Supporting Information

Copper-catalyzed Tandem Trifluoromethylation/Cyclization of Internal Alkynes

Yun-Long Ji,[a] Jin-Hong Lin, [a]* Ji-Chang Xiao[a]* and Yu-Cheng Gu[b]

[a]Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China.

Dr. Jin-Hong Lin

Tel: (+86) 21-5492-5380; E-mail: jlin@sioc.ac.cn.

Prof. Ji-Chang Xiao

Fax: (+86) 21-6416-6128; Tel: (+86)21-5492-5340; E-mail: jchxiao@sioc.ac.cn.

[b]Syngenta, Jealott's Hill International Research Centre, Bracknell, Berkshire, RG42 6EY, UK

Contents

1. General Information……S2

2. General Procedure for the Preparation of Internal Alkynes S2

3. General Procedure for the Trifluoromethylation of Alkynes…….

S10

4. Procedure for the synthesis of **3**, **4**, **5**……..…..S20

5. Crystal Data and Structure Refinement for **2h**…….……S24

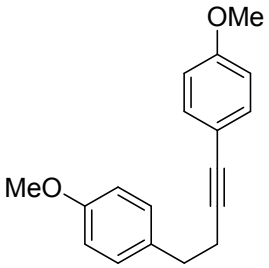
6. Copies of NMR Spectra……..…….....S25

1. General Information

^{1}H, ^{13}C and ^{19}F NMR spectra were detected on a 500 MHz, 400 MHz or 300 MHz NMR spectrometer. Data for ^{1}H NMR, ^{13}C NMR and ^{19}F NMR were recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, coupling constant (s) in Hz). Mass spectra were obtained on a GC-MS. High resolution mass data were recorded on a high resolution mass spectrometer in the EI or ESI mode.

2. General Procedure for the Preparation of Internal Alkynes.

Internal Alkynes were synthesized according to the procedure reported in literature.[1]

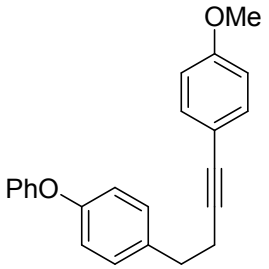


1a

4,4'-(But-1-yne-1,4-diyl)bis(methoxybenzene) (**1a**): 52%; white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.6 Hz, 2H), 7.19 (d, *J* = 8.3 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 2H), 6.81 (d, *J* = 8.6 Hz, 2H), 3.80 (s, 6H), 2.86 (t, *J* = 7.5 Hz, 2H), 2.64 (t, *J* = 7.5 Hz, 2H).

The spectra match spectra from previous report.[1]



1b

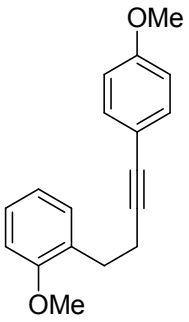
1-Methoxy-4-(4-(4-phenoxyphenyl)but-1-yn-1-yl)benzene (**1b**): 31%; yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.25 (m, 4H), 7.20 (d, *J* = 8.5 Hz, 2H), 7.05 (t, *J* = 7.4 Hz, 1H), 6.98 (d, *J* = 8.6 Hz, 2H), 6.94 (d, *J* = 8.5 Hz, 2H), 6.78 (d, *J* = 8.8 Hz, 2H), 3.74 (s, 3H), 2.86 (t, *J* = 7.4 Hz, 2H), 2.64 (t, *J* = 7.4 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.18, 157.62, 155.61, 135.86, 132.93, 129.92, 129.79, 123.09, 119.04, 118.68, 116.02, 113.92, 87.92, 81.33, 55.27, 34.62, 21.92.

IR(KBr): 3036, 2930, 2835,1589, 1505, 1486, 1233, 829, 691cm^{-1}.

HRMS (EI):calcd. For [$C_{23}H_{20}O_2$] 328.1463, found 328.1467.



1c

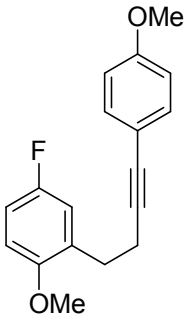
1-Methoxy-2-(4-(4-methoxyphenyl)but-3-yn-1-yl)benzene (**1c**): 40%; yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.6 Hz, 2H), 7.23 – 7.16 (m, 2H), 6.89 (t, *J* = 7.4 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 8.6 Hz, 2H), 3.80 (s, 3H), 3.75 (s, 3H), 2.92 (t, *J* = 7.6 Hz, 2H), 2.65 (t, *J* = 7.6 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.01, 157.48, 132.89, 130.28, 129.07, 127.63, 120.34, 116.22, 113.81, 110.21, 88.61, 80.71, 55.24, 55.21, 30.26, 19.93.

IR(KBr): 3000, 2933, 2835, 1604, 1507, 1240, 1030, 830, 751cm^{-1}.

HRMS (EI):calcd. For [$C_{18}H_{18}O_2$] 266.1307, found 266.1310.



1d

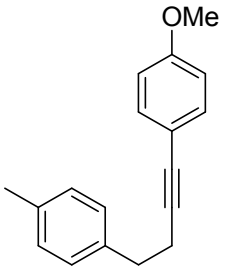
4-Fluoro-1-methoxy-2-(4-(4-methoxyphenyl)but-3-yn-1-yl)benzene (**1d**): 38%; yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.8 Hz, 2H), 6.95 (dd, *J* = 9.0, 3.0 Hz, 1H), 6.86 (td, *J* = 8.5, 3.1 Hz, 1H), 6.78 (d, *J* = 8.8 Hz, 2H), 6.72 (dd, *J* = 8.9, 4.5 Hz, 1H), 3.76 (s, 3H), 3.74 (s, 3H), 2.87 (t, *J* = 7.4 Hz, 2H), 2.64 (t, *J* = 7.4 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.09, 156.77 (d, *J* = 237.7 Hz), 153.57 (d, *J* = 1.9 Hz), 132.87, 130.72 (d, *J* = 7.2 Hz), 117.00 (d, *J* = 23.0 Hz), 116.02, 113.83, 113.12 (d, *J* = 22.6 Hz), 110.86 (d, *J* = 8.3 Hz), 88.01, 81.07, 55.74, 55.19, 29.98 (d, *J* = 1.1 Hz), 19.64.

IR(KBr): 2955, 2836, 1606, 1496, 1244, 1216, 1031, 830, 802, 708 cm^{-1}.

HRMS (EI):calcd. For [$C_{18}H_{17}FO_2$] 284.1213, found 284.1216.



1e

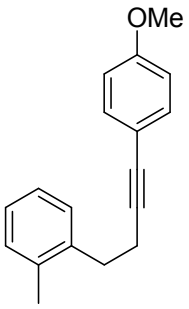
1-Methoxy-4-(4-(p-tolyl)but-1-yn-1-yl)benzene (**1e**): 27%; white solid; M.P.: 60 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.7 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.12 (d, *J* = 8.2 Hz, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 3.79 (s, 3H), 2.87 (t, *J* = 7.6 Hz, 2H), 2.65 (t, *J* = 7.6 Hz, 2H), 2.33 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.04, 137.76, 135.73, 132.84, 129.03, 128.39, 116.01, 113.79, 88.02, 80.89, 55.24, 34.91, 21.86, 21.05.

IR(KBr): 2923, 1606, 1508, 1288, 1243, 1171, 1033, 830, 806 cm^{-1}.

HRMS (EI):calcd. For [$C_{18}H_{18}O$] 250.1358, found 250.1360.

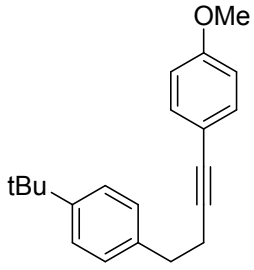


1f

1-(4-(4-Methoxyphenyl)but-3-yn-1-yl)-2-methylbenzene (**1f**): 31%; yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.8 Hz, 2H), 7.24 – 7.19 (m, 1H), 7.18 – 7.09 (m, 3H), 6.80 (d, *J* = 8.8 Hz, 2H), 3.77 (s, 3H), 2.92 (t, *J* = 7.7 Hz, 2H), 2.64 (t, *J* = 7.7 Hz, 2H), 2.35 (s, 3H).

The spectra match spectra from previous report.[1]

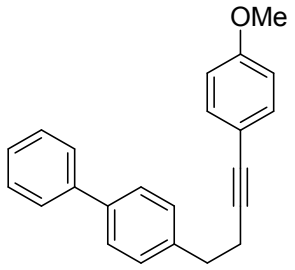


1g

1-(*tert*-Butyl)-4-(4-(4-methoxyphenyl)but-3-yn-1-yl)benzene (**1g**): 61%; white solid; M.P.: 78 °C.

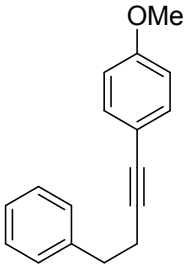
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 4H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.80 (d, *J* = 8.5 Hz, 2H), 3.78 (s, 3H), 2.89 (t, *J* = 7.6 Hz, 2H), 2.66 (t, *J* = 7.6 Hz, 2H), 1.31 (s, 9H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.08, 149.05, 137.81, 132.87, 128.18, 125.28, 116.06, 113.83, 88.16, 80.91, 55.24, 34.85, 34.42, 31.43, 21.70.
IR(KBr): 2958, 2905, 1606, 1508, 1244, 1033, 829 cm^{-1}.
HRMS (EI):calcd. For [$C_{21}H_{24}O$] 292.1827, found 292.1831.



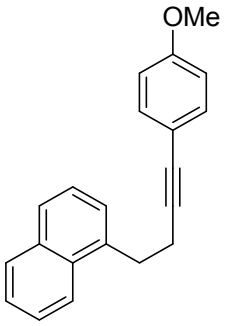
1h

4-(4-(4-Methoxyphenyl)but-3-yn-1-yl)-1,1'-biphenyl (**1h**): 56%; white solid; M.P.: 109 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.8 Hz, 2H), 7.55 (d, *J* = 7.8 Hz, 2H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.40 – 7.27 (m, 5H), 6.81 (d, *J* = 8.3 Hz, 2H), 3.80 (s, 3H), 2.96 (t, *J* = 7.3 Hz, 2H), 2.71 (t, *J* = 7.3 Hz, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.13, 141.07, 139.93, 139.26, 132.87, 128.99, 128.73, 127.11, 127.09, 127.04, 115.99, 113.85, 87.84, 81.15, 55.26, 34.95, 21.68.
IR(KBr): 3000, 2925, 2855, 1602, 1503, 1241, 1171, 1031, 826, 760, 734, 694 cm^{-1}.
HRMS (EI):calcd. For [$C_{23}H_{20}O$] 312.1514, found 312.1513.



1i

1-Methoxy-4-(4-phenylbut-1-yn-1-yl)benzene (**1i**): 50%; yellow solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.20 (m, 7H), 6.81 (d, *J* = 8.7 Hz, 2H), 3.80 (s, 3H), 2.92 (t, *J* = 7.6 Hz, 2H), 2.68 (t, *J* = 7.6 Hz, 2H).
The spectra match spectra from previous report.[1]

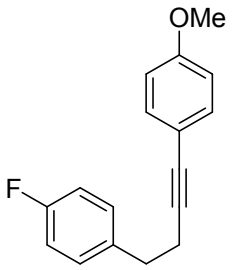


1j

1-(4-(4-Methoxyphenyl)but-3-yn-1-yl)naphthalene (**1j**): 26%; yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.3 Hz, 1H), 7.86 (d, *J* = 7.8 Hz, 1H), 7.74 (t, *J* = 4.6 Hz, 1H), 7.55 – 7.45 (m, 2H), 7.42 (d, *J* = 4.9 Hz, 2H), 7.29 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 3.78 (s, 3H), 3.39 (t, *J* = 7.7 Hz, 2H), 2.82 (t, *J* = 7.7 Hz, 2H).

The spectra match spectra from previous report.[1]

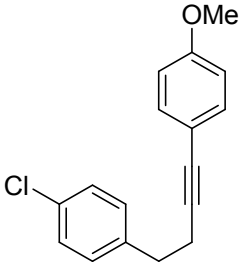


1k

1-Fluoro-4-(4-(4-methoxyphenyl)but-3-yn-1-yl)benzene (**1k**): 40%; white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 8.7 Hz, 2H), 7.22 (dd, *J* = 8.3, 5.5 Hz, 2H), 6.99 (t, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 3.79 (s, 3H), 2.87 (t, *J* = 7.4 Hz, 2H), 2.65 (t, *J* = 7.4 Hz, 2H).

The spectra match spectra from previous report.[1]



1l

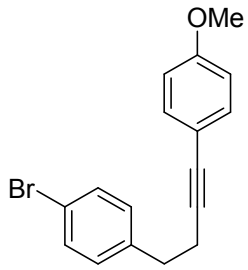
1-Chloro-4-(4-(4-methoxyphenyl)but-3-yn-1-yl)benzene (**1l**): 19%; white solid; M.P.: 58 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, *J* = 6.6 Hz, 2H), 7.27 (d, *J* = 6.3 Hz, 2H), 7.20 (d, *J* = 8.3 Hz, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 3.80 (s, 3H), 2.87 (t, *J* = 7.3 Hz, 2H), 2.65 (t, *J* = 7.3 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.17, 139.19, 132.84, 132.06, 129.95, 128.44, 115.82, 113.86, 87.37, 81.37, 55.27, 34.56, 21.58.

IR(KBr): 2927, 2854, 2541, 2150, 1602, 1504, 1243, 1087, 832, 813 cm^{-1}.

HRMS (EI):calcd. For [$C_{17}H_{15}ClO$] 270.0811, found 270.0810.

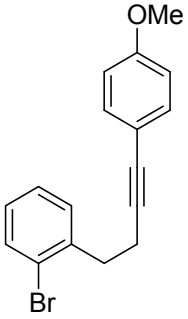


1m

1-Bromo-4-(4-(4-methoxyphenyl)but-3-yn-1-yl)benzene (**1m**): 42%; white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.3 Hz, 2H), 7.29 (d, *J* = 8.8 Hz, 2H), 7.15 (d, *J* = 8.3 Hz, 2H), 6.81 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H), 2.86 (t, *J* = 7.3 Hz, 2H), 2.65 (t, *J* = 7.4 Hz, 2H).

The spectra match spectra from previous report.[1]



1n

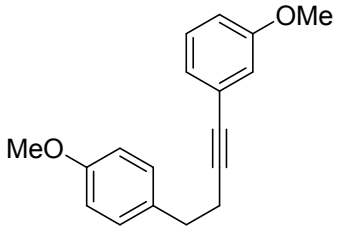
1-Bromo-2-(4-(4-methoxyphenyl)but-3-yn-1-yl)benzene (**1n**): 7%; yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (dd, *J* = 8.0, 1.1 Hz, 1H), 7.38 – 7.26 (m, 4H), 7.09 (td, *J* = 7.7, 1.7 Hz, 1H), 6.81 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 3H), 3.04 (t, *J* = 7.4 Hz, 2H), 2.71 (t, *J* = 7.4 Hz, 2H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.13, 139.86, 132.87, 132.80, 130.87, 128.08, 127.34, 124.41, 115.93, 113.83, 87.36, 81.25, 55.26, 35.52, 19.87.

IR(KBr): 2956, 2931, 2836, 1606, 1508, 1468, 1440, 1244, 1027, 830,749 cm^{-1}.

HRMS (EI):calcd. For [$C_{17}H_{15}BrO$] 314.0306, found 314.0311.



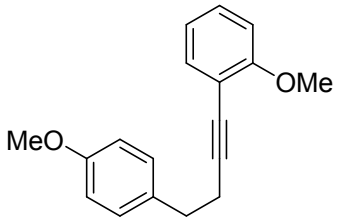
1o

1-Methoxy-3-(4-(4-methoxyphenyl)but-1-yn-1-yl)benzene (**1o**): 19%; yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 – 7.14 (m, 3H), 6.97 (d, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 2.0 Hz, 1H), 6.88 – 6.76 (m, 3H), 3.78 (s, 3H), 3.77 (s, 3H), 2.86 (t, *J* = 7.4 Hz, 2H), 2.64 (t, *J* = 7.5 Hz, 2H).

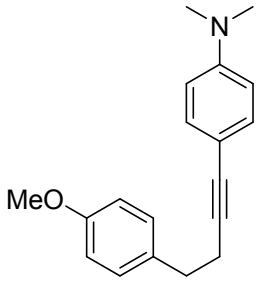
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.29, 158.18, 132.86, 129.50, 129.25, 124.93, 124.09, 116.48, 114.20, 113.82, 89.56, 81.27, 55.27, 55.23, 34.32, 21.99.

IR(KBr): 3030, 2997, 2851, 1604, 1581, 1510, 1316, 1243, 1036, 825, 779 cm^{-1}.
HRMS (EI):calcd. For [$C_{18}H_{18}O_2$] 266.1307, found 266.1302.



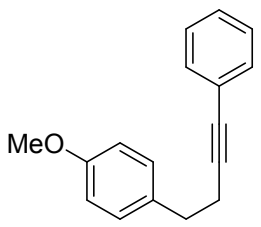
1p

1-Methoxy-2-(4-(4-methoxyphenyl)but-1-yn-1-yl)benzene (**1p**): 24%; yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 7.5, 1.5 Hz, 1H), 7.26 – 7.16 (m, 3H), 6.89 – 6.80 (m, 4H), 3.85 (s, 3H), 3.77 (s, 3H), 2.88 (t, *J* = 7.5 Hz, 2H), 2.71 (t, *J* = 7.5 Hz, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.84, 158.10, 133.67, 133.00, 129.55, 129.02, 120.41, 113.75, 112.96, 110.53, 93.86, 77.93, 55.76, 55.25, 34.43, 22.41.
IR(KBr): 2996, 2929, 2834, 1611, 1512, 1492, 1242, 1177, 1026, 820, 750 cm^{-1}.
HRMS (EI):calcd. For [$C_{18}H_{18}O_2$] 266.1307, found 266.1305.



1q

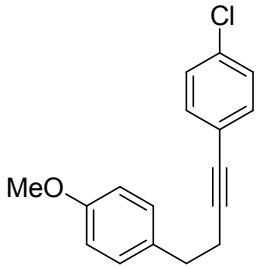
4-(4-(4-Methoxyphenyl)but-1-yn-1-yl)-N,N-dimethylaniline (**1q**): 14%; M.P.: 68 °C
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.7 Hz, 2H), 7.19 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.61 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H), 2.95 (s, 6H), 2.85 (t, *J* = 7.5 Hz, 2H), 2.63 (t, *J* = 7.5 Hz, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.08, 149.76, 133.20, 132.49, 129.51, 113.76, 111.94, 111.03, 86.97, 81.79, 55.27, 40.31, 34.67, 22.14.
IR(KBr): 2995, 2918, 2850, 1883, 1604, 1510, 1336, 1236, 1181, 1034, 814, 628 cm^{-1}.
HRMS (EI):calcd. For [$C_{19}H_{21}NO$] 279.1623, found 279.1621.



1r

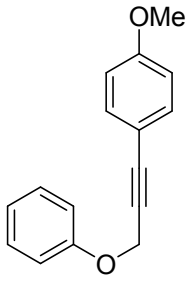
1-Methoxy-4-(4-phenylbut-3-yn-1-yl)benzene (**1r**): 45%; red oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (dd, *J* = 6.5, 3.1 Hz, 2H), 7.29 – 7.22 (m, 3H), 7.17 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 3.76 (s, 3H), 2.85 (t, *J* = 7.4 Hz, 2H), 2.64 (t, *J* = 7.4 Hz, 2H).
The spectra match spectra from previous report.[2]



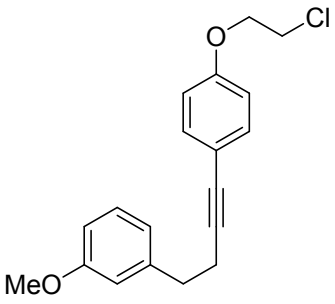
1s

1-Chloro-4-(4-(4-methoxyphenyl)but-1-yn-1-yl)benzene (**1s**): 8%; white solid; M.P.: 40 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.22 (m, 4H), 7.18 (d, *J* = 8.4 Hz, 2H), 6.85 (d, *J* = 8.5 Hz, 2H), 3.80 (s, 3H), 2.85 (t, *J* = 7.4 Hz, 2H), 2.64 (t, *J* = 7.4 Hz, 2H).
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.17, 133.54, 132.77, 131.41, 129.49, 128.52, 122.38, 113.80, 90.72, 80.27, 55.28, 34.19, 21.99.
IR(KBr): 3016, 2960, 2917, 1609, 1510, 1301, 1240, 1177, 1031, 827, 765 cm^{-1}.
HRMS (EI):calcd. For [$C_{17}H_{15}ClO$] 270.0811, found 270.0812.



1t

1-Methoxy-4-(3-phenoxyprop-1-yn-1-yl)benzene (**1t**): 76%; white solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.8 Hz, 2H), 7.30 (t, *J* = 8.0 Hz, 2H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.98 (t, *J* = 7.3 Hz, 0.85 Hz, 1H), 6.81 (d, *J* = 8.9 Hz, 2H), 4.89 (s, 2H), 3.78 (s, 3H).
The spectra match spectra from previous report.[1]



1u

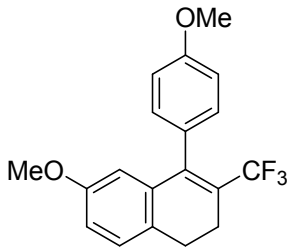
1-(4-(4-(2-chloroethoxy)phenyl)but-3-yn-1-yl)-3-methoxybenzene (**1u**): 52%; white solid.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, *J* = 8.3 Hz, 2H), 7.25 – 7.18 (m, 1H), 6.91 – 6.68 (m, 5H), 4.21 (t, *J* = 5.4 Hz, 2H), 3.86 – 3.74 (m, 5H), 2.89 (t, *J* = 7.5 Hz, 2H), 2.67 (t, *J* = 7.7 Hz, 2H).
The spectra match spectra from previous report.[1]

3. General Trifluoromethylation Procedure for Internal Alkynes.

Procedure A: CuTc (3.8mg, 0.02 mmol), Umemoto's reagent (60.3mg, 0.15 mmol), 2,2'-Dipyridyl (12.5mg, 0.08mmol), internal alkynes (0.1 mmol), and DCE (1 mL) were added sequentially to a flame-dried tube under argon. The tube was then sealed and the resulting mixture was stirred at 80 °C. When the reaction was completed, as monitored by ^{19}F NMR, the crude reaction mixture was filtered through a short pad of silica gel eluted with CH_2Cl_2. After evaporation of the solvent, the residue was purified by chromatography on silica gel (eluent: petroleum ether/dichloromethane) to afford the desired product.

Procedure B: CuTc (3.8mg, 0.02 mmol), Umemoto's reagent (60.3mg, 0.15 mmol), 2,2'-Dipyridyl (12.5mg, 0.08mmol), internal alkynes (0.1 mmol), MeOH (0.1ml) and DCE (1 mL) were added sequentially to a flame-dried tube under argon. The tube was then sealed and the resulting mixture was stirred at 80 °C. When the reaction was completed, as monitored by ^{19}F NMR, the crude reaction mixture was filtered through a short pad of silica gel eluted with CH_2Cl_2. After evaporation, the residue was purified by chromatography on silica gel (eluent: petroleum ether/dichloromethane) to afford the desired product.

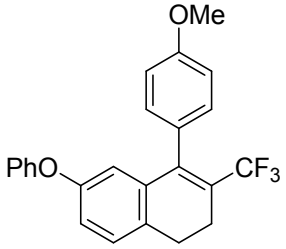
Obtained according to General Procedure **B**:



2a

6-Methoxy-4-(4-methoxyphenyl)-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2a**): 82%; white solid; M.P.: 59 °C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 – 7.05 (m, 3H), 6.92 (d, *J* = 8.5 Hz, 2H), 6.75 (dd, *J* = 8.1, 2.2 Hz, 1H), 6.29 (d, *J* = 2.0 Hz, 1H), 3.84 (s, 3H), 3.62 (s, 3H), 2.87 (t, *J* = 7.9 Hz, 2H), 2.58 (t, *J* = 7.8 Hz, 2H).
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.12 (s, 3F).
^{13}C NMR (101 MHz, $CDCl_3$) δ 157.91, 157.14, 140.63 (q, *J* = 4.1 Hz), 135.28, 129.10 (q, *J* = 1.8 Hz), 128.05, 127.18, 126.92, 124.02 (q, *J* = 28.6 Hz), 123.30 (q, *J* = 275.3 Hz), 113.37, 112.39, 112.14, 54.15, 54.13, 25.76, 21.87 (q, *J* = 2.5 Hz).
IR(KBr): 3002, 2837, 1607, 1510, 1269, 1170, 1096, 1034, 832, 787 cm^{-1}.
HRMS (EI):calcd. For [$C_{19}H_{17}F_3O_2$] 334.1181, found 334.1183.

Obtained according to General Procedure **A**:



2b

4-(4-Methoxyphenyl)-6-phenoxy-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2b**): 75%; colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.25 (m, 2H), 7.13 (d, *J* = 8.1 Hz, 1H), 7.11 – 7.00 (m, 3H), 6.94 – 6.85 (m, 4H), 6.80 (dd, *J* = 8.1, 2.3 Hz, 1H), 6.47 (d, *J* = 2.2 Hz, 1H), 3.82 (s, 3H), 2.92 (t, *J* = 8.0 Hz, 2H), 2.62 (t, *J* = 7.8 Hz, 2H).

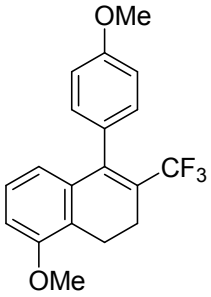
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.24 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.07, 157.27, 155.54, 141.48 (q, *J* = 3.9 Hz), 136.90, 131.05, 130.08 (q, *J* = 1.0 Hz), 129.63, 128.81, 128.26, 125.24 (q, *J* = 28.7 Hz), 124.32 (q, *J* = 272.8 Hz), 122.98, 119.23, 118.83, 118.25, 113.57, 55.19, 27.02, 22.80 (q, *J* = 2.2 Hz).

IR(KBr): 2955, 2920, 1485, 1234, 1219, 1169, 1098, 1034, 830, 815, 690 cm^{-1}.

HRMS (EI):calcd. For [$C_{24}H_{19}F_3O_2$] 396.1337, found 396.1333.

Obtained according to General Procedure **B**:



2c

8-Methoxy-4-(4-methoxyphenyl)-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2c**): 58%; yellow solid; M.P.: 90 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.5 Hz, 2H), 7.02 (t, *J* = 8.0 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.83 (d, *J* = 8.2 Hz, 1H), 6.34 (d, *J* = 7.8 Hz, 1H), 3.85 (s, 1H), 3.84 (s, 3H), 2.94 (t, *J* = 8.2 Hz, 2H), 2.56 (t, *J* = 8.2 Hz, 2H).

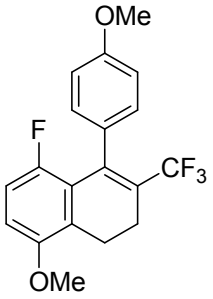
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.18 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.96, 155.76, 141.65 (q, *J* = 3.9 Hz), 136.31, 130.23 (q, *J* = 1.4 Hz), 129.63, 126.50, 124.69 (q, *J* = 28.6 Hz), 124.42 (q, *J* = 271.4 Hz), 124.34, 120.49, 113.37, 111.20, 55.68, 55.20, 21.98 (q, *J* = 2.1 Hz), 19.78.

IR(KBr): 2957, 2839, 1510, 1245, 1150, 1097, 834 cm^{-1}.

HRMS (EI):calcd. For [$C_{19}H_{17}F_3O_2$] 334.1181, found 334.1180.

Obtained according to General Procedure **A**:



2d

5-Fluoro-8-methoxy-4-(4-methoxyphenyl)-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2d**): 57%; white solid; M.P.: 110 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 6.80 (dd, *J* = 9.0, 3.7 Hz, 1H), 6.76 – 6.69 (m, 1H), 3.84 (s, 3H), 3.82 (s, 3H), 2.86 (t, *J* = 7.3 Hz, 2H), 2.48 (t, *J* = 7.3 Hz, 2H).

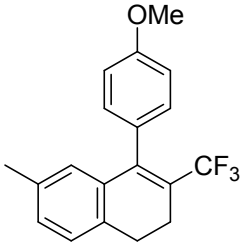
^{19}F NMR (376 MHz, $CDCl_3$) δ -57.98 (s, 3F), -117.66 (d, *J* = 10.9 Hz, 1F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.84, 155.28 (d, *J* = 248.1 Hz), 151.60 (d, *J* = 2.1 Hz), 138.95 (qd, *J* = 4.0, 1.0 Hz), 130.75 (d, *J* = 3.5 Hz), 129.45 – 129.27 (m), 127.45, 126.79 (q, *J* = 28.7 Hz), 124.17 (q, *J* = 273.1 Hz), 123.80 (d, *J* = 8.1 Hz), 114.50 (d, *J* = 25.1 Hz), 112.93, 112.53 (d, *J* = 8.9 Hz), 56.08, 55.11, 22.19 (q, *J* = 2.8 Hz), 20.98 (d, *J* = 1.8 Hz).

IR(KBr): 2963, 2916, 2839, 1608, 1475, 1241, 1148, 1084, 811 cm^{-1}.

HRMS (EI):calcd. For [$C_{19}H_{16}F_4O_2$] 352.1086, found 352.1085.

Obtained according to General Procedure **A**:



2e

4-(4-Methoxyphenyl)-6-methyl-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2e**): 64%; colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 – 7.06 (m, 3H), 7.02 (d, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 8.7 Hz, 2H), 6.51 (s, 1H), 3.85 (s, 3H), 2.89 (t, *J* = 7.9 Hz, 2H), 2.57 (t, *J* = 7.9 Hz, 2H), 2.16 (s, 3H).

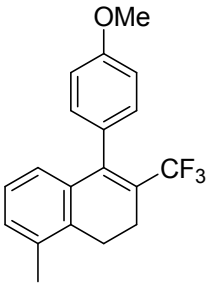
^{19}F NMR (376 MHz, $CDCl_3$) δ -58.97 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.90, 141.86 (q, *J* = 4.0 Hz), 136.05, 135.07, 133.11, 130.18 (q, *J* = 1.9 Hz), 129.39, 129.32, 128.39, 127.16, 124.53 (q, *J* = 28.5 Hz), 124.40 (q, *J* = 274.2 Hz), 113.38, 55.17, 27.34, 22.72 (q, *J* = 2.6 Hz), 21.16.

IR(KBr): 2927, 1509, 1243, 1030, 828, 785 cm^{-1}.

HRMS (EI):calcd. For [$C_{19}H_{17}F_3O$] 318.1231, found 318.1232.

Obtained according to General Procedure **A**:



2f

4-(4-Methoxyphenyl)-8-methyl-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2f**): 64%; white solid; M.P.: 70 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 – 7.04 (m, 3H), 7.00 – 6.89 (m, 3H), 6.57 (d, *J* = 7.6 Hz, 1H), 3.84 (s, 3H), 2.88 (t, *J* = 7.9 Hz, 2H), 2.59 (t, *J* = 7.8 Hz, 2H), 2.33 (s, 3H).

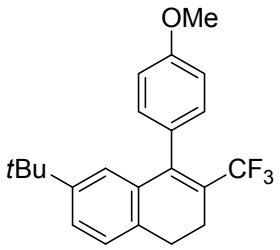
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.12 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.91, 142.03 (q, *J* = 4.0 Hz), 135.17, 134.65, 134.49, 130.82, 130.22 (q, *J* = 1.9 Hz), 129.67, 125.94, 125.77, 124.39 (q, *J* = 272.4 Hz), 123.92 (q, *J* = 28.7 Hz), 113.35, 55.17, 23.66, 22.16 (q, *J* = 2.6 Hz), 19.55.

IR(KBr): 2957, 2930, 1608, 1510, 1314, 1149, 1089, 833 cm^{-1}.

HRMS (EI):calcd. For [$C_{19}H_{17}F_3O$] 318.1231, found 318.1229.

Obtained according to General Procedure **A**:



2g

6-(Tert-butyl)-4-(4-methoxyphenyl)-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2g**): 68%; colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 8.5 Hz, 1H), 7.15 – 7.07 (m, 3H), 6.94 (d, *J* = 8.1 Hz, 2H), 6.76 (s, 1H), 3.86 (s, 3H), 2.91 (t, *J* = 7.9 Hz, 2H), 2.59 (t, *J* = 7.9 Hz, 2H), 1.13 (s, 9H).

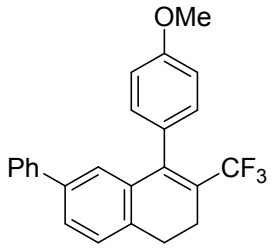
^{19}F NMR (376 MHz, $CDCl_3$) δ -58.97 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.95, 149.43, 142.21 (q, *J* = 4.0 Hz), 134.86, 133.20, 130.24 (q, *J* = 1.9 Hz), 129.42, 126.94, 125.64, 125.06, 124.49 (q, *J* = 273.4 Hz), 124.27 (q, *J* = 28.5 Hz), 113.34, 55.20, 34.46, 31.18, 27.25, 22.72 (q, *J* = 2.5 Hz).

IR(KBr): 2961, 1609, 1510, 1150, 1098, 831, 739, 621 cm^{-1}.

HRMS (EI):calcd. For [$C_{22}H_{23}F_3O$] 360.1701, found 360.1703.

Obtained according to General Procedure **A**:



2h

4-(4-Methoxyphenyl)-6-phenyl-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2h**): 74%; white solid; M.P.: 98 ^{o}C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.37 – 7.30 (m, 4H), 7.29 – 7.23 (m, 2H), 7.13 (d, *J* = 8.5 Hz, 2H), 6.96 – 6.91 (m, 3H), 3.83 (s, 3H), 2.97 (t, *J* = 7.9 Hz, 2H), 2.63 (t, *J* = 7.9 Hz, 2H).

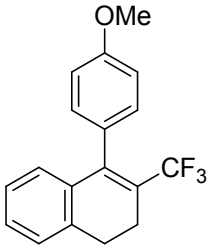
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.06 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.00, 141.84 (q, *J* = 4.0 Hz), 140.78, 139.69, 135.68, 135.20, 130.20 (q, *J* = 1.9 Hz), 129.06, 128.72, 127.75, 127.49, 127.19, 126.94, 126.56, 124.96 (q, *J* = 28.7 Hz), 124.36 (q, *J* = 272.3 Hz), 113.53, 55.19, 27.45, 22.64 (q, *J* = 2.6 Hz).

IR(KBr): 2952, 2927, 2836, 1644, 1607, 1510, 1318, 1245, 1143, 1084, 1030, 831, 760, 692 cm^{-1}.

HRMS (EI):calcd. For [$C_{24}H_{19}F_3O$] 380.1388, found 380.1389.

Obtained according to General Procedure **A**:



2i

4-(4-Methoxyphenyl)-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2i**): 73%; white solid; M.P.: 71 ^{o}C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 – 7.16 (m, 2H), 7.12 – 7.03 (m, 3H), 6.93 (d, *J* = 8.7 Hz, 2H), 6.71 (d, *J* = 7.8 Hz, 1H), 3.85 (s, 3H), 2.94 (t, *J* = 7.8 Hz, 2H), 2.60 (t, *J* = 7.8 Hz, 2H).

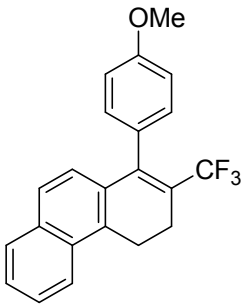
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.12 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.00, 141.78 (q, *J* = 4.0 Hz), 136.10, 135.25, 130.19 (q, *J* = 1.9 Hz), 129.27, 128.76, 127.77, 127.27, 126.54, 124.53 (q, *J* = 28.7 Hz), 124.36 (q, *J* = 273.2 Hz), 113.44, 55.20, 27.73, 22.55 (q, *J* = 2.6 Hz).

IR(KBr): 3001, 2923, 2849, 1609, 1510, 1343, 1244, 1147, 1096, 1034, 826,773 cm^{-1};

HRMS (EI):calcd. For [$C_{18}H_{15}F_3O$] 304.1075, found 304.1078.

Obtained according to General Procedure **A**:



2j

1-(4-Methoxyphenyl)-2-(trifluoromethyl)-3,4-dihydrophenanthrene (**2j**): 46%; white solid; M.P.: 147 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 8.0 Hz, 1H), 7.58 – 7.51 (m, 2H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.12 (d, *J* = 8.6 Hz, 2H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 1H), 3.86 (s, 3H), 3.37 (t, *J* = 8.4 Hz, 2H), 2.72 (t, *J* = 8.3 Hz, 2H).

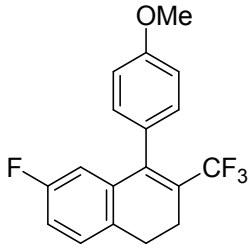
^{19}F NMR (376 MHz, $CDCl_3$) δ -58.91 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.07, 142.31 (q, *J* = 4.1 Hz), 133.59, 132.48, 132.17, 130.68, 130.29 (q, *J* = 2.0 Hz), 129.66, 128.53, 126.44, 126.31, 126.22, 125.18, 124.46 (q, *J* = 274.7 Hz), 124.02, 123.90 (q, *J* = 28.1 Hz), 113.56, 55.22, 23.14, 22.27 (q, *J* = 2.8 Hz).

IR(KBr): 2958, 2921, 2850, 1605, 1508, 1316, 1273, 1151, 1091, 822, 757 cm^{-1}.

HRMS (EI):calcd. For [$C_{22}H_{17}F_3O$] 354.1231, found 354.1234.

Obtained according to General Procedure **A**:



2k

6-Fluoro-4-(4-methoxyphenyl)-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2k**): 70%; white solid; M.P.: 74 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.14 (dd, *J* = 8.0, 5.9 Hz, 1H), 7.08 (d, *J* = 8.6 Hz, 2H), 6.94 (d, *J* = 8.7 Hz, 2H), 6.89 (td, *J* = 8.2, 2.5 Hz, 1H), 6.42 (dd, *J* = 10.4, 2.4 Hz, 1H), 3.85 (s, 3H), 2.90 (t, *J* = 8.0 Hz, 2H), 2.60 (t, *J* = 7.9 Hz, 2H).

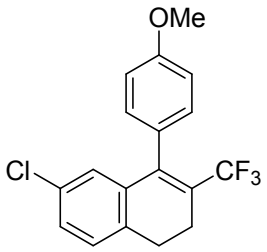
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.39 (s, 3F), -115.61 ~ -115.70 (m, 1F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.55 (d, *J* = 243.1 Hz), 159.15, 141.04 (qd, *J* = 3.7, 1.9 Hz), 137.05 (d, *J* = 7.4 Hz), 131.48 (d, *J* = 2.9 Hz), 130.07 (q, *J* = 1.9 Hz), 128.55, 128.38 (d, *J* = 7.7 Hz), 125.69 (q, *J* = 28.9 Hz), 124.15 (q, *J* = 274.5 Hz), 115.16 (d, *J* = 21.5 Hz), 114.70 (d, *J* = 23.6 Hz), 113.61, 55.19, 26.89, 22.69 (q, *J* = 2.5 Hz).

IR(KBr): 2958, 2922, 2846, 1609, 1511,1316, 1246, 1170, 1000, 790 cm^{-1}.

HRMS (EI):calcd. For [$C_{18}H_{14}F_4O$] 322.0981, found 322.0979.

Obtained according to General Procedure **A**:



2l

6-Chloro-4-(4-methoxyphenyl)-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2l**): 61%; yellow solid; M.P.: 80 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 2H), 6.67 (d, *J* = 1.0 Hz, 1H), 3.86 (s, 3H), 2.90 (t, *J* = 7.9 Hz, 2H), 2.59 (t, *J* = 7.9 Hz, 2H).

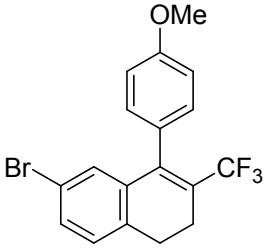
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.35 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.23, 140.97 (q, *J* = 4.0 Hz), 136.94, 134.37, 132.37, 130.13 (q, *J* = 1.8 Hz), 128.57, 128.50, 128.38, 127.66, 125.83 (q, *J* = 28.9 Hz), 124.12 (q, *J* = 273.6 Hz), 113.71, 55.23, 27.12, 22.51 (q, *J* = 2.5 Hz).

IR(KBr): 2954, 2839, 1609, 1510, 1314, 1266, 1150, 1096, 819, 779 cm^{-1}.

HRMS (EI):calcd. For [$C_{18}H_{14}ClF_3O$] 338.0685, found 338.0680.

Obtained according to General Procedure **A**:



2m

6-Bromo-4-(4-methoxyphenyl)-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2m**): 67%; white solid; M.P.: 102 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.10 – 7.05 (m, 3H), 6.95 (d, *J* = 8.5 Hz, 2H), 6.83 (d, *J* = 1.3 Hz, 1H), 3.87 (s, 3H), 2.89 (t, *J* = 8.0 Hz, 2H), 2.60 (t, *J* = 8.0 Hz, 2H).

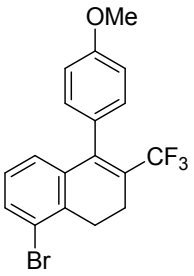
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.34 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.24, 140.89 (q, *J* = 4.0 Hz), 137.29, 134.90, 131.56, 130.50, 130.13 (q, *J* = 1.9 Hz), 128.84, 128.32, 125.86 (q, *J* = 28.9 Hz), 124.09 (q, *J* = 273.6 Hz), 120.33, 113.72, 55.23, 27.21, 22.43 (q, *J* = 2.6 Hz).

IR(KBr): 2957, 2886, 1771, 1067, 1035, 925, 835 cm^{-1}.

HRMS (EI):calcd. For [$C_{18}H_{14}BrF_3O$] 382.0180, found 382.0182.

Obtained according to General Procedure **A**:



2n

8-Bromo-4-(4-methoxyphenyl)-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2n**): 42%; yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, *J* = 8.0 Hz, 1H), 7.07 (d, *J* = 8.5 Hz, 2H), 6.96 – 6.87 (m, 3H), 6.66 (d, *J* = 7.7 Hz, 1H), 3.85 (s, 3H), 3.08 (t, *J* = 8.0 Hz, 2H), 2.62 (t, *J* = 7.9 Hz, 2H).

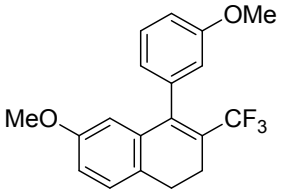
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.41 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.17, 141.28 (q, *J* = 4.0 Hz), 137.44, 135.63, 132.88, 130.22 (q, *J* = 1.9 Hz), 128.83, 127.45, 127.19, 125.32 (q, *J* = 29.0 Hz), 124.05 (d, *J* = 273.5 Hz), 123.69, 113.58, 55.23, 27.21, 22.11 (q, *J* = 2.5 Hz).

IR(KBr): 2957, 2841, 1608, 1510, 1441, 1340, 1245, 1152, 1100, 828 cm^{-1}.

HRMS (EI):calcd. For [$C_{18}H_{14}BrF_3O$] 382.0180, found 382.0179.

Obtained according to General Procedure **B**:



2o

6-Methoxy-4-(3-methoxyphenyl)-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2o**): 35%; yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 8.2 Hz, 1H), 7.12 (d, *J* = 8.2 Hz, 1H), 6.90 (dd, *J* = 8.3, 2.5 Hz, 1H), 6.82 – 6.66 (m, 3H), 6.30 (d, *J* = 2.6 Hz, 1H), 3.80 (s, 3H), 3.63 (s, 3H), 2.89 (t, *J* = 8.0 Hz, 2H), 2.59 (t, *J* = 8.0 Hz, 2H).

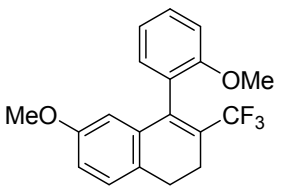
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.47 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.26, 158.26, 141.63 (q, *J* = 4.0 Hz), 138.32 (s), 135.79, 129.06, 128.13, 128.01, 124.87 (q, *J* = 28.9 Hz), 124.26 (q, *J* = 273.5 Hz), 121.50 (q, *J* = 1.6 Hz), 114.50, 113.24, 55.23, 26.80, 22.86 (q, *J* = 2.5 Hz).

IR(KBr): 3002, 2941, 1605, 1574, 1315, 1211, 1164, 1099, 1042, 812, 732, 704 cm^{-1}.

HRMS (EI):calcd. For [$C_{19}H_{17}F_3O_2$] 334.1181, found 334.1179.

Obtained according to General Procedure **B**:



2p

6-Methoxy-4-(2-methoxyphenyl)-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2p**): 57%; yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (td, *J* = 8.3, 1.7 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 1H), 7.05 (dd, *J* = 7.4, 1.6 Hz, 1H), 7.01 – 6.90 (m, 2H), 6.75 (dd, *J* = 8.2, 2.5 Hz, 1H), 6.26 (d, *J* = 2.3 Hz, 1H), 3.72 (s, 3H), 3.62 (s, 3H), 2.95 – 2.83 (m, 2H), 2.68 – 2.48 (m, 2H).

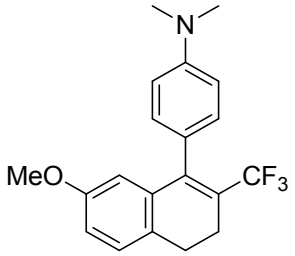
^{19}F NMR (376 MHz, $CDCl_3$) δ -61.61 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.34, 156.91 (q, *J* = 1.4 Hz), 138.47 (q, *J* = 4.2 Hz), 135.53, 130.37 (q, *J* = 1.8 Hz), 129.28, 128.19, 127.93, 126.06, 125.47 (q, *J* = 28.8 Hz), 124.36 (q, *J* = 273.3 Hz), 120.31, 113.64, 113.03, 110.82, 55.65, 55.17, 26.83, 22.92 (q, *J* = 2.2 Hz).

IR(KBr): 3002, 2941, 2837, 1601, 1574, 1315, 1169, 1146, 1096, 1068, 754 cm^{-1}.

HRMS (EI):calcd. For [$C_{19}H_{17}F_3O_2$] 334.1181, found 334.1177.

Obtained according to General Procedure **B**:



2q

4-(7-Methoxy-2-(trifluoromethyl)-3,4-dihydronaphthalen-1-yl)-N,N-dimethylaniline (**2q**): 32%; yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 (d, *J* = 8.2 Hz, 1H), 7.03 (d, *J* = 8.6 Hz, 2H), 6.81 – 6.70 (m, 3H), 6.37 (d, *J* = 2.2 Hz, 1H), 3.63 (s, 3H), 3.00 (s, 6H), 2.86 (t, *J* = 7.9 Hz, 2H), 2.57 (t, *J* = 7.9 Hz, 2H).

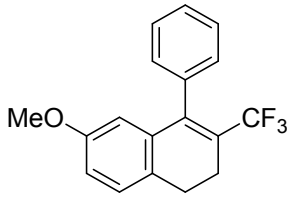
^{19}F NMR (376 MHz, $CDCl_3$) δ -58.99 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.20, 149.56, 142.26 (q, *J* = 4.1 Hz), 136.78, 129.86 (q, *J* = 2.0 Hz), 129.62, 128.40, 127.86, 124.66 (q, *J* = 28.3 Hz), 124.52 (q, *J* = 273.4 Hz), 114.66, 113.02, 112.08 , 55.26, 40.70, 26.93, 23.00 (q, *J* = 2.4 Hz).

IR(KBr): 2940, 2837, 1611, 1572, 1521, 1365, 1315, 1196, 1143, 1044, 945, 818 cm^{-1}.

HRMS (EI):calcd. For [$C_{20}H_{20}F_3NO$] 347.1497, found 347.1501.

Obtained according to General Procedure **B**:



2r

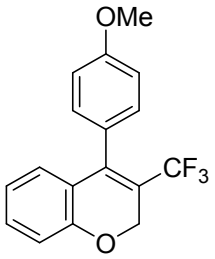
6-Methoxy-4-phenyl-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2r**): 45%; yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.33 (m, 3H), 7.19 (d, *J* = 7.4 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 1H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.26 (s, 1H), 3.62 (s, 3H), 2.90 (t, *J* = 7.8 Hz, 2H), 2.61 (t, *J* = 7.9 Hz, 2H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -59.33 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.26, 141.88 (q, *J* = 4.0 Hz), 137.03, 135.99, 128.97 (q, *J* = 2.0 Hz), 128.18, 128.01, 127.59, 124.96 (q, *J* = 28.8 Hz), 124.30 (q, *J* = 273.5 Hz), 114.45, 113.35, 55.17, 26.83, 22.89 (q, *J* = 2.4 Hz).
IR(KBr): 2932, 2839, 1607, 1573, 1494, 1313, 1171, 1099, 700 cm^{-1}.
HRMS (EI):calcd. For [$C_{18}H_{15}F_3O$] 304.1075, found 304.1079.

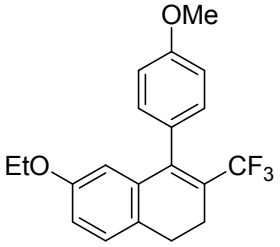
Obtained according to General Procedure **A**:



2t

4-(4-Methoxyphenyl)-3-(trifluoromethyl)-2H-chromene (**2t**): 34%; white oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 7.7 Hz, 1H), 7.13 (d, *J* = 8.3 Hz, 2H), 7.02 – 6.91 (m, 3H), 6.84 (t, *J* = 7.5 Hz, 1H), 6.73 (d, *J* = 7.6 Hz, 1H), 4.89 (s, 2H), 3.85 (s, 3H).
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.07 (s, 3F).
^{13}C NMR (101 MHz, $CDCl_3$) δ 159.55, 154.60, 140.46 (q, *J* = 4.0 Hz), 131.25, 130.12 (q, *J* = 1.8 Hz), 128.12, 126.64, 124.00, 122.84 (q, *J* = 272.8 Hz), 121.78, 117.33 (q, *J* = 29.8 Hz), 116.11, 113.64, 63.20 (q, *J* = 3.6 Hz), 55.25.
IR(KBr): 2923, 2851, 1608, 1511, 1341, 1247, 1101, 1012, 829 cm^{-1}.
HRMS (EI):calcd. For [$C_{17}H_{13}F_3O_2$] 306.0868, found 306.0869.

Compounds **2a'** was obtained according to general procedure **B** except that EtOH was used instead of MeOH:

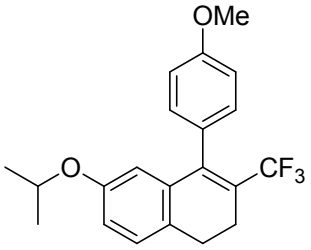


2a'

6-Ethoxy-4-(4-methoxyphenyl)-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2a'**): yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 – 7.05 (m, 3H), 6.92 (d, *J* = 8.7 Hz, 2H), 6.74 (dd, *J* = 8.2, 2.4 Hz, 1H), 6.28 (d, *J* = 2.3 Hz, 1H), 3.88 – 3.79 (m, 5H), 2.87 (t, *J* = 7.9 Hz, 2H), 2.58 (t, *J* = 8.0 Hz, 2H), 1.29 (t, *J* = 7.0 Hz, 3H).
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.12 (s, 3F).
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.99, 157.61, 141.77 (q, *J* = 4.0 Hz), 136.30, 130.19 (d, *J* = 1.9 Hz), 129.19, 128.14, 127.94, 125.04 (q, *J* = 28.5 Hz), 124.38 (q, *J* = 273.4 Hz), 114.98, 113.94, 113.47, 63.43, 55.21, 26.87, 22.95 (q, *J* = 2.5 Hz), 14.71.

IR(KBr): 2978, 2929, 2847, 1608, 1511, 1315, 1245, 1179, 1101, 833 cm^{-1}.
HRMS (EI):calcd. For [$C_{20}H_{19}F_3O_2$] 348.1337, found 348.1332.

Compound **2a''** was prepared according to general procedure **B** except that *i*PrOH was used instead of MeOH:

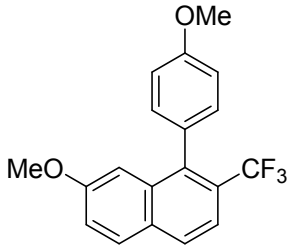


2a''

6-Isopropoxy-4-(4-methoxyphenyl)-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2a''**): yellow oil.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 – 7.02 (m, 3H), 6.93 (d, *J* = 8.6 Hz, 2H), 6.74 (dd, *J* = 8.2, 2.3 Hz, 1H), 6.26 (d, *J* = 2.1 Hz, 1H), 4.29 (sept, *J* = 5.6 Hz, 1H), 3.85 (s, 3H), 2.86 (t, *J* = 7.8 Hz, 2H), 2.58 (t, *J* = 7.9 Hz, 2H), 1.20 (d, *J* = 6.0 Hz, 6H).
^{19}F NMR (376 MHz, $CDCl_3$) δ -59.12 (s, 3F).
^{13}C NMR (101 MHz, $CDCl_3$) δ 158.91, 156.40, 141.73 (q, *J* = 3.8 Hz), 136.28, 130.13 (q, *J* = 1.2 Hz), 129.17, 128.02, 127.90, 124.88 (q, *J* = 28.8 Hz), 124.34 (q, *J* = 273.0 Hz), 116.23, 115.37, 113.40, 69.80, 55.19, 26.82, 22.91 (q, *J* = 2.2 Hz), 21.85.
IR(KBr): 2975, 2931, 2839, 1608, 1510, 1314, 1245, 1175, 1098, 830 cm^{-1}.
HRMS (EI):calcd. For [$C_{21}H_{21}F_3O_2$] 362.1494, found 362.1493.

4. Procedure for the synthesis of 3, 4, 5.

Into the solution of **2a** (33.4mg, 0.1 mmol) in toluene (3.0 mL) was added DDQ (25.0mg, 0.11 mmol). The resulting mixture was refluxed for 12 h. The reaction was quenched with sat. $NaHCO_3$ at room temperature. The mixture was extracted with CH_2Cl_2. The combined organic phase was washed with brine and then dried over $MgSO_4$. The solvent was removed by concentration. The residue was subjected to flash column chromatography to give the desired product **3** as a white solid.



3

7-Methoxy-1-(4-methoxyphenyl)-2-(trifluoromethyl)naphthalene (**3**): 92%; white solid; M.P.: 101 ^{o}C.
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.6 Hz, 1H), 7.80 (d, *J* = 8.9 Hz, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 7.25 – 7.19 (m, 3H), 7.01 (d, *J* = 8.6 Hz, 2H), 6.72 (s, 1H), 3.90 (s, 3H), 3.65 (s, 3H).

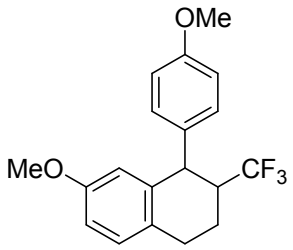
^{19}F NMR (376 MHz, CDCl3) δ -56.31 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.16, 158.24, 138.31 (q, *J* = 2.2 Hz), 134.99, 131.20 (d, *J* = 1.2 Hz), 130.17, 129.32, 129.08, 127.60, 126.70 (q, *J* = 28.8 Hz), 124.53 (q, *J* = 274.4 Hz), 120.32, 119.56 (q, *J* = 5.1 Hz), 113.33, 105.87, 55.24, 55.12.

IR(KBr): 2959, 2924, 2852, 1622, 1609, 1512, 1461, 1339, 1223, 1120, 1034, 843 cm^{-1}.

HRMS (EI):calcd. For [$C_{19}H_{15}F_3O_2$] 332.1024, found 332.1023.

Into the solution of **2a** (33.4mg, 0.1mmol) in ethanol (1 mL) was added 15% Pd/C. The reaction mixture was stirred at room temperature for overnight under H_2 atmosphere. After filtration followed by concentration, the residue was purified by flash chromatography to give the product **4**.



4

7-Methoxy-1-(4-methoxyphenyl)-2-(trifluoromethyl)-1,2,3,4-tetrahydronaphthalene (**4**): quantitative yield; colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.5 Hz, 1H), 6.96 (d, *J* = 8.6 Hz, 2H), 6.81 – 6.64 (m, 3H), 6.43 (d, *J* = 2.5 Hz, 1H), 4.40 (d, *J* = 4.6 Hz, 1H), 3.75 (s, 3H), 3.65 (s, 3H), 3.09 - 3.00 (m, 1H), 2.98 – 2.82 (m, 1H), 2.78 – 2.61 (m, 1H), 2.11 – 1.90 (m, 2H).

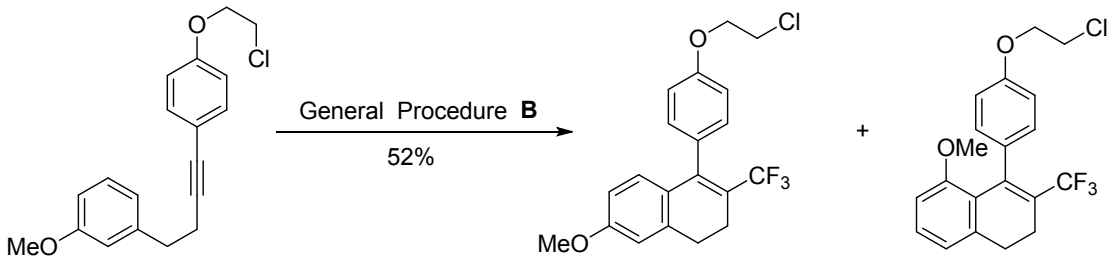
^{19}F NMR (376 MHz, $CDCl_3$) δ -68.16 (d, *J* = 9.4 Hz, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 158.34, 157.98, 139.22, 133.43, 131.30, 129.77, 127.31 (q, *J* = 279.6 Hz), 127.23, 114.59, 113.67, 113.22, 55.18, 55.11, 44.21 (q, *J* = 25.4 Hz), 43.23 (q, *J* = 1.8 Hz), 27.45, 17.22 (q, *J* = 2.5 Hz).

IR(KBr): 2954, 2917, 2839, 1611, 1507, 1254, 1096, 1035, 814 cm^{-1}.

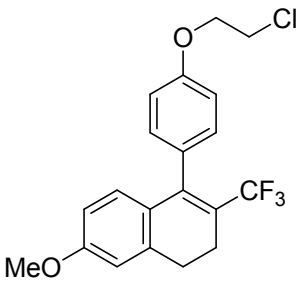
HRMS (EI):calcd. For [$C_{19}H_{19}F_3O_2$] 336.1337, found 336.1339.

Procedure for the synthesis of 5:



1u **2u** **2u'**

2.3 : 1



2u

4-(4-(2-Chloroethoxy)phenyl)-7-methoxy-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2u**): colorless oil.

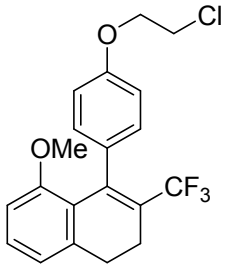
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8.6 Hz, 2H), 6.94 (d, *J* = 8.6 Hz, 2H), 6.74 (d, *J* = 1.7 Hz, 1H), 6.64 – 6.54 (m, 2H), 4.26 (t, *J* = 5.8 Hz, 2H), 3.84 (t, *J* = 5.9 Hz, 2H), 3.78 (s, 3H), 2.91 (t, *J* = 7.9 Hz, 2H), 2.58 (t, *J* = 7.9 Hz, 2H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -58.68 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 160.01, 157.58, 141.37 (q, *J* = 4.1 Hz), 138.10, 130.41, 130.30 (q, *J* = 1.8 Hz), 129.31, 128.23, 124.57 (q, *J* = 273.0 Hz), 121.98 (q, *J* = 28.7 Hz), 114.18, 113.35, 111.26, 68.00, 55.29, 41.96, 28.22, 22.52 (q, *J* = 2.6 Hz).

IR(KBr): 2920,2851, 1607, 1244, 1149, 1069, 801, 737 cm^{-1}.

HRMS (EI):calcd. For [$C_{20}H_{18}ClF_3O_2$] 382.0947, found 382.0945.



