculated: 224.0881.

3,3-difluoro-1-(3-methoxyphenyl)-4-methylenepyrrolidin-2-one (41)



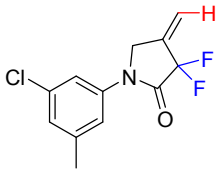
White solid, m. p. 78.3-80.2 °C, 55% (33 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.47 (t, J = 2.0 Hz, 1H), 7.35 (t, J = 8.0 Hz, 1H), 7.20 (dd, J = 8.0 Hz, J = 2.0 Hz, 1H), 6.83 (dd, J = 8.4 Hz, J = 2.4 Hz, 1H), 6.08 (s, 1H), 5.78 (s, 1H), 4.50 (t, J = 2.0 Hz, 2H), 3.85 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.02 (t, J_{F-C} = 30.6 Hz), 160.20, 138.73, 132.57 (t, J_{F-C} = 19.8 Hz), 129.97, 118.34 (t, J_{F-C} = 2.7 Hz), 112.11, 111.88, 110.84 (t J_{F-C} = 244.8 Hz), 106.25, 55.46, 48.52 (t, J_{F-C} = 2.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -102.82. HRMS: $C_{12}H_{12}F_2NO_2$ $[M + H]^+$; found: 240.0827, calculated: 240.0831.

1-(3,5-dimethylphenyl)-3,3-difluoro-4-methylenepyrrolidin-2-one (42)



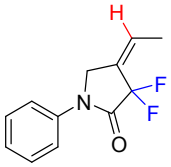
White solid, m. p. 91.4-93.6 °C, 47% (28 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.32 (s, 2H), 6.93 (s, 1H), 6.06 (s, 1H), 5.76 (s, 1H), 4.49 (t, J = 2.0 Hz, 2H), 2.36 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 161.91 (t, J_{F-C} = 30.4 Hz), 139.08, 137.41, 132.89 (t, J_{F-C} = 19.8 Hz), 128.26, 118.11, 118.07, 110.91 (t, J_{F-C} = 244.7 Hz), 48.68 (t, J_{F-C} = 12.1 Hz), 21.49. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -102.91. HRMS: $C_{13}H_{14}F_2NO$ $[M + H]^+$; found: 238.1027, calculated: 238.1038.

1-(3-chloro-5-methylphenyl)-3,3-difluoro-4-methylenepyrrolidin-2-one (43)



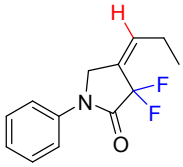
White solid, m. p. 81.6-83.0 °C, 55% (36 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.54 (s, 1H), 7.50 (s, 1H), 7.09 (s, 1H), 6.09 (s, 1H), 5.79 (s, 1H), 4.49 (t, J = 2.0 Hz, 2H), 2.39 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.02 (t, J_{F-C} = 30.8 Hz), 140.87, 138.42, 134.69, 132.30 (t, J_{F-C} = 19.8 Hz), 127.13, 118.83, 118.57, 117.24, 110.64 (t, J_{F-C} = 245.1 Hz), 48.41 (t, J_{F-C} = 2.3 Hz), 21.46. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -102.85. HRMS: $C_{12}H_{11}ClF_2NO$ $[M + H]^+$; found: 258.0484, calculated: 258.0492.

4-ethylidene-3,3-difluoro-1-phenylpyrrolidin-2-one (44)



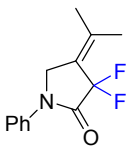
White solid, m. p. 99.2-100.9 °C, 89% (50 mg); ^{1}H NMR（400 MHz, $CDCl_3$）δ: 7.74 (t, J = 8.0 Hz, 4H), 7.47-7.42 (m, 4H), 7.30-7.25 (m, 2H), 6.57-6.50 (m, 1H), 6.27-6.20 (s, 1H), 4.47 (s, 2H), 4.43 (s, 2H), 2.11-2.08 (m, 3H), 1.92-1.89 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.58 (t, J_{F-C} = 30.8 Hz), 162.48 (t, J_{F-C} = 31.0 Hz), 137.77, 137.65, 133.62, 130.60, 129.26, 129.24, 126.33, 126.30, 124.91 (t, J_{F-C} = 19.7 Hz), 123.14 (t, J_{F-C} = 18.4 Hz), 120.19, 120.08, 112.42 (t, J_{F-C} = 243.6 Hz), 111.28 (t, J_{F-C} = 242.8 Hz), 48.40 (t, J_{F-C} = 3.0 Hz), 46.60 (t, J_{F-C} = 2.2 Hz), 14.38, 14.18 (t, J_{F-C} = 2.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -99.29, -100.67. HRMS: $C_{12}H_{12}F_2NO$ $[M + H]^+$, found: 224.0874, calculated: 224.0881.

3,3-difluoro-1-phenyl-4-propylidenepyrrolidin-2-one (45)



White solid, m. p. 91.3-92.7 °C, 82% (49 mg); ^{1}H NMR（400 MHz, $CDCl_3$）δ: 7.74 (d, J = 8.8 Hz, 4H), 7.47-7.42 (m, 4H), 7.30-7.25 (m, 2H), 6.47-6.42 (m, 1H), 6.17-6.12 (s, 1H), 4.47 (s, 2H), 4.44 (s,2H), 2.56-2.49 (m, 2H), 2.30-2.21 (m, 2H), 1.17-1.12 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.56 (t, J_{F-C} = 30.9 Hz), 162.49 (t, J_{F-C} = 31.3 Hz), 140.29, 137.77, 137.66, 137.03, 129.26, 129.25, 126.32, 126.30, 123.37 (t, J_{F-C} = 19.6 Hz), 121.79 (t, J_{F-C} = 18.6 Hz), 120.17, 120.10, 112.40 (t, J_{F-C} = 244.1 Hz), 111.41 (t, J_{F-C} = 243.0 Hz), 48.33 (t, J_{F-C} = 3.2 Hz), 46.54 (t, J_{F-C} = 2.3 Hz), 22.18 22.11 (t, J_{F-C} = 2.0 Hz),13.65 (t, J_{F-C} = 1.4 Hz), 12.84 (t, J_{F-C} = 2.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -99.29, -99.99. HRMS: $C_{13}H_{14}F_2NO$ $[M + H]^+$, found: 238.1032, calculated: 238.1038.

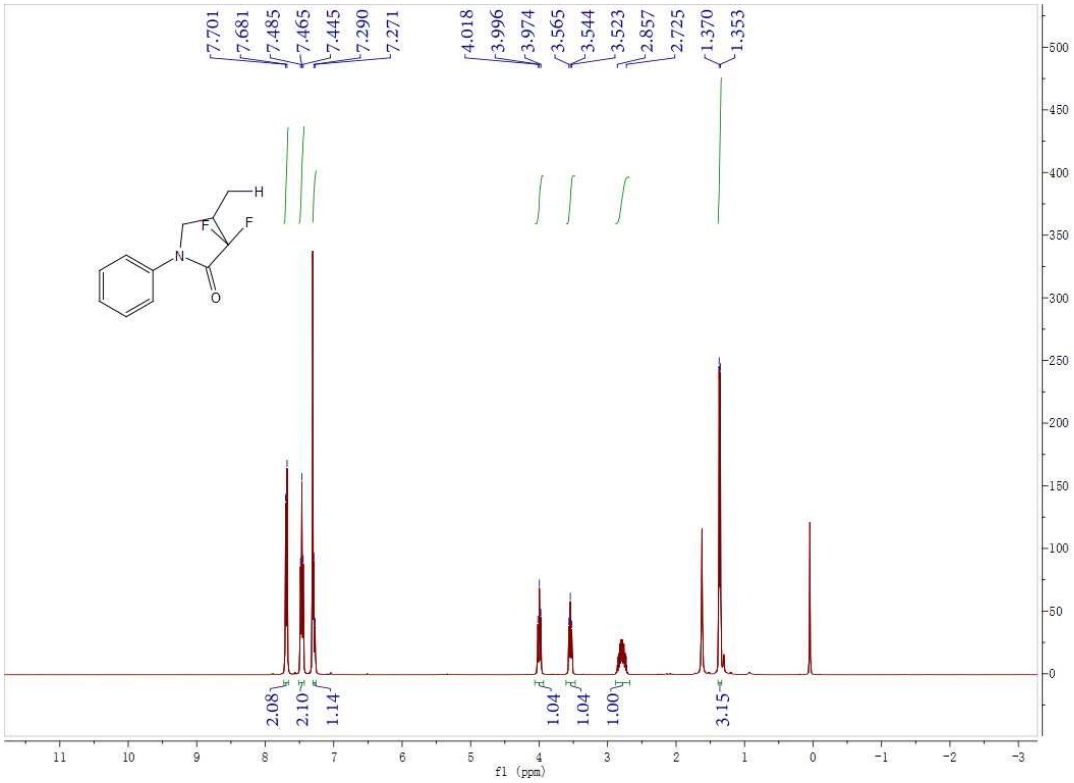
3,3-difluoro-1-phenyl-4-(propan-2-ylidene)pyrrolidin-2-one (46)

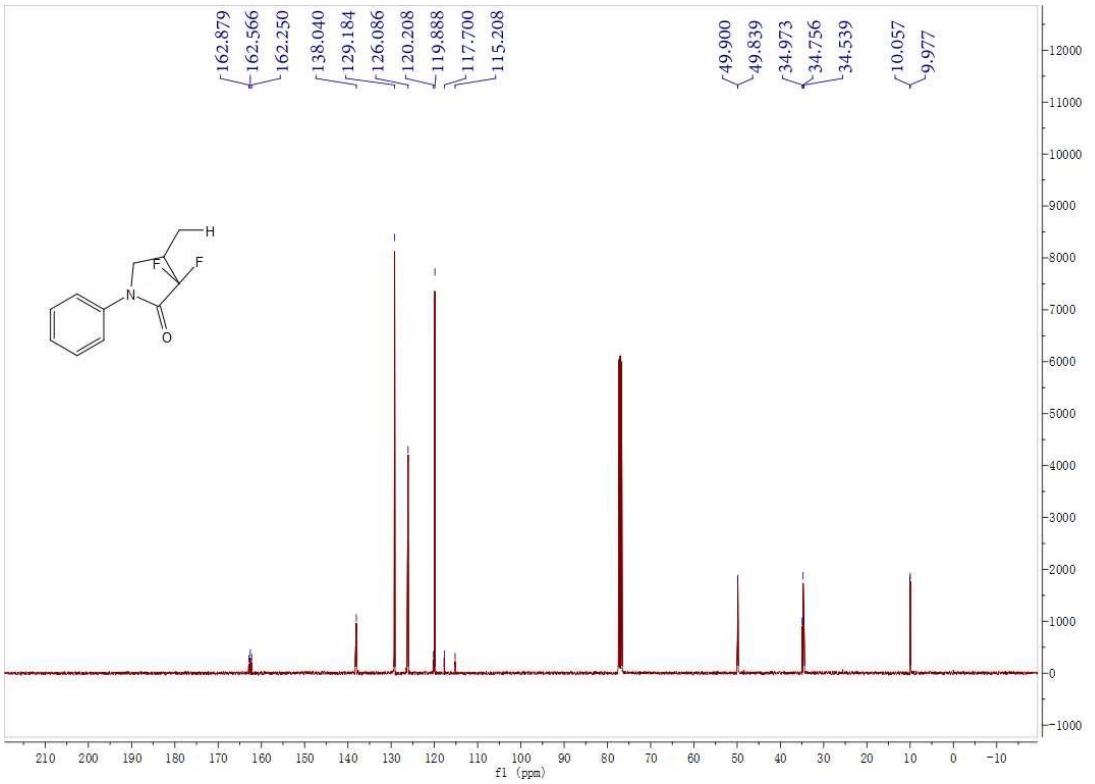


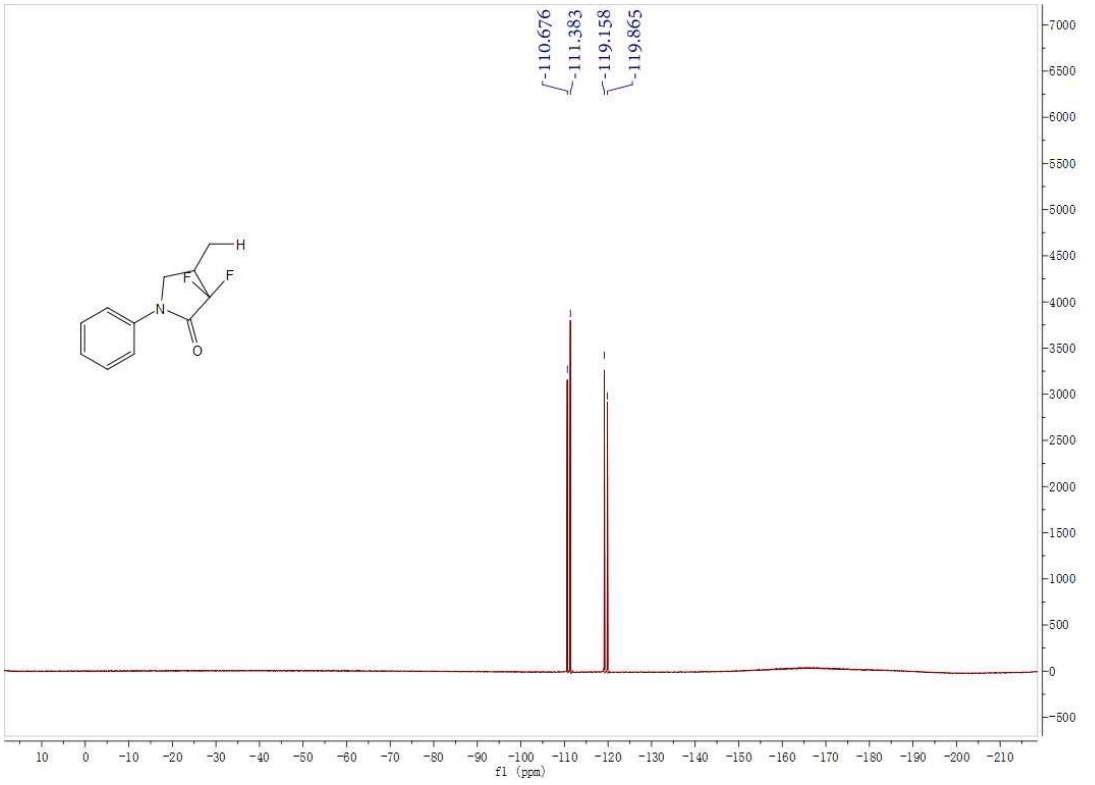
White solid, m. p. 139.2-141.7 ℃, 68% (40mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.76 (d, J = 8.0 Hz, 2H), 7.45 (t, J = 8.8 Hz, 2H), 7.27 (t, J = 7.6 Hz, 1H), 4.40 (s, 2H), 2.12 (s, 3H), 1.89 (t, J = 4.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 162.86 (t, J_{F-C} = 31.3 Hz), 143.64, 137.78, 129.23, 126.26, 120.23, 116.90 (t, J_{F-C} = 18.4 Hz), 112.59 (t, J_{F-C} = 242.2 Hz), 47.81 (t, J_{F-C} = 2.9 Hz), 21.27 (t, J_{F-C} = 1.4 Hz), 20.61. ^{19}F NMR (376 MHz, $CDCl_3$) δ: -97.70. HRMS: $C_{13}H_{13}F_2NNaO$ [M + Na]$^+$; found: 260.0847, calculated: 260.0857.

VII. Copies of NMR Spectra

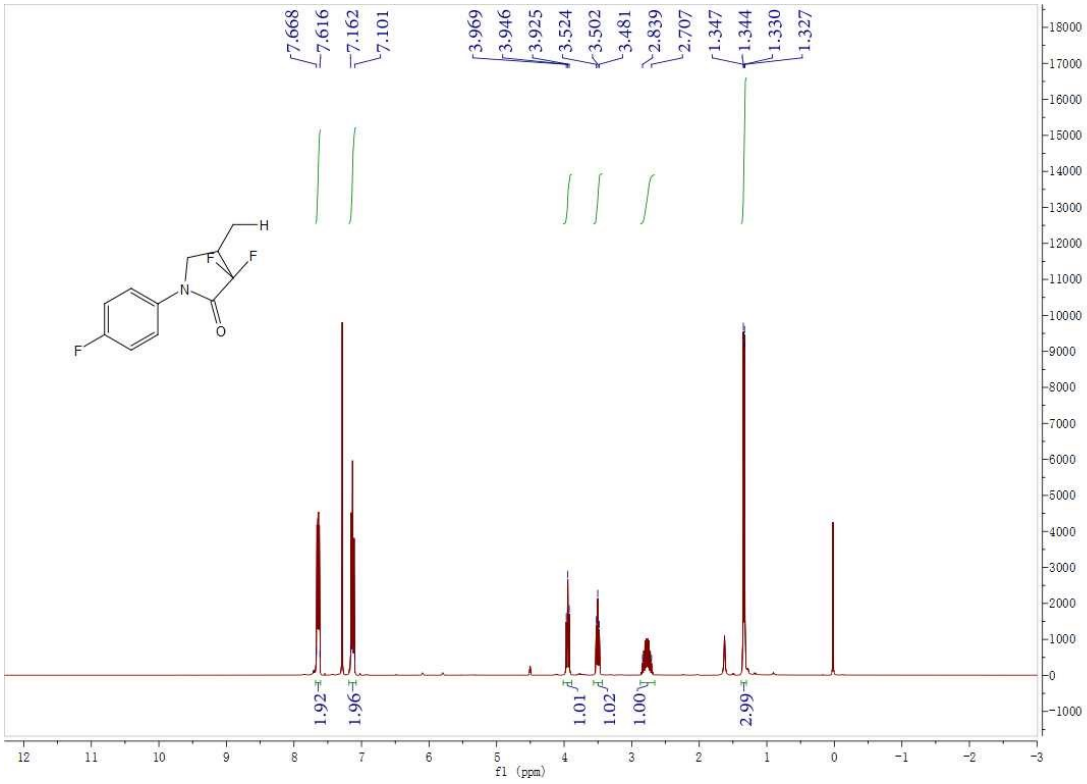
3,3-difluoro-4-methyl-1-phenylpyrrolidin-2-one (1)

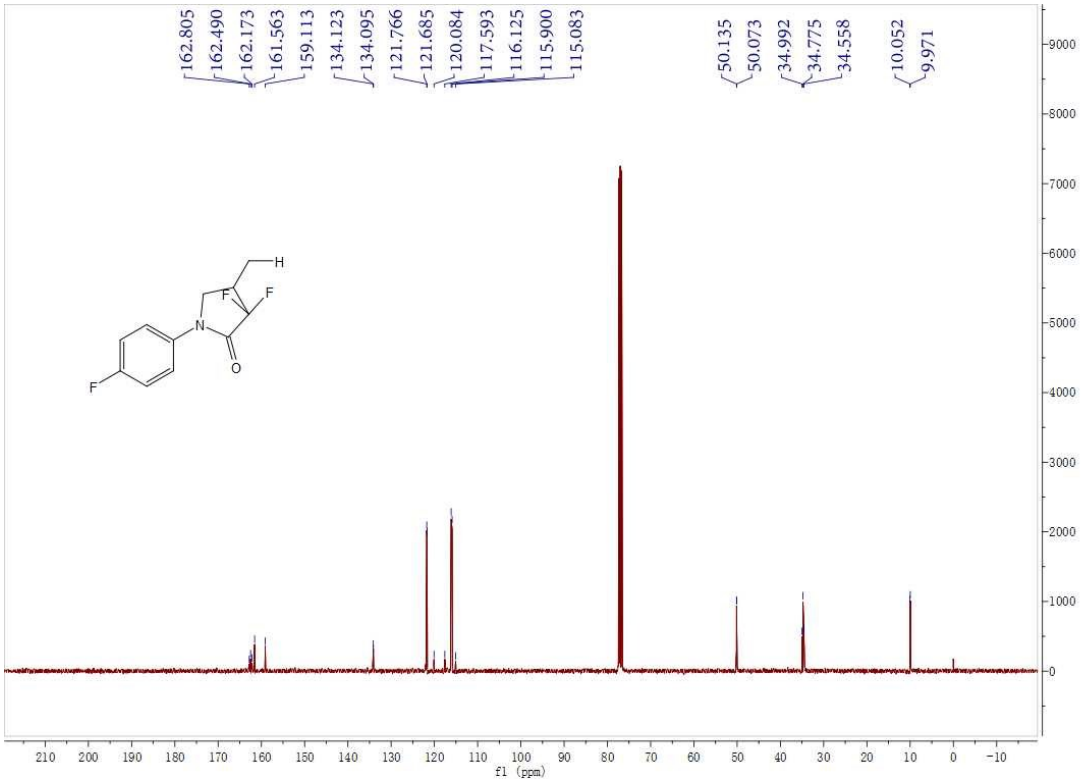


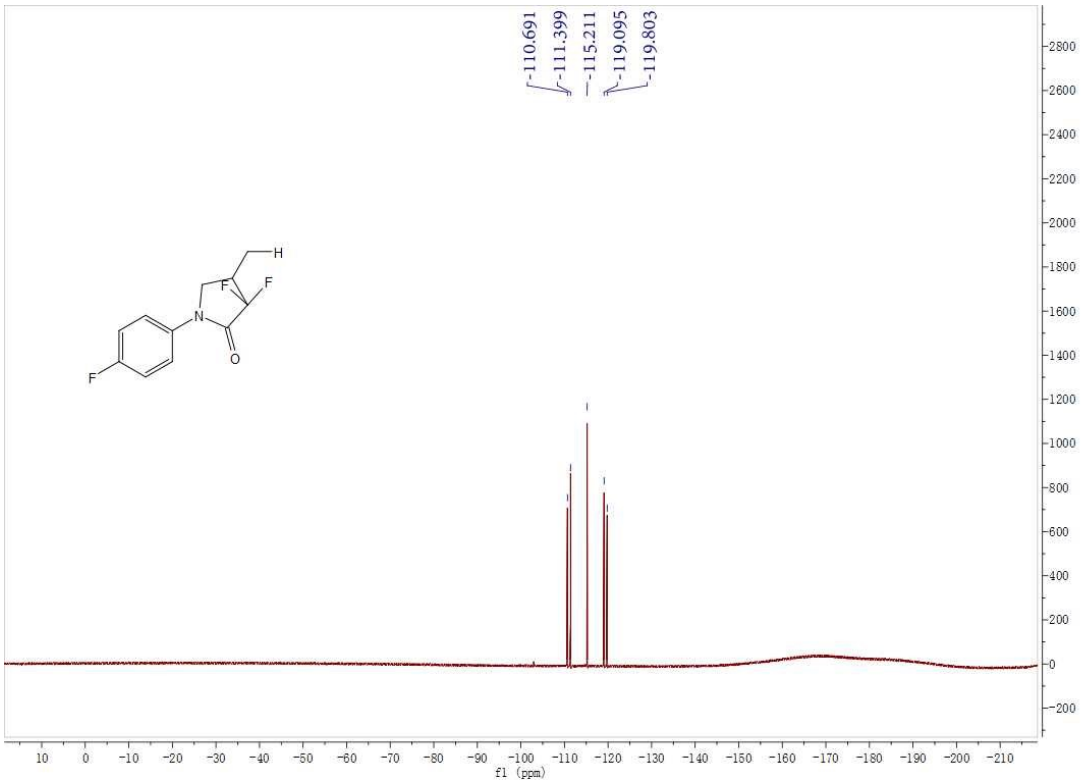

162.879
162.566
162.250
138.040
129.184
126.086
120.208
119.888
117.700
115.208
49.900
49.839
34.973
34.756
34.539
10.057
9.977
f1 (ppm)


-110.676
-111.383
-119.158
-119.865
f1 (ppm)

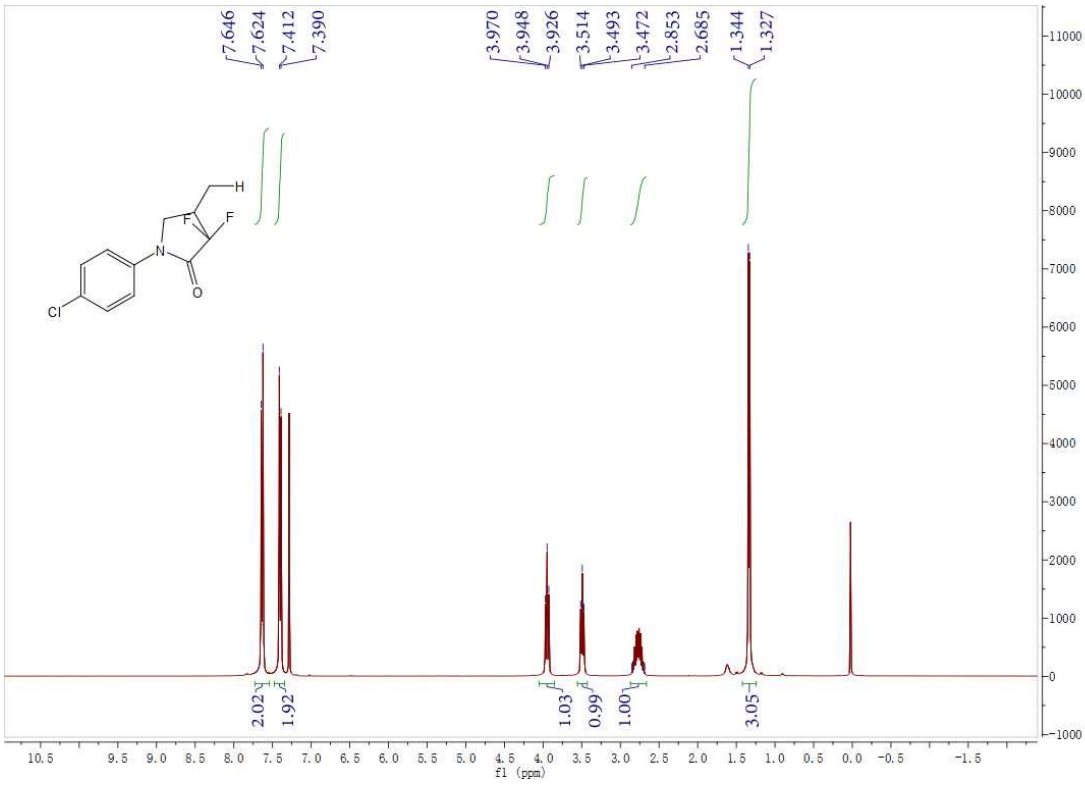
3,3-difluoro-1-(4-fluorophenyl)-4-methylpyrrolidin-2-one (2)

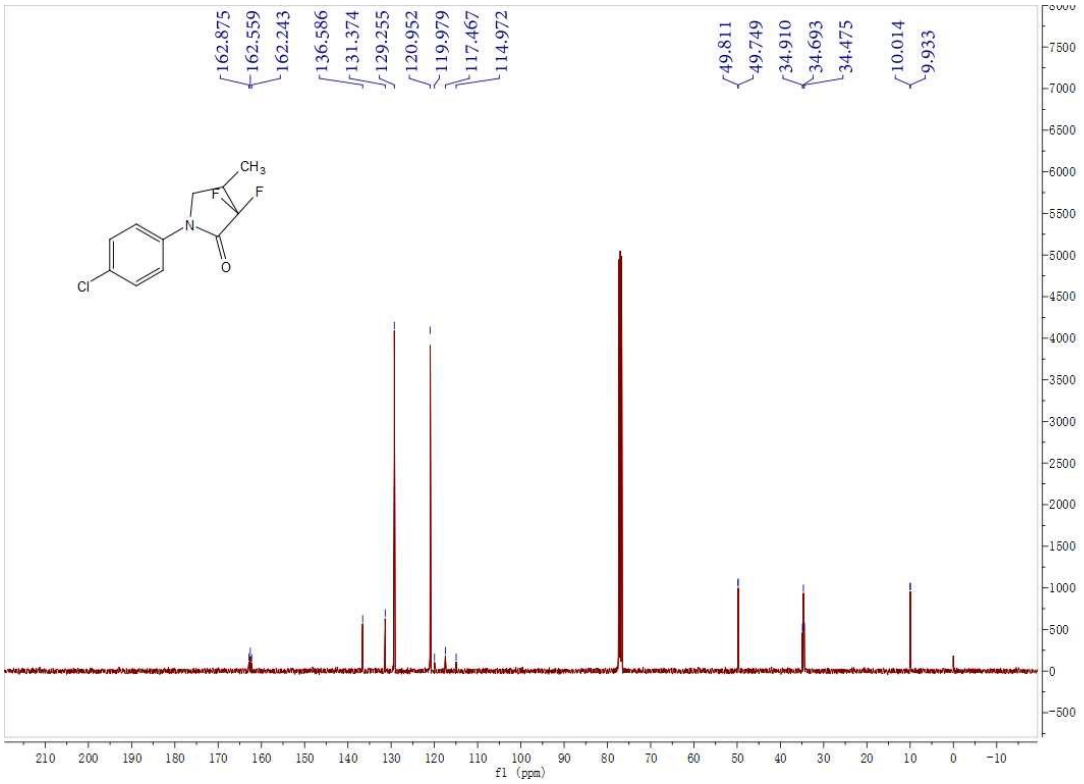


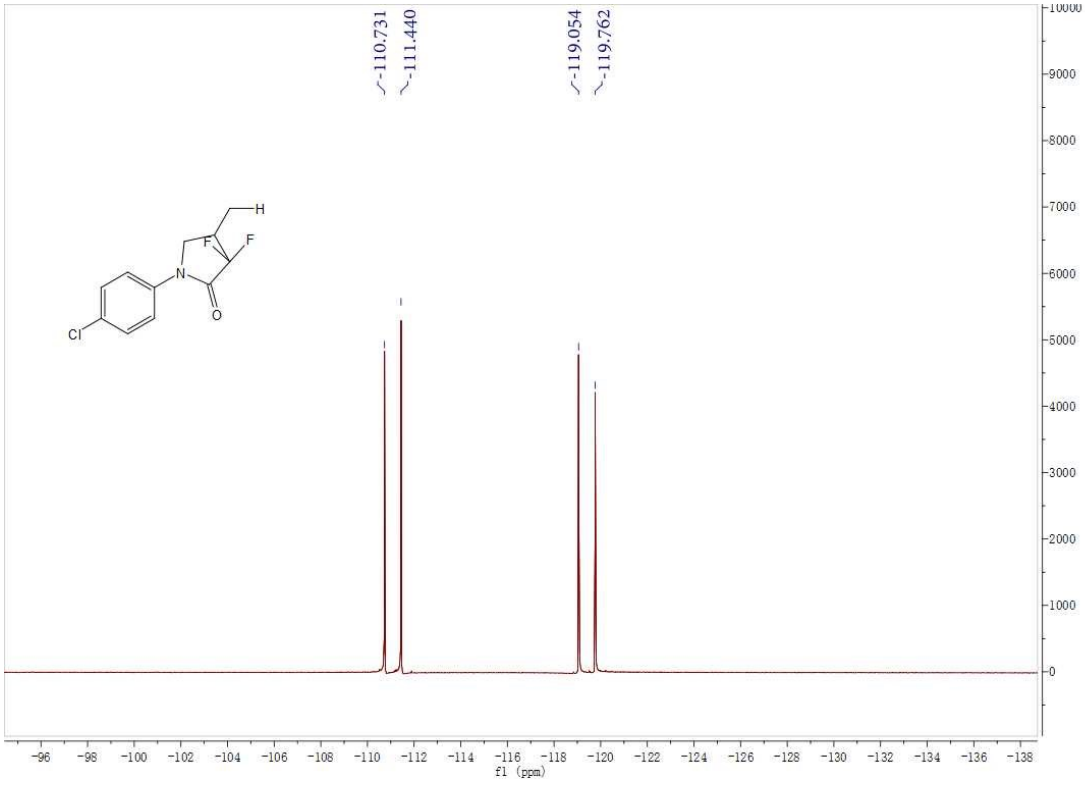




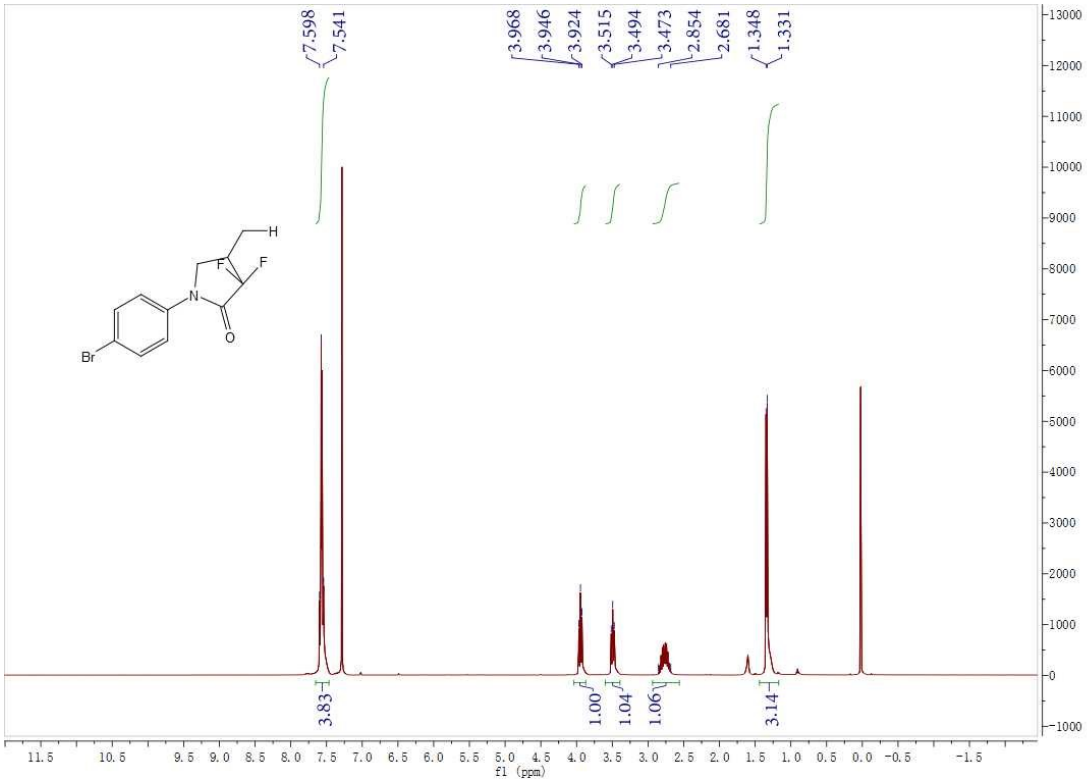
3,3-difluoro-1-(4-cholrophenyl)-4-methylpyrrolidin-2-one (3)

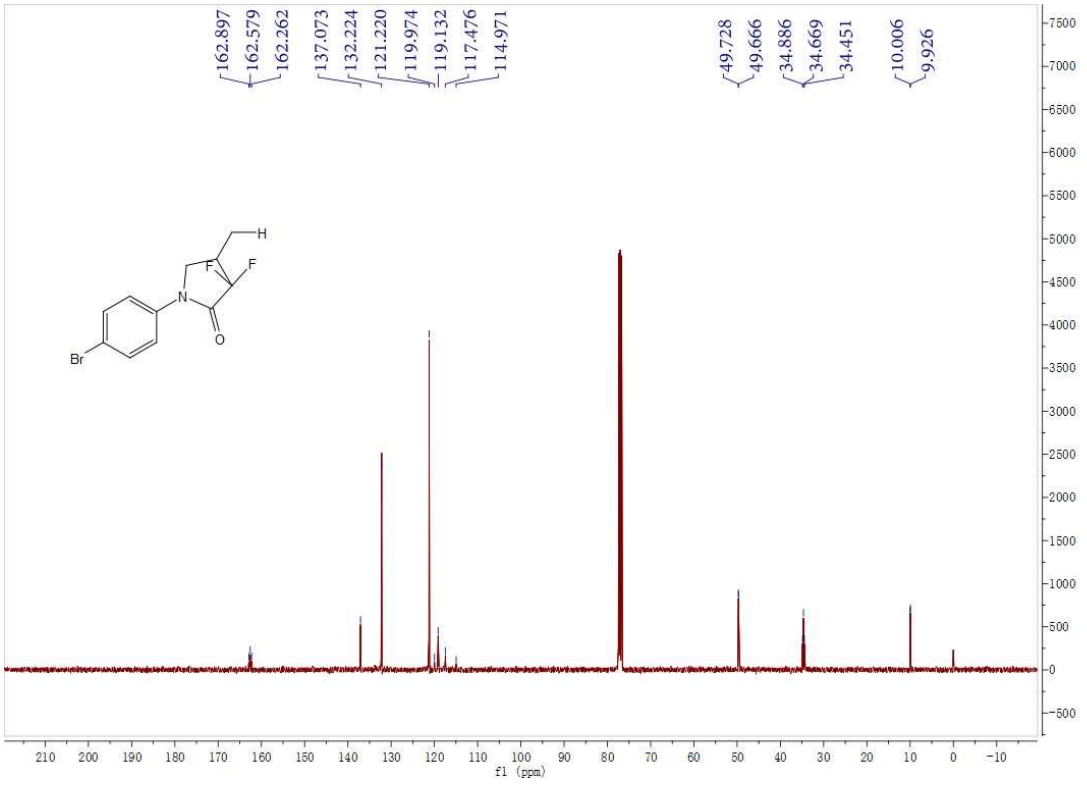


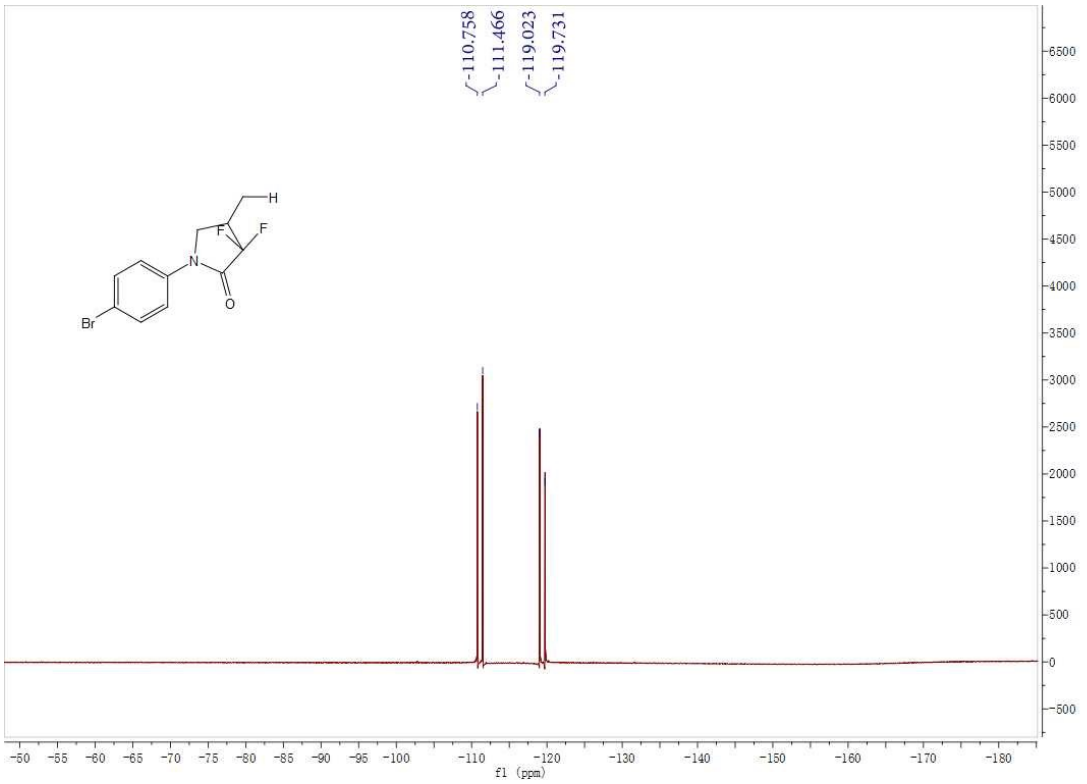

162.875
162.559
162.243
136.586
131.374
129.255
120.952
119.979
117.467
114.972
49.811
49.749
34.910
34.693
34.475
10.014
9.933
CH3
F
F
N
O
Cl
f1 (ppm)


-110.731
-111.440
-119.054
-119.762
H
F
F
N
O
Cl
f1 (ppm)

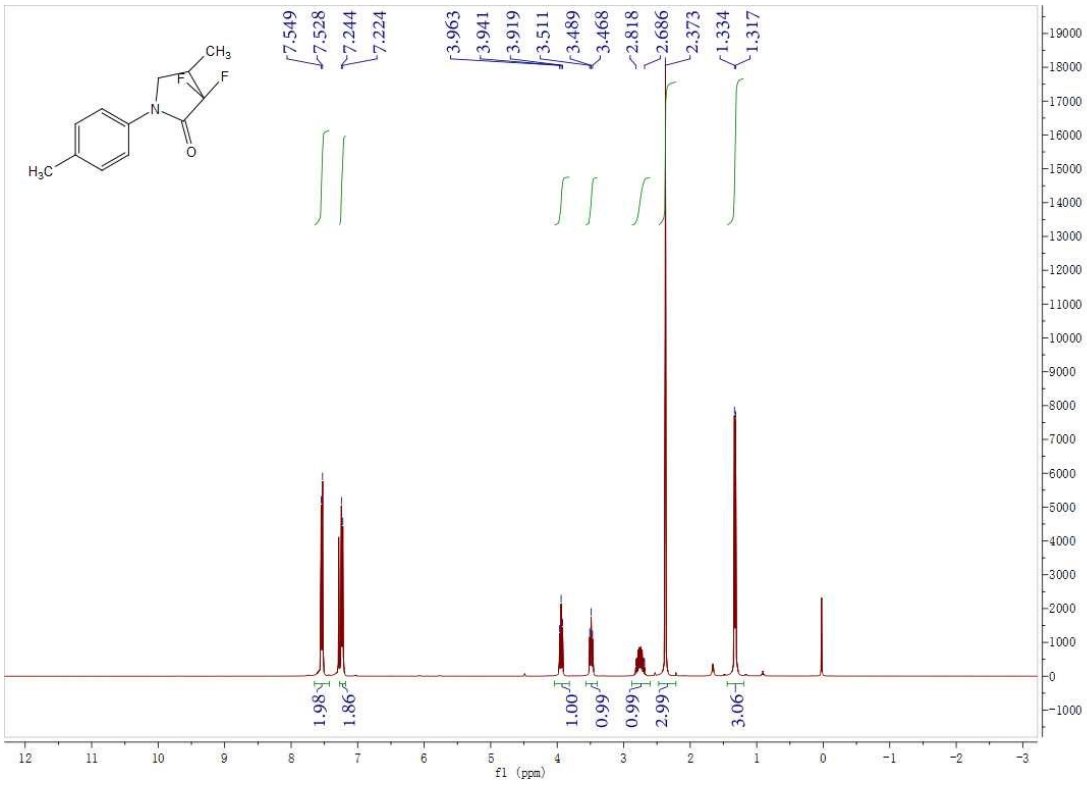
3,3-difluoro-1-(4-bromophenyl)-4-methylpyrrolidin-2-one (4)

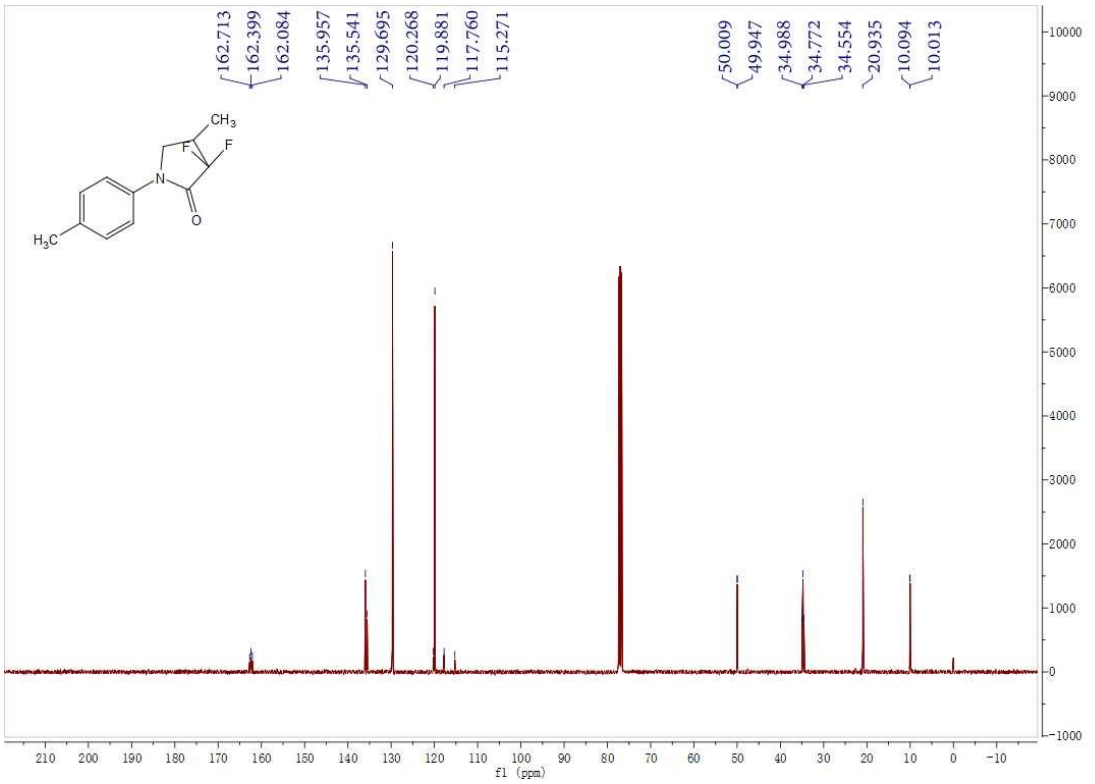


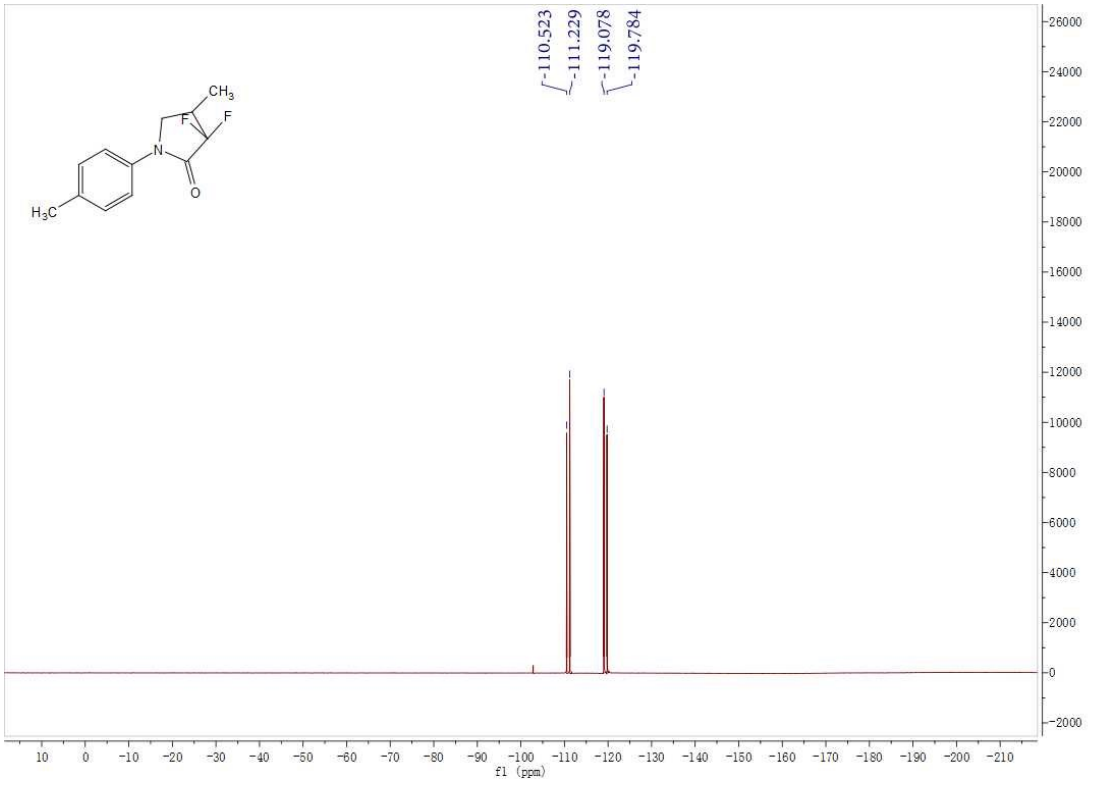




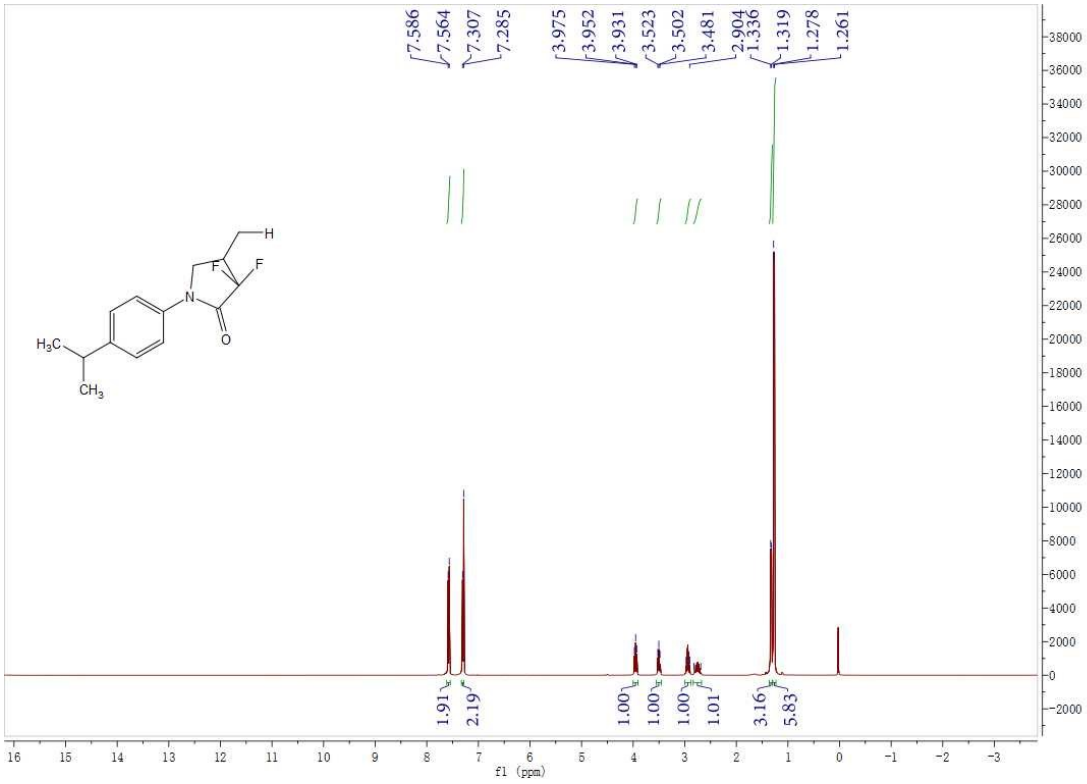
3,3-difluoro-1-(4-methylphenyl)-4-methylpyrrolidin-2-one (5)

