

Supporting Information

Synthesis of Difluoromethyl Carbinols from the Friedel-Crafts Reaction of Electron-rich Arenes with Difluorovinyl Arylsulfonates

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General Information

The solvents were dried by distillation over the drying agents indicated in parentheses: THF (Na-benzophenone). Trifluoroethanol, Anhydrous dichloromethane, EtOH were purchased from Adamas-beta. Commercially available chemicals were obtained from commercial suppliers and used without further purification unless otherwise stated.

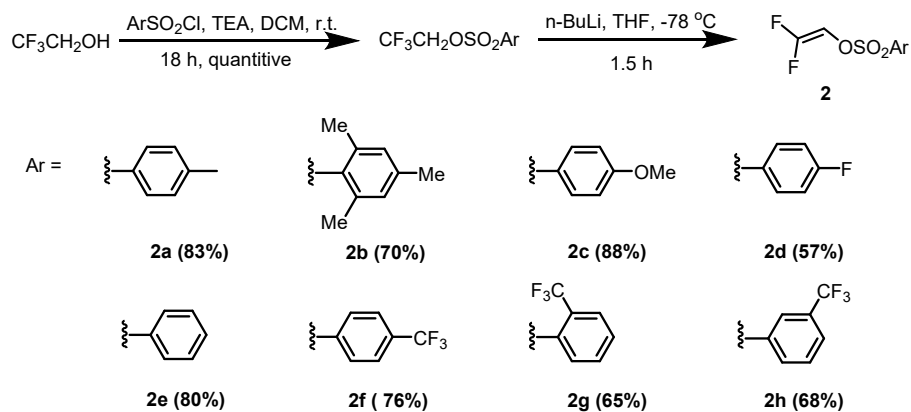
NMR-spectra were recorded on Bruker AvanceIII-500M in solvents as indicate. Chemical shifts (δ) are given in ppm relative to tetramethylsilane ($\delta = 0$). The residual solvent signals were used as references and the chemical shifts converted to the TMS scale (CDCl_3 : $\delta\text{H} = 7.26$ ppm, $\delta\text{C} = 77.16$ ppm; CD_3OD : $\delta\text{H} = 3.31$ ppm, $\delta\text{C} = 49.00$ ppm; $(\text{CD}_3)_2\text{SO}$: $\delta\text{H} = 2.49$ ppm, $\delta\text{C} = 39.52$ ppm;). The following abbreviations were used to describe peak splitting patterns: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublets), td (triplet of doublets), ddd (doublet of doublet of doublets). Coupling constants (J) were reported in hertz unit (Hz) High-resolution mass spectra (HRMS) were recorded on a BRUKER VPEXII spectrometer with EI and ESI mode unless otherwise stated.

Analytical thin layer chromatography was performed on Polygram SIL G/UV₂₅₄ plates. Visualization was accomplished with short wave UV light, or KMnO_4 staining solutions followed by heating. Flash column chromatography was performed using silica gel (200-300 mesh) with solvents distilled prior to use.

No attempts were made to optimize yields for substrate synthesis

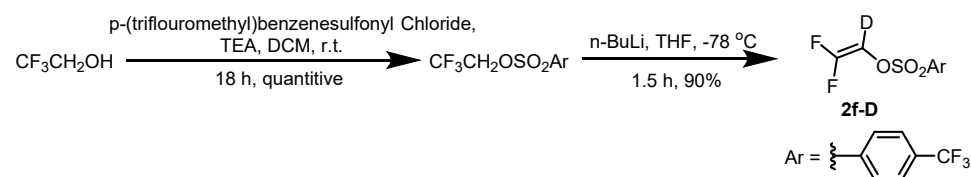
1 Synthesis of Starting Materials

1.1 Synthesis of 2,2-Difluorovinyl arylsulfonates **2**



The title compound was prepared according to a known procedure.¹

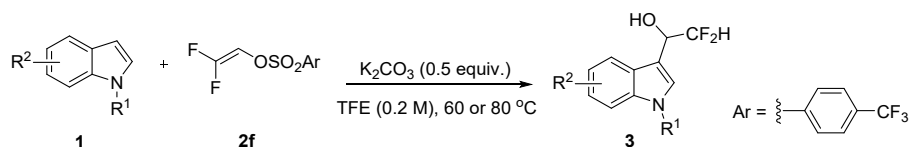
1.2 Synthesis of 2,2-Difluorovinyl-1-D 4-(trifluoromethyl)benzenesulfonate



The synthetic method of the title compound is the same as that of compound **2**, but after the final drop of n-BuLi, it is quenched with D₂O instead of H₂O.

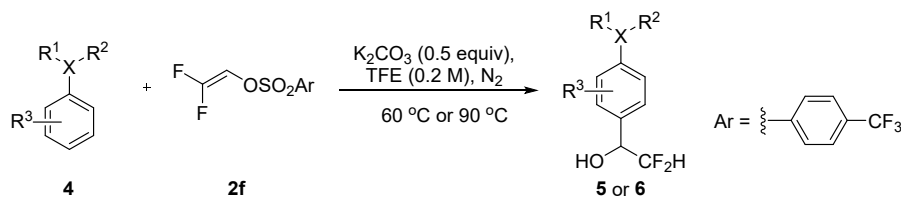
2 General Procedure for Synthesis of Difluoromethyl Carbinols

General procedure A:



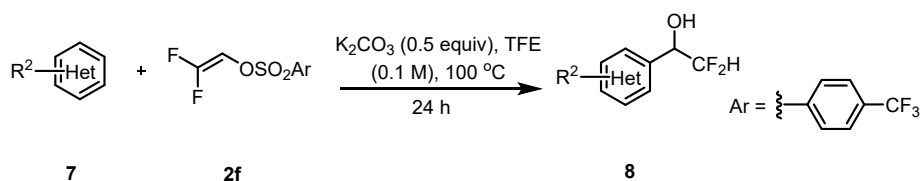
In an oven-dried Pressure tube, a mixture of Indoles **1** (0.2 mmol, 1.0 equiv), 2,2-Difluorovinyl 4-(trifluoromethyl)benzenesulfonate **2f** (115.3 mg, 0.4 mmol, 2 equiv), K_2CO_3 (13.8 mg, 0.1 mmol, 0.5 equiv) in TFE (1 ml) was stirred at 60 °C or 80 °C for 16 h. The reaction mixture was then diluted with Ethyl acetate (10 ml) and washed with brine. The aqueous phase was extracted with Ethyl acetate. The organic layers were combined, washed with brine and dried over Na_2SO_4 . The solvent was removed in vacuo, and the residue was purified by column chromatography (PE/EA) to afford the desired product **3**.

General procedure B:



In an oven-dried Pressure tube, a mixture of Phenyl **4** (0.2 mmol, 1.0 equiv), 2,2-Difluorovinyl 4-(trifluoromethyl)benzenesulfonate **2f** (115.3 mg, 0.4 mmol, 2 equiv), K_2CO_3 (13.8 mg, 0.1 mmol, 0.5 equiv) in TFE (1 ml) was stirred at 60-90 °C Under nitrogen protection for 16 h. The reaction mixture was then diluted with ethyl acetate (10 ml) and washed with brine. The aqueous phase was extracted with Ethyl acetate. The organic layers were combined, washed with brine and dried over Na_2SO_4 . The solvent was removed in vacuo, and the residue was purified by column chromatography (PE/EA) to afford the desired product **5 or 6**.

General procedure C:

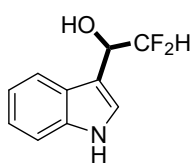


In an oven-dried Pressure tube, a mixture of Heteroarenyl **7** (0.2 mmol, 1.0

equiv), 2,2-Difluorovinyl 4-(trifluoromethyl)benzenesulfonate **2f** (115.3 mg, 0.4 mmol, 2 equiv), K₂CO₃ (13.8 mg, 0.1 mmol, 0.5 equiv) in TFE (2 ml) was stirred at 100 °C for 24 h. The reaction mixture was then diluted with ethyl acetate (10 ml) and washed with brine. The aqueous phase was extracted with Ethyl acetate. The organic layers were combined, washed with brine and dried over Na₂SO₄. The solvent was removed in vacuo, and the residue was purified by column chromatography (PE/EA) to afford the desired product **8**.

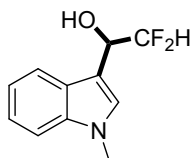
3 Characterization of Products

2,2-Difluoro-1-(1H-indol-3-yl)ethan-1-ol (3a)



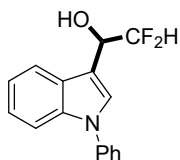
Following general procedure A at the temperature of 60 °C, the title compound was afforded as a brown oil (35.8 mg, 91%). TLC (PE: EA, 2:1 v/v): R_f = 0.5; ^1H NMR (500 MHz, Chloroform-*d*) δ 8.30 (s, 1H), 7.72 (d, J = 7.9 Hz, 1H), 7.38 (d, J = 8.2 Hz, 1H), 7.25 (s, 1H), 7.24 (t, J = 7.5 Hz, 1H), 7.17 (t, J = 7.5 Hz, 1H), 6.00 (td, J = 56.0, 4.3 Hz, 1H), 5.17-5.11 (m, 1H), 2.45 (d, J = 4.2 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 137.2, 128.0, 126.5, 122.5, 120.1, 119.5, 115.8 (t, J = 245.0 Hz), 109.8, 68.3 (t, J = 25.4 Hz), 33.0. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -126.10 (ddd, J = 282.3, 55.8, 10.0 Hz), -127.32 (ddd, J = 281.6, 56.4, 11.6 Hz). **HRMS (ESI):** calcd for $\text{C}_{10}\text{H}_8\text{F}_2\text{NO}$ [$\text{M} + \text{H}$]: 196.0568, found: 196.0559.

2,2-Difluoro-1-(1-methyl-1H-indol-3-yl)ethan-1-ol (3b)



Following general procedure A at the temperature of 60 °C to afford the title compound as a yellow oil (36.7 mg, 87%). TLC (PE: EA, 4:1 v/v): R_f = 0.3; ^1H NMR (500 MHz, Chloroform-*d*) δ 7.71 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 8.2 Hz, 1H), 7.27 (td, J = 7.5, 1.0 Hz, 1H), 7.16 (td, J = 7.4, 1.0 Hz, 1H), 7.16 (s, 1H), 5.98 (td, J = 56.1, 4.5 Hz, 1H), 5.15-5.10 (m, 1H), 3.78 (s, 3H), 2.34 (s, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 137.0, 127.9, 126.4, 122.3, 119.9, 119.4, 115.7 (t, J = 244.7 Hz), 109.6, 109.6 (t, J = 3.4 Hz), 68.1 (t, J = 25.2 Hz), 32.9. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -126.17 (ddd, J = 282.5, 56.7, 10.0 Hz), -127.21 (ddd, J = 282.5, 57.4, 12.1 Hz). **HRMS (ESI):** calcd for $\text{C}_{11}\text{H}_{12}\text{F}_2\text{NO}$ [$\text{M} + \text{H}$] $^+$: 212.0881, found: 212.0878.

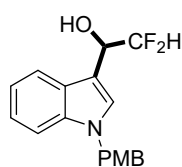
2,2-Difluoro-1-(1-phenyl-1H-indol-3-yl)ethan-1-ol (3c)



Following general procedure A at the temperature of 60 °C to afford the title compound as a yellow oil (48.6 mg, 89%). TLC (PE: EA, 4:1 v/v): R_f = 0.5; ^1H NMR (500 MHz, Chloroform-*d*) δ 7.78 (d, J = 7.9 Hz, 1H), 7.56-7.48 (m, 5H), 7.45 (s, 1H), 7.39 (t, J = 7.1 Hz, 1H), 7.28-7.21 (m, 2H), 6.05 (td, J = 56.12, 4.4 Hz, 1H), 5.21 (t, J = 10.1 Hz, 1H), 2.41 (s, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 139.1, 136.3, 129.7, 127.1, 127.0, 124.5, 123.1, 120.9, 119.7, 115.6 (t, J = 245.4 Hz), 112.1 (t, J = 3.7 Hz), 110.9, 68.2 (t, J = 25.5 Hz), 29.7. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -126.10 (ddd, J = 282.4, 55.7, 9.4 Hz), -127.09 (ddd, J = 282.5, 56.5, 11.5 Hz). **HRMS (ESI):** calcd for

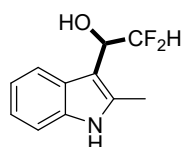
C₁₆H₁₂F₂NO [M + H]⁻: 272.0881, found: 272.0883.

2,2-Difluoro-1-(1-(4-methoxybenzyl)-1H-indol-3-yl)ethan-1-ol (3d)



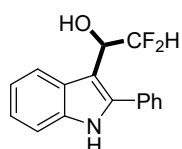
Following general procedure A at the temperature of 60 °C to afford the title compound as a colorless oil (28.5 mg, 45%). TLC (PE: EA, 2:1 v/v): R_f = 0.7; ¹H NMR (500 MHz, Chloroform-*d*) δ 7.74 (d, *J* = 7.9 Hz, 1H), 7.33 (d, *J* = 8.2 Hz, 1H), 7.26 - 7.21 (m, 2H), 7.17 (td, *J* = 8.0, 0.96 Hz, 1H), 7.09 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.7 Hz, 2H), 5.99 (td, *J* = 56.0, 4.5 Hz, 1H), 5.24 (s, 2H), 5.17-5.11 (m, 1H), 3.78 (s, 3H). ¹³C NMR (125 MHz, Chloroform-*d*) δ 159.4, 136.8, 128.9, 128.5, 127.2, 126.7, 122.6, 120.2, 119.7, 115.8 (t, *J* = 244.7 Hz), 114.3, 110.4 (t, *J* = 3.7 Hz), 110.3, 68.4 (t, *J* = 25.4 Hz), 55.4, 49.8. ¹⁹F NMR (470 MHz, Chloroform-*d*) δ -126.00 (ddd, *J* = 281.4, 55.8, 9.1 Hz), -127.18 (ddd, *J* = 281.4, 57.1, 12.1 Hz). **HRMS (ESI)**: calcd for C₁₈H₁₈F₂NO₂ [M + H]⁺: 318.1300, found: 318.1297.

2,2-Difluoro-1-(2-methyl-1H-indol-3-yl)ethan-1-ol (3e)



Following general procedure A at the temperature of 60 °C to afford the title compound as a brown oil (37.5 mg, 89%). TLC (PE: EA, 2:1 v/v): R_f = 0.6; ¹H NMR (500 MHz, Chloroform-*d*) δ 7.95 (s, 1H), 7.69 (d, *J* = 7.8 Hz, 1H), 7.28 (d, *J* = 7.9 Hz, 1H), 7.15 (td, *J* = 7.5, 1.1 Hz, 1H), 7.11 (td, *J* = 7.6, 1.1 Hz, 1H), 6.05 (td, *J* = 56.5, 5.8 Hz, 1H), 5.09-5.03 (m, 1H), 2.43 (s, 3H), 2.32 (s, 1H). ¹³C NMR (125 MHz, Chloroform-*d*) δ 135.3, 134.3, 126.7, 121.8, 120.2, 119.1, 115.5 (t, *J* = 244.5 Hz), 110.6, 106.6z (t, *J* = 3.6 Hz), 68.8 (t, *J* = 26.5 Hz), 12.1. ¹⁹F NMR (470 MHz, Chloroform-*d*) δ -125.72 (d, *J* = 10.1 Hz), -125.84 (d, *J* = 10.2 Hz). **HRMS (ESI)**: calcd for C₁₁H₁₀F₂NO [M + H]⁻: 210.0724, found: 210.0720.

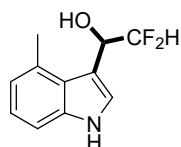
2,2-Difluoro-1-(2-phenyl-1H-indol-3-yl)ethan-1-ol (3f)



Following general procedure A at the temperature of 60 °C to afford the title compound as a yellow oil (27.3 mg, 50%). TLC (PE: EA, 4:1 v/v): R_f = 0.3; ¹H NMR (500 MHz, Chloroform-*d*) δ 8.24 (s, 1H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.51 (d, *J* = 6.7 Hz, 2H), 7.47 - 7.40 (m, 3H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.22 (t, *J* = 7.6 Hz, 1H), 7.15 (t, *J* = 7.5 Hz, 1H), 6.21 (td, *J* = 56.5, 5.7 Hz, 1H), 5.13-5.08 (m, 1H), 2.35 (s, 1H). ¹³C NMR (125 MHz, Chloroform-*d*) δ 138.4, 136.0, 131.7, 129.1, 129.1, 128.9, 126.6, 123.0, 120.8, 120.5, 115.6 (t, *J* =

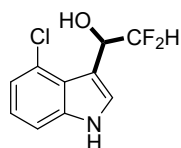
244.5 Hz), 111.4, 107.7 (d, $J = 6.6$ Hz), 68.7 (t, $J = 26.6$ Hz). ^{19}F NMR (470 MHz, Chloroform-*d*) δ -123.67 (ddd, $J = 283.1, 55.8, 8.7$ Hz), -124.95 (ddd, $J = 283.1, 57.1, 10.5$ Hz). **HRMS (ESI):** calcd for $\text{C}_{16}\text{H}_{12}\text{F}_2\text{NO}$ [$\text{M} + \text{H}$]: 272.0881, found: 272.0883.

2,2-Difluoro-1-(4-methyl-1H-indol-3-yl)ethan-1-ol (3g)



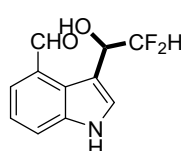
Following general procedure A at the temperature of 60 °C to afford the title compound as a white solid (30.4 mg, 72%). TLC (PE: EA, 2:1 *v/v*): $R_f = 0.5$; ^1H NMR (500 MHz, Chloroform-*d*) δ 8.24 (s, 1H), 7.23 - 7.18 (m, 2H), 7.11 (t, $J = 7.6$ Hz, 1H), 6.91 (d, $J = 7.5$ Hz, 1H), 6.01 (td, $J = 55.8, 3.6$ Hz, 1H), 5.42-5.36 (m, 1H), 2.70 (s, 3H), 2.31 (d, $J = 5.5$ Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 136.3, 130.4, 125.1, 123.3, 122.8, 122.3, 116.2 (t, $J = 245.0$ Hz), 112.1, 109.4, 67.6 (t, $J = 24.3$ Hz), 20.5. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -124.97 (ddd, $J = 281.3, 55.5, 9.5$ Hz), -127.85 (ddd, $J = 281.4, 56.1, 13.0$ Hz). **HRMS (ESI):** calcd for $\text{C}_{11}\text{H}_{10}\text{F}_2\text{NO}$ [$\text{M} + \text{H}$]: 210.0724, found: 210.0724.

1-(4-chloro-1H-indol-3-yl)-2,2-Difluoroethan-1-ol (3h)



Following general procedure A at the temperature of 60 °C to afford the title compound as a colorless oil (40.6 mg, 88%). TLC (PE: EA, 2:1 *v/v*): $R_f = 0.5$; ^1H NMR (500 MHz, Chloroform-*d*) δ 8.47 (s, 1H), 7.34 (d, $J = 2.6$ Hz, 1H), 7.27 (dd, $J = 7.4, 1.6$ Hz, 1H), 7.14 - 7.09 (m, 2H), 6.12 (td, $J = 55.5, 3.0$ Hz, 1H), 5.82 - 5.75 (m, 1H), 2.61 (d, $J = 5.2$ Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 137.6, 125.3, 124.8, 123.3, 121.5, 115.8 (t, $J = 245.6$ Hz), 111.7 (t, $J = 3.9$ Hz), 110.5, 67.2 (t, $J = 23.9$ Hz). ^{19}F NMR (470 MHz, Chloroform-*d*) δ -125.63 (ddd, $J = 279.2, 55.2, 9.1$ Hz), -131.17 (ddd, $J = 279.2, 55.7, 14.9$ Hz). **HRMS (ESI):** calcd for $\text{C}_{10}\text{H}_7\text{ClF}_2\text{NO}$ [$\text{M} + \text{H}$]: 230.0178, found: 230.0178.

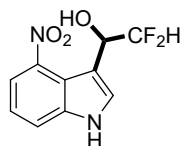
3-(2,2-Difluoro-1-hydroxyethyl)-1H-indole-4-carbaldehyde (3i)



Following general procedure A at the temperature of 80 °C to afford the title compound as a white solid (34.9 mg, 77%). TLC (PE: EA, 2:1 *v/v*): $R_f = 0.2$; ^1H NMR (500 MHz, DMSO-*d*₆) δ 11.76 (s, 1H), 10.27 (s, 1H), 7.78 (d, $J = 8.0$ Hz, 1H), 7.70 (d, $J = 7.3$ Hz, 1H), 7.67 (d, $J = 2.6$ Hz, 1H), 7.32 (t, $J = 7.7$ Hz, 1H), 6.05 (td, $J = 46.5, 4.9$ Hz, 1H), 5.98 (d, $J = 5.7$ Hz, 1H), 5.75 - 5.69 (m, 1H). ^{13}C NMR (125 MHz, DMSO-*d*₆) δ 194.0, 137.7, 129.1, 128.3, 127.0, 123.0, 120.6, 118.7, 117.0 (t, $J = 242.6$ Hz), 113.0 (t, $J = 4.3$ Hz),

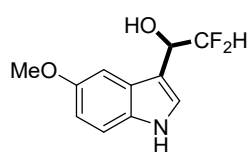
67.0 (t, $J = 22.8$ Hz). ^{19}F NMR (470 MHz, $\text{DMSO-}d_6$) δ -125.11 (ddd, $J = 273.8, 55.5, 8.8$ Hz), -129.28 (ddd, $J = 273.8, 56.3, 14.8$ Hz). **HRMS (ESI):** calcd for $\text{C}_{11}\text{H}_8\text{F}_2\text{NO}_2$ [$\text{M} + \text{H}$] $^-$: 224.0517, found: 224.0521.

2,2-Difluoro-1-(4-nitro-1H-indol-3-yl)ethan-1-ol (3j)



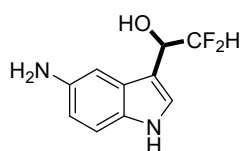
Following general procedure A at the temperature of 80 °C to afford the title compound as a yellow solid (36.8 mg, 76%). TLC (PE: EA, 2:1 v/v): $R_f = 0.2$; ^1H NMR (500 MHz, Chloroform- d) δ 7.78 (ddd, $J = 28.4, 8.0, 0.9$ Hz, 2H), 7.70 (s, 1H), 7.23 (t, $J = 8.0$ Hz, 1H), 5.86 (td, $J = 56.2, 4.0$ Hz, 1H), 5.53 (ddd, $J = 12.5, 8.6, 3.9$ Hz, 1H). ^{13}C NMR (125 MHz, Methanol- d_4) δ 144.1, 140.8, 129.7, 121.4, 119.1, 119.0, 118.6, 118.1 (t, $J = 244.0$ Hz), 112.5 (t, $J = 4.0$ Hz), 68.2 (t, $J = 24.7$ Hz). ^{19}F NMR (470 MHz, Methanol- d_4) δ -128.25 (ddd, $J = 281.2, 56.2, 8.6$ Hz), -130.25 (ddd, $J = 281.2, 56.5, 12.9$ Hz). **HRMS (ESI):** calcd for $\text{C}_{10}\text{H}_7\text{F}_2\text{N}_2\text{O}_3$ [$\text{M} + \text{H}$] $^-$: 241.0419, found: 241.0419.

2,2-Difluoro-1-(5-methoxy-1H-indol-3-yl)ethan-1-ol (3k)



Following general procedure A at the temperature of 60 °C to afford the title compound as a white solid (27.2 mg, 60%). TLC (PE: EA, 2:1 v/v): $R_f = 0.4$; ^1H NMR (500 MHz, Chloroform- d) δ 8.17 (s, 1H), 7.29 (d, $J = 8.9$ Hz, 2H), 7.17 (d, $J = 2.3$ Hz, 1H), 6.90 (dd, $J = 8.8, 2.4$ Hz, 1H), 6.03 (td, $J = 56.3, 3.9$ Hz, 1H), 5.13 (td, $J = 11.6, 4.3$ Hz, 1H), 3.86 (s, 3H), 2.31 (s, 1H). ^{13}C NMR (125 MHz, Chloroform- d) δ 154.7, 131.4, 126.5, 124.0, 115.8 (t, $J = 245.1$ Hz), 113.4, 112.3, 111.3 – 111.3 (m), 101.1, 68.5 (t, $J = 25.8$ Hz), 56.0. ^{19}F NMR (470 MHz, Chloroform- d) δ -125.55 – -127.80 (m). **HRMS (ESI):** calcd for $\text{C}_{11}\text{H}_{10}\text{F}_2\text{NO}_2$ [$\text{M} + \text{H}$] $^-$: 226.0674, found: 226.0673.

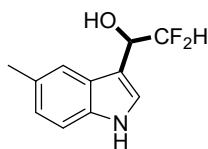
1-(5-amino-1H-indol-3-yl)-2,2-Difluoroethan-1-ol (3l)



Following general procedure A at the temperature of 60 °C to afford the title compound as a brown oil (22.5 mg, 53%). TLC (PE: EA, 1:2 v/v): $R_f = 0.2$; ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ 10.64 (s, 1H), 7.16 (d, $J = 2.6$ Hz, 1H), 7.07 (d, $J = 8.5$ Hz, 1H), 6.78 (d, $J = 1.8$ Hz, 1H), 6.50 (dd, $J = 8.5, 2.1$ Hz, 1H), 6.04 (td, $J = 56.4, 4.7$ Hz, 1H), 5.73 (d, $J = 4.6$ Hz, 1H), 5.08 (s, 2H), 4.84- 4.79 (m, 1H). ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) δ 141.1, 130.0, 127.1, 123.8, 116.6 (t, $J = 243.2$ Hz), 112.1, 111.6, 110.1 (t, $J = 3.9$ Hz), 102.4, 66.8 (t, $J = 24.6$ Hz). ^{19}F NMR (470 MHz, $\text{DMSO-}d_6$) δ -124.77

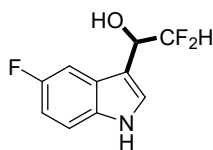
(dd, $J = 21.2, 11.3$ Hz), -124.89 (dd, $J = 20.3, 11.3$ Hz). **HRMS (ESI):** calcd for $C_{10}H_{11}F_2N_2O$ $[M + H]^+$: 213.0833, found: 213.0831.

2,2-Difluoro-1-(5-methyl-1H-indol-3-yl)ethan-1-ol (3m)



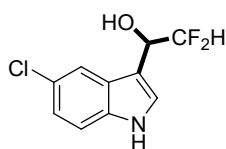
Following general procedure A at the temperature of 60 °C to afford the title compound as a yellow solid (30.4 mg, 72%). TLC (PE: EA, 2:1 v/v): $R_f = 0.5$; 1H NMR (500 MHz, Chloroform- d) δ 8.14 (s, 1H), 7.53 (s, 1H), 7.29 (d, $J = 8.3$ Hz, 1H), 7.25 (s, 1H), 7.08 (d, $J = 9.1$ Hz, 1H), 6.02 (td, $J = 56.1, 4.3$ Hz, 1H), 5.16-5.10 (m, 1H), 2.47 (s, 3H), 2.28 (d, $J = 4.3$ Hz, 1H). ^{13}C NMR (125 MHz, Chloroform- d) δ 134.7, 129.9, 126.2, 124.6, 123.5, 119.1, 115.8 (t, $J = 245.0$ Hz), 111.2, 111.1 (t, $J = 3.7$ Hz), 68.5 (t, $J = 25.4$ Hz), 21.6. ^{19}F NMR (470 MHz, Chloroform- d) δ -126.08 (ddd, $J = 281.3, 55.7, 9.1$ Hz), -127.38 (ddd, $J = 281.7, 55.6, 12.1$ Hz). **HRMS (ESI):** calcd for $C_{11}H_{10}F_2NO$ $[M + H]^+$: 210.0724, found: 210.0725.

2,2-Difluoro-1-(5-fluoro-1H-indol-3-yl)ethan-1-ol (3n)



Following general procedure A at the temperature of 80 °C to afford the title compound as a green oil (37.8 mg, 88%). TLC (PE: EA, 2:1 v/v): $R_f = 0.4$; 1H NMR (500 MHz, Chloroform- d) δ 8.26 (s, 1H), 7.36 (dd, $J = 9.6, 2.5$ Hz, 1H), 7.30 – 7.27 (m, 2H), (td, $J = 9.0, 2.5$ Hz, 1H), 5.94 (td, $J = 56.2, 4.2$ Hz, 1H), 5.10 – 5.04 (m, 1H), 2.43 (d, $J = 4.2$ Hz, 1H). ^{13}C NMR (125 MHz, Chloroform- d) δ 158.1 (d, $J = 235.7$ Hz), 132.7, 126.2 (d, $J = 9.9$ Hz), 125.0, 115.5 (t, $J = 245.2$ Hz), 112.2 (d, $J = 9.7$ Hz), 111.4 (d, $J = 26.0$ Hz), 110.8 (t, $J = 3.2$ Hz), 104.5 (d, $J = 23.9$ Hz), 68.2 (t, $J = 25.3$ Hz). ^{19}F NMR (470 MHz, Chloroform- d) δ -123.27 – -123.32 (m), -126.35 (ddd, $J = 282.7, 55.6, 10.2$ Hz), -127.25 (ddd, $J = 282.8, 56.8, 11.8$ Hz). **HRMS (ESI):** calcd for $C_{10}H_7F_3NO$ $[M + H]^+$: 214.0474, found: 214.0473.

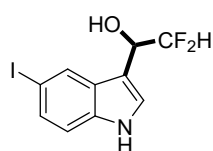
1-(5-chloro-1H-indol-3-yl)-2,2-Difluoroethan-1-ol (3o)



Following general procedure A at the temperature of 60 °C to afford the title compound as a yellow oil (37.9 mg, 82%). TLC (PE: EA, 2:1 v/v): $R_f = 0.5$; 1H NMR (500 MHz, Chloroform- d) δ 8.34 (s, 1H), 7.67 (d, $J = 1.6$ Hz, 1H), 7.24 (d, $J = 8.2$ Hz, 1H), 7.22 (d, $J = 2.6$ Hz, 1H), 7.15 (dd, $J = 8.7, 2.0$ Hz, 1H), 5.93 (td, $J = 56.0, 4.2$ Hz, 1H), 5.07 – 5.01 (m, 1H), 2.62 (d, $J = 3.6$ Hz, 1H). ^{13}C NMR (125 MHz, Chloroform- d) δ

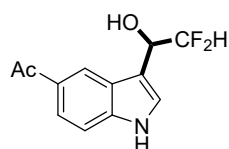
134.6, 126.9, 126.1, 124.7, 123.1, 118.9, 115.5 (t, $J = 245.0$ Hz), 112.5, 110.9 (t, $J = 3.6$ Hz), 68.1 (t, $J = 25.4$ Hz). ^{19}F NMR (470 MHz, Chloroform-*d*) δ -126.23 (ddd, $J = 282.6, 55.8, 10.0$ Hz), -127.20 (ddd, $J = 282.5, 56.8, 11.8$ Hz). **HRMS (ESI):** calcd for $\text{C}_{10}\text{H}_7\text{ClF}_2\text{NO}$ [$\text{M} + \text{H}$]: 230.0178, found: 230.0179.

2,2-Difluoro-1-(5-iodo-1H-indol-3-yl)ethan-1-ol (3p)



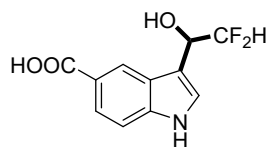
Following general procedure A at the temperature of 60 °C to afford the title compound as a brown oil (56.2 mg, 87%). TLC (PE: EA, 2:1 *v/v*): $R_f = 0.5$; ^1H NMR (500 MHz, Chloroform-*d*) δ 8.33 (s, 1H), 8.02 (s, 1H), 7.44 (d, $J = 10.0$ Hz, 1H), 7.13 (d, $J = 2.4$ Hz, 1H), 7.08 (d, $J = 8.6$ Hz, 1H), 5.92 (td, $J = 56.0, 4.2$ Hz, 1H), 5.02 (t, $J = 10.4$ Hz, 1H), 2.64 (s, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 135.2, 131.1, 128.3, 128.2, 124.2, 115.4 (t, $J = 245.0$ Hz), 113.4, 110.4 (t, $J = 3.6$ Hz), 83.9, 68.0 (t, $J = 25.4$ Hz). ^{19}F NMR (470 MHz, Chloroform-*d*) δ -126.17 (ddd, $J = 282.6, 55.6, 10.2$ Hz), -127.20 (ddd, $J = 282.4, 56.3, 11.6$ Hz). **HRMS (ESI):** calcd for $\text{C}_{10}\text{H}_7\text{F}_2\text{INO}$ [$\text{M} + \text{H}$]: 321.9534, found: 321.9530.

1-(3-(2,2-Difluoro-1-hydroxyethyl)-1H-indol-5-yl)ethan-1-one (3q)



Following general procedure A at the temperature of 80 °C to afford the title compound as a yellow oil (38.9 mg, 81%). TLC (PE: EA, 1:1 *v/v*): $R_f = 0.4$; ^1H NMR (500 MHz, DMSO-*d*₆) δ 11.51 (s, 1H), 8.40 (s, 1H), 7.76 (dd, $J = 8.6, 1.6$ Hz, 1H), 7.50 (d, $J = 2.4$ Hz, 1H), 7.47 (d, $J = 8.6$ Hz, 1H), 6.18 (td, $J = 55.9, 4.3$ Hz, 1H), 6.04 (d, $J = 5.2$ Hz, 1H), 5.13- 5.07 (m, 1H), 2.61 (s, 3H). ^{13}C NMR (125 MHz, DMSO-*d*₆) δ 197.6, 138.9, 128.8, 126.1, 125.7, 122.0, 121.4, 116.4 (t, $J = 243.7$ Hz), 113.6 (t, $J = 3.5$ Hz), 111.5, 66.5 (t, $J = 24.6$ Hz), 26.7. ^{19}F NMR (470 MHz, DMSO-*d*₆) δ -125.20 (ddd, $J = 276.7, 56.6, 12.8$ Hz), -126.32 (ddd, $J = 275.1, 55.6, 11.3$ Hz). **HRMS (ESI):** calcd for $\text{C}_{12}\text{H}_{12}\text{F}_2\text{NO}_2$ [$\text{M} + \text{H}$]⁺: 240.0830, found: 240.0829.

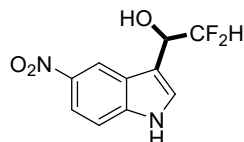
3-(2,2-Difluoro-1-hydroxyethyl)-1H-indole-5-carboxylic acid (3r)



Following general procedure A at the temperature of 80 °C to afford the title compound as a white solid (32 mg, 66%). TLC (PE: EA, 1:1 *v/v*): $R_f = 0.4$; ^1H NMR (500 MHz, Methanol-*d*₄) δ 8.49 (d, $J = 1.0$ Hz, 1H), 7.85 (dd, $J = 8.6, 1.6$ Hz, 1H), 7.43 (d, $J = 7.2$ Hz, 2H), 6.02 (td, $J = 56.0, 4.4$ Hz, 1H), 5.12 (td, $J = 10.9, 4.5$ Hz, 1H), 1.99 (s, 2H). ^{13}C NMR (125

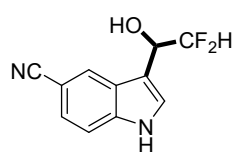
MHz, Methanol-*d*₄) δ 171.4z, 140.8, 127.3, 126.5, 124.3, 123.8, 122.7, 117.5 (t, J = 244.0 Hz), 114.1 (t, J = 3.5 Hz), 112.2, 68.7 (t, J = 24.8 Hz). ¹⁹F NMR (470 MHz, Methanol-*d*₄) δ -127.50 (ddd, J = 281.2, 56.1, 10.8 Hz), -128.18 (ddd, J = 281.1, 55.6, 12.0 Hz). **HRMS (ESI)**: calcd for C₁₁H₈F₂NO₃ [M + H]⁺: 240.0466, found: 240.0465.

2,2-Difluoro-1-(5-nitro-1H-indol-3-yl)ethan-1-ol (3s)



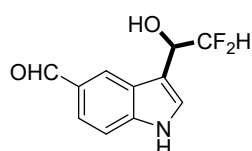
Following general procedure A at the temperature of 80 °C to afford the title compound as a yellow solid (41.6 mg, 86%). TLC (PE: EA, 2:1 v/v): R_f = 0.2; ¹H NMR (500 MHz, Methanol-*d*₄) δ 8.71 (s, 1H), 8.05 (dd, J = 9.0, 2.2 Hz, 1H), 7.52 (s, 1H), 7.48 (d, J = 9.0 Hz, 1H), 6.02 (td, J = 56.1, 4.1 Hz, 1H), 5.14 (td, J = 11.5, 4.1 Hz, 1H). ¹³C NMR (125 MHz, Methanol-*d*₄) δ 142.7, 141.1, 128.5, 127.0, 118.1, 118.0, 117.5 (t, J = 244.0 Hz), 115.3 (t, J = 3.4 Hz), 112.6, 68.6 (t, J = 25.2 Hz). ¹⁹F NMR (470 MHz, Methanol-*d*₄) δ -128.20 (ddd, J = 55.9, 49.3, 11.7 Hz). **HRMS (ESI)**: calcd for C₁₀H₇F₂N₂O₃ [M + H]⁺: 241.0419, found: 241.0419.

3-(2,2-Difluoro-1-hydroxyethyl)-1H-indole-5-carbonitrile (3t)



Following general procedure A at the temperature of 80 °C to afford the title compound as a yellow oil (37.3 mg, 84%). TLC (PE: EA, 2:1 v/v): R_f = 0.2; ¹H NMR (500 MHz, Chloroform-*d*) δ 8.66 (s, 1H), 8.12 (s, 1H), 7.45-7.43 (m, 3H), 6.95 (td, J = 56.0, 4.4 Hz, 1H), 5.19 – 5.13 (m, 1H), 2.59 (d, J = 4.0 Hz, 1H). ¹³C NMR (125 MHz, Chloroform-*d*) δ 138.1, 126.0, 125.8, 125.8, 125.5, 120.5, 115.6 (t, J = 245.5 Hz), 112.5, 112.4 (t, J = 3.7 Hz), 103.7, 68.3 (t, J = 25.9 Hz). ¹⁹F NMR (470 MHz, Chloroform-*d*) δ -126.42 (ddd, J = 285.2, 56.7, 10.8 Hz), -127.18 (ddd, J = 284.0, 55.6, 9.9 Hz). **HRMS (ESI)**: calcd for C₁₁H₇F₂N₂O [M + H]⁺: 221.0520, found: 221.0520.

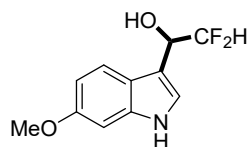
3-(2,2-Difluoro-1-hydroxyethyl)-1H-indole-5-carbaldehyde (3u)



Following general procedure A at the temperature of 80 °C to afford the title compound as a white solid (40 mg, 89%). TLC (PE: EA, 2:1 v/v): R_f = 0.2; ¹H NMR (500 MHz, DMSO-*d*₆) δ 11.65 (s, 1H), 9.99 (s, 1H), 8.32 (s, 1H), 7.66 (dd, J = 8.5, 1.4 Hz, 1H), 7.55 (dd, J = 5.4, 3.0 Hz, 2H), 6.18 (td, J = 56.5, 4.5 Hz, 1H), 6.09 (s, 1H), 5.10 (t, J = 9.9 Hz, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆) δ 192.7, 139.8, 128.8, 126.5,

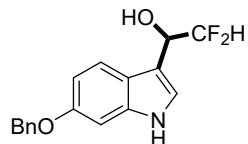
126.0, 125.5, 121.2, 116.4 (t, $J = 243.6$ Hz), 113.8 (t, $J = 7.1$ Hz), 112.4, 66.6 (t, $J = 24.7$ Hz). ^{19}F NMR (470 MHz, $\text{DMSO-}d_6$) δ -125.13 (ddd, $J = 276.5, 56.3, 12.2$ Hz), -126.10 (ddd, $J = 276.2, 55.7, 11.4$ Hz). **HRMS (ESI):** calcd for $\text{C}_{11}\text{H}_8\text{F}_2\text{NO}_2$ $[\text{M} + \text{H}]^+$: 224.0517, found: 224.0521.

2,2-Difluoro-1-(6-methoxy-1H-indol-3-yl)ethan-1-ol (3v)



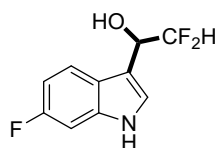
Following general procedure A at the temperature of 60 °C to afford the title compound as a white solid (40.8 mg, 90%). TLC (PE: EA, 2:1 v/v): $R_f = 0.4$; ^1H NMR (500 MHz, Methanol- d_4) δ 7.53 (d, $J = 8.7$ Hz, 1H), 7.18 (s, 1H), 6.90 (d, $J = 2.2$ Hz, 1H), 6.71 (dd, $J = 8.7, 2.3$ Hz, 1H), 5.98 (td, $J = 55.9, 4.5$ Hz, 1H), 5.01 (td, $J = 9.1, 4.8$ Hz, 1H), 3.80 (s, 3H). ^{13}C NMR (125 MHz, Methanol- d_4) δ 157.8, 138.8, 123.6, 121.9, 120.8, 117.6 (t, $J = 243.7$ Hz), 112.4-112.4 (m), 110.6, 95.4, 69.2-68.8 (m), 55.9. ^{19}F NMR (470 MHz, Methanol- d_4) δ -126.94 (ddd, $J = 279.3, 55.7, 9.1$ Hz), -128.30 (ddd, $J = 280.4, 57.1, 13.1$ Hz). **HRMS (ESI):** calcd for $\text{C}_{11}\text{H}_{10}\text{F}_2\text{NO}_2$ $[\text{M} + \text{H}]^+$: 226.0674, found: 226.0672.

1-(6-(benzyloxy)-1H-indol-3-yl)-2,2-Difluoroethan-1-ol (3w)



Following general procedure A at the temperature of 60 °C to afford the title compound as a yellow solid (52.1 mg, 86%). TLC (PE: EA, 2:1 v/v): $R_f = 0.4$; ^1H NMR (500 MHz, Chloroform- d) δ 8.11 (s, 1H), 7.57 (d, $J = 8.7$ Hz, 1H), 7.43 (d, $J = 7.2$ Hz, 2H), 7.37 (t, $J = 7.4$ Hz, 2H), 7.32 (t, $J = 7.2$ Hz, 1H), 7.07 (d, $J = 2.4$ Hz, 1H), 6.90 (dd, $J = 8.7, 2.2$ Hz, 1H), 6.85 (d, $J = 2.1$ Hz, 1H), 5.94 (td, $J = 56.1, 4.3$ Hz, 1H), 5.05 (s, 3H), 2.51 (s, 1H). ^{13}C NMR (125 MHz, Chloroform- d) δ 155.9, 137.2, 136.9, 128.6, 127.9, 127.5, 122.3, 120.3, 120.0, 115.6 (t, $J = 245.1$ Hz), 111.2 (t, $J = 3.6$ Hz), 111.1, 96.2, 70.6, 68.3 (t, $J = 25.3$ Hz). ^{19}F NMR (470 MHz, Methanol- d_4) δ -126.98 (d, $J = 280.6$ Hz), -128.27 (d, $J = 280.6$ Hz). **HRMS (ESI):** calcd for $\text{C}_{17}\text{H}_{14}\text{F}_2\text{NO}_2$ $[\text{M} + \text{H}]^+$: 302.0987, found: 302.0988.

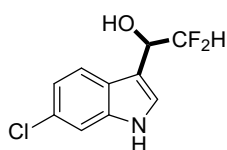
2,2-Difluoro-1-(6-fluoro-1H-indol-3-yl)ethan-1-ol (3x)



Following general procedure A at the temperature of 60 °C to afford the title compound as a brown oil (37.4 mg, 87%). TLC (PE: EA, 2:1 v/v): $R_f = 0.4$; ^1H NMR (500 MHz, Chloroform- d) δ 8.28 (s, 1H), 7.62 (dd, $J = 8.7, 5.3$ Hz, 1H), 7.20 (d, $J = 2.5$ Hz, 1H), 7.02

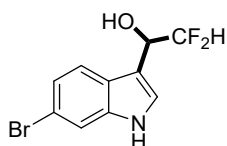
(dd, $J = 9.4, 2.3$ Hz, 1H), 6.92 (td, $J = 9.2, 2.3$ Hz, 1H), 5.95 (td, $J = 56.0, 4.3$ Hz, 1H), 5.11-5.06 (m, 1H), 2.56 (d, $J = 4.1$ Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 160.2 (d, $J = 238.9$ Hz), 136.3 (d, $J = 12.5$ Hz), 123.7, 122.4, 120.3 (d, $J = 10.1$ Hz), 115.6 (t, $J = 245.0$ Hz), 111.3 (t, $J = 3.6$ Hz), 109.3 (d, $J = 24.7$ Hz), 97.8 (d, $J = 26.6$ Hz), 68.2 (t, $J = 25.5$ Hz). ^{19}F NMR (470 MHz, Chloroform-*d*) δ -120.02 (td, $J = 10.4, 9.6, 5.4$ Hz), -126.17 (ddd, $J = 282.3, 55.9, 9.9$ Hz), -127.24 (ddd, $J = 282.4, 56.3, 11.8$ Hz). **HRMS (ESI):** calcd for $\text{C}_{10}\text{H}_7\text{F}_3\text{NO}$ [$\text{M} + \text{H}$] $^+$: 214.0474, found: 214.0465.

1-(6-chloro-1H-indol-3-yl)-2,2-Difluoroethan-1-ol (3y)



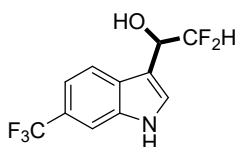
Following general procedure A at the temperature of 60 °C to afford the title compound as a yellow solid (41.1 mg, 89%). TLC (PE: EA, 2:1 v/v): $R_f = 0.5$; ^1H NMR (500 MHz, Chloroform-*d*) δ 8.25 (s, 1H), 7.64 (d, $J = 8.5$ Hz, 1H), 7.37 (d, $J = 1.7$ Hz, 1H), 7.28 (d, $J = 2.5$ Hz, 1H), 7.14 (dd, $J = 8.5, 1.7$ Hz, 1H), 5.96 (td, $J = 56.1, 4.3$ Hz, 1H), 5.15-5.09 (m, 1H), 2.38 (d, $J = 4.3$ Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 136.6, 128.8, 124.5, 123.9, 121.2, 120.4, 115.6 (t, $J = 245.0$ Hz), 111.6 (t, $J = 3.6$ Hz), 111.4, 68.2 (t, $J = 25.0$ Hz). ^{19}F NMR (470 MHz, Chloroform-*d*) δ -126.41 (ddd, $J = 282.2, 56.9, 10.1$ Hz), -127.18 (ddd, $J = 283.5, 56.4, 11.1$ Hz). **HRMS (ESI):** calcd for $\text{C}_{10}\text{H}_7\text{ClF}_2\text{NO}$ [$\text{M} + \text{H}$] $^+$: 230.0178, found: 230.0179.

1-(6-bromo-1H-indol-3-yl)-2,2-Difluoroethan-1-ol (3z)



Following general procedure A at the temperature of 60 °C to afford the title compound as a white solid (47.7 mg, 87%). TLC (PE: EA, 2:1 v/v): $R_f = 0.5$; ^1H NMR (500 MHz, Chloroform-*d*) δ 8.27 (s, 1H), 7.56 (d, $J = 8.5$ Hz, 1H), 7.50 (d, $J = 1.5$ Hz, 1H), 7.25 (dd, $J = 8.5, 1.5$ Hz, 1H), 7.21 (d, $J = 2.5$ Hz, 1H), 5.94 (td, $J = 56.0, 4.3$ Hz, 1H), 5.12 – 5.06 (m, 1H), 2.49 (d, $J = 4.2$ Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 137.0, 124.7, 123.9, 123.7, 120.7, 116.3, 115.5 (t, $J = 245.0$ Hz), 114.4, 111.5 (t, $J = 3.5$ Hz), 68.1 (t, $J = 25.5$ Hz). ^{19}F NMR (470 MHz, Chloroform-*d*) δ -126.34 (d, $J = 282.7$ Hz), -127.22 (d, $J = 282.7$ Hz). **HRMS (ESI):** calcd for $\text{C}_{10}\text{H}_7\text{BrF}_2\text{NO}$ [$\text{M} + \text{H}$] $^+$: 273.9673, found: 273.9676.

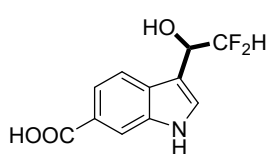
2,2-Difluoro-1-(6-(trifluoromethyl)-1H-indol-3-yl)ethan-1-ol (3a')



Following general procedure A at the temperature of 80 °C to afford the title compound as a brown oil (40.3 mg, 76%). TLC

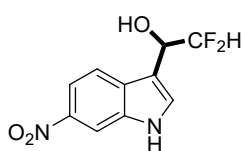
(PE: EA, 2:1 v/v): $R_f = 0.5$; $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 8.54 (s, 1H), 7.83 (d, $J = 8.4$ Hz, 1H), 7.68 (s, 1H), 7.44 (s, 1H), 7.41 (d, $J = 8.4$ Hz, 1H), 5.98 (td, $J = 56.1, 4.4$ Hz, 1H), 5.21-5.15 (m, 1H), 2.48 (d, $J = 3.7$ Hz, 1H). $^{13}\text{C NMR}$ (125 MHz, Chloroform-*d*) δ 135.1, 128.2, 125.9, 124.9 (q, $J = 271.8$ Hz), 125.0 (q, $J = 32.1$ Hz), 120.0, 117.1 (q, $J = 3.6$ Hz), 115.6 (t, $J = 245.5$ Hz), 111.7 (t, $J = 3.6$ Hz), 109.1 (q, $J = 4.5$ Hz), 68.2 (t, $J = 25.6$ Hz). $^{19}\text{F NMR}$ (470 MHz, Chloroform-*d*) δ -60.81, -126.77 (t, $J = 10.3$ Hz), -126.89 (t, $J = 9.9$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{11}\text{H}_7\text{F}_5\text{NO}$ [$\text{M} + \text{H}$] $^-$: 264.0442, found: 264.0443.

3-(2,2-Difluoro-1-hydroxyethyl)-1H-indole-6-carboxylic acid (3b')



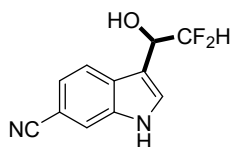
Following general procedure A at the temperature of 80 °C to afford the title compound as a white solid (30 mg, 62%). TLC (PE: EA, 1:1 v/v): $R_f = 0.4$; $^1\text{H NMR}$ (500 MHz, Methanol-*d*₄) δ 8.14 (s, 1H), 7.75 (s, 2H), 7.52 (s, 1H), 6.02 (td, $J = 56.0, 4.1$ Hz, 1H), 5.11 (td, $J = 10.6, 4.3$ Hz, 1H). $^{13}\text{C NMR}$ (125 MHz, Methanol-*d*₄) δ 171.4, 137.3, 131.3, 128.5, 124.9, 121.5, 119.9, 117.5 (t, $J = 243.8$ Hz), 115.1, 113.1 (t, $J = 3.6$ Hz), 68.6 (t, $J = 25.2$ Hz). $^{19}\text{F NMR}$ (470 MHz, Methanol-*d*₄) δ -127.58 (ddd, $J = 281.8, 56.2, 10.8$ Hz), -128.30 (dd, $J = 281.1, 56.6, 12.2$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{11}\text{H}_8\text{F}_2\text{NO}_3$ [$\text{M} + \text{H}$] $^-$: 240.0466, found: 240.0466.

2,2-Difluoro-1-(6-nitro-1H-indol-3-yl)ethan-1-ol (3c')



Following general procedure A at the temperature of 80 °C to afford the title compound as a yellow solid (42.6 mg, 88%). TLC (PE: EA, 2:1 v/v): $R_f = 0.3$; $^1\text{H NMR}$ (500 MHz, Methanol-*d*₄) δ 8.36 (d, $J = 1.8$ Hz, 1H), 7.97 (dd, $J = 8.9, 2.1$ Hz, 1H), 7.83 (d, $J = 8.9$ Hz, 1H), 7.68 (s, 1H), 6.01 (td, $J = 56.2, 4.0$ Hz, 1H), 5.13 (td, $J = 11.3, 4.2$ Hz, 1H). $^{13}\text{C NMR}$ (125 MHz, Methanol-*d*₄) δ 144.4, 136.5, 132.4, 131.2, 120.6, 117.5 (t, $J = 243.7$ Hz), 115.4, 114.0 (t, $J = 3.6$ Hz), 109.2, 68.5 (t, $J = 25.4$ Hz). $^{19}\text{F NMR}$ (470 MHz, Methanol-*d*₄) δ -127.84 (ddd, $J = 280.8, 55.9, 10.8$ Hz), -128.58 (ddd, $J = 280.4, 55.5, 10.5$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{10}\text{H}_7\text{F}_2\text{N}_2\text{O}_3$ [$\text{M} + \text{H}$] $^-$: 241.0419, found: 241.0420.

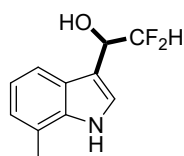
3-(2,2-Difluoro-1-hydroxyethyl)-1H-indole-6-carbonitrile (3d')



Following general procedure A at the temperature of 80 °C to afford the title compound as a white solid (39.1 mg, 88%). TLC

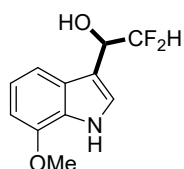
(PE: EA, 2:1 v/v): $R_f = 0.2$; $^1\text{H NMR}$ (500 MHz, Methanol- d_4) δ 7.03 (d, $J = 8.3$ Hz, 1H), 6.98 (s, 1H), 6.78 (s, 1H), 6.51 (d, $J = 9.5$ Hz, 1H), 5.18 (td, $J = 56.1, 4.2$ Hz, 1H), 4.30 (td, $J = 11.3, 4.1$ Hz, 1H). $^{13}\text{C NMR}$ (125 MHz, Methanol- d_4) δ 136.9, 130.9, 129.3, 122.9, 121.6, 121.5, 117.5, 117.5 (t, $J = 243.6$ Hz), 113.7 (t, $J = 3.5$ Hz), 104.8, 68.5 (t, $J = 25.2$ Hz). $^{19}\text{F NMR}$ (470 MHz, Methanol- d_4) δ -127.78 (ddd, $J = 280.8, 56.3, 10.7$ Hz), -128.43 (ddd, $J = 281.5, 55.9, 11.4$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{11}\text{H}_7\text{F}_2\text{N}_2\text{O}$ [$\text{M} + \text{H}$] $^+$: 221.0520, found: 221.0520.

2,2-Difluoro-1-(7-methyl-1H-indol-3-yl)ethan-1-ol (3e')



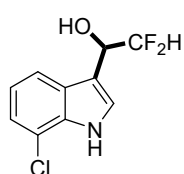
Following general procedure A at the temperature of 60 °C to afford the title compound as a yellow oil (37.1 mg, 88%). TLC (PE: EA, 2:1 v/v): $R_f = 0.4$; $^1\text{H NMR}$ (500 MHz, Chloroform- d) δ 8.17 (s, 1H), 7.57 (d, $J = 7.8$ Hz, 1H), 7.26 (s, 1H), 7.09 (t, $J = 7.5$ Hz, 1H), 7.05 (d, $J = 6.9$ Hz, 1H), 5.98 (td, $J = 55.6, 3.0$ Hz, 1H), 5.15-5.10 (m, 1H), 2.47 (s, 3H), 2.37 (d, $J = 3.4$ Hz, 1H). $^{13}\text{C NMR}$ (125 MHz, Chloroform- d) δ 136.0, 125.5, 123.4, 123.1, 120.8, 120.7, 117.1, 115.8 (t, $J = 244.7$ Hz), 112.0 (t, $J = 3.7$ Hz), 68.5 (t, $J = 25.4$ Hz), 16.7. $^{19}\text{F NMR}$ (470 MHz, Chloroform- d) δ -126.14 (ddd, $J = 282.1, 55.7, 9.7$ Hz), -127.34 (ddd, $J = 282.1, 56.6, 12.0$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{11}\text{H}_{10}\text{F}_2\text{NO}$ [$\text{M} + \text{H}$] $^+$: 210.0724, found: 210.0715.

2,2-Difluoro-1-(7-methoxy-1H-indol-3-yl)ethan-1-ol (3f')



Following general procedure A at the temperature of 60 °C to afford the title compound as a yellow oil (39.9 mg, 88%). TLC (PE: EA, 2:1 v/v): $R_f = 0.4$; $^1\text{H NMR}$ (500 MHz, Chloroform- d) δ 8.53 (s, 1H), 7.32 (d, $J = 8.0$ Hz, 1H), 7.24 (d, $J = 2.4$ Hz, 1H), 7.08 (t, $J = 7.9$ Hz, 1H), 6.68 (d, $J = 7.7$ Hz, 1H), 5.99 (td, $J = 56.1, 4.4$ Hz, 1H), 5.14-5.09 (m, 1H), 3.95 (s, 3H), 2.47 (s, 1H). $^{13}\text{C NMR}$ (125 MHz, Chloroform- d) δ 146.2, 127.1, 126.9, 122.9, 120.9, 115.6 (t, $J = 244.9$ Hz), 111.9, 111.8 (t, $J = 3.8$ Hz), 102.4, 68.3 (t, $J = 25.4$ Hz), 55.4. $^{19}\text{F NMR}$ (470 MHz, Chloroform- d) δ -126.18 (dd, $J = 282.3, 55.5, 10.3$ Hz), -127.38 (ddd, $J = 282.5, 57.1, 11.9$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{11}\text{H}_{10}\text{F}_2\text{NO}_2$ [$\text{M} + \text{H}$] $^+$: 226.0674, found: 226.0681.

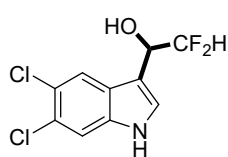
1-(7-chloro-1H-indol-3-yl)-2,2-Difluoroethan-1-ol (3g')



Following general procedure A at the temperature of 60 °C to afford the title compound as a yellow oil (41.6 mg, 90%). TLC (PE: EA, 2:1

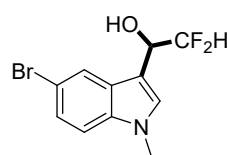
v/v): $R_f = 0.7$; $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 8.50 (s, 1H), 7.63 (d, $J = 8.0$ Hz, 1H), 7.33 (d, $J = 2.5$ Hz, 1H), 7.25 (d, $J = 2.0$ Hz, 1H), 7.10 (t, $J = 7.8$ Hz, 1H), 5.97 (td, $J = 56.1, 4.4$ Hz, 1H), 5.13 (td, $J = 10.6, 4.3$ Hz, 1H), 2.51 (s, 1H). $^{13}\text{C NMR}$ (125 MHz, Chloroform-*d*) δ 133.6, 127.3, 123.9, 122.1, 121.2, 118.2, 116.9, 115.5 (t, $J = 245.3$ Hz), 112.5 (t, $J = 3.6$ Hz), 68.3 (t, $J = 25.7$ Hz). $^{19}\text{F NMR}$ (470 MHz, Chloroform-*d*) δ -126.00 (ddd, $J = 281.6, 54.9, 9.9$ Hz), -127.23 (ddd, $J = 281.6, 56.9, 12.0$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{10}\text{H}_7\text{ClF}_2\text{NO}$ [$\text{M} + \text{H}$] $^+$: 230.0178, found: 230.0179.

1-(5,6-dichloro-1H-indol-3-yl)-2,2-difluoroethan-1-ol (3h')



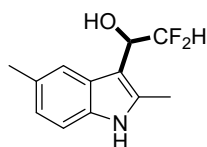
Following general procedure A at the temperature of 60 °C to afford the title compound as a yellow oil (42.4 mg, 80%). TLC (PE: EA, 2:1 *v/v*): $R_f = 0.4$; $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 8.42 (s, 1H), 7.78 (s, 1H), 7.43 (s, 1H), 7.26 (s, 1H), 5.93 (td, $J = 56.1, 4.3$ Hz, 1H), 5.06 (td, $J = 10.7, 4.2$ Hz, 1H), 2.76 (s, 1H). $^{13}\text{C NMR}$ (125 MHz, Chloroform-*d*) δ 134.9, 126.6, 125.5, 125.2, 124.4, 120.6, 115.4 (t, $J = 245.3$ Hz), 112.9, 110.9 (t, $J = 3.6$ Hz), 68.0 (t, $J = 25.5$ Hz). $^{19}\text{F NMR}$ (470 MHz, Chloroform-*d*) δ -126.39 (ddd, $J = 282.8, 55.6, 10.3$ Hz), -127.27 (ddd, $J = 282.2, 55.3, 10.2$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{10}\text{H}_6\text{Cl}_2\text{F}_2\text{NO}$ [$\text{M} + \text{H}$] $^+$: 263.9789, found: 263.9789.

1-(5-bromo-1-methyl-1H-indol-3-yl)-2,2-Difluoroethan-1-ol (3i')



Following general procedure A at the temperature of 60 °C to afford the title compound as a white solid (42.6 mg, 74%). TLC (PE: EA, 2:1 *v/v*): $R_f = 0.4$; $^1\text{H NMR}$ (500 MHz, Methanol-*d*₄) δ 7.72 (s, 1H), 7.19 – 7.15 (m, 3H), 5.85 (td, $J = 56.2, 4.2$ Hz, 1H), 4.90 (td, $J = 11.4, 4.3$ Hz, 1H), 3.66 (s, 3H). $^{13}\text{C NMR}$ (125 MHz, Methanol-*d*₄) δ 137.3, 130.6, 129.8, 125.6, 123.2, 117.5 (t, $J = 243.7$ Hz), 113.7, 112.2, 111.5 (t, $J = 3.6$ Hz), 68.5 (t, $J = 25.1$ Hz), 33.0. $^{19}\text{F NMR}$ (470 MHz, Methanol-*d*₄) δ -127.61 (ddd, $J = 281.2, 56.4, 11.1$ Hz), -128.27 (ddd, $J = 281.4, 57.0, 11.7$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{11}\text{H}_9\text{BrF}_2\text{NO}$ [$\text{M} + \text{H}$] $^+$: 287.9830, found: 287.9840.

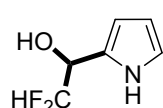
1-(2,5-dimethyl-1H-indol-3-yl)-2,2-Difluoroethan-1-ol (3j')



Following general procedure A at the temperature of 80 °C to afford the title compound as a red oil (15.7 mg, 35%). TLC (PE: EA, 2:1 *v/v*): $R_f = 0.6$; $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 7.89 (s, 1H),

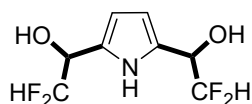
7.48 (s, 1H), 7.17 (d, $J = 8.2$ Hz, 1H), 6.98 (d, $J = 8.2$ Hz, 1H), 6.06 (td, $J = 56.6, 5.6$ Hz, 1H), 5.05 – 5.0 (m, 1H), 2.42 (d, $J = 9.8$ Hz, 6H), 2.35 (s, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 134.3, 133.5, 129.5, 126.8, 123.2, 118.7, 115.5 (t, $J = 244.4$ Hz), 110.2, 106.0 (t, $J = 4.0$ Hz), 68.8 (t, $J = 26.5$ Hz), 21.5, 12.1. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -125.63 (d, $J = 10.2$ Hz), -125.75 (d, $J = 10.2$ Hz). **HRMS (ESI):** calcd for $\text{C}_{12}\text{H}_{12}\text{F}_2\text{NO}$ [$\text{M} + \text{H}$] $^+$: 224.0881, found: 224.0881.

2,2-Difluoro-1-(1H-pyrrol-2-yl)ethan-1-ol (3l')



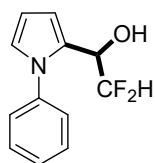
Following general procedure A at the temperature of 60 °C to afford the title compound as a colorless oil (13.4 mg, 45%). TLC (PE: EA, 2:1 v/v): $R_f = 0.5$; ^1H NMR (500 MHz, Chloroform-*d*) δ 8.55 (s, 1H), 6.87 – 6.81 (m, 1H), 6.24 (s, 1H), 6.21 (q, $J = 2.8$ Hz, 1H), 5.84 (td, $J = 55.8, 3.6$ Hz, 1H), 4.91 (t, $J = 9.9$ Hz, 1H), 2.54 (s, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 127.6, 118.1, 114.0 (t, $J = 245.3$ Hz), 107.8, 107.0, 67.0 (t, $J = 24.8$ Hz). ^{19}F NMR (470 MHz, Chloroform-*d*) δ -127.26 (ddd, $J = 284.3, 55.5, 10.4$ Hz), -129.17 (ddd, $J = 283.5, 56.0, 12.8$ Hz). **HRMS (ESI):** calcd for $\text{C}_6\text{H}_6\text{F}_2\text{NO}$ [$\text{M} + \text{H}$] $^+$: 146.0411, found: 146.0411.

1,1'-(1H-pyrrole-3,4-diyl)bis(2,2-Difluoroethan-1-ol) (3l')



Following general procedure A to afford the title compound as a yellow oil (10.4 mg, 23%). TLC (PE: EA, 2:1 v/v): $R_f = 0.2$; ^1H NMR (500 MHz, Chloroform-*d*) δ 9.01 (s, 1H), 6.19 (s, 2H), 5.82 (td, $J = 55.6, 3.2$ Hz, 2H), 4.84 (t, $J = 11.2$ Hz, 2H), 3.08 (s, 2H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 126.8 (q, $J = 3.2$ Hz), 114.8 (t, $J = 245.2$ Hz), 108.4, 108.3, 67.9 (td, $J = 25.0, 2.7$ Hz). ^{19}F NMR (470 MHz, Chloroform-*d*) δ -127.26 (ddd, $J = 285.2, 55.5, 10.0$ Hz), -129.06 (ddd, $J = 284.9, 55.9, 12.0, 8.5$ Hz). **HRMS (ESI):** calcd for $\text{C}_8\text{H}_8\text{F}_4\text{NO}_2$ [$\text{M} + \text{H}$] $^+$: 226.0485, found: 226.0483.

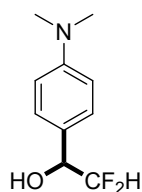
2,2-Difluoro-1-(1-phenyl-1H-pyrrol-2-yl)ethan-1-ol (3m')



Following general procedure A to afford the title compound as a yellow oil (28.7 mg, 64%). TLC (PE: EA, 2:1 v/v): $R_f = 0.2$; ^1H NMR (500 MHz, Chloroform-*d*) δ 7.47 (t, $J = 7.6$ Hz, 2H), 7.42 – 7.40 (m, 3H), 6.89 (dd, $J = 2.7, 1.7$ Hz, 1H), 6.48 (d, $J = 3.5$ Hz, 1H), 6.31 (t, $J = 3.2$ Hz, 1H), 5.92 (td, $J = 55.7, 4.2$ Hz, 1H), 4.68-4.62 (m, 1H), 2.23 (d, $J = 6.3$ Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 139.1, 129.4, 128.2 (t, $J = 4.0$ Hz), 127.9, 126.3, 124.2,

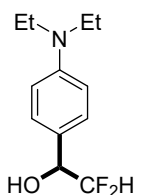
115.2 (t, $J = 245.0$ Hz), 109.4, 109.0, 65.7 (t, $J = 25.5$ Hz). ^{19}F NMR (470 MHz, Chloroform-*d*) δ -125.17 (ddd, $J = 282.8, 55.4, 9.3$ Hz), -127.70 (ddd, $J = 283.4, 56.3, 12.5$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{12}\text{H}_{10}\text{F}_2\text{NO}$ [$\text{M} + \text{H}$] $^-$: 222.0724, found: 222.0733.

1-(4-(dimethylamino)phenyl)-2,2-Difluoroethan-1-ol (5a)



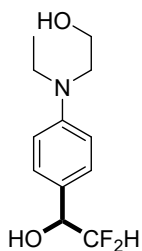
Following general procedure B at the temperature of 90 °C to afford the title compound as a white solid (30 mg, 75%). TLC (PE: EA, 8:1 v/v): $R_f = 0.3$; ^1H NMR (500 MHz, Chloroform-*d*) δ 7.27 (d, $J = 8.7$ Hz, 2H), 6.73 (d, $J = 8.7$ Hz, 2H), 5.75 (td, $J = 56.2, 4.8$ Hz, 1H), 4.70 (td, $J = 10.2, 4.8$ Hz, 1H), 2.96 (s, 6H), 2.36 (s, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 151.1, 128.2, 123.7, 116.2 (t, $J = 245.0$ Hz), 112.6, 73.6 (t, $J = 24.6$ Hz), 40.6. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -127.01 (ddd, $J = 282.4, 56.1, 10.1$ Hz), -127.69 (ddd, $J = 282.7, 57.0, 10.6$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{10}\text{H}_{14}\text{F}_2\text{NO}$ [$\text{M} + \text{H}$] $^+$: 202.1037, found: 202.1034.

1-(4-(diethylamino)phenyl)-2,2-Difluoroethan-1-ol (5b)



Following general procedure B at the temperature of 90 °C to afford the title compound as a yellow oil (32.5 mg, 71%). TLC (PE: EA, 8:1 v/v): $R_f = 0.3$; ^1H NMR (500 MHz, Chloroform-*d*) δ 7.24 (d, $J = 8.7$ Hz, 2H), 6.68 (d, $J = 8.8$ Hz, 2H), 5.76 (td, $J = 56.2, 4.8$ Hz, 1H), 4.68 (td, $J = 10.3, 4.8$ Hz, 1H), 3.36 (q, $J = 7.1$ Hz, 4H), 2.33 (s, 1H), 1.17 (t, $J = 7.1$ Hz, 6H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 148.4, 128.5, 122.3 (t, $J = 3.2$ Hz), 116.2 (t, $J = 244.5$ Hz), 111.6, 73.9 – 73.5 (m), 44.5, 12.6. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -126.88 (ddd, $J = 281.8, 56.4, 9.6$ Hz), -127.65 (ddd, $J = 281.8, 55.9, 10.6$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{12}\text{H}_{18}\text{F}_2\text{NO}$ [$\text{M} + \text{H}$] $^+$: 230.1350, found: 230.1347.

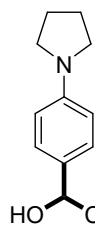
1-(4-(ethyl(2-hydroxyethyl)amino)phenyl)-2,2-Difluoroethan-1-ol (5c)



Following general procedure B at the temperature of 90 °C to afford the title compound as a colorless oil (30.9 mg, 63%). TLC (PE: EA, 1:1 v/v): $R_f = 0.4$; ^1H NMR (500 MHz, Chloroform-*d*) δ 7.16 (d, $J = 8.6$ Hz, 2H), 6.66 (d, $J = 8.7$ Hz, 2H), 5.66 (td, $J = 56.2, 4.8$ Hz, 1H), 4.61-4.56 (m, 1H), 3.68 (t, $J = 5.8$ Hz, 2H), 3.38-3.31 (m, 4H), 2.72 (s, 1H), 1.95 (s, 1H), 1.07 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 148.8, 128.5, 123.6 (t, $J = 3.3$ Hz), 116.1 (t, $J = 245.0$ Hz), 112.4, 73.4 (t, $J = 25.0$ Hz), 60.2, 52.4, 45.6, 11.9. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -126.94 (ddd, $J = 282.3,$

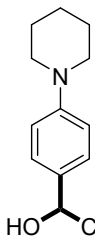
56.2, 9.8 Hz), -127.60 (ddd, $J = 281.8, 56.7, 10.0$ Hz). **HRMS (ESI):** calcd for $C_{12}H_{16}F_2NO_2$ $[M + H]^+$: 244.1143, found: 244.1142.

2,2-Difluoro-1-(4-(pyrrolidin-1-yl)phenyl)ethan-1-ol (5d)



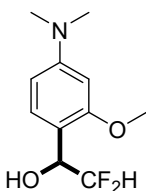
Following general procedure B at the temperature of 90 °C to afford the title compound as a yellow oil (28.4 mg, 62%). TLC (PE: EA, 8:1 v/v): $R_f = 0.3$; 1H NMR (500 MHz, Chloroform-*d*) δ 7.25 (d, $J = 8.1$ Hz, 2H), 6.57 (d, $J = 8.7$ Hz, 2H), 5.75 (td, $J = 56.3, 4.8$ Hz, 1H), 4.68 (td, $J = 10.1, 4.7$ Hz, 1H), 3.30 (t, $J = 6.6$ Hz, 4H), 2.46 (s, 1H), 2.08 – 1.95 (m, 4H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 148.6, 128.4, 122.5, 116.3 (t, $J = 244.9$ Hz), 111.8, 73.8 (t, $J = 24.6$ Hz), 47.8, 25.7. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -126.90 (ddd, $J = 283.2, 55.9, 9.8$ Hz), -127.59 (ddd, $J = 280.3, 55.4, 10.9$ Hz). **HRMS (ESI):** calcd for $C_{12}H_{16}F_2NO$ $[M + H]^+$: 228.1194, found: 228.1190.

2,2-Difluoro-1-(4-(piperidin-1-yl)phenyl)ethan-1-ol (5e)



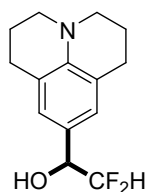
Following general procedure B at the temperature of 90 °C to afford the title compound as a red oil (29.9 mg, 62%). TLC (PE: EA, 2:1 v/v): $R_f = 0.5$; 1H NMR (500 MHz, Chloroform-*d*) δ 7.24 (d, $J = 8.6$ Hz, 2H), 6.91 (d, $J = 8.7$ Hz, 2H), 5.72 (td, $J = 56.2, 4.9$ Hz, 1H), 4.68 (td, $J = 10.2, 4.8$ Hz, 1H), 3.16 (t, $J = 5.5$ Hz, 4H), 2.71 (s, 1H), 1.70 (p, $J = 5.8$ Hz, 4H), 1.58 (q, $J = 5.9$ Hz, 2H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 152.6, 128.1, 126.2 (t, $J = 3.2$ Hz), 116.3, 116.1 (t, $J = 244.9$ Hz), 73.5 (t, $J = 24.6$ Hz), 50.4, 25.7, 24.3. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -126.65– -127.29 (m), -127.37– -128.01 (m). **HRMS (ESI):** calcd for $C_{13}H_{18}F_2NO$ $[M + H]^+$: 242.1350, found: 242.1346.

1-(4-(dimethylamino)-2-methoxyphenyl)-2,2-Difluoroethan-1-ol (5f)



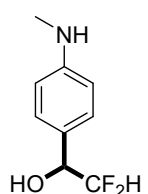
Following general procedure B at the temperature of 90 °C to afford the title compound as a yellow oil (14.3 mg, 31%). TLC (PE: EA, 2:1 v/v): $R_f = 0.4$; 1H NMR (500 MHz, Chloroform-*d*) δ 7.16 (d, $J = 8.5$ Hz, 1H), 6.32 (dd, $J = 8.5, 2.3$ Hz, 1H), 6.23z (d, $J = 2.3$ Hz, 1H), 5.94 (td, $J = 56.5, 4.8$ Hz, 1H), 4.85-4.82 (m, 1H), 3.86 (s, 3H), 2.98 (s, 6H), 1.64 (s, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 158.0, 152.2, 129.8, 117.4- 113.5 (m), 111.7-111.6 (m), 104.7, 95.4, 71.8- 71.4 (m), 55.2, 40.5. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -125.07 (ddd, $J = 280.5, 56.2, 7.9$ Hz), -128.61 (ddd, $J = 280.6, 57.3, 13.9$ Hz). **HRMS (ESI):** calcd for $C_{11}H_{16}F_2NO_2$ $[M + H]^+$: 232.1143, found: 232.1141.

2,2-Difluoro-1-(2,3,6,7-tetrahydro-1H,5H-pyrido[3,2,1-ij]quinolin-9-yl)ethan-1-ol (5g)



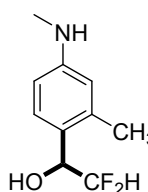
Following general procedure B at the temperature of 90 °C to afford the title compound as a white solid (33.4 mg, 66%). TLC (PE: EA, 2:1 v/v): $R_f = 0.8$; $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 6.79 (s, 2H), 5.74 (td, $J = 56.3, 4.9$ Hz, 1H), 4.59 – 4.54 (m, 1H), 3.14 (t, $J = 3.6$ Hz, 4H), 2.74 (t, $J = 6.5$ Hz, 4H), 2.36 (s, 1H), 1.98-1.93 (m, 4H). $^{13}\text{C NMR}$ (125 MHz, Chloroform-*d*) δ 143.6, 125.9, 122.7 (t, $J = 3.2$ Hz), 121.6, 116.2 (t, $J = 244.8$ Hz), 73.8 (t, $J = 25.0$ Hz), 50.0, 27.8, 21.9. $^{19}\text{F NMR}$ (470 MHz, Chloroform-*d*) δ -126.59 (ddd, $J = 282.2, 55.7, 9.0$ Hz), -127.46 (ddd, $J = 281.4, 56.7, 11.2$ Hz). **HRMS (ESI):** calcd for $\text{C}_{14}\text{H}_{18}\text{F}_2\text{NO}$ $[\text{M} + \text{H}]^+$: 254.1350, found:254.1345.

2,2-Difluoro-1-(4-(methylamino)phenyl)ethan-1-ol (5h)



Following general procedure B at the temperature of 90 °C to afford the title compound as a white solid (26.2 mg, 70%). TLC (PE: EA, 2:1 v/v): $R_f = 0.3$; $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 7.21 (d, $J = 8.5$ Hz, 2H), 6.61 (d, $J = 8.6$ Hz, 2H), 5.73 (td, $J = 56.2, 4.8$ Hz, 1H), 4.68 (td, $J = 10.2, 4.8$ Hz, 1H), 2.83 (s, 3H). $^{13}\text{C NMR}$ (125 MHz, Chloroform-*d*) δ 150.0, 128.4, 124.4 (t, $J = 3.3$ Hz), 116.2 (t, $J = 244.3$ Hz), 112.5, 73.7 (t, $J = 24.6$ Hz), 30.7. $^{19}\text{F NMR}$ (470 MHz, Chloroform-*d*) δ -127.00 (ddd, $J = 282.1, 56.3, 9.6$ Hz), -127.67 (ddd, $J = 281.2, 55.3, 10.4$ Hz). **HRMS (ESI):** calcd for $\text{C}_9\text{H}_{12}\text{F}_2\text{NO}$ $[\text{M} + \text{H}]^+$: 188.0881, found:188.0878.

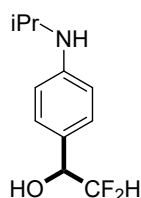
2,2-Difluoro-1-(3-methyl-5-(methylamino)phenyl)ethan-1-ol (5i)



Following general procedure B at the temperature of 90 °C to afford the title compound as a yellow oil (22.1 mg, 55%). TLC (PE: EA, 2:1 v/v): $R_f = 0.4$; $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 7.28 (d, $J = 8.5$ Hz, 1H), 6.50 (dd, $J = 8.4, 2.5$ Hz, 1H), 6.43 (d, $J = 2.3$ Hz, 1H), 5.80 (td, $J = 56.2, 5.2$ Hz, 1H), 5.02-4.97 (m, 1H), 2.83 (s, 3H), 2.32 (s, 3H), 1.59 (s, 1H), 1.25 (s, 1H). $^{13}\text{C NMR}$ (125 MHz, Chloroform-*d*) δ 149.5, 137.6, 127.7, 123.0 (t, $J = 6.0$ Hz), 116.5 (t, $J = 245.0$ Hz), 114.2, 110.3, 69.8 (t, $J = 24.9$ Hz), 30.5, 19.6. $^{19}\text{F NMR}$ (470 MHz, Chloroform-*d*) δ -126.12 (ddd, $J = 282.4, 57.0, 11.7$ Hz), -127.24 (ddd, $J =$

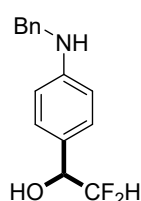
282.5, 55.4, 8.2 Hz). **HRMS (ESI):** calcd for C₁₀H₁₄F₂NO [M + H]⁺: 202.1037, found:202.1035.

1-(4-(dimethylamino)phenyl)-2,2-Difluoroethan-1-ol (5j)



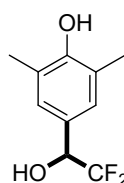
Following general procedure B at the temperature of 90 °C to afford the title compound as a white solid (26.6 mg, 62%). TLC (PE: EA, 2:1 v/v): R_f = 0.5; ¹H NMR (500 MHz, Chloroform-*d*) δ 7.18 (d, *J* = 8.5 Hz, 2H), 6.57 (d, *J* = 8.6 Hz, 2H), 5.73 (td, *J* = 56.2, 4.8 Hz, 1H), 4.66 (td, *J* = 10.2, 4.8 Hz, 1H), 3.62 (p, *J* = 6.3 Hz, 1H), 1.20 (d, *J* = 6.3 Hz, 6H). ¹³C NMR (125 MHz, Chloroform-*d*) δ 148.2, 128.5, 124.1 (t, *J* = 3.4 Hz), 116.2 (t, *J* = 245.0 Hz), 113.2, 73.6 (t, *J* = 24.6 Hz), 44.3, 23.0. ¹⁹F NMR (470 MHz, Chloroform-*d*) δ -126.93 (ddd, *J* = 281.7, 56.3, 9.5 Hz), -127.66 (ddd, *J* = 281.7, 56.3, 10.8 Hz). **HRMS (ESI):** calcd for C₁₁H₁₆F₂NO [M + H]⁺: 216.1194, found: 216.1192.

1-(4-(benzylamino)phenyl)-2,2-Difluoroethan-1-ol (5k)



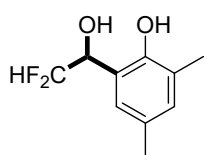
Following general procedure B at the temperature of 90 °C to afford the title compound as a yellow oil (29.4 mg, 56%). TLC (PE: EA, 2:1 v/v): R_f = 0.5; ¹H NMR (500 MHz, Chloroform-*d*) δ 7.35 (s, 2H), 7.34 (d, *J* = 2.3 Hz, 2H), 7.30-7.26 (m, 1H), 7.19 (d, *J* = 8.4 Hz, 2H), 6.63 (d, *J* = 8.4 Hz, 2H), 5.73 (td, *J* = 56.0, 4.9 Hz, 1H), 4.67 (td, *J* = 10.1, 4.8 Hz, 1H), 4.33 (s, 2H), 4.17 (s, 1H), 2.37 (s, 1H). ¹³C NMR (125 MHz, Chloroform-*d*) δ 148.7, 139.0, 128.7, 128.3, 127.4, 127.3, 124.5 (t, *J* = 3.5 Hz), 116.0 (t, *J* = 245.1 Hz), 112.7, 73.5 (t, *J* = 24.5 Hz), 48.1. ¹⁹F NMR (470 MHz, Chloroform-*d*) δ -126.98 (ddd, *J* = 282.9, 55.9, 9.9 Hz), -127.68 (ddd, *J* = 282.7, 57.3, 11.5 Hz). **HRMS (ESI):** calcd for C₁₅H₁₅F₂NO [M + H]⁺: 264.1194, found: 264.1190.

4-(2,2-Difluoro-1-hydroxyethyl)-2,6-dimethylphenol (6a)



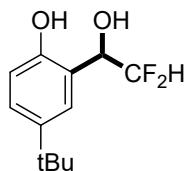
Following general procedure B at the temperature of 90 °C to afford the title compound as a white solid (24.2 mg, 60%). TLC (PE: EA, 2:1 v/v): R_f = 0.5; ¹H NMR (500 MHz, Methanol-*d*₄) δ 6.97 (s, 2H), 5.75 (td, *J* = 56.2, 4.7 Hz, 1H), 4.58-4.52 (m, 1H), 2.21 (s, 6H). ¹³C NMR (125 MHz, Methanol-*d*₄) δ 154.6, 129.5 (t, *J* = 3.2 Hz), 128.5, 125.5, 117.8 (t, *J* = 243.8 Hz), 74.2 (t, *J* = 24.3 Hz), 16.7. ¹⁹F NMR (470 MHz, Methanol-*d*₄) δ -128.26 (ddd, *J* = 281.0, 55.6, 9.6 Hz), -129.11 (ddd, *J* = 281.2, 55.5, 12.0 Hz). **HRMS (ESI):** calcd for C₁₀H₁₁F₂O₂ [M + H]⁺: 201.0721, found:201.0721.

2-(2,2-Difluoro-1-hydroxyethyl)-4,6-dimethylphenol (6b)



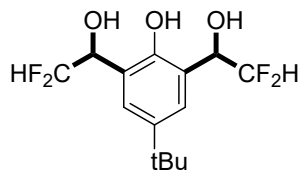
Following general procedure B at the temperature of 60 °C to afford the title compound as a white solid (18.2 mg, 45%). TLC (PE: EA, 2:1 v/v): $R_f = 0.8$; $^1\text{H NMR}$ (500 MHz, $\text{DMSO-}d_6$) δ 8.36 (s, 1H), 6.97 (s, 1H), 6.85 (s, 1H), 6.13 (d, $J = 5.4$ Hz, 1H), 5.98 (td, $J = 55.8$, 3.6 Hz, 1H), 5.11-5.04 (m, 1H), 2.17 (s, 3H), 2.13 (s, 3H). $^{13}\text{C NMR}$ (125 MHz, $\text{DMSO-}d_6$) δ 150.3, 130.8, 127.8, 126.1, 124.5, 124.3 (t, $J = 3.3$ Hz), 116.1 (t, $J = 243.3$ Hz), 67.4 (t, $J = 22.9$ Hz), 20.3, 16.5. $^{19}\text{F NMR}$ (470 MHz, $\text{DMSO-}d_6$) δ -125.43 (ddd, $J = 275.4$, 55.4, 8.2 Hz), -129.51 (ddd, $J = 275.6$, 56.3, 16.9 Hz). **HRMS (ESI)**: calcd for $\text{C}_{10}\text{H}_{11}\text{F}_2\text{O}_2$ [$\text{M} + \text{H}$] $^+$: 201.0721, found:201.0721.

4-(tert-butyl)-2-(2,2-Difluoro-1-hydroxyethyl)phenol (6c)



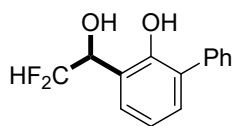
Following general procedure B at the temperature of 60 °C to afford the title compound as a colorless oil (20.2 mg, 44%). TLC (PE: EA, 2:1 v/v): $R_f = 0.7$; $^1\text{H NMR}$ (500 MHz, $\text{Chloroform-}d$) δ 7.28 (dd, $J = 8.5$, 2.5 Hz, 1H), 7.11 (d, $J = 2.3$ Hz, 1H), 6.98 (s, 1H), 6.82 (d, $J = 8.5$ Hz, 1H), 5.94 (td, $J = 55.2$, 4.7 Hz, 1H), 4.96-4.91 (m, 1H), 1.81 (s, 1H), 1.28 (s, 9H). $^{13}\text{C NMR}$ (125 MHz, $\text{Chloroform-}d$) δ 153.0, 143.6, 127.5, 126.0, 119.1-119.1 (m), 116.8, 114.9 (t, $J = 245.6$ Hz), 75.1-74.7 (m), 34.2, 31.6. $^{19}\text{F NMR}$ (470 MHz, $\text{Chloroform-}d$) δ -125.83 (ddd, $J = 284.2$, 55.2, 7.9 Hz), -128.91 (ddd, $J = 284.3$, 57.1, 13.1 Hz). **HRMS (ESI)**: calcd for $\text{C}_{12}\text{H}_{15}\text{F}_2\text{O}_2$ [$\text{M} + \text{H}$] $^+$: 229.1034, found:229.1041.