2u'

4-(4-(2-Chloroethoxy)phenyl)-5-methoxy-3-(trifluoromethyl)-1,2-dihydronaphthalene (**2u'**): white solid; M.P.: 95 °C.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 7.9 Hz, 1H), 7.09 (d, *J* = 8.6 Hz, 2H), 6.87 – 6.81 (m, 3H), 6.67 (d, *J* = 8.3 Hz, 1H), 4.25 (t, *J* = 6.0 Hz, 2H), 3.83 (t, *J* = 5.9 Hz, 2H), 3.22 (s, 3H), 2.81 (t, *J* = 7.7 Hz, 2H), 2.46 (t, *J* = 7.7 Hz, 2H).

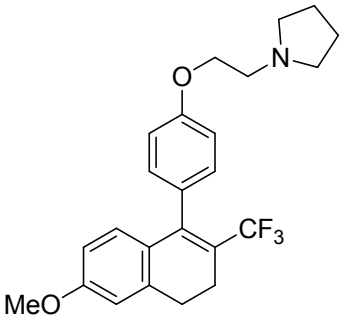
^{19}F NMR (376 MHz, $CDCl_3$) δ -57.22 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 157.88, 156.83, 140.89 (q, *J* = 3.9 Hz), 139.98, 133.40, 129.88, 129.48 (q, *J* = 2.1 Hz), 125.53 (q, *J* = 28.4 Hz), 124.64, 124.41 (q, *J* = 273.2 Hz), 119.90, 113.17, 111.85, 68.04, 55.57, 42.01, 29.32, 22.80 (q, *J* = 2.8 Hz).

IR(KBr): 3002, 2922, 2849, 1606, 1569, 1509, 1243, 1146, 1068, 831 cm^{-1}.

HRMS (EI):calcd. For [$C_{20}H_{18}ClF_3O_2$] 382.0947, found 382.0944.

Into the solution of **2u** (38.2mg, 0.1mmol) in ethanol (0.5mL) was added pyrrolidine (0.5 mL). The resulting mixture was stirred at 100 °C for 4 h. After evaporation, the residue was purified by flash chromatography to give the pure Nafoxidine analogue **5.**



5

1-(2-(4-(6-Methoxy-2-(trifluoromethyl)-3,4-dihydronaphthalen-1-yl)phenoxy)ethyl)pyrrolidine (**5**): 82%; colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, *J* = 8.5 Hz, 2H), 6.91 (d, *J* = 8.6 Hz, 2H), 6.72 (d, *J* = 1.2 Hz, 1H), 6.63 – 6.46 (m, 2H), 4.22 (t, *J* = 5.6 Hz, 2H), 3.77 (s, 3H), 3.04 (t, *J* = 5.3 Hz, 2H), 2.89 (t, *J* = 7.8 Hz, 2H), 2.86 – 2.72 (m, 4H), 2.56 (t, *J* = 7.8 Hz, 2H), 1.96 – 1.82 (m, 4H).

^{19}F NMR (376 MHz, $CDCl_3$) δ -58.69 (s, 3F).

^{13}C NMR (101 MHz, $CDCl_3$) δ 159.98, 157.89, 141.43 (q, *J* = 4.5 Hz), 138.07, 130.19, 129.96, 129.36, 128.30, 124.58 (q, *J* = 271.9 Hz), 121.89 (q, *J* = 28.6 Hz), 114.04, 113.32, 111.23, 66.24, 55.29, 54.90, 54.68, 28.24, 23.48, 22.51 (q, *J* = 2.5 Hz).

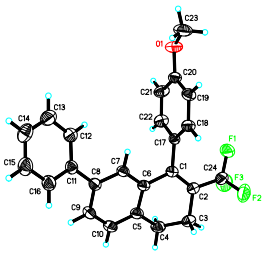
IR(KBr): 2960, 2934, 1608, 1510, 1246, 1149, 1096, 1069, 1036, 833, 804 cm^{-1}.

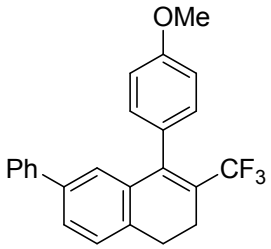
HRMS (ESI):calcd. For $[C_{24}H_{27}F_3NO_2]$ $[M+H]^+$ 418.1988, found 418.1990.

References

1. A. Walkinshaw, W. Xu, M. Suero and M. Gaunt, *J. Am. Chem. Soc.*, 2013, **135**, 12532-12535.
2. T. Satoh, Y. Hayashi and K. Yamakawa, *Bull. Chem. Soc. Jpn.*, 1993, **66**, 1866-1869.

5. Crystal data and structure refinement for 2h.



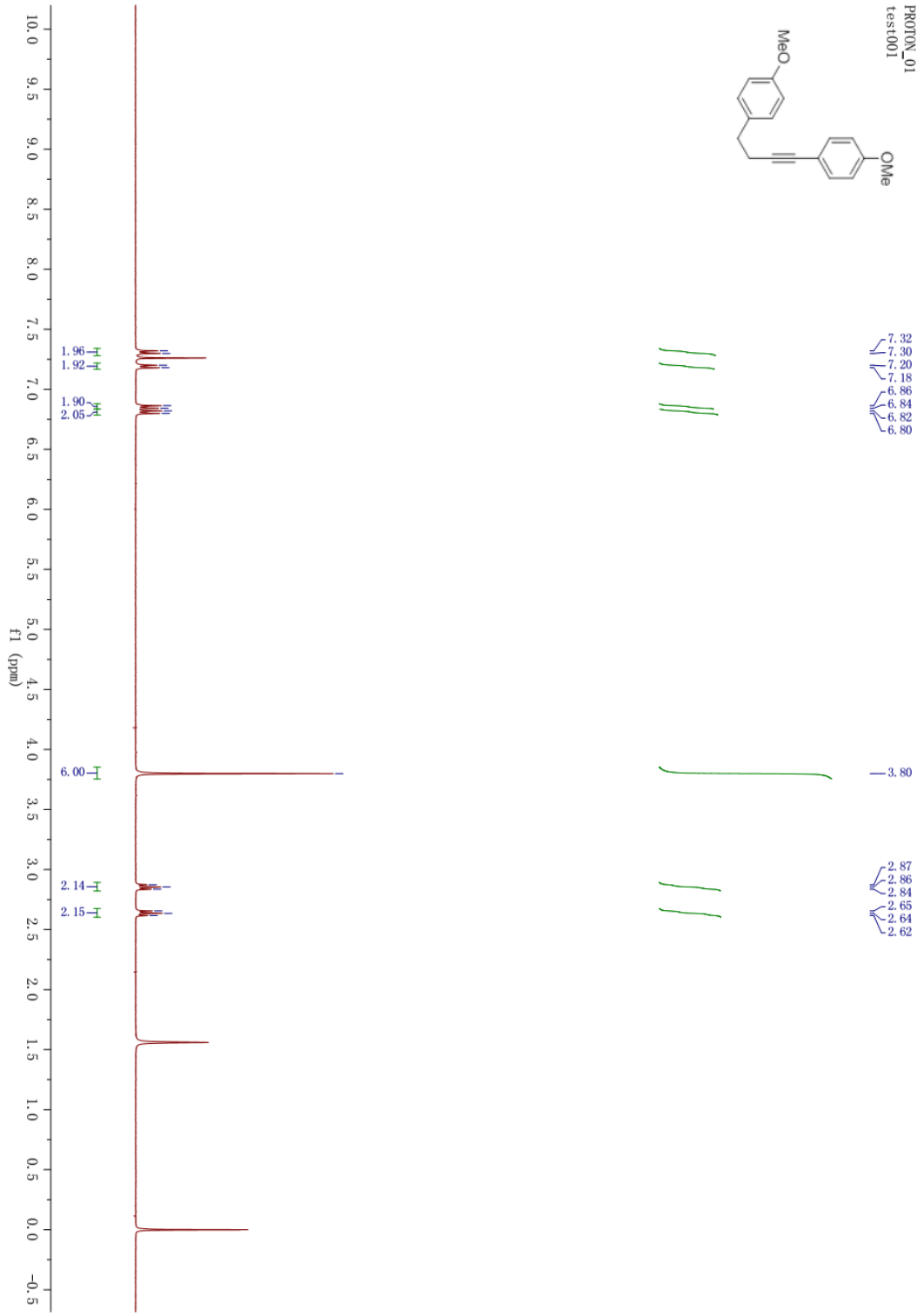


2h

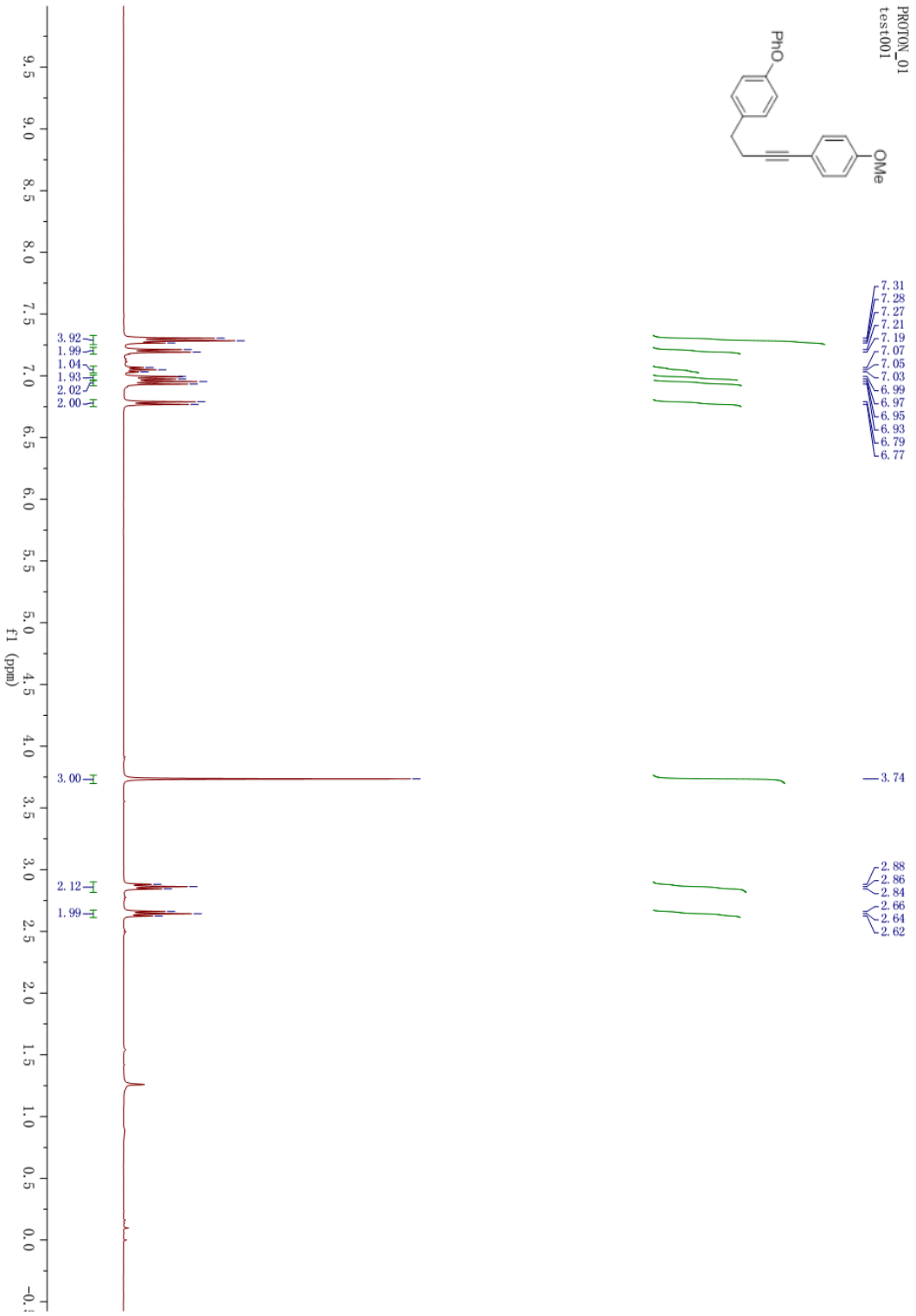
Empirical formula	$C_{24}H_{19}F_3O$	
Formula weight	380.39	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 5.3668(8) Å	α= 82.874(3)°.
	b = 9.6287(15) Å	β= 86.417(4)°.
	c = 18.804(3) Å	γ = 82.471(4)°.
Volume	954.8(3) $Å^3$	
Z	2	
Density (calculated)	1.323 Mg/m^3	
Absorption coefficient	0.099 mm^{-1}	
F(000)	396	
Crystal size	0.211 x 0.143 x 0.078 mm^3	
Theta range for data collection	2.148 to 25.994°.	
Index ranges	-6<=h<=5, -10<=k<=11, -23<=l<=22	
Reflections collected	5822	
Independent reflections	3747 [R(int) = 0.0342]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7457 and 0.4299	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3747 / 0 / 254	
Goodness-of-fit on F^2	1.053	
Final R indices [I>2sigma(I)]	R1 = 0.0619, wR2 = 0.1801	
R indices (all data)	R1 = 0.0872, wR2 = 0.2022	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.368 and -0.253 $e.Å^{-3}$	

