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Supporting Information

Synthesis of Biologically Active [1,5]Diazocino[2,1-b]quinazolinones through [4+4] Cycloaddition of 2-Akynyl Quinazolinones with Aza-ortho-quinone Methides

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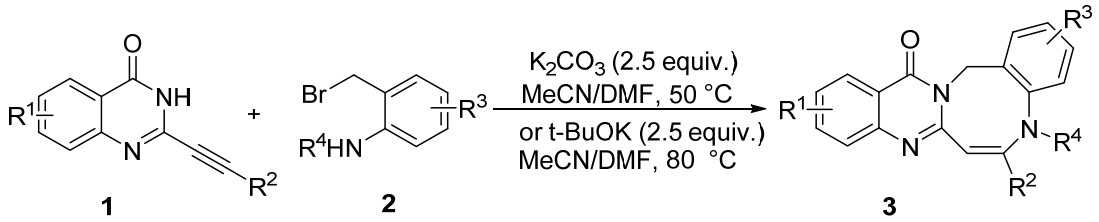
Contents

1. General experimental information

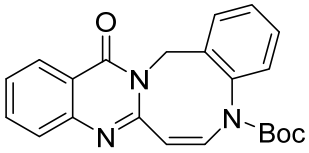
^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature using 400 MHz, 600 MHz spectrometers. The data are reported as follows: chemical shift in ppm from internal tetramethylsilane on the δ scale, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. High resolution mass spectra were acquired on an LTQ FT spectrometer, and were obtained by peak matching. Melting points are reported uncorrected. Analytical thin layer chromatography was performed on 0.25 mm extra hard silica gel plates with UV254 fluorescent indicator. Chromatography was performed using with 300-400 mesh silica gel (SiO_2). Unless otherwise noted, all reagents and solvents were obtained from commercial sources and, where appropriate, purified prior to use. All reagents and solvents were obtained from commercial sources and, where appropriate, purified prior to use. 2-(Bromomethyl)anilines **2** were prepared according to literature methods[1, 2].

2. Synthesis of [1,5]diazocino[2,1-*b*]quinazolines 3



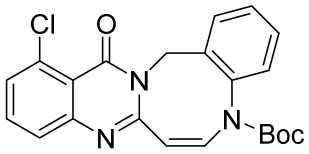
General procedure A: In a 25 mL reaction flask was charged with K_2CO_3 (69 mg, 2.5 equiv.), **1** (0.2 mmol), **2** (0.24 mmol), DMF (5.0 mL), and MeCN (0.5 mL). The reaction mixture was stirred vigorously at 50 °C until compound **1** was completely consumed (monitored by TLC). At this time, the reaction was quenched with water (20 mL) and extracted with EtOAc (20 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and filtered. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (PE/EtOAc = 10/1 to 2/1) to afford compounds **3aa**-**3ma**, **3ra**-**3sa** and **3ab**-**3am**.

General procedure B: In a 25 mL reaction flask was charged with *t*-BuOK (56 mg, 2.5 equiv.), **1** (0.2 mmol), **2** (0.24 mmol), DMF (5.0 mL), and MeCN (0.5 mL). The mixture was stirred vigorously at 80 °C for 1.5~15 h until compound **1** was completely consumed (monitored by TLC). At this time, the reaction was quenched with water (20 mL) and extracted with EtOAc (20 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and filtered. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (PE/EtOAc = 6/1 to 1/1) to afford compounds **3na-3pa** and **3ta-3va**.



3aa

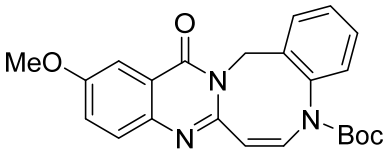
(*Z*)-Tert-butyl 13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazoline-5-carboxylate (3aa). 1a (34 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 0.5 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3aa**. A light yellow solid, 0.073 g, 97% yield; mp: 184−185 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (dd, J = 8.0, 1.3 Hz, 1H), 7.73 (dd, J = 7.5, 1.7 Hz, 1H), 7.69 – 7.62 (m, 1H), 7.51 (dd, J = 13.7, 10.1 Hz, 2H), 7.42 – 7.37 (m, 1H), 7.32 – 7.21 (m, 3H), 7.13 (dd, J = 7.8, 1.3 Hz, 1H), 6.16 (d, J = 13.6 Hz, 1H), 5.64 (d, J = 12.0 Hz, 1H), 4.98 (d, J = 13.6 Hz, 1H), 1.49 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6, 152.7, 152.0, 148.0, 138.1, 134.7, 134.5, 134.0, 130.1, 129.2, 128.8, 128.7, 127.2, 127.1, 126.8, 120.1, 105.1, 84.0, 42.5, 28.1. HRMS (ESI) m/z calcd for $C_{22}H_{22}N_3O_3$ $(M+H)^+$: 376.1656, found 376.1653.



3ba

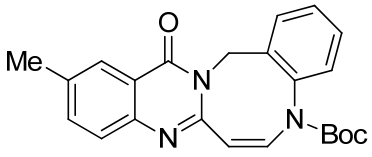
(*Z*)-*Tert*-butyl 12-chloro-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazoline-5-carboxylate (3ba). **1b** (41 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 2 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3ba**. A white solid, 0.074 g, 90% yield; mp: 206−207 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (dd, J

= 7.4, 1.9 Hz, 1H), 7.53 – 7.46 (m, 2H), 7.42 – 7.36 (m, 2H), 7.32 – 7.23 (m, 2H), 7.12 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.13 (d, *J* = 13.7 Hz, 1H), 5.57 (d, *J* = 12.0 Hz, 1H), 4.94 (d, *J* = 13.7 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 159.7, 152.7, 152.6, 150.4, 138.2, 134.7, 134.4, 134.3, 133.8, 130.3, 129.4, 129.2, 128.9, 128.7, 126.6, 117.2, 104.6, 84.1, 42.5, 28.1. HRMS (ESI) m/z calcd for $C_{22}H_{21}ClN_3O_3$ $(M+H)^+$: 410.1266, found 410.1268.



3ca

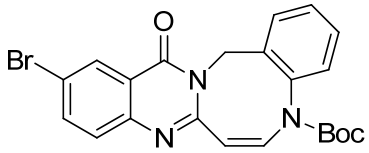
(*Z*)-*Tert*-butyl 11-methoxy-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocineo[2, 1-*b*]quinazoline-5-carboxylate (3ca). 1c (40 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 3 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3ca**. A white solid, 0.080 g, 99% yield; mp: 192−193 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.72 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.60 (d, *J* = 2.9 Hz, 1H), 7.45 (t, *J* = 9.7 Hz, 2H), 7.31 – 7.20 (m, 3H), 7.12 (dd, *J* = 7.8, 1.3 Hz, 1H), 6.17 (d, *J* = 13.6 Hz, 1H), 5.63 (d, *J* = 12.0 Hz, 1H), 4.98 (d, *J* = 13.6 Hz, 1H), 3.90 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 161.4, 158.5, 152.7, 149.7, 142.7, 138.2, 134.8, 133.2, 130.0, 129.1, 128.9, 128.8, 125.0, 120.8, 106.3, 105.4, 83.8, 55.9, 42.6, 28.1. HRMS (ESI) m/z calcd for $C_{23}H_{24}N_3O_4$ $(M+H)^+$: 406.1761, found 406.1762.



3da

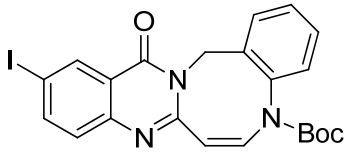
(*Z*)-*Tert*-butyl 11-methyl-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2, 1-*b*]quinazoline-5-carboxylate (3da). 1d (36 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 2 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3da**. A white solid, 0.067 g, 85% yield; mp: 173−174 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.05 – 7.98 (m, 1H), 7.71 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.50 – 7.40 (m, 3H), 7.30 – 7.20 (m, 2H), 7.12 (dd, *J* = 7.8, 1.5 Hz, 1H), 6.16 (d, *J* = 13.6 Hz, 1H), 5.63 (d, *J* = 12.0 Hz, 1H), 4.96 (d, *J* = 13.6 Hz, 1H), 2.44 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 161.6,

152.7, 151.1, 146.0, 138.1, 137.0, 136.0, 134.8, 133.6, 130.0, 129.1, 128.8, 127.0, 126.5, 119.8, 105.2, 83.9, 42.5, 28.1, 21.5. HRMS (ESI) m/z calcd for $C_{23}H_{24}N_3O_3$ $(M+H)^+$: 390.1812 found 390.1820.



3ea

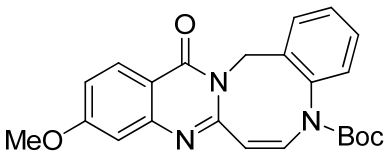
(*Z*)-*Tert*-butyl 11-bromo-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*] quinazoline-5-carboxylate (3ea). 1e (50 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 5 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3ea**. A white solid, 0.148 g, 95% yield; mp: 202−203 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.34 (d, J = 2.2 Hz, 1H), 7.73 – 7.67 (m, 2H), 7.51 (d, J = 12.0 Hz, 1H), 7.37 (d, J = 8.7 Hz, 1H), 7.32 – 7.21 (m, 2H), 7.14 – 7.09 (m, 1H), 6.12 (d, J = 13.6 Hz, 1H), 5.59 (d, J = 12.0 Hz, 1H), 4.97 (d, J = 13.6 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.4, 152.6, 152.4, 146.8, 138.0, 137.6, 134.5, 134.4, 130.0, 129.6, 129.3, 129.0, 128.9, 128.8, 121.3, 120.2, 104.7, 84.1, 42.7, 28.1. HRMS (ESI) m/z calcd for $C_{22}H_{21}BrN_3O_3$ $(M+H)^+$: 454.0761, found 454.0762.



3fa

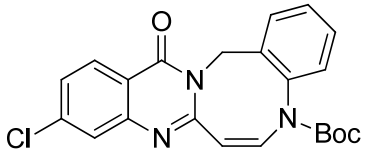
(*Z*)-*Tert*-butyl 11-iodo-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*] quinazoline-5-carboxylate (3fa). 1f (59 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 3 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3fa**. A white solid, 0.093 g, 93% yield; mp: 194−195 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.56 (d, J = 2.0 Hz, 1H), 7.90 (dd, J = 8.6, 2.1 Hz, 1H), 7.69 (dd, J = 7.6, 1.7 Hz, 1H), 7.51 (d, J = 12.0 Hz, 1H), 7.32 – 7.21 (m, 4H), 7.12 (dd, J = 7.9, 1.2 Hz, 1H), 6.12 (d, J = 13.6 Hz, 1H), 5.59 (d, J = 12.0 Hz, 1H), 4.97 (d, J = 13.6 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.2, 152.6, 147.3, 143.2, 138.0, 135.9, 134.5, 130.0, 129.3,

129.0, 128.9, 128.8, 121.6, 104.7, 91.0, 84.1, 42.7, 28.1. HRMS (ESI) m/z calcd for $C_{22}H_{22}IN_3O_3$ $(M+H)^+$: 502.0622, found 502.0623.



3ga

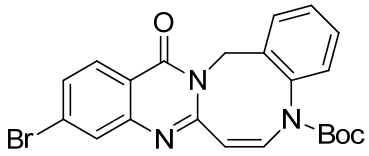
(*Z*)-*Tert*-butyl 10-methoxy-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2, 1-*b*]quinazoline-5-carboxylate (3ga). 1g (40 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 3 h. Purification by column chromatography (2/1, PE/EtOAc) afforded **3ga**. A white solid, 0.079 g, 98% yield; mp: 184−185 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (d, J = 8.9 Hz, 1H), 7.72 (dd, J = 7.5, 1.7 Hz, 1H), 7.48 (d, J = 12.0 Hz, 1H), 7.26 (dd, J = 7.4, 1.5 Hz, 2H), 7.12 (dd, J = 7.8, 1.3 Hz, 1H), 6.97 (dd, J = 8.9, 2.5 Hz, 1H), 6.90 (d, J = 2.4 Hz, 1H), 6.14 (d, J = 13.6 Hz, 1H), 5.60 (d, J = 12.0 Hz, 1H), 4.95 (d, J = 13.6 Hz, 1H), 3.85 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.7, 161.0, 152.7, 152.6, 150.2, 138.1, 134.8, 134.1, 130.1, 129.2, 128.7, 128.6, 107.4, 105.1, 84.0, 55.8, 42.3, 28.1. HRMS (ESI) m/z calcd for $C_{23}H_{24}N_3O_4$ $(M+H)^+$: 406.1761, found 406.1758.



3ha

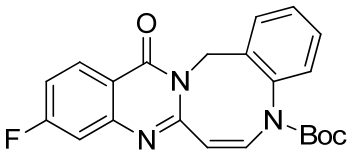
(*Z*)-*Tert*-butyl 10-chloro-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*] quinazoline-5-carboxylate (3ha). 1h (61 mg, 0.3 mmol), **2a** (103 mg, 0.36 mmol) ran for 3 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3ha**. A white solid, 0.112 g, 91% yield; mp: 201−202 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (d, J = 8.6 Hz, 1H), 7.70 (dd, J = 7.6, 1.8 Hz, 1H), 7.54 – 7.47 (m, 2H), 7.35 – 7.21 (m, 3H), 7.12 (dd, J = 7.9, 1.5 Hz, 1H), 6.12 (d, J = 13.7 Hz, 1H), 5.60 (d, J = 12.0 Hz, 1H), 4.97 (d, J = 13.6 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.0, 153.2, 152.6, 149.0, 140.6, 138.1, 134.6, 134.5, 130.0, 129.2, 128.9, 128.8, 128.5, 127.2, 126.6, 118.5,

104.7, 84.1, 42.6, 28.1. HRMS (ESI) m/z calcd for $C_{22}H_{21}ClN_3O_3$ $(M+H)^+$: 410.1266, found 410.1264.



3ia

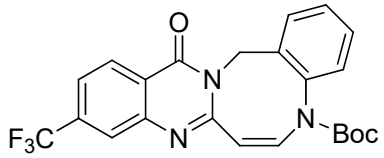
(*Z*)-*Tert*-butyl 10-bromo-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*] quinazoline-5-carboxylate (3ia). 1i (50 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 2 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3ia**. A white solid, 0.076 g, 83% yield; mp: 205−206 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 8.5 Hz, 1H), 7.70 (dd, J = 6.7, 1.6 Hz, 2H), 7.54 – 7.46 (m, 2H), 7.33 – 7.21 (m, 2H), 7.13 (dd, J = 7.9, 1.2 Hz, 1H), 6.12 (d, J = 13.7 Hz, 1H), 5.60 (d, J = 12.0 Hz, 1H), 4.97 (d, J = 13.7 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.1, 153.2, 152.6, 149.1, 138.1, 134.6, 134.5, 130.0, 129.9, 129.8, 129.3, 129.1, 128.9, 128.8, 128.5, 118.8, 104.7, 84.1, 42.6, 28.1. HRMS (ESI) m/z calcd for $C_{22}H_{21}BrN_3O_3$ $(M+H)^+$: 454.0761, found 454.0771.



3ja

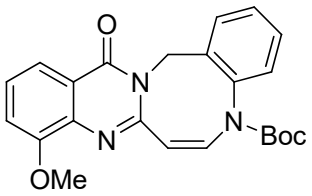
(*Z*)-*Tert*-butyl 10-fluoro-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*] quinazoline-5-carboxylate (3ja). 1j (38 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 3 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3ja**. A white solid, 0.060 g, 75% yield; mp: 199−200 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (dd, J = 8.8, 6.1 Hz, 1H), 7.70 (dd, J = 7.5, 1.6 Hz, 1H), 7.51 (d, J = 12.0 Hz, 1H), 7.33 – 7.22 (m, 2H), 7.18 – 7.06 (m, 3H), 6.13 (d, J = 13.7 Hz, 1H), 5.60 (d, J = 12.0 Hz, 1H), 4.97 (d, J = 13.6 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.6 (d, J = 252.6 Hz), 160.9, 153.3, 152.6, 150.2, 150.1, 138.1, 134.6, 134.5, 130.1, 129.8 (d, J = 10.7 Hz), 129.2, 128.8 (d, J = 7.9 Hz), 116.8 (d, J = 1.9 Hz), 115.5 (d, J = 23.6 Hz), 112.3

(d, J = 21.5 Hz), 104.7, 84.1, 42.5, 28.1. ^{19}F NMR (375 MHz, DMSO-d_6): δ –104.1. HRMS (ESI) m v/z calcd for $C_{22}H_{21}FN_3O_3$ $(M+H)^+$: 394.1561, found 394.1571.



3ka

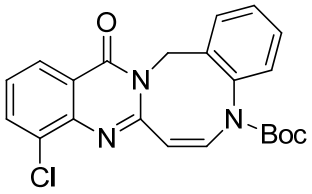
(*Z*)-*Tert*-butyl 13-oxo-10-(trifluoromethyl)-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazoline-5-carboxylate (3ka). 1k (47 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 3 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3ka**. A white solid, 0.076 g, 85% yield; mp: 172−173 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, J = 8.3 Hz, 1H), 7.82 – 7.77 (m, 1H), 7.70 (dd, J = 7.6, 1.8 Hz, 1H), 7.60 – 7.50 (m, 2H), 7.34 – 7.21 (m, 2H), 7.14 (dd, J = 7.9, 1.5 Hz, 1H), 6.14 (d, J = 13.7 Hz, 1H), 5.63 (d, J = 12.0 Hz, 1H), 5.01 (d, J = 13.7 Hz, 1H), 1.49 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8, 153.4, 152.5, 148.0, 138.1, 136.0 (q, J = 32.5 Hz), 134.9, 134.3, 130.0, 129.3, 129.0, 128.8, 128.2, 124.8 (q, J = 4.1 Hz), 123.5 (q, J = 271.5 Hz), 122.4 (q, J = 3.3 Hz), 122.2, 104.4, 84.2, 42.7, 28.1. ^{19}F NMR (375 MHz, $CDCl_3$): δ -63.4. HRMS (ESI) m/z calcd for $C_{23}H_{21}F_3N_3O_3$ $(M+H)^+$: 444.1530, found 444.1541.



3la

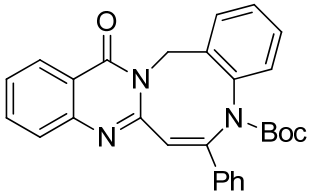
(*Z*)-*Tert*-butyl 9-methoxy-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2, 1-*b*]quinazoline-5-carboxylate (3la). 1l (40 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 3 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3la**. A white solid, 0.080 g, 99% yield; mp: 120−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (dd, J = 8.1, 1.2 Hz, 1H), 7.69 (dd, J = 7.6, 1.7 Hz, 1H), 7.45 (d, J = 12.0 Hz, 1H), 7.33 (t, J = 8.0 Hz, 1H), 7.30 – 7.18 (m, 3H), 7.10 (ddd, J = 8.0, 4.0, 1.2 Hz, 2H), 6.16 (d, J = 13.6 Hz, 1H), 5.78 (d, J = 12.0 Hz, 1H), 4.99 (d, J = 13.6 Hz, 1H), 3.94 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4, 154.2, 152.7, 151.3, 138.7, 138.1, 134.7,

133.6, 130.0, 129.1, 128.8, 128.7, 127.0, 121.2, 118.4, 113.9, 105.6, 83.9, 56.3, 42.6, 28.1. HRMS (ESI) m/z calcd for $C_{23}H_{24}N_3O_4$ $(M+H)^+$: 406.1761, found 406.1772.



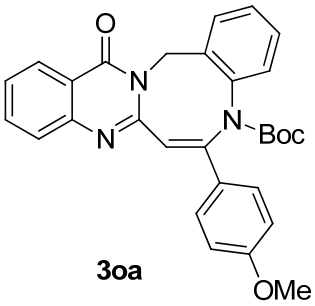
3ma

(*Z*)-*Tert*-butyl 9-chloro-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*] quinazol (3ma). 1m (40 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 3 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3ma**. A white solid, 0.071 g, 87% yield; mp: 213−214 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (dd, J = 8.0, 1.4 Hz, 1H), 7.71 (dd, J = 7.7, 1.5 Hz, 2H), 7.51 (d, J = 12.0 Hz, 1H), 7.32 – 7.20 (m, 3H), 7.12 (dd, J = 7.9, 1.2 Hz, 1H), 6.13 (d, J = 13.6 Hz, 1H), 5.75 (d, J = 12.0 Hz, 1H), 5.01 (d, J = 13.6 Hz, 1H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.1, 152.7, 152.6, 144.8, 138.1, 134.6, 134.5, 134.4, 131.5, 129.9, 129.2, 128.9, 128.8, 126.6, 125.9, 121.6, 105.2, 84.1, 42.7, 28.1. HRMS (ESI) m/z calcd for $C_{22}H_{21}ClN_3O_3$ $(M+H)^+$: 410.1266, found 410.1271.



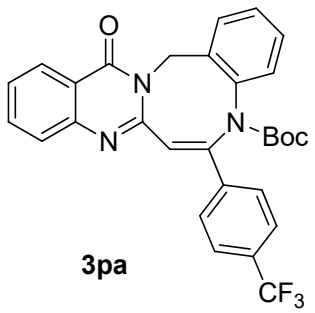
3na

(*Z*)-*Tert*-butyl 13-oxo-6-phenyl-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocineo [2,1-*b*]quinazoline-5-carboxylate (3na). 1n (44 mg, 0.18 mmol), **2a** (61 mg, 0.22 mmol) ran for 1.5 h. Purification by column chromatography (2/1, PE/EtOAc) afforded **3na**. A white solid, 0.075 g, 93% yield; mp: 232−233 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, J = 7.9 Hz, 1H), 7.77 – 7.61 (m, 4H), 7.51 – 7.31 (m, 8H), 7.28 – 7.24 (m, 1H), 5.62 (d, J = 14.9 Hz, 1H), 5.05 (d, J = 15.7 Hz, 1H), 1.14 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.9, 152.7, 152.4, 147.4, 143.0, 134.6, 134.4, 131.9, 130.6, 130.1, 129.0, 128.9, 127.4, 127.0, 126.6, 122.6, 121.4, 81.7, 48.4, 27.8. HRMS (ESI) m/z calcd for $C_{28}H_{26}N_3O_3$ $(M+H)^+$: 452.1969, found 452.1979.



3oa

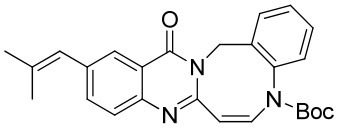
(*Z*)-*Tert*-butyl 6-(4-methoxyphenyl)-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazoline-5-carboxylate (3oa). 1o (55 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 20 h. Purification by column chromatography (2/1, PE/EtOAc) afforded **3oa**. A white solid, 0.086 g, 90% yield; mp: 210−211 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (dd, J = 8.0, 1.1 Hz, 1H), 7.75 – 7.66 (m, 2H), 7.62 – 7.56 (m, 2H), 7.51 – 7.29 (m, 4H), 7.27 – 7.19 (m, 2H), 6.94 – 6.86 (m, 2H), 5.60 (d, J = 15.3 Hz, 1H), 5.05 (d, J = 15.4 Hz, 1H), 3.81 (s, 3H), 1.13 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0, 161.2, 152.8, 147.4, 142.7, 134.4, 132.0, 130.6, 130.5, 128.9, 128.2, 127.3, 127.0, 126.9, 121.3, 120.5, 114.5, 81.7, 55.5, 48.5, 27.8. HRMS (ESI) m/z calcd for $C_{29}H_{28}N_3O_4$ $(M+H)^+$: 482.2074, found 482.2085.



3pa

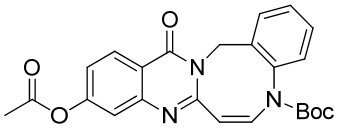
(*Z*)-*Tert*-butyl 13-oxo-6-(4-(trifluoromethyl)phenyl)-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazoline-5-carboxylate (3pa). 1p (63 mg, 0.2 mmol), **2a** (69 mg, 0.24 mmol) ran for 5 h. Purification by column chromatography (2/1, PE/EtOAc) afforded **3pa**. A white solid, 0.087 g, 83% yield; mp: 245−245.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 – 8.22 (m, 1H), 7.80 – 7.69 (m, 4H), 7.66 (d, J = 8.3 Hz, 2H), 7.53 – 7.38 (m, 4H), 7.38 – 7.27 (m, 2H), 5.63 (d, J = 15.5 Hz, 1H), 5.00 (d, J = 15.6 Hz, 1H), 1.13 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8, 152.6, 151.8, 147.3, 141.7, 138.2, 136.2, 134.6, 131.9, 131.8 (q, J = 32.6 Hz), 130.8, 130.5, 129.2, 127.7, 127.5, 127.3, 126.9, 126.1 (q, J = 3.8 Hz), 124.8, 123.9 (q, J = 270.6 Hz), 121.4, 82.2, 48.3,

27.7. ^{19}F NMR (375 MHz, $CDCl_3$): δ -62.8. HRMS (ESI) m/z calcd for $C_{29}H_{25}F_3N_3O_3$ $(M+H)^+$: 520.1843, found 520.1844.



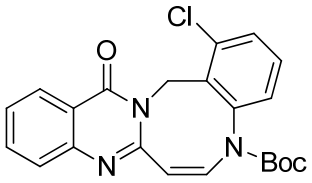
3ra

(*Z*)-*tert*-butyl 11-(2-methylprop-1-en-1-yl)-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazoline-5-carboxylate (3ra). 1r (58 mg, 0.26 mmol), **2a** (89 mg, 0.31 mmol) ran for 5 h. Purification by column chromatography (4/1, PE/EtOAc) afforded **3ra**. A white solid, 0.100 g, 90% yield; mp: 85−86 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, J = 2.2 Hz, 1H), 7.72 (dd, J = 7.5, 1.8 Hz, 1H), 7.54 – 7.43 (m, 3H), 7.30 – 7.20 (m, 2H), 7.12 (dd, J = 7.8, 1.6 Hz, 1H), 6.30 (s, 1H), 6.16 (d, J = 13.7 Hz, 1H), 5.63 (d, J = 12.0 Hz, 1H), 4.97 (d, J = 13.5 Hz, 1H), 1.97 – 1.85 (m, 6H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6, 152.7, 151.3, 146.0, 138.1, 137.5, 137.4, 135.4, 134.7, 133.6, 130.1, 129.1, 128.7, 126.8, 126.2, 124.2, 119.7, 105.3, 83.9, 42.5, 28.1, 27.2, 19.7. HRMS (ESI) m/z calcd for $C_{26}H_{28}N_3O_3$ $(M+H)^+$: 430.2125, found 430.2127. #



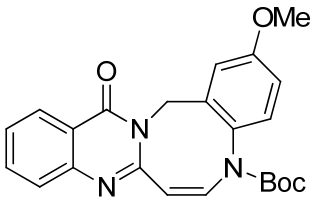
3sa

(*Z*)-*tert*-butyl 10-acetoxy-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazoline-5-carboxylate (3sa). 1s (52 mg, 0.23 mmol), **2a** (79 mg, 0.28 mmol) ran for 4 h. Purification by column chromatography (2/1, PE/EtOAc) afforded **3sa**. A light yellow solid, 0.025 g, 25% yield; mp: 87−88 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (d, J = 8.7 Hz, 1H), 7.70 (dd, J = 7.6, 1.8 Hz, 1H), 7.51 (d, J = 12.0 Hz, 1H), 7.33 – 7.22 (m, 3H), 7.16 – 7.07 (m, 2H), 6.14 (d, J = 13.7 Hz, 1H), 5.61 (d, J = 12.0 Hz, 1H), 4.98 (d, J = 13.6 Hz, 1H), 2.32 (s, 3H), 1.49 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.8, 161.0, 155.4, 152.9, 152.6, 149.3, 138.0, 134.6, 134.4, 130.0, 129.2, 128.9, 128.8, 128.7, 121.0, 119.1, 117.8, 104.8, 84.0, 42.5, 28.1, 21.3. HRMS (ESI) m/z calcd for $C_{24}H_{24}N_3O_5$ $(M+H)^+$: 434.1710, found 434.1714.



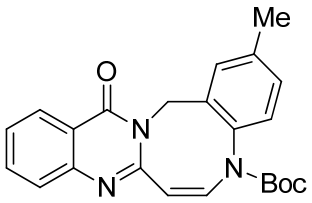
3ab

(*Z*)-*Tert*-butyl 1-chloro-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocineo [2,1-*b*]quinazoline-5-carboxylate (3ab). 1a (34 mg, 0.2 mmol), **2b** (77 mg, 0.24 mmol) ran for 0.5 h. Purification by column chromatography (4/1, PE/EtOAc) afforded **3ab**. A white solid, 0.080 g, 97% yield; mp: 197−198 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (dd, J = 8.0, 1.5 Hz, 1H), 7.69 – 7.64 (m, 1H), 7.51 (d, J = 8.2 Hz, 1H), 7.44 – 7.22 (m, 4H), 7.11 (d, J = 8.0 Hz, 1H), 6.52 (d, J = 14.4 Hz, 1H), 5.65 (d, J = 11.8 Hz, 1H), 4.98 (d, J = 14.3 Hz, 1H), 1.50 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.9, 152.2, 151.9, 147.5, 141.4, 135.1, 134.4, 133.0, 132.6, 129.9, 129.4, 127.3, 127.1, 127.0, 126.9, 120.3, 107.7, 84.2, 40.1, 28.1. HRMS (ESI) m/z calcd for $C_{22}H_{21}ClN_3O_3$ $(M+H)^+$: 410.1266, found 410.1268.