1,1'-(5-(tert-butyl)-2-hydroxy-1,3-phenylene)bis(2,2-Difluoroethan-1-ol) (6c')



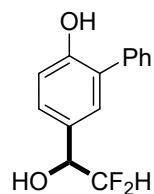
Following general procedure B at the temperature of 60 °C to afford the title compound as a colorless oil (6.5 mg, 11%). TLC (PE: EA, 2:1 v/v): $R_f = 0.6$; $^1\text{H NMR}$ (500 MHz, $\text{Chloroform-}d$) δ 8.19 (d, $J = 21.7$ Hz, 1H), 7.19 (s, 2H), 6.96 (td, 2H), 4.97-4.96 (m, 2H), 1.72 (s, 2H), 1.28 (s, 9H). $^{13}\text{C NMR}$ (125 MHz, $\text{Chloroform-}d$) δ 151.7 (d, $J = 4.6$ Hz), 143.5, 126.8 (d, $J = 6.0$ Hz), 120.8-120.8 (m), 120.7-120.7 (m), 114.7 (t, $J = 245.7$ Hz), 74.2-73.8 (m), 74.1-73.7 (m), 34.2, 31.3. $^{19}\text{F NMR}$ (470 MHz, $\text{Chloroform-}d$) δ -125.56 (ddd, $J = 283.3$, 54.3, 7.7 Hz), -125.81 (ddd, $J = 284.1$, 55.5, 8.8 Hz), -129.33 (ddd, $J = 284.4$, 57.2, 14.2 Hz), -129.33 (ddd, $J = 284.4$, 56.8, 13.8 Hz). **HRMS (ESI)**: calcd for $\text{C}_{14}\text{H}_{17}\text{F}_4\text{O}_3$ [$\text{M} + \text{H}$] $^+$: 309.1108, found:309.1118.

3-(2,2-Difluoro-1-hydroxyethyl)-[1,1'-biphenyl]-2-ol (6d)



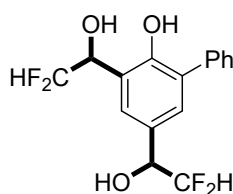
Following general procedure B at the temperature of 60 °C to afford the title compound as a yellow oil (7 mg, 14%). TLC (PE: EA, 2:1 v/v): $R_f = 0.7$; $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 7.51 – 7.46 (m, 5H), 7.43 – 7.40 (m, 1H), 7.28 (d, $J = 7.7$ Hz, 2H), 7.03 (t, $J = 7.6$ Hz, 1H), 6.04 (td, $J = 55.4, 4.5$ Hz, 1H), 5.09 – 5.04 (m, 1H). $^{13}\text{C NMR}$ (125 MHz, Chloroform-*d*) δ 150.9, 136.5, 131.0, 129.3, 129.2, 129.2, 128.5, 128.1, 121.4 (t, $J = 3.3$ Hz), 120.8, 114.8 (t, $J = 245.1$ Hz), 72.9-72.5 (m). $^{19}\text{F NMR}$ (470 MHz, Chloroform-*d*) δ -125.68 (ddd, $J = 282.8, 55.2, 7.5$ Hz), -129.56 (ddd, $J = 282.9, 56.5, 14.0$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{14}\text{H}_{11}\text{F}_2\text{O}_2$ [$\text{M} + \text{H}$] $^+$: 249.0721, found:249.0730.

5-(2,2-Difluoro-1-hydroxyethyl)-[1,1'-biphenyl]-2-ol (6d')



Following general procedure B at the temperature of 60 °C to afford the title compound as a colorless oil (12.5 mg, 25%). TLC (PE: EA, 2:1 v/v): $R_f = 0.5$; $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 7.51 – 7.45 (m, 4H), 7.41 (t, $J = 7.1$ Hz, 1H), 7.31 (d, $J = 7.0$ Hz, 2H), 7.00 (d, $J = 9.0$ Hz, 1H), 5.76 (td, $J = 56.0, 5.0$ Hz, 1H), 5.40 (s, 1H), 4.79 (td, $J = 10.0, 4.8$ Hz, 1H), 2.50 (s, 1H). $^{13}\text{C NMR}$ (125 MHz, Chloroform-*d*) δ 153.1, 136.5, 129.4, 129.2, 129.0, 128.4, 128.2, 128.0, 116.2, 115.8 (t, $J = 245.2$ Hz), 73.3 (t, $J = 24.6$ Hz). $^{19}\text{F NMR}$ (470 MHz, Chloroform-*d*) δ -127.36 (dd, $J = 9.7, 5.3$ Hz), -127.48 (dd, $J = 9.7, 5.8$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{14}\text{H}_{11}\text{F}_2\text{O}_2$ [$\text{M} + \text{H}$] $^+$: 249.0721, found:249.0730.

1,1'-(2-hydroxy-[1,1'-biphenyl]-3,5-diyl)bis(2,2-Difluoroethan-1-ol) (6d'')

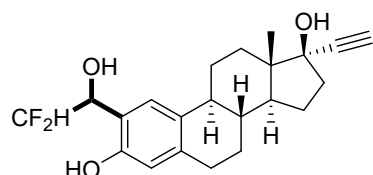


Following general procedure B at the temperature of 60 °C to afford the title compound as a red oil (29.7 mg, 45%). TLC (PE: EA, 2:1 v/v): $R_f = 0.4$; $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 7.53 – 7.47 (m, 4H), 7.44 (t, $J = 7.4$ Hz, 1H), 7.35 (dd, $J = 5.7, 4.1$ Hz, 2H), 6.67 (d, $J = 19.7$ Hz, 1H), 6.13 – 5.66 (m, 2H), 5.13 – 5.03 (m, 1H), 4.79 (tt, $J = 10.0, 4.1$ Hz, 1H), 2.67 (s, 2H). $^{13}\text{C NMR}$ (125 MHz, Chloroform-*d*) δ 151.7 (d, $J = 10.9$ Hz), 136.1 (d, $J = 3.7$ Hz), 129.9, 129.6 (d, $J = 8.5$ Hz), 129.2 (d, $J = 5.3$ Hz), 128.3 (d, $J = 2.7$ Hz), 128.1 (d, $J = 5.3$ Hz), 127.1 (d, $J = 5.0$ Hz), 121.7, 121.6, 115.7 (t, $J = 245.4$ Hz), 114.6 (t, $J = 245.4$ Hz), 73.0 (t, $J = 25.0$ Hz), 72.3 (t, $J = 24.4$ Hz). $^{19}\text{F NMR}$ (470 MHz, Chloroform-*d*) δ -125.45 – -126.45 (m), -127.19 – -127.80 (m), -

129.49 (ddd, $J = 149.2, 56.0, 14.1$ Hz), -130.10 (ddd, $J = 149.2, 55.8, 14.1$ Hz).

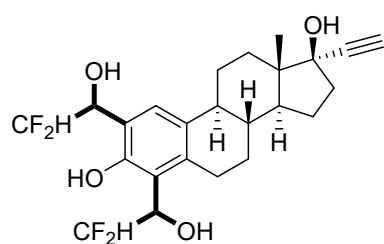
HRMS (ESI): calcd for $C_{16}H_{13}F_4O_3$ $[M + H]^+$: 329.0795, found:329.0806.

(8R,9S,13S,14S,17R)-2-(2,2-Difluoro-1-hydroxyethyl)-17-ethynyl-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene-3,17-diol (6f)



Following general procedure B at the temperature of 60 °C to afford the title compound as a white solid (30.1 mg, 40%). TLC (PE: EA, 2:1 v/v): $R_f = 0.3$; 1H NMR (500 MHz, $DMSO-d_6$) δ 9.31 (s, 1H), 7.25 (s, 1H), 6.49 (s, 1H), 5.97 (t, $J = 55.7$ Hz, 1H), 5.83 (d, $J = 5.3$ Hz, 1H), 5.34 (s, 1H), 4.98 – 4.95 (m, 1H), 2.69 (s, 2H), 2.30 (s, 1H), 2.10 – 2.06 (m, 2H), 1.86 (t, $J = 12.7$ Hz, 1H), 1.78 – 1.76 (m, 2H), 1.69 – 1.57 (m, 3H), 1.32 - 1.24 (m, 4H), 0.76 (s, 3H). ^{13}C NMR (125 MHz, $DMSO-d_6$) δ 152.1, 136.8, 130.4 (d, $J = 7.9$ Hz), 124.9 (d, $J = 7.6$ Hz), 121.4 (d, $J = 3.4$ Hz), 116.1 (t, $J = 243.2$ Hz), 114.7, 89.0 (d, $J = 2.7$ Hz), 78.1, 75.1, 66.5 (t, $J = 23.8$ Hz), 49.0, 46.7 (d, $J = 2.5$ Hz), 43.4 (d, $J = 13.2$ Hz), 40.4, 38.8, 32.6 (d, $J = 5.1$ Hz), 28.9 (d, $J = 12.7$ Hz), 27.0 (d, $J = 8.8$ Hz), 26.3 (d, $J = 13.3$ Hz), 22.5, 12.7. ^{19}F NMR (470 MHz, $DMSO-d_6$) δ -125.41 (dd, $J = 274.0, 56.2$ Hz), -128.85 – -130.04 (m). **HRMS (ESI):** calcd for $C_{22}H_{25}F_2O_3$ $[M + H]^+$: 375.1766, found:375.1762.

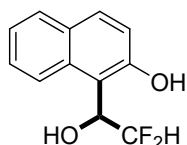
(8R,9S,13S,14S,17R)-2,4-bis(2,2-difluoro-1-hydroxyethyl)-17-ethynyl-13-methyl-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthrene-3,17-diol (6f')



Following general procedure B at the temperature of 60 °C to afford the title compound as a white solid (21.9 mg, 24%). TLC (PE: EA, 2:1 v/v): $R_f = 0.2$; 1H NMR (500 MHz, $DMSO-d_6$) δ 7.40 (d, $J = 5.0$ Hz, 1H), 6.22 (t, $J = 55.3$ Hz, 1H), 6.05 (t, $J = 56.4$ Hz, 1H), 5.41 (s, 1H), 5.27 (s, 1H), 5.08 (s, 1H), 2.89 (d, $J = 16.2$ Hz, 1H), 2.75 – 2.52 (m, 2H), 2.39 (s, 1H), 2.17 (d, $J = 2.2$ Hz, 2H), 1.96-1.84 (m, 3H), 1.76 – 1.65 (m, 3H), 1.40-1.30 (m, 4H), 0.82 (s, 3H). ^{13}C NMR (125 MHz, $DMSO-d_6$) δ 153.4, 135.7, 131.6, 125.9 (d, $J = 10.4$ Hz), 122.8, 119.3, 116.4 (t, $J = 245.6$ Hz), 116.0 (t, $J = 245.6$ Hz), 89.4, 78.6, 75.6, 69.5, 69.4, 49.5, 47.0 (d, $J = 1.8$ Hz), 44.2 (d, $J = 8.9$ Hz), 39.3, 38.7 (d, $J = 4.6$ Hz), 33.0 (d, $J = 5.3$ Hz), 27.5, 26.9 (d,

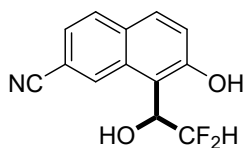
$J = 13.5$ Hz), 26.7, 22.9, 13.1. ^{19}F NMR (470 MHz, $\text{DMSO-}d_6$) δ -124.14 – -127.60 (m), -127.93 – -130.59 (m). **HRMS (ESI):** calcd for $\text{C}_{24}\text{H}_{27}\text{F}_4\text{O}_4$ $[\text{M} + \text{H}]^+$: 455.1839, found:455.1843.

1-(2,2-Difluoro-1-hydroxyethyl)naphthalen-2-ol (6g)



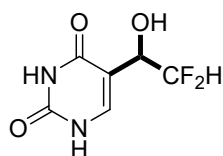
Following general procedure B at the temperature of 60 °C to afford the title compound as a black solid (19.7 mg, 44%). TLC (PE: EA, 4:1 v/v): $R_f = 0.3$; ^1H NMR (500 MHz, Chloroform- d) δ 8.47 (s, 1H), 7.77 (t, $J = 8.7$ Hz, 2H), 7.73 (d, $J = 8.6$ Hz, 1H), 7.49 (t, $J = 7.7$ Hz, 1H), 7.35 (t, $J = 7.5$ Hz, 1H), 7.12 (d, $J = 8.9$ Hz, 1H), 6.06 (td, $J = 55.7, 4.4$ Hz, 1H), 5.86 (dt, $J = 13.8, 5.5$ Hz, 1H), 3.88 (s, 1H). ^{13}C NMR (125 MHz, Chloroform- d) δ 155.4, 131.9, 131.4, 129.0, 128.9, 127.3, 123.5, 121.0, 119.5, 114.7 (t, $J = 246.2$ Hz), 109.6 (t, $J = 3.2$ Hz), 71.2-70.8 (m). ^{19}F NMR (470 MHz, Chloroform- d) δ -125.47 (ddd, $J = 282.8, 55.1, 6.7$ Hz), -128.50 (ddd, $J = 282.8, 56.6, 14.0$ Hz). **HRMS (ESI):** calcd for $\text{C}_{12}\text{H}_9\text{F}_2\text{O}_2$ $[\text{M} + \text{H}]^+$: 223.0565, found:223.0570.

8-(2,2-Difluoro-1-hydroxyethyl)-7-hydroxy-2-naphthonitrile (6h)



Following general procedure B at the temperature of 60 °C to afford the title compound as a white solid (28.4 mg, 57%). TLC (PE: EA, 2:1 v/v): $R_f = 0.4$; ^1H NMR (500 MHz, $\text{DMSO-}d_6$) δ 10.67 (s, 1H), 8.52 (d, $J = 9.0$ Hz, 1H), 8.42 (d, $J = 1.7$ Hz, 1H), 7.92 (d, $J = 8.9$ Hz, 1H), 7.66 (dd, $J = 9.0, 1.8$ Hz, 1H), 7.32 (d, $J = 8.9$ Hz, 1H), 6.50 (s, 1H), 6.34 (td, $J = 56.0, 5.0$ Hz, 1H), 5.69 (td, $J = 13.0, 12.5, 5.0$ Hz, 1H). ^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) δ 156.4, 134.9, 134.6, 131.1, 127.3, 126.4, 126.3, 119.6, 119.6, 116.2 (t, $J = 243.8$ Hz), 115.1 (t, $J = 3.1$ Hz), 104.6, 66.5 (t, $J = 25.2$ Hz). ^{19}F NMR (470 MHz, $\text{DMSO-}d_6$) δ -124.01 (t, $J = 10.8$ Hz), -124.13 (t, $J = 10.8$ Hz). **HRMS (ESI):** calcd for $\text{C}_{13}\text{H}_8\text{F}_2\text{NO}_2$ $[\text{M} + \text{H}]^+$: 248.0517, found:248.0526.

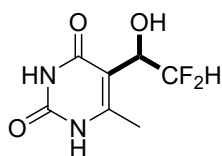
5-(2,2-Difluoro-1-hydroxyethyl)pyrimidine-2,4(1H,3H)-dione (8a)



Following general procedure C at the temperature of 100 °C to afford the title compound as a white solid (32.6 mg, 85%). TLC (PE: EA, 1:2 v/v): $R_f = 0.3$; ^1H NMR (500 MHz, Methanol- d_4) δ 7.48 (s, 1H), 5.97 (td, $J = 56.0, 3.3$ Hz, 1H), 4.76-4.70 (m, 1H). ^{13}C NMR (125 MHz, Methanol- d_4) δ 165.5, 153.1, 142.1, 116.2 (t, $J = 243.4$ Hz), 110.0 (t, $J = 3.6$ Hz), 67.6 (t, $J = 24.3$ Hz). ^{19}F NMR (470 MHz, Methanol- d_4) δ -

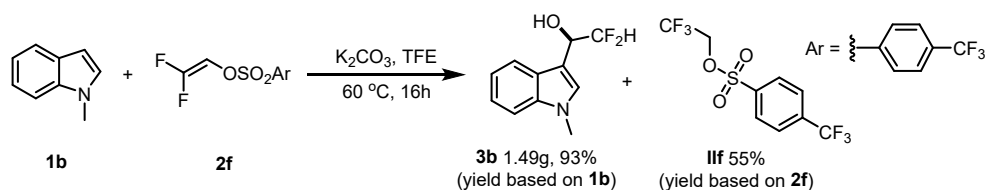
129.88 (ddd, $J = 281.2, 55.6, 7.7$ Hz), -133.04 (ddd, $J = 281.3, 56.2, 15.5$ Hz). **HRMS (ESI)**: calcd for $C_6H_5F_2N_2O_3$ [$M + H$] $^-$: 191.0262, found:191.0260.

5-(2,2-Difluoro-1-hydroxyethyl)-6-methylpyrimidine-2,4(1H,3H)-dione (8b)



Following general procedure C at the temperature of 100 °C to afford the title compound as a white solid (30.5 mg, 74%). TLC (PE: EA, 1:2 v/v): $R_f = 0.2$; 1H NMR (500 MHz, Chloroform-*d*) δ 6.11 (td, $J = 56.8, 5.4$ Hz, 1H), 4.84 – 4.79 (m, 1H), 2.27 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 166.2, 154.8, 152.7, 116.9 (t, $J = 242.2$ Hz), 107.1 (t, $J = 3.7$ Hz), 68.5 (t, $J = 27.3$ Hz), 16.7. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -123.49 (ddd, $J = 284.2, 57.0, 11.7$ Hz), -123.61 (ddd, $J = 285.7, 56.6, 10.0$ Hz). **HRMS (ESI)**: calcd for $C_7H_7F_2N_2O_3$ [$M + H$] $^-$: 205.0419, found:205.0424.

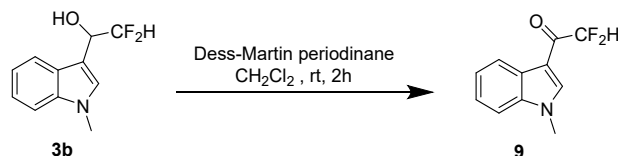
4 Gram-scale Synthesis of product **3b**



In an oven-dried 100 ml round bottom flask, a mixture of 1-methylindole **1b** (7.6 mmol, 1.0 equiv), 2,2-Difluorovinyl 4-(trifluoromethyl)benzenesulfonate **2f** (4.380 g, 15.2 mmol, 2 equiv), K_2CO_3 (525.2 mg, 3.8 mmol, 0.5 equiv) in TFE (20 ml) was stirred at 60 °C for 16 h. The reaction mixture was then diluted with Ethyl acetate (30 ml) and washed with brine. The aqueous phase was extracted with Ethyl acetate. The organic layers were combined, washed with brine and dried over Na_2SO_4 . The solvent was removed in vacuo, and the residue was purified by column chromatography (PE/EA= 4/1) to afford the desired 1.49 g of product **3b**, yield 93% and product **IIIf**, yield 55%.

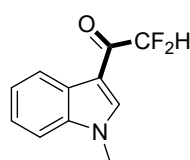
5 Derivatization of product 3b and Characterization Data of Compounds 9-13.

5.1 Compound 9



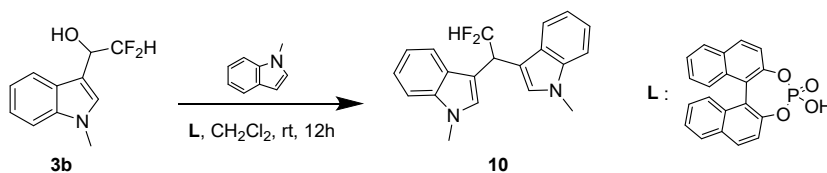
In an oven-dried Pressure tube, a mixture of 2,2-Difluoro-1-(1-methyl-1H-indol-3-yl)ethan-1-ol **3b** (0.2 mmol, 1.0 equiv), Dess-Martin periodinane (313.8 mg, 0.74 mmol, 3.7 equiv), in CH₂Cl₂ (5 ml) was stirred at room temperature for 2 h. The reaction mixture was then diluted with ethyl acetate (10 ml) and washed with brine. The aqueous phase was extracted with Ethyl acetate. The organic layers were combined, washed with brine and dried over Na₂SO₄. The solvent was removed in vacuo, and the residue was purified by column chromatography (PE/EA= 4/1) to afford the desired 14 mg of product **9**, yield 53%.²

2,2-Difluoro-1-(1-methyl-1H-indol-3-yl)ethan-1-one (9)



According to the above procedure and provide the title compound as a yellow oil (22.2 mg, 53%). TLC (PE: EA, 4:1 v/v): R_f = 0.4; ¹H NMR (500 MHz, Chloroform-*d*) δ 8.41 – 8.39 (m, 1H), 8.00 (s, 1H), 7.39 – 7.35 (m, 3H), 6.10 (t, *J* = 54.3 Hz, 1H), 3.89 (s, 3H). ¹³C NMR (125 MHz, Chloroform-*d*) δ 182.8 (t, *J* = 25.3 Hz), 137.9 (t, *J* = 7.1 Hz), 137.2, 126.9, 124.3, 123.6, 122.6, 112.2 (t, *J* = 254.0 Hz), 110.4 (t, *J* = 2.1 Hz), 109.9, 33.9. ¹⁹F NMR (470 MHz, Chloroform-*d*) δ -112.25- -120.00 (m), -120.11- -126.03 (m). **HRMS (ESI)**: calcd for C₁₁H₁₀F₂NO [M + H]⁺: 210.0724, found:210.0722.

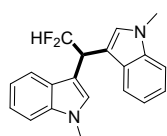
5.2 Compound 10



In an oven-dried Pressure tube, a mixture of 2,2-Difluoro-1-(1-methyl-1H-indol-3-yl)ethan-1-ol **3b** (0.2 mmol, 1.0 equiv), 1-Methyl-1H-indole (26.2 mg, 0.2

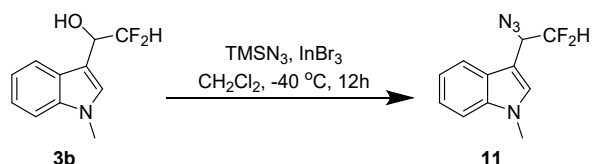
mmol, 1 equiv), 1,1'-Binaphthyl-2,2'-diyl hydrogenphosphate (6.9mg, 0.02 mmol, 0.1 equiv) in CH₂Cl₂ (1 ml) was stirred at room temperature for 12 h. The reaction mixture was then diluted with ethyl acetate (10 ml) and washed with brine. The aqueous phase was extracted with Ethyl acetate. The organic layers were combined, washed with brine and dried over Na₂SO₄. The solvent was removed in vacuo, and the residue was purified by column chromatography (PE/EA= 4/1) to afford the desired 35.7 mg of product **10**, yield 55%.^{2,3}

3,3'-(2,2-Difluoroethane-1,1-diyl)bis(1-methyl-1H-indole) (**10**)



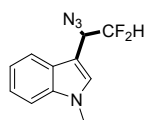
According to the above procedure and provide the title compound as a yellow oil (35.6 mg, 55%). TLC (PE: EA, 4:1 v/v): $R_f = 0.6$; ¹H NMR (500 MHz, Chloroform-*d*) δ 7.66 (d, $J = 7.9$ Hz, 2H), 7.36 (d, $J = 8.1$ Hz, 2H), 7.29 (t, $J = 7.6$ Hz, 2H), 7.15 (t, $J = 7.1$ Hz, 2H), 7.07 (s, 2H), 6.39 (tt, $J = 26.7, 3.0$ Hz, 1H), 5.08 (td, $J = 16.3, 2.9$ Hz, 1H), 3.77 (s, 6H). ¹³C NMR (125 MHz, Chloroform-*d*) δ 136.9, 128.0, 127.5, 121.7, 119.3, 119.1, 117.2 (t, $J = 245.0$ Hz), 110.2 (t, $J = 3.6$ Hz), 109.3, 38.4 (t, $J = 22.1$ Hz), 32.8. ¹⁹F NMR (470 MHz, Chloroform-*d*) δ -117.61 (d, $J = 16.1$ Hz), -117.73 (d, $J = 16.5$ Hz). **HRMS (ESI)**: calcd for C₂₀H₁₈F₂N₂Na [M + Na]⁺: 347.1330, found:347.1326.

5.3 Compound **11**



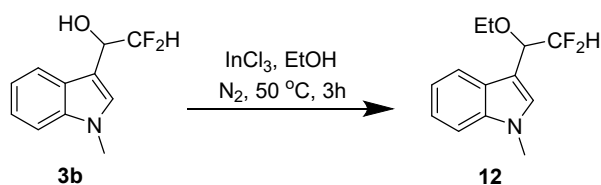
In an oven-dried Pressure tube, a mixture of 2,2-Difluoro-1-(1-methyl-1H-indol-3-yl)ethan-1-ol **3b** (0.2 mmol, 1.0 equiv), TMSN₃ (34.6 mg, 0.3 mmol, 1.5 equiv), InBr₃ (35.5mg, 0.1 mmol, 0.5 equiv) in CH₂Cl₂ (1 ml) was stirred at -40°C for 12 h. The reaction mixture was then diluted with ethyl acetate (10 ml). The aqueous phase was extracted with Ethyl acetate. The organic layers were combined and dried over Na₂SO₄. The solvent was removed in vacuo, and the residue was purified by column chromatography (PE/EA= 4/1) to afford the desired 19 mg of product **11**, yield 57%.⁴

3-(1-azido-2,2-Difluoroethyl)-1-methyl-1H-indole (**11**)



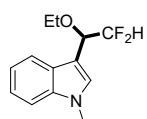
According to the above procedure and provide the title compound as a yellow oil (26.9 mg, 57%). TLC (PE: EA, 4:1 *v/v*): $R_f = 0.7$; $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 7.66 (d, $J = 8.0$ Hz, 1H), 7.35 (d, $J = 8.2$ Hz, 1H), 7.30 (t, $J = 7.6$ Hz, 1H), 7.20 (s, 1H), 7.19 (t, $J = 7.3$ Hz, 1H), 6.00 (td, $J = 55.6, 3.8$ Hz, 1H), 4.97 (td, $J = 12.5, 3.7$ Hz, 1H), 3.80 (s, 3H). $^{13}\text{C NMR}$ (125 MHz, Chloroform-*d*) δ 137.0, 128.7, 126.6, 122.6, 120.3, 118.9, 114.9 (t, $J = 246.3$ Hz), 109.8, 104.7 (t, $J = 3.1$ Hz), 59.6 (t, $J = 24.0$ Hz), 33.1. $^{19}\text{F NMR}$ (470 MHz, Chloroform-*d*) δ -122.32 (ddd, $J = 279.3, 55.5, 12.0$ Hz), -123.78 (ddd, $J = 279.4, 55.5, 13.3$ Hz). **HRMS (ESI)**: calcd for $\text{C}_{11}\text{H}_{11}\text{F}_2\text{N}_4$ $[\text{M} + \text{H}]^+$: 237.0946, found:237.0944.

5.4 Compound 12



In an oven-dried Pressure tube, a mixture of 2,2-Difluoro-1-(1-methyl-1H-indol-3-yl)ethan-1-ol **3b** (0.2 mmol, 1.0 equiv), InCl_3 (8.4 mg, 0.04 mmol, 0.2 equiv) in EtOH (1 ml) was stirred at 50°C with nitrogen protection for 3h. The reaction mixture was then diluted with ethyl acetate (10 ml). The aqueous phase was extracted with Ethyl acetate. The organic layers were combined and dried over Na_2SO_4 . The solvent was removed in vacuo, and the residue was purified by column chromatography (PE/EA= 32/1) to afford the desired 26.3 mg of product **12**, yield 75%.⁴

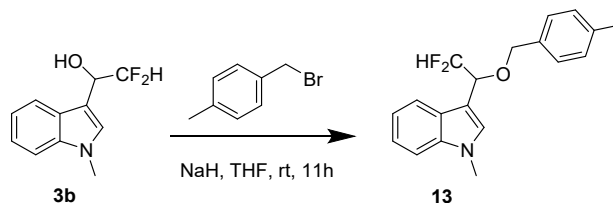
3-(1-ethoxy-2,2-Difluoroethyl)-1-methyl-1H-indole (12)



According to the above procedure and provide the title compound as a yellow oil (33.9 mg, 75%). TLC (PE: EA, 32:1 *v/v*): $R_f = 0.3$; $^1\text{H NMR}$ (500 MHz, Chloroform-*d*) δ 7.73 (d, $J = 8.0$ Hz, 1H), 7.33 (d, $J = 8.2$ Hz, 1H), 7.26 (t, $J = 7.9$ Hz, 1H), 7.15 (t, $J = 7.5$ Hz, 1H), 7.13 (s, 1H), 5.98 (td, $J = 56.1, 4.5$ Hz, 1H), 4.76 (td, $J = 10.8, 4.5$ Hz, 1H), 3.80 (s, 3H), 3.61 – 3.49 (m, 2H), 1.21 (t, $J = 7.0$ Hz, 3H). $^{13}\text{C NMR}$ (125 MHz, Chloroform-*d*) δ 137.2, 128.8, 127.0, 122.1, 119.8, 117.1-113.2 (m), 109.5, 108.2-108.1 (m), 77.2, 75.4-75.0 (m), 64.7, 32.9, 15.2. $^{19}\text{F NMR}$ (470 MHz, Chloroform-*d*) δ -124.78 (ddd, $J = 282.3, 56.8, 10.6$ Hz), -

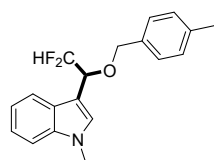
125.95 (ddd, $J = 282.3, 56.8, 12.1$ Hz). **HRMS (ESI):** calcd for $C_{13}H_{16}F_2NO$ $[M + H]^+$: 226.1037, found:226.1034.

5.5 Compound 13



In an oven-dried Pressure tube, a mixture of 2,2-Difluoro-1-(1-methyl-1H-indol-3-yl)ethan-1-ol **3b** (0.2 mmol, 1.0 equiv), p-Methylbenzyl bromide (44.4 mg, 0.24 mmol, 1.2 equiv), NaH (19.2 mg, 0.8 mmol, 4 equiv) in dry THF (1 ml) was stirred at room temperature for 1h. The reaction mixture was then diluted with ethyl acetate (10 ml). The aqueous phase was extracted with Ethyl acetate. The organic layers were combined and dried over Na_2SO_4 . The solvent was removed in vacuo, and the residue was purified by column chromatography (PE/EA= 32/1) to afford the desired 20 mg of product **13**, yield 52%.

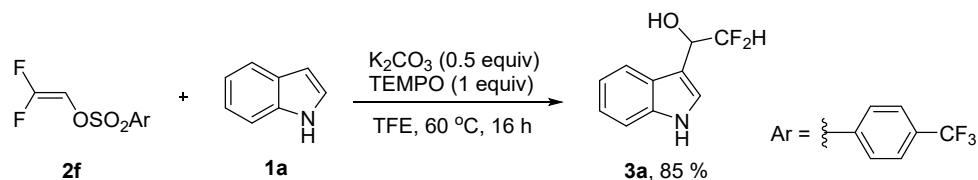
3-(2,2-Difluoro-1-((4-methylbenzyl)oxy)ethyl)-1-methyl-1H-indole (**13**)



According to the above procedure and provide the title compound as a yellow oil (35.1 mg, 52%). TLC (PE: EA, 32:1 v/v): $R_f = 0.2$; 1H NMR (500 MHz, Chloroform-*d*) δ 7.71 (d, $J = 8.0$ Hz, 1H), 7.34 (d, $J = 8.2$ Hz, 1H), 7.27 (t, $J = 7.6$ Hz, 1H), 7.23 – 7.12 (m, 6H), 6.00 (td, $J = 56.1, 4.5$ Hz, 1H), 4.80 (td, $J = 10.9, 4.5$ Hz, 1H), 4.61 (d, $J = 11.7$ Hz, 1H), 4.38 (d, $J = 11.7$ Hz, 1H), 3.79 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 137.6, 137.4, 134.7, 129.3, 129.2, 128.2, 127.1, 122.3, 120.0, 120.0, 115.3(t, $J = 247.1$ Hz), 109.7, 107.6(d, $J = 1.7$ Hz), 74.1 (t, $J = 25.2$ Hz), 70.3, 33.1, 21.3. ^{19}F NMR (470 MHz, Chloroform-*d*) δ -124.39 (ddd, $J = 282.3, 56.4, 10.4$ Hz), -125.95 (ddd, $J = 282.0, 56.1, 11.6$ Hz). **HRMS (ESI):** calcd for $C_{19}H_{19}F_2NONa$ $[M + Na]^+$: 338.1326, found:338.1320.

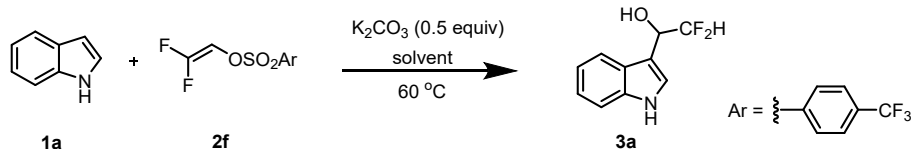
6 Mechanism Study

6.1 Free radical inhibition experiment



In an oven-dried Pressure tube, a mixture of Indoles **1a** (0.2 mmol, 1.0 equiv), 2,2-Difluorovinyl 4-(trifluoromethyl)benzenesulfonate **2f** (115.3 mg, 0.4 mmol, 2 equiv), TEMPO (31.2 mg, 0.2 mmol, 1 equiv), K_2CO_3 (13.8 mg, 0.1 mmol, 0.5 equiv) in TFE (1 ml) was stirred at 60 °C for 16 h. The reaction mixture was then diluted with Ethyl acetate (10 ml) and washed with brine. The aqueous phase was extracted with ethyl acetate. The organic layers were combined, washed with brine and dried over Na_2SO_4 . The pure product was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product **3a**, yield: 85%.

6.2 Reaction solvent screening



In an oven-dried Pressure tube, a mixture of Indoles **1a** (0.2 mmol, 1.0 equiv), 2,2-Difluorovinyl 4-(trifluoromethyl)benzenesulfonate **2f** (115.3 mg, 0.4 mmol, 2 equiv), K_2CO_3 (13.8 mg, 0.1 mmol, 0.5 equiv) in different solvent, Solvents include MeOH, EtOH, TFE and HFIP, the reaction was stirred at 60 °C. TLC monitoring reaction.

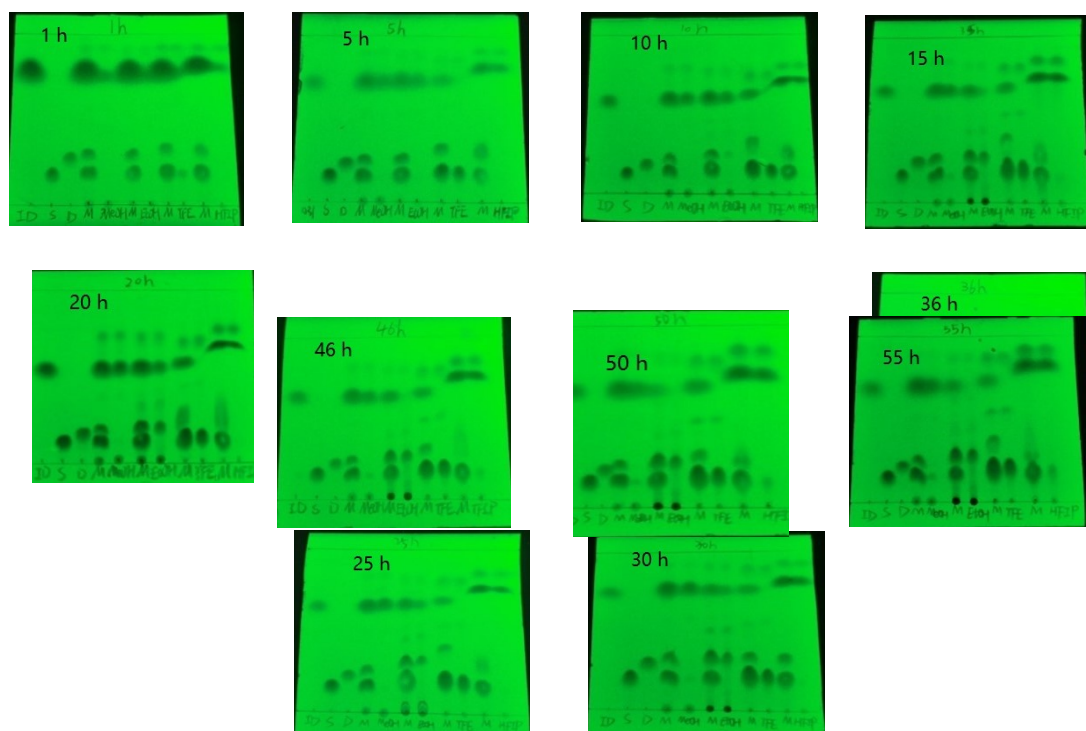
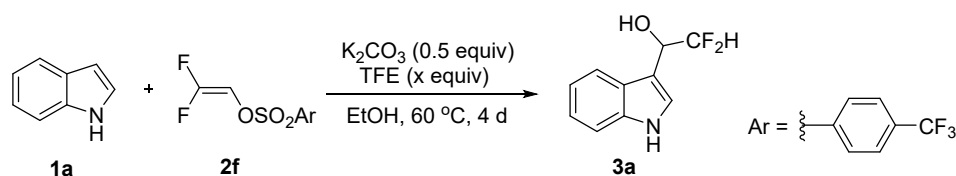


Fig 1: TLC monitoring reaction

(ID: Indole, S: **3a**, D: 3,3'-(2,2-difluoroethane-1,1-diyl)bis(1H-indole), M: Mixing point, MeOH, EtOH, TFE and HFIP represents the reaction of different solvents)

6.3 Effect of trifluoroethanol



In an oven-dried Pressure tube, a mixture of Indoles **1a** (0.2 mmol, 1.0 equiv), 2,2-Difluorovinyl 4-(trifluoromethyl)benzenesulfonate (115.3 mg, 0.4 mmol, 2 equiv), TFE (x equiv), K_2CO_3 (13.8 mg, 0.1 mmol, 0.5 equiv) in EtOH (1 ml) was stirred at 60 °C for 4 days. The reaction mixture was then diluted with Ethyl acetate (10 ml) and washed with brine. The aqueous phase was extracted with ethyl acetate. The organic layers were combined, washed with brine and dried over Na_2SO_4 . The pure product was purified by flash column

chromatography on silica with an appropriate solvent to afford the pure product **3a**.

Table 1 Effect of trifluoroethanol on Yield

| TFE (x equiv) | Yield |
|---------------|-------|
| 0 | 0 |
| 10 | 9 % |
| 20 | 14 % |
| 30 | 19 % |
| 40 | 22 % |

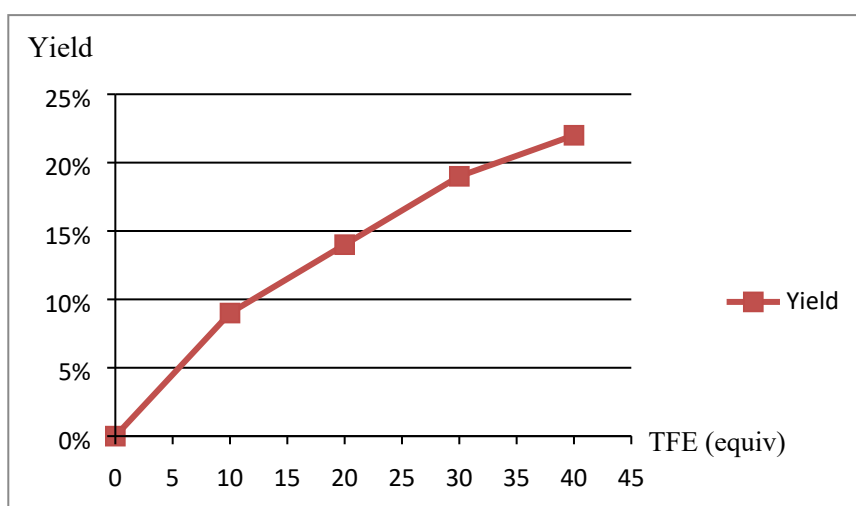
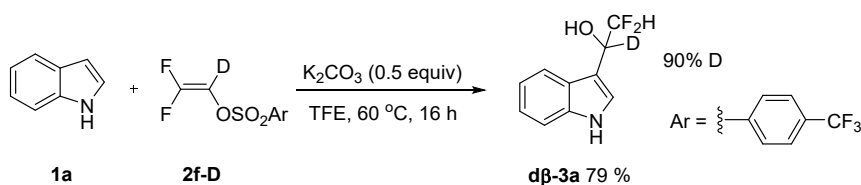


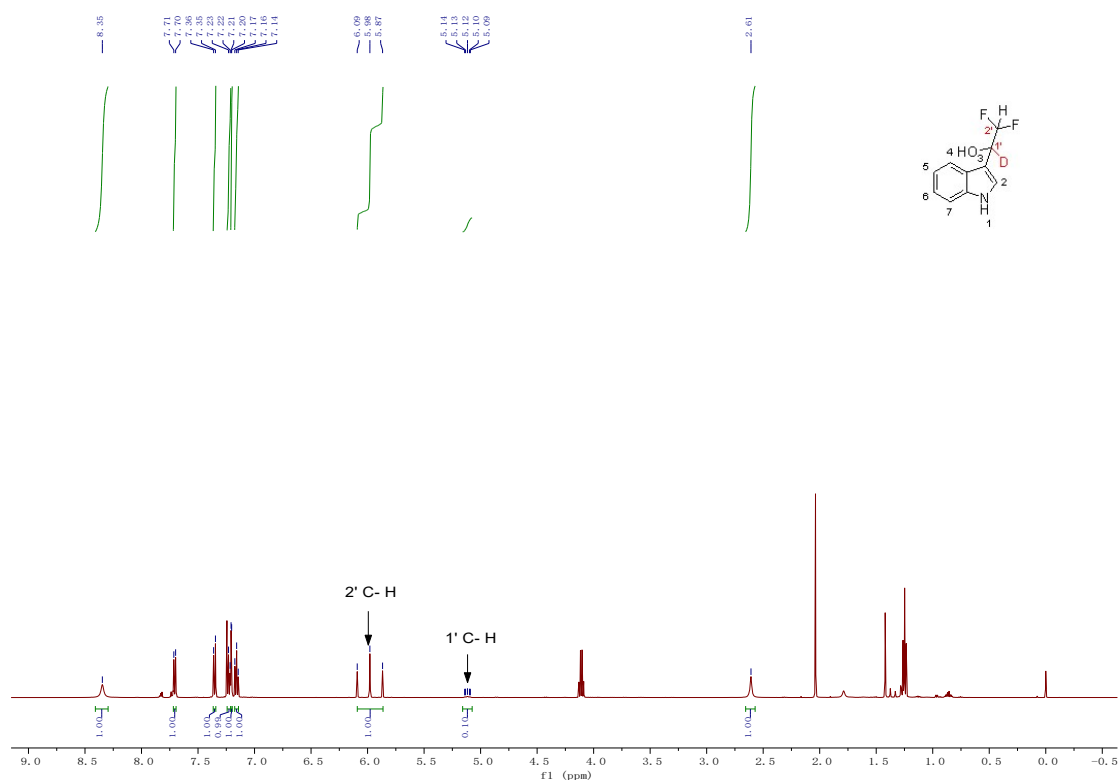
Fig. 2 Effect of trifluoroethanol on Yield

6.4 Deuterium experiment

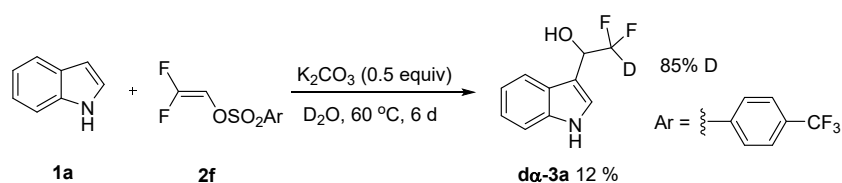


In an oven-dried Pressure tube, a mixture of Indoles **1a** (0.2 mmol, 1.0 equiv), 2,2-Difluorovinyl-1-D 4-(trifluoromethyl)benzenesulfonate **2f-D** (114.8 mg, 0.4 mmol, 2 equiv), K_2CO_3 (13.8 mg, 0.1 mmol, 0.5 equiv) in TFE (1 ml) was stirred at 60 °C for 16 h. The reaction mixture was then diluted with Ethyl acetate (10 ml) and washed with brine. The aqueous phase was extracted with

ethyl acetate. The organic layers were combined, washed with brine and dried over Na₂SO₄. The pure product was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product **dβ-3a**, yield: 79%.

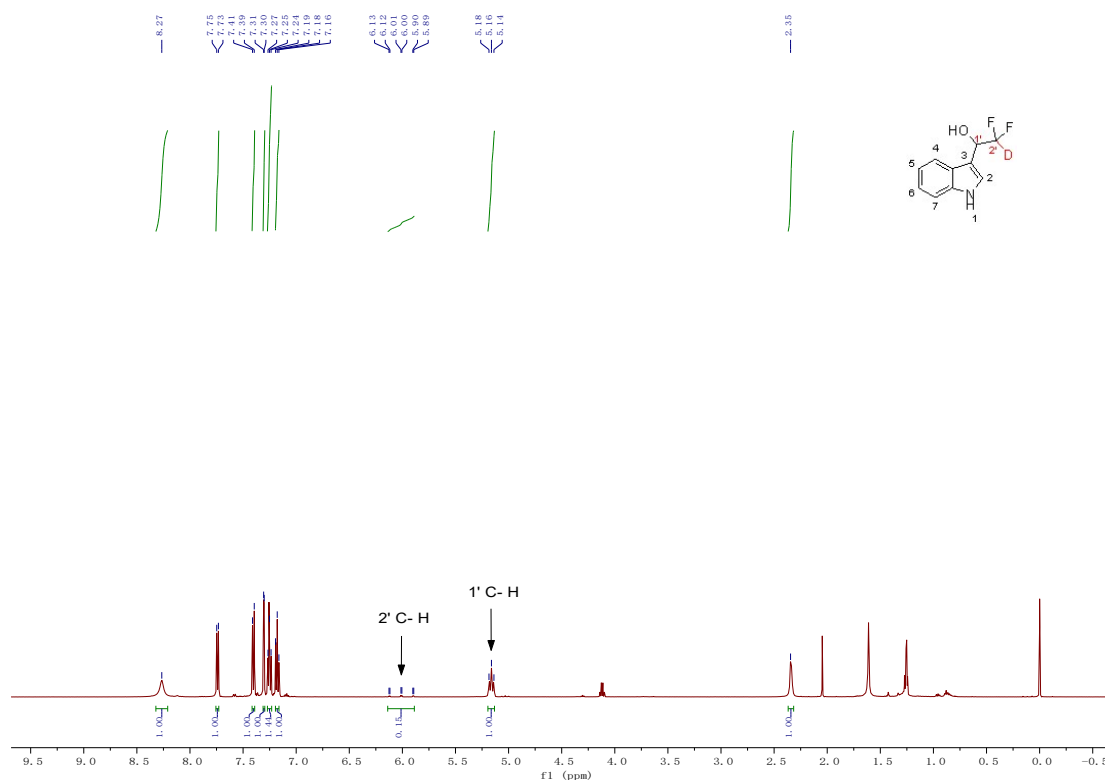


Supplementary scheme 5 ¹H NMR spectra for compound **dβ-3a**.



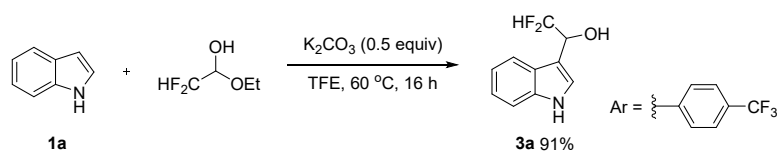
In an oven-dried Pressure tube, a mixture of Indoles **1a** (0.2 mmol, 1.0 equiv), 2,2-Difluorovinyl 4-(trifluoromethyl)benzenesulfonate (115.3mg, 0.4 mmol, 2 equiv), K₂CO₃ (13.8 mg, 0.1 mmol, 0.5 equiv) in D₂O (1 ml) was stirred at 60 °C for 6 days. The reaction mixture was then diluted with Ethyl acetate (10 ml) and washed with brine. The aqueous phase was extracted with ethyl acetate. The organic layers were combined, washed with brine and dried over Na₂SO₄. The pure product was purified by flash column chromatography on silica with

an appropriate solvent to afford the pure product **da-3a**, yield: 12%.

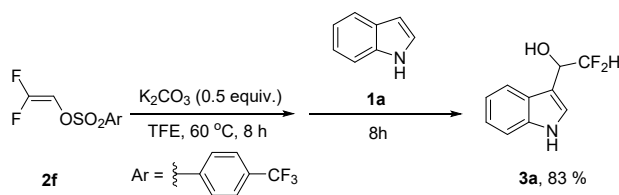


Supplementary scheme 5 ¹H NMR spectra for compound **da-3a**.

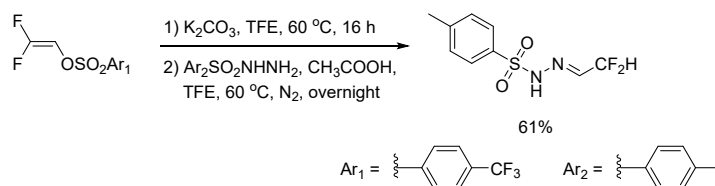
6.5 Capture of active difluoroacetaldehyde intermediate



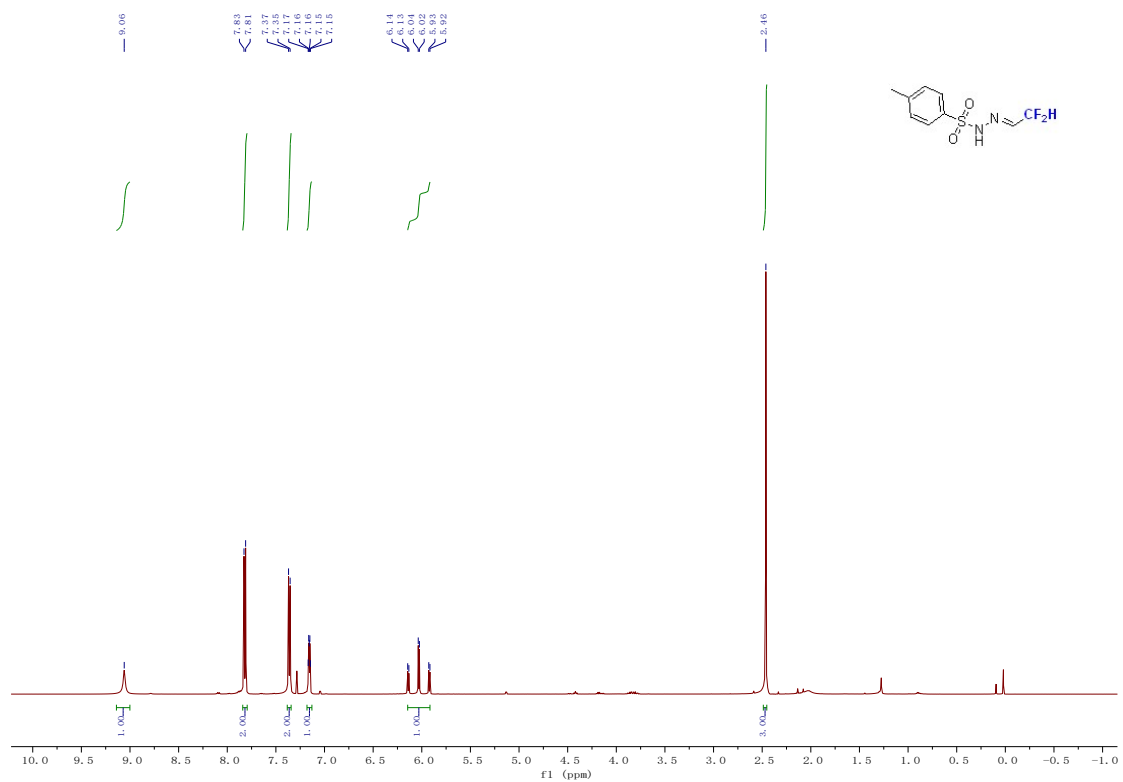
In an oven-dried Pressure tube, a mixture of Indoles **1a** (0.2 mmol, 1.0 equiv), 1-ethoxy-2,2-difluoroethan-1-ol (0.4 mmol, 2 equiv), K_2CO_3 (13.8 mg, 0.1 mmol, 0.5 equiv) in TFE (1 ml) was stirred at 60 °C for 16 h. The reaction mixture was then diluted with Ethyl acetate (10 ml) and washed with brine. The aqueous phase was extracted with ethyl acetate. The organic layers were combined, washed with brine and dried over Na_2SO_4 . The pure product was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product **3a**, yield: 91%.



In an oven-dried Pressure tube, a mixture of 2,2-Difluorovinyl 4-(trifluoromethyl)benzenesulfonate **2f** (115.3 mg, 0.4 mmol, 2 equiv), K_2CO_3 (13.8 mg, 0.1 mmol, 0.5 equiv) in TFE (1 ml) was stirred at 60 °C for 8 h. Then Indoles **1a** (0.2 mmol, 1.0 equiv) were added. The mixture was stirred at 60 °C for 8 h. The reaction mixture was then diluted with Ethyl acetate (10 ml) and washed with brine. The aqueous phase was extracted with ethyl acetate. The organic layers were combined, washed with brine and dried over Na_2SO_4 . The pure product was purified by flash column chromatography on silica with an appropriate solvent to afford the pure product **3a**, yield: 83%.



In an oven-dried Pressure tube, a mixture of 2,2-Difluorovinyl 4-(trifluoromethyl)benzenesulfonate (115.3 mg, 0.4 mmol, 2 equiv), K_2CO_3 (13.8 mg, 0.1 mmol, 0.5 equiv) in TFE (1 ml) was stirred at 60 °C for 16 h. Then CH_3COOH (800 μl), P-toluenesulfonyl hydrazide (37.24 mg, 0.2 mmol, 1 equiv) were added dropwise under N_2 atmosphere. Then the mixture was transferred to 60 °C and stirred for overnight,⁵ and monitored by TLC (PE:EA=4:1). The pure product was purified by flash column chromatography on silica with an appropriate solvent to afford the product Difluoroacetaldehyde N-tosylhydrazone, yield: 61%. The index of this compound is consistent with the reference.



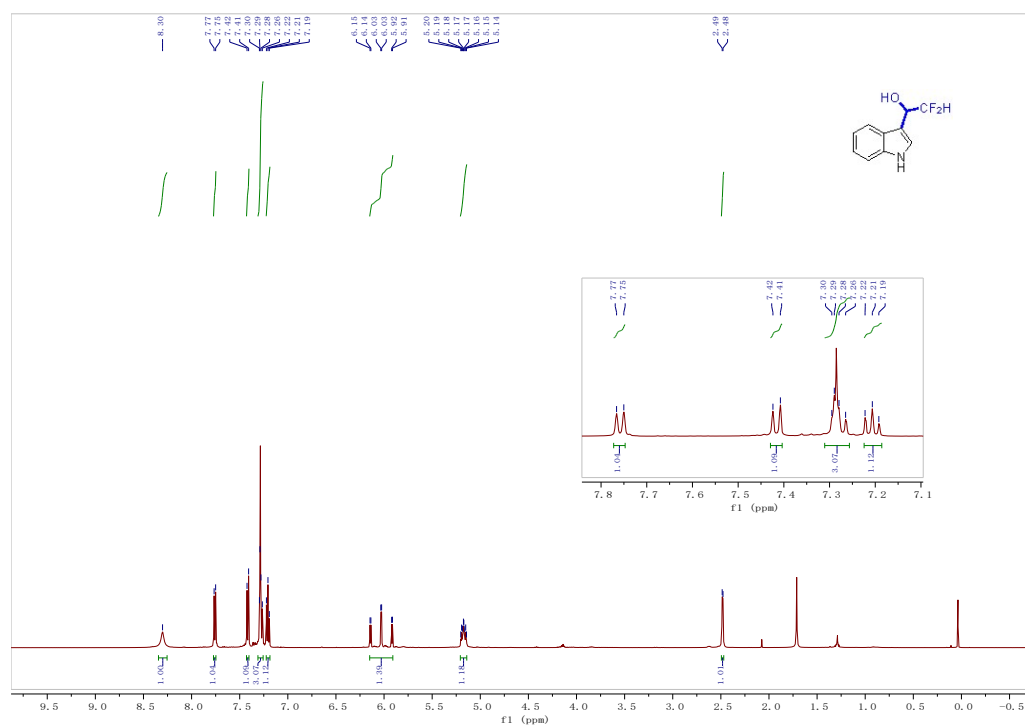
Supplementary scheme 5 ^1H NMR spectra for product Difluoroacetaldehyde N-tosylhydrazone.

7 References

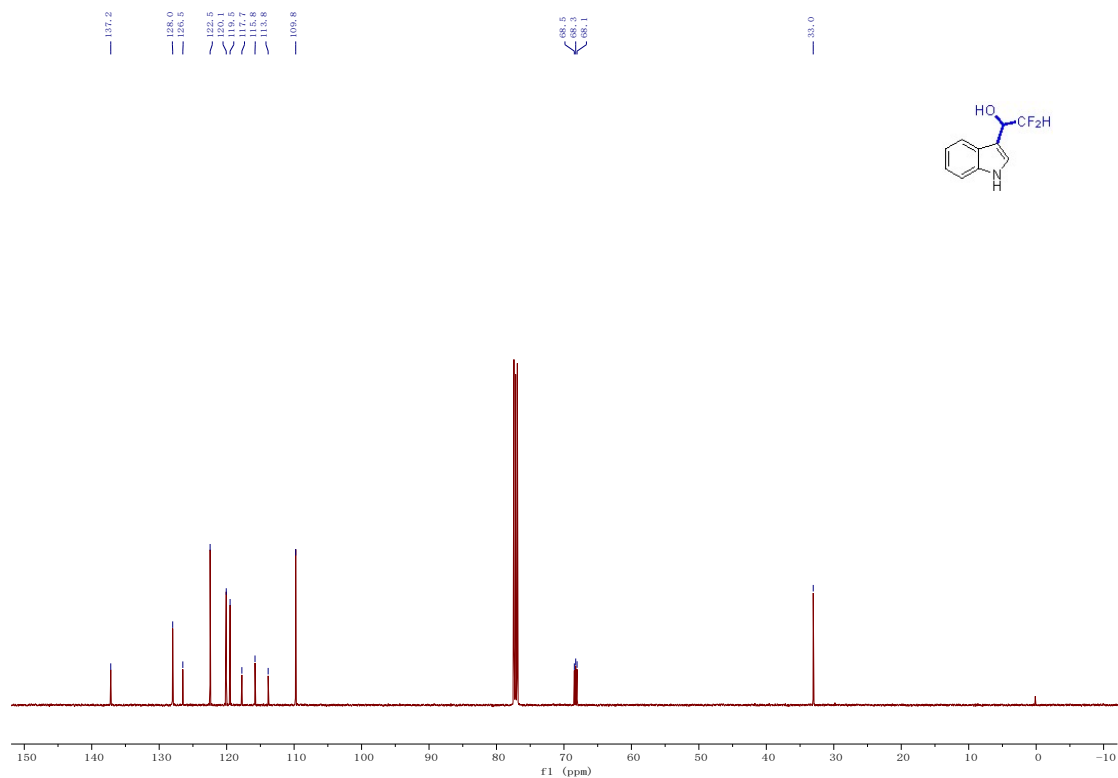
1. (a) Gøgsig, T. M.; Søbjerg, L. S.; Lindhardt (né Hansen), A. T.; Jensen, K. L.; Skrydstrup, T.; *J. Org. Chem.* **2008**, *73*, 3404. (b) Zhang, B.; Zhang, X. *Chem. Commun.* **2016**, *52*, 1238.
2. Xu Z, Hang Z, Chai L, Liu ZQ. *Org Lett.* **2016**, *18*, 4662.
3. Wang W, Xiong W, Wang J, Wang QA, Yang W. Brønsted. *J Org Chem.* **2020**, *85*, 4398.
4. Guo, S., Chen, J., Yi, M., Dong, L., Lin, A., Yao, H. *Org. Chem. Front.* **2021**, *8*, 1783.
5. Bi, X., Gai, Y., Zhang, X., Dong, Y., Sivaguru, P., Wang, Y., Ning, Y. *Angew Chem Int Ed Engl.* **2020**, *59*, 6473.

8 ¹H, ¹³C and ¹⁹F NMR Spectra of Synthesized Compounds

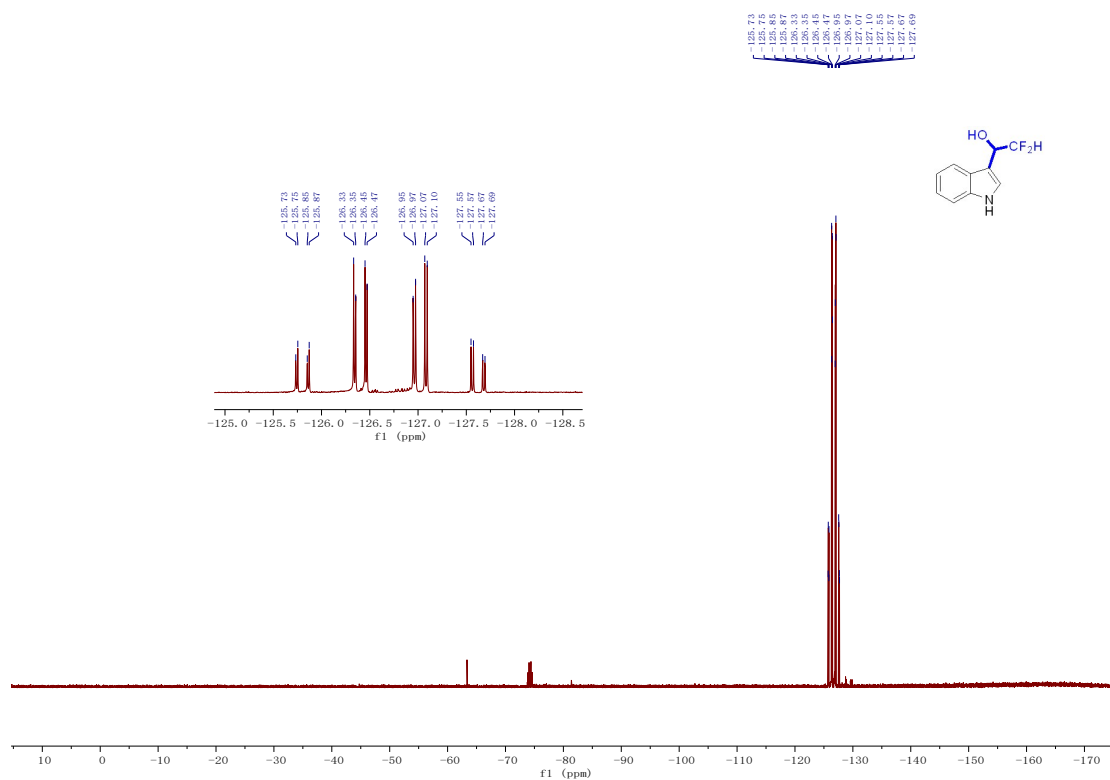
¹H NMR (500 MHz, Chloroform-*d*) spectra of **3a**



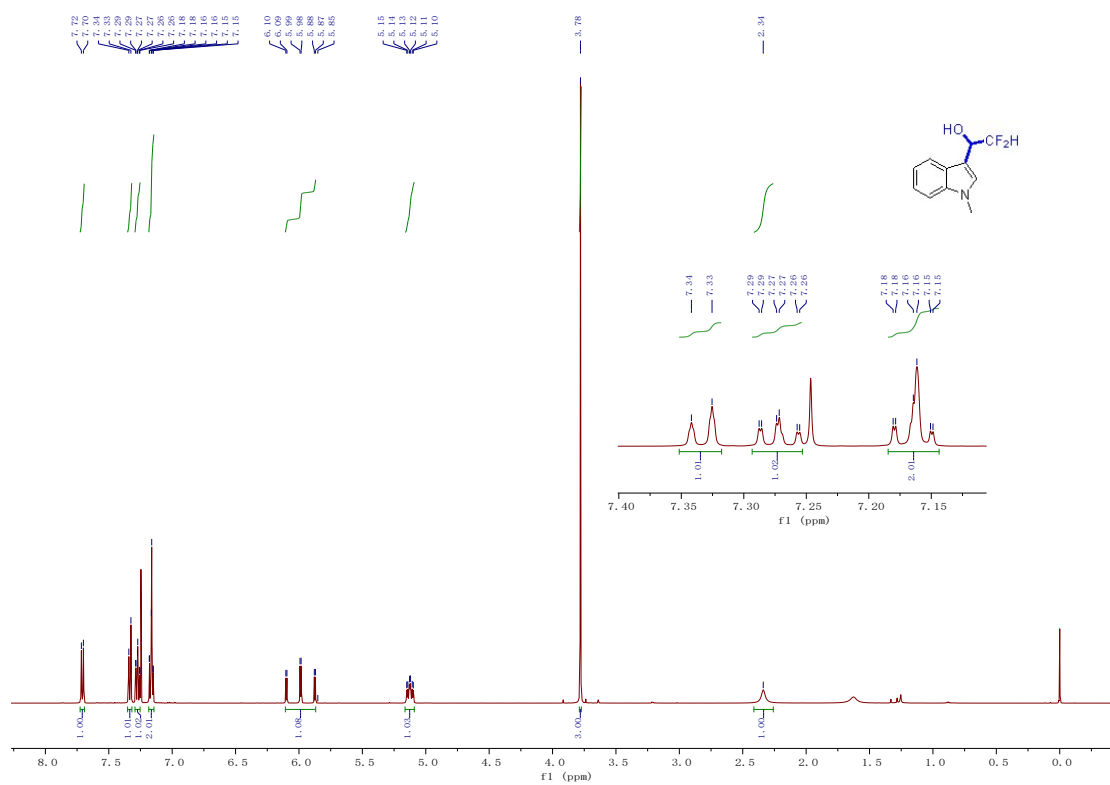
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **3a**



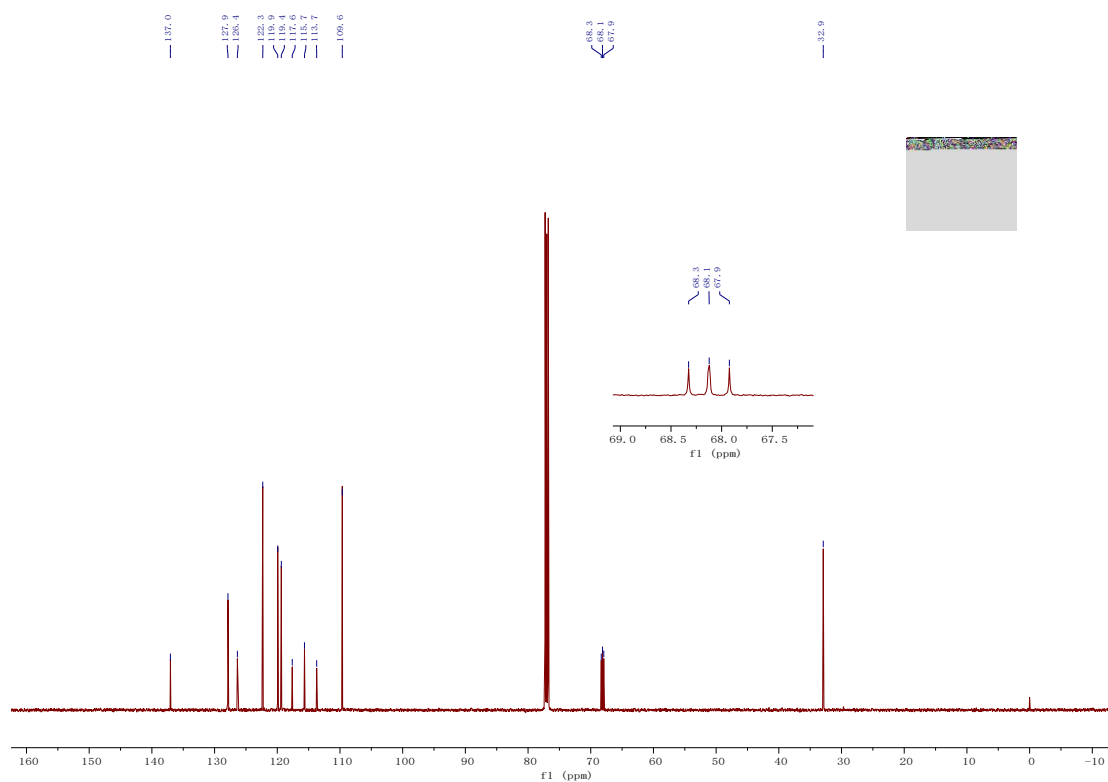
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **3a**



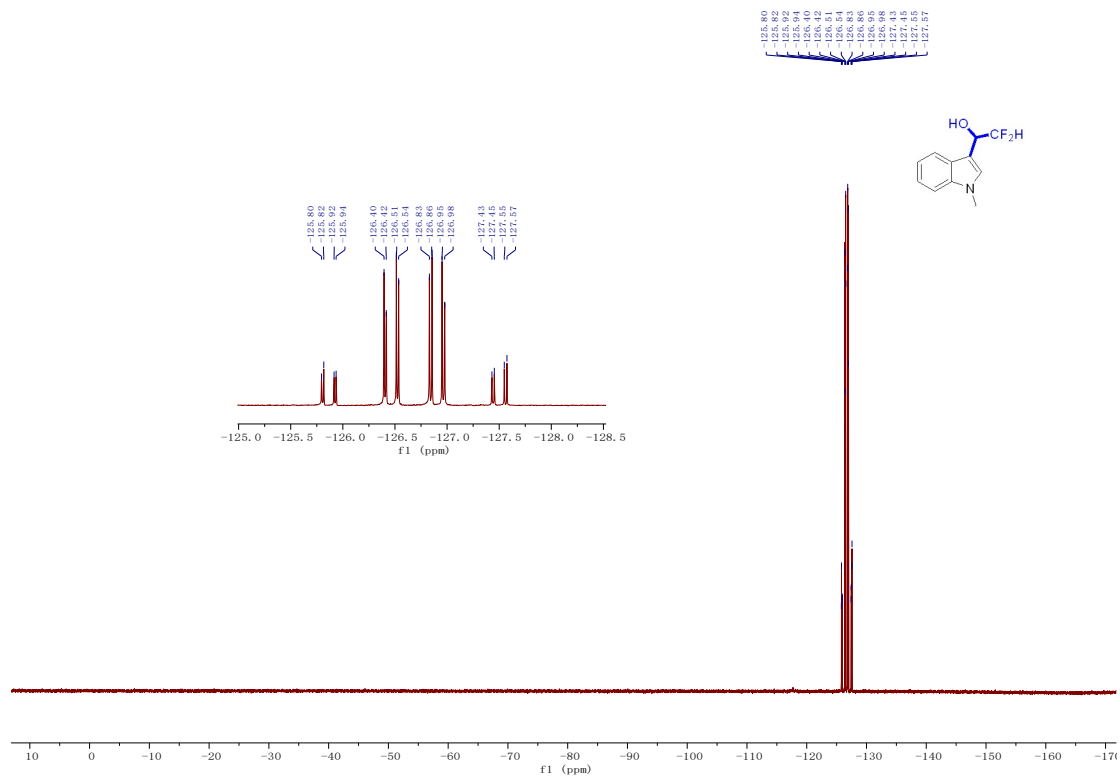
¹H NMR (500 MHz, Chloroform-*d*) spectra of **3b**



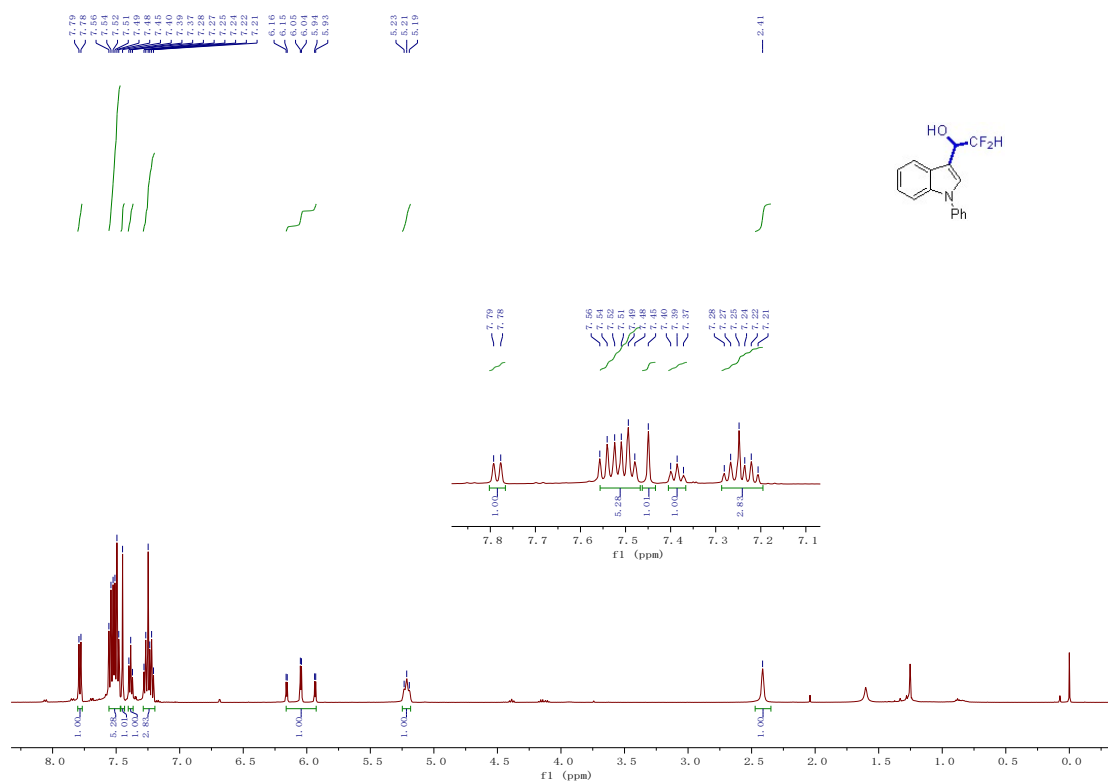
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **3b**



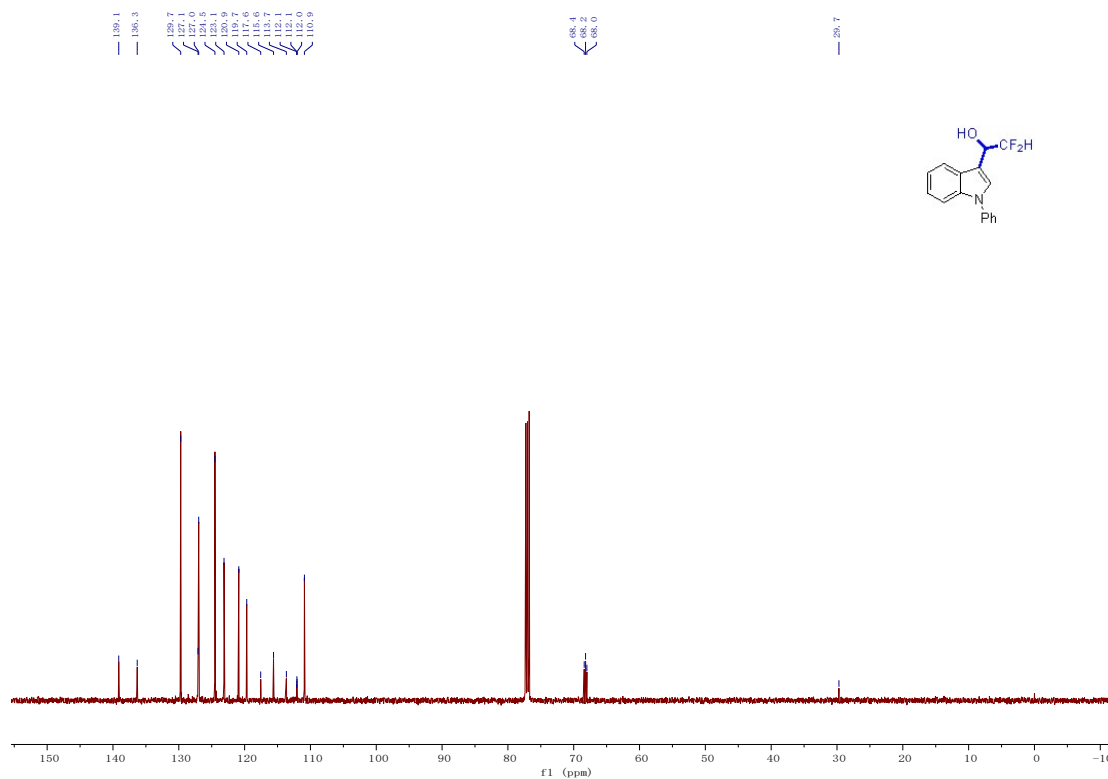
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **3b**



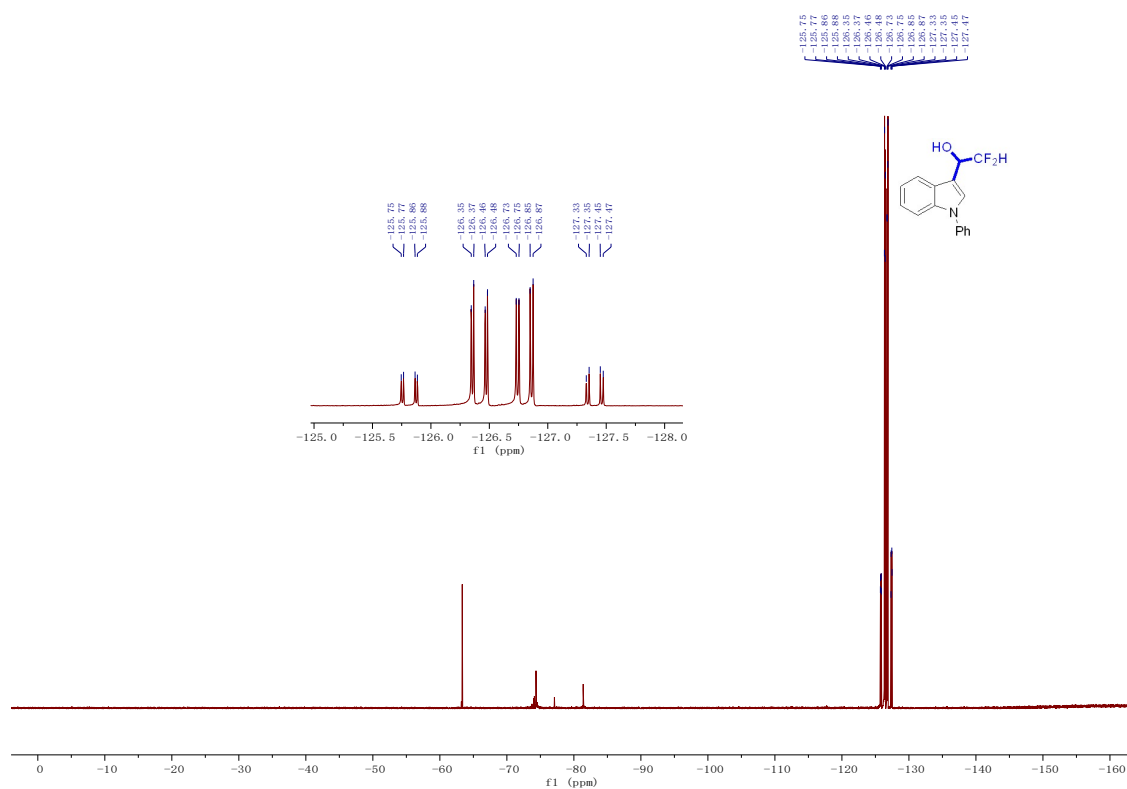
^1H NMR (500 MHz, Chloroform-*d*) spectra of **3c**