6. Copies of NMR Spectra.

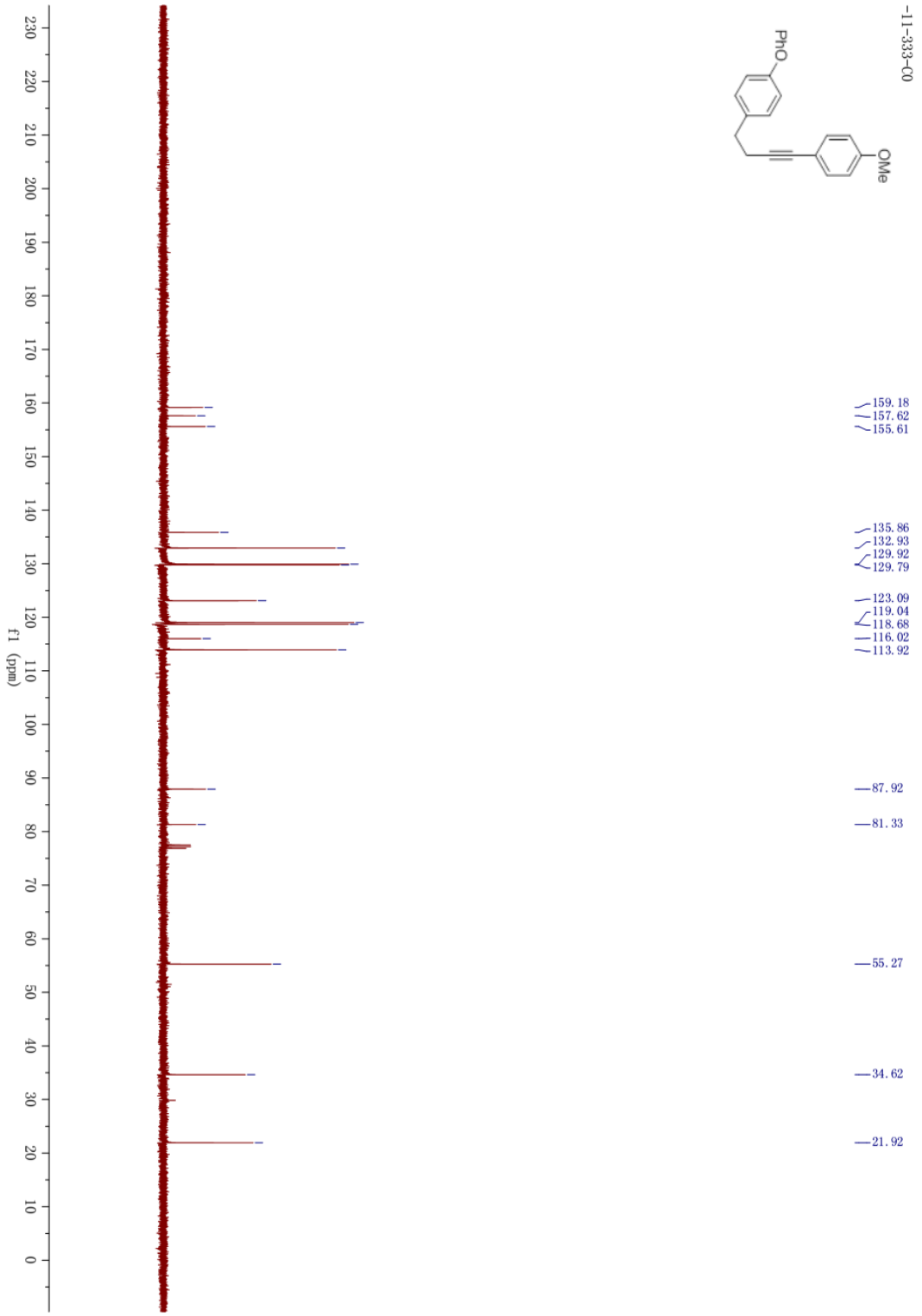
^{1}H NMR spectrum of compound **1a**



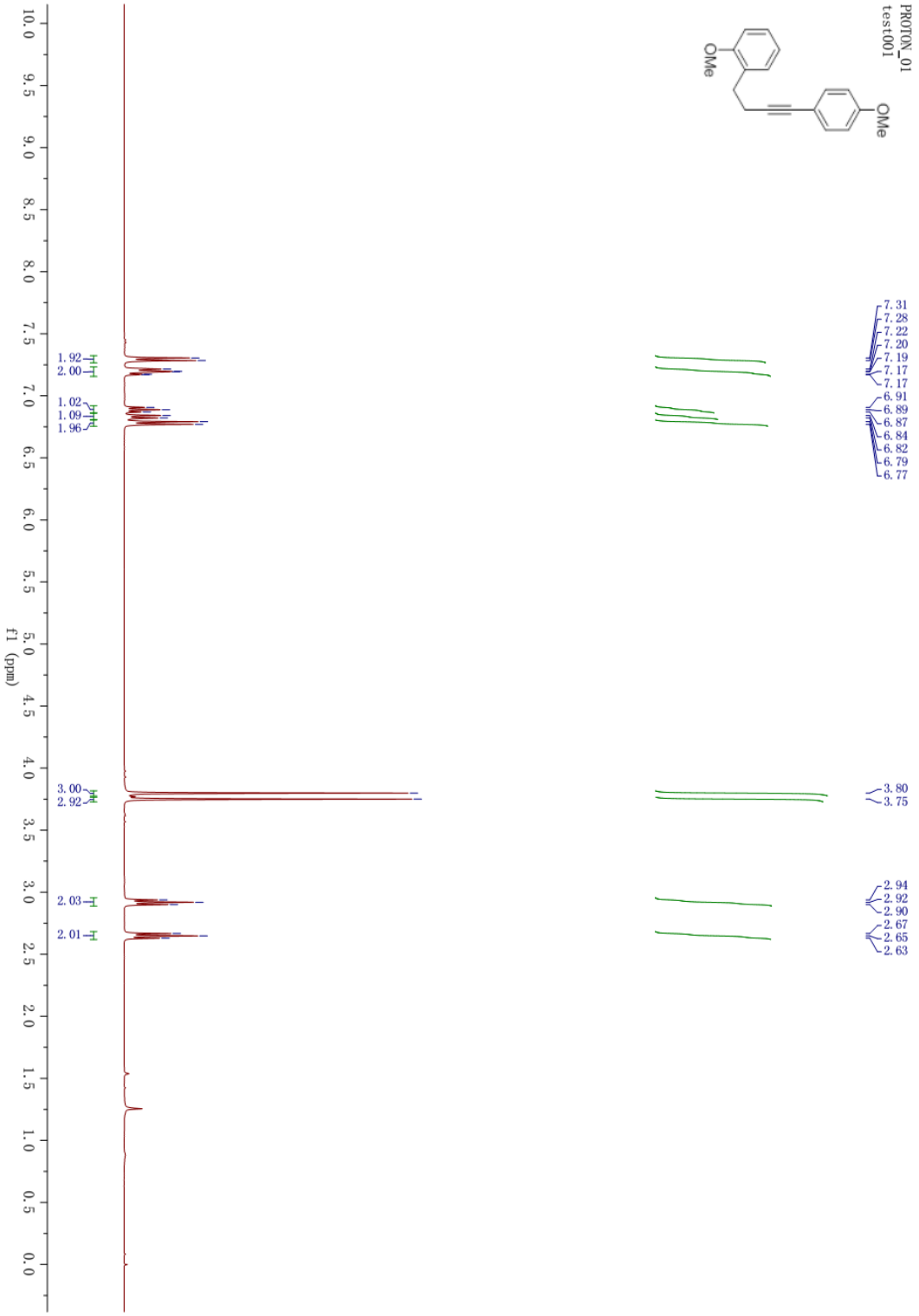
^{1}H NMR spectrum of compound **1b**



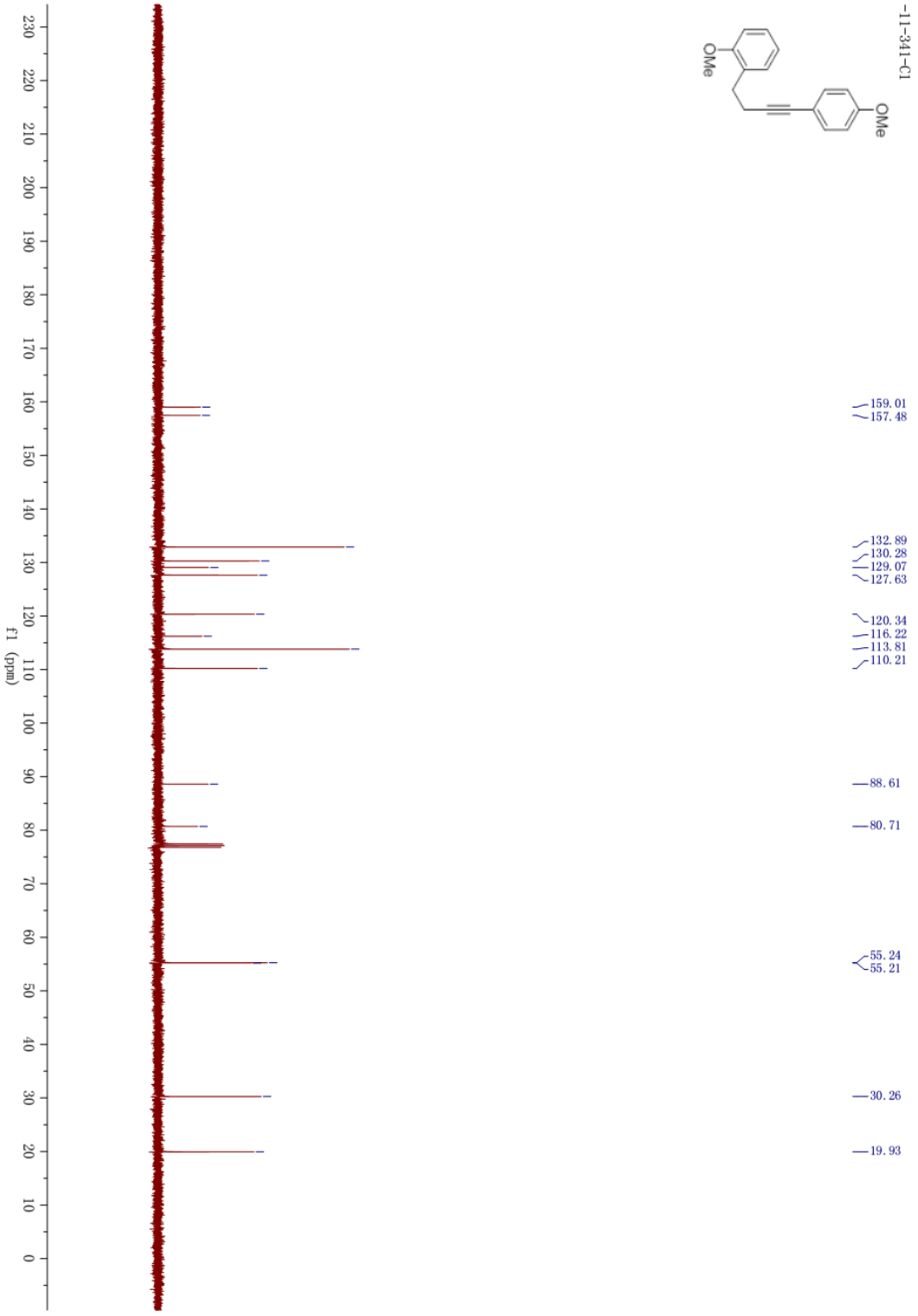
^{13}C NMR spectrum of compound **1b**



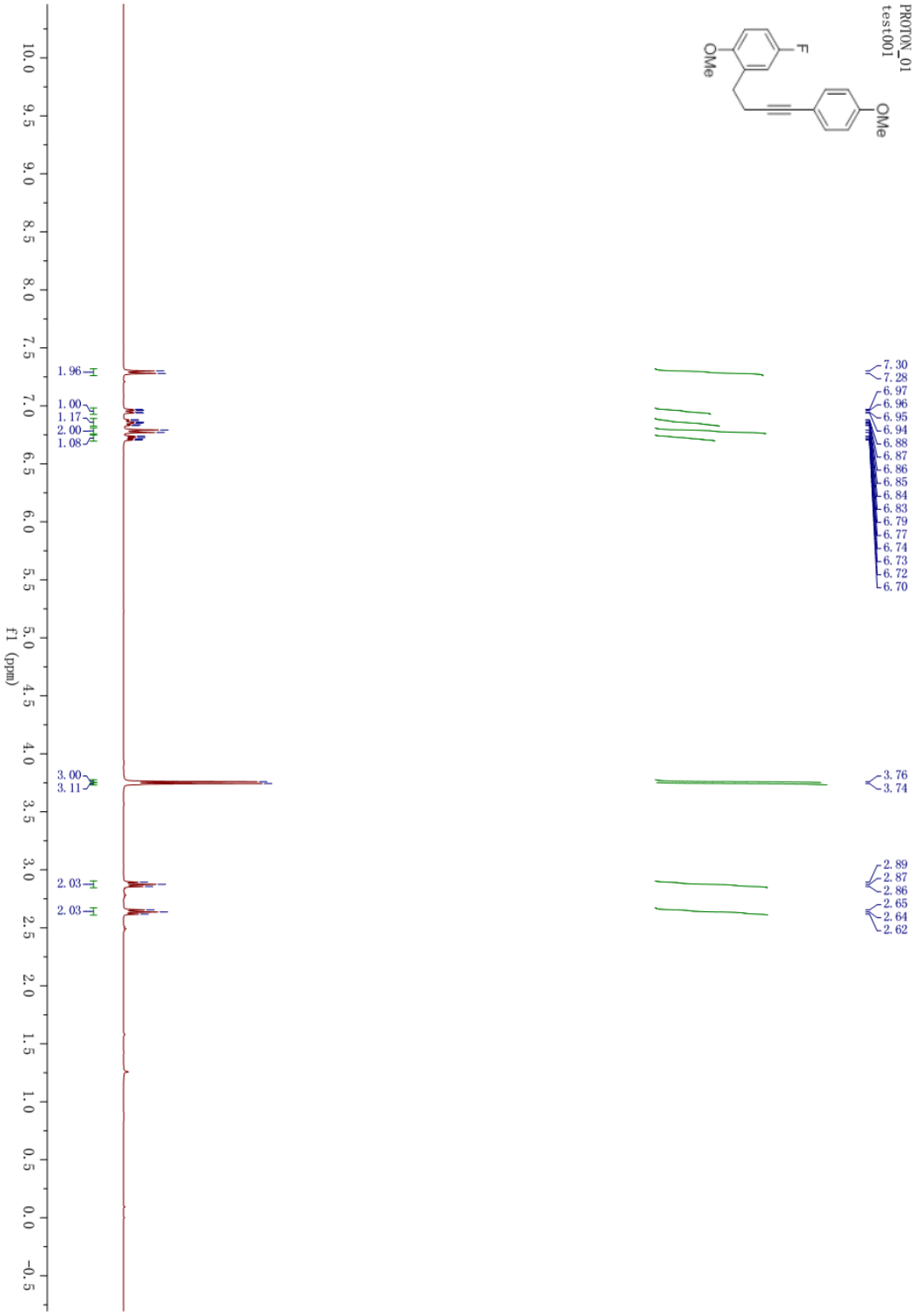
^{1}H NMR spectrum of compound **1c**



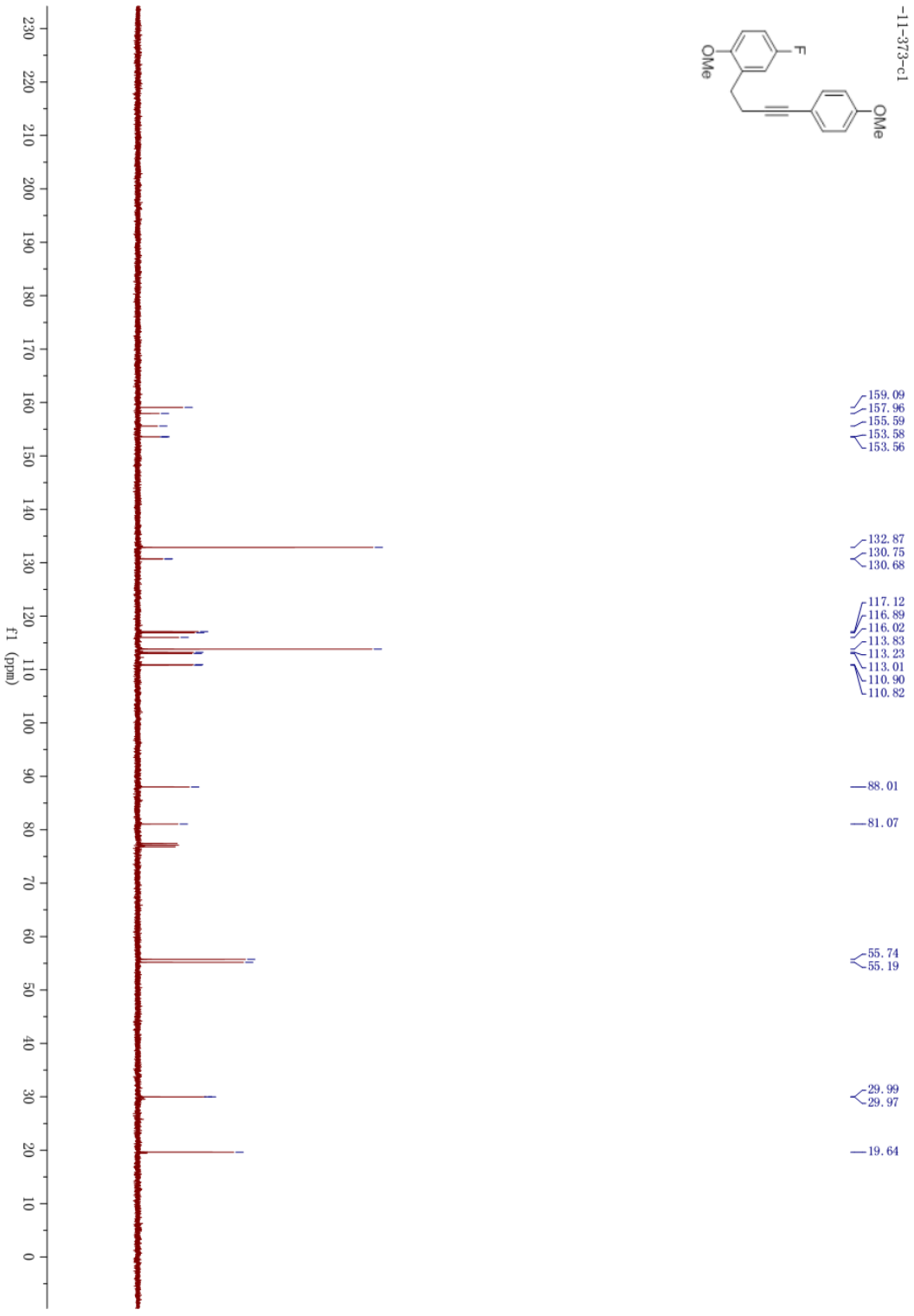
^{13}C NMR spectrum of compound **1c**



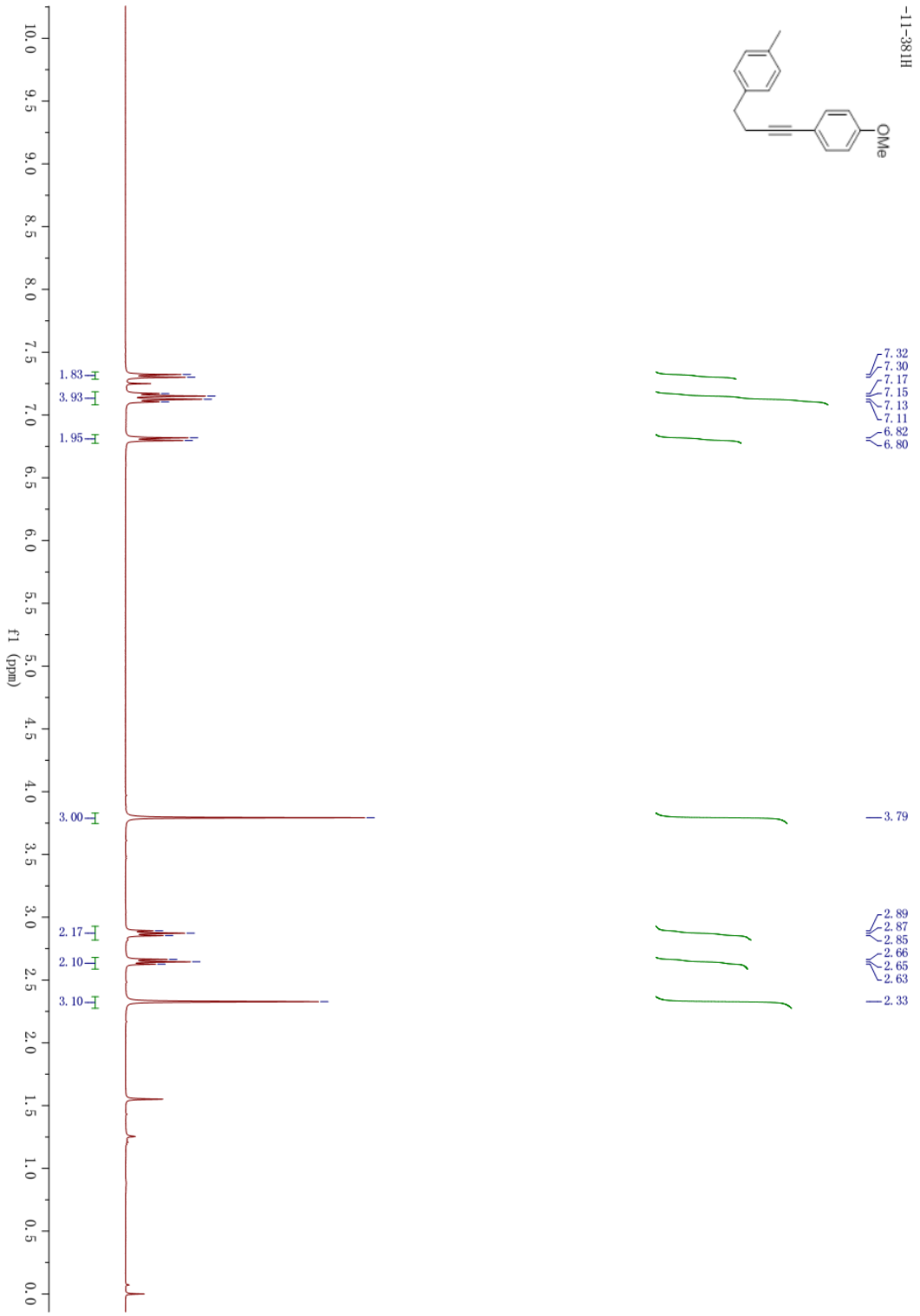
^{1}H NMR spectrum of compound **1d**



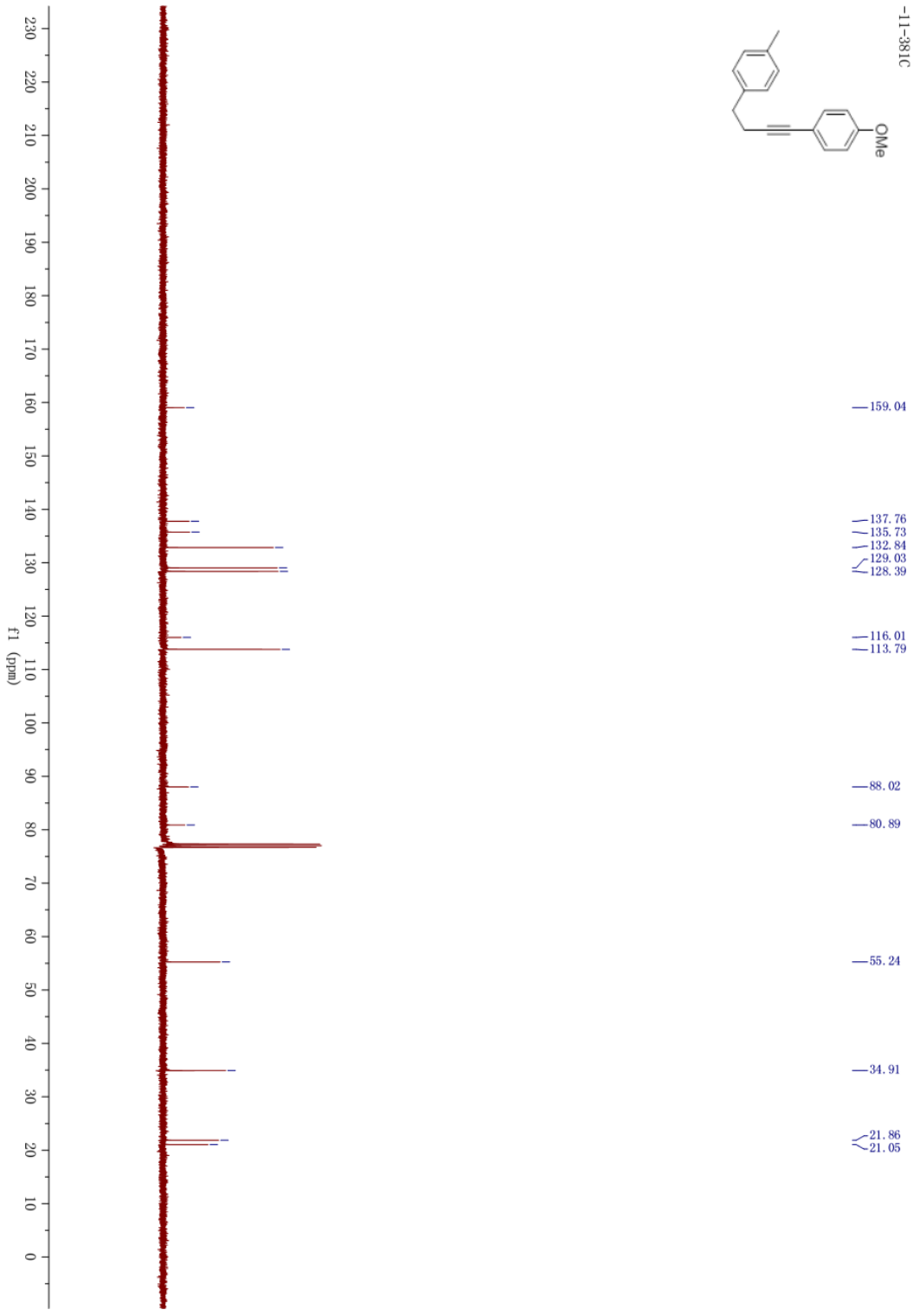
^{13}C NMR spectrum of compound **1d**



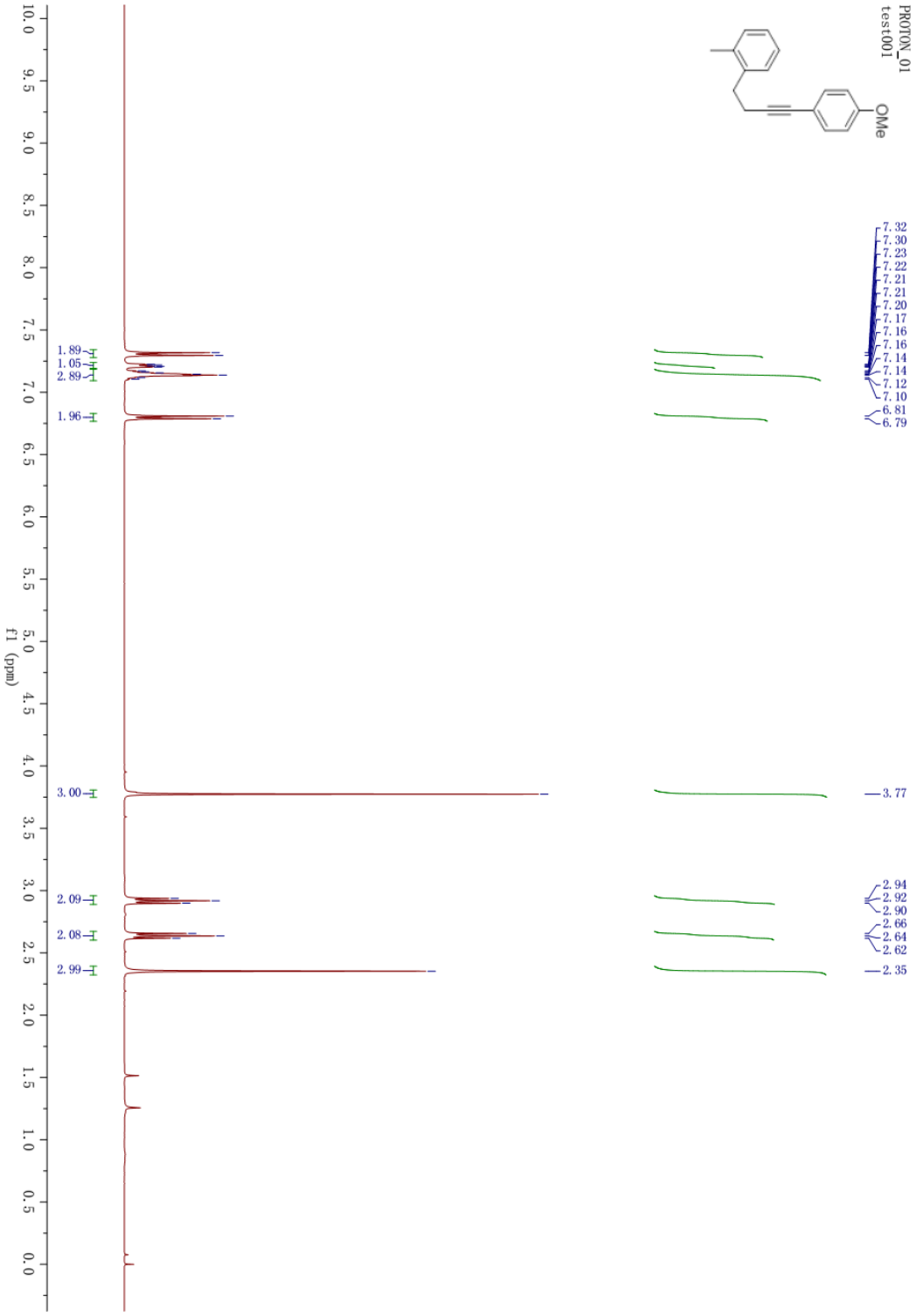
^{1}H NMR spectrum of compound **1e**



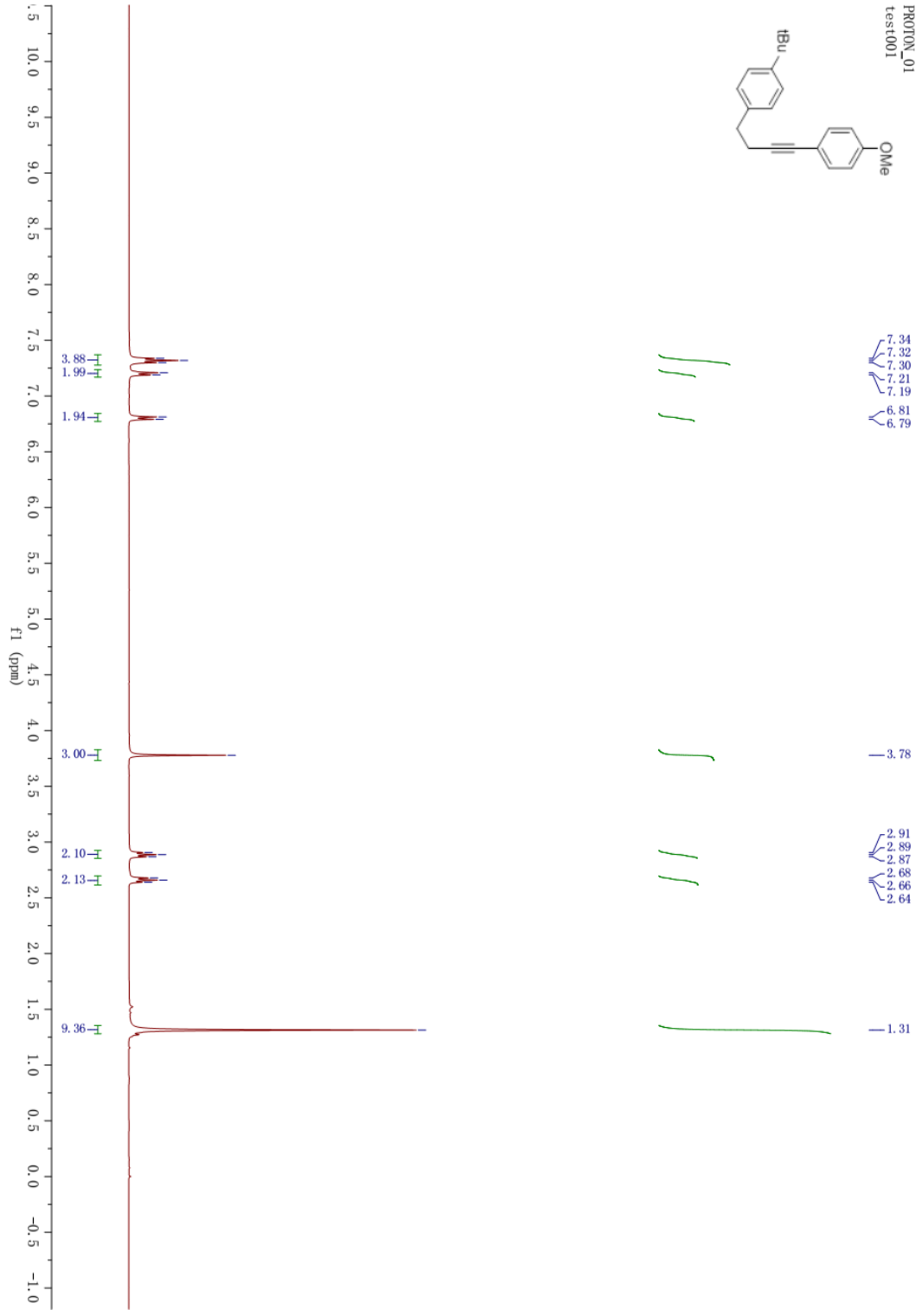
^{13}C NMR spectrum of compound **1e**



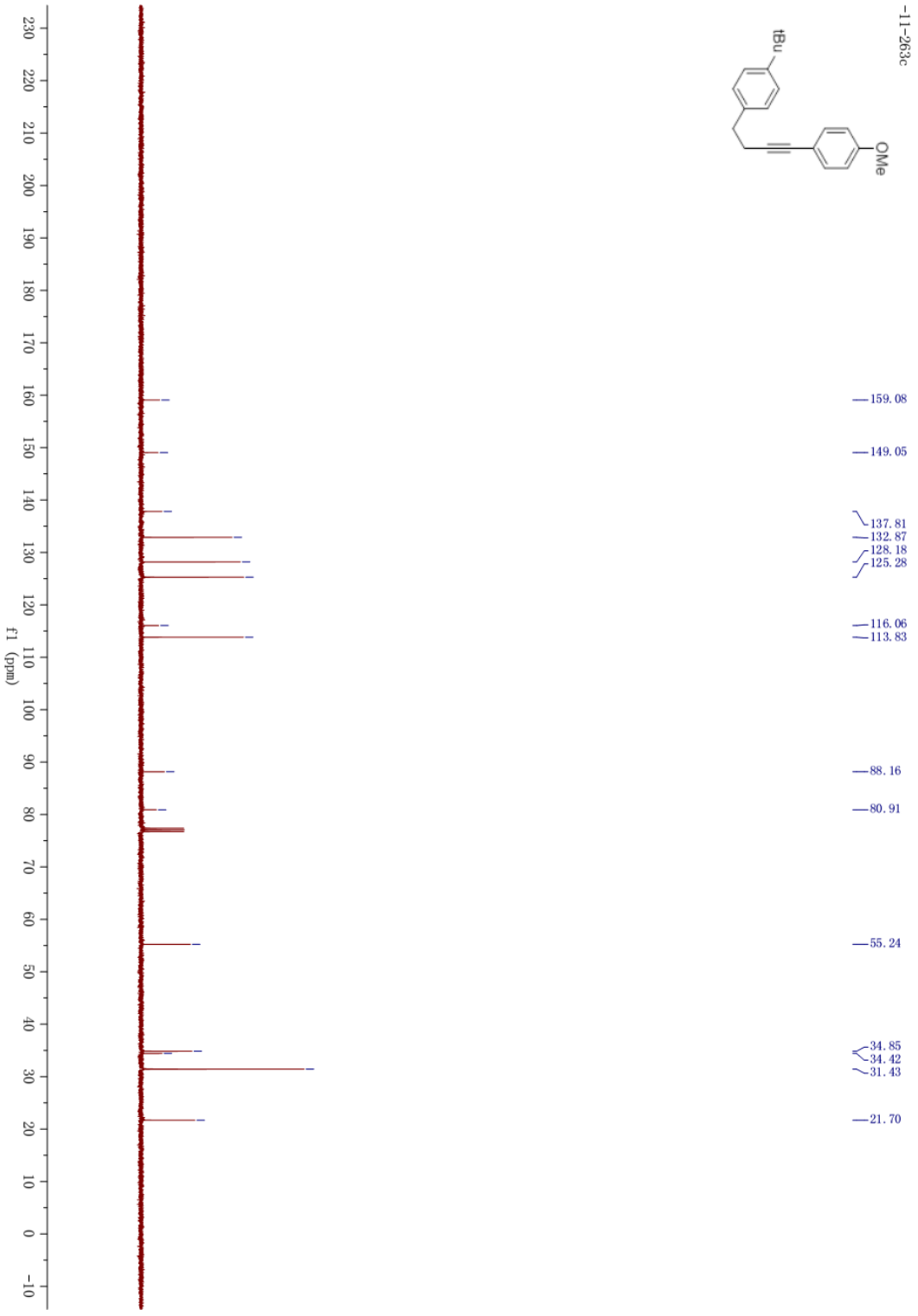
^{1}H NMR spectrum of compound **1f**



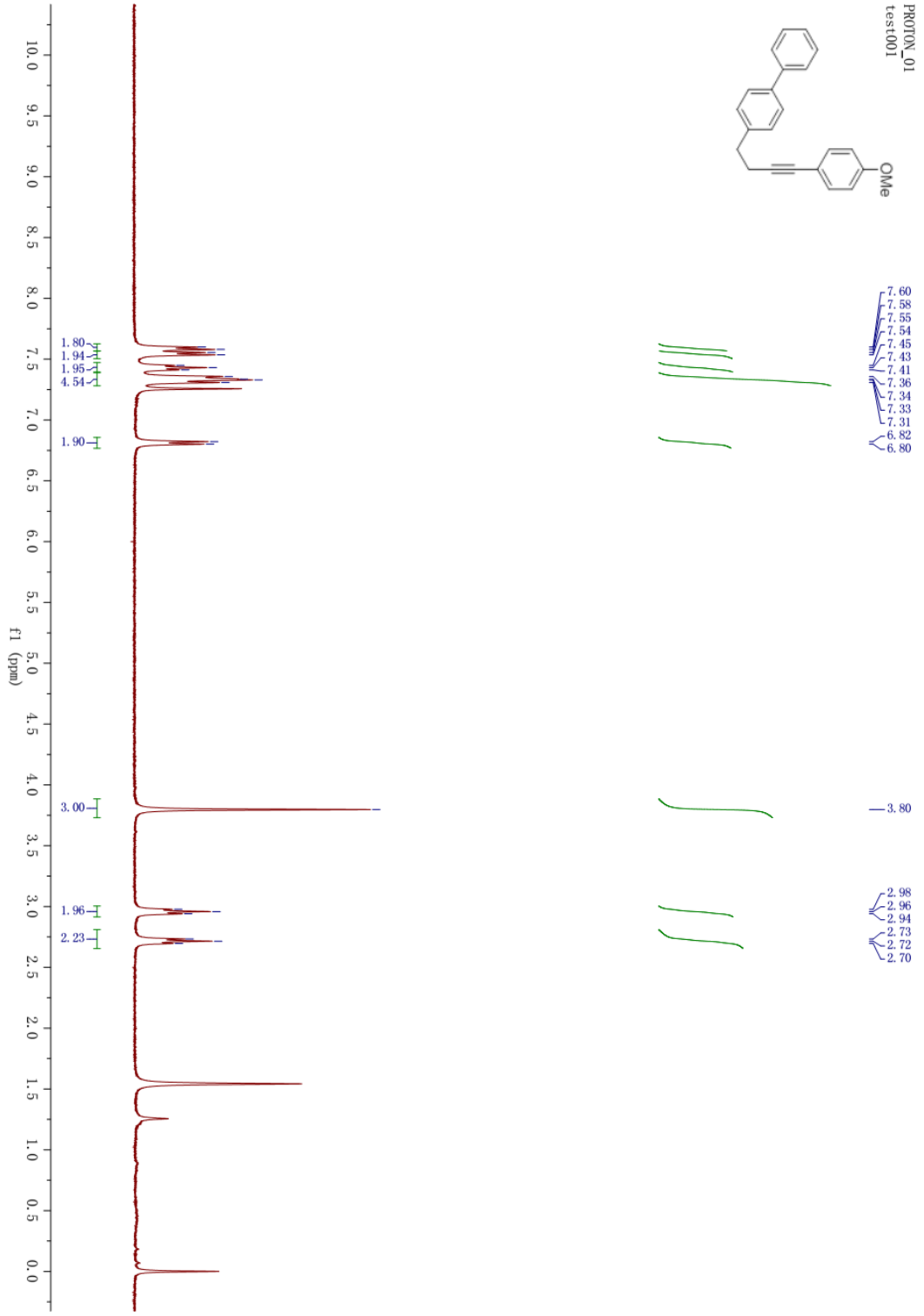
^{1}H NMR spectrum of compound **1g**



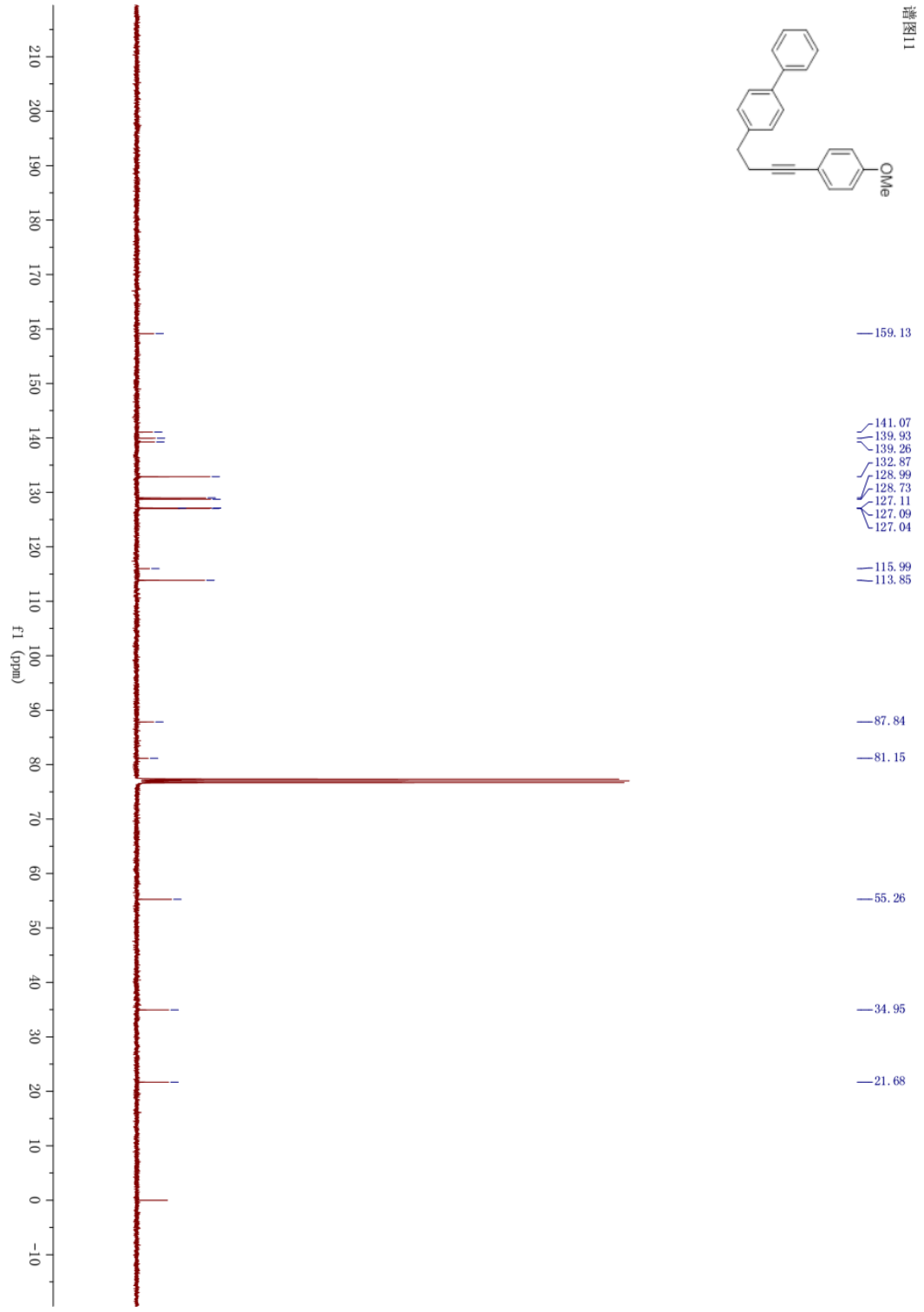
^{13}C NMR spectrum of compound **1g**



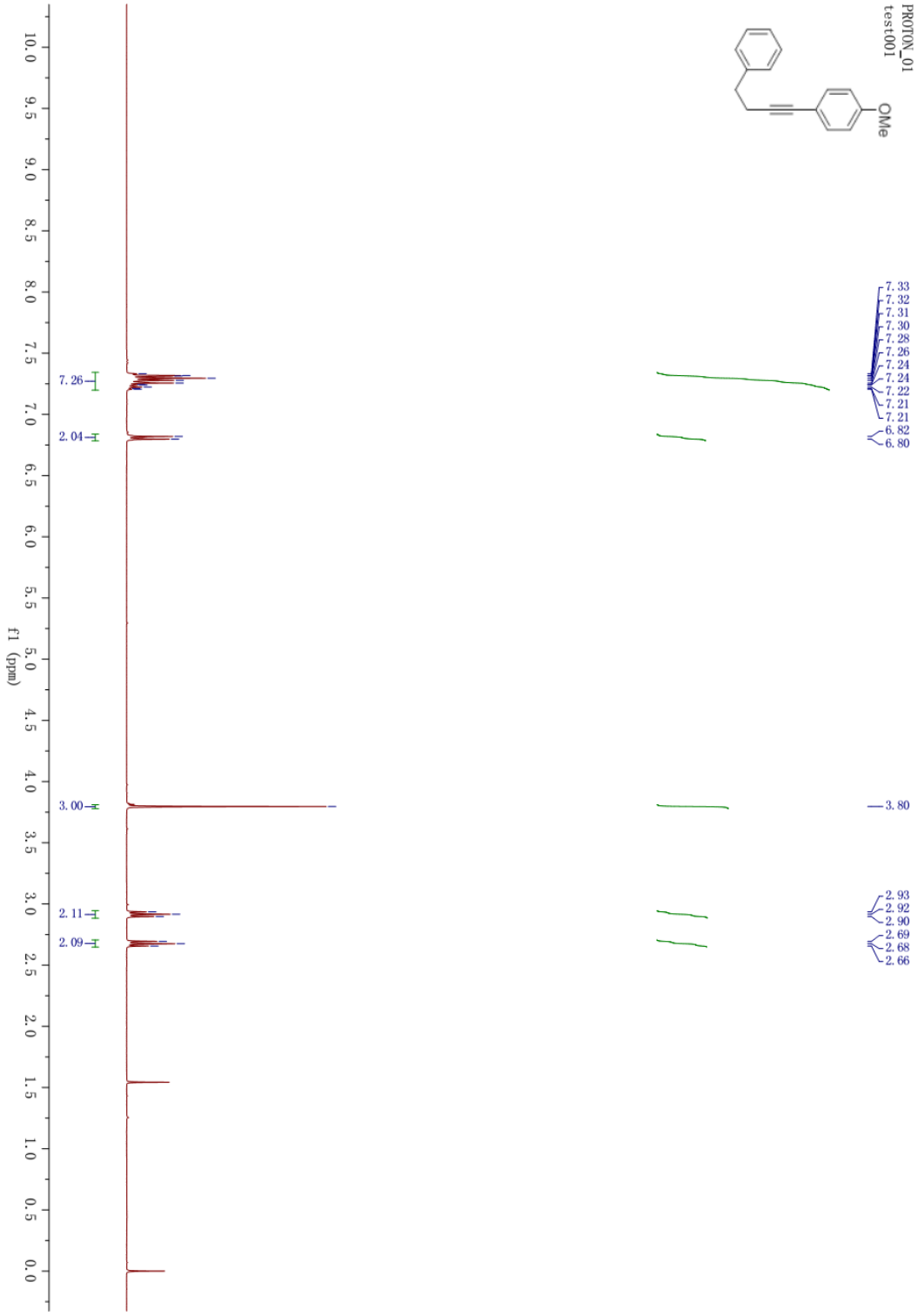
^{1}H NMR spectrum of compound **1h**



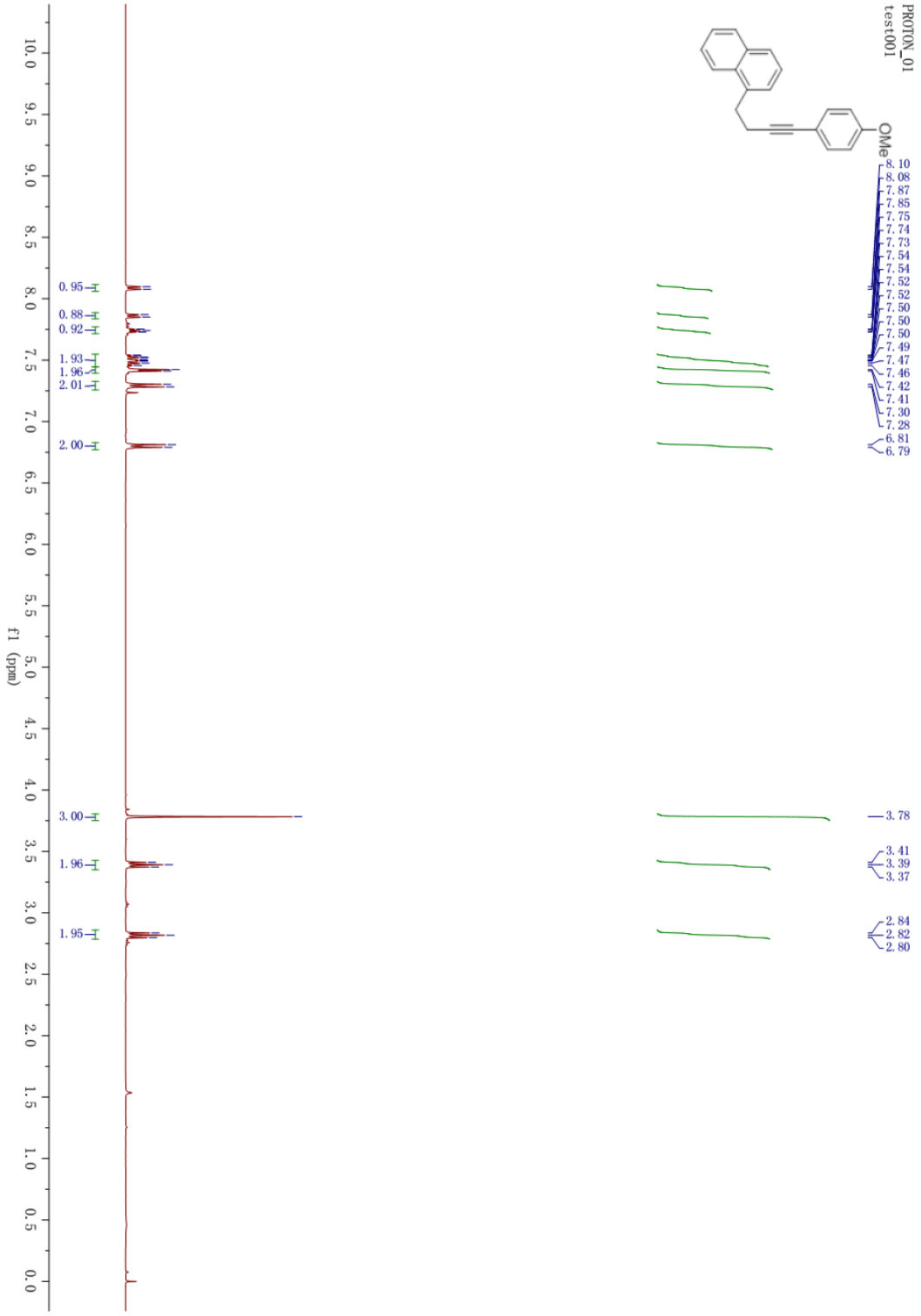
^{13}C NMR spectrum of compound **1h**



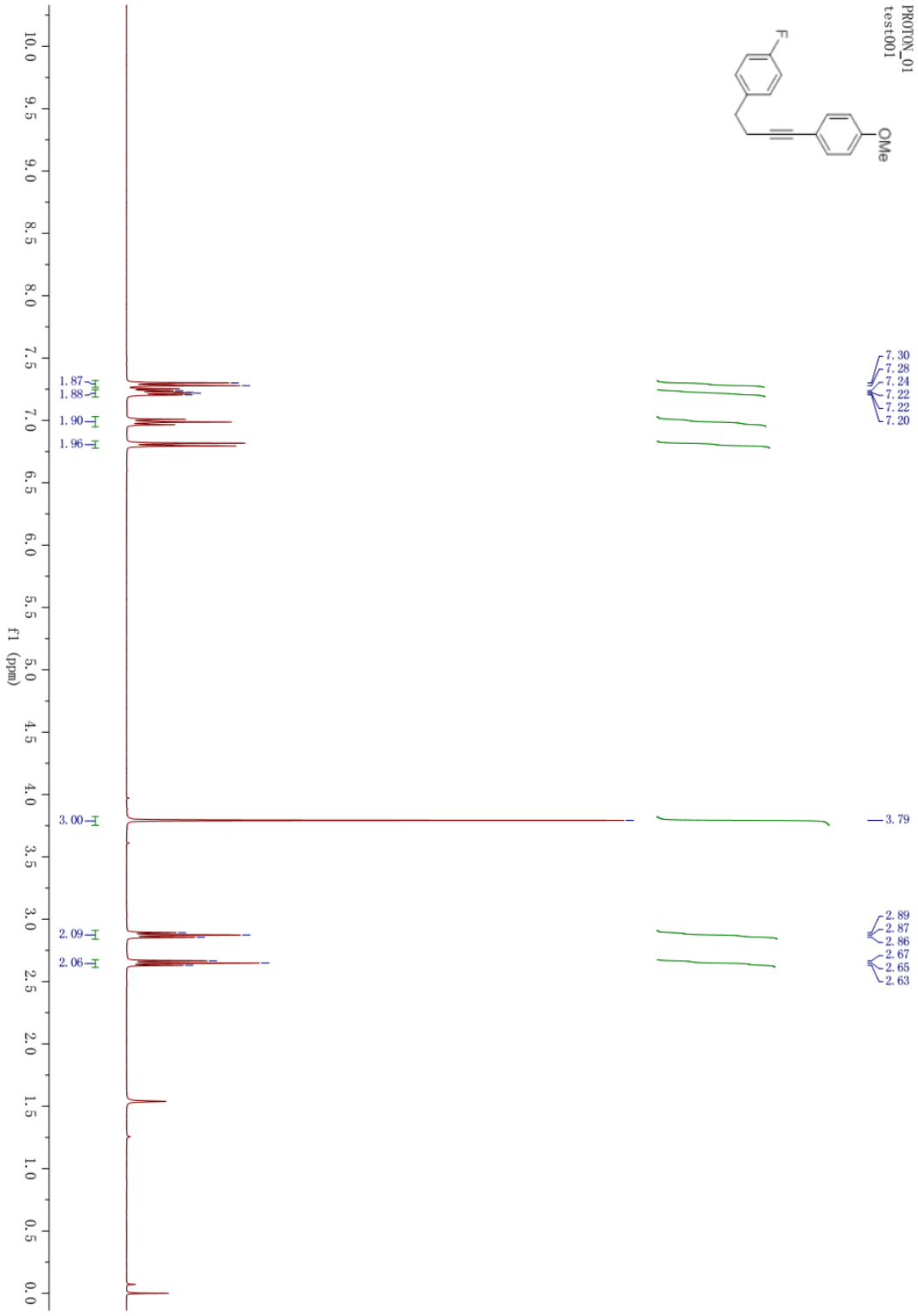
^{1}H NMR spectrum of compound **1i**



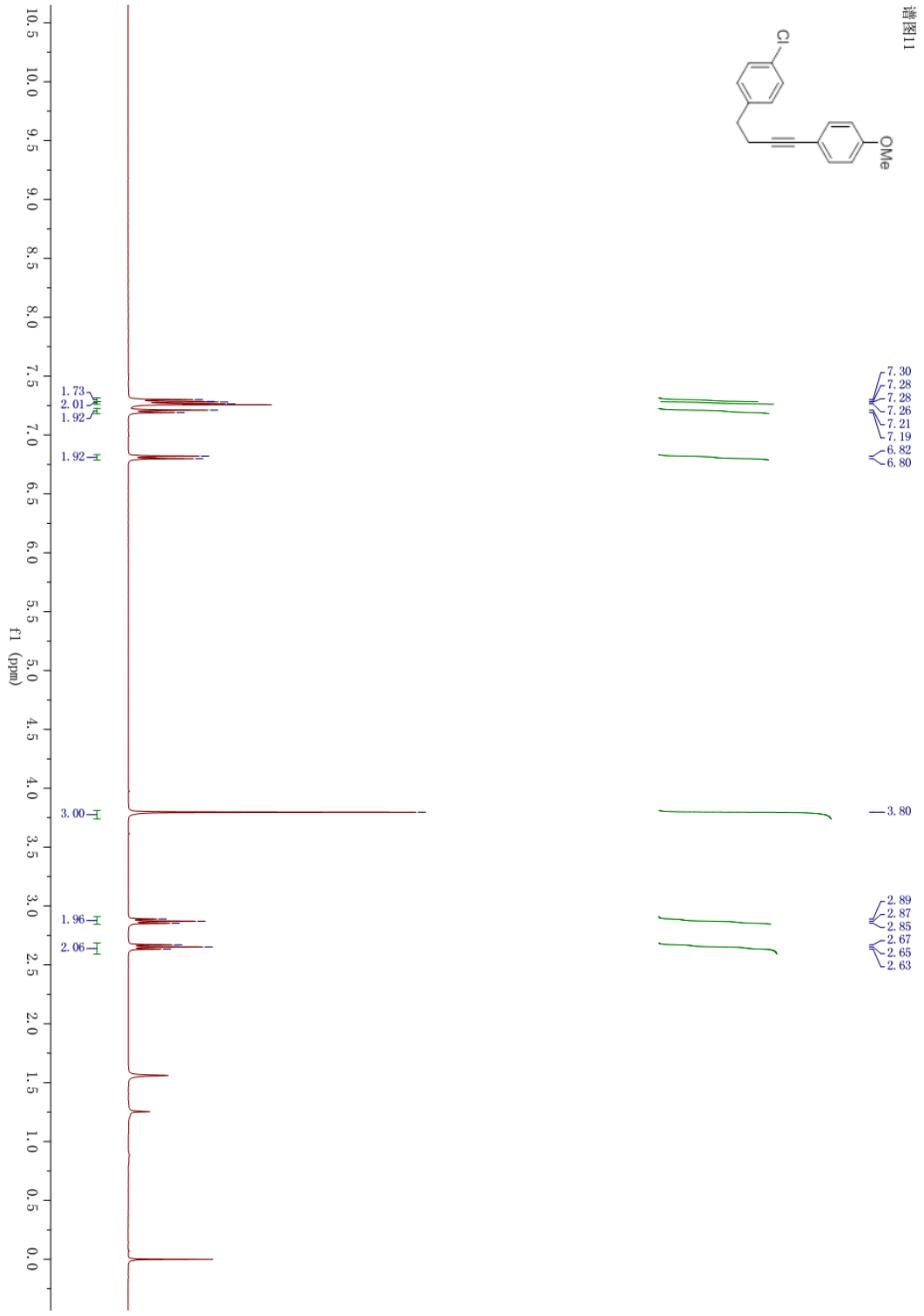
^{1}H NMR spectrum of compound **1j**



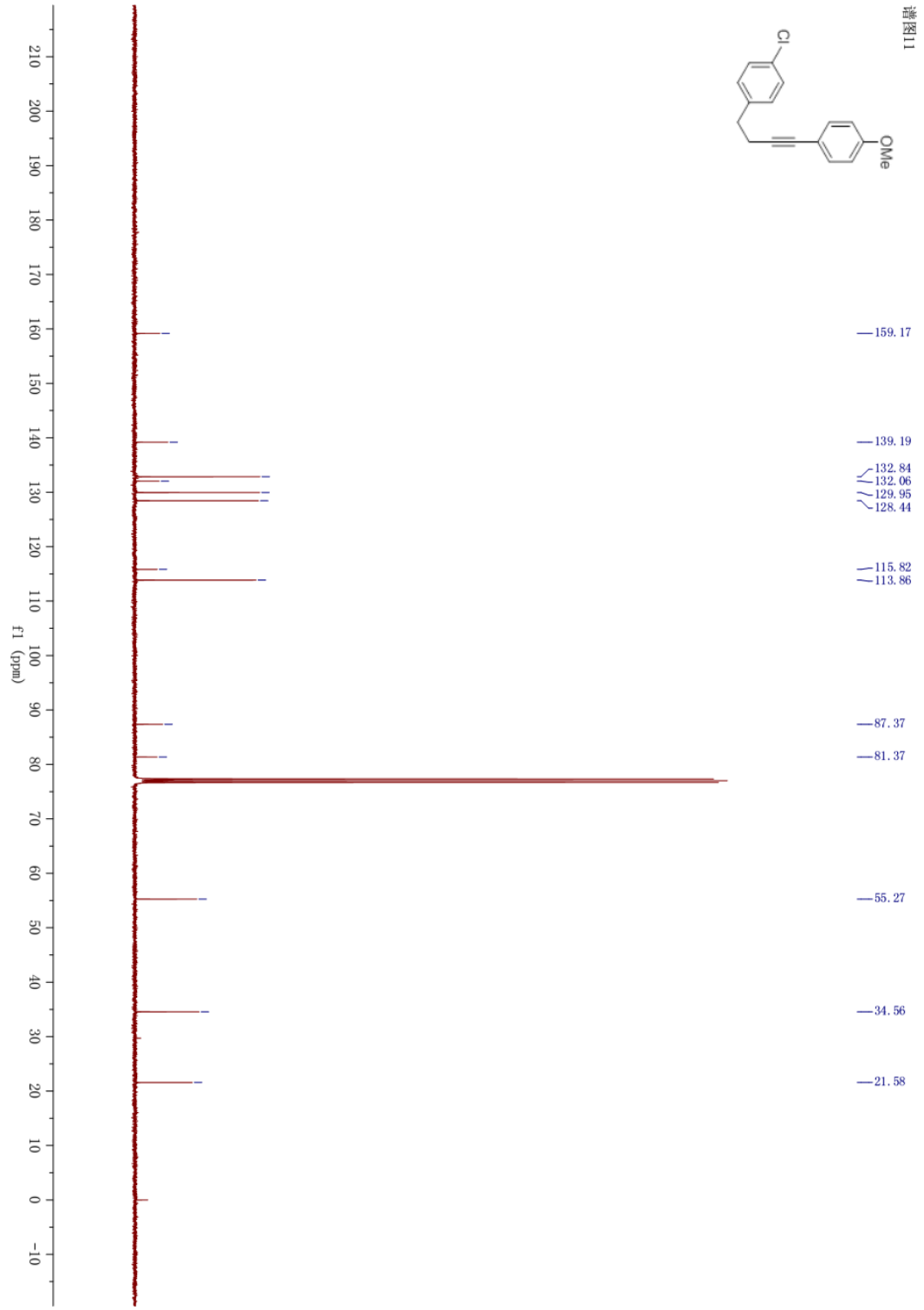
^{1}H NMR spectrum of compound **1k**



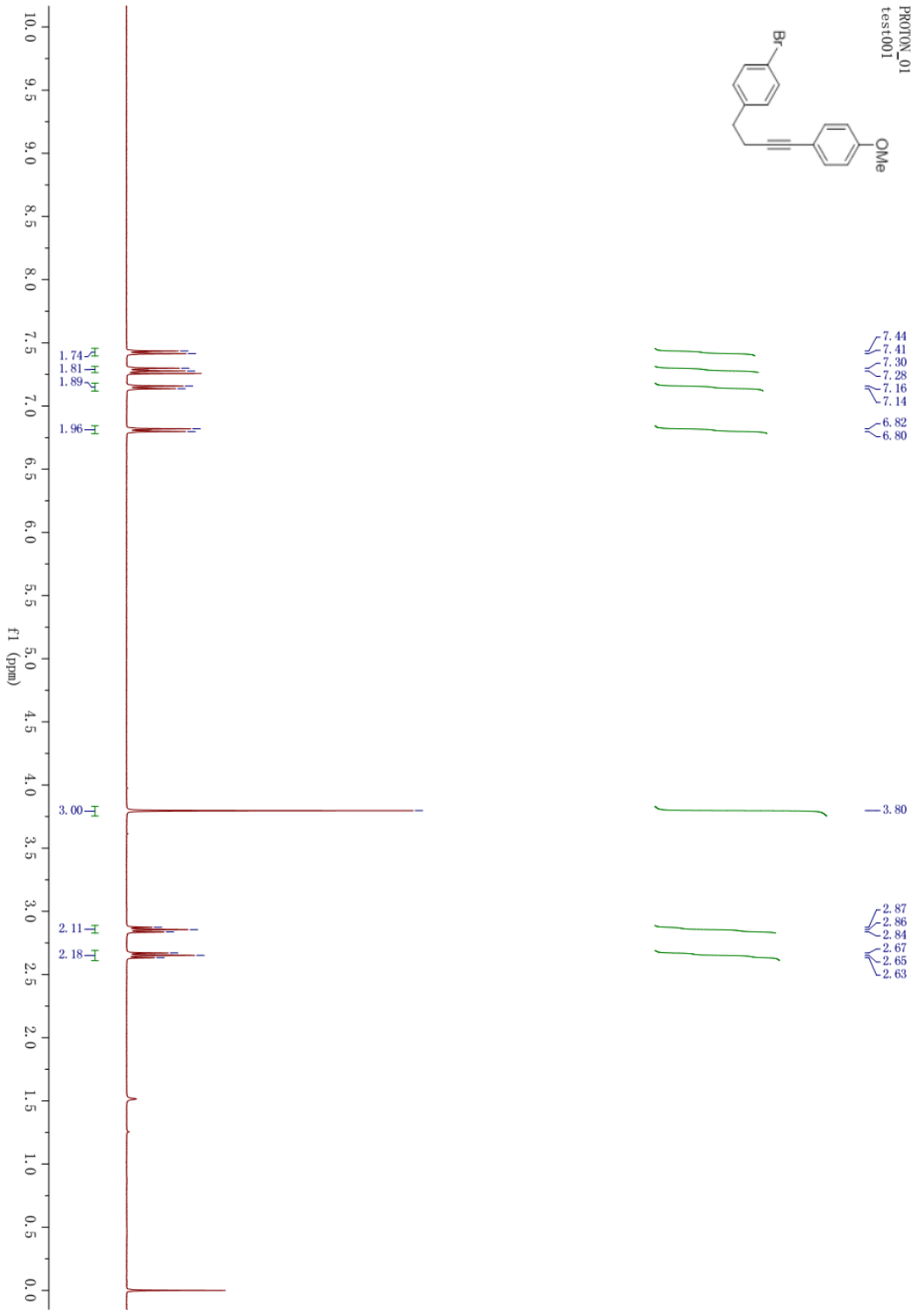
^{1}H NMR spectrum of compound **1l**