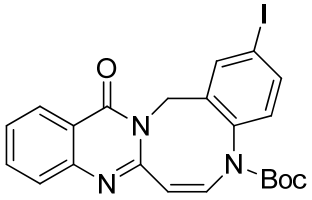
3ac

(*Z*)-*Tert*-butyl 2-methoxy-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocineo [2,1-*b*]quinazoline-5-carboxylate (3ac). 1a (34 mg, 0.2 mmol), **2c** (76 mg, 0.24 mmol) ran for 0.5 h. Purification by column chromatography (4/1, PE/EtOAc) afforded **3ac**. A white solid, 0.081 g, 99% yield; mp: 148−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (dd, J = 8.0, 1.5 Hz, 1H), 7.66 (ddd, J = 8.5, 7.1, 1.5 Hz, 1H), 7.55 – 7.44 (m, 2H), 7.39 (ddd, J = 8.2, 7.1, 1.2 Hz, 1H), 7.21 (d, J = 3.0 Hz, 1H), 7.03 (d, J = 8.9 Hz, 1H), 6.81 (dd, J = 8.9, 3.0 Hz, 1H), 6.09 (d, J = 13.6 Hz, 1H), 5.61 (d, J = 11.9 Hz, 1H), 4.92 (d, J = 13.6 Hz, 1H), 3.75 (s, 3H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6, 159.5, 152.9, 152.1, 148.0, 135.7, 134.4, 134.3, 130.6, 129.9, 127.1, 127.0, 126.7, 120.0, 115.7, 113.1, 104.9, 83.8, 55.7, 42.7, 28.1. HRMS (ESI) m/z calcd for $C_{23}H_{24}N_3O_4$ $(M+H)^+$: 406.1761, found 406.1775.



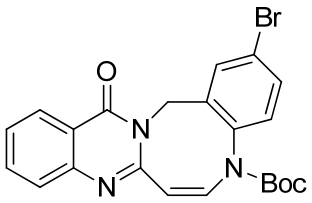
3ad

(*Z*)-*Tert*-butyl 2-methyl-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*] quinazoline-5-carboxylate (3ad). 1a (34 mg, 0.2 mmol), **2d** (72 mg, 0.24 mmol) ran for 2 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3ad**. A white solid, 0.078 g, 99% yield; mp: 204−205 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (dd, J = 8.0, 1.5 Hz, 1H), 7.66 (ddd, J = 8.5, 7.1, 1.6 Hz, 1H), 7.55 – 7.43 (m, 3H), 7.40 (ddd, J = 8.1, 7.0, 1.2 Hz, 1H), 7.08 (dd, J = 8.4, 2.1 Hz, 1H), 7.00 (d, J = 8.2 Hz, 1H), 6.11 (d, J = 13.6 Hz, 1H), 5.61 (d, J = 11.9 Hz, 1H), 4.92 (d, J = 13.6 Hz, 1H), 2.27 (s, 3H), 1.49 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.6, 152.8, 152.1, 148.0, 139.3, 135.5, 134.4, 134.3, 134.2, 130.2, 129.7, 128.4, 127.2, 127.1, 126.7, 120.1, 105.0, 83.8, 42.5, 28.1, 21.2. HRMS (ESI) m/z calcd for $C_{23}H_{24}N_3O_3$ $(M+H)^+$: 390.1812 found 390.1818.



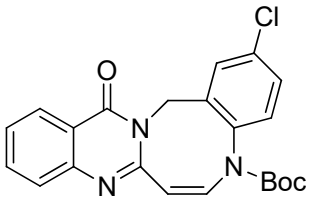
3ae

(*Z*)-*Tert*-butyl 2-iodo-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazoline-5-carboxylate (3ae). 1a (34 mg, 0.2 mmol), **2e** (99 mg, 0.24 mmol) ran for 3 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3ae**. A white solid, 0.091 g, 91% yield; mp: 194−195 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (dd, J = 8.0, 1.4 Hz, 1H), 8.06 (d, J = 2.0 Hz, 1H), 7.68 (ddd, J = 8.4, 7.2, 1.5 Hz, 1H), 7.61 (dd, J = 8.5, 2.1 Hz, 1H), 7.55 (d, J = 8.1 Hz, 1H), 7.47 – 7.38 (m, 2H), 6.87 (d, J = 8.5 Hz, 1H), 6.10 (d, J = 13.7 Hz, 1H), 5.66 (d, J = 12.0 Hz, 1H), 4.90 (d, J = 13.7 Hz, 1H), 1.49 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4, 152.3, 151.5, 148.0, 138.8, 138.0, 136.6, 134.6, 133.4, 130.5, 127.3, 127.2, 126.9, 120.0, 105.4, 94.1, 84.4, 41.9, 28.1. HRMS (ESI) m/z calcd for $C_{22}H_{21}IN_3O_3(M+H)^+$: 502.0622, found 502.0617.



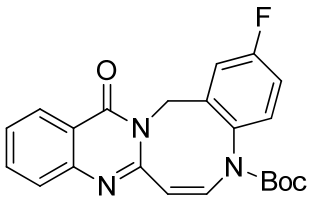
3af

(*Z*)-*Tert*-butyl 2-bromo-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*] quinazoline-5-carboxylate (3af). 1a (34 mg, 0.2 mmol), **2f** (87 mg, 0.24 mmol) ran for 0.3 h. Purification by column chromatography (4/1, PE/EtOAc) afforded **3af**. A white solid, 0.080 g, 88% yield; mp: 193−194 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (dd, J = 8.0, 1.2 Hz, 1H), 7.88 (d, J = 2.3 Hz, 1H), 7.68 (ddd, J = 8.5, 7.2, 1.5 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.43 (ddd, J = 11.0, 7.5, 3.6 Hz, 3H), 7.01 (d, J = 8.6 Hz, 1H), 6.11 (d, J = 13.7 Hz, 1H), 5.66 (d, J = 12.0 Hz, 1H), 4.92 (d, J = 13.7 Hz, 1H), 1.49 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4, 152.3, 151.5, 147.9, 137.2, 136.5, 134.6, 133.6, 132.8, 132.1, 130.4, 127.2, 127.0, 122.5, 120.0, 105.4, 84.4, 42.1, 28.1. HRMS (ESI) m/z calcd for $C_{22}H_{21}BrN_3O_3$ $(M+H)^+$: 454.0761, found 454.0750.



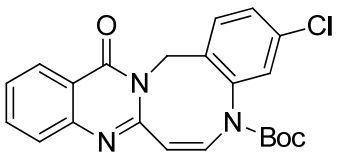
3ag

(*Z*)-*Tert*-butyl 2-chloro-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*] quinazoline-5-carboxylate (3ag). 1a (34 mg, 0.2 mmol), **2g** (77 mg, 0.24 mmol) ran for 2 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3ag**. A white solid, 0.081 g, 99% yield; mp: 202−203 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (dd, J = 8.0, 1.3 Hz, 1H), 7.73 (d, J = 2.4 Hz, 1H), 7.71 – 7.64 (m, 1H), 7.54 (d, J = 8.1 Hz, 1H), 7.49 – 7.39 (m, 2H), 7.29 – 7.23 (m, 1H), 7.08 (d, J = 8.6 Hz, 1H), 6.11 (d, J = 13.7 Hz, 1H), 5.66 (d, J = 12.0 Hz, 1H), 4.93 (d, J = 13.7 Hz, 1H), 1.49 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.4, 152.4, 151.5, 147.9, 136.7, 136.2, 134.6, 134.5, 133.6, 130.2, 129.9, 129.2, 127.3, 127.2, 127.0, 120.0, 105.3, 84.4, 42.2, 28.1. HRMS (ESI) m/z calcd for $C_{22}H_{21}ClN_3O_3$ $(M+H)^+$: 410.1266, found 410.1269.



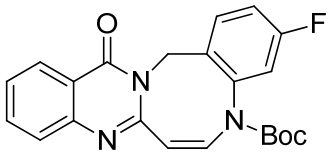
3ah

(*Z*)-*Tert*-butyl 2-fluoro-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*] quinazoline-5-carboxylate (3ah). 1a (34 mg, 0.2 mmol), **2h** (73 mg, 0.24 mmol) ran for 3 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3ah**. A white solid, 0.078 g, 99% yield; mp: 195−196 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (dd, J = 8.1, 1.5 Hz, 1H), 7.67 (ddd, J = 8.5, 7.1, 1.6 Hz, 1H), 7.54 (dd, J = 8.3, 1.2 Hz, 1H), 7.49 – 7.39 (m, 3H), 7.12 (dd, J = 8.9, 5.0 Hz, 1H), 6.99 (ddd, J = 9.0, 7.8, 3.0 Hz, 1H), 6.11 (d, J = 13.6 Hz, 1H), 5.65 (d, J = 11.9 Hz, 1H), 4.94 (dd, J = 13.7, 1.4 Hz, 1H), 1.49 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.0 (J = 248.1 Hz), 161.5, 152.6, 151.6, 147.9, 136.6 (d, J = 8.4 Hz), 134.6, 134.0, 133.9, 133.8, 130.7 (d, J = 8.7 Hz), 127.1, 127.0 (d, J = 28.9 Hz), 120.0, 116.4 (d, J = 4.7 Hz), 116.2 (d, J = 4.6 Hz), 105.3, 84.2, 42.4, 28.1. ^{19}F NMR (375 MHz, $CDCl_3$): δ -111.0. HRMS (ESI) m/z calcd for $C_{22}H_{21}FN_3O_3$ $(M+H)^+$: 394.1561, found 394.1568.



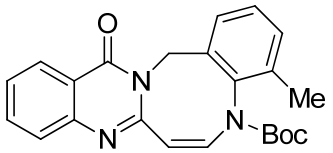
3ai

(*Z*)-*Tert*-butyl 3-chloro-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*] quinazoline-5-carboxylate (3ai). 1a (34 mg, 0.2 mmol), **2i** (77 mg, 0.24 mmol) ran for 0.3 h. Purification by column chromatography (6/1, PE/EtOAc) afforded **3ai**. A white solid, 0.079 g, 96% yield; mp: 200−201 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.21 (dd, J = 8.0, 1.5 Hz, 1H), 7.70 – 7.64 (m, 2H), 7.53 (dd, J = 8.2, 1.1 Hz, 1H), 7.47 – 7.37 (m, 2H), 7.22 (dd, J = 8.4, 2.1 Hz, 1H), 7.15 (d, J = 2.1 Hz, 1H), 6.12 (d, J = 13.7 Hz, 1H), 5.66 (d, J = 12.0 Hz, 1H), 4.94 (d, J = 13.8 Hz, 1H), 1.50 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5, 152.2, 151.5, 148.0, 139.0, 134.6, 134.1, 133.4, 133.3, 131.2, 129.4, 129.0, 127.3, 127.0, 126.9, 120.0, 105.4, 84.5, 42.0, 28.1. HRMS (ESI) m/z calcd for $C_{22}H_{21}ClN_3O_3$ $(M+H)^+$: 410.1266, found 410.1270.



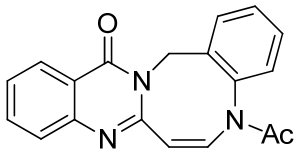
3aj

(*Z*)-*Tert*-butyl 3-fluoro-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocineo[2,1-*b*] quinazoline-5-carboxylate (3aj). 1a (34 mg, 0.2 mmol), **2j** (73 mg, 0.24 mmol) ran for 0.17 h. Purification by column chromatography (4/1, PE/EtOAc) afforded **3aj**. A white solid, 0.066 g, 85% yield; mp: 170−171 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (dd, J = 8.0, 1.5 Hz, 1H), 7.75 – 7.64 (m, 2H), 7.57 – 7.51 (m, 1H), 7.48 – 7.38 (m, 2H), 6.98 (ddd, J = 8.6, 8.0, 2.6 Hz, 1H), 6.86 (dd, J = 9.4, 2.6 Hz, 1H), 6.12 (d, J = 13.8 Hz, 1H), 5.66 (d, J = 12.0 Hz, 1H), 4.94 (d, J = 13.8 Hz, 1H), 1.50 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1 (J = 247.1 Hz), 161.6, 152.3, 151.6, 148.0, 139.4 (d, J = 10.3 Hz), 134.6, 133.4, 131.5 (d, J = 9.1 Hz), 130.9 (d, J = 3.5 Hz), 127.3, 127.0, 126.9, 120.0, 116.7 (d, J = 21.2 Hz), 115.8 (d, J = 23.2 Hz), 105.5, 84.5, 42.0, 28.1. ^{19}F NMR (375 MHz, $CDCl_3$): δ -112.0. HRMS (ESI) m/z calcd for $C_{22}H_{21}FN_3O_3$ $(M+H)^+$: 394.1561, found 394.1571.



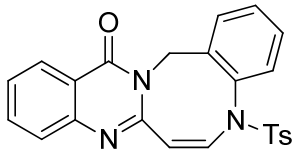
3ak

(*Z*)-*Tert*-butyl 4-methyl-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocineeo-[2,1-*b*]quinazoline-5-carboxylate (3ak). 1a (34 mg, 0.2 mmol), **2k** (72 mg, 0.24 mmol) ran for 0.5 h. Purification by column chromatography (4/1, PE/EtOAc) afforded **3ak**. A white solid, 0.076 g, 87% yield; mp: 174−175 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (dd, J = 8.1, 1.5 Hz, 1H), 7.66 – 7.62 (m, 1H), 7.57 – 7.54 (m, 1H), 7.52 – 7.35 (m, 3H), 7.18 – 7.12 (m, 2H), 6.19 (d, J = 13.5 Hz, 1H), 5.69 (d, J = 11.5 Hz, 1H), 4.92 (d, J = 13.6 Hz, 1H), 2.17 (s, 3H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5, 151.8, 147.8, 137.2, 135.9, 135.3, 134.4, 134.1, 131.1, 129.2, 127.4, 127.1, 127.0, 126.8, 120.0, 106.9, 83.6, 42.9, 28.1, 18.1. HRMS (ESI) m/z calcd for $C_{23}H_{24}N_3O_3$ $(M+H)^+$: 390.1812 found 390.1812.



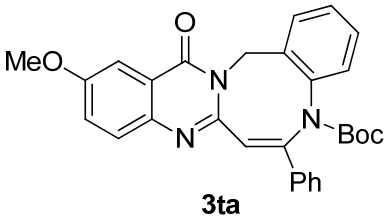
3al

(*Z*)-5-Acetyl-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazolin-13(15*H*)-one (3al). **1a** (34 mg, 0.2 mmol), **2l** (54 mg, 0.24 mmol) ran for 0.5 h. Purification by column chromatography (4/1, PE/EtOAc) afforded **3al**. A white solid, 0.064 g, 99% yield; mp: 195.4−196.9 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.22 (dd, J = 8.0, 1.5 Hz, 1H), 7.81 – 7.79 (m, 1H), 7.72 – 7.65 (m, 2H), 7.53 (d, J = 8.0 Hz, 1H), 7.43 – 7.40 (m, 1H), 7.37 – 7.32 (m, 2H), 7.17 – 7.12 (m, 1H), 6.20 (d, J = 13.7 Hz, 1H), 5.82 (d, J = 12.0 Hz, 1H), 4.92 (d, J = 13.6 Hz, 1H), 2.03 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.7, 161.5, 151.3, 147.8, 139.1, 135.5, 134.6, 132.7, 130.7, 130.4, 129.8, 128.0, 127.3, 127.1, 127.0, 120.0, 108.0, 42.2, 23.6. HRMS (ESI) m/z calcd for $C_{19}H_{16}N_3O_2$ $(M+H)^+$: 318.1237 found 318.1239.



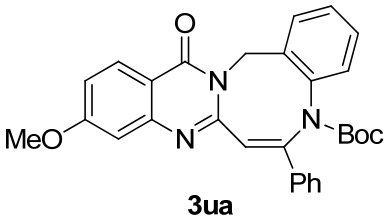
3am

(*Z*)-5-Tosyl-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazolin-13(15*H*)-one (3am). **1a** (85 mg, 0.5 mmol), **2m** (255 mg, 0.6 mmol) ran for 28 h. Purification by column chromatography (2/1, PE/EtOAc) afforded **3am**. A white solid, 0.040 g, 18% yield; mp: 280−281 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.15 (dd, J = 8.1, 1.5 Hz, 1H), 7.65 – 7.62 (m, 1H), 7.60 (dd, J = 7.7, 1.6 Hz, 1H), 7.50 – 7.48 (m, 4H), 7.40 – 7.36 (m, 3H), 7.34 – 7.30 (m, 3H), 5.66 (d, J = 11.5 Hz, 1H), 5.44 (d, J = 13.8 Hz, 1H), 3.69 (d, J = 13.9 Hz, 1H), 2.47 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 160.0, 150.6, 147.2, 145.5, 136.2, 134.8, 134.6, 133.7, 133.0, 130.8, 130.7, 130.6, 129.7, 129.6, 127.2, 127.1, 127.0, 126.4, 119.1, 41.2, 21.2. HRMS (ESI) m/z calcd for $C_{24}H_{20}N_3O_3S$ $(M+H)^+$: 430.1220 found 430.1224.



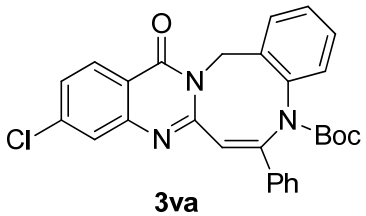
3ta

(*Z*)-*Tert*-butyl 11-methoxy-13-oxo-6-phenyl-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazoline-5-carboxylate (3ta). 1t (47 mg, 0.17 mmol), **2a** (58 mg, 0.20 mmol) ran for 1.5 h. Purification by column chromatography (1/1, PE/EtOAc) afforded **3ta**. A white solid, 0.068 g, 85% yield; mp: 200−201 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 – 7.59 (m, 4H), 7.53 – 7.29 (m, 8H), 7.28 – 7.22 (m, 1H), 5.60 (d, J = 12.2 Hz, 1H), 5.04 (d, J = 14.8 Hz, 1H), 3.88 (s, 3H), 1.14 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7, 158.6, 152.8, 150.3, 142.8, 141.9, 136.6, 134.7, 132.0, 130.6, 130.1, 129.0, 128.9, 127.3, 126.6, 124.7, 122.6, 122.2, 106.4, 81.8, 55.9, 48.5, 27.8. HRMS (ESI) m/z calcd for $C_{29}H_{28}N_3O_4$ $(M+H)^+$: 482.2074, found 482.2077.



3ua

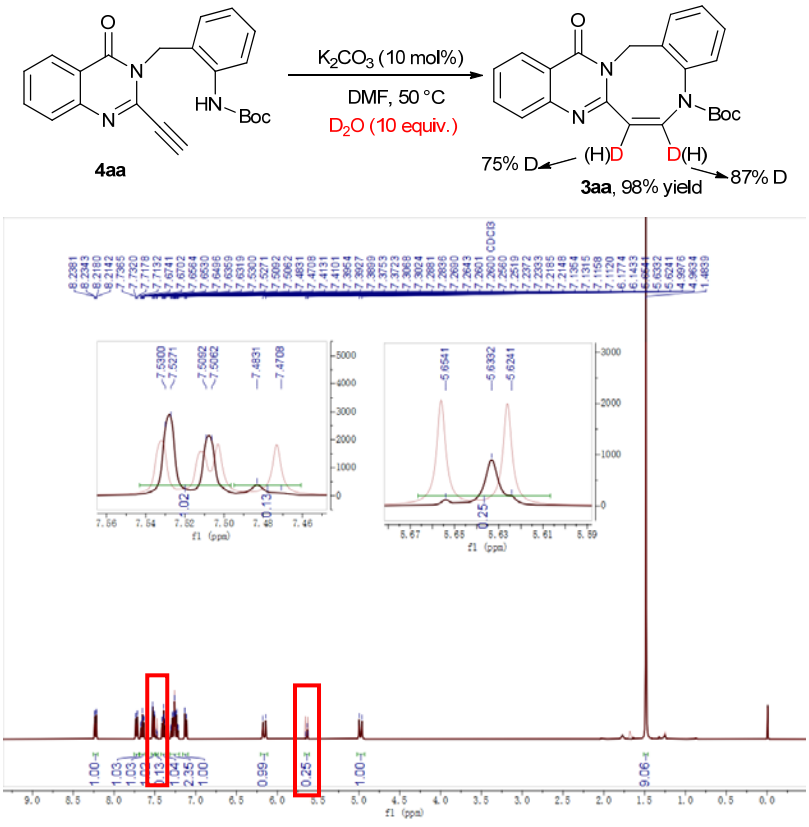
(*Z*)-*Tert*-butyl 10-methoxy-13-oxo-6-phenyl-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazoline-5-carboxylate (3ua). **1u** (47 mg, 0.17 mmol), **2a** (58 mg, 0.20 mmol) ran for 1.5 h. Purification by column chromatography (1/1, PE/EtOAc) afforded **3ua**. A white solid, 0.065 g, 82% yield; mp: 211−212 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 8.8 Hz, 1H), 7.69 – 7.61 (m, 2H), 7.52 – 7.21 (m, 8H), 7.15 – 6.93 (m, 2H), 5.60 (d, J = 14.4 Hz, 1H), 5.01 (d, J = 12.0 Hz, 1H), 3.90 (s, 3H), 1.16 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.7, 161.5, 153.1, 152.7, 149.6, 142.9, 134.7, 132.0, 130.6, 130.1, 129.1, 128.9, 128.6, 127.4, 126.7, 116.9, 115.0, 108.1, 81.7, 55.8, 48.3, 27.8. HRMS (ESI) m/z calcd for $C_{29}H_{28}N_3O_4$ $(M+H)^+$: 482.2074, found 482.2078.



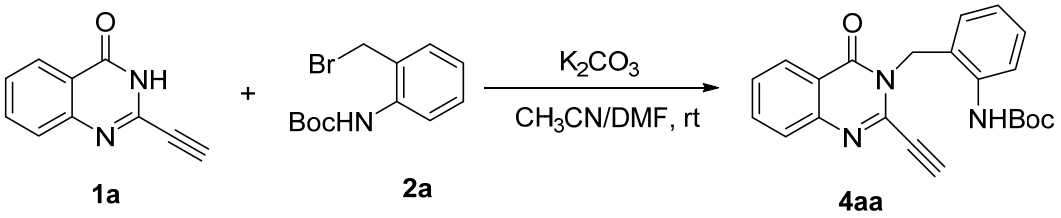
3va

(*Z*)-*Tert*-butyl 10-chloro-13-oxo-6-phenyl-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocineo[2,1-*b*]quinazoline-5-carboxylate (3va). 1v (56 mg, 0.2 mmol), **2a** (68 mg, 0.24 mmol) ran for 1.5 h. Purification by column chromatography (1/1, PE/EtOAc) afforded **3va**. A white solid, 0.081 g, 84% yield; mp: 213−214 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (d, J = 8.5 Hz, 1H), 7.77 – 7.56 (m, 3H), 7.50 – 7.23 (m, 9H), 5.59 (d, J = 15.2 Hz, 1H), 5.03 (d, J = 15.6 Hz, 1H), 1.16 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.3, 153.7, 152.7, 148.4, 143.3, 140.6, 134.4, 131.7, 130.6, 130.3, 129.1, 128.6, 127.7, 127.5, 126.7, 122.4, 119.8, 81.9, 48.5, 27.8. HRMS (ESI) m/z calcd for $C_{28}H_{25}ClN_3O_3$ $(M+H)^+$: 486.1579, found 486.1586.

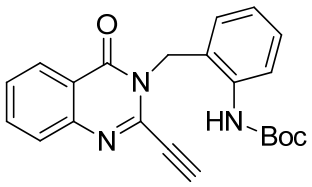
3. Synthesis of compound D-3aa.



4. Synthesis of compound 4aa.



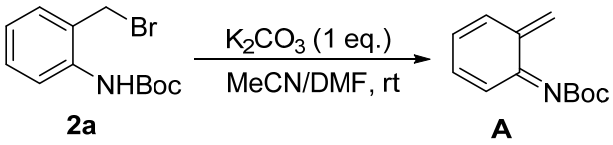
To a stirred mixture of quinazolin-4(3*H*)-one **1a** (340 mg, 2 mmol, 1.0 equiv.) and 2-(bromomethyl)phenyl **2a** (1140 mg, 4 mmol) in MeCN/DMF (1:10, 0.1 M), K_2CO_3 (552 mg, 2.0 equiv.) was added at 25 °C. The resulting mixture was stirred at 25 °C for 1.5 h. After completion indicated by TLC, the mixture was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (PE/EtOAc = 6/1) to afford compound **4aa** (86% yield, 0.65 g).



4aa

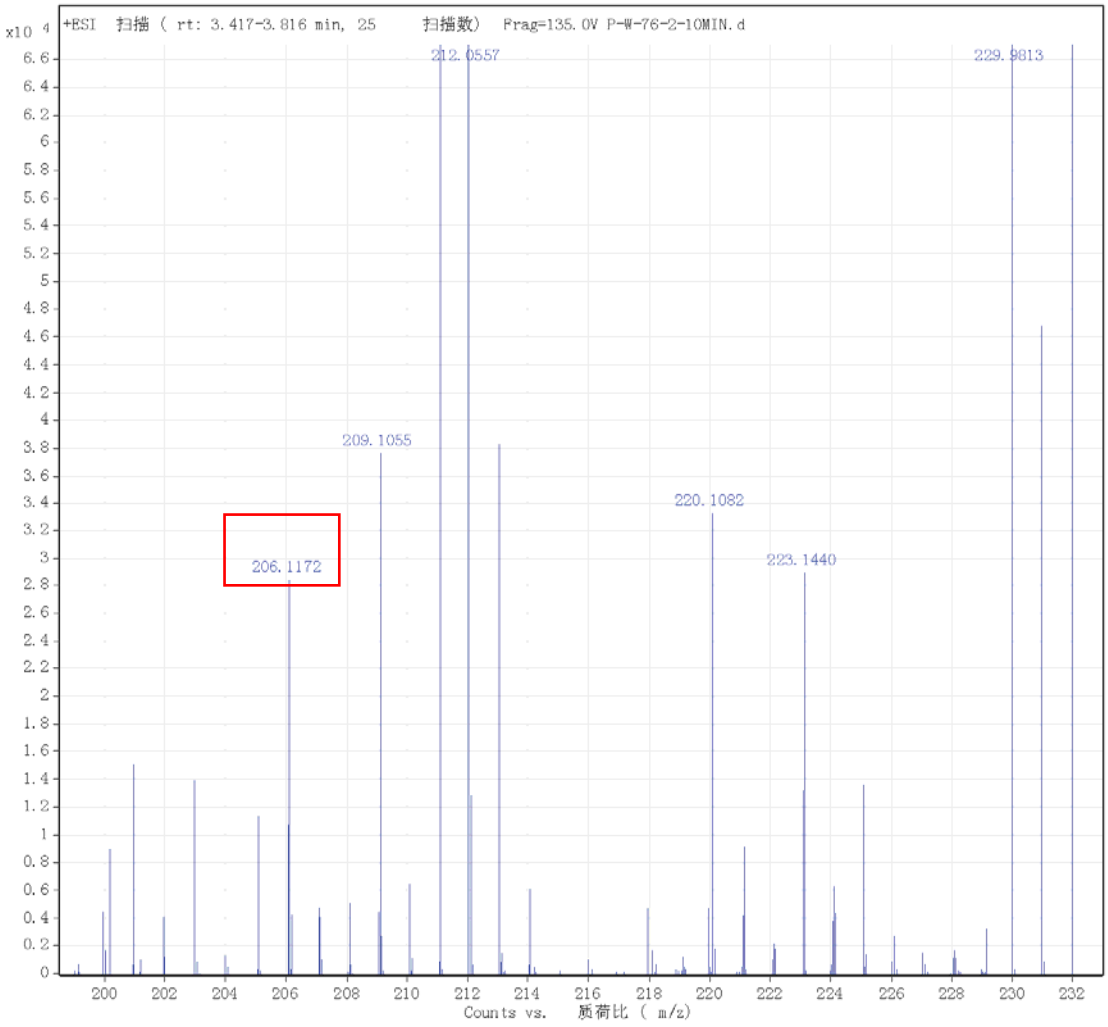
***Tert*-butyl (2-((2-ethynyl-4-oxoquinazolin-3(4*H*)-yl)methyl)phenyl)carbamate (4aa)**. A white solid, 0.646 g, 86% yield; mp: 227–228 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.02 (s, 1H), 8.15 (dd, J = 8.0, 1.5 Hz, 1H), 7.91 – 7.87 (m, 1H), 7.73 (dd, J = 8.3, 1.1 Hz, 1H), 7.63 – 7.59 (m, 1H), 7.39 – 7.32 (m, 1H), 7.23 (td, J = 7.6, 1.5 Hz, 1H), 7.06 (td, J = 7.6, 1.4 Hz, 1H), 6.80 (dd, J = 7.8, 1.5 Hz, 1H), 5.40 (s, 2H), 4.75 (s, 1H), 1.49 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.4, 153.6, 147.0, 139.4, 135.8, 134.9, 130.2, 128.2, 127.3, 127.2, 126.4, 125.2, 125.1, 125.0, 121.3, 85.4, 79.1, 76.3, 45.3, 28.1. HRMS (ESI) m/z calcd for $C_{22}H_{22}N_3O_3$ $(M+H)^+$: 376.1656, found 376.1666.