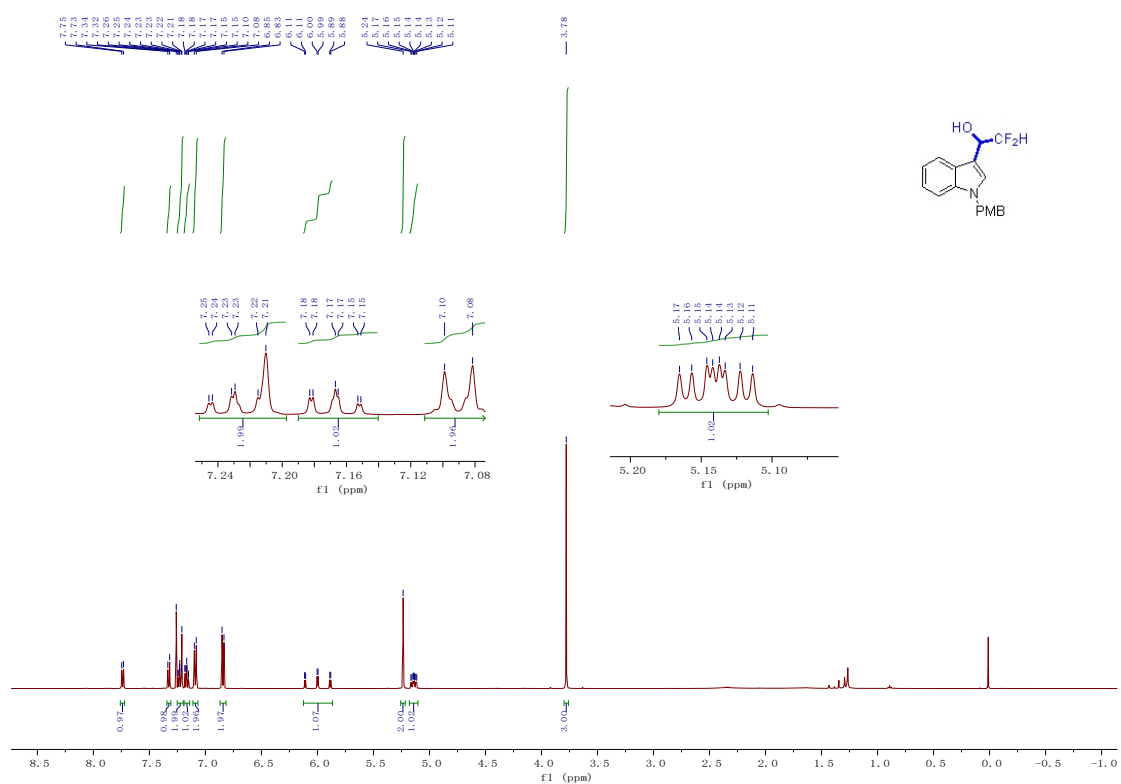
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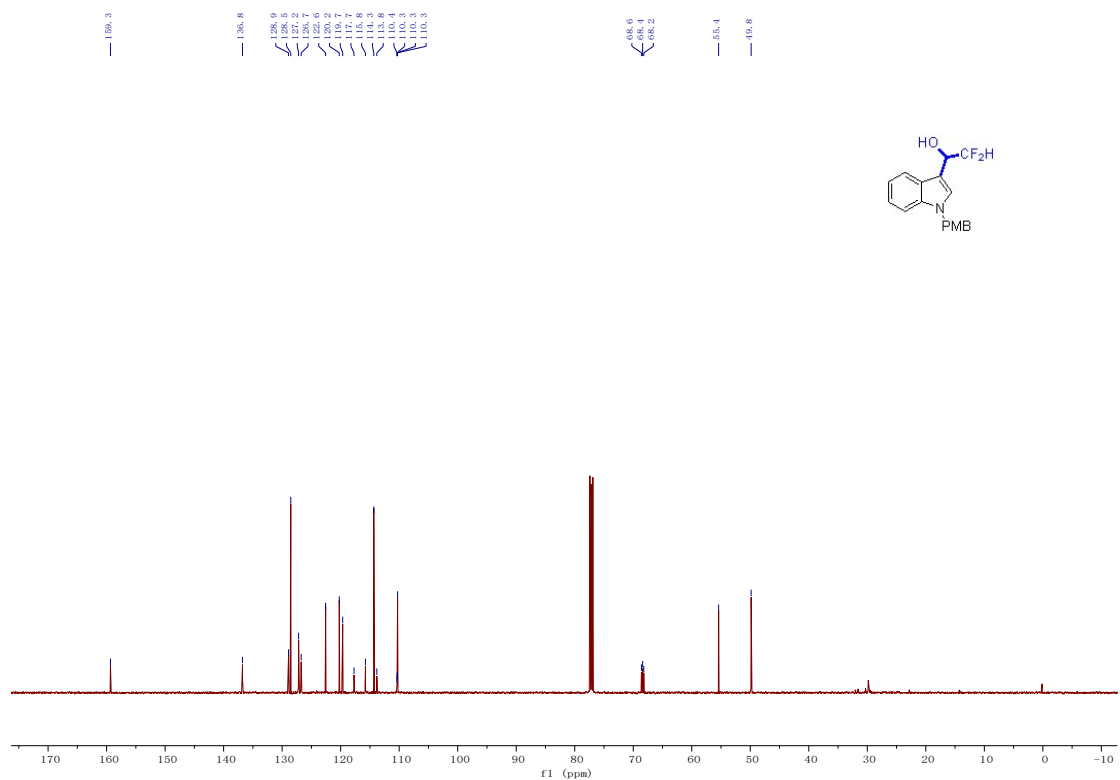
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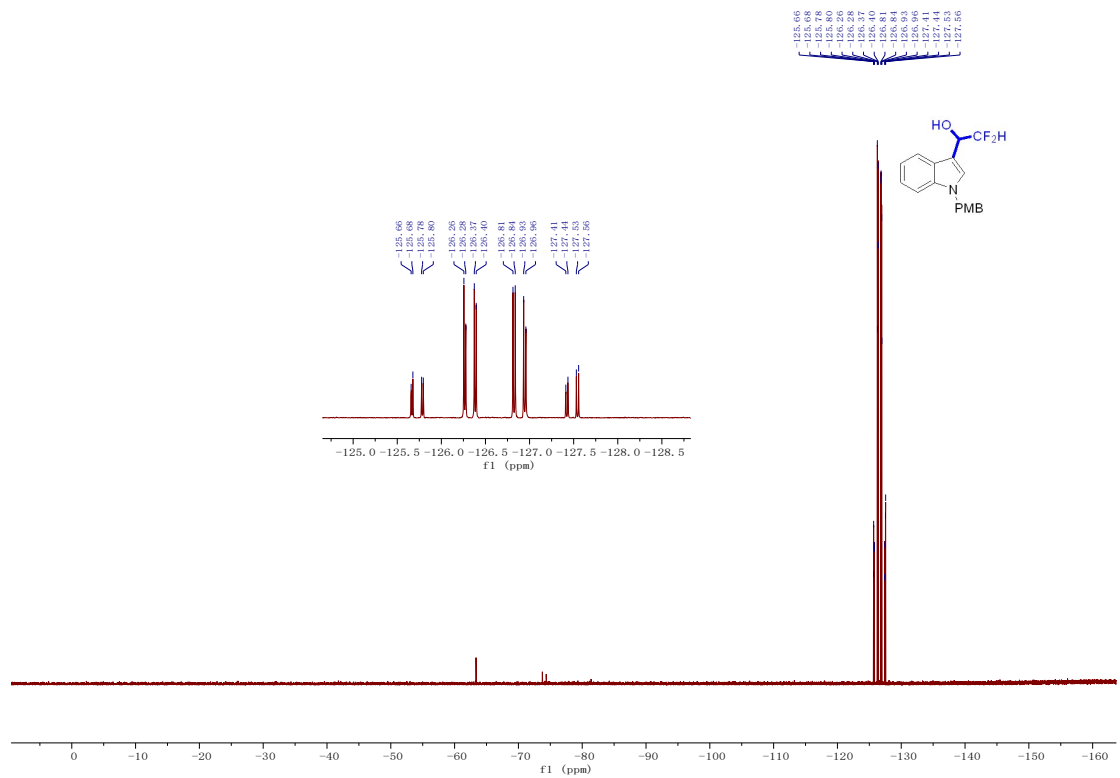
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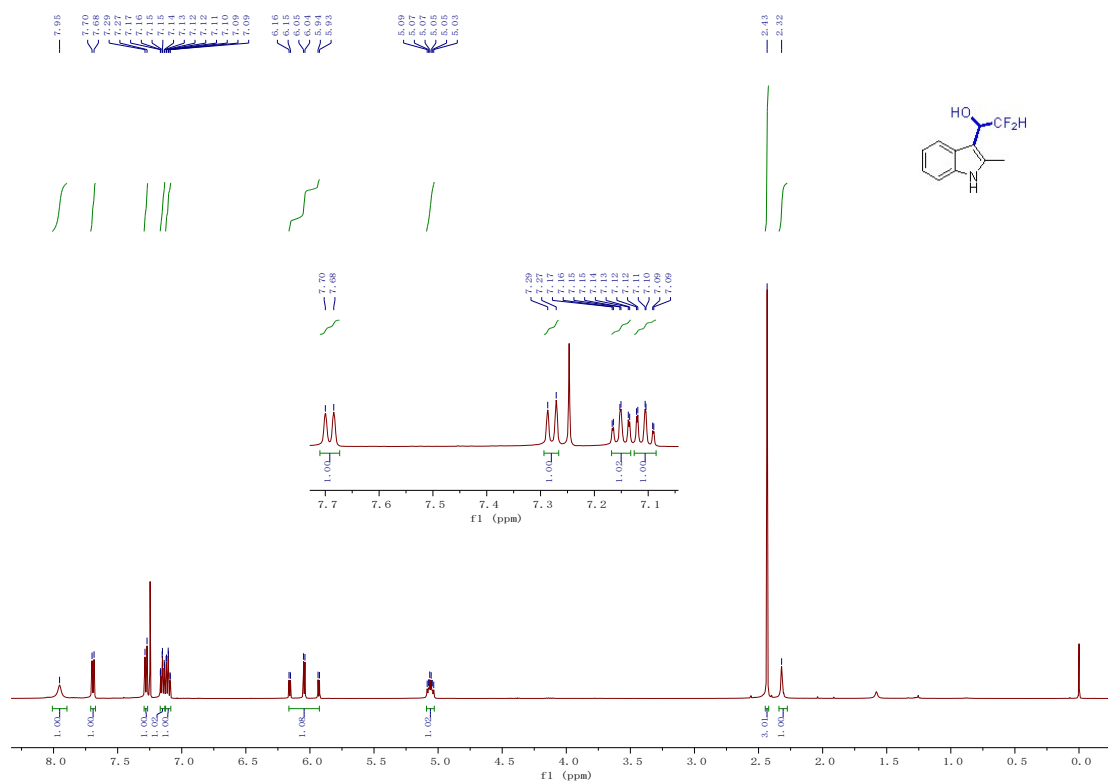
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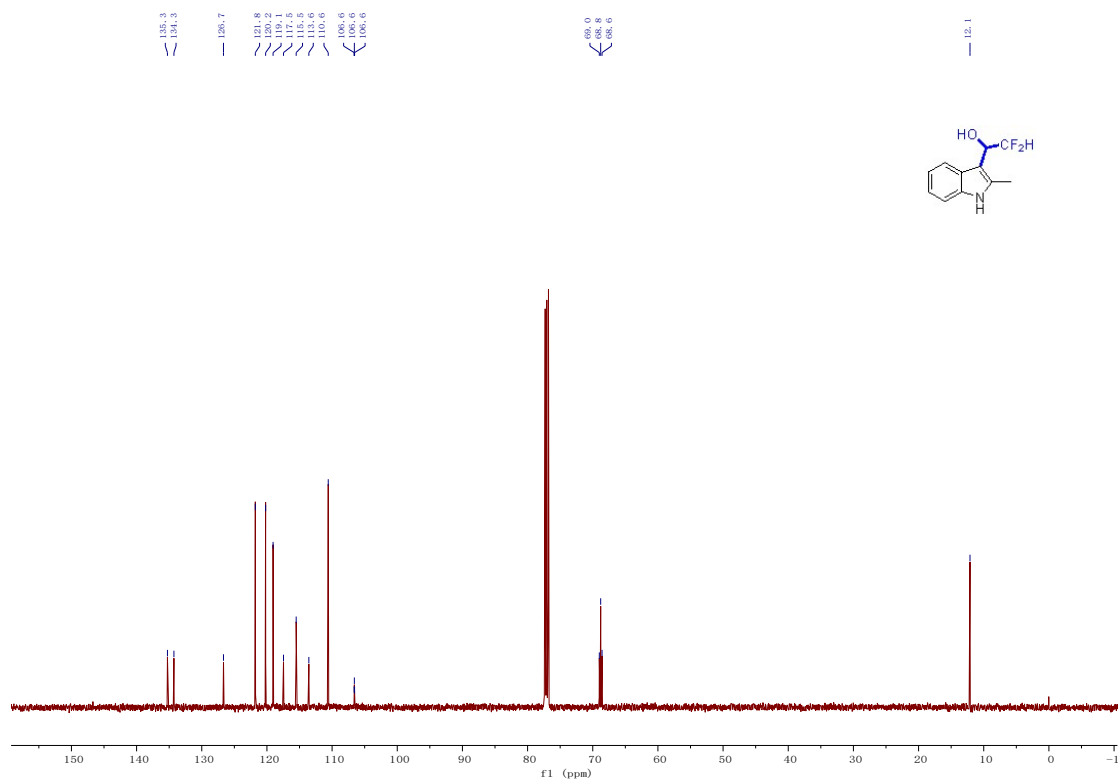
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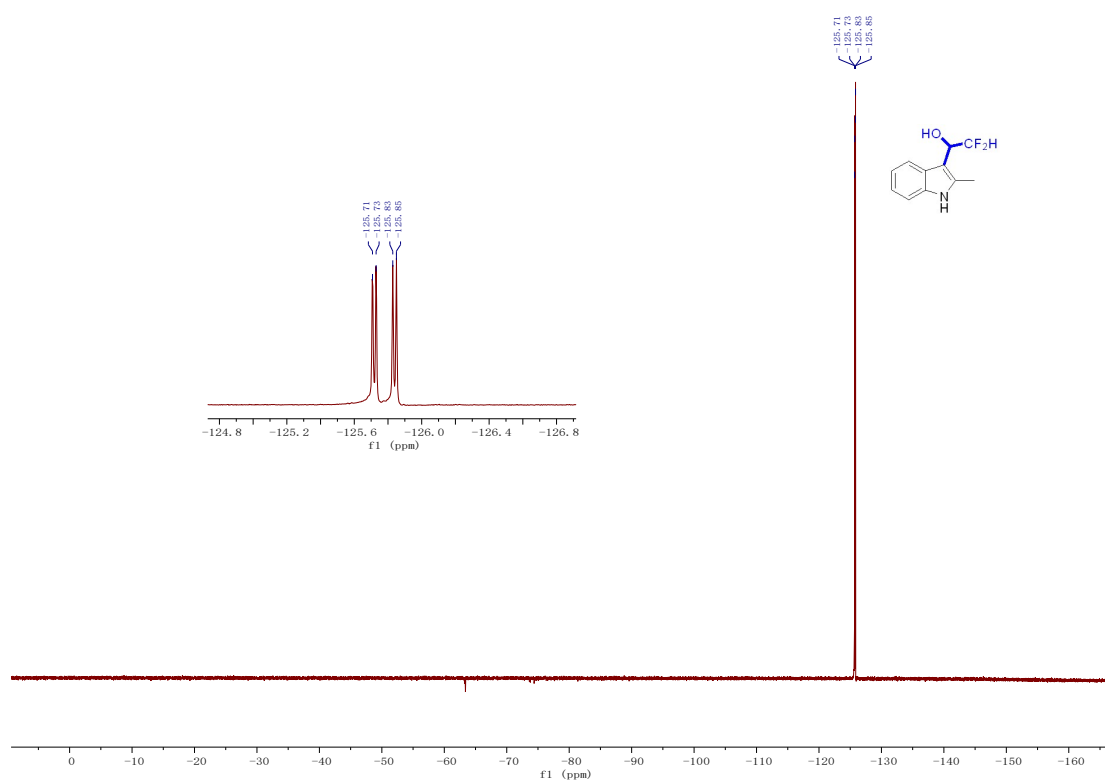
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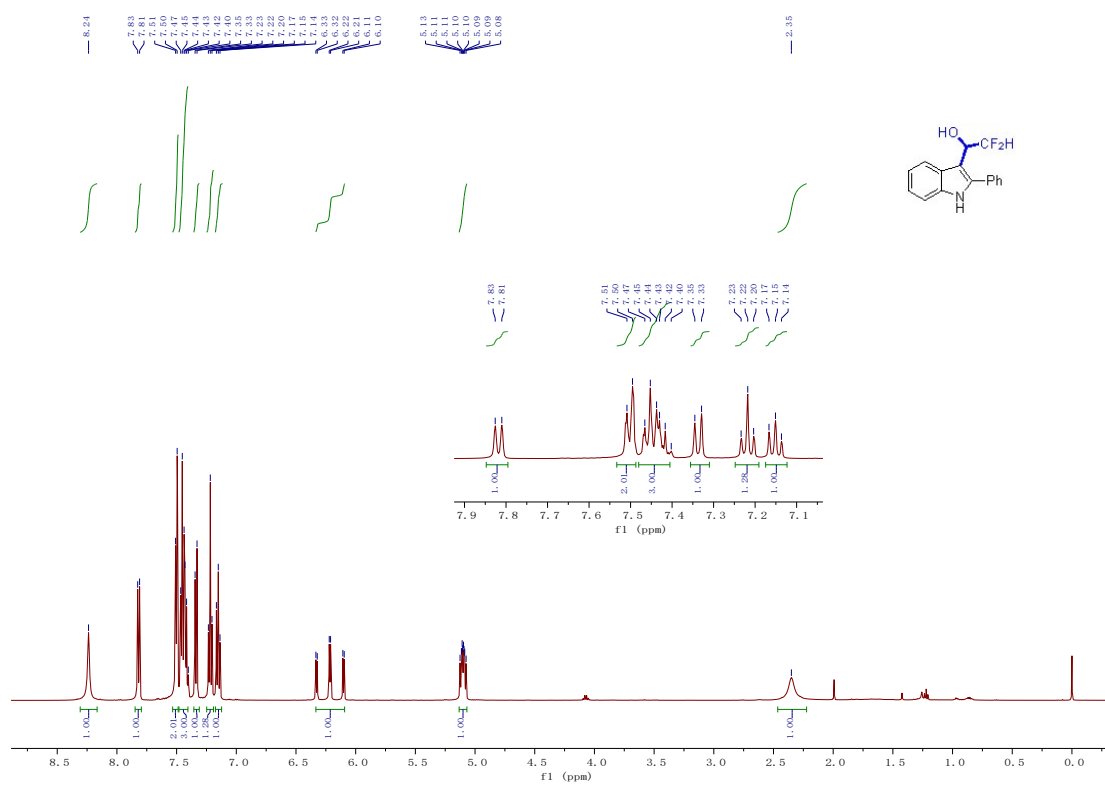
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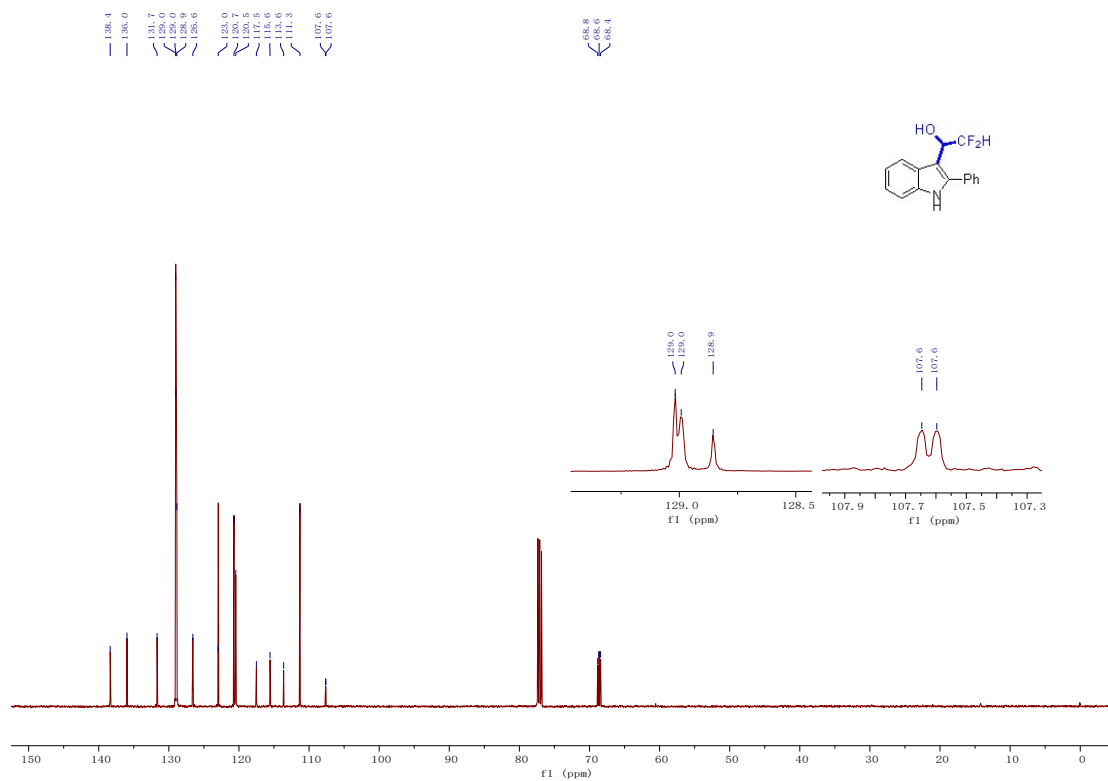
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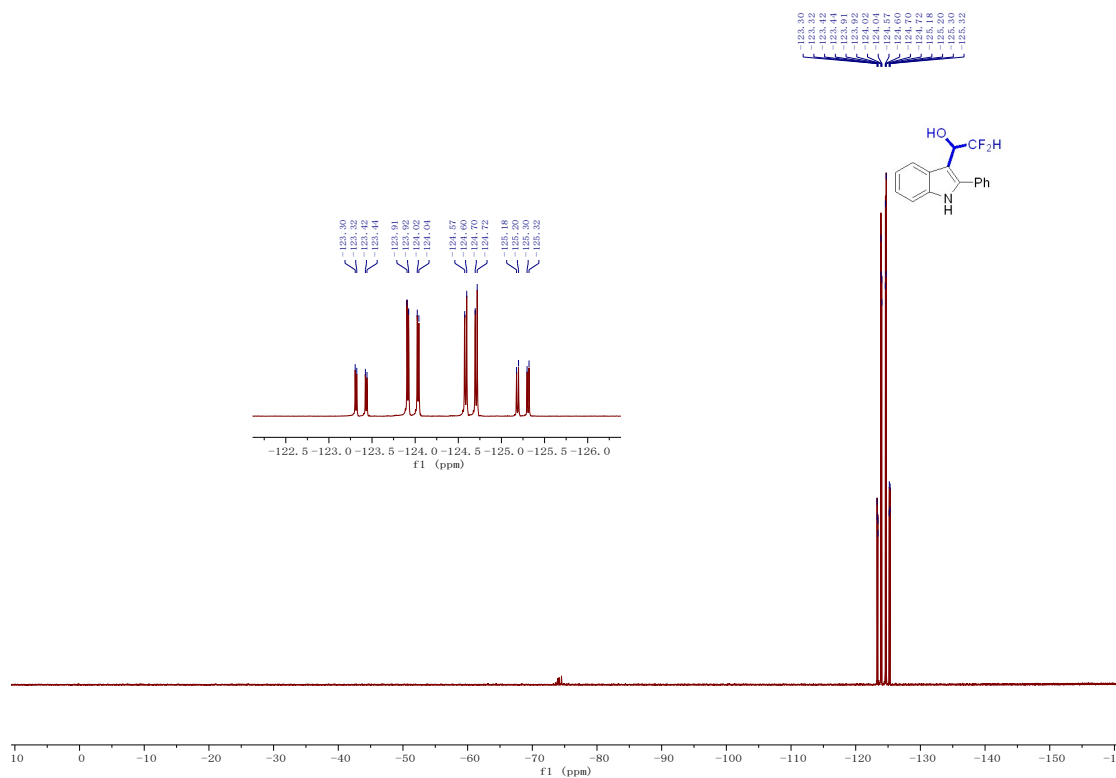
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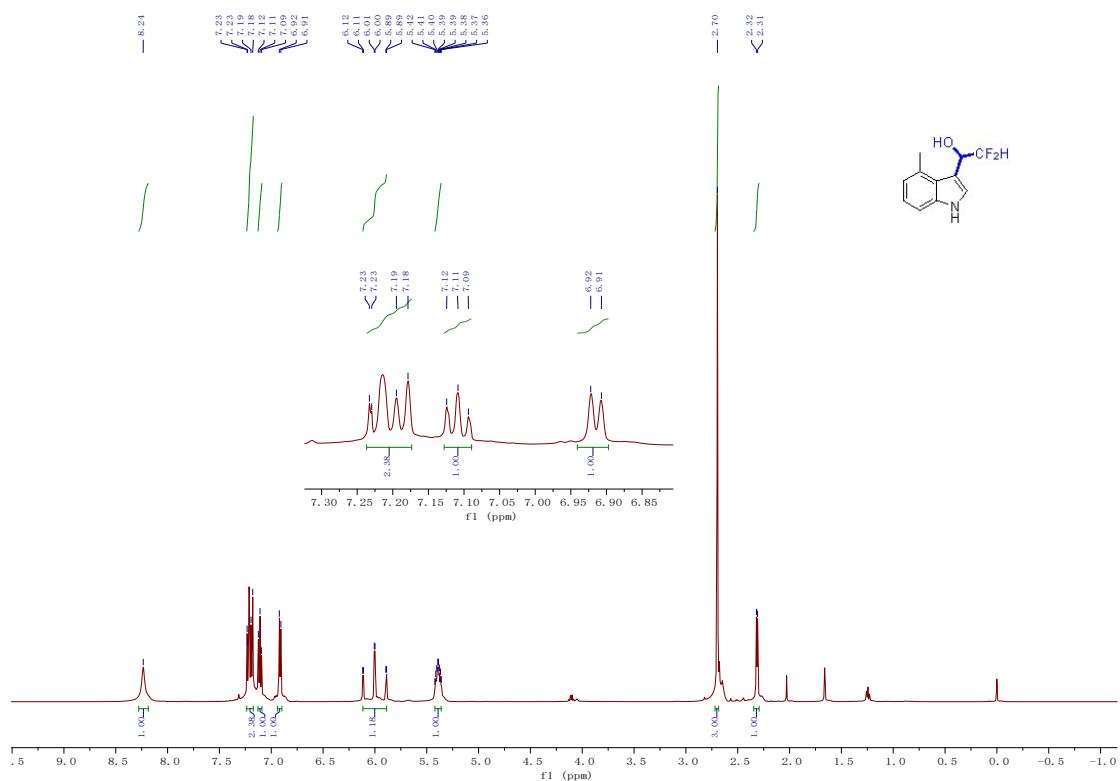
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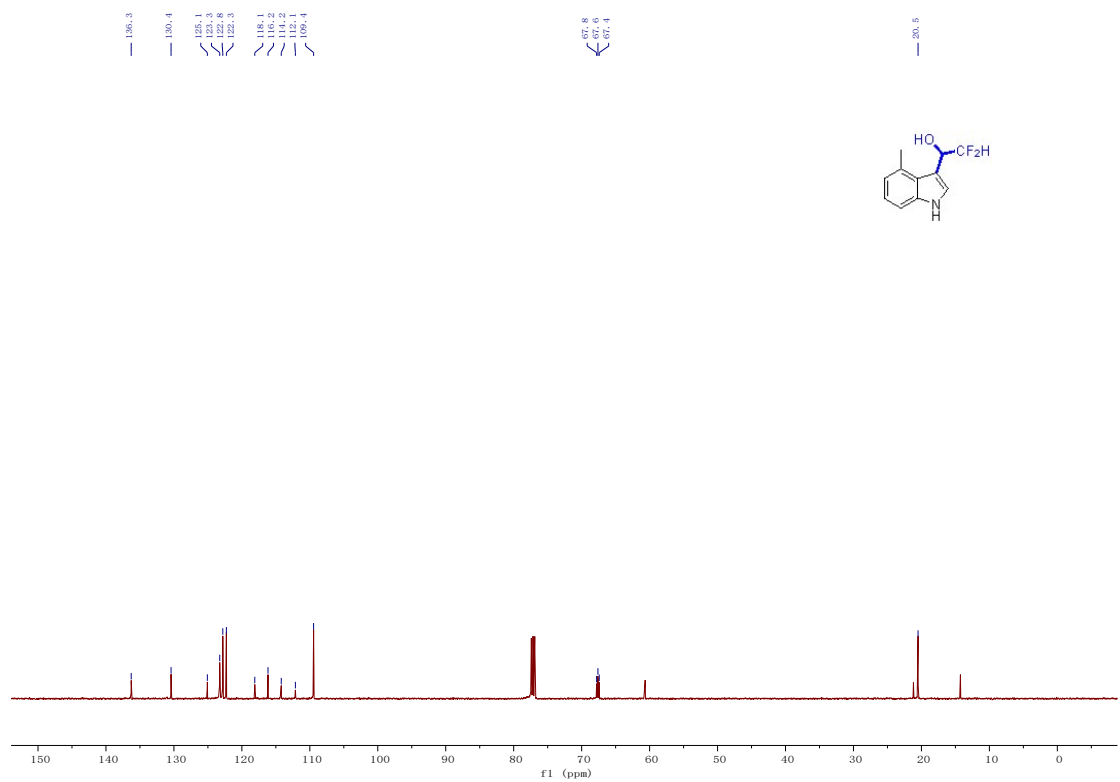
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **3f**



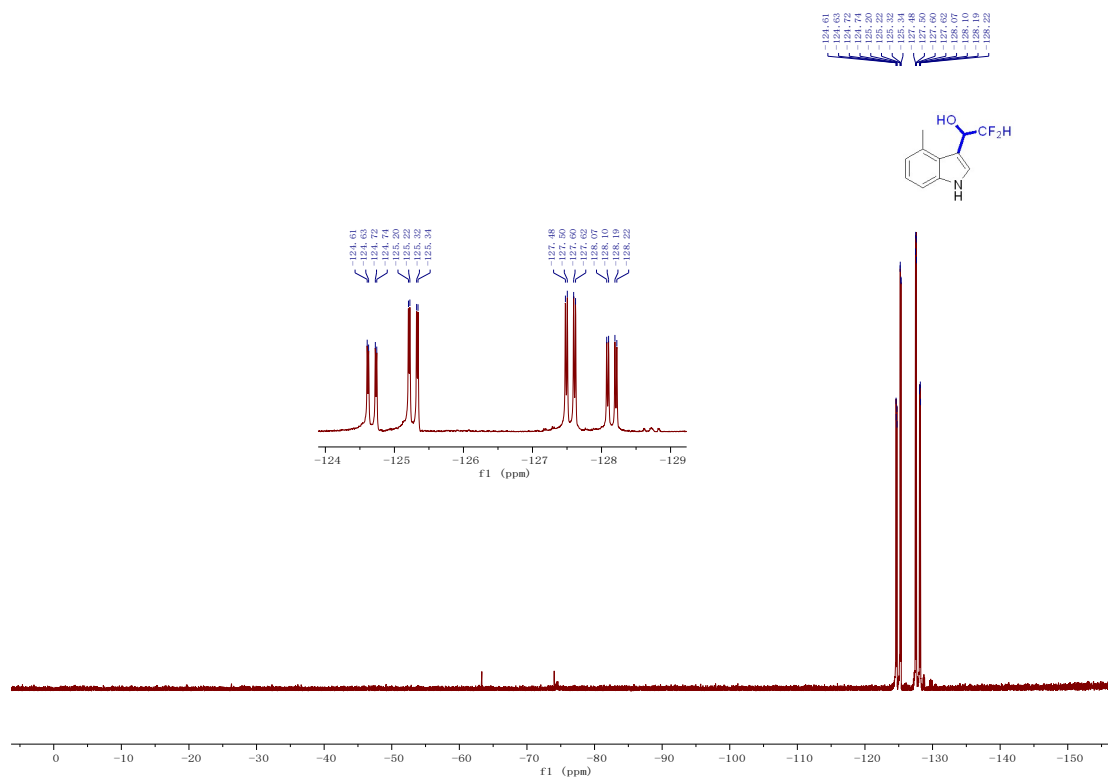
¹H NMR (500 MHz, Chloroform-*d*) spectra of **3g**



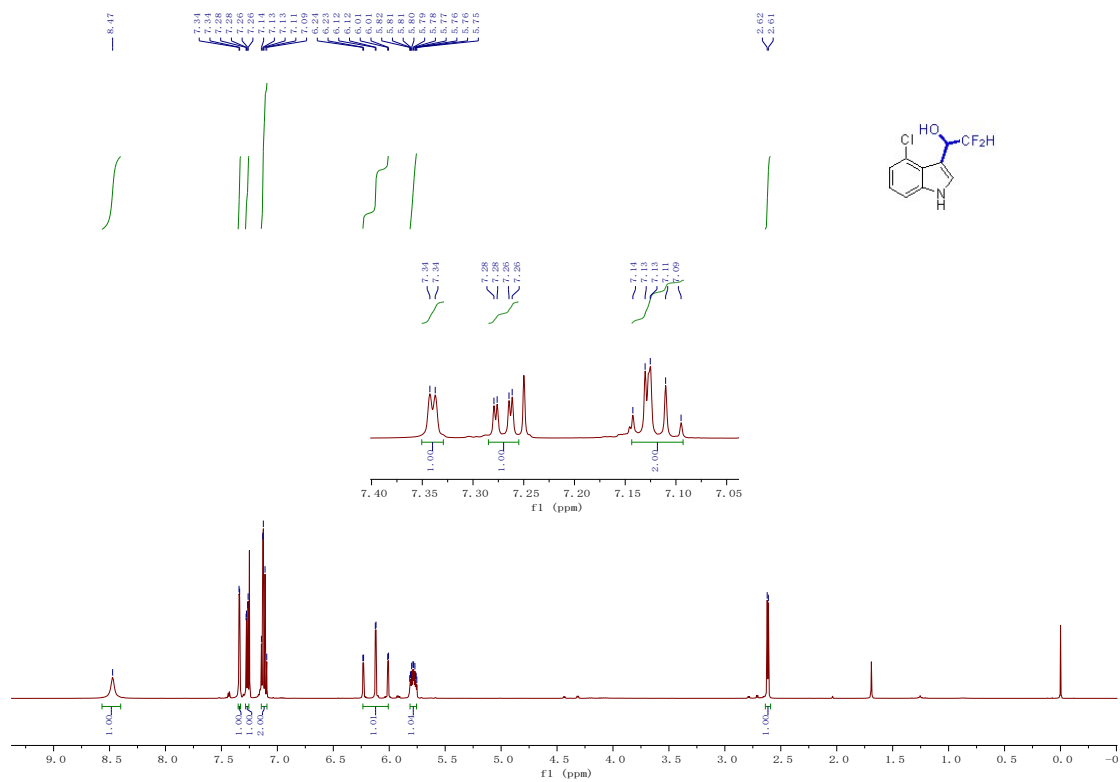
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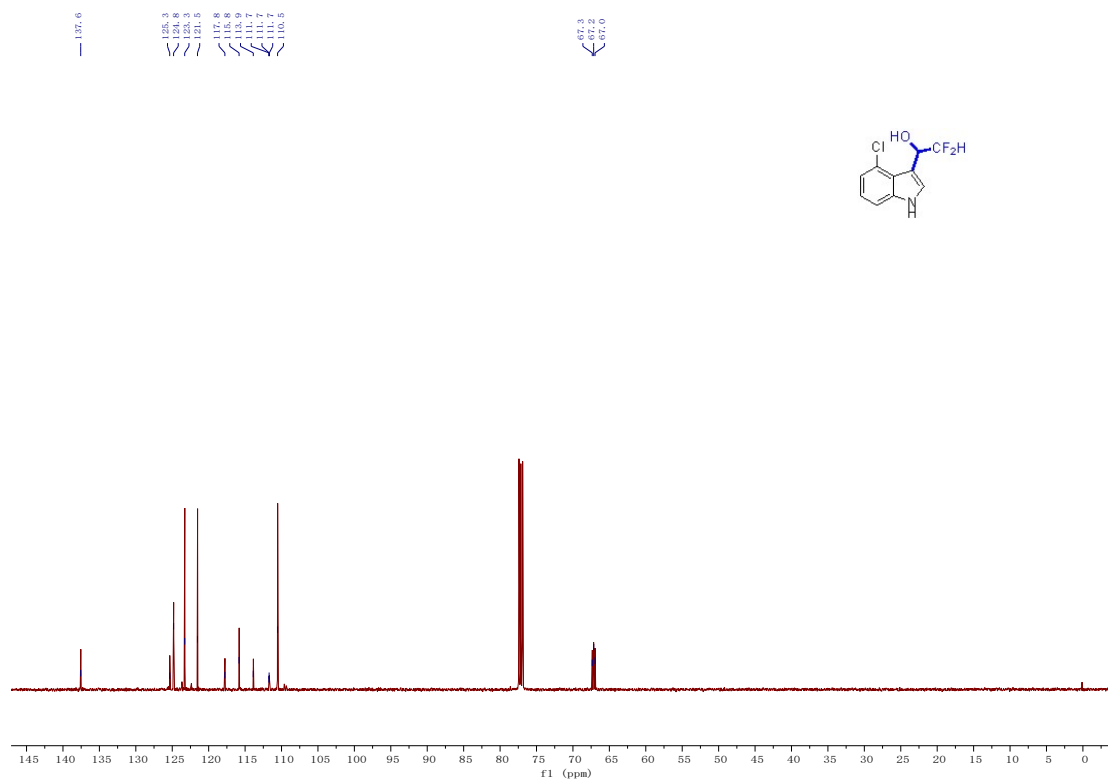
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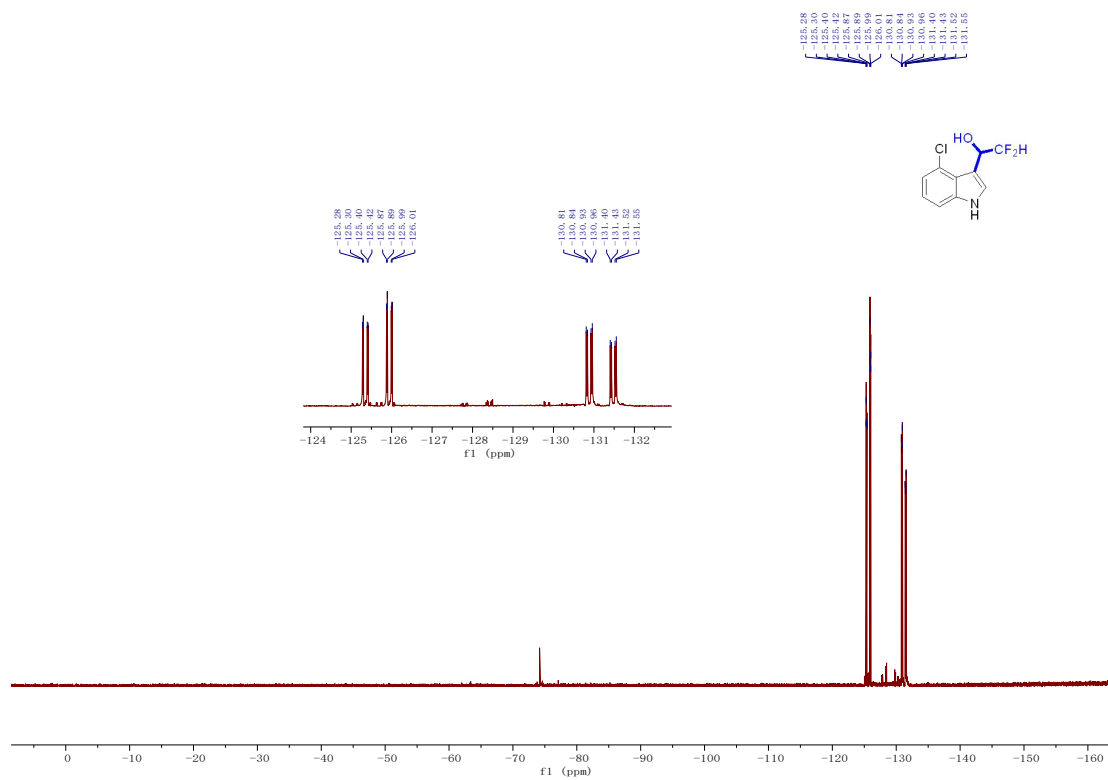
¹H NMR (500 MHz, Chloroform-*d*) spectra of **3h**



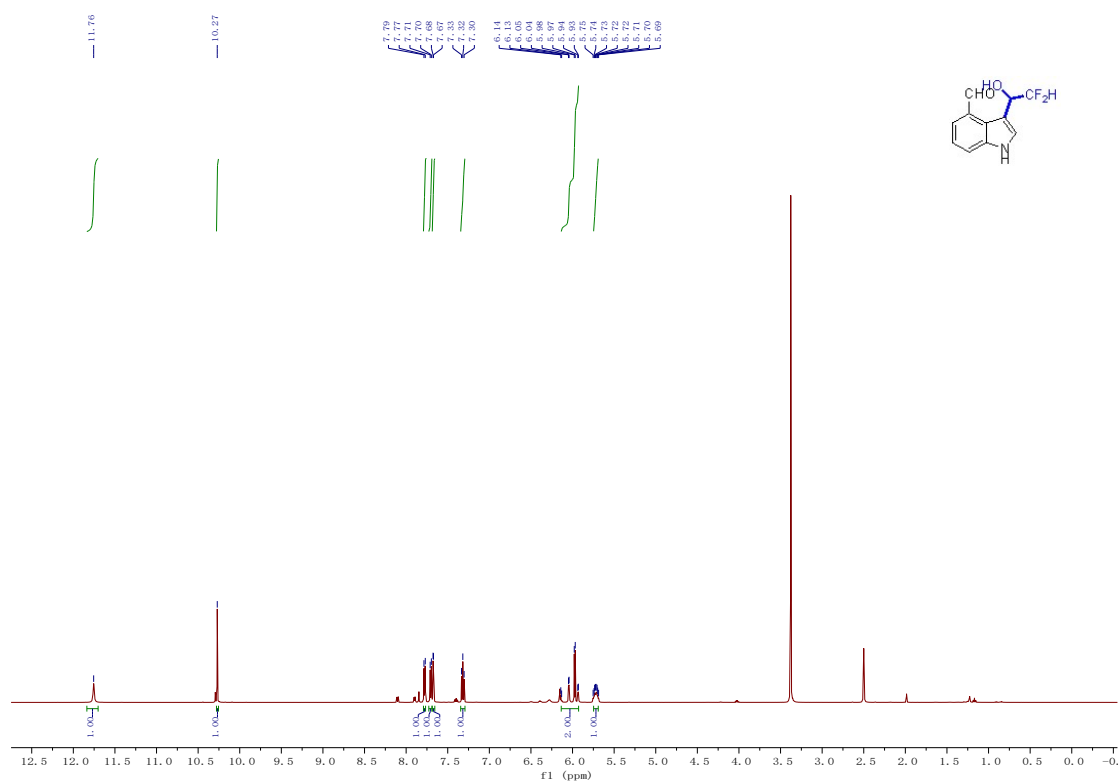
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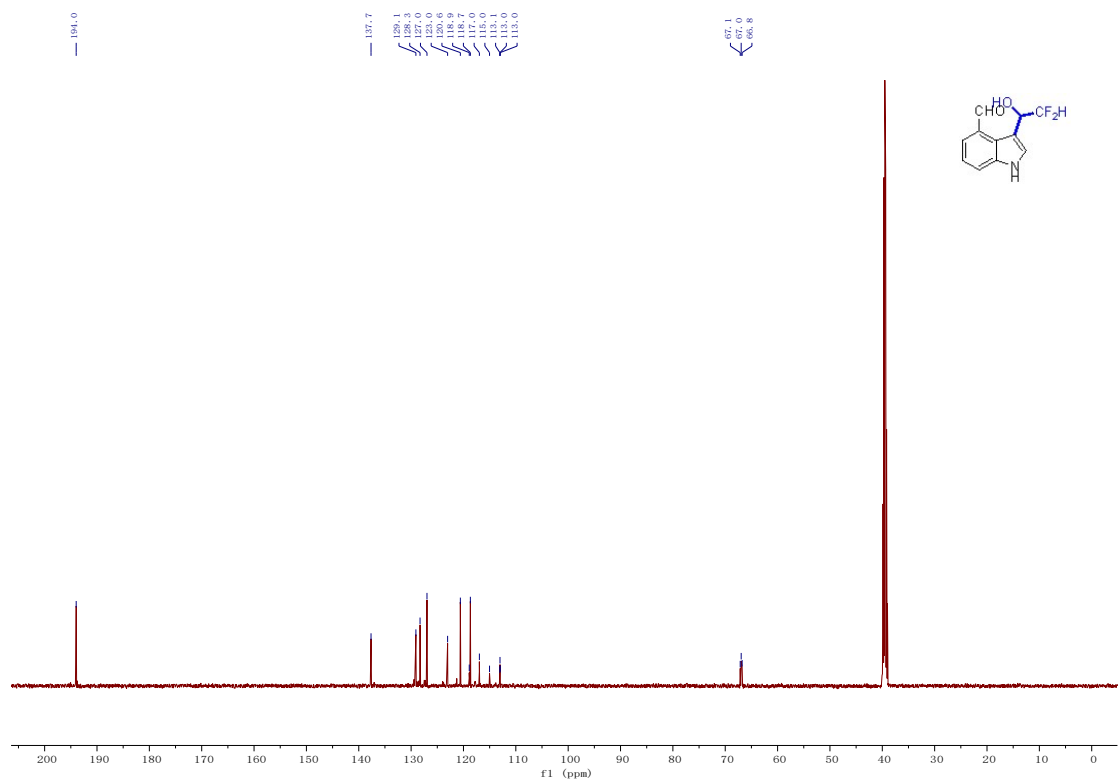
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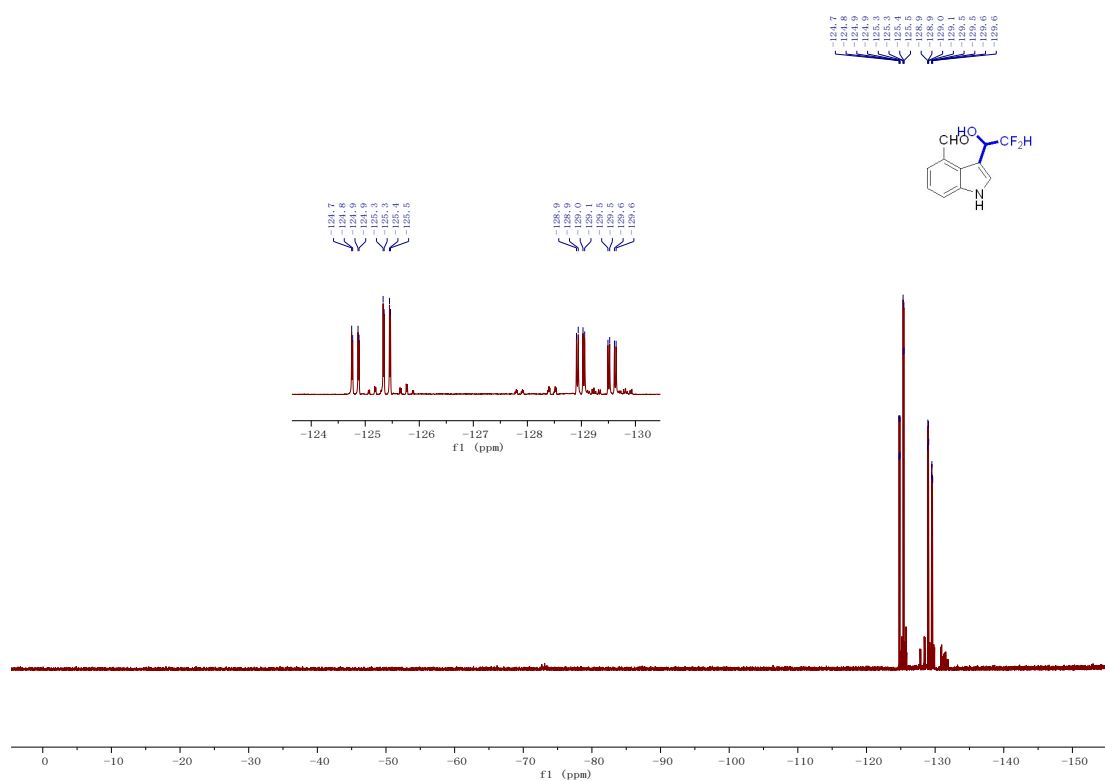
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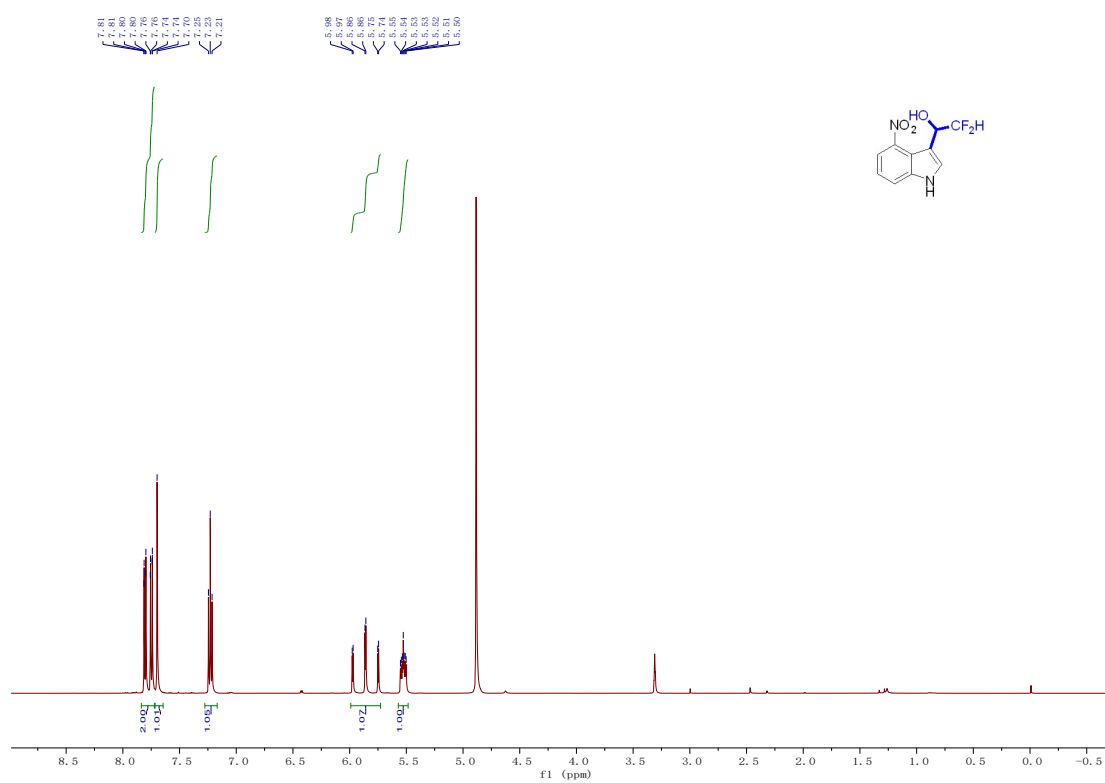
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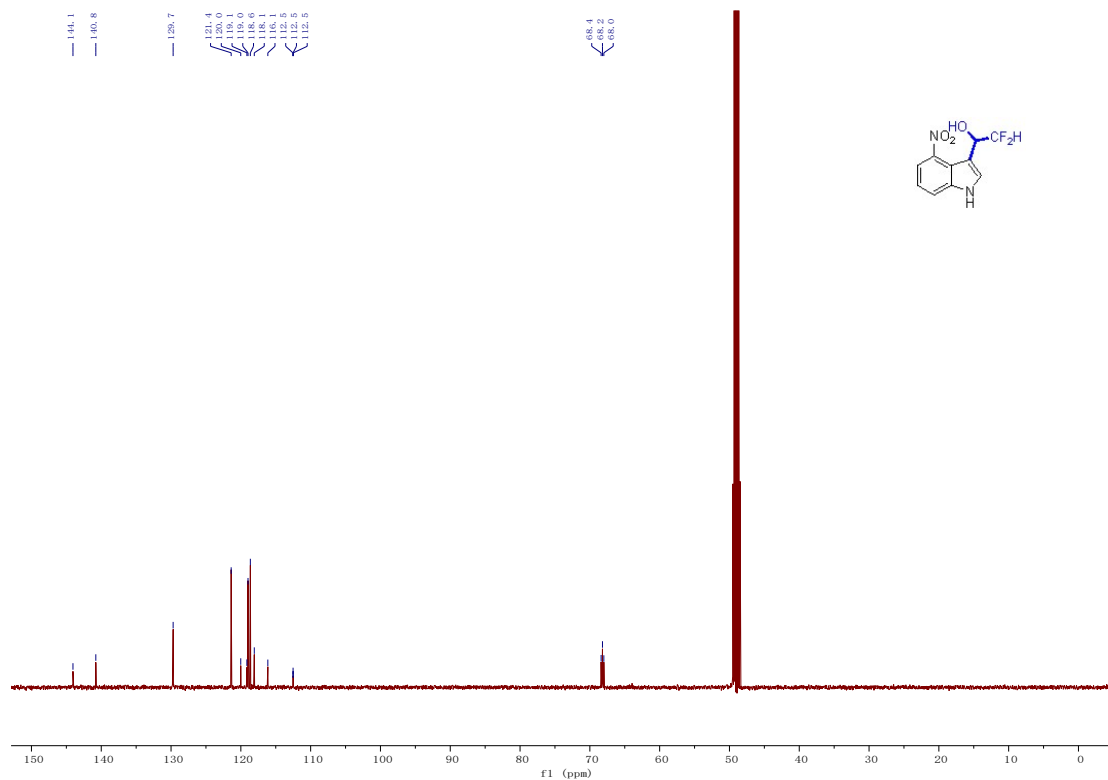
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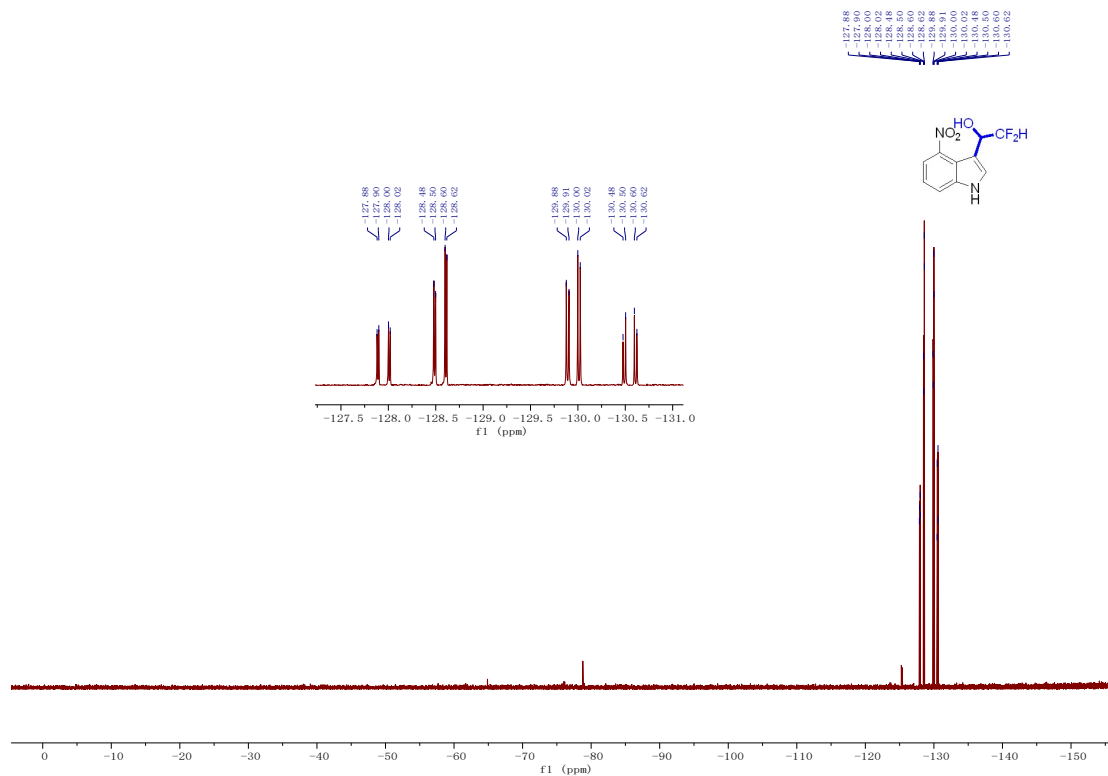
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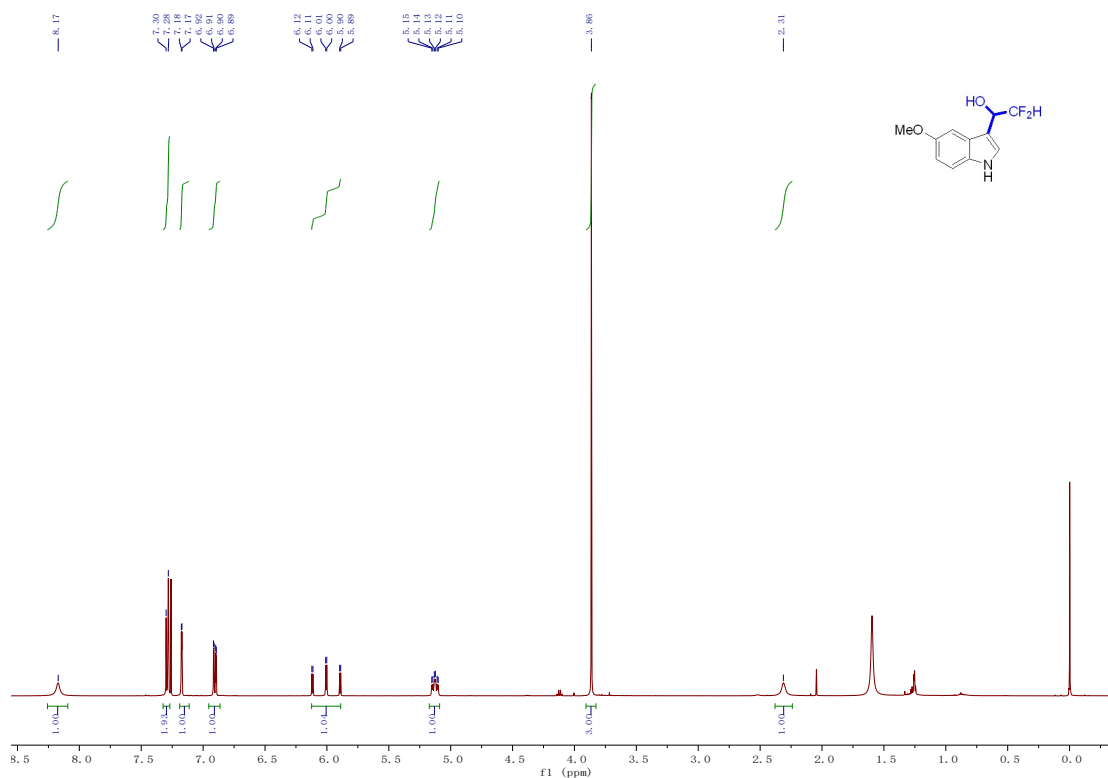
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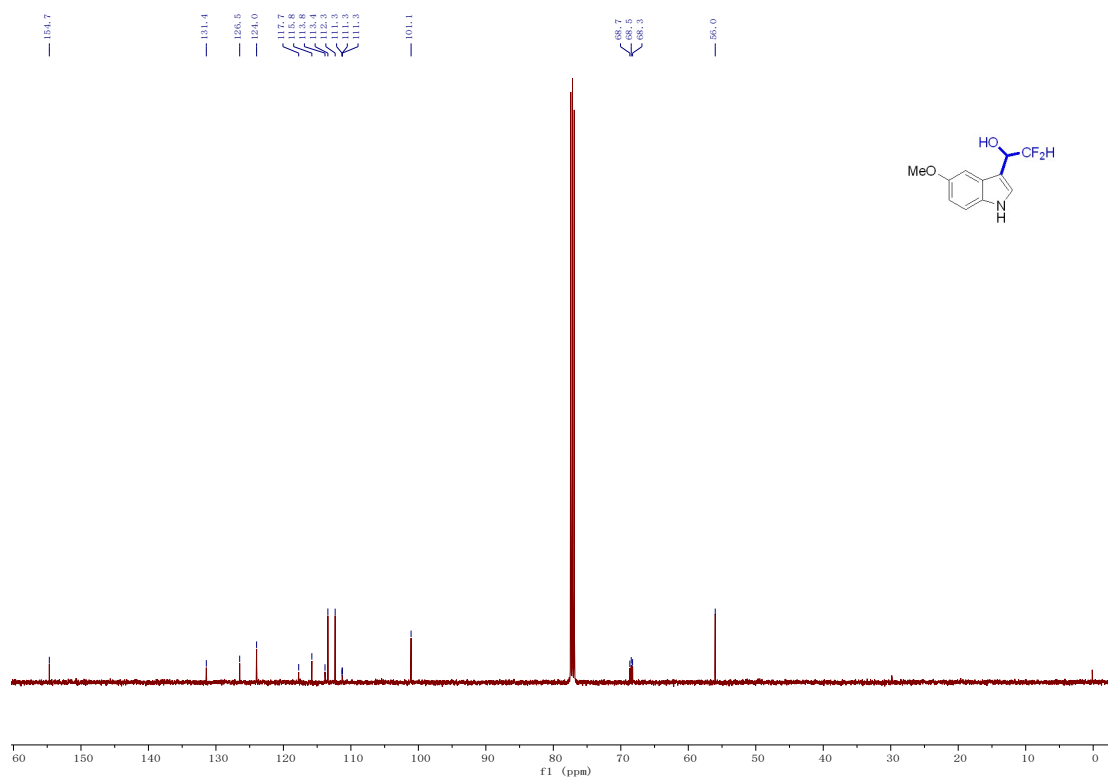
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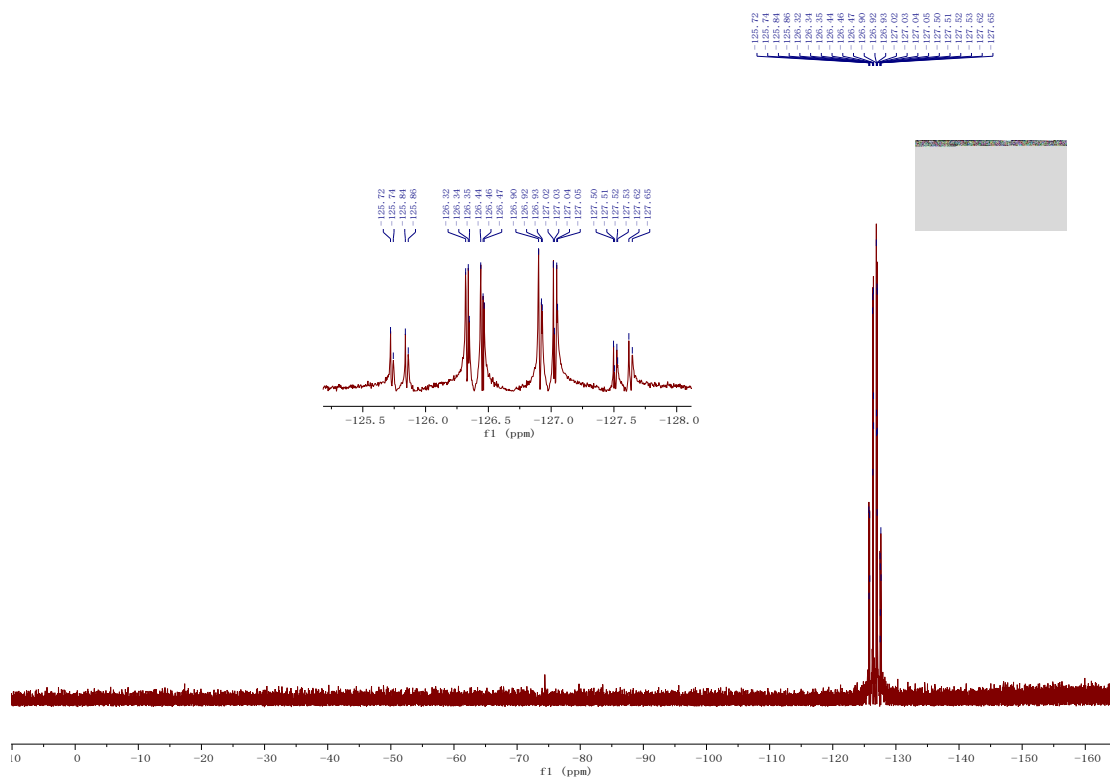
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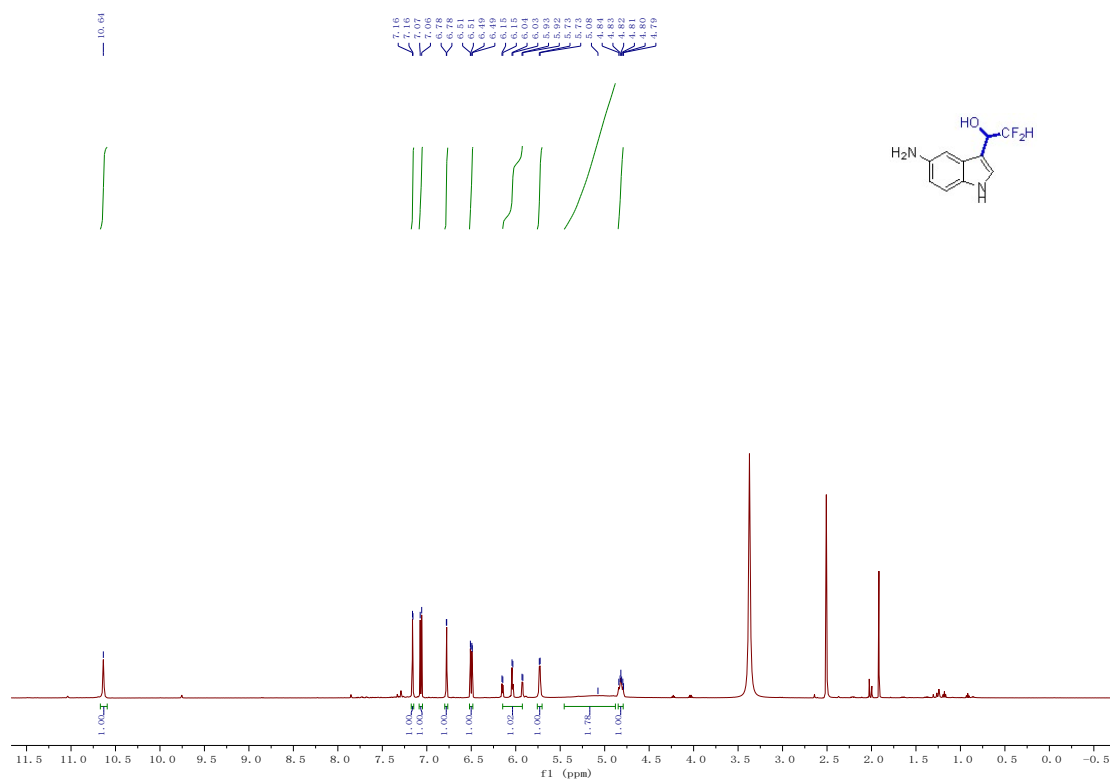
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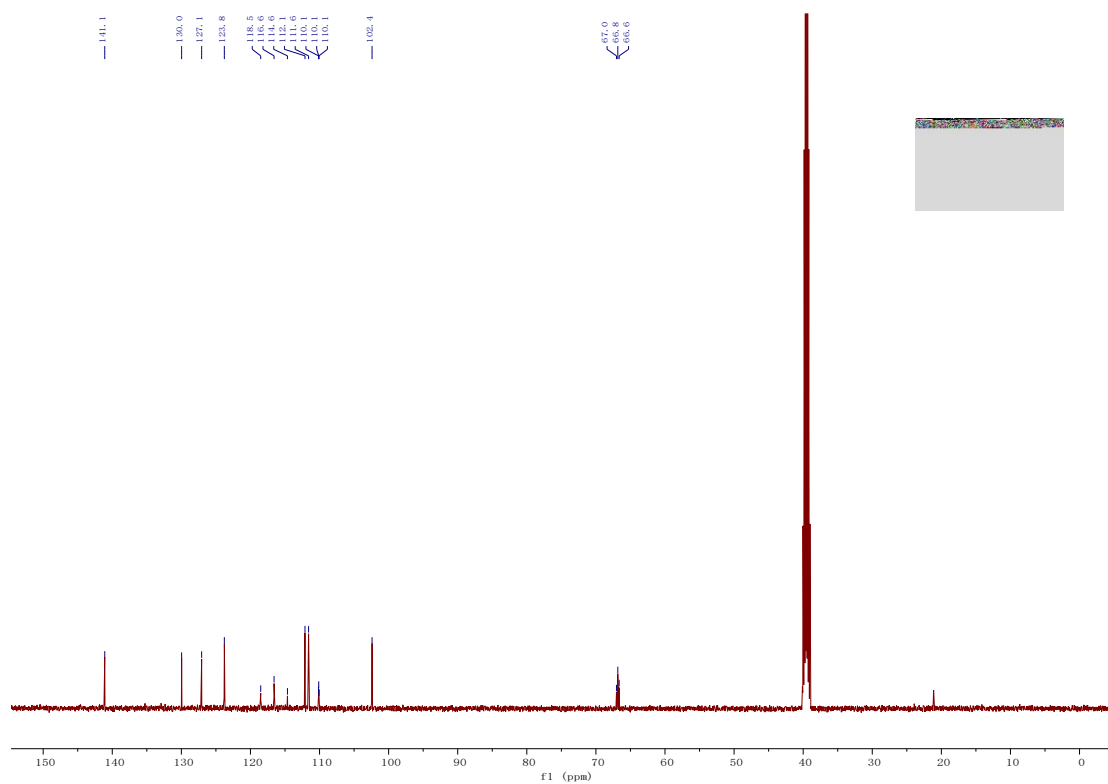
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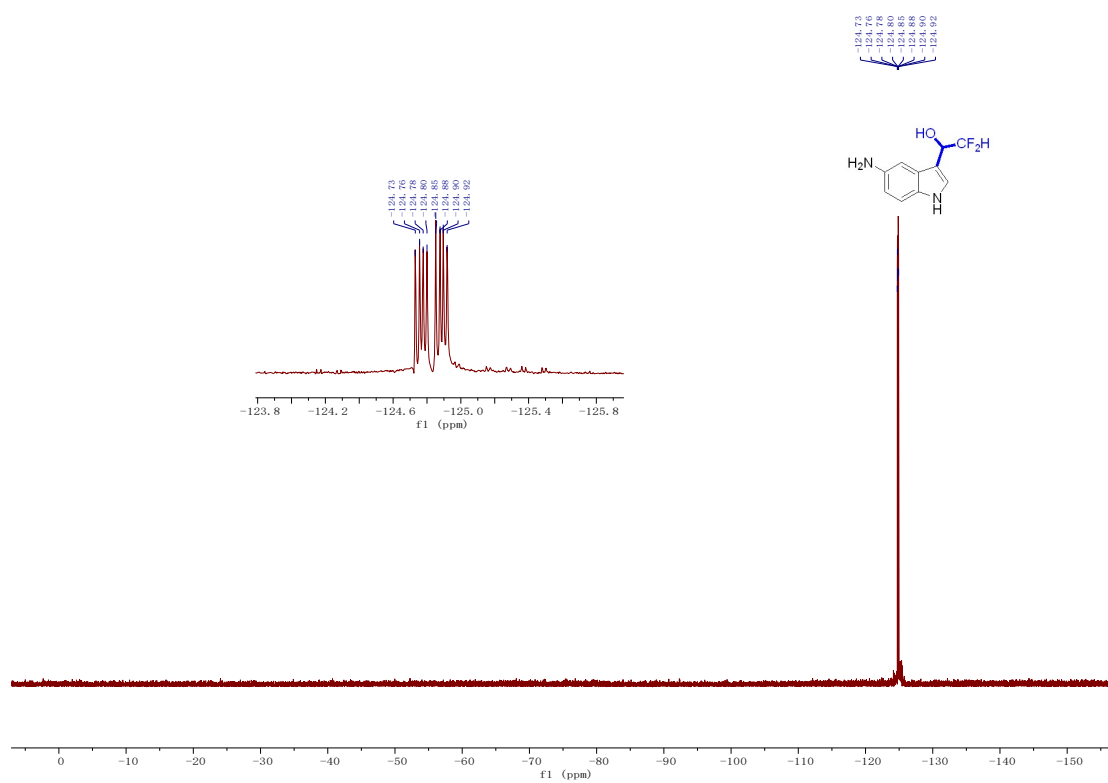
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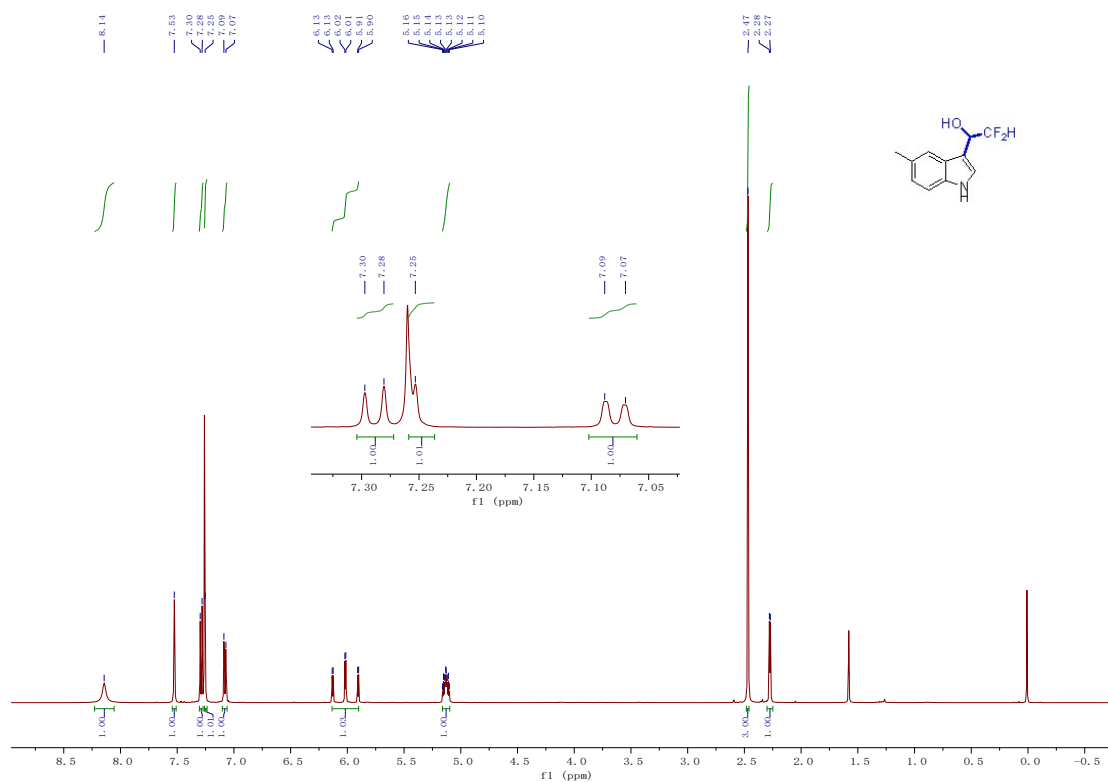
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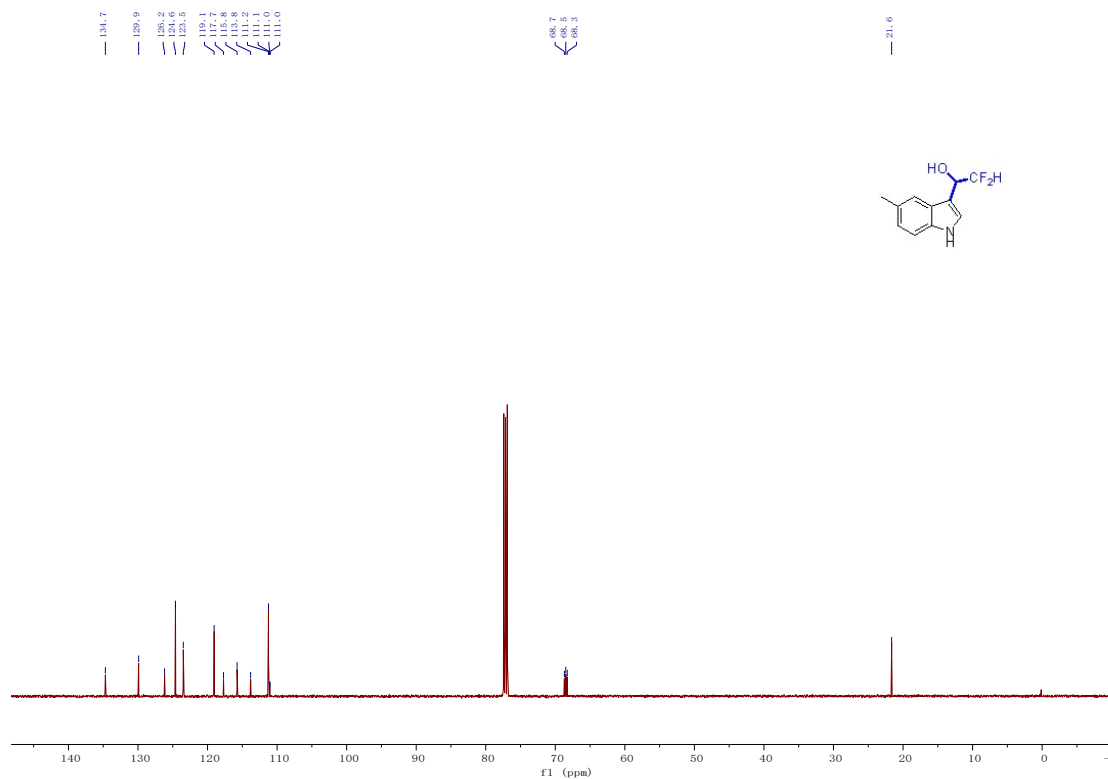
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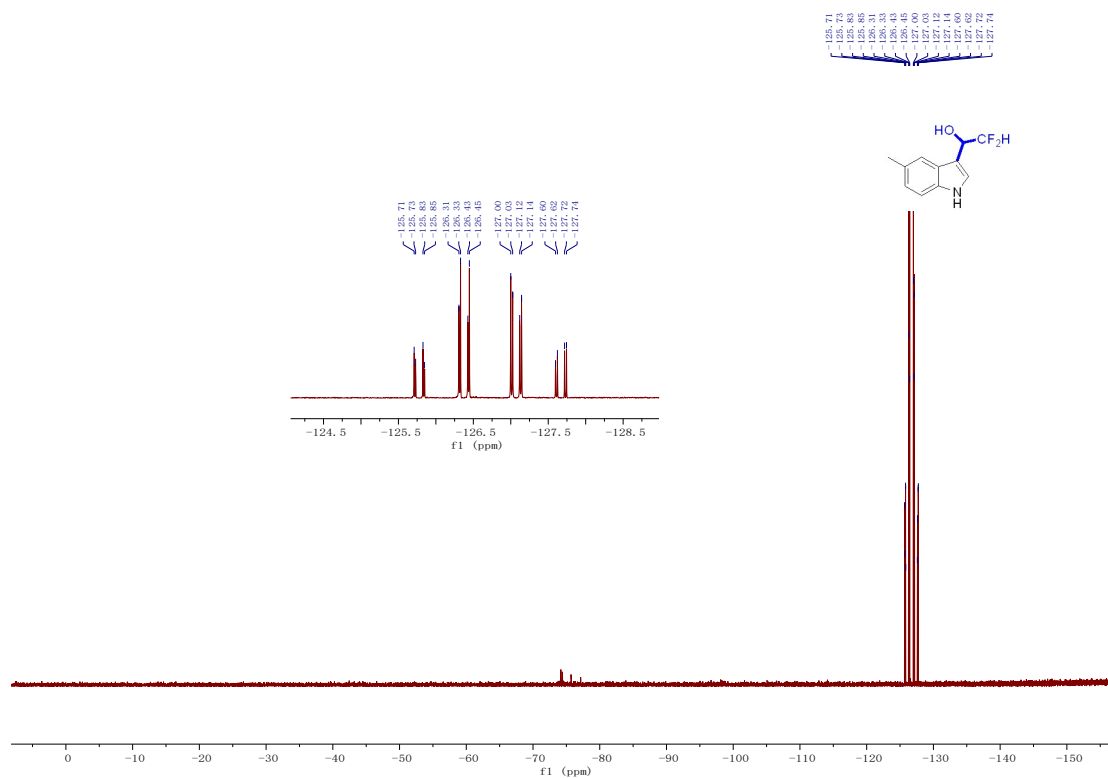
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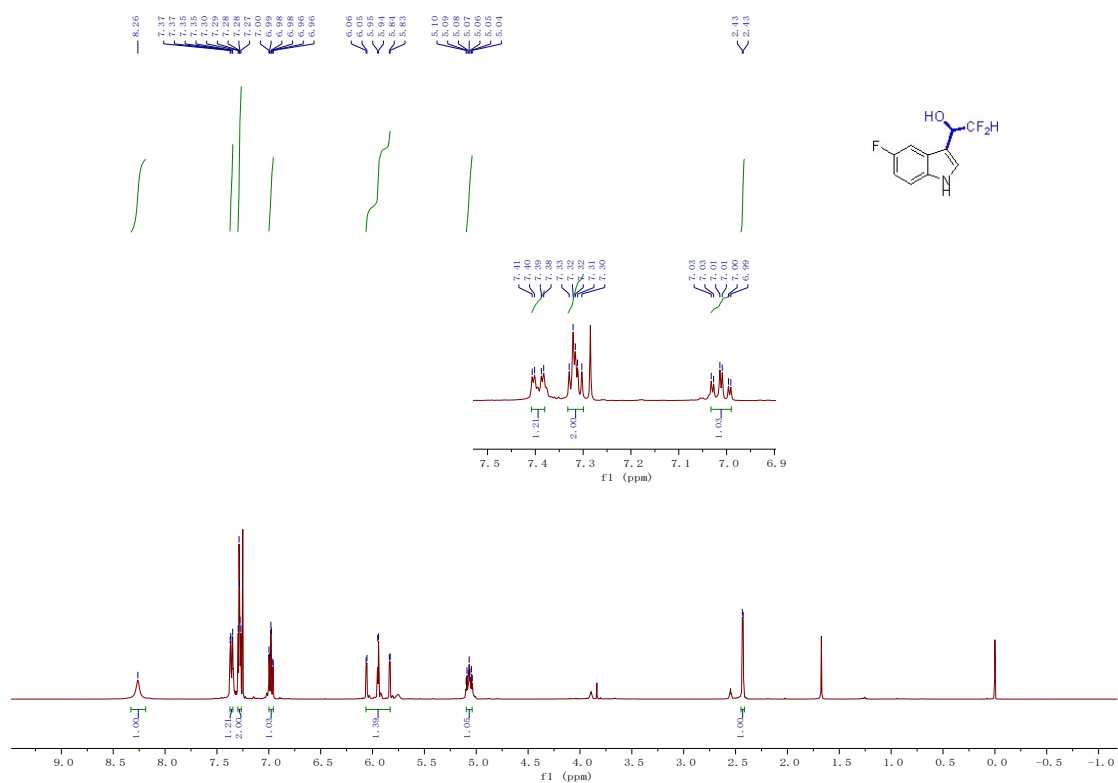
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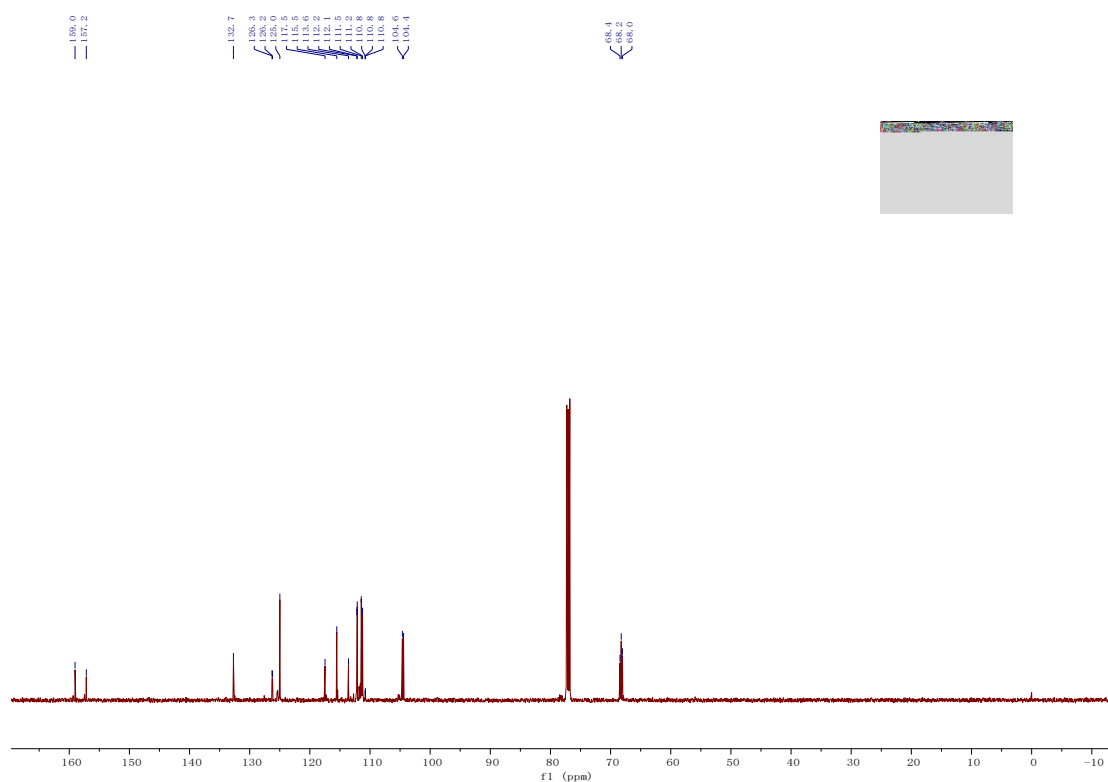
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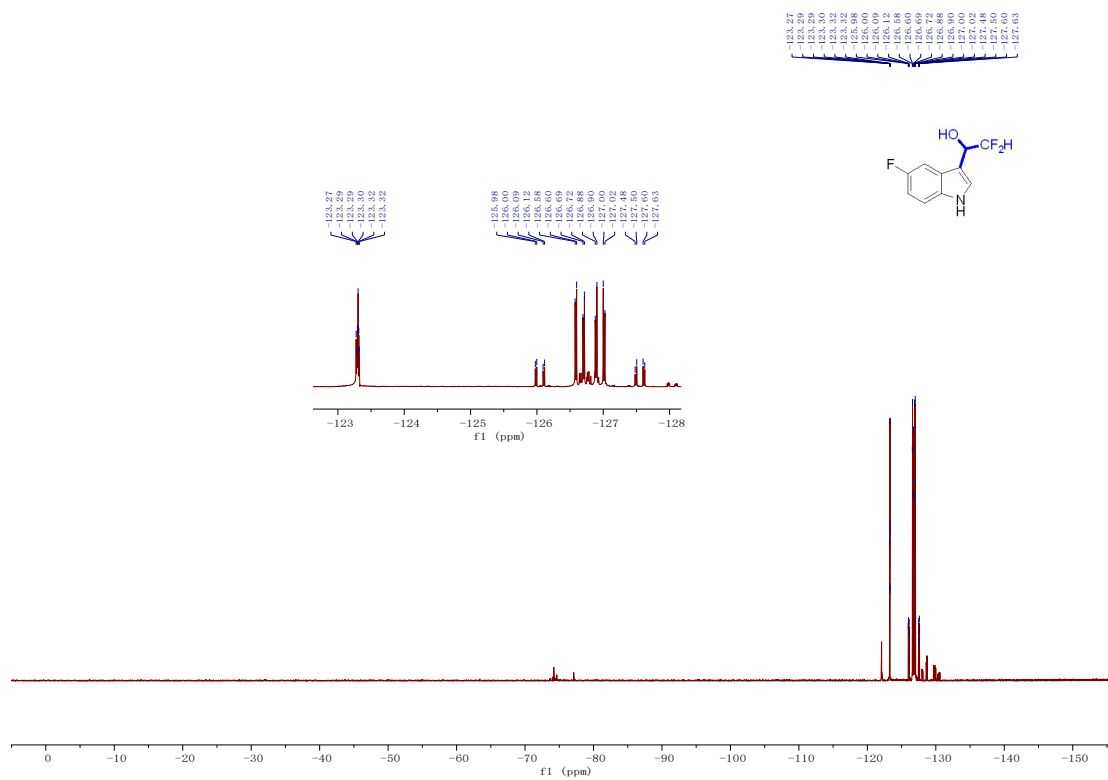
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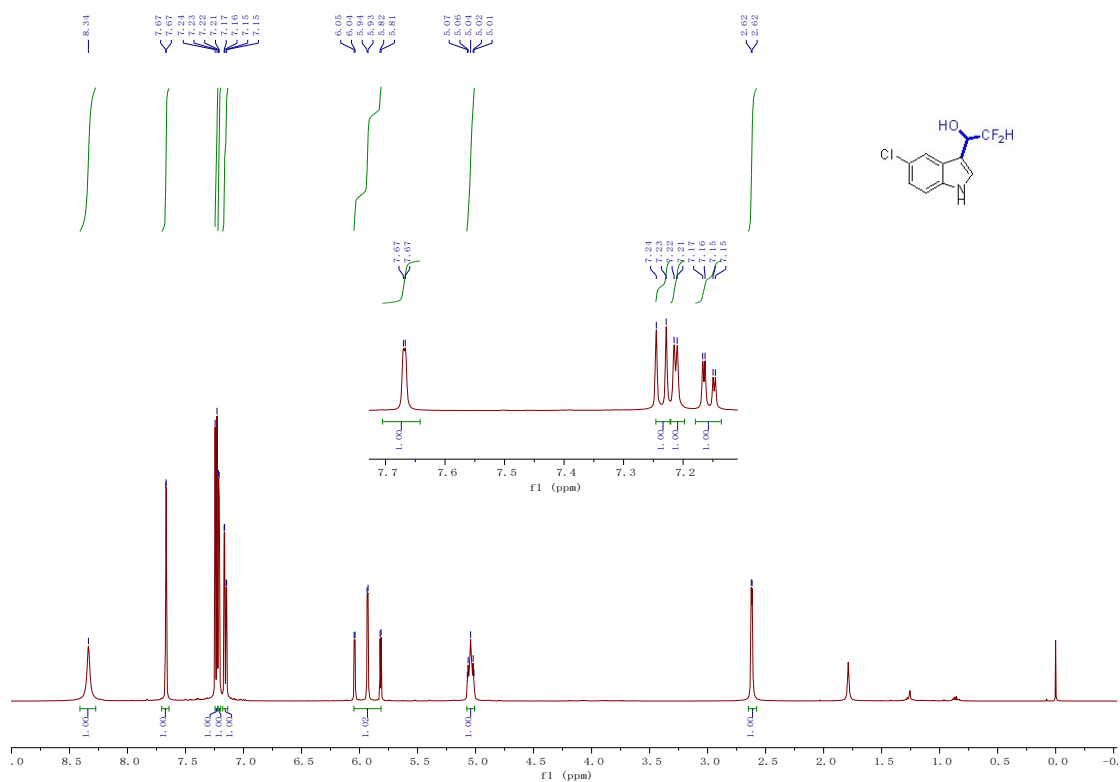
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **3n**



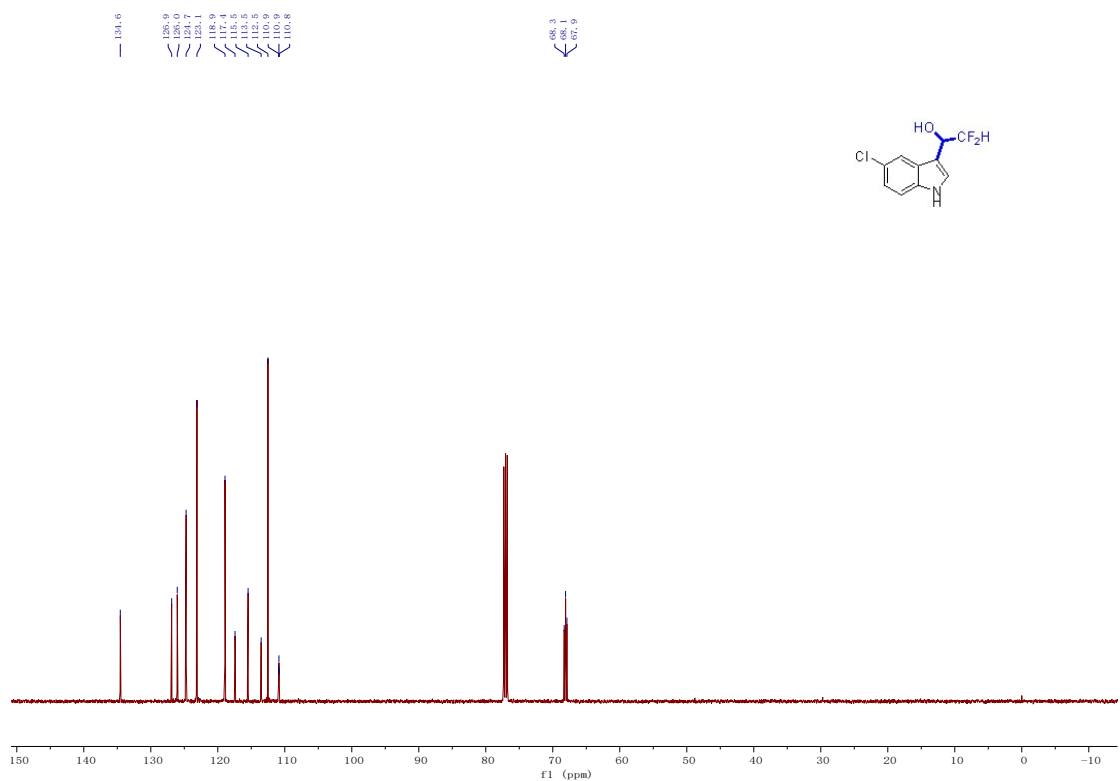
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **3n**