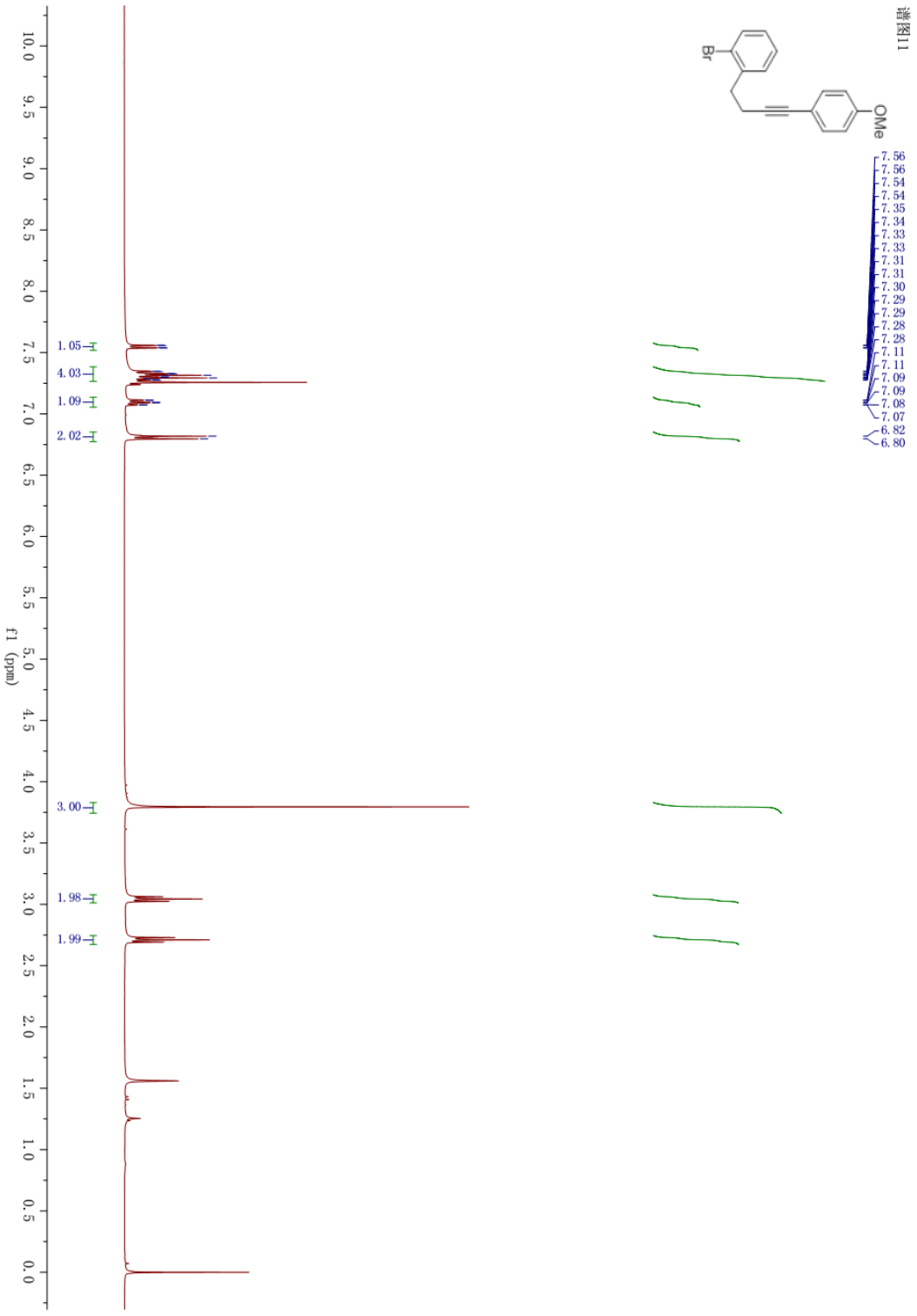
^{13}C NMR spectrum of compound **1l**



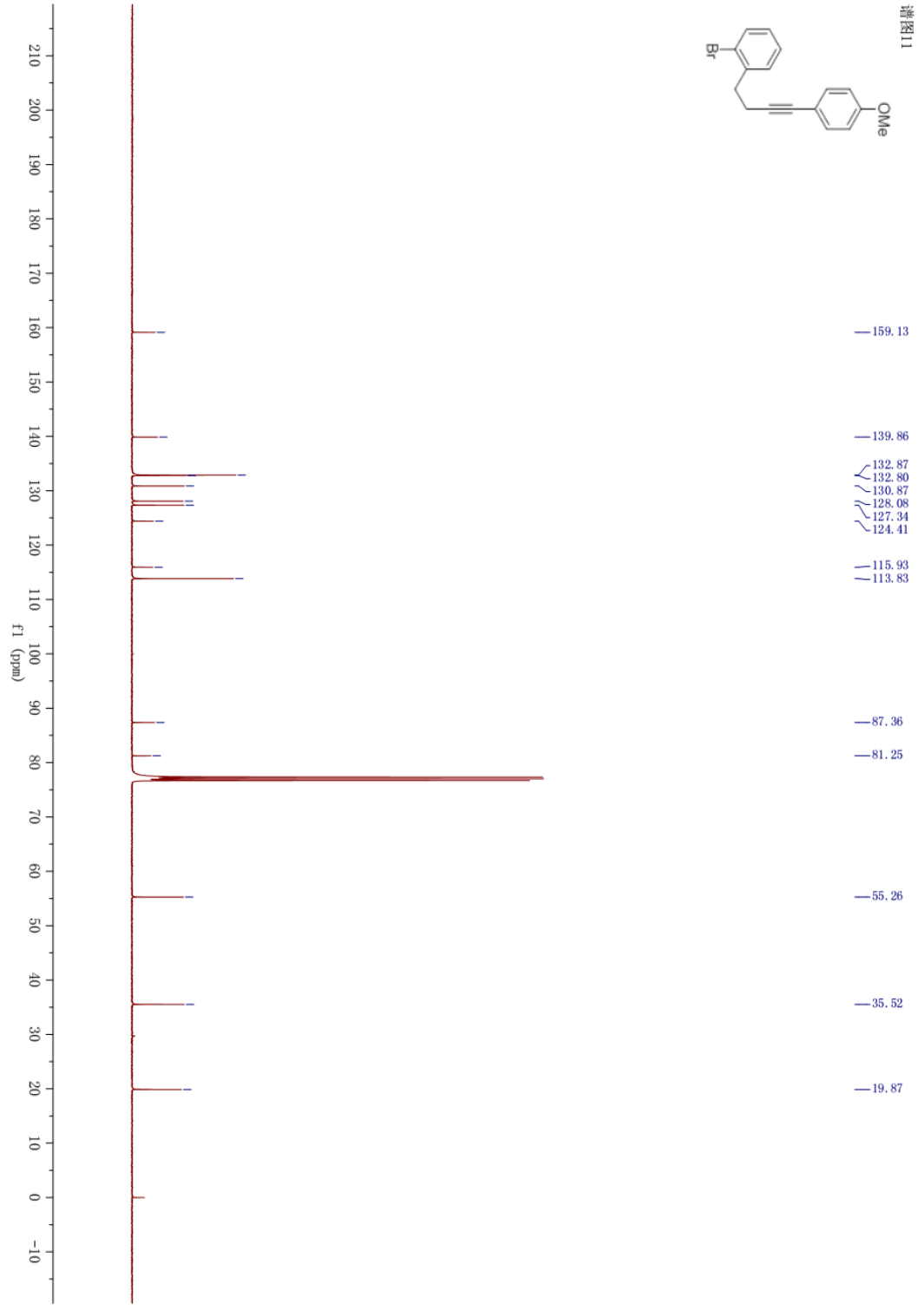
^{1}H NMR spectrum of compound **1m**



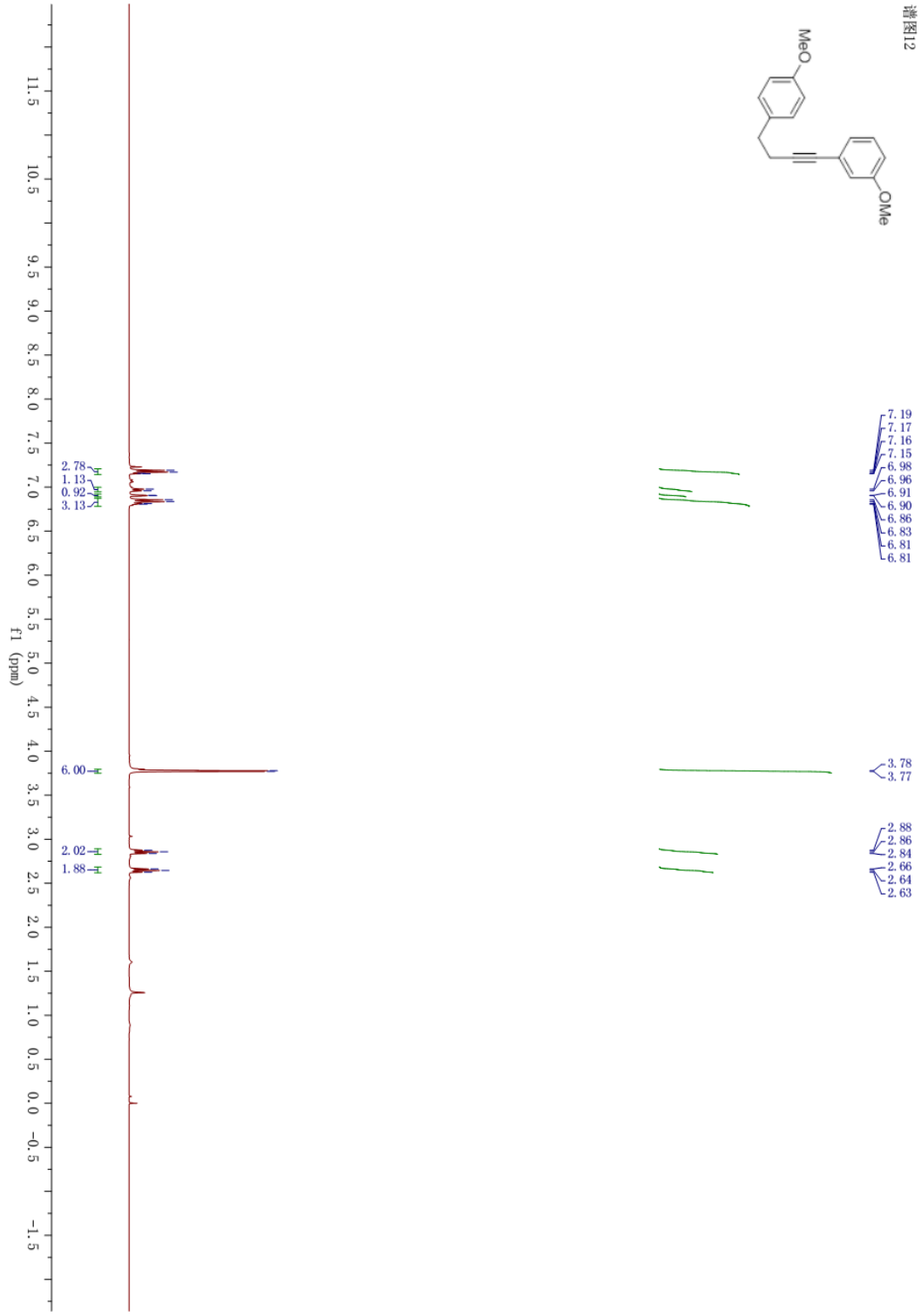
^{1}H NMR spectrum of compound **1n**



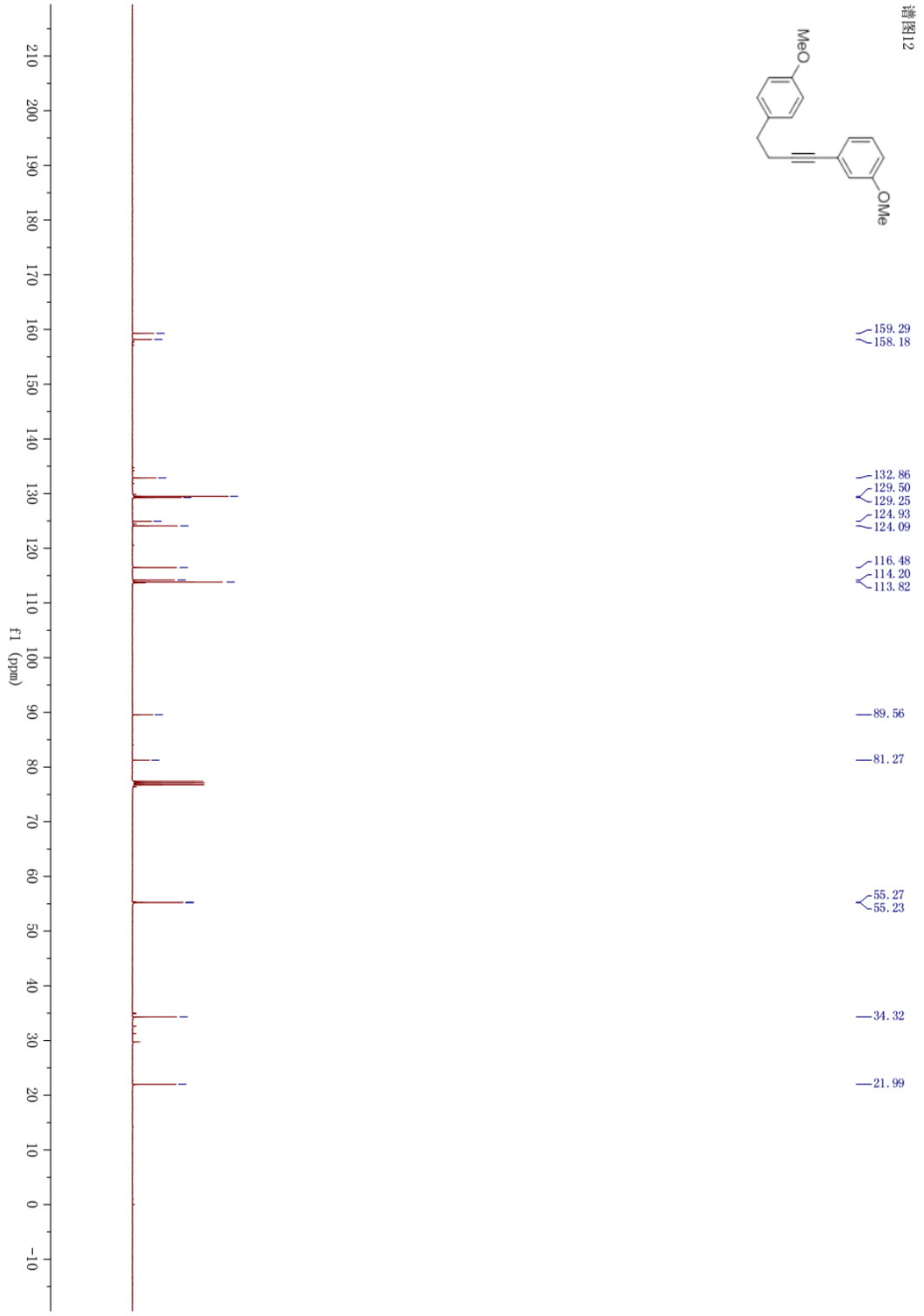
^{13}C NMR spectrum of compound **1n**



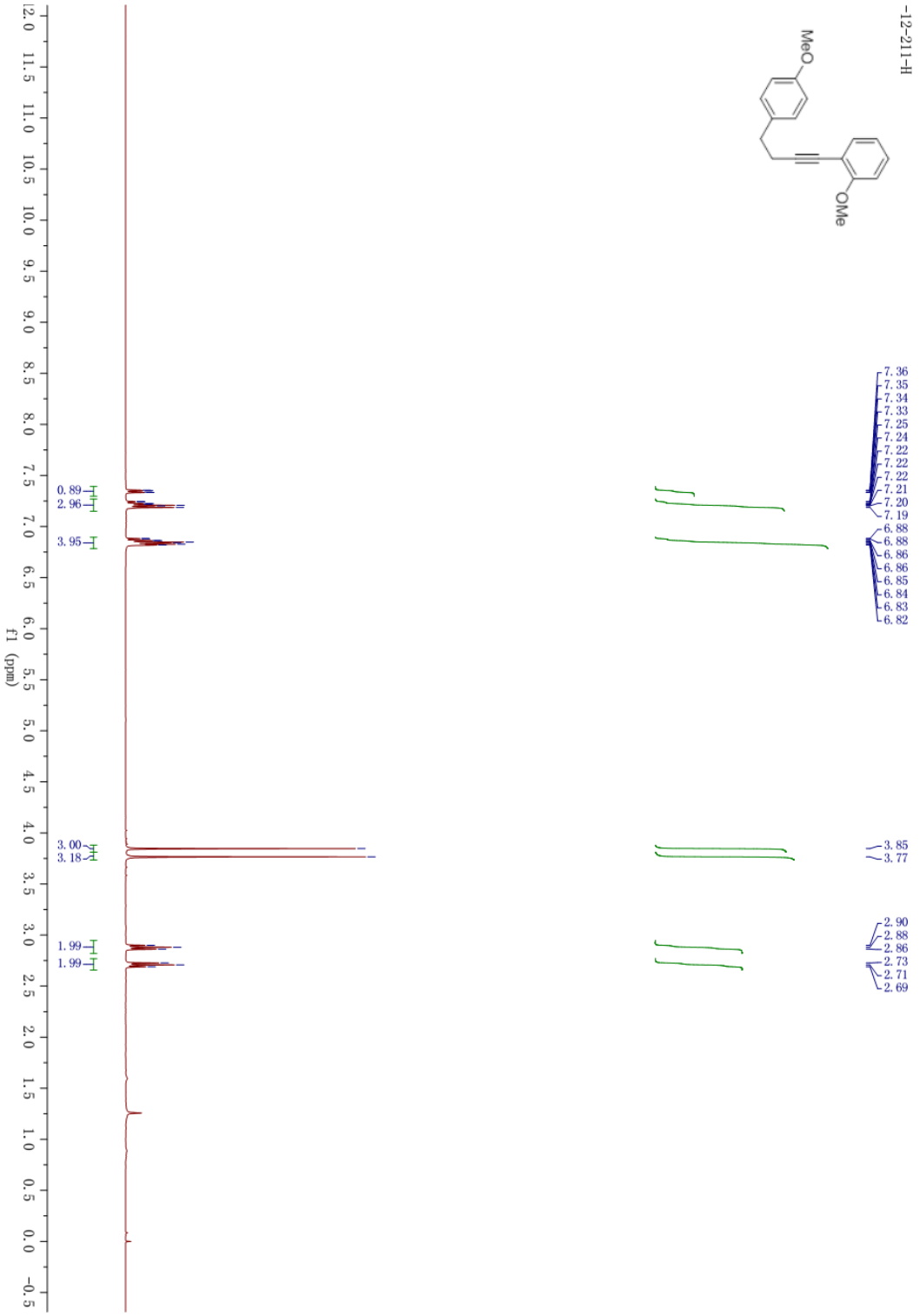
^{1}H NMR spectrum of compound **1o**



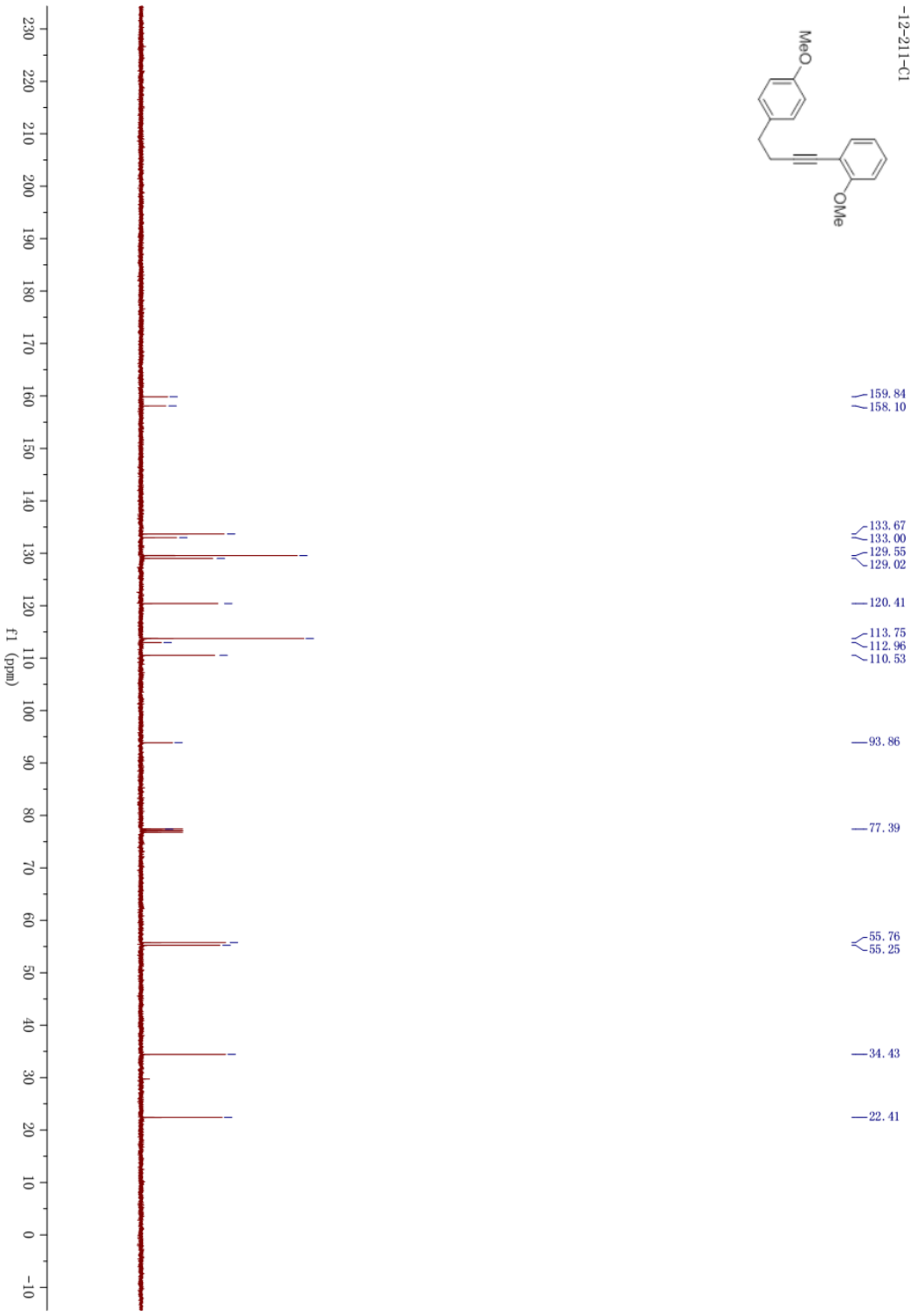
^{13}C NMR spectrum of compound **1o**



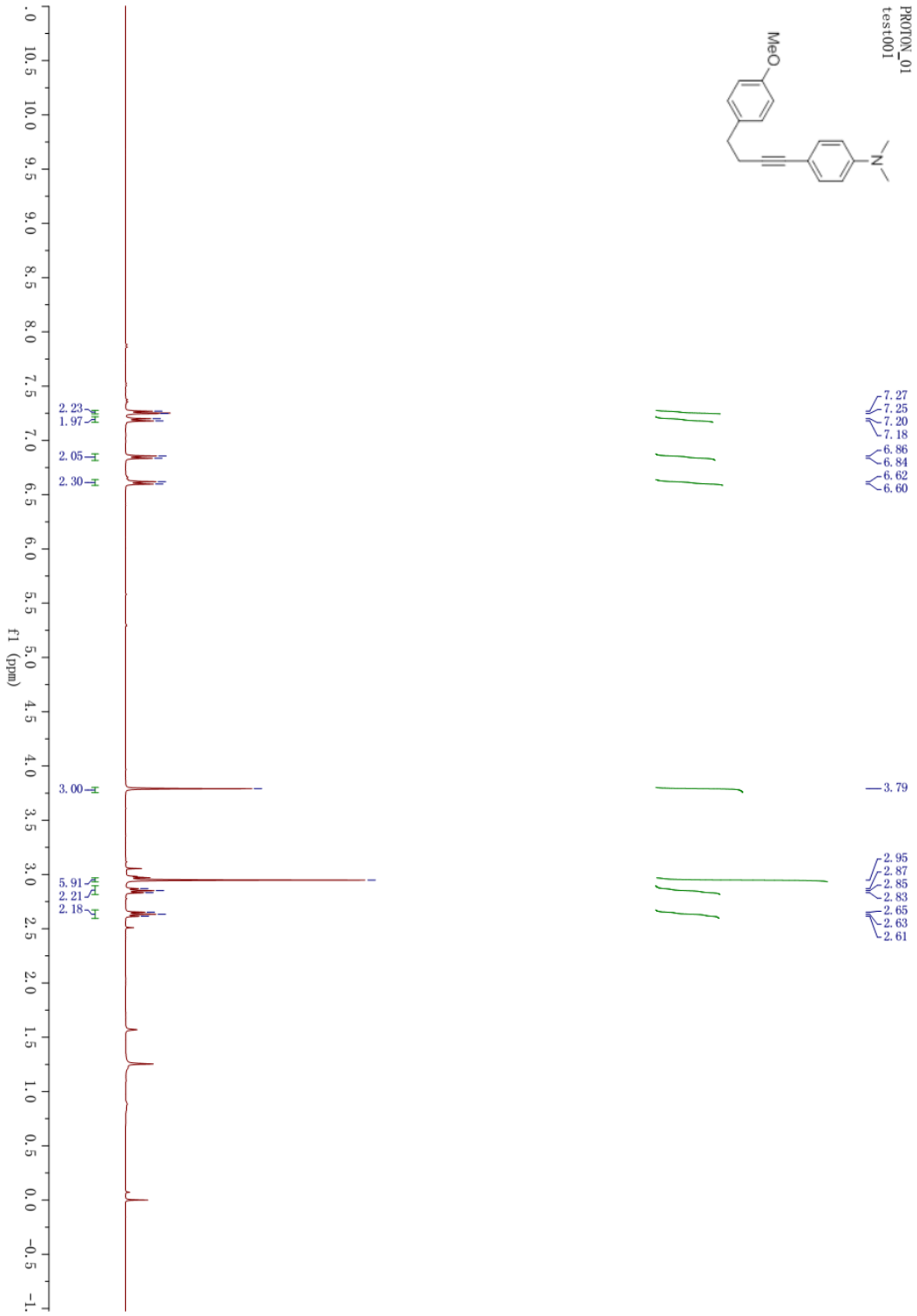
^{1}H NMR spectrum of compound **1p**



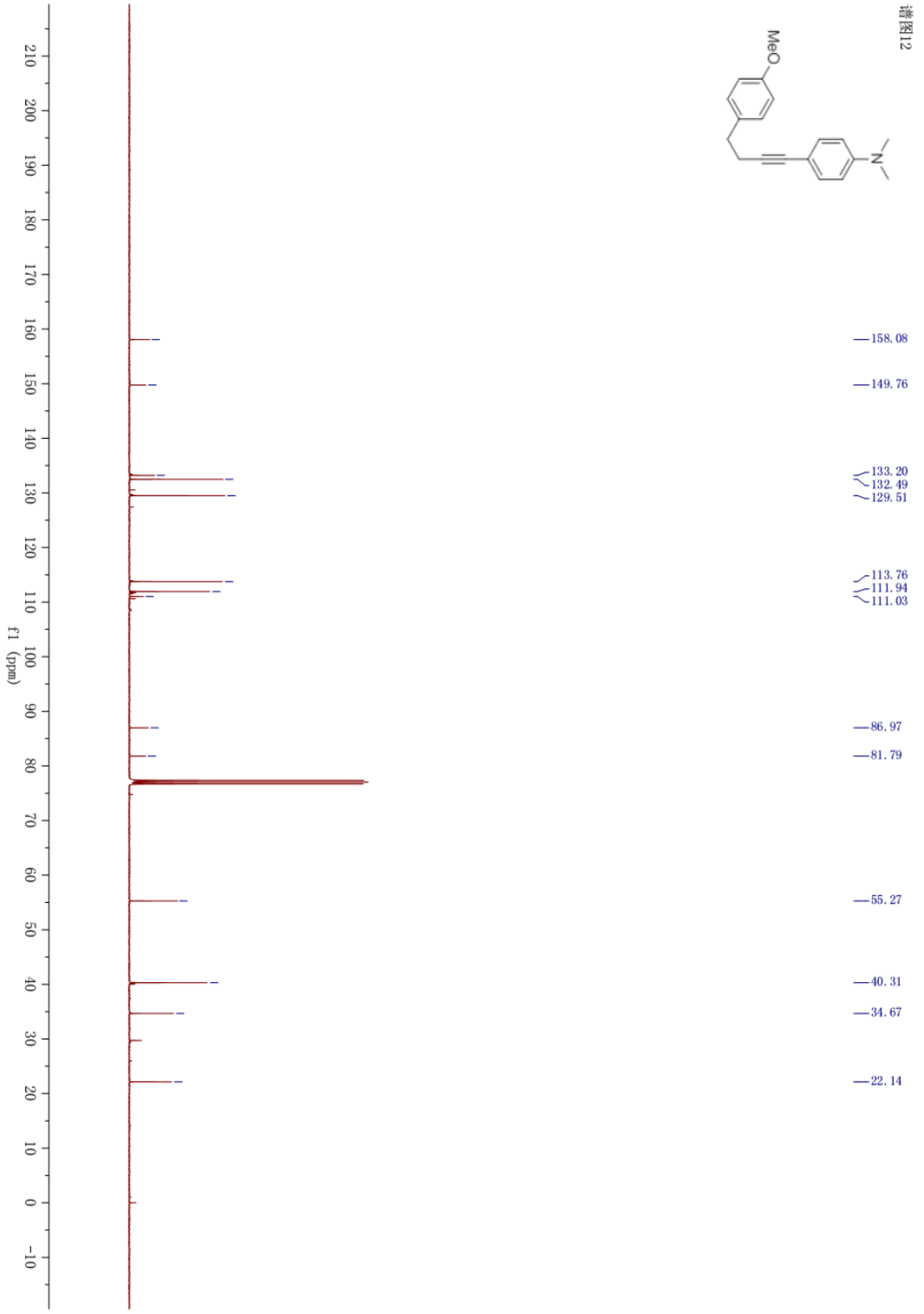
^{13}C NMR spectrum of compound **1p**



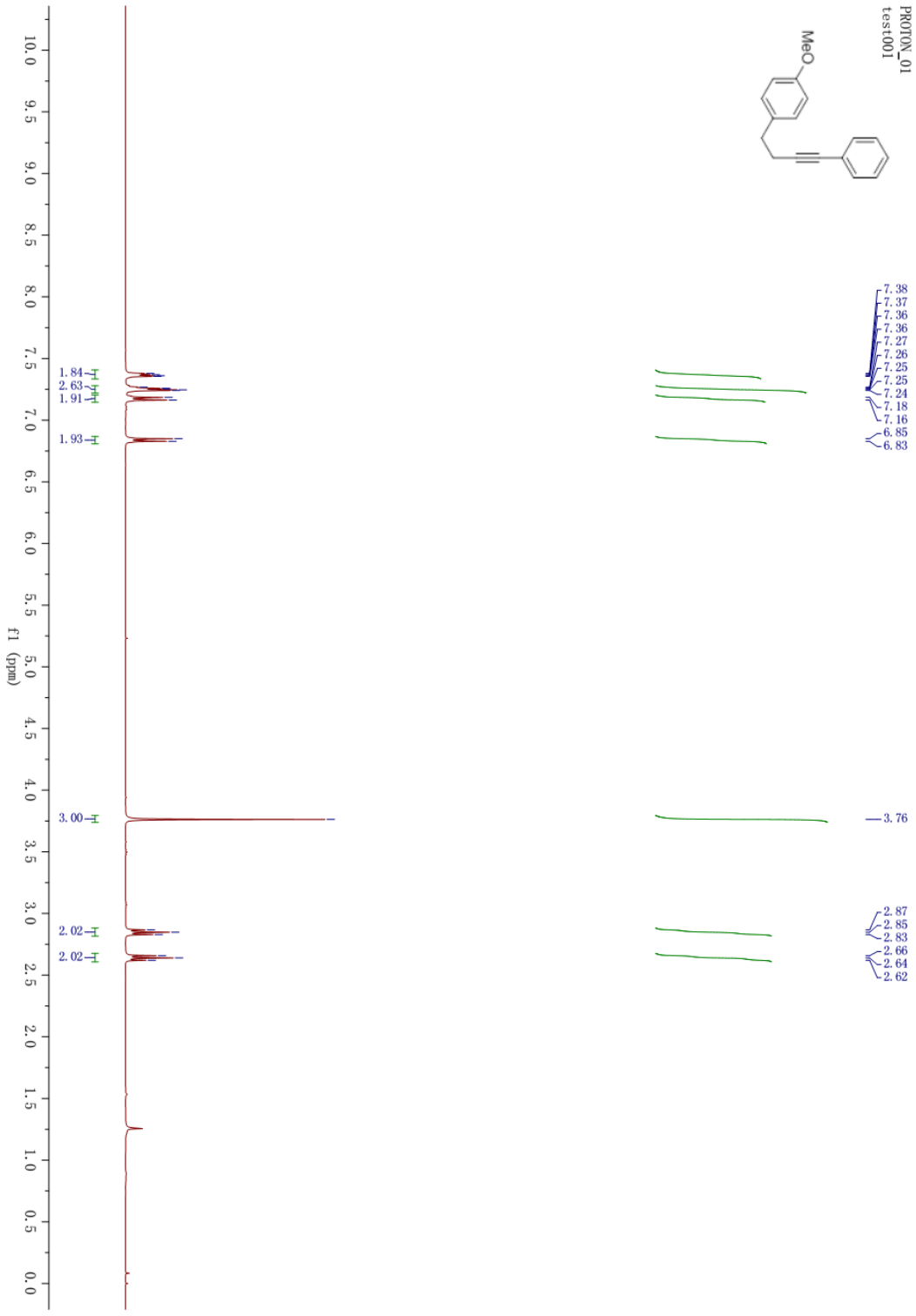
^{1}H NMR spectrum of compound **1q**



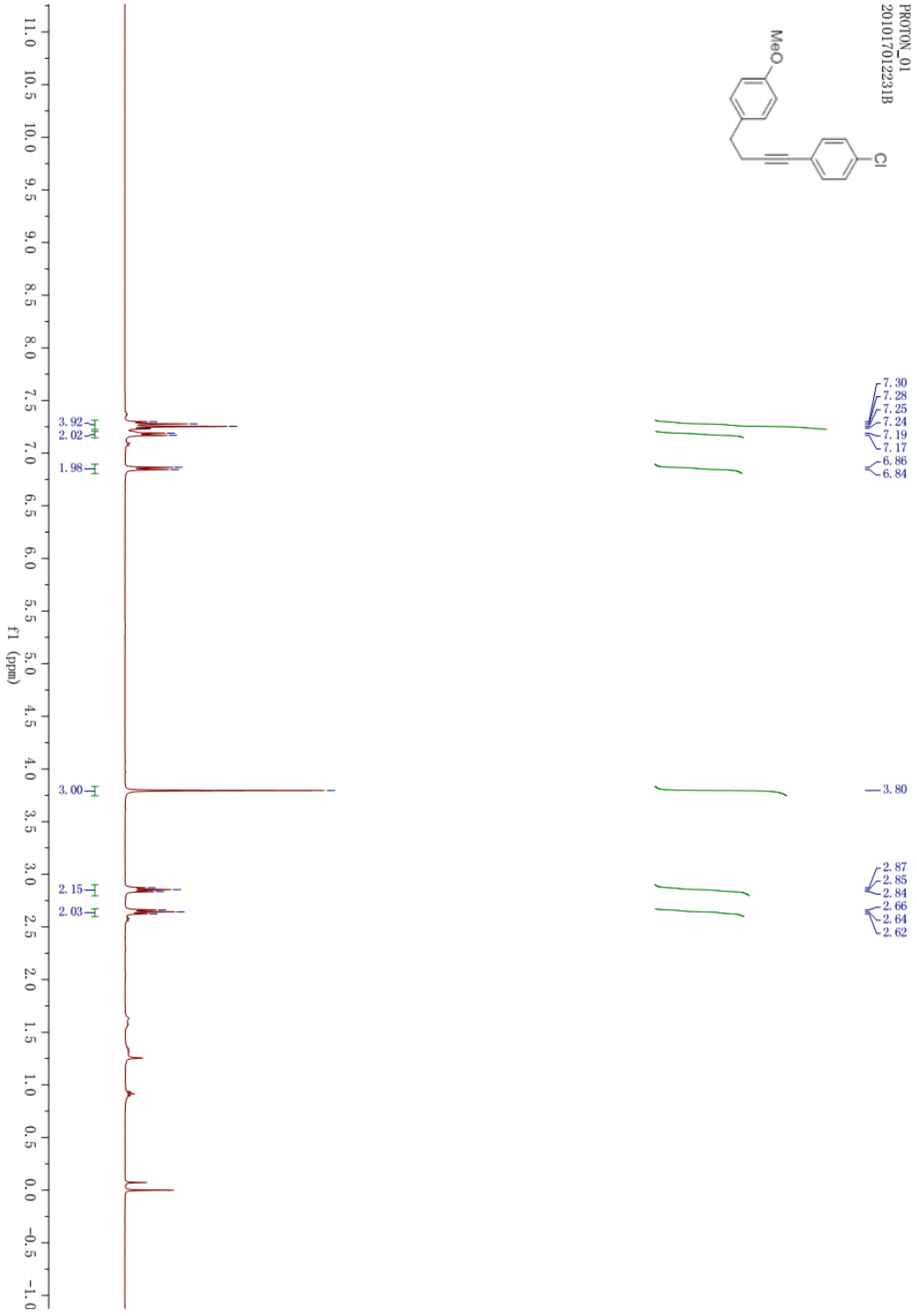
^{13}C NMR spectrum of compound **1q**



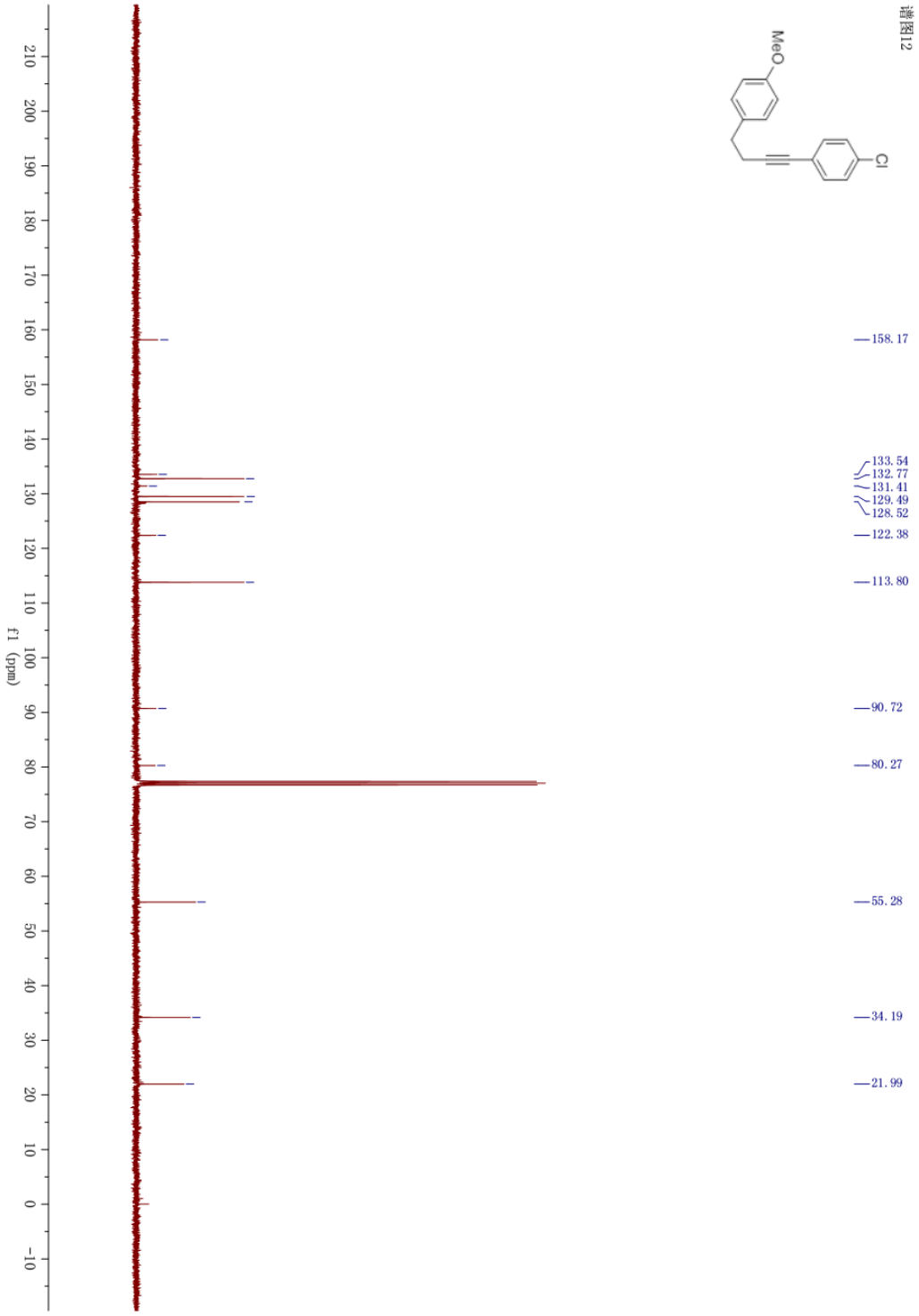
^{1}H NMR spectrum of compound **1r**



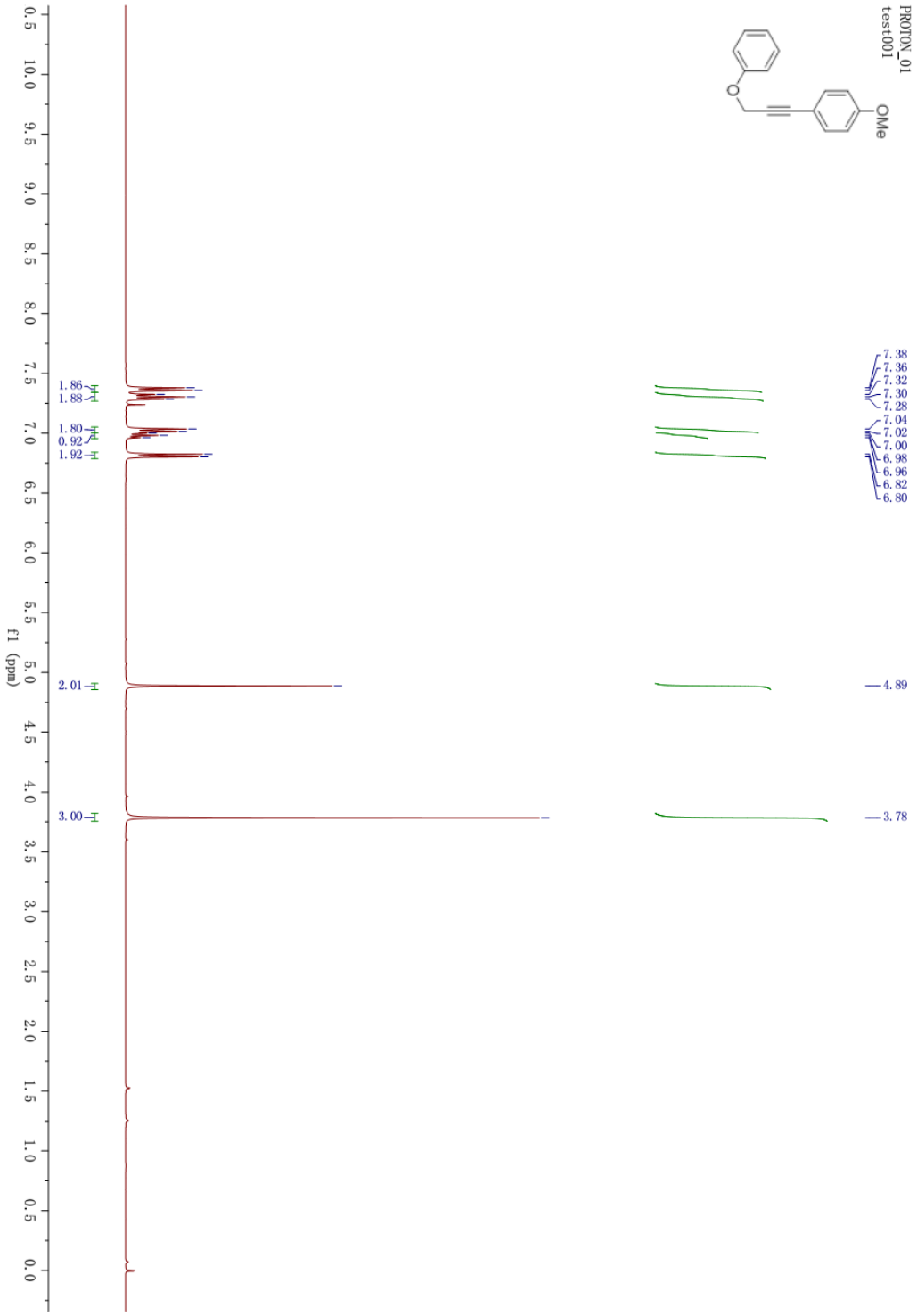
^{1}H NMR spectrum of compound **1s**



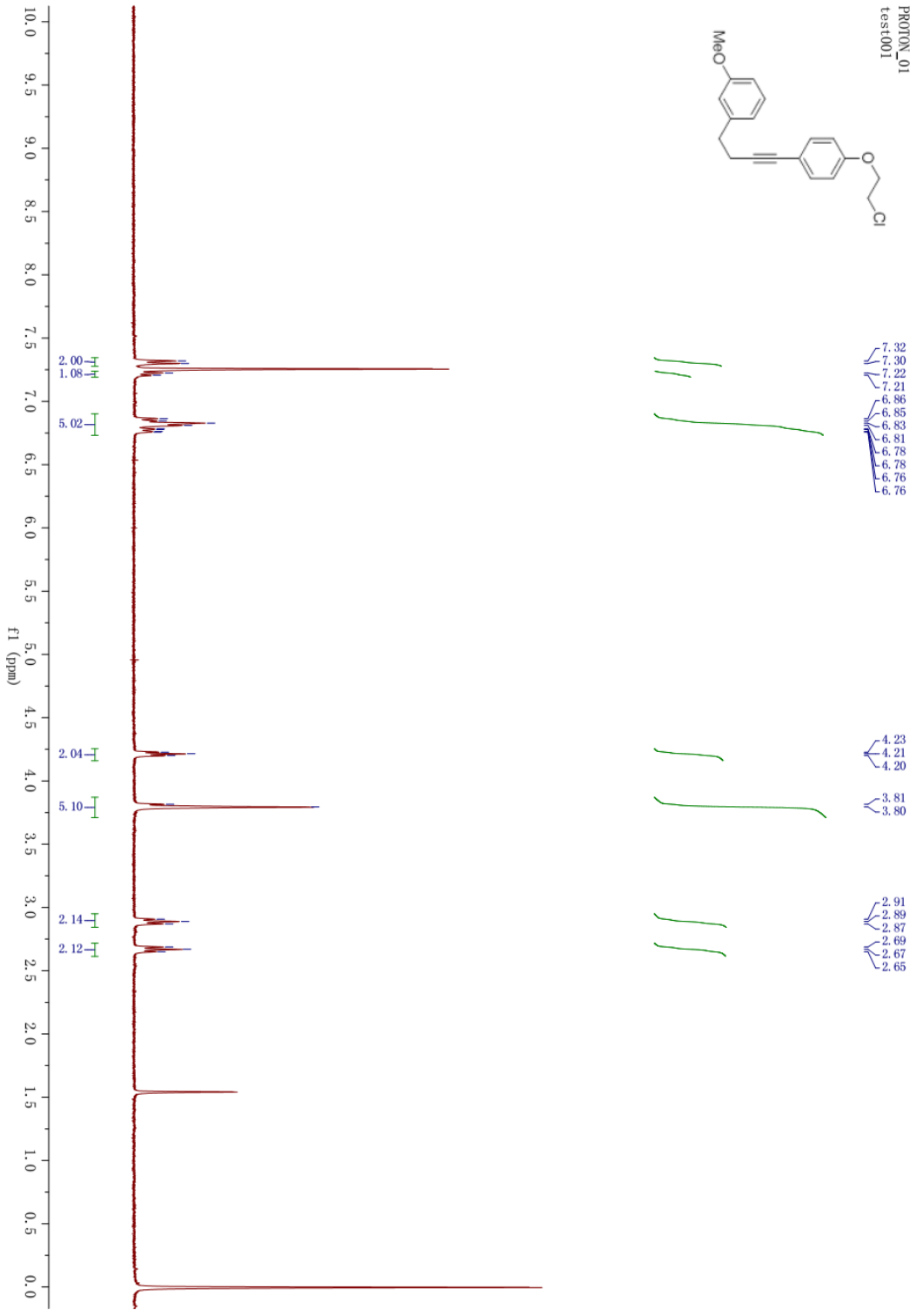
^{13}C NMR spectrum of compound **1s**



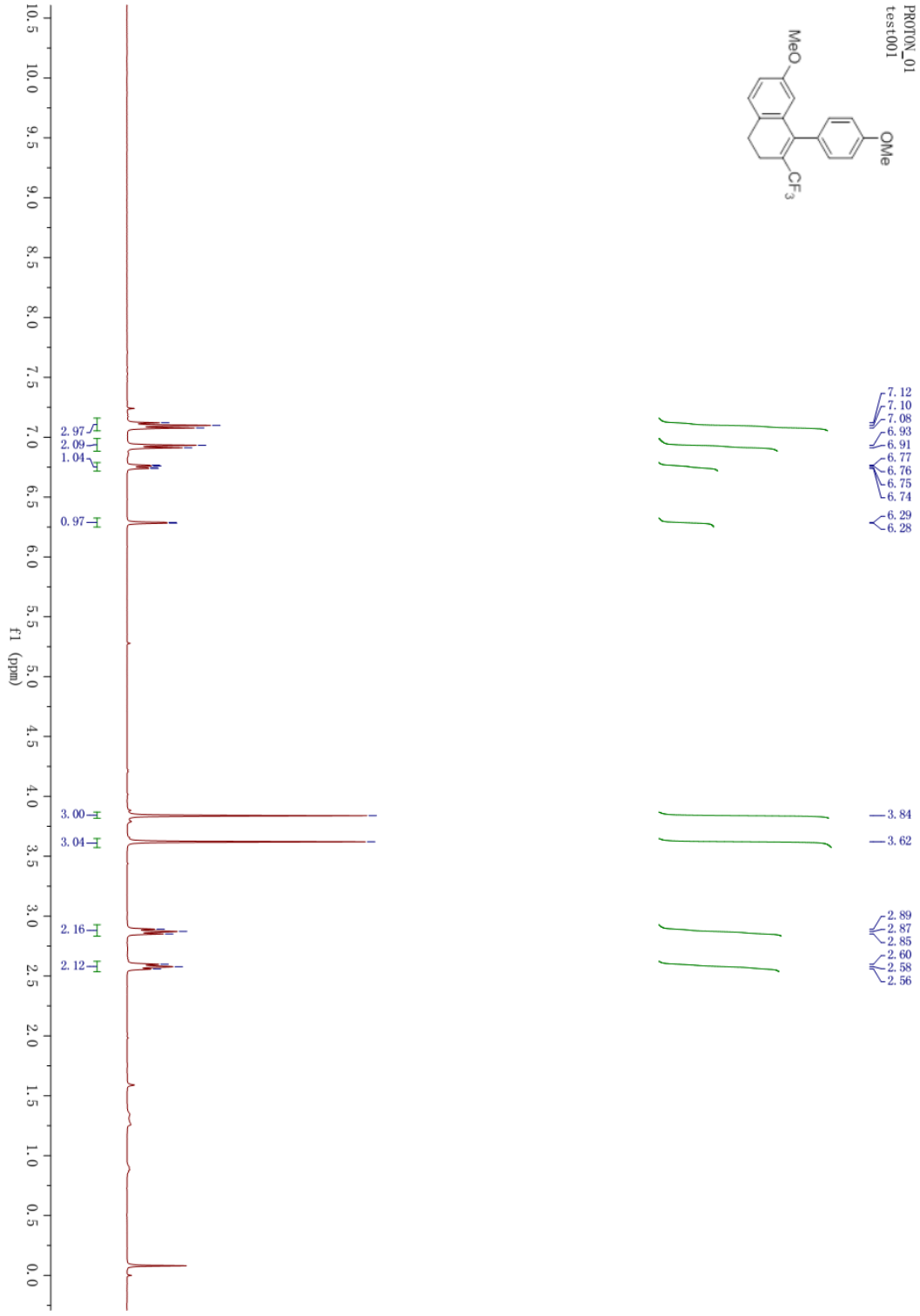
^{1}H NMR spectrum of compound **1t**



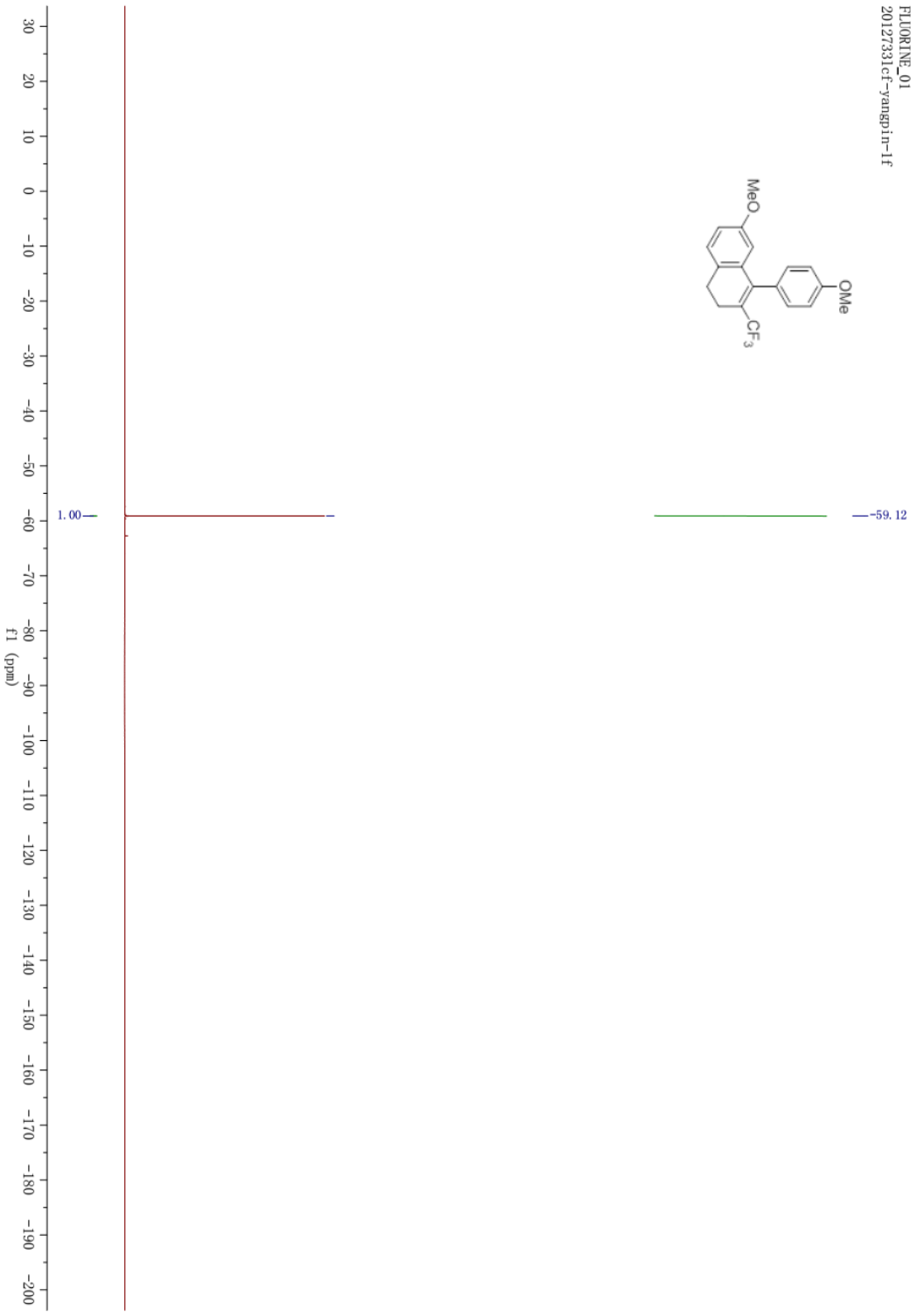
^{1}H NMR spectrum of compound **1u**



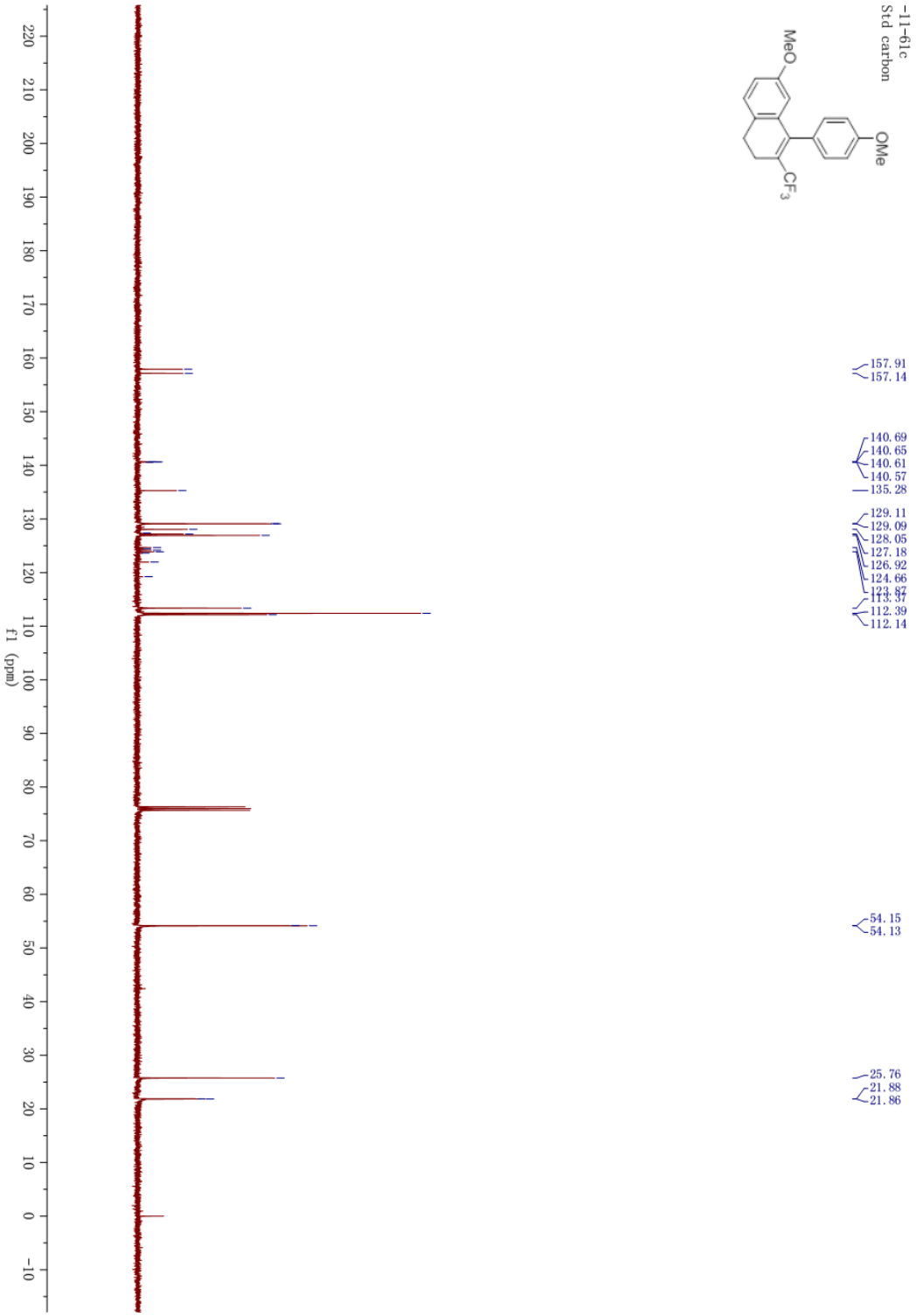
^{1}H NMR spectrum of compound **2a**



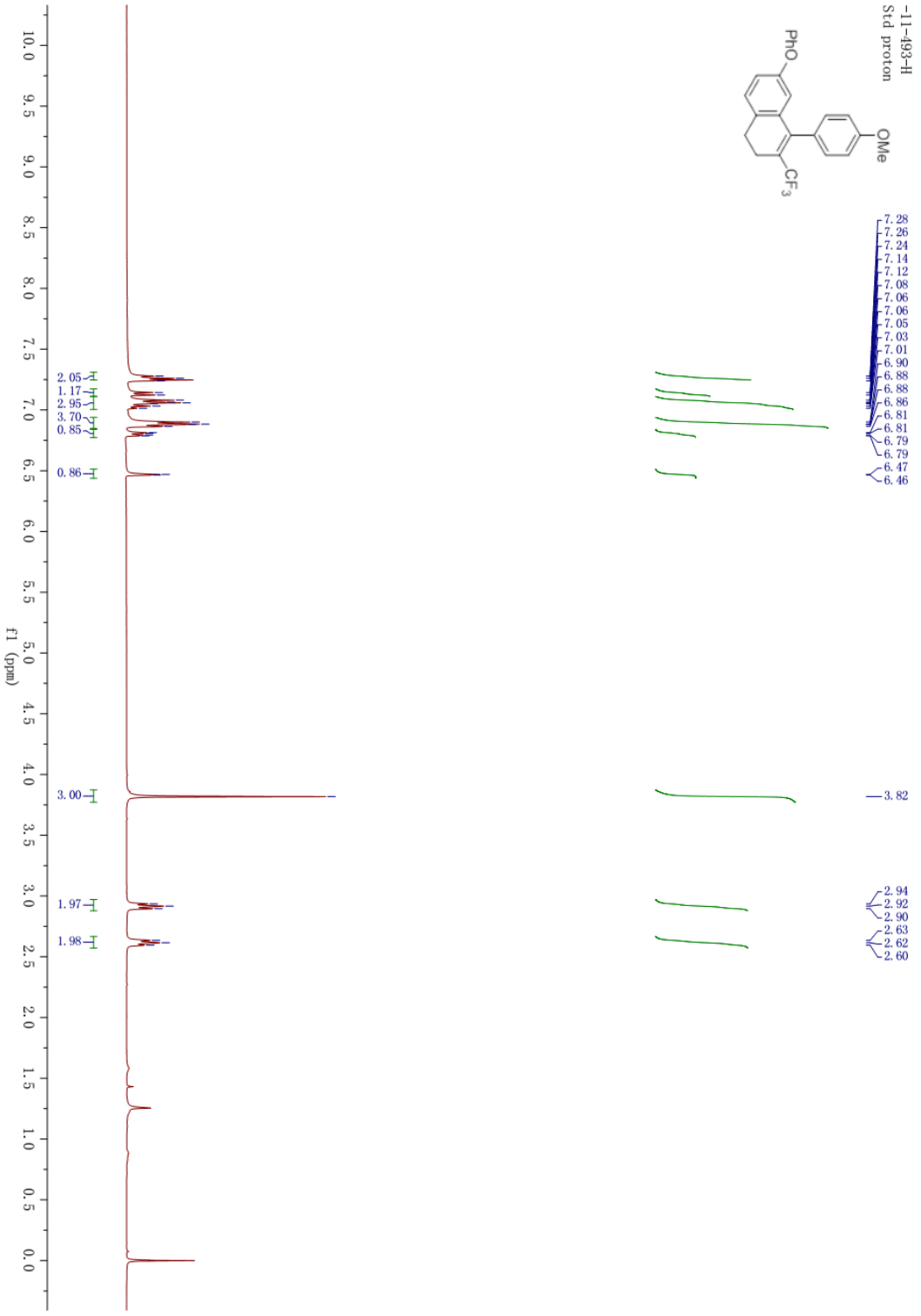
^{19}F NMR spectrum of compound **2a**



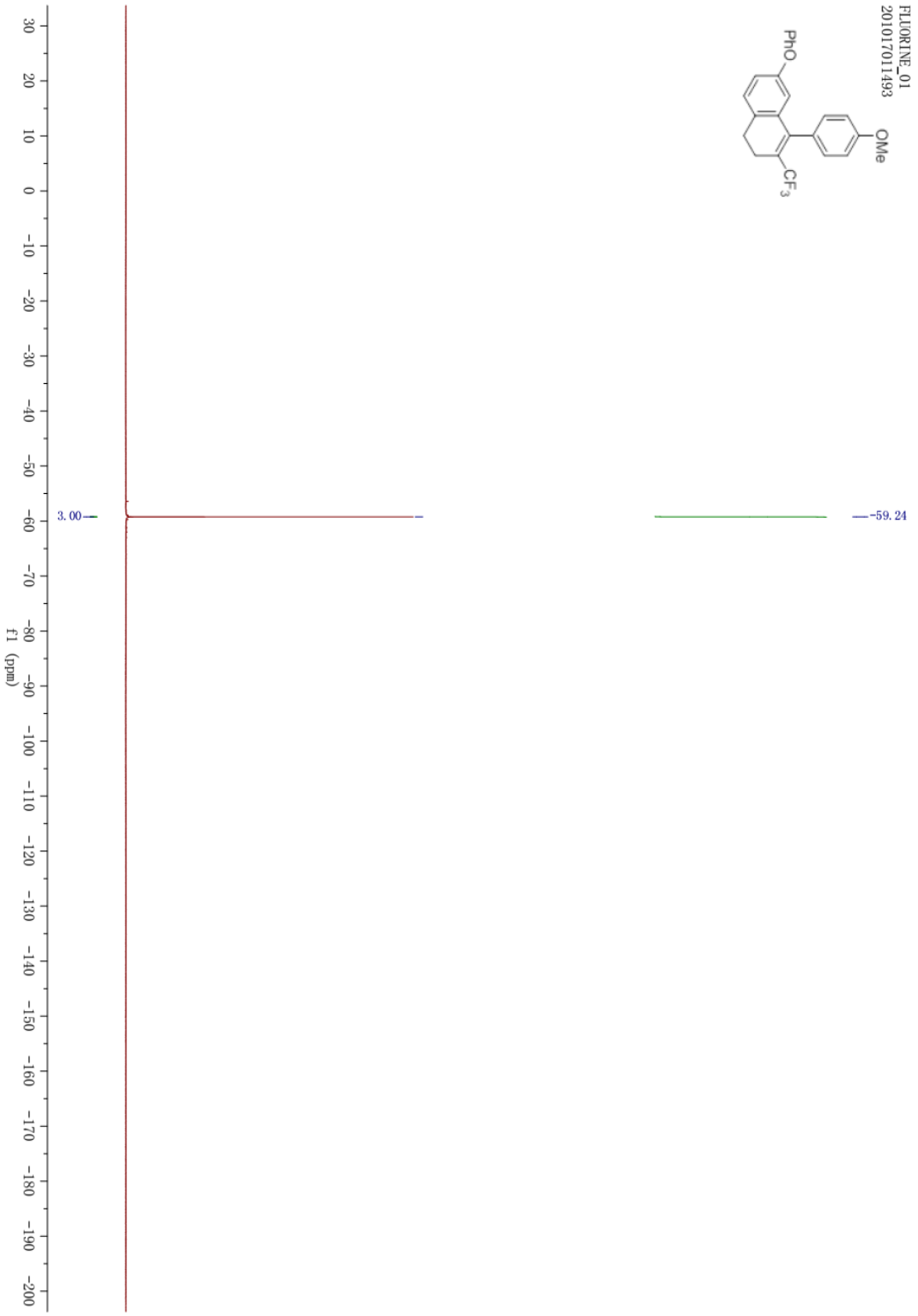
^{13}C NMR spectrum of compound **2a**



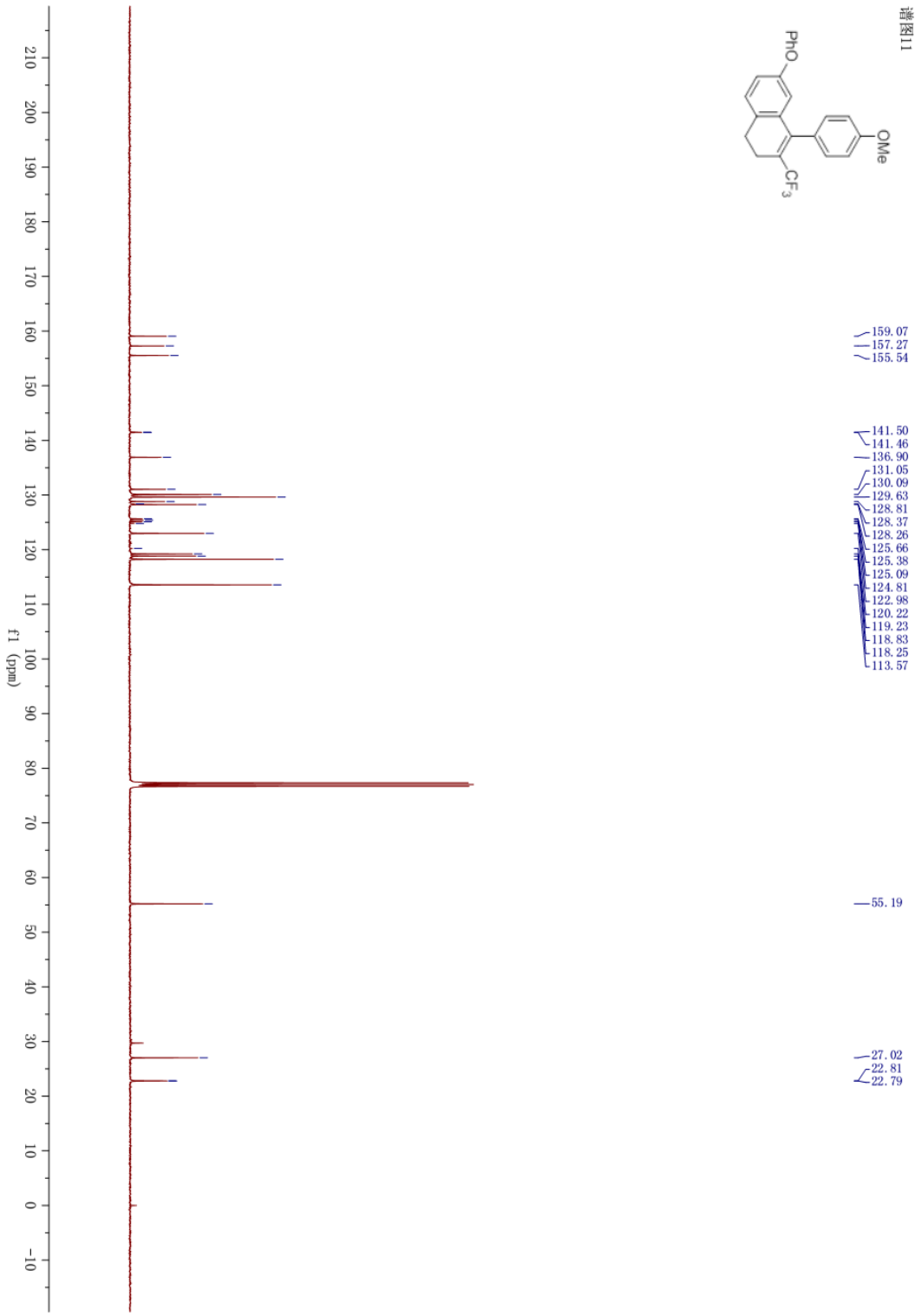