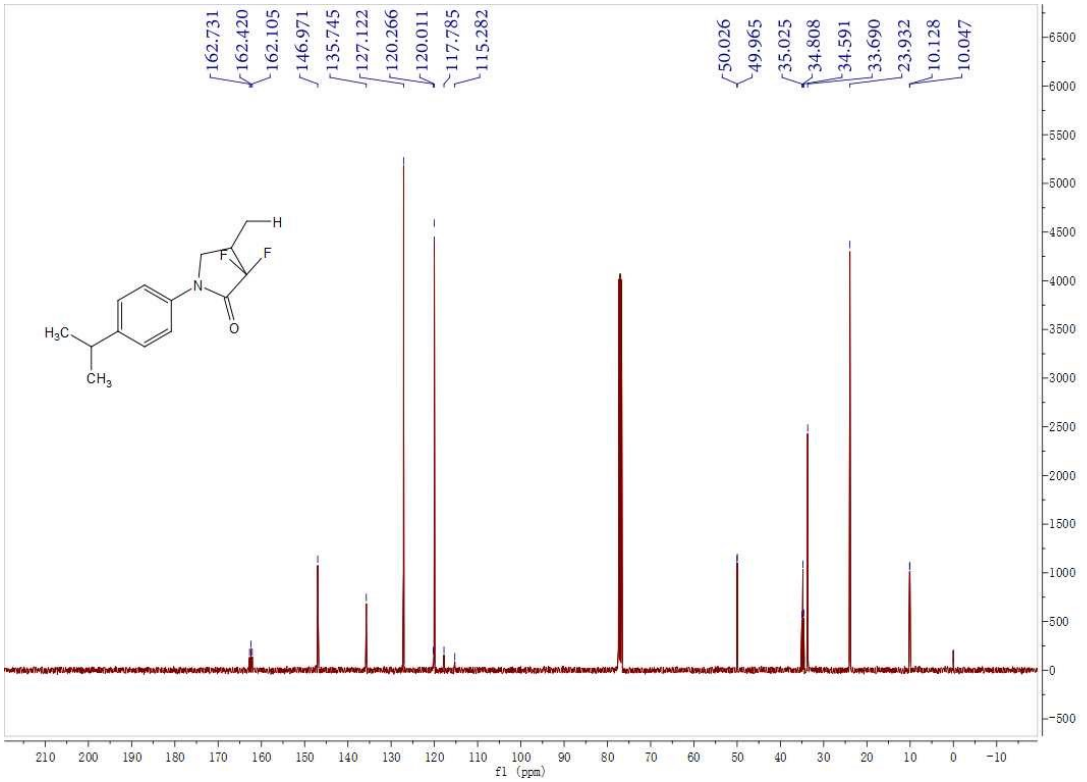


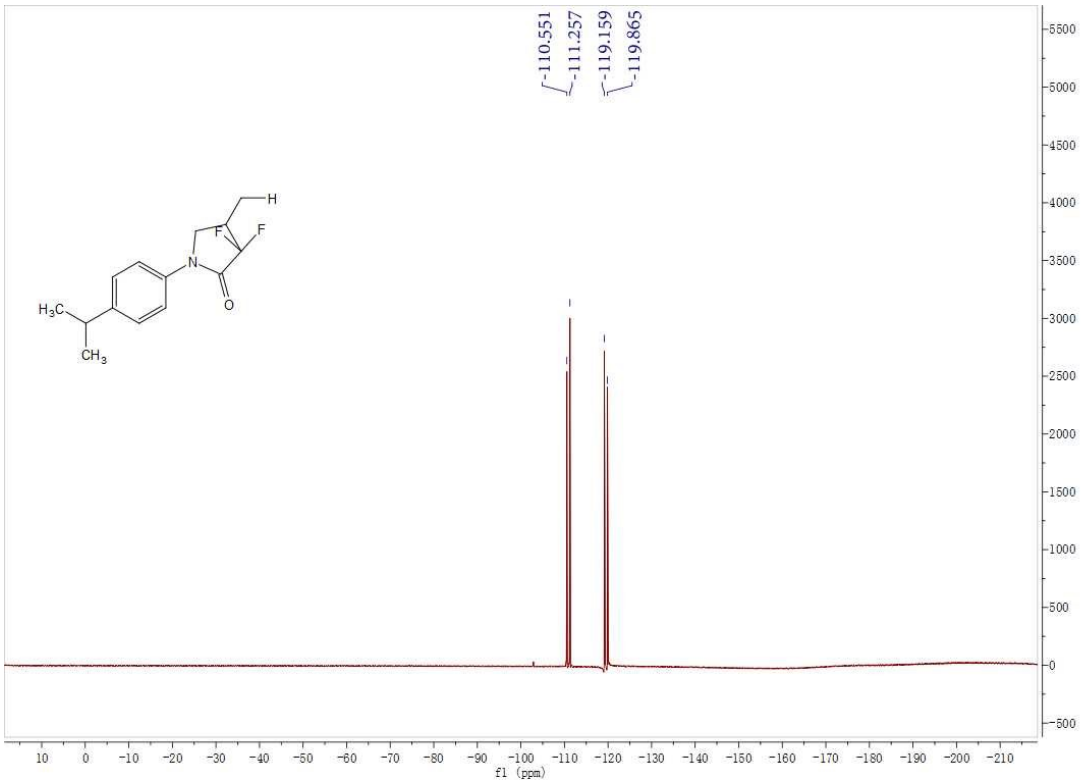

162.713
162.399
162.084
135.957
135.541
129.695
120.268
119.881
117.760
115.271
50.009
49.947
34.988
34.772
34.554
20.935
10.094
10.013
CH3
F
F
N
O
H3C
f1 (ppm)


-110.523
-111.229
-119.078
-119.784
CH3
F
F
N
O
H3C
f1 (ppm)

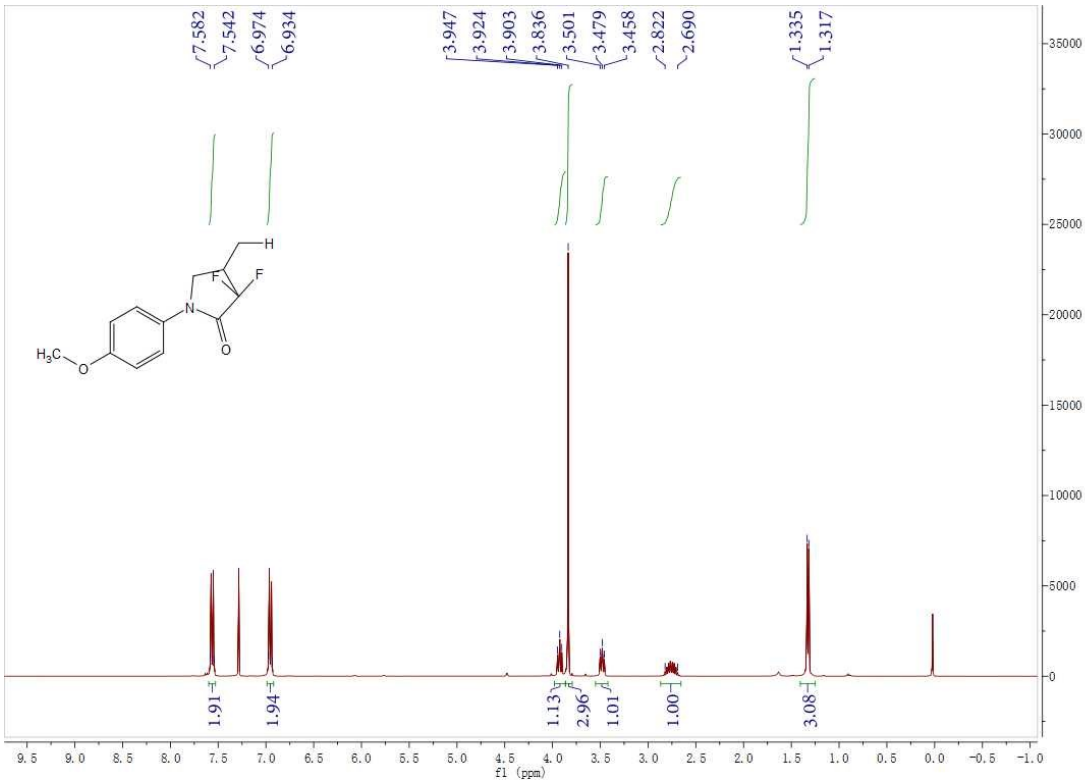
3,3-difluoro-1-(4-isopropylphenyl)-4-methylpyrrolidin-2-one (6)

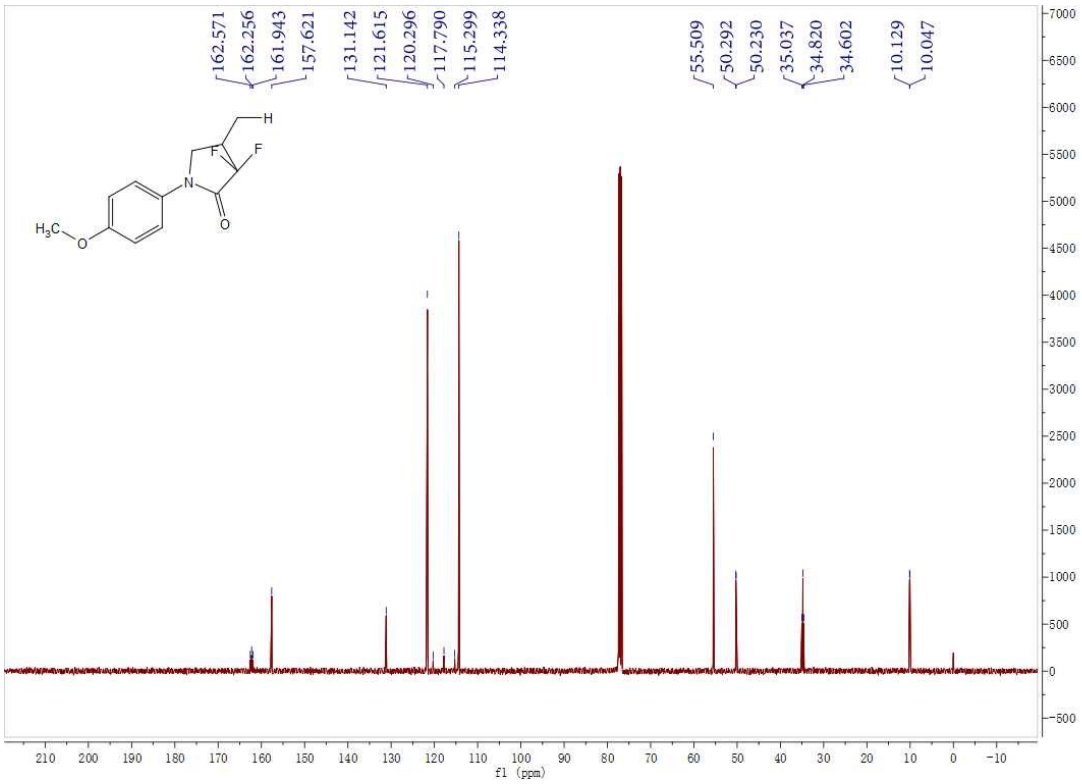


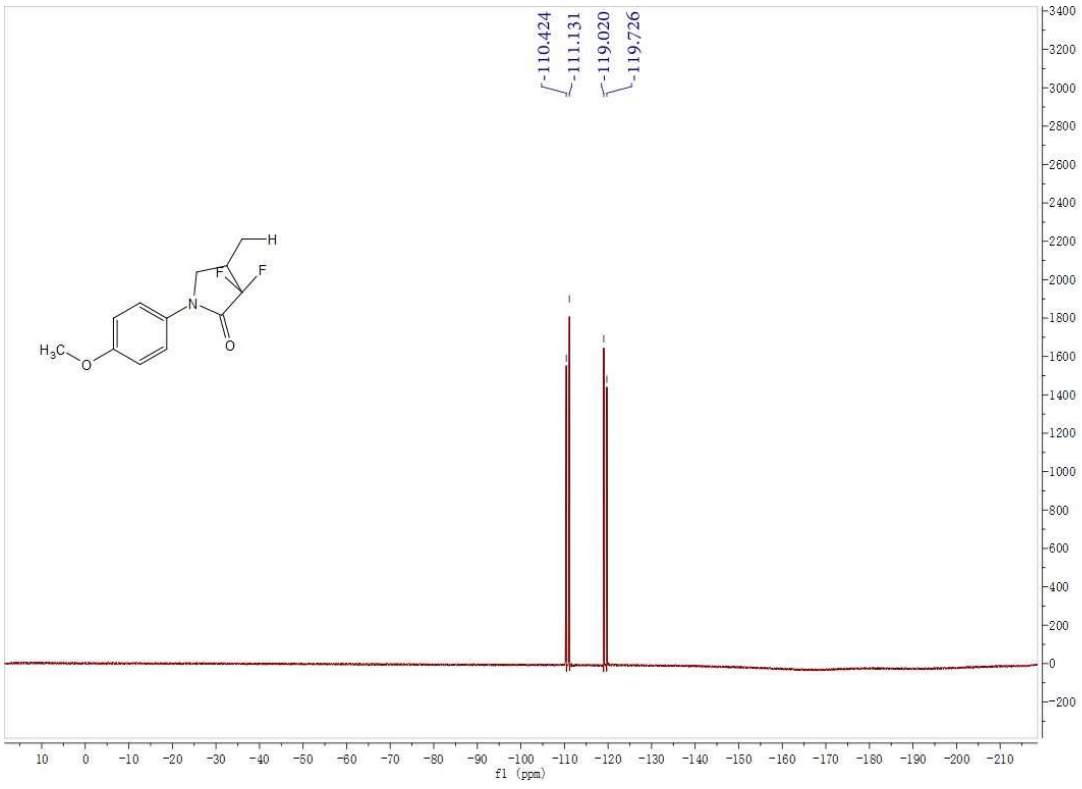




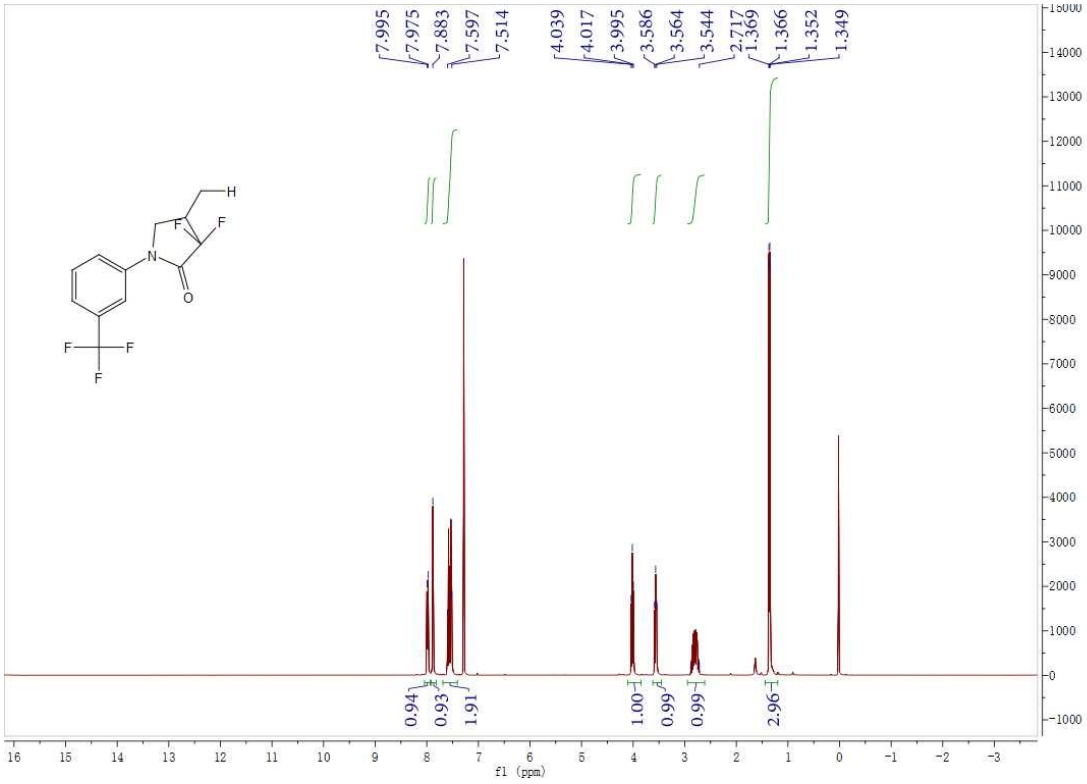
3,3-difluoro-1-(4-methoxyphenyl)-4-methylpyrrolidin-2-one (7)

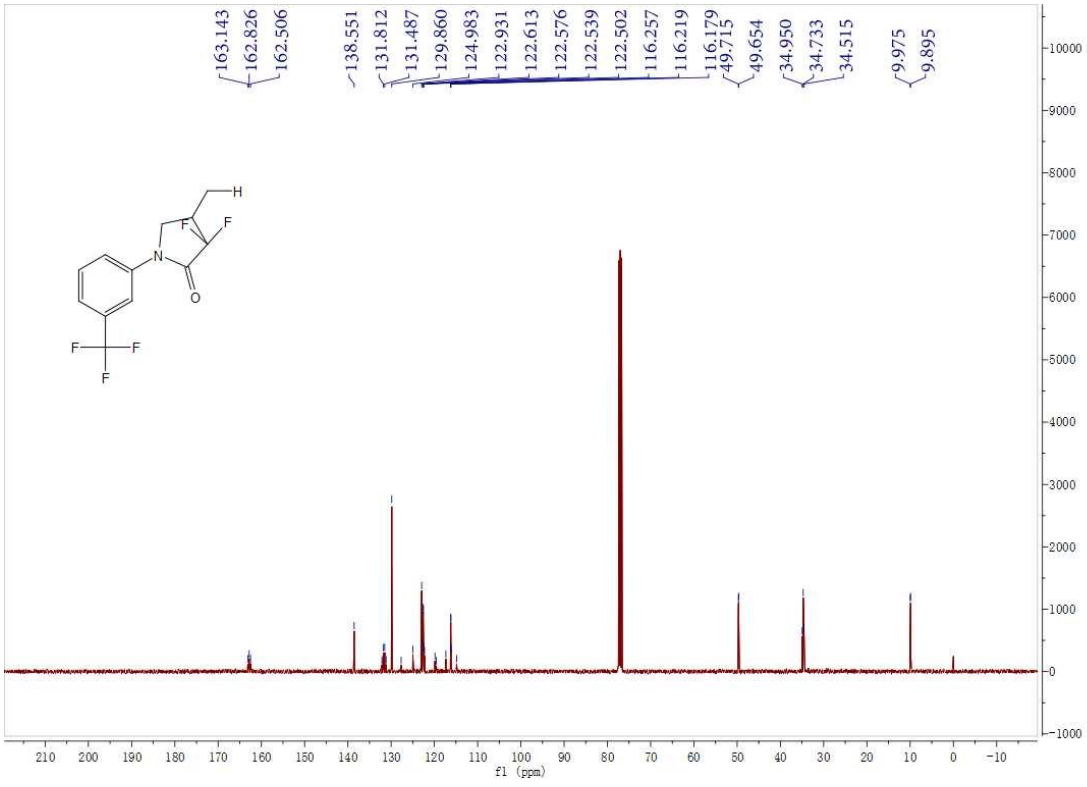


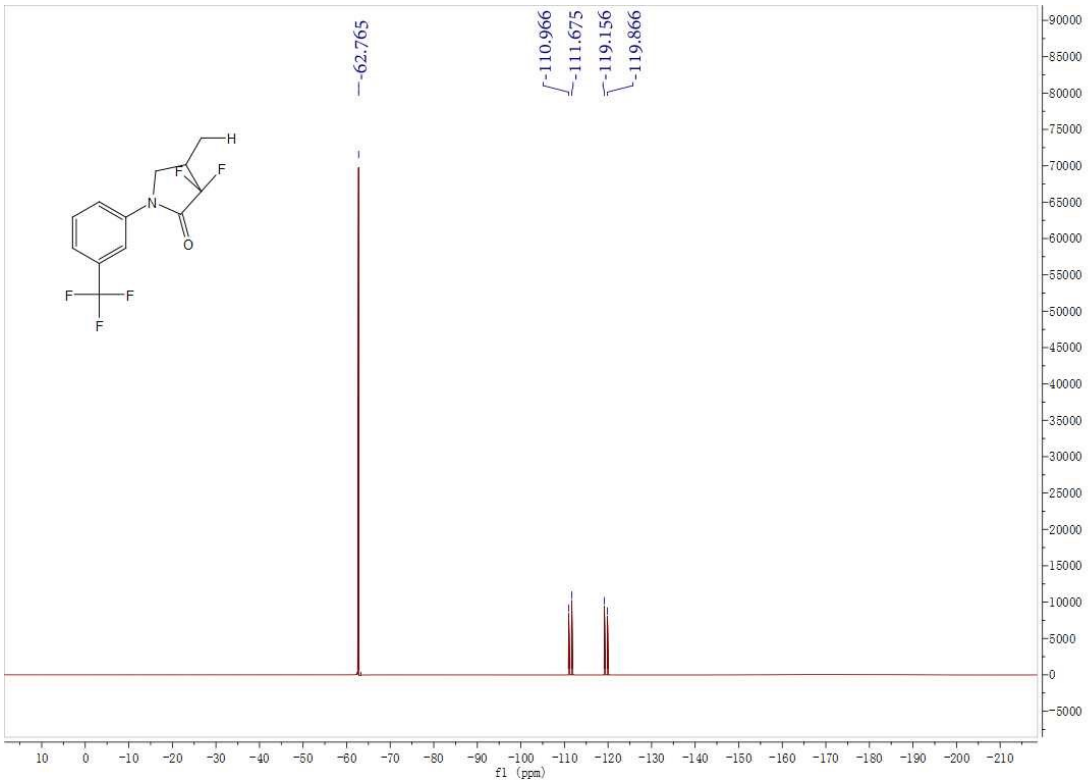

162.571
162.256
161.943
157.621
131.142
121.615
120.296
117.790
115.299
114.338
55.509
50.292
50.230
35.037
34.820
34.602
10.129
10.047
f1 (ppm)


-110.424
-111.131
-119.020
-119.726
f1 (ppm)

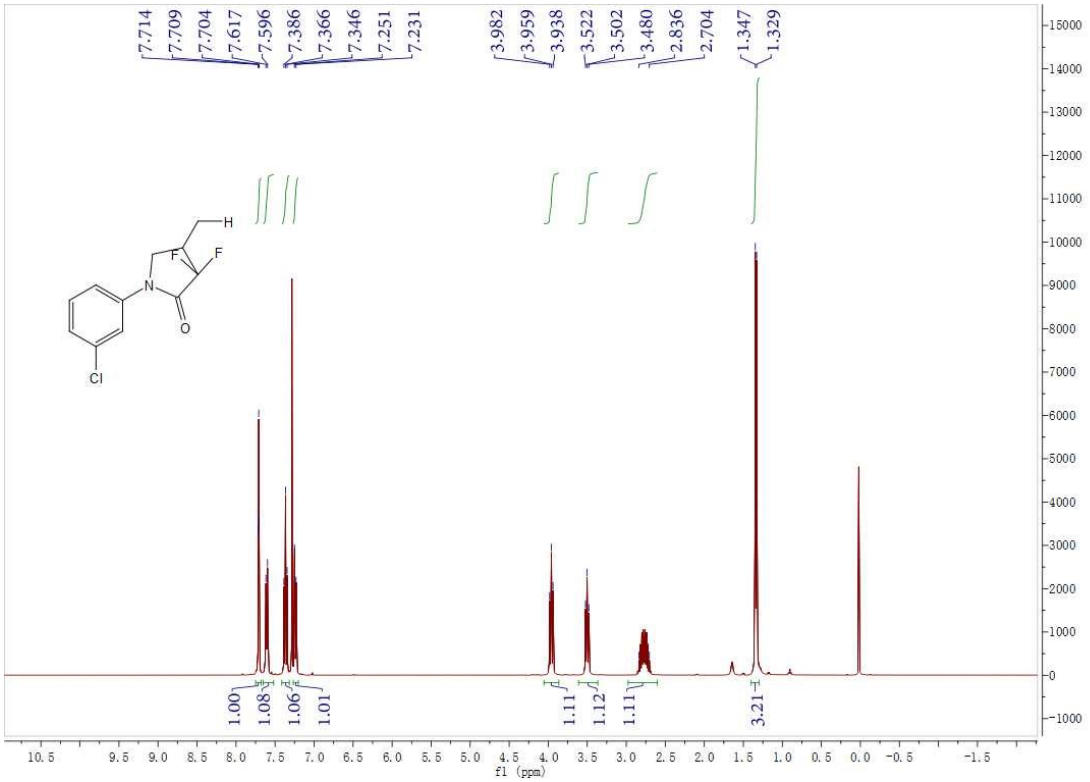
3,3-difluoro-4-methyl-1-(3-(trifluoromethyl)phenyl)pyrrolidin-2-one (8)

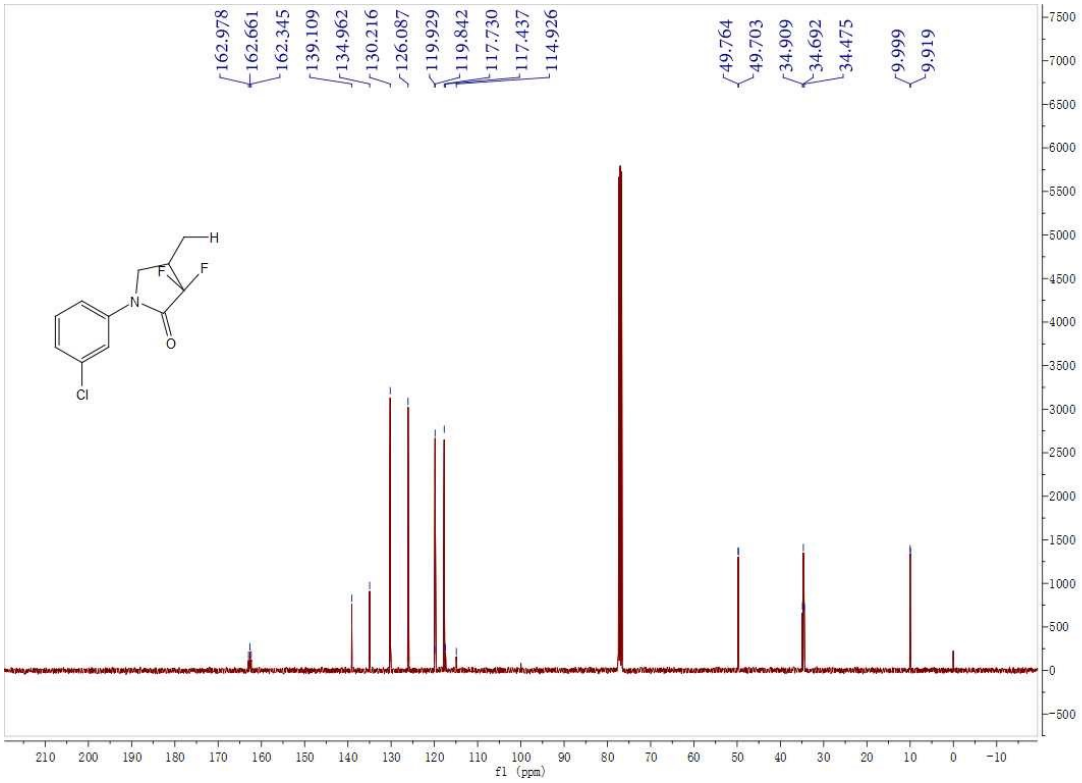


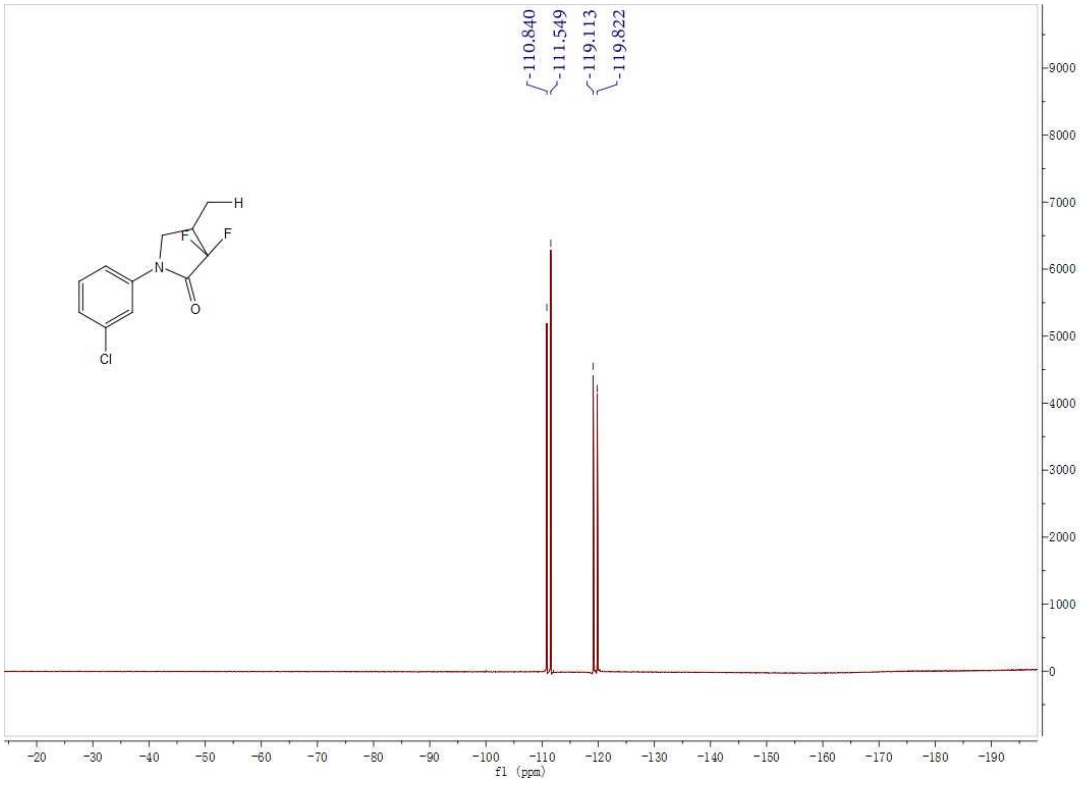




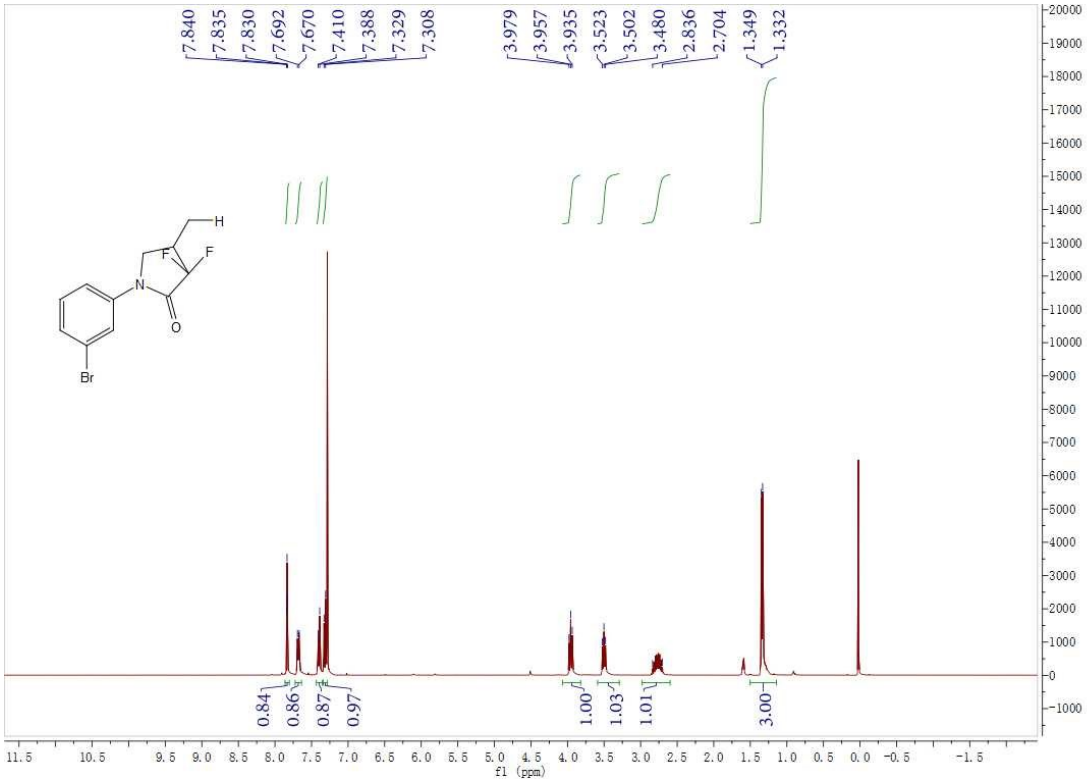
3,3-difluoro-4-methyl-1-(3-chlorophenyl)pyrrolidin-2-one (9)

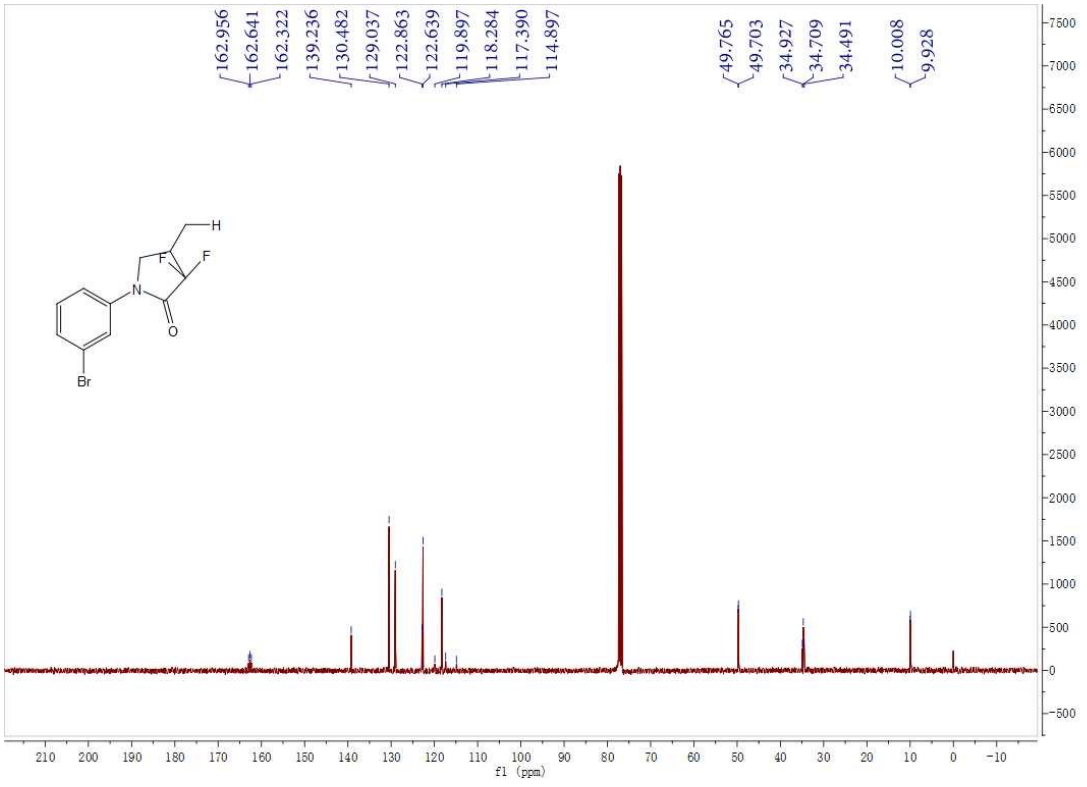


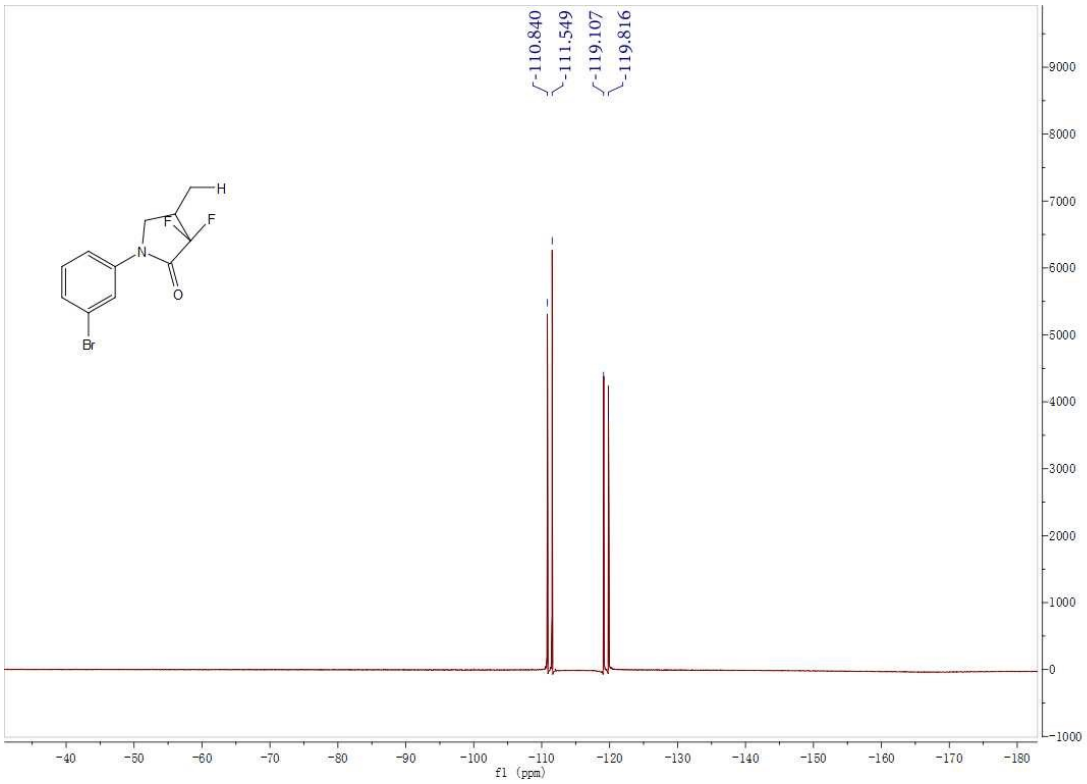

162.978
162.661
162.345
139.109
134.962
130.216
126.087
119.929
119.842
117.730
117.437
114.926
49.764
49.703
34.909
34.692
34.475
9.999
9.919
H
F
F
N
O
Cl
f1 (ppm)


-110.840
-111.549
-119.113
-119.822
H
F
F
N
O
Cl
f1 (ppm)

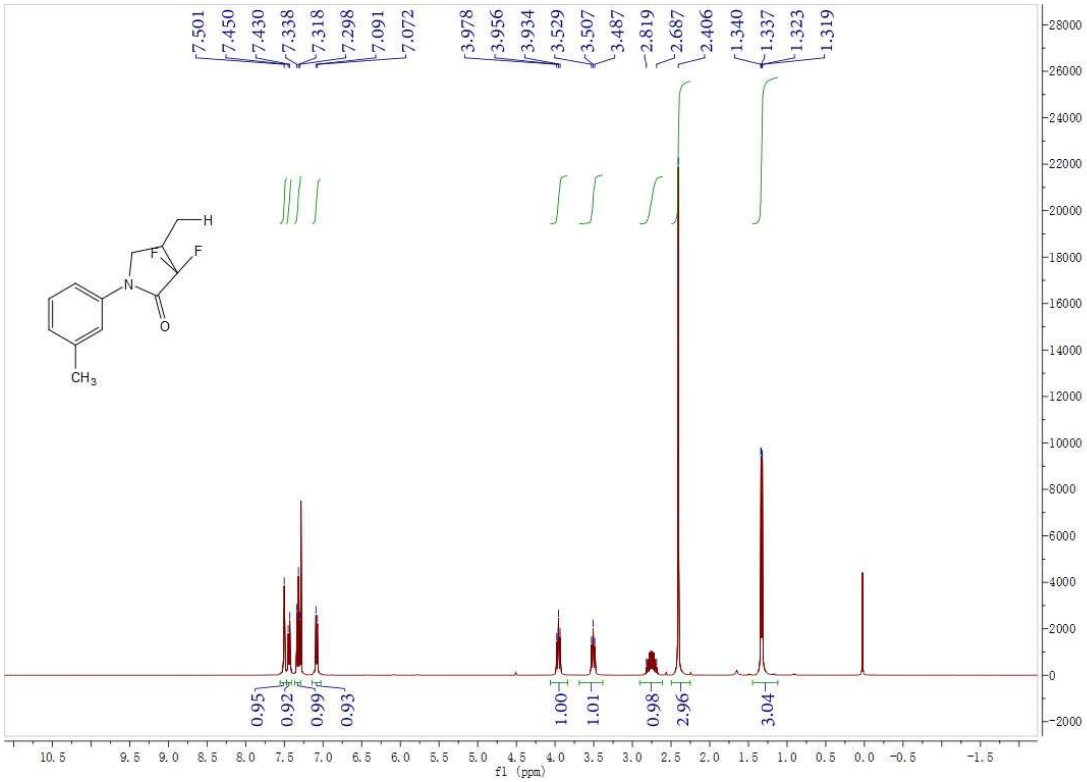
3,3-difluoro-4-methyl-1-(3-bromophenyl)pyrrolidin-2-one (10)

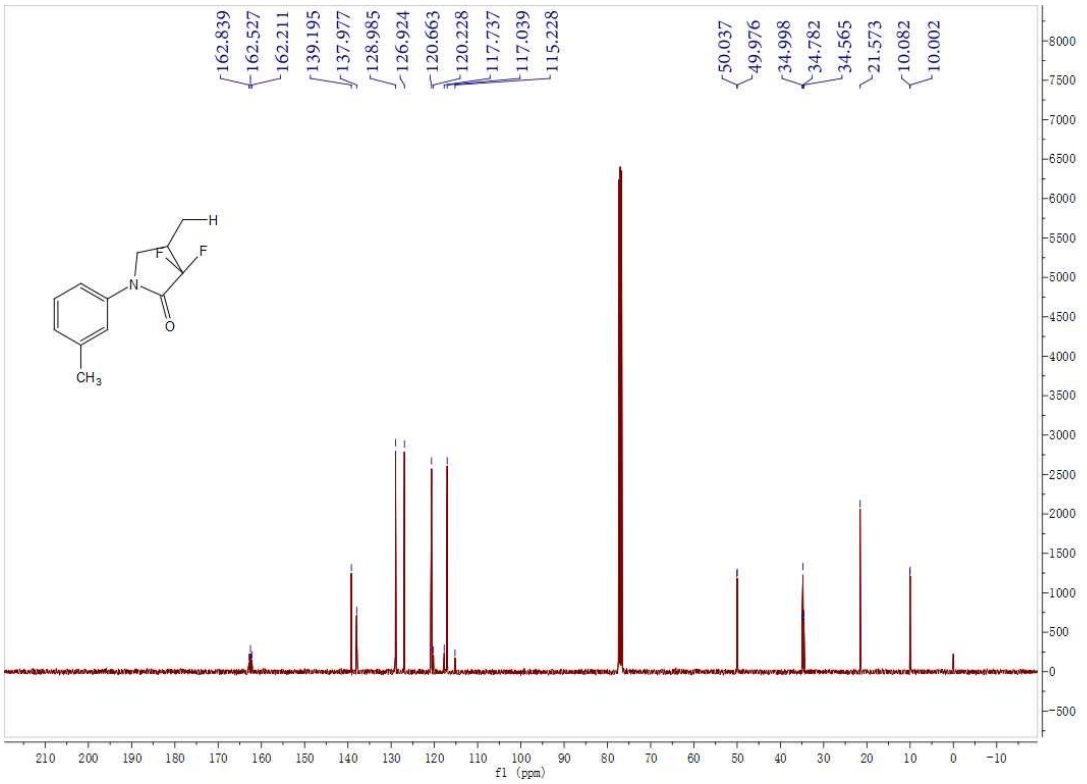


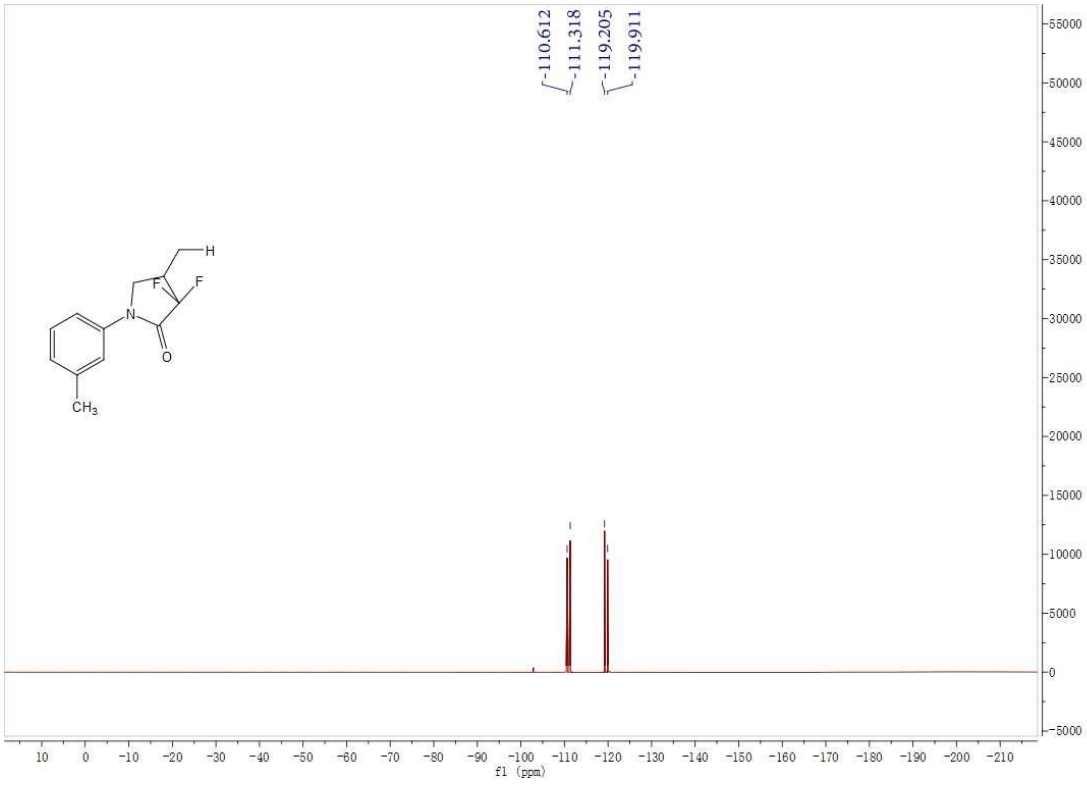




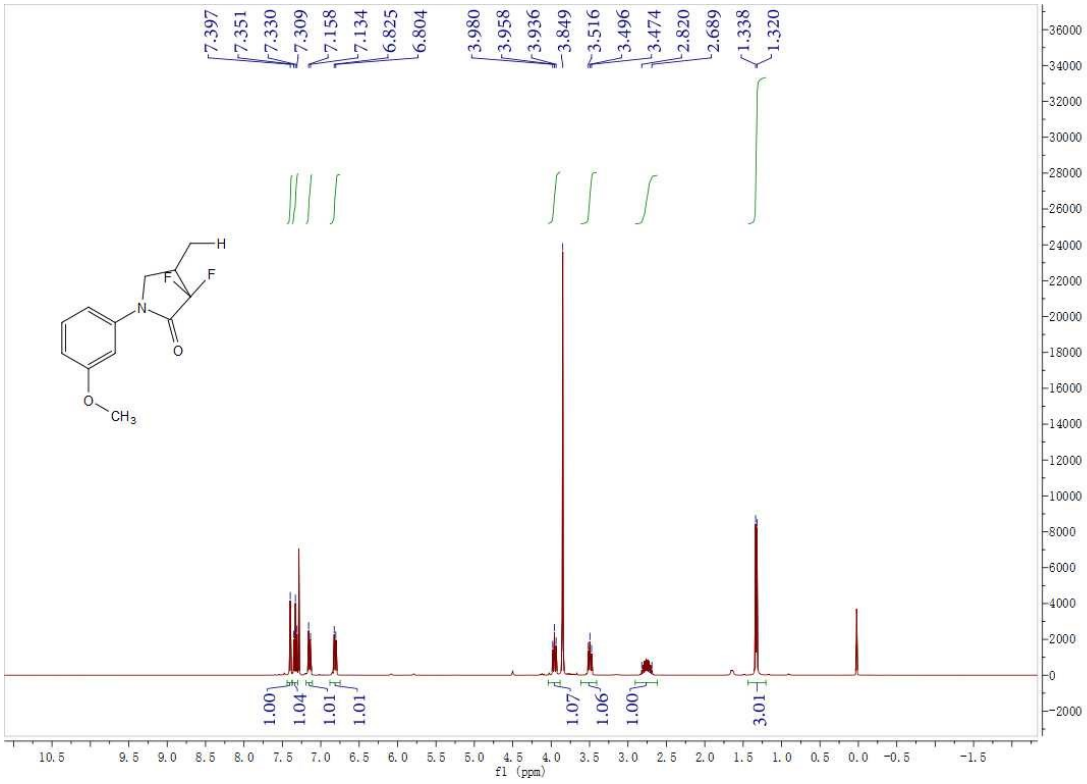
3,3-difluoro-4-methyl-1-(3-methylphenyl)pyrrolidin-2-one (11)

