Supporting Information

NIS-Mediated Oxidative Cyclization of *N*-(2-Trifluoromethyl-3-alkynyl)hydroxylamines: A Facile Access to 4-Trifluoromethyl-5-acylisoxazoles

Li Zhang, Qin Zeng, Ao Mao, Ziang Wu, Tian Luo, Yuanjing Xiao[a]*and Junliang Zhang[a,b]*

Shanghai Key Laboratory of Green Chemistry and Chemical Processes, Department of Chemistry, East China Normal University, 3663 N. Zhongshan Road, Shanghai 200062 (P. R. China).

E-mail: yjxiao@chem.ecnu.edu.cn, jlzhang@chem.ecnu.edu.cn

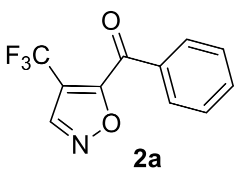
1. General information.

^1H NMR spectra, ^{13}C NMR spectra were recorded on a Bruker 400 MHz and 500 MHz spectrometer in chloroform-d^3 or d^6-DMSO. All signals are reported in ppm with the internal TMS signal at 0 ppm as a standard. The data is being reported as (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad signal, coupling constant(s) in Hz, integration). $ClCH_2CH_2Cl$ (DCE), CH_2Cl_2 (DCM), CH_3CN, DMSO, DMF were freshly distilled from CaH_2;

toluene and THF was freshly distilled from sodium metal prior to use. *N*-(2–(Trifluoromethyl)-3-alkynyl) hydroxylamines **1** were synthesized according to our previously published paper.[1]

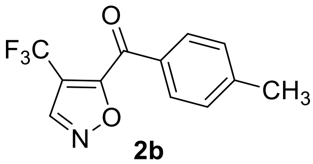
2. General Procedure for the synthesis of 4-trifluoromethyl -5-acylisoxazole 2

To a solution of *N*-(2–(trifluoromethyl)-3-alkynyl)hydroxylamine **1** (0.2 mmol) in DMF(2.0 mL), NIS (90.0 mg, 0.4 mmol) was added at room temperature or at 0℃, the reaction mixture was stirred at room temperature or at 0℃ for 12~36 h. The reaction was quenched with saturated aqueous solution of $Na_2S_2O_3$ (2.0 mL), Then extracted with ethyl acetate (3x4.0 mL) and the combined organic extracts were dried over $MgSO_4$. After filtration and evaporation, the residue was purified by flash column chromatography on silica gel to afford **2**. [Eluent: petroleum ether : ethyl acetate = 50:1～5:1].



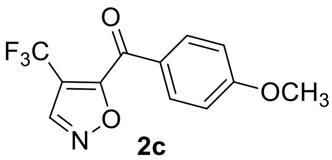
2a

Colorless oil. 79% isolated yield.^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.04 (d, *J* = 7.7 Hz, 2H), 7.72 (t, *J* = 7.3 Hz, 1H), 7.57 (t, *J* = 7.7 Hz, 2H).^{19}F NMR (377 MHz, $CDCl_3$) δ -57.31. ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.58, 164.66, 148.35 (q, *J* = 2.6 Hz), 135.18, 134.47, 130.23, 129.02, 120.21 (q, J = 268.1 Hz), 114.87 (q, J = 40.9 Hz). MS (70 eV): m/z (%): 241 (M^+, 1.99), 46 (100). HRMS calcd for $C_{11}H_6F_3NO_2$: 241.0351, found: 241.0353.



2b

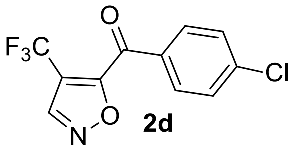
White solid. mp 43-45 ^oC. 65% isolated yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.93 (d, J = 8.1 Hz, 2H), 7.35 (d, J = 8.1 Hz, 2H), 2.46 (s, 3H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.27. ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.18, 165.01 (q, J = 3.2 Hz), 148.22 (q, J = 5.2, 2.6 Hz), 146.69, 132.07, 130.36, 129.75, 120.27 (q, J = 268.1 Hz), 114.48 (q, J = 40.9 Hz), 21.90. MS (70 eV): m/z (%): 255 (M^+, 25.92), 119 (100). HRMS calcd for $C_{12}H_8F_3NO_2$: 255.0507, found: 255.0508.



2c

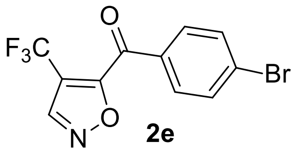
Yellow solid. 32-34 ^oC. 81% isolated yield. ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.03 (d, J = 9.0 Hz, 2H), 7.01 (d, J = 9.0 Hz, 2H), 3.91 (s, 3H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.22. ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.81, 165.25, 165.23 (q, J = 4.1 Hz), 148.20 (q, J = 2.5 Hz), 132.84, 127.42, 120.27 (q, J = 268.0 Hz), 114.34, 114.26 (q, J = 41.0 Hz), 55.67. MS (70 eV): m/z (%): 271

(M^+, 25.97), 135 (100). HRMS calcd for $C_{12}H_8F_3NO_3$: 271.0456, found: 271.0455.



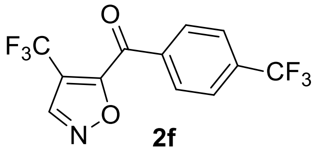
2d

White solid. mp 68-69 °C. 77% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 8.02 (d, *J* = 8.7 Hz, 2H), 7.55 (d, *J* = 8.7 Hz, 2H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.41. ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.15, 164.24 (q, *J* = 3.2 Hz), 148.49 (q, *J* = 2.7 Hz), 142.03, 132.76, 131.56, 129.47, 120.12 (q, *J* = 268.3 Hz), 115.28 (q, *J* = 41.1 Hz). MS (70 eV): m/z (%): 275 (M^+, 23.95), 277 (M^++2, 7.96), 139 (100). HRMS calcd for $C_{11}H_5ClF_3NO_2$: 274.9961, found: 274.9959.



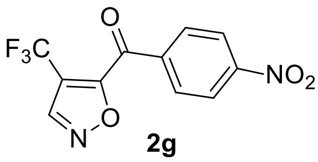
2e

White solid. mp 66-68 °C. 60% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.93 (d, *J* = 8.7 Hz, 2H), 7.72 (d, *J* = 8.7 Hz, 2H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.40. ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.39, 164.21 (q, *J* = 3.2 Hz), 148.49 (q, *J* = 2.7 Hz), 133.18, 132.47, 131.55, 130.95, 120.12 (q, *J* = 268.3 Hz), 115.31 (q, *J* = 41.2 Hz). MS (70 eV): m/z (%): 319 (M^+, 29.16), 321 (M^++2, 28.35), 183(100). HRMS calcd for $C_{11}H_5BrF_3NO_2$: 318.9456, found: 318.9459.



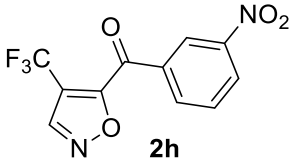
2f

White solid. mp 37-39 °C. 75% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.19 (d, J = 8.2 Hz, 2H), 7.84 (d, J = 8.2 Hz, 2H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.55, -63.45. ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.41, 163.80 (q, J = 3.2 Hz), 148.64 (q, J = 2.7 Hz), 137.11, 136.09 (q, J = 33.0 Hz), 130.53, 126.05 (q, J = 3.7 Hz), 123.24 (q, J = 271.0 Hz), 120.07 (q, J = 266.0 Hz), 115.79 (q, J = 41.0 Hz). MS (70 eV): m/z (%): 309 (M^+, 20.39), 173(100). HRMS calcd for $C_{12}H_5F_6NO_2$: 309.0224, found: 309.0222.



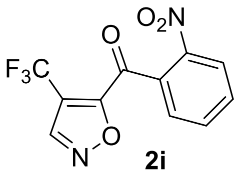
2g

Yellow solid. mp 92-94 °C. 65% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.67 (s, 1H), 8.42 (d, J = 9.0 Hz, 2H), 8.27 (d, J = 9.0 Hz, 2H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.60. ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.69, 163.31 (q, J = 3.3 Hz), 151.17, 148.81 (q, J = 2.7 Hz), 138.76, 131.26, 124.09, 119.95 (q, J = 268.6 Hz), 116.26 (q, J = 41.4 Hz). MS (70 eV): m/z (%): 286 (M^+, 38.15), 150 (100). HRMS calcd for $C_{11}H_5F_3N_2O_4$: 286.0201, found: 286.0203.



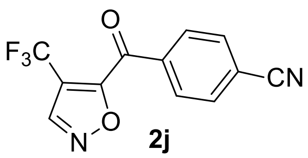
2h

Yellow oil. 91% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.93 (s, 1H), 8.67 (s, 1H), 8.57 (d, J = 7.8 Hz, 1H), 8.43 (d, J = 7.8 Hz, 1H), 7.82 (t, J = 8.0 Hz, 1H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.57. ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.13, 163.28 (q, J = 3.1 Hz), 148.80 (q, J = 2.7 Hz), 148.52, 135.63, 135.46, 130.42, 129.07, 125.01, 119.97 (q, J = 268.6 Hz), 116.26 (q, J = 41.3 Hz). MS (70 eV): m/z (%): 286 (M^+, 25.88), 150 (100). HRMS calcd for $C_{11}H_5F_3N_2O_4$: 286.0201, found: 286.0199.



2i

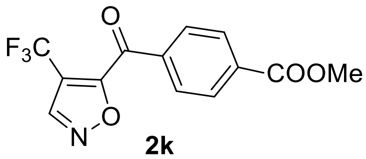
Yellow solid. mp 104-106 ^{o}C. 86% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.32 (d, J = 7.6 Hz, 1H), 7.94-7.87 (m, 1H), 7.86 – 7.80 (m, 1H), 7.64 (d, J = 7.6 Hz, 1H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.69. ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.99, 162.78 (q, J = 3.3 Hz), 149.12 (q, J = 2.8 Hz), 146.50, 135.06, 132.75, 132.68, 129.52, 124.62, 120.00 (q, J = 268.6 Hz), 114.21 (q, J = 41.9 Hz). MS (70 eV): m/z (%): 286 (M^+, 8.61), 134 (100). HRMS calcd for $C_{11}H_5F_3N_2O_4$: 286.0201, found: 286.0200.



2j

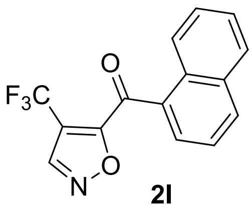
Yellow solid. mp 120-122 ^{o}C. 74% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ

8.66 (s, 1H), 8.19 (d, J = 8.4 Hz, 2H), 7.88 (d, J = 8.4 Hz, 2H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.56. ^{13}C NMR (101 MHz, $CDCl_3$) δ 178.90, 163.40 (q, J = 3.2 Hz), 148.75 (q, J = 2.8 Hz), 137.30, 132.72, 130.51, 119.95 (q, J = 268.5 Hz), 118.15, 117.39, 116.13 (q, J = 41.4 Hz). MS (70 eV): m/z (%): 266 (M^+, 20.42), 130 (100). HRMS calcd for $C_{12}H_5F_3N_2O_2$: 266.0303, found: 266.0305.



2k

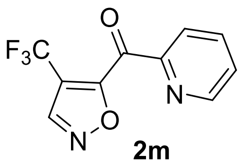
White solid. mp 68-69 °C. 75% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.21 (d, J = 8.2 Hz, 2H), 8.11 (d, J = 8.2 Hz, 2H), 3.97 (s, 3H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.45. ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.88, 165.73, 164.03 (q, J = 3.2 Hz), 148.55 (q, J = 2.7 Hz), 137.51, 135.49, 130.09, 130.02, 120.09 (q, J = 268.3 Hz), 115.50 (q, J = 41.2 Hz), 52.69. MS (70 eV): m/z (%): 299 (M^+, 27.30), 163 (100). HRMS calcd for $C_{13}H_8F_3NO_4$: 299.0405 found: 299.0407.



2l

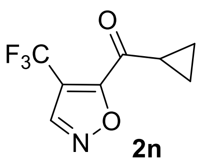
White solid. mp 105-107 °C. 65% isolated yield.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 8.2 Hz, 1H), 8.62 (s, 1H), 8.16 (d, J = 8.2 Hz, 1H), 7.96 (d, J = 7.7

Hz, 1H), 7.83 (d, J = 7.7Hz, 1H), 7.73-7.66 (m, 1H), 7.65-7.59(m, 1H), 7.56 (dd, J = 8.0, 7.5 Hz, 1H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.14. ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.22, 165.55 (q, J = 3.2 Hz), 148.36 (q, J = 2.6 Hz), 135.71, 133.82, 132.82, 131.21, 130.64, 129.25, 128.81, 127.23, 125.07, 124.17, 120.32 (q, J = 268.2 Hz), 114.47 (q, J = 40.9 Hz). MS (70 eV): m/z (%): 291 (M^+, 38.15), 127 (100). HRMS calcd for $C_{15}H_8F_3NO_2$: 291.0507, found: 291.0509.



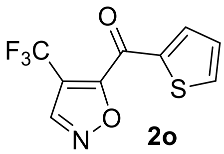
2m

Brown oil. 39% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, J = 4.7 Hz, 1H), 8.58 (s, 1H), 8.18 (d, J = 7.8 Hz, 1H), 8.00-7.94 (m, 1H), 7.63-7.58 (m, 1H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -56.95. ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.96, 164.52 (q, J = 3.3 Hz), 151.69, 149.65, 147.71 (q, J = 2.4 Hz), 137.31, 128.49, 124.12, 120.32 (q, J = 267.8 Hz), 114.12 (q, J = 40.5 Hz). MS (70 eV): m/z (%): 242(M^+, 1.13), 78 (100). HRMS calcd for $C_{10}H_5F_3N_2O_2$: 242.0303, found: 242.0304.



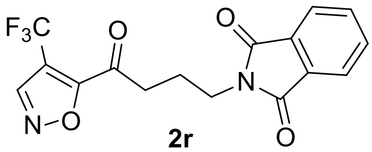
2n

Faint yellow solid. mp 65-67 ^{o}C. 33% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 2.87-2.78 (m, 1H), 1.47 – 1.37 (m, 2H), 1.29-1.24 (m, 2H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.63. ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.14, 163.68 (q, J = 3.2 Hz), 148.99 (q, J = 3.0 Hz), 120.14 (q, J = 268.2 Hz), 112.96 (q, J = 41.5 Hz), 19.46, 14.04 (2C). MS (70 eV): m/z (%): 205(M^+, 25.36), 164 (100). HRMS calcd for $C_8H_6F_3NO_2$: 205.0351, found:.



2o

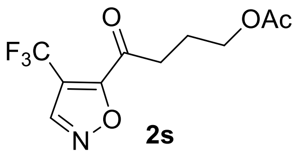
Light yellow solid. mp 38-41 ^{o}C. 47% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.20 (d, J = 3.9 Hz, 1H), 7.90 (d, J = 4.9 Hz, 1H), 7.28 – 7.25 (m, 1H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.45. ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.18, 163.87 (q, J = 3.2 Hz), 148.73 (q, J = 2.9 Hz), 140.96, 137.76, 136.62, 129.10, 120.14 (q, J = 268.3 Hz), 115.13 (q, J = 41.3 Hz). MS (70 eV): m/z (%): 247(M^+, 30.50), 111(100). HRMS calcd for $C_9H_4F_3NO_2S$: 246.9915, found:.



2r

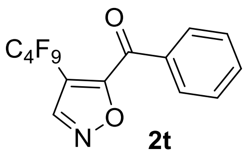
White solid. mp 92-94 ^{o}C. 69% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (s, 1H), 7.84 (dd, J = 5.5, 3.0 Hz, 2H), 7.73 (dd, J = 5.5, 3.0 Hz, 2H), 3.83 (t, J = 6.5 Hz, 2H), 3.14 (t, J = 7.0 Hz, 2H), 2.22-2.12 (m, 2H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.80. ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.68, 168.41, 163.24 (q, J = 3.2 Hz), 148.95 (q, J = 3.0 Hz), 134.05, 131.93, 123.33, 120.03 (q, J = 268.4 Hz), 113.62 (q, J = 41.6 Hz), 37.62, 36.73, 21.78. MS (70 eV): m/z (%): 352 (M^+, 0.45), 160 (100). HRMS calcd for $C_{16}H_{11}F_3N_2O_4$: 352.0671, found:

352.0675.



2s

Colorless oil. 78% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 4.17 (t, *J* = 6.2 Hz, 2H), 3.15 (t, *J* = 7.0 Hz, 2H), 2.17 – 2.08 (m, 2H), 2.03 (s, 3H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.78. ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.00, 170.92, 163.27, 149.01 (q, *J* = 3.0 Hz), 120.05 (q, *J* = 268.4 Hz), 113.73 (q, *J* = 41.7 Hz), 62.99, 37.14, 22.05, 20.79. MS (70 eV): m/z (%): 205(M^+-CH_3COOH, 12.62), 43(100). HRMS-ESI calcd for $C_{10}H_{10}F_3NNaO_4$ [$M+Na^+$]: 288.0454, found: 288.0469.

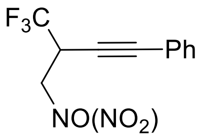


2t

Yellow oil. 69% isolated yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 7.90 (d, *J* = 7.3 Hz, 2H), 7.71 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.8 Hz, 2H). ^{19}F NMR (377 MHz, $CDCl_3$) δ 80.95 – -81.05 (m, 3F), -105.30 – -105.50 (m, 2F), -122.25 – -122.45 (m, 2F), -125.60 – -125.80 (m, 2F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.49, 166.17 (t, *J* = 3.1 Hz), 149.43 – 144.87 (m, 1C), 135.35, 134.63, 130.14, 129.05, 119.01-112.57 (m, 2C), 111.39 (t, *J* = 30.3 Hz), 110.31-107.99 (m, 2C). MS (70 eV): m/z (%): 391 (M^+, 6.42), 105 (100). HRMS calcd for $C_{14}H_6F_9NO_2$: 391.0255, found: 391.0253.

3. Synthesis of 3a/3a’

To a solution of *N*-(4-phenyl-2-(trifluoromethyl)but-3-yn-1-yl)hydroxyl amine **1a** (0.2 mmol, 45.8 mg) in Toluene(2.0 mL), NIS (90.0 mg. 0.4 mmol) was added at room temperature, the reaction mixture was stirred at room temperature for 13 h. The reaction was quenched with saturated aqueous solution of $Na_2S_2O_3$ (2.0 mL), then extracted with ethyl acetate (3x4.0 mL) and the combined organic extracts were dried over Na_2SO_4. After filtration and evaporation, the residue was purified by flash column chromatography on silica gel to afford two inseparable nitro/nitroso compound **3a**/**3a’** in 1:1 ratio (39.4 mg) in 84% isolated yield as a White solid. [eluent: petroleum ether/dichloromethane 2:1].

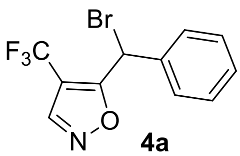


3a/3a'

^{1}H NMR (400 MHz, $CDCl_3$) δ [7.46 – 7.41 (m, 2H)], [7.39 – 7.28 (m, 3H)], [4.85 – 4.63 (m, 2H)], [4.46-4.33 (m, 1H)]. ^{19}F NMR (377 MHz, $CDCl_3$) δ -70.22，70.24. ^{13}C NMR (100 MHz, $CDCl_3$) δ 131.96, 129.21, (128.33, 128.31), [123.78 (q, *J* = 278.0 Hz), 123.76 (q, *J* = 279.0 Hz)], (121.10,121.08), (86.59, 86.53), [77.47 (q, *J* = 3.4 Hz), 77.43 (q, *J* = 3.4 Hz)], (57.49, 57.34), [34.72 (q, *J* = 32.0 Hz), 34.63 (q, *J* = 33.0 Hz)]. MS (70 eV): m/z (%): 227 (M^+, 18.11), 197(100). HRMS calcd for $C_{11}H_8F_3NO$: 227.0558, found: 227.0560; HRMS calcd for $C_{11}H_8F_3NO_2$: 243.0507, found: 243.0505.

4. Synthesis of 4a

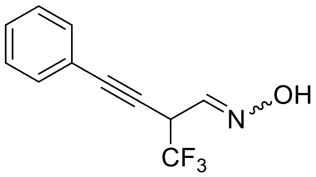
To a solution of *N*-(4-phenyl-2-(trifluoromethyl)but-3-yn-1-yl) hydroxyl amine **1a** (0.2 mmol, 45.8 mg) in DMF(2.0 mL) , NBS (71.0 mg. 0.4 mmol) was added at room temperature, the reaction mixture was stirred at room temperature for 13 h. the reaction was quenched with saturated aqueous solution of $Na_2S_2O_3$ (2.0 mL), then extracted with ethyl acetate (3x4.0 mL) and the combined organic extracts were dried over Na_2SO_4. After filtration and evaporation, the residue was purified by flash column chromatography on silica gel to afford **4a** (32.0 mg) in 53% isolated yield as a colorless oil. [Eluent: petroleum ether : ethyl acetate = 50:1].


4a

^{1}H NMR (400 MHz, CD_2Cl_2) δ 8.45 (s, 1H), 7.64 (dd, *J* = 7.5, 1.4 Hz, 2H), 7.52 – 7.30 (m, 3H), 6.33 (s, 1H). ^{19}F NMR (377 MHz, CD_2Cl_2) δ -57.35. ^{13}C NMR (100 MHz, CD_2Cl_2) δ 168.78 (q, *J* = 3.1 Hz), 148.37 (q, *J* = 2.2 Hz), 135.90 (s), 130.06 (s), 129.50 (s), 128.88 (s), 121.31 (q, *J* = 267.5 Hz), 108.03 (q, *J* = 39.5 Hz), 38.16. MS (70 eV): m/z (%): 226 (M^+-Br, 100). HRMS calcd for $C_{11}H_7BrF_3NO$: 304.9663, found: 304.9659.

5. Synthesis of 5a/5a'

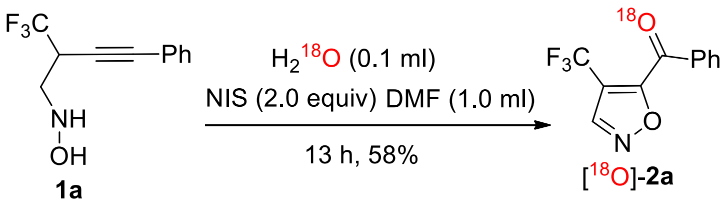
To a solution of *N*-(4-phenyl-2-(trifluoromethyl)but-3-yn-1-yl)hydroxyl amine **1a** (3.0 mmol, 687.0 mg) in DMF (30.0 mL), NIS (810.0 mg. 3.6 mmol) was added at -20℃, and the reaction mixture was stirred at -20℃ for 3 h. After complete conversion of the material (monitored by TLC), the reaction was quenched with saturated aqueous solution of $Na_2S_2O_3$ (10.0 mL), The reaction mixture was extracted with ethyl acetate (15x3.0 mL) and the combined organic extracts were dried over Na_2SO_4. After filtration and evaporation, the residue was purified by flash column chromatography on silica gel to afford two inseparable isomers of oxime **5a/5a'** (490.0 mg) in 72% isolated yield as a yellow oil .[Eluent: petroleum ether : ethyl acetate = 10:1].



5a / 5a'

^{1}H NMR (400 MHz, $CDCl_3$) δ [9.54 (brs, 0.69 H), 9.12 (brs, 0.31 H)]; [7.56 – 7.45(m, 1.38 H), 7.56 – 7.45 (m, 0.62 H)]; [7.42 – 7.29(m, 2.07 H), 7.42 – 7.29 (m, 0.93 H)]; [7.56 – 7.45 (m, 0.31 H), 6.98 – 6.90 (m, 0.69 H)]; [5.25 – 5.05 (m, 0.69 H), 4.35 – 4.24(m, 0.31 H)]. ^{19}F NMR (377 MHz, $CDCl_3$) δ -69.49, -69.55. ^{13}C NMR (126 MHz, $CDCl_3$) δ (142.61, 140.60), 131.99, (129.17, 129.08), 128.33, [123.45 (q, *J* = 280.9 Hz), 123.40 (q, *J* = 280.4 Hz)], (121.49, 121.34), (87.28, 87.22), 85.17, [39.92 (q, *J* = 32.7 Hz), 33.91 (q, *J* = 33.5 Hz)]. MS (70 eV): m/z (%): 227 (M^+, 62.80), 91(100). HRMS calcd for $C_{11}H_8F_3NO$: 227.0558, found: 227.0556.

6. $H_2{}^{18}O$ Labelling Experiments



To a solution of *N*-(4-phenyl-2-(trifluoromethyl)but-3-yn-1-yl) hydroxylamine **1a** (0.1 mmol, 22.9 mg) in DMF(1.0 mL) and $H_2{}^{18}O$(0.1 mL), NIS (45.0 mg. 0.2 mmol) was added at room temperature, the reaction mixture was stirred at room temperature for 13 h. The reaction was quenched with saturated aqueous solution of $Na_2S_2O_3$ (1.0 mL), then extracted with ethyl acetate (3x2.0 mL) and the combined organic extracts were dried over Na_2SO_4. After filtration and evaporation, the residue was purified by flash column chromatography on silica gel to afford **[^{18}O]-2a** and 2a in 58% isolated yield as a Colorless oil . [Eluent: petroleum ether : ethyl acetate = 50:1].

HRMS Cacld for $C_{11}H_6F_3NO^{18}O$: 243.0393, Found: 243.0391.

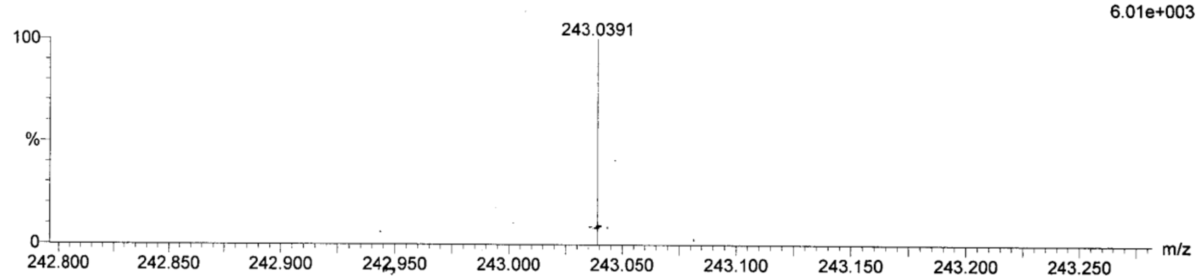
Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off

Monoisotopic Mass, Odd and Even Electron Ions
28 formula(e) evaluated with 1 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-11 H: 0-10 N: 0-1 F: 0-3 16O: 0-1 18O: 0-1

ZL-2-149
20140527009 35 (0.583)

TOF MS EI+
6.01e+003

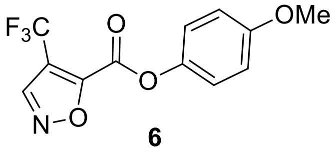


Minimum:				-1.5		
Maximum:		5.0	10.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Formula
243.0391	243.0393	-0.2	-0.8	8.0	2775900.3	C11 H6 N F3 16O 18O

7. Synthesis of isoxazole ester 6

To a solution of (4-methoxyphenyl)(4-(trifluoromethyl)isoxazol-5-yl) methanone **2c** (0.96 mmol, 260.0mg) in Hexafluoroisopropanol (HFIP, 5.0 mL), DCM (5.0 mL) and PH=7.5 buffer (1.3 mL), 3-chloroperoxybenzoic acid (830.0 mg, 4.8 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for 15 h. After complete consumption of the material **2c** (monitored by TLC), the reaction was quenched with saturated aqueous solution of $Na_2S_2O_3$ (16.0 mL), and $NaHCO_3$ (36.0 mL). The reaction mixture was extracted with dichloromethane (3x10.0 mL) and the combined organic extracts were dried over Na_2SO_4. After filtration and evaporation, the residue was purified by flash column chromatography on silica gel to afford isoxazole ester **6**

(198.4 mg) in 72% isolated yield as a yellow oil.[Eluent: petroleum ether : dichloromethane = 10:1].

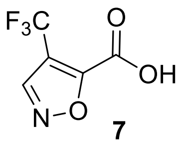


6

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (s, 1H), 7.21 (d, *J* = 9.1 Hz, 1H), 6.95 (d, *J* = 9.1 Hz, 1H), 3.83 (s, 2H). ^{19}F NMR (377 MHz, $CDCl_3$) δ -57.32. ^{13}C NMR (126 MHz, $CDCl_3$) δ 158.04, 157.98 (q, *J* = 3.3 Hz), 153.26, 148.94 (q, *J* = 2.6 Hz), 143.01, 121.64, 119.95 (q, *J* = 268.5 Hz), 116.07 (q, *J* = 41.4 Hz), 114.65, 55.57. MS (70 eV): m/z (%): 287 (M^+, 76.80), 123(100). HRMS calcd for $C_{12}H_8F_3NO_4$: 287.0405, found: 287.0406.

8. Synthesis of isoxazole acid 7

A solution of isoxazole ester 6 (0.66 mmol, 189.4 mg) in HCl:HOAc:H2O = 1:1:1 (2.0 mL) was stirred at 105℃ for 5 h. After complete consumption of the isoxazole ester 6 (monitored by TLC), the reaction mixture was cooled to room temperature. After cooling, acetone was added and the mixture was removed under reduced pressure, the residue was purified by flash column chromatography on silica gel to afford 7 (95.0 mg) in 80% isolated yield as a Colorless oil. [eluent: dichloromethane / Methanol = 100:5]

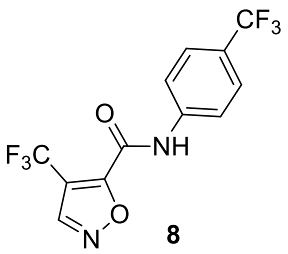


7

^{1}H NMR (400 MHz, d^6-DMSO) δ 13.42 (brs, 1H), 9.26 (s, 1H). ^{19}F NMR (377 MHz, d^6-DMSO) δ -56.04. ^{13}C NMR (100 MHz, d^{6-}DMSO) δ 161.36 (q, J = 3.3 Hz), 156.58, 150.30 (q, J = 2.6 Hz), 120.97 (q, J = 267.6 Hz), 113.27 (q, J = 40.2 Hz). MS (70 eV): m/z (%): 181 (M^+, 5.68), 84(100). HRMS-ESI calcd for $C_5H_2F_3NO_3$ $[M-H]^-$: 179.9914, found: 179.9865.

9. Synthesis of Leflunomide Analogue 8

To a solution of isoxazole acid **7**(0.1 mmol, 18.0 mg), 2-(7-aza-1H-benzotri-azole-1-yl)-1,1,3,3-tetramethyluronium hexafluoro phosphate (HATU) (0.2 mmol, 76.0 mg) in DCE (2.0 mL),was added Et_3N (0.2 mmol, 28.0 uL) at 0℃. The rection mixture was stirred for 5 minute, Then 4-(trifluoromethyl) aniline (0.2 mmol, 25.0 uL) was added, the reaction mixture was warmed to room temperature and stirred for 4h. After complete consumption of the isoxazole acid **7** (monitored by TLC), the solvent was removed under reduced pressure and the crude reaction mixture was purified by flash column chromatography on silica gel to afford Leflunomide Analogue **8** (23.2 mg) in 72% isolated yield as a white solid. [eluent: petroleum ether : ethyl acetate = 10:1].



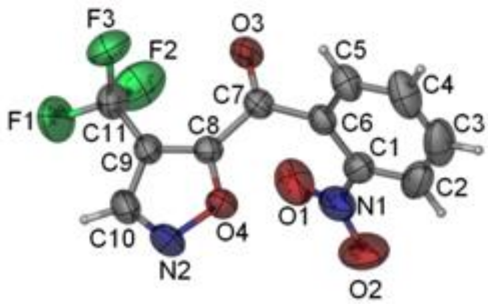
8

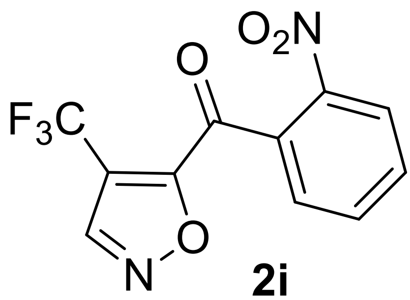
Mp 136-139 °C. ^{1}H NMR (500 MHz, d^6-DMSO) δ 11.52 (s, 1H), 9.42 (s, 1H), 7.99 (d, J = 7.7 Hz, 2H), 7.77 (d, J = 7.7 Hz, 2H). ^{19}F NMR (377 MHz, d^6-DMSO) δ -57.21, -62.39. ^{13}C NMR (126 MHz, d^6-DMSO) δ 162.10 (q, J = 3.3 Hz), 153.32, 150.44, 141.38, 126.68 (q, J = 3.8 Hz), 125.62 (q, J = 32.0 Hz), 124.65 (q, J = 272.2 Hz). 121.28, 120.89 (q, J = 268.4 Hz), 112.92 (q, J = 40.4 Hz). MS (70 eV): m/z (%): 324 (M^+, 100). HRMS calcd for $C_{12}H_6F_6N_2O_2$: 324.0333, found: 324.0331.

10. References

[1] Q. Zeng, L. Zhang, J. Yang, B. Xu, Y. Xiao and J. Zhang. *Chem. Commun*. 2014, **50**, 4203.

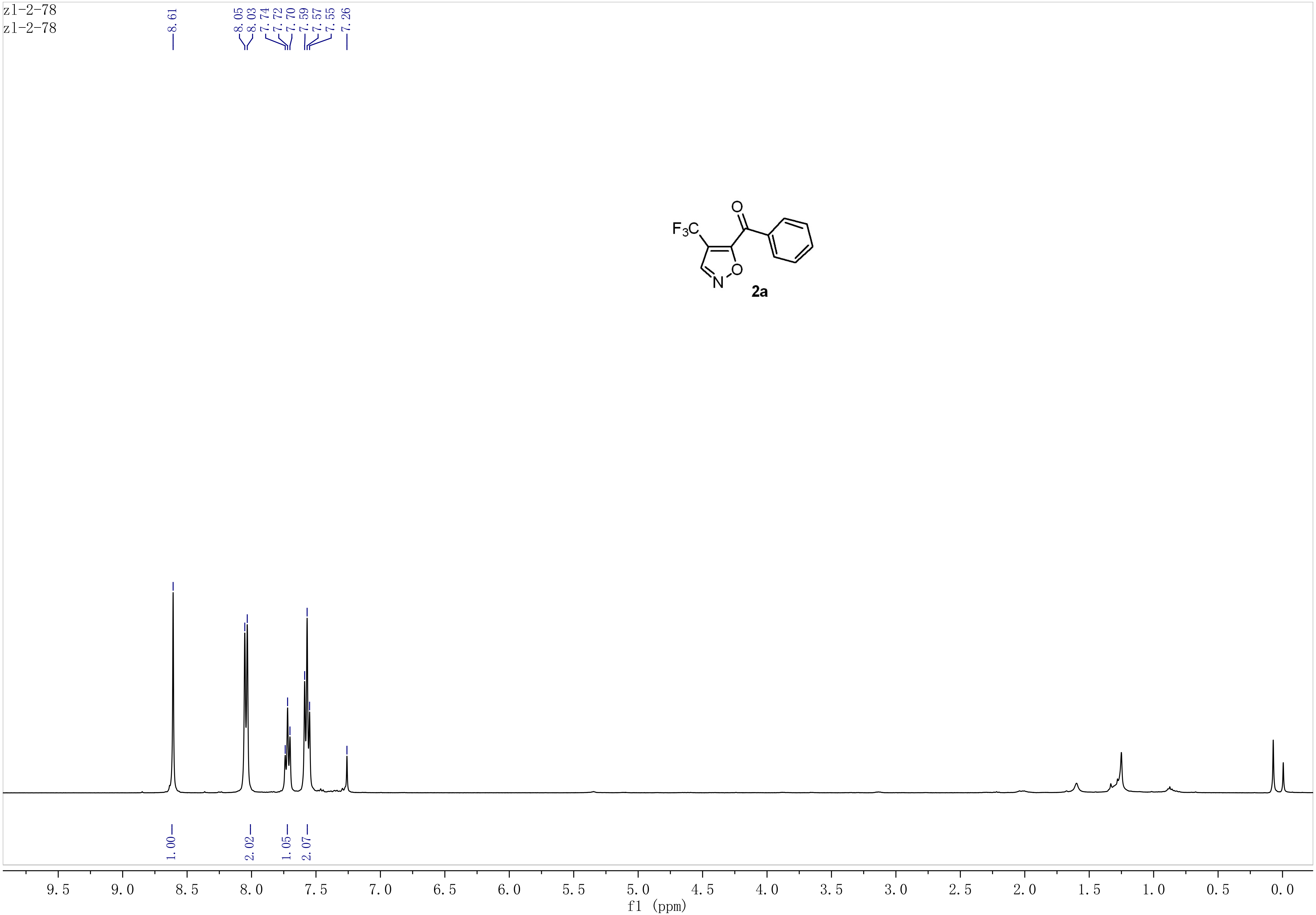
11. X-ray structures of 2i.