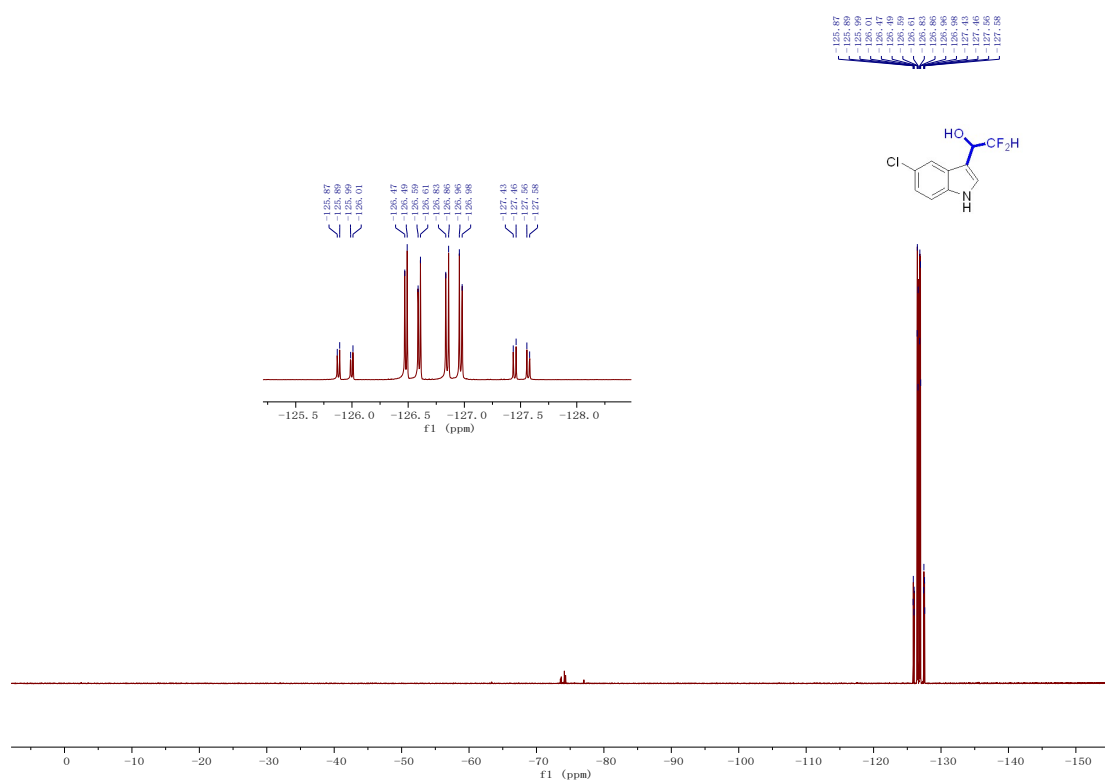
^1H NMR (500 MHz, Chloroform-*d*) spectra of **3o**



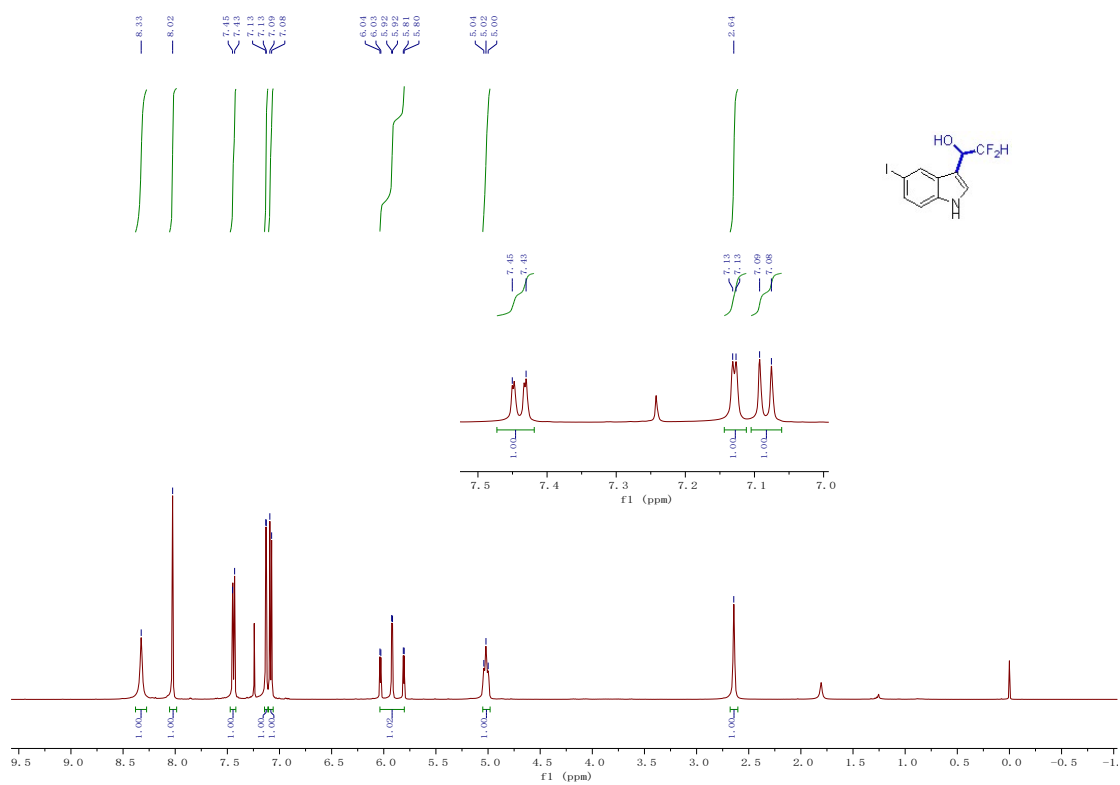
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **3o**



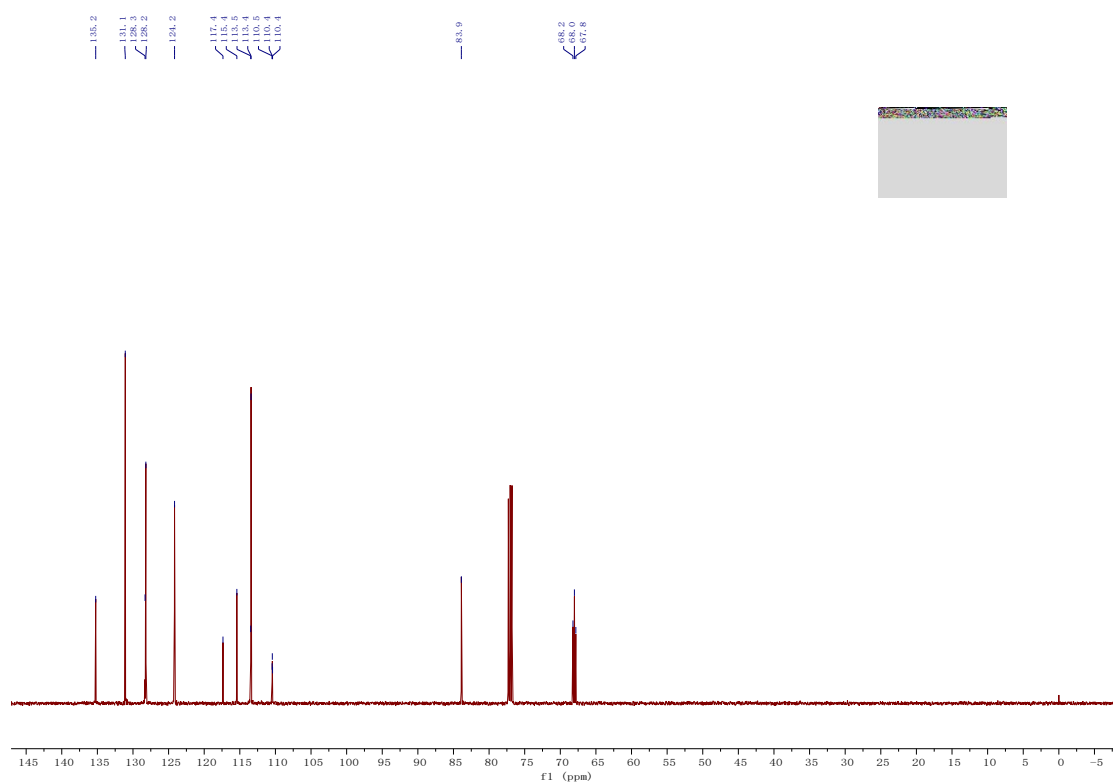
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **3o**



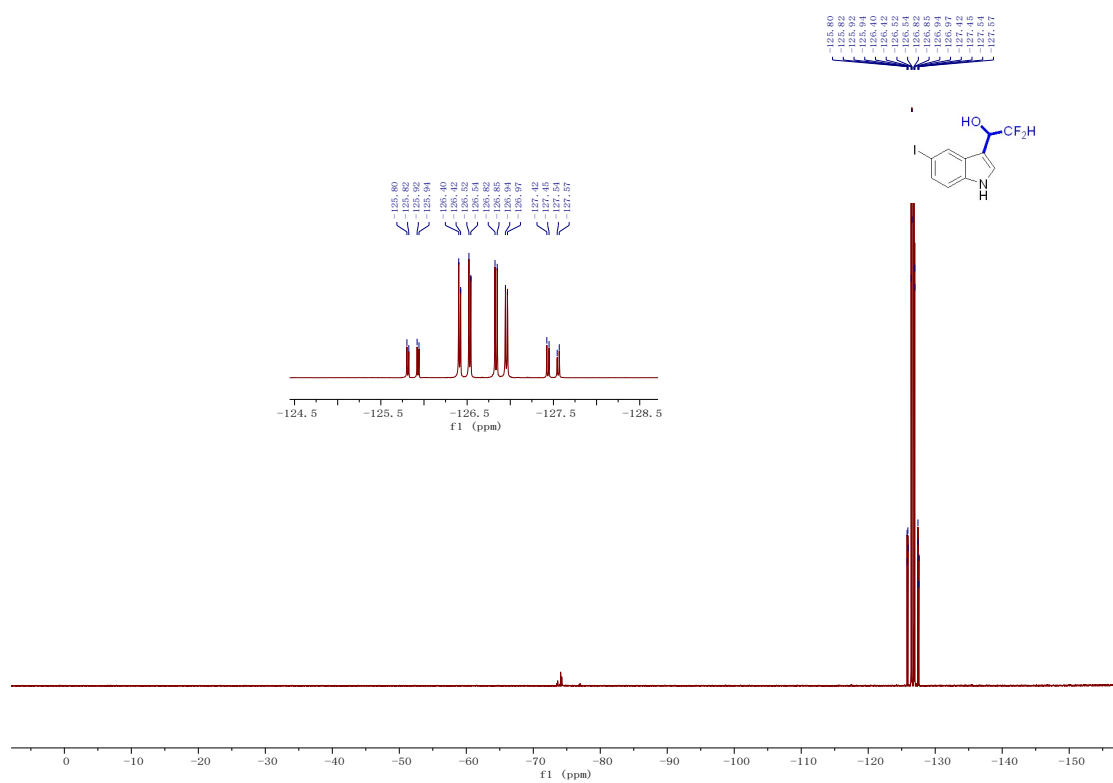
^1H NMR (500 MHz, Chloroform-*d*) spectra of **3p**



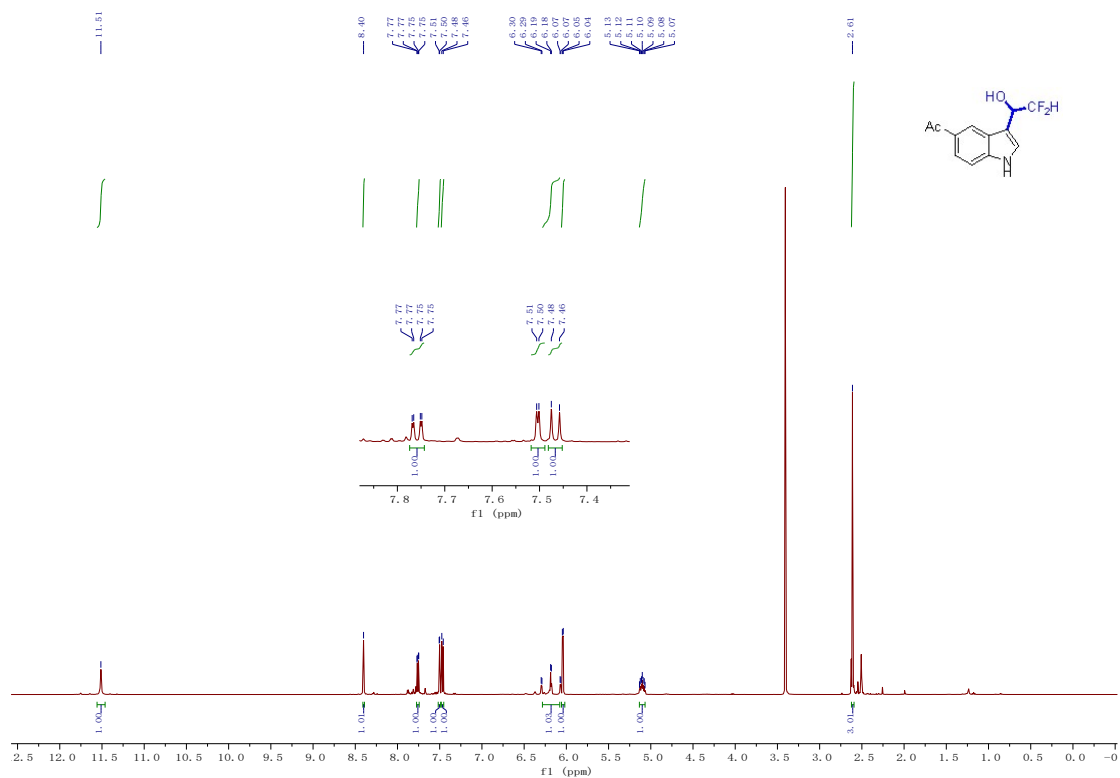
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **3p**



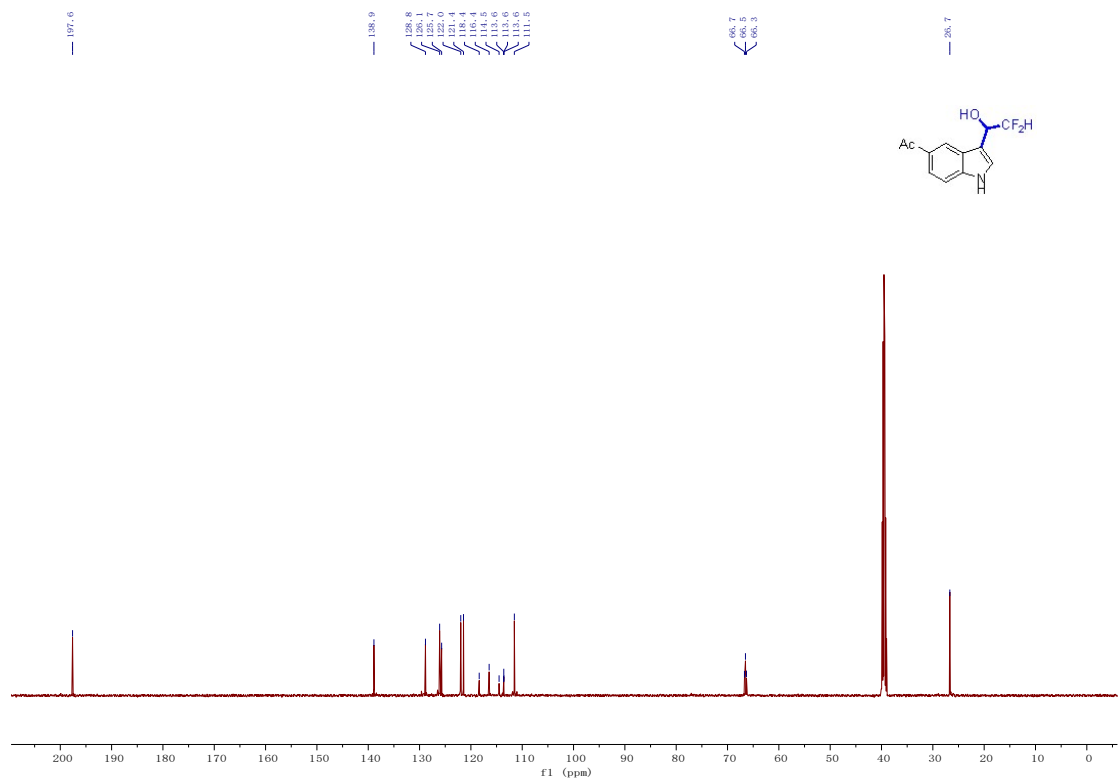
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **3p**



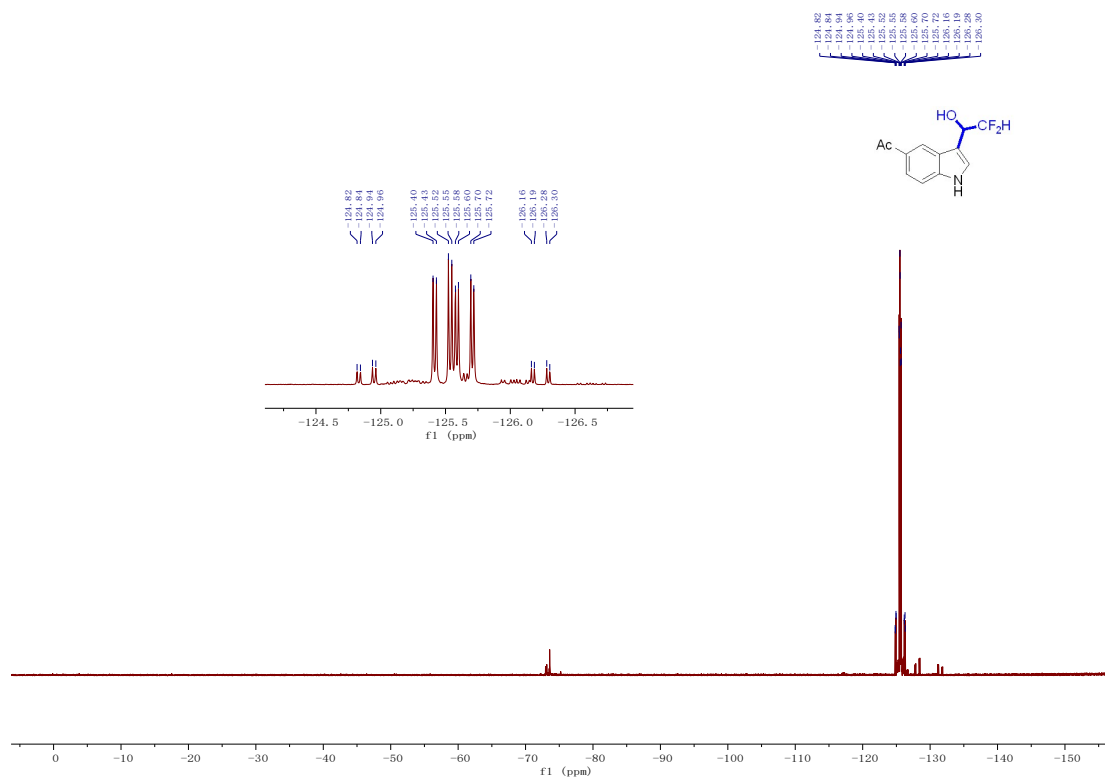
¹H NMR (500 MHz, DMSO-*d*₆) spectra of **3q**



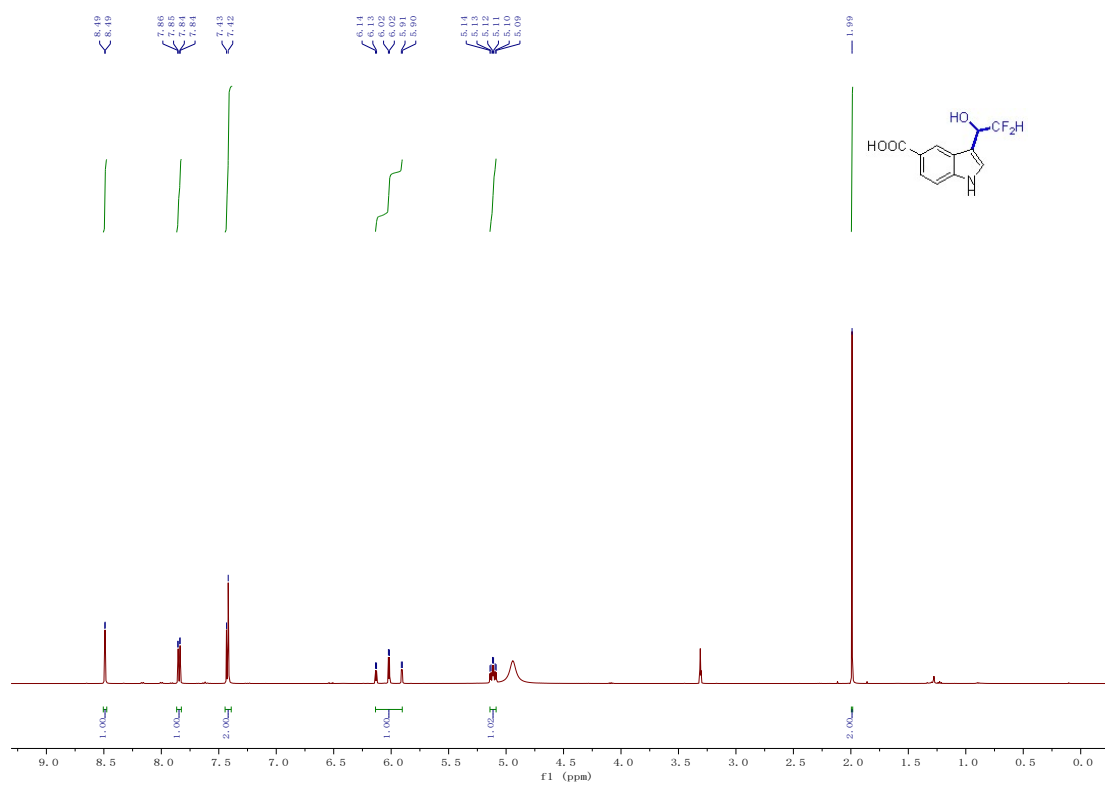
¹³C NMR (125 MHz, DMSO-*d*₆) spectra of **3q**



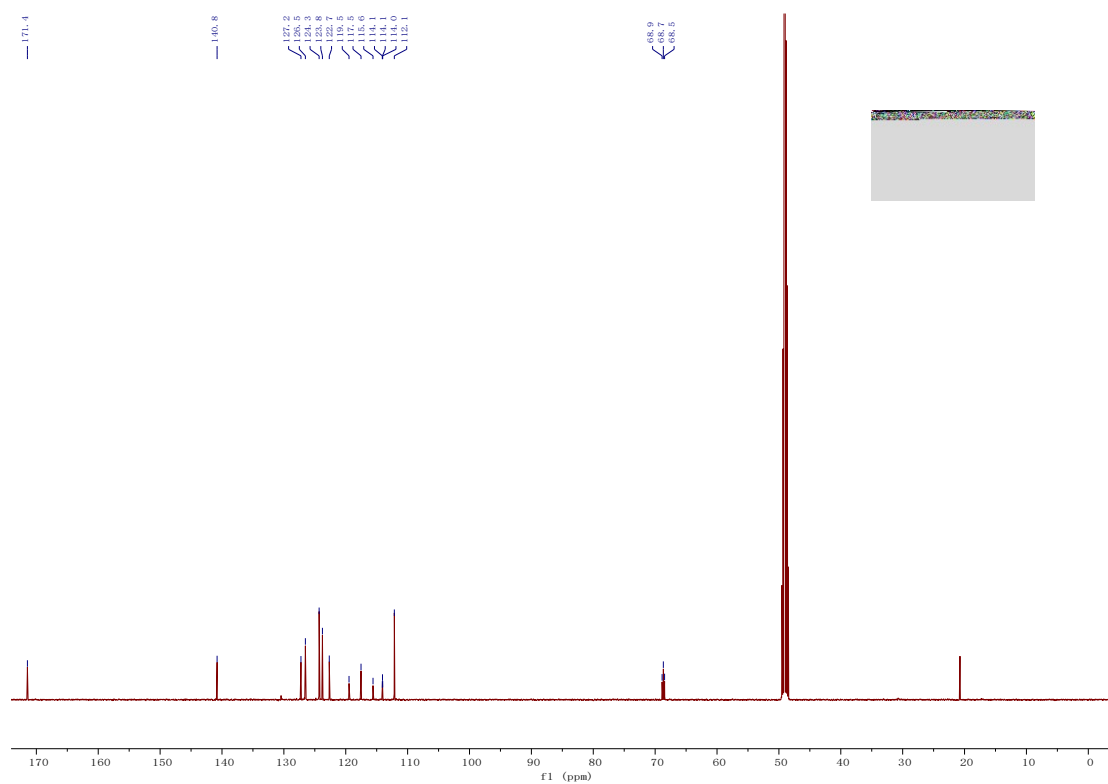
¹⁹F NMR (470 MHz, DMSO-*d*₆) spectra of **3q**



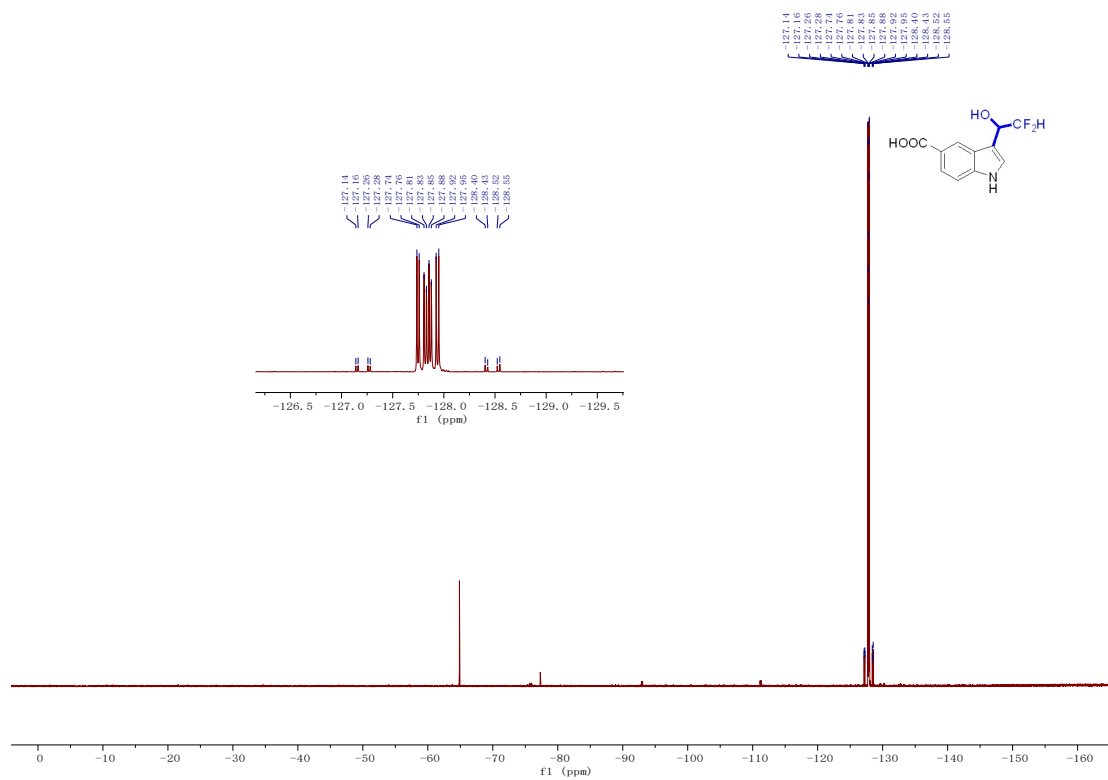
¹H NMR (500 MHz, Methanol-*d*₄) spectra of **3r**



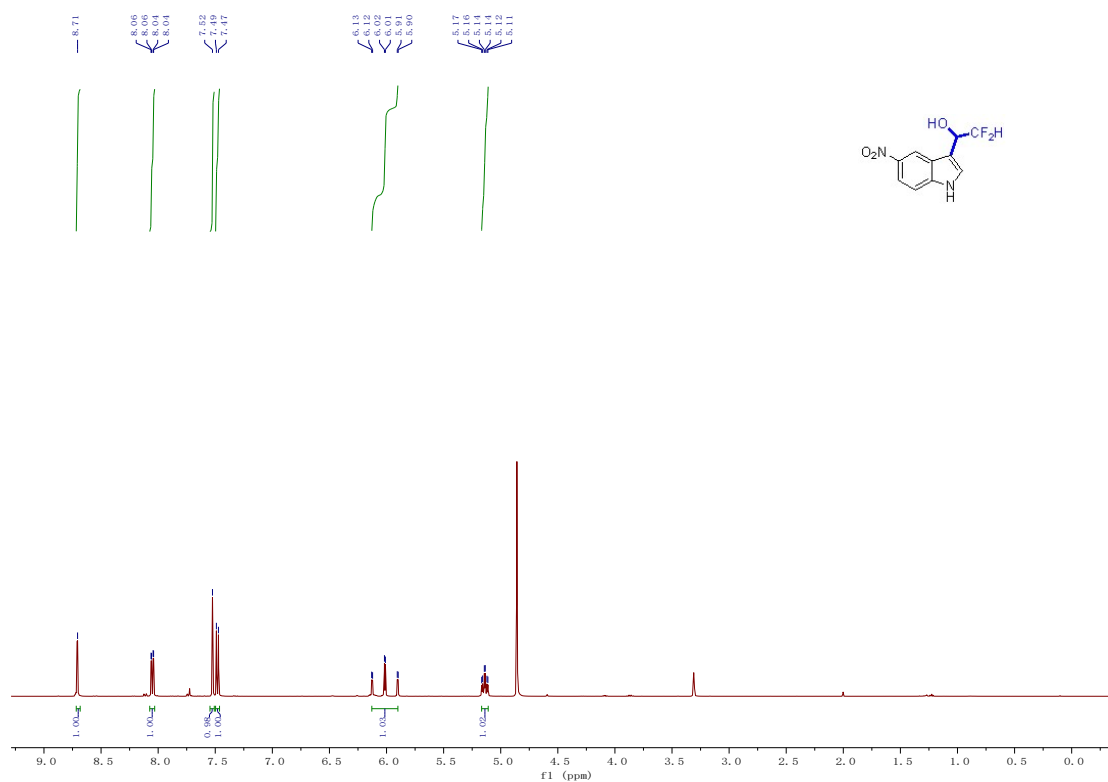
¹³C NMR (125 MHz, Methanol-*d*₄) spectra of **3r**



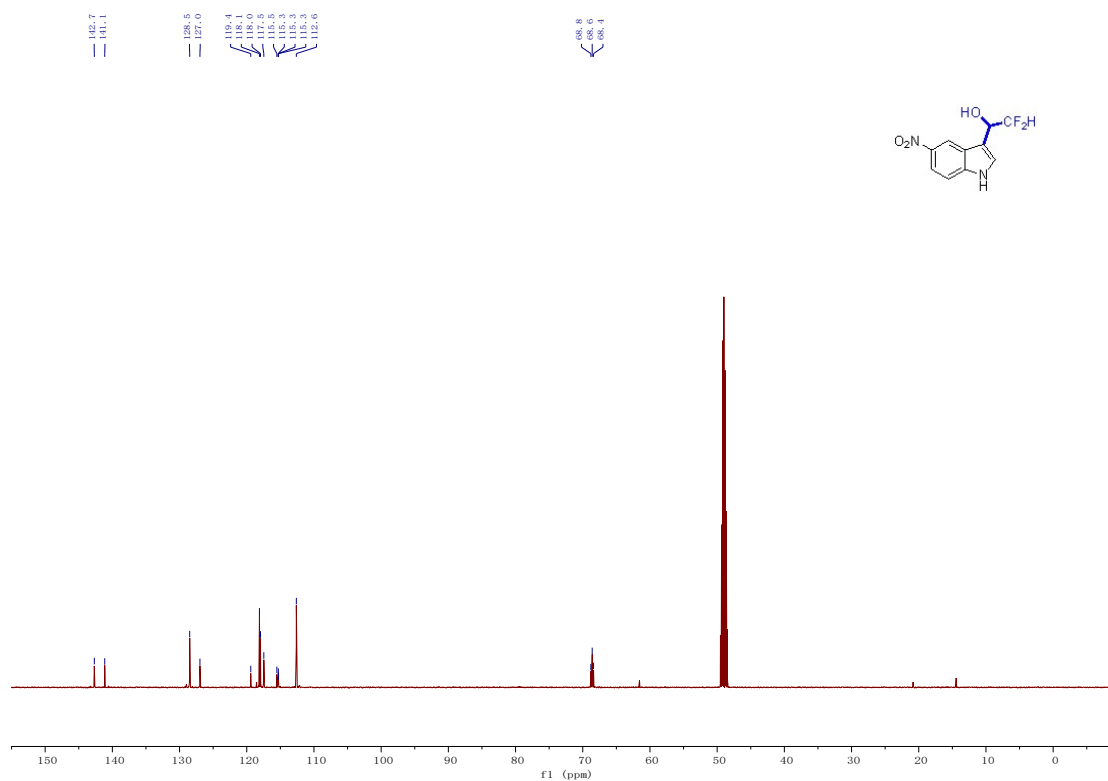
¹⁹F NMR (470 MHz, Methanol-*d*₄) spectra of **3r**



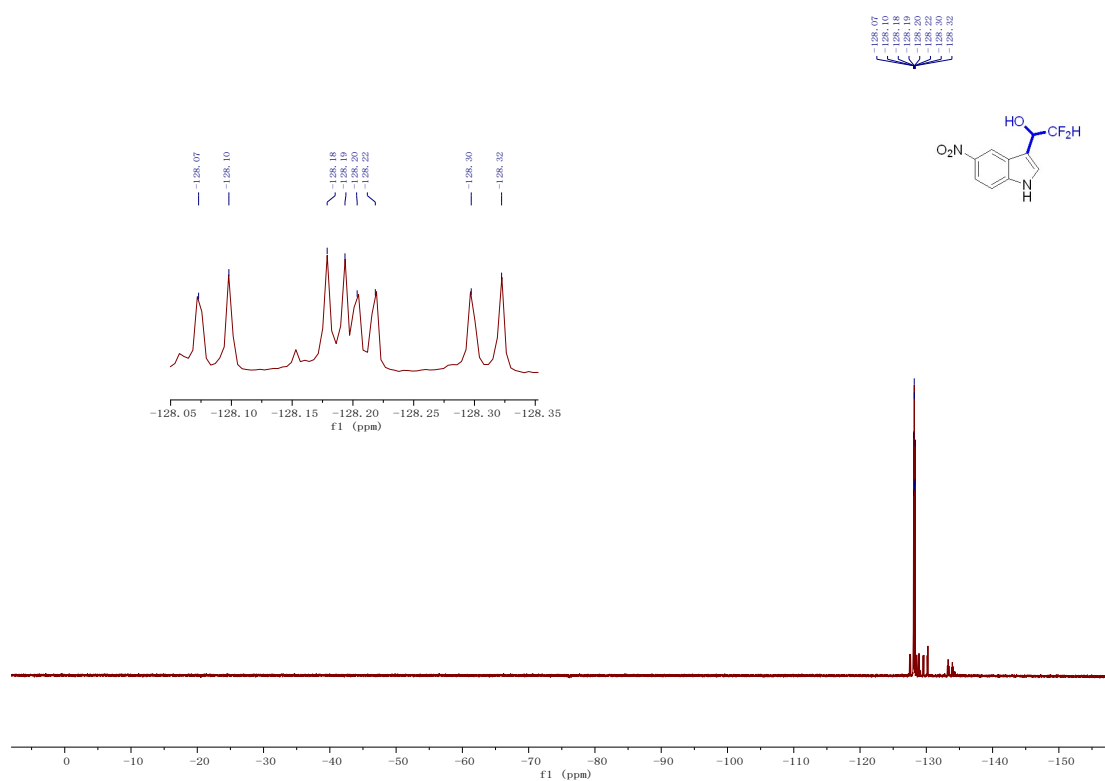
¹H NMR (500 MHz, Methanol-*d*₄) spectra of **3s**



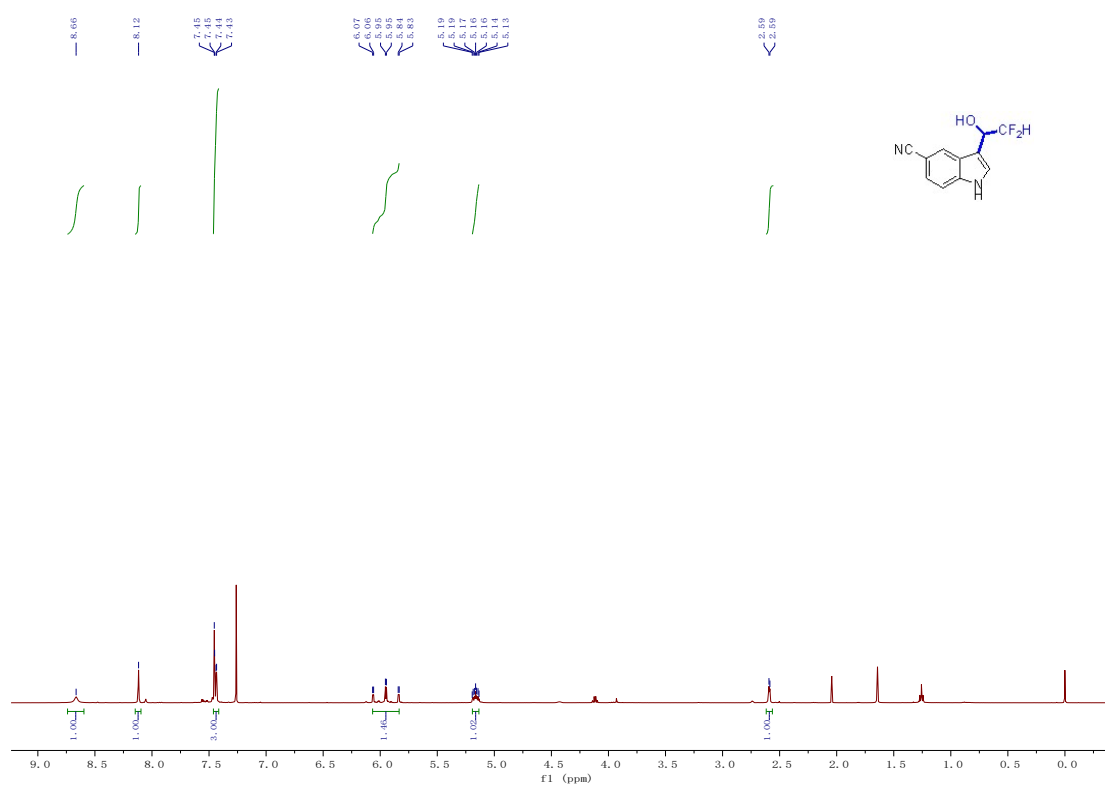
¹³C NMR (125 MHz, Methanol-*d*₄) spectra of **3s**



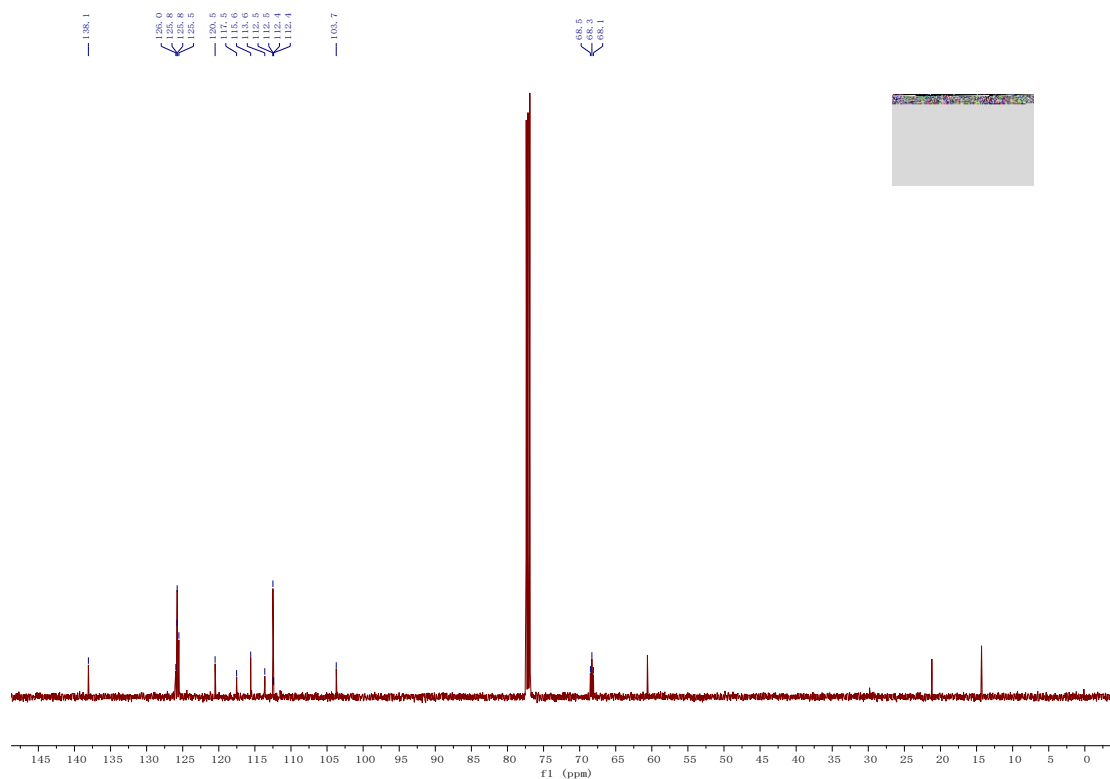
^{19}F NMR (470 MHz, Methanol- d_4) spectra of **3s**



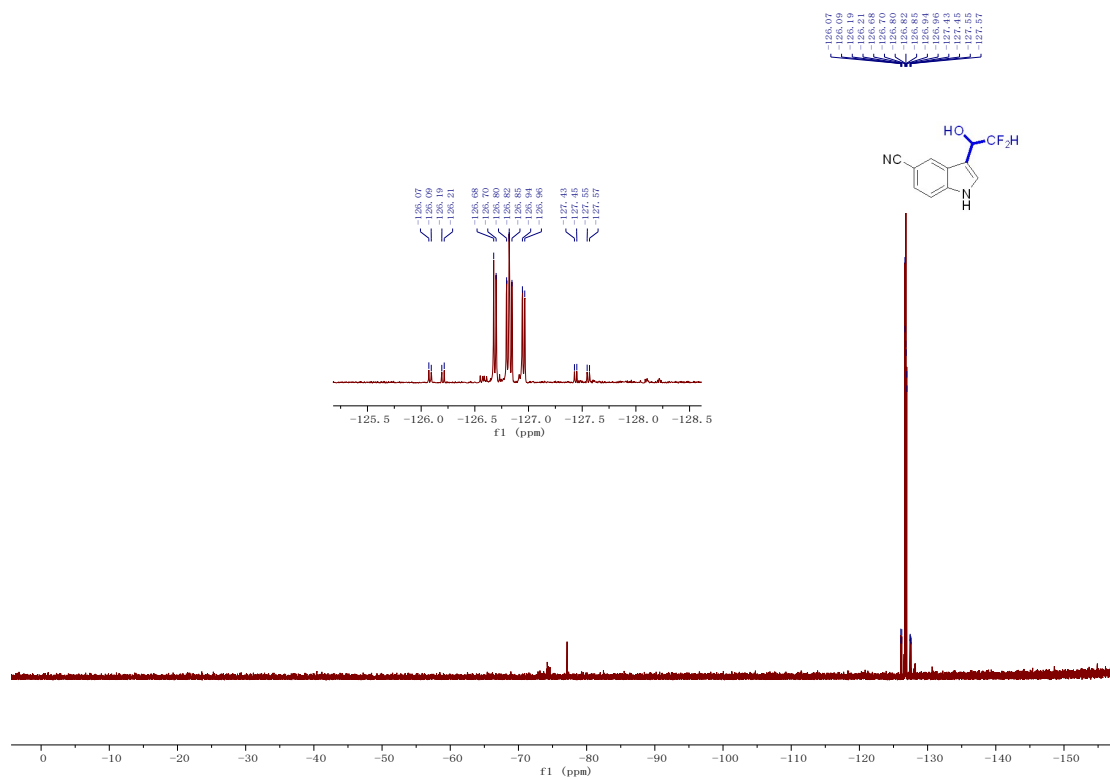
^1H NMR (500 MHz, Chloroform- d) spectra of **3t**



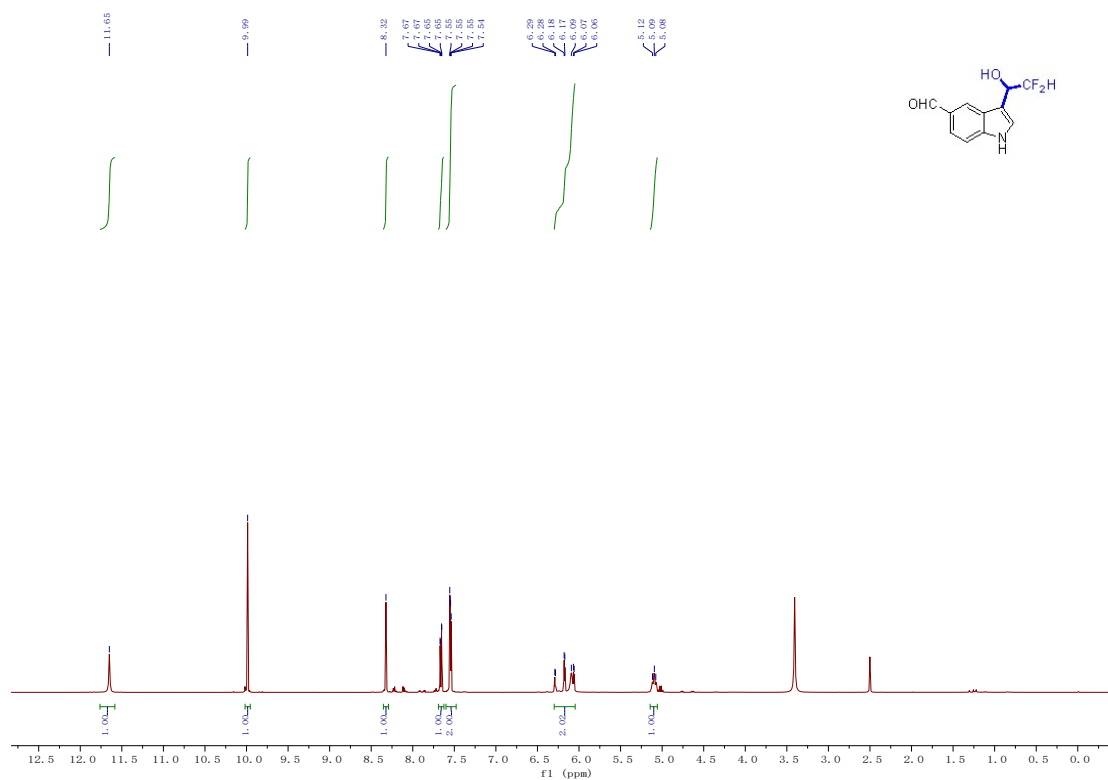
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **3t**



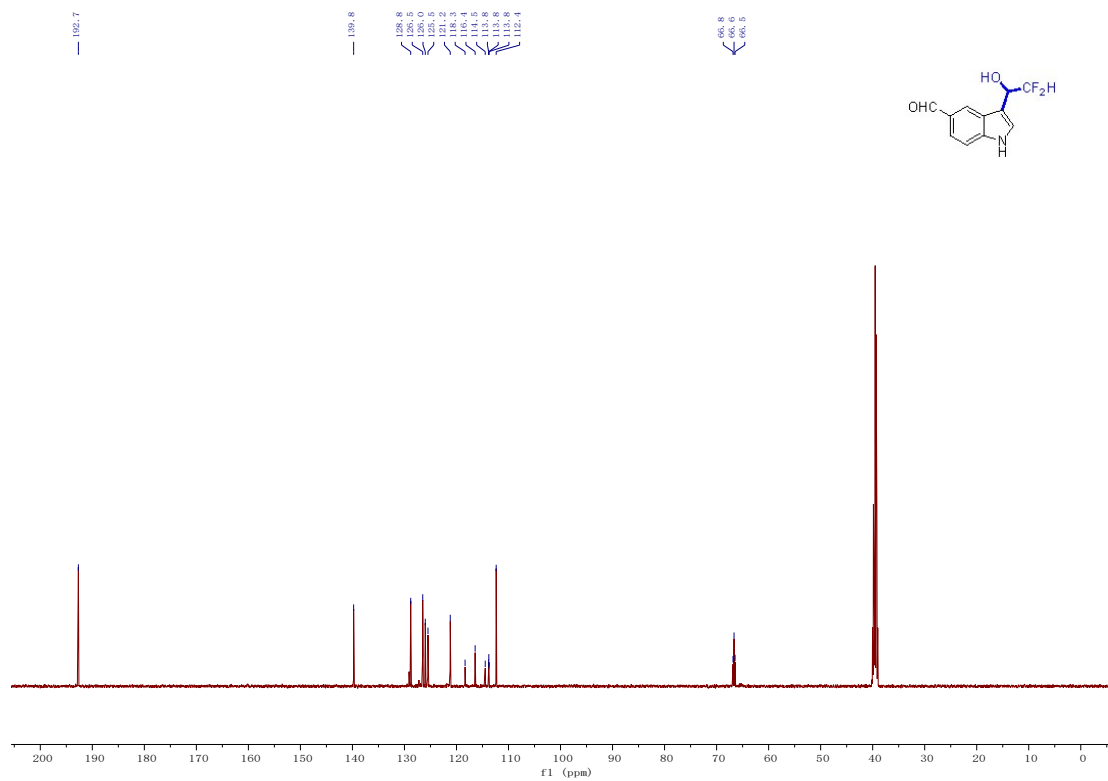
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **3t**



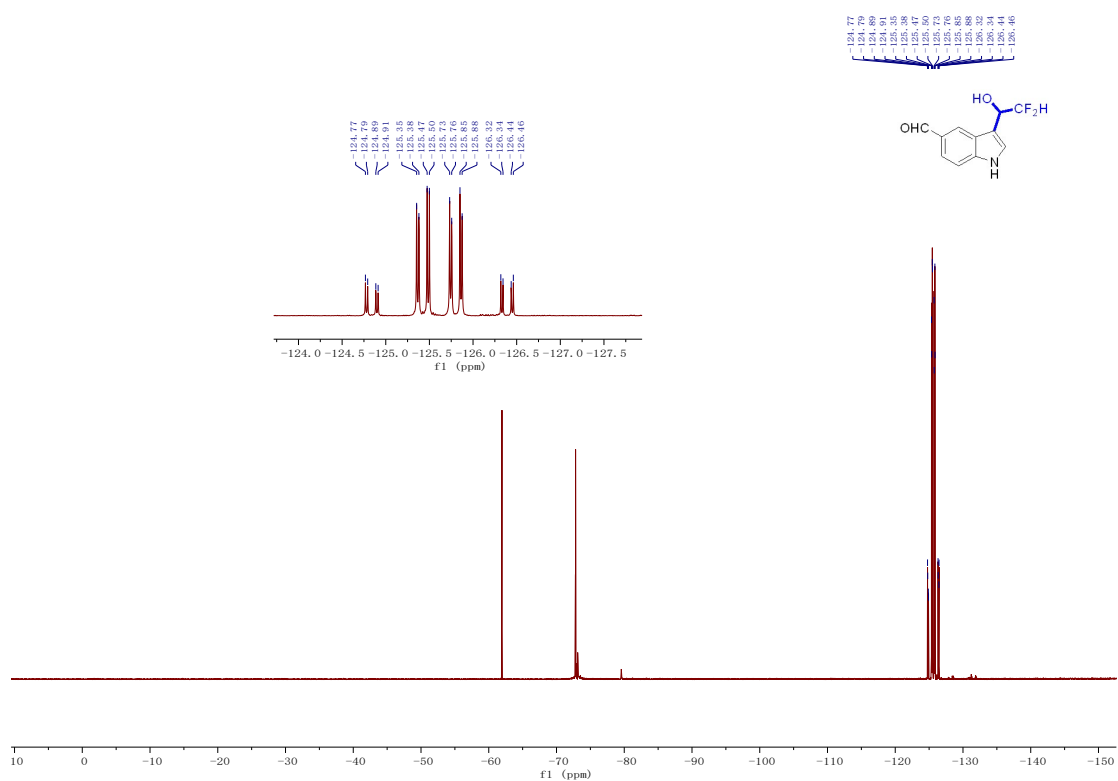
^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectra of **3u**



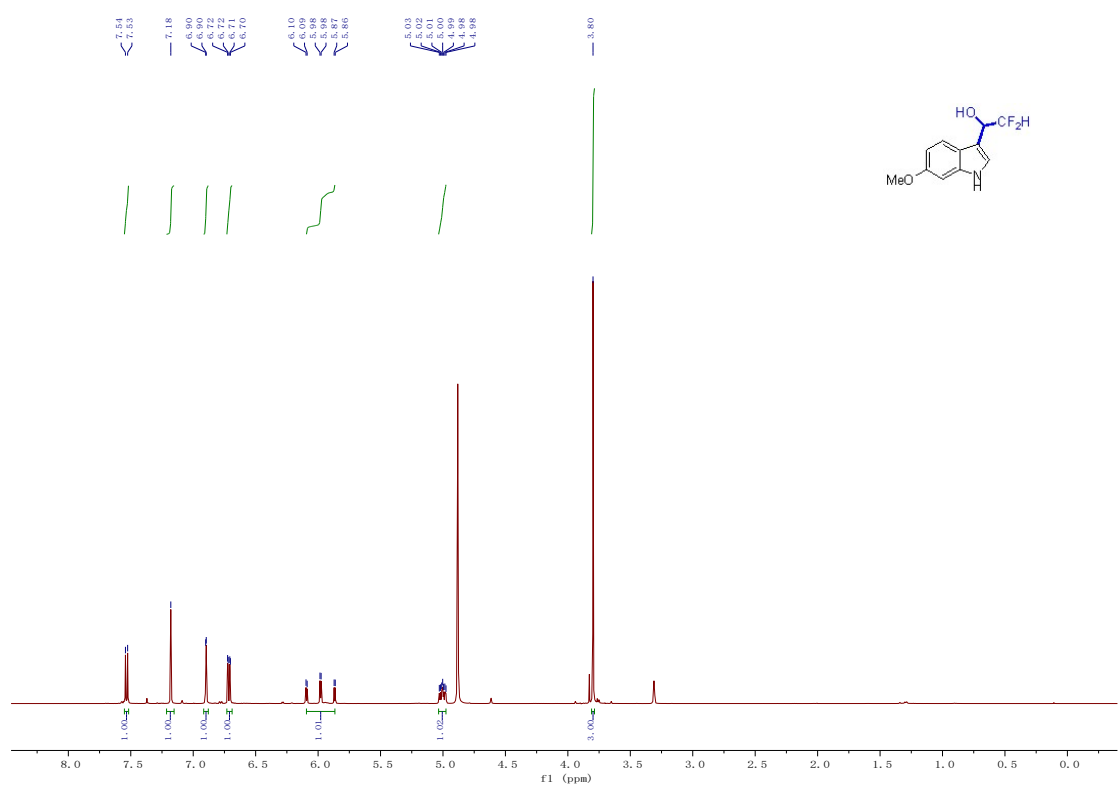
^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectra of **3u**



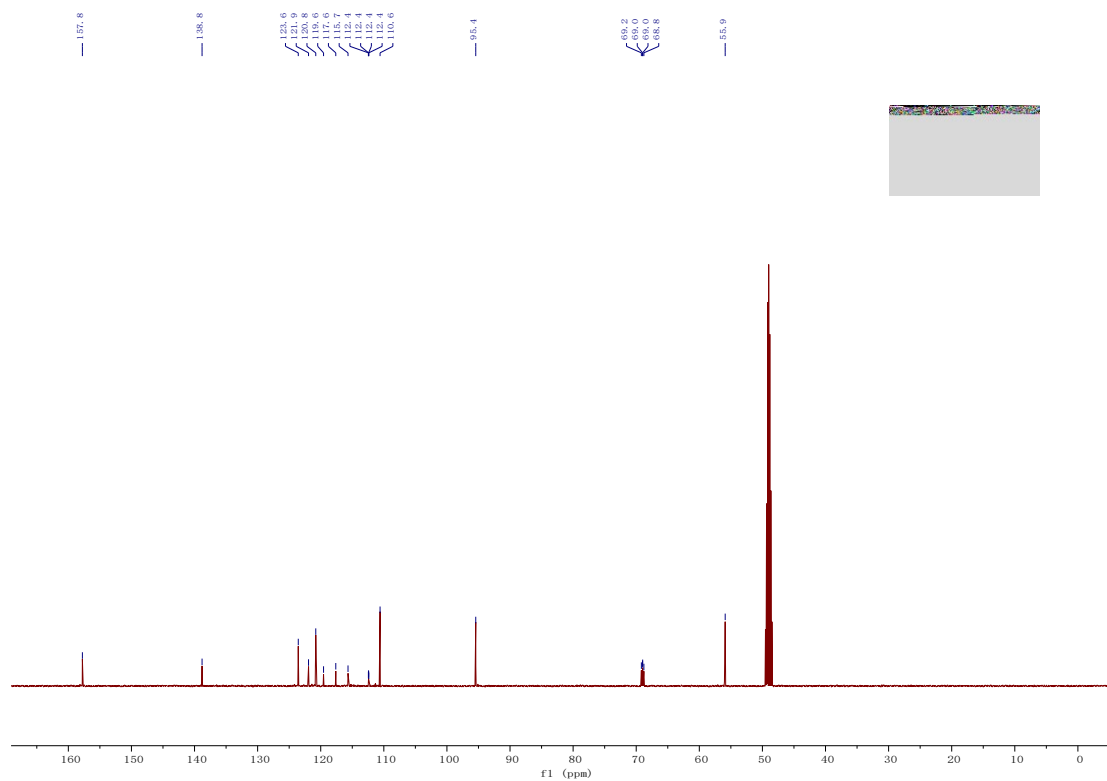
^{19}F NMR (470 MHz, $\text{DMSO-}d_6$) spectra of **3u**



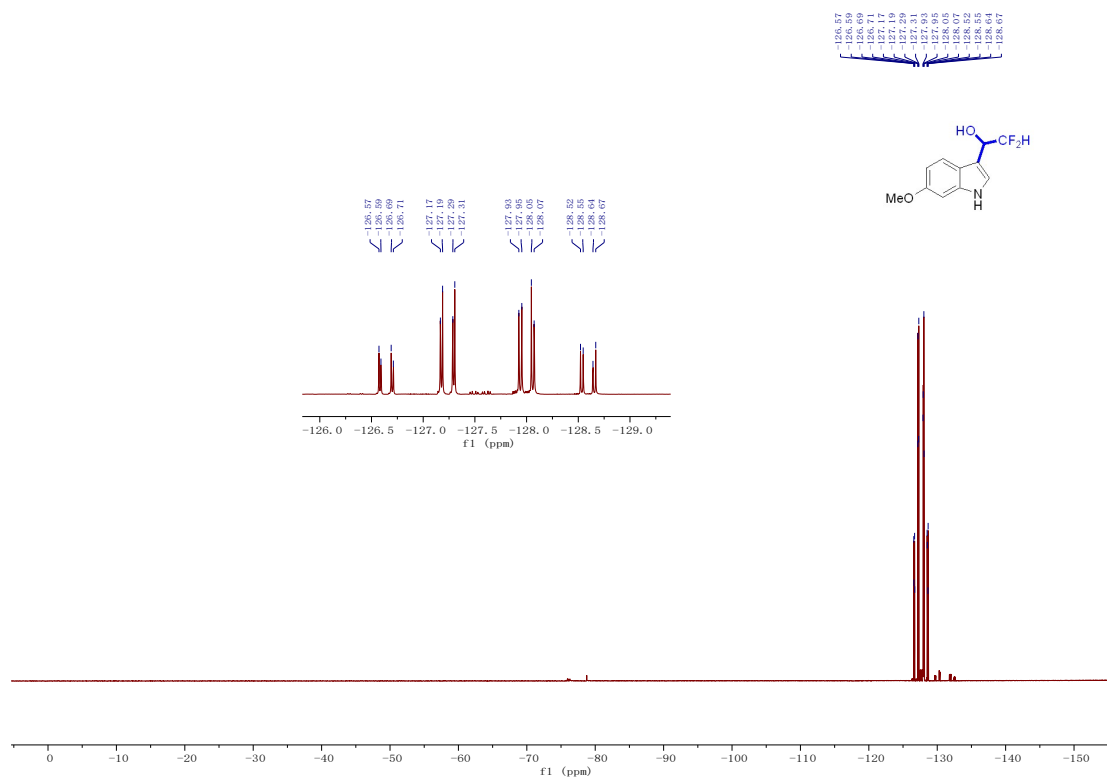
^1H NMR (500 MHz, $\text{Methanol-}d_4$) spectra of **3v**



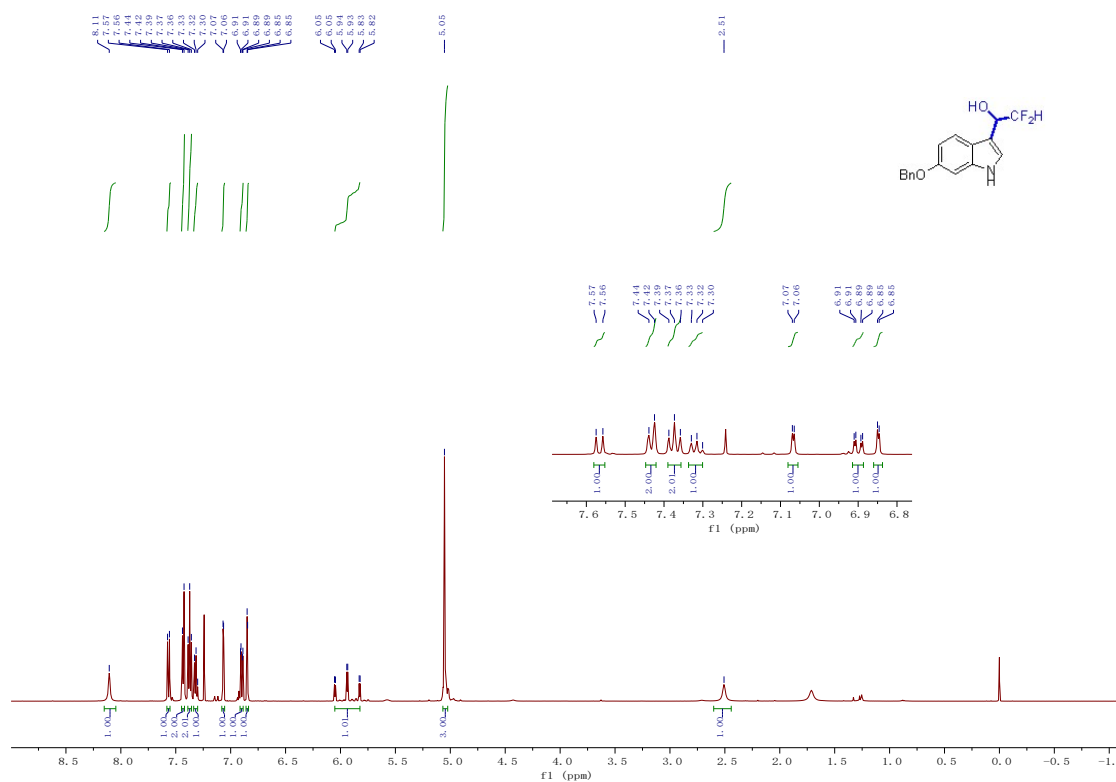
¹³C NMR (125 MHz, Methanol-*d*₄) spectra of **3v**



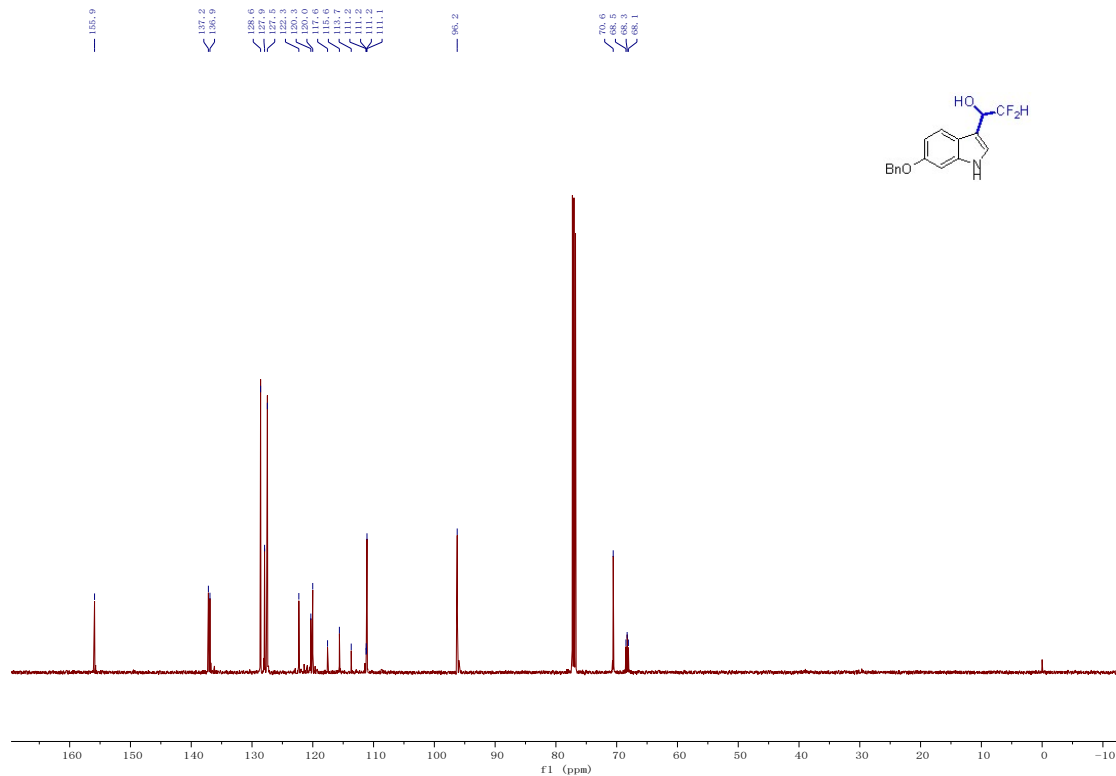
¹⁹F NMR (470 MHz, Methanol-*d*₄) spectra of **3v**



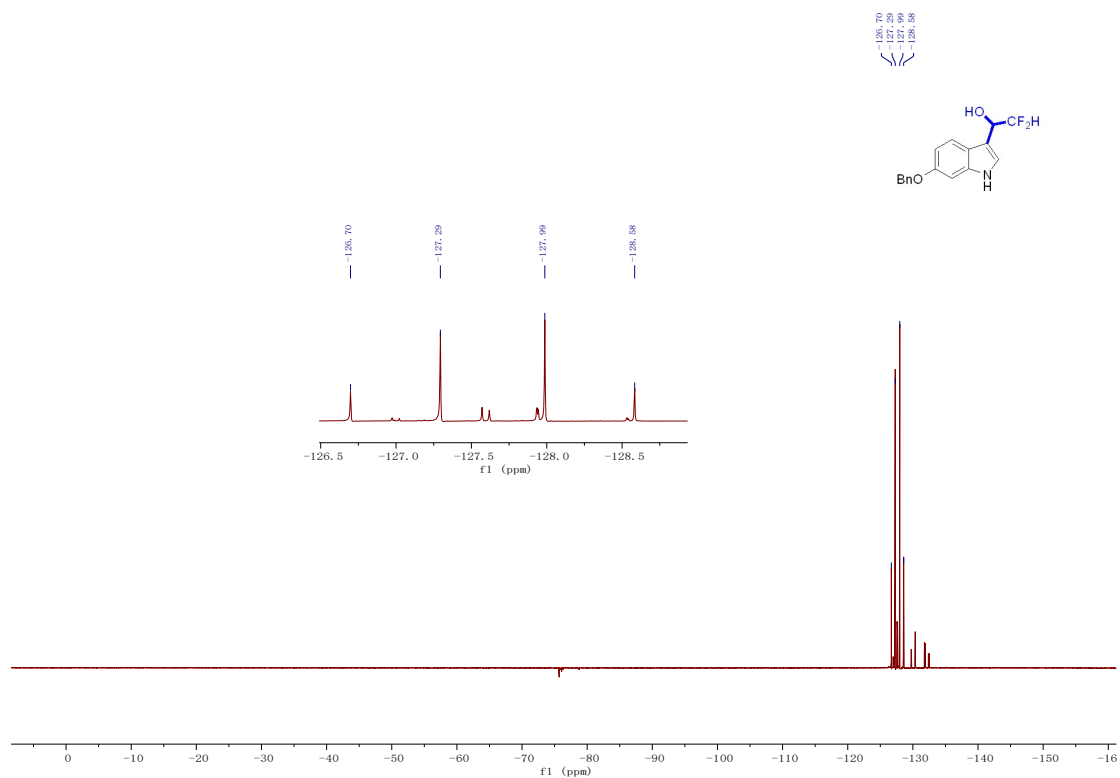
^1H NMR (500 MHz, Chloroform-*d*) spectra of **3w**



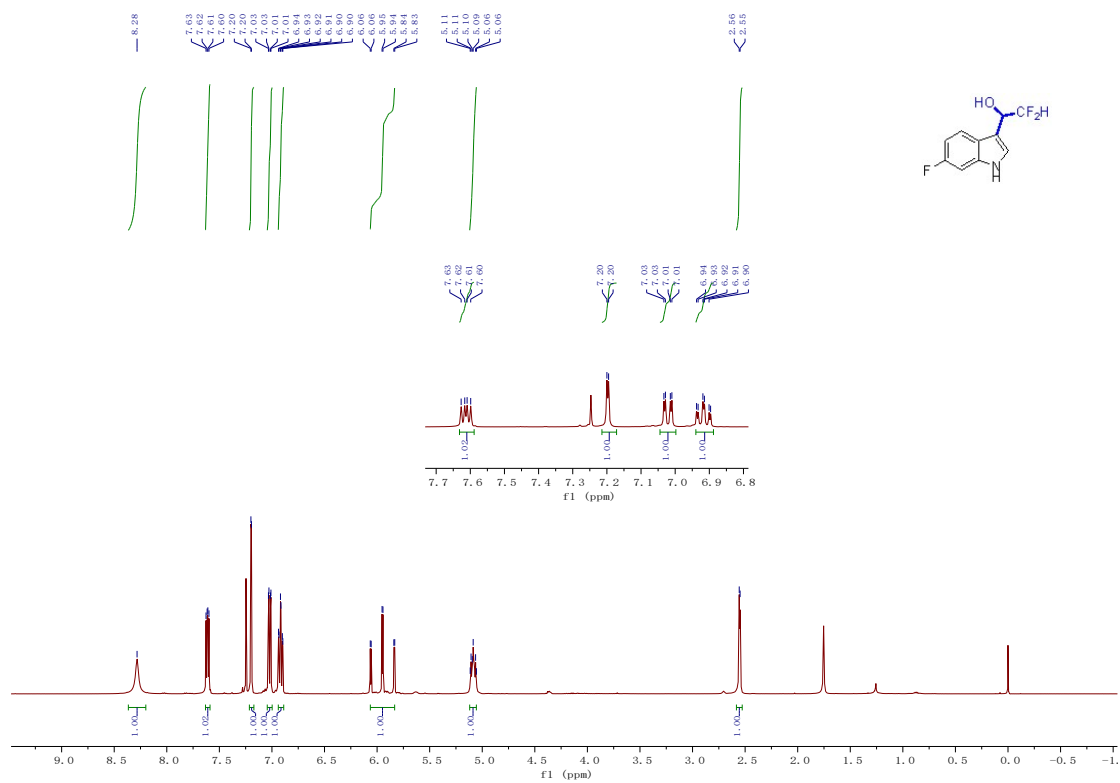
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **3w**



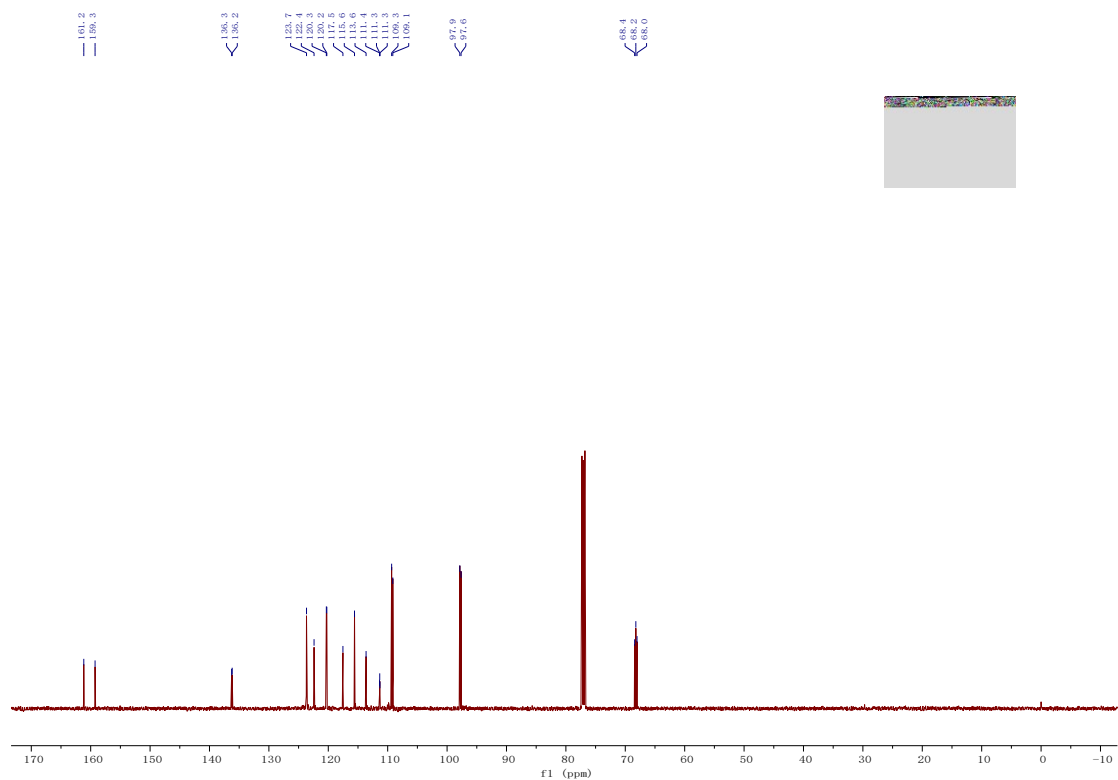
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **3w**



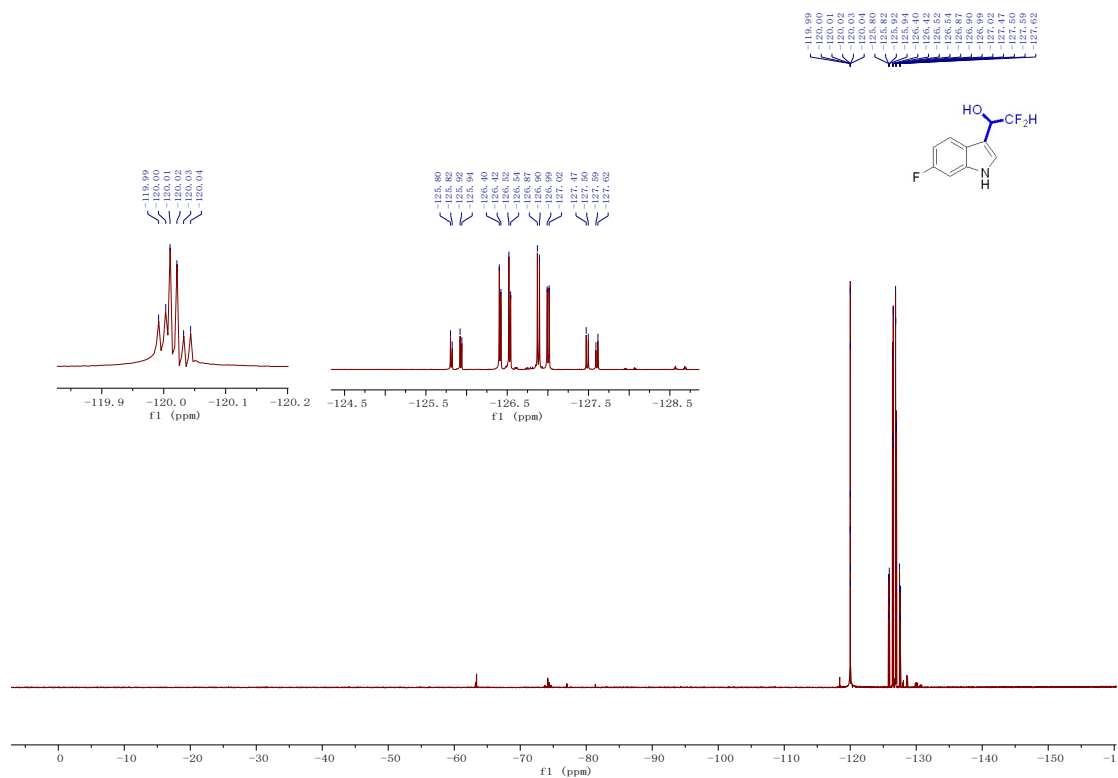
^1H NMR (500 MHz, Chloroform-*d*) spectra of **3x**



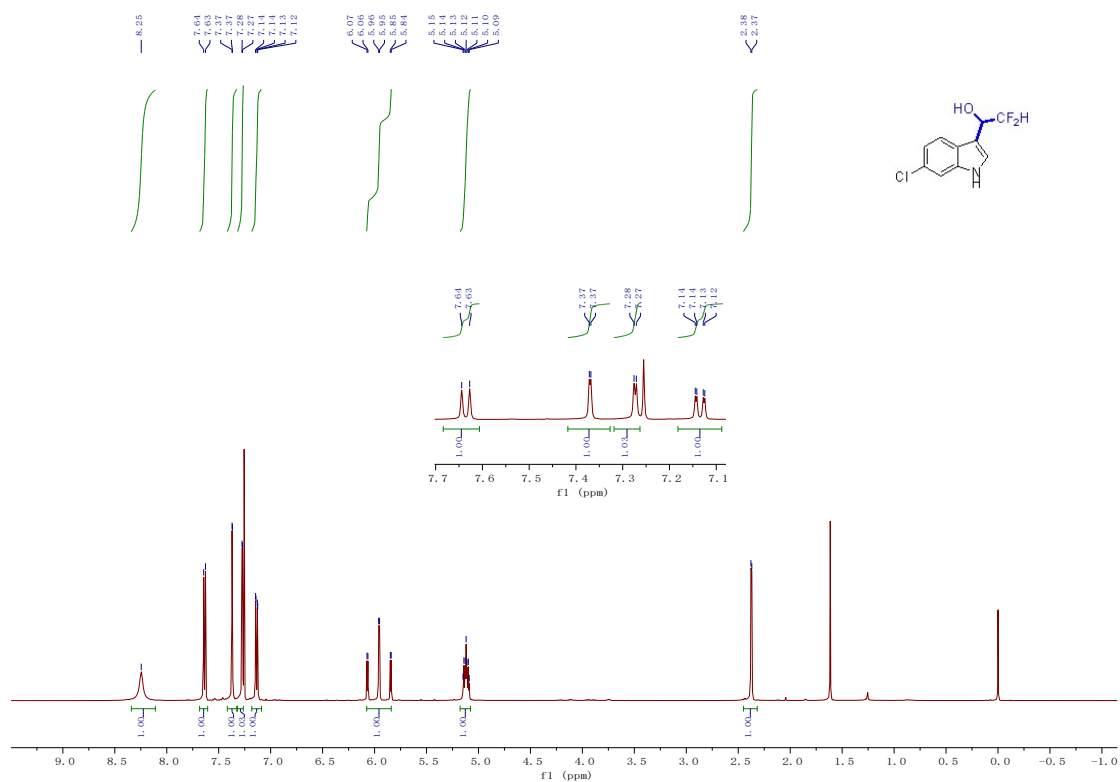
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **3x**



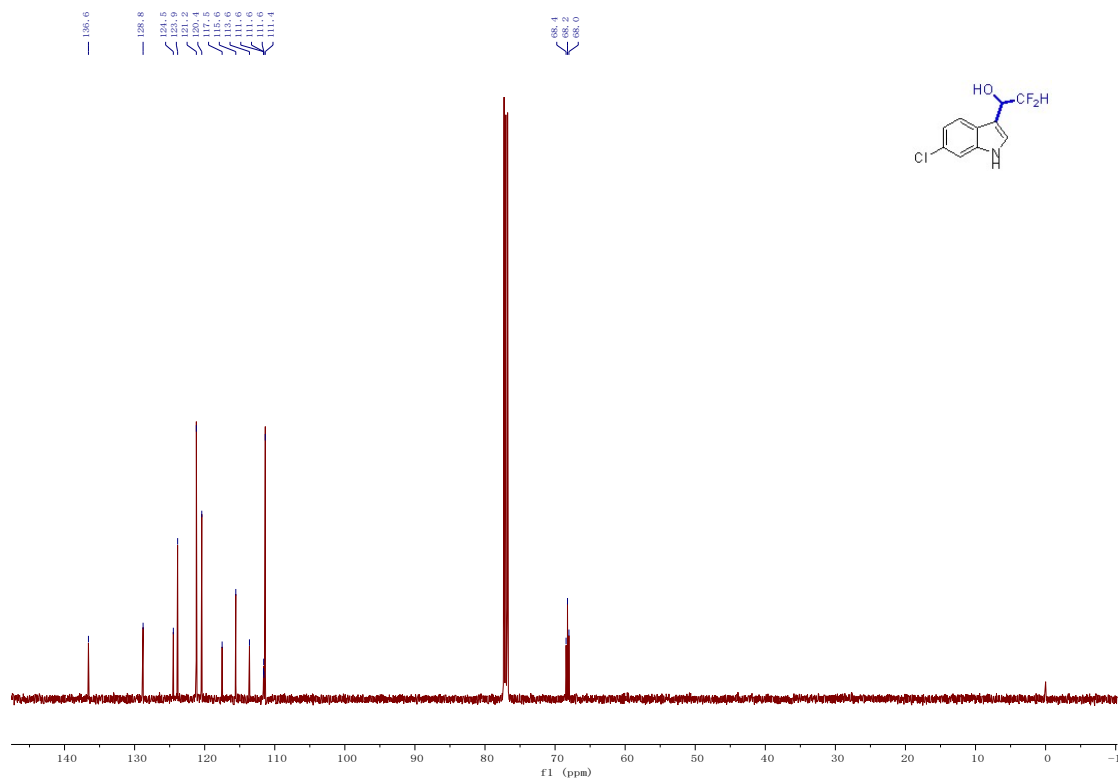
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **3x**



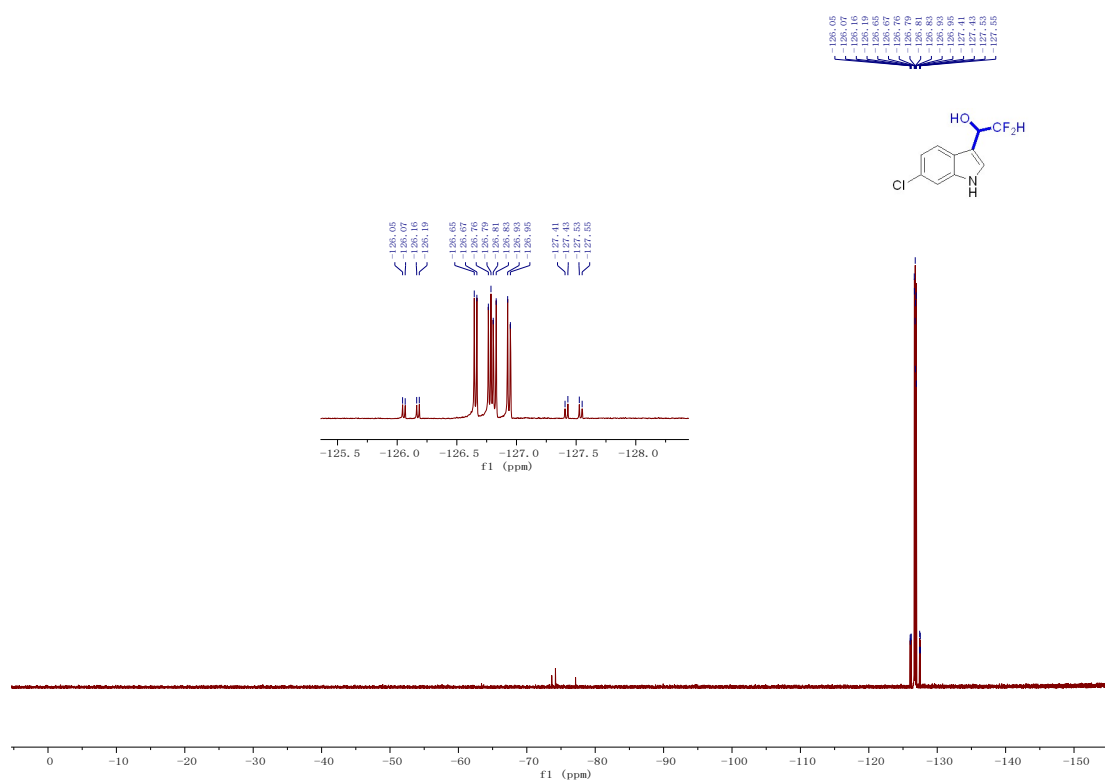
¹H NMR (500 MHz, Chloroform-*d*) spectra of **3y**



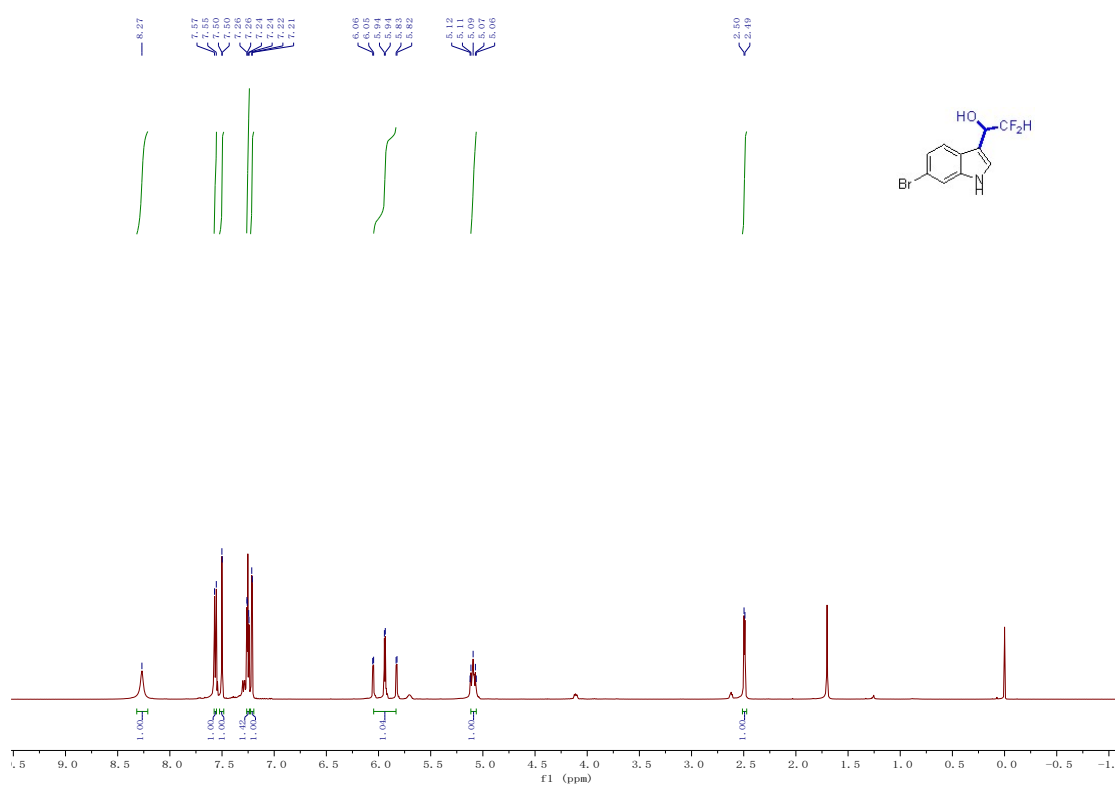
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **3y**