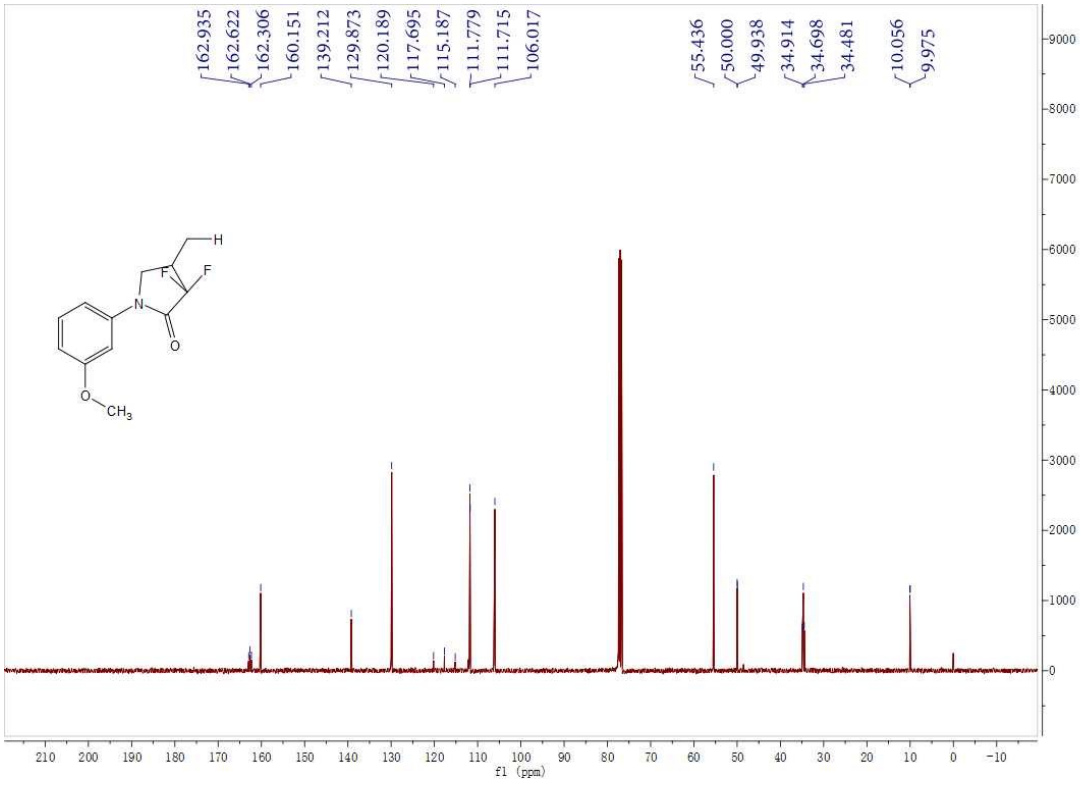


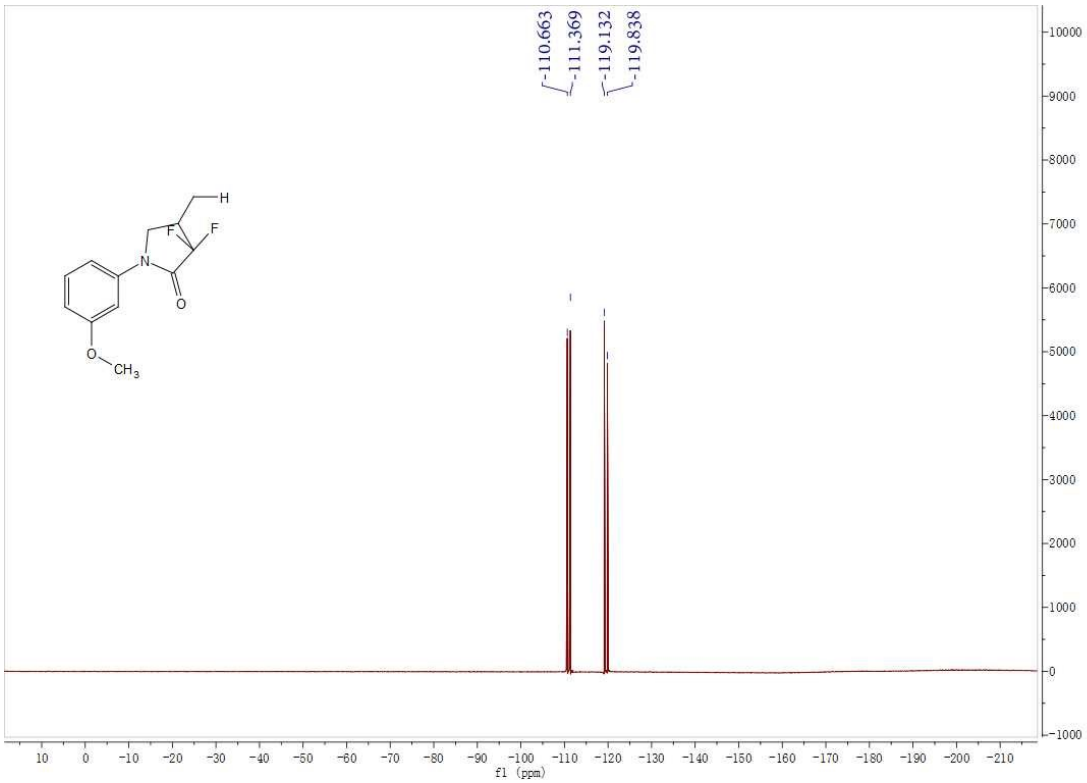

162.839
162.527
162.211
139.195
137.977
128.985
126.924
120.663
120.228
117.737
117.039
115.228
50.037
49.976
34.998
34.782
34.565
21.573
10.082
10.002
f1 (ppm)


-110.612
-111.318
-119.205
-119.911
f1 (ppm)

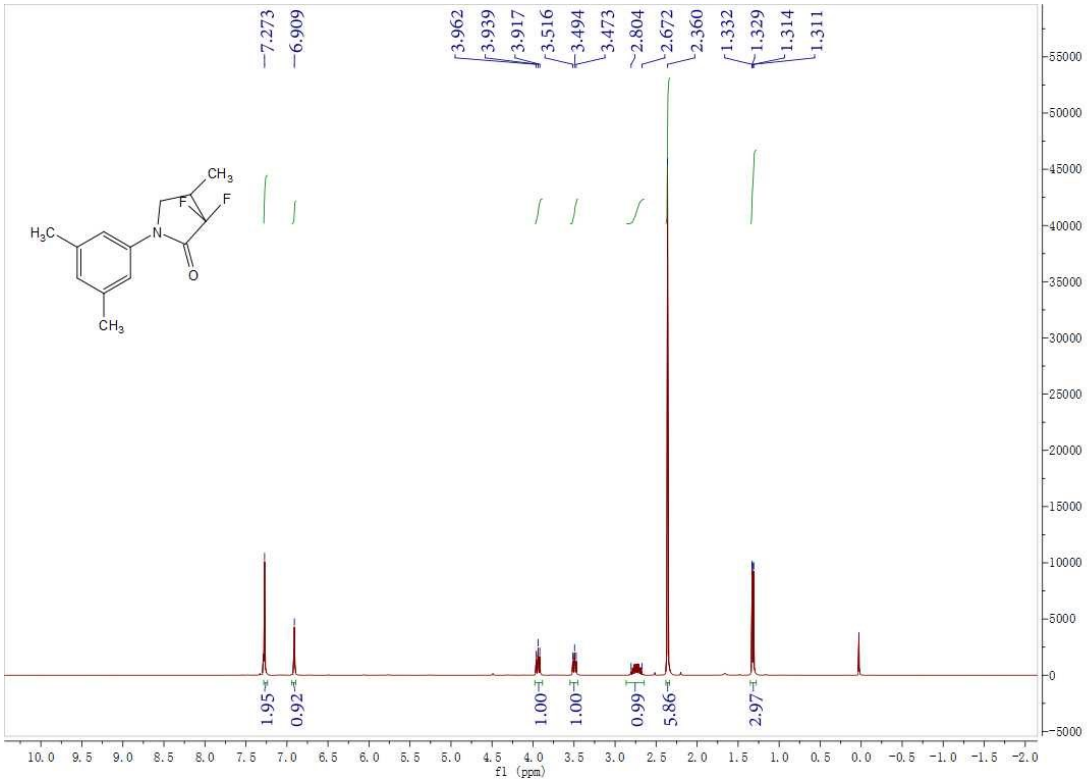
3,3-difluoro-4-methyl-1-(3-methoxyphenyl)pyrrolidin-2-one (12)

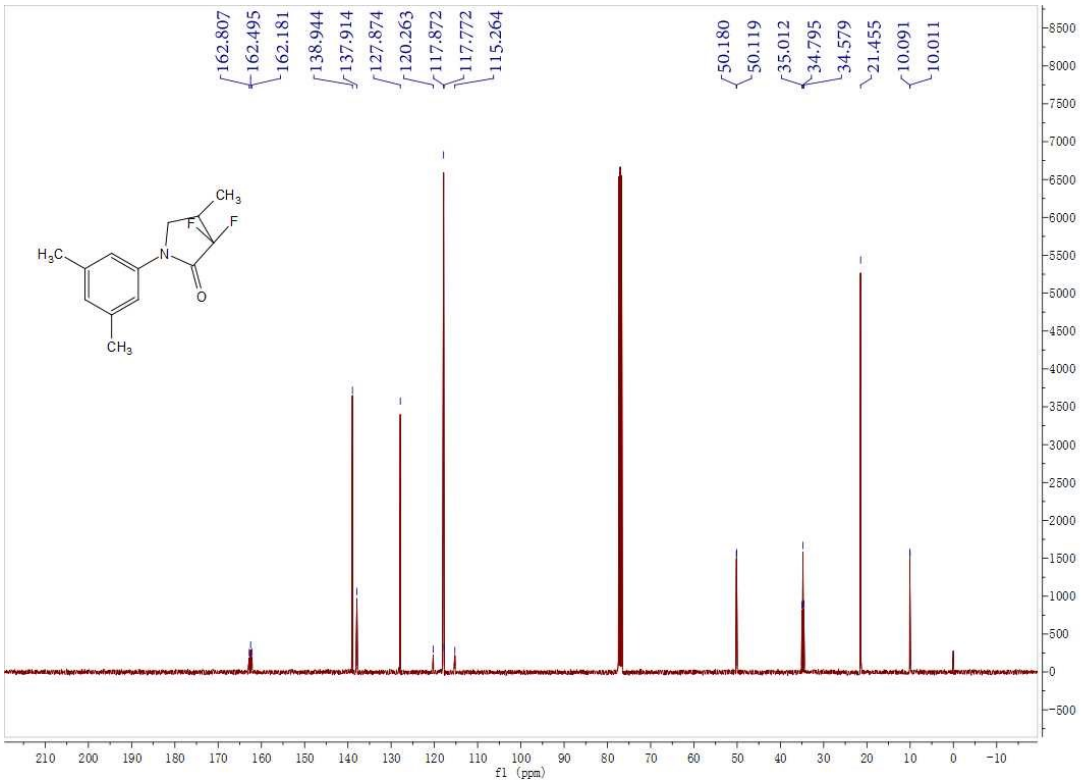


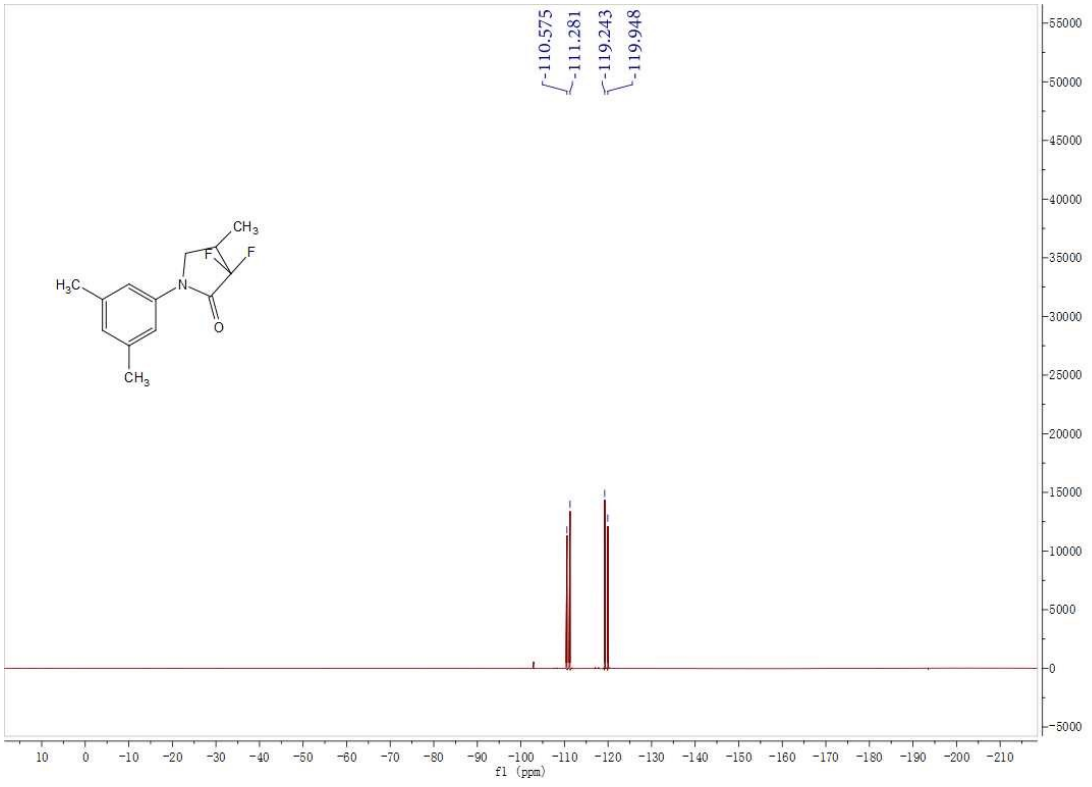




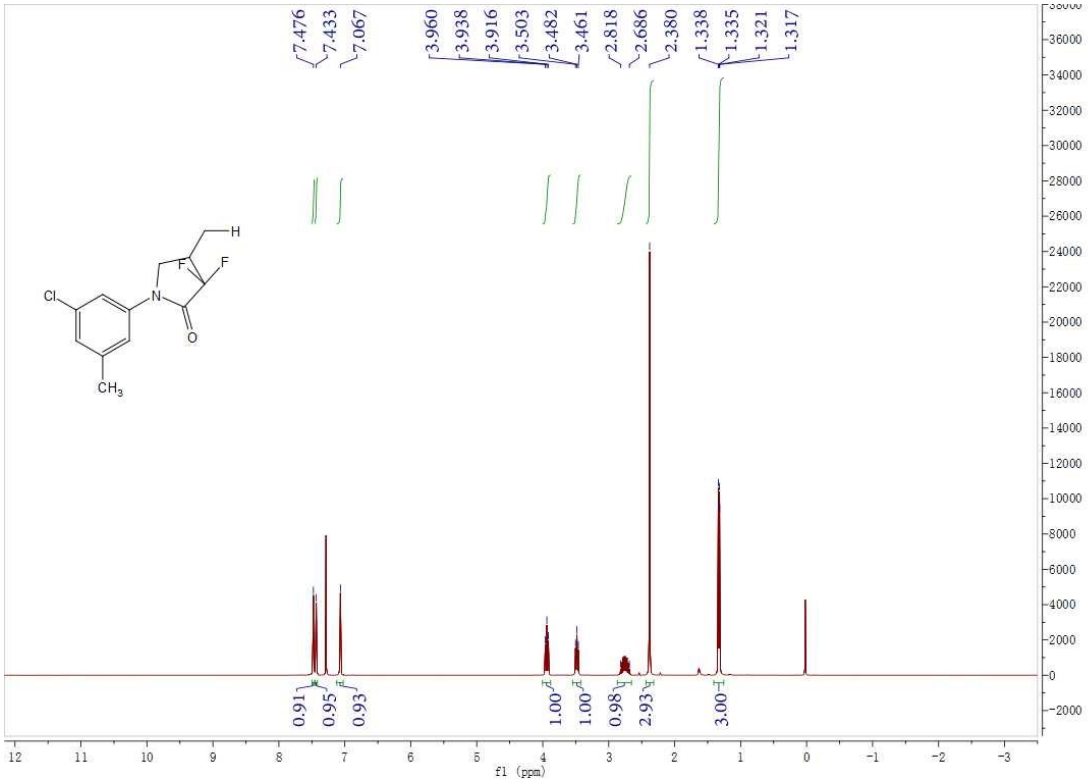
3,3-difluoro-4-methyl-1-(3,5-dimethylphenyl)pyrrolidin-2-one (13)

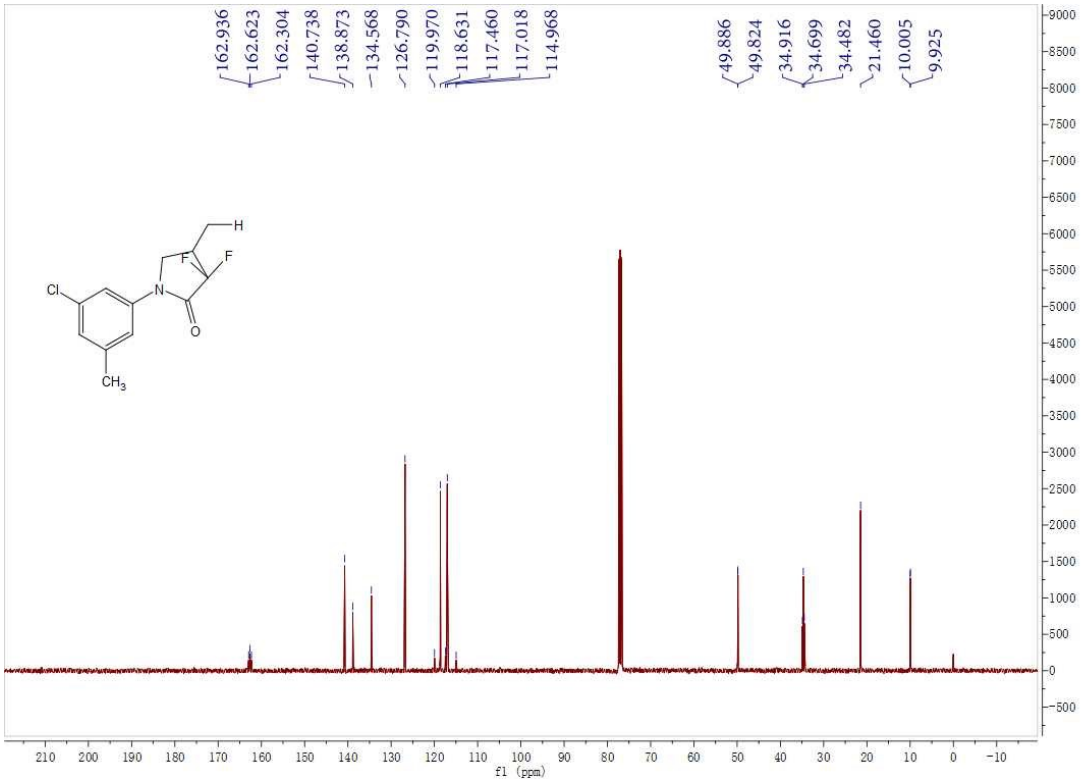


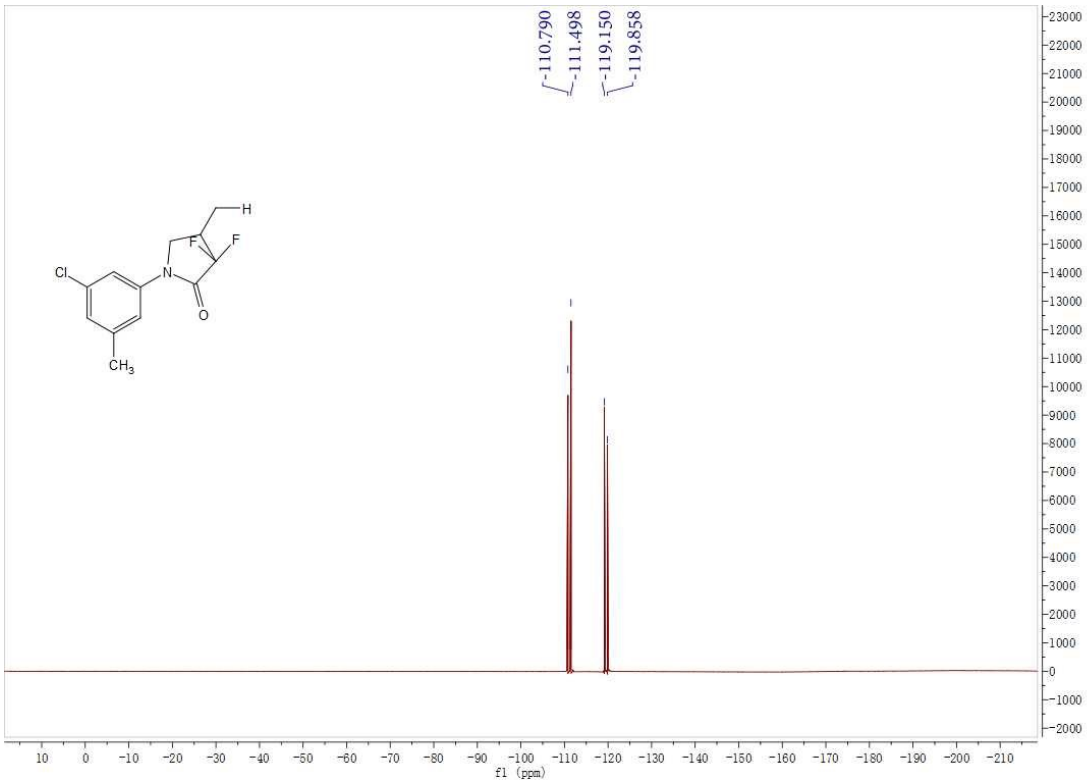

162.807
162.495
162.181
138.944
137.914
127.874
120.263
117.872
117.772
115.264
50.180
50.119
35.012
34.795
34.579
21.455
10.091
10.011
f1 (ppm)


-110.575
-111.281
-119.243
-119.948
f1 (ppm)

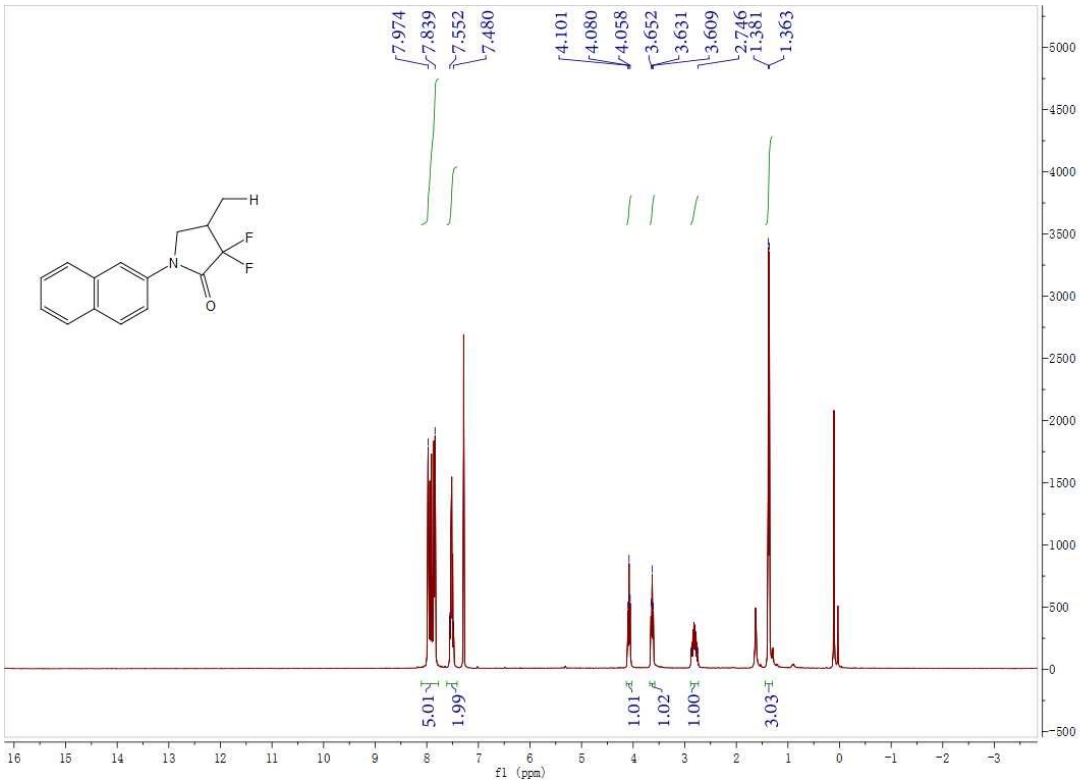
3,3-difluoro-4-methyl-1-(3-chloro-5-dimethylphenyl)pyrrolidin-2-one (14)

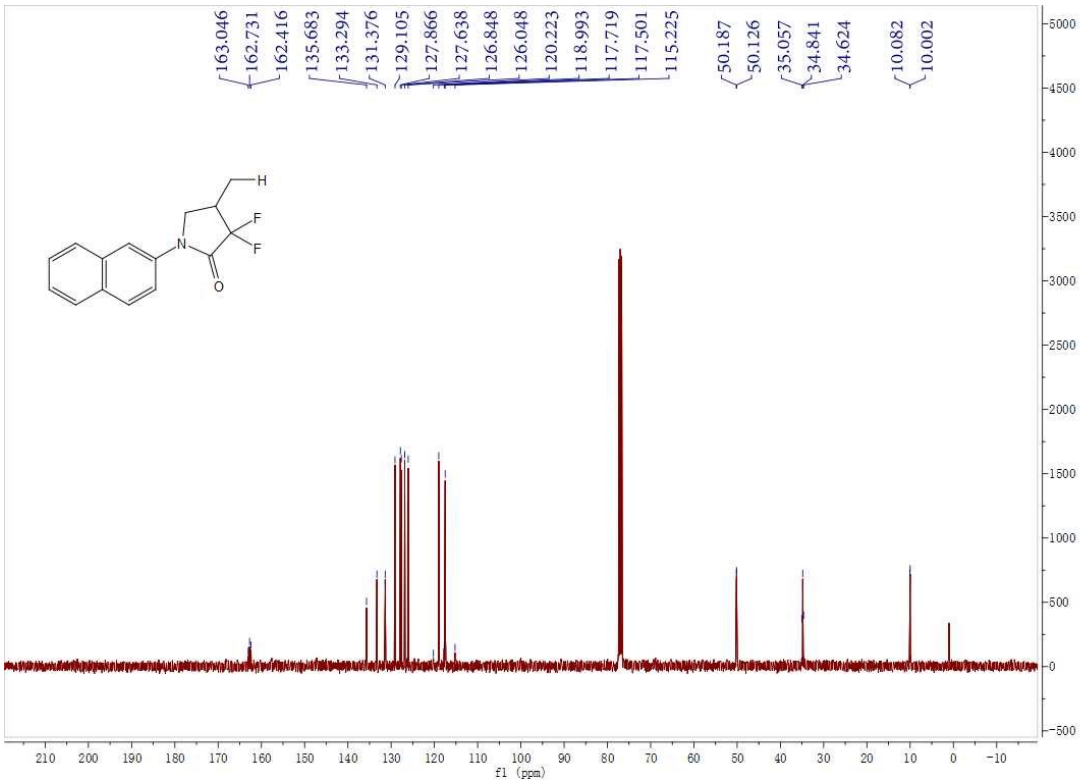


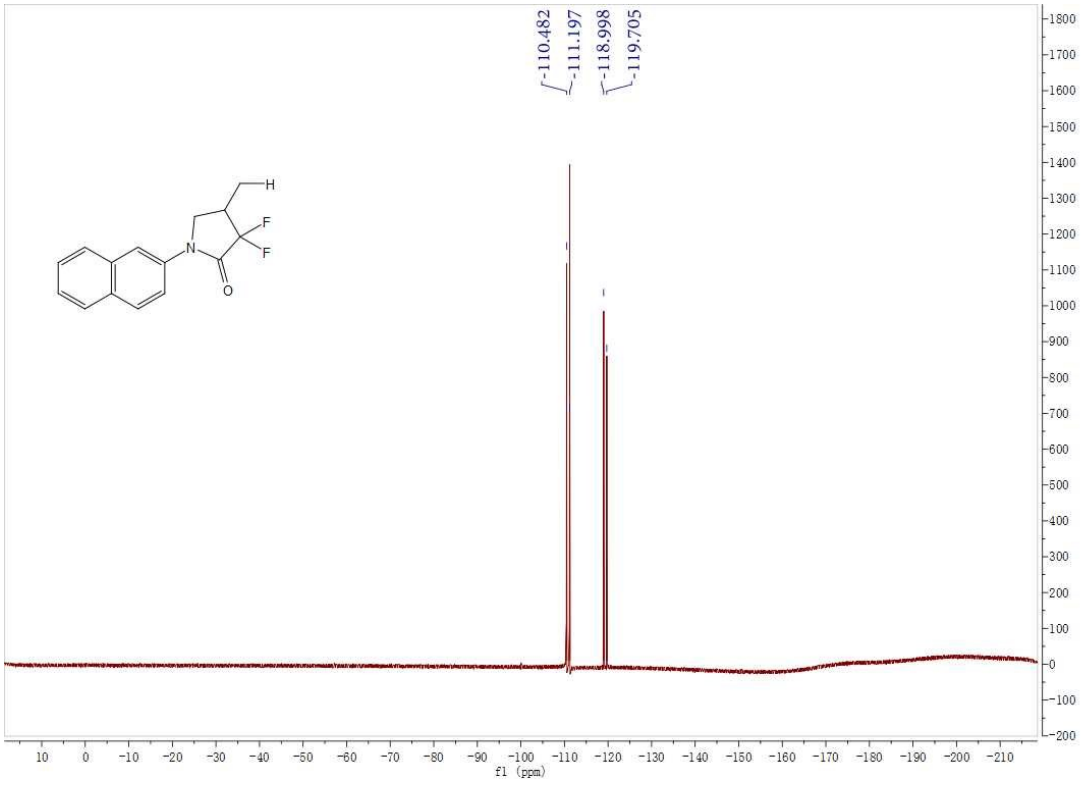




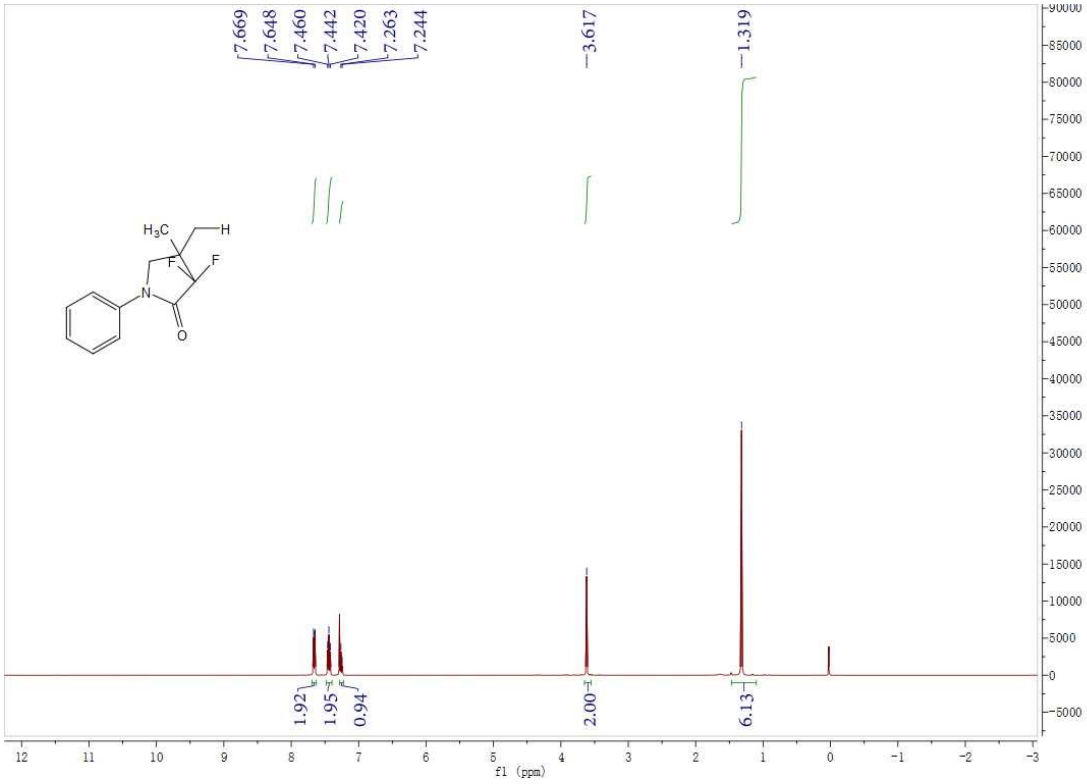
3,3-difluoro-4-methyl-1-(naphthalen-2-yl)pyrrolidin-2-one (15)

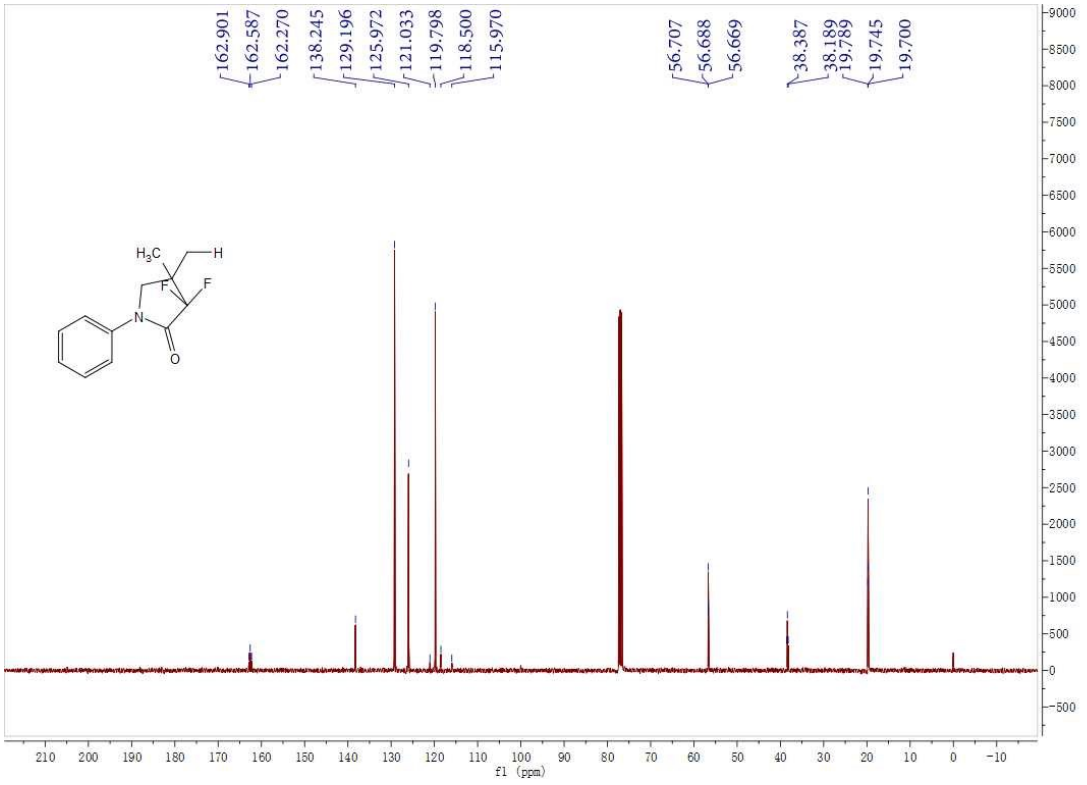


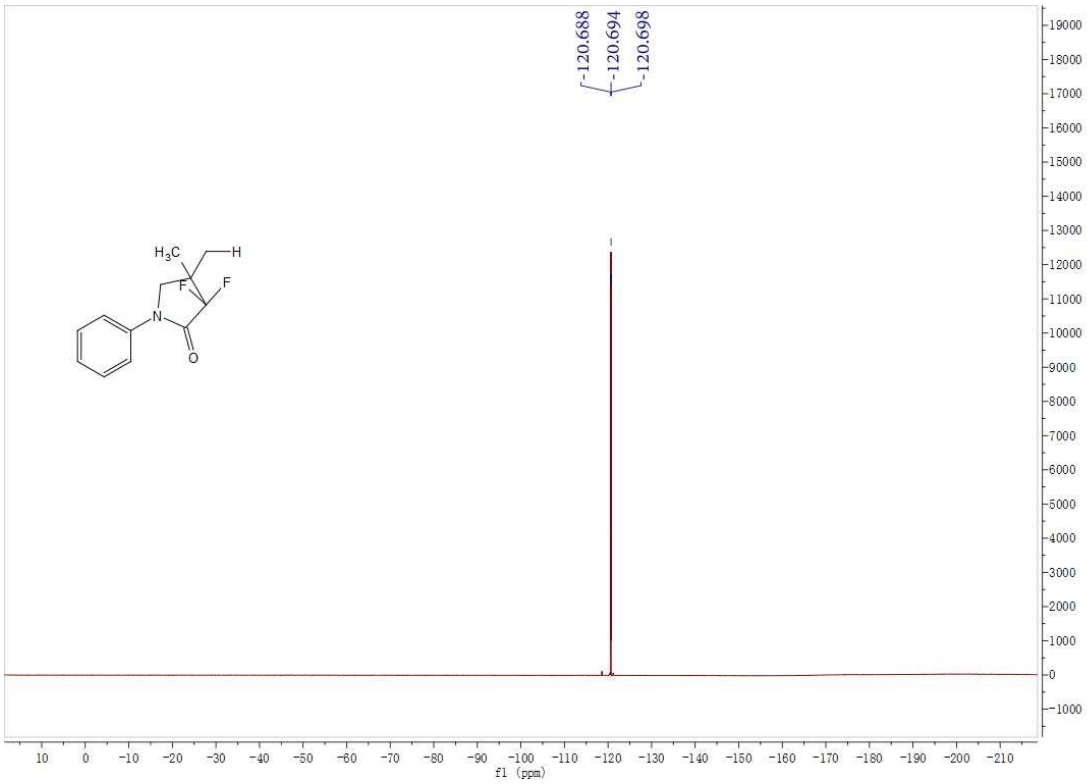

163.046
162.731
162.416
135.683
133.294
131.376
129.105
127.866
127.638
126.848
126.048
120.223
118.993
117.719
117.501
115.225
50.187
50.126
35.057
34.841
34.624
10.082
10.002
H
F
F
N
O
f1 (ppm)


-110.482
-111.197
-118.998
-119.705
H
F
F
N
O
f1 (ppm)

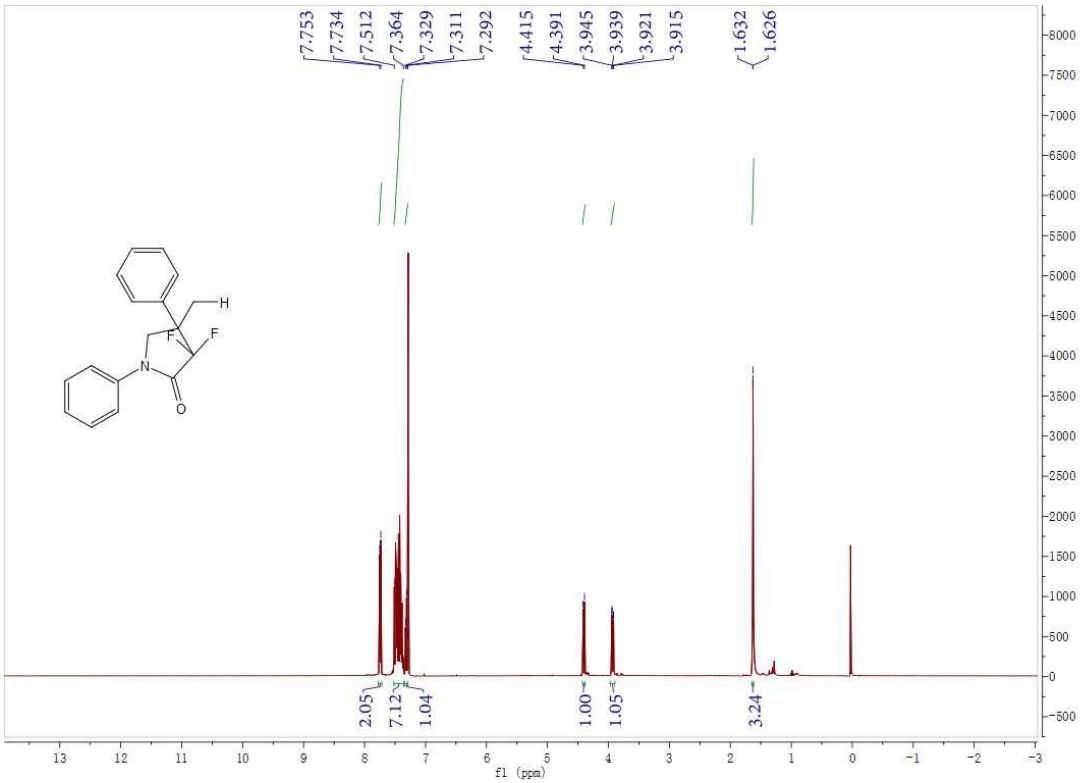
3,3-difluoro-4,4-dimethyl-1-phenylpyrrolidin-2-one (16)