5. Ao-QMs intermediate detection by HRMS.

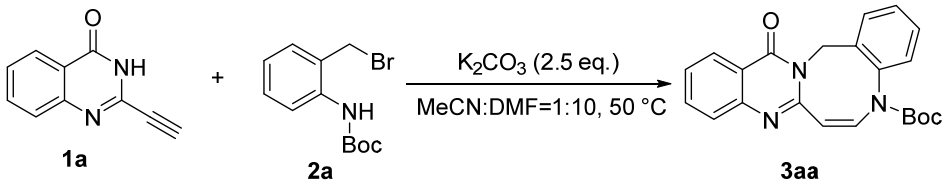


$[M+H]^+$: 206.1176
found: 206.1172

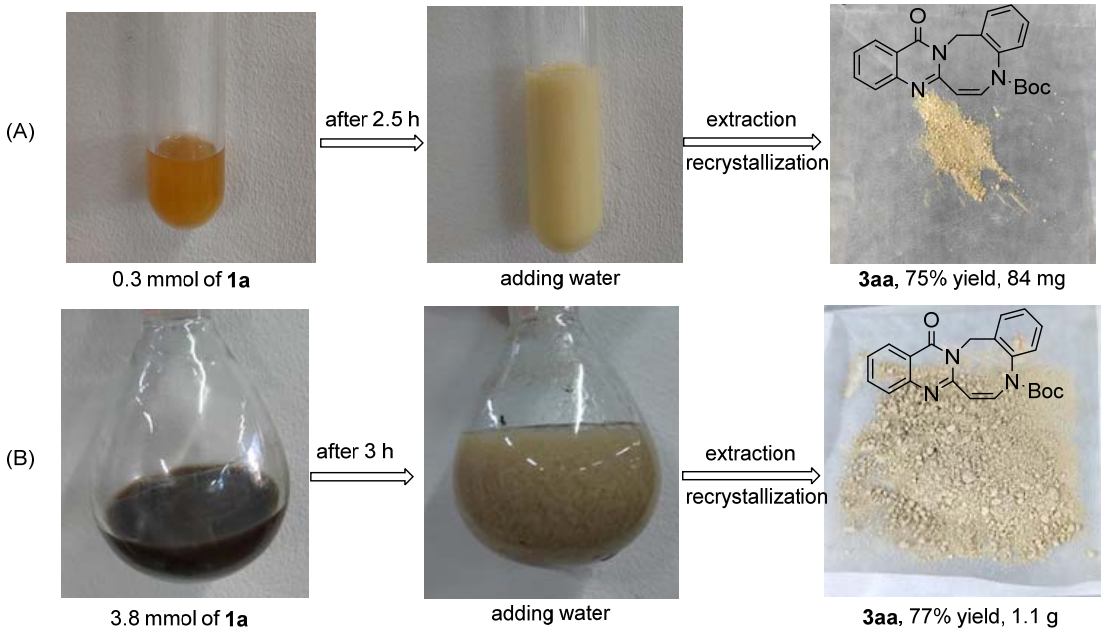
K_2CO_3 and 2-(bromomethyl)phenyl (**2a**) were carried out with 1:1 ratio at rt for 10 min, then, the reaction mixture was directly detected by HRMS (ESI) and we found azadiene. The HRMS(ESI) spectra of components were listed as below:



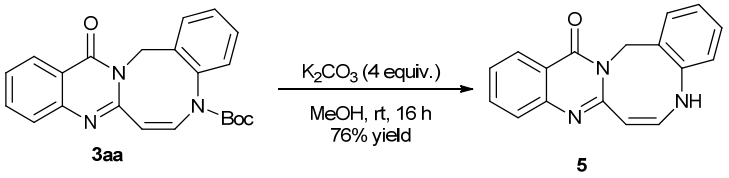
6. Preparations of compound 3aa by simple operations.



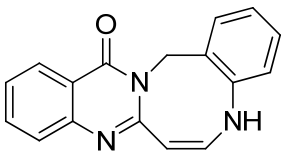
To a stirred mixture of **1a** (0.3 mmol or 3.8 mmol, 1.0 equiv.) in DMF and MeCN (*V*:*V* = 10:1), K_2CO_3 (2.5 equiv.) and **2a** (1.2 equiv.) was added. The resulting mixture was stirred at 50 °C for 2.5~3 h until compound **1a** was completely consumed (monitored by TLC). At this time, the reaction was quenched with water (8 or 30 mL) and extracted with ethyl ether (30 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and concentrated *in vacuo*. Recrystallization with ethyl ether and PE to afford compound **3aa** as a yellow solid. Product **3aa** obtained from this protocol showed a clean ^1H NMR.



7. Synthesis of compound 5.



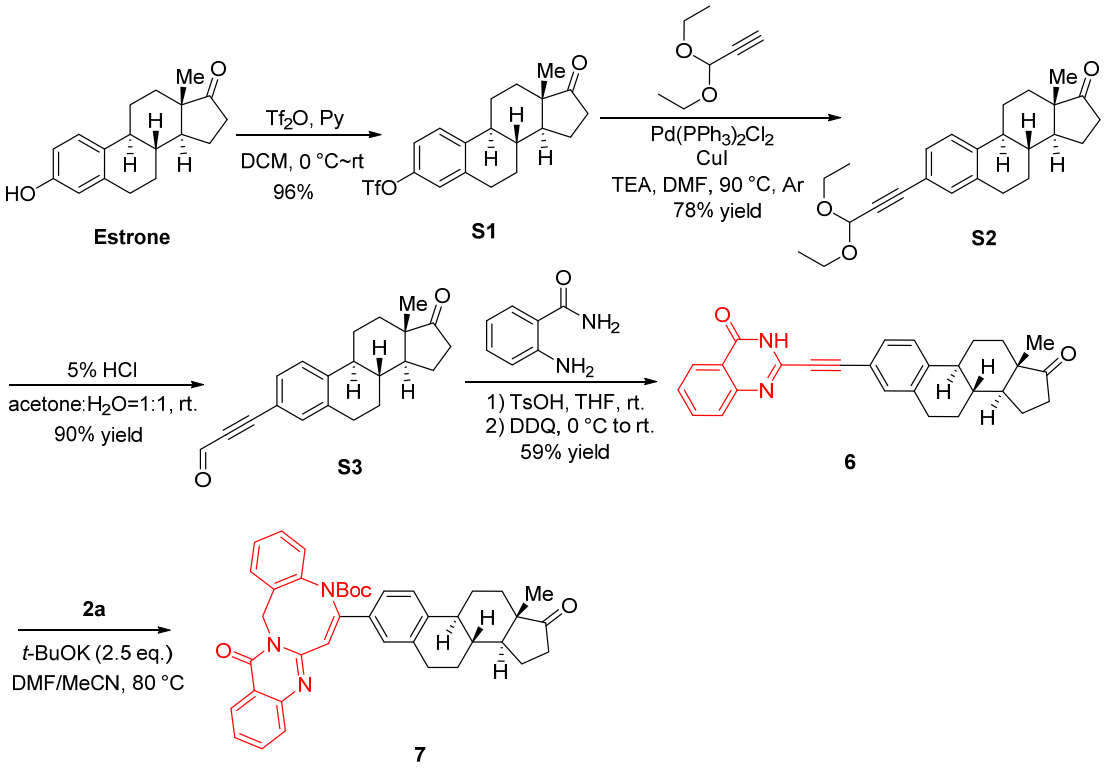
In a 25 mL reaction flask was charged with K_2CO_3 (147 mg, 4.0 equiv.), **3aa** (100 mg, 0.27 mmol) and MeOH (4.0 mL). The mixture was stirred vigorously at 25 °C for 16 h until compound **3aa** was completely consumed (monitored by TLC). At this time, the mixture was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (PE/EtOAc = 2/1 to 1/2) to afford compound **5**.



5

(*Z*)-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazolin-13(15*H*)-one (5). 3aa (100 mg, 0.27 mmol) ran for 16 h. Purification by column chromatography (1/2, PE/EtOAc) afforded **5**. A yellow solid, 0.056 g, 76% yield; mp: 282−283 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (dd, J = 8.1, 1.6 Hz, 1H), 7.77 (dd, J = 7.6, 1.6 Hz, 1H), 7.65 – 7.61 (m, 1H), 7.54 – 7.49 (m, 1H), 7.36 – 7.32 (m, 1H), 7.20 (dd, J = 7.6, 1.6 Hz, 1H), 7.04 (dd, J = 7.5, 1.2 Hz, 1H), 6.76 (dd, J = 8.0, 1.3 Hz, 1H), 6.37 (dd, J = 11.7, 7.9 Hz, 1H), 6.24 (s, 1H), 5.87 (d, J = 13.7 Hz, 1H), 5.52 (d, J = 13.7 Hz, 1H), 5.11 (d, J = 11.7 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.1, 155.0, 140.7, 136.3, 134.4, 132.9, 129.8, 128.6, 126.9, 126.6, 125.9, 125.2, 121.1, 119.7, 94.6, 44.0. HRMS (ESI) m/z calcd for $C_{17}H_{14}N_3O$ $(M+H)^+$: 276.1131 found 276.1140.

8. Synthesis of compounds 6 and 7.



Estrone (10 mmol, 1.0 equiv.) and pyridine (1.61 mL, 2.0 equiv.) was sequentially dissolved in 40 mL of dry DCM. The resulting mixture was stirred at 25 °C for 0.5 h, following by dropwise addition of Tf_2O (2.02 mL, 1.2 equiv.) at 0 °C. After that, the mixture was warmed to rt, and stirred overnight. When the reaction completed, 10% HCl was added to the solution to quench the reaction, and then the mixture was extracted with DCM. The organic layer was washed with saturated $NaHCO_3$ and saturated brine, dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (PE/EtOAc = 10/1) to afford compound **S1** with 96% yield (3.80 g).

A mixture of **S1** (1.81 g, 4.5 mmol), 3,3-diethoxyprop-1-yne (0.81 mL, 1.25 equiv.), triethylamine (3.0 mL), and $Pd(PPh_3)_2Cl_2$ (316 mg, 0.1 equiv.), CuI (86 mg, 0.1 equiv.) was dissolved in 15 mL of DMF and stirred at 90 °C for 16 h under argon gas. The reaction mixture was diluted with water (150 mL) and extracted with EA (3×50 mL), the combined organic layers were washed with brine for three times (3×30 mL), dried by Na_2SO_4, filtered and concentrated *in vacuo*. The crude product was purified by silica

gel column chromatography (PE/EtOAc = 10/1) to afford compound **S2** with 78% yield (1.30 g).

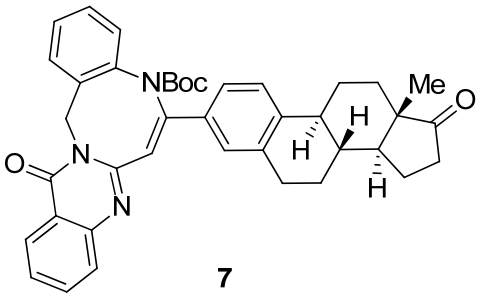
S2 (1.00 g, 2.71 mmol) was dissolved in mixed solvents (20 mL) of acetone and H_2O (*V*:*V* = 1:1), then 5% HCl (8 mL, 5.0 equiv.) was added to the solution, and the mixture was allowed to react overnight at room temperature. Upon completion of the reaction, acetone was removed under reduced pressure, after that the aqueous layer was extracted with DCM (3×20 mL), the combined organic layers were dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (PE/EtOAc = 10/1) to afford compound **S3** with 90% yield (0.9 g).[3]

To a stirred mixture of 2-aminobenzamide (75 mg, 0.55 mmol, 1.0 equiv.), anhydrous magnesium sulfate (198 mg, 3.0 equiv.) in THF (0.2 M) was added *p*-toluene sulfonic acid (29 mg, 0.3 equiv.) and **S3** (167 mg, 0.55 mmol, 1.0 equiv.) at 25 °C under argon gas. The resulting mixture was stirred at 25 °C for 2.5 h. After completion indicated by TLC, 2,3-dicyano-5,6-dichlorobenzoquinone (DDQ, 150 mg, 1.2 equiv.) was added. The resultant reaction mixture was stirred at room temperature for an additional 0.5 h (monitored by TLC). The mixture was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (DCM/MeOH = 100/1) to afford **6**.

2-(((8*R*,9*S*,13*S*,14*S*)-13-Methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)ethynyl)quinazolin-4(3*H*)-one (6). A white solid, 0.136 g, 59% yield; mp: 299–300 °C; ^{1}H NMR (600 MHz, Pyr-d_5): δ 8.59 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.79 – 7.77 (m, 1H), 7.55 – 7.41 (m, 2H), 7.33 – 7.23 (m, 2H), 2.75 (dd, *J* = 9.1, 4.3 Hz, 2H), 2.53 – 2.40 (m, 1H), 2.23 – 2.22 (m, 1H), 2.15 – 2.03 (m, 2H), 2.02 – 1.94 (m, 1H), 1.87 – 1.74 (m, 2H), 1.49 – 1.21 (m, 6H), 0.83 (s, 3H). ^{13}C NMR (150 MHz, Pyr-d_5): δ 219.9, 162.9, 159.0, 143.7, 140.5, 138.2, 135.2, 133.7, 130.3, 128.6, 128.0, 127.3, 126.9, 118.4, 91.4, 84.5, 50.8, 48.4, 45.1, 38.2, 36.3, 32.5, 29.6, 26.7, 26.1, 22.1, 14.2. HRMS (ESI) m/z calcd for $C_{28}H_{27}N_2O_2$ $(M+H)^+$: 423.2067, found 423.2080.

In a 25 mL reaction flask was charged with *t*-BuOK (50 mg, 2.5 eq.), **6** (76 mg, 0.18 mmol), **2a** (62 mg, 1.2 eq.) and DMF (5.0 mL), MeCN (0.5 mL). The mixture was

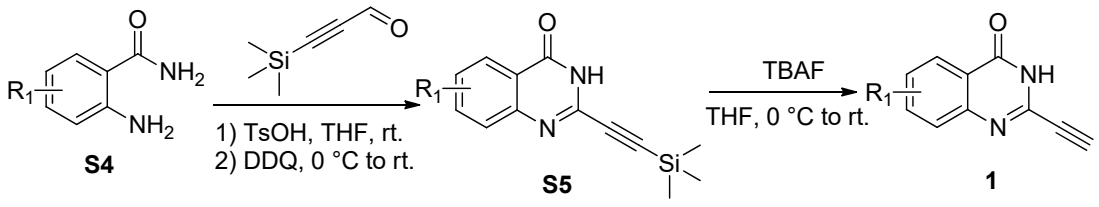
stirred vigorously at 80 °C for 3 h until compound **6** was completely consumed (monitored by TLC). At this time, the reaction was quenched with water (20 mL) and extracted with EtOAc (30 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and filtered. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (PE/EtOAc = 1/6 to 1/1) to afford compound **7**.



7

(*Z*)-*Tert*-butyl 6-((8*R*,9*S*,13*S*,14*S*)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6*H*-cyclopenta[*a*]phenanthren-3-yl)-13-oxo-13,15-dihydro-5*H*-benzo[6,7][1,5]diazocino[2,1-*b*]quinazoline-5-carboxylate (7). A white solid, 0.088 g, 78% yield; mp: 189−190 °C; ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.24 (dt, J = 8.0, 1.1 Hz, 1H), 7.80 – 7.61 (m, 2H), 7.54 – 7.21 (m, 9H), 5.60 (d, J = 15.4 Hz, 1H), 5.03 (d, J = 15.4 Hz, 1H), 2.96 – 2.91 (m, 2H), 2.51 (dd, J = 19.1, 8.7 Hz, 1H), 2.43 – 2.40 (m, 1H), 2.31 – 2.27 (m, 1H), 2.18 – 2.11 (m, 1H), 2.09 – 2.01 (m, 2H), 1.98 – 1.95 (m, 1H), 1.68 (d, J = 19.1 Hz, 1H), 1.65 – 1.57 (m, 2H), 1.55 – 1.42 (m, 4H), 1.30 – 1.04 (m, 9H), 0.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 220.8, 161.9, 152.8, 152.6, 147.4, 142.8, 142.3, 137.2, 134.4, 132.0, 130.6, 128.9, 127.3, 127.2, 127.0, 126.1, 124.0, 121.8, 121.3, 81.7, 50.5, 48.5, 48.0, 44.6, 38.0, 35.9, 31.6, 29.6, 27.8, 26.4, 25.7, 21.7, 13.9. HRMS (ESI) m/z calcd for $C_{40}H_{42}N_3O_4$ $(M+H)^+$: 628.3170, found 628.3169.

9. Synthesis of 2-ethynylquinazolin-4(3*H*)-one 1.

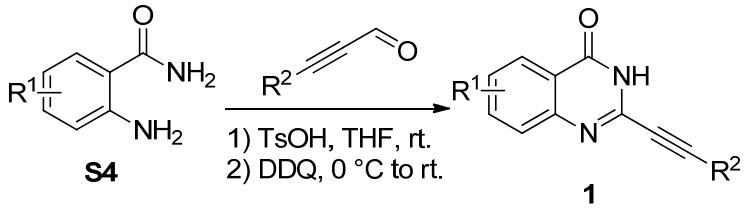


S4 **S5** **1**

2-aminobenzamides **S4** was prepared according to literature method [4].

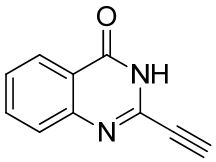
General procedure C: To a stirred mixture of 2-aminobenzamide **S4** (4.0 mmol, 1.0 equiv.), anhydrous magnesium sulfate (1440 mg, 3.0 equiv.) in THF (0.2 M) was added *p*-toluene sulfonic acid (200 mg, 0.3 equiv.) and 3-(Trimethylsilyl)-2-propynal (4.0 mmol, 1.0 equiv.) at 25 °C under argon gas. The resulting mixture was stirred at 25 °C for 1~12 h. After completion indicated by TLC, 2,3-dicyano-5,6-dichlorobenzo- -quinone (DDQ, 1090 mg, 1.2 equiv.) was added. The resultant reaction mixture was stirred at room temperature for an additional 0.5 h (monitored by TLC). The mixture was concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (PE/EtOAc = 20/1 to 1/1) to afford **S5**.

To a solution of **S5** (4.4 mmol) in THF (20 mL) at 0 °C was added slowly a solution of Tetrabutylammonium fluoride (1 mol/L in THF) (4.8 mmol, 1.1 equiv.). The resulting mixture was allowed to warm to room temperature and stirred for 1 h. Upon completion, the reaction mixture was quenched by addition of an aqueous saturated solution of NH_4Cl (20 mL) and extracted with ethyl acetate (3×30 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography (DCM/MeOH = 100/1 to 50/1) to afford **1a**-**1m** and **1r**-**1s**.



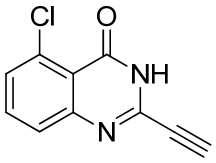
General procedure D: To a stirred mixture of 2-aminobenzamide **S4** (1.5 mmol, 1.0 equiv.), anhydrous magnesium sulfate (540 mg, 3.0 equiv.) in THF (0.2 M) was added *p*-toluene sulfonic acid (80 mg, 0.3 equiv.) and 3-phenylpropiolaldehyde or methylpropiolic aldehyde (1.5 mmol, 1.0 equiv.) at 25 °C under argon gas. The resulting mixture was stirred at 25 °C for 1~12 h. After completion indicated by TLC, 2,3-dicyano-5,6-dichlorobenzoquinone (DDQ, 410 mg, 1.2 equiv.) was added. The resultant reaction mixture was stirred at room temperature for an additional 0.5 h (monitored by TLC). The mixture was concentrated under reduced pressure. The crude

product was purified by silica gel column chromatography (PE/EtOAc = 20/1 to 1/1) to afford **1n**-**1q, 1t**-**1v**.



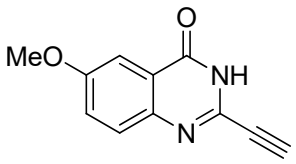
1a

2-Ethynylquinazolin-4(3*H*)-one (1a). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1a**. A white solid, 0.491 g, 81% yield; mp: 222.7–223.6 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.86 (s, 1H), 8.14 – 8.07 (m, 1H), 7.82 (t, J = 7.7 Hz, 1H), 7.65 (d, J = 8.1 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 4.71 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.0, 148.2, 137.7, 134.7, 127.7, 127.3, 125.9, 122.3, 82.5, 77.1. HRMS (ESI) m/z calcd for $C_{10}H_7N_2O$ $(M+H)^+$: 171.0553, found 171.0560.



1b

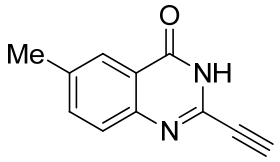
5-Chloro-2-ethynylquinazolin-4(3*H*)-one (1b). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1b**. A grey solid, 0.170 g, 81% yield; mp: 251–252 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.89 (s, 1H), 7.72 (t, J = 8.0 Hz, 1H), 7.55 (dd, J = 8.0, 1.2 Hz, 2H), 4.75 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.3, 150.8, 138.6, 134.4, 132.5, 129.9, 126.9, 119.3, 83.2, 76.7. HRMS (ESI) m/z calcd for $C_{10}H_6ClN_2O$ $(M+H)^+$: 205.0163, found 205.0167.



1c

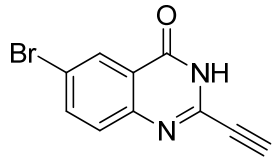
2-Ethynyl-6-methoxyquinazolin-4(3*H*)-one (1c). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1c**. A grey solid, 0.122 g, 28% yield; mp: 233–234 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.79 (s, 1H), 7.61 (d, J =

8.9 Hz, 1H), 7.49 (d, J = 2.9 Hz, 1H), 7.42 (dd, J = 8.9, 3.0 Hz, 1H), 4.65 (s, 1H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.7, 158.5, 142.6, 135.3, 129.1, 124.0, 123.3, 106.0, 82.0, 77.1, 55.7. HRMS (ESI) m/z calcd for $C_{11}H_9N_2O_2$ $(M+H)^+$: 201.0659, found 201.0662.



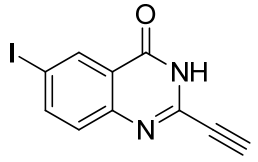
1d

2-Ethynyl-6-methylquinazolin-4(3*H*)-one (1d). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1d**. A yellow solid, 0.360 g, 66% yield; mp: 243–244 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.75 (s, 1H), 7.92 – 7.86 (m, 1H), 7.63 (dd, J = 8.4, 2.1 Hz, 1H), 7.54 (d, J = 8.3 Hz, 1H), 4.68 (s, 1H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.8, 146.2, 137.6, 136.8, 135.9, 127.2, 125.3, 122.0, 82.2, 77.1, 20.9. HRMS (ESI) m/z calcd for $C_{11}H_9N_2O$ $(M+H)^+$: 185.0709, found 185.0709.



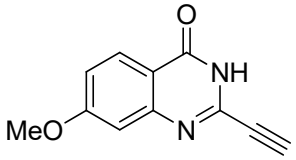
1e

6-Bromo-2-ethynylquinazolin-4(3*H*)-one (1e). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1e**. A white solid, 0.248 g, 86% yield; mp: 220–221 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.03 (s, 1H), 8.16 (d, J = 2.4 Hz, 1H), 7.96 (dd, J = 8.7, 2.4 Hz, 1H), 7.59 (d, J = 8.7 Hz, 1H), 4.77 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 159.9, 147.2, 138.1, 137.5, 129.6, 128.0, 123.9, 120.2, 83.1, 76.9. HRMS (ESI) m/z calcd for $C_{10}H_6BrN_2O$ $(M+H)^+$: 248.9658, found 248.9663.



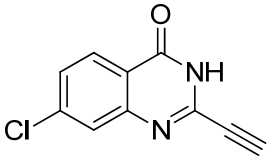
1f

2-Ethynyl-6-iodoquinazolin-4(3*H*)-one (1f). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1f**. A yellow solid, 0.340 g, 93% yield; mp: 242–243 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.00 (s, 1H), 8.35 (d, J = 2.1 Hz, 1H), 8.10 (dd, J = 8.5, 2.1 Hz, 1H), 7.43 (d, J = 8.5 Hz, 1H), 4.76 (s, 1H). 13C NMR (100 MHz, DMSO-d_6): δ 159.7, 147.5, 143.0, 138.1, 134.2, 129.4, 124.0, 93.1, 83.1, 77.0. HRMS (ESI) m/z calcd for $C_{10}H_6IN_2O$ $(M+H)^+$: 296.9519, found 296.9527.



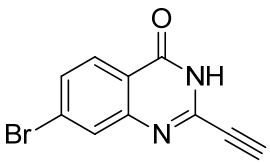
1g

2-Ethynyl-7-methoxyquinazolin-4(3*H*)-one (1g). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1g**. A white solid, 0.376 g, 95% yield; mp: 246–247 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.72 (s, 1H), 8.02 – 7.97 (m, 1H), 7.13 – 7.09 (m, 2H), 4.70 (s, 1H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.1, 160.5, 150.5, 138.2, 127.5, 117.0, 115.7, 108.6, 82.4, 77.0, 55.8. HRMS (ESI) m/z calcd for $C_{11}H_6N_2O_2$ $(M+H)^+$: 201.0659, found 201.0664.



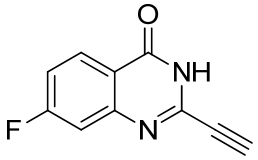
1h

7-Chloro-2-ethynylquinazolin-4(3*H*)-one (1h). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1h**. A white solid, 0.140 g, 74% yield; mp: 281–282 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.00 (s, 1H), 8.08 (d, J = 8.6 Hz, 1H), 7.71 (d, J = 2.1 Hz, 1H), 7.56 (dd, J = 8.5, 2.1 Hz, 1H), 4.78 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.4, 149.3, 139.2, 139.0, 127.9, 127.8, 126.5, 121.1, 83.3, 76.8. HRMS (ESI) m/z calcd for $C_{10}H_6ClN_2O$ $(M+H)^+$: 205.0163, found 205.0165.



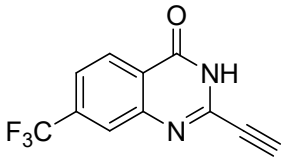
1i

7-Bromo-2-ethynylquinazolin-4(3*H*)-one (1i). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1i**. A yellow solid, 0.385 g, 95% yield; mp: 251–252 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.00 (s, 1H), 7.99 (d, J = 8.5 Hz, 1H), 7.86 (d, J = 1.9 Hz, 1H), 7.69 (dd, J = 8.5, 2.0 Hz, 1H), 4.78 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.6, 149.4, 138.9, 130.5, 129.5, 128.2, 127.9, 121.4, 83.3, 76.8. HRMS (ESI) m/z calcd for $C_{10}H_6BrN_2O$ $(M+H)^+$: 248.9658, found 248.9665.



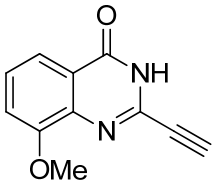
1j

2-Ethynyl-7-fluoroquinazolin-4(3*H*)-one (1j). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1j**. A white solid, 0.186 g, 99% yield; mp: 224–225 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.96 (s, 1H), 8.15 (dd, J = 8.8, 6.2 Hz, 1H), 7.48 – 7.37 (m, 2H), 4.77 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 165.7 (J = 249.8 Hz), 160.3, 150.4 (d, J = 13.1 Hz), 139.0, 129.0 (d, J = 10.8 Hz), 119.3 (d, J = 1.9 Hz), 116.1 (d, J = 23.6 Hz), 112.5 (d, J = 21.8 Hz), 83.2, 76.8. ^{19}F NMR (375 MHz, DMSO-d_6): δ –104.0. HRMS (ESI) m/z calcd for $C_{10}H_6FN_2O$ $(M+H)^+$: 189.0459, found 189.0464.



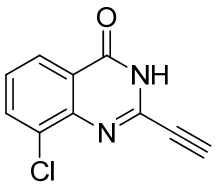
1k

2-Ethynyl-7-(trifluoromethyl)quinazolin-4(3*H*)-one (1k). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1k**. A white solid, 0.251 g, 80% yield; mp: 222–223 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.16 (s, 1H), 7.98 – 7.97 (m, 1H), 7.98 (dt, J = 1.6, 0.8 Hz, 1H), 7.87 – 7.80 (m, 1H), 4.82 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.3, 148.4, 139.2, 134.2 (q, J = 32.1 Hz), 127.7, 125.2, 124.5 (q, J = 34.0 Hz), 123.4 (q, J = 271.4 Hz), 123.3 (q, J = 3.5 Hz), 83.6, 76.8. ^{19}F NMR (375 MHz, DMSO-d_6): δ –61.7. HRMS (ESI) m/z calcd for $C_{11}H_6F_3N_2O$ $(M+H)^+$: 239.0427, found 239.0433.



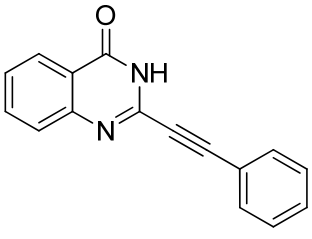
1l

2-Ethynyl-8-methoxyquinazolin-4(3*H*)-one (1l). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1l**. A white solid, 0.200 g, 50% yield; mp: 230–231 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.85 (s, 1H), 7.69 – 7.60 (m, 1H), 7.47 (t, J = 8.0 Hz, 1H), 7.40 – 7.31 (m, 1H), 4.68 (s, 1H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.9, 154.4, 138.6, 136.1, 128.1, 123.3, 116.8, 115.2, 82.2, 77.3, 56.0. HRMS (ESI) m/z calcd for $C_{11}H_9N_2O_2$ $(M+H)^+$: 201.0659, found 201.0660.



1m

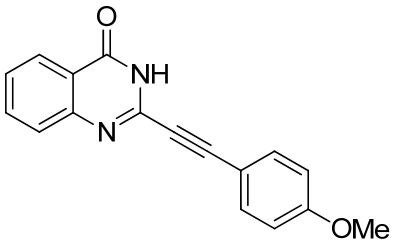
8-Chloro-2-ethynylquinazolin-4(3*H*)-one (1m). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1m**. A white solid, 0.201 g, 86% yield; mp: 256–257 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.10 (s, 1H), 8.05 (dd, J = 7.9, 1.5 Hz, 1H), 7.96 (dd, J = 7.8, 1.5 Hz, 1H), 7.50 (t, J = 7.9 Hz, 1H), 4.81 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.5, 144.8, 138.4, 134.8, 130.8, 127.9, 125.0, 124.1, 83.6, 77.0. HRMS (ESI) m/z calcd for $C_{10}H_6ClN_2O$ $(M+H)^+$: 205.0163, found 205.0167.