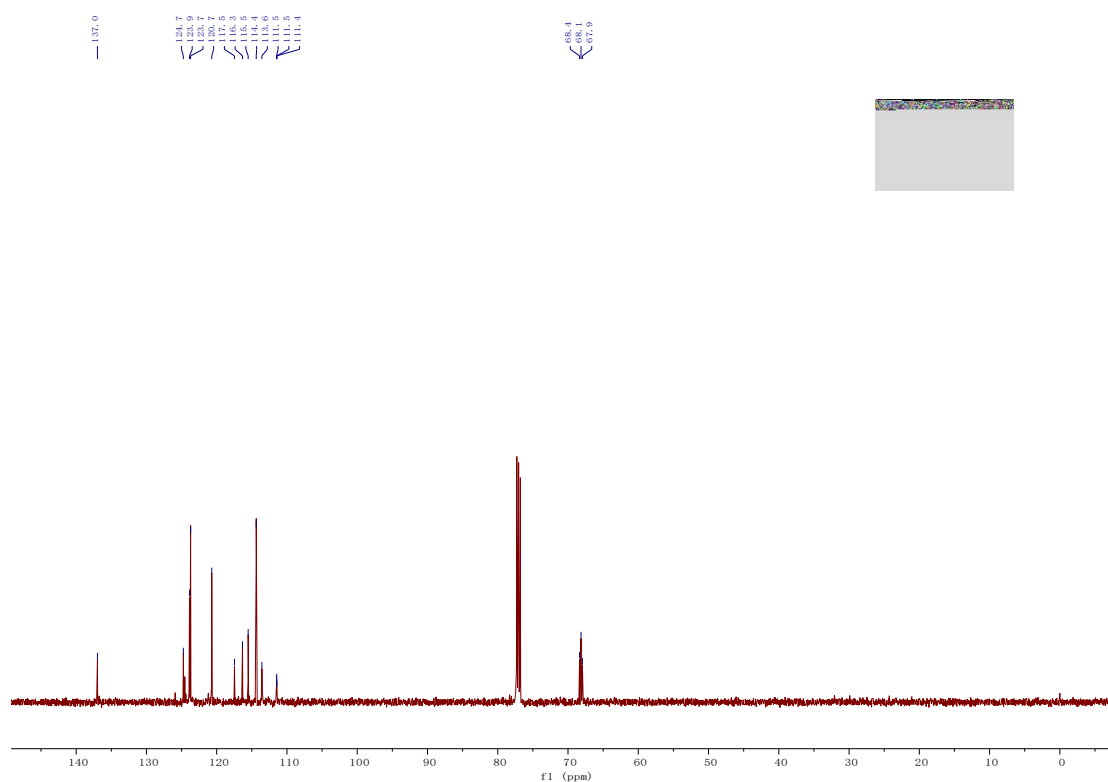
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **3y**



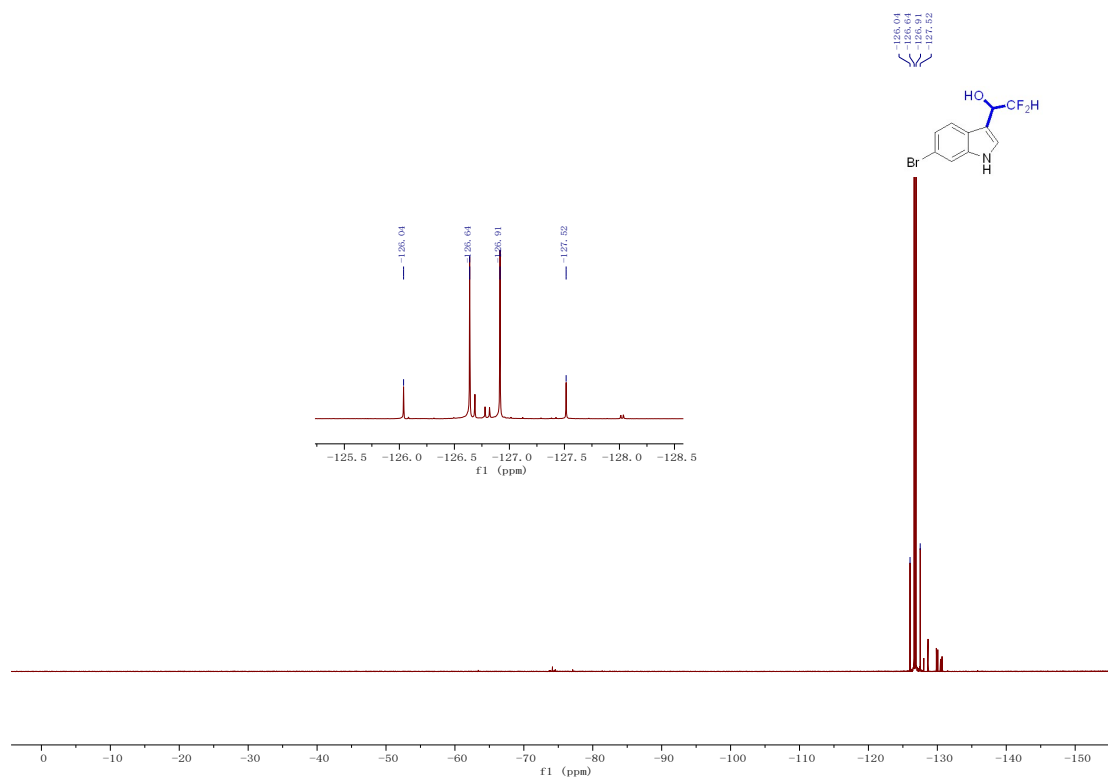
¹H NMR (500 MHz, Chloroform-*d*) spectra of **3z**



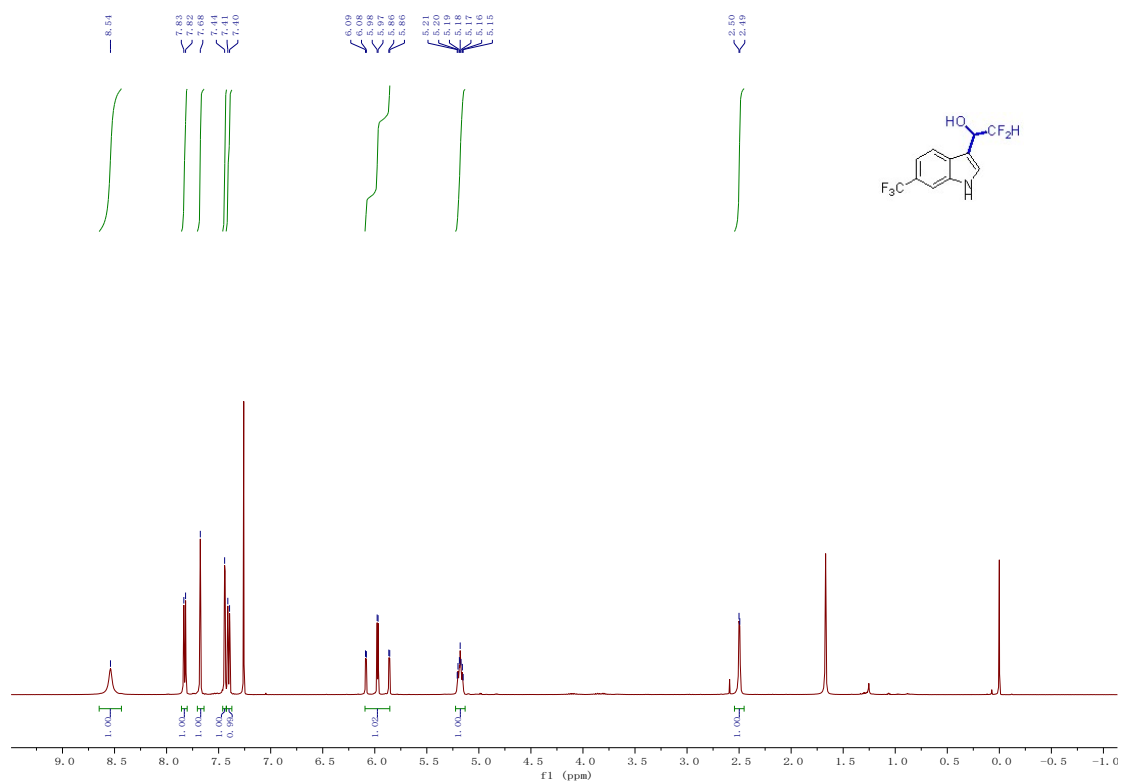
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **3z**



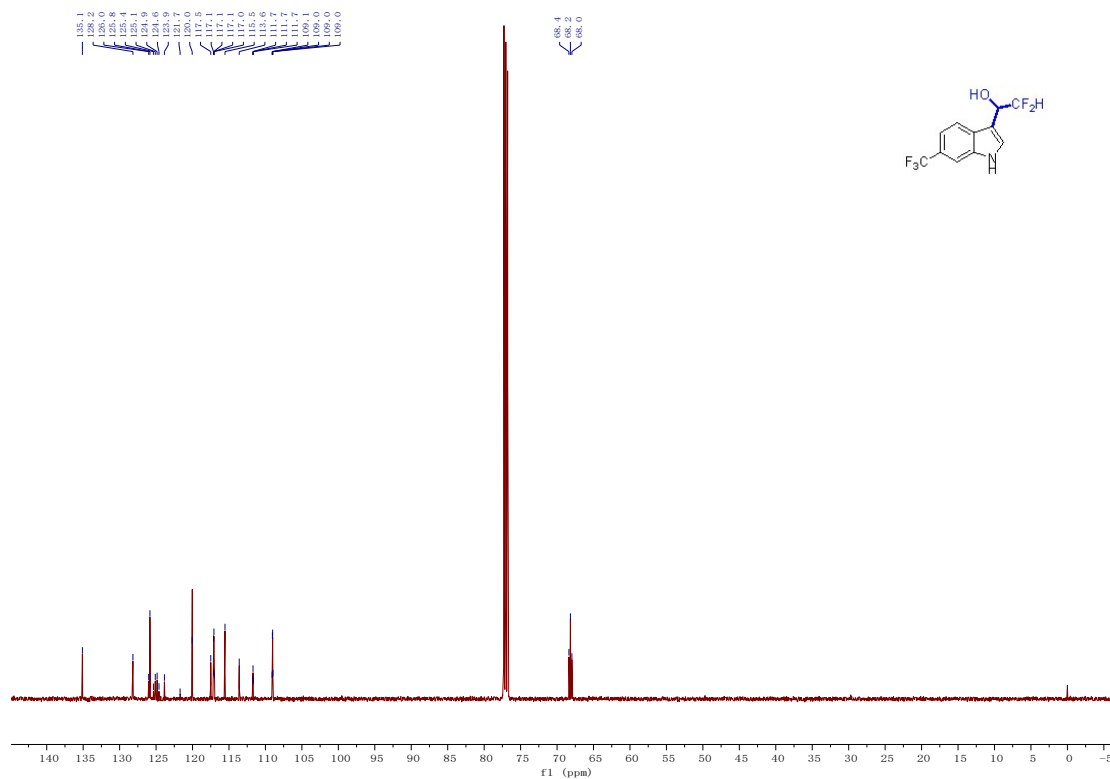
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **3z**



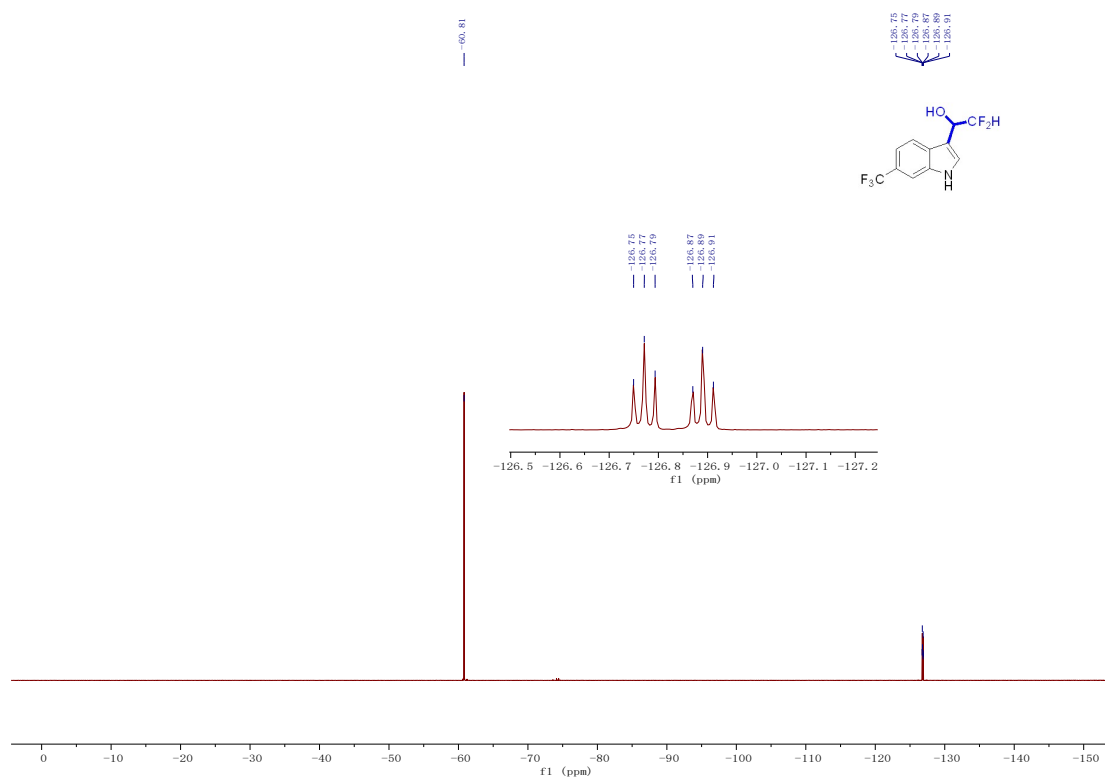
^1H NMR (500 MHz, Chloroform-*d*) spectra of **3a'**



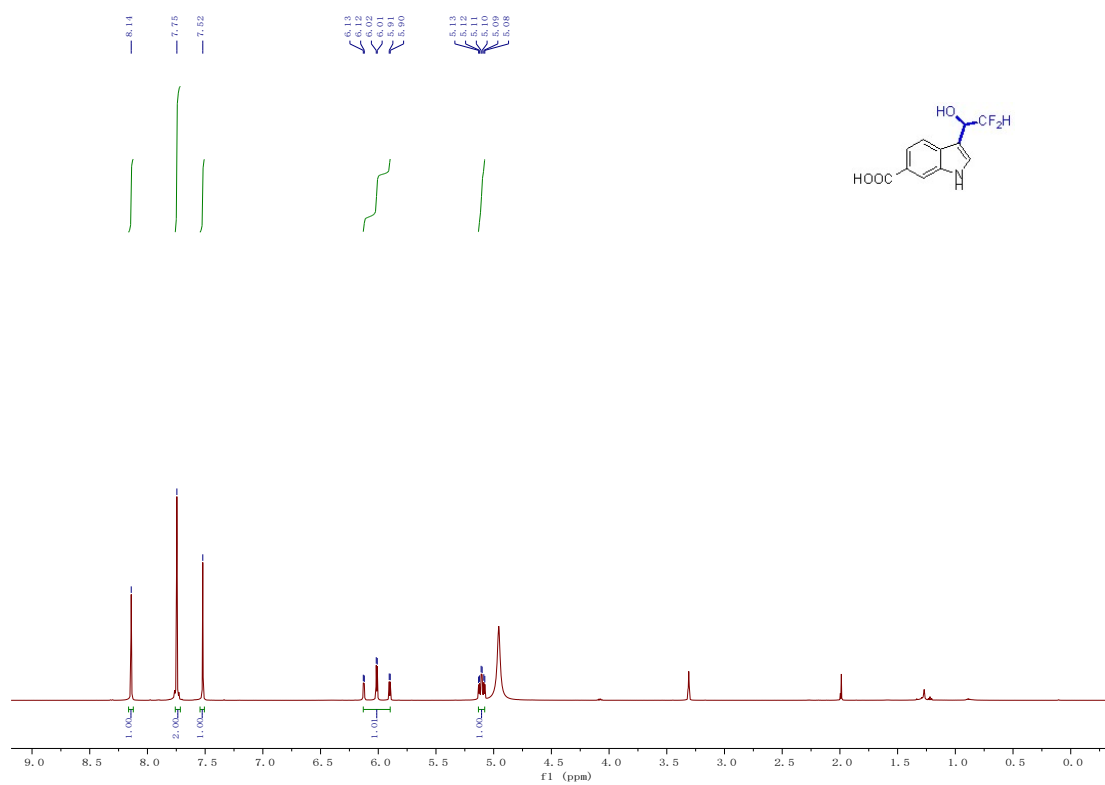
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **3a'**



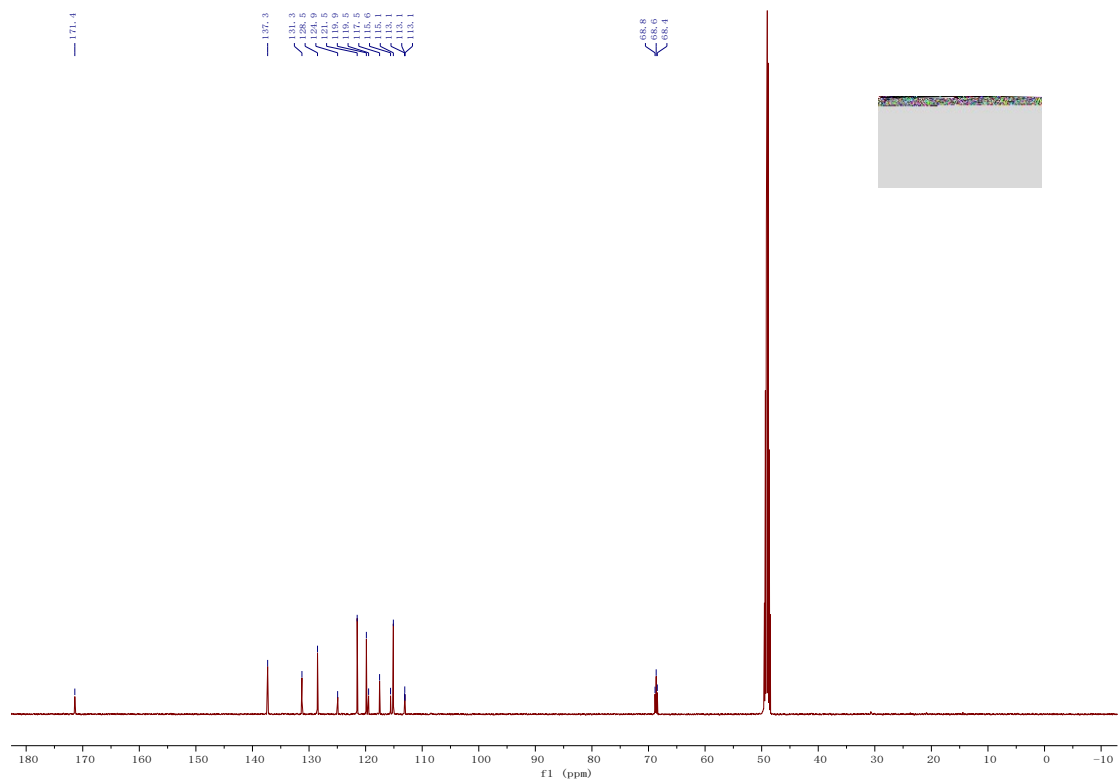
^{19}F NMR (470 MHz, Chloroform- d) spectra of **3a'**



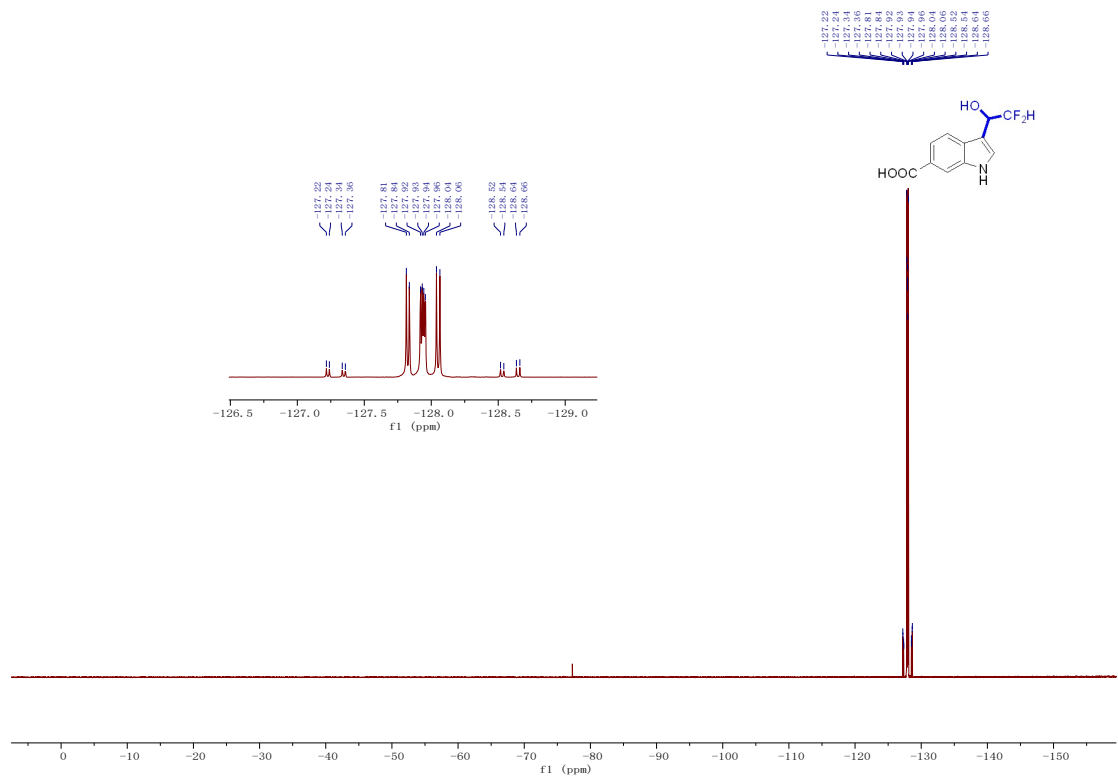
^1H NMR (500 MHz, Methanol- d_4) spectra of **3b'**



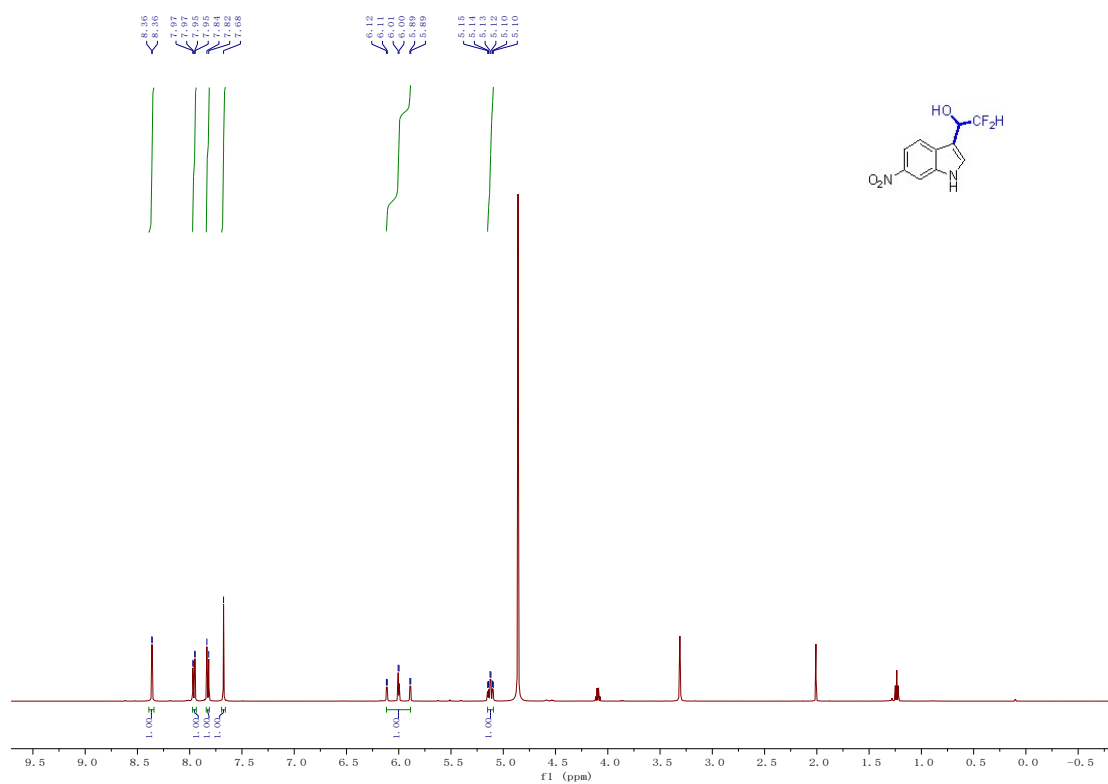
^{13}C NMR (125 MHz, Methanol- d_4) spectra of **3b'**



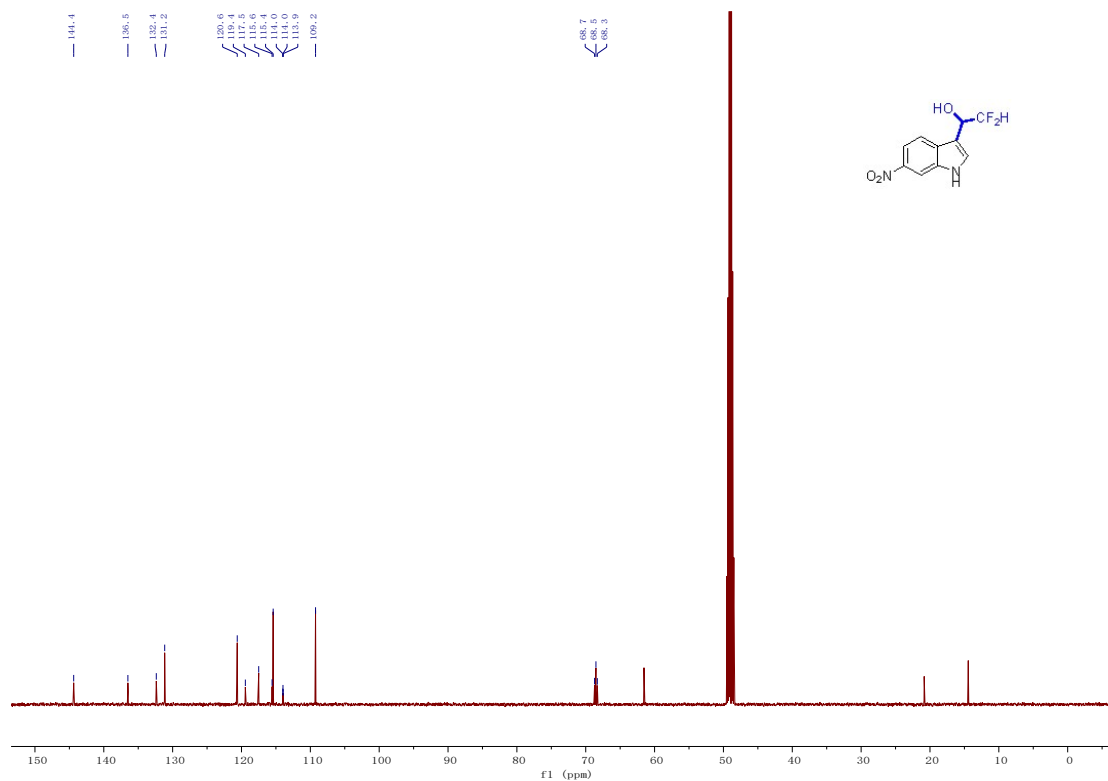
^{19}F NMR (470 MHz, Methanol- d_4) spectra of **3b'**



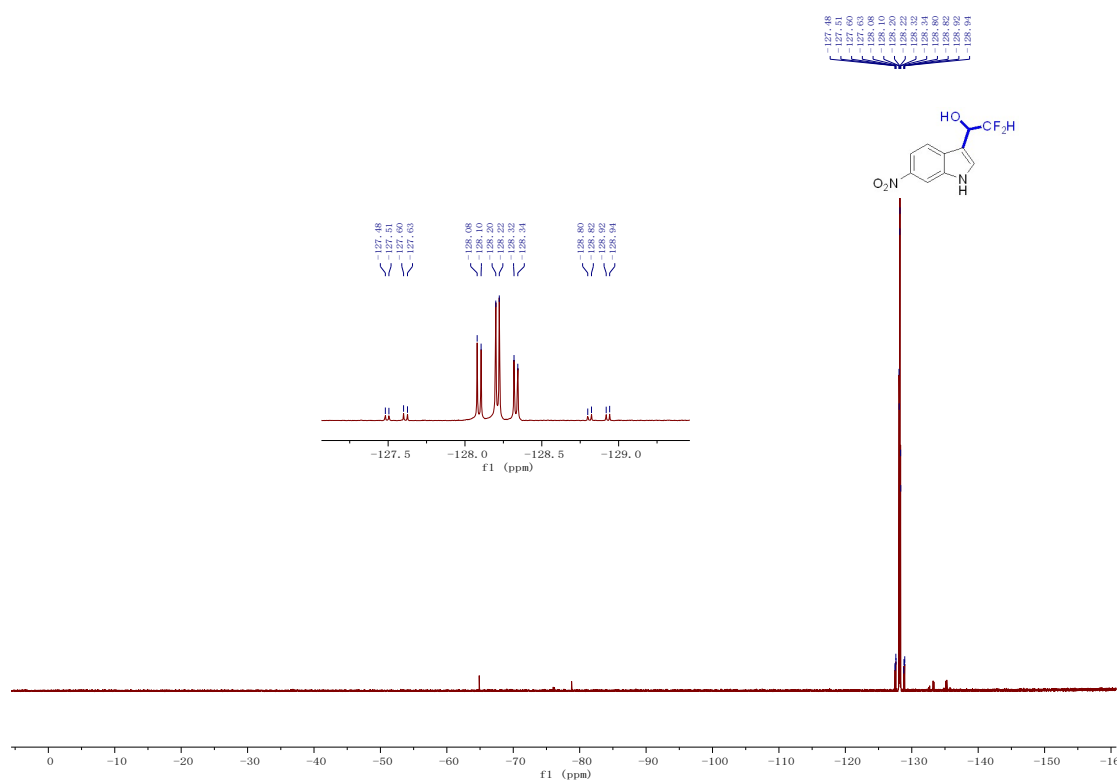
^1H NMR (500 MHz, Methanol- d_4) spectra of **3c'**



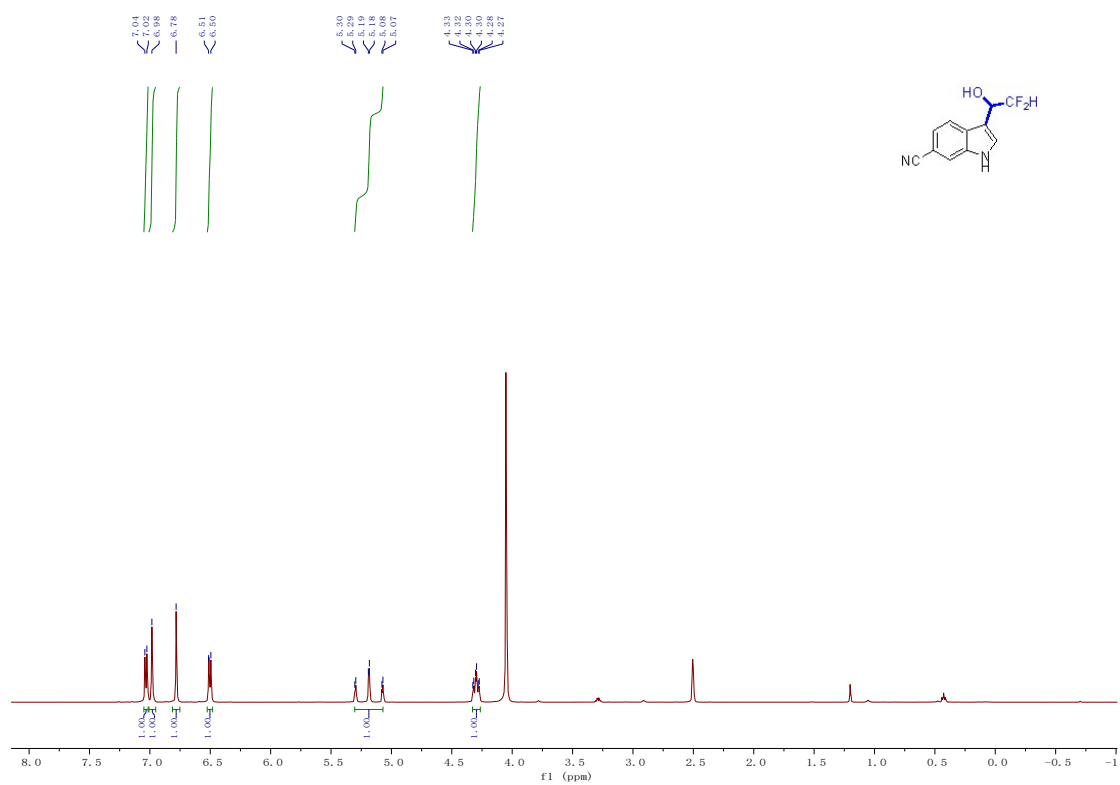
^{13}C NMR (125 MHz, Methanol- d_4) spectra of **3c'**



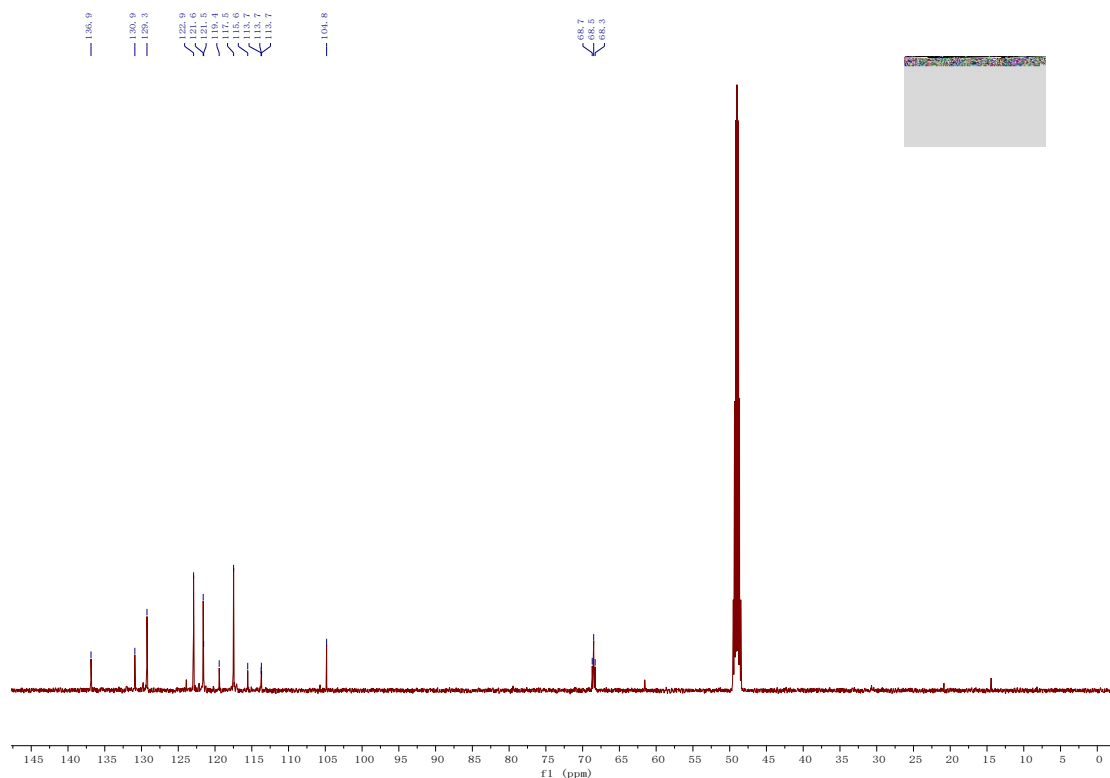
^{19}F NMR (470 MHz, Methanol- d_4) spectra of **3c'**



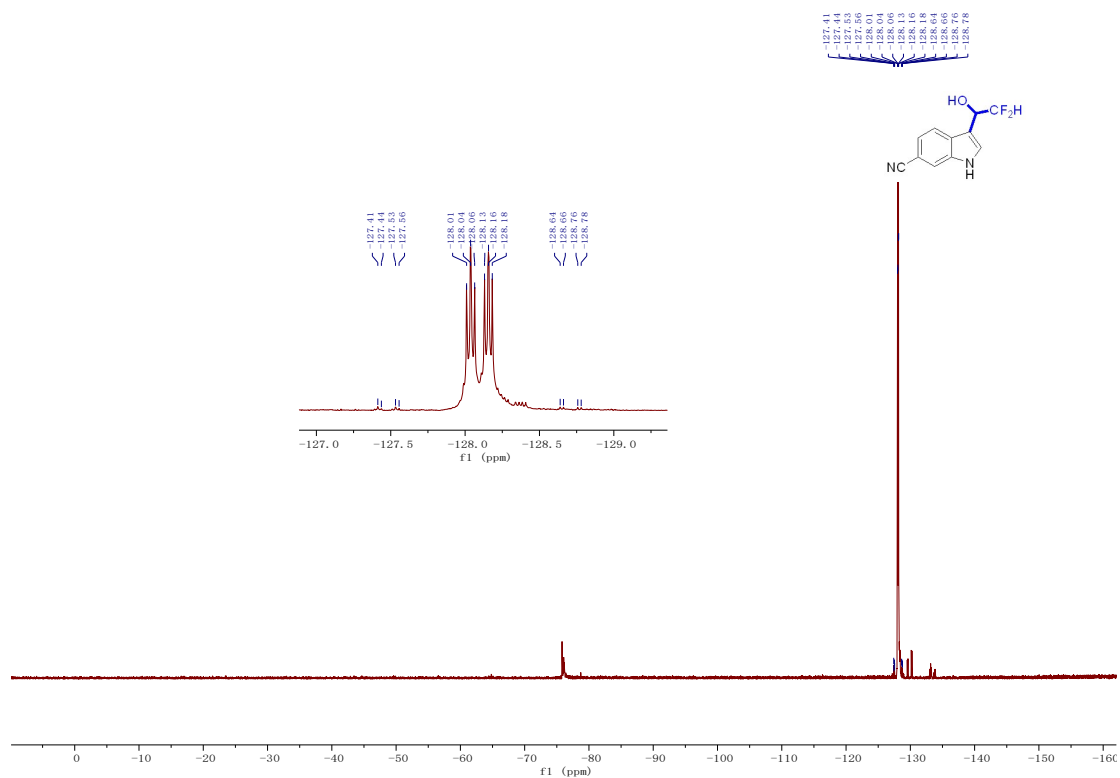
^1H NMR (500 MHz, Methanol- d_4) spectra of **3d'**



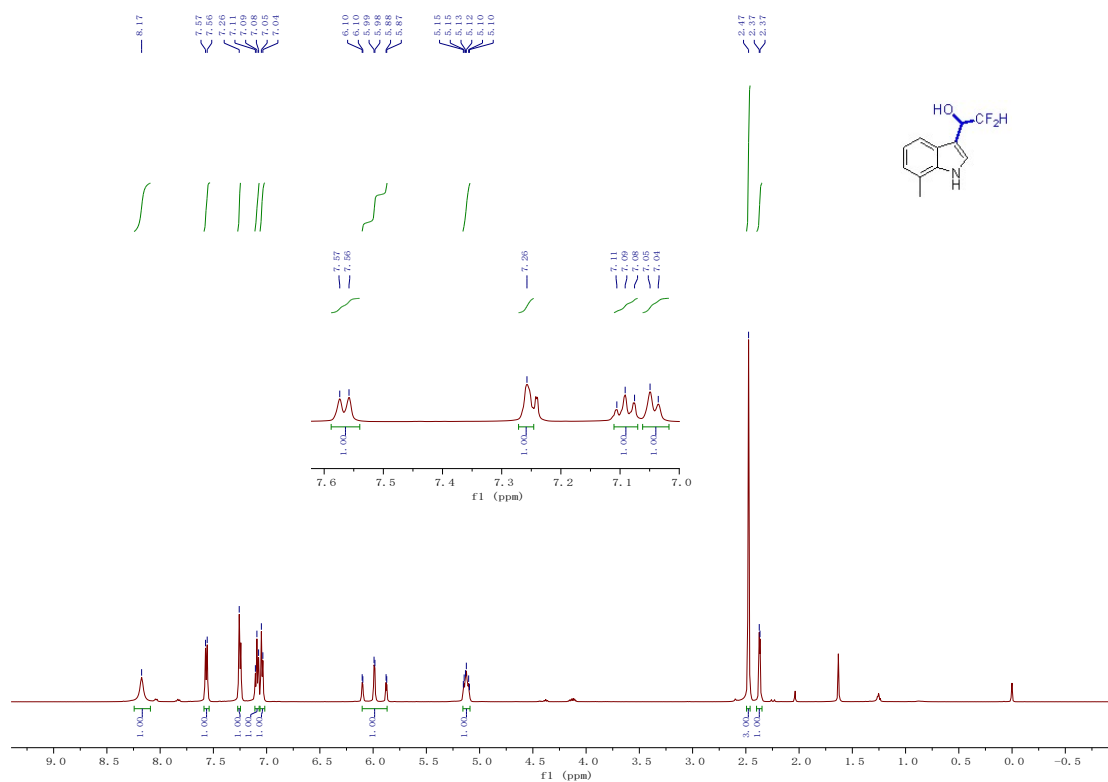
^{13}C NMR (125 MHz, Methanol- d_4) spectra of **3d**'



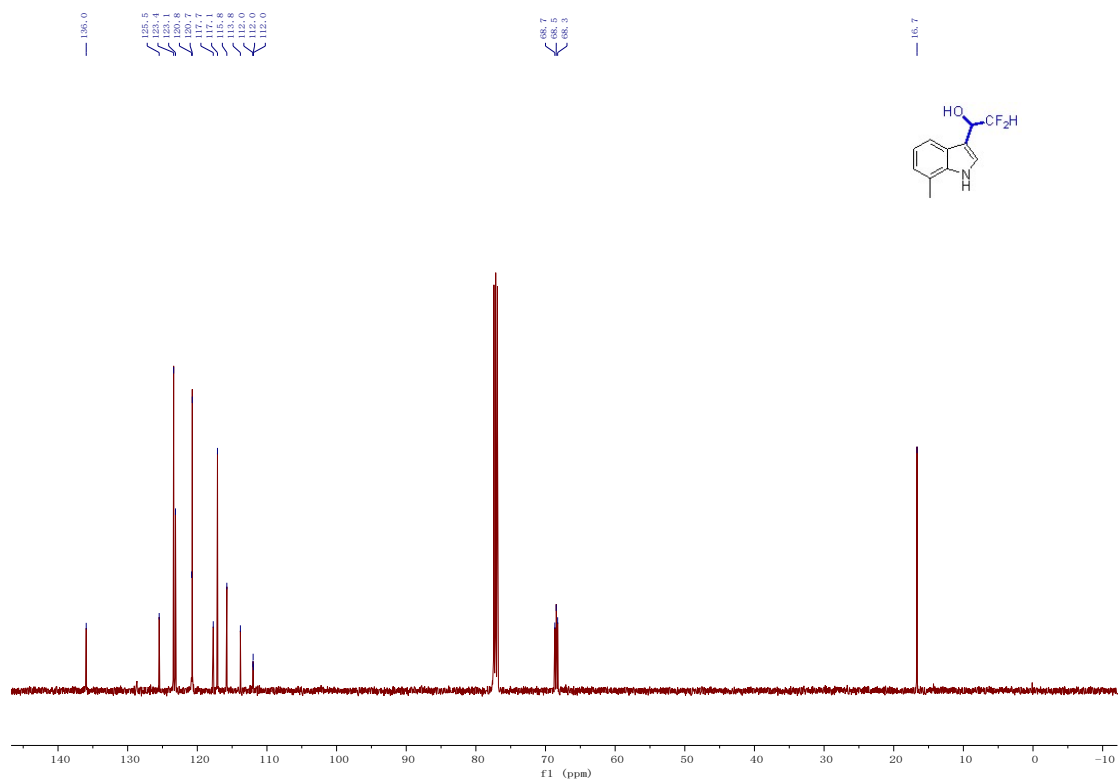
^{19}F NMR (470 MHz, Methanol- d_4) spectra of **3d**'



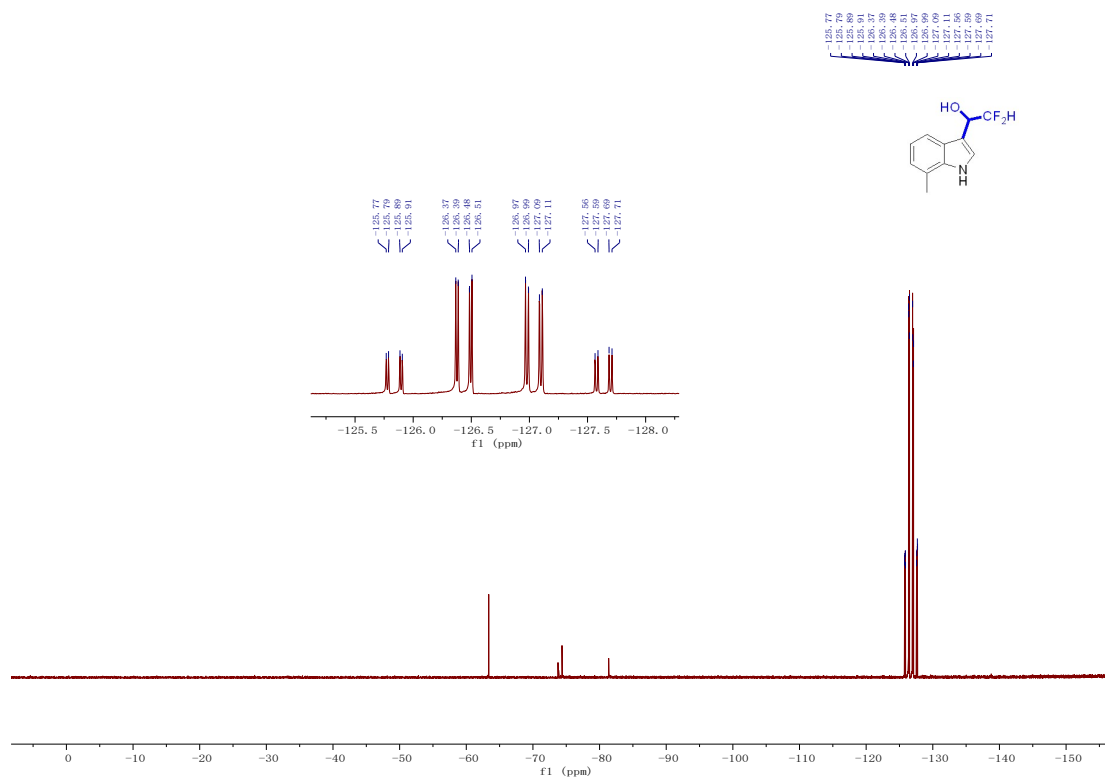
¹H NMR (500 MHz, Chloroform-*d*) spectra of **3e'**



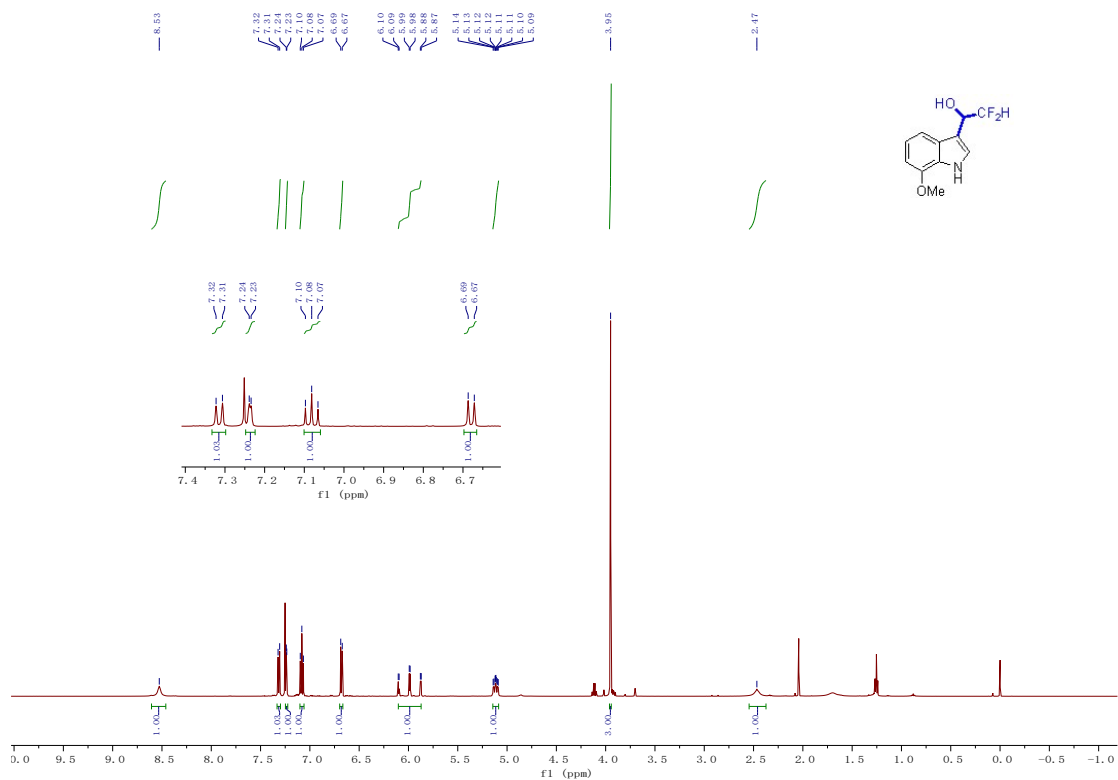
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **3e'**



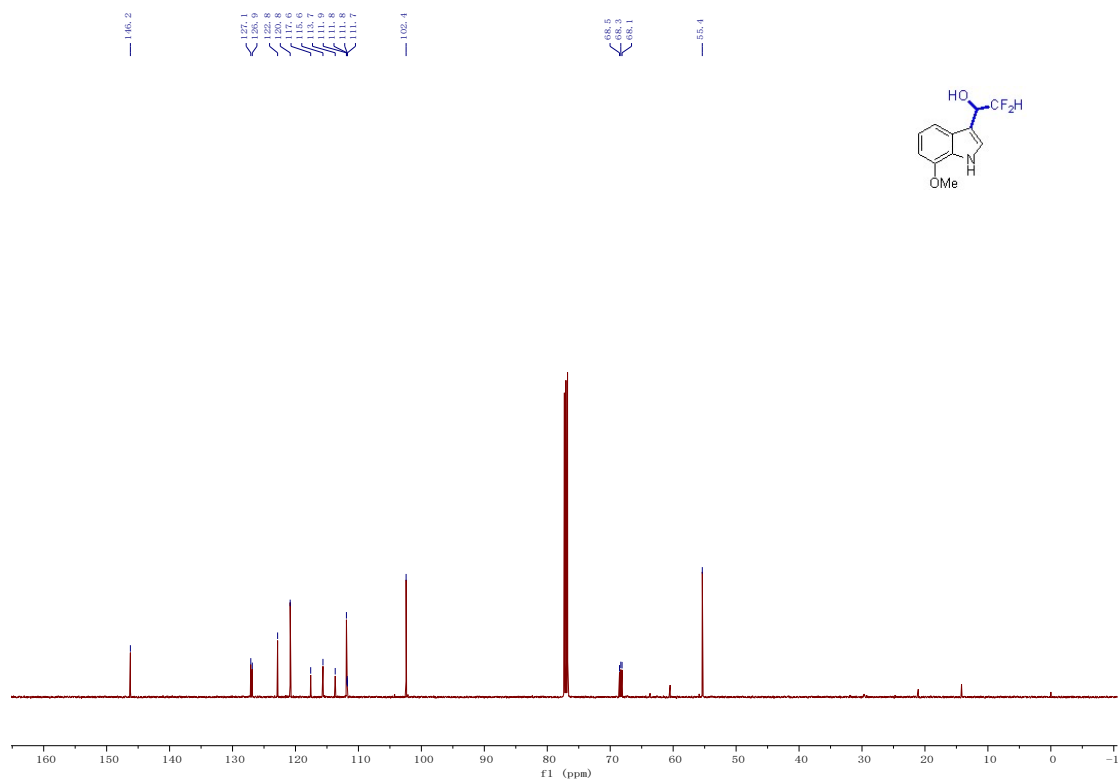
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **3e'**



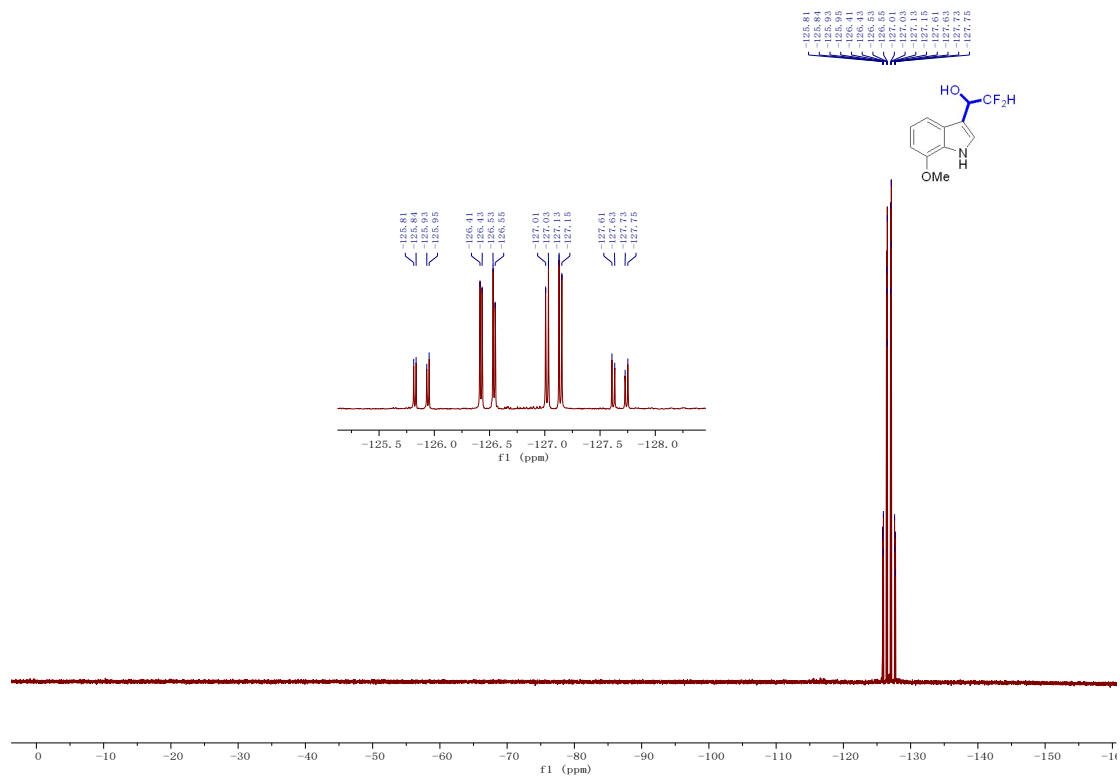
^1H NMR (500 MHz, Chloroform-*d*) spectra of **3f'**



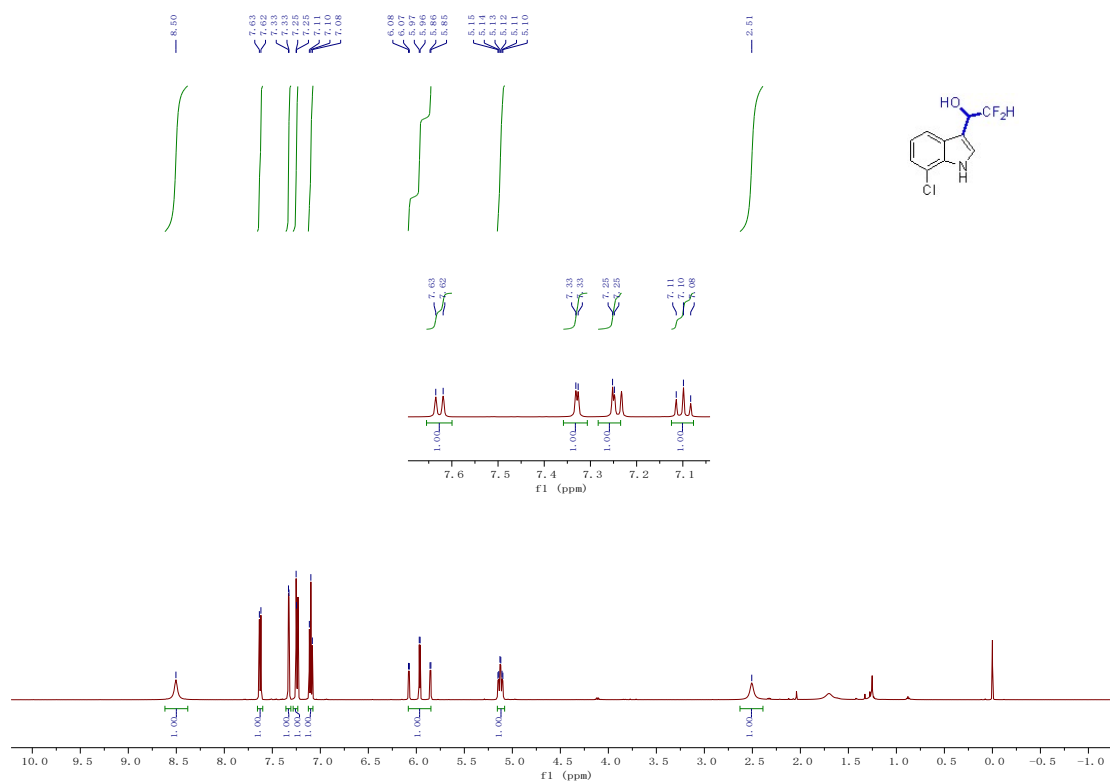
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **3f**



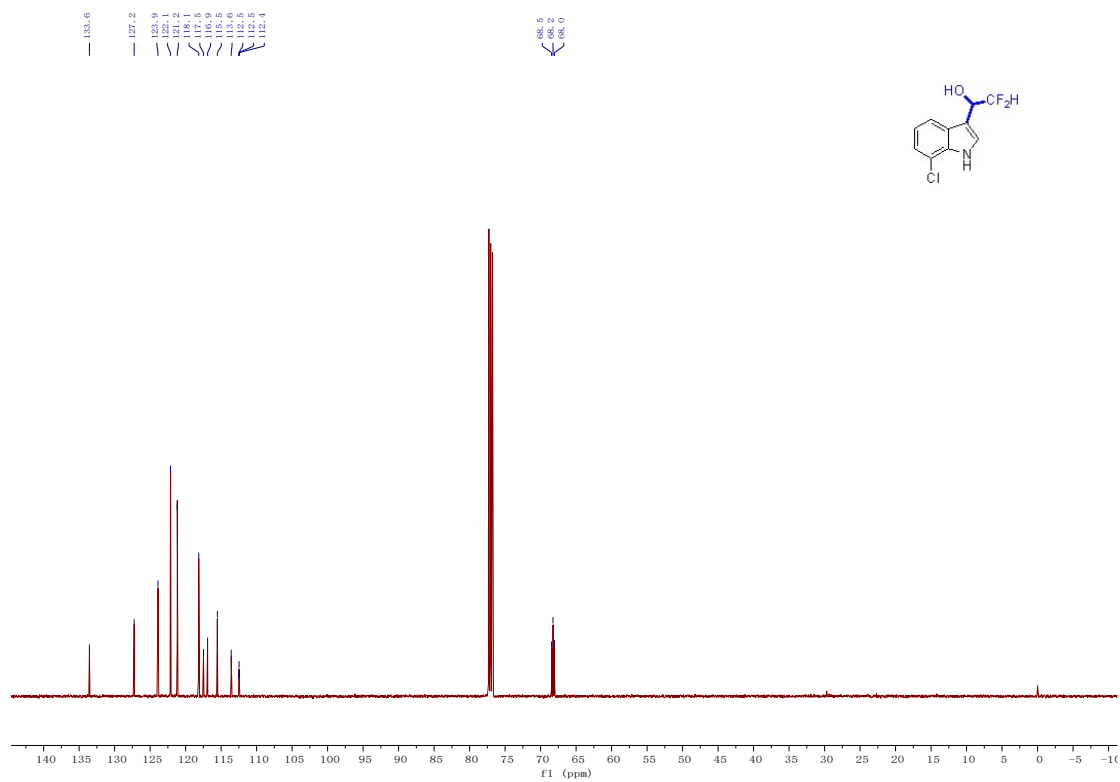
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **3f**



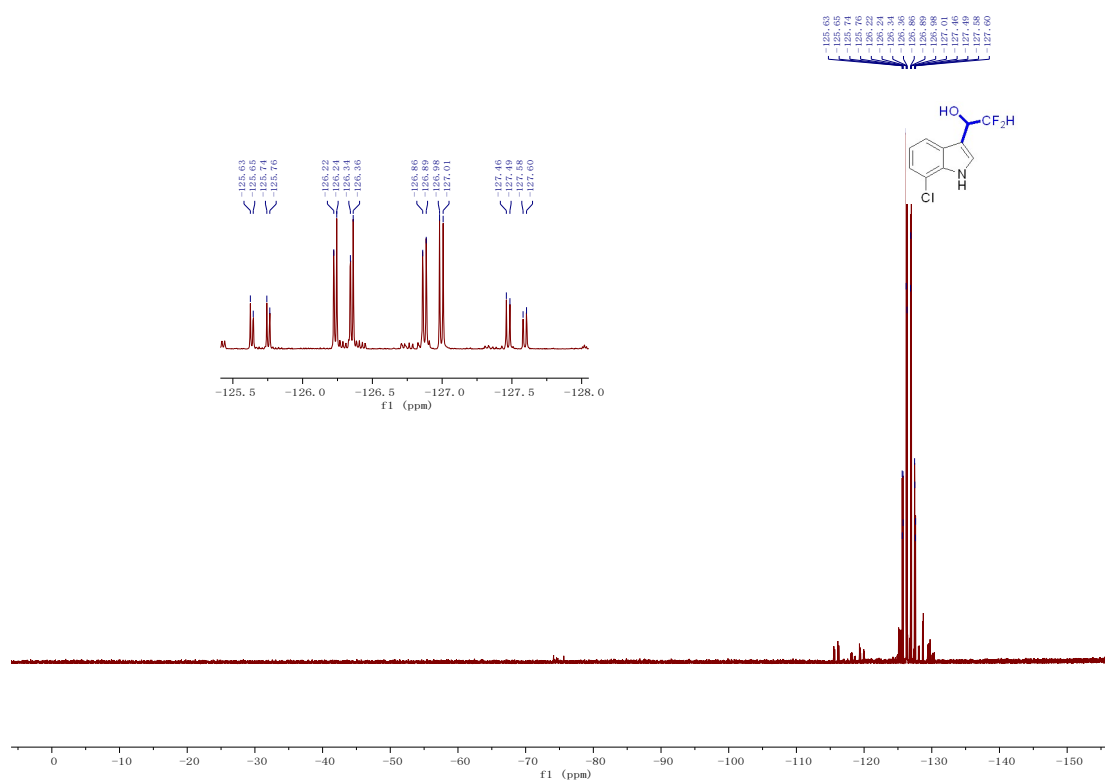
^1H NMR (500 MHz, Chloroform-*d*) spectra of **3g'**



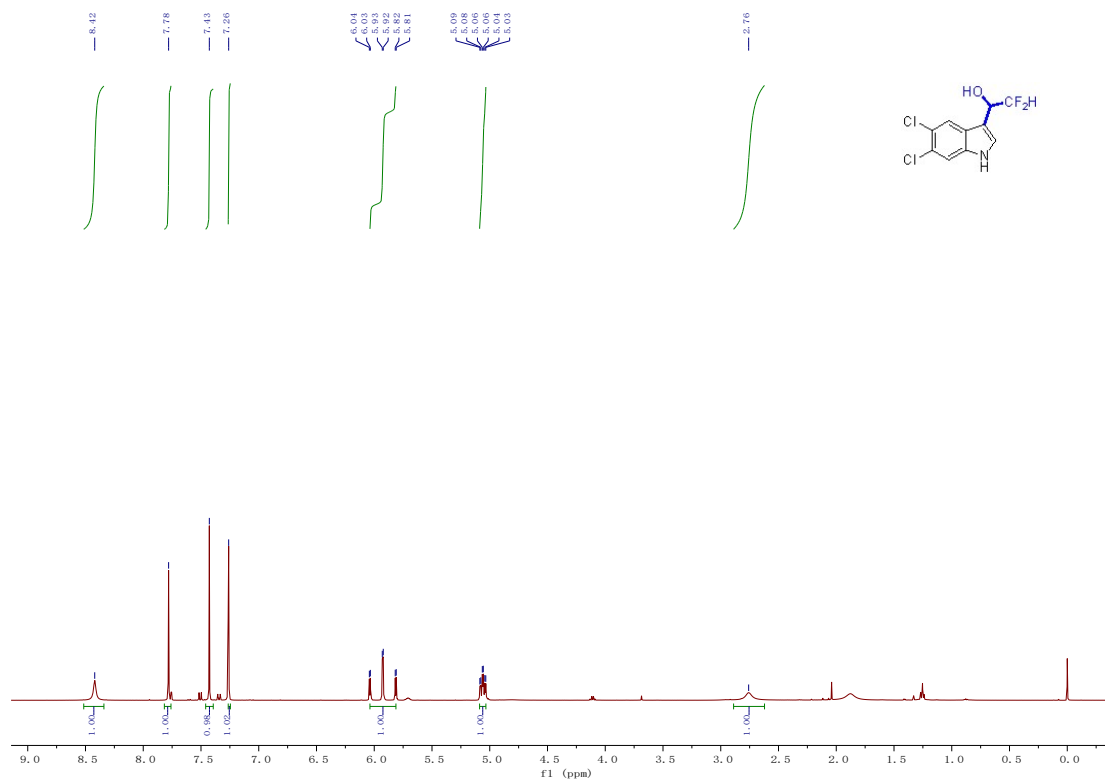
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **3g'**



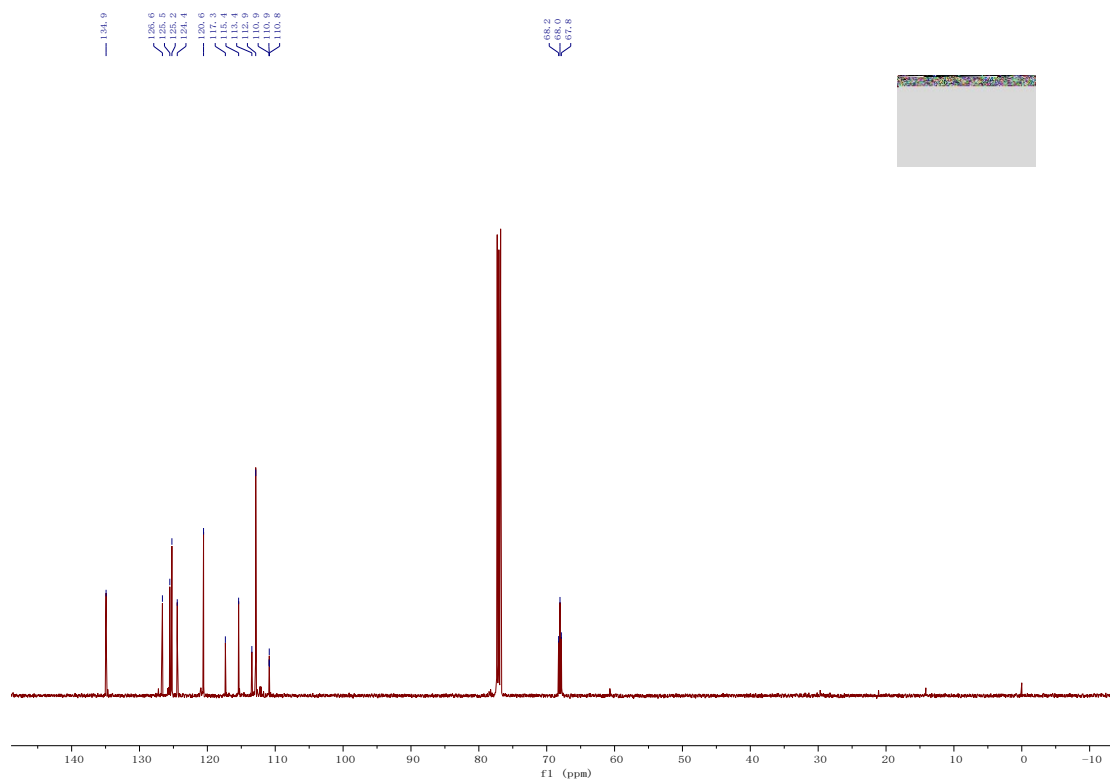
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **3g'**



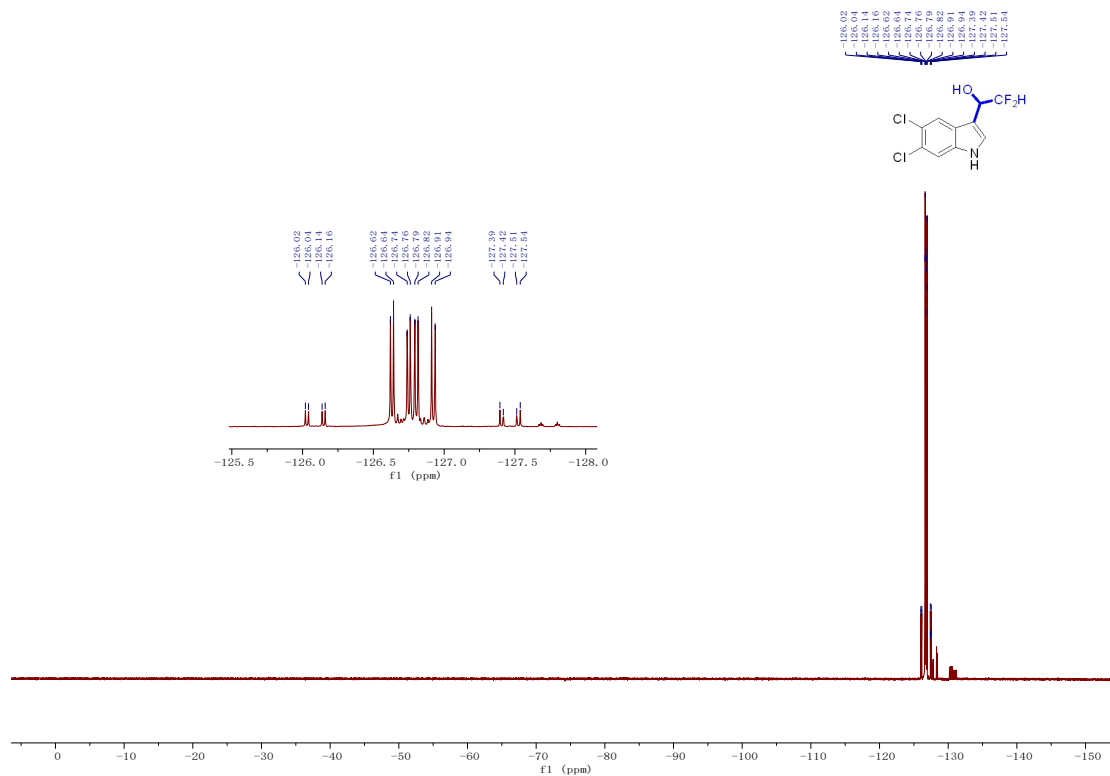
¹H NMR (500 MHz, Chloroform-*d*) spectra of **3h'**



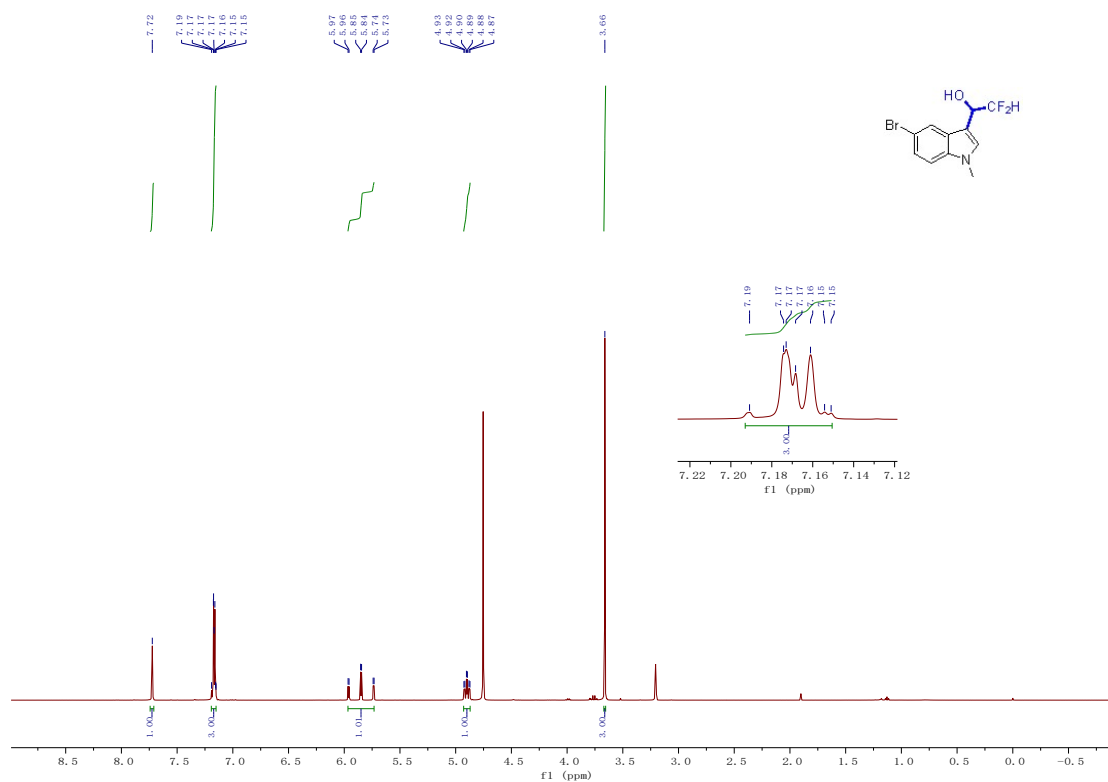
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **3h'**



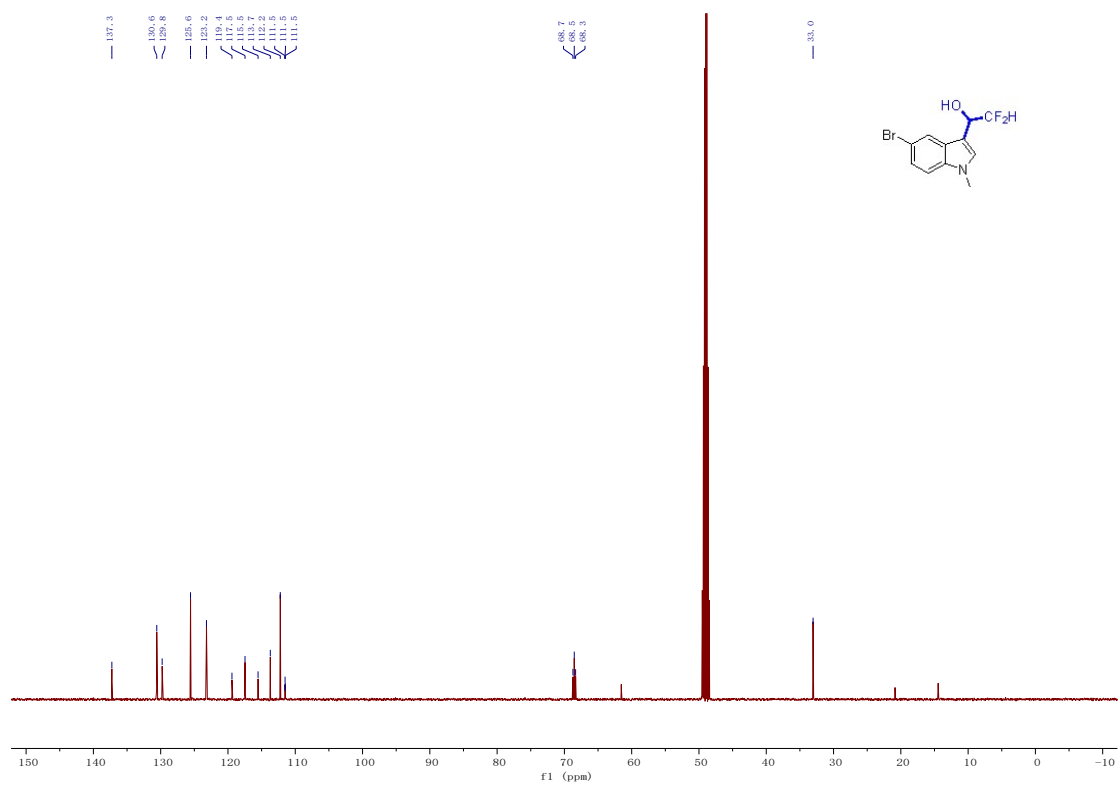
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **3h'**



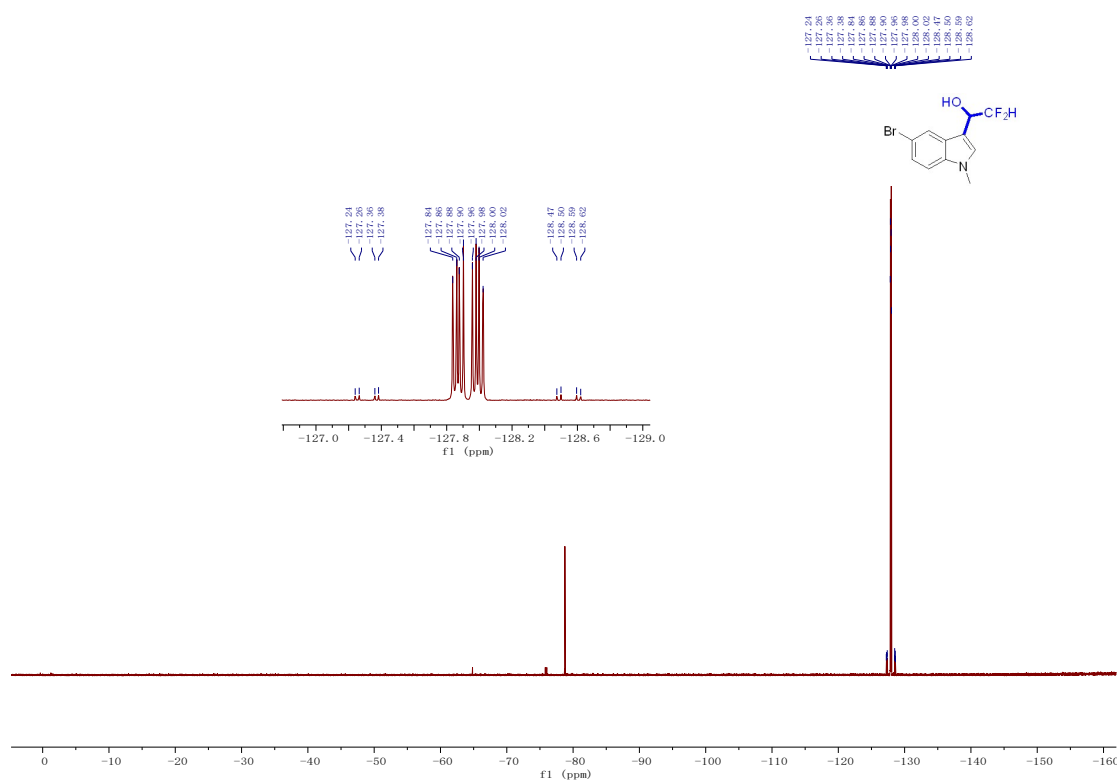
^1H NMR (500 MHz, Methanol- d_4) spectra of **3i'**



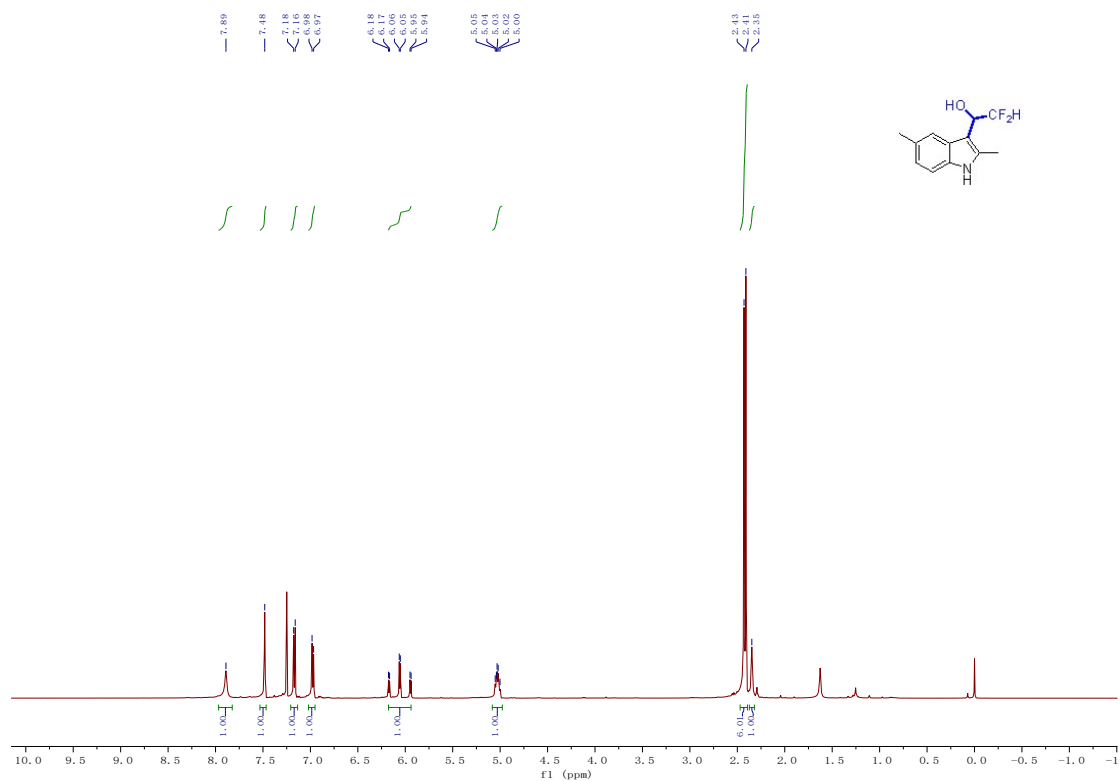
^{13}C NMR (125 MHz, Methanol- d_4) spectra of **3i'**



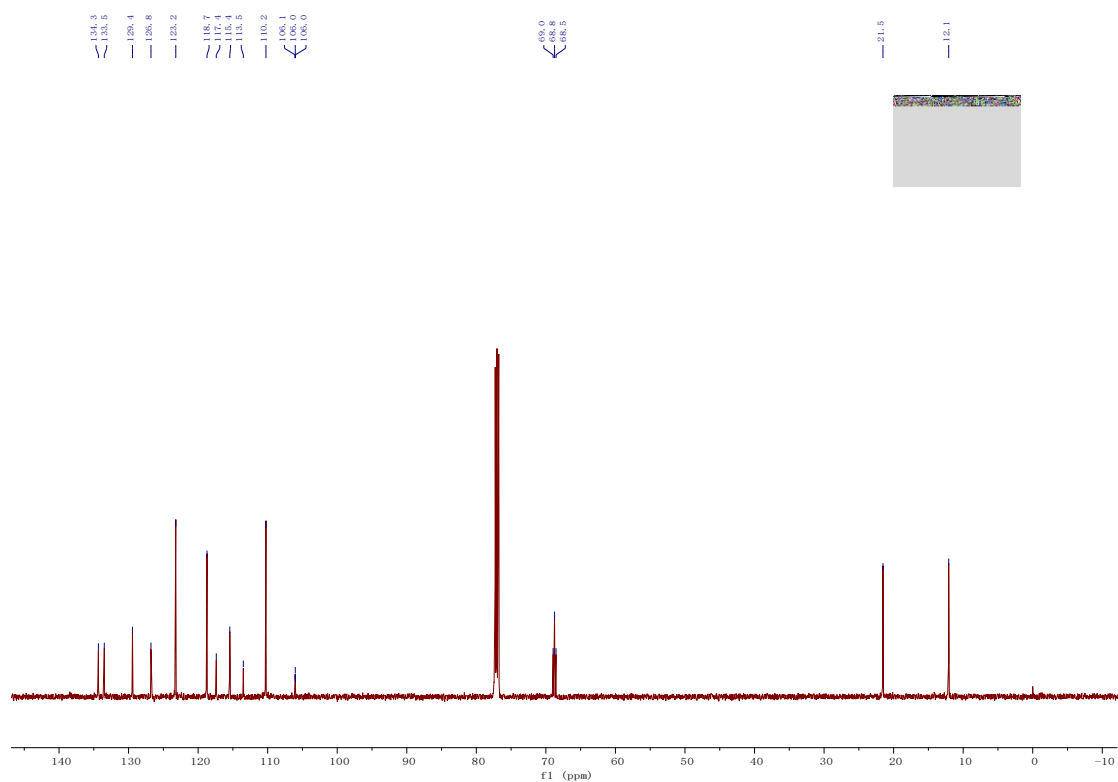
^{19}F NMR (470 MHz, Methanol- d_4) spectra of **3i'**



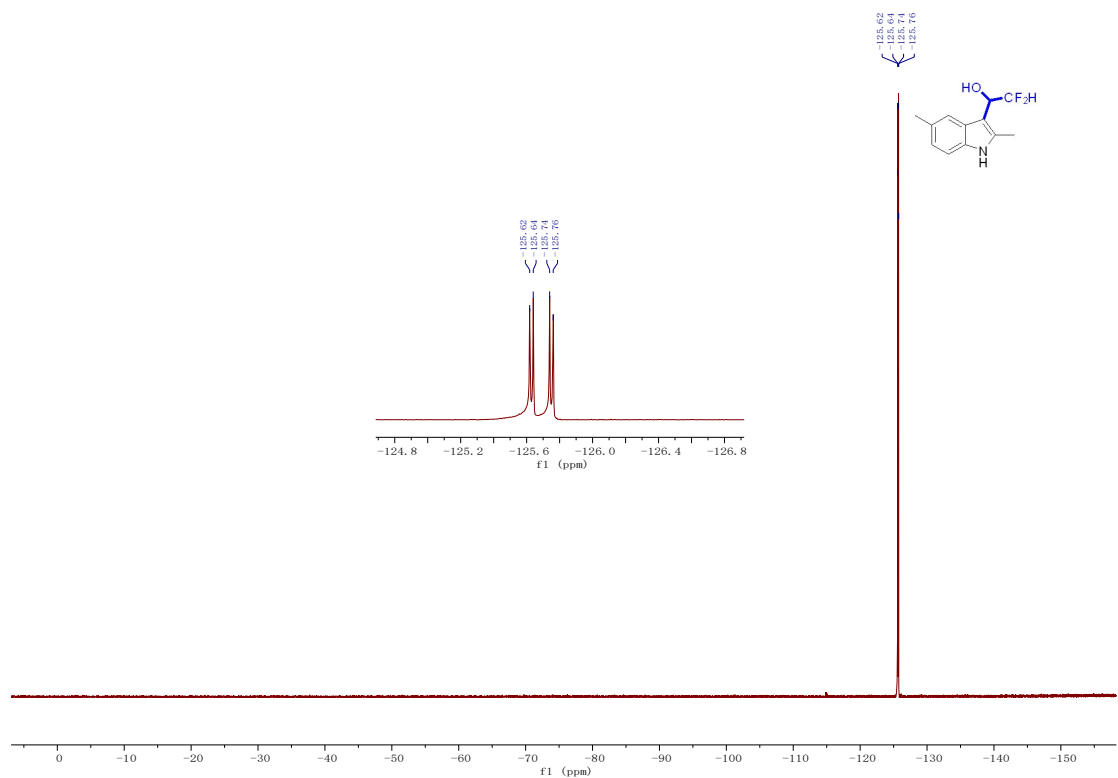
^1H NMR (500 MHz, Chloroform- d) spectra of **3j'**