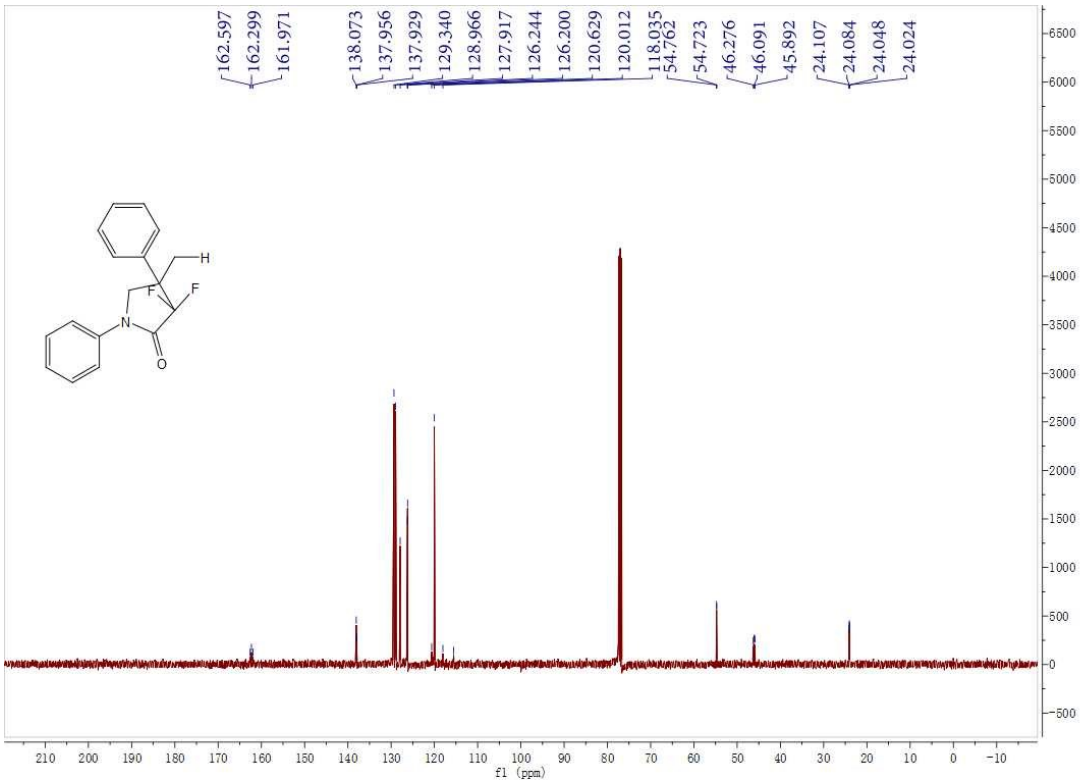


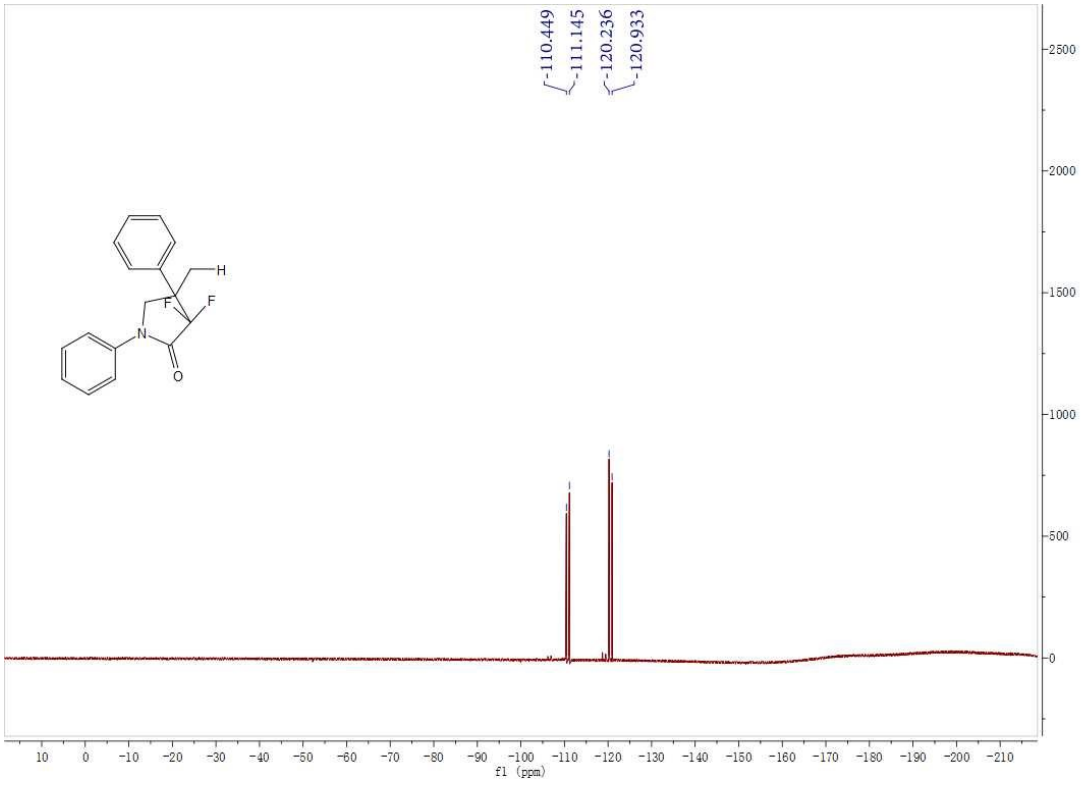




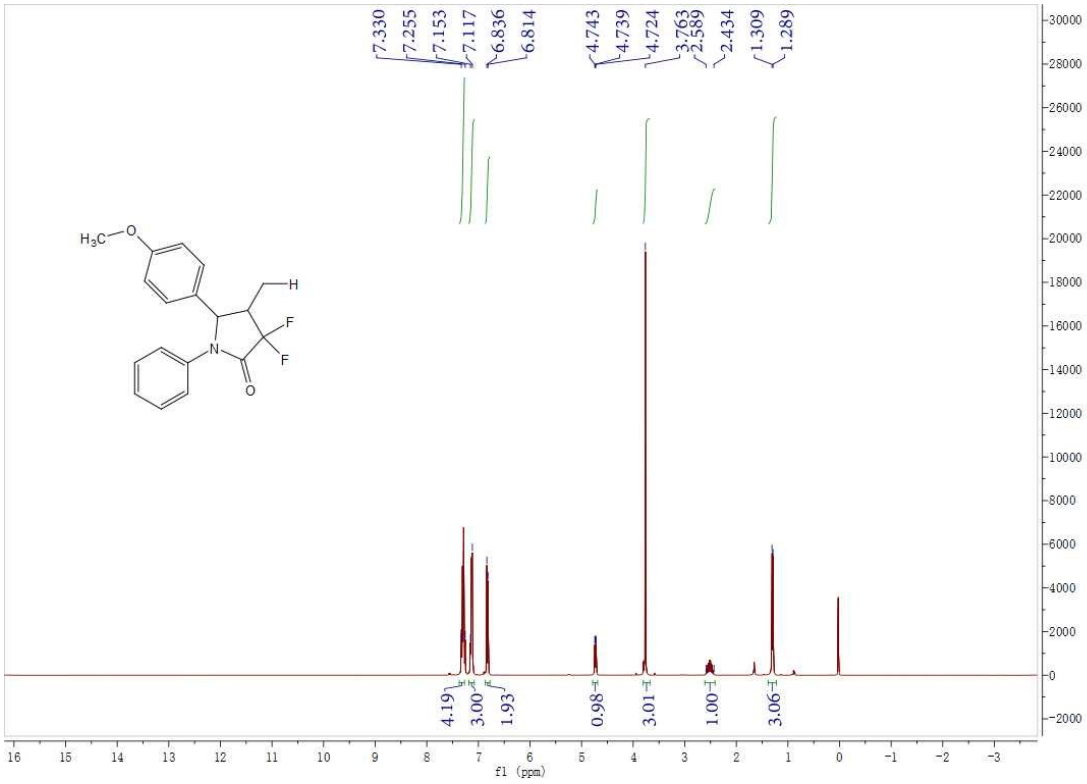
3,3-difluoro-4-methyl-1,4-diphenylpyrrolidin-2-one (17)

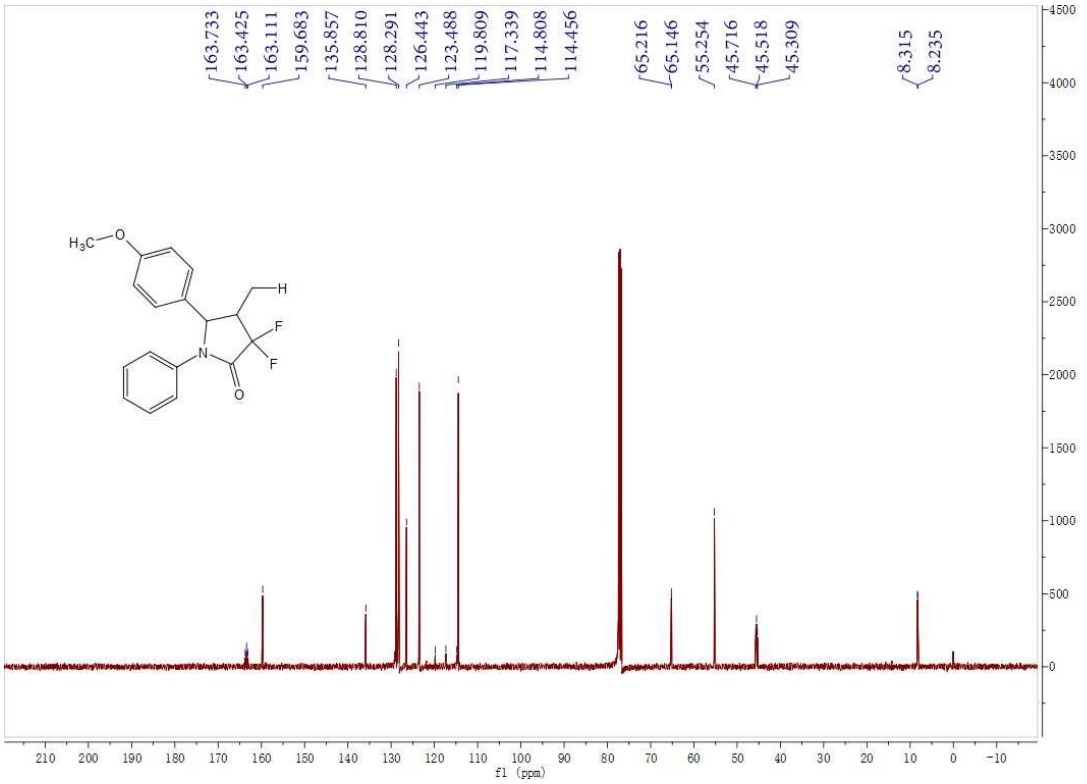


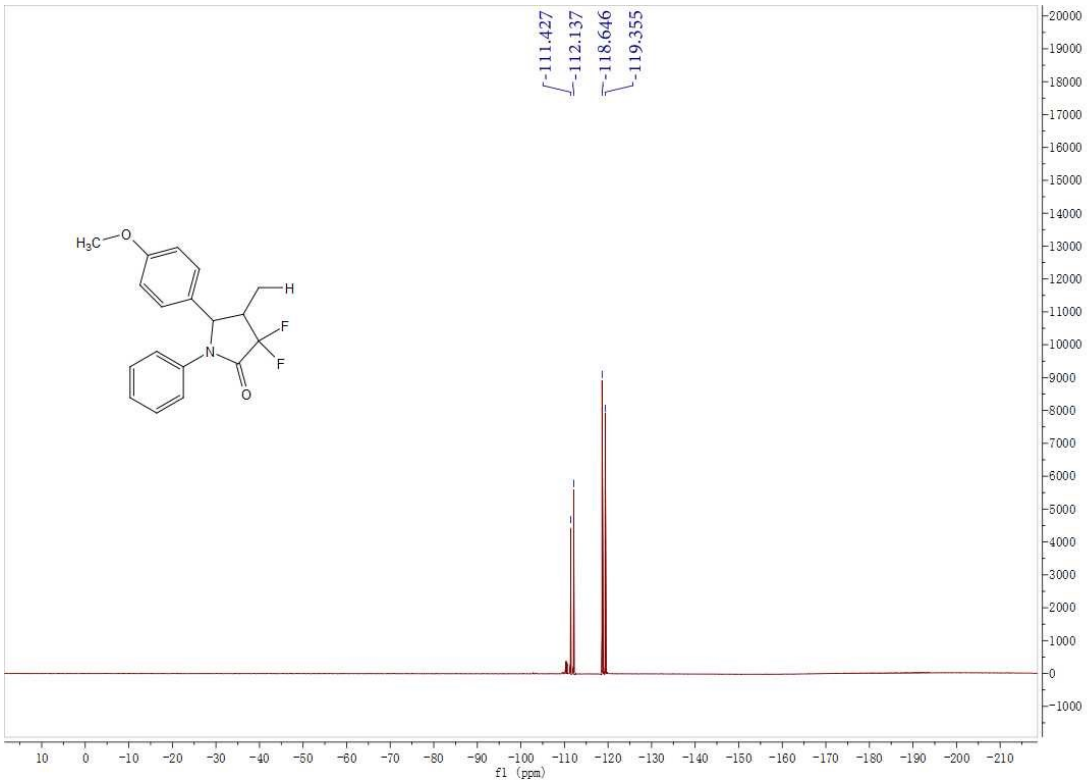

162.597
162.299
161.971
138.073
137.956
137.929
129.340
128.966
127.917
126.244
126.200
120.629
120.012
118.035
54.762
54.723
46.276
46.091
45.892
24.107
24.084
24.048
24.024
H
F
F
N
O
f1 (ppm)


-110.449
-111.145
-120.236
-120.933
H
F
F
N
O
f1 (ppm)

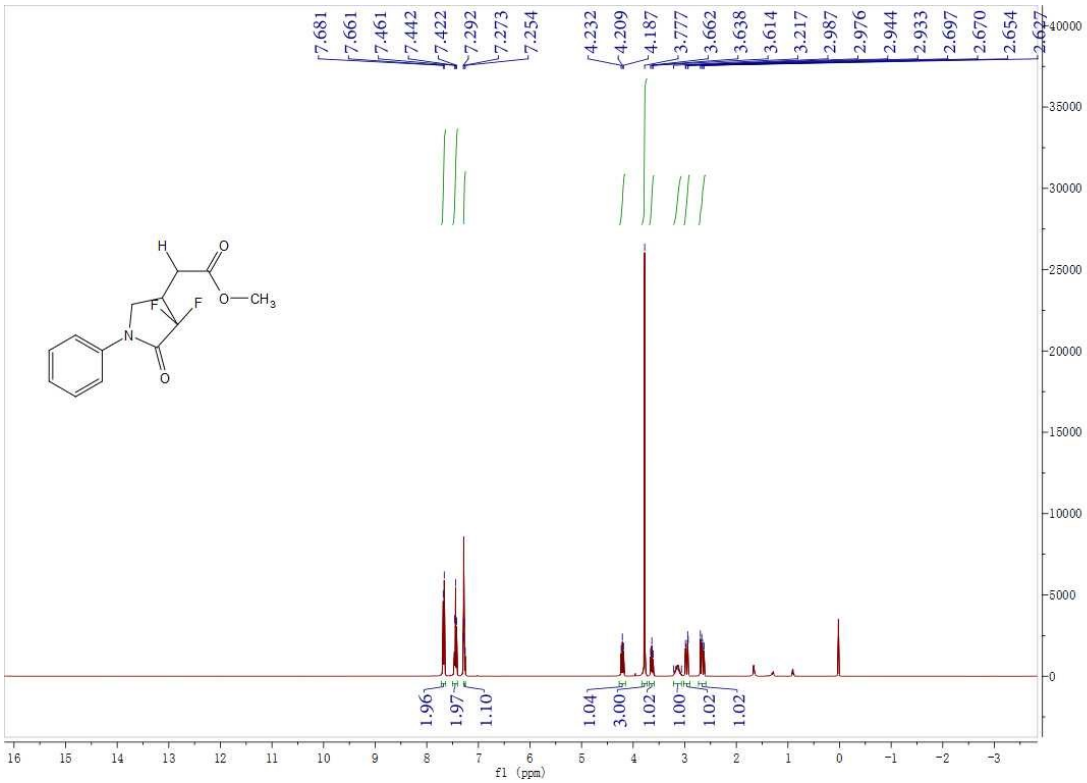
3,3-difluoro-5-(4-methoxyphenyl)-4-methyl-1-phenylpyrrolidin-2-one (18)

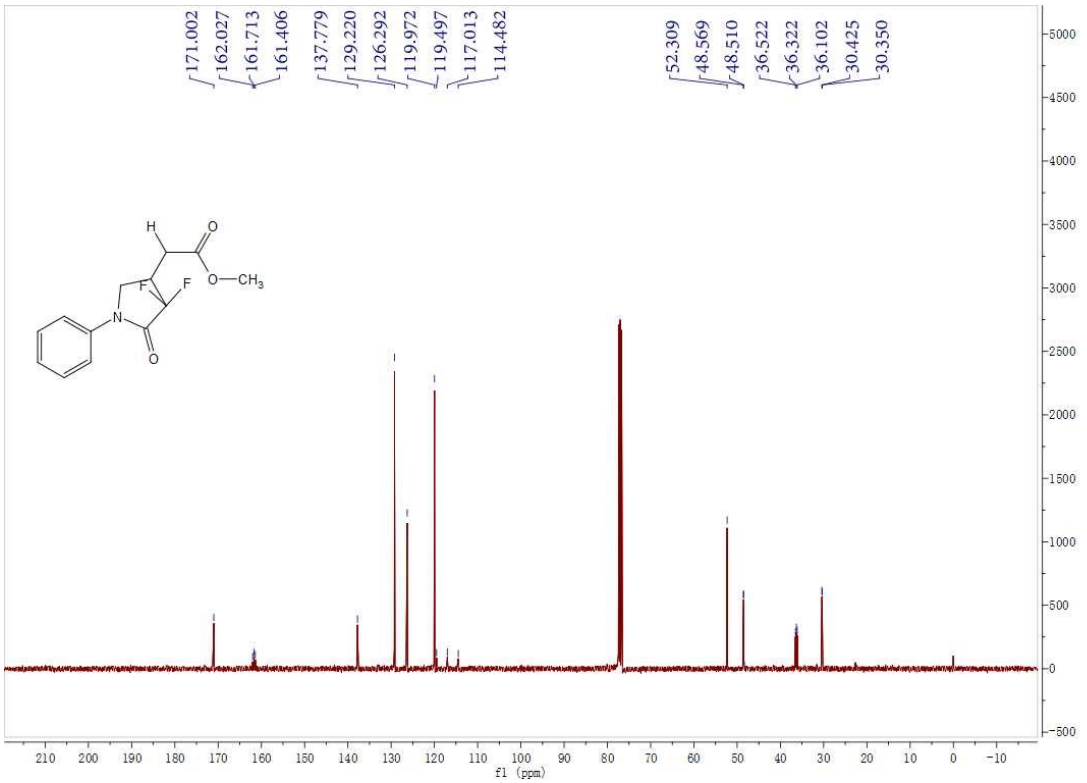


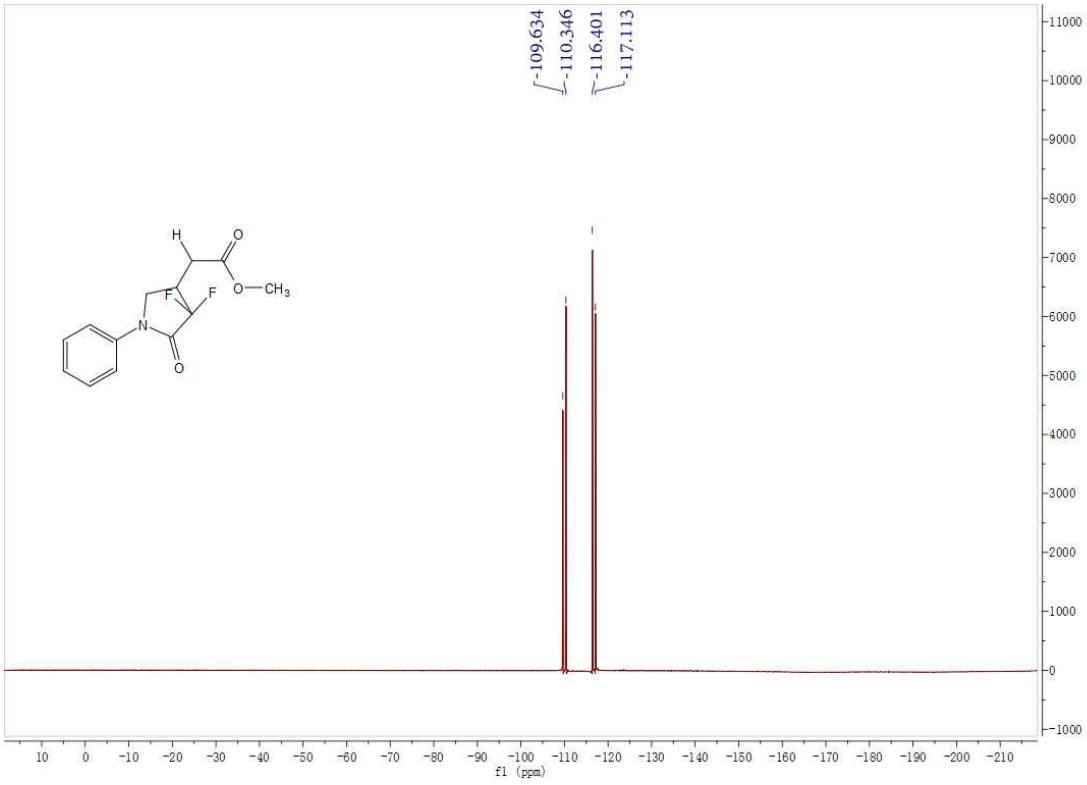




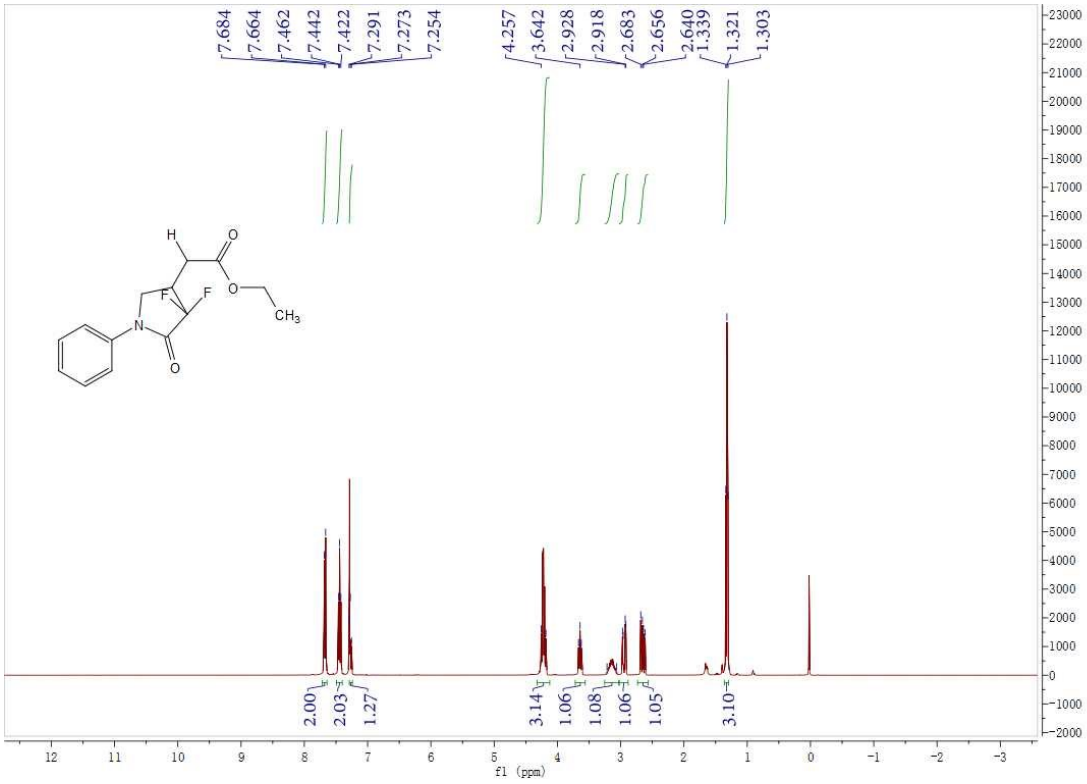
methyl 2-(4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)acetate (19)

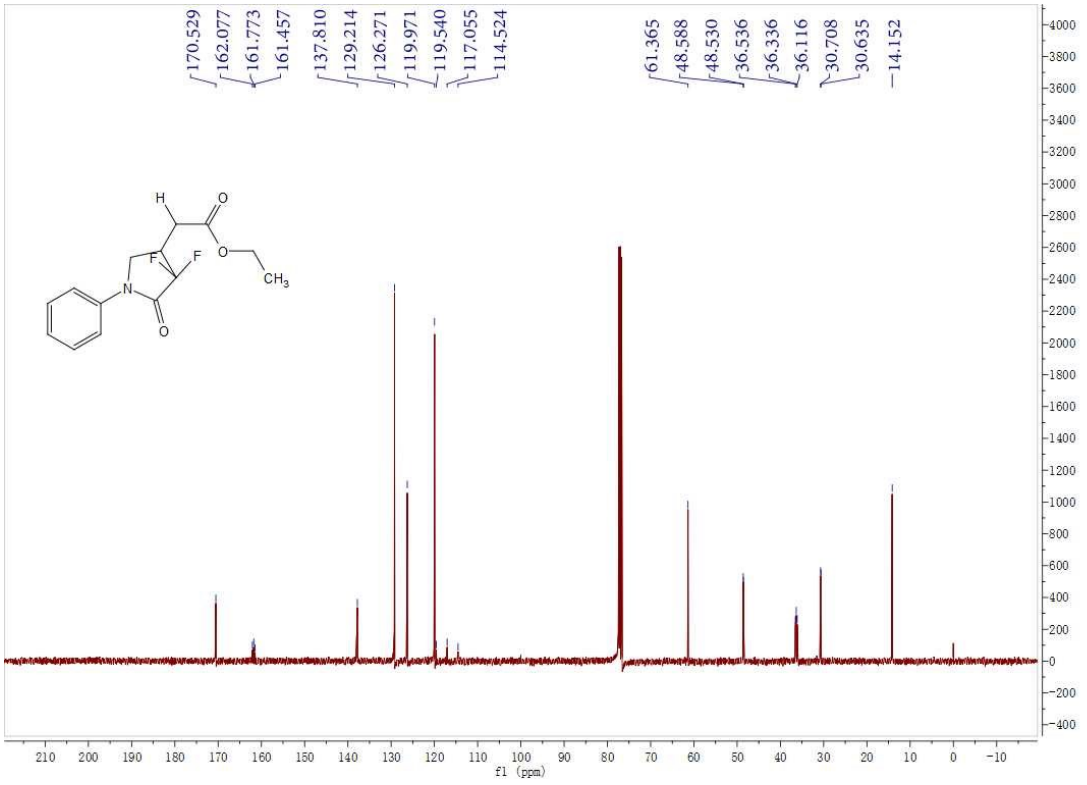


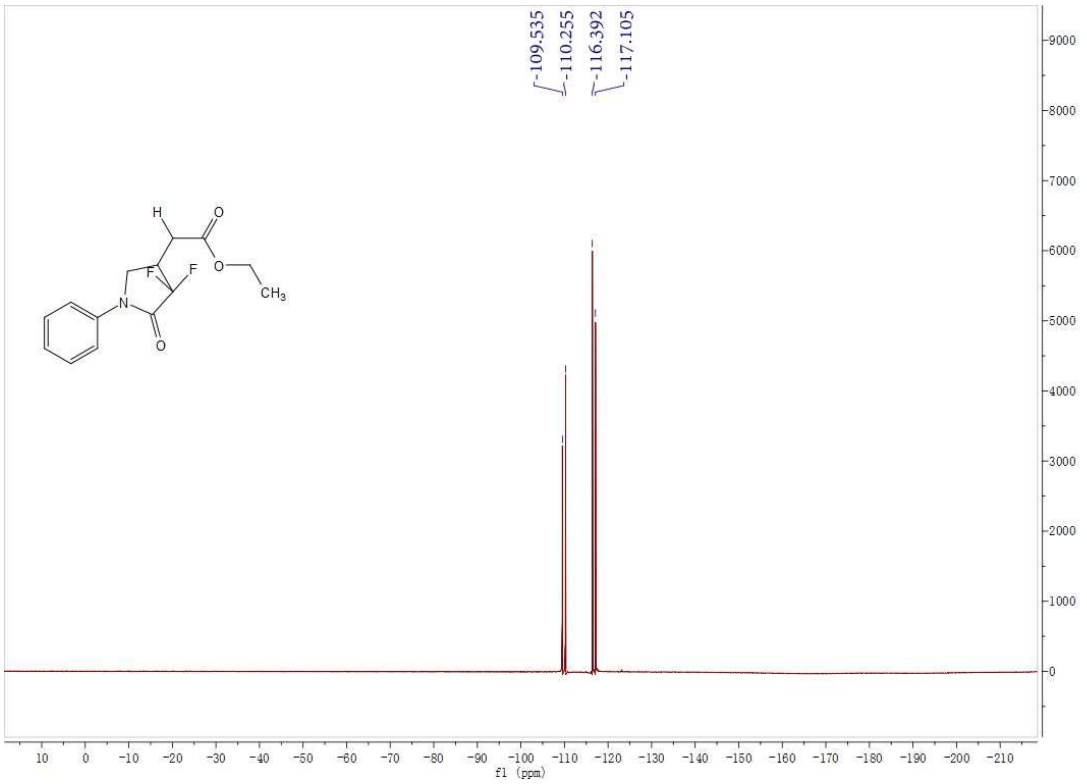

171.002
162.027
161.713
161.406
137.779
129.220
126.292
119.972
119.497
117.013
114.482
52.309
48.569
48.510
36.522
36.322
36.102
30.425
30.350
f1 (ppm)


-109.634
-110.346
-116.401
-117.113
f1 (ppm)

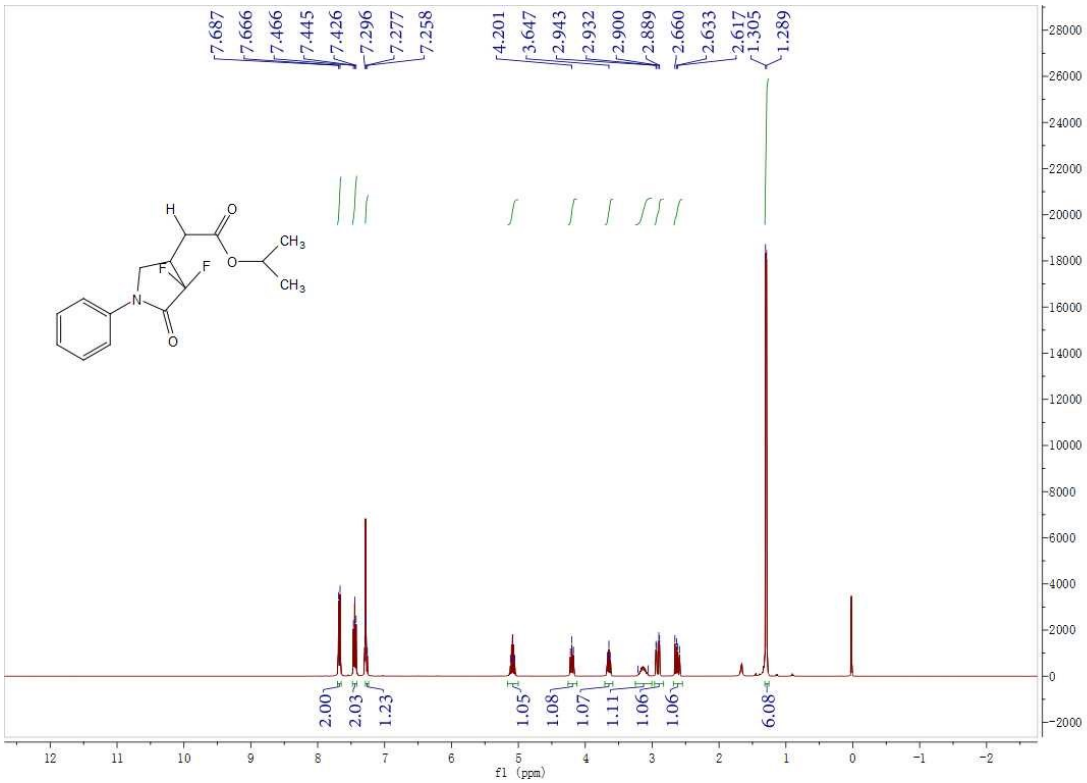
ethyl 2-(4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)acetate (20)

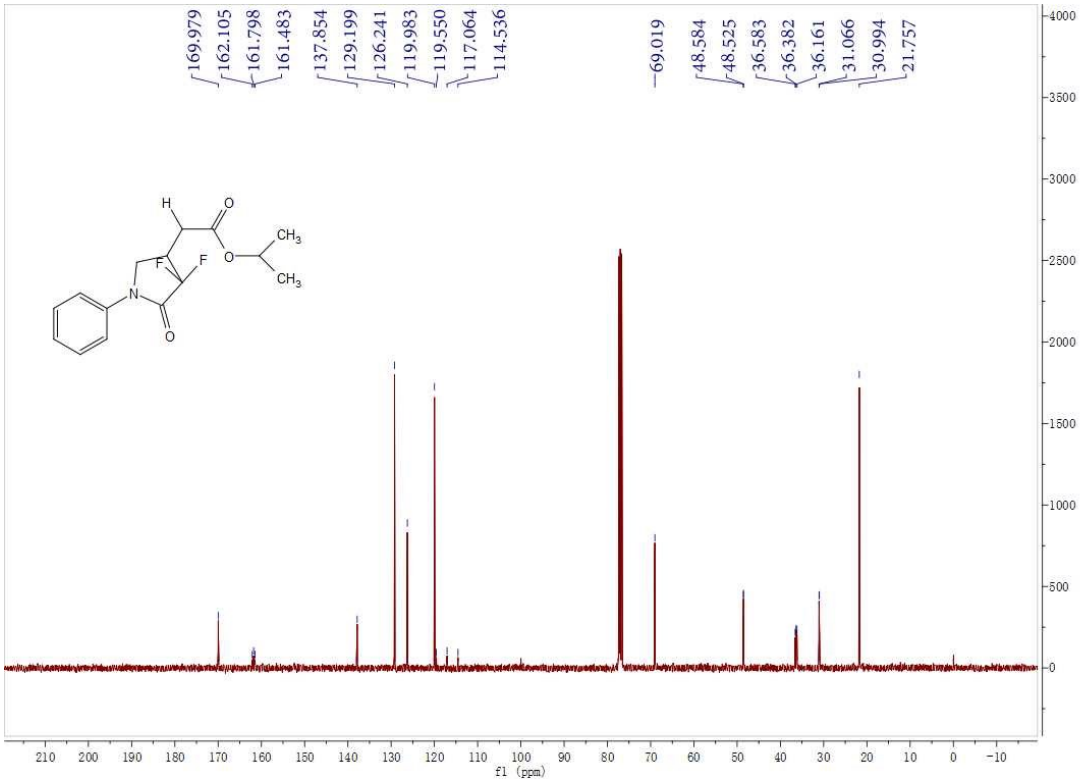


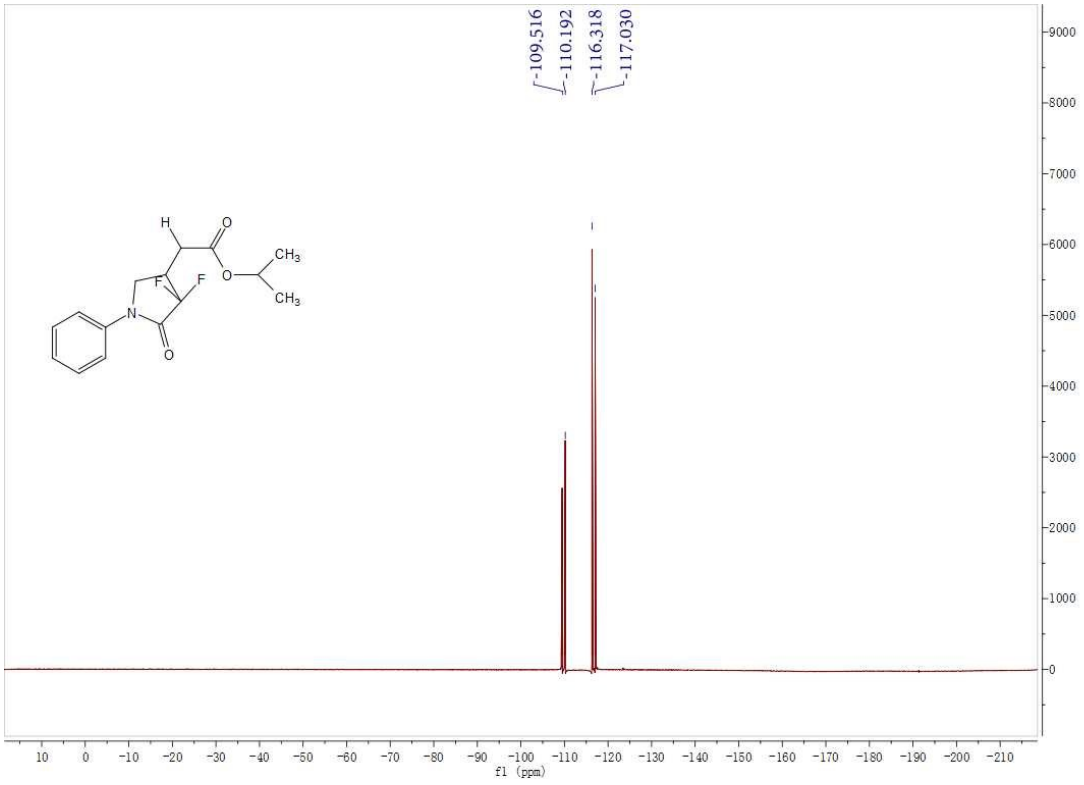




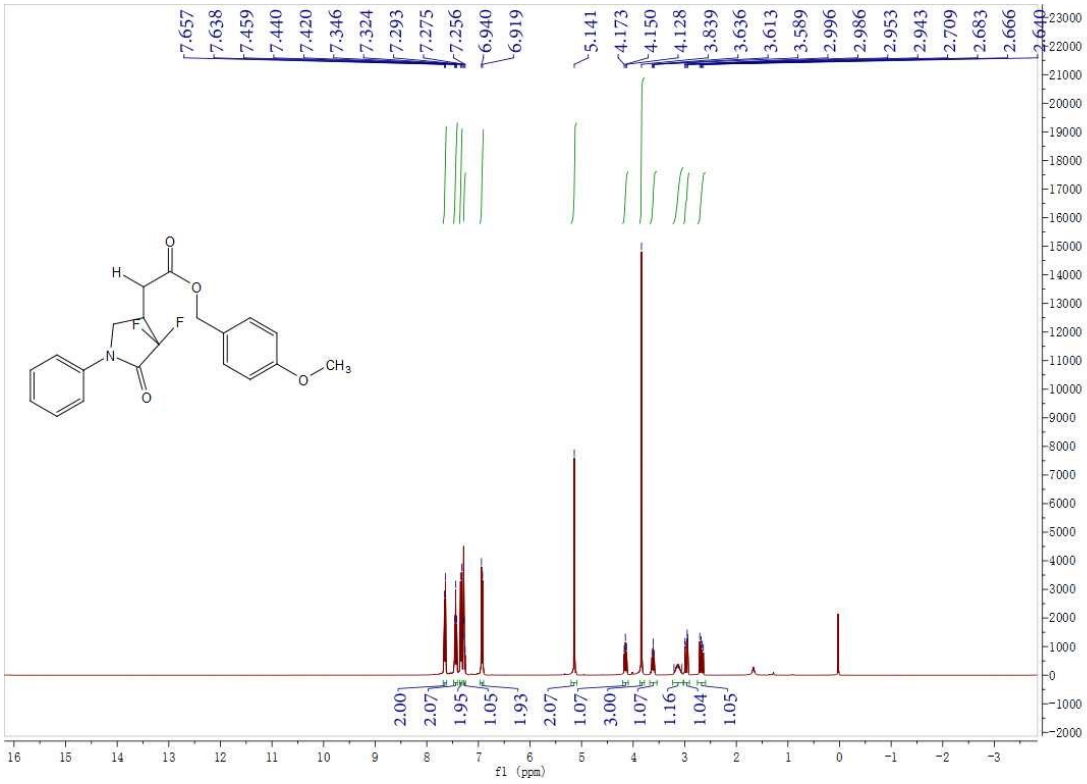
isopropyl 2-(4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)acetate (21)

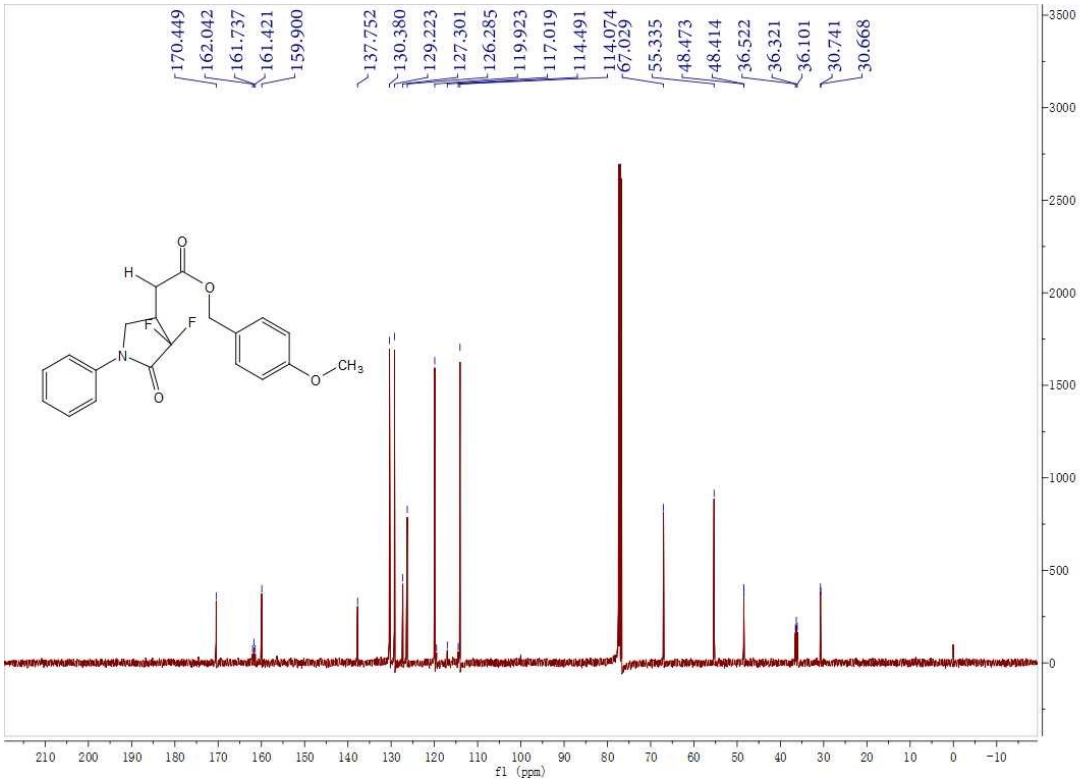


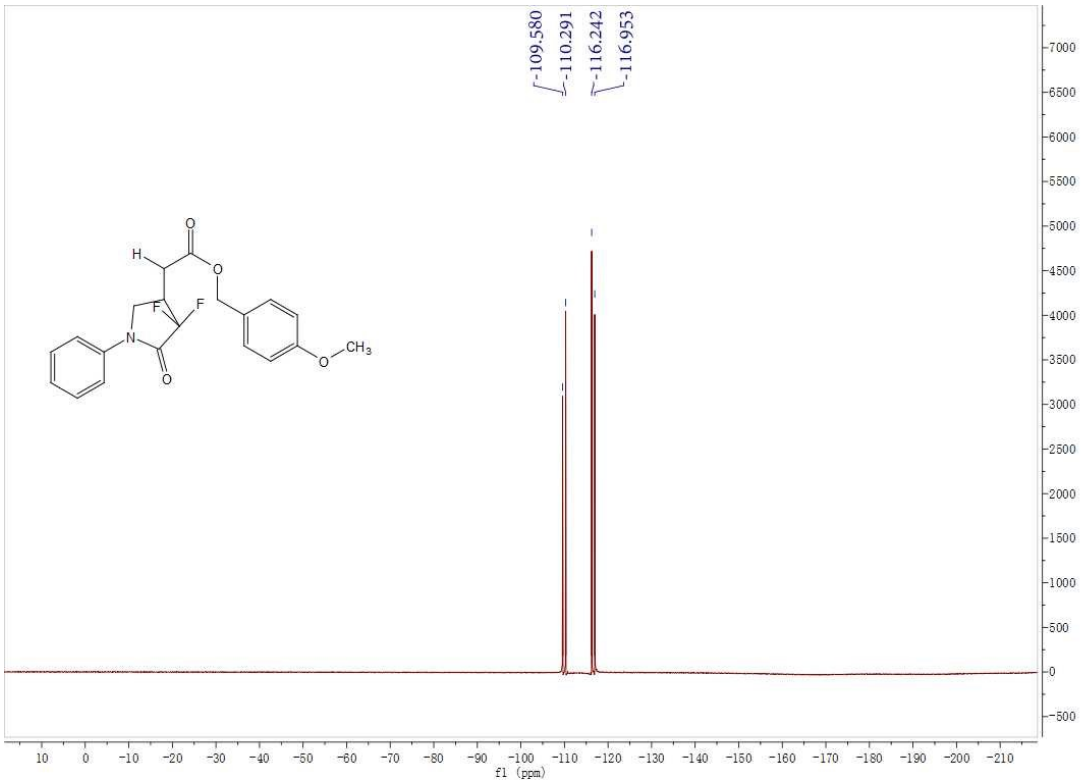

169.979
162.105
161.798
161.483
137.854
129.199
126.241
119.983
119.550
117.064
114.536
69.019
48.584
48.525
36.583
36.382
36.161
31.066
30.994
21.757
H
O
CH3
F
F
O
CH3
N
O
f1 (ppm)


-109.516
-110.192
-116.318
-117.030
H
O
CH3
F
F
O
CH3
N
O
f1 (ppm)

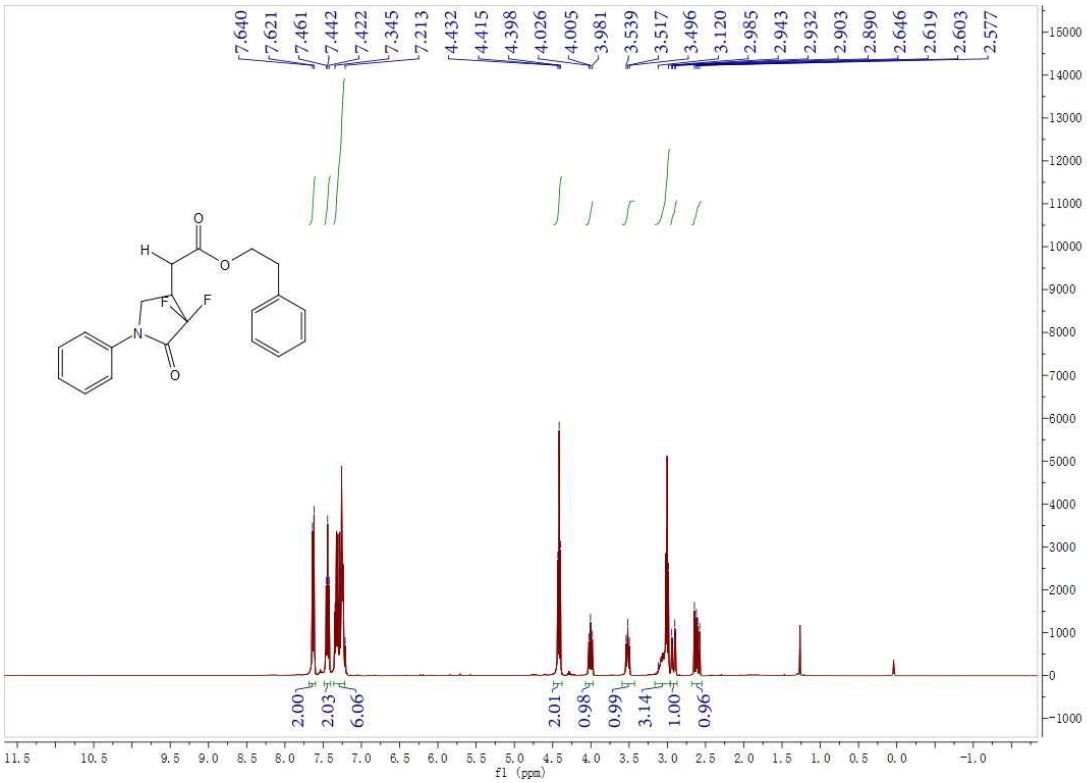
4-methoxybenzyl 2-(4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)acetate (22)