^{1}H NMR spectrum of compound **2b**



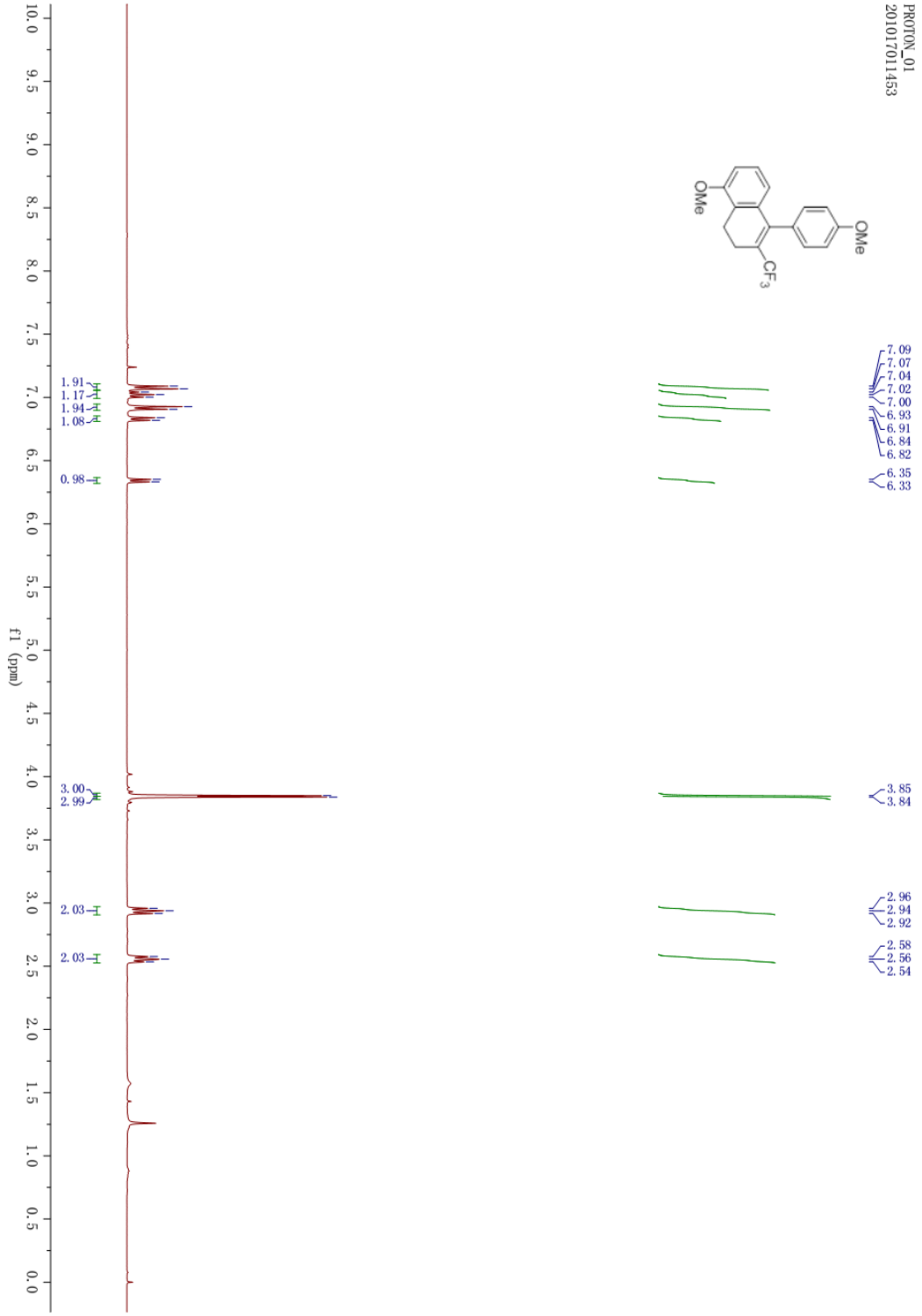
^{19}F NMR spectrum of compound **2b**



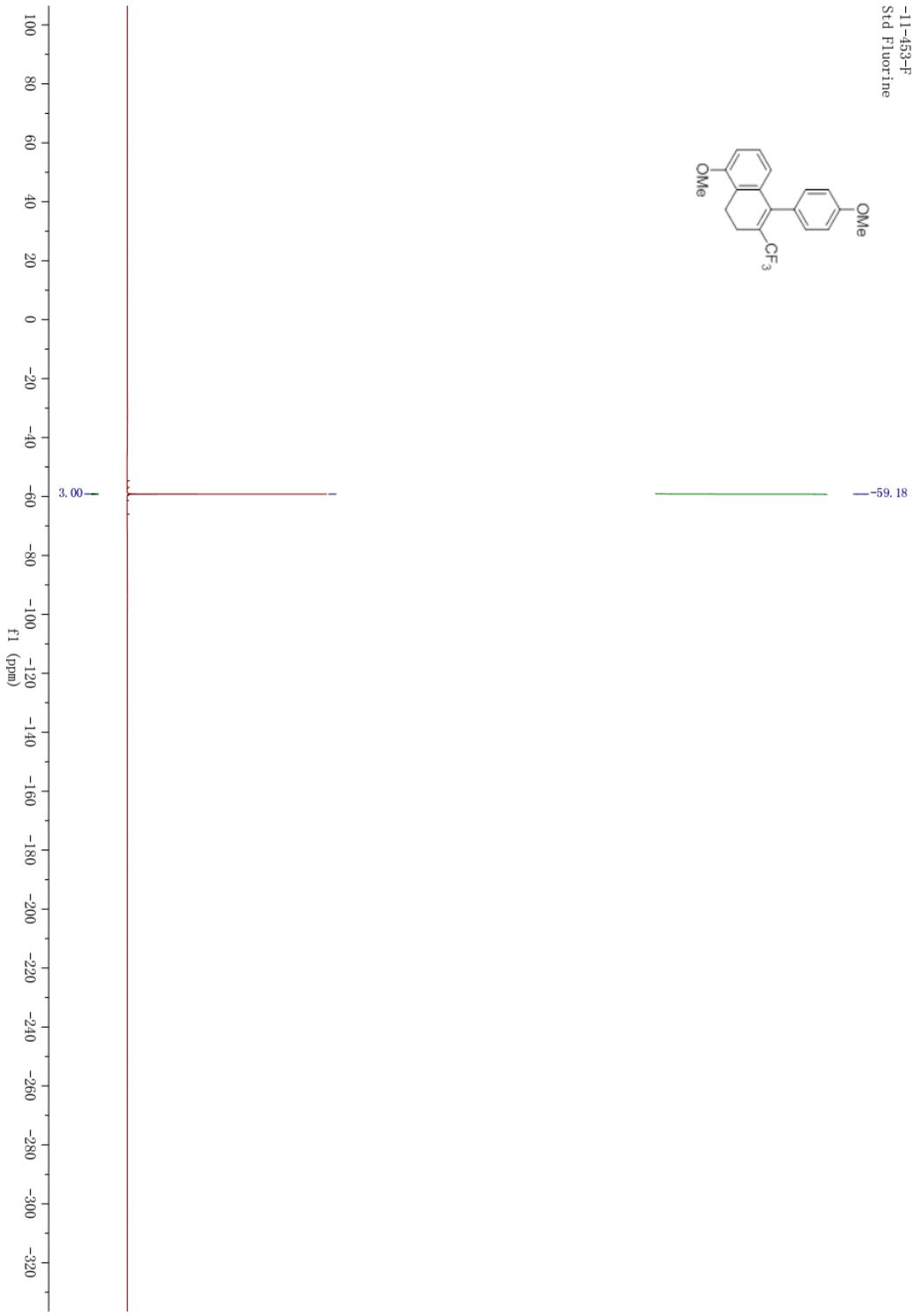
^{13}C NMR spectrum of compound **2b**



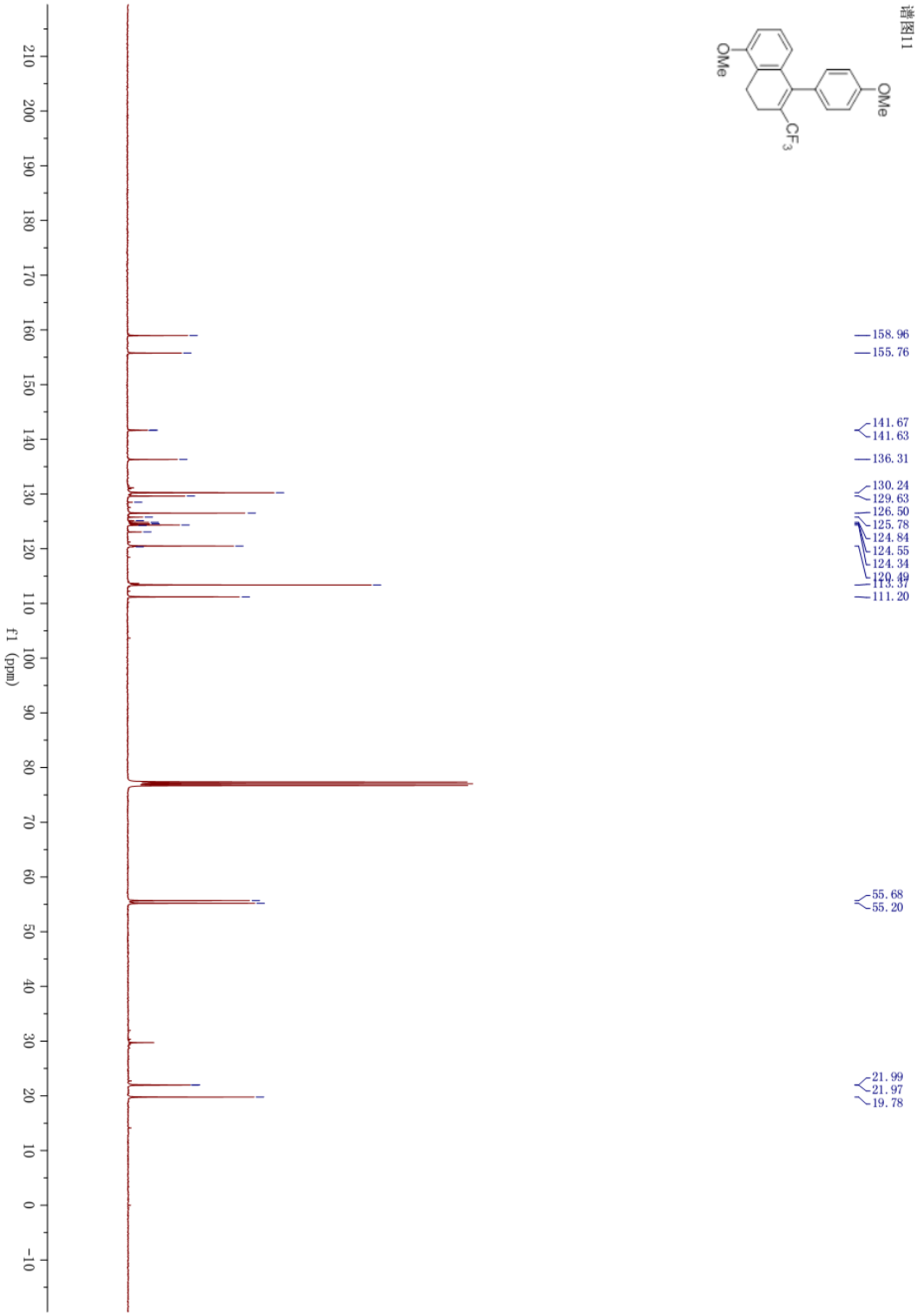
^{1}H NMR spectrum of compound **2c**



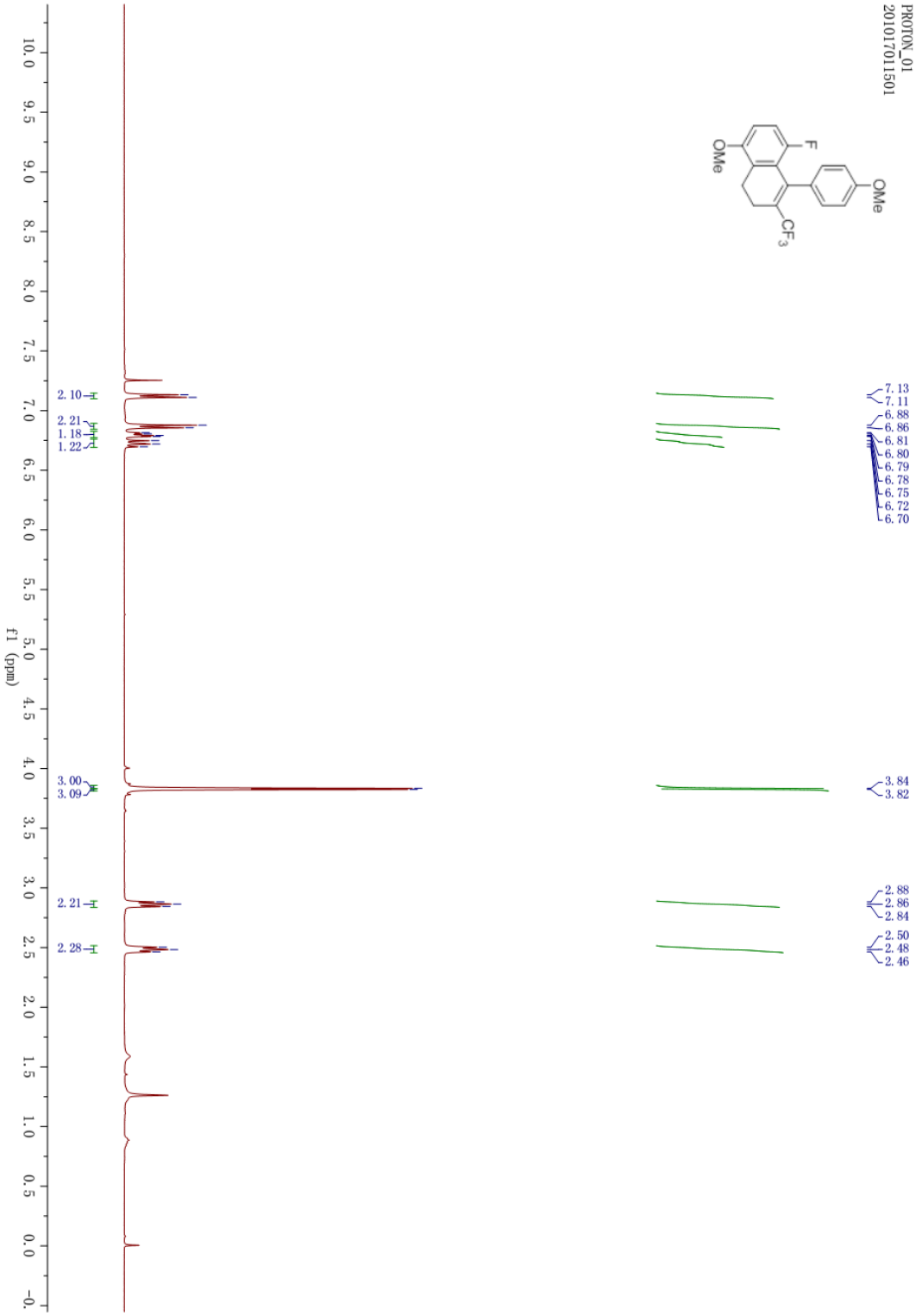
^{19}F NMR spectrum of compound **2c**



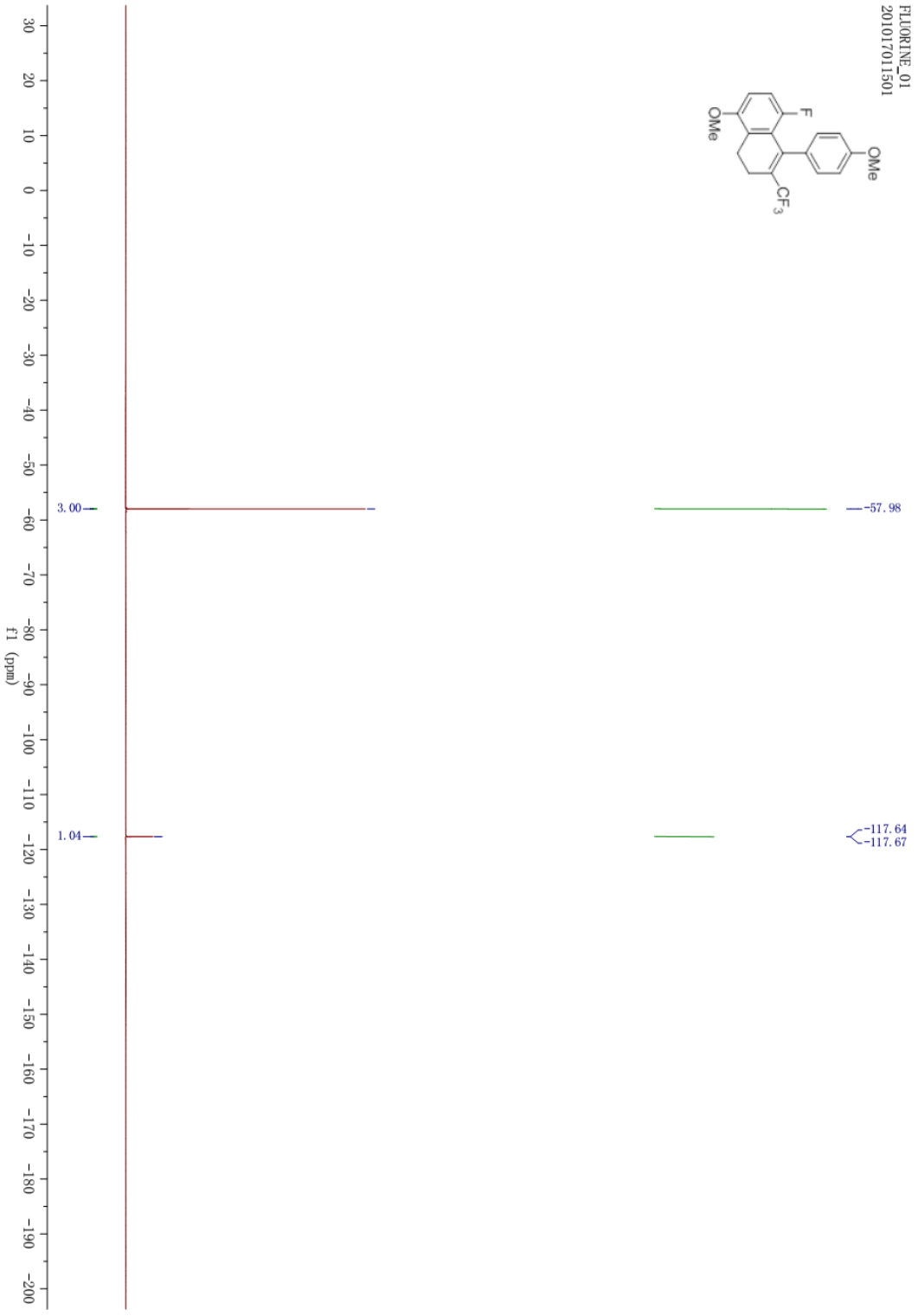
^{13}C NMR spectrum of compound **2c**



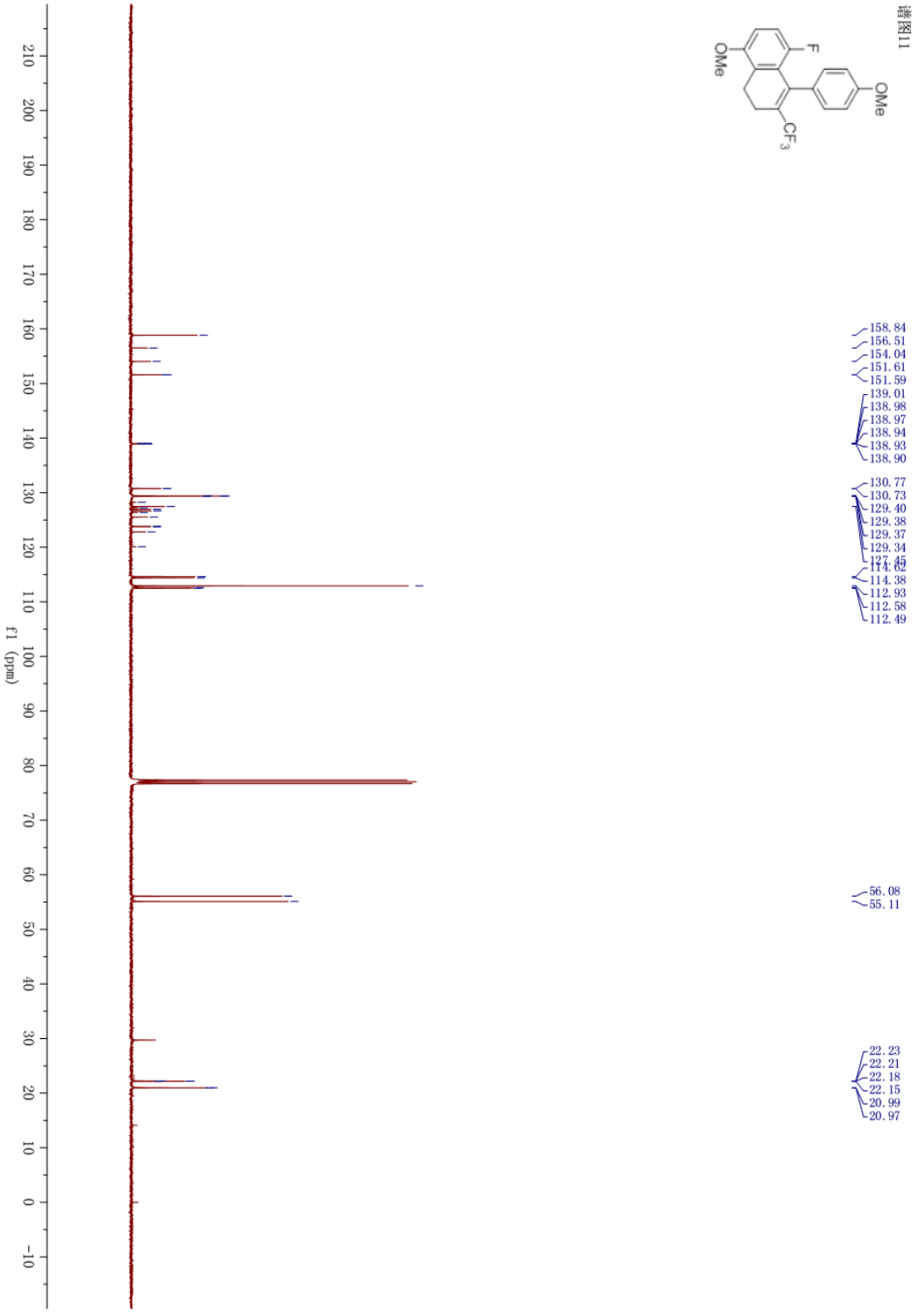
^{1}H NMR spectrum of compound **2d**



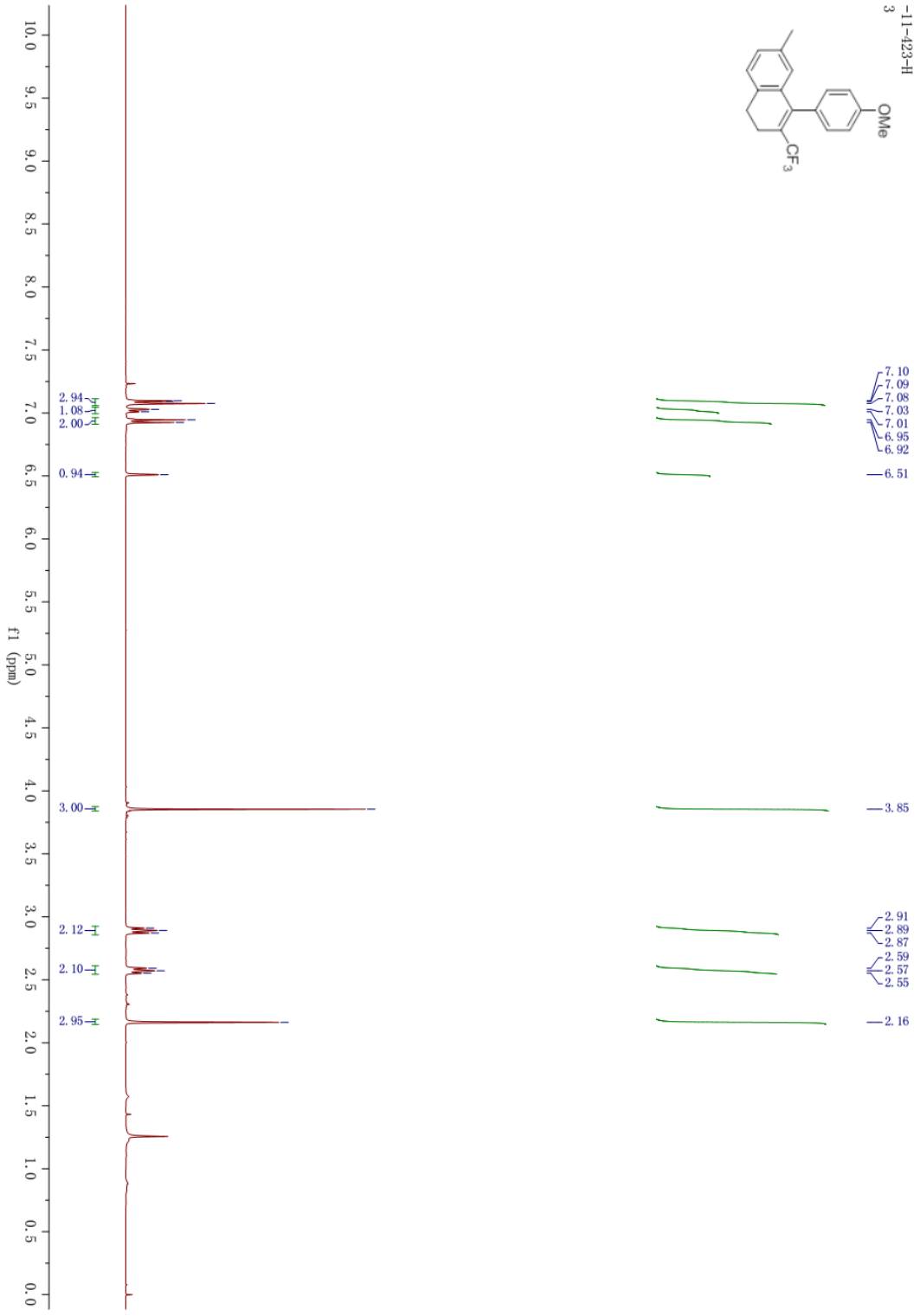
^{19}F NMR spectrum of compound **2d**



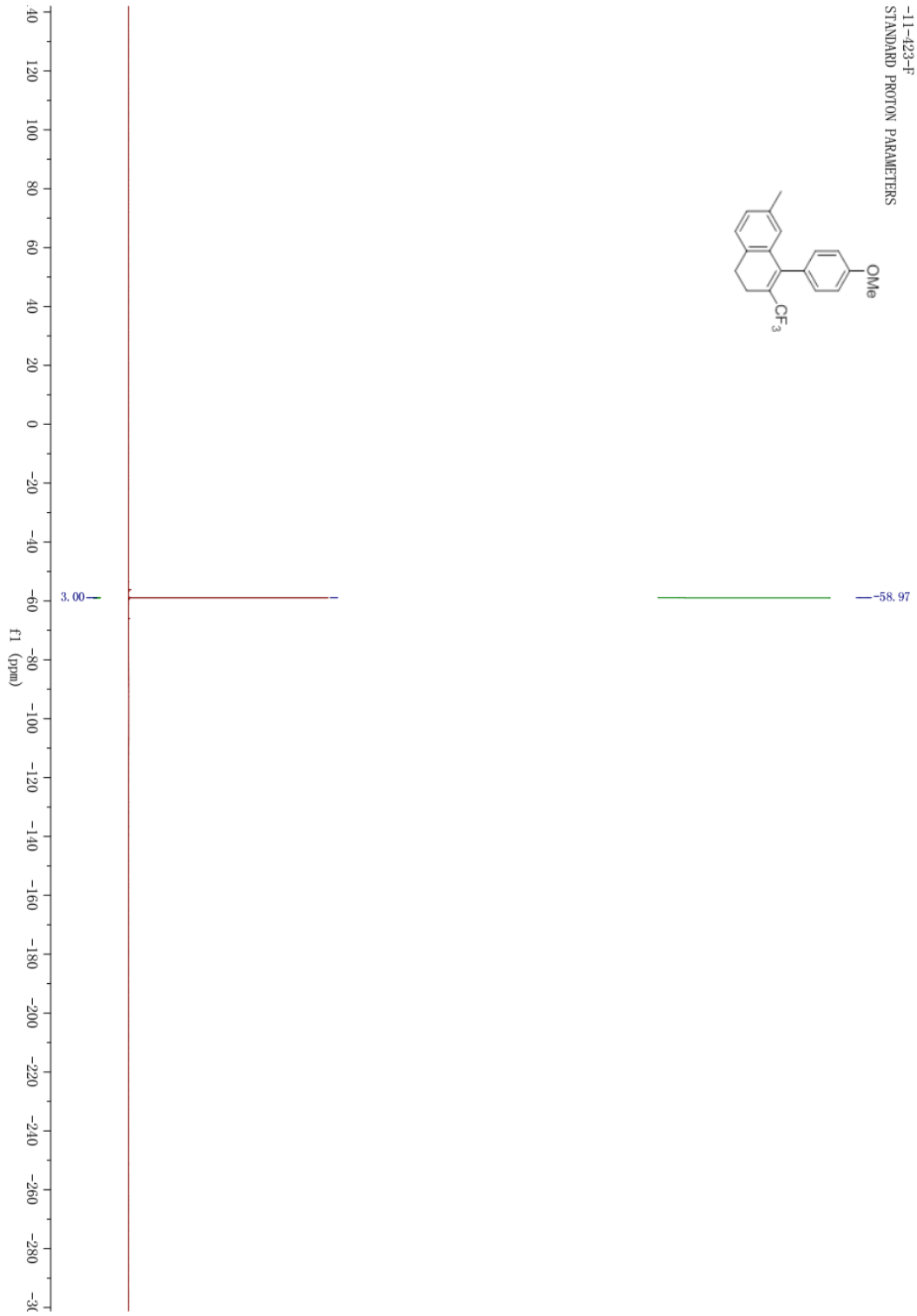
^{13}C NMR spectrum of compound **2d**



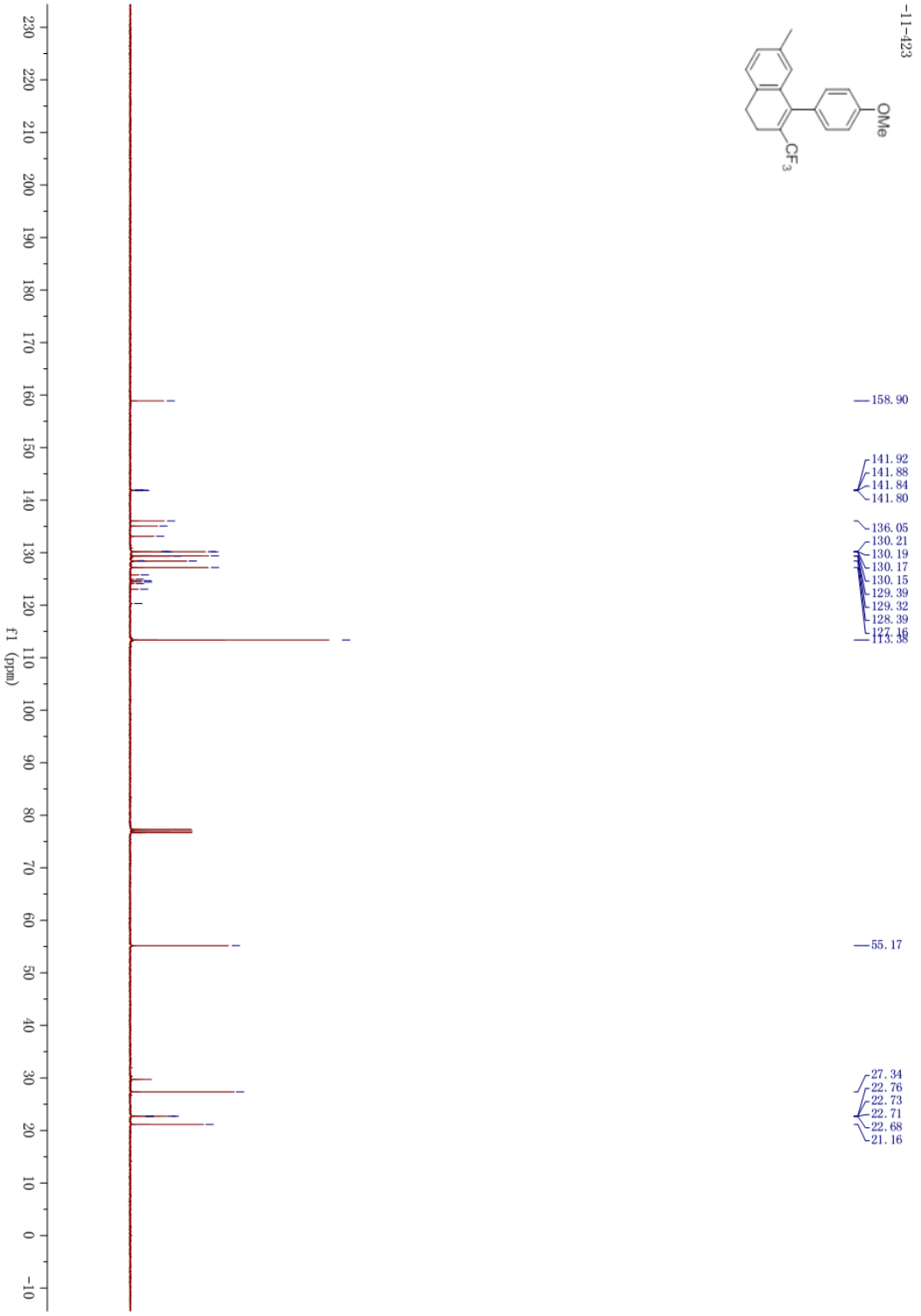
^{1}H NMR spectrum of compound **2e**



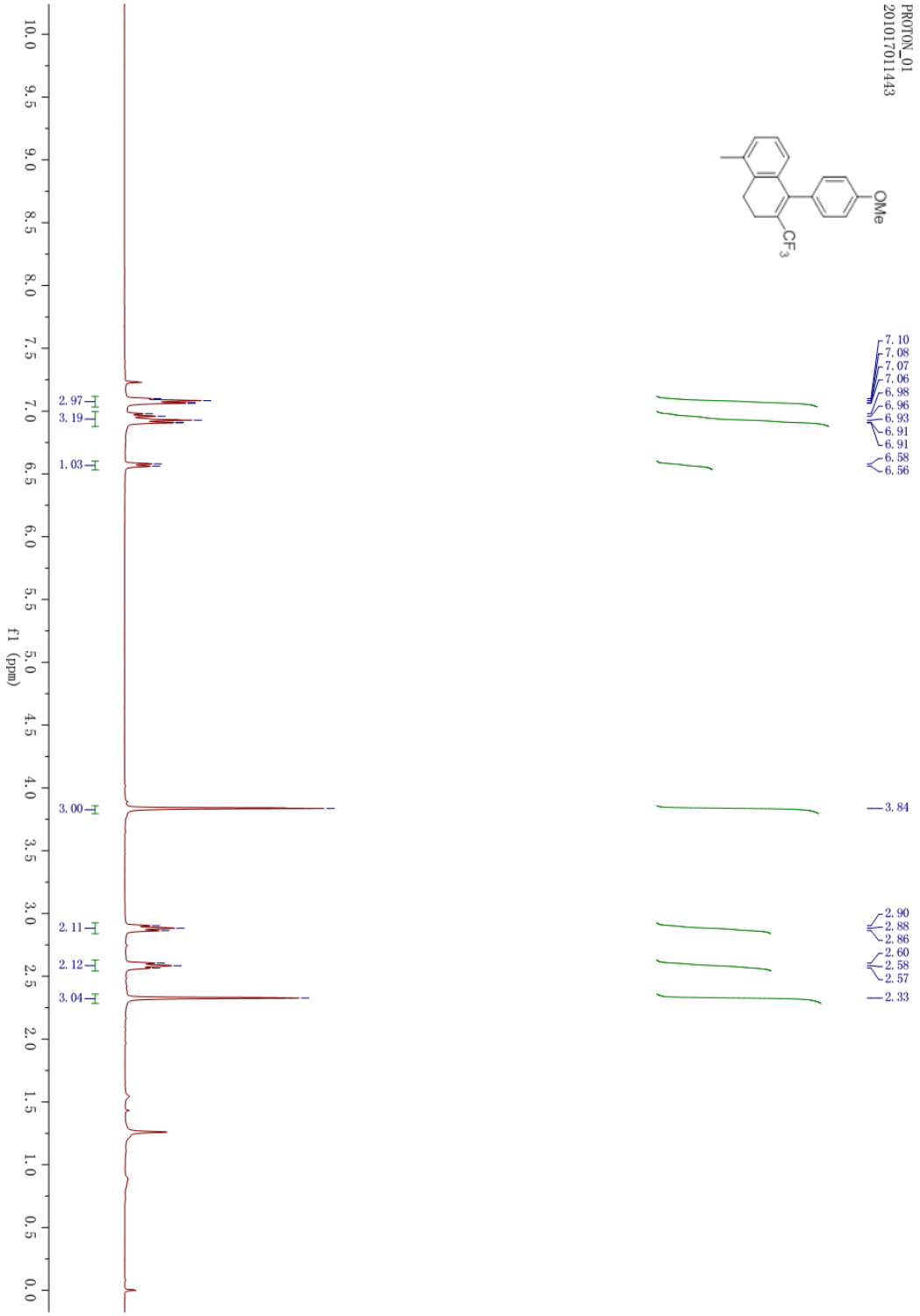
^{19}F NMR spectrum of compound **2e**



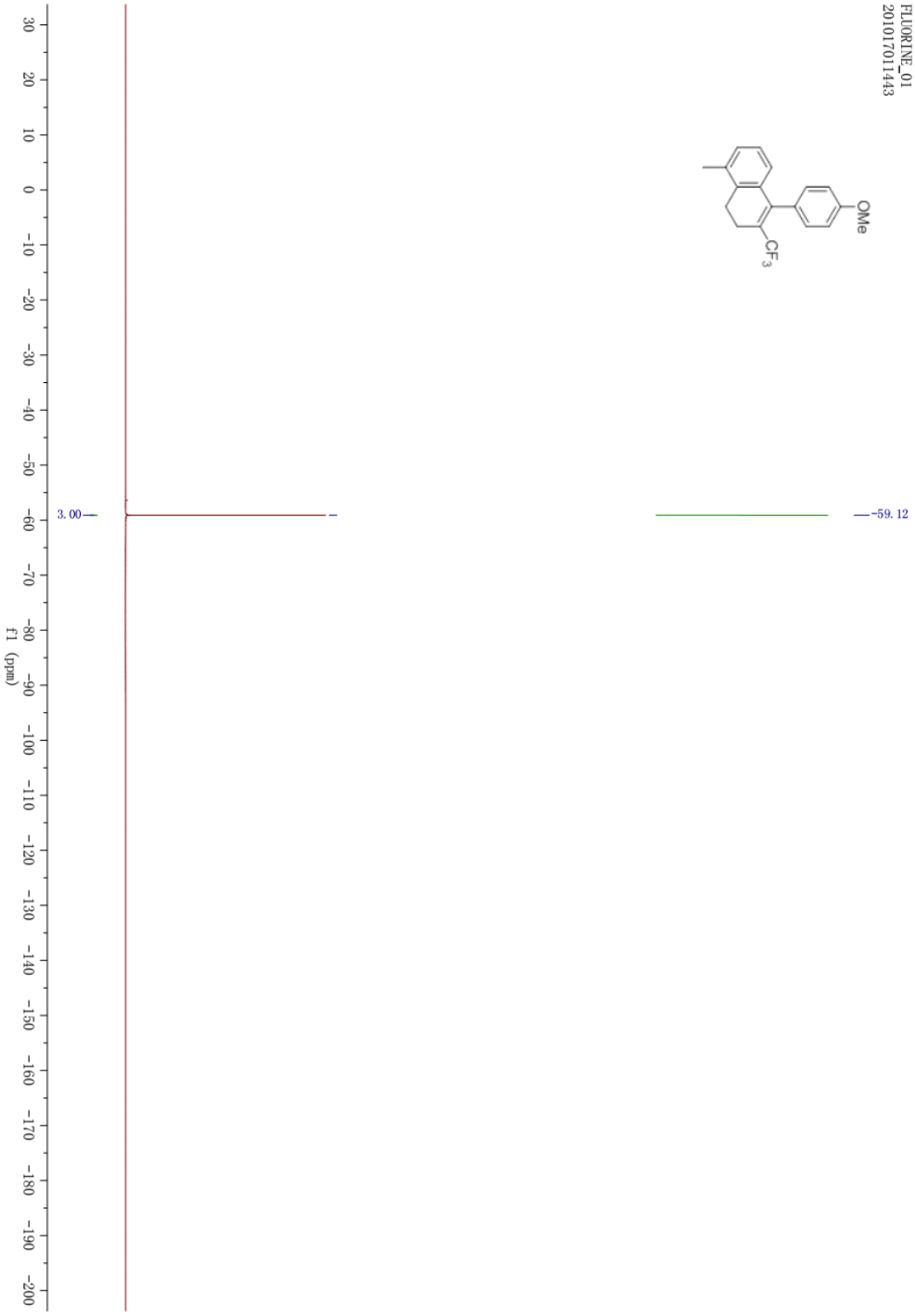
^{13}C NMR spectrum of compound **2e**



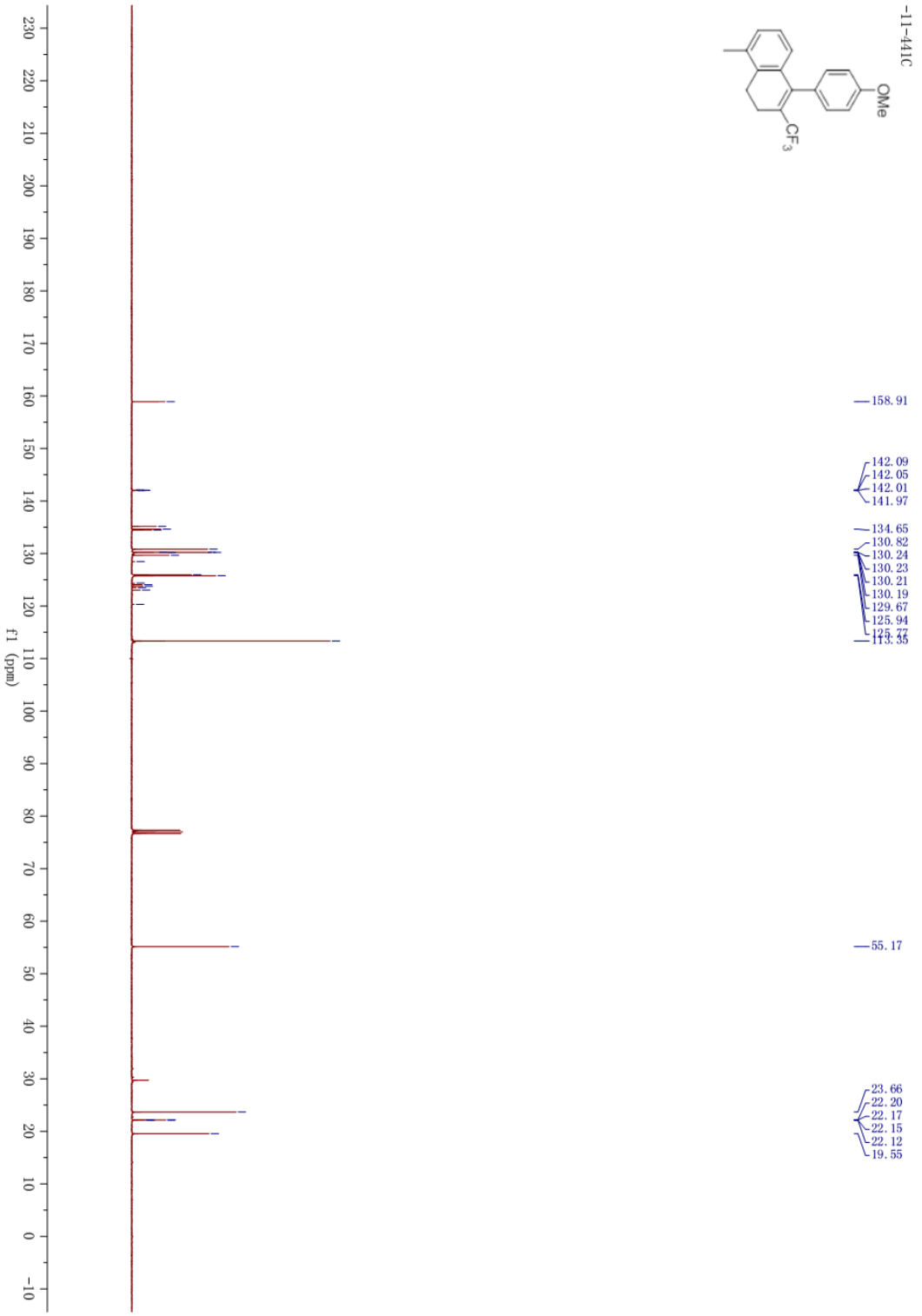
^{1}H NMR spectrum of compound **2f**



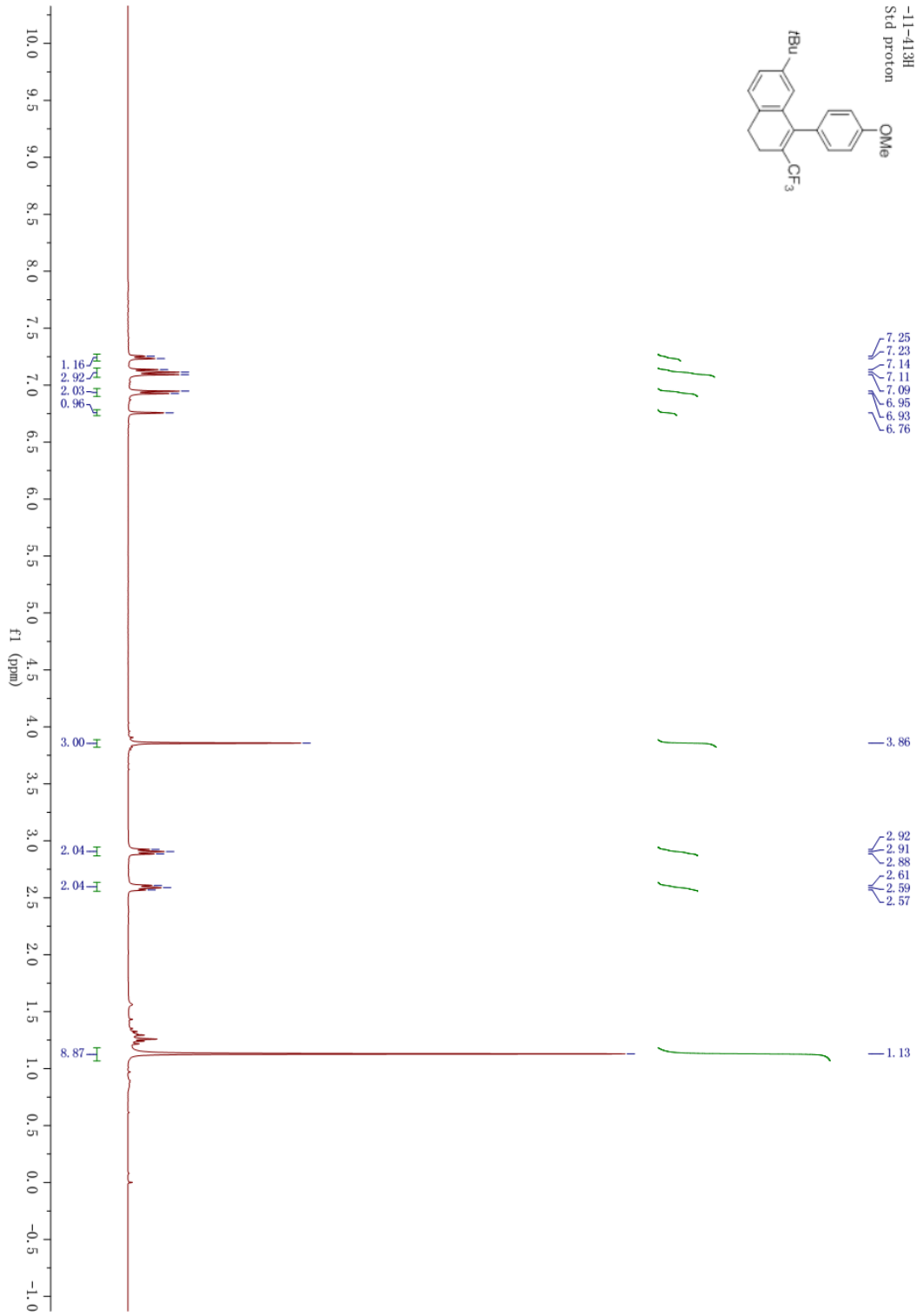
^{19}F NMR spectrum of compound **2f**



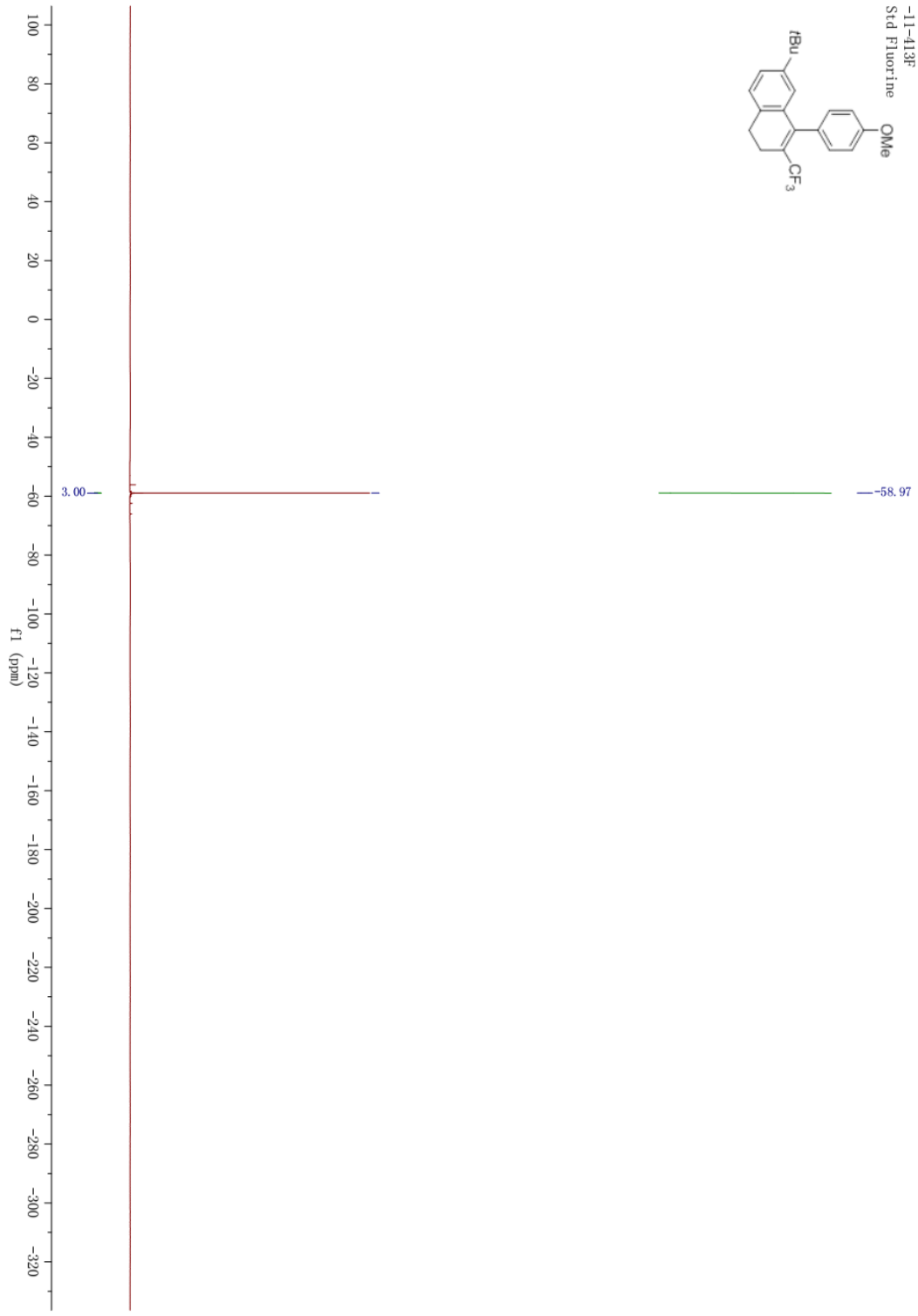
^{13}C NMR spectrum of compound **2f**



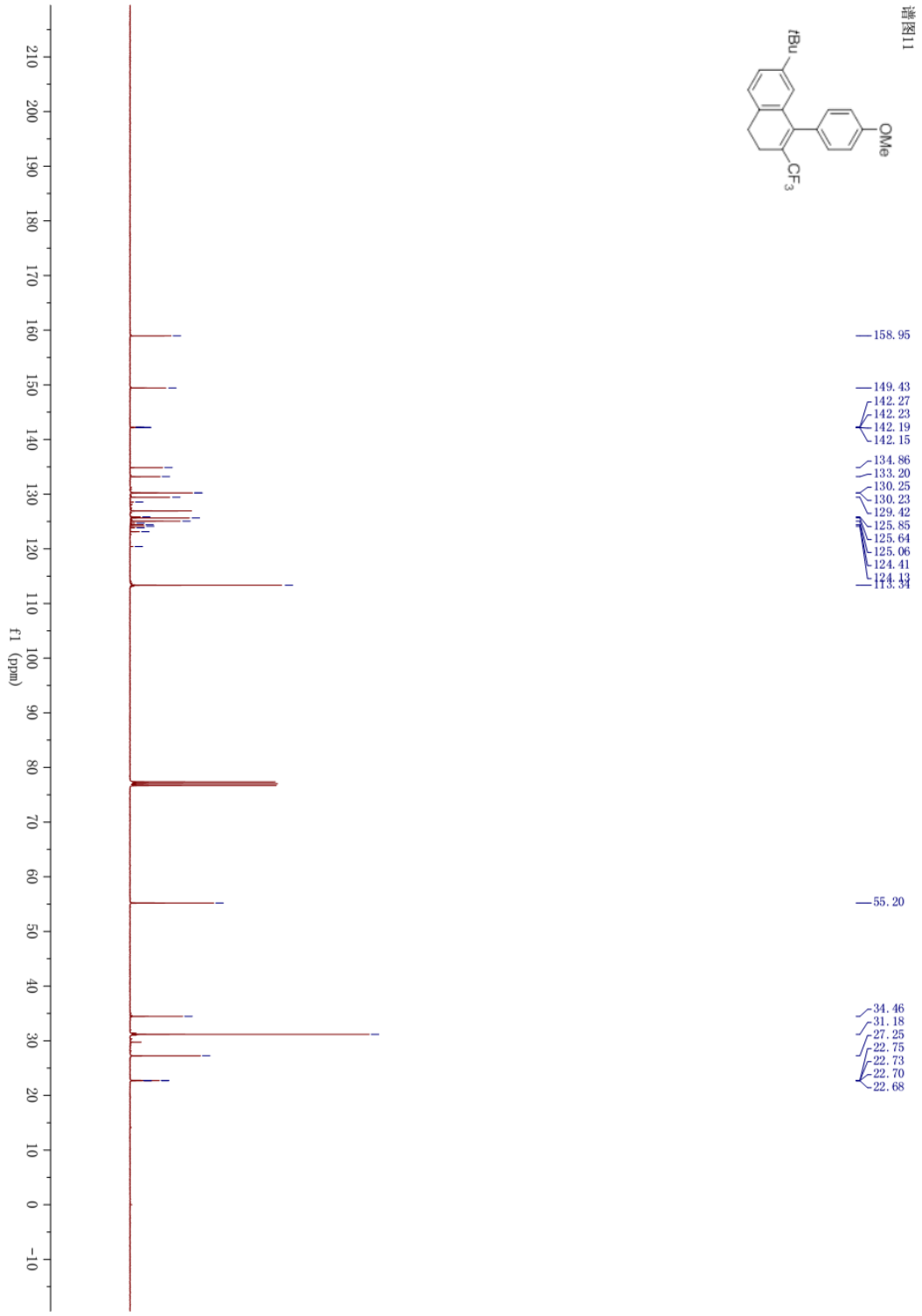
^{1}H NMR spectrum of compound **2g**



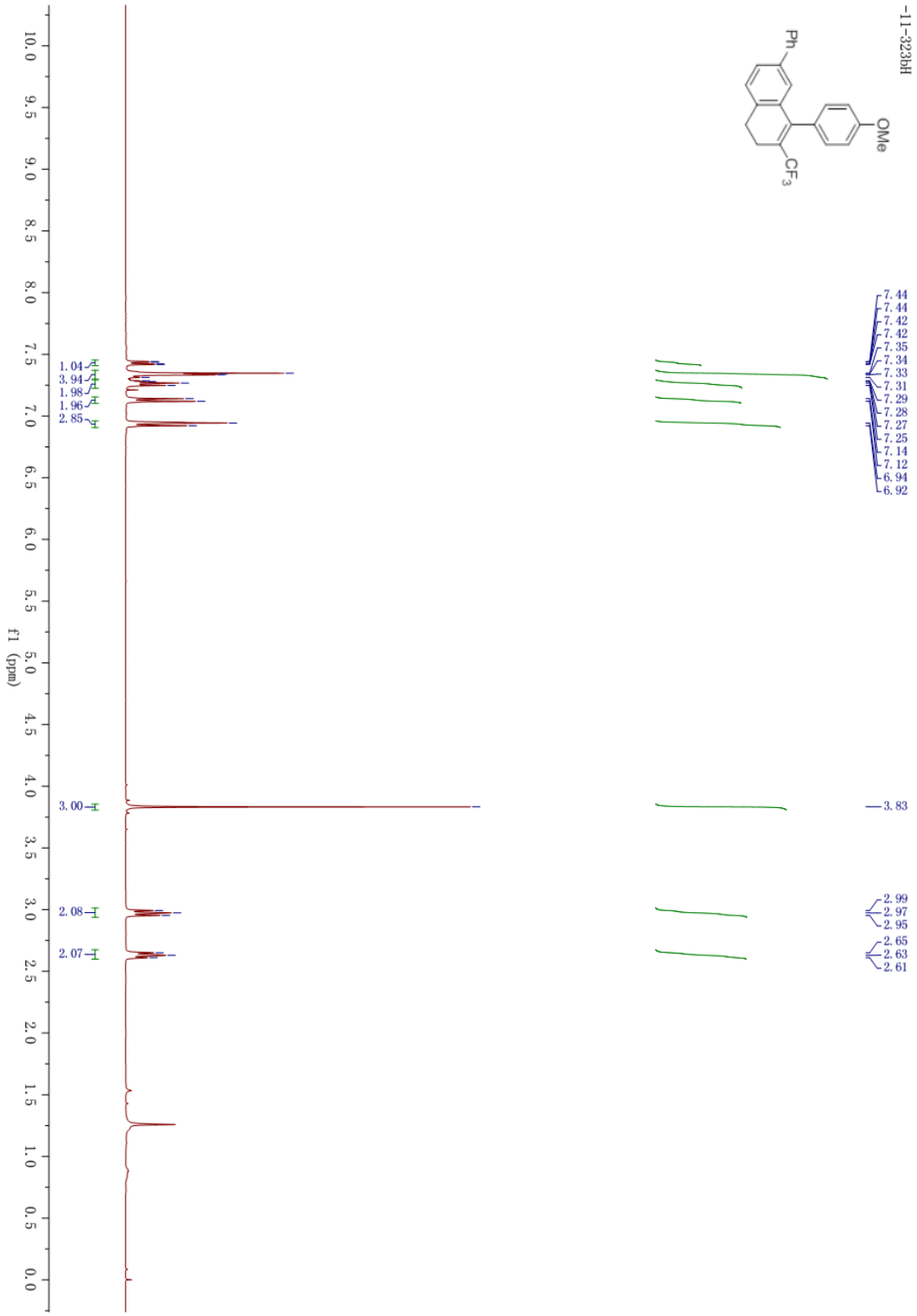
^{19}F NMR spectrum of compound **2g**



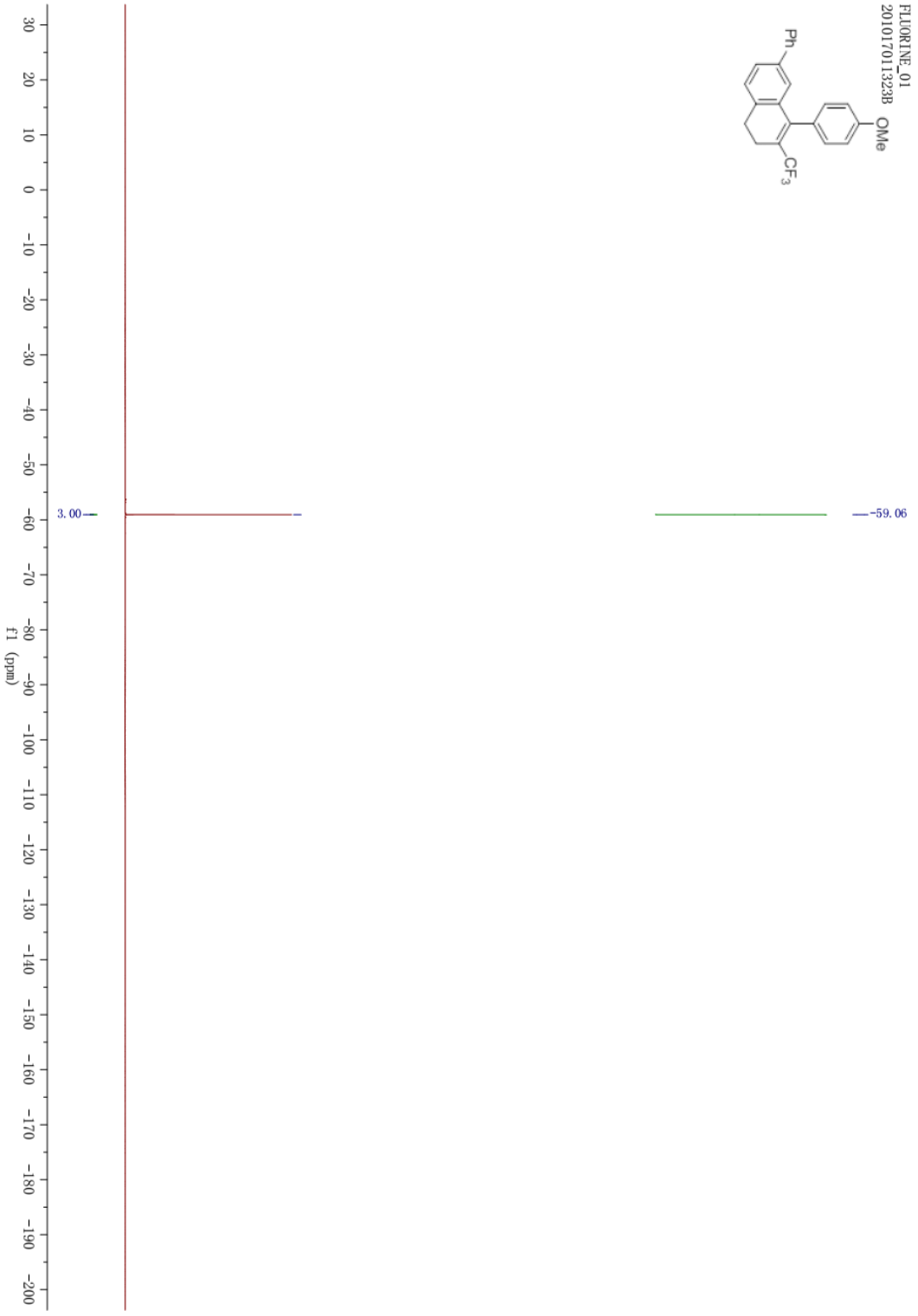
^{13}C NMR spectrum of compound **2g**



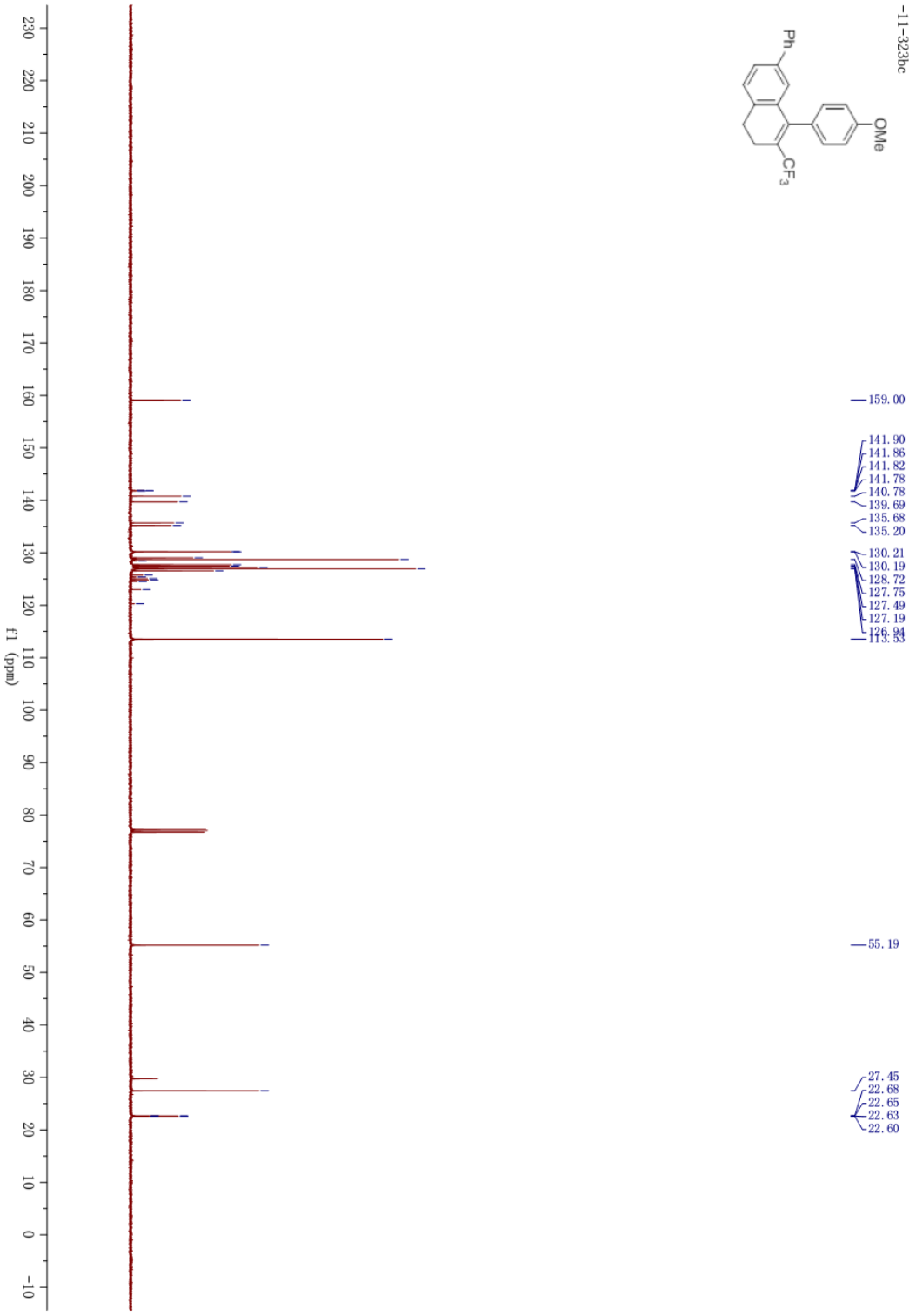