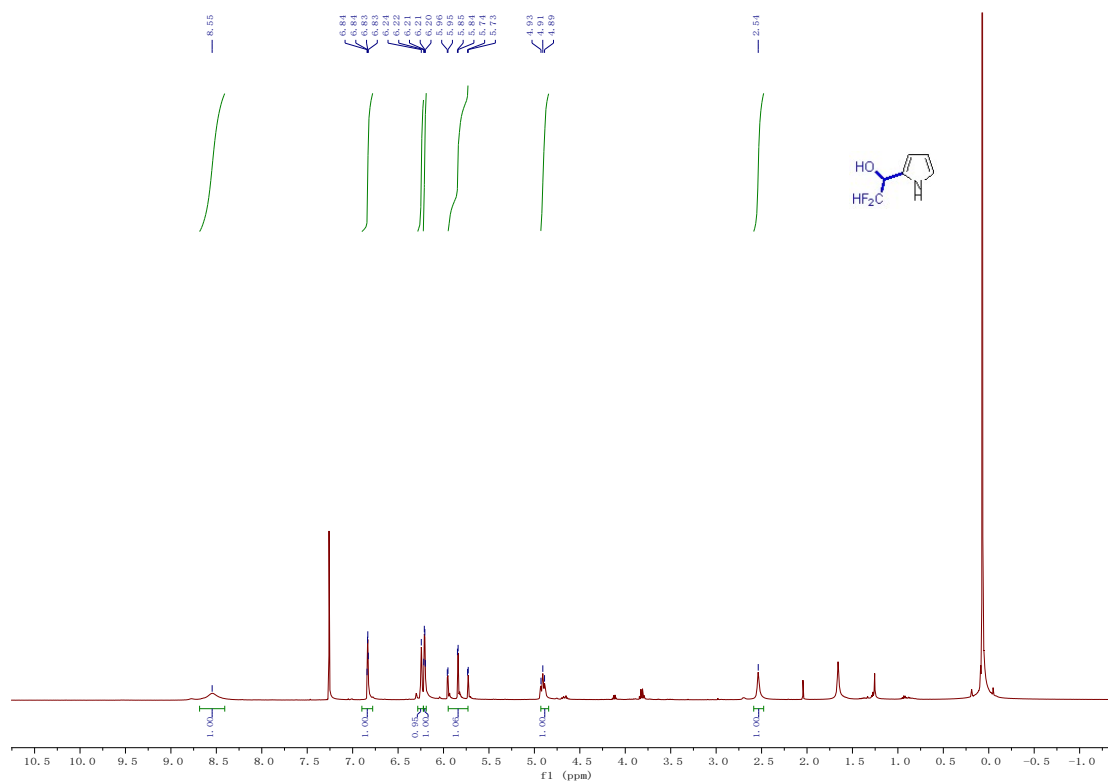
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **3j'**



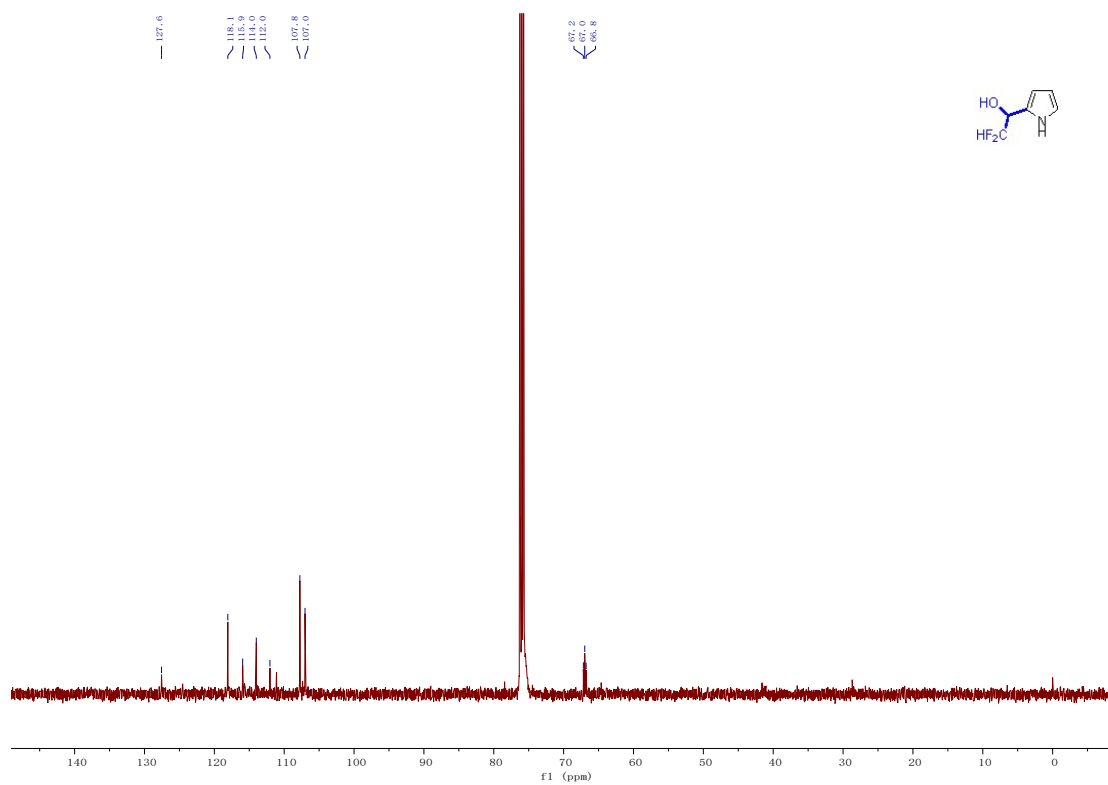
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **3j'**



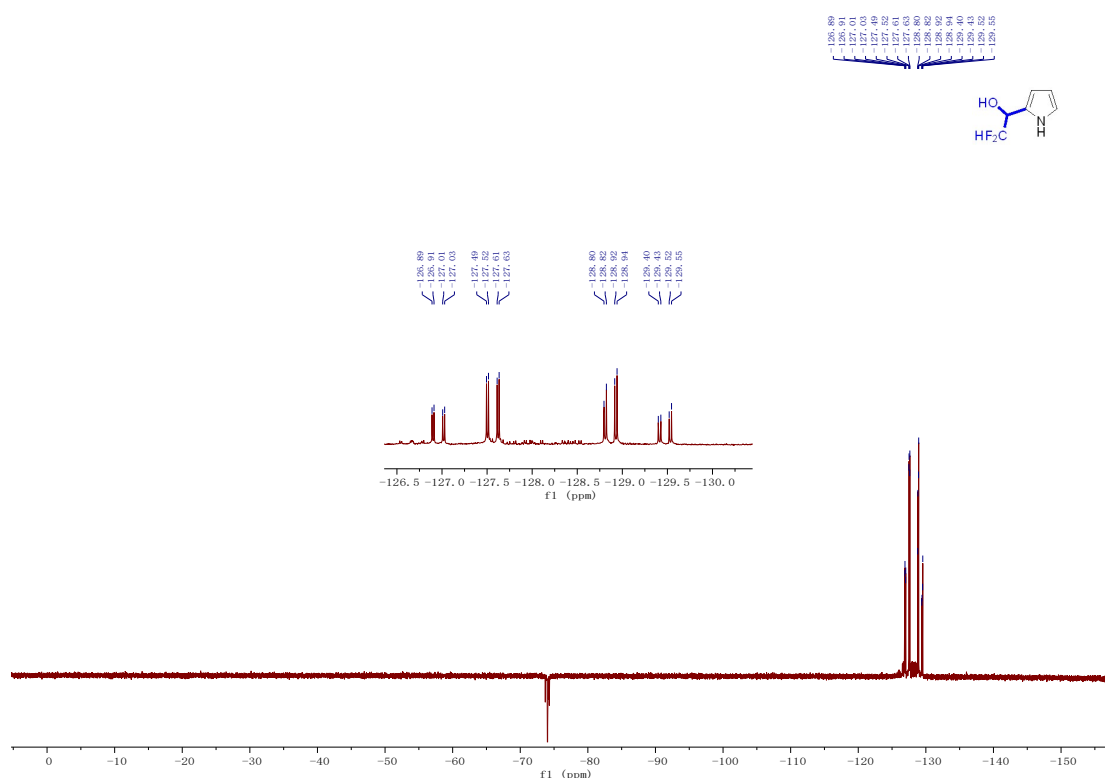
^1H NMR (500 MHz, Chloroform-*d*) spectra of **31'**



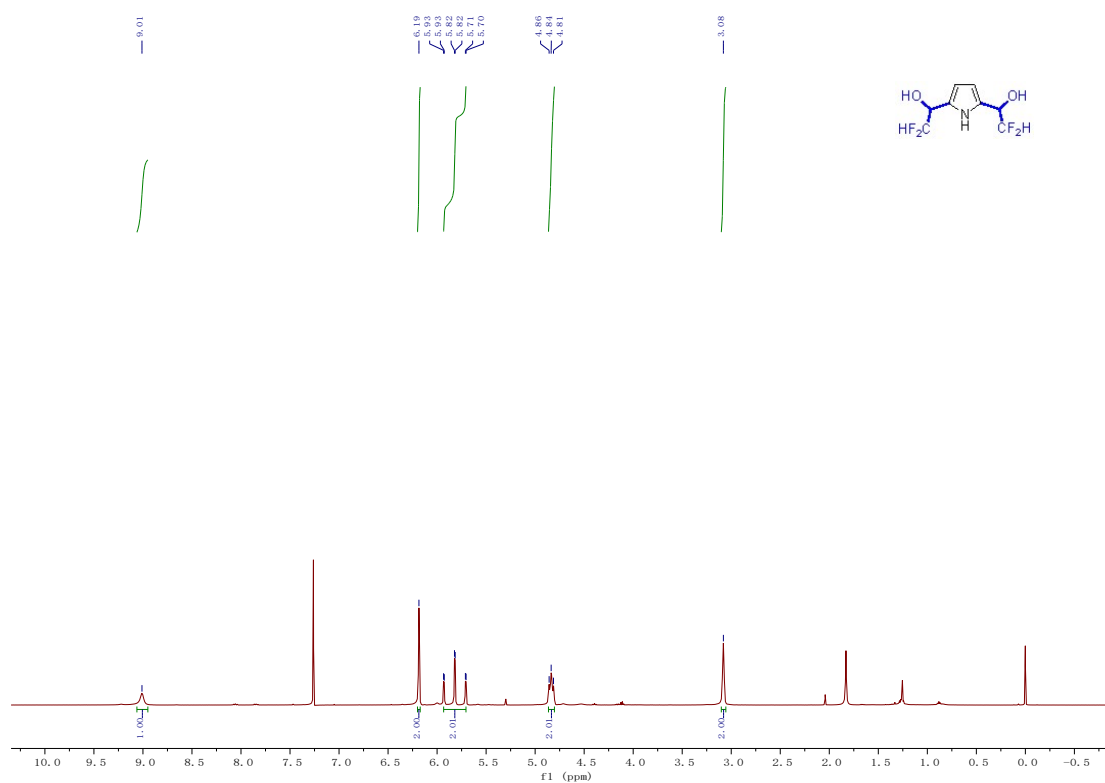
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **31'**



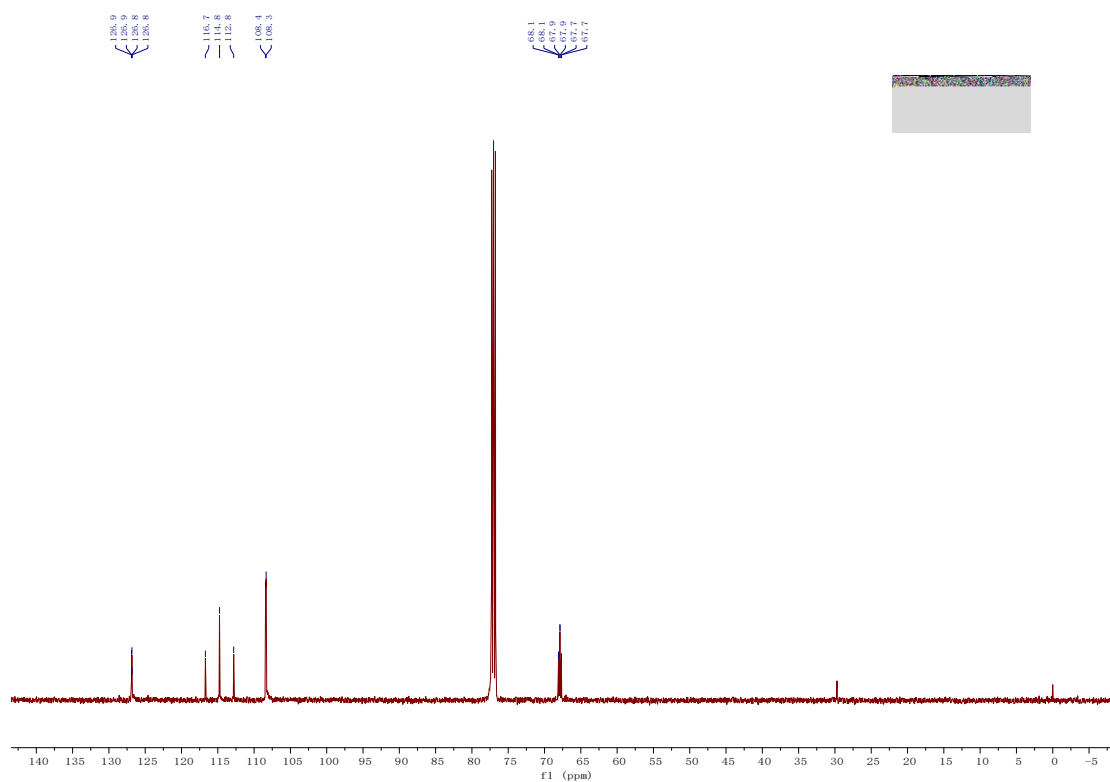
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **3I'**



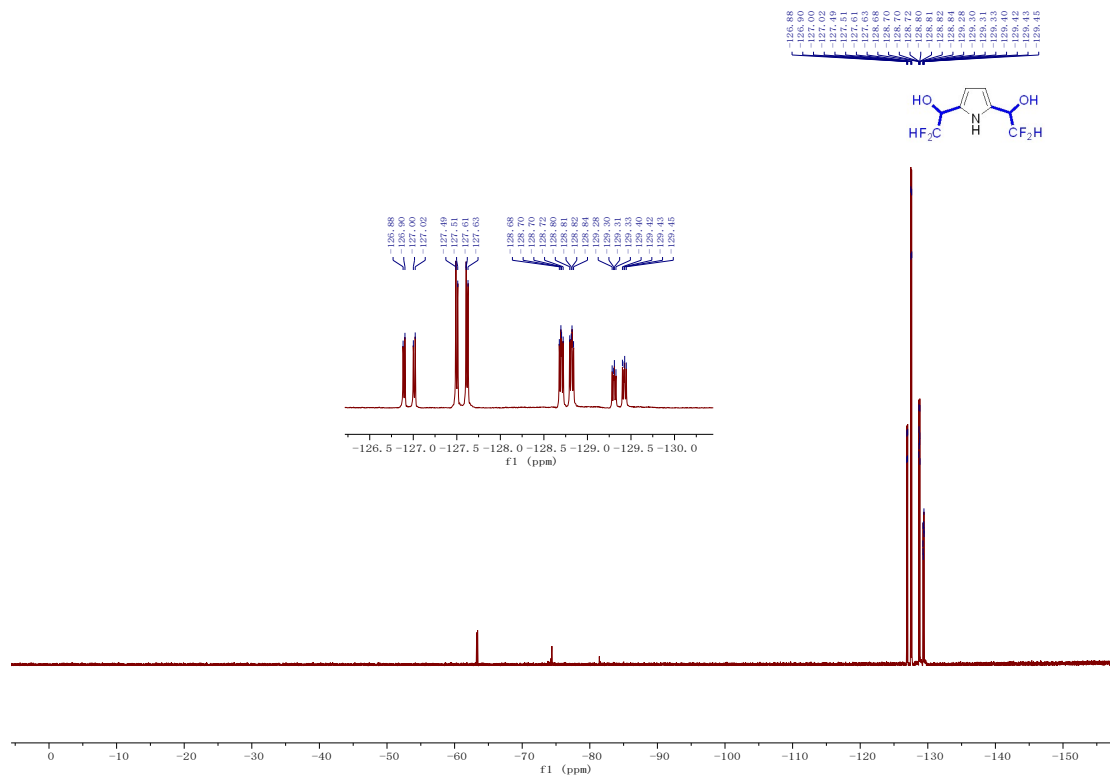
^1H NMR (500 MHz, Chloroform-*d*) spectra of **3I''**



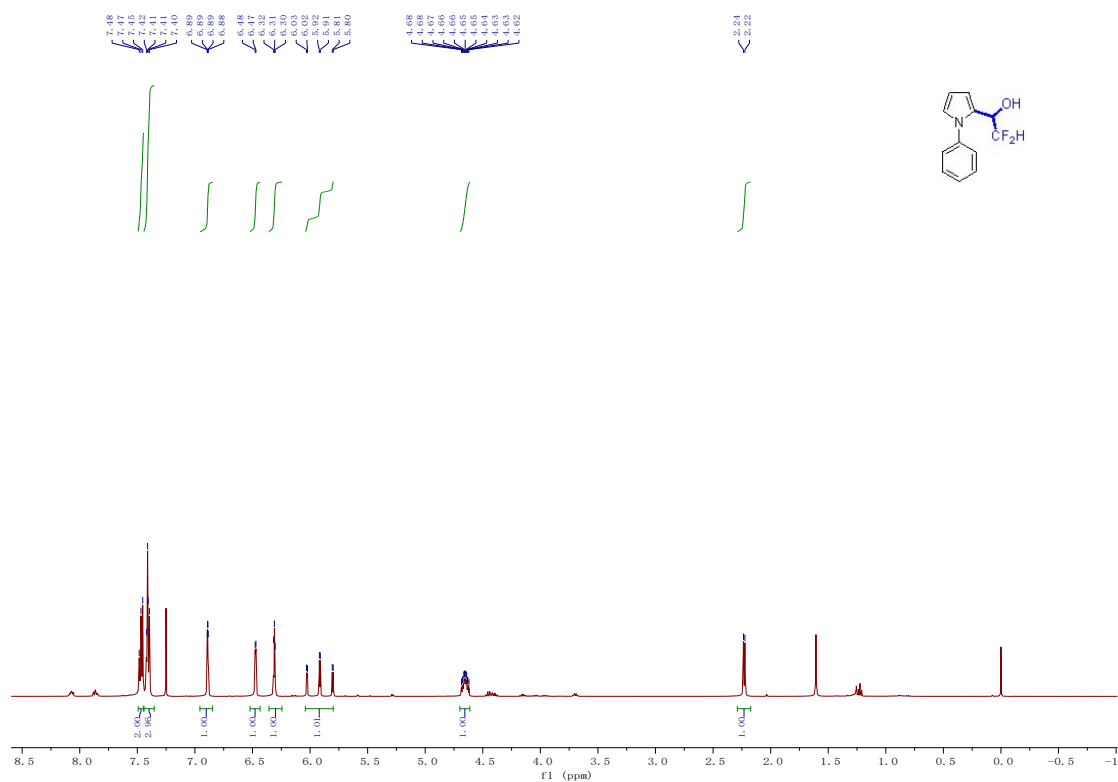
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **31''**



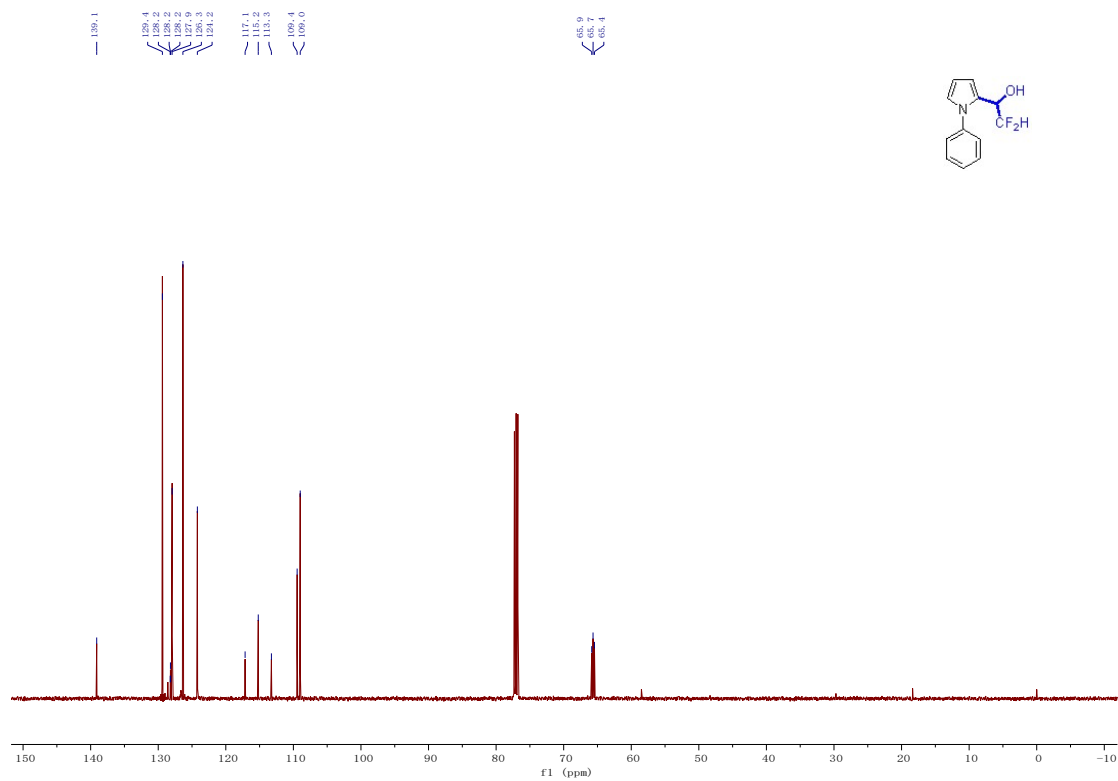
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **31''**



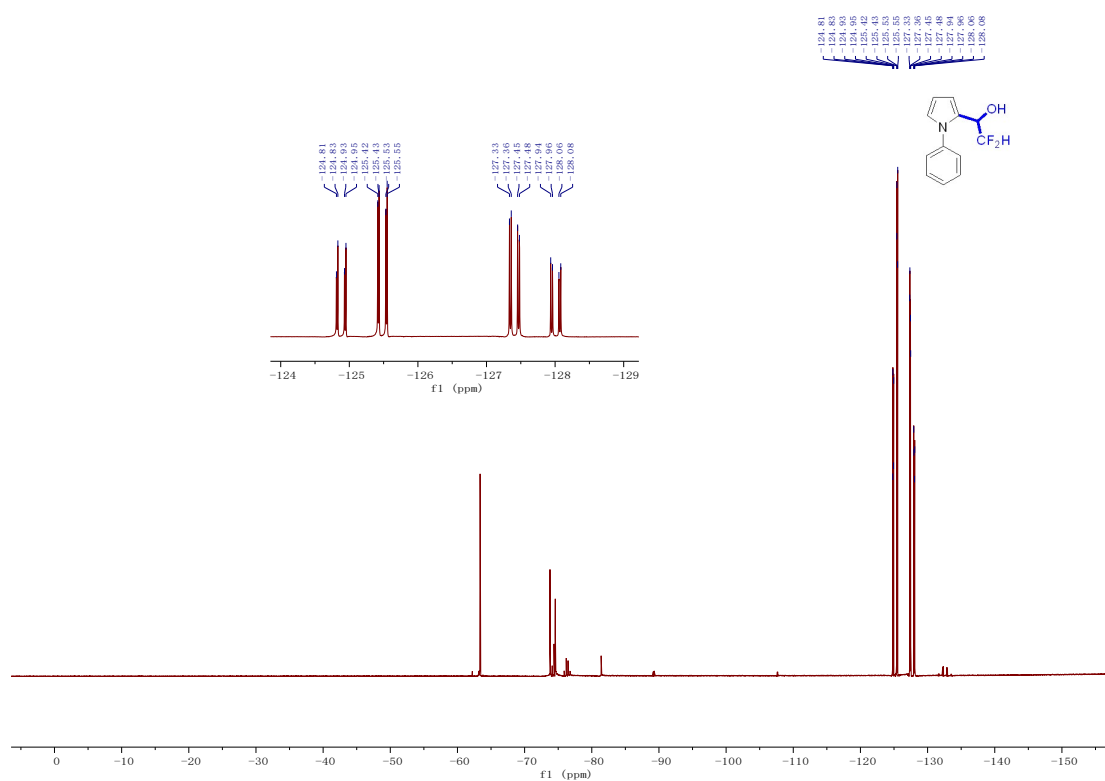
^1H NMR (500 MHz, Chloroform-*d*) spectra of **3m'**



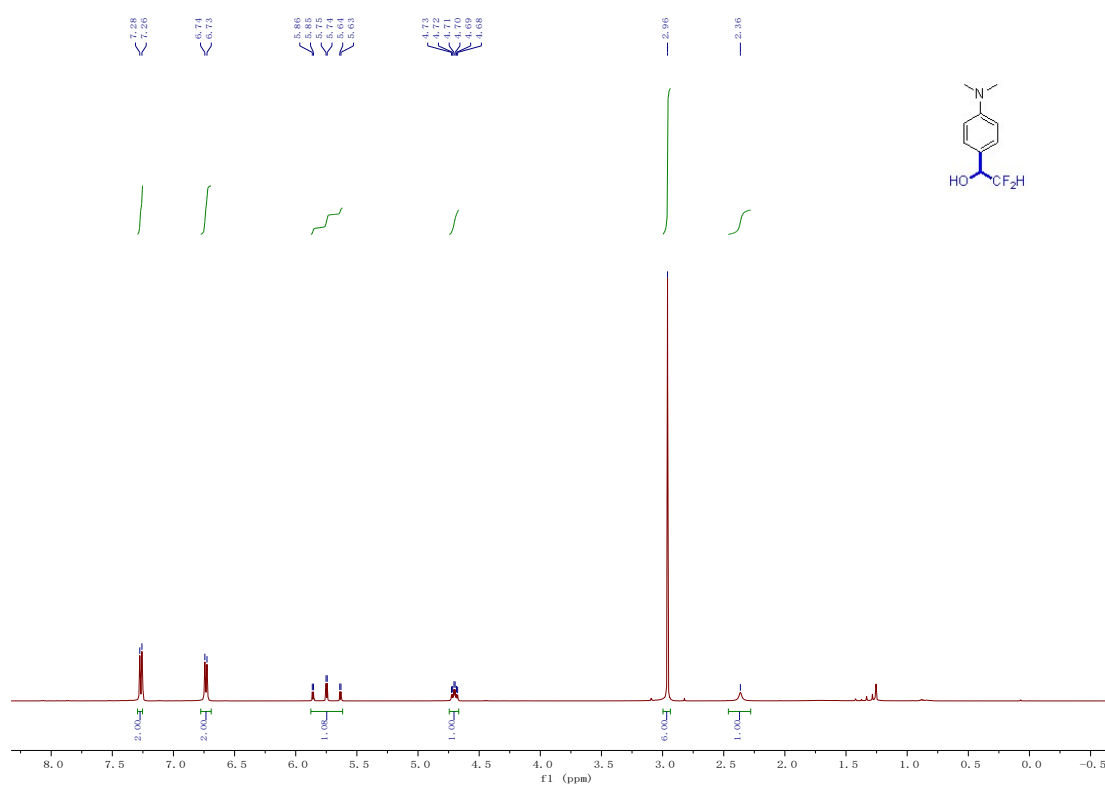
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **3m'**



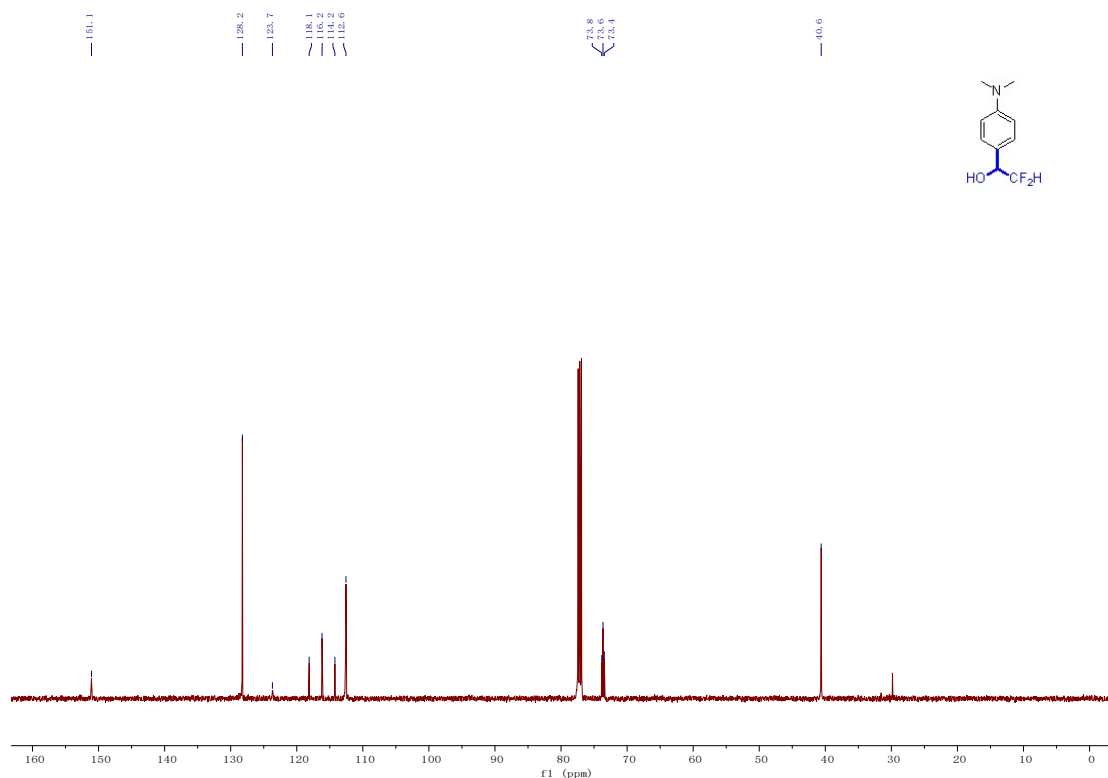
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **3m'**



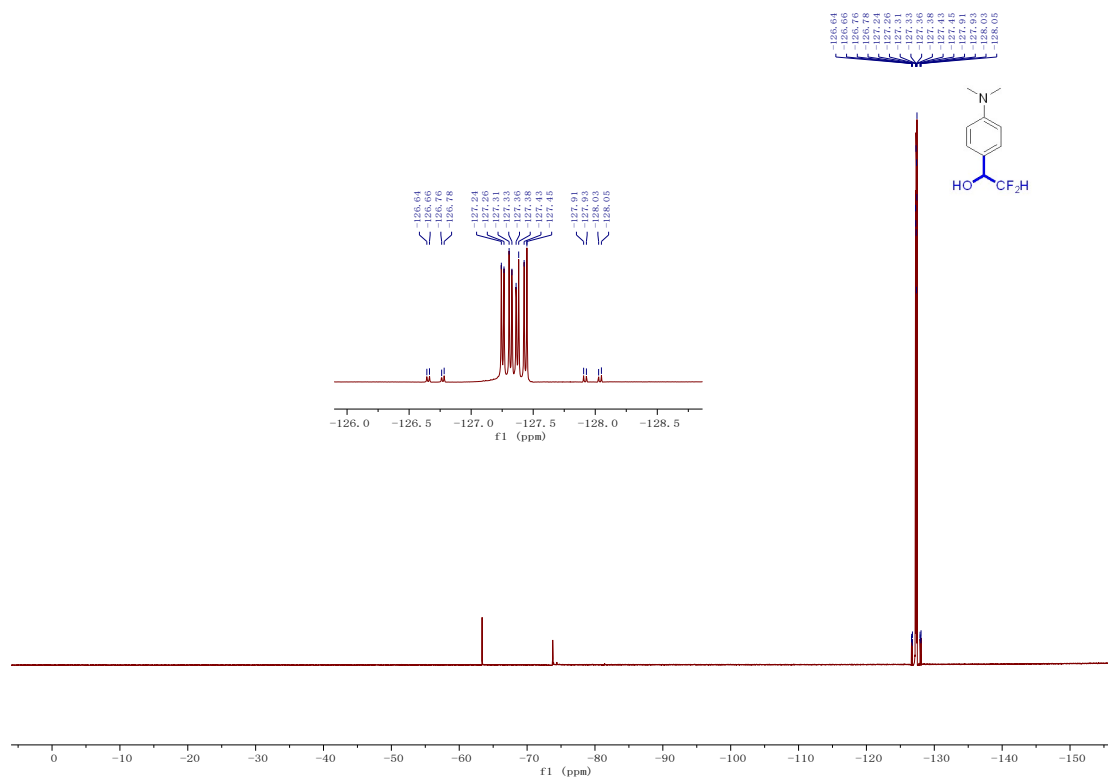
¹H NMR (500 MHz, Chloroform-*d*) spectra of **5a**



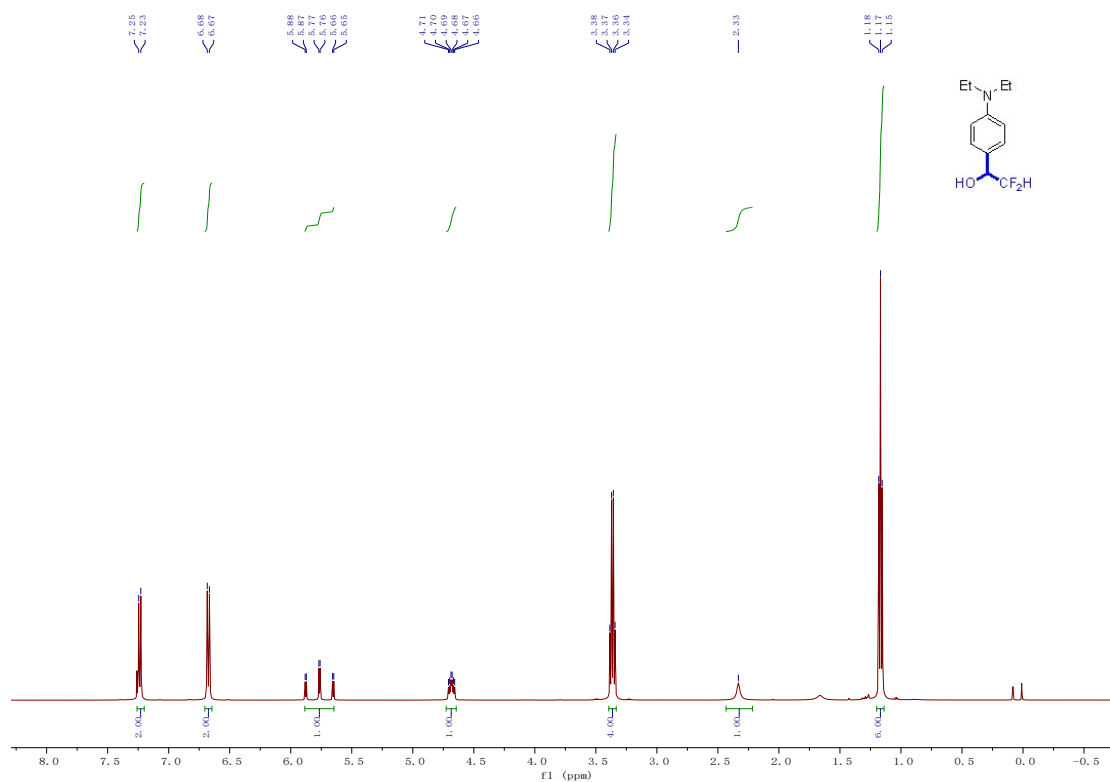
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **5a**



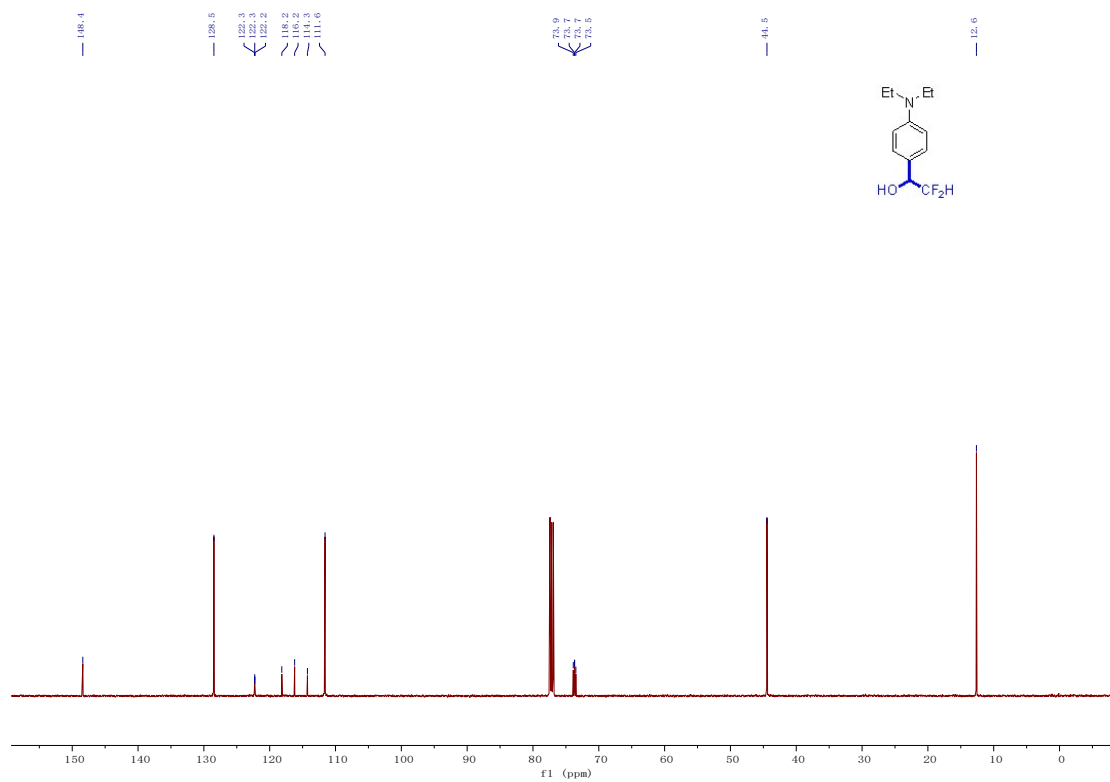
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **5a**



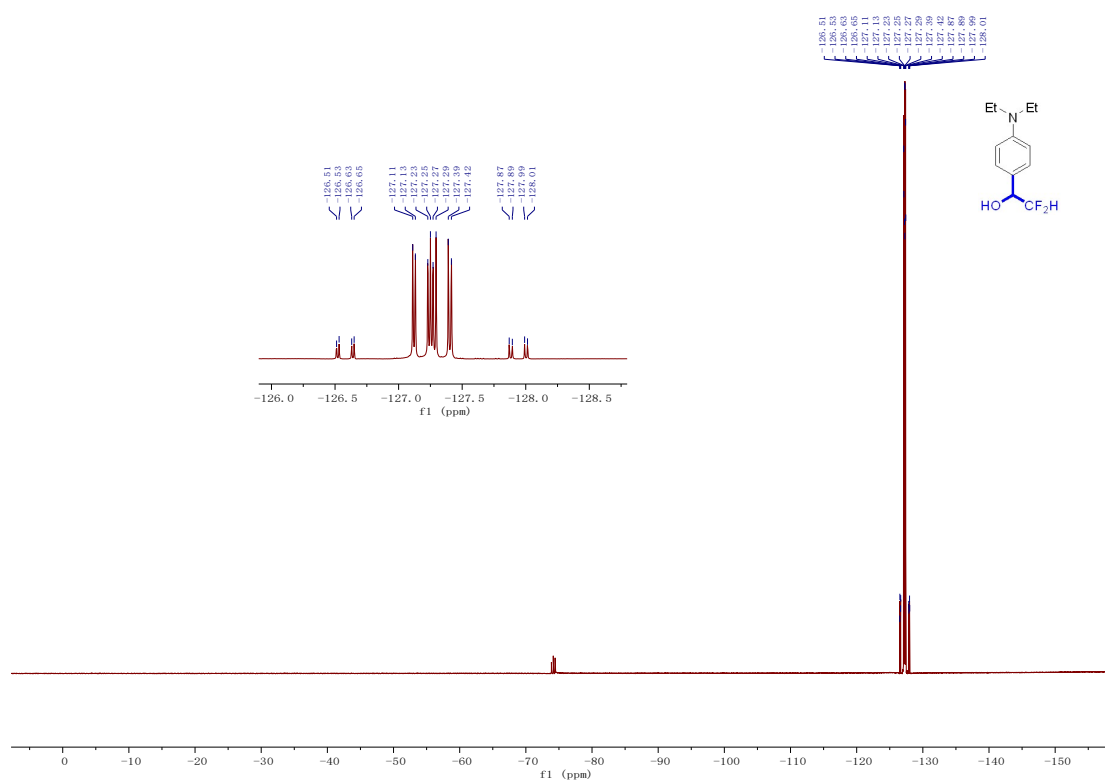
¹H NMR (500 MHz, Chloroform-*d*) spectra of **5b**



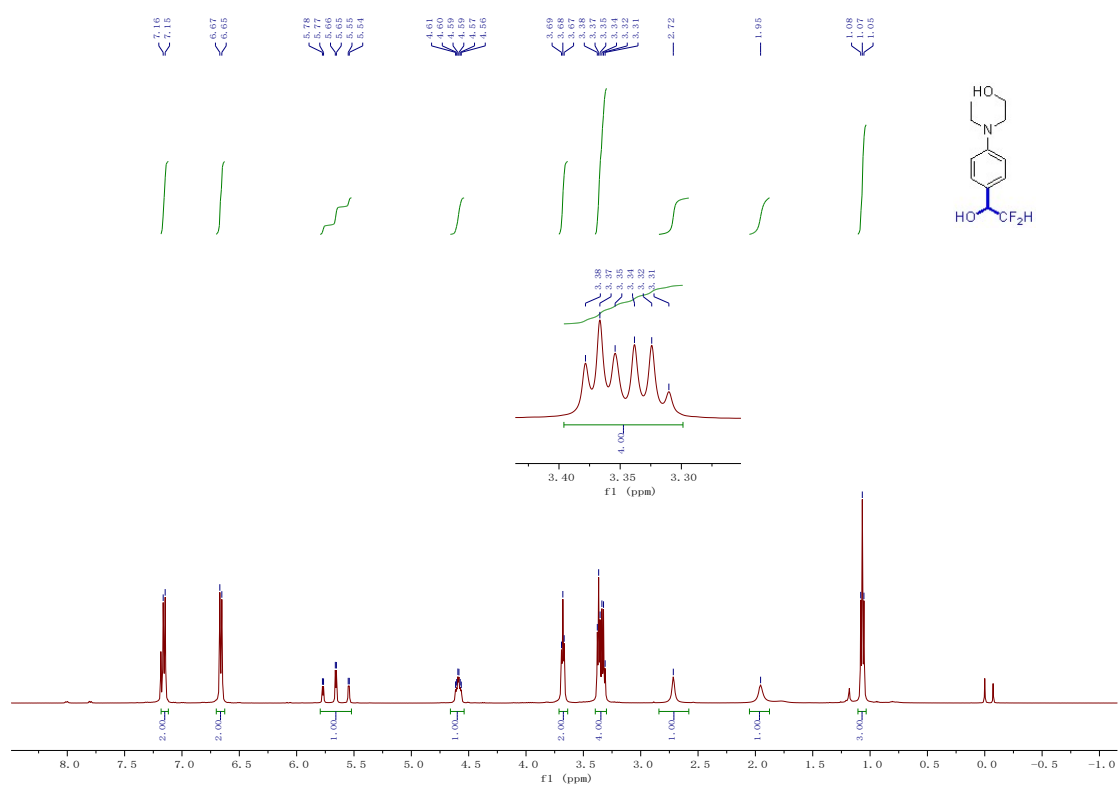
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **5b**



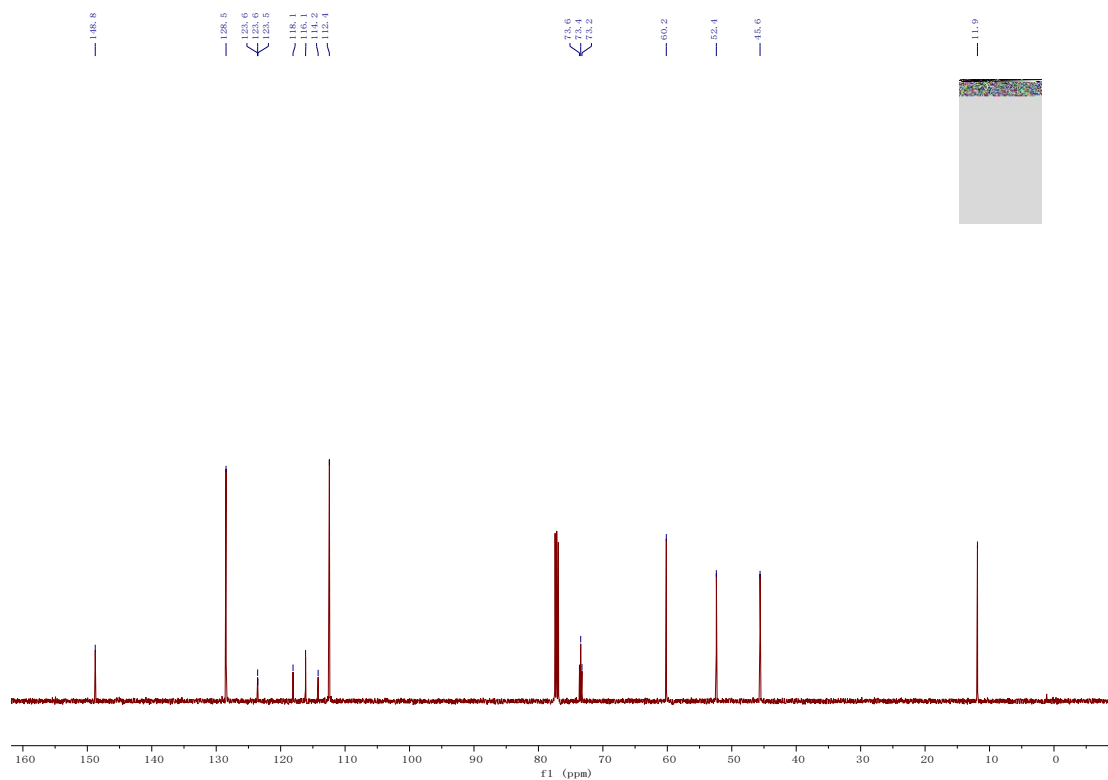
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **5b**



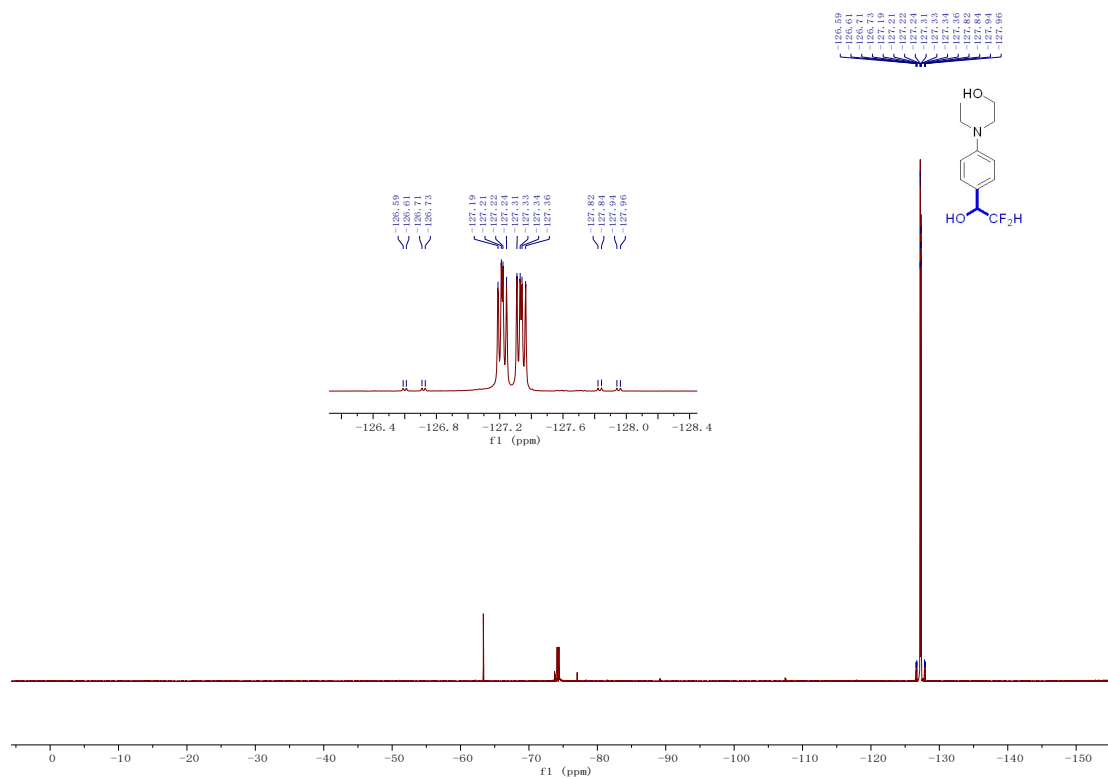
^1H NMR (500 MHz, Chloroform-*d*) spectra of **5c**



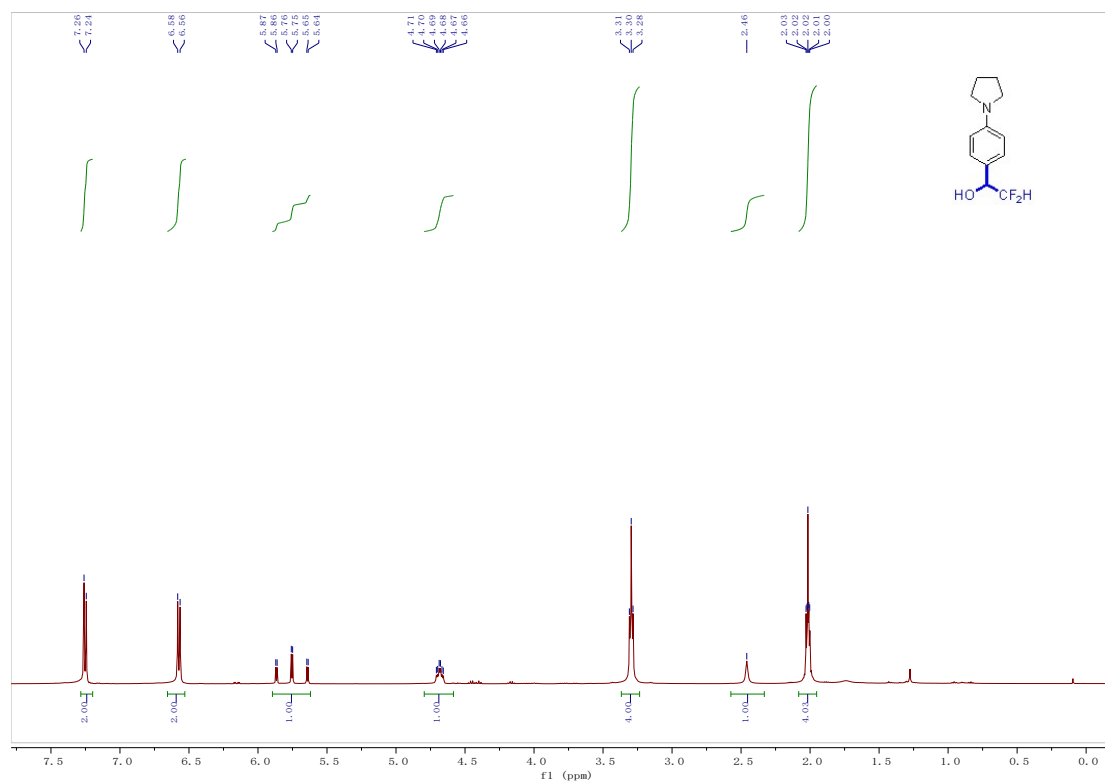
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **5c**



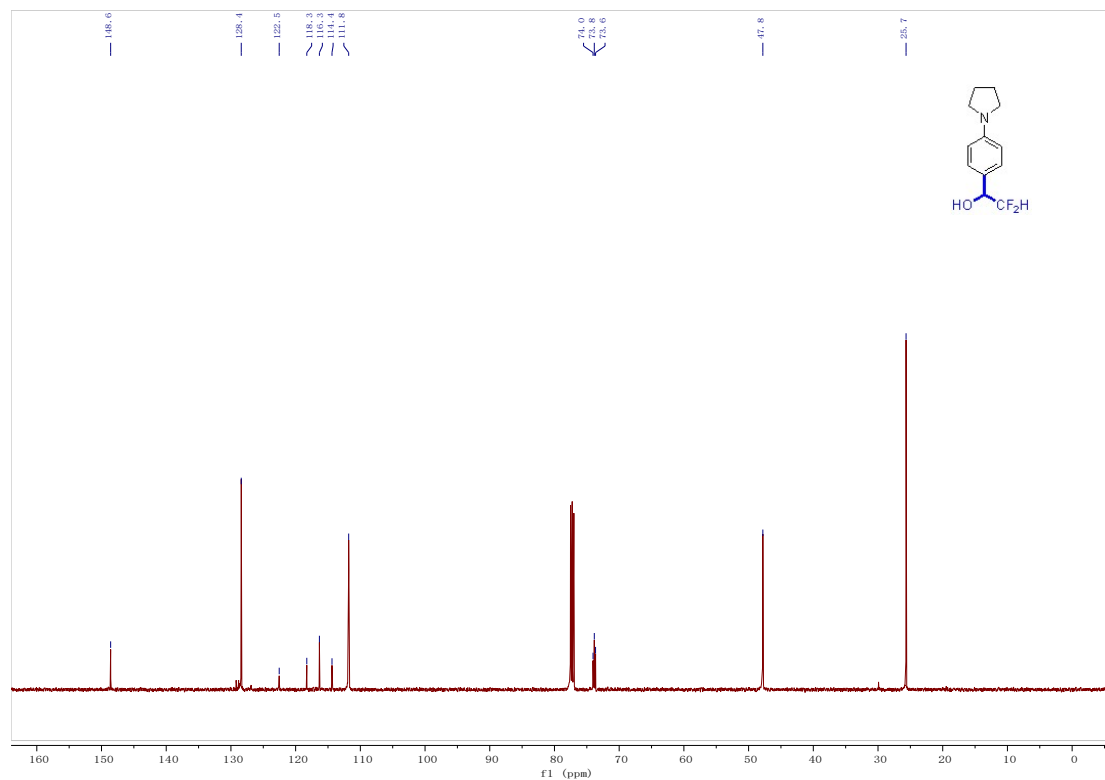
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **5c**



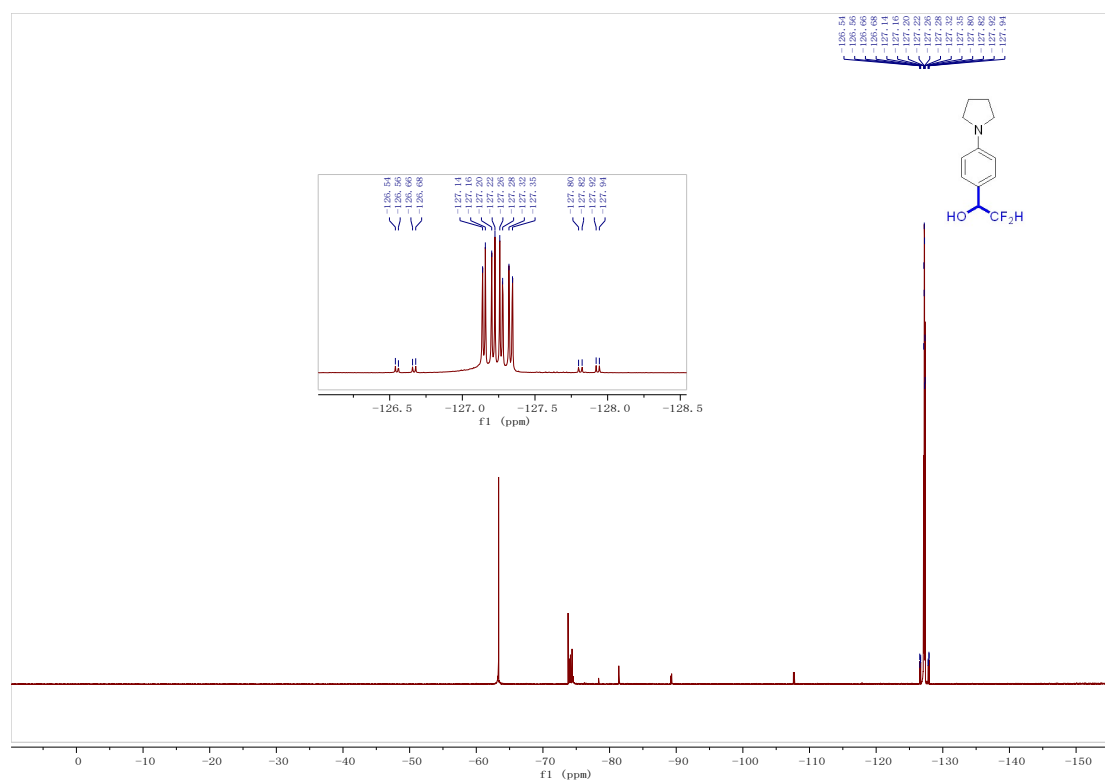
¹H NMR (500 MHz, Chloroform-*d*) spectra of **5d**



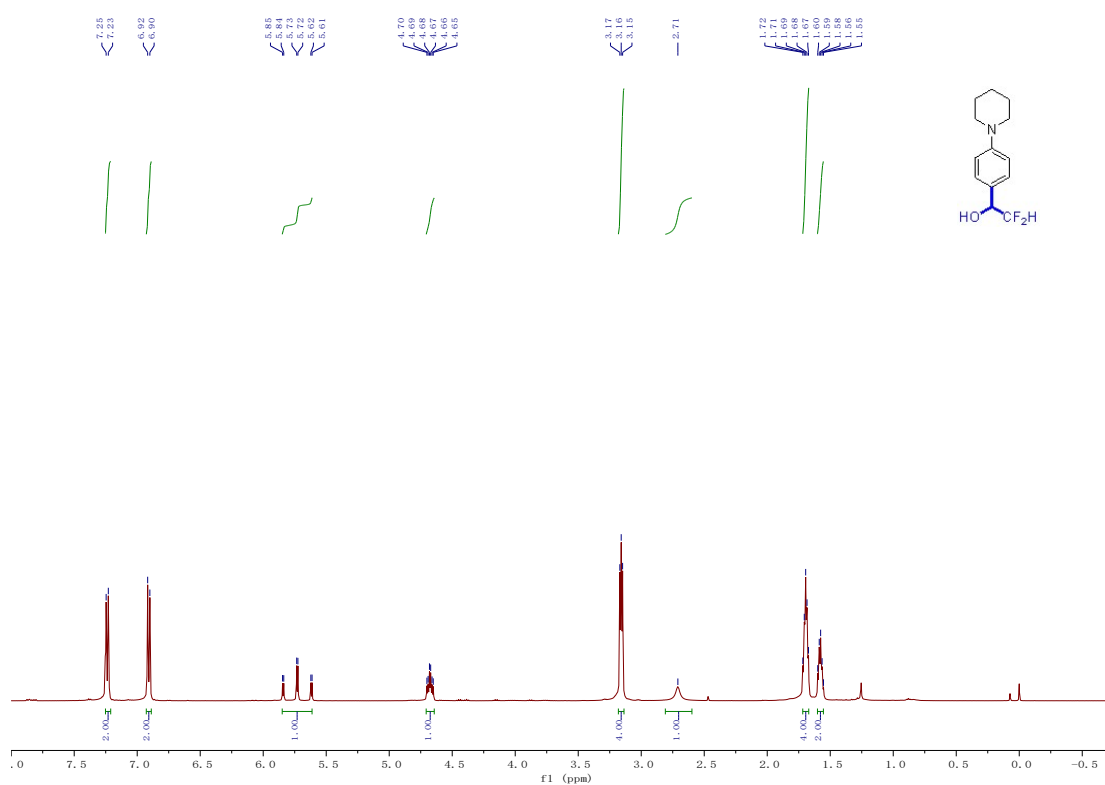
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **5d**



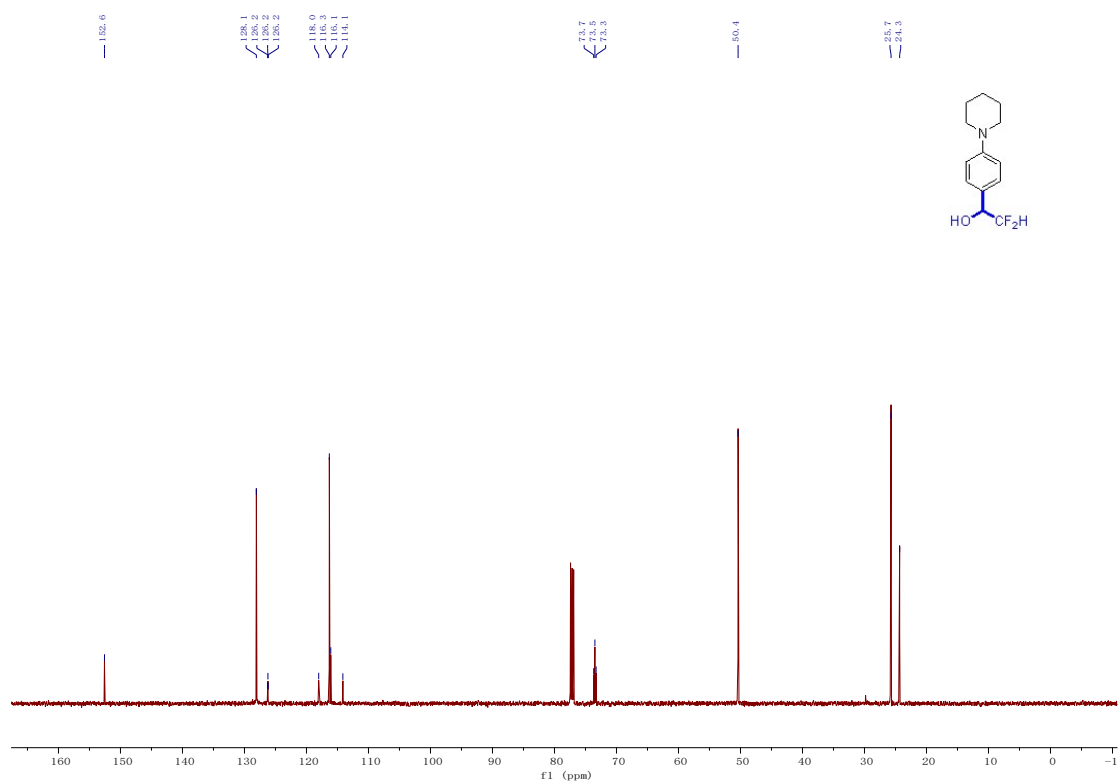
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **5d**



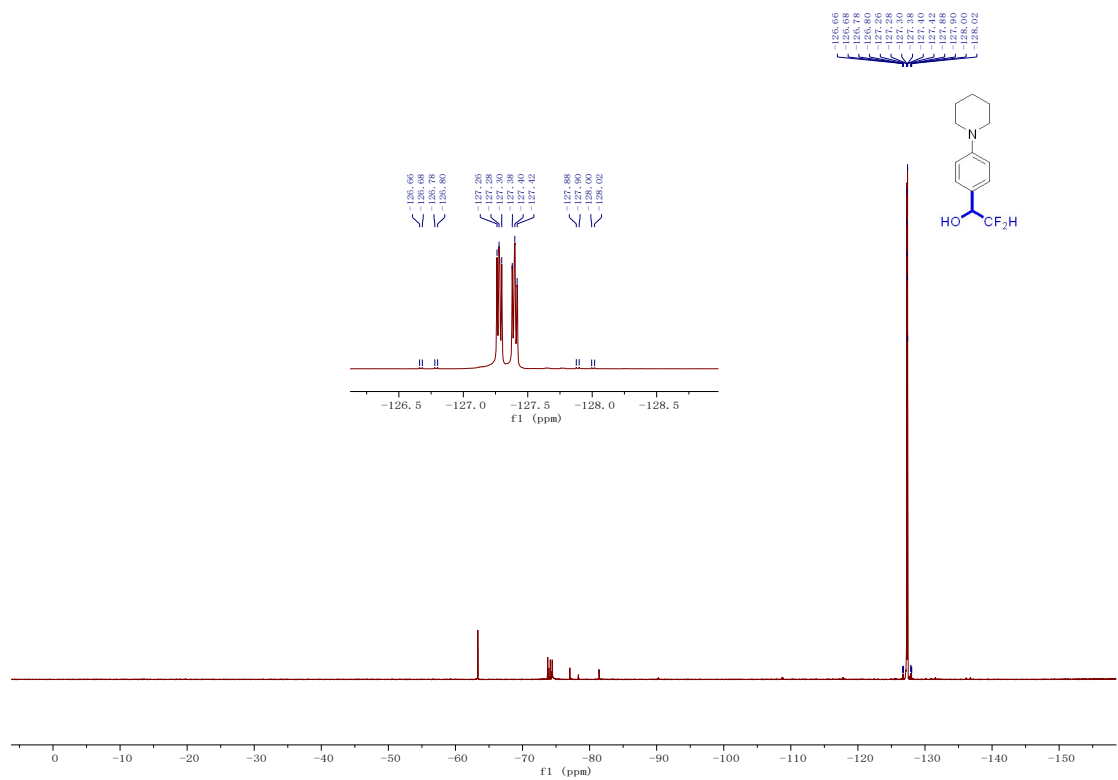
^1H NMR (500 MHz, Chloroform-*d*) spectra of **5e**



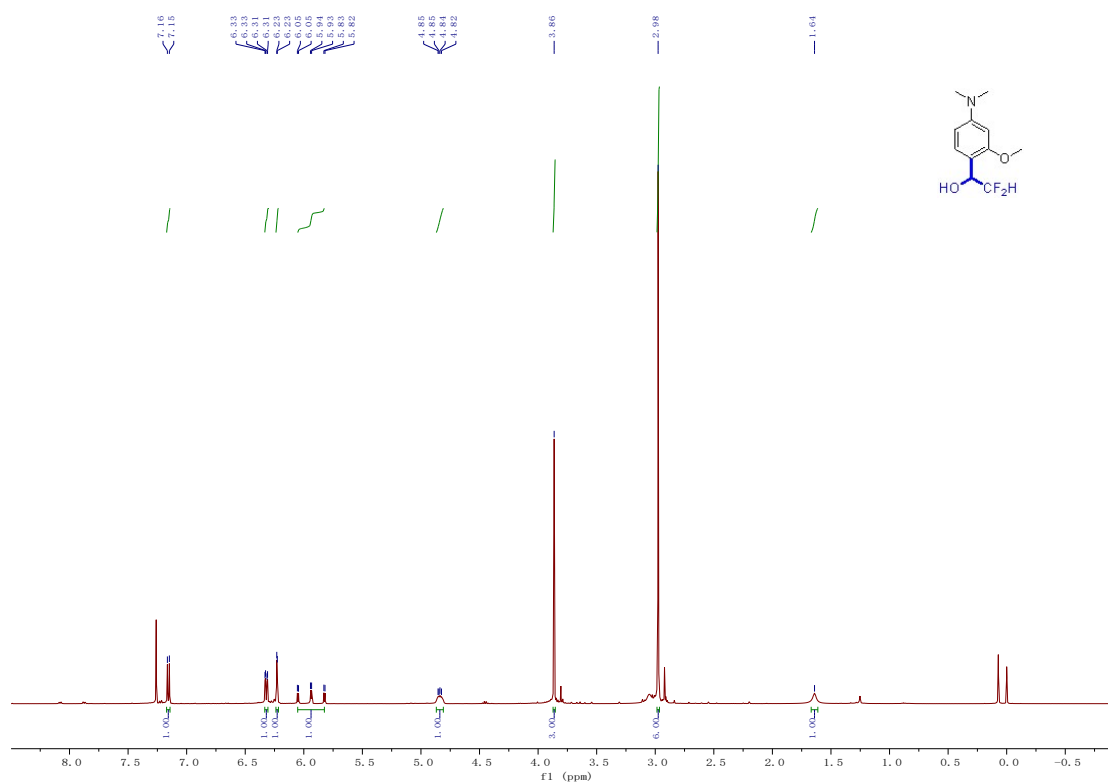
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **5e**



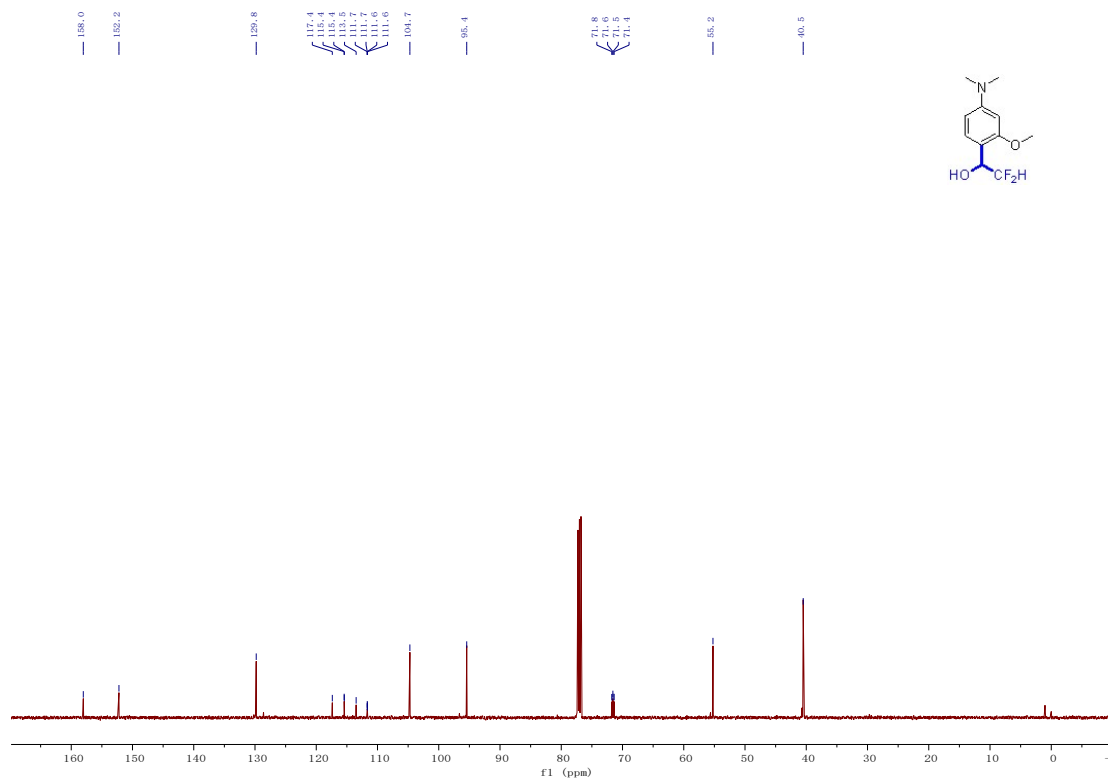
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **5e**



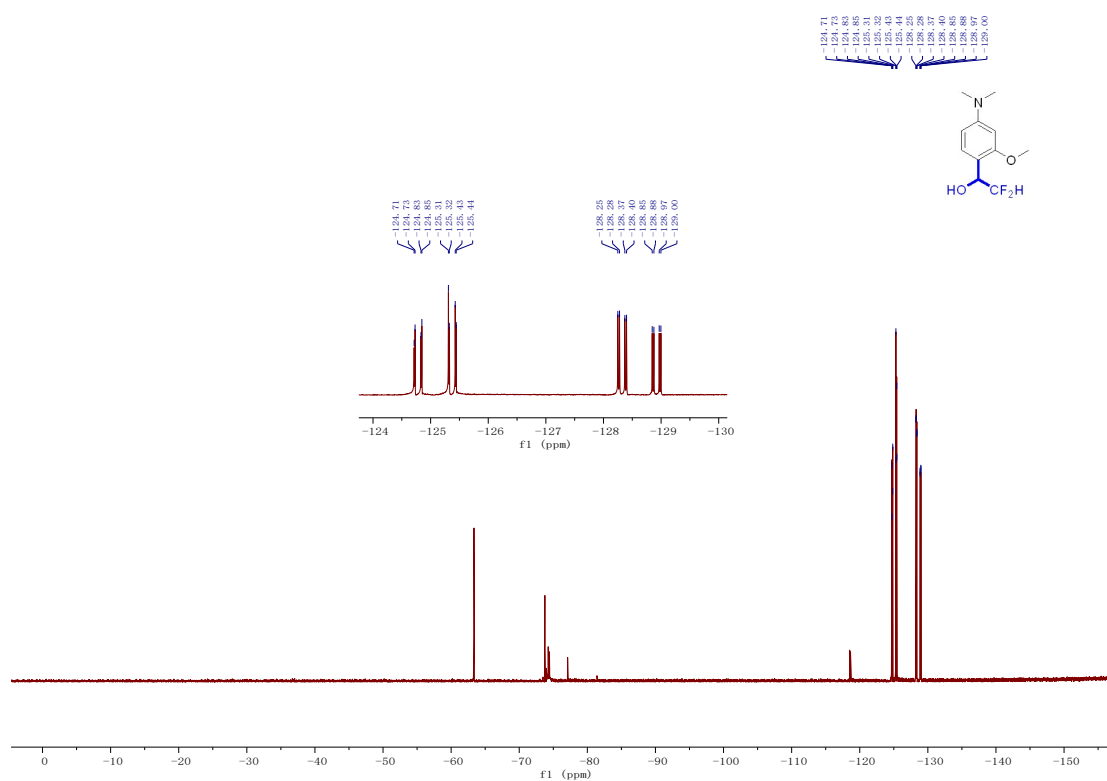
¹H NMR (500 MHz, Chloroform-*d*) spectra of **5f**



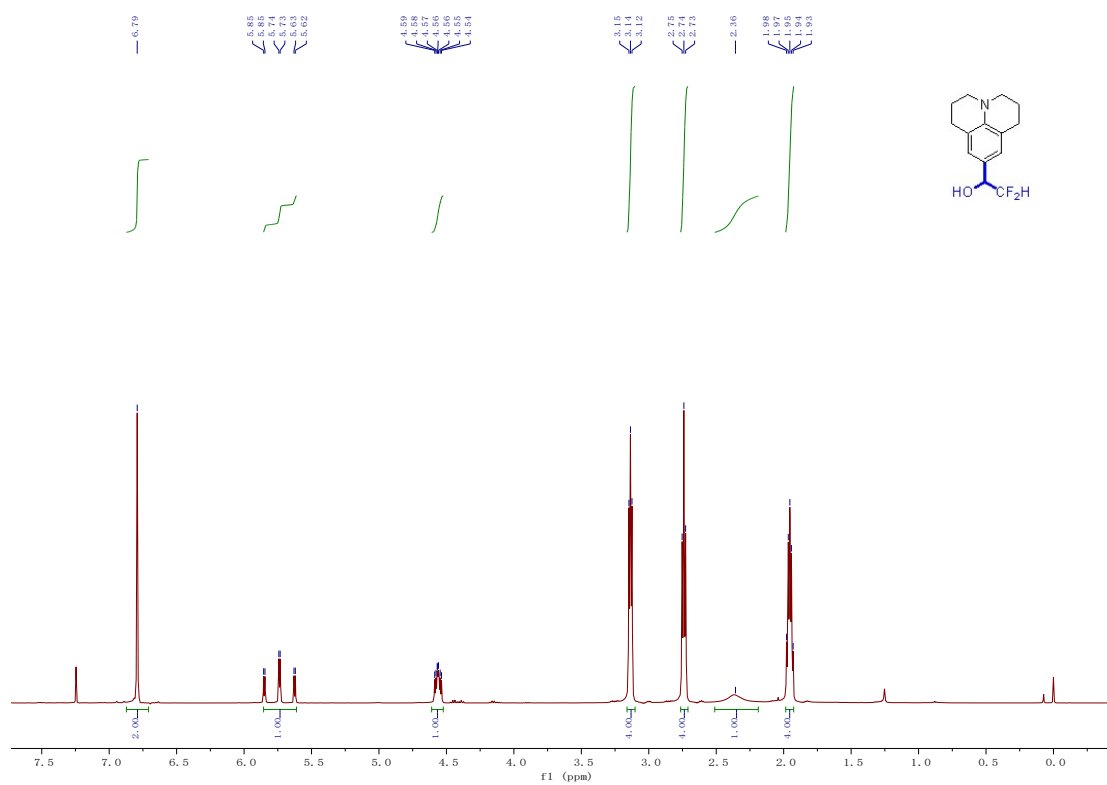
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **5f**



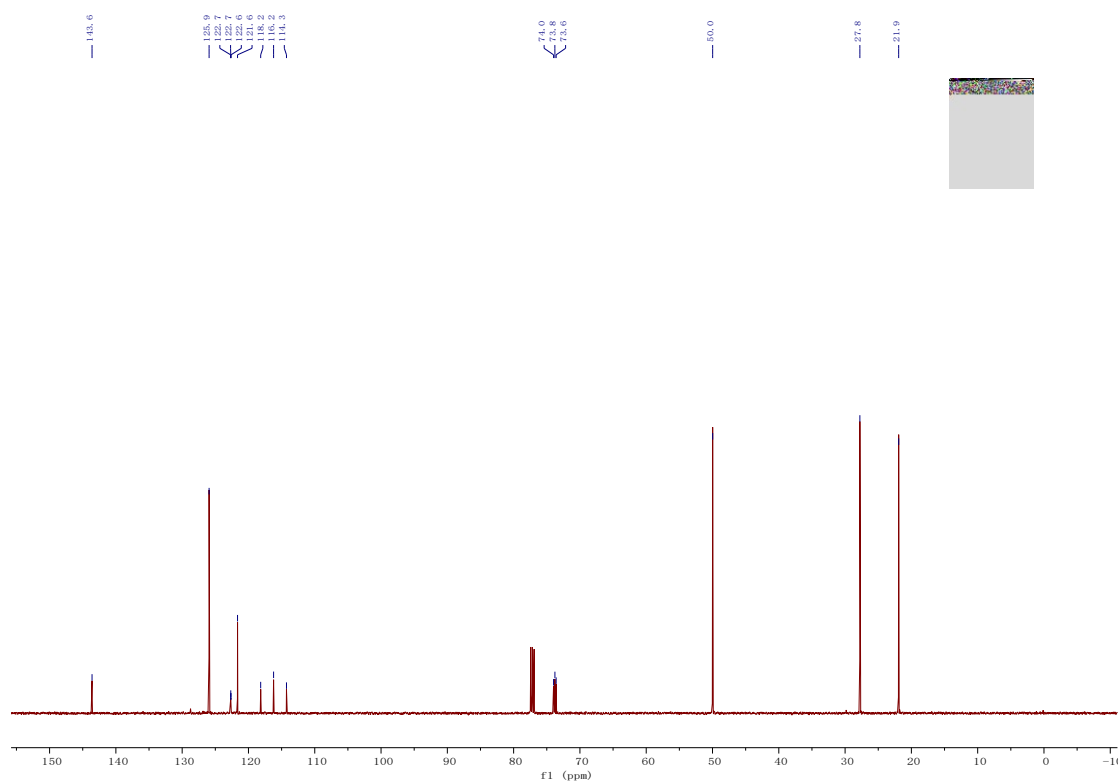
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **5f**



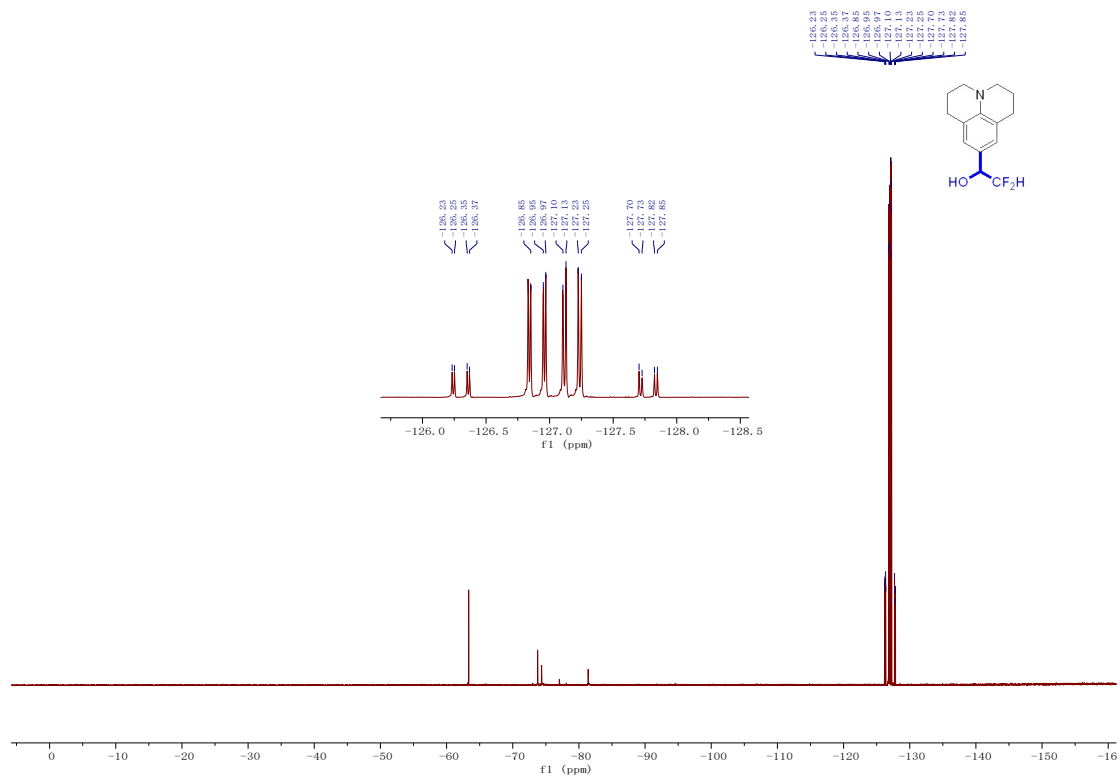
^1H NMR (500 MHz, Chloroform-*d*) spectra of **5g**



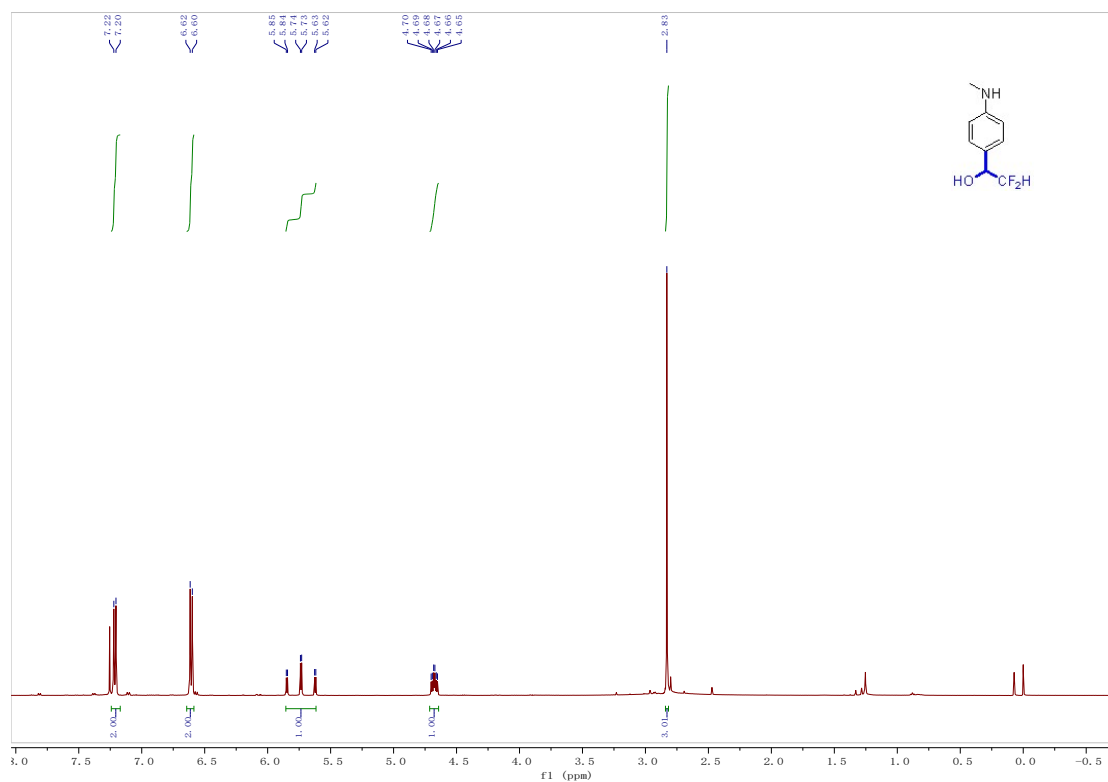
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **5g**



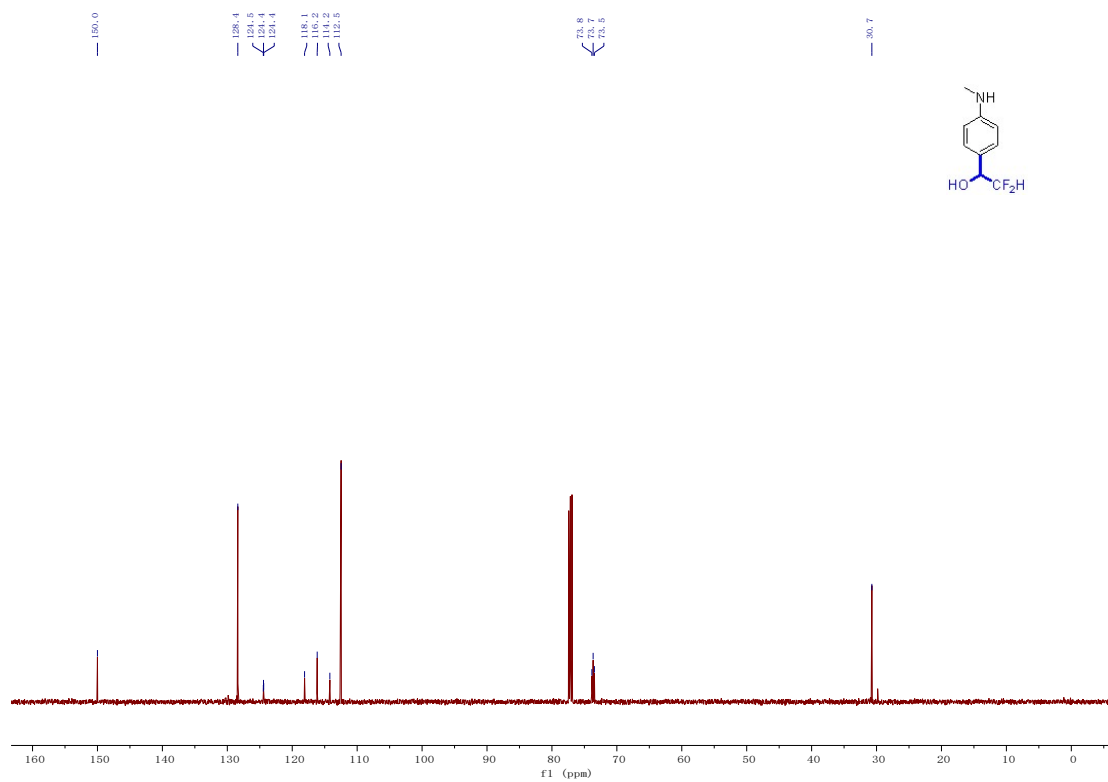
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **5g**