1n

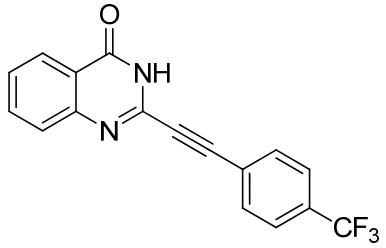
2-(Phenylethynyl)quinazolin-4(3*H*)-one (1n). Purification by flash column chromatography (1/20 to 1/1, EtOAc/PE) to afford **1n**. A white solid, 0.493 g, 50% yield; mp: 211–212 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.91 (s, 1H), 8.13 (dd, J =

7.9, 1.5 Hz, 1H), 7.86 – 7.82 (m, 1H), 7.73 – 7.65 (m, 3H), 7.58 – 7.48 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.3, 149.2, 138.4, 135.1, 132.8, 130.5, 128.7, 128.0, 127.7, 126.5, 121.8, 120.4, 92.3, 82.6. HRMS (ESI) m/z calcd for $C_{16}H_{11}N_2O$ $(M+H)^+$: 247.0866, found 247.0867.



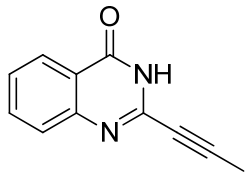
1o

2-((4-Methoxyphenyl)ethynyl)quinazolin-4(3*H*)-one (1o). Purification by flash column chromatography (1/20 to 1/1, EtOAc/PE) to afford **1o**. A white solid, 0.286 g, 52% yield; mp: 279–280 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.81 (s, 1H), 8.11 (dd, J = 8.0, 1.5 Hz, 1H), 7.84 – 7.80 (m, 1H), 7.70 – 7.61 (m, 3H), 7.55 – 7.51 (m, 1H), 7.09 – 7.02 (m, 2H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 161.1, 161.0, 148.7, 138.7, 134.6, 134.1, 127.2, 125.9, 121.9, 114.8, 111.5, 91.0, 82.3, 55.5. HRMS (ESI) m/z calcd for $C_{17}H_{13}N_2O_2$ $(M+H)^+$: 277.0972, found 277.0975.



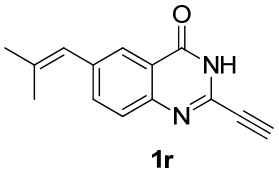
1p

2-((4-(Trifluoromethyl)phenyl)ethynyl)quinazolin-4(3*H*)-one (1p). Purification by flash column chromatography (1/20 to 1/1, EtOAc/PE) to afford **1p**. A white solid, 0.475 g, 50% yield; mp: 256–257 °C; ^{1}H NMR (400 MHz, Pyr-d_5): δ 8.57 (d, J = 7.9 Hz, 1H), 7.95 (d, J = 8.0 Hz, 1H), 7.81 – 7.74 (m, 1H), 7.66 (d, J = 2.5 Hz, 4H), 7.51 (t, J = 7.6 Hz, 1H). ^{13}C NMR (100 MHz, Pyr-d_5): δ 162.7, 139.7, 135.2, 135.1, 133.5, 131.7 (q, J = 32.4 Hz), 129.6, 128.9, 128.7, 128.3, 127.3, 127.2, 126.5 (q, J = 238.4 Hz), 126.4 (q, J = 3.7 Hz), 126.1, 88.5, 86.7. ^{19}F NMR (375 MHz, Pyr-d_5): δ –61.03. HRMS (ESI) m/z calcd for $C_{17}H_{10}F_3N_2O$ $(M+H)^+$: 315.0740, found 315.0747.



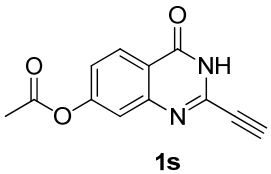
1q

2-(Prop-1-yn-1-yl)quinazolin-4(3*H*)-one (1q). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1q**. A white solid, 0.372 g, 20% yield; mp: 197–198 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ 12.66 (s, 1H), 8.08 (dd, J = 7.9, 1.5 Hz, 1H), 7.81 – 7.78 (m, 1H), 7.60 (d, J = 8.1 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 2.13 (s, 3H). ^{13}C NMR (150 MHz, DMSO-d_6): δ 161.1, 148.6, 138.5, 134.6, 127.2, 127.1, 125.9, 121.9, 89.9, 74.3, 3.8. HRMS (ESI) m/z calcd for $C_{11}H_9N_2O$ $(M+H)^+$: 185.0709 , found 185.0707.



1r

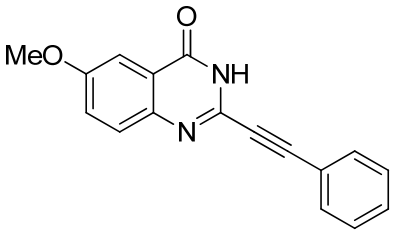
2-ethynyl-6-(2-methylprop-1-en-1-yl)quinazolin-4(3*H*)-one (1r). Purification by flash column chromatography (1/100 to 1/50, MeOH/DCM) to afford **1r**. A white solid, 0.130 g, 88% yield; mp: 192.6–193 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.83 (s, 1H), 7.91 (d, J = 2.1 Hz, 1H), 7.69-7.66 (m, 1H), 7.60 (d, J = 8.4 Hz, 1H), 6.38 (s, 1H), 4.71 (s, 1H), 1.91 (d, J = 1.5 Hz, 3H), 1.88 (d, J = 1.4 Hz, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.9, 146.3, 137.4, 137.0, 135.1, 127.2, 124.7, 123.8, 122.1, 82.5, 77.1, 26.9, 19.4. HRMS (ESI) m/z calcd for $C_{14}H_{13}N_2O$ $(M+H)^+$: 225.1022, found 225.1024. #



1s

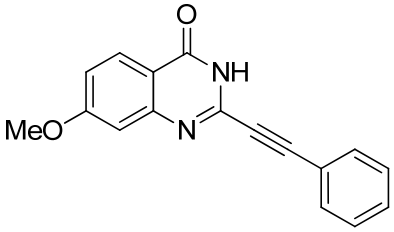
2-ethynyl-4-oxo-3,4-dihydroquinazolin-7-yl acetate (1s). Purification by flash column chromatography (1/100 to 1/20, MeOH/DCM) to afford **1s**. A white solid, 0.242 g, 84% yield; mp: 206.4–207.3 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.93 (s, 1H), 8.13 (d, J = 8.6 Hz, 1H), 7.41 (d, J = 2.3 Hz, 1H), 7.33 (dd, J = 8.7, 2.3 Hz, 1H), 4.76 (s, 1H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 168.8, 160.5, 155.1, 149.5,

138.5, 127.6, 122.2, 120.1, 119.5, 83.0, 76.9, 21.0. HRMS (ESI) m/z calcd for $C_{12}H_9N_2O_3$ $(M+H)^+$: 229.0608, found 229.0609.



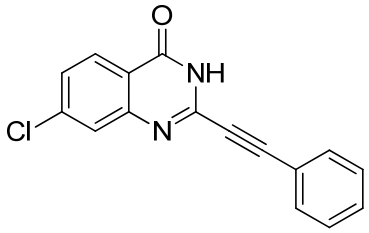
1t

6-Methoxy-2-(phenylethynyl)quinazolin-4(3*H*)-one (1t). Purification by flash column chromatography (1/20 to 1/1, EtOAc/PE) to afford **1t**. A white solid, 0.186 g, 34% yield; mp: 265–266 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.84 (s, 1H), 7.70 – 7.62 (m, 3H), 7.57 – 7.47 (m, 4H), 7.44 (dd, J = 8.9, 3.0 Hz, 1H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.8, 158.4, 143.0, 136.1, 132.2, 130.5, 129.1, 129.0, 124.0, 123.0, 120.0, 106.1, 89.6, 83.1, 55.7. HRMS (ESI) m/z calcd for $C_{17}H_{13}N_2O_2$ $(M+H)^+$: 277.0972, found 277.0974.



1u

7-Methoxy-2-(phenylethynyl)quinazolin-4(3*H*)-one (1u). Purification by flash column chromatography (1/20 to 1/1, EtOAc/PE) to afford **1u**. A white solid, 0.142 g, 26% yield; mp: 288–289 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 12.76 (s, 1H), 8.02 (d, J = 8.6 Hz, 1H), 7.71 – 7.65 (m, 2H), 7.56 – 7.48 (m, 3H), 7.15 – 7.09 (m, 2H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 164.1, 160.6, 150.7, 139.0, 132.3, 130.7, 129.1, 127.5, 119.8, 116.8, 115.4, 108.6, 90.0, 83.0, 55.8. HRMS (ESI) m/z calcd for $C_{17}H_{13}N_2O_2$ $(M+H)^+$: 277.0972, found 277.0979.



1v

7-Chloro-2-(phenylethynyl)quinazolin-4(3*H*)-one (1v). Purification by flash column chromatography (1/20 to 1/1, EtOAc/PE) to afford **1v**. A white solid, 0.550 g, 98% yield; mp: 241–242 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 13.04 (s, 1H), 8.10 (d, J = 8.5 Hz, 1H), 7.79 – 7.65 (m, 3H), 7.59 – 7.48 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 160.5, 149.7, 139.8, 139.2, 132.4, 130.8, 129.1, 128.0, 127.6, 126.4, 120.9, 119.6, 90.9, 82.9. HRMS (ESI) m/z calcd for $C_{16}H_{10}ClN_2O$ $(M+H)^+$: 281.0476, found 281.0478.

10. Biological activity studies of compounds 3, 5, and 7.

Cell Culture: Murine monocyte-macrophage RAW264.7 cells maintained in DMEM (Giboc, USA) incubated at 37 °C in a humidified atmosphere containing 5% CO_2. Mouse peritoneal macrophages purchased from Procell Life Science & Technology Co., Ltd.

Cell Viability assay: Cell cytotoxicity was evaluated by MTT. The MTT solution was added into each well and after incubation at 37 °C for 4 h, the culture media containing MTT were removed, and then DMSO was added into each well and the absorbance at 570 nm was measured by a microplate reader.[5]

Assay for NO production: NO production was quantified by nitrite accumulation in the culture medium using the Griess reaction. Briefly, Raw264.7 cells were pretreated with compounds for 1 h, and then stimulated with or without LPS (1 mg/mL) for 24 h. The isolated supernatants were mixed with an equal volume of Griess reagent (Beyotime Biotechnology, China). $NaNO_2$ was used to generate a standard curve, and nitrite production was determined by measuring the optical density at 540 nm by a microplate reader.[5]

Table S1. The effects of the target compounds on the cell viability of RAW264.7 at the concentration of 25 μM. (the MTT assay).

Compounds	Cell survival (% of normal)	Compounds	Cell survival (% of normal)
3aa	68.00±4.34	**3al**	73.33±8.96
3ab	108.33±5.13	**3da**	98.67±2.52
3ac	94.00±7.00	**3fa**	95.00±6.56
3ad	104.00±2.64	**3ia**	74.00±4.58
3ae	104.33±8.08	**3ka**	85.67±2.08
3af	96.76±6.11	**3oa**	123.67±6.11
3ag	92.33±6.03	**5**	87±6.08
3ai	54.00±9.16	**7**	117.67±11.06
3aj	57.33±12.05	**Indometacin**	93.67±0.57

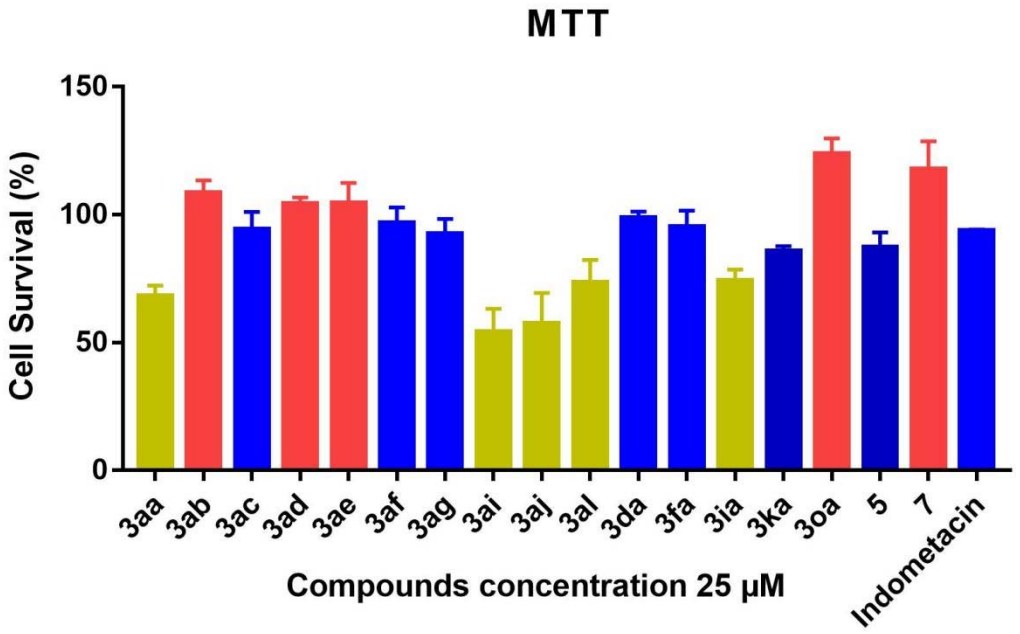
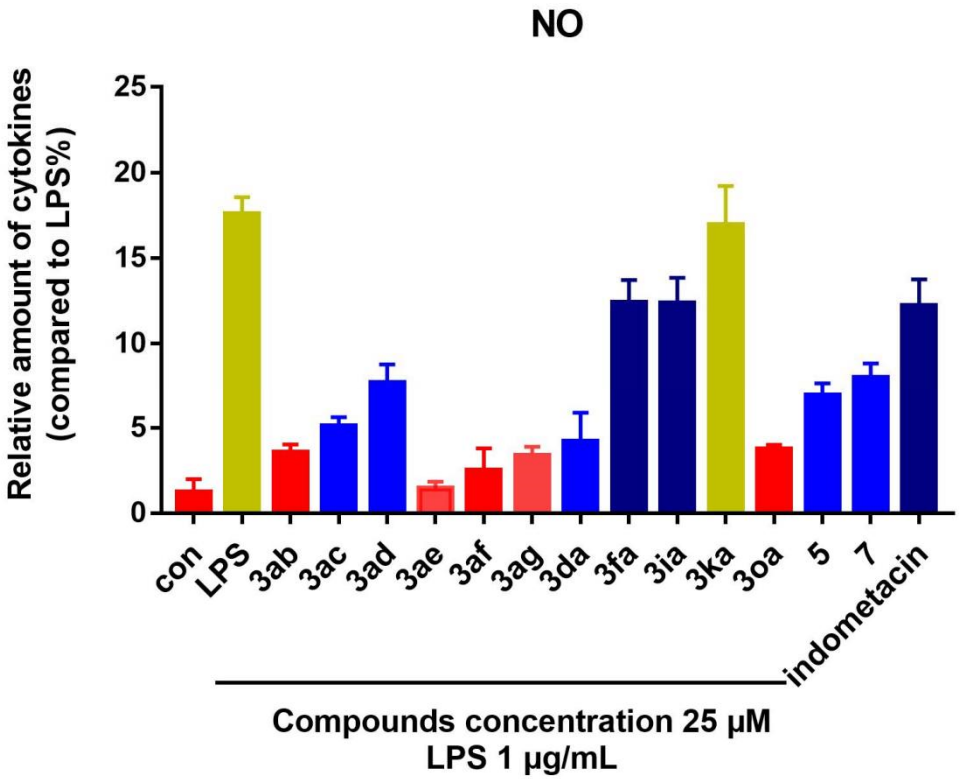


Table S2. The Effect of the compounds **3ab**, **3ac**, **3ad**, **3ae**, **3af**, **3ag**, **3da**, **3fa**, **3ia**, **3ka**, **3oa**, **5**, **7** on the inhibition of NO produced by RAW264.7 cell induced by LPS. In the 25 μM compound concentration, LPS concentration 1 μg/mL.

Compounds	Concentration of NO (μmol/L)	Compounds	Concentration of NO (μmol/L)

con	1.20±0.79	**3da**	4.20±1.69
LPS	17.56±0.98	**3fa**	12.38±1.32
3ab	3.56±0.46	**3ia**	12.35±1.48
3ac	5.10±0.53	**3ka**	16.92±2.27
3ad	7.71±1.06	**3oa**	3.73±0.27
3ae	1.44±0.41	**5**	6.87±0.79
3af	2.5±1.29	**7**	7.99±0.84
3ag	3.36±0.54	**Indometacin**	12.18±1.55



The concentration-dependently suppressed LPS-induced NO generation of **3ab**, **3ae**, **3af**, **3ag**, and **3oa**, are shown in table S3, S4, S5, S6 and S7, respectively.

Table S3. The concentration-dependently suppressed LPS-induced NO generation of the compound **3ab**.

3ab (μmol/L)	Concentration of NO (μmol/L)
0	15.85±0.82
5	10.31±0.51

15	5.44±0.32
25	1.89±0.68

Table S4. The concentration-dependently suppressed LPS-induced NO generation of the compound **3ae**.

3ae (μmol/L)	Concentration of NO (μmol/L)
0	15.85±0.82
5	10.63±0.88
15	5.22±0.15
25	2.31±0.16

Table S5. The concentration-dependently suppressed LPS-induced NO generation of the compound **3af**.

3af (μmol/L)	Concentration of NO (μmol/L)
0	15.85±0.82
5	9.06±0.56
15	3.64±0.02
25	1.78±0.23

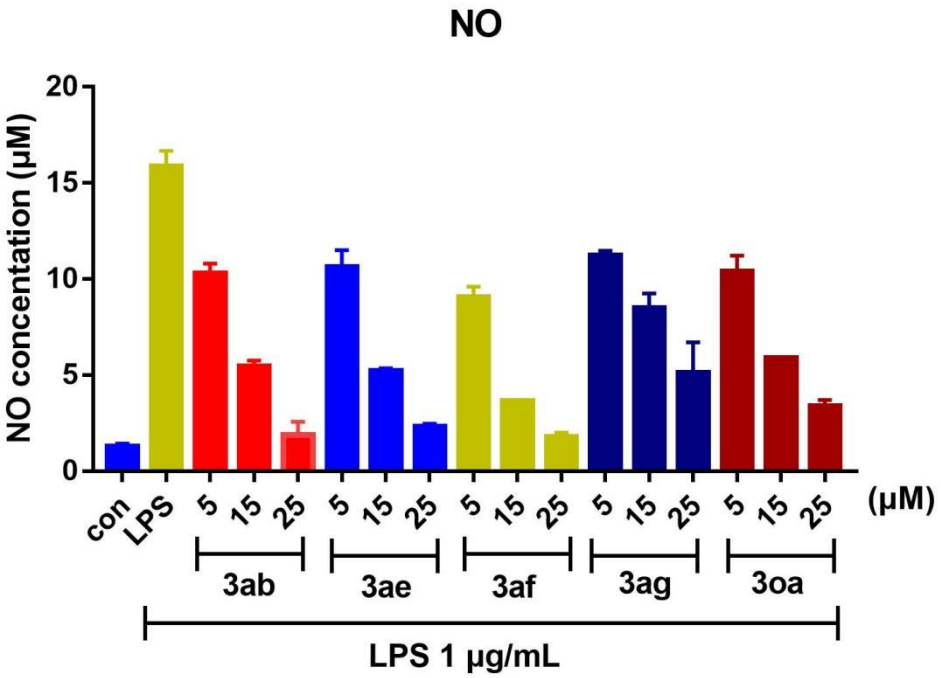
Table S6. The concentration-dependently suppressed LPS-induced NO generation of the compound **3ag**.

3ag (μmol/L)	Concentration of NO (μmol/L)
0	15.85±0.82
5	11.22±0.26
15	8.50±0.76
25	5.12±1.58

Table S7. The concentration-dependently suppressed LPS-induced NO generation of the compound **3oa**.

3oa (μmol/L)	Concentration of NO (μmol/L)
0	15.85±0.82
5	10.39±0.84
15	5.89±0.03

25		3.37±0.34



11. X-ray structure of compound 3na

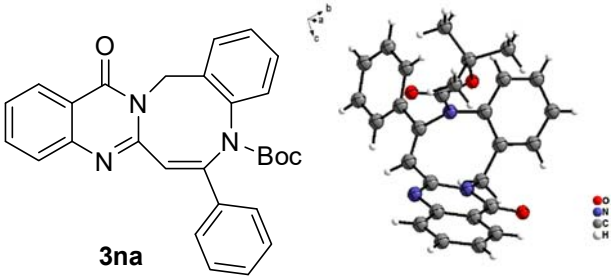


Figure S1: ORTEP diagram of **3na** at 50% ellipsoid probability

Table S8. Crystal data and structure refinement details for compound **3na**.

Compound	**3na**
Empirical formula	$C_{28}H_{25}N_3O_3$
Formula weight	451.51
Crystal system	monoclinic
Space group	C2/c
a (Å)	15.5445(2)
b (Å)	9.50890(10)

c (Å)	31.2275(3)
α (°)	90
β (°)	91.2180(10)
γ (°)	90
V (Å^3)	4614.73(9)
Z	8
ρ_{calc} (g/cm^3)	1.300
μ (mm^{-1})	0.687
F (000)	1904.0
Radiation	Cu Kα (λ = 1.54184)
2θ range for data collection (°)	5.662–151.118
Reflections collected	16222
Independent reflections	4600 [R_{int} = 0.0280, R_{sigma} = 0.0242]
Data/restraints/parameters	4600/0/310
Goodness-of-fit on F^2	1.073
Final R indexes [$I >= 2\sigma(I)$]	R_1 = 0.0445, ωR_2 = 0.1149
Final R indexes [all data]	R_1 = 0.0472, ωR_2 = 0.1169

12. References

[1] C.-V. Vo, M.-U. Luescher, J.-W. Bode. *Nat. Chem.* **2014**, *6*, 310.

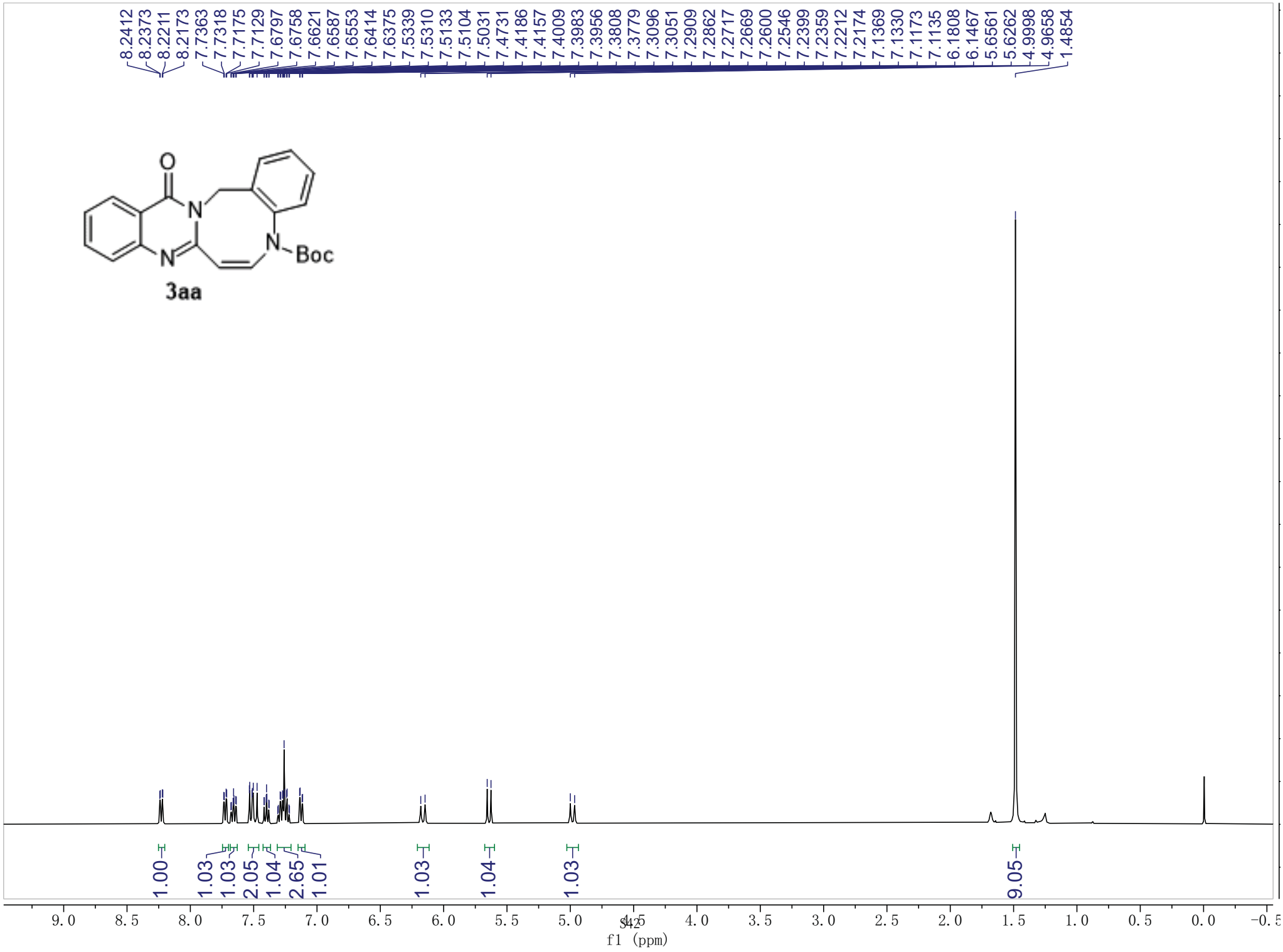
[2] N.-V. Borrero, L.-G. DeRatt, L. Ferreira Barbosa, K.-A. Abboud, A. Aponick. *Org. Lett.* **2015**, *17*, 1754.

[3] B. Zhou, Q. Wu, Z. Dong, J. Xu, Z. Yang. *Org. Lett.* **2019**, *21*, 3594.

[4] G. Wang, X. Chen, Y. Deng, Z. Li, X. Xu. *J. Agric. Food. Chem.* **2015**, *63*, 6883.

[5] X.-F. Kong, F. Zhan, G.-X. He, C.-X. Pan, X. Gu, K. Lu, D.-L. Mo, and G.-F. Su, *J. Org. Chem.* **2018**, *83*, 2006.

