

Supporting Information

General Radical Difluoromethylation using Difluoroacetic Anhydride via Photoredox Catalysis

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Aiwen Lei

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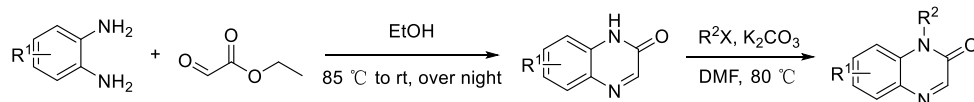
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General Information

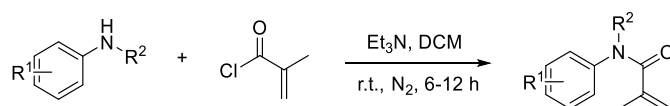
All manipulations were carried out by standard Schlenk techniques. Unless otherwise stated, analytical grade solvents and commercially available reagents were used to conduct the reactions. LED irradiation was accomplished using the blue photochemical reactors. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel. Gradient flash chromatography was conducted and eluted with a continuous gradient from petroleum ether to ethyl acetate. All new compounds were characterized by ^1H NMR, ^{13}C NMR, ^{19}F NMR and HRMS. The known compounds were characterized by ^1H NMR and ^{13}C NMR. ^1H NMR, ^{19}F NMR and ^{13}C NMR spectra were recorded on a Bruker 400 MHz NMR spectrometer. The chemical shifts (δ) were given in part per million relative to internal tetramethyl silane (TMS, 0 ppm for ^1H NMR), CDCl_3 (77.16 ppm for ^{13}C NMR) and $\text{DMSO}-d_6$ (2.50 ppm for ^1H NMR, 39.52 ppm for ^{13}C NMR), respectively. High resolution mass spectra (HRMS) were measured with a Bruker UltiMate3000 & Compact instrument and accurate masses were reported for the molecular $(\text{M}+\text{H})^+$, $(\text{M}-\text{OH})^+$, $(\text{M})^+$, $(\text{M}+\text{NH}_4)^+$. GC-MS spectra were recorded on Varian GC MS 3900-2100T or SHIMADZU GC MS-2010.

Experimental Procedures

General procedure for synthesis of substrates

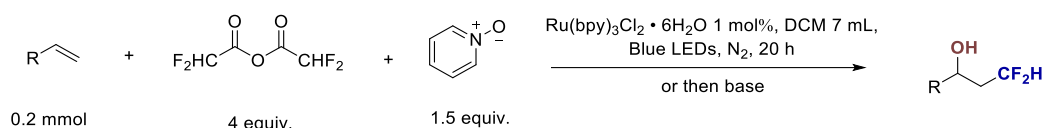


To a solution of *o*-phenylenediamine (1.0 equiv., 15 mmol) in EtOH (40 mL), ethyl glyoxalate (1.1 equiv.) was added. The mixture was heated at 85 °C for 1 h and kept in room temperature overnight. After the reaction, the product was collected by filtration. The crude product was washed by EtOH (10 mL) for 3 times and then dried to obtain quinoxalinone. A round-bottom bottle equipped with a magnetic stir bar was charged with obtained quinoxalinone (1.0 equiv., 15 mmol), organic halide (R^2X , 1.8 equiv.) and K_2CO_3 (1.2 equiv.) in DMF (40 mL) at 80 °C for 2 h. After completion of the reaction, the reaction was quenched with H_2O (80 mL). The aqueous layers were extracted with EA (60 mL \times 3), and the combined organic layers were washed with brine, dried over anhydrous Na_2SO_4 , and concentrated in vacuo. The residue was purified by flash column chromatography conducted with a continuous gradient from petroleum ether (bp. 60-90 °C) to ethyl acetate on silica gel.

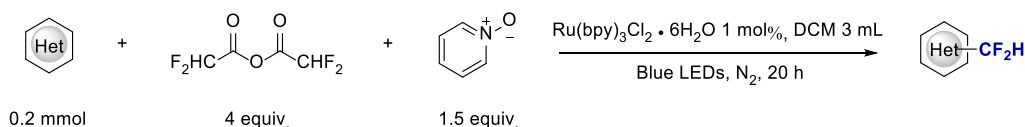


To a 50 mL round-bottom flask was added the solution of corresponding aniline (2.0 mmol) in DCM (15 mL) and triethylamine (0.4 g, 4.0 mmol, 2.0 equiv.). The mixture was stirred at 0 °C, and added methacryloyl chloride (0.31 g, 3.0 mmol, 1.5 equiv.) slowly under nitrogen atmosphere. The resulting solution was stirred at room temperature for 6~12 h, quenched with H_2O (30 mL), extracted with DCM (15 mL \times 3). The combined organic layer was washed with brine (15 mL \times 3), dried over Na_2SO_4 , and concentrated. The residue was purified by flash chromatography on a silica gel using petroleum ether and ethyl acetate (15:1~10:1, v/v) as the eluent to give corresponding substrates.

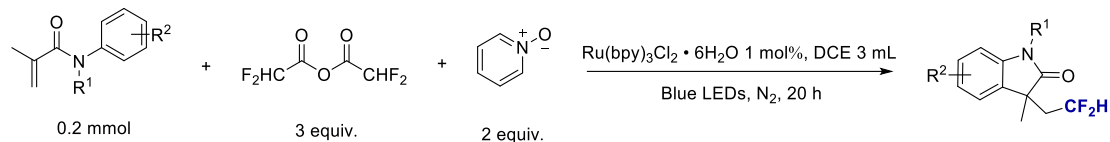
General procedure for visible-light-induced general radical difluoromethylation reaction with difluoroacetic anhydride



In a flame-dried 15 mL Schlenk tube equipped with a stir bar, $Ru(bpy)_3Cl_2 \cdot 6H_2O$ (0.002 mmol) was added. Pyridine-*N*-oxide (0.3 mmol) was added to the glovebox. Under nitrogen atmosphere, difluoroacetic anhydride (0.8 mmol), olefin (0.2 mmol) and DCM (7.0 mL) were injected respectively into the bottle via syringes. The mixture was stirred at 4 \times 6 W blue LEDs at 25 °C for 20 h. With or without post processing steps (removing the solvent, then added NaOH 0.1 g, EtOH 2.5 mL and H_2O 0.5 mL at 60 °C stirred for 3 h), the residue was purified by flash column chromatography conducted with a continuous gradient from petroleum ether (bp. 60-90 °C) to ethyl acetate on silica gel.

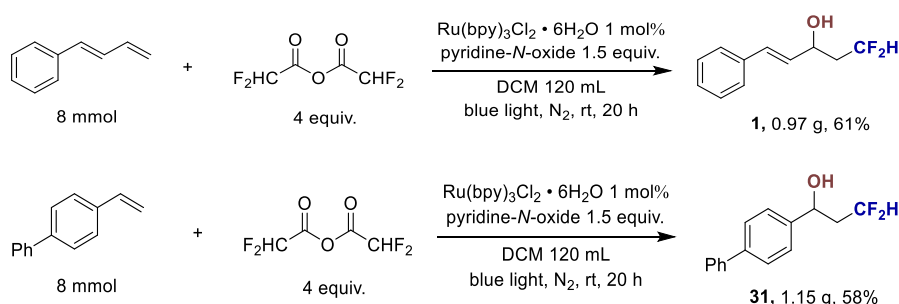


In a flame-dried 15 mL Schlenk tube equipped with a stir bar, Ru(bpy)₃Cl₂·6H₂O (0.002 mmol) and aromatic heterocycle (0.2 mmol) were added. Pyridine-*N*-oxide (0.3 mmol) was added to the glovebox. Under nitrogen atmosphere, difluoroacetic anhydride (0.8 mmol) and DCM (3.0 mL) were injected respectively into the bottle via syringes. At last, the mixture was stirred at 4×6 W blue LEDs at 25 °C for 20 h. The residue was purified by flash column chromatography conducted with a continuous gradient from petroleum ether (bp. 60-90 °C) to ethyl acetate on silica gel.



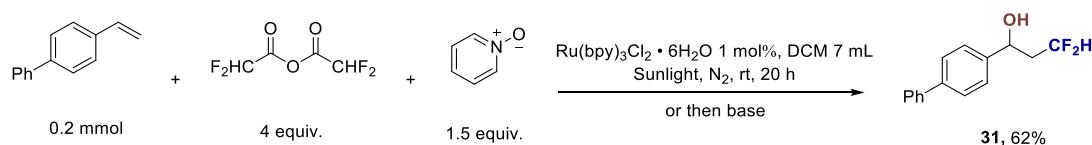
In a flame-dried 15 mL Schlenk tube equipped with a stir bar, Ru(bpy)₃Cl₂·6H₂O (0.002 mmol) and *N*-arylacrylamides (0.2 mmol) were added. Pyridine-*N*-oxide (0.4 mmol) was added to the glovebox. Under nitrogen atmosphere, difluoroacetic anhydride (0.6 mmol) and DCE (3.0 mL) were injected respectively into the bottle via syringes. At last, the mixture was stirred at 4×6 W blue LEDs at 25 °C for 20 h. The residue was purified by flash column chromatography conducted with a continuous gradient from petroleum ether (bp. 60-90 °C) to ethyl acetate on silica gel.

Scale-up procedure for Substrates 1 and 31



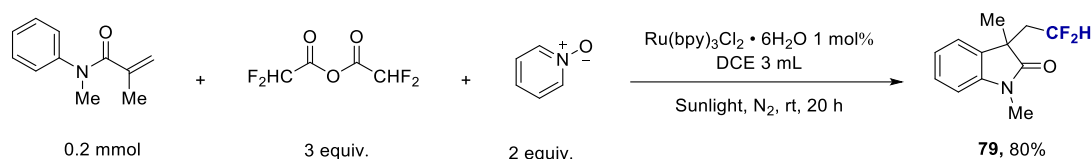
In a flame-dried 100 mL Schlenk tube equipped with a stir bar, Ru(bpy)₃Cl₂·6H₂O (1 mol%, 0.08 mmol) was added. Pyridine-*N*-oxide (1.5 equiv., 12 mmol) was added to the glovebox. Under nitrogen atmosphere, difluoroacetic anhydride (4 equiv., 32 mmol), olefin (8 mmol) and DCM (120 mL) were injected respectively into the bottle via syringes. The mixture was stirred at 4×6 W purple LEDs at 25 °C for 20 h. With or without post processing steps (removing the solvent, then added NaOH (4.0 g), EtOH 100 mL and H₂O 20 mL at 60 °C for 3 h), removing the solvent, then the reaction mixture was washed with water and extracted with EA (60 mL×3). The organic layers were combined, dried over Na₂SO₄ and concentrated in vacuum. The residue was purified by flash column chromatography conducted with a continuous gradient from petroleum ether (bp. 60-90 °C) to ethyl acetate on silica gel.

Sunlight experiments



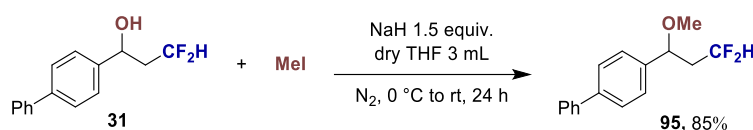
In a flame-dried 15 mL flask, Ru(bpy)₃Cl₂·6H₂O (0.002 mmol) was added. Pyridine-*N*-oxide (0.3 mmol) was added to the glovebox. Under nitrogen atmosphere, difluoroacetic anhydride (0.8 mmol), olefin (0.2 mmol) and DCM (7.0 mL) were injected respectively into the bottle via syringes. After 20 h. removing the solvent, NaOH 0.1 g, EtOH 2.5 mL and H₂O 0.5 mL were added, then stirring at 60 °C for 3 h. The residue was purified by flash column chromatography conducted with a continuous gradient

from petroleum ether (bp. 60-90 °C) to ethyl acetate on silica gel.

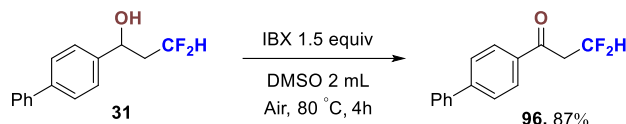


In a flame-dried 15 mL flask equipped, Ru(bpy)₃Cl₂·6H₂O (0.002 mmol) and *N*-arylacrylamides (0.2 mmol) were added. Pyridine-*N*-oxide (0.4 mmol) was added to the glovebox. Under nitrogen atmosphere, difluoroacetic anhydride (0.6 mmol) and DCE (3.0 mL) were injected respectively into the bottle via syringes. After 20 h. The residue was purified by flash column chromatography conducted with a continuous gradient from petroleum ether (bp. 60-90 °C) to ethyl acetate on silica gel.

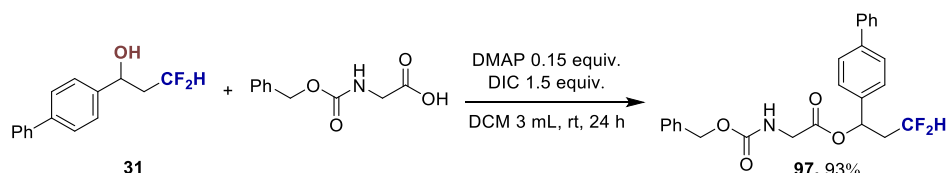
Derivatization experiments



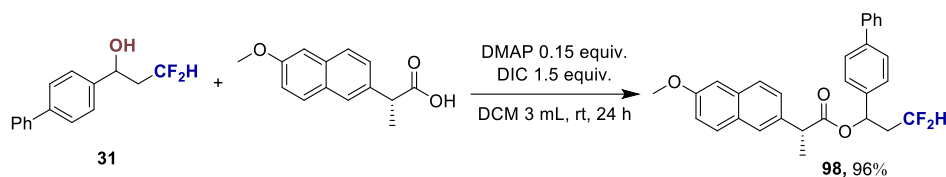
To a 50 mL round-bottom flask 1-([1,1'-biphenyl]-4-yl)-3,3-difluoropropan-1-ol (24.8 mg, 0.1 mmol) and dry THF (3 mL) were added. The mixture was stirred at 0 °C, and added NaH (0.15 mmol, 1.5 equiv.) slowly under nitrogen atmosphere. After stirring for 30 minutes, and added the MeI (2 equiv.) slowly under nitrogen atmosphere. The resulting solution was stirred at room temperature for 24 h, quenched with H₂O (30 mL), extracted with DCM (15 mL×3). The combined organic layer was washed with brine (15 mL×3), dried over Na₂SO₄, and concentrated in vacuum. The residue was purified by flash column chromatography conducted with a continuous gradient from petroleum ether (bp. 60-90 °C) to ethyl acetate on silica gel.



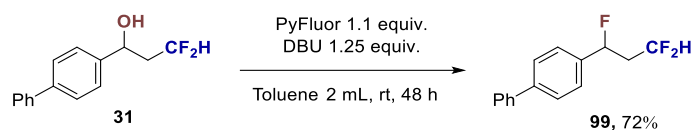
To a solution of 1-([1,1'-biphenyl]-4-yl)-3,3-difluoropropan-1-ol (24.8 mg, 0.1 mmol, 1 equiv.) in DMSO (2 mL) was added 2-iodoxybenzoic acid (42 mg, 0.15 mmol, 1.5 equiv.). Then the reaction was stirred for 4 hours at 80 °C. The solution was then diluted with water and extracted with EA (20 mL), the organic layers were then pooled and washed with saturated aqueous NaHCO₃, brine, dried over Na₂SO₄. After removal of the solvent, the crude reaction mixture was purified on silica gel to afford the desired product (21.4 mg, 87%) as a faint yellow liquid.



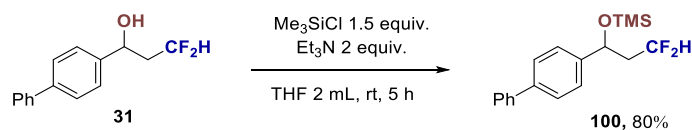
To a 50 mL round-bottom flask, ((benzyloxy)carbonyl)glycine (0.2 mmol, 2equiv.), 1-([1,1'-biphenyl]-4-yl)-3,3-difluoropropan-1-ol (24.8 mg, 0.1 mmol), 4-dimethylaminopyridine (0.015 mmol, 0.15 equiv.), *N,N*-diisopropylcarbodiimide (0.15 mmol, 1.5 equiv.) and DCM (3.0 mL) were added. The solution was stirred for 24 h at 25 °C. Then, the solution was concentrated in vacuum. The residue was purified by flash column chromatography conducted with a continuous gradient from petroleum ether (bp. 60-90 °C) to ethyl acetate on silica gel.



To a 50 mL round-bottom flask, (*R*)-2-(6-methoxynaphthalen-2-yl)propanoic acid (0.2 mmol, 2equiv.), 1-([1,1'-biphenyl]-4-yl)-3,3-difluoropropan-1-ol (24.8 mg, 0.1 mmol), 4-dimethylaminopyridine (0.015 mmol, 0.15 equiv.), *N,N*-diisopropylcarbodiimide (0.15 mmol, 1.5 equiv.) and DCM (3.0 mL) were added. The solution was stirred for 24 h at 25 °C. Then, the solution was concentrated in vacuum. The residue was purified by flash column chromatography conducted with a continuous gradient from petroleum ether (bp. 60-90 °C) to ethyl acetate on silica gel.

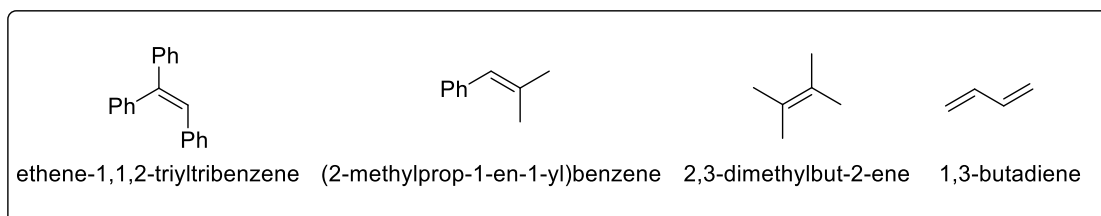


In a flame-dried 15 mL Schlenk tube equipped with a stir bar 1-([1,1'-biphenyl]-4-yl)-3,3-difluoropropan-1-ol (24.8 mg, 0.1 mmol), toluene (1 mL), PyFluor (1.1 equiv.), and DBU (2 equiv.). The mixture is stirred at room temperature for 48 hours under ambient atmosphere. After removal of the solvent, the crude reaction mixture was purified by flash column chromatography on silica gel to afford the desired product (18 mg, 72%) as a white solid.

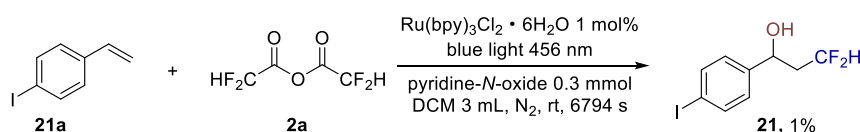


To a solution of 1-([1,1'-biphenyl]-4-yl)-3,3-difluoropropan-1-ol (24.8 mg, 0.1 mmol) in THF (2 mL) was added triethylamine (0.2 mmol, 2 equiv.) and trimethylsilyl chloride (1.5 mmol, 1.5 equiv.). The suspension was stirred for 5 h at room temperature. Subsequently, water (2 mL) was added, and the organic layer was separated. The aqueous layer was washed with ethyl acetate (2 mL) three times. Combined organic layers were dried over anhydrous MgSO_4 and concentrated under high vacuum. The crude product was purified by column chromatography on silica gel (hexanes:ethyl acetate, 10:1) to yield **100** (80% yield).

Substrates Incompatible with the Reaction



Determination of Quantum Yield



A cuvette was charged with 21a (0.2 mmol), 2a (0.8 mmol), Ru(bpy)₃Cl₂·6H₂O (0.002 mmol), pyridine-*N*-oxide (0.3 mmol), and 3.0 mL DCM. The sample was irradiated ($\lambda = 456$ nm, slit width = 3.0 mm, slit height 5.0 mm with intensity of 0.371 mW·cm⁻²) for 6794 s. After irradiation, the yield of product formed was determined by ¹⁹F NMR based on a (trifluoromethyl)benzene standard. The quantum yield was determined as follows.

ϕ = Mole number for product/Mole number for absorption of photons = 0.00465

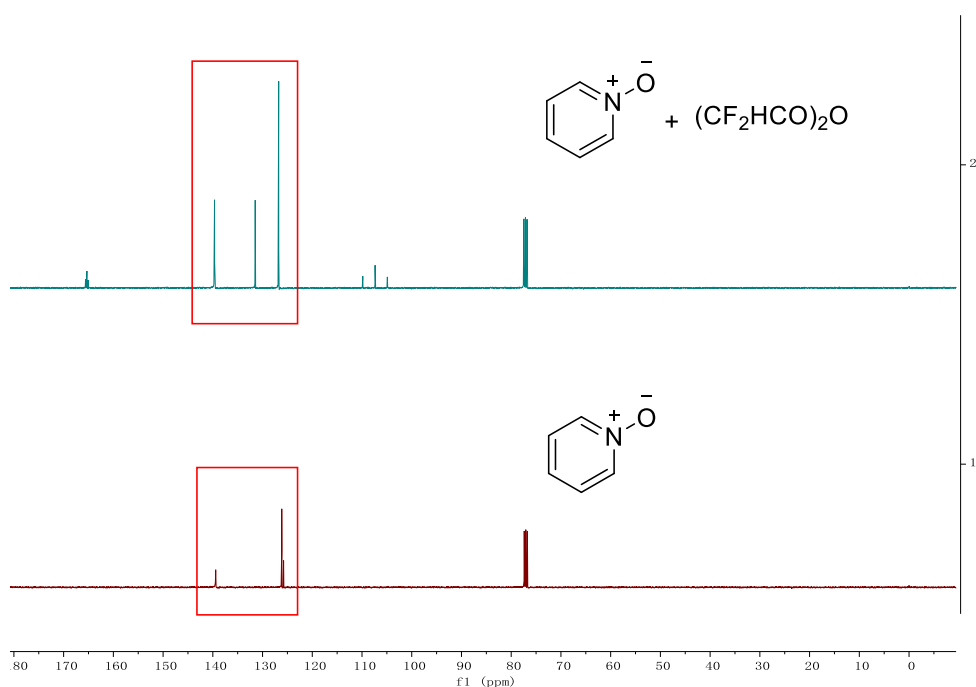
$$\phi = \frac{n_{21} N_A / t}{f P \lambda / h c}$$

n_{21} : the mole number of the product 21; t : reaction time (6794 s); N_A : 6.02×10²³/mol; f : 1-10^{-A}(456 nm, A = 0.154); P : $P = E \cdot S$ (E : illumination intensity, $E = 0.371$ mW/cm²; S : the area that irradiated $S = 0.15$ cm²); λ : wavelength ($\lambda = 4.56 \times 10^7$ m); h : planck constant ($h = 6.626 \times 10^{-34}$ J*s); c : velocity of light ($c = 3 \times 10^8$ m/s).

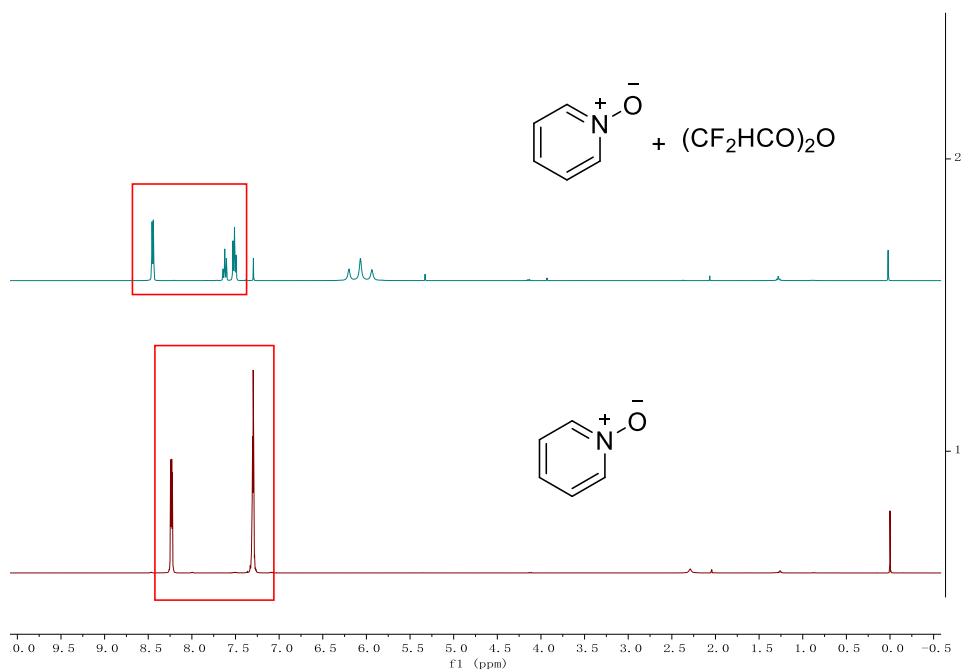
These low quantum yields were obtained, which suggest that the reaction may not have undergone a free radical chain reaction process.

¹³C/¹H NMR chemical shifts

In a NMR tube, pyridine-*N*-oxide, difluoroacetic anhydride and CDCl₃ were added. The mixture was determined by ¹³C/¹H NMR spectroscopy.

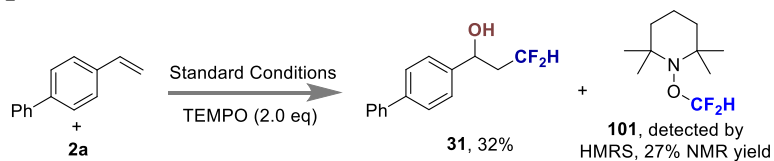


¹³C NMR chemical shift

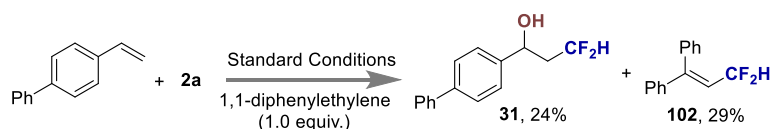
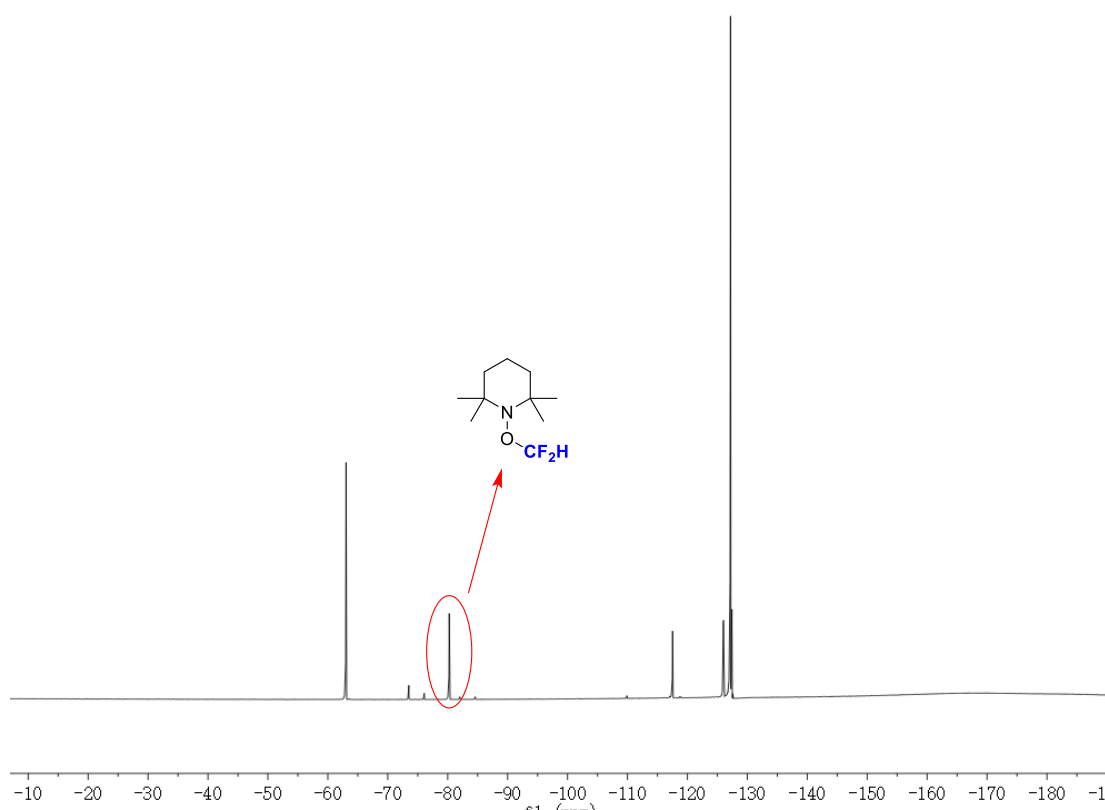


¹H NMR chemical shift

Trapping experiment



In a flame-dried 15 mL Schlenk tube equipped with a stir bar, Ru(bpy)₃Cl₂·6H₂O (0.002 mmol) and TEMPO (0.4 mmol, 2 equiv.) was added. Pyridine-*N*-oxide (0.3 mmol) was added to the glovebox. Under nitrogen atmosphere, difluoroacetic anhydride (0.8 mmol), olefin (0.2 mmol) and DCM (7.0 mL) were injected respectively into the bottle via syringes. The mixture was stirred at 4×6 W blue LEDs at 25 °C for 20 h. The yields were determined by ¹⁹F NMR spectroscopy using (trifluoromethyl)benzene standard. ¹⁹F NMR (377 MHz,) δ -80.25¹. HRMS (ESI) calcd for C₁₀H₂₀F₂NO⁺, [M+H]⁺ 208.1508, found 208.1513¹.

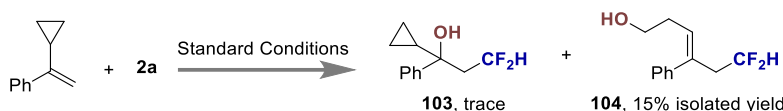


In a flame-dried 15 mL Schlenk tube equipped with a stir bar, Ru(bpy)₃Cl₂·6H₂O (0.002 mmol) and 1,1-diphenylethylene (0.2 mmol) were added. Pyridine-*N*-oxide (0.3 mmol) was added to the glovebox. Under nitrogen atmosphere, difluoroacetic anhydride (0.8 mmol), olefin (0.2 mmol) and DCM (7.0 mL) were injected respectively into the bottle via syringes. The mixture was stirred at 4×6 W blue LEDs at 25 °C for 20 h. With or without post processing steps (removing the solvent, then added NaOH 0.1 g, EtOH 2.5 mL and H₂O 0.5 mL at 60 °C stirred for 3 h), the residue was purified by flash column chromatography conducted with a continuous gradient from petroleum ether (bp. 60-90 °C) to ethyl acetate on silica gel.



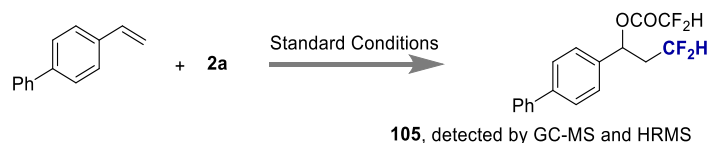
In a flame-dried 15 mL Schlenk tube equipped with a stir bar, Ru(bpy)₃Cl₂·6H₂O (0.002 mmol) and 1,1-diphenylethylene (0.2 mmol, 1.0 equiv.) were added. Pyridine-*N*-oxide (0.3 mmol) was added to the glovebox. Under nitrogen atmosphere, difluoroacetic anhydride (0.8 mmol), and DCM (7.0 mL) were injected respectively into the bottle via syringes. The mixture was stirred at 4×6 W blue LEDs at 25 °C for 20 h. The residue was purified by flash column chromatography conducted with a continuous gradient from petroleum ether (bp. 60-90 °C) to ethyl acetate on silica gel.

Radical clock experiment



In a flame-dried 15 mL Schlenk tube equipped with a stir bar, Ru(bpy)₃Cl₂·6H₂O (0.002 mmol) was added. Pyridine-*N*-oxide (0.3 mmol) was added to the glovebox. Under nitrogen atmosphere, difluoroacetic anhydride (0.8 mmol), (1-cyclopropylvinyl)benzene (0.2 mmol) and DCM (7.0 mL) were injected respectively into the bottle via syringes. The mixture was stirred at 4×6 W blue LEDs at 25 °C for 20 h. With or without post processing steps (removing the solvent, then added NaOH 0.1 g, EtOH 2.5 mL and H₂O 0.5 mL at 60 °C stirred for 3 h), the residue was purified by flash column chromatography conducted with a continuous gradient from petroleum ether (bp. 60-90 °C) to ethyl acetate on silica gel.

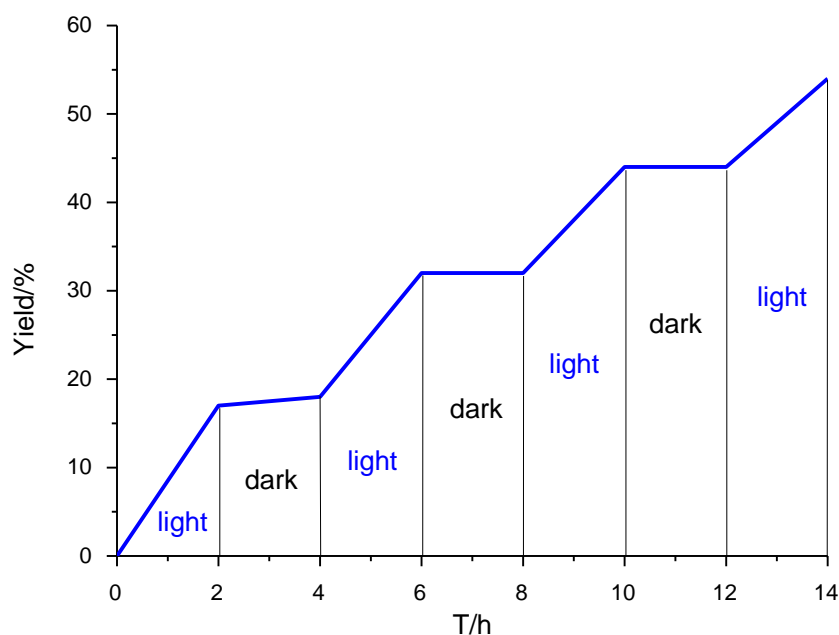
The detection of intermediate



In a flame-dried 15 mL Schlenk tube equipped with a stir bar, Ru(bpy)₃Cl₂·6H₂O (0.002 mmol) was added. Pyridine-*N*-oxide (0.3 mmol) was added to the glovebox. Under nitrogen atmosphere, difluoroacetic anhydride (0.8 mmol), olefin (0.2 mmol) and DCM (7.0 mL) were injected respectively into the bottle via syringes. The mixture was stirred at 4×6 W blue LEDs at 25 °C for 20 h. Reaction mixture was taken out from the reaction system for High resolution mass spectra analysis. **HRMS (ESI)** calcd for C₁₇H₁₅F₄O₂⁺, [M+H]⁺ 327.1003, found 327.1005.

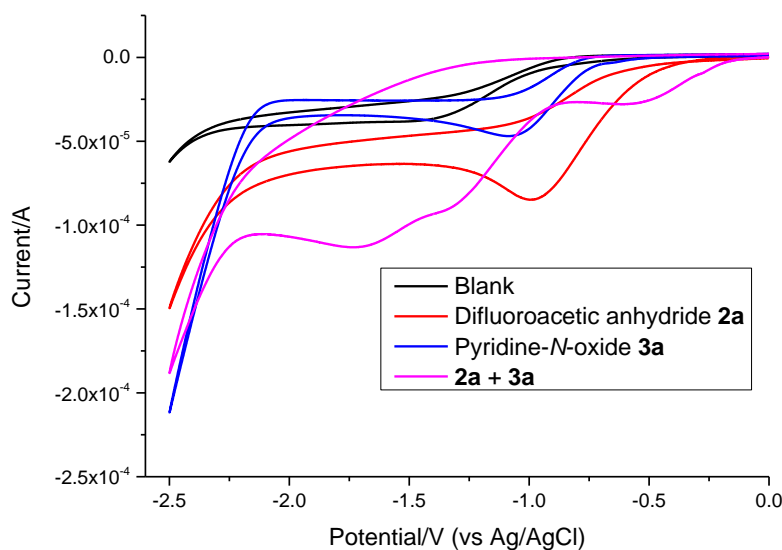
Light off/on over time experiments

In a flame-dried 15 mL Schlenk tube equipped with a stir bar, Ru(bpy)₃Cl₂·6H₂O (0.002 mmol) was added. Pyridine-*N*-oxide (0.3 mmol) was added to the glovebox. Under nitrogen atmosphere, difluoroacetic anhydride (0.8 mmol), (trifluoromethyl)benzene (0.2 mmol), olefin (0.2 mmol) and DCM (7.0 mL) were injected respectively into the bottle via syringes. The mixture was stirred at 4×6 W blue LEDs at 25 °C. The mixture was stirred under blue light irradiation at 25 °C for the 2 h. 0.4 mL reaction mixture was taken out from the reaction system under N₂ protection for ¹⁹F NMR spectroscopy analysis. The remaining mixture was stirred in the absence of light for an additional 2 h. Then another 0.4 mL reaction mixture was taken out from the reaction system under N₂ protection for ¹⁹F NMR spectroscopy analysis. The lamps were turned back on to irradiate the remaining mixture. After an additional 2 h of irradiation, the lamps were turned off. ¹⁹F NMR spectroscopy analysis was performed every 2 h until the reaction time reached 14 h. The total yield was determined by ¹⁹F NMR spectroscopy of the unpurified mixture with (trifluoromethyl)benzene as an internal standard.



General procedure for cyclic voltammetry (CV)

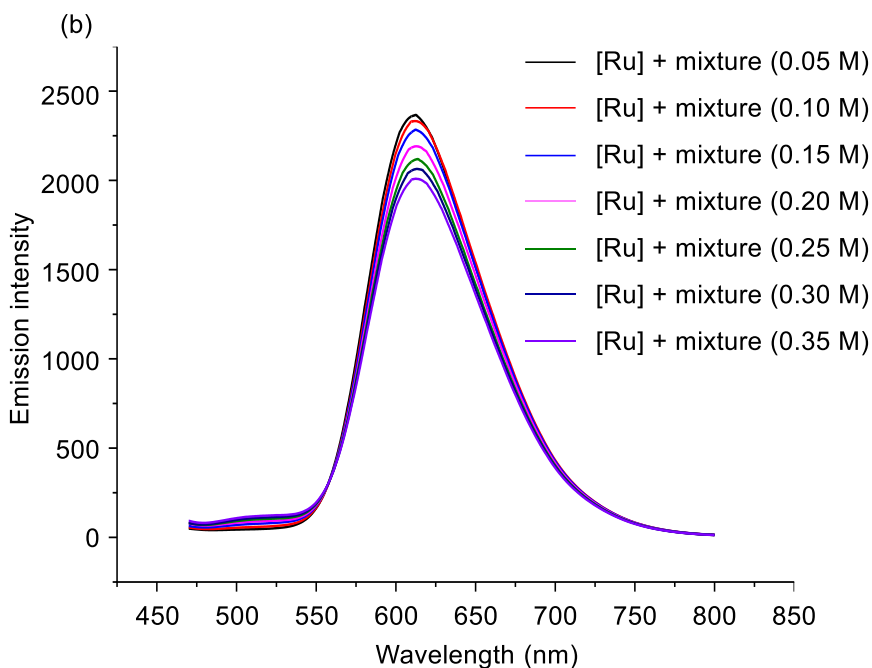
Cyclic voltammetry experiment was performed in a three-electrode cell connected to a Schlenk line under air at room temperature. The working electrode was a glass carbon electrode, the counter electrode was a platinum wire. The reference was an Ag/AgCl electrode submerged in 10 mL DCM. Corresponding undetested matter: difluoroacetic anhydride (0.1 mmol), pyridine-*N*-oxide (0.1 mmol), in a three-electrode cell, solvent DCM 10 mL containing $n\text{-Bu}_4\text{NBF}_4$ (0.5 mmol) were poured into the electrochemical cell in all experiments. The scan rate is 0.1 V/s.



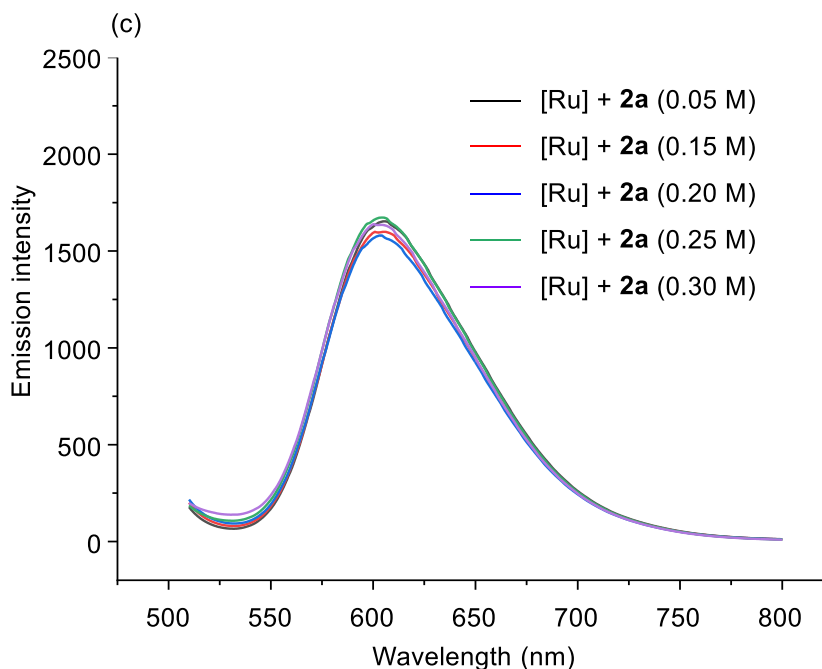
Luminescence quenching experiments

Quenching data was obtained using a Hitachi F4600 Fluorimeter. All quenching data was recorded

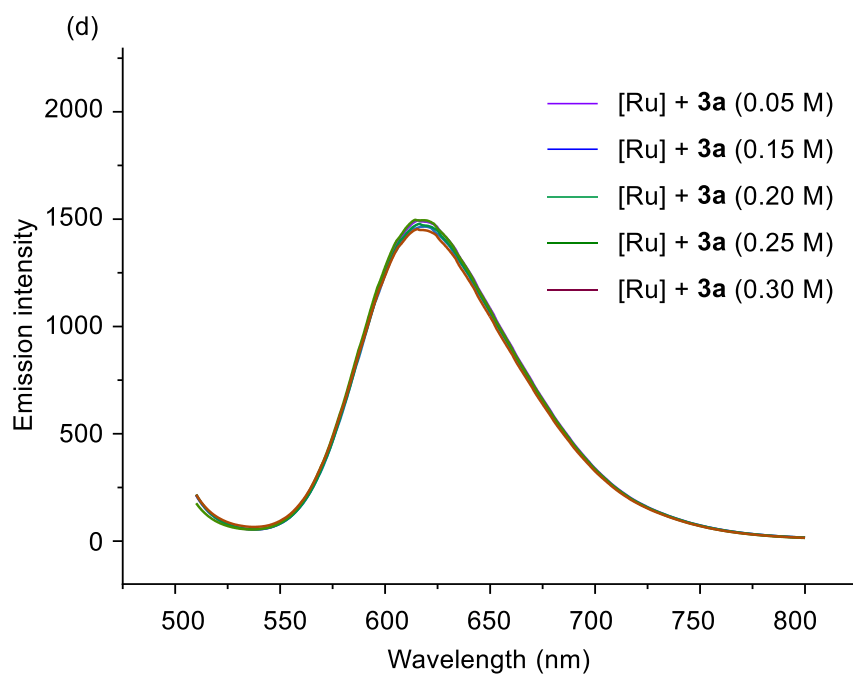
using a quartz cuvette. Under nitrogen atmosphere, $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ (1×10^{-5} M) and the mixture (pyridine-*N*-oxide:difluoroacetic anhydride 1:1) were run in dry DCM at 25 °C. Excitation was performed at 450 nm. All values are the average of 3 measurements.



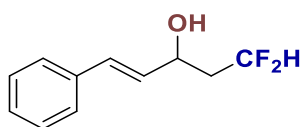
Quenching data was obtained using a Hitachi F4600 Fluorimeter. All quenching data was recorded using a quartz cuvette. $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ (1×10^{-5} M) and pyridine-*N*-oxide were run in DCM at 25 °C. Excitation was performed at 450 nm.



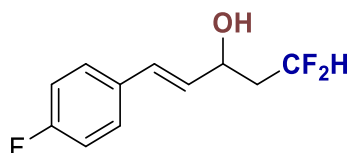
Quenching data was obtained using a Hitachi F4600 Fluorimeter. All quenching data was recorded using a quartz cuvette. $\text{Ru}(\text{bpy})_3\text{Cl}_2 \cdot 6\text{H}_2\text{O}$ (1×10^{-5} M) and difluoroacetic anhydride were run in DCM at 25 °C. Excitation was performed at 450 nm.



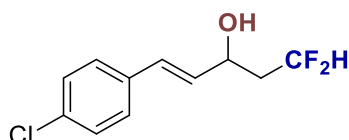
Characterization of Products



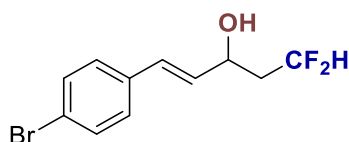
(E)-5,5-difluoro-1-phenylpent-1-en-3-ol (1). Faint yellow liquid was obtained in 75% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.42 – 7.21 (m, 5H), 6.63 (d, J = 15.9 Hz, 1H), 6.27 – 5.84 (m, 2H), 4.56 (q, J = 6.8 Hz, 1H), 2.30 – 2.07 (m, 2H), 1.88 (s, 1H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 136.14, 131.55, 130.48, 128.82, 128.27, 126.73, 116.04 (t, J = 238.4 Hz), 68.31 (dd, J = 7.9, 5.7 Hz), 41.53 (t, J = 20.7 Hz). $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -115.89 – -118.07 (m). **HRMS (ESI)** calcd for $\text{C}_{11}\text{H}_{11}\text{F}_2$, $[\text{M}-\text{OH}]^+$ 181.0823, found 181.0820.



(E)-5,5-difluoro-1-(4-fluorophenyl)pent-1-en-3-ol (2). Faint yellow liquid was obtained in 82% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.39 – 7.29 (m, 2H), 7.07 – 6.96 (m, 2H), 6.59 (dd, J = 15.9, 1.1 Hz, 1H), 6.21 – 5.84 (m, 2H), 4.54 (td, J = 7.9, 4.7 Hz, 1H), 2.27 – 1.97 (m, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 162.69 (d, J = 247.5 Hz), 132.31 (d, J = 3.3 Hz), 130.32, 130.22 (d, J = 2.2 Hz), 128.27 (d, J = 8.2 Hz), 116.01 (t, J = 238.4 Hz), 115.74 (d, J = 21.7 Hz), 68.19 (dd, J = 7.9, 5.6 Hz), 41.50 (t, J = 20.6 Hz). $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -113.59, -115.54 – -118.14 (m). **HRMS (ESI)** calcd for $\text{C}_{11}\text{H}_{10}\text{F}_3$, $[\text{M}-\text{OH}]^+$ 199.0729, found 199.0727.

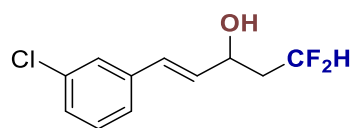


(E)-1-(4-chlorophenyl)-5,5-difluoropent-1-en-3-ol (3). Faint yellow liquid was obtained in 81% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.29 (s, 4H), 6.59 (dd, J = 15.9, 1.2 Hz, 1H), 6.24 – 5.85 (m, 2H), 4.66 – 4.46 (m, 1H), 2.27 – 2.04 (m, 2H), 1.96 (s, 1H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 134.66, 133.89, 131.13, 130.20, 128.98, 127.92, 115.97 (t, J = 238.5 Hz), 68.11 (dd, J = 7.9, 5.6 Hz), 41.46 (t, J = 20.7 Hz). $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -115.93 – -117.89 (m). **HRMS (ESI)** calcd for $\text{C}_{11}\text{H}_{10}\text{ClF}_2$, $[\text{M}-\text{OH}]^+$ 215.0434, found 215.0432.

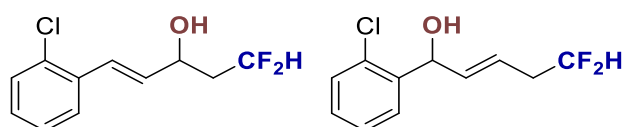


(E)-1-(4-bromophenyl)-5,5-difluoropent-1-en-3-ol (4). Faint yellow liquid was obtained in 75% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.45 (d, J = 8.5 Hz, 2H), 7.23 (d, J = 8.5 Hz, 2H), 6.57 (d, J = 15.9, 1.1 Hz, 1H), 6.29 – 5.76 (m, 2H), 4.55 (td, J = 7.5, 4.9 Hz, 1H), 2.24 – 2.03 (m, 2H), 2.00 (s, 1H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 135.10, 131.92, 131.25, 130.22, 128.22, 122.04, 115.95 (t, J = 238.5 Hz), 68.08 (dd, J = 7.9, 5.6 Hz), 41.42 (t, J = 20.7 Hz). $^{19}\text{F NMR}$ (377 MHz,

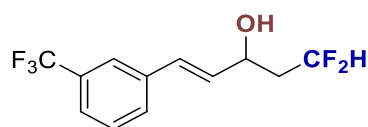
Chloroform-*d*) δ -115.76 – -117.83 (m). **HRMS (ESI)** calcd for $C_{11}H_{10}BrF_2^+$, $[M-OH]^+$ 258.9929, found 258.9928.



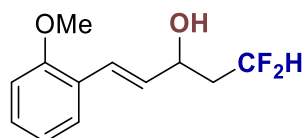
(*E*)-1-(3-chlorophenyl)-5,5-difluoropent-1-en-3-ol (5). Faint yellow liquid was obtained in 51% isolated yield. **1H NMR** (400 MHz, Chloroform-*d*) δ 7.25 (m, 3H), 6.59 (d, J = 15.9 Hz, 1H), 6.31 – 5.85 (m, 2H), 4.57 (d, J = 6.6 Hz, 1H), 2.14 (m, 2H), 1.90 (s, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 138.07, 134.77, 132.04, 130.03 (d, J = 1.8 Hz), 128.17, 126.62, 124.97, 115.94 (t, J = 238.6 Hz), 68.44 – 67.57 (dd, J = 7.9, 5.6 Hz), 41.45 (t, J = 20.7 Hz). **^{19}F NMR** (377 MHz, Chloroform-*d*) δ -116.06 – -117.92 (m). **HRMS (ESI)** calcd for $C_{11}H_{10}ClF_2^+$, $[M-OH]^+$ 215.0434, found 215.0432.



(*E*)-1-(2-chlorophenyl)-5,5-difluoropent-1-en-3-ol/(*E*)-1-(2-chlorophenyl)-5,5-difluoropent-2-en-1-ol (6). Faint yellow liquid was obtained in 73% (4:1) isolated yield. **1H NMR** (400 MHz, Chloroform-*d*) δ 7.76 – 7.10 (m, 4H), 7.08 – 4.41 (m, 4H), 2.72 – 1.97 (m, 3H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 142.61, 139.86, 136.12, 134.35, 133.41, 132.42, 129.90, 129.70, 129.21, 129.05, 127.62, 127.60, 127.40, 127.07, 121.95 (t, J = 6.6 Hz), 116.14 (t, J = 238.6 Hz), 115.96 (t, J = 238.6 Hz), 70.93, 68.17 (dd, J = 7.9, 5.5 Hz), 41.37 (t, J = 20.8 Hz), 37.38 (t, J = 22.0 Hz). **^{19}F NMR** (377 MHz, Chloroform-*d*) δ -115.70 (d, J = 2.4 Hz), -115.86 – -117.81 (m). **HRMS (ESI)** calcd for $C_{11}H_{10}ClF_2^+$, $[M-OH]^+$ 215.0434, found 215.0434.

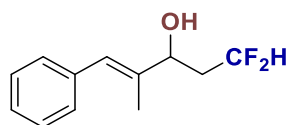


(*E*)-5,5-difluoro-1-(3-(trifluoromethyl)phenyl)pent-1-en-3-ol (7). Faint yellow liquid was obtained in 35% isolated yield. **1H NMR** (400 MHz, Chloroform-*d*) δ 7.62 (s, 1H), 7.53 (m, 2H), 7.44 (t, J = 7.7 Hz, 1H), 6.68 (dd, J = 15.9, 1.2 Hz, 1H), 6.30 (dd, J = 15.9, 6.5 Hz, 1H), 6.05 (tdd, J = 56.6, 5.7, 3.8 Hz, 1H), 4.60 (m, 1H), 2.26 – 2.08 (m, 2H), 2.02 (s, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 137.02, 132.53, 131.26 (q, J = 32.3 Hz), 129.90, 129.88, 129.30, 124.74 (q, J = 3.8 Hz), 124.16 (q, J = 272.7 Hz), 123.34 (q, J = 3.9 Hz), 115.94 (t, J = 238.5 Hz), 67.94 (dd, J = 7.9, 5.6 Hz), 41.45 (t, J = 20.8 Hz). **^{19}F NMR** (377 MHz, Chloroform-*d*) δ -62.82, -115.57 – -118.46 (m). **HRMS (ESI)** calcd for $C_{12}H_{10}F_5^+$, $[M-OH]^+$ 249.0697, found 249.0697.

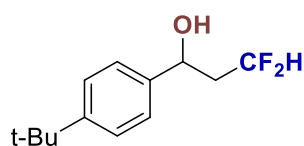


(*E*)-5,5-difluoro-1-(2-methoxyphenyl)pent-1-en-3-ol (8). Faint yellow liquid was obtained in 60% isolated yield. **1H NMR** (400 MHz, Chloroform-*d*) δ 7.41 (d, J = 7.6 Hz, 1H), 7.28 – 7.23 (m, 1H), 6.92 (m, 3H), 6.32 – 5.85 (m, 2H), 4.56 (dt, J = 12.4, 5.9 Hz, 1H), 3.85 (s, 3H), 2.15 (m, 2H), 1.90 (s, 1H). **^{13}C NMR** (101 MHz, Chloroform-*d*) δ 157.00, 131.14, 129.34, 127.20, 126.58, 125.10, 120.82, 116.15

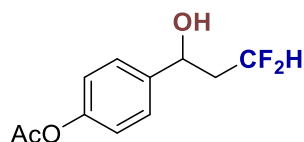
(t, $J = 238.2$ Hz), 111.02, 68.94 – 68.66 (m), 55.56, 41.57 (t, $J = 20.6$ Hz). **^{19}F NMR** (377 MHz, Chloroform- d) δ -115.87 – -118.01 (m). **HRMS (ESI)** calcd for $\text{C}_{12}\text{H}_{13}\text{F}_2\text{O}^+$, $[\text{M}-\text{OH}]^+$ 211.0929, found 211.0932.



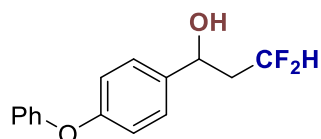
(E)-5,5-difluoro-2-methyl-1-phenylpent-1-en-3-ol (9). Colorless liquid was obtained in 65% isolated yield. **^1H NMR** (400 MHz, Chloroform- d) δ 7.35 (m, 2H), 7.30 – 7.22 (m, 3H), 6.57 (s, 1H), 6.04 (tdd, $J = 56.9, 6.3, 3.3$ Hz, 1H), 4.44 (dt, $J = 9.9, 2.7$ Hz, 1H), 2.38 – 1.99 (m, 2H), 1.89 (s, 3H), 1.86 (s, 1H). **^{13}C NMR** (101 MHz, Chloroform- d) δ 138.83, 137.01, 129.06, 128.35, 126.95, 126.49, 116.36 (t, $J = 238.5$ Hz), 72.94 (dd, $J = 8.4, 4.8$ Hz), 39.80 (t, $J = 20.7$ Hz), 13.44. **^{19}F NMR** (377 MHz, Chloroform- d) δ -115.03 – -118.72 (m). **HRMS (ESI)** calcd for $\text{C}_{12}\text{H}_{13}\text{F}_2^+$, $[\text{M}-\text{OH}]^+$ 195.0980, found 195.0977.



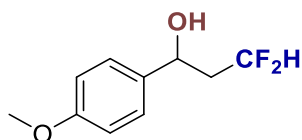
1-(4-(tert-butyl)phenyl)-3,3-difluoropropan-1-ol (10)⁶. Faint yellow liquid was obtained in 75% isolated yield. **^1H NMR** (400 MHz, Chloroform- d) δ 7.40 (d, $J = 8.1$ Hz, 2H), 7.29 (d, $J = 8.1$ Hz, 2H), 6.16 – 5.80 (m, 1H), 4.90 (dd, $J = 9.8, 3.9$ Hz, 1H), 2.42 – 2.24 (m, 1H), 2.15 (m, 1H), 2.06 (s, 1H), 1.32 (s, 9H). **^{13}C NMR** (101 MHz, Chloroform- d) δ 151.48, 140.10, 125.87, 125.54, 116.23 (t, $J = 238.4$ Hz), 69.45 (dd, $J = 8.0, 5.5$ Hz), 43.13 (t, $J = 20.8$ Hz), 34.73, 31.44. **^{19}F NMR** (377 MHz, Chloroform- d) δ -115.80 – -120.12 (m).



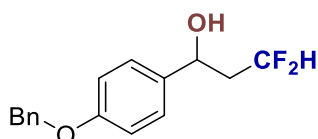
4-(3,3-difluoro-1-hydroxypropyl)phenyl acetate (11)⁷. Faint yellow liquid was obtained in 72% isolated yield. **^1H NMR** (400 MHz, Chloroform- d) δ 7.37 (d, $J = 8.5$ Hz, 2H), 7.09 (d, $J = 8.5$ Hz, 2H), 6.00 (tdd, $J = 56.7, 6.4, 3.3$ Hz, 1H), 4.93 (dt, $J = 9.8, 3.3$ Hz, 1H), 2.39 – 2.21 (m, 4H), 2.21 – 2.06 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform- d) δ 169.72, 150.48, 140.76, 126.90, 122.08, 116.03 (t, $J = 238.6$ Hz), 69.08 (dd, $J = 8.0, 5.5$ Hz), 43.27 (t, $J = 20.9$ Hz), 21.24. **^{19}F NMR** (377 MHz, Chloroform- d) δ -116.01 – -119.70 (m).



3,3-difluoro-1-(4-phenoxyphenyl)propan-1-ol (12). Colorless liquid was obtained in 71% isolated yield. **^1H NMR** (400 MHz, Chloroform- d) δ 7.39 – 7.27 (m, 4H), 7.15 – 7.08 (m, 1H), 7.05 – 6.96 (m, 4H), 5.99 (tdd, $J = 56.7, 6.3, 3.4$ Hz, 1H), 4.92 (dd, $J = 9.8, 3.8$ Hz, 1H), 2.33 (m, 1H), 2.23 – 2.06 (m, 2H). **^{13}C NMR** (101 MHz, Chloroform- d) δ 157.44, 156.99, 137.82, 129.96, 127.27, 123.70, 119.21, 119.03, 116.13 (t, $J = 238.5$ Hz), 69.19 (dd, $J = 7.9, 5.6$ Hz), 43.27 (t, $J = 20.8$ Hz). **^{19}F NMR** (377 MHz, Chloroform- d) δ -116.10 – -118.74 (m). **HRMS (ESI)** calcd for $\text{C}_{15}\text{H}_{13}\text{F}_2\text{O}^+$, $[\text{M}-\text{OH}]^+$ 247.0929, found 247.0921.

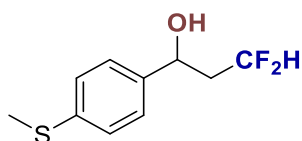


3,3-difluoro-1-(4-methoxyphenyl)propan-1-ol (13)⁶. Faint yellow liquid was obtained in 63% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.28 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.7 Hz, 2H), 5.96 (tdd, *J* = 56.8, 6.3, 3.5 Hz, 1H), 4.88 (dd, *J* = 9.7, 4.0 Hz, 1H), 3.81 (s, 3H), 2.33 (m, 1H), 2.21 – 2.07 (m, 1H), 2.05 (s, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 159.64, 135.26, 127.09, 116.22 (t, *J* = 238.5 Hz), 114.29, 69.25 (dd, *J* = 8.0, 5.7 Hz), 55.46, 43.22 (t, *J* = 20.7 Hz). ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -115.95 – -118.92 (m).

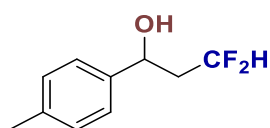


1-(4-(benzyloxy)phenyl)-3,3-difluoropropan-1-ol (14). Faint yellow liquid was obtained in 70% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.36 (m, 4H), 7.33 (m, 1H), 7.30 – 7.25 (m, 2H), 7.00 – 6.92 (m, 2H), 5.96 (tdd, *J* = 56.7, 6.3, 3.4 Hz, 1H), 5.06 (s, 2H), 4.87 (dd, *J* = 9.7, 4.0 Hz, 1H), 2.32 (m, 1H), 2.20 – 2.05 (m, 1H), 2.02 (s, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 158.72, 136.81, 135.42, 128.65, 128.07, 127.48, 127.01, 116.11 (t, *J* = 238.5 Hz), 115.13, 70.09, 69.13 (dd, *J* = 8.0, 5.7 Hz), 43.10 (t, *J* = 20.6 Hz). ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -115.48-119.03 (m).

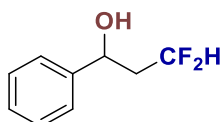
HRMS (ESI) calcd for C₁₆H₁₅F₂O⁺, [M-OH]⁺ 261.1086, found 261.1086.



3,3-difluoro-1-(4-(methylthio)phenyl)propan-1-ol (15). Faint yellow liquid was obtained in 53% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.27 (m, 4H), 5.99 (tt, *J* = 55.9, 4.6 Hz, 1H), 4.91 (dd, *J* = 9.8, 4.0 Hz, 1H), 2.49 (s, 3H), 2.42 – 1.93 (m, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 139.92, 138.78, 126.95, 126.31, 116.10 (t, *J* = 238.4 Hz), 69.49 – 69.10 (m), 43.22 (t, *J* = 20.8 Hz), 15.91. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -116.53 – -118.21 (m). **HRMS (ESI)** calcd for C₁₀H₁₁F₂S⁺, [M+H]⁺ 201.0544, found 201.0542.

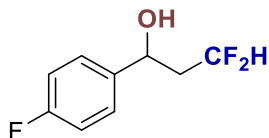


3,3-difluoro-1-(4-(methylthio)phenyl)propan-1-ol (16)⁶. Faint yellow liquid was obtained in 70% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.21 (m, 2H), 7.18 (d, *J* = 7.9 Hz, 2H), 5.98 (tdd, *J* = 56.8, 6.4, 3.4 Hz, 1H), 4.90 (dt, *J* = 9.7, 3.2 Hz, 1H), 2.43 – 2.23 (m, 4H), 2.14 (m, 1H), 2.00 (d, *J* = 3.0 Hz, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 140.06, 138.08, 129.49, 125.60, 116.09 (t, *J* = 238.4 Hz), 69.40 (dd, *J* = 8.0, 5.6 Hz), 43.12 (t, *J* = 20.7 Hz), 21.14. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -115.78 – -118.78 (m).

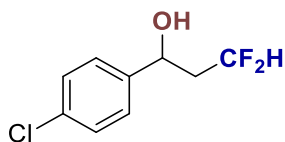


3,3-difluoro-1-phenylpropan-1-ol (17)⁶. Faint yellow liquid was obtained in 60% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.28 (m, 5H), 5.99 (tdd, *J* = 56.7, 6.3, 3.3 Hz, 1H), 4.93 (dd, *J* = 9.7, 3.9 Hz, 1H), 2.43 – 2.23 (m, 1H), 2.16 (m, 2H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 143.14, 128.95, 128.38, 125.75, 116.15 (t, *J* = 238.4 Hz), 69.66 (dd, *J* = 7.9, 5.5 Hz), 43.28 (t, *J* = 20.8 Hz).

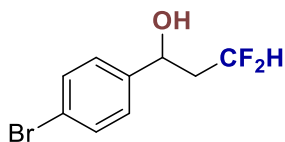
¹⁹F NMR (377 MHz, Chloroform-*d*) δ -116.25 – -118.19 (m).



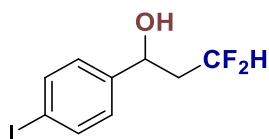
3,3-difluoro-1-(4-fluorophenyl)propan-1-ol (18)⁶. Faint yellow liquid was obtained in 70% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.33 (t, *J* = 6.6 Hz, 2H), 7.05 (t, *J* = 8.4 Hz, 2H), 5.98 (tt, *J* = 56.7, 4.4 Hz, 1H), 4.92 (dd, *J* = 9.3, 4.0 Hz, 1H), 2.40 – 2.02 (m, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 162.62 (d, *J* = 246.5 Hz), 138.94 (d, *J* = 3.2 Hz), 127.48 (d, *J* = 8.2 Hz), 116.02 (t, *J* = 238.4 Hz), 115.81 (d, *J* = 21.6 Hz), 68.96 (dd, *J* = 6.6 Hz), 43.33 (t, *J* = 20.8 Hz). ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -116.57 – -118.22 (m).



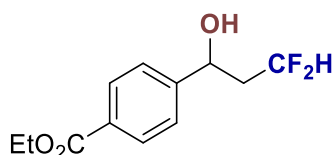
1-(4-chlorophenyl)-3,3-difluoropropan-1-ol (19)⁶. Faint yellow liquid was obtained in 71% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.33 (m, 4H), 6.00 (tdd, *J* = 56.7, 6.3, 3.3 Hz, 1H), 4.98 – 4.92 (m, 1H), 2.41 – 2.05 (m, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 141.64, 134.09, 129.12, 127.14, 115.94 (t, *J* = 238.4 Hz), δ 69.01 (dd, *J* = 7.9, 5.5 Hz), 43.31 (t, *J* = 20.9 Hz). ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -116.44 – -118.69 (m).



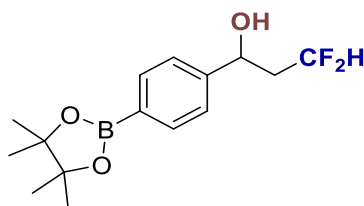
1-(4-bromophenyl)-3,3-difluoropropan-1-ol (20)⁶. Faint yellow liquid was obtained in 58% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.50 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 5.99 (tdd, *J* = 56.6, 6.3, 3.3 Hz, 1H), 4.91 (dt, *J* = 10.0, 2.8 Hz, 1H), 2.39 – 2.01 (m, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 142.14, 132.05, 127.46, 122.16, 115.91 (t, *J* = 238.7 Hz), 69.02 (dd, *J* = 7.8, 5.5 Hz), 43.22 (t, *J* = 20.9 Hz). ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -116.26 – -118.68 (m).



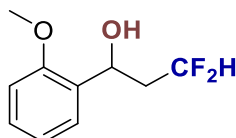
3,3-difluoro-1-(4-iodophenyl)propan-1-ol (21). Faint yellow liquid was obtained in 65% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.86 – 7.62 (m, 2H), 7.24 – 7.00 (m, 2H), 5.98 (tdd, *J* = 59.8, 56.6, 6.4, 3.4 Hz, 1H), 5.08 – 4.78 (m, 1H), 2.41 – 2.05 (m, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 142.79, 138.02, 127.67, 118.27, 115.90, 113.52, 93.78, 69.10 (dd, *J* = 7.8, 5.6 Hz), 43.18 (t, *J* = 20.9 Hz). ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -116.30 – -118.41 (m). HRMS (ESI) calcd for C₉H₈F₂I⁺, [M-OH]⁺ 280.9633, found 280.9638.



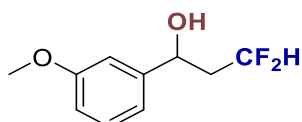
ethyl 4-(3,3-difluoro-1-hydroxypropyl)benzoate (22). Faint yellow liquid was obtained in 41% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.02 (d, J = 8.2 Hz, 2H), 7.43 (d, J = 8.1 Hz, 2H), 6.03 (tdd, J = 56.6, 6.4, 3.2 Hz, 1H), 5.01 (dt, J = 10.0, 3.1 Hz, 1H), 4.37 (q, J = 7.1 Hz, 2H), 2.47 (d, J = 3.3 Hz, 1H), 2.41 – 2.08 (m, 2H), 1.39 (t, J = 7.1 Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 166.46, 148.11, 130.35, 130.18, 125.62, 115.91 (t, J = 238.7 Hz), 69.40 – 69.04 (dd, J = 7.8, 5.5 Hz), 61.26, 43.25 (t, J = 21.0 Hz), 14.43. $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -116.39 – -118.38 (m). **HRMS (ESI)** calcd for $\text{C}_{12}\text{H}_{15}\text{F}_2\text{O}_3^+$, $[\text{M}+\text{H}]^+$ 245.0984, found 245.0980.



3,3-difluoro-1-(4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)propan-1-ol (23)⁶. Faint yellow liquid was obtained in 71% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.81 (d, J = 8.1 Hz, 2H), 7.36 (d, J = 7.9 Hz, 2H), 5.99 (tdd, J = 56.8, 6.4, 3.3 Hz, 1H), 4.95 (dd, J = 9.7, 3.7 Hz, 1H), 2.43 – 2.06 (m, 3H), 1.34 (s, 12H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 146.17, 135.42, 125.02, 116.09 (t, J = 238.7 Hz), 115.63, 84.08, 69.64 (dd, J = 7.9, 5.6 Hz), 43.25 (t, J = 20.9 Hz), 25.31 – 24.40 (m). $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -116.35 – -118.52 (m).

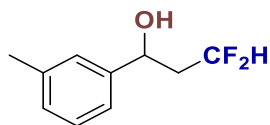


3,3-difluoro-1-(2-methoxyphenyl)propan-1-ol (24). Faint yellow liquid was obtained in 62% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.39 – 7.30 (m, 2H), 7.02 (td, J = 7.5, 1.1 Hz, 1H), 6.94 (dd, J = 8.2, 1.0 Hz, 1H), 6.08 (tdd, J = 57.0, 6.5, 3.3 Hz, 1H), 5.13 (dd, J = 9.7, 6.0, 3.8 Hz, 1H), 3.91 (s, 3H), 2.80 (d, J = 6.2 Hz, 1H), 2.56 – 2.19 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 156.53, 130.64, 129.16, 126.80, 121.11, 116.54 (t, J = 238.2 Hz), 110.74, 66.55 (dd, J = 8.5, 5.6 Hz), 55.43, 41.39 (t, J = 20.7 Hz). $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -116.01 – -118.31 (m). **HRMS (ESI)** calcd for $\text{C}_{10}\text{H}_{12}\text{F}_2\text{O}_2$, $[\text{M}]^+$ 202.0800, found 202.0796.

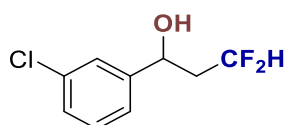


3,3-difluoro-1-(3-methoxyphenyl)propan-1-ol (25). Faint yellow liquid was obtained in 69% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.32 – 7.25 (m, 1H), 6.93 (dd, J = 8.5, 1.8 Hz, 2H), 6.85 (m, 1H), 5.99 (tdd, J = 56.8, 6.4, 3.4 Hz, 1H), 4.91 (dd, J = 9.7, 3.9 Hz, 1H), 3.81 (s, 3H), 2.41 – 2.06 (m, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 160.09, 144.84, 130.04, 117.94, 116.13 (t, J = 238.2 Hz), 113.74, 111.28, 69.59 (dd, J = 8.0, 5.6 Hz), 55.41, 43.26 (t, J = 20.8 Hz). $^{19}\text{F NMR}$ (377 MHz,

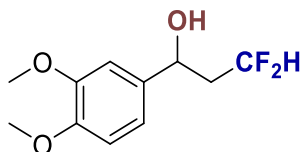
Chloroform-*d*) δ -116.18 – -118.54 (m). **HRMS (ESI)** calcd for $C_{10}H_{12}F_2O_2^+$, $[M]^+$ 202.0800, found 202.0798.



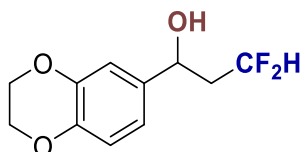
3,3-difluoro-1-(m-tolyl)propan-1-ol (26). Faint yellow liquid was obtained in 57% isolated yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.30 – 7.23 (m, 1H), 7.15 (dd, J = 16.8, 7.4 Hz, 3H), 5.99 (tdd, J = 56.7, 6.3, 3.4 Hz, 1H), 4.91 (dt, J = 9.7, 3.1 Hz, 1H), 2.42 – 2.08 (m, 5H), 2.03 (d, J = 3.3 Hz, 1H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 143.11, 138.74, 129.13, 128.87, 126.44, 122.79, 116.21 (t, J = 238.2 Hz), δ 69.70 (dd, J = 7.9, 5.6 Hz), 43.28 (t, J = 20.8 Hz), 21.58. **¹⁹F NMR** (377 MHz, Chloroform-*d*) δ -116.53 – -118.20 (m). **HRMS (ESI)** calcd for $C_{10}H_{11}F_2^+$, $[M-OH]^+$ 169.0823, found 169.0821.



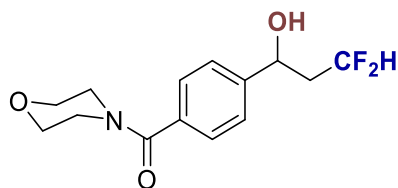
1-(3-chlorophenyl)-3,3-difluoropropan-1-ol (27)⁷. Faint yellow liquid was obtained in 45% isolated yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.45 – 7.19 (m, 4H), 6.01 (tdd, J = 59.6, 56.5, 5.7, 2.5 Hz, 1H), 5.08 – 4.81 (m, 1H), 2.44 – 2.01 (m, 3H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 145.22, 134.92, 130.26, 128.50, 125.99, 123.88, 118.27, 115.90, 113.53, 69.07 (dd, J = 7.9, 5.5 Hz), 43.28 (t, J = 21.0 Hz). **¹⁹F NMR** (377 MHz, Chloroform-*d*) δ -116.64 – -118.30 (m).



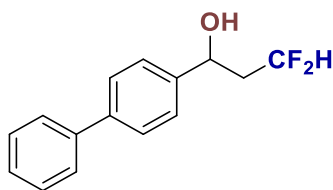
1-(3,4-dimethoxyphenyl)-3,3-difluoropropan-1-ol (28). Colorless liquid was obtained in 78% isolated yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 6.96 – 6.79 (m, 3H), 5.97 (tdd, J = 56.8, 6.3, 3.5 Hz, 1H), 4.88 (dd, J = 9.6, 4.0 Hz, 1H), 3.88 (d, J = 5.6 Hz, 6H), 2.43 – 2.06 (m, 3H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 149.38, 148.99, 135.78, 118.00, 116.18 (t, J = 238.6 Hz), 111.25, 108.75, 69.47 (dd, J = 7.9, 5.7 Hz), 56.07, 56.01, 43.29 (t, J = 20.7 Hz). **¹⁹F NMR** (377 MHz, Chloroform-*d*) δ -116.35 – -118.29 (m). **HRMS (ESI)** calcd for $C_{11}H_{14}F_2O_3^+$, $[M]^+$ 232.0906, found 232.0912.



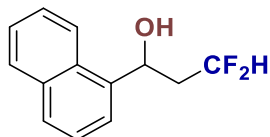
1-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-3,3-difluoropropan-1-ol (29). Colorless liquid was obtained in 74% isolated yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 6.93 – 6.76 (m, 3H), 5.96 (tdd, J = 56.8, 6.3, 3.5 Hz, 1H), 4.81 (dd, J = 9.5, 4.1 Hz, 1H), 4.25 (s, 4H), 2.41 – 1.89 (m, 3H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 143.80, 143.56, 136.52, 118.79, 117.66, 116.18 (t, J = 238.6 Hz), 114.77, 69.19 (dd, J = 8.0, 5.7 Hz), 64.49, 64.47, 43.16 (t, J = 20.7 Hz). **¹⁹F NMR** (377 MHz, Chloroform-*d*) δ -116.37 – -118.40 (m). **HRMS (ESI)** calcd for $C_{11}H_{12}F_2O_3^+$, $[M]^+$ 230.0749, found 230.0755.



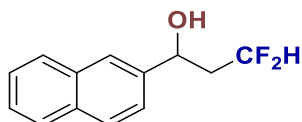
(4-(3,3-difluoro-1-hydroxypropyl)phenyl)(morpholino)methanone (30). Faint yellow solid was obtained in 50% isolated yield. $^1\text{H NMR}$ (400 MHz, DMSO- d_6) δ 7.47 (d, J = 8.0 Hz, 2H), 7.41 (d, J = 8.0 Hz, 2H), 6.16 (tdd, J = 56.9, 6.4, 3.4 Hz, 1H), 5.74 (d, J = 4.7 Hz, 1H), 4.80 (dt, J = 9.2, 4.5 Hz, 1H), 3.61 (s, 6H), 3.40 (s, 2H), 2.19 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, DMSO- d_6) δ 169.46, 146.56, 134.89, 127.55, 126.20, 117.19 (t, J = 237.0 Hz), 67.70 (dd, J = 8.7, 4.8 Hz), 66.55, 43.30 (t, J = 20.0 Hz). $^{19}\text{F NMR}$ (377 MHz, DMSO- d_6) δ -114.35 – -117.65 (m). **HRMS (ESI)** calcd for $\text{C}_{14}\text{H}_{18}\text{F}_2\text{NO}_3^+$, $[\text{M}+\text{H}]^+$ 286.1249, found 286.1241.



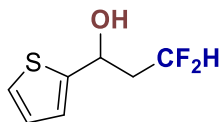
1-([1,1'-biphenyl]-4-yl)-3,3-difluoropropan-1-ol (31)⁷. White solid was obtained in 80% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform- d) δ 7.62 – 7.53 (m, 4H), 7.43 (dt, J = 8.2, 6.8 Hz, 4H), 7.38 – 7.31 (m, 1H), 6.01 (tdd, J = 56.7, 6.4, 3.4 Hz, 1H), 4.96 (dd, J = 9.7, 3.9 Hz, 1H), 2.45 – 2.08 (m, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform- d) δ 142.05, 141.33, 140.63, 128.96, 127.66, 127.62, 127.21, 126.21, 116.14 (t, J = 238.5 Hz), 69.41 (dd, J = 7.9, 5.5 Hz), 43.21 (t, J = 20.8 Hz). $^{19}\text{F NMR}$ (377 MHz, Chloroform- d) δ -110.15 – -123.26 (m).



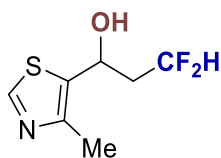
3,3-difluoro-1-(naphthalen-1-yl)propan-1-ol (32). Faint yellow liquid was obtained in 47% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform- d) δ 8.05 (dd, J = 8.4, 1.4 Hz, 1H), 7.89 (dd, J = 7.8, 1.7 Hz, 1H), 7.81 (d, J = 8.2 Hz, 1H), 7.68 (d, J = 7.1 Hz, 1H), 7.60 – 7.44 (m, 3H), 6.16 (tdd, J = 56.7, 6.3, 3.4 Hz, 1H), 5.84 – 5.66 (m, 1H), 2.51 – 2.30 (m, 2H), 2.17 (d, J = 3.2 Hz, 1H). $^{13}\text{C NMR}$ (101 MHz, Chloroform- d) δ 138.75, 133.94, 129.90, 129.21, 128.75, 126.68, 126.00, 125.61, 122.81, 122.65, 116.43 (t, J = 238.6 Hz), 66.43 (dd, J = 9.2, 4.4 Hz), 42.68 (t, J = 20.8 Hz). $^{19}\text{F NMR}$ (377 MHz, Chloroform- d) δ -116.19 – -118.98 (m). **HRMS (ESI)** calcd for $\text{C}_{13}\text{H}_{11}\text{F}_2^+$, $[\text{M}-\text{OH}]^+$ 205.0823, found 205.0826.



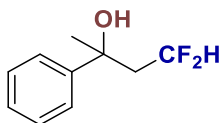
3,3-difluoro-1-(naphthalen-2-yl)propan-1-ol (33). Faint yellow liquid was obtained in 67% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform- d) δ 7.98 – 7.70 (m, 1H), 7.57 – 7.36 (m, 1H), 6.01 (tdd, J = 56.7, 6.3, 3.4 Hz, 0H), 5.16 – 5.01 (m, 0H), 2.57 – 2.14 (m, 1H). $^{13}\text{C NMR}$ (101 MHz, Chloroform- d) δ 140.41, 133.37, 133.32, 128.92, 128.12, 127.88, 126.61, 126.40, 124.66, 123.55, 118.53, 116.16, 113.79, 69.79 (dd, J = 7.9, 5.7 Hz), 43.20 (t, J = 20.8 Hz). $^{19}\text{F NMR}$ (377 MHz, Chloroform- d) δ -116.42 – -118.07 (m). $\text{C}_{13}\text{H}_{11}\text{F}_2^+$, $[\text{M}-\text{OH}]^+$ 205.0823, found 205.0825.



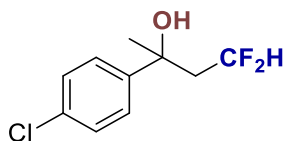
3,3-difluoro-1-(thiophen-2-yl)propan-1-ol (34). Colorless liquid was obtained in 60% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.38 – 7.20 (m, 1H), 7.14 – 6.90 (m, 2H), 5.98 (tdd, J = 56.6, 6.3, 3.5 Hz, 1H), 5.27 – 5.09 (m, 1H), 2.66 – 2.16 (m, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 146.79, 127.04, 125.46, 124.31, 118.18, 115.81, 113.44, 65.49 (dd, J = 8.4, 6.1 Hz), 43.41 (t, J = 21.2 Hz). $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -116.86 – -118.51 (m). **HRMS (ESI)** calcd for $\text{C}_7\text{H}_7\text{F}_2\text{S}^+$, $[\text{M}-\text{OH}]^+$ 161.0231, found 161.0228.



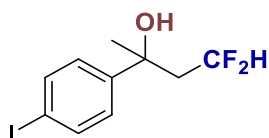
3,3-difluoro-1-(4-methylthiazol-5-yl)propan-1-ol (35). Colorless liquid was obtained in 79% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 8.59 (s, 1H), 6.00 (tdd, J = 56.6, 6.3, 3.3 Hz, 1H), 5.25 (dd, J = 9.6, 4.1 Hz, 1H), 3.84 (s, 1H), 2.35 (m, 4H), 2.27 – 2.07 (m, 1H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 151.53, 148.45, 135.23, 115.48 (t, J = 238.8 Hz), 62.63 (dd, J = 8.8, 5.7 Hz), 43.45 (t, J = 21.3 Hz), 15.07. $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -116.99 – -118.86 (m). **HRMS (ESI)** calcd for $\text{C}_7\text{H}_{10}\text{F}_2\text{NOS}^+$, $[\text{M}+\text{H}]^+$ 194.0446, found 194.0440.



4,4-difluoro-2-phenylbutan-2-ol (36)⁶. Colorless liquid was obtained in 47% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.47 – 7.42 (m, 2H), 7.38 (m, 2H), 7.29 (m, 1H), 5.80 (tdd, J = 56.3, 5.6, 3.8 Hz, 1H), 2.38 (m, 2H), 2.11 (s, 1H), 1.64 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 146.62, 128.72, 127.43, 124.50, 116.40 (t, J = 238.1 Hz), 72.41, 47.56 (t, J = 19.9 Hz), 30.66. $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -112.86 – -112.87(m).

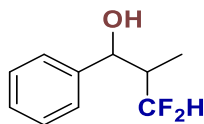


2-(4-chlorophenyl)-4,4-difluorobutan-2-ol (37). Colorless liquid was obtained in 68% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.37 (m, 4H), 5.80 (tdd, J = 56.2, 5.4, 4.0 Hz, 1H), 2.44 – 2.27 (m, 2H), 2.12 (s, 1H), 1.62 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 145.09, 133.26, 128.79, 126.09, 116.15 (t, J = 238.4 Hz), 72.16 (t, J = 5.9 Hz), 47.40 (t, J = 20.0 Hz), 30.74. $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -112.93. **HRMS (ESI)** calcd for $\text{C}_{10}\text{H}_{10}\text{ClF}_2^+$, $[\text{M}-\text{OH}]^+$ 203.434, found 203.0437.

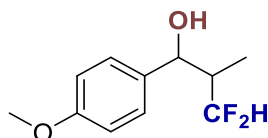


4,4-difluoro-2-(4-iodophenyl)butan-2-ol (38). Colorless liquid was obtained in 66% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.73 – 7.66 (m, 2H), 7.22 – 7.16 (m, 2H), 5.80 (tdd, J = 56.2, 5.3, 4.0

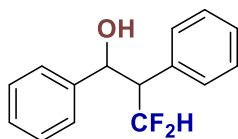
Hz, 1H), 2.42 – 2.26 (m, 2H), 2.11 (t, $J = 1.5$ Hz, 1H), 1.61 (s, 3H). ^{13}C NMR (101 MHz, Chloroform- d) δ 146.40, 137.74, 126.71, 116.13 (t, $J = 238.4$ Hz), 93.00, 72.24 (t, $J = 5.8$ Hz), 47.35 (t, $J = 20.0$ Hz), 30.64. ^{19}F NMR (377 MHz, Chloroform- d) δ -112.88. HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{17}\text{O}_2^+$, $[\text{M}+\text{H}]^+$ 193.1223, found 193.1217. HRMS (ESI) calcd for $\text{C}_{10}\text{H}_{10}\text{F}_2\text{I}^+$, $[\text{M}-\text{OH}]^+$ 294.9790, found 294.9787.



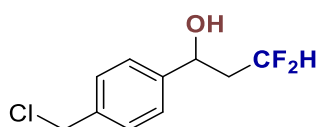
3,3-difluoro-2-methyl-1-phenylpropan-1-ol (39)⁶. Faint yellow liquid was obtained in 40% isolated yield. dr = 3:2. ^1H NMR (400 MHz, Chloroform- d) δ 7.50 – 7.28 (m, 5H), 6.19 (td, $J = 57.1$, 2.2 Hz, 0.6H), 5.69 (td, $J = 56.8$, 5.0 Hz, 0.42H), 4.94 (dd, $J = 4.7$, 2.2 Hz, 0.4H), 4.55 (d, $J = 9.5$ Hz, 0.59H), 2.47 – 1.89 (m, 2.05H), 1.00 (d, $J = 7.0$ Hz, 1.25H), 0.76 (d, $J = 7.0$ Hz, 1.8H). ^{13}C NMR (101 MHz, Chloroform- d) δ 142.04, 128.84, 128.66, 128.55, 127.94, 126.88, 125.99, 118.37 (t, $J = 242.4$ Hz), 117.34, 117.32 (t, $J = 242.4$ Hz), 75.11 (dd, $J = 8.1$, 2.1 Hz), 72.46 (t, $J = 5.8$ Hz), 44.91 (t, $J = 18.8$ Hz), 44.19 (t, $J = 18.8$ Hz), 7.86 (t, $J = 5.05$ Hz), 6.74 (dd, $J = 5.7$, 3.9 Hz). ^{19}F NMR (377 MHz, Chloroform- d) δ -119.23 – -133.77 (m).



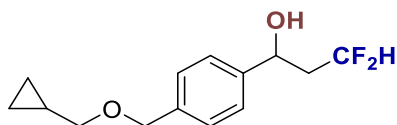
3,3-difluoro-1-(4-methoxyphenyl)-2-methylpropan-1-ol (40). Faint yellow liquid was obtained in 65% isolated yield. dr = 3:2. ^1H NMR (400 MHz, Chloroform- d) δ 7.24 (dd, $J = 8.8$, 2.7 Hz, 2H), 6.89 (d, $J = 8.3$ Hz, 2H), 6.18 (td, $J = 57.2$, 2.1 Hz, 0.6H), 5.64 (td, $J = 56.8$, 4.7 Hz, 0.4H), 4.85 (d, $J = 5.0$ Hz, 0.4H), 4.50 (d, $J = 9.6$ Hz, 0.6H), 3.80 (s, 3H), 2.47 – 1.79 (m, 2H), 1.03 (d, $J = 6.9$ Hz, 1H), 0.74 (d, $J = 7.0$ Hz, 2H). ^{13}C NMR (101 MHz, Chloroform- d) δ 159.71, 159.32, 134.24, 134.11, 128.26, 128.07, 127.62, 127.24, 118.28 (t, $J = 242.4$ Hz), 117.40 (dd, $J = 241.39$, 2.02 Hz), 114.29, 114.17, 114.05, 74.64 (dd, $J = 8.2$, 2.0 Hz), 72.43 – 72.25 (dd, $J = 8.2$, 2.0 Hz), 55.42, 51.32, 44.98 (t, $J = 18.7$ Hz), 44.57 – 43.67 (t, $J = 18.7$ Hz), 7.84 (t, $J = 4.7$ Hz), 6.92 (dd, $J = 5.5$, 4.1 Hz). ^{19}F NMR (377 MHz, Chloroform- d) δ -120.06 – -133.90 (m). HRMS (ESI) calcd for $\text{C}_{11}\text{H}_{13}\text{F}_2\text{O}^+$, $[\text{M}-\text{OH}]^+$ 199.0929, found 199.0931.



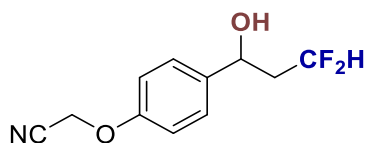
3,3-difluoro-1,2-diphenylpropan-1-ol (41)⁶. Colorless liquid was obtained in 35% isolated yield. dr > 10:1. ^1H NMR (400 MHz, Chloroform- d) δ 7.23 – 7.03 (m, 10H), 6.45 (td, $J = 56.5$, 2.8 Hz, 1H), 5.14 (dd, $J = 9.7$, 2.3 Hz, 1H), 3.40 (m, 1H), 2.23 (d, $J = 3.0$ Hz, 1H). ^{13}C NMR (101 MHz, Chloroform- d) δ 141.57, 133.54, 130.10 (d, $J = 1.7$ Hz), 128.44, 128.33, 128.22, 127.71, 126.82, 116.63 (dd, $J = 244.1$, 241.3 Hz), 74.76 (dd, $J = 6.5$, 2.9 Hz), 56.80 (t, $J = 19.2$ Hz). ^{19}F NMR (377 MHz, Chloroform- d) δ -121.30 – -125.91 (m).



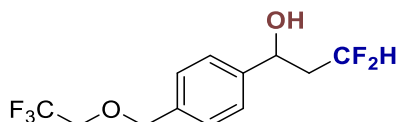
1-(4-(chloromethyl)phenyl)-3,3-difluoropropan-1-ol (42). Faint yellow liquid was obtained in 55% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.39 (q, J = 8.3 Hz, 4H), 6.00 (tdd, J = 56.7, 6.3, 3.3 Hz, 1H), 4.96 (dd, J = 9.7, 3.8 Hz, 1H), 4.59 (s, 2H), 2.41 – 2.04 (m, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 143.42, 137.65, 129.20, 126.17, 116.03 (t, J = 238.6 Hz), 69.30 (dd, J = 8.0, 5.5 Hz), 45.90, 43.25 (t, J = 20.8 Hz). $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -113.71 – -120.82 (m). **HRMS (ESI)** calcd for $\text{C}_{10}\text{H}_{10}\text{ClF}_2^+$, $[\text{M}-\text{OH}]^+$ 203.434, found 203.0437.



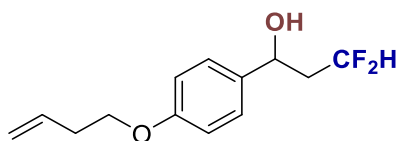
1-(4-((cyclopropylmethoxy)methyl)phenyl)-3,3-difluoropropan-1-ol (43). Colorless liquid was obtained in 71% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.37 – 7.30 (m, 4H), 5.97 (tdd, J = 56.8, 6.4, 3.4 Hz, 1H), 4.90 (dt, J = 9.6, 3.0 Hz, 1H), 4.51 (s, 2H), 3.30 (d, J = 6.9 Hz, 2H), 2.39 – 2.01 (m, 3H), 1.17 – 0.99 (m, 1H), 0.65 – 0.43 (m, 2H), 0.20 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 142.51, 138.71, 128.25, 125.78, 116.14 (t, J = 238.4 Hz), 75.21, 72.25, 69.36 (dd, J = 8.0, 5.5 Hz), 43.27 (t, J = 20.8 Hz), 10.71, 3.18. $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -116.41 – -118.33 (m). **HRMS (ESI)** calcd for $\text{C}_{14}\text{H}_{17}\text{F}_2\text{O}^+$, $[\text{M}+\text{H}]^+$ 239.1242, found 239.1234.



2-(4-(3,3-difluoro-1-hydroxypropyl)phenoxy)acetonitrile (44). Faint yellow liquid was obtained in 53% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.40 – 7.32 (m, 2H), 7.03 – 6.94 (m, 2H), 5.99 (tdd, J = 56.6, 6.3, 3.4 Hz, 1H), 4.93 (dd, J = 9.7, 3.8 Hz, 1H), 4.77 (s, 2H), 2.41 – 2.05 (m, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 156.42, 137.99, 127.44, 116.06 (t, J = 238.4 Hz), 115.41, 115.11, 68.98 (dd, J = 7.9, 5.7 Hz), 53.78, 43.28 (t, J = 20.8 Hz). $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -116.01 – -118.73 (m). **HRMS (ESI)** calcd for $\text{C}_{11}\text{H}_{10}\text{F}_2\text{NO}^+$, $[\text{M}-\text{OH}]^+$ 210.0725, found 210.0724.

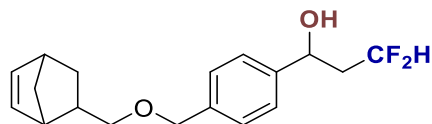


3,3-difluoro-1-(4-((2,2,2-trifluoroethoxy)methyl)phenyl)propan-1-ol (45). Faint yellow liquid was obtained in 65% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.36 (s, 4H), 5.98 (tdd, J = 56.7, 6.3, 3.3 Hz, 1H), 4.93 (dd, J = 10.1, 3.5 Hz, 1H), 4.67 (s, 2H), 3.83 (q, J = 8.7 Hz, 2H), 2.43 – 2.04 (m, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 143.29, 136.69, 128.43, 126.04, 124.16 (q, J = 279.777 Hz), 116.07 (t, J = 238.5 Hz), 73.85, 69.33 (dd, J = 7.9, 5.6 Hz), 67.40 (q, J = 34.2 Hz), 43.26 (t, J = 20.8 Hz). $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -73.89, -116.53 – -118.19 (m). **HRMS (ESI)** calcd for $\text{C}_{12}\text{H}_{12}\text{F}_5\text{O}^+$, $[\text{M}-\text{OH}]^+$ 267.0803, found 267.0796.

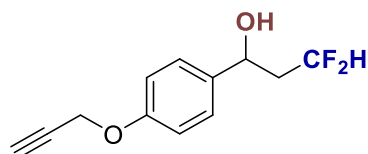


1-(4-(but-3-en-1-yloxy)phenyl)-3,3-difluoropropan-1-ol (46). Faint yellow liquid was obtained in 41% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.27 (d, J = 8.1 Hz, 2H), 6.90 (d, J = 7.9 Hz, 2H),

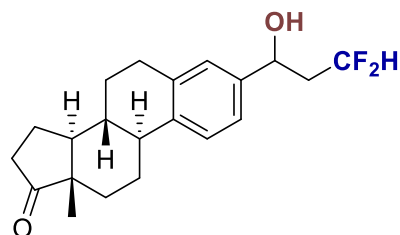
6.18 – 5.63 (m, 2H), 5.31 – 4.39 (m, 3H), 4.26 – 3.84 (m, 2H), 2.61 – 1.72 (m, 5H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 159.00, 135.27, 134.46, 127.07, 117.25, 116.23 (t, J = 238.5 Hz), 114.94, 69.28, 67.44, 43.22 (t, J = 20.7 Hz), 33.73. **¹⁹F NMR** (377 MHz, Chloroform-*d*) δ -116.49 – -118.18 (m). **HRMS (ESI)** calcd for C₁₃H₁₅F₂O⁺, [M-OH]⁺ 225.1086, found 225.1084.



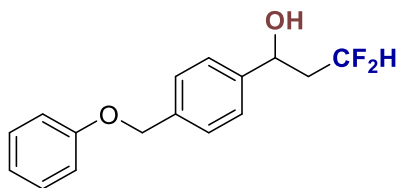
1-(4-((bicyclo[2.2.1]hept-5-en-2-ylmethoxy)methyl)phenyl)-3,3-difluoropropan-1-ol (47). Colorless solid was obtained in 66% isolated yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.47 – 7.27 (m, 4H), 6.24 – 5.75 (m, 3H), 4.92 (dd, J = 10.5, 3.8 Hz, 1H), 4.65 – 4.31 (m, 2H), 3.69 – 2.61 (m, 4H), 2.49 – 2.02 (m, 3H), 1.96 – 1.56 (m, 1H), 1.49 – 1.02 (m, 4H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 142.44, 142.39, 139.01, 138.90, 137.35, 136.81, 136.68, 132.49, 129.18, 128.18, 128.15, 126.16, 125.81, 125.76, 116.14 (t, J = 238.5 Hz), 75.29, 74.35, 72.74, 72.64, 69.44 (dd, J = 7.9, 5.6 Hz), 49.53, 45.14, 44.10, 43.86, 43.28 (t, J = 20.8 Hz), 42.31, 41.66, 39.02, 38.91, 29.87, 29.27. **¹⁹F NMR** (377 MHz, Chloroform-*d*) δ -116.42 – -118.28 (m). **HRMS (ESI)** calcd for C₁₈H₂₃F₂O₂⁺, [M+H]⁺ 309.1661, found 309.1661.



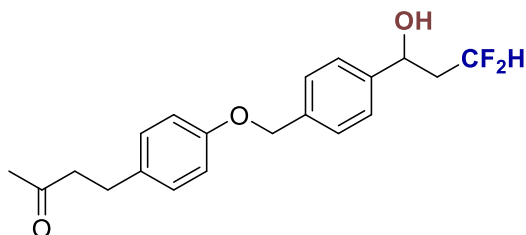
3,3-difluoro-1-(4-(prop-2-yn-1-yloxy)phenyl)propan-1-ol (48). Yellow liquid was obtained in 45% isolated yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.31 (d, J = 8.7 Hz, 2H), 6.98 (d, J = 8.7 Hz, 2H), 5.98 (tdd, J = 56.8, 6.3, 3.4 Hz, 1H), 4.90 (dd, J = 9.6, 4.0 Hz, 1H), 4.70 (d, J = 2.4 Hz, 2H), 2.53 (t, J = 2.4 Hz, 1H), 2.42 – 2.23 (m, 1H), 2.22 – 2.06 (m, 1H), 2.00 (s, 1H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 157.56, 136.23, 127.10, 116.18 (t, J = 238.4 Hz), 115.31, 78.51, 75.82, 69.25 (dd, J = 7.9, 5.6 Hz), 55.98, 43.24 (t, J = 20.6 Hz). **¹⁹F NMR** (377 MHz, Chloroform-*d*) δ -116.48 – -118.30 (m). **HRMS (ESI)** calcd for C₁₂H₁₁F₂O⁺, [M+H]⁺ 209.0773, found 209.0774.



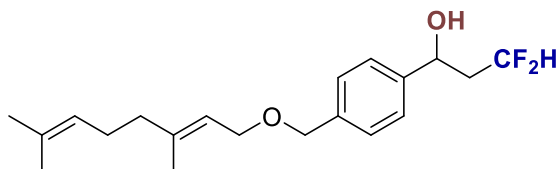
(8R,9S,13S,14S)-3-(3,3-difluoro-1-hydroxypropyl)-13-methyl-6,7,8,9,11,12,13,14,15,16-decahydro-17H-cyclopenta[a]phenanthren-17-one (49). Faint yellow solid was obtained in 65% isolated yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.30 (d, J = 8.0 Hz, 1H), 7.17 – 7.07 (m, 2H), 5.99 (tdd, J = 56.8, 6.4, 3.3 Hz, 1H), 4.87 (dd, J = 9.8, 3.8 Hz, 1H), 2.92 (dd, J = 9.0, 4.2 Hz, 2H), 2.58 – 2.38 (m, 2H), 2.38 – 2.22 (m, 3H), 2.21 – 1.99 (m, 4H), 1.99 – 1.90 (m, 1H), 1.72 – 1.38 (m, 6H), 0.90 (s, 3H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 140.67, 139.90, 137.13, 126.38, 126.36, 125.91, 123.17, 123.15, 116.21 (t, J = 238.4 Hz), 69.31 (dd, J = 7.9, 5.6 Hz), 69.30 (dd, J = 7.9, 5.6 Hz), 50.57, 48.08, 44.46, 43.17 (t, J = 20.6 Hz), 43.15 (t, J = 20.6 Hz), 38.19 (d, J = 1.3 Hz), 35.94, 31.65, 29.55, 29.51, 26.53, 25.82, 21.68, 13.91. **¹⁹F NMR** (377 MHz, Chloroform-*d*) δ -116.06 – -118.34 (m). **HRMS (ESI)** calcd for C₂₁H₂₅F₂O⁺, [M-OH]⁺ 331.1868, found 331.1867.



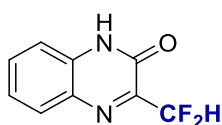
3,3-difluoro-1-(4-(benzoxymethyl)phenyl)propan-1-ol (50). Colorless solid was obtained in 80% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.44 (d, J = 8.2 Hz, 2H), 7.37 (d, J = 8.2 Hz, 2H), 7.29 (m, 2H), 6.96 (m, 3H), 5.99 (tdd, J = 56.8, 6.4, 3.4 Hz, 1H), 5.05 (s, 2H), 4.94 (dt, J = 9.6, 2.8 Hz, 1H), 2.43 – 2.03 (m, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 158.75, 142.88, 137.28, 129.65, 128.07, 126.01, 121.19, 116.10 (t, J = 238.5 Hz), 114.94, 69.61, 69.40 (dd, J = 8.0, 5.5 Hz), 43.25 (t, J = 20.8 Hz). $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -116.38 – -118.33 (m). **HRMS (ESI)** calcd for $\text{C}_{16}\text{H}_{16}\text{F}_2\text{O}_2$, $[\text{M}]^+$ 278.1113, found 278.1108.



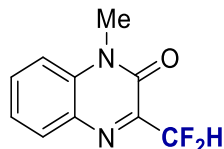
4-(4-((4-(3,3-difluoro-1-hydroxypropyl)benzyl)oxy)phenyl)butan-2-one (51). Colorless solid was obtained in 66% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.49 – 7.31 (m, 4H), 7.14 – 7.03 (m, 2H), 6.95 – 6.81 (m, 2H), 6.00 (tdd, J = 56.8, 6.4, 3.3 Hz, 1H), 5.02 (s, 2H), 4.94 (dd, J = 9.7, 3.8 Hz, 1H), 2.87 – 2.66 (m, 4H), 2.30 (m, 2H), 2.12 (m, 4H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 208.47, 157.17, 142.92, 137.28, 133.54, 129.40, 128.02, 125.99, 116.10 (t, J = 238.5 Hz), 114.96, 69.75, 69.35 (dd, J = 7.9, 5.4 Hz), 45.49, 43.28 (t, J = 20.8 Hz), 30.21, 28.98. $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -115.42 – -119.37 (m). **HRMS (ESI)** calcd for $\text{C}_{20}\text{H}_{26}\text{F}_2\text{O}_3\text{N}^+$, $[\text{M}+\text{NH}_4]^+$ 366.1875, found 366.1876.



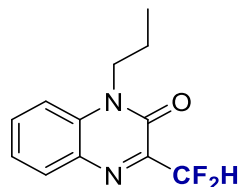
(E)-1-(4-(((3,7-dimethylocta-2,6-dien-1-yl)oxy)methyl)phenyl)-3,3-difluoropropan-1-ol (52). Faint yellow liquid was obtained in 65% isolated yield. $^1\text{H NMR}$ (400 MHz, Chloroform-*d*) δ 7.46 – 7.29 (m, 4H), 5.97 (tdd, J = 56.8, 6.4, 3.4 Hz, 1H), 5.38 (ddt, J = 6.8, 5.4, 1.3 Hz, 1H), 5.10 (tt, J = 6.6, 1.6 Hz, 1H), 4.90 (dt, J = 9.8, 2.8 Hz, 1H), 4.48 (s, 2H), 4.03 (d, J = 6.8 Hz, 2H), 2.40 – 2.21 (m, 2H), 2.20 – 2.01 (m, 5H), 1.68 (d, J = 1.5 Hz, 3H), 1.64 (d, J = 1.3 Hz, 3H), 1.60 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, Chloroform-*d*) δ 142.50, 140.76, 138.77, 131.83, 128.38, 125.76, 124.08, 120.75, 116.14 (t, J = 238.4 Hz), 71.61, 69.39 (dd, J = 8.0, 5.5 Hz), 66.85, 43.29 (t, J = 20.8 Hz), 39.72, 26.48, 25.83, 17.82, 16.62. $^{19}\text{F NMR}$ (377 MHz, Chloroform-*d*) δ -115.25 – -119.85 (m). **HRMS (ESI)** calcd for $\text{C}_{20}\text{H}_{29}\text{F}_2\text{O}_2^+$, $[\text{M}+\text{H}]^+$ 339.2130, found 339.2134.



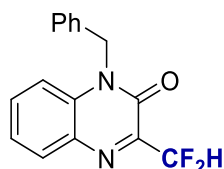
3-(difluoromethyl)quinoxalin-2(1H)-one (53)⁸. Faint yellow solid was obtained in 65% isolated yield. ¹H NMR (400 MHz, DMSO-*d*₆) δ 12.87 (s, 1H), 7.93 – 7.84 (m, 1H), 7.66 (td, *J* = 7.8, 1.4 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.07 (t, *J* = 53.3 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 153.67, 150.20 (t, *J* = 20.8 Hz), 133.32, 132.76, 131.16, 129.95, 124.37, 116.25, 110.82 (t, *J* = 239.3 Hz). ¹⁹F NMR (377 MHz, DMSO-*d*₆) δ -124.31.



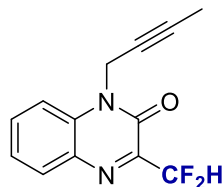
3-(difluoromethyl)-1-methylquinoxalin-2(1H)-one (54)⁸. White solid was obtained in 70% isolated yield. ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.95 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.79 (m, 1H), 7.67 (dd, *J* = 8.5, 1.1 Hz, 1H), 7.53 – 7.43 (m, 1H), 7.12 (t, *J* = 53.2 Hz, 1H), 3.67 (s, 3H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 153.14 (t, *J* = 2.2 Hz), 148.71 (t, *J* = 21.6 Hz), 134.48, 133.06, 131.53, 130.78, 124.57, 115.67, 110.91 (t, *J* = 239.6 Hz), 29.36. ¹⁹F NMR (377 MHz, DMSO-*d*₆) δ -124.26.



3-(difluoromethyl)-1-propylquinoxalin-2(1H)-one (55)⁸. Faint yellow solid was obtained in 60% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.01 (d, *J* = 8.0 Hz, 1H), 7.68 (t, *J* = 7.9 Hz, 1H), 7.48 – 7.32 (m, 2H), 6.98 (t, *J* = 53.7 Hz, 1H), 4.25 (t, *J* = 7.9 Hz, 2H), 1.82 (m, 2H), 1.07 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 153.17, 148.76, 133.43, 132.65, 132.31, 131.81, 124.31, 114.10, 110.14 (t, *J* = 241.8 Hz), 43.94, 20.79, 11.47. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -124.35.

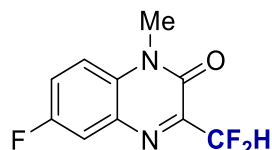


1-benzyl-3-(difluoromethyl)quinoxalin-2(1H)-one (56)⁸. White solid was obtained in 62% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.04 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.65 – 7.53 (m, 1H), 7.48 – 7.24 (m, 7H), 7.06 (t, *J* = 53.7 Hz, 1H), 5.55 (s, 2H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 153.38, 148.78 (t, *J* = 22.5 Hz), 134.55, 133.41, 132.65, 132.21, 131.58, 129.09, 128.03, 126.96, 124.46, 114.78, 110.05 (t, *J* = 241.8 Hz), 45.88. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -124.16.

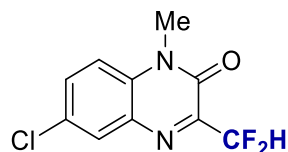


1-(but-2-yn-1-yl)-3-(difluoromethyl)quinoxalin-2(1H)-one (57). Faint yellow solid was obtained in 51% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.01 (d, *J* = 8.0 Hz, 1H), 7.72 (t, *J* = 7.9 Hz, 1H), 7.56 (d, *J* = 8.5 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H), 6.96 (t, *J* = 53.7 Hz, 1H), 5.09 – 4.93 (s, 2H), 1.87 – 1.70 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 152.43, 148.74 (t, *J* = 22.5 Hz), 132.86, 132.77,

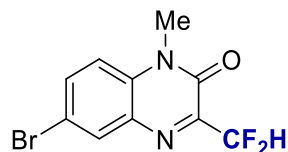
132.24, 131.56, 124.67, 114.89, 110.09 (t, $J = 241.8$ Hz), 81.91, 71.57, 32.11, 3.68. **^{19}F NMR** (377 MHz, Chloroform- d) δ -124.26. **HRMS (ESI)** calcd for $\text{C}_{13}\text{H}_{10}\text{F}_2\text{N}_2\text{O}_1^+$, $[\text{M}+\text{H}]^+$ 249.0834, found 249.0829.



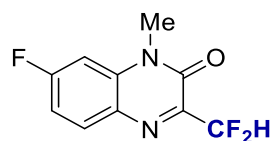
3-(difluoromethyl)-6-fluoro-1-methylquinoxalin-2(1H)-one (58)⁸. Faint yellow solid was obtained in 65% isolated yield. **^1H NMR** (400 MHz, Chloroform- d) δ 7.70 (dd, $J = 8.3, 2.9$ Hz, 1H), 7.46 (m, 1H), 7.37 (m, 1H), 6.95 (t, $J = 53.6$ Hz, 1H), 3.75 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform- d) δ 158.99 (d, $J = 245.8$ Hz), 152.96, 150.15 (t, $J = 22.22$ Hz), 132.51 (d, $J = 11.2$ Hz), 130.88, 120.79 (d, $J = 24.1$ Hz), 116.77 (d, $J = 22.5$ Hz), 115.35 (d, $J = 8.7$ Hz), 110.00 (t, $J = 242.1$ Hz), 29.41. **^{19}F NMR** (377 MHz, Chloroform- d) δ -117.26, -124.68.



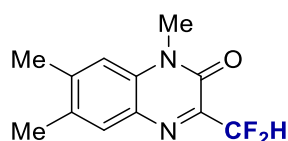
6-chloro-3-(difluoromethyl)-1-methylquinoxalin-2(1H)-one (59)⁸. Faint yellow solid was obtained in 60% isolated yield. **^1H NMR** (400 MHz, Chloroform- d) δ 7.98 (d, $J = 2.4$ Hz, 1H), 7.64 (dd, $J = 8.9, 2.4$ Hz, 1H), 7.34 (d, $J = 9.0$ Hz, 1H), 6.93 (t, $J = 53.6$ Hz, 1H), 3.73 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform- d) δ 152.92, 149.86 (t, $J = 22.7$ Hz), 132.79, 132.39, 130.68, 129.94, 115.28, 110.02 (t, $J = 242.2$ Hz), 29.31. **^{19}F NMR** (377 MHz, Chloroform- d) δ -124.61.



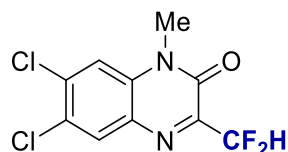
6-bromo-3-(difluoromethyl)-1-methylquinoxalin-2(1H)-one (60)⁸. Faint yellow solid was obtained in 68% isolated yield. **^1H NMR** (400 MHz, Chloroform- d) δ 8.22 – 8.05 (m, 1H), 7.85 – 7.66 (m, 1H), 7.27 (d, $J = 8.9$ Hz, 1H), 6.93 (t, $J = 53.5$ Hz, 1H), 3.72 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform- d) δ 152.90, 150.00 (t, $J = 22.7$ Hz), 135.49, 133.76, 133.24, 132.67, 117.08, 115.53, 110.00 (t, $J = 242.2$ Hz), 29.27. **^{19}F NMR** (377 MHz, Chloroform- d) δ -124.59.



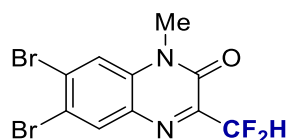
3-(difluoromethyl)-7-fluoro-1-methylquinoxalin-2(1H)-one (61)⁹. White solid was obtained in 68% isolated yield. **^1H NMR** (400 MHz, Chloroform- d) δ 8.07 – 7.98 (m, 1H), 7.37 – 6.68 (m, 3H), 3.73 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform- d) δ 164.94 (d, $J = 254.8$ Hz), 153.18, 147.62 (t, $J = 20.2$ Hz), 135.89 (d, $J = 12.2$ Hz), 133.82 (d, $J = 11.0$ Hz), 128.82, 112.76 (d, $J = 23.7$ Hz), 110.16 (t, $J = 242.1$ Hz), 101.10 (d, $J = 27.9$ Hz), 29.39. **^{19}F NMR** (377 MHz, Chloroform- d) δ -117.26, -124.68.



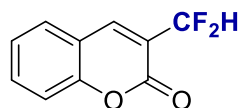
3-(difluoromethyl)-1,6,7-trimethylquinoxalin-2(1H)-one (62)⁹. Yellow solid was obtained in 71% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.72 (s, 1H), 7.20 – 6.65 (m, 2H), 3.70 (s, 3H), 2.45 (s, 3H), 2.37 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 153.45, 147.30, 143.31, 133.73, 132.22, 131.35, 130.50, 114.50, 110.37 (t, *J* = 241.4 Hz), 28.98, 20.96, 19.29. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -123.99.



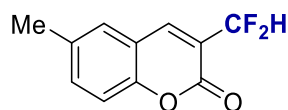
6,7-dichloro-3-(difluoromethyl)-1-methylquinoxalin-2(1H)-one (63)⁸. Faint yellow solid was obtained in 68% isolated yield. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.24 (s, 1H), 8.00 (s, 1H), 7.10 (t, *J* = 53.0 Hz, 1H), 3.64 (s, 3H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 152.84 (t, *J* = 2.0 Hz), 150.33 (t, *J* = 21.6 Hz), 135.40, 134.47, 131.38, 130.95, 126.59, 117.55, 110.62 (t, *J* = 240.3 Hz), 29.82. ¹⁹F NMR (377 MHz, DMSO-*d*₆) δ -124.75.



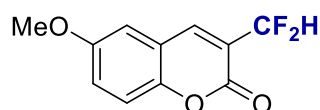
6,7-dibromo-3-(difluoromethyl)-1-methylquinoxalin-2(1H)-one (64). Faint yellow solid was obtained in 65% isolated yield. ¹H NMR (400 MHz, DMSO-*d*₆) δ 8.31 (s, 1H), 8.09 (s, 1H), 7.09 (t, *J* = 53.0 Hz, 1H), 3.63 (s, 3H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 152.84 (t, *J* = 2.0 Hz), 150.34 (t, *J* = 21.6 Hz), 134.75, 134.30, 131.54, 128.60, 120.51, 118.66, 110.65 (t, *J* = 240.2 Hz), 29.72. ¹⁹F NMR (377 MHz, DMSO-*d*₆) δ -124.74. HRMS (ESI) calcd for C₁₀H₇Br₂F₂N₂O⁺, [M+H]⁺ 366.8888, found 366.8895.



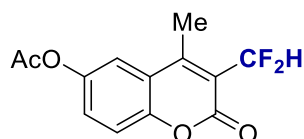
3-(difluoromethyl)-2H-chromen-2-one (65)¹⁰. White solid was obtained in 47% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.08 (s, 1H), 7.62 (m, 2H), 7.43 – 7.31 (m, 2H), 6.76 (t, *J* = 54.7 Hz, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 158.78, 154.27, 141.48 (t, *J* = 6.1 Hz), 133.61, 129.25, 125.23, 121.71 (t, *J* = 23.4 Hz), 117.86, 117.08, 110.28 (t, *J* = 238.9 Hz). ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -119.40.



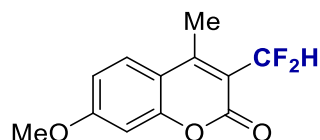
3-(difluoromethyl)-6-methyl-2H-chromen-2-one (66)¹⁰. Faint yellow solid was obtained in 46% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.01 (d, *J* = 1.8 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.38 (s, 1H), 7.32 – 7.23 (m, 1H), 6.75 (td, *J* = 54.7, 1.5 Hz, 1H), 2.44 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 158.92 (t, *J* = 5.0 Hz), 152.31, 141.34 (t, *J* = 6.1 Hz), 134.97, 134.56, 128.84, 121.42 (t, *J* = 23.6 Hz), 117.49, 116.67, 110.25 (t, *J* = 238.8 Hz), 20.74. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -119.30.