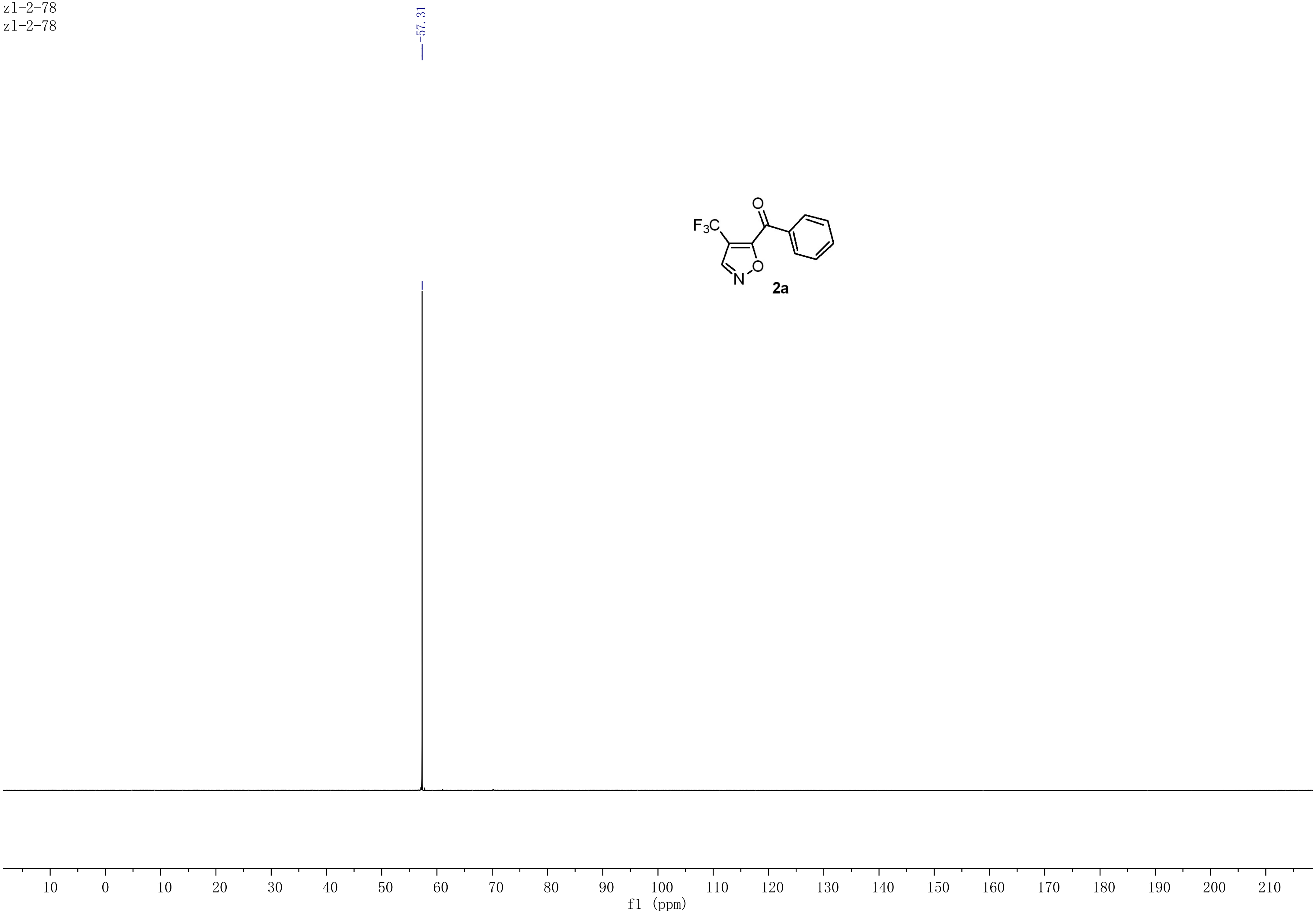




2i

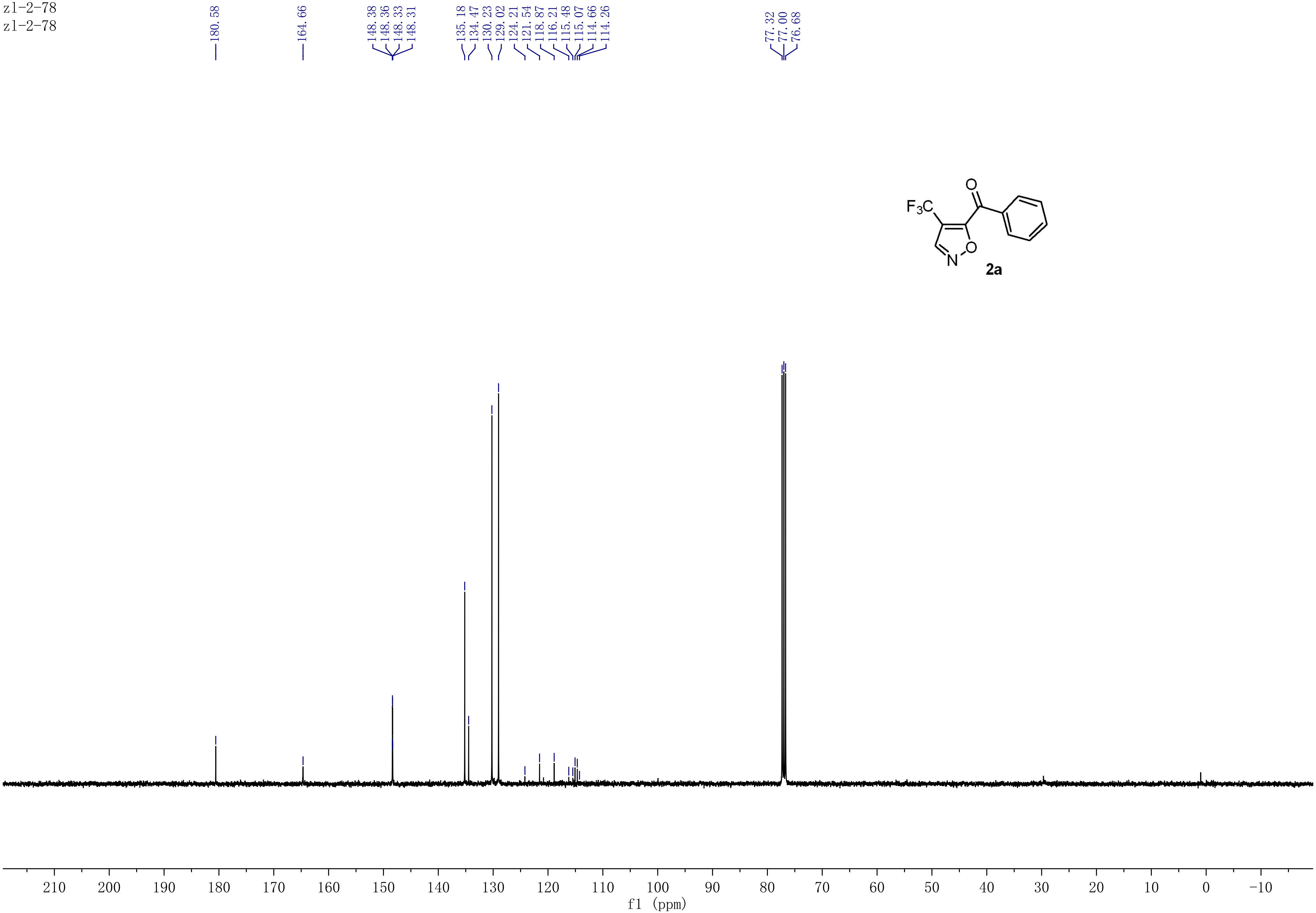
Figure 1. ORTEP depiction of compound **2i**, CCDC 1005152 .


zl-2-78
zl-2-78
8.61
8.05
8.03
7.74
7.72
7.70
7.59
7.57
7.55
7.26
F_3C
O
N
2a
1.00
2.02
1.05
2.07
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

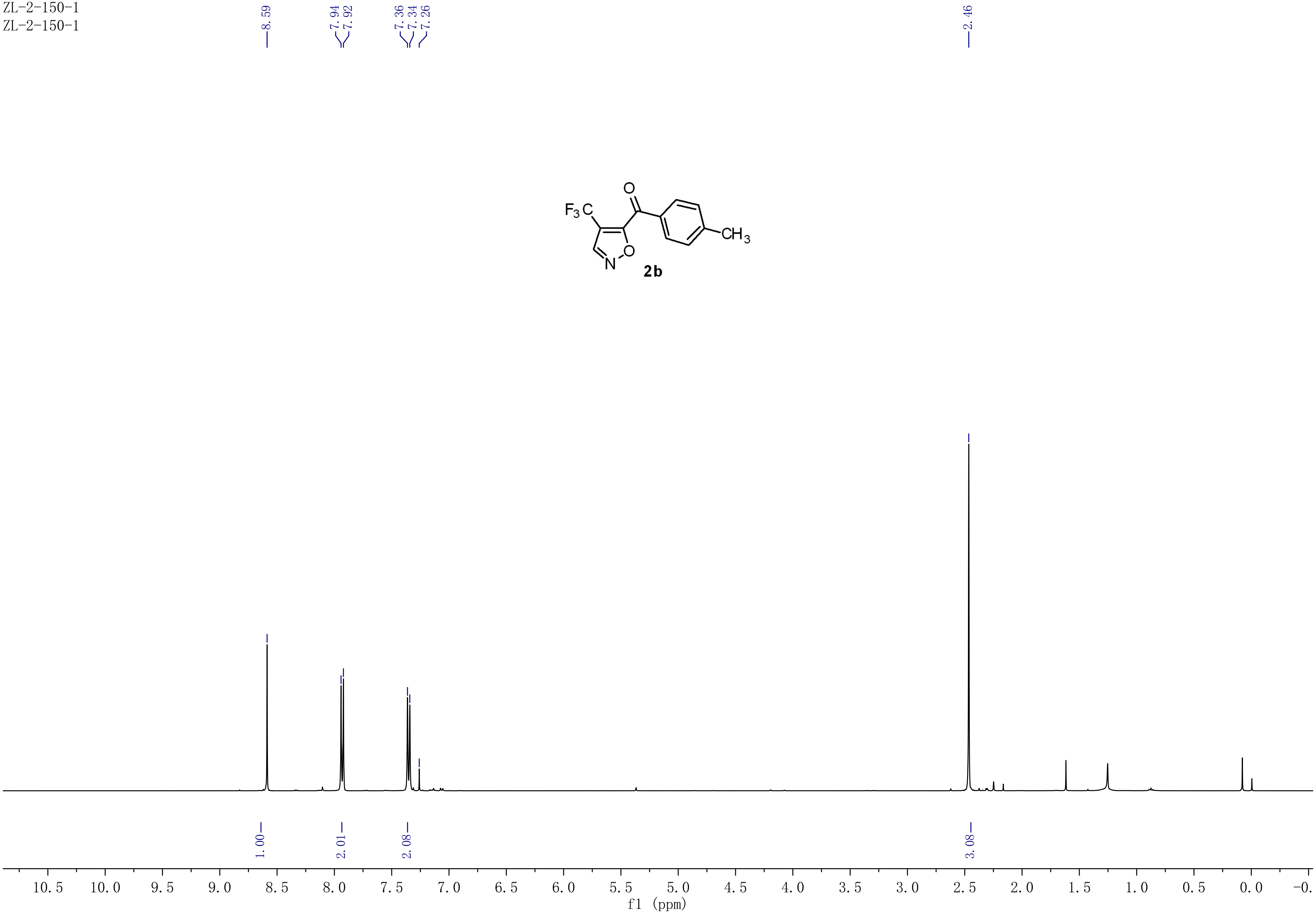


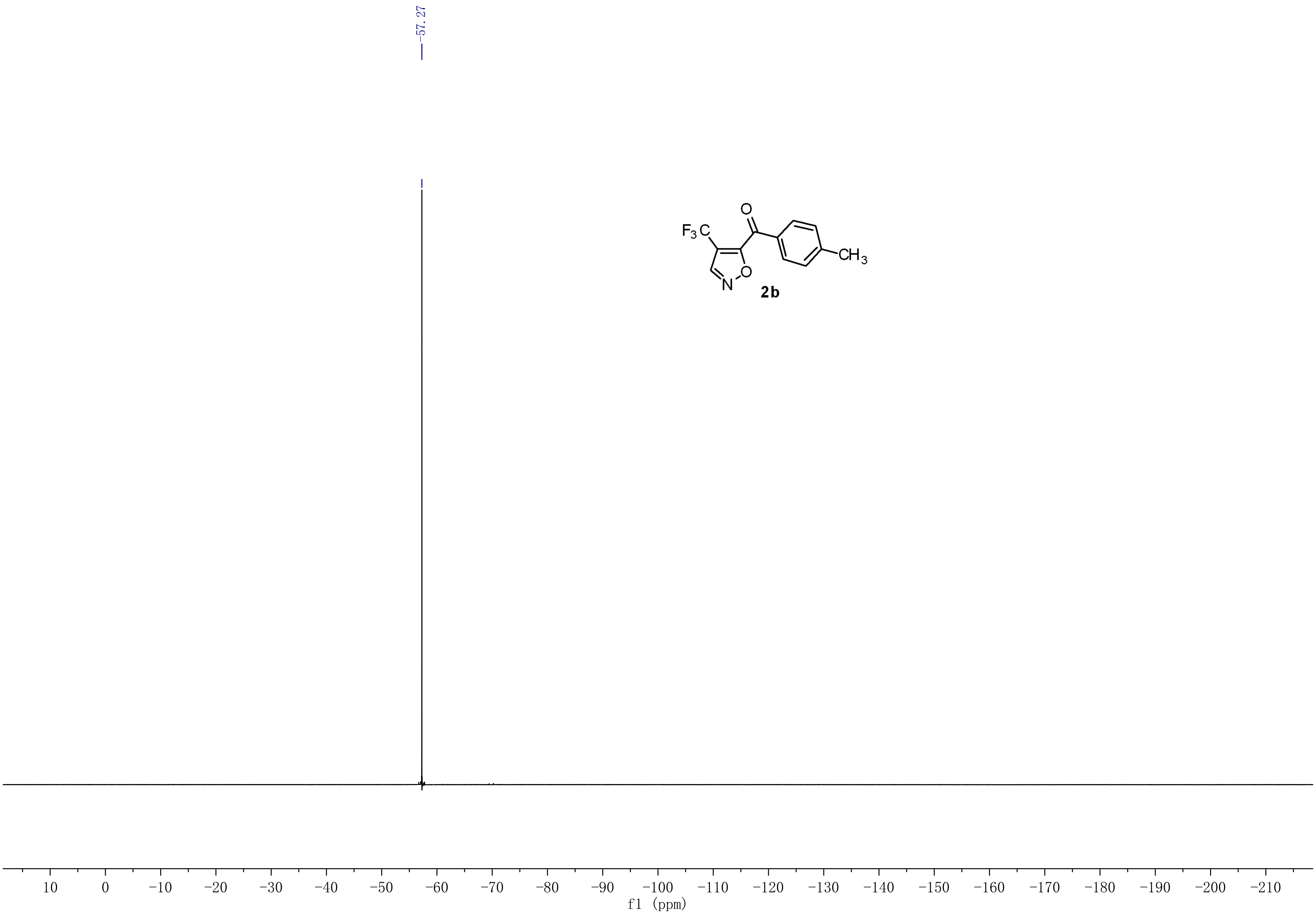
zl-2-78
zl-2-78
-57.31
F_3C
O
N
2a
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

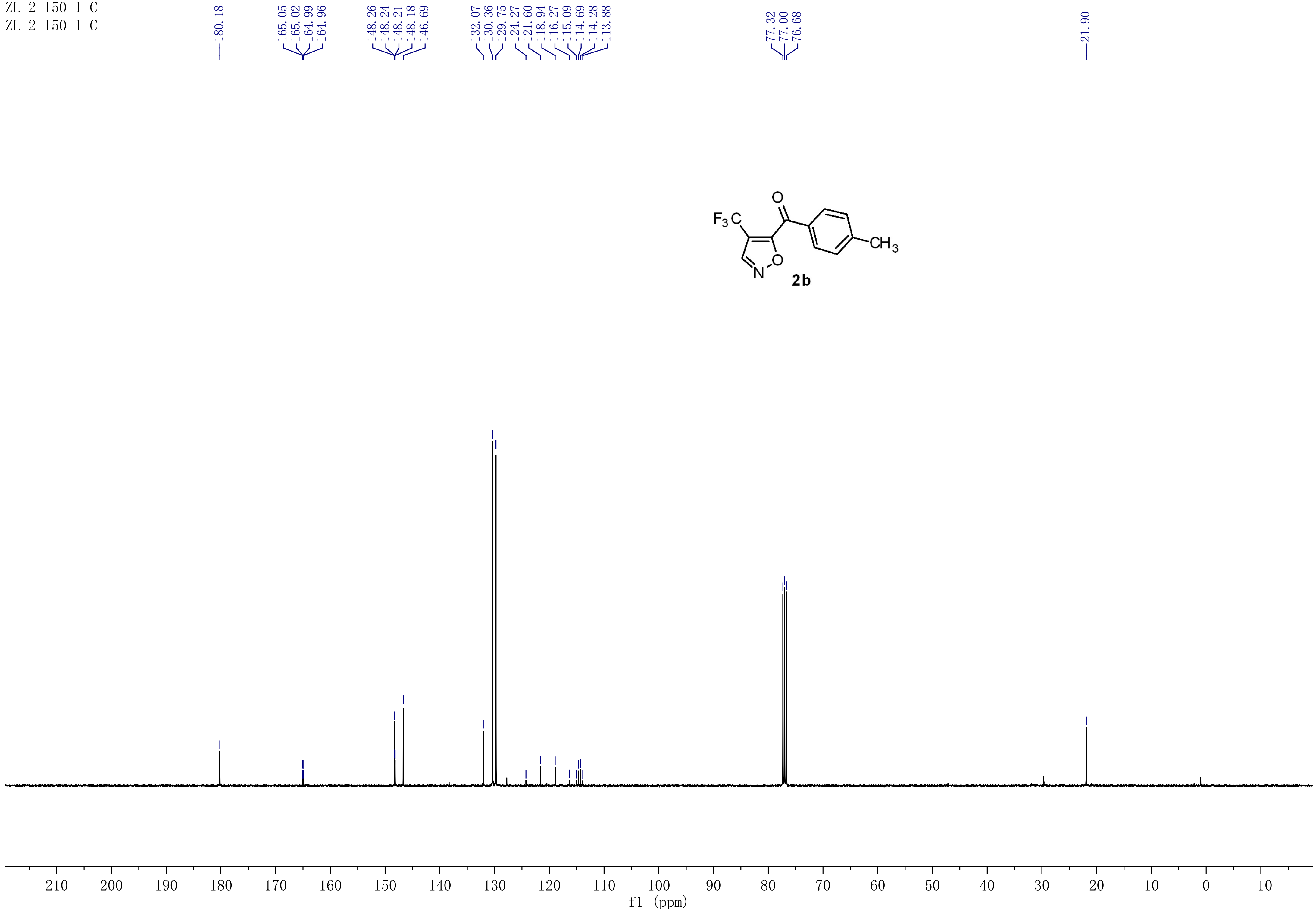
zl-2-78
zl-2-78



2a


ZL-2-150-1
ZL-2-150-1
8.59
7.94
7.92
7.36
7.34
7.26
2.46
F_3C
O
N
O
CH_3
2b
1.00
2.01
2.08
3.08
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.
f1 (ppm)


-57.27
F_3C
O
N
O
CH_3
2b
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)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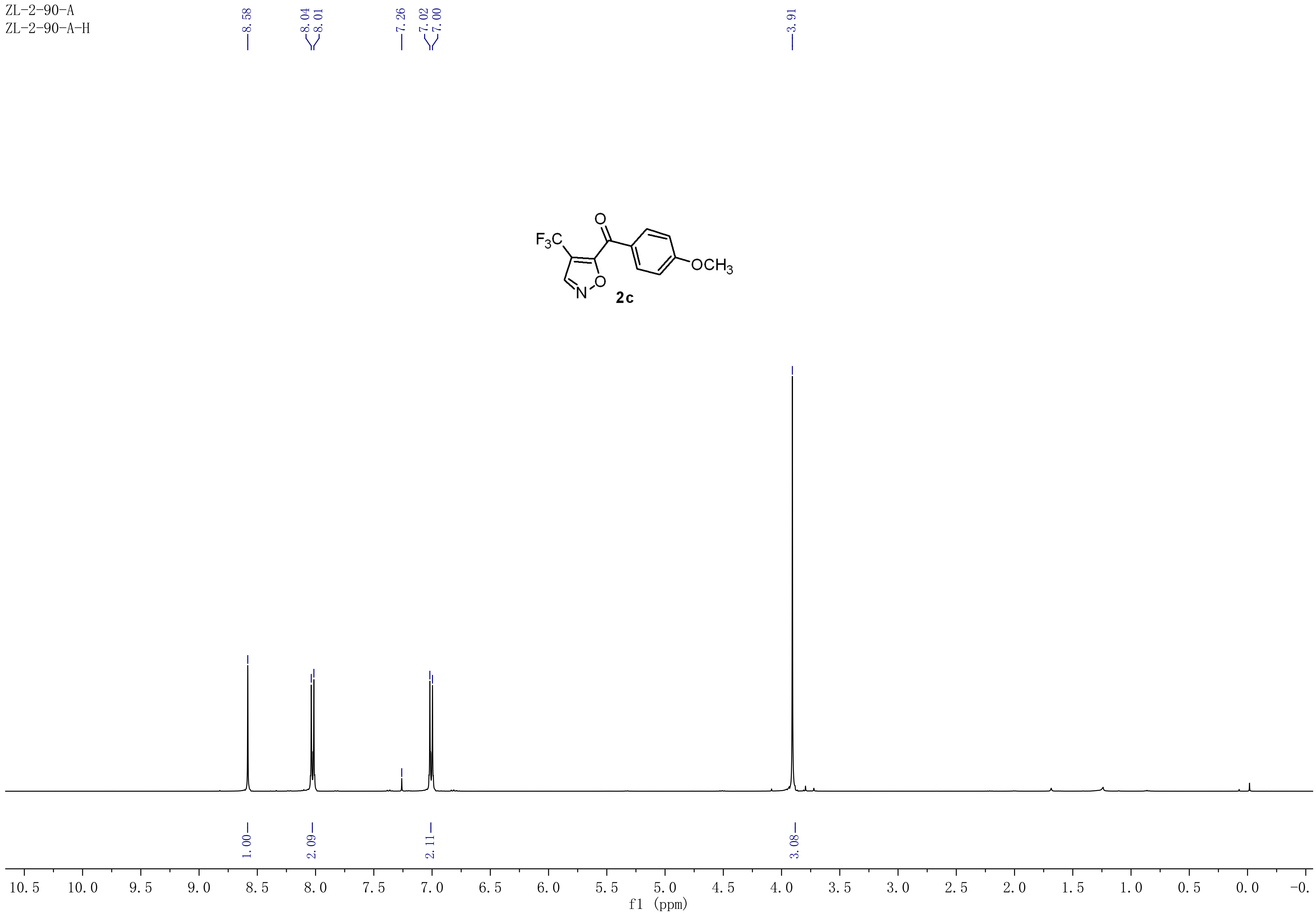
ZL-2-150-1-C
180.18
165.05
165.02
164.99
164.96
148.26
148.24
148.21
148.18
146.69
132.07
130.36
129.75
124.27
121.60
118.94
116.27
115.09
114.69
114.28
113.88
77.32
77.00
76.68
21.90
F_3C
O
N
CH_3
2b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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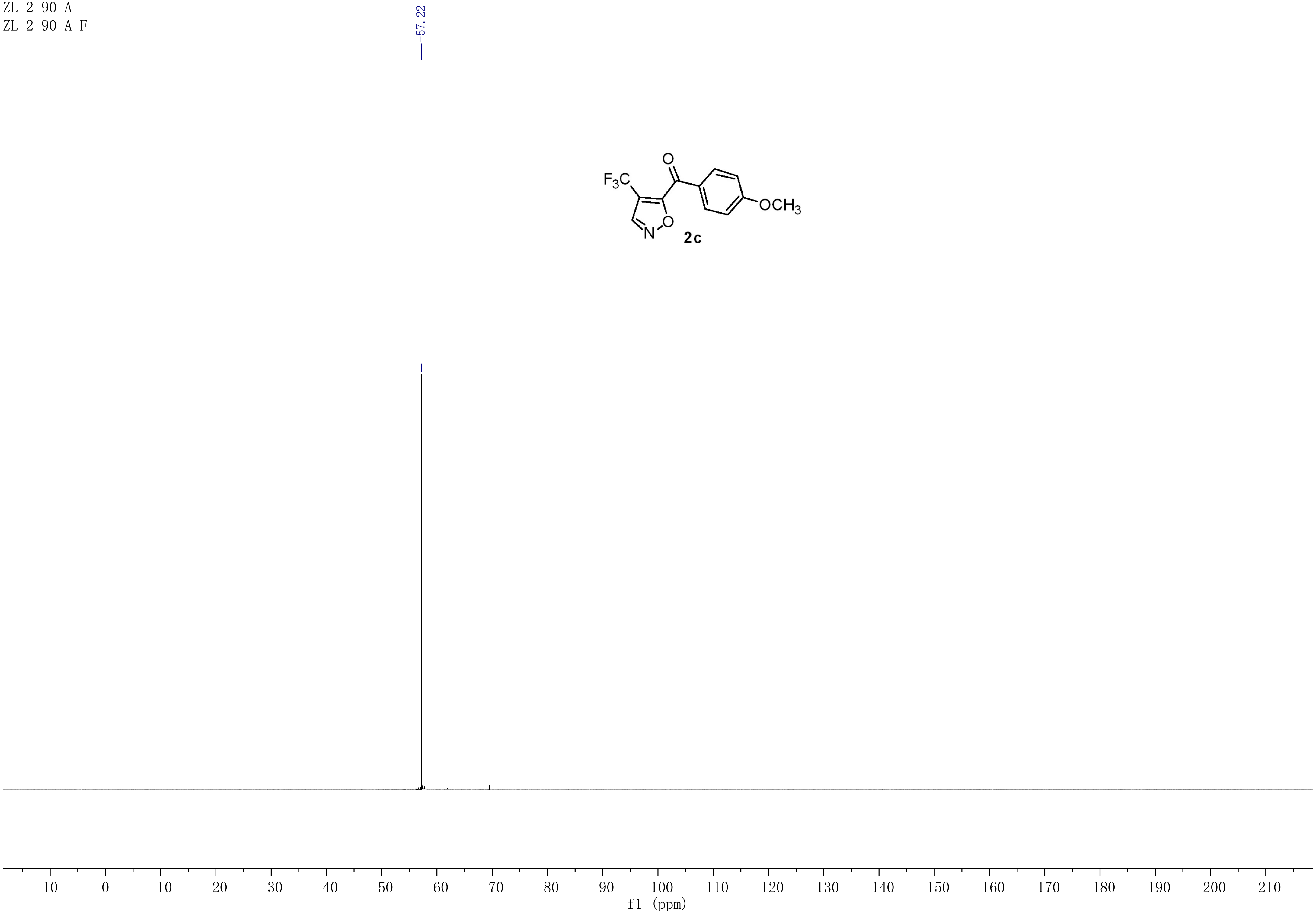
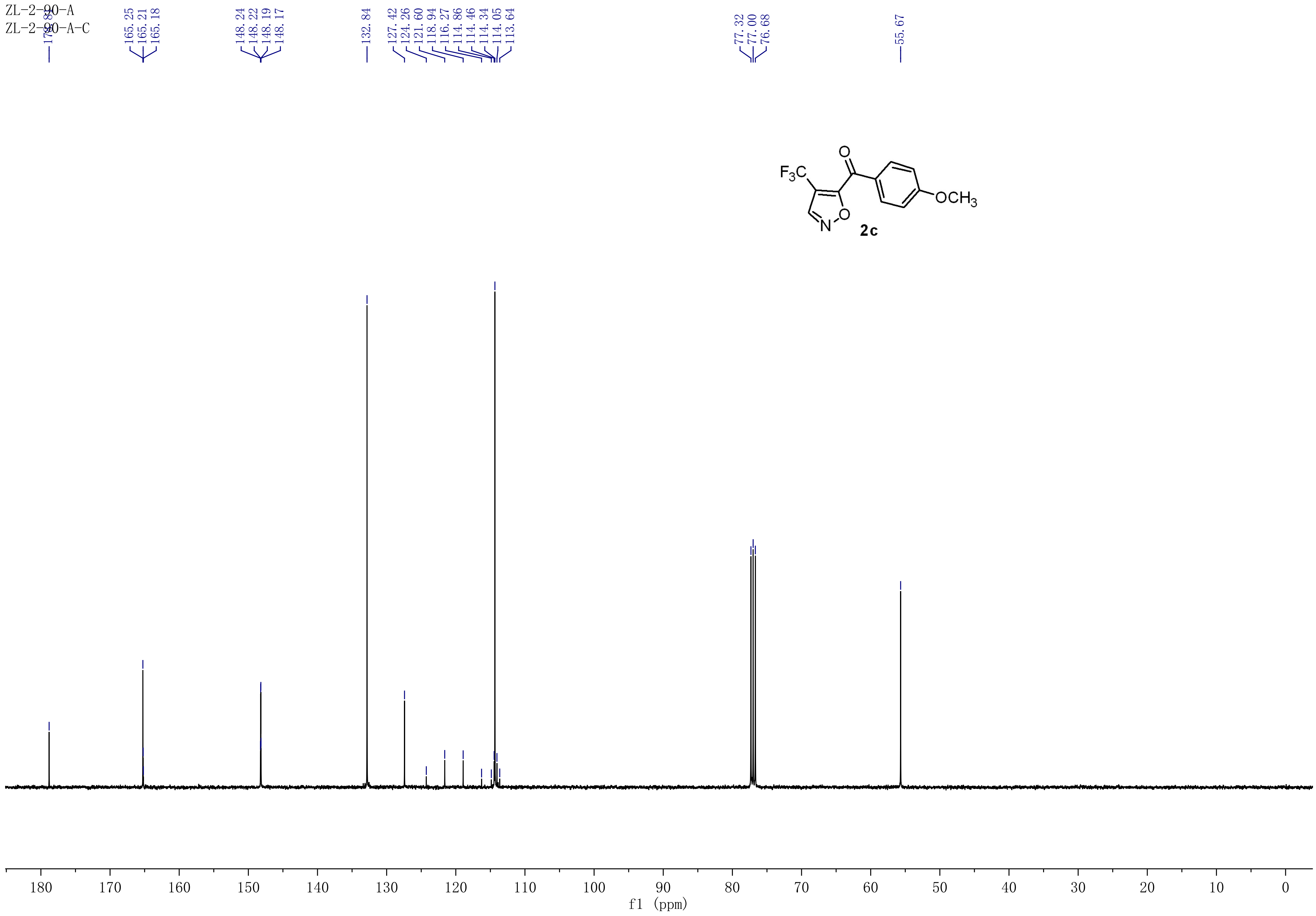
ZL-2-90-A-H
8.58
8.04
8.01
7.26
7.02
7.00
3.91
F3C
O
N
OCH3
2c
1.00
2.09
2.11
3.08
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.
f1 (ppm)

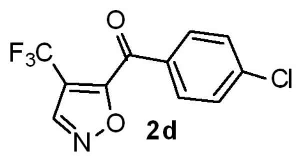


ZL-2-90-A
ZL-2-90-A-F
-57.22
F3C
O
N
OCH3
2c
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

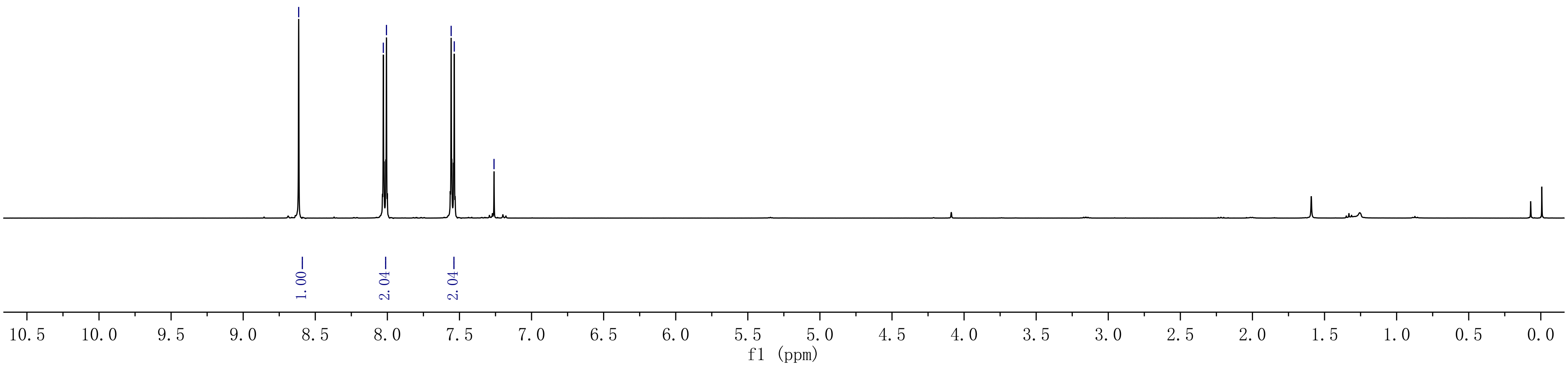


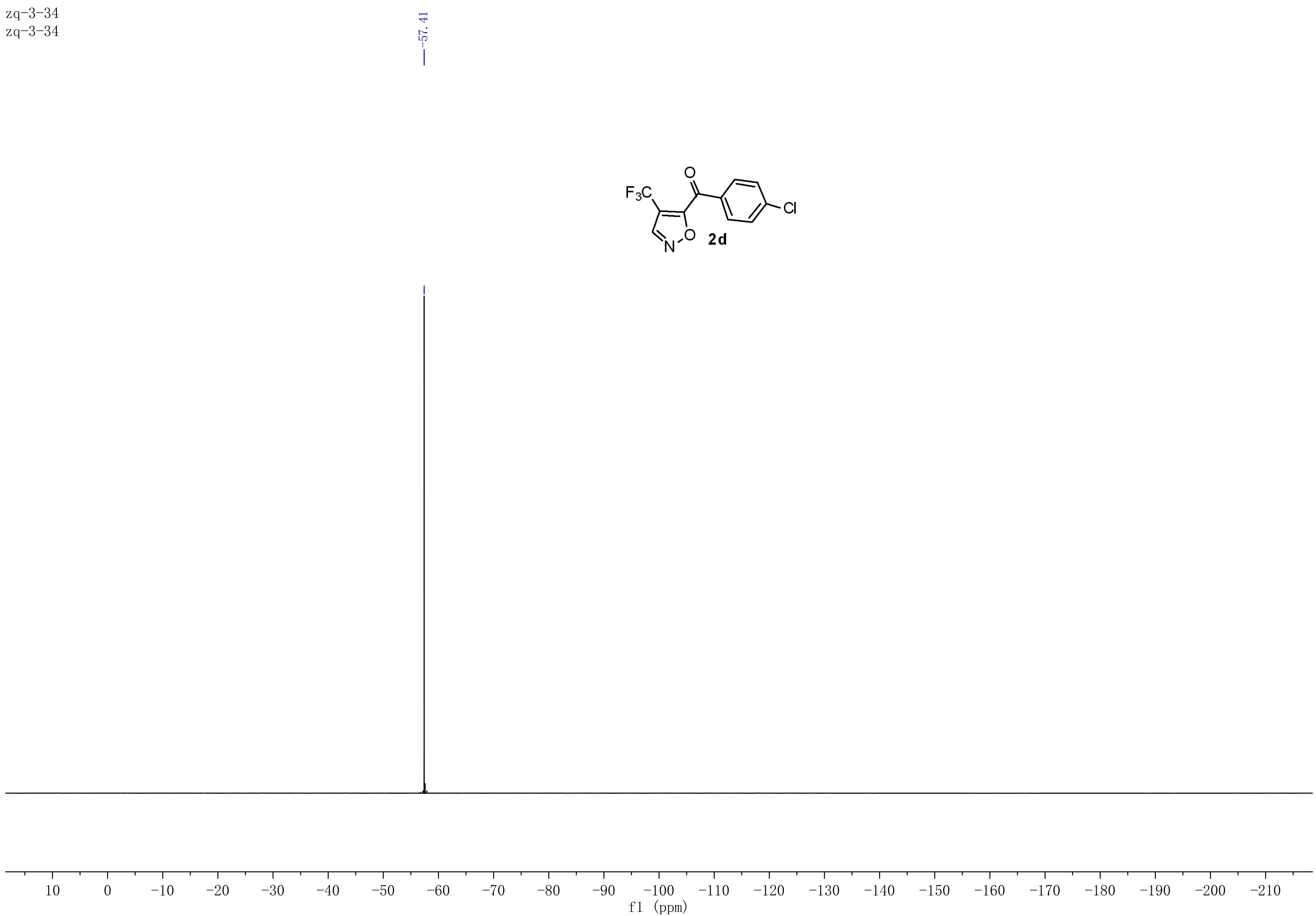
ZL-2-90-A
ZL-2-90-A-C
165.25
165.21
165.18
148.24
148.22
148.19
148.17
132.84
127.42
124.26
121.60
118.94
116.27
114.86
114.46
114.34
114.05
113.64
77.32
77.00
76.68
55.67
F3C
O
N
OCH3
2c
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

zq-3-34
zq-3-34



2d




zq-3-34
zq-3-34
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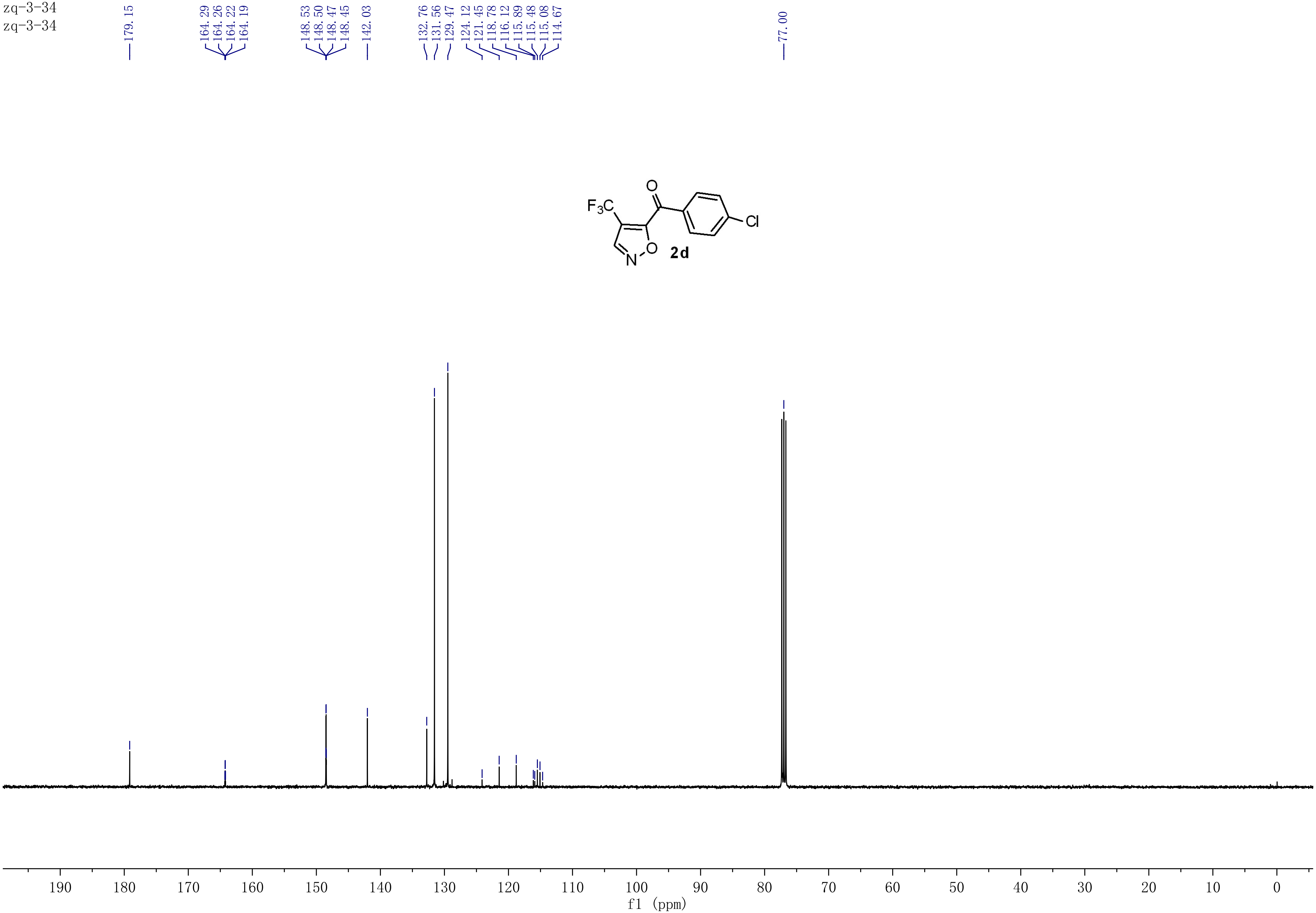
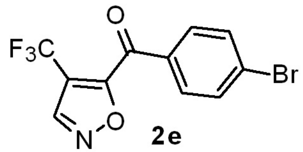
F3C
O
N
Cl
2d
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

