Supporting Information

Aromatic Ring Substituted Aaptamine Analogues as Potential Cytotoxic Agents against Extranodal Natural Killer/T-Cell Lymphoma

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1. Table S1. Attempts of bromination condition of aaptamine

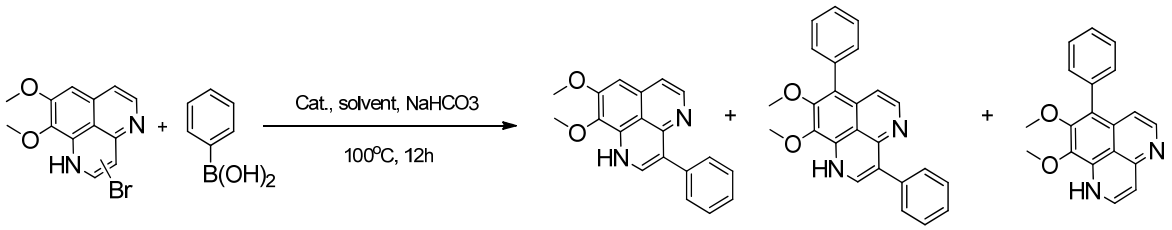
	Reagent	Solve	Yield (%)[a]
1	NBS	DMF	<10%
2	NBS	DCM	<10%
3	Br_2	DMF	60%
4	Br_2	DCM	>90%

[a]Estimated by LCMS

2. Table S2. Optimization of the condition of Suzuki coupling reaction of brominated aaptamine

	Cat.	Solvent	Suzuki products total yield (%)[a]
1	$Pd(OAc)_2$	DMF	35
2	$Pd(OAc)_2$	1,4-Dioxane	32
3	$Pd(OAc)_2$	1,4-Dioxane/H_2O, 3:1	42
4	$Pd(dppf)_2Cl_2$	DMF	38
5	$Pd(dppf)_2Cl_2$	1,4-Dioxane	41
6	$Pd(dppf)_2Cl_2$	1,4-Dioxane/H_2O, 3:1	81
7	$Pd(CH_3CN)_2Cl_2$	DMF	Trace
8	$Pd(CH_3CN)_2Cl_2$	1,4-Dioxane	22
9	$Pd(CH_3CN)_2Cl_2$	1,4-Dioxane/H_2O, 3:1	24

General condition: $NaHCO_3$, 100° C, 12 h, [a]Estimated by LCMS



3. The physical and spectroscopic characterizations of compounds 3a-i, 4a-f, 5a-l, and 6a-c.

*3-Phenyl-aaptamine (**3a**)*: yellow solid; 72.9 mg, yield 24%; UV (MeOH) λ_{max} (log ε) 240 (3.33), 260 (3.33) nm; HRESIMS *m/z* 305.1306 $[M + H]^+$ (calcd. 305.1290, $C_{19}H_{17}N_2O_2$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.67 (s, 1H), 7.56-7.59 (ov, 2H), 7.50-7.53 (m, 2H), 7.12 (d, J = 7.2 Hz, 1H), 7.06 (br.s, 1H), 6.89 (d, J = 7.2 Hz, 1H), 4.05 (s, 3H), 3.96 (s, 3H). ^{13}C NMR (125 MHz, CD_3OD) δ 158.8, 150.4, 142.0, 141.3, 135.2, 134.9, 134.8, 133.4, 131.3, 131.3, 130.8, 130.7, 130.7, 130.5, 118.4, 115.1, 102.9, 61.6, 57.3.

*3-(4-Ethylphenyl)-aaptamine (**3b**)*: yellow solid; 73.0 mg, yield 22%; UV (MeOH) λ_{max} (log ε) 218 (2.55), 270 (2.13) nm; HRESIMS *m/z* 333.1609 $[M + H]^+$ (calcd. 333.1603, $C_{21}H_{21}N_2O_2$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.67 (s, 1H), 7.41 (ov, J = 2.0 Hz, 4H), 7.11 (d, J = 7.2 Hz, 1H), 7.07 (s, 1H), 6.89 (d, J = 7.2 Hz, 1H), 4.05 (s, 3H), 3.96 (s, 3H), 2.74 (d, J = 7.6 Hz, 2H), 1.29 (t, J = 7.6 Hz, 3H).^{13}C NMR (125 MHz, CD_3OD) δ 158.9, 150.3, 147.3, 142.2, 135.3, 134.8, 133.8, 130.8, 130.8, 130.7, 130.6, 130.6, 129.6, 118.4, 115.0, 114.6, 102.7, 61.6, 57.4, 30.0, 16.4.

*3-(3-isopropylphenyl)-aaptamine (**3c**)*: yellow solid; 69.2 mg, yield 20%; UV (MeOH) λ_{max} (log ε) 216 (2.89), 270 (2.80) nm; HRESIMS *m/z* 347.1772 $[M + H]^+$ (calcd. 347.1760, $C_{22}H_{23}N_2O_2$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.69 (s, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.43 (d, J = 7.7 Hz, 1H), 7.36 (s, 1H), 7.31 (d, J = 7.6 Hz, 1H), 7.13 (s, 1H), 7.11 (d, J = 7.4 Hz, 1H), 6.93 (d, J = 7.4 Hz, 1H), 4.08 (s, 3H), 3.98 (s, 3H), 3.00 (m, 1H), 1.32 (d, J = 6.9 Hz, 3H), 1.32 (d, J = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, CD_3OD) δ 157.3, 150.8, 148.6, 140.4, 133.5, 133.1, 132.1, 131.6, 129.6, 128.8, 127.2, 126.3, 116.7, 116.6, 113.4, 113.1, 101.2, 59.8, 55.8, 34.1, 22.9, 22.9.

*3-(4-methoxyphenyl)-aaptamine (**3d**)*: yellow solid; 66.8 mg, yield 20%; UV (MeOH) λ_{max} (log ε) 242 (4.03), 264 (4.06) nm; HRESIMS *m/z* 335.1406 $[M + H]^+$ (calcd. 335.1396, $C_{20}H_{19}N_2O_3$); ^{1}H NMR and ^{13}C NMR data: see Table 1.

*3-(3-fluorophenyl)-aaptamine (**3e**)*: green yellow solid; 48.3 mg, yield 15%; UV (MeOH) λ_{max} (log ε) 201 (3.42), 217 (3.26) nm; HRESIMS *m/z* 323.1197 $[M + H]^+$

(calcd. 323.1196, $C_{19}H_{16}N_2O_2F$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.26 (s, 1H), 7.16 (td, J = 8.1, 6.1 Hz, 1H), 6.87-6.92 (ov, 2H), 6.82-6.79 (m, 1H), 6.74 (d, J = 7.1 Hz, 1H), 6.61 (s, 1H), 6.46 (d, J = 7.2 Hz, 1H), 3.61 (s, 3H), 3.52 (s, 3H).^{13}C NMR (125 MHz, CD_3OD) δ 166.1, 164.2, 158.8, 150.3, 142.3, 136.3, 135.5, 1345.0, 133.7, 133.0, 131.8, 126.6, 118.6, 117.6, 115.0, 113.6, 102.4, 61.5, 57.3.

*3-(4-chlorophenyl)-aaptamine (**3f**)*: yellow liquid; 50.7 mg, yield 15%; UV (MeOH) λ_{max} (log ε) 321 (1.86); 368 (1.87) nm; HRESIMS *m/z* 339.0899 [M + H]$^+$ (calcd. 339.0900, $C_{19}H_{16}N_2O_2Cl$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.73 (s, 1H), 7.62-7.58 (ov, 2H), 7.54-7.51 (ov, 2H), 7.15 (d, J = 7.4 Hz, 1H), 7.13 (s, 1H), 6.95 (d, J = 7.2 Hz, 1H), 4.07 (s, 3H), 3.98 (s, 3H). ^{13}C NMR (125 MHz, CD_3OD) δ 157.3, 148.5, 140.6, 134.9, 133.5, 133.1, 132.1, 130.7, 130.7, 130.5, 129.6, 129.6, 129.1, 116.7, 113.4, 111.6, 101.1, 59.8, 55.7.

*3-(3-(trifluoromethyl)phenyl)-aaptamine (**3g**)*: dark green solid; 52.1 mg, yield 14%; UV (MeOH) λ_{max} (log ε) 248 (3.33), 271 (3.17) nm; HRESIMS *m/z* 373.1174 [M + H]$^+$ (calc. 373.1164, $C_{20}H_{16}N_2O_2F_3$); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.89 (s, 1H), 7.84 (ov, 2H), 7.78 (m, 2H), 7.27 (d, J = 6.9 Hz, 1H), 7.19 (s, 1H), 6.96 (d, J = 6.9 Hz, 1H), 4.00 (s, 3H), 3.84 (s, 3H).^{13}C NMR (125 MHz, DMSO-d_6) δ 157.2, 148.5, 141.9, 134.2, 133.7, 133.7, 133.5, 131.9, 131.0, 126.8, 126.8, 125.9, 125.4, 123.7, 116.8, 113.7, 111.4, 101.5, 61.0, 57.0.

*3-(m-tolyl)-aaptamine (**3h**)*: yellow solid; 63.6 mg, yield 20%; UV (MeOH) λ_{max} (log ε) 274 (3.17), 322 (2.84) nm; HRESIMS *m/z* 319.1450 [M + H]$^+$ (calc.319.1447, $C_{20}H_{19}N_2O_2$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.69 (s, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.37-7.31 (m, 2H), 7.28 (d, J = 7.6 Hz, 1H), 7.12 (ov, 2H), 6.92 (d, J = 7.2 Hz, 1H), 4.06 (s, 3H), 3.97 (s, 3H), 2.44 (s, 3H).^{13}C NMR (125 MHz, CD_3OD) δ 159.0, 150.3, 142.1, 141.4, 135.2, 134.8, 133.8, 133.3, 131.5, 131.2, 131.1, 130.6, 127.6, 118.4, 115.1, 114.7, 102.9, 61.6, 57.4, 21.8.

*3-(3-hydroxyphenyl)-aaptamine (**3i**)*: dark yellow solid; 16.0 mg, yield 5%; UV (MeOH) λ_{max} (log ε) 260 (3.57), 318 (3.08) nm; HRESIMS *m/z* 321.1241 [M + H]$^+$ (calcd. 321.1239, $C_{19}H_{17}N_2O_3$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.70 (s, 1H), 7.44-7.36 (m, 1H), 7.31 (dd, J = 7.5, 1.6 Hz, 1H), 7.18 (d, J = 7.2 Hz, 1H), 7.14 (s,

1H), 7.08-7.00 (m, 2H), 6.94 (d, J = 7.2 Hz, 1H), 4.08 (s, 3H), 3.99 (s, 3H).^{13}C NMR (125 MHz, CD_3OD) δ 157.2, 155.8, 148.4, 140.9, 133.4, 133.1, 132.0, 131.6, 130.7, 129.0, 120.2, 118.2, 116.4, 115.9, 113.1, 110.2, 101.0, 59.9, 55.7.

*7-phenyl-aaptamine (**4a**)*: black solid; 48.6 mg, yield 16%; UV (MeOH) λ_{max} (log ε) 218 (3.99), 270 (3.97) nm; HRESIMS *m/z* 305.1296 $[M + H]^+$ (calcd. 305.1290, $C_{19}H_{17}N_2O_2$); ^{1}H NMR (400 MHz, CD_3OD) δ 7.91 (d, J = 6.6 Hz, 1H), 7.51 (dt, J = 14.5, 7.0 Hz, 3H), 7.31 (d, J = 6.9 Hz, 2H), 7.14 (d, J = 7.3 Hz, 1H), 6.54 – 6.41 (m, 2H), 4.02 (s, 3H), 3.74 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 157.0, 152.3, 142.6, 137.9, 135.9, 135.1, 131.9, 131.4, 131.4, 130.9, 130.0, 130.0, 129.3, 126.0, 120.0, 112.5, 100.3, 61.6, 61.5.

*7-(3-isopropylphenyl)-aaptamine (**4b**)*: dark yellow solid; 51.9 mg, yield 15%; UV (MeOH) λ_{max} (log ε) 315 (1.86) nm; HRESIMS *m/z* 347.1753 $[M + H]^+$ (calcd. 347.1760, $C_{22}H_{23}N_2O_2$); ^{1}H NMR (400 MHz, CD_3Cl) δ 7.94 (br.s, 1H), 7.41 (t, J = 7.6 Hz, 1H), 7.30 (br.s, 1H), 7.08 (ov, 2H), 6.94 (br.s, 1H), 6.43 (d, J = 6.4 Hz, 1H), 4.06 (s, 3H), 3.74 (s, 3H), 2.97 (m, 1H), 1.28 (d, J = 6.4 Hz, 6H). ^{13}C NMR (100 MHz, CD_3Cl) δ 155.4, 150.7, 149.5, 140.5, 136.4, 134.1, 133.4, 130.5, 128.7, 128.5, 128.1, 127.3, 126.1, 124.5, 118.6, 111.3, 99.5, 61.2, 61.0, 34.0, 24.0, 23.9.

*7-(4-chlorophenyl)-aaptamine (**4c**)*: light green solid; 33.8 mg, yield 10%; UV (MeOH) λ_{max} (log ε) 239 (2.36), 317 (1.97), 389 (1.85) nm; HRESIMS *m/z* 339.0909 $[M + H]^+$ (calcd. 339.0900, $C_{19}H_{16}N_2O_2Cl$); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.97 (d, J = 7.0 Hz, 1H), 7.59-7.56 (m, 2H), 7.35-7.26 (m, 3H), 6.60 (d, J = 7.0 Hz, 1H), 6.28 (d, J = 7.4 Hz, 1H), 3.87 (s, 3H), 3.72 (s, 3H).^{13}C NMR (125 MHz, DMSO-d_6) δ 154.6, 150.1, 142.0, 135.7, 134.6, 132.6, 132.5, 132.0, 132.0, 130.1, 130.1, 128.8, 128.8, 121.4, 118.0, 109.9, 99.5, 60.9, 60.7.

*7-(4-methoxyphenyl)-aaptamine (**4d**)*: yellow solid; 60.1 mg, yield 18%; UV (MeOH) λ_{max} (log ε) 231.00 (4.43), 322.80 (4.04) nm; HRESIMS *m/z* 335.1396 $[M + H]^+$ (calcd. 335.1396, $C_{19}H_{16}N_2O_3$); ^{1}H NMR and ^{13}C NMR data see Table 1.

*7-(4-(trifluoromethyl)phenyl)-aaptamine (**4e**)*: dark yellow solid; 37.2 mg, yield 10%; UV (MeOH) λ_{max} (log ε) 246 (3.11) nm; HRESIMS *m/z* 373.1165 $[M + H]^+$ (calcd. 373.1164, $C_{20}H_{16}N_2O_2F_3$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.93 (s, 1H), 7.83 (d, J =

8.0 Hz, 2H), 7.53 (d, J = 7.9 Hz, 2H), 7.17 (s, 1H), 6.55 (s, 1H), 6.40 (d, J = 7.1 Hz, 1H), 4.01 (s, 3H), 3.79 (s, 3H).^{13}C NMR (125 MHz, CD_3OD) δ 155.2, 150.8, 141.3, 138.0, 136.3, 135.0, 130.9, 130.9, 130.3, 129.1, 125.4, 125.4, 125.3, 125.3, 122.6, 118.5, 110.5, 99.2, 60.3, 60.1.

*7-(3-(trifluoromethyl)phenyl)-aaptamine (**4f**)*: green solid; 29.8 mg, yield 8%; UV (MeOH) λ_{max} (log ε) 255 (3.14), 317 (2.75) nm; HRESIMS *m/z* 373.1165 [M + H]$^+$ (calcd. 373.1164, $C_{20}H_{16}N_2O_2F_3$); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.00 (d, J = 6.9 Hz, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.76 (t, J = 7.6 Hz, 1H), 7.62 (d, J = 8.6 Hz, 2H), 7.30 (d, J = 7.4 Hz, 1H), 6.69 (d, J = 6.9 Hz, 1H), 6.22 (d, J = 7.4 Hz, 1H), 3.88 (s, 3H), 3.73 (s, 3H).^{13}C NMR (125 MHz, DMSO-d_6) δ 155.1, 150.6, 142.5, 136.2, 135.4, 135.3, 134.9, 130.8, 130.7, 130.5, 130.2, 127.2, 127.1, 125.1, 121.4, 118.5, 110.2, 100.0, 61.4, 61.3.

*3,7-diphenyl-aaptamine (**5a**)*: dark yellow solid; 152.0 mg, yield 40%; UV (MeOH) λ_{max} (log ε) 273 (3.67), 324 (3.35) nm; HRESIMS *m/z* 381.1613 [M + H]$^+$ (calcd. 381.1603, $C_{25}H_{21}N_2O_2$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.83 (s, 1H), 7.59 (d, J = 7.3 Hz, 2H), 7.56-7.51 (m, 5H), 7.46 (d, J = 7.5 Hz, 1H), 7.37-7.28 (m, 2H), 7.01 (d, J = 7.5 Hz, 1H), 6.48 (d, J = 7.5 Hz, 1H), 4.05 (s, 3H), 3.75 (s, 3H).^{13}C NMR (125 MHz, CD_3OD) δ 156.7, 150.5, 142.1, 137.9, 135.6, 135.3, 133.1, 132.1, 131.4, 131.4, 131.1, 131.1, 130.6, 130.4, 130.4, 130.2, 130.0, 130.0, 129.3, 125.9, 120.0, 115.4, 112.7, 61.6, 61.6.

*3,7-bis(4-(trifluoromethyl)phenyl)-aaptamine (**5b**):* red solid; 103.2 mg, yield 20%; UV (MeOH) λ_{max} (log ε) 246 (3.97), 326 (3.62) nm; HRESIMS *m/z* 517.1343 [M + H]$^+$ (calcd. 517.1351, $C_{27}H_{19}N_2O_2F_6$); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.89 (ov, 5H), 7.78 (d, J = 8.0 Hz, 2H), 7.54 (d, J = 8.0 Hz, 2H), 7.20 (d, J = 7.1 Hz, 1H), 6.32 (d, J = 7.2 Hz, 1H), 3.90 (s, 3H), 3.76 (s, 3H).^{13}C NMR (125 MHz, CD_3OD) δ 154.5, 149.1, 141.3, 138.5, 136.9, 136.6, 135.8, 130.9, 130.9, 130.9, 130.9, 129.8, 129.8, 129.8, 129.8, 126.2, 126.2, 125.3, 125.3, 122.9, 122.8, 121.7, 119.0, 113.2, 110.4, 60.5, 60.0.

*3,7-bis(4-chlorophenyl)-aaptamine (**5c**):* green yellow solid; 89.8 mg, yield 20%; UV (MeOH) λ_{max} (log ε) 274 (3.16), 324 (2.84) nm; HRESIMS *m/z* 449.0820 [M + H]$^+$

(calc. 449.0824, $C_{25}H_{19}N_2O_2Cl_2$); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.91 (s, 1H), 7.63 (dd, J = 18.3, 8.4 Hz, 4H), 7.57 (t, J = 7.3 Hz, 2H), 7.34 (d, J = 8.4 Hz, 2H), 7.14 (d, J = 7.4 Hz, 1H), 6.36 (d, J = 7.4 Hz, 1H), 3.92 (s, 3H), 3.76 (s, 3H).^{13}C NMR (125 MHz, DMSO-d_6) δ 154.4, 148.4, 141.5, 135.7, 134.1, 133.6, 132.6, 132.5, 132.0, 132.0, 131.4, 131.4, 130.6, 130.3, 129.5, 129.5, 128.8, 128.8, 121.4, 118.0, 112.4, 110.4, 109.4, 60.9, 60.8.

*3,7-bis(4-methoxyphenyl)-aaptamine (**5d**):* yellow solid; 167.4 mg, yield 38%; UV (MeOH) λ_{max} (log ε) 253 (2.73), 324 (2.44) nm; HRESIMS *m/z* 441.1807 $[M + H]^+$ (calc. 441.1814, $C_{27}H_{25}N_2O_4$); ^{1}H NMR and ^{13}C NMR data see Table 1.

*3,7-bis(4-fluorophenyl)-aaptamine (**5e**)*: light green solid; 62.4 mg, yield 15%; UV (MeOH) λ_{max} (log ε) 241 (3.11), 272 (3.14) nm; HRESIMS *m/z* 417.1410 $[M + H]^+$ (calc. 417.1415, $C_{25}H_{19}N_2O_2F_2$); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.81 (s, 1H), 7.57-7.54 (m, 2H), 7.48-7.23 (m, 7H), 7.16 (d, J = 7.3 Hz, 1H), 6.29 (d, J = 7.3 Hz, 1H), 3.89 (s, 3H), 3.71 (s, 3H).^{13}C NMR (125 MHz, DMSO-d_6) δ 162.7, 161.1, 154.3, 148.7, 141.0, 135.7, 134.3, 132.2, 132.2, 131.7, 131.6, 130.6, 130.1, 130.1, 128.5, 121.2, 118.2, 116.3, 116.2, 115.8, 115.6, 112.8, 110.2, 60.8, 60.8.

*3,7-di-p-tolyl-aaptamine (**5f**)*: yellow solid; 122.4 mg, yield 30%; UV (MeOH) λ_{max} (log ε) 273 (2.46), 324 (2.16) nm; HRESIMS 409.1916 $[M + H]^+$ (calc. 409.1916, $C_{27}H_{25}N_2O_2$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.79 (s, 1H), 7.40 (ov, 4H), 7.34 (d, J = 7.8 Hz, 2H), 7.20 (d, J = 8.0 Hz, 2H), 6.99 (d, J = 7.5 Hz, 1H), 6.49 (d, J = 7.5 Hz, 1H), 4.04 (s, 3H), 3.74 (s, 3H), 2.43 (s, 3H), 2.43 (s, 3H). ^{13}C NMR (125 MHz, CD_3OD) δ 156.7, 150.6, 141.9, 140.8, 139.3, 137.9, 135.4, 132.2, 132.1, 131.7, 131.7, 131.3, 131.3, 130.6, 130.6, 130.3, 130.3, 130.0, 130.0, 125.9, 120.0, 115.4, 112.7, 61.6, 61.6, 21.4, 21.4.

*3,7-bis(3-isopropylphenyl)-aaptamine (**5g**):* dark yellow solid; 139.2 mg, yield 30%; UV (MeOH) λ_{max} (log ε) 273 (3.00), 322 (2.67) nm; HRESIMS 465.2544 (calc. 465.2542 $[M+H]^+$, $C_{31}H_{33}N_2O_2$); ^{1}H NMR (400 MHz, CD_3Cl) δ 8.07 (s, 1H), 7.54-7.41 (m, 4H), 7.07-7.39 (m, 5H), 6.37 (d, J = 7.5 Hz, 1H), 4.05 (s, 3H), 3.75 (s, 3H), 2.89 (t, J = 7.2 Hz, 1H), 2.86 (t, J = 7.2 Hz, 1H), 1.29 (d, J = 7.3 Hz, 3H), 1.28 (d, J = 7.3 Hz, 3H), 1.25 (d, J = 7.3 Hz, 3H), 1.24 (d, J = 7.3 Hz, 3H). ^{13}C NMR (100

MHz, CD_3Cl) δ 155.0, 150.6, 149.4, 148.2, 141.9, 136.9, 134.3, 133.6, 131.2, 130.2, 129.7, 129.3, 128.6, 128.0, 127.2, 127.1, 127.1, 126.1, 125.9, 124.3, 118.4, 113.5, 110.8, 61.2, 60.9, 33.9, 33.9, 23.9, 23.9, 23.7, 23.7.

*3,7-bis(3-(trifluoromethyl)phenyl)-aaptamine (**5h**)*: green yellow solid; 77.4 mg, yield 15%; UV (MeOH) λ_{max} (log ε) 331 (3.08), 377 (2.97) nm; HRESIMS *m/z* 517.1354 (calc. 517.1351 $[M+H]^+$, $C_{27}H_{19}N_2O_2F_6$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.86 (s, 1H), 7.81-7.74 (m, 5H), 7.72 (d, J = 7.8 Hz, 1H), 7.61 (d, J = 10.6 Hz, 2H), 7.11 (d, J = 7.2 Hz, 1H), 6.36 (d, J = 7.1 Hz, 1H), 4.01 (s, 3H), 3.78 (s, 3H).^{13}C NMR (125 MHz, CD_3OD) δ 154.3, 149.4, 141.2, 136.5, 136.1, 135.6, 134.4, 134.1, 132.9, 131.6, 131.2, 130.9, 130.6, 130.1, 130.1, 129.3, 129.3, 126.9, 125.9, 125.1, 124.2, 121.0, 119.3, 113.5, 110.1, 60.1, 59.9.

*3,7-di-m-tolyl-aaptamine (**5i**)*: dark yellow solid; 102.0 mg, yield 25%; UV (MeOH) λ_{max} (log ε) 272 (2.58), 324 (2.23), 379 (2.04) nm; HRESIMS *m/z* 409.1916 (calc. 409.1916 $[M+H]^+$, $C_{27}H_{25}N_2O_2$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.82 (s, 1H), 7.48 (s, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.36 (d, J = 7.8 Hz, 2H), 7.33-7.27 (m, 2H), 7.14 (s, 1H), 7.11 (d, J = 7.5 Hz, 1H), 7.01 (d, J = 7.4 Hz, 1H), 6.48 (d, J = 7.3 Hz, 1H), 4.06 (s, 3H), 3.76 (s, 3H), 2.45 (s, 3H), 2.42 (s, 3H).^{13}C NMR (125 MHz, CD_3OD) δ 157.0, 150.7, 142.1, 141.5, 140.2, 138.1, 135.6, 135.5, 133.1, 132.3, 132.2, 131.6, 131.3, 131.1, 130.3, 130.3, 130.2, 130.2, 128.7, 127.6, 126.4, 120.2, 115.8, 113.1, 61.9, 21.8, 21.8.

*3,7-bis(3-fluorophenyl)-aaptamine (**5j**)*: yellow solid; 62.4 mg, yield 15%; UV (MeOH) λ_{max} (log ε) 269 (1.87), 325 (1.56), 394 (1.41) nm; HRESIMS *m/z* 417.1413 (calc. 417.1415 $[M+H]^+$, $C_{27}H_{25}N_2O_2F_2$), ^{1}H NMR (500 MHz, CD_3OD) δ 7.84 (s, 1H), 7.59 (td, J = 8.0, 6.1 Hz, 1H), 7.54 (td, J = 8.0, 6.1 Hz, 1H), 7.36-7.31 (m, 2H), 7.25 (td, J = 8.6, 2.2 Hz, 1H), 7.21-7.16 (m, 1H), 7.14 (dt, J = 7.6, 1.0 Hz, 1H), 7.11-7.03 (m, 2H), 6.44 (d, J = 7.4 Hz, 1H), 4.02 (s, 3H), 3.79 (s, 3H). ^{13}C NMR (125 MHz, CD_3OD) δ 165.5, 163.9, 156.2, 150.3, 142.7, 138.1, 137.9, 137.8, 136.7, 136.0, 132.9, 132.9, 132.2, 131.7, 131.5, 127.5, 126.4, 123.8, 120.2, 118.3, 117.3, 117.1, 115.9, 114.5, 112.1, 61.7, 61.5.

*3,7-bis(3,5-dimethylphenyl)-aaptamine (**5k**):* light green solid; 130.8 mg, yield 30%; UV (MeOH) λ_{max} (log ε) 273 (3.56), 323 (3.26) nm; HRESIMS m/z 437.2226 (calc. 437.2229 $[M+H]^+$, $C_{29}H_{29}N_2O_2$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.69 (s, 1H), 7.09 (s, 1H), 7.02 (d, J = 11.3 Hz, 3H), 6.90 (d, J = 7.5 Hz, 1H), 6.82 (s, 2H), 6.37 (d, J = 7.5 Hz, 1H), 3.95 (s, 3H), 3.65 (s, 3H), 2.31 (s, 6H), 2.28 (s, 6H).^{13}C NMR (125 MHz, CD_3OD) δ 155.2, 149.0, 140.4, 139.6, 139.6, 138.3, 138.3, 136.4, 133.9, 133.7, 131.4, 130.7, 130.6, 129.2, 128.5, 127.5, 127.5, 127.5, 126.4, 126.4, 126.4, 124.8, 118.4, 114.1, 111.4, 60.2, 60.2, 20.0, 20.0.

*3,7-di-p-tolyl-aaptamine (**5l**)*: yellow solid; 152.6 mg, yield 35%; UV (MeOH) λ_{max} (log ε) 272 (2.19), 323 (2.22) nm; HRESIMS m/z 437.2231 (calc. 437.2229 $[M+H]^+$, $C_{29}H_{29}N_2O_2$); ^{1}H NMR (500 MHz, CD_3OD) δ 7.81 (s, 1H), 7.44 (ov, 4H), 7.38 (d, J = 7.8 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 7.00 (d, J = 7.5 Hz, 1H), 6.48 (d, J = 7.5 Hz, 1H), 4.05 (s, 3H), 3.75 (s, 3H), 2.74-2.78 (ov, 4H), 1.33 (t, J = 7.5 Hz, 3H), 1.31 (t, J = 7.5 Hz, 3H). ^{13}C NMR (125 MHz, CD_3OD) δ 155.1, 149.0, 145.5, 144.1, 140.9, 136.6, 134.5, 132.2, 130.7, 130.0, 130.0, 129.1, 129.1, 129.0, 129.0, 128.9, 128.9, 128.0, 128.0, 124.1, 118.7, 114.0, 111.0, 60.2, 60.1, 28.3, 28.3, 14.7, 14.7.

*3-(naphthalen-1-yl)-aaptamine (**6a**)*: dark solid; 53.1 mg, yield 15%; UV (MeOH) λ_{max} (log ε) 217 (3.25), 239 (3.05) nm; HRESIMS *m/z* 355.1449 (calc. 355.1447 $[M+H]^+$, $C_{23}H_{19}N_2O_2$); ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.11 (1H, br.d), 8.10 (1H, ov), 8.02 (1H, m), 7.87 (1H, s), 7.61 (3H, ov), 7.23 (1H, br.d, J = 5 Hz), 7.22 (1H, br.s), 6.96 (1H, d, J = 5 Hz), 3.97 (3H, s), 3.75 (3H, s). ^{13}C NMR (125 MHz, DMSO-d_6) δ 158.0, 149.4, 142.5, 134.6, 134.2, 134.2, 132.7, 130.6, 130.4, 129.8, 129.4, 128.9, 128.9, 128.2, 128.0, 127.8, 117.7, 114.4, 114.4, 113.5, 102.4, 61.8, 57.8.

*3,7-di(naphthalen-1-yl)-aaptamine (**6b**)*: dark solid; 144.0 mg, yield 30%; UV (MeOH) λ_{max} (log ε) 201 (4.10), 221 (4.37) nm; HRESIMS *m/z* 481.1920 (calc. 481.1916 $[M+H]^+$, $C_{33}H_{25}N_2O_2$), ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.13-8.08 (4H, ov), 8.03-7.98 (5H, ov), 7.90 (1H, br.s), 7.66 (1H, br.d, J = 5 Hz), 7.62-7.59 (4H, ov), 7.46 (1H, d, J = 5 Hz), 7.14 (1H, d, J = 5 Hz), 6.39 (1H, d, J = 5 Hz), 3.97 (3H, s), 3.75 (3H, s). ^{13}C NMR (125 MHz, DMSO-d_6) δ 154.9, 136.5, 133.8, 133.6, 133.3, 132.8, 132.1, 131.3, 130.5, 129.5, 129.4, 129.4, 128.8, 128.8, 128.7, 128.7, 128.6, 128.4,

128.4, 128.1, 128.1, 127.4, 127.2, 127.0, 127.0, 126.9, 126.9, 122.6, 119.0, 114.3, 110.9, 61.4, 61.3.

*7-(naphthalen-1-yl)-aaptamine (**6c**)*: dark solid; 35.4 mg, yield 10%; UV (MeOH) λ_{max} (log ε) 219 (2.75), 256 (2.43), 316 (1.92) nm; HRESIMS *m/z* 355.1453 (calc. 355.1447 $[M+H]^+$, $C_{23}H_{19}N_2O_2$); ^{1}H NMR (500 MHz, CD_3OD) δ 8.02 (1H, d, J = 5 Hz), 7.95-7.89 (3H, ov), 7.82 (1H, br.s), 7.57-7.53 (2H, ov), 7.41 (1H, d, J = 5 Hz), 7.12 (1H, br.d, J = 5 Hz), 6.51-6.47 (2H, ov), 4.03 (3H, s), 3.73 (3H, s). ^{13}C NMR (125 MHz, CD_3OD) δ 155.7, 150.9, 141.2, 136.4, 134.6, 133.5, 133.0, 131.1, 130.6, 129.0, 128.1, 127.7, 127.6, 127.4, 127.4, 126.2, 126.1, 118.6, 111.0, 111.0, 99.0, 60.2, 60.1.

4. HRMS and NMR spectra of 3a-i, 4a-f, 5a-l, and 6a-c

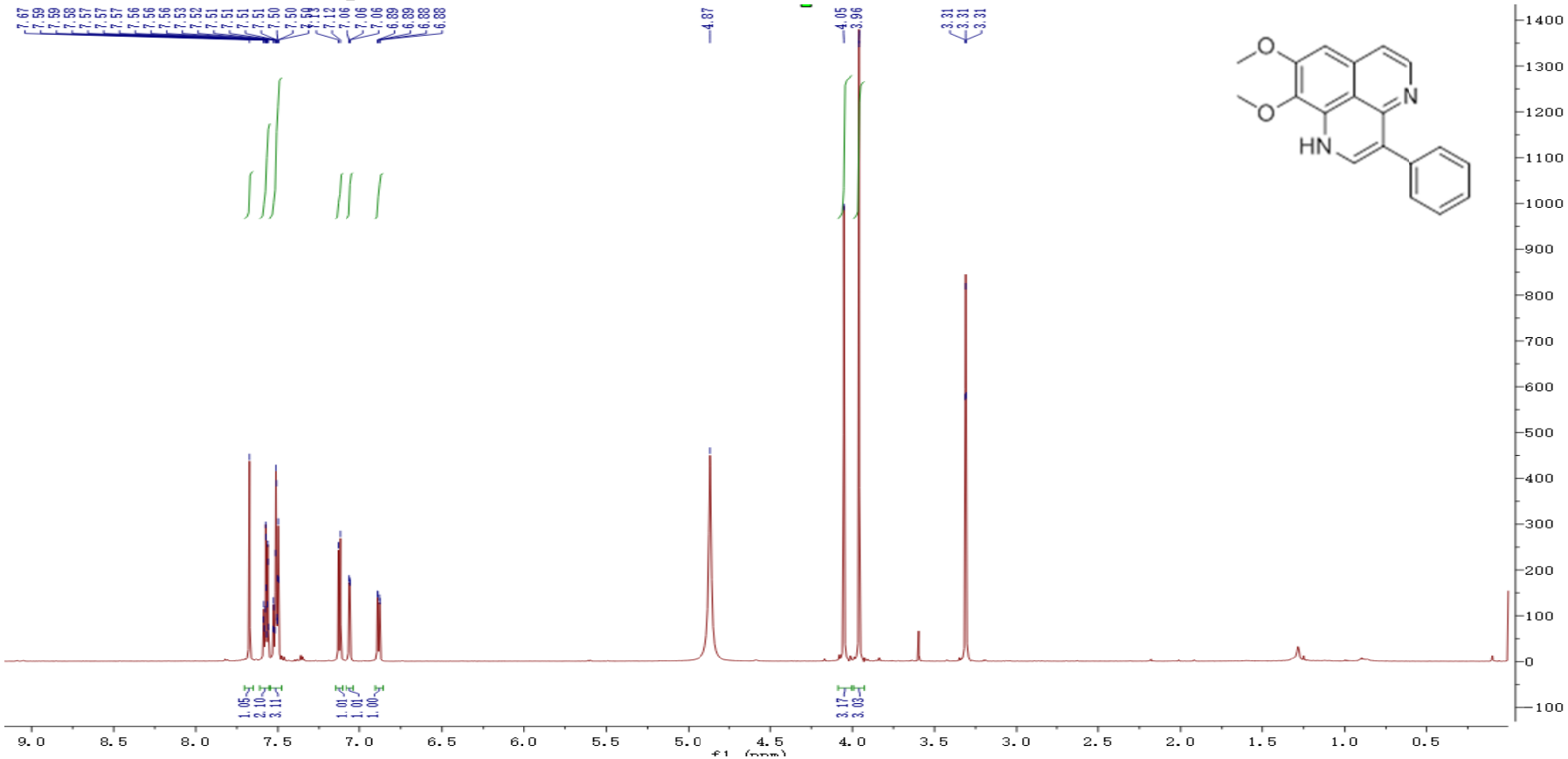


Figure S1. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 3a

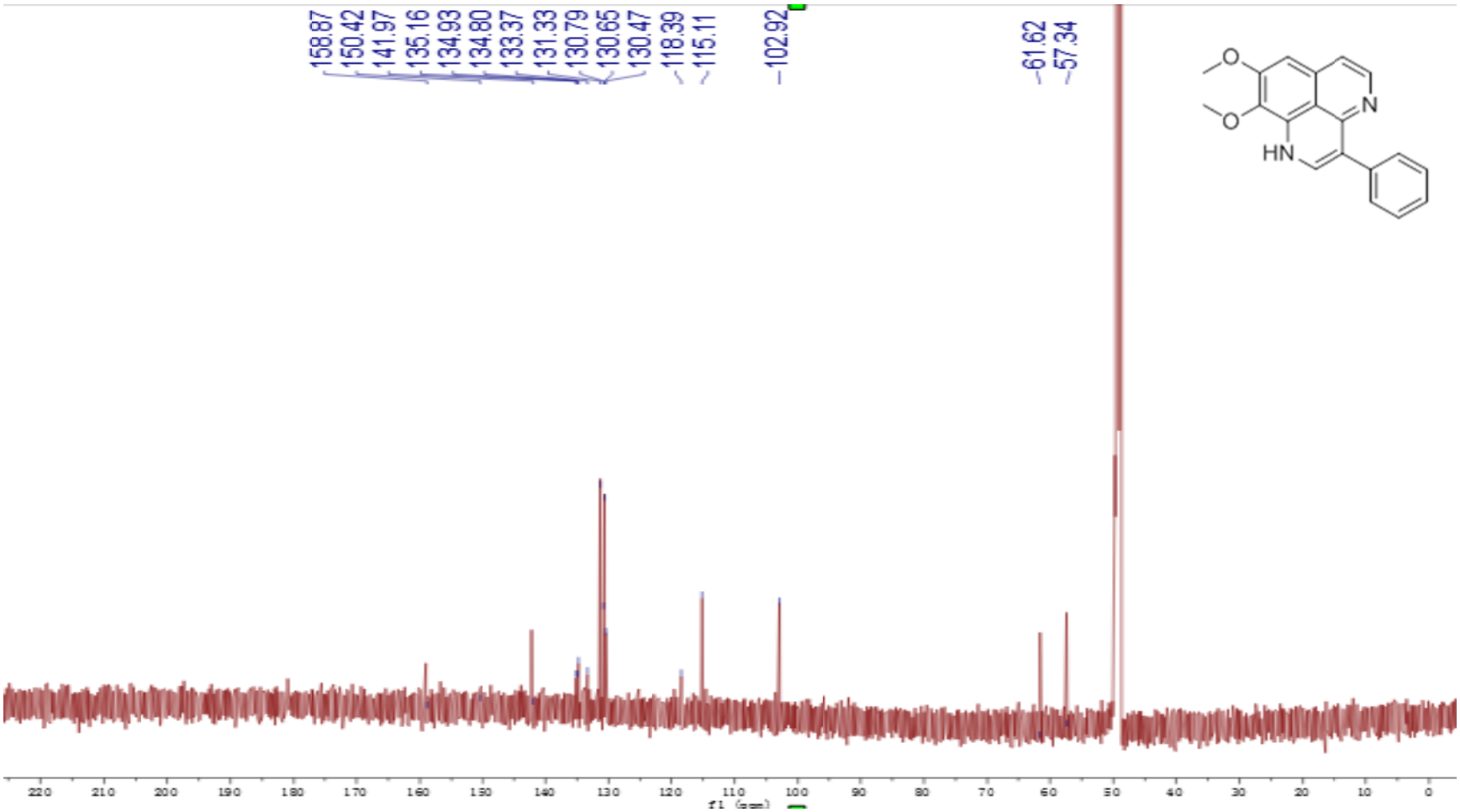


Figure S2. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 3a

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
472 formula(e) evaluated with 5 results within limits (up to 50 closest results for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
305.1306	305.1290	1.6	5.2	12.5	C19 H17 N2 O2	565.5	0.023	97.74	19	17	2	2
	305.1330	-2.4	-7.9	16.5	C24 H17	569.3	3.806	2.22	24	17		
	305.1322	-1.6	-5.2	4.5	C8 H17 N8 O5	573.7	8.210	0.03	8	17	8	5
	305.1309	-0.3	-1.0	-0.5	C7 H21 N4 O9	574.6	9.071	0.01	7	21	4	9
	305.1282	2.4	7.9	0.5	C3 H17 N10 O7	576.0	10.535	0.00	3	17	10	7

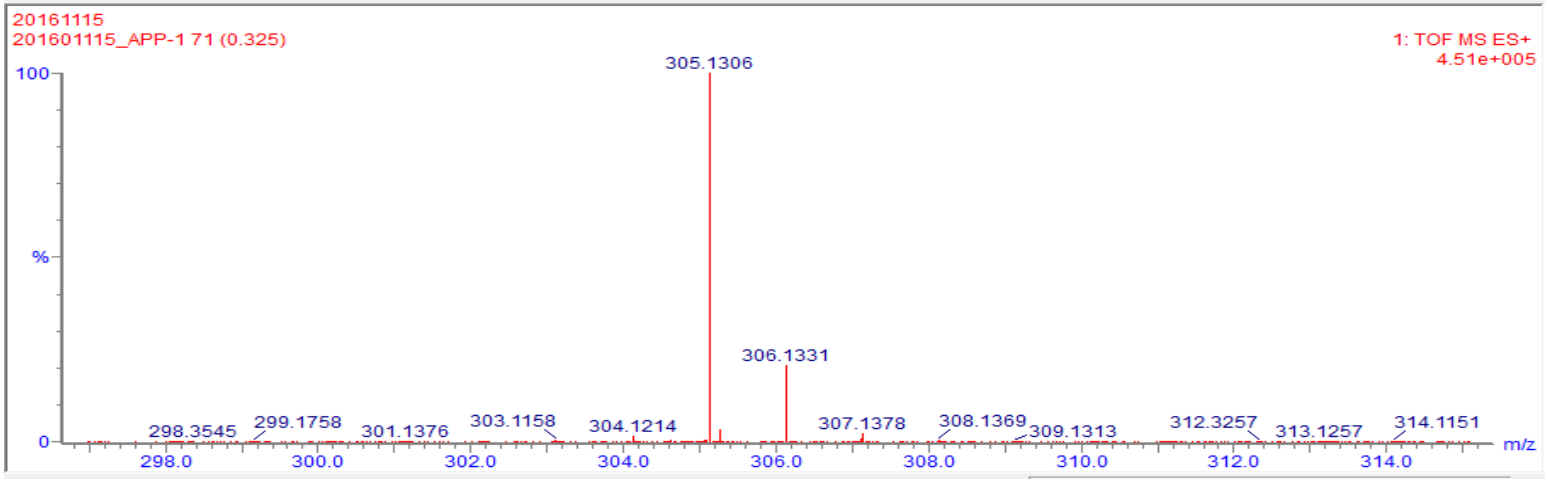


Figure S3. HRESIMS of compound 3a

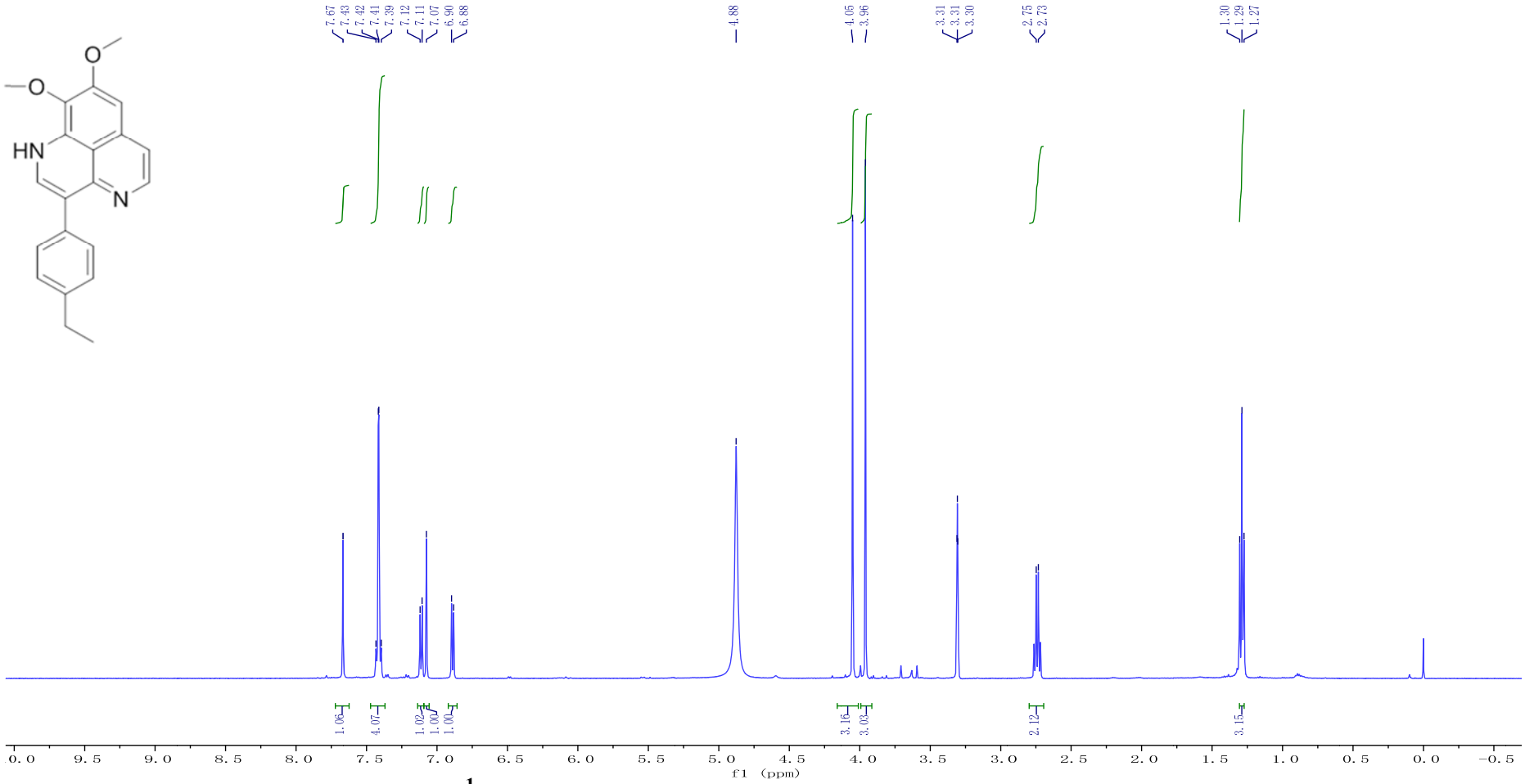


Figure S4. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 3b

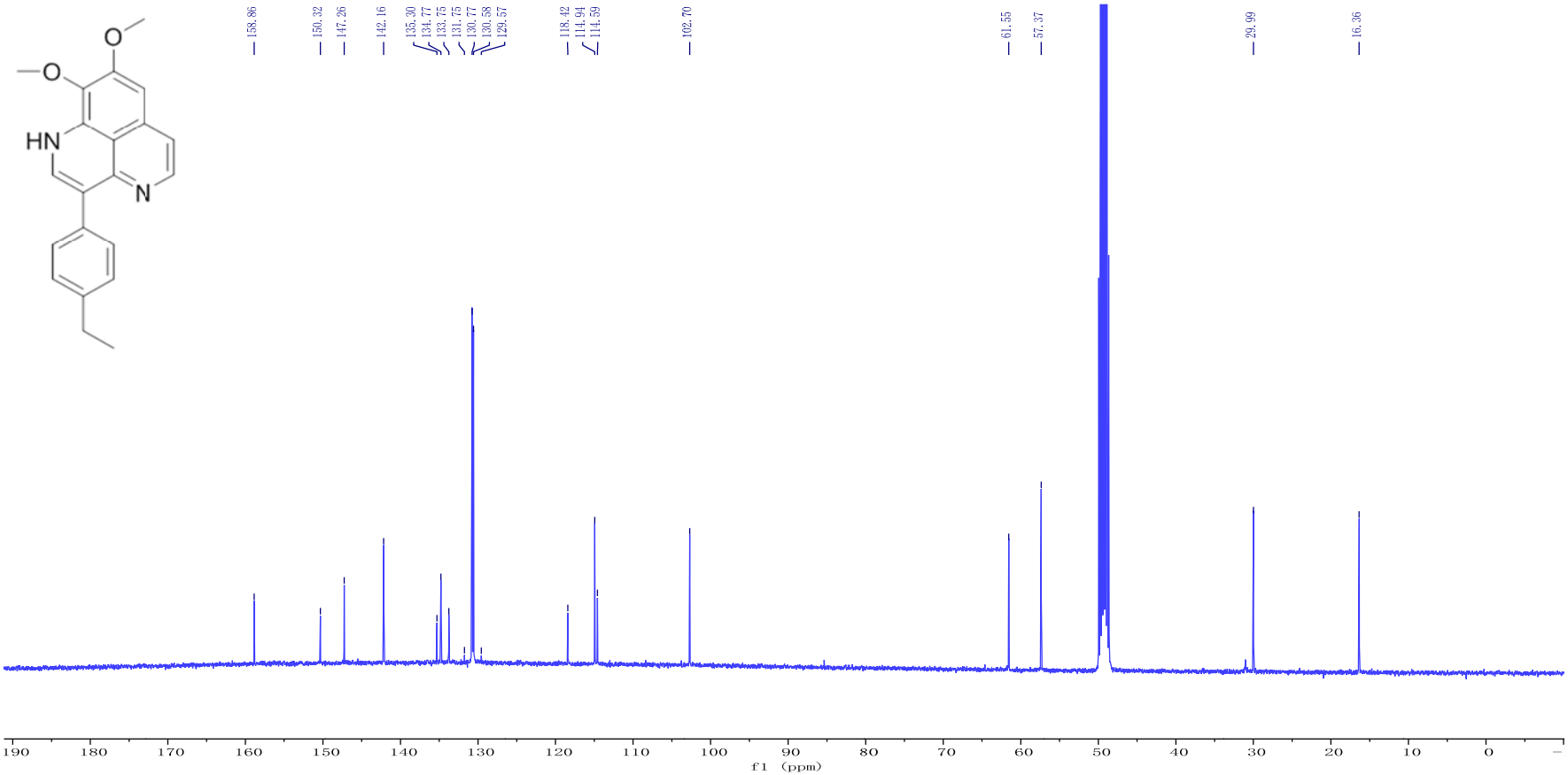


Figure S5. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 3b

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
314 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
333.1609	333.1643	-3.4	-10.2	16.5	C26 H21	2015.0	0.583	55.81	26	21		
	333.1603	0.6	1.8	12.5	C21 H21 N2 O2	2015.3	0.842	43.09	21	21	2	2
	333.1576	3.3	9.9	13.5	C17 H17 N8	2019.4	4.952	0.71	17	17	8	
	333.1563	4.6	13.8	8.5	C16 H21 N4 O4	2020.1	5.614	0.36	16	21	4	4
	333.1635	-2.6	-7.8	4.5	C10 H21 N8 O5	2022.3	7.897	0.04	10	21	8	5