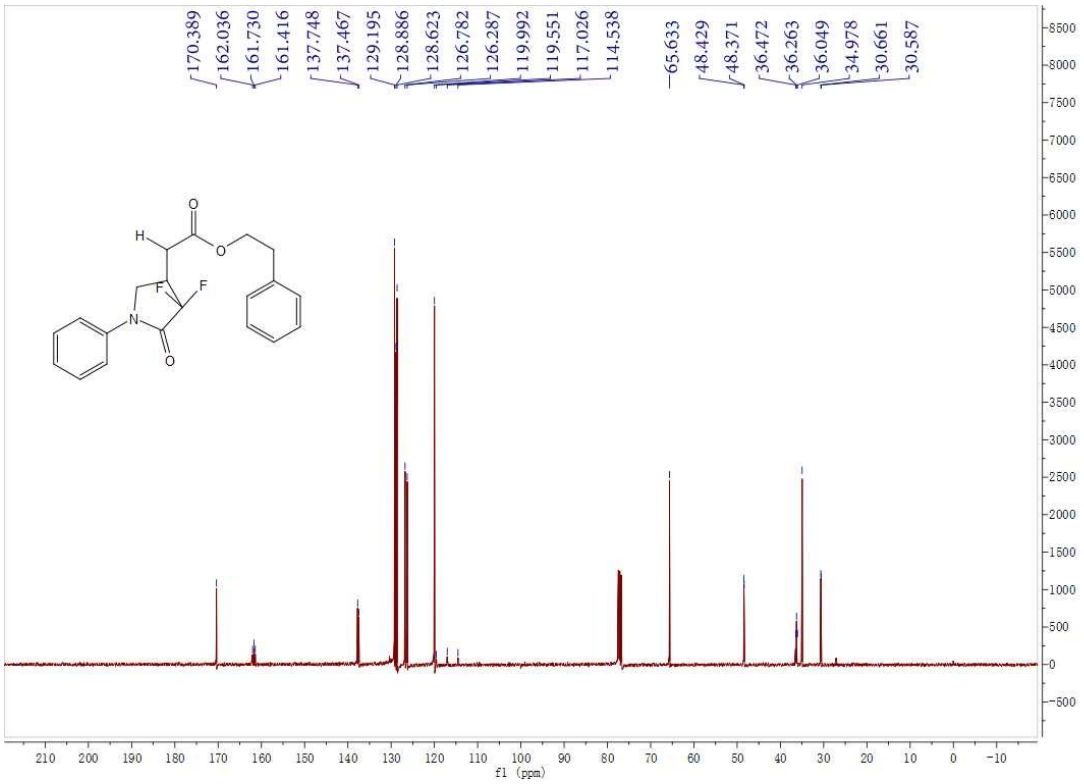


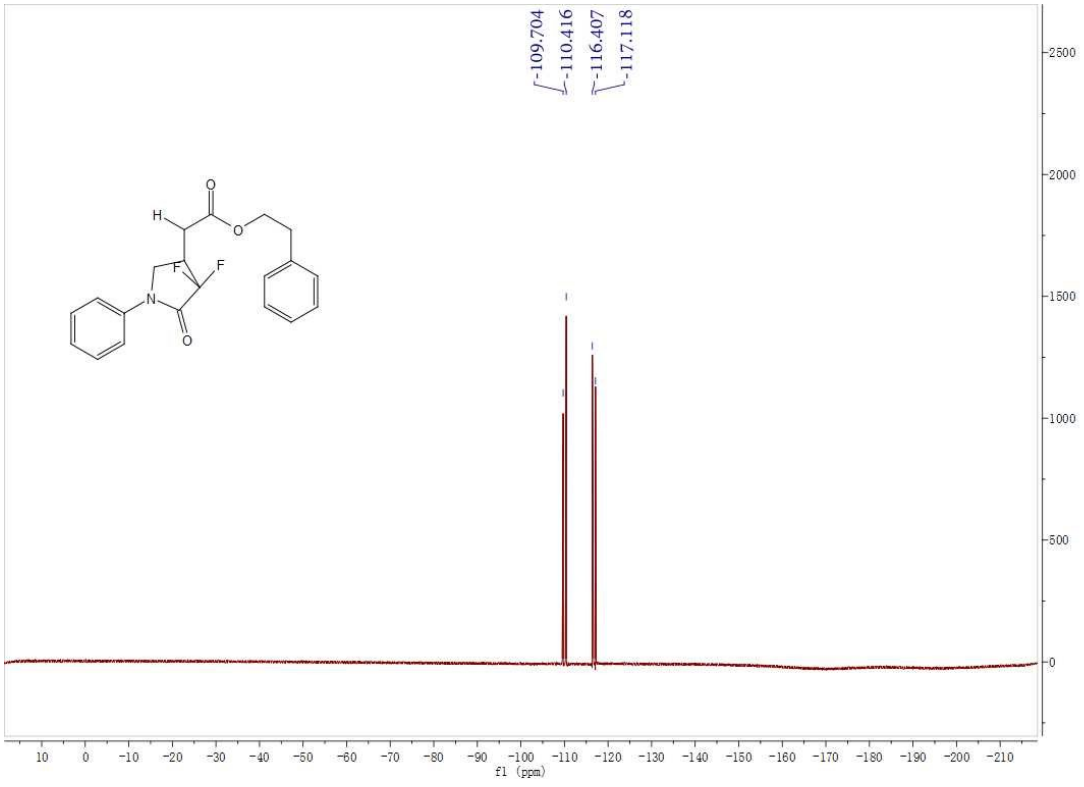




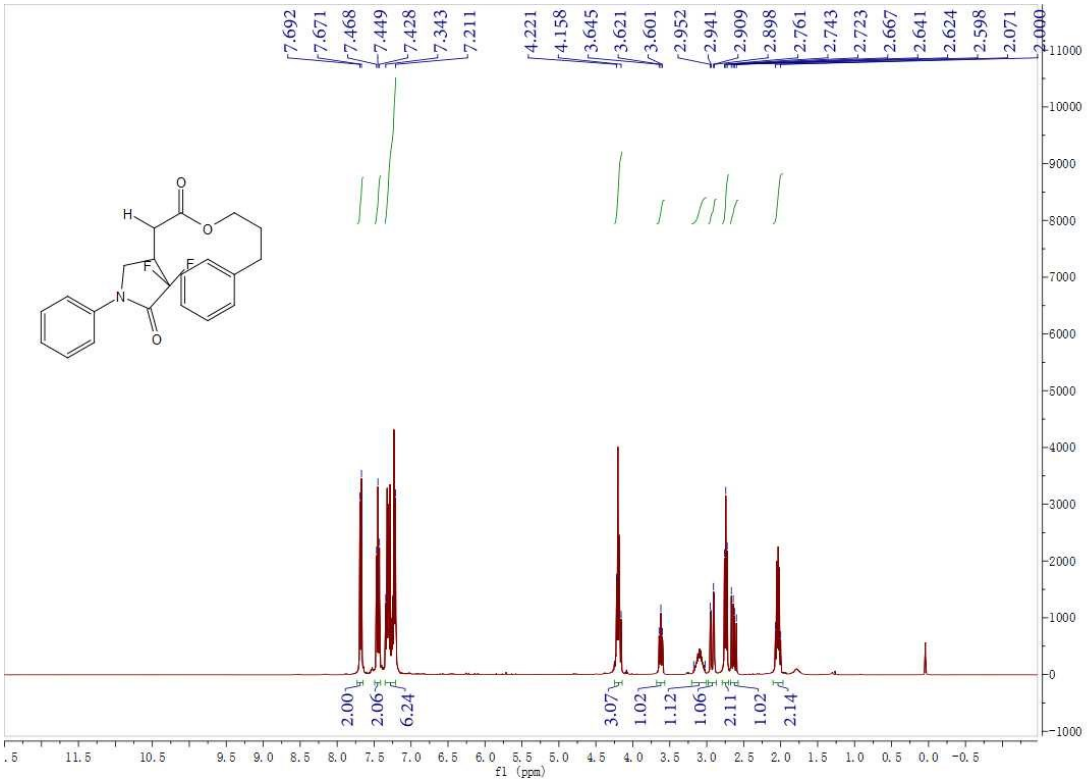
phenethyl 2-(4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)acetate (23)

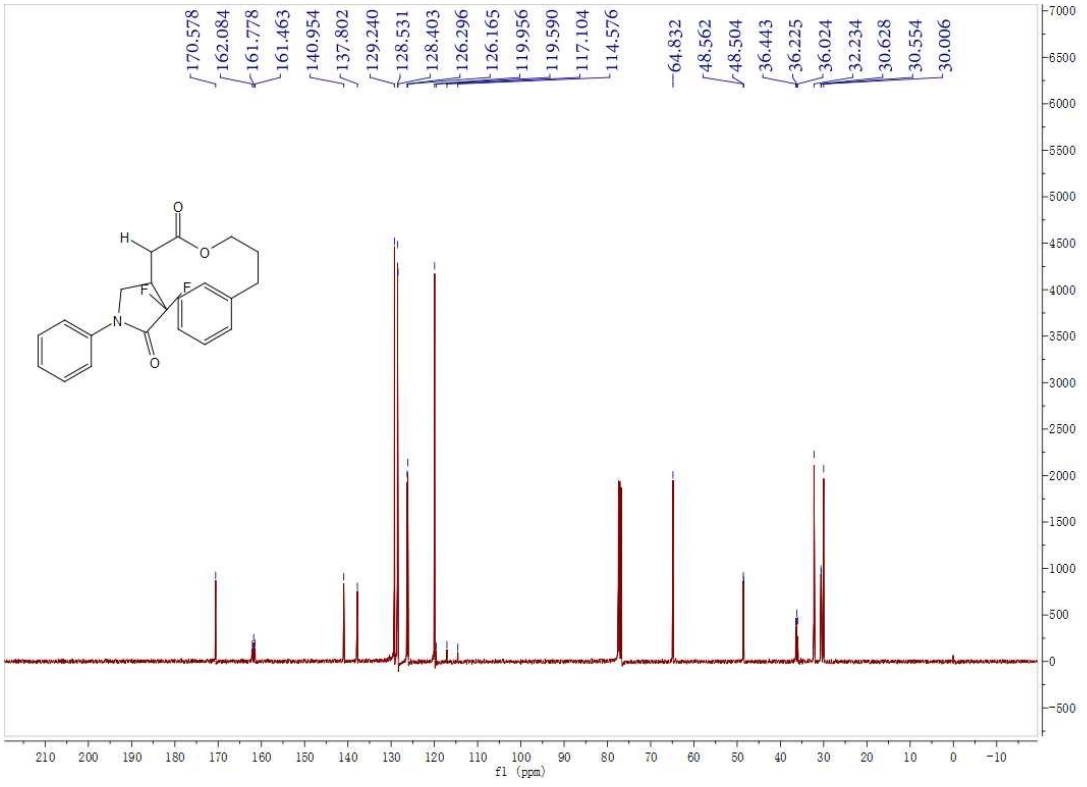


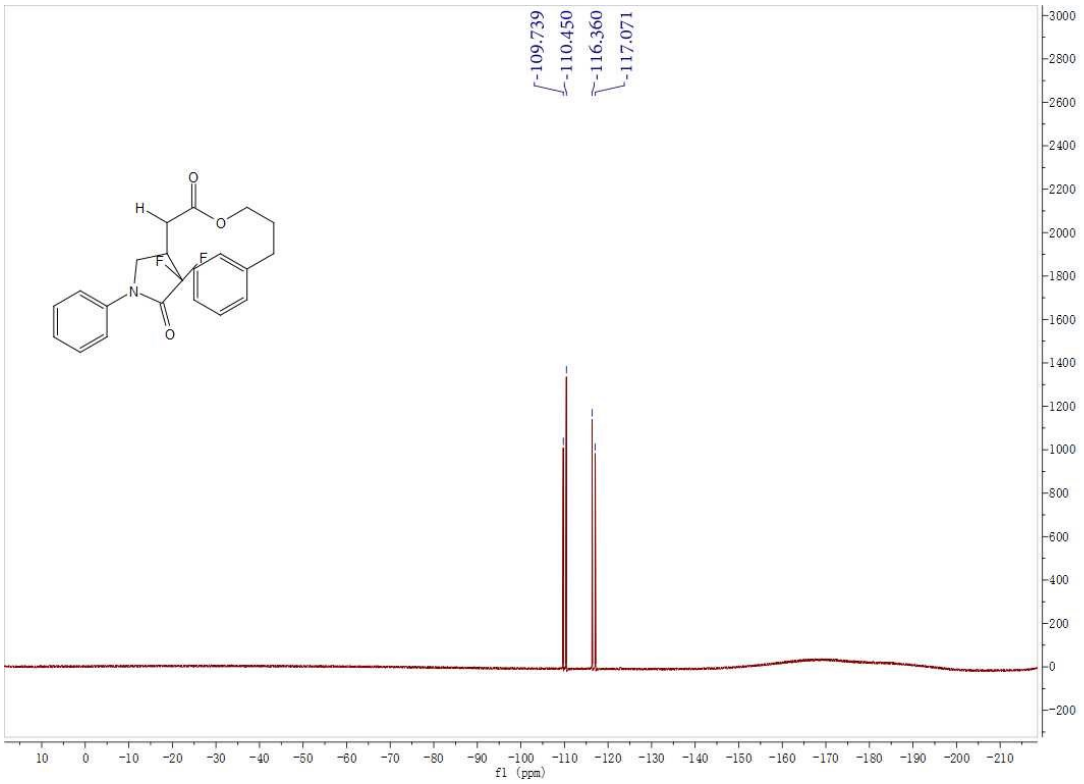

170.389
162.036
161.730
161.416
137.748
137.467
129.195
128.886
128.623
126.782
126.287
119.992
119.551
117.026
114.538
65.633
48.429
48.371
36.472
36.263
36.049
34.978
30.661
30.587
f1 (ppm)


-109.704
-110.416
-116.407
-117.118
f1 (ppm)

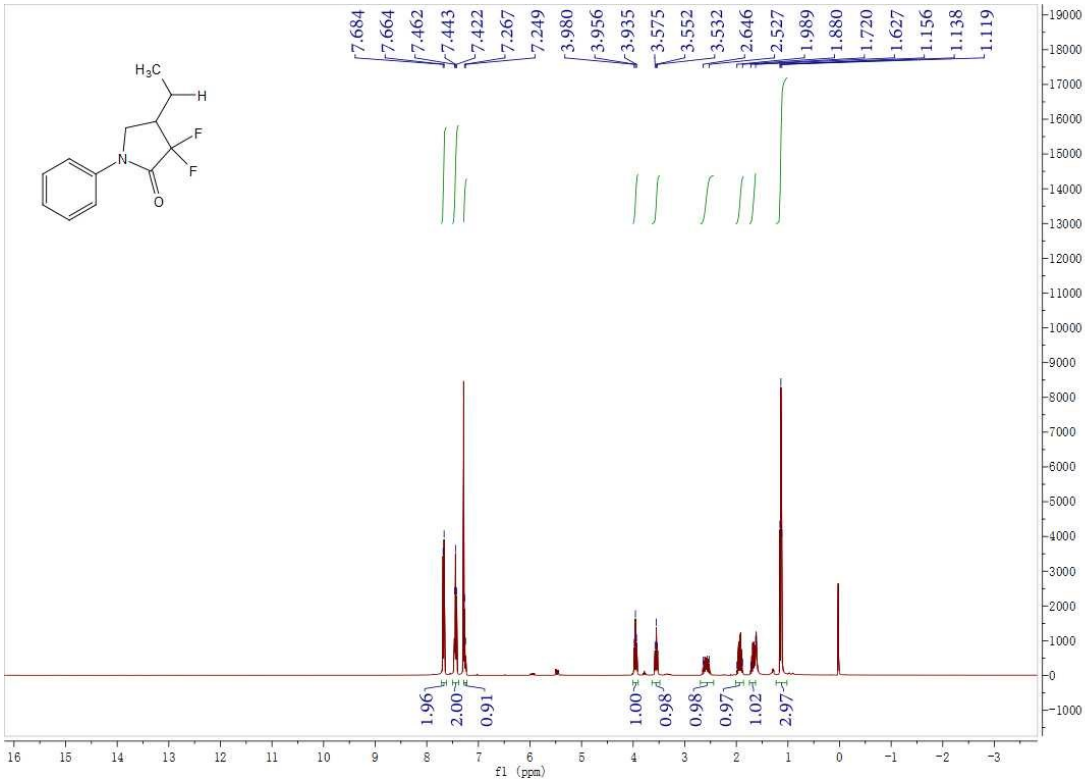
3-phenylpropyl 2-(4,4-difluoro-5-oxo-1-phenylpyrrolidin-3-yl)acetate (24)

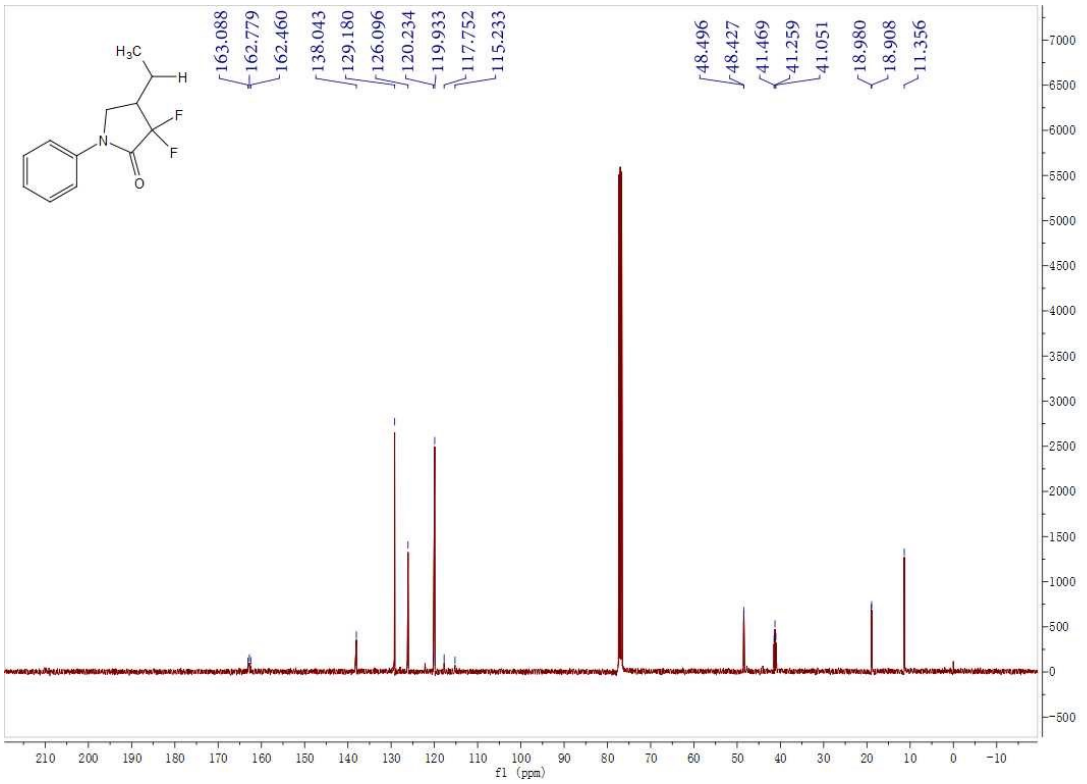


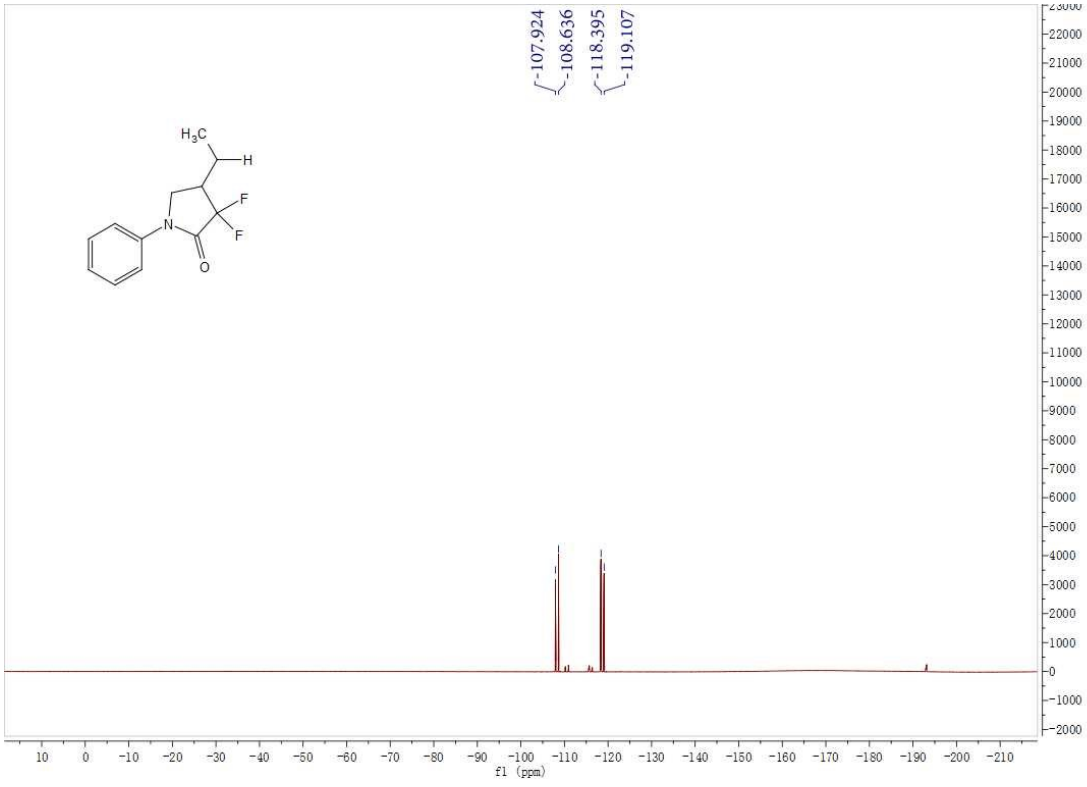




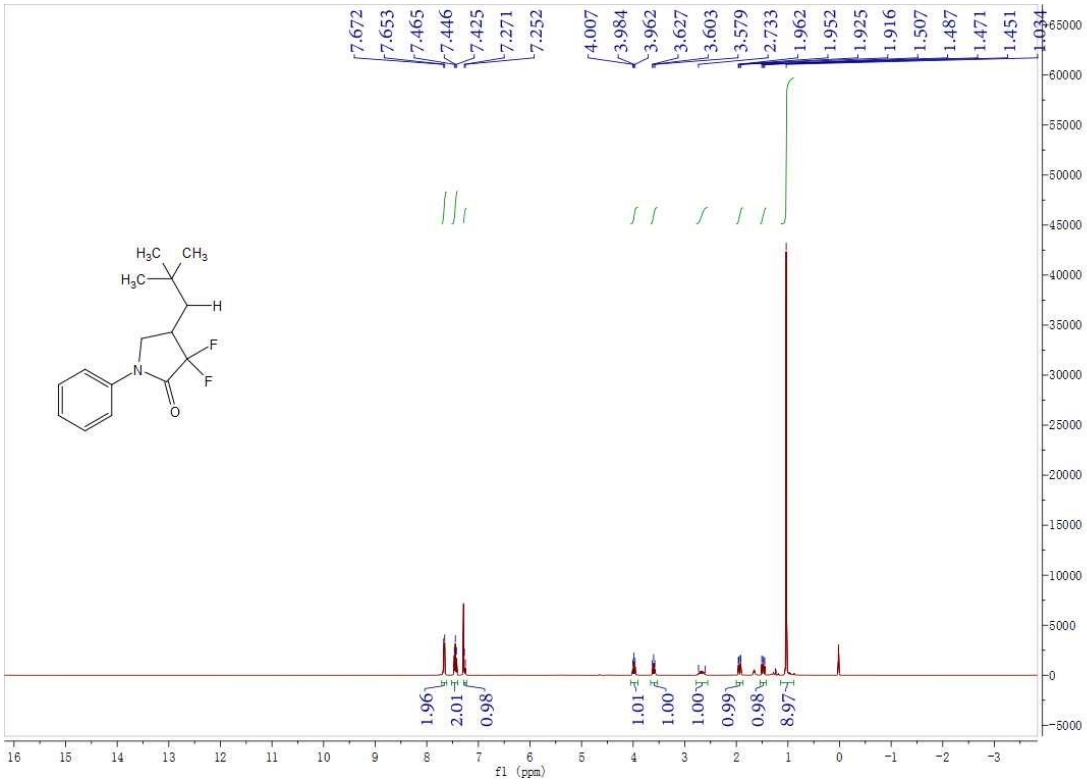
3,3-difluoro-4-ethyl-1-phenylpyrrolidin-2-one (25)

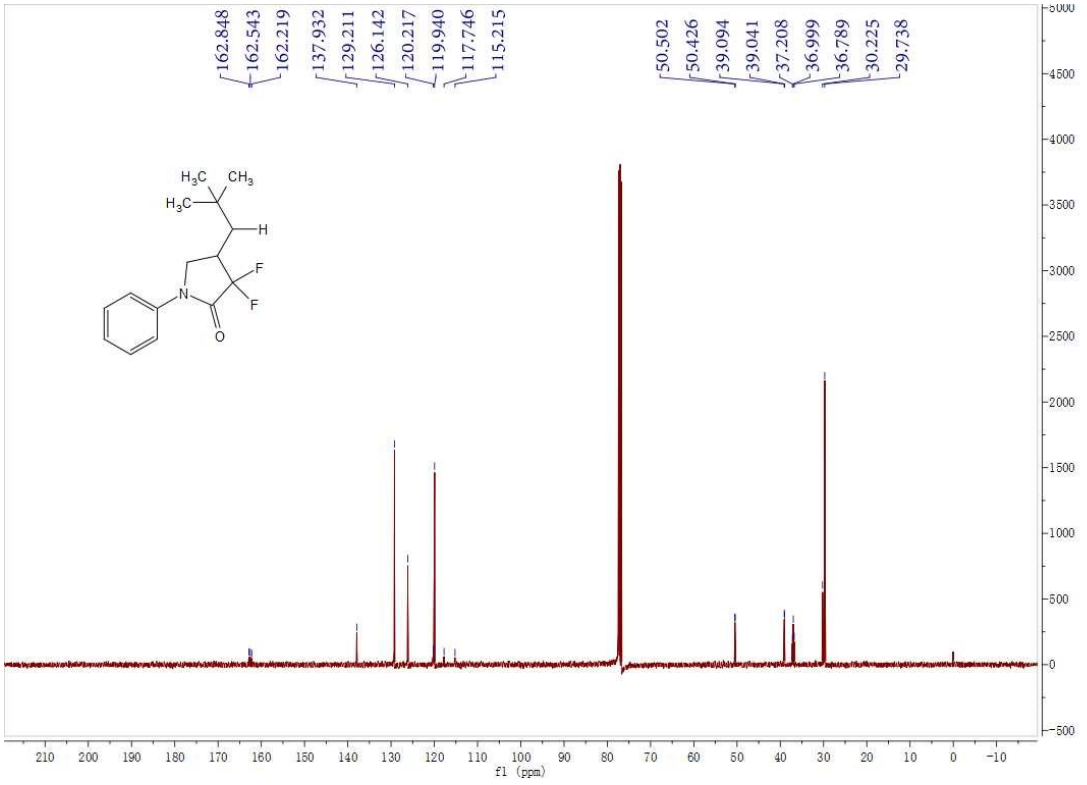


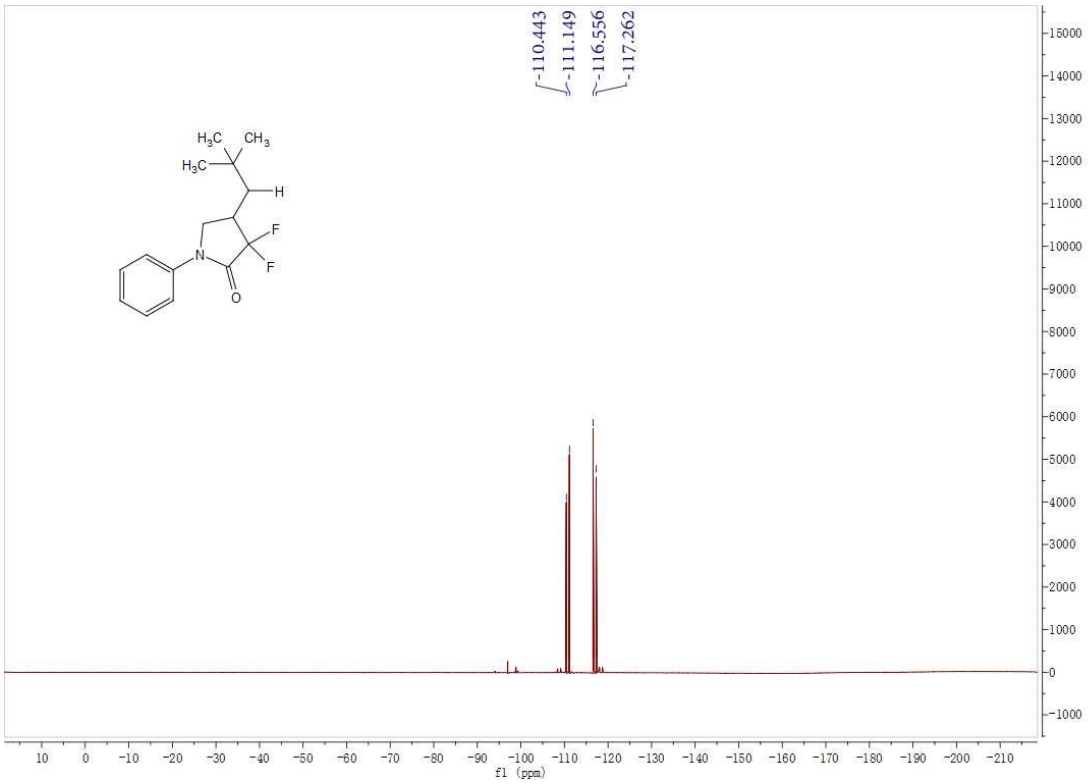

163.088
162.779
162.460
138.043
129.180
126.096
120.234
119.933
117.752
115.233
48.496
48.427
41.469
41.259
41.051
18.980
18.908
11.356
H3C
H
F
F
N
O
f1 (ppm)


-107.924
-108.636
-118.395
-119.107
H3C
H
F
F
N
O
f1 (ppm)

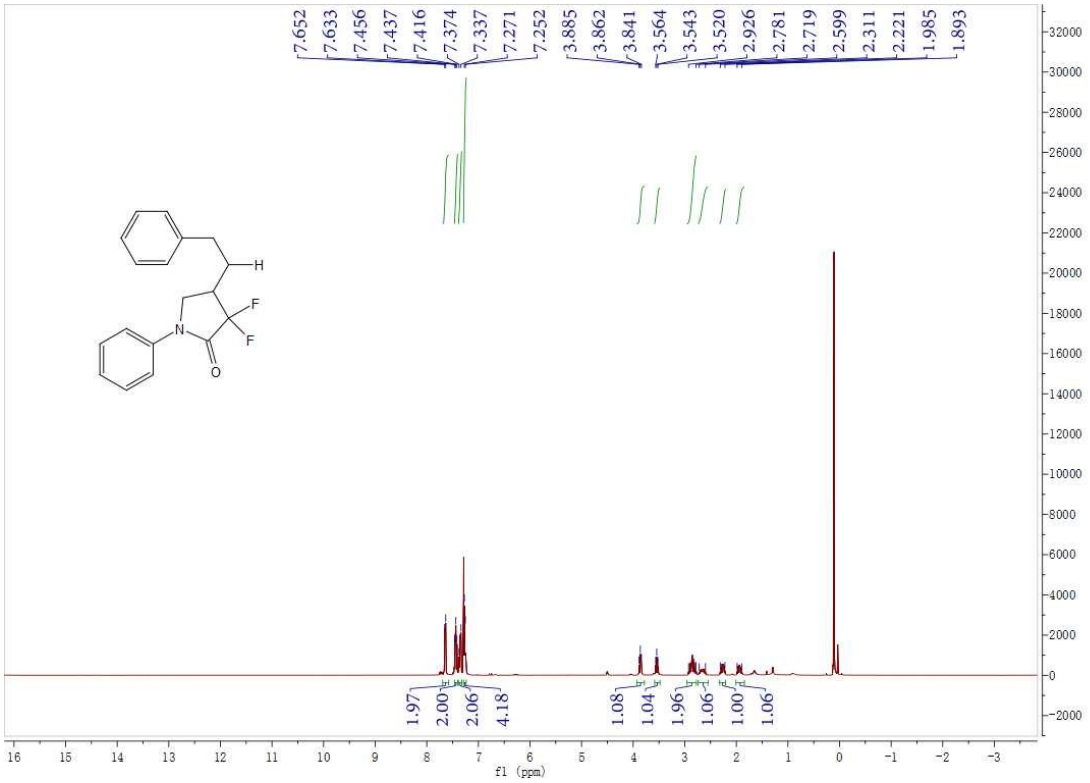
3,3-difluoro-4-neopentyl-1-phenylpyrrolidin-2-one (2x) (26)

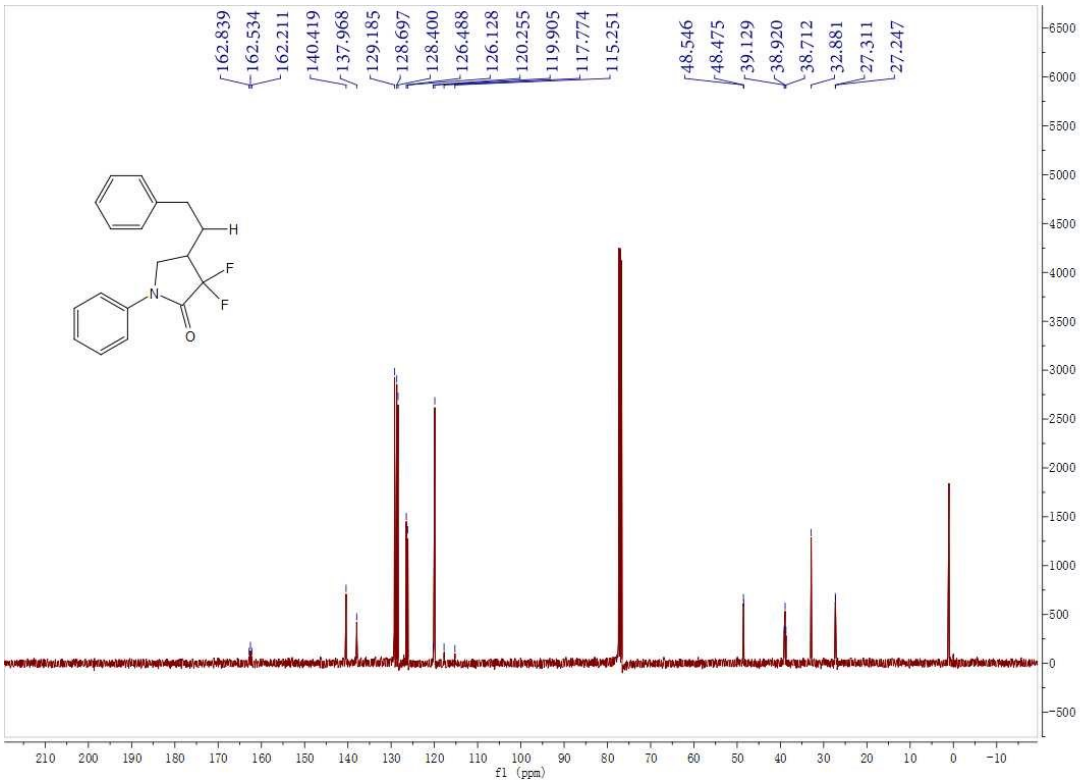


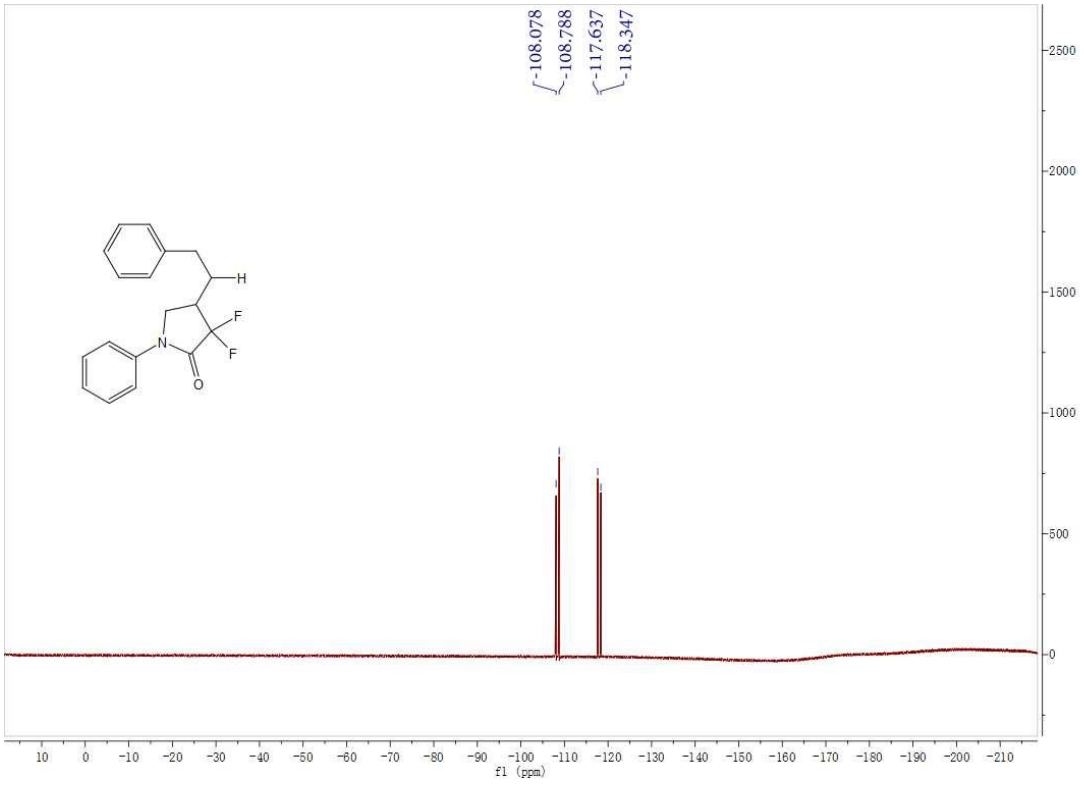




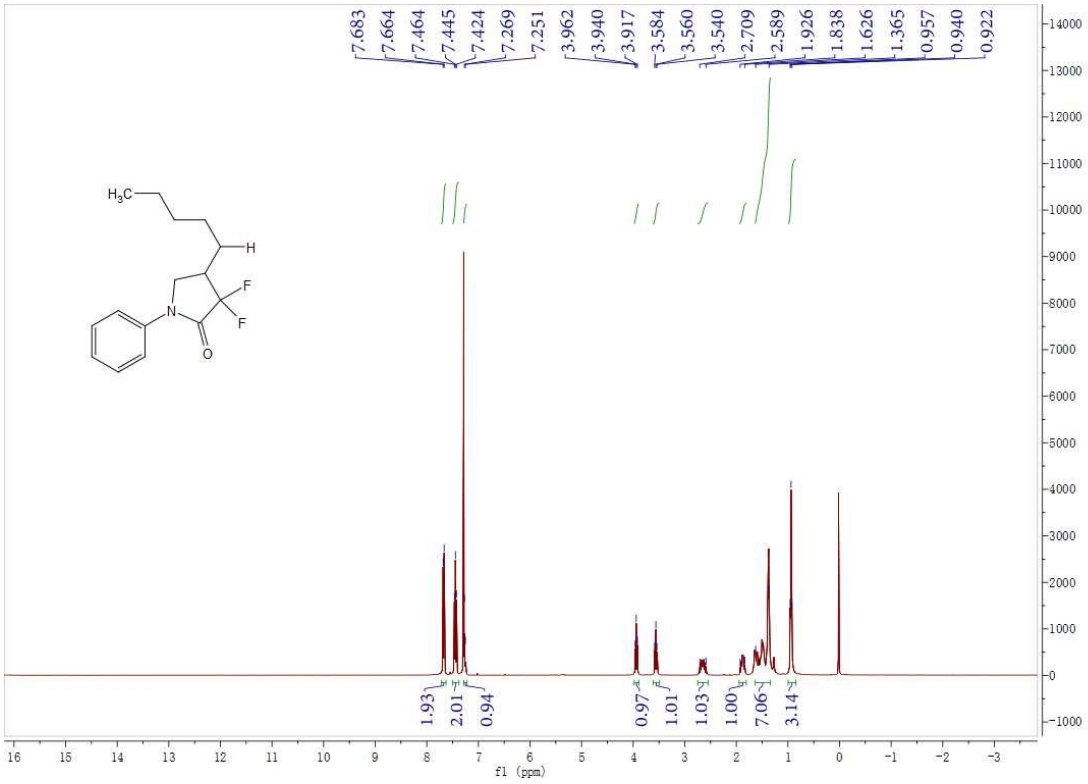
3,3-difluoro-4-phenethyl-1-phenylpyrrolidin-2-one (27)

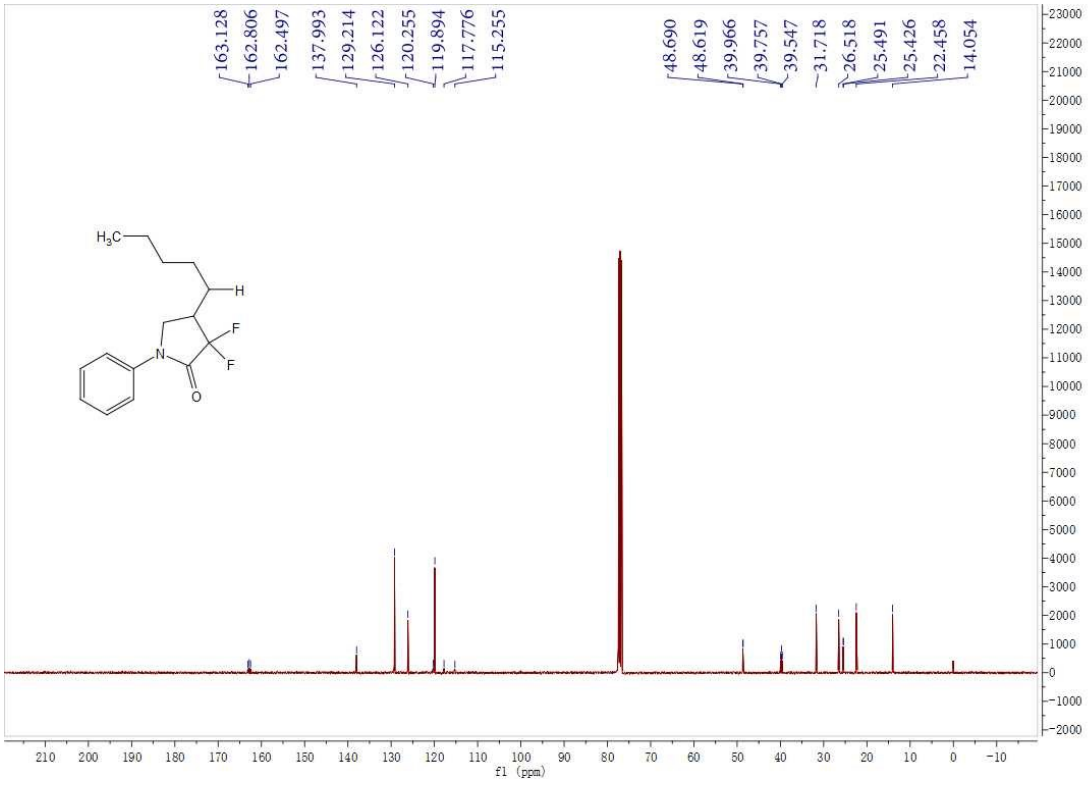


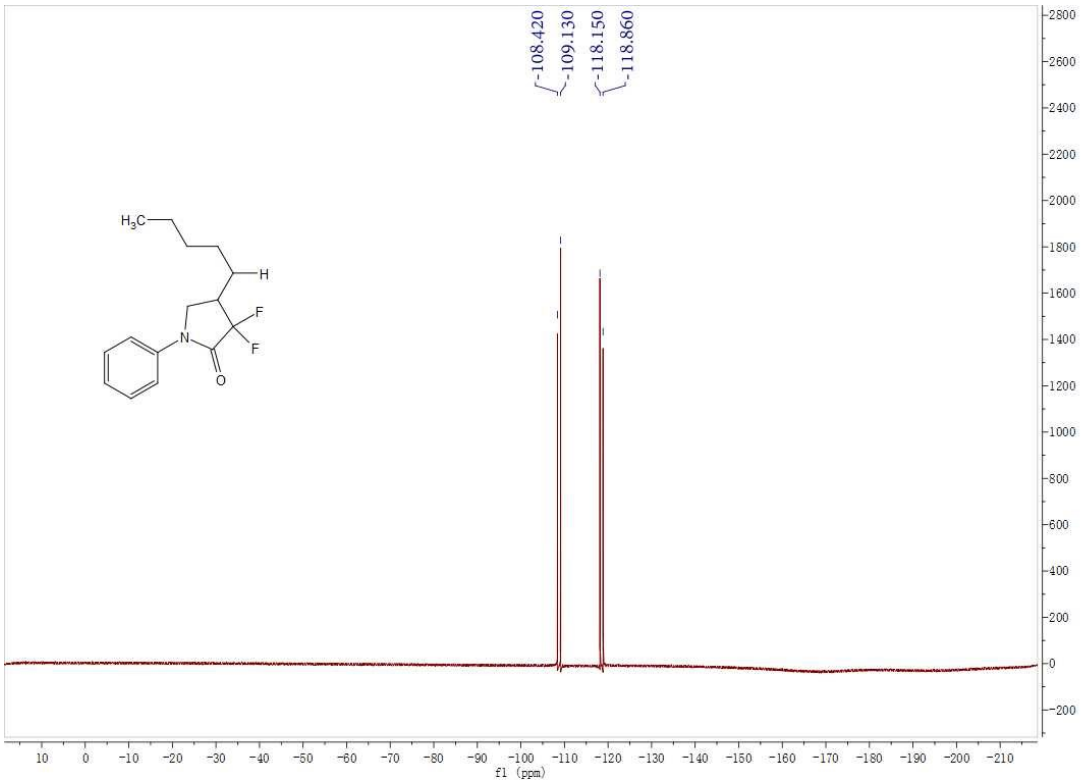

162.839
162.534
162.211
140.419
137.968
129.185
128.697
128.400
126.488
126.128
120.255
119.905
117.774
115.251
48.546
48.475
39.129
38.920
38.712
32.881
27.311
27.247
H
F
F
N
O
f1 (ppm)


-108.078
-108.788
-117.637
-118.347
H
F
F
N
O
f1 (ppm)

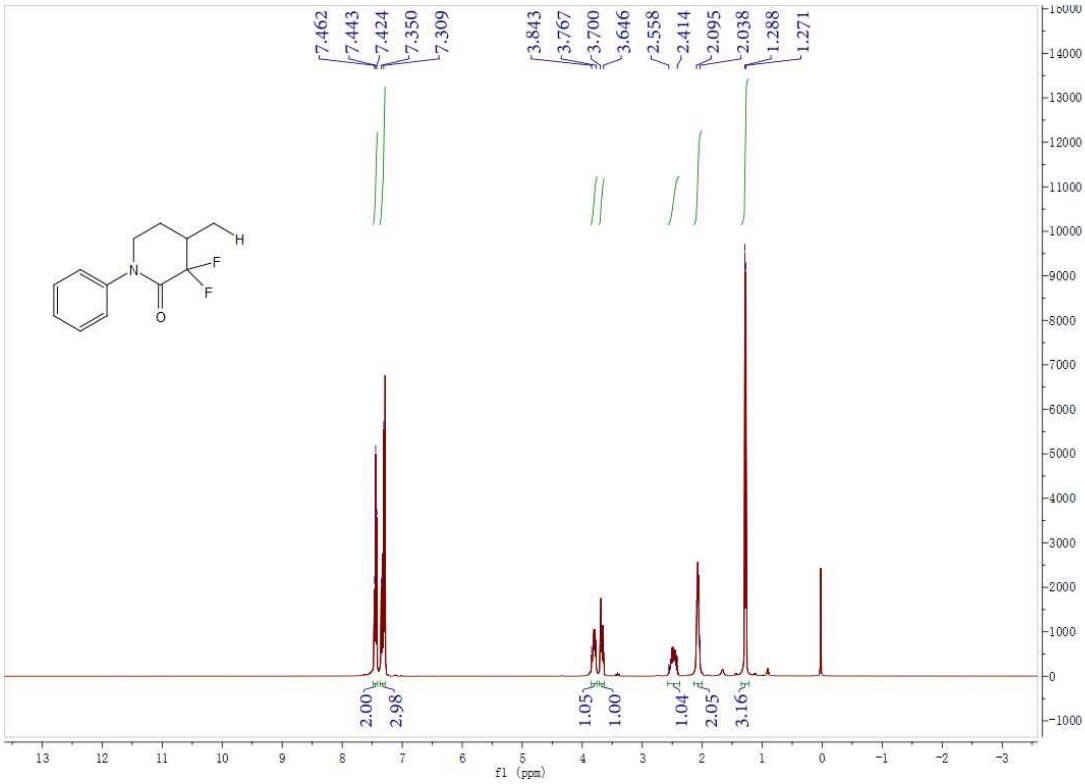
3,3-difluoro-4-pentyl-1-phenylpyrrolidin-2-one (28)