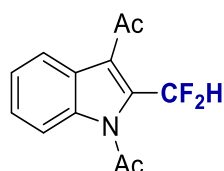
3-(difluoromethyl)-6-methoxy-2H-chromen-2-one (67)¹⁰. Faint yellow solid was obtained in 48% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.00 (s, 1H), 7.49 (d, *J* = 8.7 Hz, 1H), 6.92 (dd, *J* = 8.7, 2.4 Hz, 1H), 6.89 – 6.55 (m, 2H), 3.91 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 164.33, 159.24 (t, *J* = 5.4 Hz), 156.34, 141.53 (t, *J* = 6.0 Hz), 130.26, 117.94 (t, *J* = 23.7 Hz), 113.63, 112.97, 111.47, 110.60 (t, *J* = 238.8 Hz), 100.90, 56.08. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -118.50. HRMS (ESI) calcd for C₁₂H₁₇O₂⁺, [M+H]⁺ 193.1223, found 193.1217.



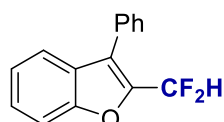
3-(difluoromethyl)-4-methyl-2-oxo-2H-chromen-6-yl acetate (68). Faint yellow solid was obtained in 60% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.78 (m, 1H), 7.32 – 6.90 (m, 3H), 2.68 (s, 3H), 2.36 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 168.70, 159.63 (t, *J* = 6.2 Hz), 154.41, 154.35, 153.79, 126.61, 118.96, 117.77 (t, *J* = 23.0 Hz), 117.73, 112.01 (t, *J* = 238.36 Hz), 110.59, 21.25, 15.12 (t, *J* = 3.2 Hz). ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -113.67. HRMS (ESI) calcd for C₁₃H₁₁F₂O₄⁺, [M+H]⁺ 269.0620, found 269.0622.



3-(difluoromethyl)-6-methoxy-4-methyl-2H-chromen-2-one (69). Faint yellow solid was obtained in 56% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 8.9 Hz, 1H), 7.24 – 6.88 (m, 2H), 6.80 (d, *J* = 2.5 Hz, 1H), 3.90 (s, 3H), 2.64 (t, *J* = 1.9 Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 164.02, 160.20 (t, *J* = 6.3 Hz), 155.15, 154.94, 126.76, 115.08 (t, *J* = 22.9 Hz), 113.47, 113.35, 112.47 (t, *J* = 238.36 Hz), 100.75, 56.02, 14.98. HRMS (ESI) calcd for C₁₂H₁₁F₂O₃⁺, [M+H]⁺ 241.0671, found 241.0670.

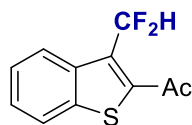


1,1'-(2-(difluoromethyl)-1H-indole-1,3-diyl)bis(ethan-1-one) (70). White solid was obtained in 42% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.85 (m, 2H), 7.61 – 7.20 (m, 3H), 2.85 (t, *J* = 1.1 Hz, 3H), 2.74 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 197.16, 171.05, 135.81, 131.85 (t, *J* = 26.26 Hz), 127.20, 125.60, 124.61, 121.66, 114.75, 109.85 (t, *J* = 237.7 Hz), 32.42 (t, *J* = 2.1 Hz), 29.83, 27.48 (t, *J* = 4.5 Hz). ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -109.53. HRMS (ESI) calcd for C₁₃H₁₂F₂NO₂⁺, [M+H]⁺ 252.0831, found 252.0823.

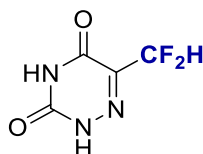


2-(difluoromethyl)-3-phenylbenzofuran (71)¹¹. Faint yellow solid was obtained in 63% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.72 (d, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 1H), 7.62 – 7.45 (m, 6H), 7.38 (t, *J* = 7.5 Hz, 1H), 6.78 (t, *J* = 52.4 Hz, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 154.67,

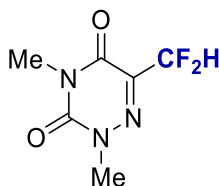
142.87 (t, $J = 23.3$ Hz), 129.78, 129.41, 129.27, 128.77, 127.15, 126.93, 124.10 (t, $J = 6.6$ Hz), 123.80, 121.30, 112.31, 108.46 (t, $J = 234.9$ Hz). **^{19}F NMR** (377 MHz, Chloroform- d) δ -113.84.



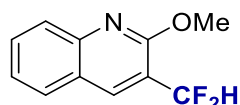
1-(3-(difluoromethyl)benzo[*b*]thiophen-2-yl)ethan-1-one (72). Faint yellow solid was obtained in 52% isolated yield. **^1H NMR** (400 MHz, Chloroform- d) δ 8.31 – 8.22 (m, 1H), 8.01 – 7.67 (m, 2H), 7.49 (m, 2H), 3.97 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform- d) δ 162.35, 140.49, 136.11, 134.99 (t, $J = 25.7$ Hz), 132.78 (t, $J = 8.6$ Hz), 127.82, 125.92 (t, $J = 3.0$ Hz), 125.66, 122.61, 110.78 (t, $J = 234.7$ Hz), 53.11. **^{19}F NMR** (377 MHz, Chloroform- d) δ -112.27. **HRMS (ESI)** calcd for $\text{C}_{11}\text{H}_9\text{F}_2\text{OS}^+$, $[\text{M}+\text{H}]^+$ 227.0337, found 227.0341.



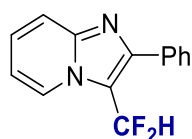
6-(difluoromethyl)-1,2,4-triazine-3,5(2H,4H)-dione (73)⁸. White solid was obtained in 56% isolated yield. **^1H NMR** (400 MHz, DMSO- d_6) δ 12.59 (d, $J = 178.5$ Hz, 2H), 6.80 (t, $J = 52.7$ Hz, 1H). **^{13}C NMR** (101 MHz, DMSO- d_6) δ 155.68, 149.55, 136.41 (t, $J = 23.8$ Hz), 111.26 (t, $J = 237.8$ Hz). **^{19}F NMR** (377 MHz, DMSO- d_6) δ -122.18.



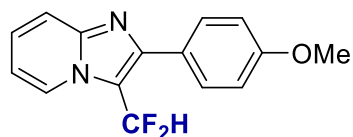
6-(difluoromethyl)-2,4-dimethyl-1,2,4-triazine-3,5(2H,4H)-dione (74). White solid was obtained in 60% isolated yield. **^1H NMR** (400 MHz, Chloroform- d) δ 6.59 (t, $J = 53.0$ Hz, 1H), 3.72 (s, 3H), 3.37 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform- d) δ 154.11, 148.76, 134.62 (t, $J = 24.8$ Hz), 110.03 (t, $J = 240.8$ Hz), 40.22, 27.34. **^{19}F NMR** (377 MHz, Chloroform- d) δ -121.93. **HRMS (ESI)** calcd for $\text{C}_6\text{H}_8\text{F}_2\text{N}_3\text{O}_2^+$, $[\text{M}+\text{H}]^+$ 192.0579, found 192.0584.



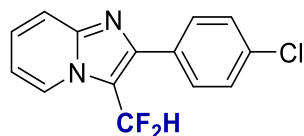
3-(difluoromethyl)-2-methoxyquinoline (75). Faint yellow solid was obtained in 71% isolated yield. **^1H NMR** (400 MHz, Chloroform- d) δ 8.04 (d, $J = 1.7$ Hz, 1H), 7.66 (ddd, $J = 7.5, 6.5, 1.7$ Hz, 2H), 7.40 (d, $J = 9.0$ Hz, 1H), 7.31 (td, $J = 7.5, 1.0$ Hz, 1H), 6.92 (t, $J = 55.1$ Hz, 1H), 3.75 (s, 3H). **^{13}C NMR** (101 MHz, Chloroform- d) δ 160.20, 140.48, 136.98 (t, $J = 6.4$ Hz), 132.33, 130.18, 125.36 (t, $J = 22.5$ Hz), 122.93, 119.28, 114.44, 111.27 (t, $J = 237.2$ Hz), 29.58. **^{19}F NMR** (377 MHz, Chloroform- d) δ -119.68. **HRMS (ESI)** calcd for $\text{C}_{11}\text{H}_{10}\text{F}_2\text{NO}^+$, $[\text{M}+\text{H}]^+$ 210.0725, found 210.0719.



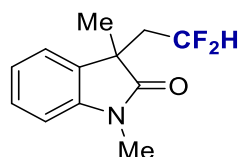
3-(difluoromethyl)-2-phenylimidazo[1,2-*a*]pyridine (76). Yellow solid was obtained in 48% isolated yield. ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.68 (dt, *J* = 7.0, 1.3 Hz, 1H), 7.97 (dt, *J* = 9.0, 1.2 Hz, 1H), 7.86 (m, 1H), 7.69 (dd, *J* = 7.5, 2.0 Hz, 2H), 7.59 (m, 3H), 7.46 (td, *J* = 6.9, 1.4 Hz, 1H), 6.16 (t, *J* = 53.6 Hz, 1H). ¹³C NMR (101 MHz, DMSO-*d*₆) δ 176.90 (t, *J* = 24.9 Hz), 157.04, 148.20, 134.51, 132.51, 130.23, 130.07, 129.25, 128.92, 117.87, 117.26, 107.30. ¹⁹F NMR (377 MHz, DMSO-*d*₆) δ -124.71. HRMS (ESI) calcd for C₁₄H₁₁F₂N₂⁺, [M+H]⁺ 245.0885, found 245.0876.



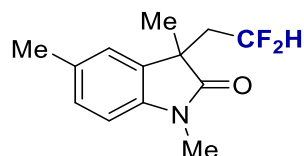
3-(difluoromethyl)-2-(4-methoxyphenyl)imidazo[1,2-*a*]pyridine (77). Faint yellow solid was obtained in 81% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 9.76 (d, *J* = 6.9 Hz, 1H), 7.89 – 7.47 (m, 4H), 7.22 (t, *J* = 7.0 Hz, 1H), 7.07 (d, *J* = 8.2 Hz, 2H), 5.98 (t, *J* = 53.4 Hz, 1H), 3.90 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 177.20 (t, *J* = 25.0 Hz), 161.30, 157.54, 148.56, 131.57, 131.28, 129.42, 125.89, 117.61, 116.05, 114.38, 106.02 (t, *J* = 245.7 Hz), 55.54. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -124.27. HRMS (ESI) calcd for C₁₅H₁₃F₂N₂O⁺, [M+H]⁺ 275.0990, found 275.0993.



2-(4-chlorophenyl)-3-(difluoromethyl)imidazo[1,2-*a*]pyridine (78). White solid was obtained in 50% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 9.77 (dd, *J* = 6.9, 1.3 Hz, 1H), 7.85 (dd, *J* = 8.9, 1.3 Hz, 1H), 7.70 (m, 1H), 7.63 – 7.46 (m, 4H), 7.39 – 7.21 (m, 1H), 5.92 (td, *J* = 53.3, 1.1 Hz, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 177.11 (t, *J* = 25.1 Hz), 156.17, 148.55, 136.70, 132.32, 131.78, 131.15, 129.47, 129.21, 117.85, 116.47, 106.24 (t, *J* = 246.7 Hz). ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -124.15. HRMS (ESI) calcd for C₁₄H₁₀ClF₂N₂⁺, [M+H]⁺ 279.0495, found 279.0489.

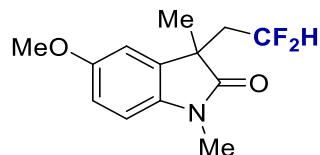


3-(2,2-difluoroethyl)-1,3-dimethylindolin-2-one (79)¹². Faint yellow liquid was obtained in 95% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.31 (td, *J* = 7.7, 1.3 Hz, 1H), 7.23 (dd, *J* = 7.4, 1.3 Hz, 1H), 7.09 (td, *J* = 7.5, 1.0 Hz, 1H), 6.88 (d, *J* = 7.8 Hz, 1H), 5.59 (tdd, *J* = 56.1, 6.4, 3.5 Hz, 1H), 3.23 (s, 3H), 2.50 (m, 1H), 2.39 – 2.19 (m, 1H), 1.41 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 179.22, 143.02, 132.12, 128.60, 122.91, 122.86, 115.23 (t, *J* = 239.7 Hz), 108.59, 45.14 – 44.32 (m), 41.46 (t, *J* = 21.9 Hz), 26.47, 24.46. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -113.47 – -115.04 (m).

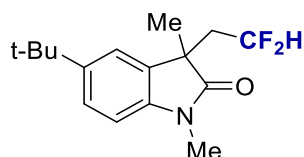


3-(2,2-difluoroethyl)-1,3,5-trimethylindolin-2-one (80)¹². Faint yellow liquid was obtained in 93% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.14 – 7.07 (m, 1H), 7.04 (d, *J* = 1.6 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 5.59 (tdd, *J* = 56.2, 6.5, 3.4 Hz, 1H), 3.21 (s, 3H), 2.49 (m, 1H), 2.36 (s, 3H), 2.26 (m, 1H), 1.40 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 179.25, 140.59, 132.48, 132.15, 128.83,

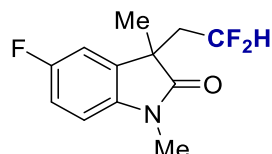
123.70, 115.27 (t, $J = 239.7$ Hz), 108.35, 44.75 (dd, $J = 6.4, 4.2$ Hz), 41.46 (t, $J = 21.8$ Hz), 26.50, 24.47, 21.24. ^{19}F NMR (377 MHz, Chloroform- d) δ -113.46 – -115.08 (m).



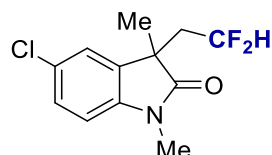
3-(2,2-difluoroethyl)-5-methoxy-1,3-dimethylindolin-2-one (81)¹². Faint yellow liquid was obtained in 95% isolated yield. ^1H NMR (400 MHz, Chloroform- d) δ 6.92 – 6.72 (m, 3H), 5.61 (tdd, $J = 56.1, 6.4, 3.5$ Hz, 1H), 3.81 (s, 3H), 3.20 (s, 3H), 2.49 (m, 1H), 2.26 (m, 1H), 1.40 (s, 3H). ^{13}C NMR (101 MHz, Chloroform- d) δ 178.87, 156.27, 136.47, 133.52, 115.21 (t, $J = 239.7$ Hz), 112.44, 110.67, 108.88, 55.92, 45.09 (dd, $J = 6.4, 4.2$ Hz), 41.45 (t, $J = 21.9$ Hz), 26.55, 24.50. ^{19}F NMR (377 MHz, Chloroform- d) δ -113.45 – -115.03 (m).



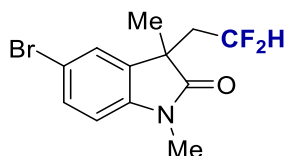
5-(tert-butyl)-3-(2,2-difluoroethyl)-1,3-dimethylindolin-2-one (82)¹². White solid was obtained in 95% isolated yield. ^1H NMR (400 MHz, Chloroform- d) δ 7.33 (dd, $J = 8.2, 2.0$ Hz, 1H), 7.25 (d, $J = 2.0$ Hz, 1H), 6.81 (d, $J = 8.2$ Hz, 1H), 5.60 (tdd, $J = 56.2, 6.5, 3.4$ Hz, 1H), 3.21 (s, 3H), 2.49 (m, 1H), 2.28 (m, 1H), 1.42 (s, 3H), 1.33 (s, 9H). ^{13}C NMR (101 MHz, Chloroform- d) δ 179.42, 146.22, 140.58, 131.83, 125.14, 120.02, 115.31 (t, $J = 239.6$ Hz), 107.98, 44.91 (dd, $J = 6.4, 4.3$ Hz), 41.50 (t, $J = 21.8$ Hz), 34.72, 31.71, 26.47, 24.41. ^{19}F NMR (377 MHz, Chloroform- d) δ -113.25 – -114.85 (m).



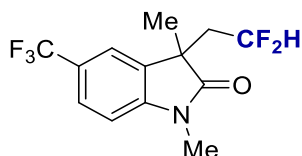
3-(2,2-difluoroethyl)-5-fluoro-1,3-dimethylindolin-2-one (83)¹². Colorless liquid was obtained in 95% isolated yield. ^1H NMR (400 MHz, Chloroform- d) δ 7.07 – 6.94 (m, 2H), 6.81 (dd, $J = 8.3, 4.1$ Hz, 1H), 5.62 (tdd, $J = 55.9, 6.1, 3.6$ Hz, 1H), 3.22 (s, 3H), 2.51 (m, 1H), 2.28 (m, 1H), 1.41 (s, 3H). ^{13}C NMR (101 MHz, Chloroform- d) δ 178.88, 159.45 (d, $J = 241.3$ Hz), 138.88 (d, $J = 2.0$ Hz), 133.79 (d, $J = 7.8$ Hz), 114.99, 114.81 (d, $J = 23.4$ Hz), 111.22 (d, $J = 24.7$ Hz), 109.12 (d, $J = 8.2$ Hz), 45.14 (t, $J = 4.4$ Hz), 41.27 (t, $J = 22.0$ Hz), 26.61, 24.43. ^{19}F NMR (377 MHz, Chloroform- d) δ -114.25 (d, $J = 3.4$ Hz), -120.12.



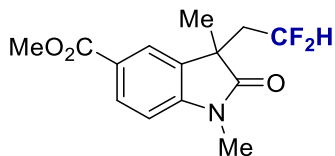
5-chloro-3-(2,2-difluoroethyl)-1,3-dimethylindolin-2-one (84)¹². Colorless liquid was obtained in 91% isolated yield. ^1H NMR (400 MHz, Chloroform- d) δ 7.29 (dd, $J = 8.3, 2.1$ Hz, 1H), 7.22 (d, $J = 2.1$ Hz, 1H), 6.81 (d, $J = 8.2$ Hz, 1H), 5.62 (tdd, $J = 56.0, 6.2, 3.6$ Hz, 1H), 3.22 (s, 3H), 2.51 (m, 1H), 2.28 (m, 1H), 1.41 (s, 3H). ^{13}C NMR (101 MHz, Chloroform- d) δ 178.73, 141.57, 133.86, 128.56, 128.28, 123.55, 114.95 (t, $J = 240.1$ Hz), 109.55, 44.92 (t, $J = 5.2$ Hz), 41.27 (t, $J = 22.0$ Hz), 26.62, 24.47. ^{19}F NMR (377 MHz, Chloroform- d) δ -114.35.



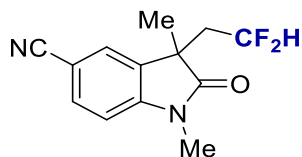
5-bromo-3-(2,2-difluoroethyl)-1,3-dimethylindolin-2-one (85)¹². White solid was obtained in 98% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.44 (dd, *J* = 8.3, 1.9 Hz, 1H), 7.35 (d, *J* = 2.0 Hz, 1H), 6.76 (d, *J* = 8.3 Hz, 1H), 5.62 (tdd, *J* = 55.9, 6.3, 3.6 Hz, 1H), 3.21 (s, 3H), 2.51 (m, 1H), 2.28 (m, 1H), 1.41 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 178.59, 142.07, 134.24, 131.46, 126.27, 115.50, 114.93 (t, *J* = 240.1 Hz), 110.05, 44.86 (t, *J* = 5.2 Hz), 41.28 (t, *J* = 22.0 Hz), 26.58, 24.47. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -114.34.



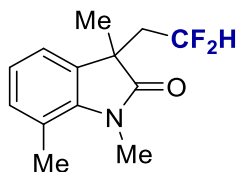
3-(2,2-difluoroethyl)-1,3-dimethyl-5-(trifluoromethyl)indolin-2-one (86)¹². Faint yellow liquid was obtained in 98% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.61 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.47 (s, 1H), 6.96 (d, *J* = 8.2 Hz, 1H), 5.61 (tdd, *J* = 55.8, 6.2, 3.5 Hz, 1H), 3.27 (s, 3H), 2.55 (m, 1H), 2.33 (m, 1H), 1.45 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 179.15, 146.01, 132.78, 126.46 (q, *J* = 4.0 Hz), 125.17 (q, *J* = 121 Hz), 124.40 (q, *J* = 272.7 Hz), 120.06 (d, *J* = 3.7 Hz), 114.85 (t, *J* = 240.1 Hz), 108.40, 44.66 (t, *J* = 5.2 Hz), 41.23 (t, *J* = 21.9 Hz), 26.71, 24.48. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -61.42, -114.44 (d, *J* = 9.7 Hz).



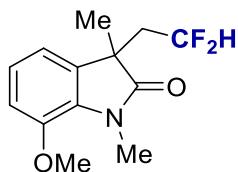
methyl 3-(2,2-difluoroethyl)-1,3-dimethyl-2-oxoindoline-5-carboxylate (87)¹². White solid was obtained in 96% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 8.08 (dd, *J* = 8.2, 1.7 Hz, 1H), 7.93 (d, *J* = 1.6 Hz, 1H), 6.94 (d, *J* = 8.2 Hz, 1H), 5.59 (tdd, *J* = 56.0, 6.4, 3.5 Hz, 1H), 3.94 (s, 3H), 3.28 (s, 3H), 2.57 (m, 1H), 2.36 (m, 1H), 1.46 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 179.49, 166.81, 147.14, 132.07, 131.32, 124.81, 124.20, 114.94 (t, *J* = 240.0 Hz), 108.16, 52.26, 44.46 (t, *J* = 21.9 Hz), 41.28 (t, *J* = 21.9 Hz), 26.70, 24.53. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -114.58 (d, *J* = 6.6 Hz).



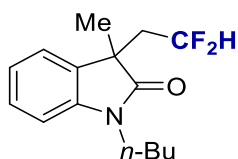
3-(2,2-difluoroethyl)-1,3-dimethyl-2-oxoindoline-5-carbonitrile (88)¹². White solid was obtained in 98% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.66 (dd, *J* = 8.1, 1.6 Hz, 1H), 7.51 (d, *J* = 1.6 Hz, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 5.62 (tdd, *J* = 55.7, 5.9, 3.6 Hz, 1H), 3.27 (s, 3H), 2.55 (m, 1H), 2.35 (m, 1H), 1.44 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 178.88, 146.84, 133.90, 133.24, 126.47, 119.07, 114.69 (t, *J* = 240.3 Hz), 109.04, 106.00, 44.44 (dd, *J* = 6.2, 3.8 Hz), 41.04 (t, *J* = 21.9 Hz), 26.73, 24.46. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -113.44 – -115.43 (m).



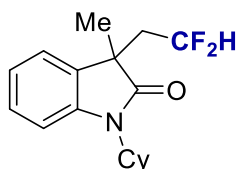
3-(2,2-difluoroethyl)-1,3,7-trimethylindolin-2-one (89)¹². Colorless liquid was obtained in 67% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.09 – 7.00 (m, 2H), 6.98 (d, *J* = 7.4 Hz, 1H), 5.57 (tdd, *J* = 56.2, 6.5, 3.4 Hz, 1H), 3.51 (s, 3H), 2.59 (s, 3H), 2.50 (m, 1H), 2.34 – 2.14 (m, 1H), 1.38 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 179.99, 140.78, 132.73, 132.28, 122.78, 120.76, 120.29, 115.27 (t, *J* = 239.6 Hz), 44.02 (dd, *J* = 6.5, 4.2 Hz), 41.75 (t, *J* = 21.8 Hz), 29.82, 24.91, 19.20. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -113.51 – -115.15 (m).



3-(2,2-difluoroethyl)-7-methoxy-1,3-dimethylindolin-2-one (90)¹³. Colorless liquid was obtained in 62% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.03 (m, 1H), 6.85 (m, 2H), 5.57 (tdd, *J* = 56.2, 6.4, 3.5 Hz, 1H), 3.87 (s, 3H), 3.49 (s, 3H), 2.49 (m, 1H), 2.24 (m, 1H), 1.39 (s, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 179.48, 145.69, 133.74, 130.78, 123.48, 115.42, 115.26 (t, *J* = 239.6 Hz), 112.20, 55.99, 44.83 – 44.67 (m), 41.62 (t, *J* = 21.9 Hz), 29.80, 24.73. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -114.13 – -114.41 (m).

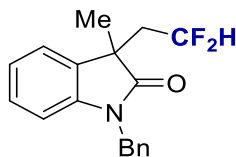


1-butyl-3-(2,2-difluoroethyl)-3-methylindolin-2-one (91)¹³. Faint yellow liquid was obtained in 90% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.25 (m, 1H), 7.23 (dd, *J* = 7.4, 1.2 Hz, 1H), 7.08 (td, *J* = 7.5, 1.0 Hz, 1H), 6.89 (d, *J* = 7.9 Hz, 1H), 5.57 (tdd, *J* = 56.2, 6.4, 3.5 Hz, 1H), 3.80 – 3.61 (m, 2H), 2.51 (m, 1H), 2.28 (m, 1H), 1.70 – 1.60 (m, 2H), 1.44 – 1.32 (m, 5H), 0.96 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 179.11, 142.49, 132.25, 128.49, 123.02, 122.57, 115.26 (t, *J* = 239.8 Hz), 108.88, 44.56 (t, *J* = 5.3 Hz), 41.41 (t, *J* = 21.9 Hz), 39.92, 29.46, 24.75, 20.21, 13.87. ¹⁹F NMR (377 MHz, Chloroform-*d*) δ -114.20.

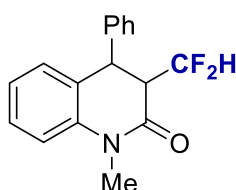


1-cyclohexyl-3-(2,2-difluoroethyl)-3-methylindolin-2-one (92). Colorless crystal was obtained in 85% isolated yield. ¹H NMR (400 MHz, Chloroform-*d*) δ 7.32 – 7.18 (m, 2H), 7.13 – 7.00 (m, 2H), 5.50 (tdd, *J* = 56.2, 6.6, 3.3 Hz, 1H), 4.17 (tt, *J* = 12.7, 3.8 Hz, 1H), 2.51 (m, 1H), 2.35 – 2.22 (m, 1H), 2.14 (m, 2H), 1.88 (s, 2H), 1.83 – 1.68 (m, 3H), 1.50 – 1.34 (m, 5H), 1.26 (m, 1H). ¹³C NMR (101 MHz, Chloroform-*d*) δ 179.08, 142.13, 132.43, 128.23, 123.06, 122.17, 115.30 (t, *J* = 239.8 Hz), 110.52, 52.32, 44.28 (t, *J* = 5.3 Hz), 41.69 (t, *J* = 21.8 Hz), 29.14, 29.03, 26.08, 26.07, 25.50, 24.81. ¹⁹F NMR (377

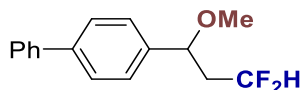
MHz, Chloroform-*d*) δ -114.38 (d, J = 3.2 Hz). **HRMS (ESI)** calcd for $C_{17}H_{22}F_2NO^+$, $[M+H]^+$ 297.1644, found 294.1659.



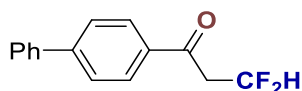
1-benzyl-3-(2,2-difluoroethyl)-3-methylindolin-2-one (93)¹³. Colorless crystal was obtained in 84% isolated yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.35 – 7.21 (m, 6H), 7.17 (td, J = 7.8, 1.3 Hz, 1H), 7.05 (td, J = 7.5, 1.0 Hz, 1H), 6.77 – 6.73 (m, 1H), 5.61 (tdd, J = 56.1, 6.5, 3.4 Hz, 1H), 5.03 – 4.81 (m, 2H), 2.59 (m, 1H), 2.34 (m, 1H), 1.47 (s, 3H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 179.32, 142.12, 135.84, 132.00, 128.90, 128.50, 127.77, 127.36, 122.93, 122.88, 115.24 (t, J = 239.9 Hz), 109.71, 44.69 (t, J = 5.3 Hz), 43.97, 41.32 (t, J = 21.9 Hz), 25.08. **¹⁹F NMR** (377 MHz, Chloroform-*d*) δ -114.10 (d, J = 2.7 Hz).



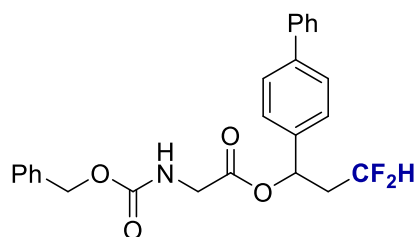
3-(difluoromethyl)-1-methyl-4-phenyl-3,4-dihydroquinolin-2(1H)-one (94)¹⁴. Light yellow solid was obtained in 67% isolated yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.49 – 6.96 (m, 11H), 6.00 (td, J = 55.6, 4.3 Hz, 1H), 4.54 – 4.34 (m, 1H), 3.43 (s, 4H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 164.67, 140.44, 139.19, 129.34, 129.11, 128.65, 127.61, 127.51, 125.90, 124.07, 115.24, 114.94 (t, J = 239.9 Hz), 53.02 (t, J = 20.8 Hz), 41.34, 30.13. **¹⁹F NMR** (377 MHz, Chloroform-*d*) δ -119.65 – -122.97 (m).



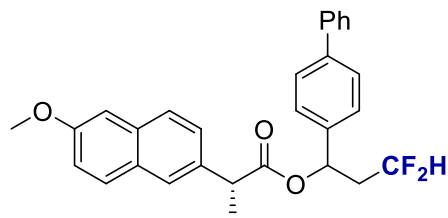
4-(3,3-difluoro-1-methoxypropyl)-1,1'-biphenyl (95). Faint yellow liquid was obtained in 85% isolated yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 7.66 – 7.55 (m, 4H), 7.50 – 7.41 (m, 2H), 7.40 – 7.32 (m, 3H), 5.97 (tdd, J = 57.1, 6.8, 3.2 Hz, 1H), 4.49 – 4.24 (m, 1H), 3.24 (s, 3H), 2.59 – 2.21 (m, 1H), 2.24 – 2.01 (m, 1H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 141.35, 140.77, 139.46, 128.96, 127.64, 127.58, 127.23, 127.05, 115.96 (t, J = 238.4 Hz), 56.79, 42.92 (t, J = 21.4 Hz). **¹⁹F NMR** (377 MHz, Chloroform-*d*) δ -116.55 – -119.59 (m). **HRMS (ESI)** calcd for $C_{16}H_{17}F_2O^+$, $[M+H]^+$ 263.1242, found 263.1244.



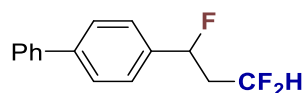
1-([1,1'-biphenyl]-4-yl)-3,3-difluoropropan-1-one (96). Faint yellow liquid was obtained in 87% isolated yield. **¹H NMR** (400 MHz, Chloroform-*d*) δ 8.06 – 7.96 (m, 2H), 7.79 – 7.69 (m, 2H), 7.67 – 7.60 (m, 2H), 7.54 – 7.45 (m, 2H), 7.45 – 7.37 (m, 1H), 6.43 (tt, J = 55.6, 4.7 Hz, 1H), 3.57 (td, J = 15.2, 4.7 Hz, 2H). **¹³C NMR** (101 MHz, Chloroform-*d*) δ 193.47 (t, J = 6.8 Hz), 146.85, 139.66, 134.85, 129.17, 128.93, 128.64, 127.61, 127.43, 115.00 (t, J = 238.5 Hz), 43.15 (t, J = 23.5 Hz). **¹⁹F NMR** (377 MHz, Chloroform-*d*) δ -116.72. **HRMS (ESI)** calcd for $C_{15}H_{13}F_2O^+$, $[M+H]^+$ 247.0929, found 247.0927.



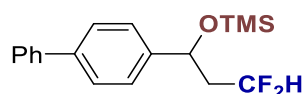
1-([1,1'-biphenyl]-4-yl)-3,3-difluoropropyl ((benzyloxy)carbonyl)glycinate (97). White solid was obtained in 93% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.63 (t, J = 8.3 Hz, 4H), 7.55 – 7.33 (m, 10H), 6.09 (dd, J = 9.1, 4.9 Hz, 1H), 5.89 (tt, J = 56.0, 4.8 Hz, 1H), 5.35 (t, J = 5.7 Hz, 1H), 5.16 (s, 2H), 4.06 (m, 2H), 2.73 – 2.47 (m, 1H), 2.38 (m, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.15, 156.35, 141.94, 140.40, 137.19, 136.74, 136.24, 129.29, 129.00, 128.95, 128.64, 128.34, 128.23, 128.01, 127.74, 127.22, 126.93, 115.78, 114.93 (t, J = 239.8 Hz), 71.84 (t, J = 6.3 Hz), 67.26, 42.98, 40.71 (t, J = 22.0 Hz). ^{19}F NMR (377 MHz, Chloroform-*d*) δ -116.69 (d, J = 13.6 Hz). HRMS (ESI) calcd for $\text{C}_{25}\text{H}_{24}\text{F}_2\text{NO}_4^+$, $[\text{M}+\text{H}]^+$ 440.1668, found 440.1669.



1-([1,1'-biphenyl]-4-yl)-3,3-difluoropropyl (2R)-2-(6-methoxynaphthalen-2-yl)propanoate (98). White solid was obtained in 96% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.78 – 7.25 (m, 12H), 7.18 – 7.03 (m, 3H), 6.02 – 5.61 (m, 1.5H), 5.45 (tdd, J = 56.3, 6.1, 3.7 Hz, 0.5H), 3.90 (d, J = 4.6 Hz, 4H), 2.61 – 2.08 (m, 2H), 1.55 (d, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.52, 173.35, 157.84, 157.78, 141.62, 141.28, 140.56, 140.56, 137.96, 137.80, 135.44, 135.23, 133.85, 133.79, 129.40, 129.36, 129.03, 128.98, 128.94, 128.88, 127.66, 127.64, 127.58, 127.39, 127.36, 127.25, 127.23, 127.17, 126.84, 126.56, 126.43, 126.11, 126.09, 126.06, 119.27, 119.12, 115.14 (t, J = 239.8 Hz), 114.95 (t, J = 239.8 Hz), 105.74, 105.67, 71.09 (t, J = 6.3 Hz), 71.04 (t, J = 6.3 Hz), 55.42, 55.40, 45.68, 45.54, 40.96 (t, J = 22.0 Hz), 40.87 (t, J = 22.0 Hz), 29.84, 18.39, 18.35. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -116.68, -116.90 (m). HRMS (ESI) calcd for $\text{C}_{29}\text{H}_{26}\text{F}_2\text{O}_3^+$, $[\text{M}]^+$ 460.1850, found 460.1857.

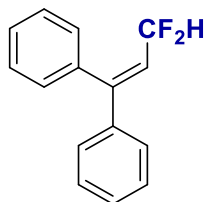


4-(1,3,3-trifluoropropyl)-1,1'-biphenyl (99). White solid was obtained in 72% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.84 – 7.30 (m, 9H), 6.27 – 5.85 (m, 1H), 5.71 (dd, J = 47.4, 10.0 Hz, 1H), 2.59 (m, 1H), 2.35 (m, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 142.06 (d, J = 1.7 Hz), 140.36, 137.17 (d, J = 19.6 Hz), 128.90, 127.69, 127.57, 127.17, 125.97 (d, J = 6.5 Hz), 114.88 (td, J = 239.2, 3.7 Hz), 89.35 (dq, J = 170.7, 4.0 Hz), 42.43 – 41.35 (q, J = 23.23 Hz). ^{19}F NMR (377 MHz, Chloroform-*d*) δ -116.15 – -118.83 (m), -176.11. HRMS (ESI) calcd for $\text{C}_{15}\text{H}_{13}\text{F}_3^+$, $[\text{M}]^+$ 250.0964, found 250.0962.

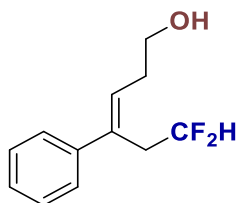


1-([1,1'-biphenyl]-4-yl)-3,3-difluoropropoxytrimethylsilane (100). White solid was obtained in 80% isolated yield. ^1H NMR (400 MHz, Chloroform-*d*) δ 7.73 – 7.55 (m, 4H), 7.49 (t, J = 7.6 Hz, 2H), 7.46

– 7.37 (m, 3H), 5.99 (tdd, $J = 57.1, 7.2, 2.9$ Hz, 1H), 4.96 (dd, $J = 10.0, 3.5$ Hz, 1H), 2.43 – 2.03 (m, 2H), 0.10 (s, 9H). ^{13}C NMR (101 MHz, Chloroform- d) δ 142.72, 140.79, 140.65, 128.91, 127.46, 127.32, 127.18, 126.17, 116.33 (t, $J = 238.3$ Hz), 69.95 (dd, $J = 8.4, 5.6$ Hz), 44.91 (t, $J = 20.5$ Hz), 0.09. HRMS (ESI) calcd for $\text{C}_{18}\text{H}_{22}\text{F}_2\text{OSi}^+$, $[\text{M}]^+$ 320.1403, found 320.1406.



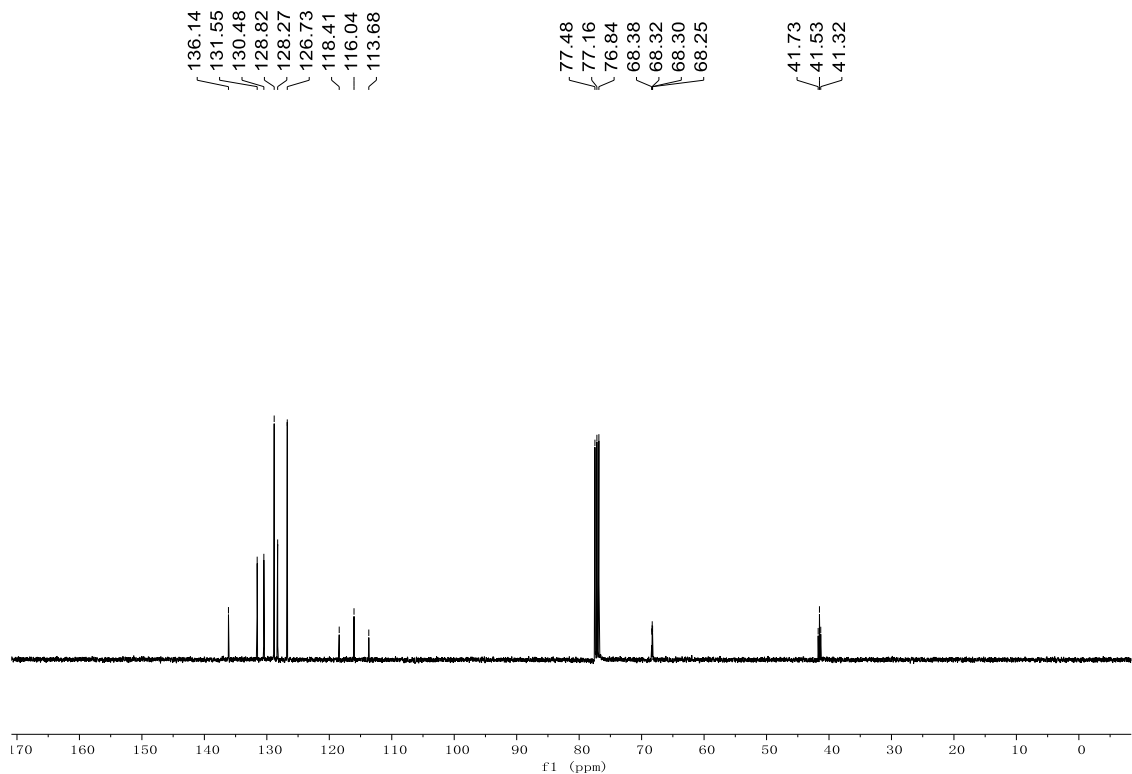
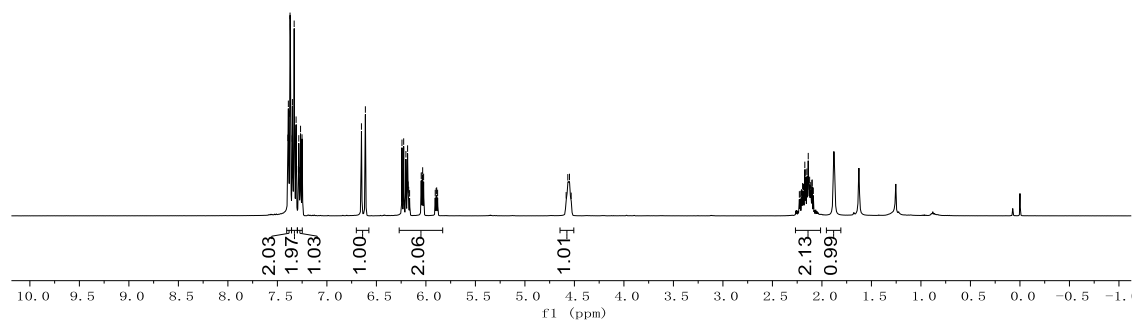
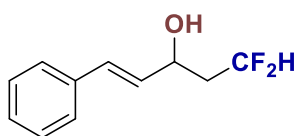
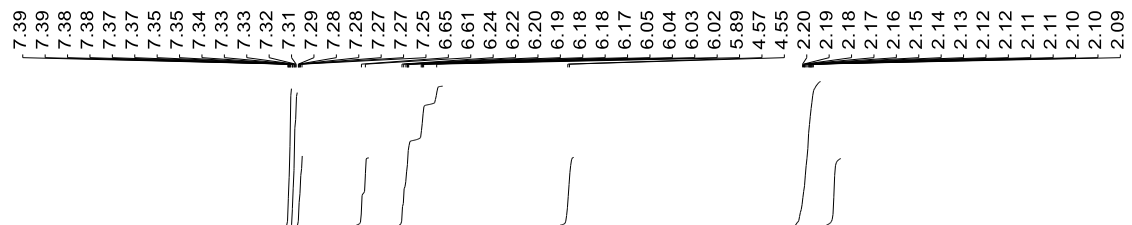
(3,3-difluoroprop-1-ene-1,1-diyl)dibenzene (102)¹⁵. Faint yellow solid was obtained in 87% isolated yield. ^1H NMR (400 MHz, Chloroform- d) δ 7.62 – 7.05 (m, 10H), 6.36 – 5.77 (m, 2H). ^{13}C NMR (101 MHz, Chloroform- d) δ 150.78 (t, $J = 12.8$ Hz), 140.18, 137.34, 129.94, 129.17, 128.82, 128.59, 128.55, 128.16, 120.19 (t, $J = 26.7$ Hz), 113.88 (t, $J = 229.4$ Hz). ^{19}F NMR (377 MHz, Chloroform- d) δ -106.75.

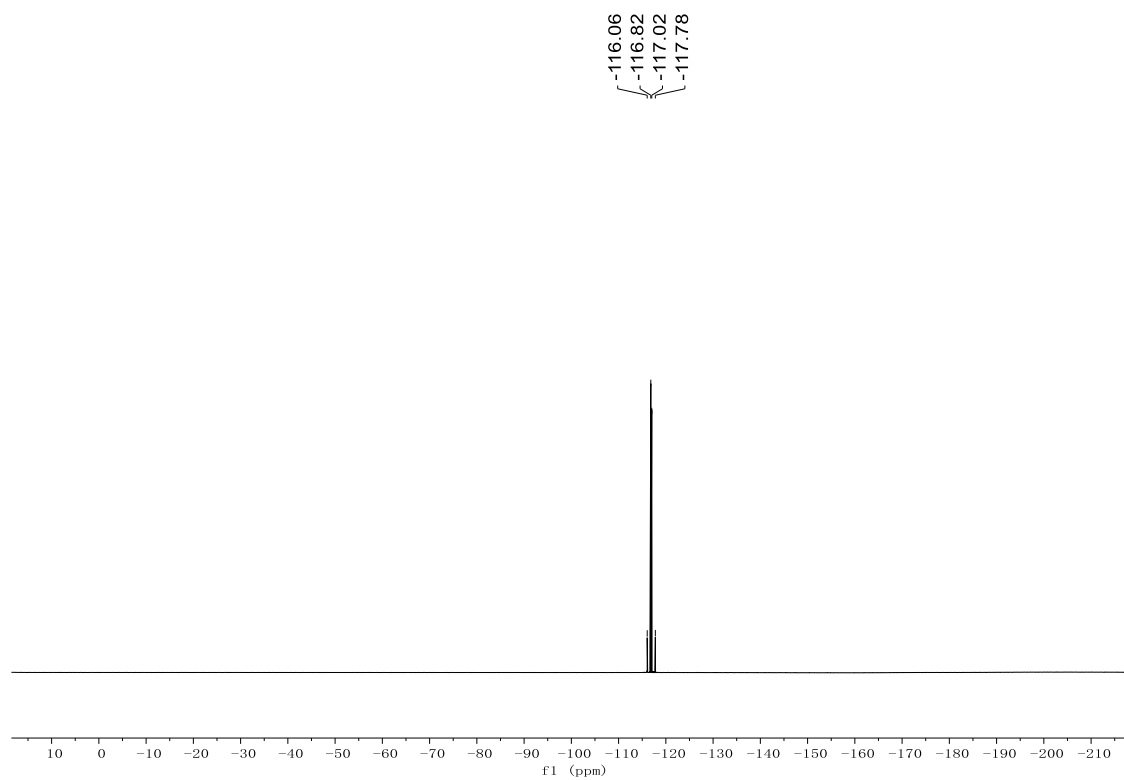


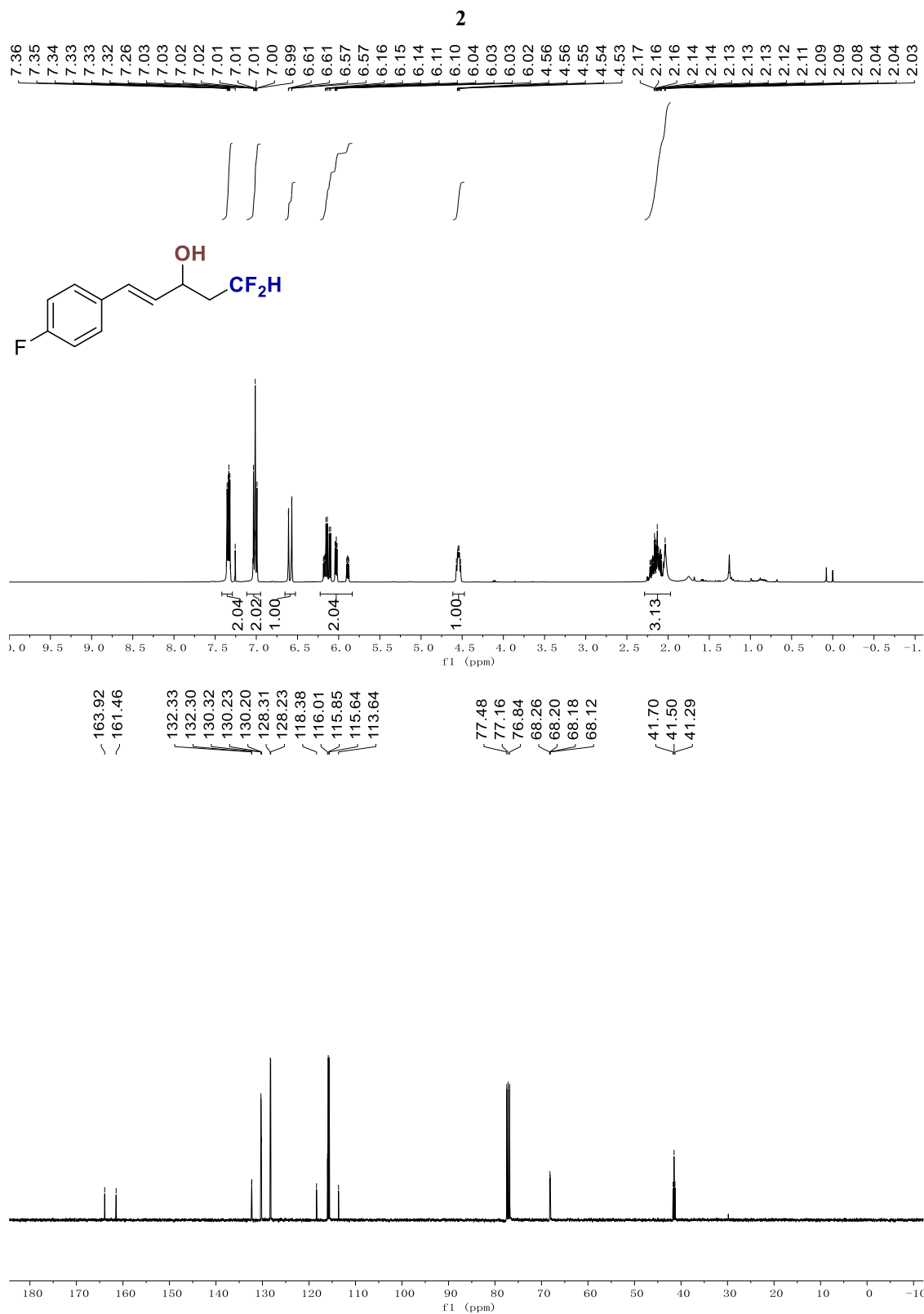
6,6-difluoro-4-phenylhex-3-en-1-ol (104). Faint yellow liquid was obtained in 15% isolated yield. ^1H NMR (400 MHz, Chloroform- d) δ 7.40 – 7.26 (m, 5H), 5.94 (t, $J = 7.5$ Hz, 1H), 5.75 (tt, $J = 56.7, 4.9$ Hz, 1H), 3.77 (t, $J = 6.4$ Hz, 2H), 3.12 (td, $J = 16.5, 4.9$ Hz, 2H), 2.53 (q, $J = 6.7$ Hz, 2H), 1.67 (s, 1H). ^{13}C NMR (101 MHz, Chloroform- d) δ 141.67, 134.02 (t, $J = 6.0$ Hz), 129.96, 128.67, 127.61, 126.43, 116.02 (t, $J = 241.2$ Hz), 62.18, 35.50 (t, $J = 22.6$ Hz), 32.49. ^{19}F NMR (377 MHz, Chloroform- d) δ -114.56. HRMS (ESI) calcd for $\text{C}_{12}\text{H}_{13}\text{F}_2^+$, $[\text{M}-\text{OH}]^+$ 195.0980, found 195.0977.

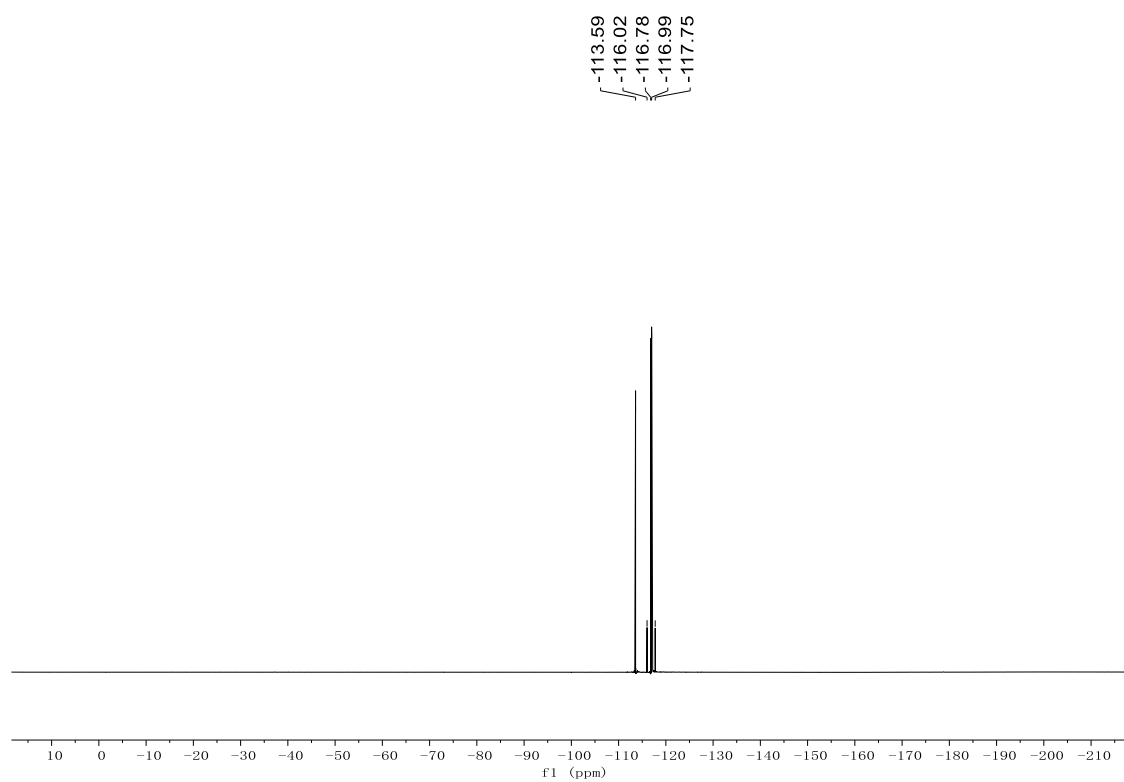
NMR Spectra of Products

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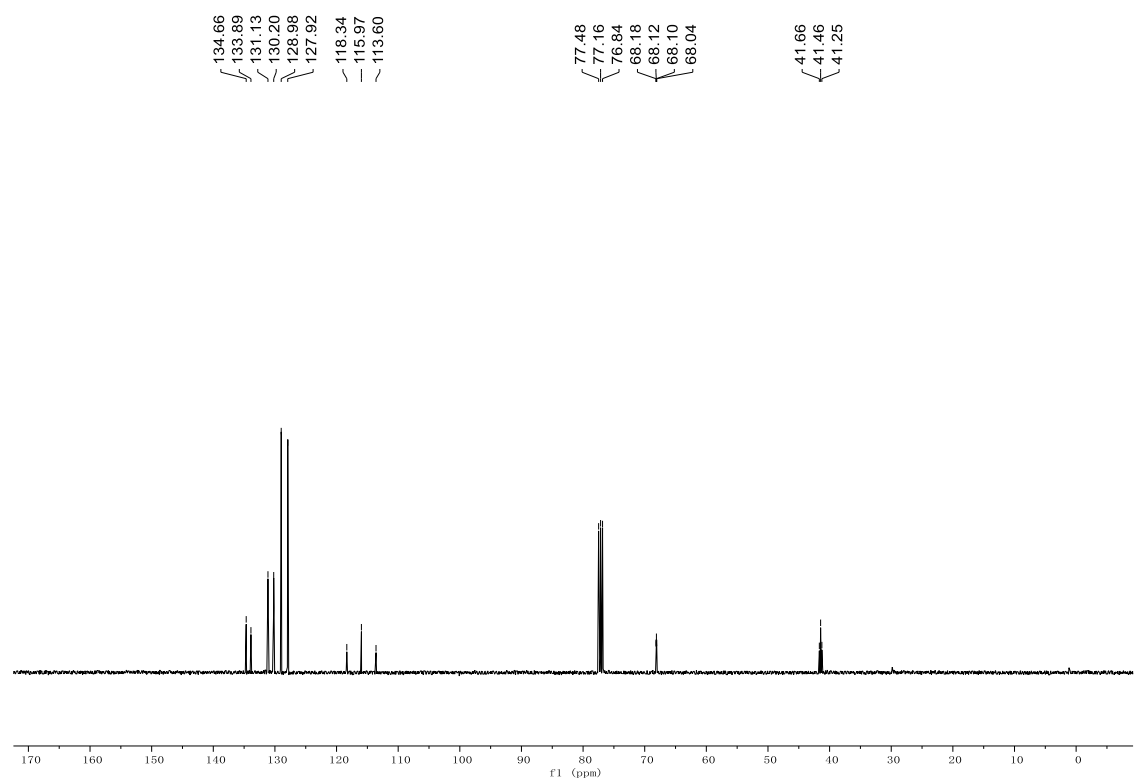
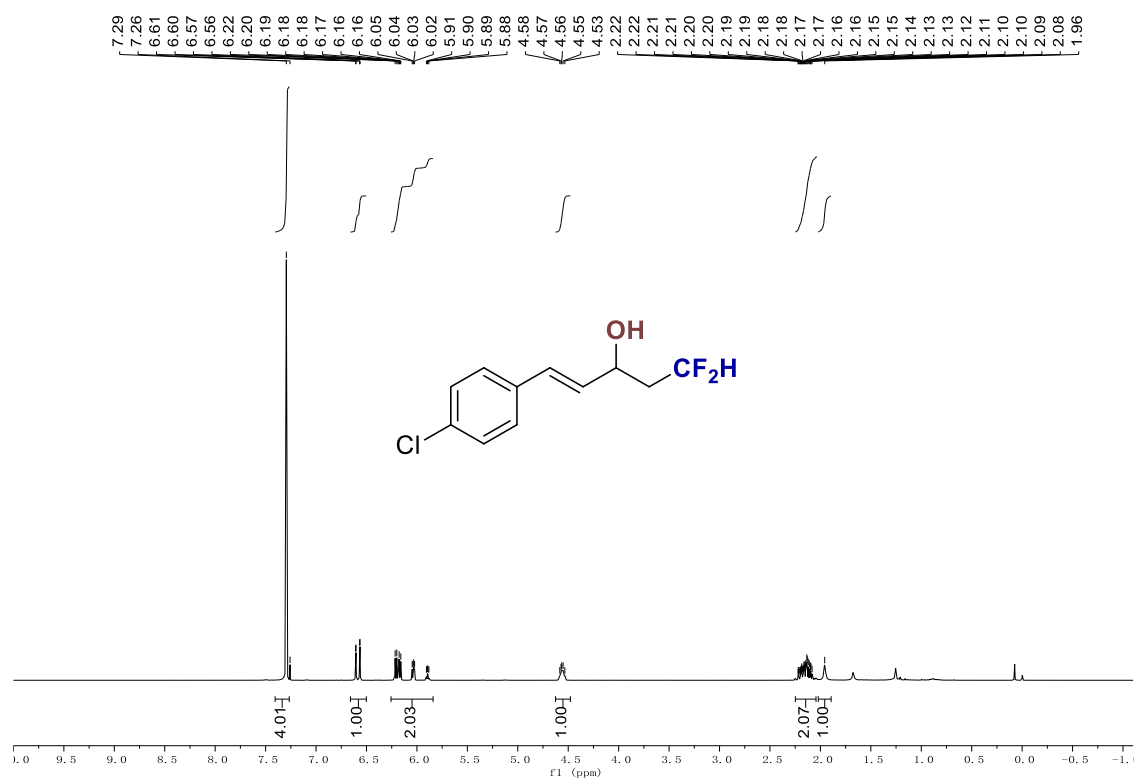


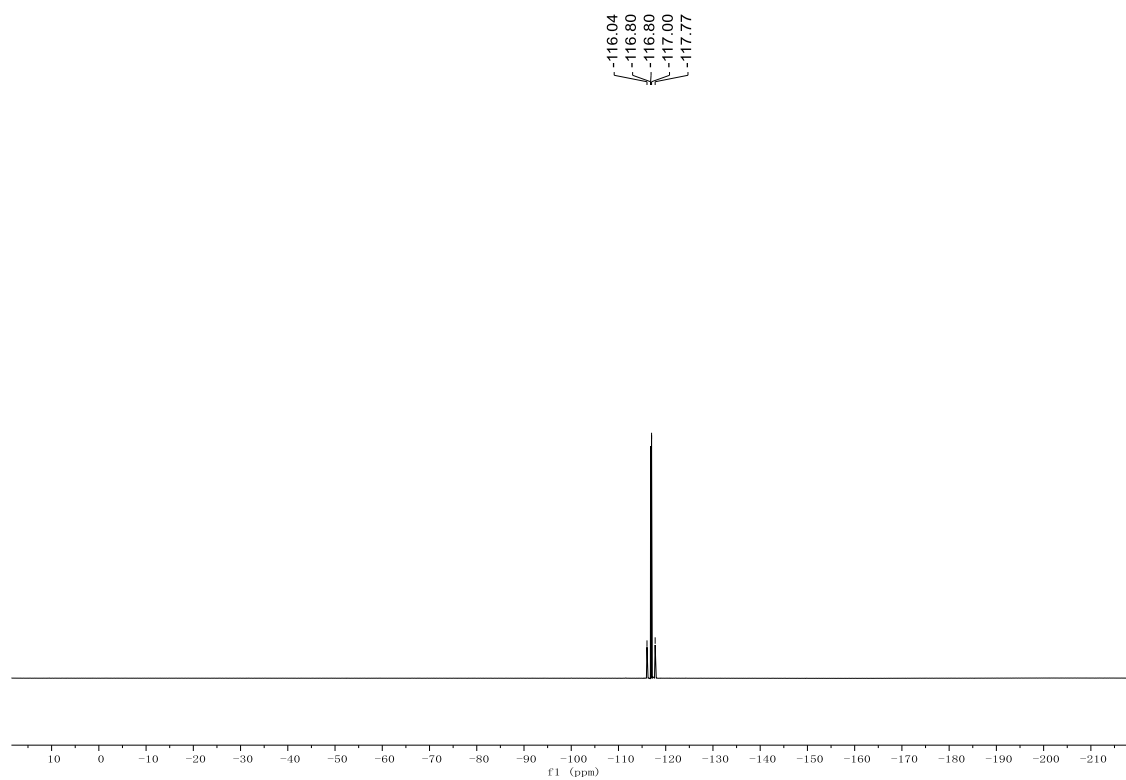


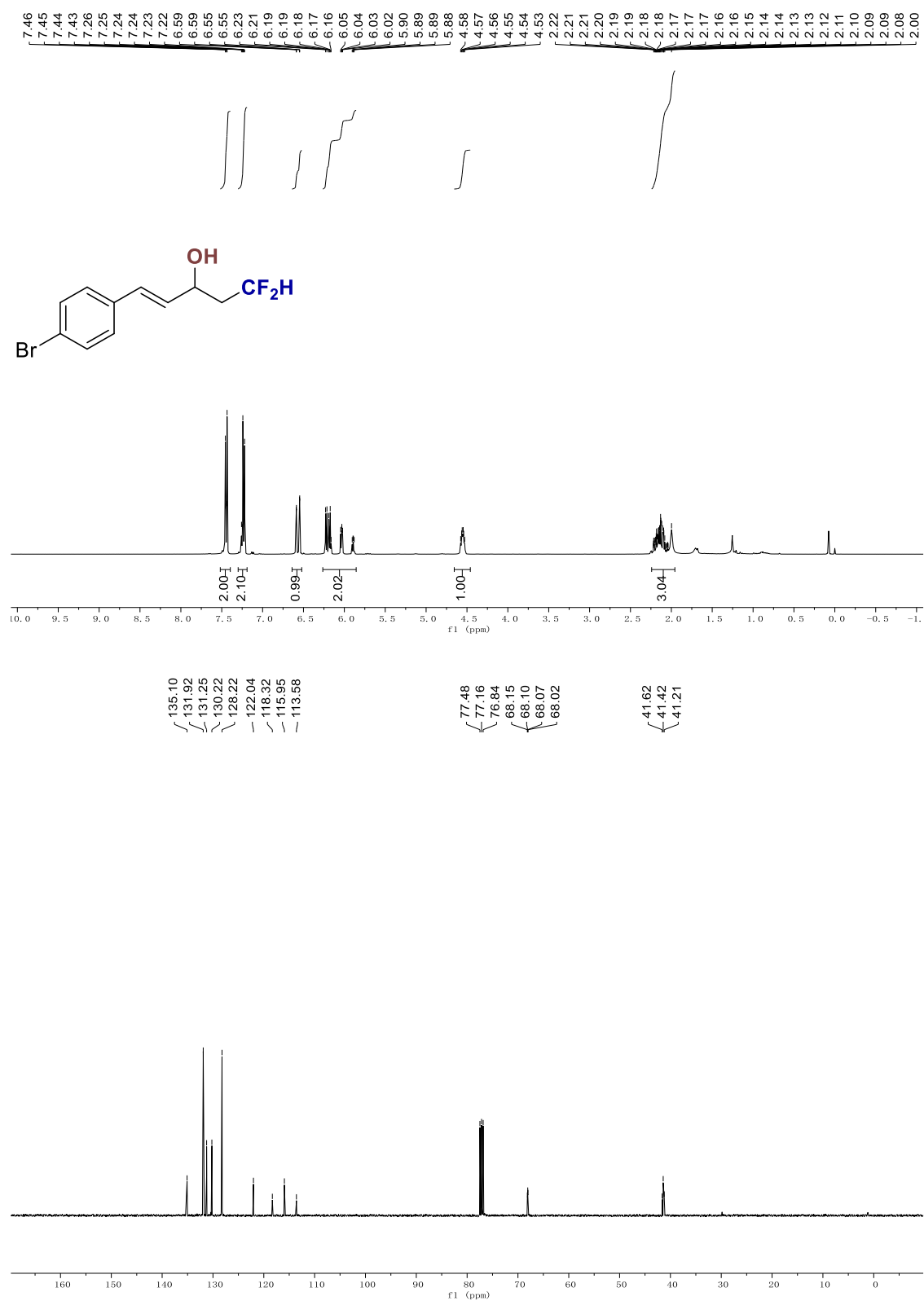


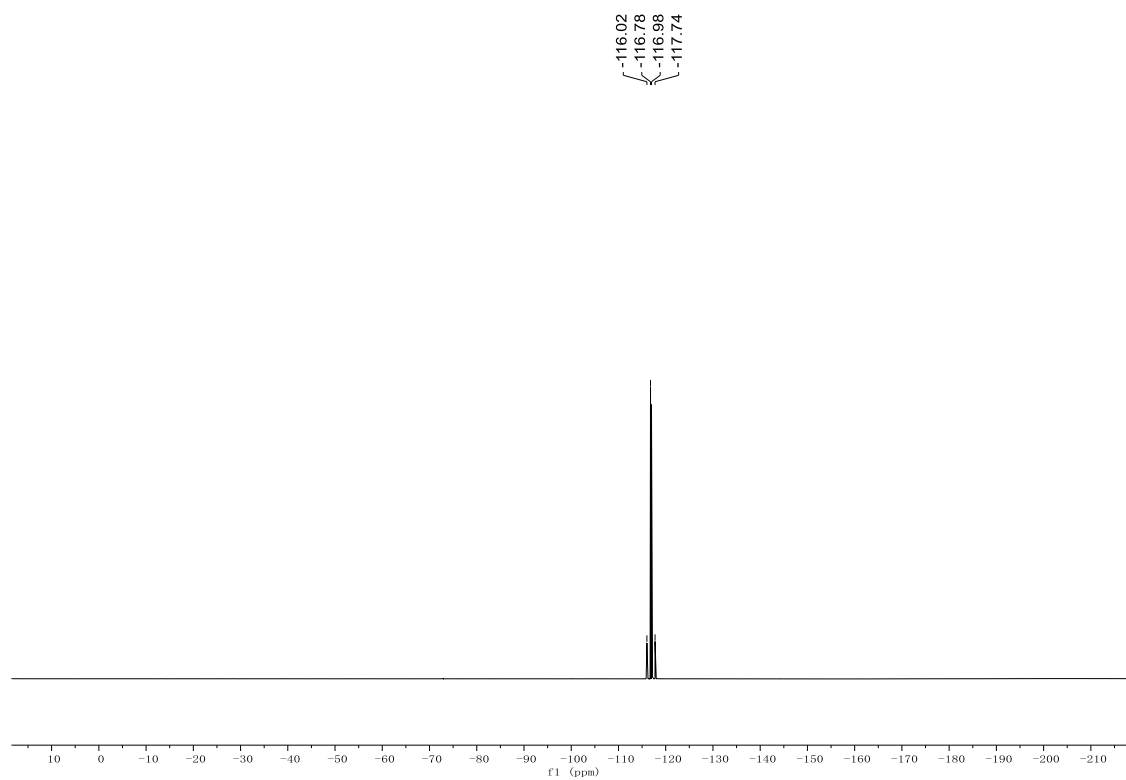


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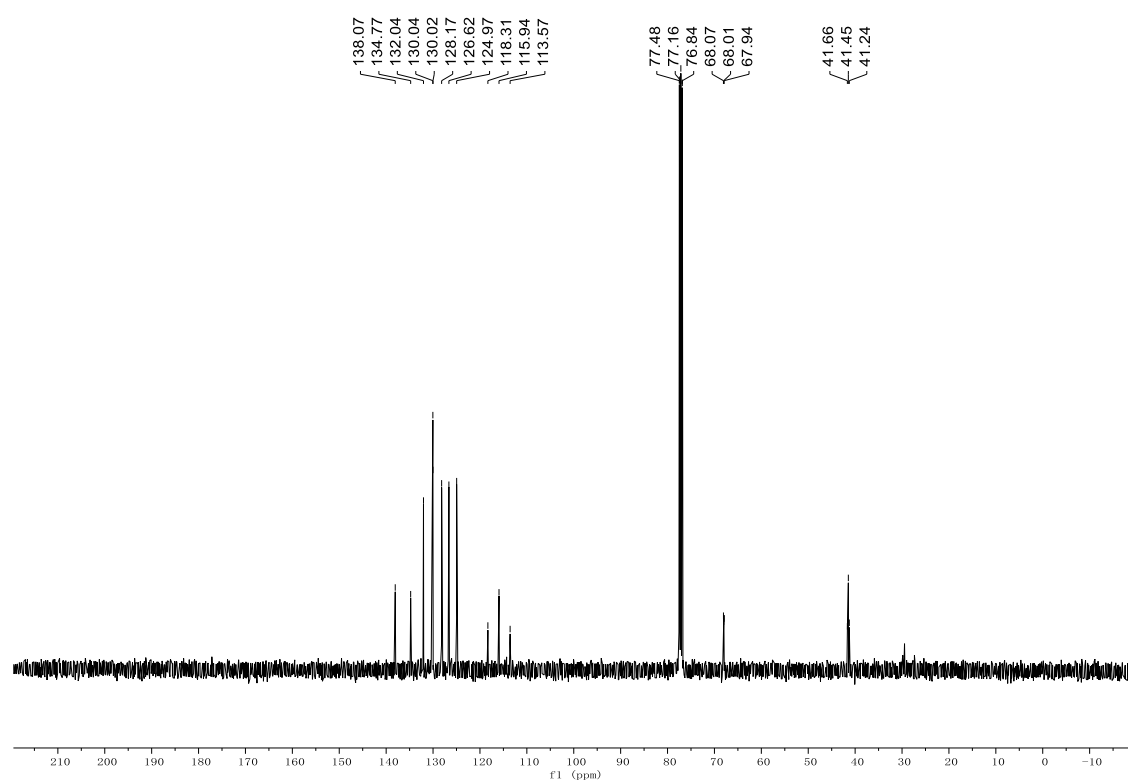
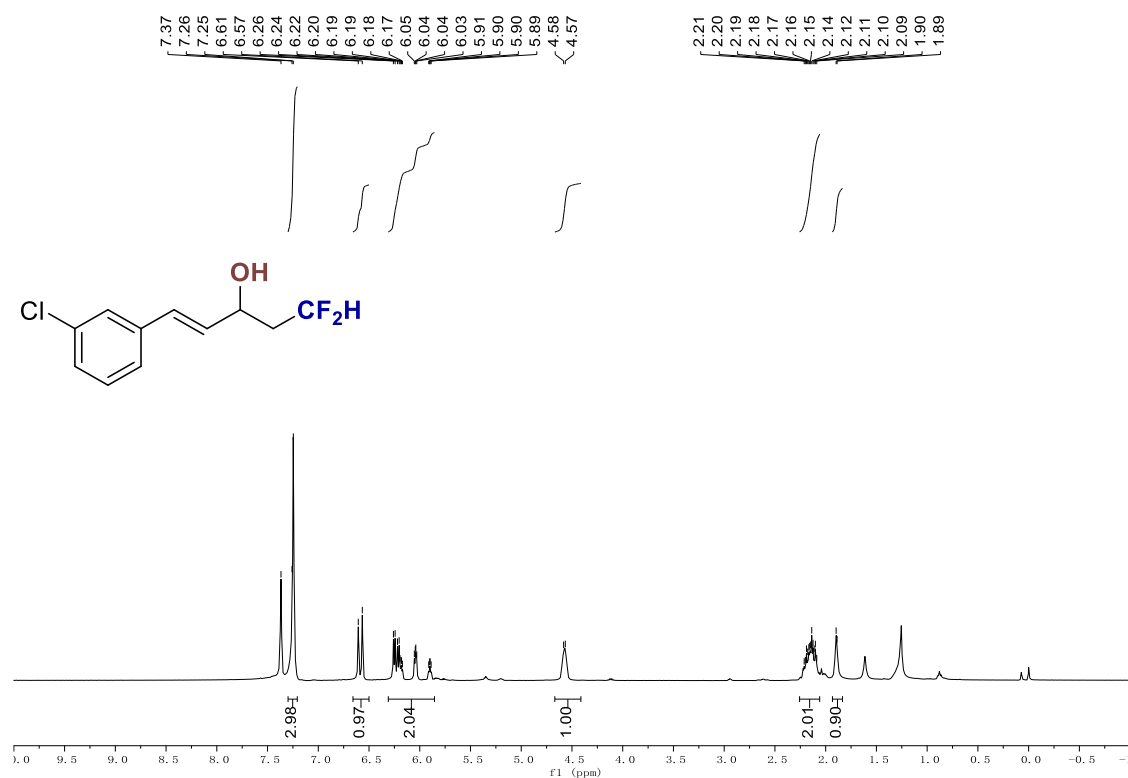


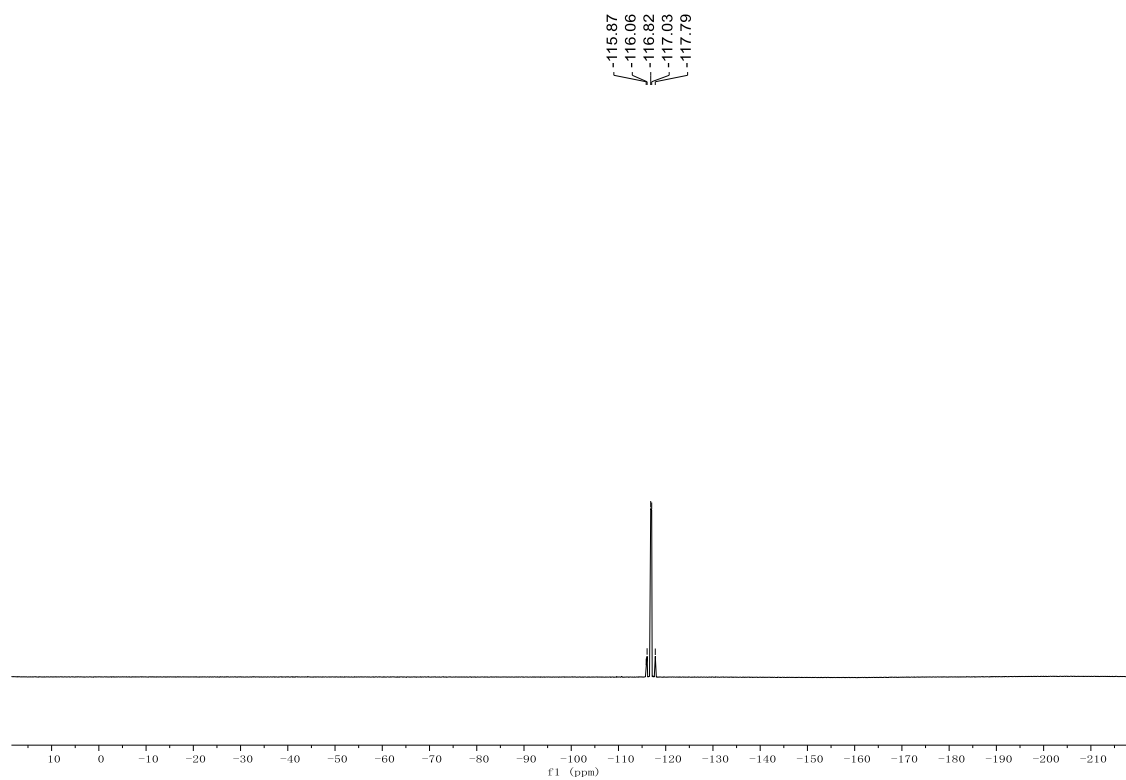


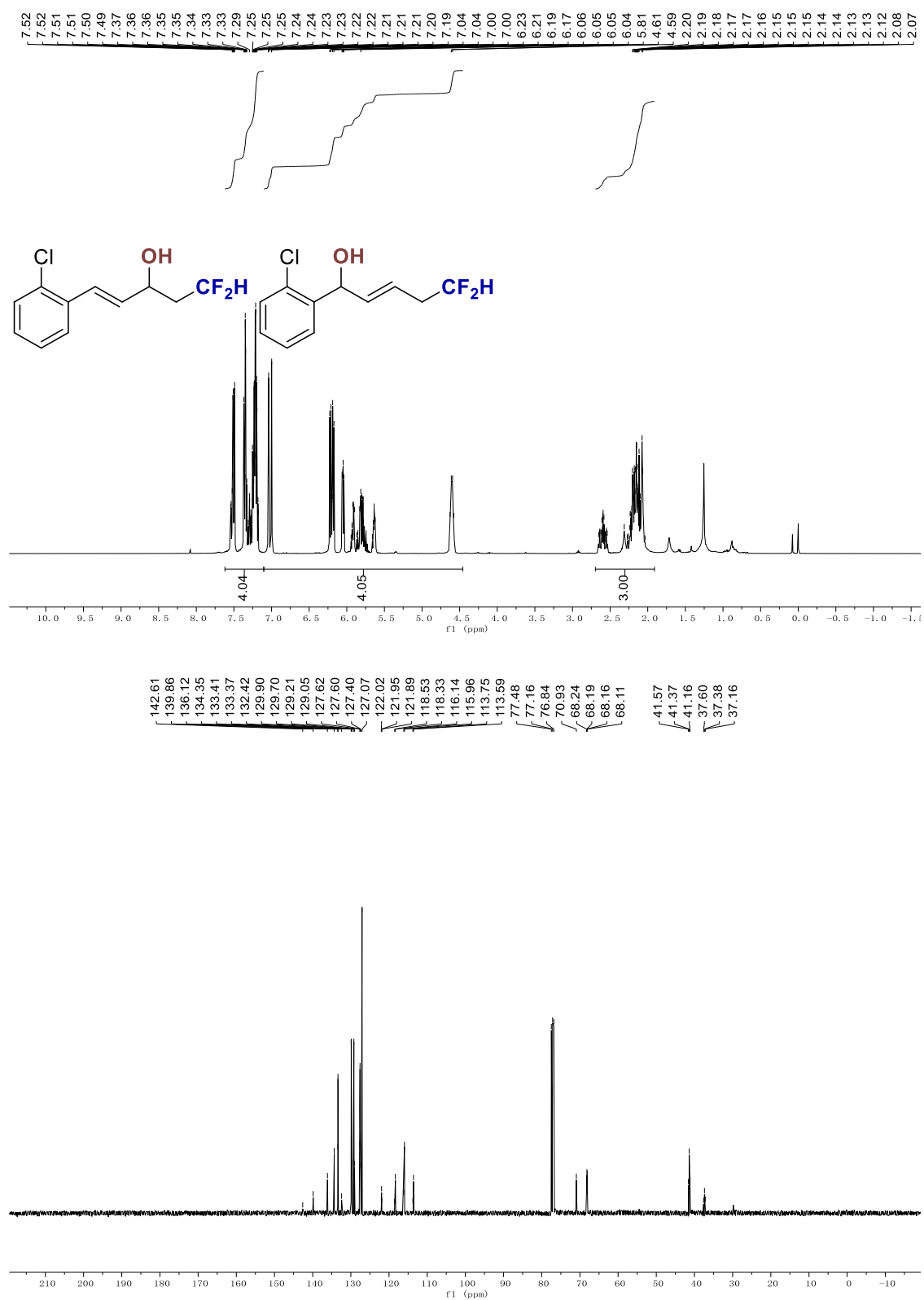


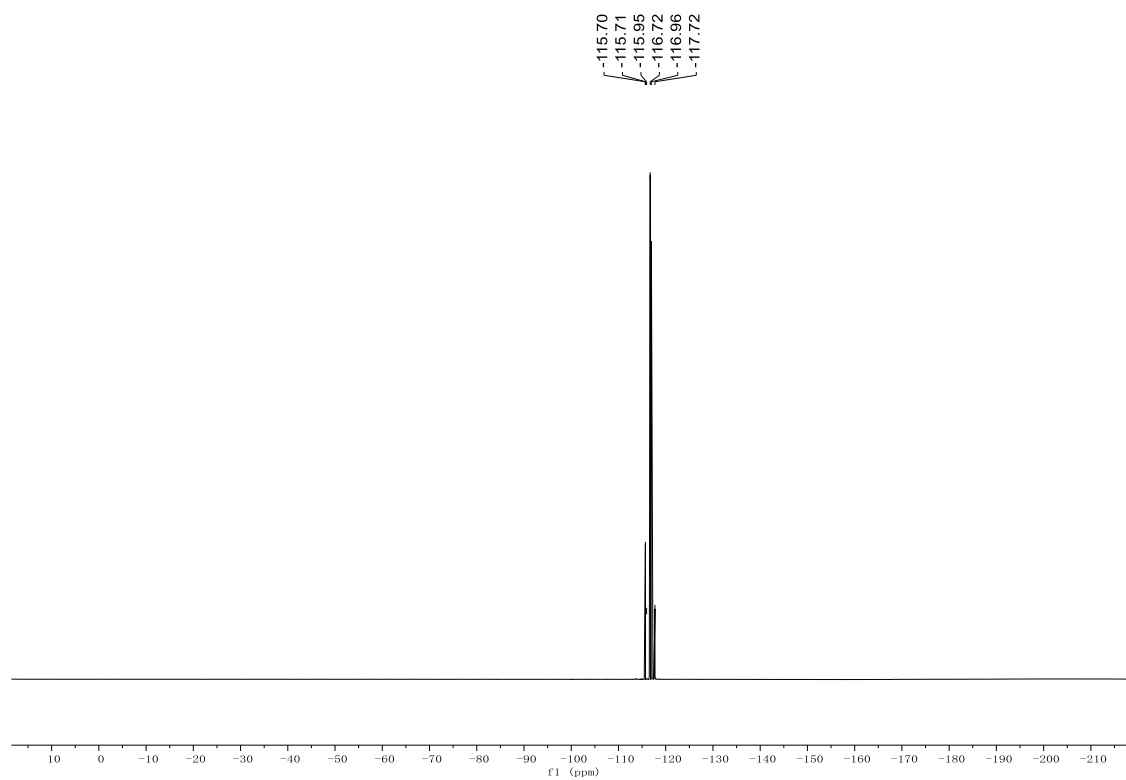


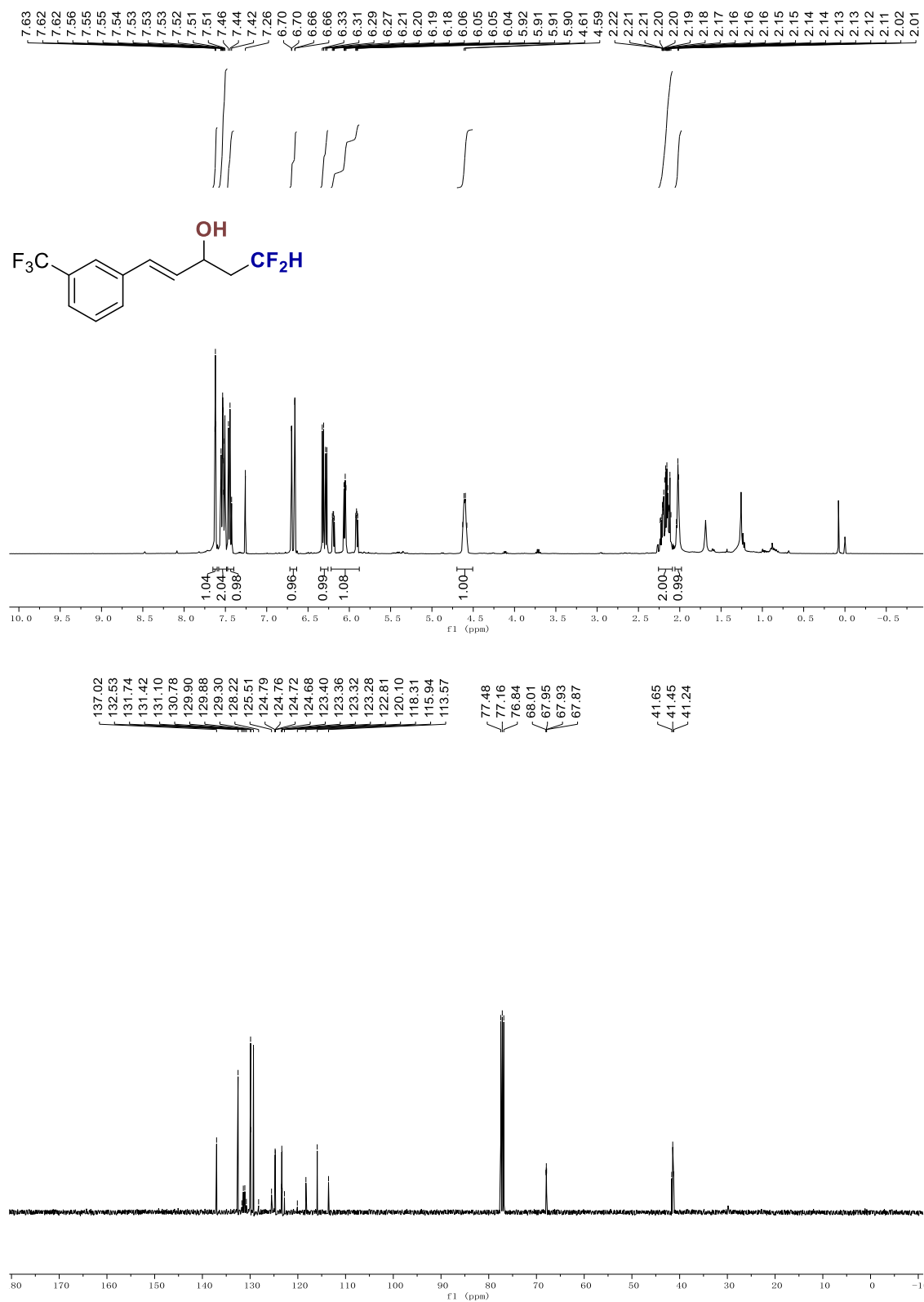
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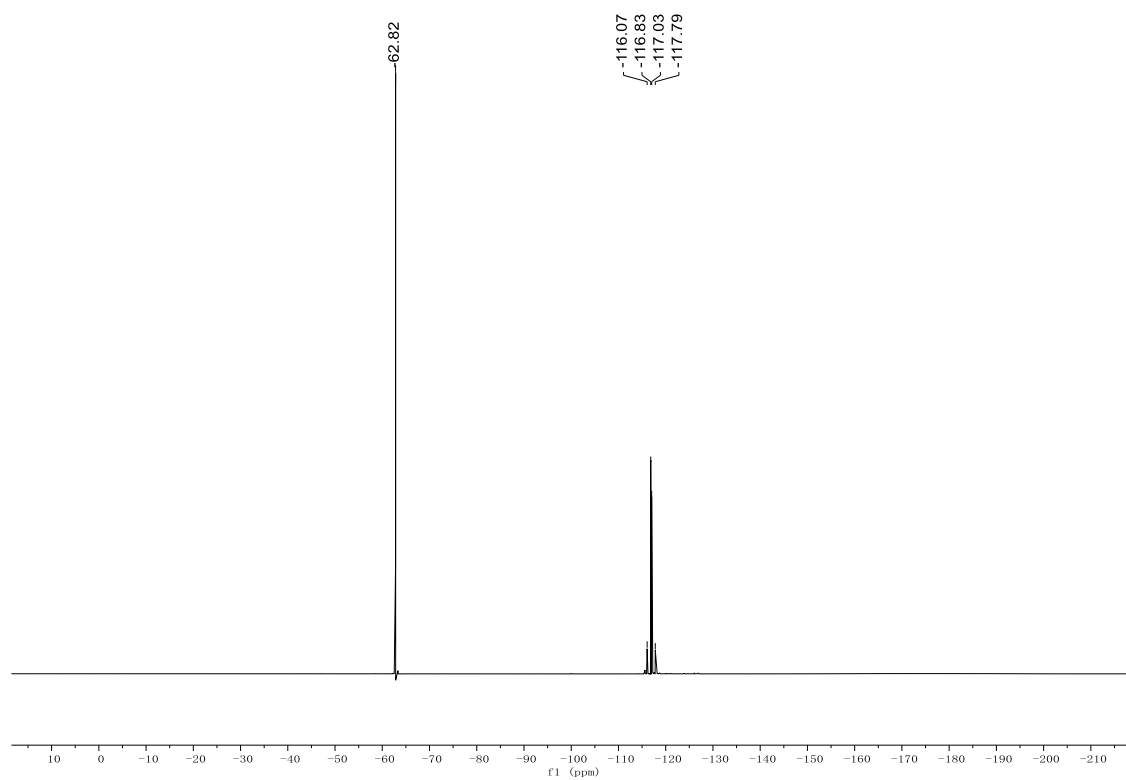


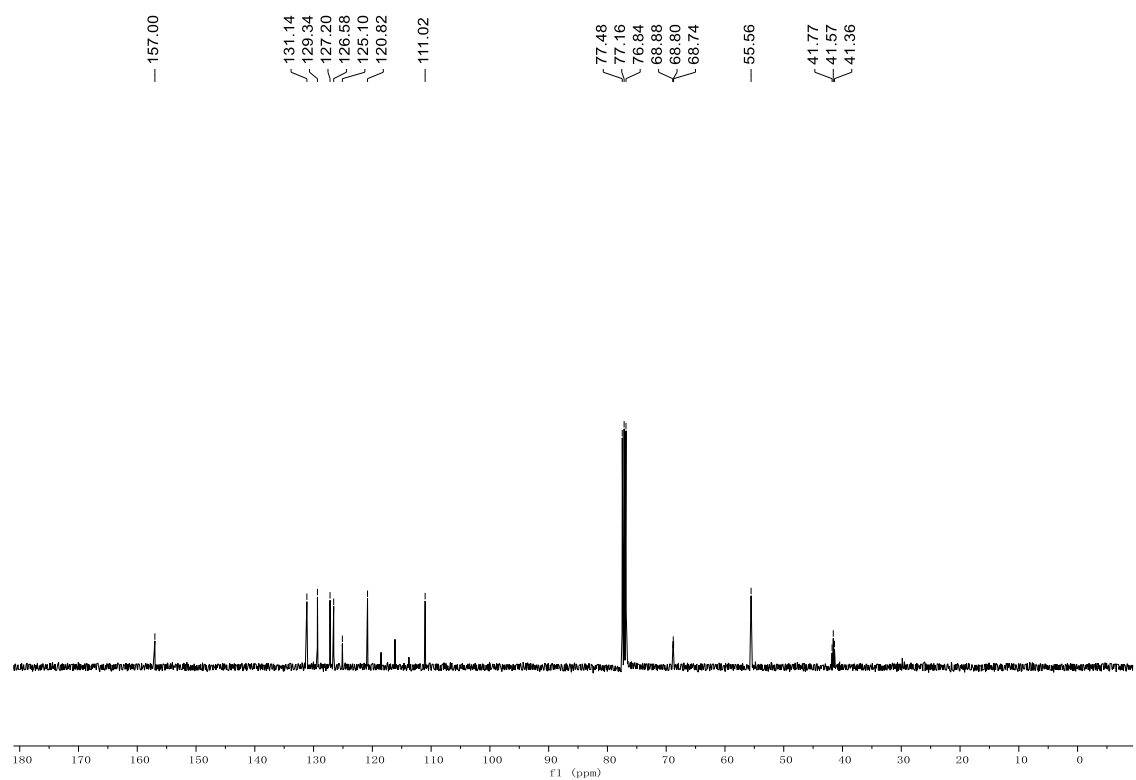
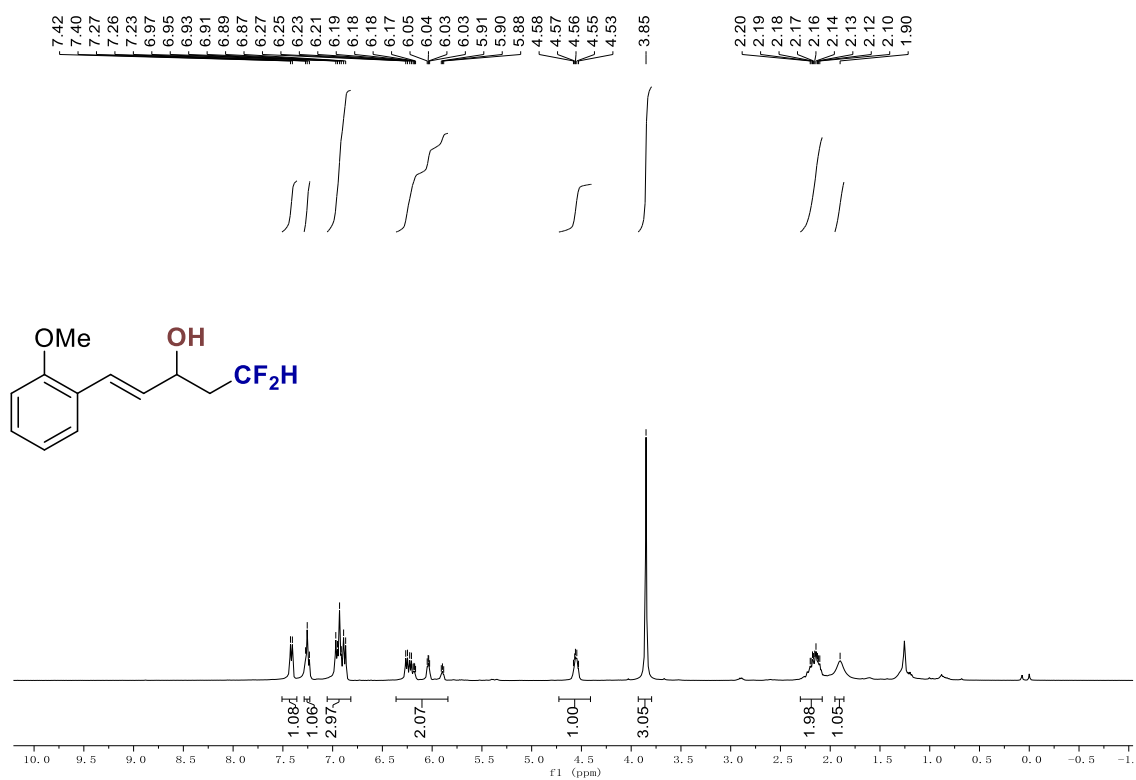


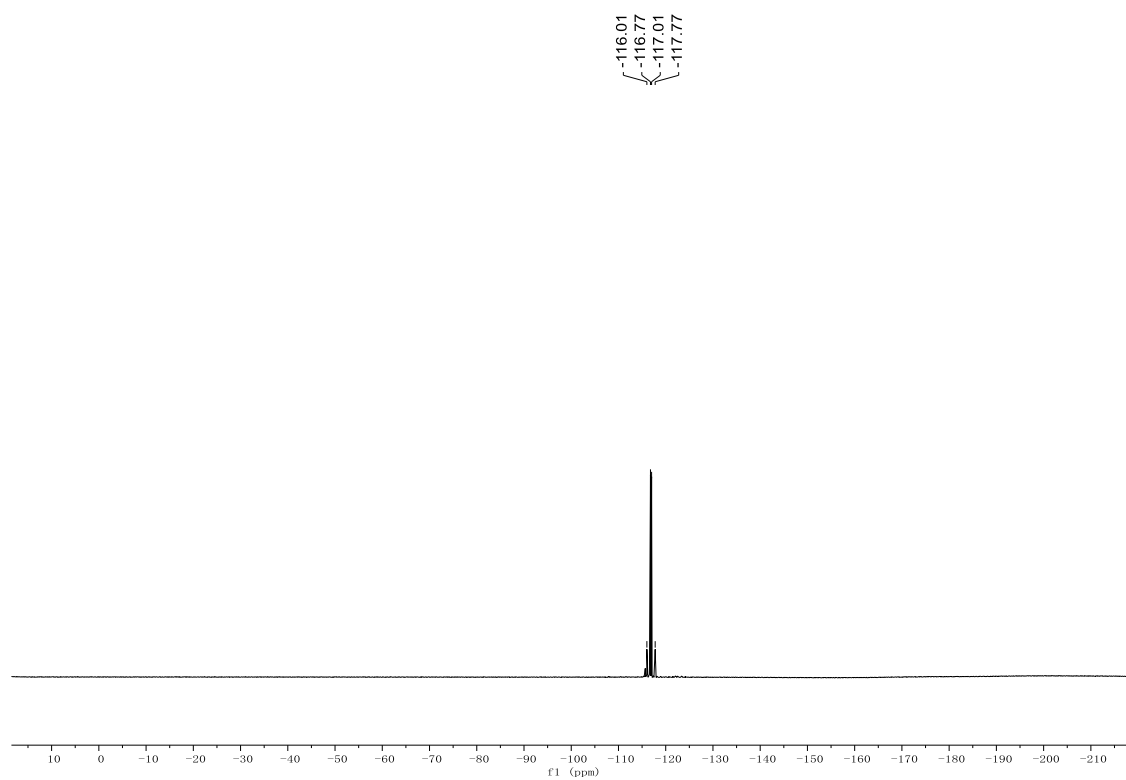


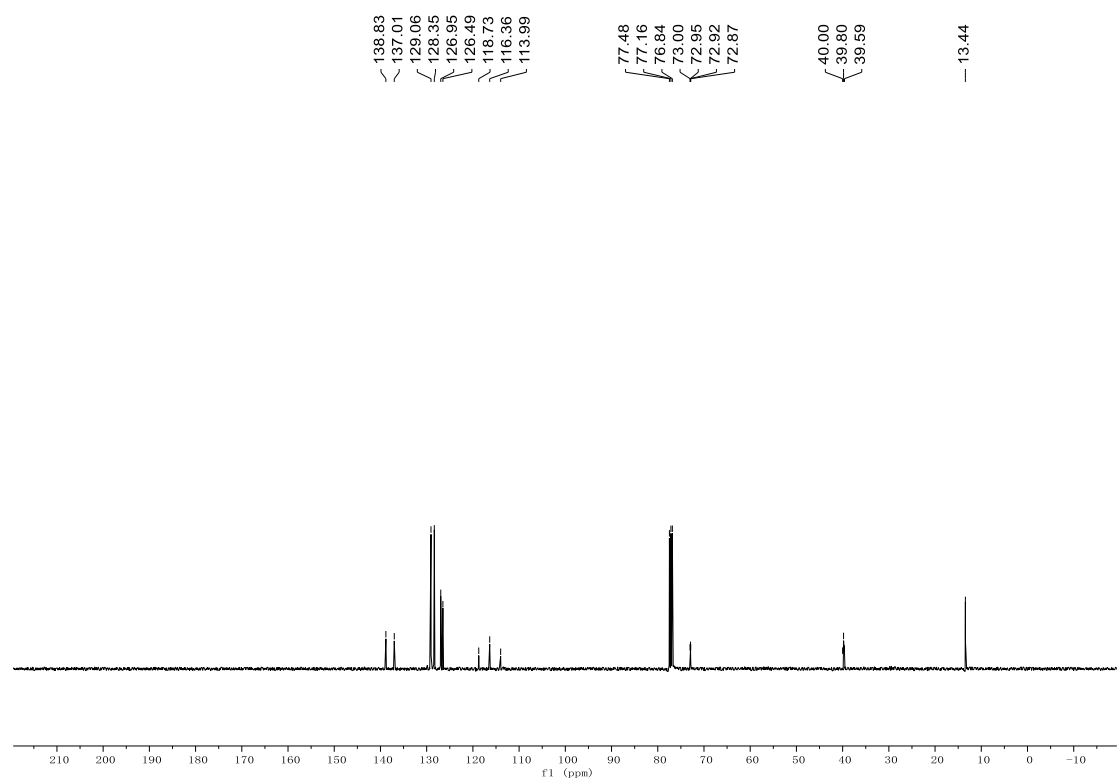
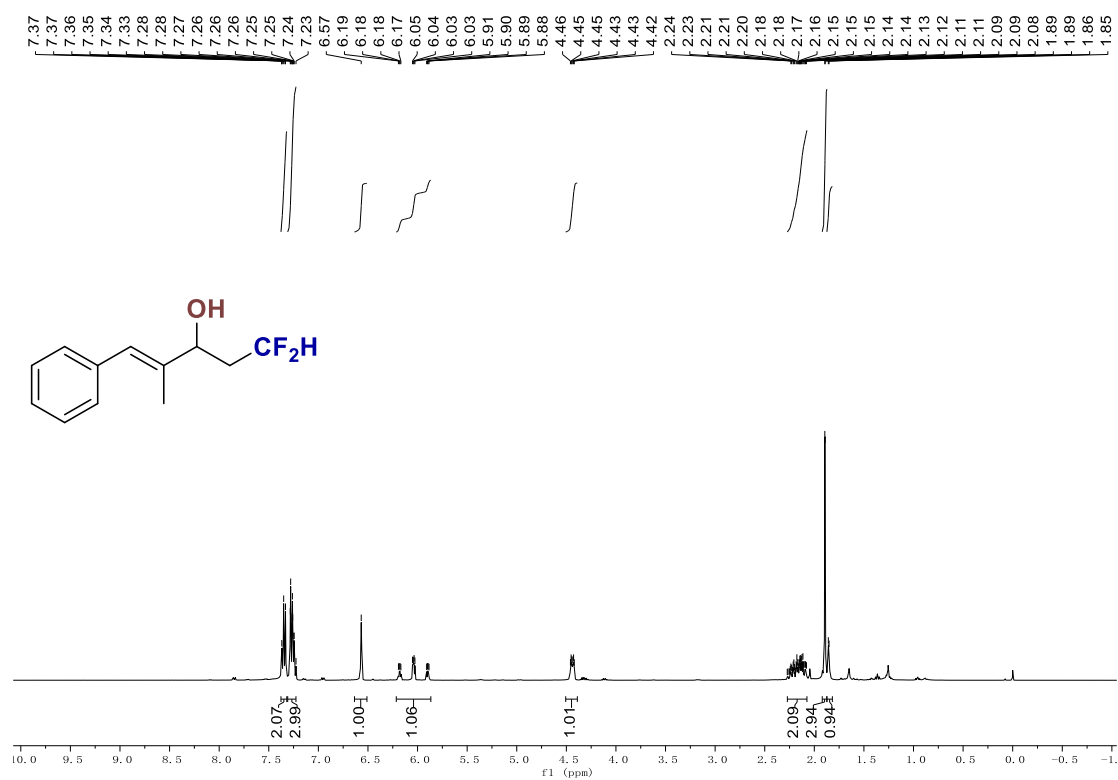


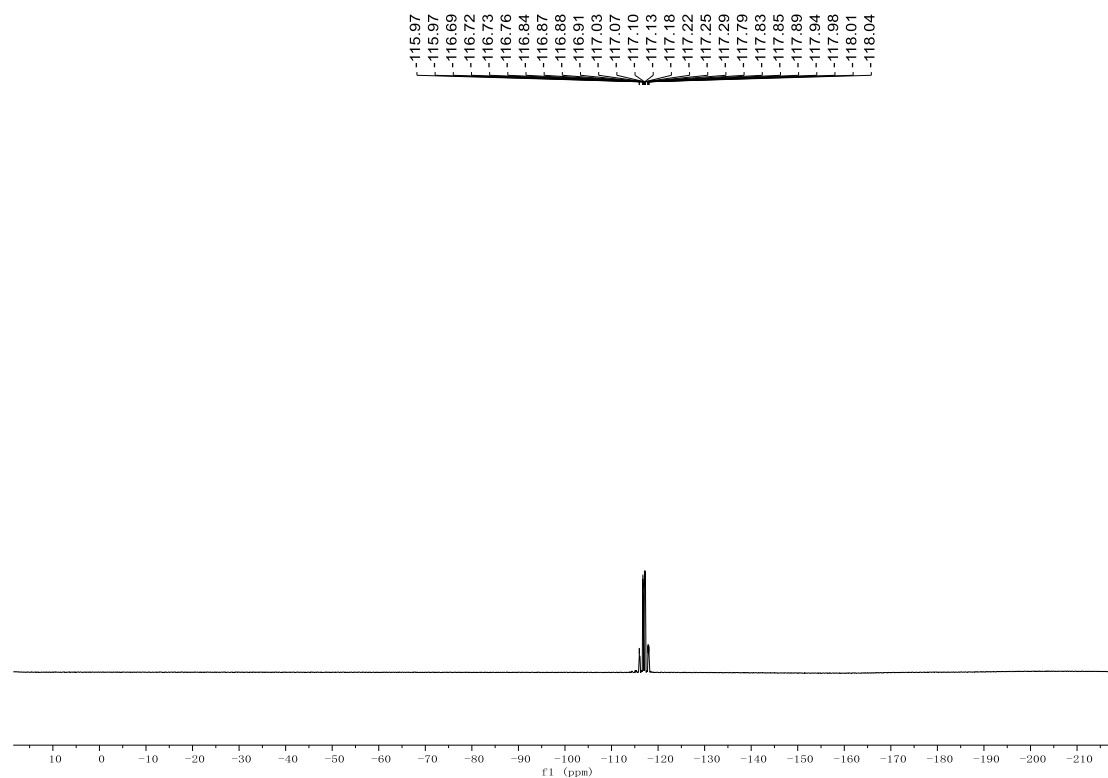


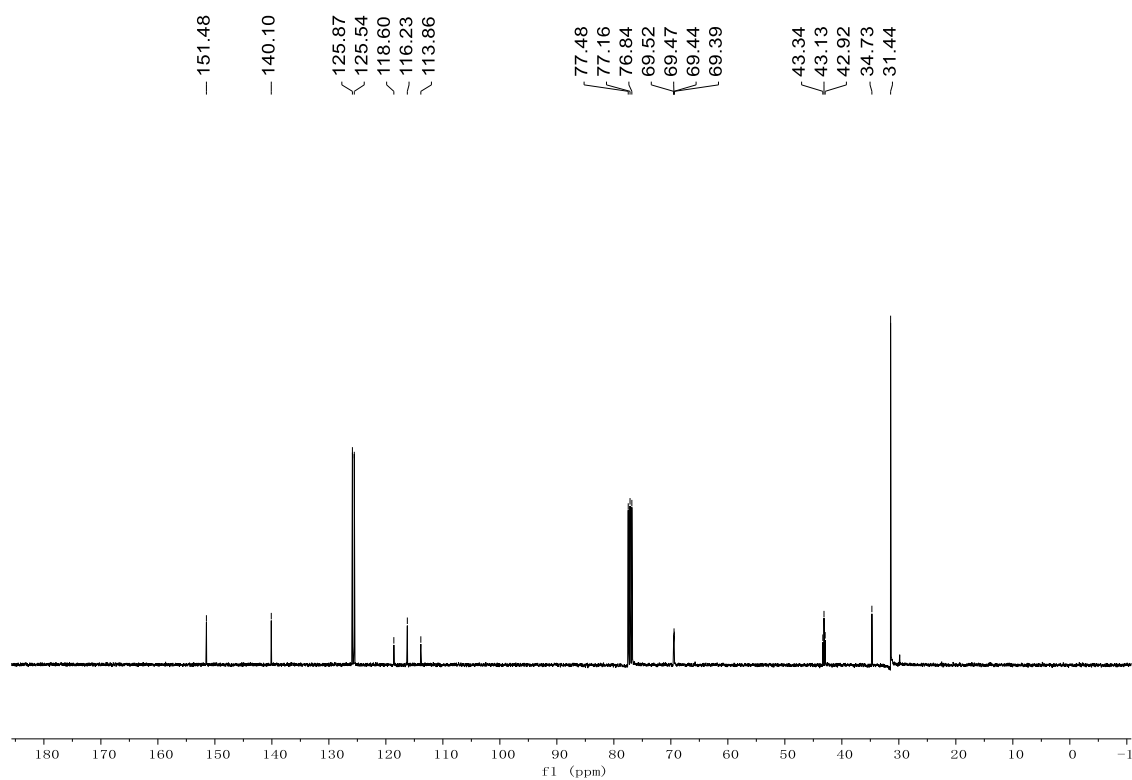
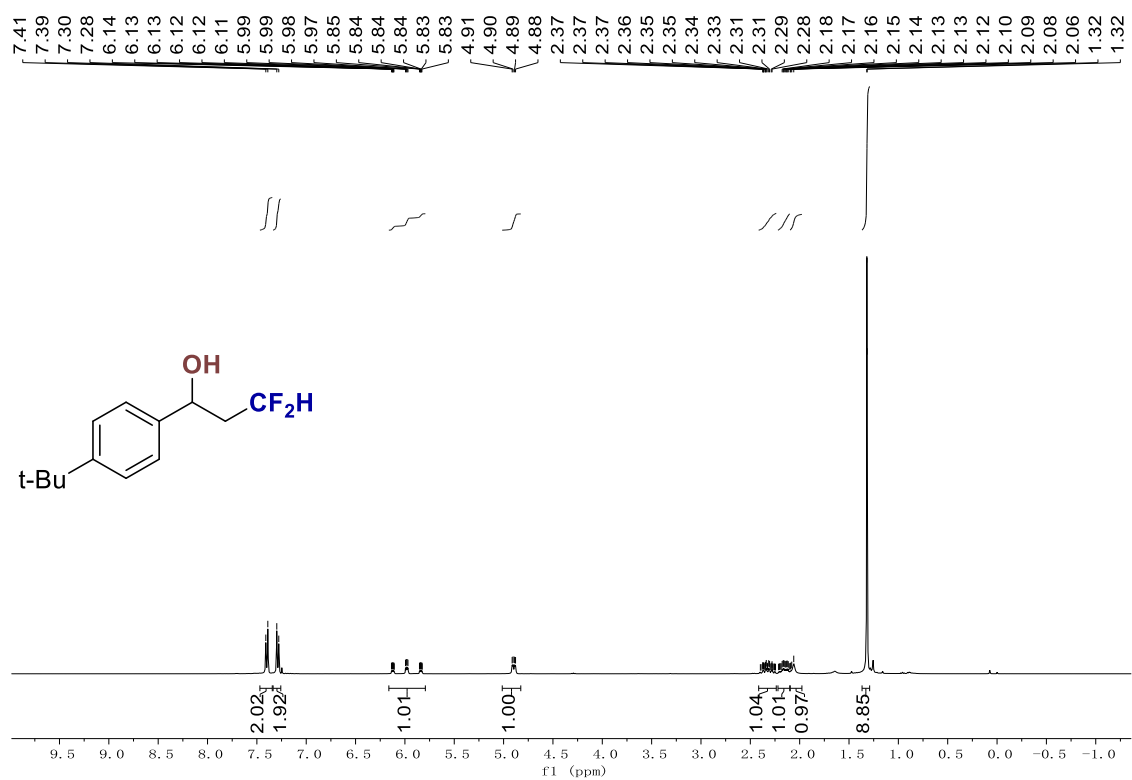


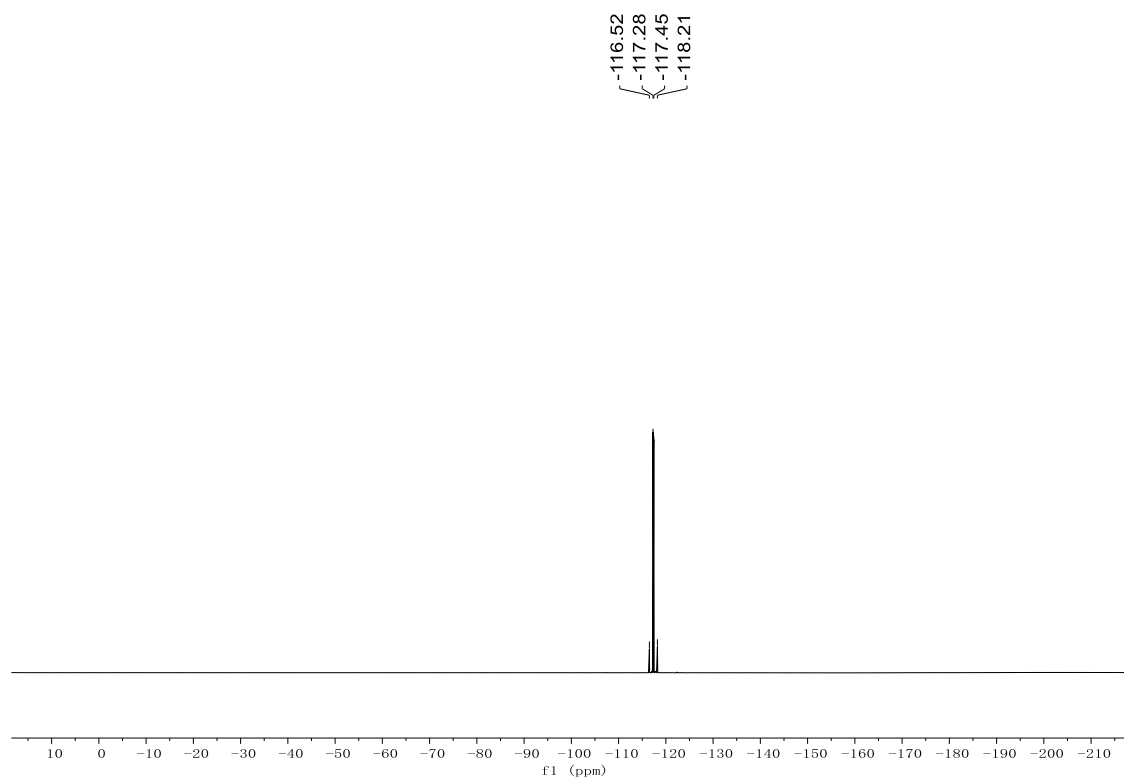


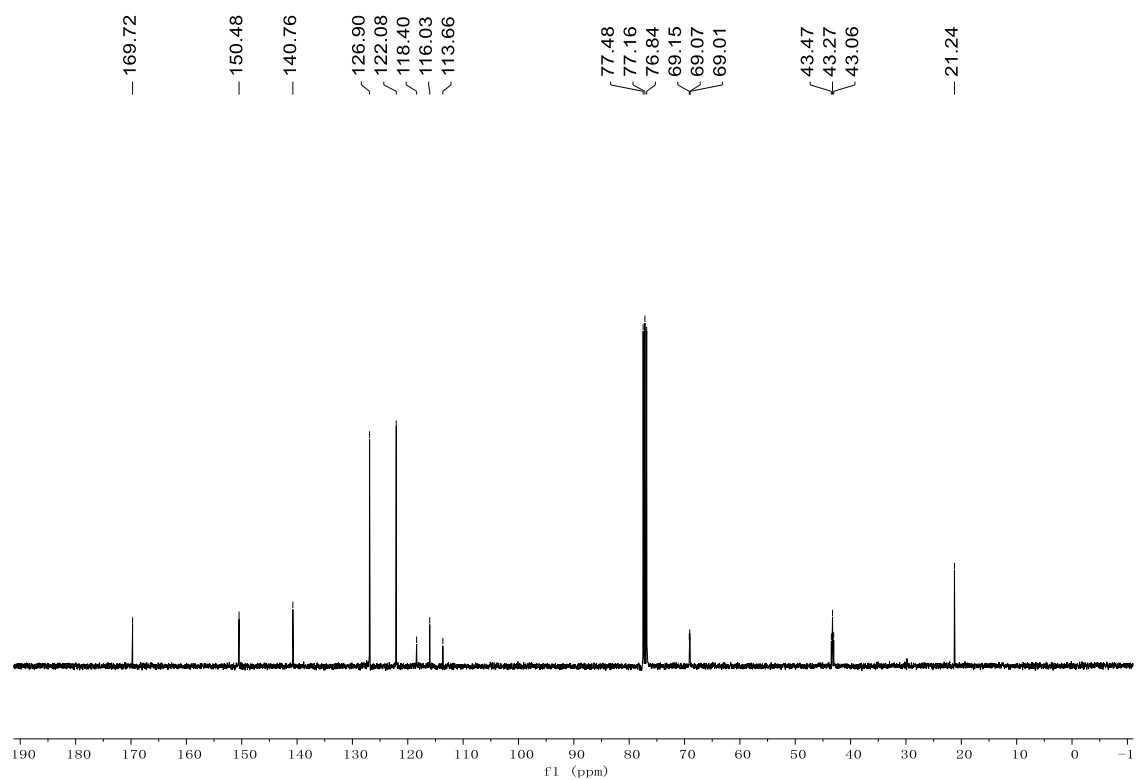
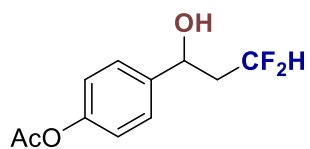
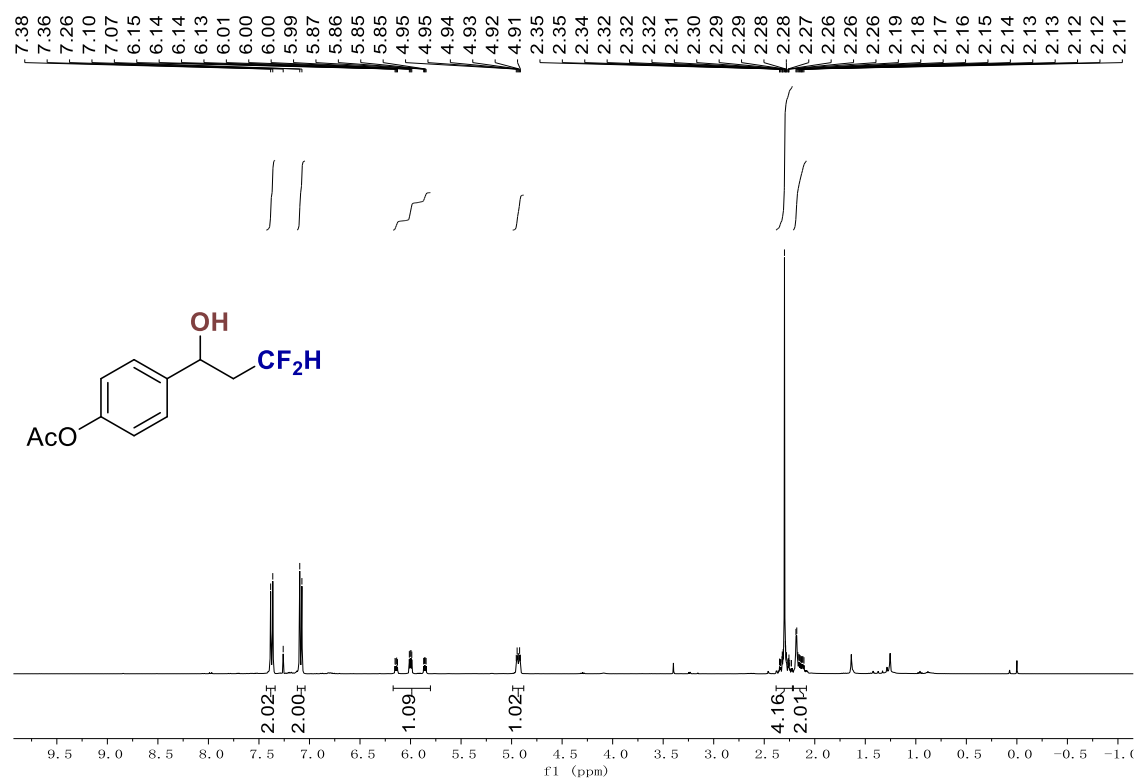