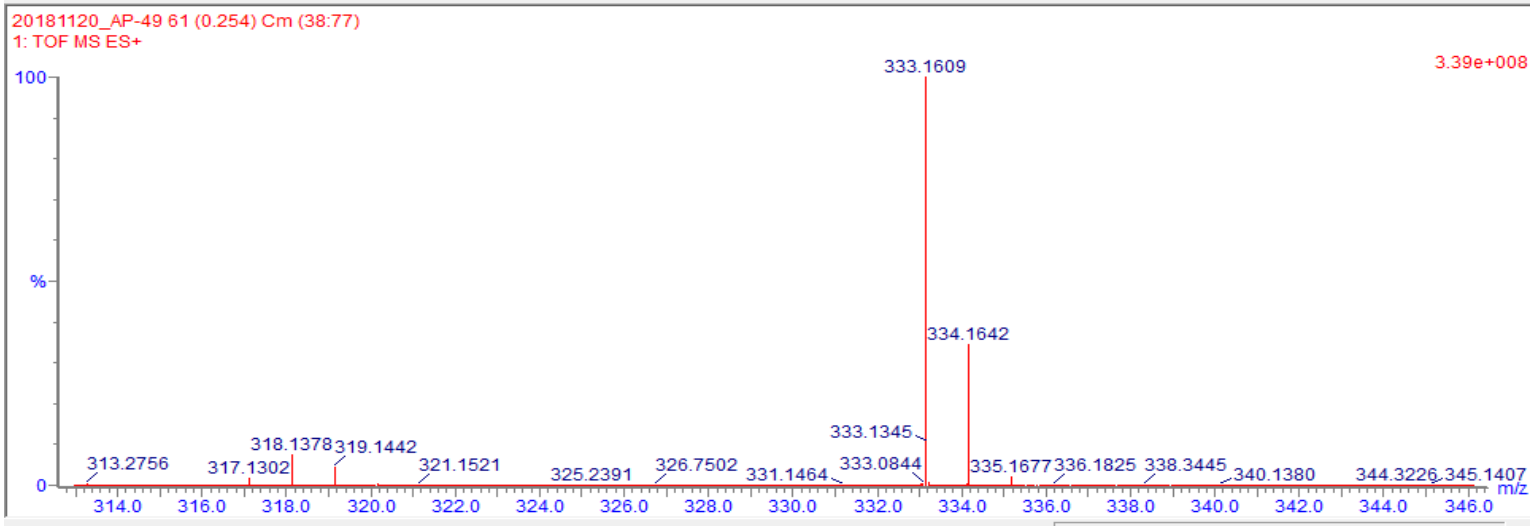


Figure S6. HRESIMS of compound 3b

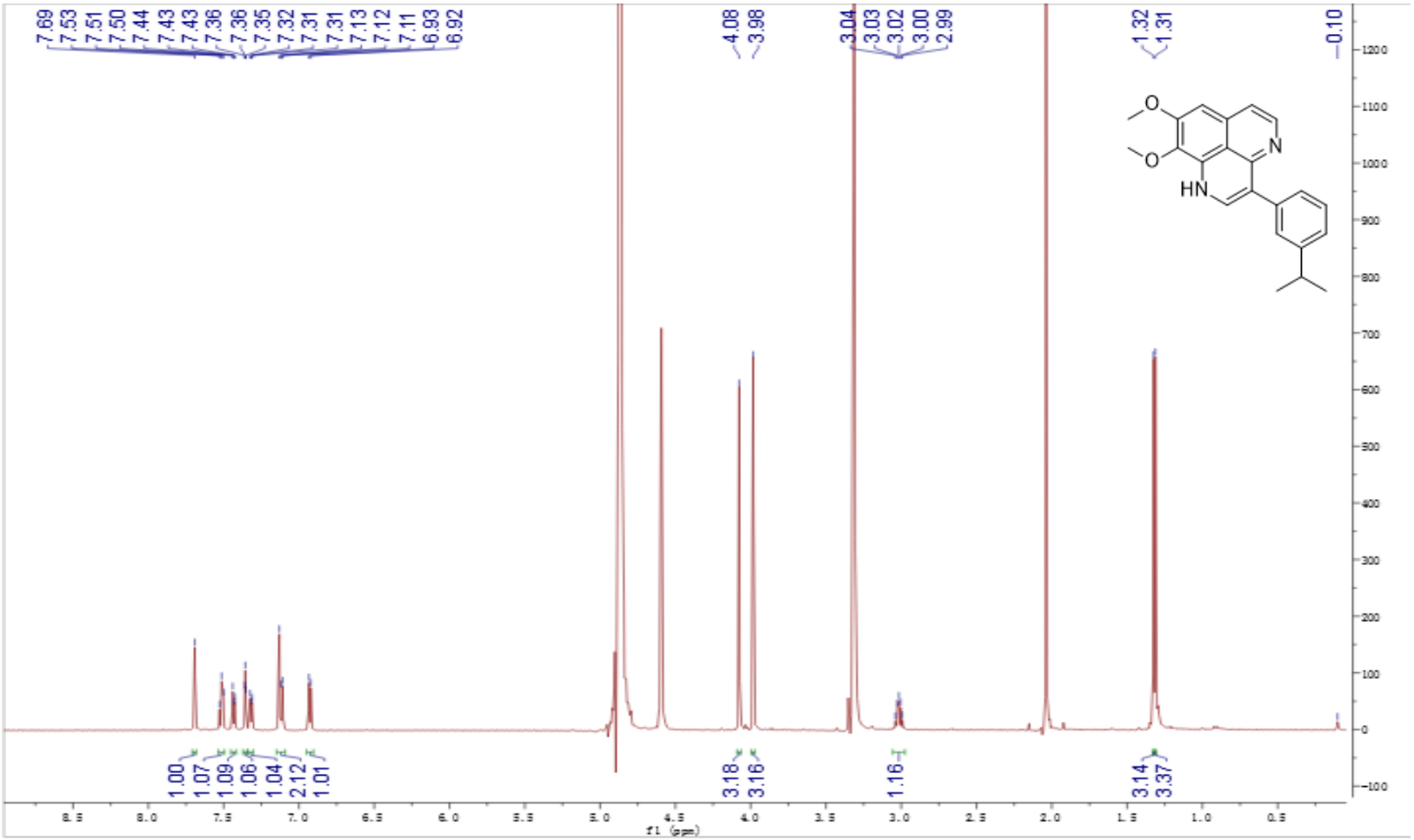


Figure S7. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 3c

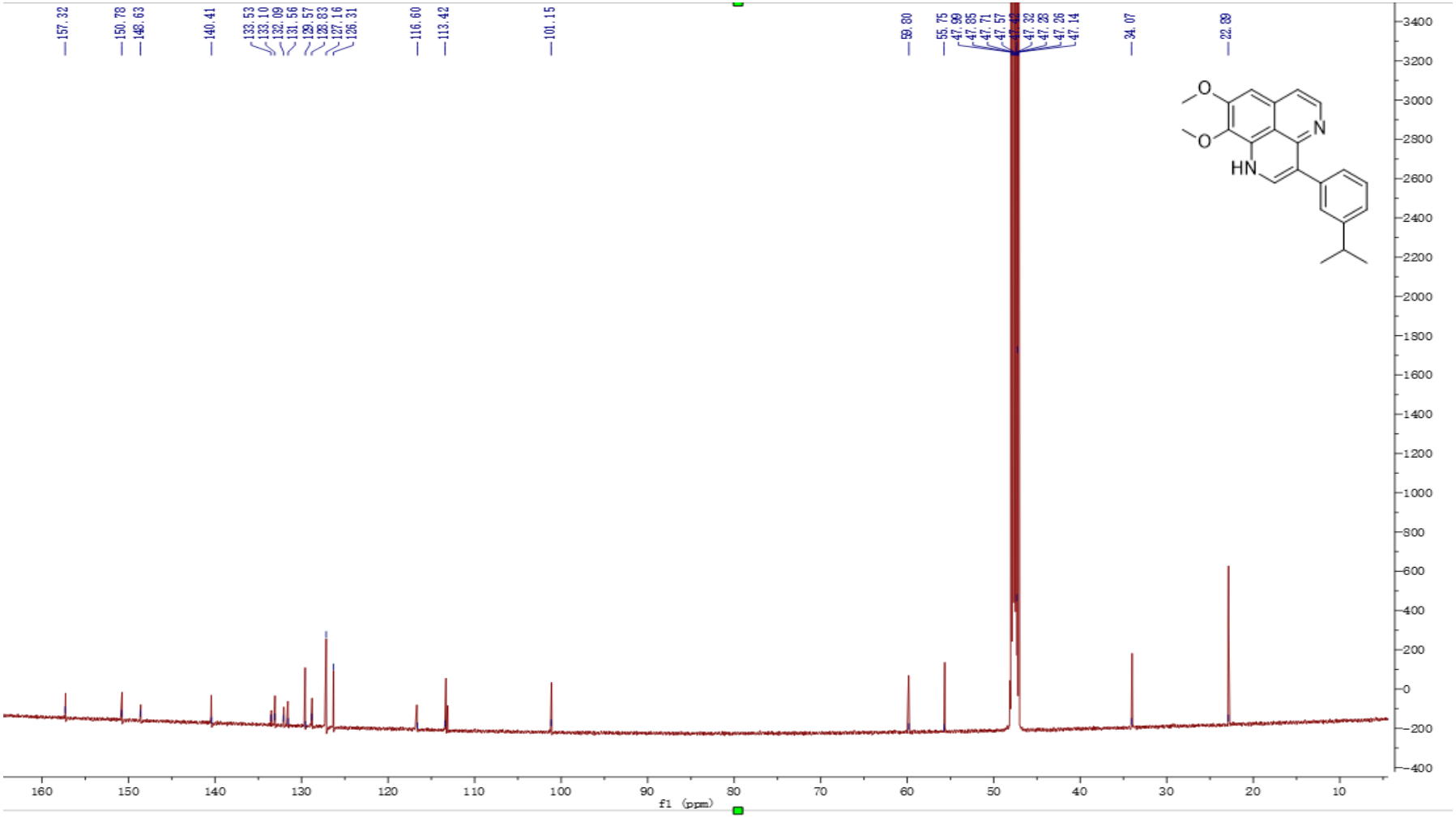


Figure S8. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 3c

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
601 formula(e) evaluated with 5 results within limits (up to 50 closest results for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
347.1772	347.1760	1.2	3.5	12.5	C22 H23 N2 O2	2841.7	0.001	99.92	22	23	2	2
	347.1800	-2.8	-8.1	16.5	C27 H23	2849.1	7.379	0.06	27	23		
	347.1791	-1.9	-5.5	4.5	C11 H23 N8 O5	2851.2	9.541	0.01	11	23	8	5
	347.1778	-0.6	-1.7	-0.5	C10 H27 N4 O9	2851.5	9.842	0.01	10	27	4	9
	347.1751	2.1	6.0	0.5	C6 H23 N10 O7	2854.7	13.018	0.00	6	23	10	7

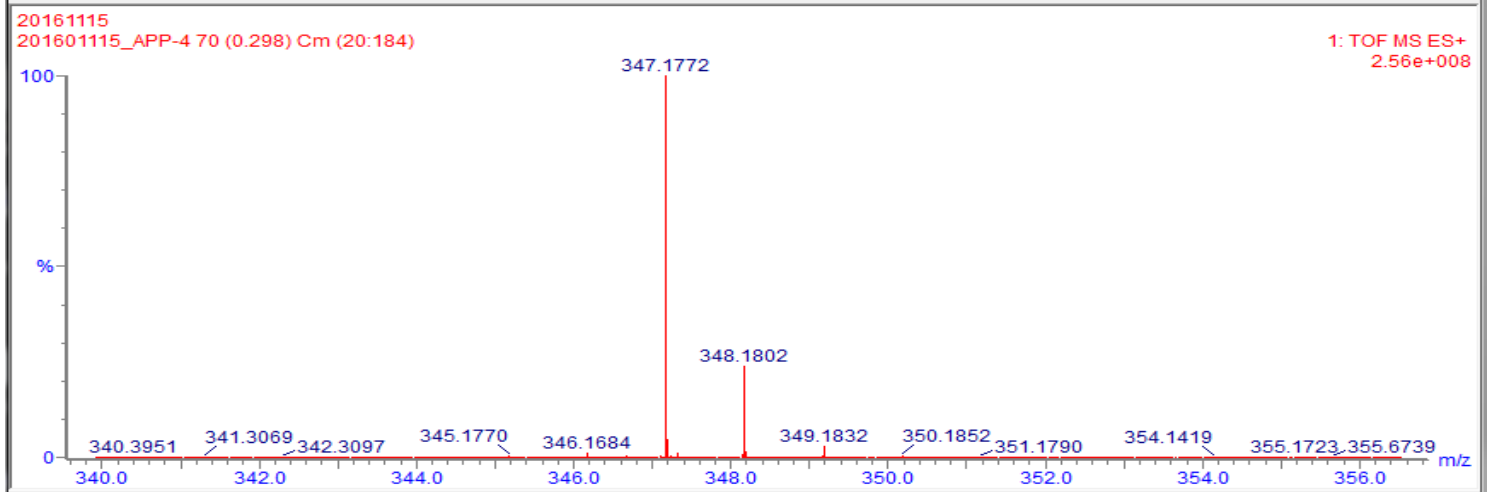


Figure S9. HRESIMS of compound 3c

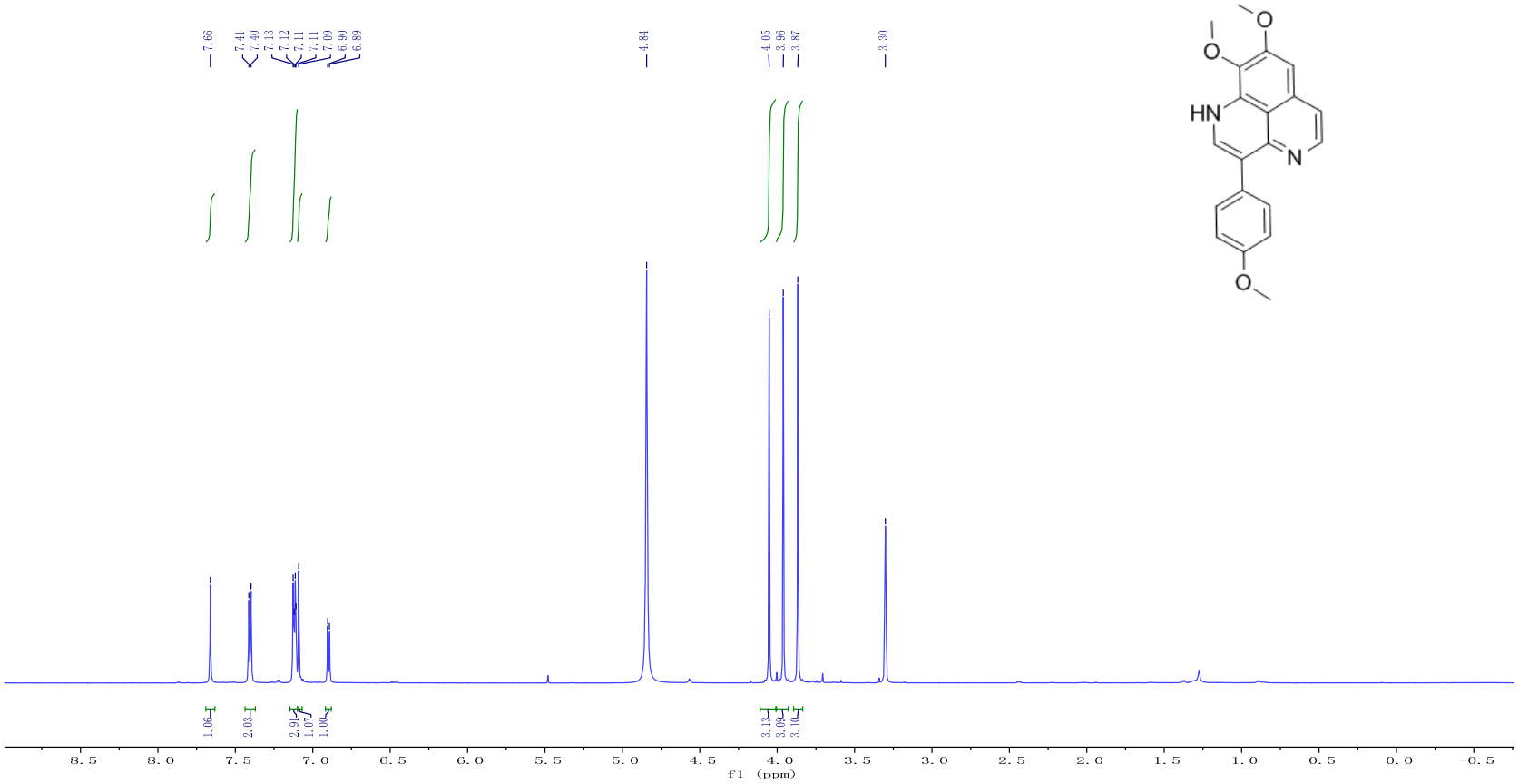


Figure S10. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 3d

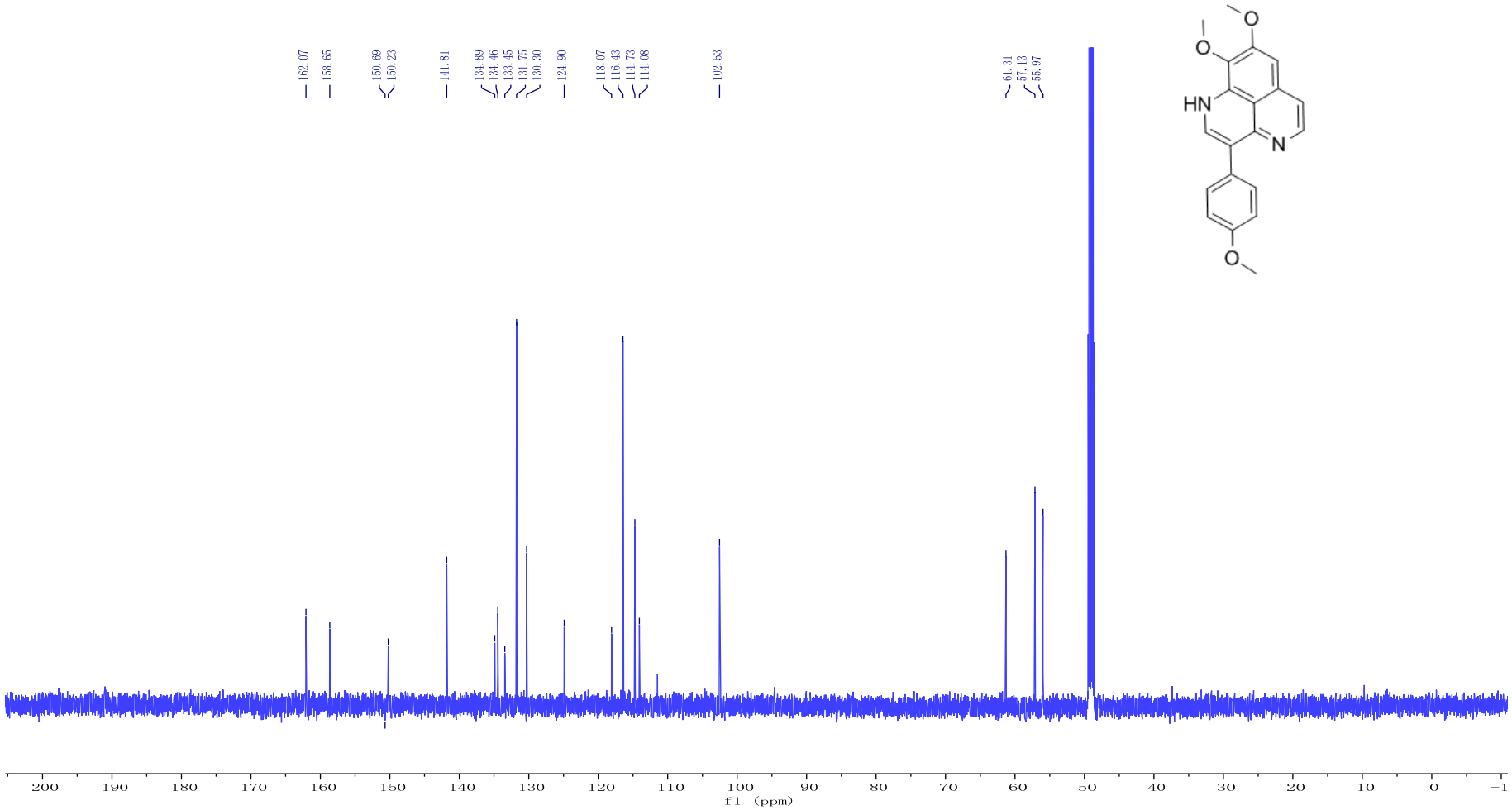


Figure S11. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 3d

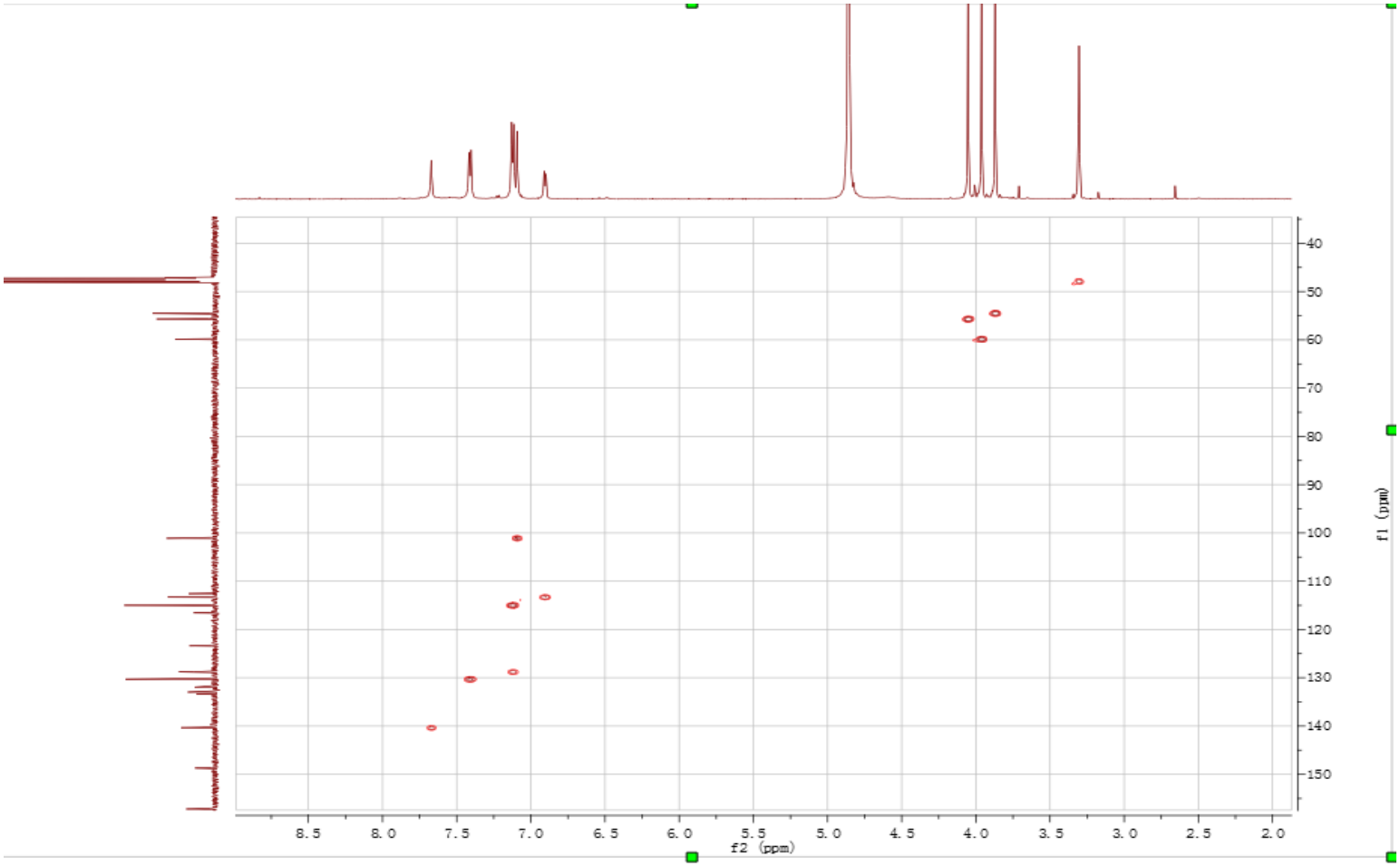


Figure S12. HSQC spectrum of compound 3d

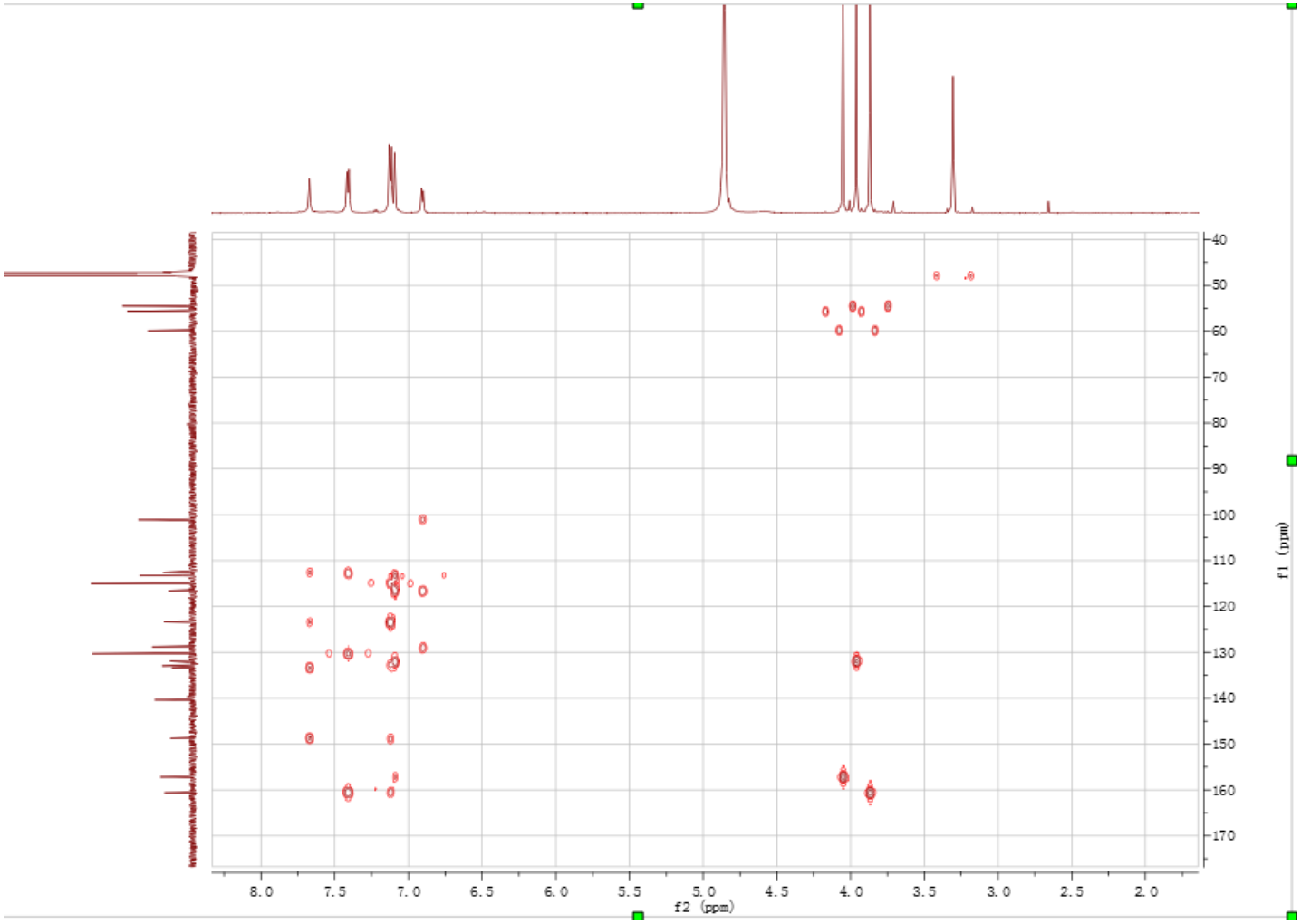


Figure S13. HMBC spectrum of compound 3d

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
319 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
335.1406	335.1436	-3.0	-9.0	16.5	C25 H19 O	230.5	1.511	22.07	25	19		1
	335.1396	1.0	3.0	12.5	C20 H19 N2 O3	230.5	1.571	20.79	20	19	2	3
	335.1369	3.7	11.0	13.5	C16 H15 N8 O	230.6	1.610	20.00	16	15	8	1
	335.1454	-4.8	-14.3	3.5	C13 H23 N2 O8	230.6	1.664	18.94	13	23	2	8
	335.1428	-2.2	-6.6	4.5	C9 H19 N8 O6	230.7	1.704	18.19	9	19	8	6

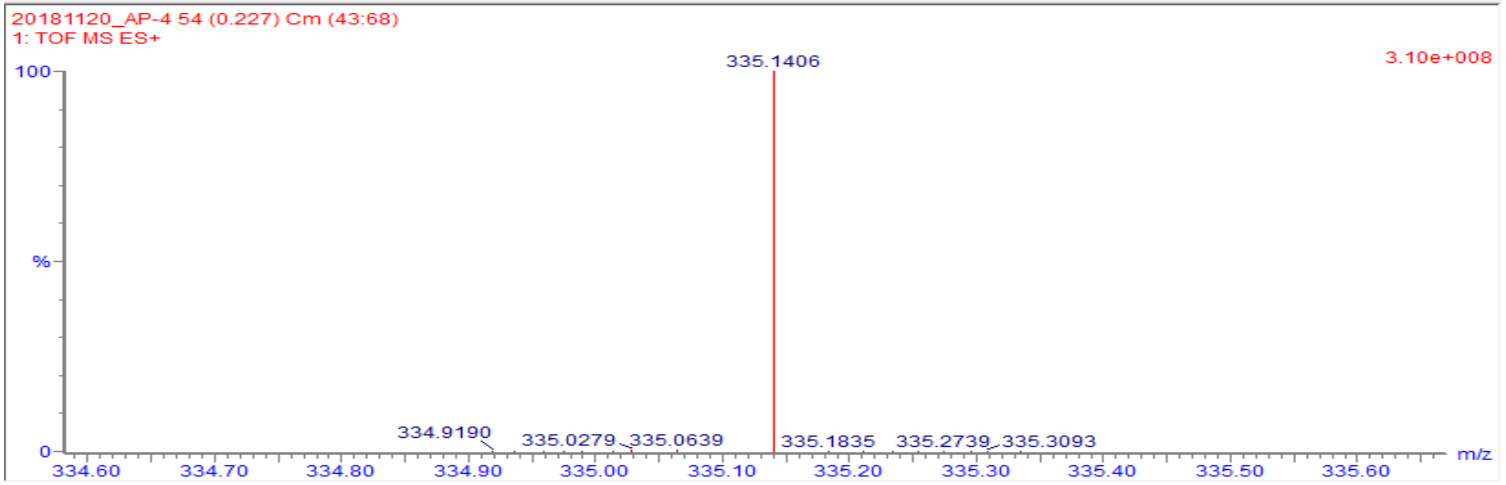


Figure S14. HRESIMS of compound 3d

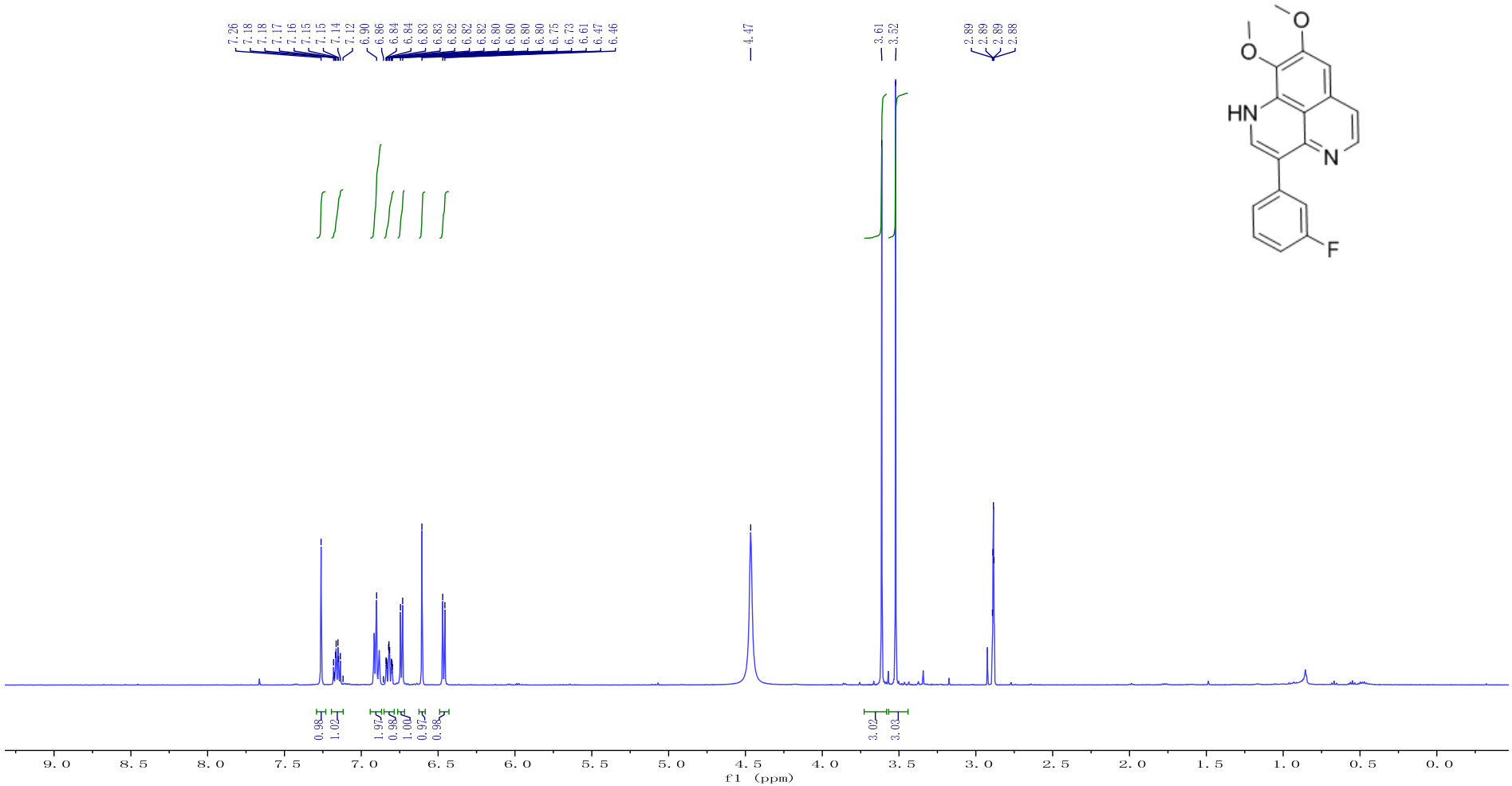


Figure S15. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 3e

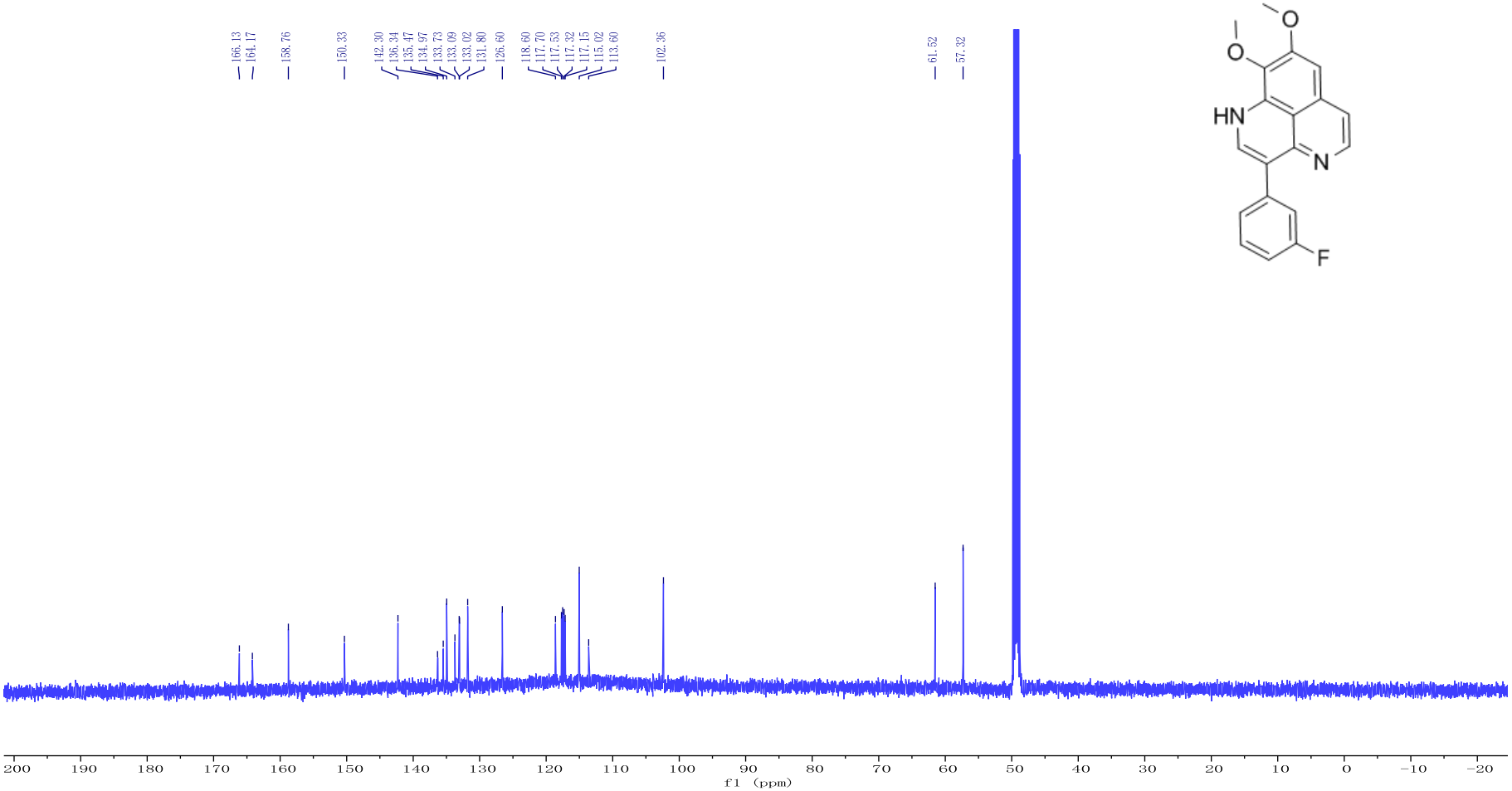


Figure S16. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 3e

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
274 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	RA	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O	F
323.1197	100.00	323.1196	0.1	0.3	12.5	C19 H16 N2 O2 F	2124.4	0.064	93.77	19	16	2	2	1
		323.1236	-3.9	-12.1	16.5	C24 H16 F	2127.5	3.180	4.16	24	16			1
		323.1169	2.8	8.7	13.5	C15 H12 N8 F	2128.5	4.103	1.65	15	12	8		1
		323.1156	4.1	12.7	8.5	C14 H16 N4 O4 F	2129.9	5.524	0.40	14	16	4	4	1
		323.1228	-3.1	-9.6	4.5	C8 H16 N8 O5 F	2133.1	8.690	0.02	8	16	8	5	1

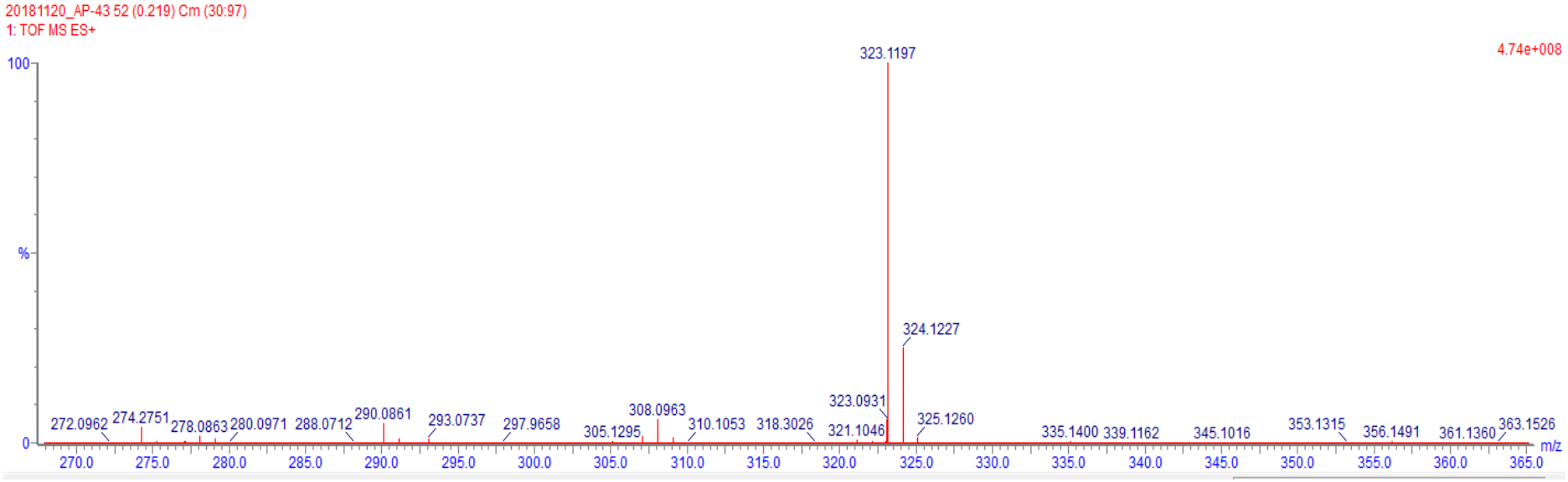


Figure S17. HRESIMS of compound 3e

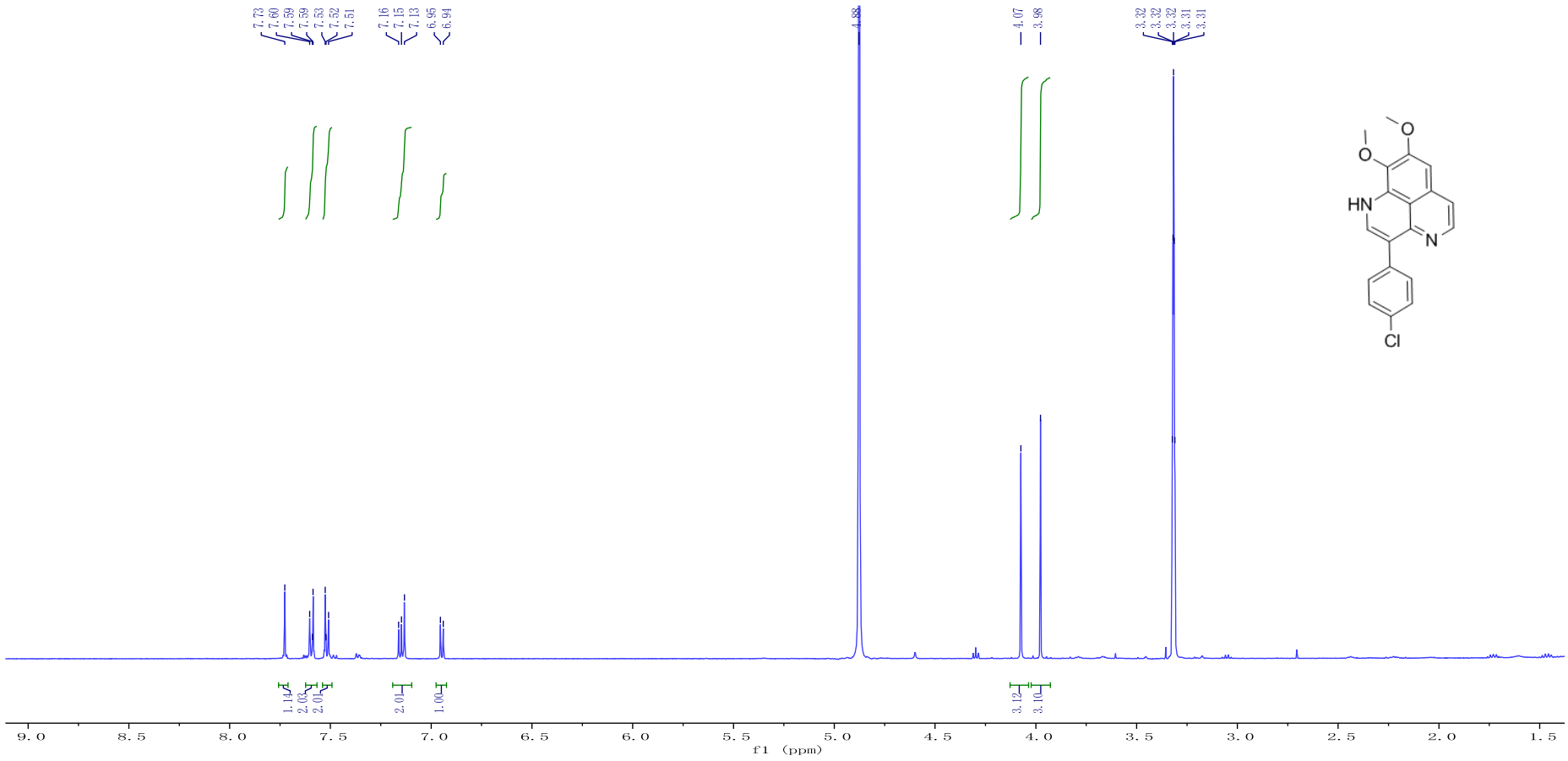


Figure S18. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 3f

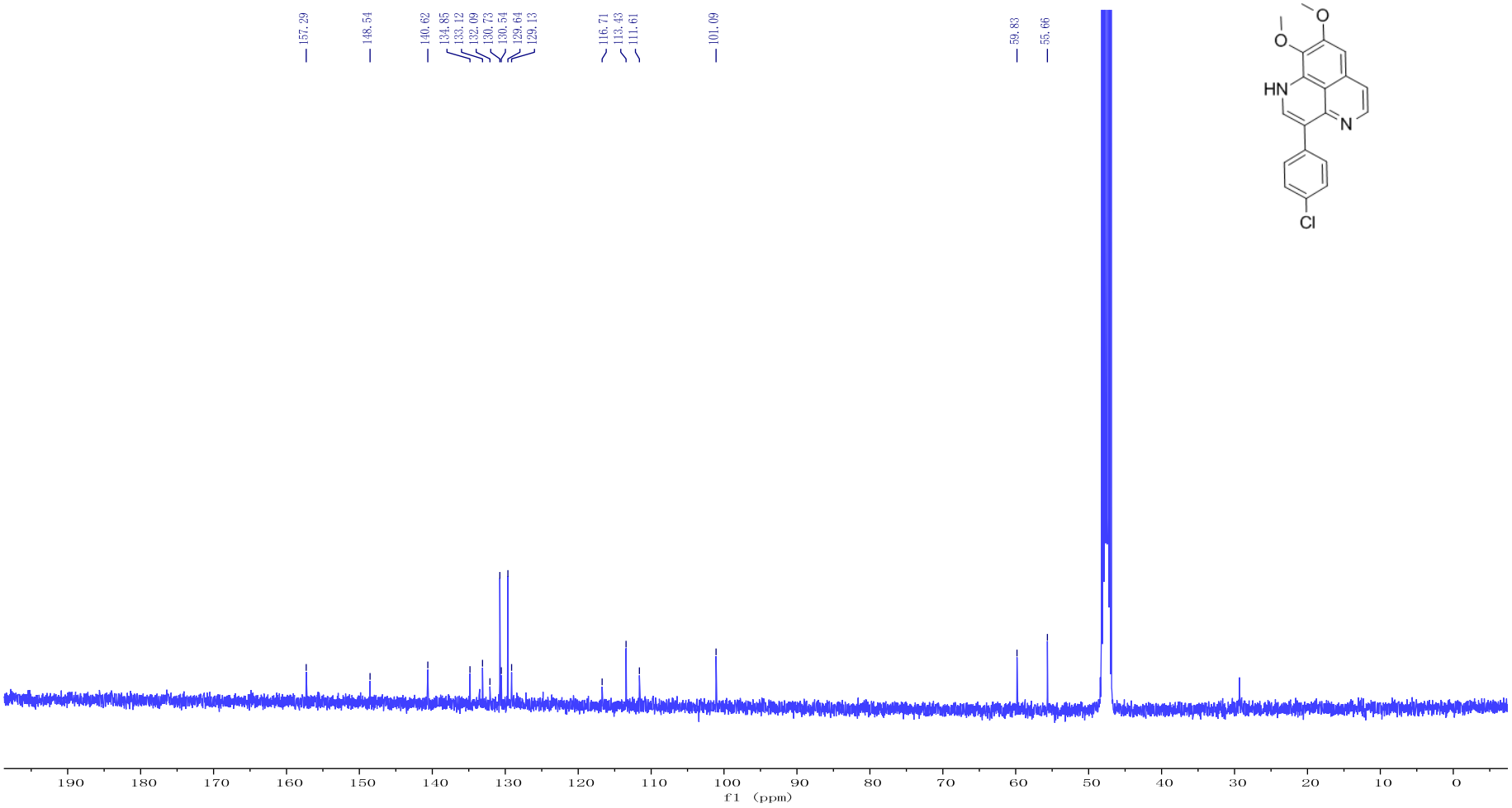


Figure S19. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 3f

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

274 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O	Cl
339.0899	339.0900	-0.1	-0.3	12.5	C19 H16 N2 O2 Cl	1825.2	0.277	75.80	19	16	2	2	1
	339.0860	3.9	11.5	8.5	C14 H16 N4 O4 Cl	1827.1	2.173	11.38	14	16	4	4	1
	339.0873	2.6	7.7	13.5	C15 H12 N8 Cl	1827.5	2.525	8.00	15	12	8		1
	339.0932	-3.3	-9.7	4.5	C8 H16 N8 O5 Cl	1828.4	3.451	3.17	8	16	8	5	1
	339.0941	-4.2	-12.4	16.5	C24 H16 Cl	1829.1	4.106	1.65	24	16			1