^{1}H NMR spectrum of compound **2h**



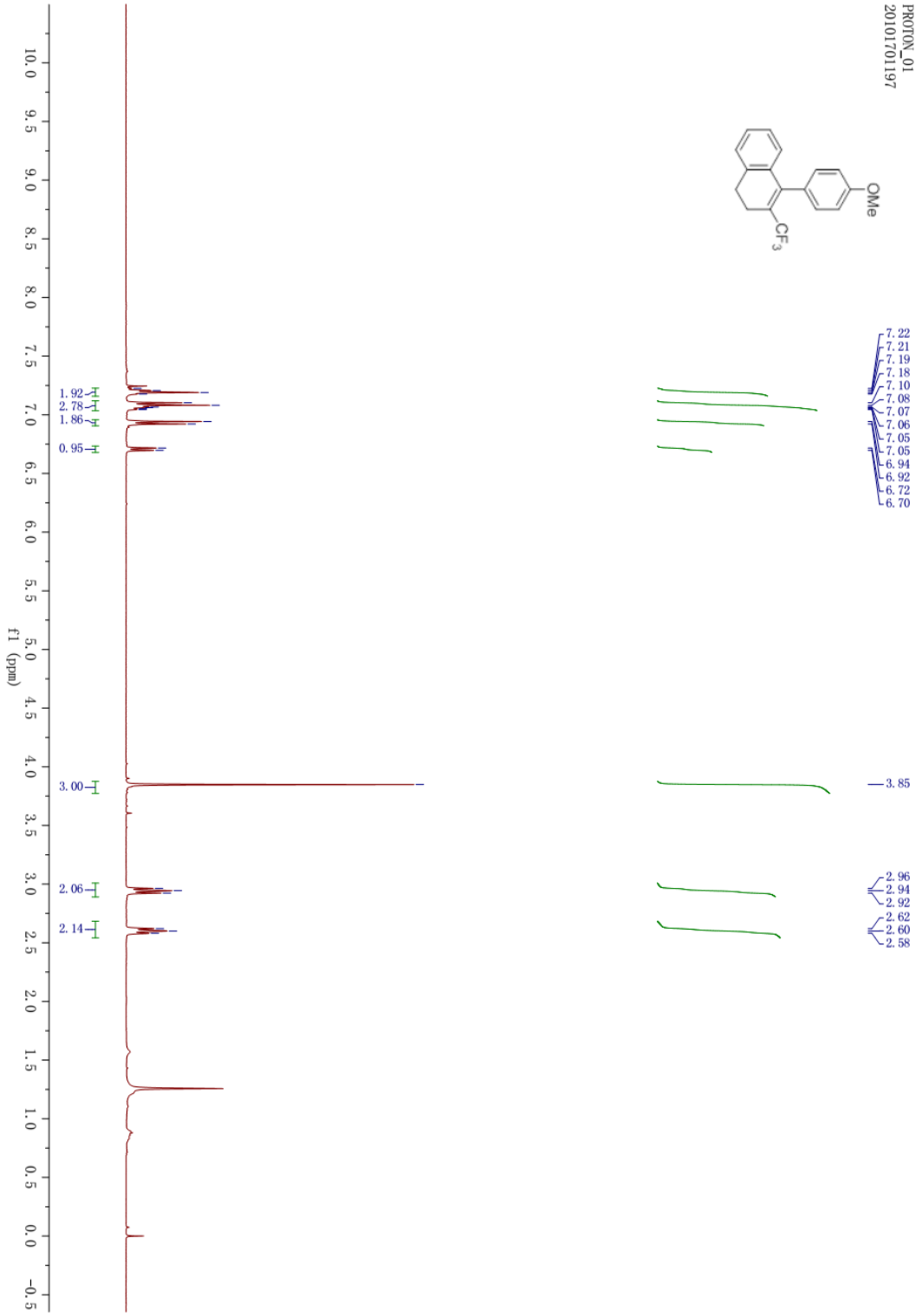
^{19}F NMR spectrum of compound **2h**



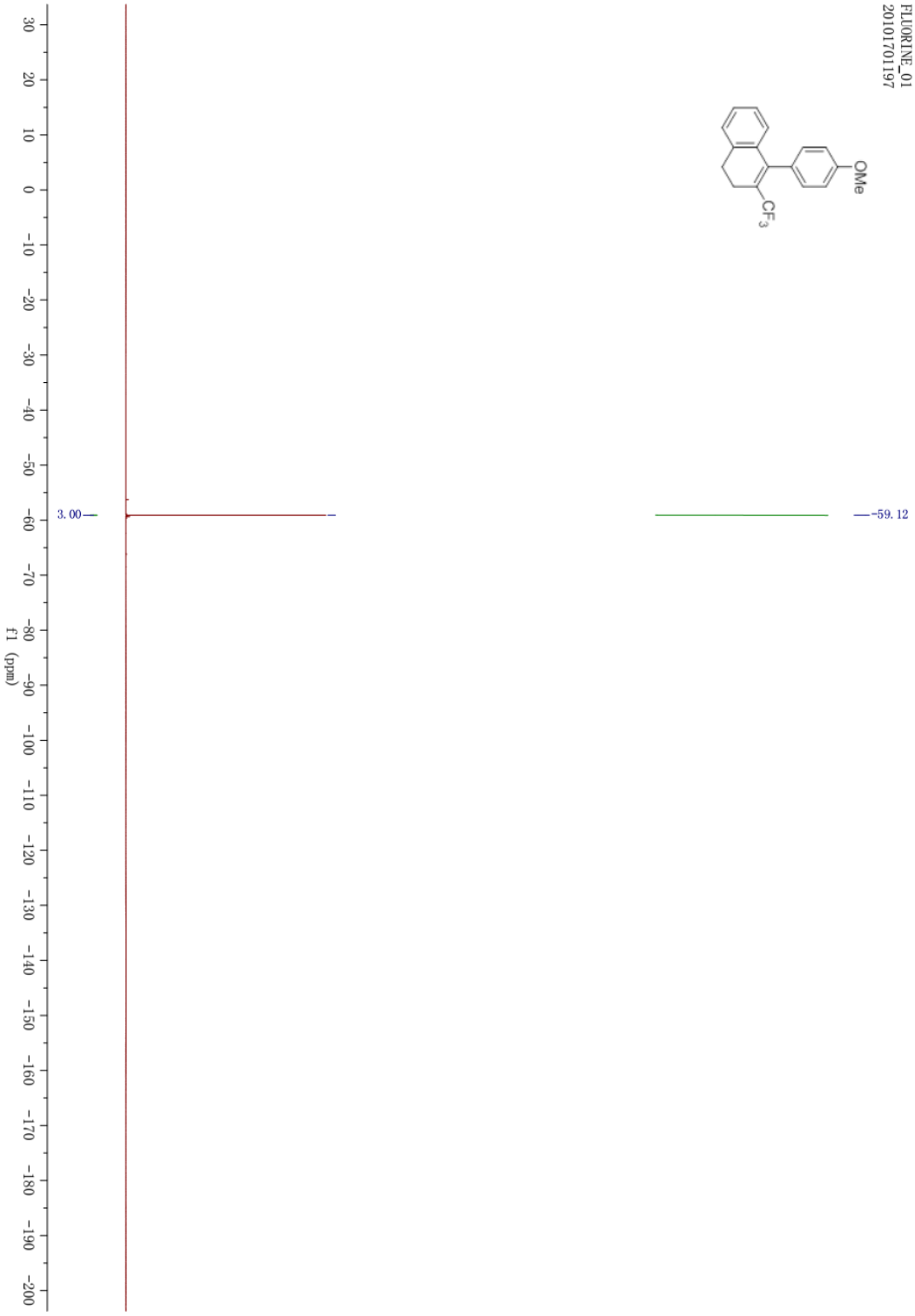
^{13}C NMR spectrum of compound **2h**



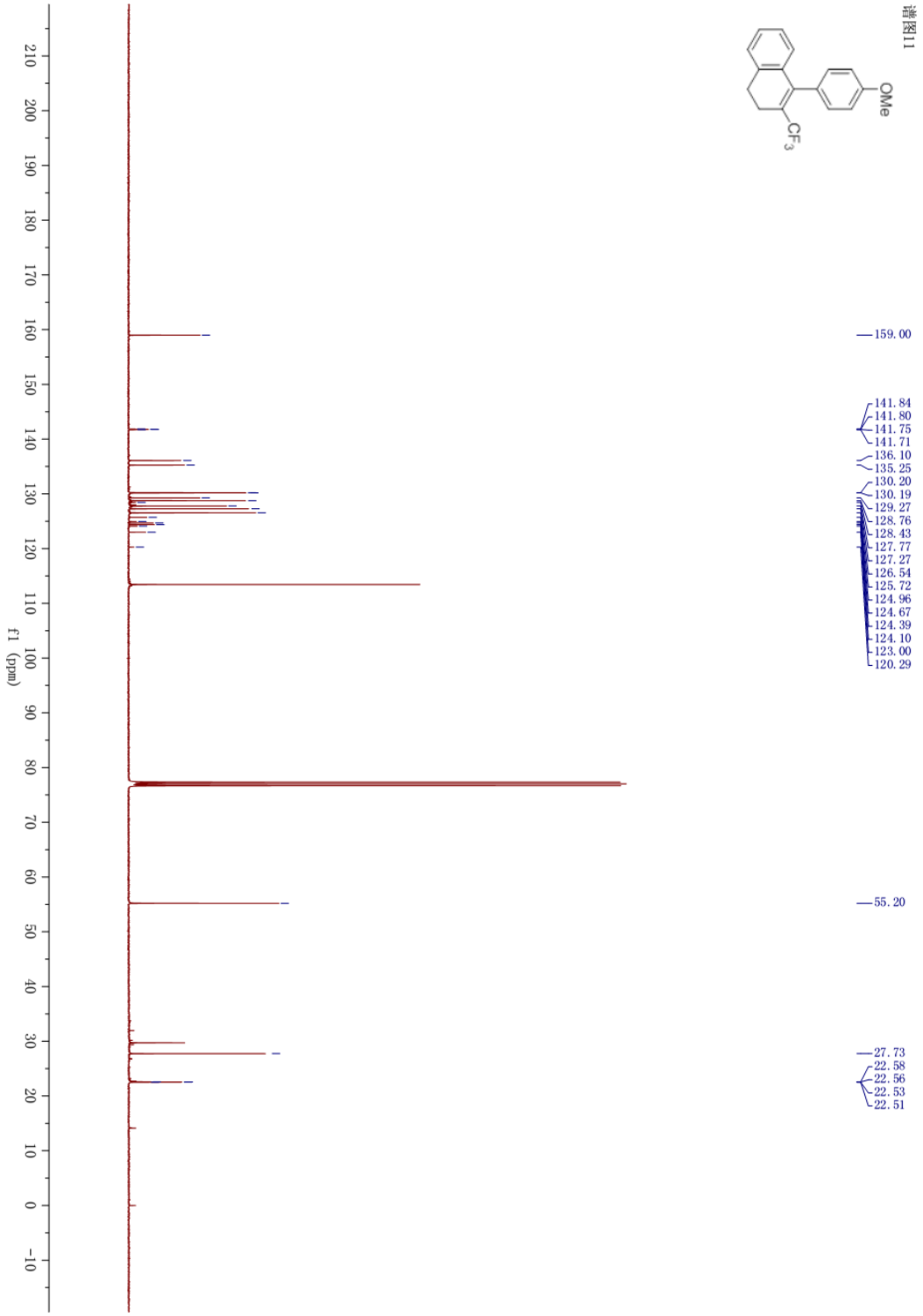
^{1}H NMR spectrum of compound **2i**



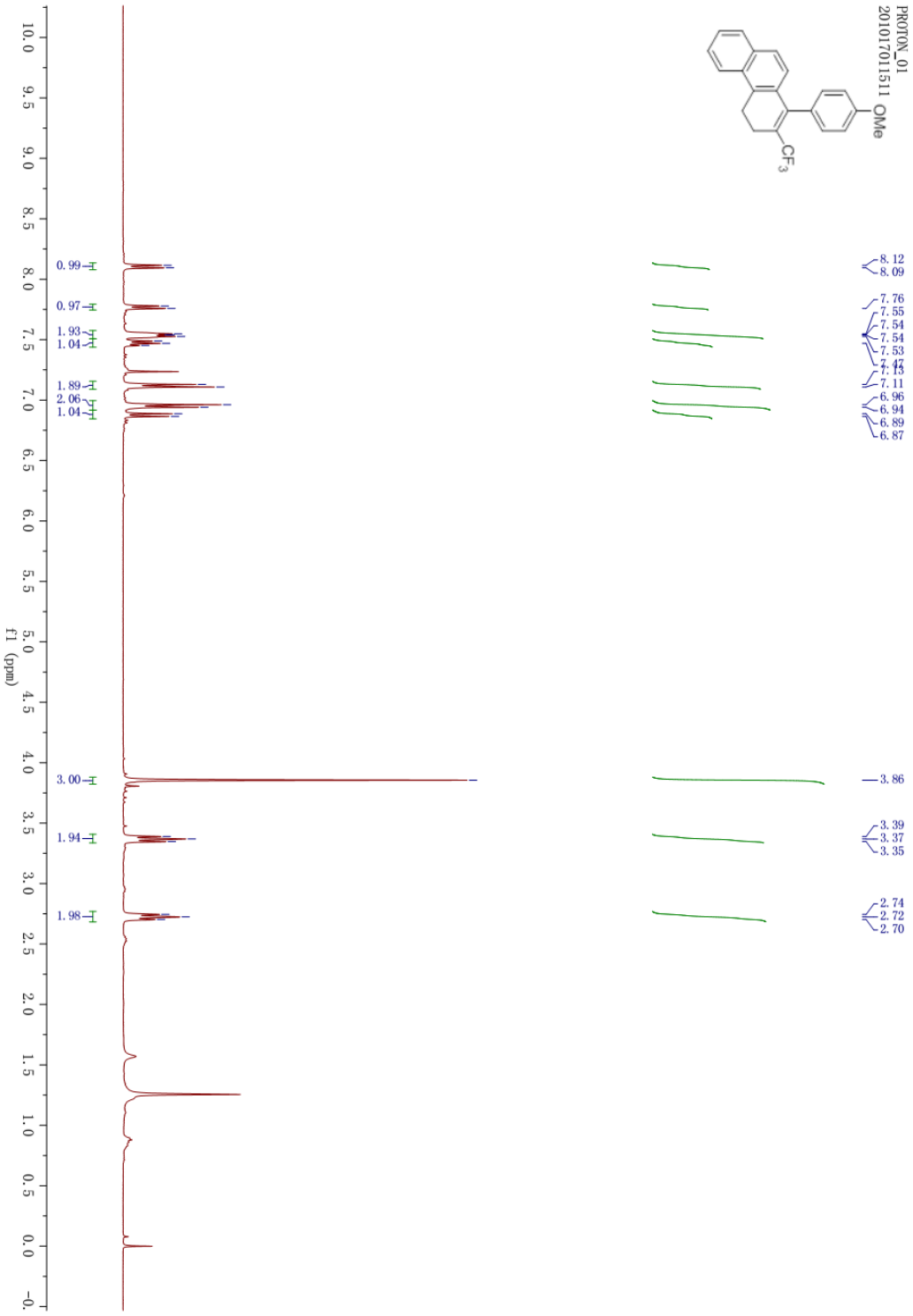
^{19}F NMR spectrum of compound **2i**



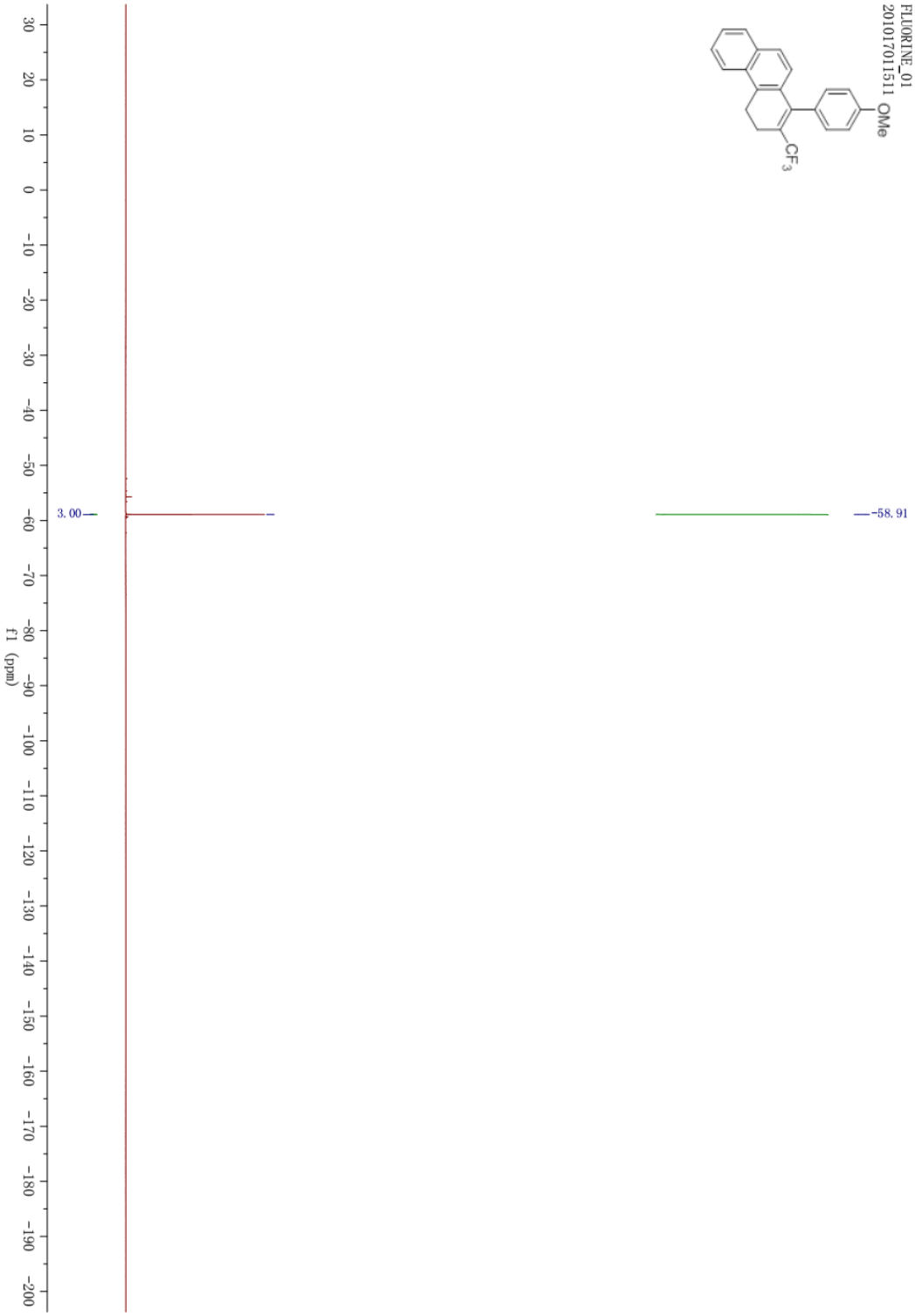
^{13}C NMR spectrum of compound **2i**



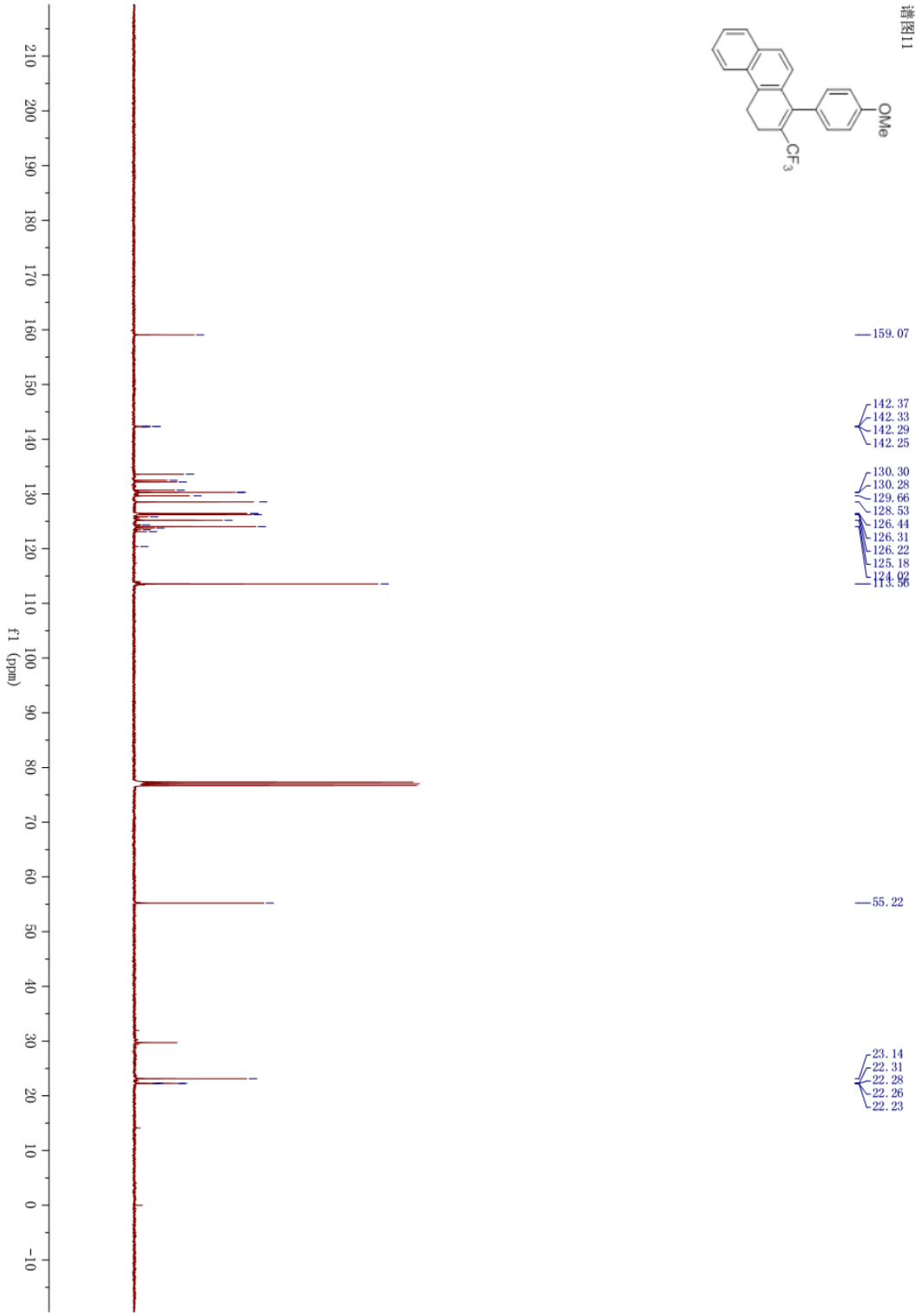
^{1}H NMR spectrum of compound **2j**



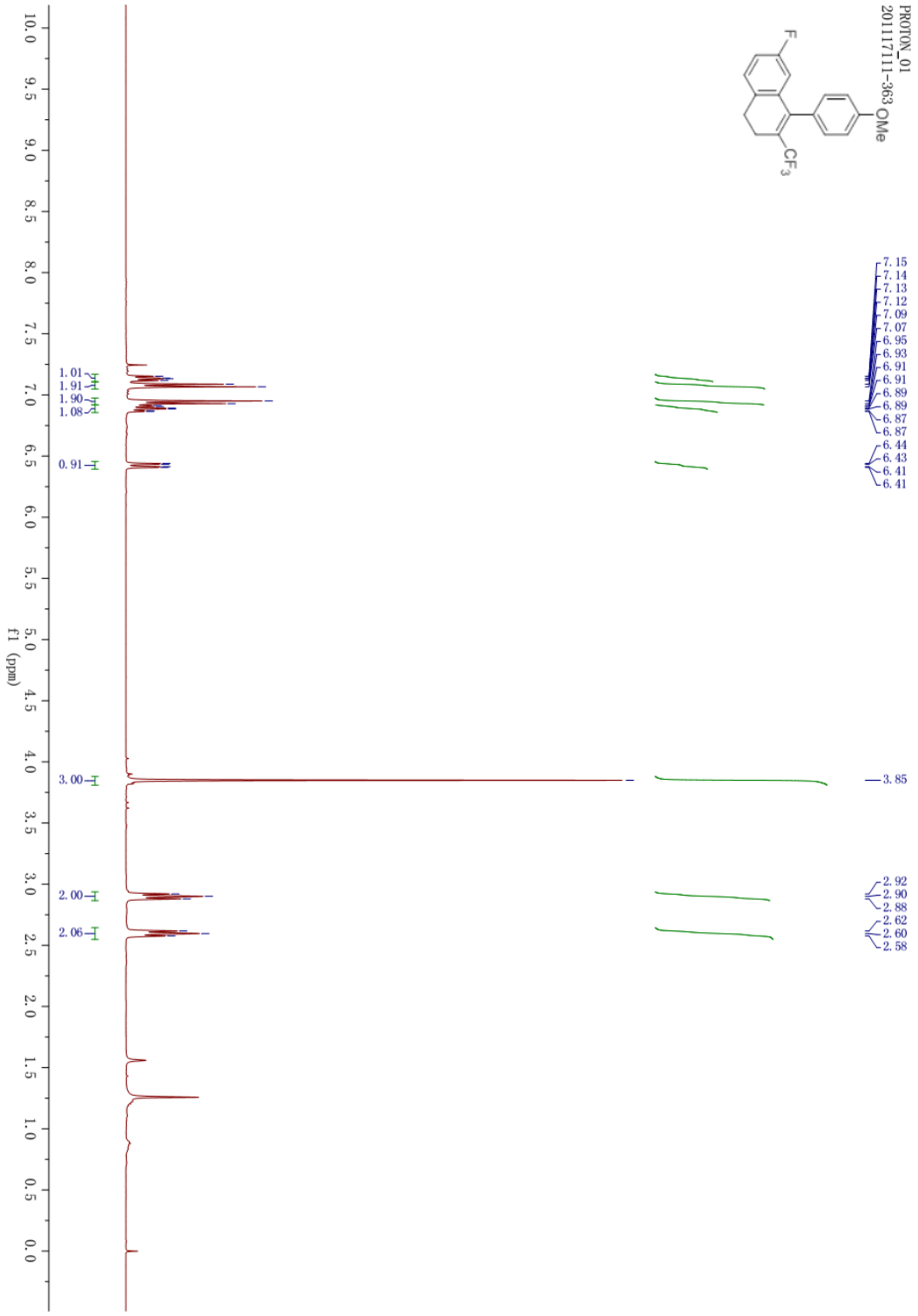
^{19}F NMR spectrum of compound **2j**



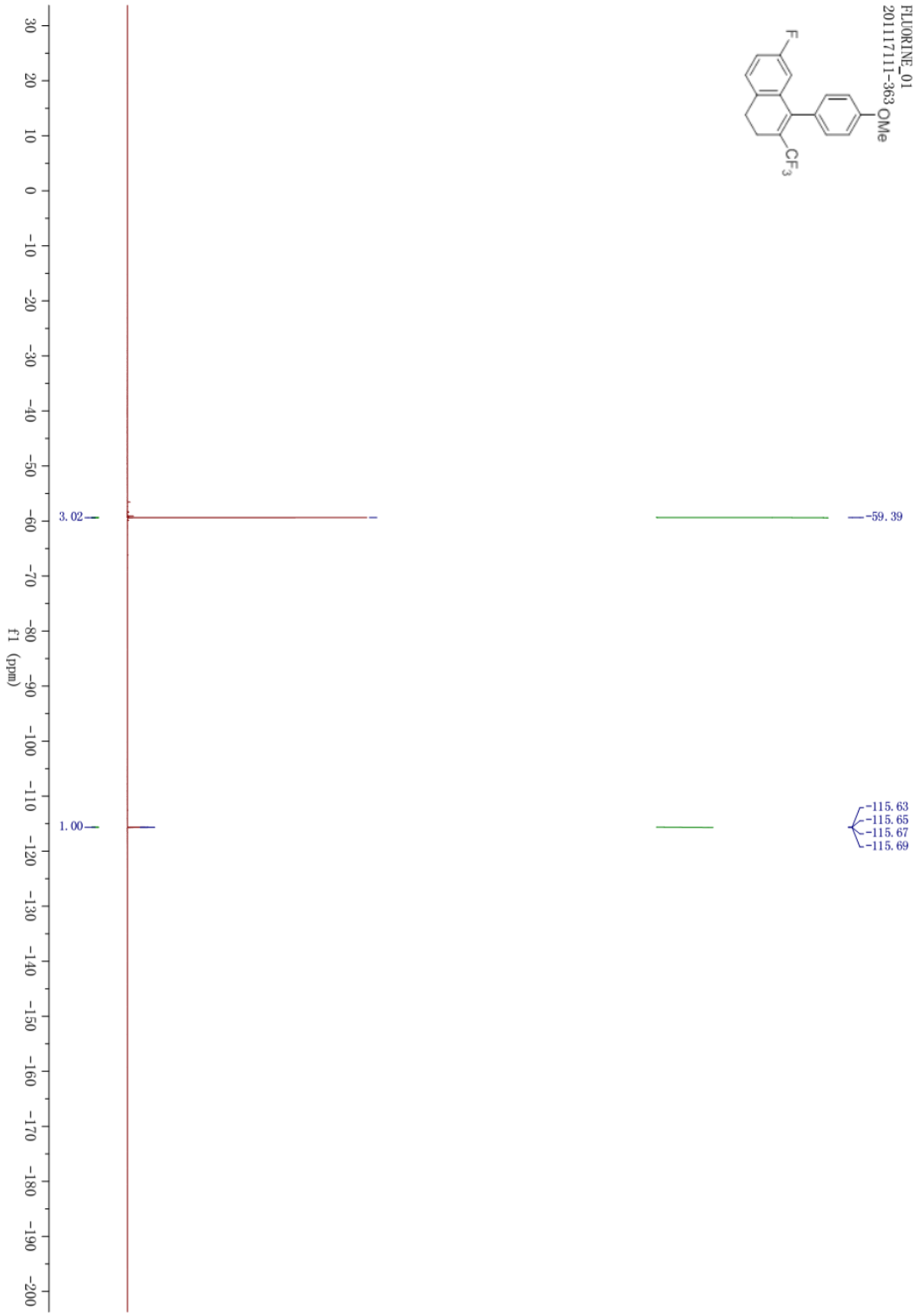
^{13}C NMR spectrum of compound **2j**



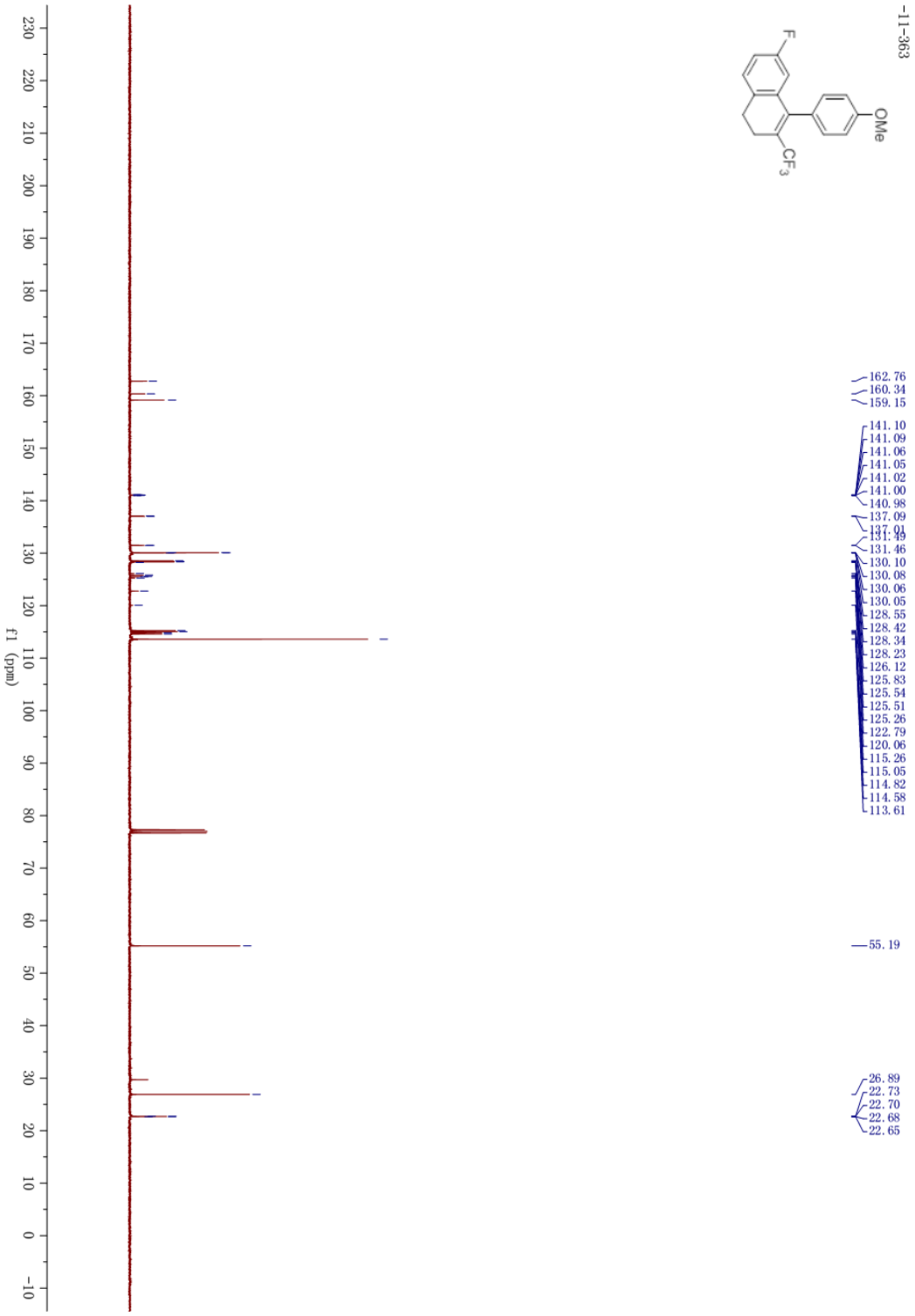
^{1}H NMR spectrum of compound **2k**



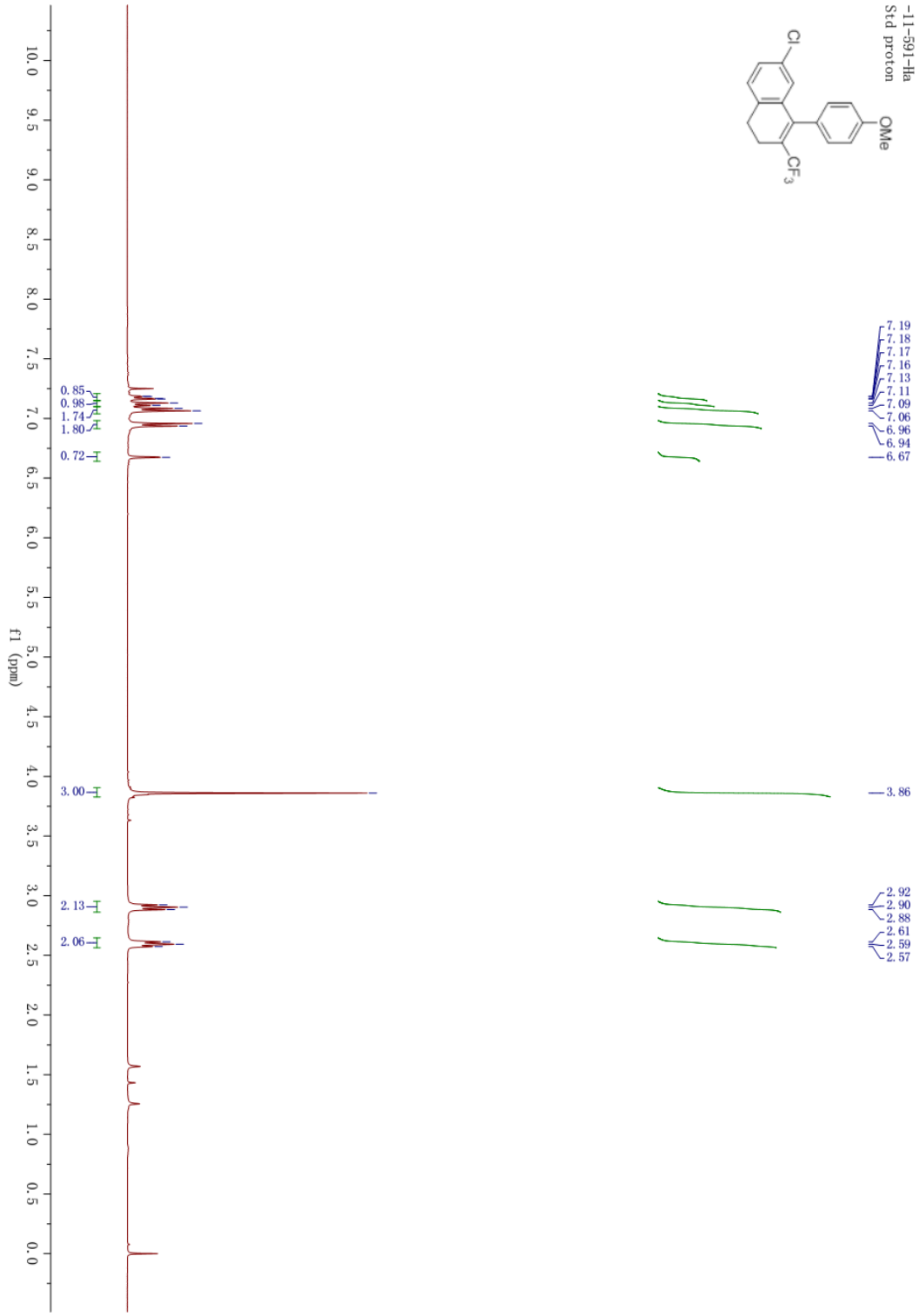
^{19}F NMR spectrum of compound **2k**



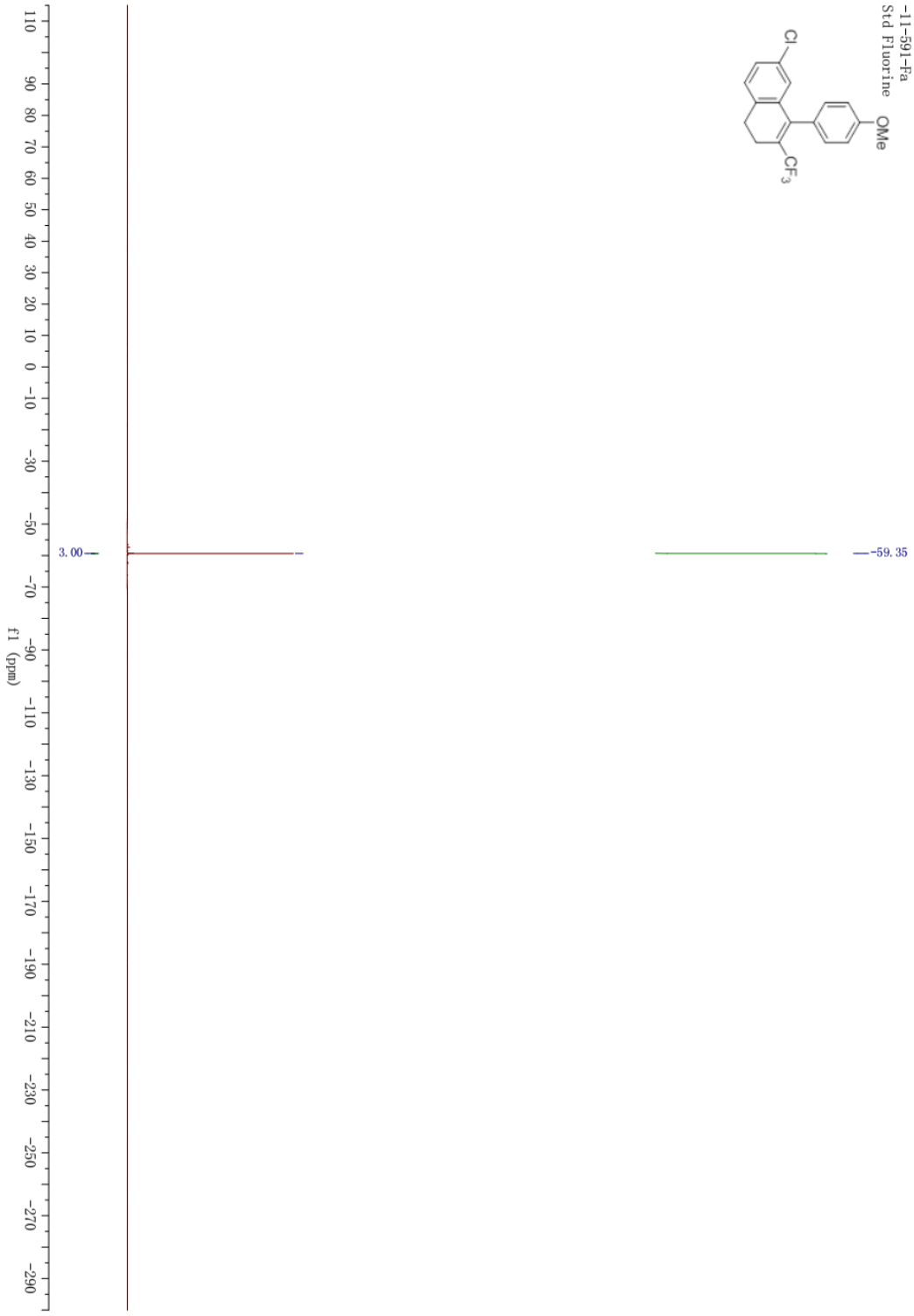
^{13}C NMR spectrum of compound **2k**



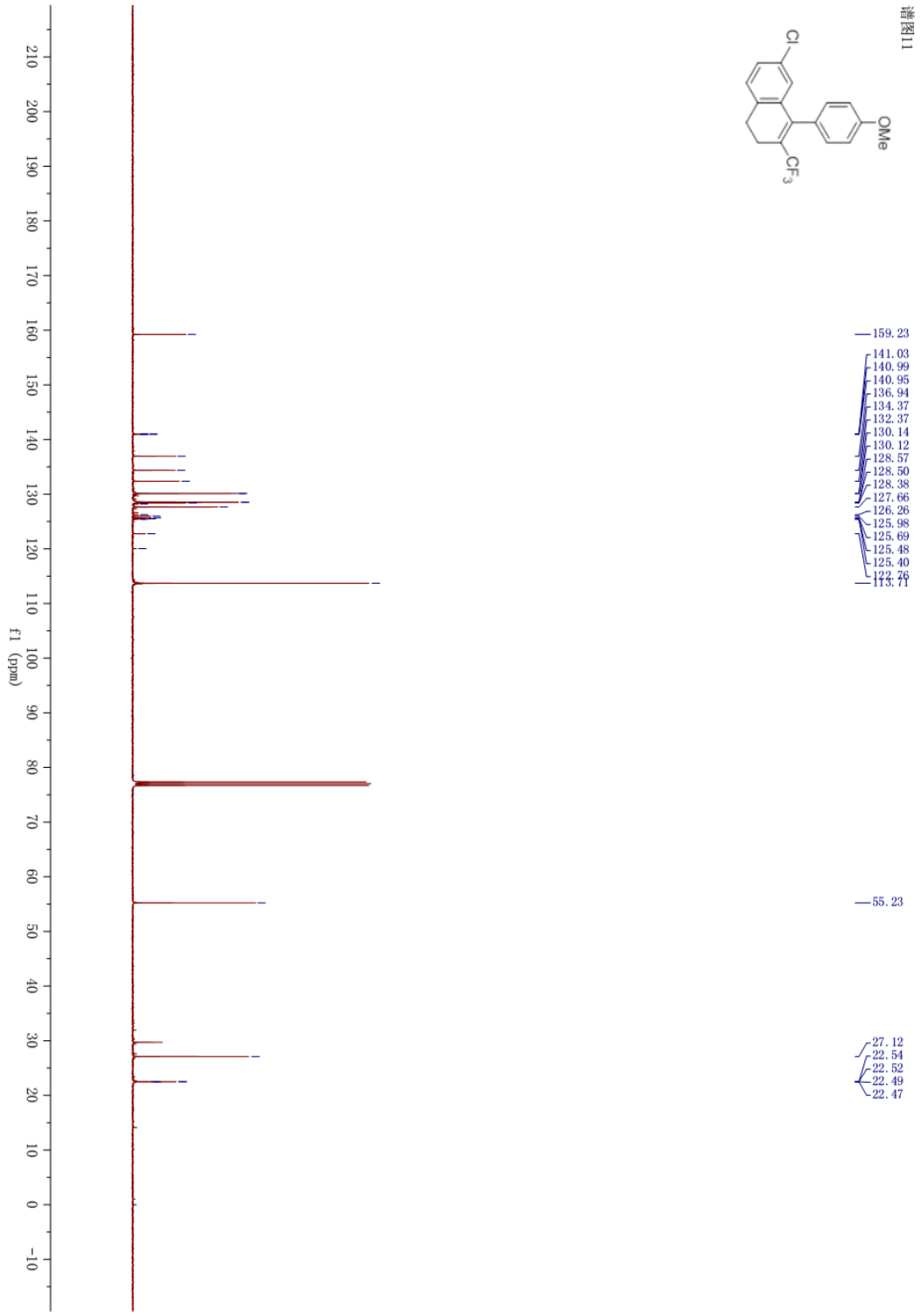
^{1}H NMR spectrum of compound **2l**



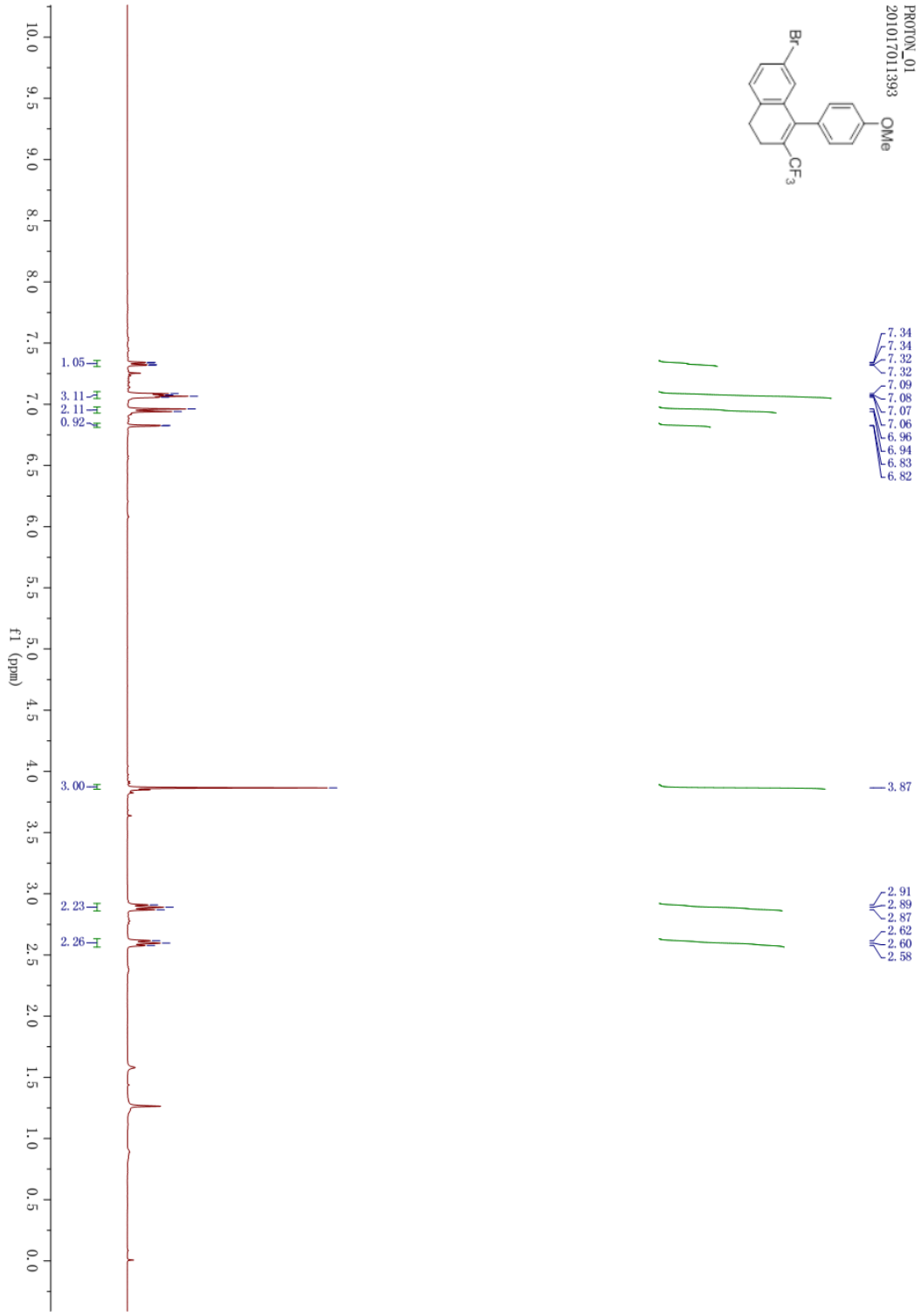
^{19}F NMR spectrum of compound **2l**



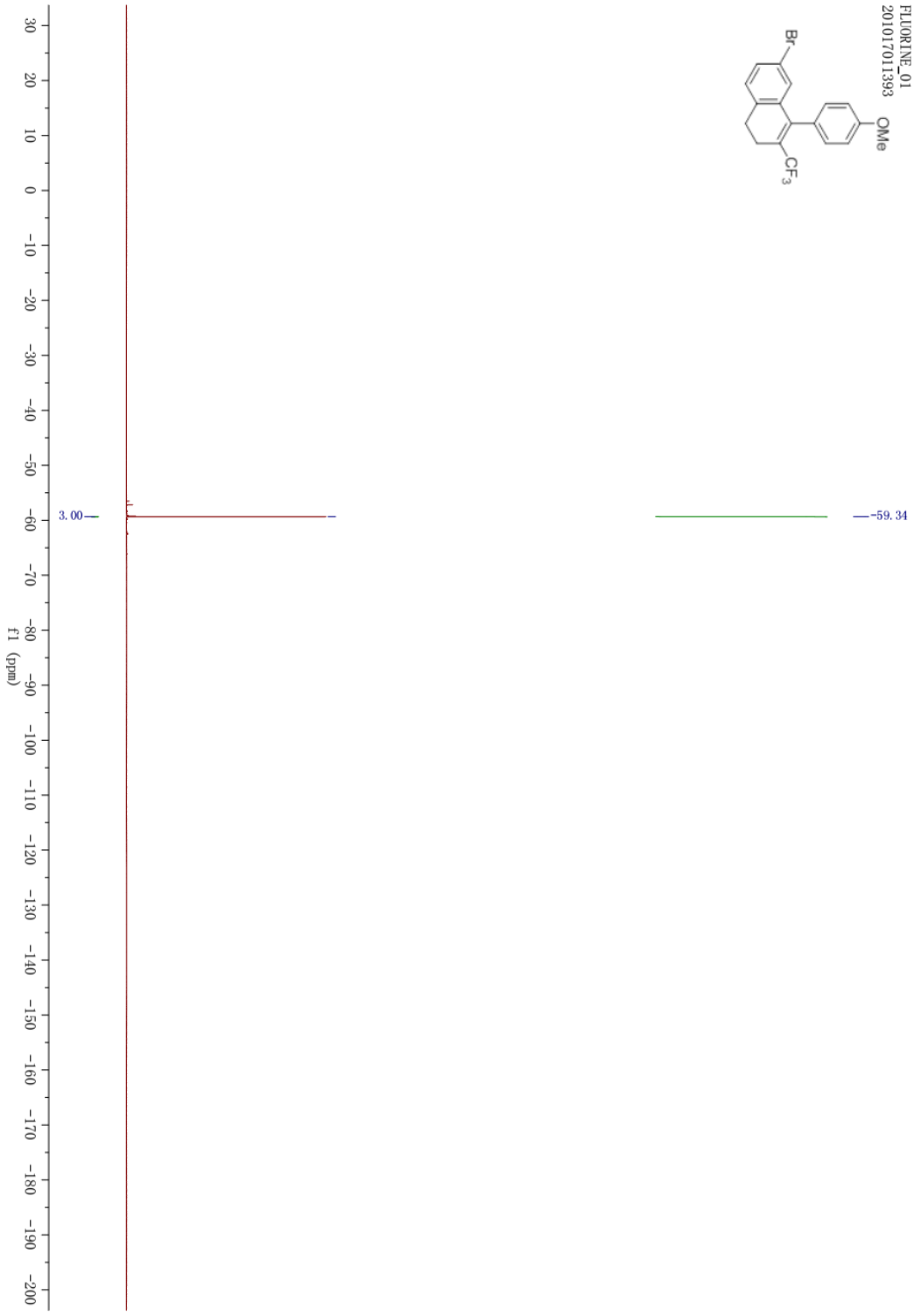
^{13}C NMR spectrum of compound **2l**



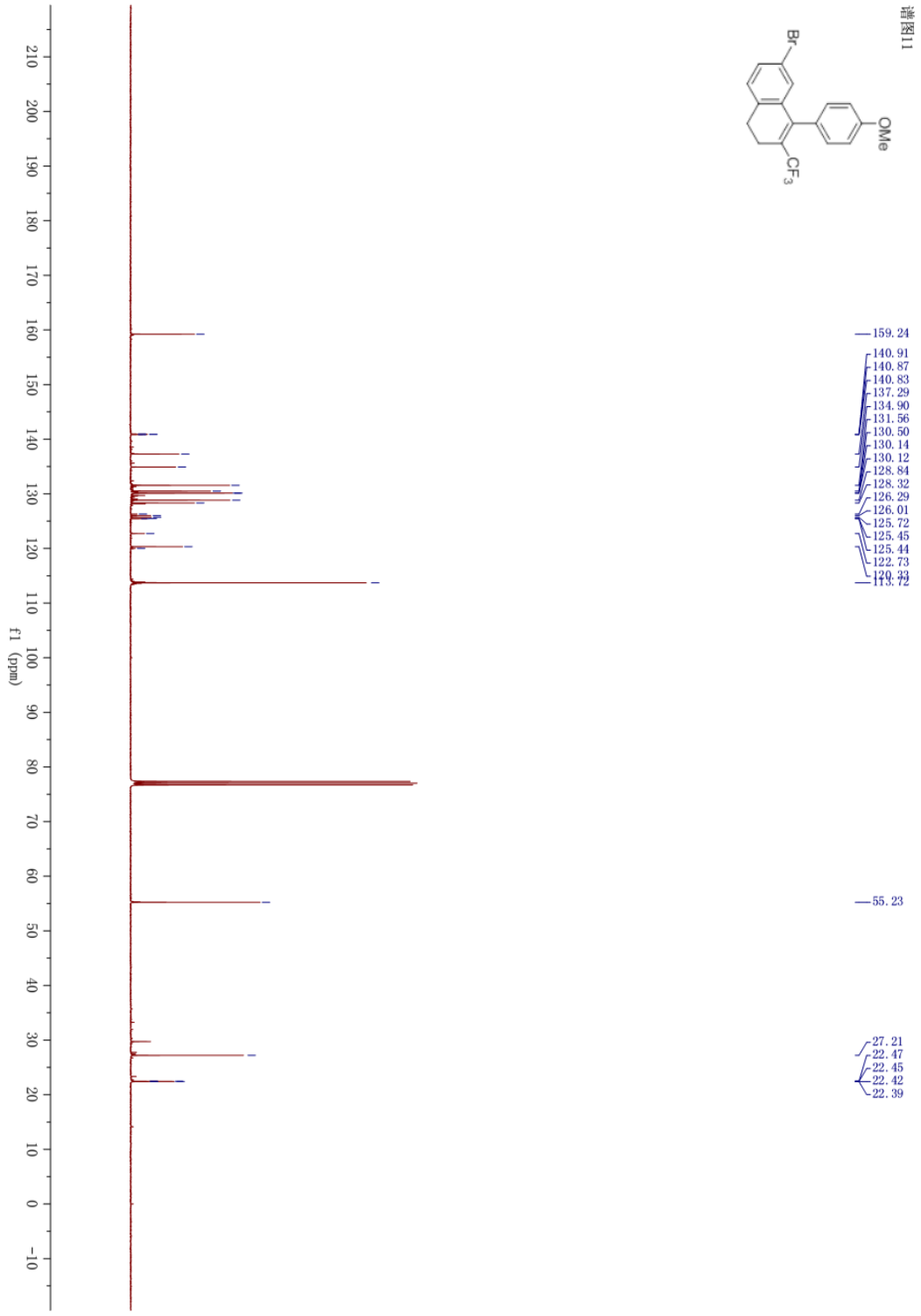
^{1}H NMR spectrum of compound **2m**



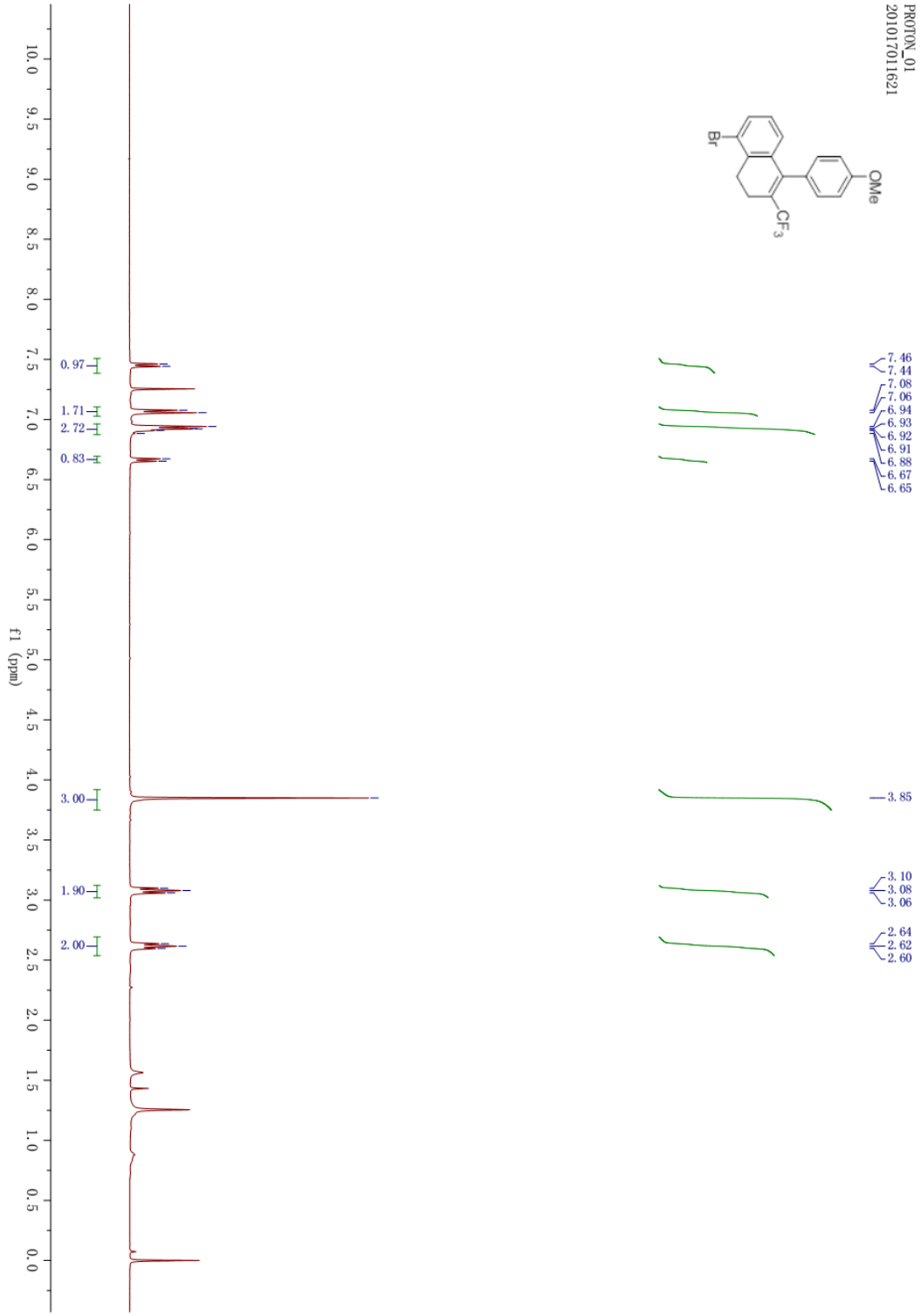
^{19}F NMR spectrum of compound **2m**



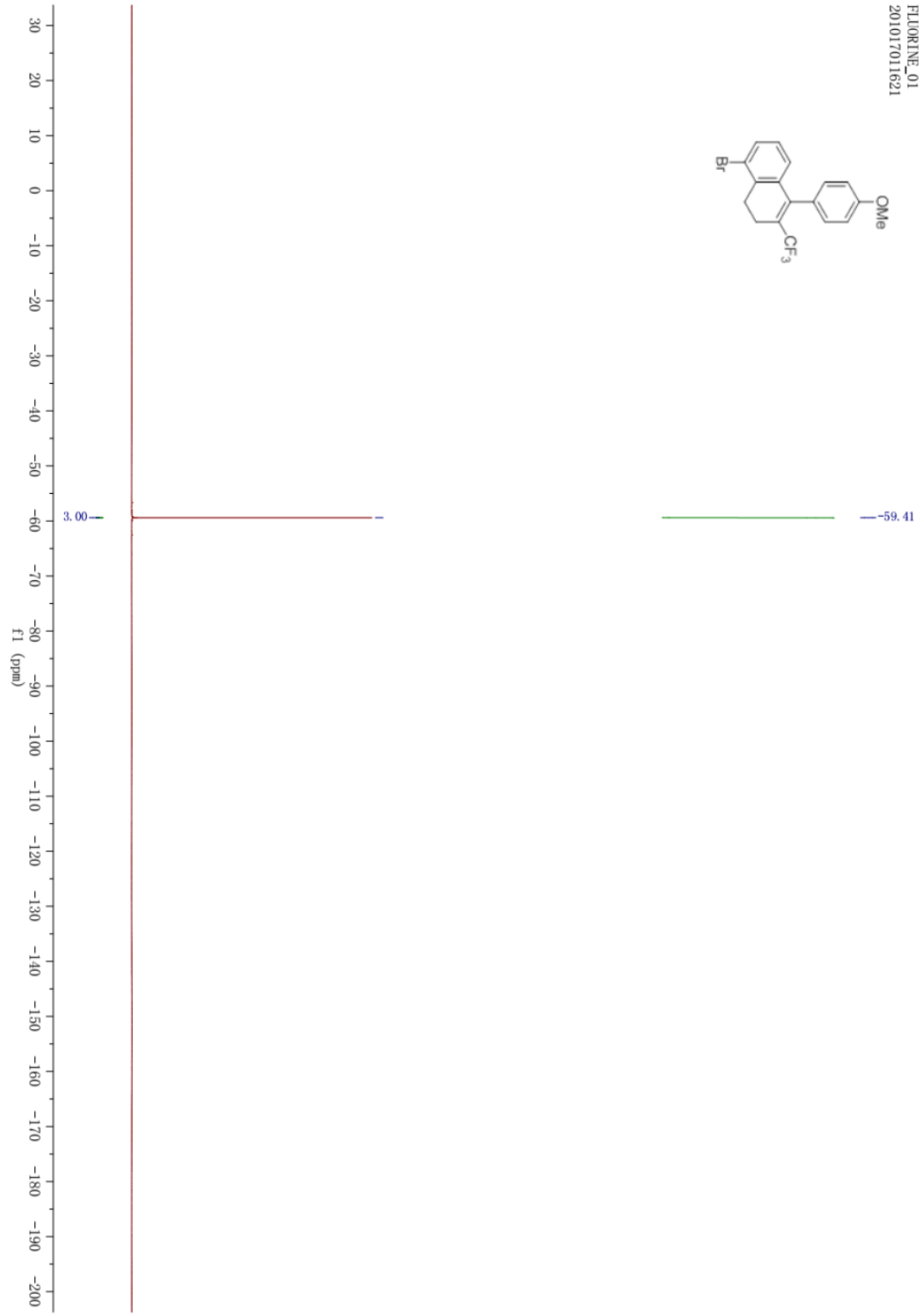
^{13}C NMR spectrum of compound **2m**



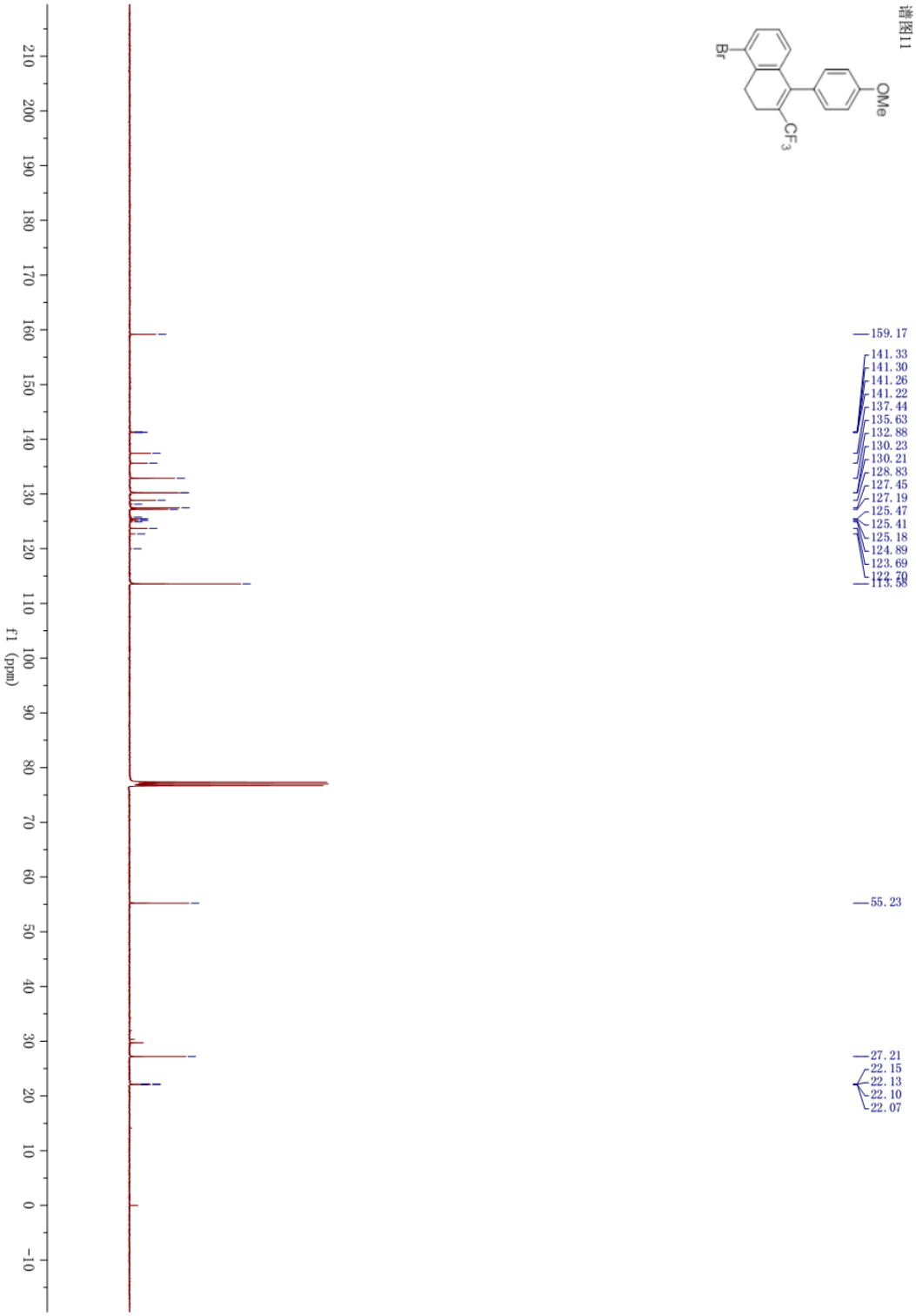
^{1}H NMR spectrum of compound **2n**