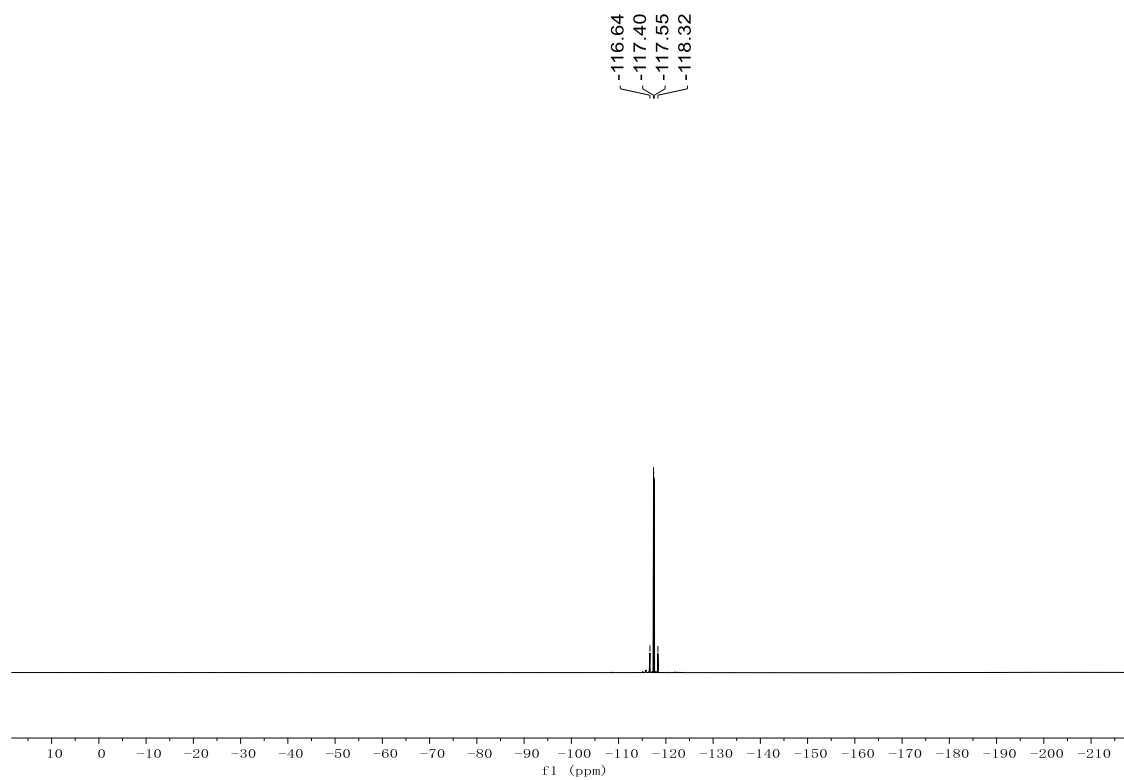


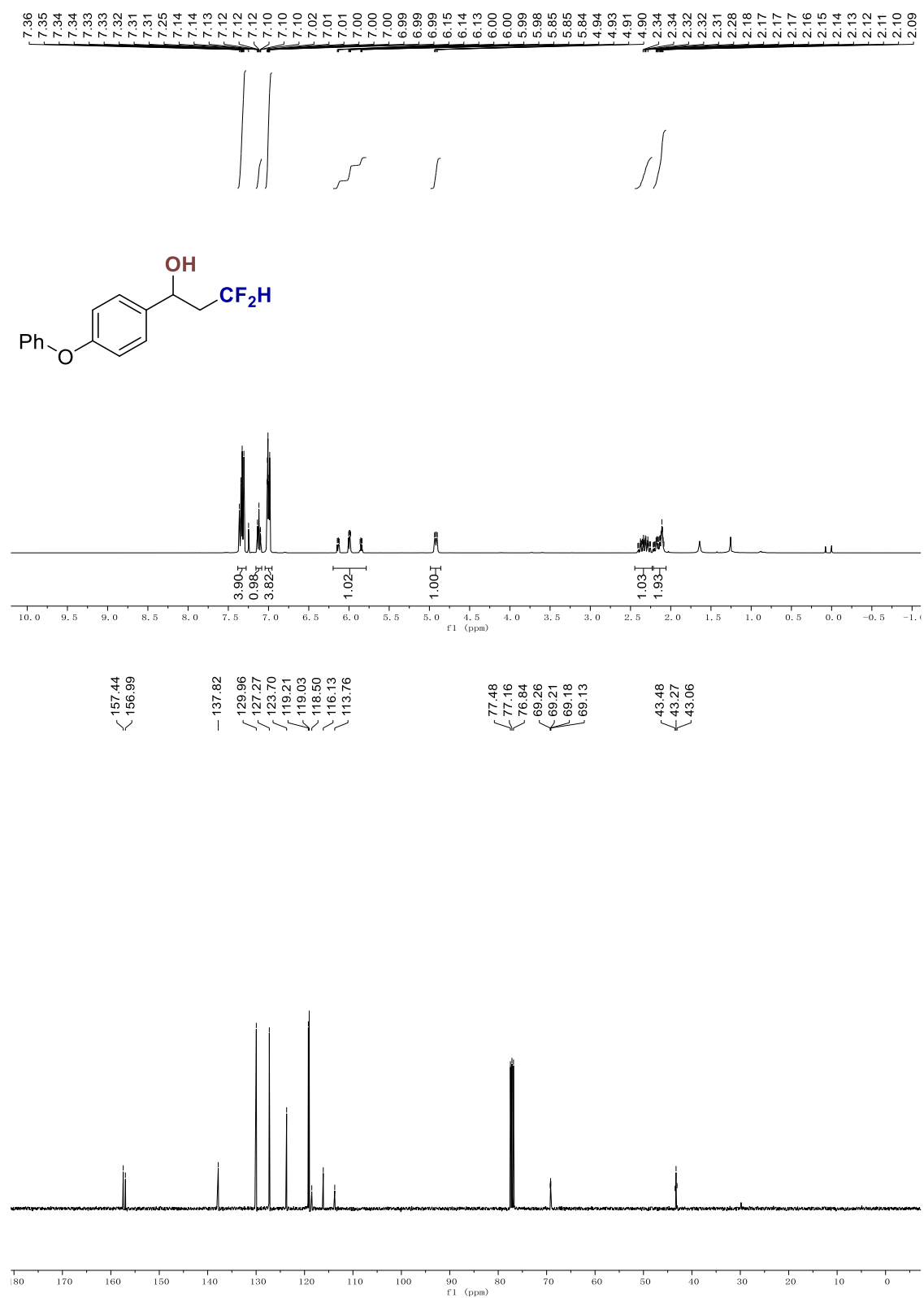


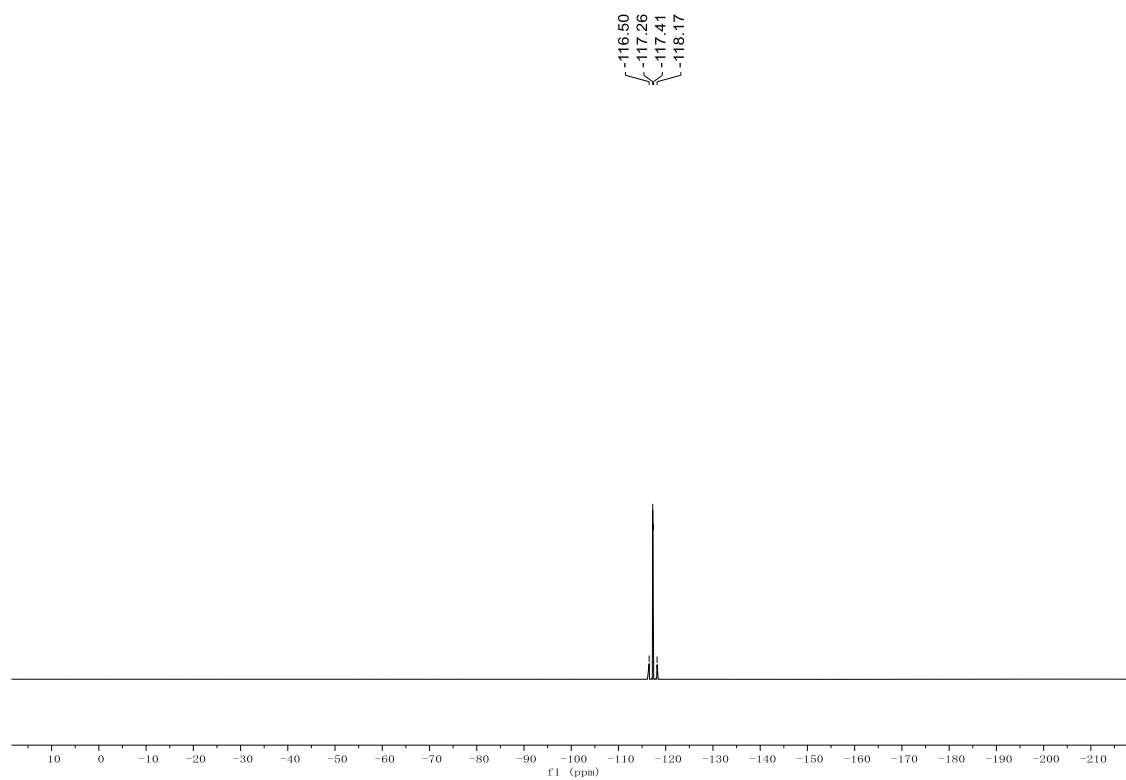


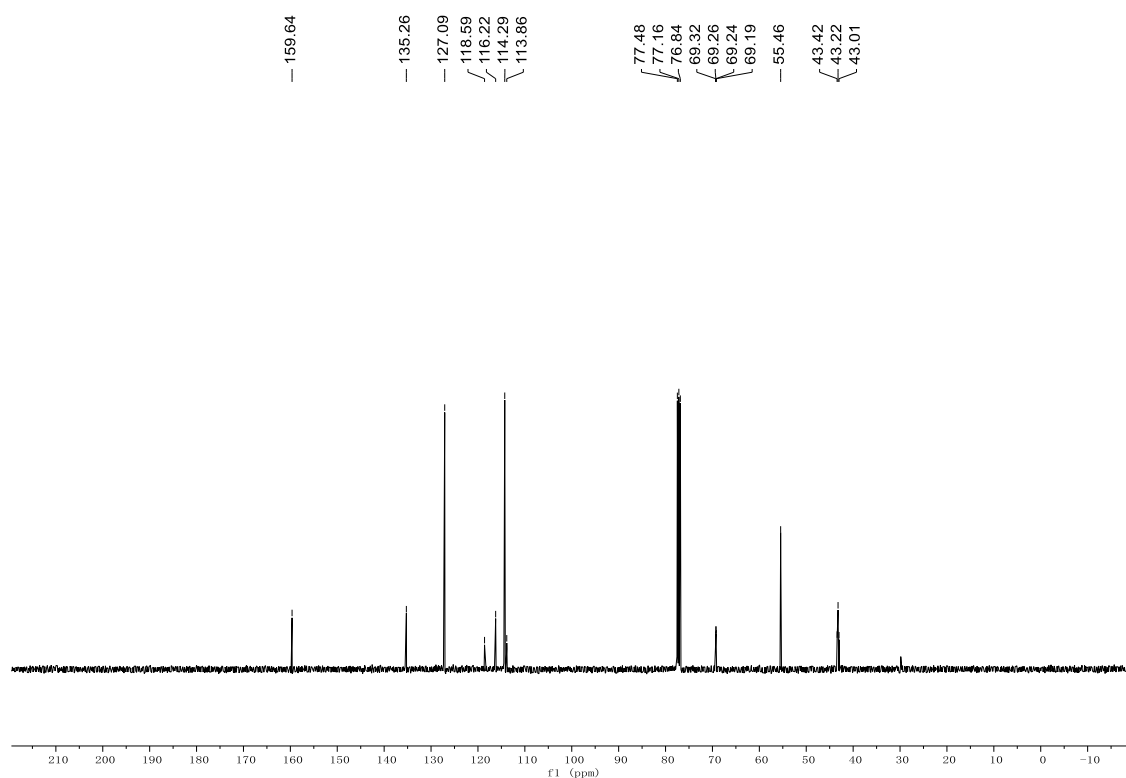
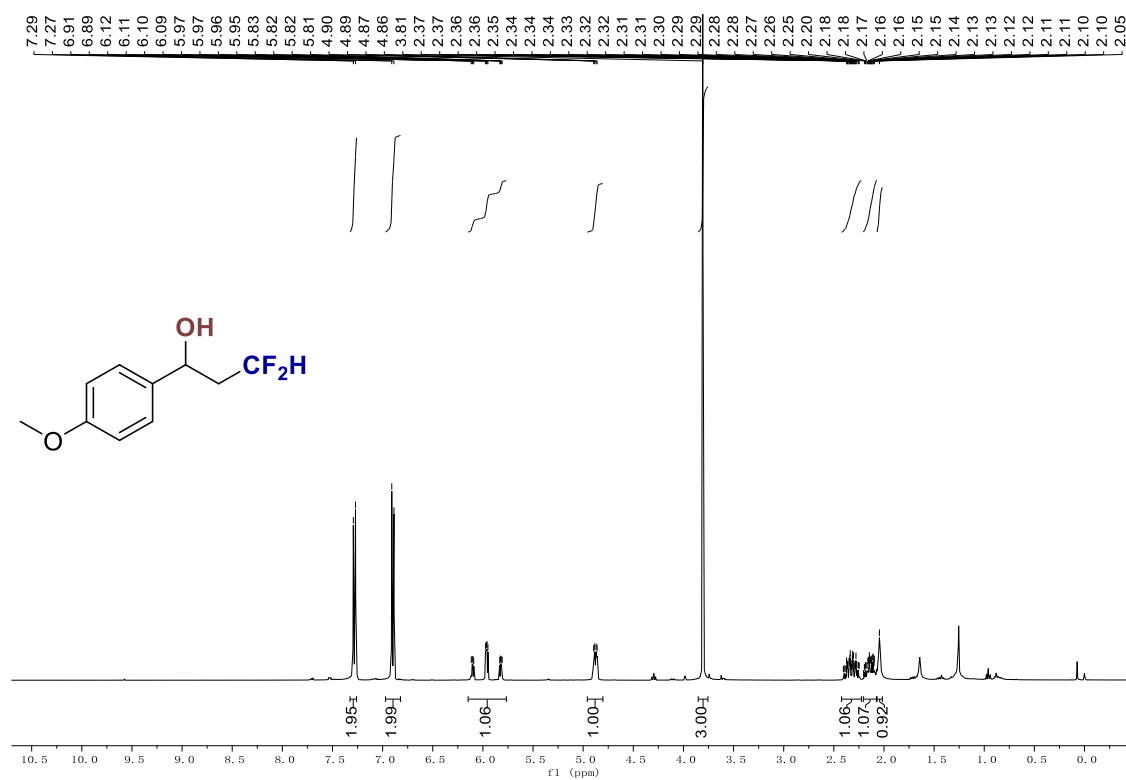


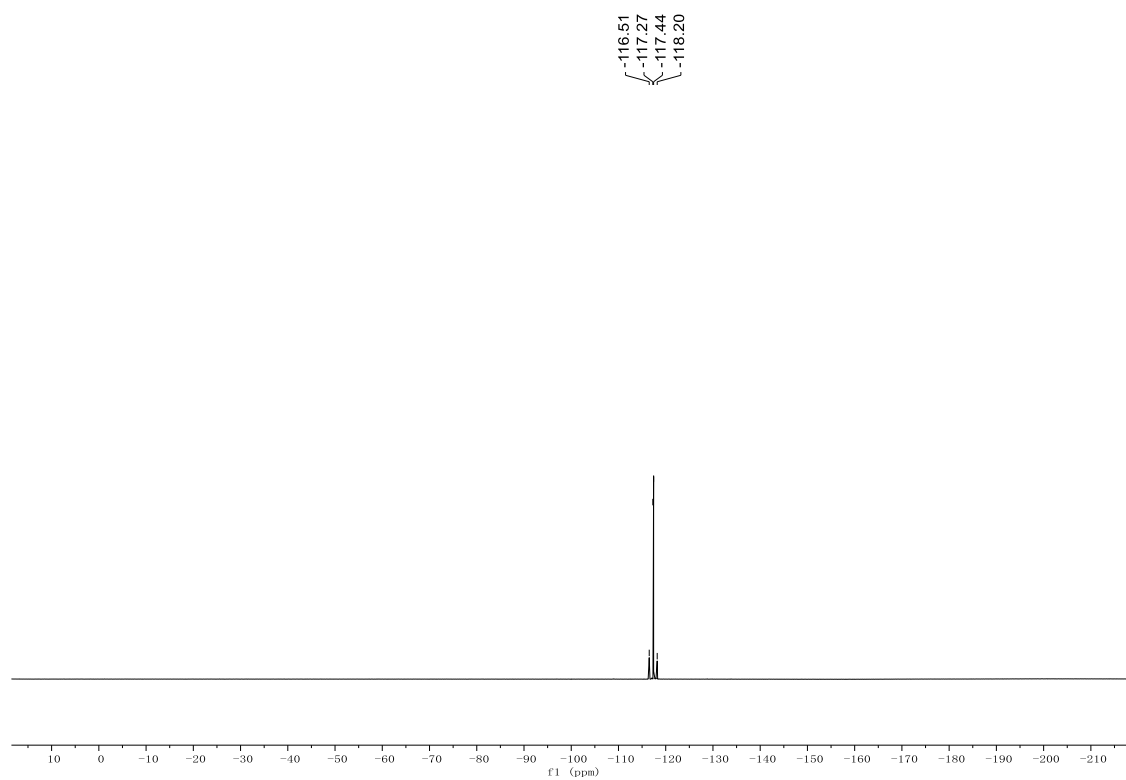


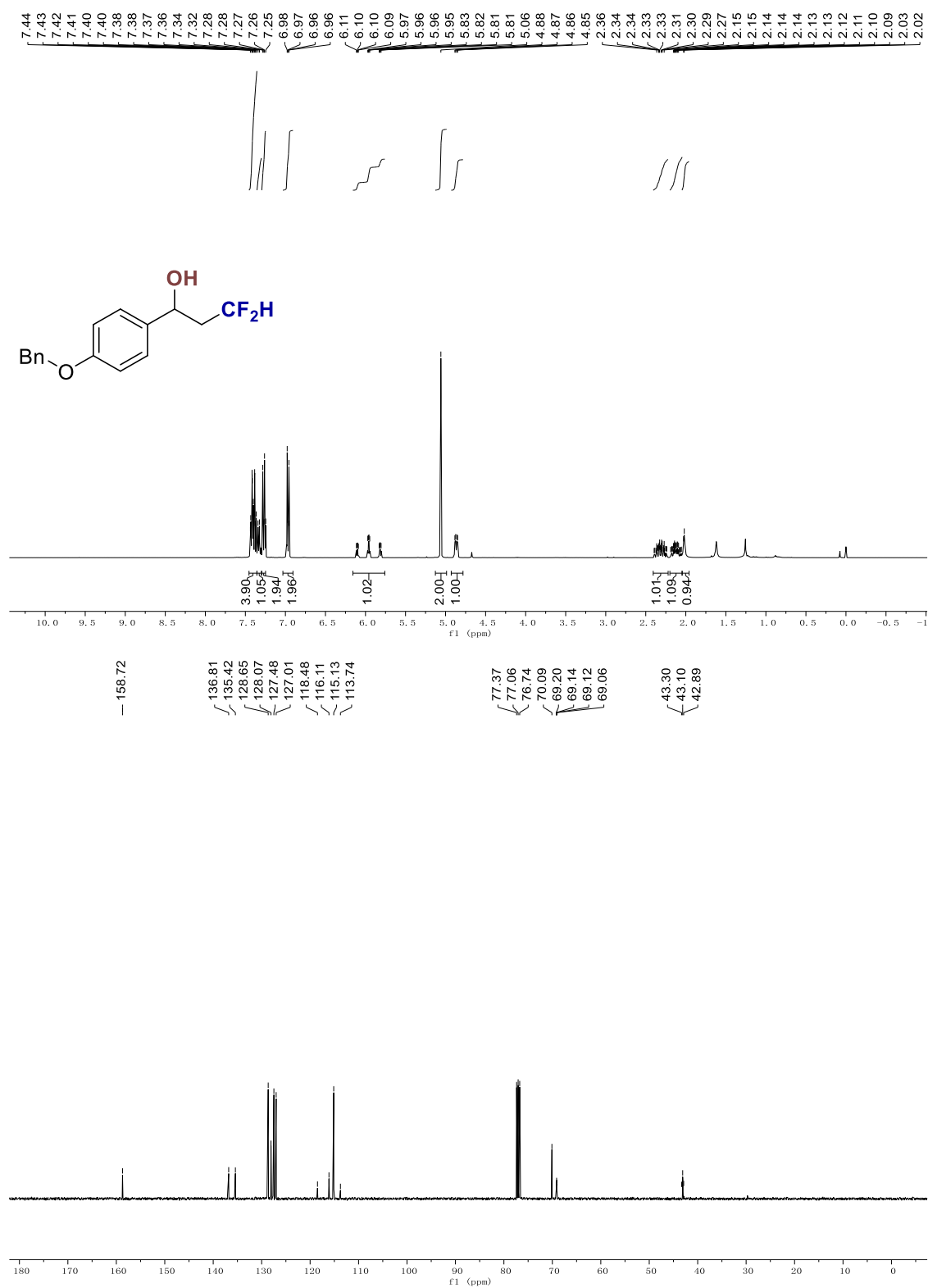


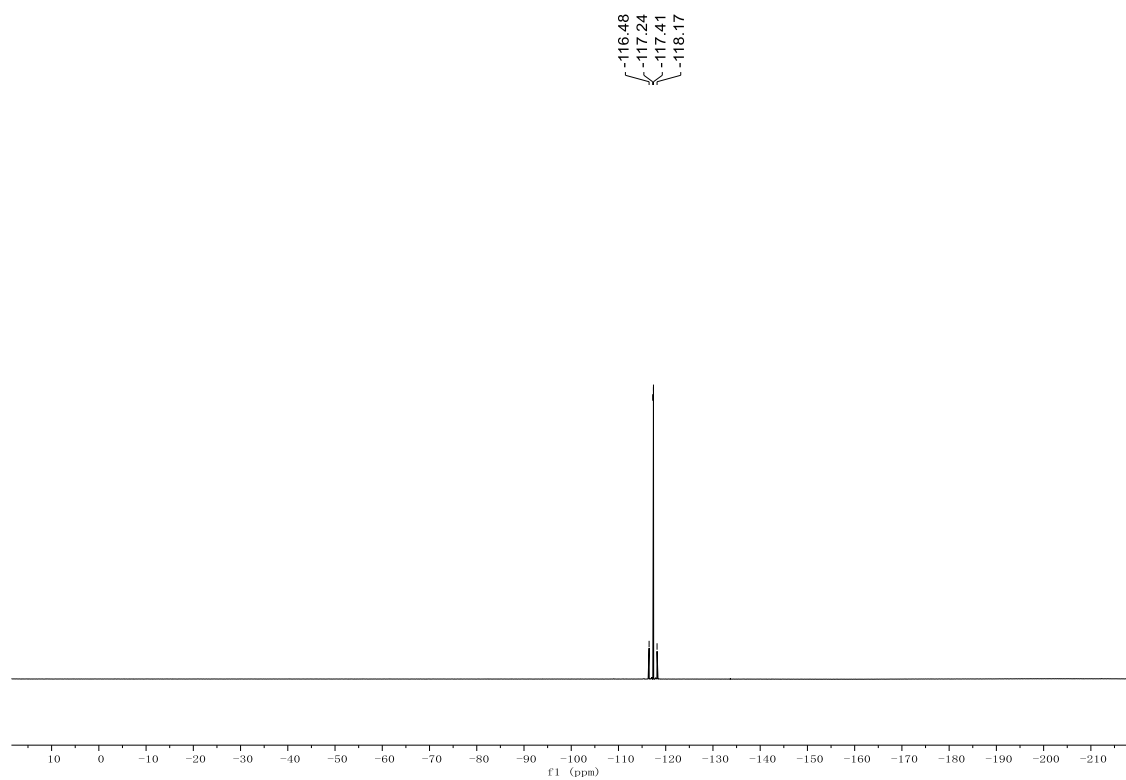




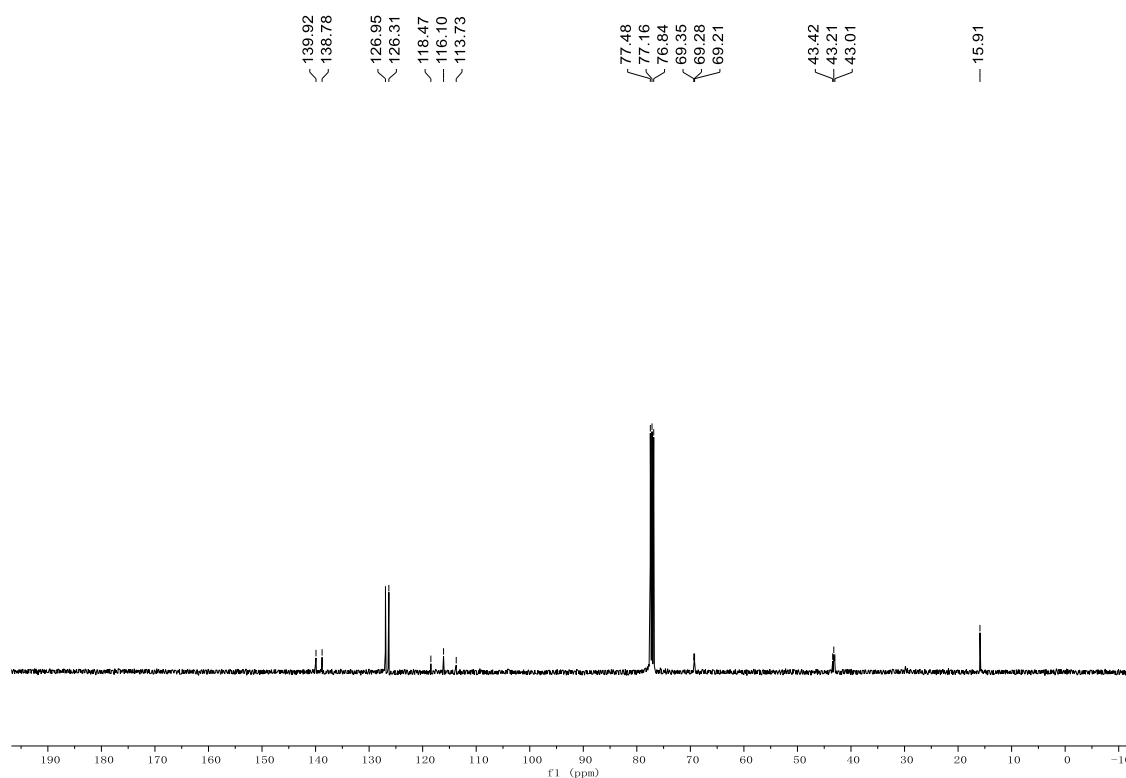
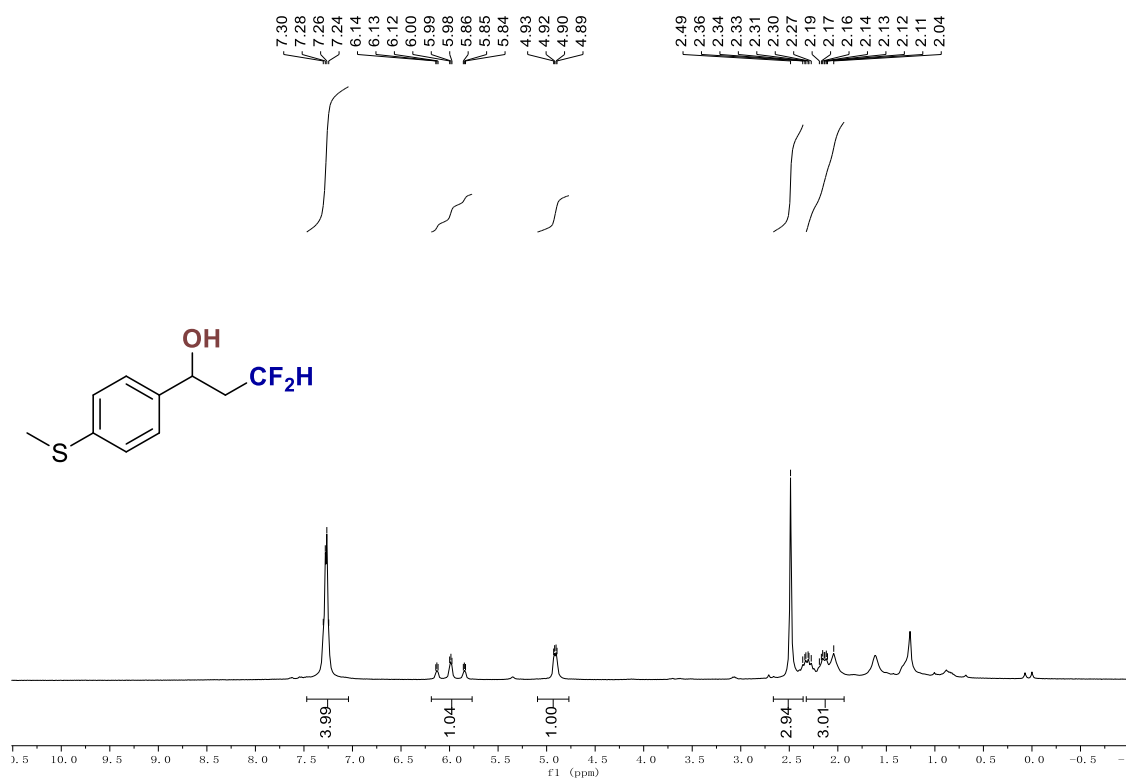


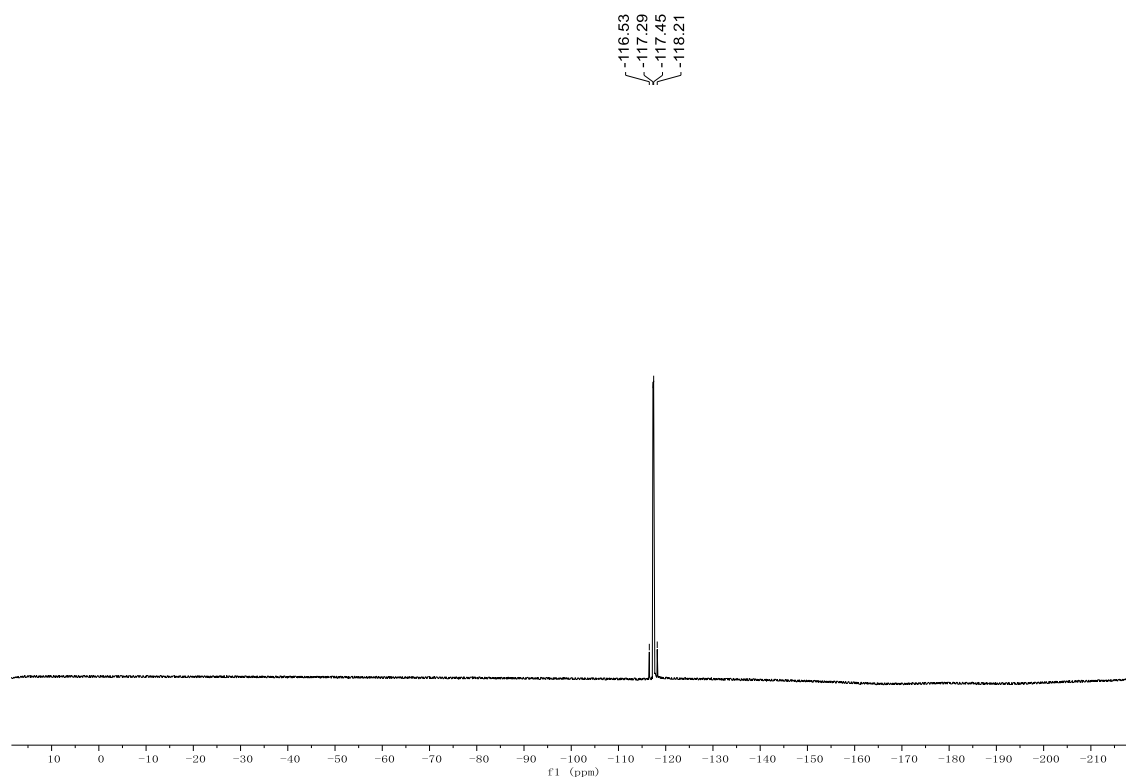


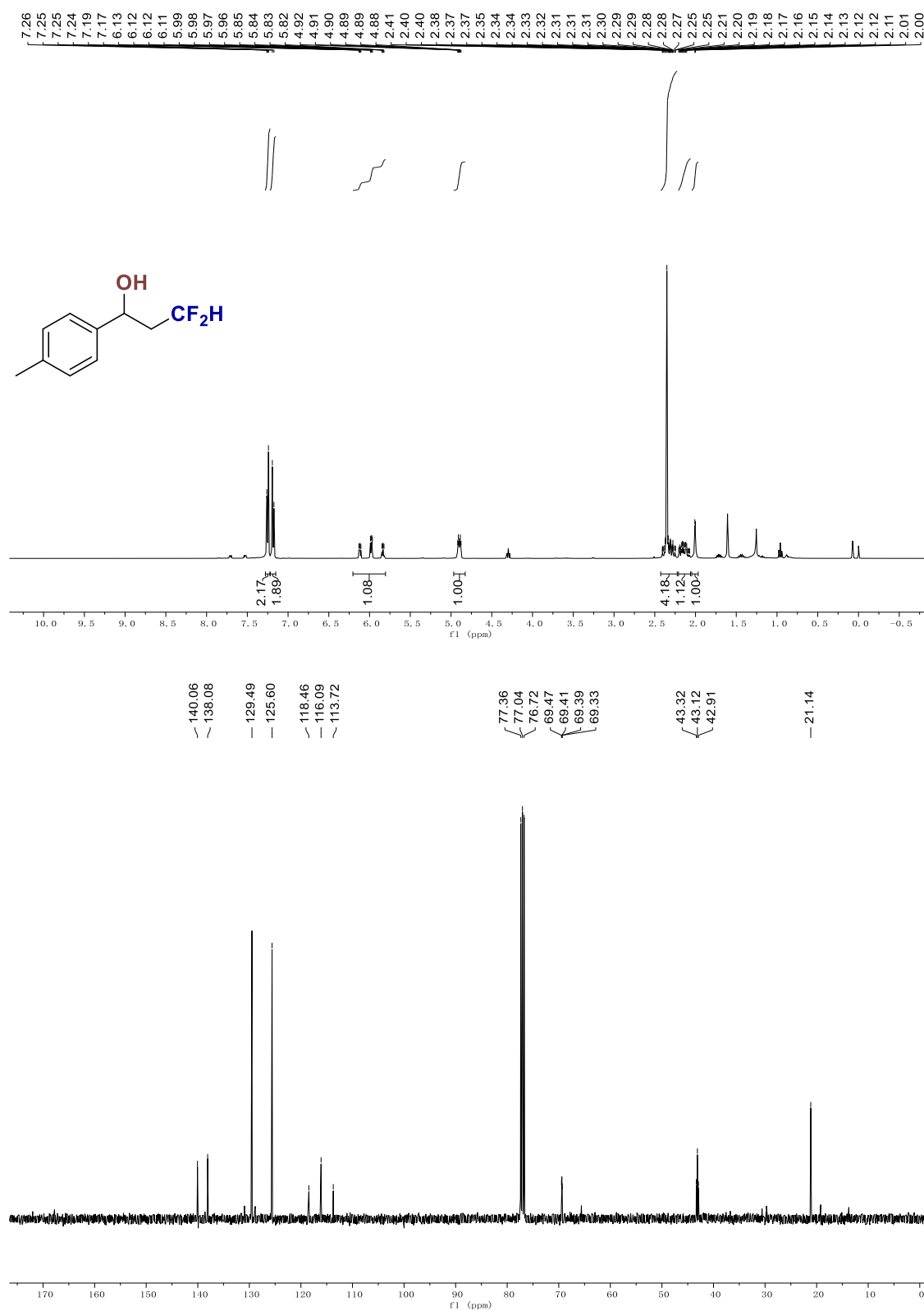


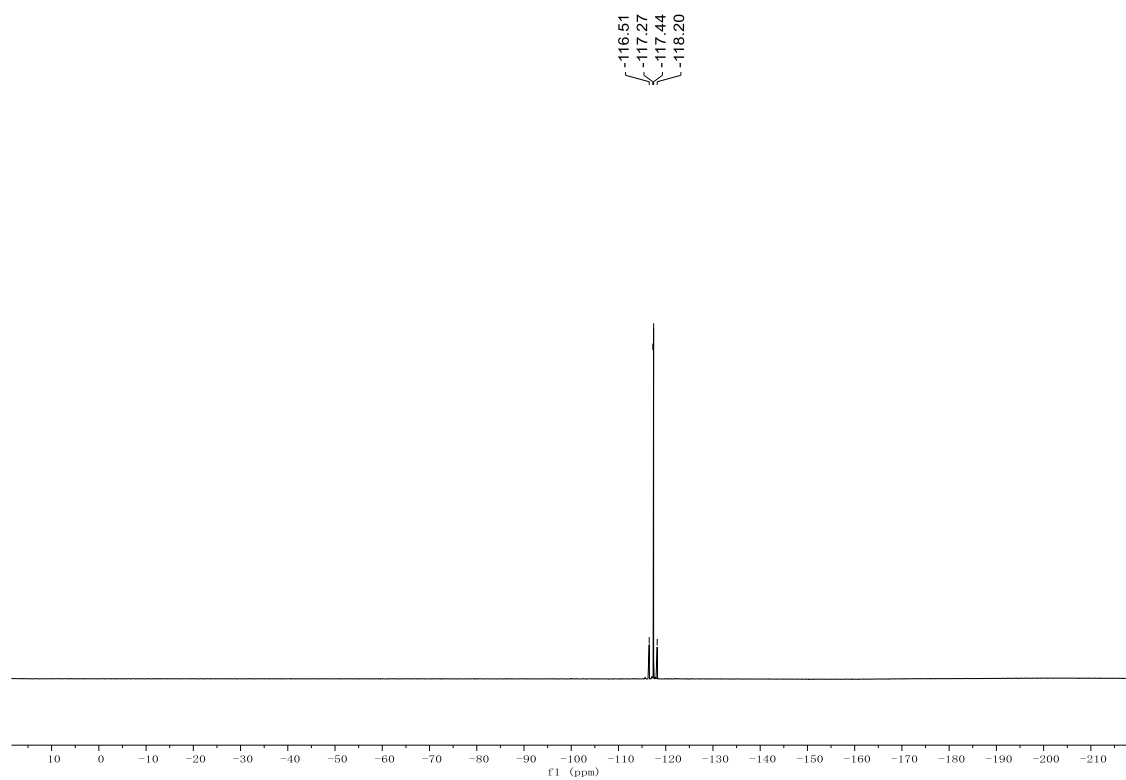


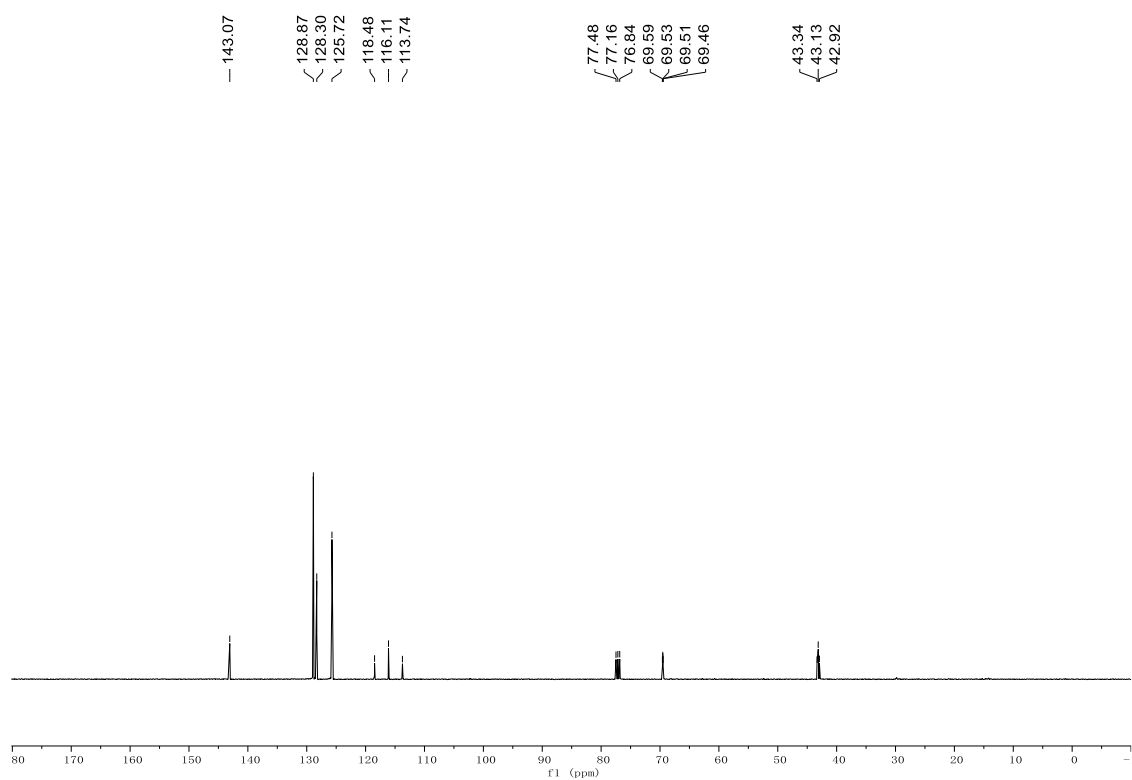
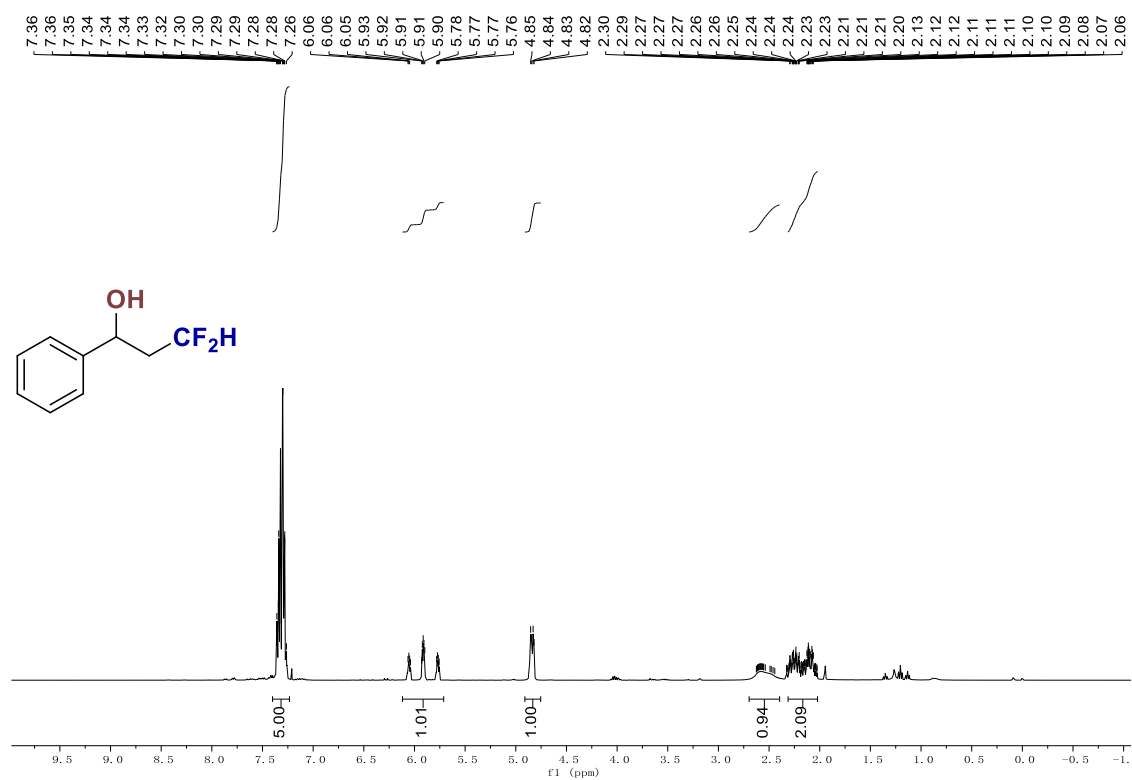
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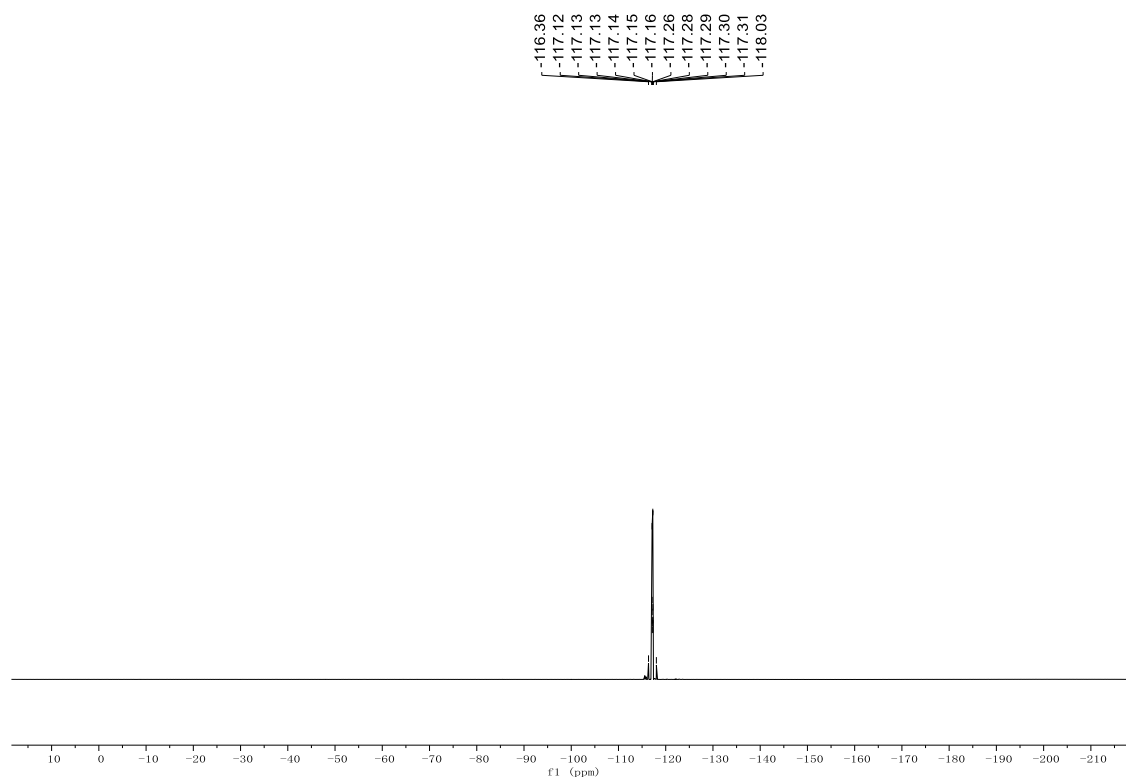




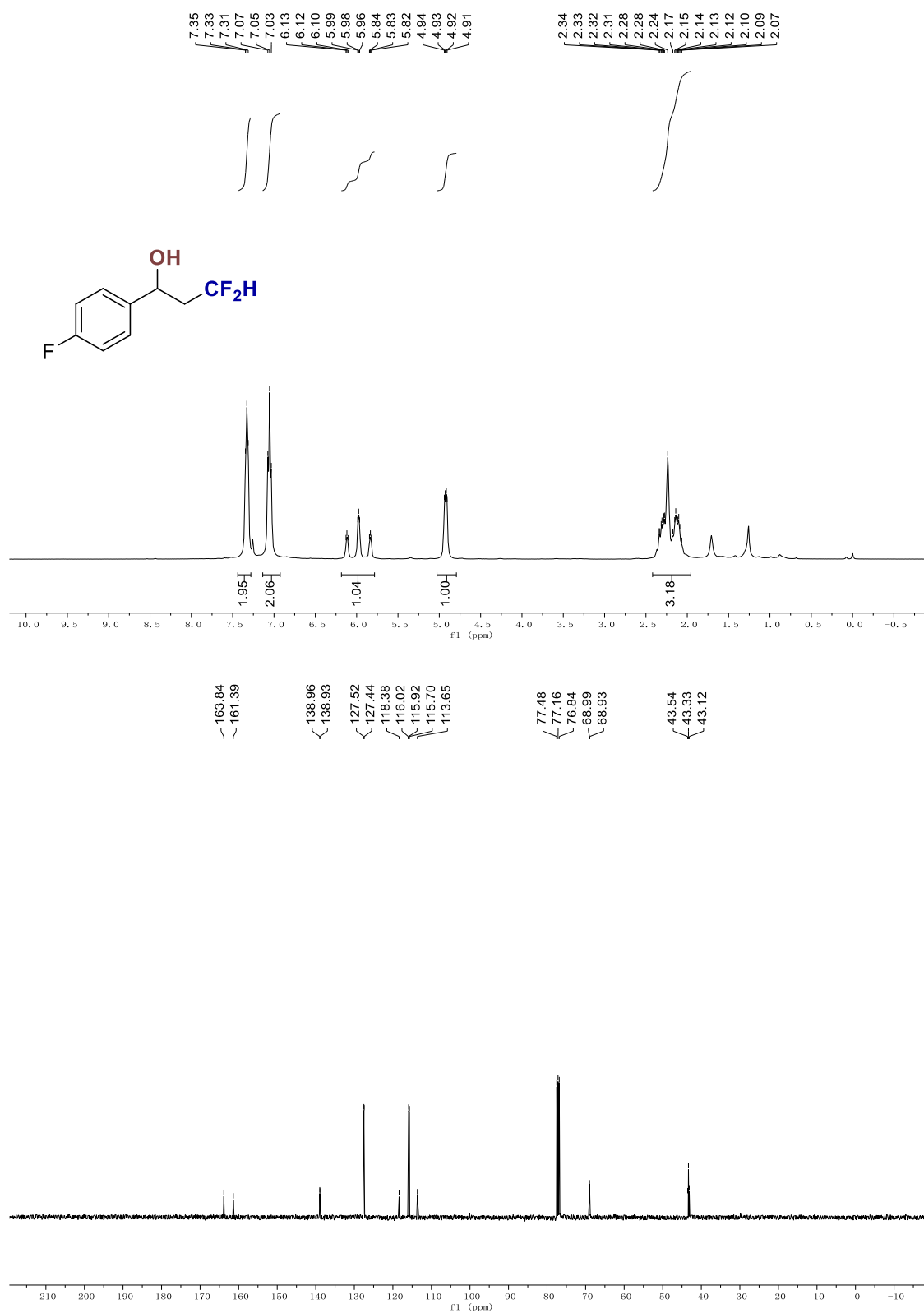




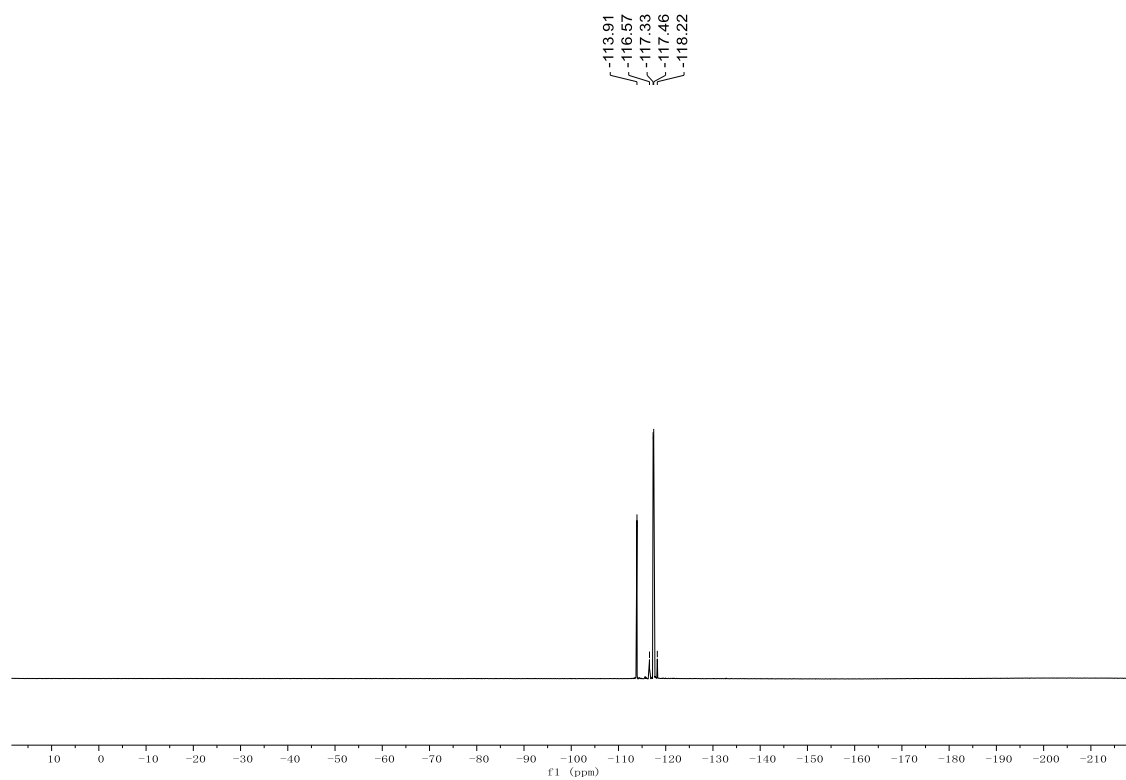


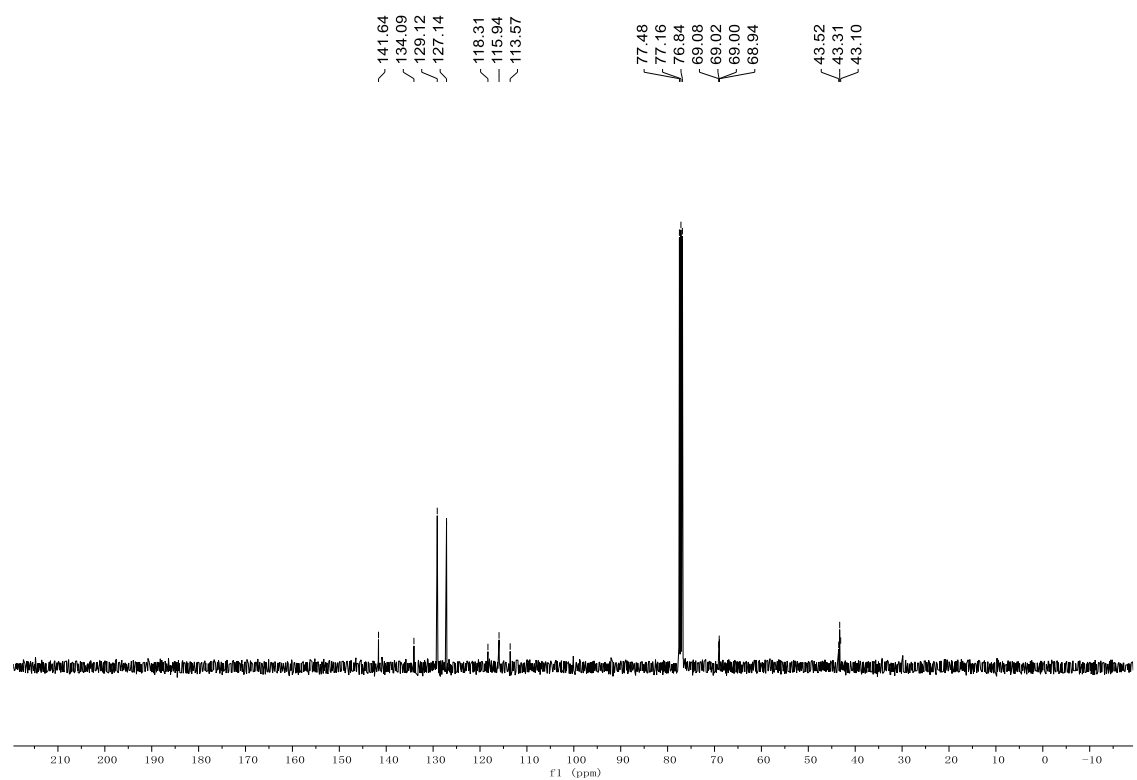
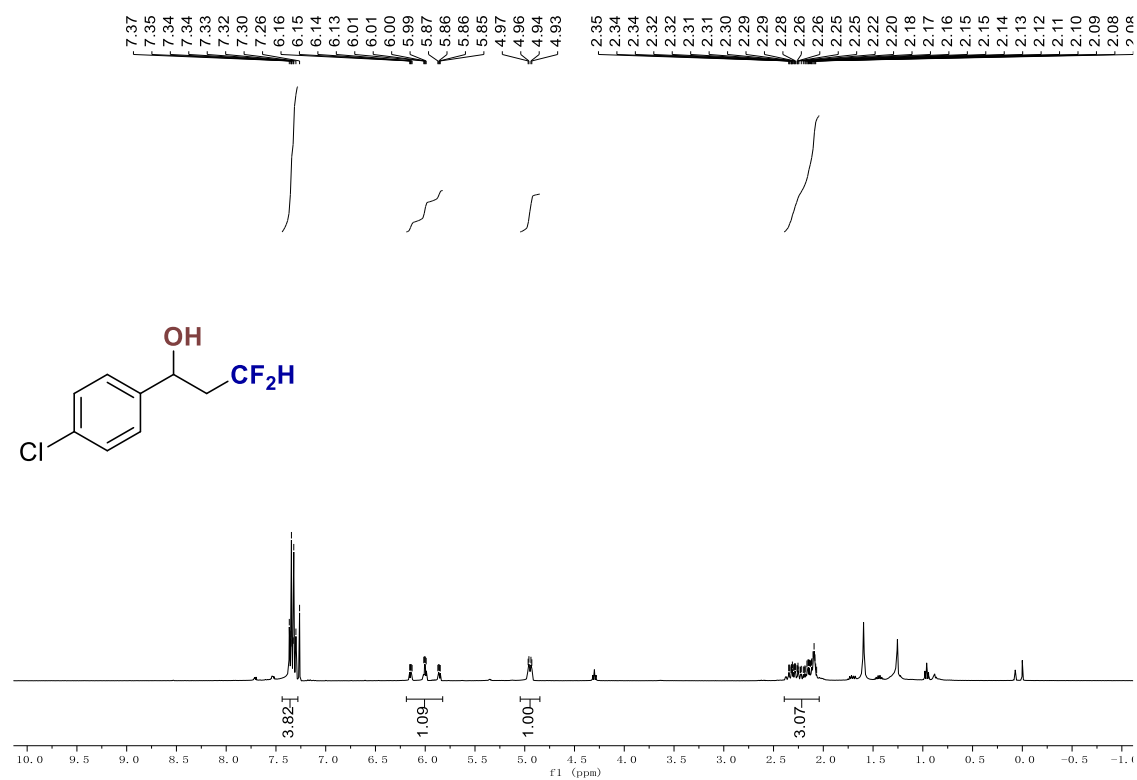


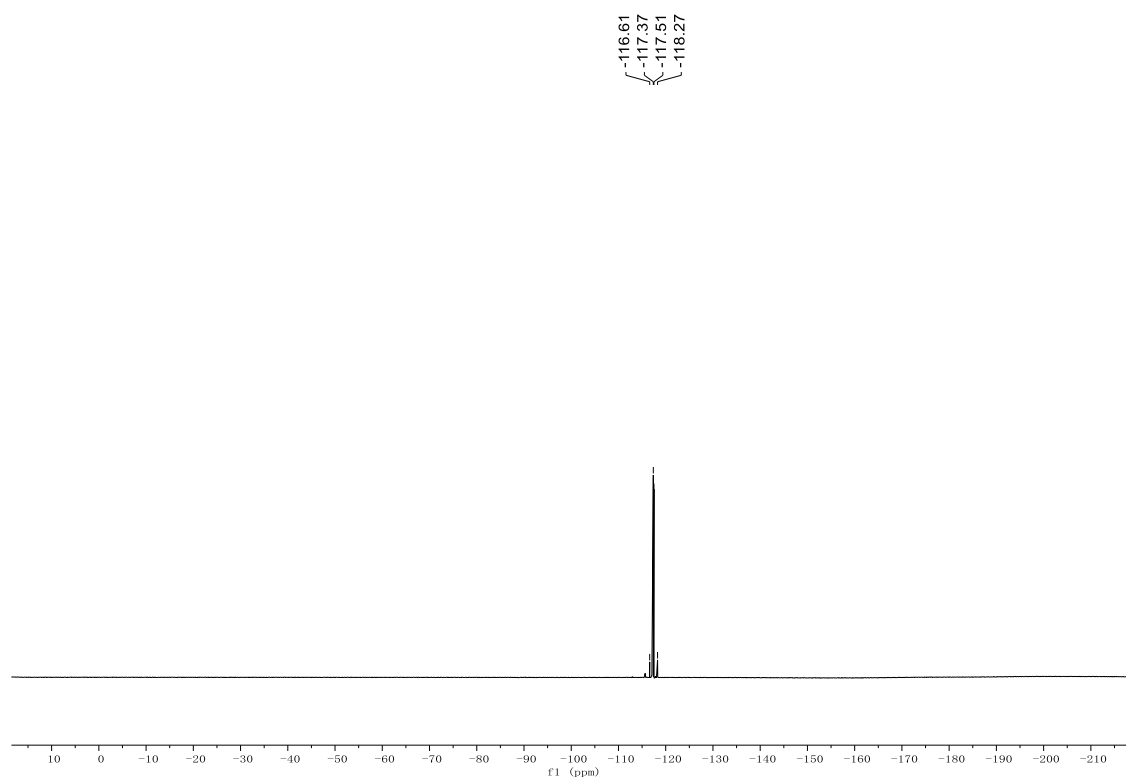
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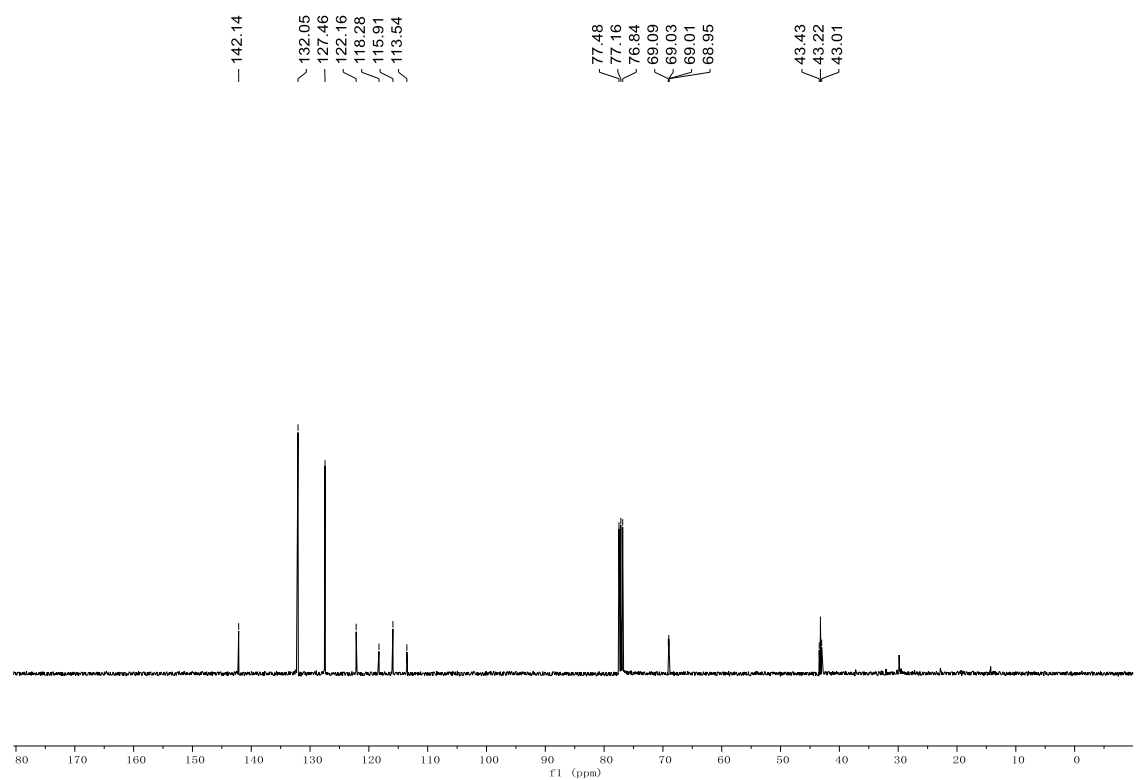
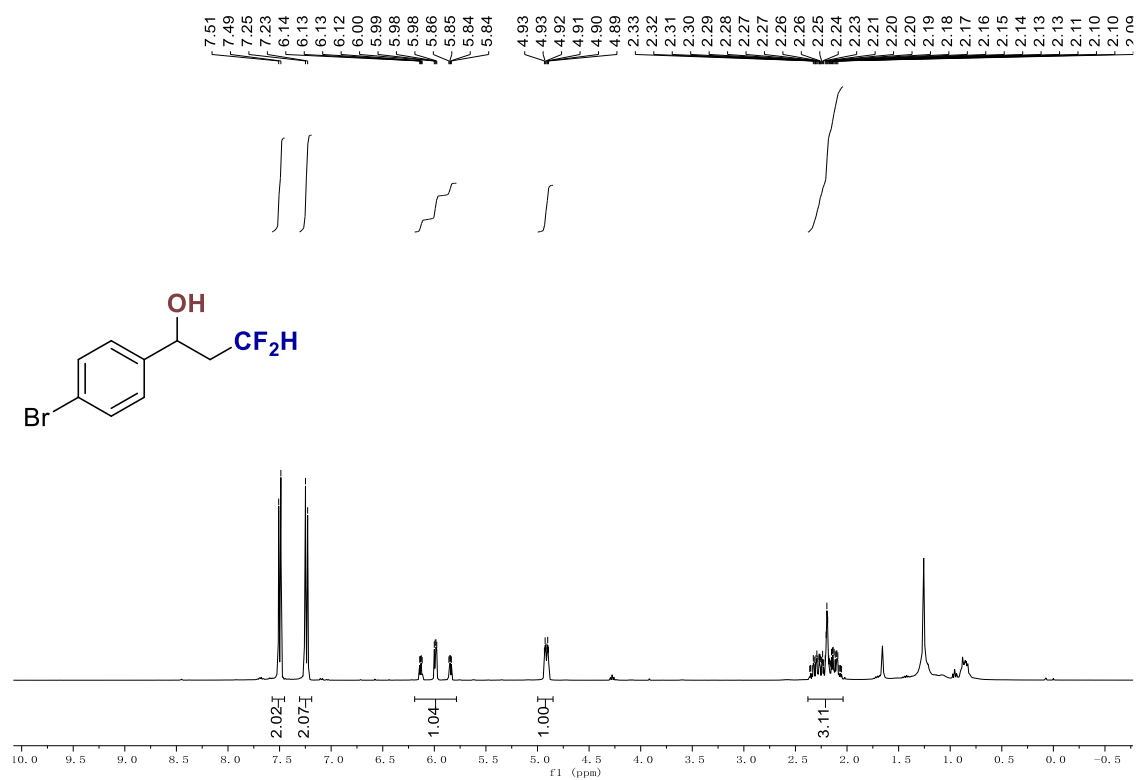


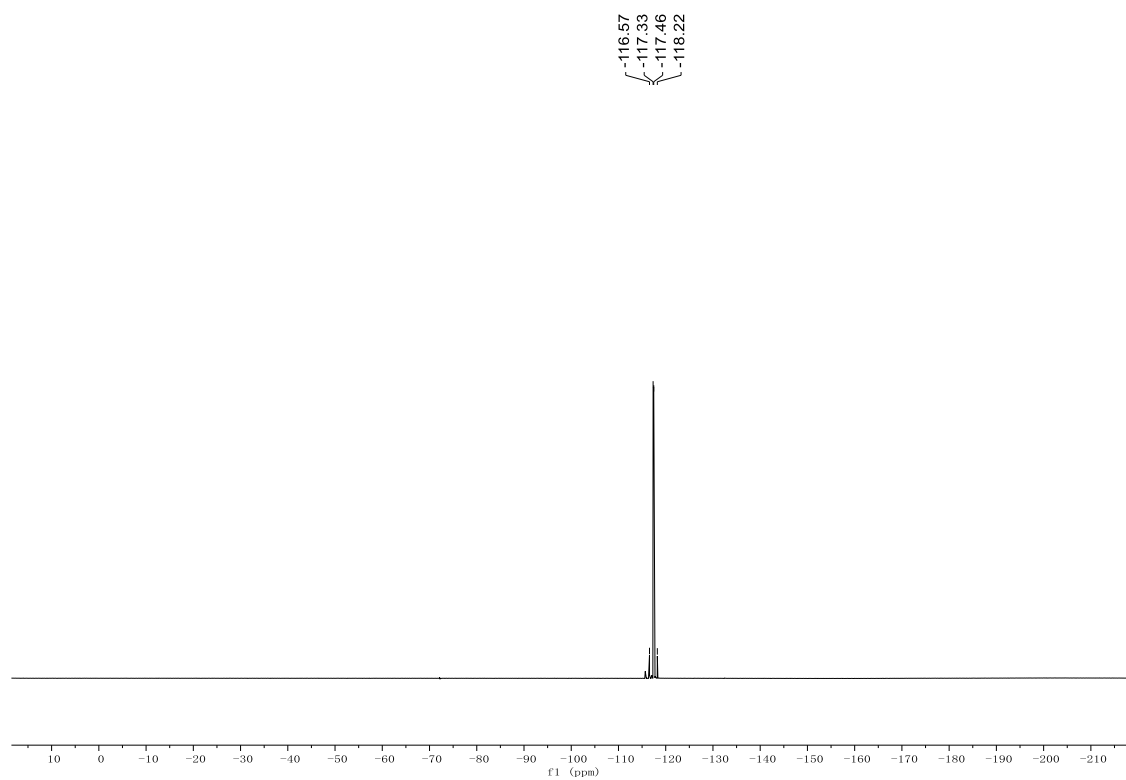
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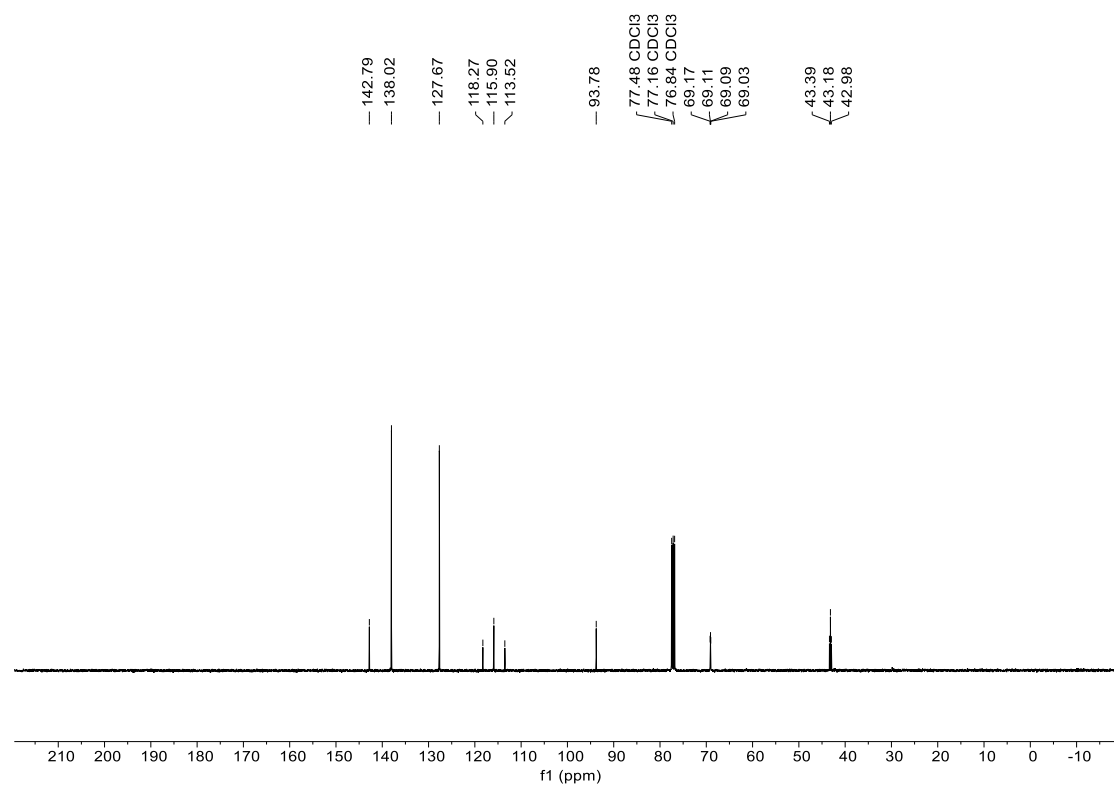
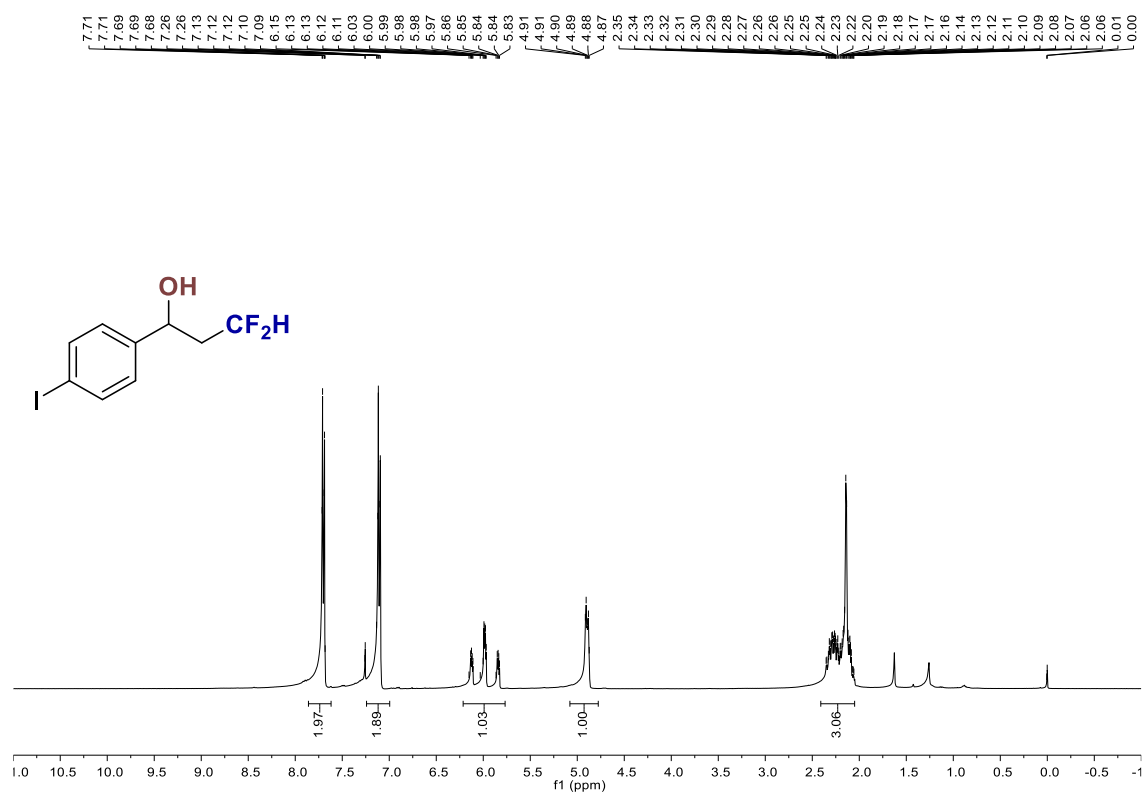


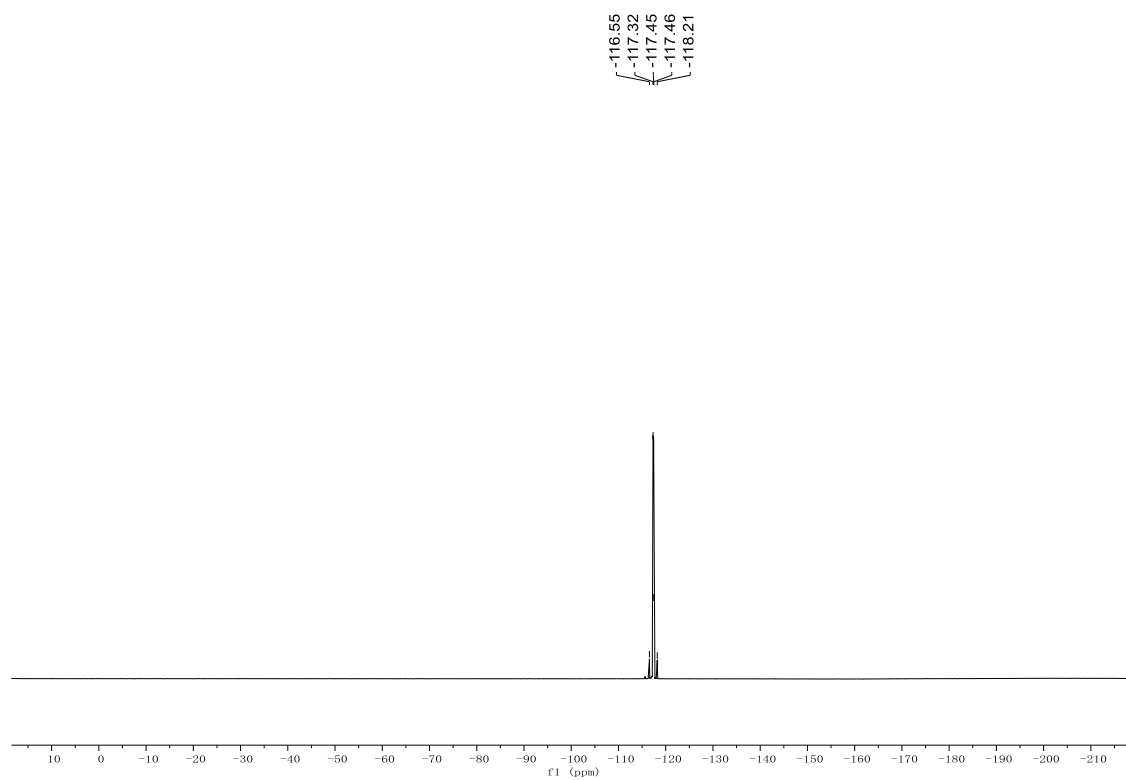


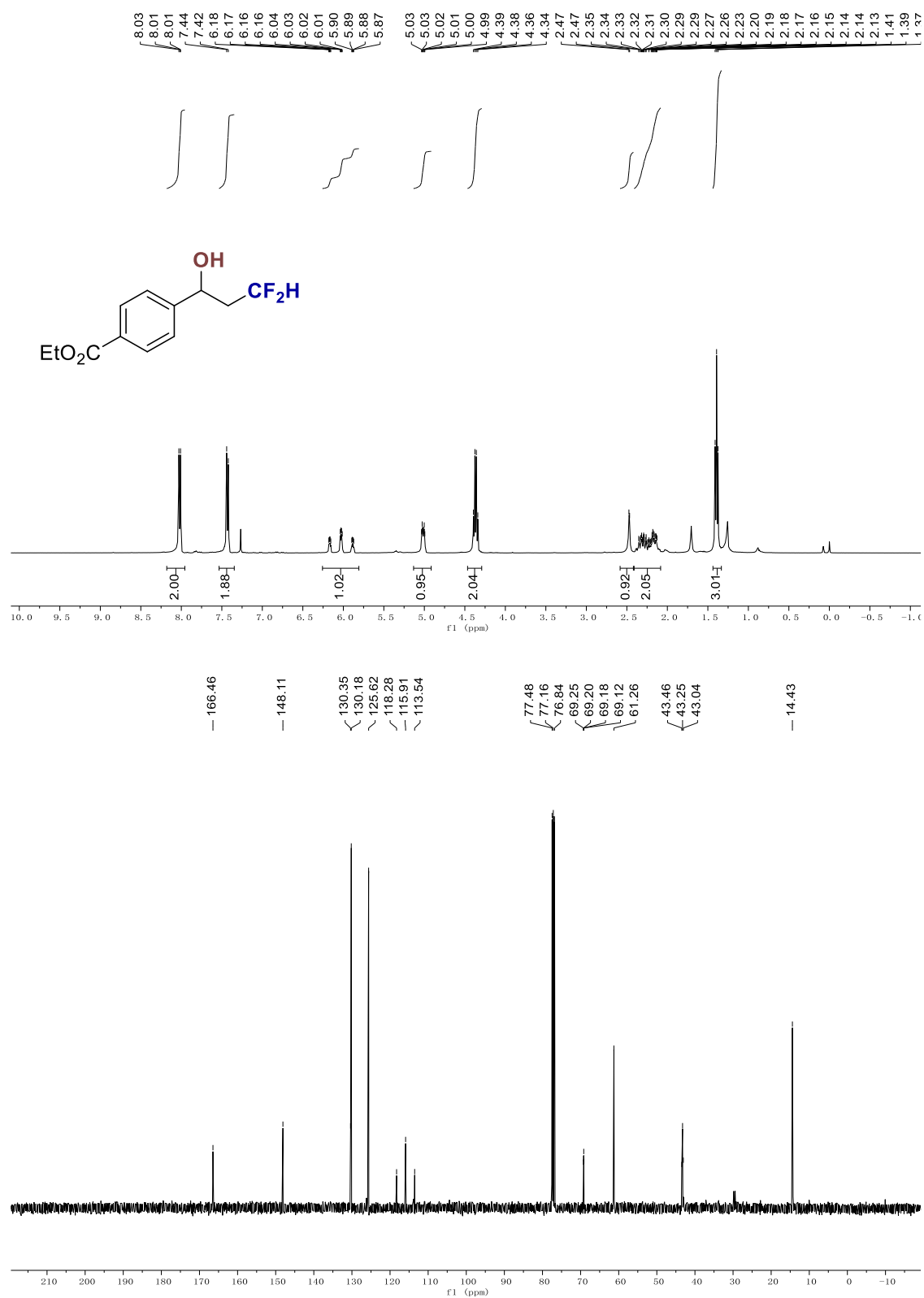


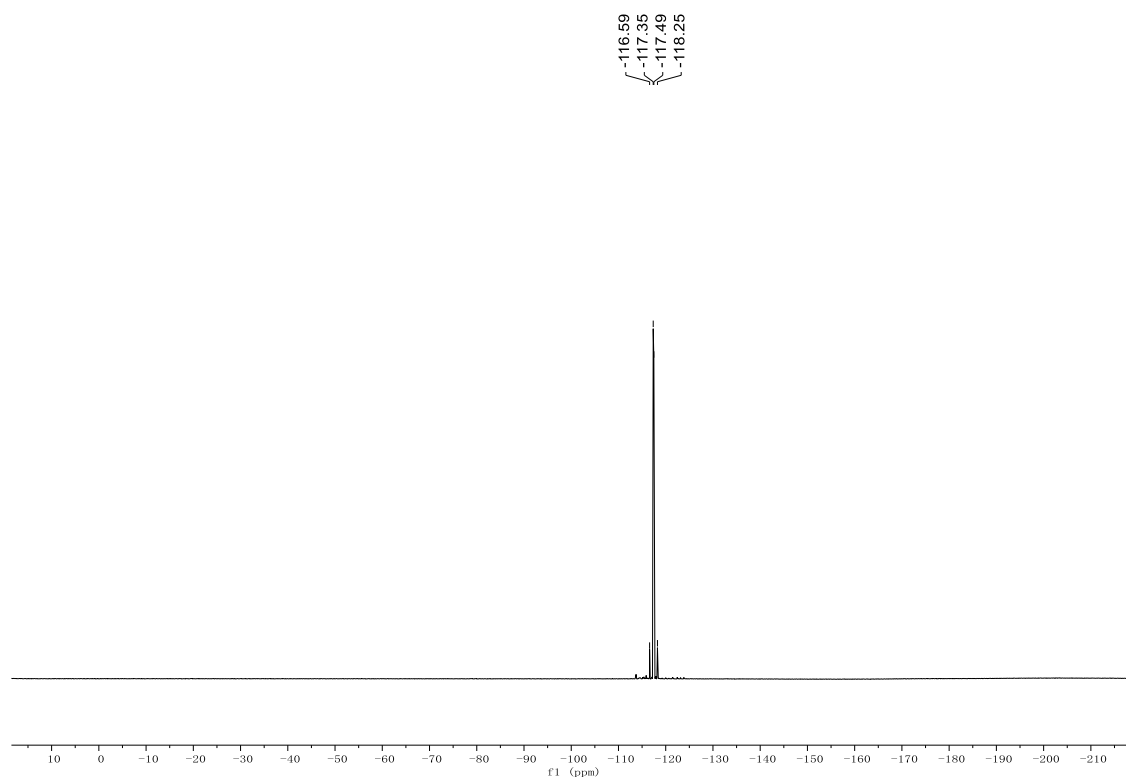


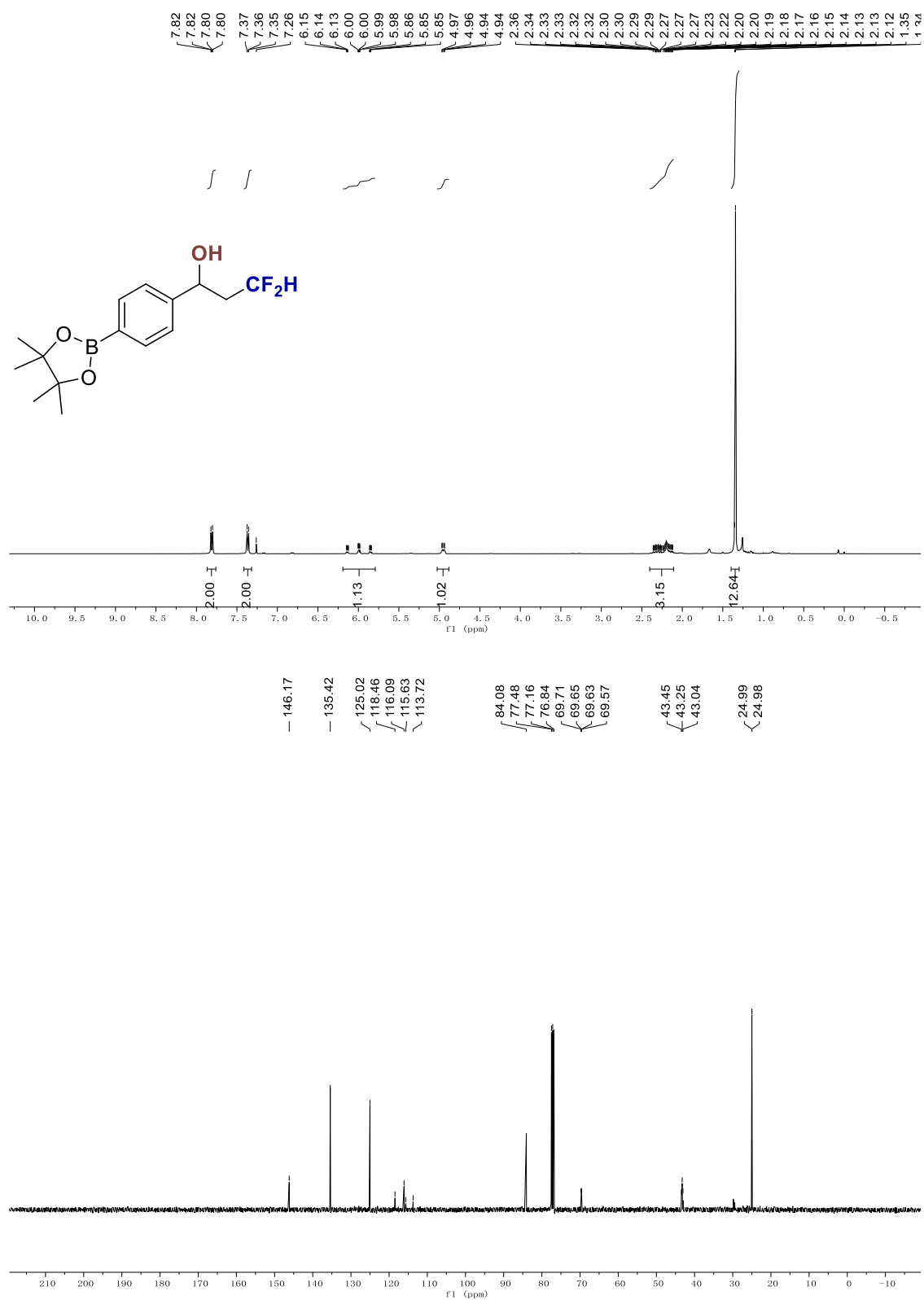


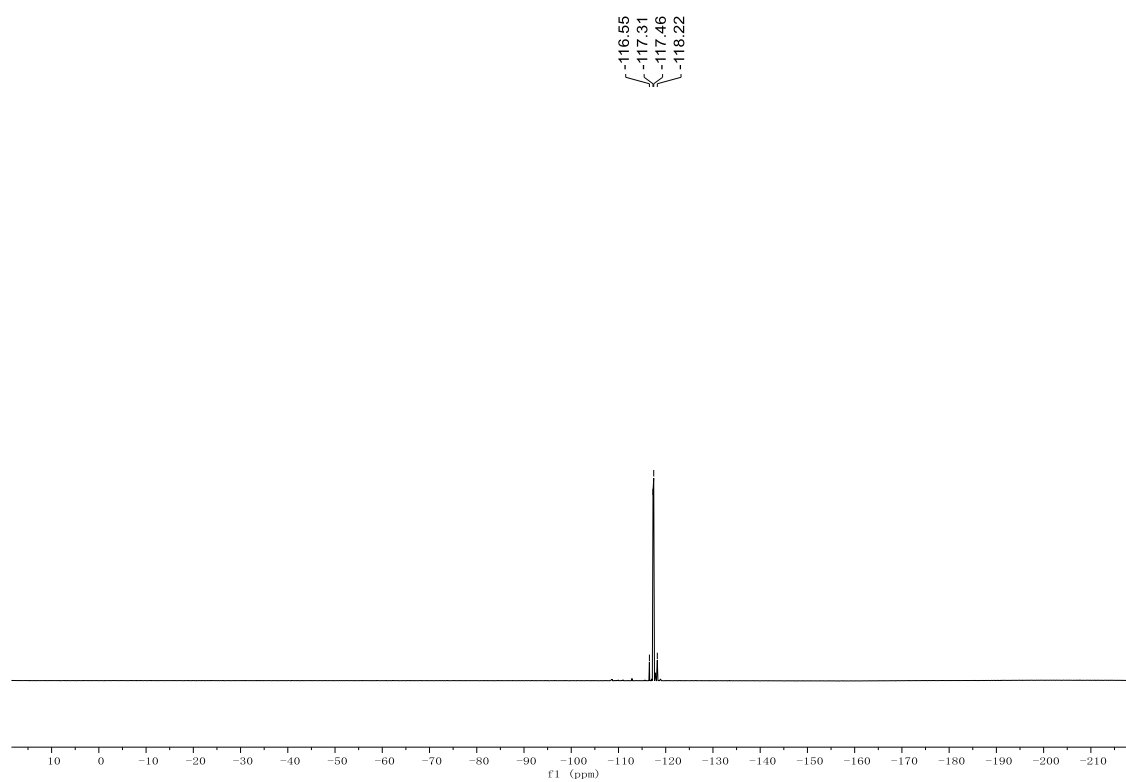


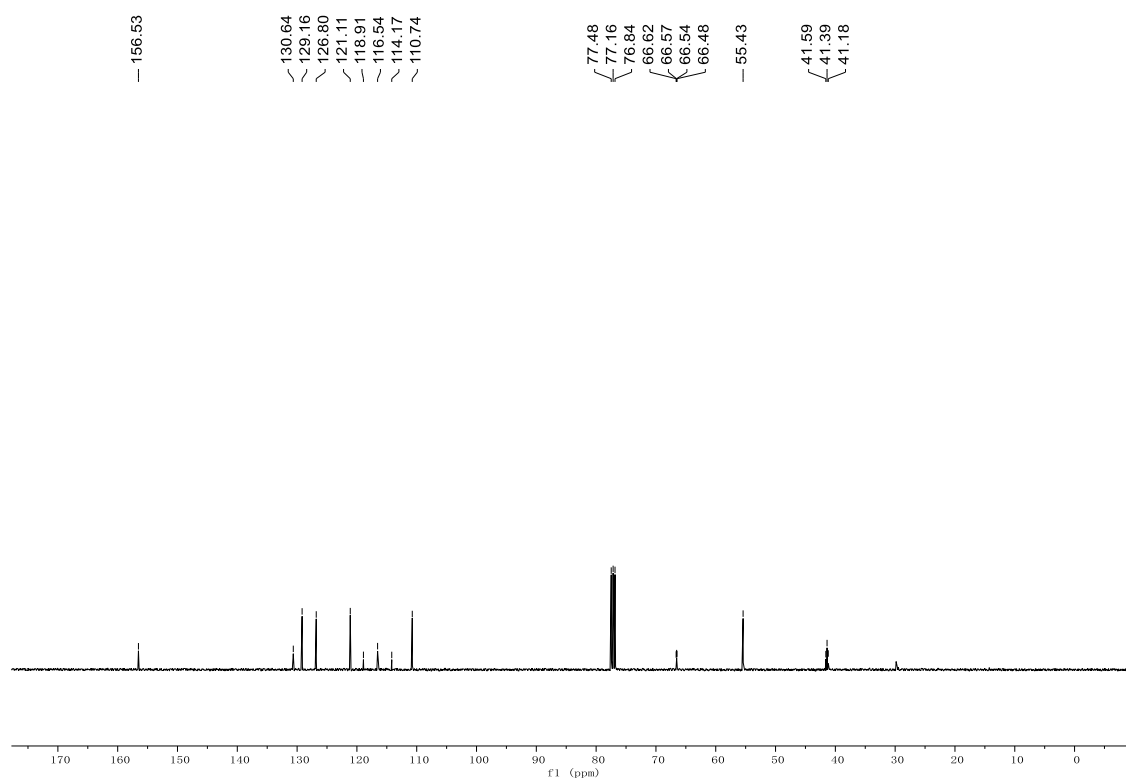
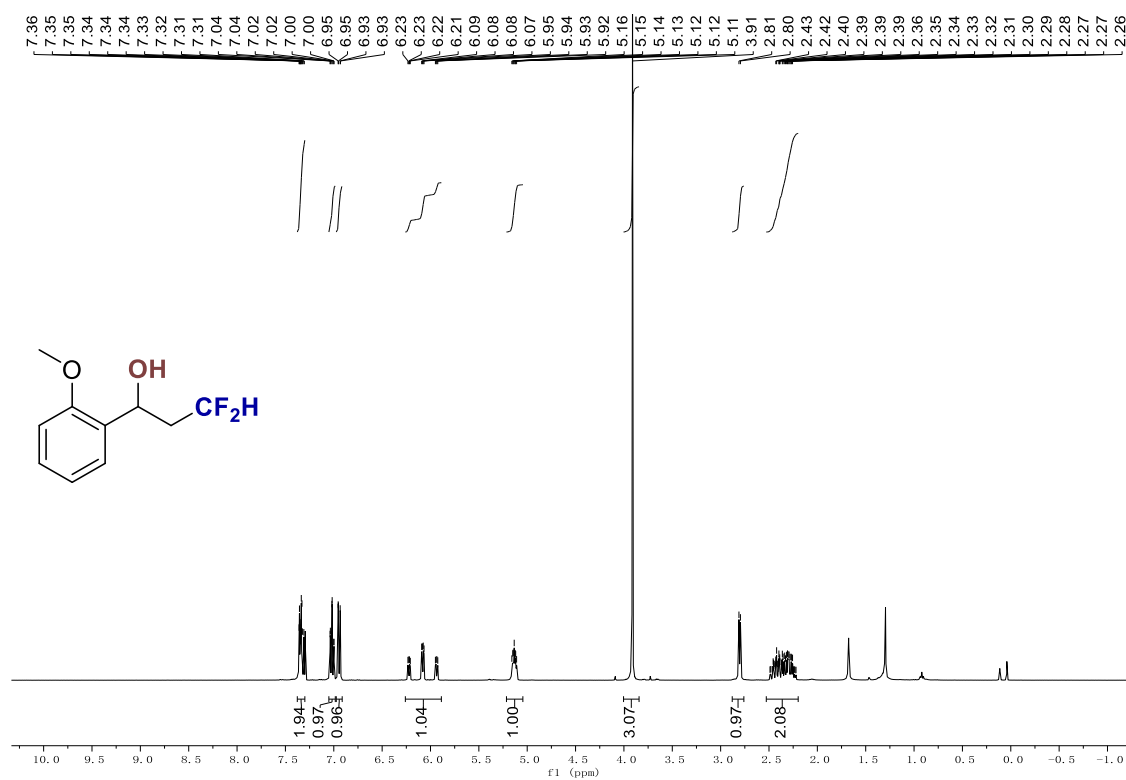


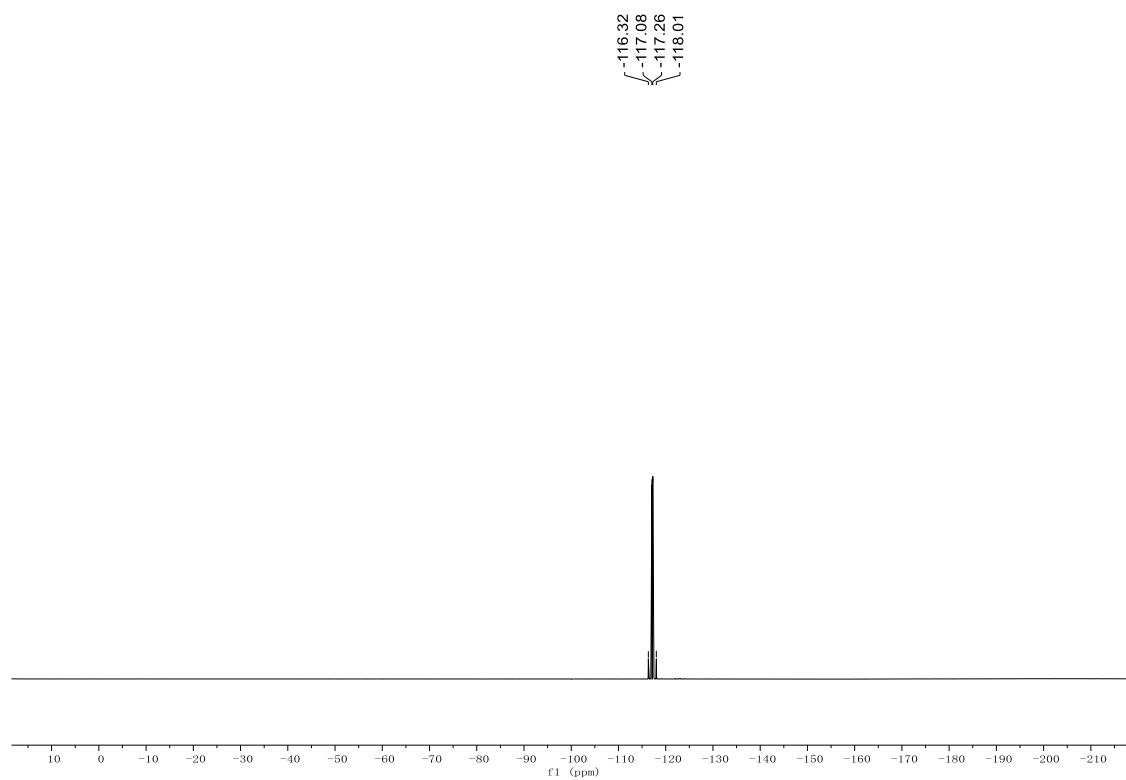


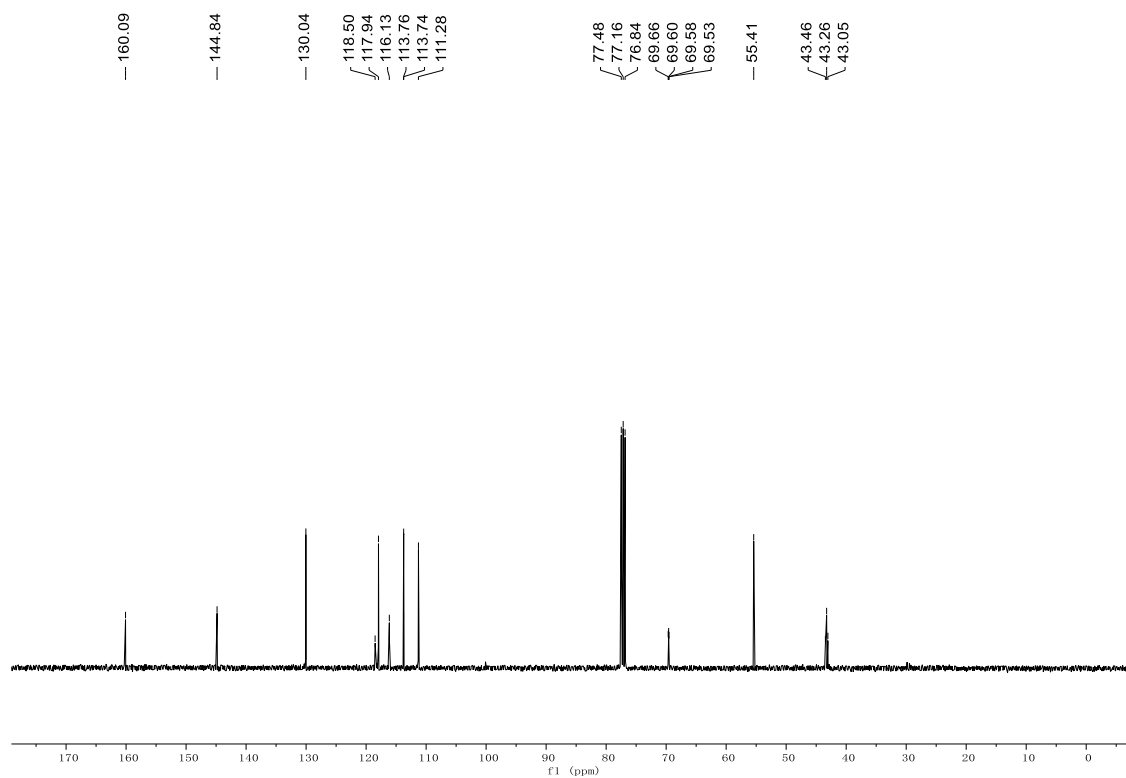
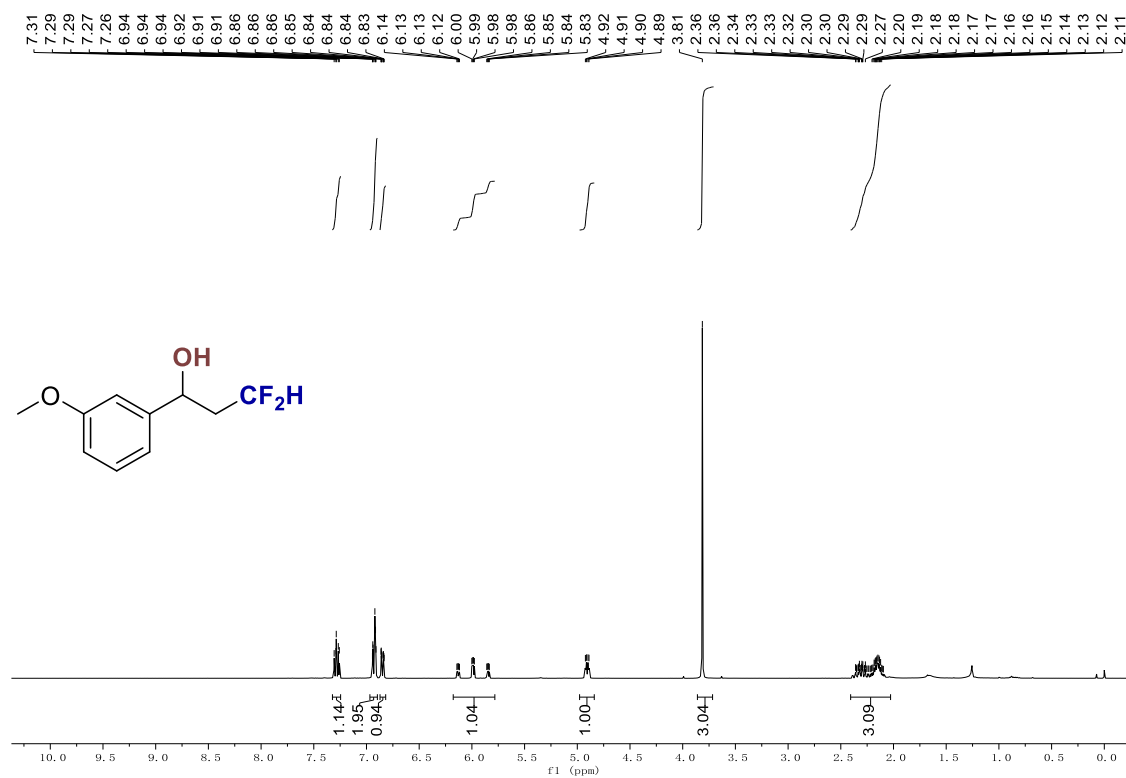