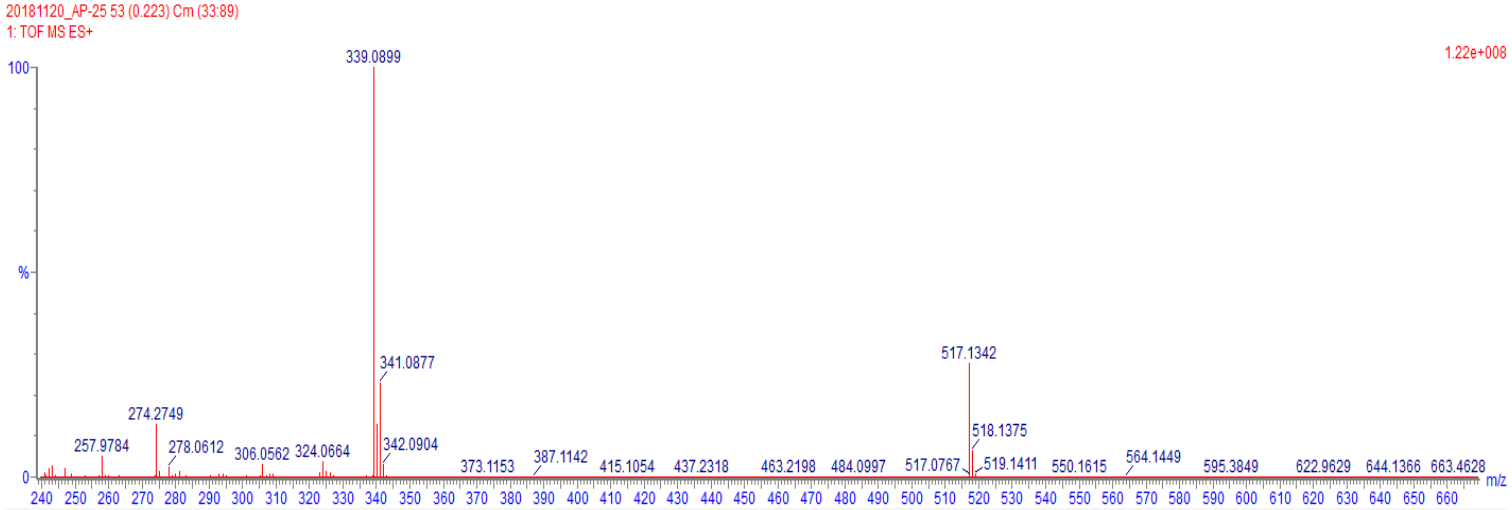


Figure S20. HRESIMS of 3f

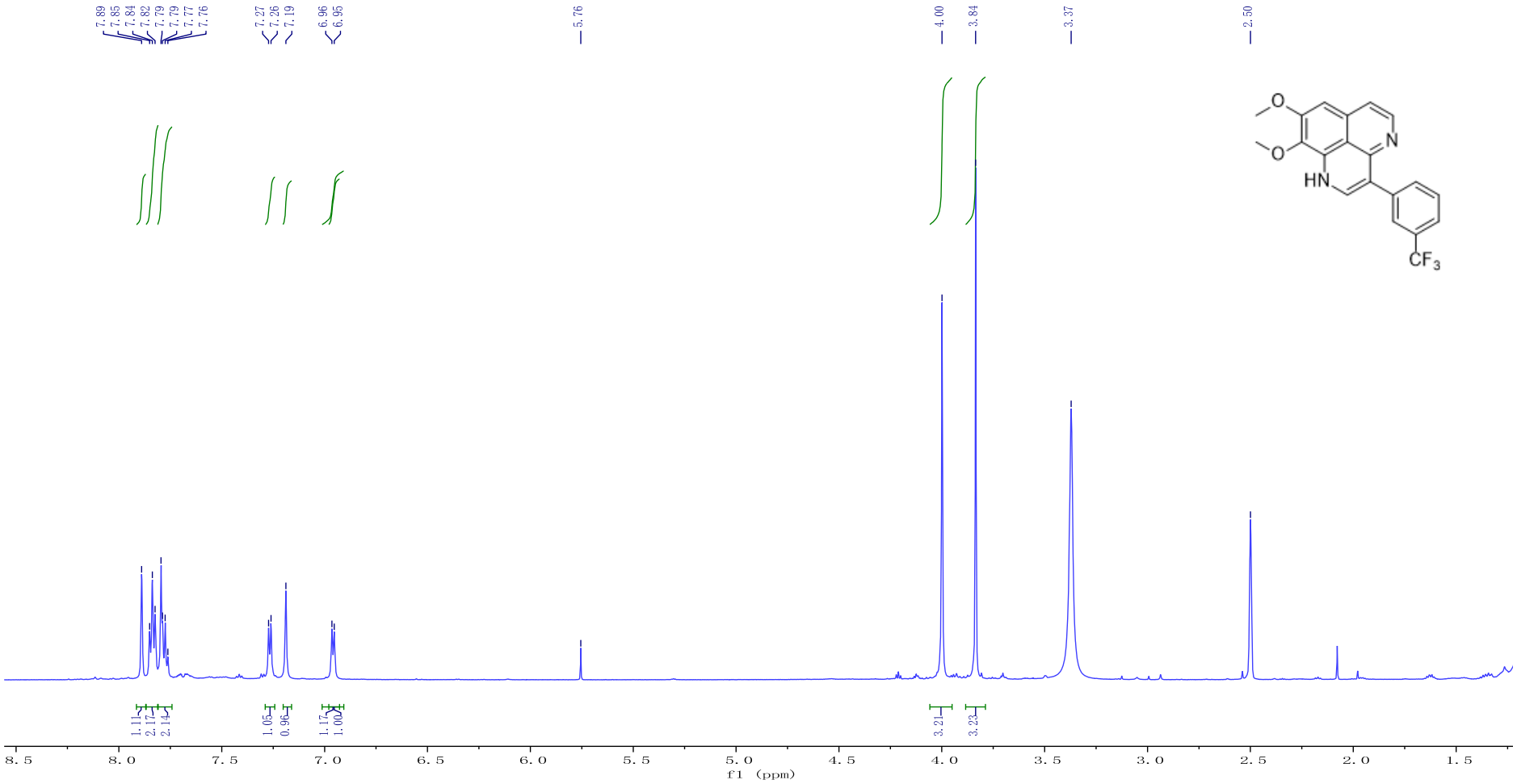


Figure S21. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of compound 3g

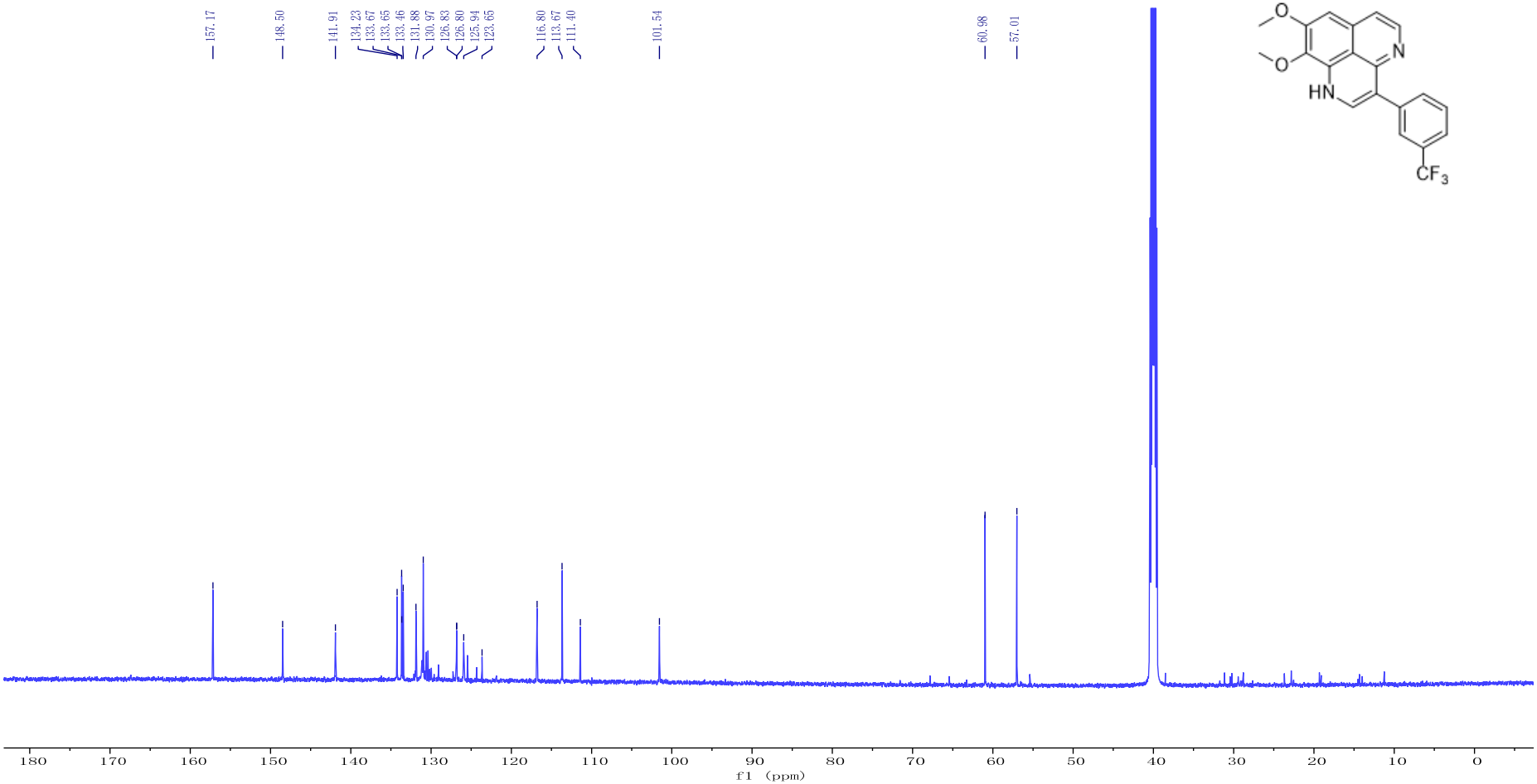


Figure S22. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of compound 3g

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
275 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	RA	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O	F
373.1174	100.00	373.1164	1.0	2.7	12.5	C20 H16 N2 O2 F3	1976.7	0.384	68.13	20	16	2	2	3
		373.1204	-3.0	-8.0	16.5	C25 H16 F3	1977.5	1.171	31.02	25	16			3
		373.1137	3.7	9.9	13.5	C16 H12 N8 F3	1981.4	5.090	0.62	16	12	8		3
		373.1223	-4.9	-13.1	3.5	C13 H20 N2 O7 F3	1982.7	6.311	0.18	13	20	2	7	3
		373.1196	-2.2	-5.9	4.5	C9 H16 N8 O5 F3	1983.9	7.585	0.05	9	16	8	5	3

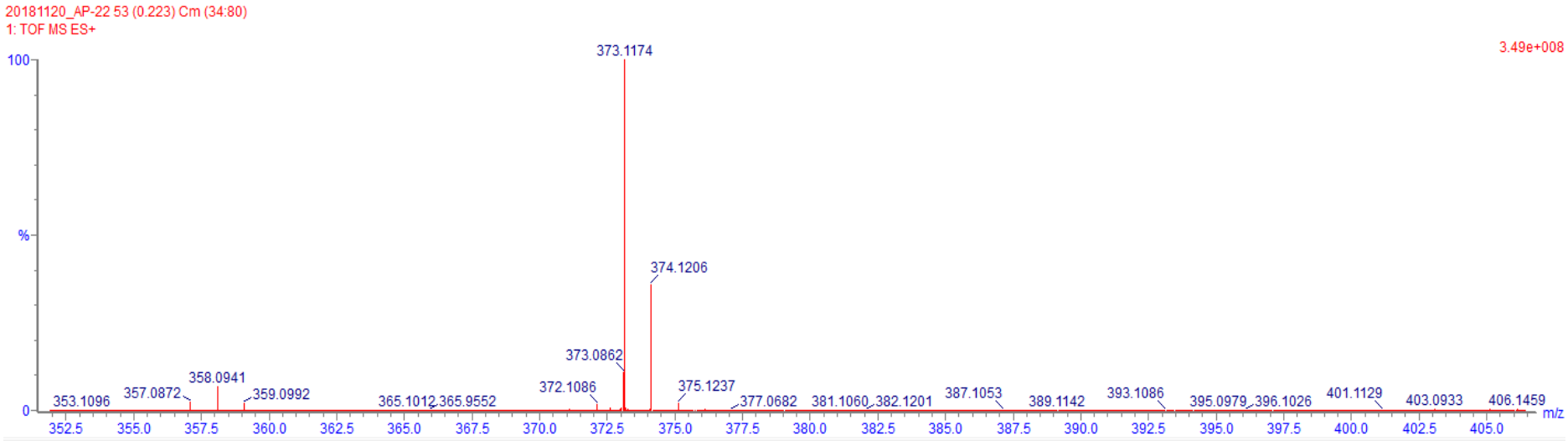


Figure S23. HRESIMS of compound 3g

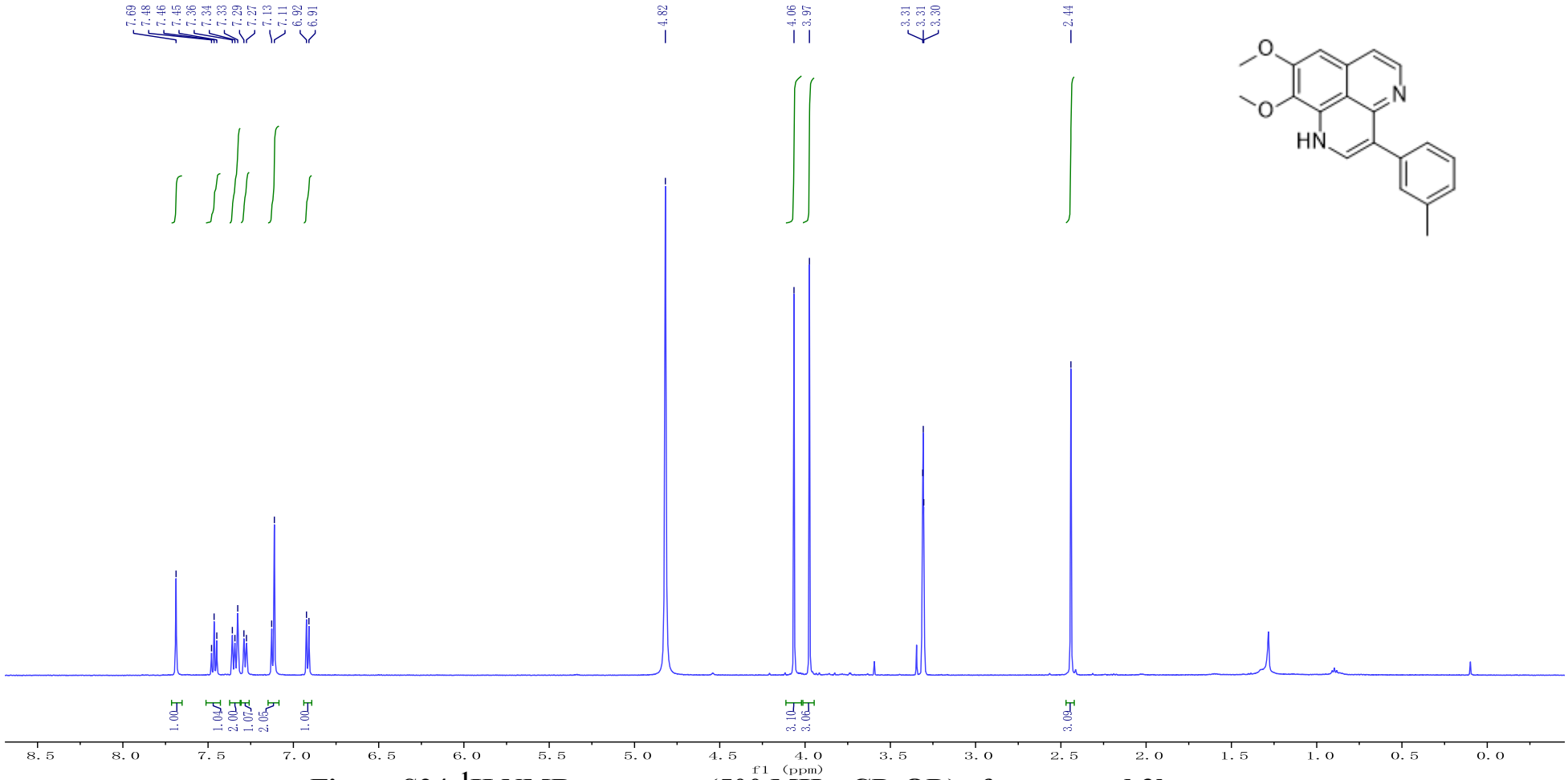


Figure S24. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 3h

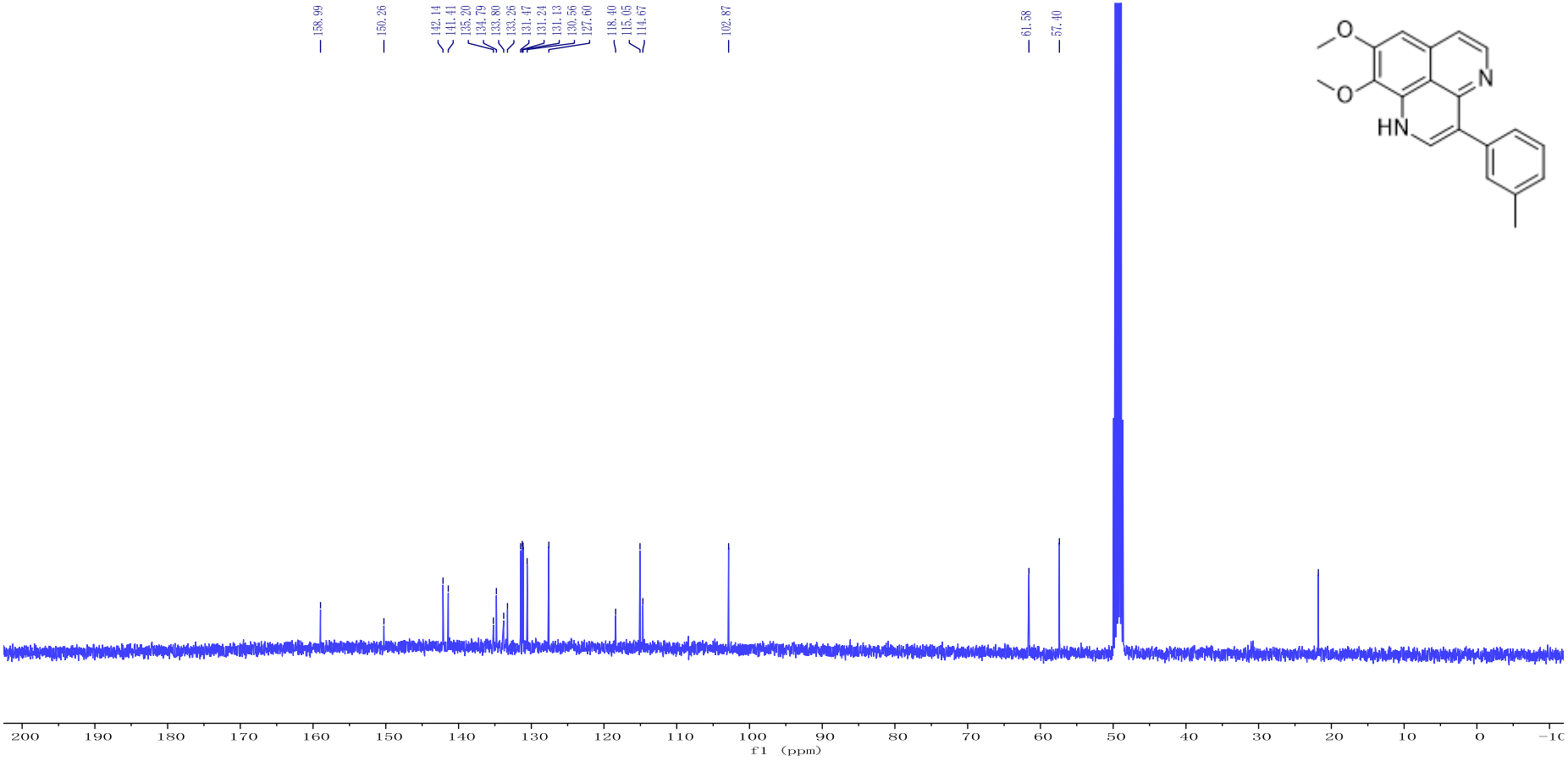


Figure S25. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 3h

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
302 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
319.1450	319.1487	-3.7	-11.6	16.5	C25 H19	240.4	1.517	21.94	25	19		
	319.1447	0.3	0.9	12.5	C20 H19 N2 O2	240.4	1.577	20.67	20	19	2	2
	319.1420	3.0	9.4	13.5	C16 H15 N8	240.5	1.616	19.88	16	15	8	
	319.1406	4.4	13.8	8.5	C15 H19 N4 O4	240.5	1.638	19.43	15	19	4	4
	319.1478	-2.8	-8.8	4.5	C9 H19 N8 O5	240.6	1.710	18.08	9	19	8	5

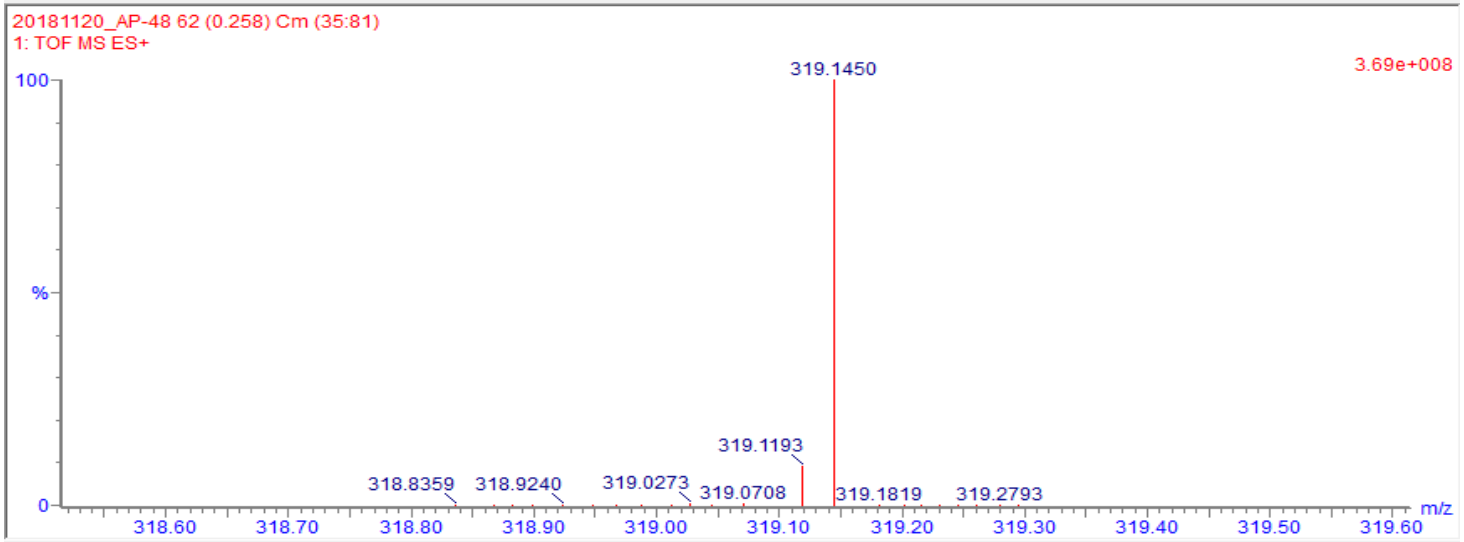


Figure S26. HRESIMS of compound 3h

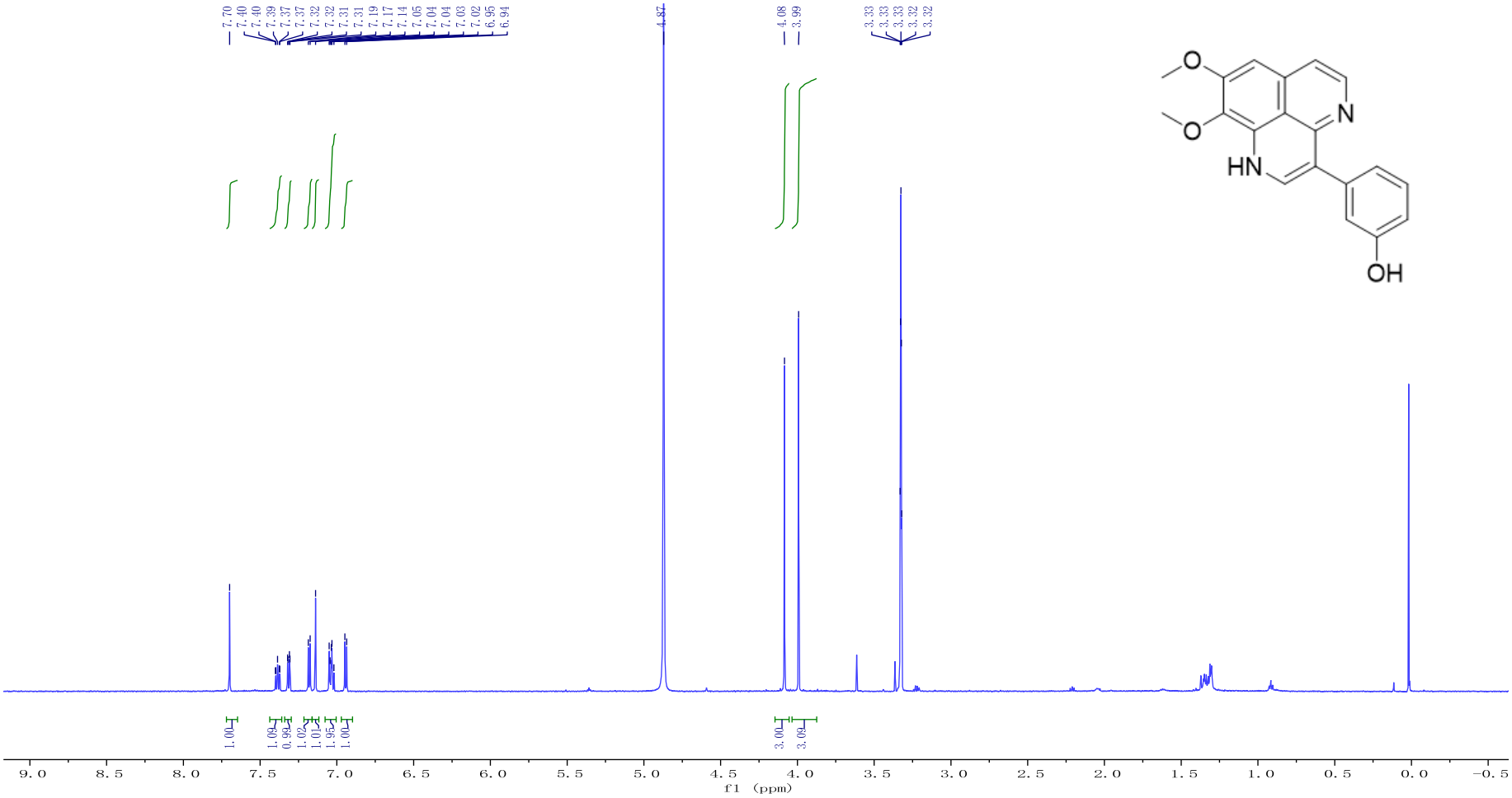


Figure S27. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 3i

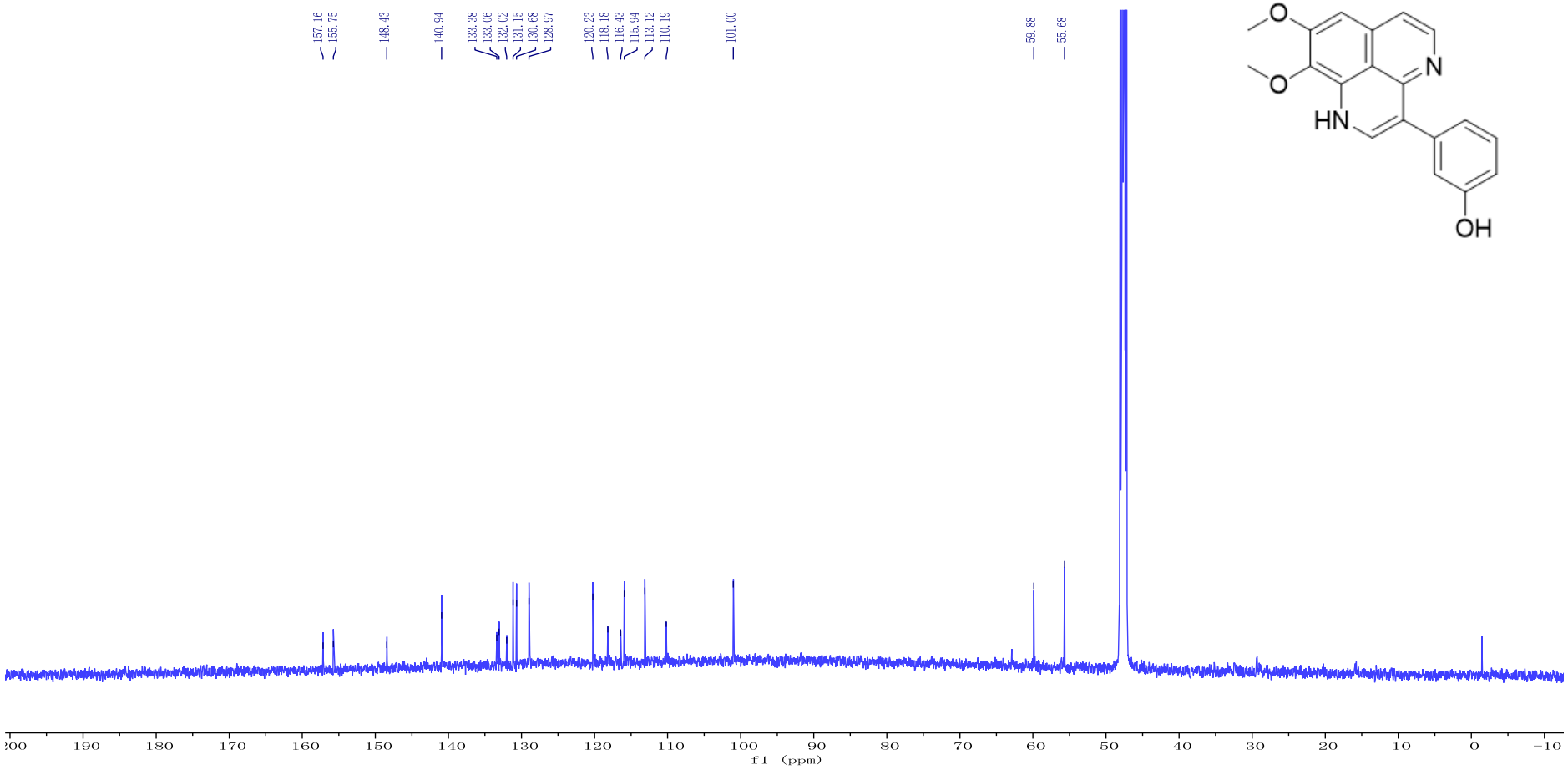


Figure S28. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 3i

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
304 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
321.1241	321.1271	-3.0	-9.3	4.5	C8 H17 N8 O6	1728.7	0.340	71.16	8	17	8	6
	321.1199	4.2	13.1	8.5	C14 H17 N4 O5	1730.5	2.059	12.76	14	17	4	5
	321.1212	2.9	9.0	13.5	C15 H13 N8 O	1730.8	2.408	9.00	15	13	8	1
	321.1239	0.2	0.6	12.5	C19 H17 N2 O3	1731.5	3.077	4.61	19	17	2	3
	321.1279	-3.8	-11.8	16.5	C24 H17 O	1732.1	3.703	2.47	24	17		1

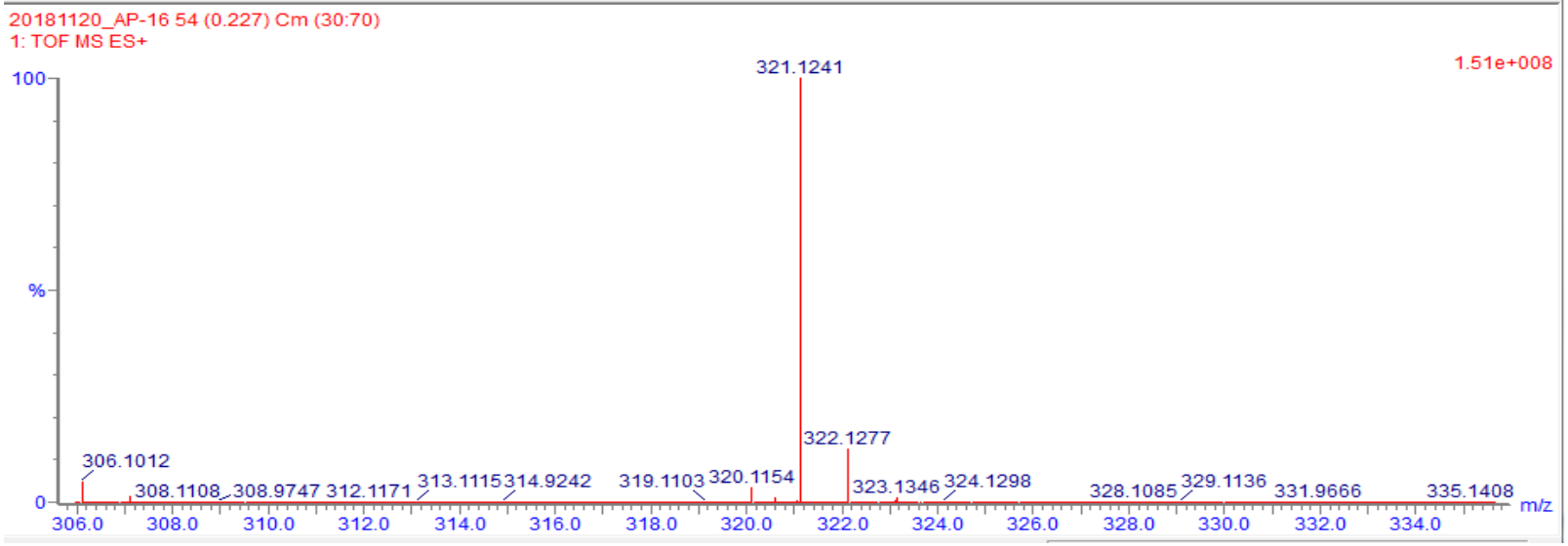


Figure S29. HRESIMS of compound 3i

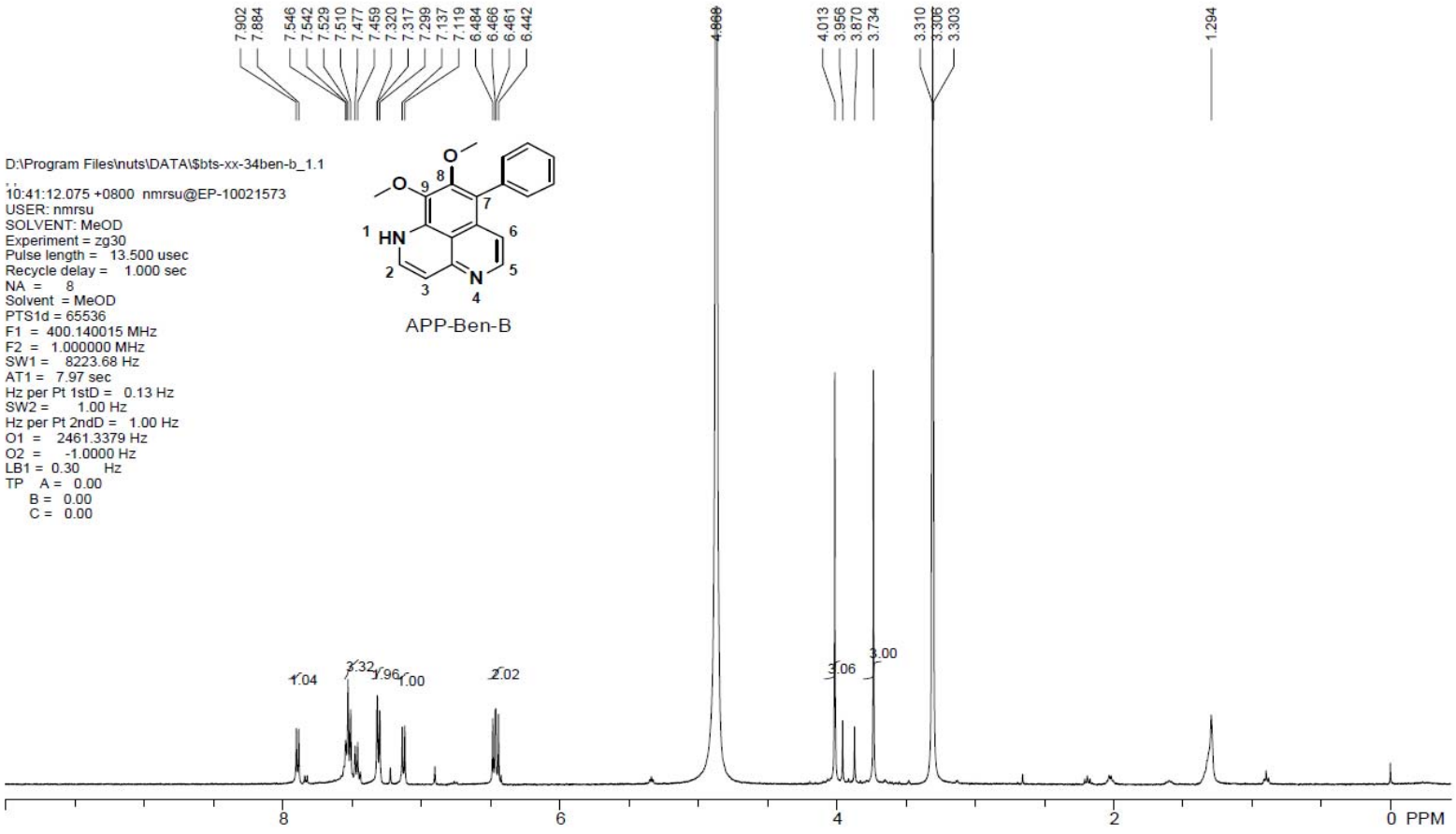


Figure S30. ^{1}H NMR spectrum (400 MHz, CD_3OD) of compound 4a

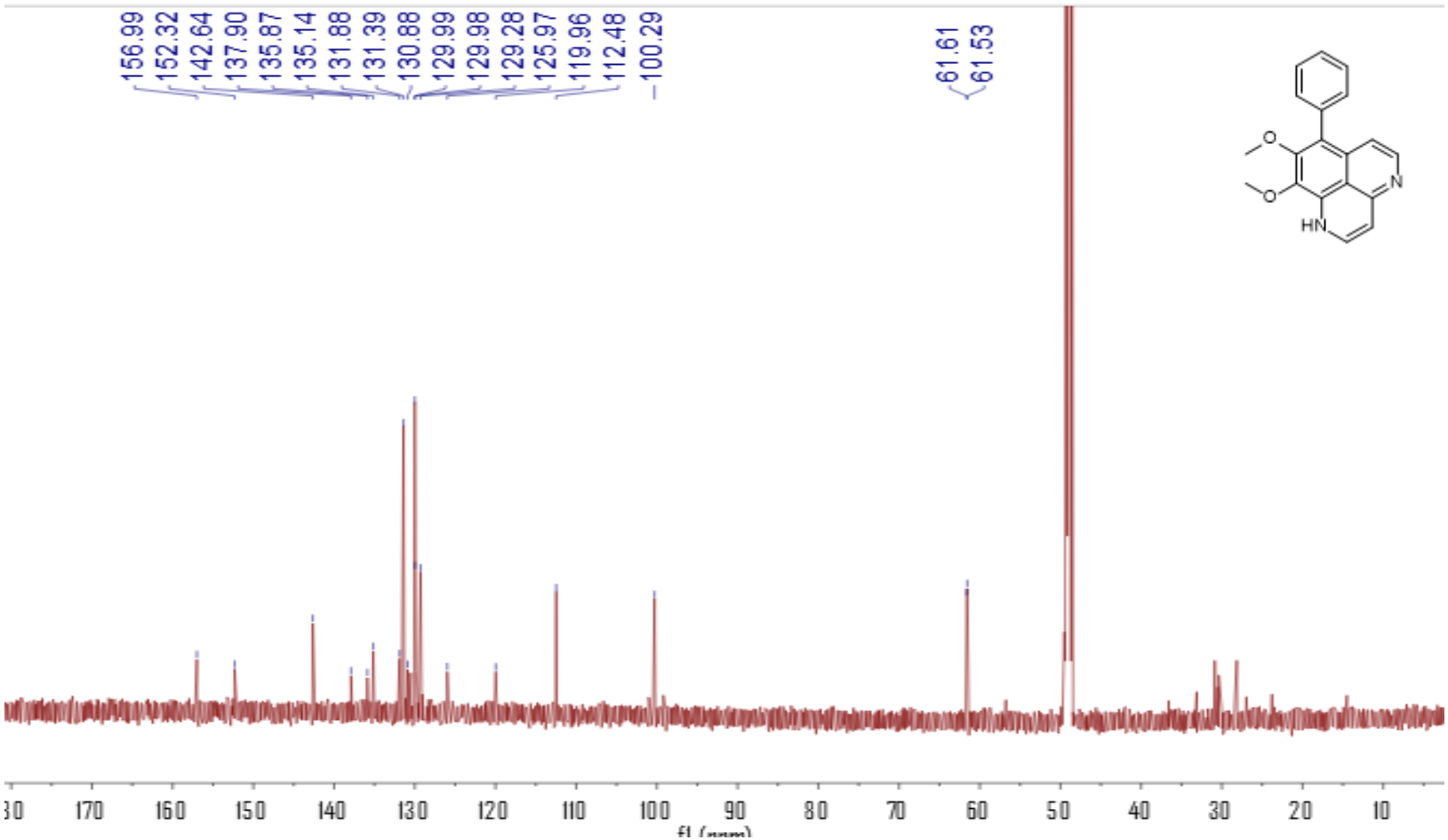


Figure S31. ^{13}C NMR spectrum (100 MHz, CD_3OD)of compound 4a

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
122 formula(e) evaluated with 2 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
305.1296	305.1290	0.6	2.0	12.5	C19 H17 N2 O2	413.4	0.077	92.62	19	17	2	2
	305.1330	-3.4	-11.1	16.5	C24 H17	416.0	2.606	7.38	24	17		