13. NMR spectra for compounds **3**, **4**, **5**, **6**, **7**, and **1**.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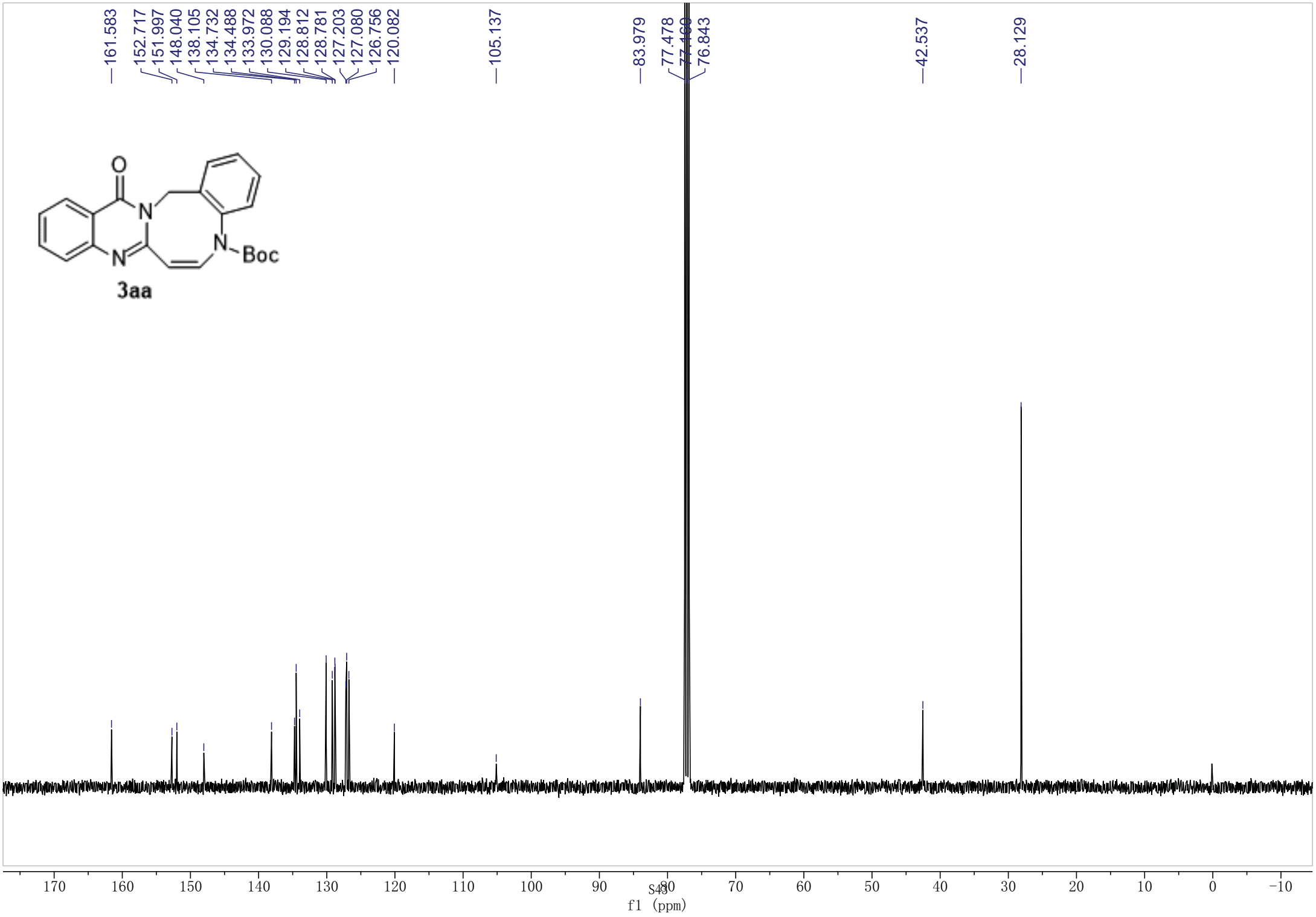
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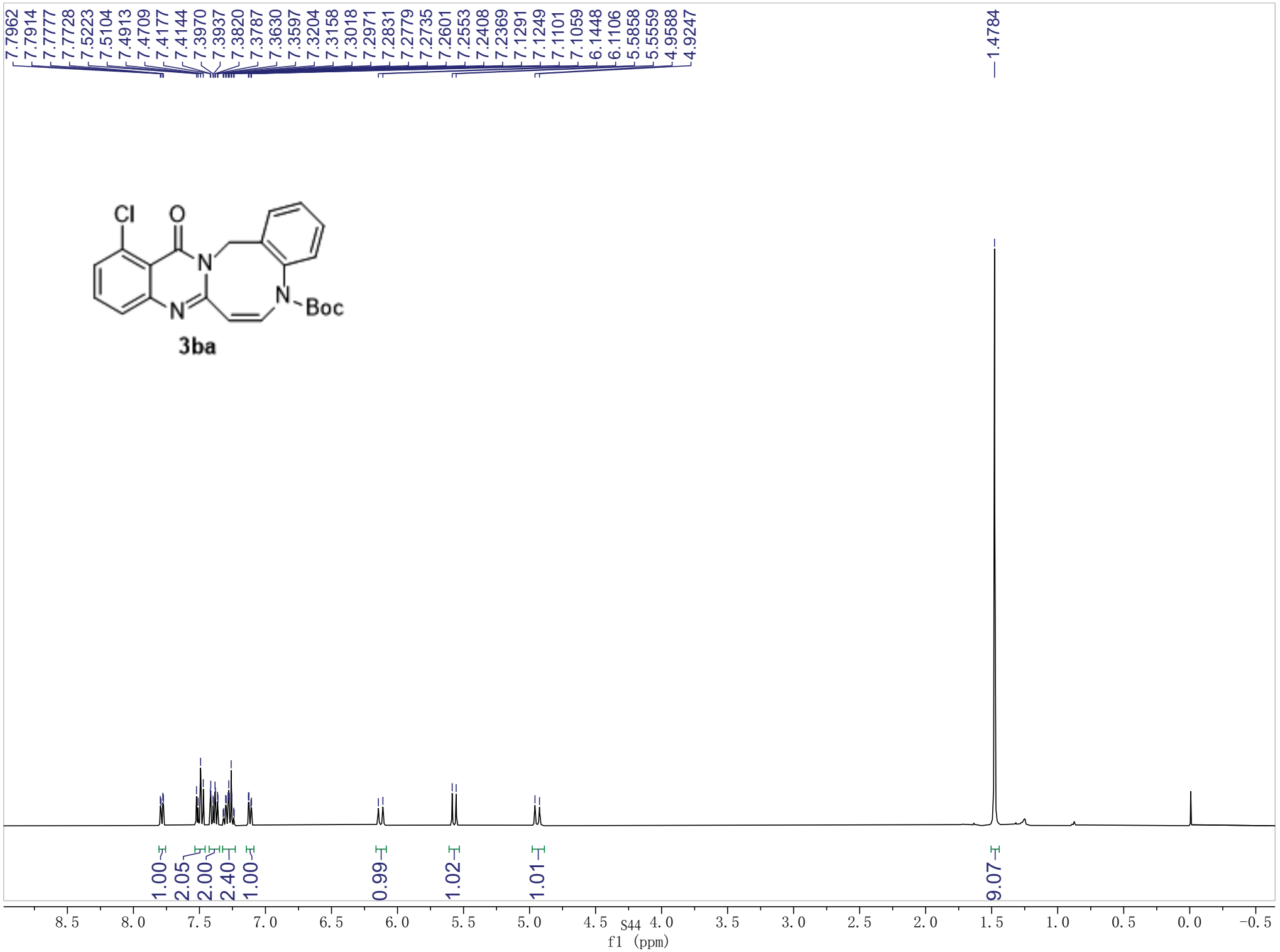
20
10
0
−10
f1 (ppm)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7.7914
7.7777
7.7728
7.5223
7.5104
7.4913
7.4709
7.4177
7.4144
7.3970
7.3937
7.3820
7.3787
7.3630
7.3597
7.3204
7.3158
7.3018
7.2971
7.2831
7.2779
7.2735
7.2601
7.2553
7.2408
7.2369
7.1291
7.1249
7.1101
7.1059
6.1448
6.1106
5.5858
5.5559
4.9588
4.9247
1.4784
Cl
O
N
N
N
Boc
3ba
1.00
2.05
2.00
2.40
1.00
0.99
1.02
1.01
9.07
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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0.5
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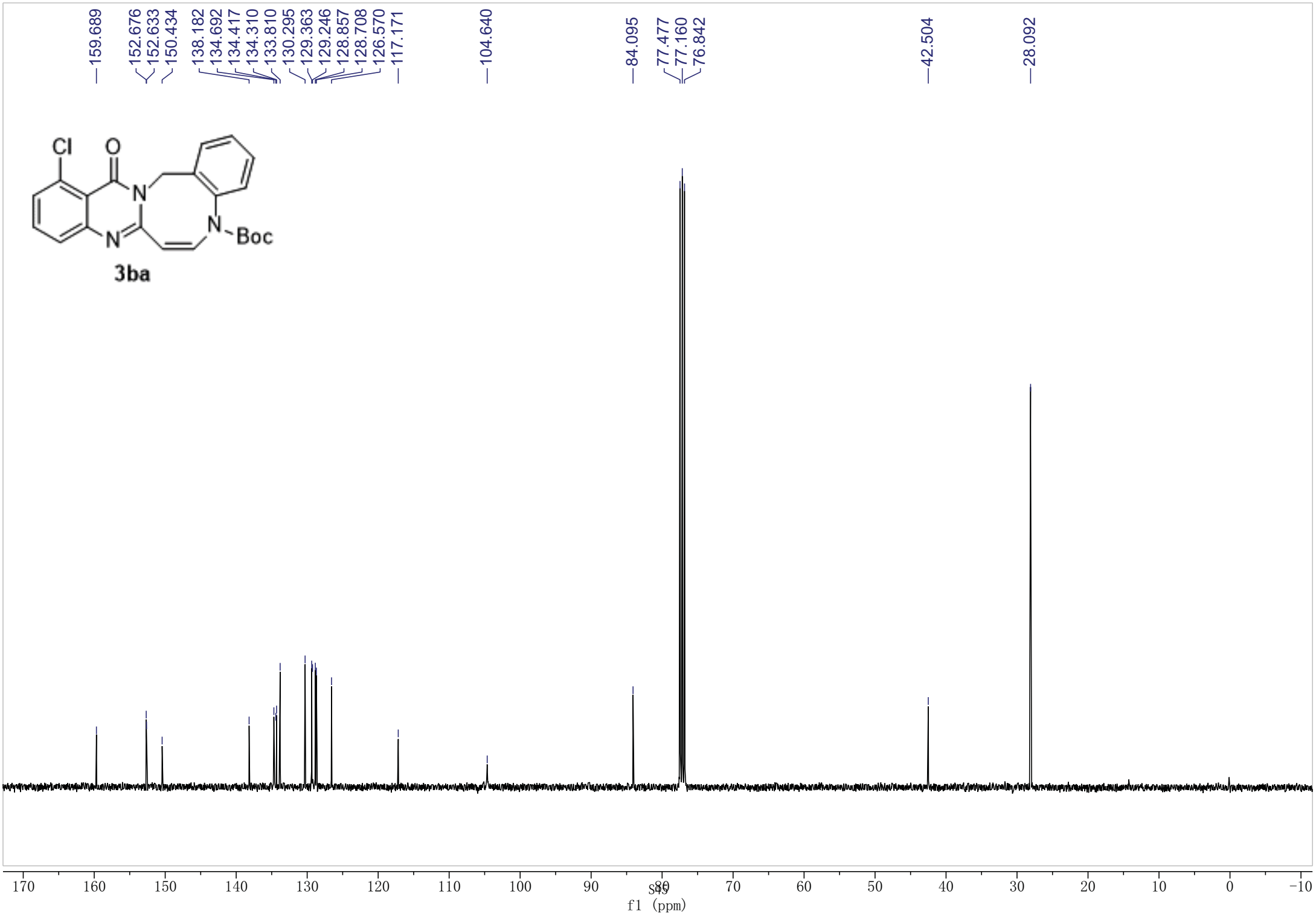
-0.5
f1 (ppm)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134.310
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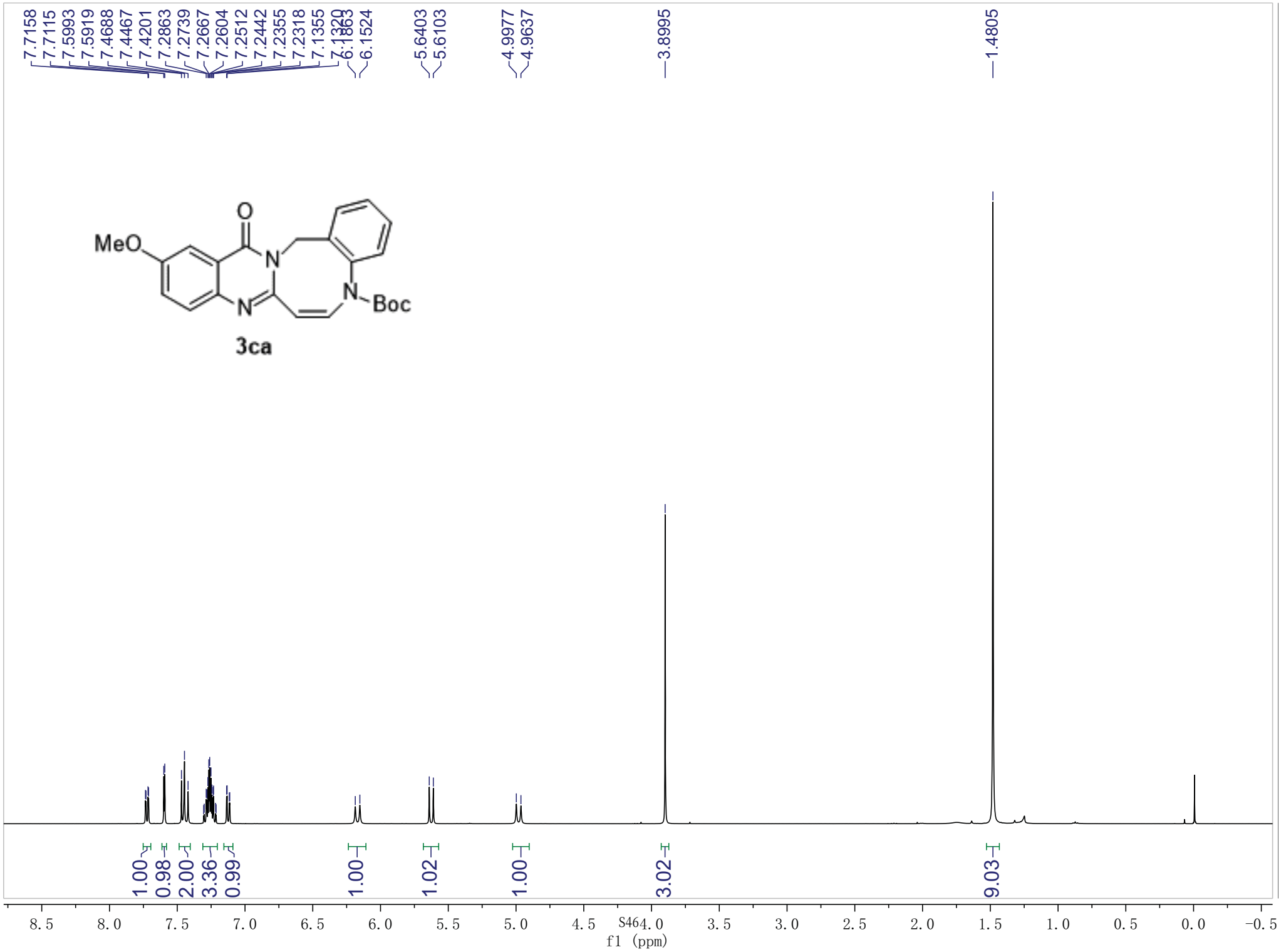
130.295
129.363
129.246
128.857
128.708
126.570
117.171
104.640
84.095
77.477
77.160
76.842
42.504
28.092
Cl
O
N
N
N
Boc
3ba
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.5993
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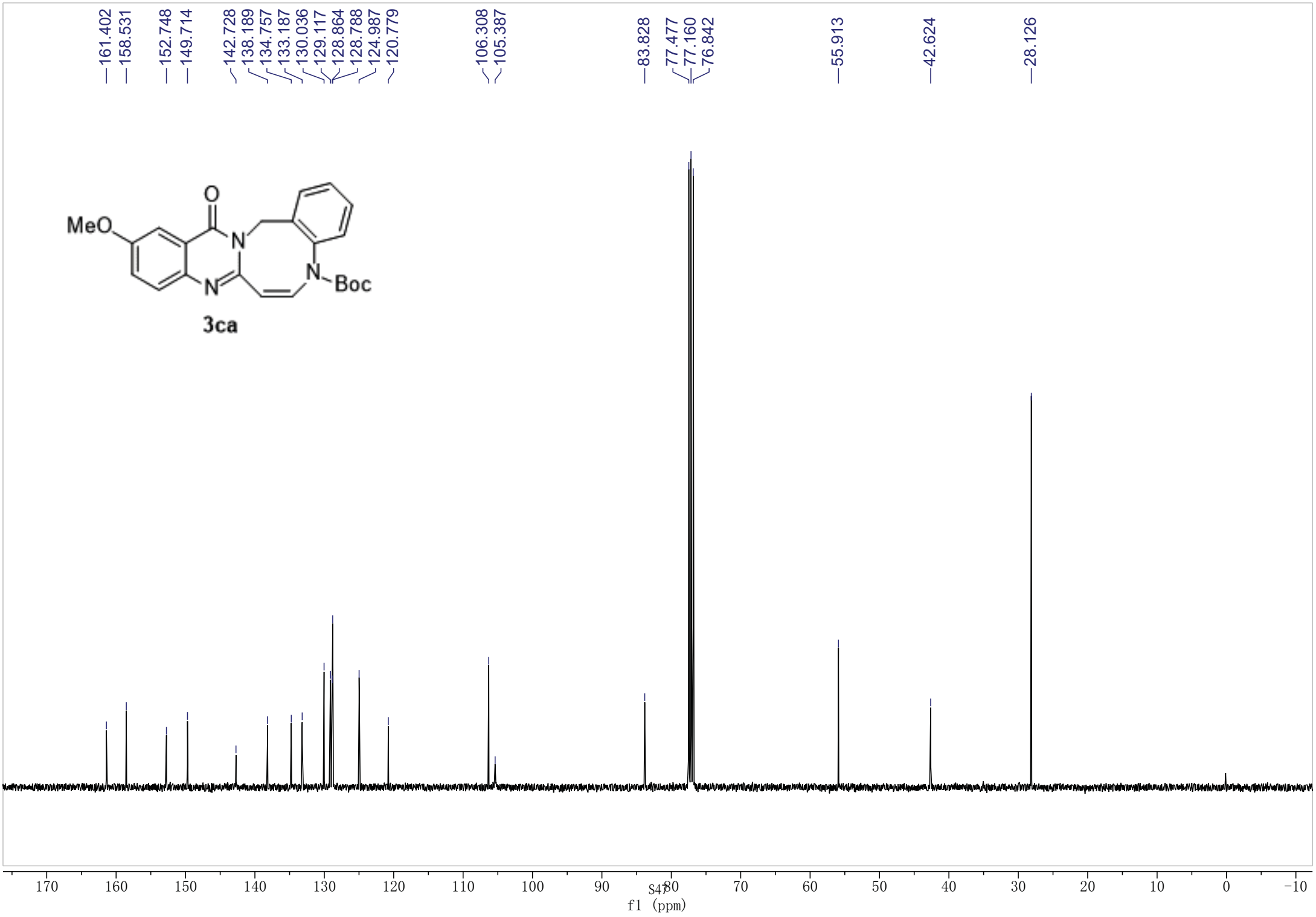
7.4688
7.4467
7.4201
7.2863
7.2739
7.2667
7.2604
7.2512
7.2442
7.2355
7.2318
7.1355
6.1524
5.6403
5.6103
4.9977
4.9637
3.8995
1.4805
MeO
O
N
N
N
Boc
3ca
1.00
0.98
2.00
3.36
0.99
1.00
1.02
1.00
3.02
9.03
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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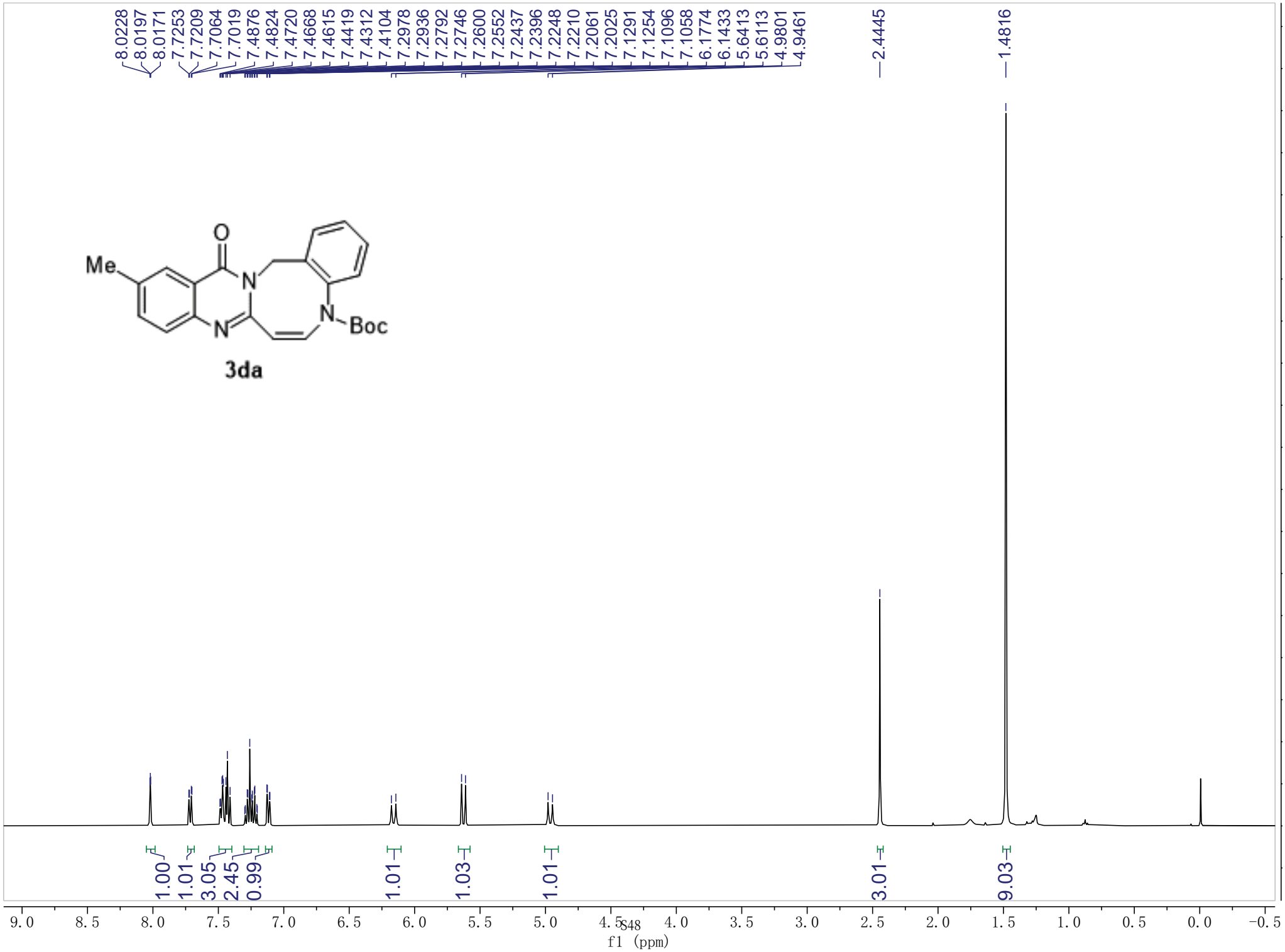
152.748
149.714
142.728
138.189
134.757
133.187
130.036
129.117
128.864
128.788
124.987
120.779
106.308
105.387
83.828
77.477
77.160
76.842
55.913
42.624
28.126
MeO
O
N
N
N
Boc
3ca
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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8.0171
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7.7019
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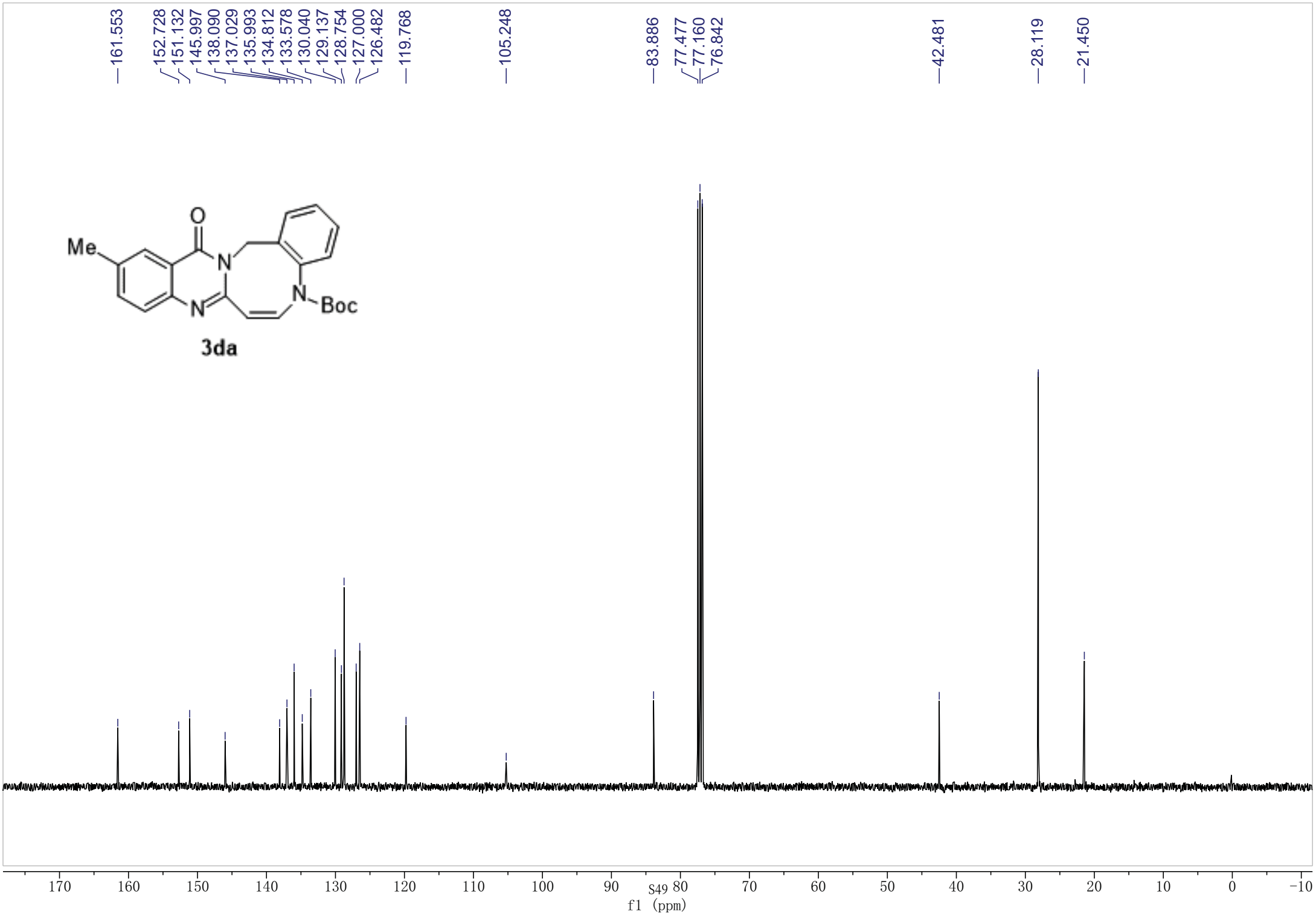
7.4824
7.4720
7.4668
7.4615
7.4419
7.4312
7.4104
7.2978
7.2936
7.2792
7.2746
7.2600
7.2552
7.2437
7.2396
7.2248
7.2210
7.2061
7.2025
7.1291
7.1254
7.1096
7.1058
6.1774
6.1433
5.6413
5.6113
4.9801
4.9461
2.4445
1.4816
Me
O
N
N
N
Boc
3da
1.00
1.01
3.05
2.45
0.99
1.01
1.03
1.01
3.01
9.03
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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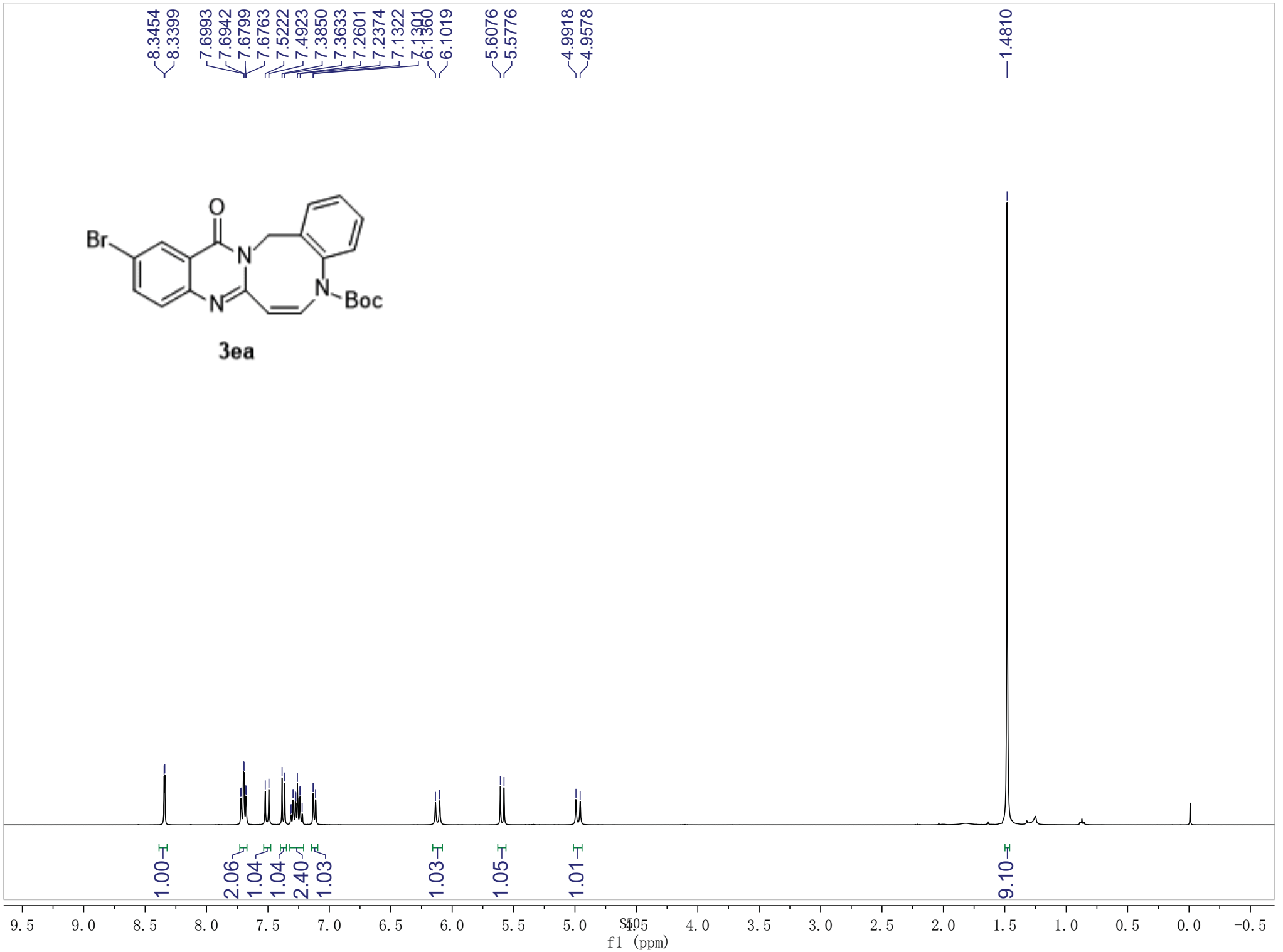
151.132
145.997
138.090
137.029
135.993
134.812
133.578
130.040
129.137
128.754
127.000
126.482
119.768
105.248
83.886
77.477
77.160
76.842
42.481
28.119
21.450
Me
O
N
N
N
Boc
3da
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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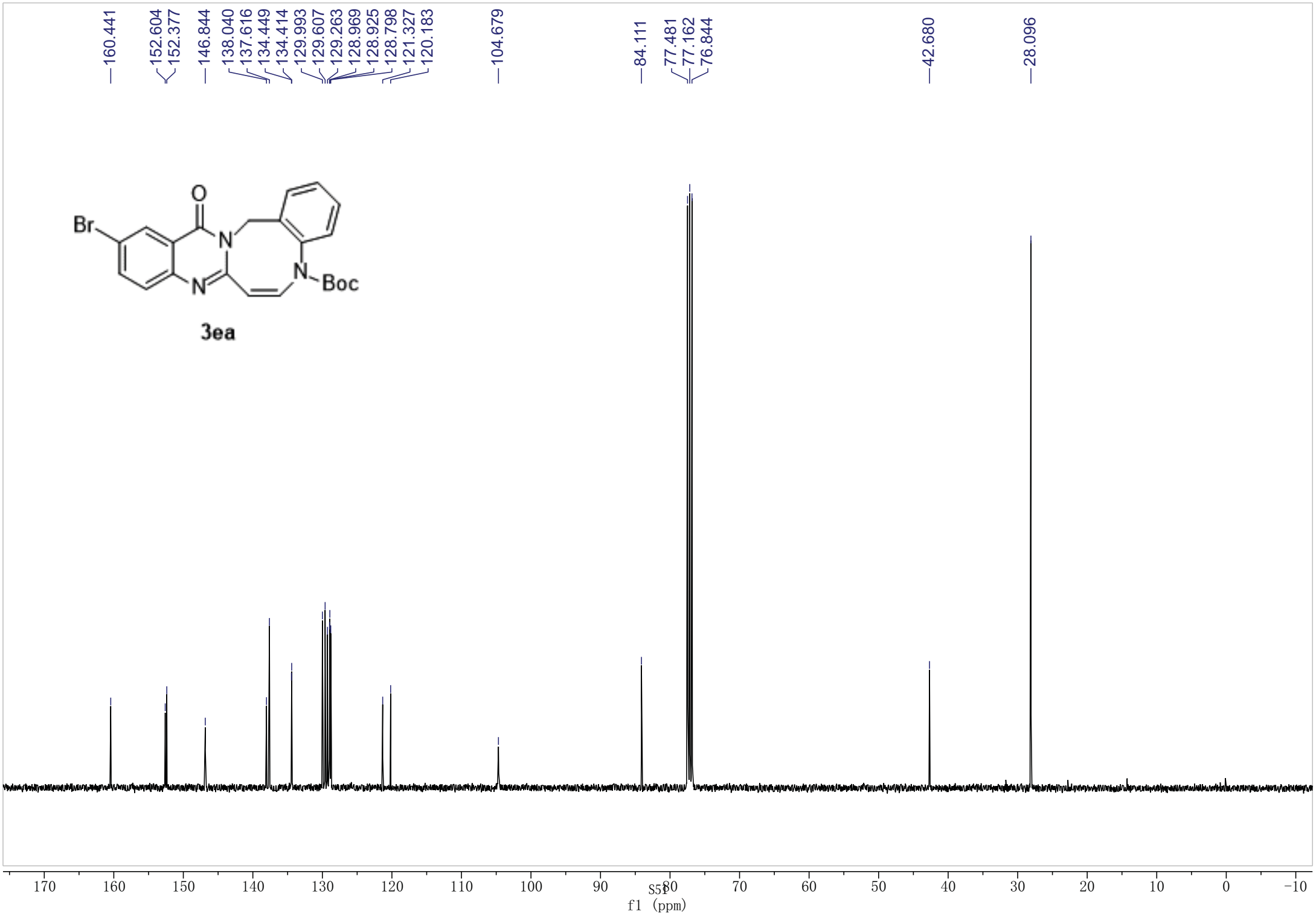
7.6993
7.6942
7.6799
7.6763
7.5222
7.4923
7.3850
7.3633
7.2601
7.2374
7.1322
7.1301
7.1260
6.1019
5.6076
5.5776
4.9918
4.9578
1.4810
Br
O
N
N
N
Boc
3ea
1.00
2.06
1.04
1.04
2.40
1.03
1.03
1.05
1.01
9.10
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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146.844
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134.449
134.414
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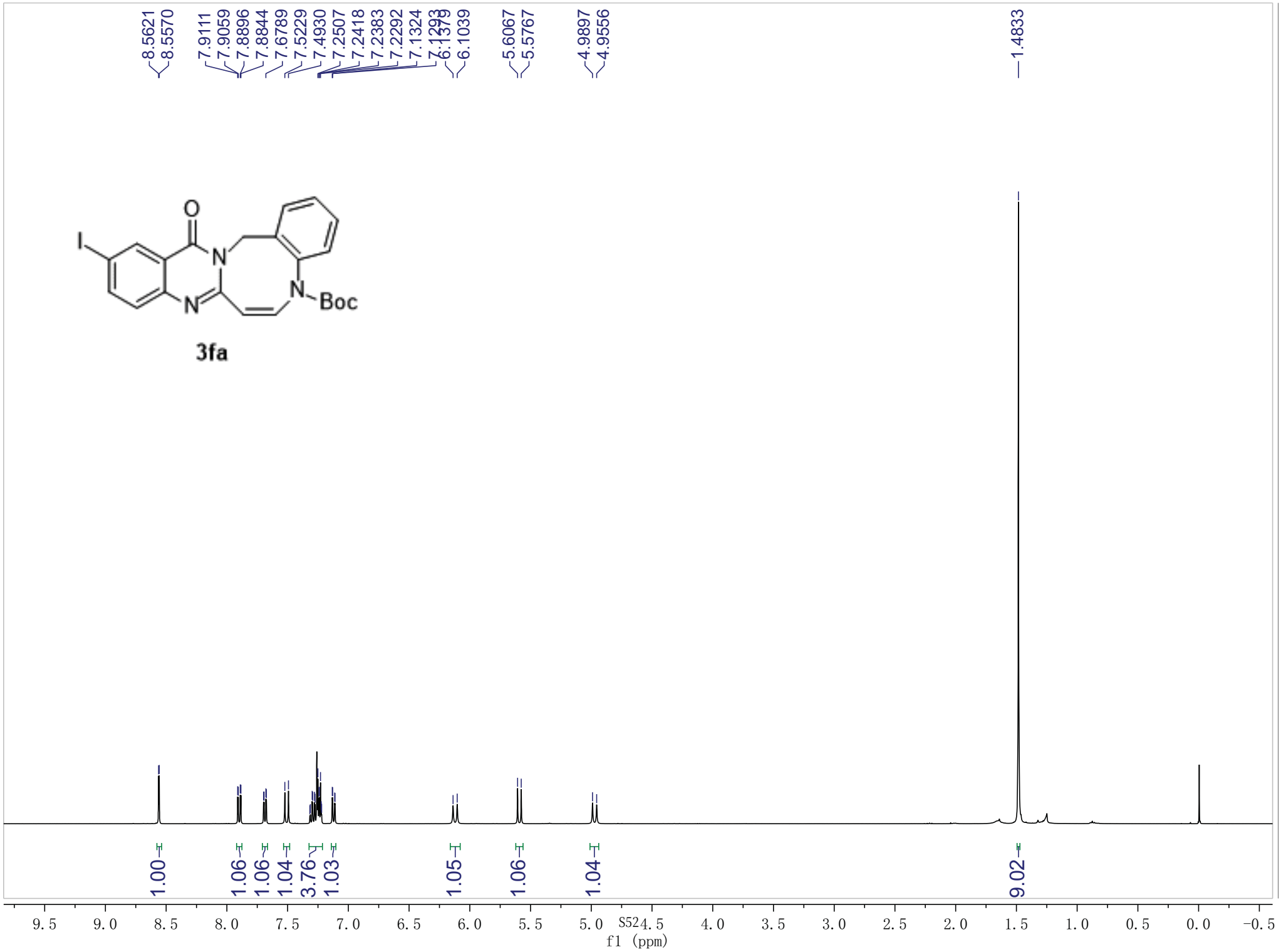