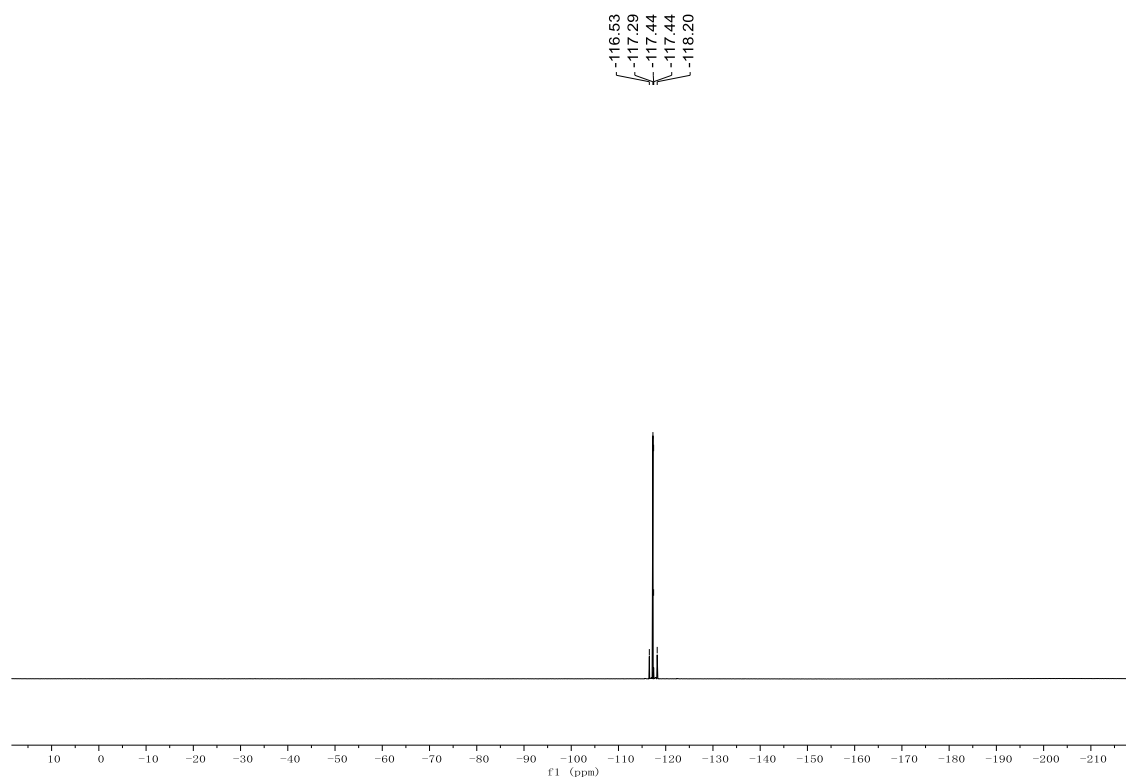


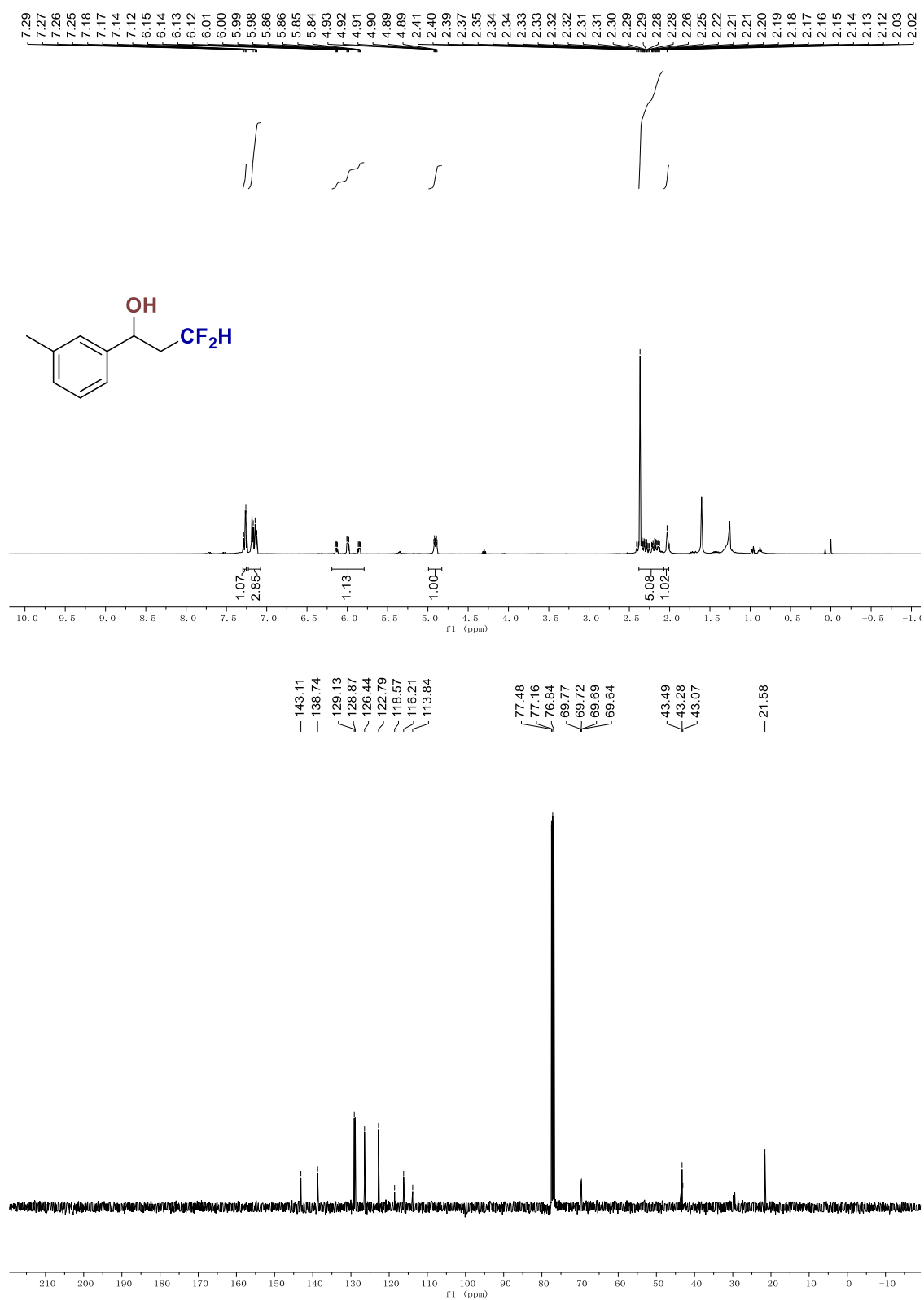


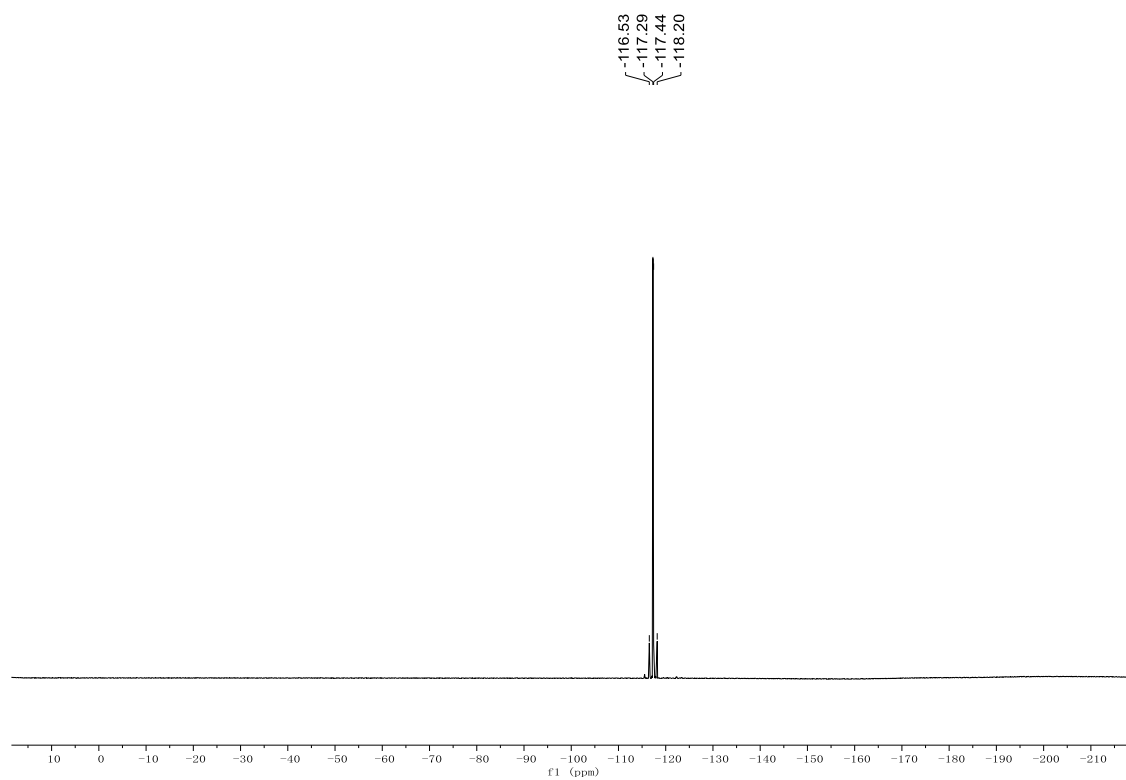


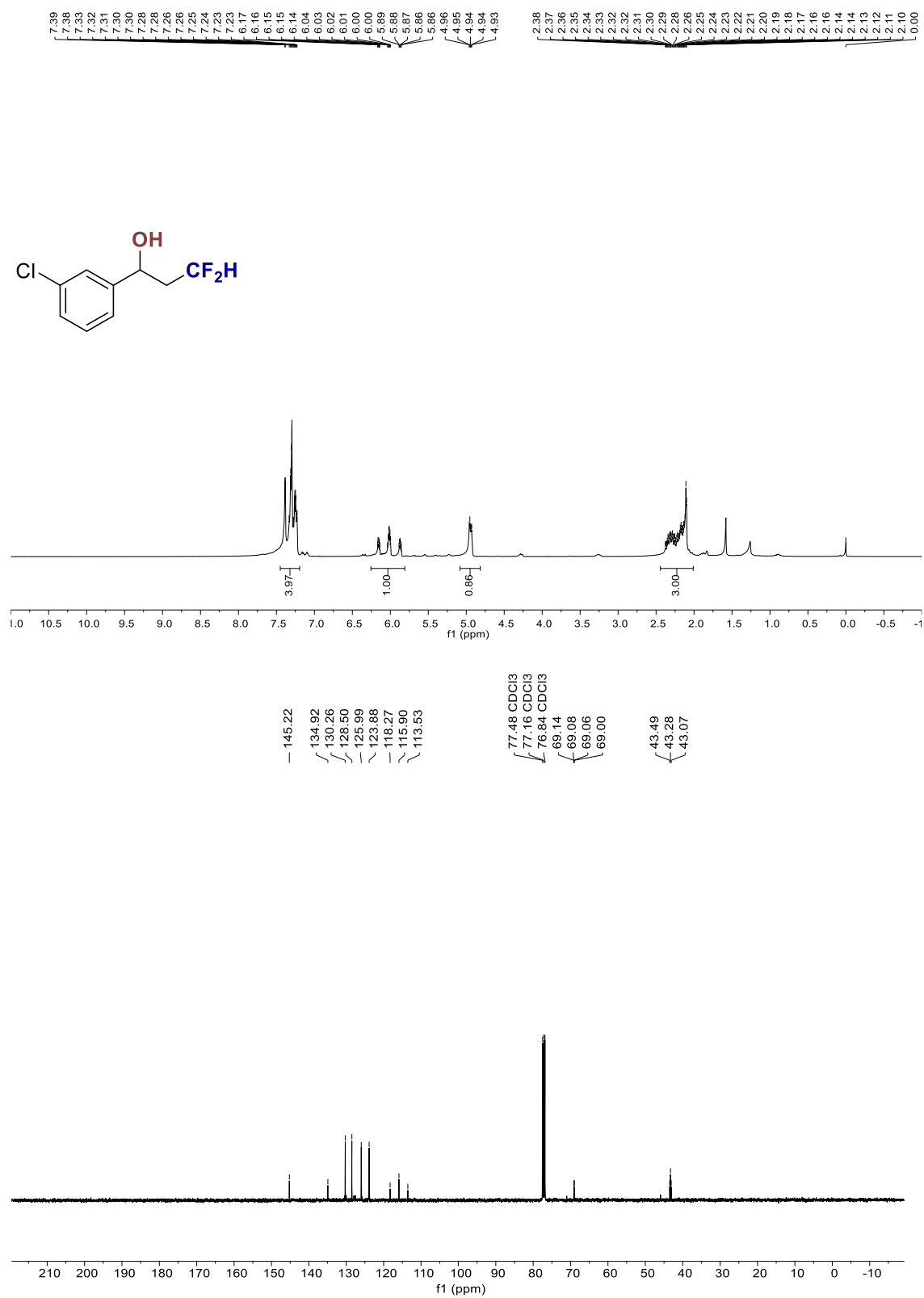


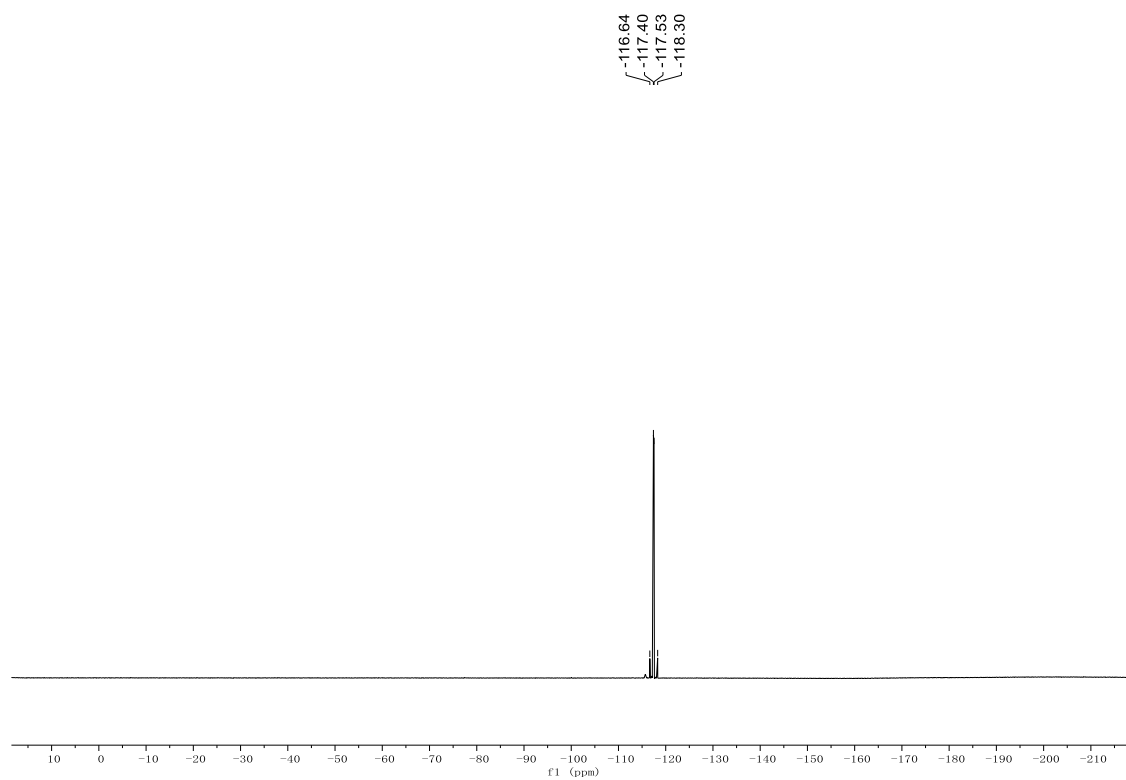


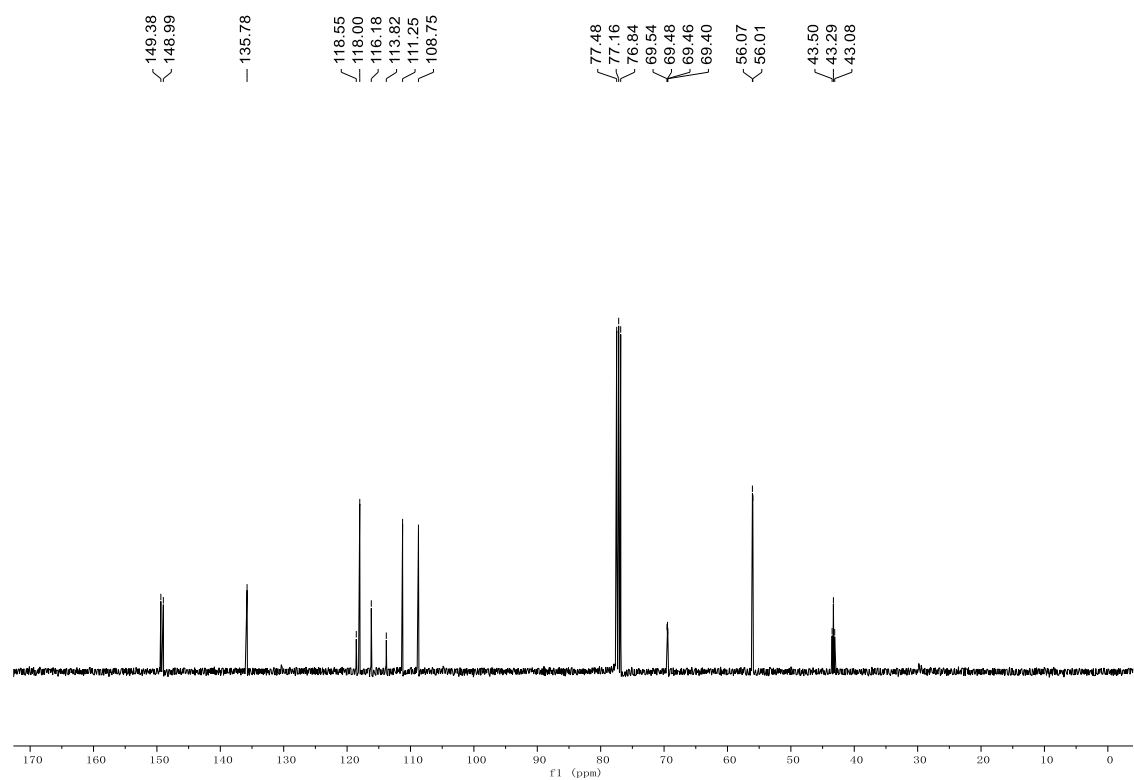
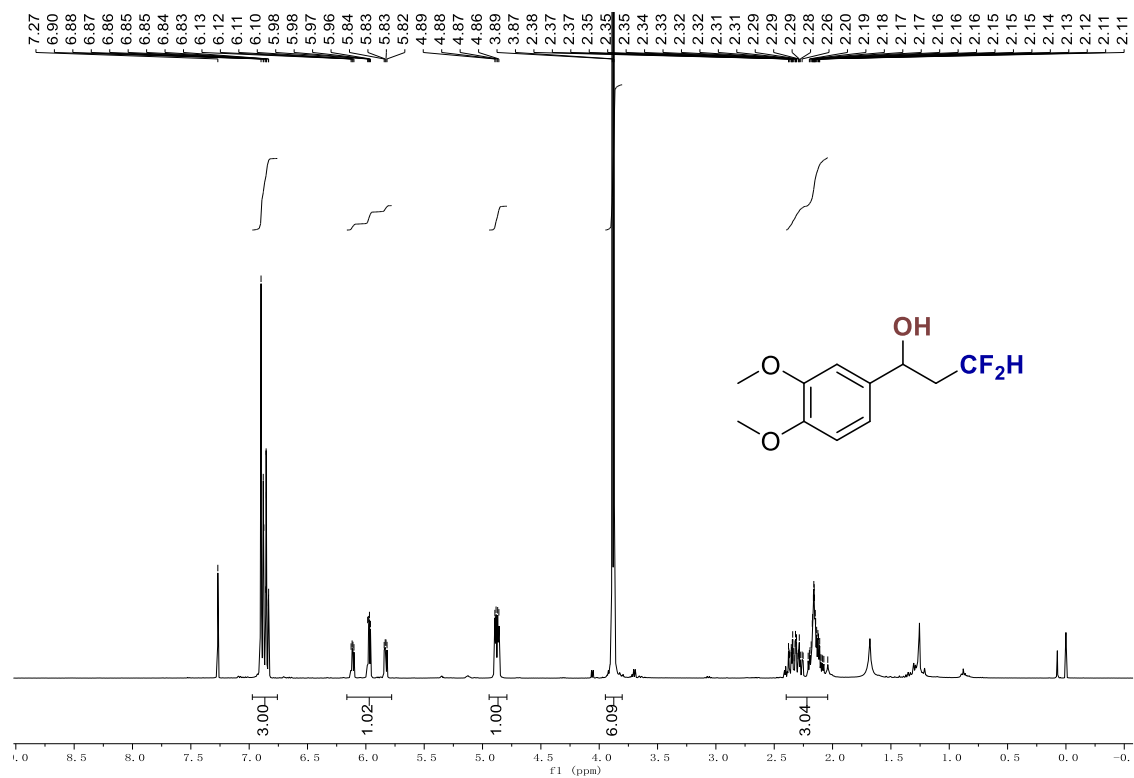


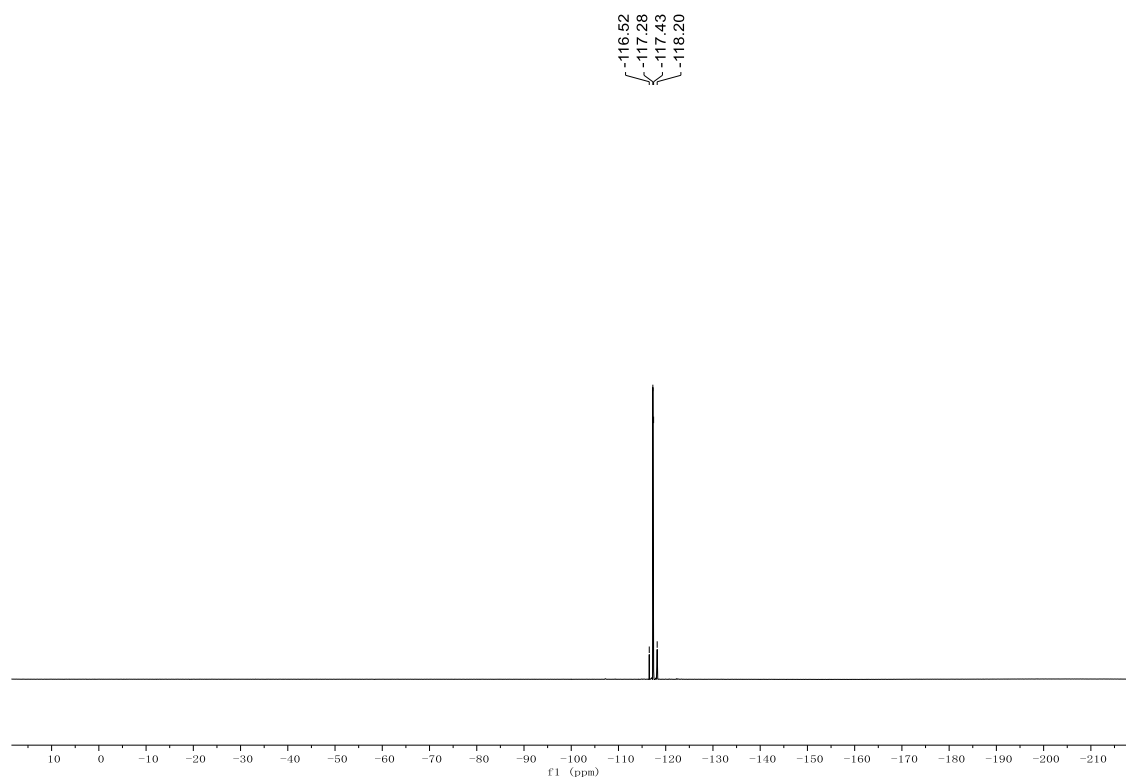




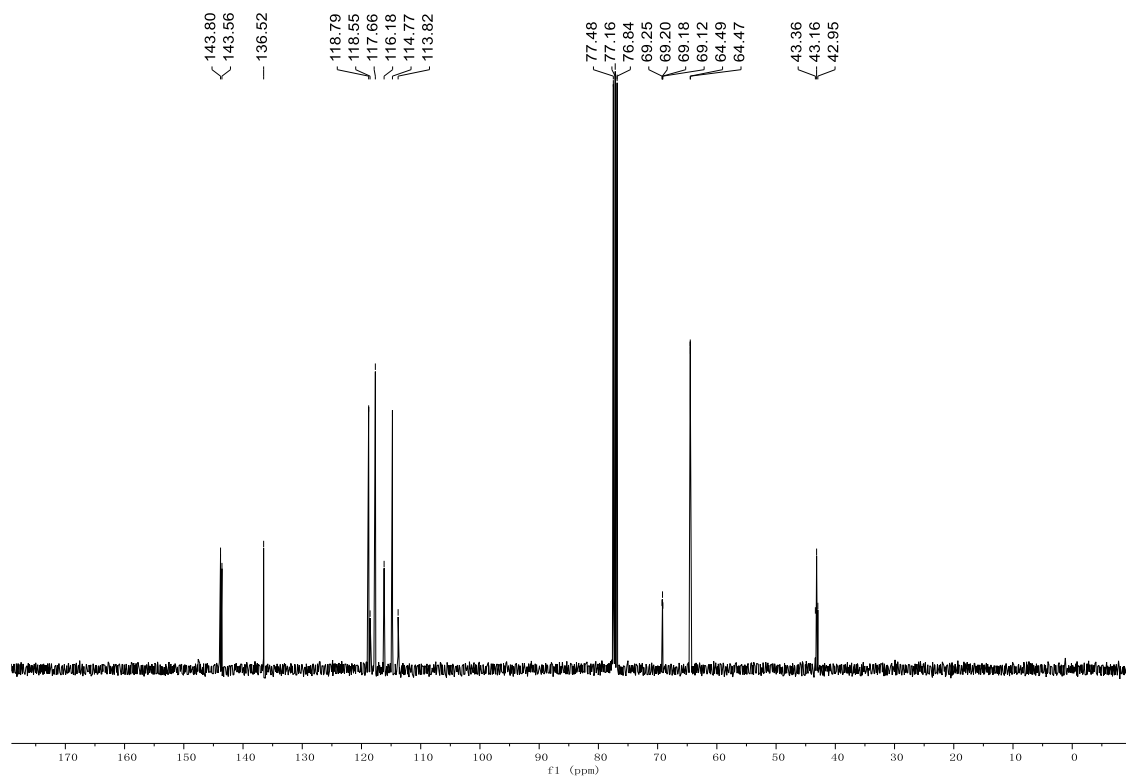
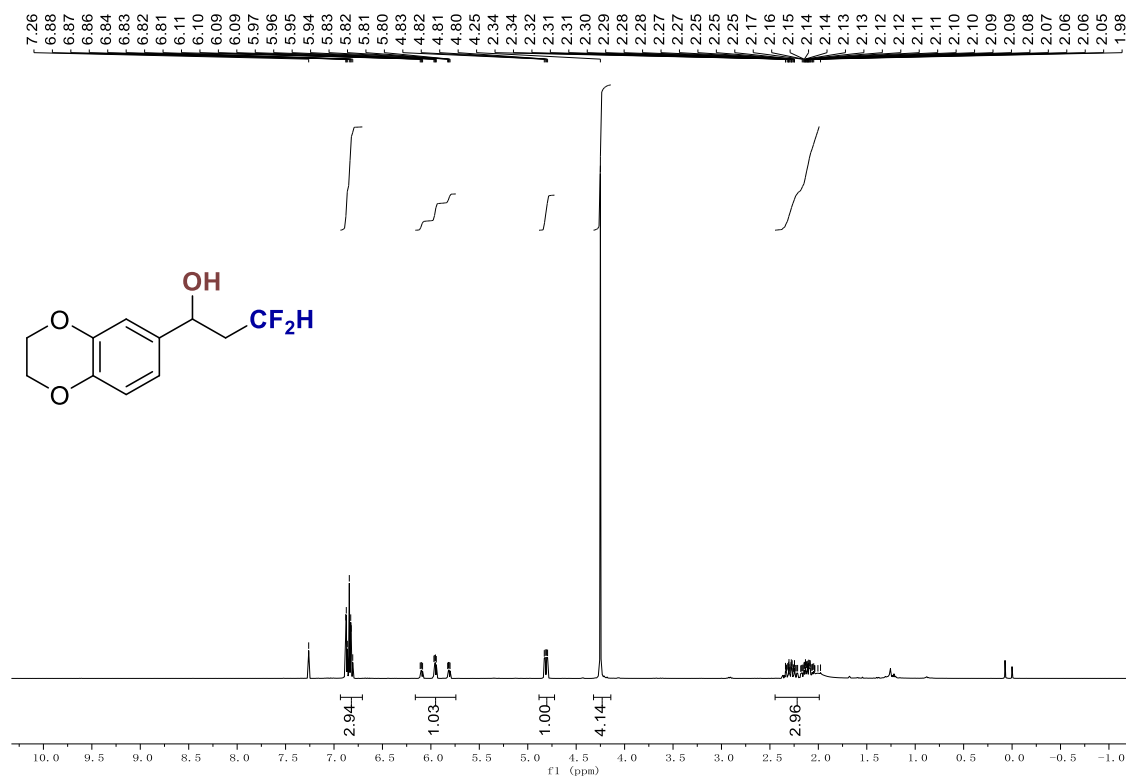


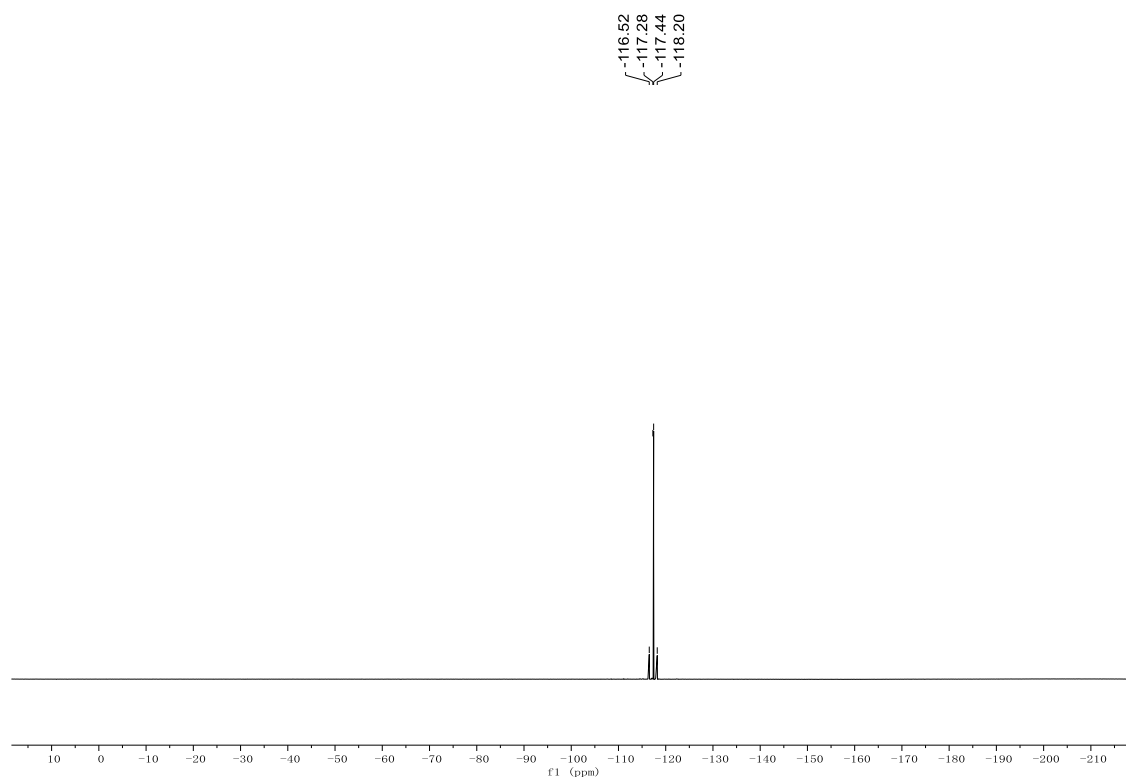


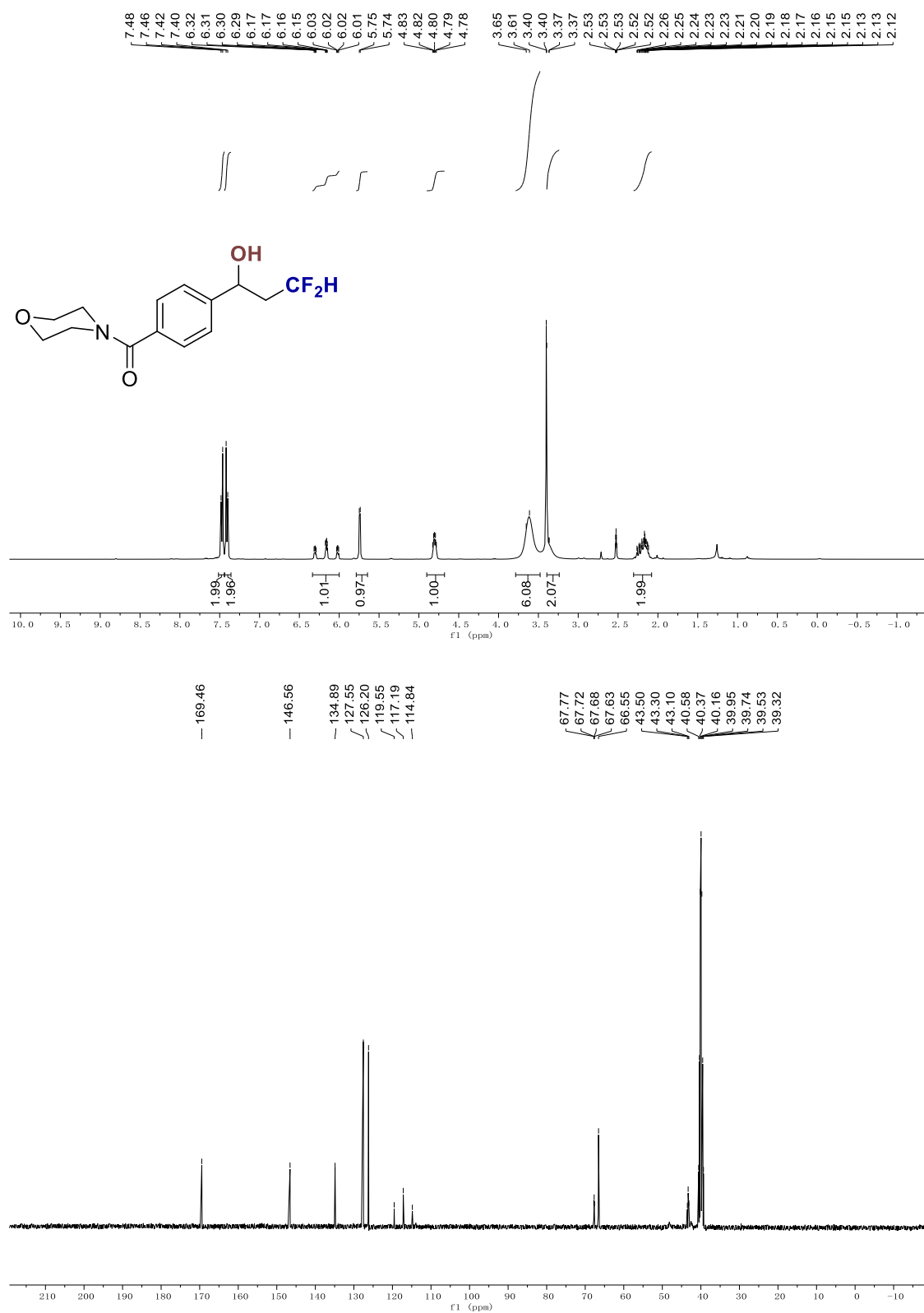


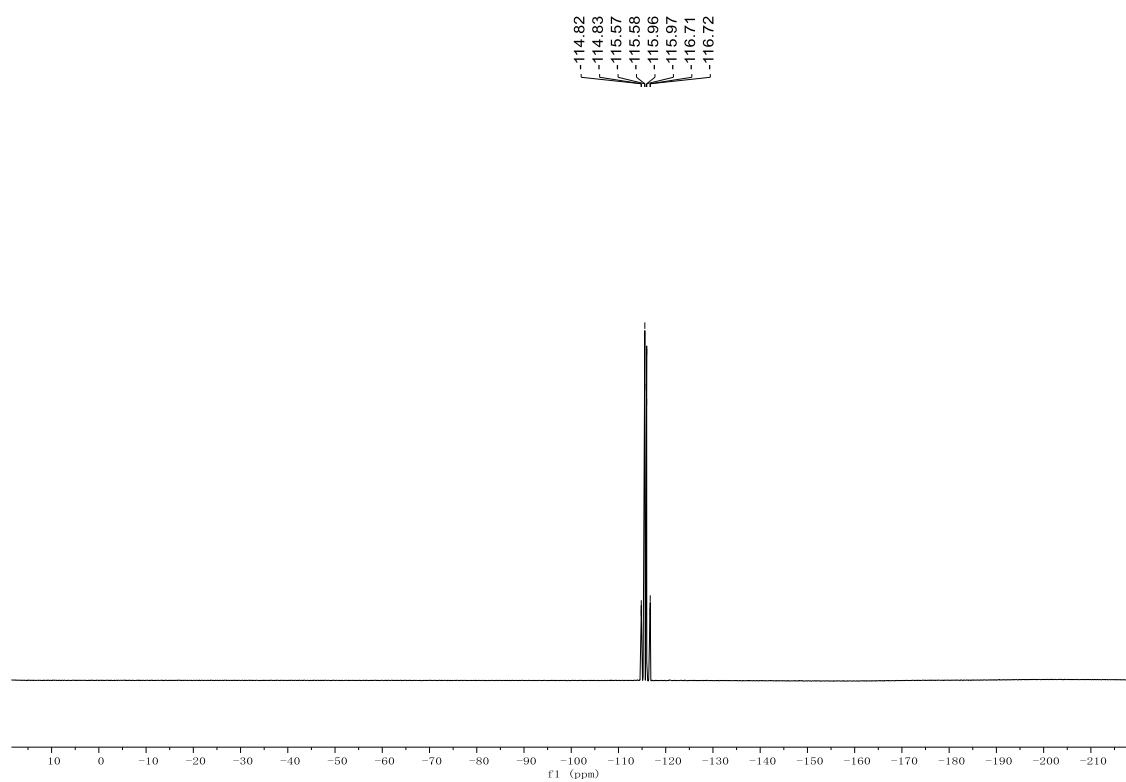


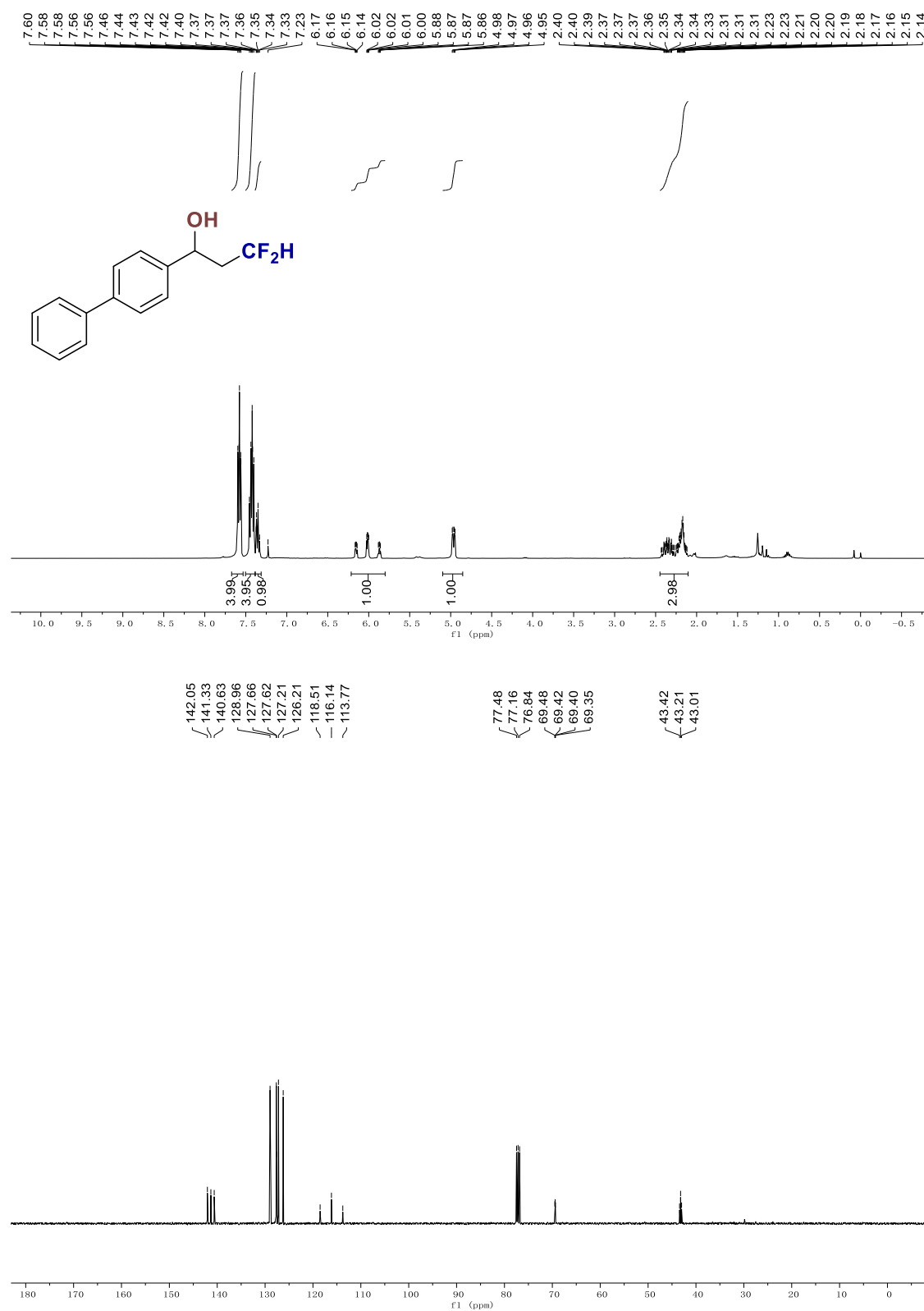
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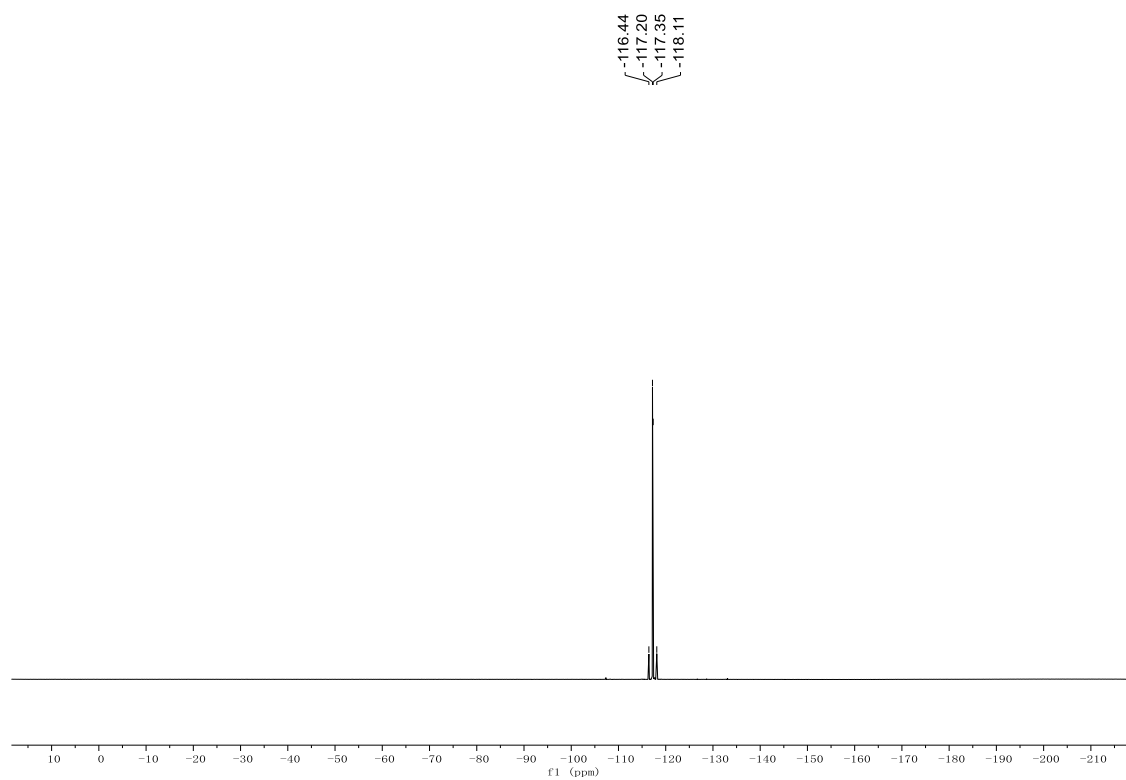


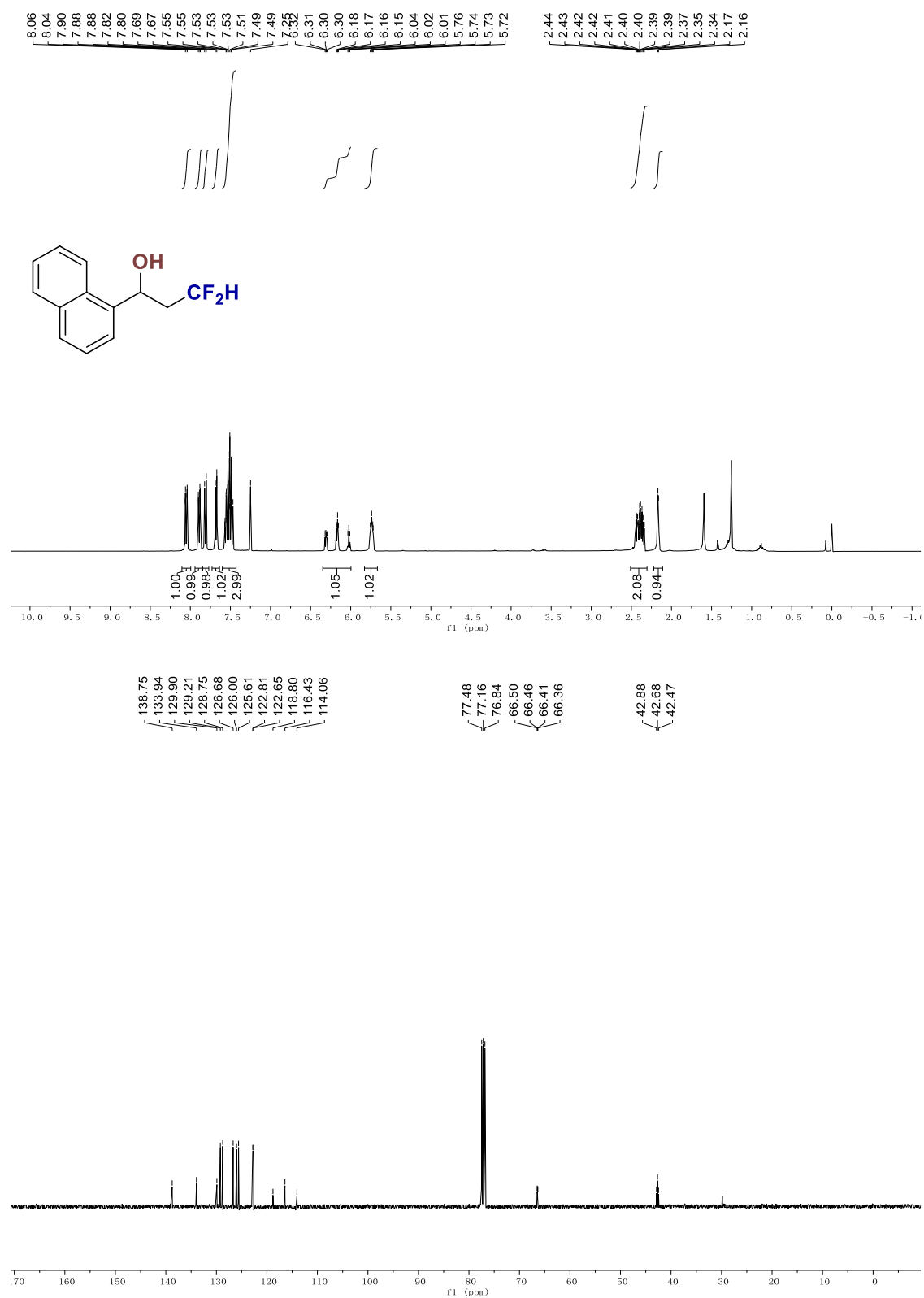


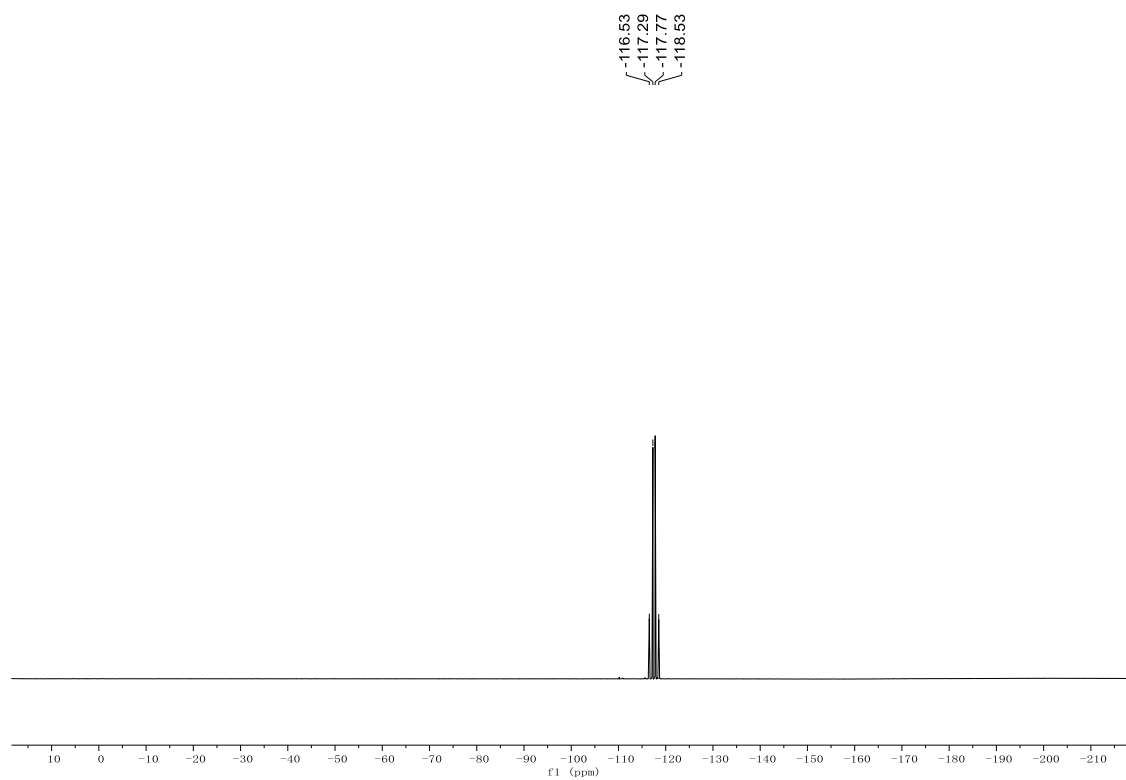


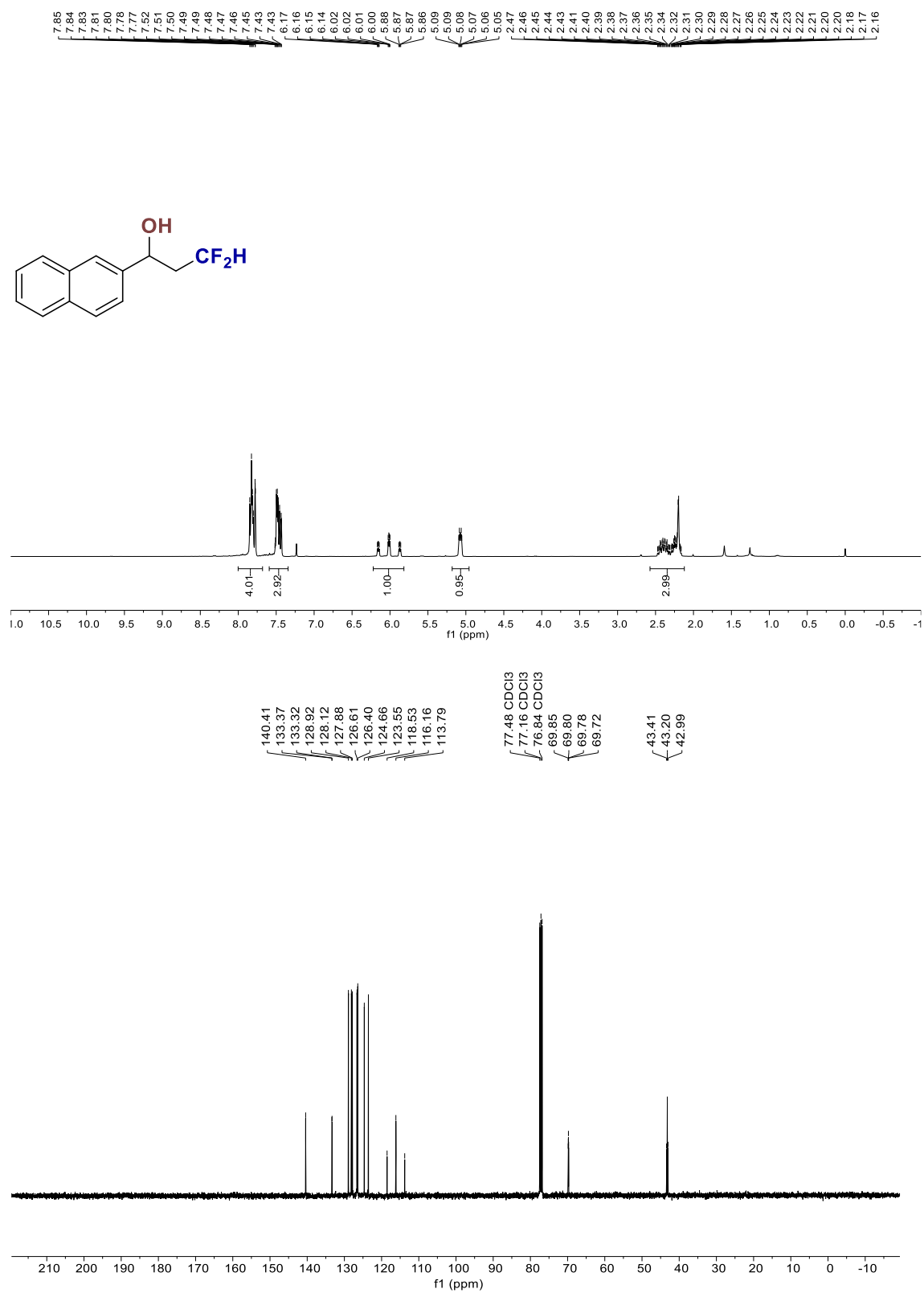


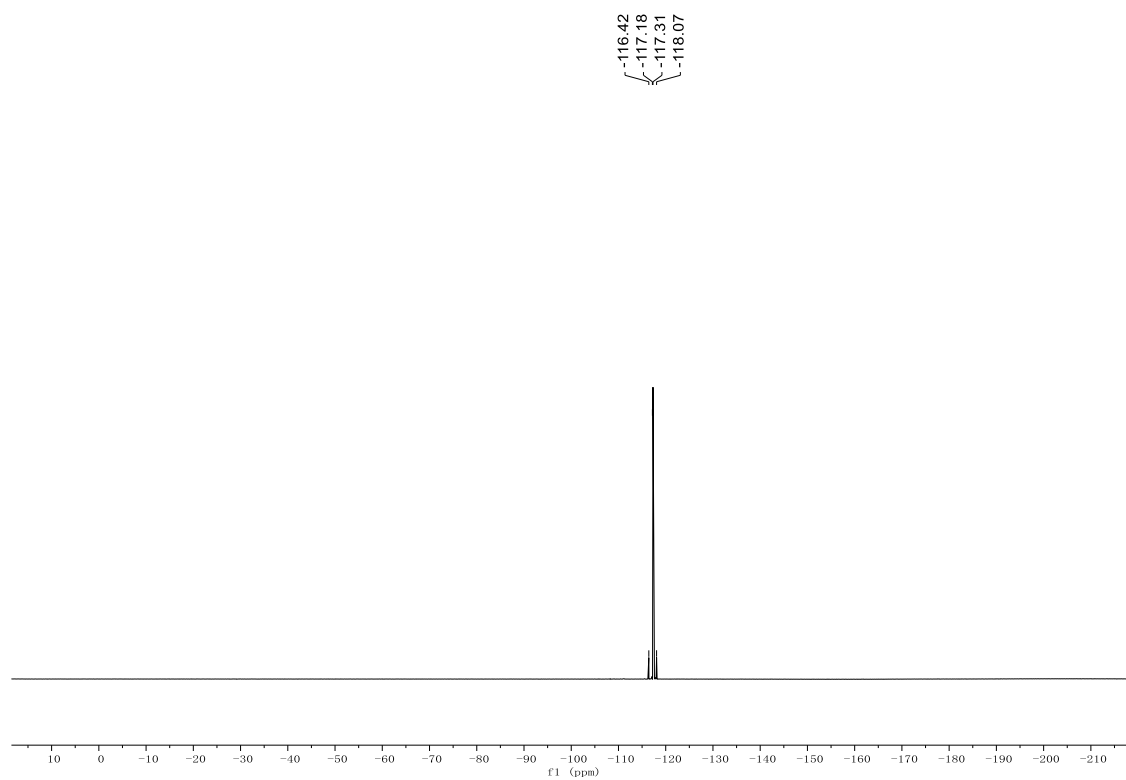


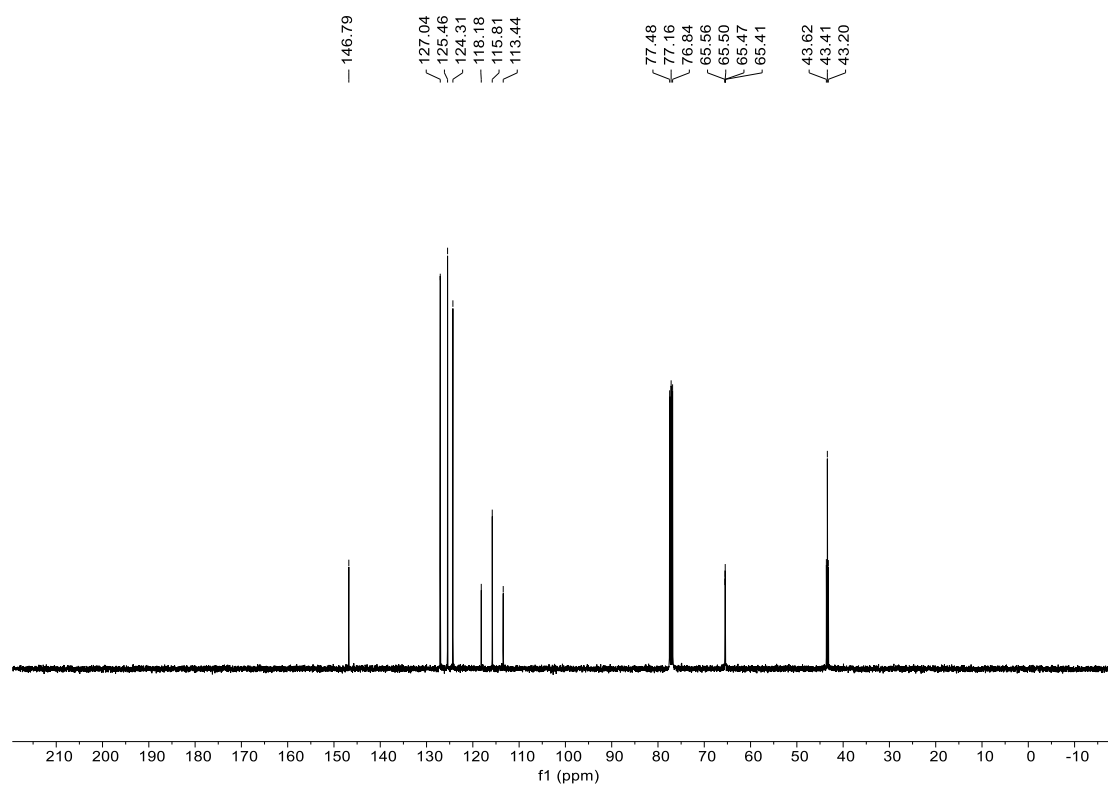
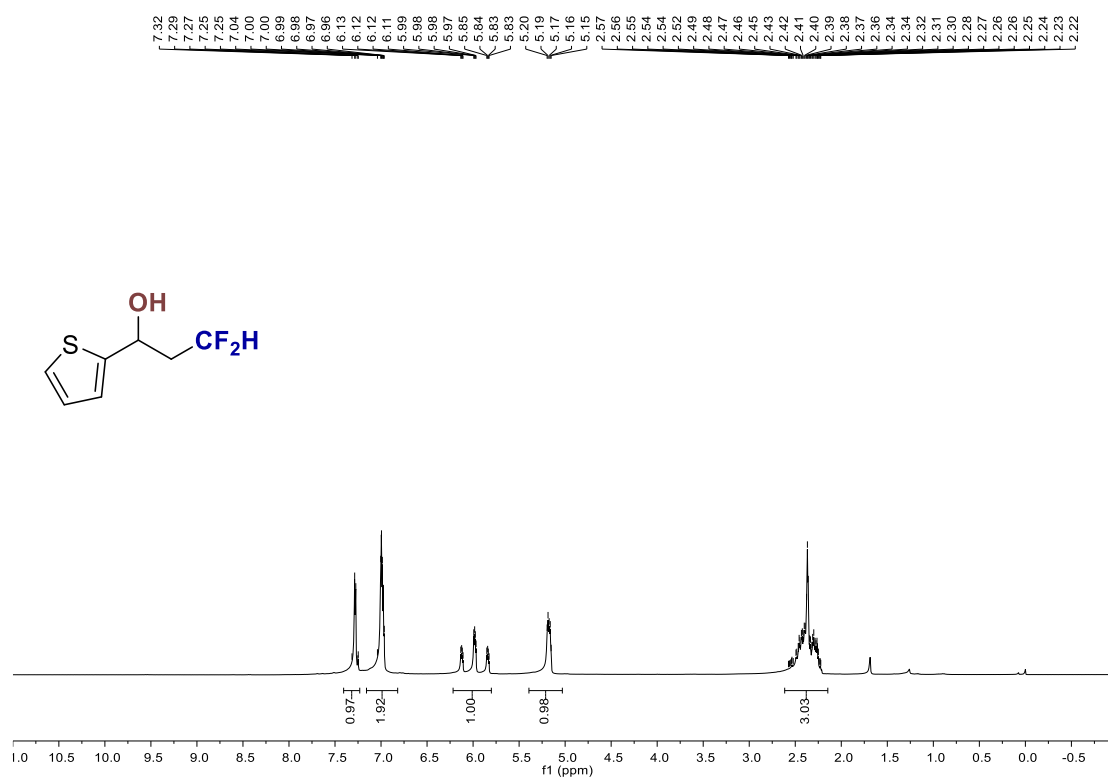


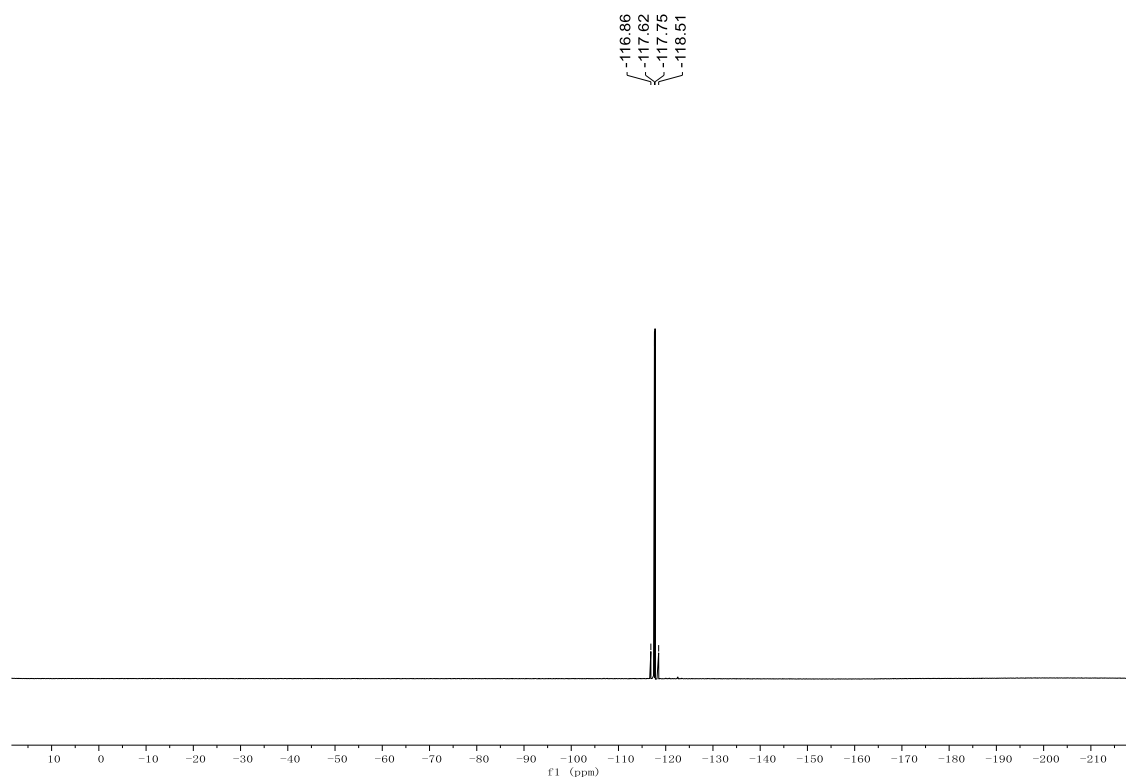


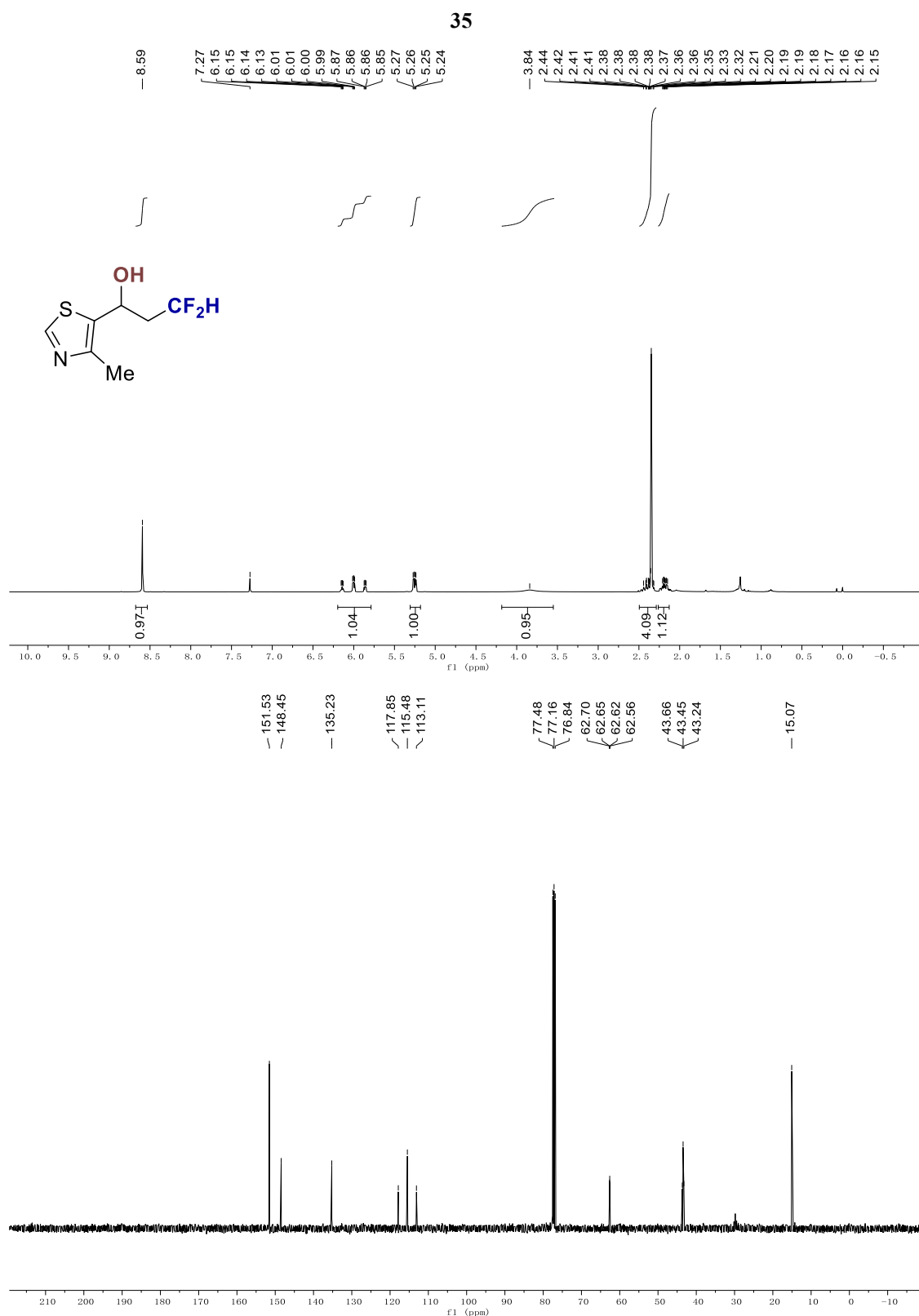


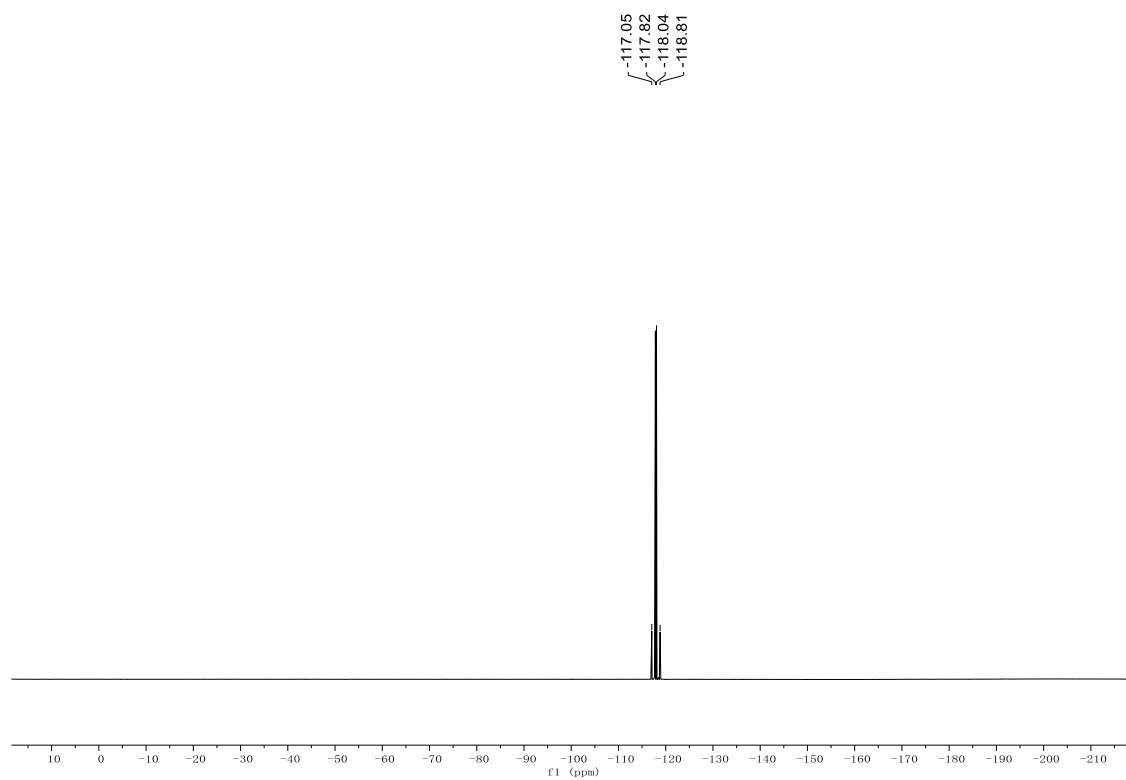


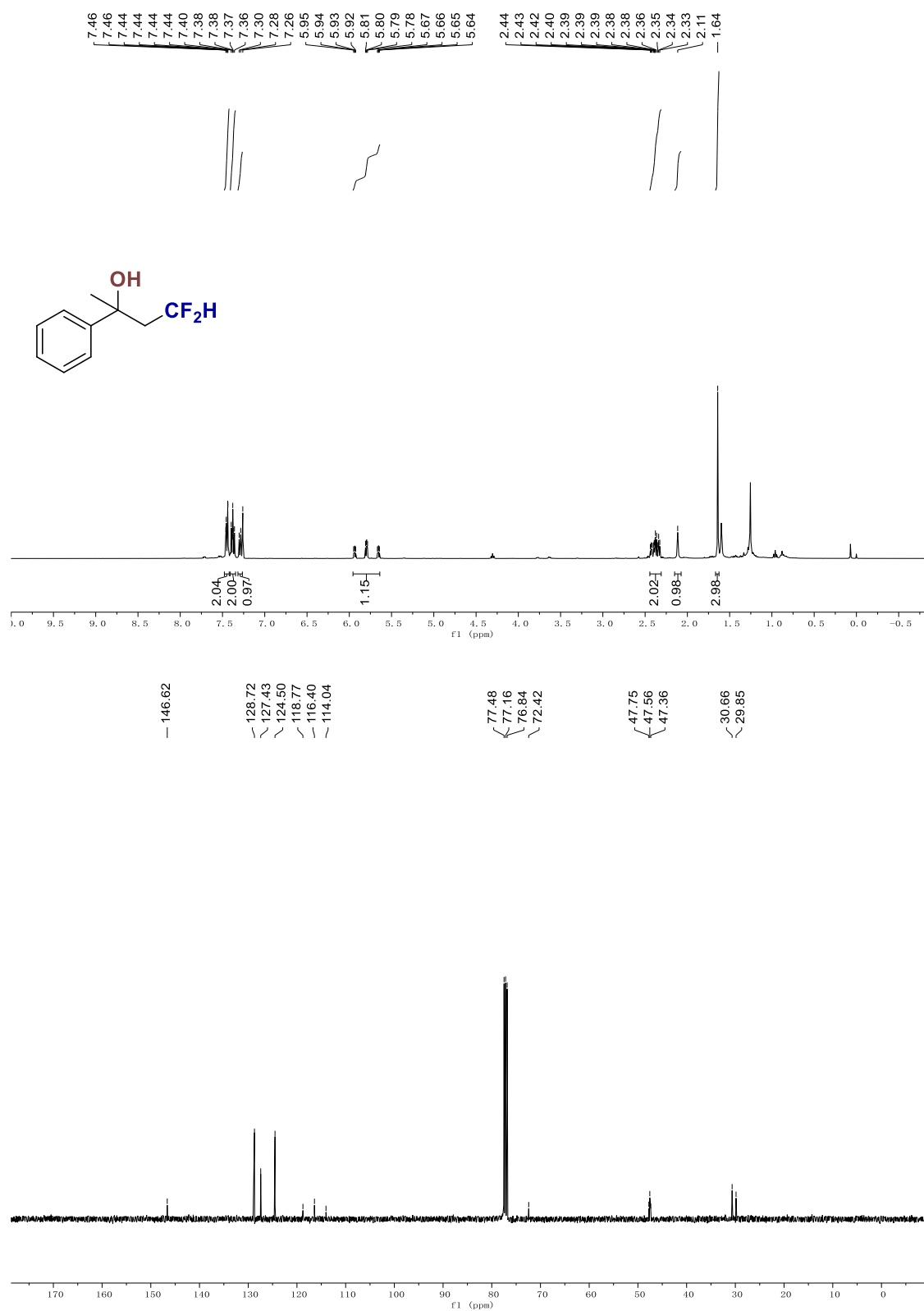


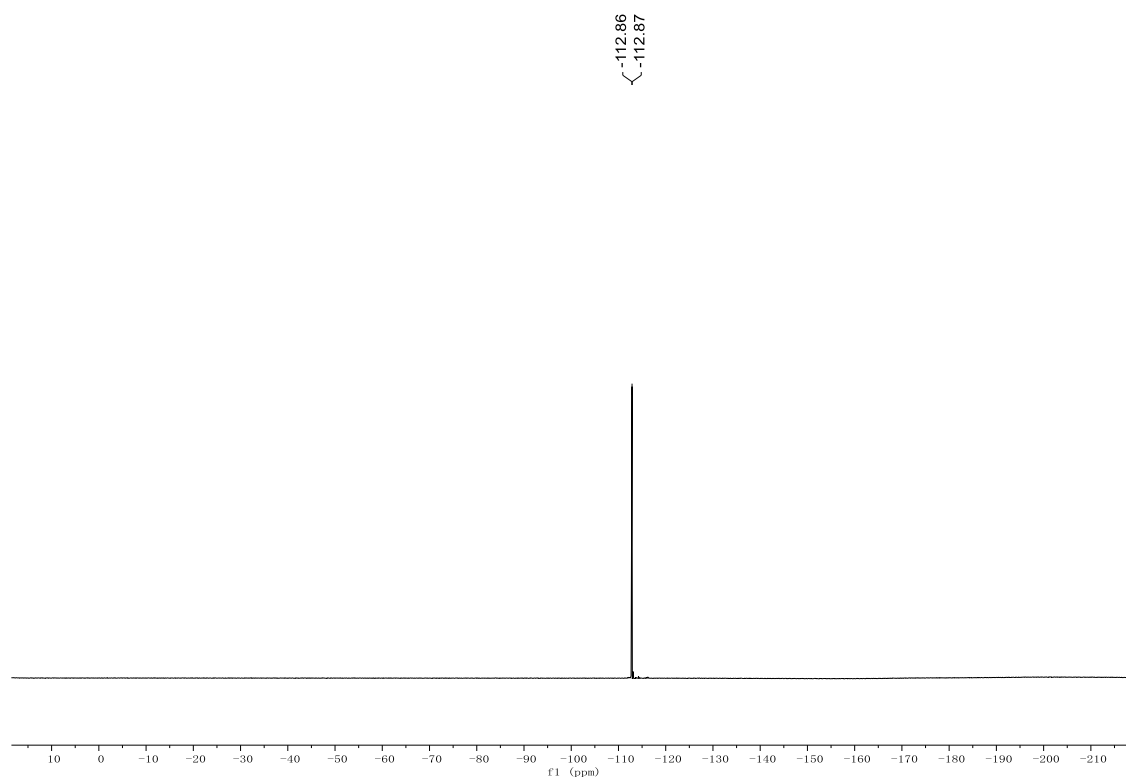


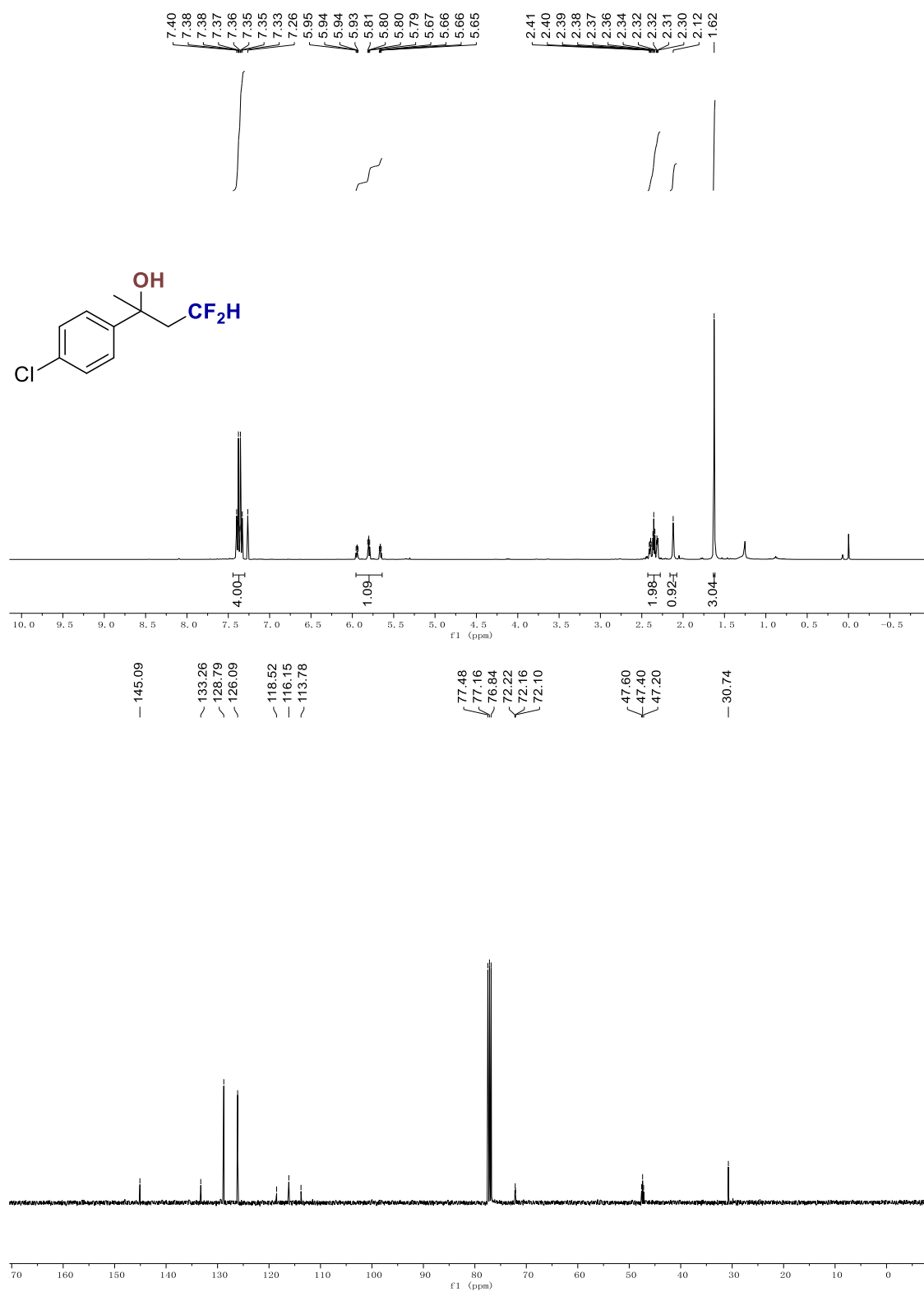


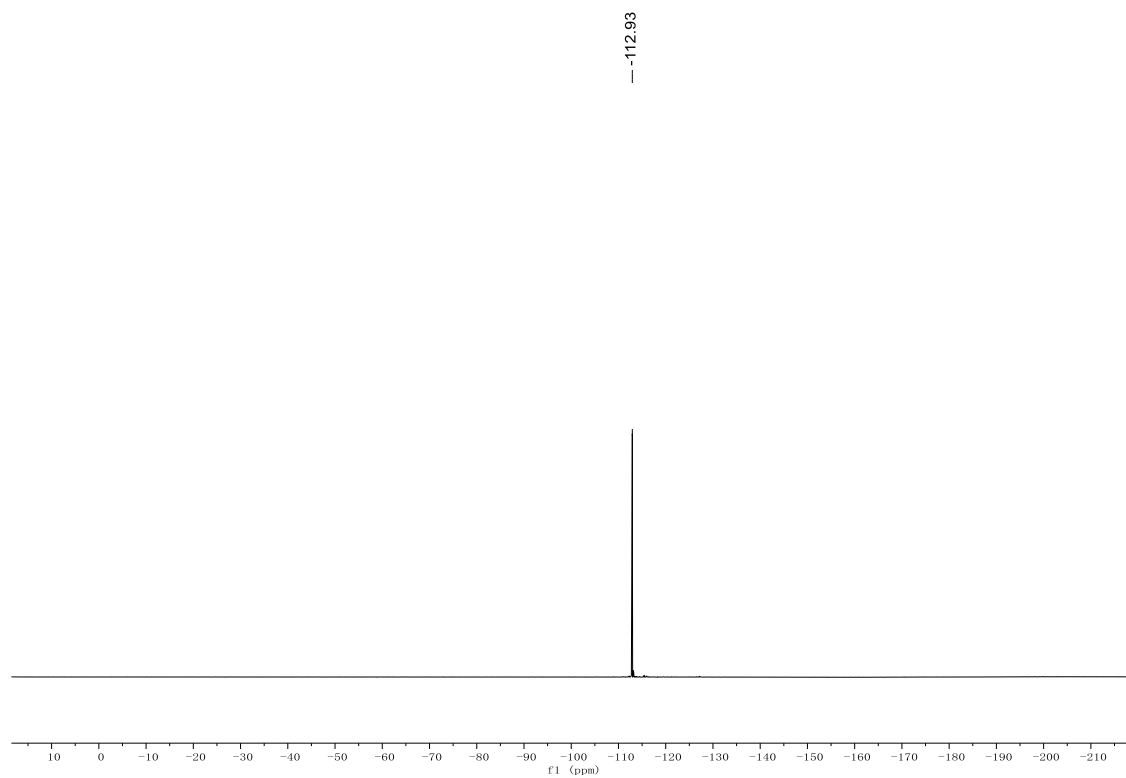




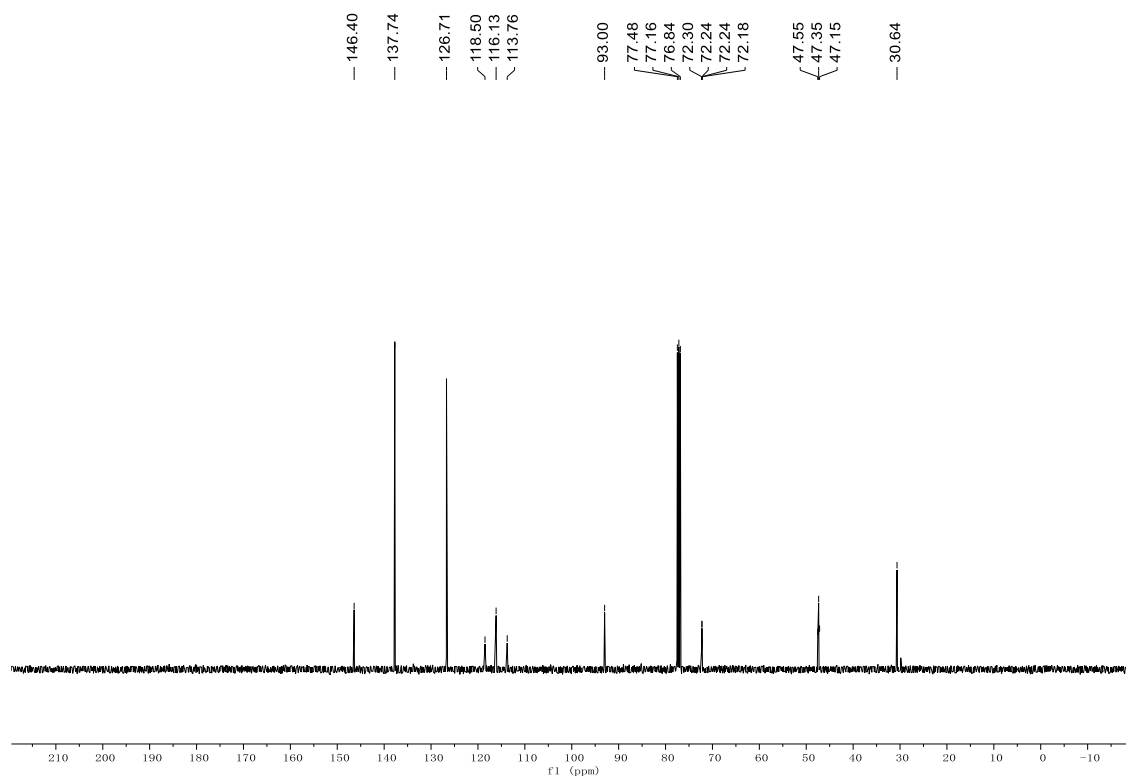
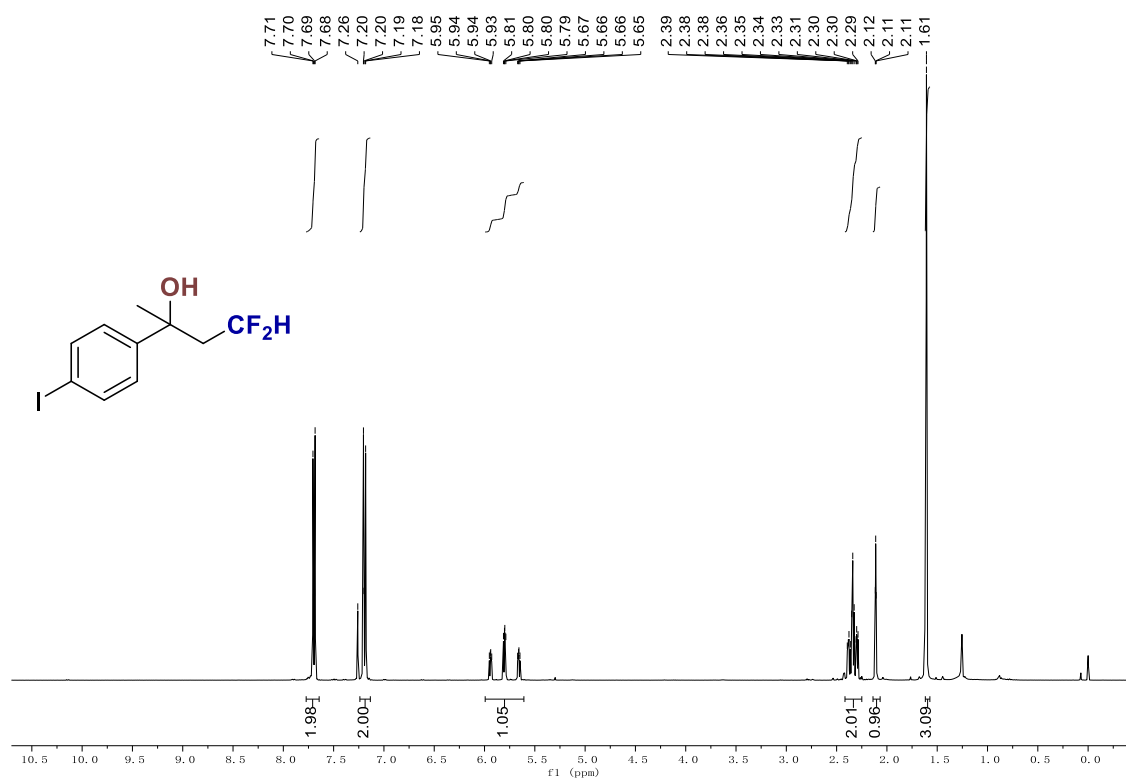


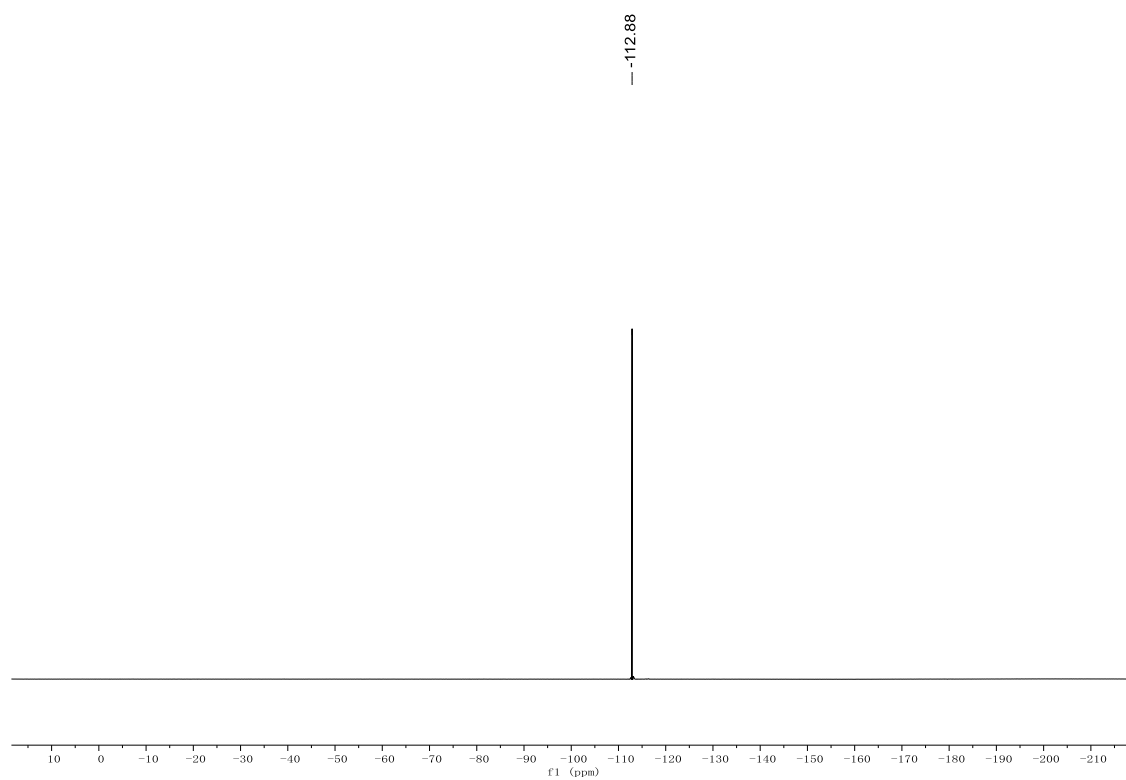


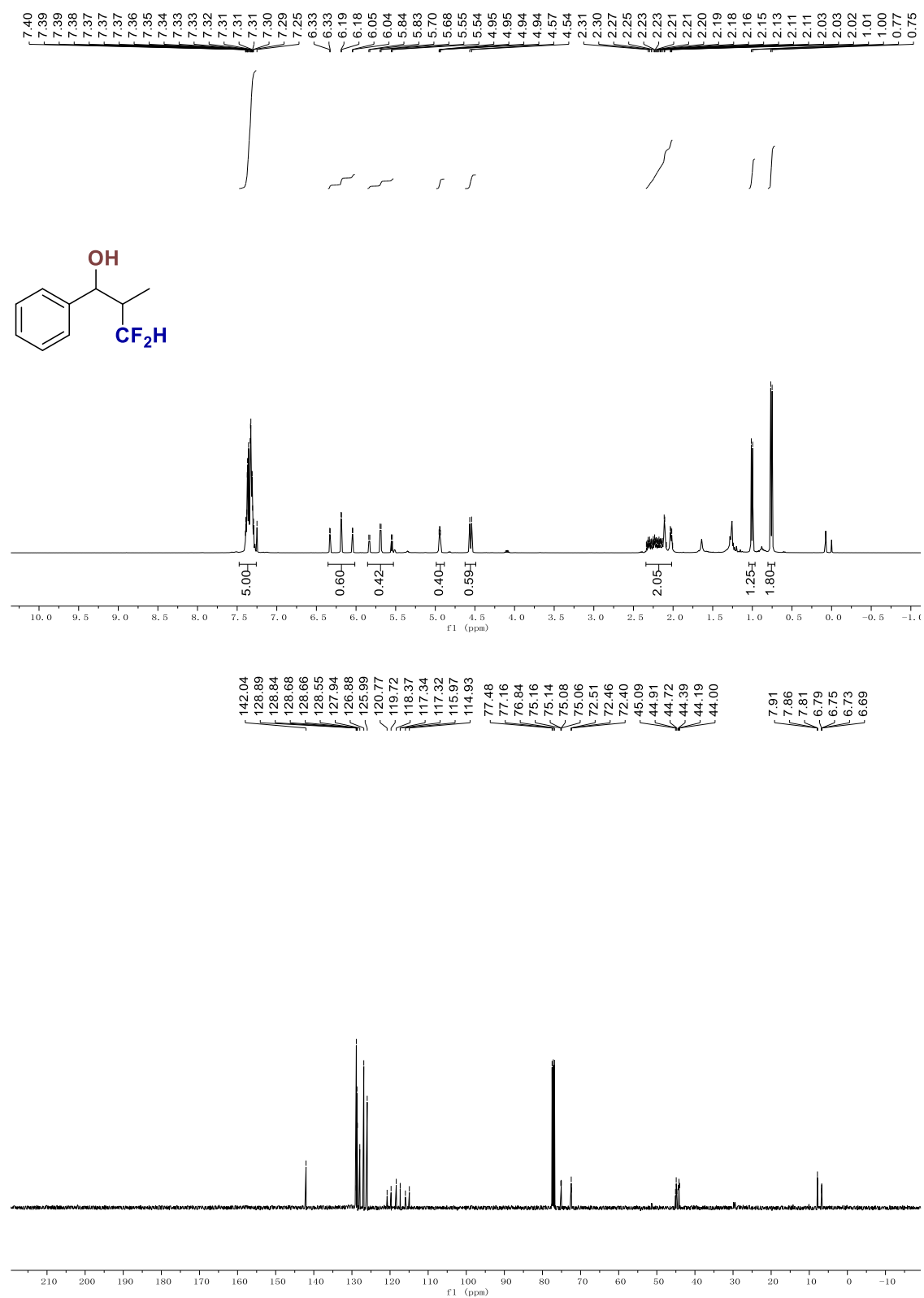


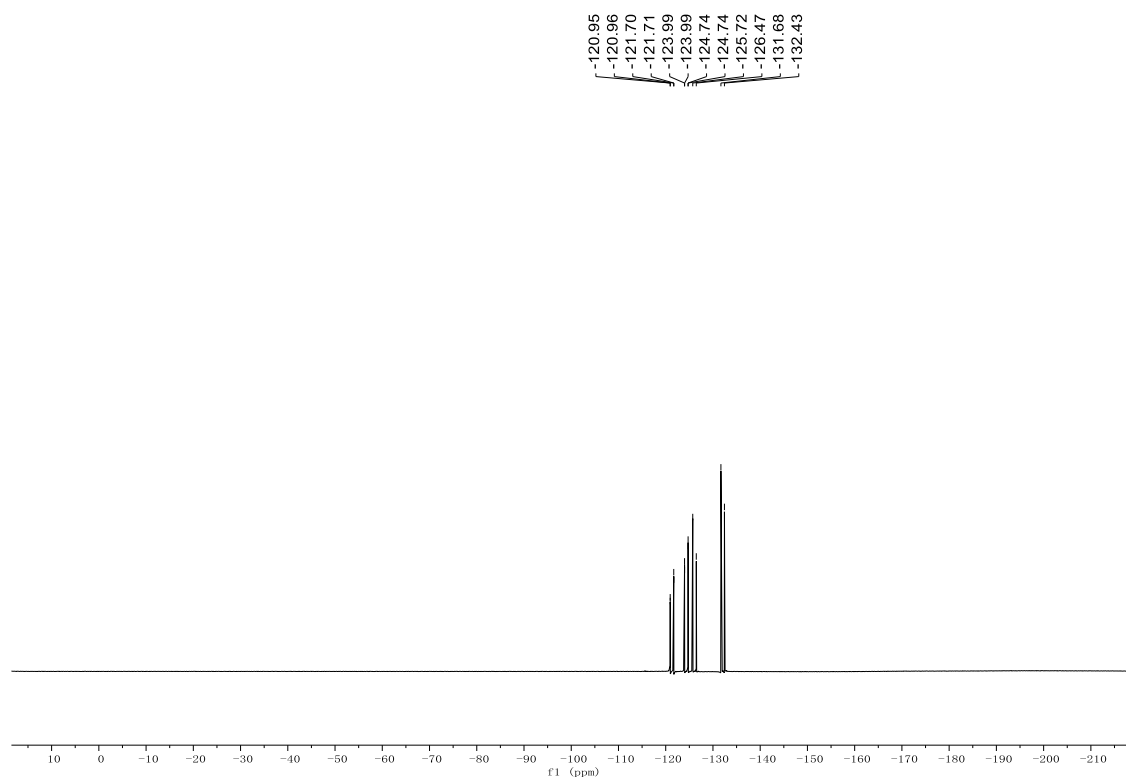


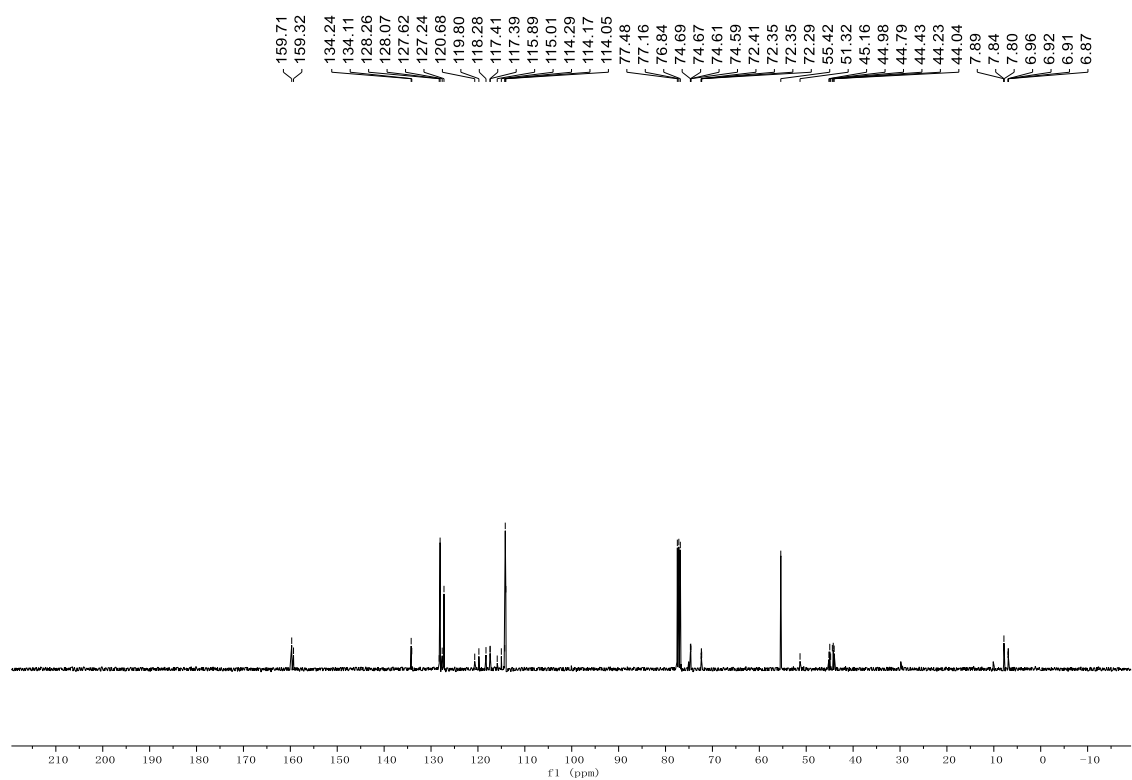
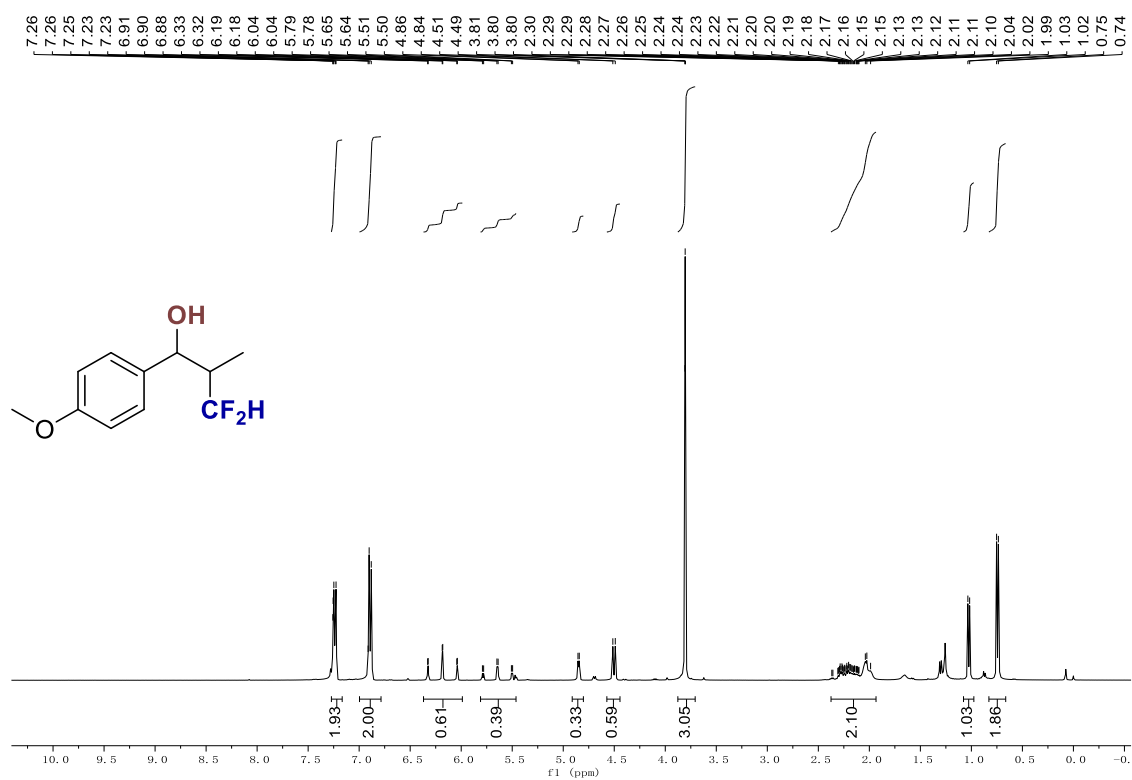
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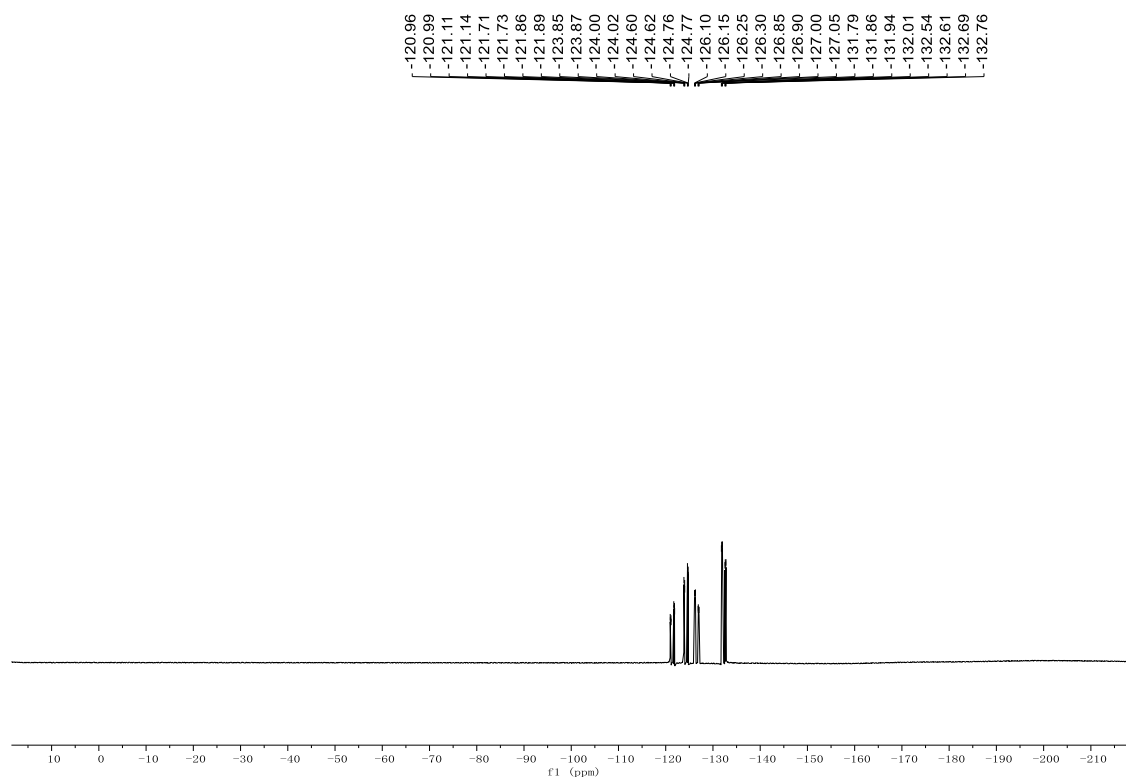


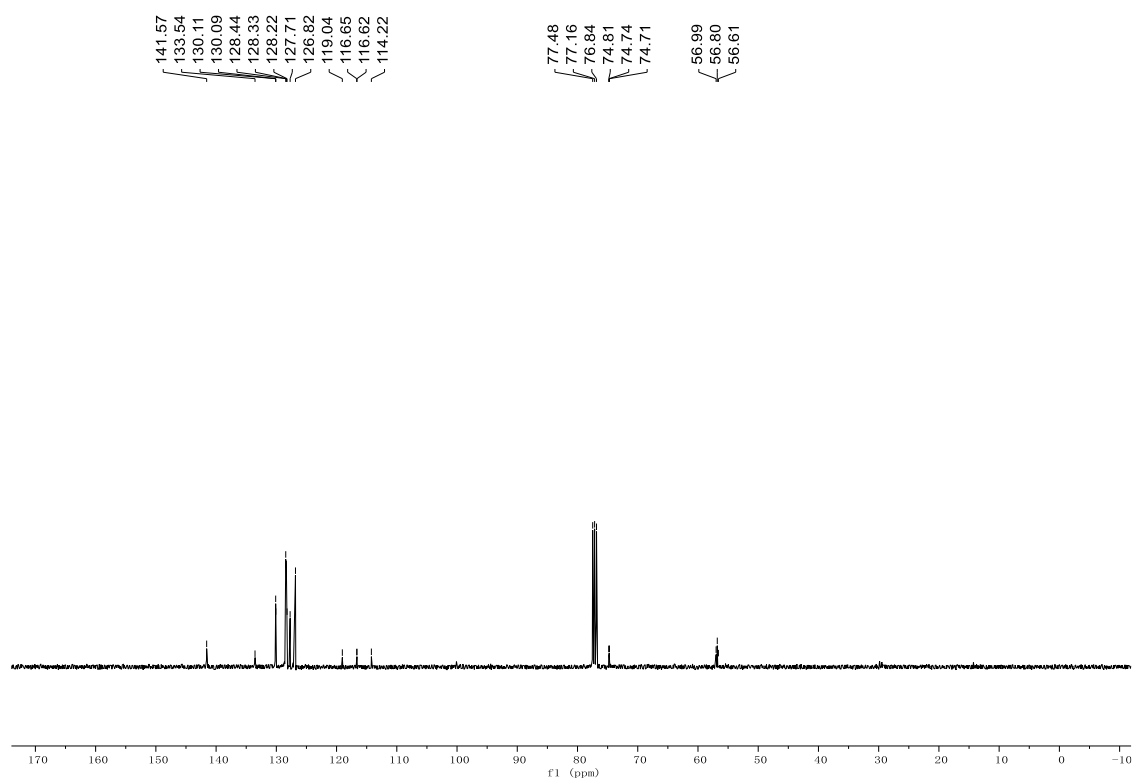
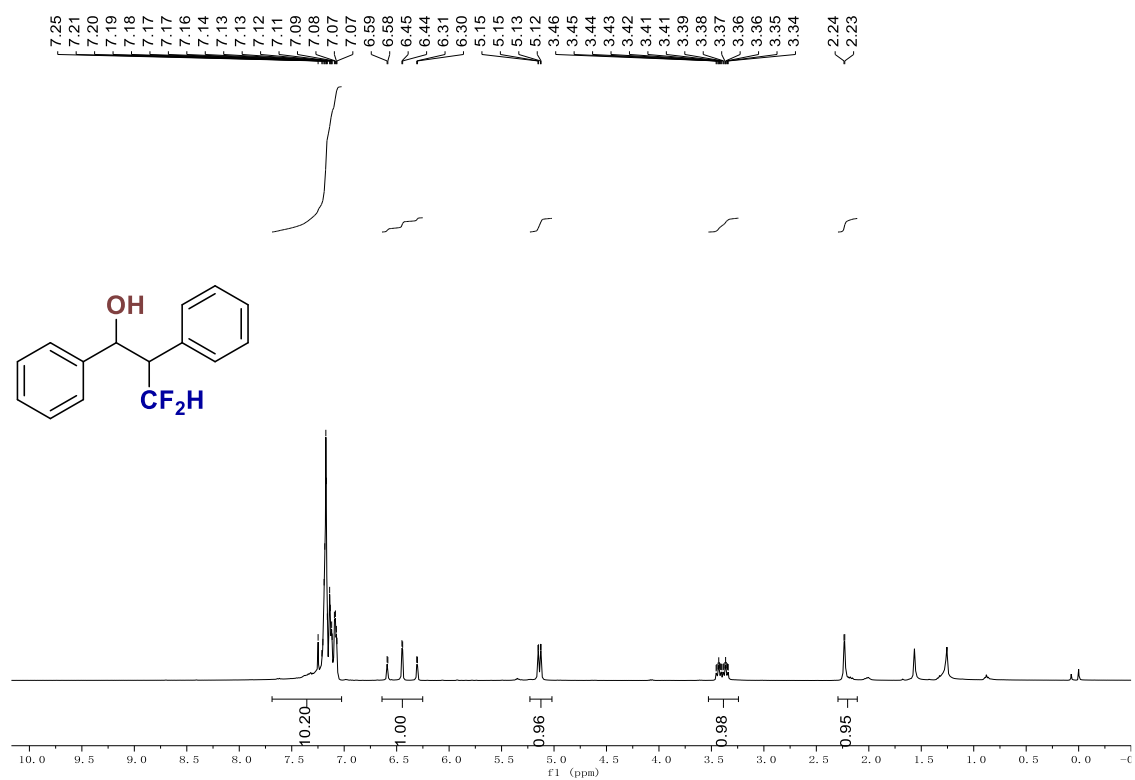


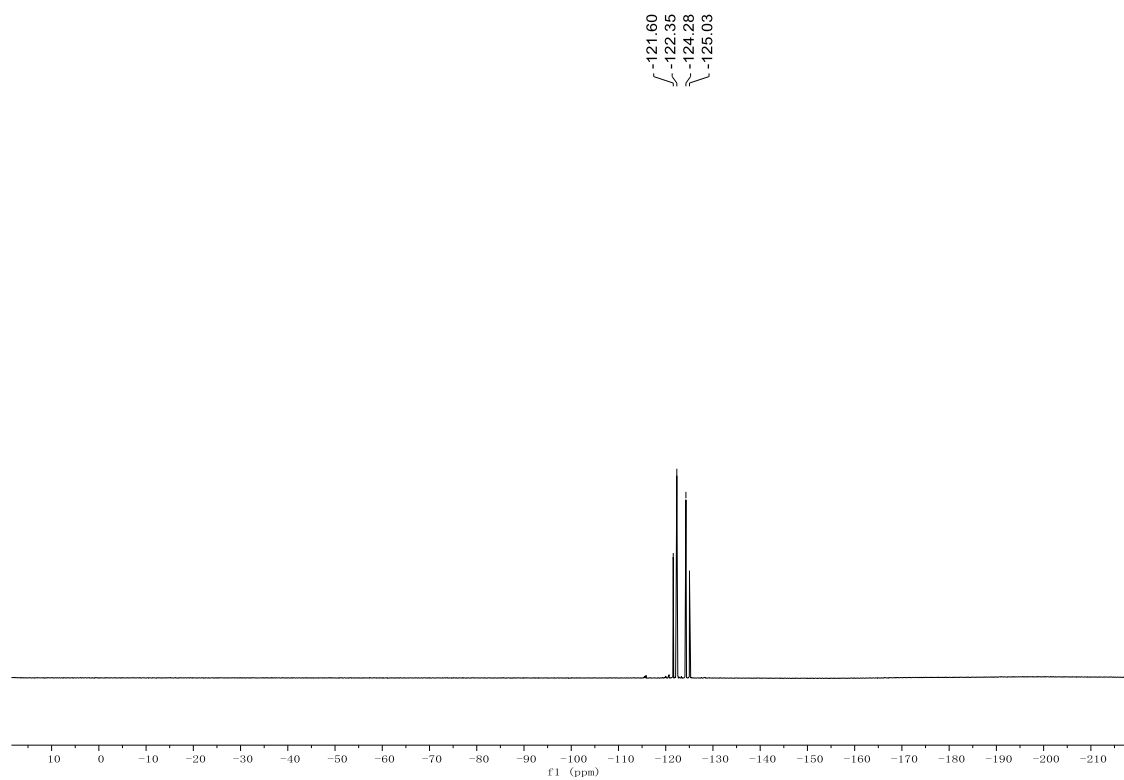


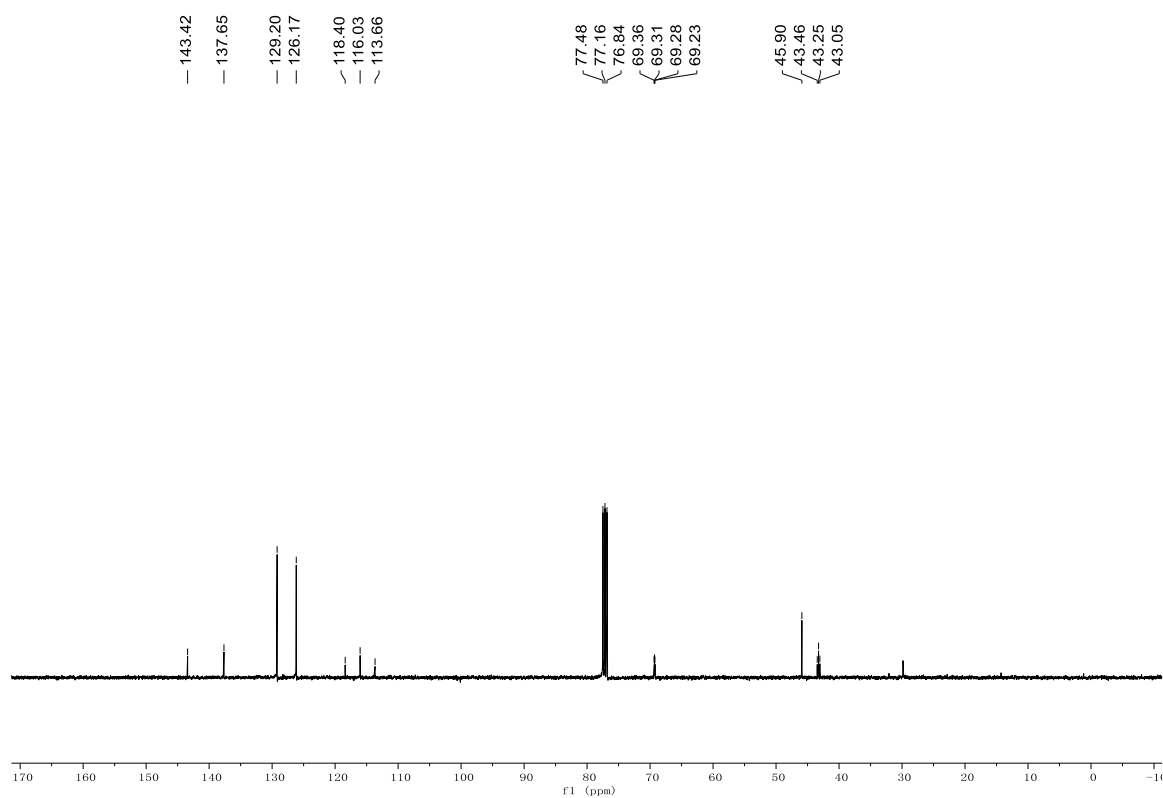
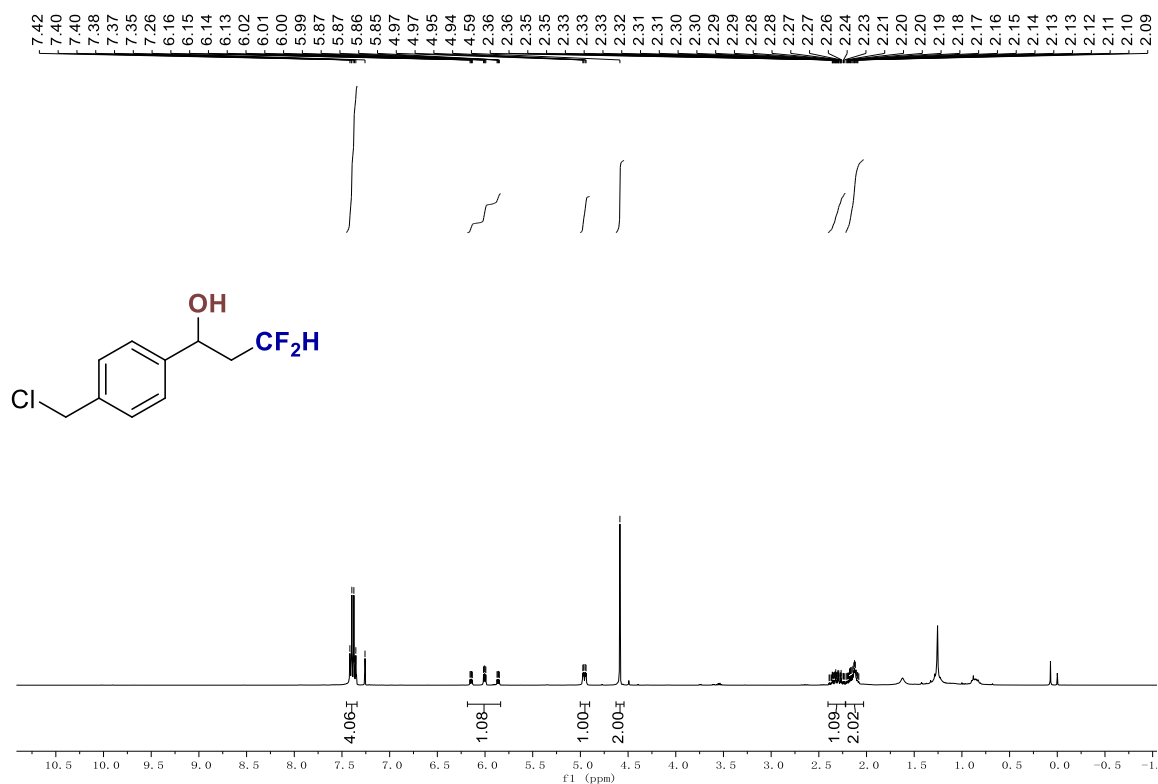