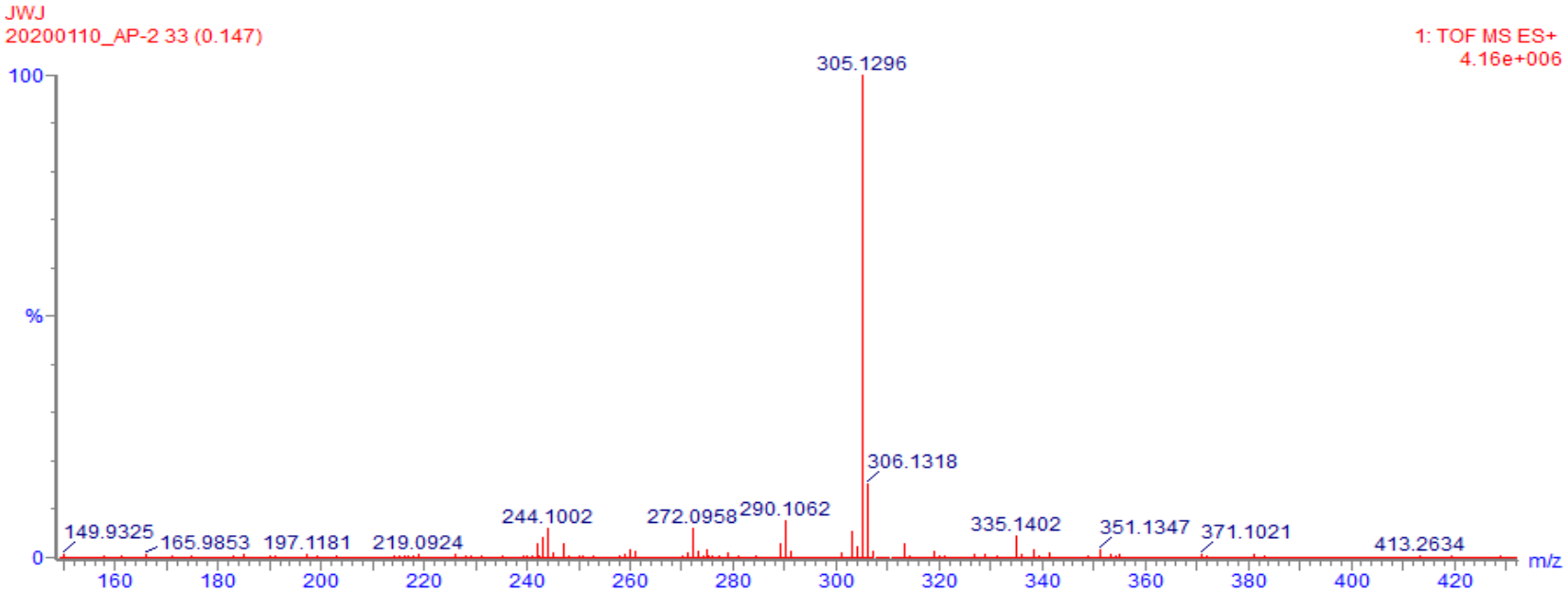


Figure S32. HRESIMS of compound 4a

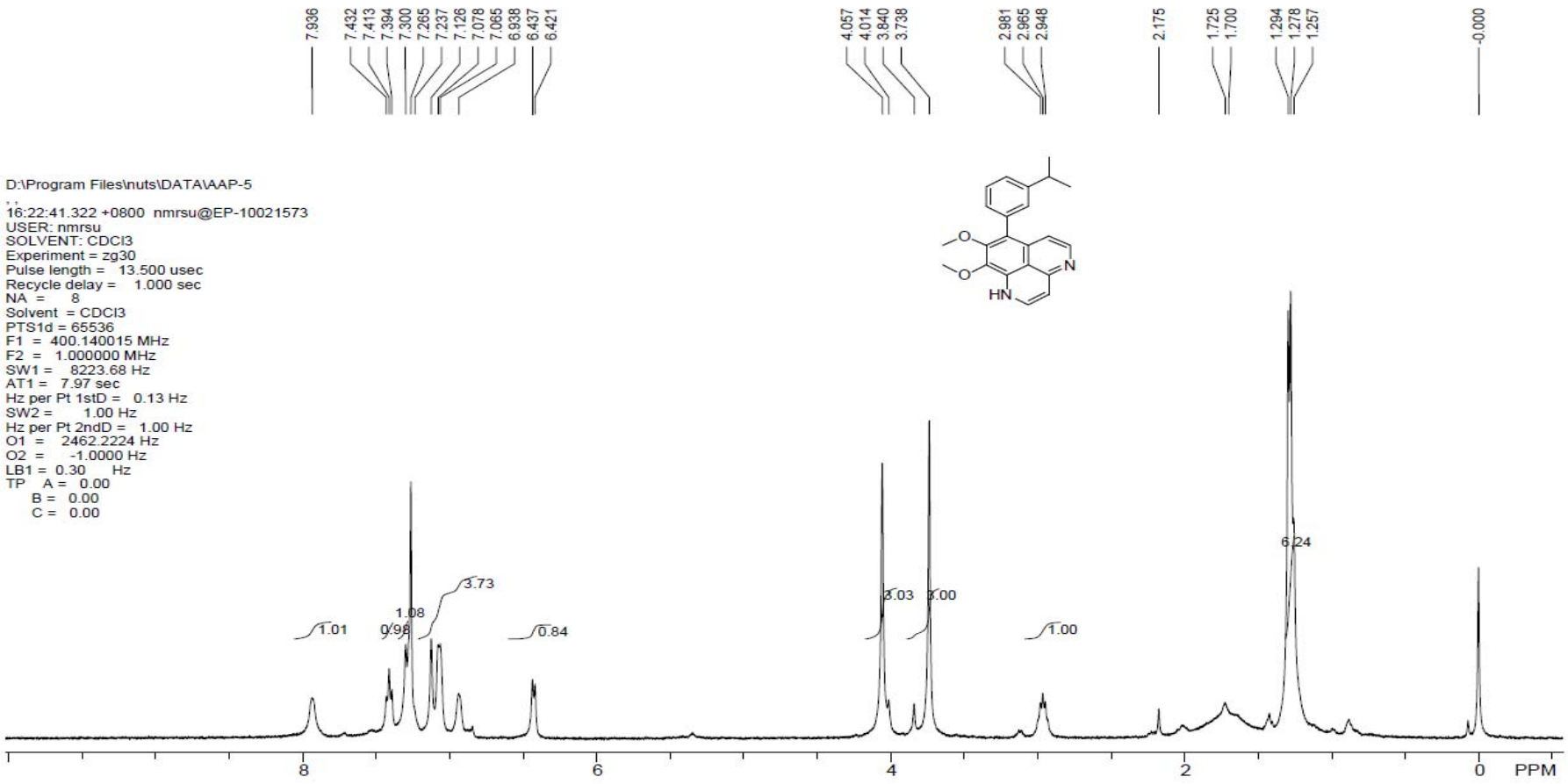


Figure S33. ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of compound 4b

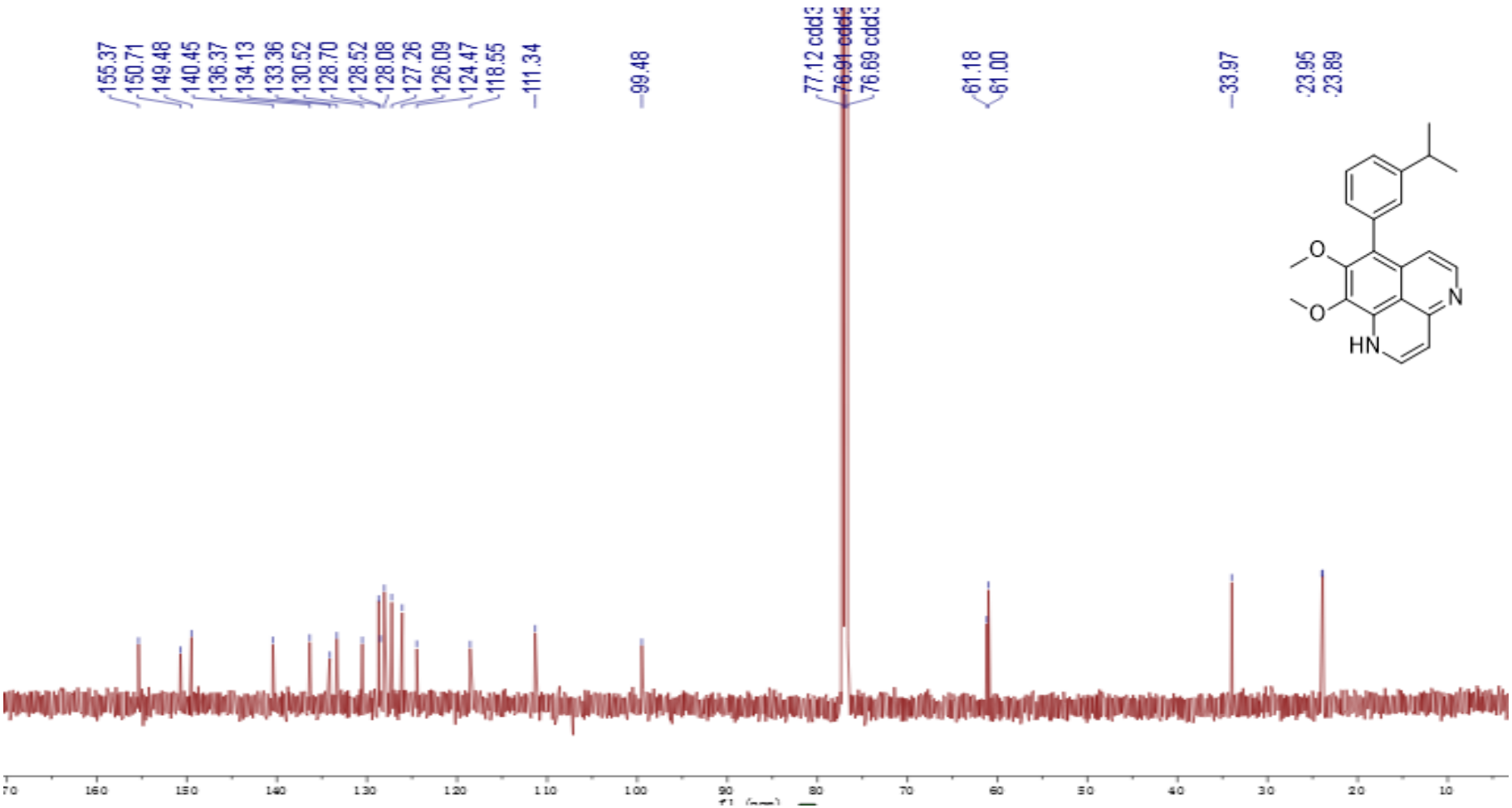


Figure S34. ^{13}C NMR spectrum (100 MHz, $CDCl_3$) of compound 4b

gle Mass Analysis
rance = 10.0 PPM / DBE: min = -1.5, max = 50.0
nent prediction: Off
ber of isotope peaks used for i-FIT = 3
oisotopic Mass, Even Electron Ions
formula(e) evaluated with 5 results within limits (up to 50 closest results for each mass)
nents Used:

	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
753	347.1760	-0.7	-2.0	12.5	C22 H23 N2 O2	2893.3	0.008	99.23	22	23	2	2
	347.1733	2.0	5.8	13.5	C18 H19 N8	2898.3	4.936	0.72	18	19	8	
	347.1719	3.4	9.8	8.5	C17 H23 N4 O4	2900.9	7.539	0.05	17	23	4	4
	347.1778	-2.5	-7.2	-0.5	C10 H27 N4 O9	2904.6	11.307	0.00	10	27	4	9
	347.1751	0.2	0.6	0.5	C6 H23 N10 O7	2908.1	14.761	0.00	6	23	10	7

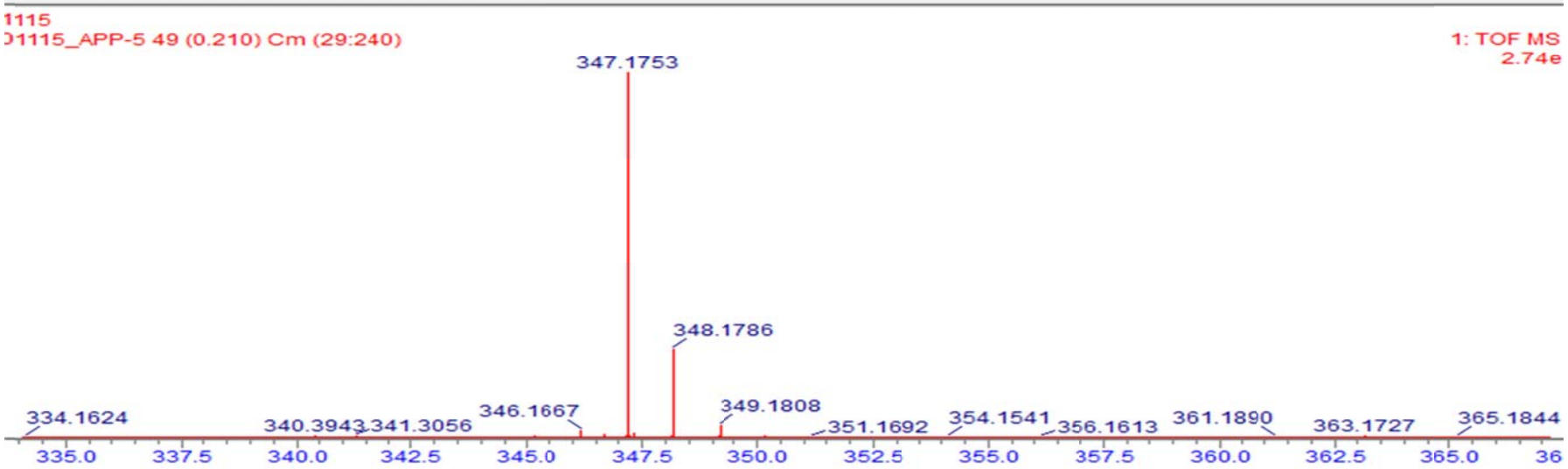


Figure S35. HRESIMS of compound 4b

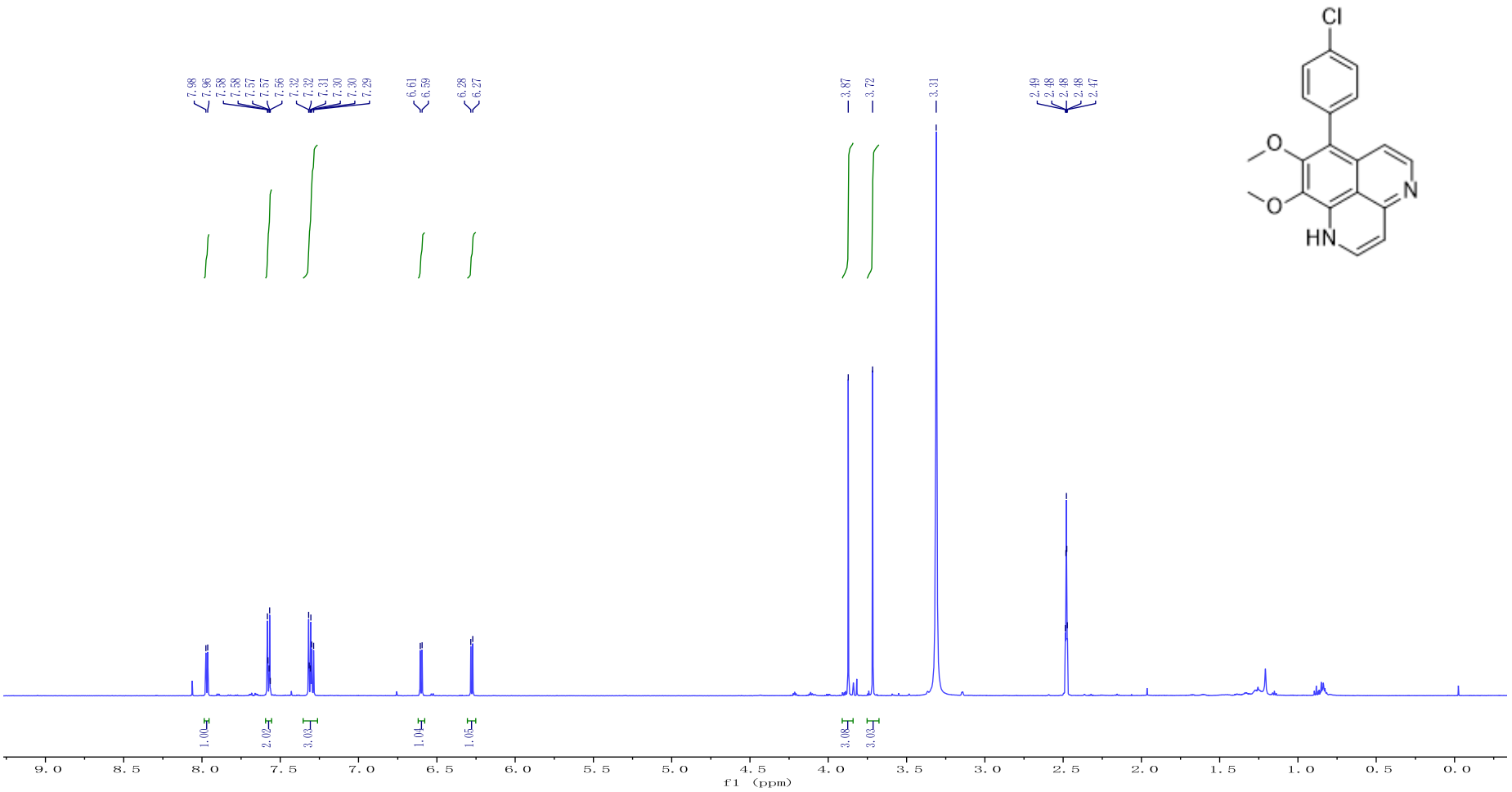


Figure S36. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of compound 4c

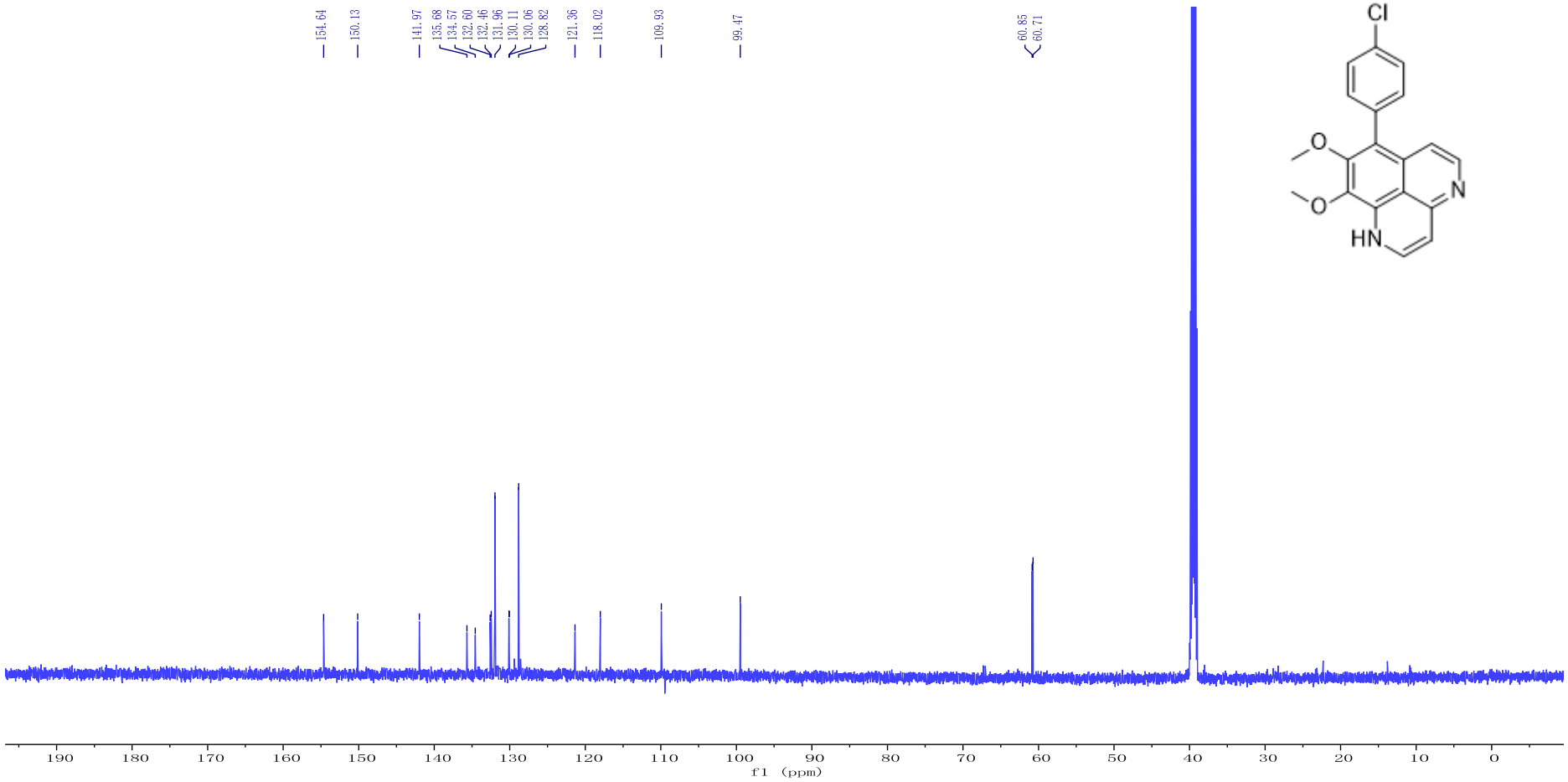


Figure S37. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of compound 4c

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
274 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	RA	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O	Cl
339.0909	100.00	339.0900	0.9	2.7	12.5	C19 H16 N2 O2 Cl	2056.0	0.309	73.45	19	16	2	2	1
		339.0860	4.9	14.5	8.5	C14 H16 N4 O4 Cl	2058.1	2.363	9.42	14	16	4	4	1
		339.0873	3.6	10.6	13.5	C15 H12 N8 Cl	2058.3	2.589	7.51	15	12	8		1
		339.0932	-2.3	-6.8	4.5	C8 H16 N8 O5 Cl	2058.4	2.695	6.75	8	16	8	5	1
		339.0941	-3.2	-9.4	16.5	C24 H16 Cl	2059.3	3.548	2.88	24	16			1

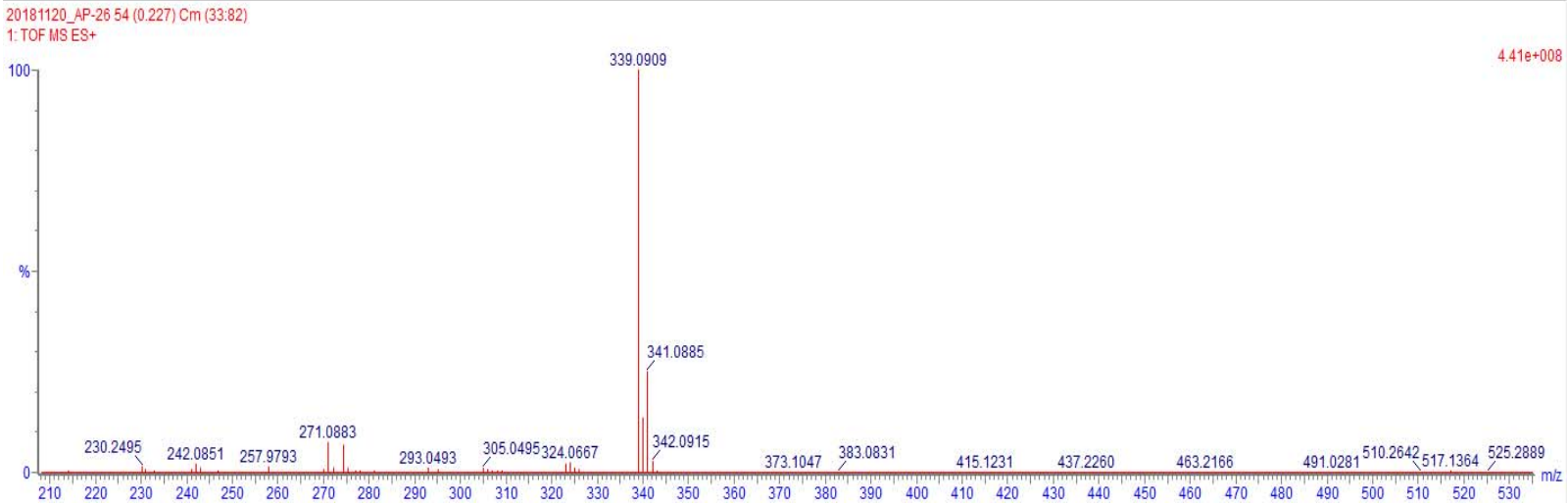


Figure S38. HRESIMS of compound 4c

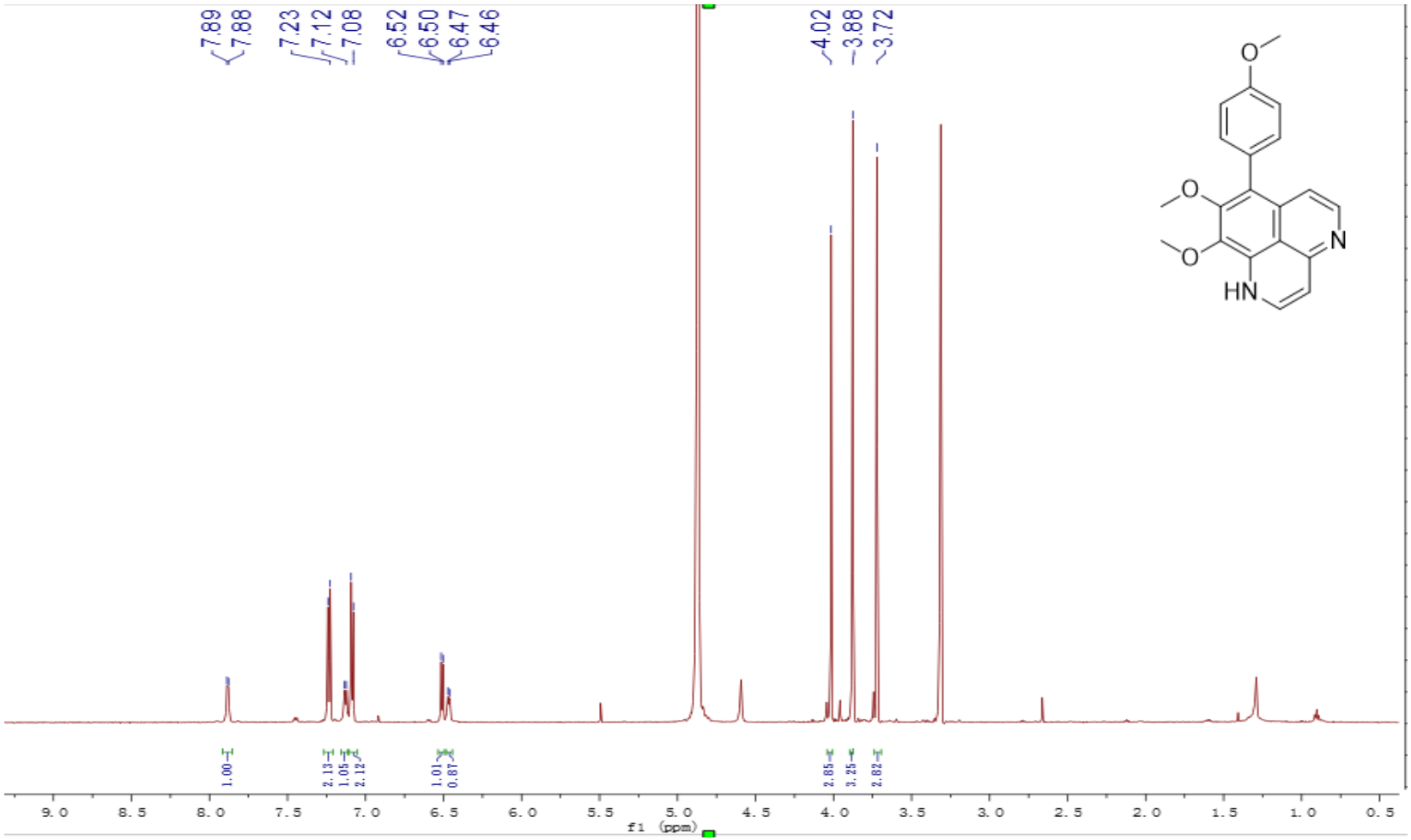


Figure S39. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 4d

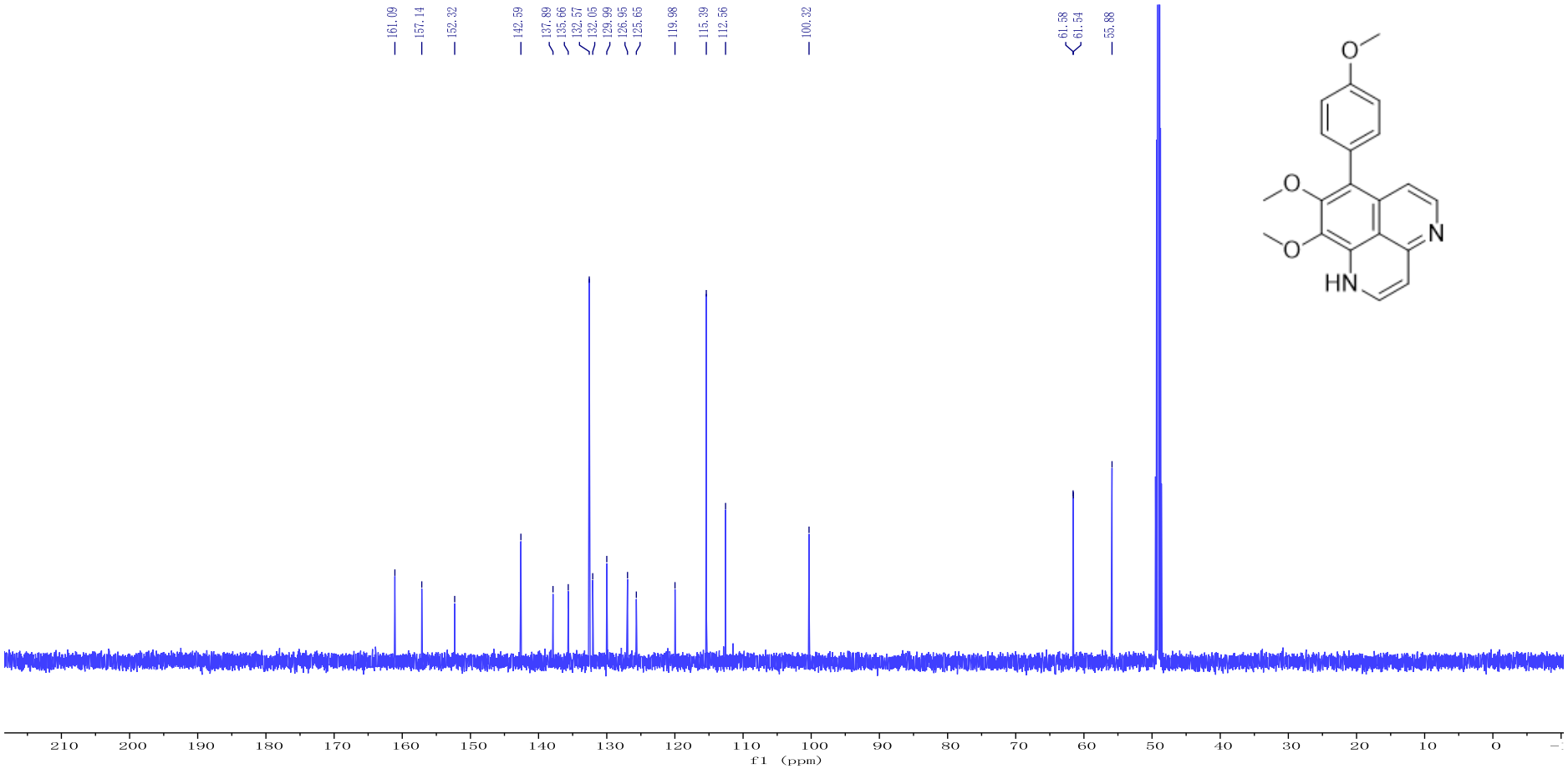


Figure S40. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 4d

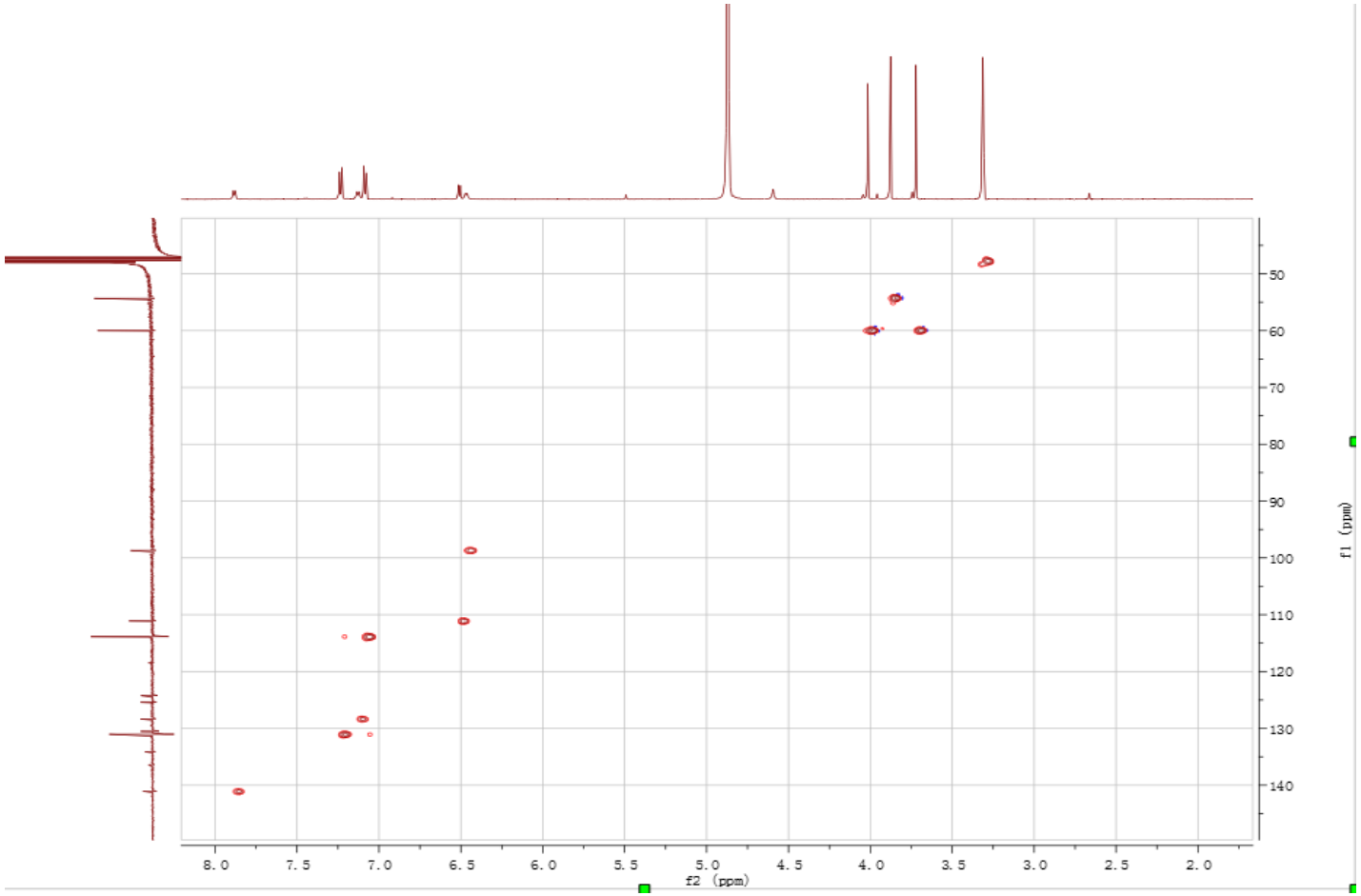


Figure S41. HSQC spectrum of compound 4d

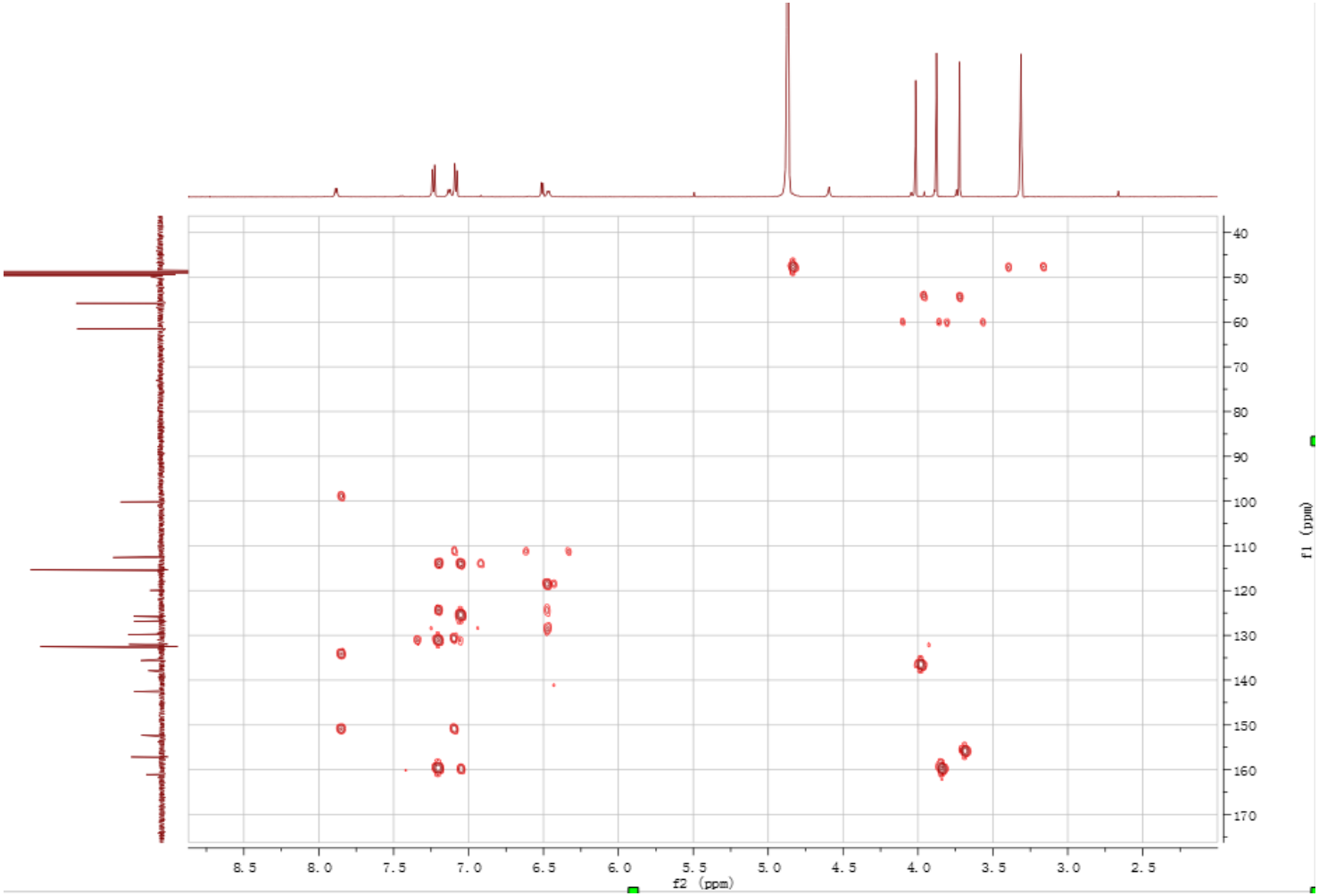


Figure S42. HMBC spectrum of compound 4d

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
319 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
335.1396	335.1436	-4.0	-11.9	16.5	C25 H19 O	56.8	1.517	21.94	25	19		1
	335.1396	0.0	0.0	12.5	C20 H19 N2 O3	56.8	1.577	20.67	20	19	2	3
	335.1369	2.7	8.1	13.5	C16 H15 N8 O	56.9	1.616	19.88	16	15	8	1
	335.1355	4.1	12.2	8.5	C15 H19 N4 O5	56.9	1.638	19.44	15	19	4	5
	335.1428	-3.2	-9.5	4.5	C9 H19 N8 O6	57.0	1.710	18.08	9	19	8	6

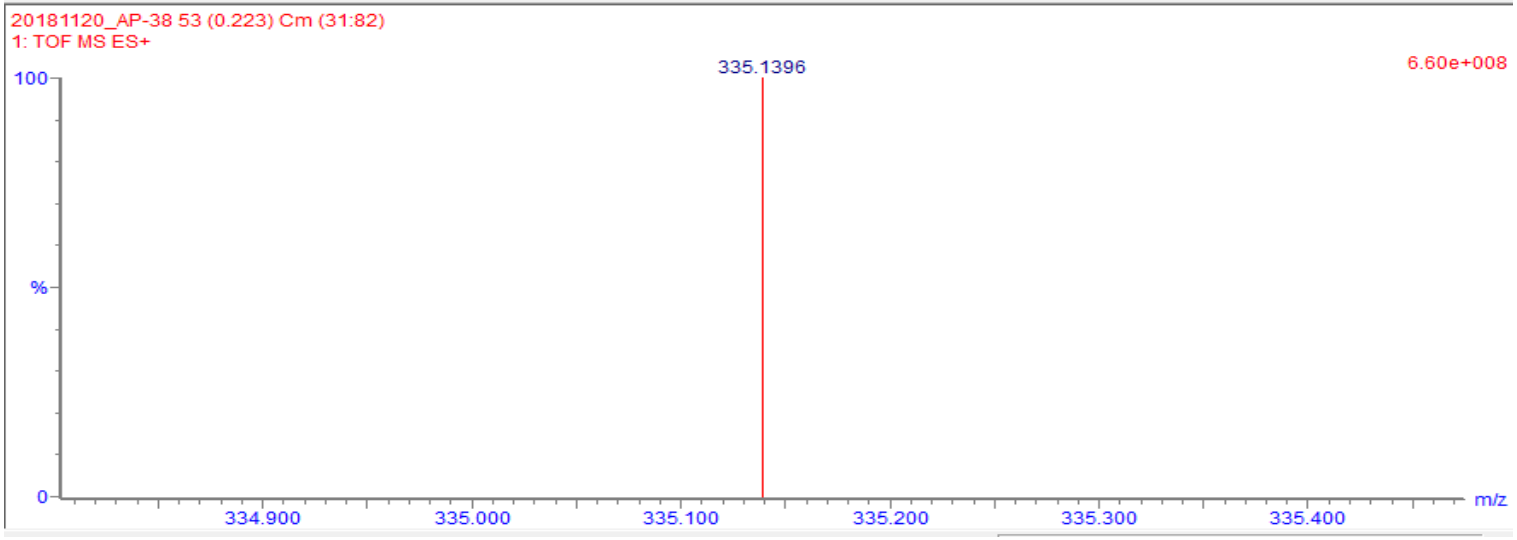


Figure S43. HRESIMS of compound 4d

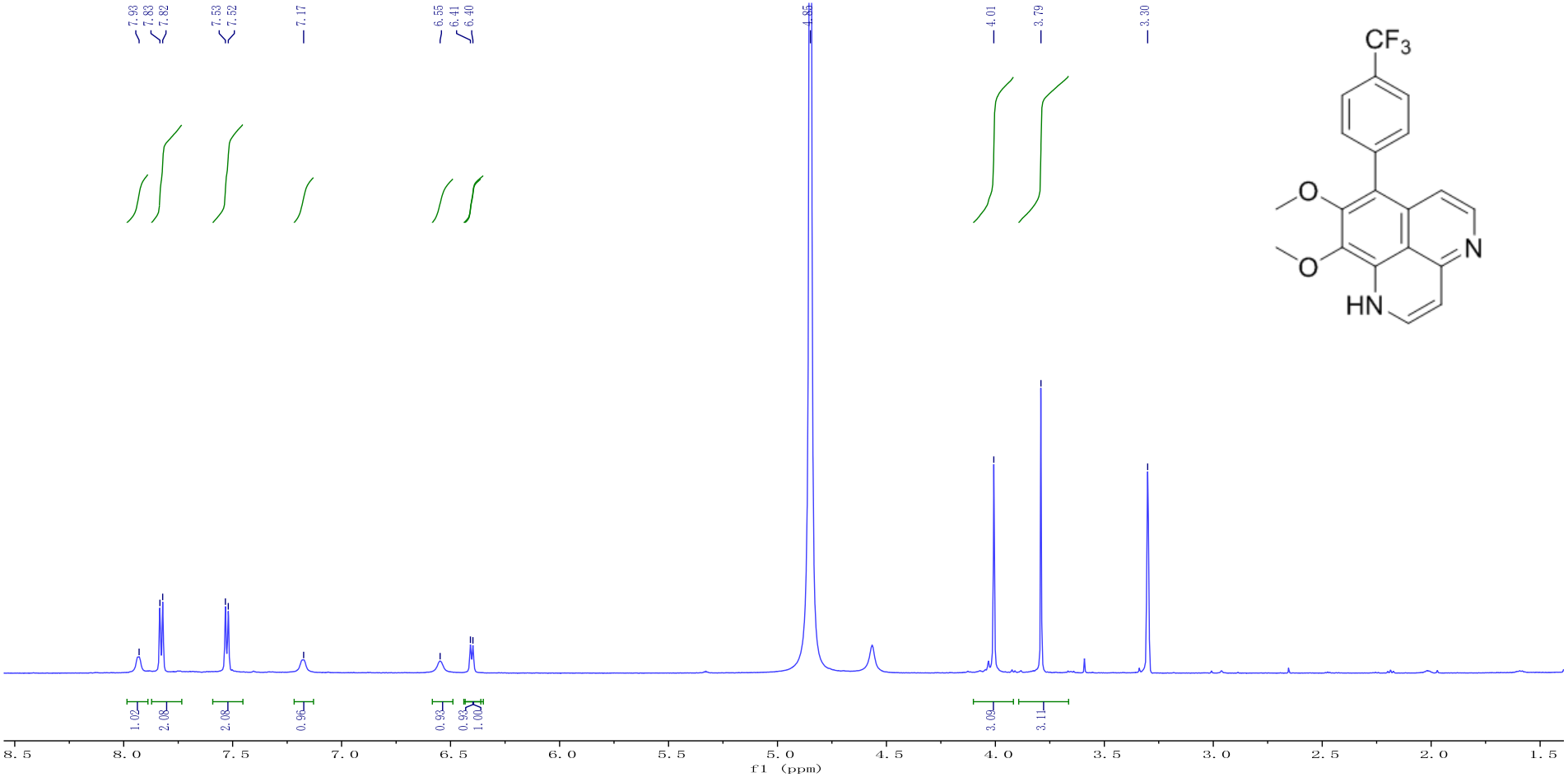


Figure S44. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 4e

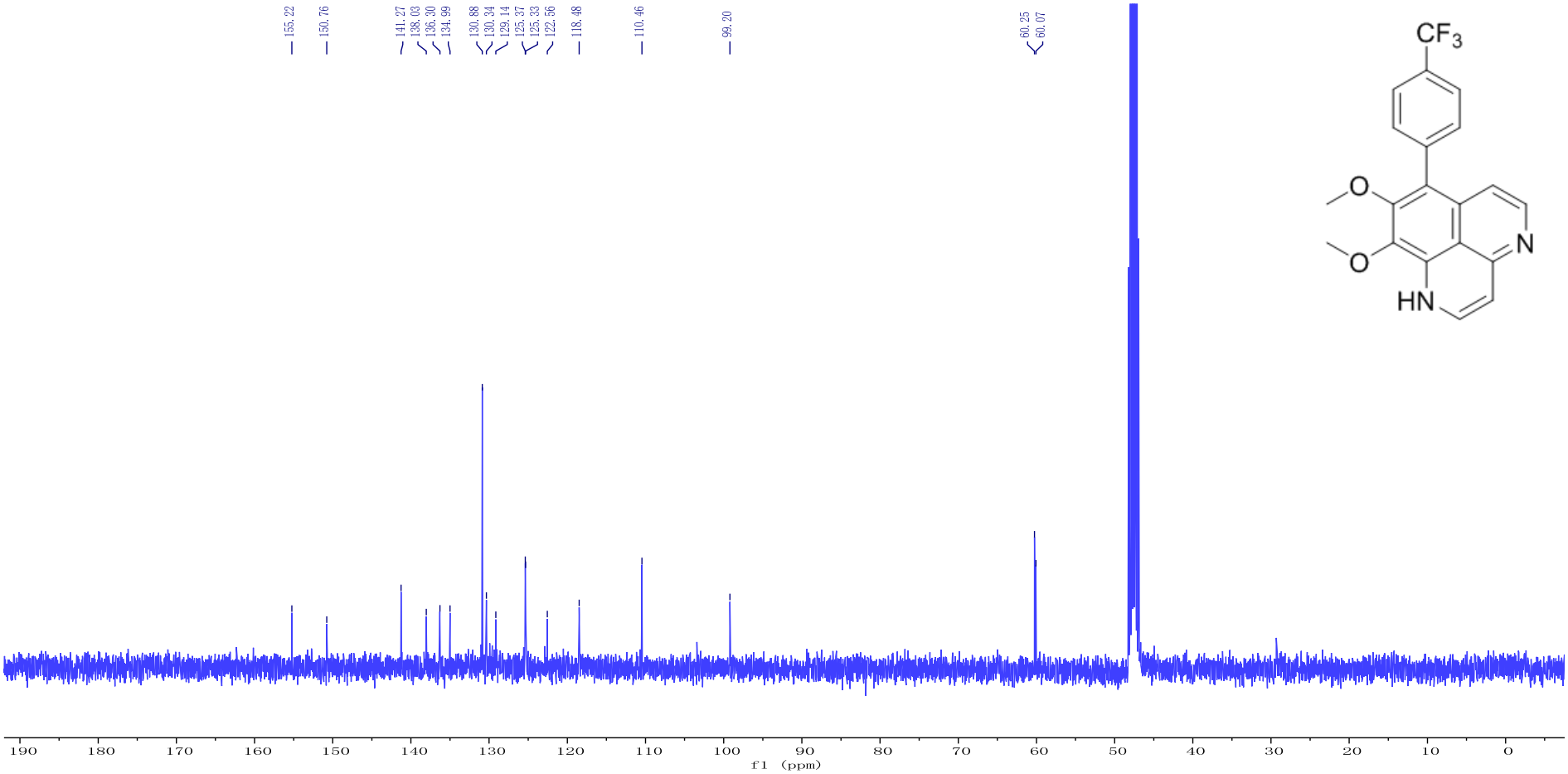


Figure S45. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 4e

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
275 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	RA	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O	F
373.1165	100.00	373.1196	-3.1	-8.3	4.5	C9 H16 N8 O5 F3	1617.0	0.524	59.23	9	16	8	5	3
		373.1137	2.8	7.5	13.5	C16 H12 N8 F3	1618.3	1.755	17.30	16	12	8		3
		373.1124	4.1	11.0	8.5	C15 H16 N4 O4 F3	1618.3	1.808	16.39	15	16	4	4	3
		373.1164	0.1	0.3	12.5	C20 H16 N2 O2 F3	1619.2	2.667	6.95	20	16	2	2	3
		373.1204	-3.9	-10.5	16.5	C25 H16 F3	1623.1	6.593	0.14	25	16			3