zq-3-34
zq-3-34

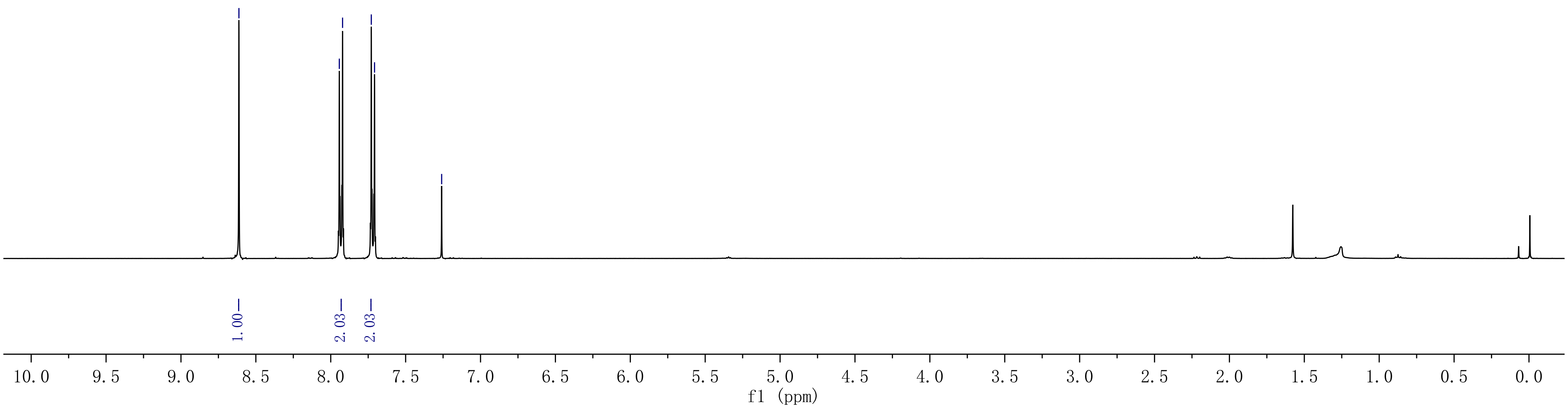


2d

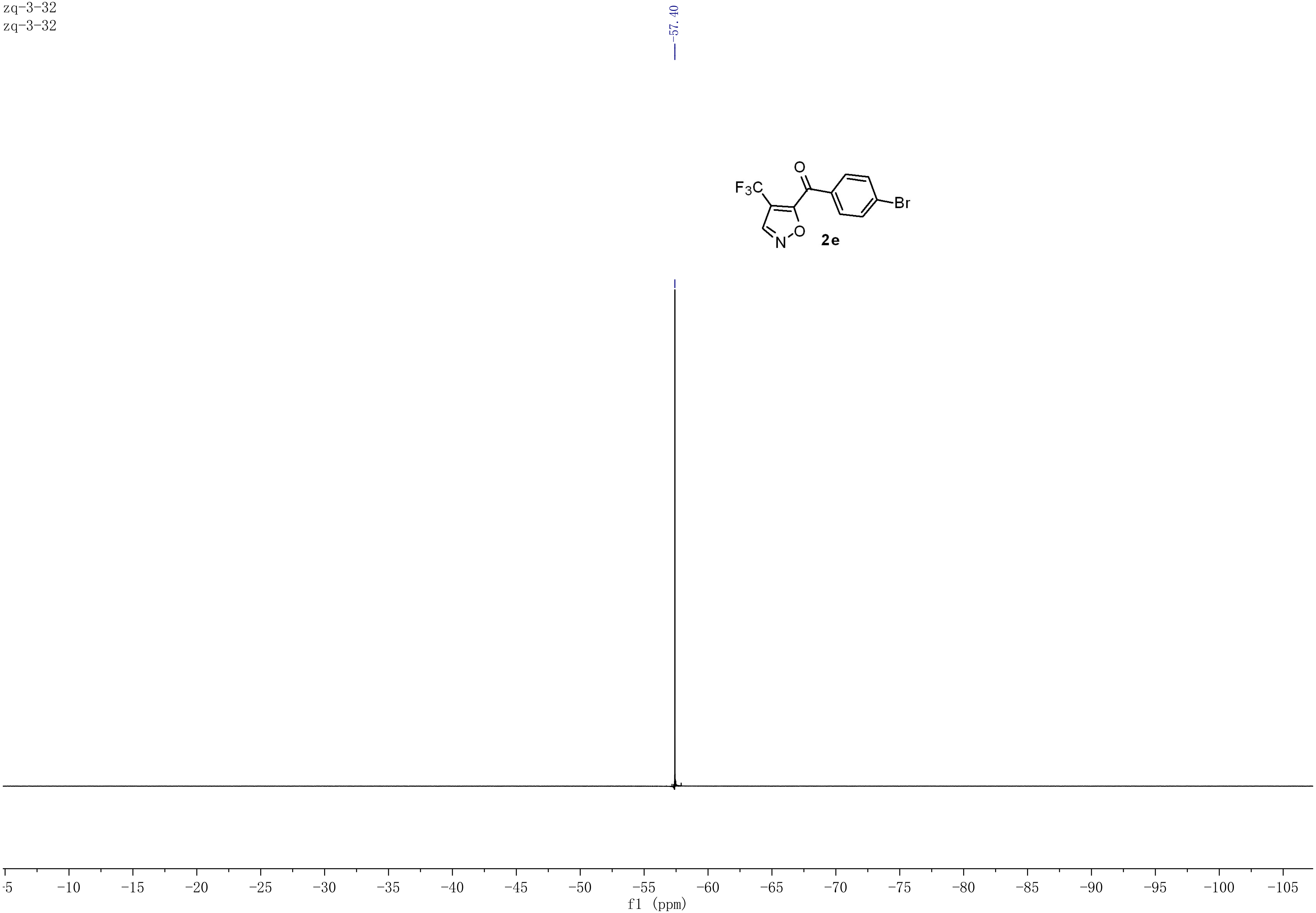
zq-3-32
zq-3-32

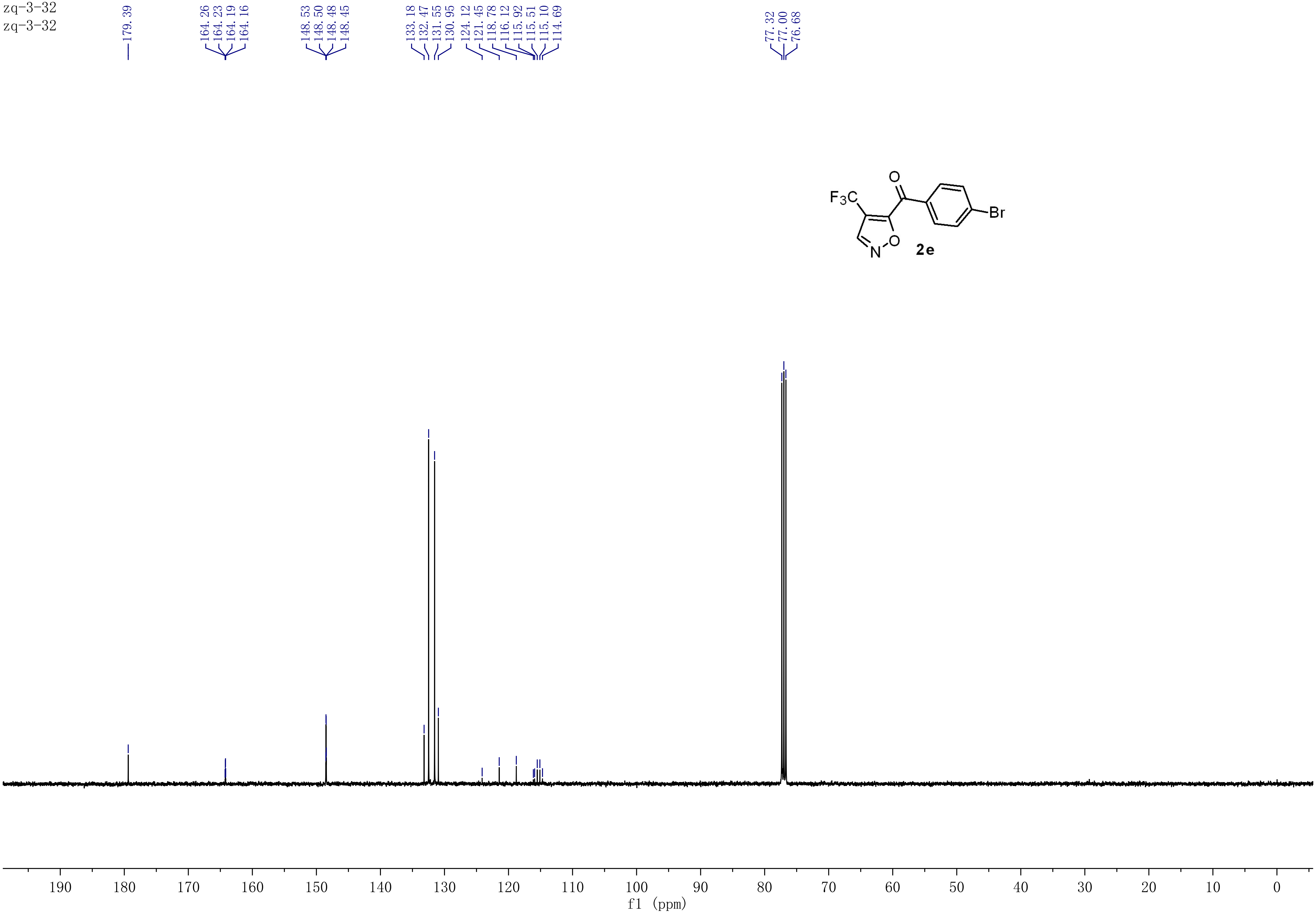


2e



zq-3-32
zq-3-32


−57.40
F3C
O
N
O
Br
2e
-5 −10 −15 −20 −25 −30 −35 −40 −45 −50 −55 −60 −65 −70 −75 −80 −85 −90 −95 −100 −105
f1 (ppm)


zq-3-32
zq-3-32
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164.26
164.23
164.19
164.16
148.53
148.50
148.48
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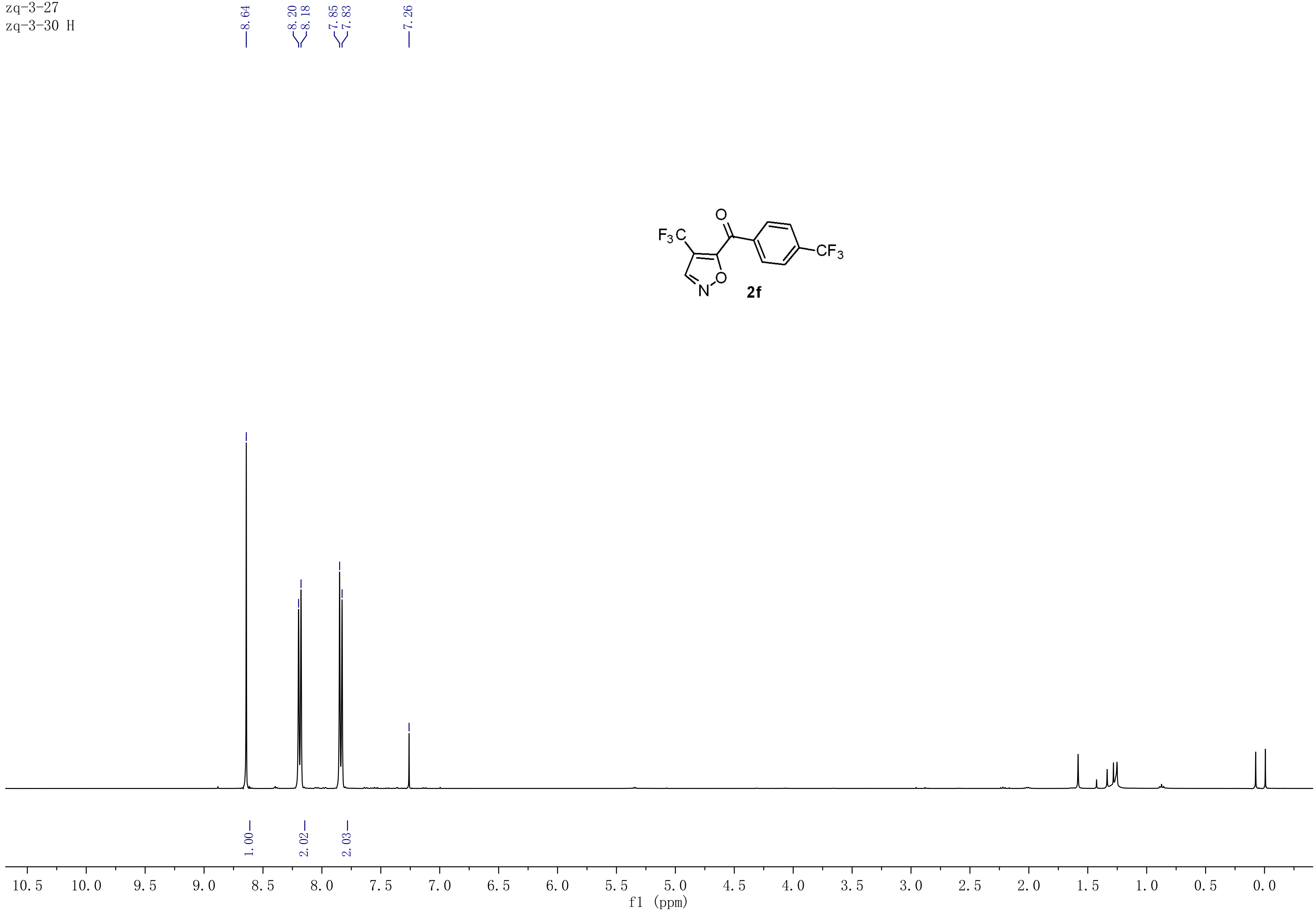
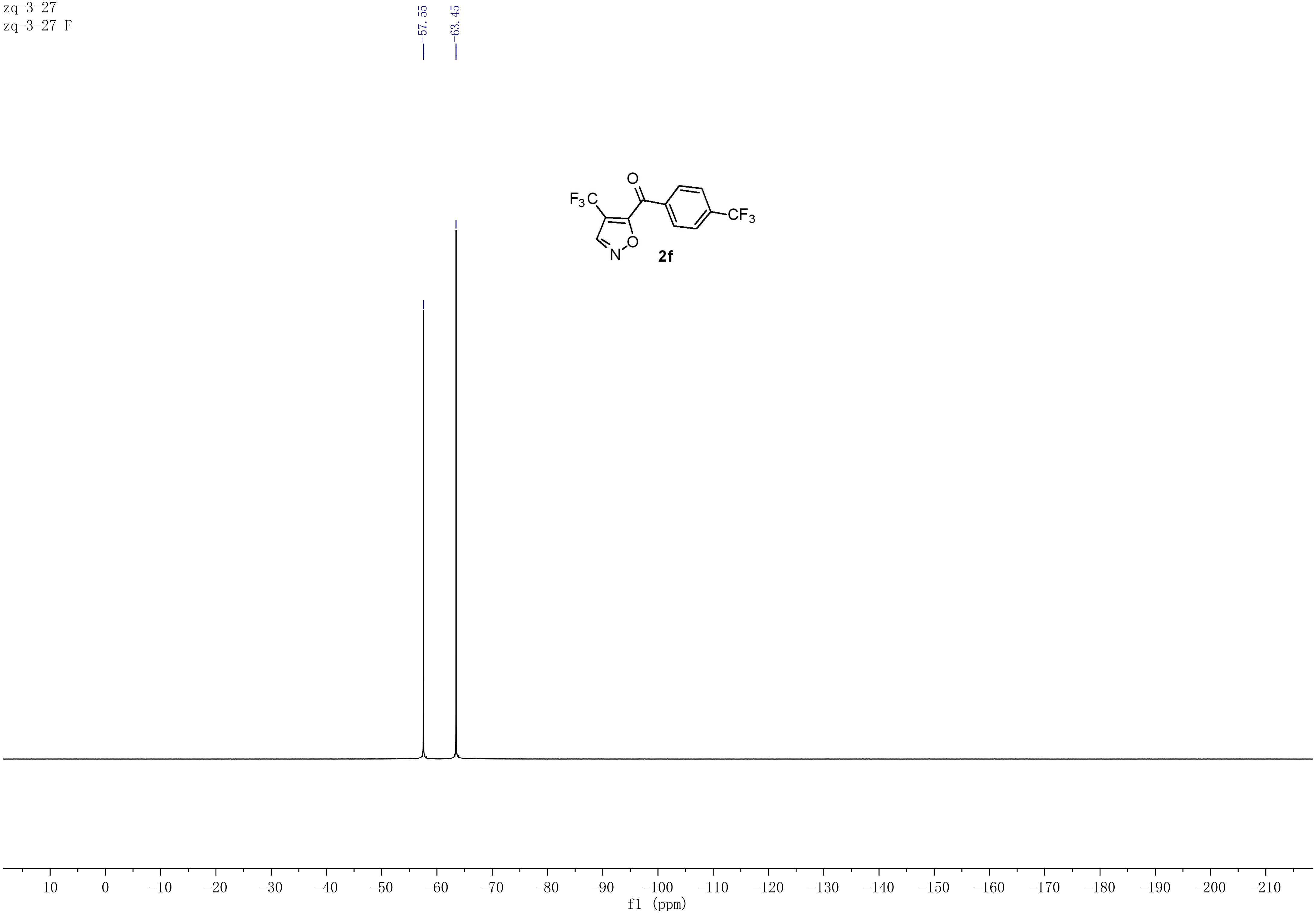
132.47
131.55
130.95
124.12
121.45
118.78
116.12
115.92
115.51
115.10
114.69
77.32
77.00
76.68
O
F_3C
Br
N
O
2e
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

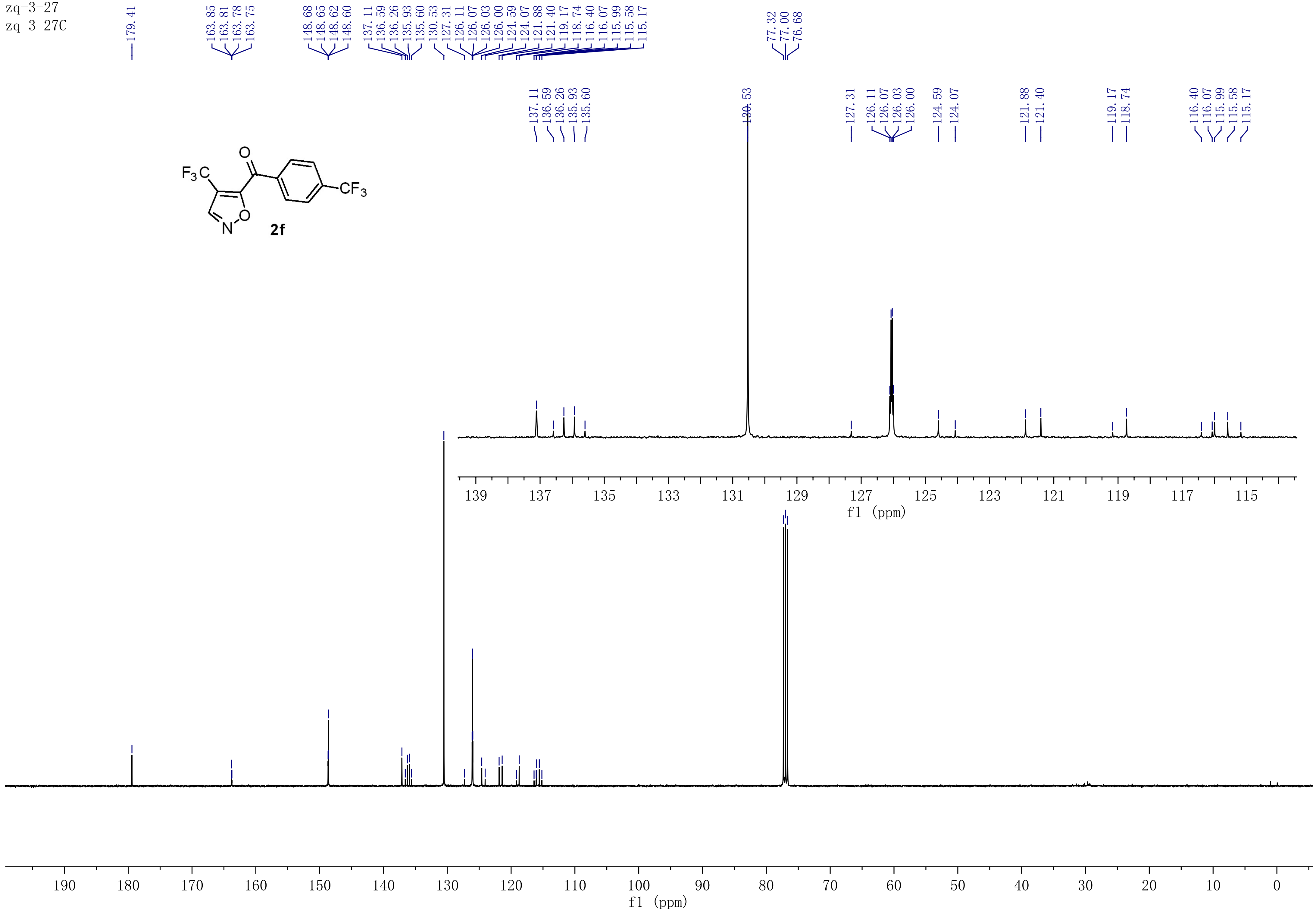


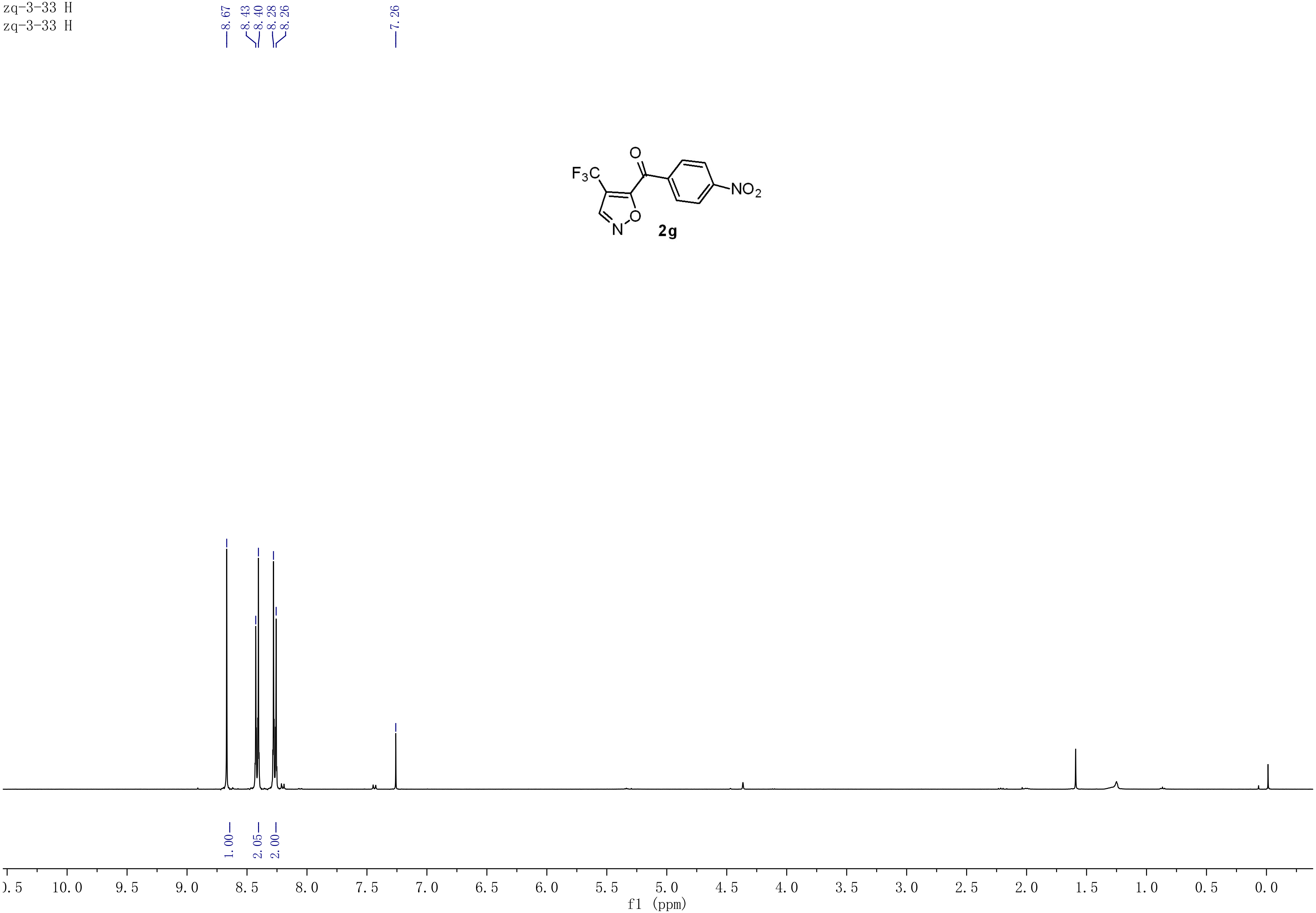
zq-3-27
zq-3-30 H
8.64
8.20
8.18
7.85
7.83
7.26
F3C
O
CF3
N
O
2f
1.00
2.02
2.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

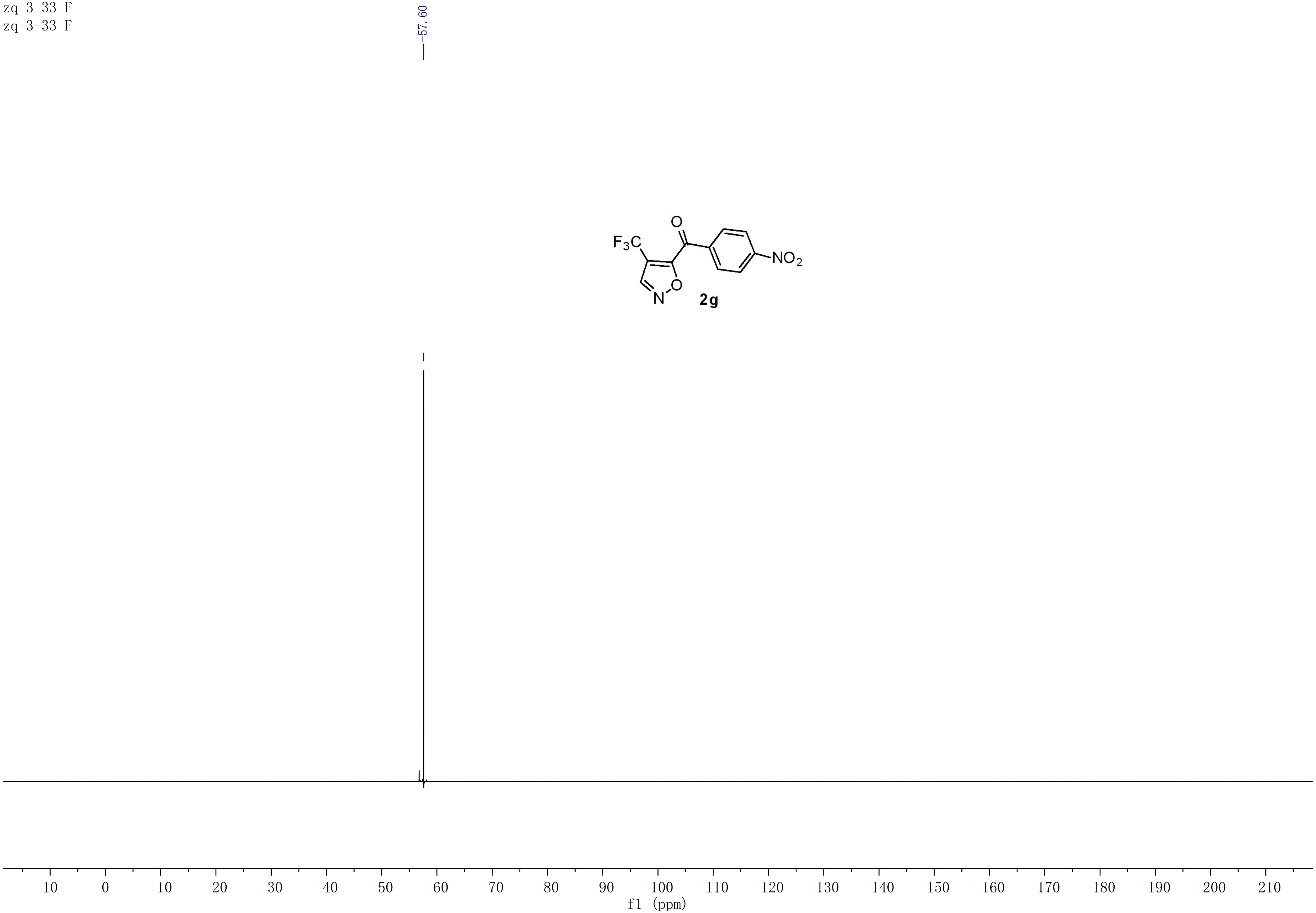
zq-3-27
zq-3-27 F

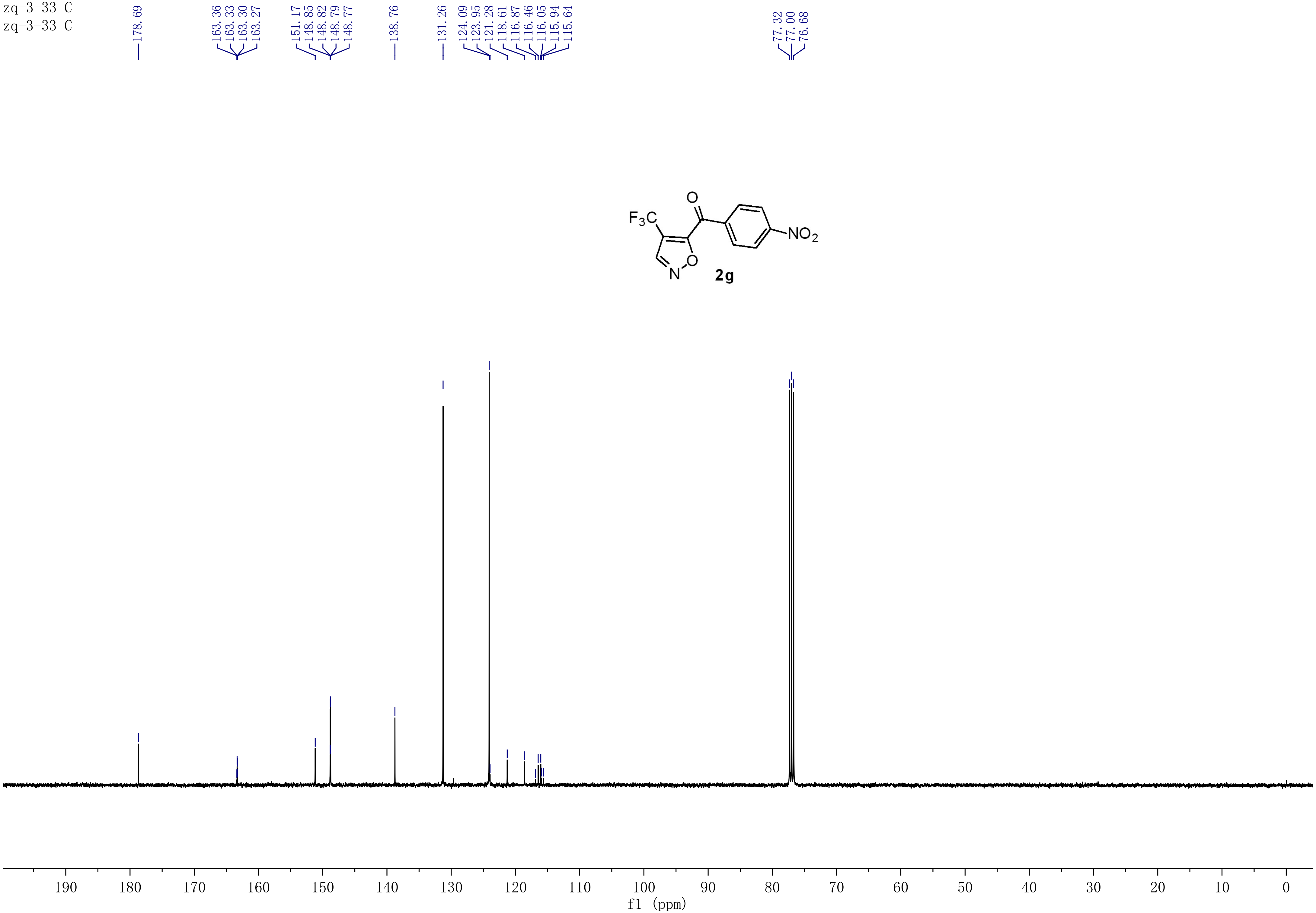


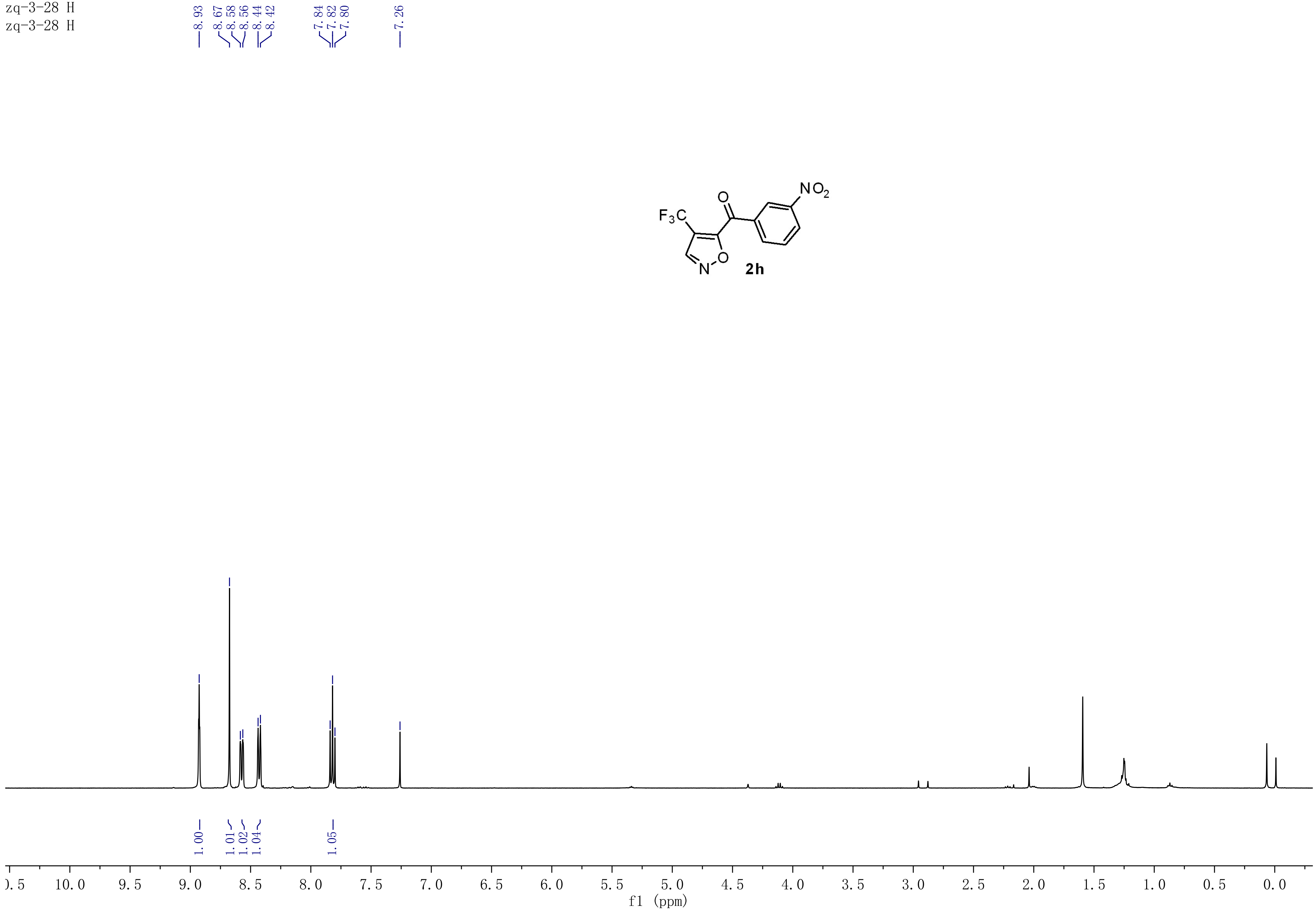
2f

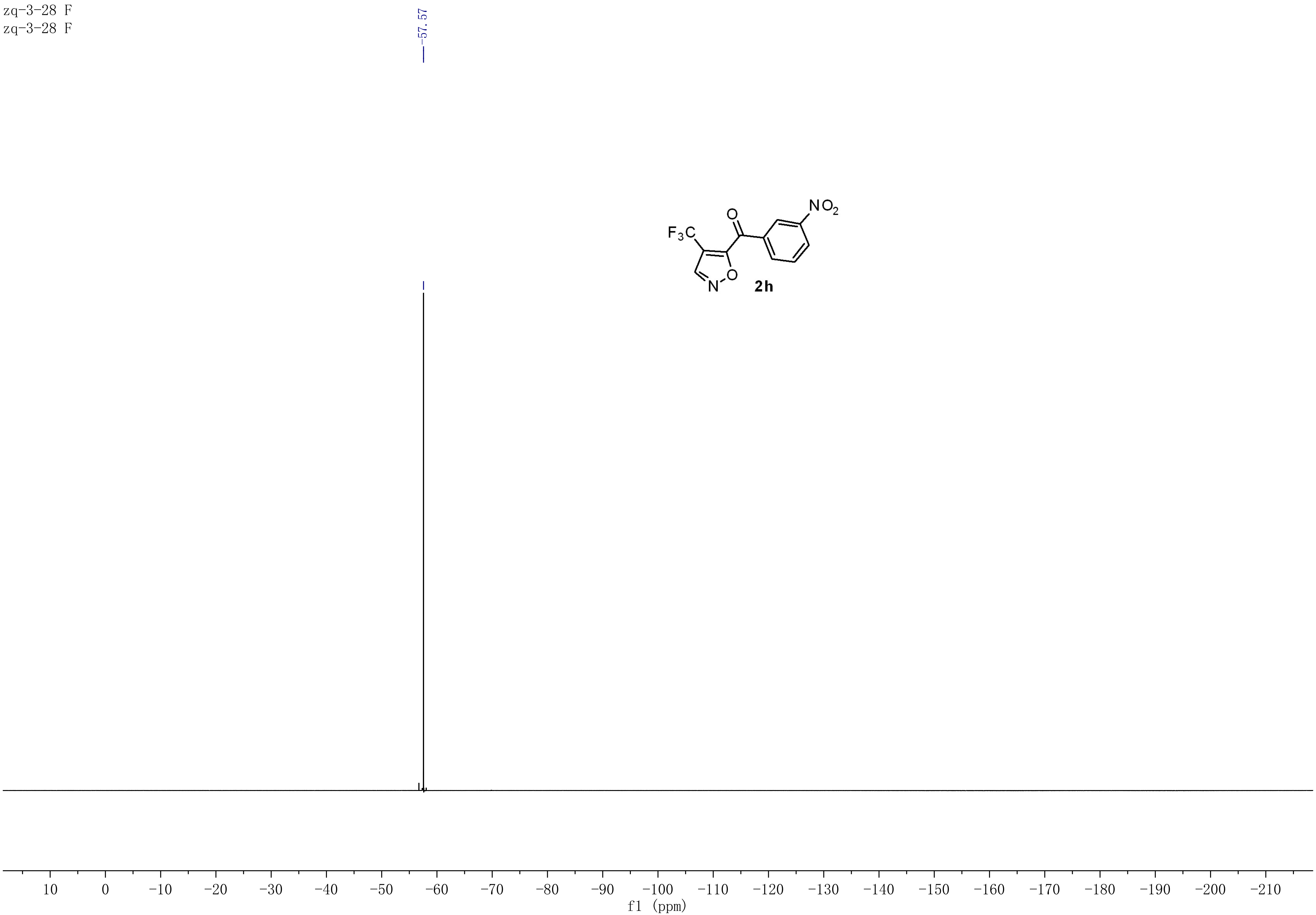

zq-3-27
zq-3-27C
179.41
163.85 163.81 163.78 163.75
148.68 148.65 148.62 148.60
137.11 136.59 136.26 135.93 135.60 130.53 127.31 126.11 126.07 126.03 126.00 124.59 124.07 121.88 121.40 119.17 118.74 116.40 116.07 115.99 115.58 115.17
77.32 77.00 76.68
2f
f1 (ppm)