129.263
128.969
128.925
128.798
121.327
120.183
104.679
84.111
77.481
77.162
76.844
42.680
28.096
Br
O
N
N
N
Boc
3ea
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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8.5570
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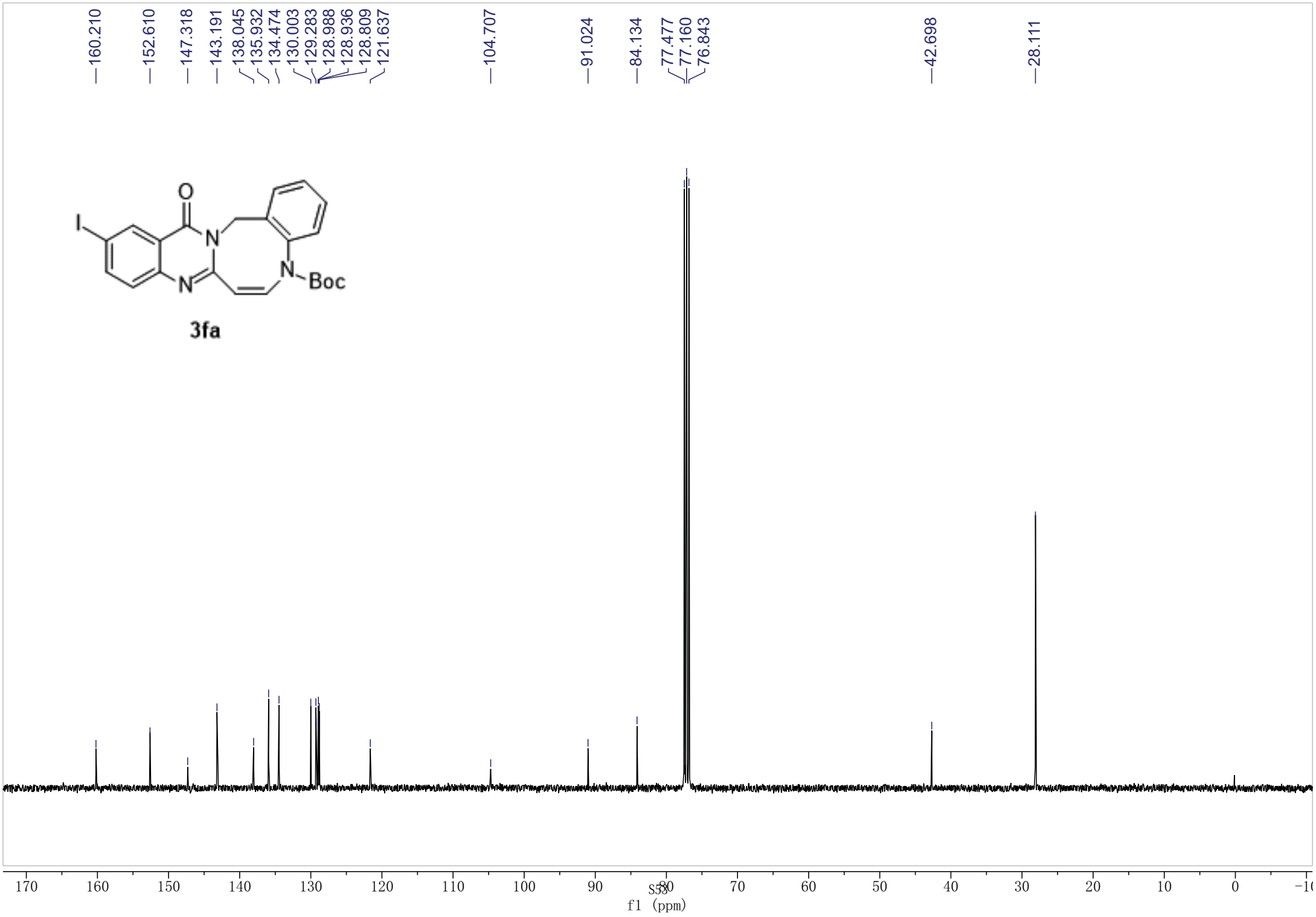
7.8896
7.8844
7.6789
7.5229
7.4930
7.2507
7.2418
7.2383
7.2292
7.1324
6.1039
5.6067
5.5767
4.9897
4.9556
1.4833
O
I
N
N
N
Boc
3fa
1.00
1.06
1.06
1.04
3.76
1.03
1.05
1.06
1.04
9.02
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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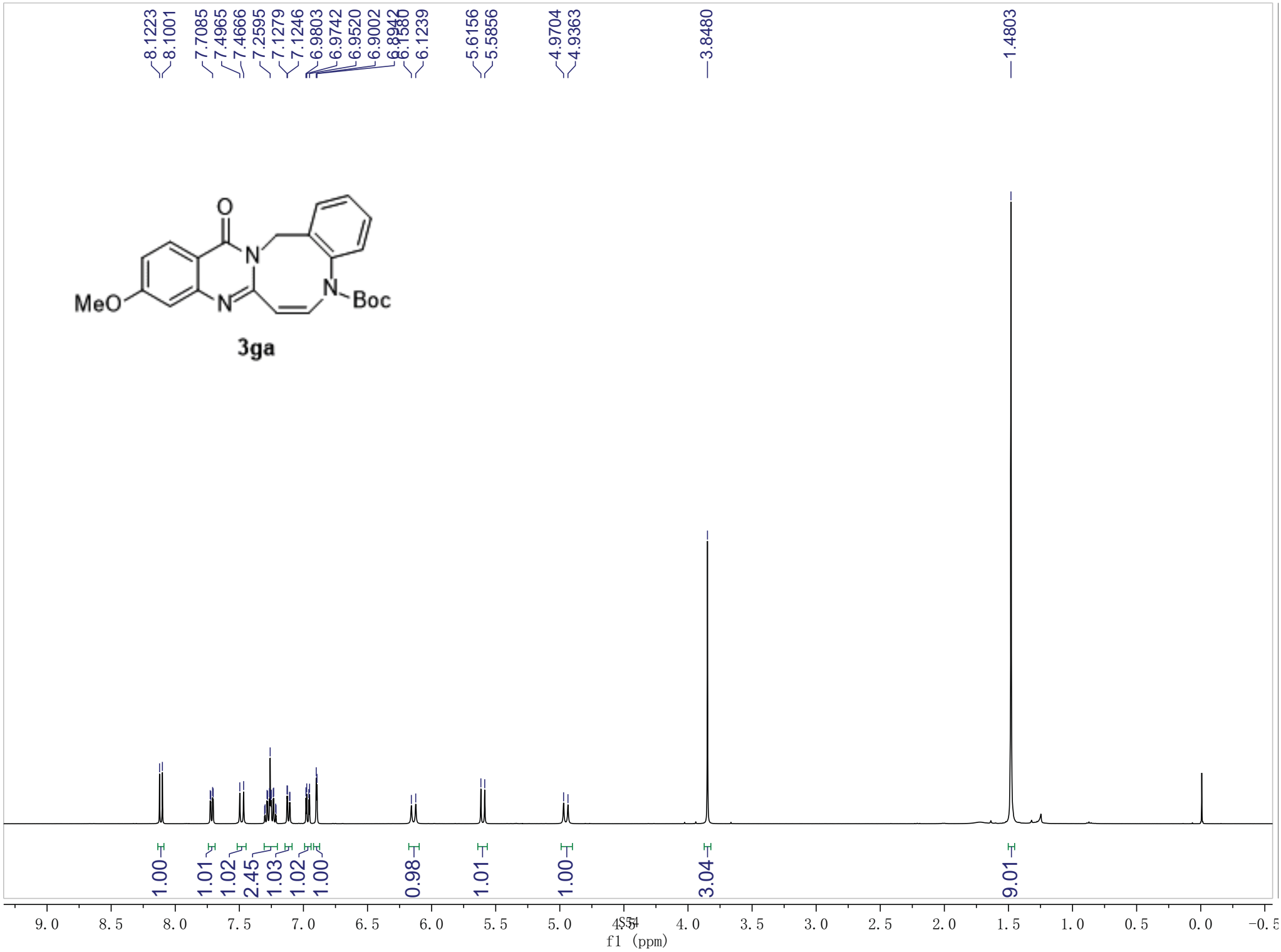
147.318
143.191
138.045
135.932
134.474
130.003
129.283
128.988
128.936
128.809
121.637
104.707
91.024
84.134
77.477
77.160
76.843
42.698
28.111
O
I
N
N
N
Boc
3fa
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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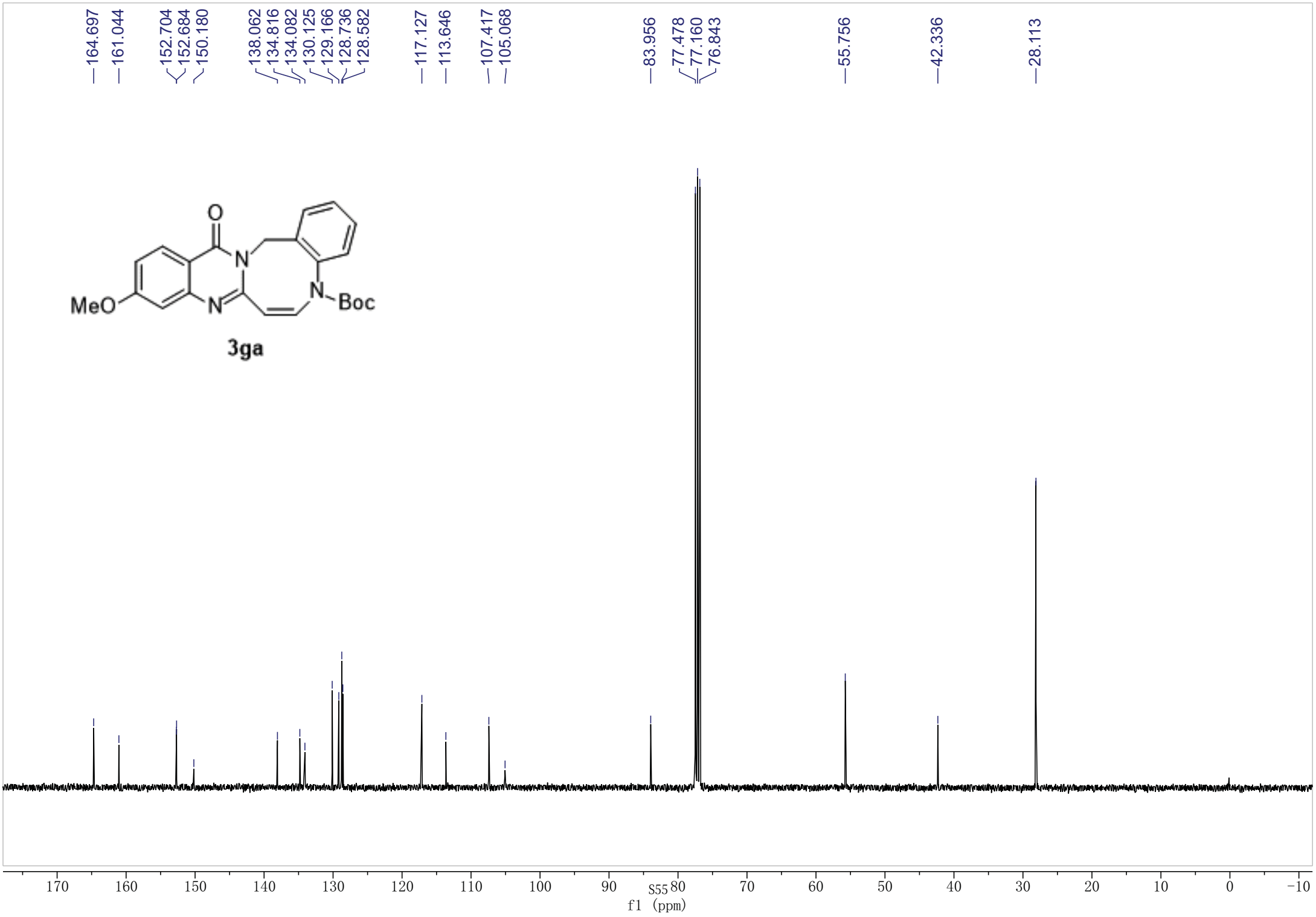
8.1001
7.7085
7.4965
7.4666
7.2595
7.1279
7.1246
6.9803
6.9742
6.9520
6.9002
6.8942
6.8580
6.1239
5.6156
5.5856
4.9704
4.9363
3.8480
1.4803
O
N
N
N
Boc
MeO
3ga
1.00
1.01
1.02
2.45
1.03
1.02
1.00
0.98
1.01
1.00
3.04
9.01
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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161.044
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134.816
134.082
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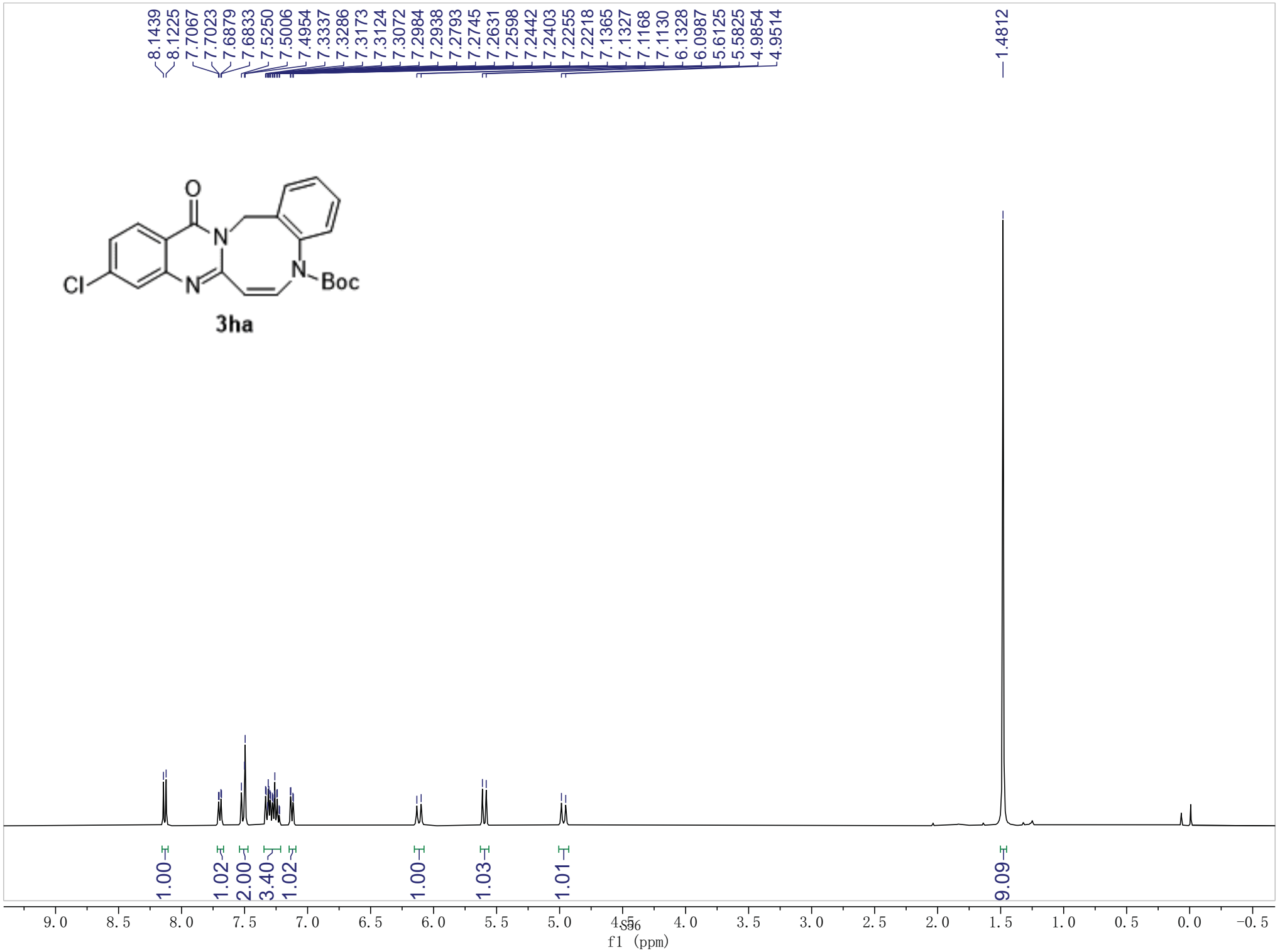
129.166
128.736
128.582
117.127
113.646
107.417
105.068
83.956
77.478
77.160
76.843
55.756
42.336
28.113
O
N
N
N
MeO
Boc
3ga
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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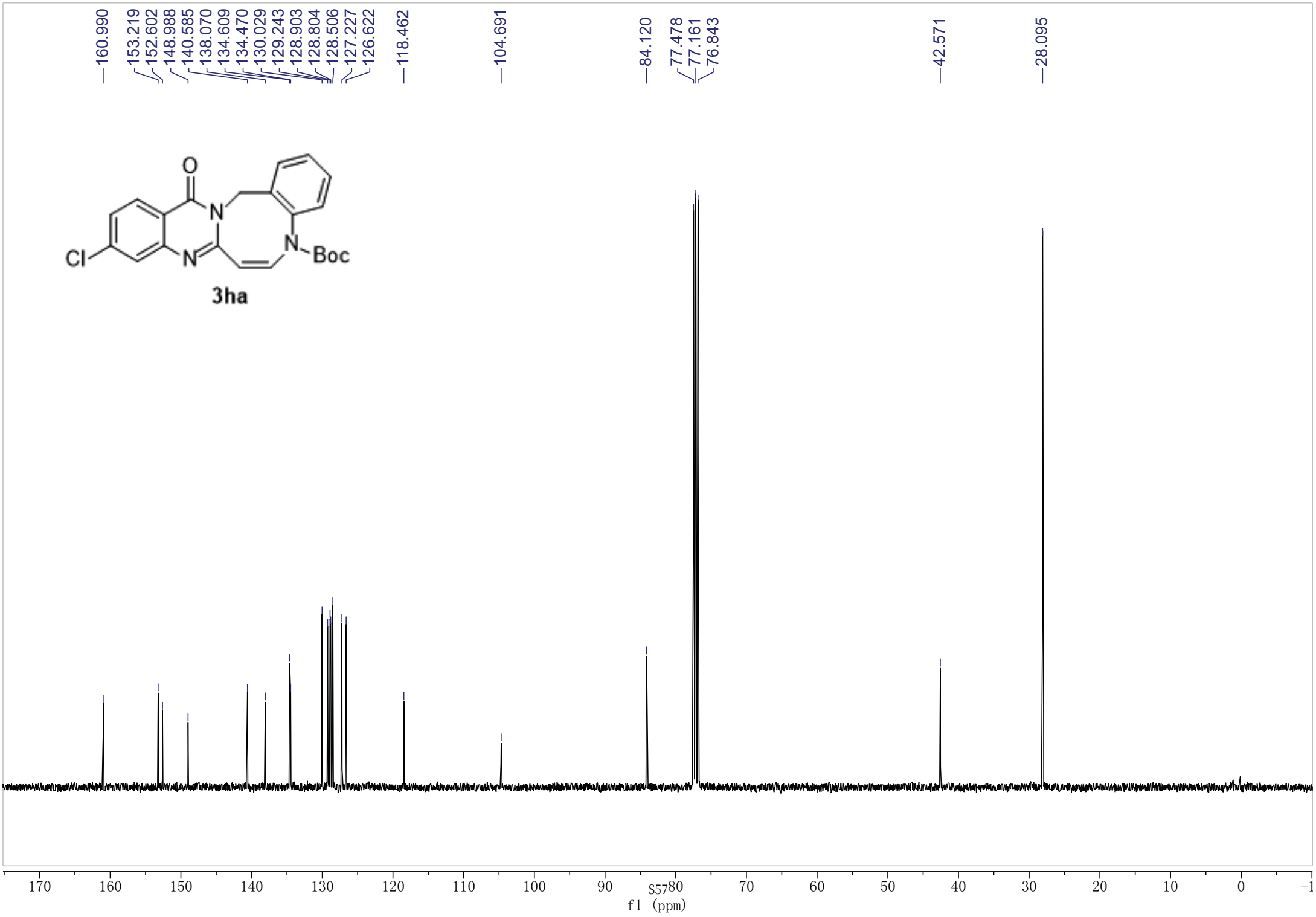
7.7023
7.6879
7.6833
7.5250
7.5006
7.4954
7.3337
7.3286
7.3173
7.3124
7.3072
7.2984
7.2938
7.2793
7.2745
7.2631
7.2598
7.2442
7.2403
7.2255
7.2218
7.1365
7.1327
7.1168
7.1130
6.1328
6.0987
5.6125
5.5825
4.9854
4.9514
1.4812
O
N
N
Boc
Cl
N
3ha
1.00
1.02
2.00
3.40
1.02
1.00
1.03
1.01
9.09
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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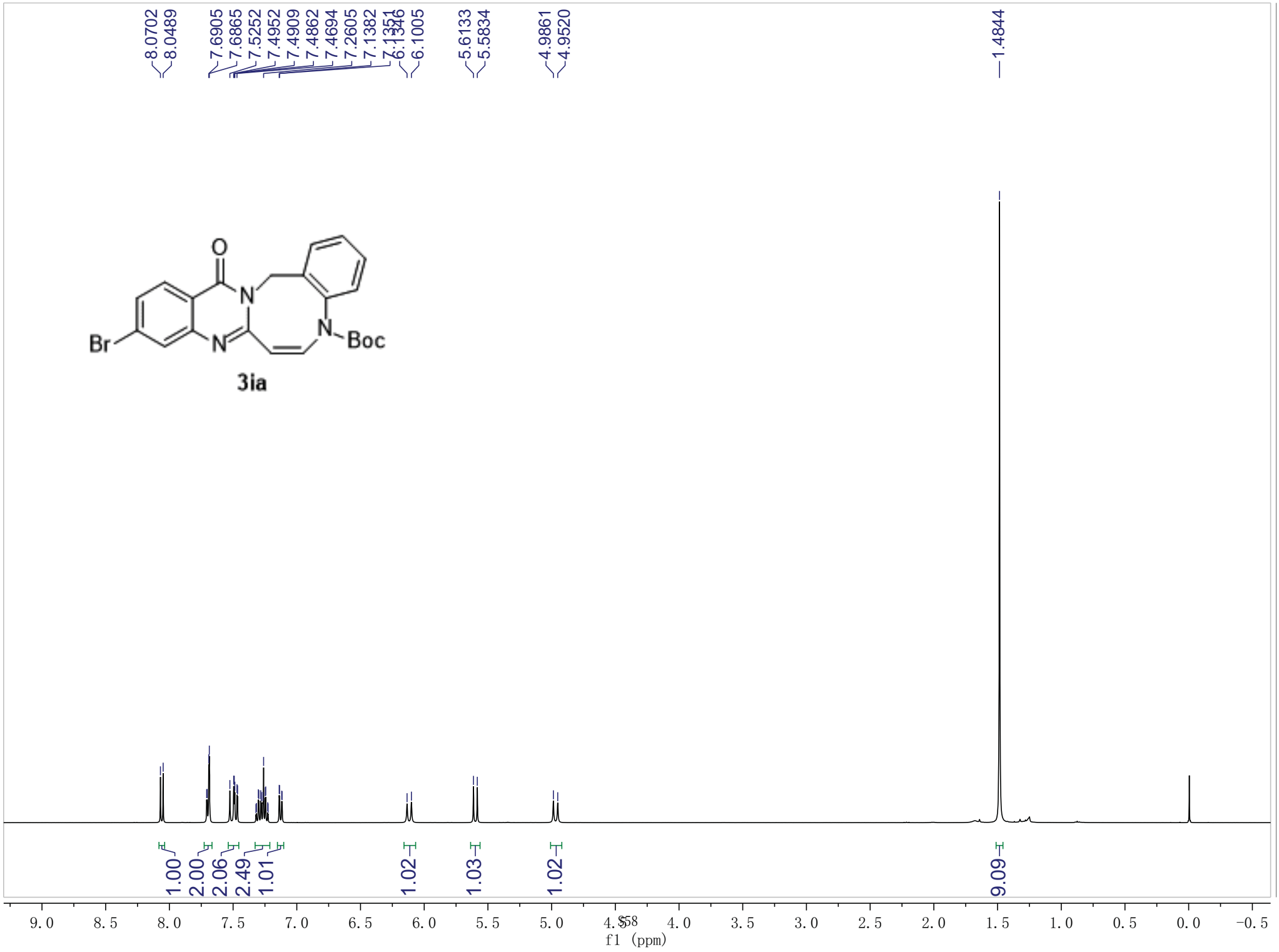
134.470
130.029
129.243
128.903
128.804
128.506
127.227
126.622
118.462
104.691
84.120
77.478
77.161
76.843
42.571
28.095
O
N
N
N
Cl
Boc
3ha
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)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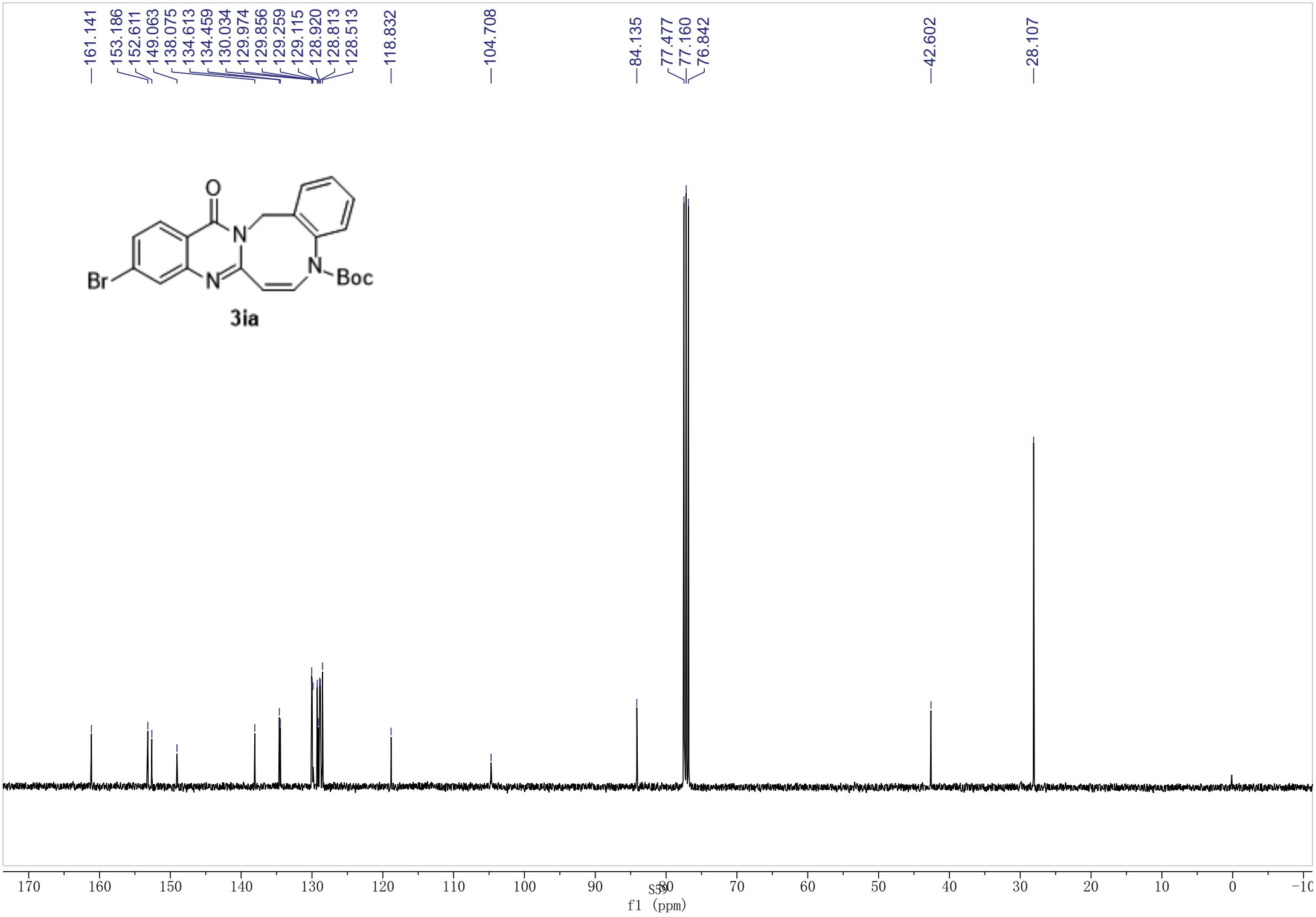
7.4909
7.4862
7.4694
7.2605
7.1382
7.1351
7.1346
6.1005
5.6133
5.5834
4.9861
4.9520
1.4844
O
N
N
N
Boc
Br
3ia
1.00
2.00
2.06
2.49
1.01
1.02
1.03
1.02
9.09
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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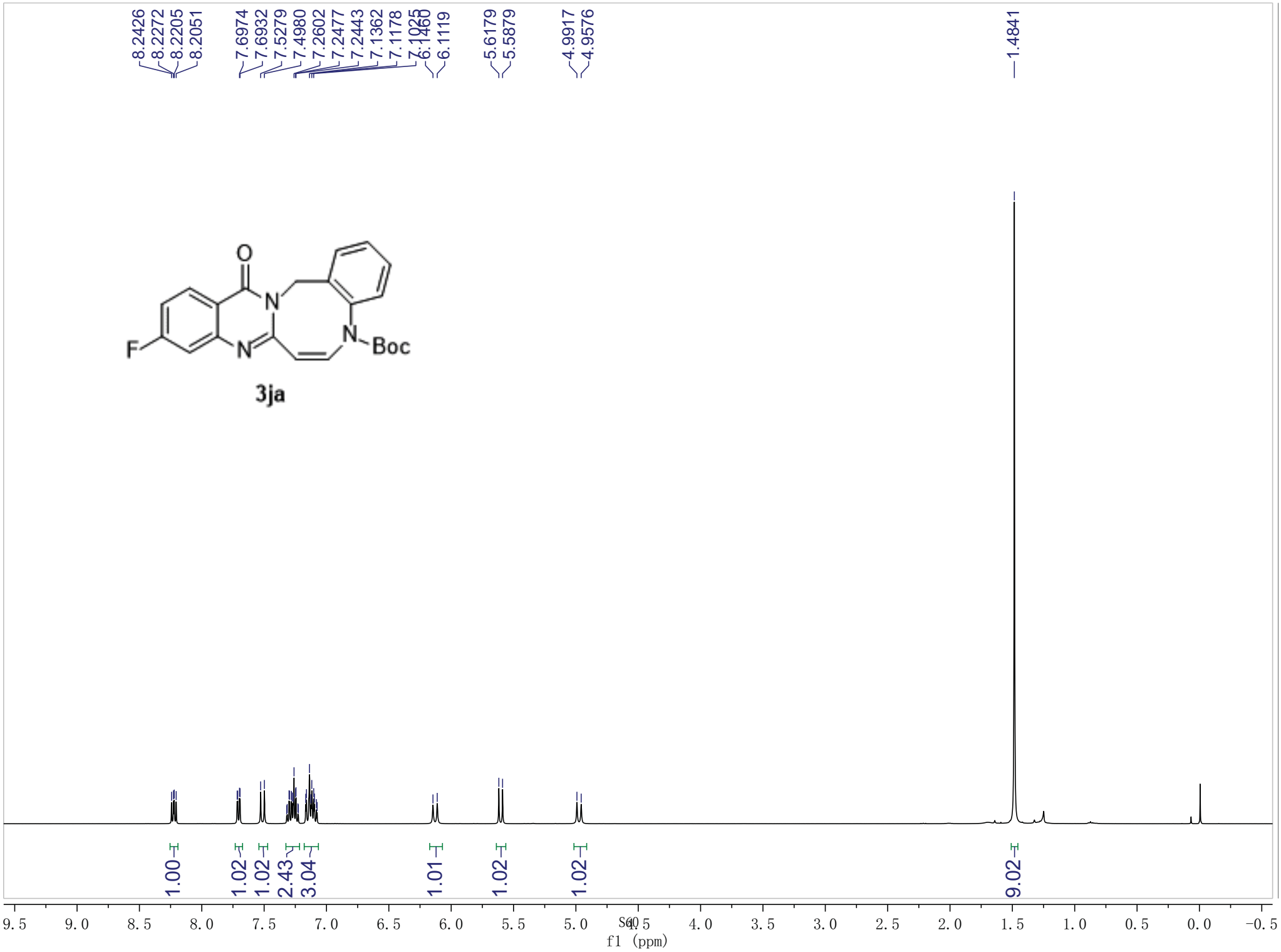
130.034
129.974
129.856
129.259
129.115
128.920
128.813
128.513
118.832
104.708
84.135
77.477
77.160
76.842
42.602
28.107
O
N
N
N
Boc
Br
3ia
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.2426
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7.5279
7.4980
7.2602
7.2477
7.2443
7.1362
7.1178
6.1119
5.6179
5.5879
4.9917
4.9576
1.4841
O
N
N
N
Boc
F
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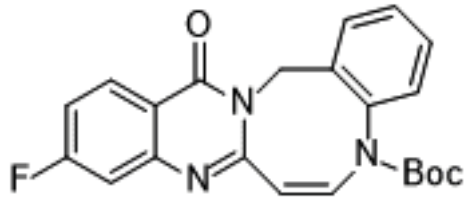
1.02
2.43
3.04
1.01
1.02
1.02
9.02
f1 (ppm)