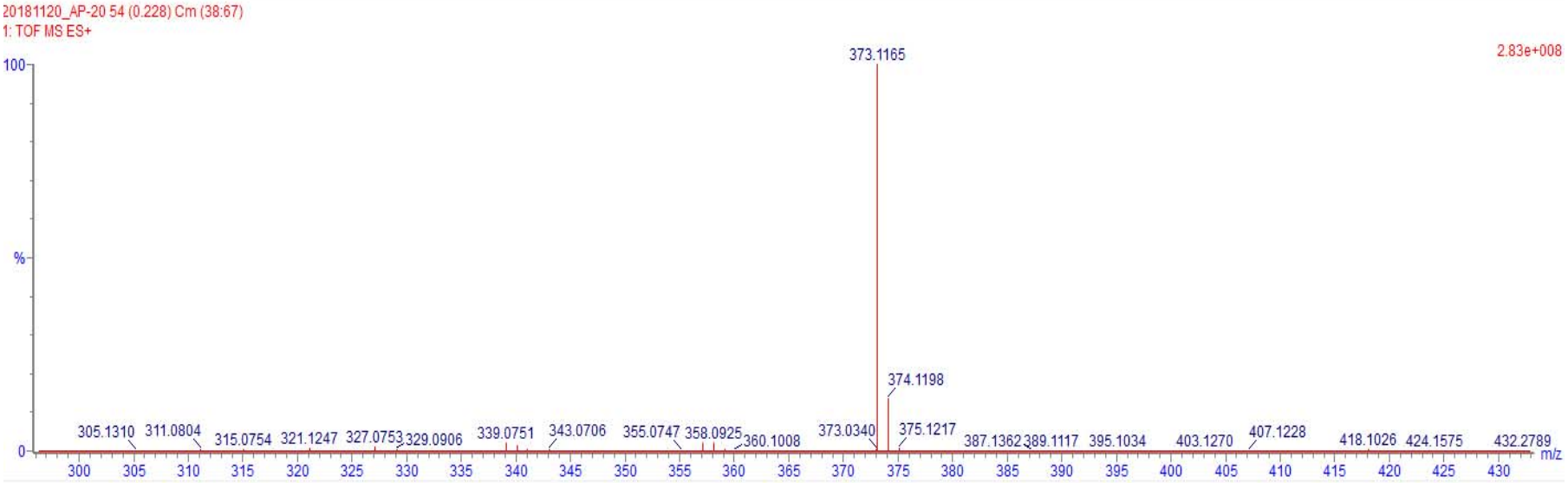


Figure S46. HRESIMS of compound 4e

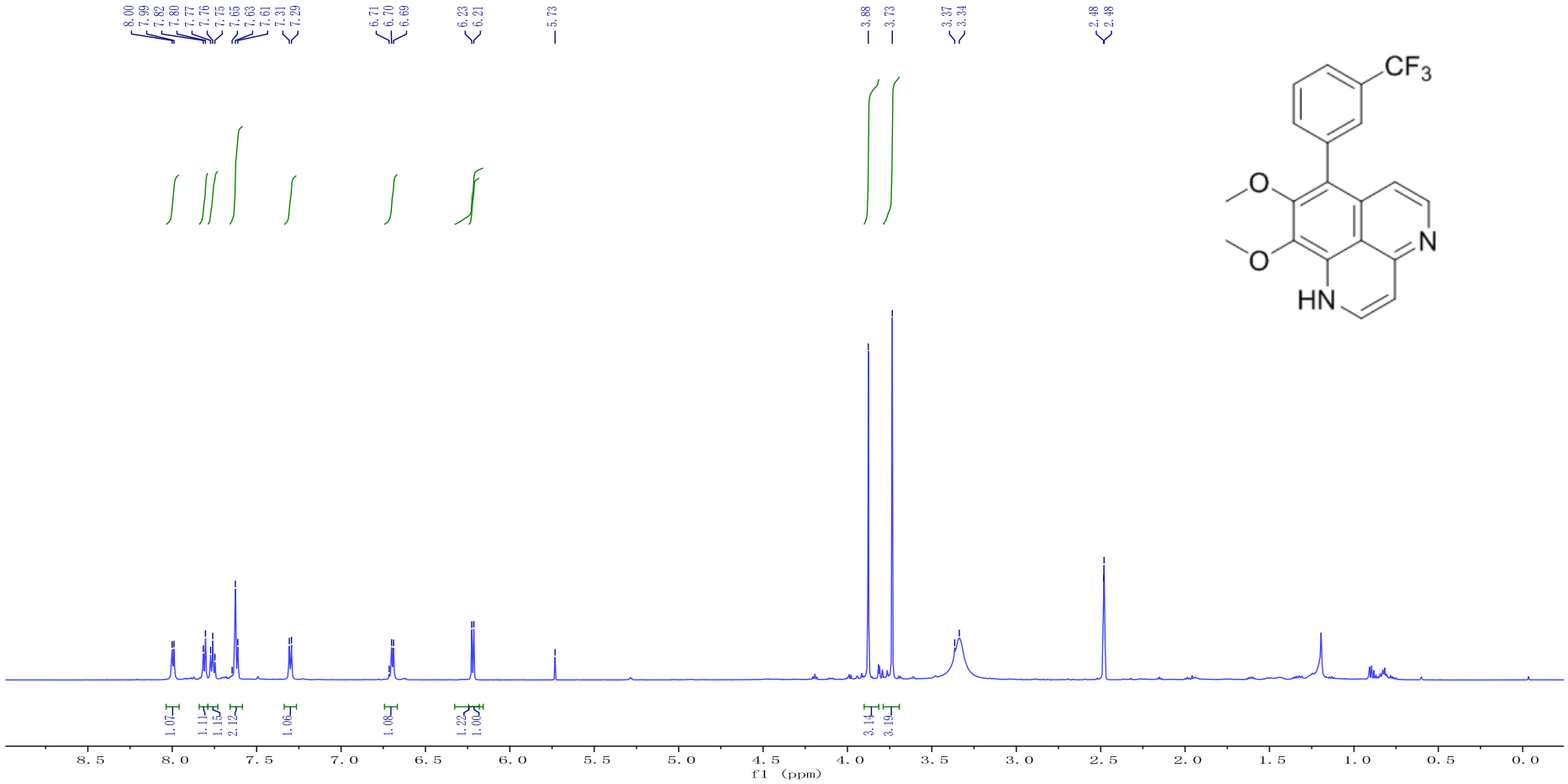


Figure S47. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of compound 4f

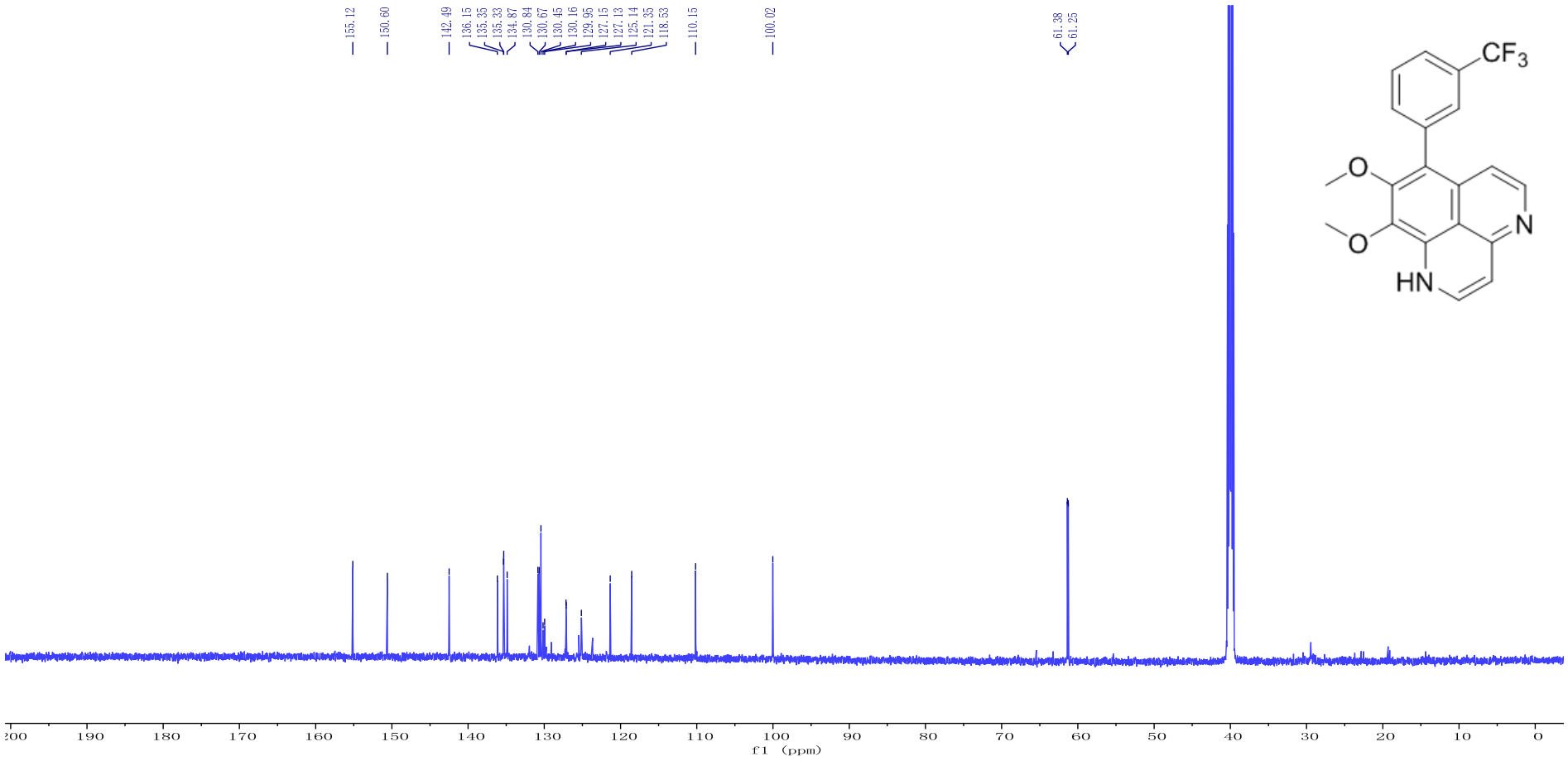


Figure S48. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of compound 4f

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
275 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	RA	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O	F
373.1165	100.00	373.1164	0.1	0.3	12.5	C20 H16 N2 O2 F3	2063.1	0.221	80.14	20	16	2	2	3
		373.1204	-3.9	-10.5	16.5	C25 H16 F3	2065.1	2.180	11.31	25	16			3
		373.1137	2.8	7.5	13.5	C16 H12 N8 F3	2065.9	3.049	4.74	16	12	8		3
		373.1124	4.1	11.0	8.5	C15 H16 N4 O4 F3	2066.3	3.377	3.41	15	16	4	4	3
		373.1196	-3.1	-8.3	4.5	C9 H16 N8 O5 F3	2068.4	5.531	0.40	9	16	8	5	3

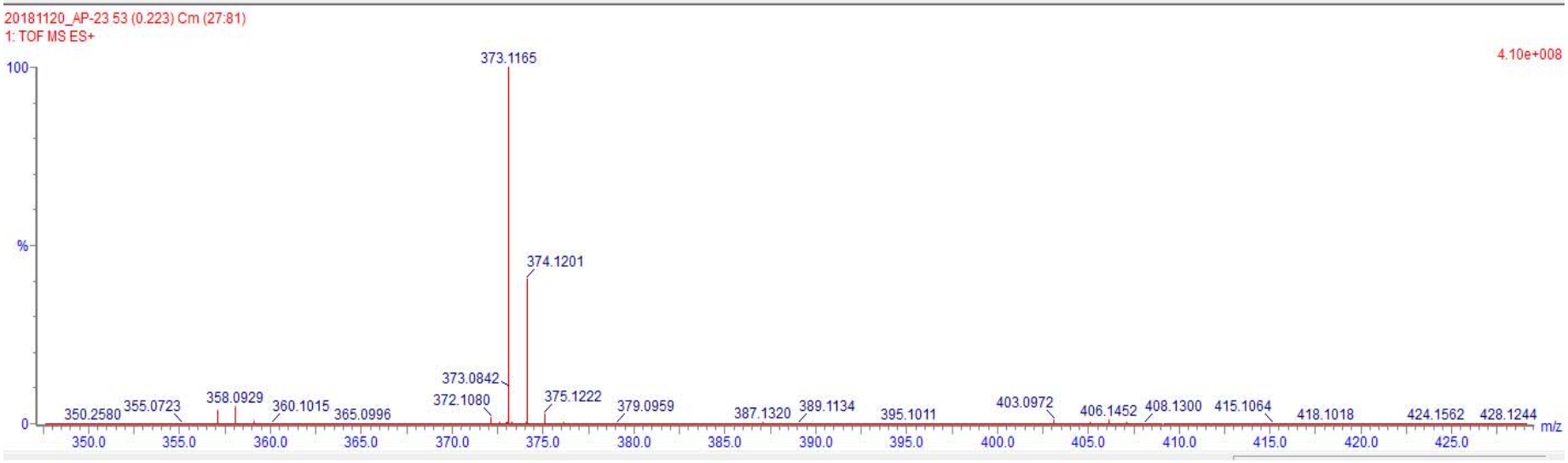


Figure S49. HRESIMS of compound 4f

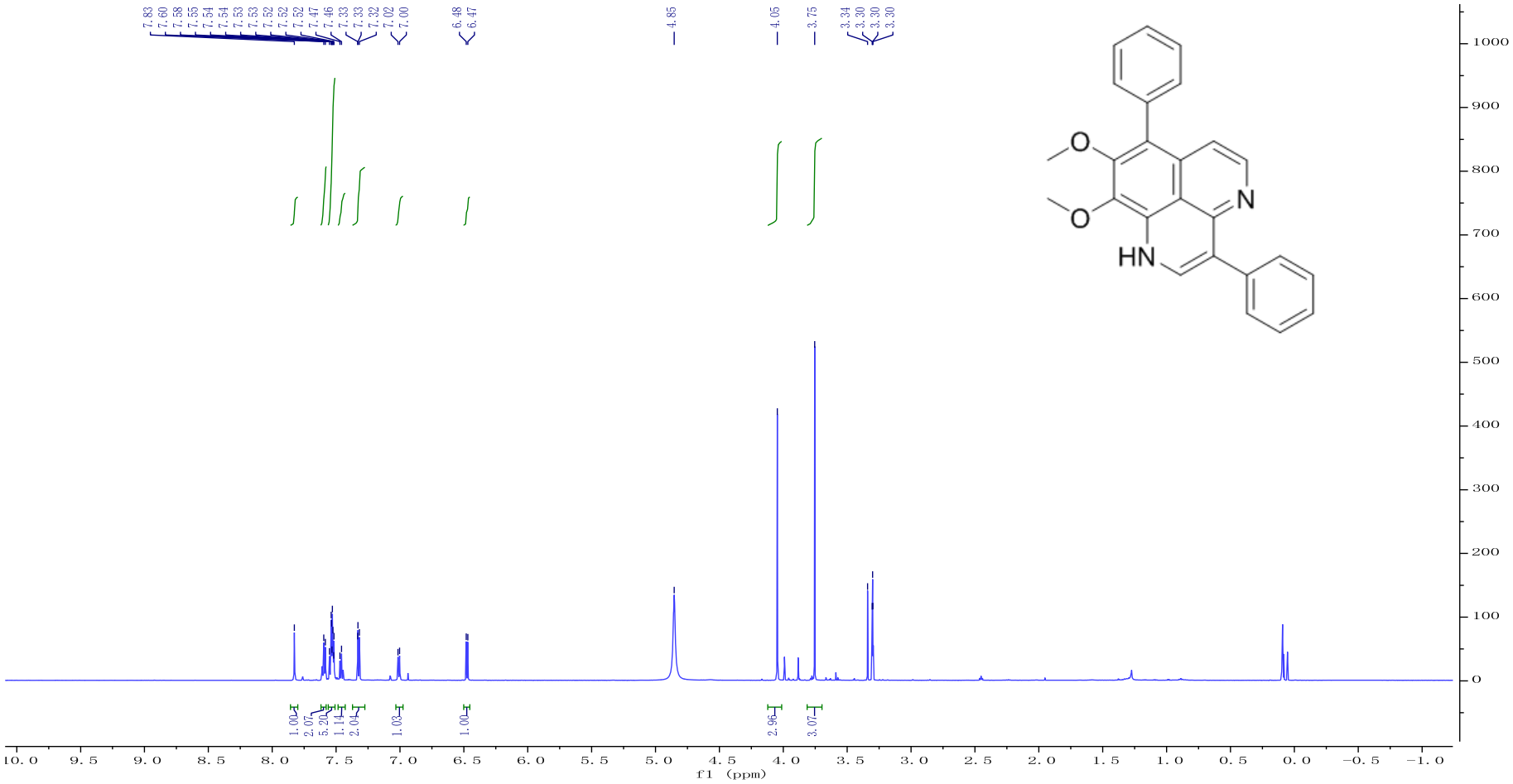


Figure S50. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 5a

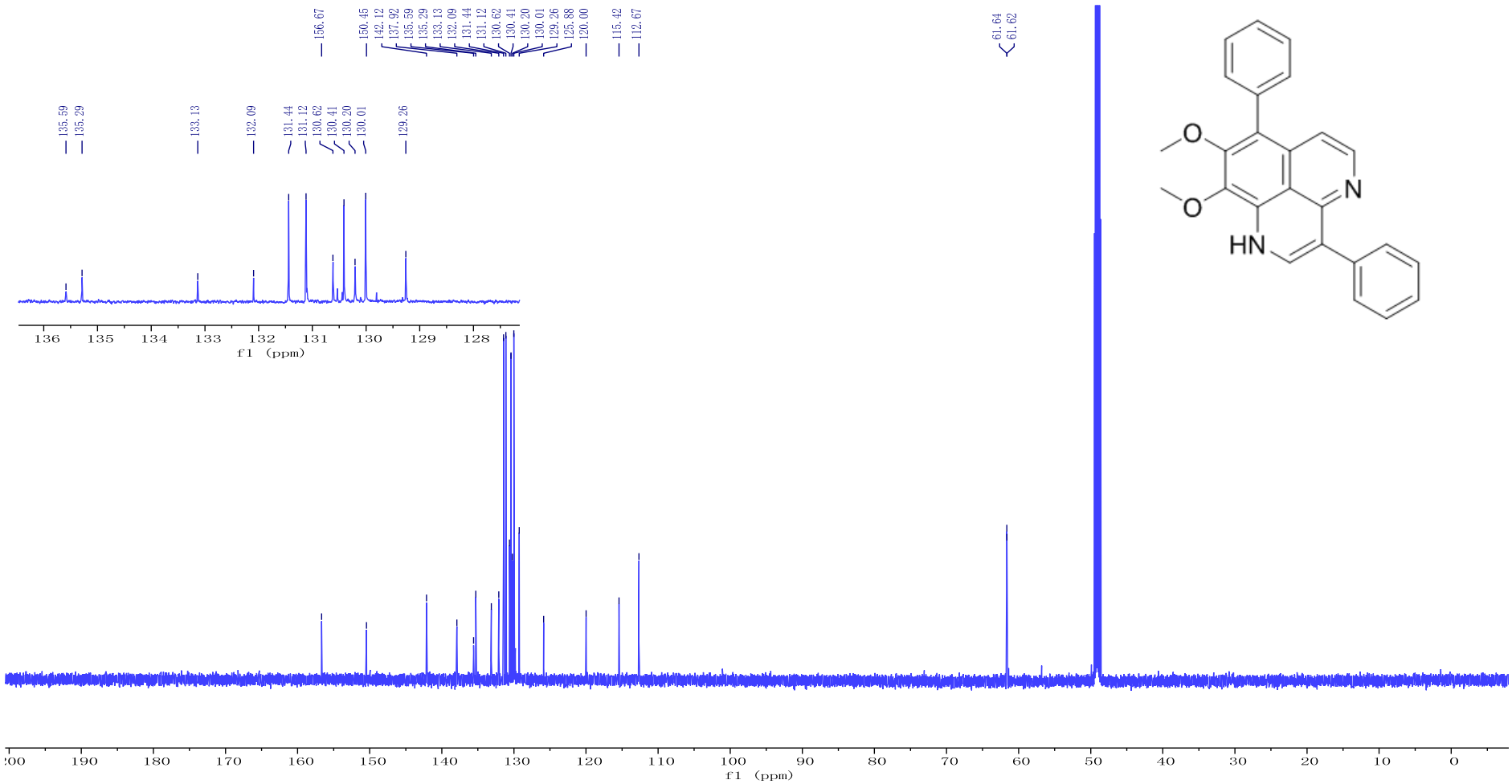


Figure S51. ^{1}H NMR spectrum (125 MHz, CD_3OD) of compound 5a

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
719 formula(e) evaluated with 8 results within limits (up to 50 closest results for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
381.1613	381.1603	1.0	2.6	16.5	C25 H21 N2 O2	442.7	0.009	99.09	25	21	2	2
	381.1576	3.7	9.7	17.5	C21 H17 N8	447.9	5.241	0.53	21	17	8	
	381.1643	-3.0	-7.9	20.5	C30 H21	448.2	5.593	0.37	30	21		
	381.1635	-2.2	-5.8	8.5	C14 H21 N8 O5	452.7	10.081	0.00	14	21	8	5
	381.1622	-0.9	-2.4	3.5	C13 H25 N4 O9	453.4	10.727	0.00	13	25	4	9
	381.1608	0.5	1.3	-1.5	C12 H29 O13	454.4	11.712	0.00	12	29		13
	381.1595	1.8	4.7	4.5	C9 H21 N10 O7	455.0	12.336	0.00	9	21	10	7
	381.1581	3.2	8.4	-0.5	C8 H25 N6 O11	455.5	12.814	0.00	8	25	6	11

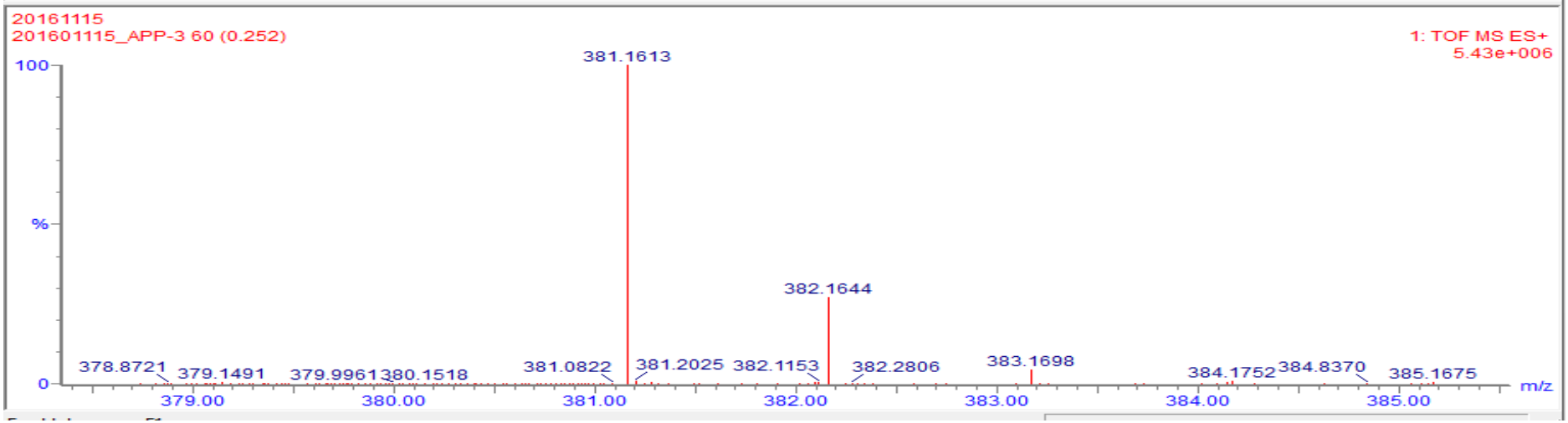


Figure S52. HRESIMS of compound 5a

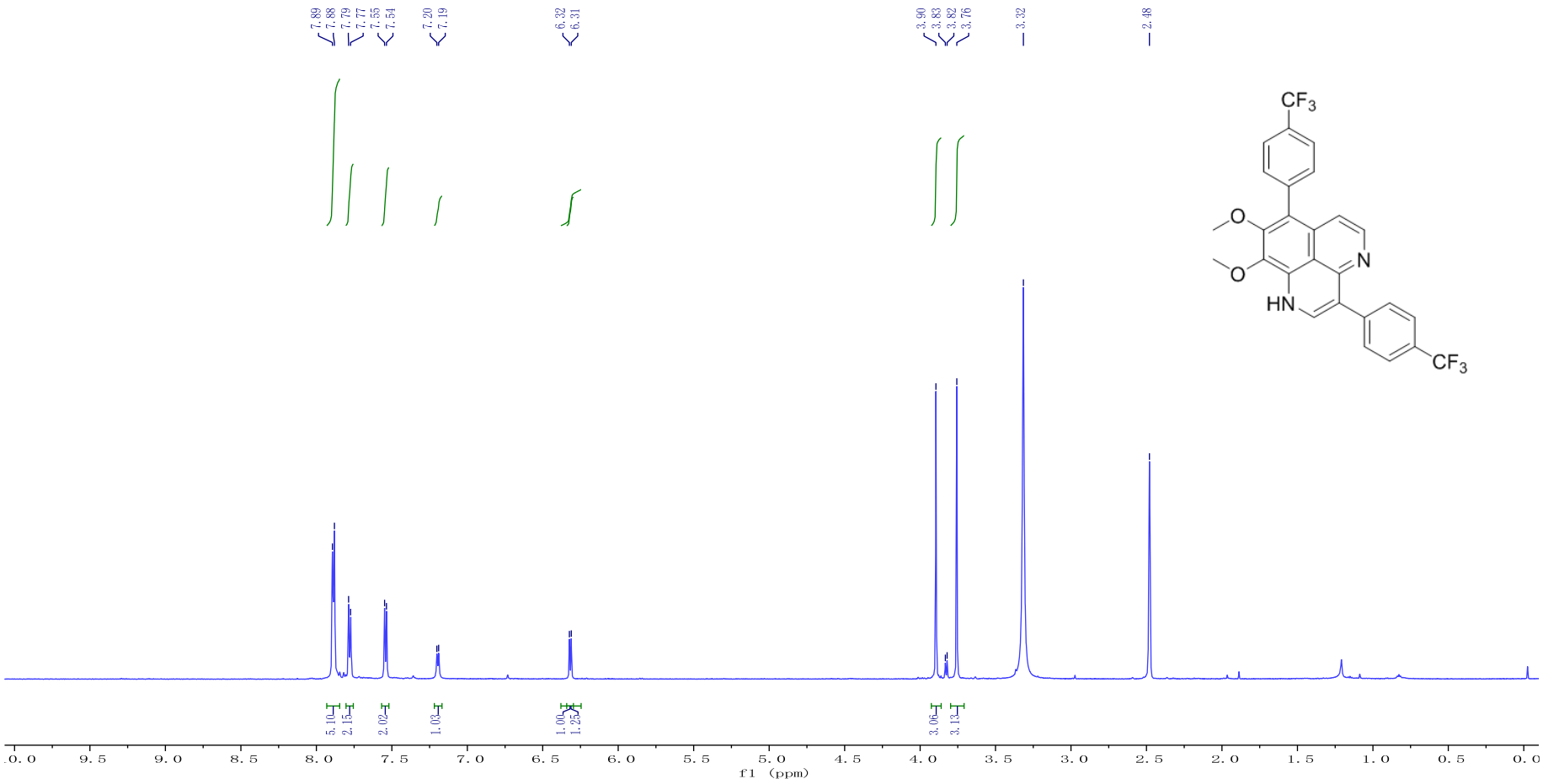


Figure S53. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of compound 5b

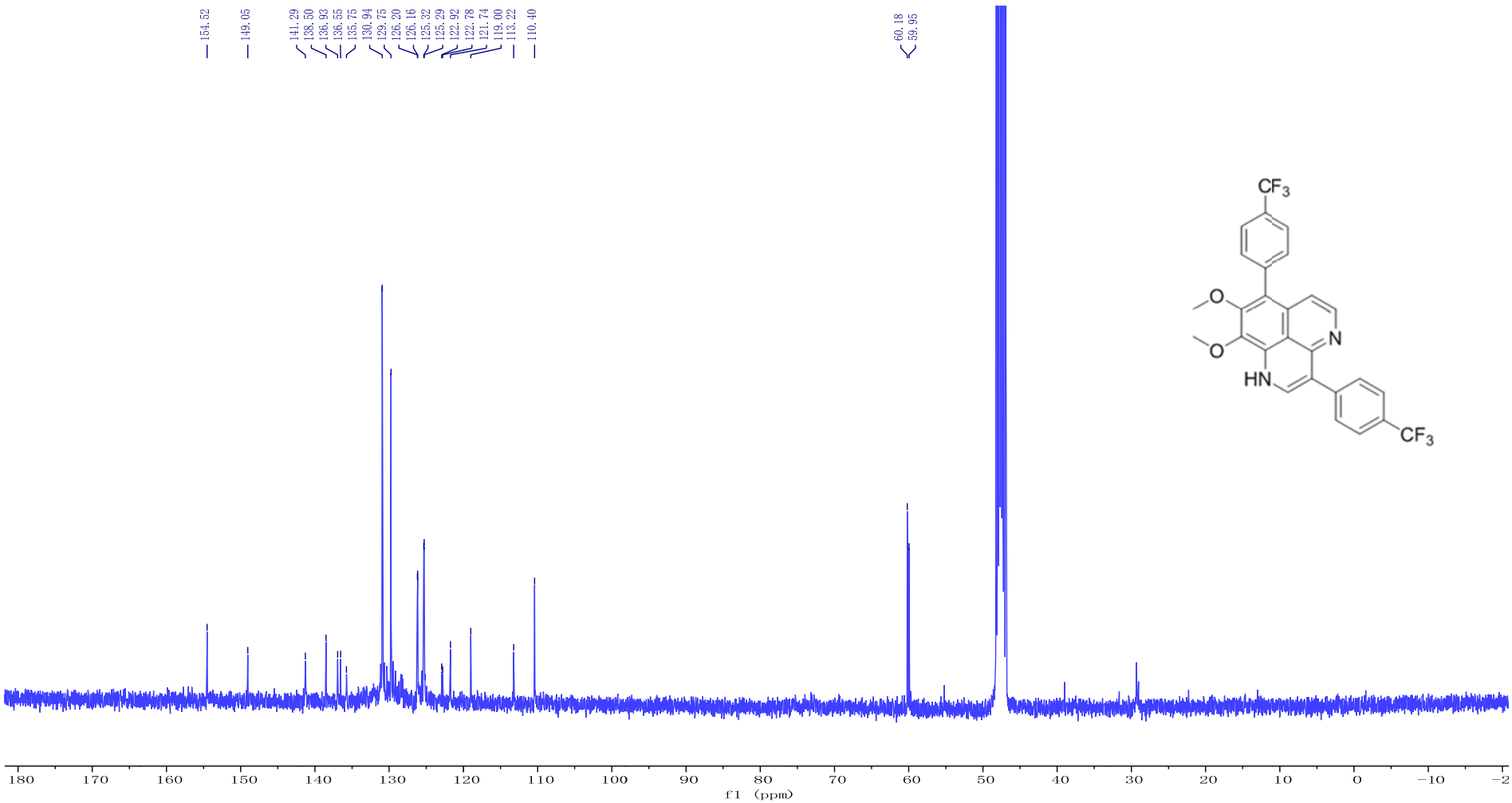


Figure S54. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 5b

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
349 formula(e) evaluated with 6 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	RA	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O	F
517.1343	100.00	517.1351	-0.8	-1.5	16.5	C27 H19 N2 O2 F6	1512.5	0.369	69.15	27	19	2	2	6
		517.1324	1.9	3.7	17.5	C23 H15 N8 F6	1513.8	1.610	20.00	23	15	8		6
		517.1310	3.3	6.4	12.5	C22 H19 N4 O4 F6	1515.0	2.847	5.80	22	19	4	4	6
		517.1391	-4.8	-9.3	20.5	C32 H19 F6	1515.6	3.458	3.15	32	19			6
		517.1297	4.6	8.9	7.5	C21 H23 O8 F6	1516.5	4.396	1.23	21	23		8	6
		517.1383	-4.0	-7.7	8.5	C16 H19 N8 O5 F6	1517.2	5.007	0.67	16	19	8	5	6

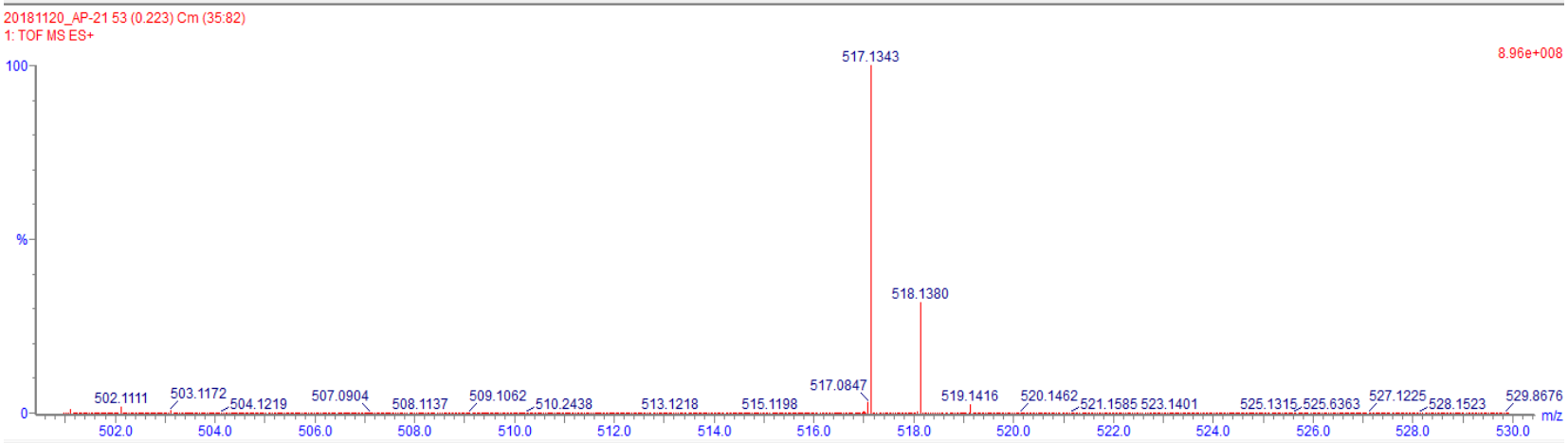


Figure S55. HRESIMS of compound 5b

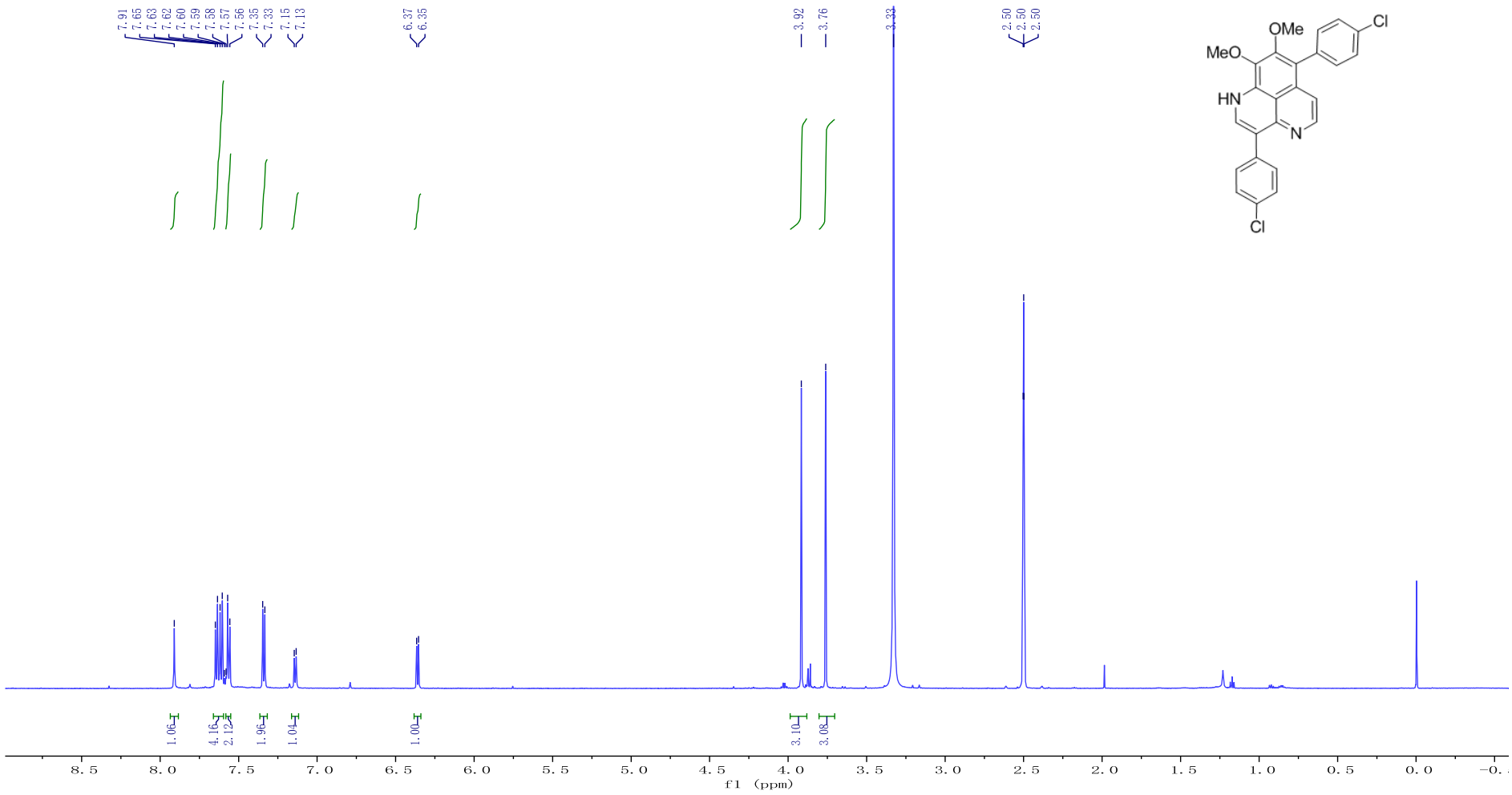


Figure S56. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of compound 5c

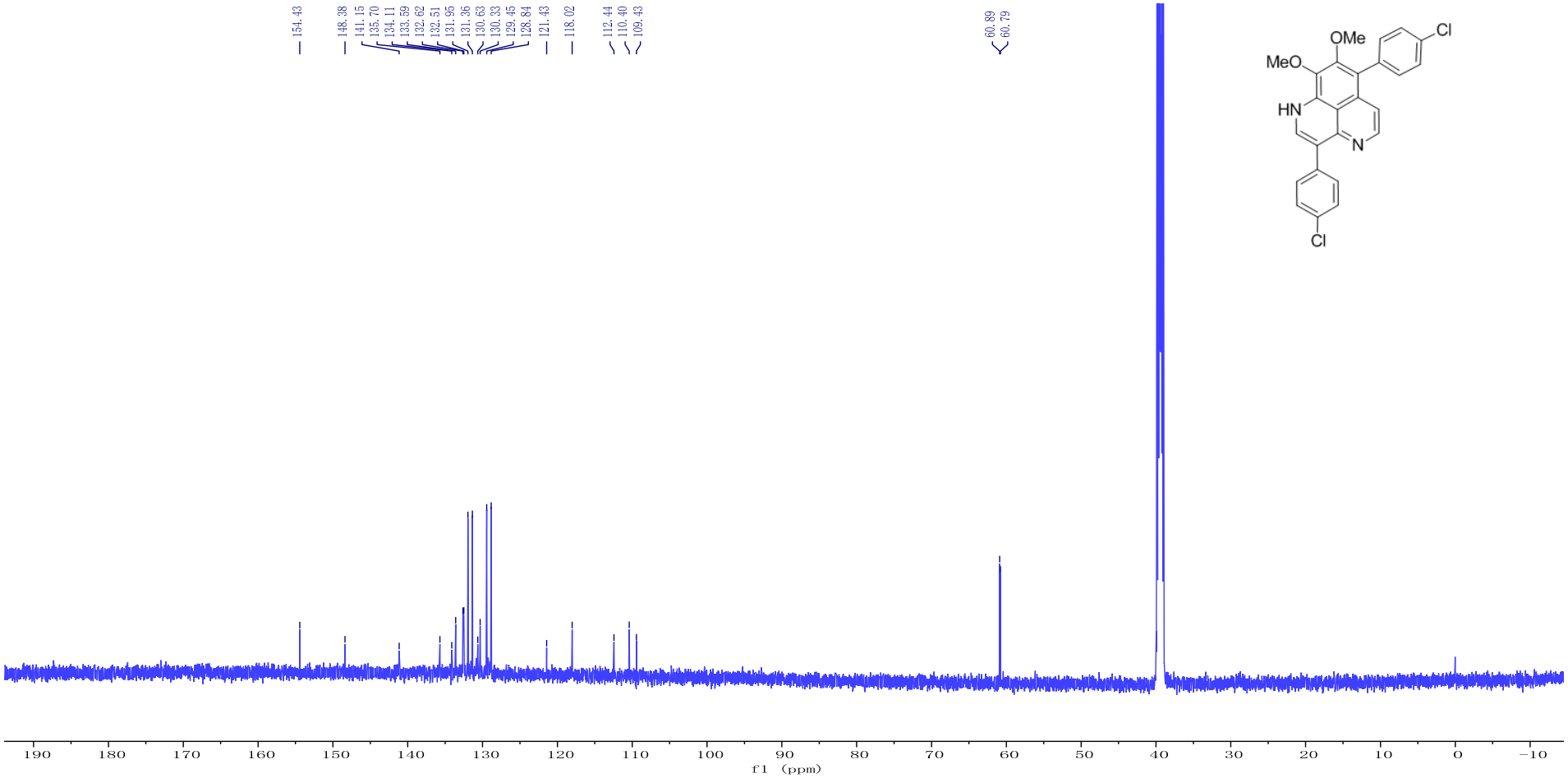


Figure S57. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of compound 5c

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
348 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	RA	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O	Cl
449.0820	100.00	449.0855	-3.5	-7.8	8.5	C14 H19 N8 O5 Cl2	1931.4	0.315	72.97	14	19	8	5	2
		449.0783	3.7	8.2	12.5	C20 H19 N4 O4 Cl2	1933.3	2.194	11.15	20	19	4	4	2
		449.0824	-0.4	-0.9	16.5	C25 H19 N2 O2 Cl2	1933.4	2.285	10.18	25	19	2	2	2
		449.0797	2.3	5.1	17.5	C21 H15 N8 Cl2	1934.0	2.884	5.59	21	15	8		2
		449.0864	-4.4	-9.8	20.5	C30 H19 Cl2	1937.8	6.748	0.12	30	19			2