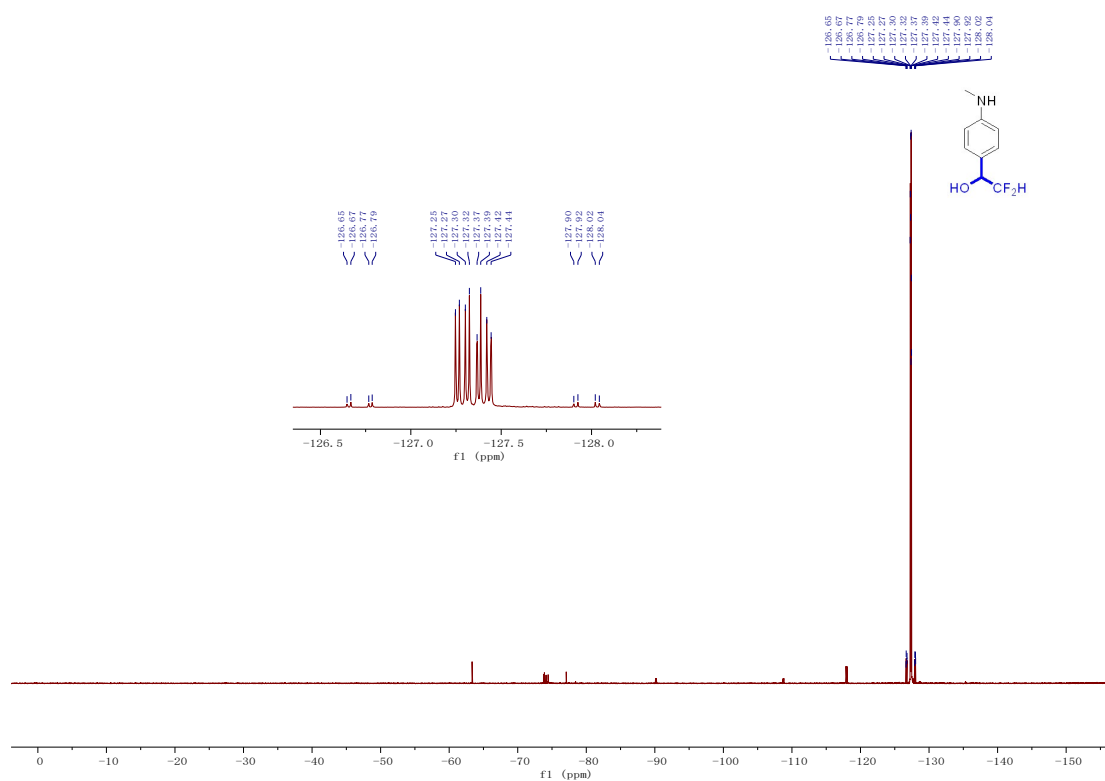
¹H NMR (500 MHz, Chloroform-*d*) spectra of **5h**



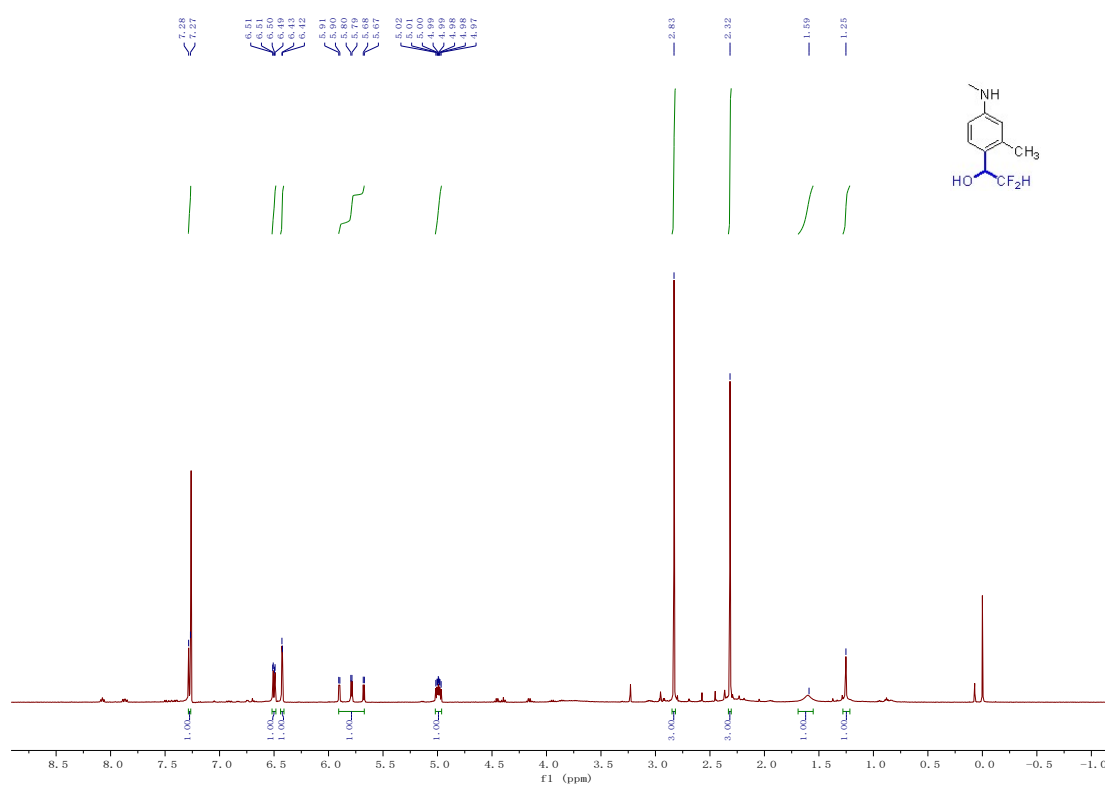
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **5h**



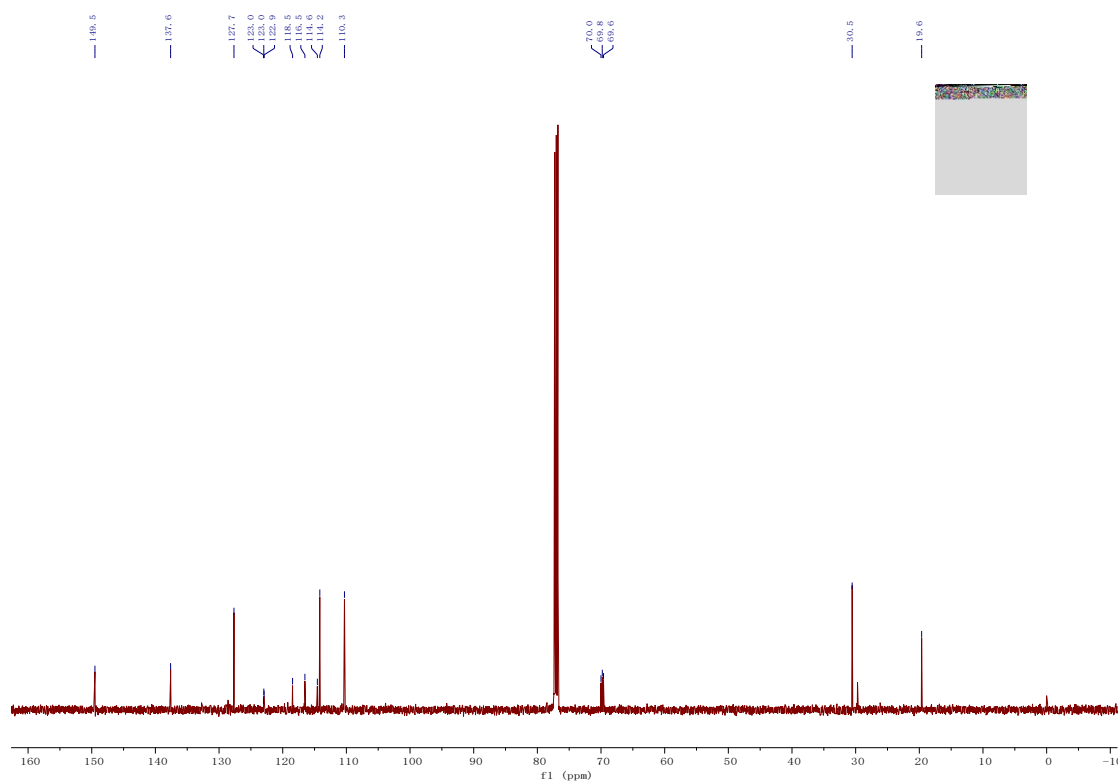
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **5h**



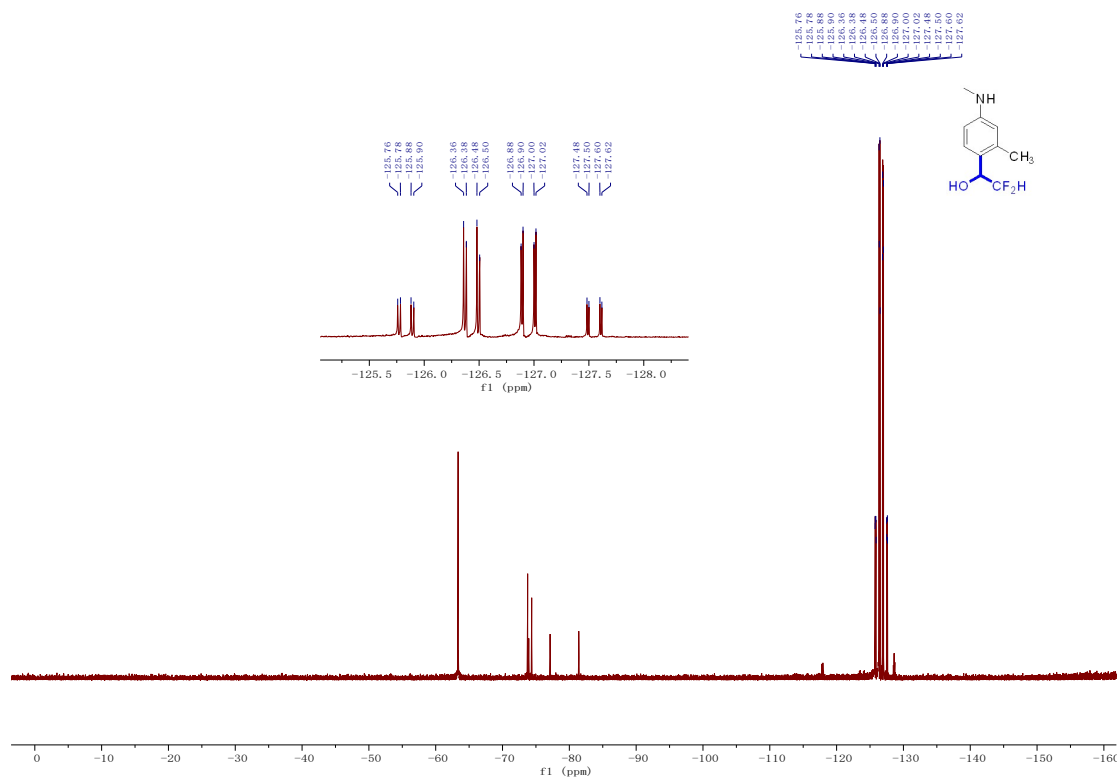
¹H NMR (500 MHz, Chloroform-*d*) spectra of **5i**



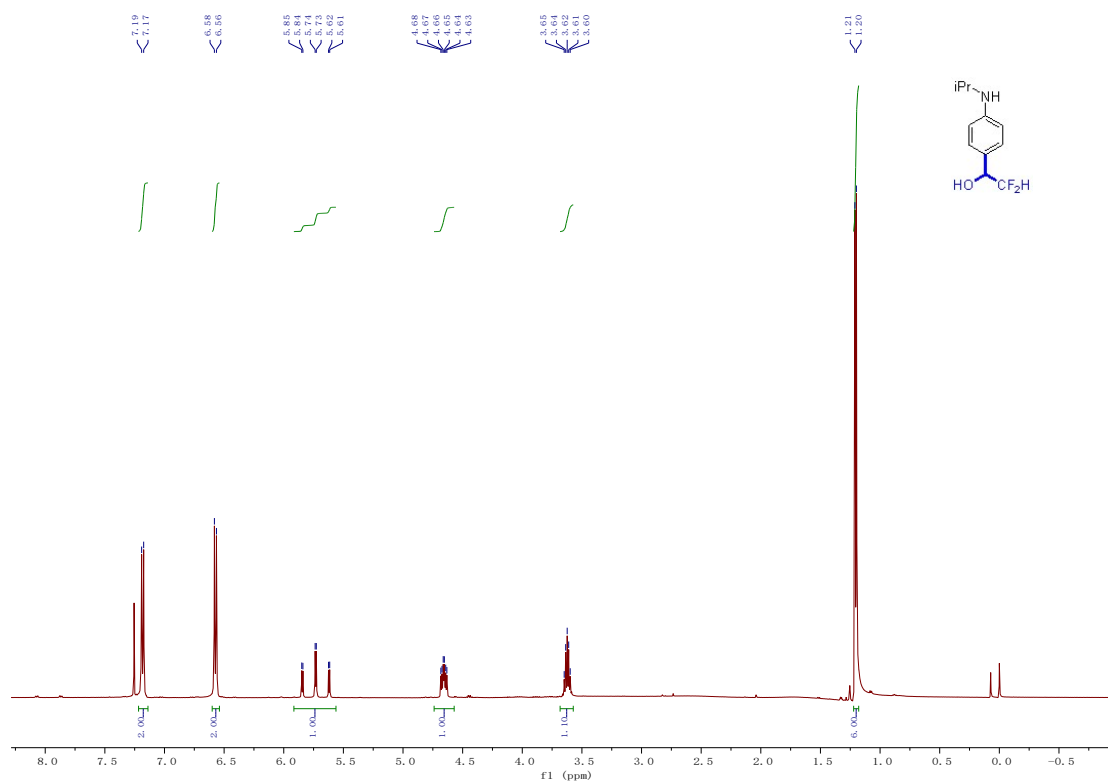
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **5i**



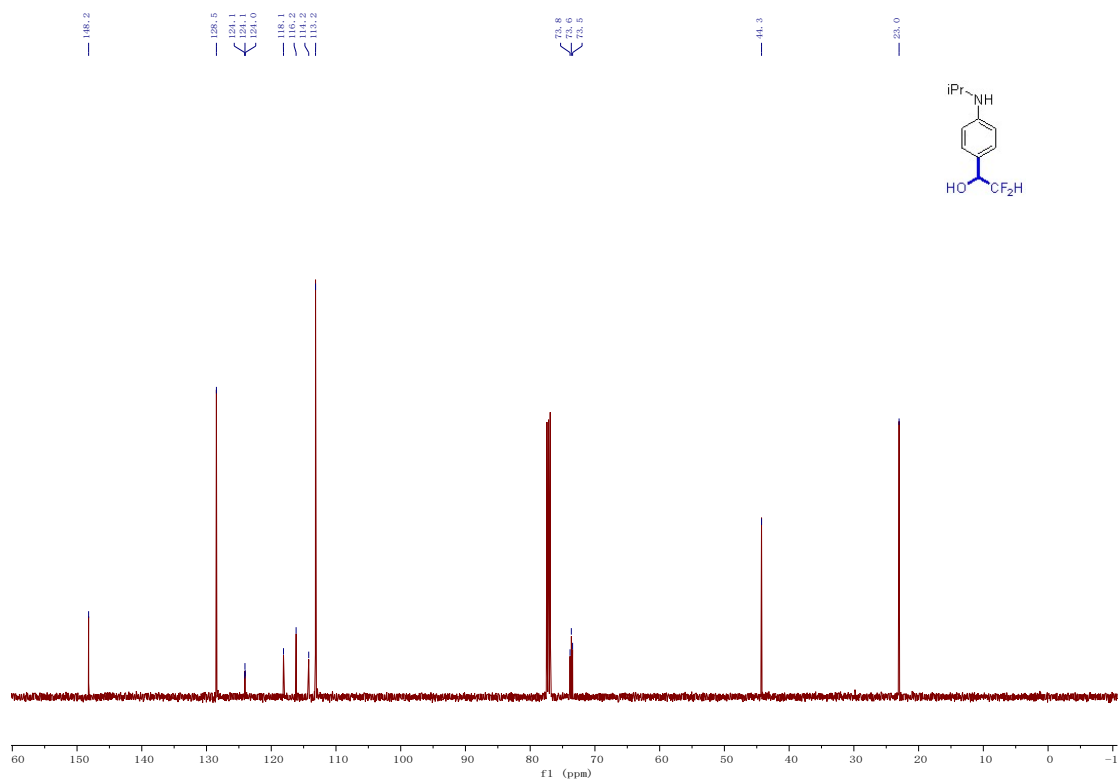
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **5i**



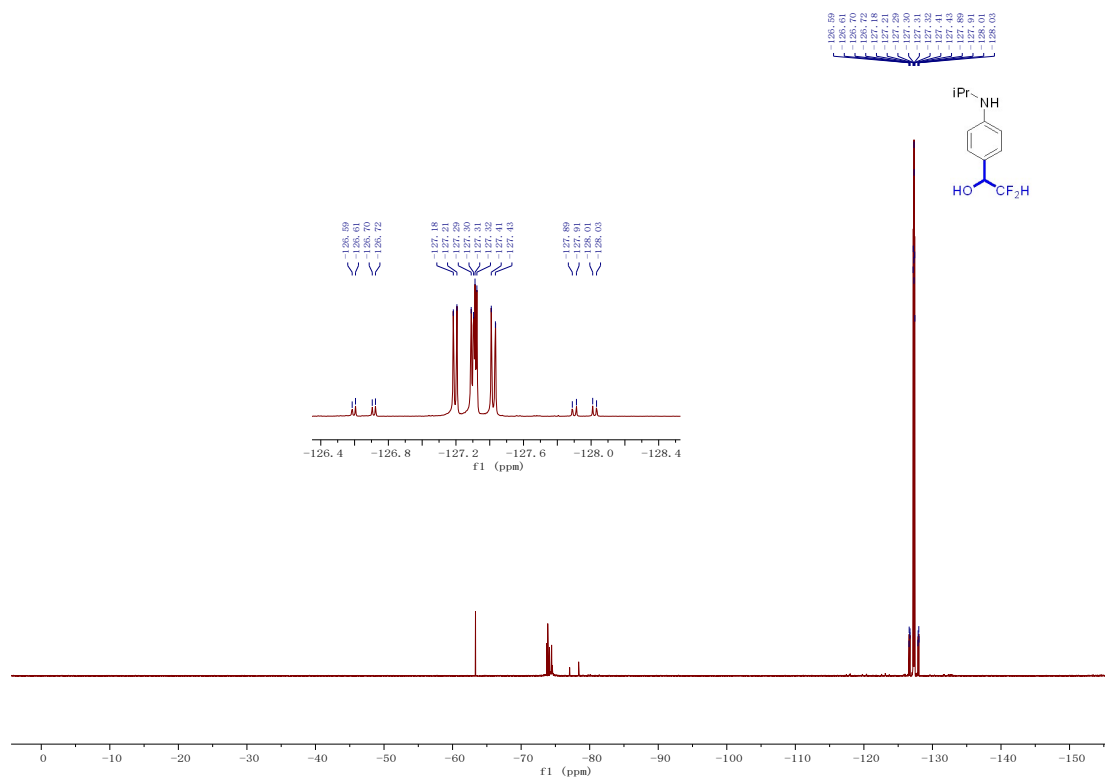
¹H NMR (500 MHz, Chloroform-*d*) spectra of **5j**



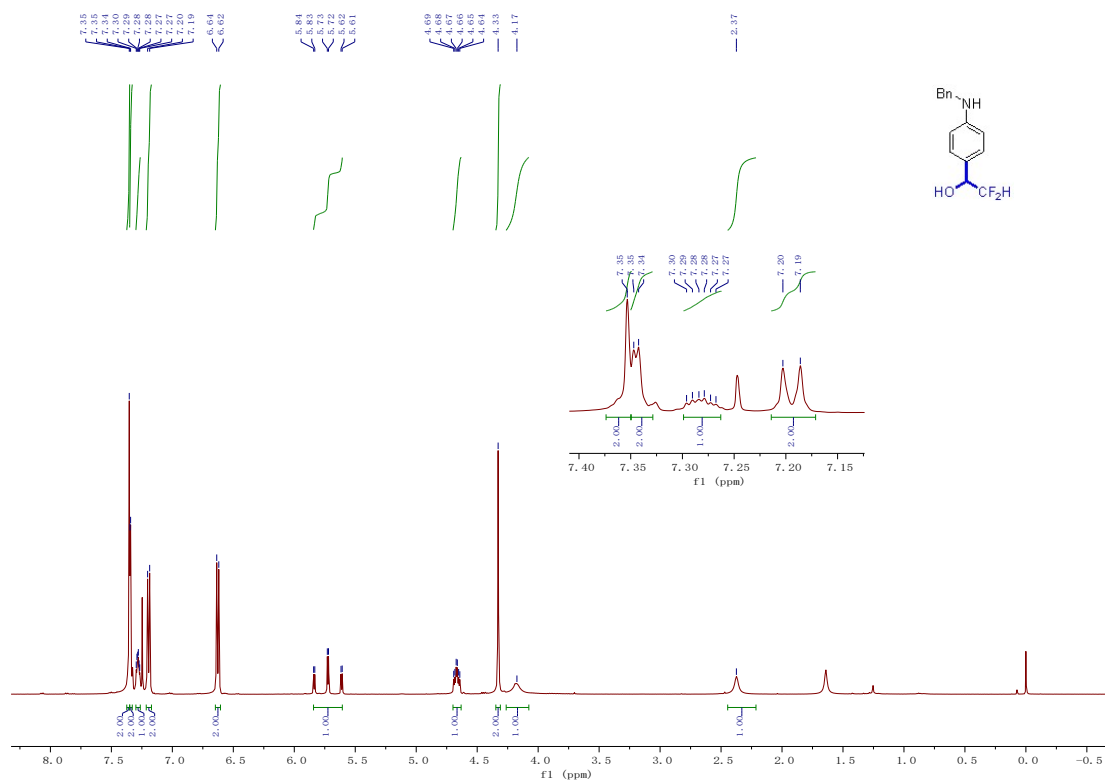
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **5j**



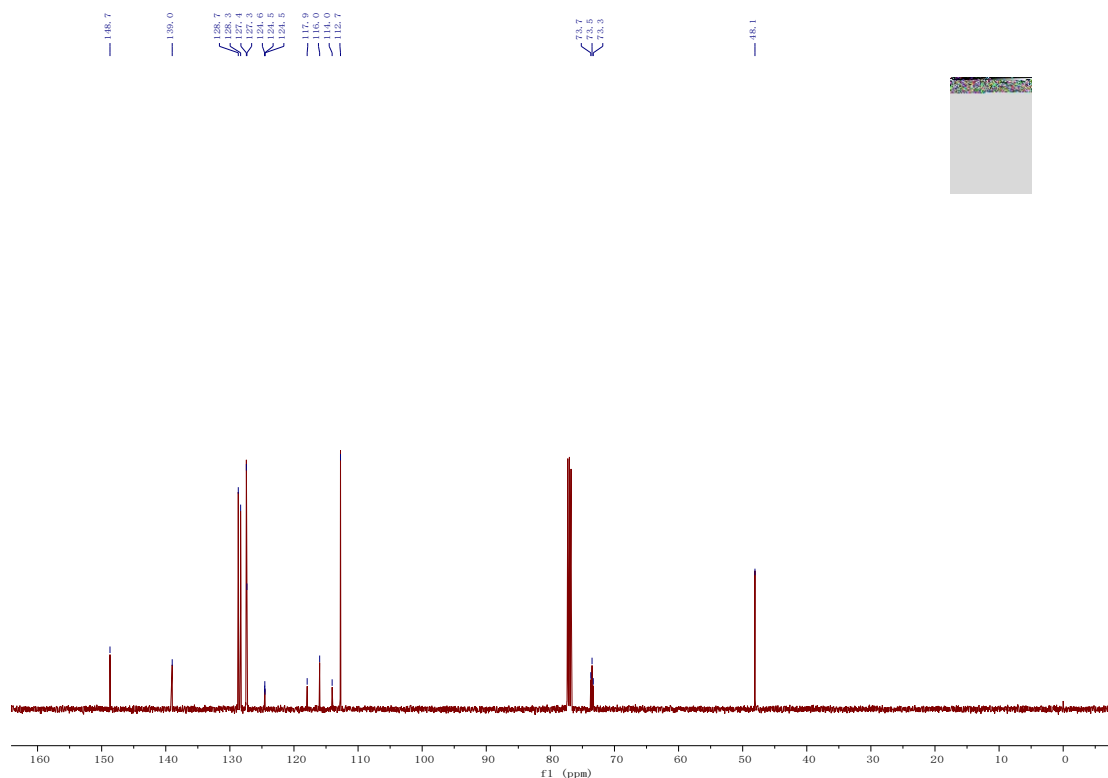
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **5j**



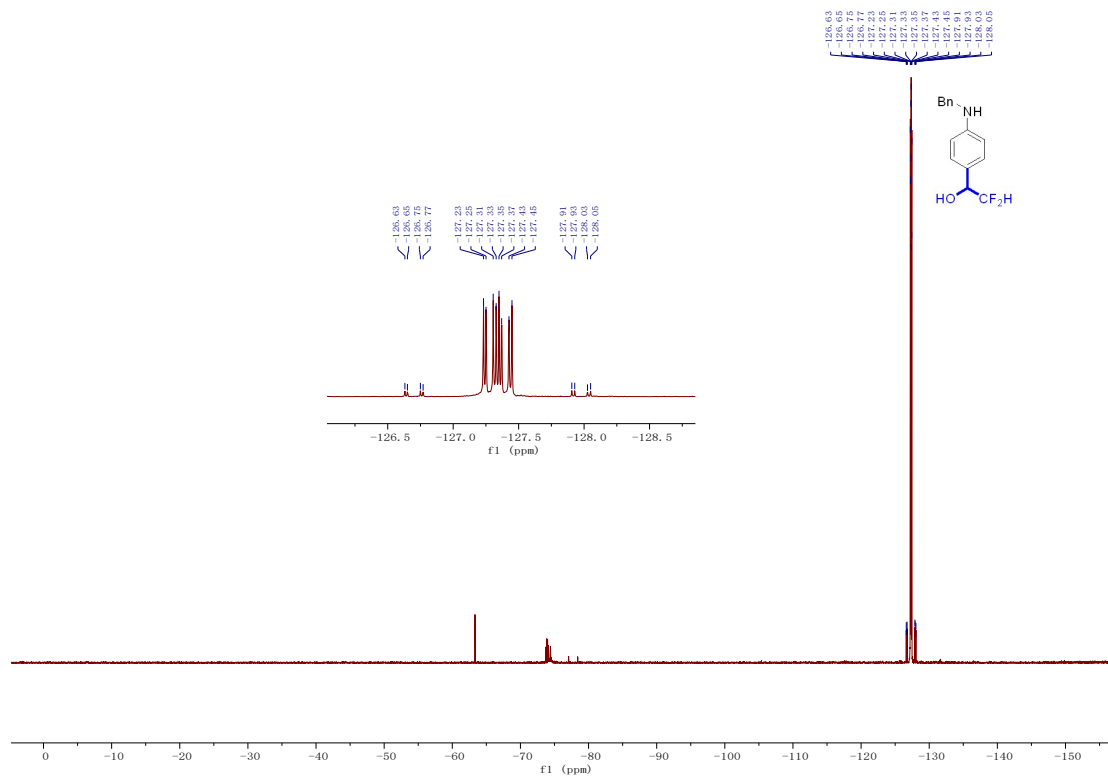
¹H NMR (500 MHz, Chloroform-*d*) spectra of **5k**



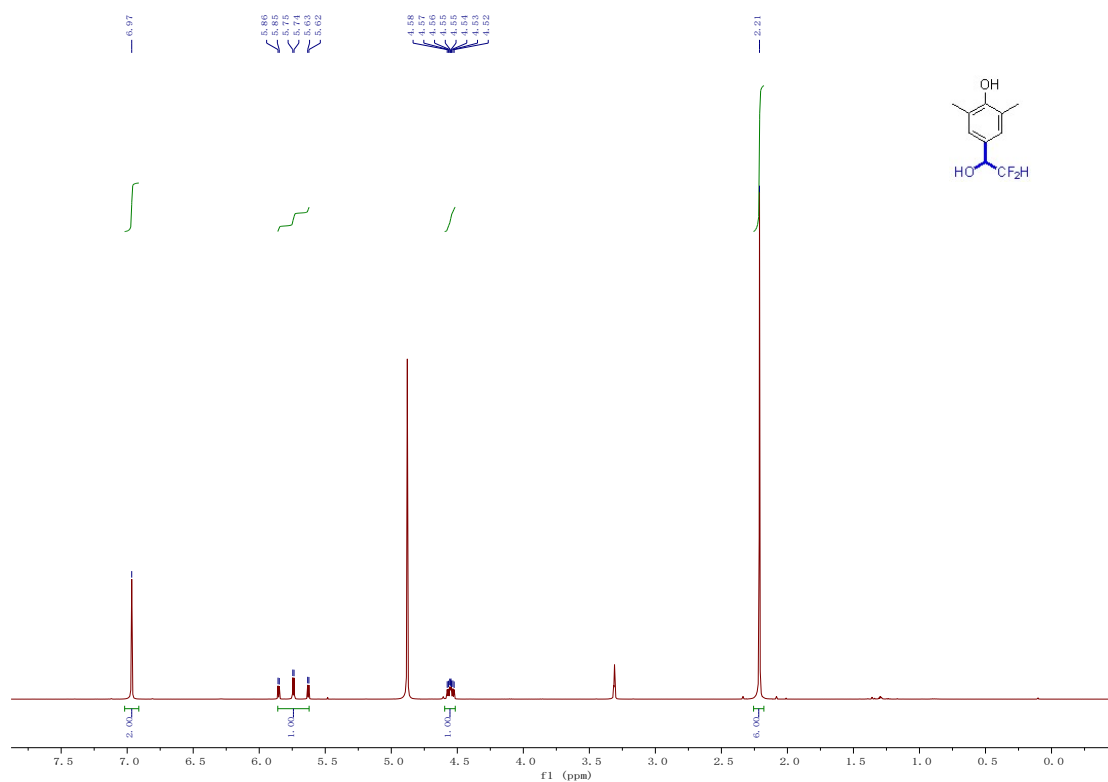
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **5k**



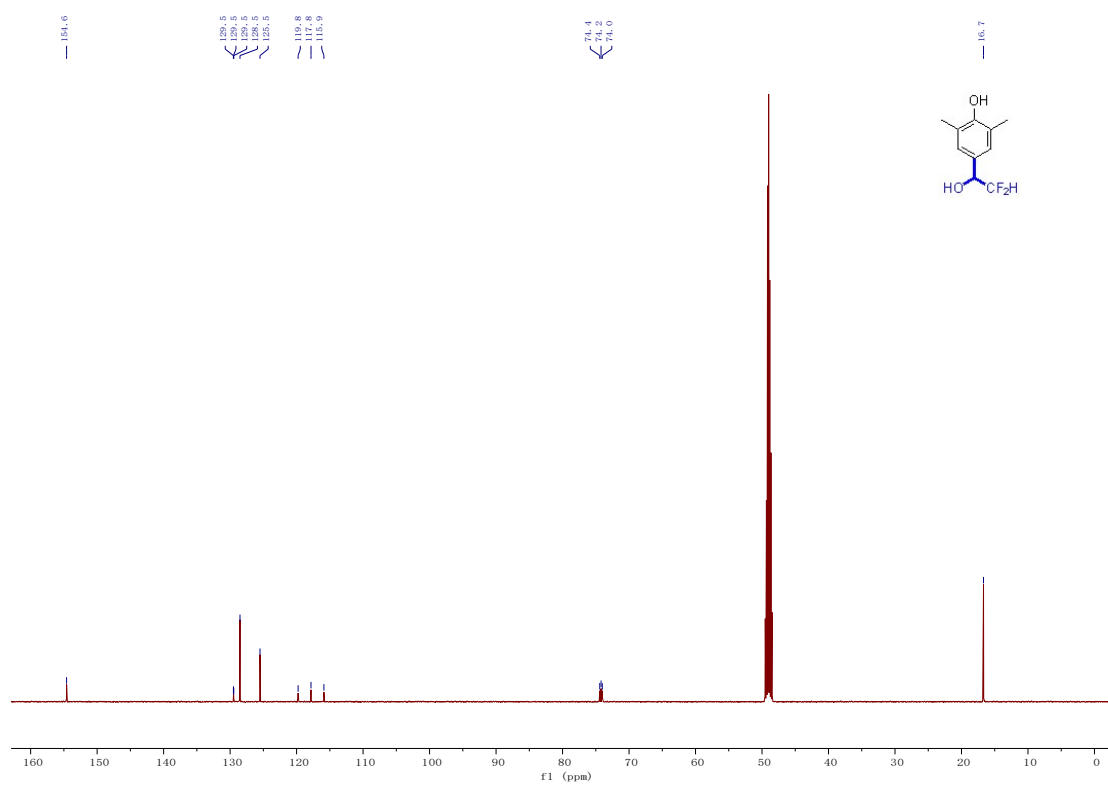
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **5k**



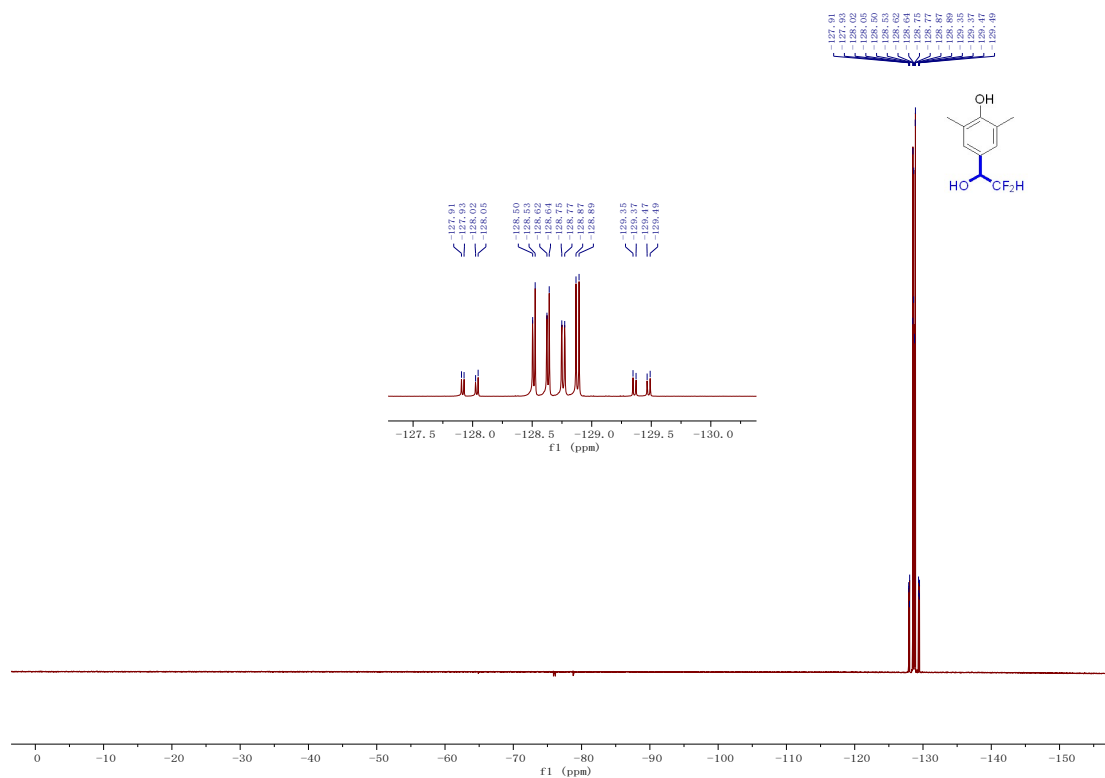
^1H NMR (500 MHz, Methanol- d_4) spectra of **6a**



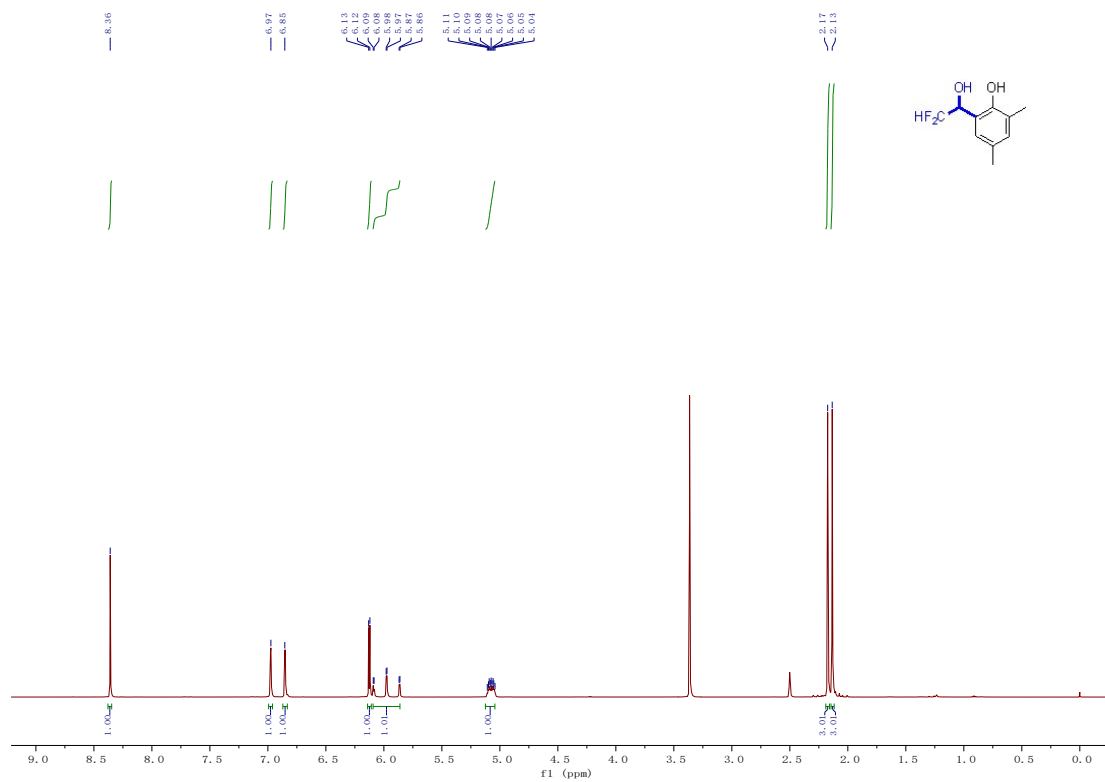
^{13}C NMR (125 MHz, Methanol- d_4) spectra of **6a**



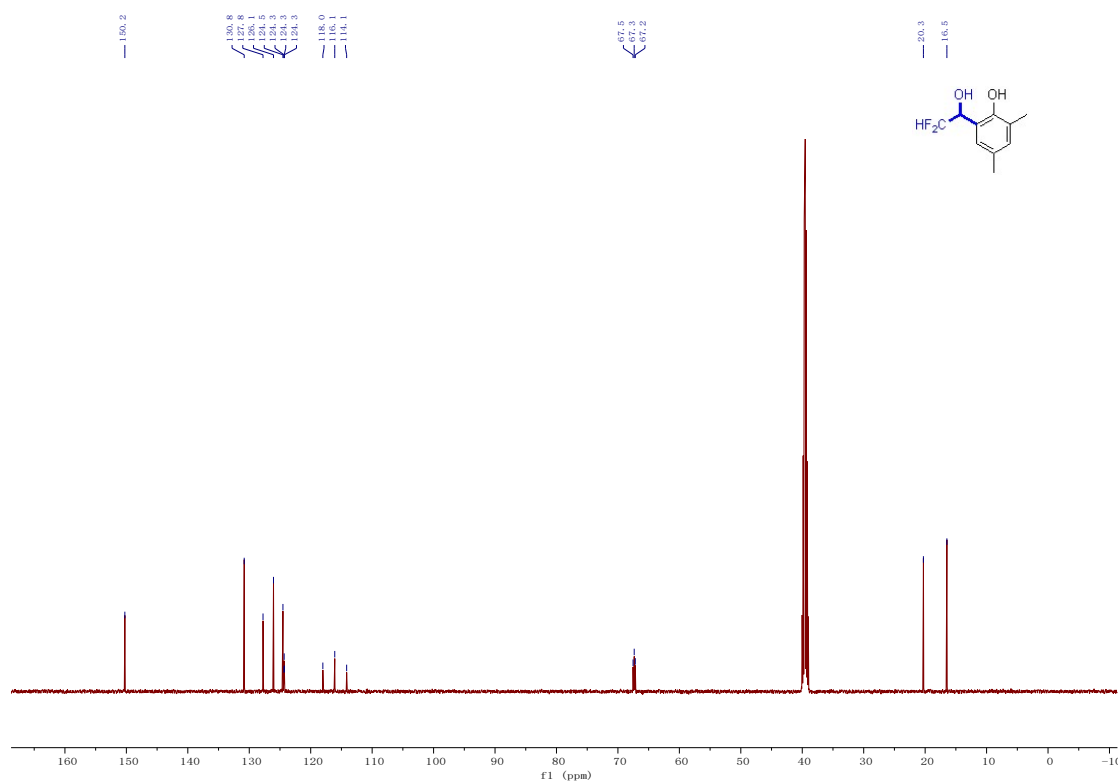
¹⁹F NMR (470 MHz, Methanol-*d*₄) spectra of **6a**



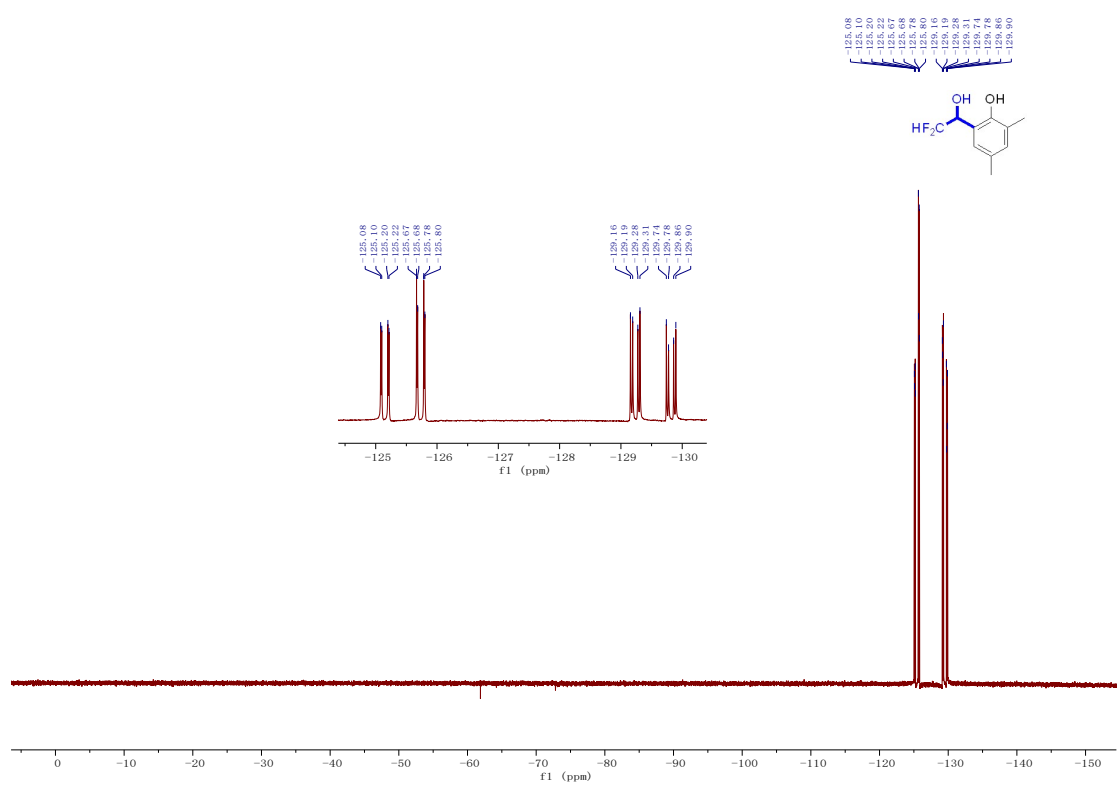
¹H NMR (500 MHz, DMSO-*d*₆) spectra of **6b**



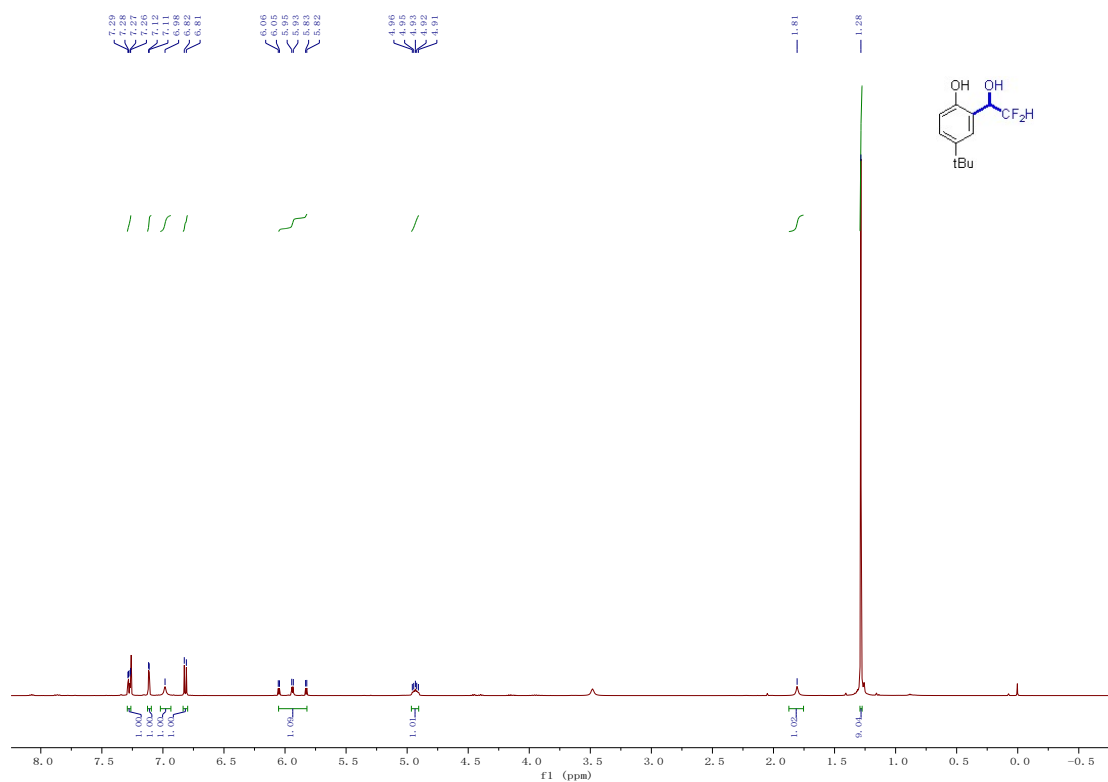
¹³C NMR (125 MHz, DMSO-*d*₆) spectra of **6b**



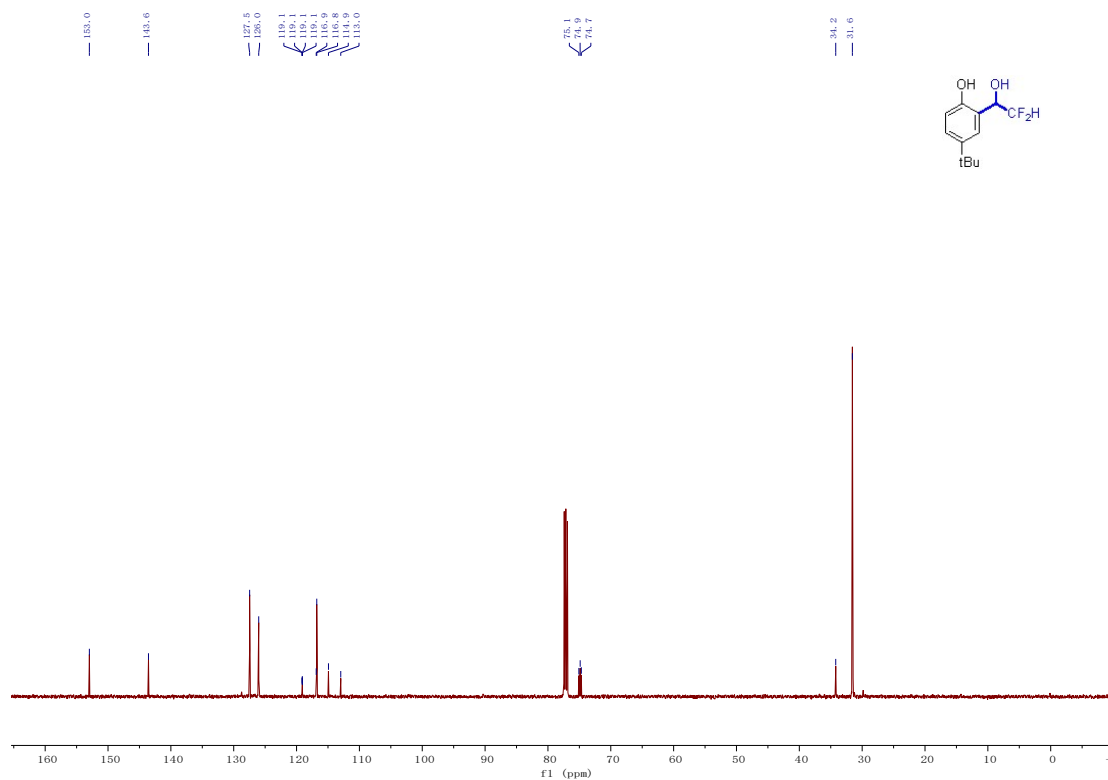
¹⁹F NMR (470 MHz, DMSO-*d*₆) spectra of **6b**



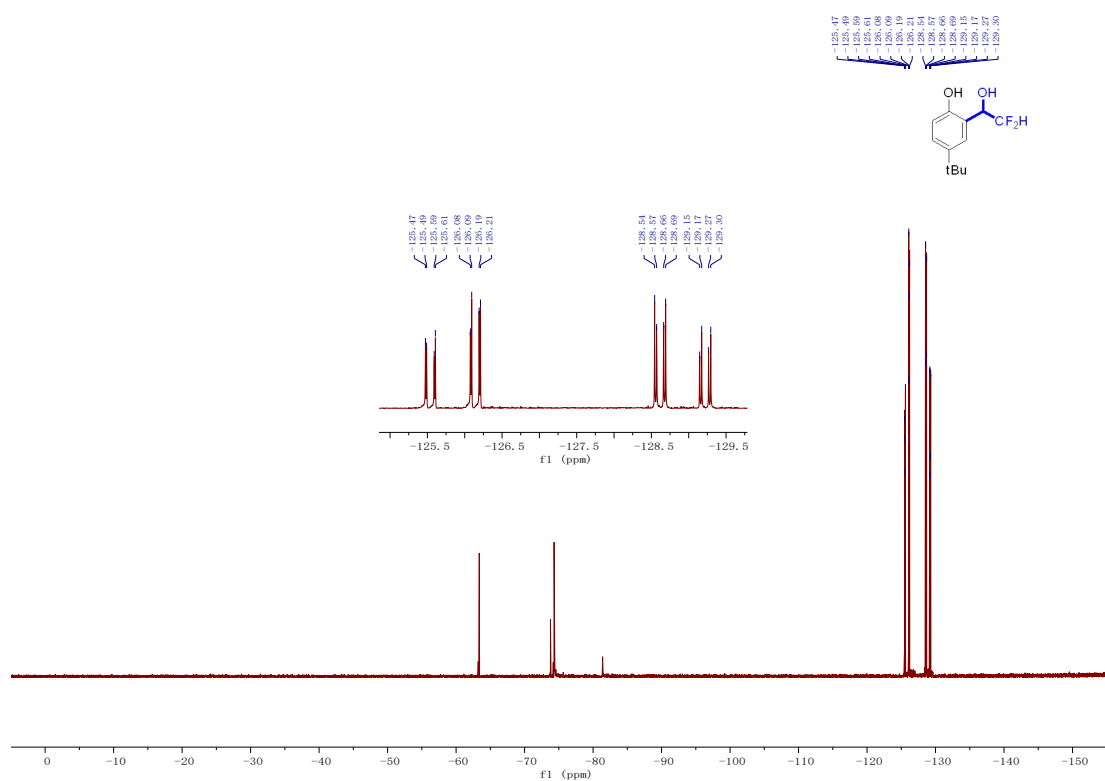
^1H NMR (500 MHz, Chloroform-*d*) spectra of **6c**



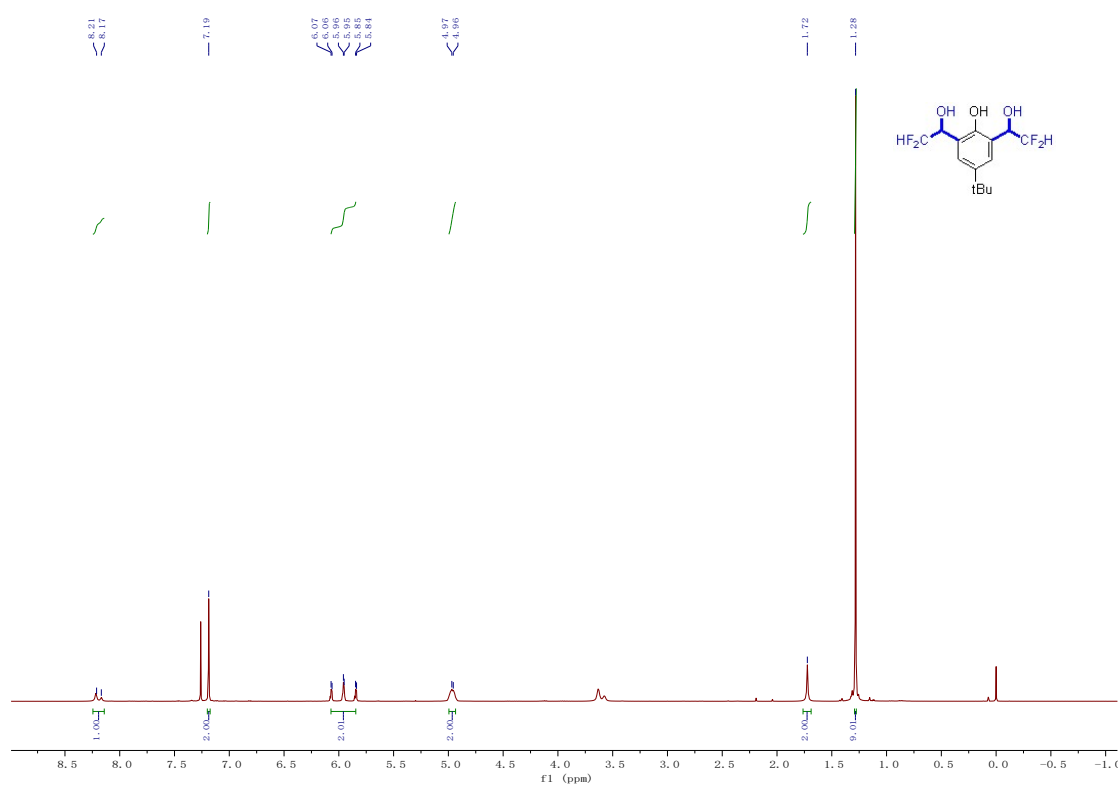
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **6c**



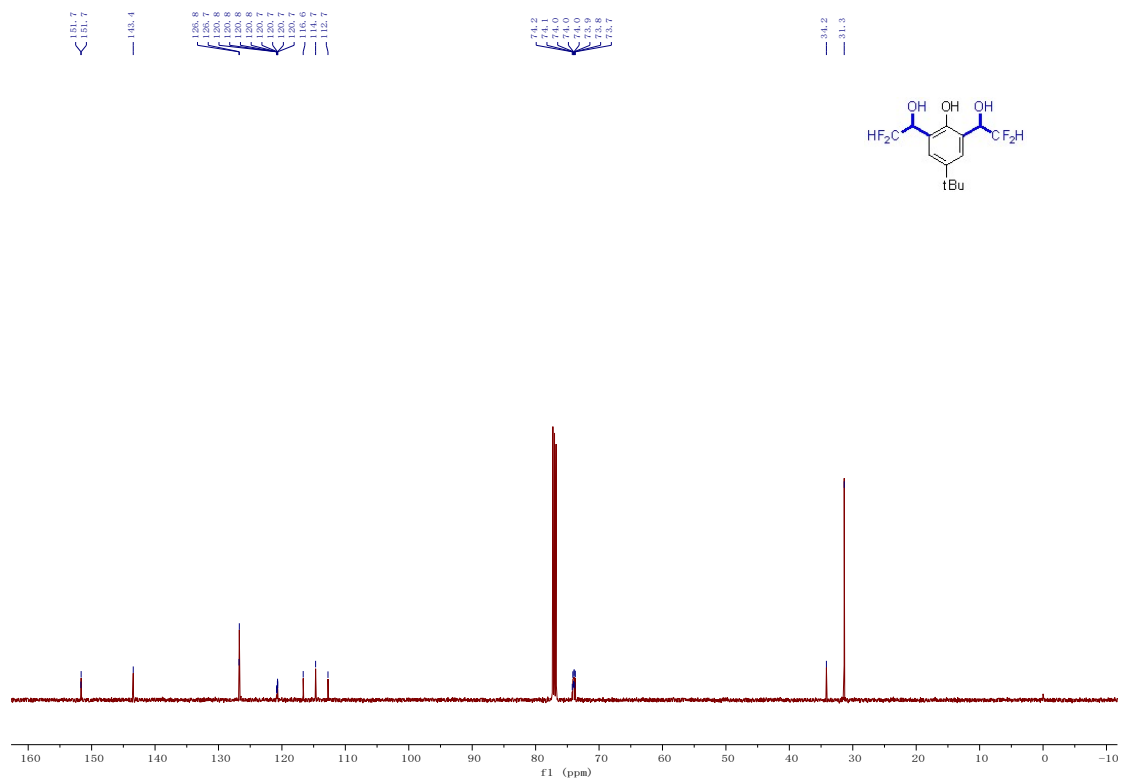
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **6c**



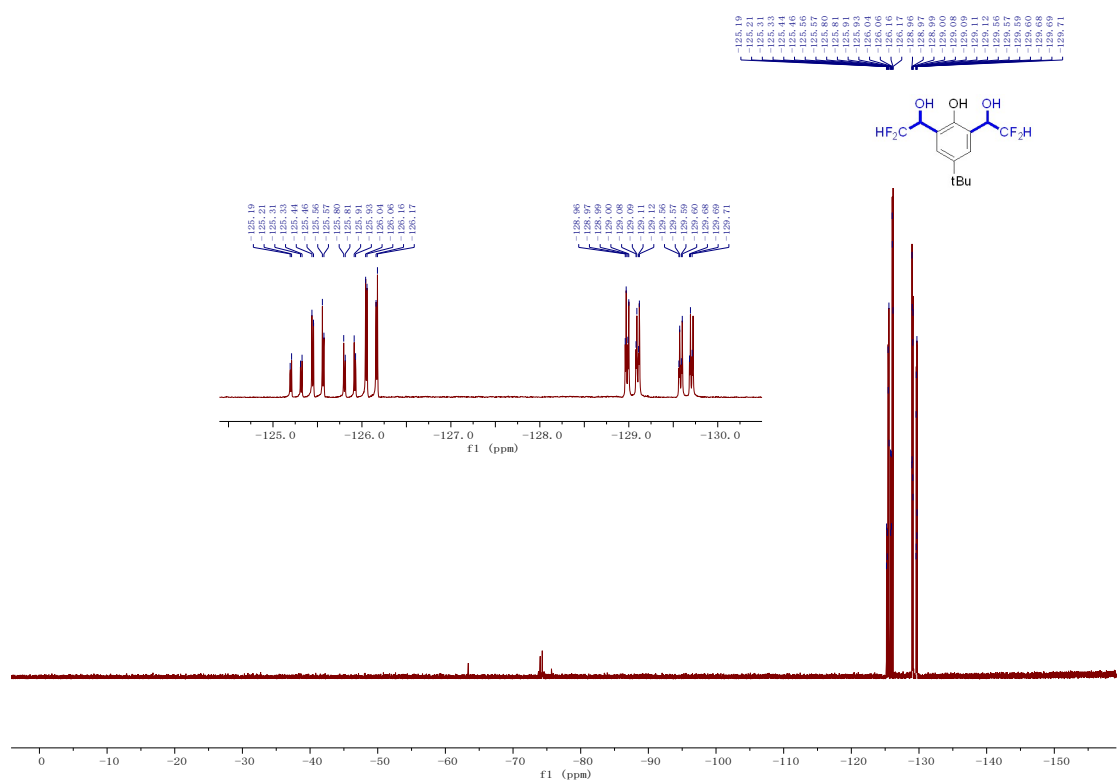
¹H NMR (500 MHz, Chloroform-*d*) spectra of **6c'**



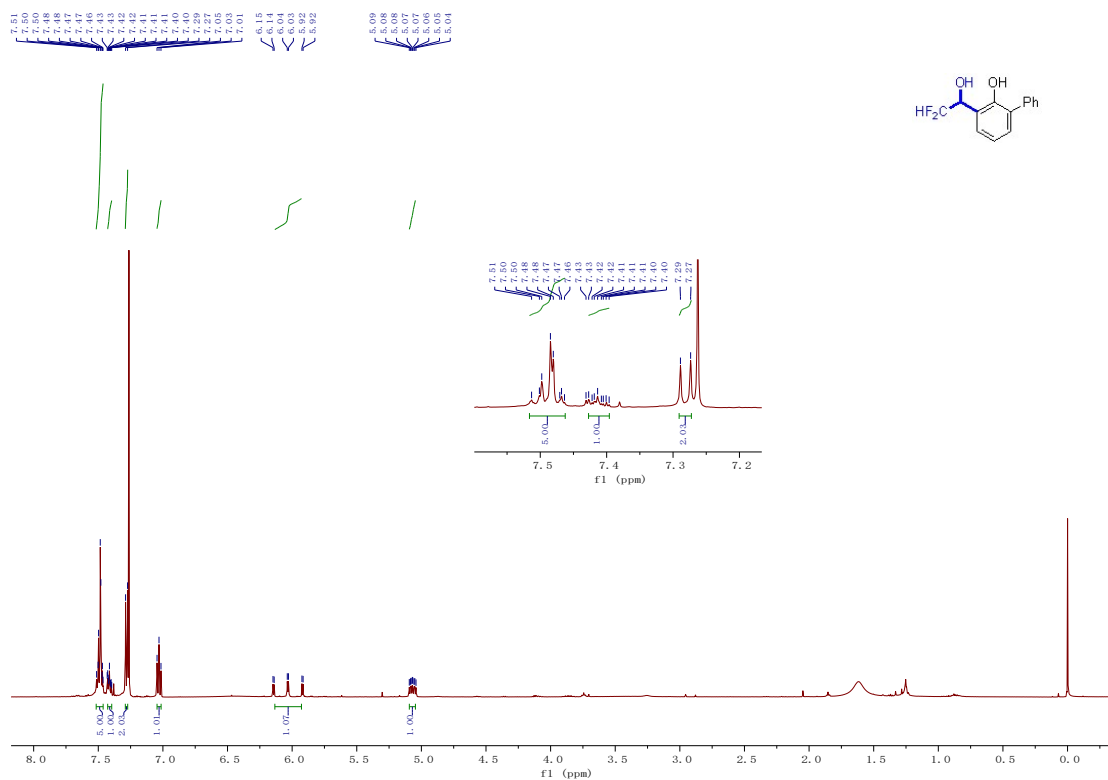
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **6c'**



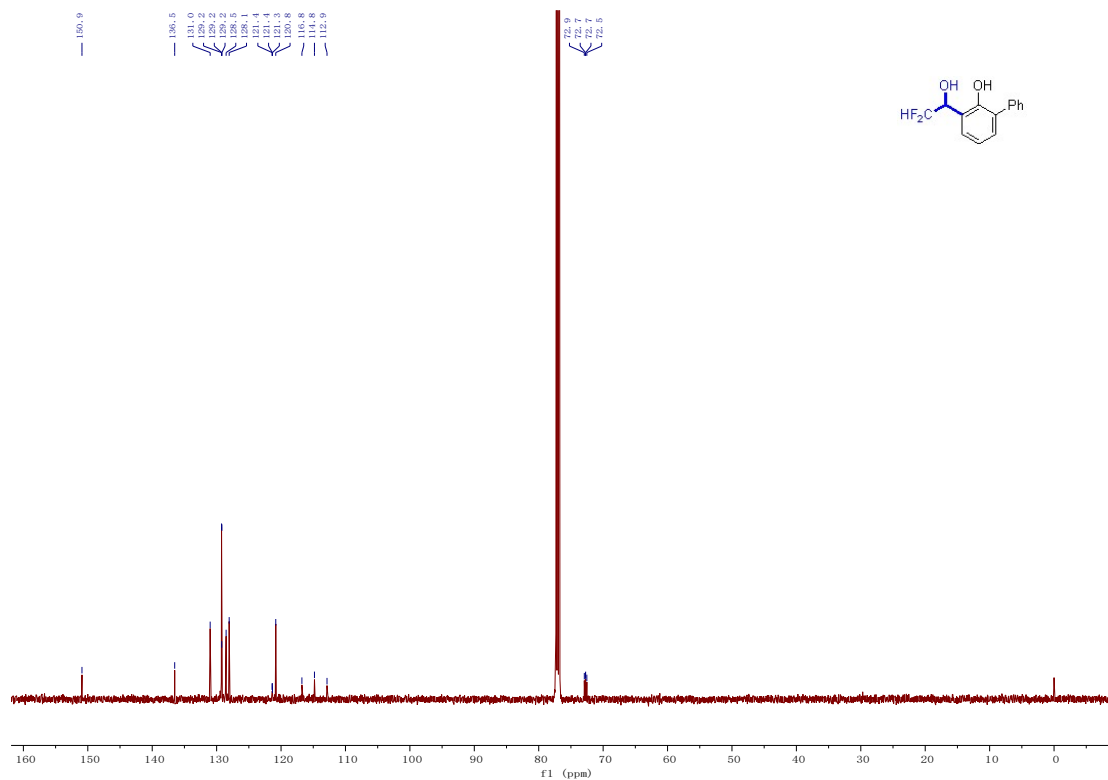
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **6c'**



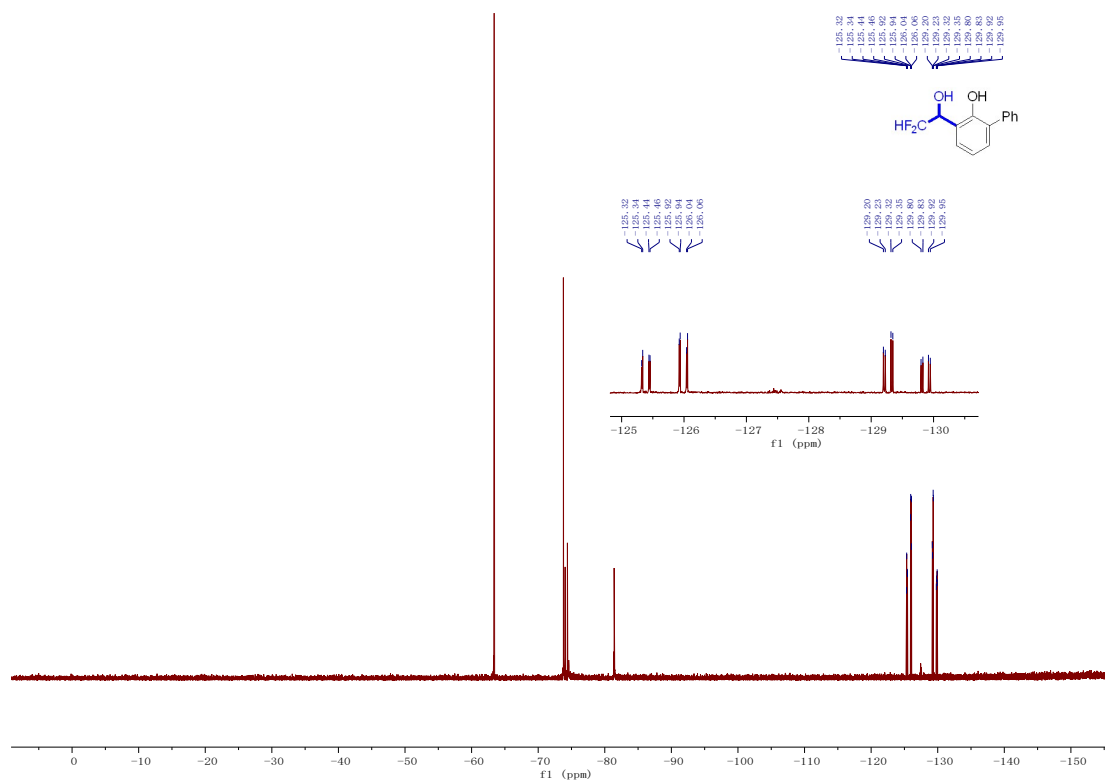
^1H NMR (500 MHz, Chloroform-*d*) spectra of **6d**



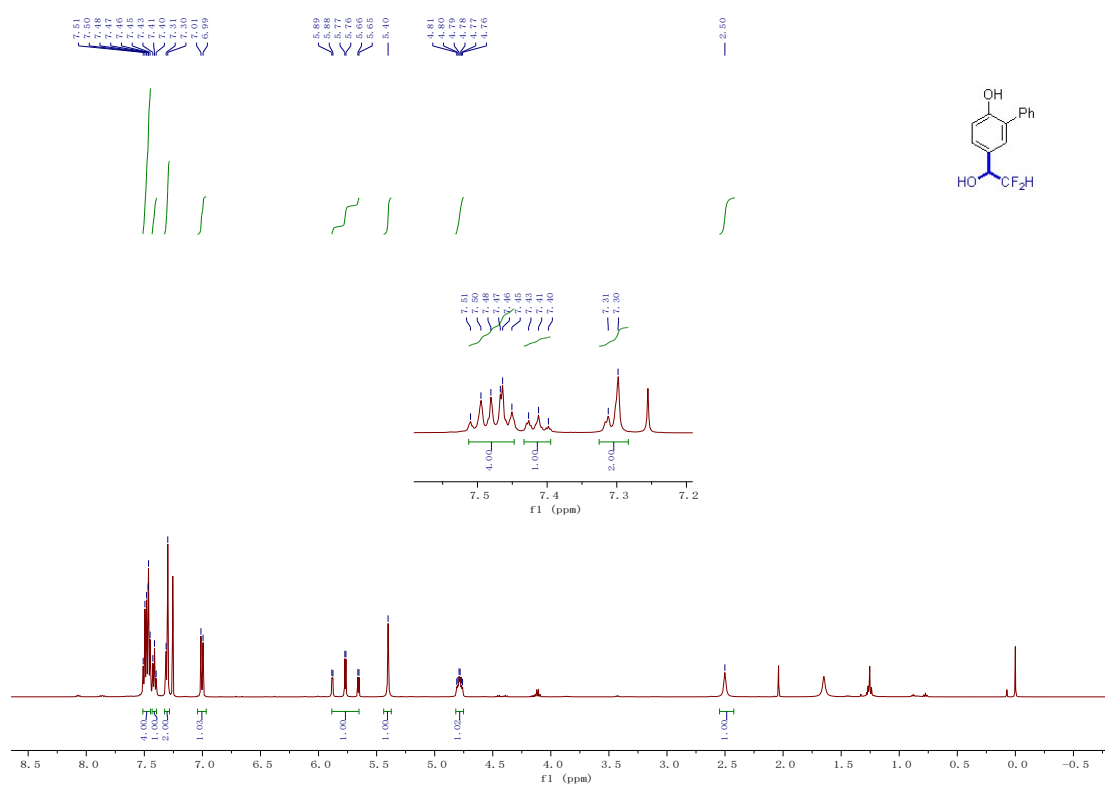
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **6d**



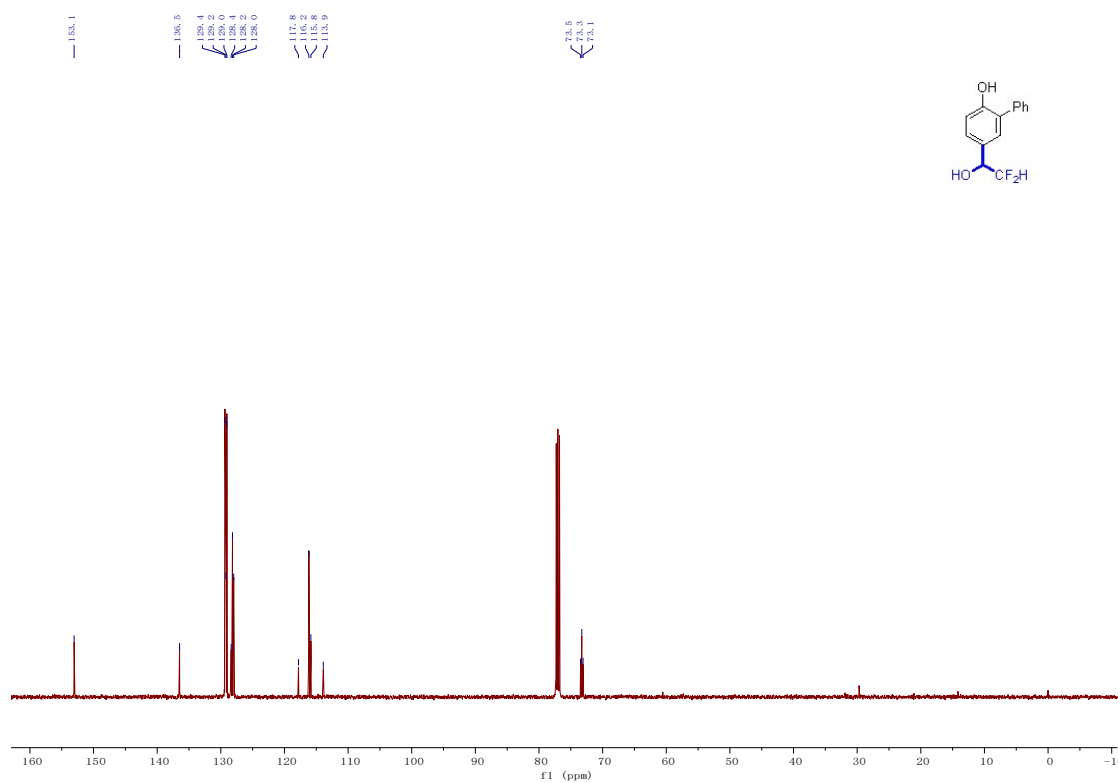
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **6d**



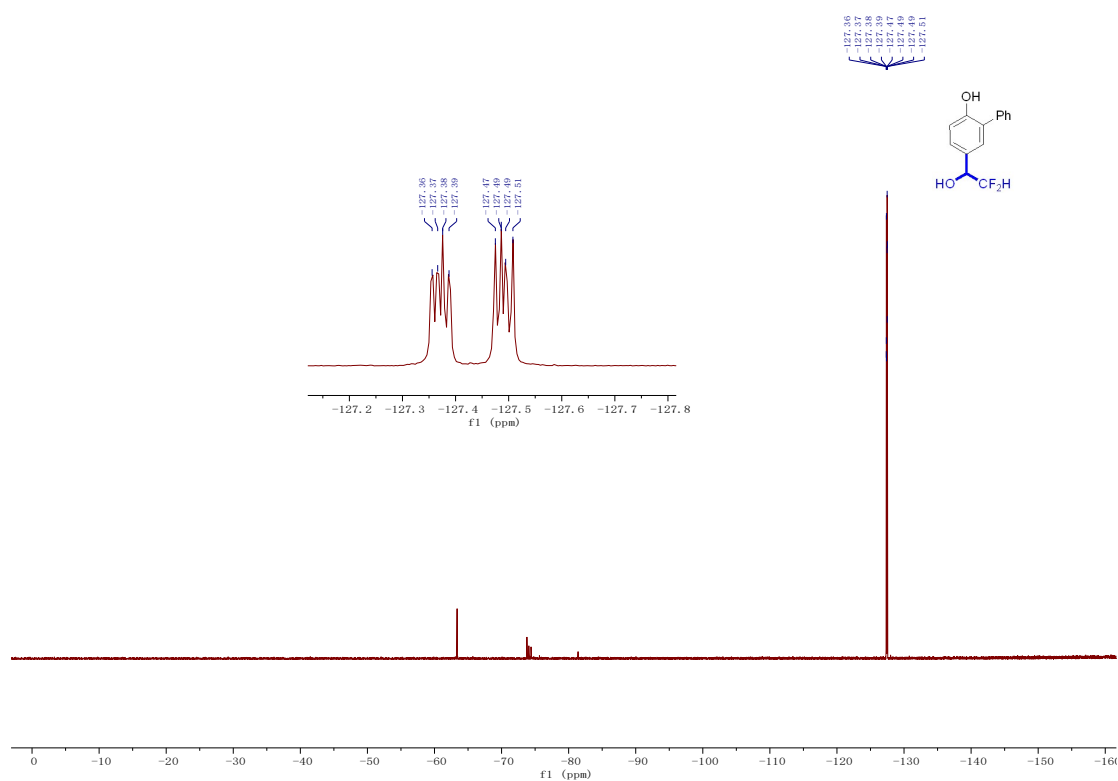
^1H NMR (500 MHz, Chloroform-*d*) spectra of **6d'**



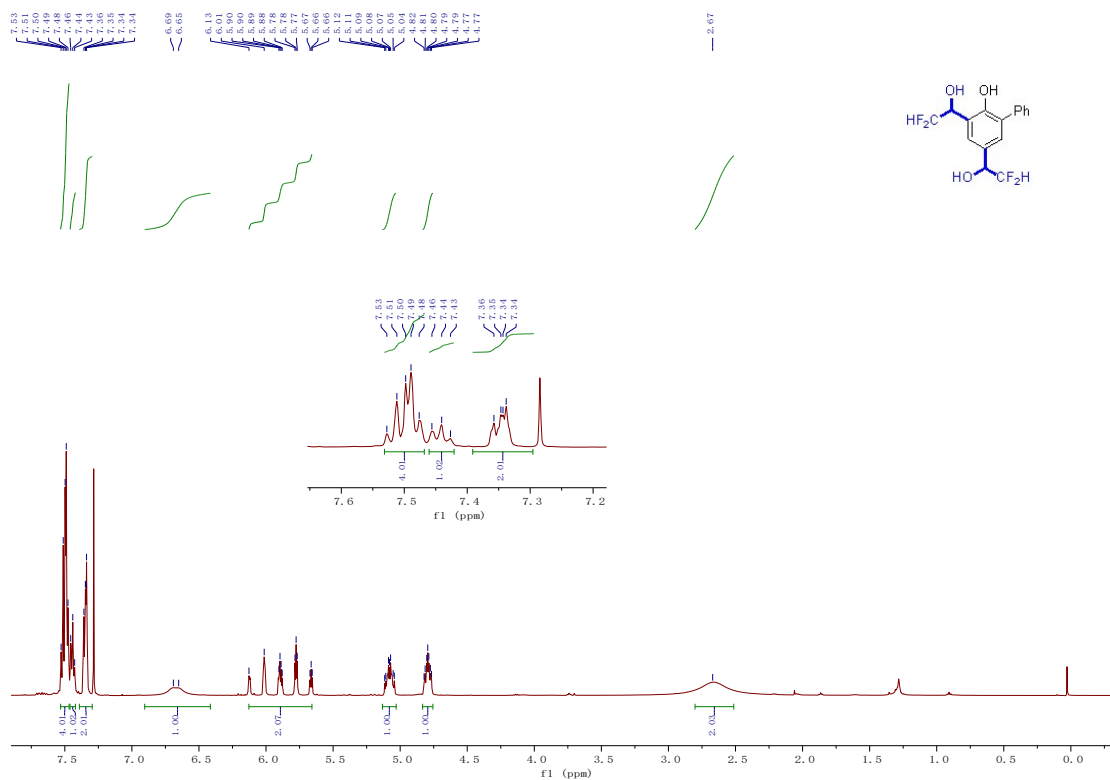
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **6d'**



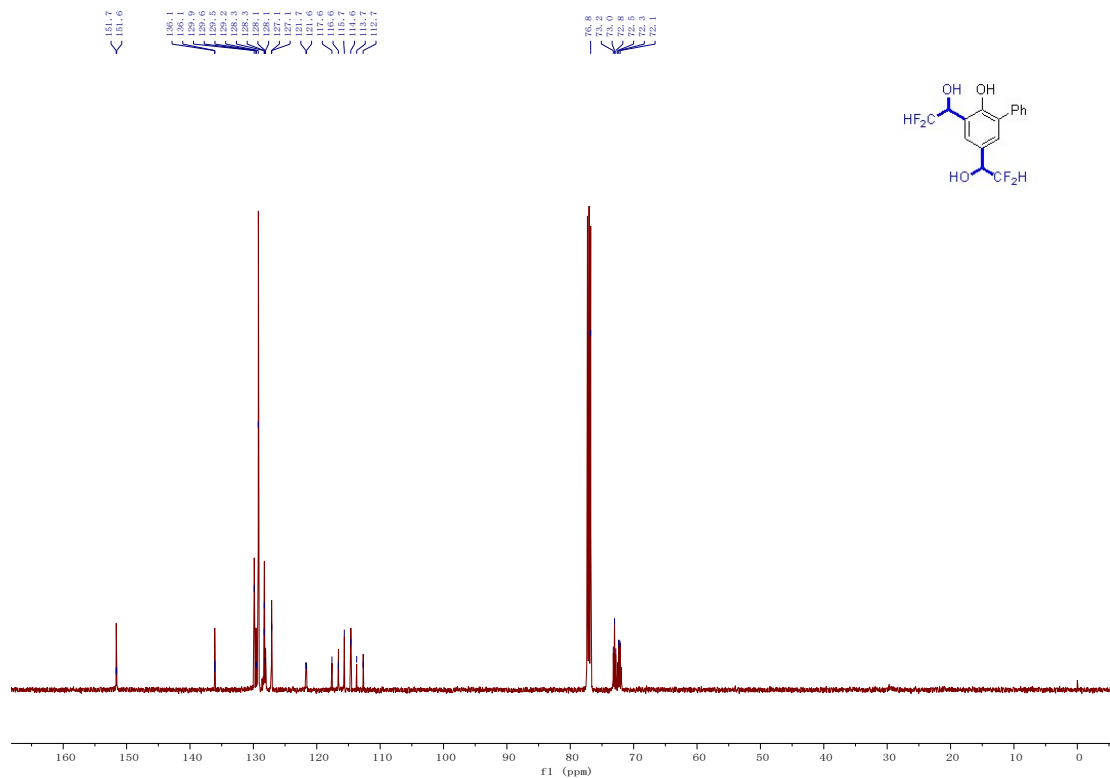
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **6d'**



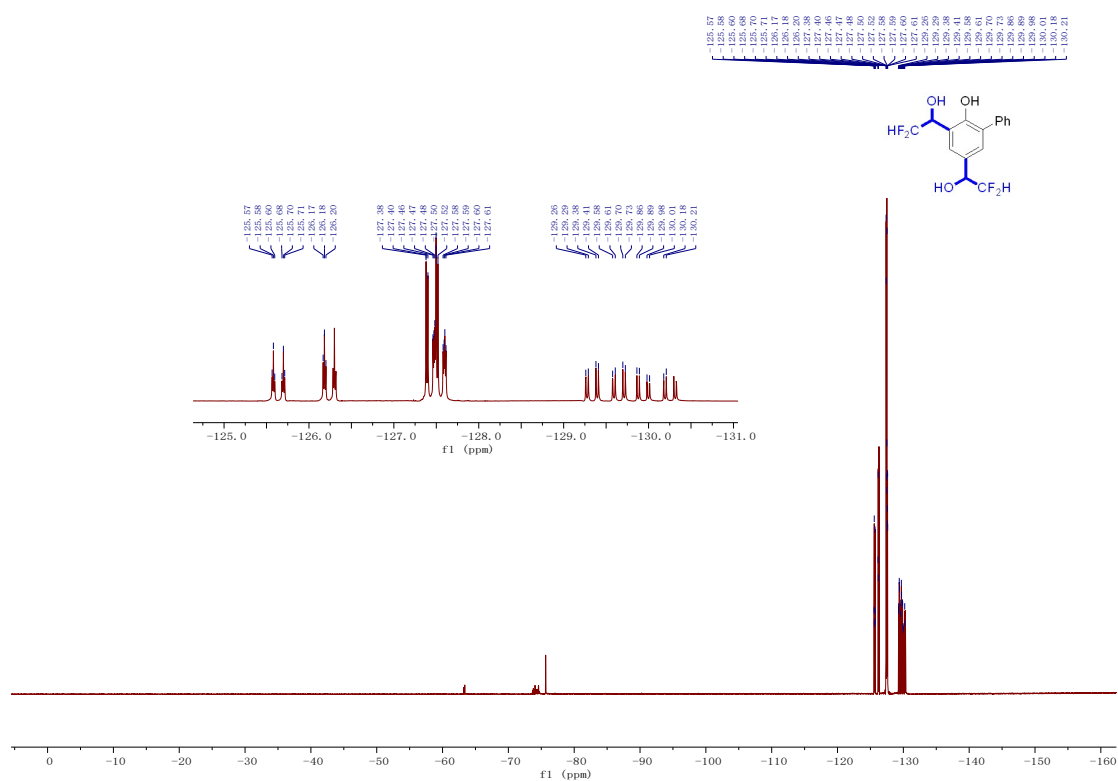
¹H NMR (500 MHz, Chloroform-*d*) spectra of **6d''**