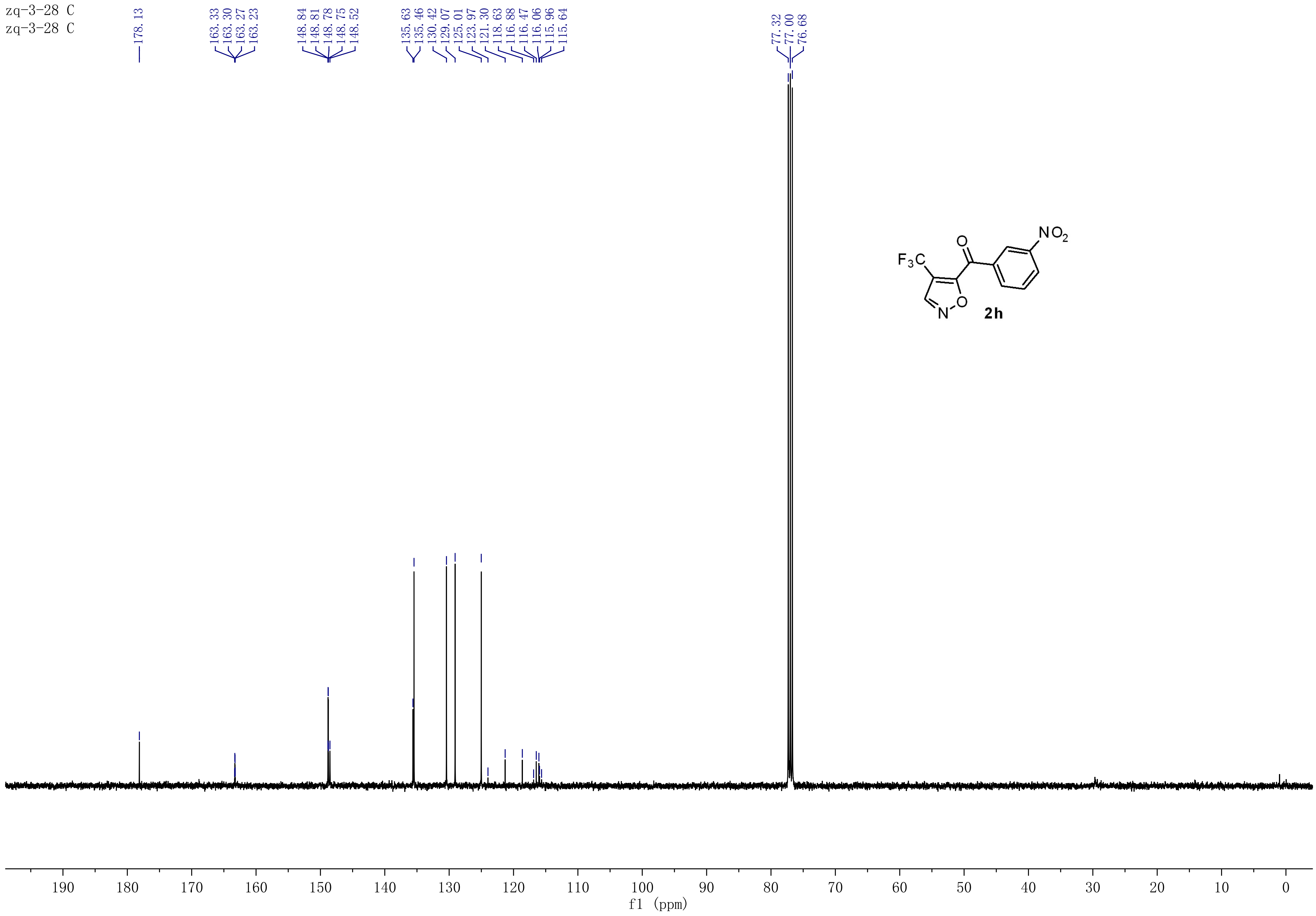

zq-3-33 H
zq-3-33 H
8.67
8.43
8.40
8.28
8.26
7.26
F_3C
O
NO_2
N
O
2g
1.00
2.05
2.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


zq-3-33 F
zq-3-33 F
-57.60
F_3C
O
NO_2
N
O
2g
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

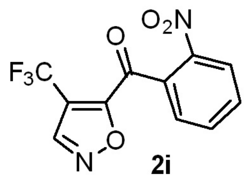

zq-3-33 C
zq-3-33 C
178.69
163.36
163.33
163.30
163.27
151.17
148.85
148.82
148.79
148.77
138.76
131.26
124.09
123.95
121.28
118.61
116.87
116.46
116.05
115.94
115.64
77.32
77.00
76.68
O
F3C
NO2
N
O
2g
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


zq-3-28 H
zq-3-28 H
8.93
8.67
8.58
8.56
8.44
8.42
7.84
7.82
7.80
7.26
F3C
O
NO2
N
O
2h
1.00
1.01
1.02
1.04
1.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

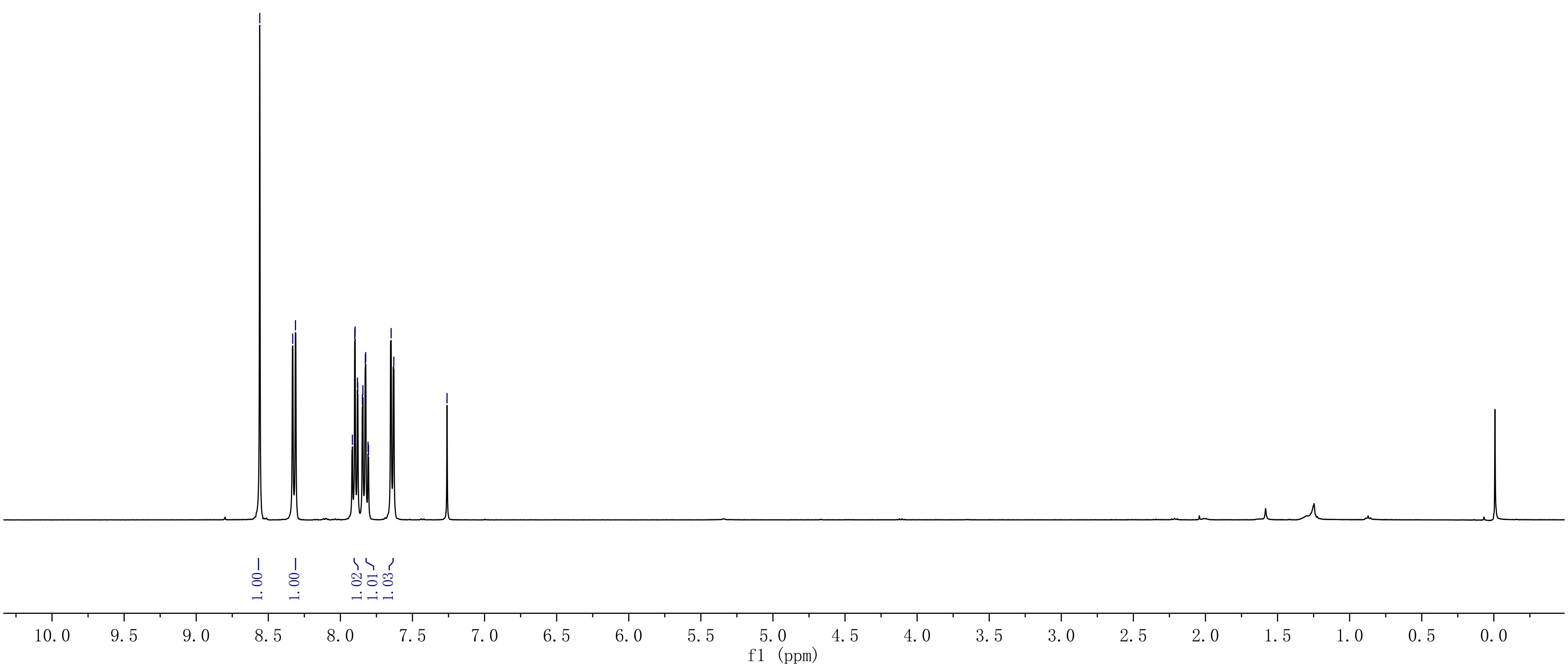

zq-3-28 F
zq-3-28 F
-57.57
F3C
O
NO2
N
O
2h
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

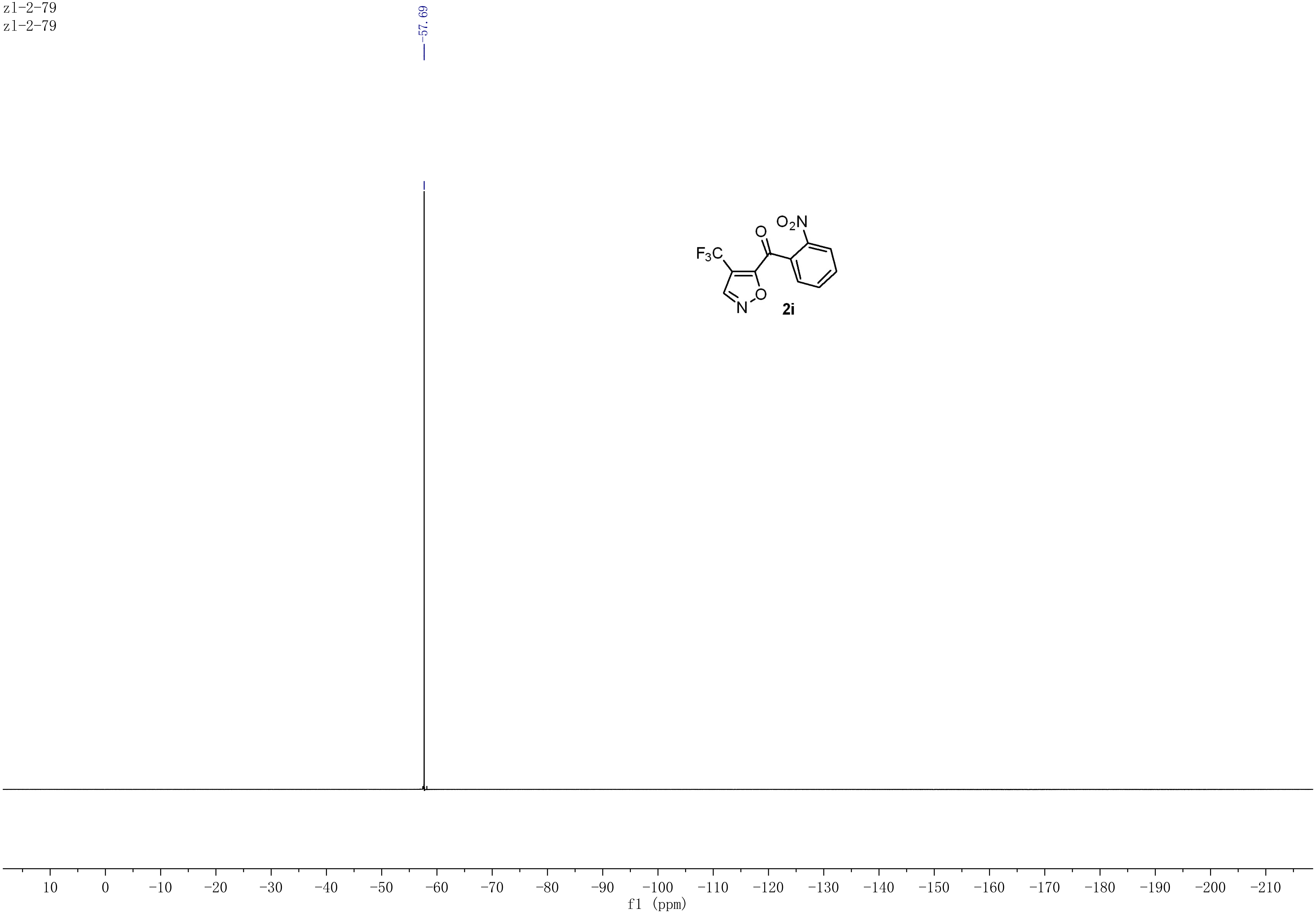

zq-3-28 C
zq-3-28 C
178.13
163.33
163.30
163.27
163.23
148.84
148.81
148.78
148.75
148.52
135.63
135.46
130.42
129.07
125.01
123.97
121.30
118.63
116.88
116.47
116.06
115.96
115.64
77.32
77.00
76.68
NO_2
O
F_3C
N
O
2h
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

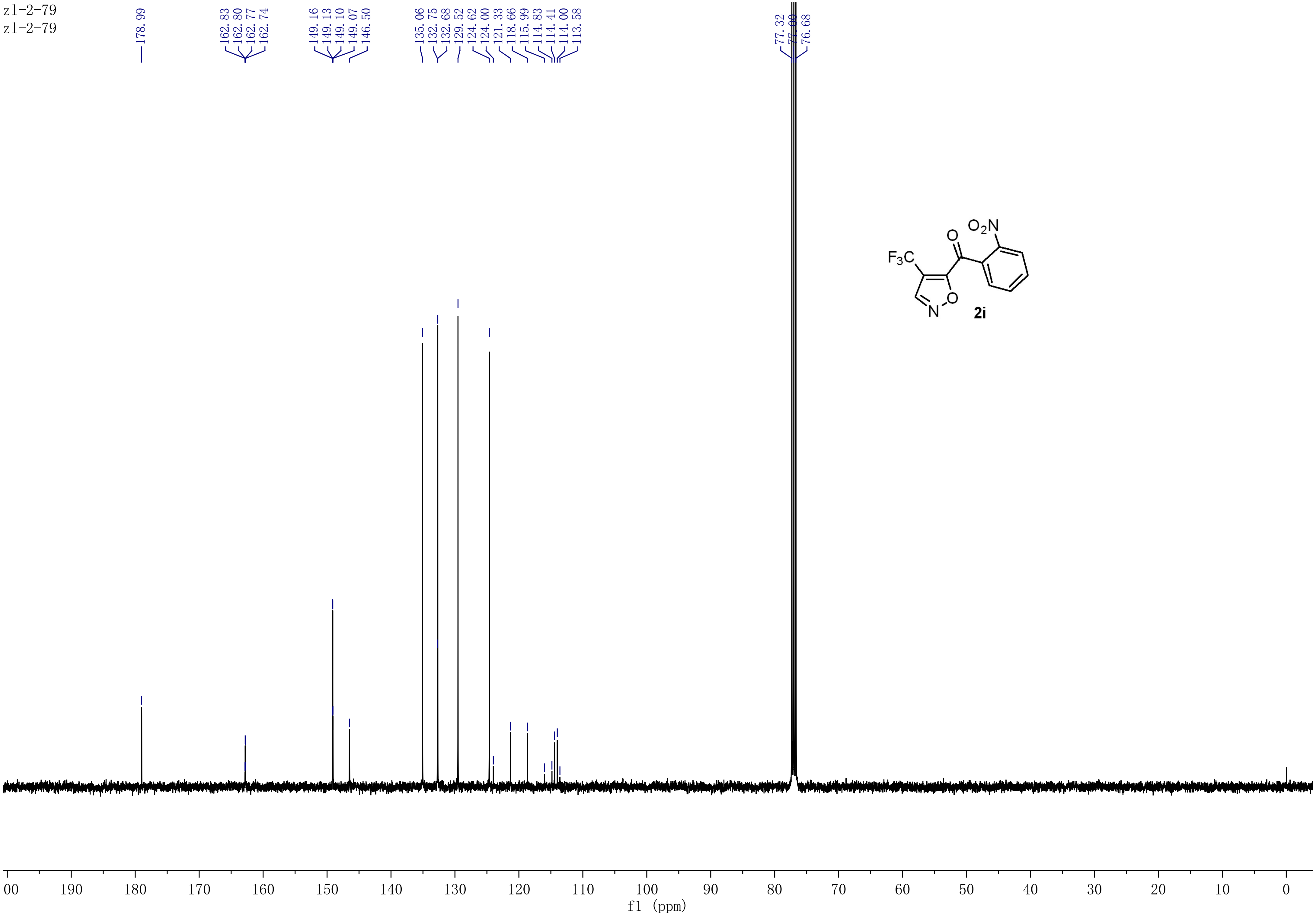
zl-2-79
zl-2-79

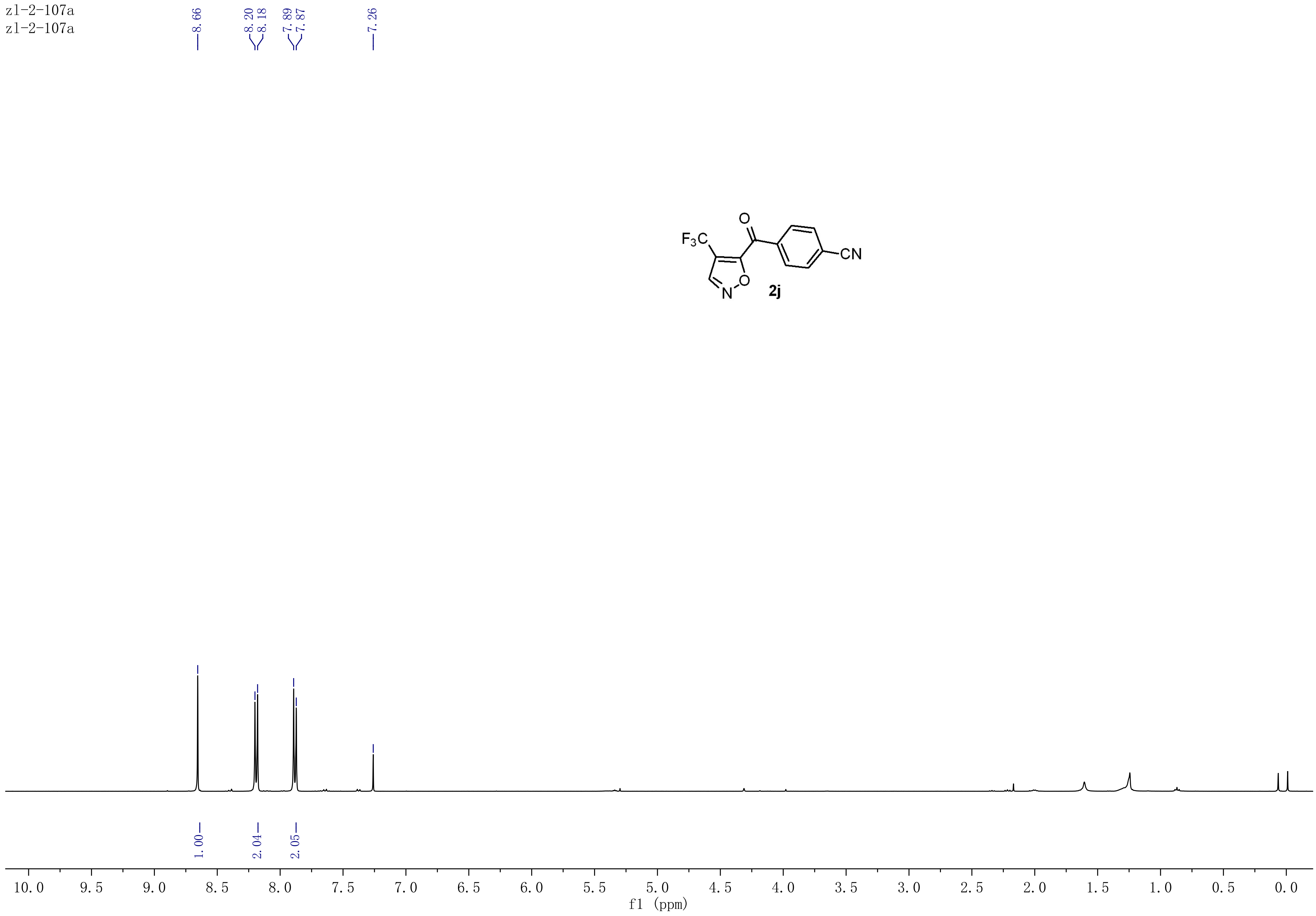


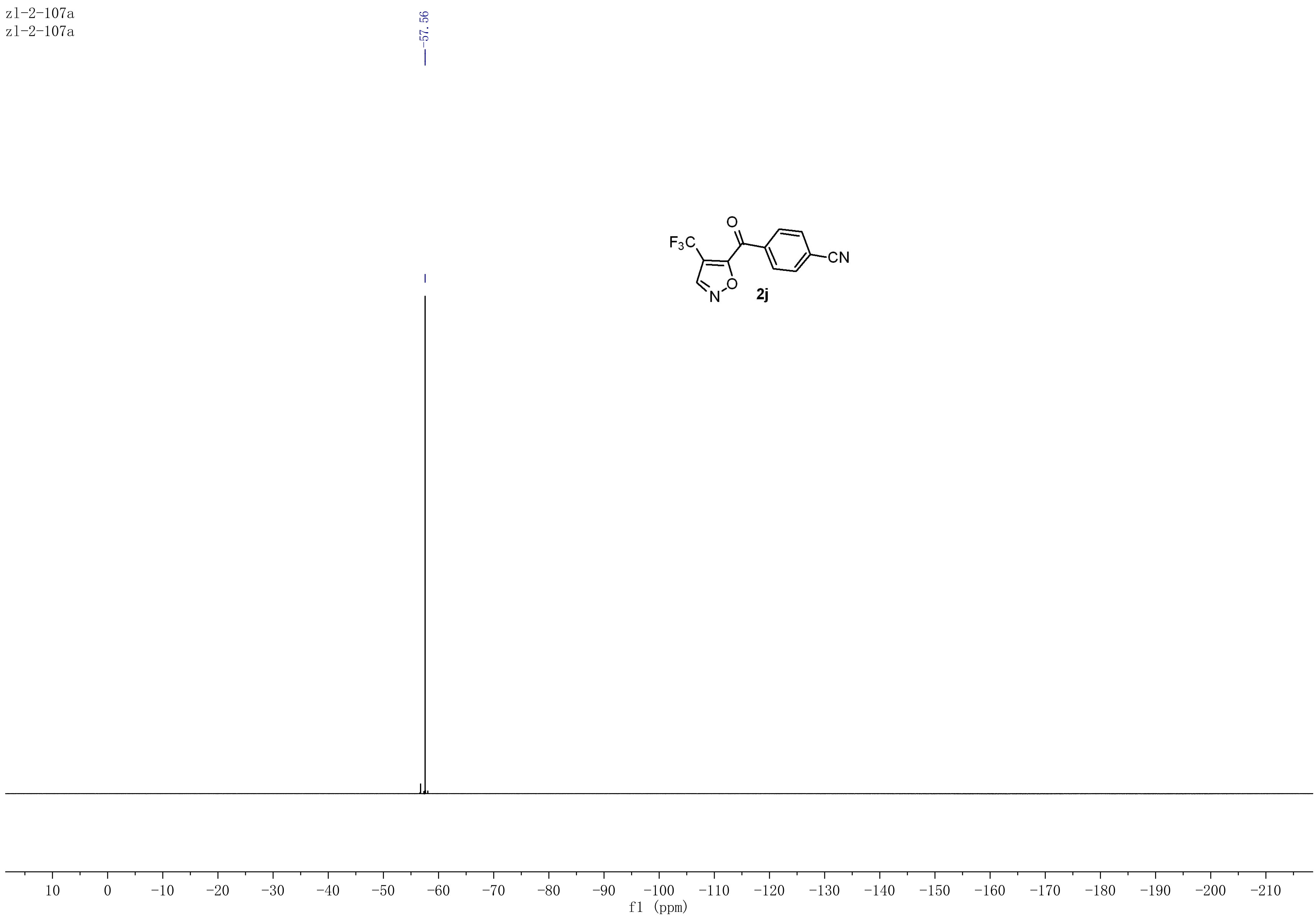
2i

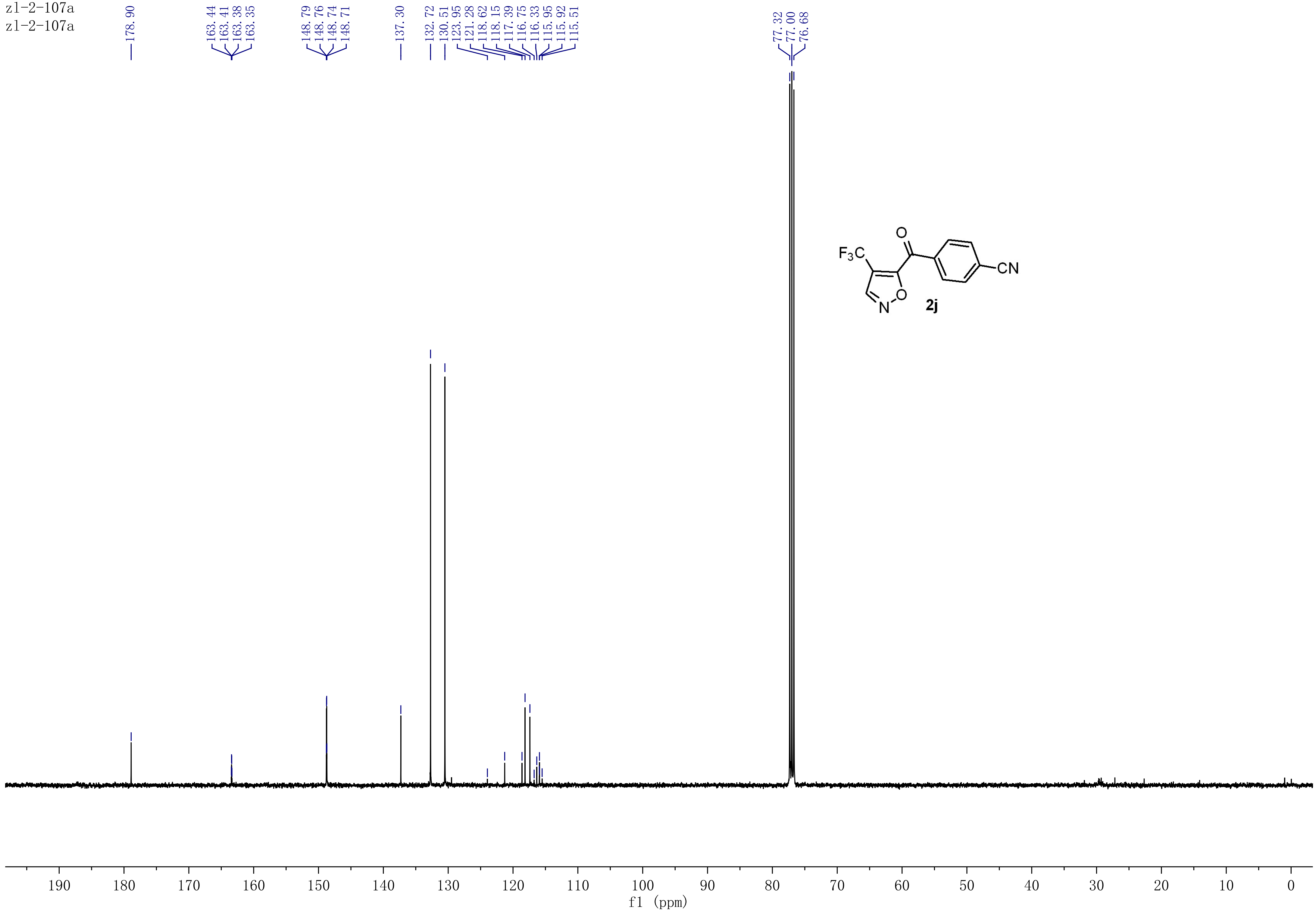



zl-2-79
zl-2-79
-57.69
O
O_2N
F_3C
O
N
2i
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)


zl-2-79
zl-2-79
178.99
162.83
162.80
162.77
162.74
149.16
149.13
149.10
149.07
146.50
135.06
132.75
132.68
129.52
124.62
124.00
121.33
118.66
115.99
114.83
114.41
114.00
113.58
77.32
77.00
76.68
O
O_2N
F_3C
N
O
2i
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

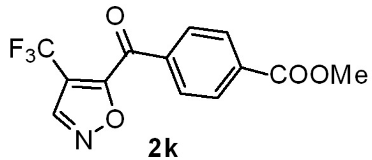

zl-2-107a
zl-2-107a
8.66
8.20
8.18
7.89
7.87
7.26
F3C
O
CN
N
O
2j
1.00
2.04
2.05
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


zl-2-107a
zl-2-107a
-57.56
F_3C
O
CN
N
O
2j
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)



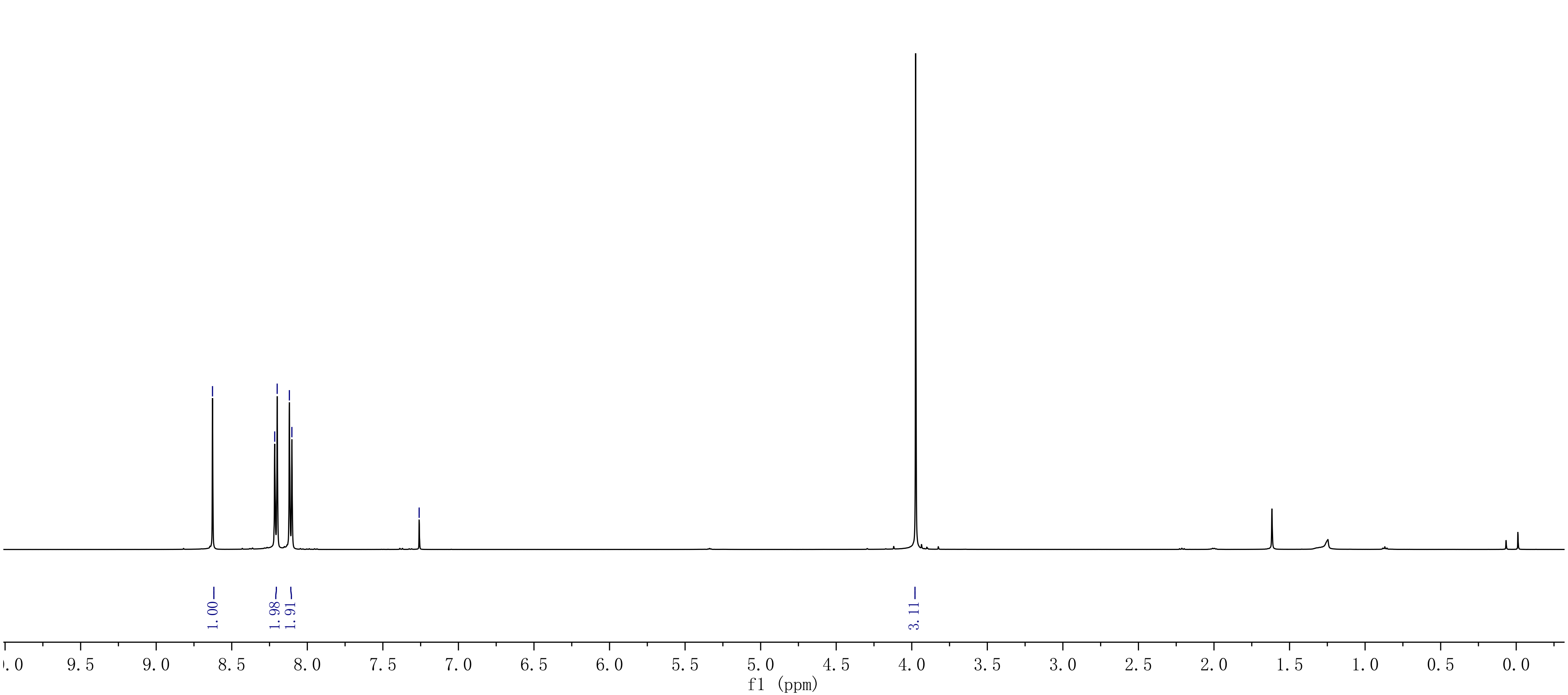
zl-2-107a
zl-2-107a
178.90
163.44
163.41
163.38
163.35
148.79
148.76
148.74
148.71
137.30
132.72
130.51
123.95
121.28
118.62
118.15
117.39
116.75
116.33
115.95
115.92
115.51
77.32
77.00
76.68
F3C
O
CN
N
O
2j
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

zl-2-115



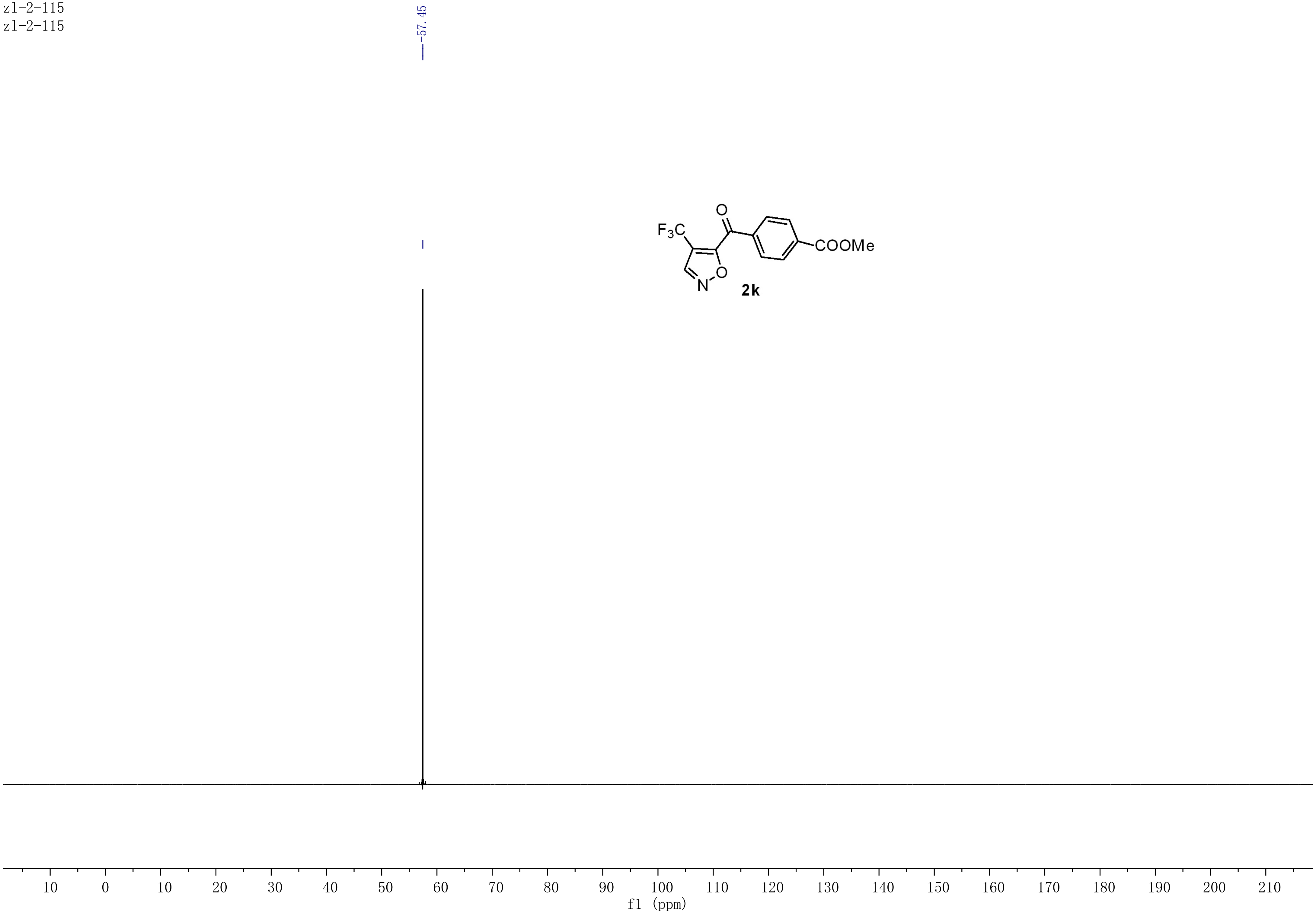
F3C
O
COOMe
N
O

2k

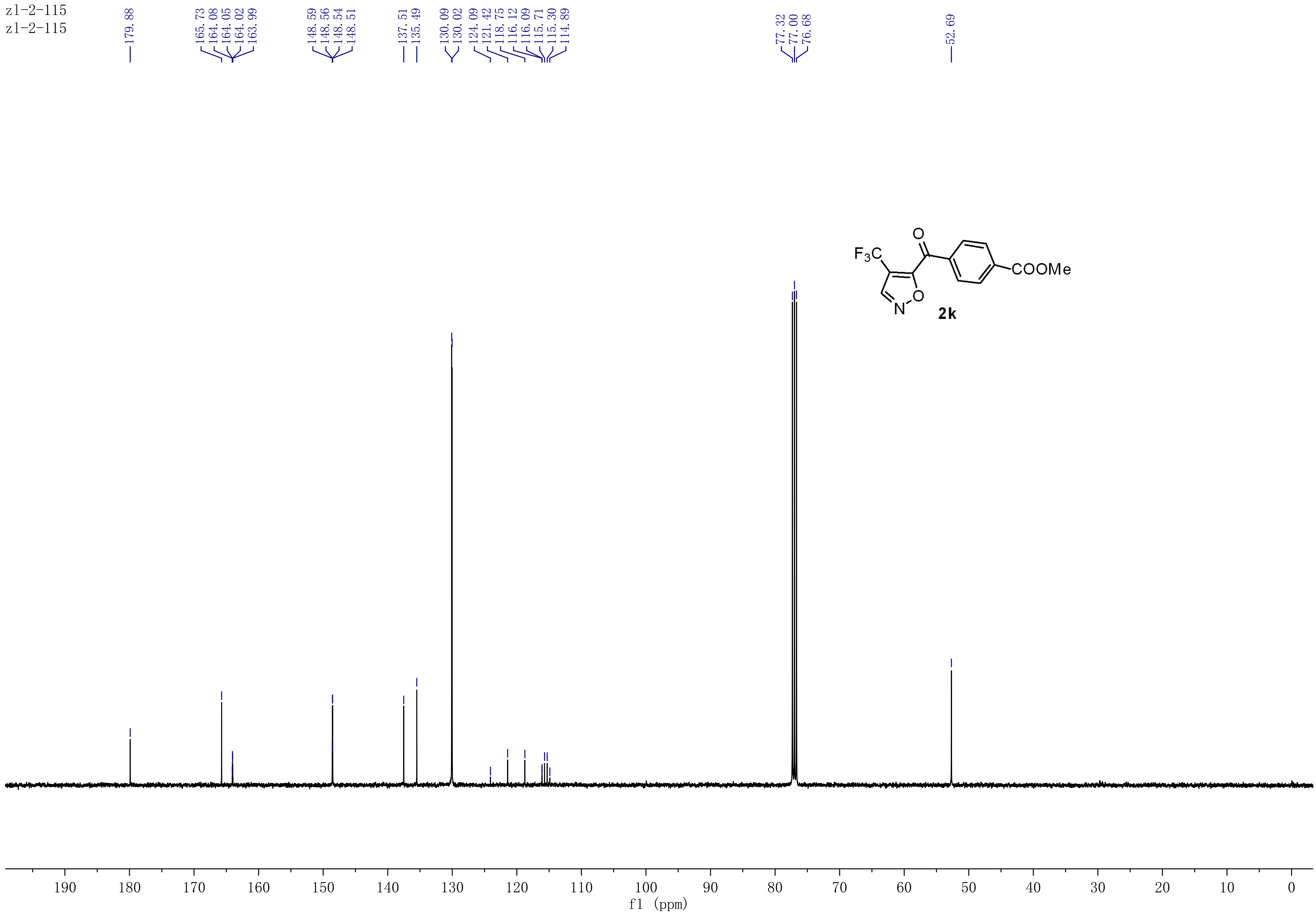


8.63
8.22
8.20
8.12
8.10
7.26
1.00
1.98
1.91
3.11
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