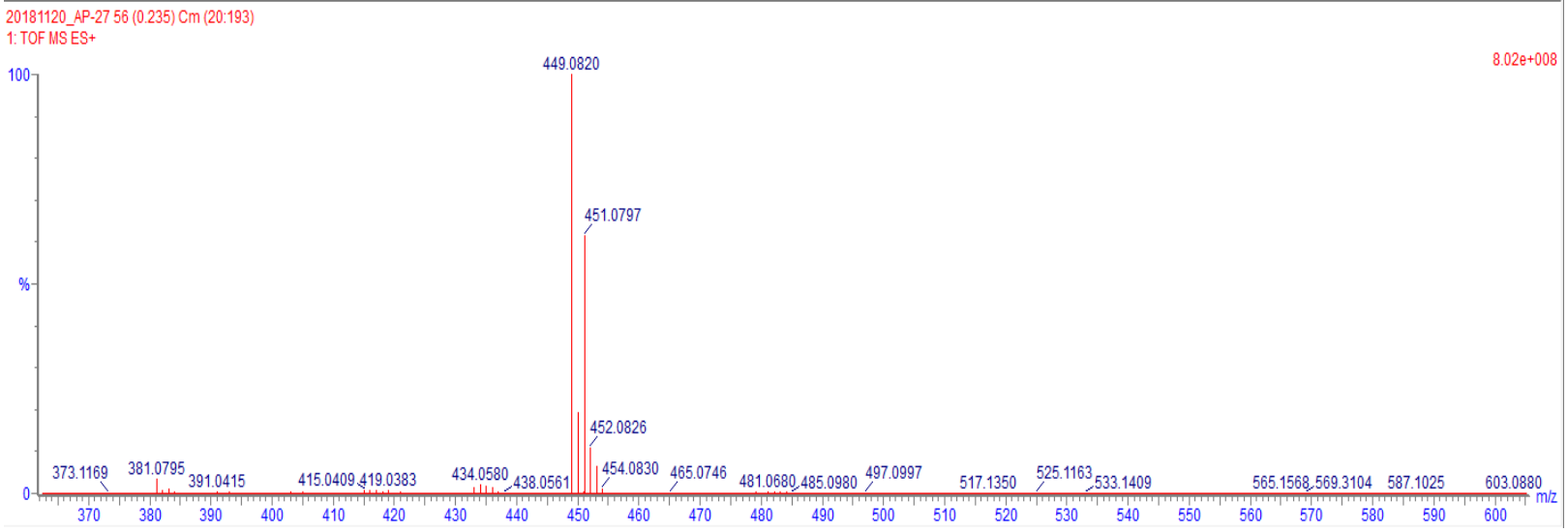


Figure S58. HRESIMS of compound 5c

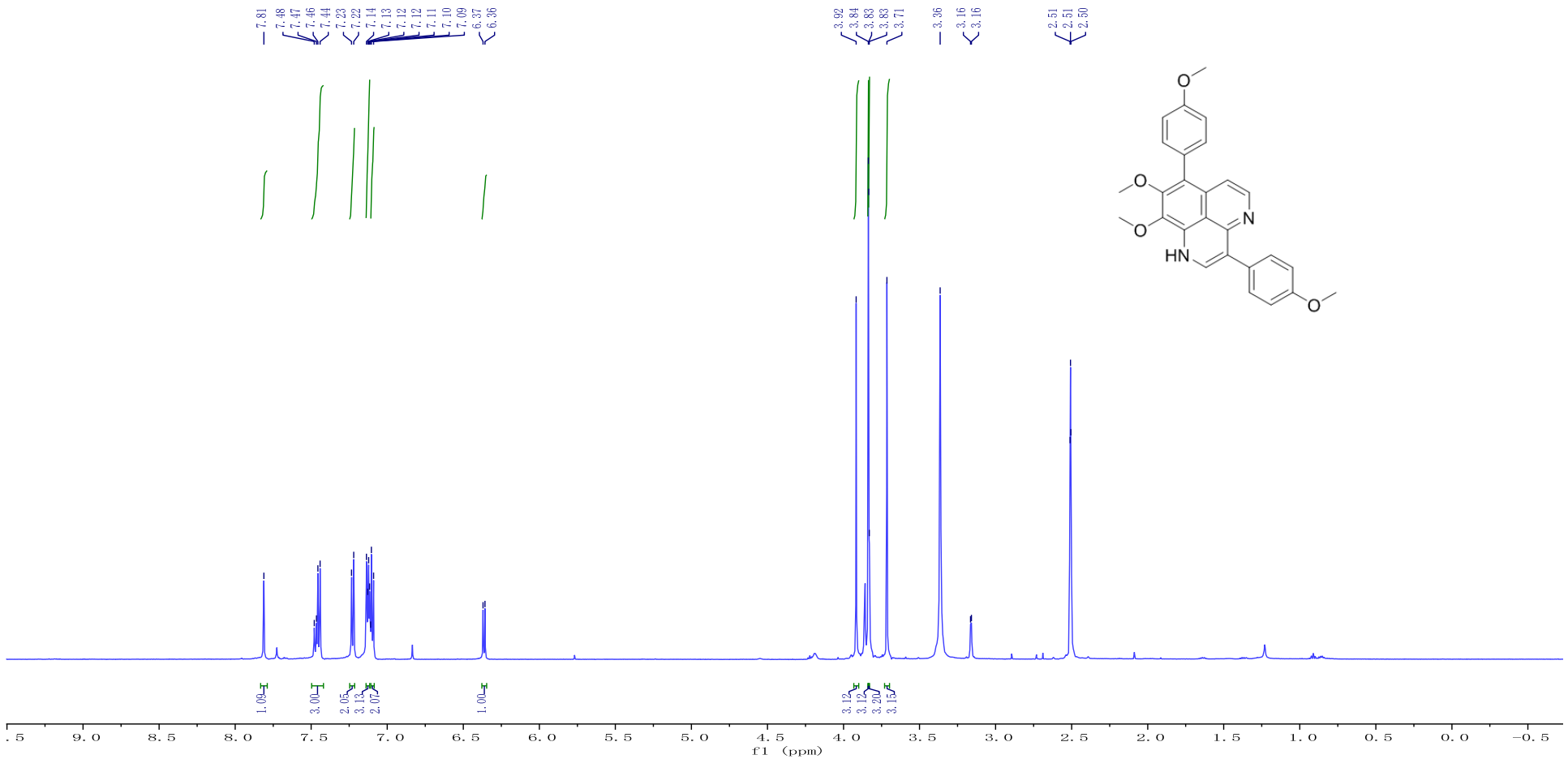


Figure S59. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of compound 5d

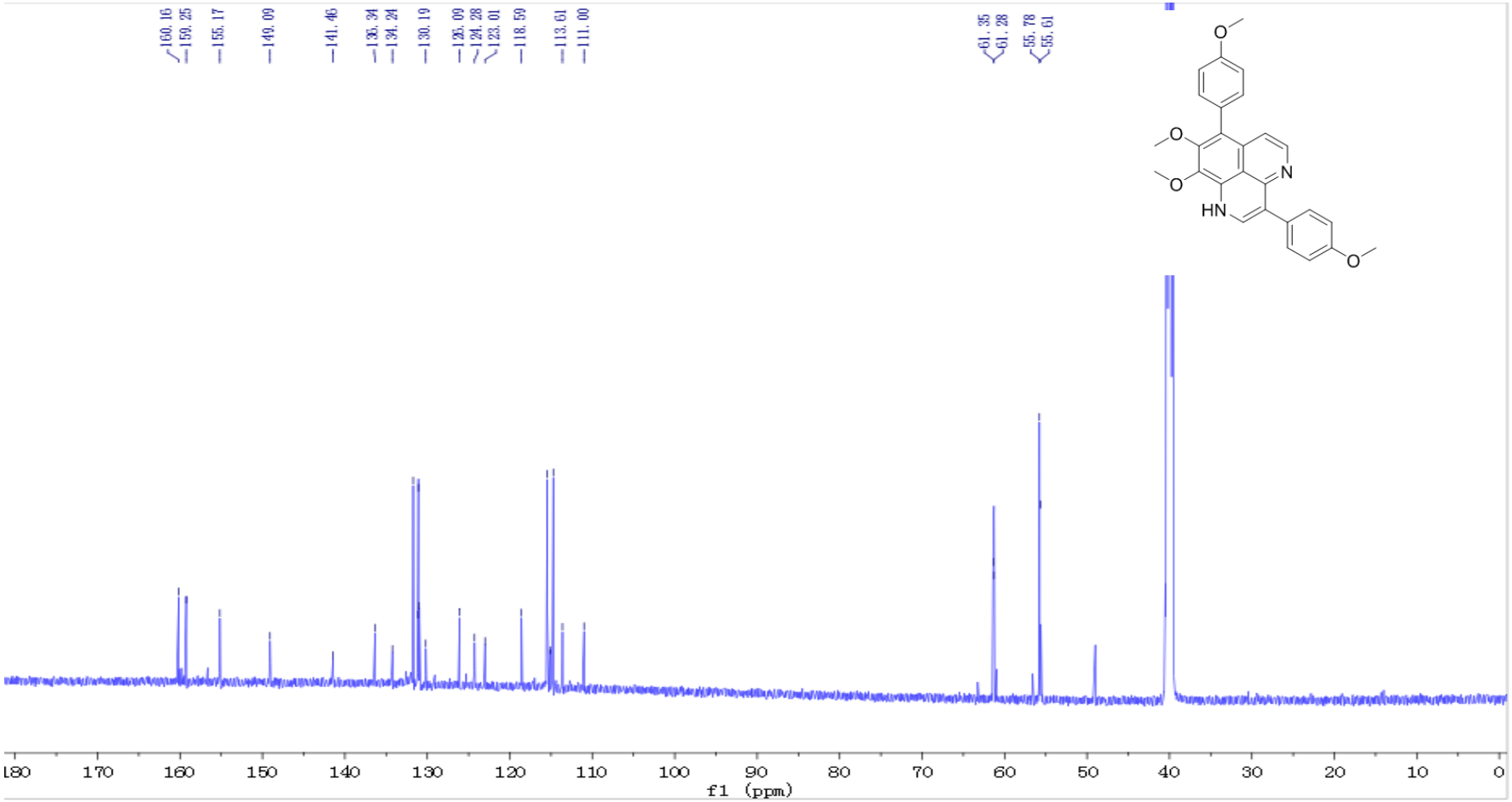


Figure S60. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of compound 5d

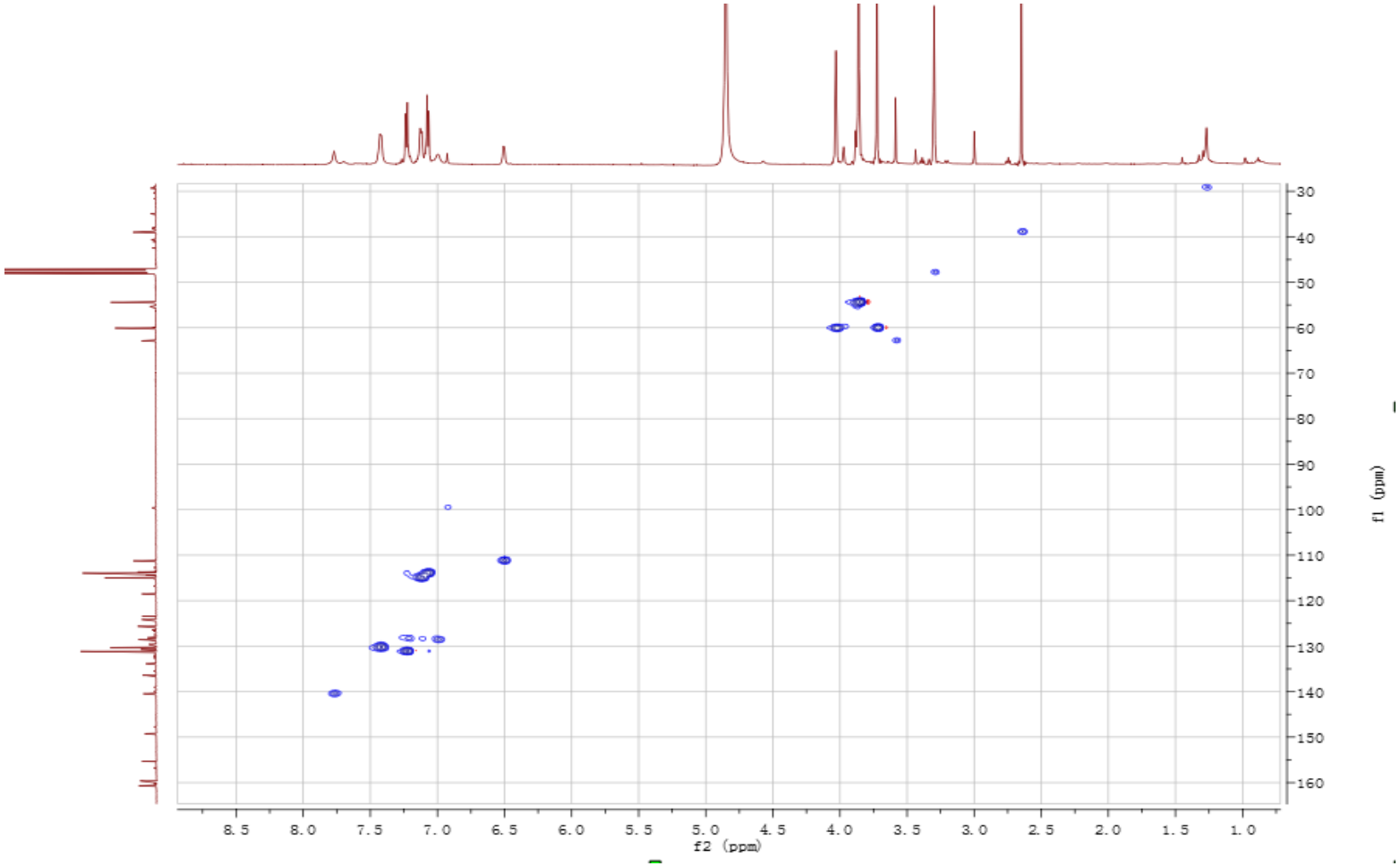


Figure S61. HSQC spectrum of compound 5d

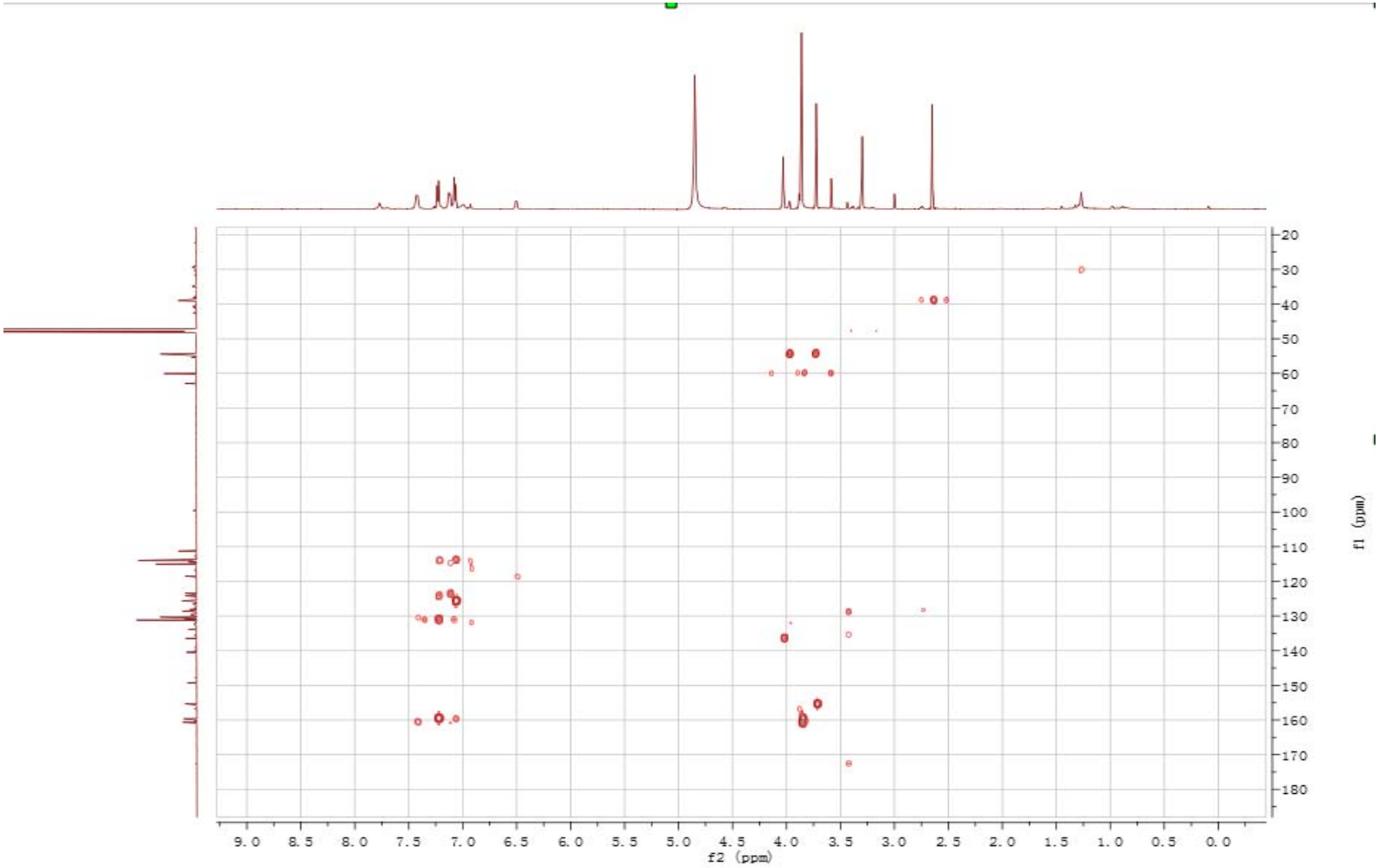


Figure S62. HSQC spectrum of compound 5d

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
415 formula(e) evaluated with 6 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
441.1807	441.1855	-4.8	-10.9	20.5	C32 H25 O2	1561.3	1.074	34.16	32	25		2
	441.1828	-2.1	-4.8	21.5	C28 H21 N6	1561.3	1.093	33.54	28	21	6	
	441.1814	-0.7	-1.6	16.5	C27 H25 N2 O4	1561.6	1.447	23.53	27	25	2	4
	441.1787	2.0	4.5	17.5	C23 H21 N8 O2	1563.1	2.945	5.26	23	21	8	2
	441.1774	3.3	7.5	12.5	C22 H25 N4 O6	1563.7	3.535	2.91	22	25	4	6
	441.1846	-3.9	-8.8	8.5	C16 H25 N8 O7	1565.3	5.112	0.60	16	25	8	7

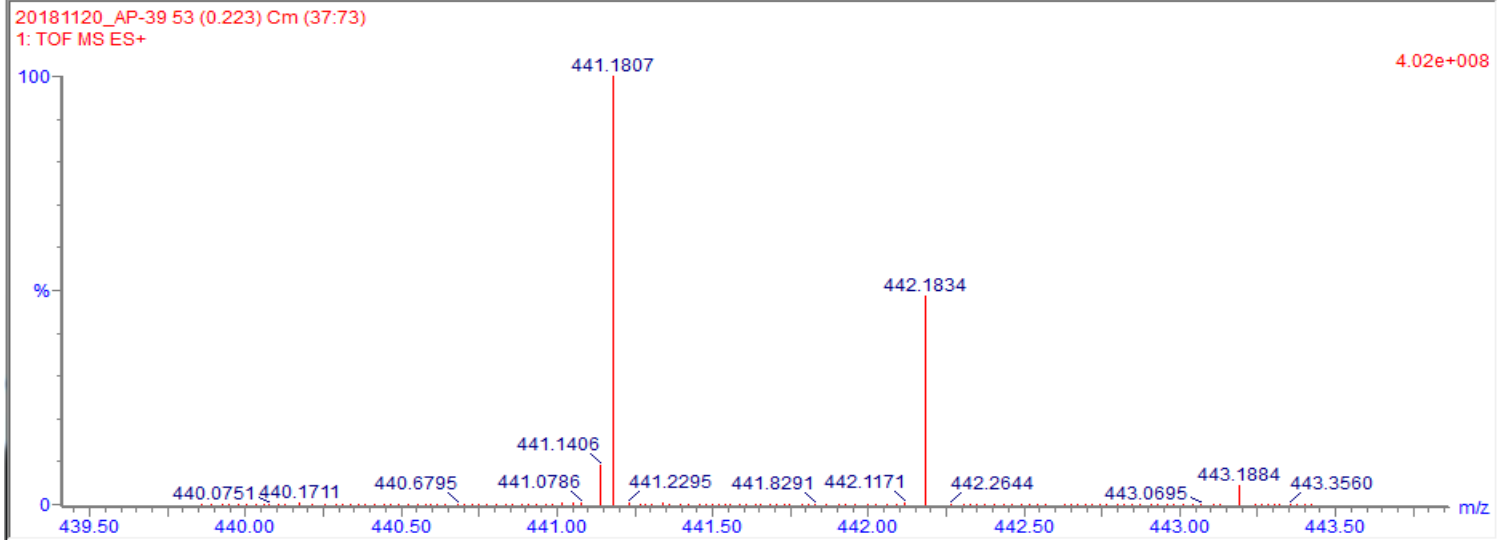


Figure S63. HRESIMS of compound 5d

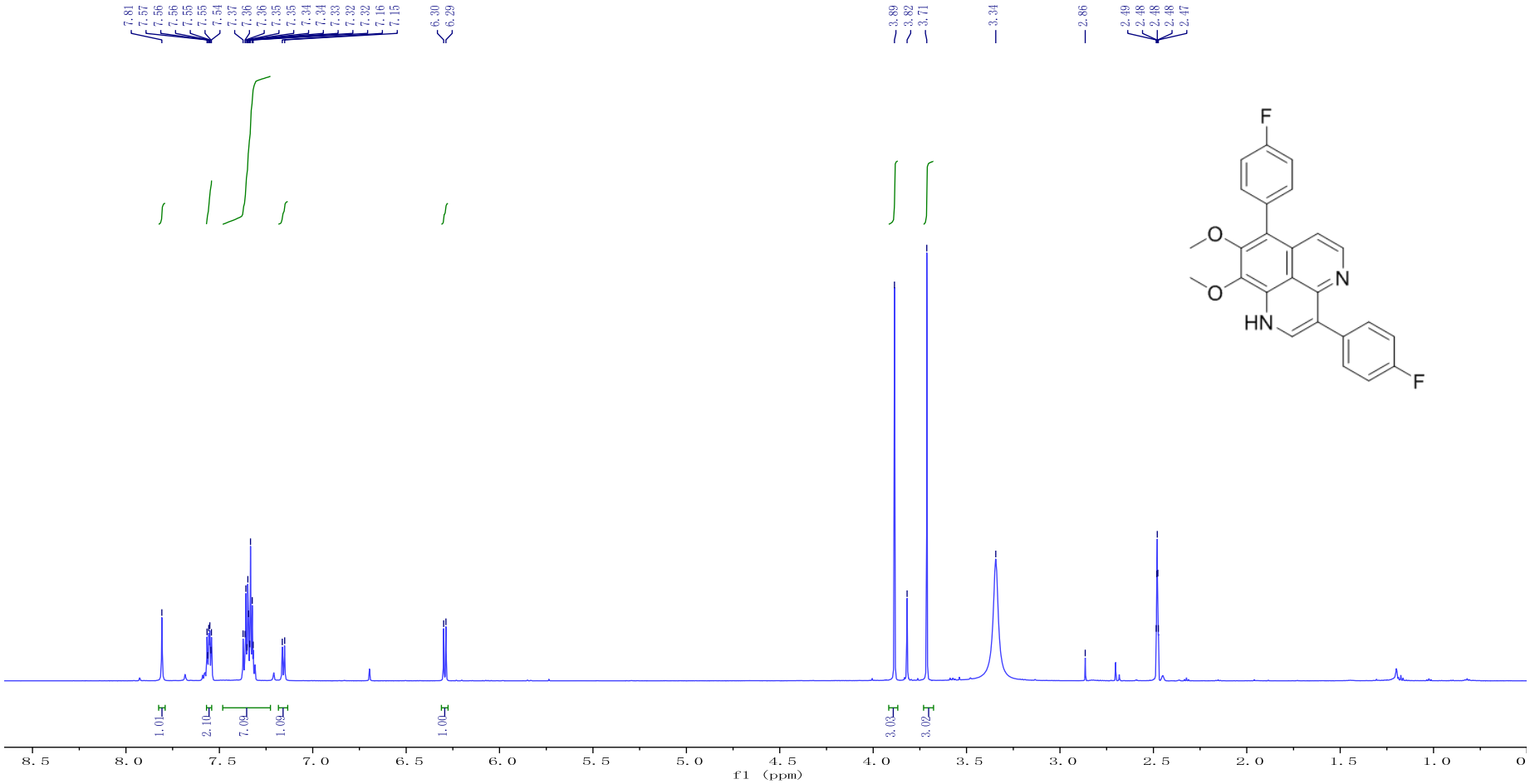


Figure S64. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of compound 5e

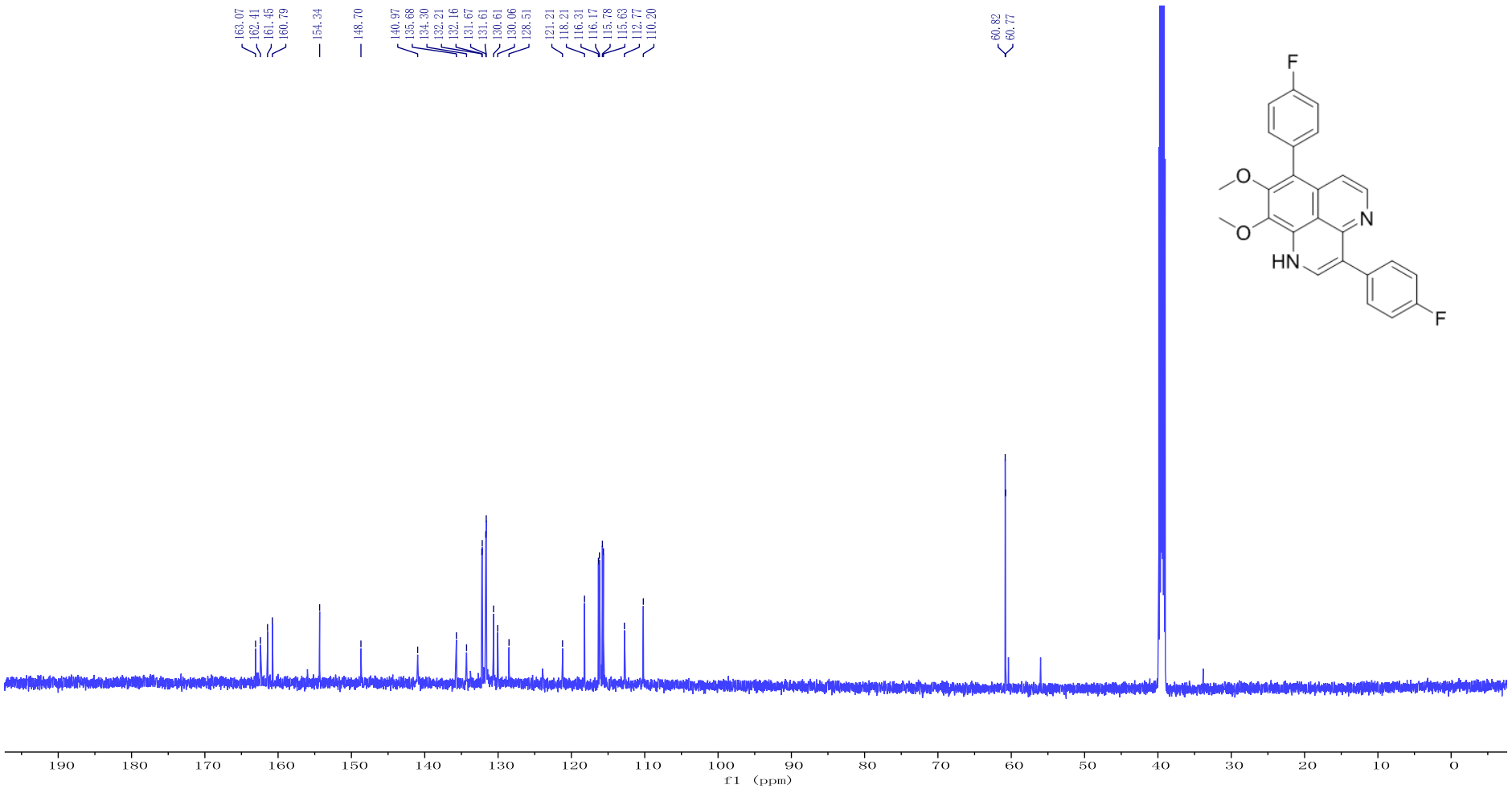


Figure S65. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of compound 5e

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
348 formula(e) evaluated with 6 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	RA	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O	F
417.1410	100.00	417.1415	-0.5	-1.2	16.5	C25 H19 N2 O2 F2	1985.0	0.247	78.09	25	19	2	2	2
		417.1388	2.2	5.3	17.5	C21 H15 N8 F2	1986.7	1.922	14.63	21	15	8		2
		417.1374	3.6	8.6	12.5	C20 H19 N4 O4 F2	1988.1	3.361	3.47	20	19	4	4	2
		417.1455	-4.5	-10.8	20.5	C30 H19 F2	1988.3	3.535	2.91	30	19			2
		417.1361	4.9	11.7	7.5	C19 H23 O8 F2	1989.8	5.070	0.63	19	23		8	2
		417.1446	-3.6	-8.6	8.5	C14 H19 N8 O5 F2	1990.7	5.903	0.27	14	19	8	5	2

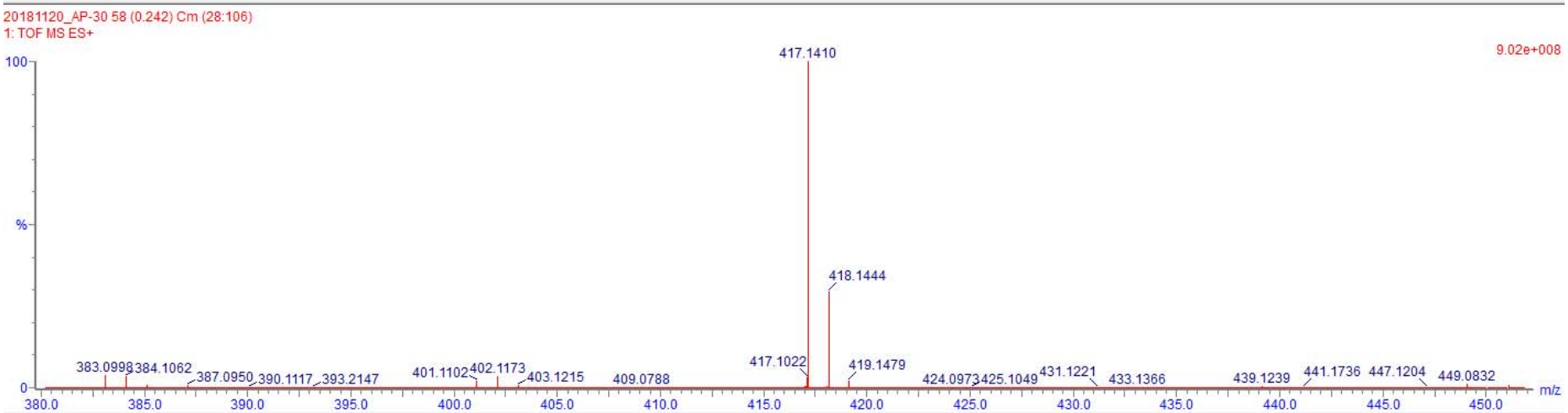


Figure S66. HRESIMS of compound 5e

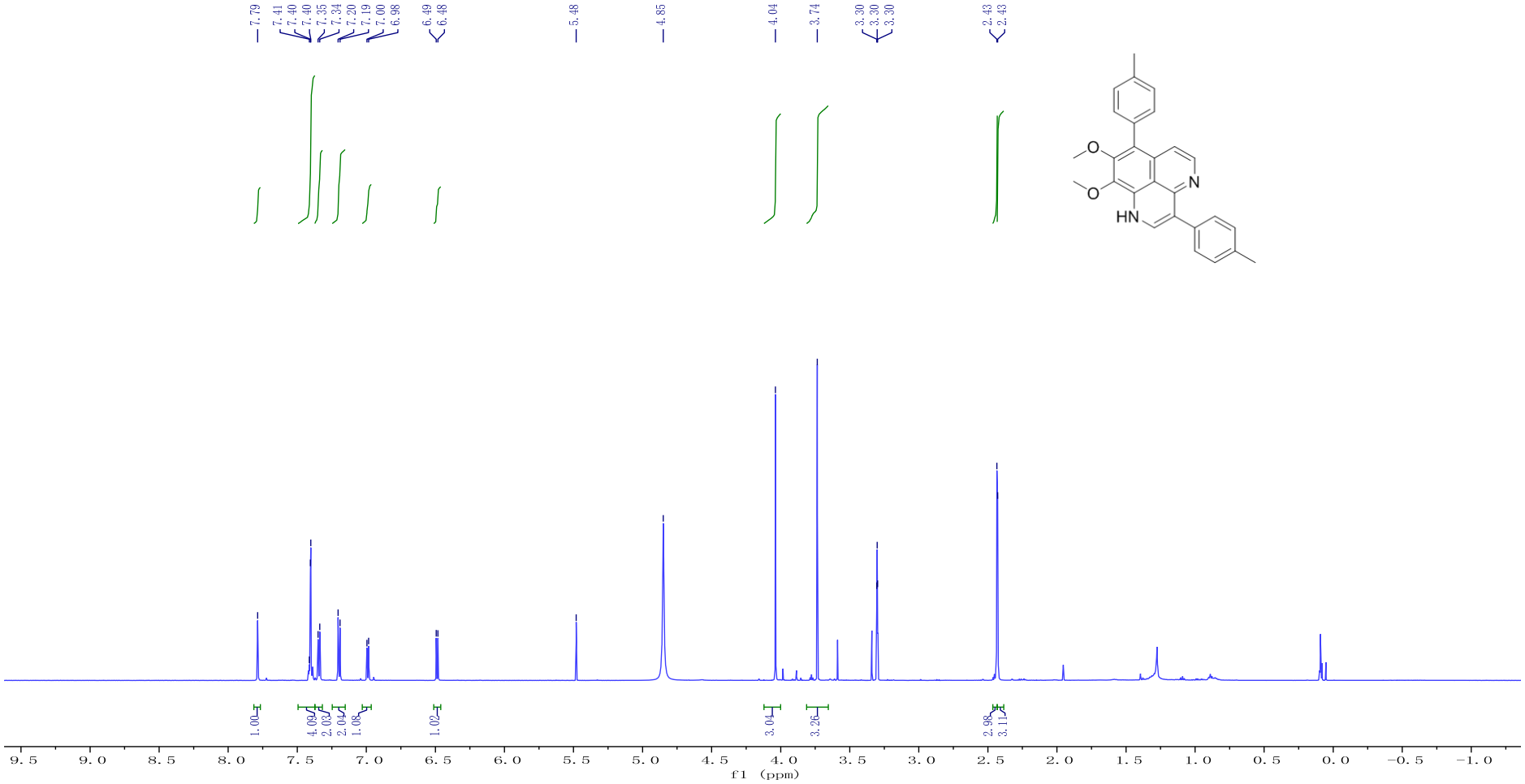


Figure S67. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 5f

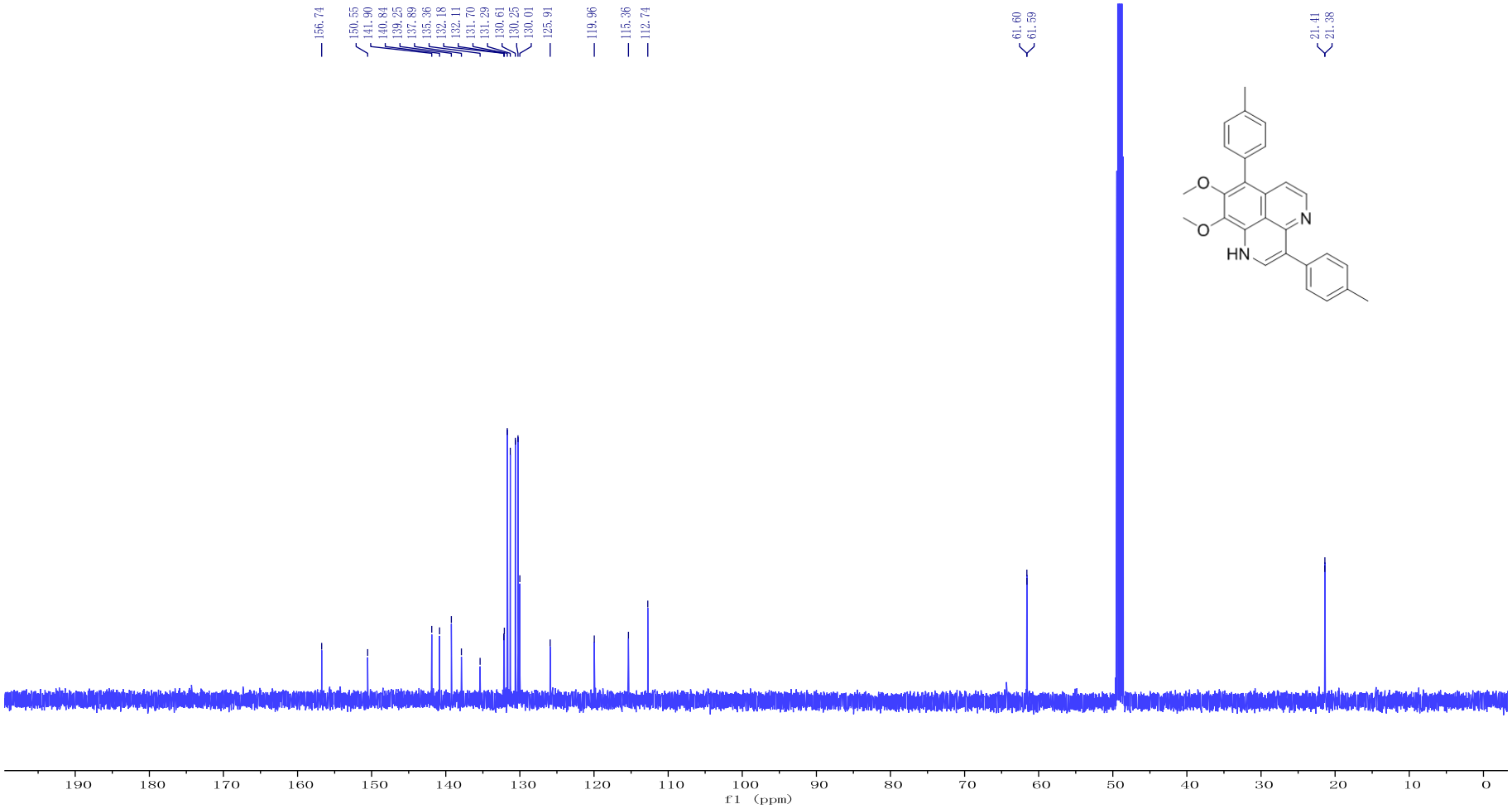


Figure S68. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 5f

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
387 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
409.1916	409.1948	-3.2	-7.8	8.5	C16 H25 N8 O5	1845.2	0.535	58.58	16	25	8	5
	409.1916	0.0	0.0	16.5	C27 H25 N2 O2	1846.6	1.981	13.79	27	25	2	2
	409.1876	4.0	9.8	12.5	C22 H25 N4 O4	1846.7	2.127	11.92	22	25	4	4
	409.1889	2.7	6.6	17.5	C23 H21 N8	1847.0	2.358	9.46	23	21	8	
	409.1956	-4.0	-9.8	20.5	C32 H25	1847.4	2.773	6.25	32	25		

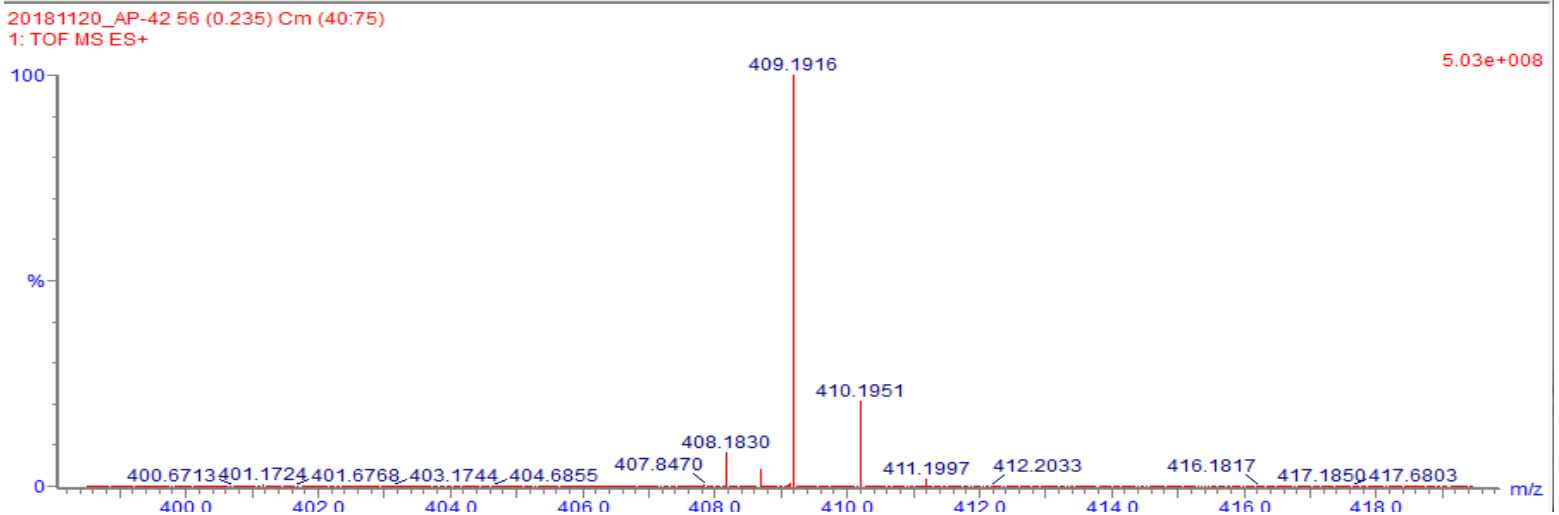


Figure S69. HRESIMS of compound 5f

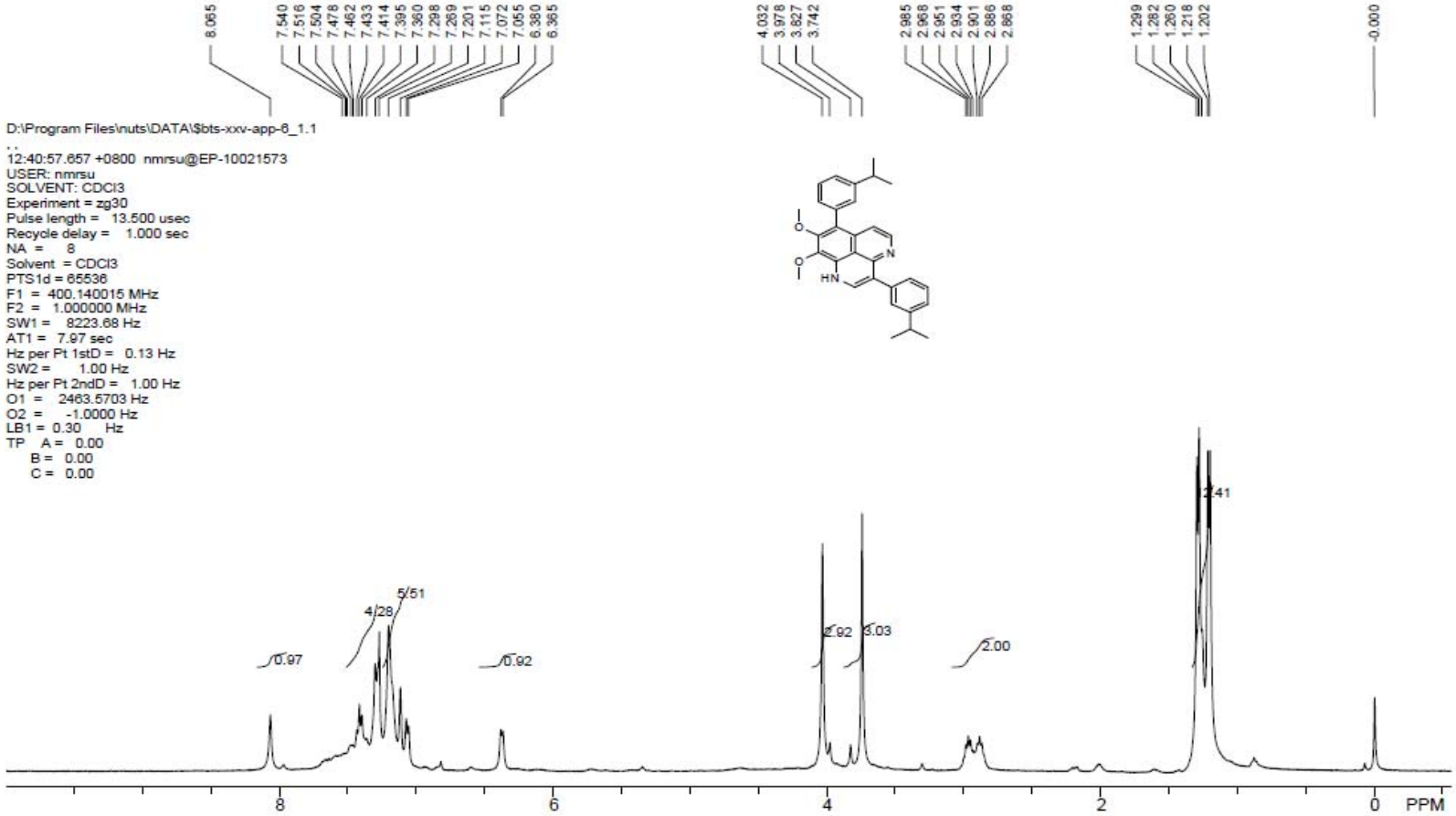


Figure S70. ^{1}H NMR spectrum (400 MHz, CD_3Cl) of compound 5g

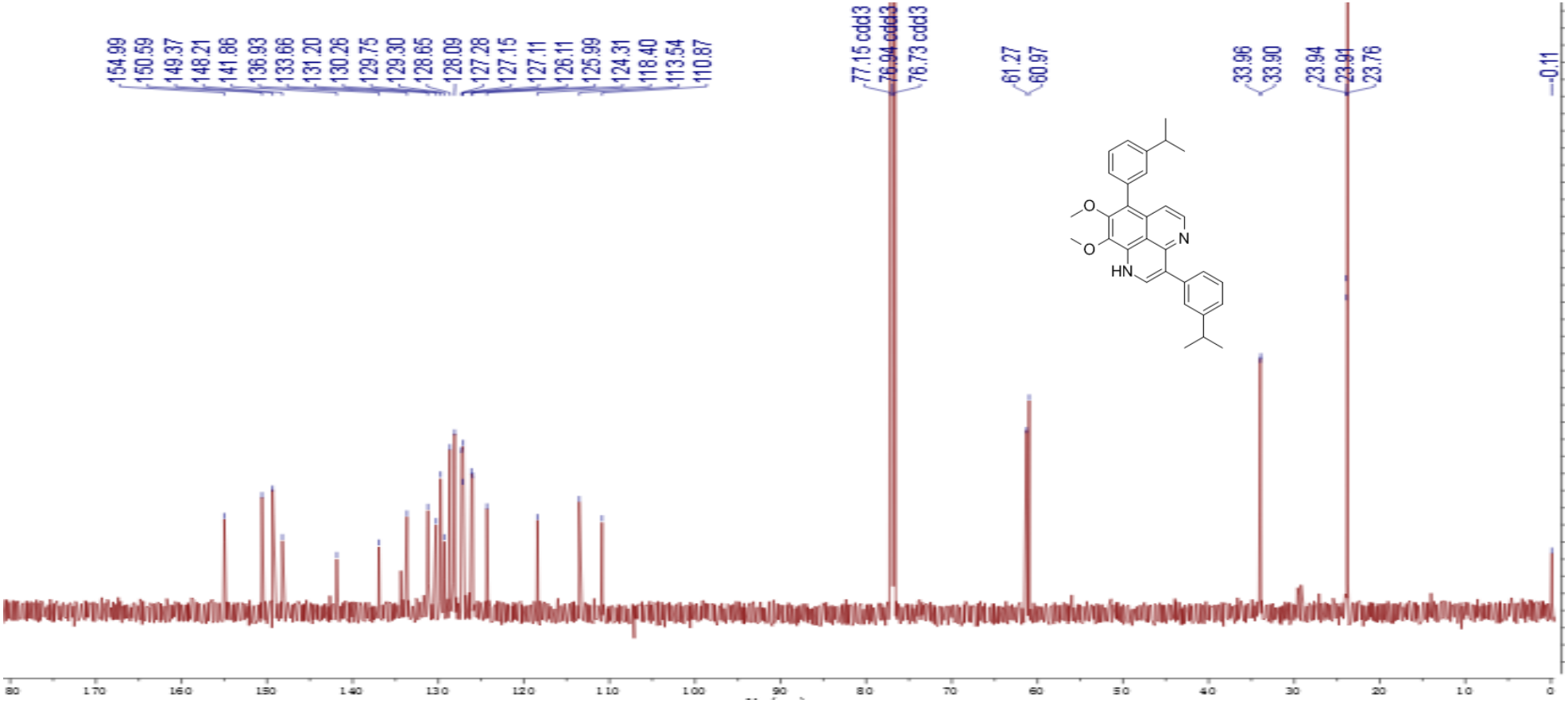


Figure S71. ^{13}C NMR spectrum (100 MHz, CD_3Cl) of compound 5g

Single Mass Analysis
Tolerance = 10.0 PPM / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
627 formula(e) evaluated with 5 results within limits (up to 50 closest results for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
465.2544	465.2542	0.2	0.4	16.5	C31 H33 N2 O2	2395.3	0.030	97.05	31	33	2	2
	465.2502	4.2	9.0	12.5	C26 H33 N4 O4	2398.9	3.655	2.59	26	33	4	4
	465.2561	-1.7	-3.7	3.5	C19 H37 N4 O9	2401.5	6.274	0.19	19	37	4	9
	465.2582	-3.8	-8.2	20.5	C36 H33	2402.2	6.958	0.10	36	33		
	465.2547	-0.3	-0.6	-1.5	C18 H41 O13	2402.4	7.153	0.08	18	41		13

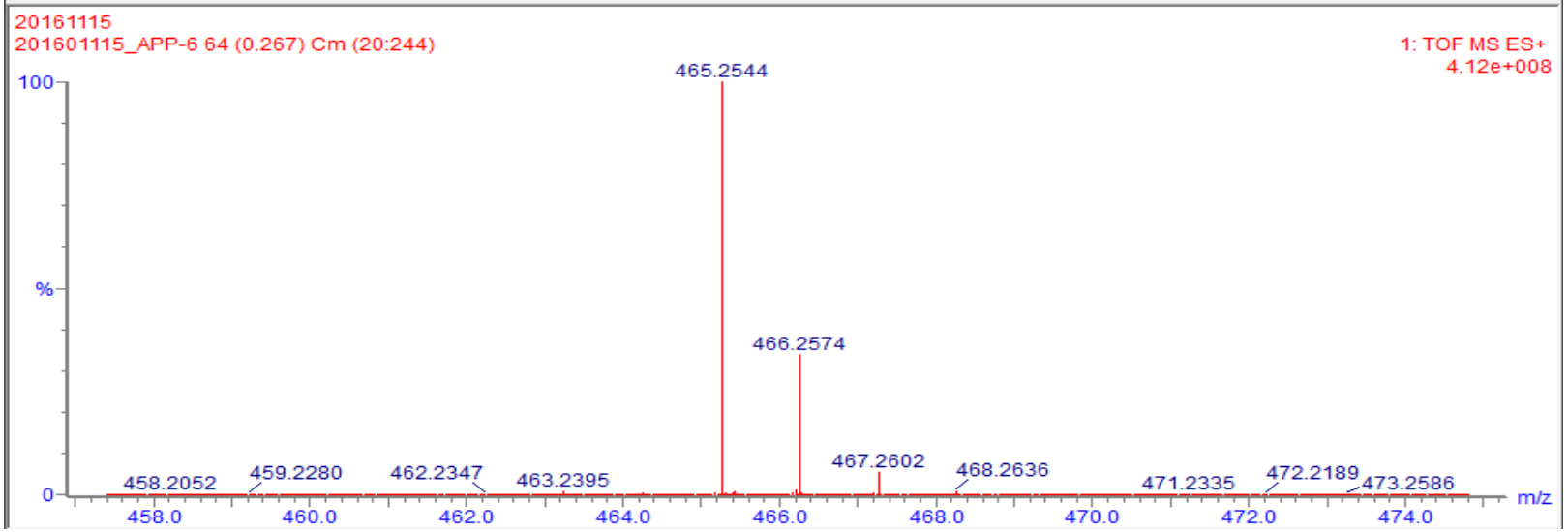


Figure S72. HRESIMS of compound 5g

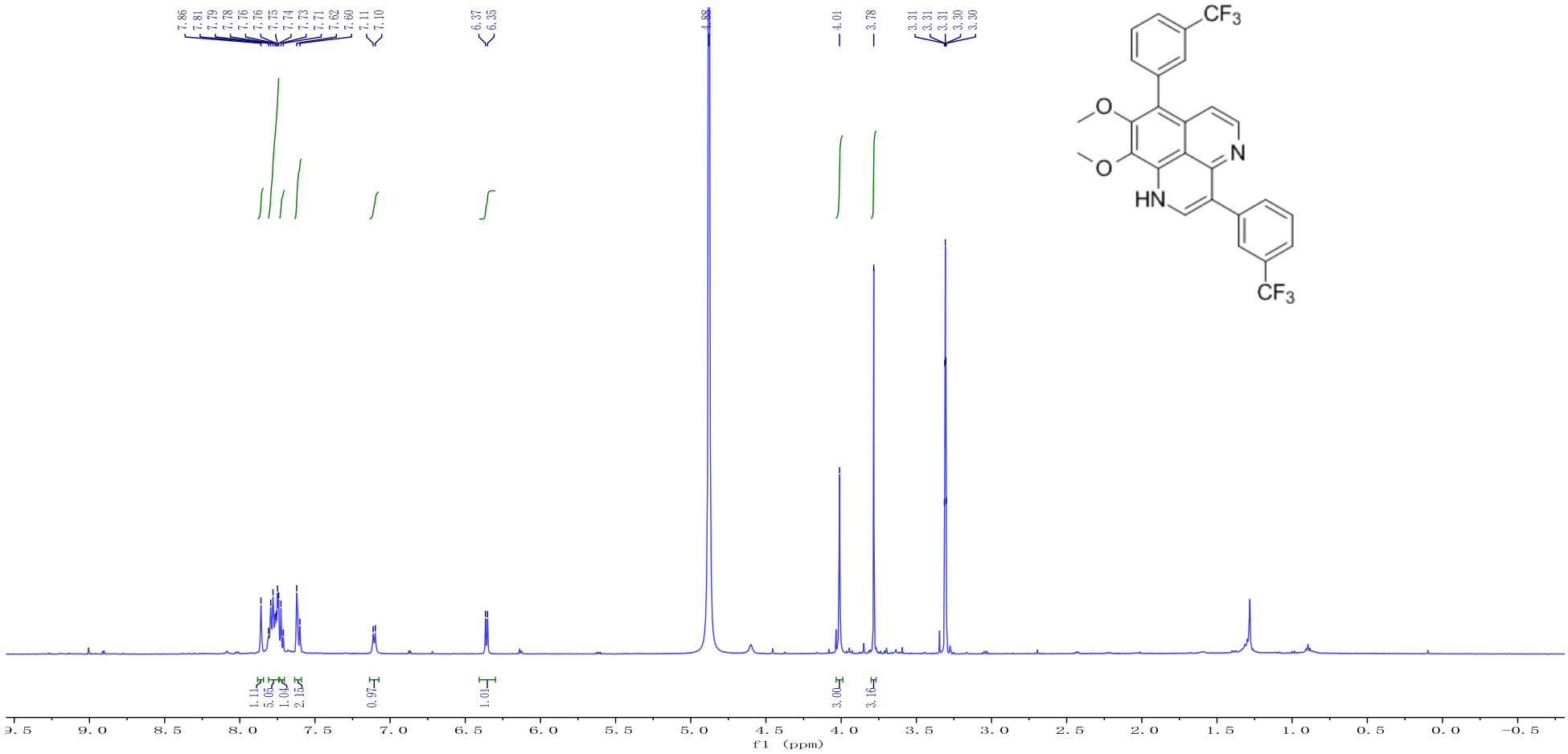


Figure S73. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 5h

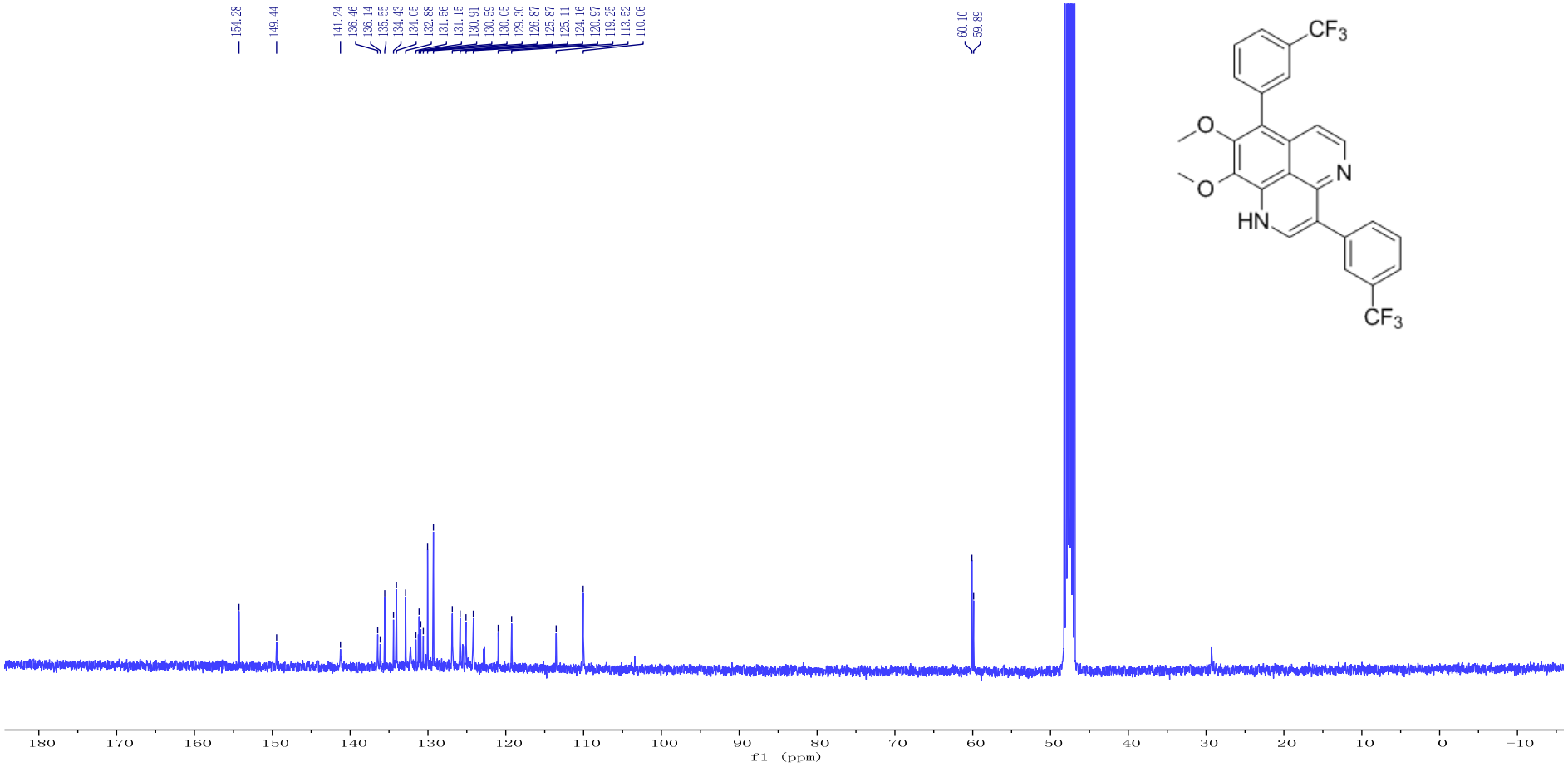


Figure S74. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 5h

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
349 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	RA	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O	F
517.1354	100.00	517.1351	0.3	0.6	16.5	C27 H19 N2 O2 F6	1740.4	0.150	86.05	27	19	2	2	6
		517.1324	3.0	5.8	17.5	C23 H15 N8 F6	1742.8	2.616	7.31	23	15	8		6
		517.1391	-3.7	-7.2	20.5	C32 H19 F6	1743.3	3.096	4.52	32	19			6
		517.1310	4.4	8.5	12.5	C22 H19 N4 O4 F6	1744.4	4.144	1.59	22	19	4	4	6
		517.1383	-2.9	-5.6	8.5	C16 H19 N8 O5 F6	1745.4	5.222	0.54	16	19	8	5	6