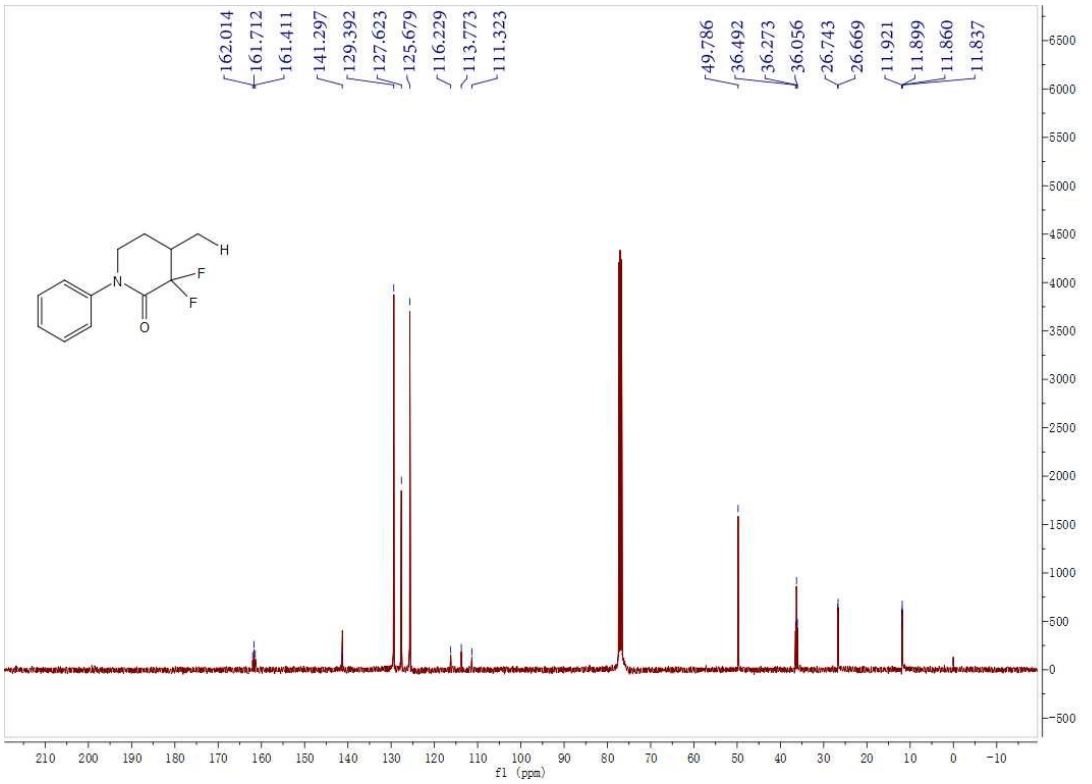


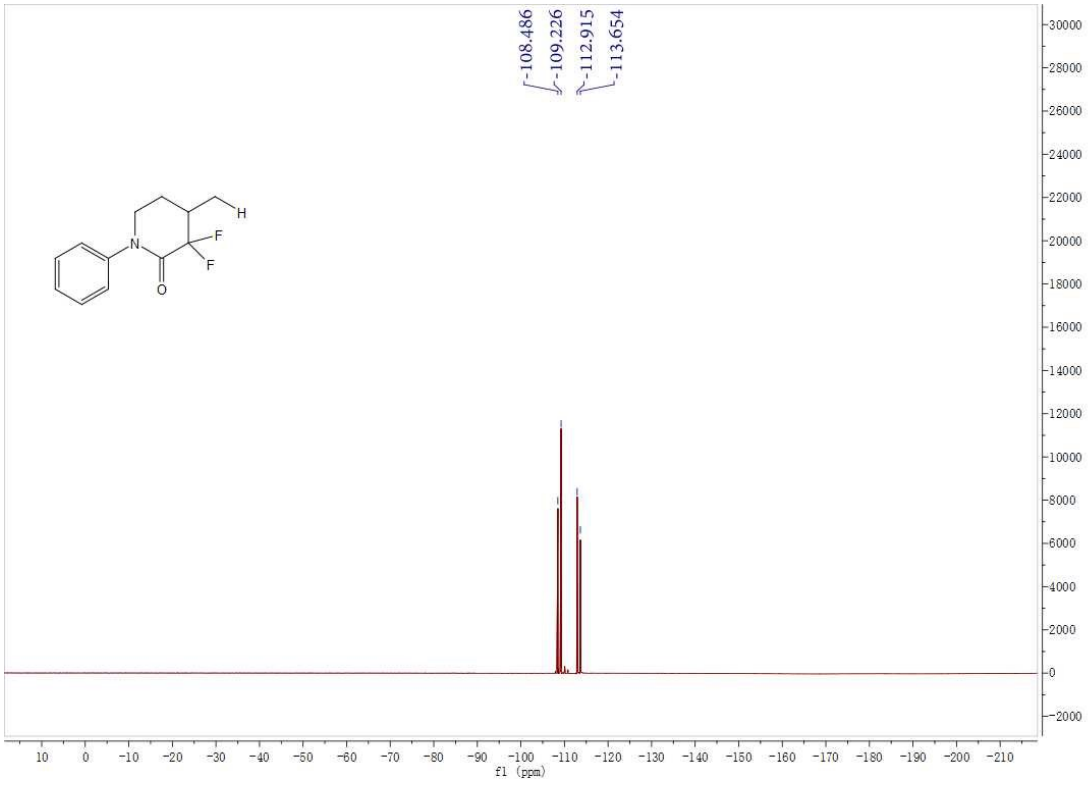




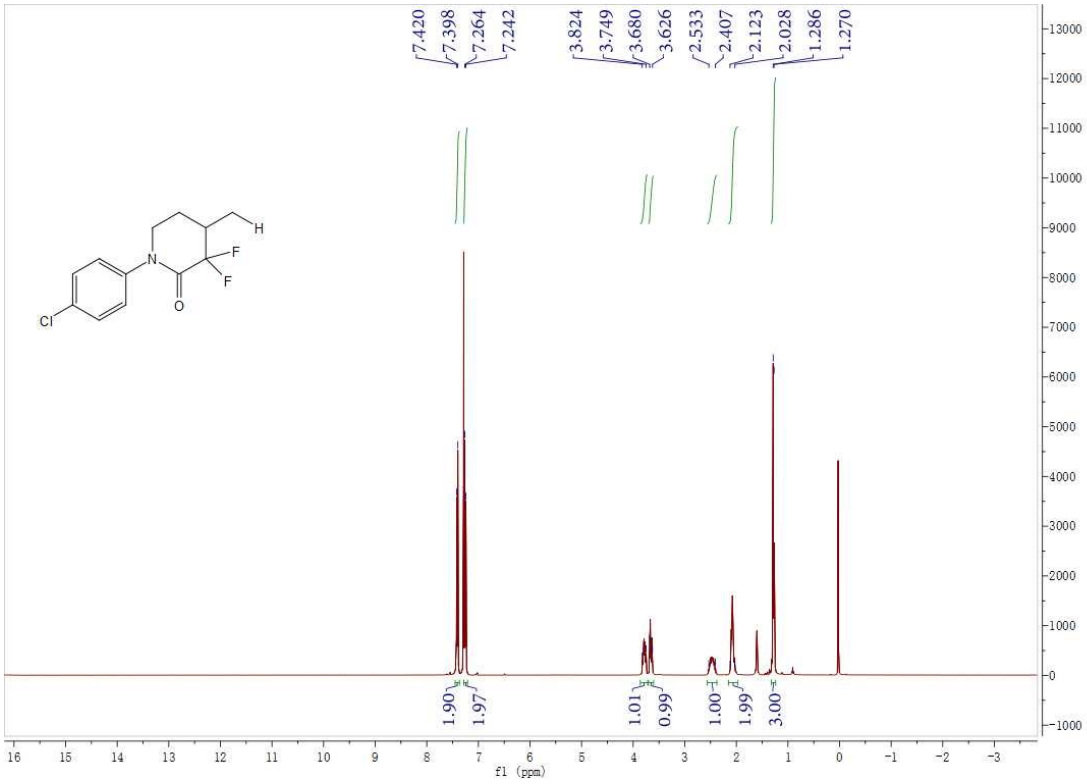
3,3-difluoro-4-methyl-1-phenylpiperidin-2-one (29)

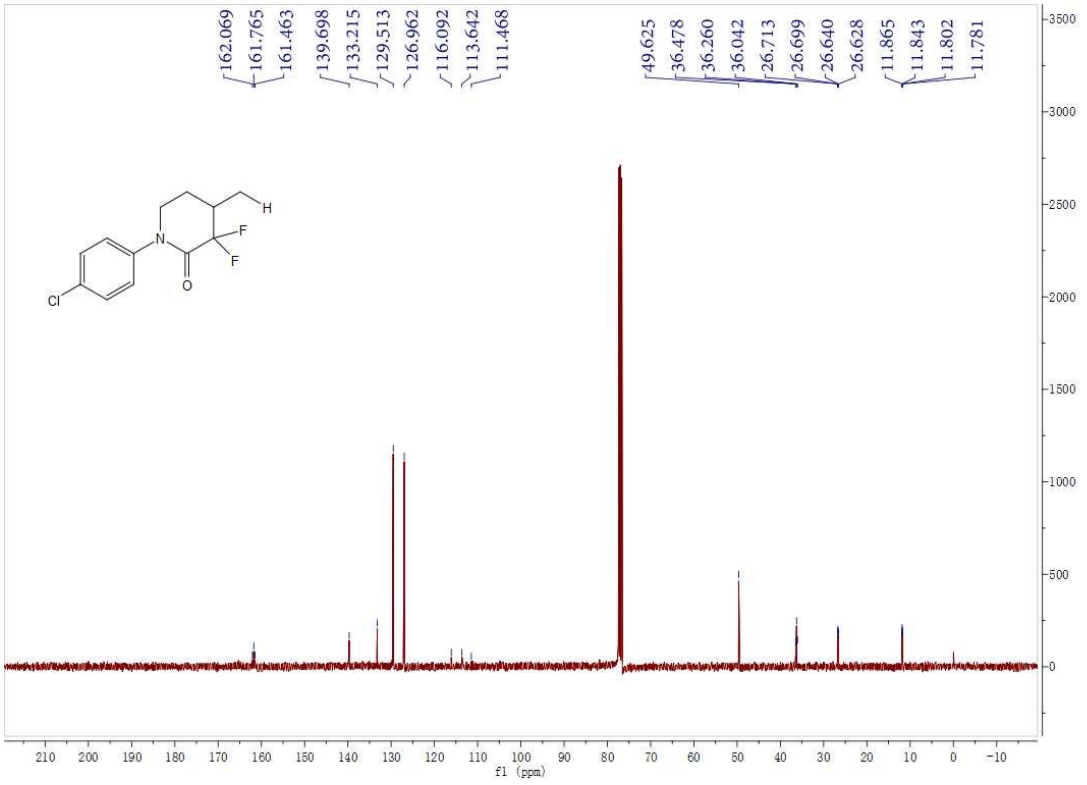


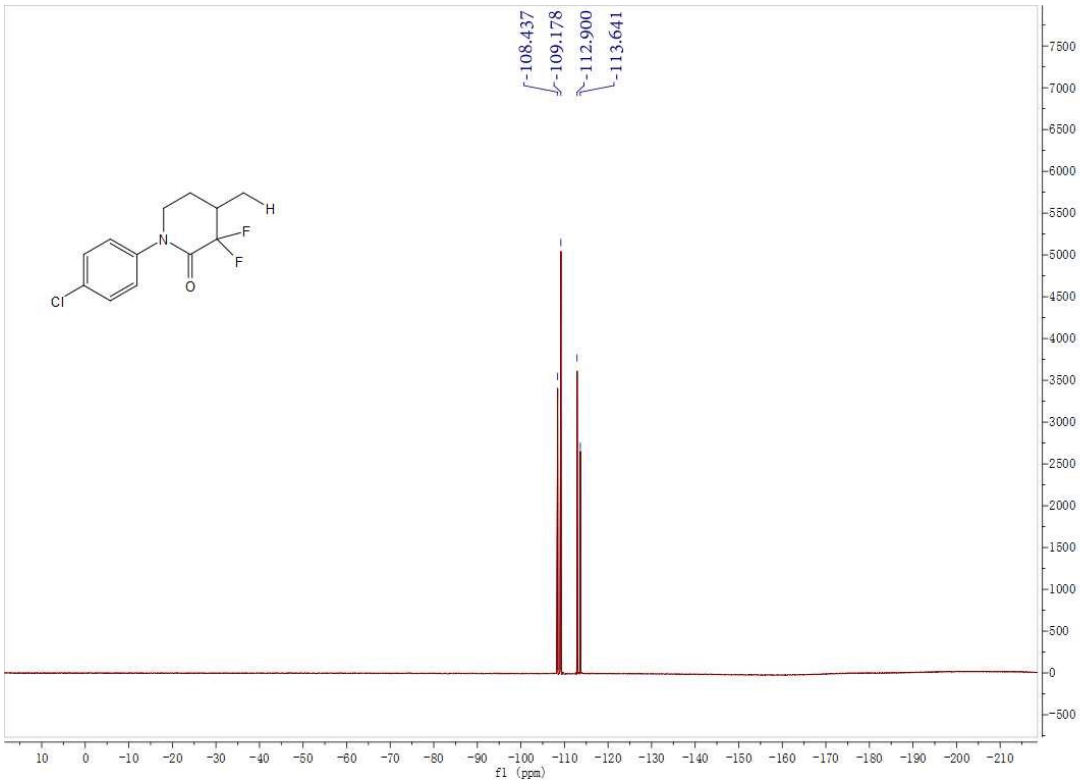

162.014
161.712
161.411
141.297
129.392
127.623
125.679
116.229
113.773
111.323
49.786
36.492
36.273
36.056
26.743
26.669
11.921
11.899
11.860
11.837
f1 (ppm)


-108.486
-109.226
-112.915
-113.654
f1 (ppm)

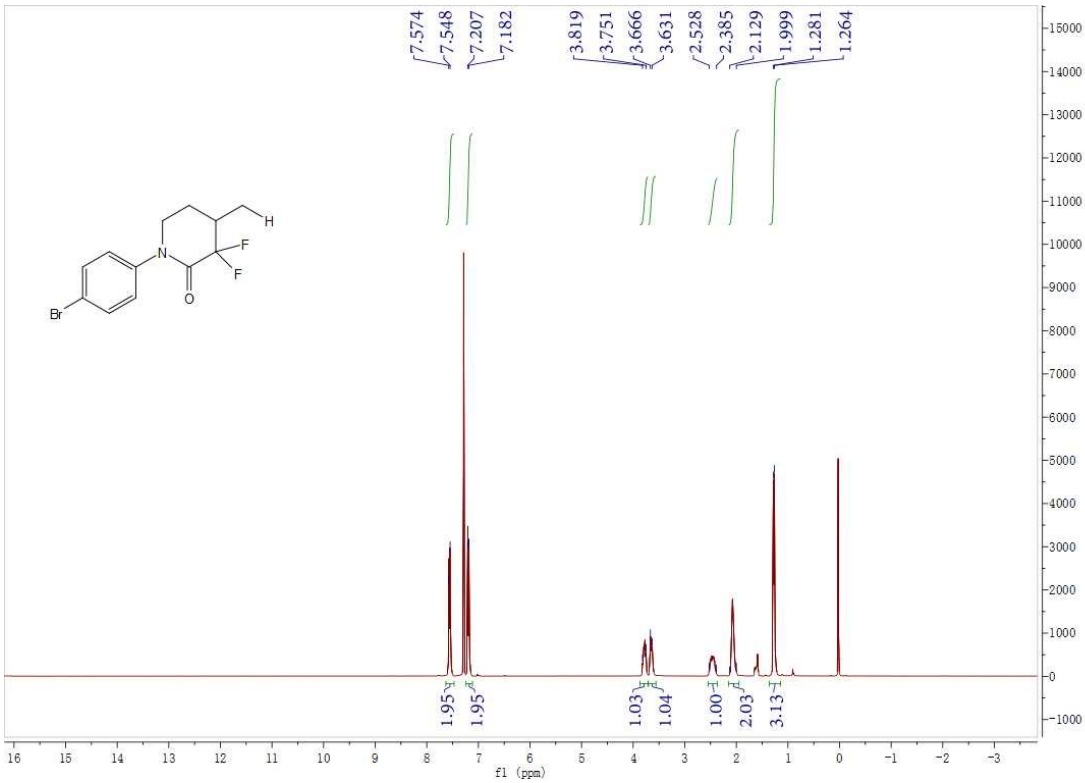
3,3-difluoro-4-methyl-1-(4-chlorophenyl)-piperidin-2-one (30)

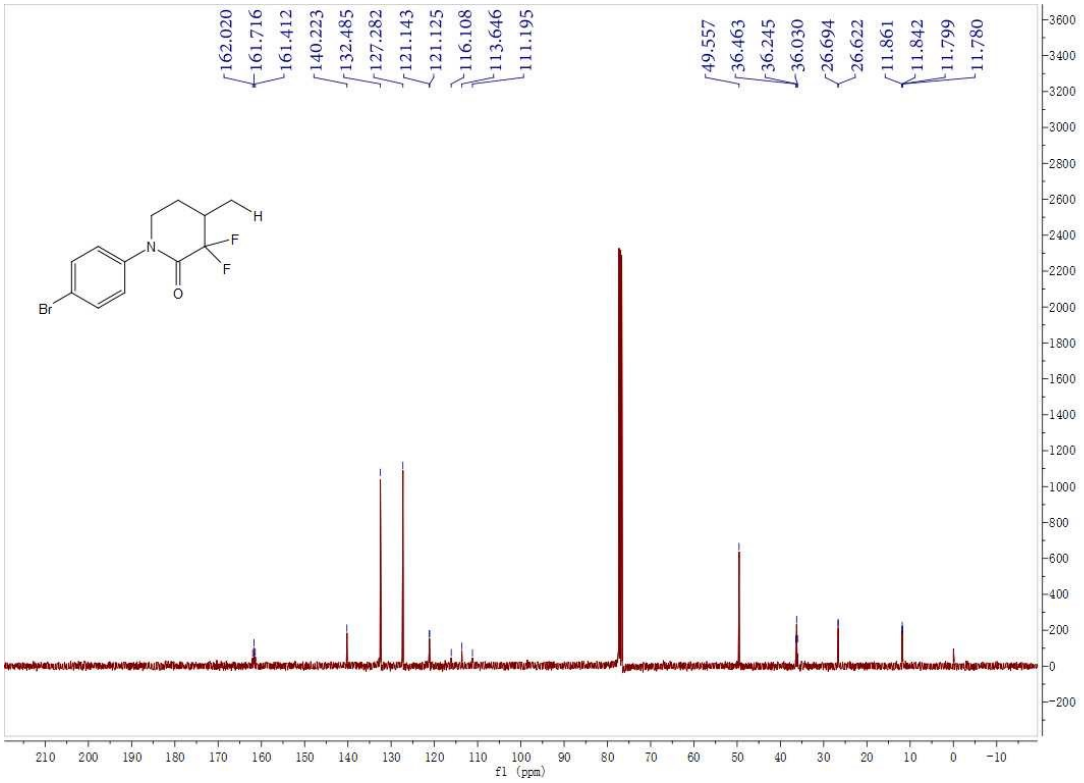


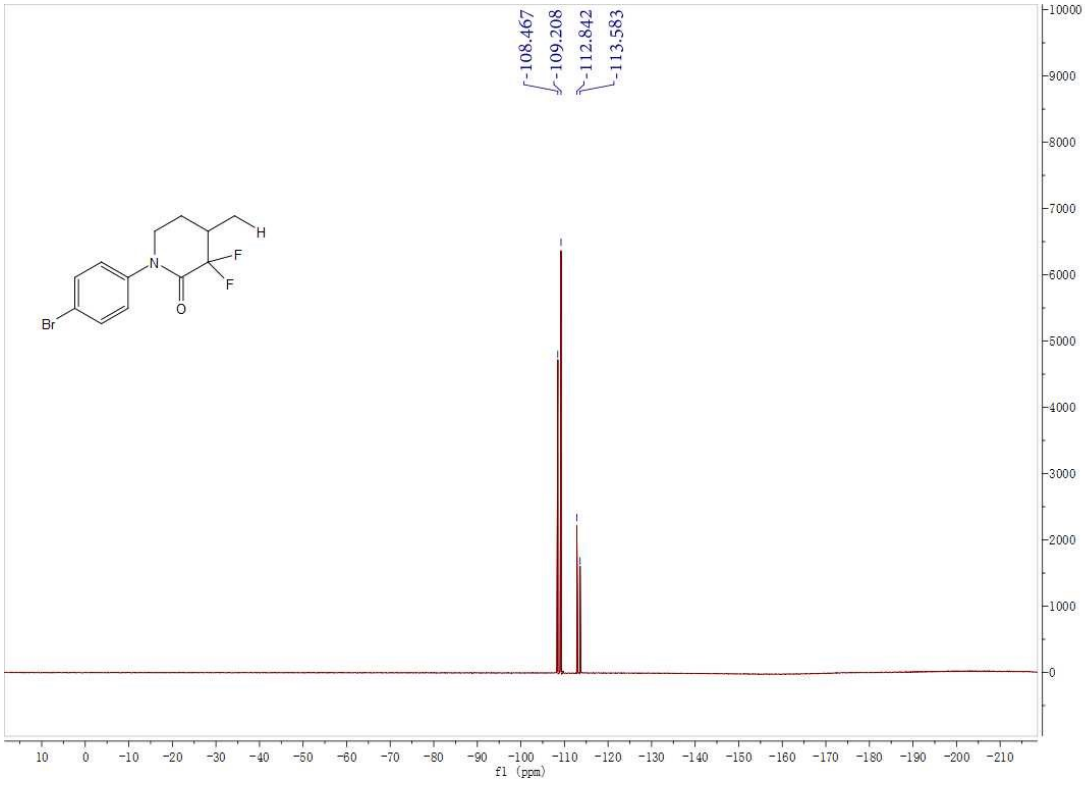




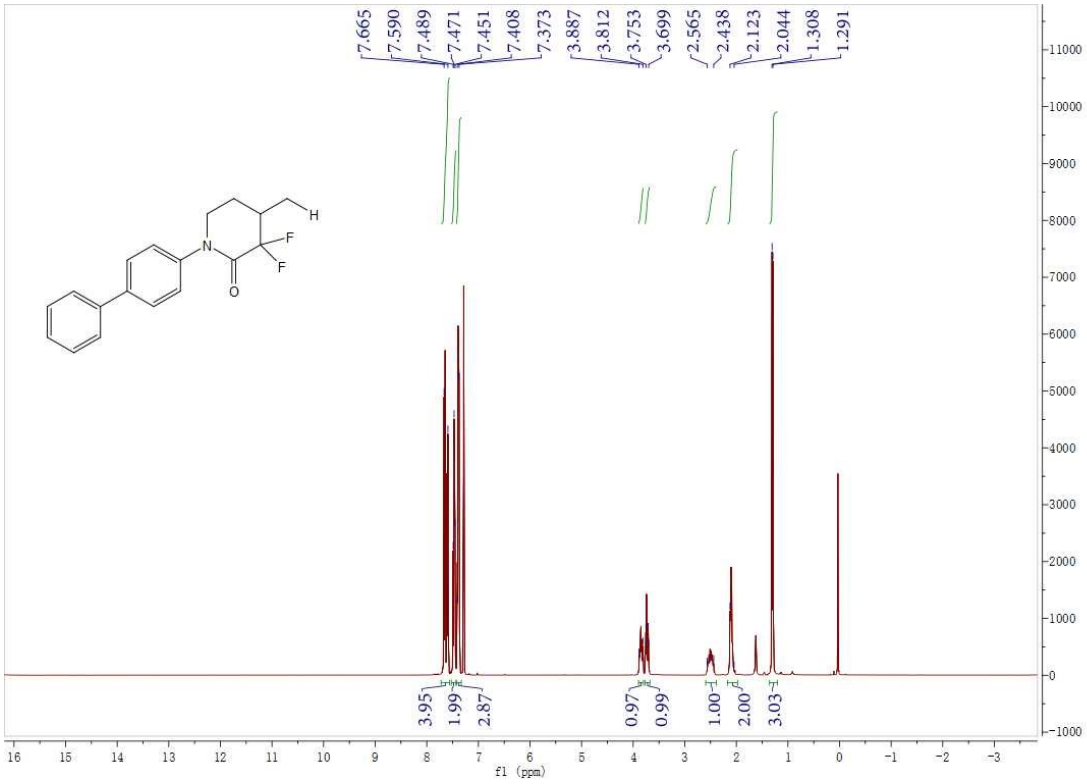
3,3-difluoro-4-methyl-1-(4-chlorophenyl)-piperidin-2-one (31)

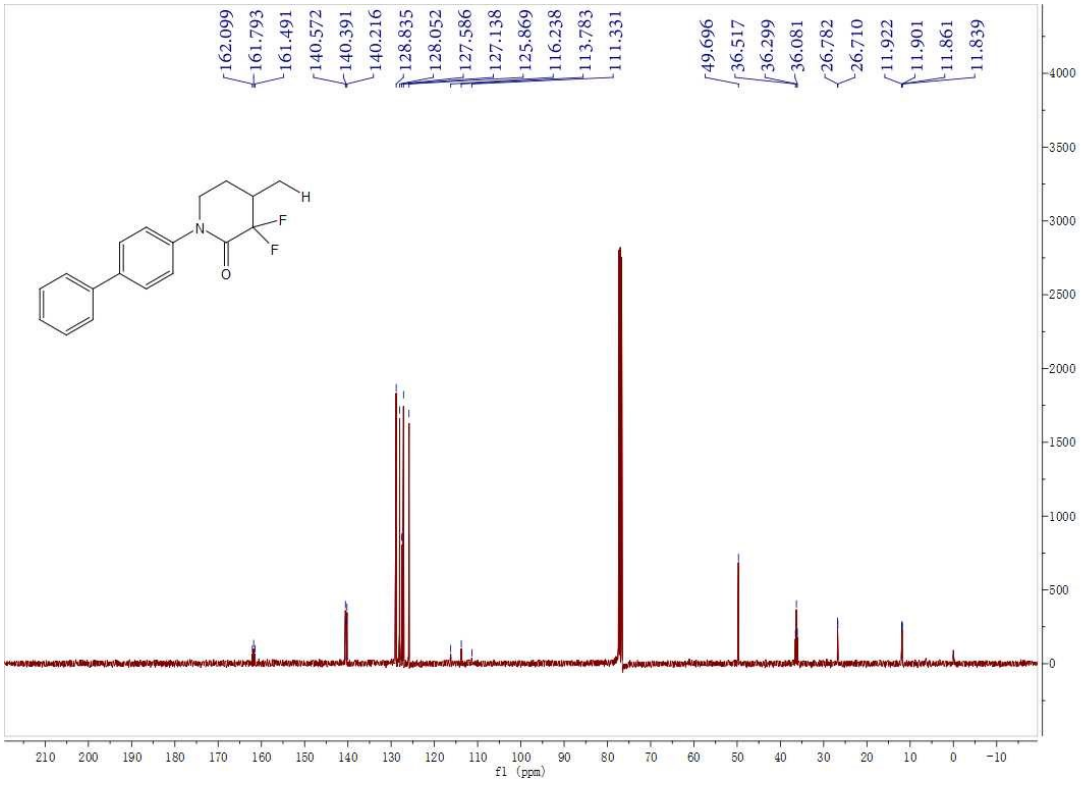


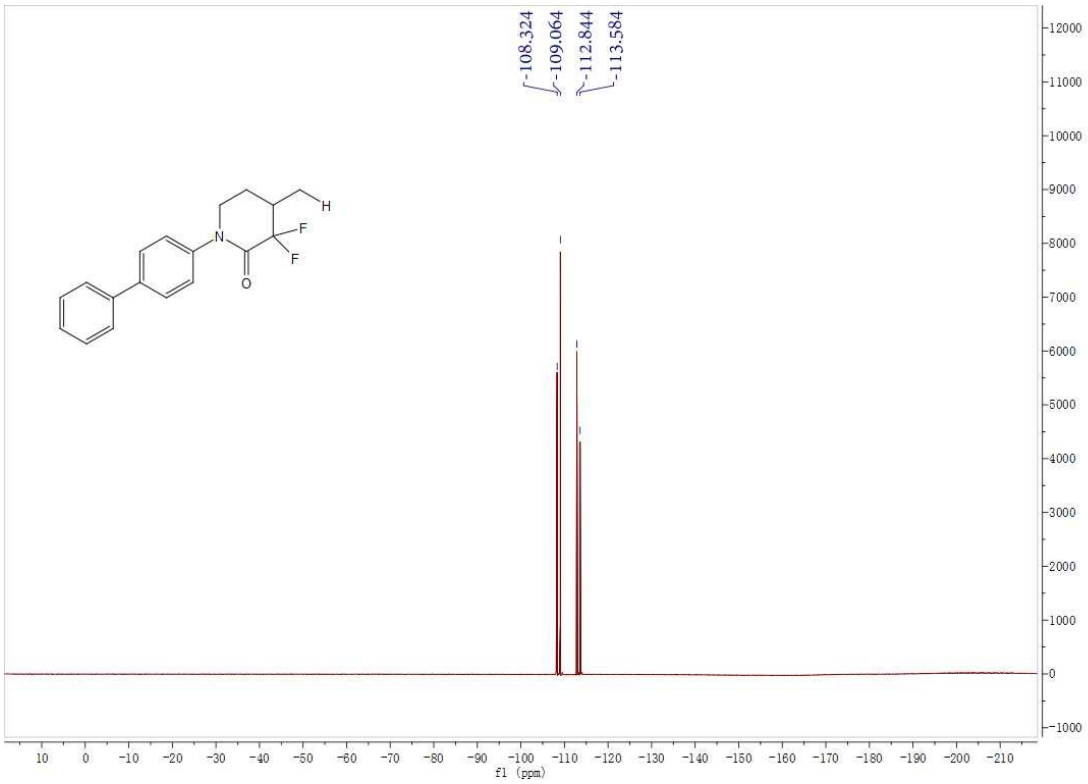

162.020
161.716
161.412
140.223
132.485
127.282
121.143
121.125
116.108
113.646
111.195
49.557
36.463
36.245
36.030
26.694
26.622
11.861
11.842
11.799
11.780
f1 (ppm)


-108.467
-109.208
-112.842
-113.583
f1 (ppm)

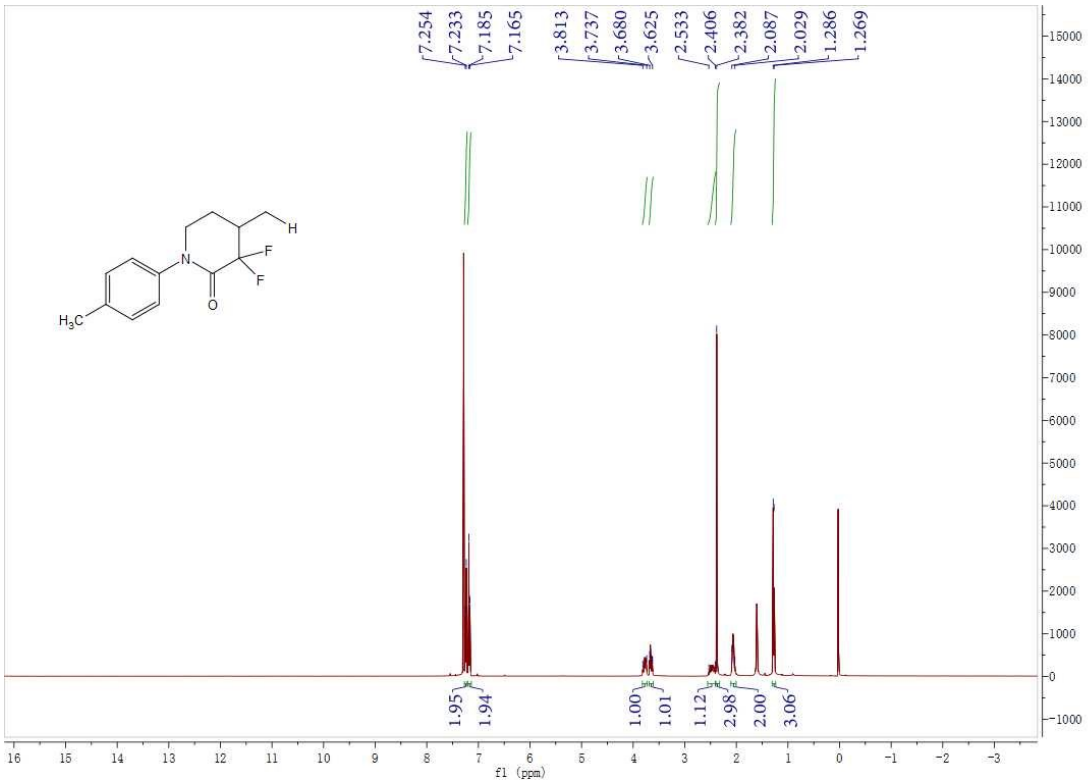
3,3-difluoro-4-methyl-1-(4-chlorophenyl)-piperidin-2-one (32)

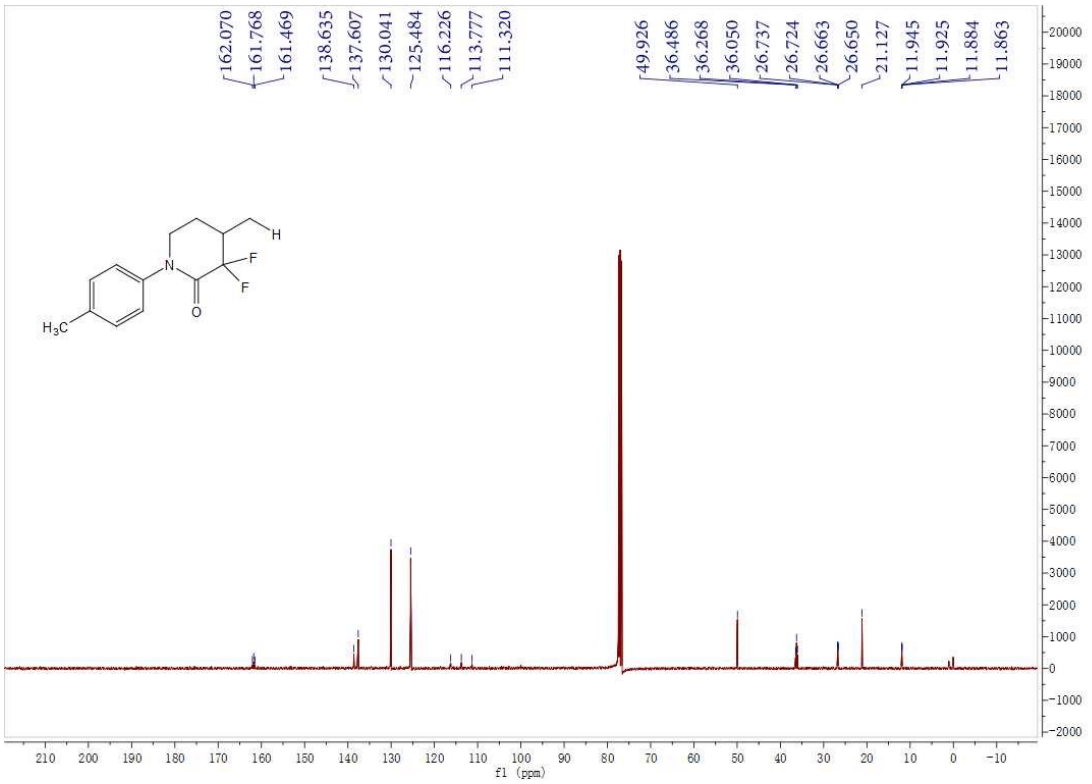


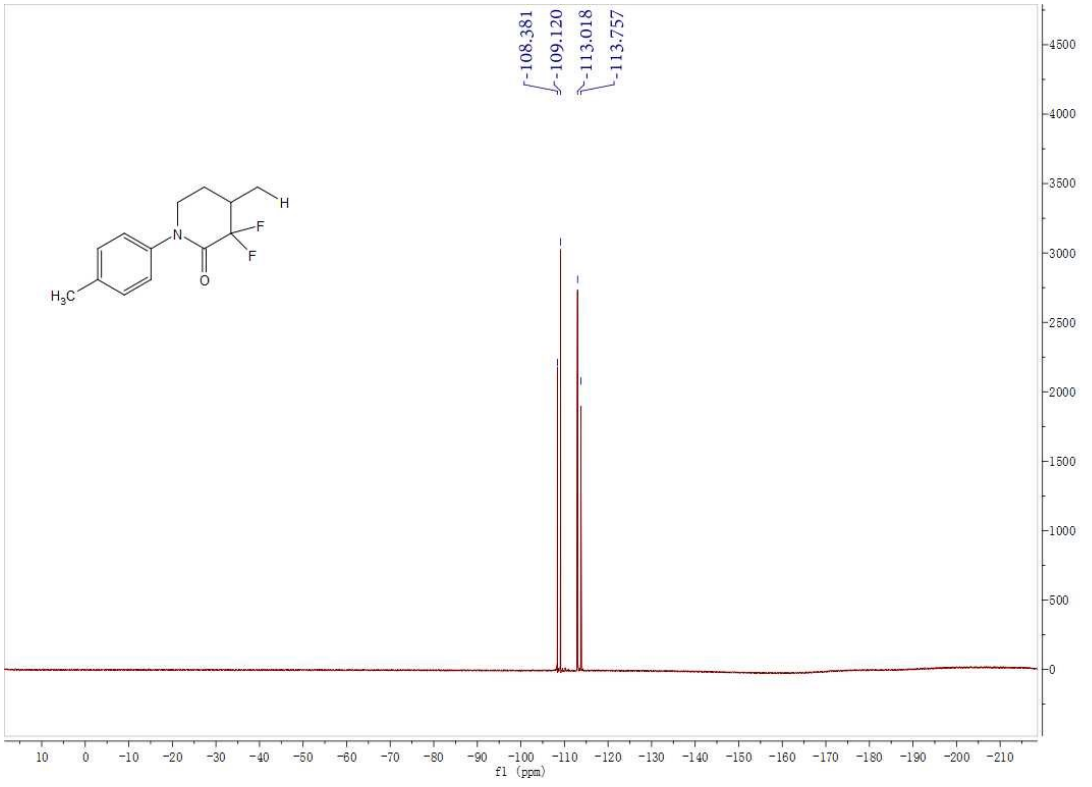




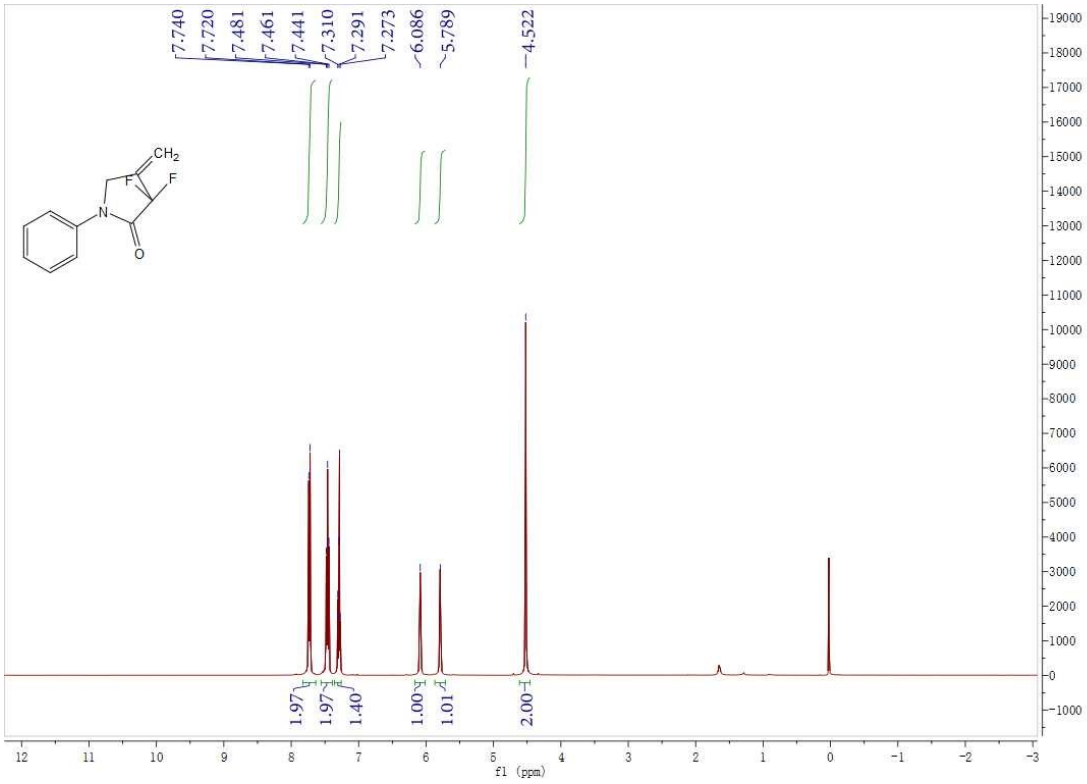
3,3-difluoro-4-methyl-1-(4-chlorophenyl)-piperidin-2-one (33)

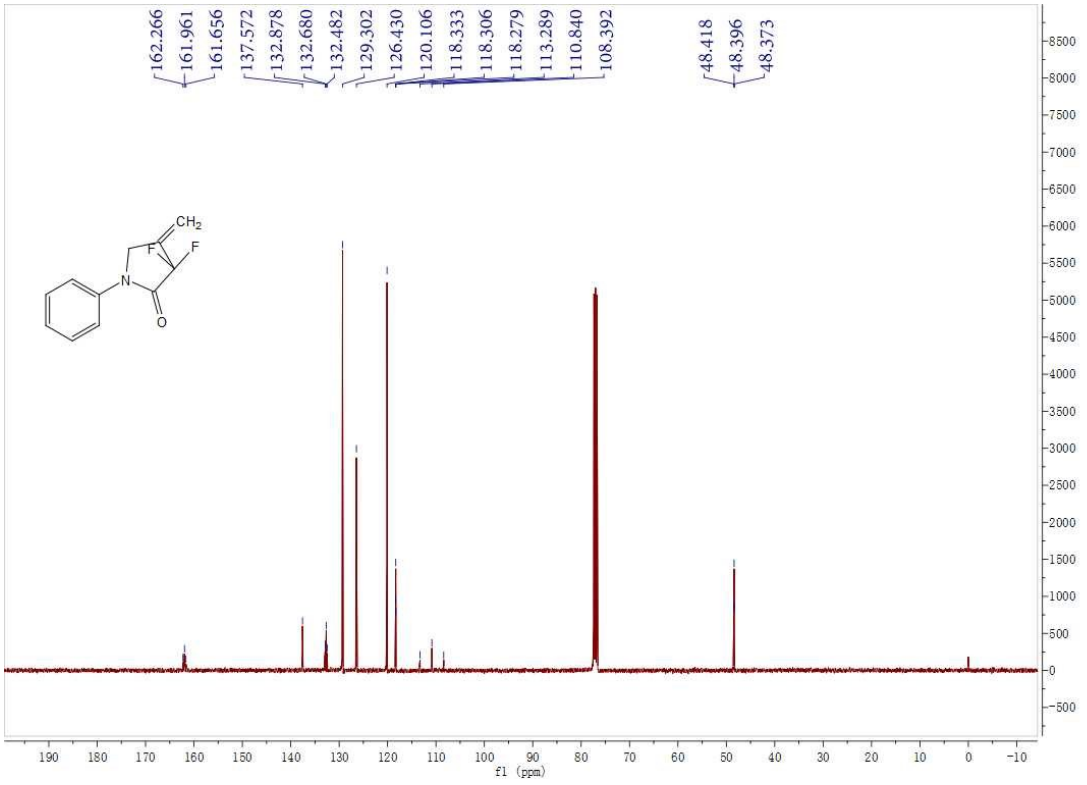


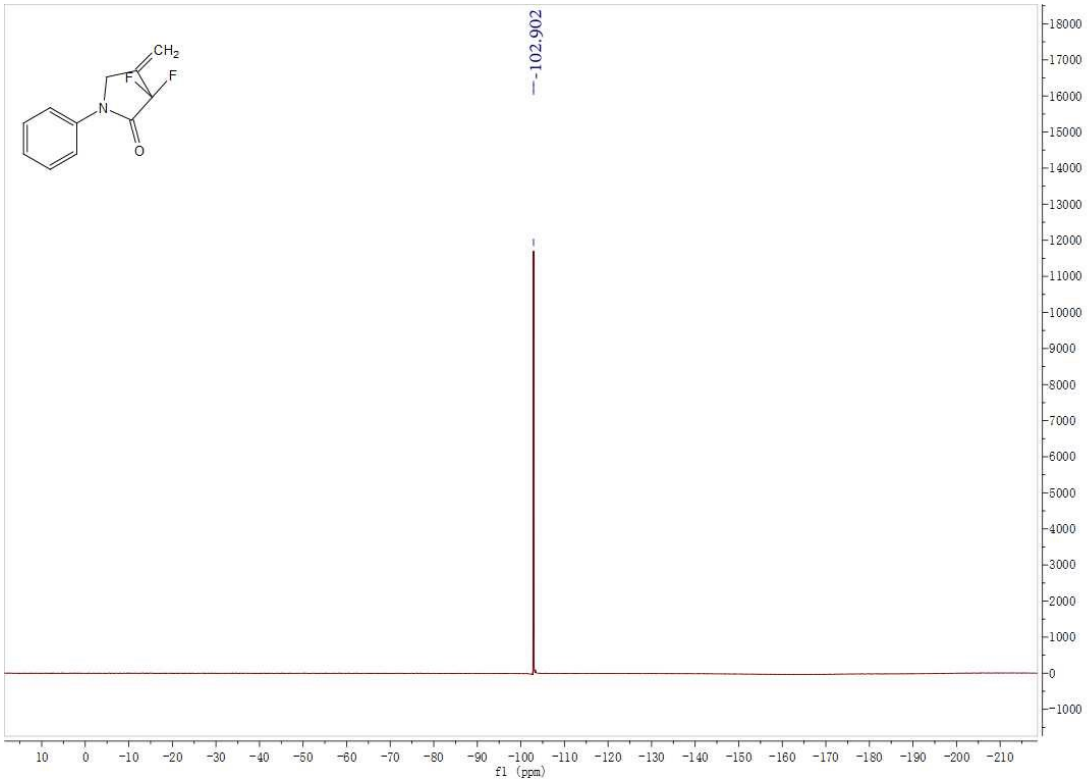

162.070
161.768
161.469
138.635
137.607
130.041
125.484
116.226
113.777
111.320
49.926
36.486
36.268
36.050
26.737
26.724
26.663
26.650
21.127
11.945
11.925
11.884
11.863
H
F
F
N
O
H3C
f1 (ppm)


-108.381
-109.120
-113.018
-113.757
H
F
F
N
O
H3C
f1 (ppm)

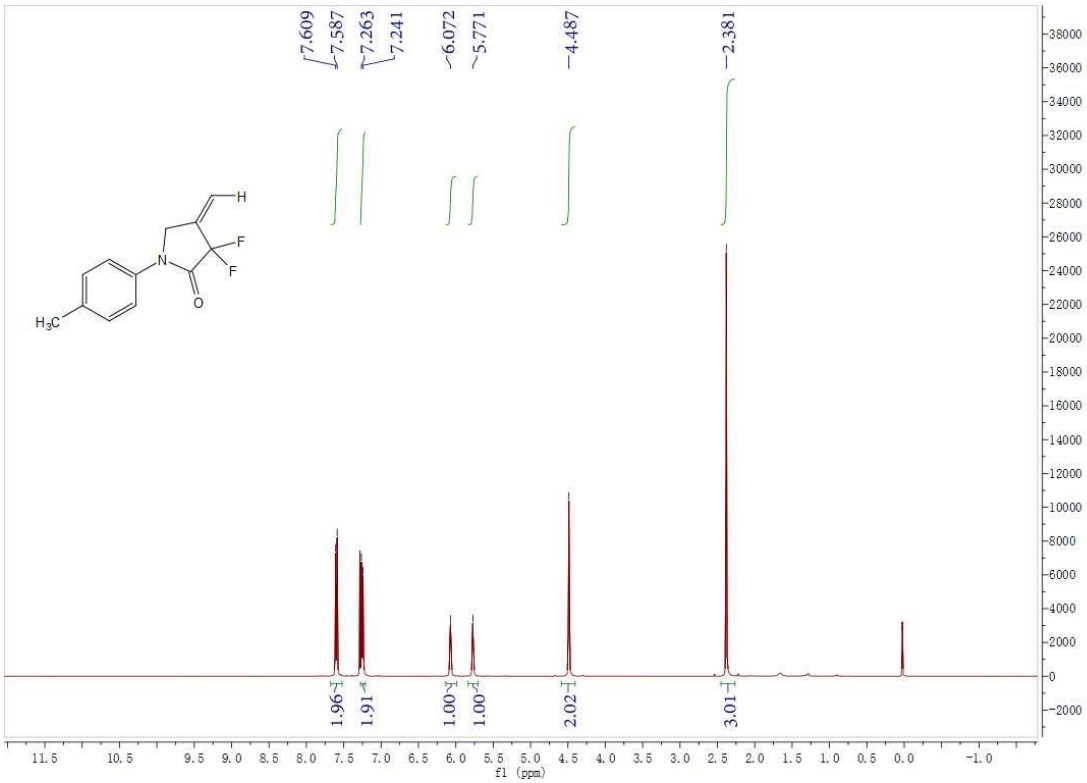
3,3-difluoro-4-methylene-1-phenylpyrrolidin-2-one (34)