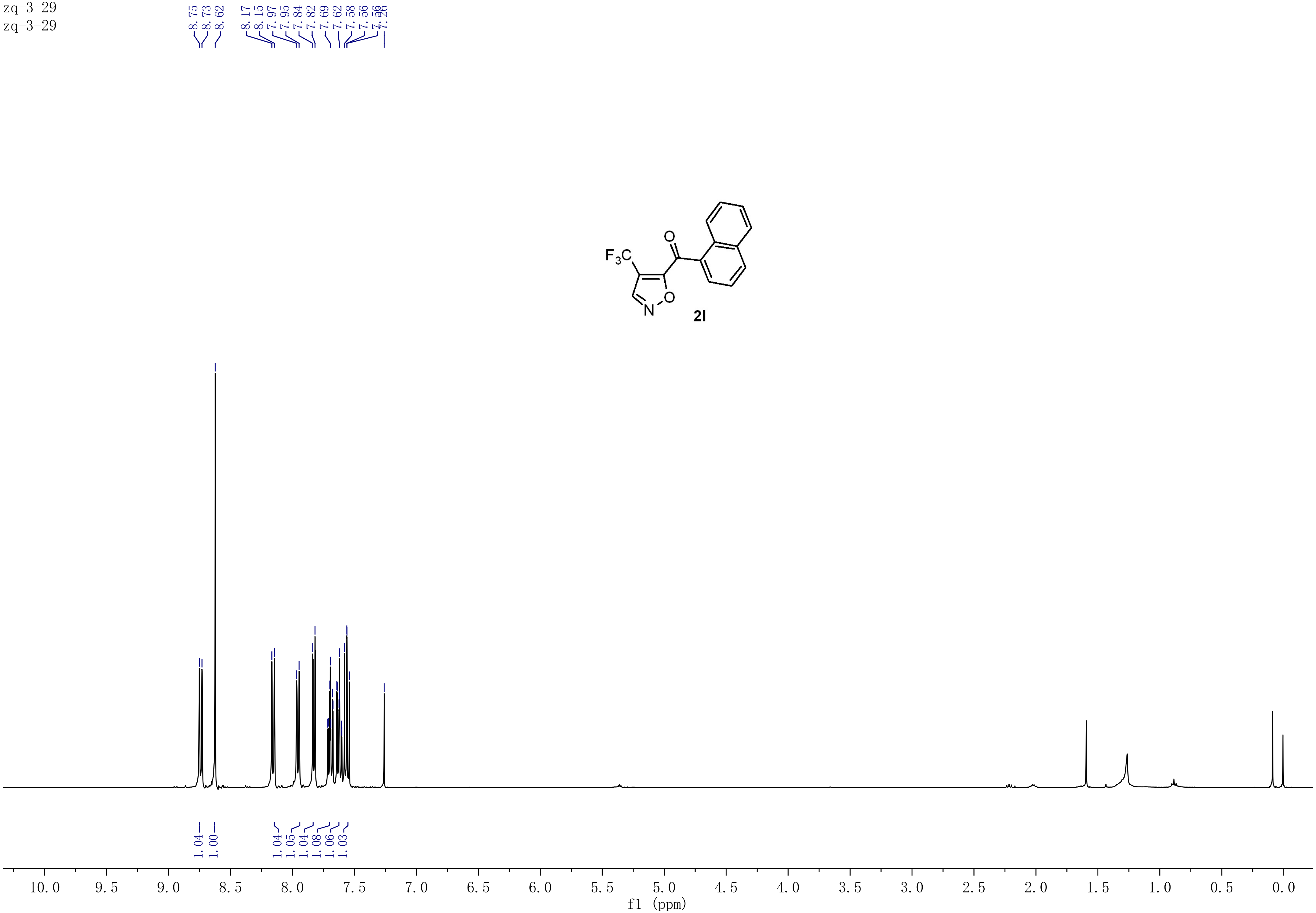
zl-2-115
zl-2-115

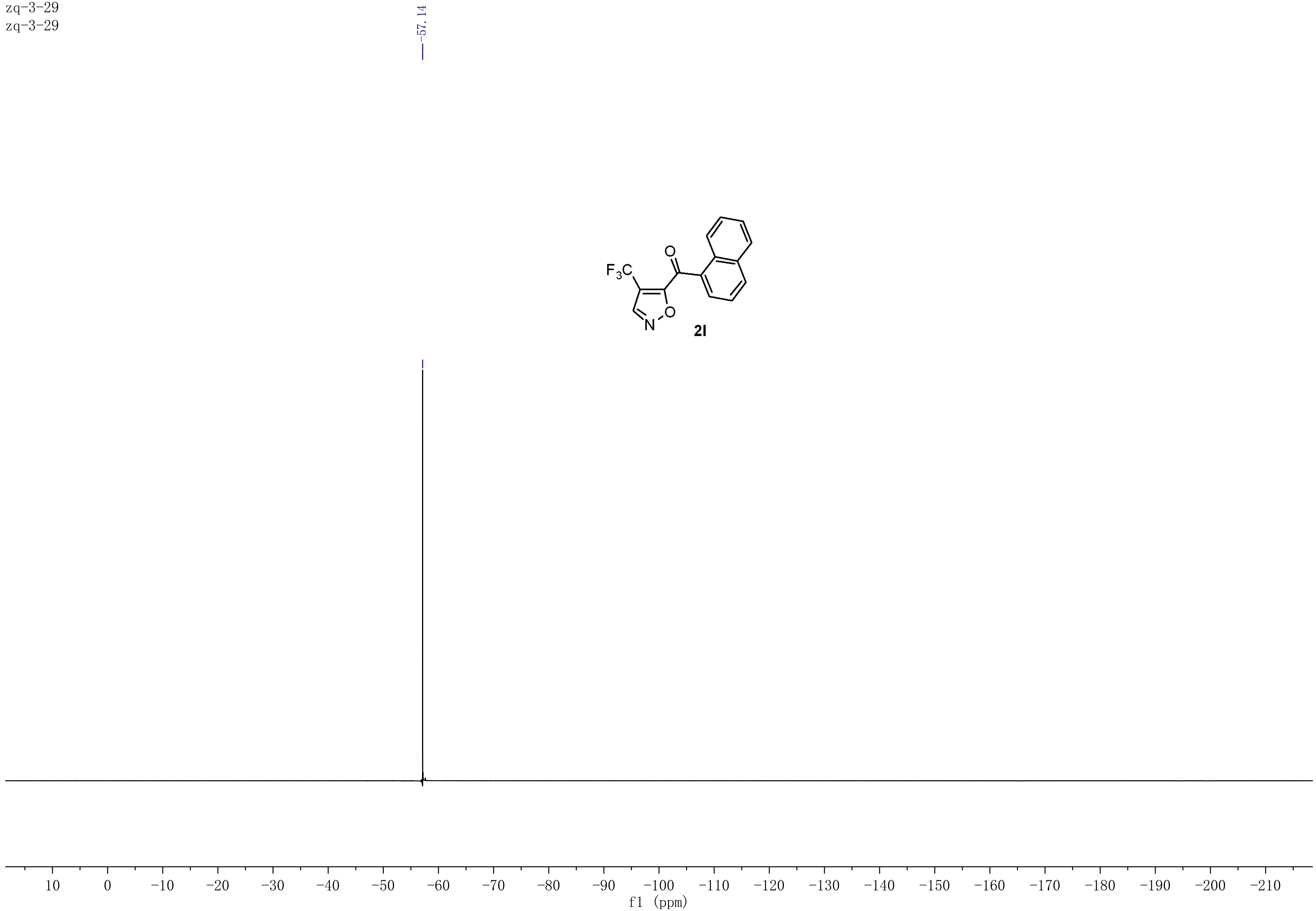


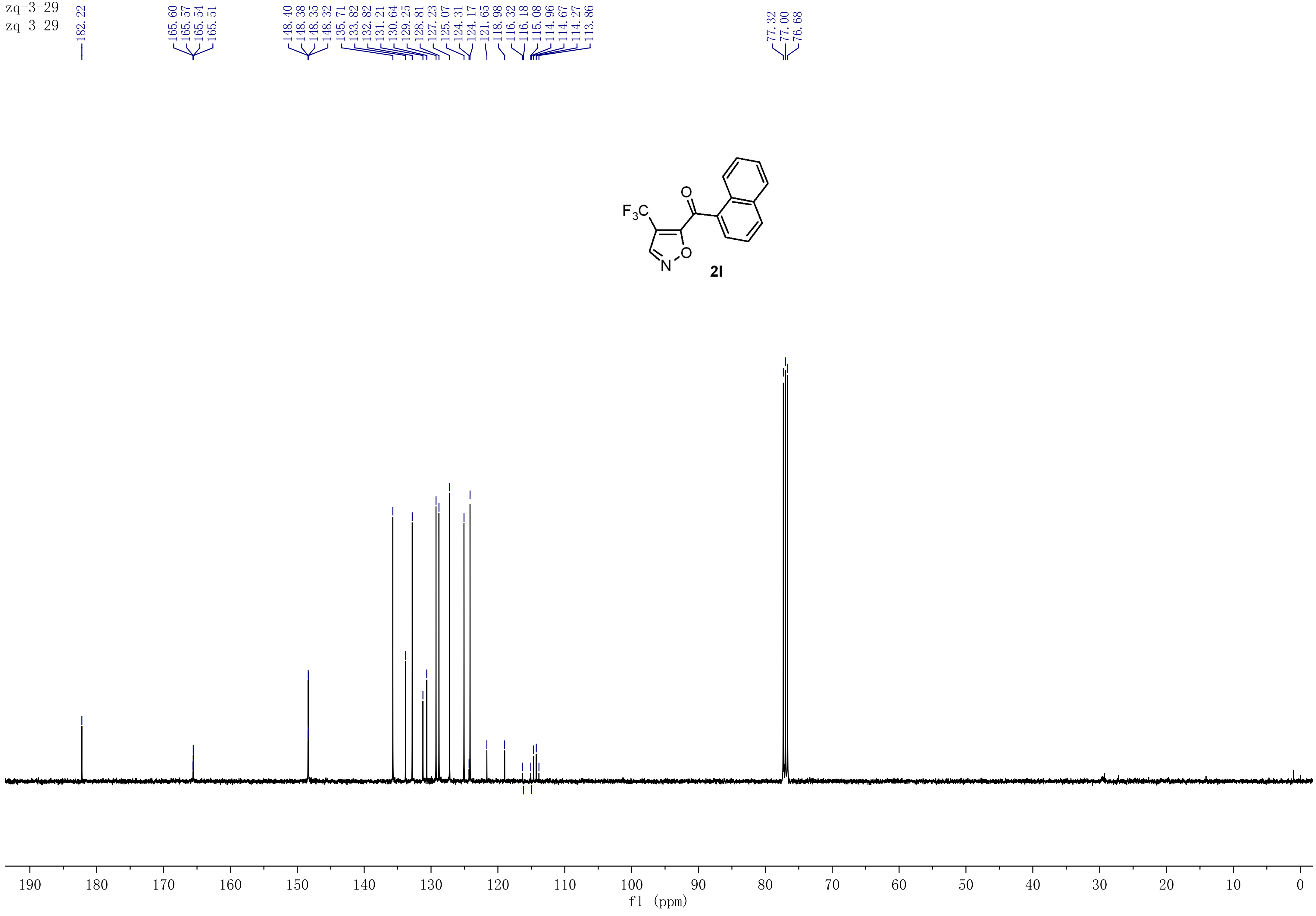
2k

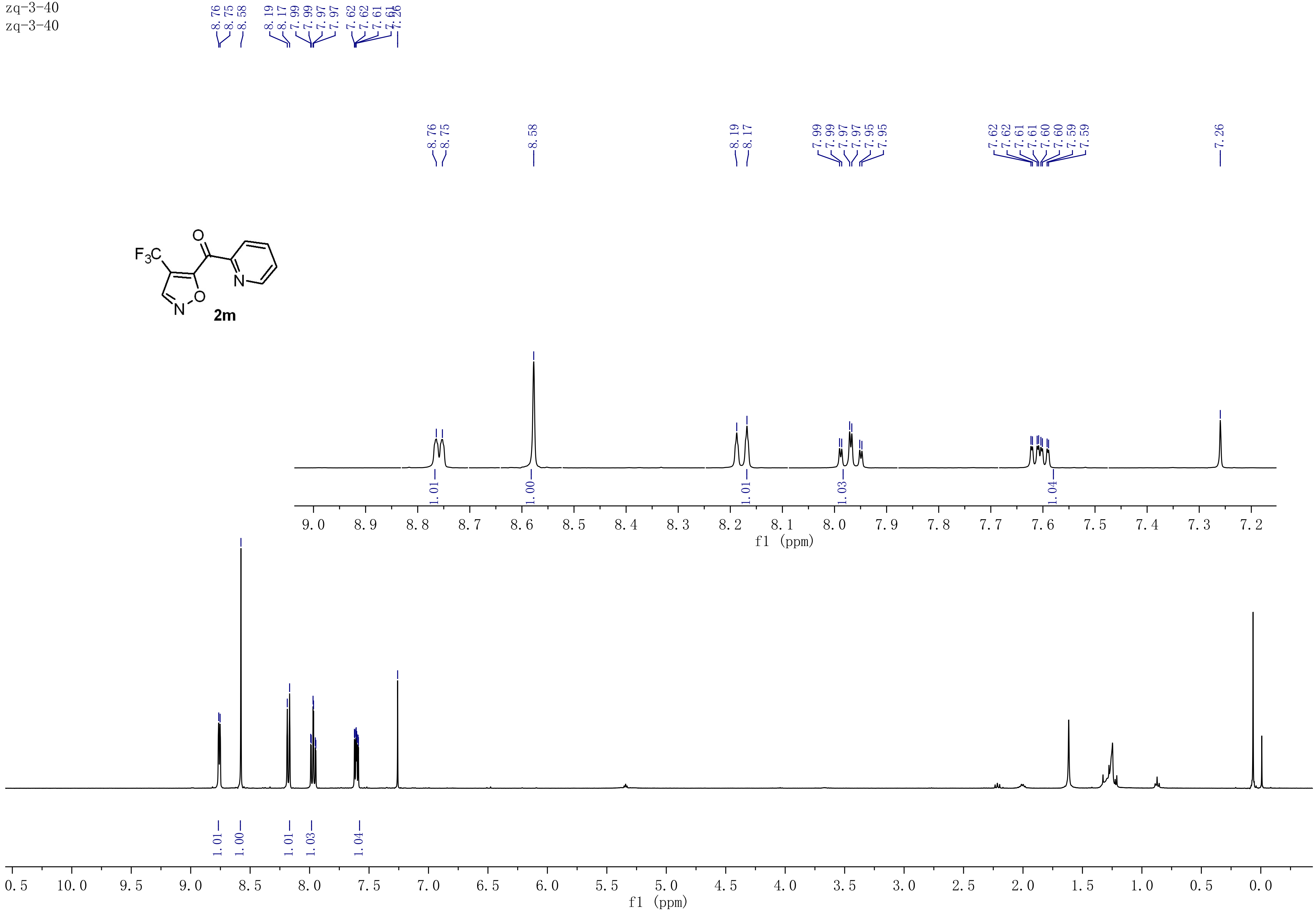

zl-2-115
zl-2-115
179.88
165.73
164.08
164.05
164.02
163.99
148.59
148.56
148.54
148.51
137.51
135.49
130.09
130.02
124.09
121.42
118.75
116.12
116.09
115.71
115.30
114.89
77.32
77.00
76.68
52.69
O
F3C
COOMe
N
O
2k
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

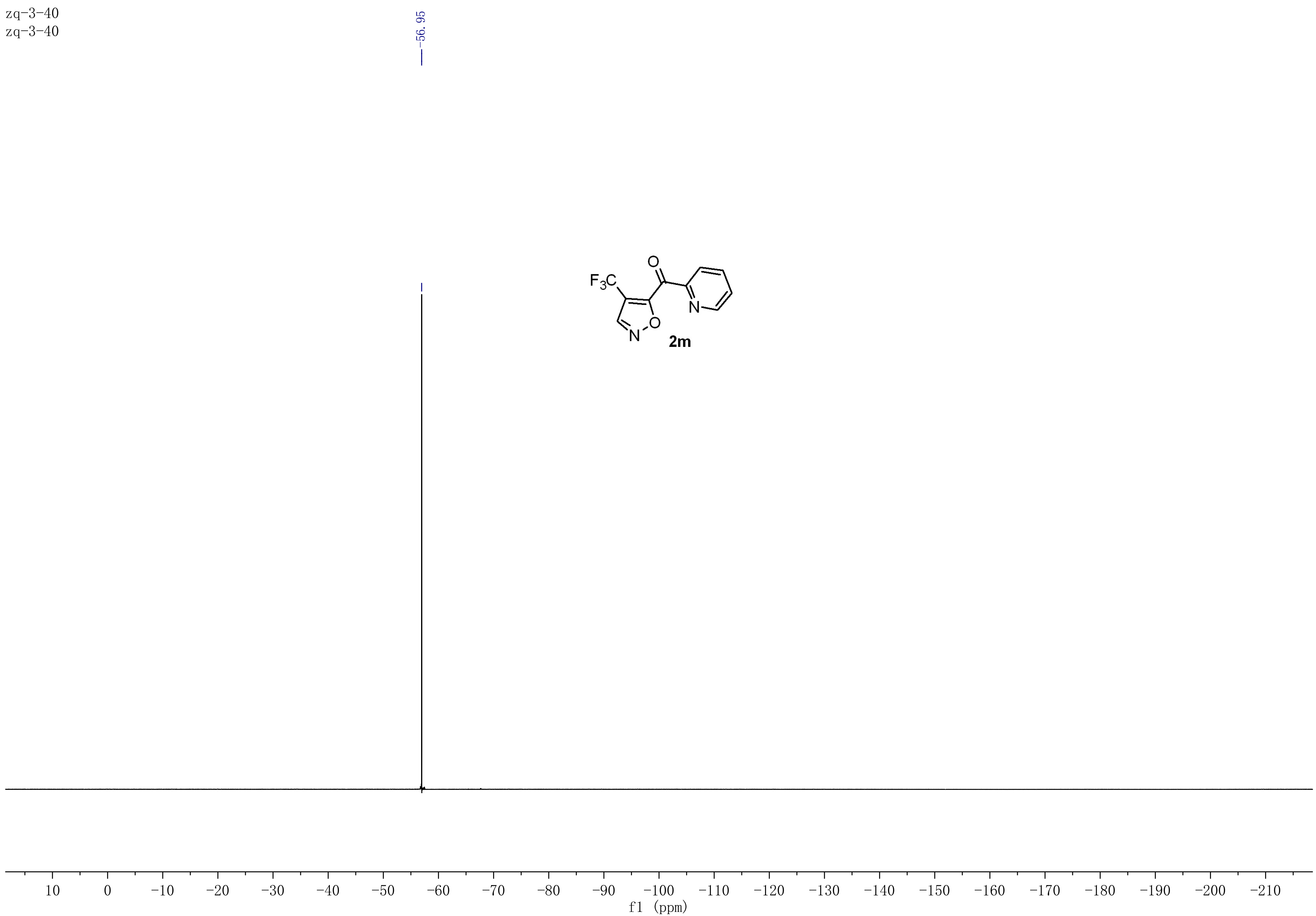
zq-3-29
zq-3-29

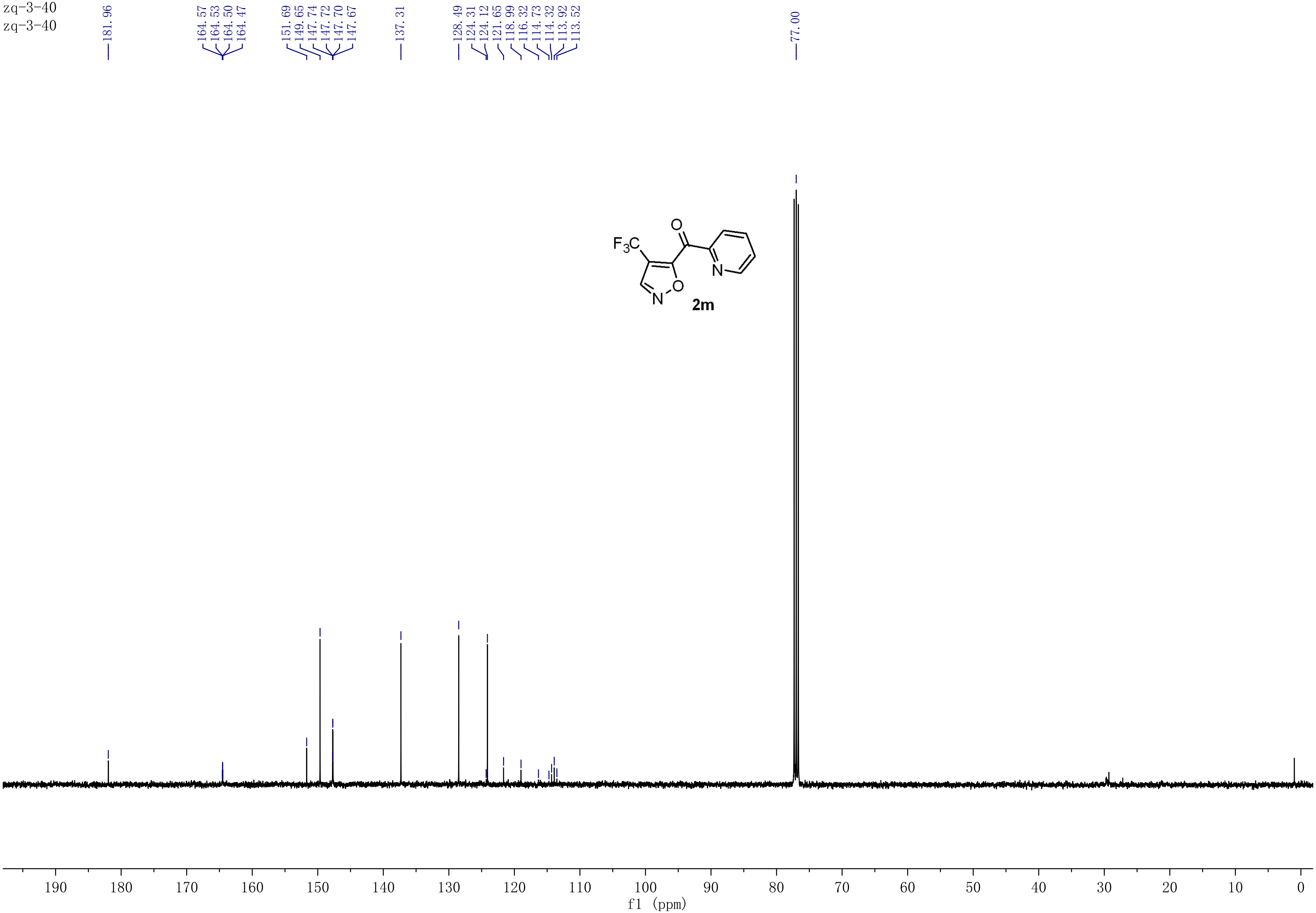

8.75
8.73
8.62
8.17
8.15
7.97
7.95
7.84
7.82
7.69
7.62
7.58
7.56
7.56
7.26
F_3C
O
N
O
2l
1.04
1.00
1.04
1.05
1.04
1.08
1.06
1.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

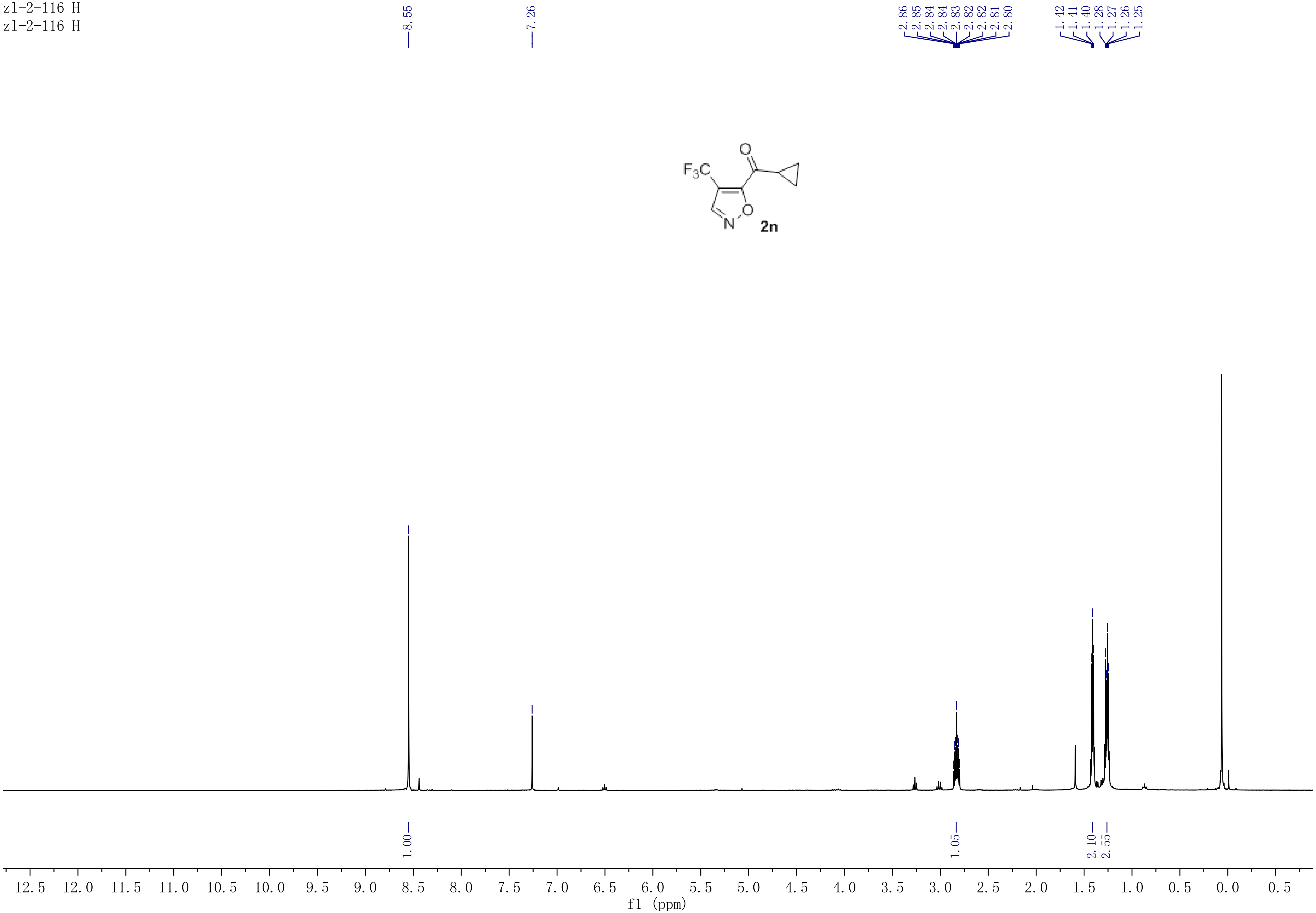

zq-3-29
zq-3-29
-57.14
F3C
O
N
O
2l
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)


zq-3-29
zq-3-29
182.22
165.60
165.57
165.54
165.51
148.40
148.38
148.35
148.32
135.71
133.82
132.82
131.21
130.64
129.25
128.81
127.23
125.07
124.31
124.17
121.65
118.98
116.32
116.18
115.08
114.96
114.67
114.27
113.86
77.32
77.00
76.68
F_3C
O
N
2l
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

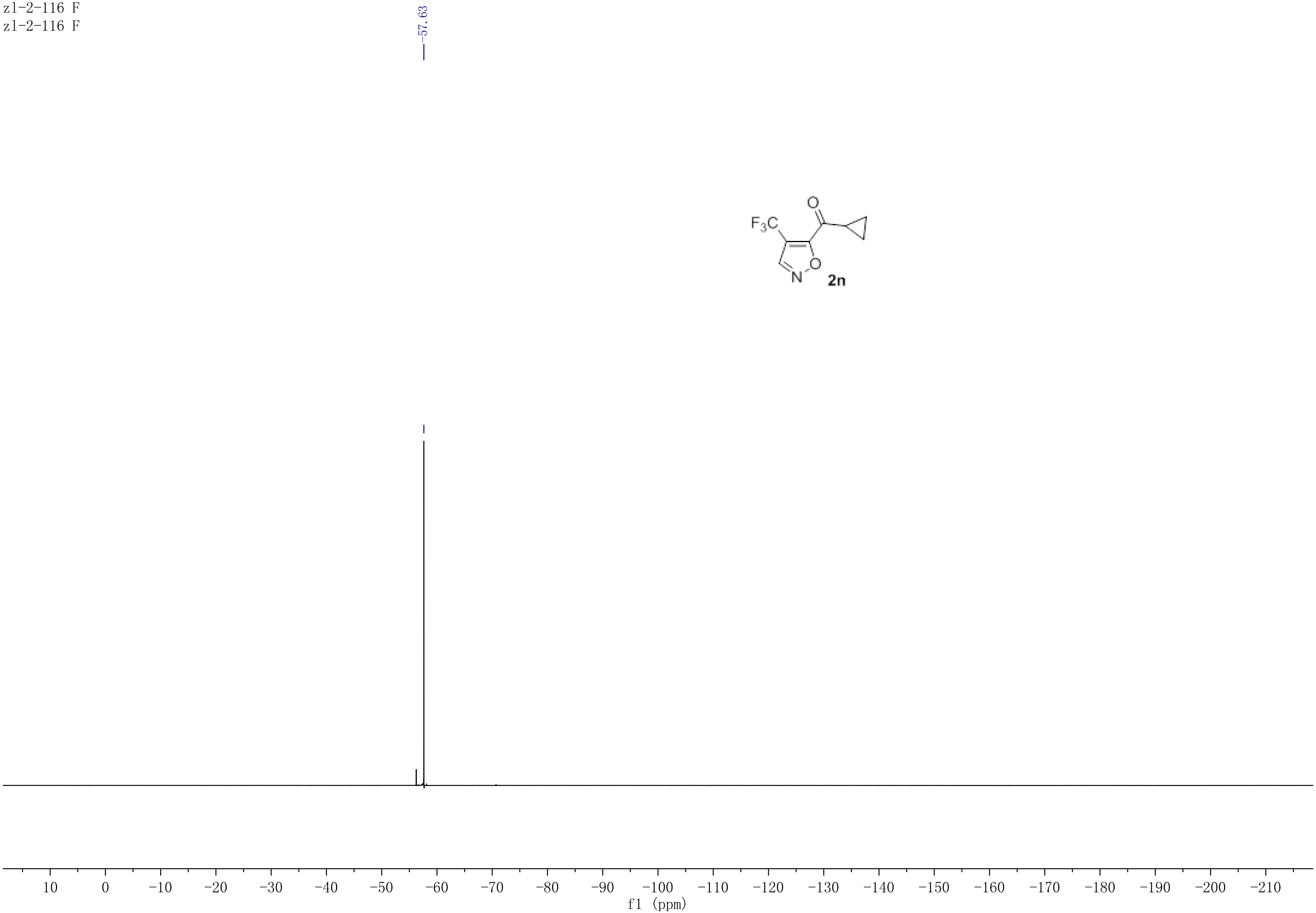

zq-3-40
zq-3-40
8.76 8.75 8.58 8.19 8.17 7.99 7.99 7.97 7.97 7.62 7.62 7.61 7.61 7.26
8.76 8.75
8.58
8.19 8.17
7.99 7.99 7.97 7.97 7.95 7.95
7.62 7.62 7.61 7.61 7.60 7.60 7.59 7.59
7.26
2m
1.01
1.00
1.01
1.03
1.04
9.0 8.9 8.8 8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2
f1 (ppm)
0.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


zq-3-40
zq-3-40
-56.95
F3C
O
N
O
N
2m
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

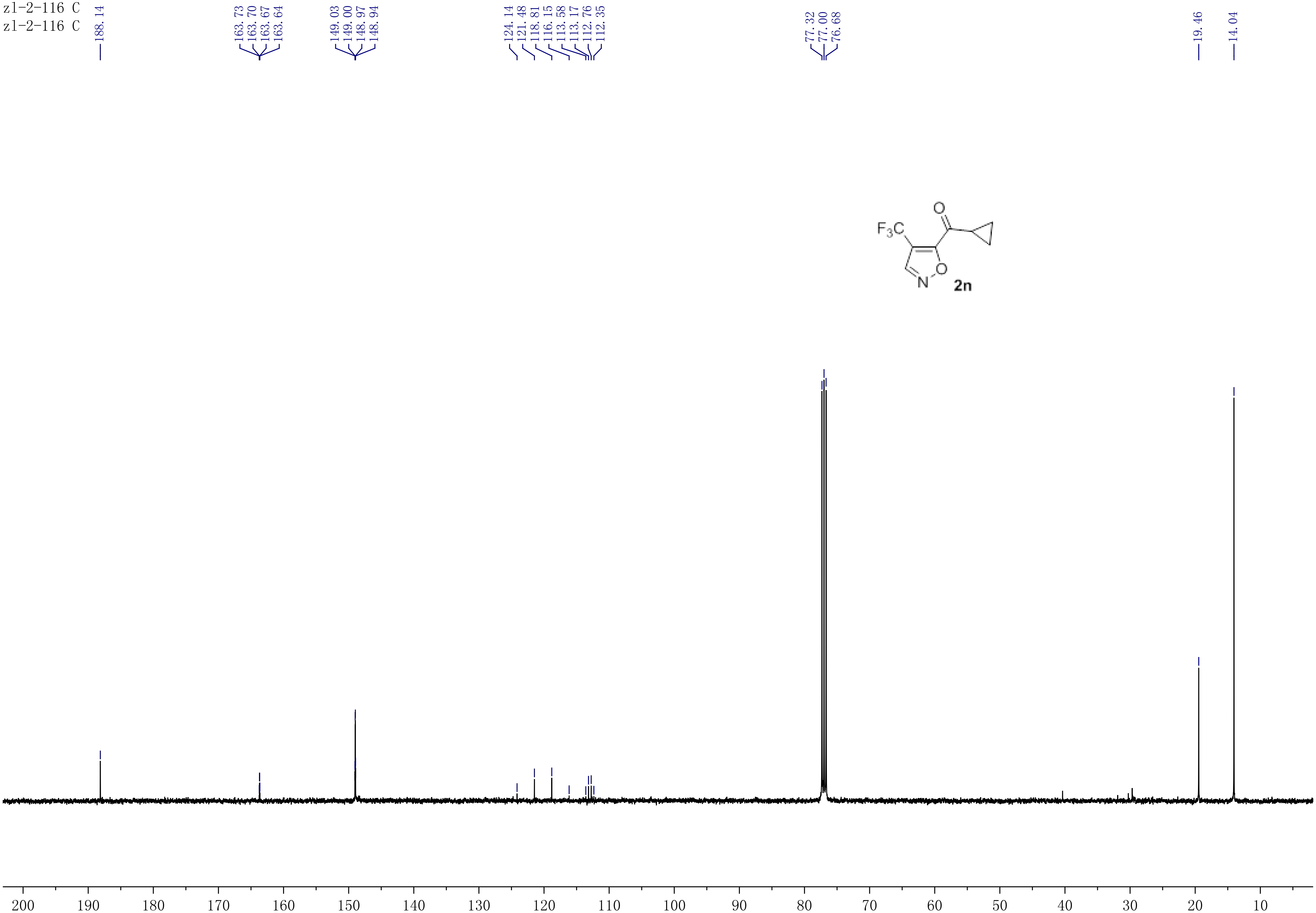

zq-3-40
zq-3-40
181.96
164.57
164.53
164.50
164.47
151.69
149.65
147.74
147.72
147.70
147.67
137.31
128.49
124.31
124.12
121.65
118.99
116.32
114.73
114.32
113.92
113.52
77.00
F3C
O
N
2m
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