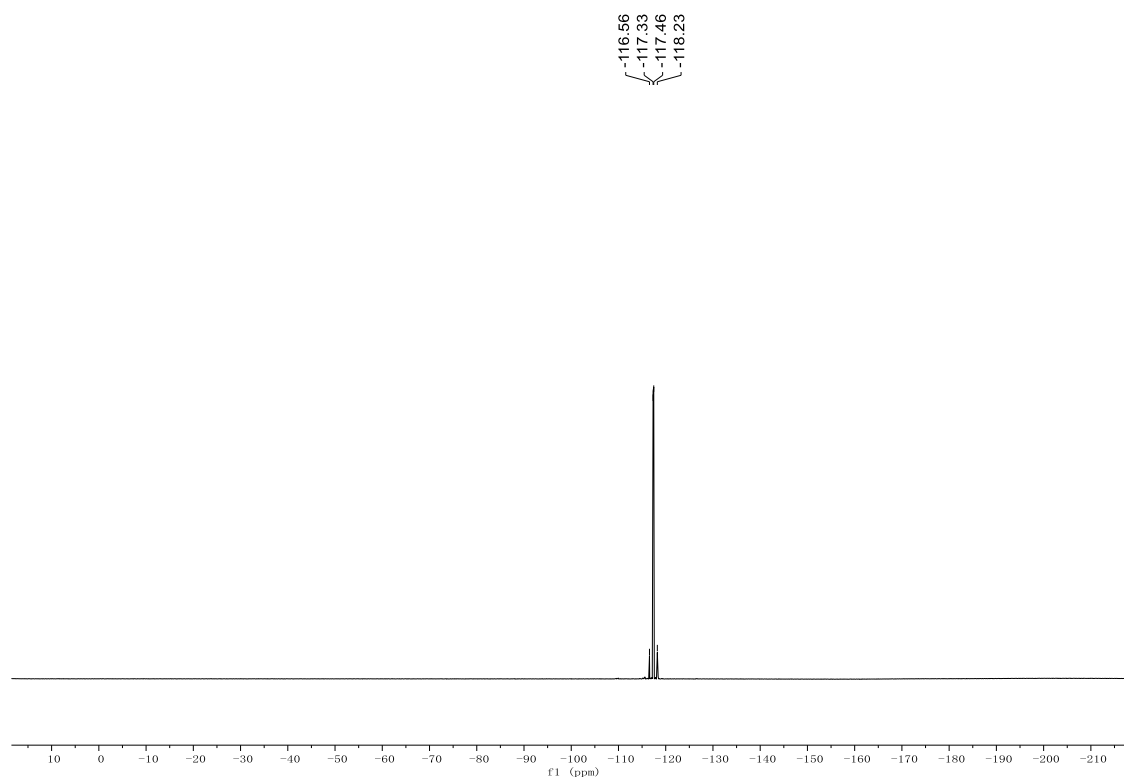


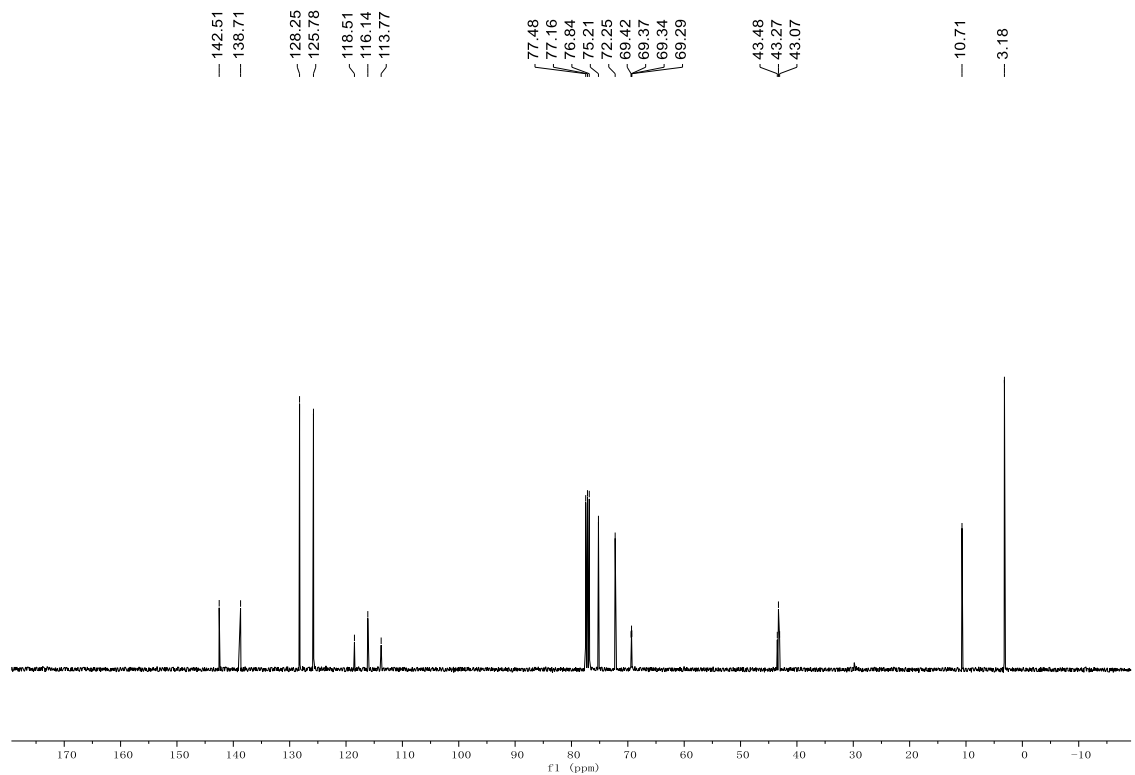
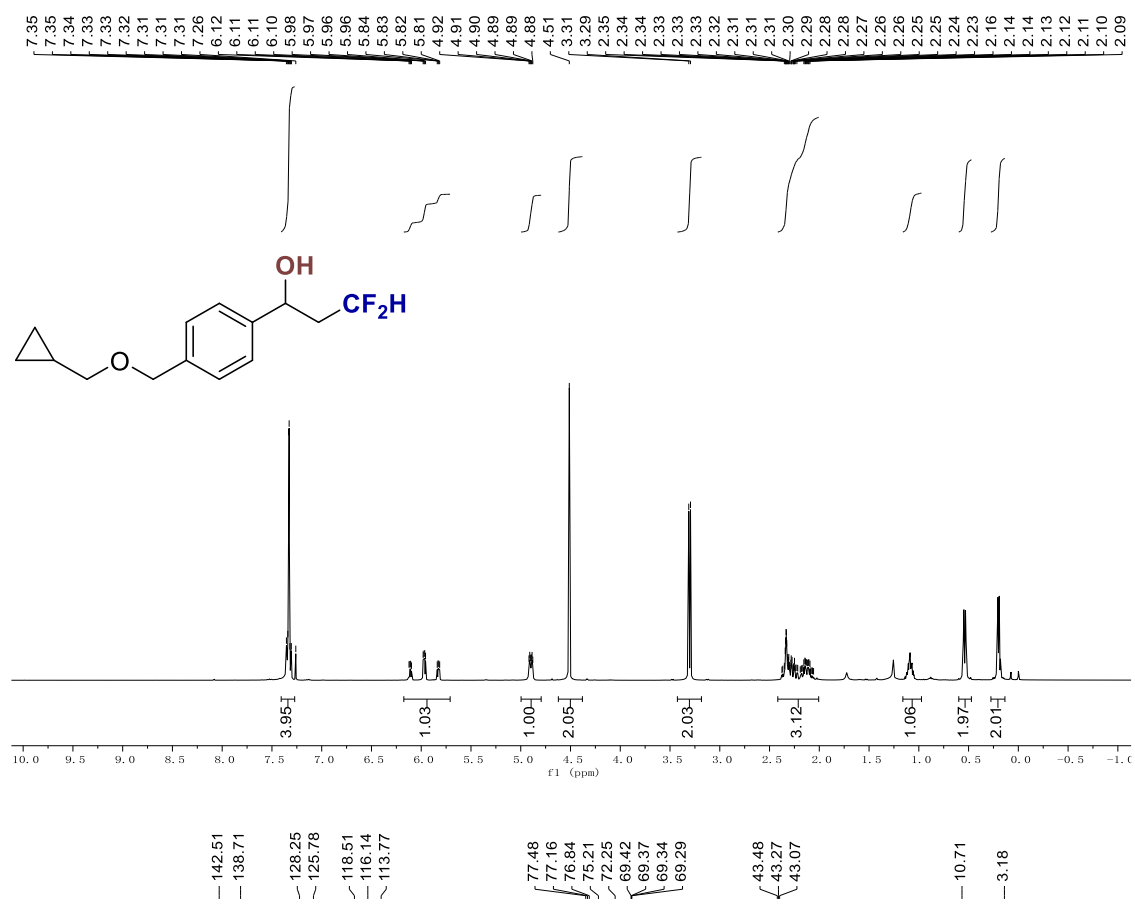


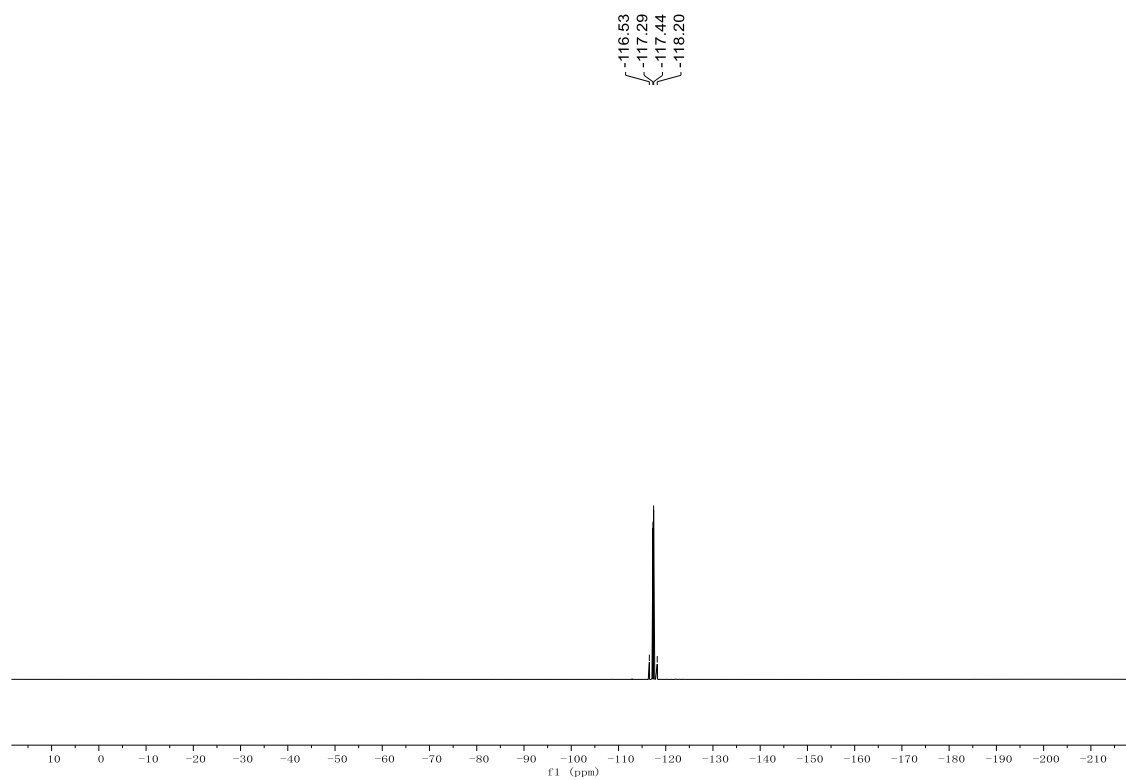


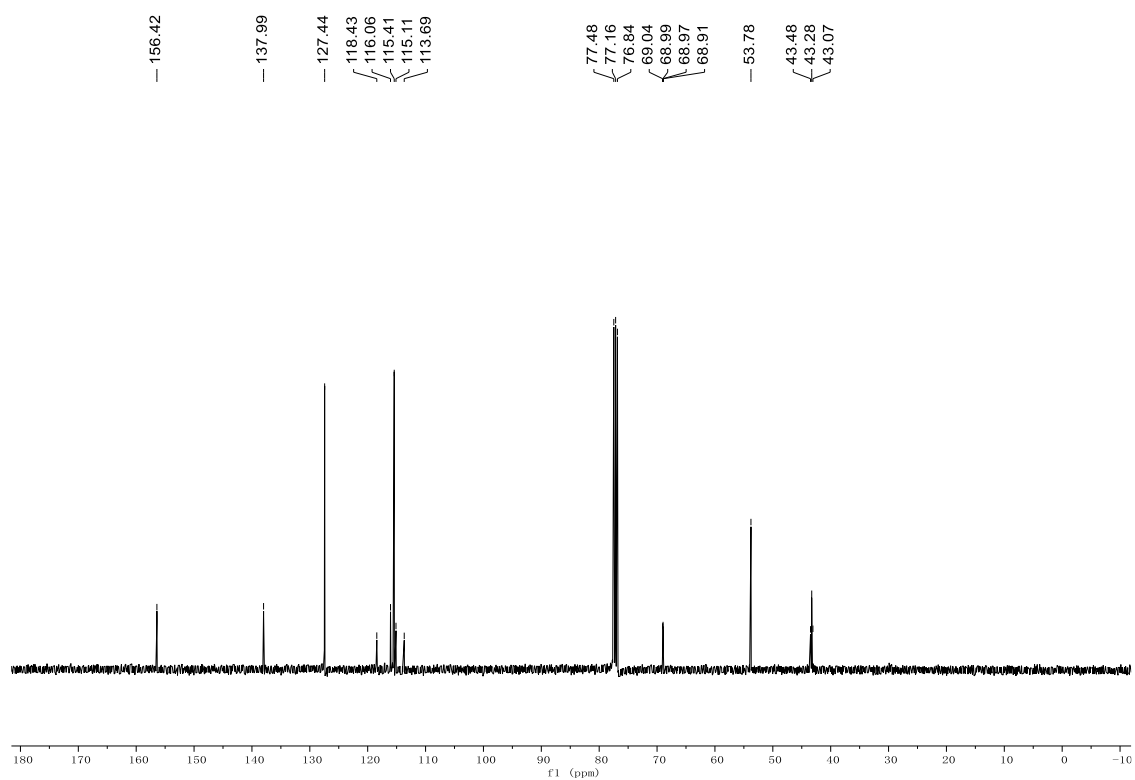
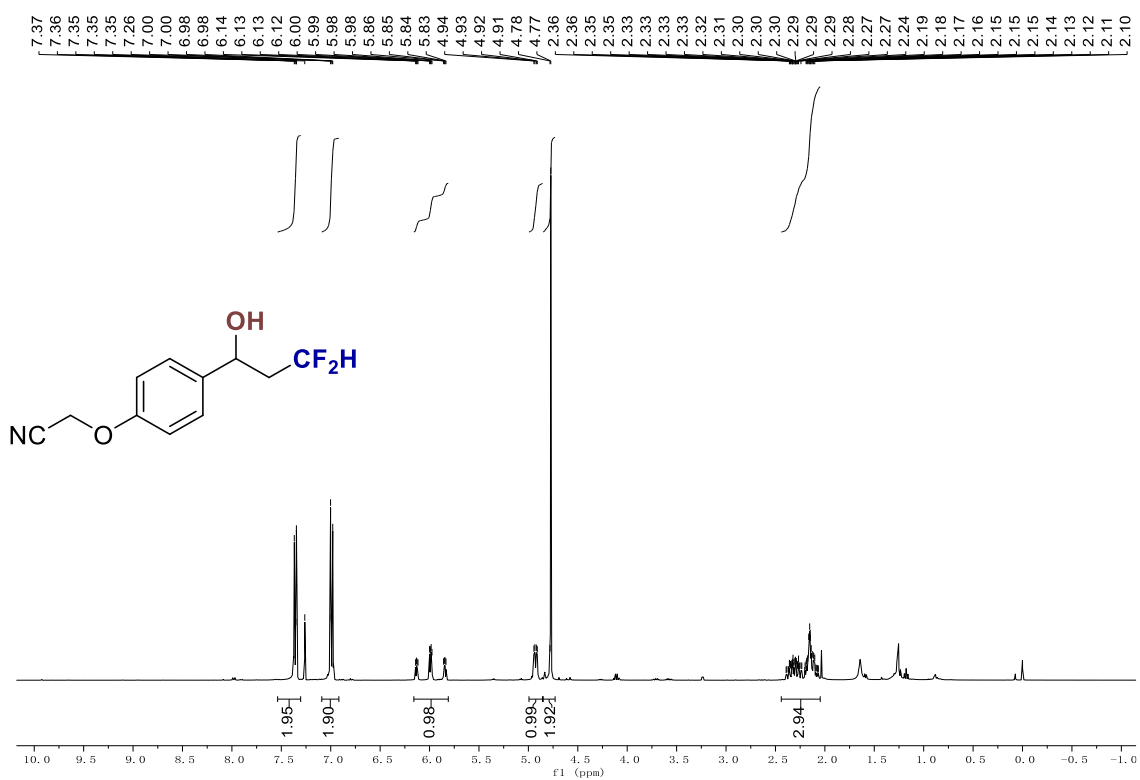


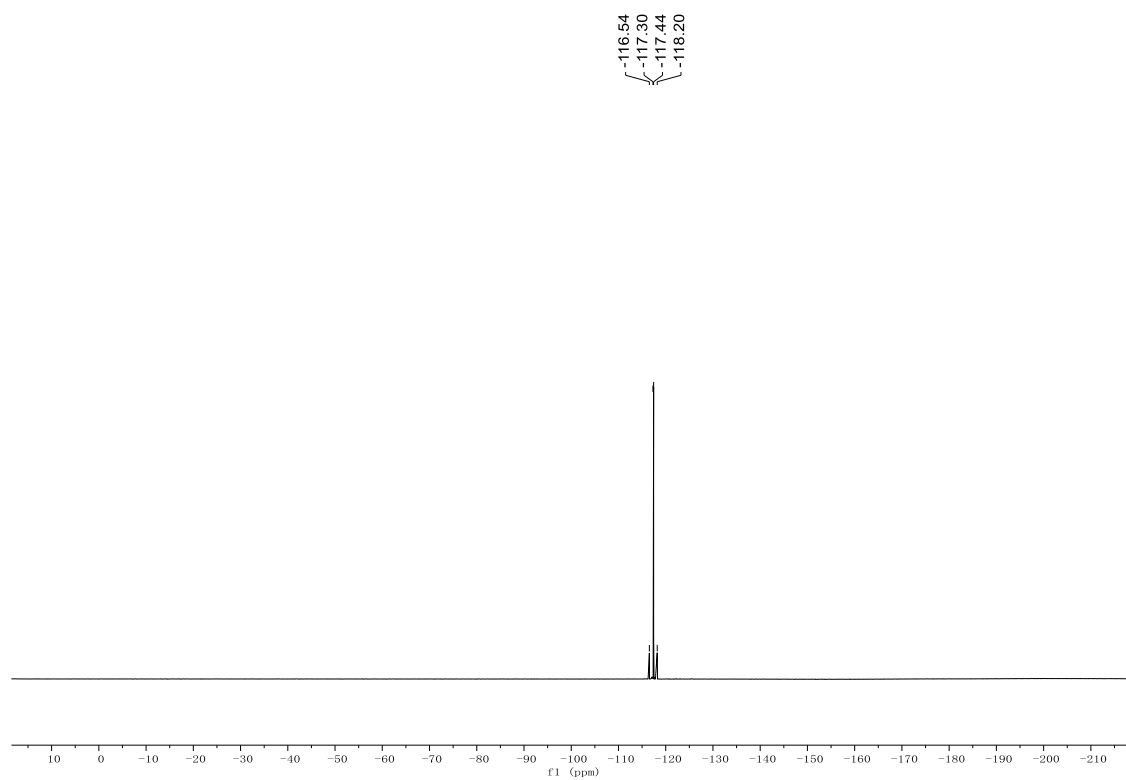




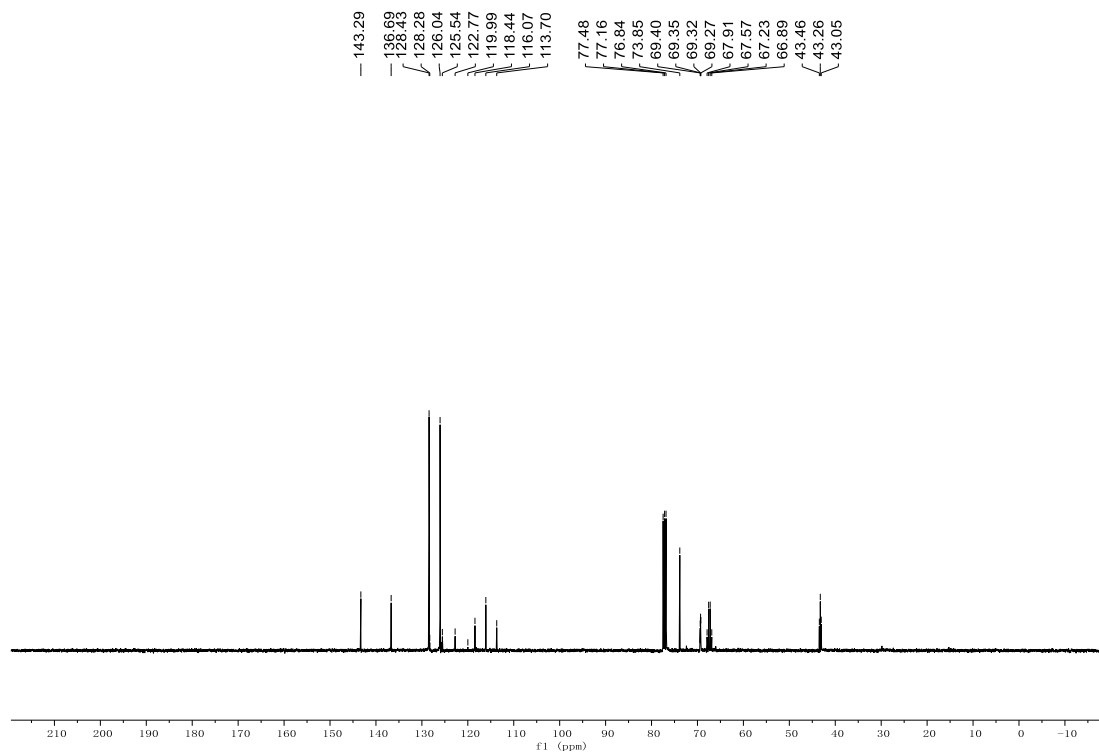
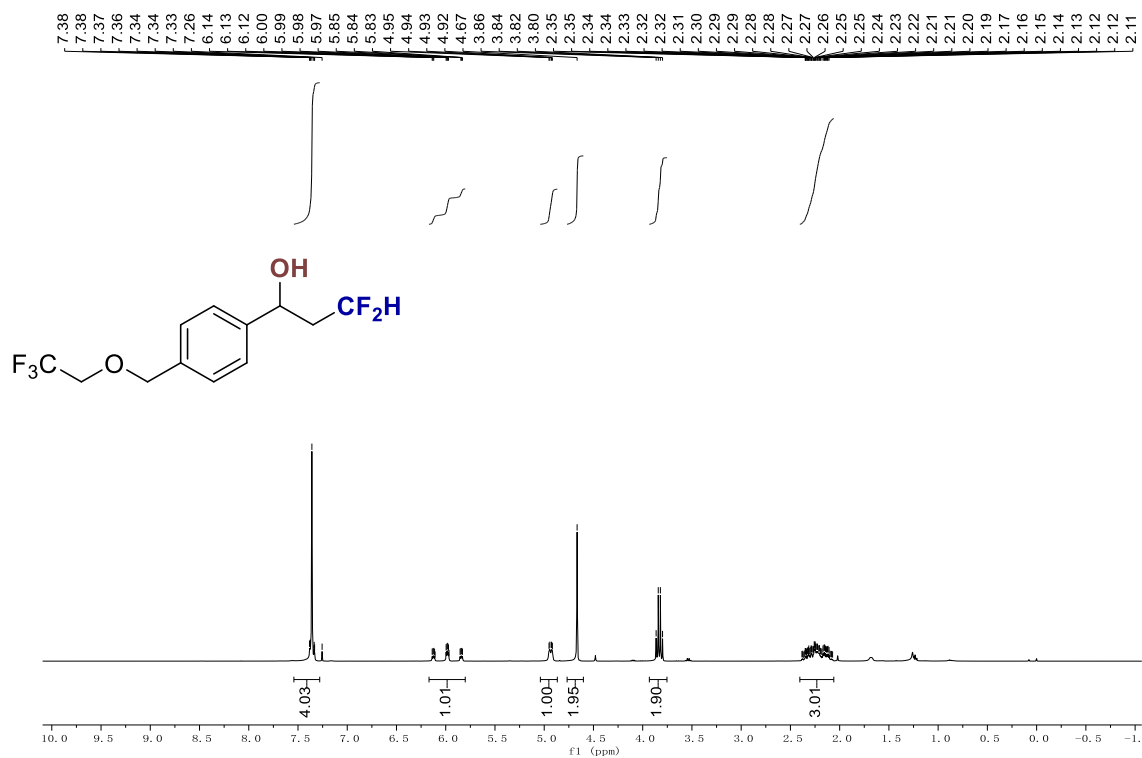


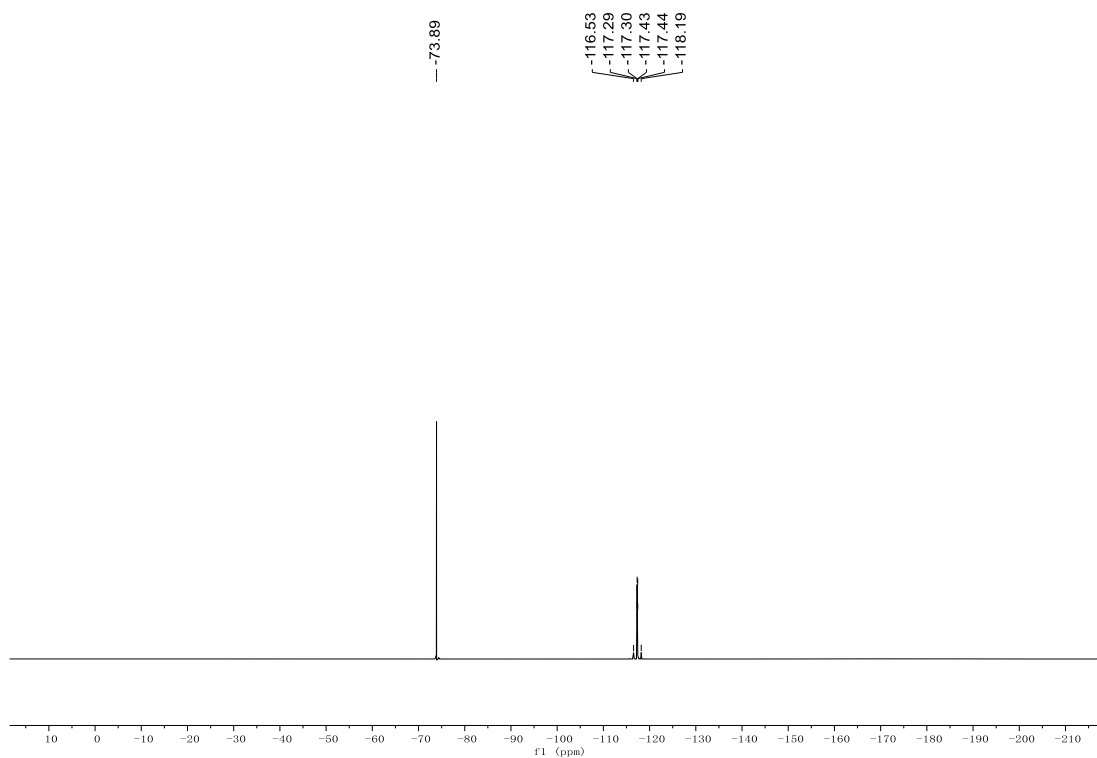


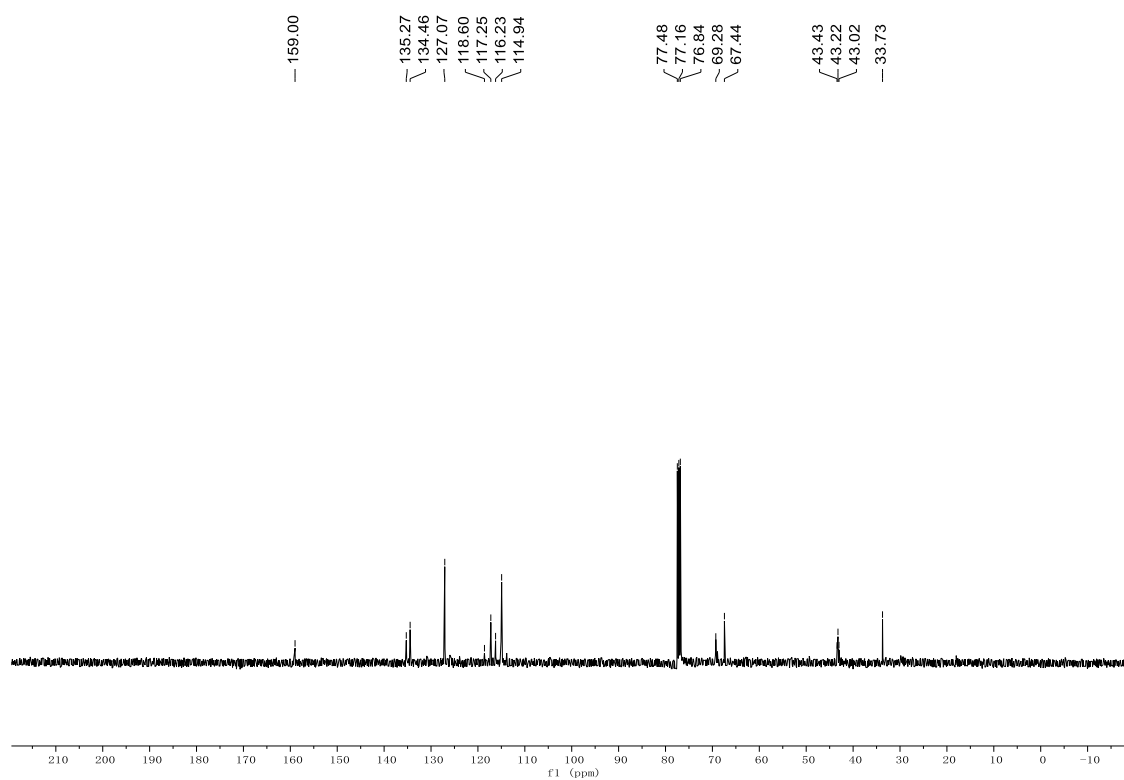
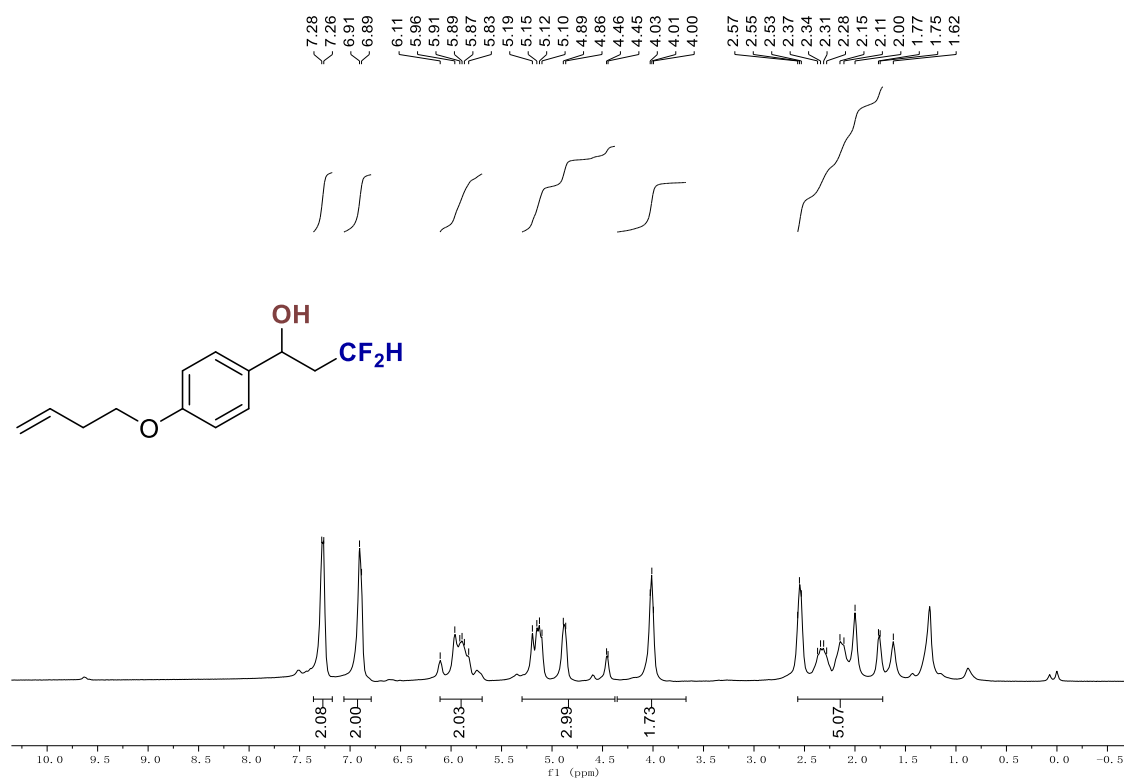


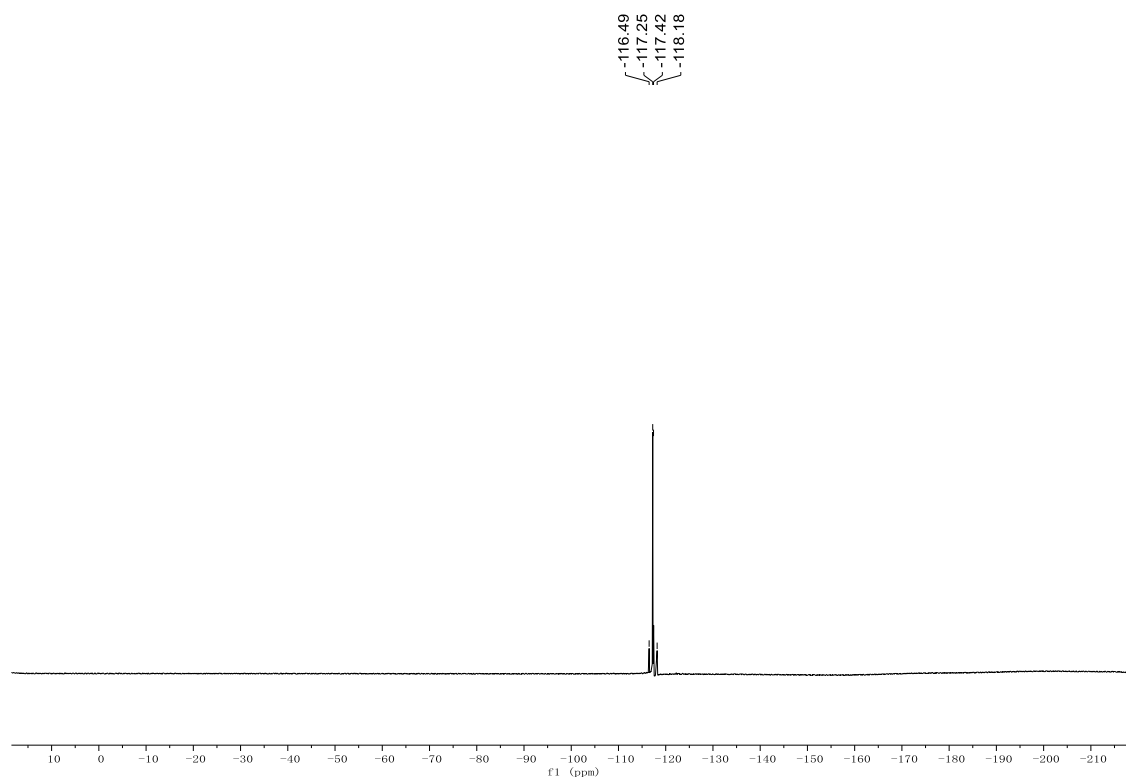


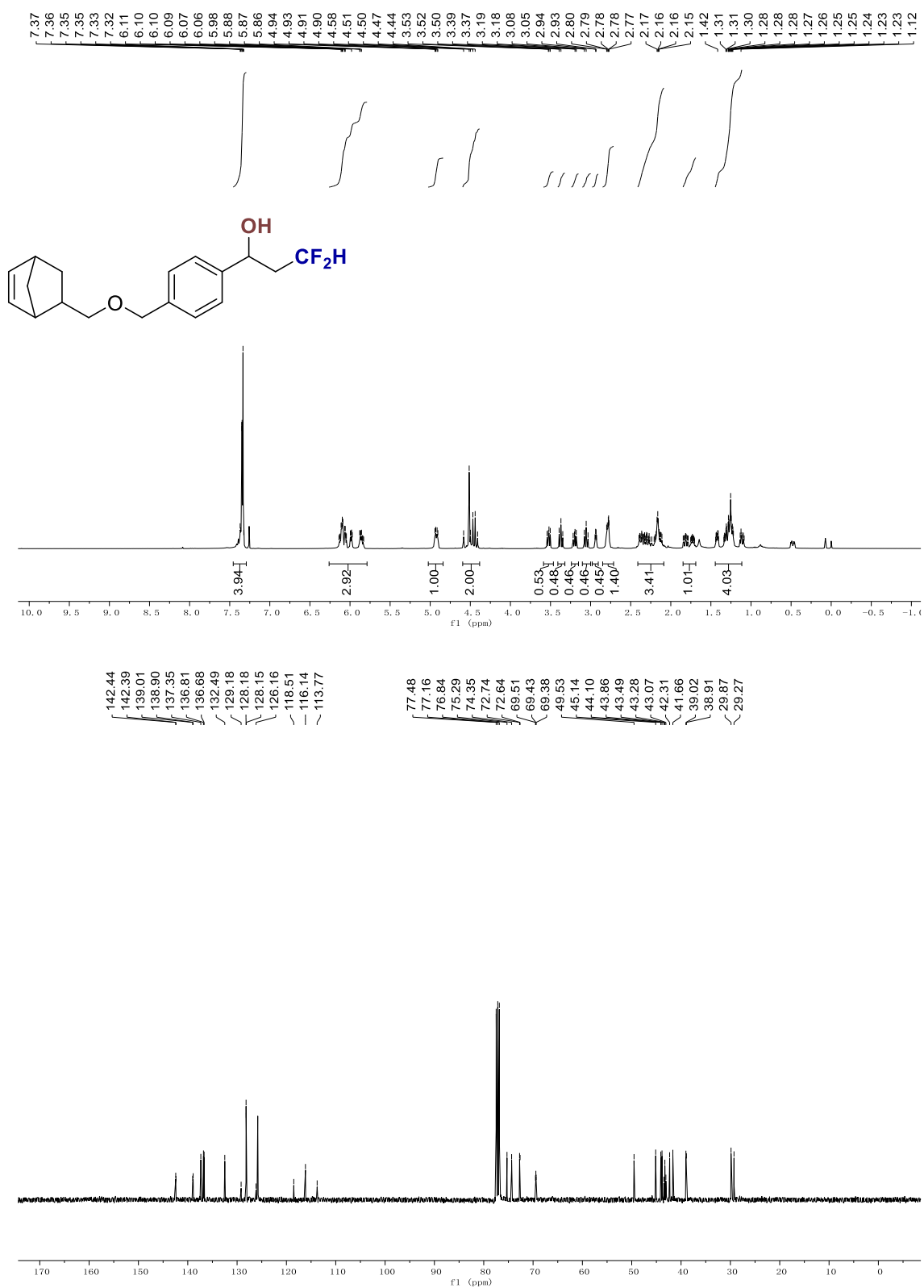
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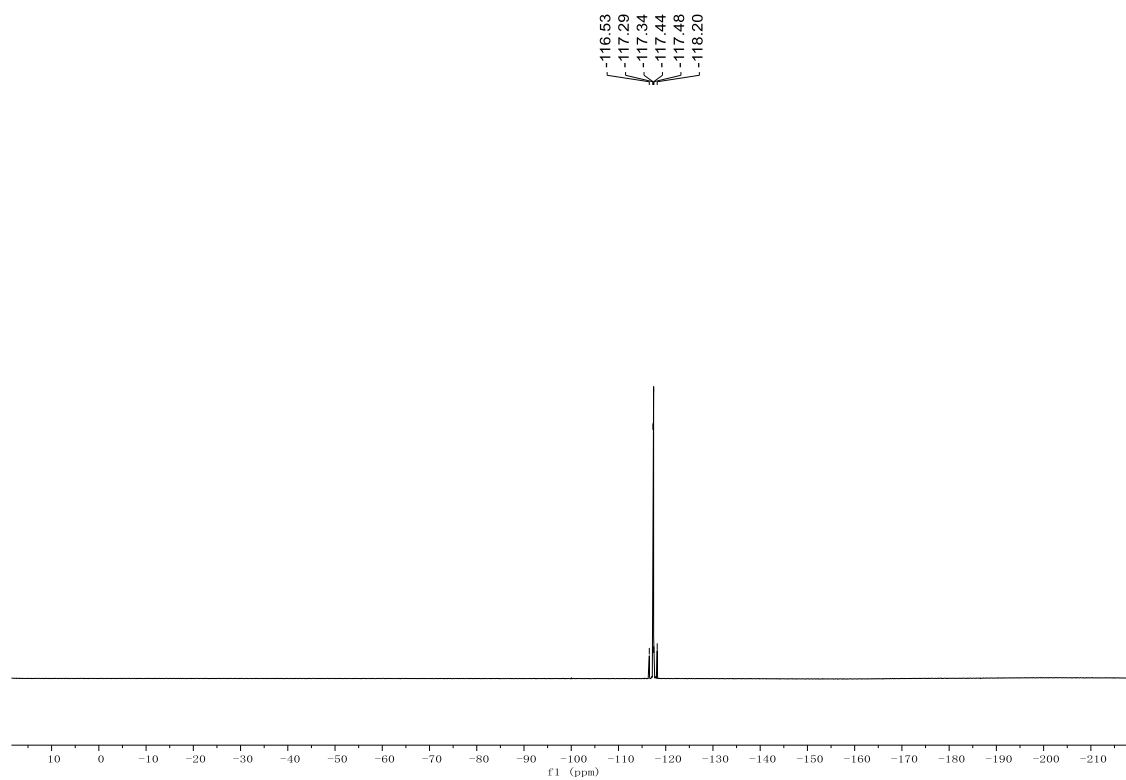


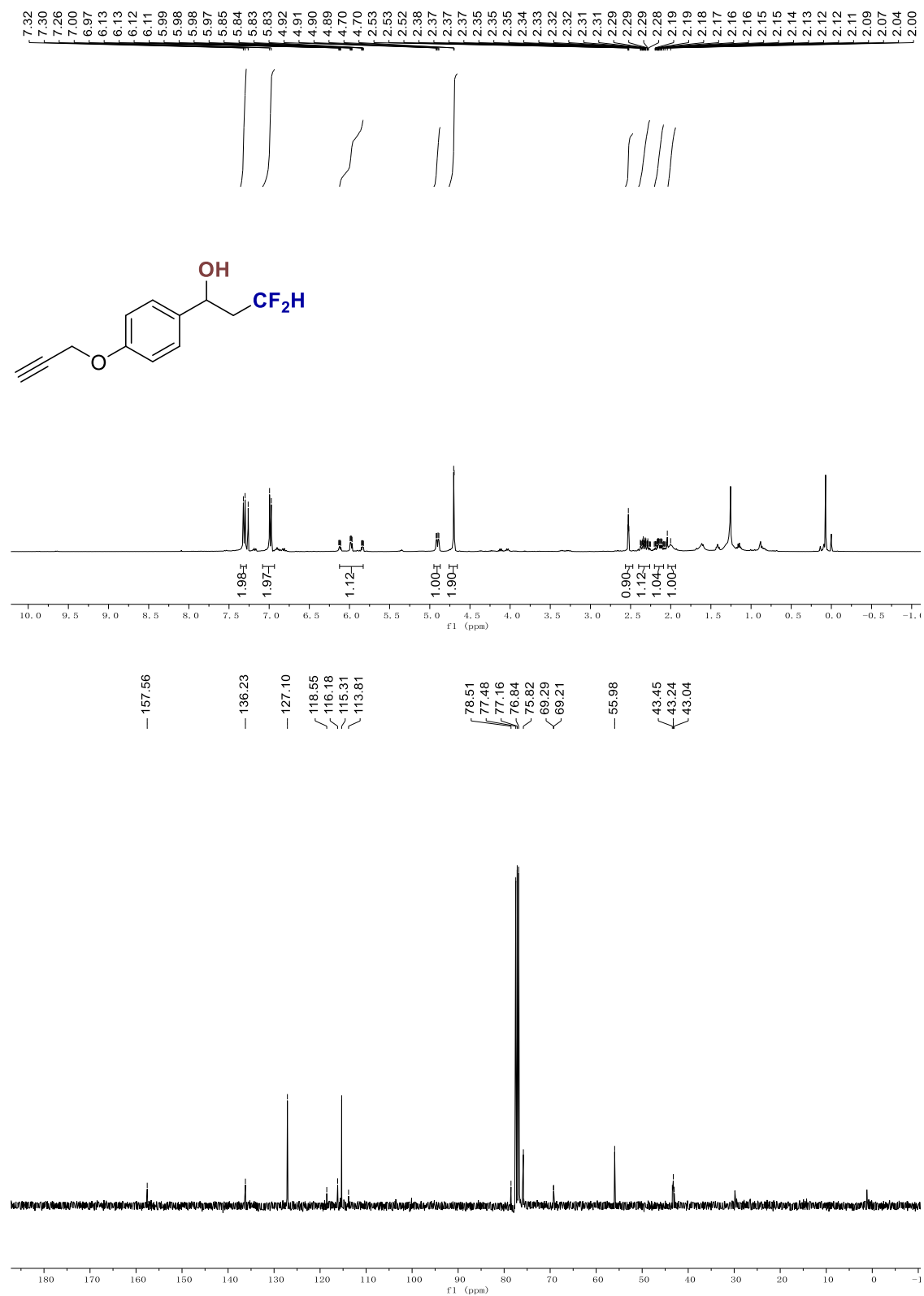


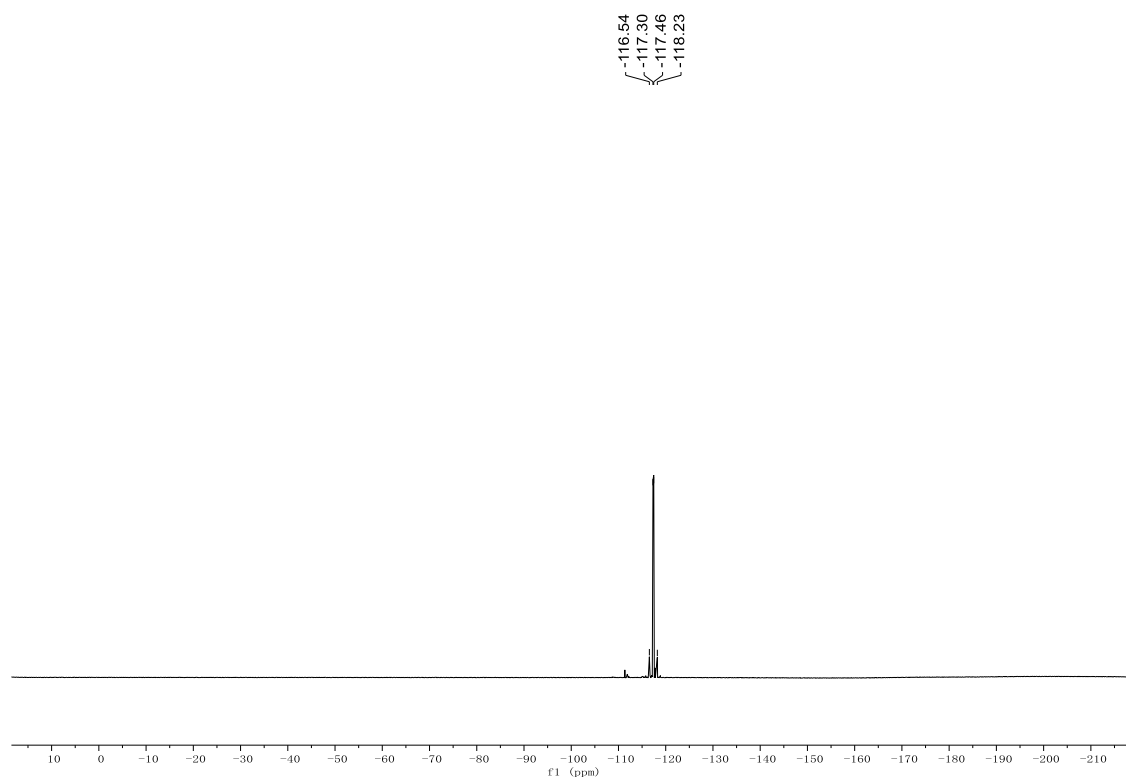


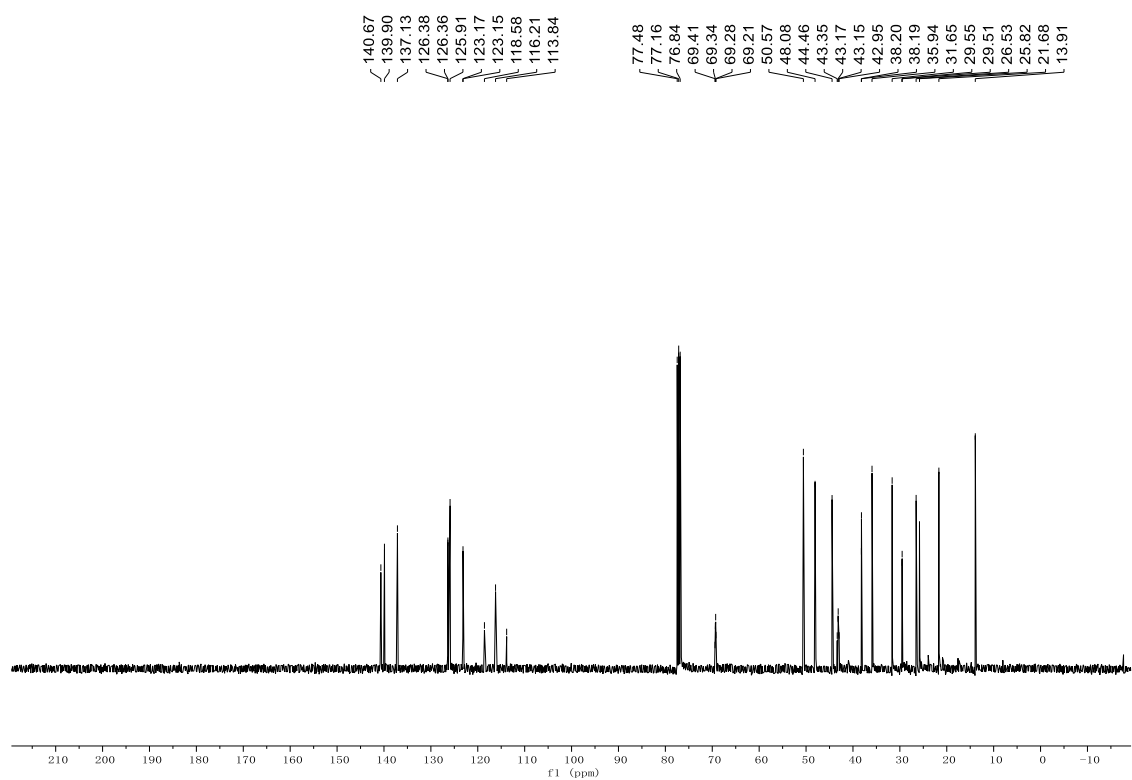
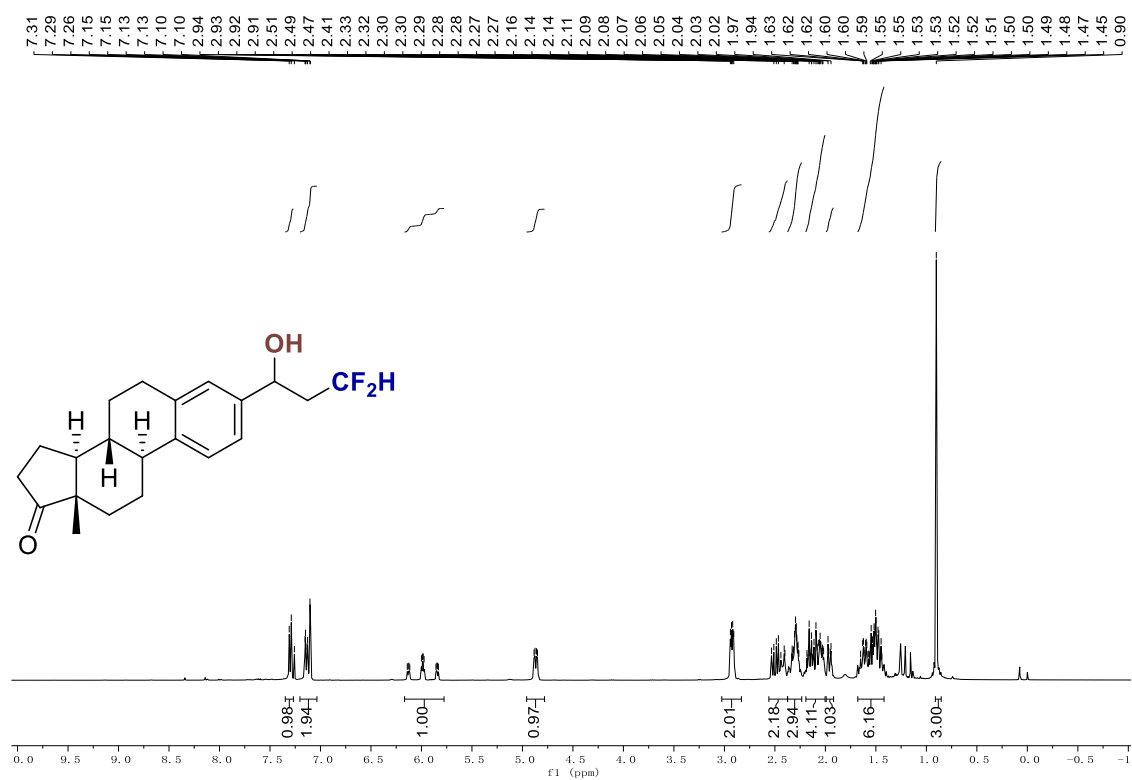


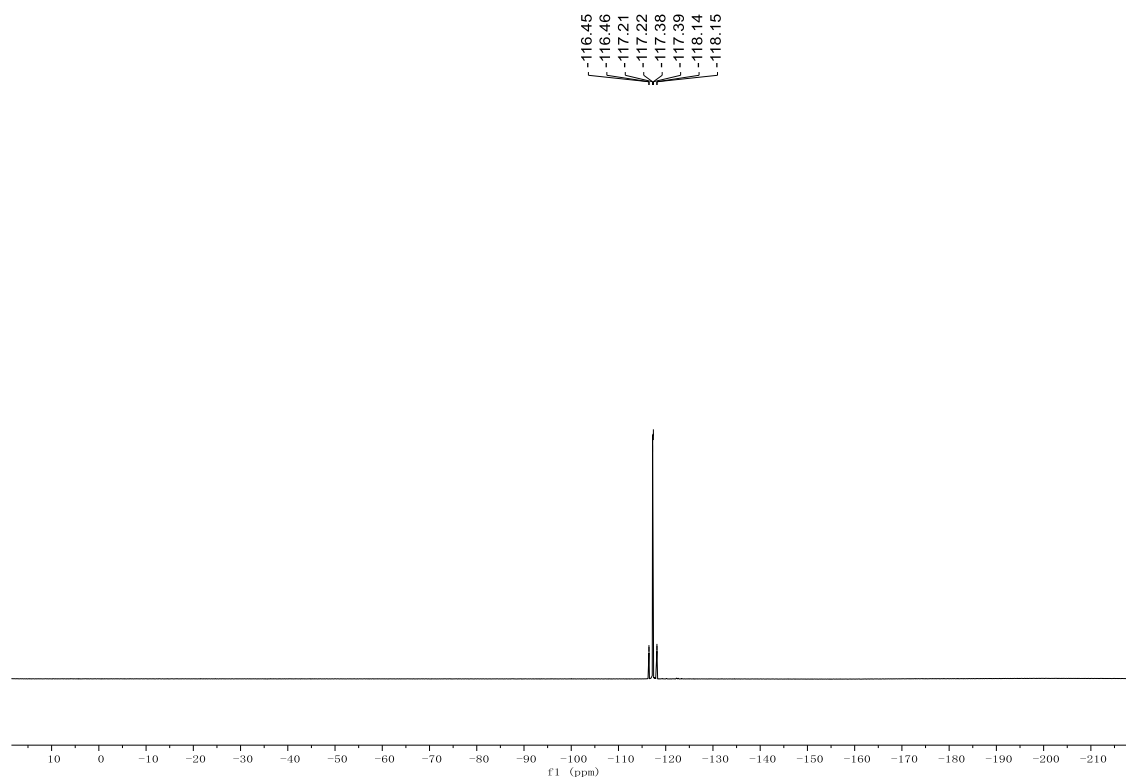


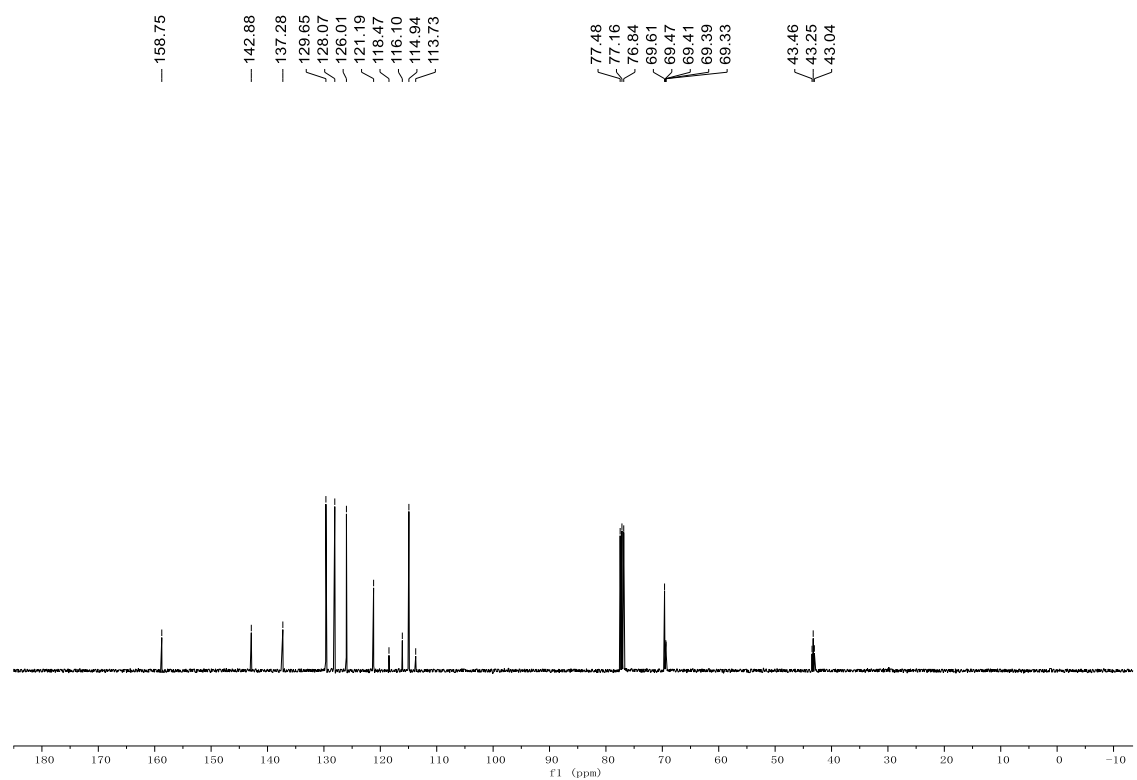
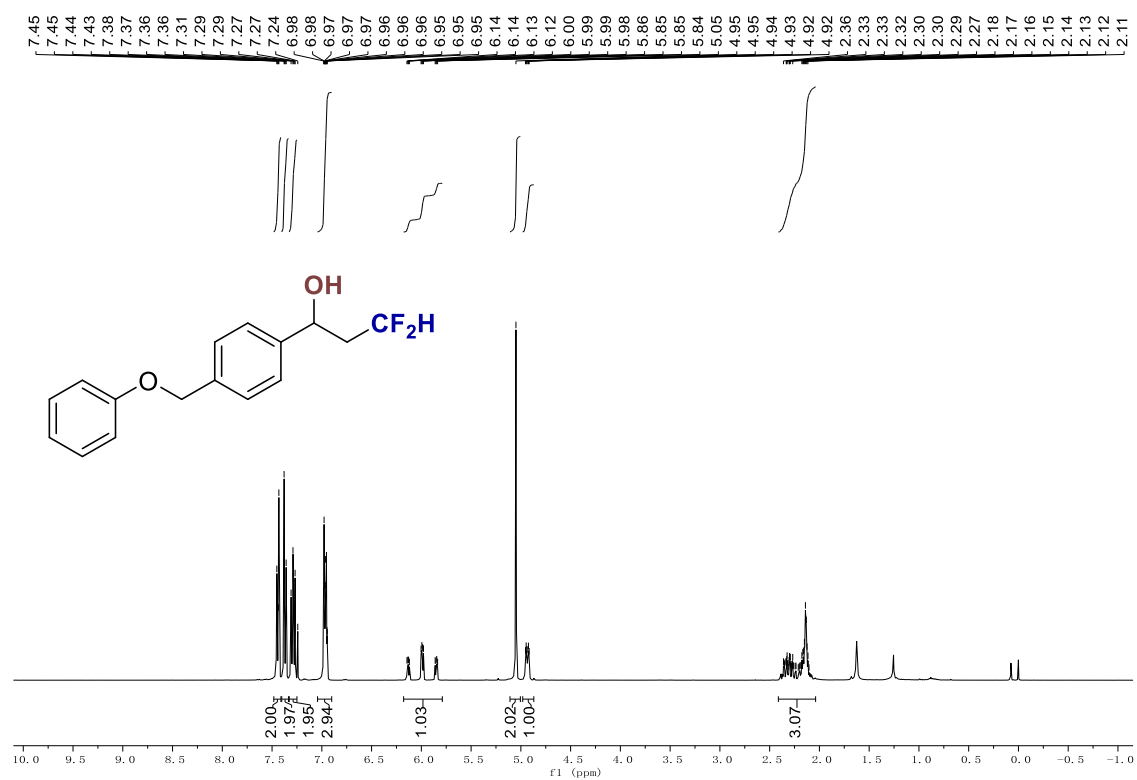


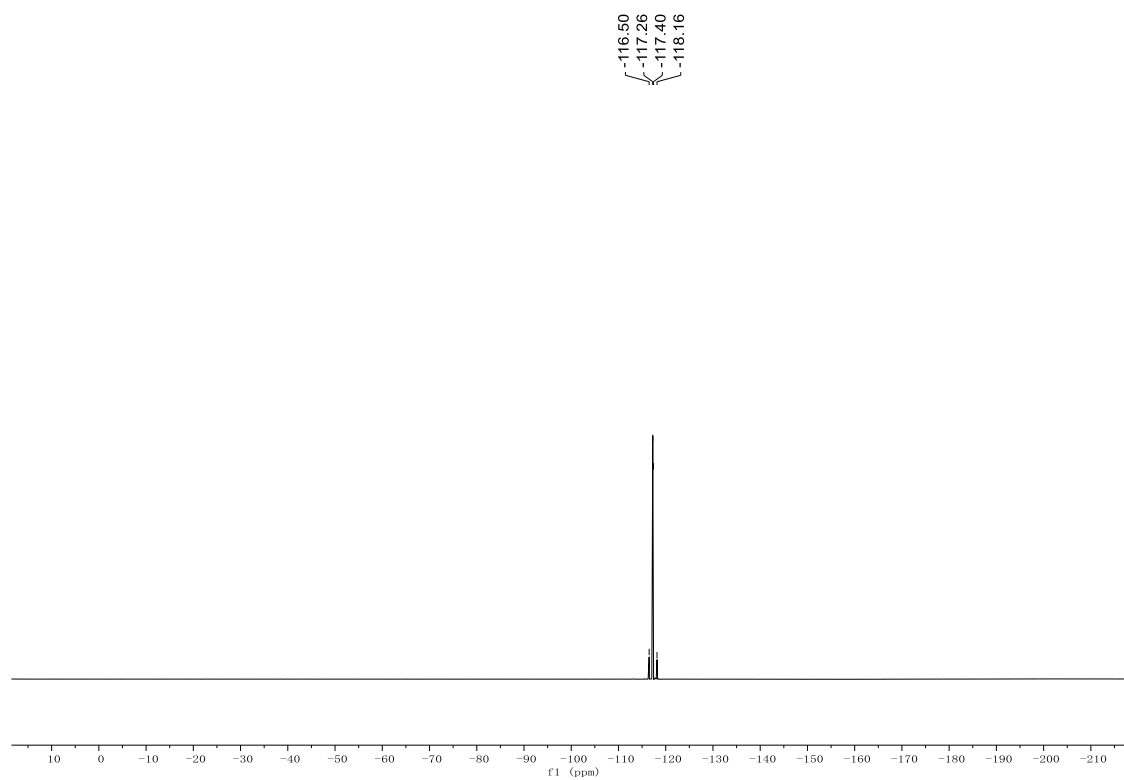


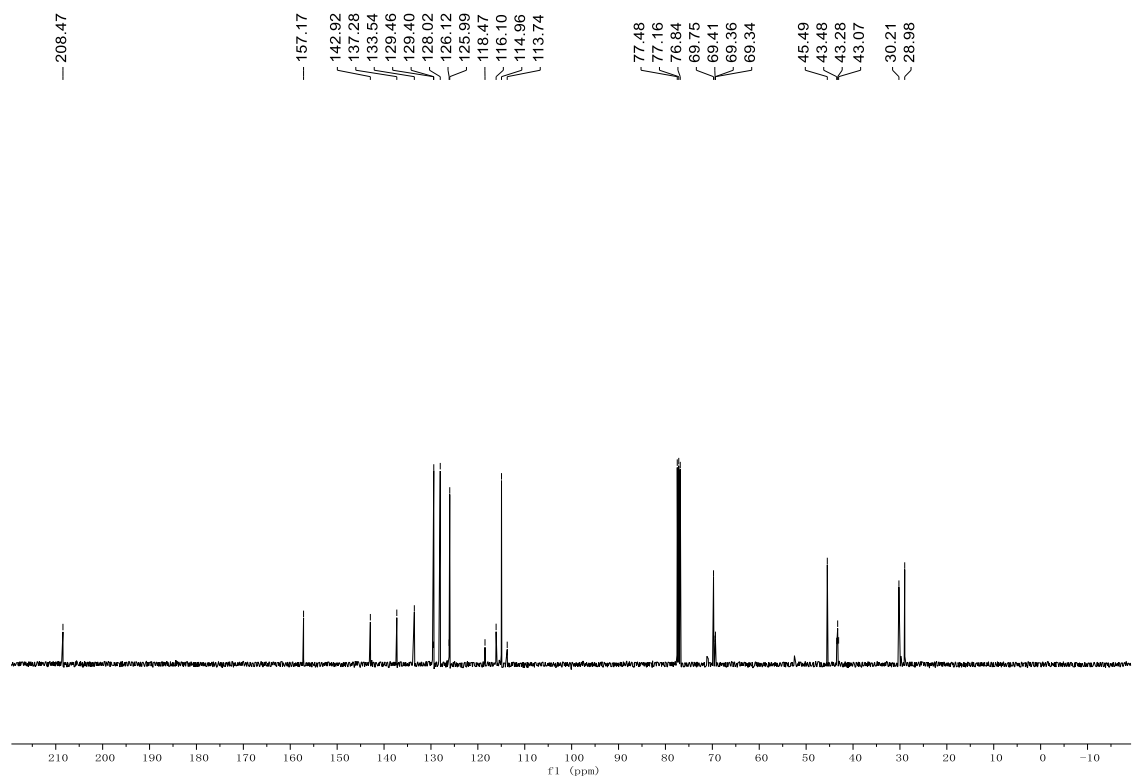
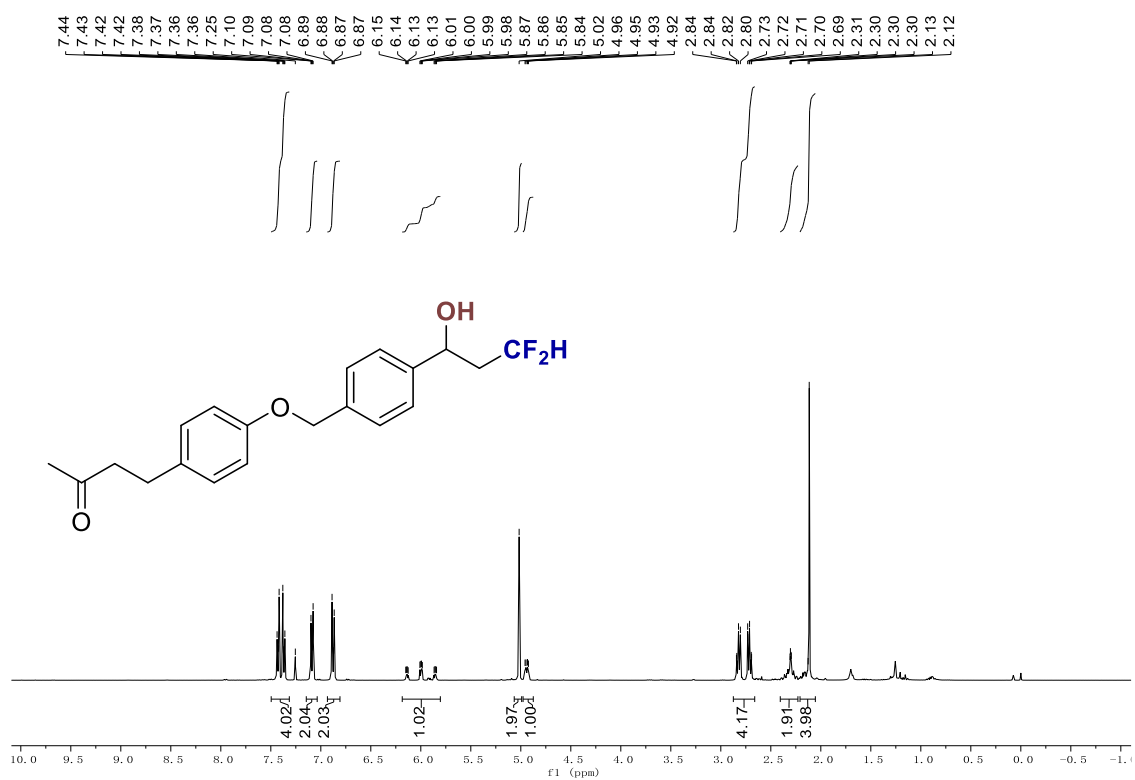


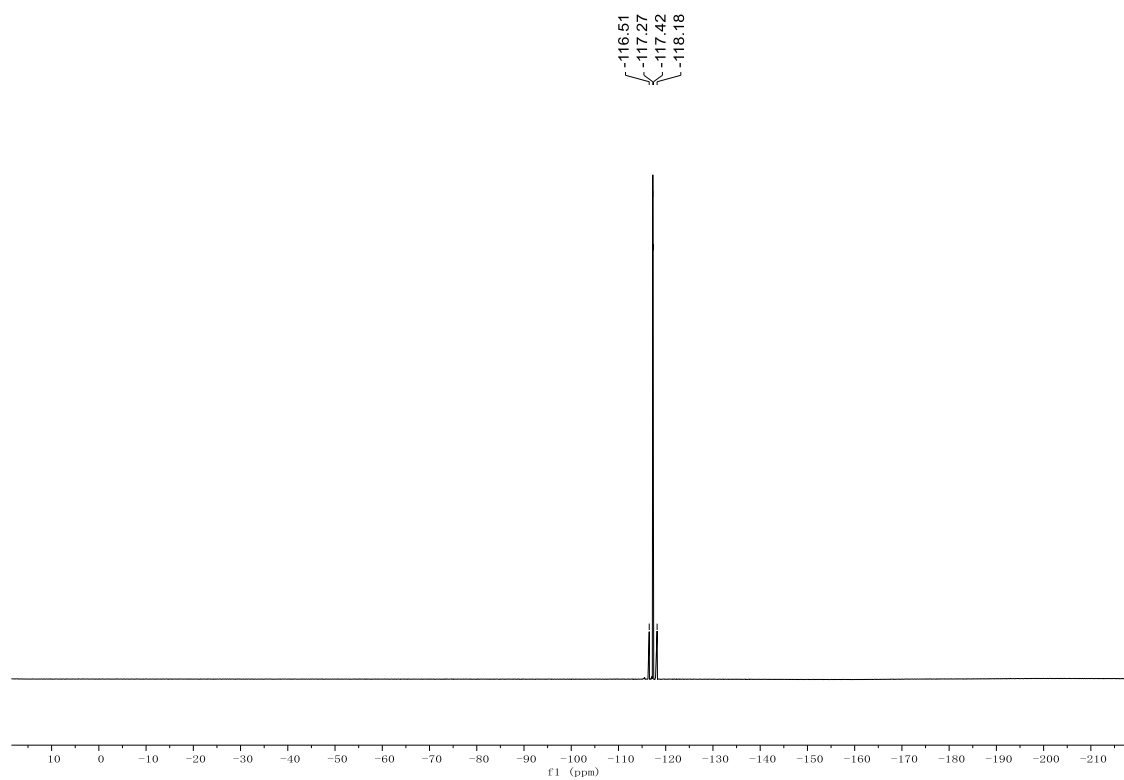


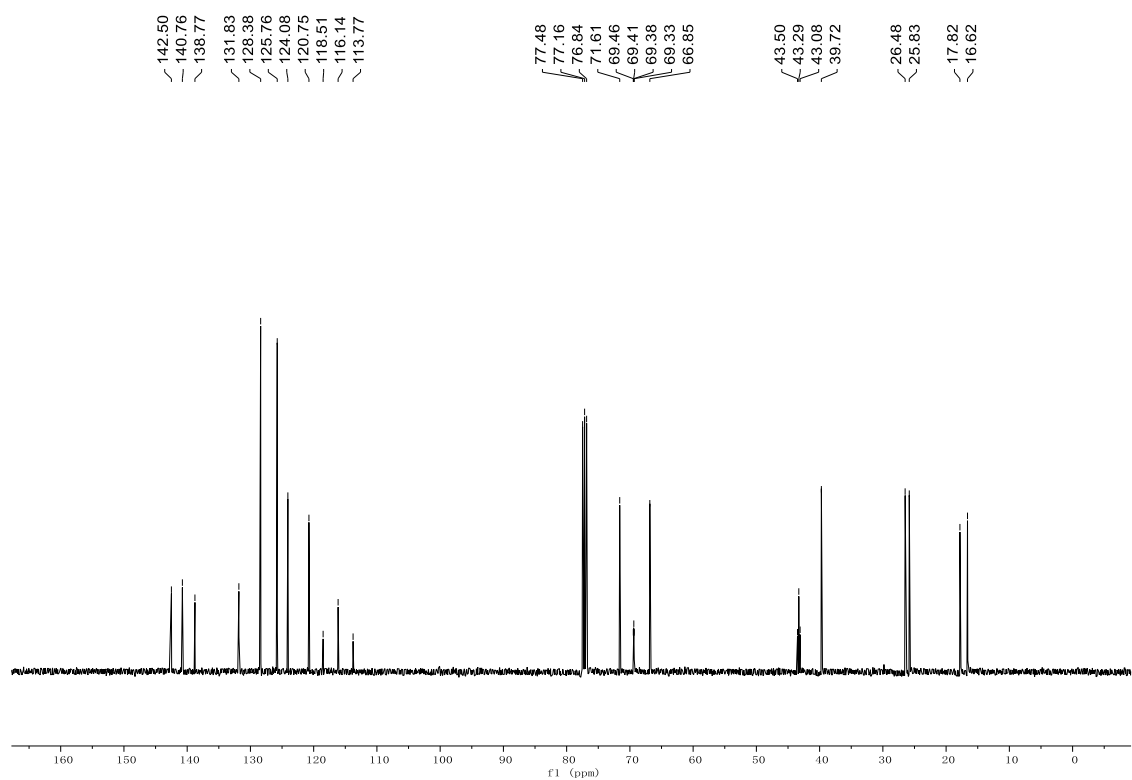
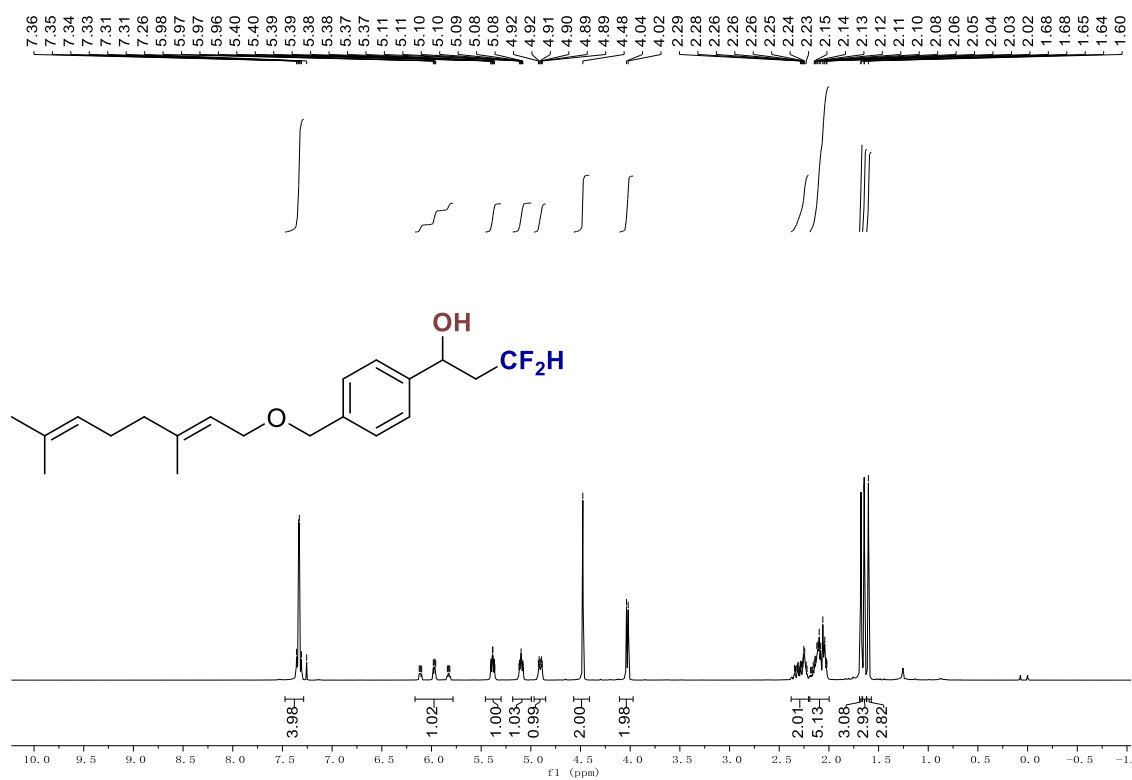


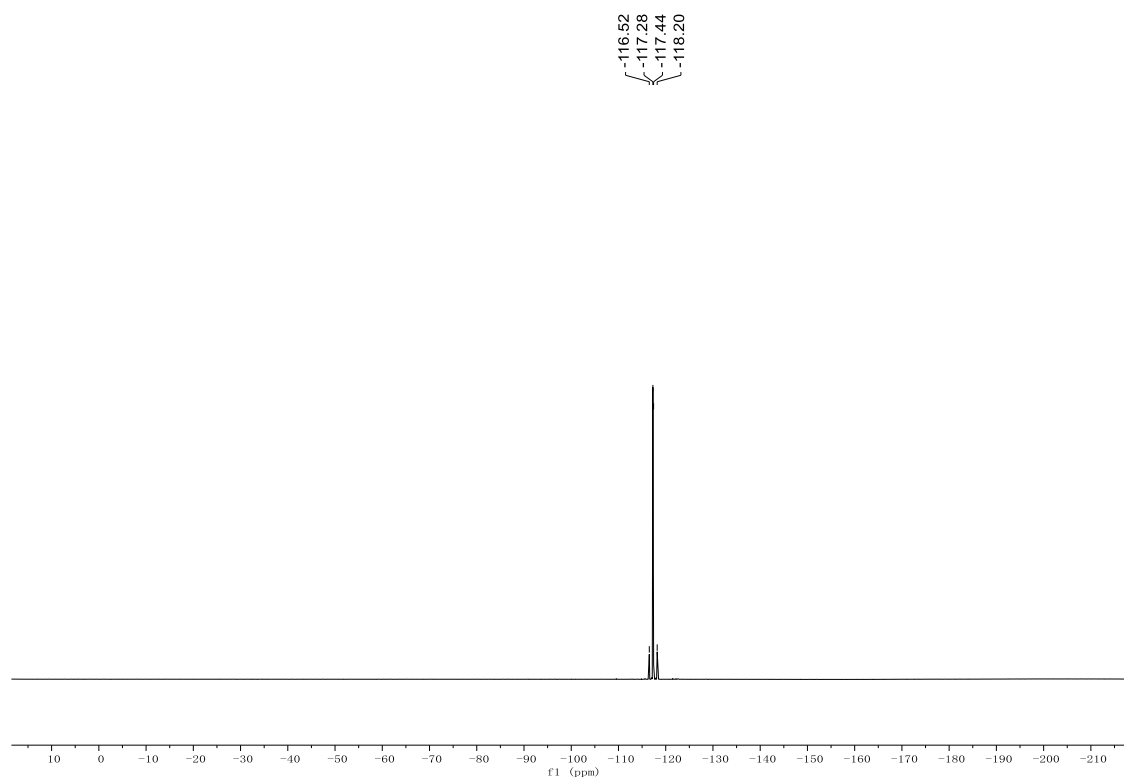




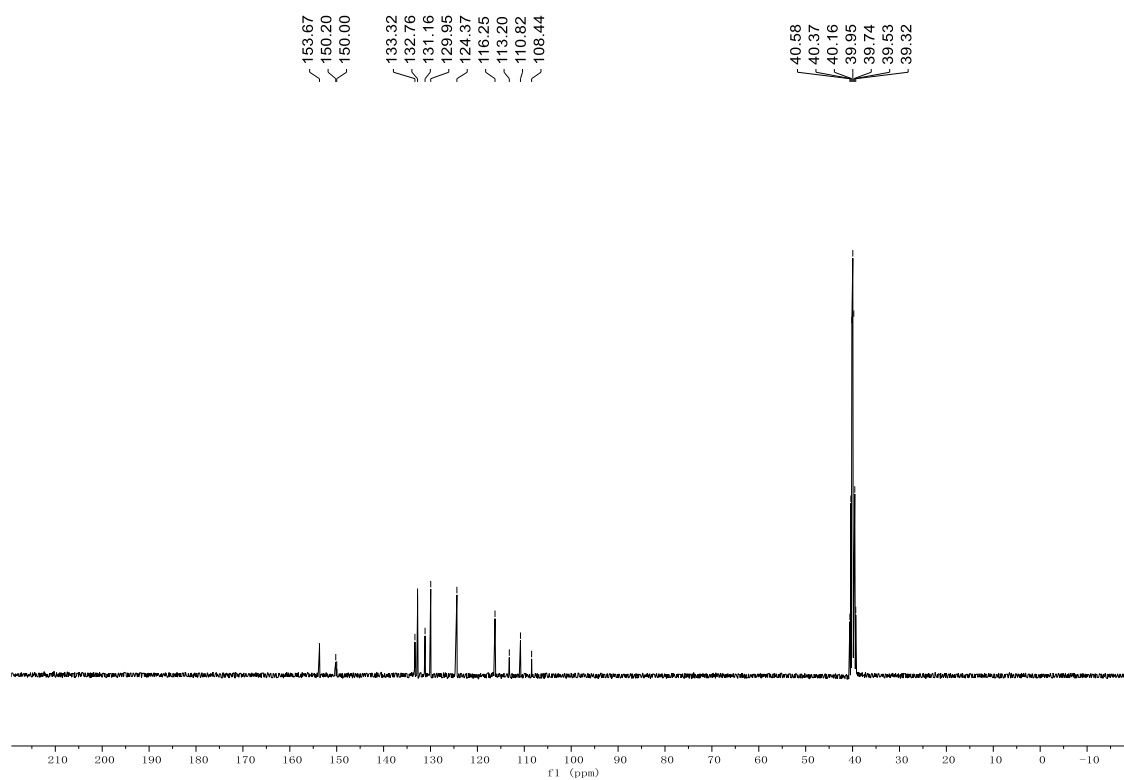
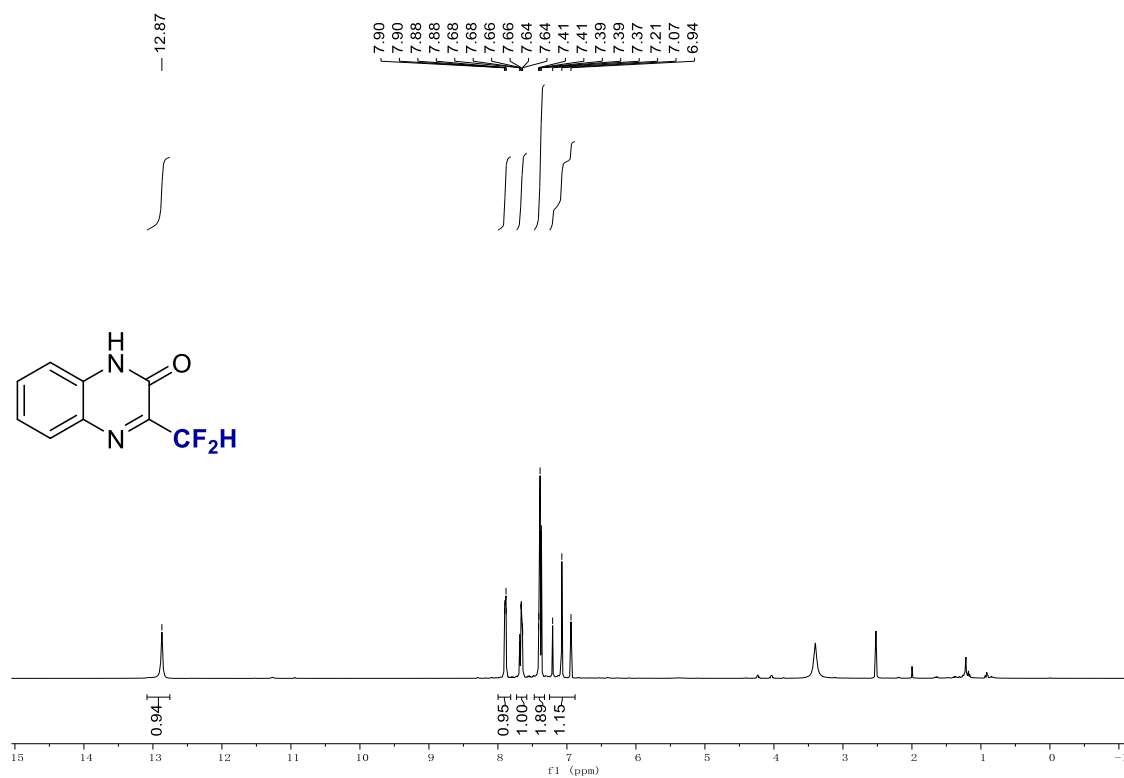


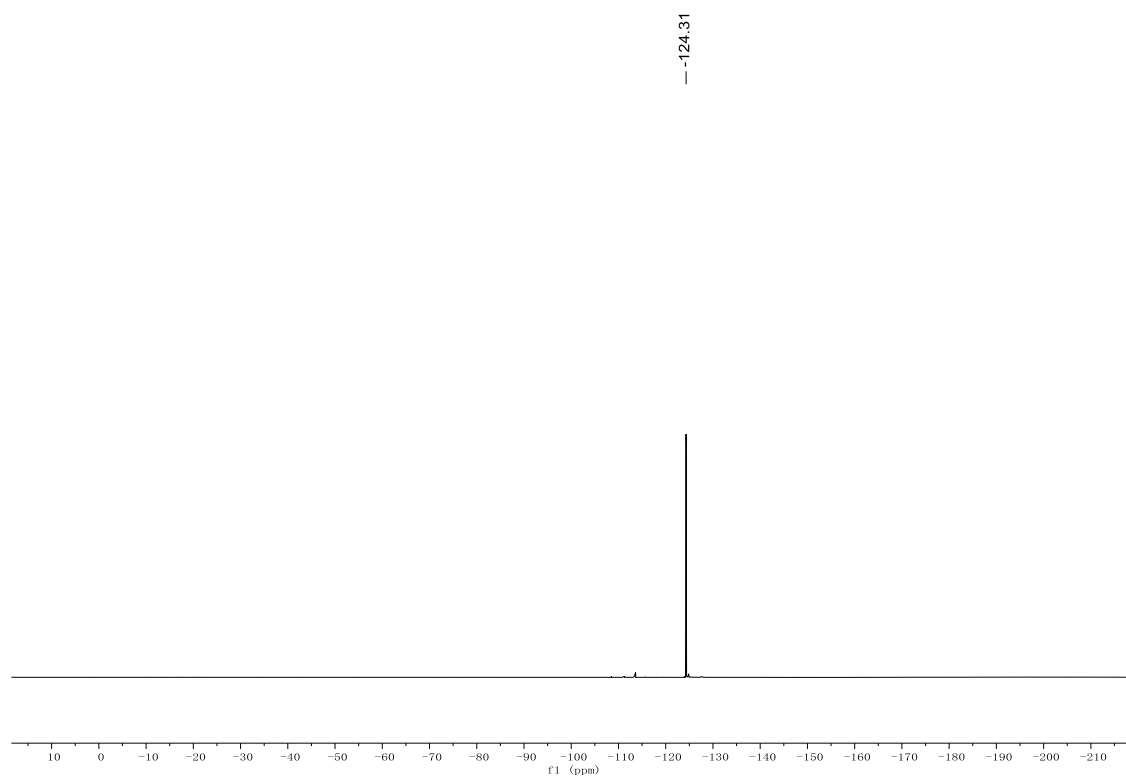


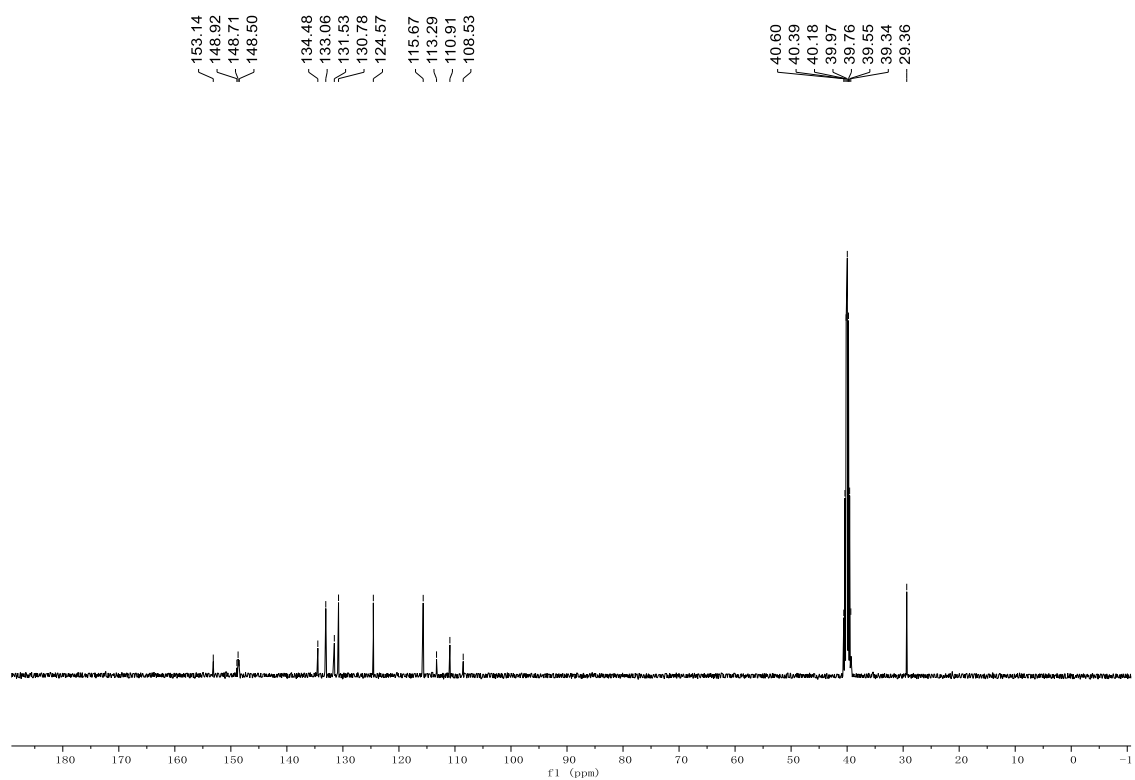
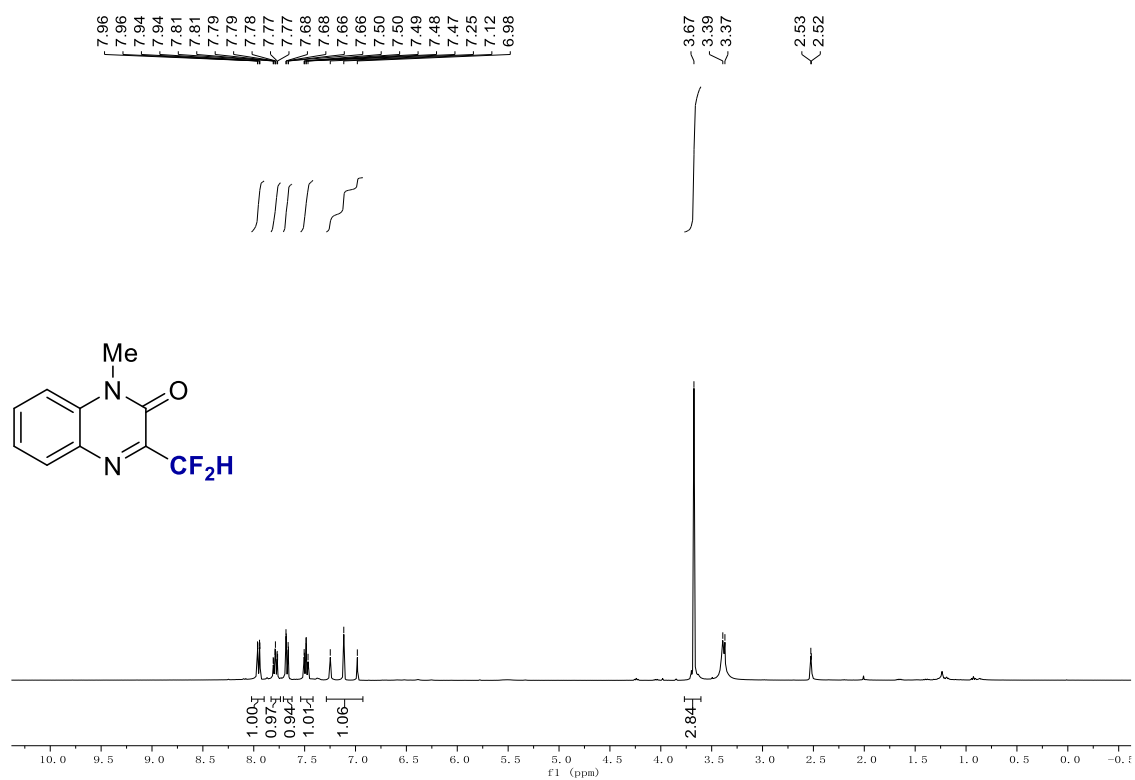


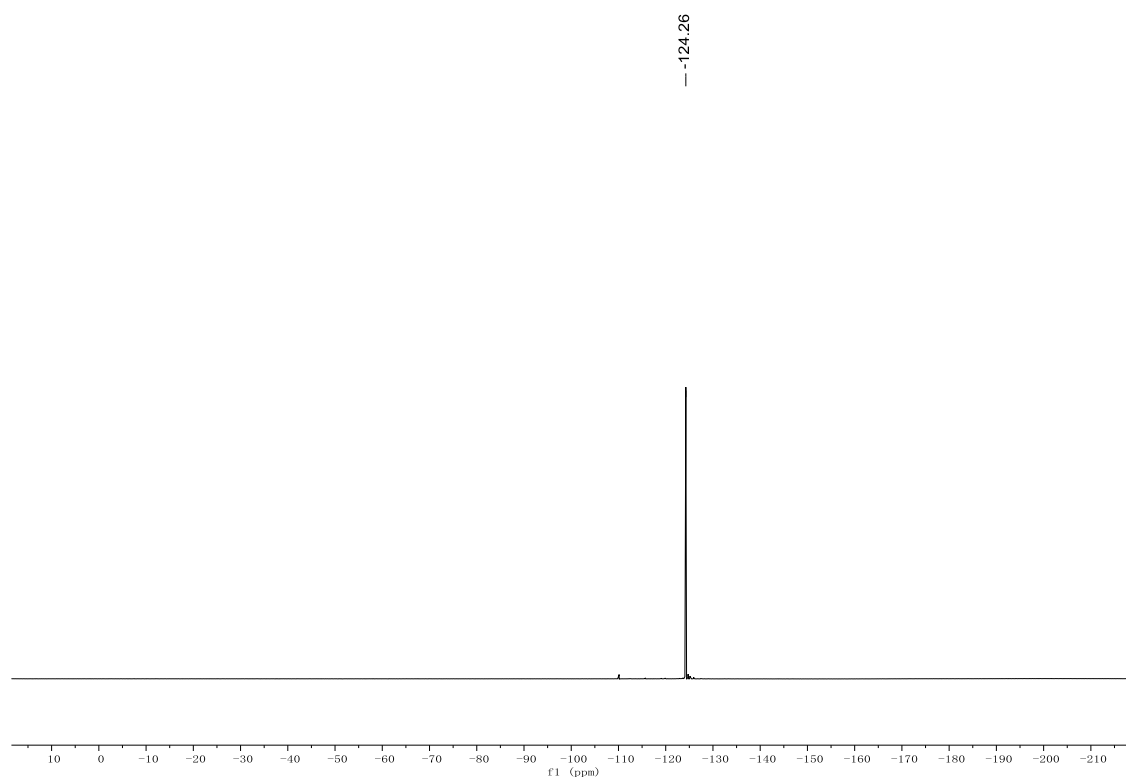


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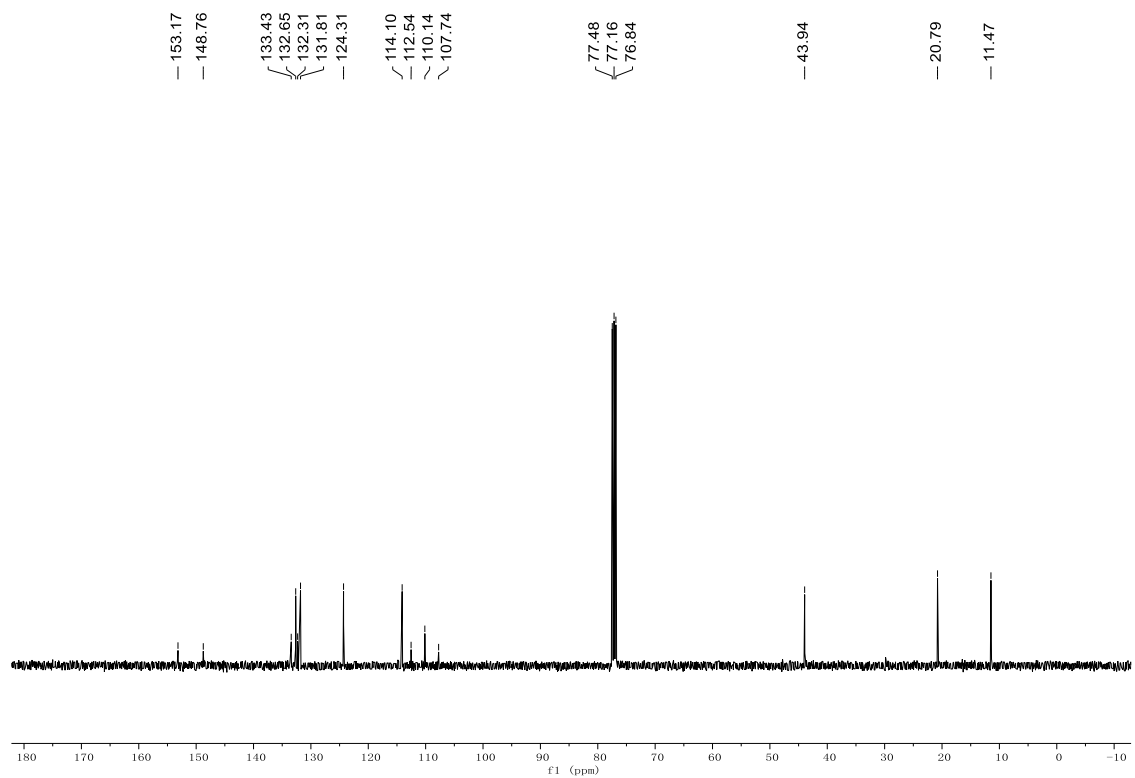
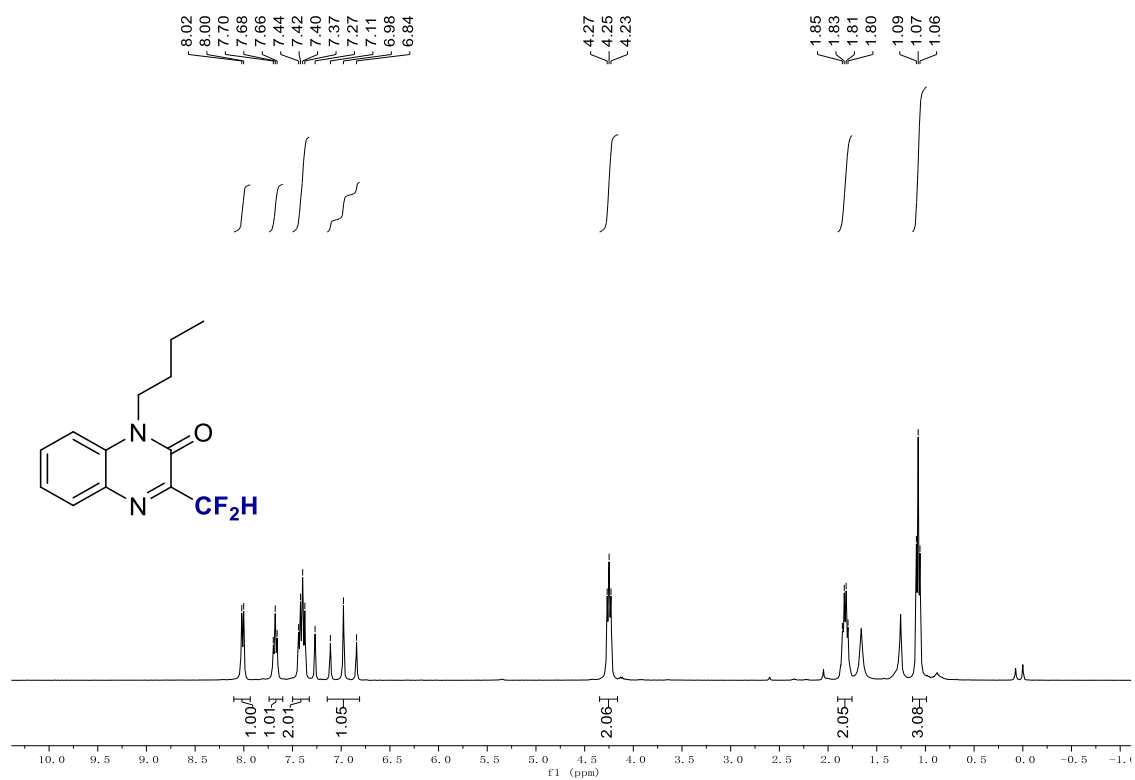




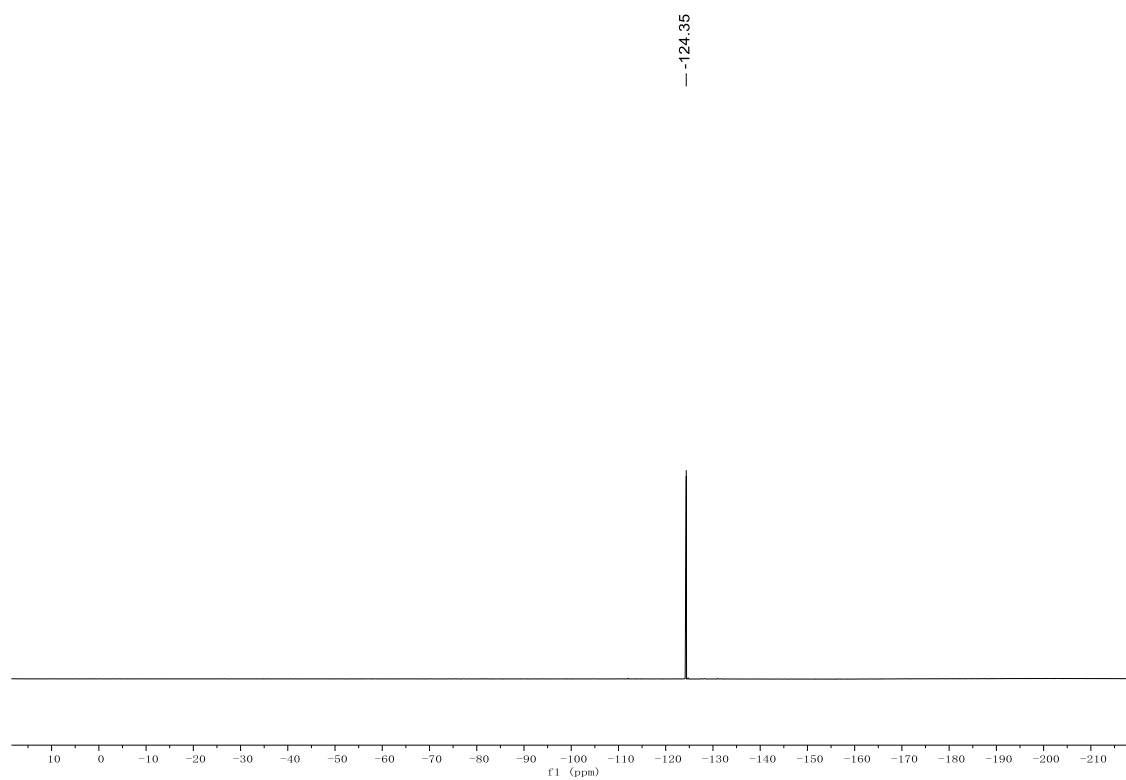




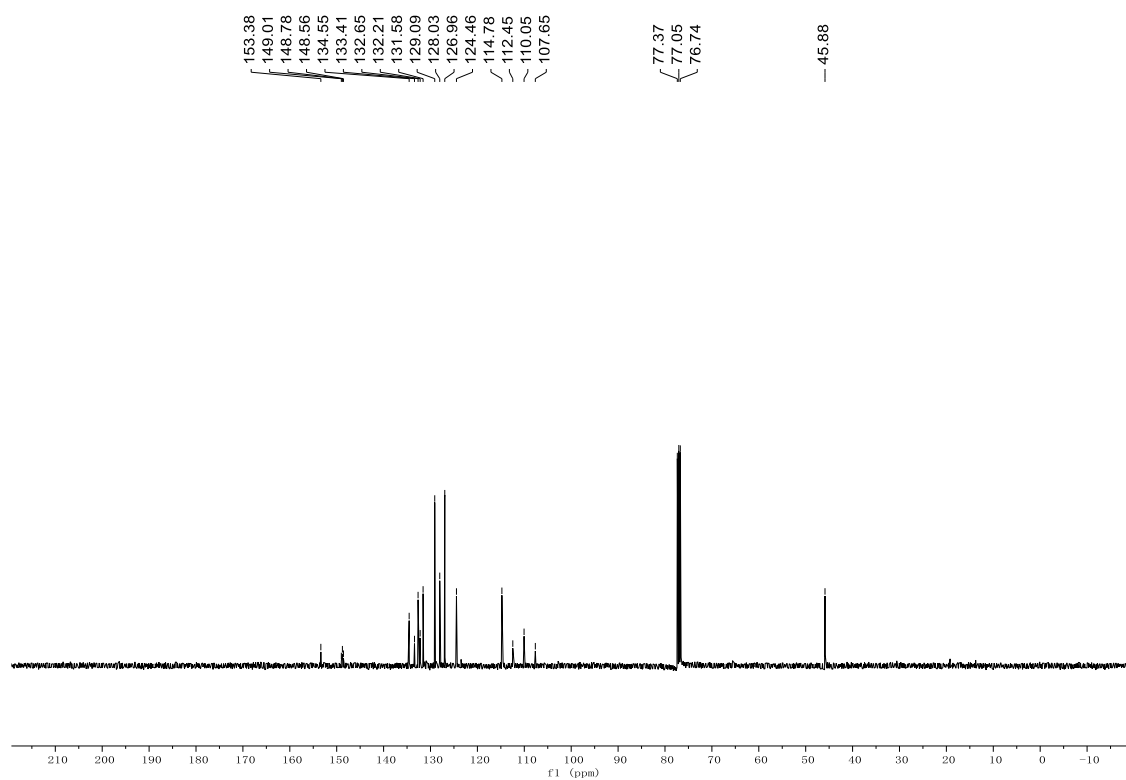
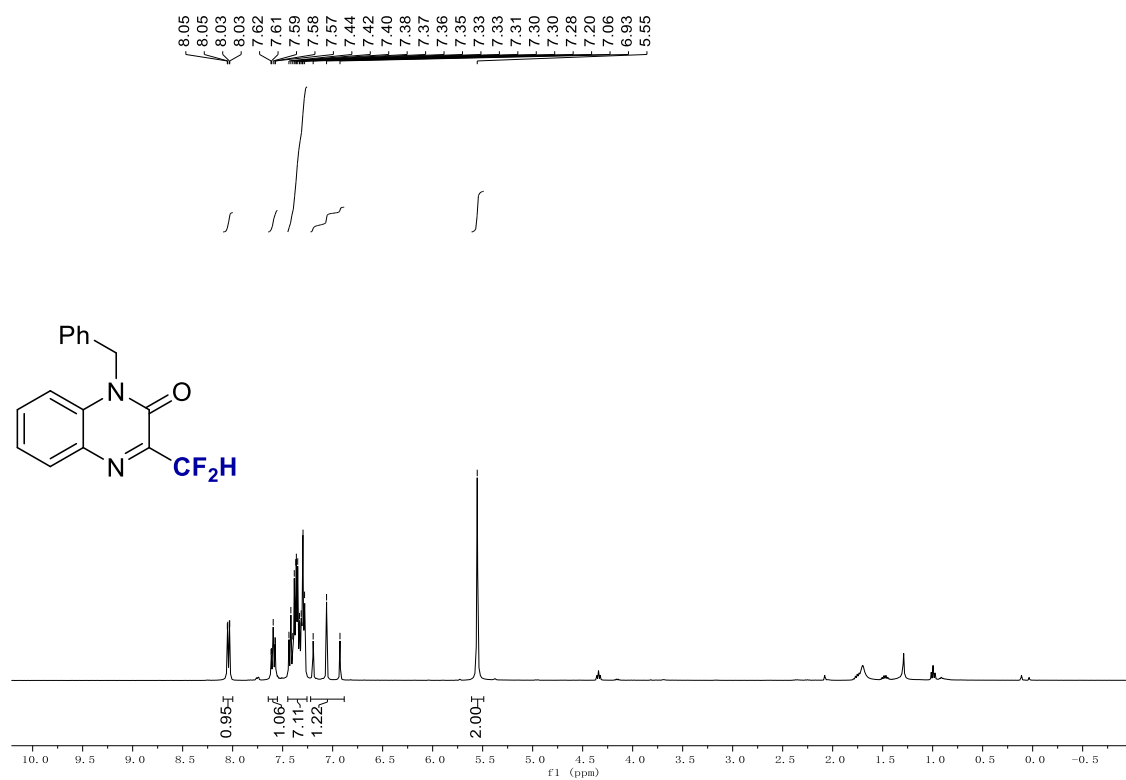
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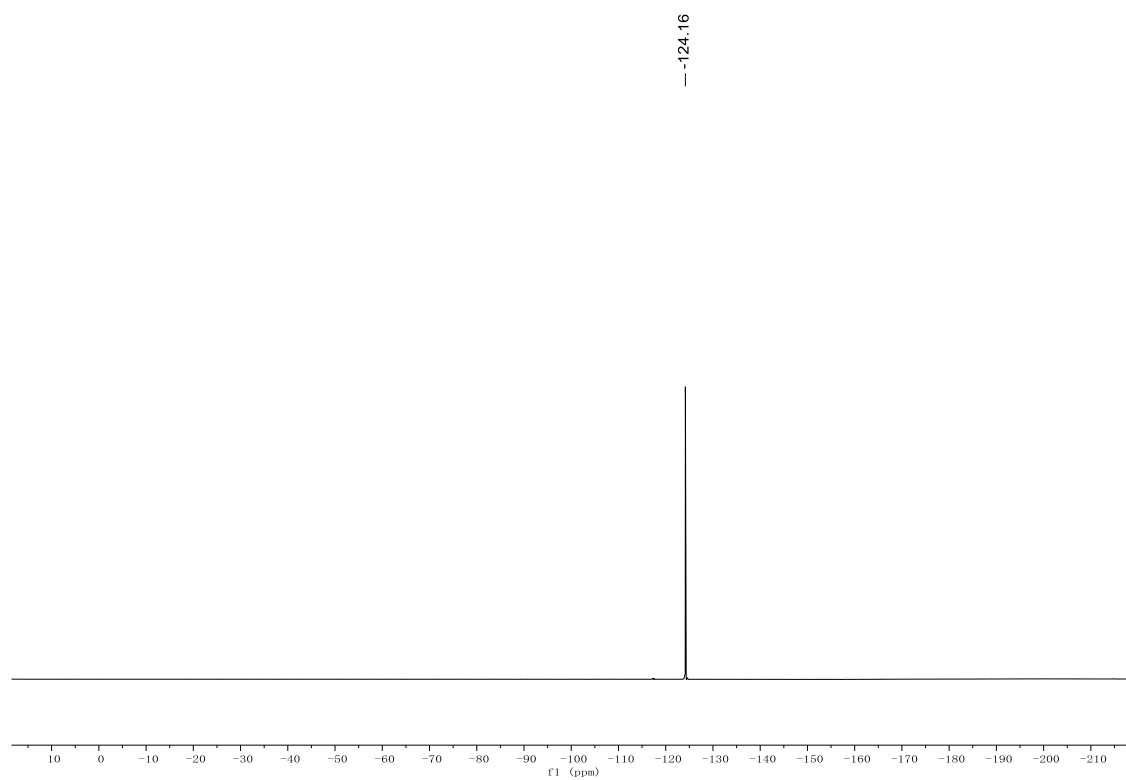


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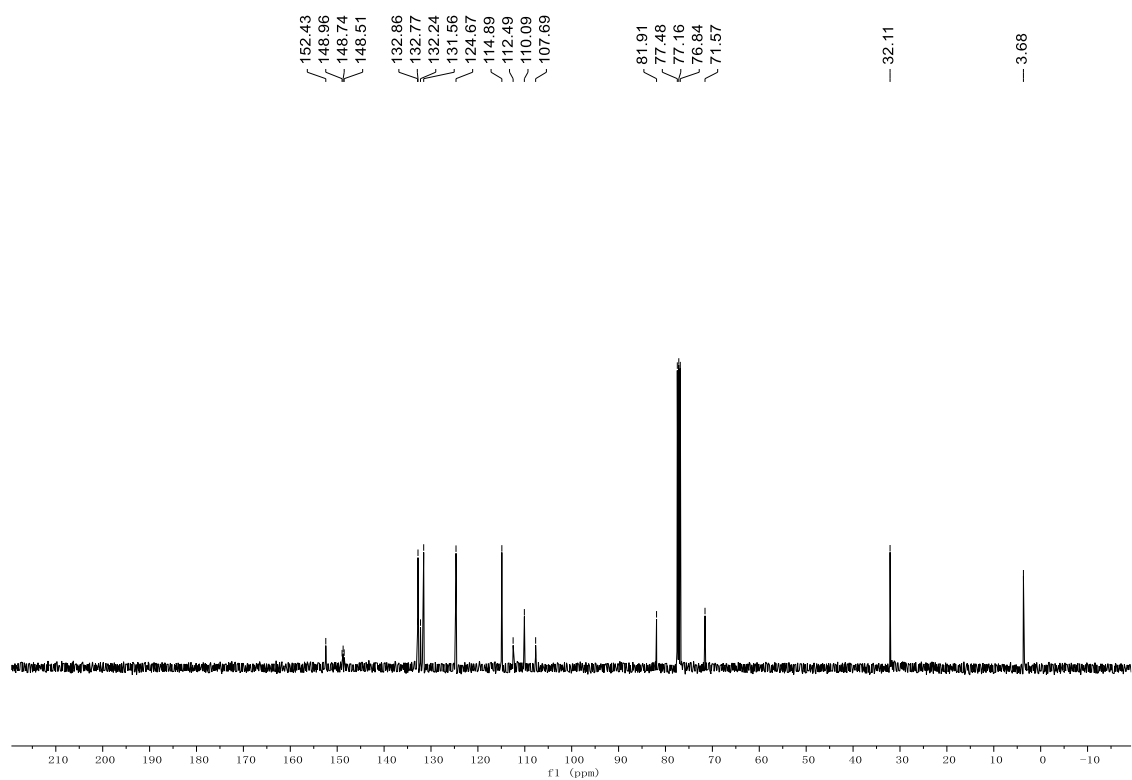
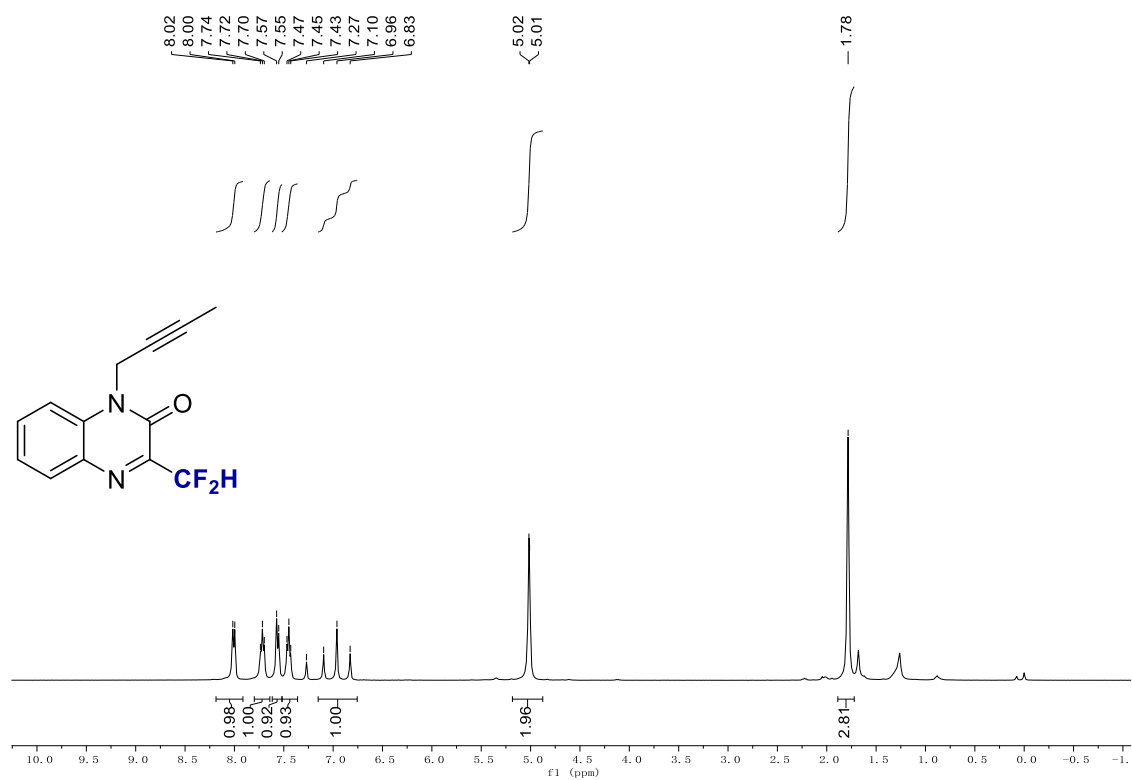