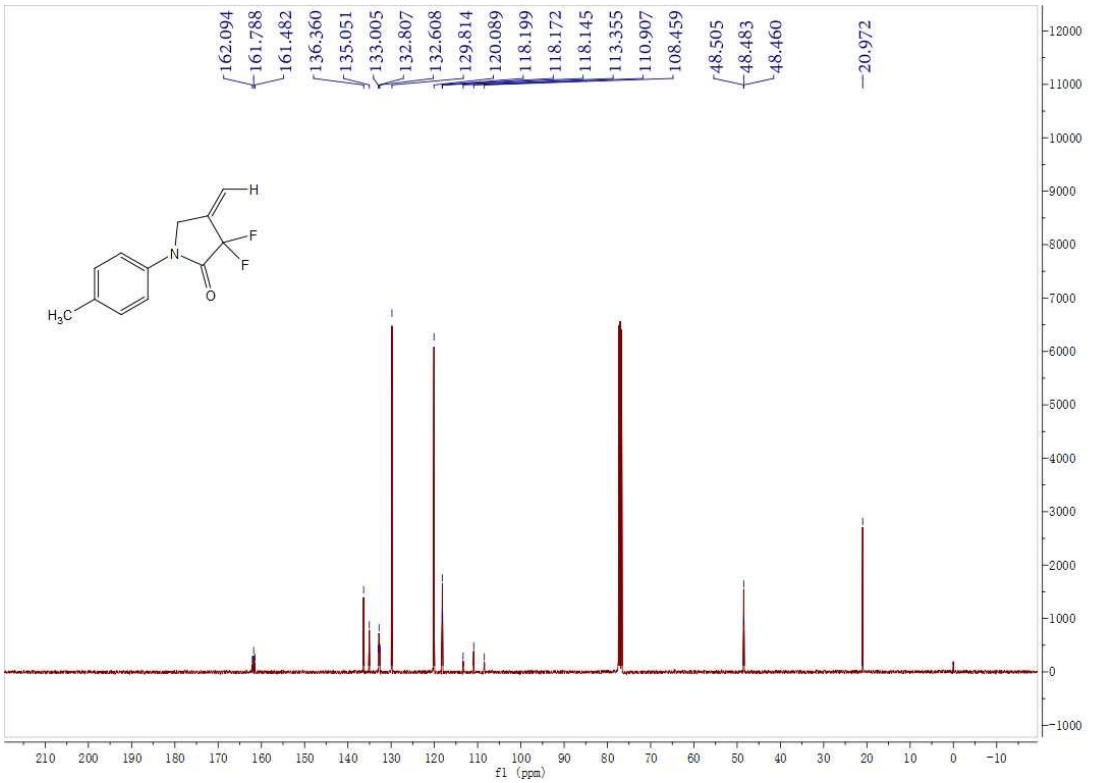


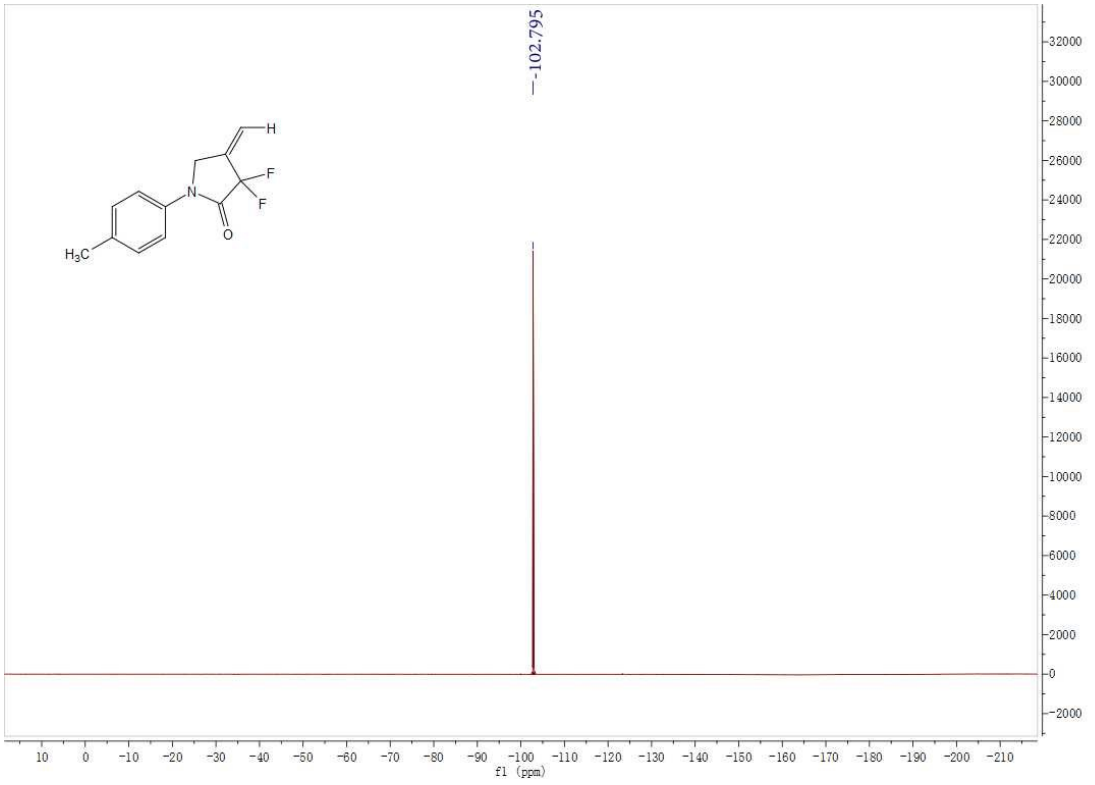




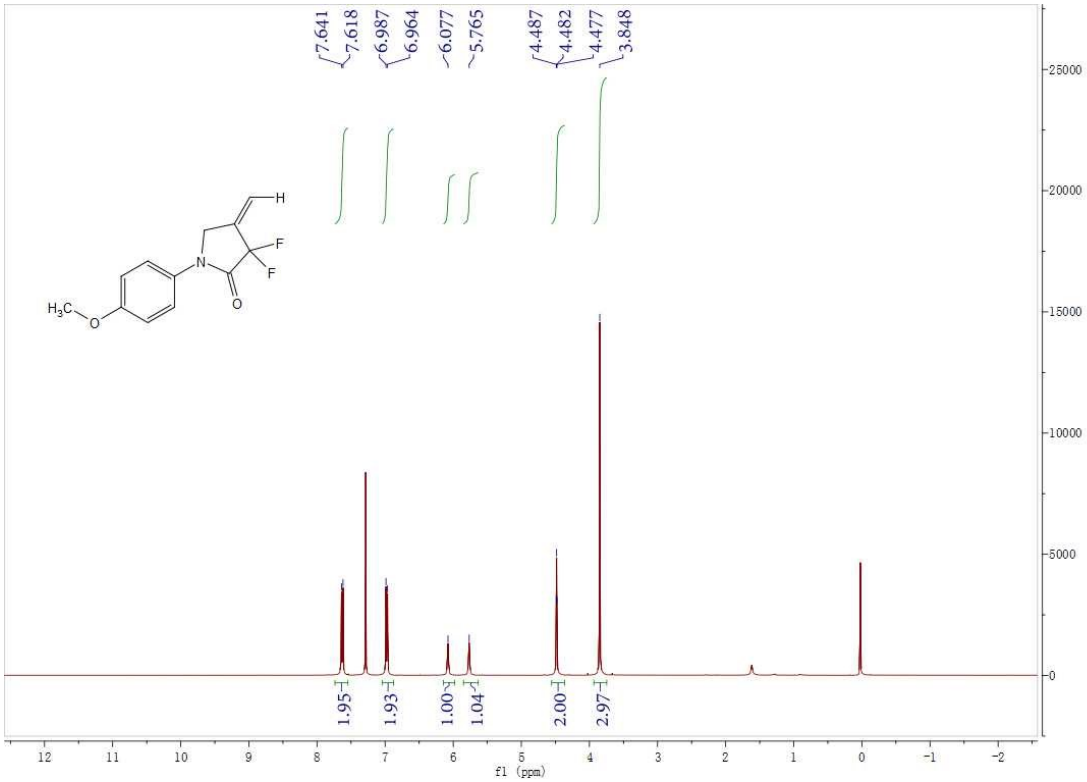
3,3-difluoro-4-methylene-1-(*p*-tolyl)pyrrolidin-2-one (35)

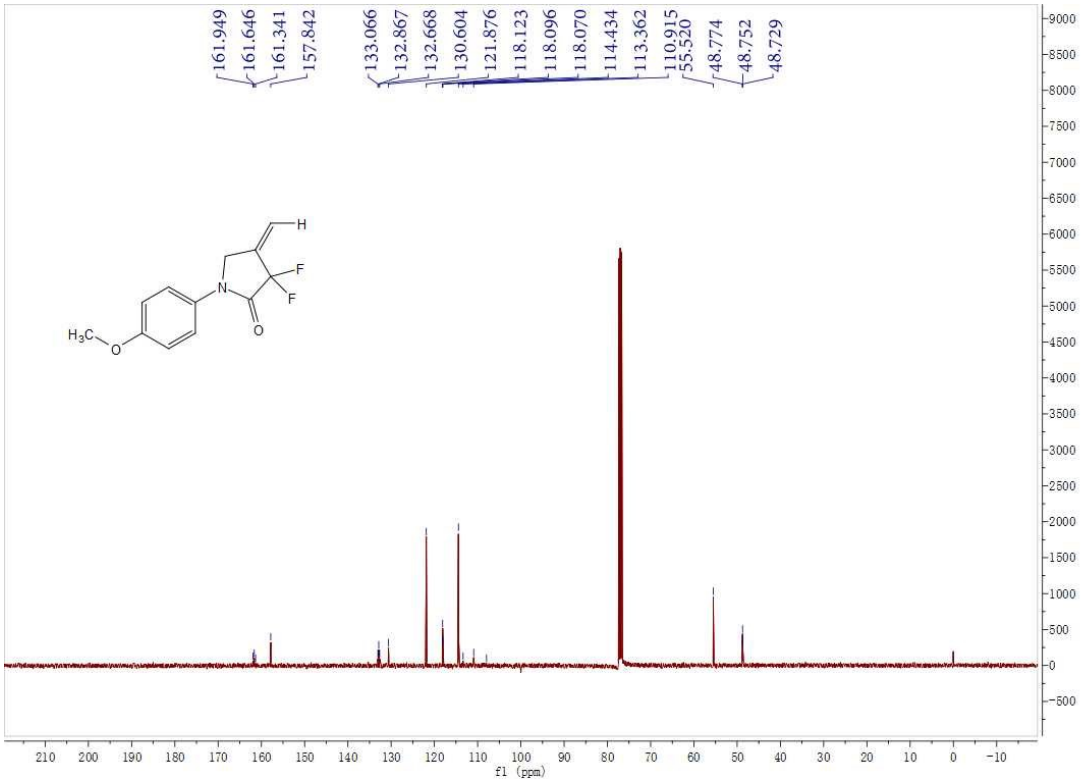


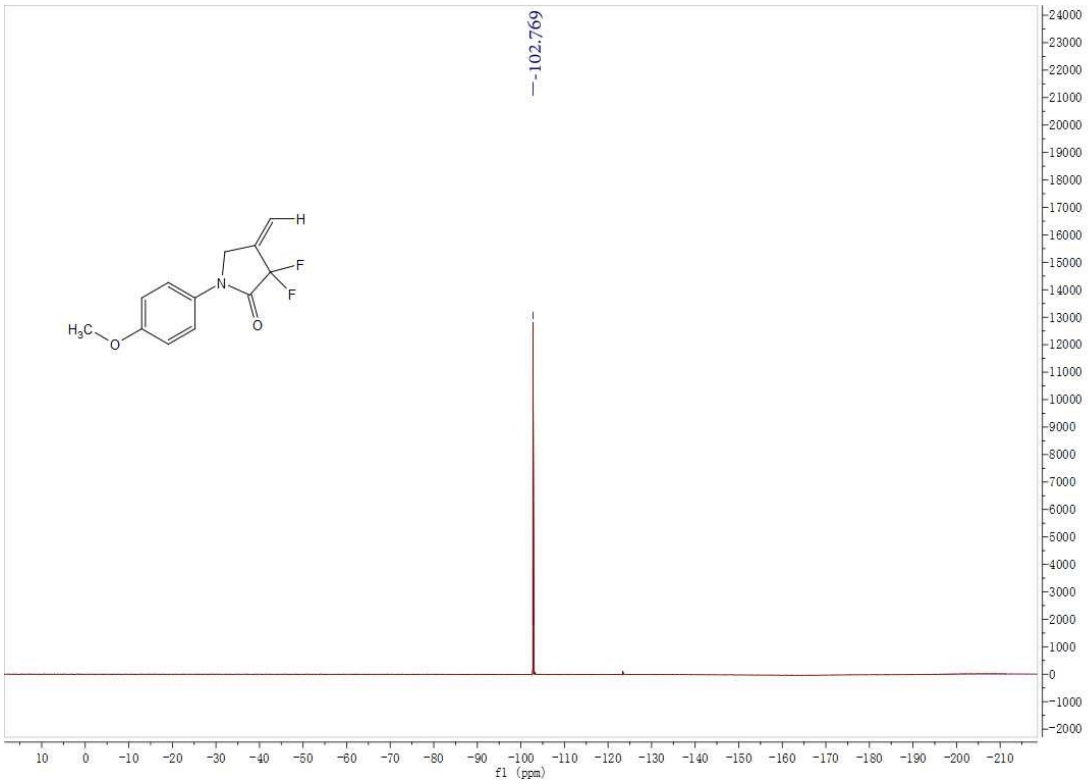

162.094
161.788
161.482
136.360
135.051
133.005
132.807
132.608
129.814
120.089
118.199
118.172
118.145
113.355
110.907
108.459
48.505
48.483
48.460
20.972
H
F
F
N
O
H3C
f1 (ppm)


-102.795
H
F
F
N
O
H3C
f1 (ppm)

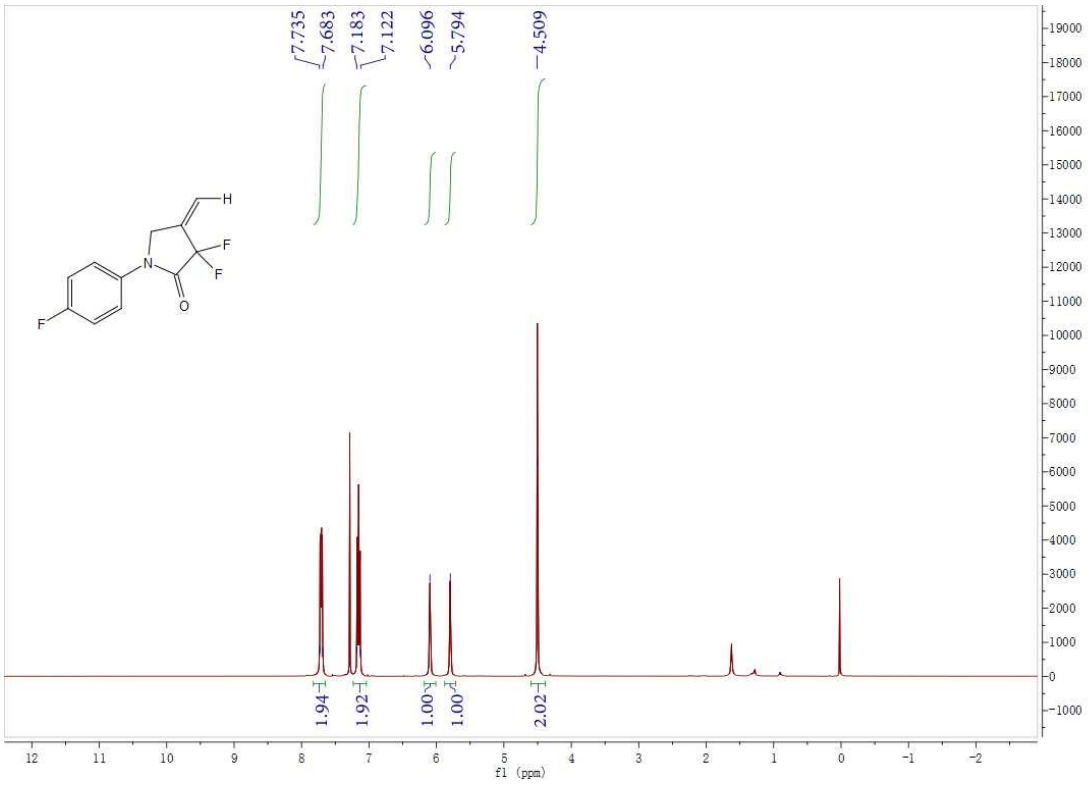
3,3-difluoro-1-(4-methoxyphenyl)-4-methylenepyrrolidin-2-one (36)[3]

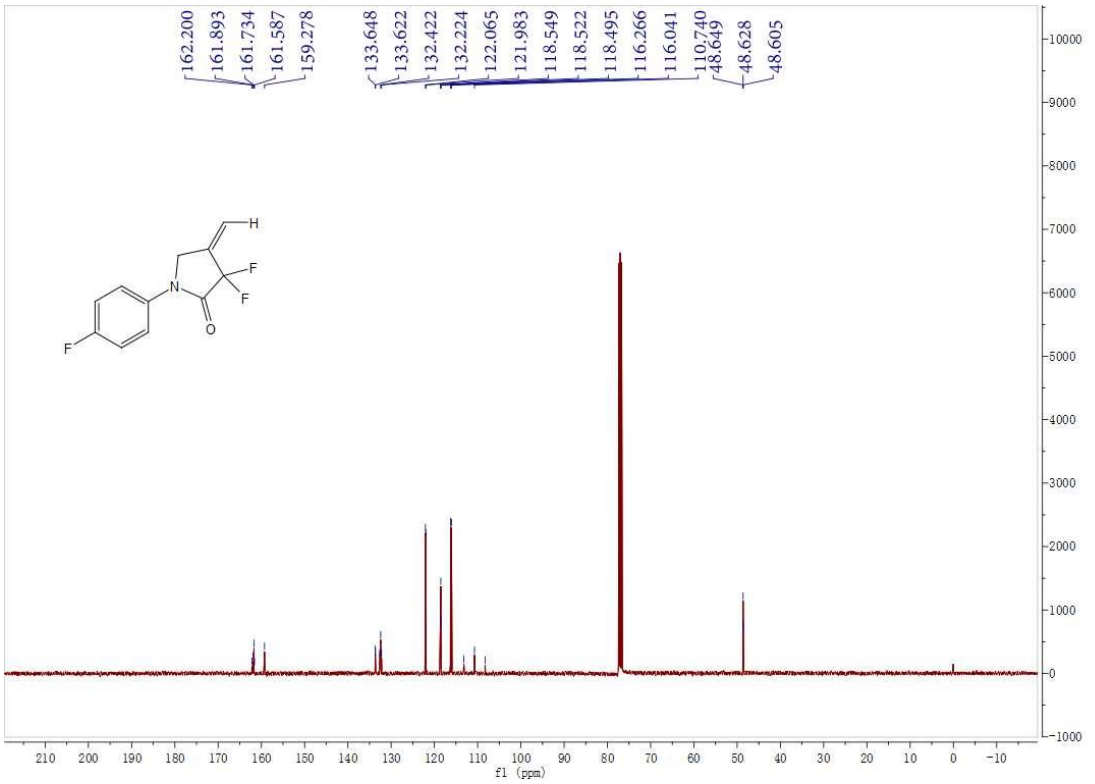


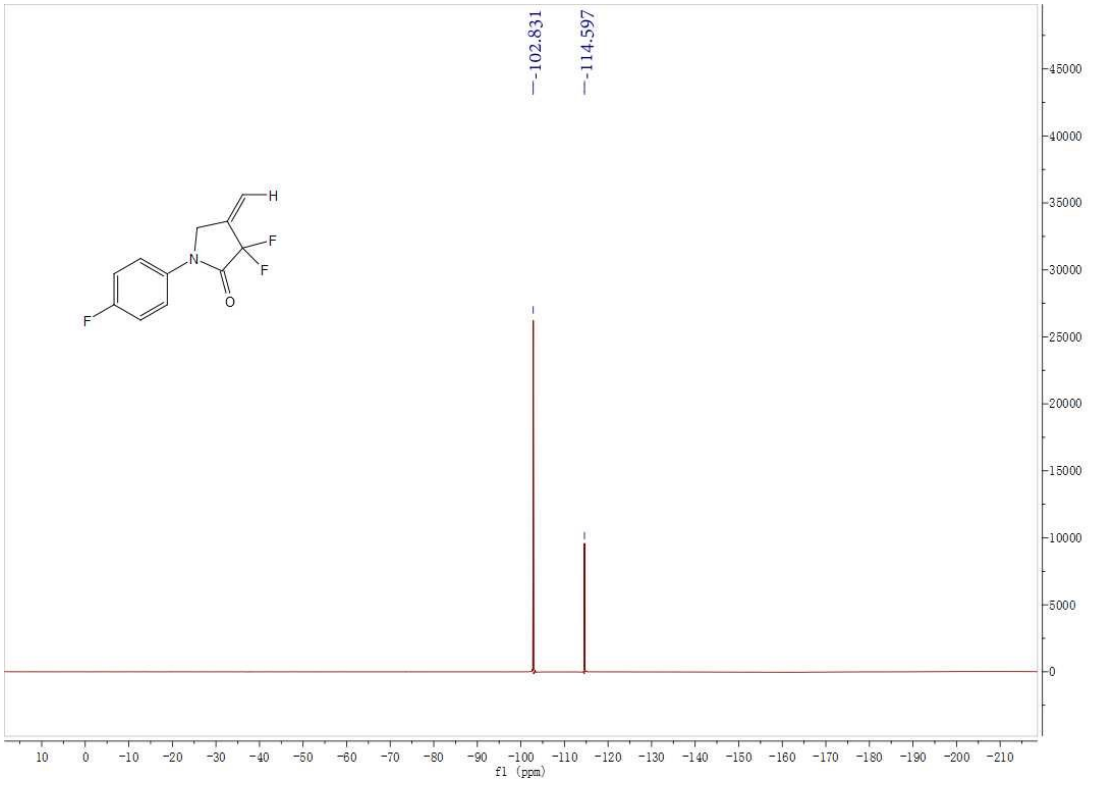




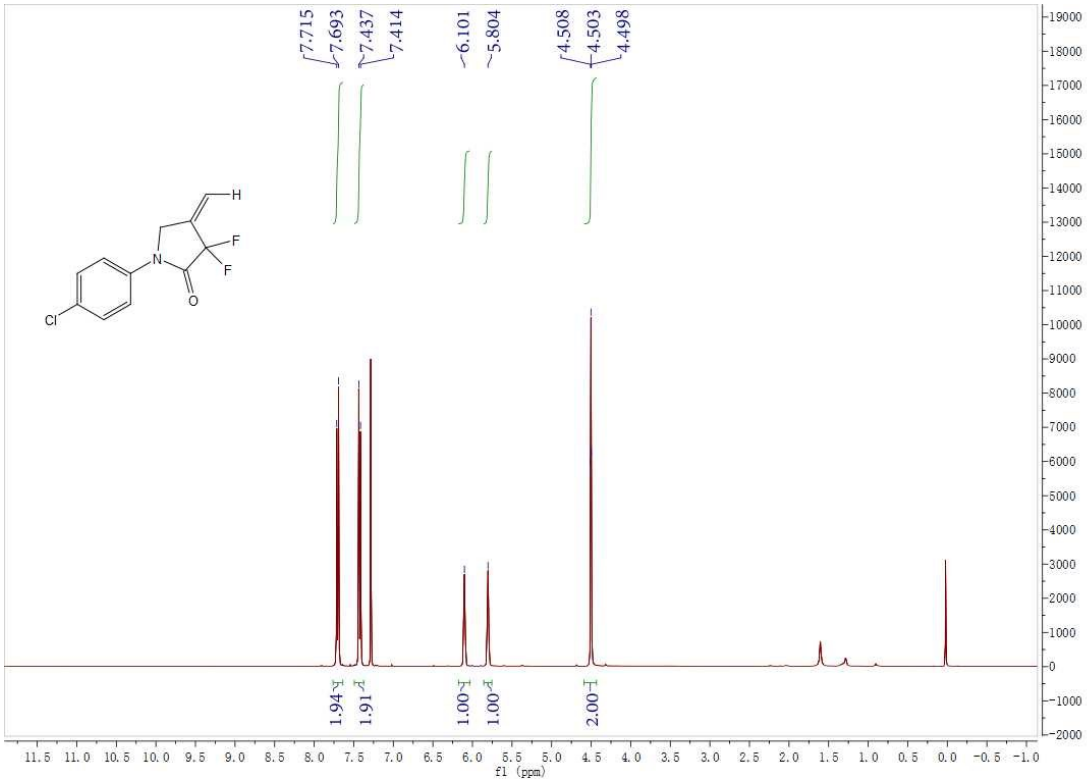
3,3-difluoro-1-(4-fluorophenyl)-4-methylenepyrrolidin-2-one (37)[3]

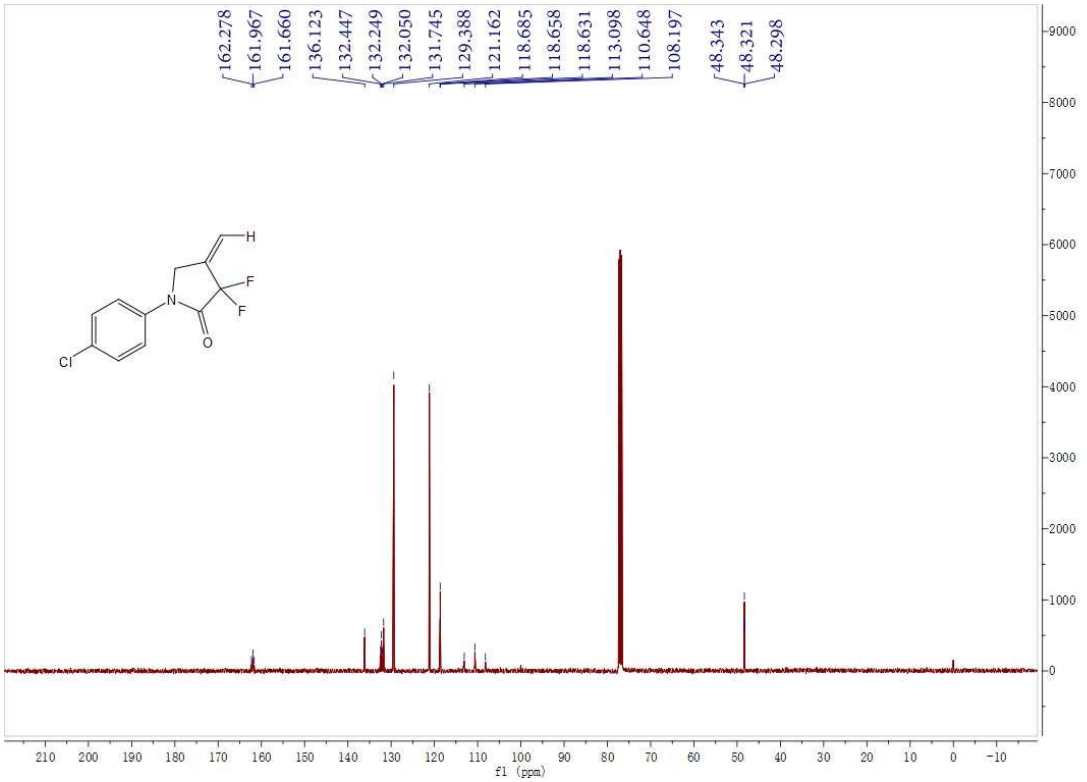


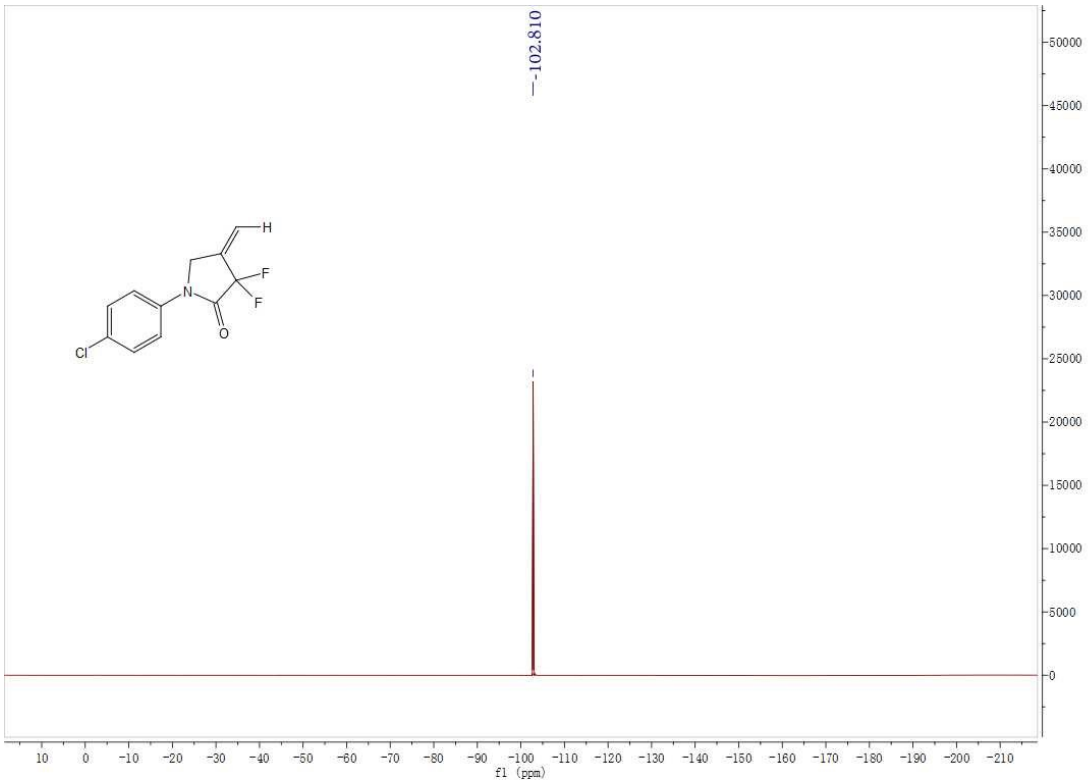

162.200
161.893
161.734
161.587
159.278
133.648
133.622
132.422
132.224
122.065
121.983
118.549
118.522
118.495
116.266
116.041
110.740
48.649
48.628
48.605
f1 (ppm)


-102.831
-114.597
f1 (ppm)

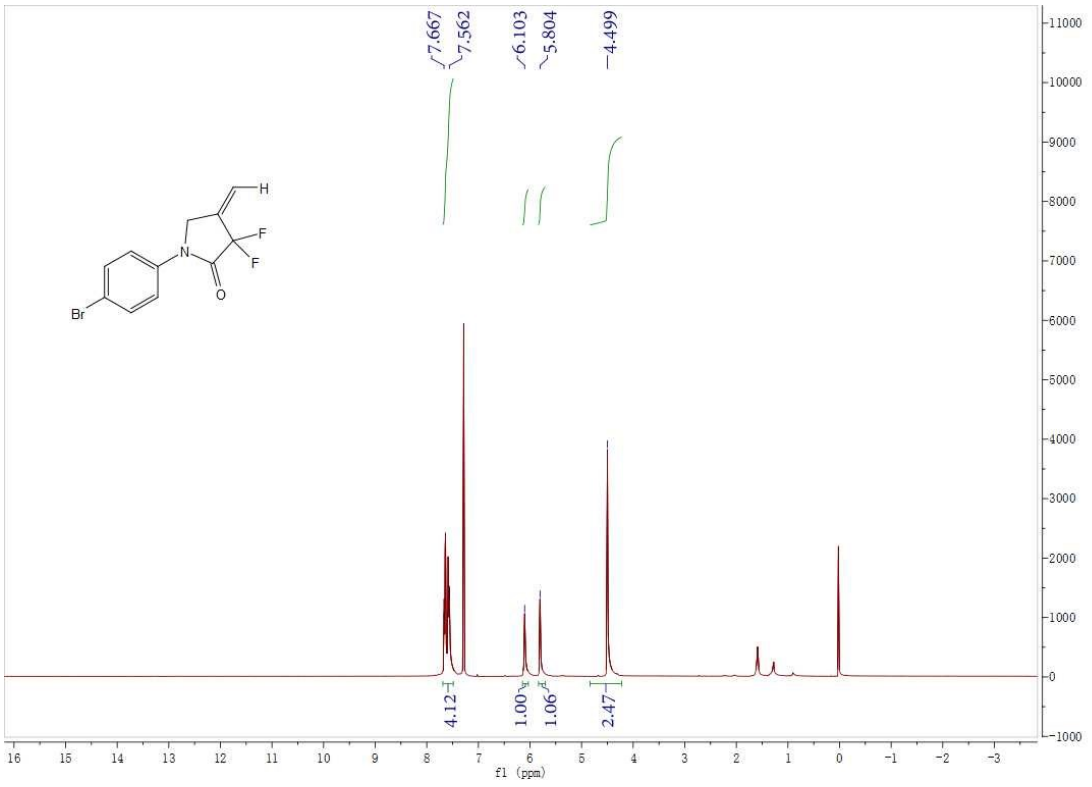
3,3-difluoro-1-(4-cholrophenyl)-4-methylenepyrrolidin-2-one (38)

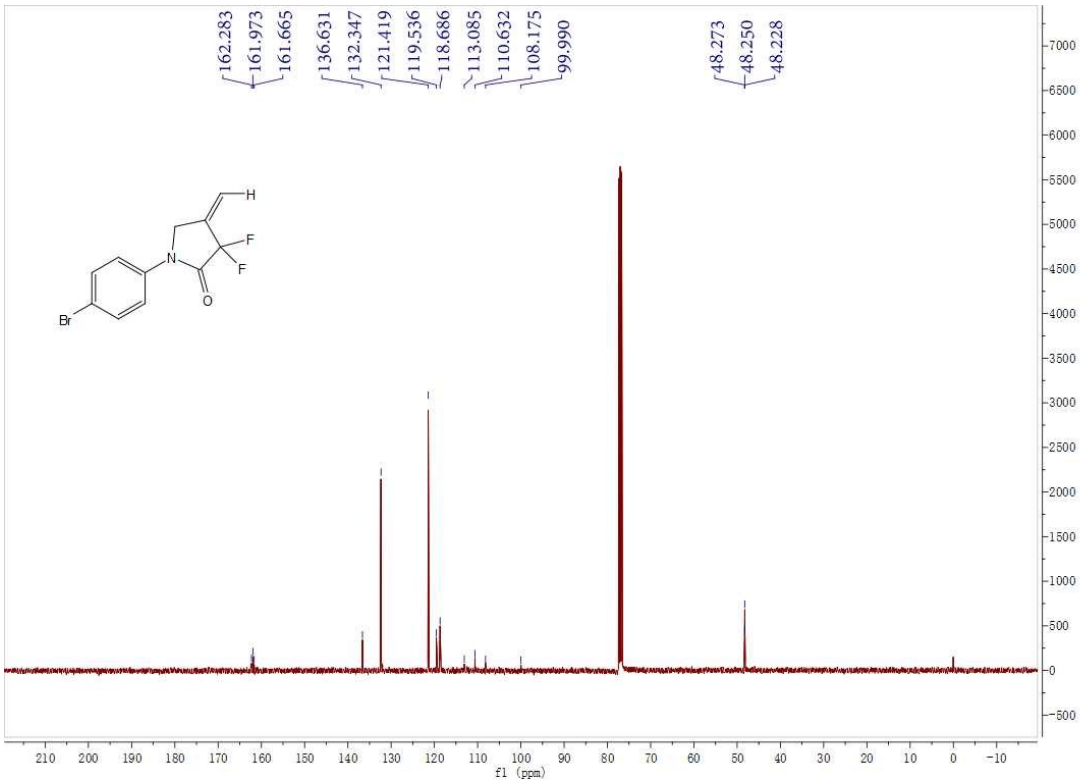


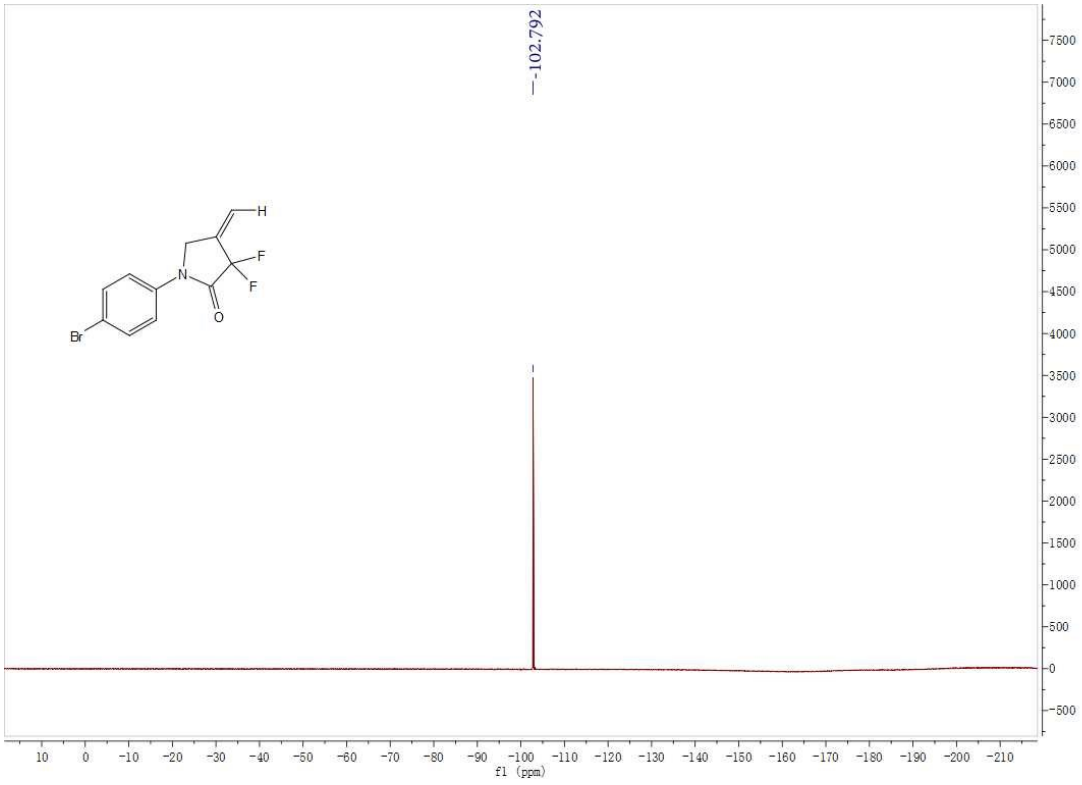




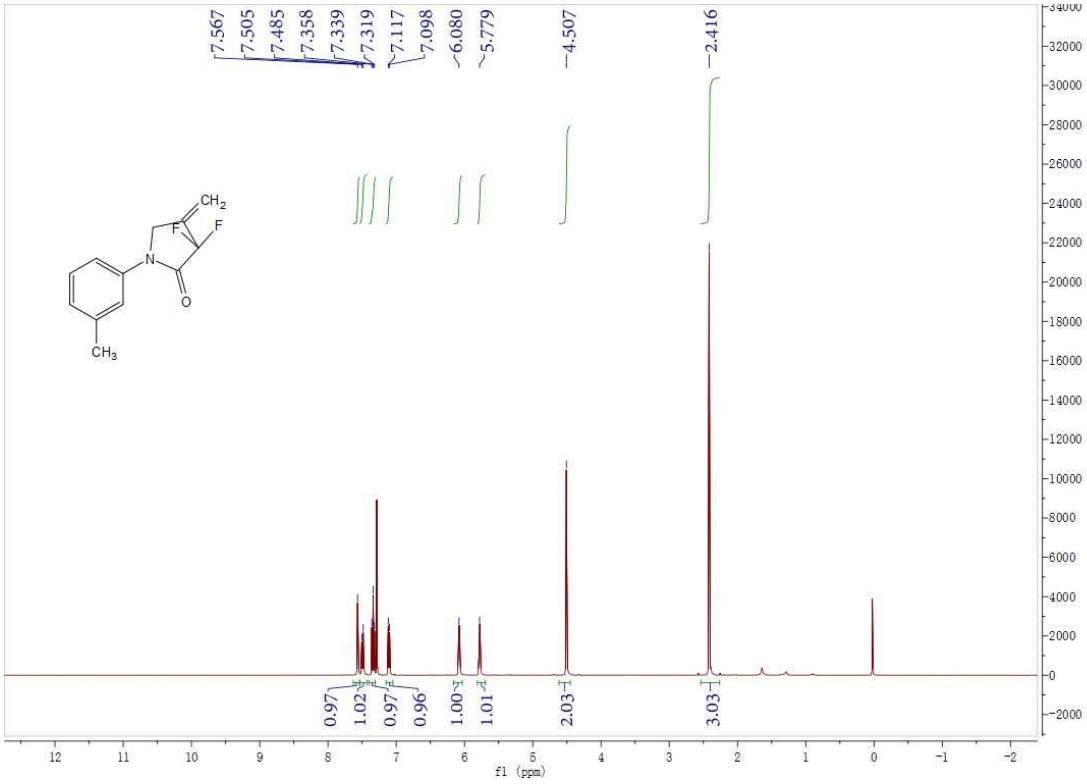
3,3-difluoro-1-(4-bromophenyl)-4-methylenepyrrolidin-2-one (39)

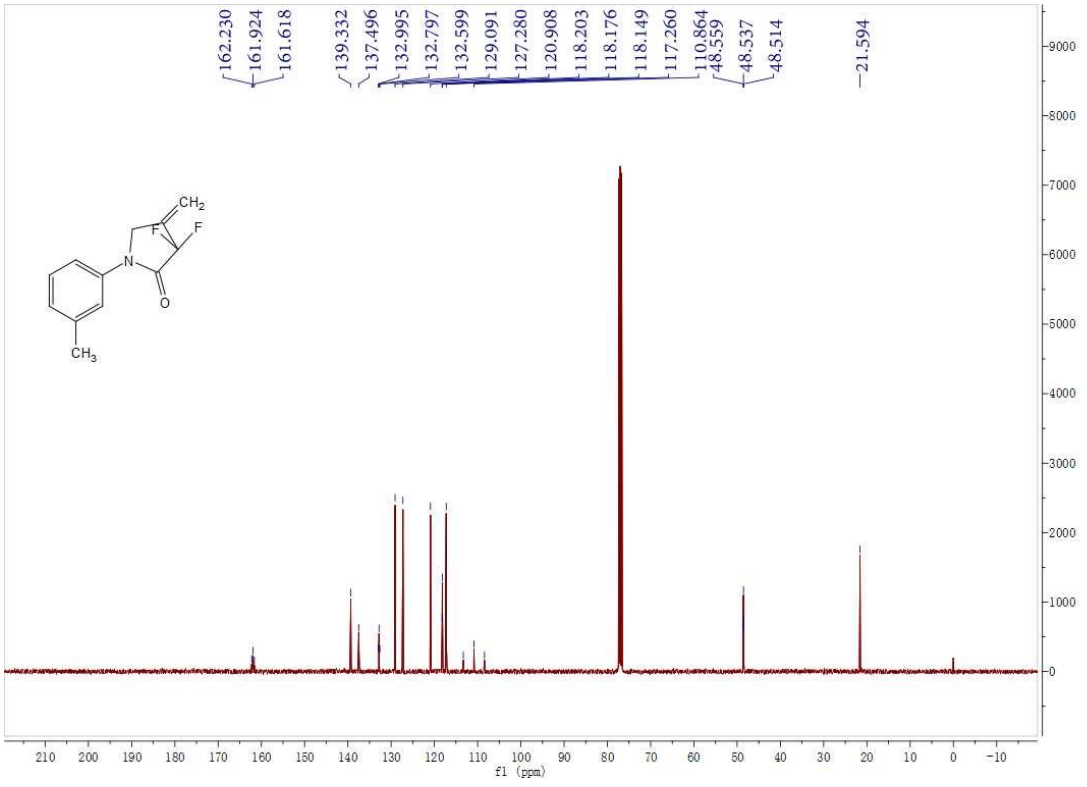


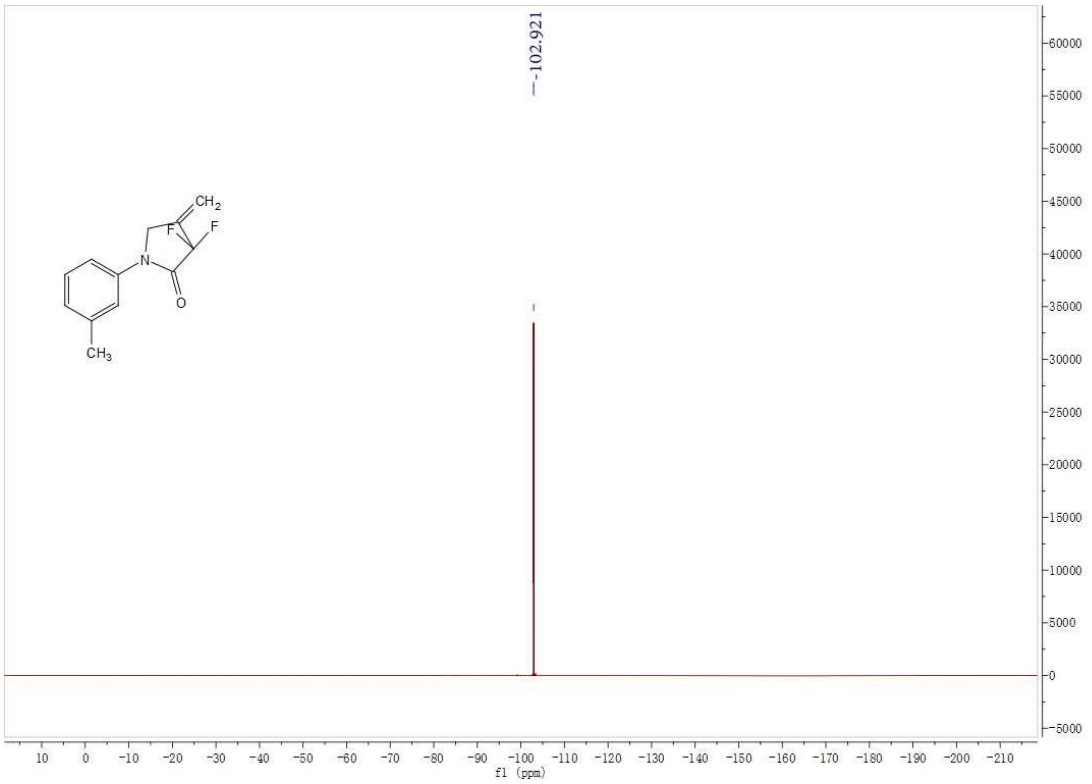

162.283
161.973
161.665
136.631
132.347
121.419
119.536
118.686
113.085
110.632
108.175
99.990
48.273
48.250
48.228
H
F
F
N
O
Br
fl (ppm)


-102.792
H
F
F
N
O
Br
fl (ppm)