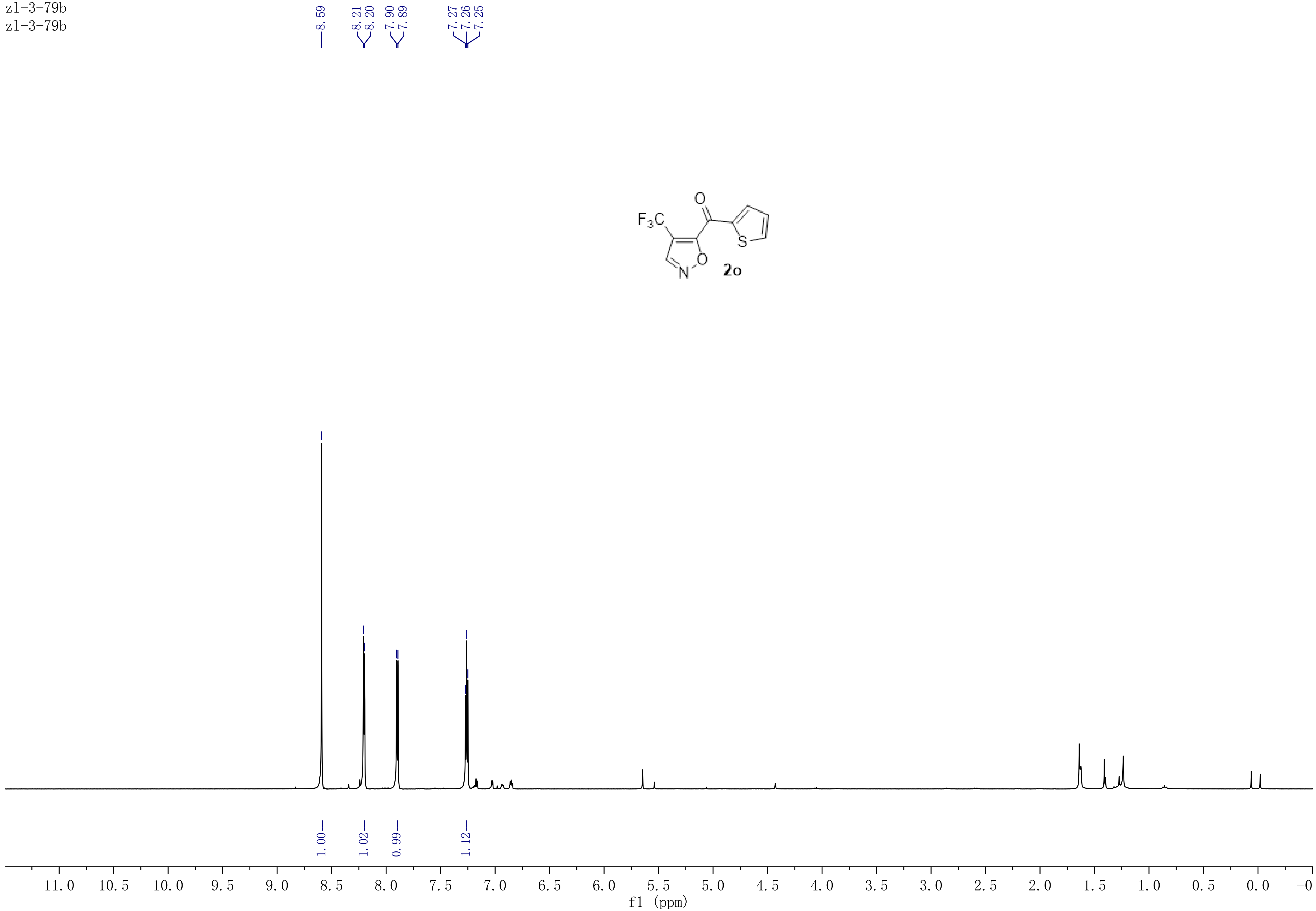

zl-2-116 H
zl-2-116 H
8.55
7.26
2.86
2.85
2.84
2.84
2.83
2.82
2.82
2.81
2.80
1.42
1.41
1.40
1.28
1.27
1.26
1.25
F_3C
O
N
2n
1.00
1.05
2.10
2.55
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

zl-2-116 F
zl-2-116 F

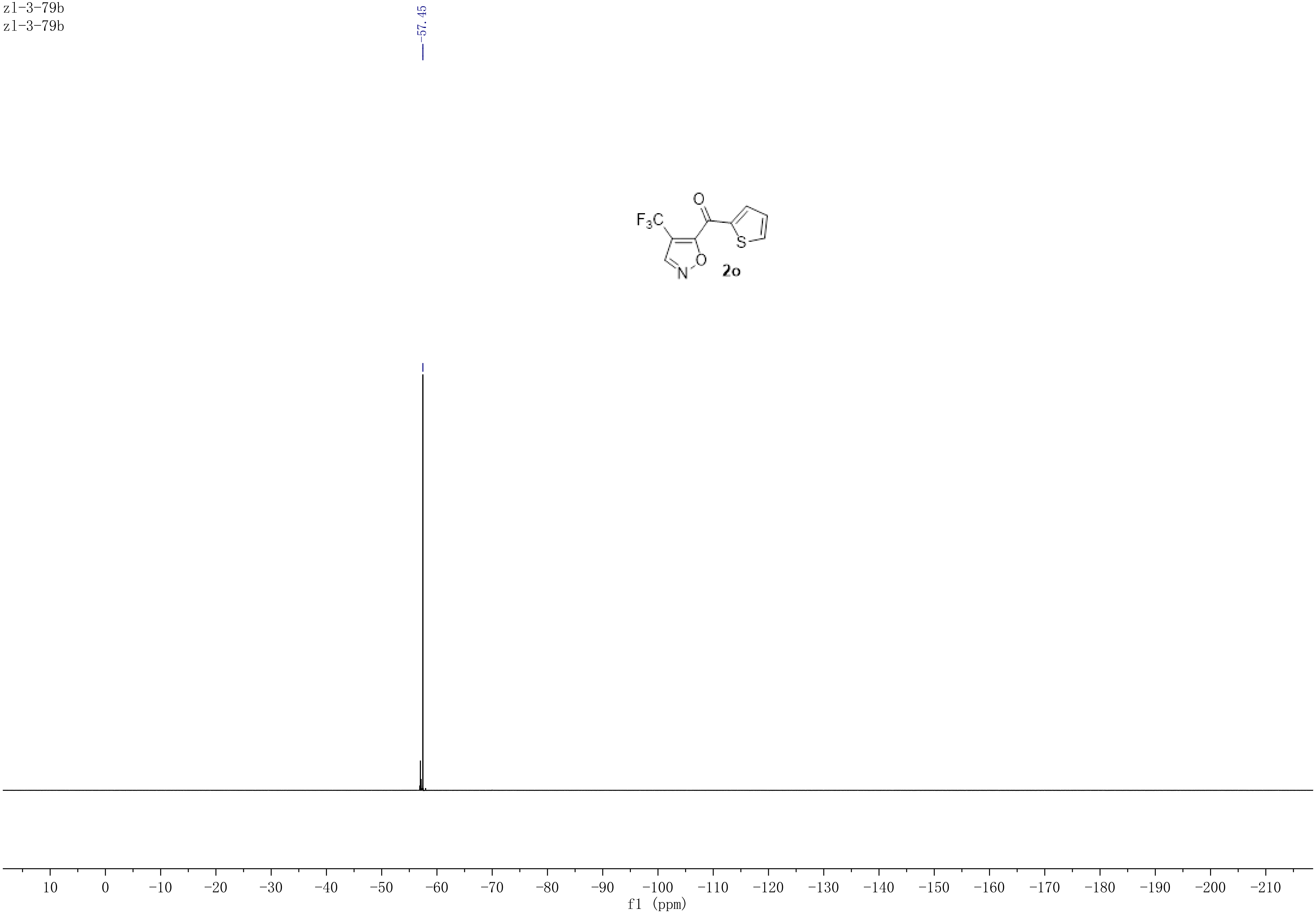


zl-2-116 C
zl-2-116 C

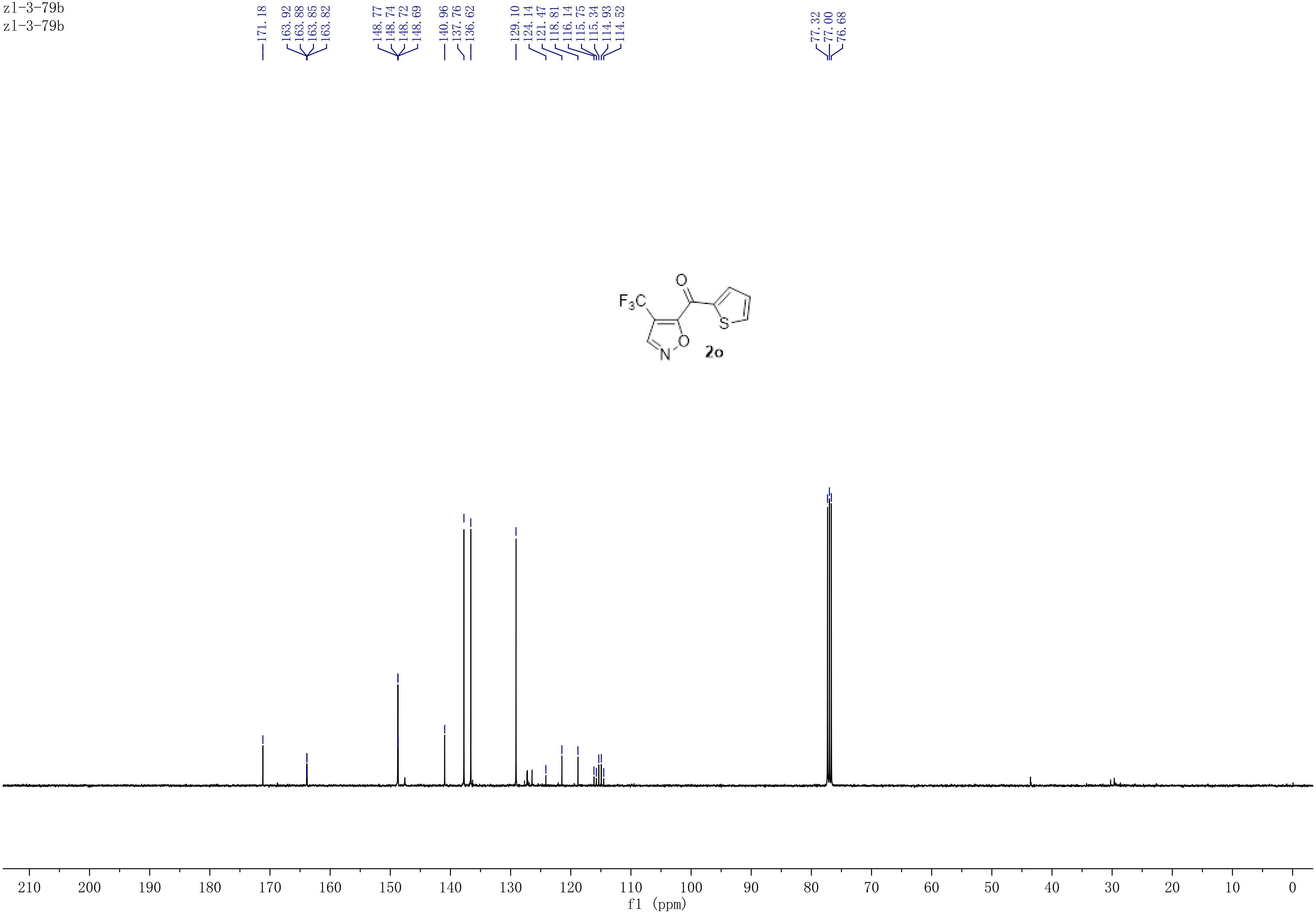


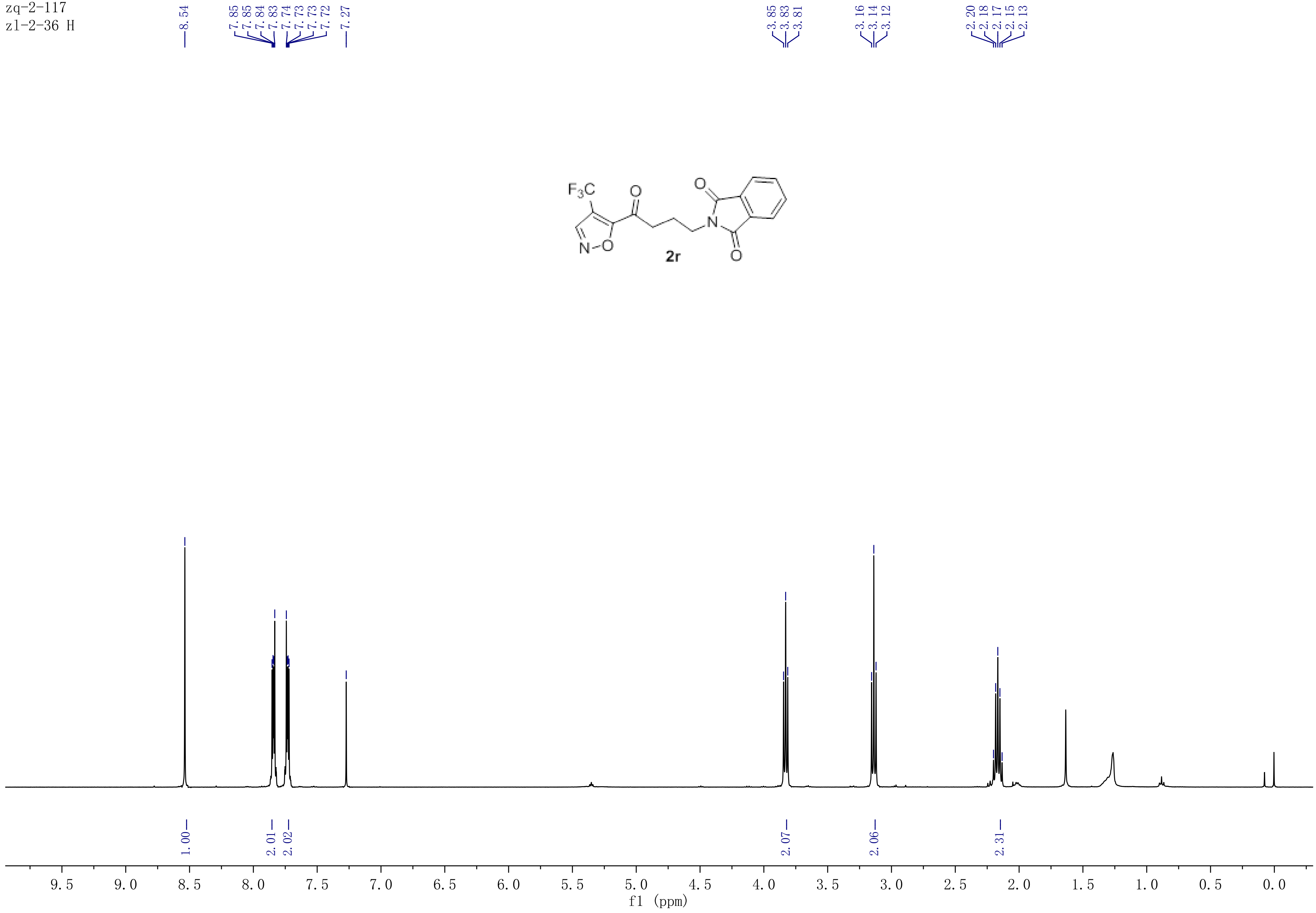

zl-3-79b
zl-3-79b
8.59
8.21
8.20
7.90
7.89
7.27
7.26
7.25
F3C
O
S
N
O
2o
1.00
1.02
0.99
1.12
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)

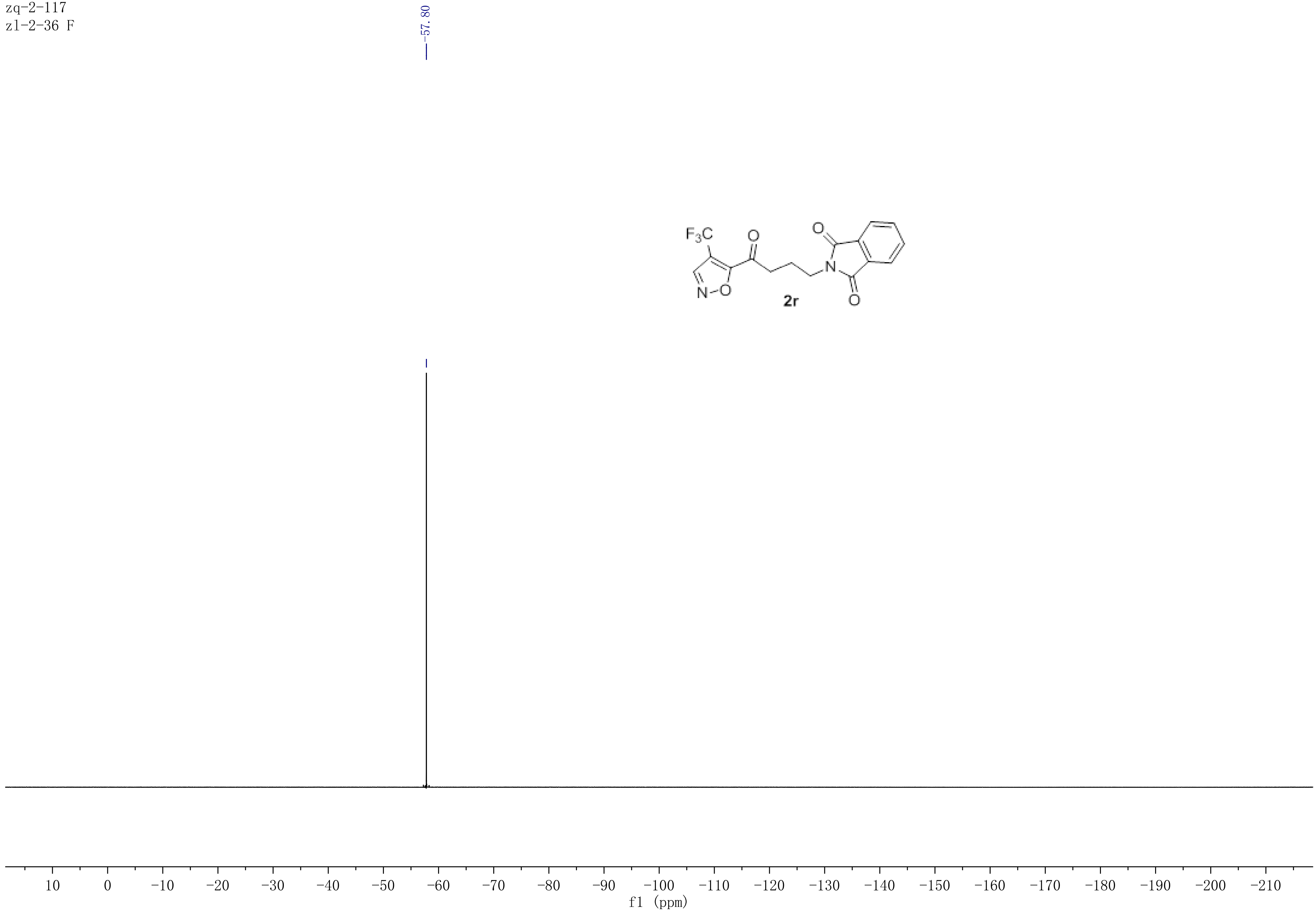
zl-3-79b
zl-3-79b

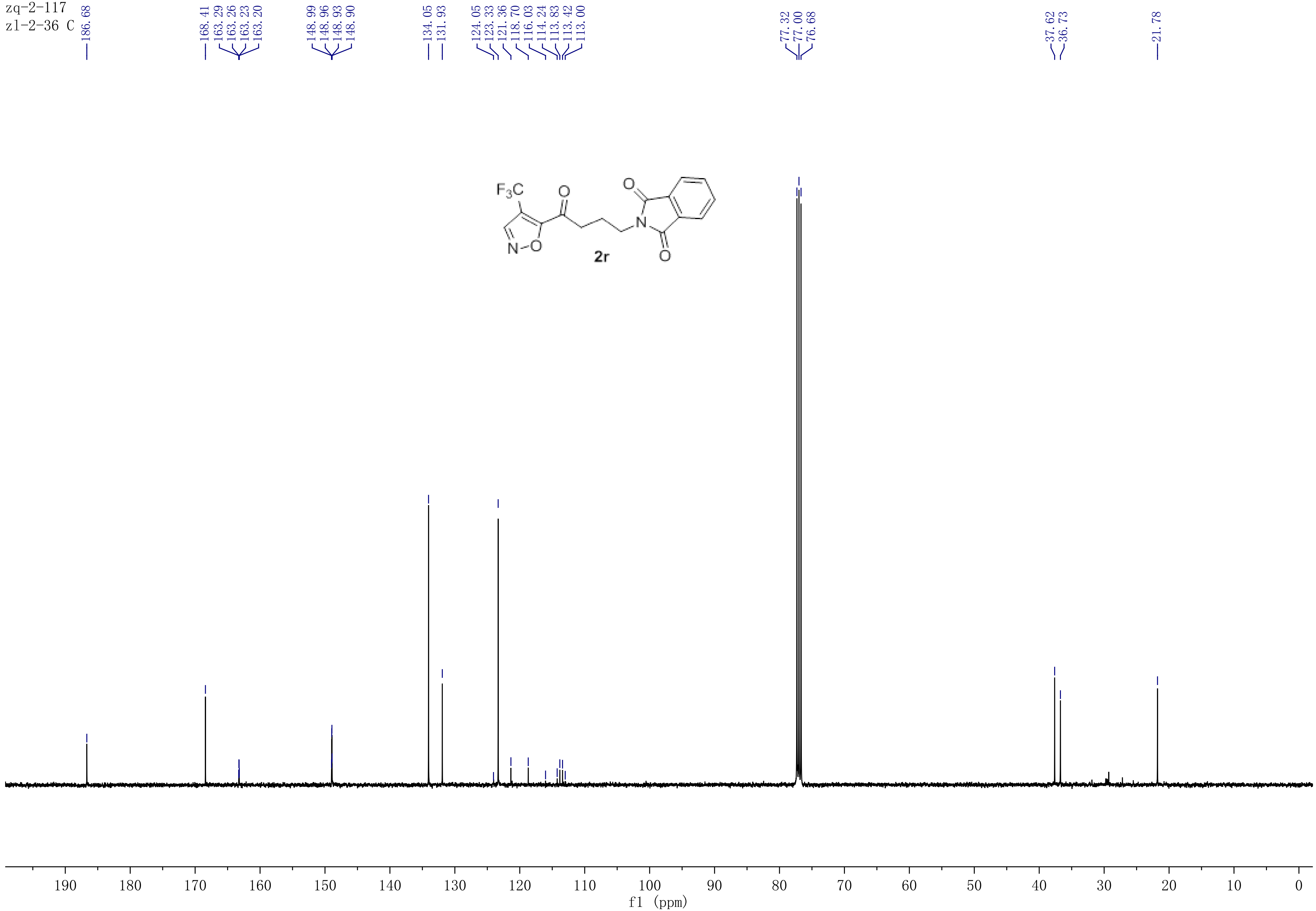


zl-3-79b
zl-3-79b

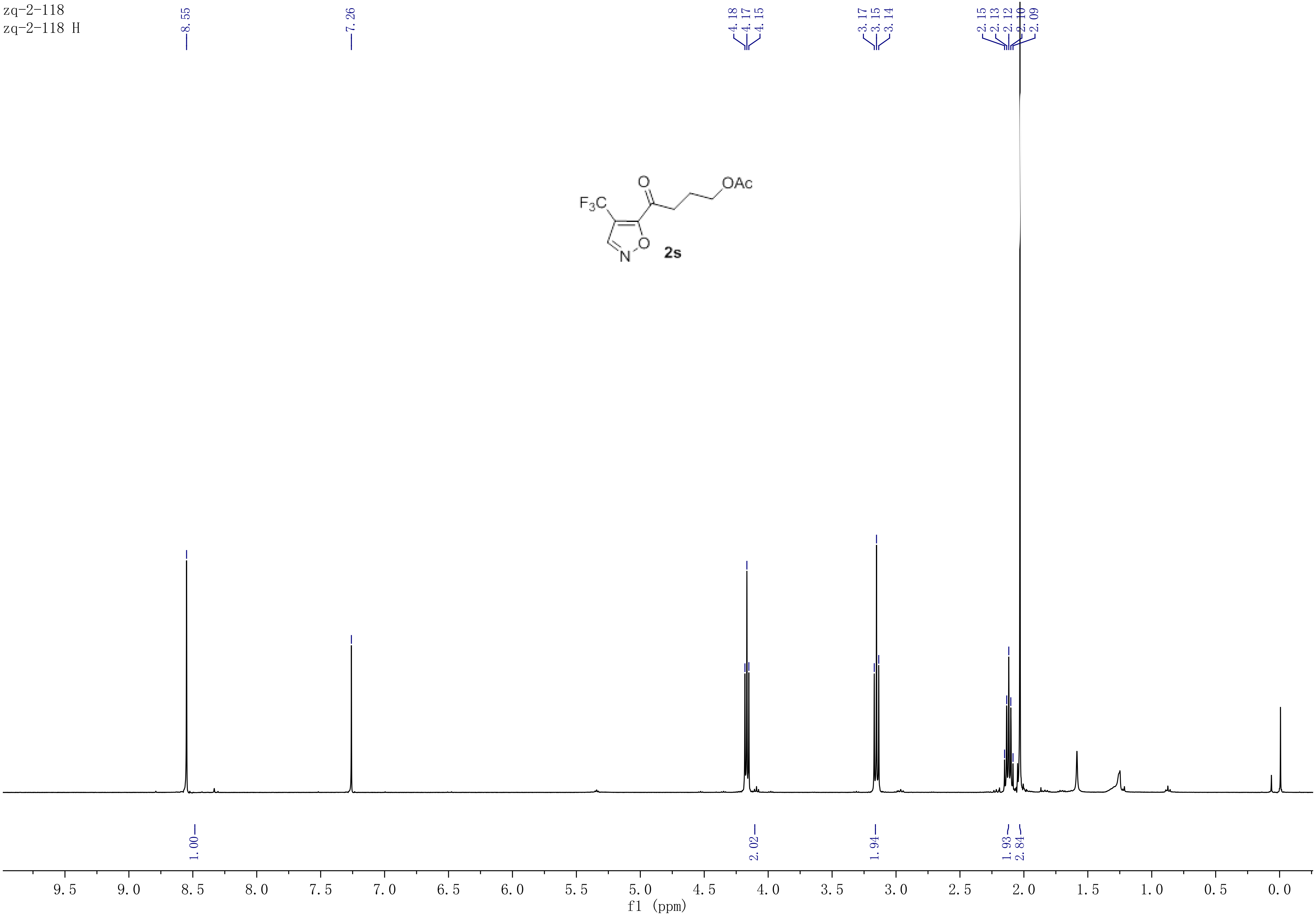



zq-2-117
zl-2-36 H
8.54
7.85
7.85
7.84
7.83
7.74
7.73
7.73
7.72
7.27
3.85
3.83
3.81
3.16
3.14
3.12
2.20
2.18
2.17
2.15
2.13
F_3C
O
N
O
O
N
O
2r
1.00
2.01
2.02
2.07
2.06
2.31
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

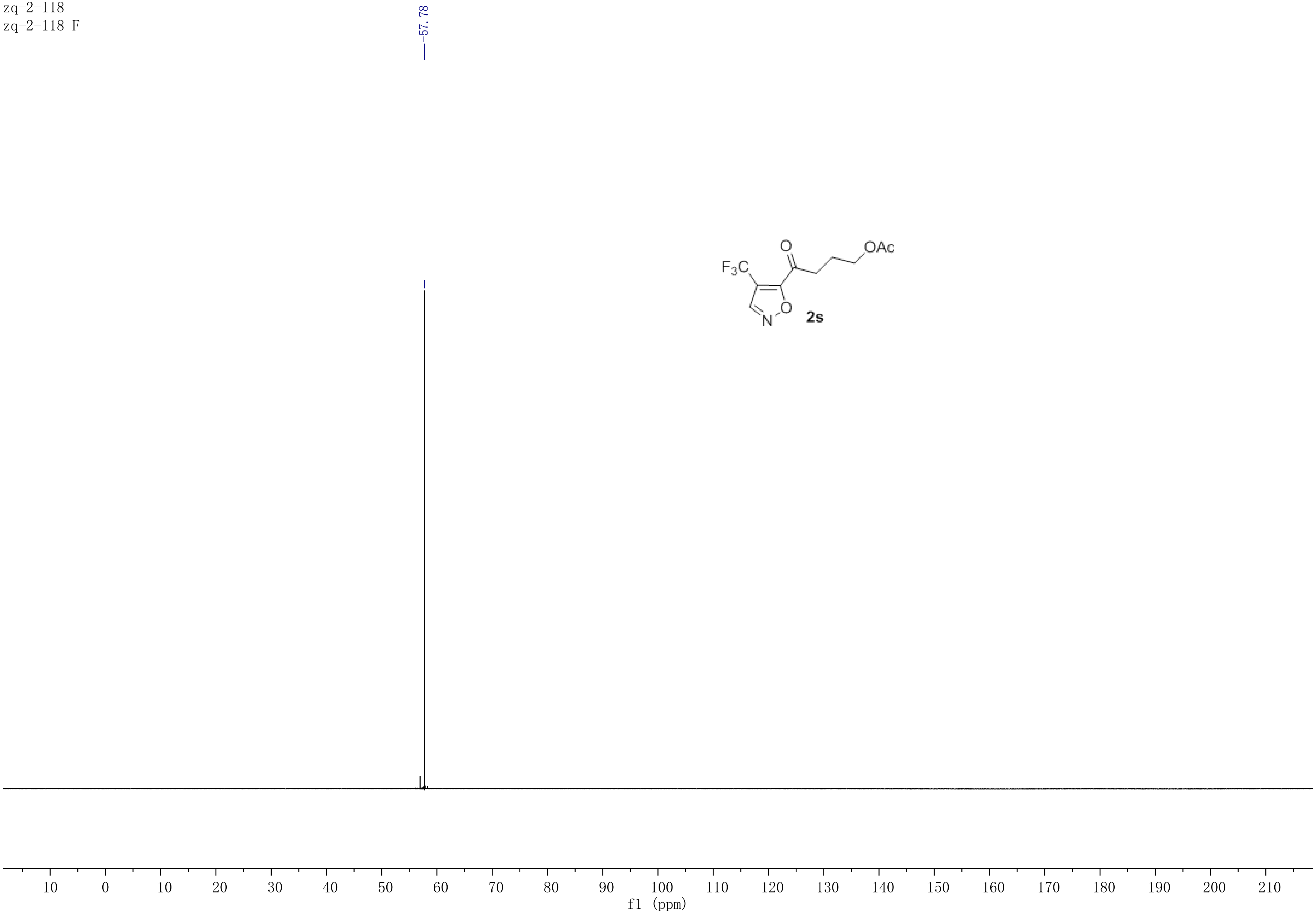

zq-2-117
zl-2-36 F
-57.80
F_3C
2r
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

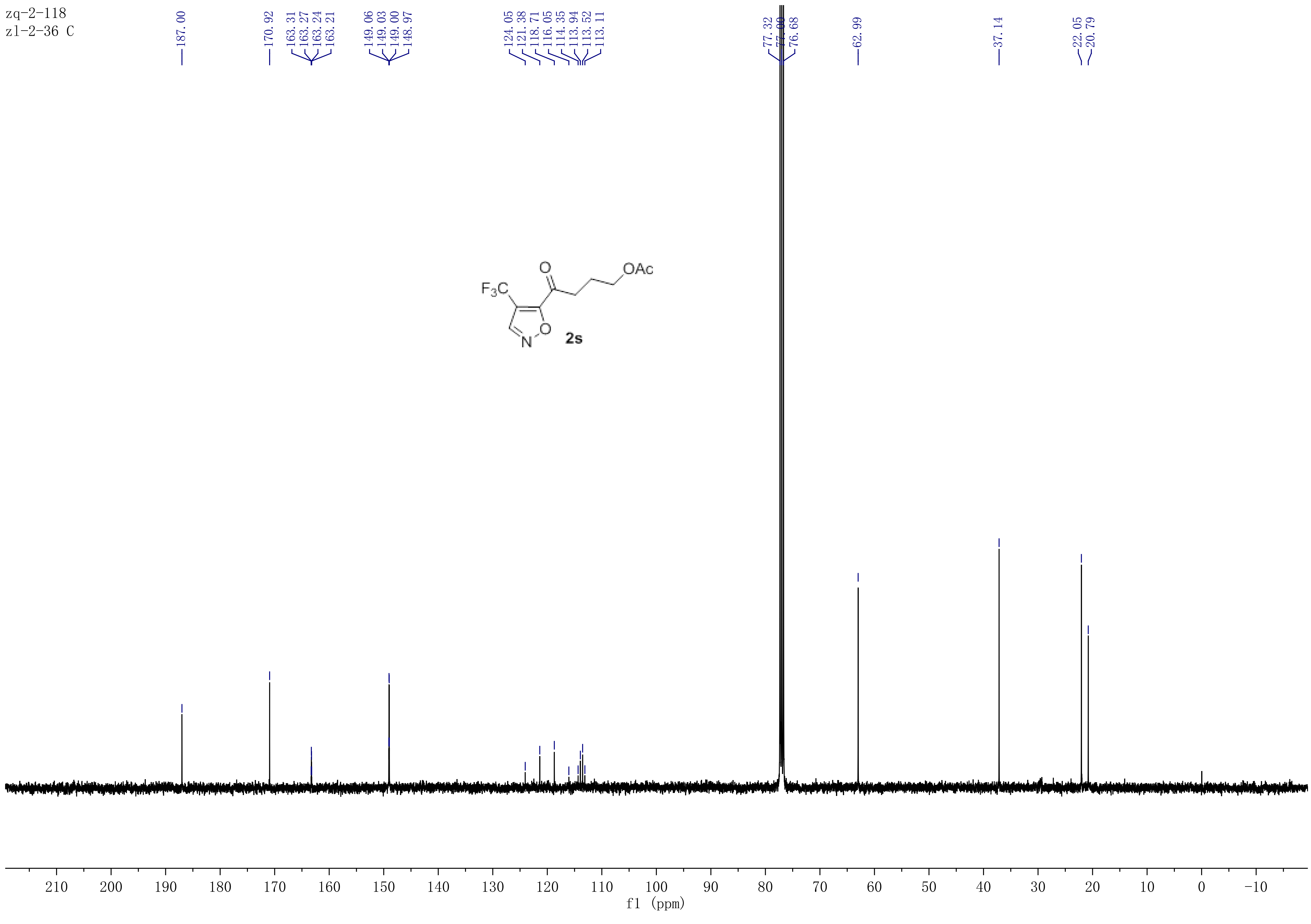

zq-2-117
zl-2-36 C
186.68
168.41
163.29
163.26
163.23
163.20
148.99
148.96
148.93
148.90
134.05
131.93
124.05
123.33
121.36
118.70
116.03
114.24
113.83
113.42
113.00
77.32
77.00
76.68
37.62
36.73
21.78
F3C
O
N
O
N
O
O
2r
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

zq-2-118
zq-2-118 H

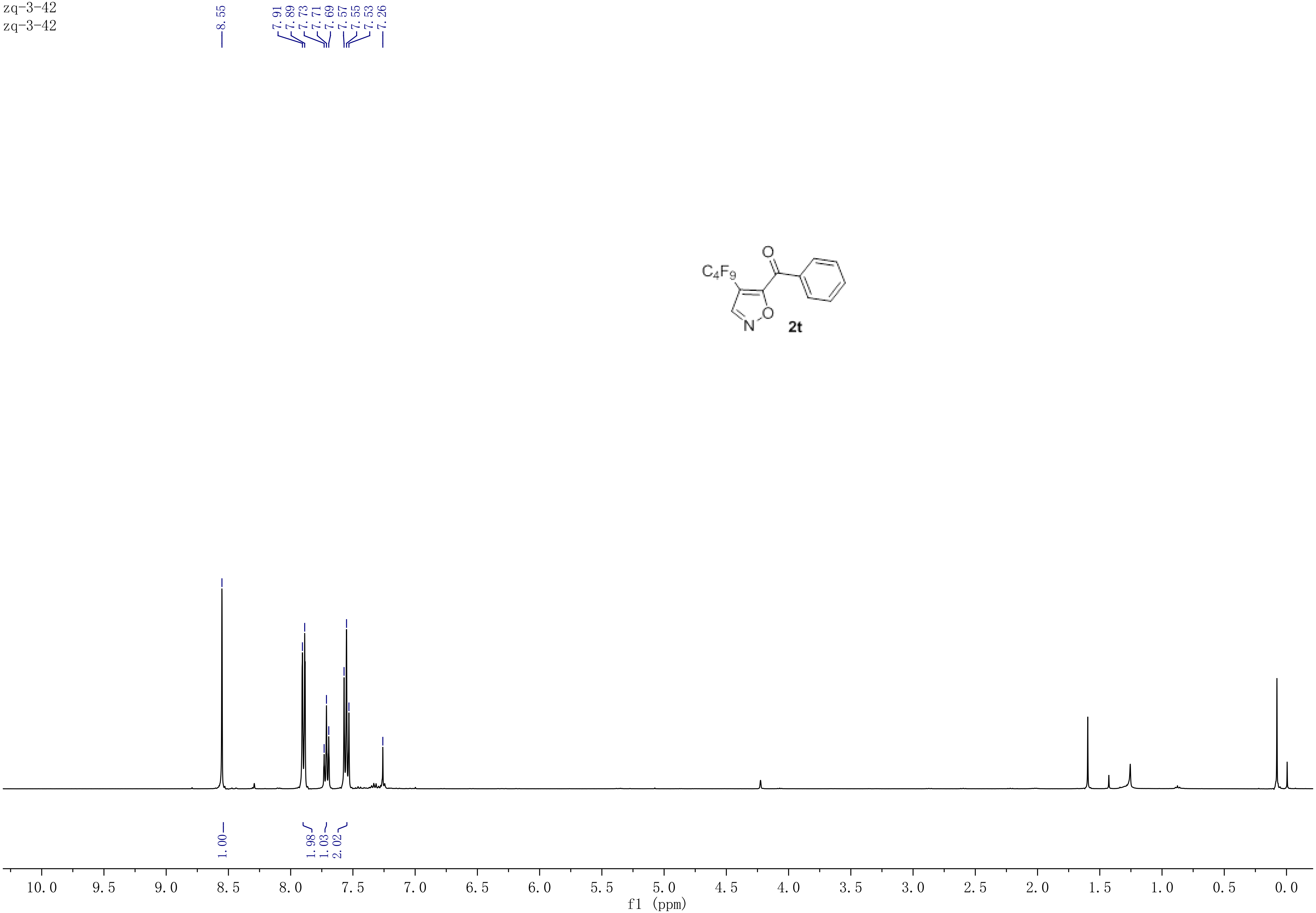


zq-2-118
zq-2-118 F

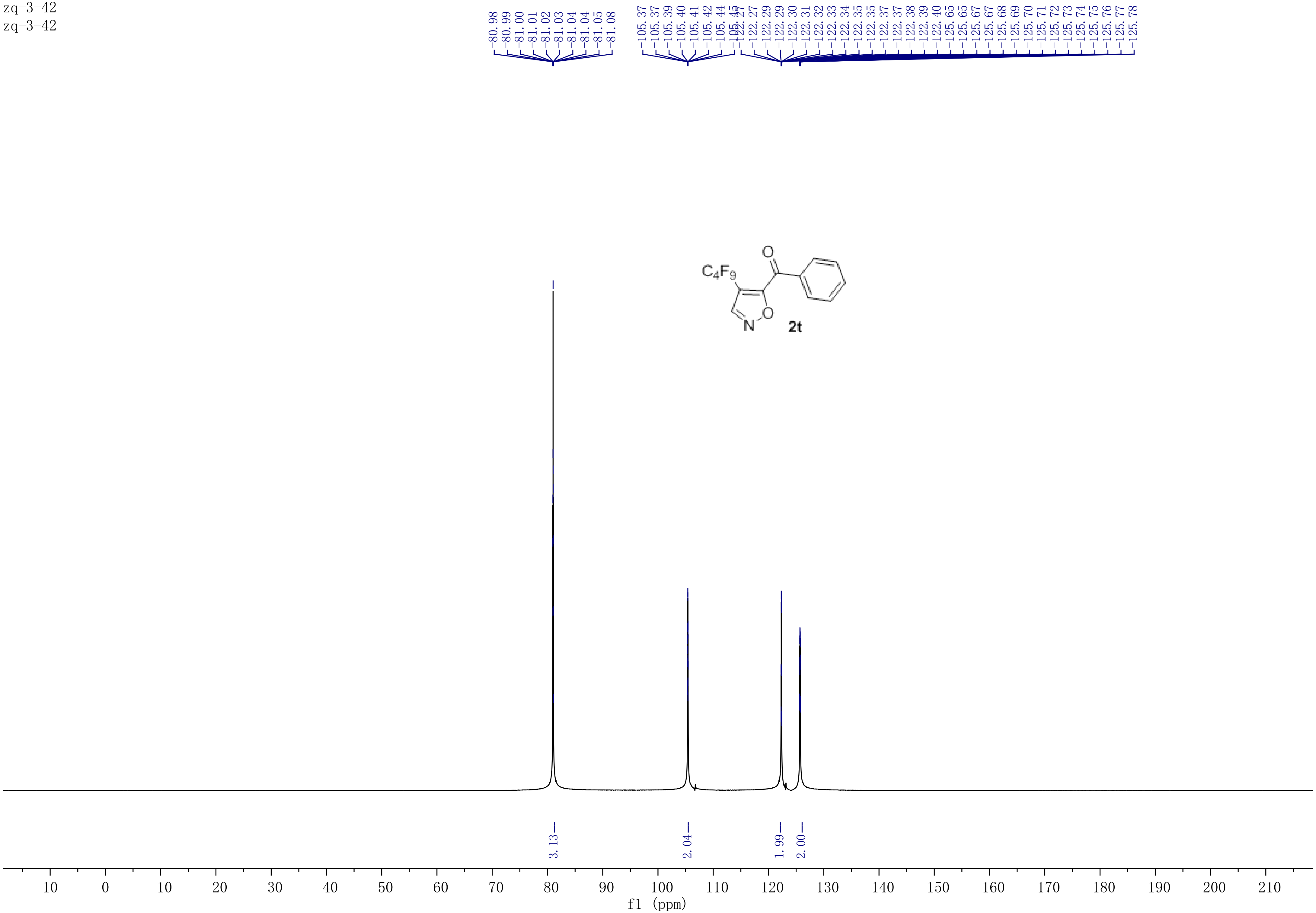



zq-2-118
zl-2-36 C
187.00
170.92
163.31
163.27
163.24
163.21
149.06
149.03
149.00
148.97
124.05
121.38
118.71
116.05
114.35
113.94
113.52
113.11
77.32
77.00
76.68
62.99
37.14
22.05
20.79
F3C
O
OAc
N
O
2s
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