3ja

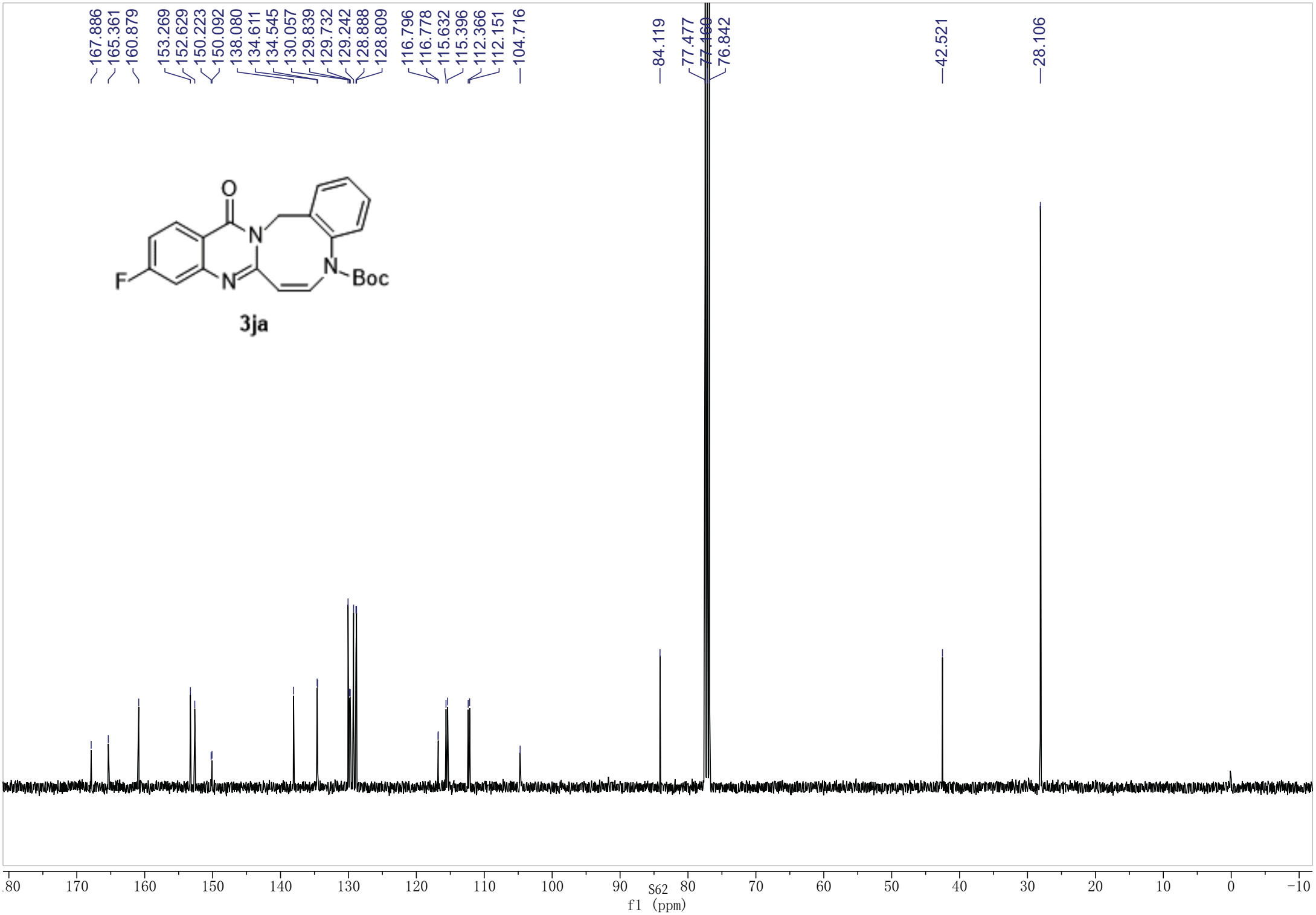


3ja

-104.1

10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

f1 (ppm)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138.080
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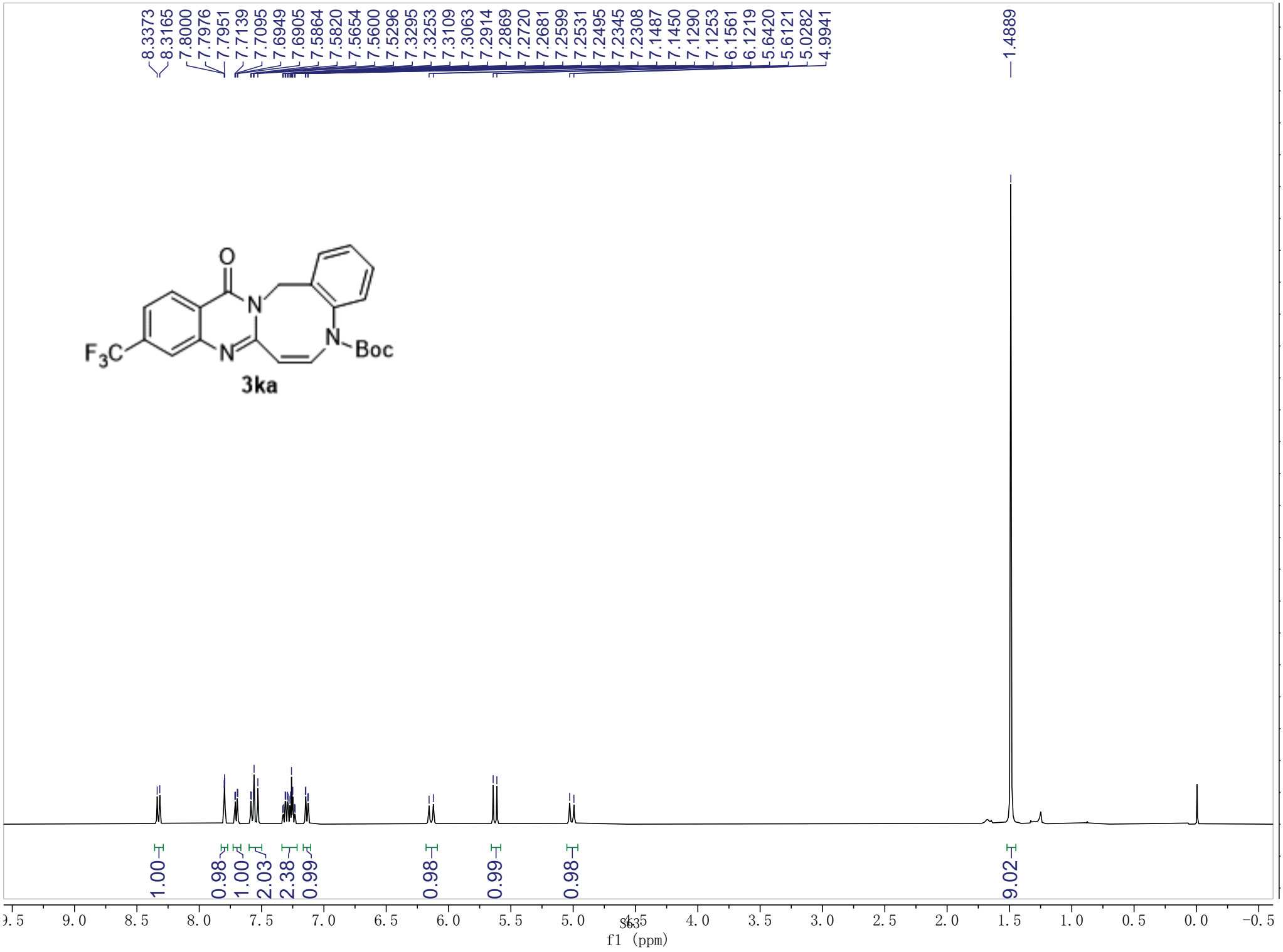
130.057
129.839
129.732
129.242
128.888
128.809
116.796
116.778
115.632
115.396
112.366
112.151
104.716
84.119
77.477
77.160
76.842
42.521
28.106
O
N
N
Boc
F
3ja
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)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7.6905
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7.5820
7.5654
7.5600
7.5296
7.3295
7.3253
7.3109
7.3063
7.2914
7.2869
7.2720
7.2681
7.2599
7.2531
7.2495
7.2345
7.2308
7.1487
7.1450
7.1290
7.1253
6.1561
6.1219
5.6420
5.6121
5.0282
4.9941
1.4889
O
N
N
N
Boc
F3C
3ka
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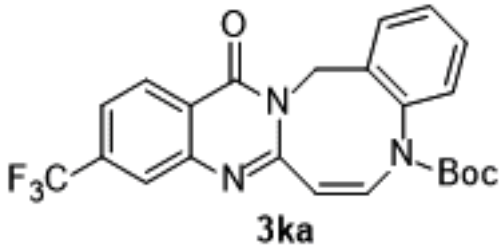
1.00
2.03
2.38
0.99
0.98
0.99
0.98
9.02
f1 (ppm)