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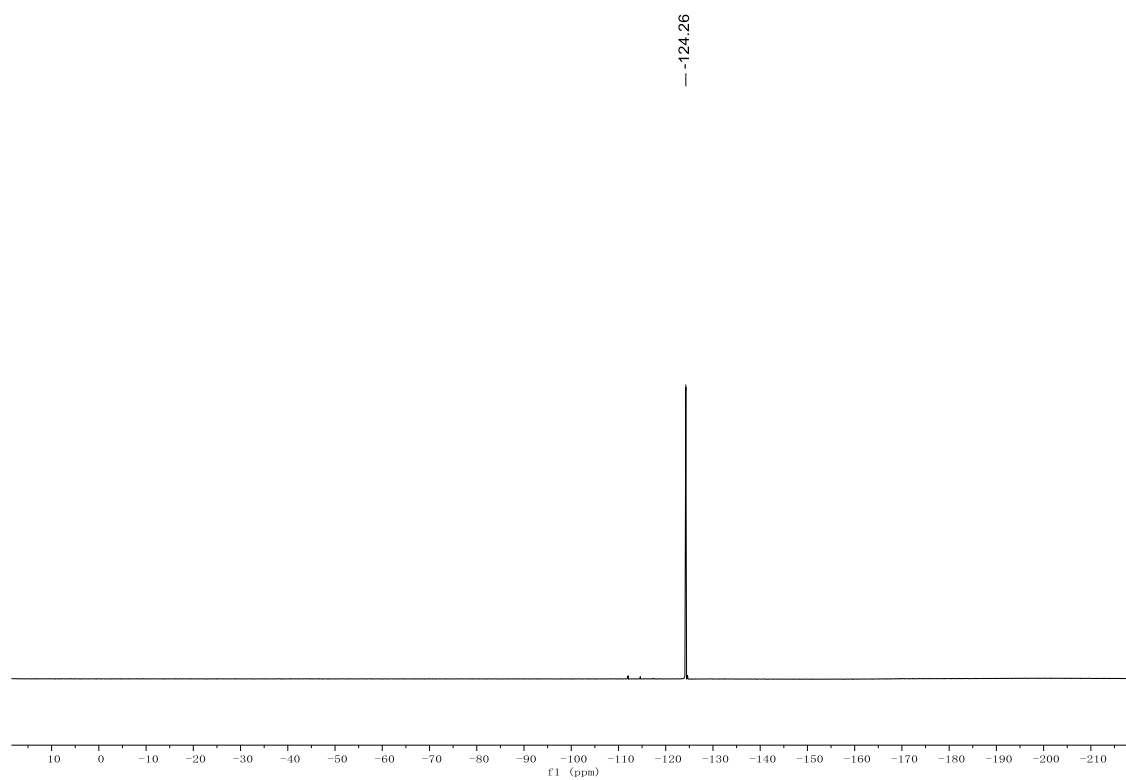


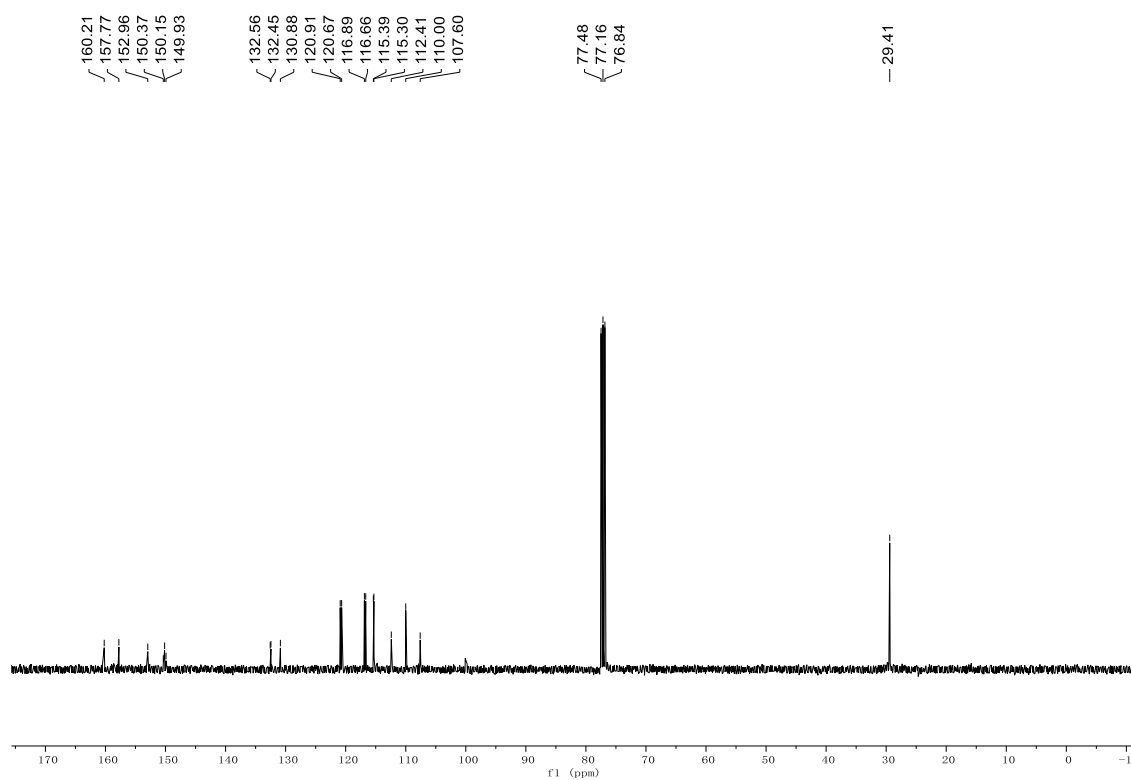
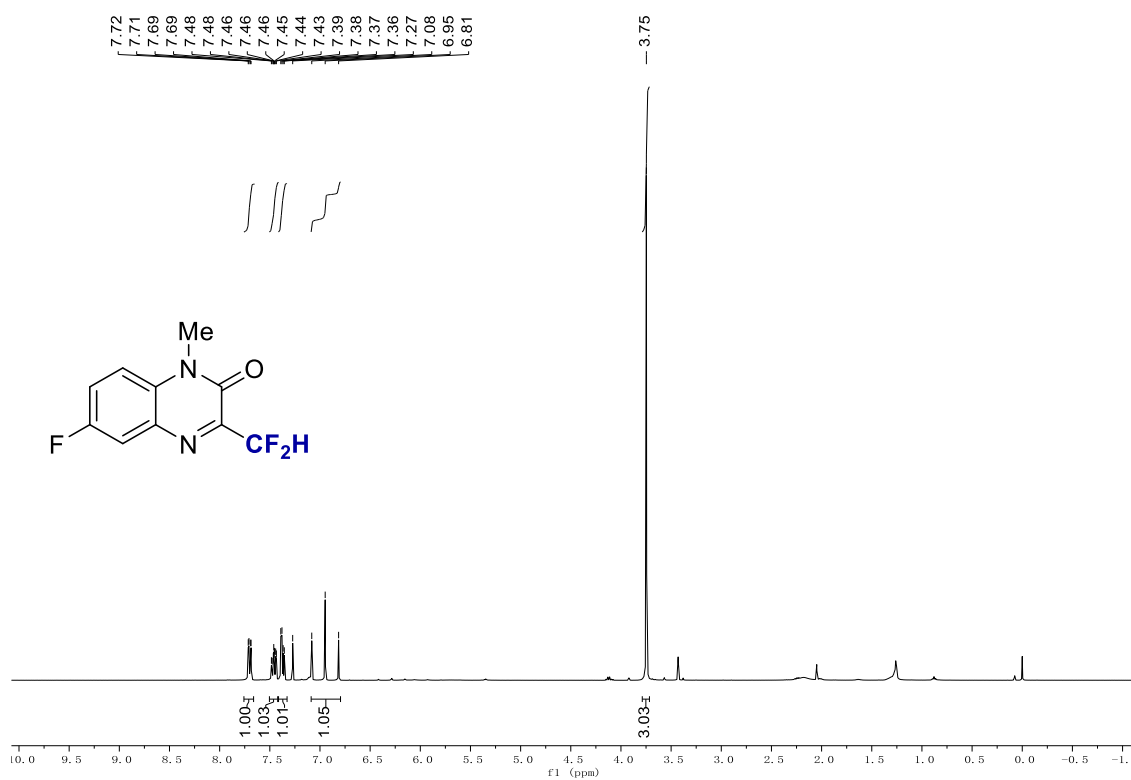


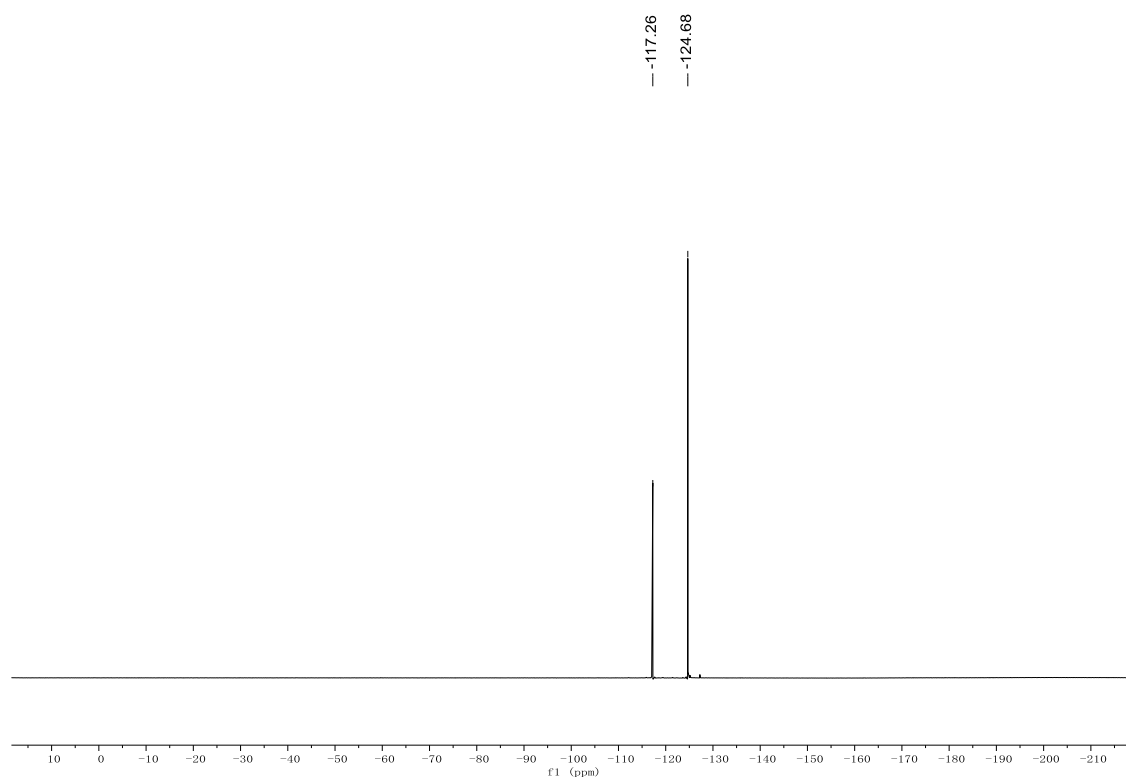
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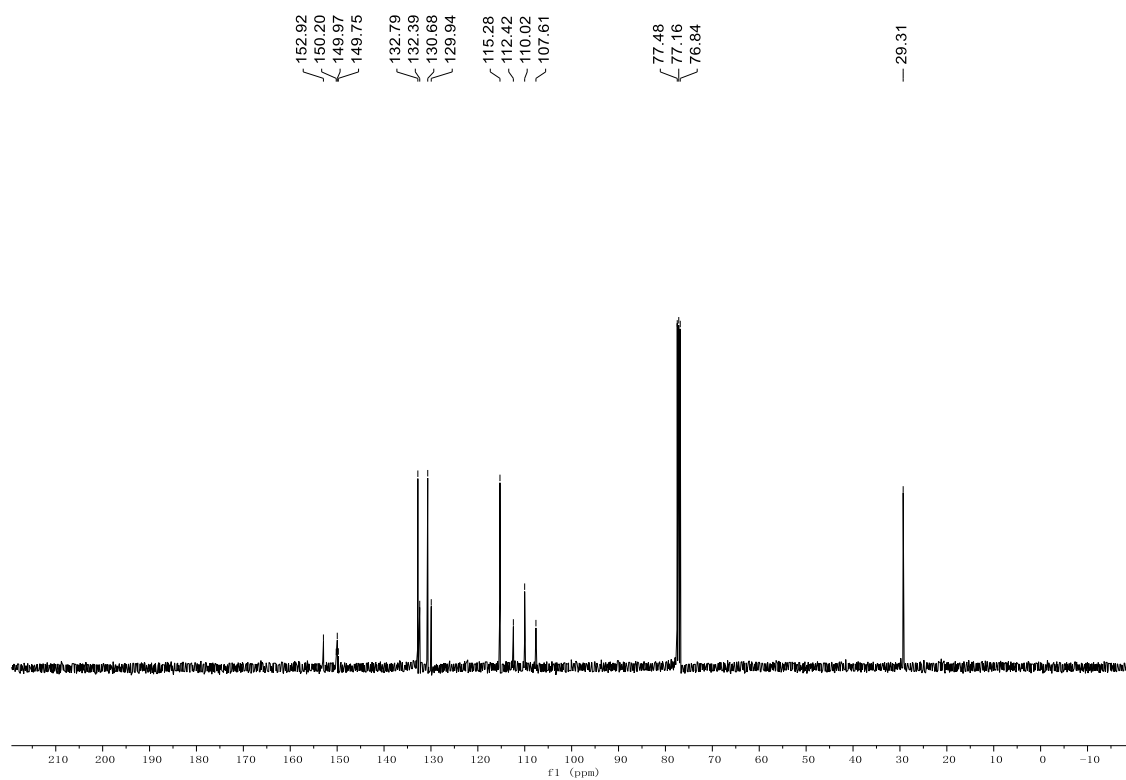
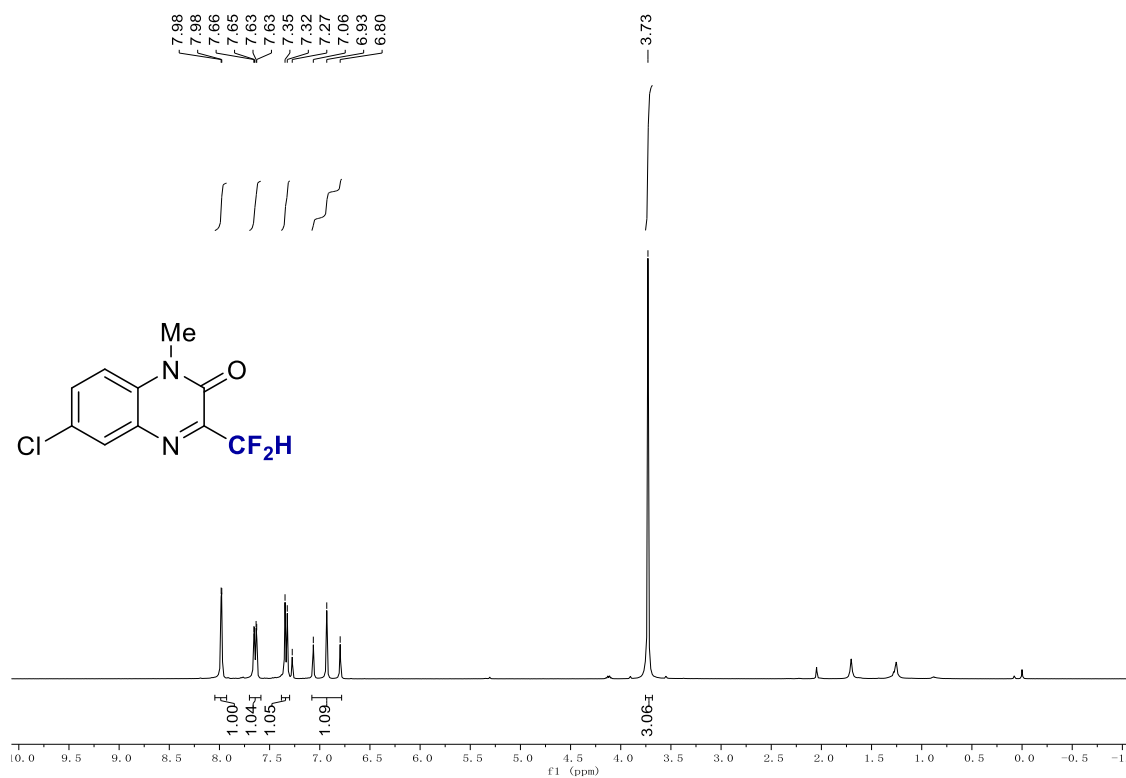
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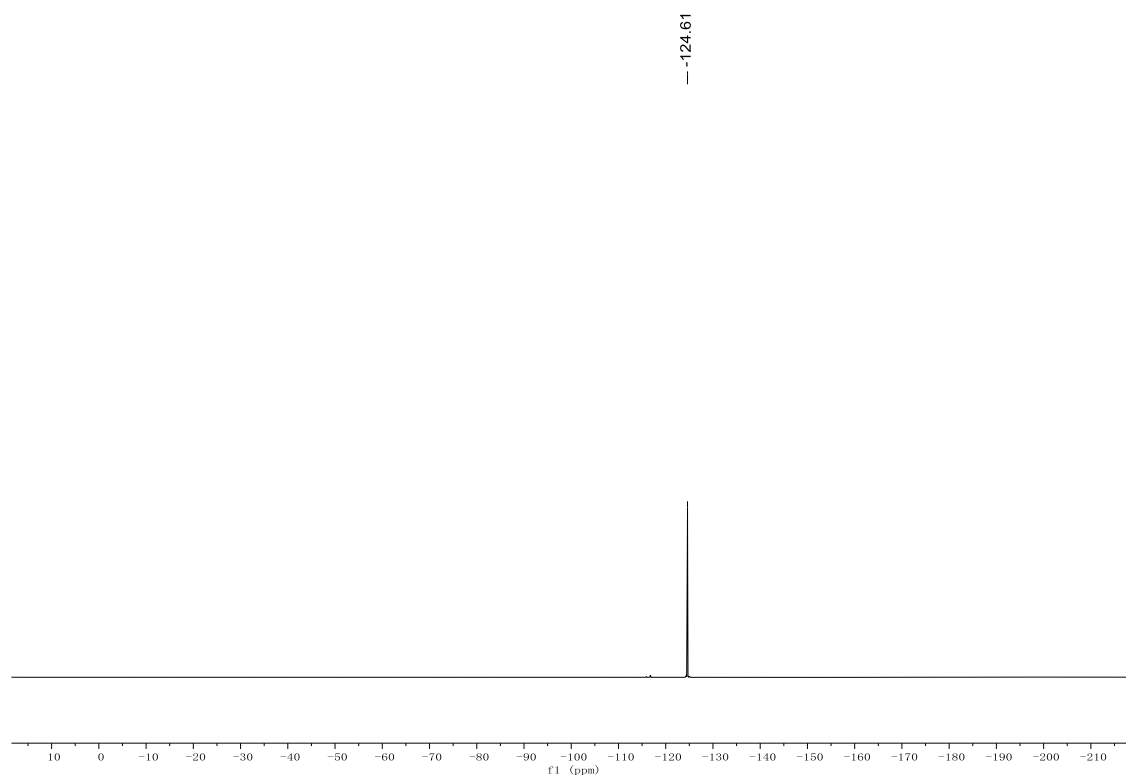


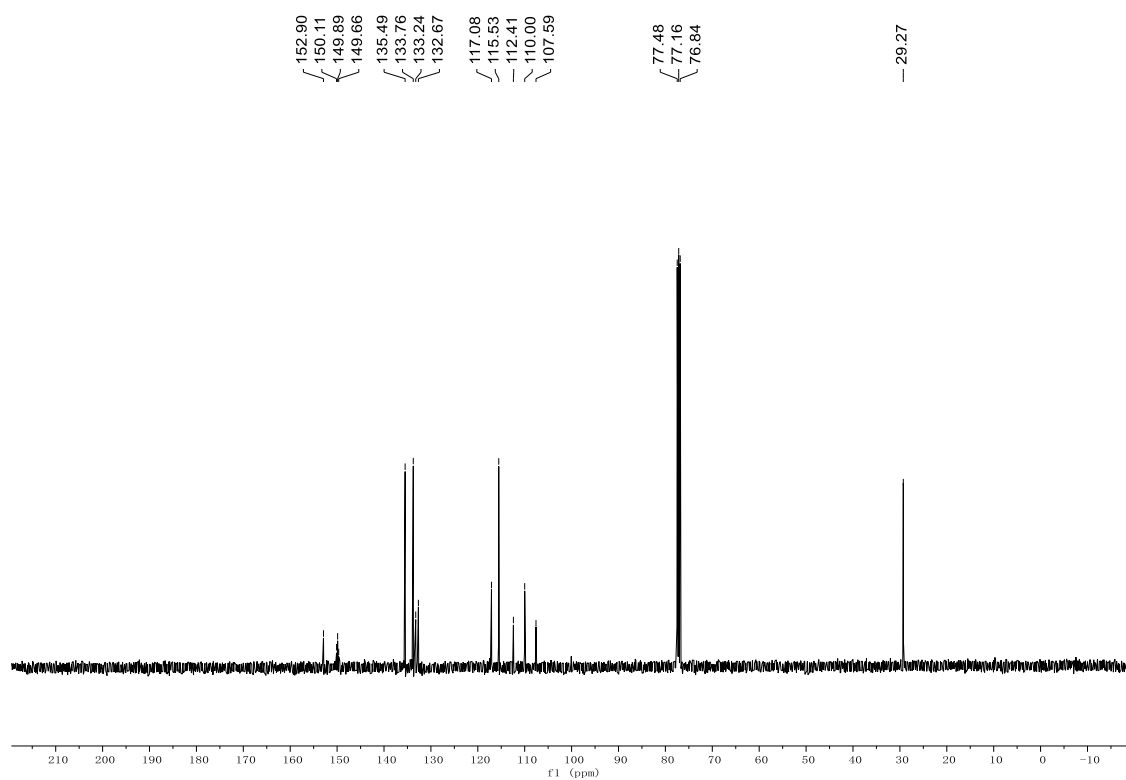
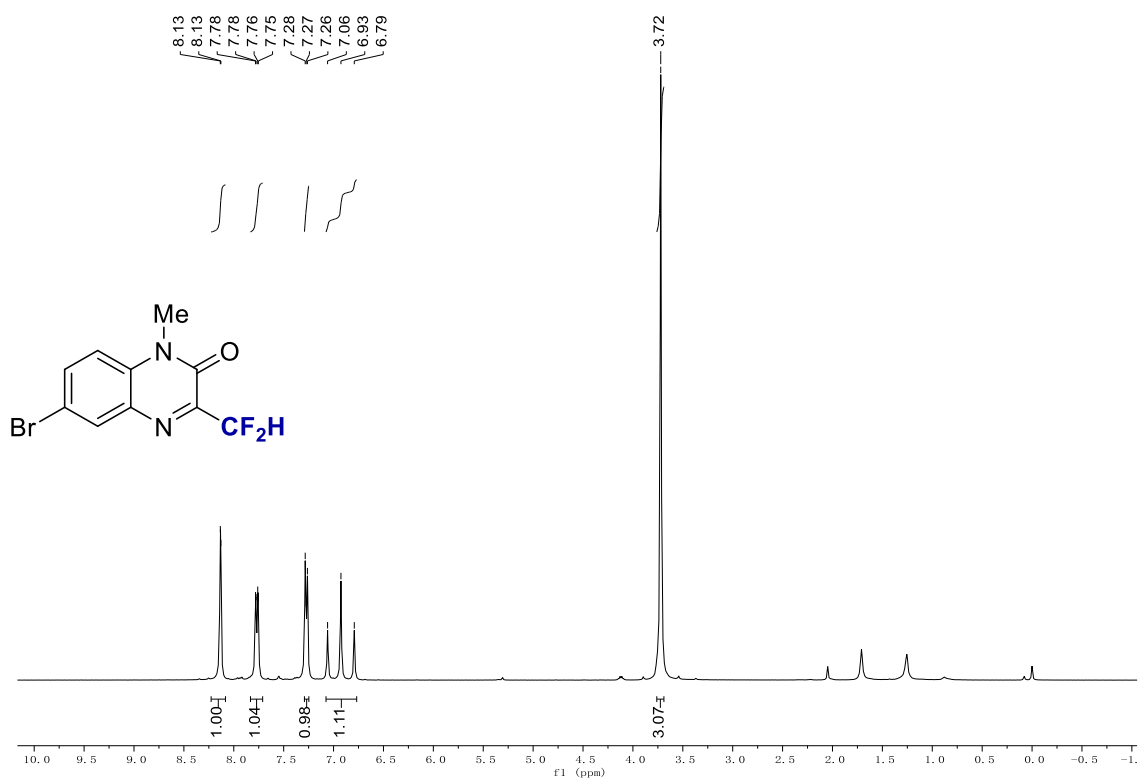


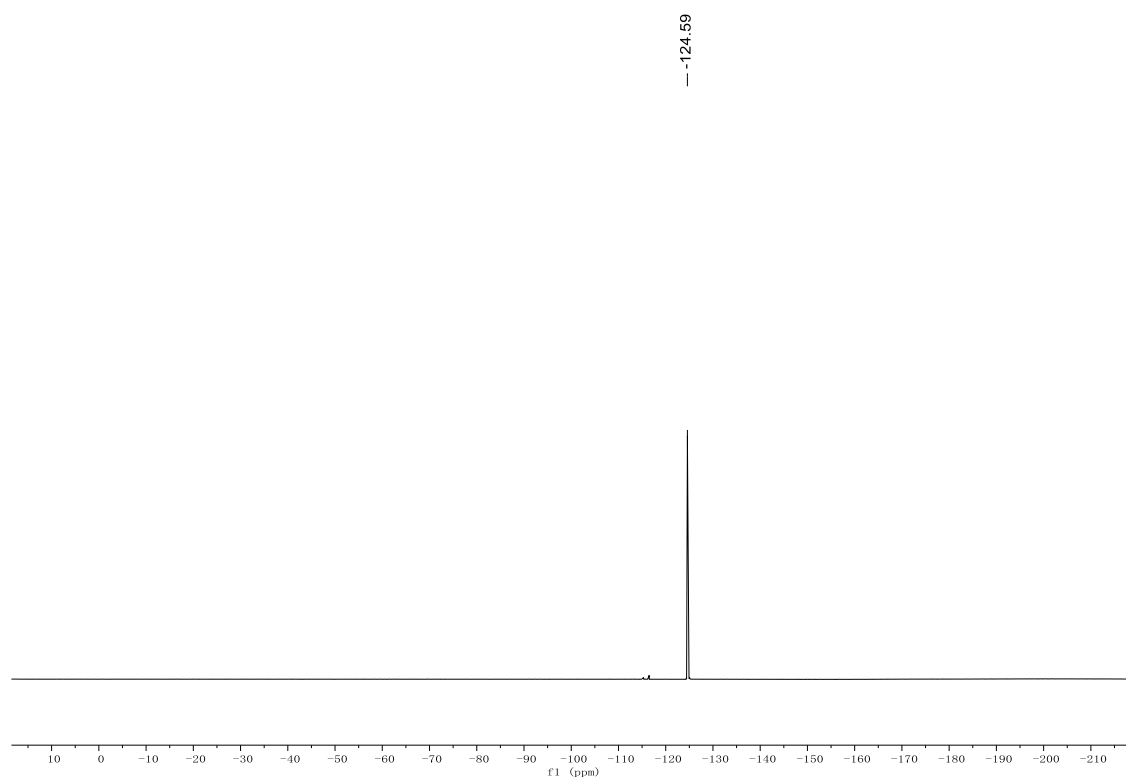
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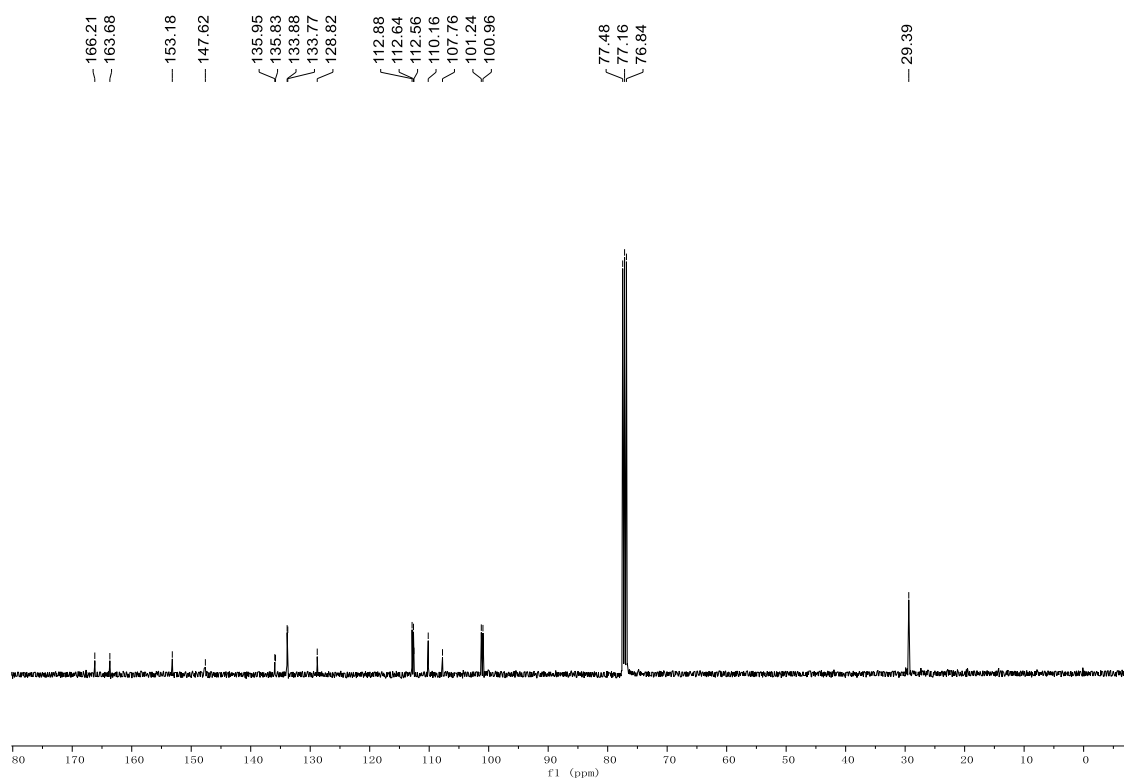
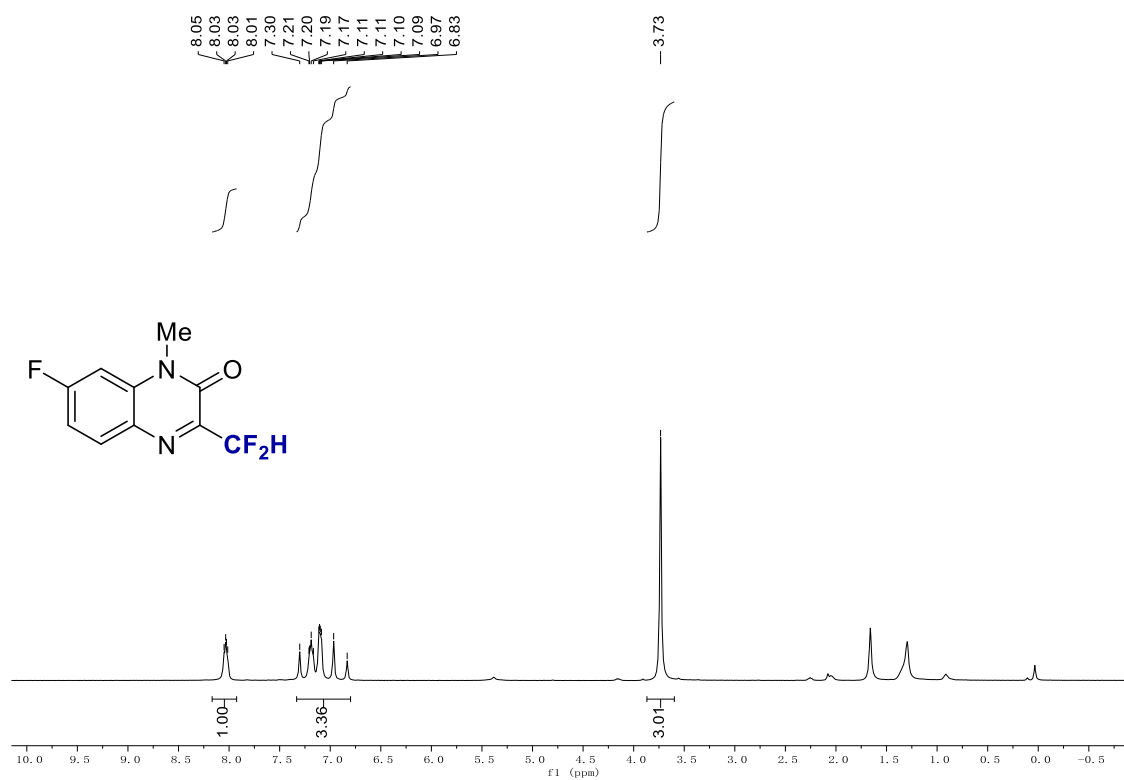
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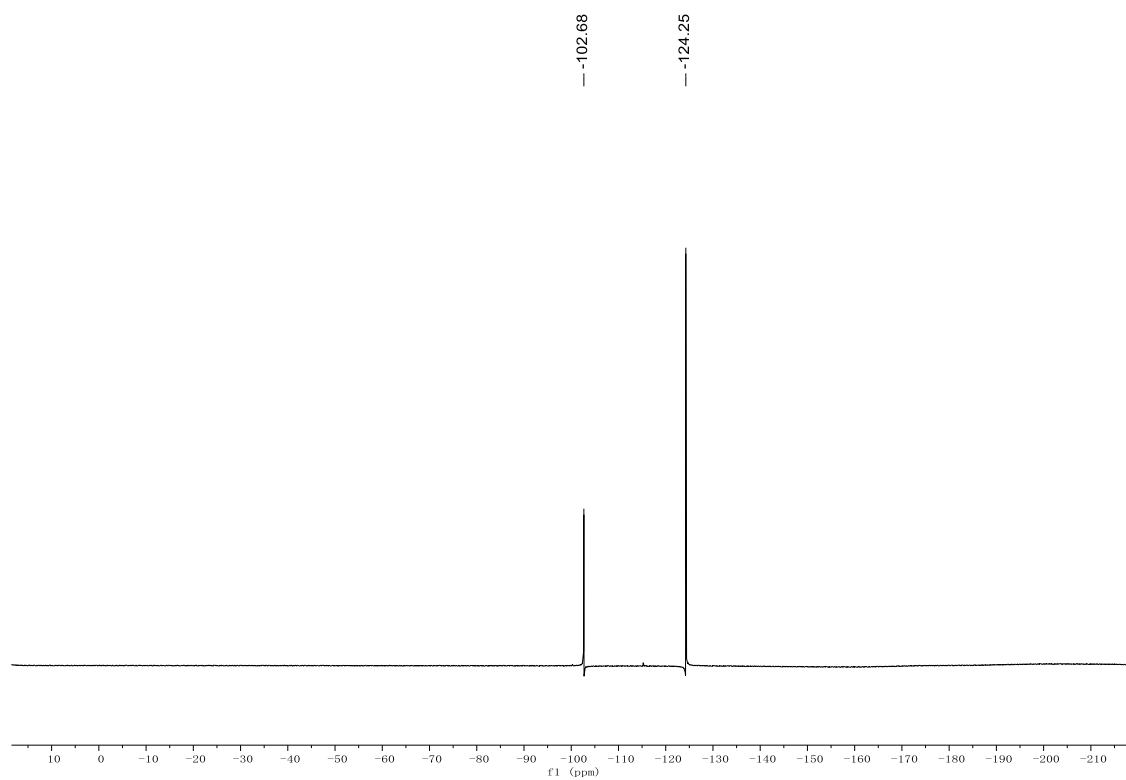


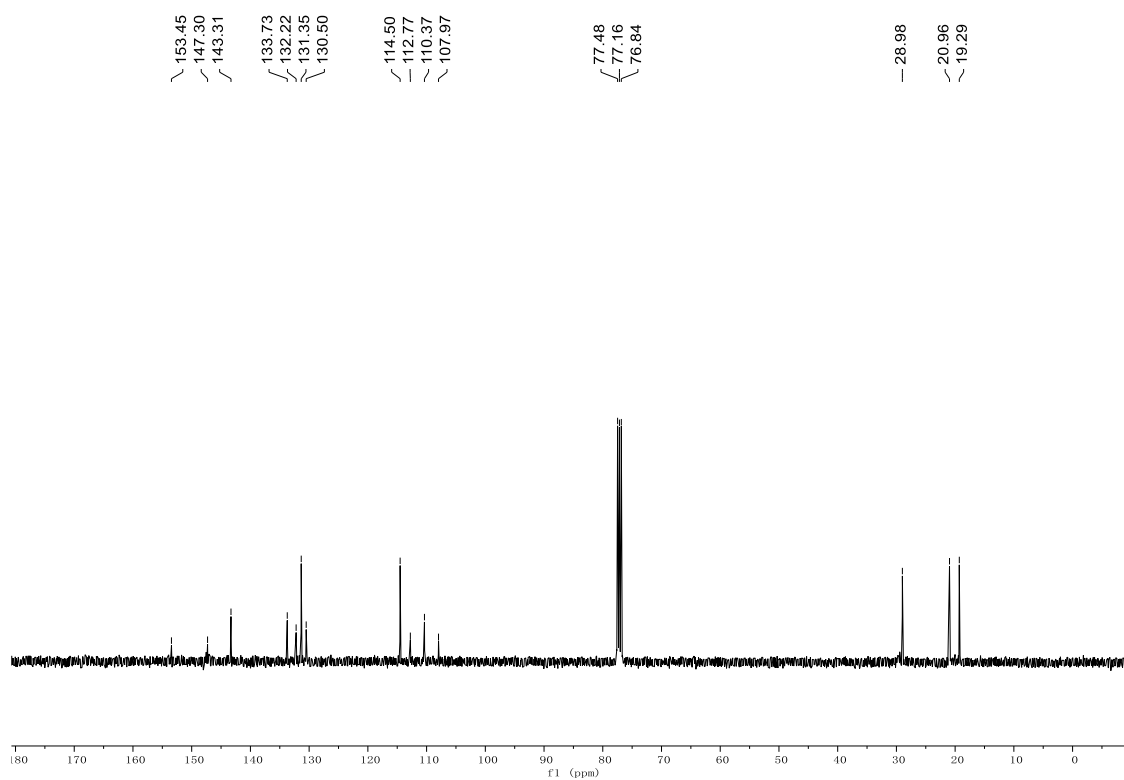
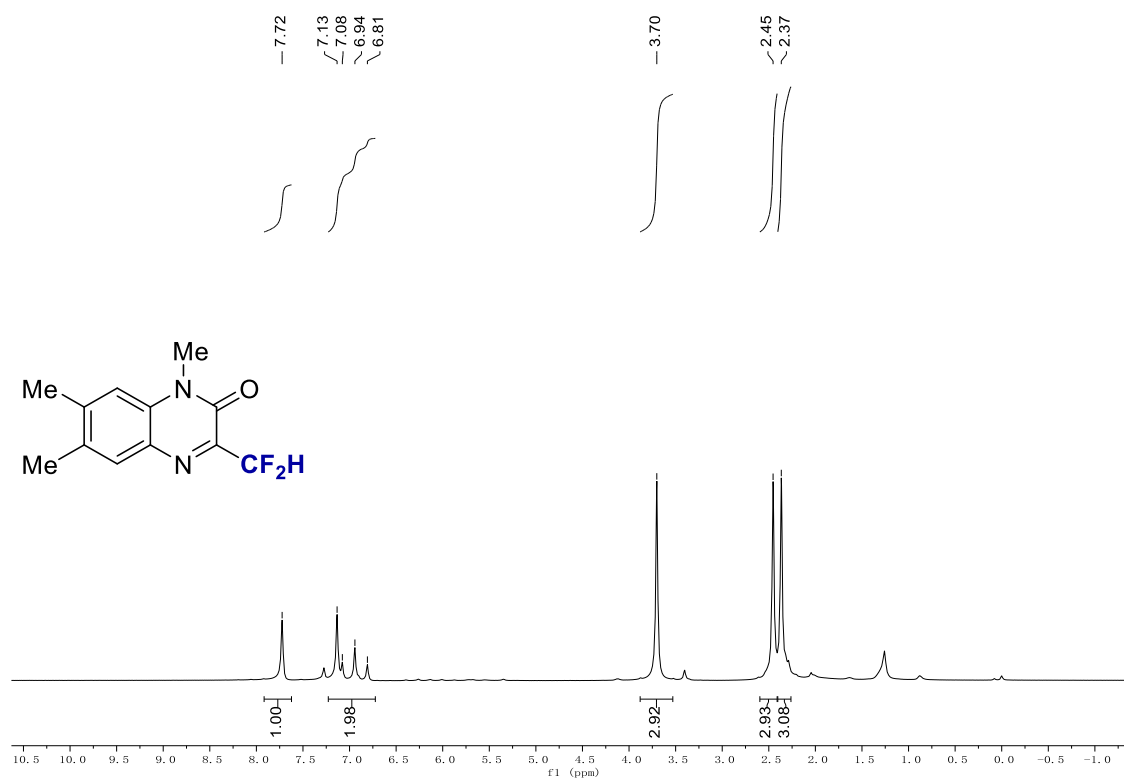


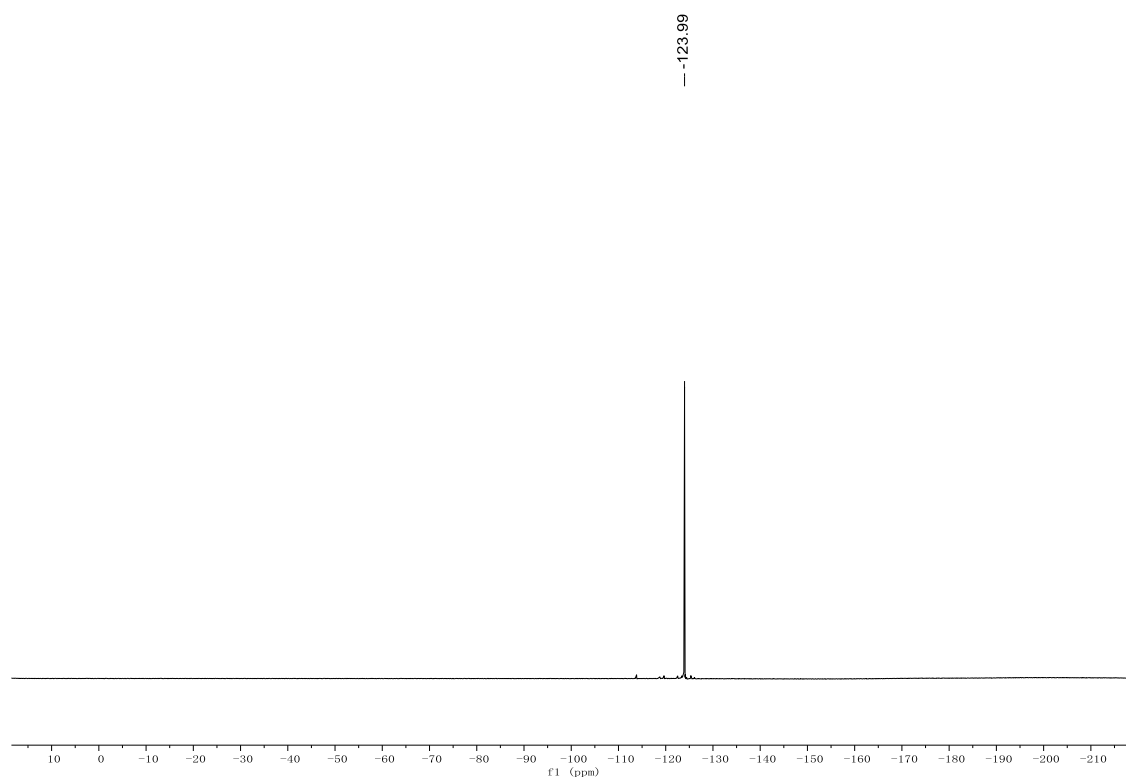
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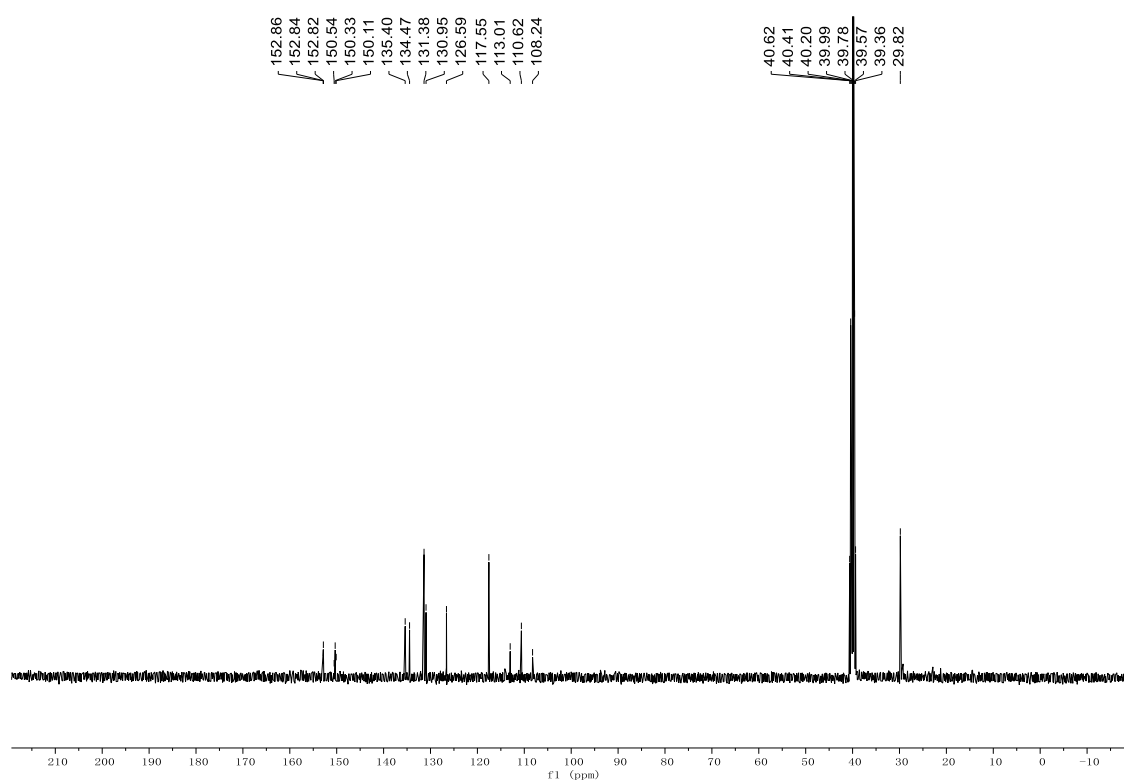
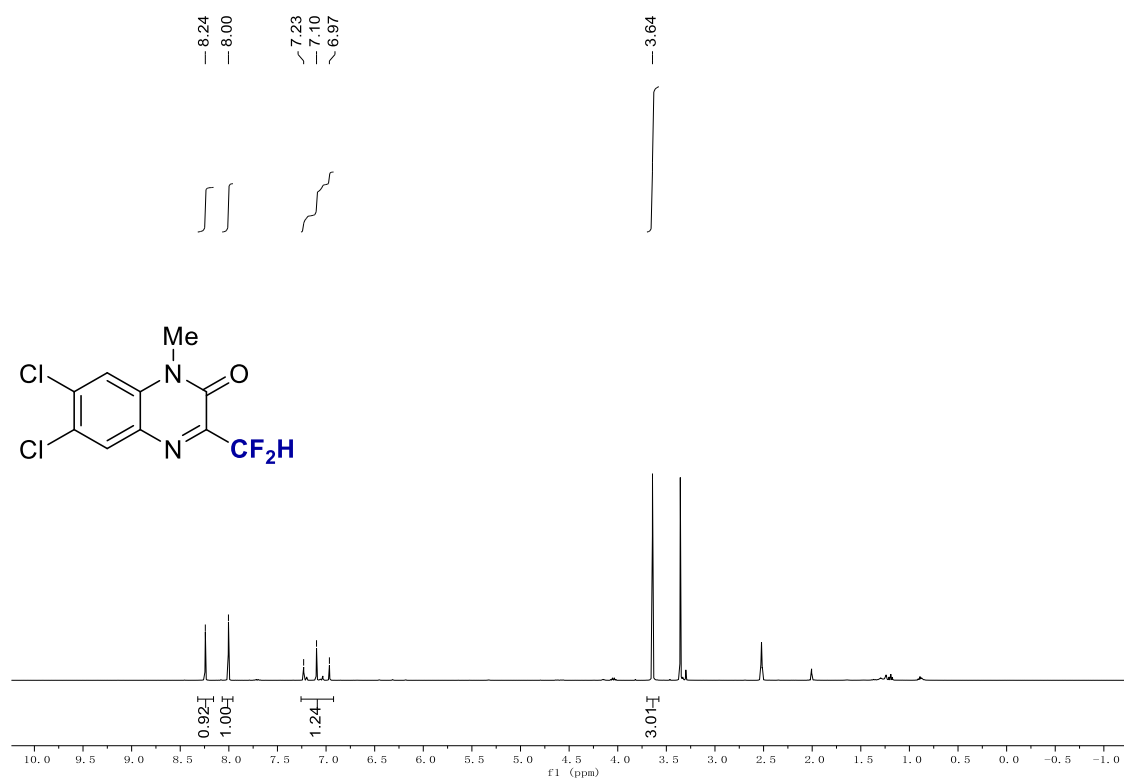


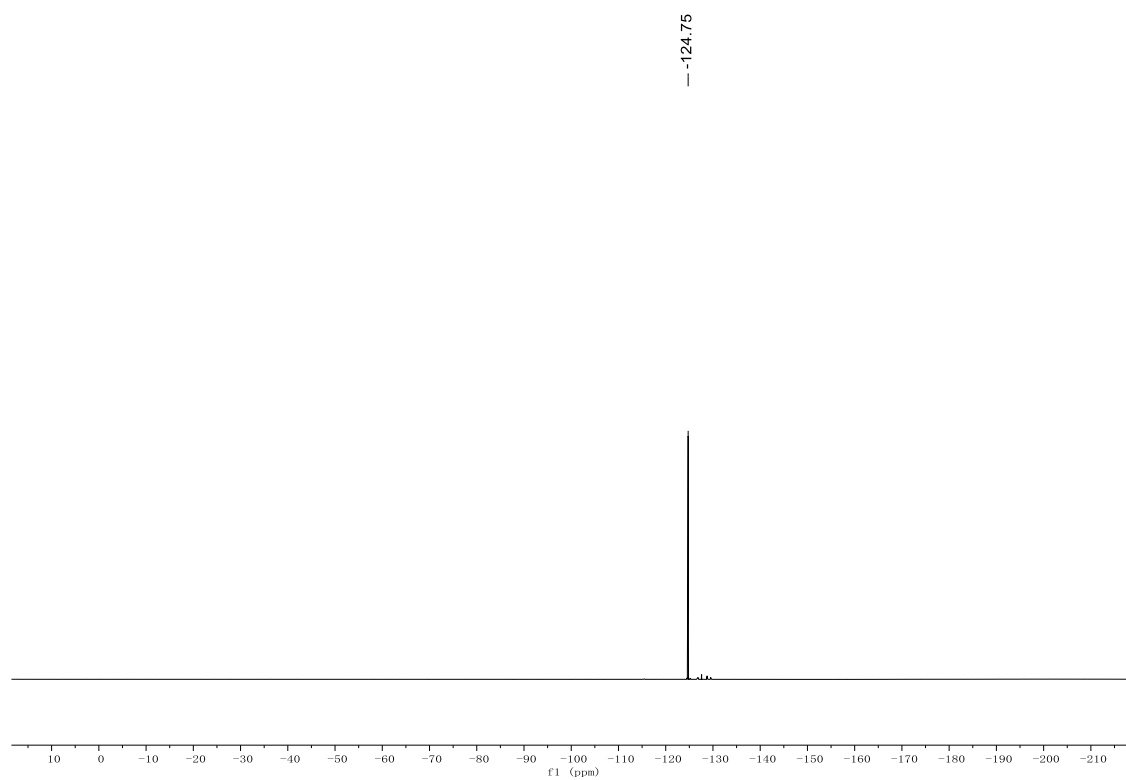
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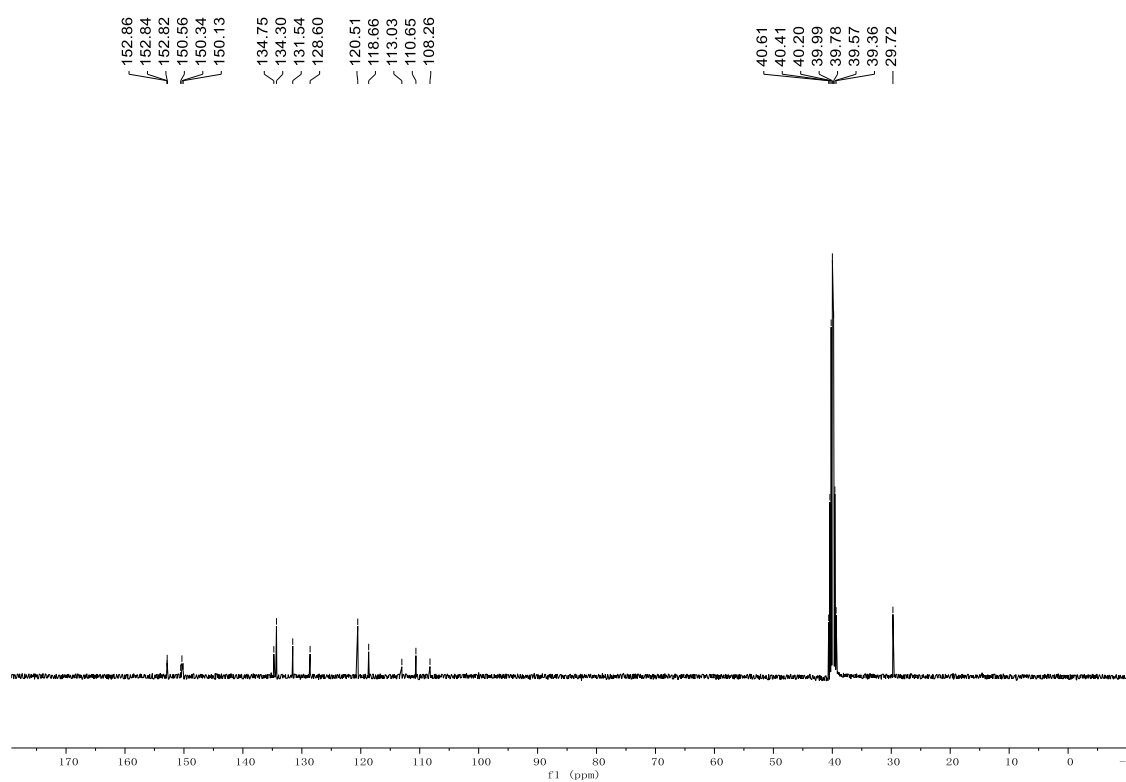
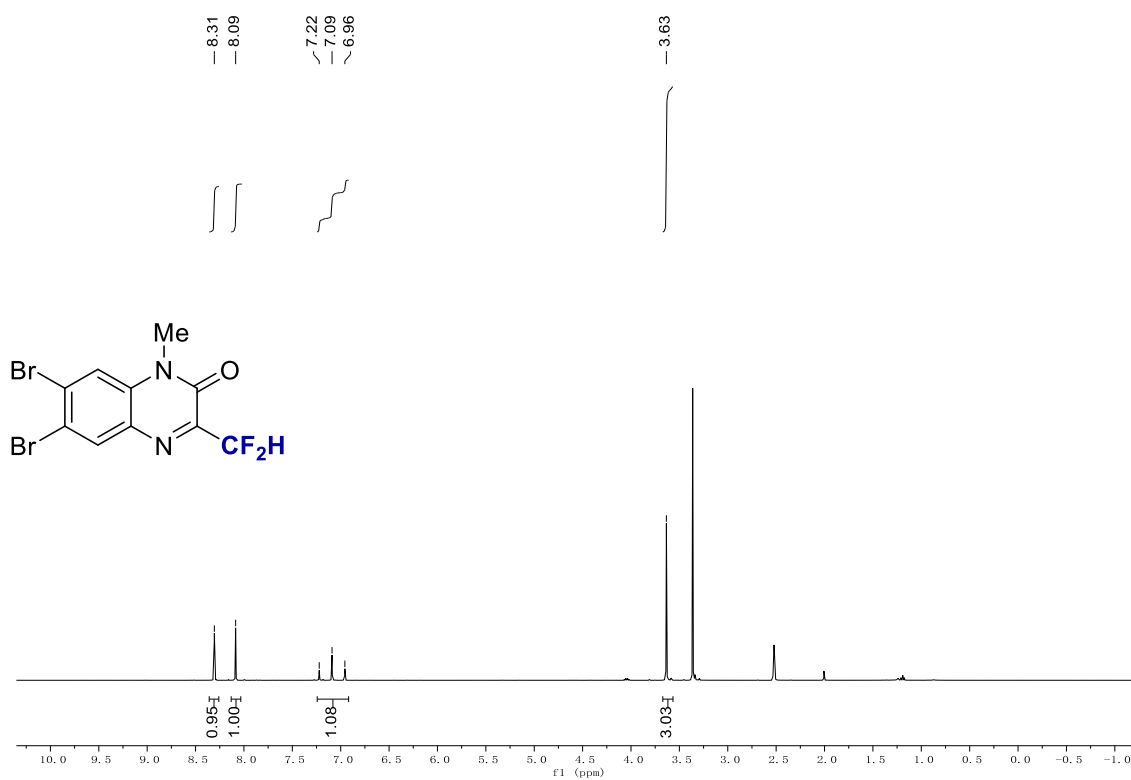


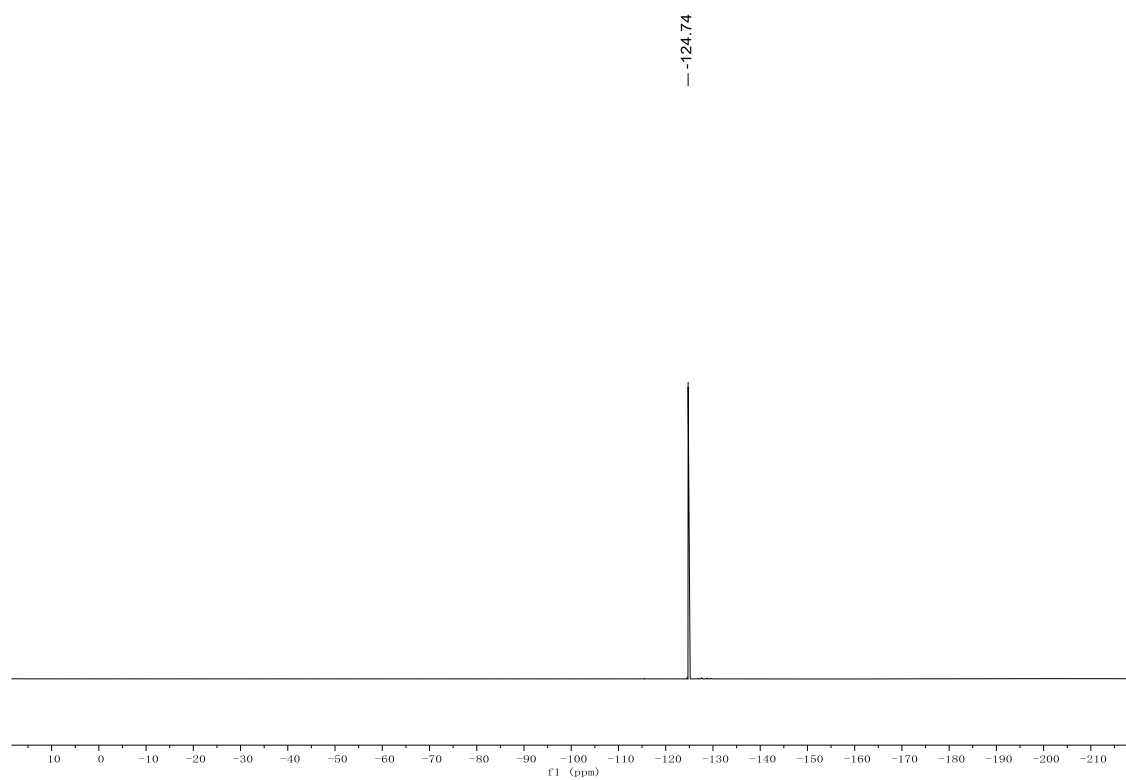


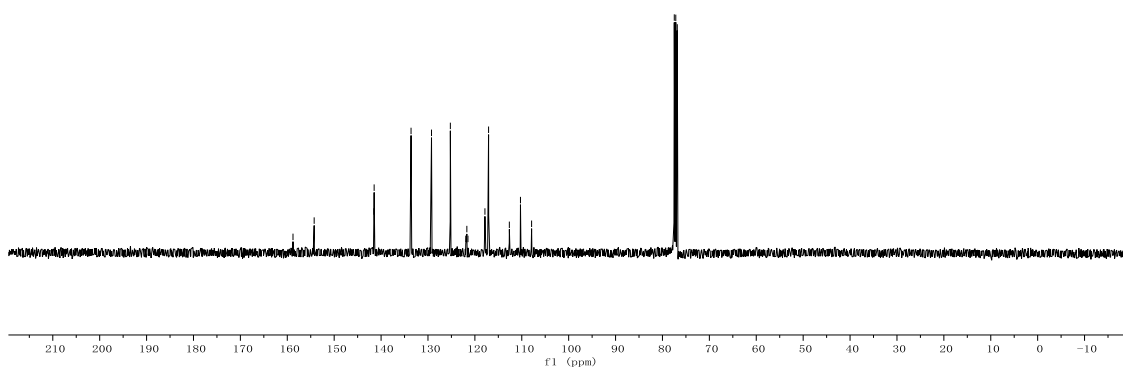
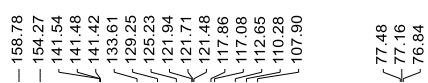
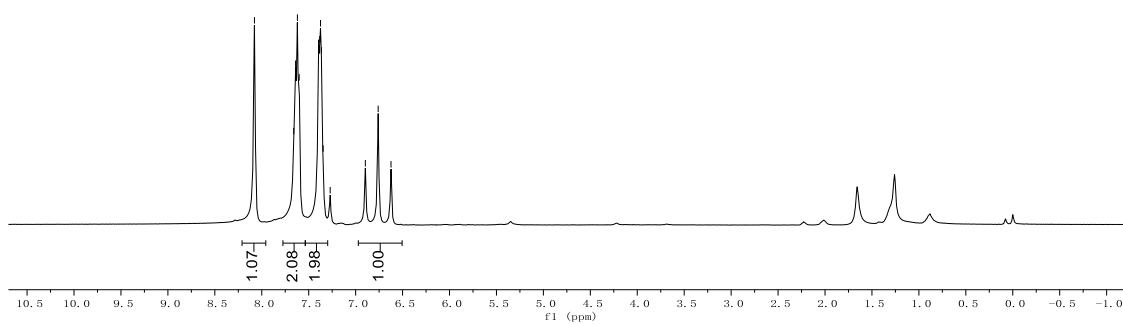
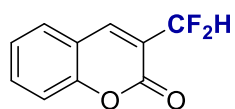
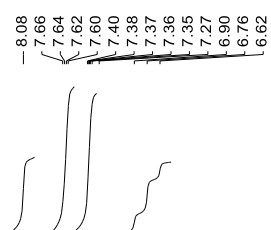


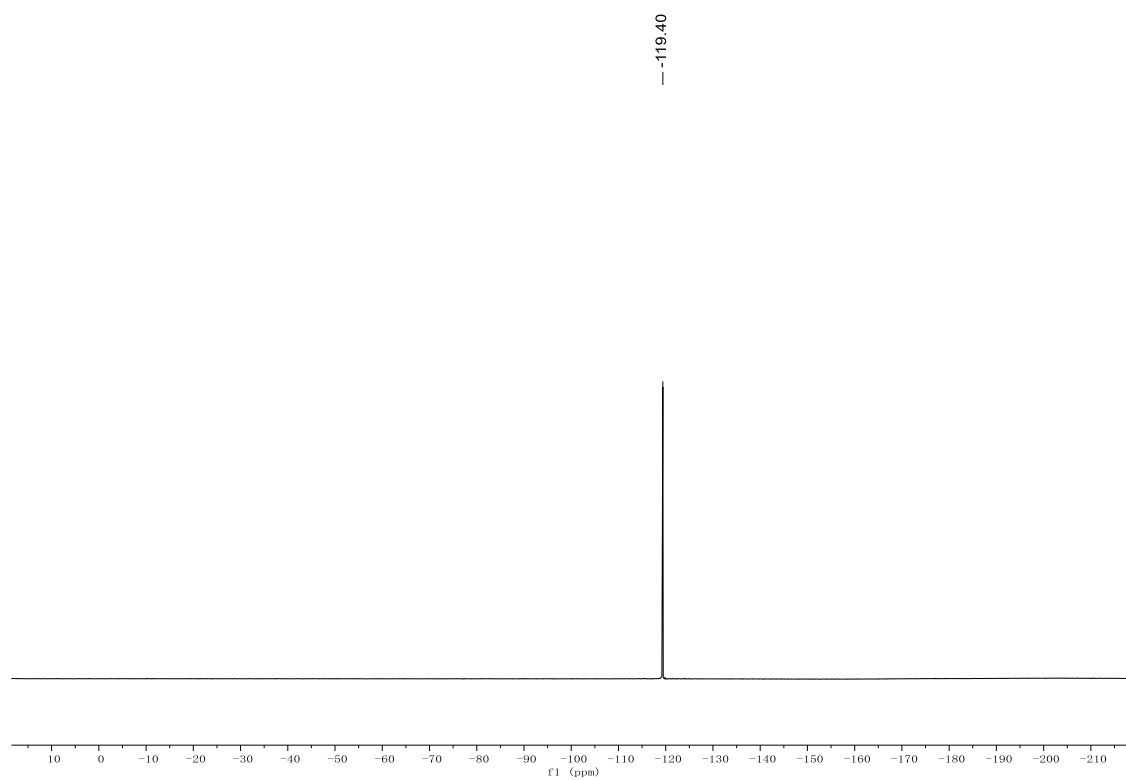


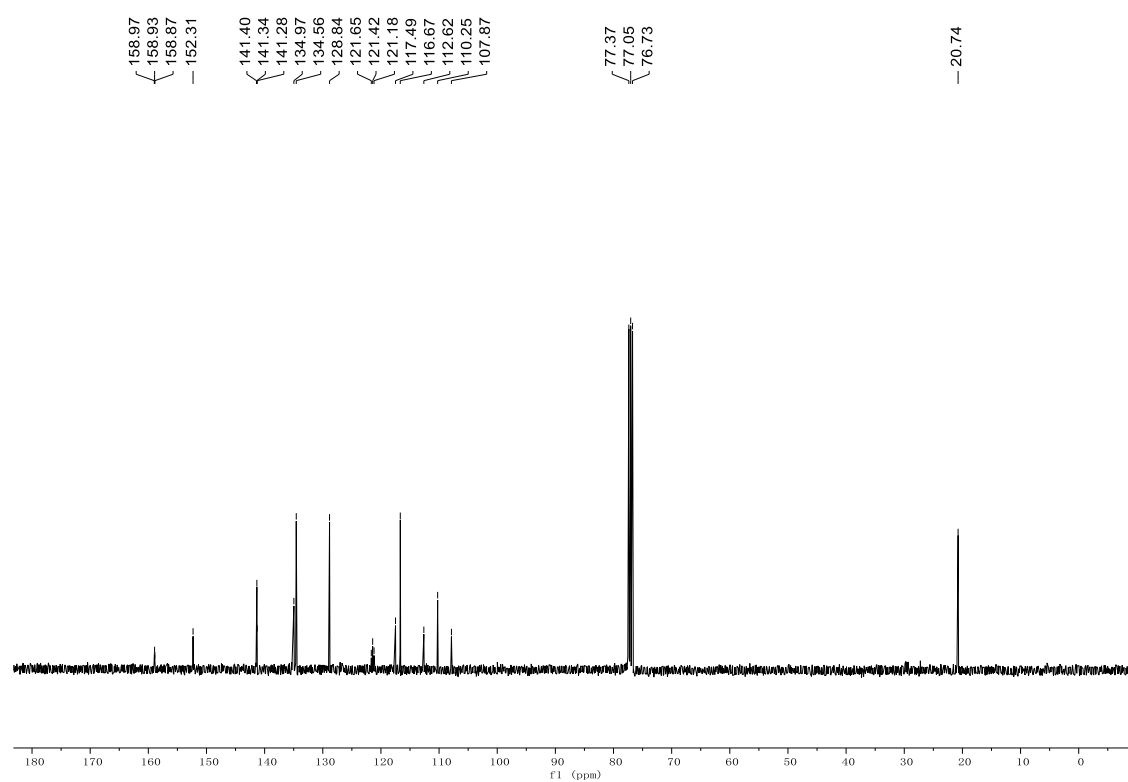
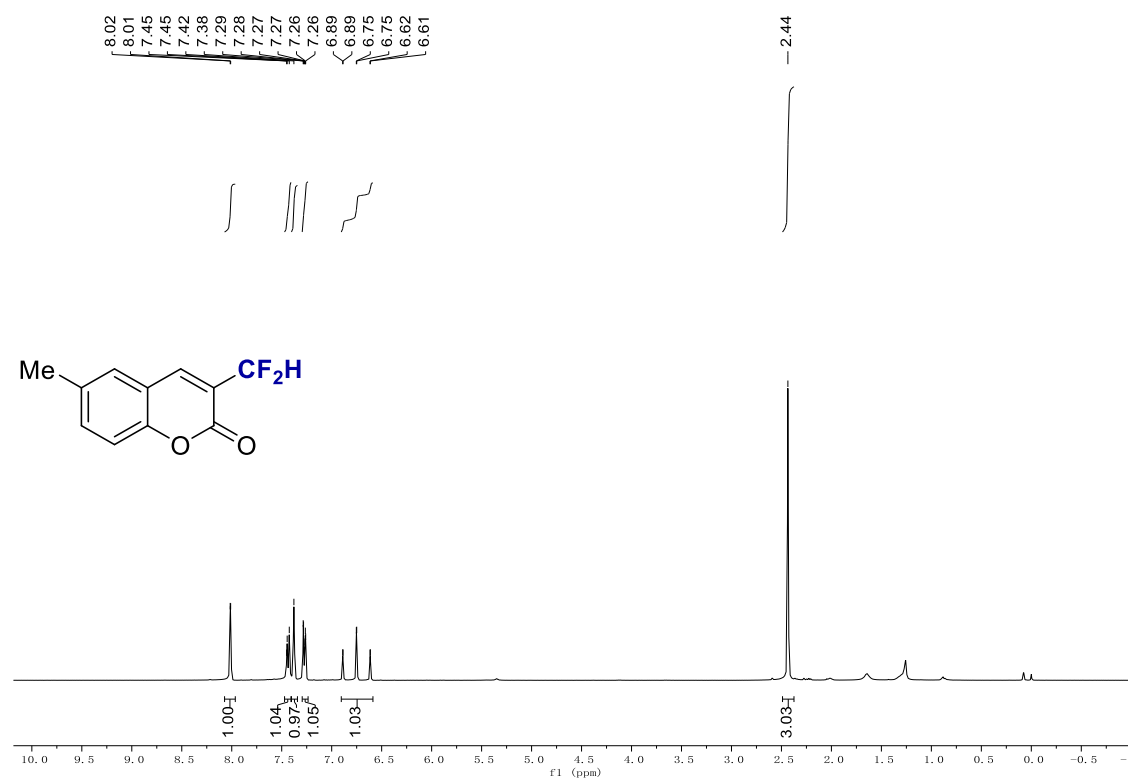


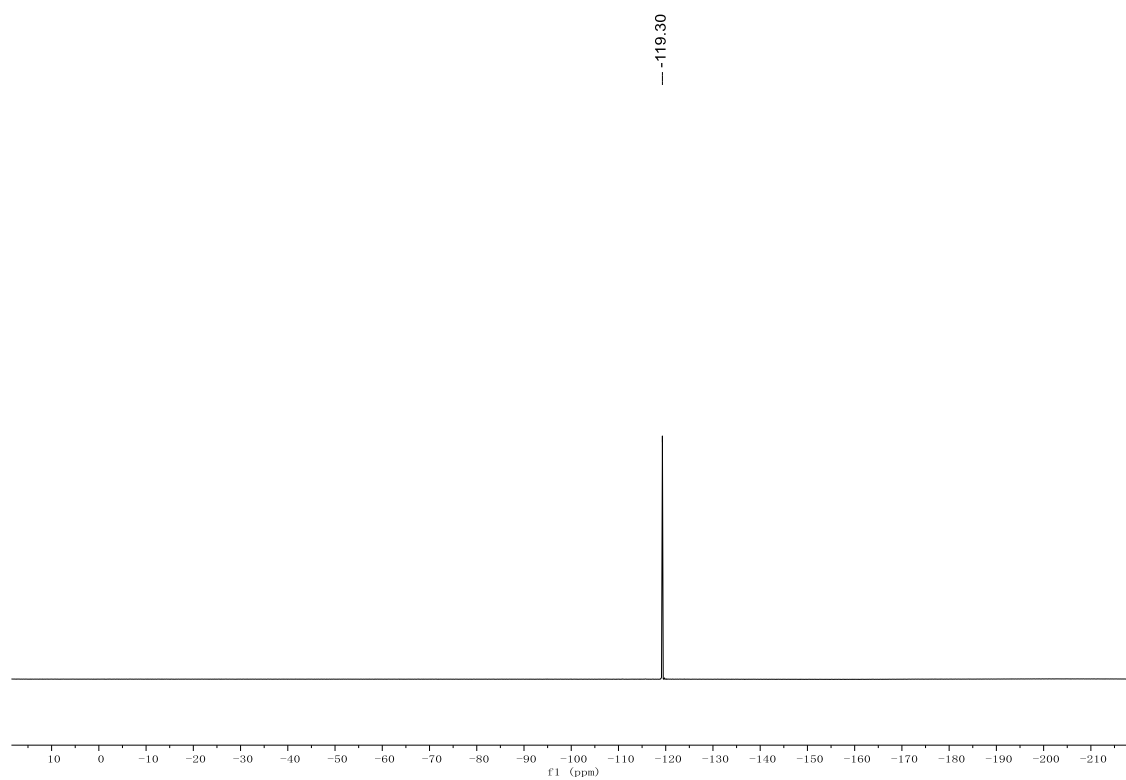


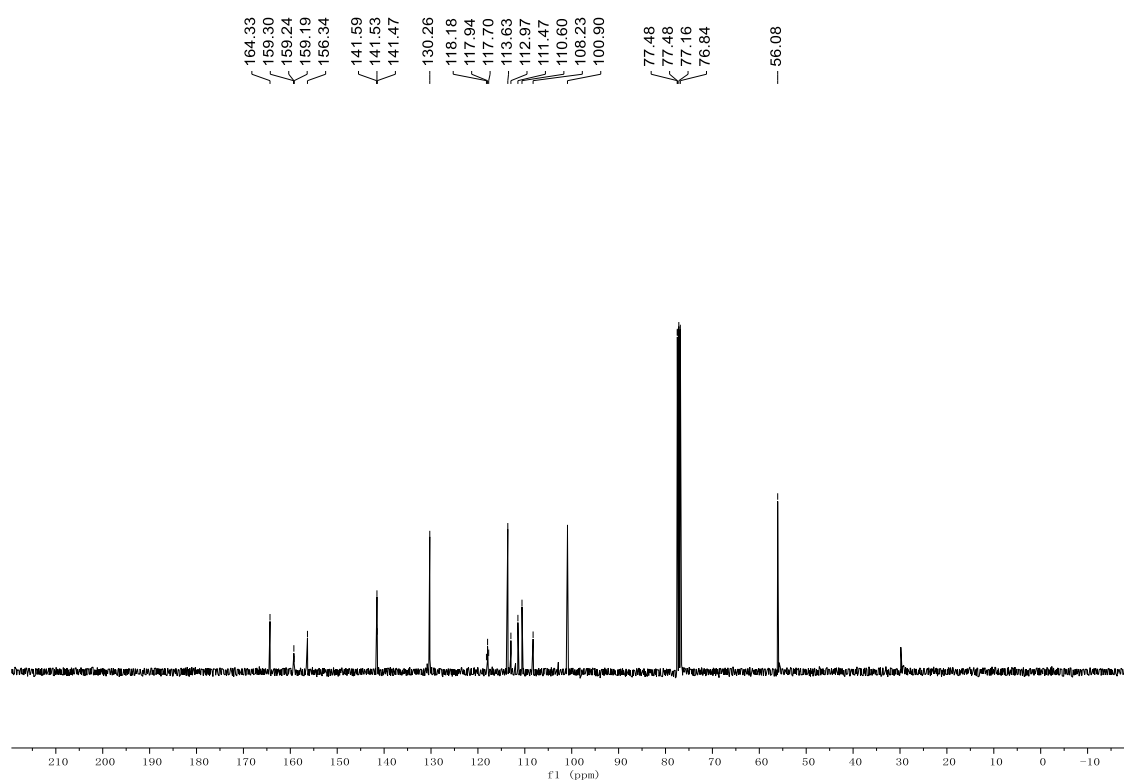
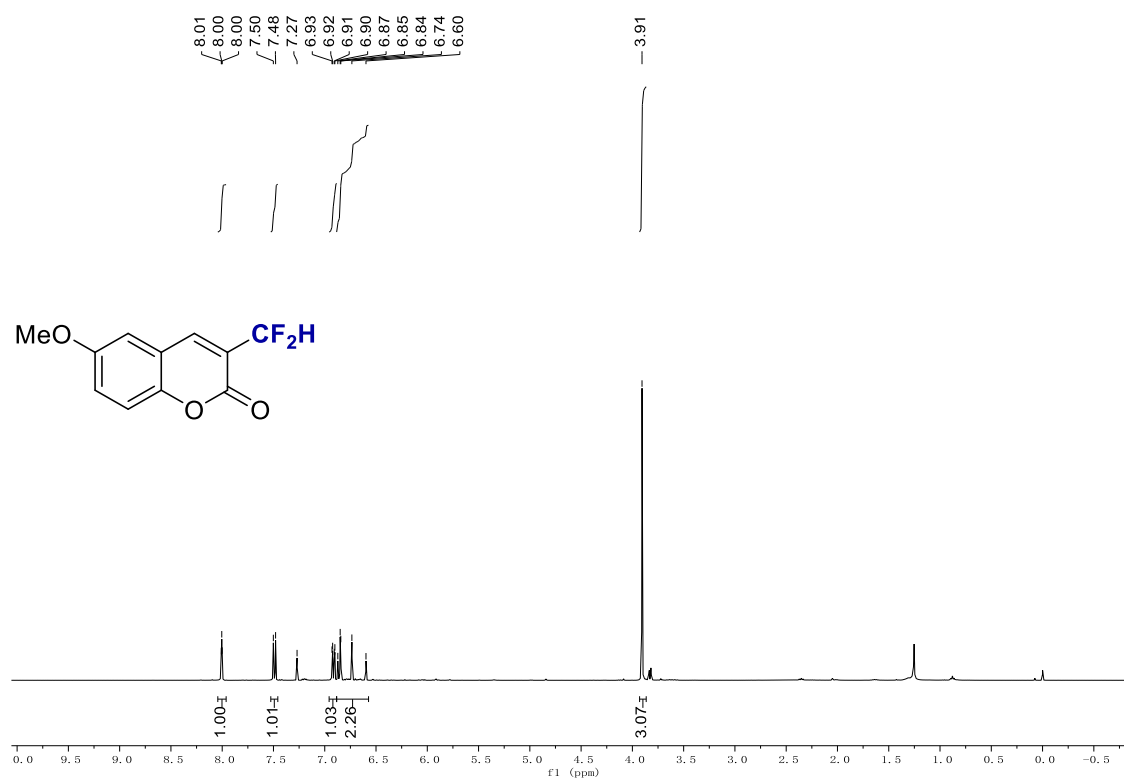


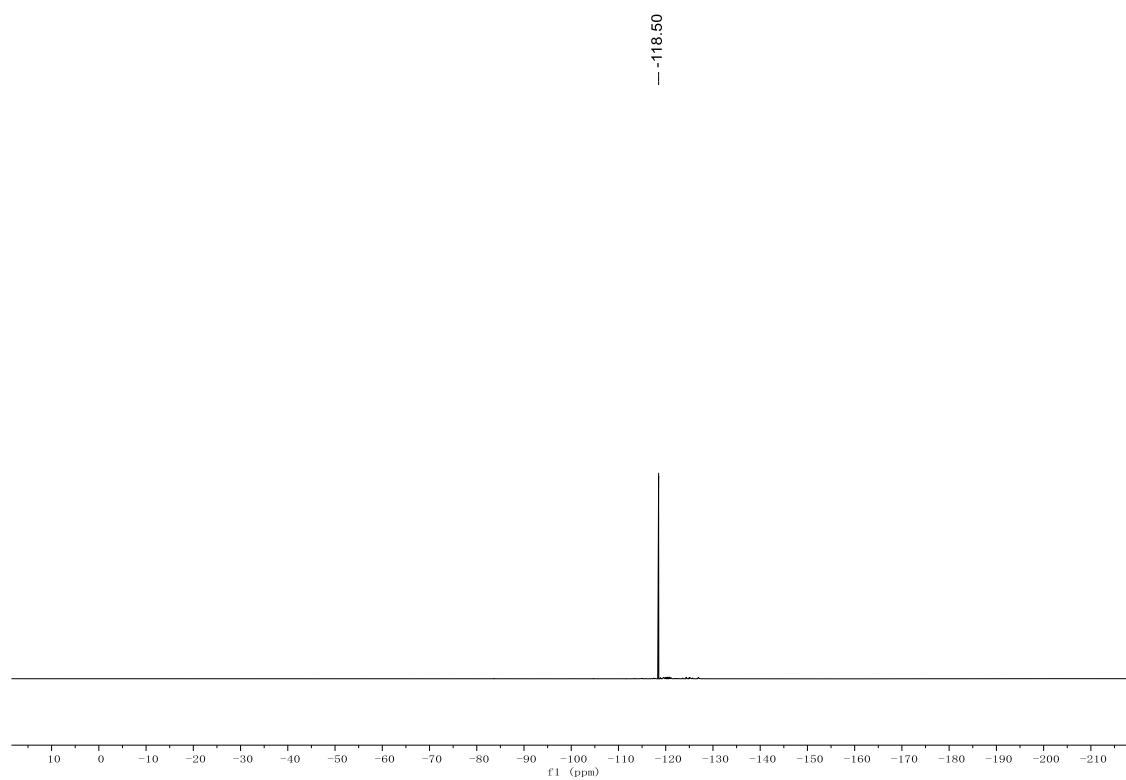




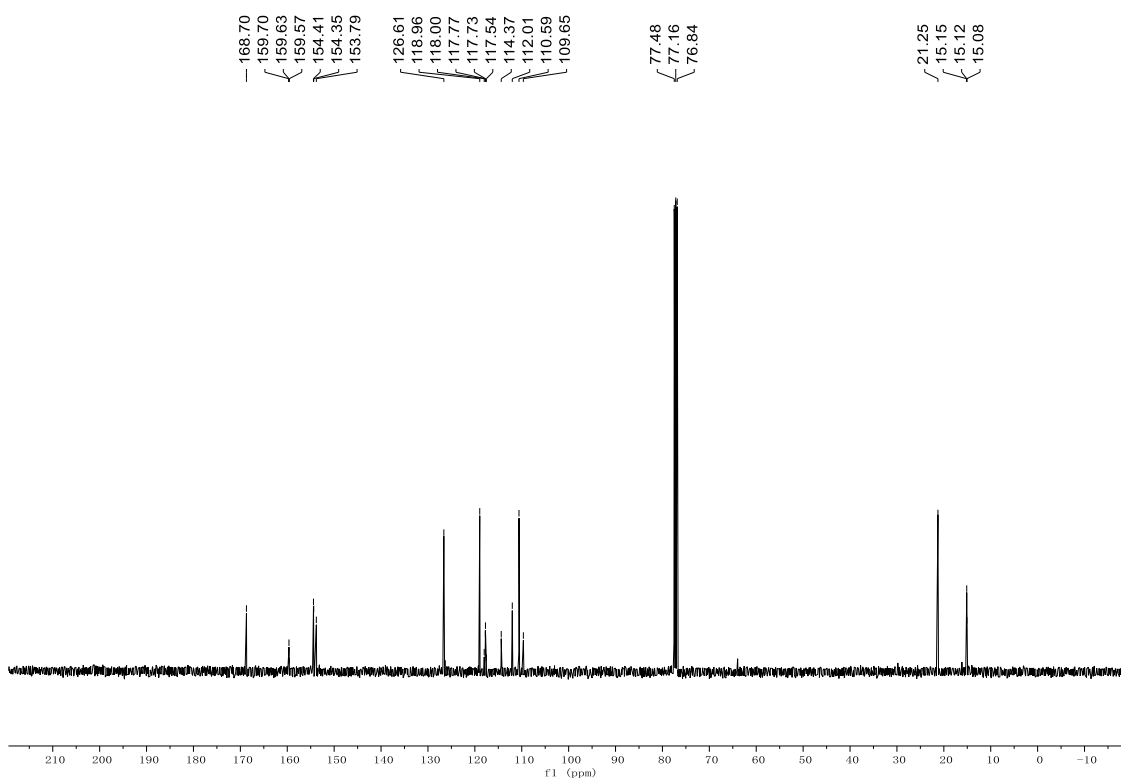
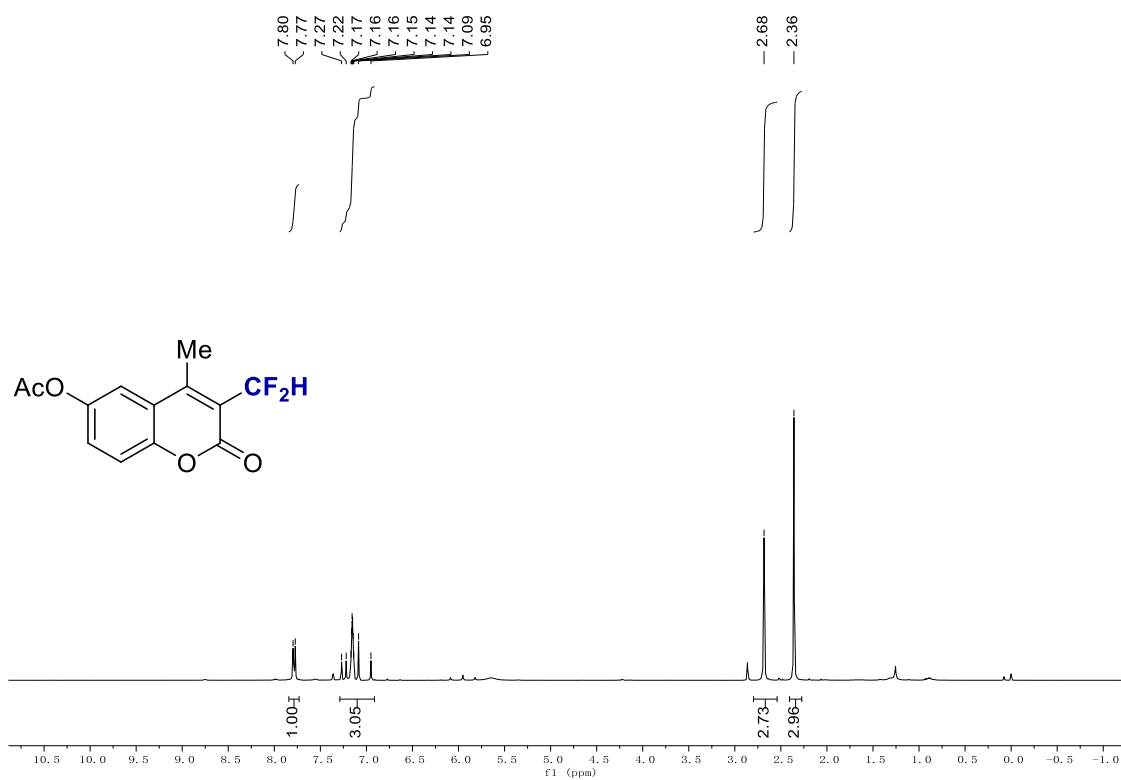




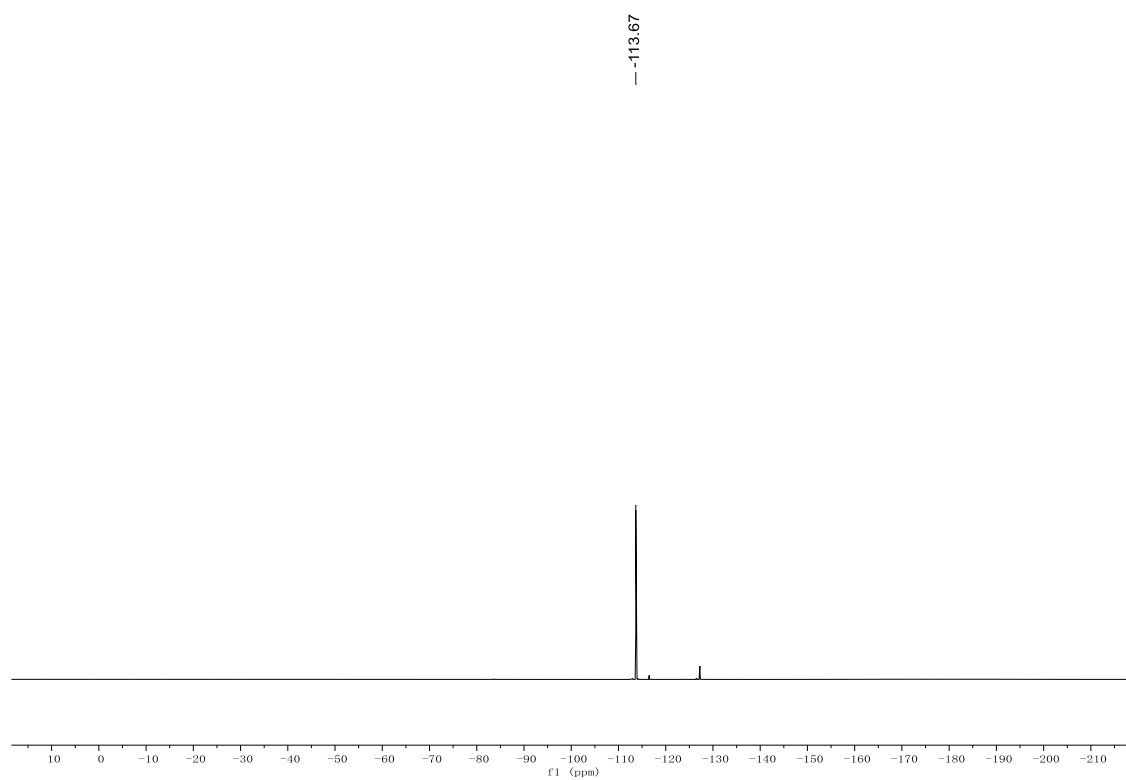


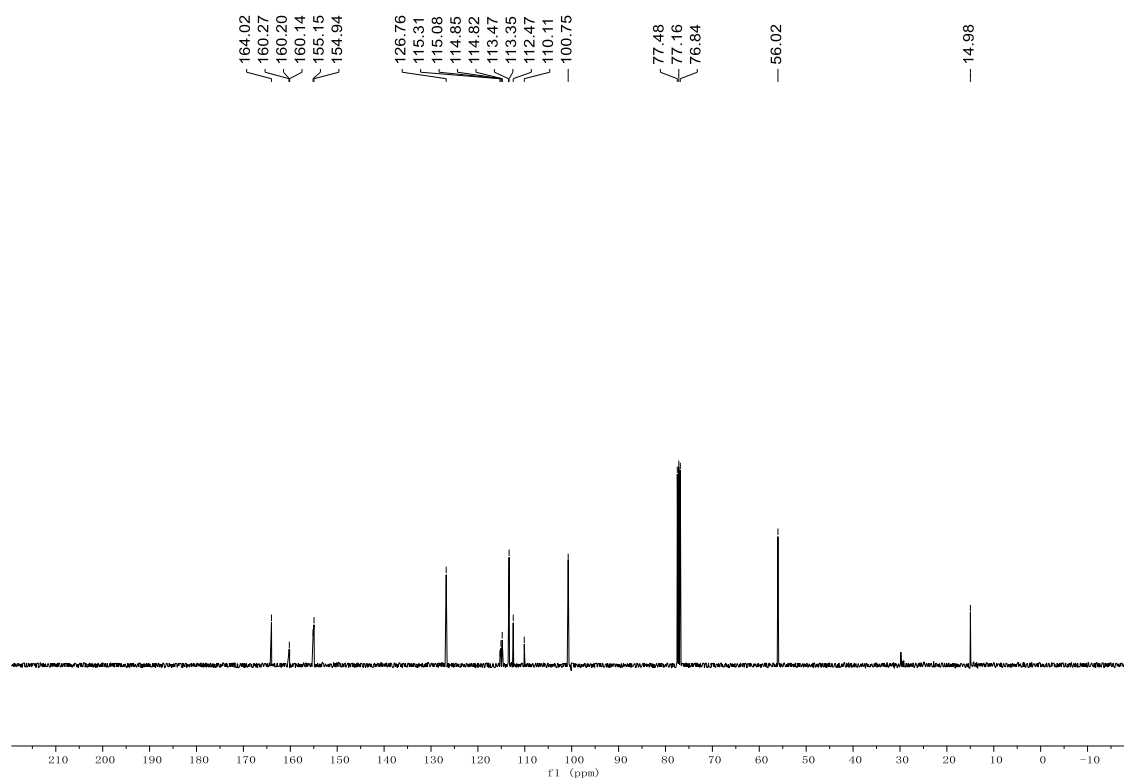
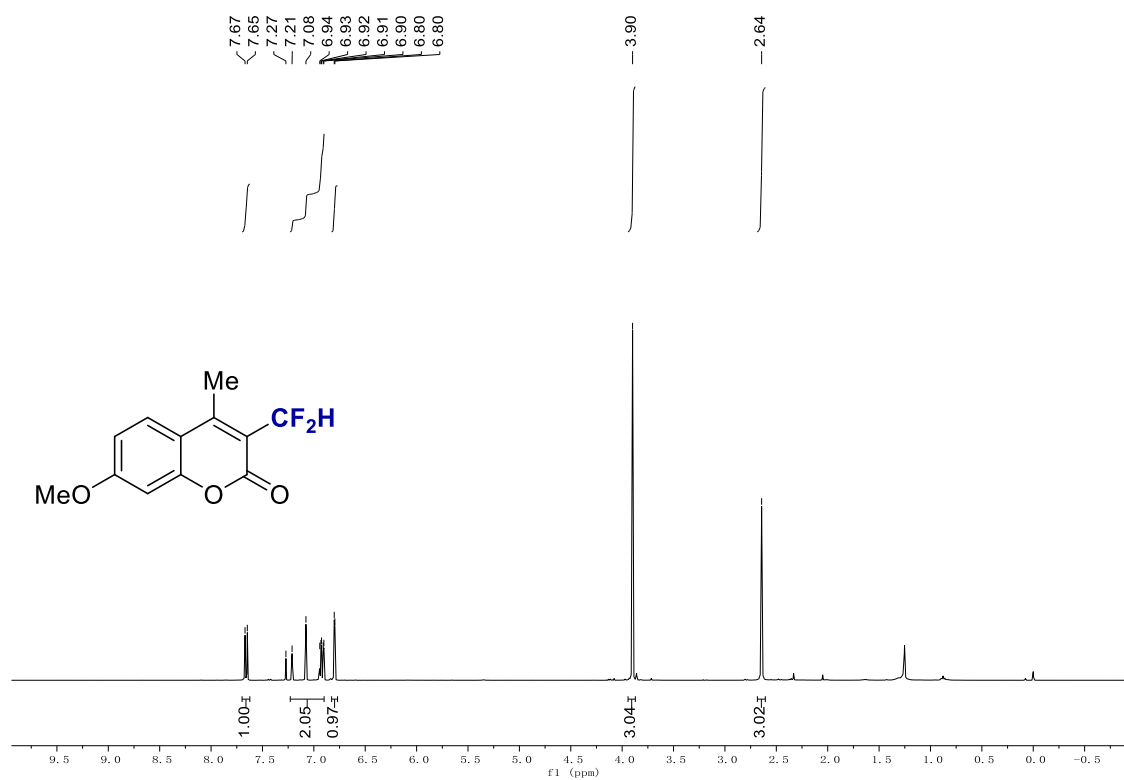


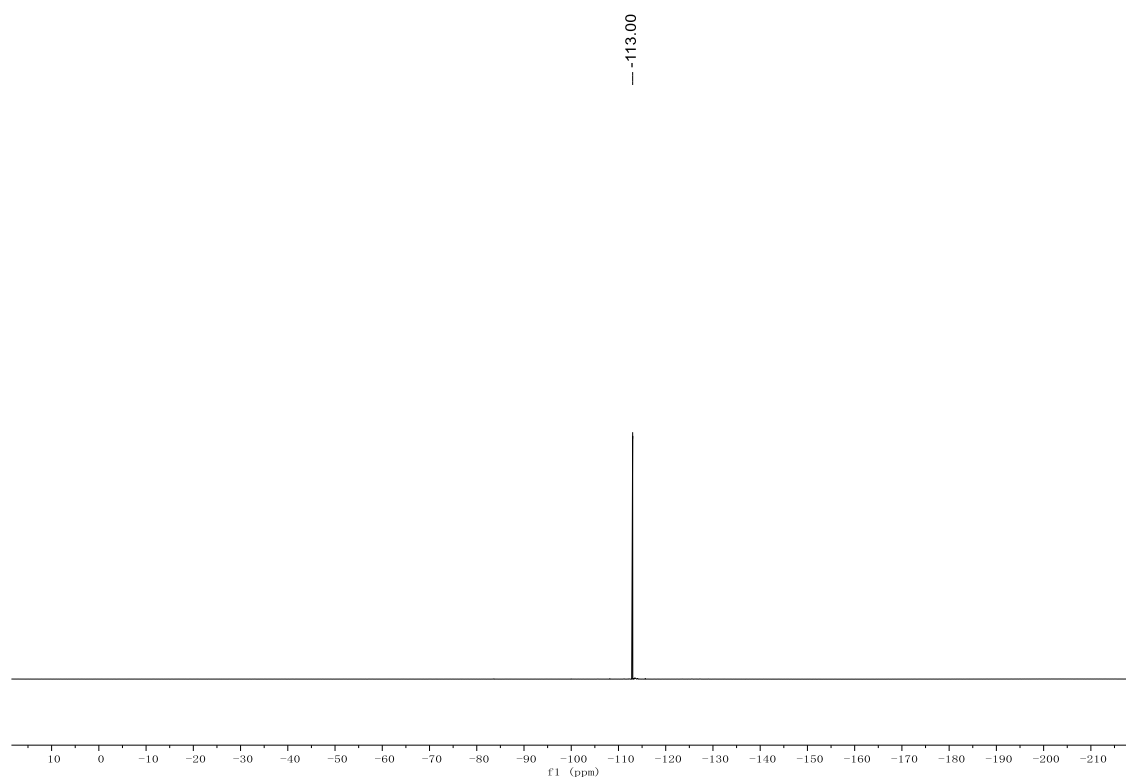
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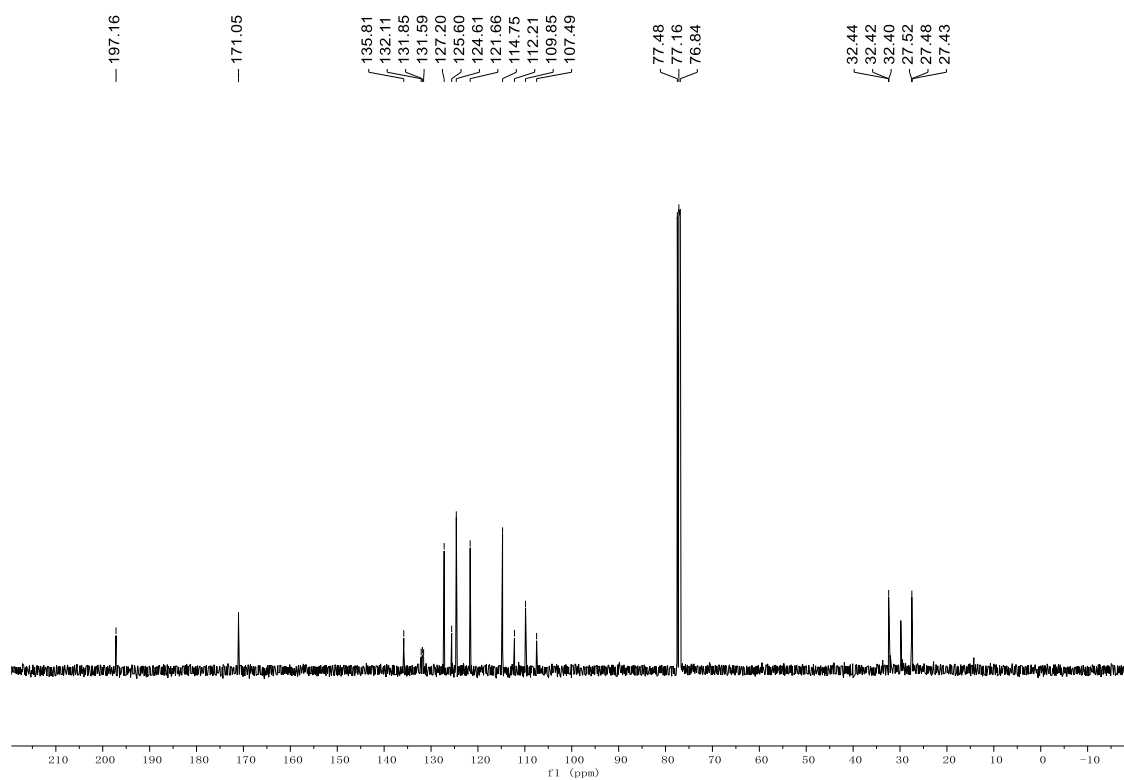
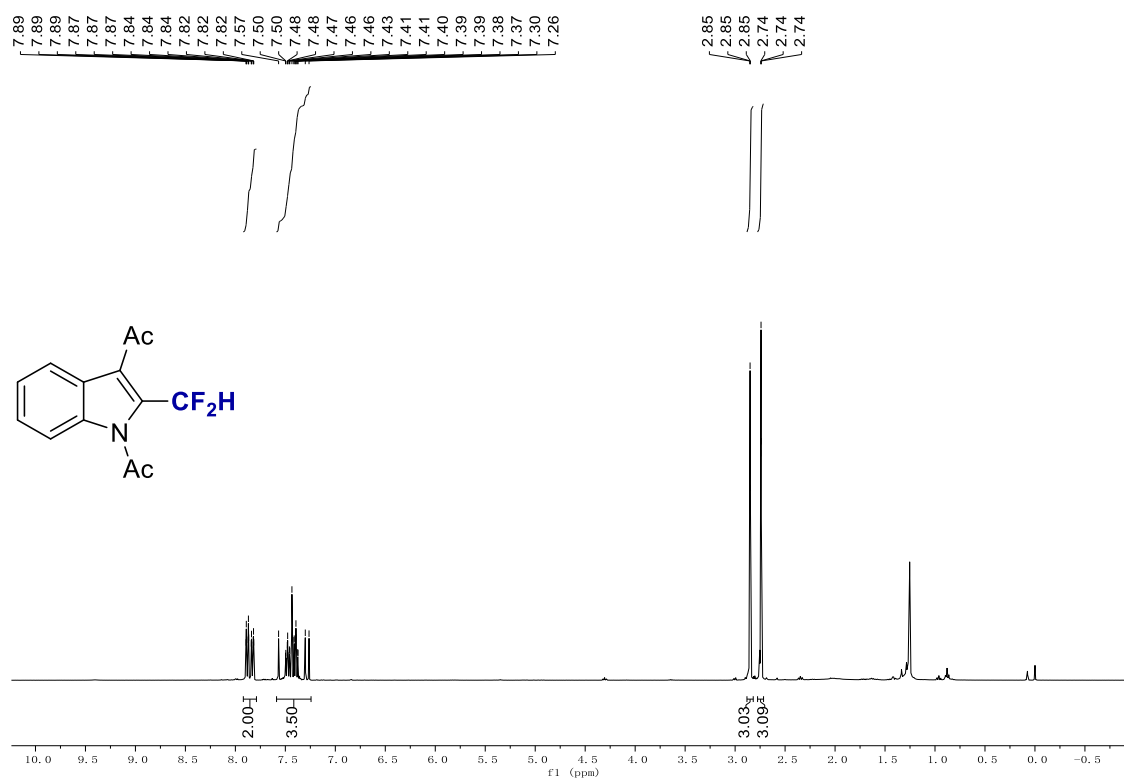


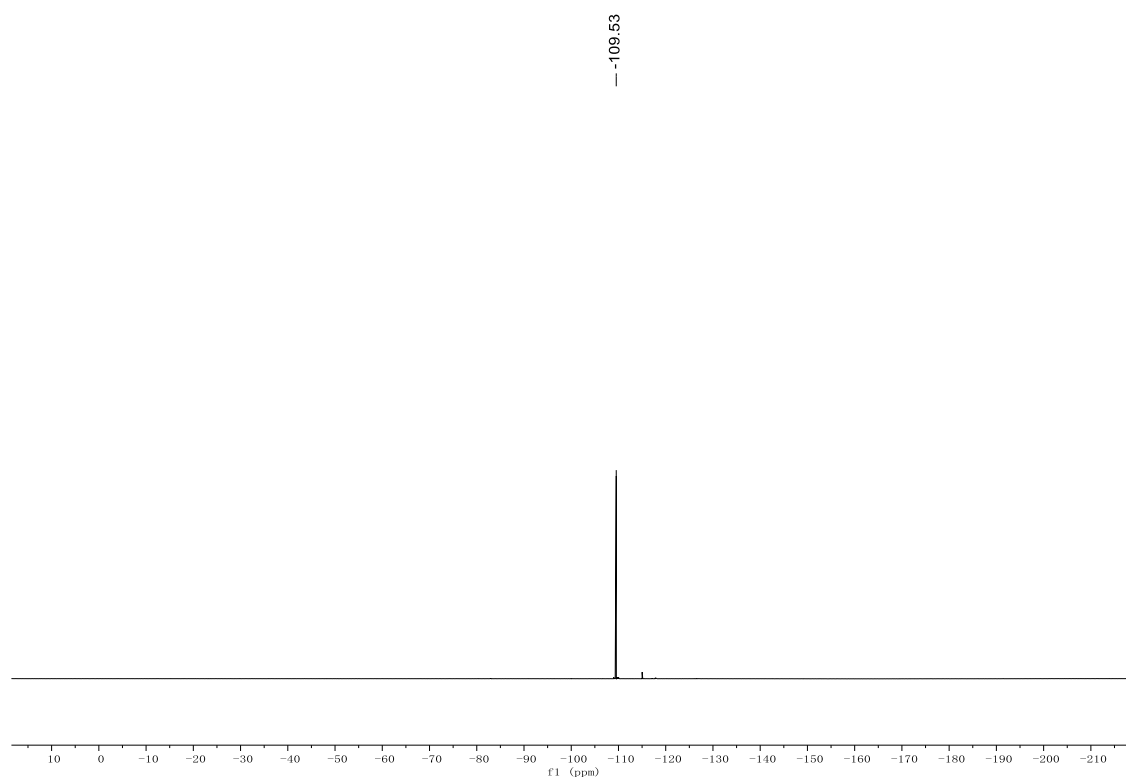
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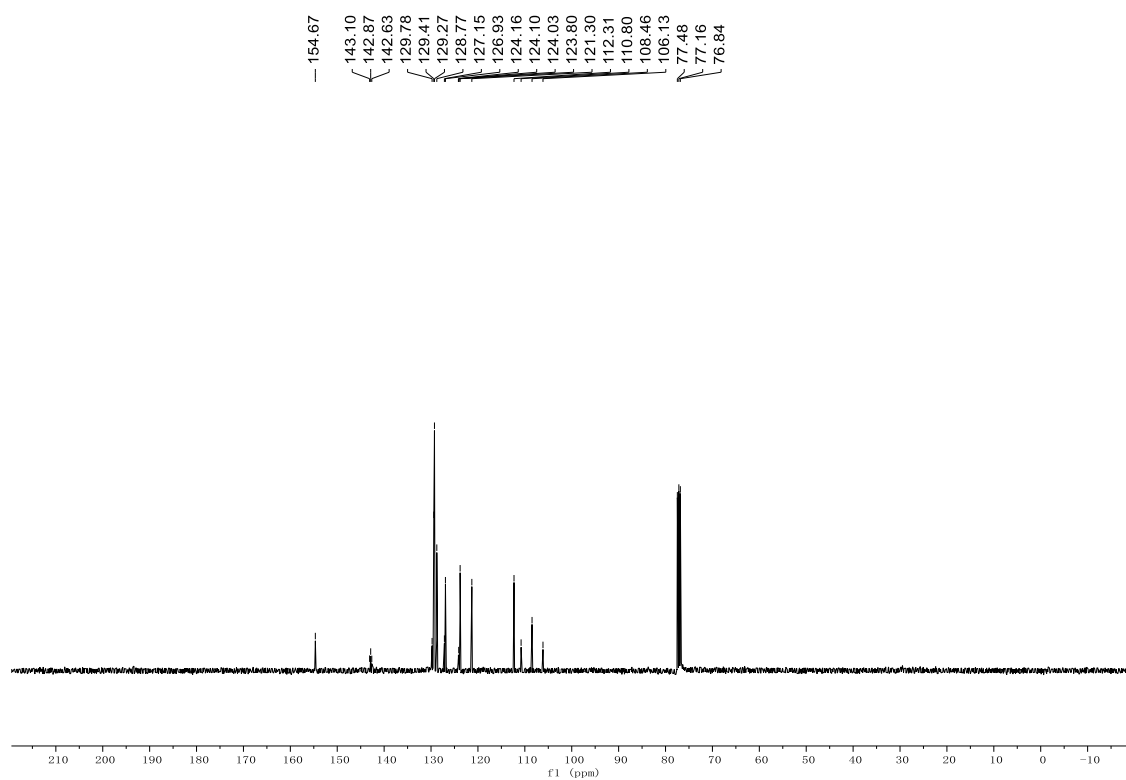
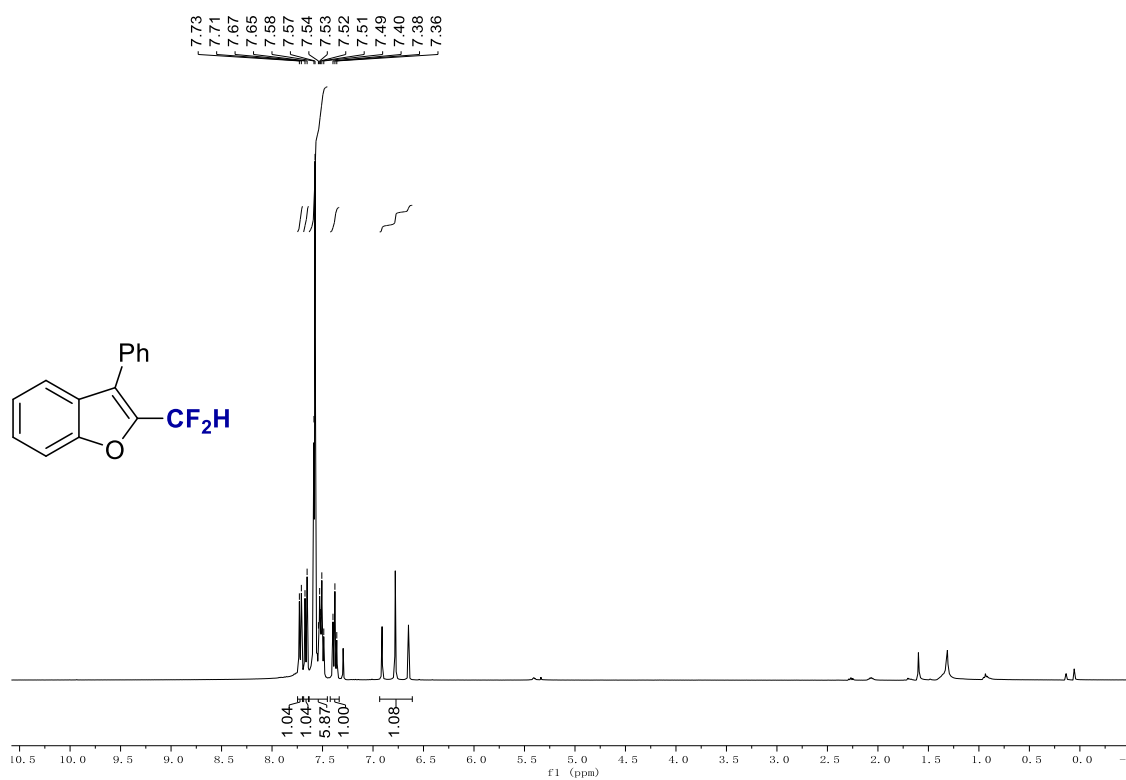


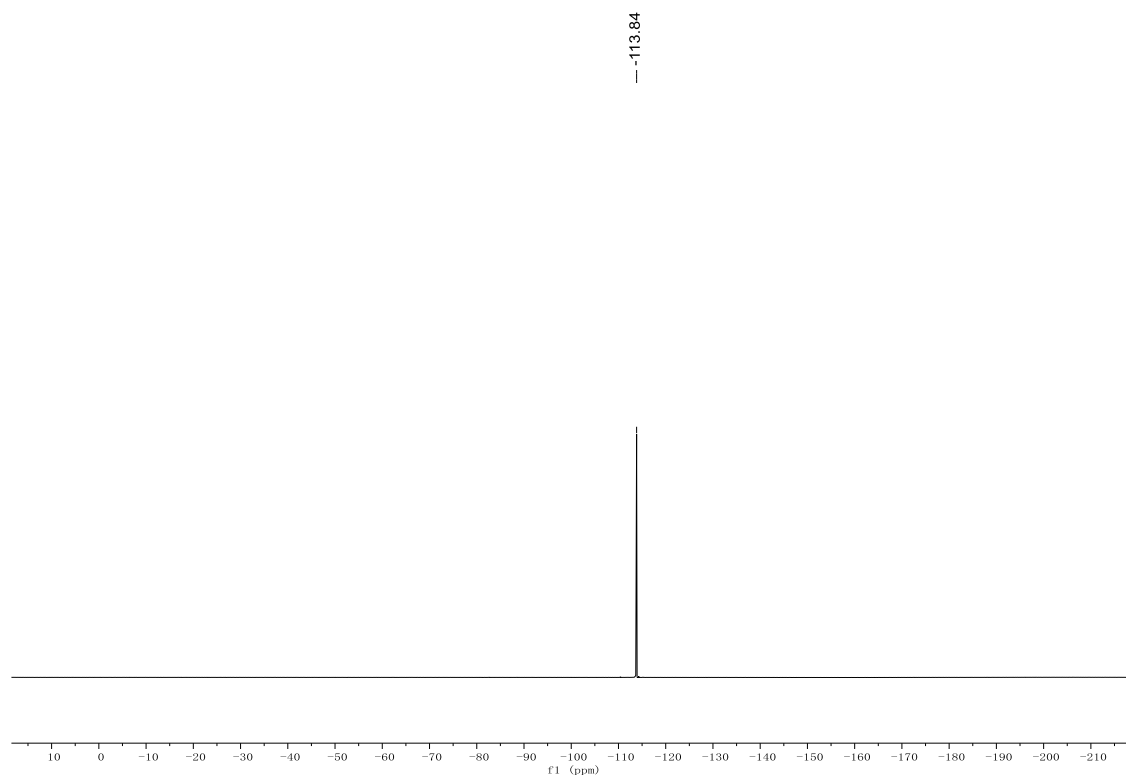


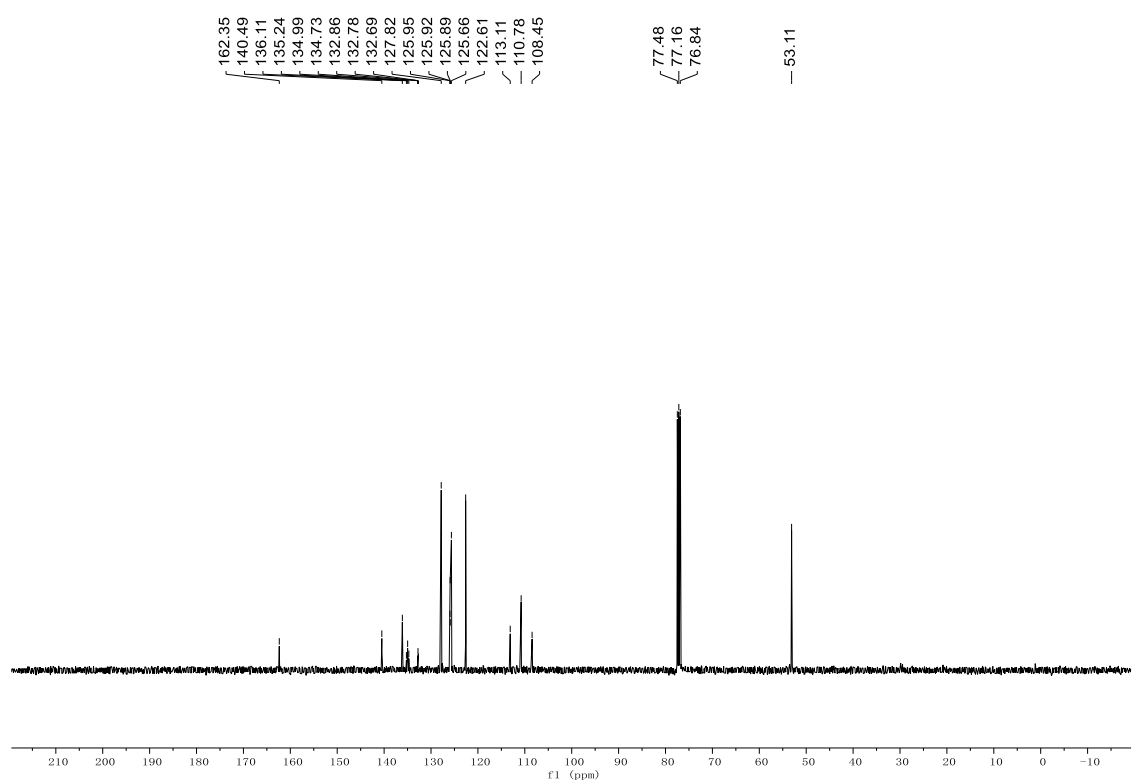
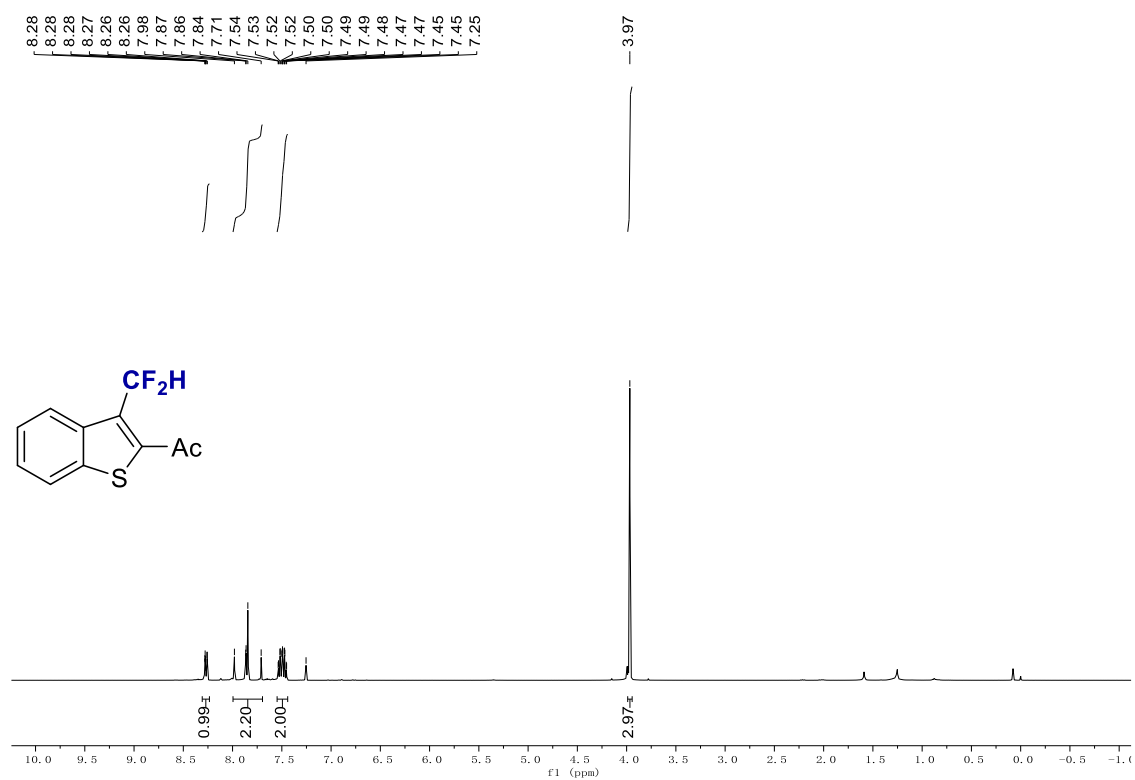