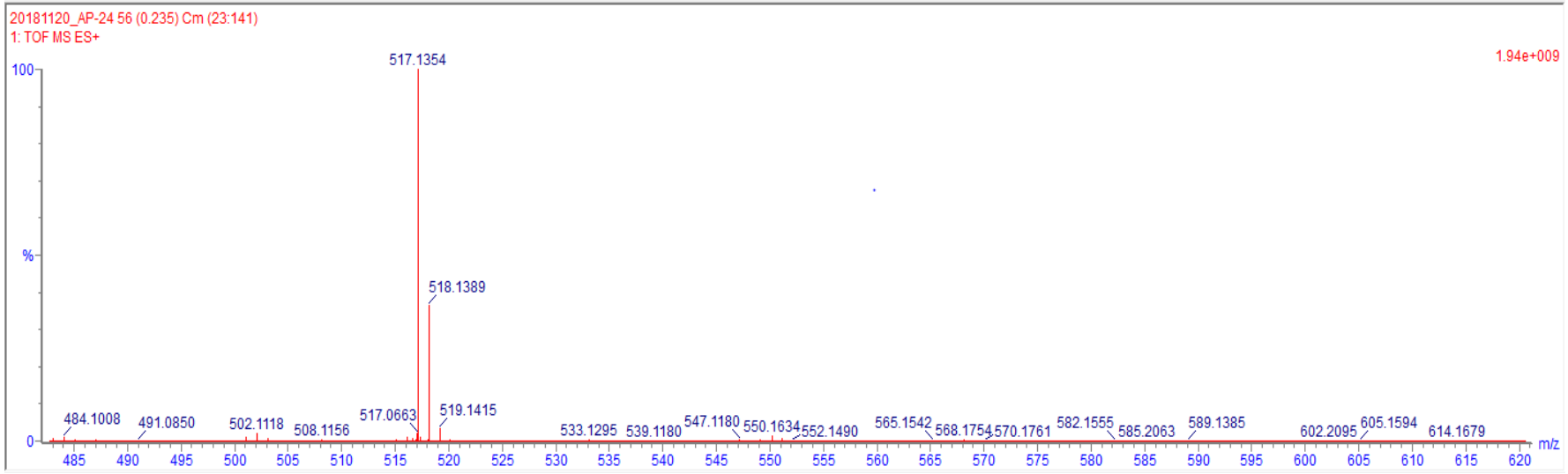


Figure S75. HRESIMS of compound 5h

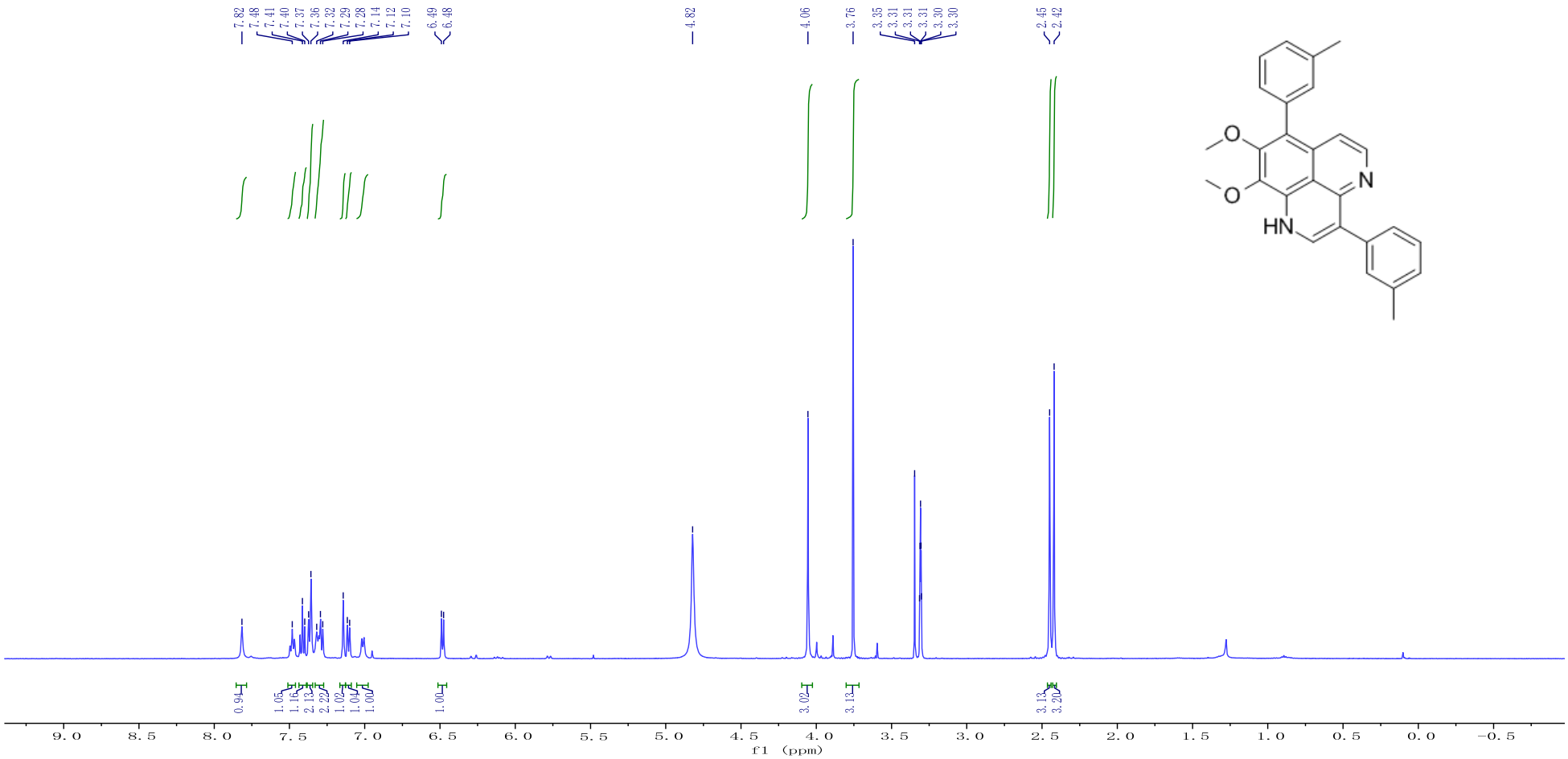


Figure S76. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 5i

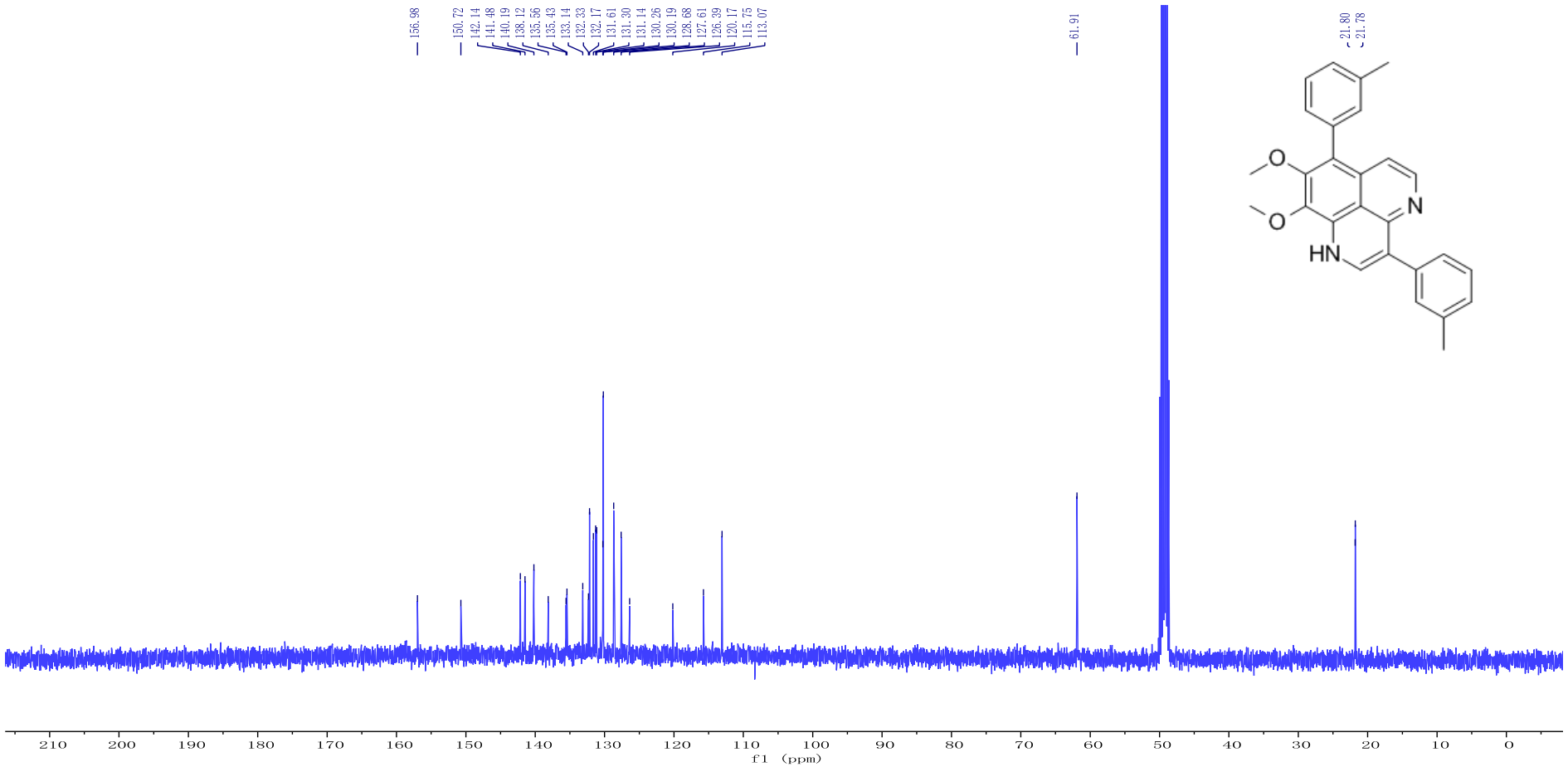


Figure S77. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 5i

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
387 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
409.1916	409.1916	0.0	0.0	16.5	C27 H25 N2 O2	2075.4	0.271	76.24	27	25	2	2
	409.1889	2.7	6.6	17.5	C23 H21 N8	2077.0	1.915	14.73	23	21	8	
	409.1956	-4.0	-9.8	20.5	C32 H25	2078.1	3.013	4.91	32	25		
	409.1876	4.0	9.8	12.5	C22 H25 N4 O4	2078.5	3.393	3.36	22	25	4	4
	409.1948	-3.2	-7.8	8.5	C16 H25 N8 O5	2080.0	4.880	0.76	16	25	8	5

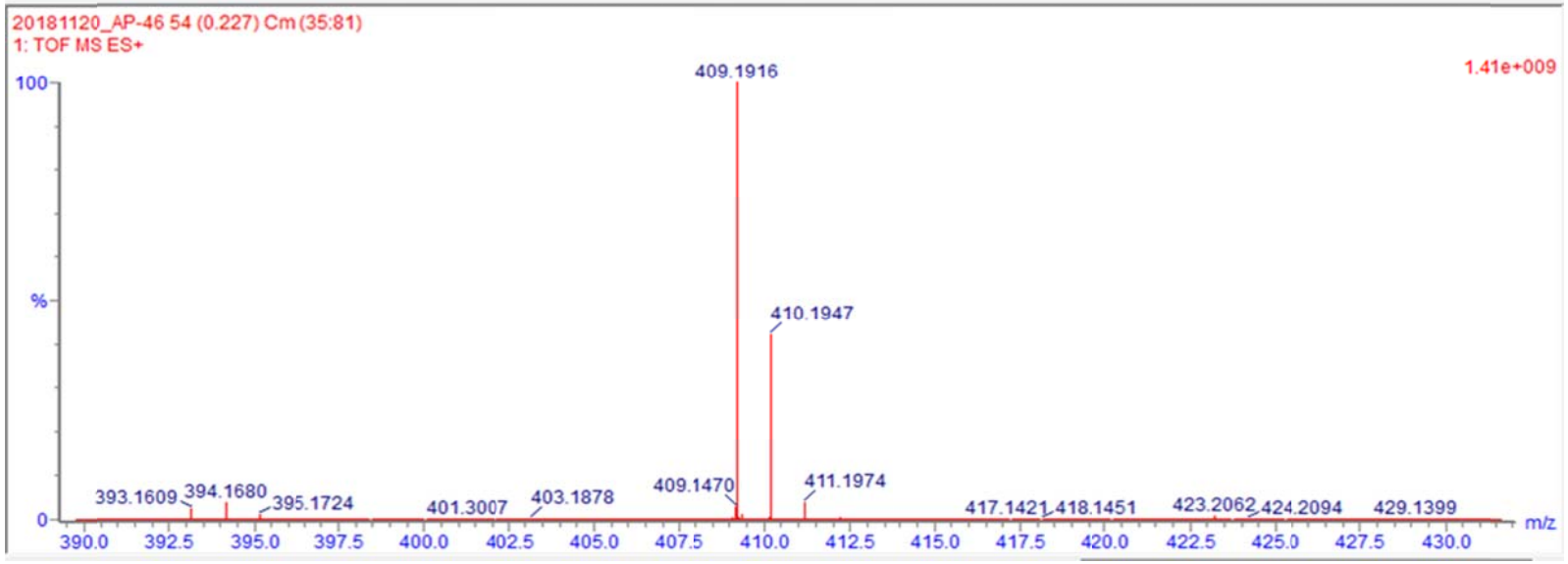


Figure S78. HRESIMS of compound 5i

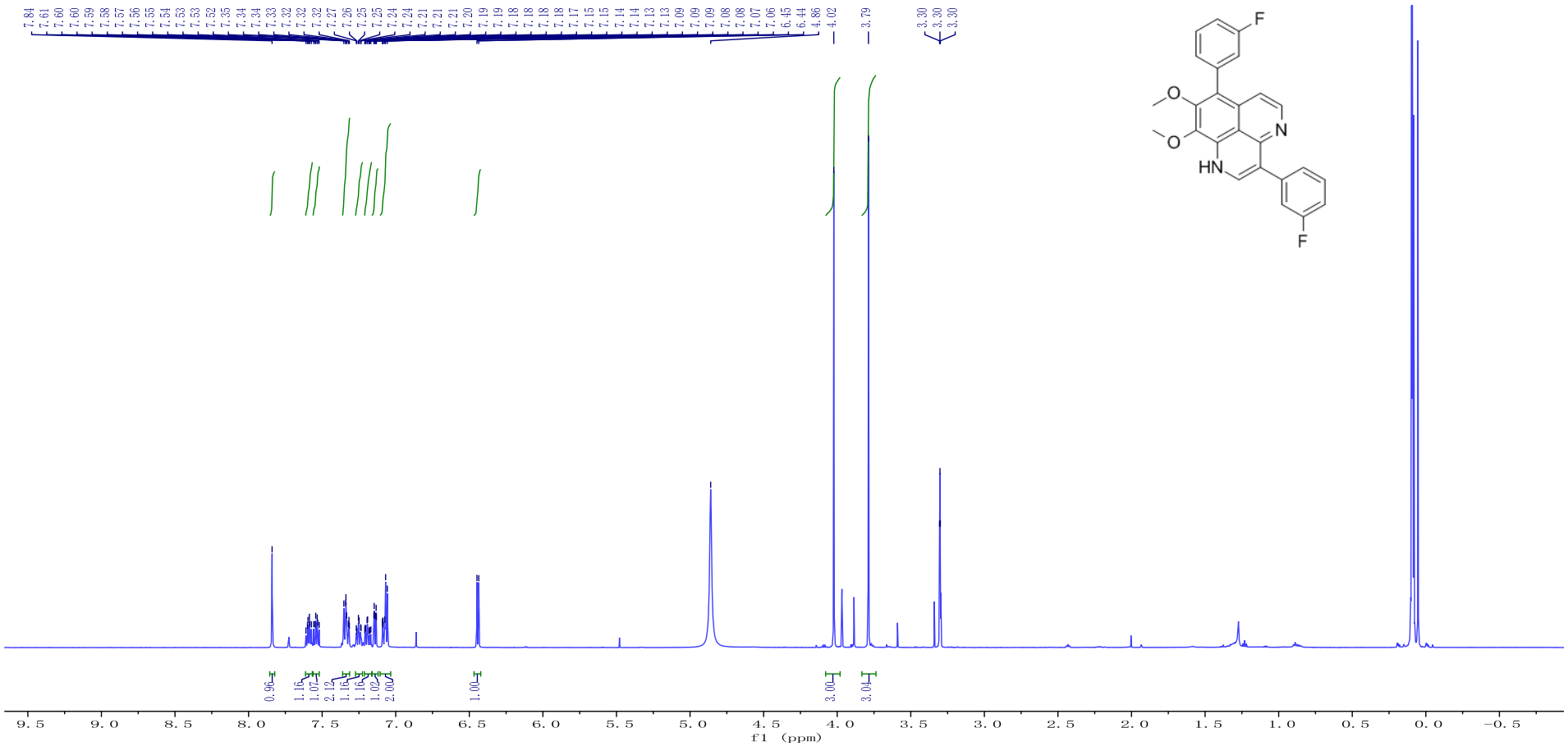


Figure S79. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 5j

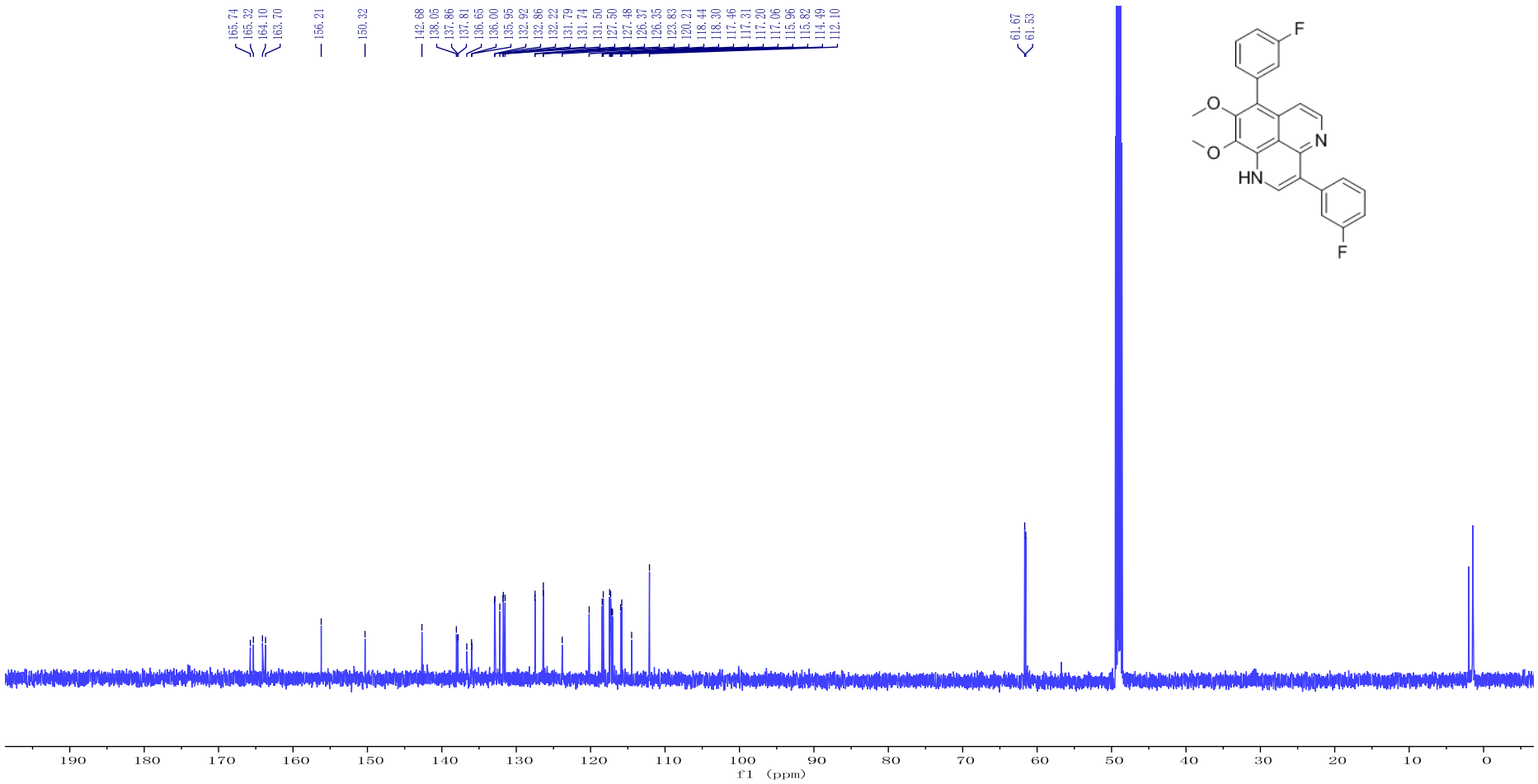


Figure S80. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 5j

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
348 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	RA	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O	F
417.1413	100.00	417.1415	-0.2	-0.5	16.5	C25 H19 N2 O2 F2	1776.3	0.634	53.03	25	19	2	2	2
		417.1446	-3.3	-7.9	8.5	C14 H19 N8 O5 F2	1777.4	1.703	18.22	14	19	8	5	2
		417.1388	2.5	6.0	17.5	C21 H15 N8 F2	1777.5	1.795	16.61	21	15	8		2
		417.1374	3.9	9.3	12.5	C20 H19 N4 O4 F2	1777.8	2.178	11.32	20	19	4	4	2
		417.1455	-4.2	-10.1	20.5	C30 H19 F2	1780.5	4.807	0.82	30	19			2

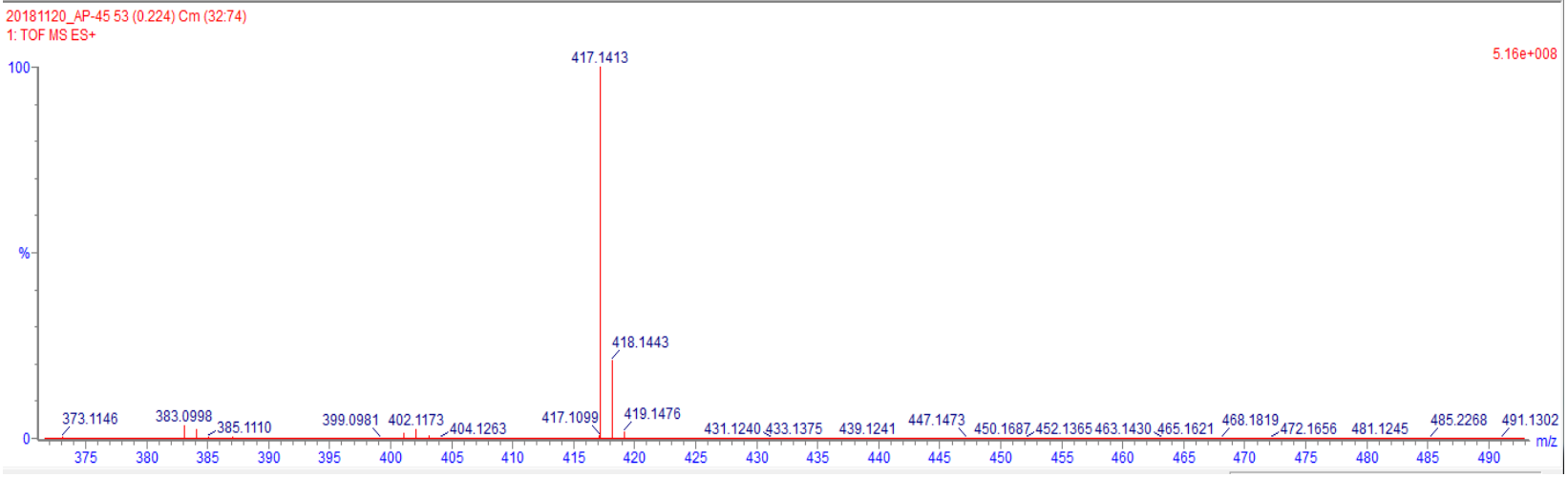


Figure S81. HRESIMS of compound 5j

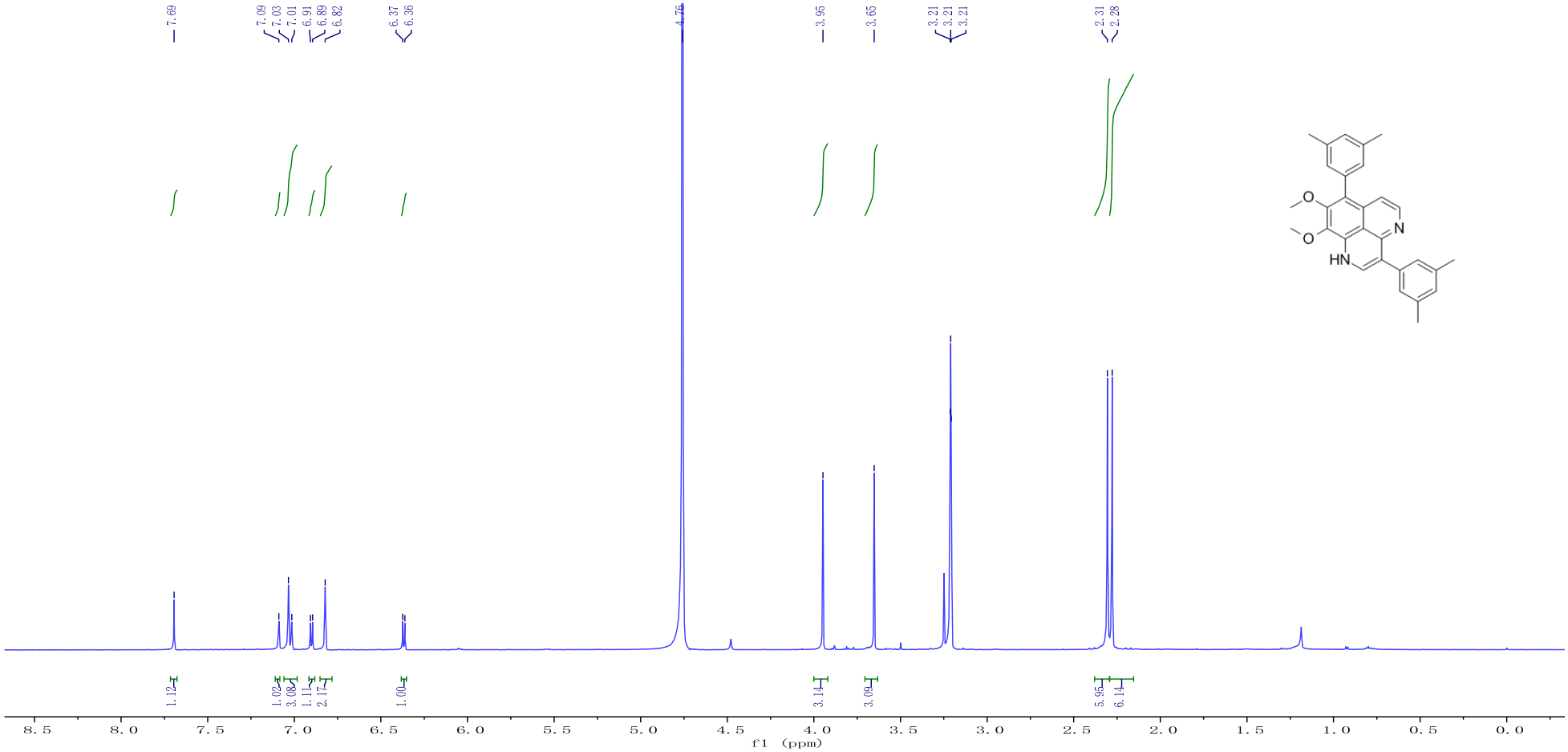


Figure S82. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 5k

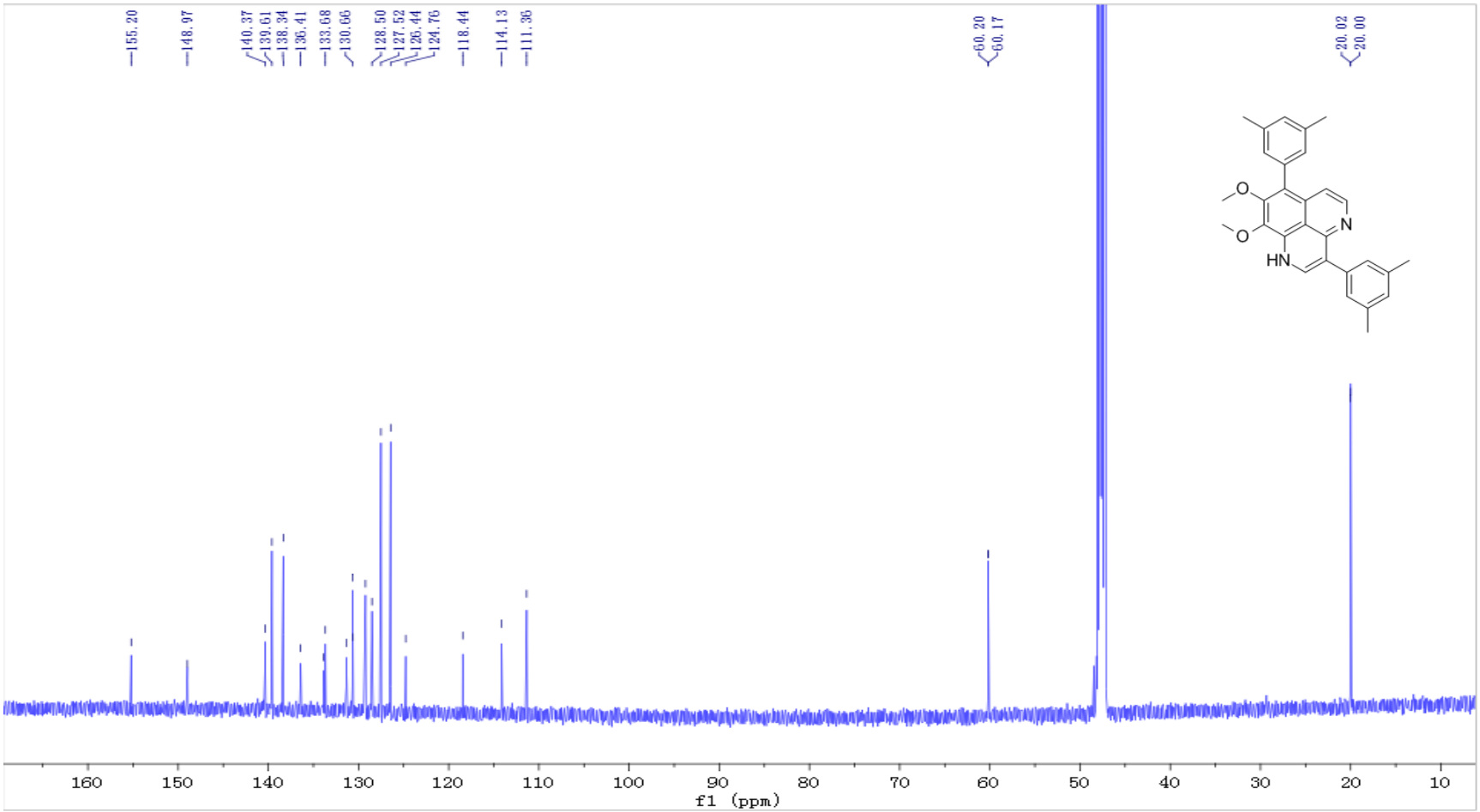


Figure S83. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 5k

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
414 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
437.2226	437.2261	-3.5	-8.0	8.5	C18 H29 N8 O5	1554.5	0.609	54.41	18	29	8	5
	437.2229	-0.3	-0.7	16.5	C29 H29 N2 O2	1555.4	1.531	21.62	29	29	2	2
	437.2202	2.4	5.5	17.5	C25 H25 N8	1555.8	1.939	14.39	25	25	8	
	437.2189	3.7	8.5	12.5	C24 H29 N4 O4	1556.2	2.374	9.31	24	29	4	4
	437.2269	-4.3	-9.8	20.5	C34 H29	1559.8	5.929	0.27	34	29		

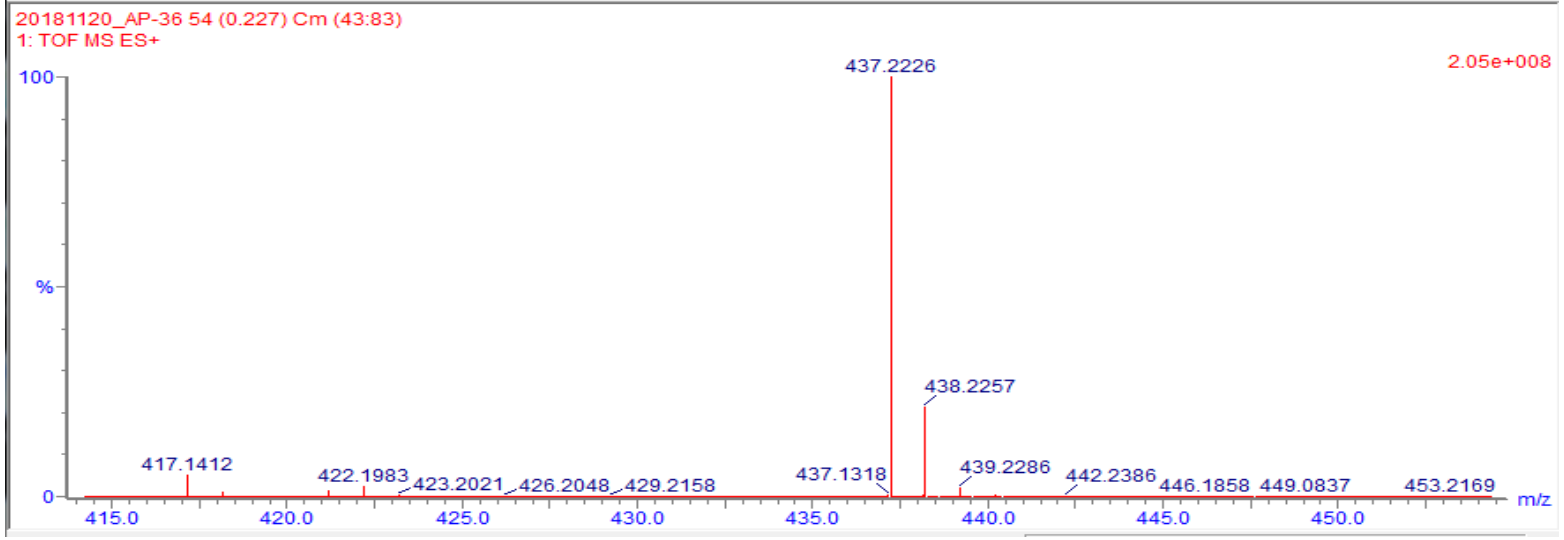


Figure S84. HRESIMS of compound 5k

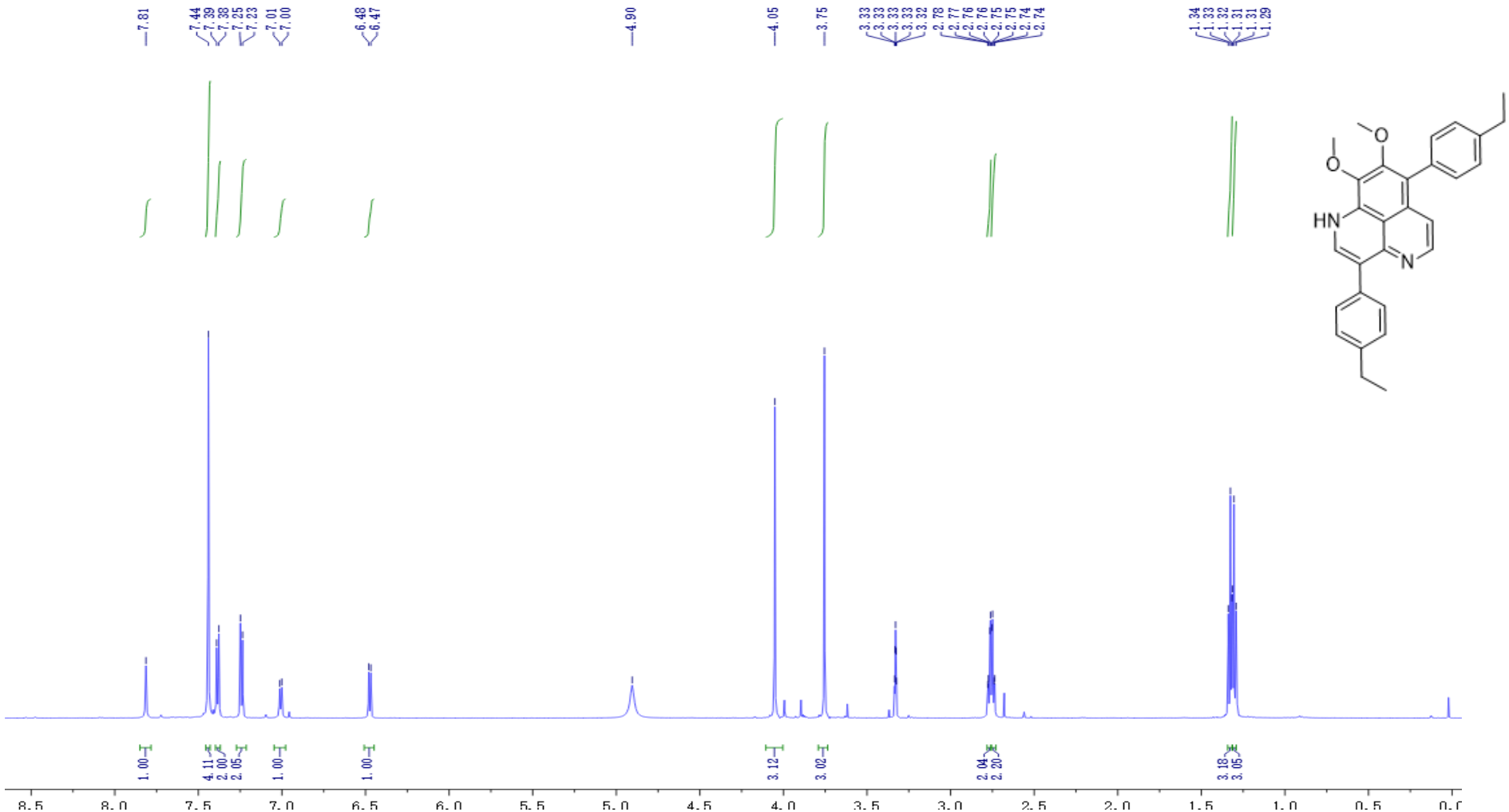


Figure S85. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 5l

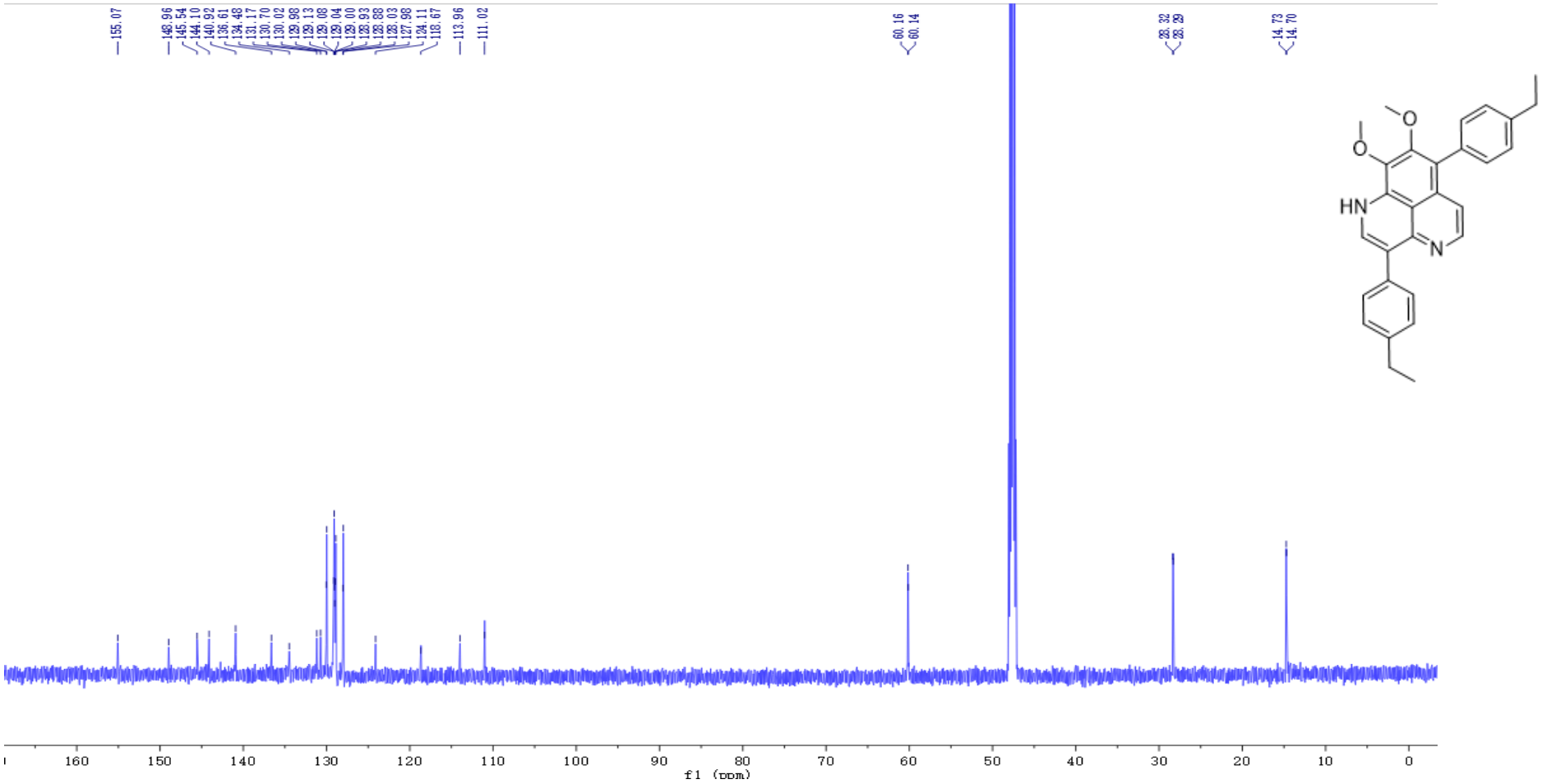


Figure S86. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 5l

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
414 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
437.2231	437.2229	0.2	0.5	16.5	C29 H29 N2 O2	1079.0	0.598	54.98	29	29	2	2
	437.2261	-3.0	-6.9	8.5	C18 H29 N8 O5	1080.1	1.717	17.96	18	29	8	5
	437.2202	2.9	6.6	17.5	C25 H25 N8	1080.3	1.902	14.92	25	25	8	
	437.2189	4.2	9.6	12.5	C24 H29 N4 O4	1081.1	2.714	6.62	24	29	4	4
	437.2269	-3.8	-8.7	20.5	C34 H29	1081.3	2.897	5.52	34	29		