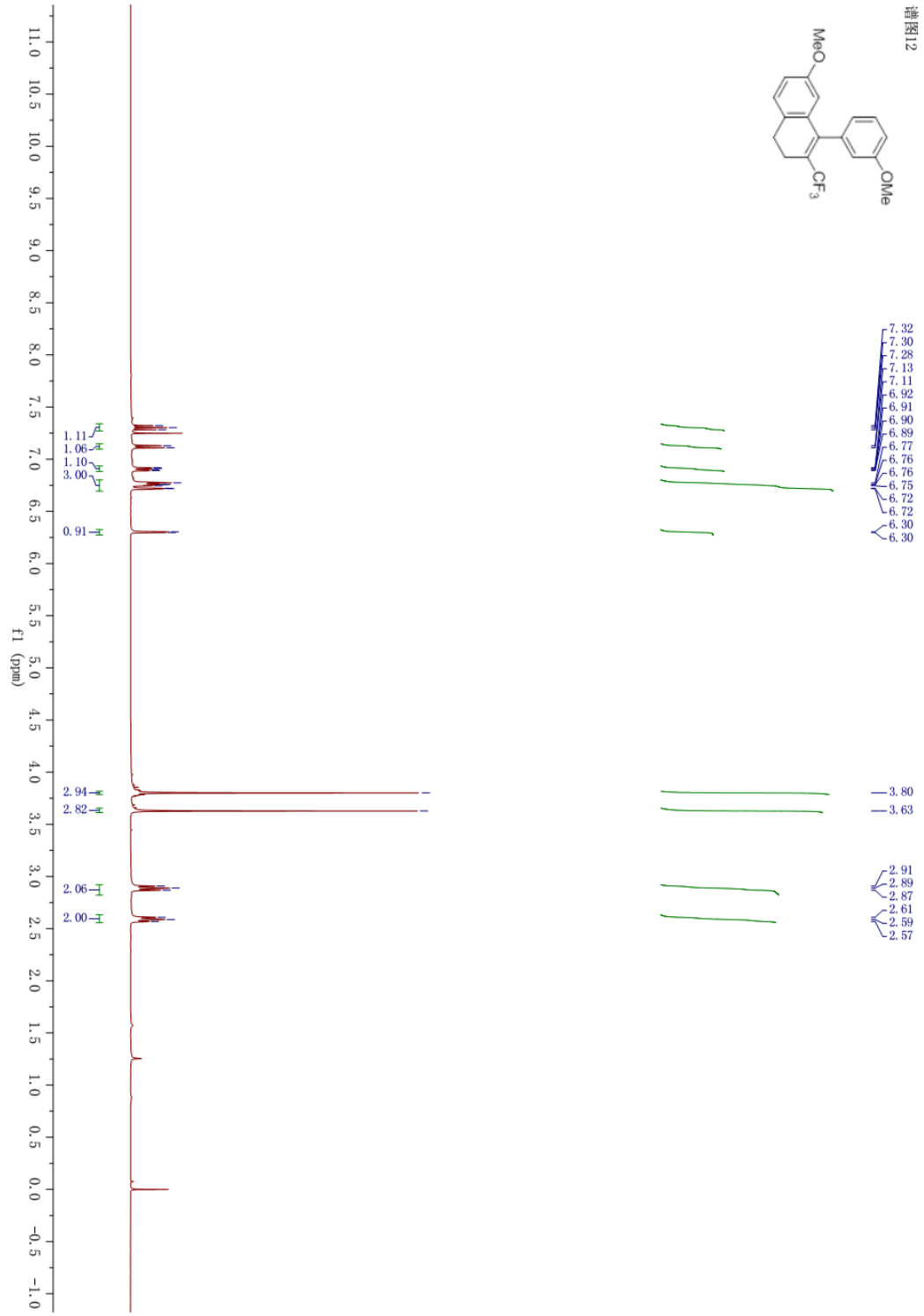
^{19}F NMR spectrum of compound **2n**



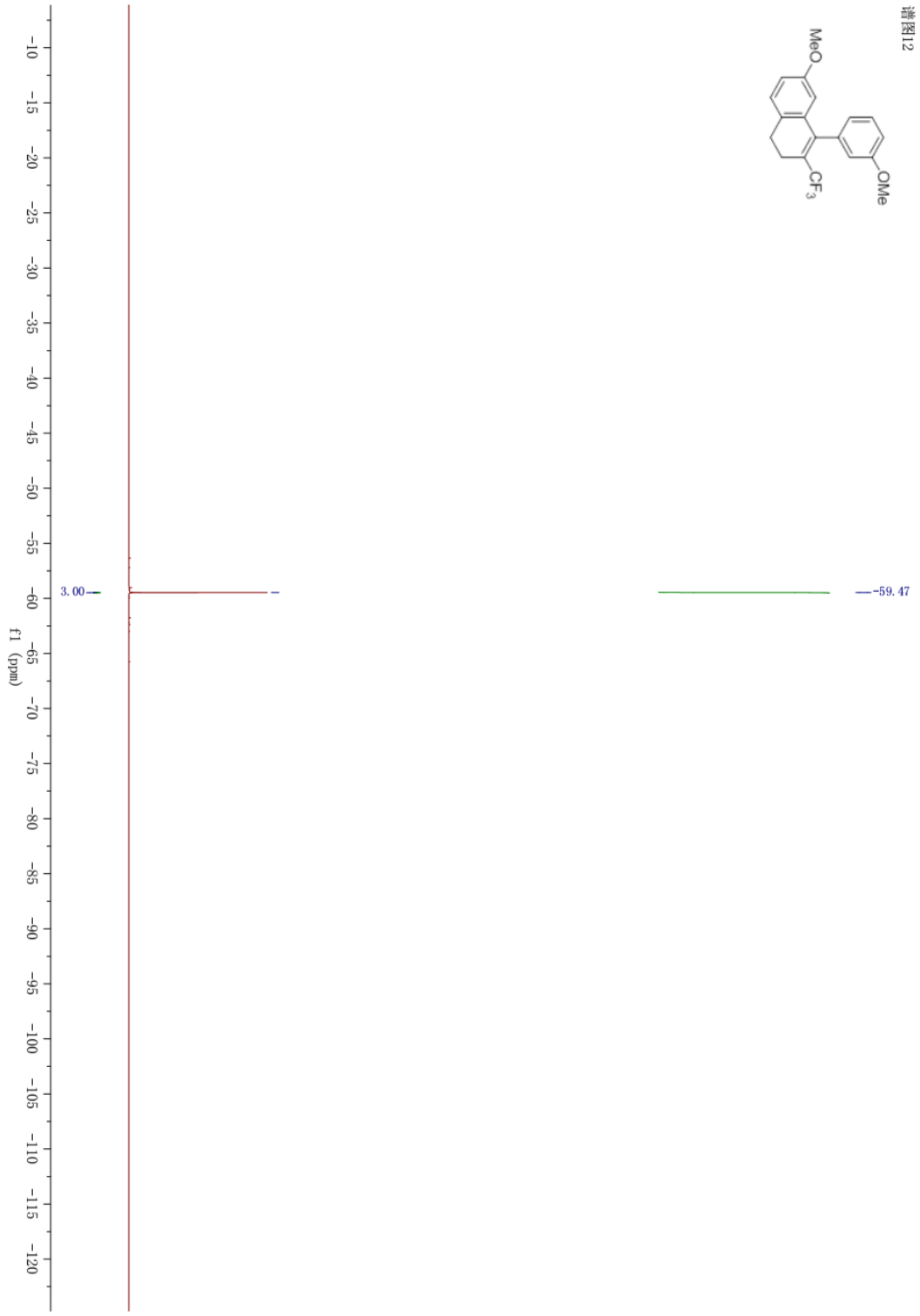
^{13}C NMR spectrum of compound **2n**



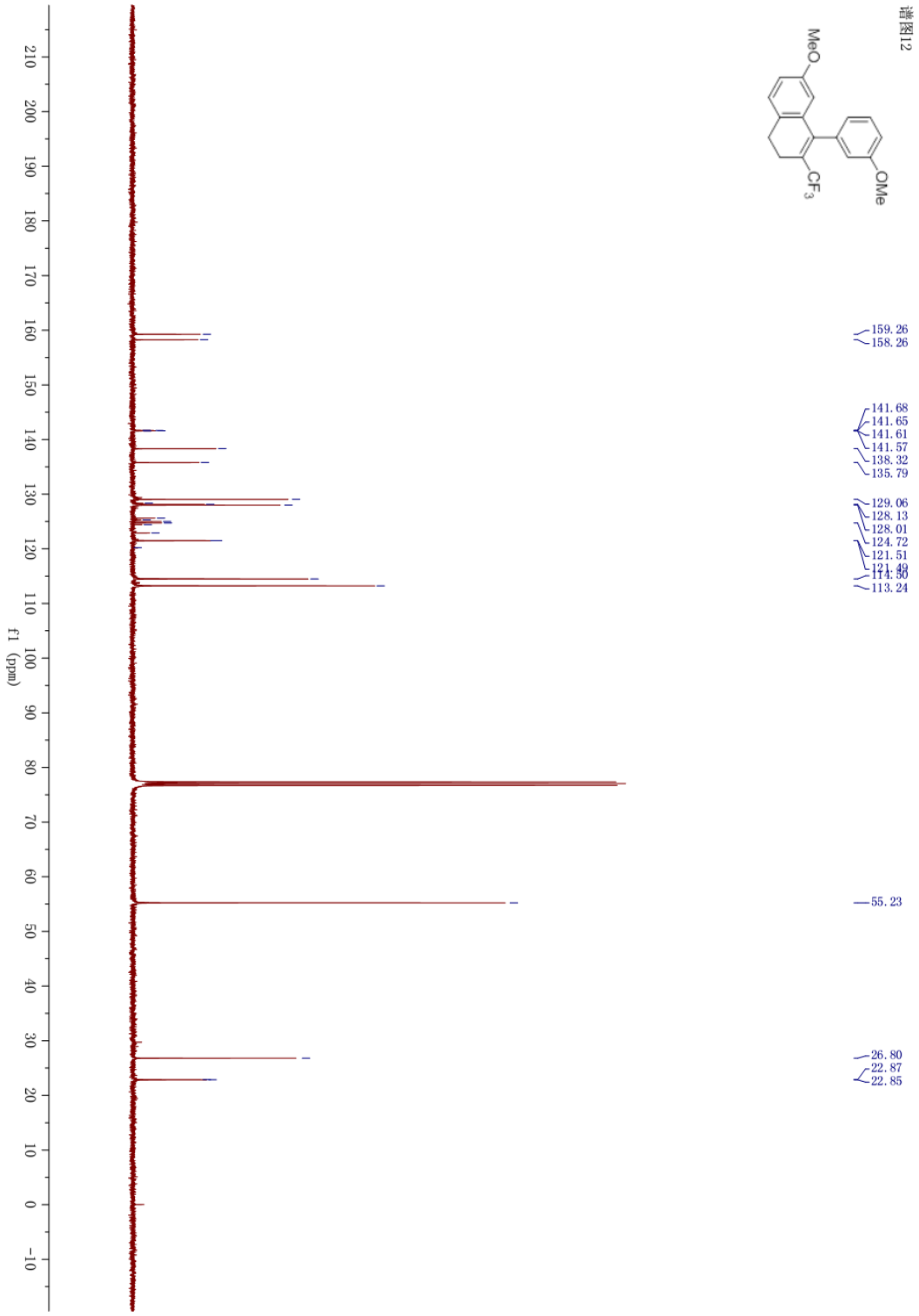
^{1}H NMR spectrum of compound **2o**



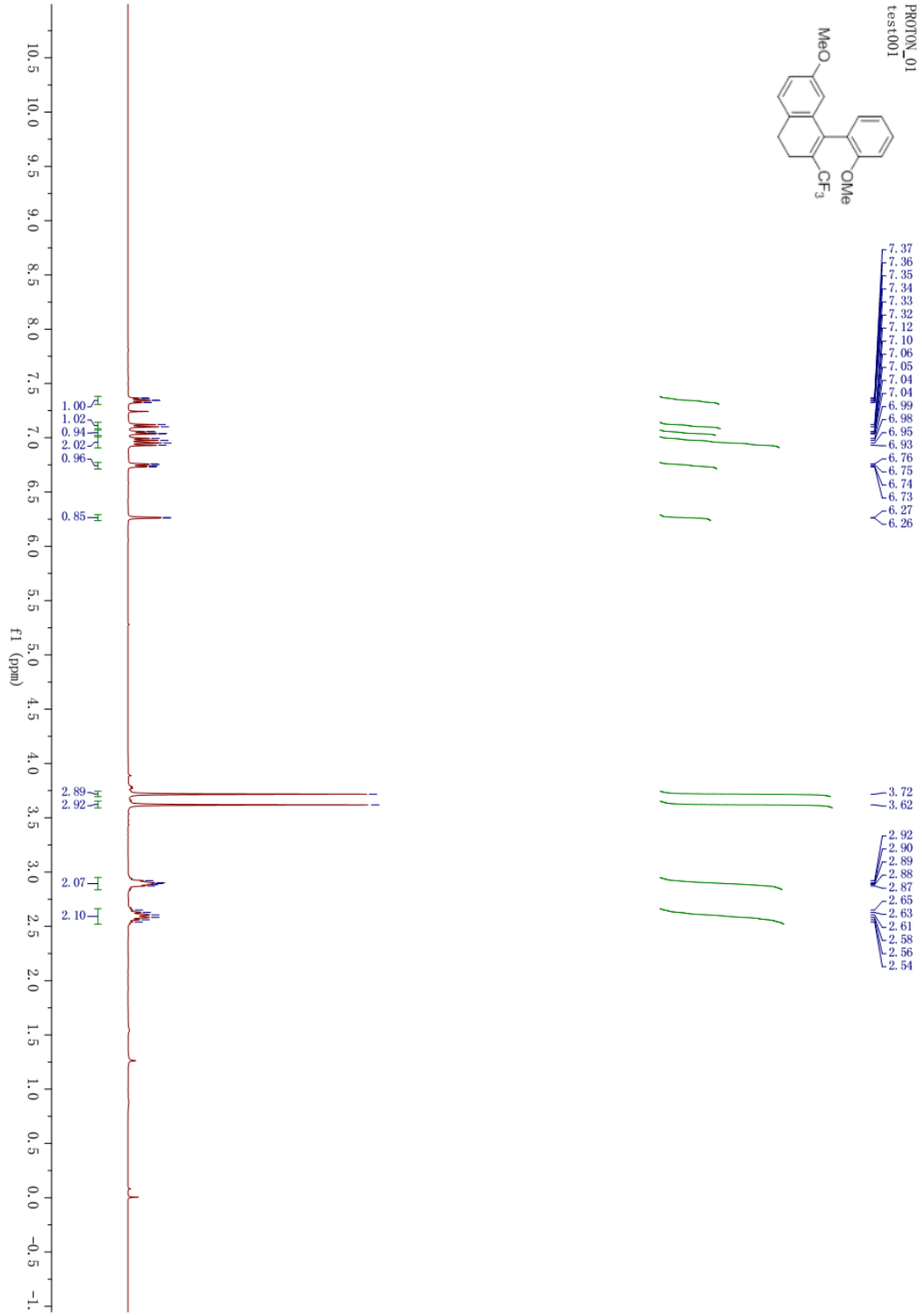
^{19}F NMR spectrum of compound **2o**



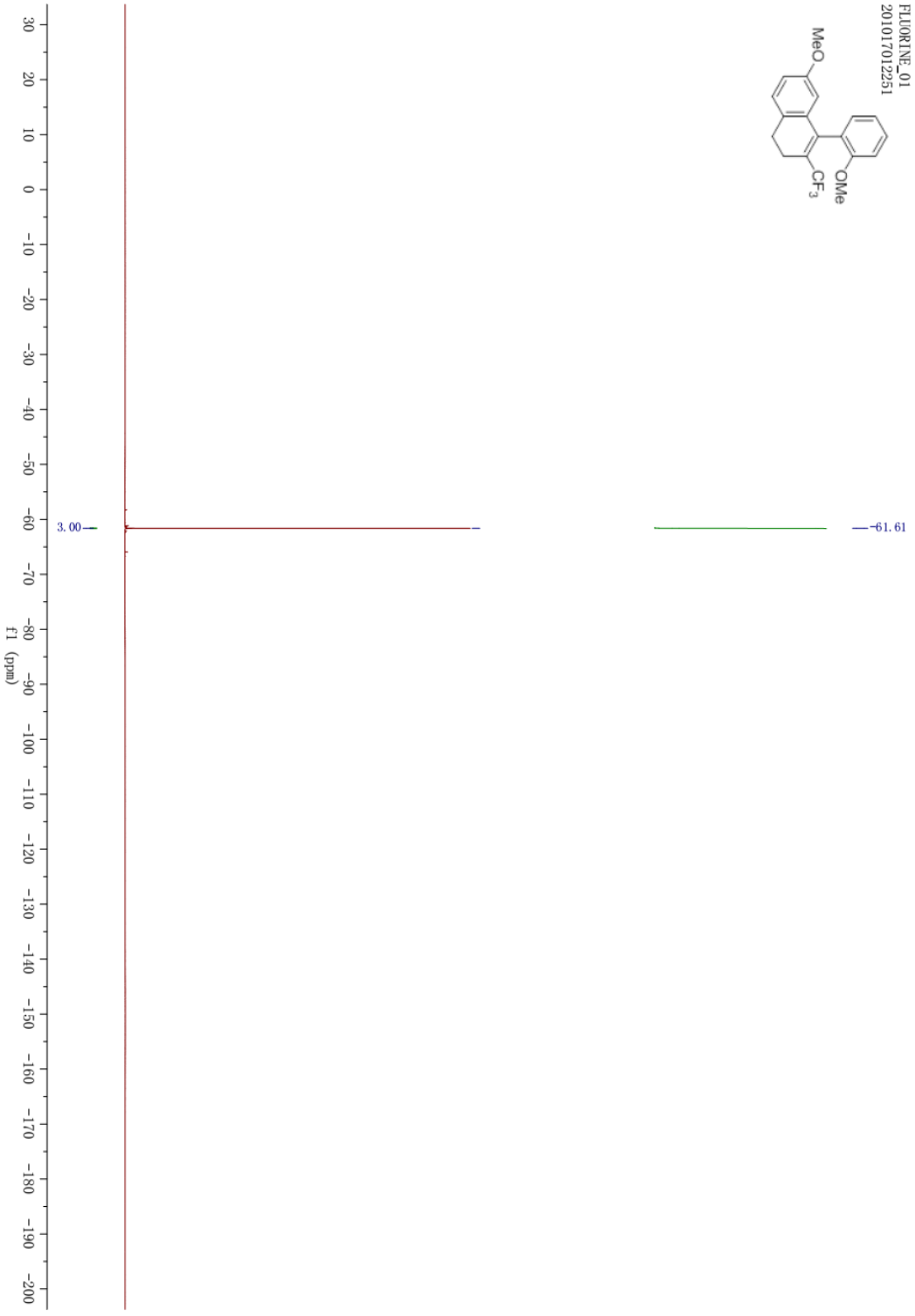
^{13}C NMR spectrum of compound **2o**



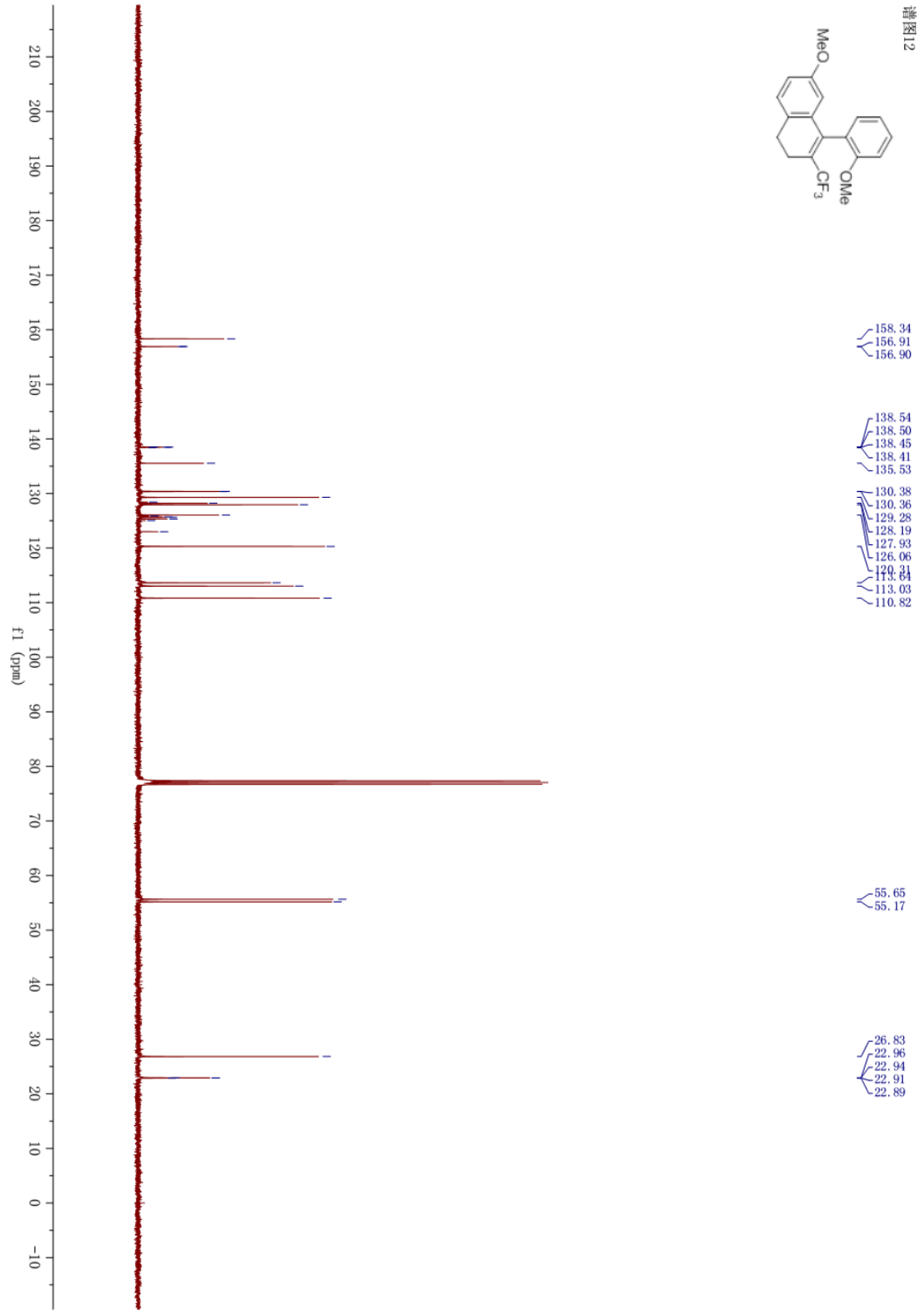
^{1}H NMR spectrum of compound **2p**



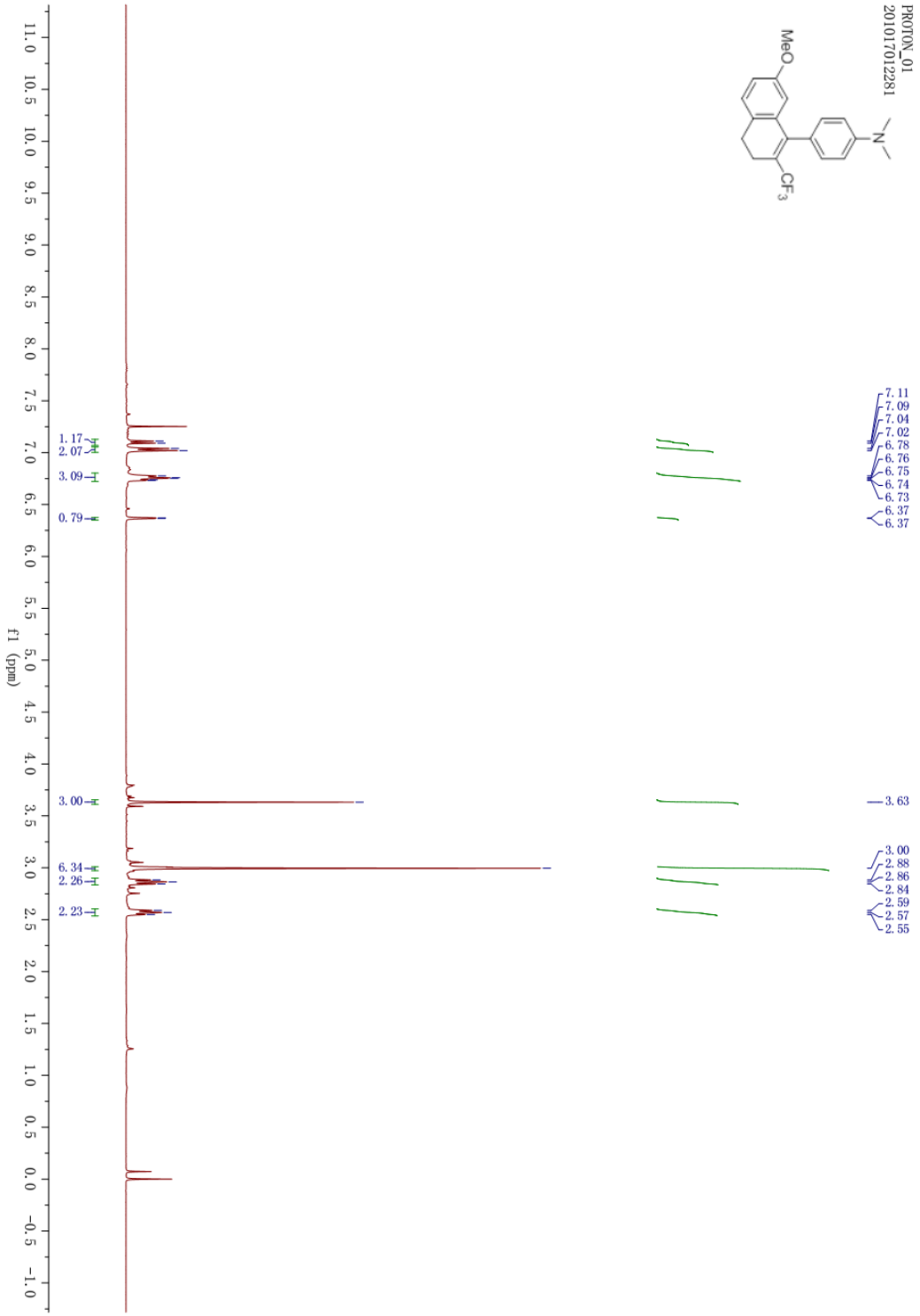
^{19}F NMR spectrum of compound **2p**



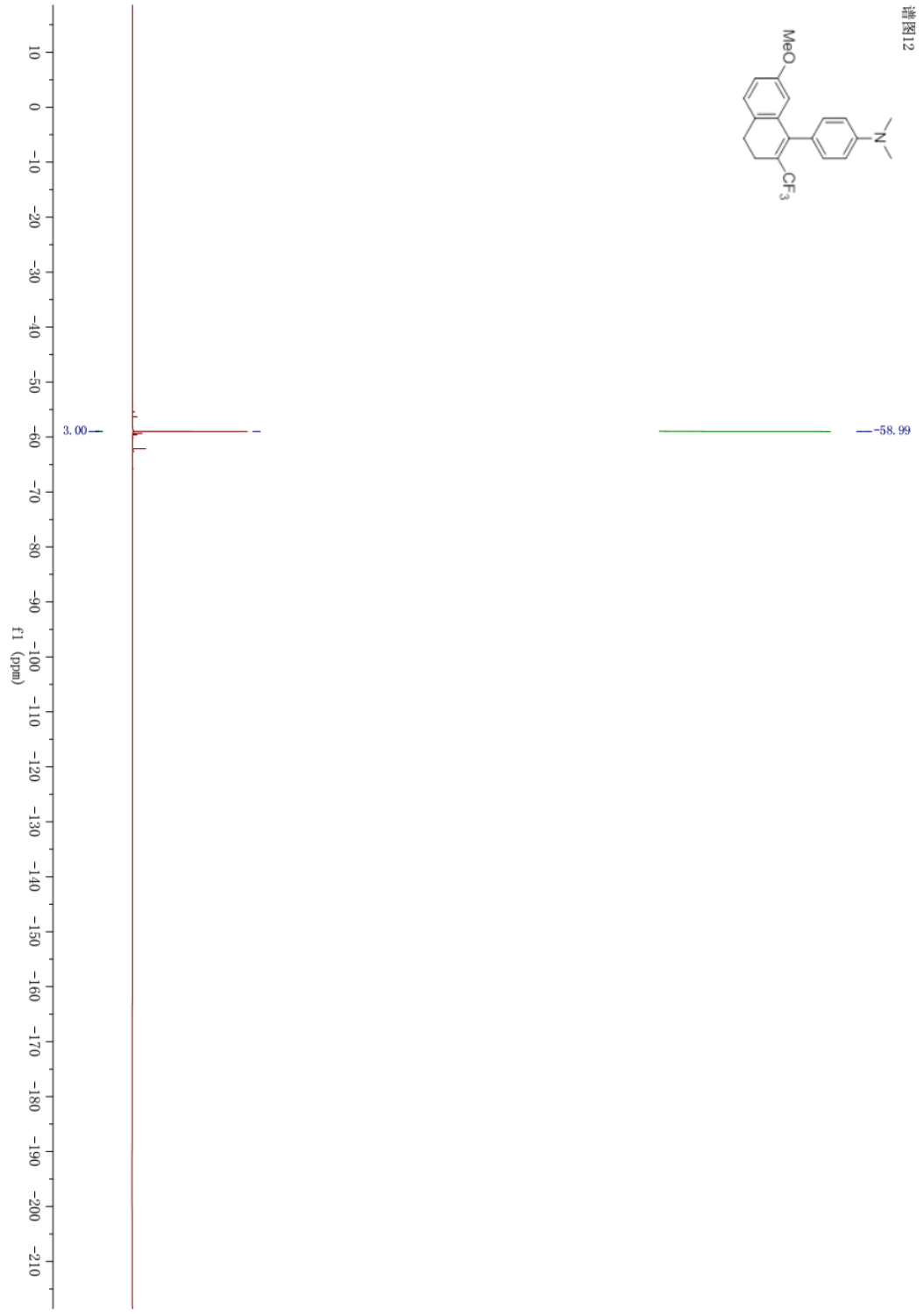
^{13}C NMR spectrum of compound **2p**



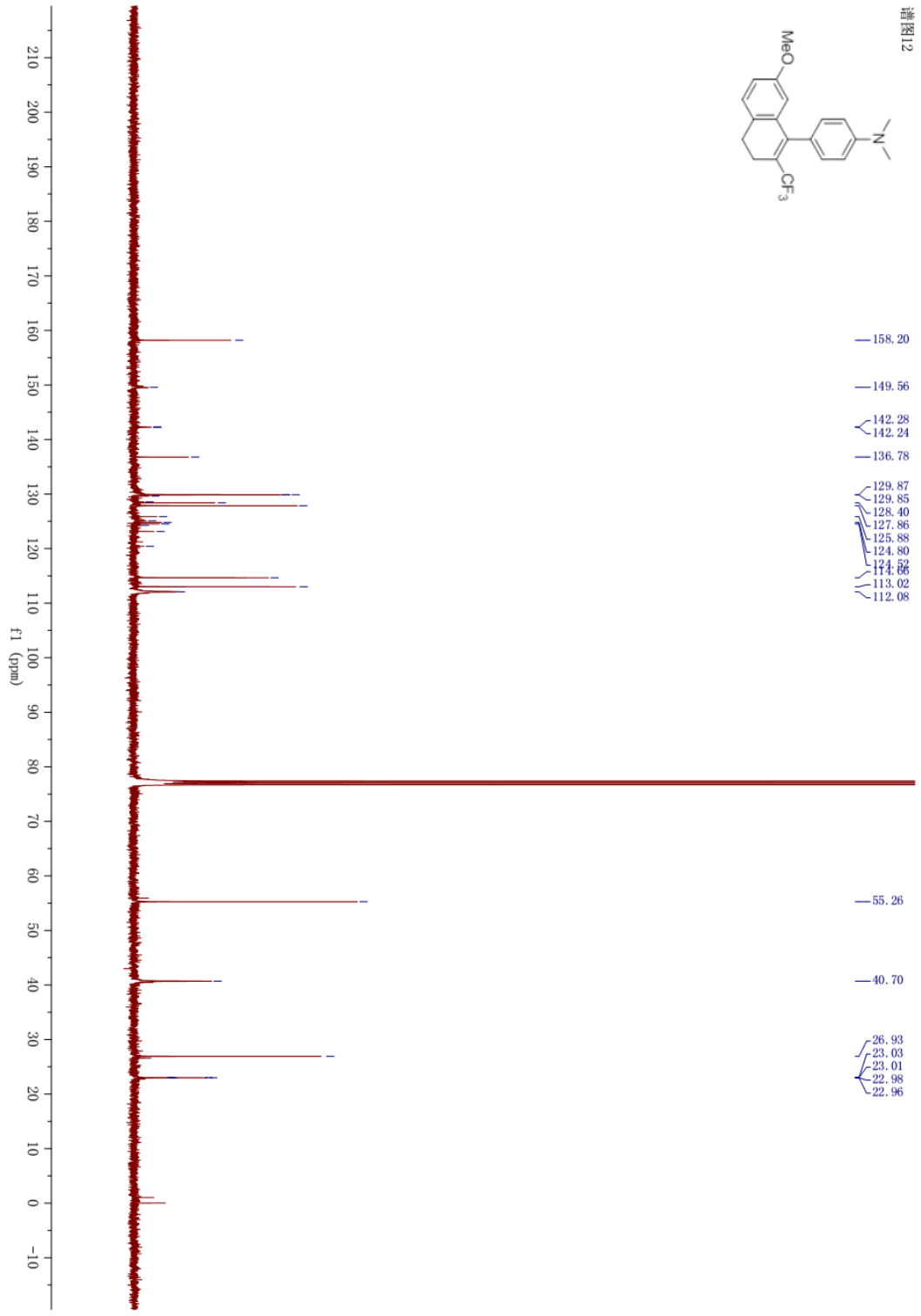
^{1}H NMR spectrum of compound **2q**



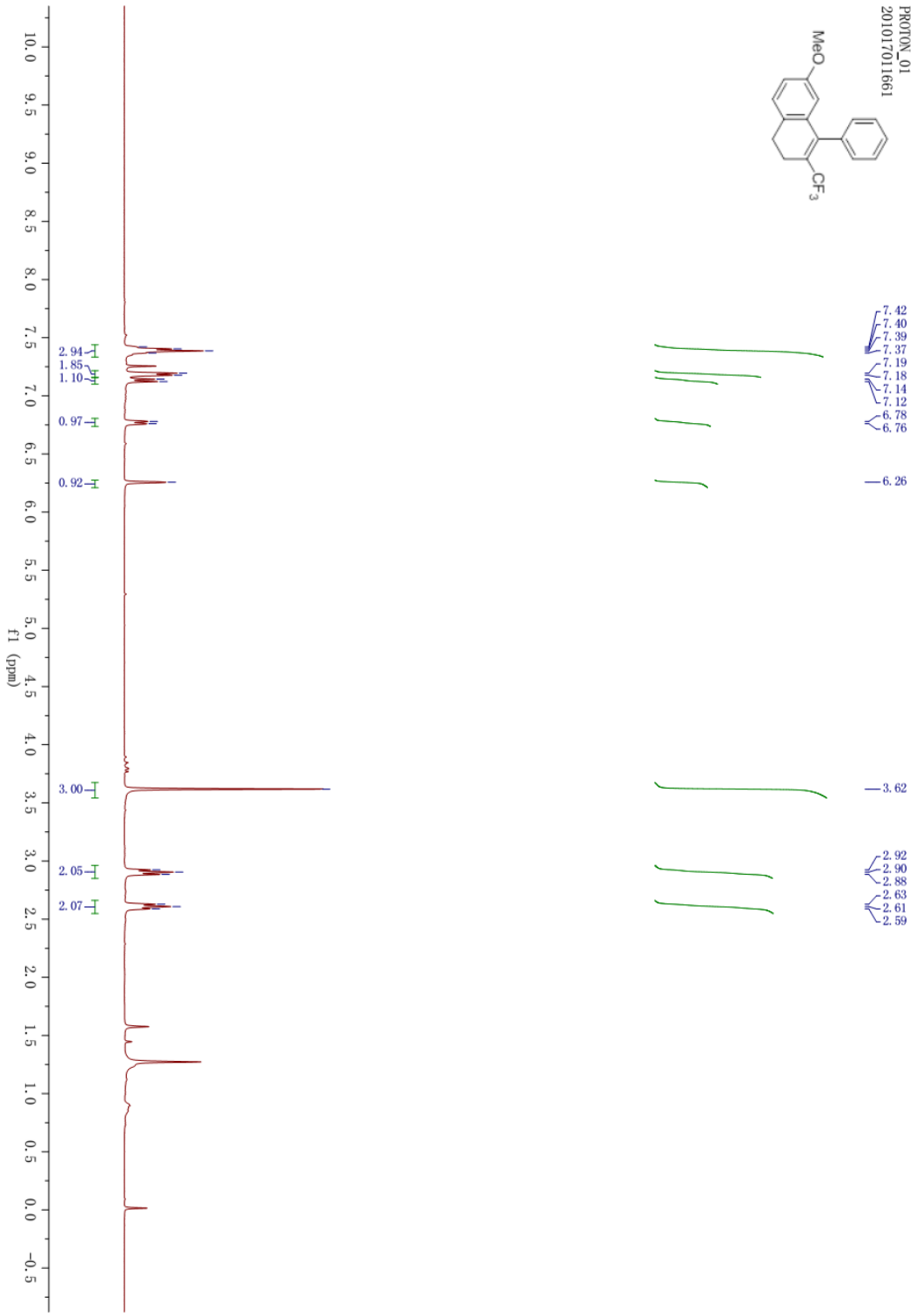
^{19}F NMR spectrum of compound **2q**



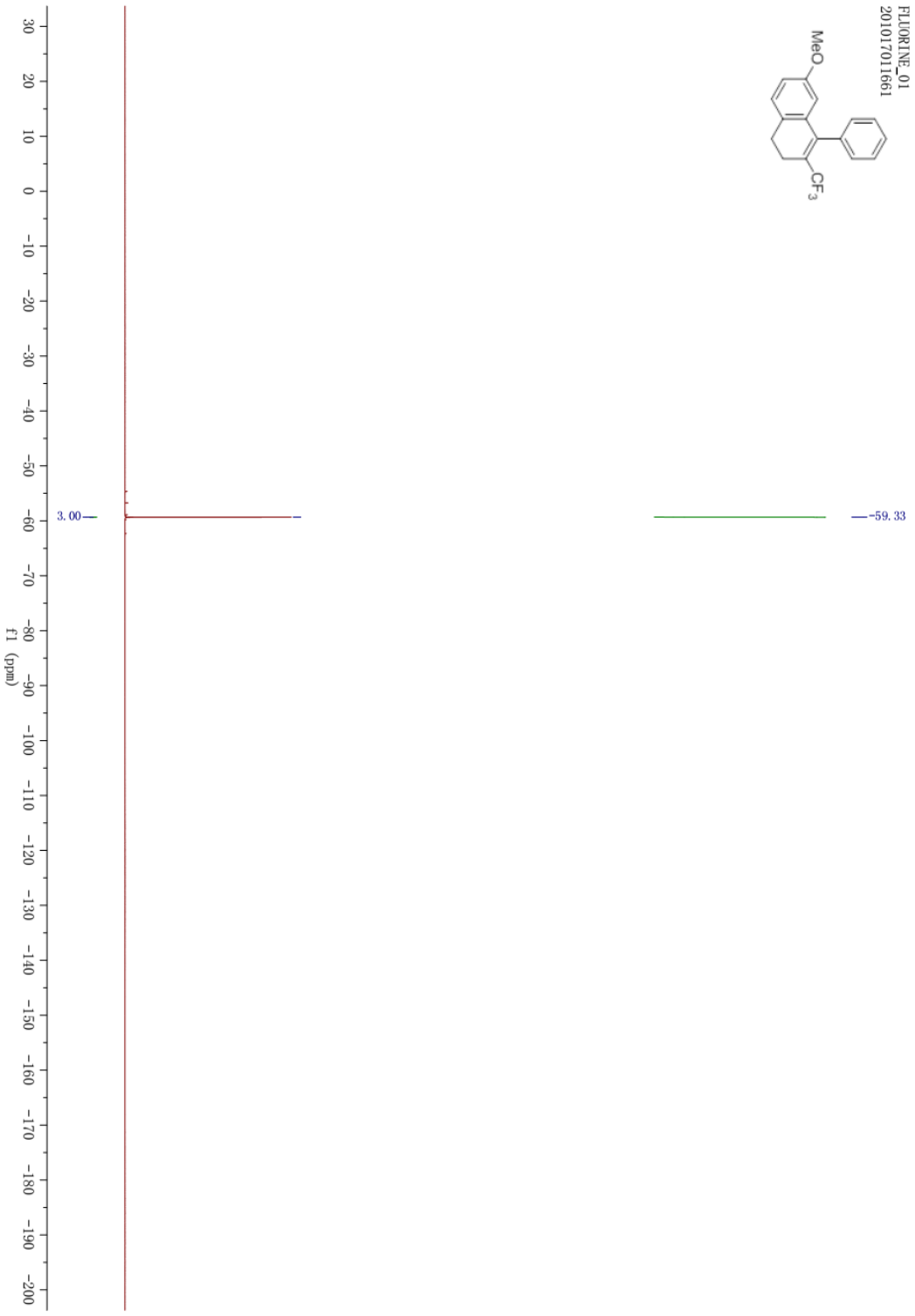
^{13}C NMR spectrum of compound **2q**



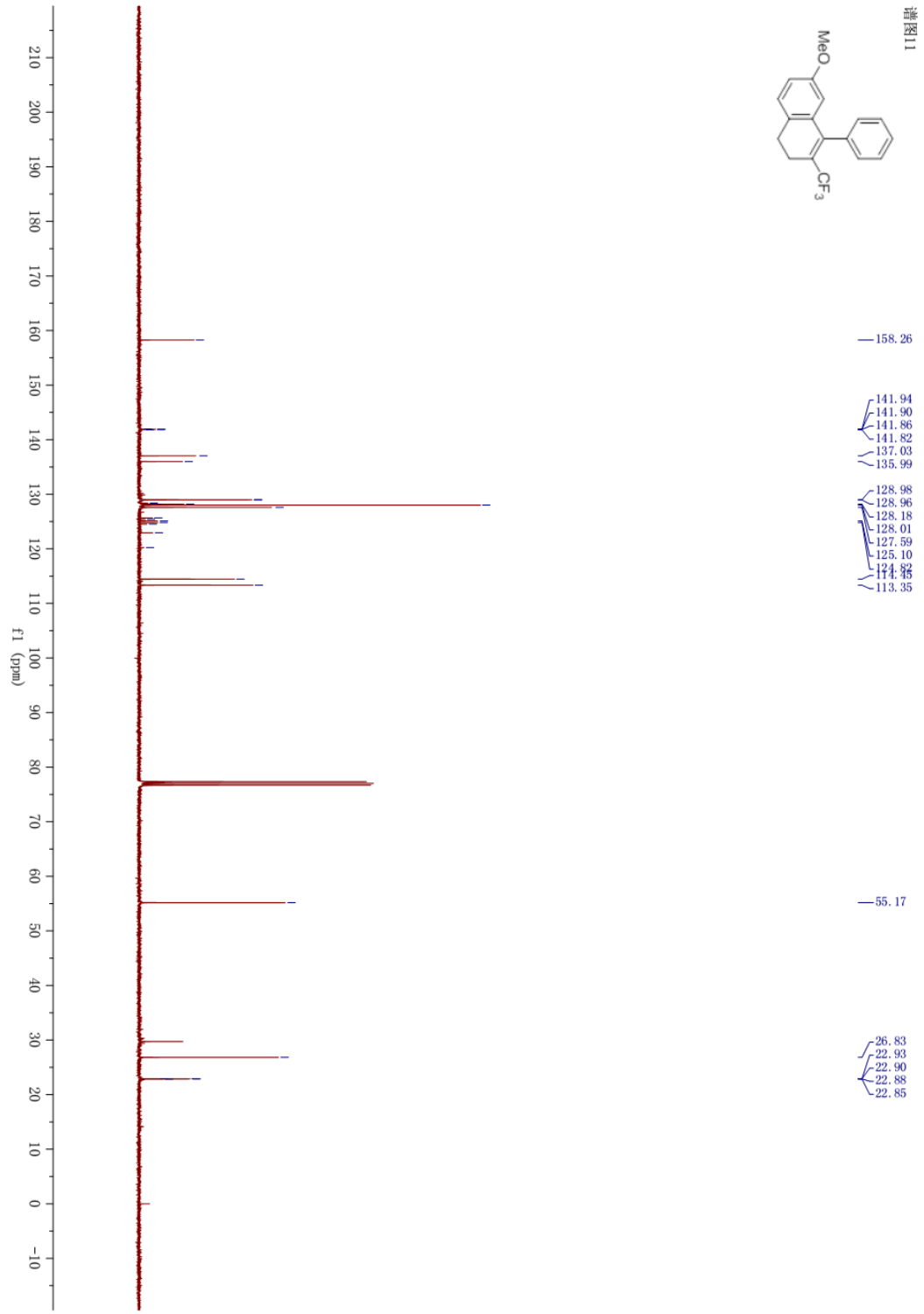
^{1}H NMR spectrum of compound **2r**



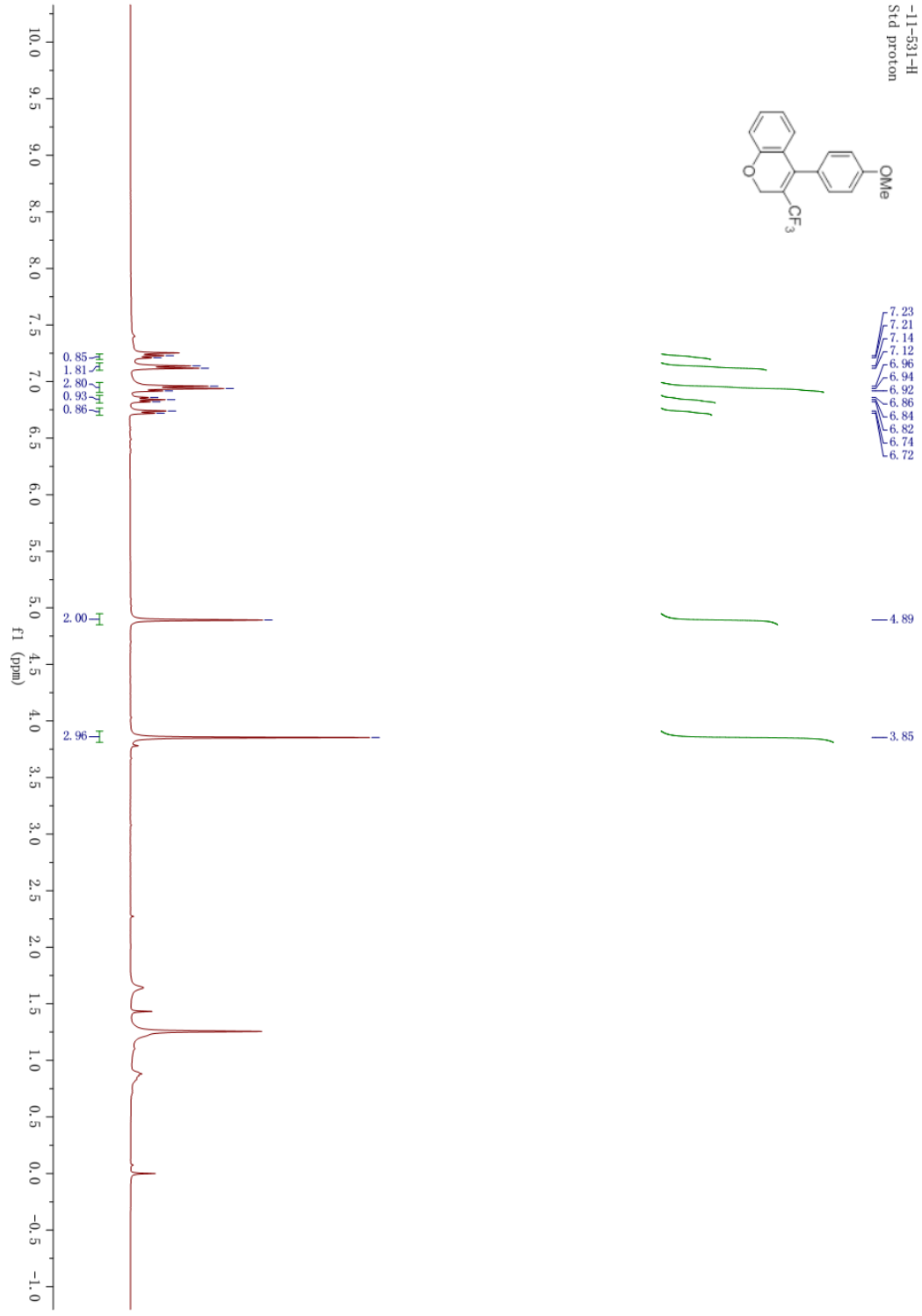
^{19}F NMR spectrum of compound **2r**



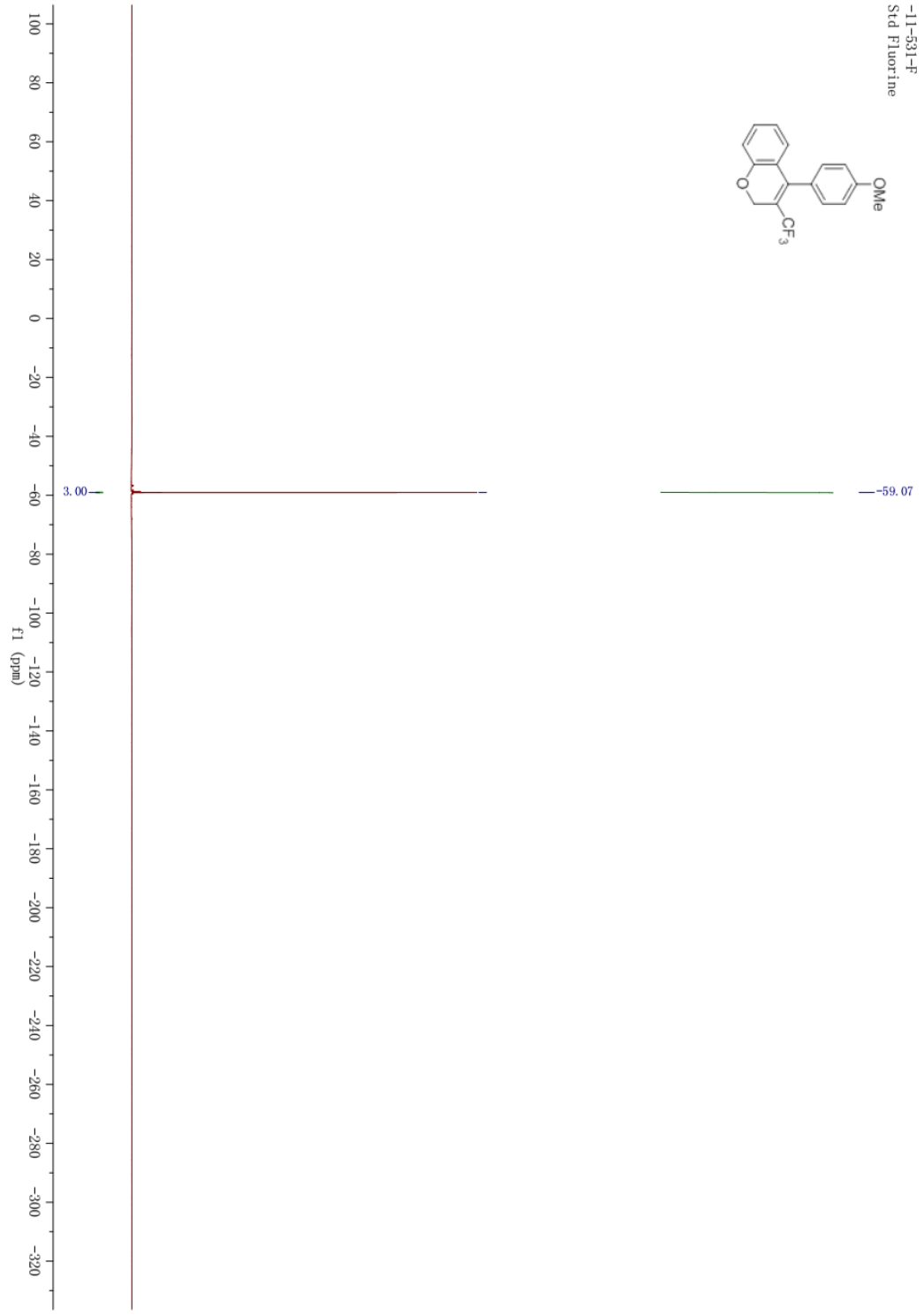
^{13}C NMR spectrum of compound **2r**



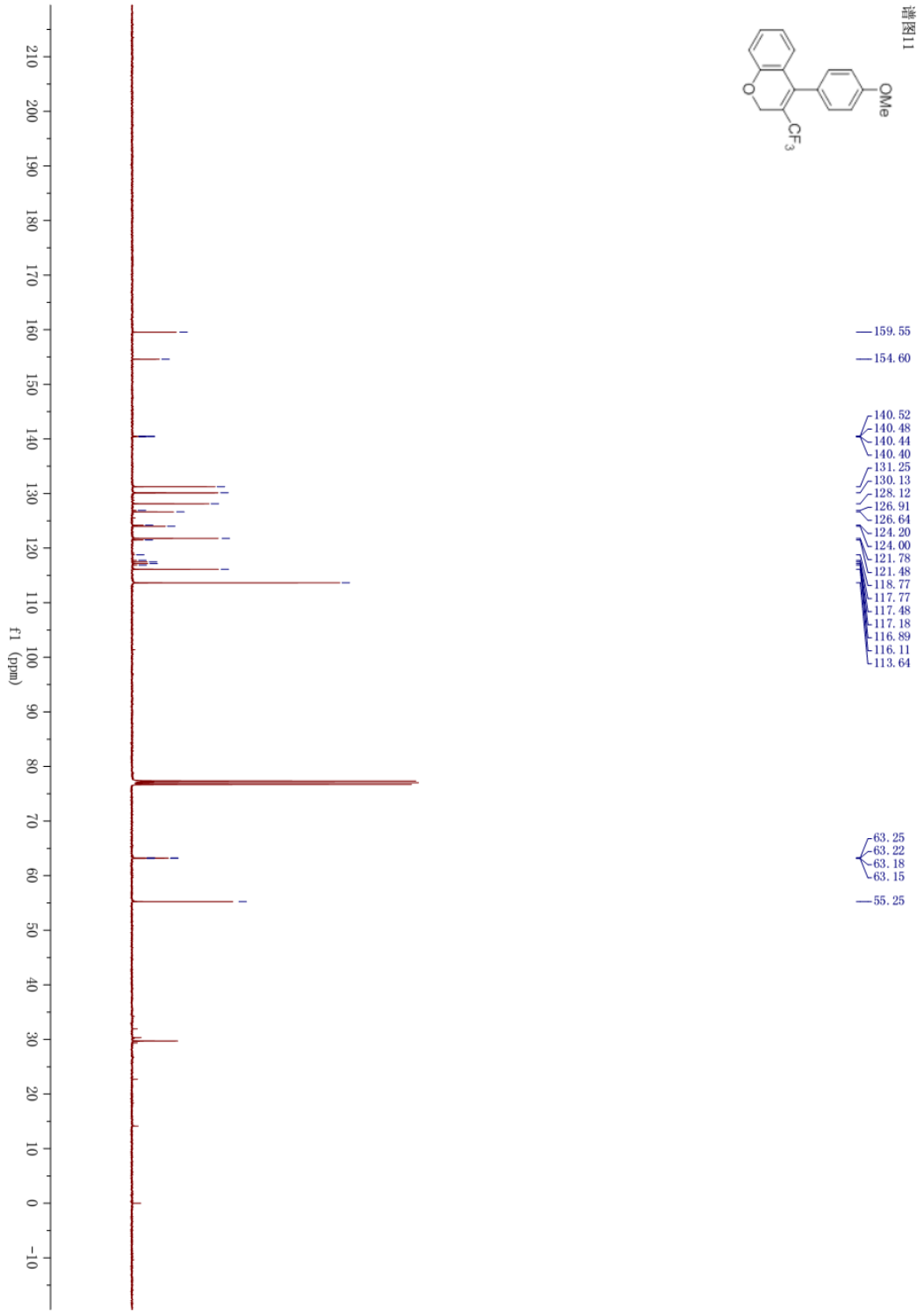
^{1}H NMR spectrum of compound **2t**



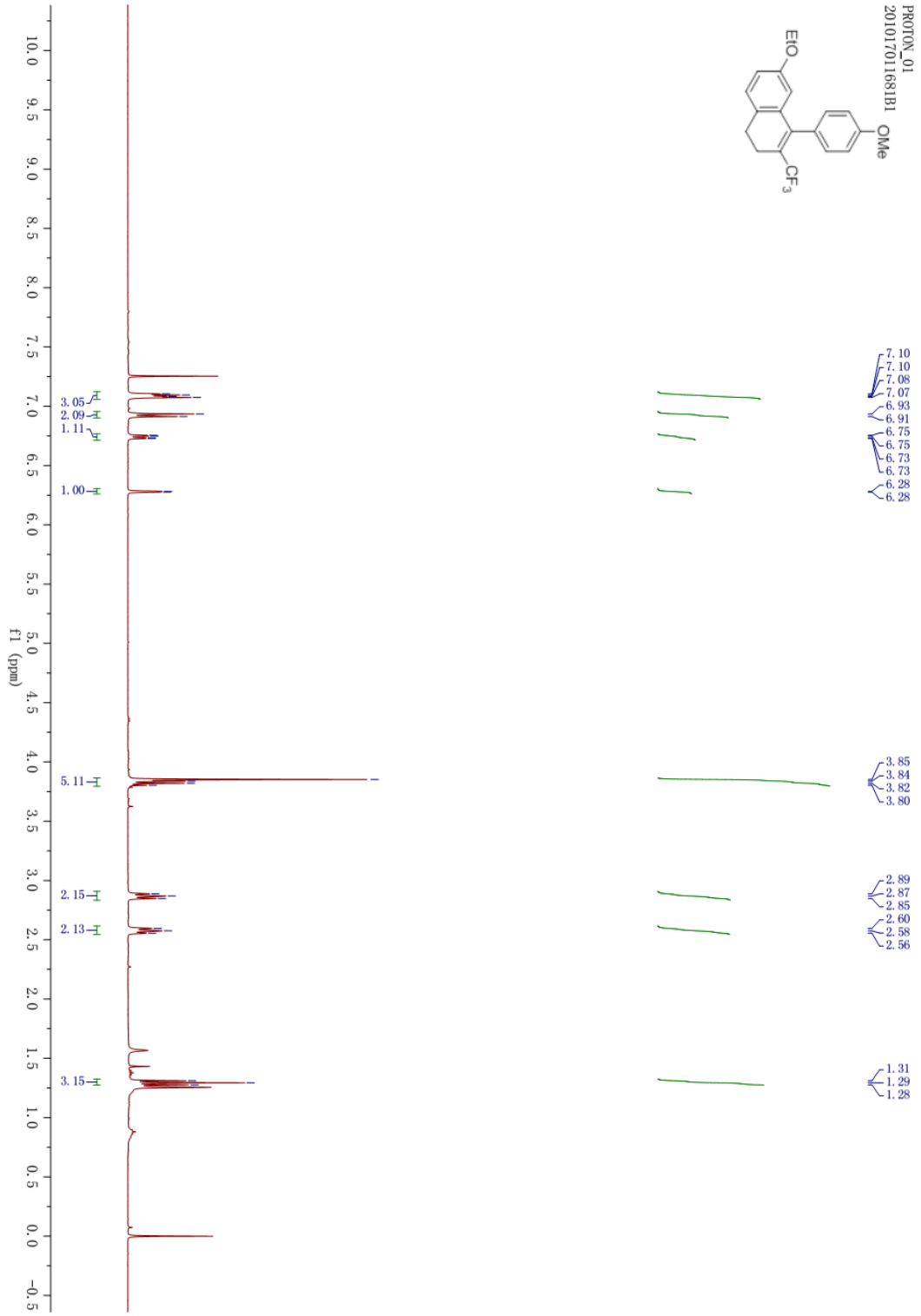
^{19}F NMR spectrum of compound **2t**



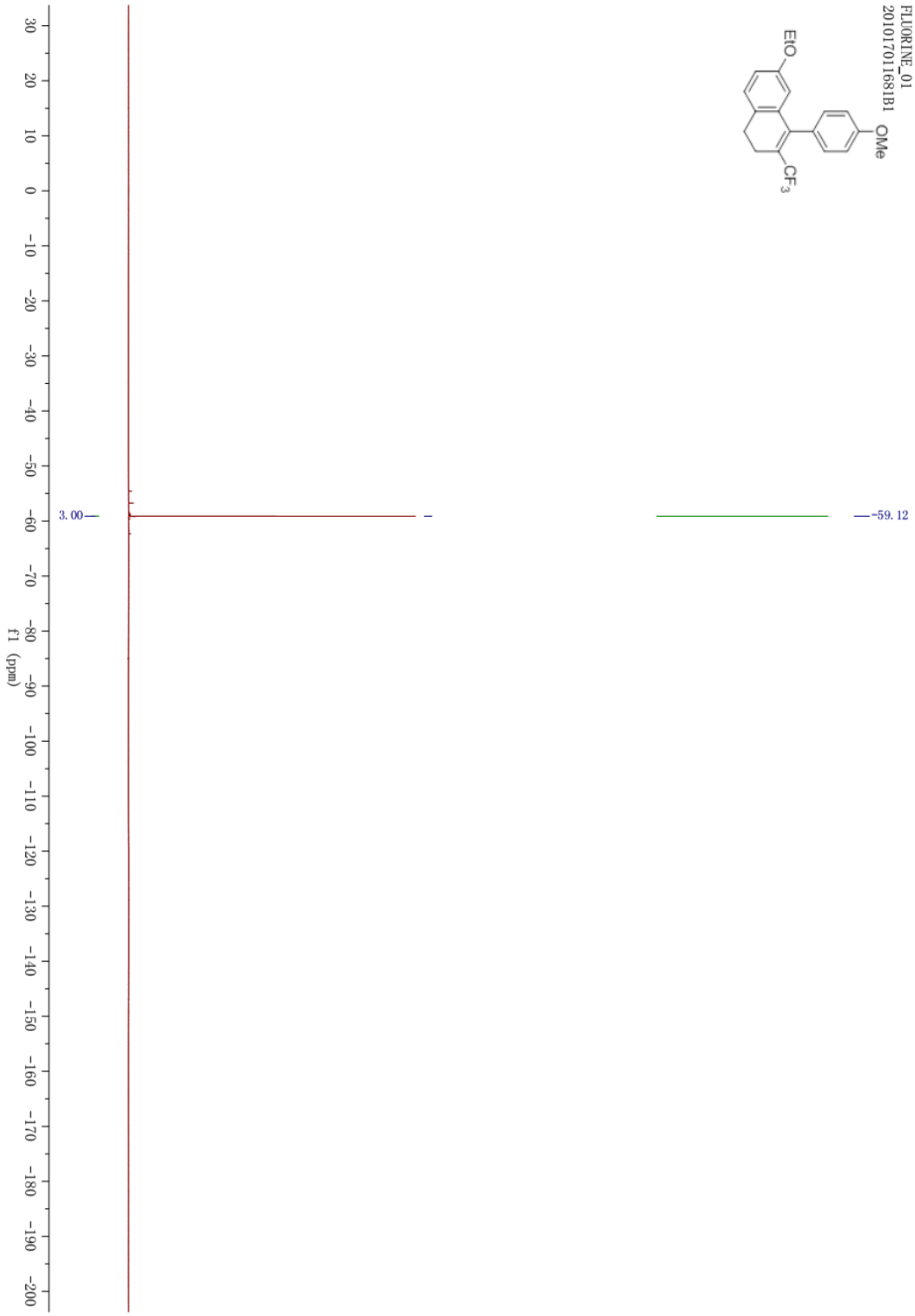
^{13}C NMR spectrum of compound **2t**



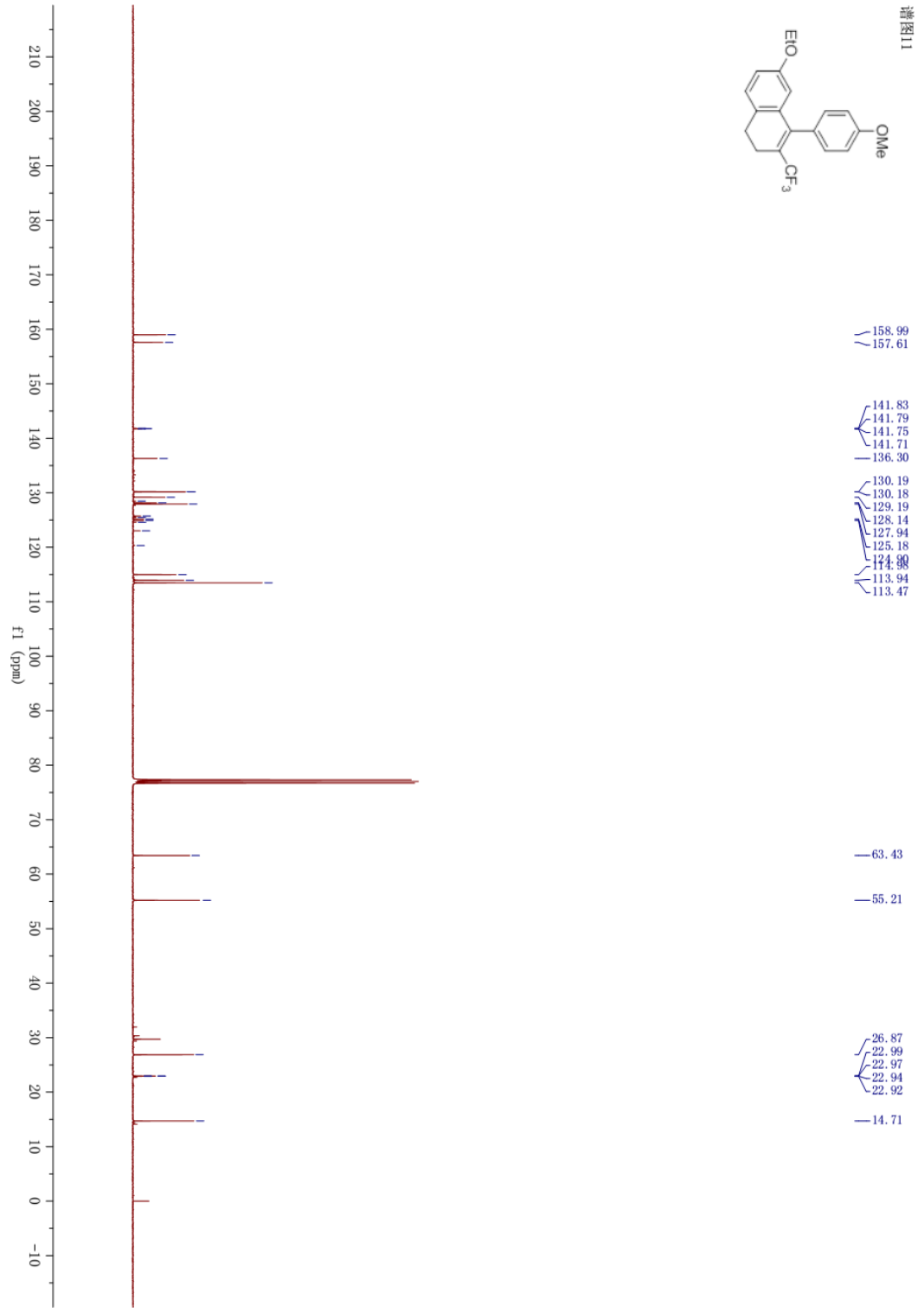
^{1}H NMR spectrum of compound **2a'**