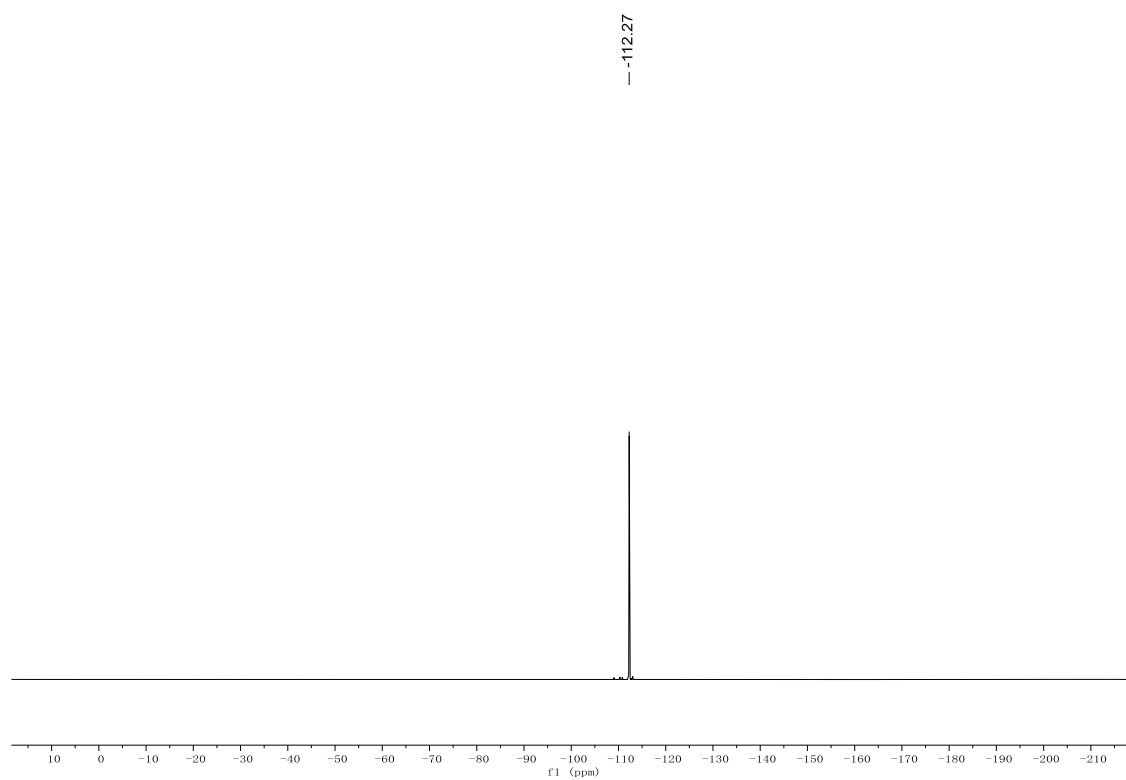




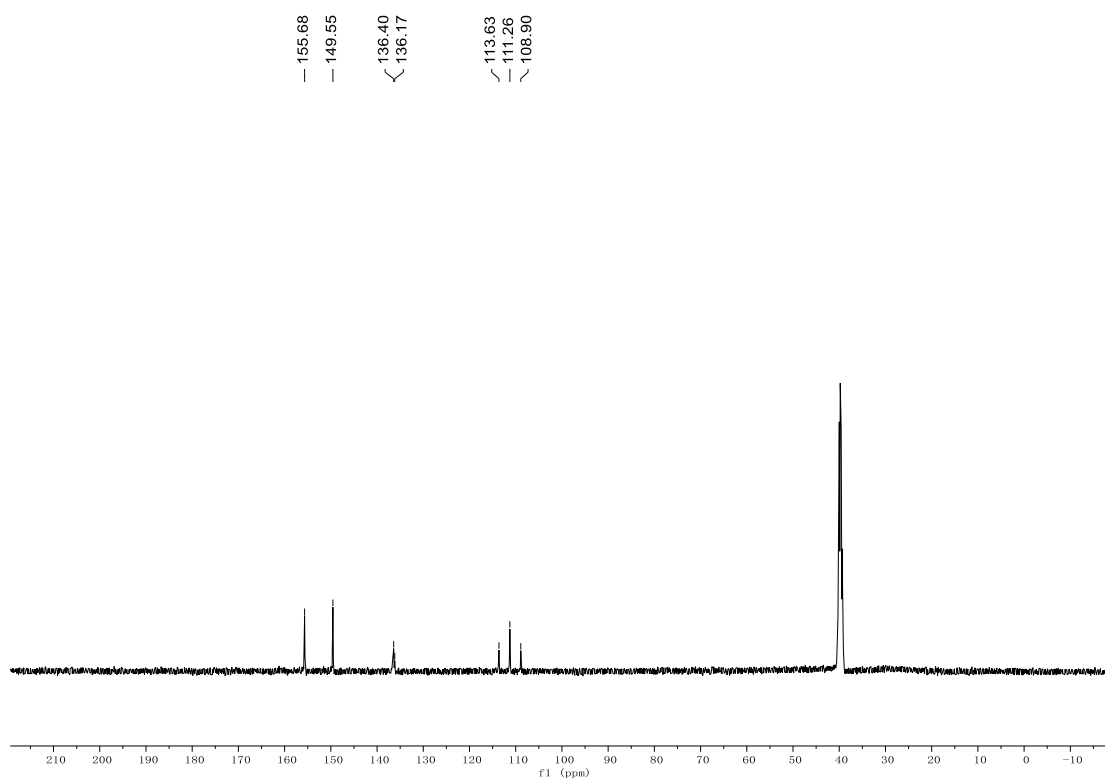
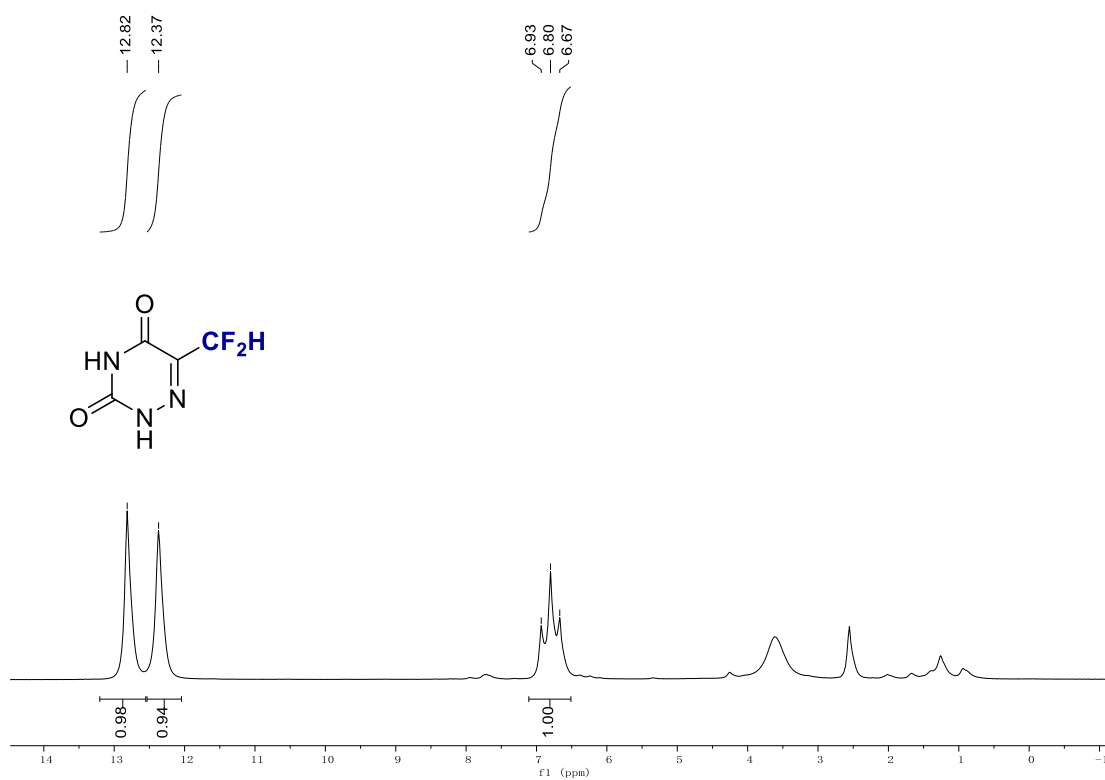


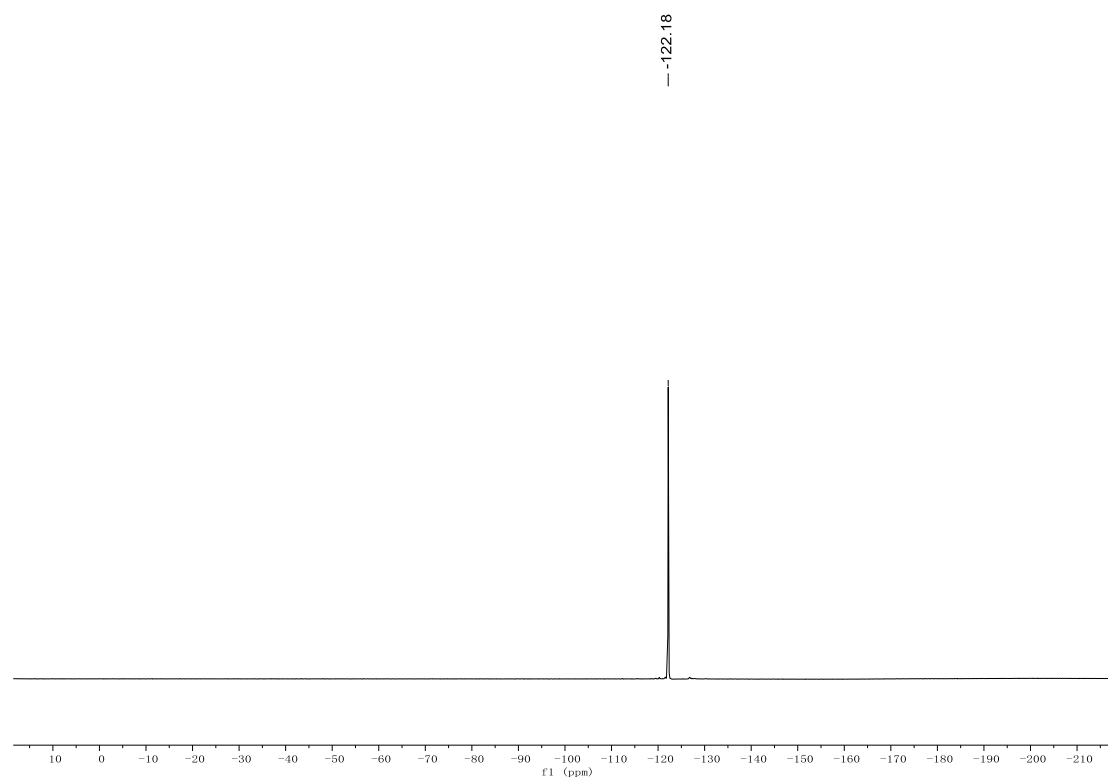




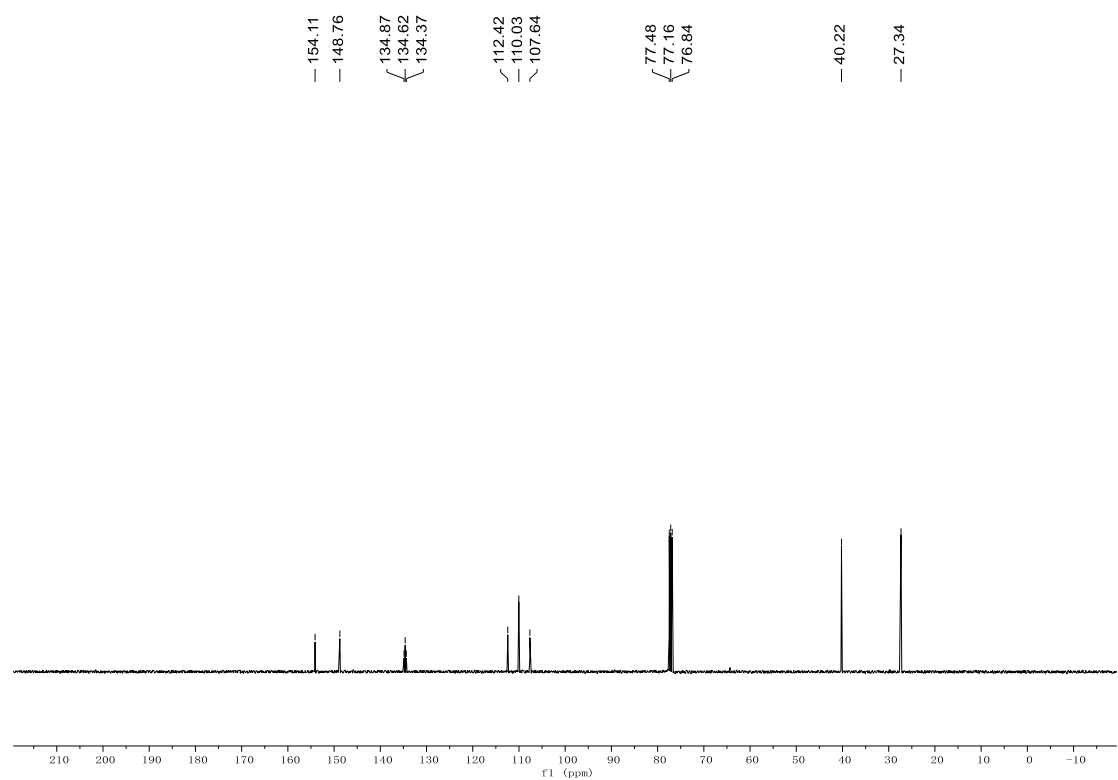
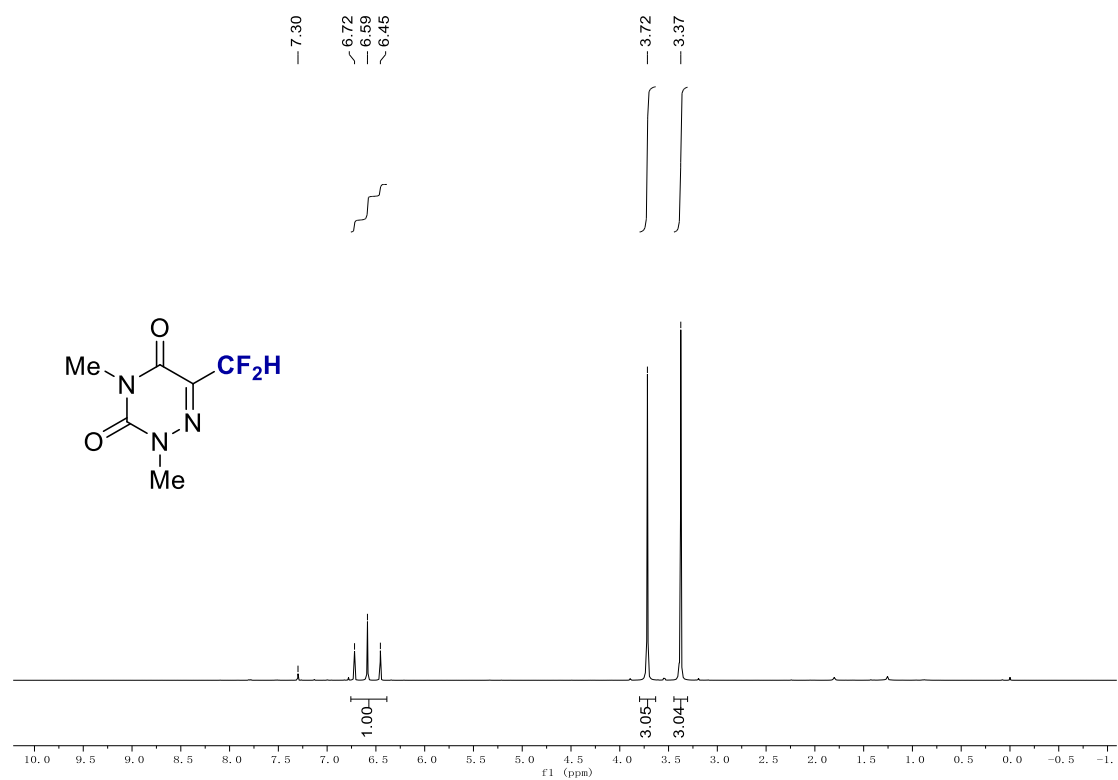


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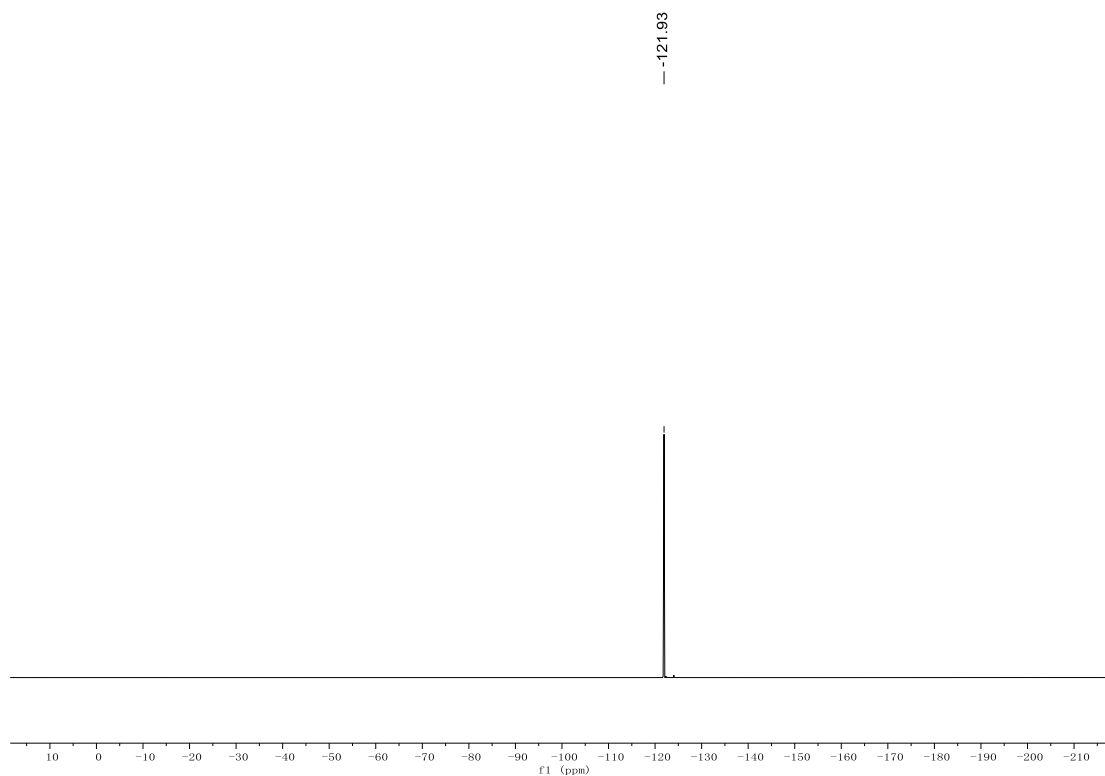




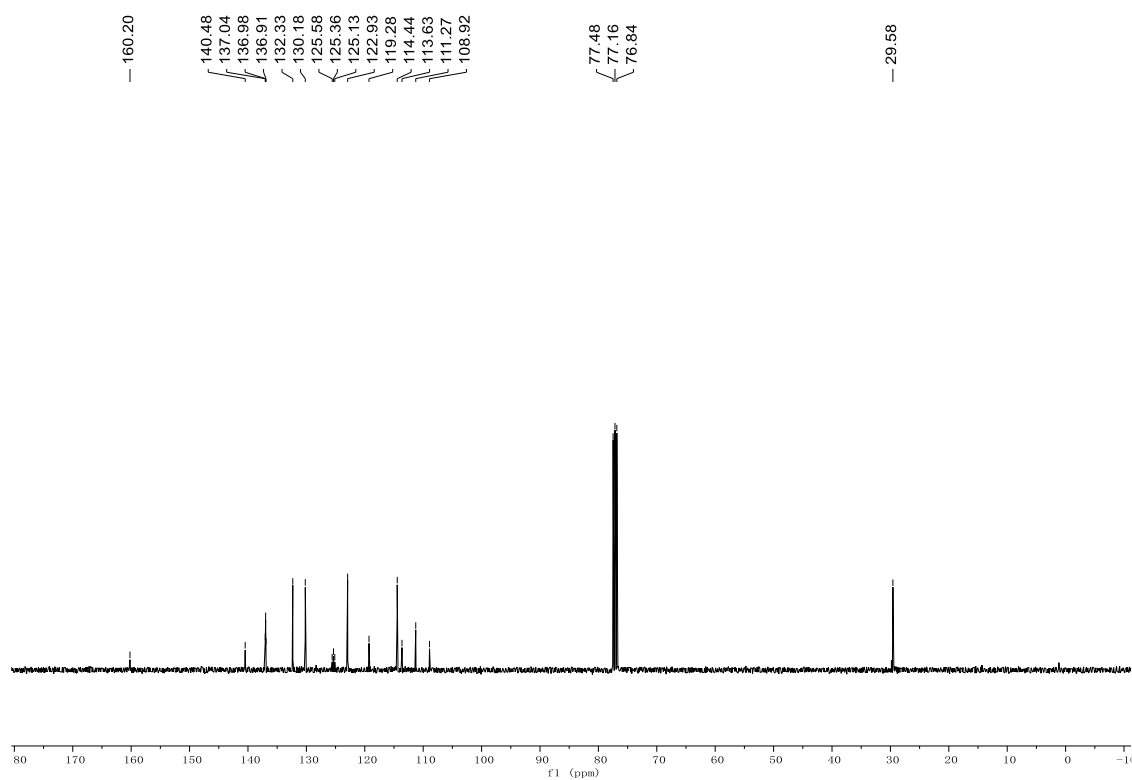
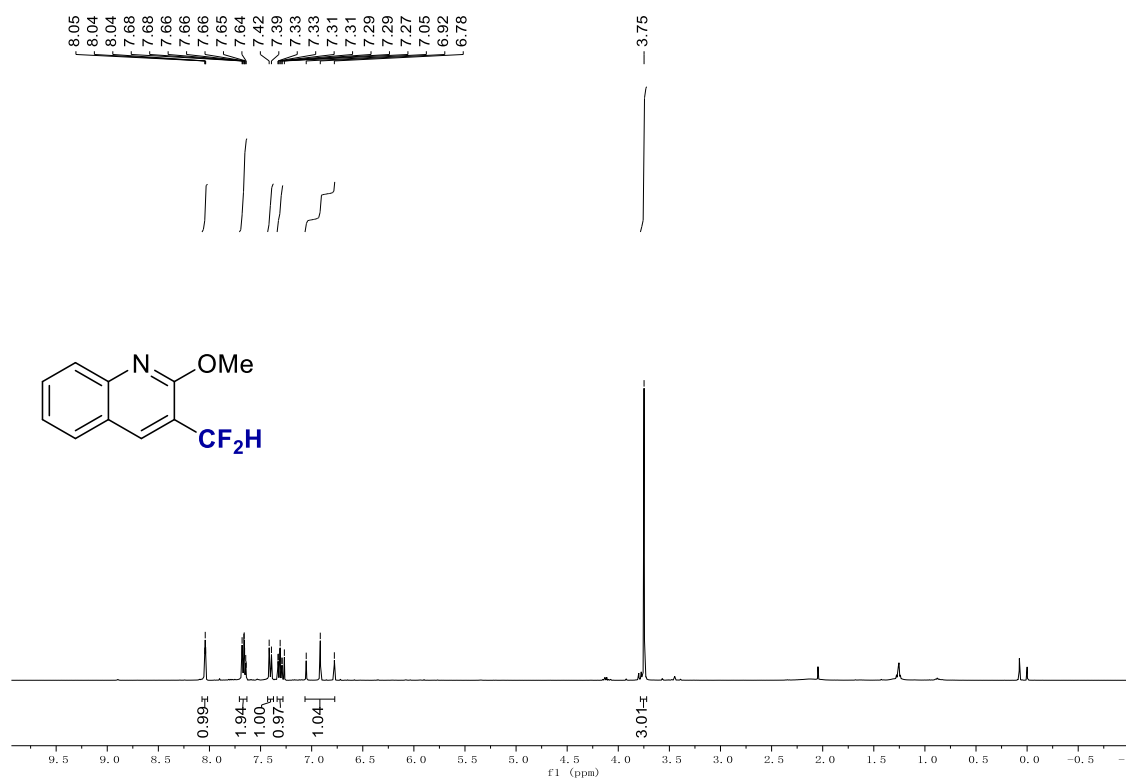
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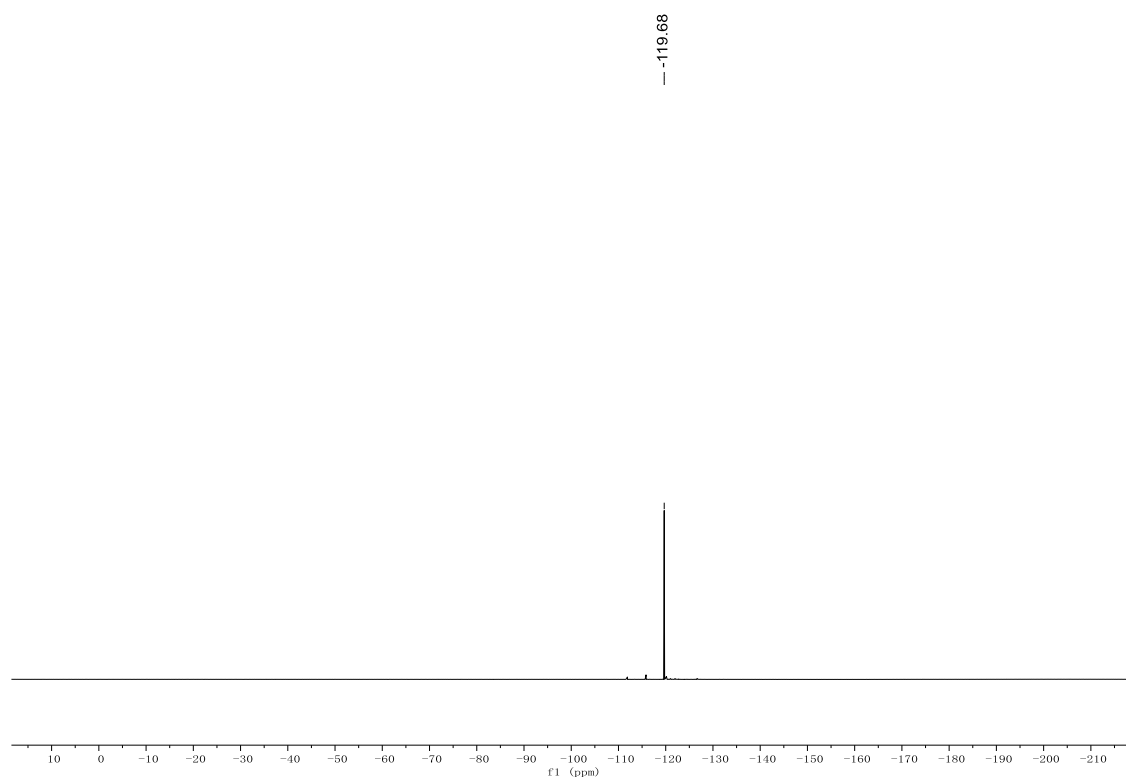


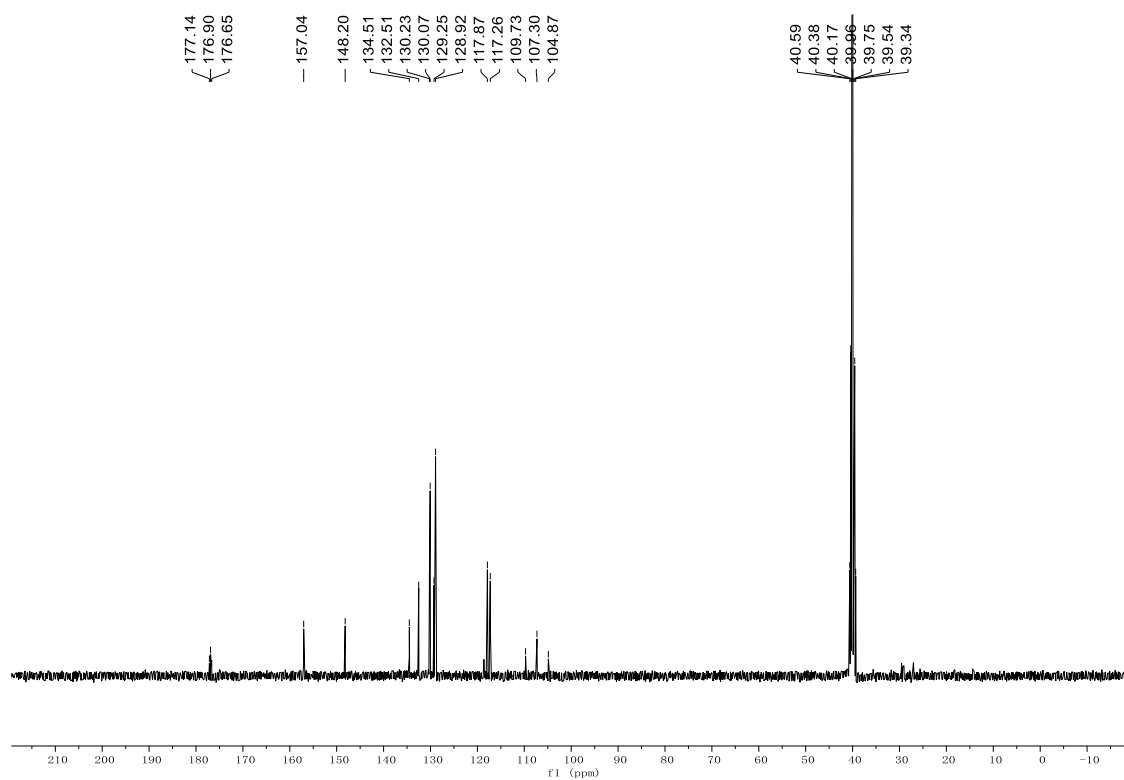
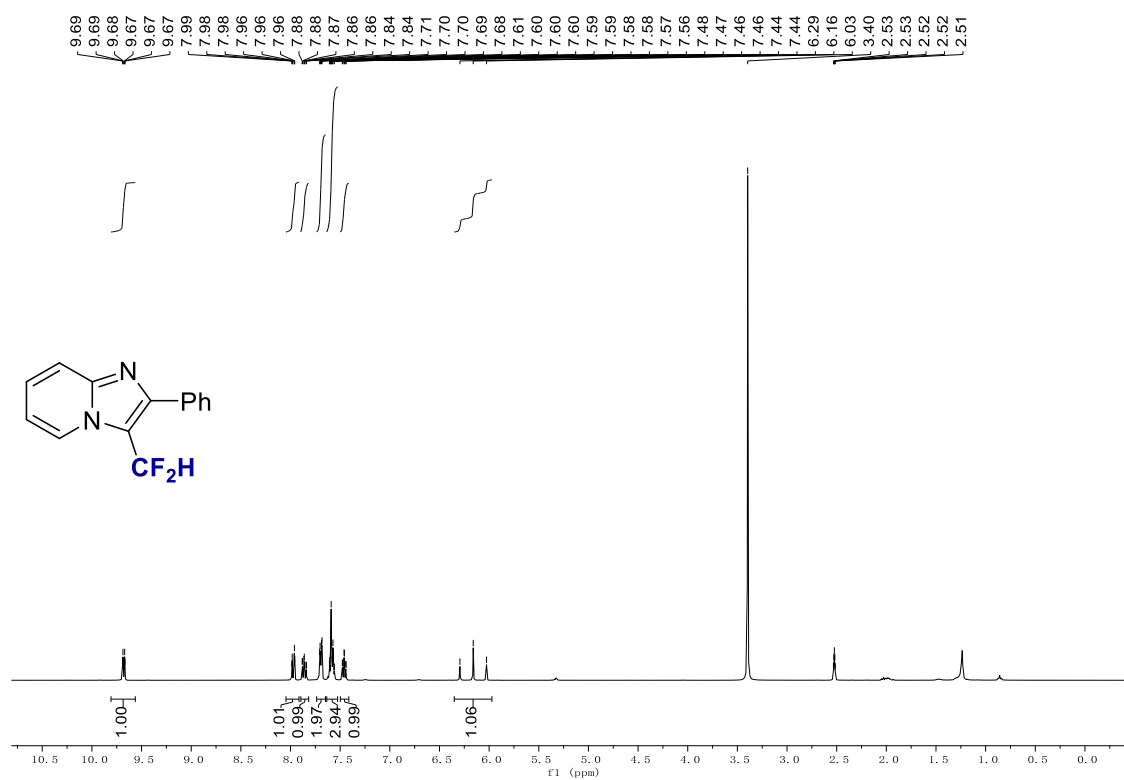
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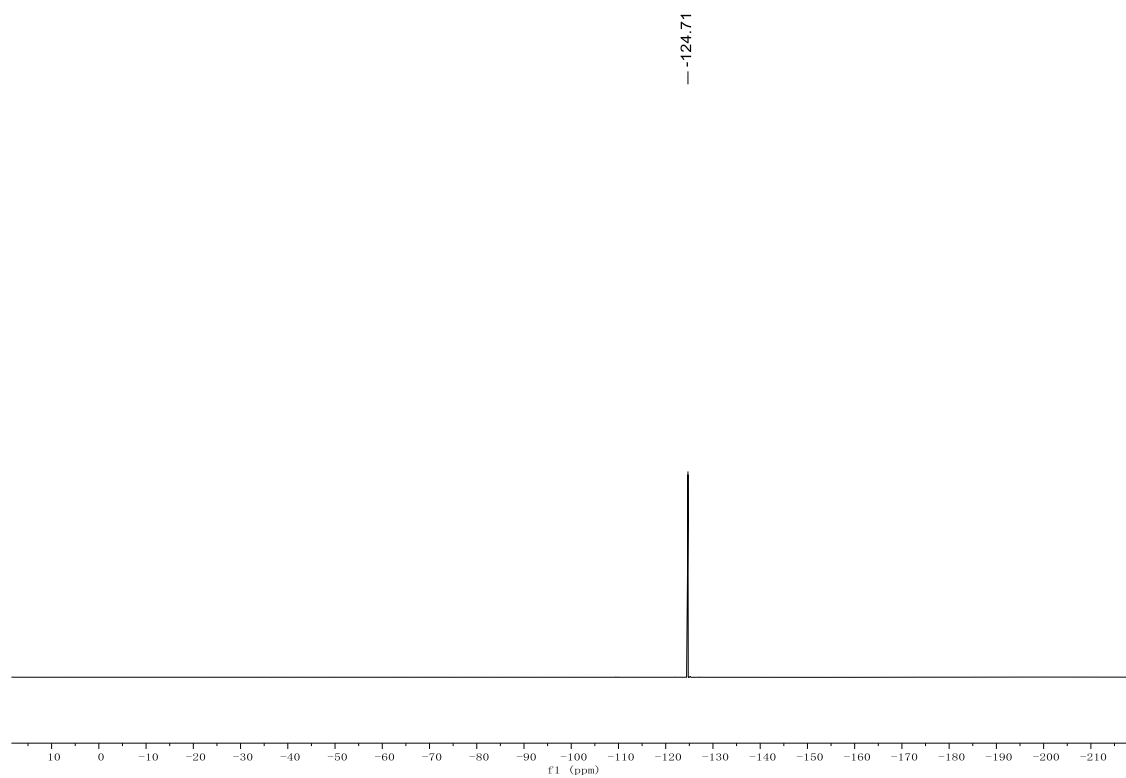


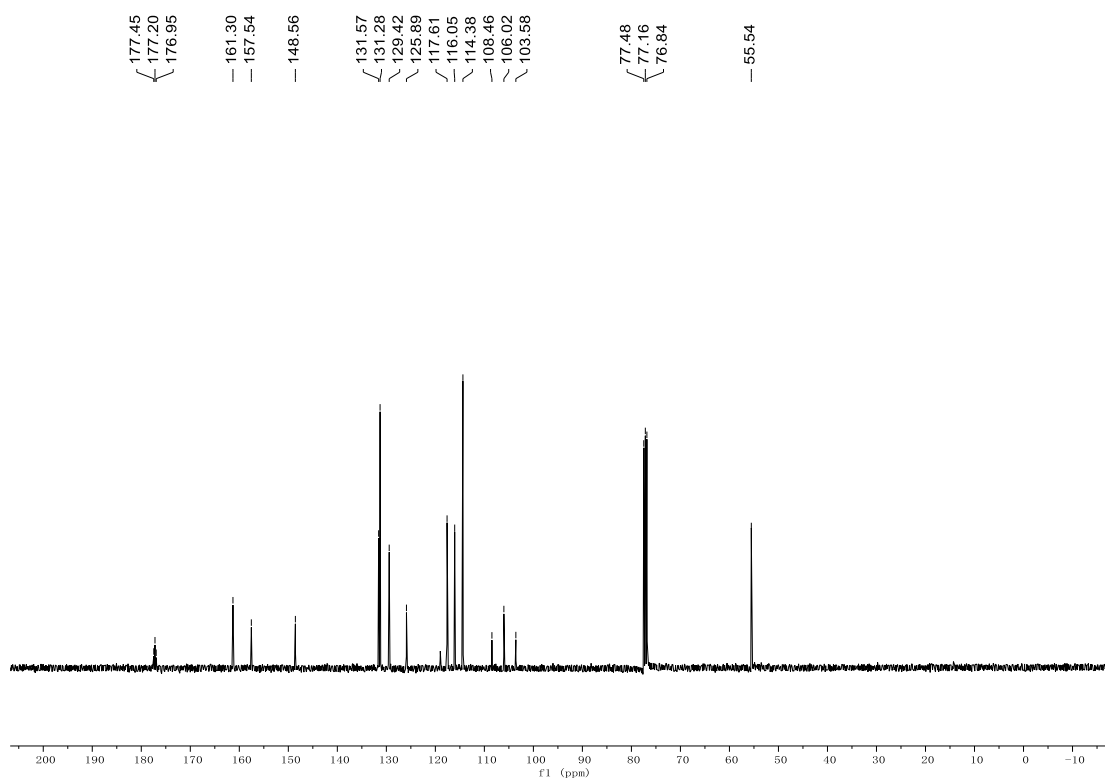
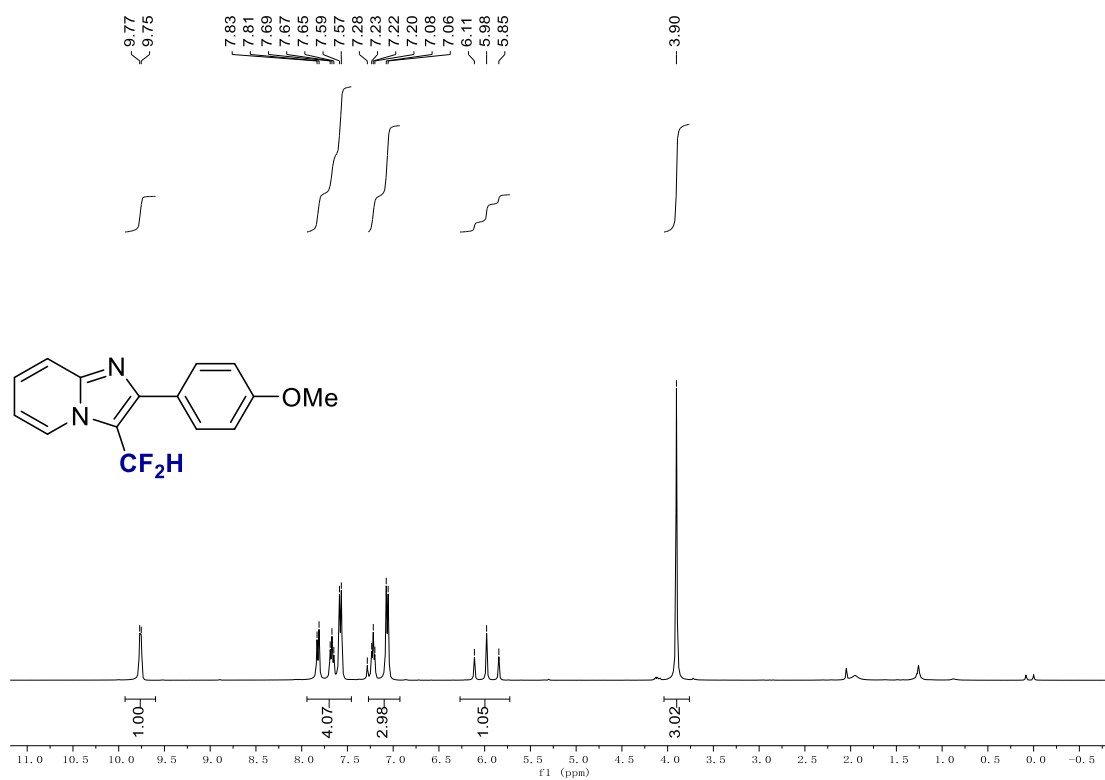
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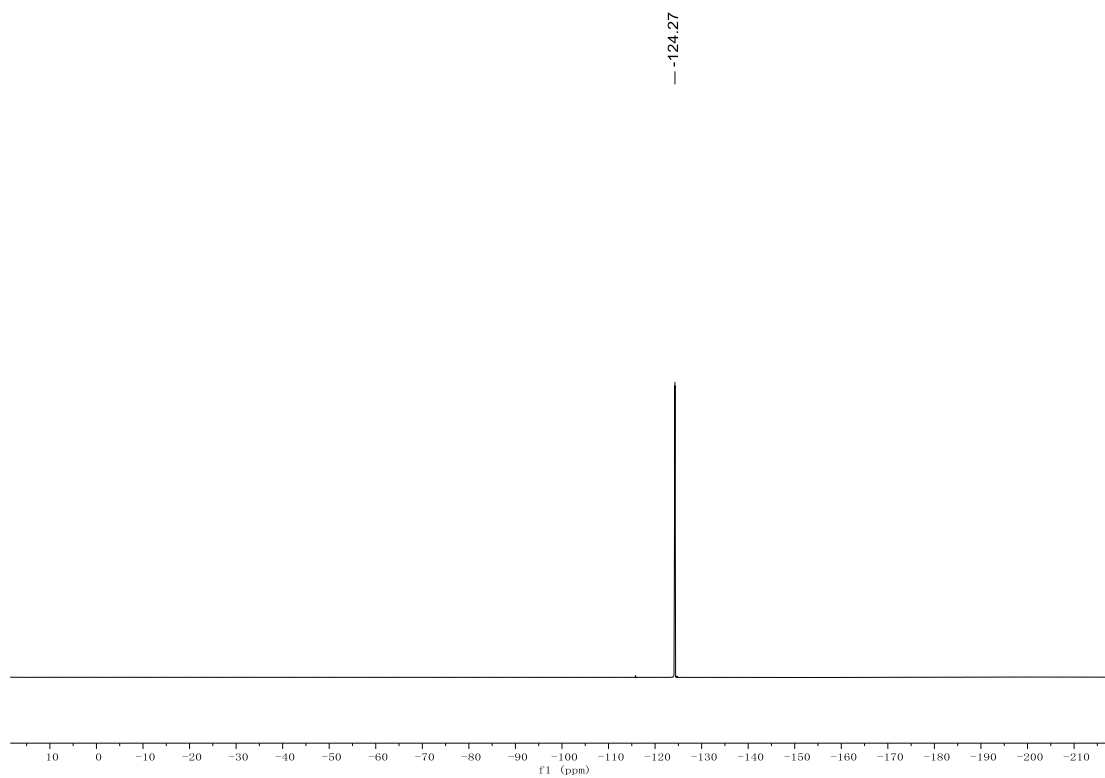




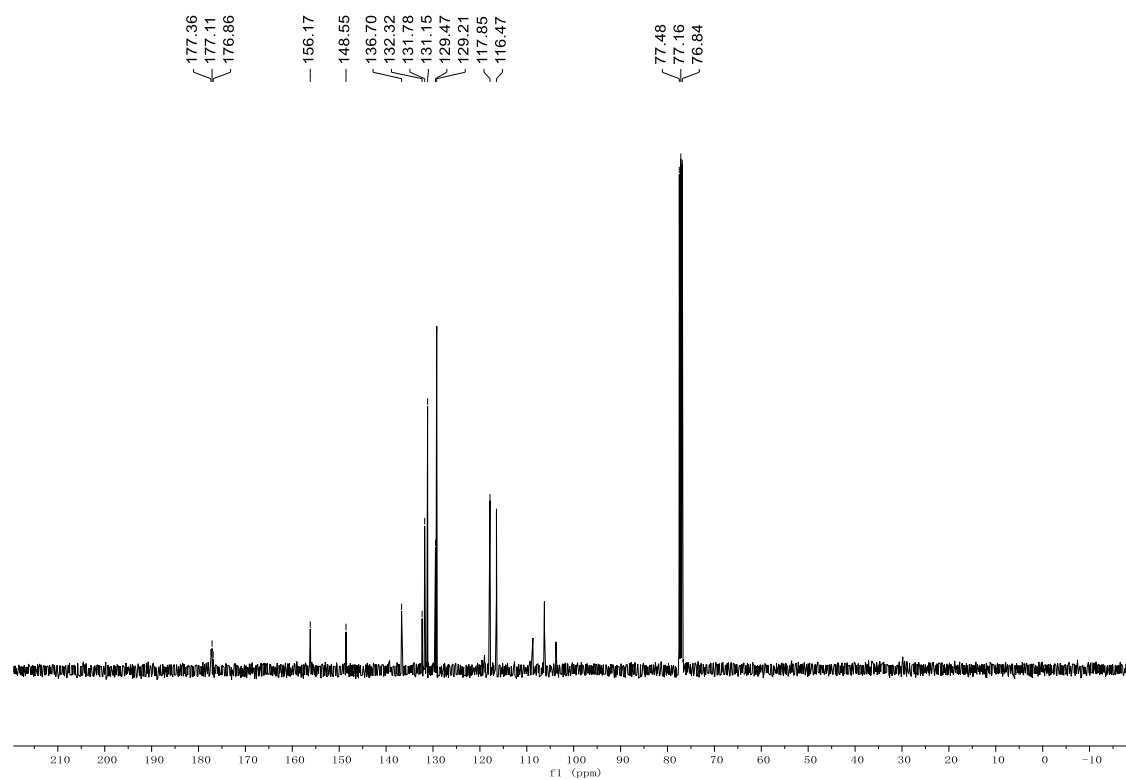
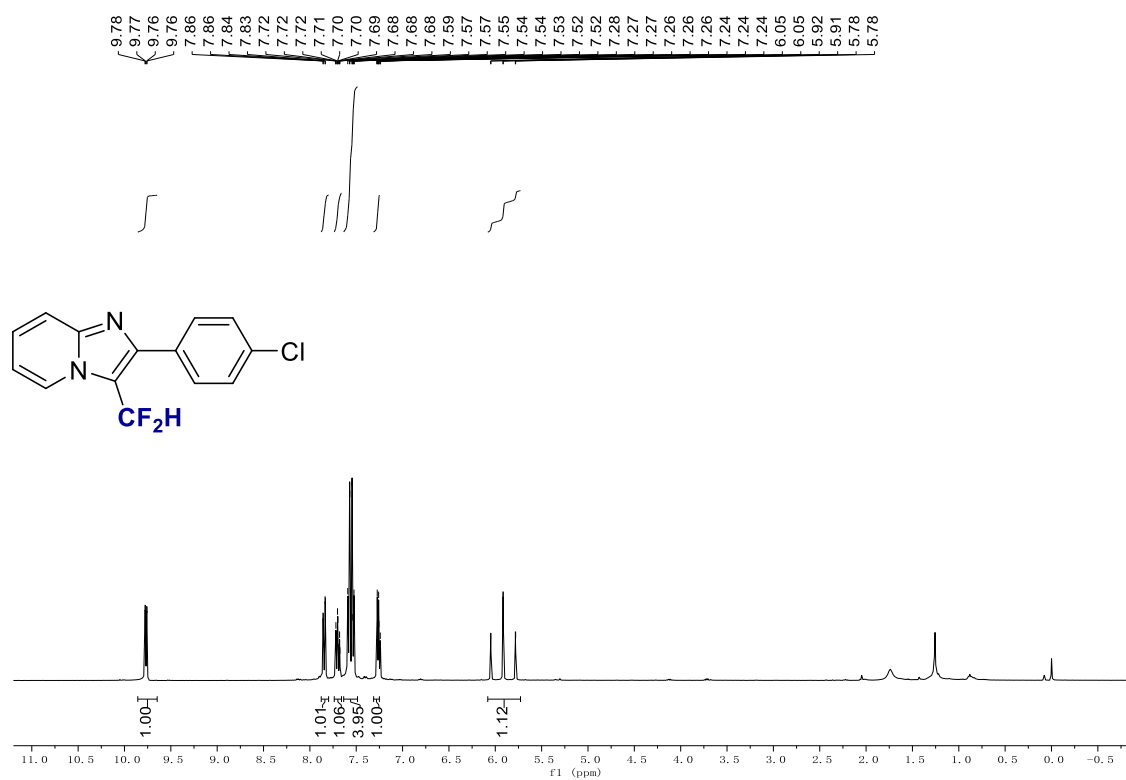




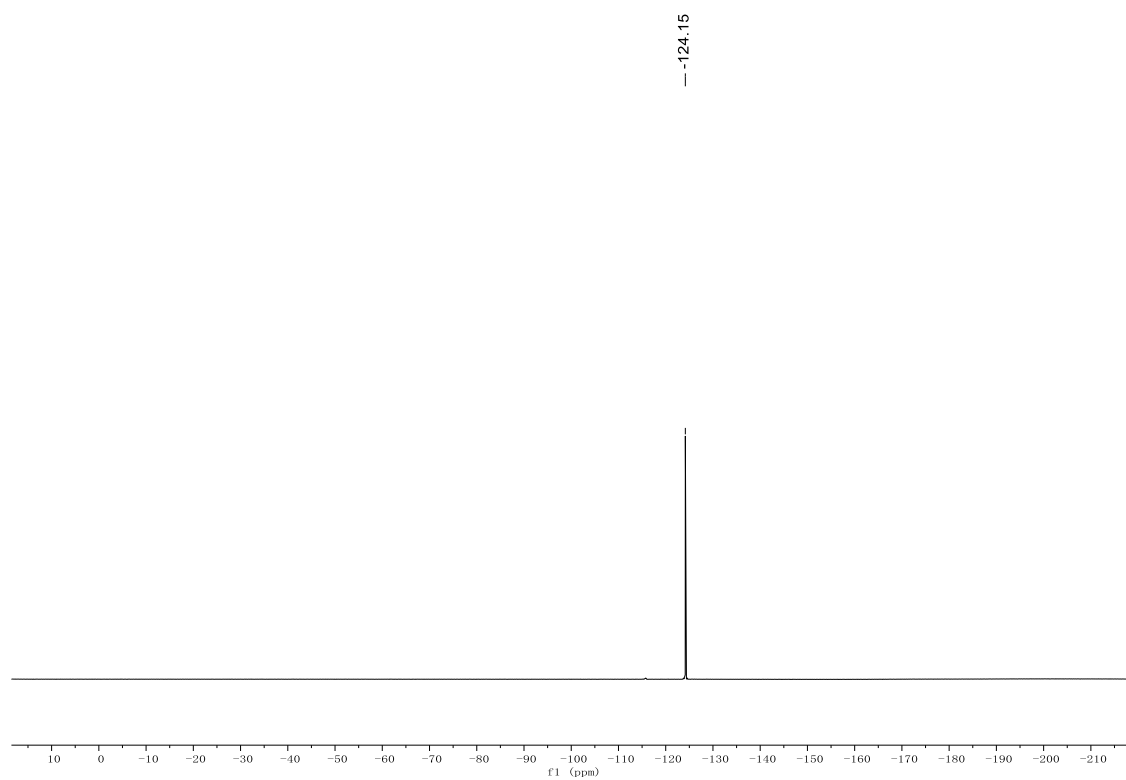


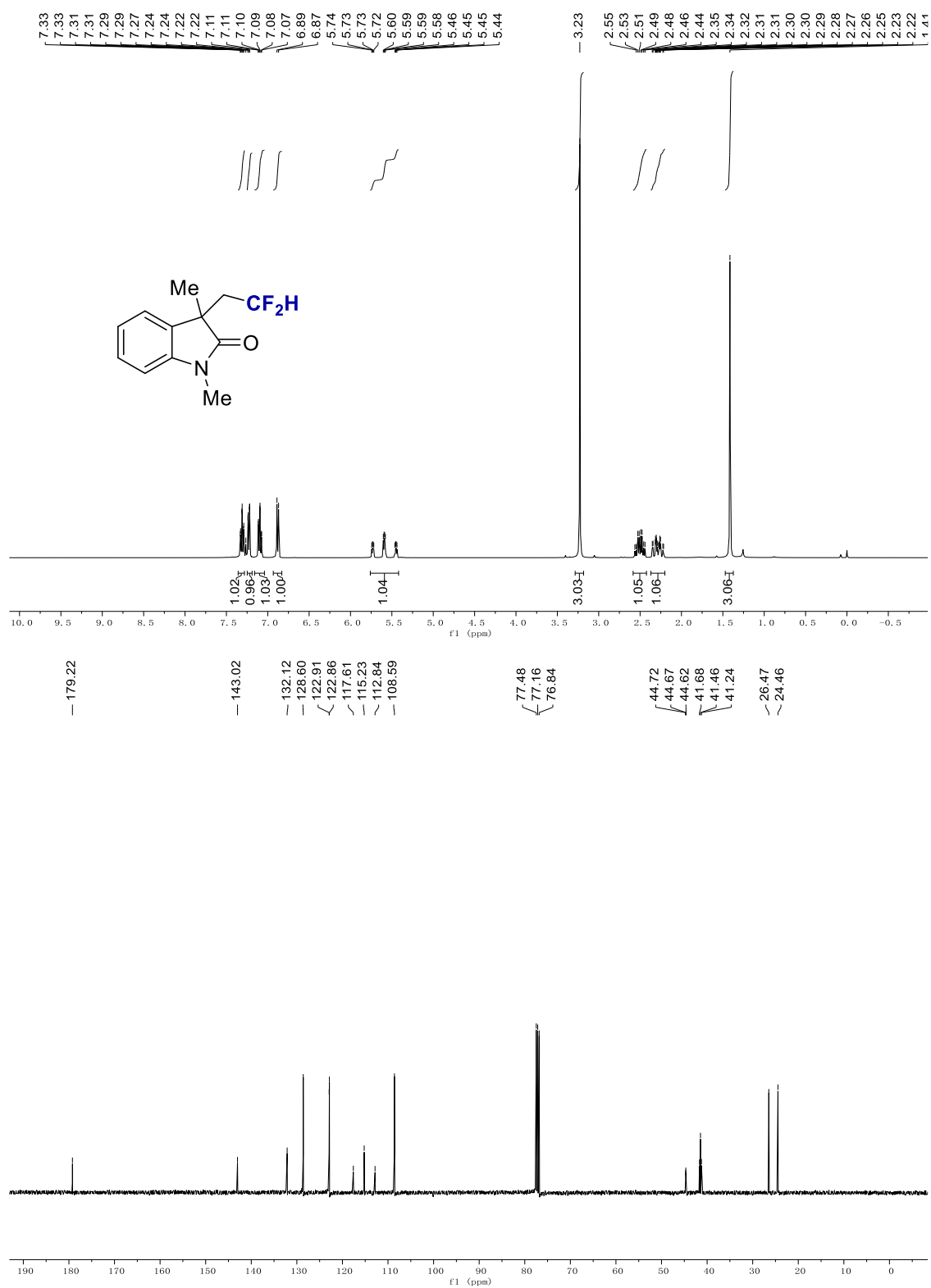


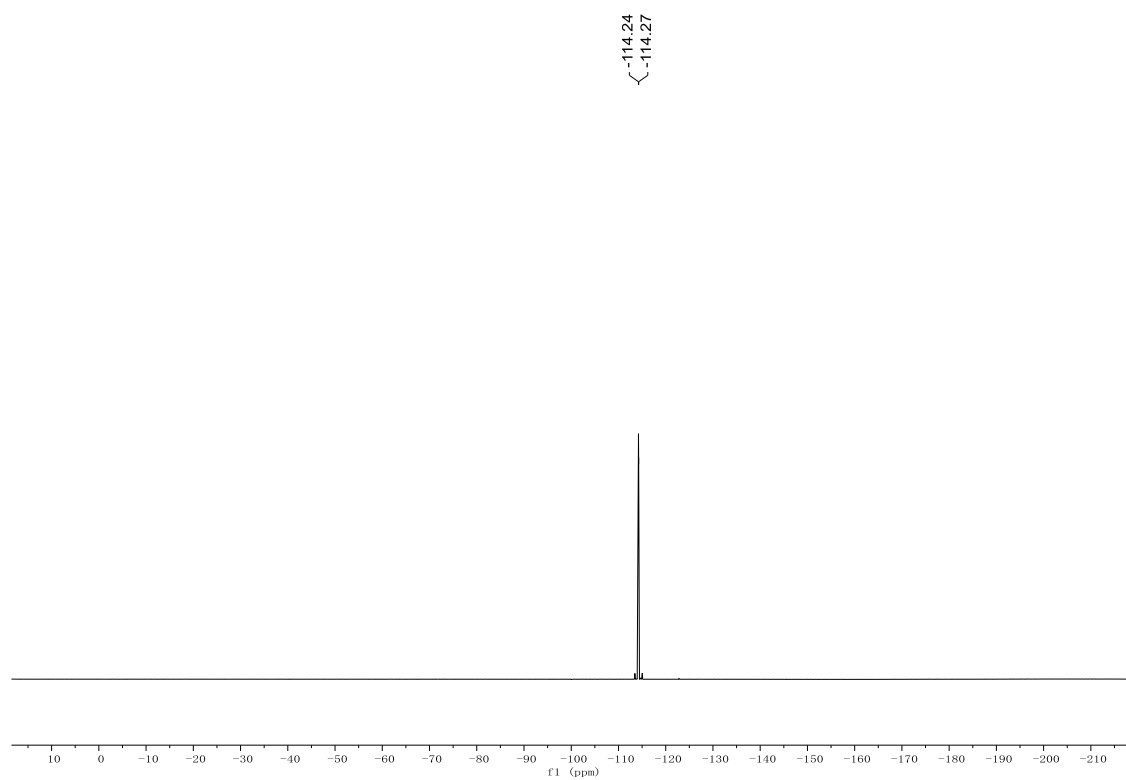
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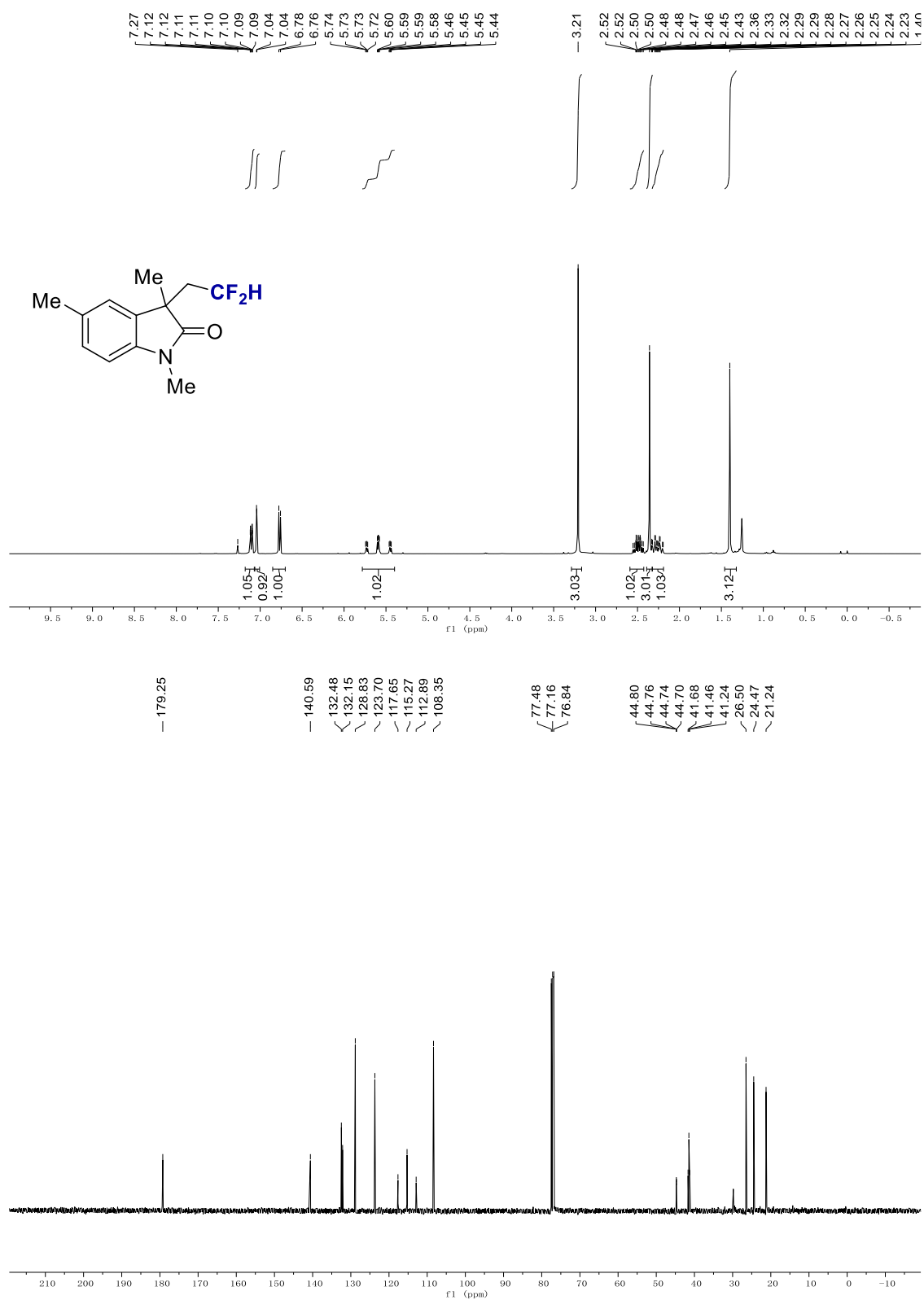


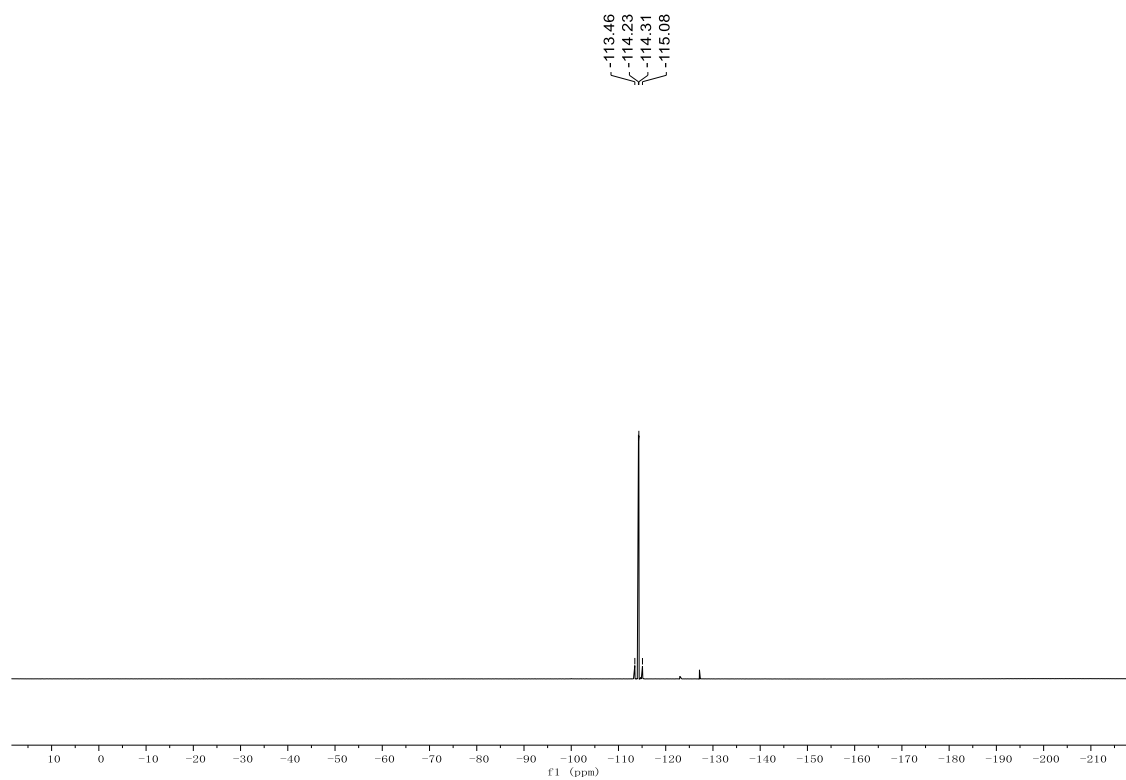
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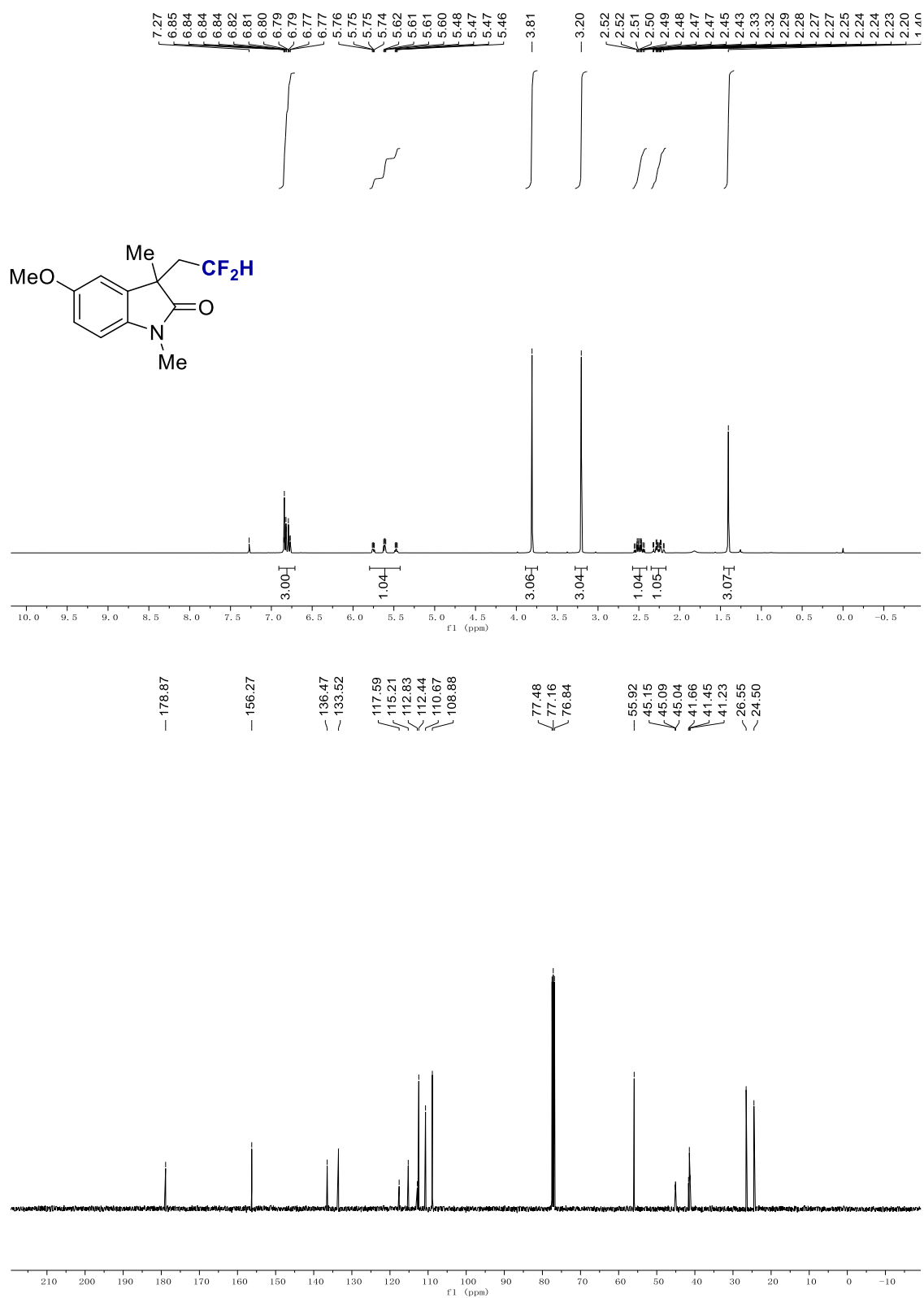


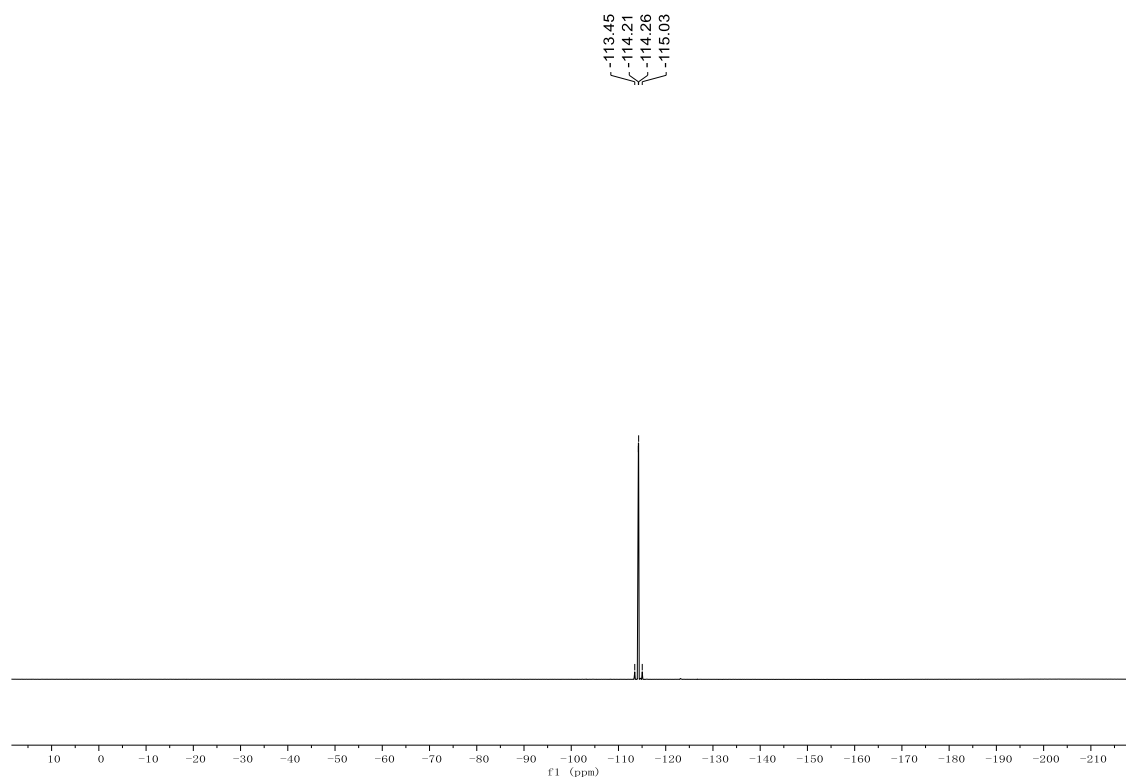


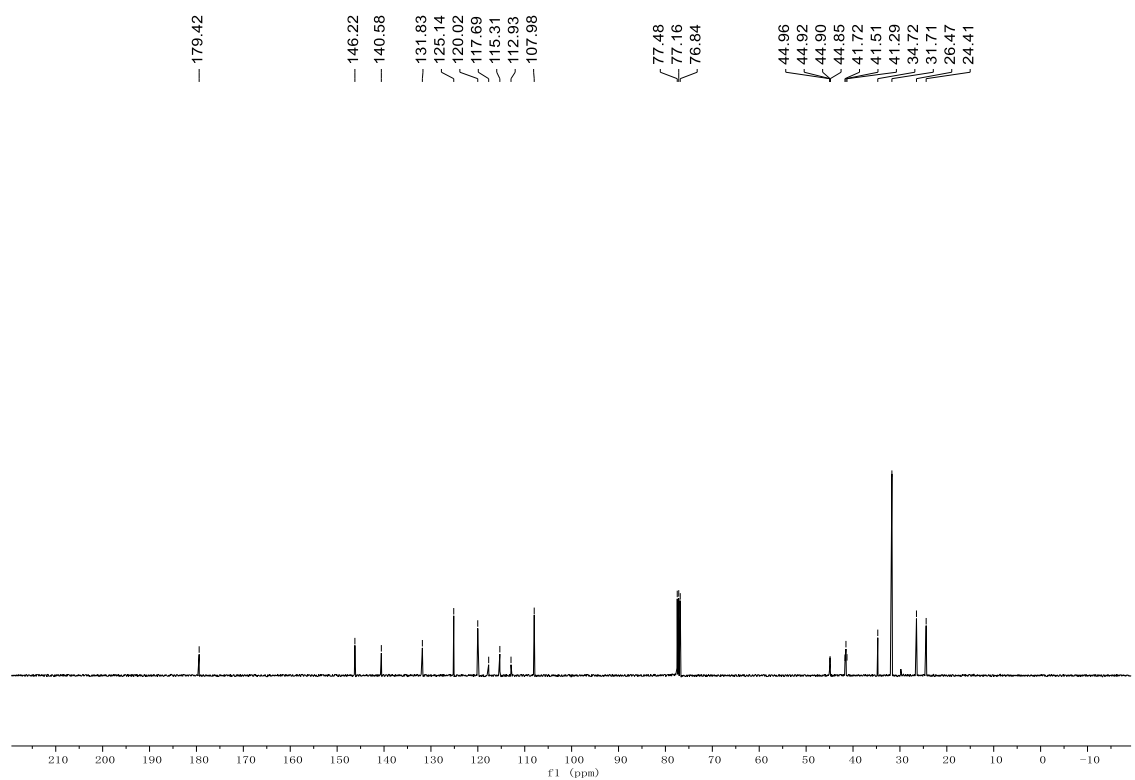
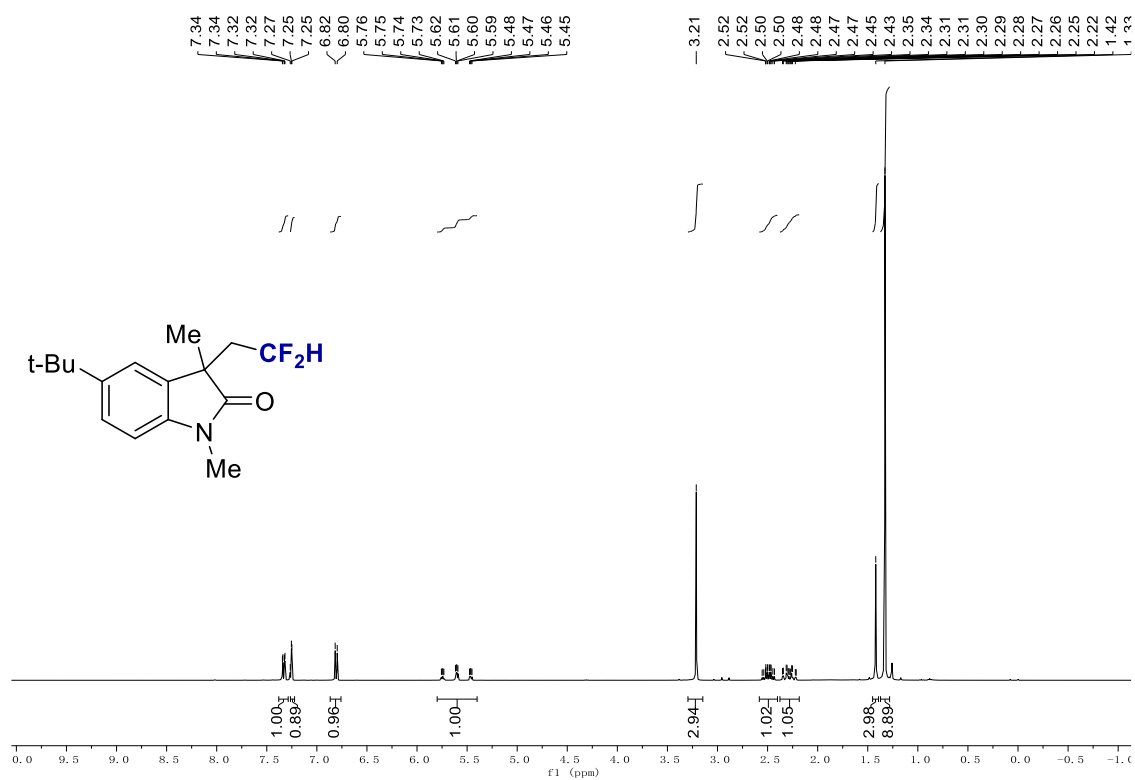


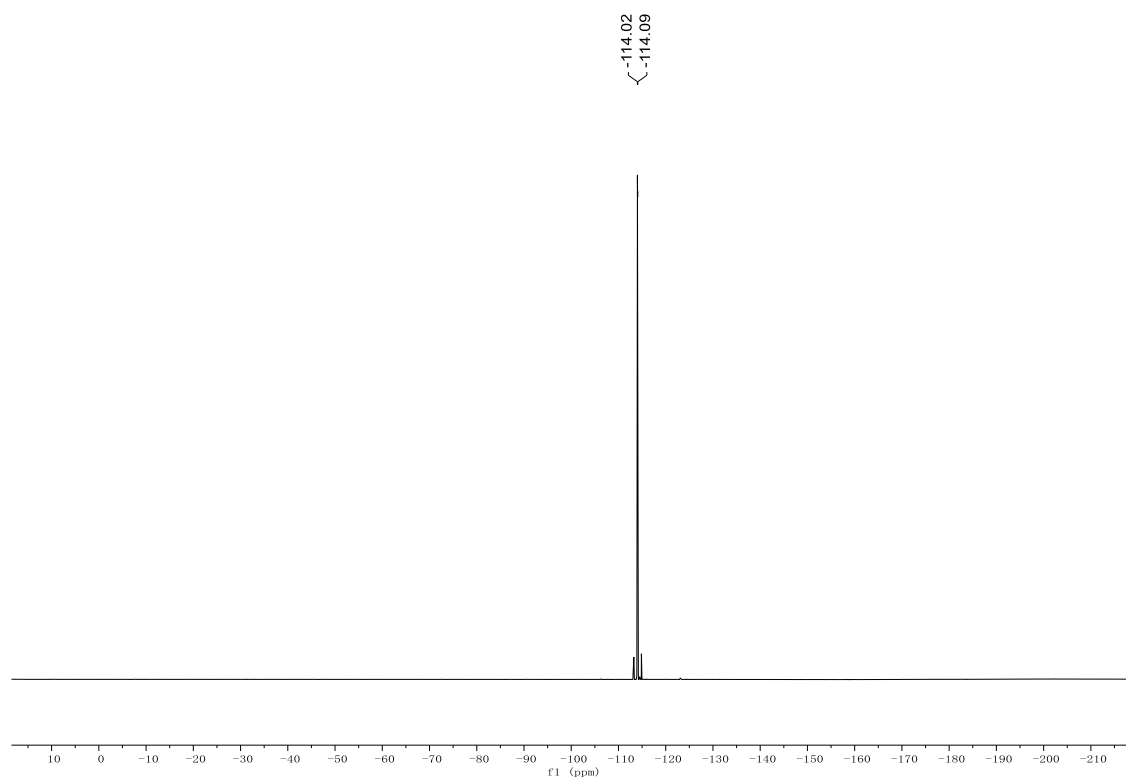


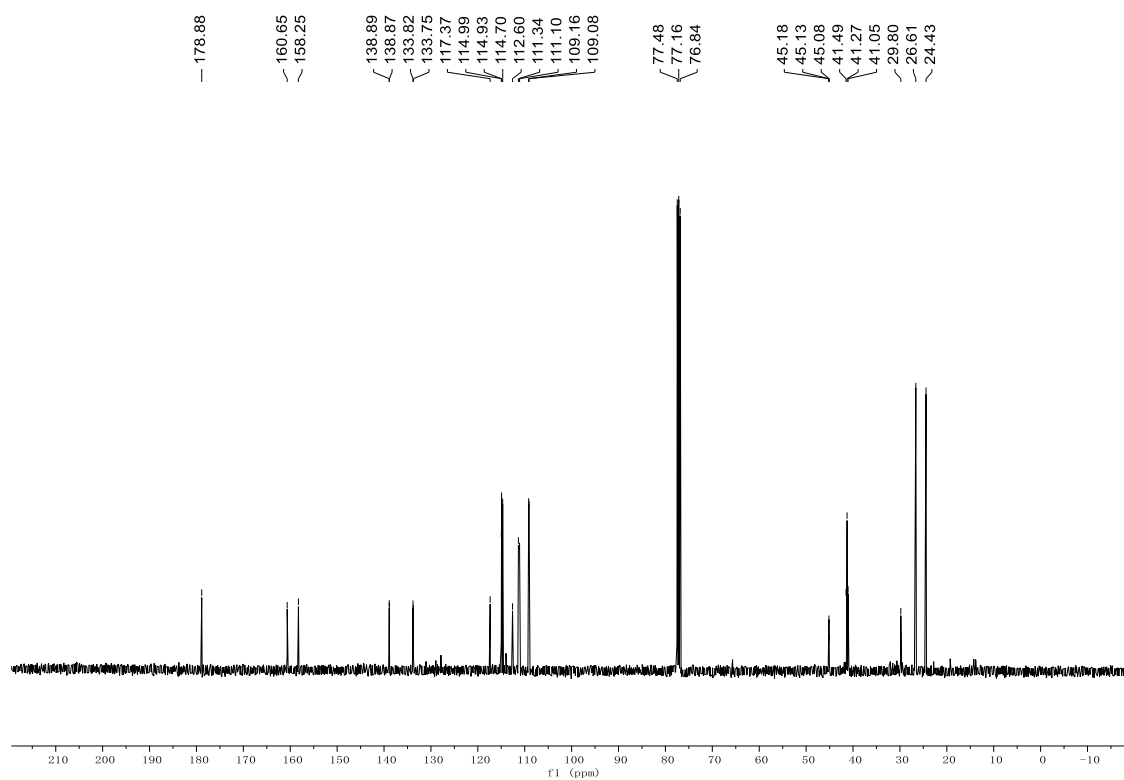
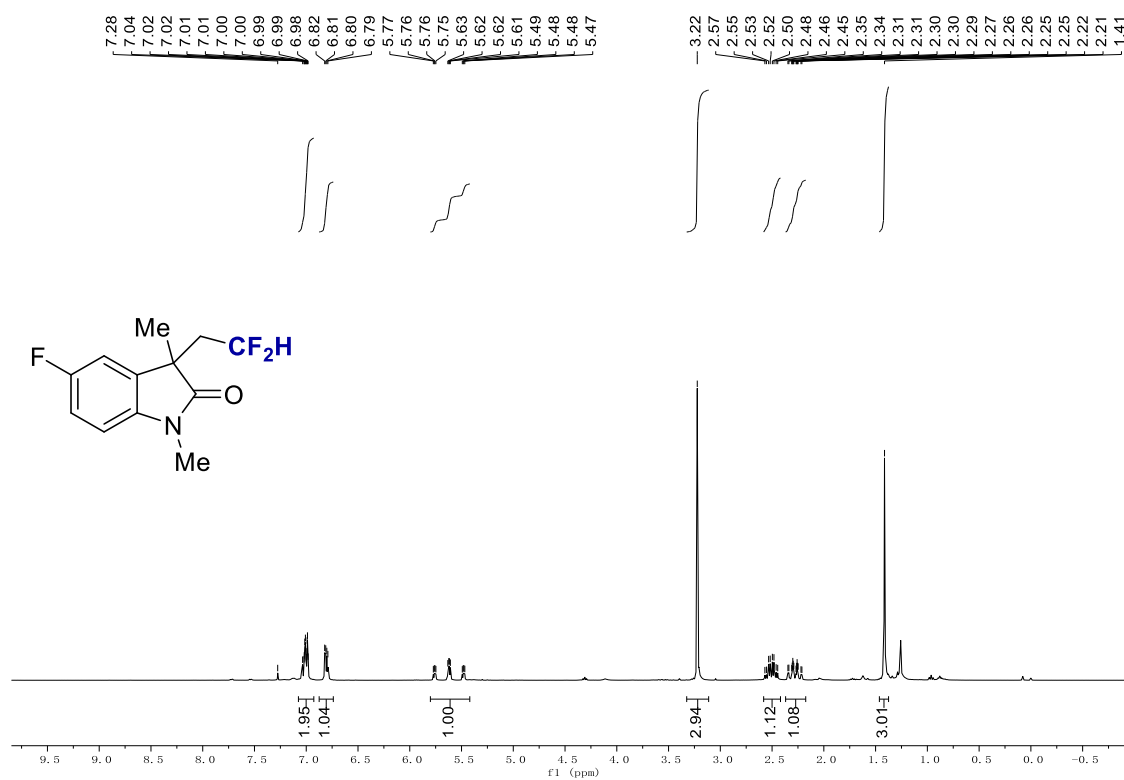


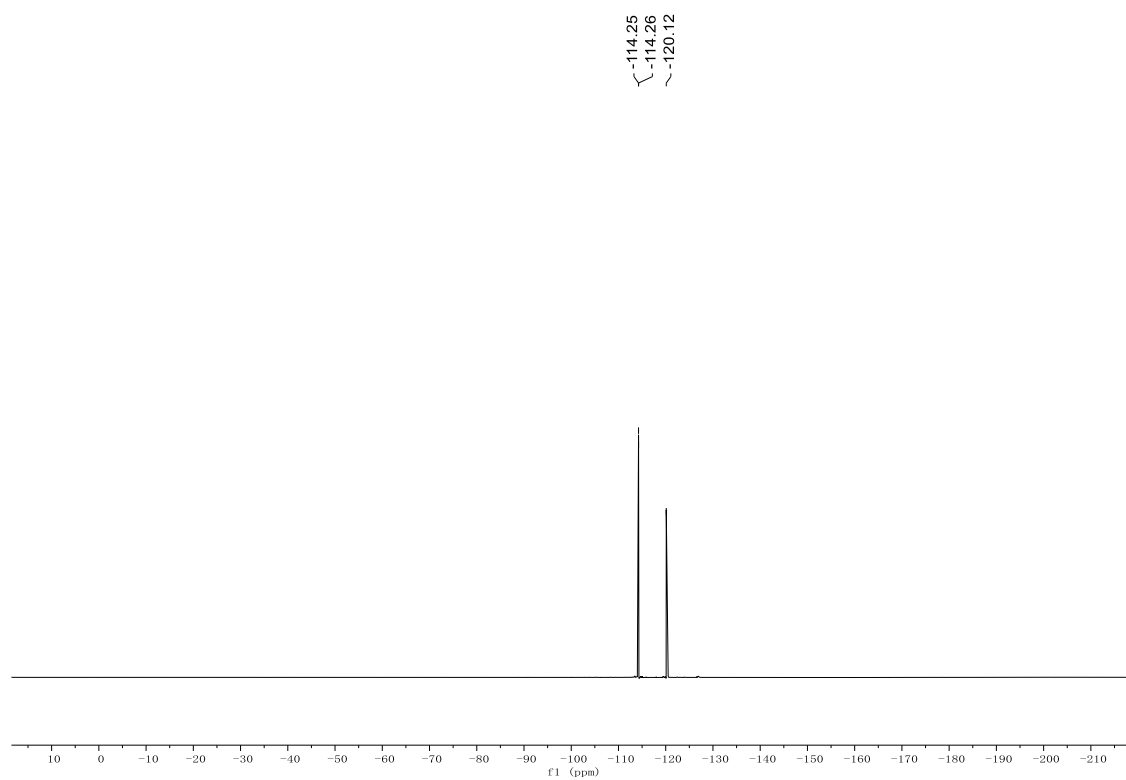


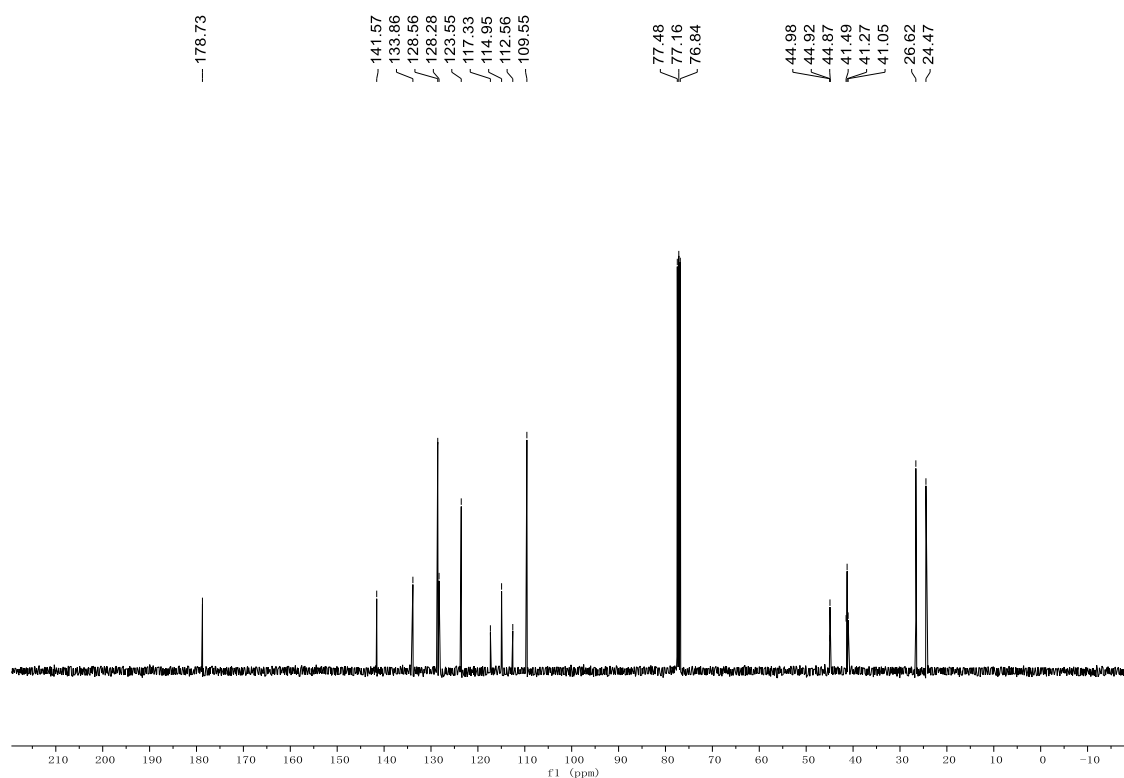
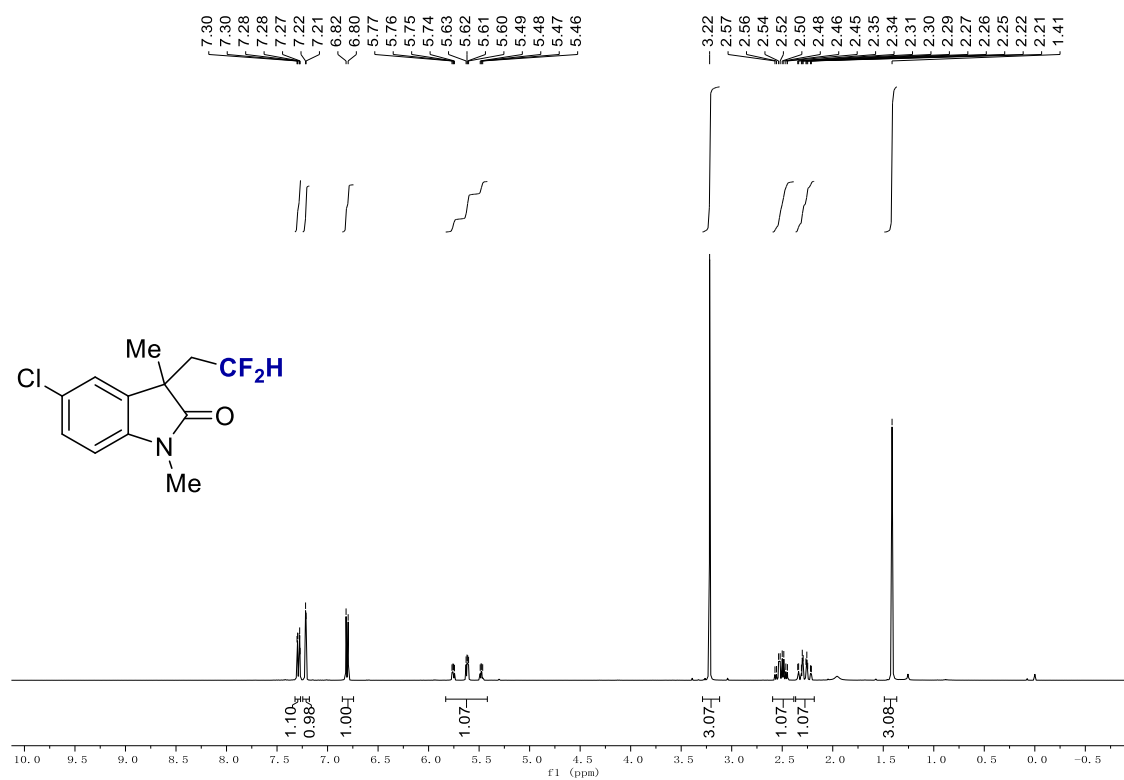


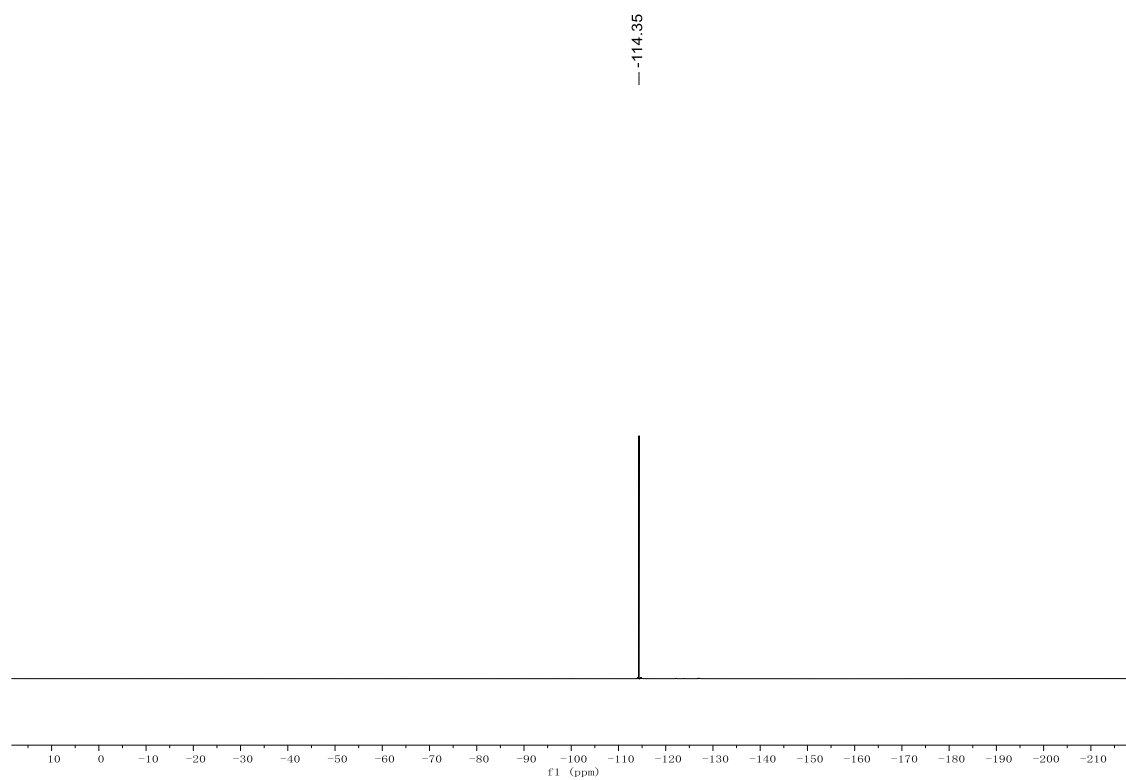


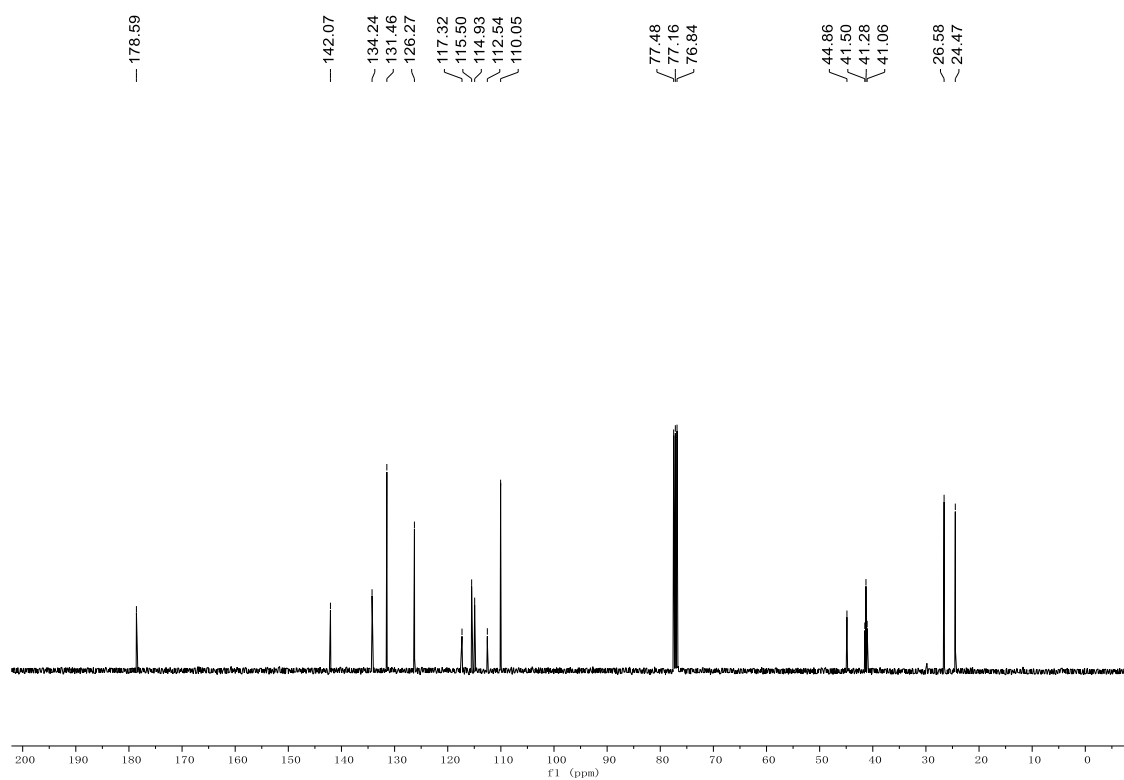
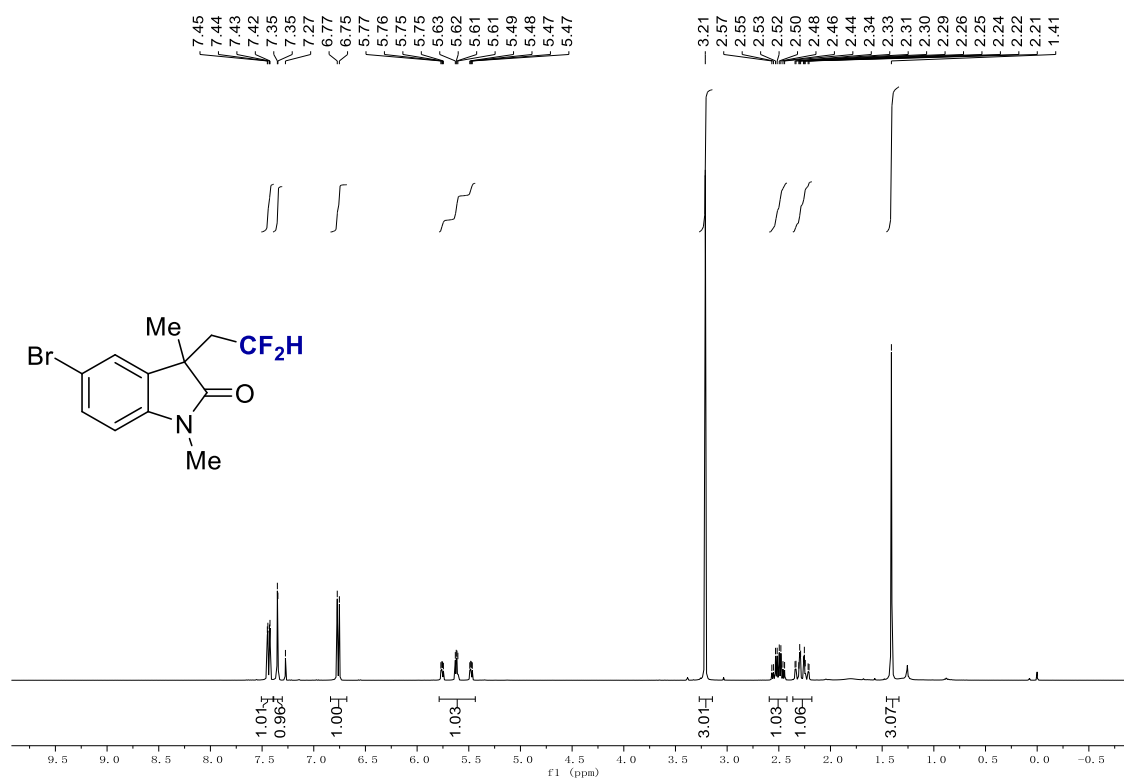


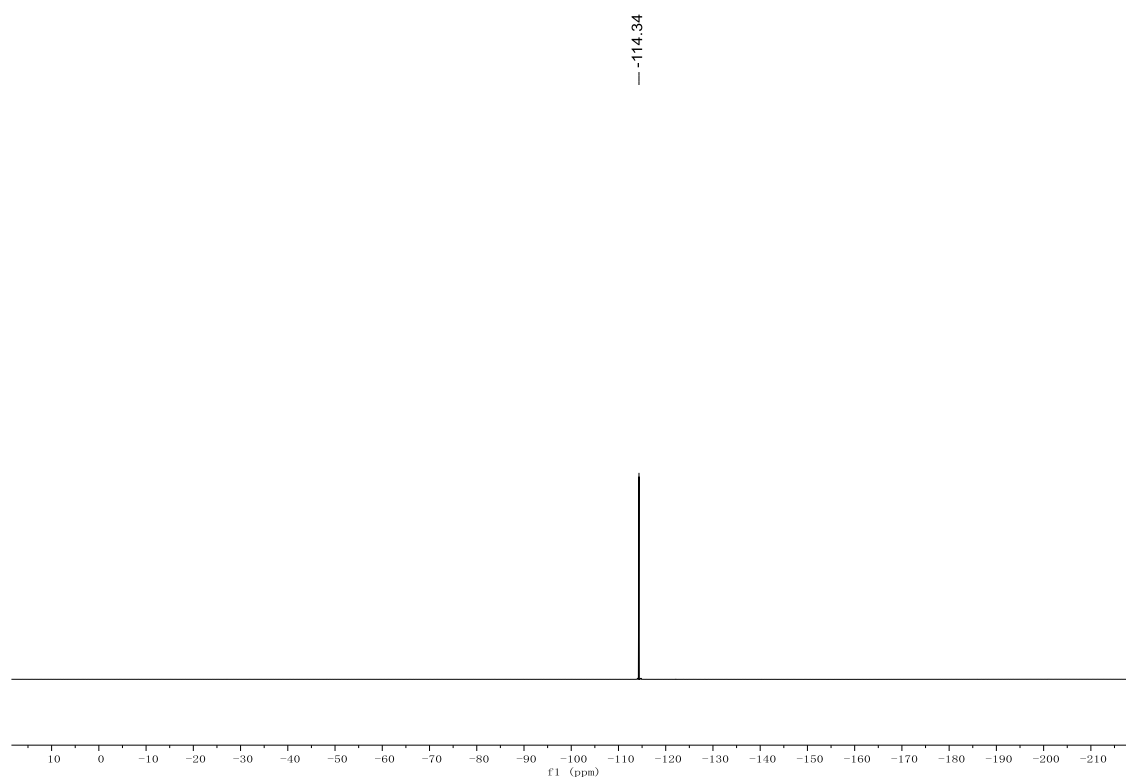


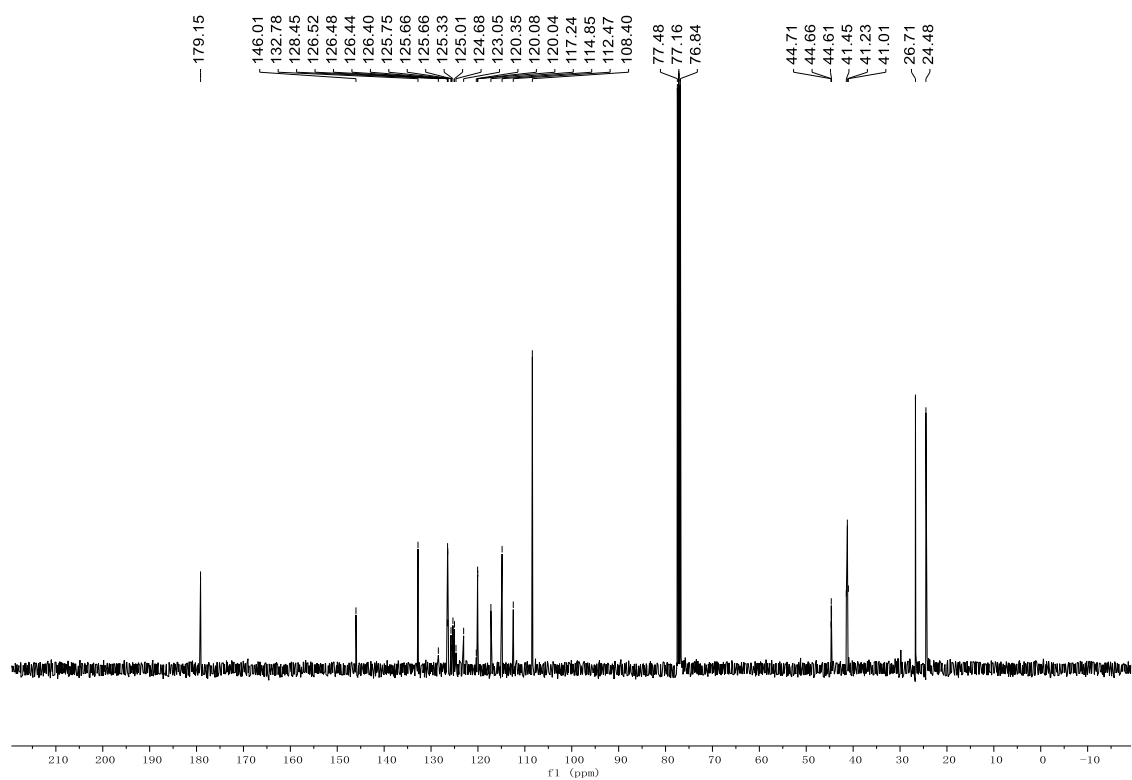
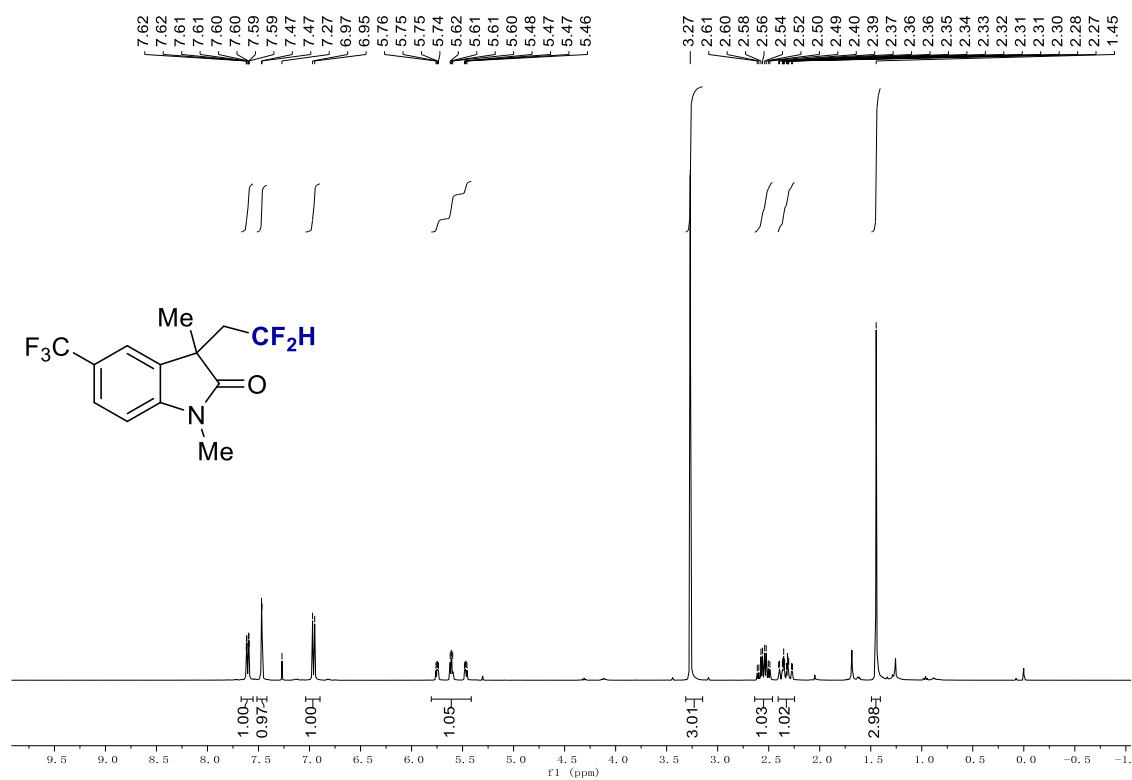