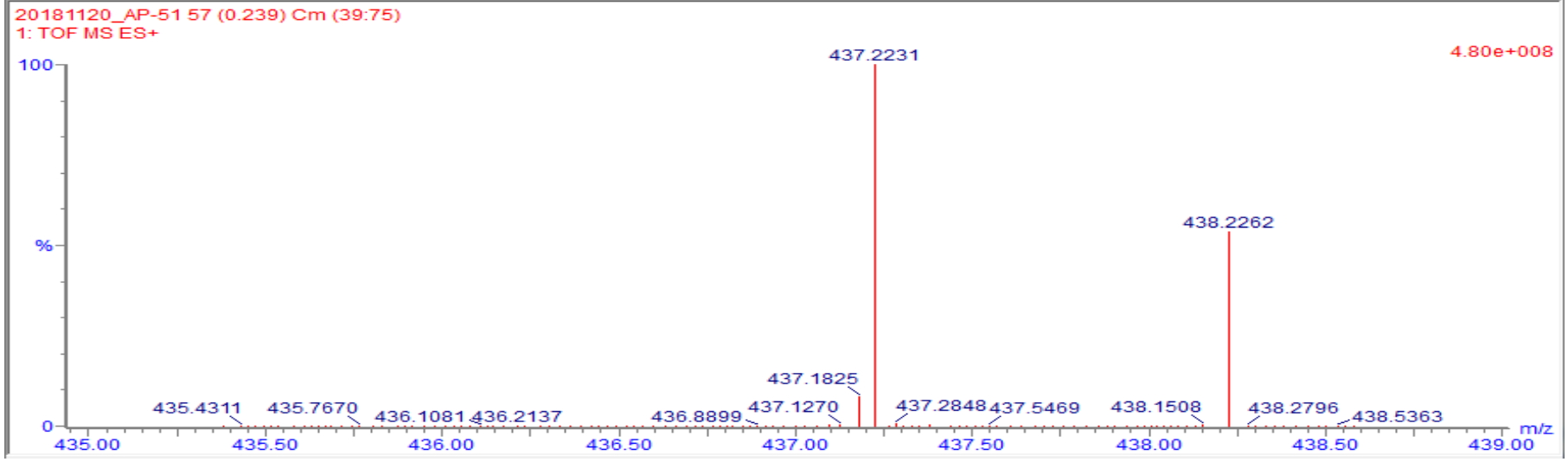


Figure S87. HRESIMS of compound 5l

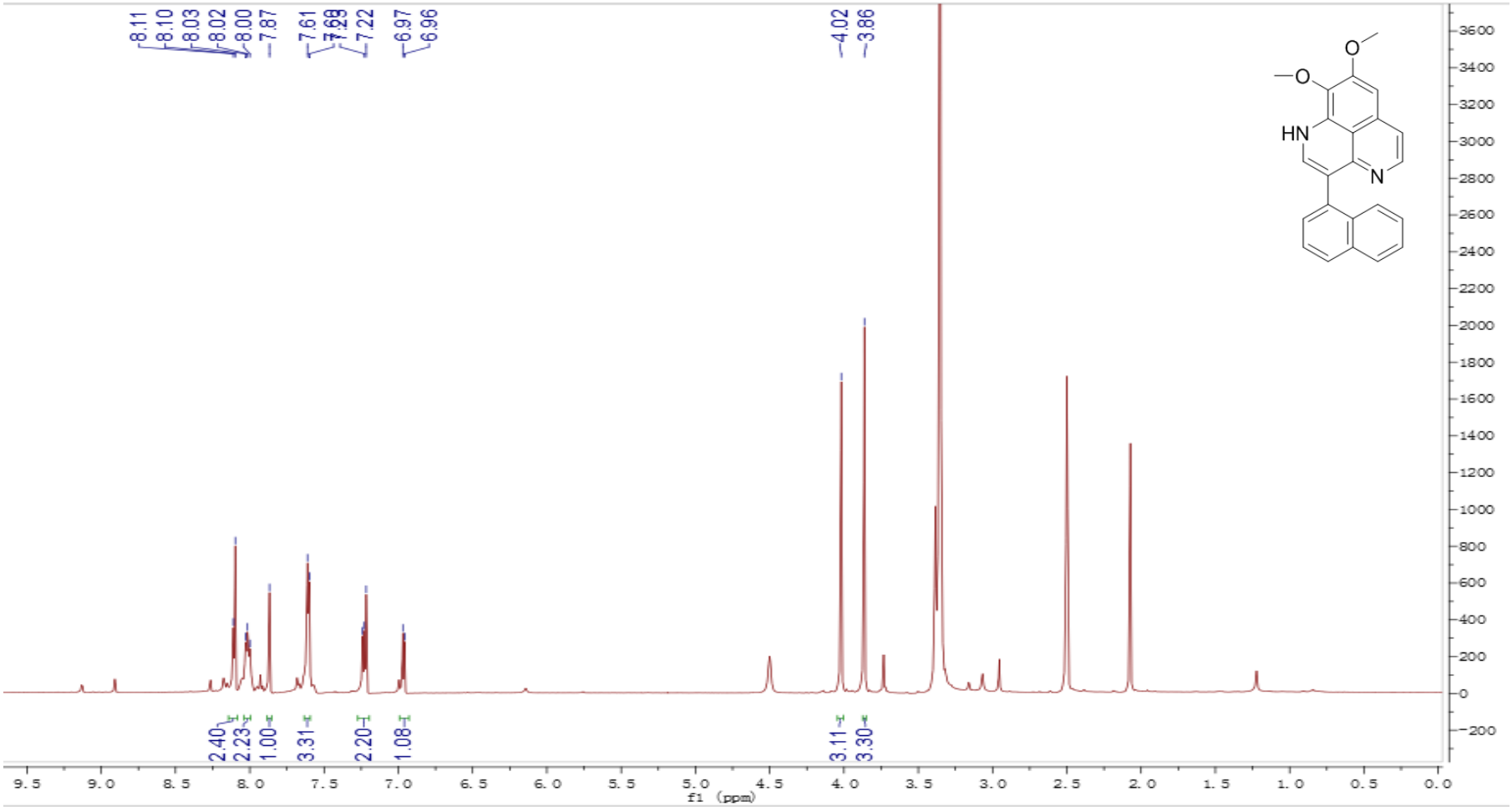


Figure S88. ^{1}H NMR spectrum of (500 MHz, DMSO-d_6) of compound 6a

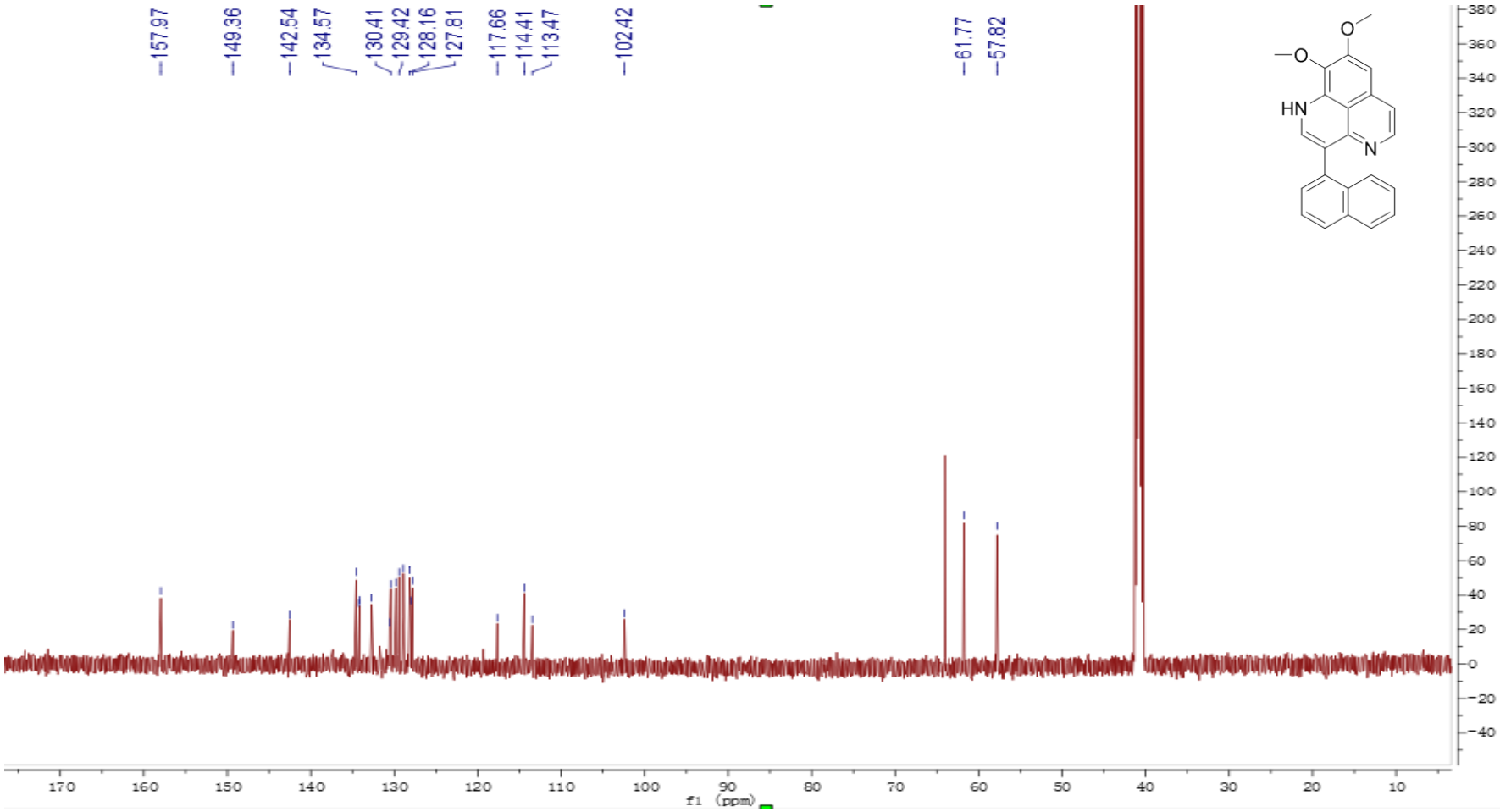


Figure S89. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of compound 6a

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
335 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
355.1449	355.1447	0.2	0.6	15.5	C23 H19 N2 O2	1509.2	0.622	53.71	23	19	2	2
	355.1478	-2.9	-8.2	7.5	C12 H19 N8 O5	1509.9	1.286	27.65	12	19	8	5
	355.1406	4.3	12.1	11.5	C18 H19 N4 O4	1511.2	2.559	7.74	18	19	4	4
	355.1487	-3.8	-10.7	19.5	C28 H19	1511.5	2.867	5.69	28	19		
	355.1420	2.9	8.2	16.5	C19 H15 N8	1511.6	2.955	5.21	19	15	8	

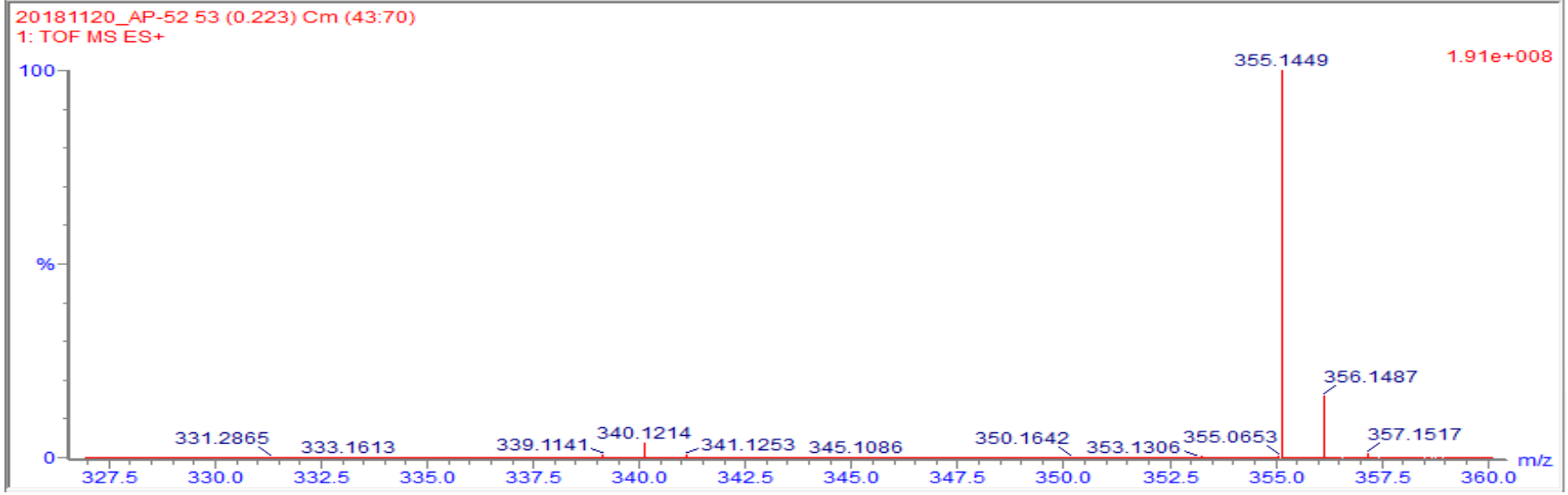


Figure S90. HRESIMS of compound 6a

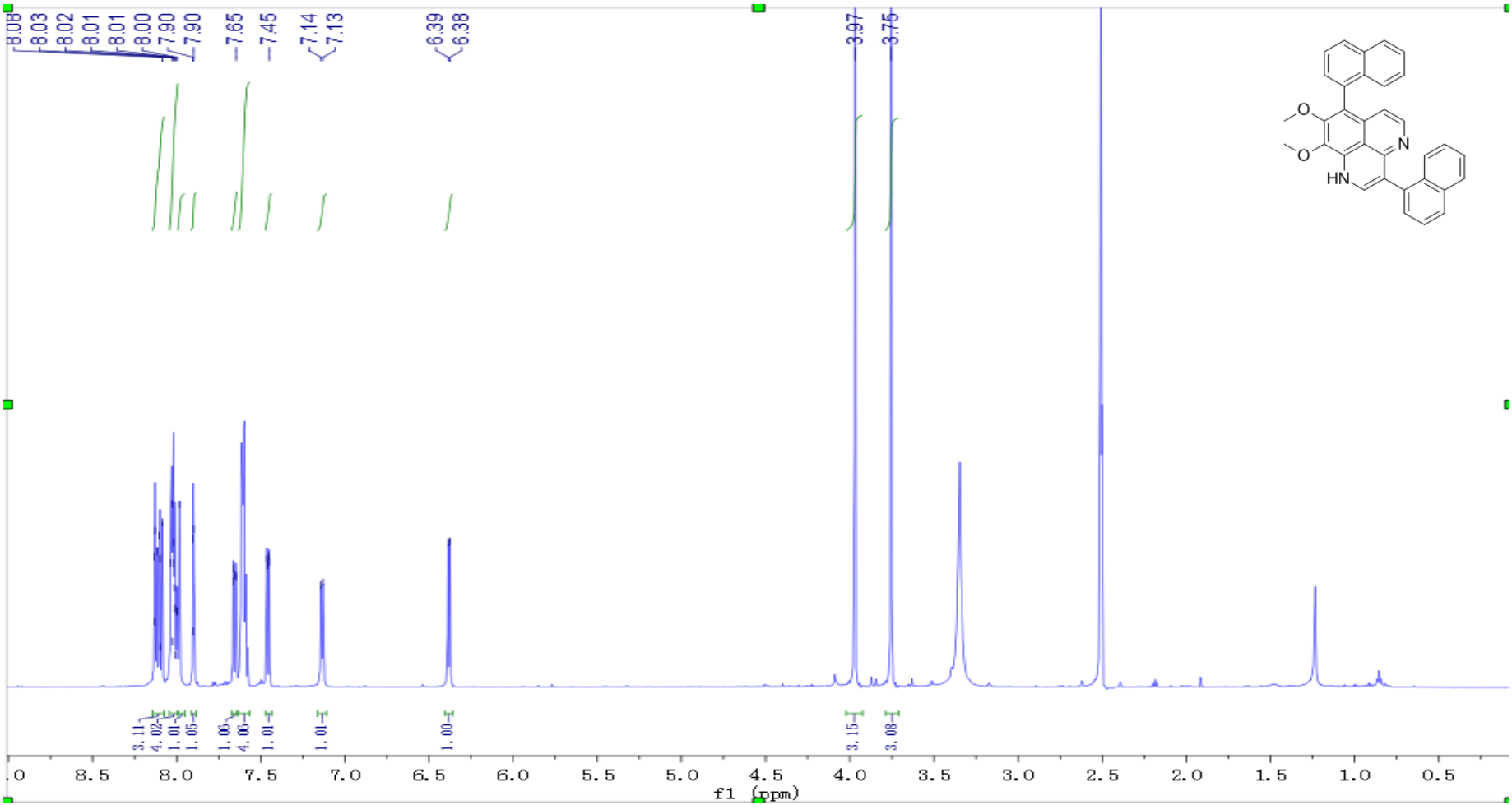


Figure S91. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of compound 6b

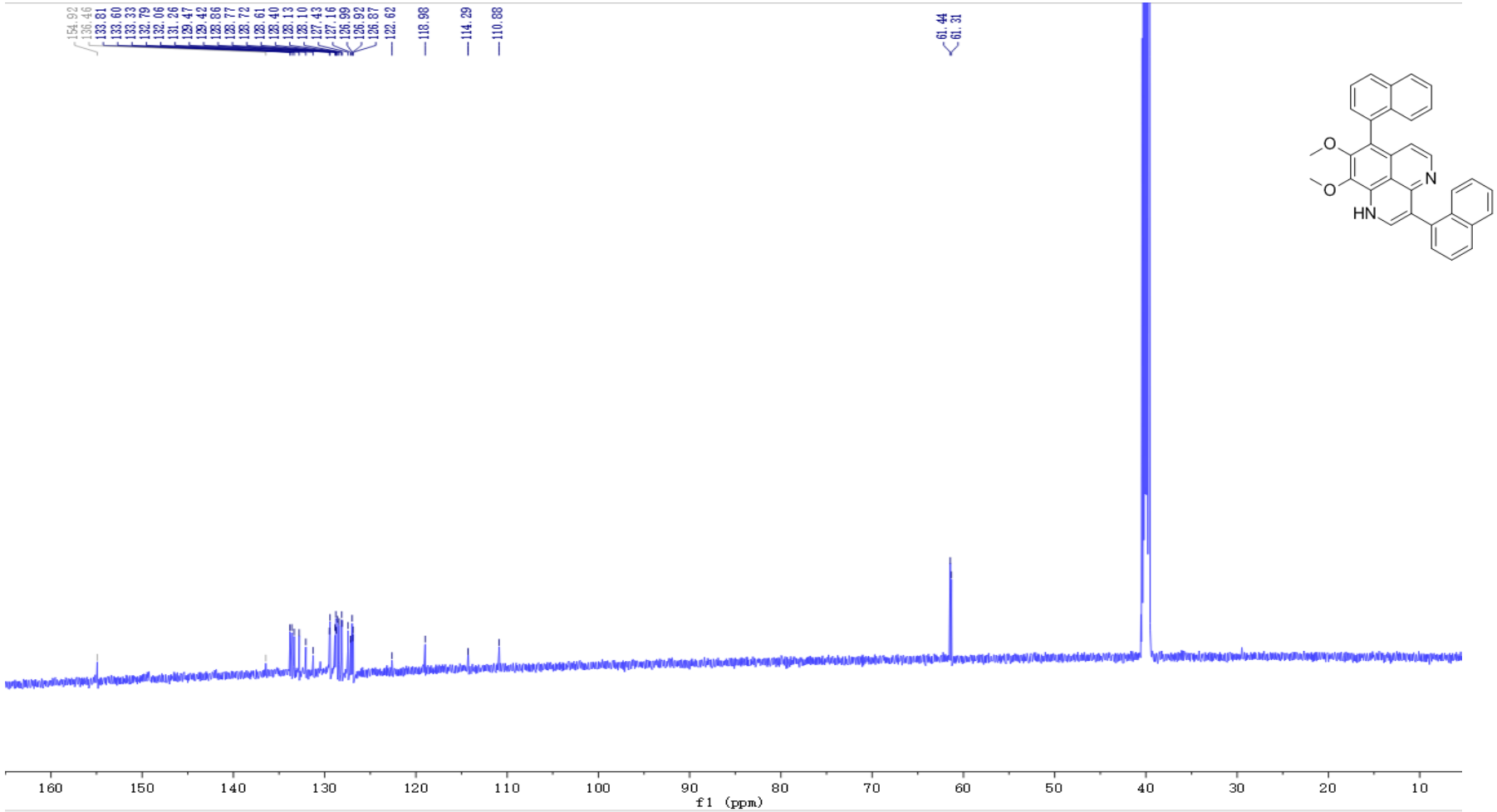
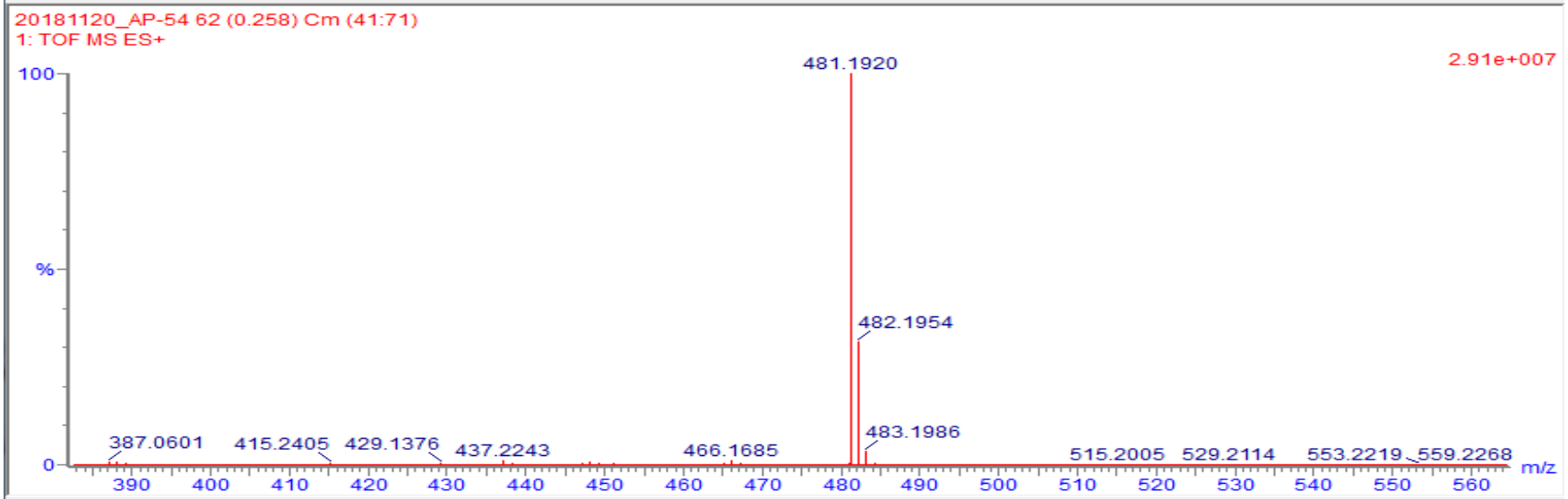


Figure S92. ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of compound 6b

Single Mass Analysis
Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3
Monoisotopic Mass, Even Electron Ions
455 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)
Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
481.1920	481.1916	0.4	0.8	22.5	C33 H25 N2 O2	1196.1	0.765	46.55	33	25	2	2
	481.1948	-2.8	-5.8	14.5	C22 H25 N8 O5	1196.5	1.177	30.83	22	25	8	5
	481.1889	3.1	6.4	23.5	C29 H21 N8	1197.3	2.014	13.34	29	21	8	
	481.1876	4.4	9.1	18.5	C28 H25 N4 O4	1197.9	2.555	7.77	28	25	4	4
	481.1956	-3.6	-7.5	26.5	C38 H25	1199.5	4.191	1.51	38	25		



For Help, press F1

Figure S93. HRESIMS of compound 6b

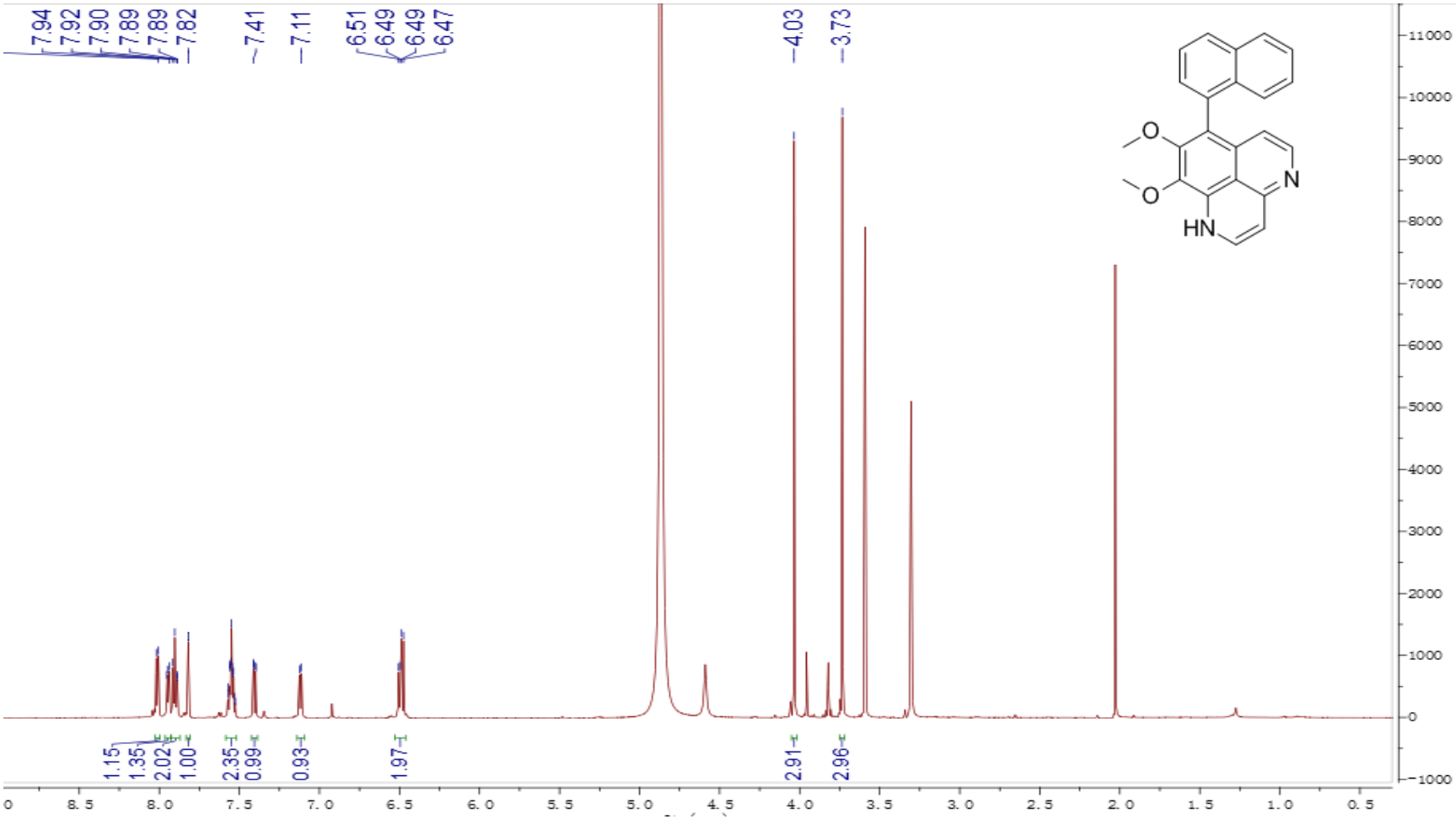


Figure S94. ^{1}H NMR spectrum (500 MHz, CD_3OD) of compound 6c

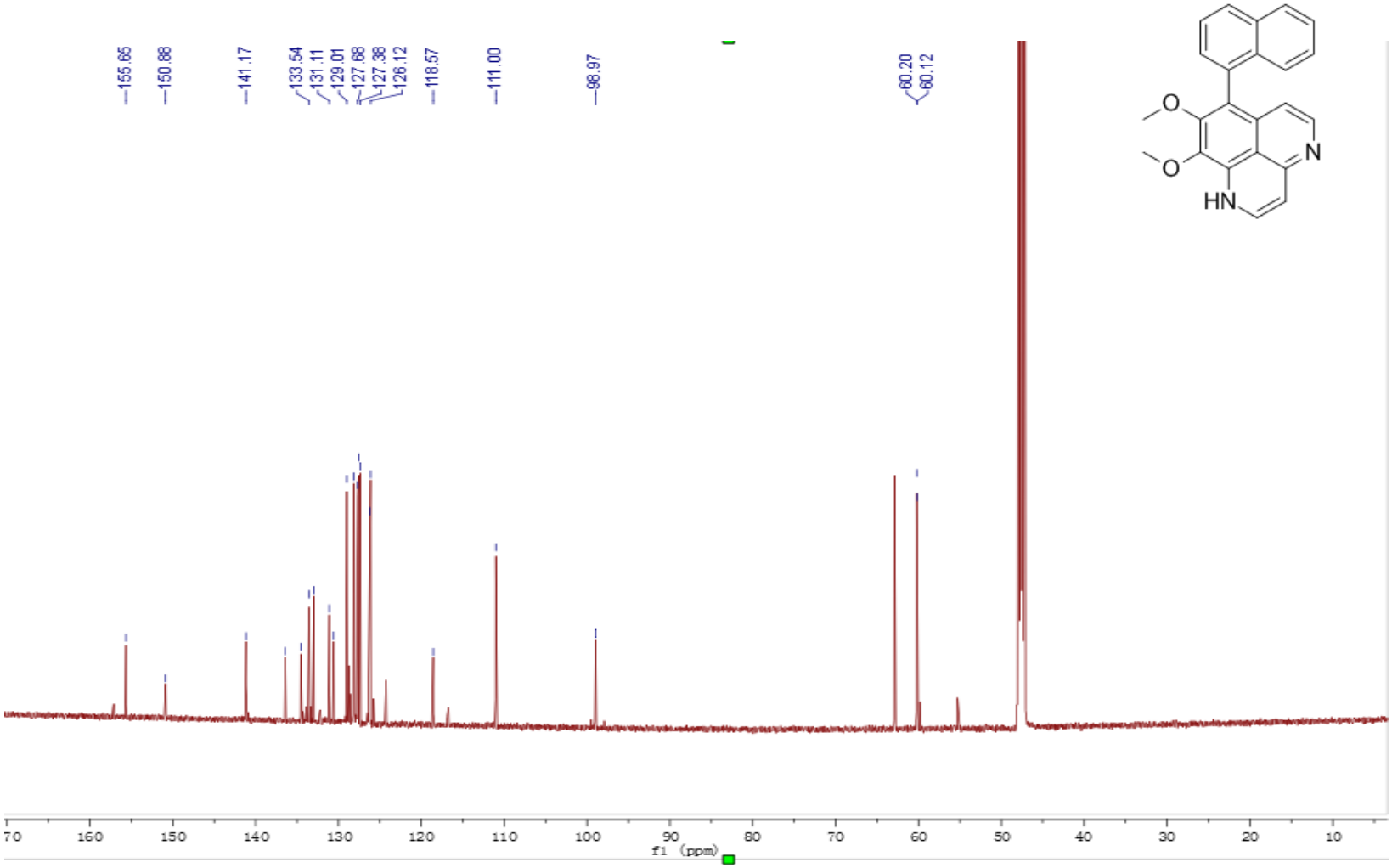


Figure S95. ^{13}C NMR spectrum (125 MHz, CD_3OD) of compound 6c

Single Mass Analysis

Tolerance = 5.0 mDa / DBE: min = -1.5, max = 50.0

Element prediction: Off

Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions

335 formula(e) evaluated with 5 results within limits (up to 50 best isotopic matches for each mass)

Elements Used:

Mass	Calc. Mass	mDa	PPM	DBE	Formula	i-FIT	i-FIT Norm	Fit Conf %	C	H	N	O
355.1453	355.1478	-2.5	-7.0	7.5	C12 H19 N8 O5	1626.6	0.201	81.77	12	19	8	5
	355.1447	0.6	1.7	15.5	C23 H19 N2 O2	1628.8	2.437	8.74	23	19	2	2
	355.1406	4.7	13.2	11.5	C18 H19 N4 O4	1629.3	2.950	5.23	18	19	4	4
	355.1420	3.3	9.3	16.5	C19 H15 N8	1629.6	3.199	4.08	19	15	8	
	355.1487	-3.4	-9.6	19.5	C28 H19	1632.8	6.386	0.17	28	19		

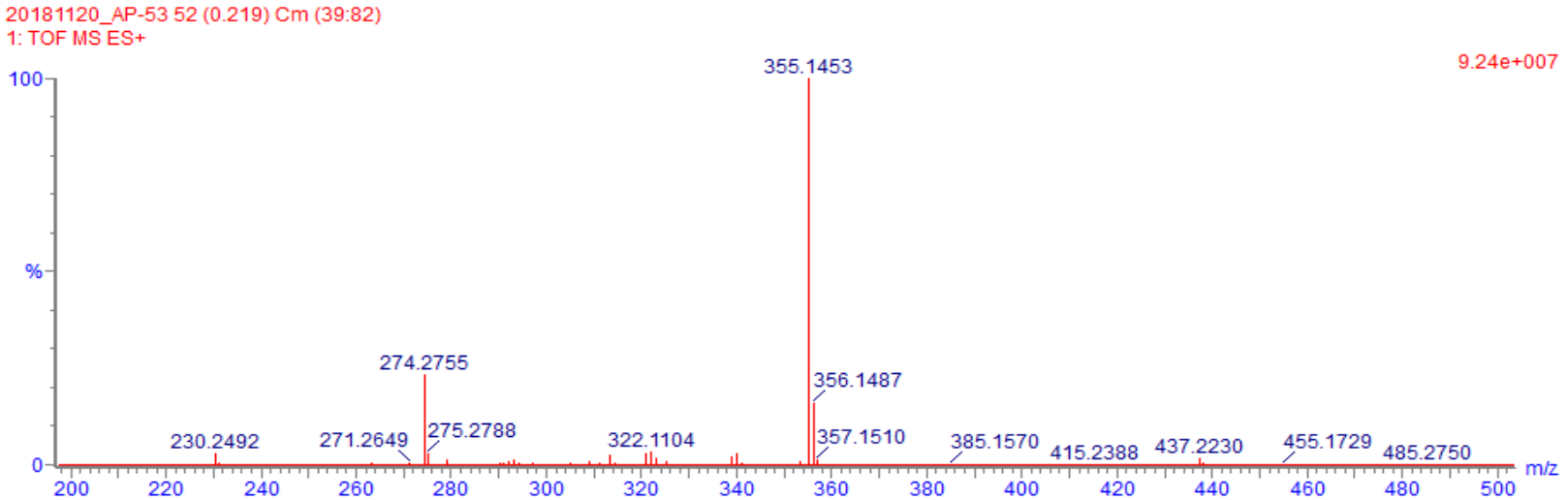


Figure S96. HRESIMS of compound 6c

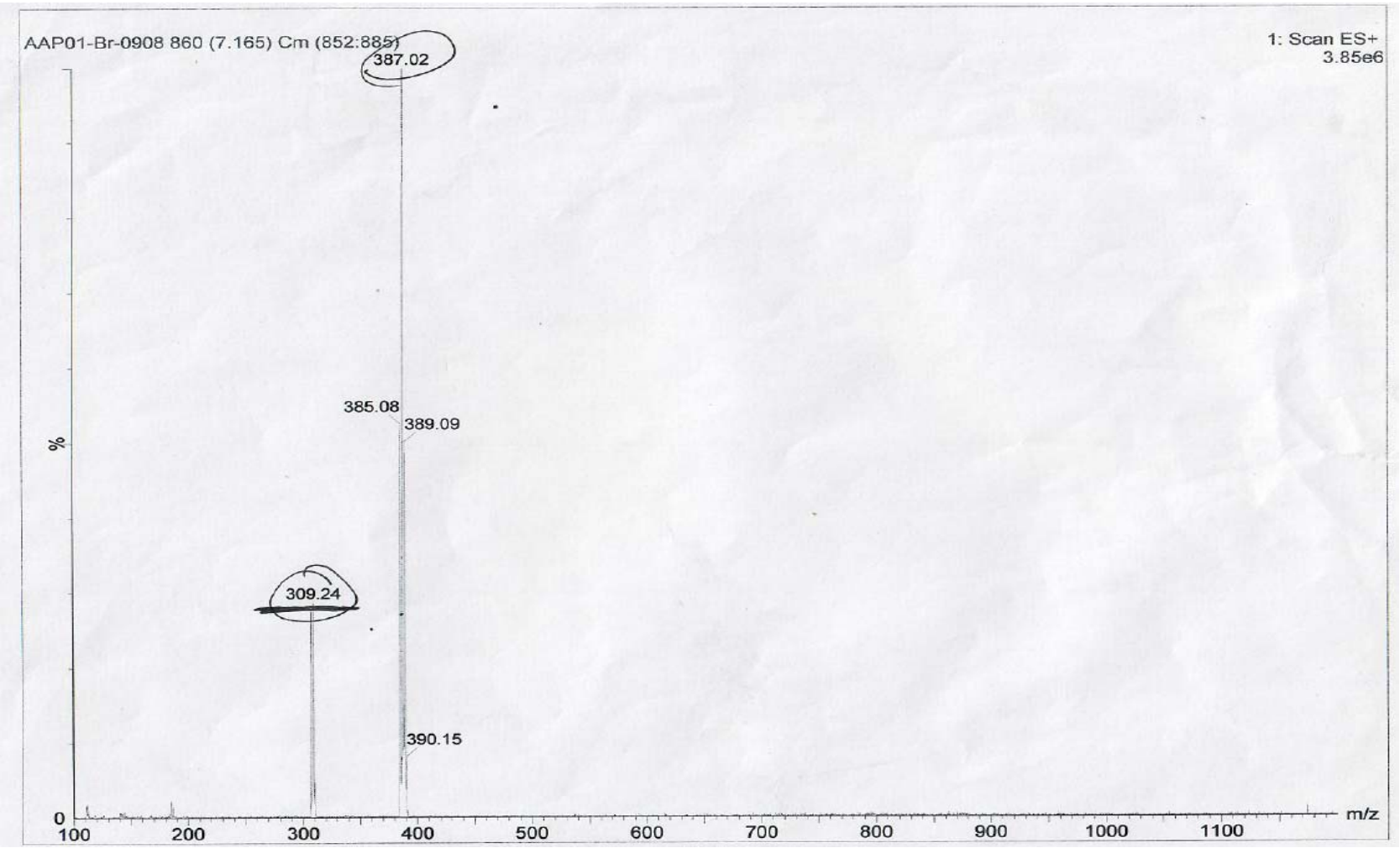


Figure S97. ESIMS of brominated aaptamine intermediate

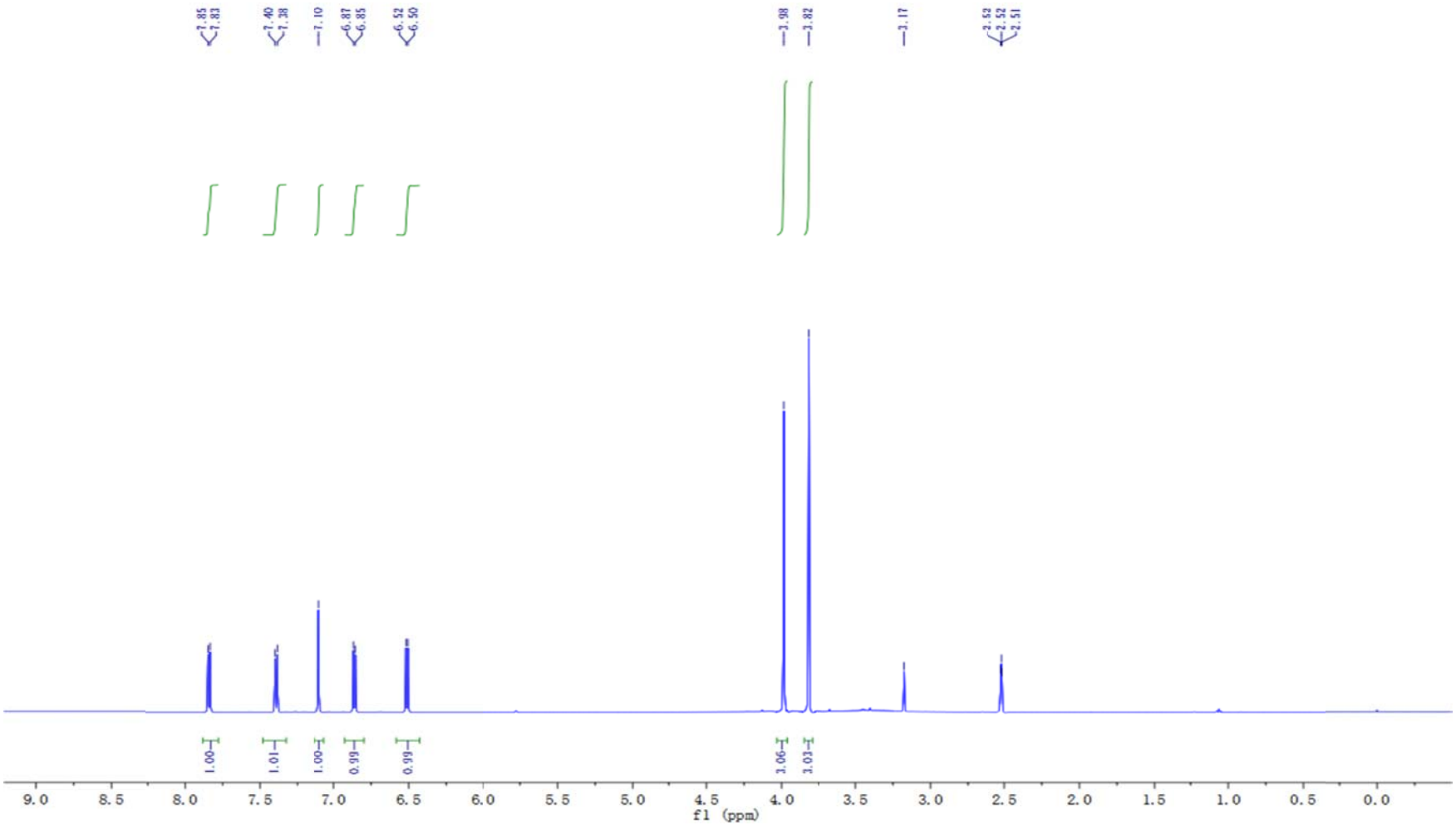


Figure S98. ^{1}H NMR spectrum (500 MHz, CD_3OD) of aaptamine (1)

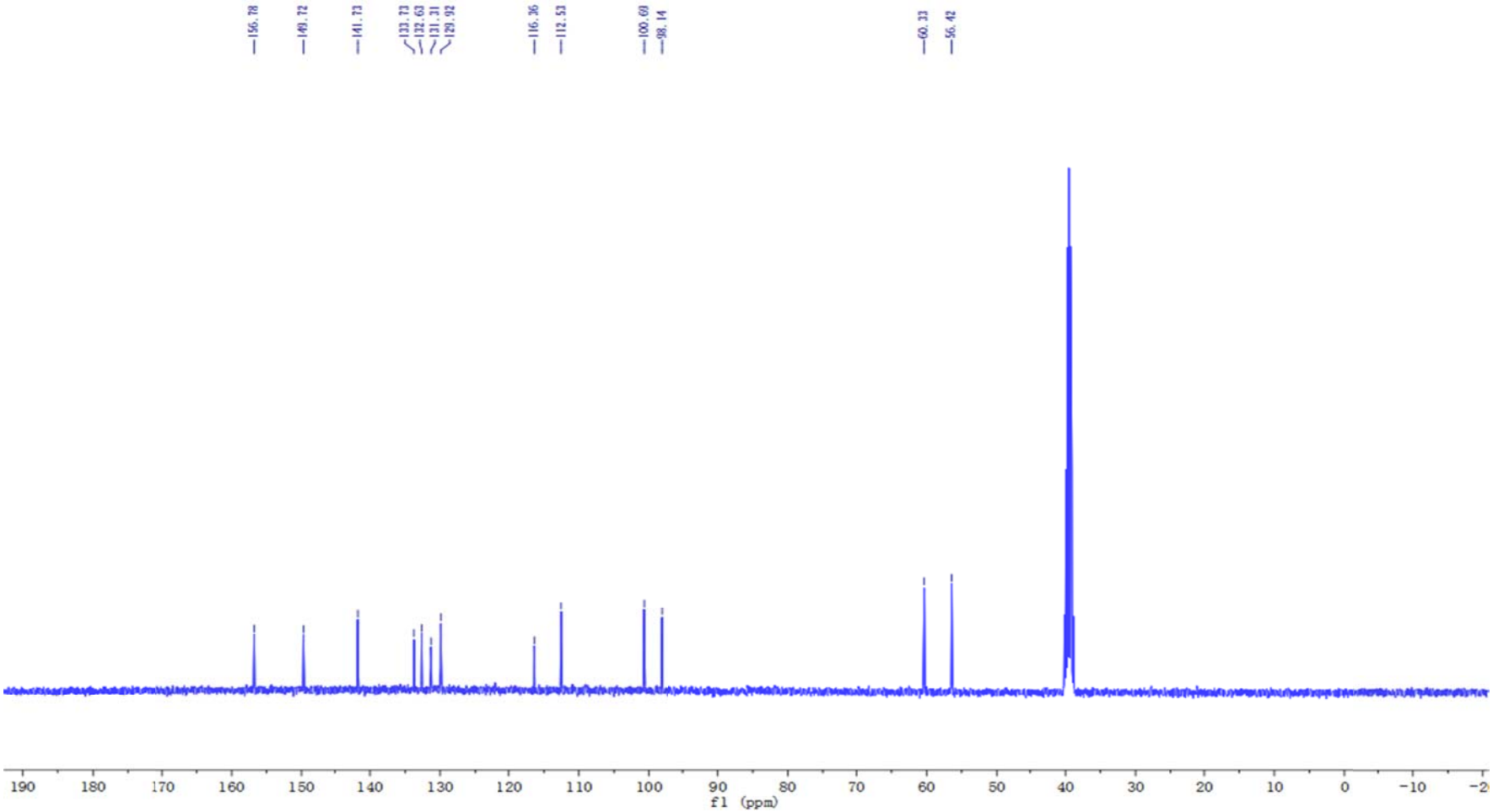


Figure S99. ^{13}C NMR spectrum (125 MHz, CD_3OD) of aaptamine (1)

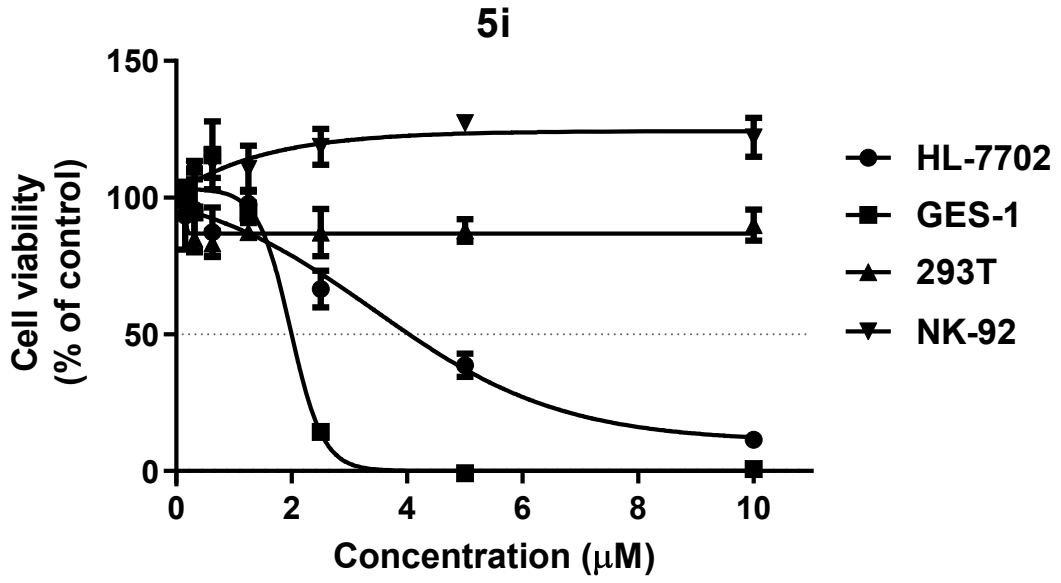


Figure S100. Cytotoxicity of compound 5i to the human normal cells HL-7702, GES-1, 293T, and NK-92

Table S3. Optimized Cartesian coordinate

Aaptamine			
C	1.202531	0.694941	-0.200333
C	-0.158932	0.941571	-0.149004
N	-0.646782	2.227270	-0.217789
C	-1.987638	2.491420	-0.174205
C	-2.907153	1.507152	-0.056080
C	-2.485563	0.125270	0.020735
N	-3.388256	-0.844531	0.135162
C	-2.913081	-2.114549	0.201556
C	-1.590117	-2.471702	0.160106
C	-0.599200	-1.457885	0.037392
C	0.789129	-1.700305	-0.019342
C	1.673363	-0.637728	-0.140595
O	3.016769	-0.760639	-0.212320
C	3.572020	-2.063616	-0.146054
H	4.651019	-1.932850	-0.215431
H	3.323984	-2.553734	0.801477
H	3.225873	-2.684716	-0.979043
H	1.144451	-2.721811	0.030413
C	-1.082933	-0.128971	-0.033134

H	-1.299168	-3.515005	0.219807
H	-3.673053	-2.887395	0.294799
H	-3.963283	1.739894	-0.020075
H	-2.255355	3.538481	-0.239314
H	0.023684	2.971995	-0.334957
O	2.054189	1.763043	-0.347226
C	2.763049	2.103675	0.844991
H	3.347881	2.995049	0.615048
H	2.066491	2.323945	1.661865
H	3.432219	1.292103	1.143970

optimization: wB97X-D/6-31G(d,p)/CPCM(CH_2Cl_2); E=-762.326425

single point energy: wB97X-D/6-311++G(2d,p)/CPCM(CH_2Cl_2); E=-762.5164003