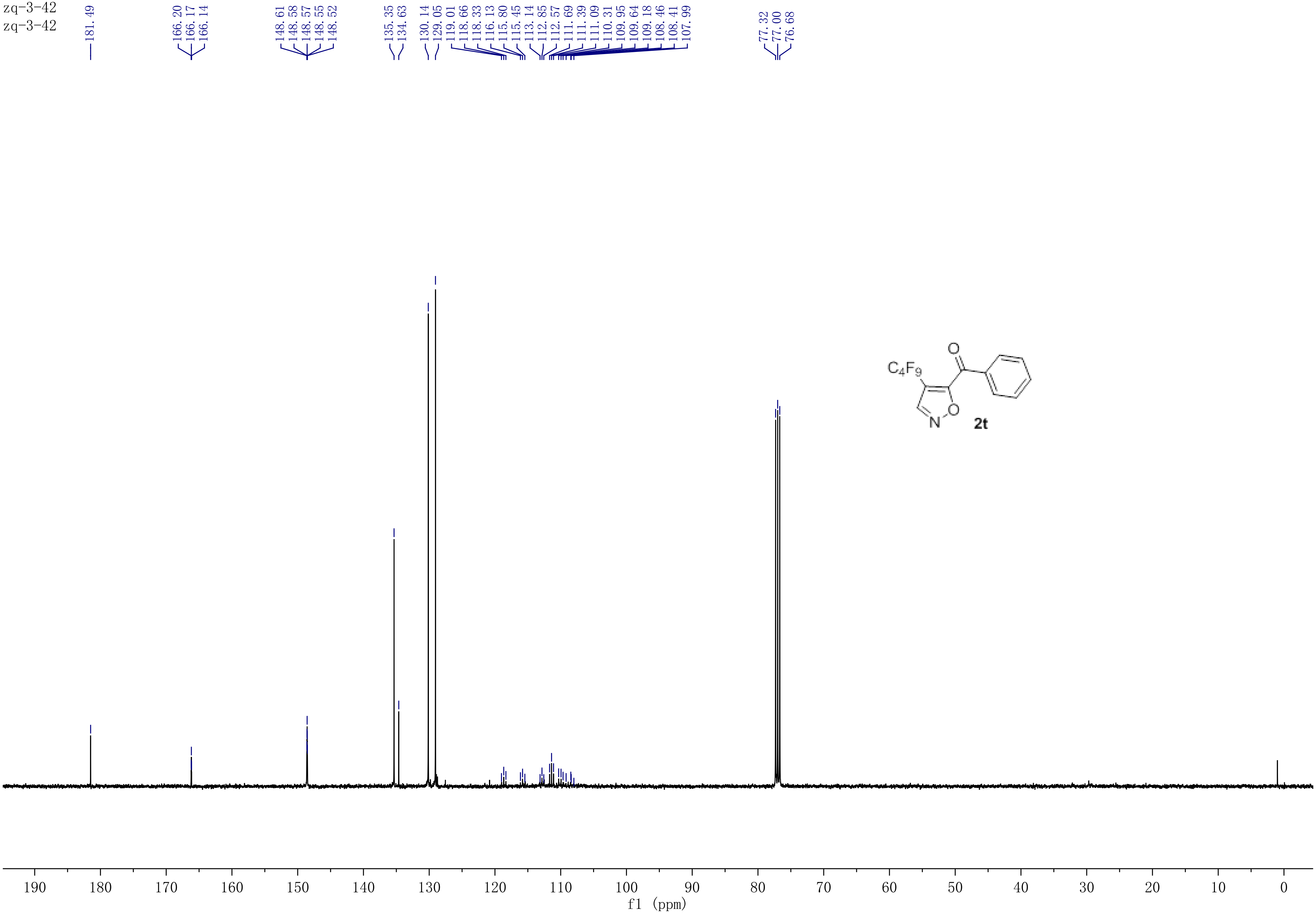
zq-3-42
zq-3-42


8.55
7.91
7.89
7.73
7.71
7.69
7.57
7.55
7.53
7.26
C4F9
O
N
O
2t
1.00
1.98
1.03
2.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

zq-3-42
zq-3-42

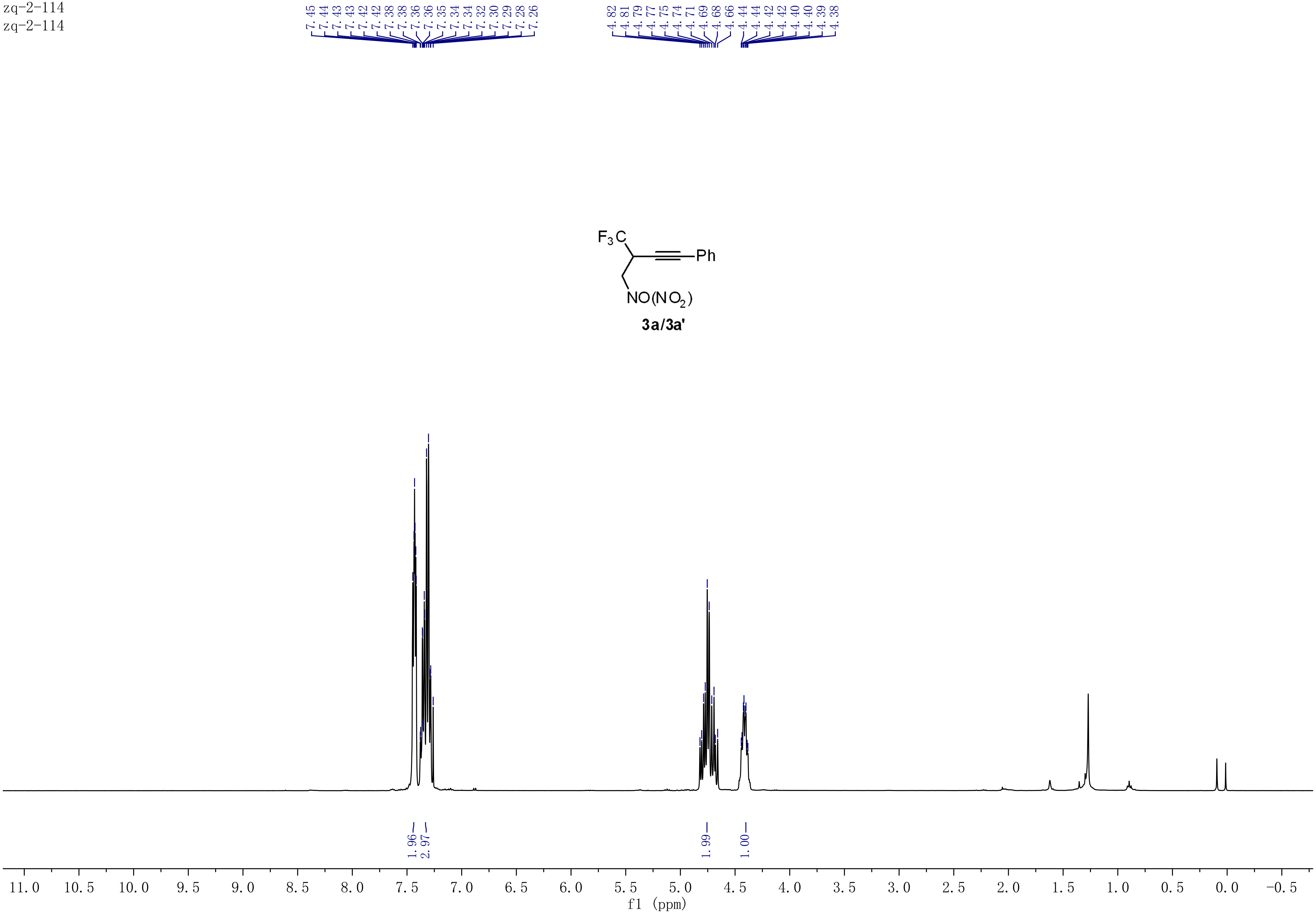

-80.98
-80.99
-81.00
-81.01
-81.02
-81.03
-81.04
-81.04
-81.05
-81.08
-105.37
-105.37
-105.39
-105.40
-105.41
-105.42
-105.44
-105.45
-122.27
-122.27
-122.29
-122.29
-122.30
-122.31
-122.32
-122.33
-122.34
-122.35
-122.35
-122.37
-122.37
-122.38
-122.39
-122.40
-125.65
-125.65
-125.67
-125.67
-125.68
-125.69
-125.70
-125.71
-125.72
-125.73
-125.74
-125.75
-125.76
-125.77
-125.78
C4F9
O
N
O
2t
3.13
2.04
1.99
2.00
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

zq-3-42
zq-3-42

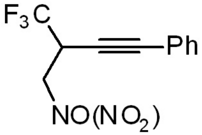


2t

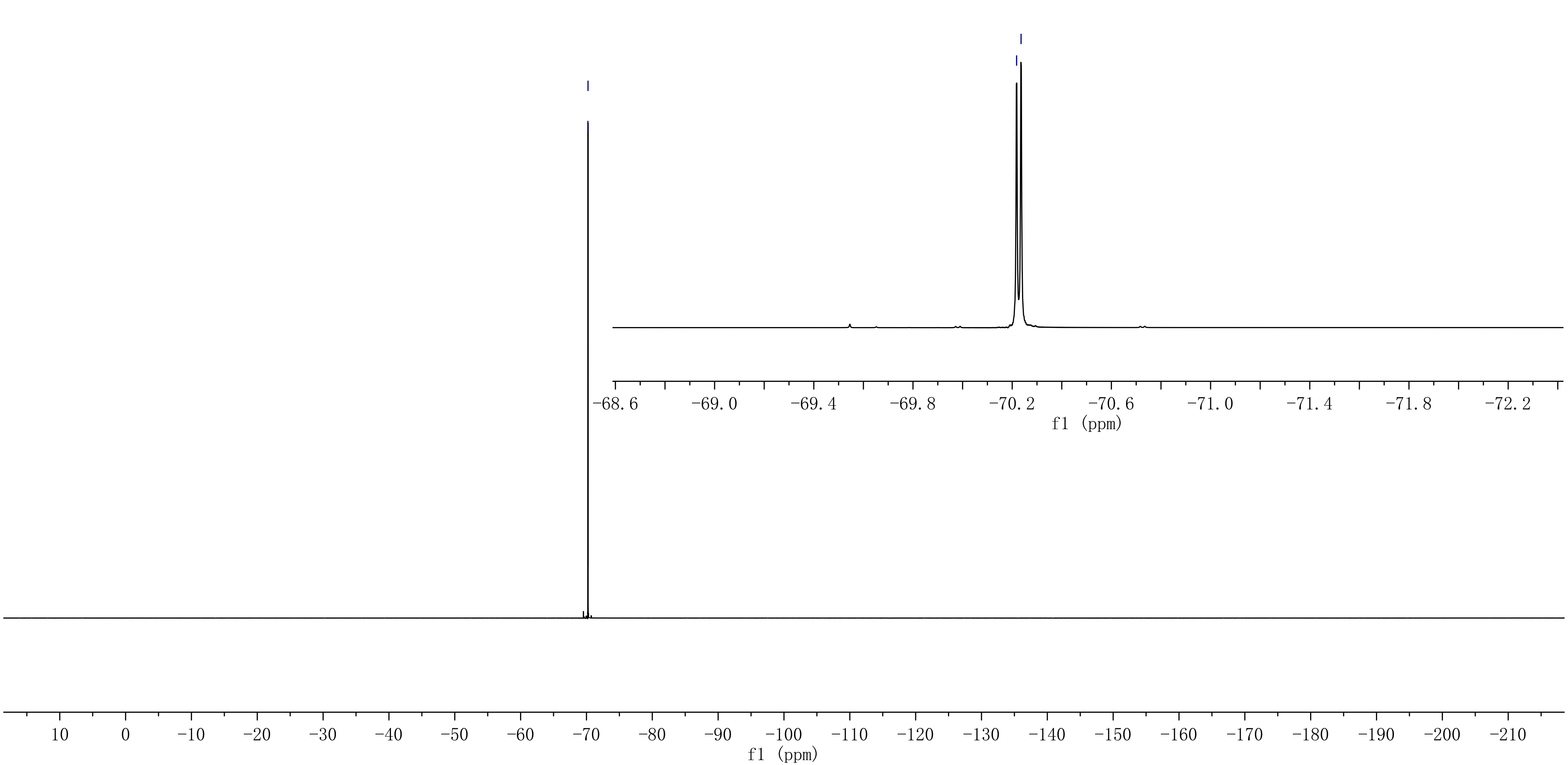
zq-2-114
zq-2-114

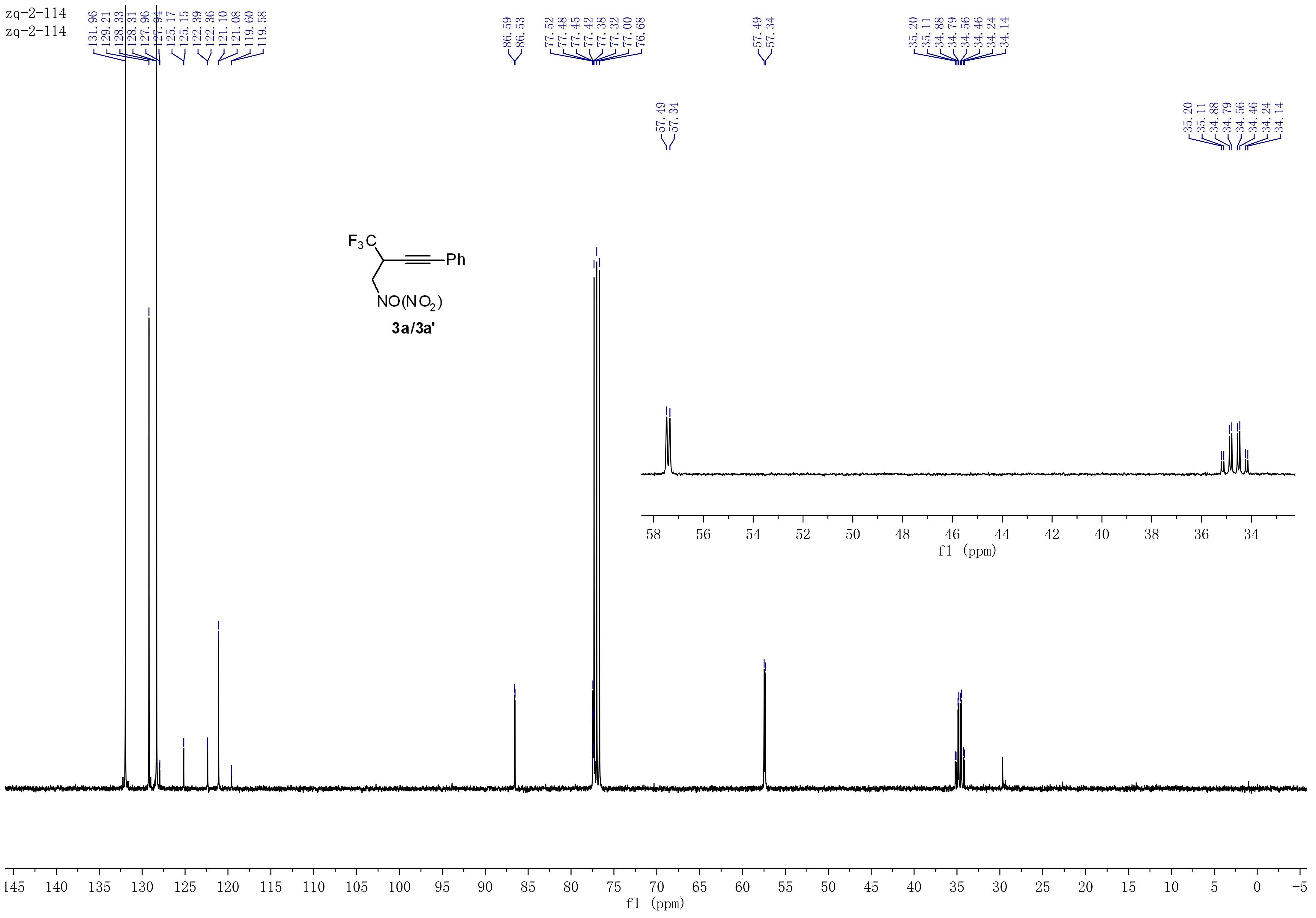


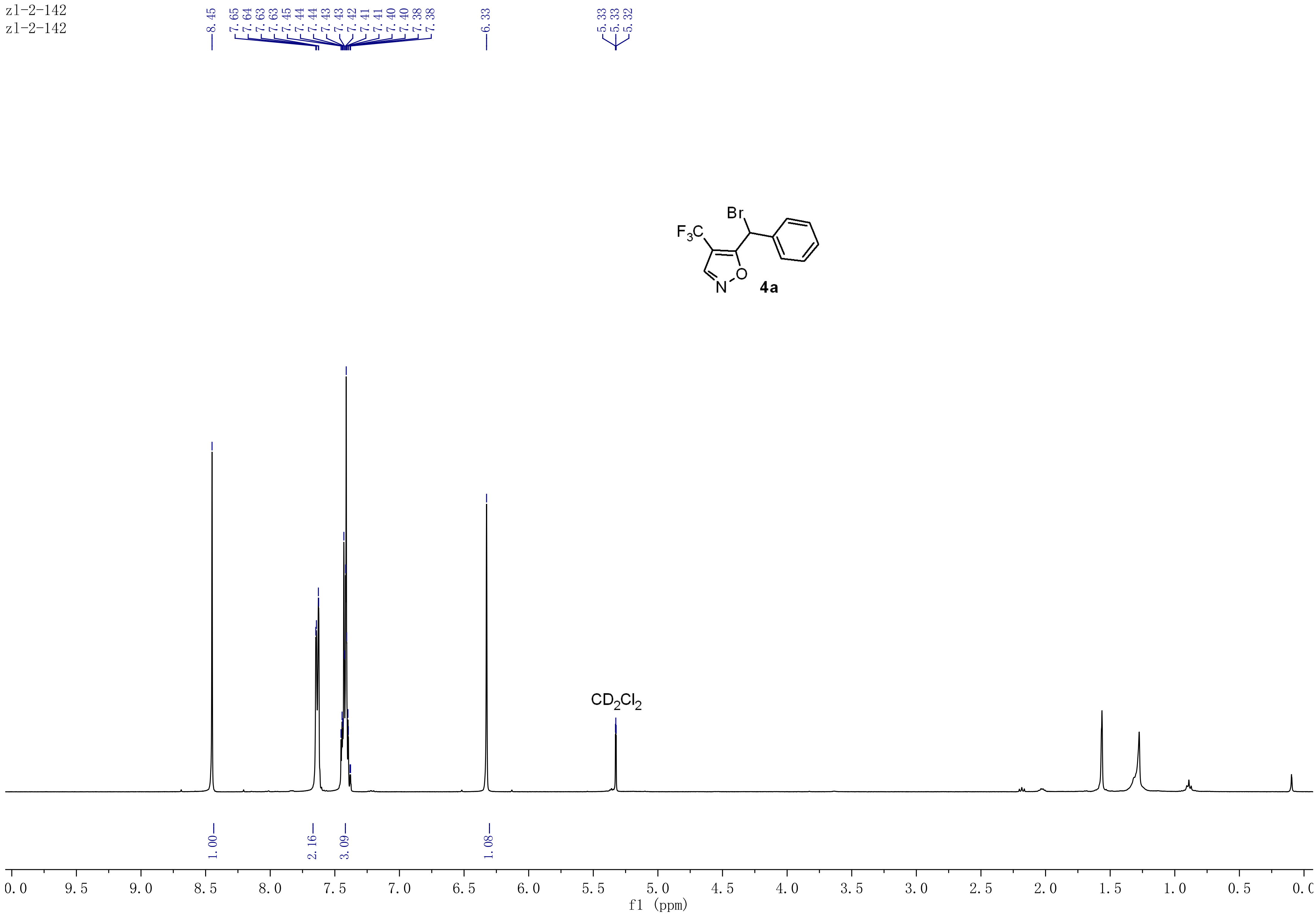
zq-2-114
zq-2-114



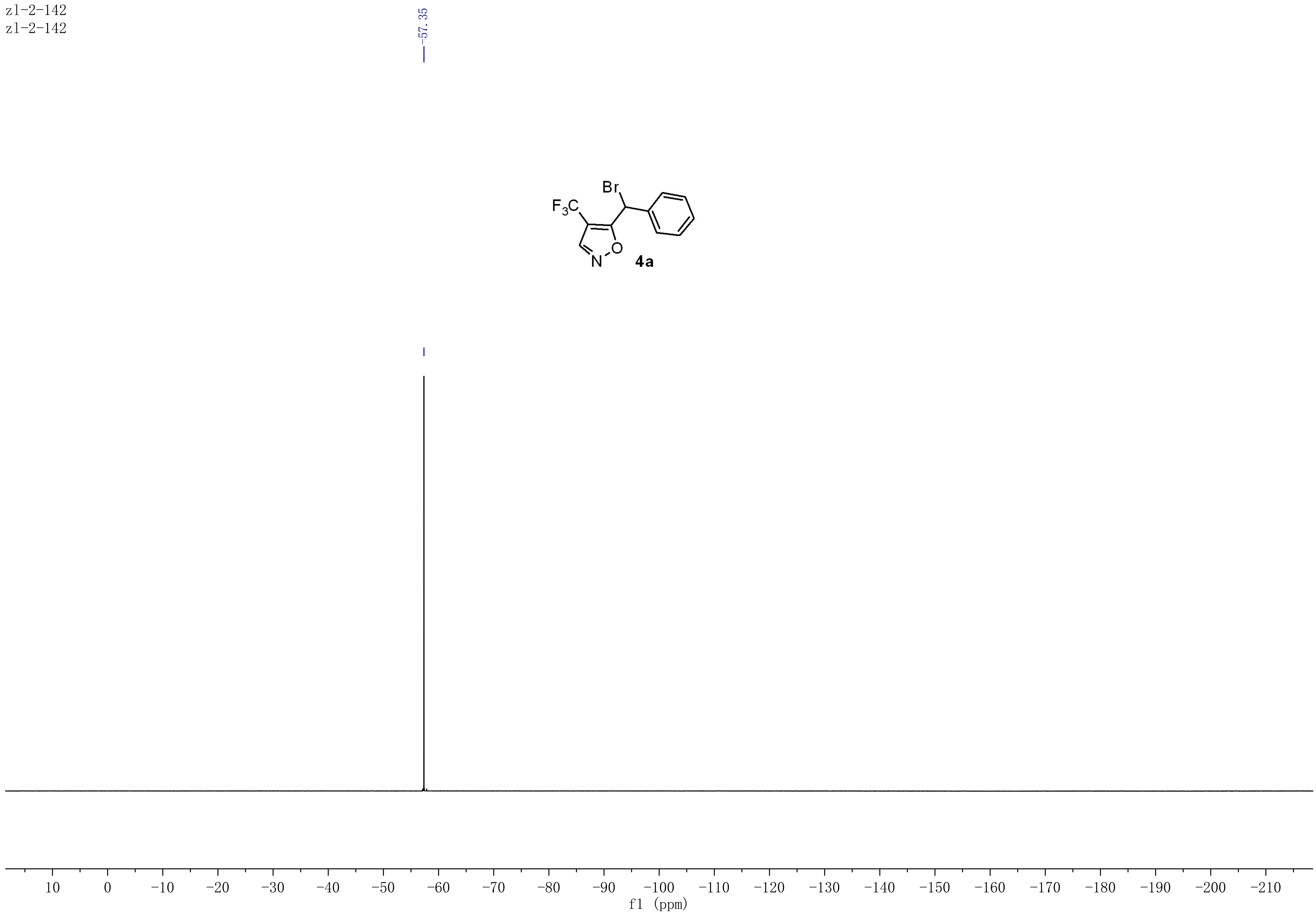
3a/3a'

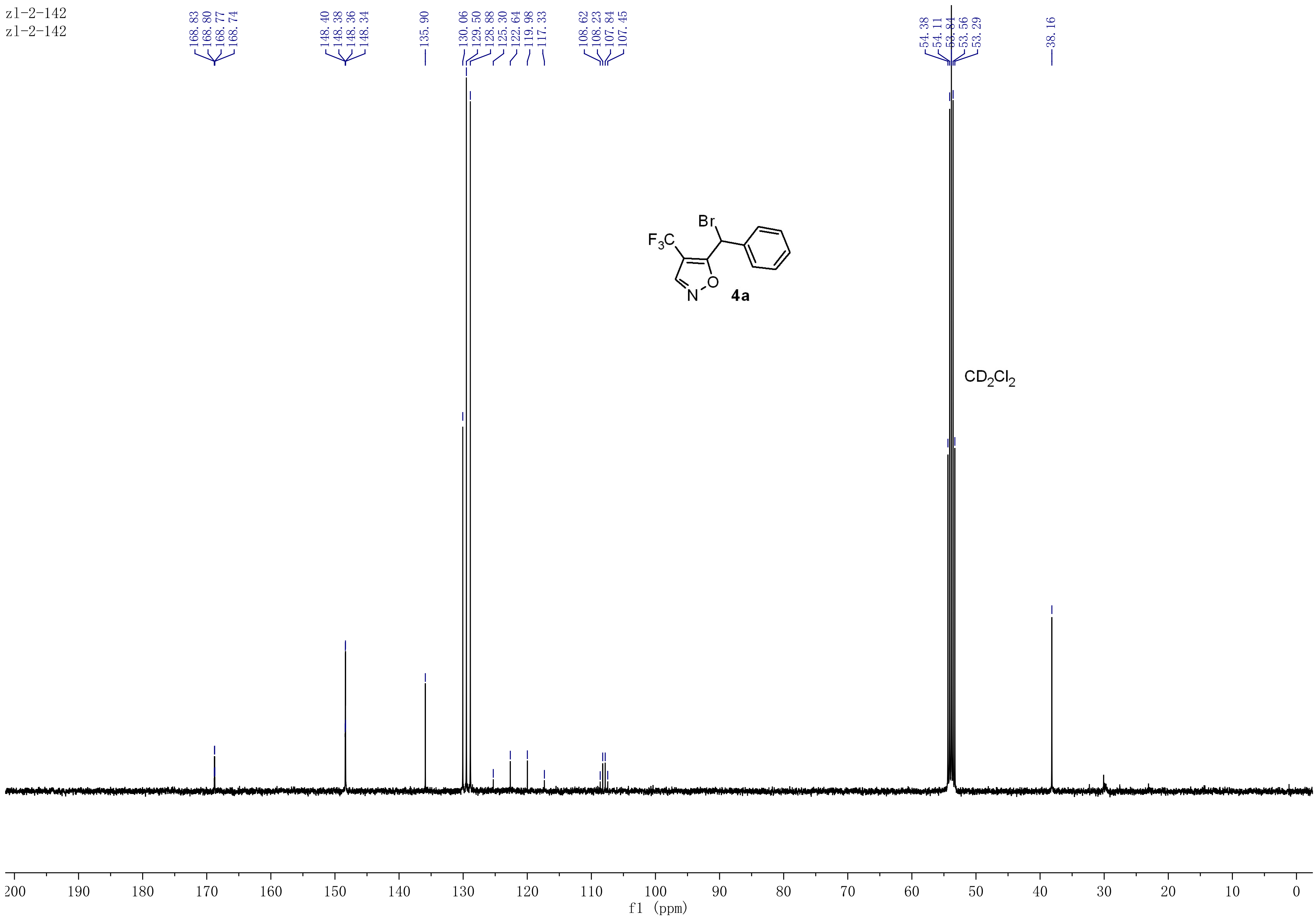



zq-2-114
zq-2-114
131.96
129.21
128.33
128.31
127.96
127.94
125.17
125.15
122.39
122.36
121.10
121.08
119.60
119.58
86.59
86.53
77.52
77.48
77.45
77.42
77.38
77.32
77.00
76.68
57.49
57.34
35.20
35.11
34.88
34.79
34.56
34.46
34.24
34.14
F3C
Ph
NO(NO2)
3a/3a'
f1 (ppm)
f1 (ppm)

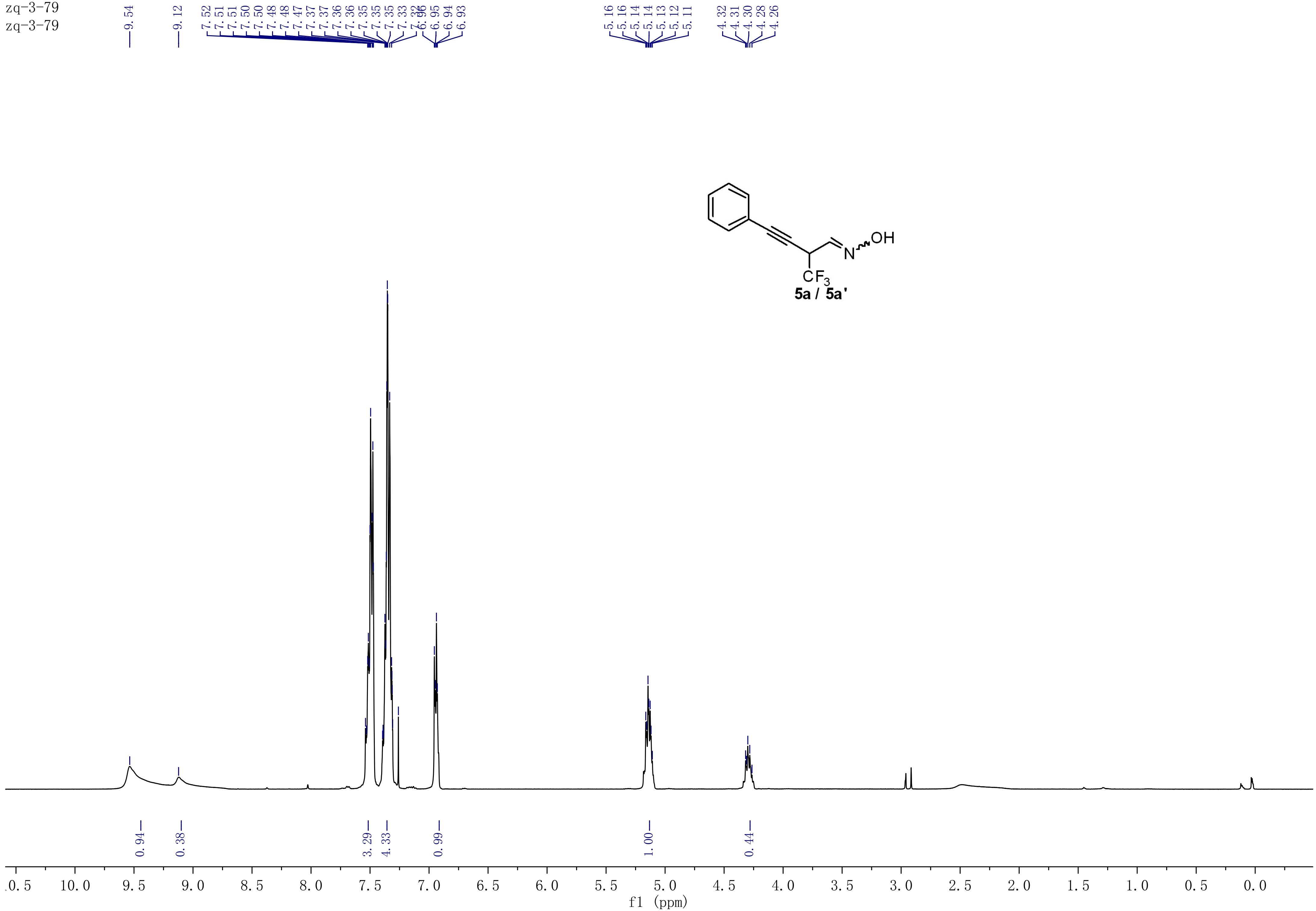


zl-2-142
zl-2-142
8.45
7.65
7.64
7.63
7.63
7.45
7.44
7.44
7.43
7.43
7.42
7.41
7.41
7.40
7.40
7.38
7.38
6.33
5.33
5.33
5.32
Br
F3C
O
N
4a
CD2Cl2
1.00
2.16
3.09
1.08
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


zl-2-142
zl-2-142
-57.35
Br
F3C
N
O
4a
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

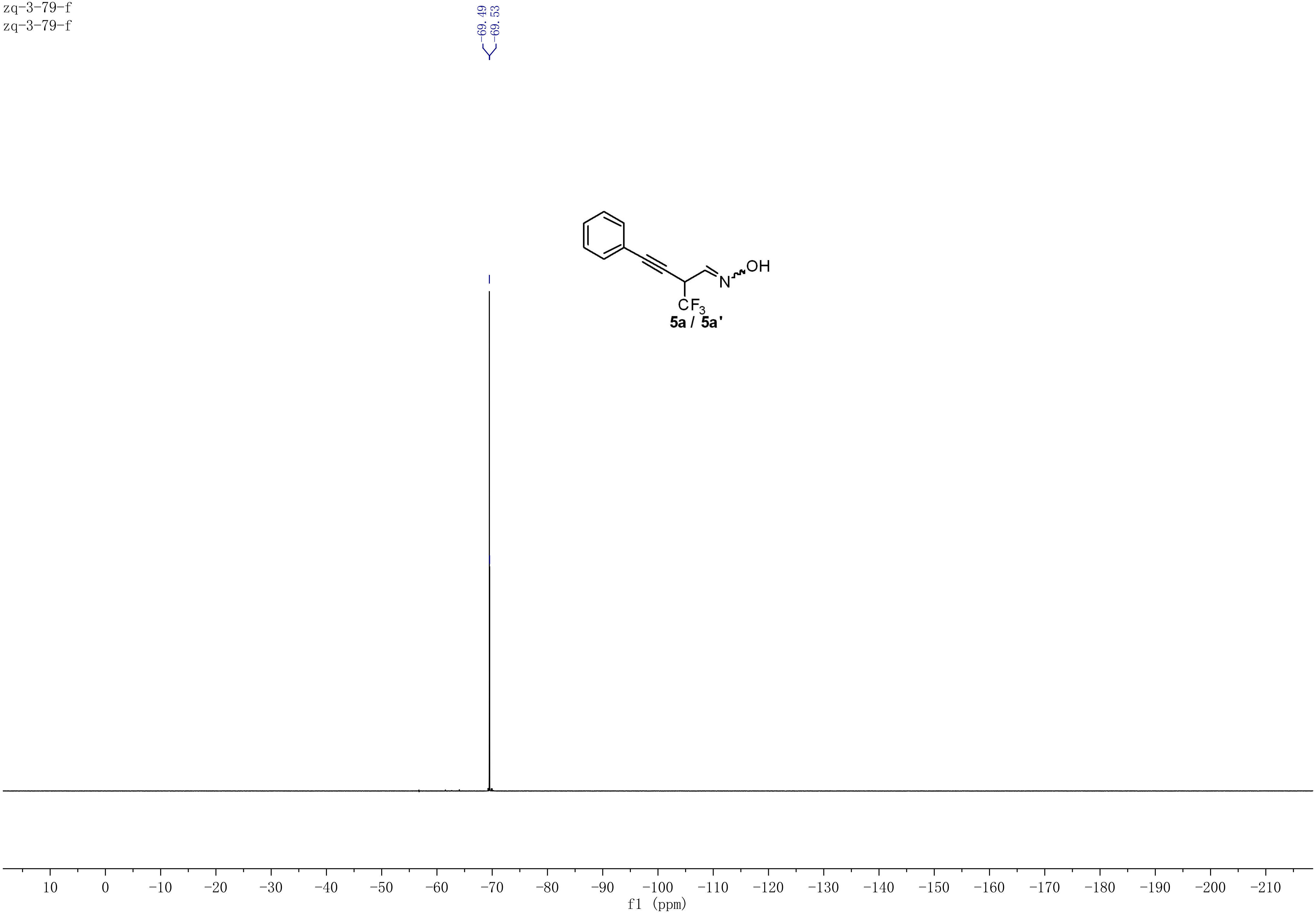


zl-2-142
zl-2-142
168.83
168.80
168.77
168.74
148.40
148.38
148.36
148.34
135.90
130.06
129.50
128.88
125.30
122.64
119.98
117.33
108.62
108.23
107.84
107.45
54.38
54.11
53.84
53.56
53.29
38.16
Br
F3C
N
O
4a
CD2Cl2
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