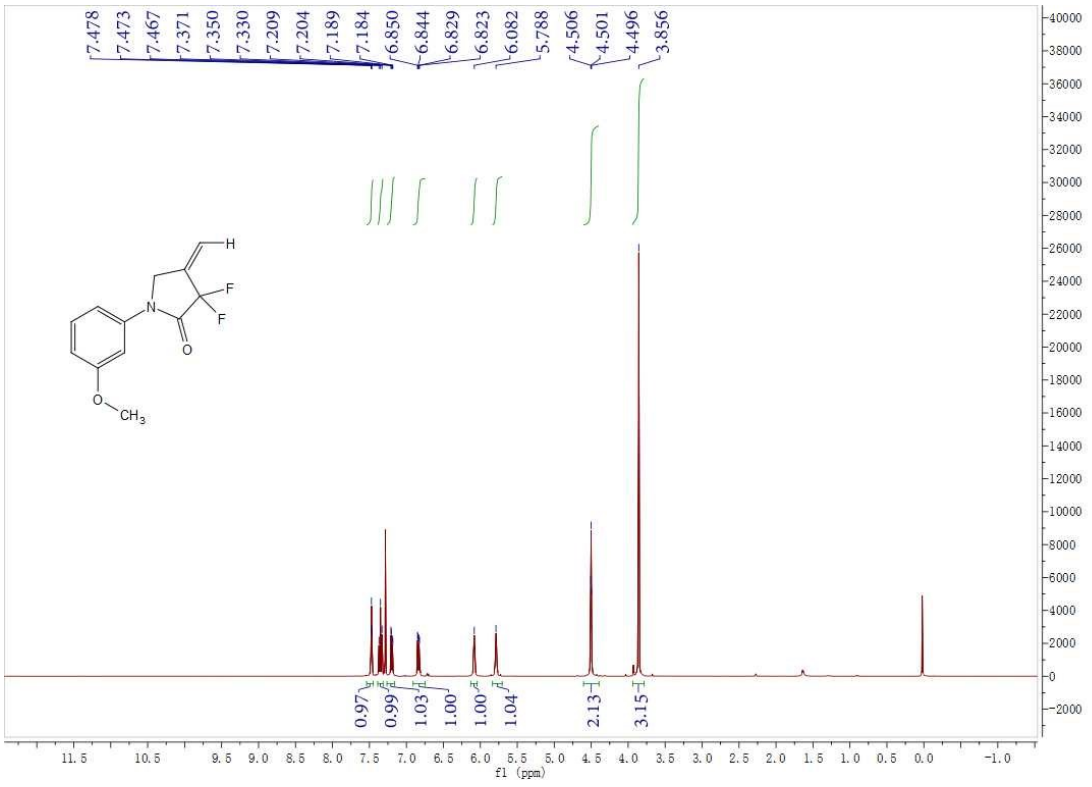
3,3-difluoro-4-methylene-1-(m-tolyl)pyrrolidin-2-one (40)

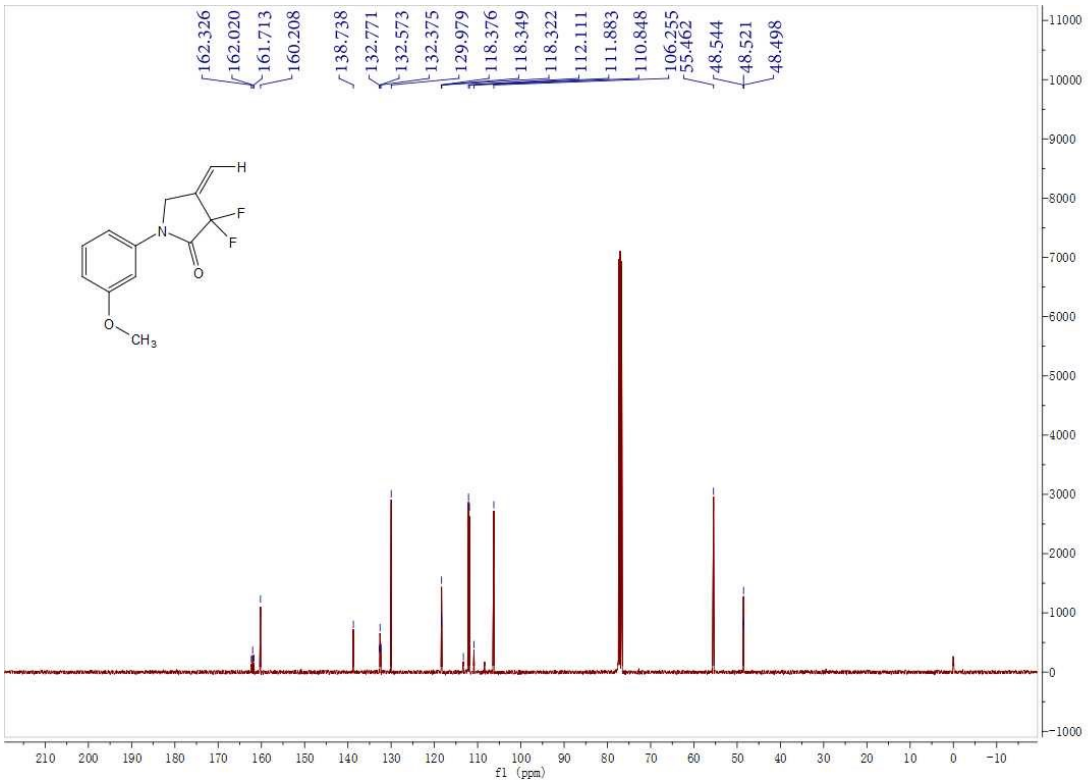


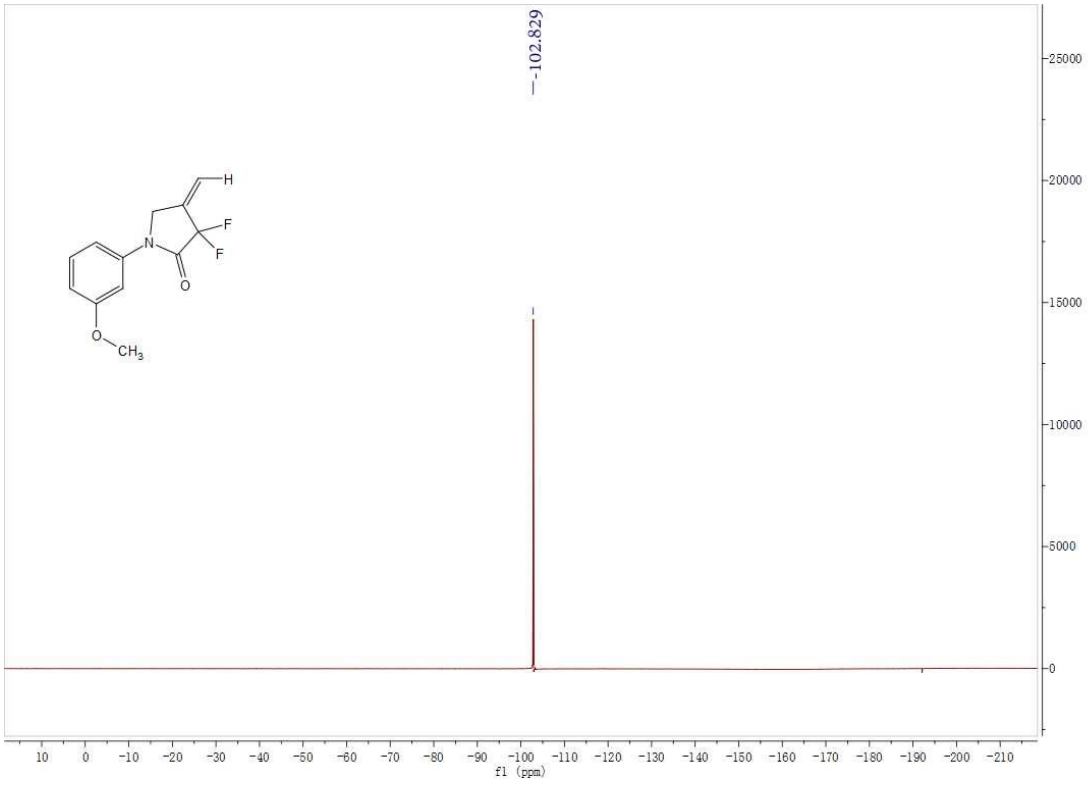




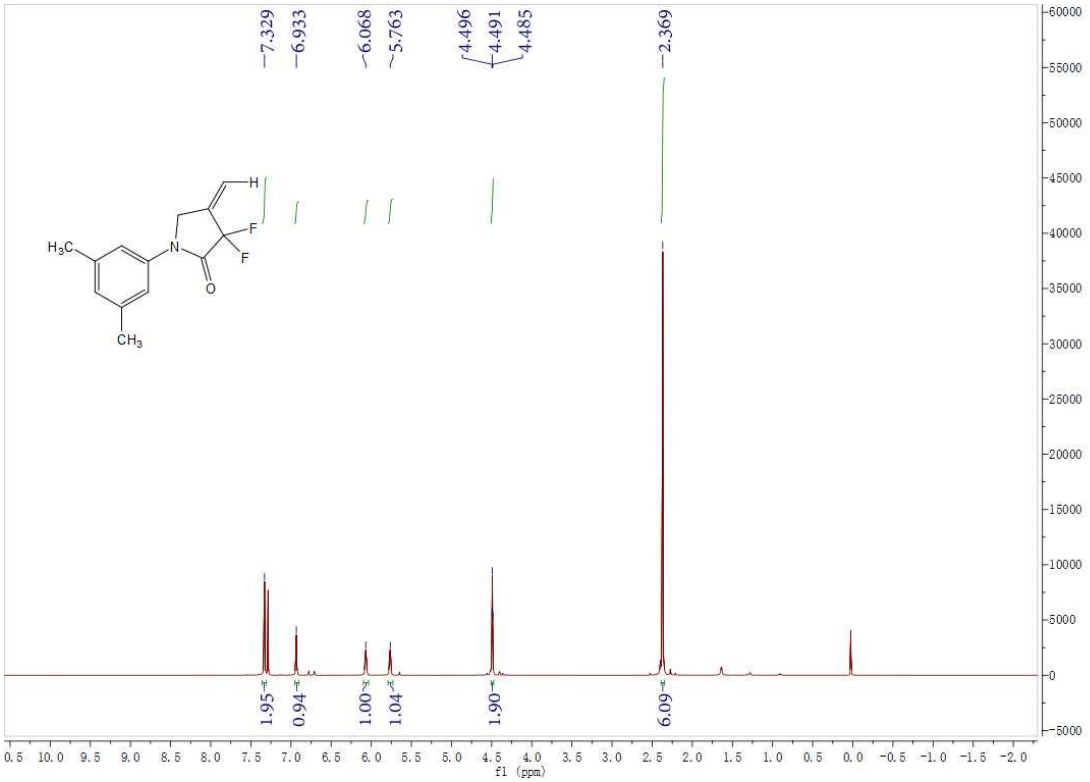
3,3-difluoro-1-(3-methoxyphenyl)-4-methylenepyrrolidin-2-one (41)

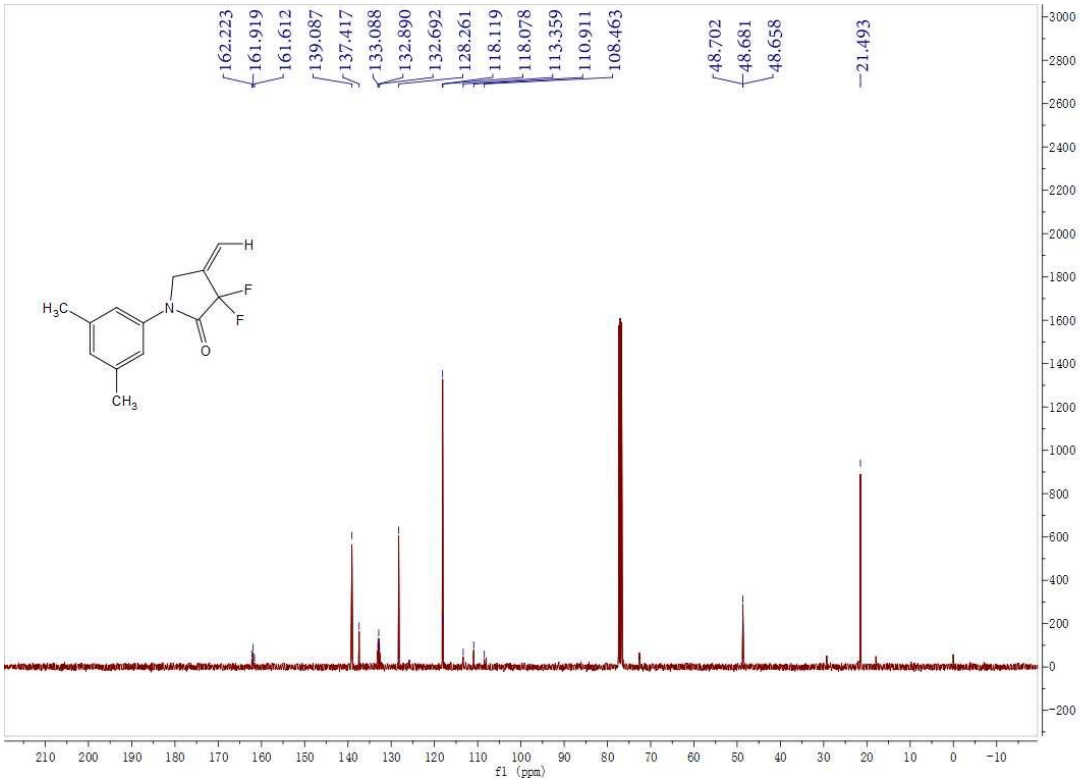


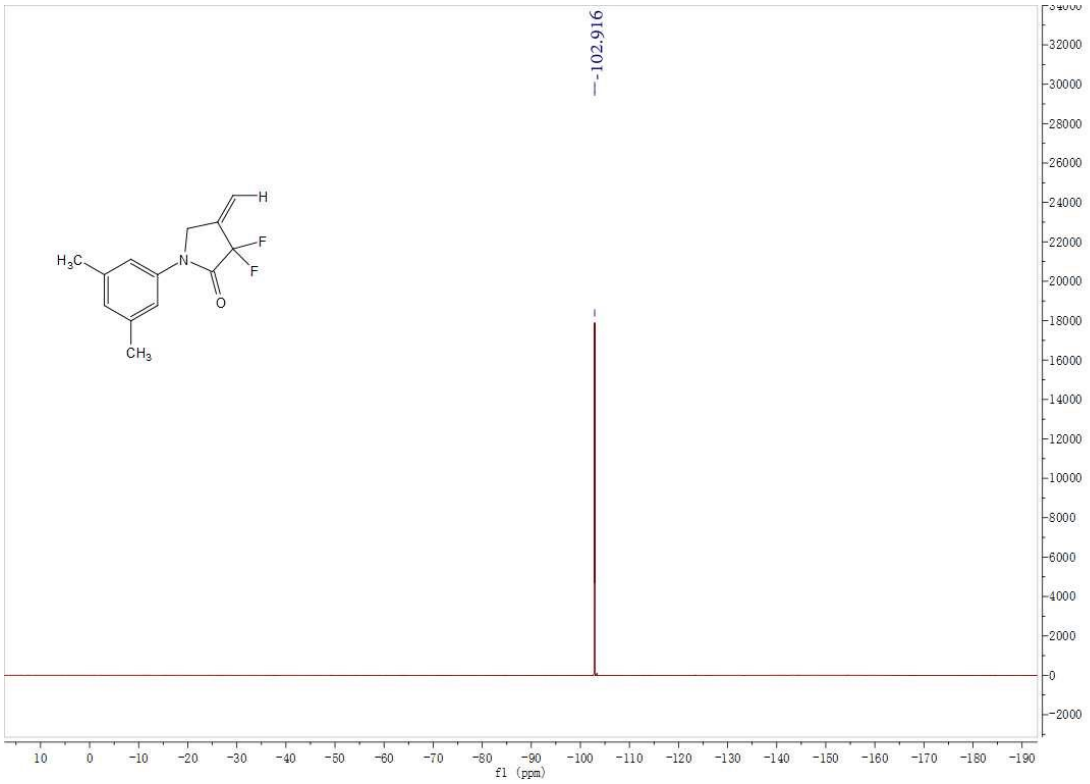

162.326
162.020
161.713
160.208
138.738
132.771
132.573
132.375
129.979
118.376
118.349
118.322
112.111
111.883
110.848
106.255
55.462
48.544
48.521
48.498
H
F
F
N
O
O
CH3
f1 (ppm)


-102.829
H
F
F
N
O
O
CH3
f1 (ppm)

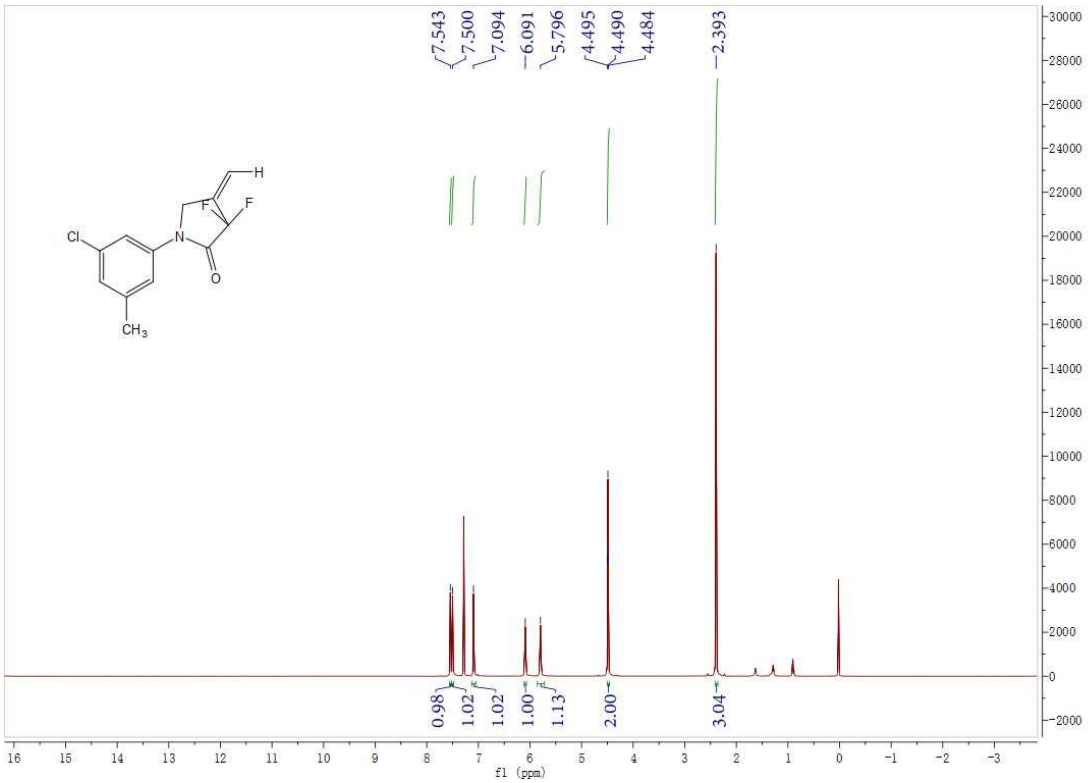
1-(3,5-dimethylphenyl)-3,3-difluoro-4-methylenepyrrolidin-2-one (42)

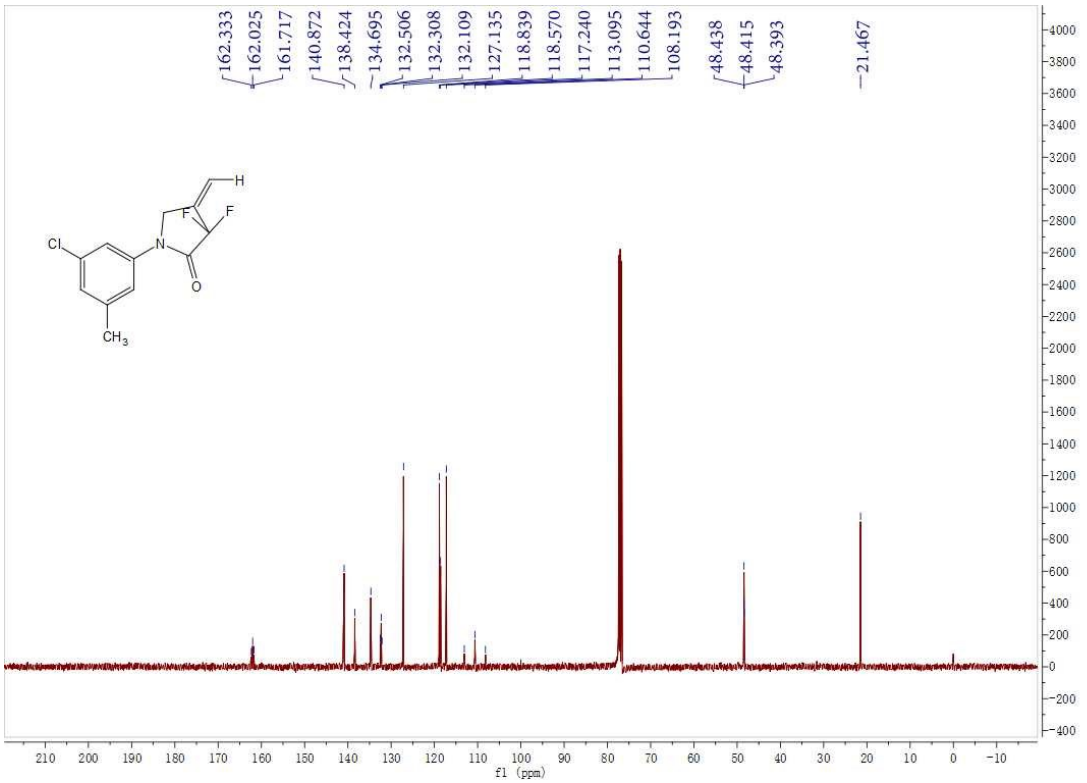


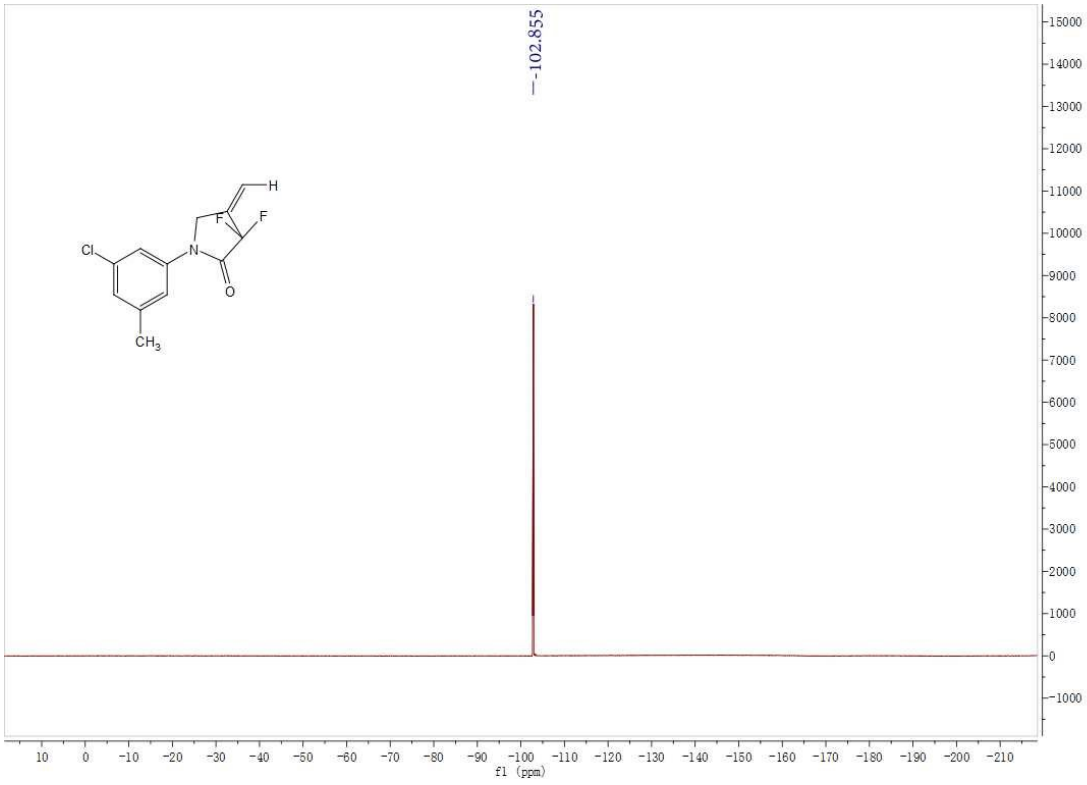




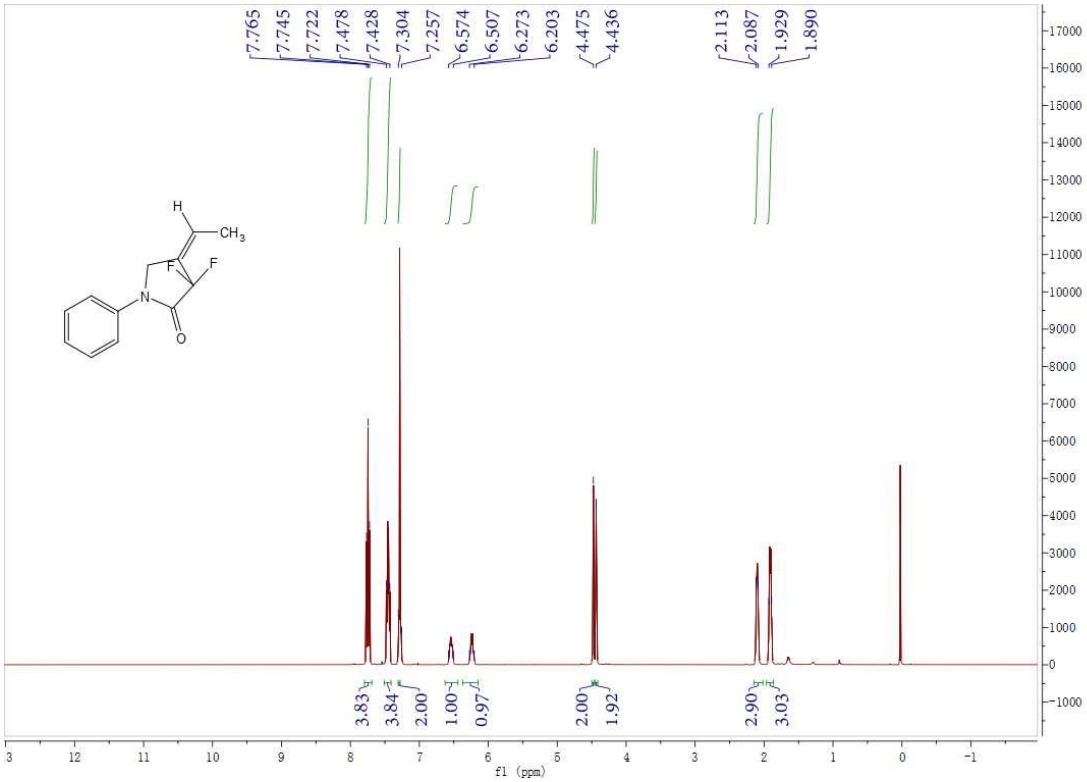
1-(3-chloro-5-methylphenyl)-3,3-difluoro-4-methylenepyrrolidin-2-one (43)

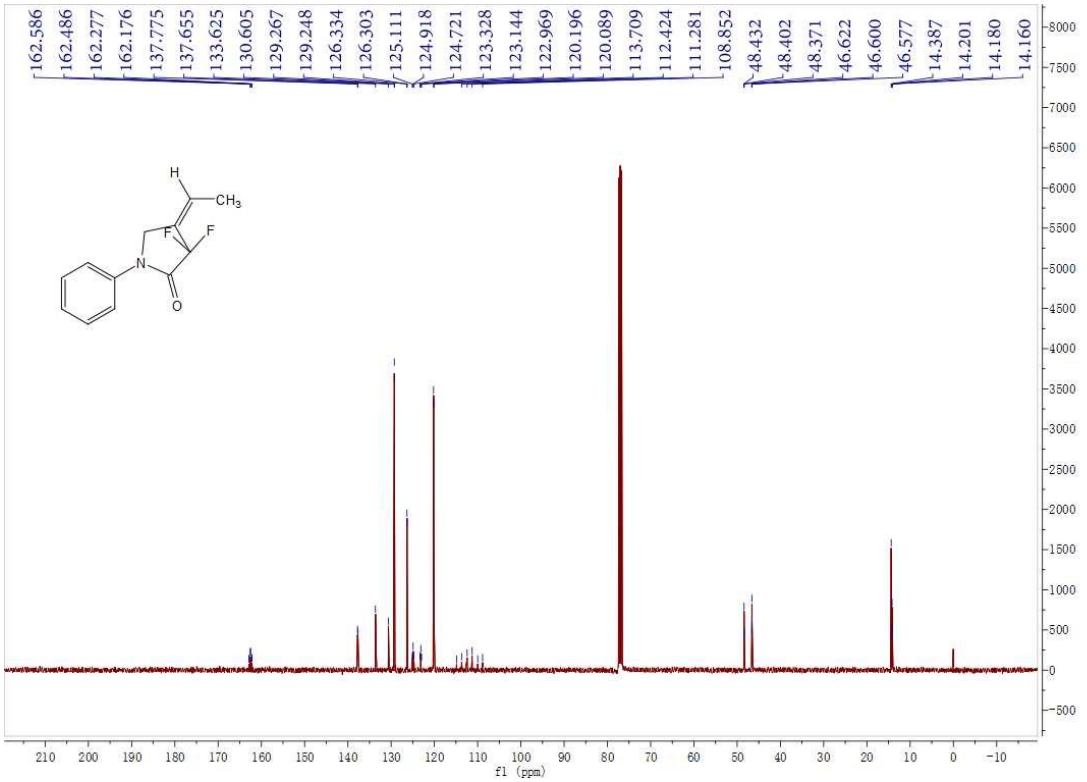


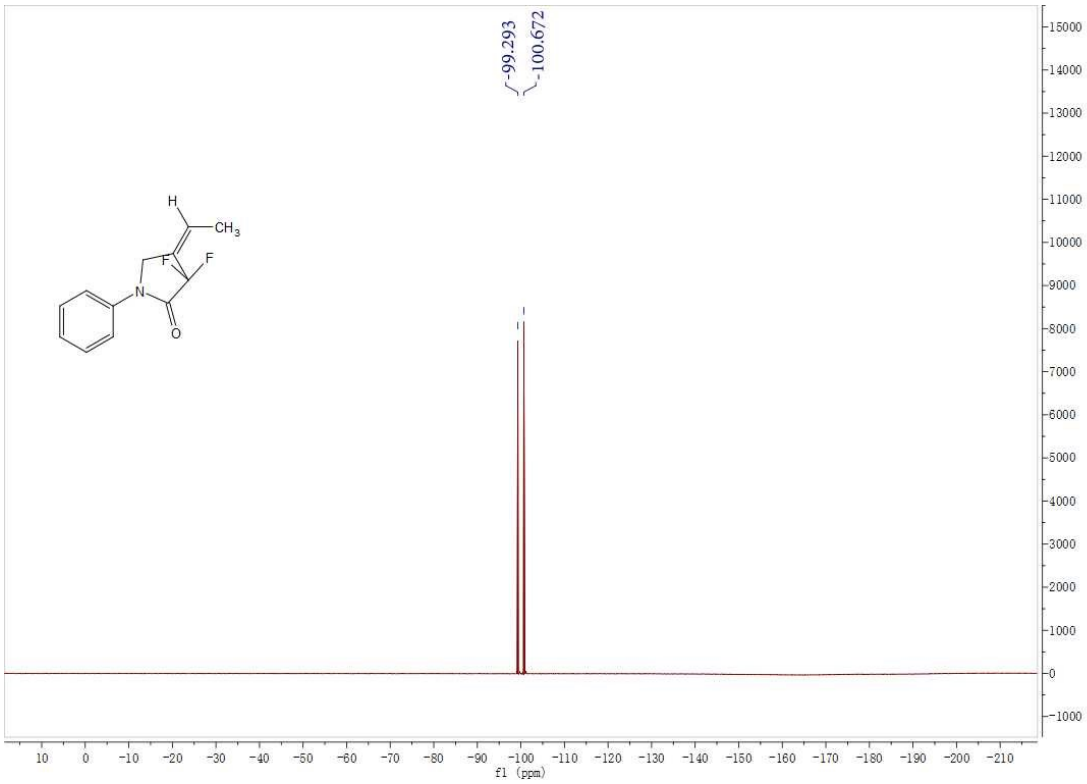

162.333
162.025
161.717
140.872
138.424
134.695
132.506
132.308
132.109
127.135
118.839
118.570
117.240
113.095
110.644
108.193
48.438
48.415
48.393
21.467
Cl
N
O
F
F
H
CH3
f1 (ppm)


-102.855
Cl
N
O
F
F
H
CH3
f1 (ppm)

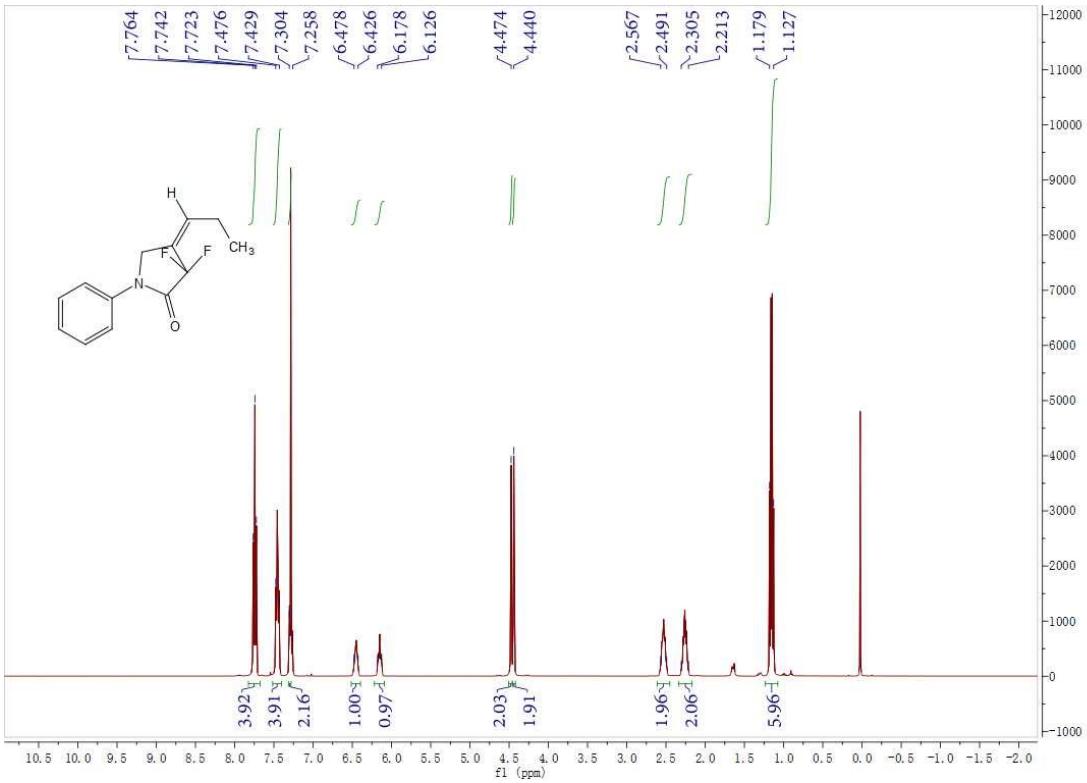
4-ethylidene-3,3-difluoro-1-phenylpyrrolidin-2-one (44)

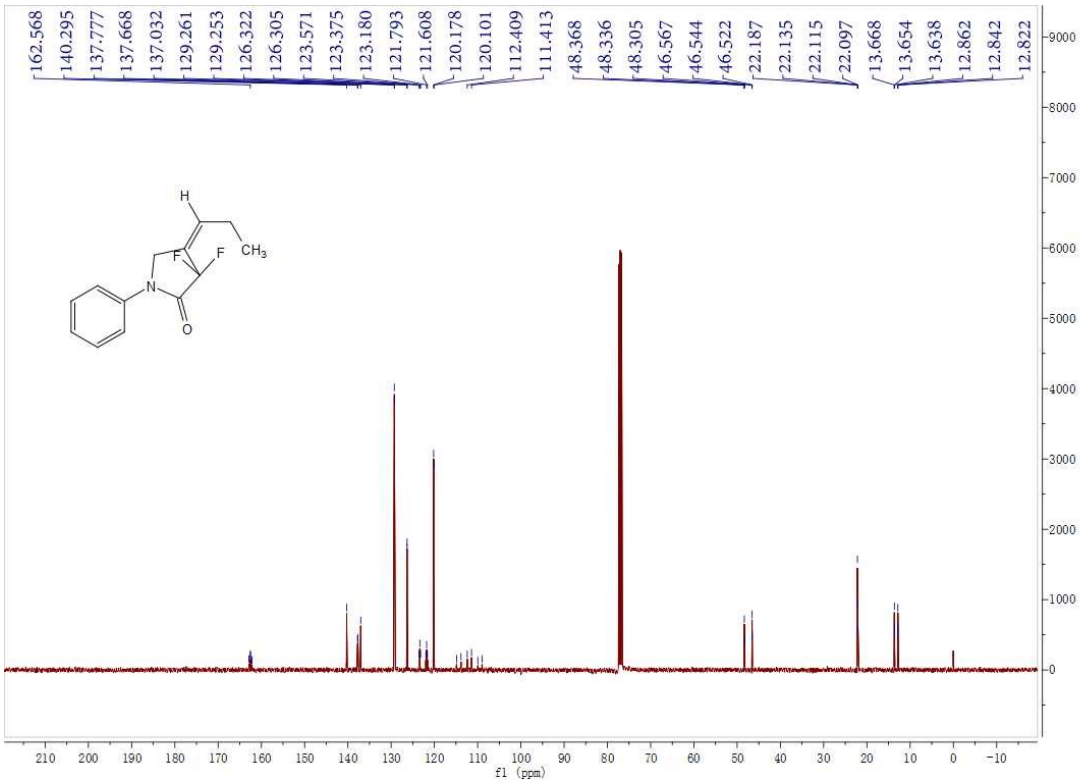


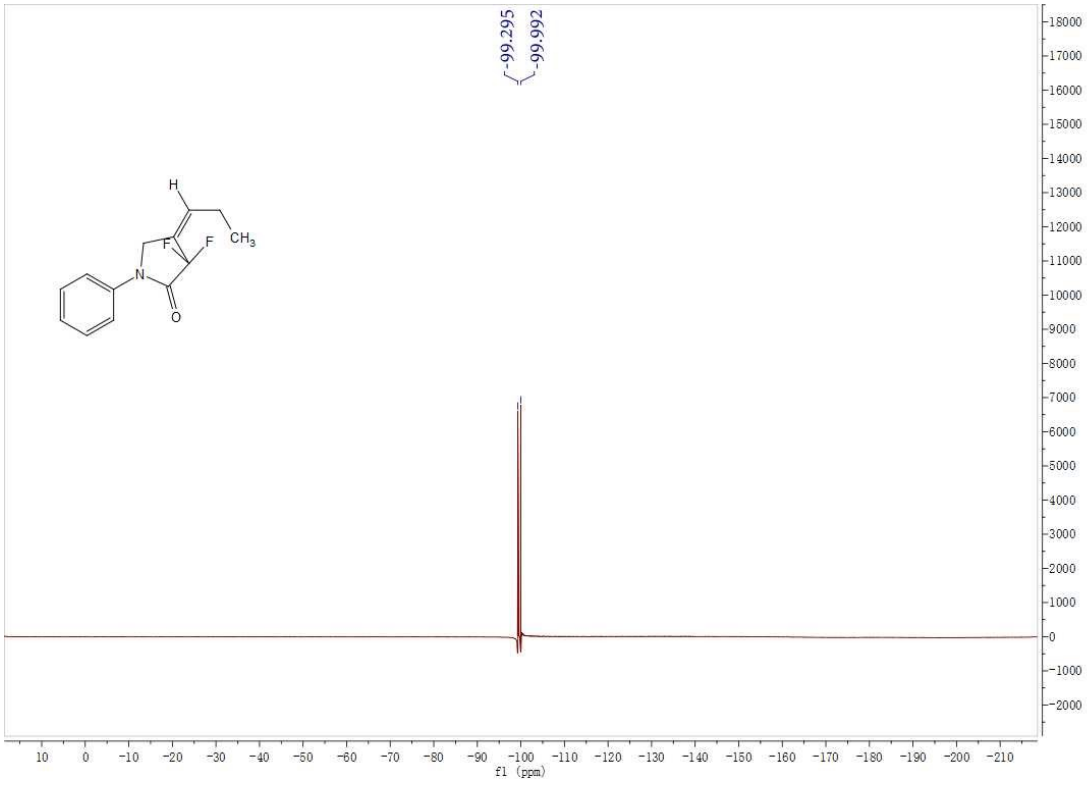




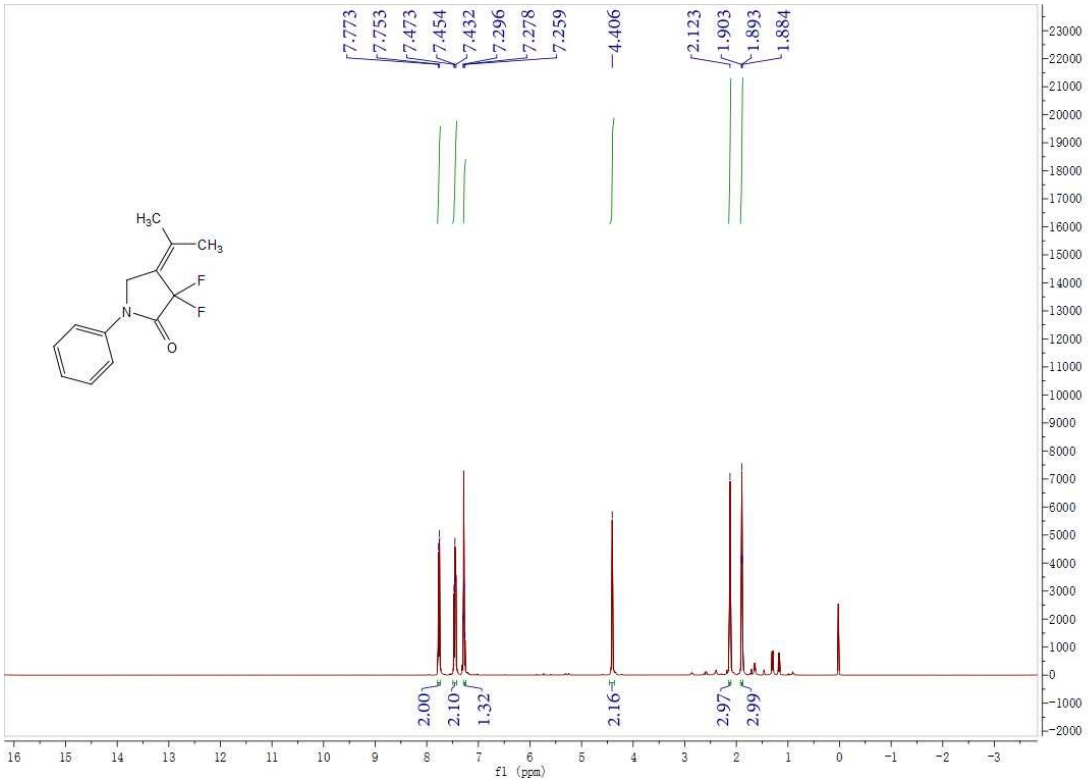
3,3-difluoro-1-phenyl-4-propylidenepyrrolidin-2-one (45)

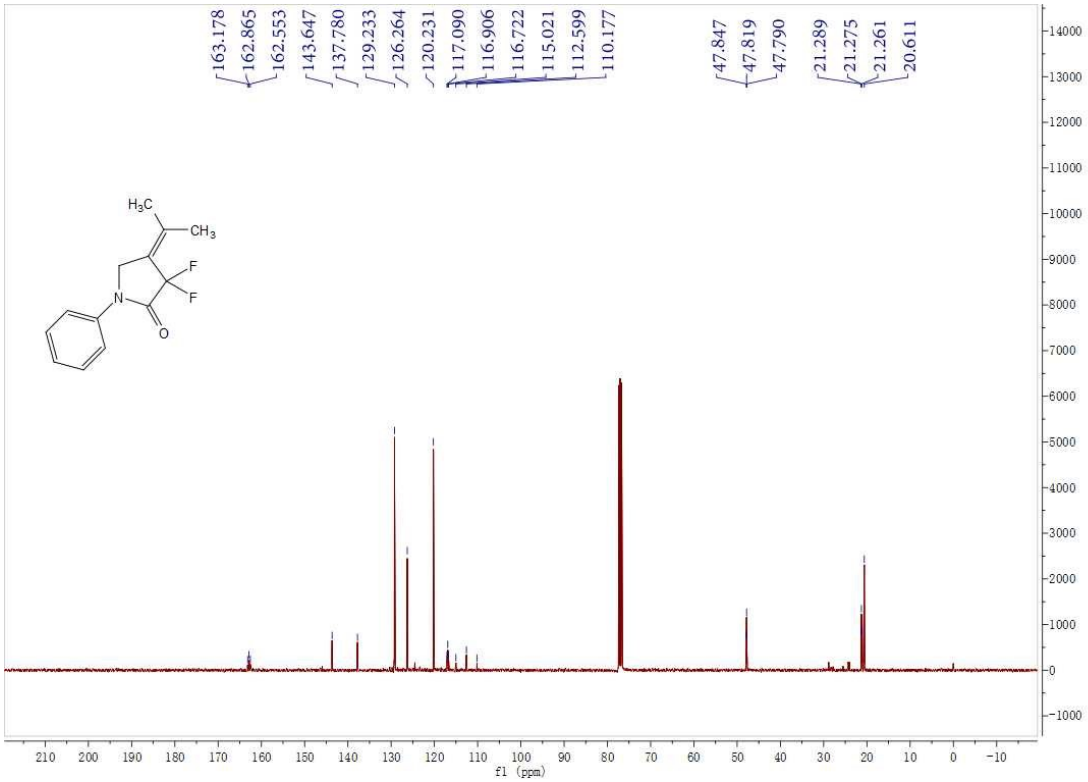


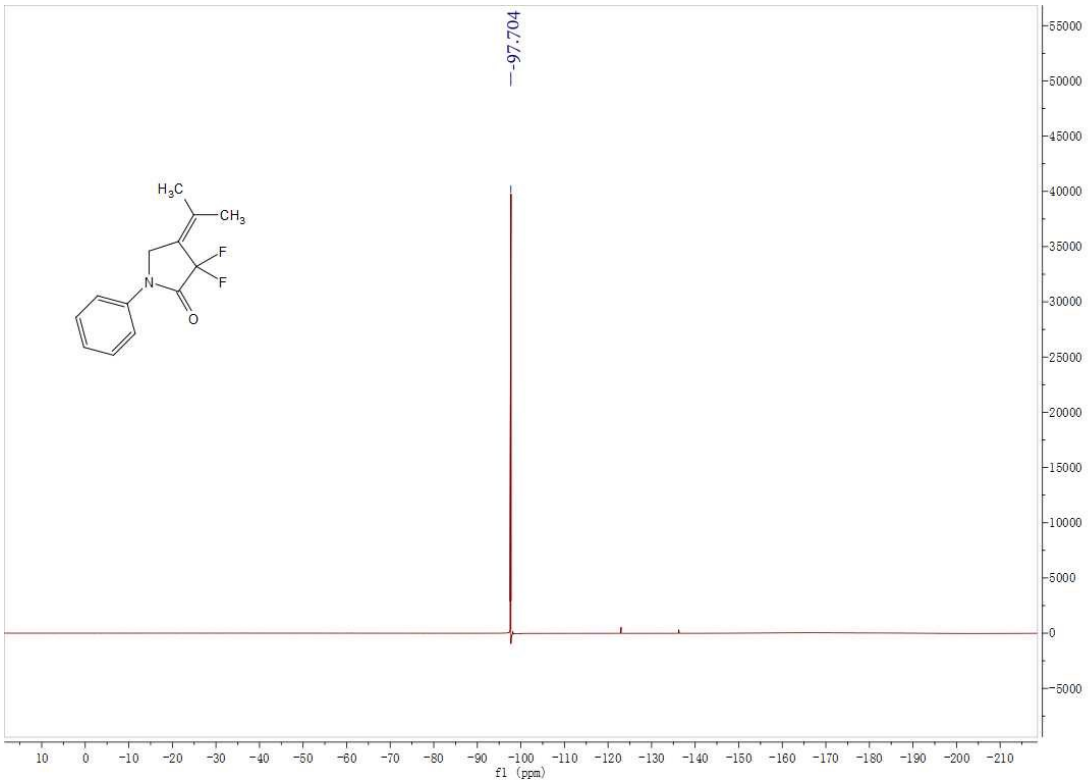

162.568
140.295
137.777
137.668
137.032
129.261
129.253
126.322
126.305
123.571
123.375
123.180
121.793
121.608
120.178
120.101
112.409
111.413
48.368
48.336
48.305
46.567
46.544
46.522
22.187
22.135
22.115
22.097
13.668
13.654
13.638
12.862
12.842
12.822
H
F
F
CH3
N
O
f1 (ppm)


-99.295
-99.992
H
F
F
CH3
N
O
f1 (ppm)

3,3-difluoro-1-phenyl-4-(propan-2-ylidene)pyrrolidin-2-one (46)






-97.704
H3C
CH3
F
F
N
O
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
-5000
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)