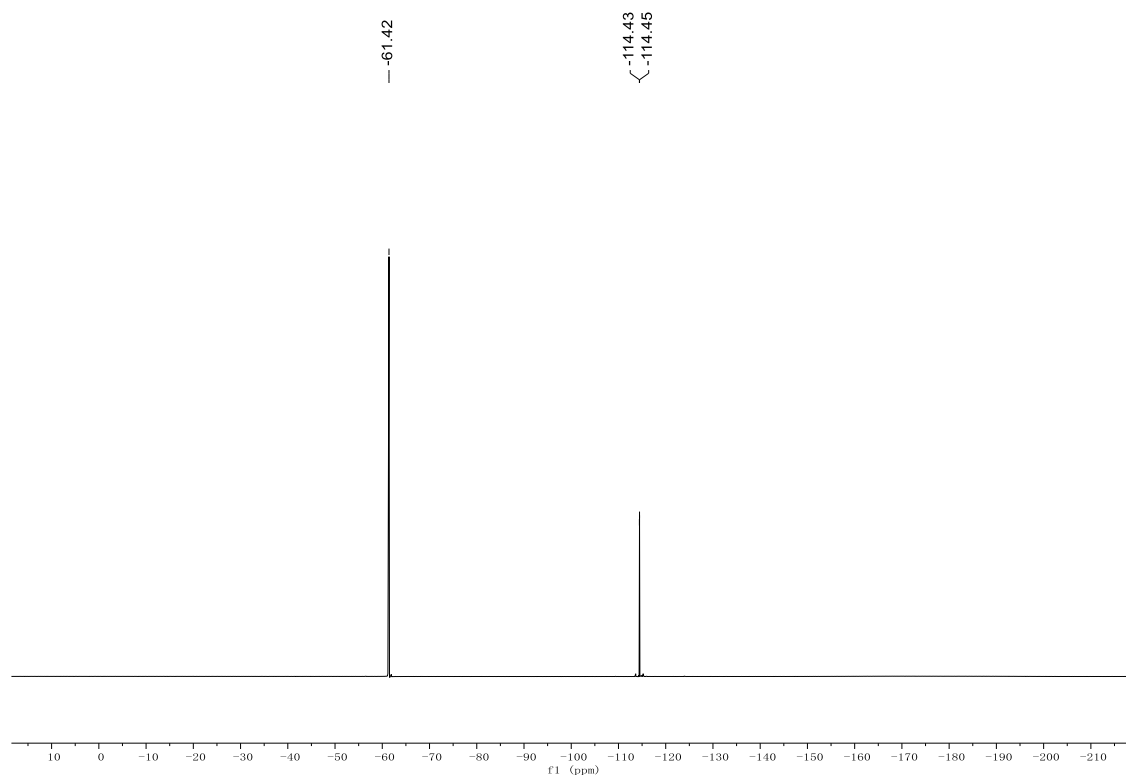


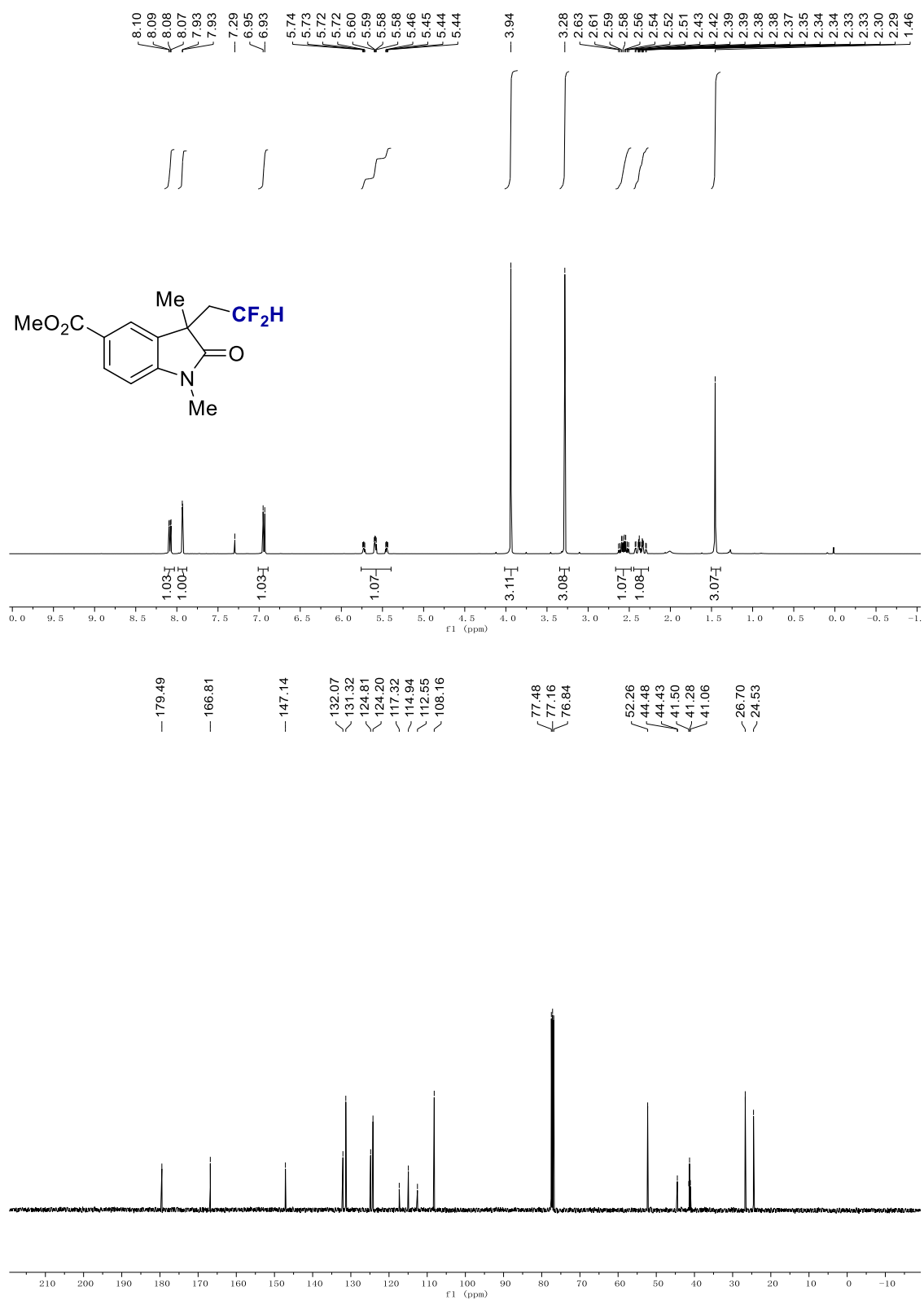


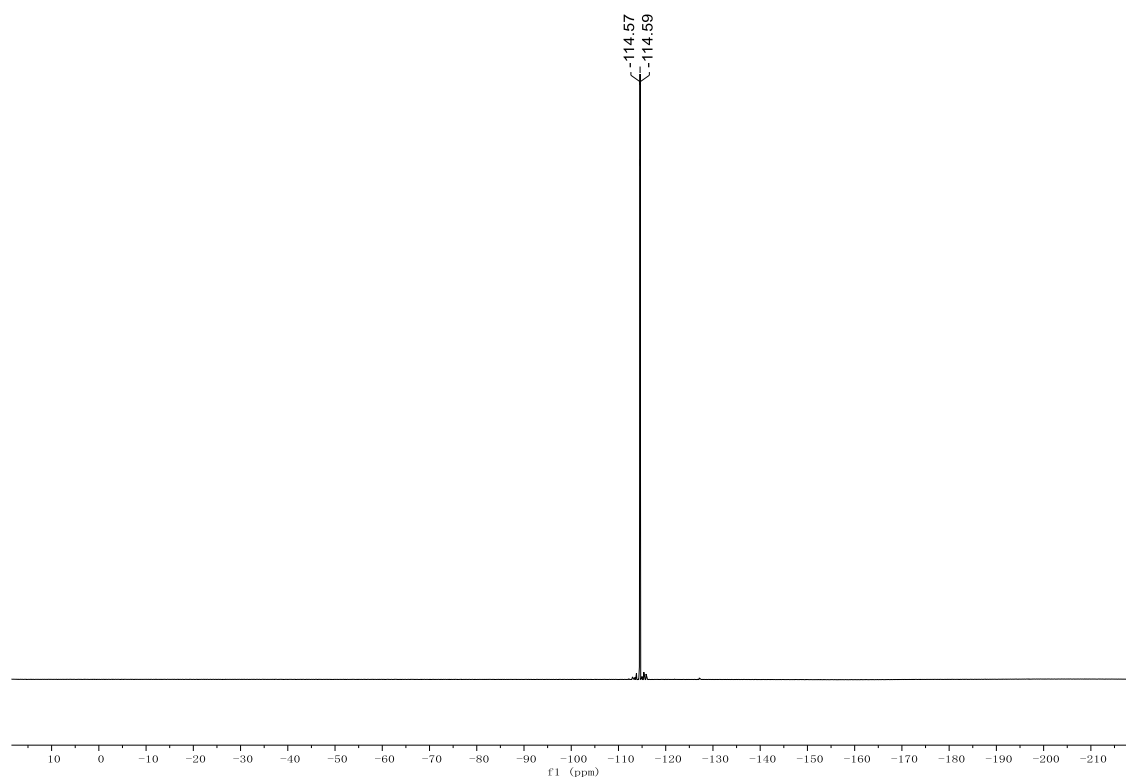


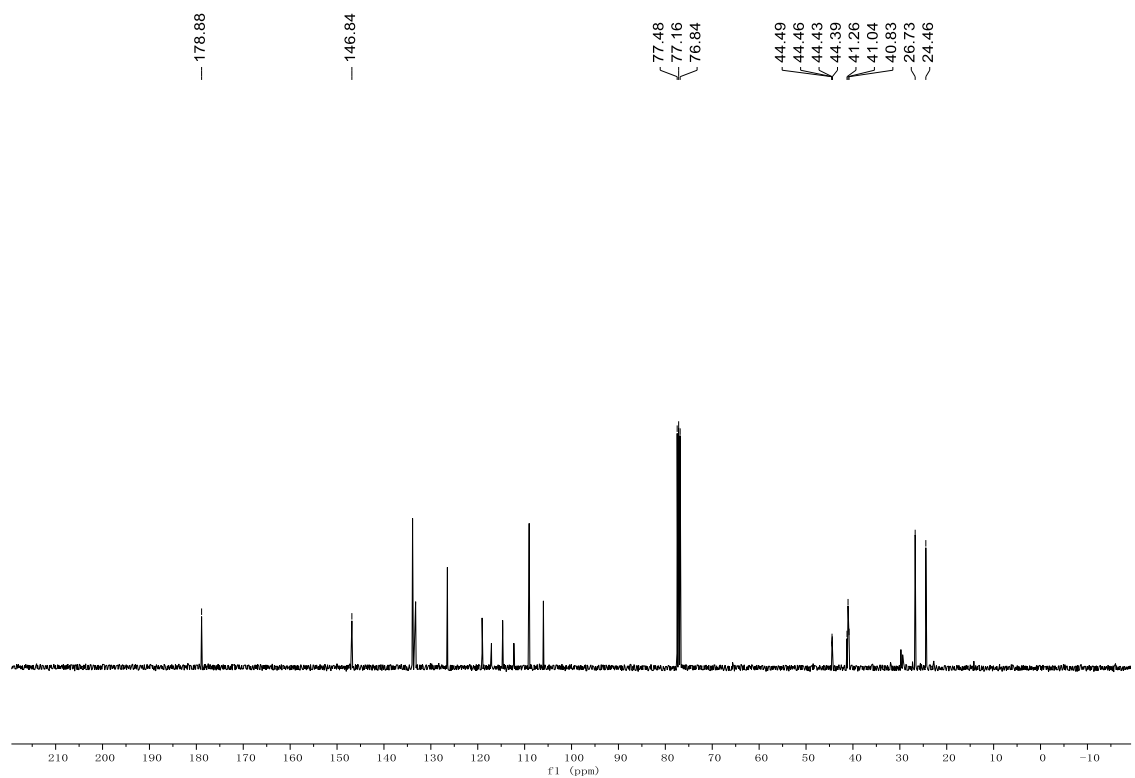
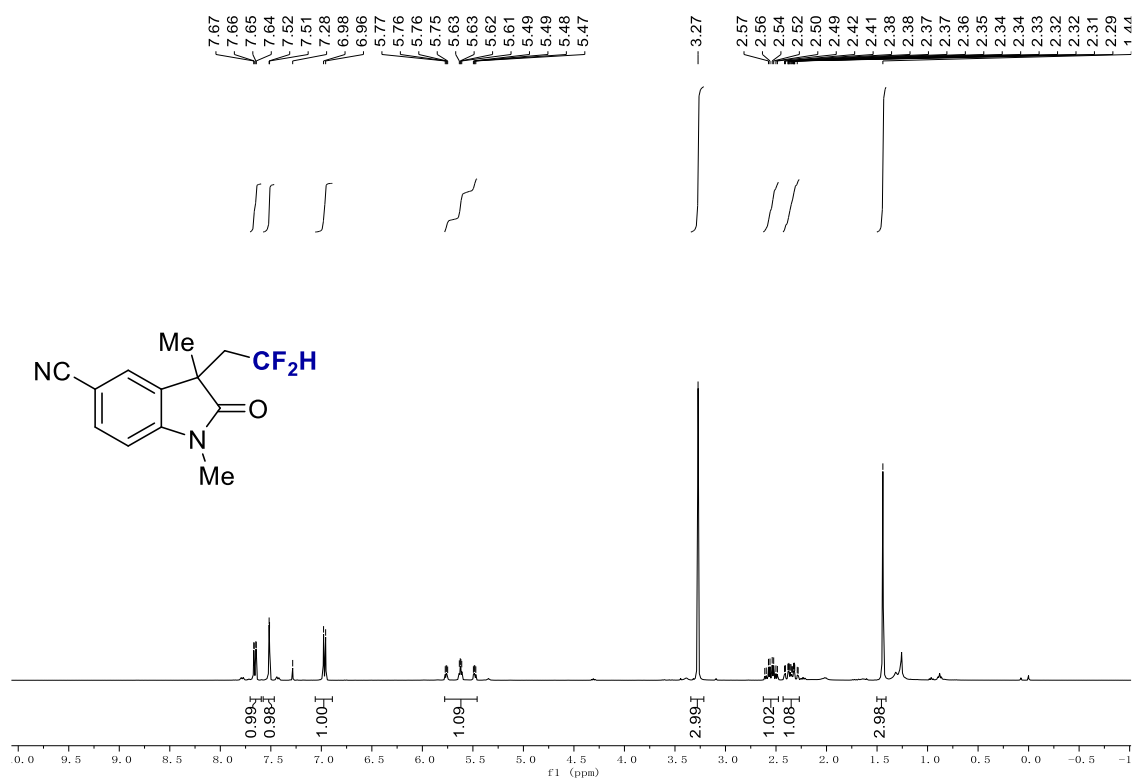


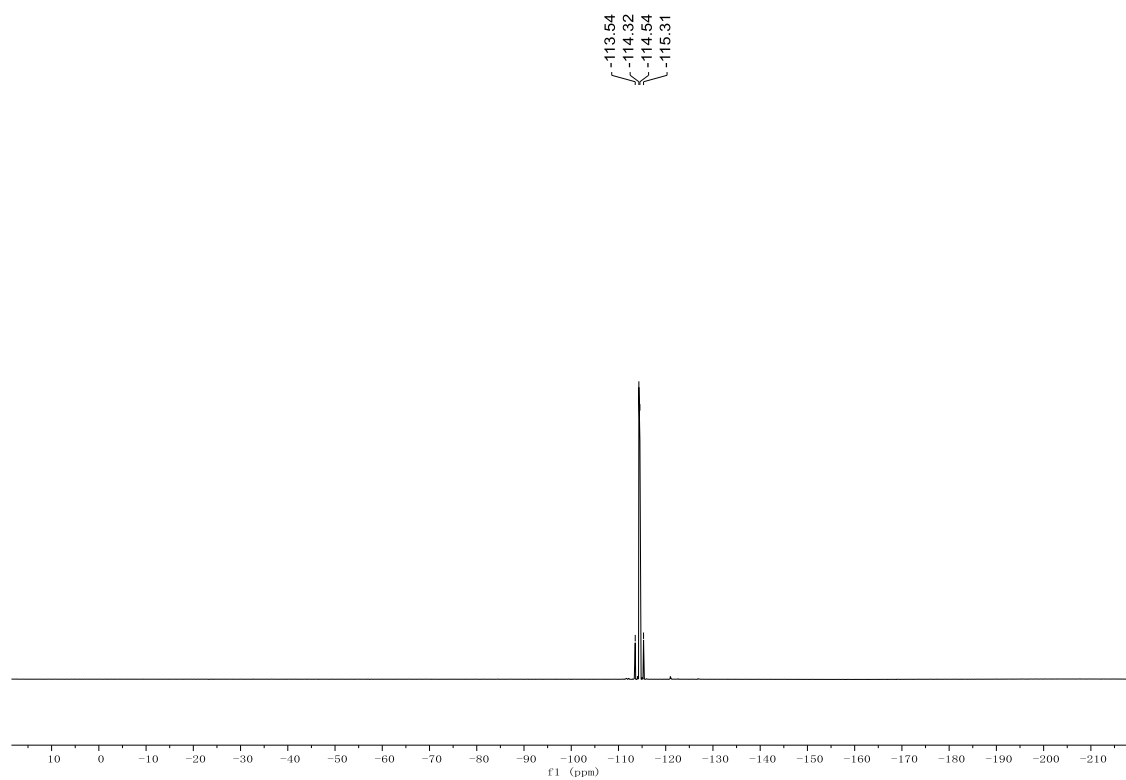


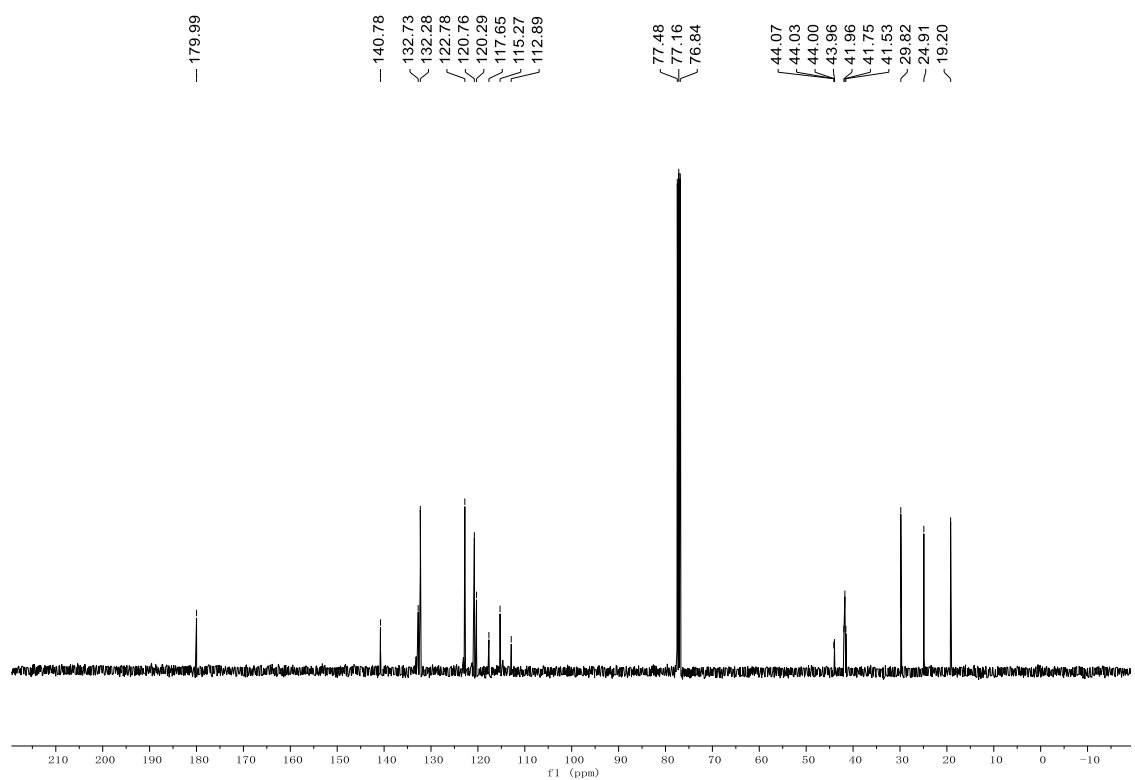
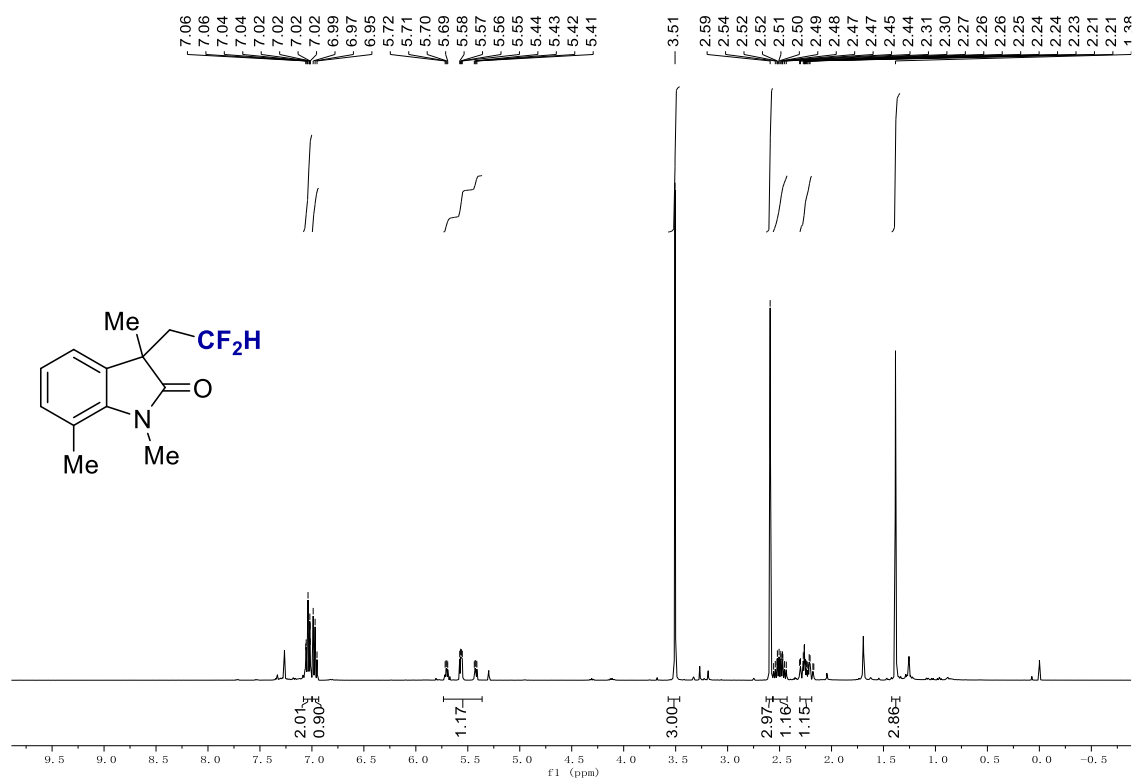


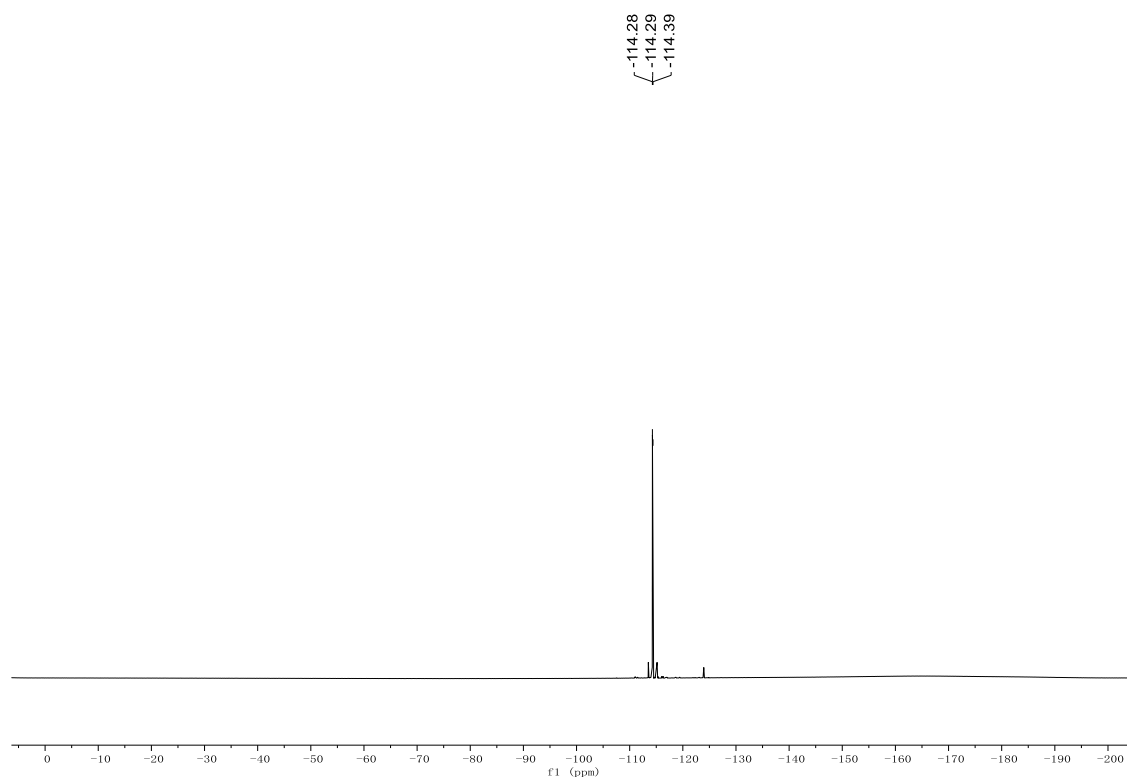


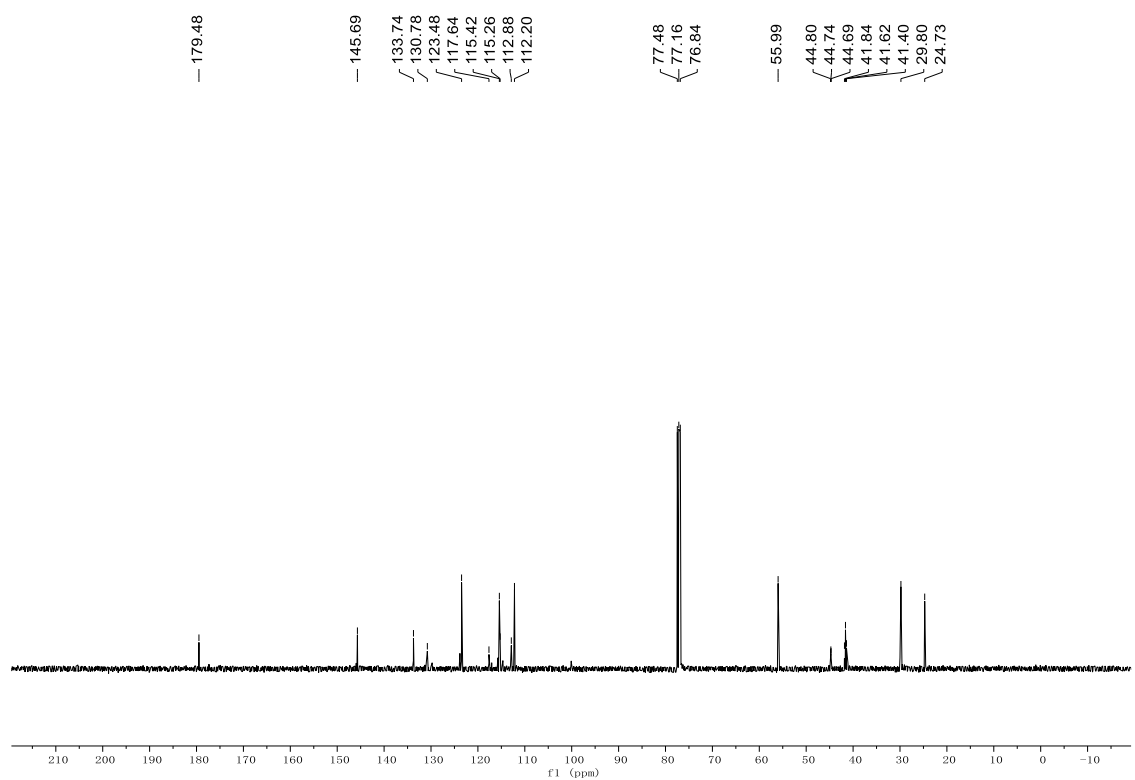
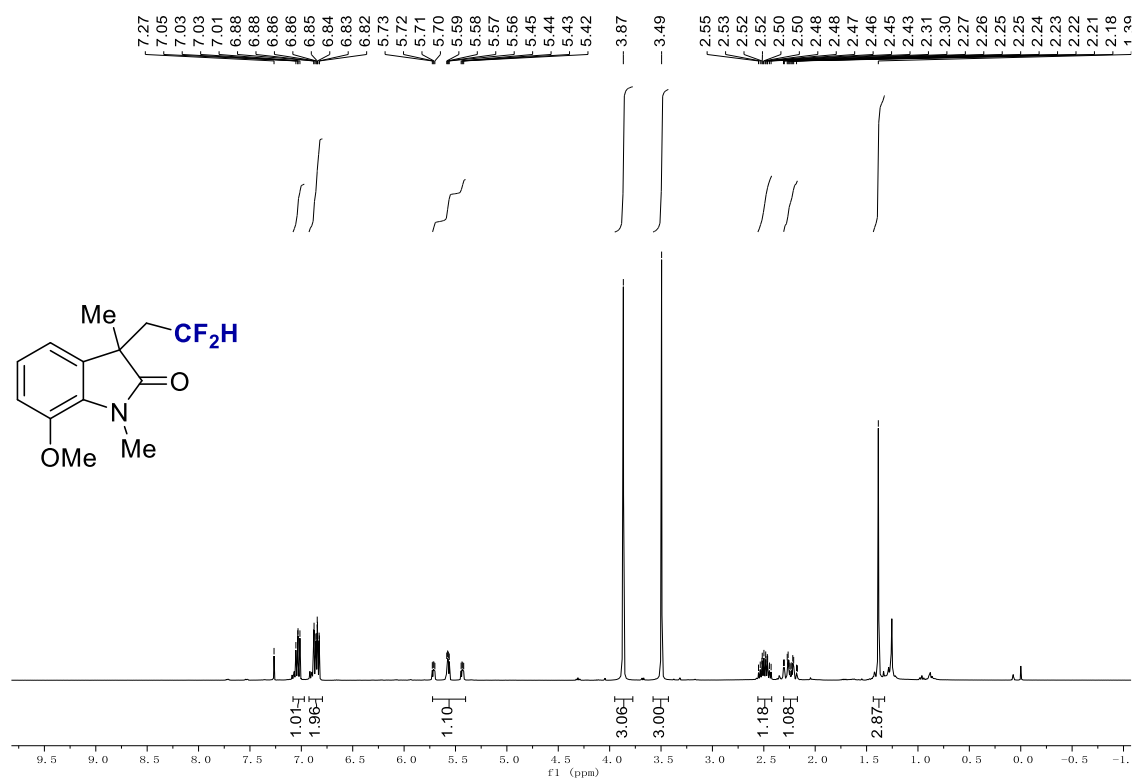


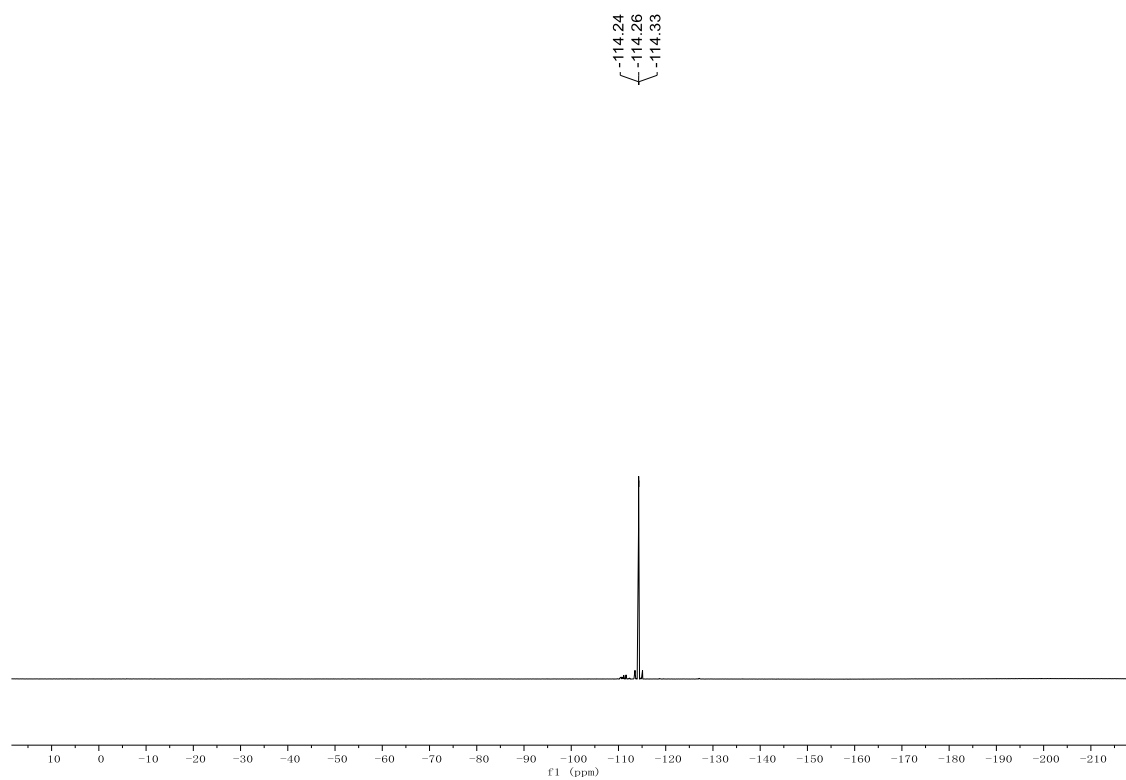


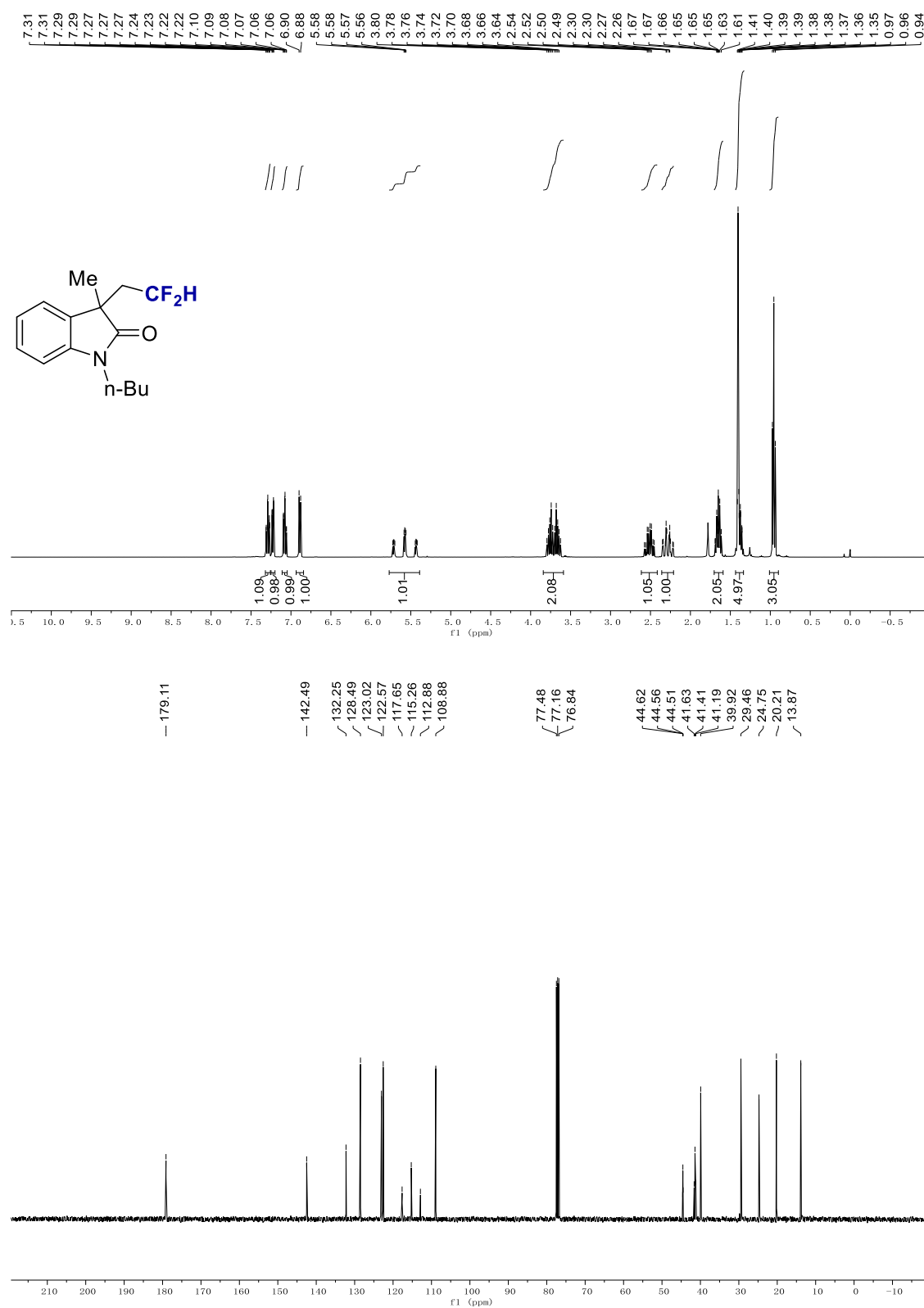


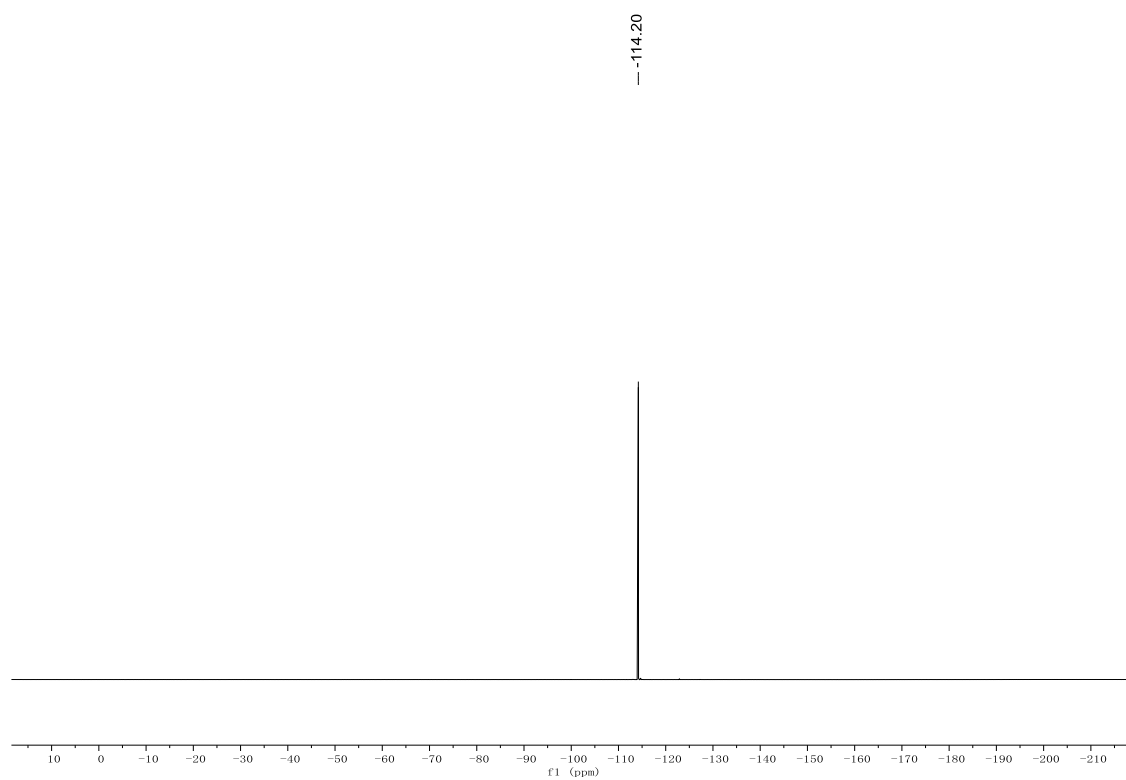


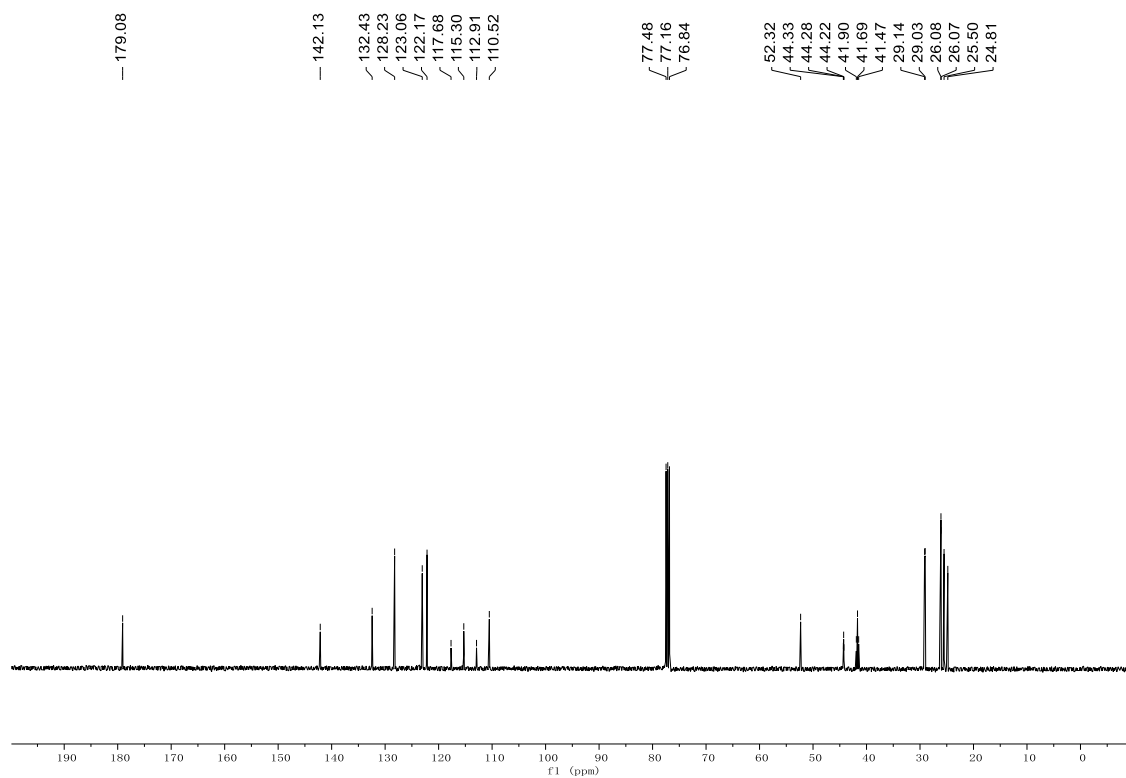
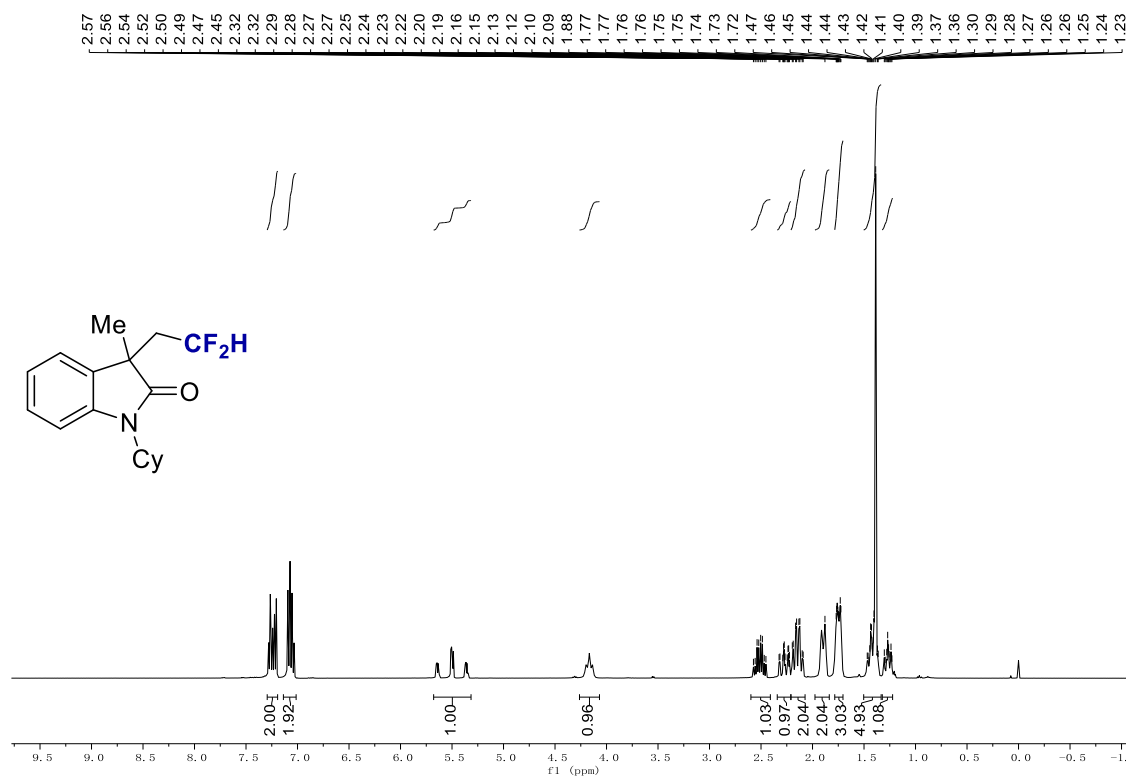


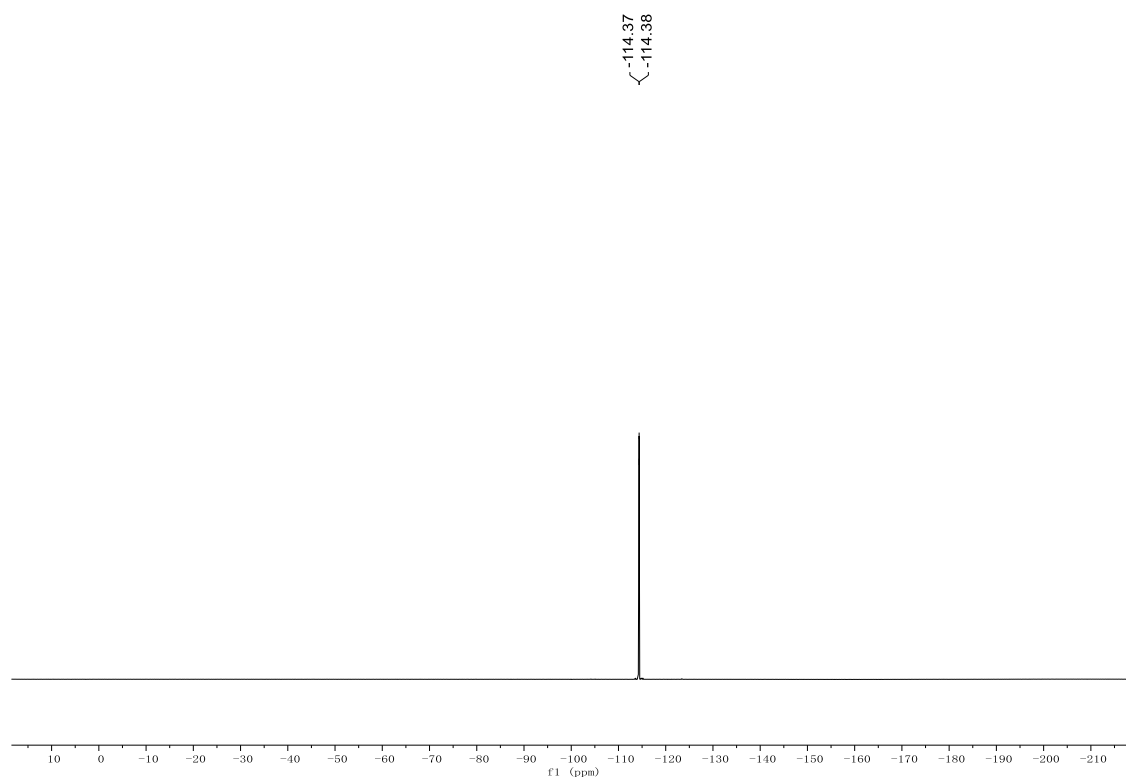


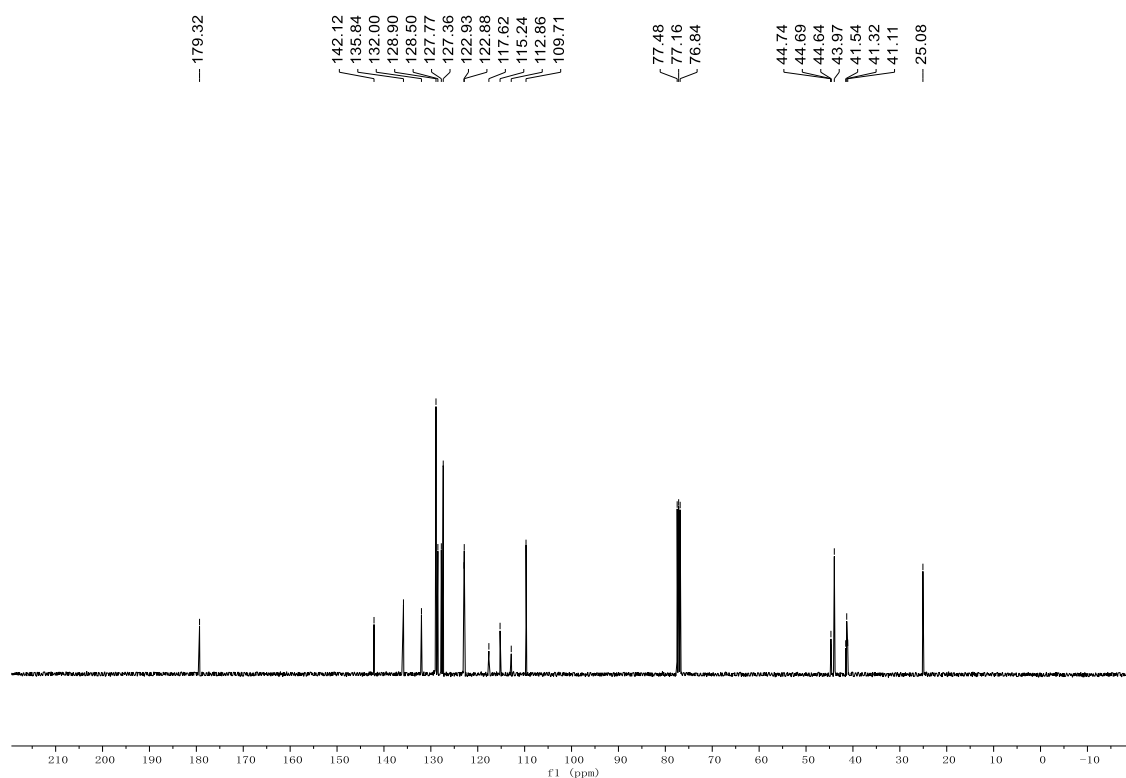
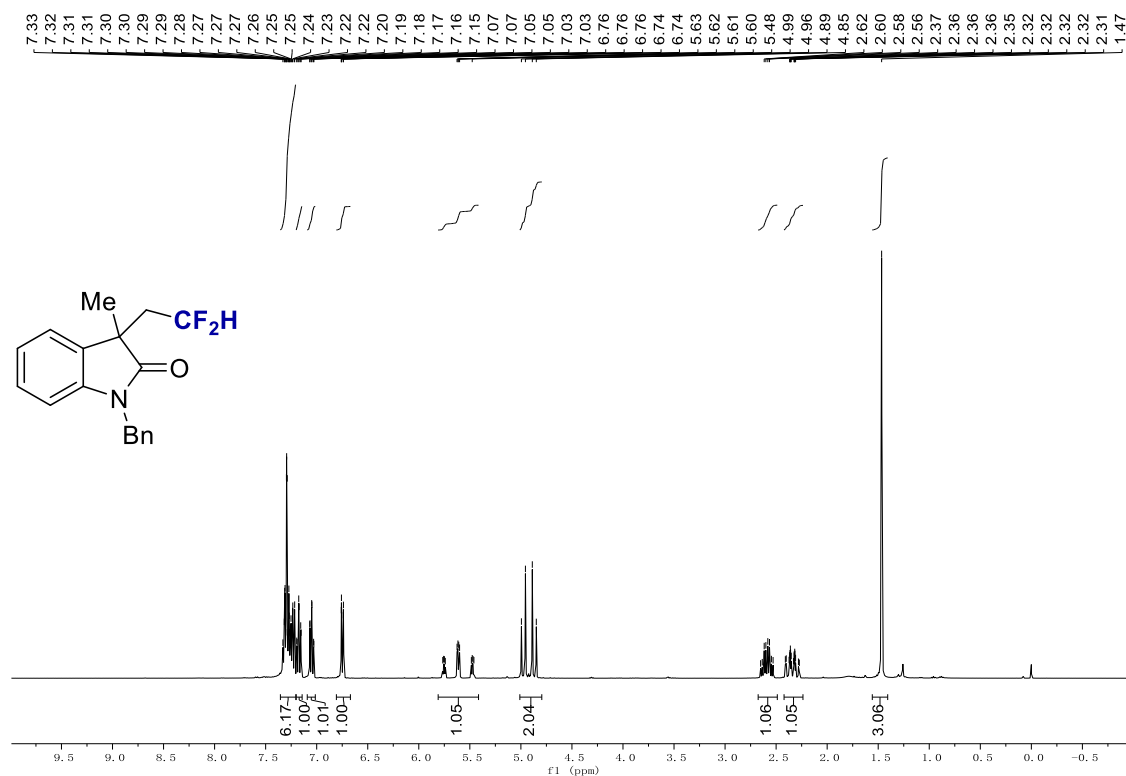


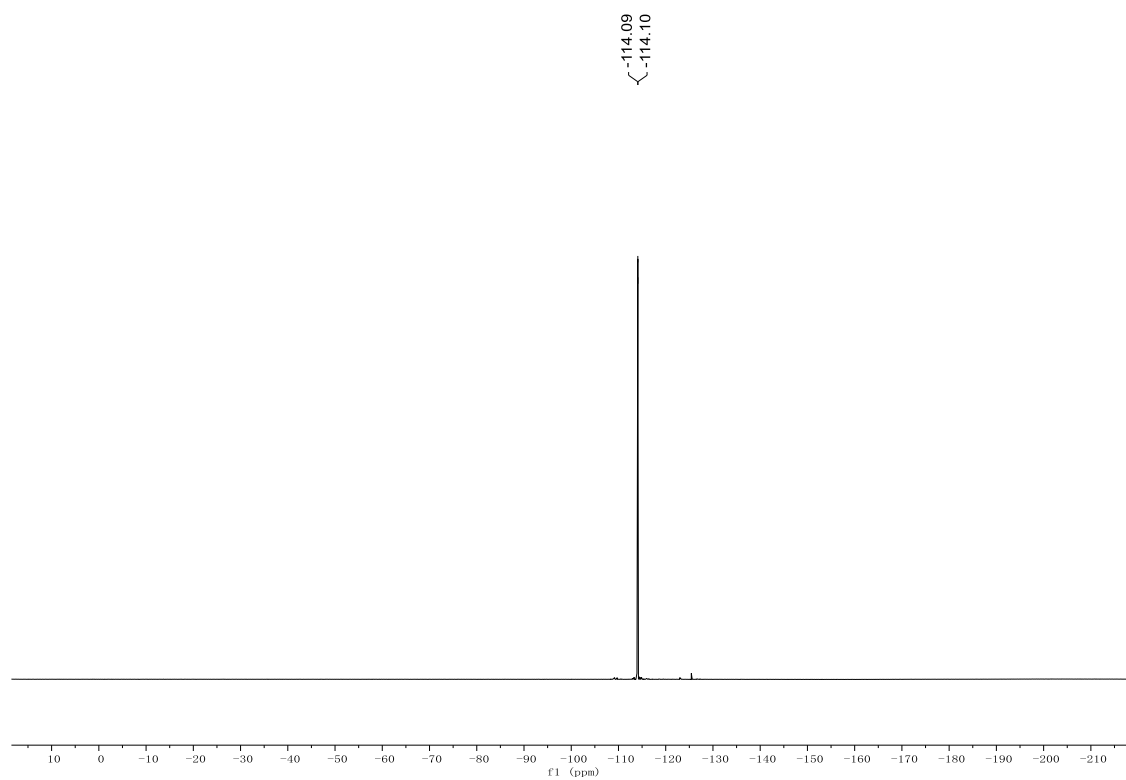


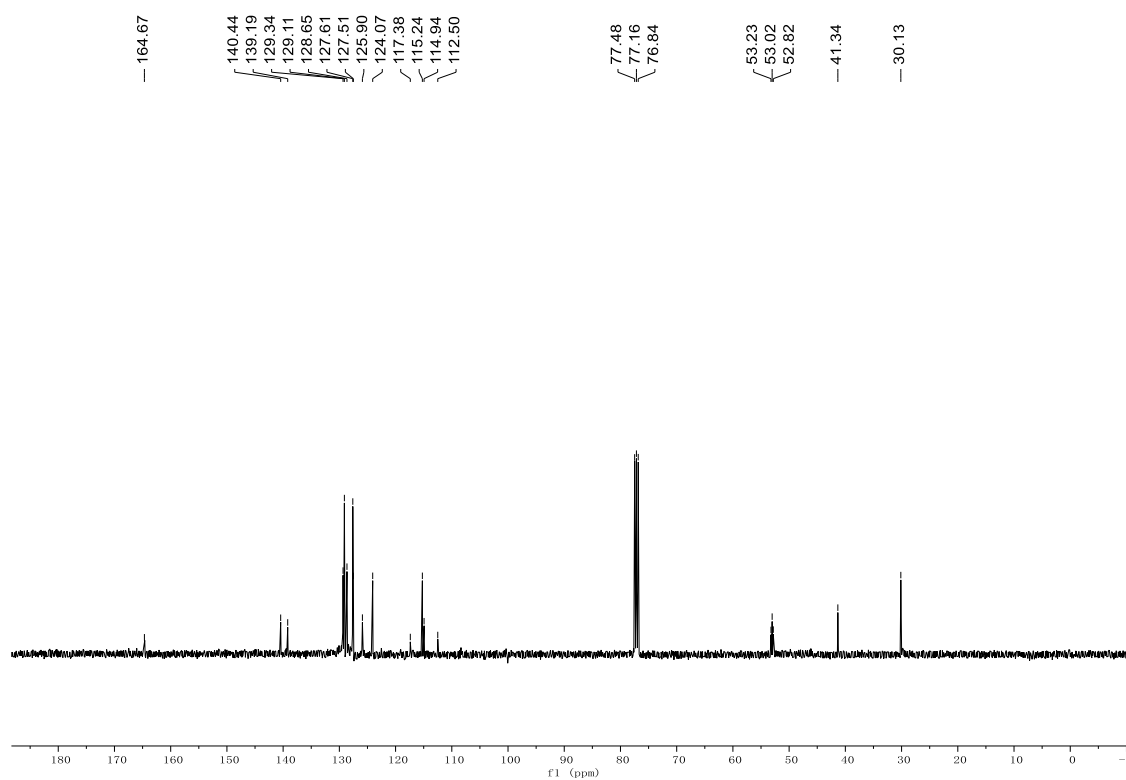
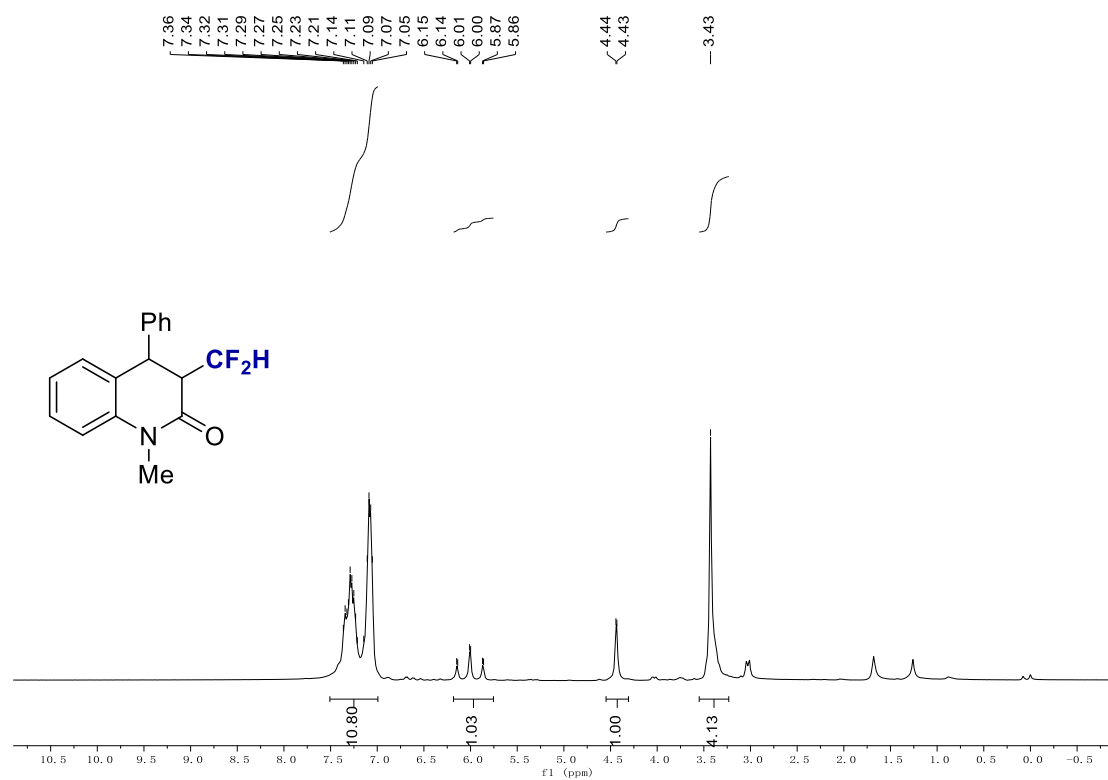


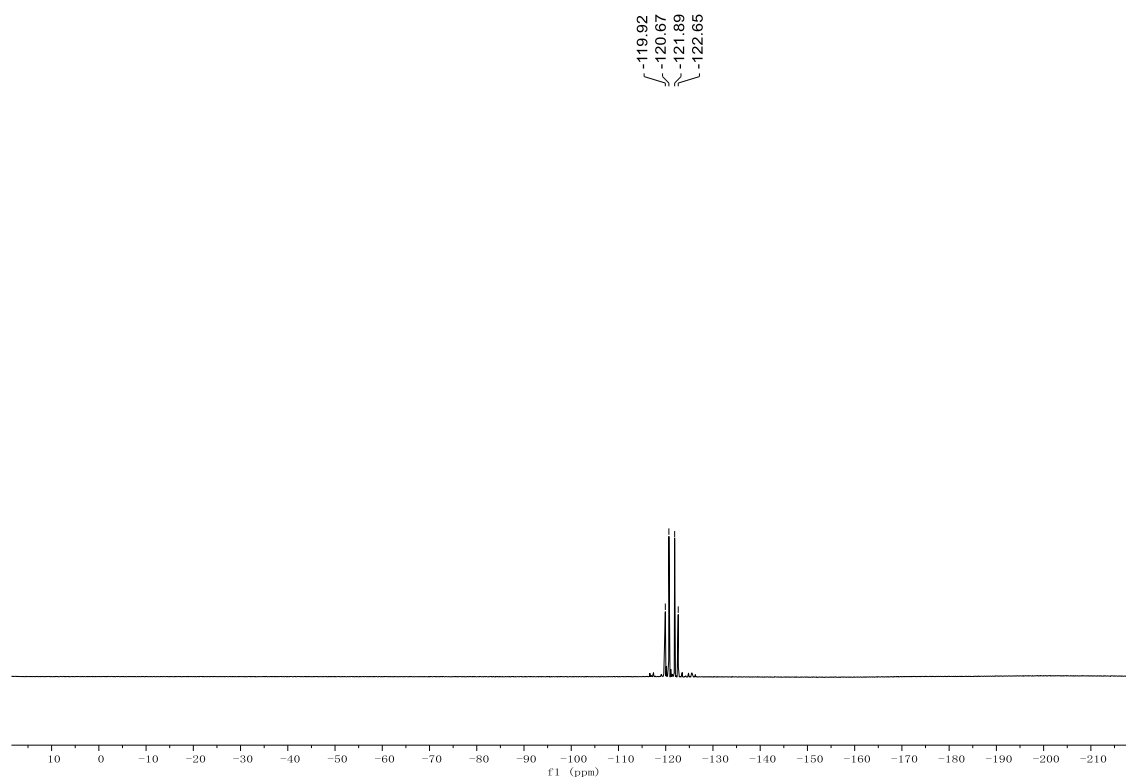


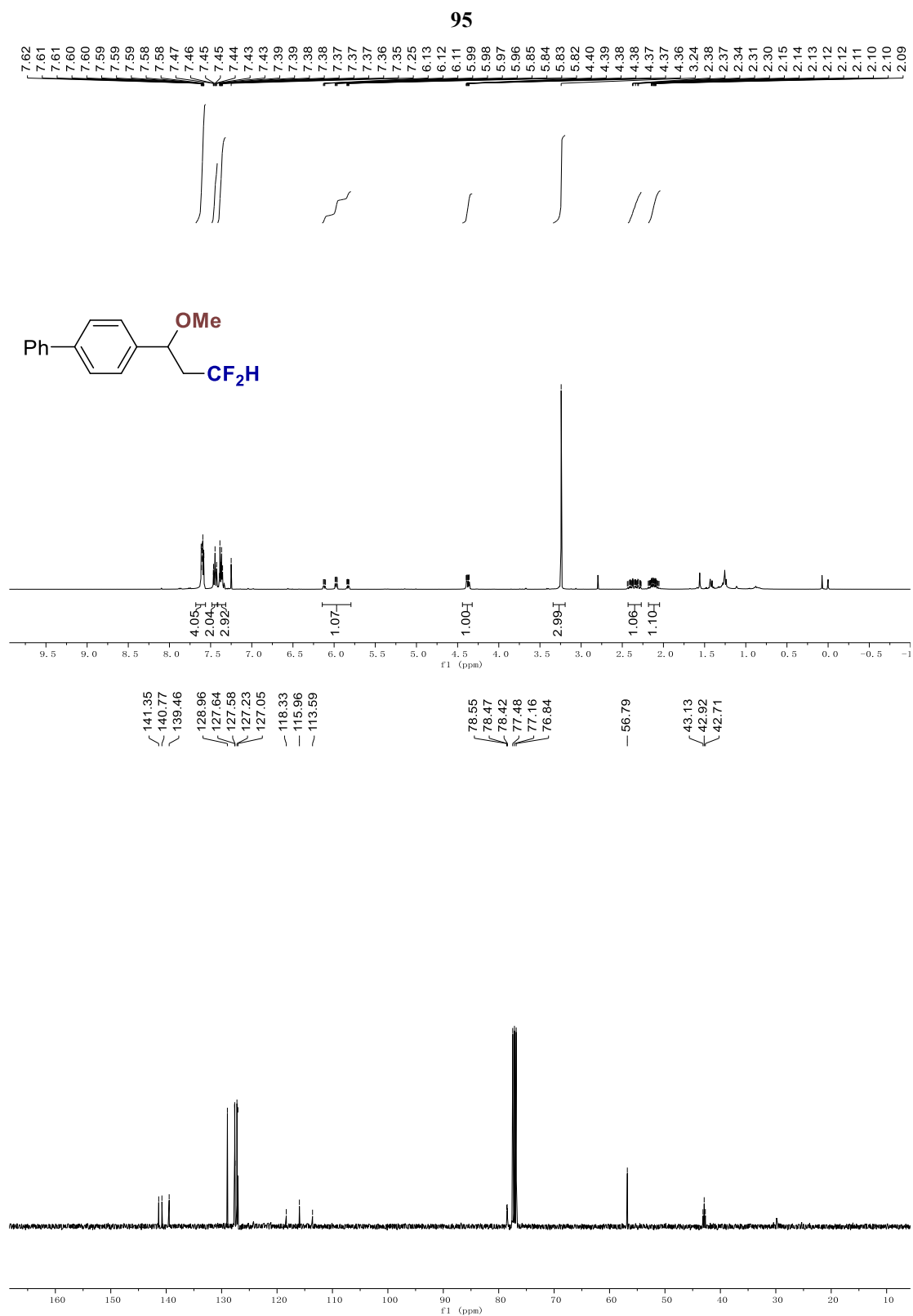


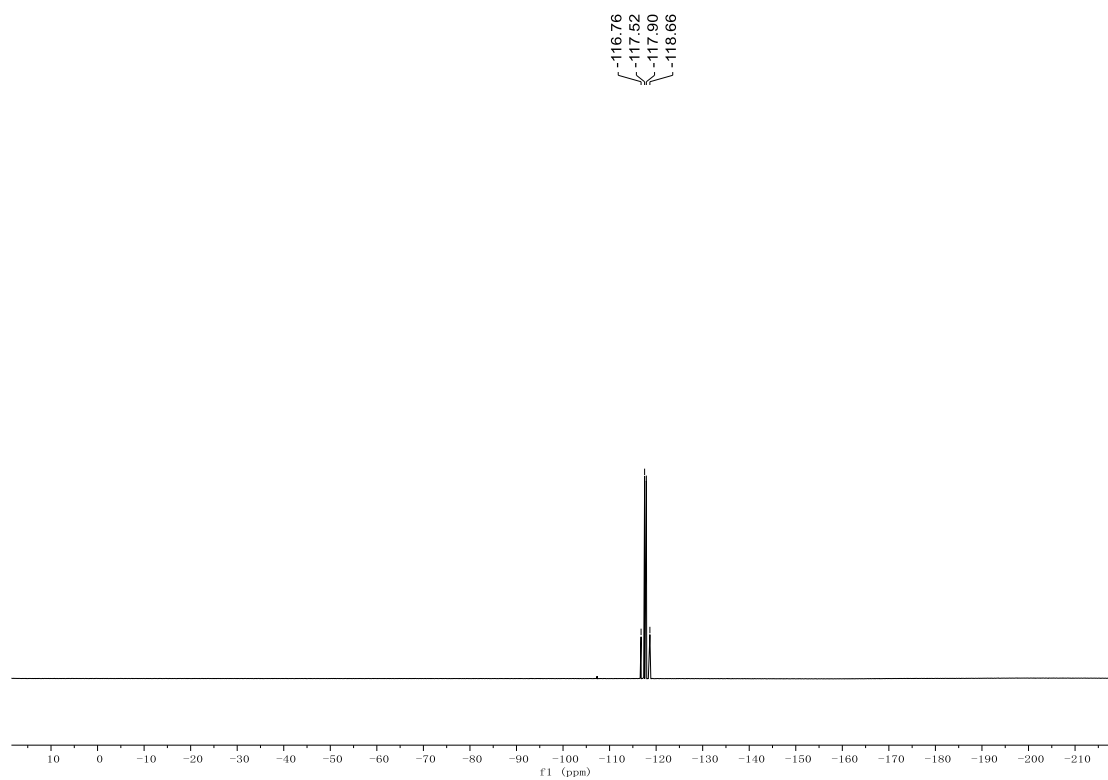


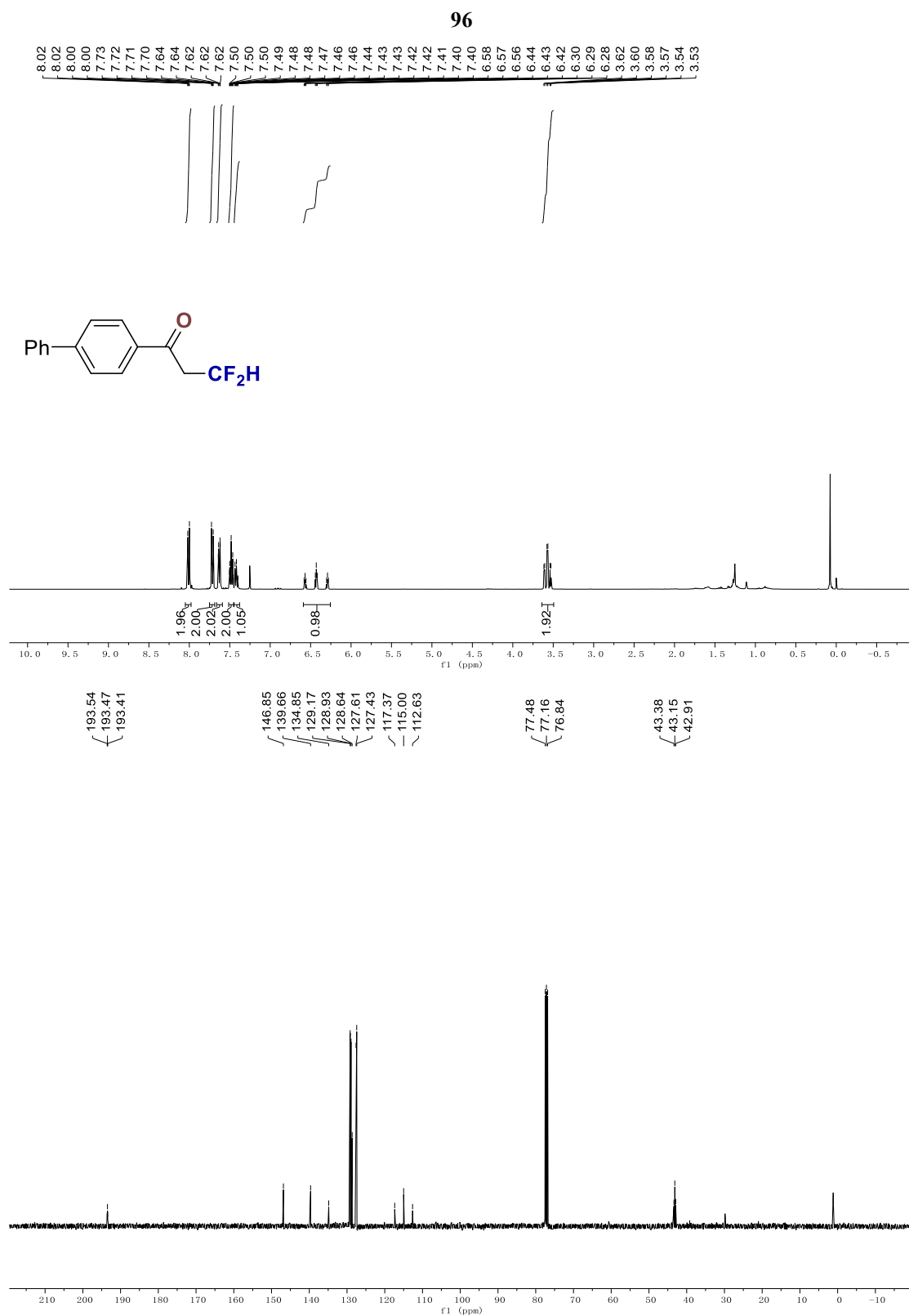


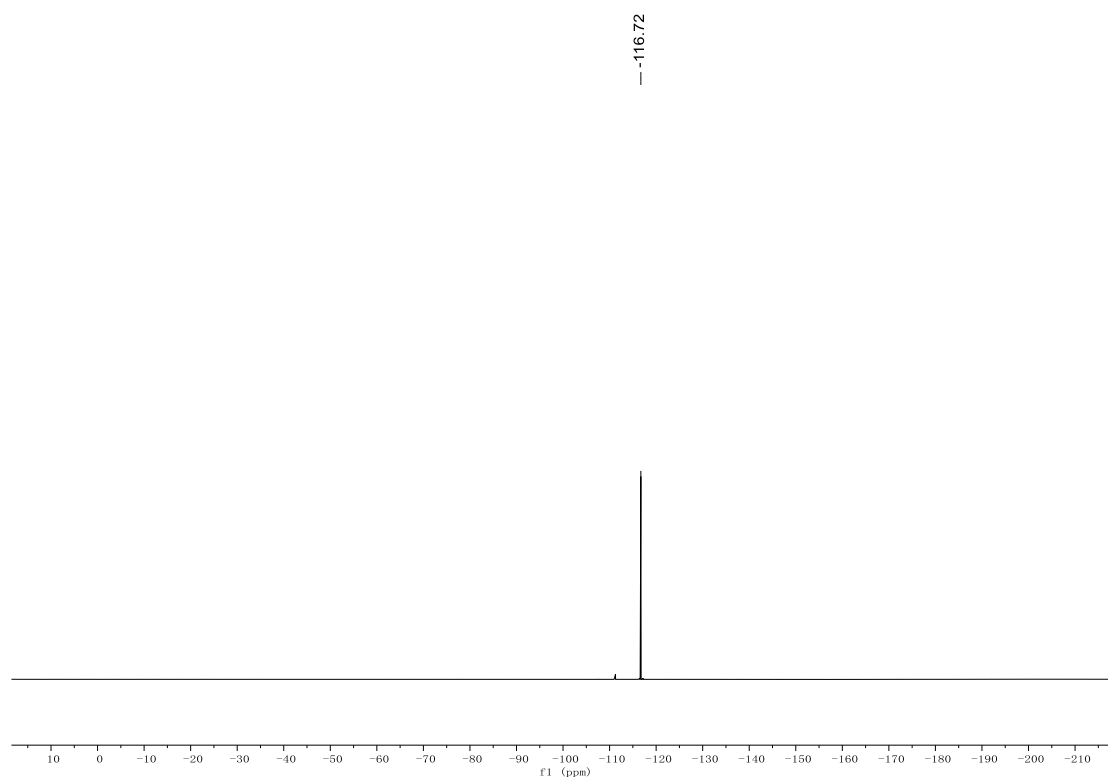


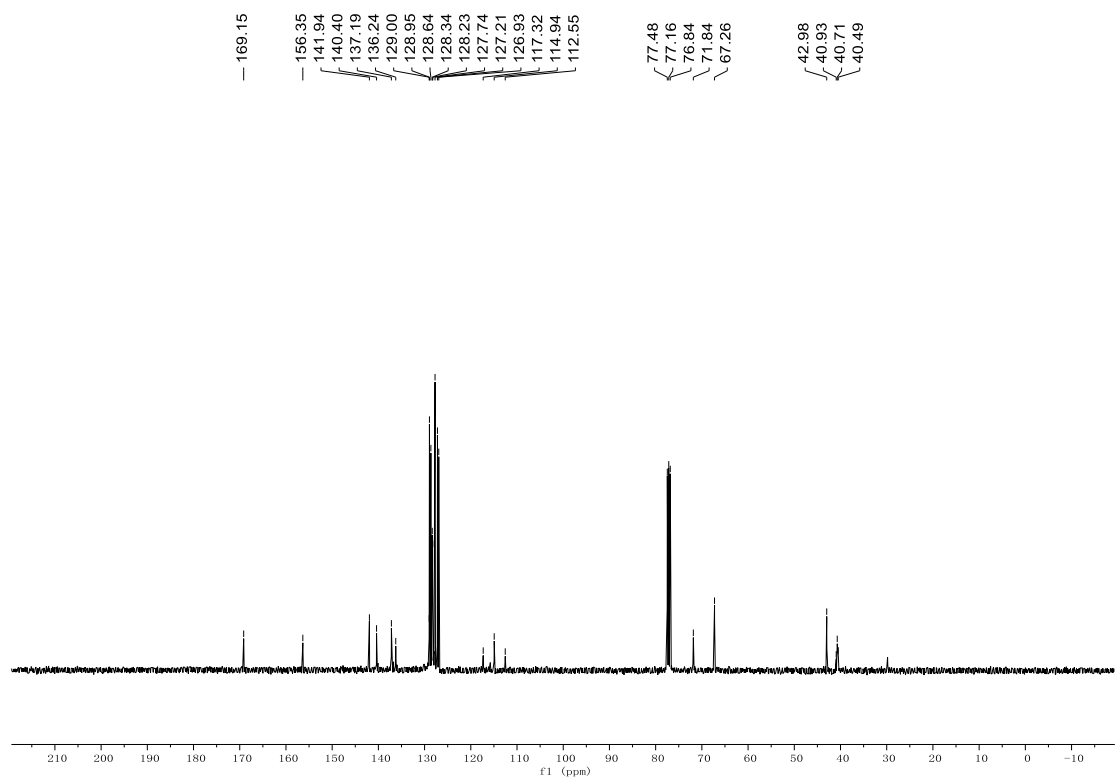
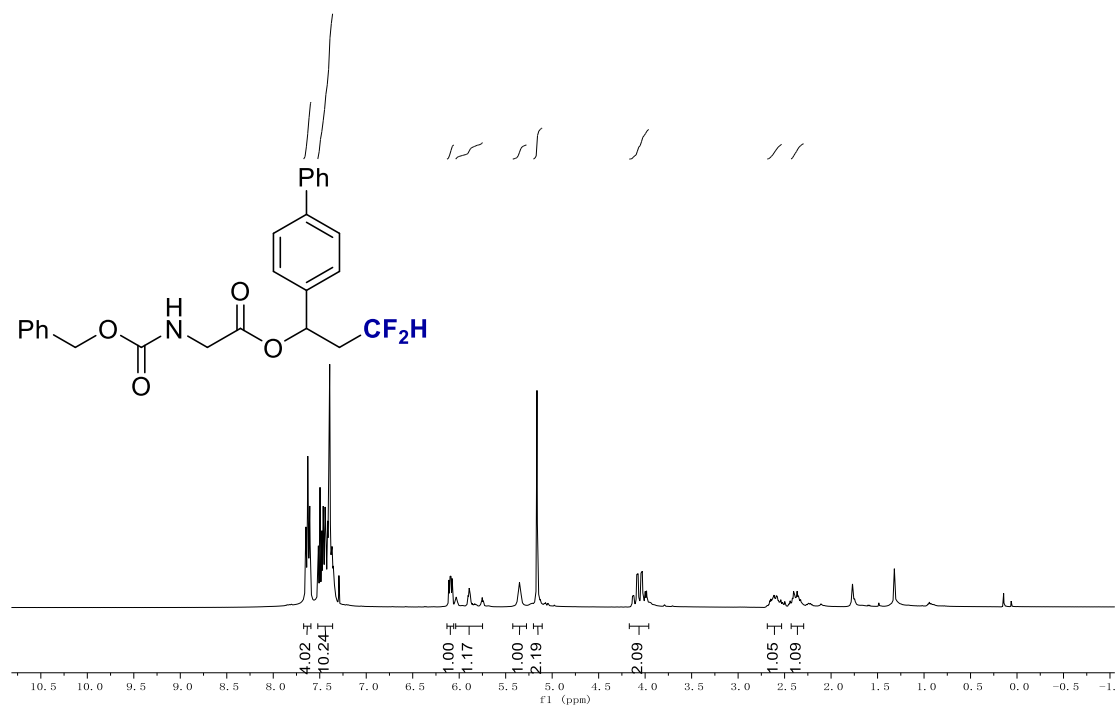


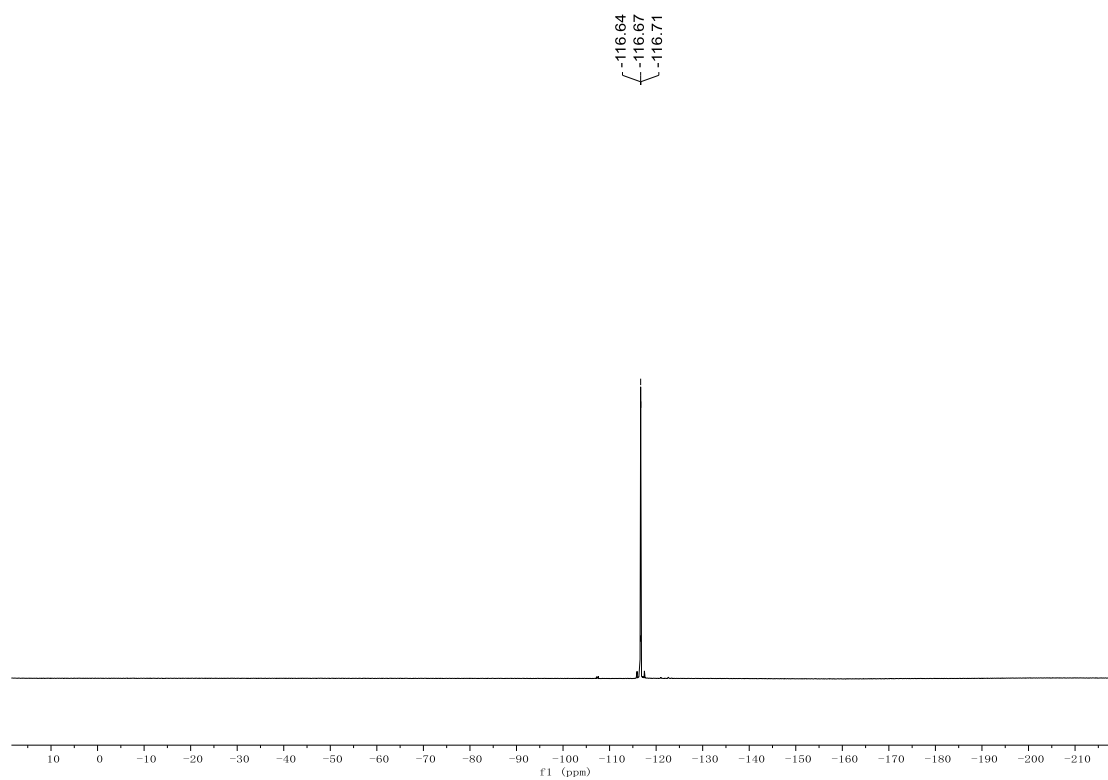


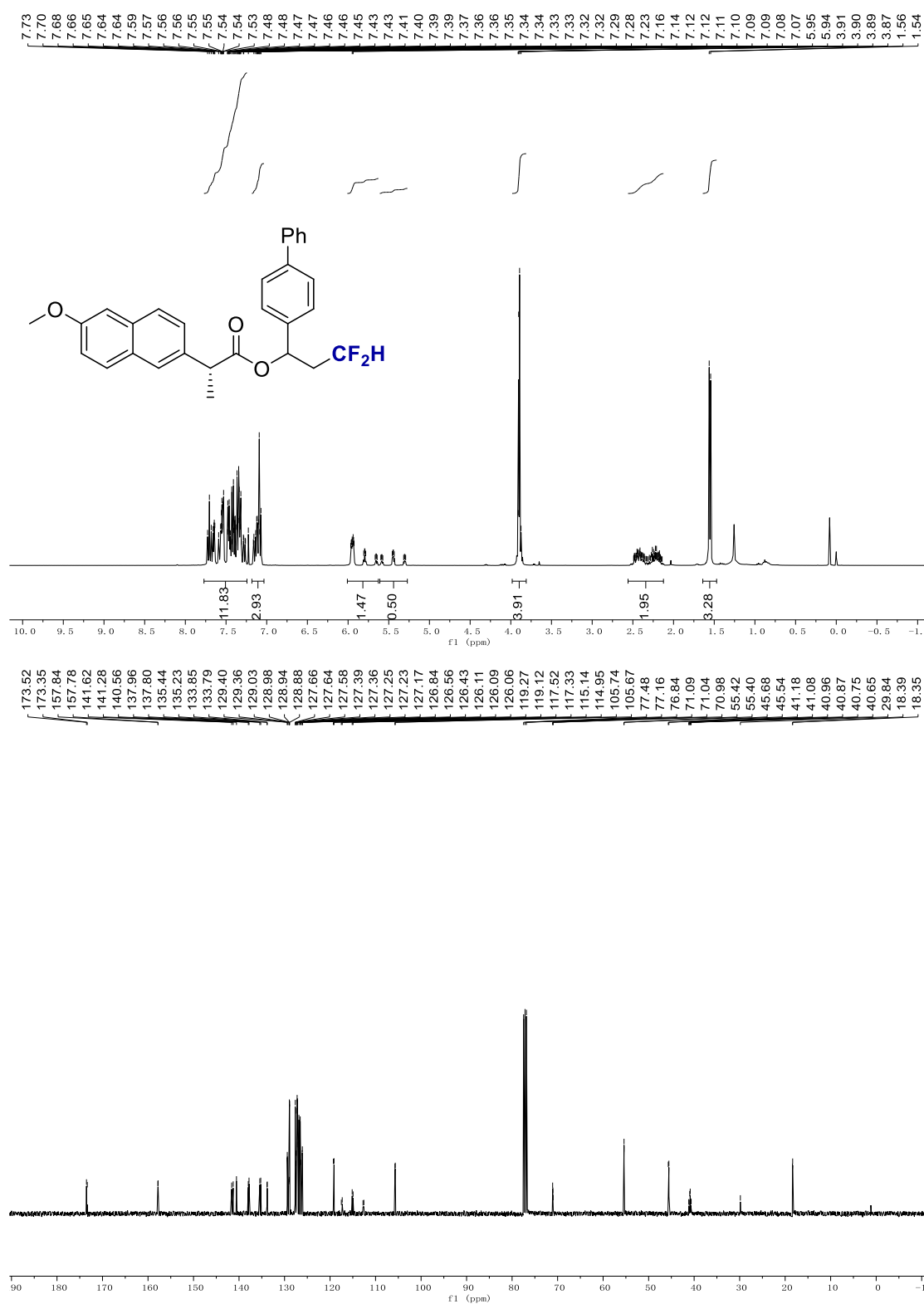


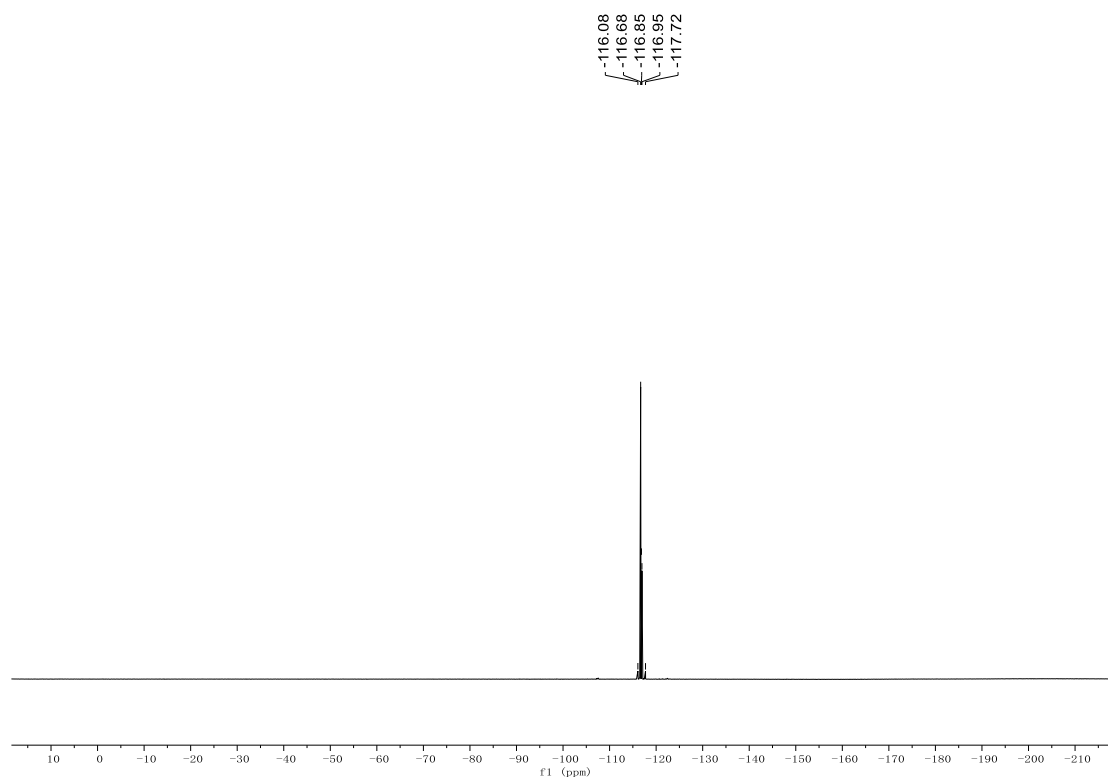




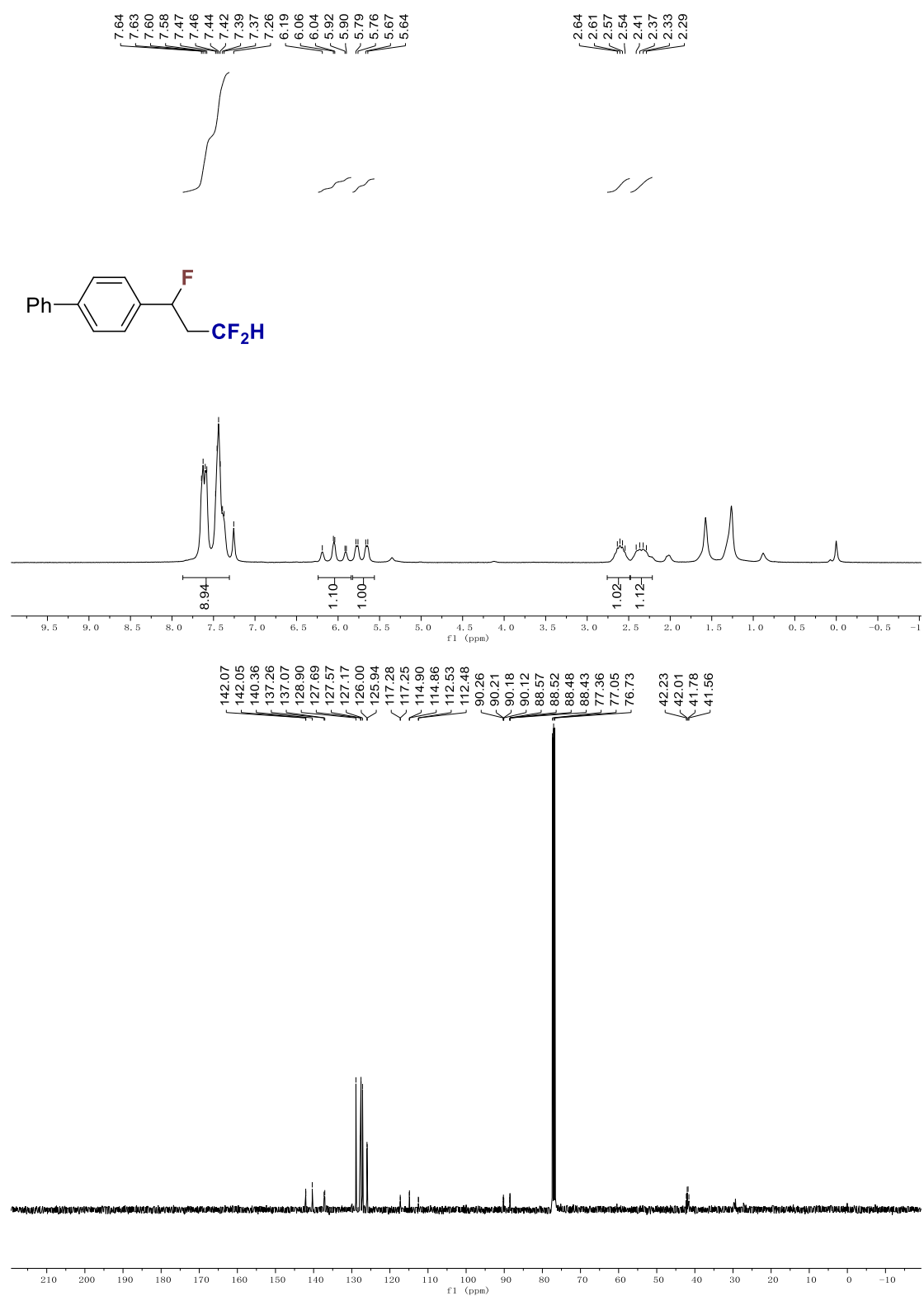


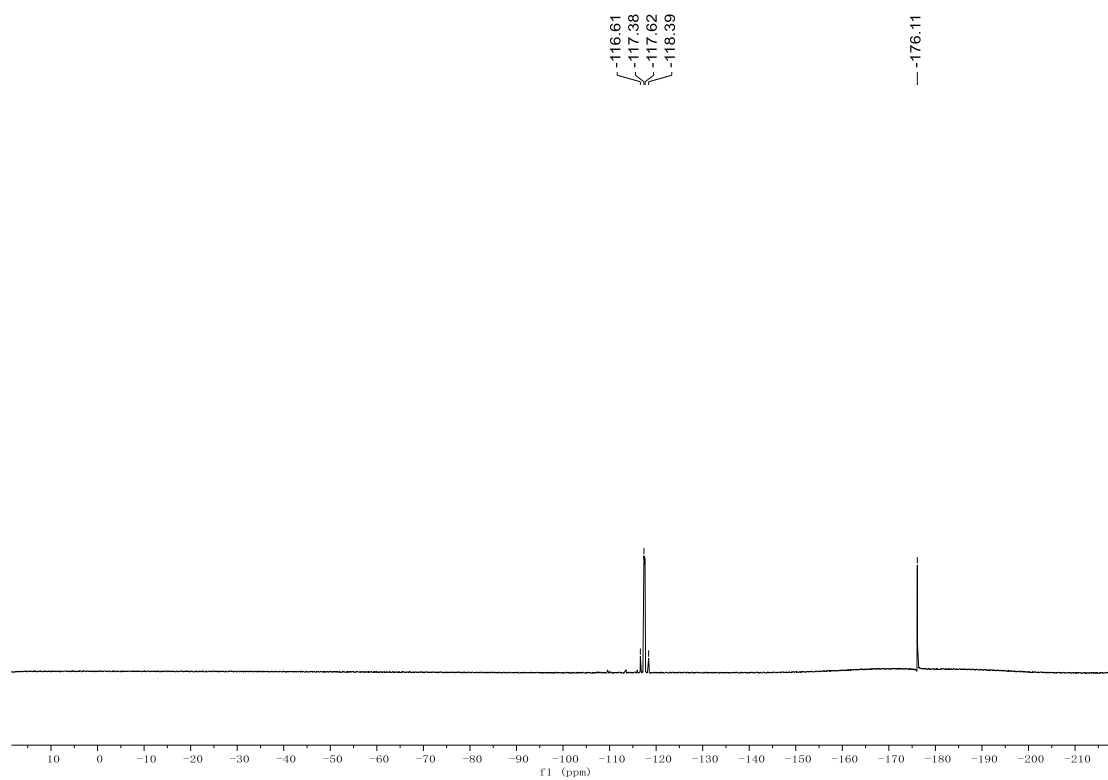


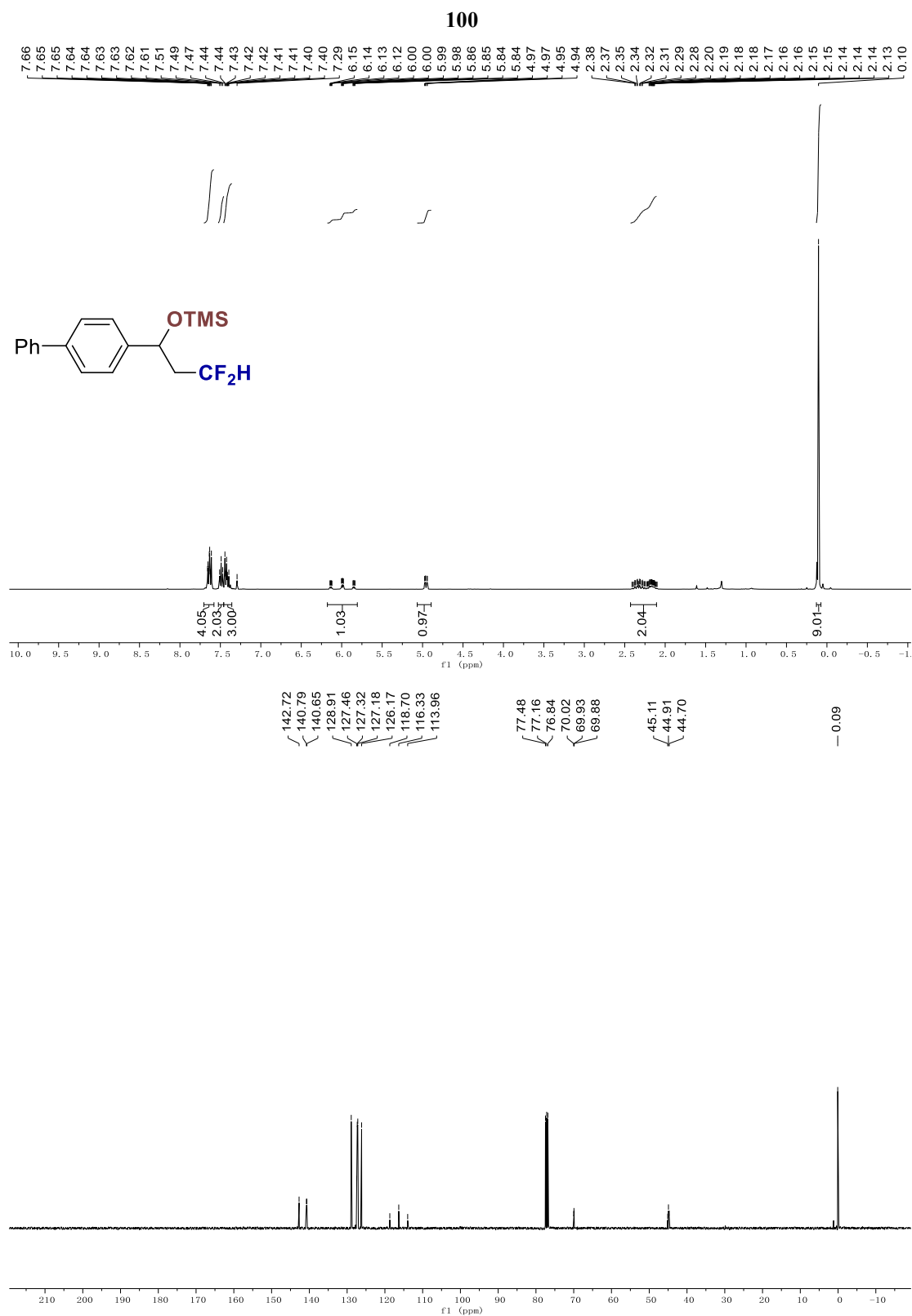


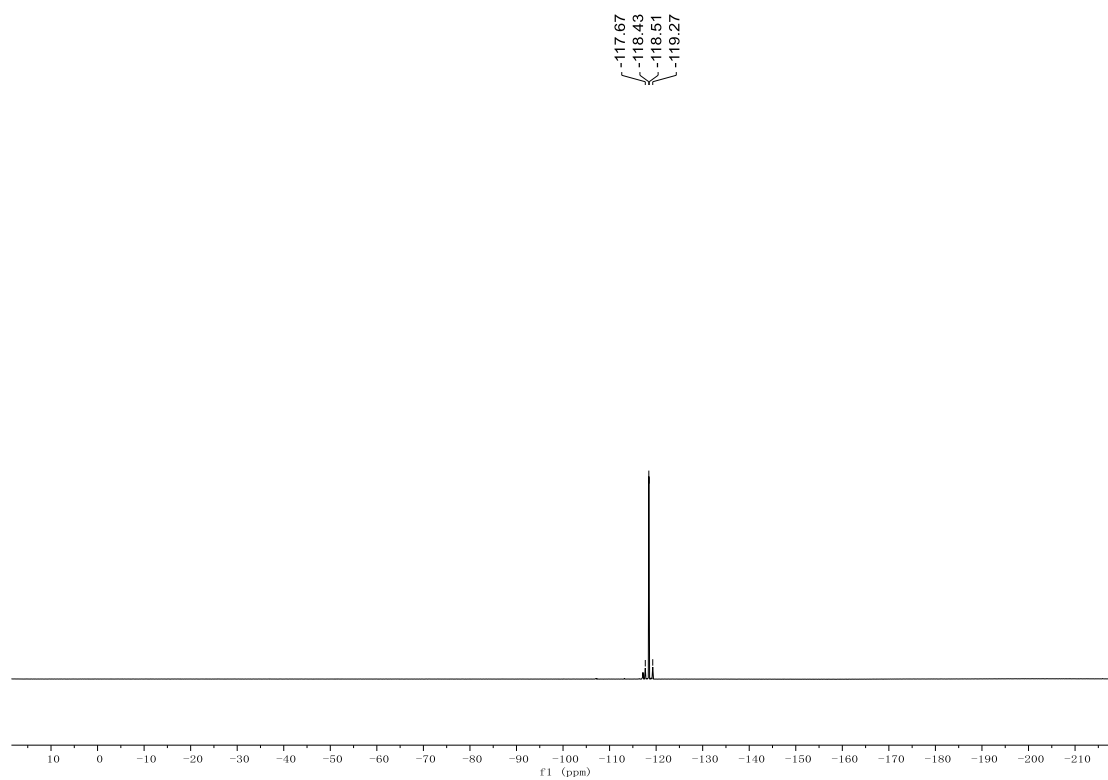


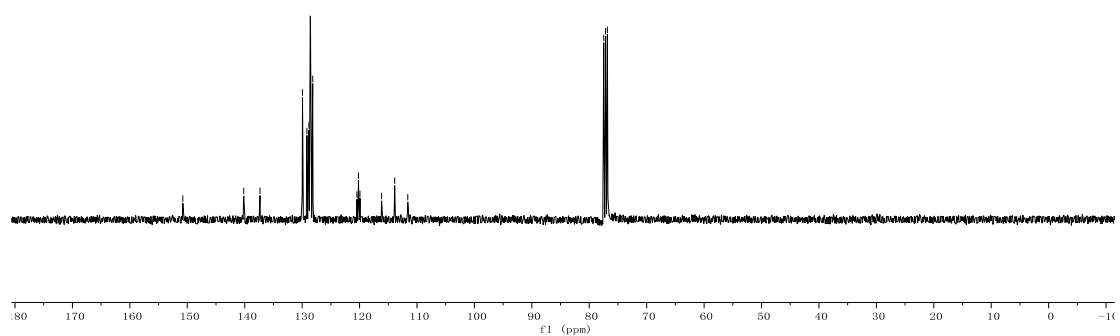
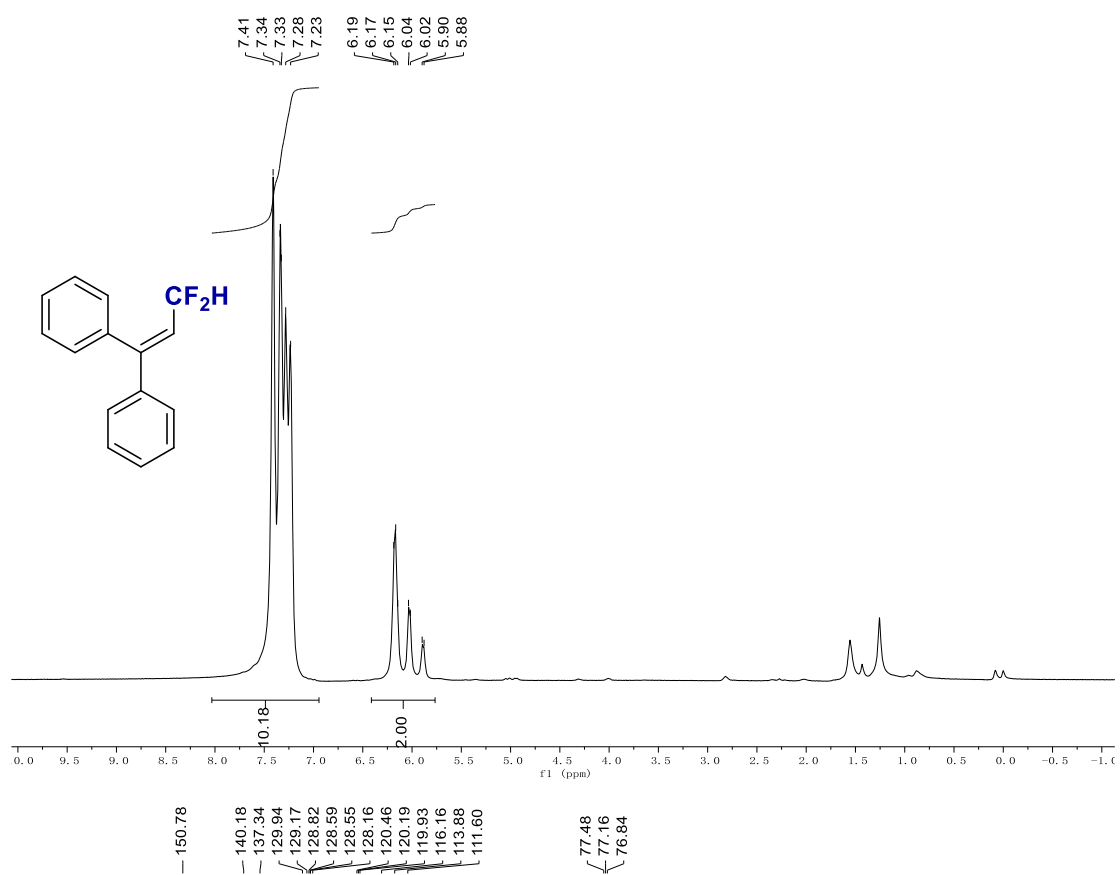
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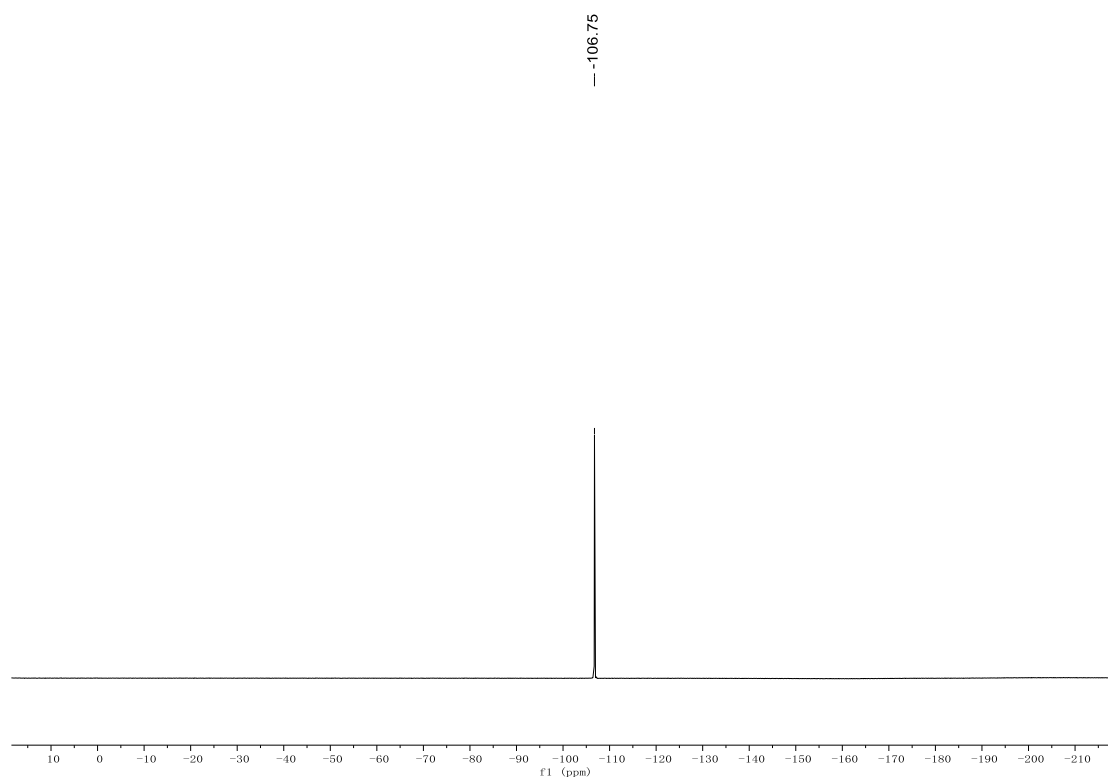




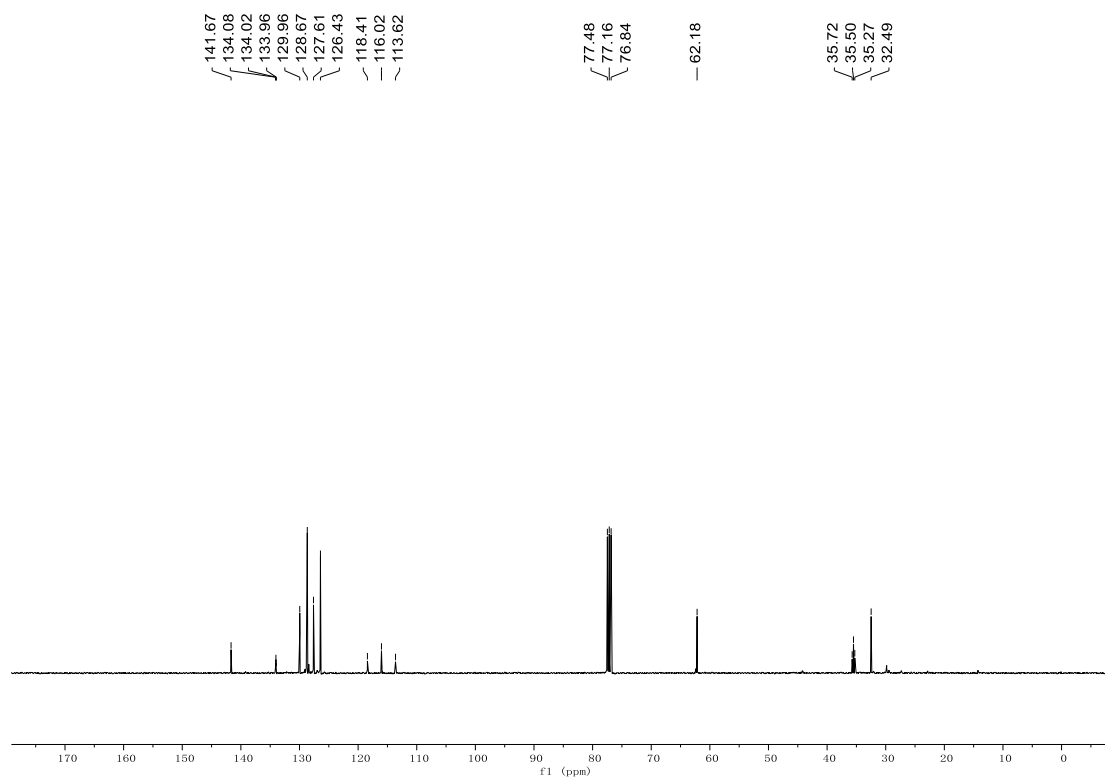
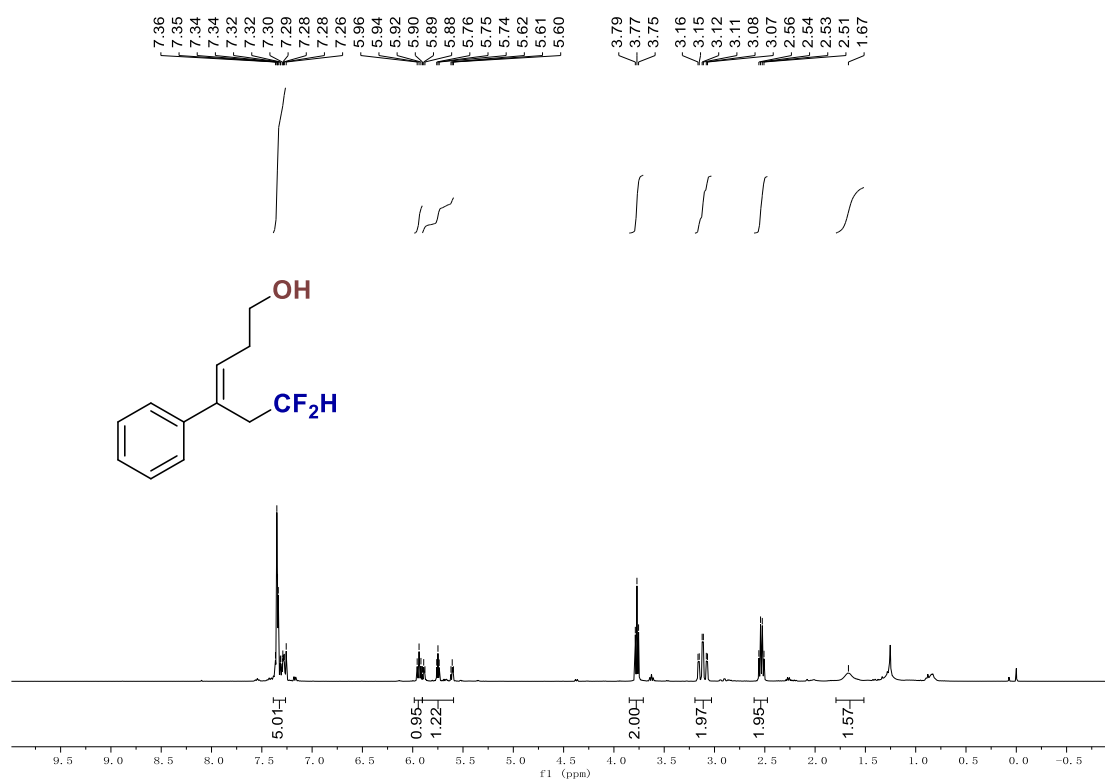


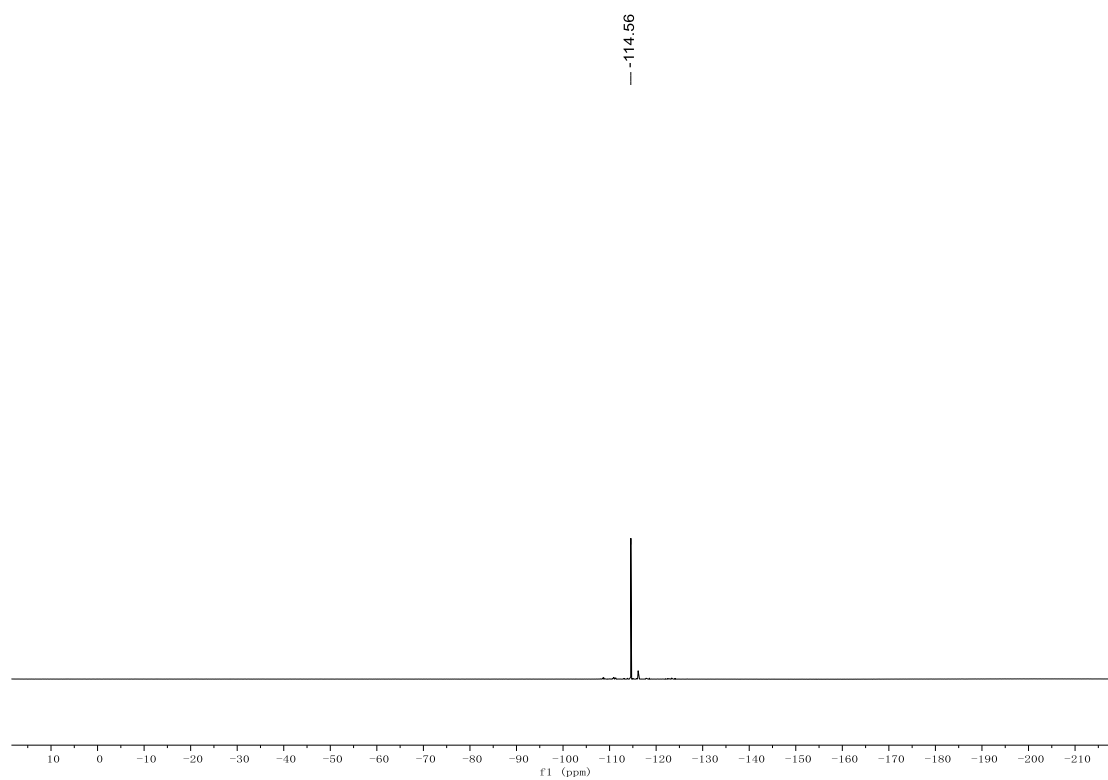






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