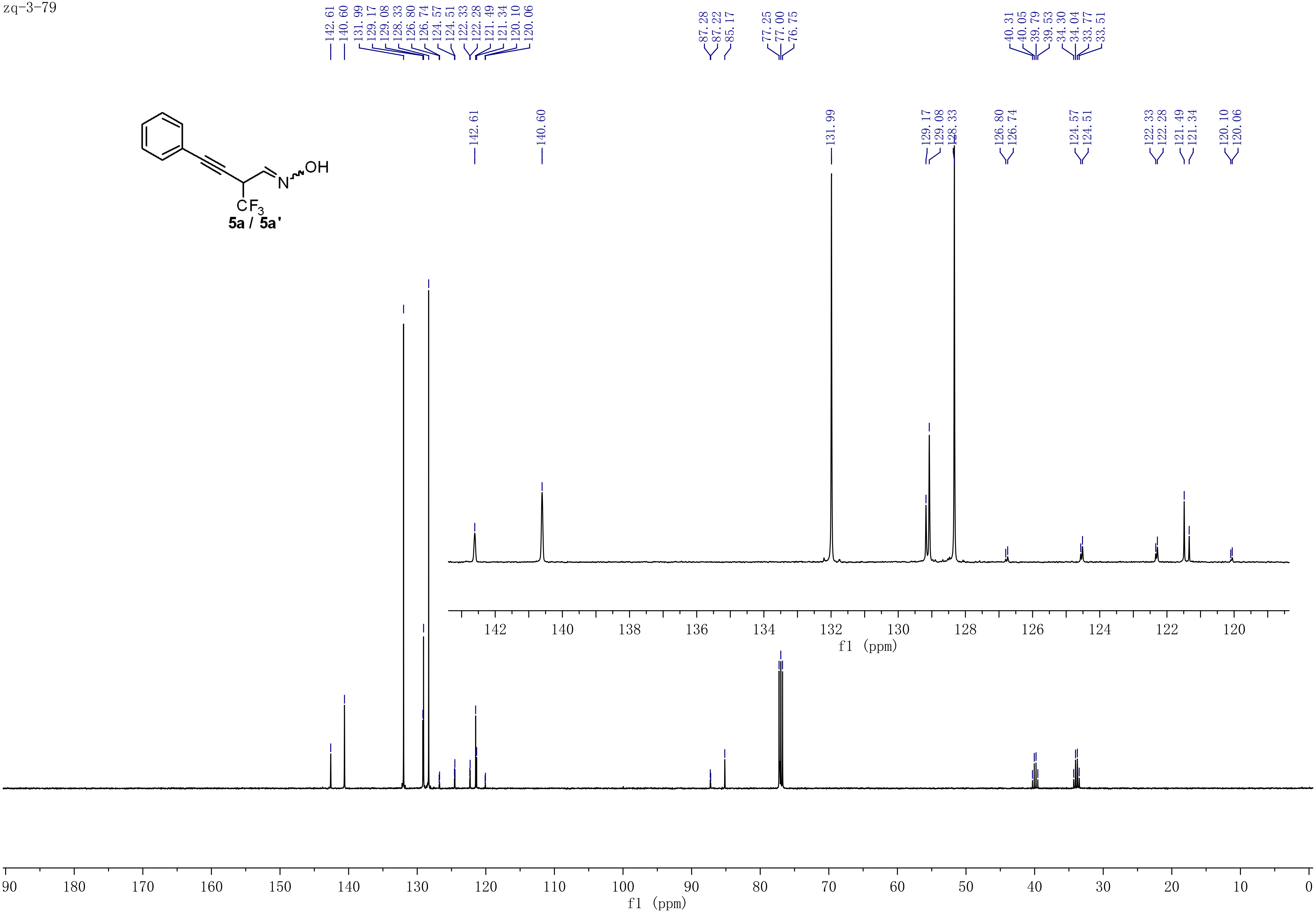


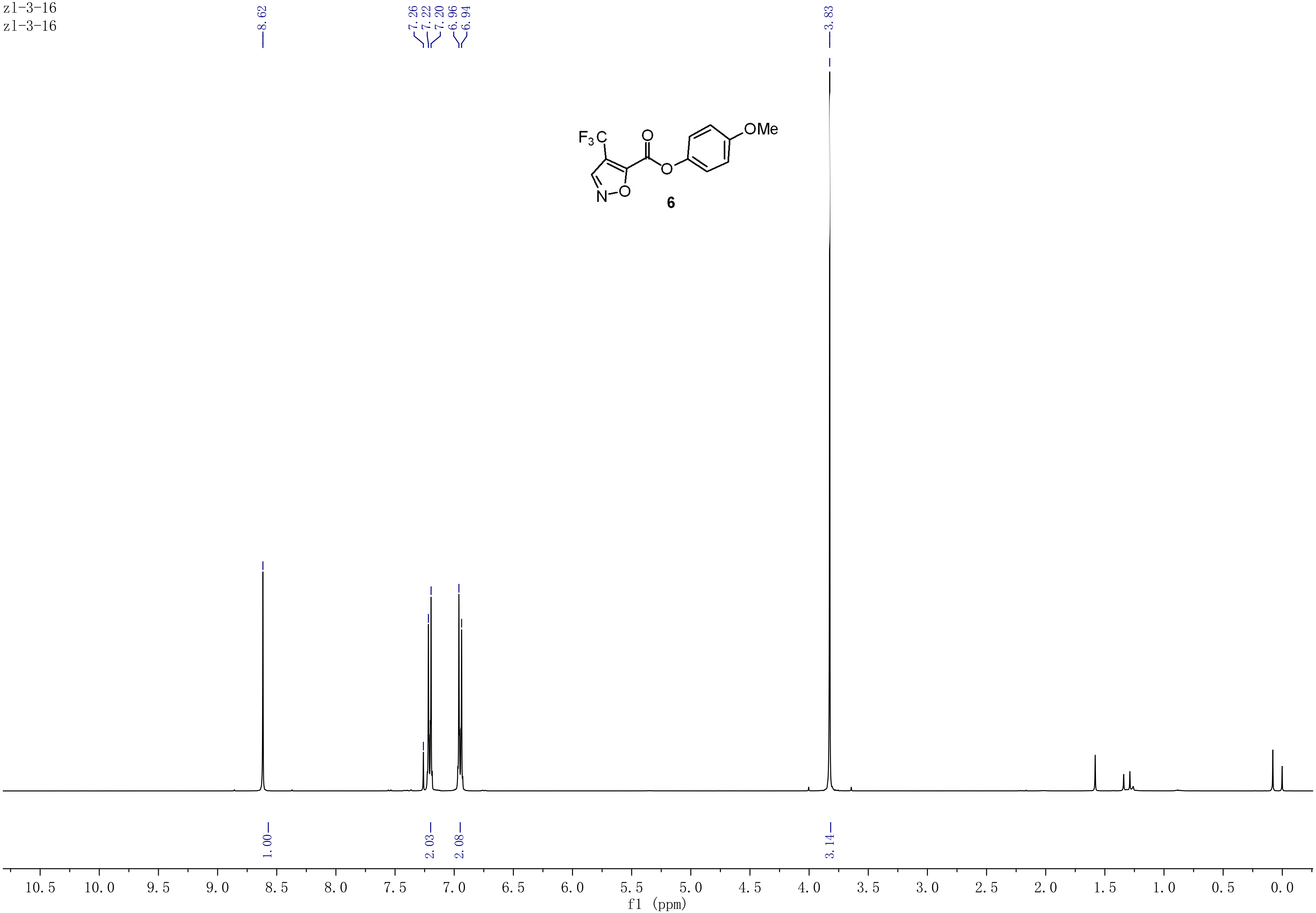
zq-3-79
zq-3-79
9.54
9.12
7.52
7.51
7.51
7.50
7.50
7.48
7.48
7.47
7.37
7.37
7.36
7.36
7.35
7.35
7.35
7.33
6.95
6.94
6.93
5.16
5.16
5.14
5.14
5.13
5.12
5.11
4.32
4.31
4.30
4.28
4.26
OH
N
CF3
5a / 5a'
0.94
0.38
3.29
4.33
0.99
1.00
0.44
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

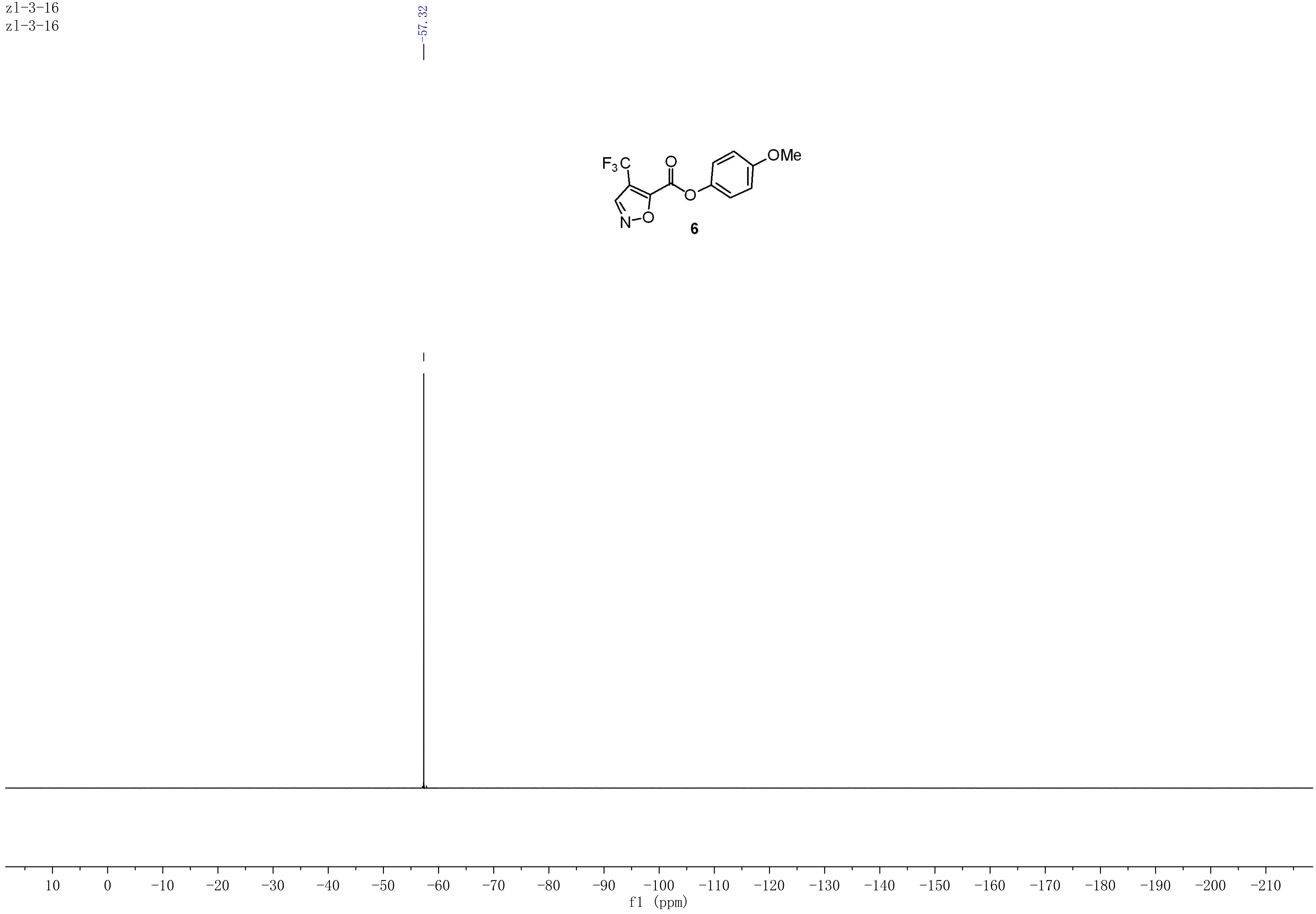
zq-3-79-f
zq-3-79-f

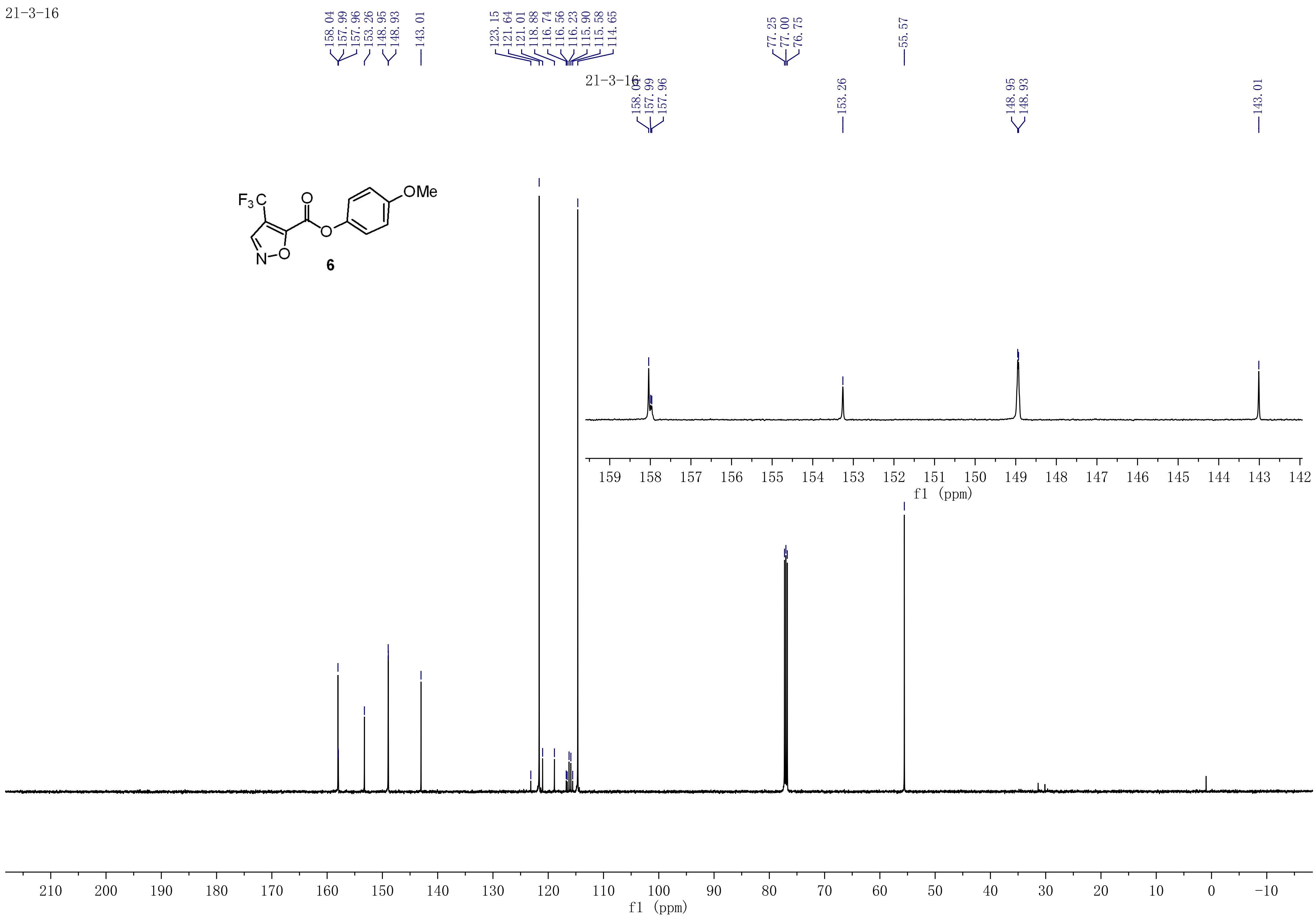


zq-3-79

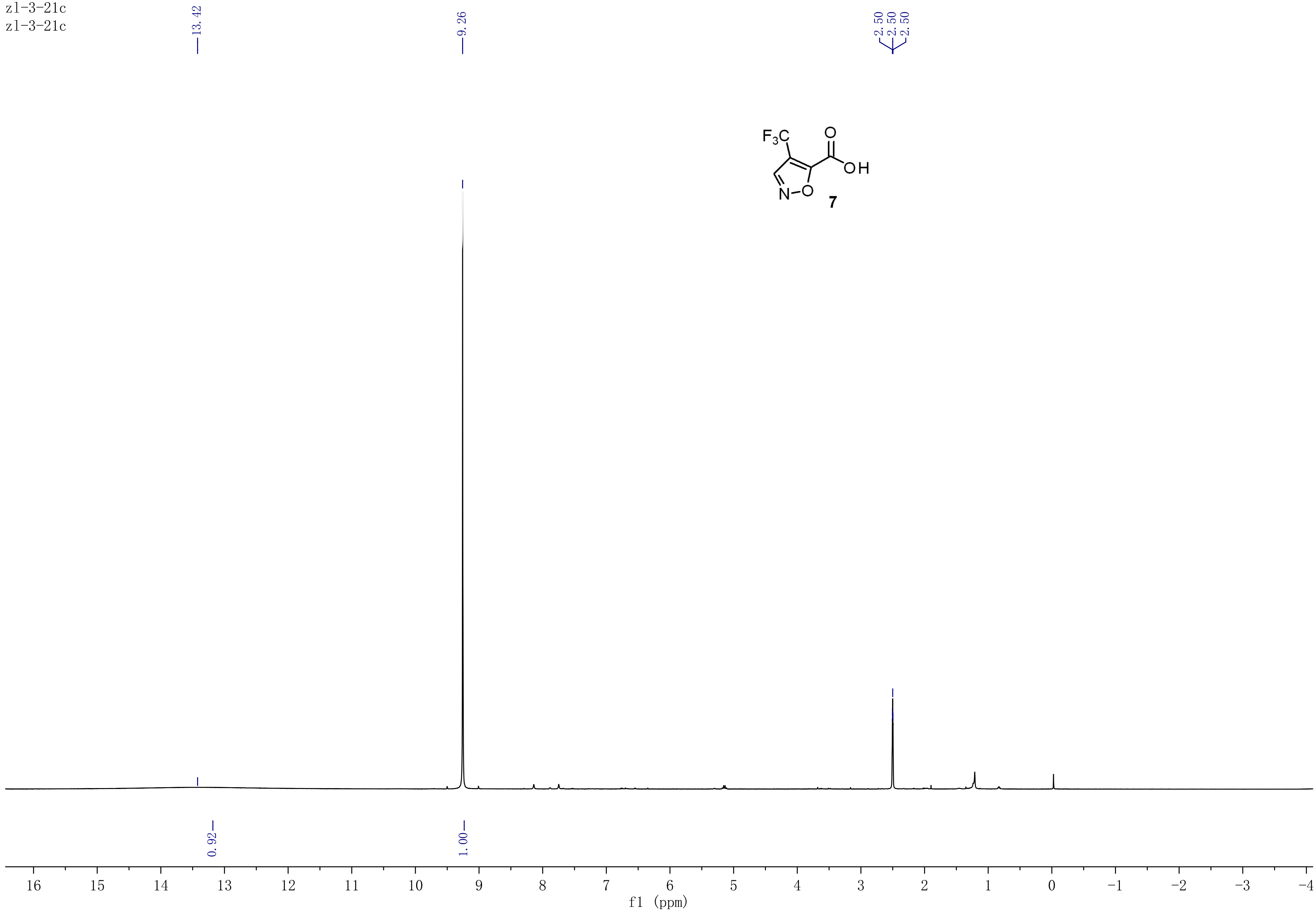

142.61
140.60
131.99
129.17
129.08
128.33
126.80
126.74
124.57
124.51
122.33
122.28
121.49
121.34
120.10
120.06
87.28
87.22
85.17
77.25
77.00
76.75
40.31
40.05
39.79
39.53
34.30
34.04
33.77
33.51
OH
N
CF3
5a / 5a'
f1 (ppm)

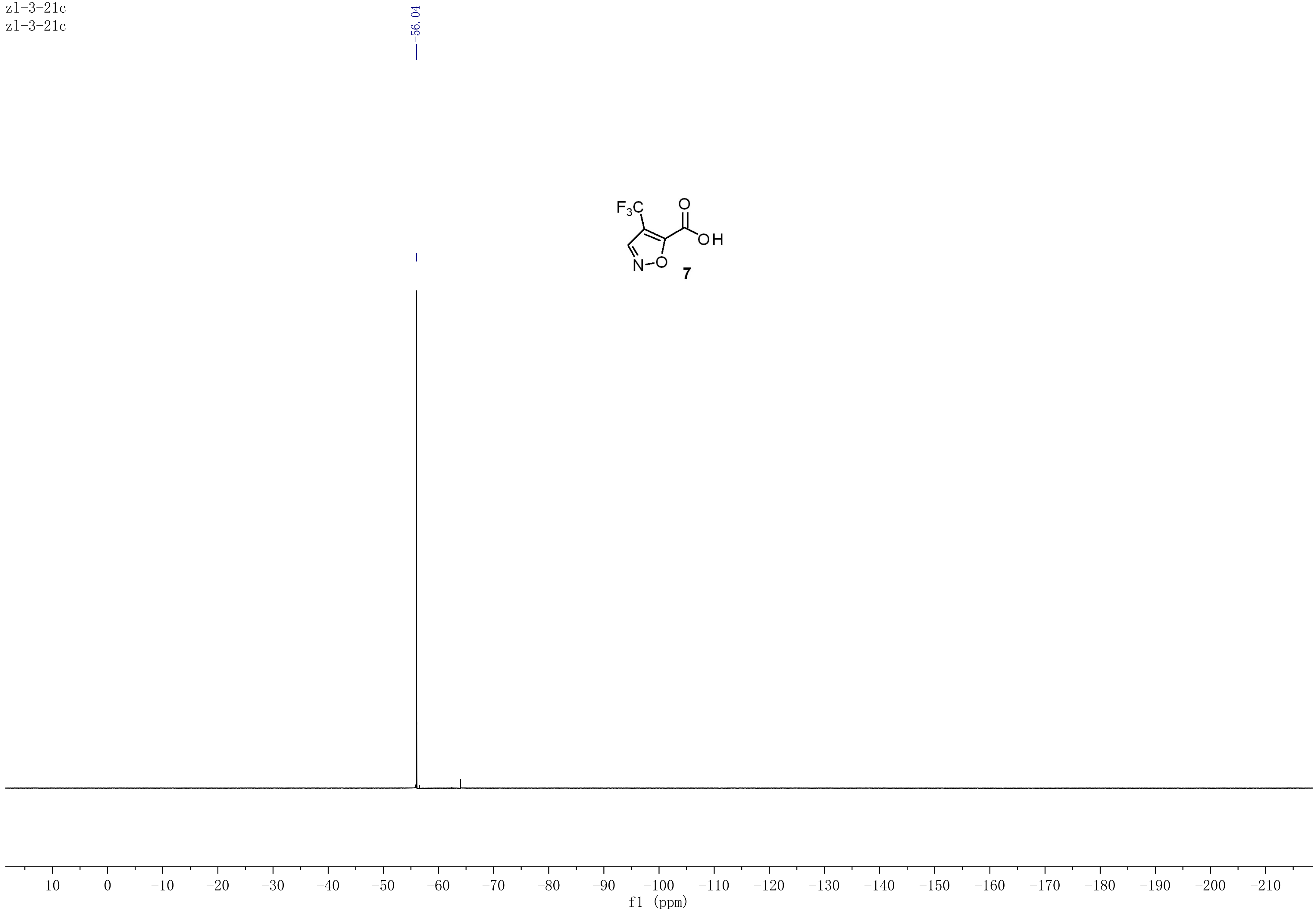

zl-3-16
zl-3-16
8.62
7.26
7.22
7.20
6.96
6.94
3.83
F_3C
O
OMe
N
O
6
1.00
2.03
2.08
3.14
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

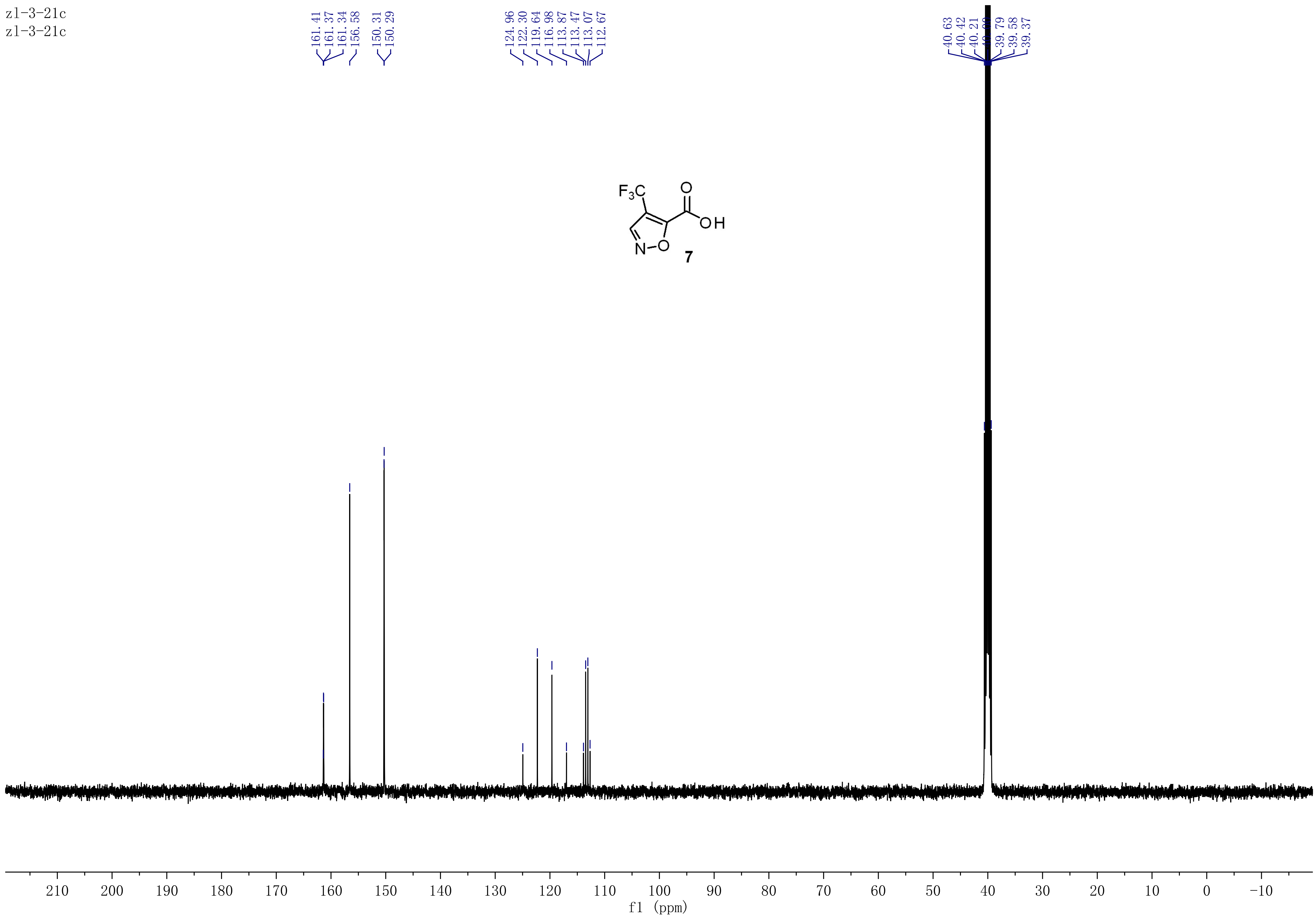

zl-3-16
zl-3-16
-57.32
F3C
O
OMe
N-O
O
6
10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190 −200 −210
f1 (ppm)

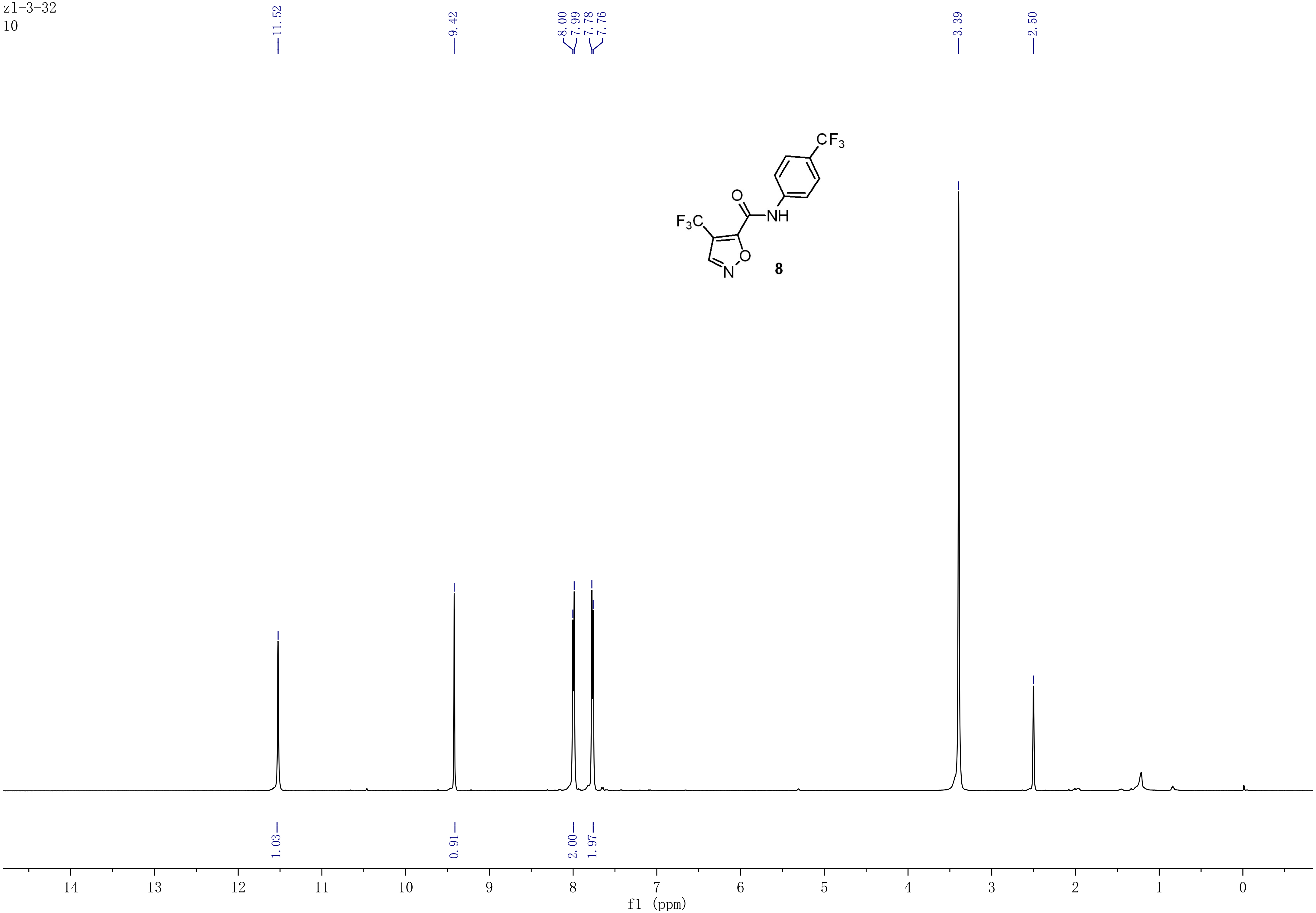


21-3-16
158.04
157.99
157.96
153.26
148.95
148.93
143.01
123.15
121.64
121.01
118.88
116.74
116.56
116.23
115.90
115.58
114.65
77.25
77.00
76.75
55.57
F_3C
OMe
N
O
6
f1 (ppm)

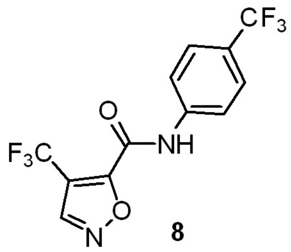

zl-3-21c
zl-3-21c
13.42
9.26
2.50
2.50
2.50
F3C
O
OH
N-O
7
0.92
1.00
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
f1 (ppm)


zl-3-21c
zl-3-21c
-56.04
F_3C
O
OH
N-O
7
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

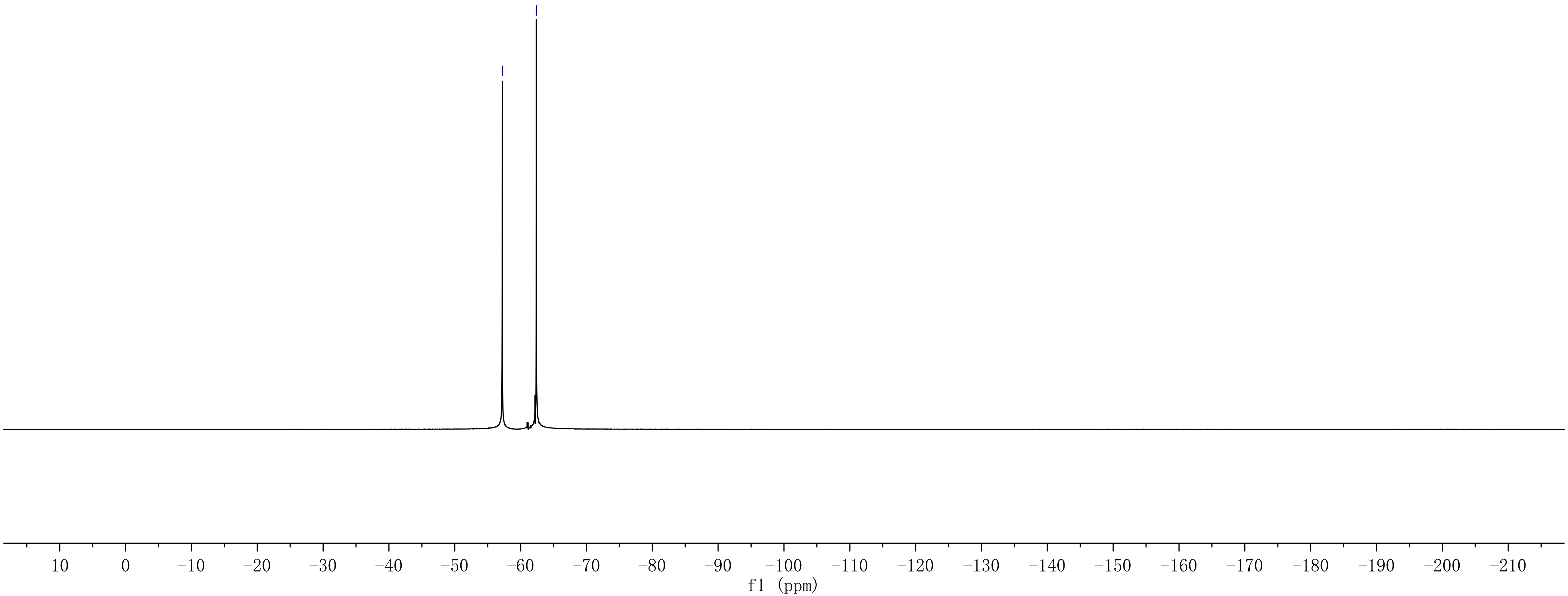

zl-3-21c
zl-3-21c
161.41
161.37
161.34
156.58
150.31
150.29
124.96
122.30
119.64
116.98
113.87
113.47
113.07
112.67
40.63
40.42
40.21
39.79
39.58
39.37
F3C
O
OH
N
O
7
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

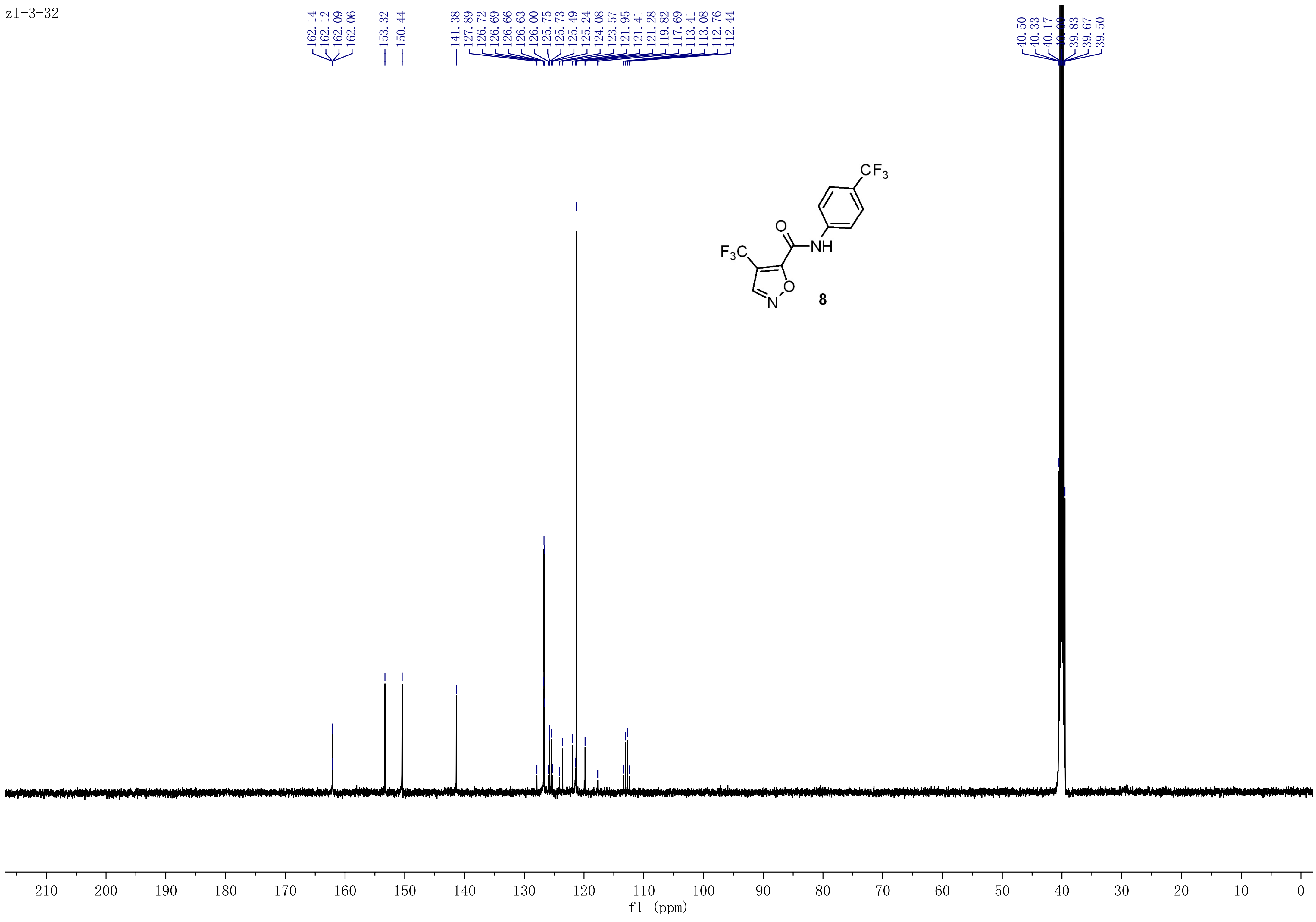

zl-3-32
10
11.52
9.42
8.00
7.99
7.78
7.76
3.39
2.50
CF3
O
NH
F3C
O
N
8
1.03
0.91
2.00
1.97
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0
f1 (ppm)

zl-3-32
zl-3-32



8




zl-3-32
162.14
162.12
162.09
162.06
153.32
150.44
141.38
127.89
126.72
126.69
126.66
126.63
126.00
125.75
125.73
125.49
125.24
124.08
123.57
121.95
121.41
121.28
119.82
117.69
113.41
113.08
112.76
112.44
40.50
40.33
40.17
39.83
39.67
39.50
CF_3
O
NH
F_3C
O
N
8
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)