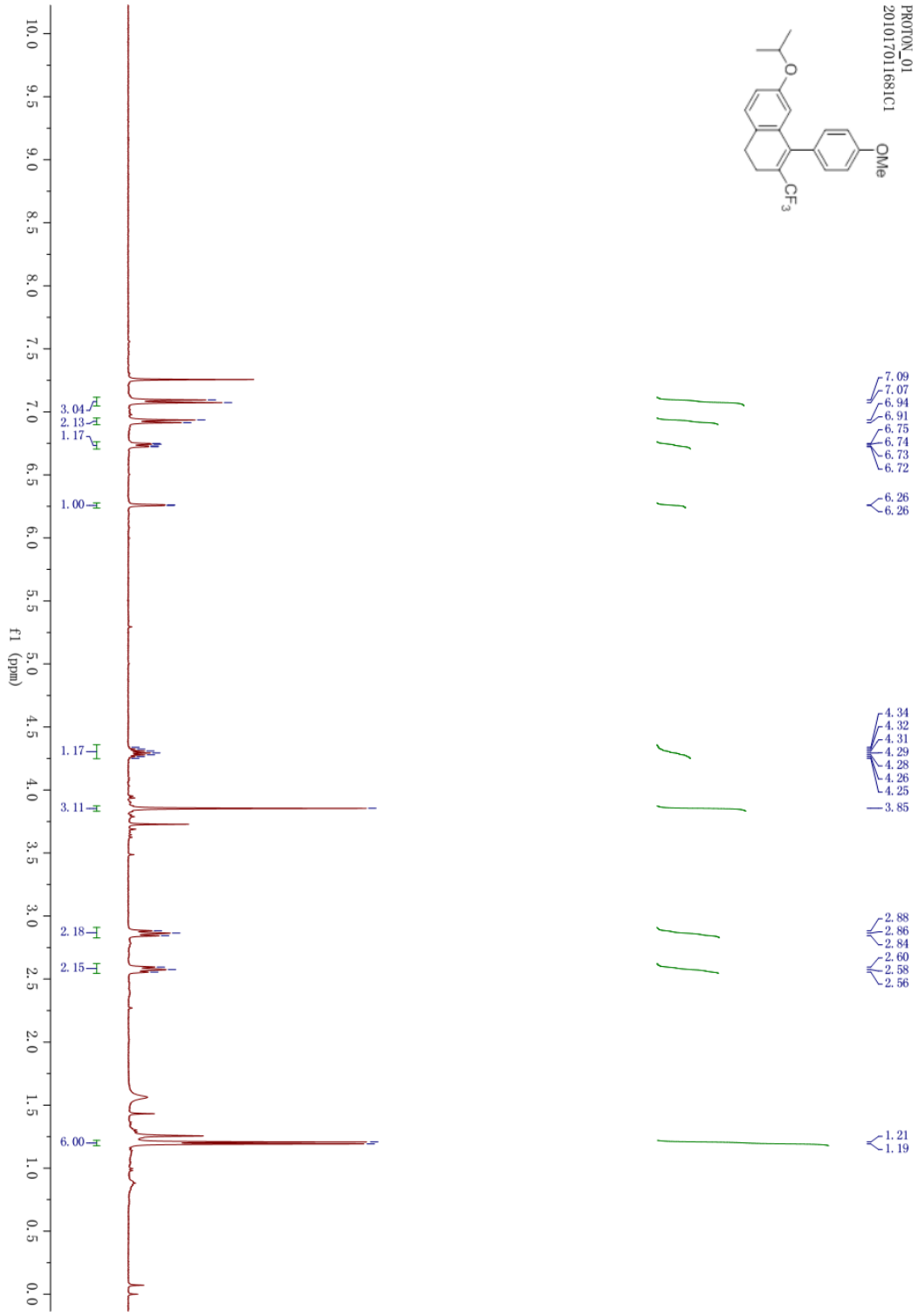
^{19}F NMR spectrum of compound **2a'**



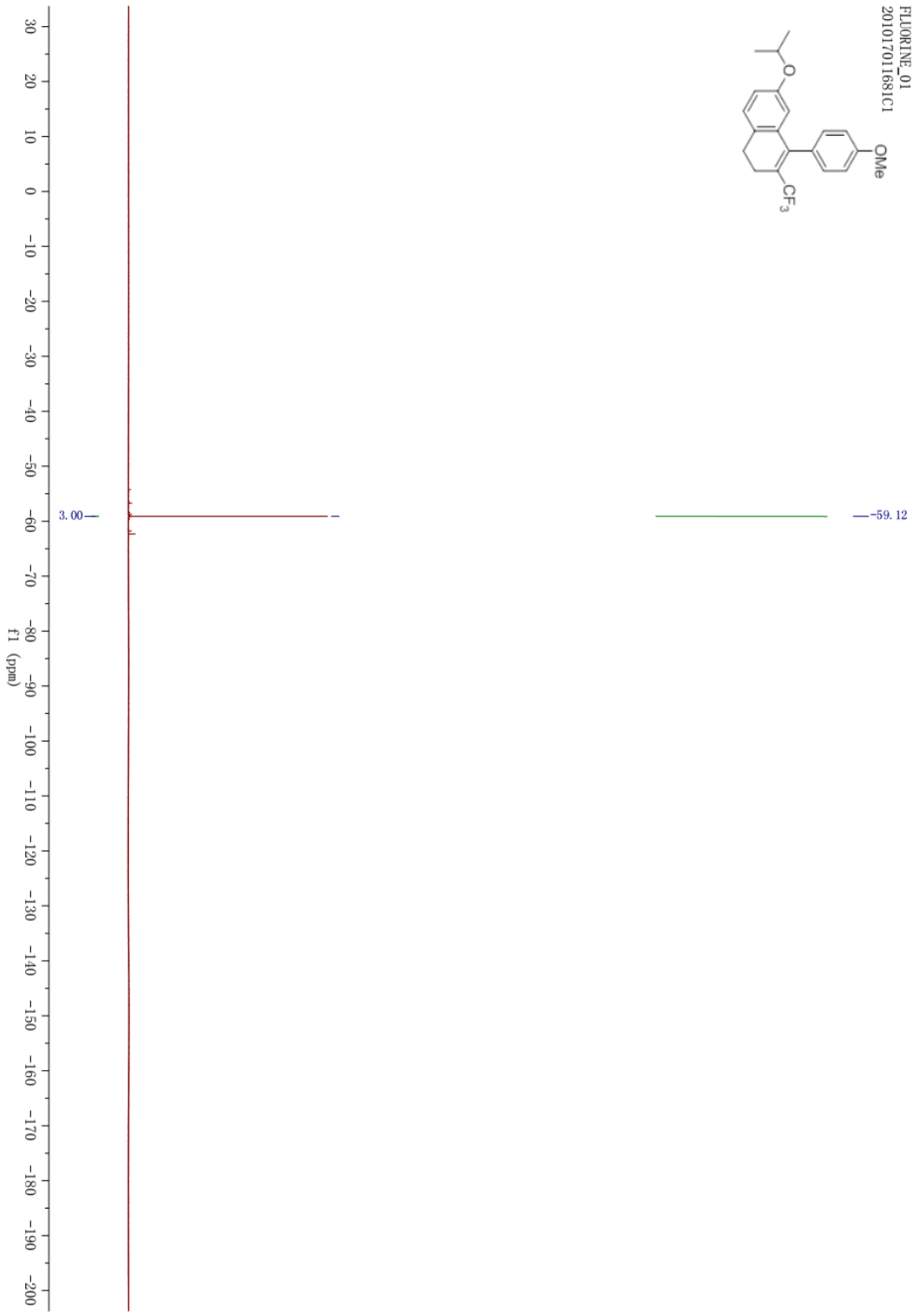
^{13}C NMR spectrum of compound **2a'**



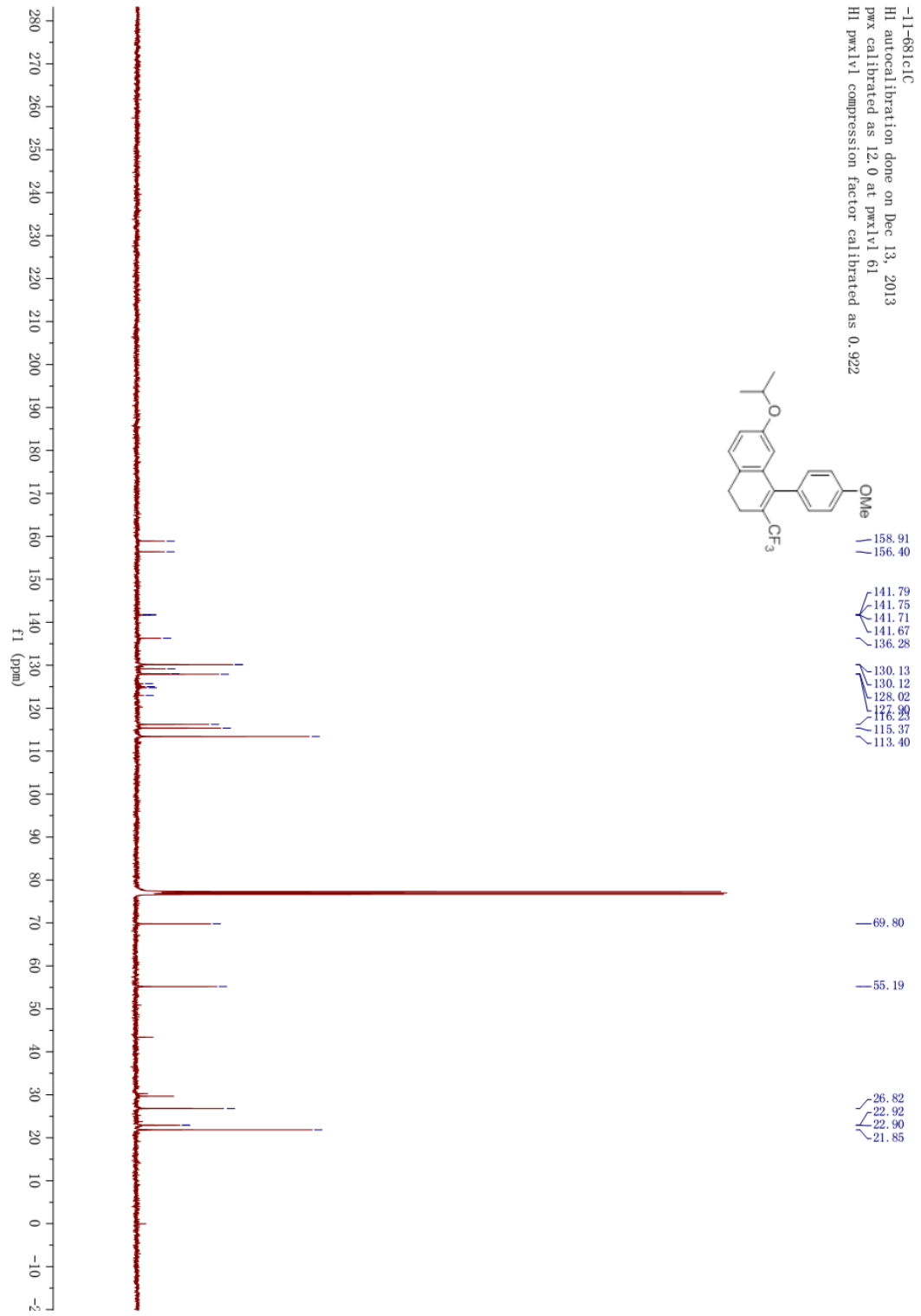
^{1}H NMR spectrum of compound **2a''**



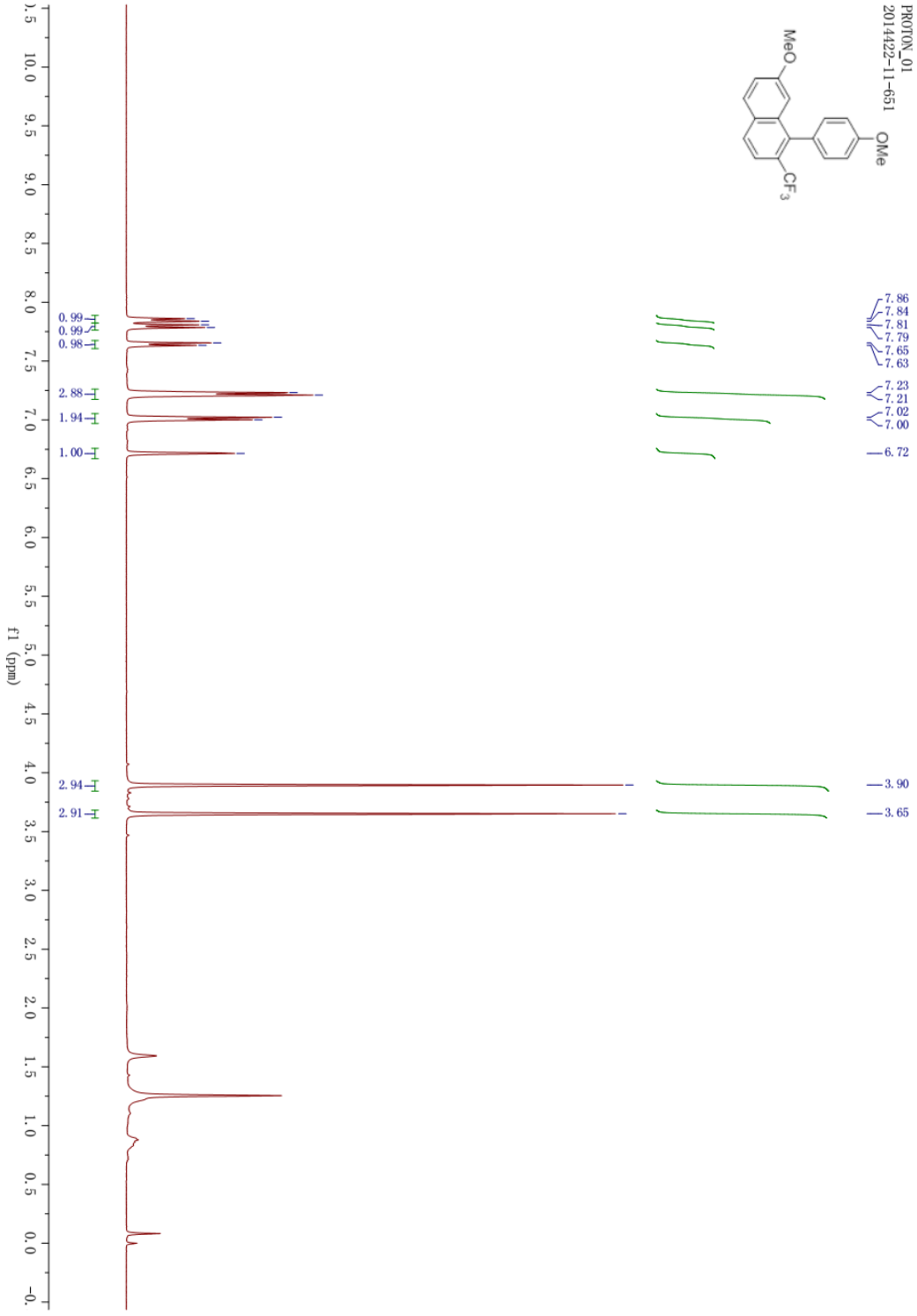
^{19}F NMR spectrum of compound **2a''**



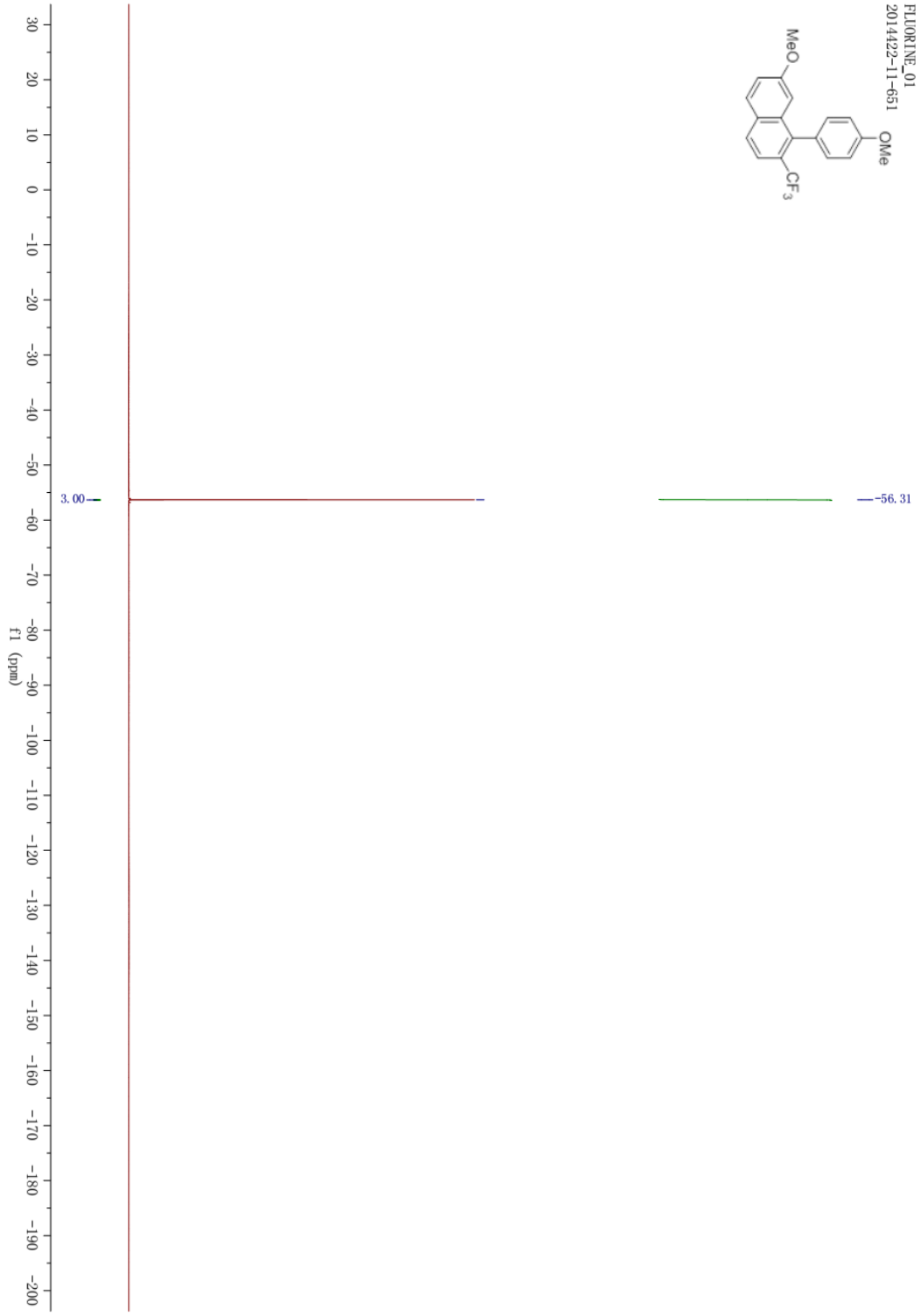
^{13}C NMR spectrum of compound **2a''**



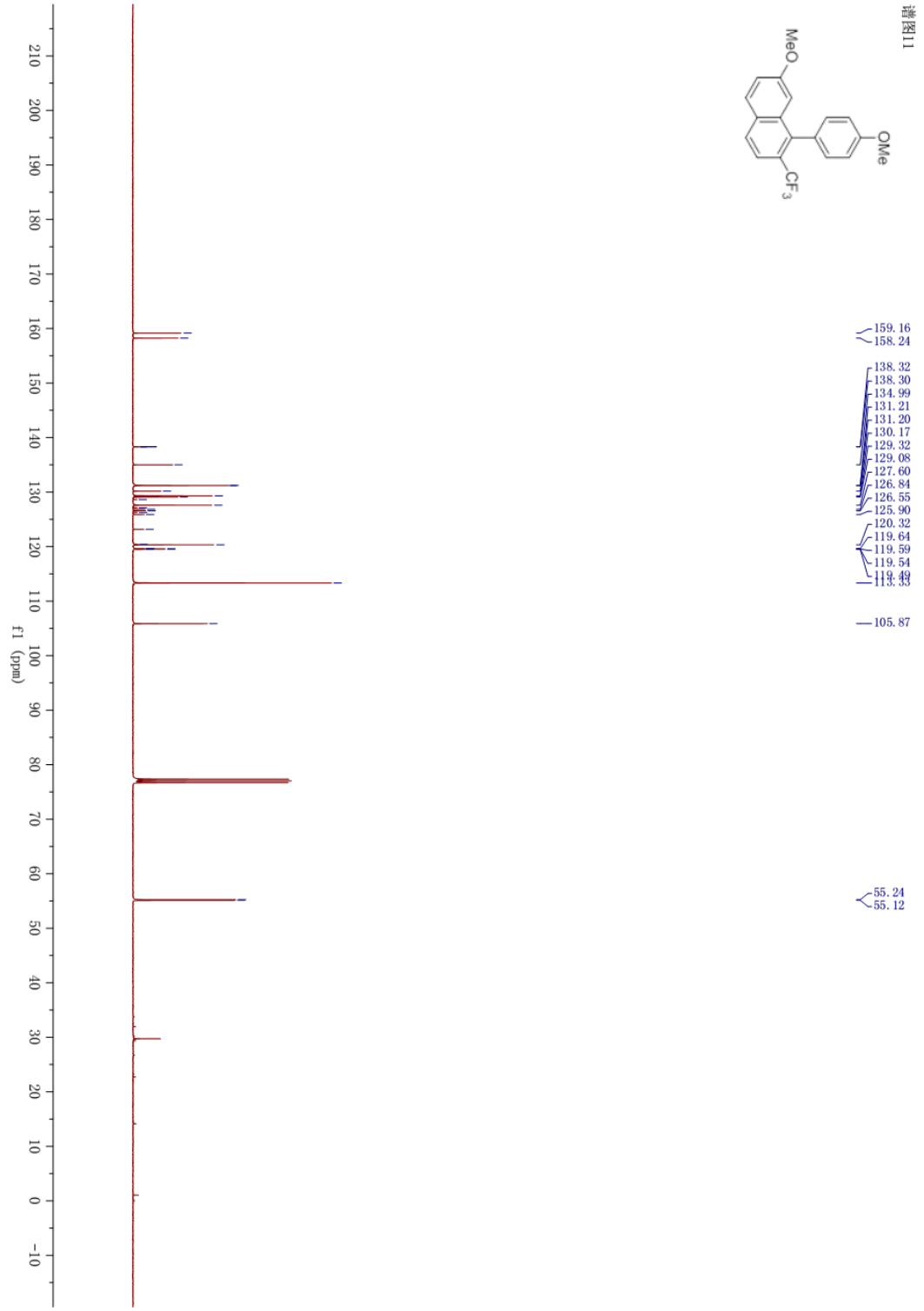
^{1}H NMR spectrum of compound **3**



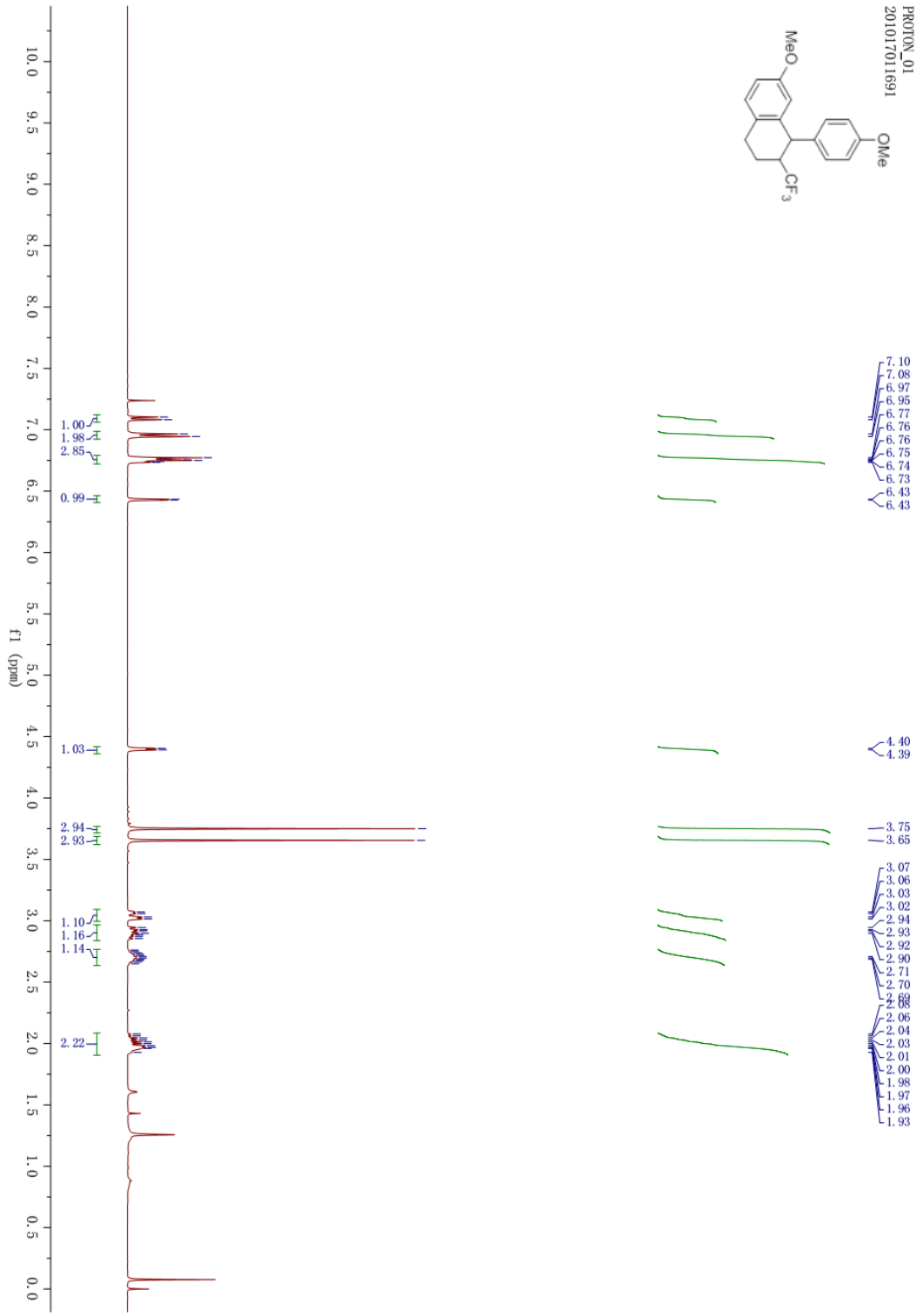
^{19}F NMR spectrum of compound **3**



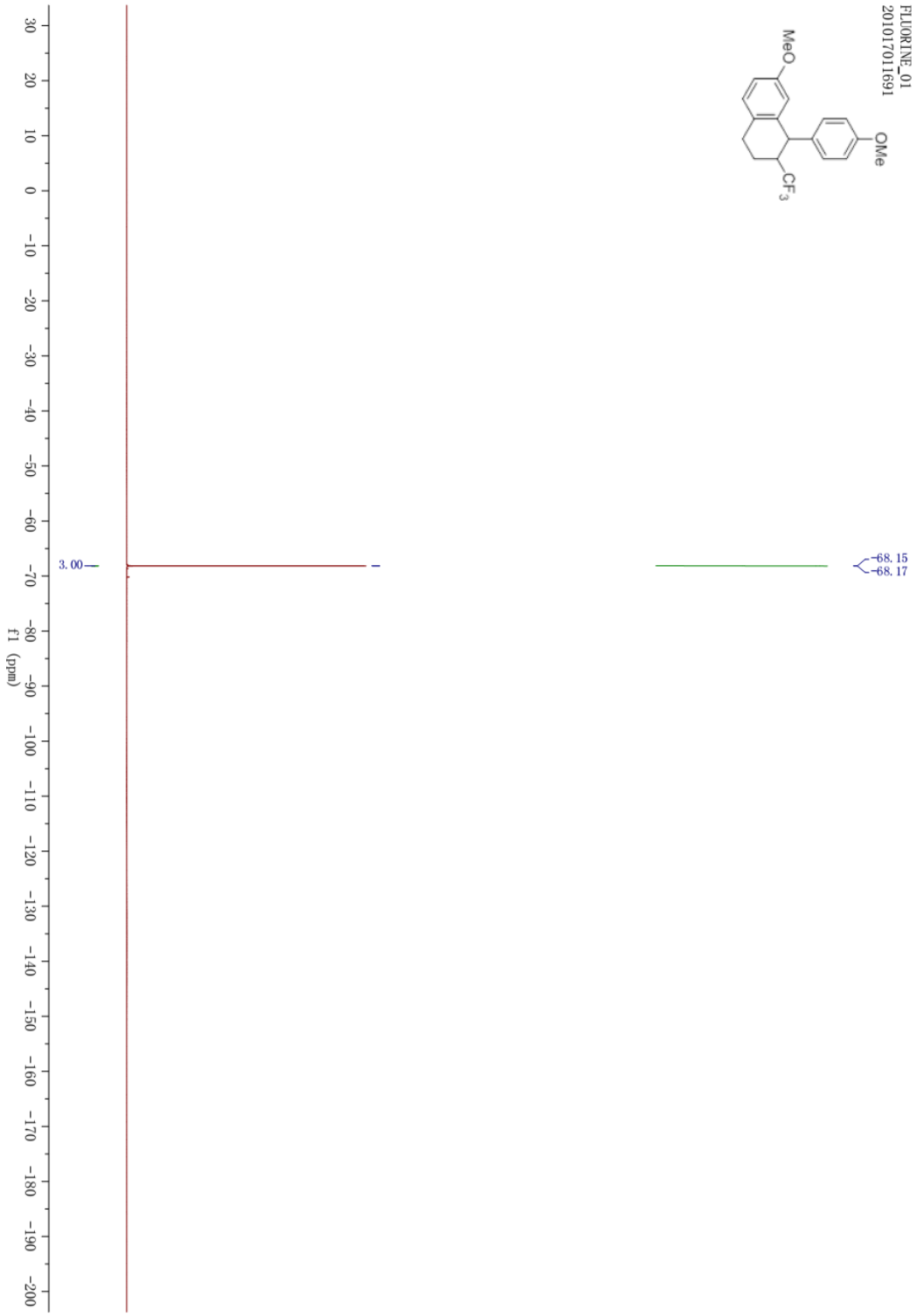
^{13}C NMR spectrum of compound **3**



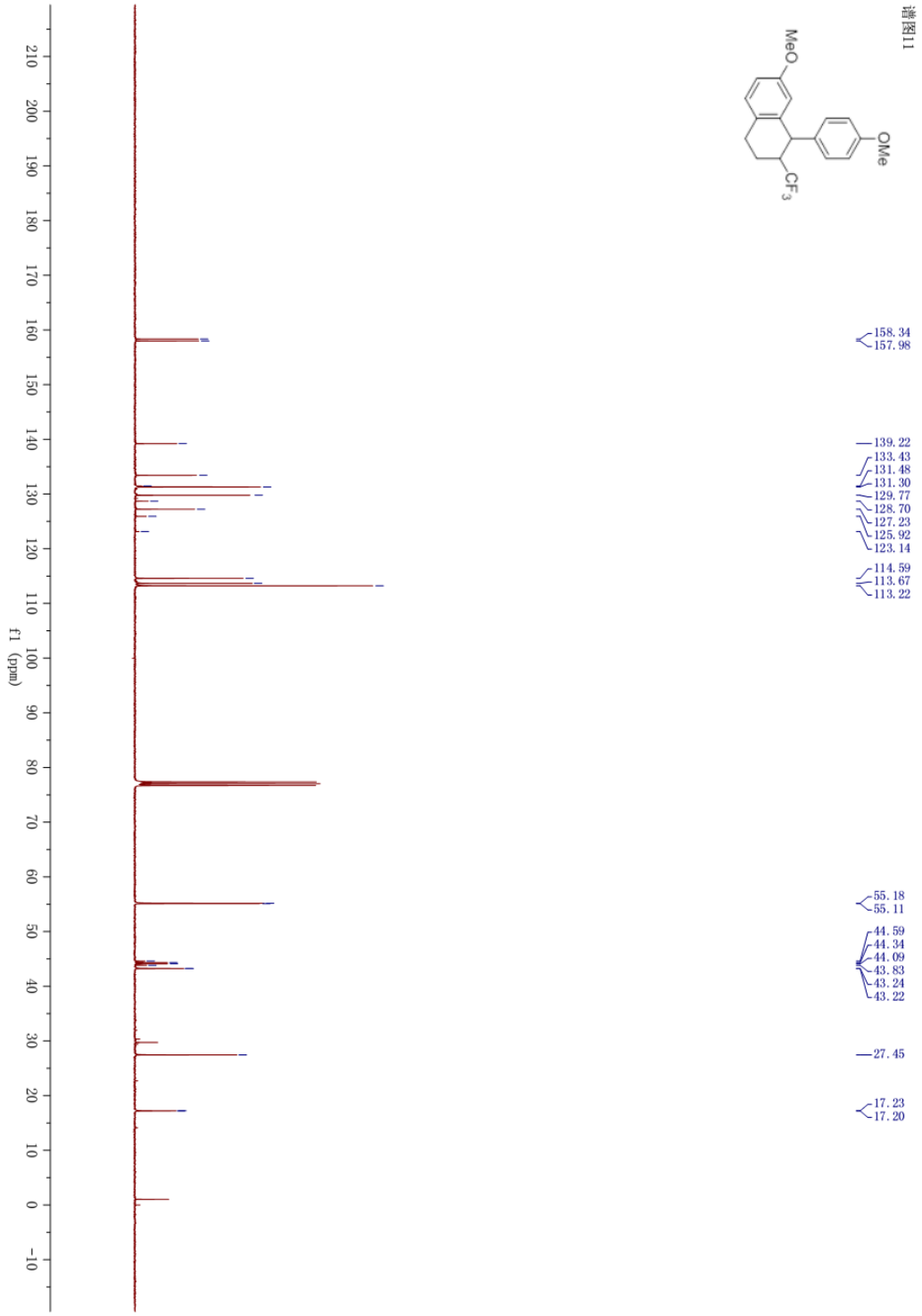
^{1}H NMR spectrum of compound **4**



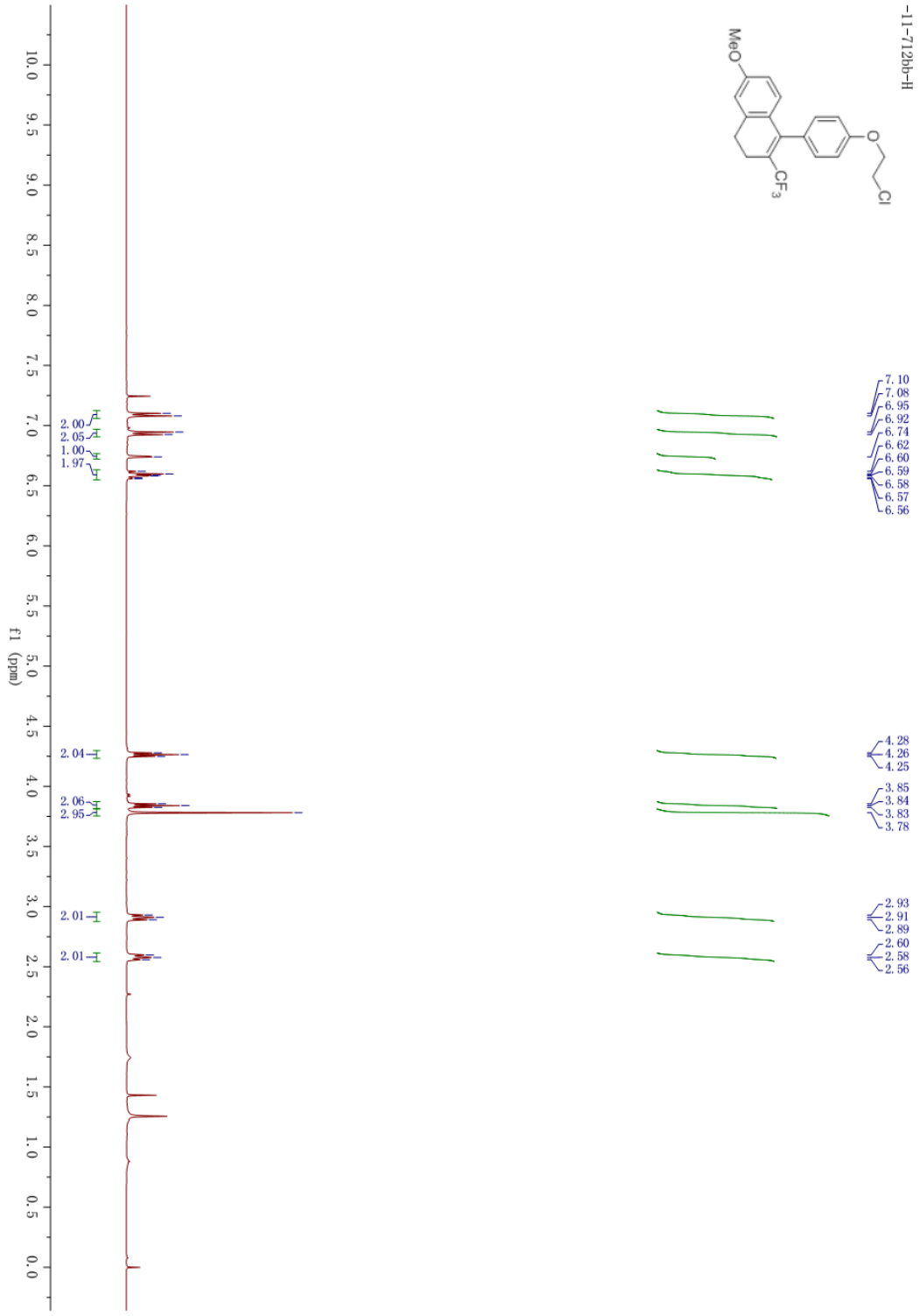
^{19}F NMR spectrum of compound **4**



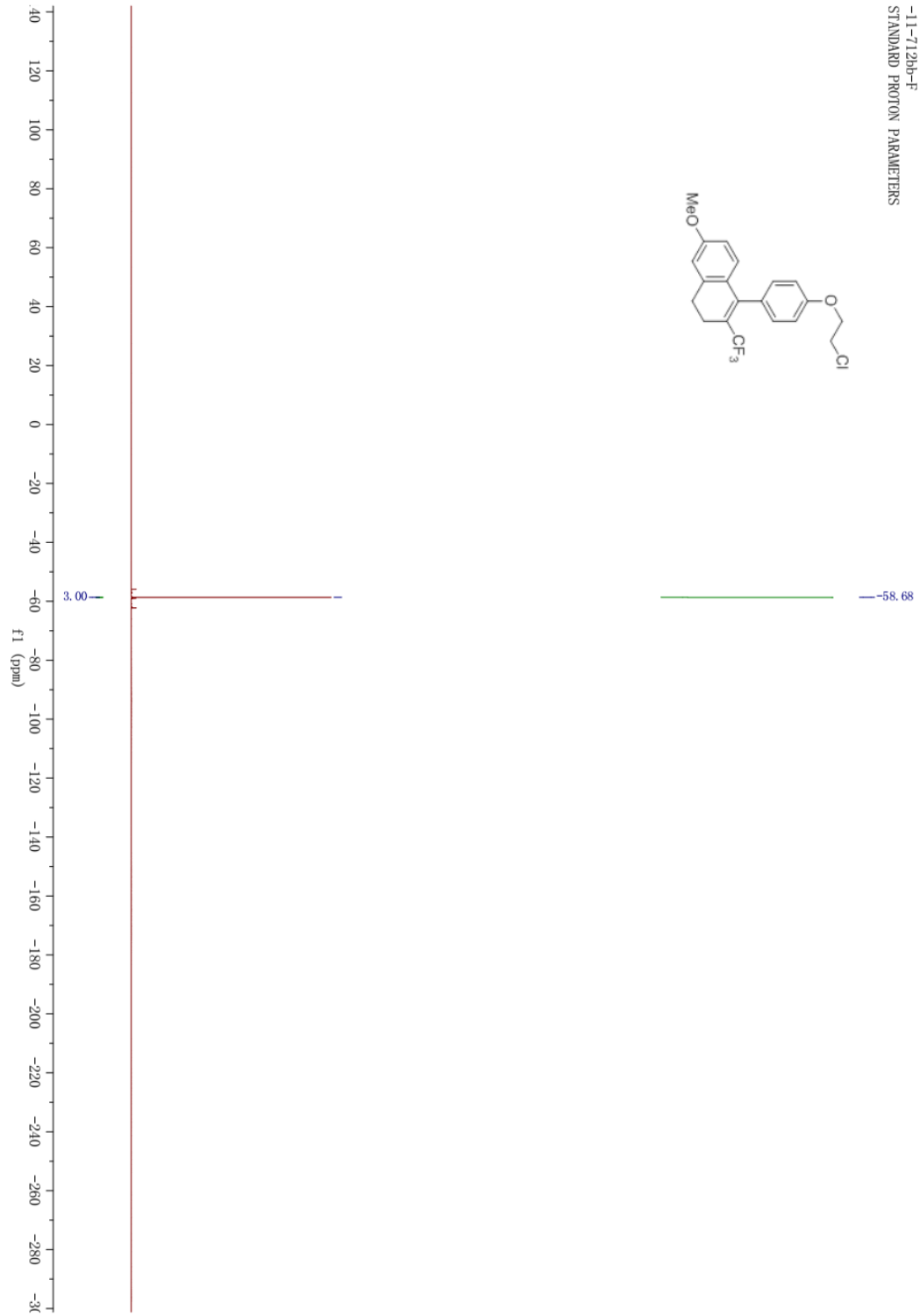
^{13}C NMR spectrum of compound **4**



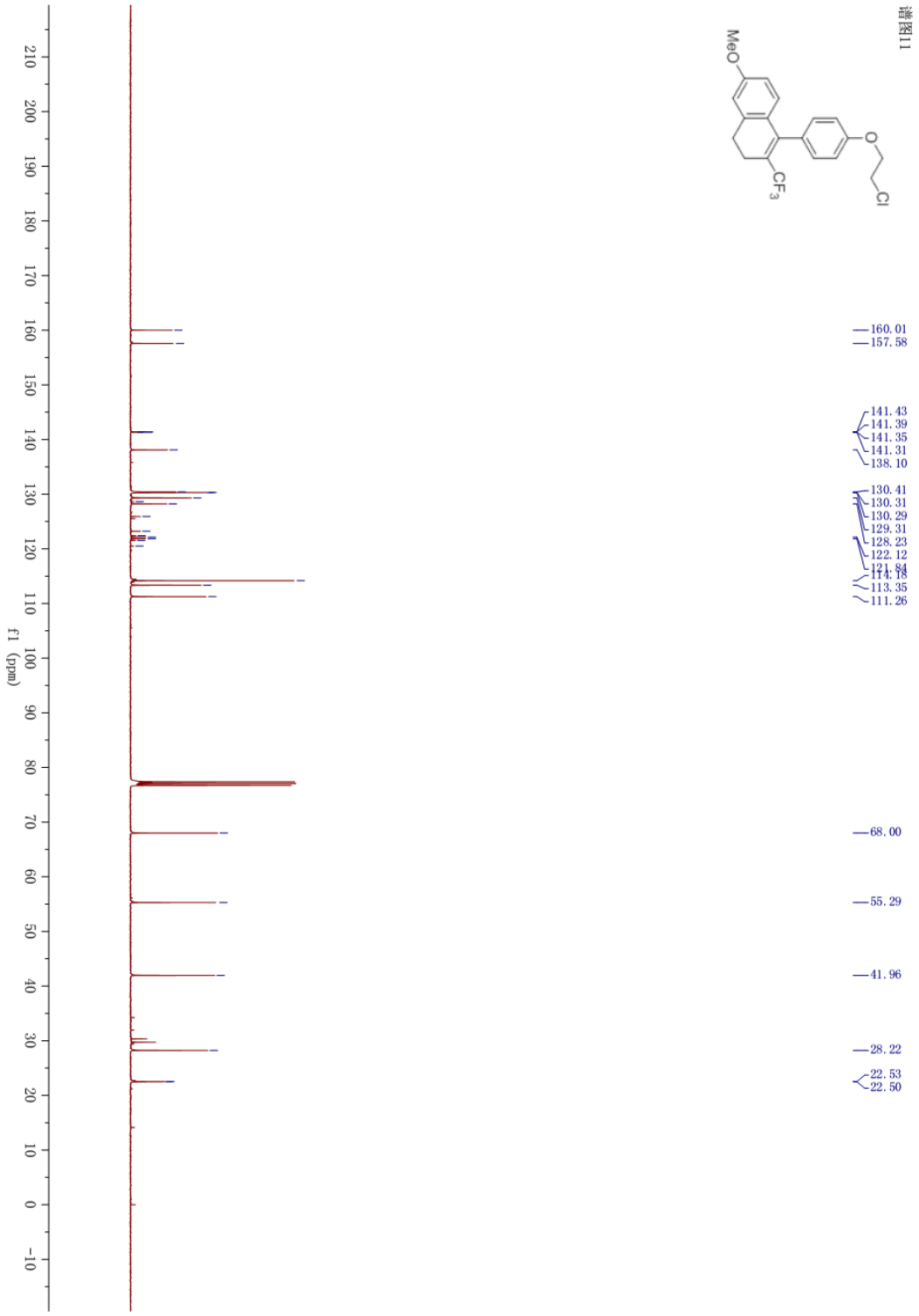
^{1}H NMR spectrum of compound **2u**



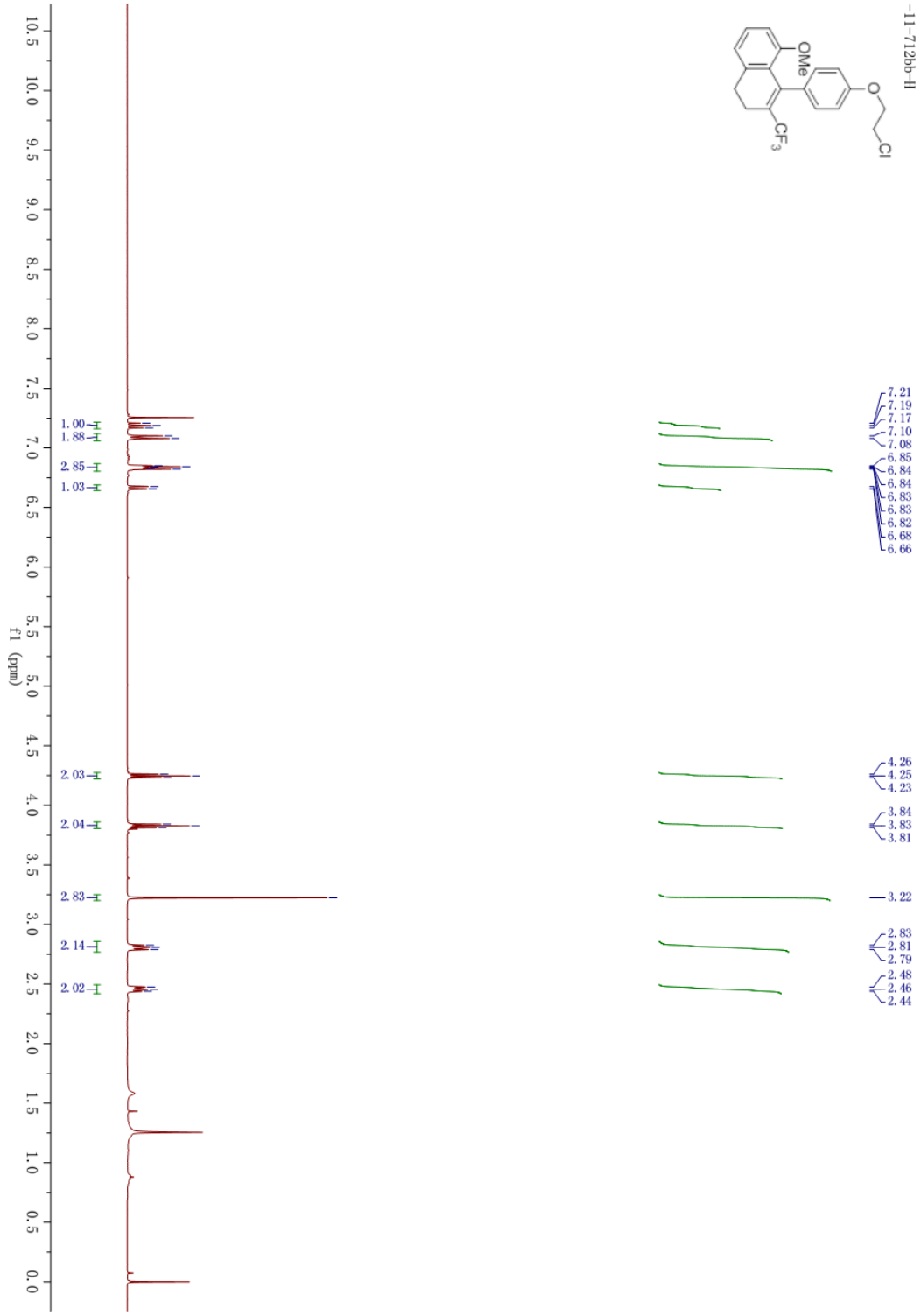
^{19}F NMR spectrum of compound **2u**



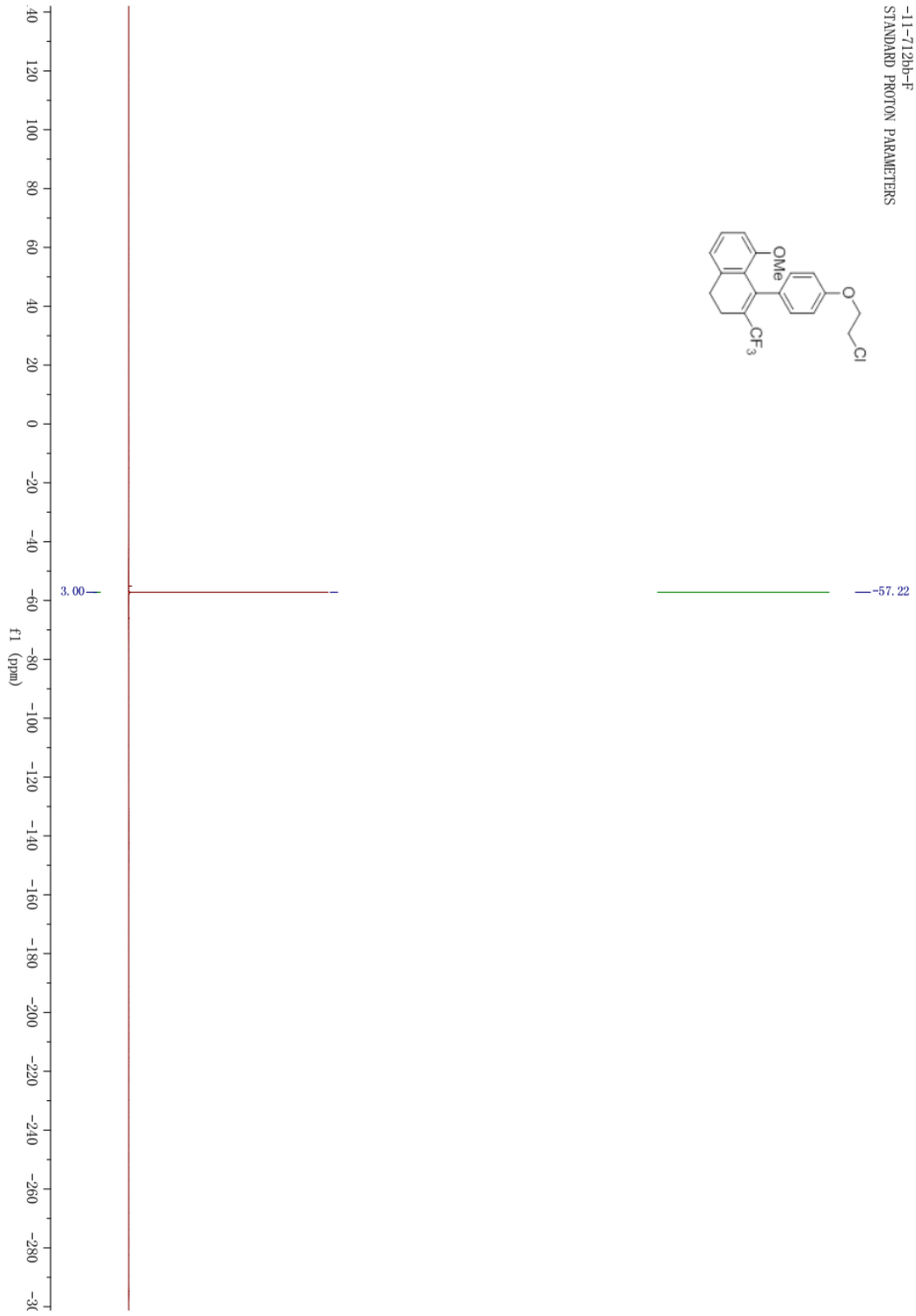
^{13}C NMR spectrum of compound **2u**



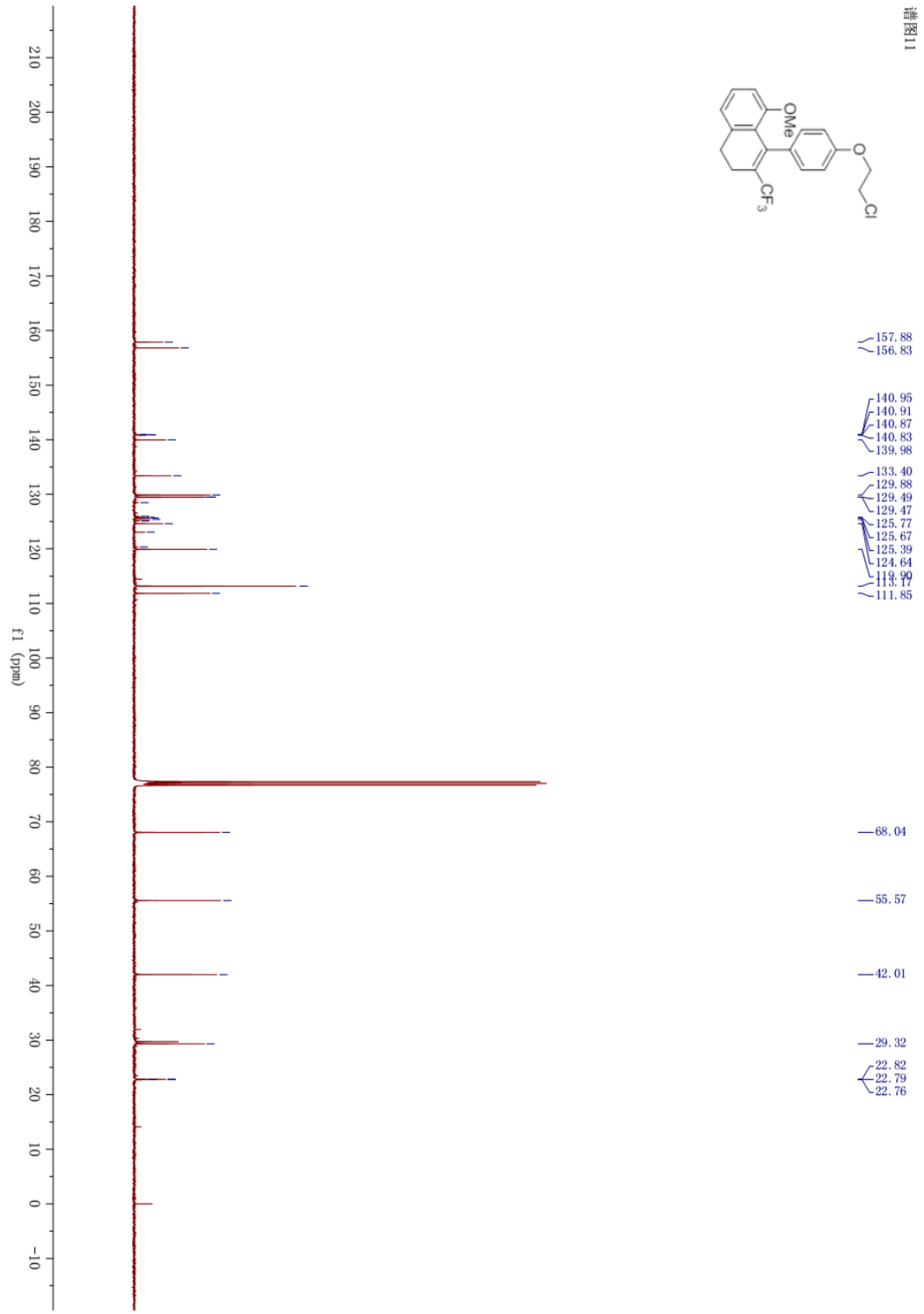
^{1}H NMR spectrum of compound **2u'**



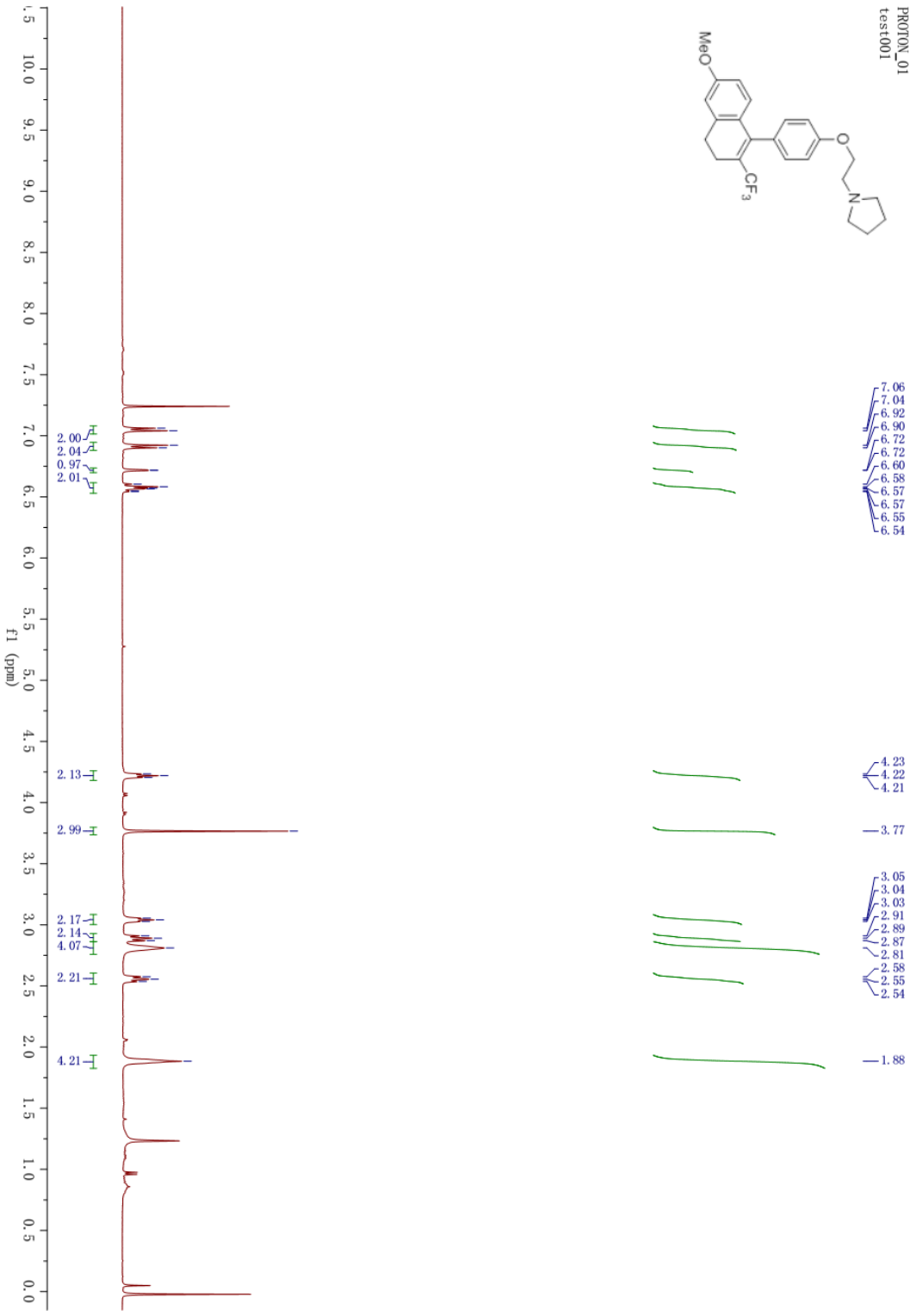
^{19}F NMR spectrum of compound **2u'**



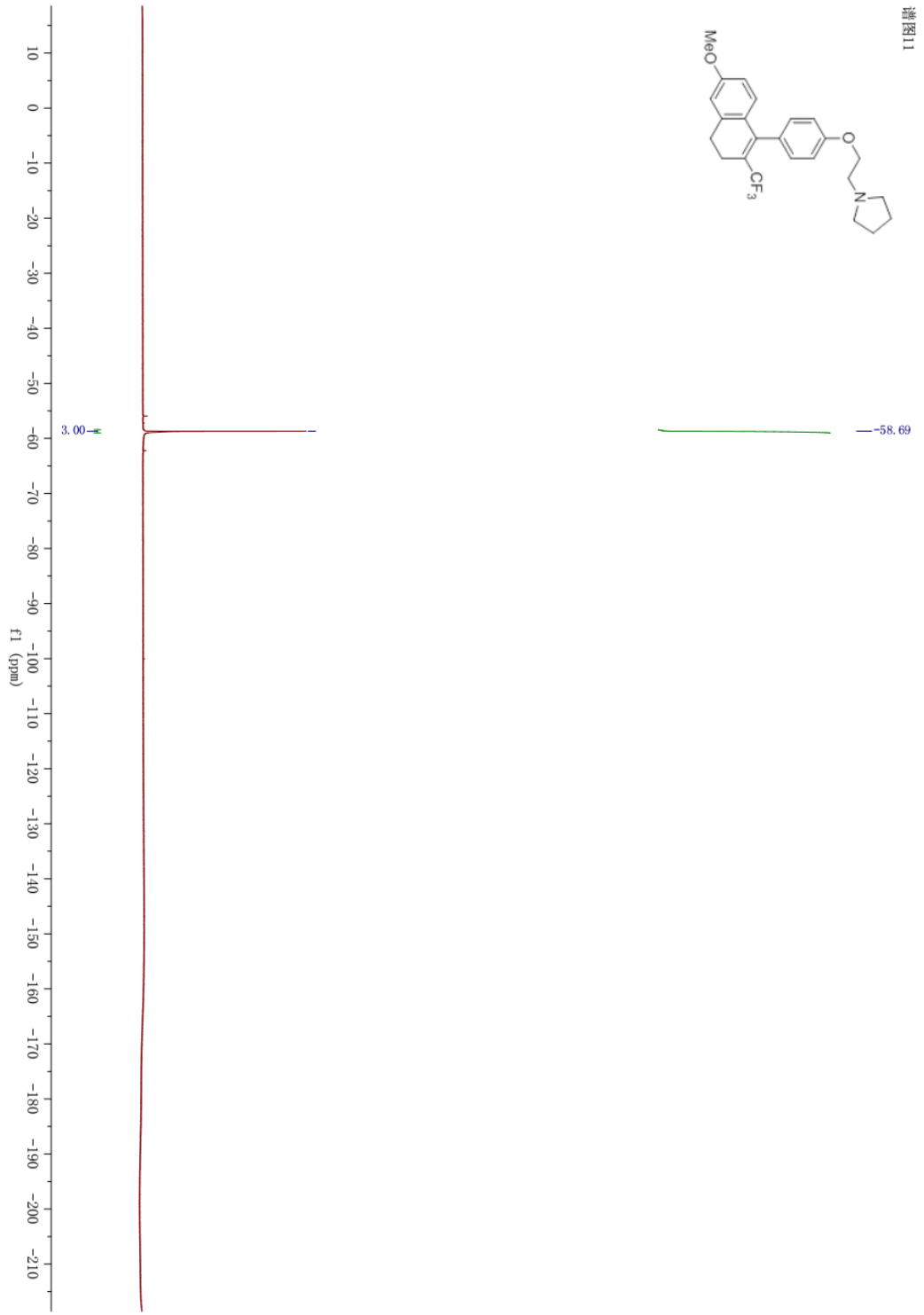
^{13}C NMR spectrum of compound **2u'**



^{1}H NMR spectrum of compound **5**



^{19}F NMR spectrum of compound **5**



^{13}C NMR spectrum of compound **5**