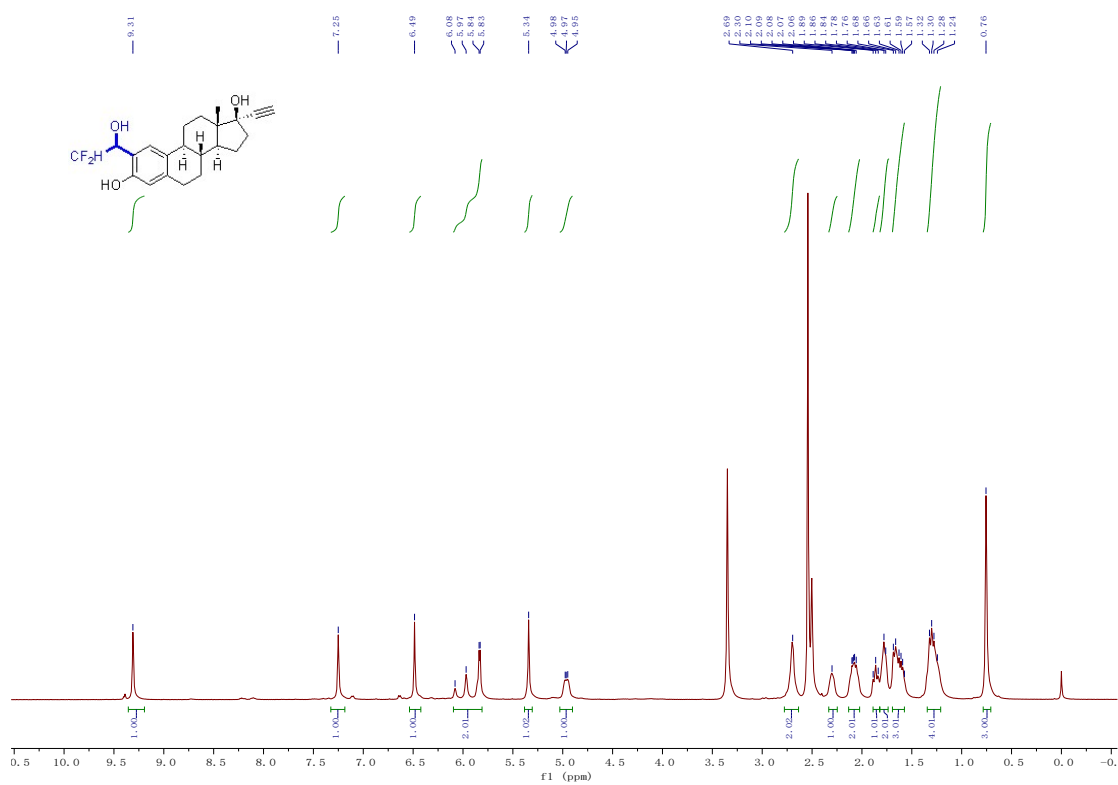
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **6d''**



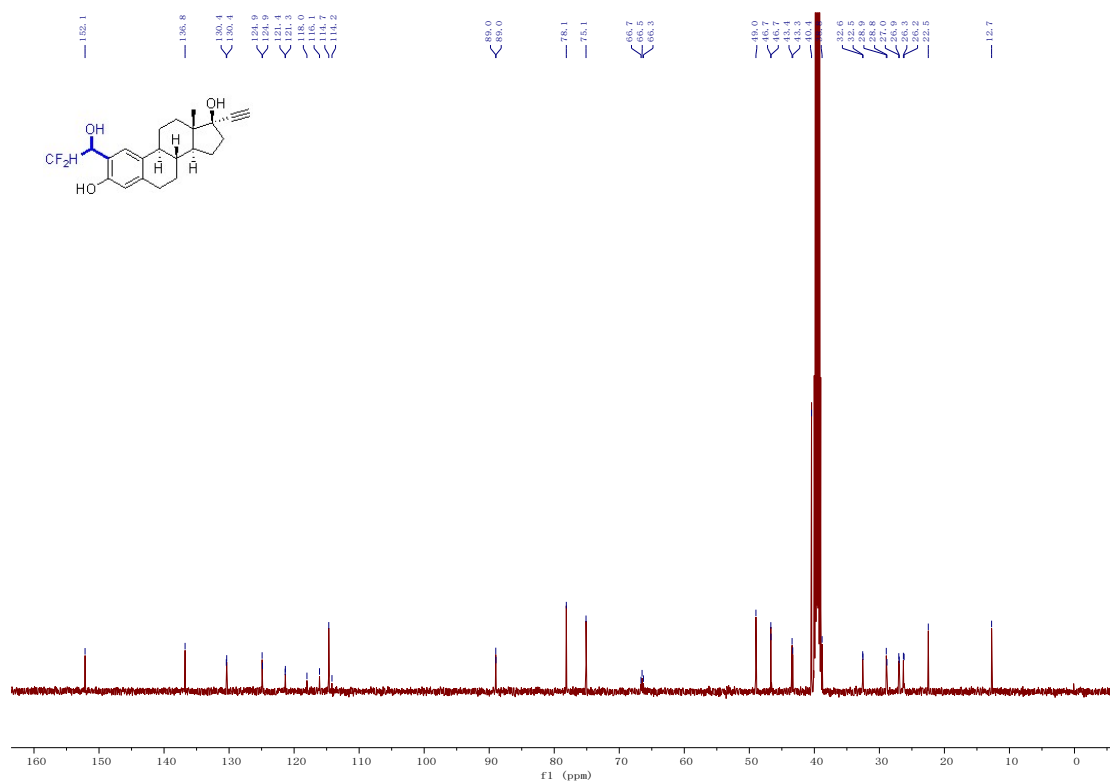
^{19}F NMR (470 MHz, Chloroform- d) spectra of **6d**'



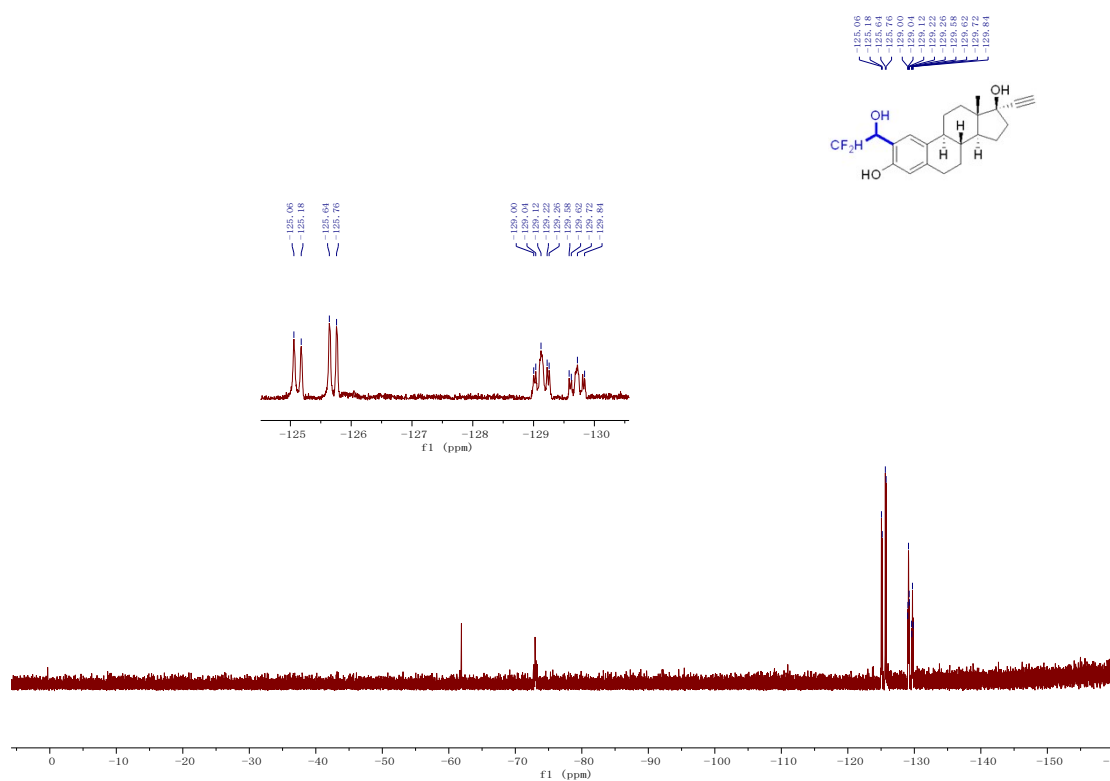
^1H NMR (500 MHz, DMSO- d_6) spectra of **6f**



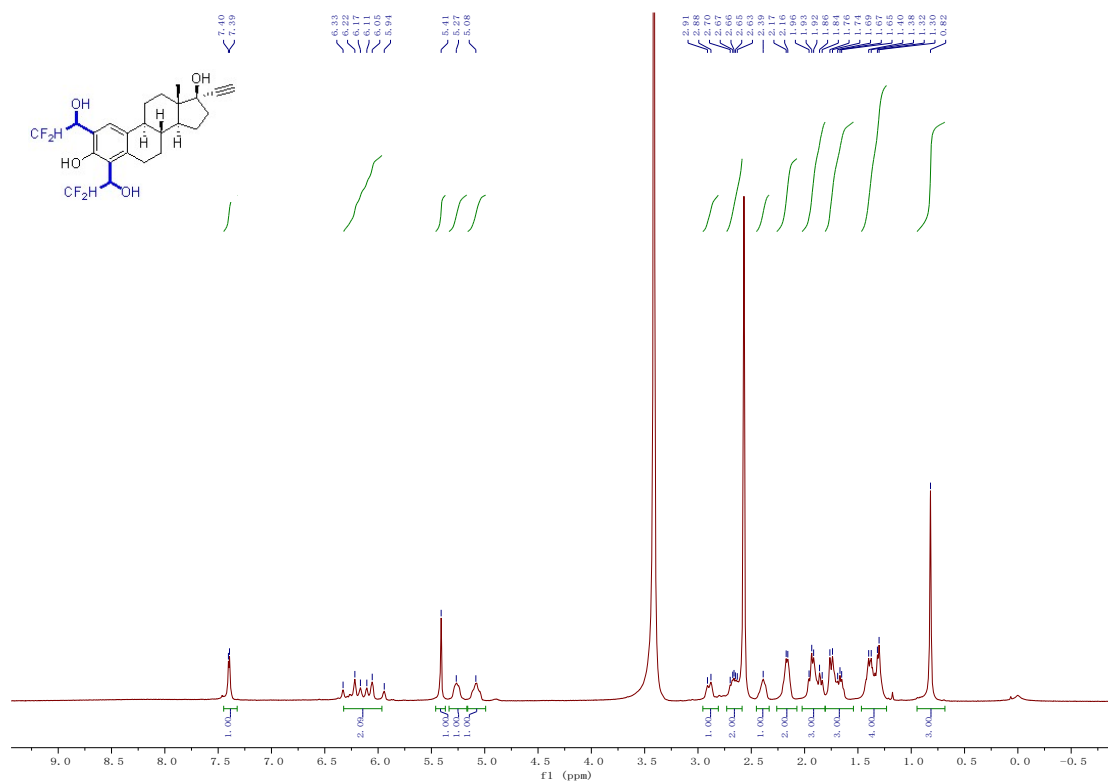
^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectra of **6f**



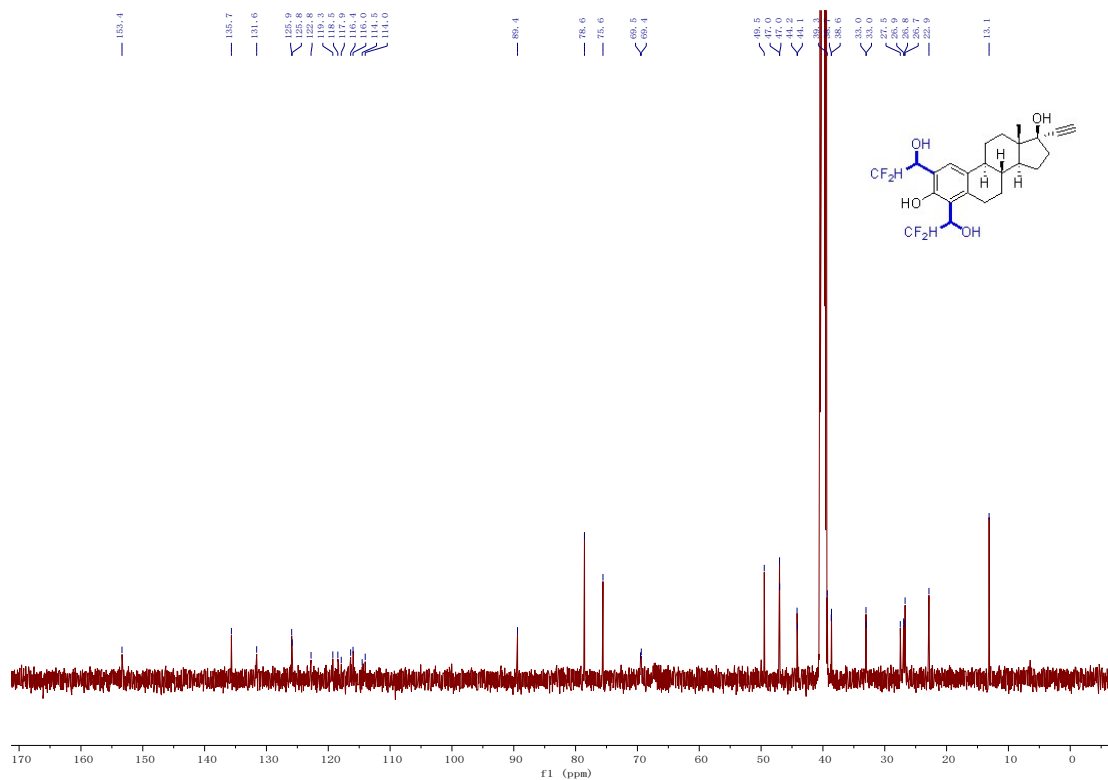
^{19}F NMR (470 MHz, $\text{DMSO-}d_6$) spectra of **6f**



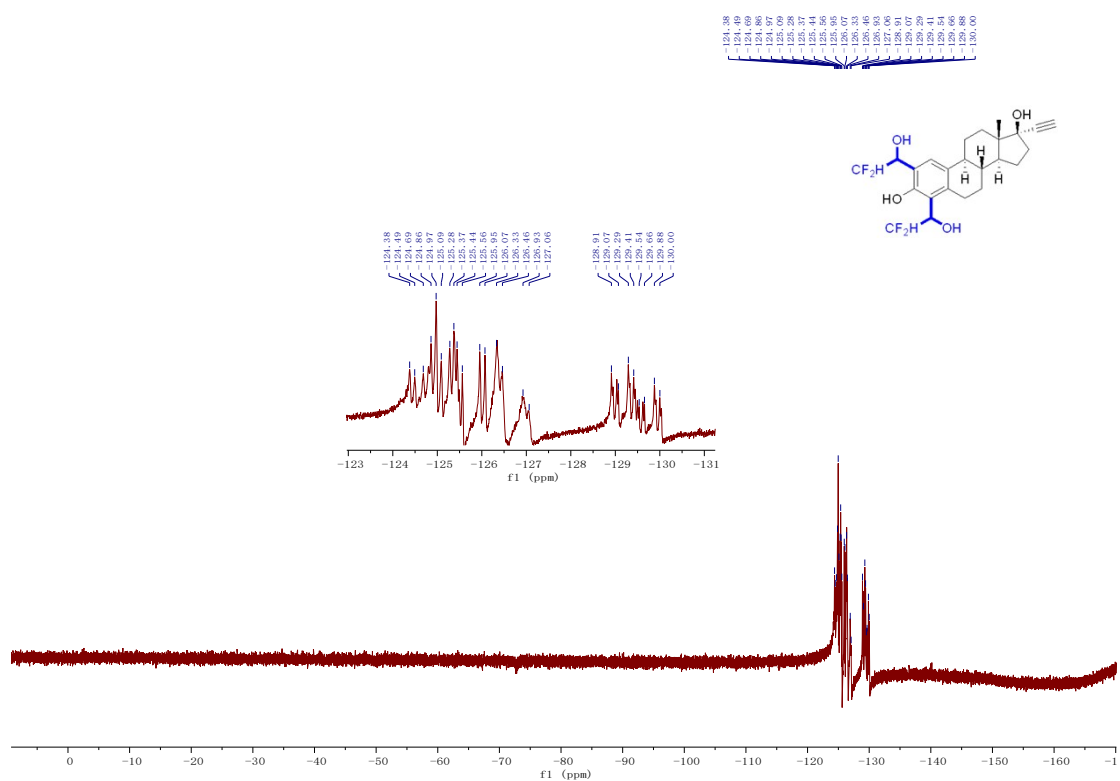
^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectra of **6f**



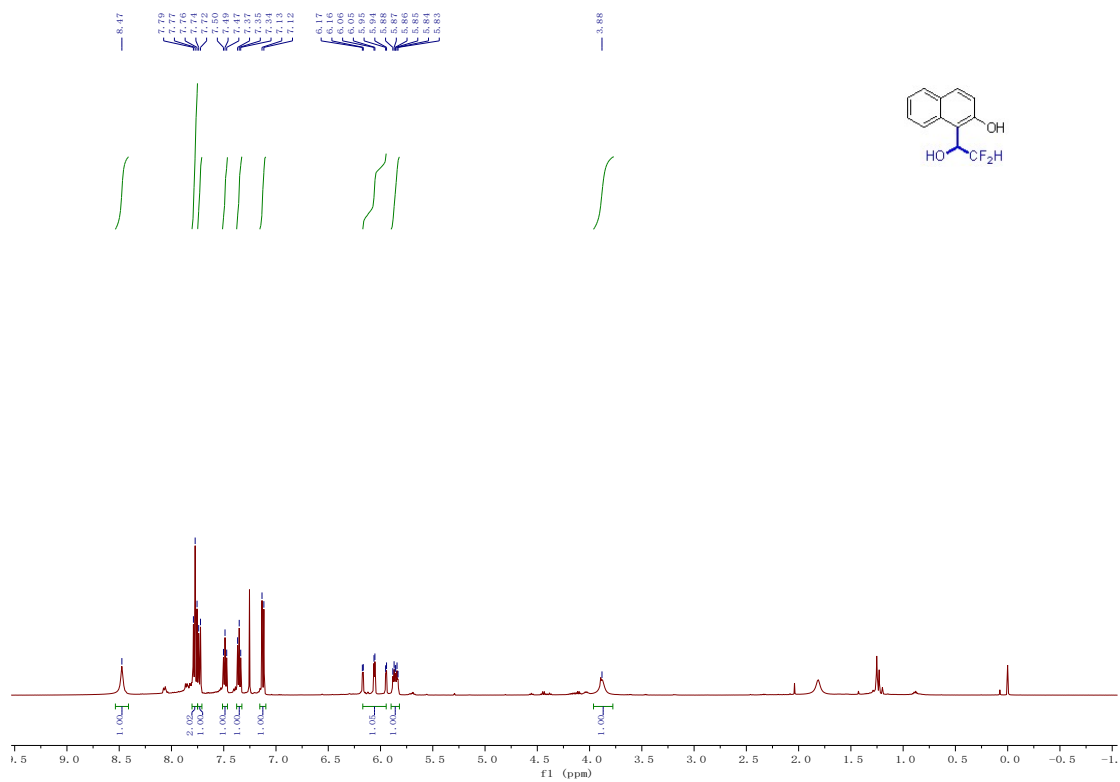
^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectra of **6f**



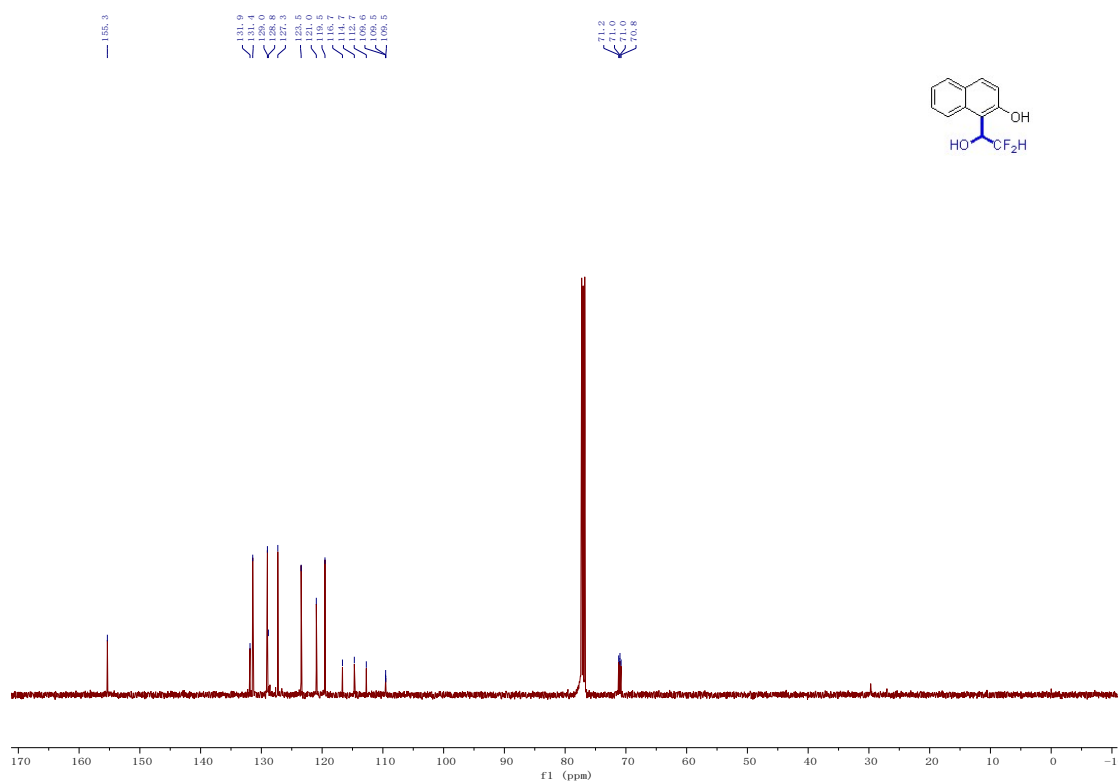
¹⁹F NMR (470 MHz, DMSO-d₆) spectra of **6f**



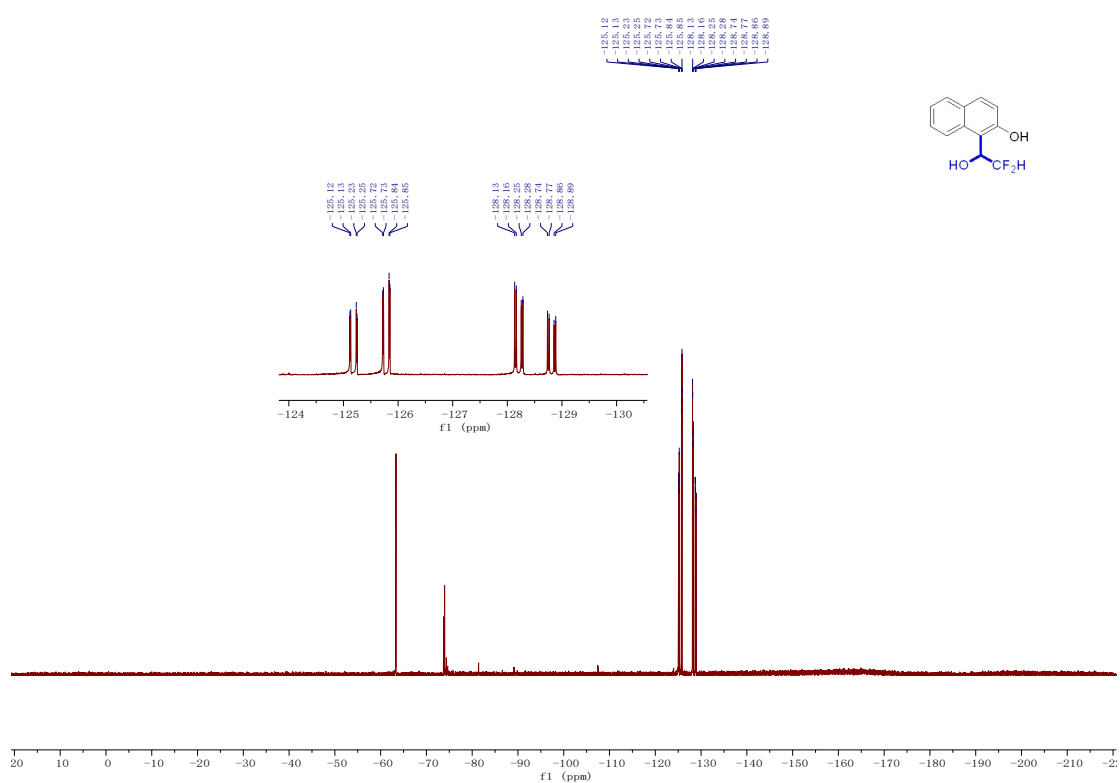
¹H NMR (500 MHz, Chloroform-d) spectra of **6g**



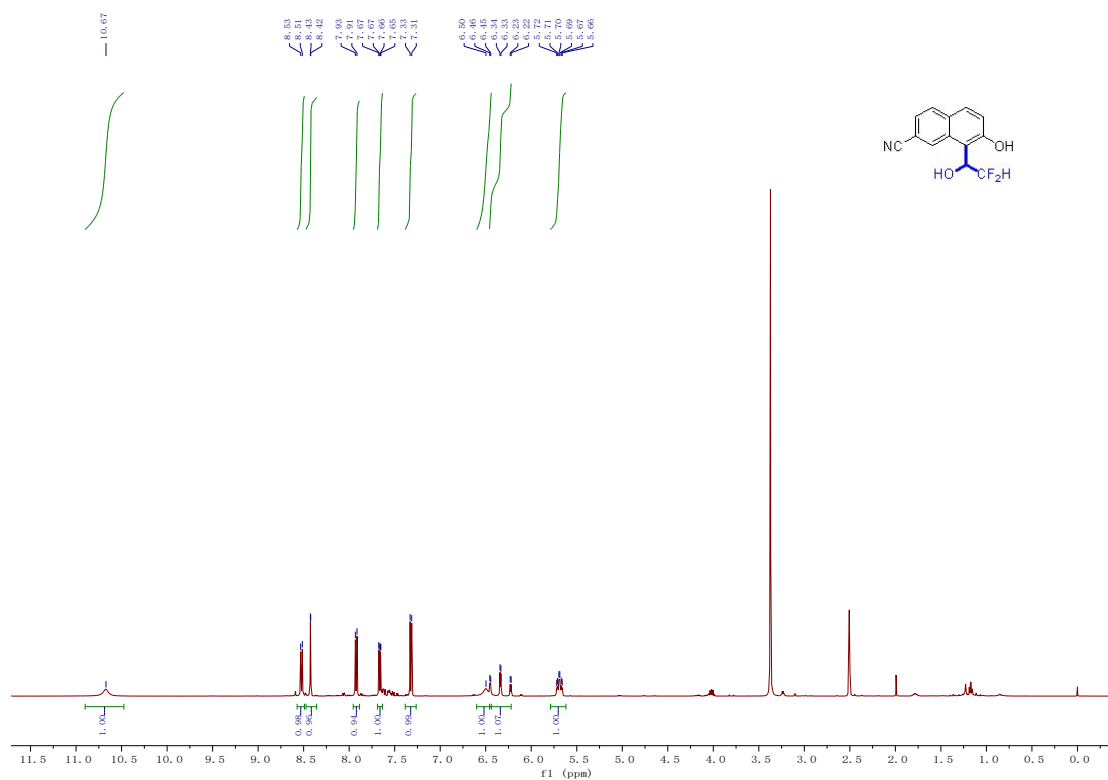
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **6g**



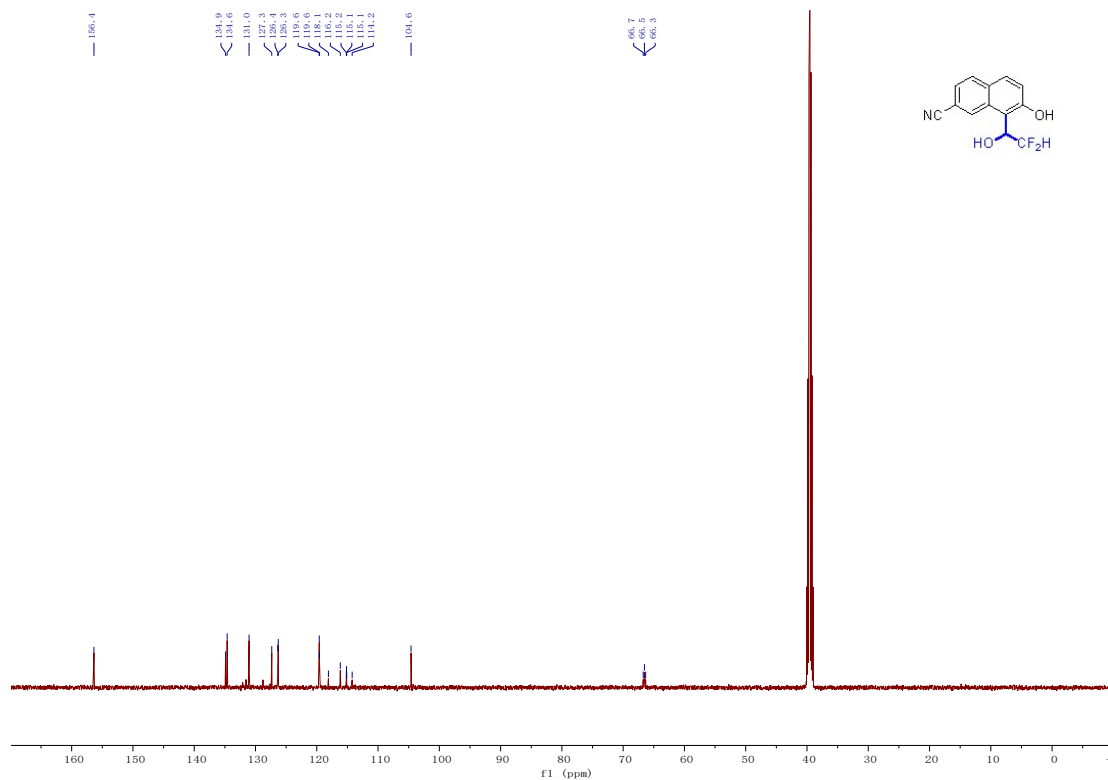
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **6g**



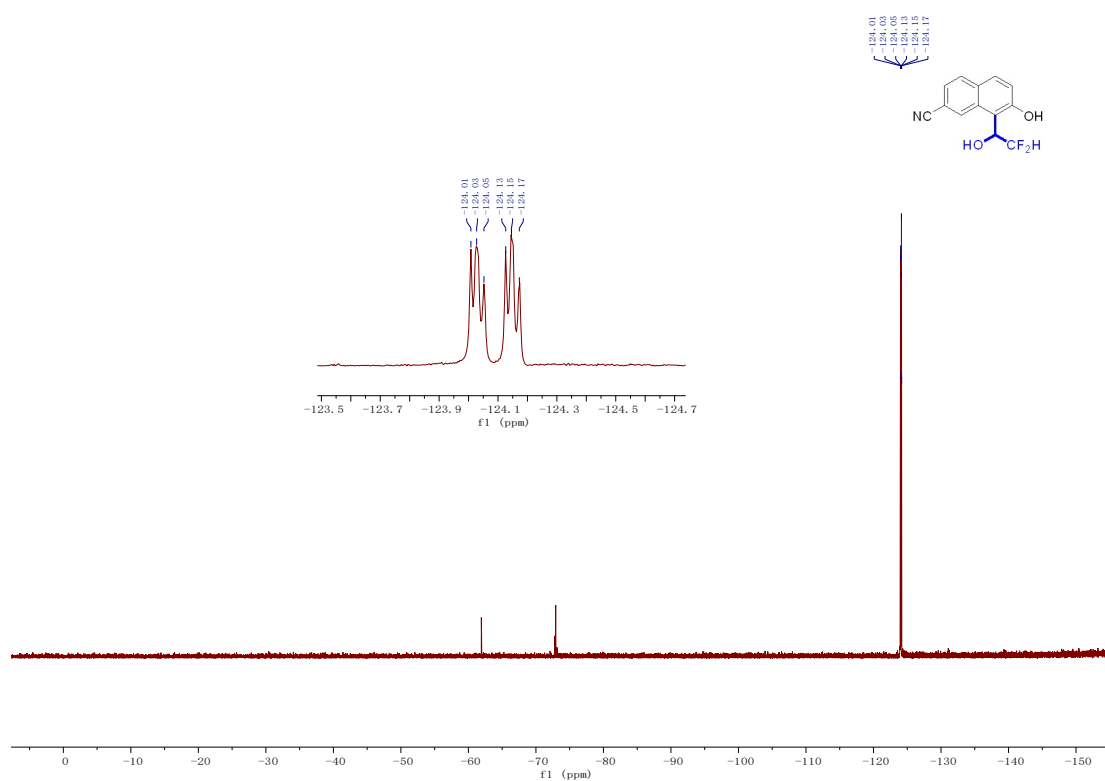
^1H NMR (500 MHz, $\text{DMSO-}d_6$) spectra of **6h**



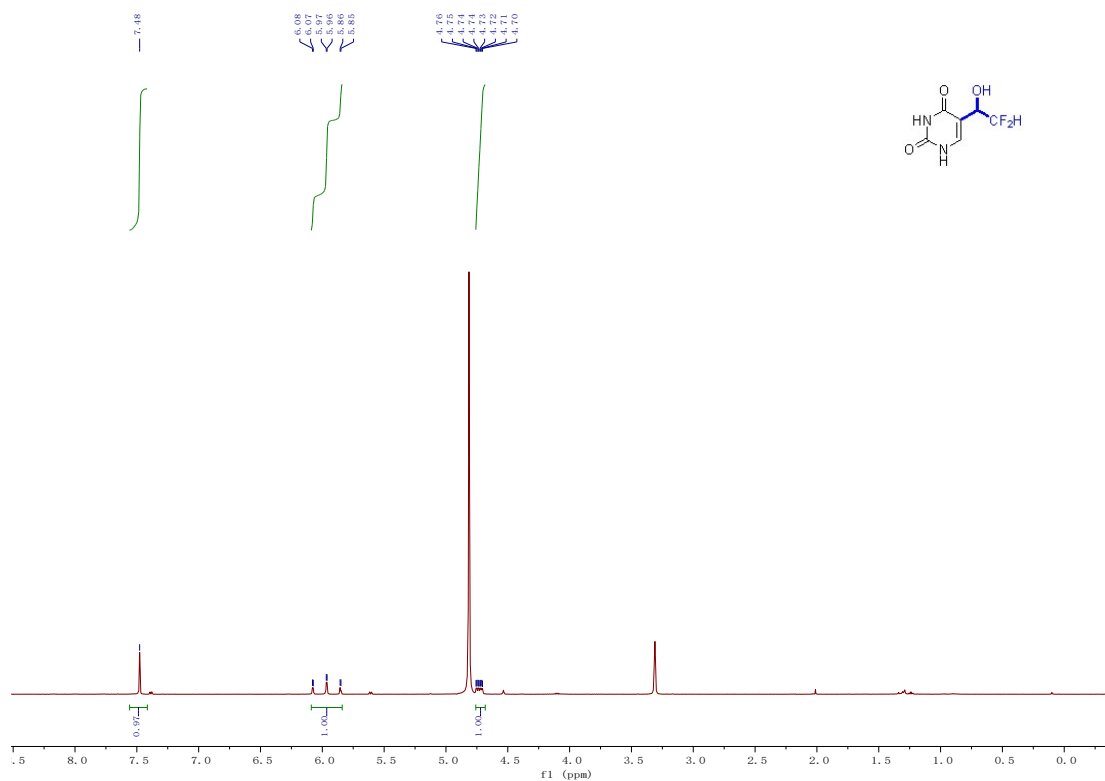
^{13}C NMR (125 MHz, $\text{DMSO-}d_6$) spectra of **6h**



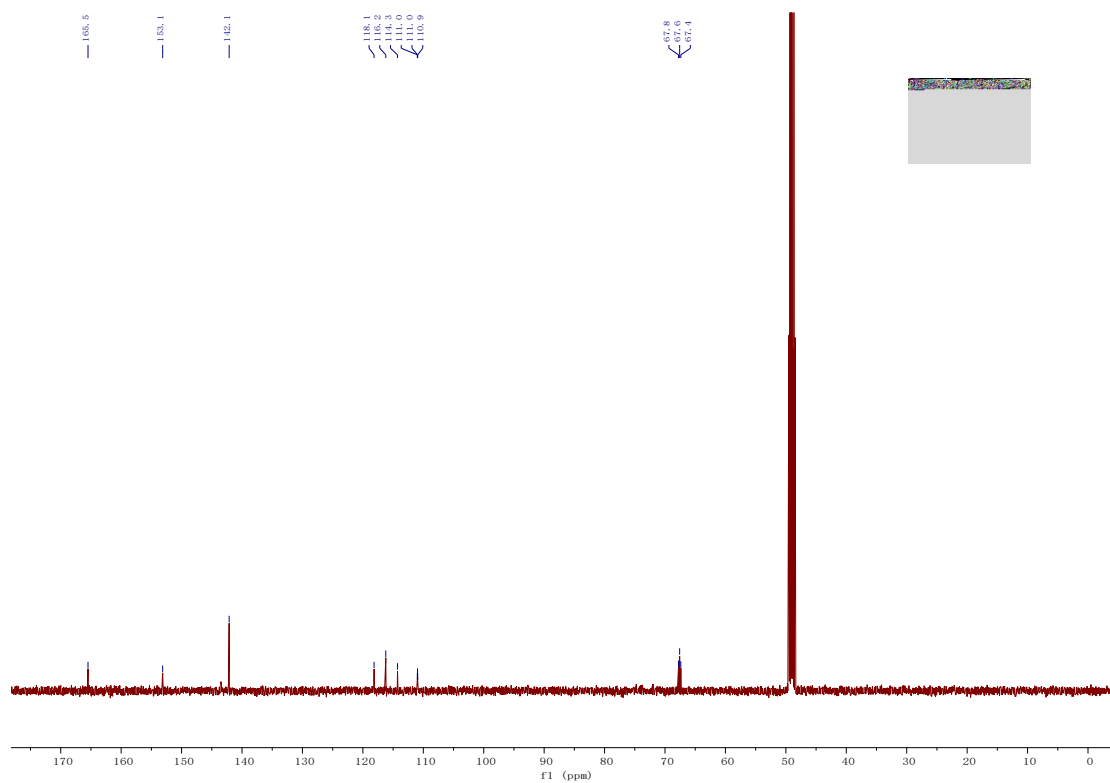
^{19}F NMR (470 MHz, $\text{DMSO-}d_6$) spectra of **6h**



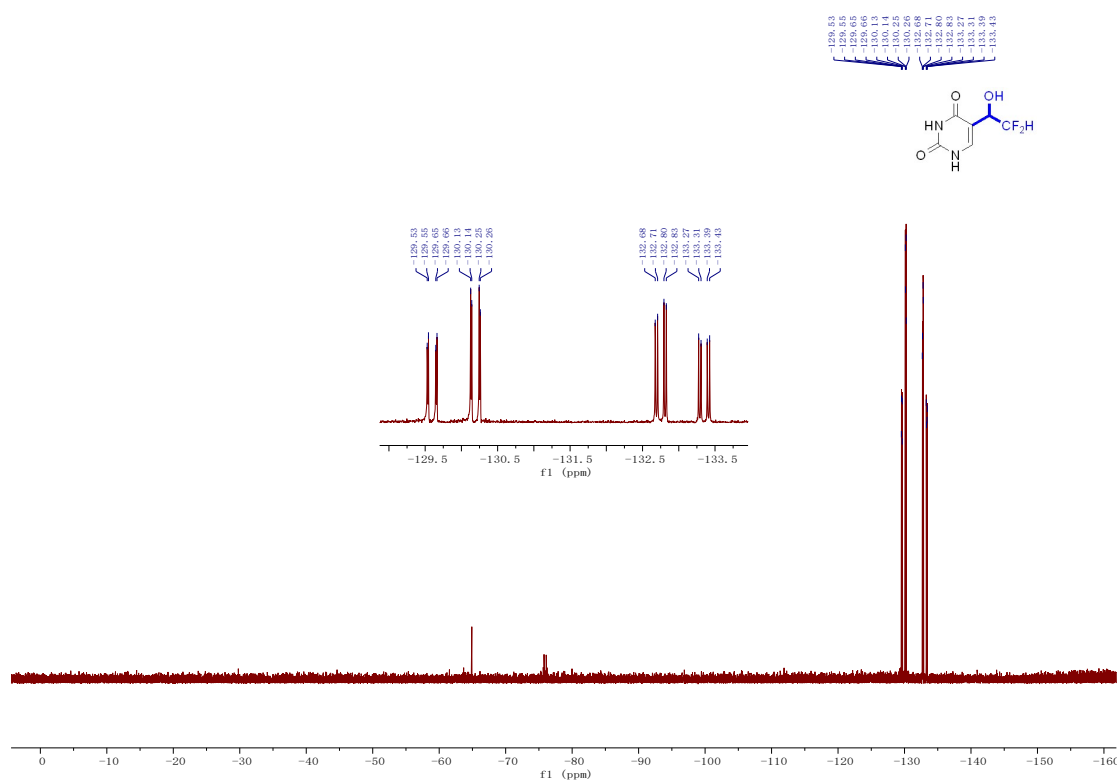
^1H NMR (500 MHz, $\text{Methanol-}d_4$) spectra of **8a**



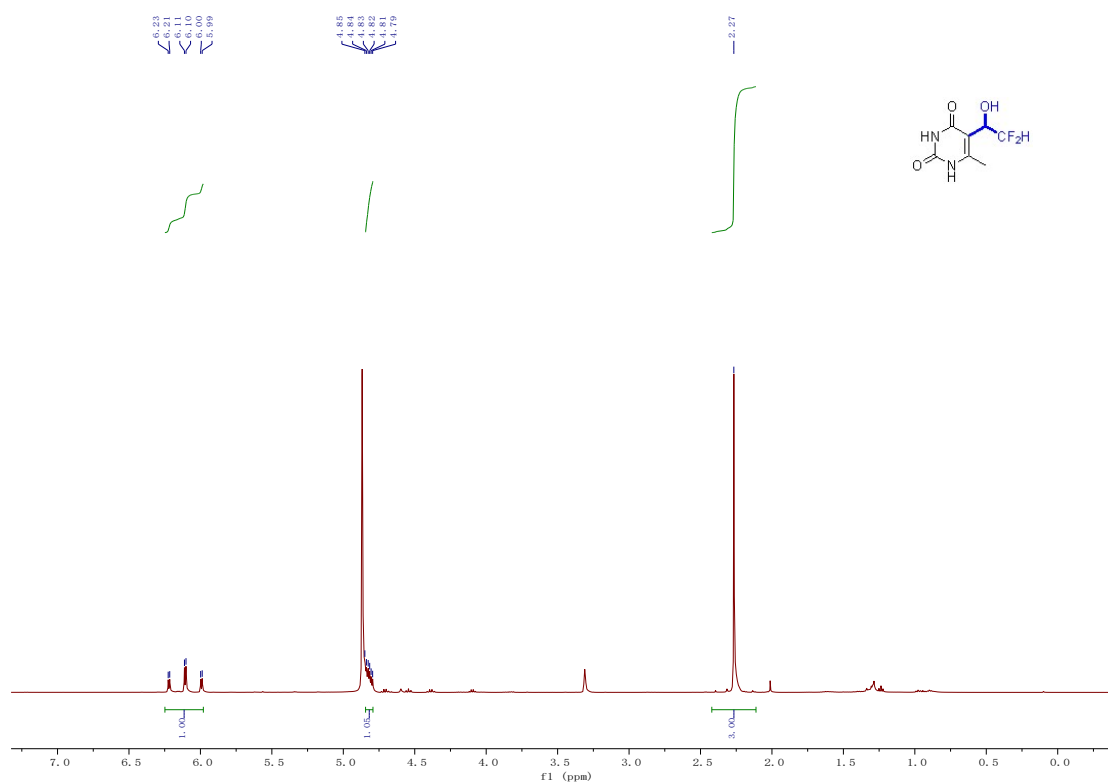
¹³C NMR (125 MHz, Methanol-*d*₄) spectra of **8a**



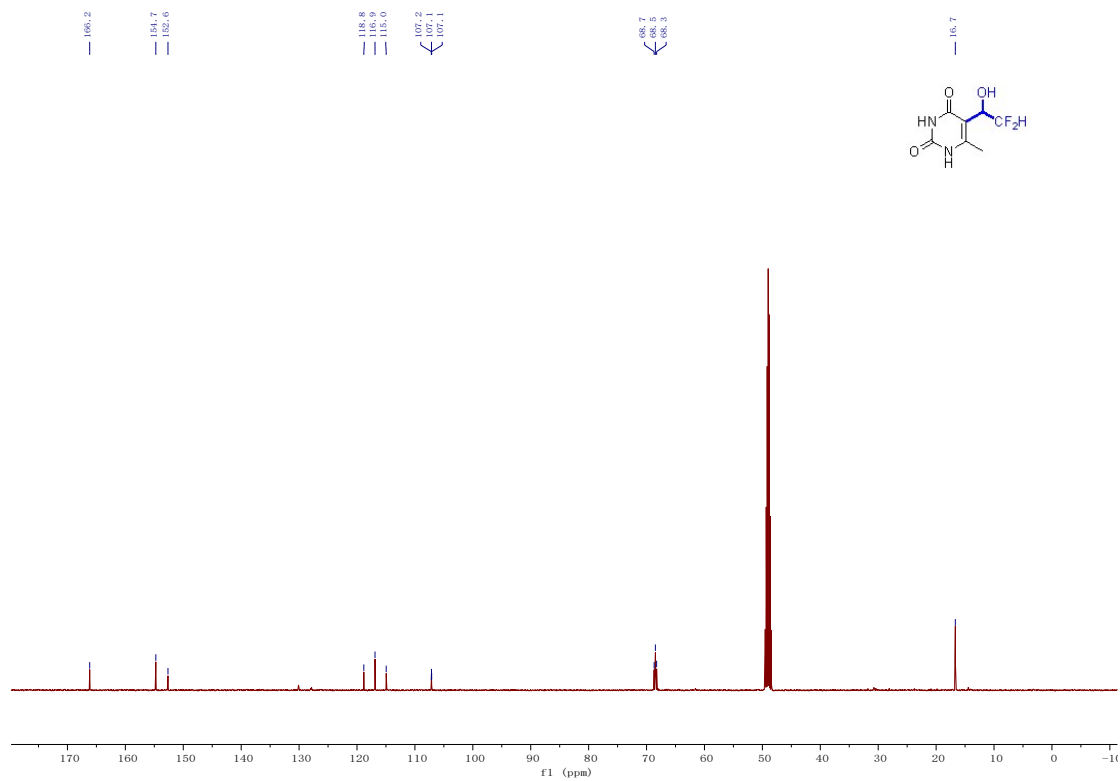
¹⁹F NMR (470 MHz, Methanol-*d*₄) spectra of **8a**



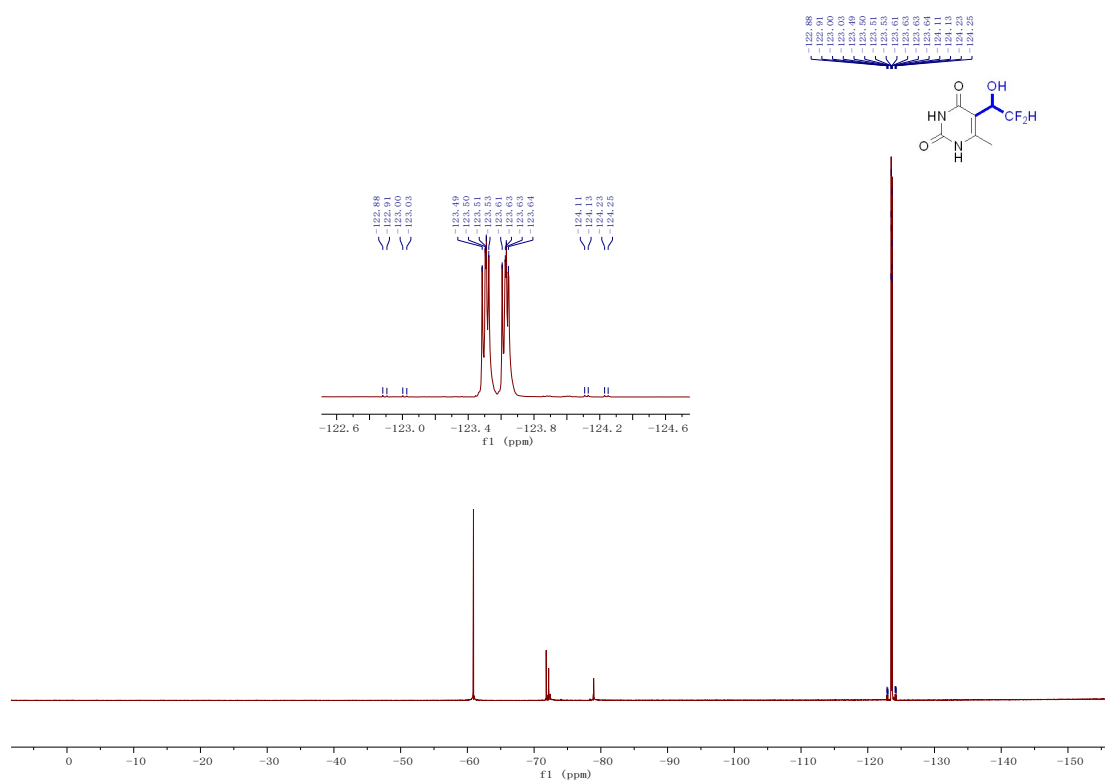
^1H NMR (500 MHz, Chloroform-*d*) spectra of **8b**



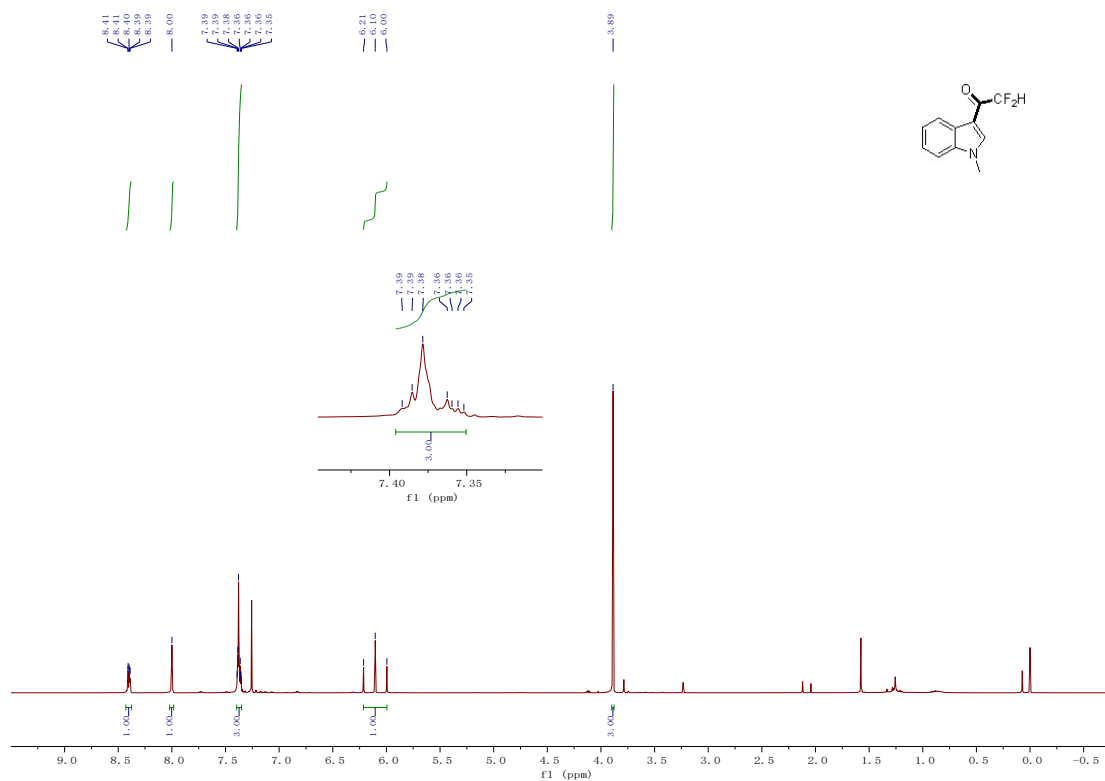
^{13}C NMR (125 MHz, Chloroform-*d*) spectra of **8b**



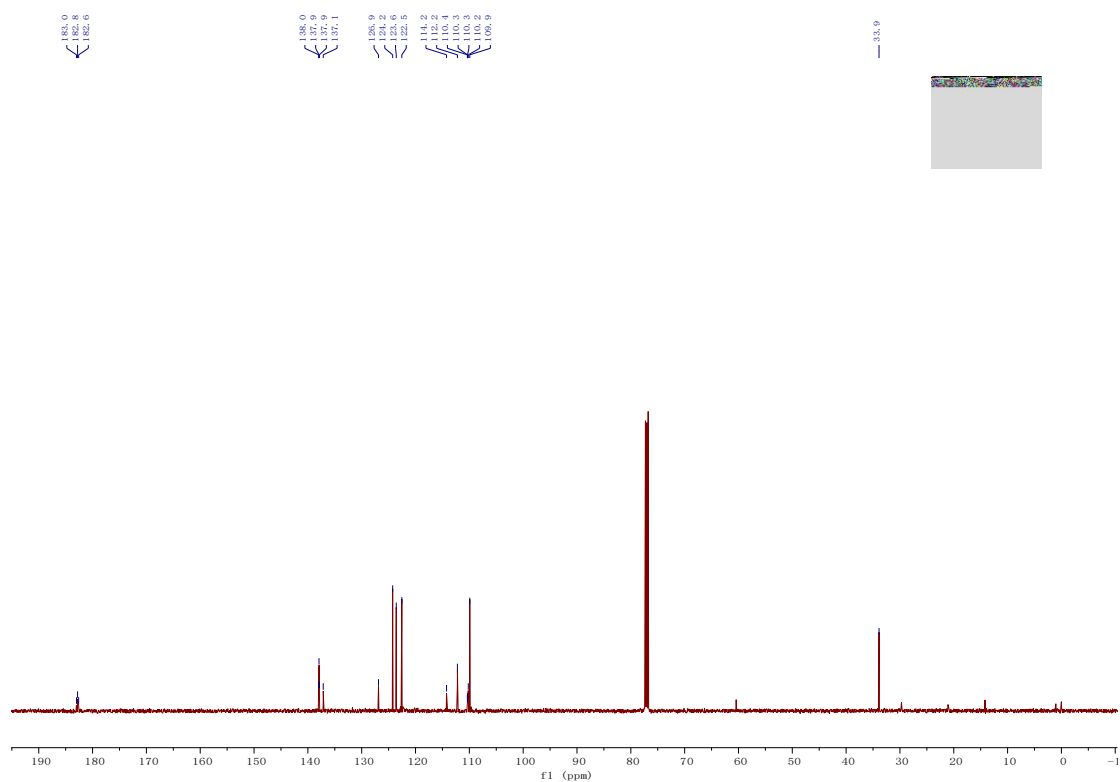
^{19}F NMR (470 MHz, Chloroform-*d*) spectra of **8b**



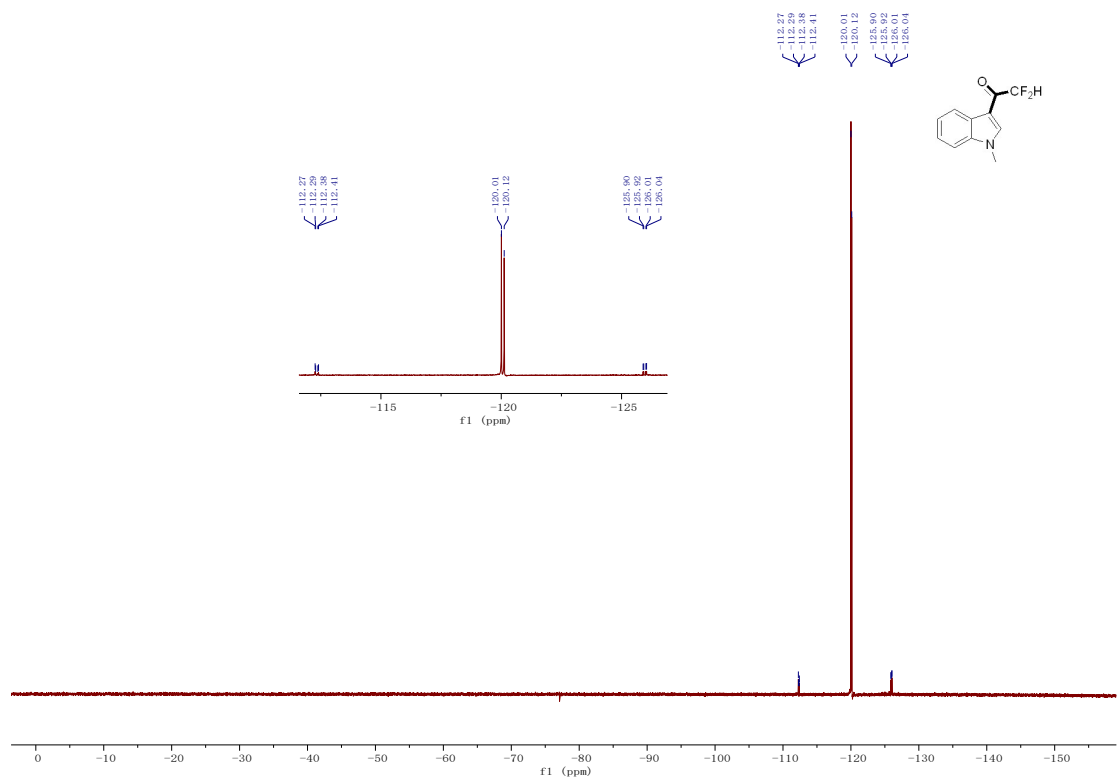
^1H NMR (500 MHz, Chloroform-*d*) spectra of **9**



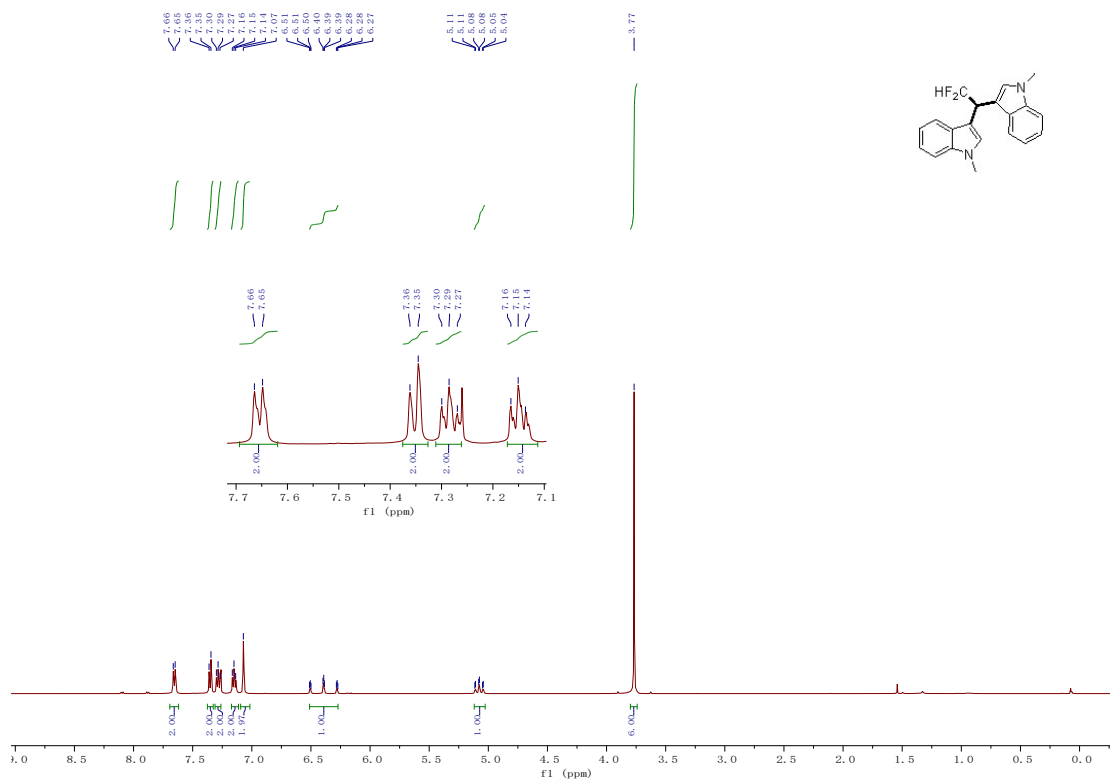
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **9**



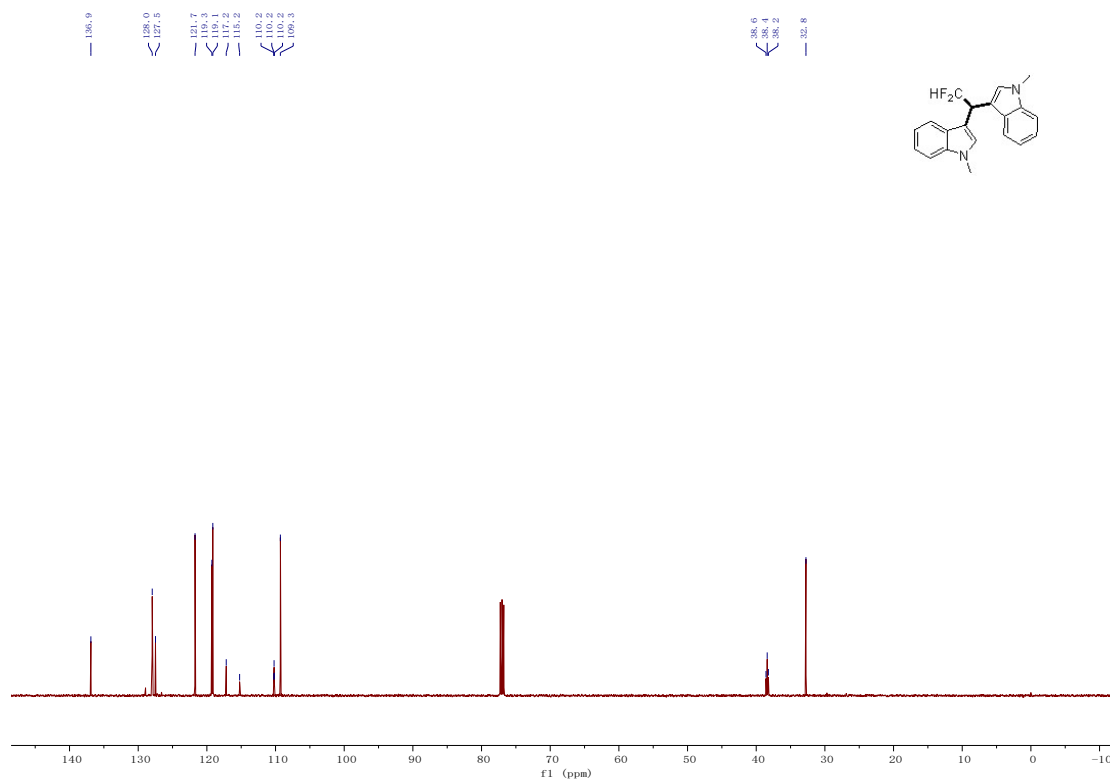
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **9**



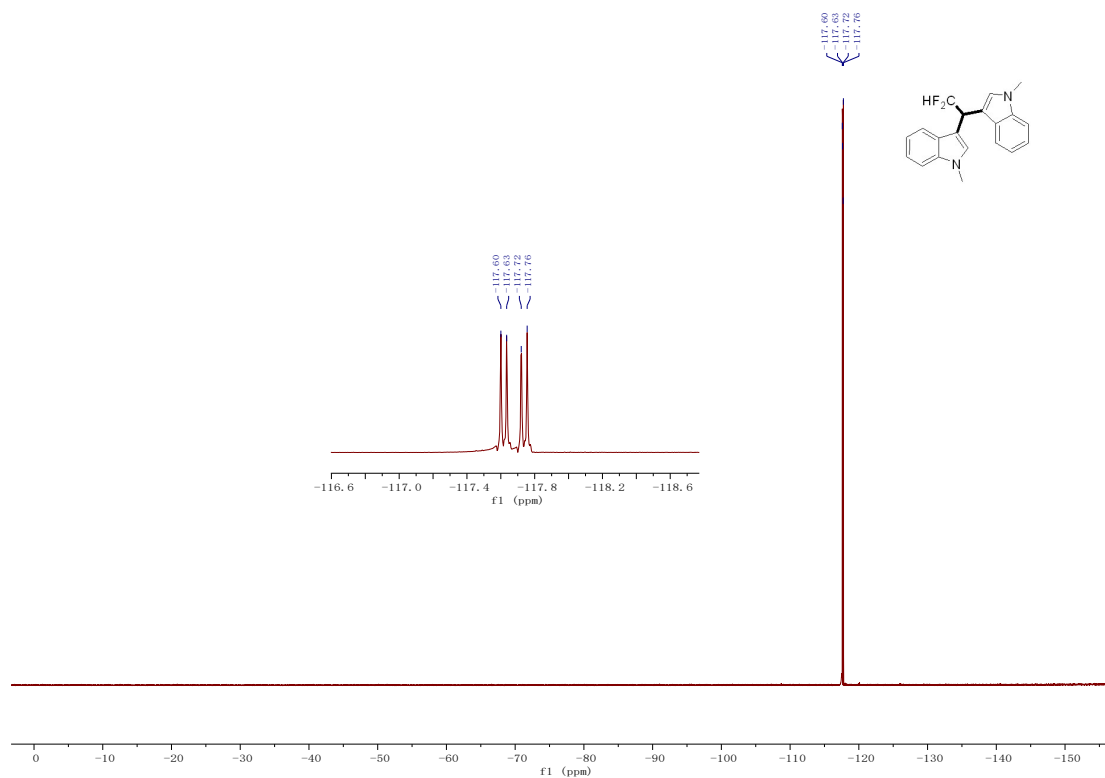
¹H NMR (500 MHz, Chloroform-*d*) spectra of **10**



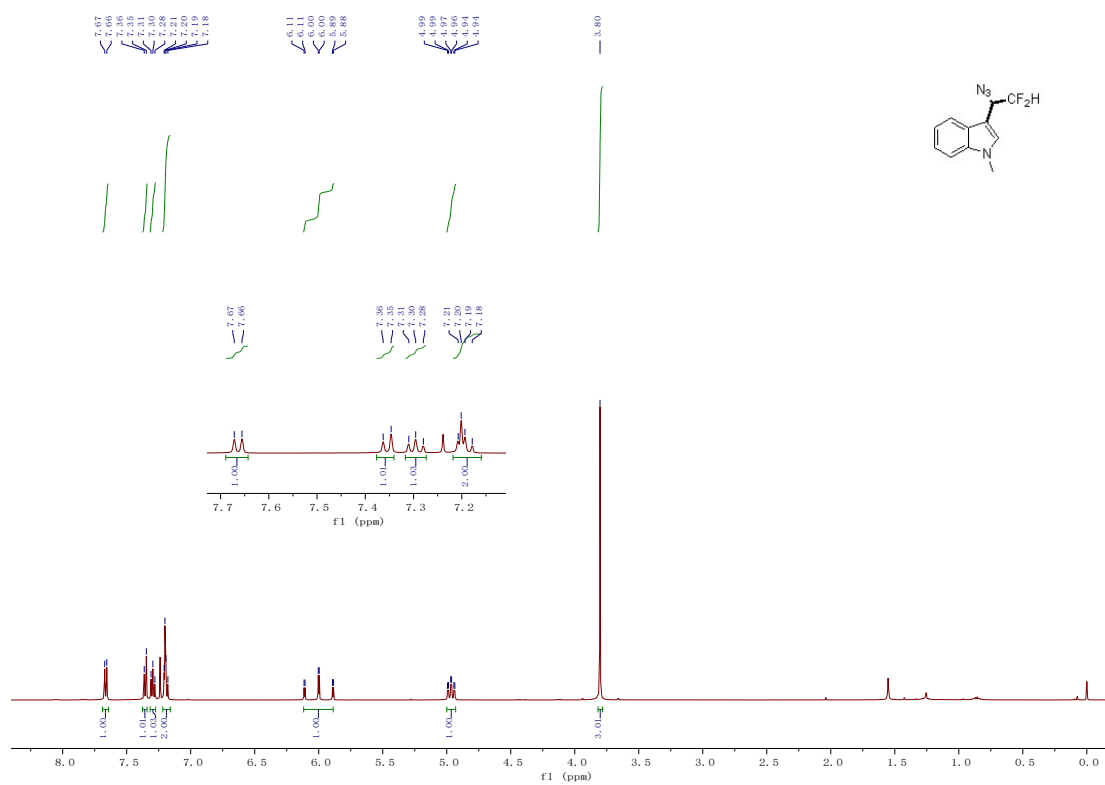
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **10**



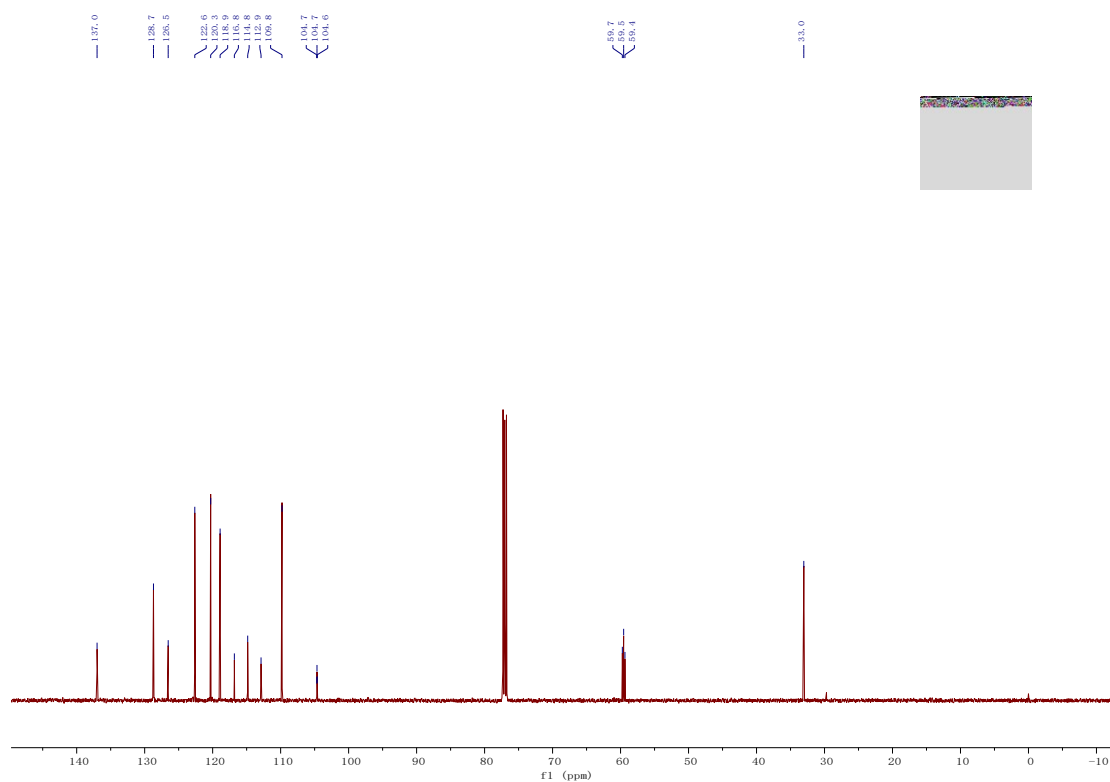
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **10**



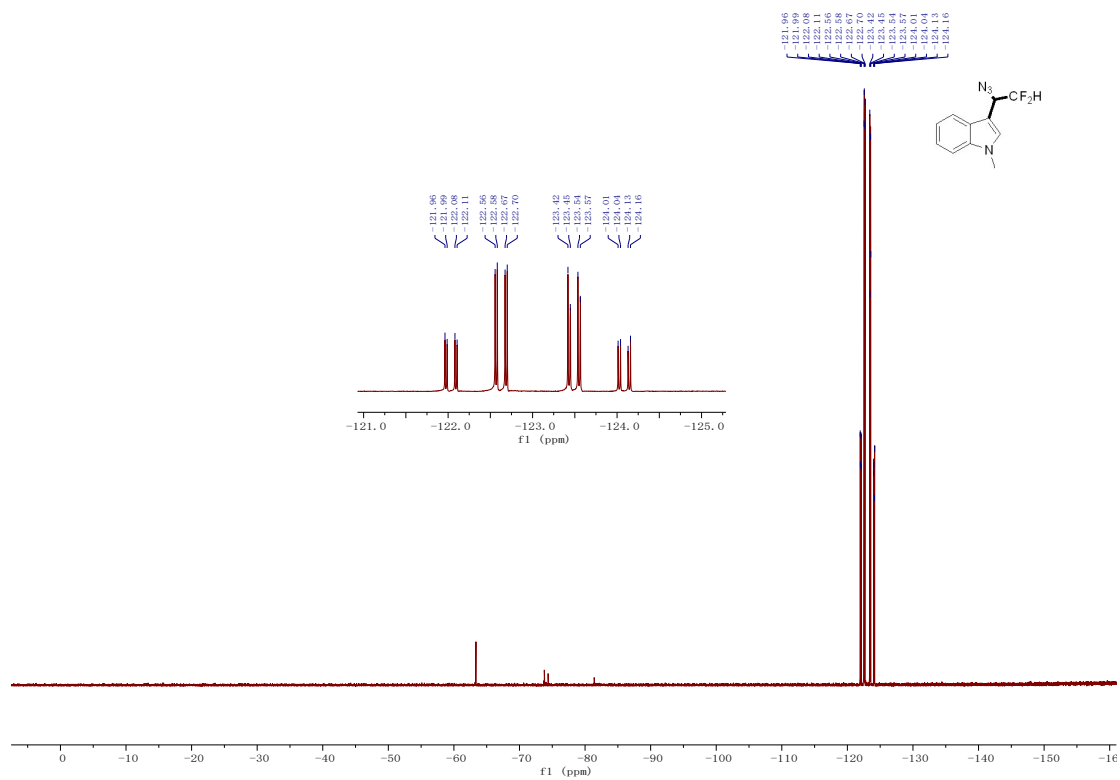
¹H NMR (500 MHz, Chloroform-*d*) spectra of **11**



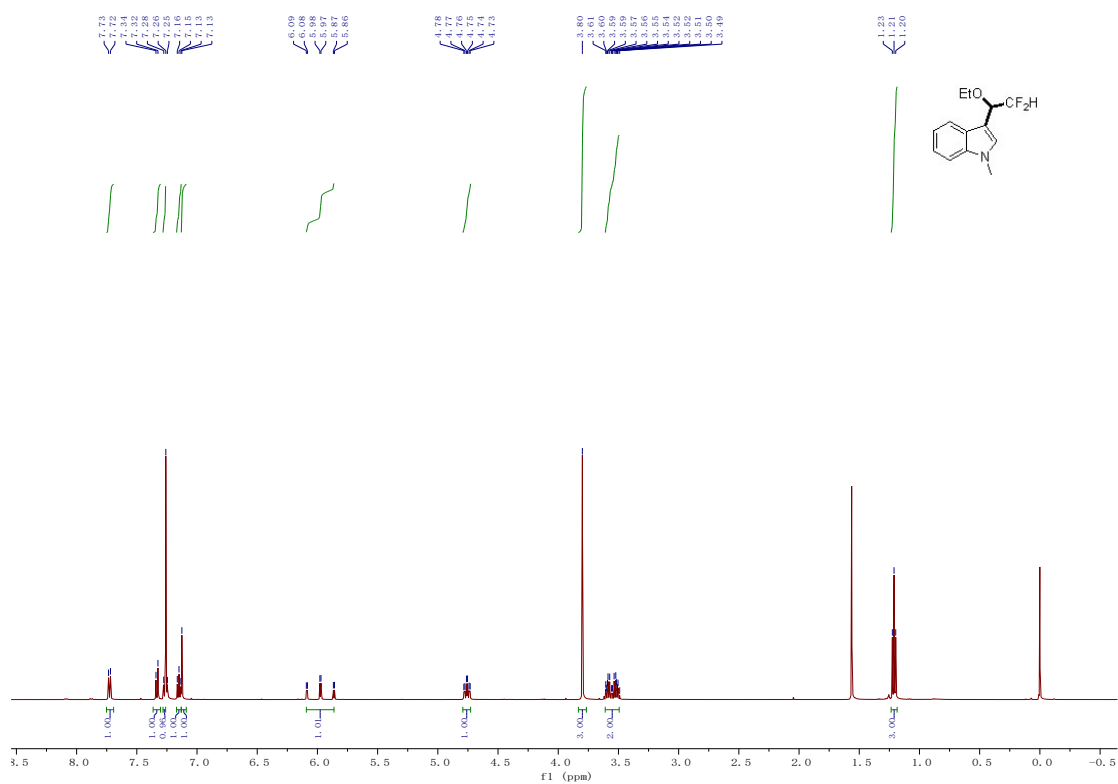
¹³C NMR (125 MHz, Chloroform-*d*) spectra of **11**



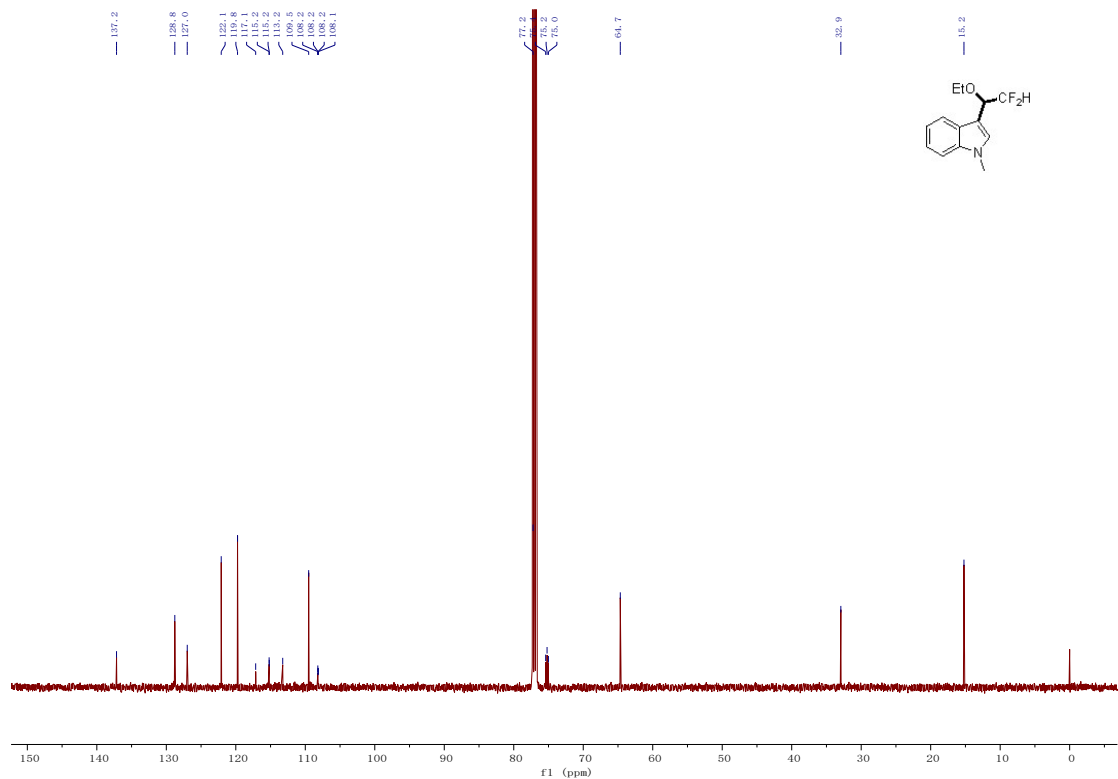
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **11**



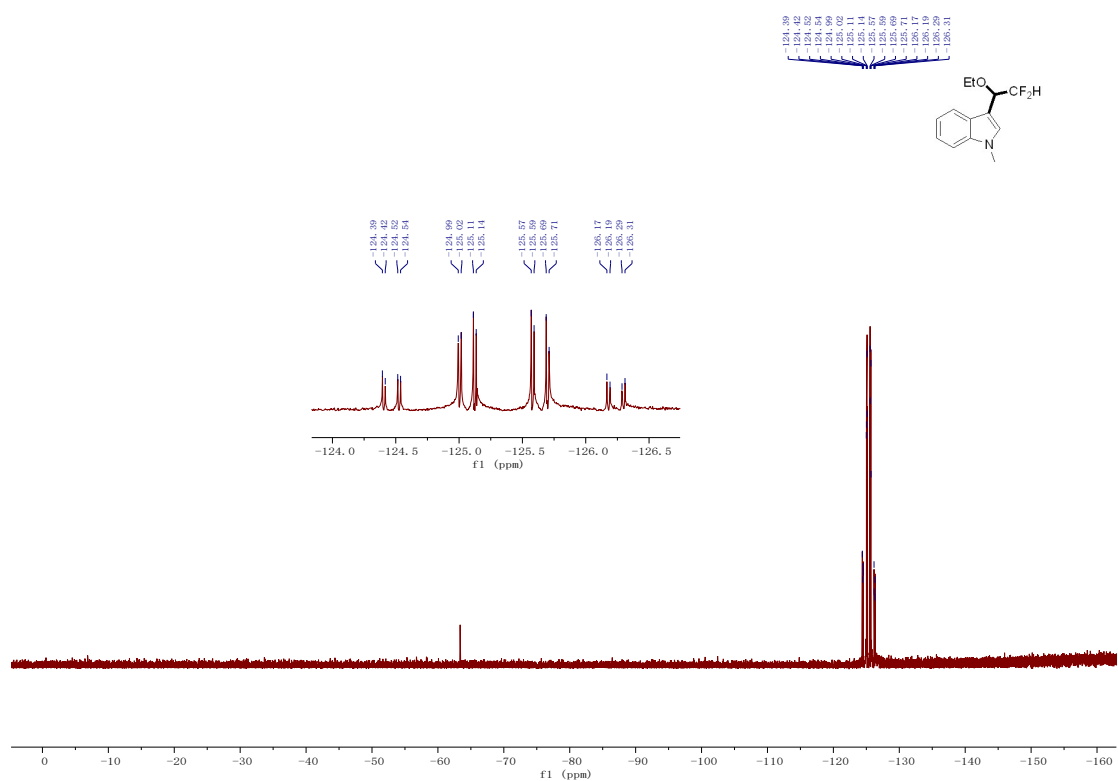
¹H NMR (500 MHz, Chloroform-*d*) spectra of 12



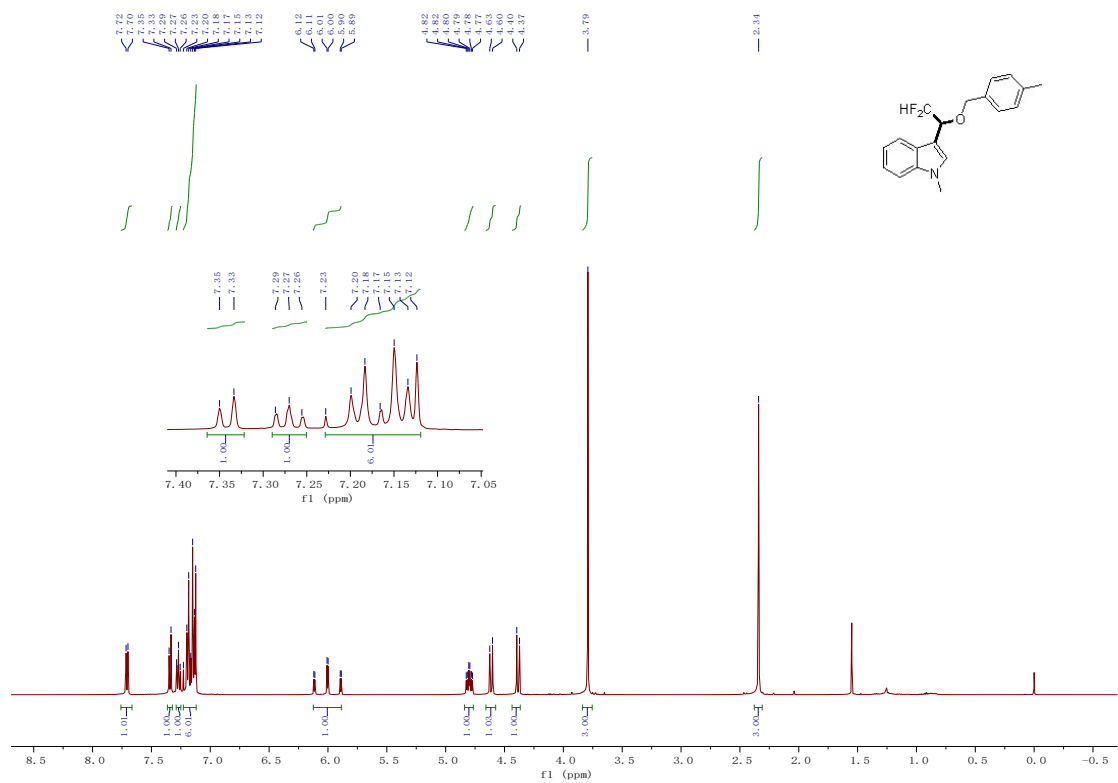
¹³C NMR (125 MHz, Chloroform-*d*) spectra of 12



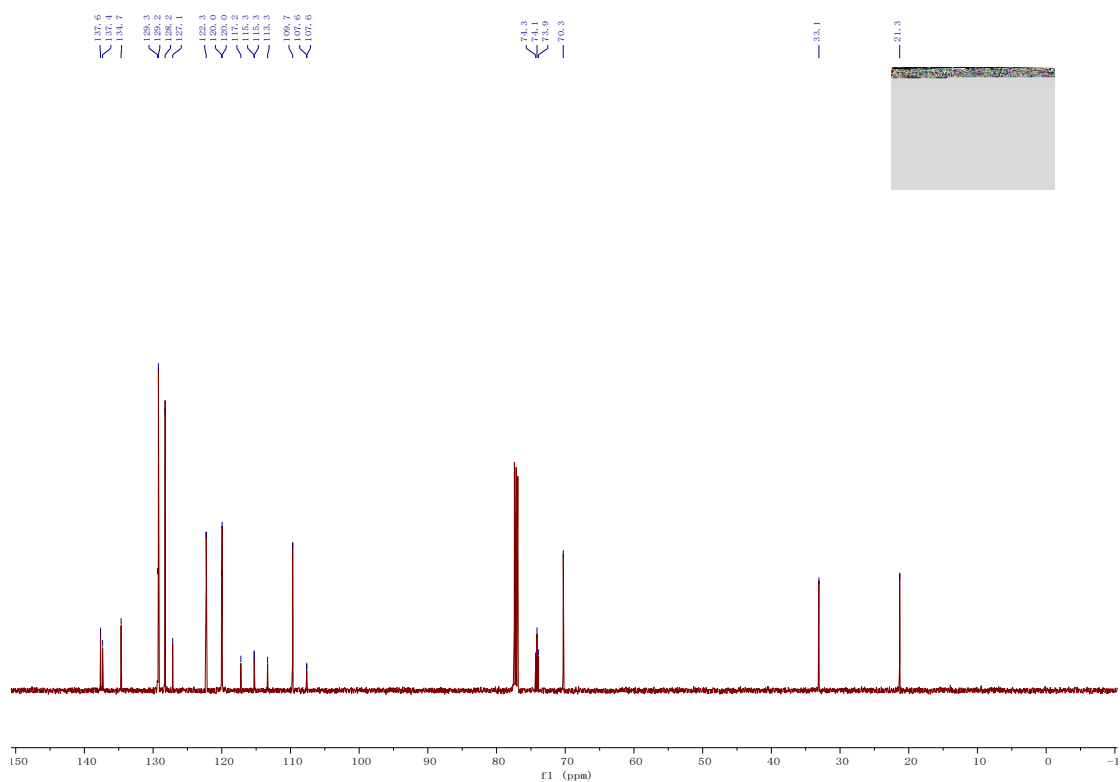
¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **12**



¹H NMR (500 MHz, Chloroform-*d*) spectra of **13**



¹³C NMR (125 MHz, Chloroform-*d*) spectra of **13**



¹⁹F NMR (470 MHz, Chloroform-*d*) spectra of **13**