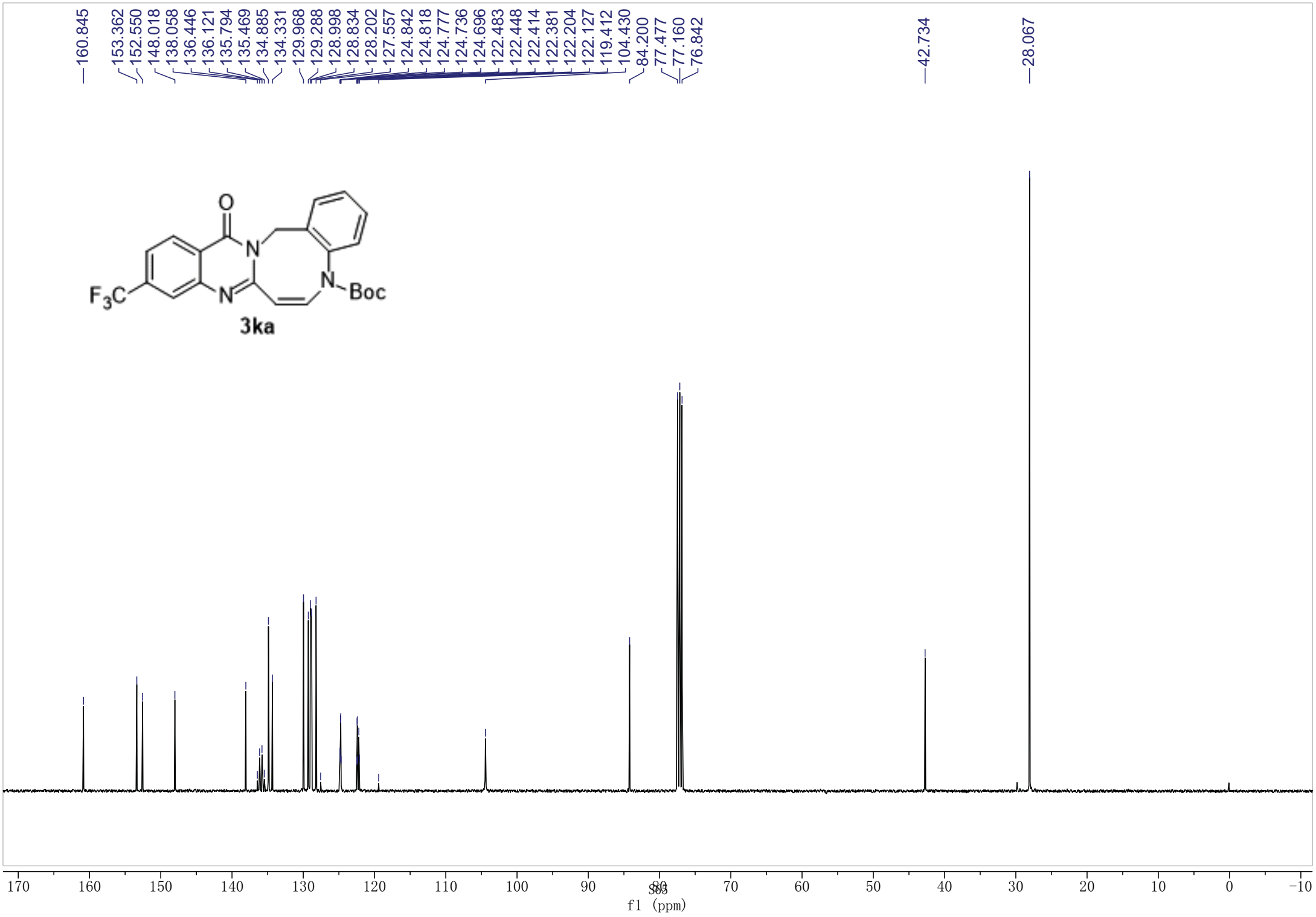


3ka

-63.4

10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

f1 (ppm)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152.550
148.018
138.058
136.446
136.121
135.794
135.469
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124.818
124.777
124.736
124.696
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122.448
122.414
122.381
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122.127
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77.160
76.842
42.734
28.067
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N
N
Boc
F3C
3ka
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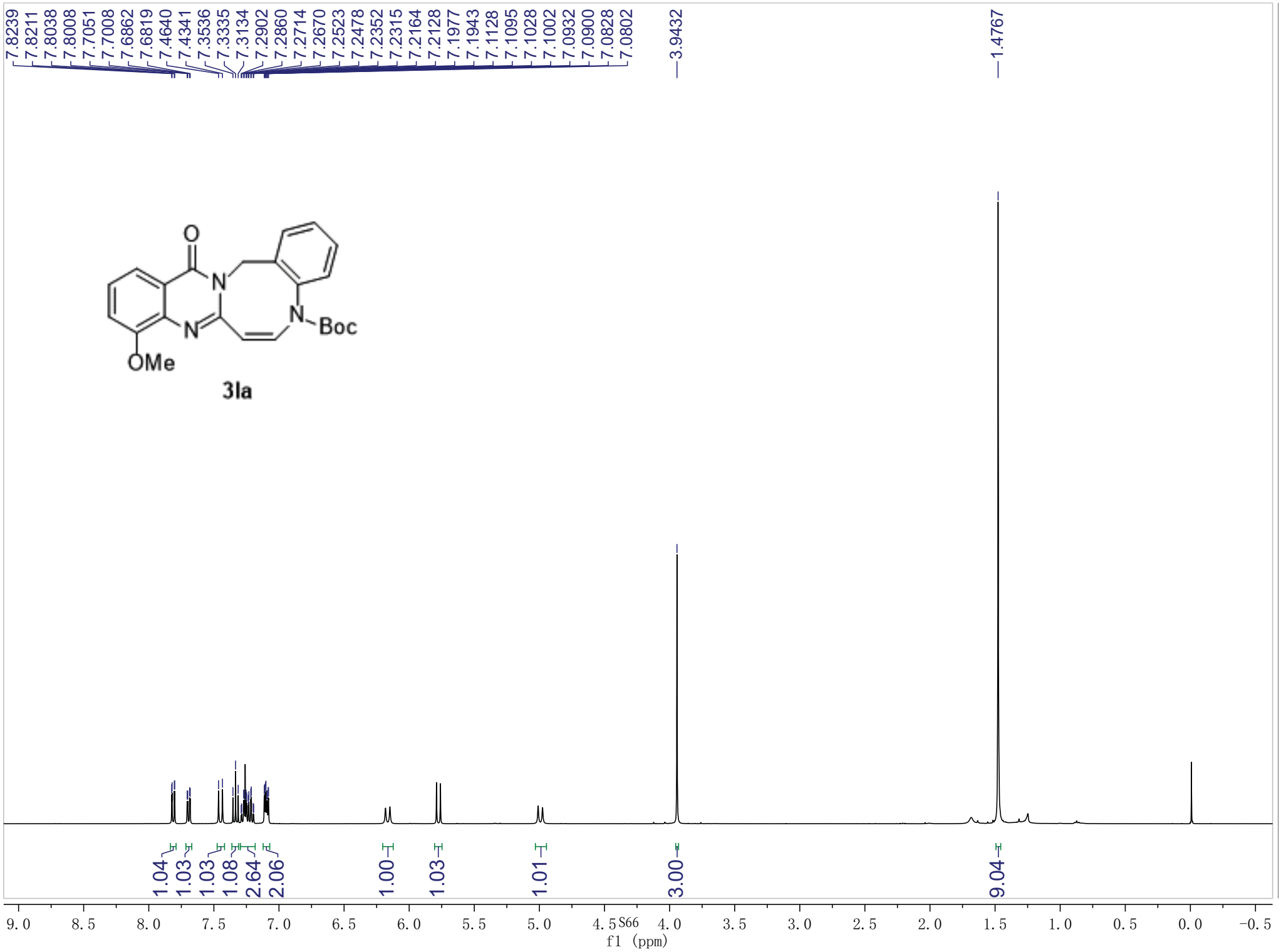
f1 (ppm)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7.2523
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7.2352
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7.1028
7.1002
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7.0828
7.0802
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N
N
N
Boc
OMe
3la
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1.03
1.03
1.08
2.64
2.06
1.00
1.03
1.01
3.00
9.04
9.0
8.5
8.0
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7.0
6.5
6.0
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5.0
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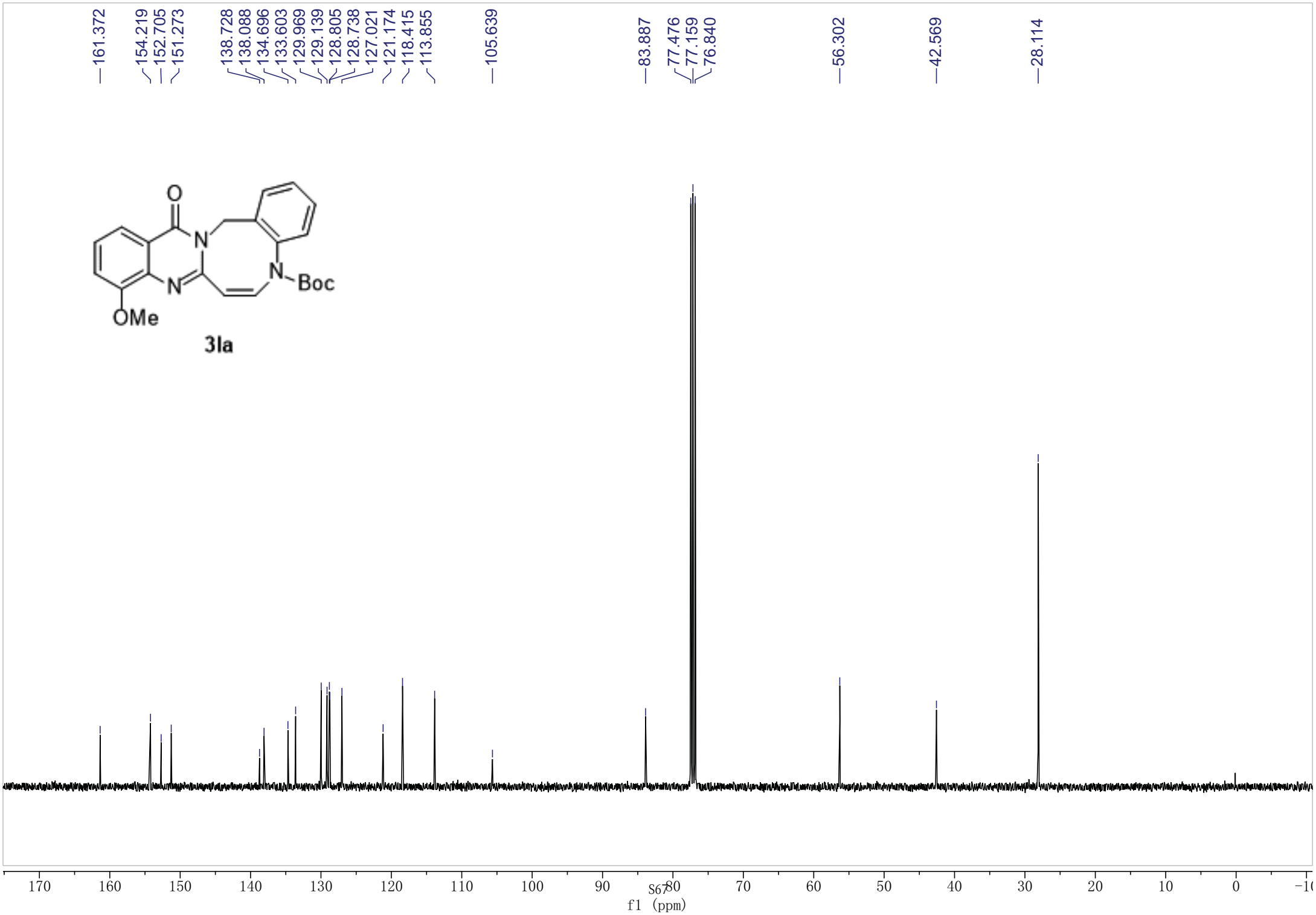
f1 (ppm)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127.021
121.174
118.415
113.855
105.639
83.887
77.476
77.159
76.840
56.302
42.569
28.114
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N
N
N
Boc
OMe
3la
170
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100
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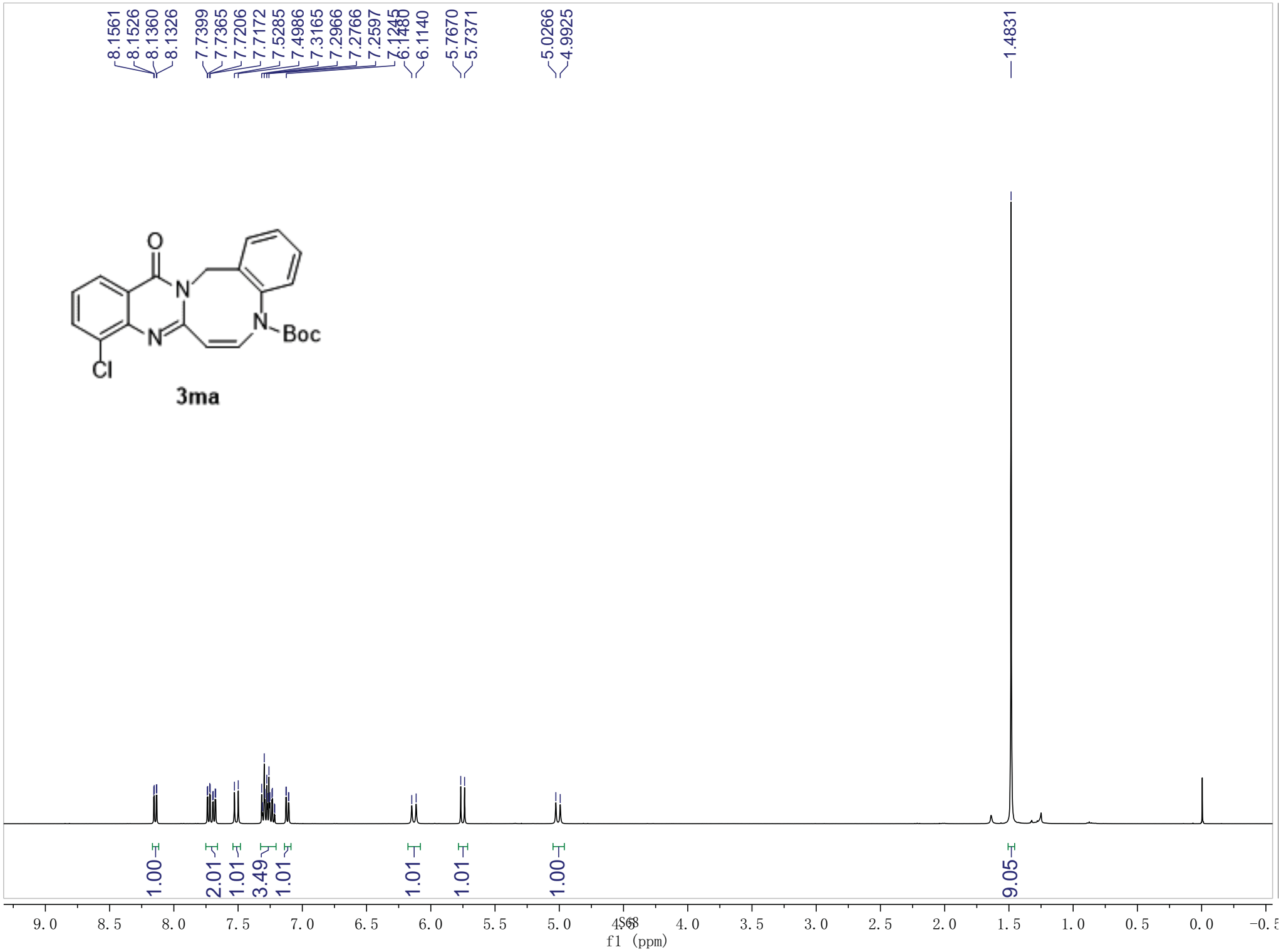
f1 (ppm)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7.3165
7.2966
7.2766
7.2597
7.1245
7.1180
6.1140
5.7670
5.7371
5.0266
4.9925
1.4831
O
N
N
N
Boc
Cl
3ma
1.00
2.01
1.01
3.49
1.01
1.01
1.01
1.00
9.05
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.5
3.0
2.5
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1.0
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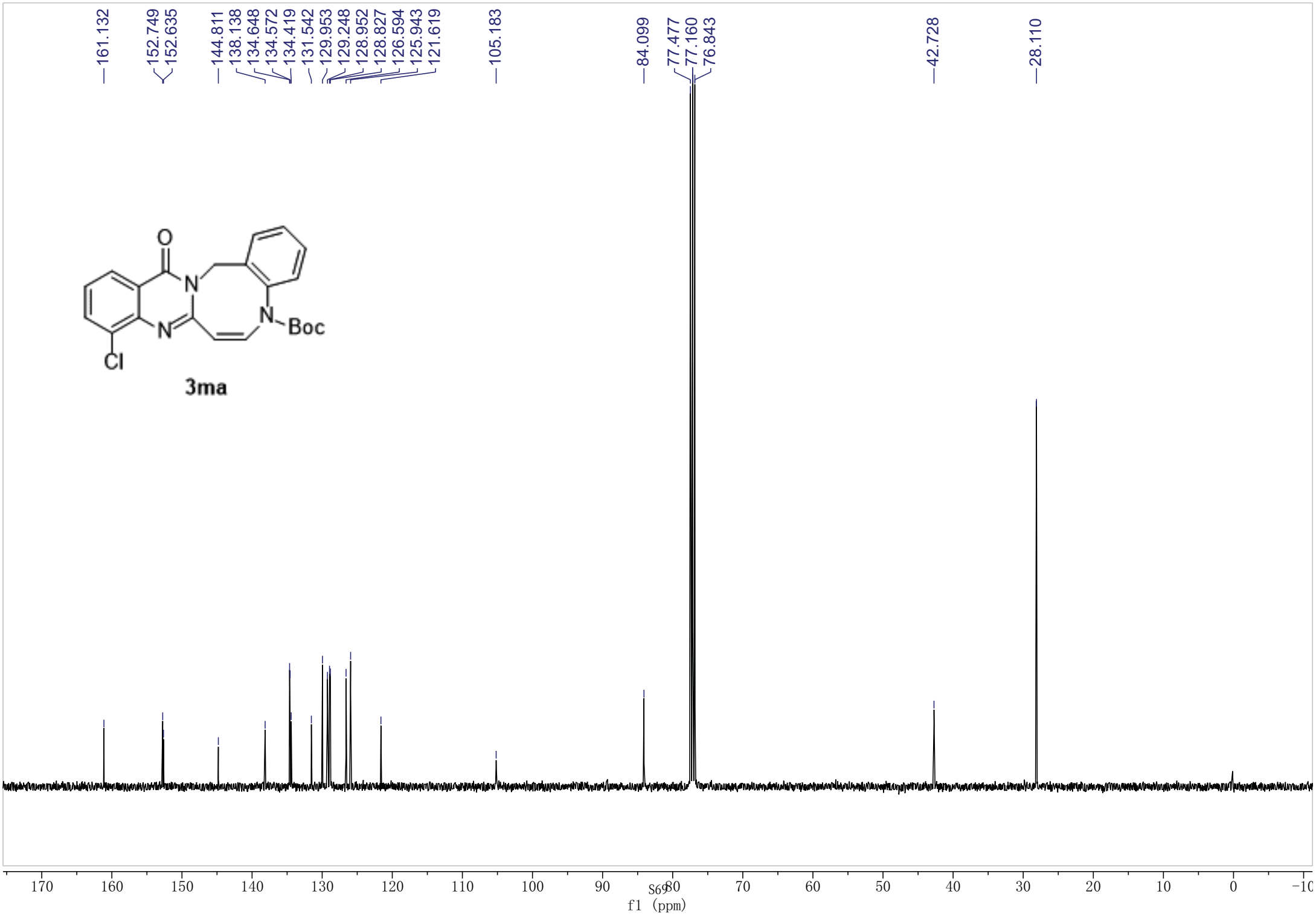
0.0
f1 (ppm)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128.827
126.594
125.943
121.619
105.183
84.099
77.477
77.160
76.843
42.728
28.110
O
N
N
N
Boc
Cl
3ma
170
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120
110
100
90
80
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30
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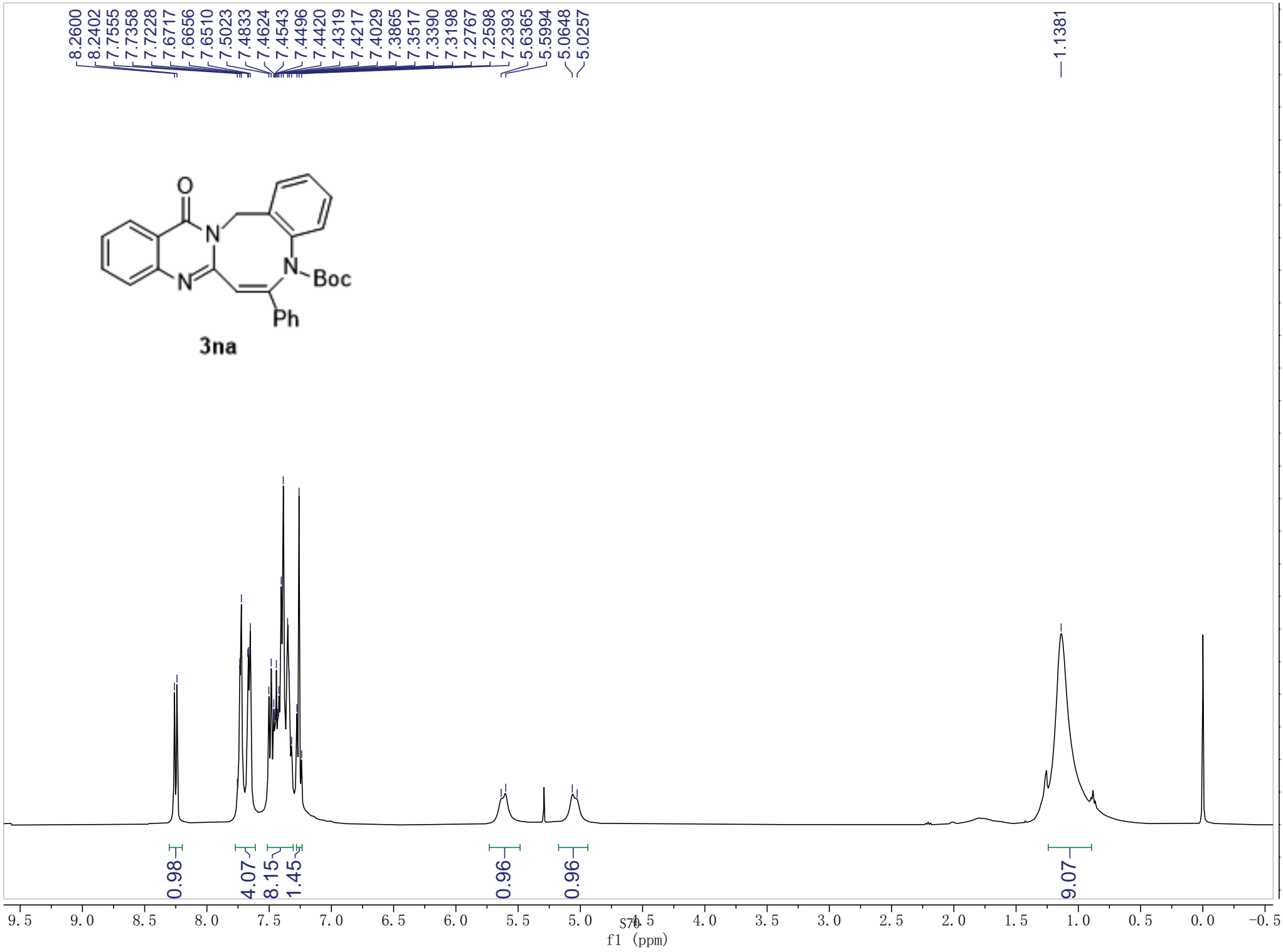
f1 (ppm)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7.4624
7.4543
7.4496
7.4420
7.4319
7.4217
7.4029
7.3865
7.3517
7.3390
7.3198
7.2767
7.2598
7.2393
5.6365
5.5994
5.0648
5.0257
1.1381
O
N
N
N
Boc
Ph
3na
0.98
4.07
8.15
1.45
0.96
0.96
9.07
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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2.5
2.0
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0.5
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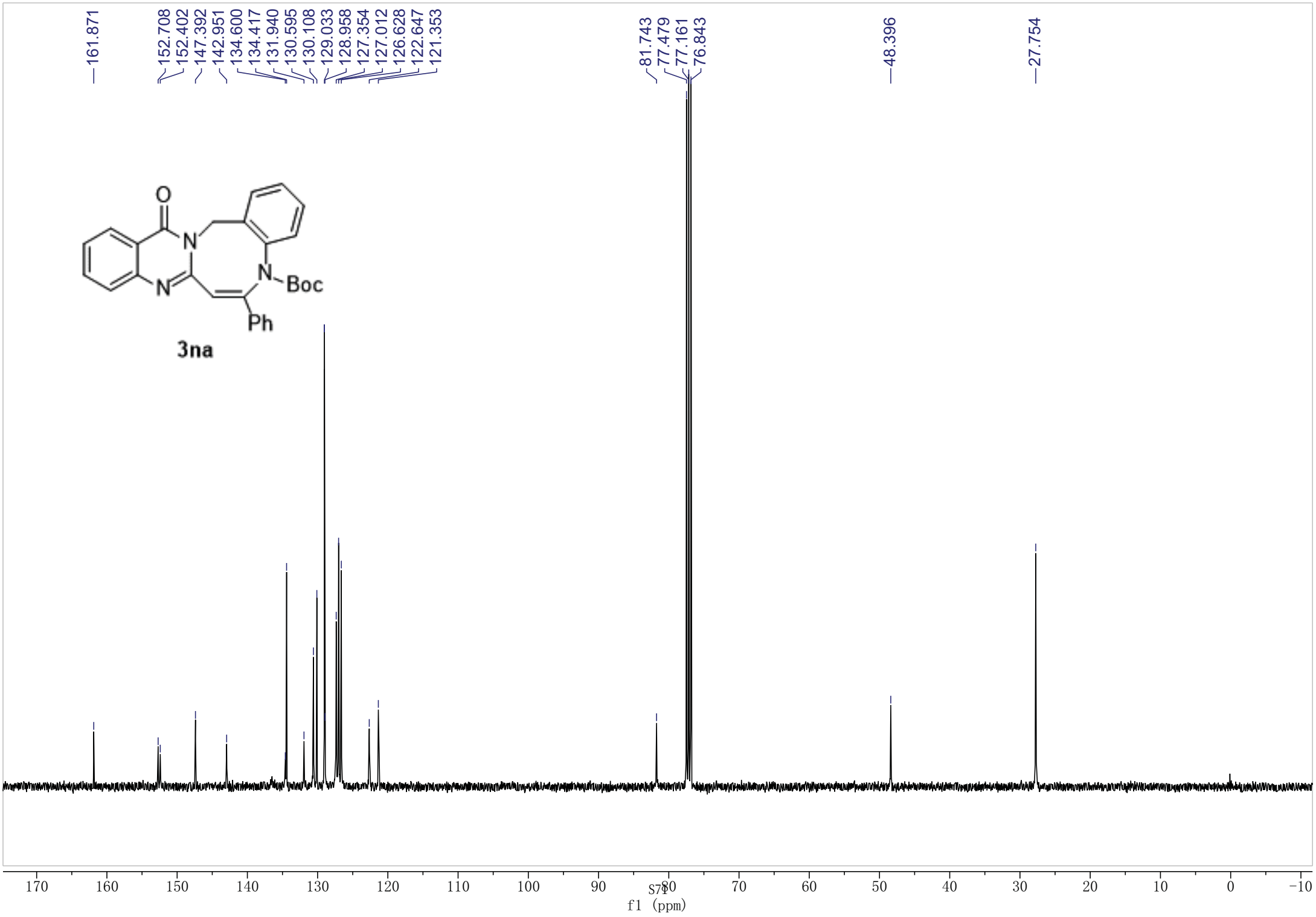
f1 (ppm)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129.033
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127.012
126.628
122.647
121.353
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77.161
76.843
48.396
27.754
O
N
N
N
Boc
Ph
3na
170
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100
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80
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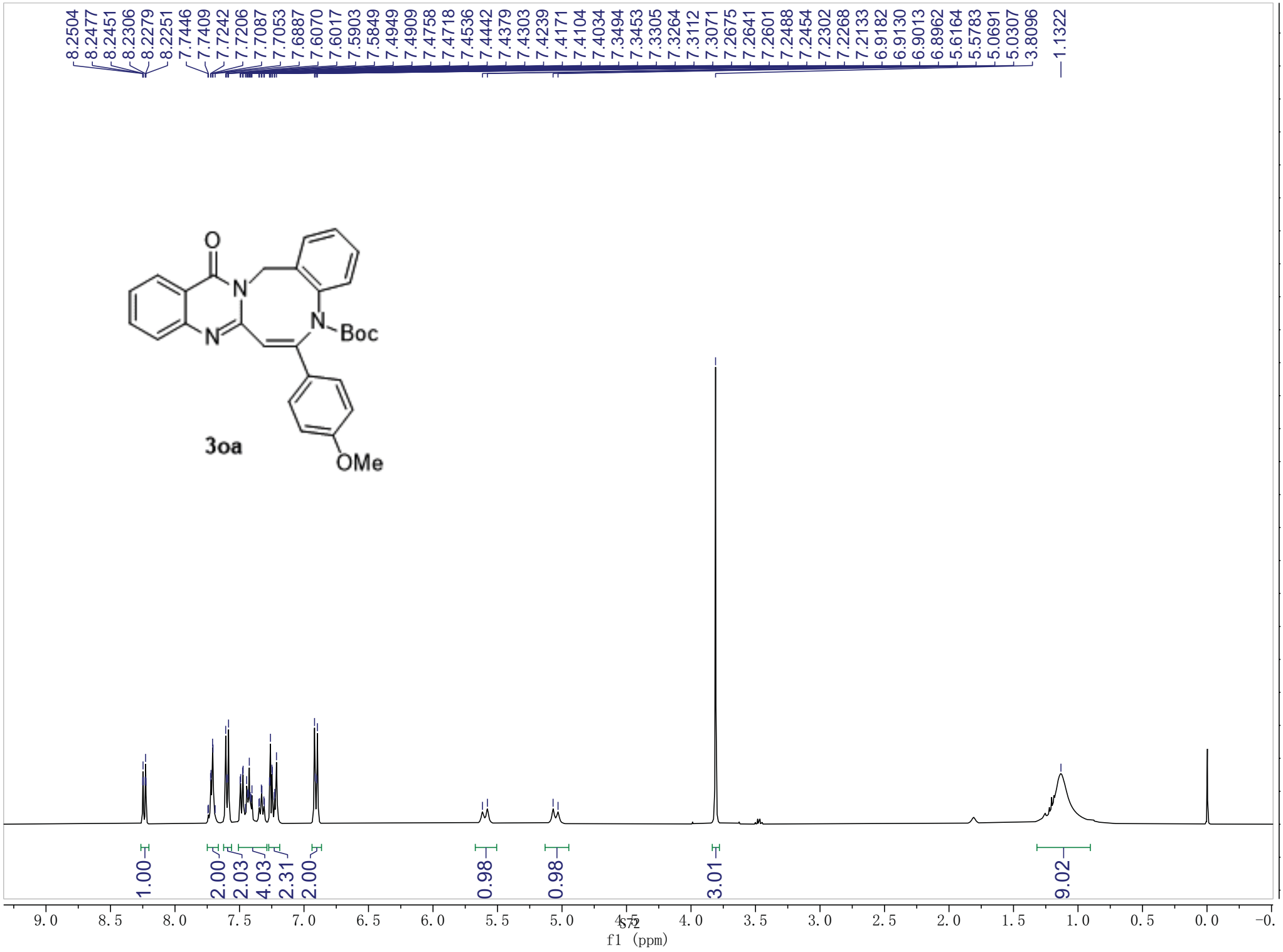
50
40
30
20
10
0
-10
f1 (ppm)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7.7087
7.7053
7.6887
7.6070
7.6017
7.5903
7.5849
7.4949
7.4909
7.4758
7.4718
7.4536
7.4442
7.4379
7.4303
7.4239
7.4171
7.4104
7.4034
7.3494
7.3453
7.3305
7.3264
7.3112
7.3071
7.2675
7.2641
7.2601
7.2488
7.2454
7.2302
7.2268
7.2133
6.9182
6.9130
6.9013
6.8962
5.6164
5.5783
5.0691
5.0307
3.8096
1.1322
O
N
N
N
Boc
OMe
3oa
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2.00
2.03
4.03
2.31
2.00
0.98
0.98
3.01
9.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
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3.0
2.5
2.0
1.5
1.0
0.5
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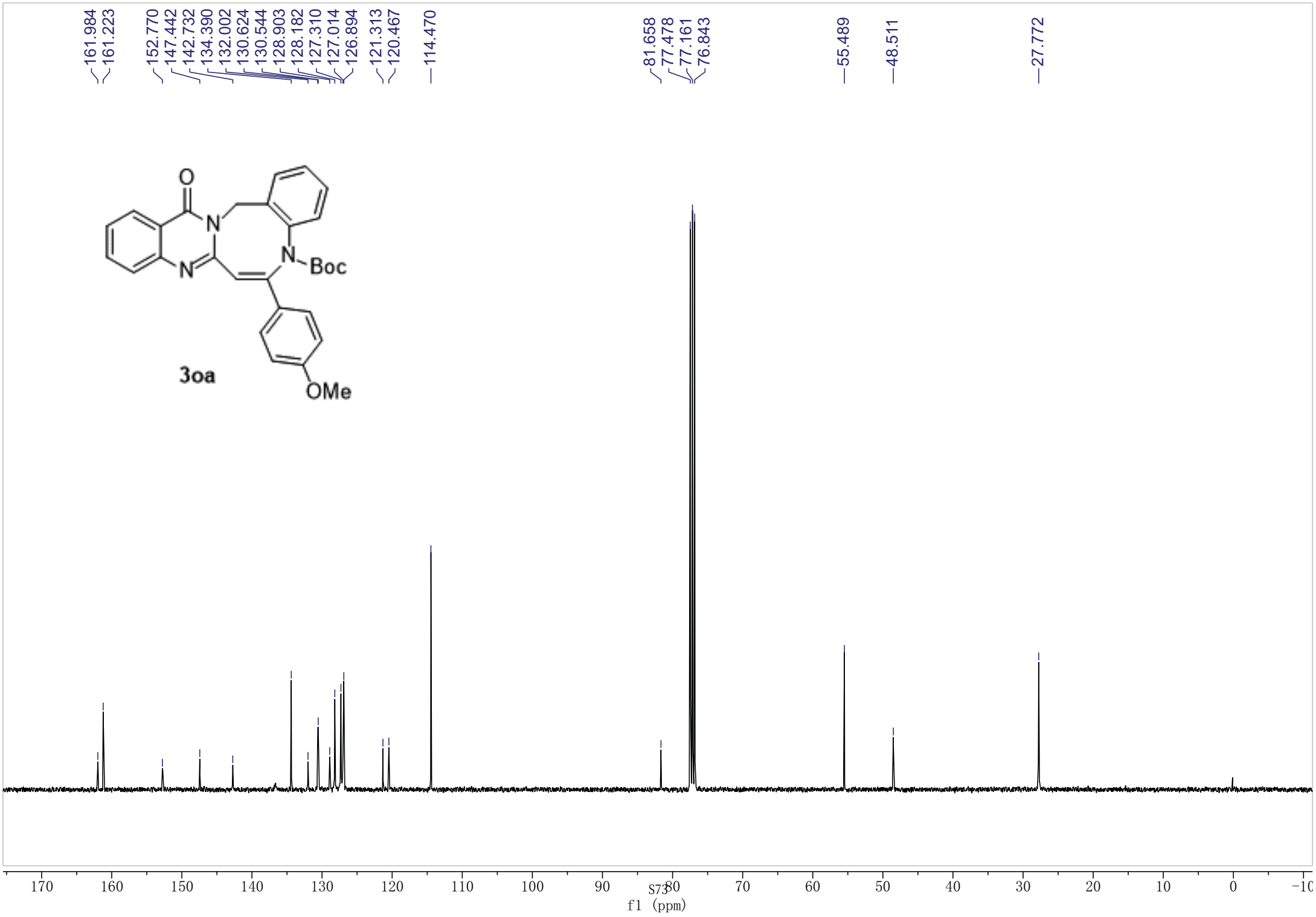
-0.
f1 (ppm)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126.894
121.313
120.467
114.470
81.658
77.478
77.161
76.843
55.489
48.511
27.772
O
N
N
N
Boc
OMe
3oa
170
160
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140
130
120
110
100
90
80
70
60
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30
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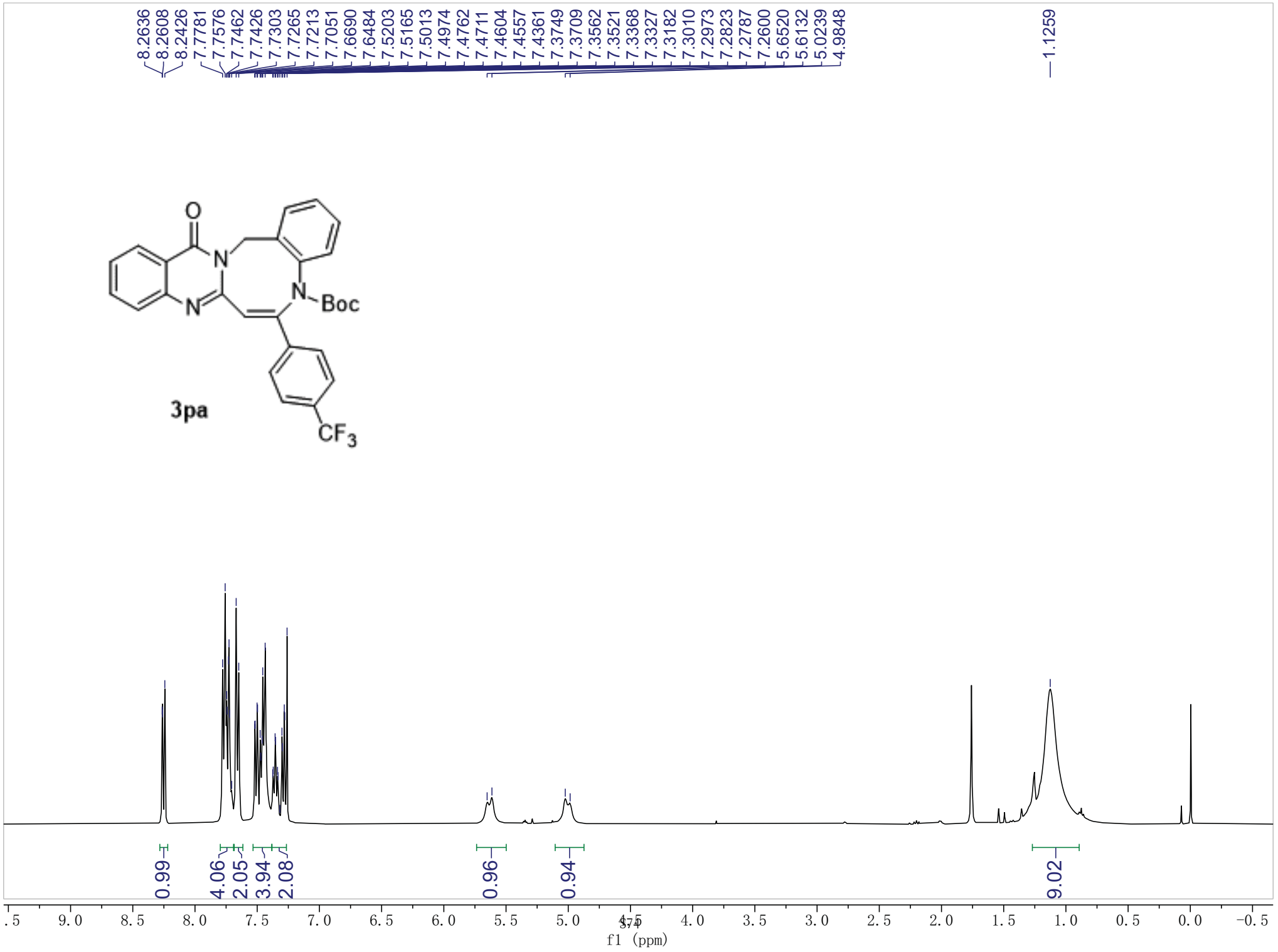
-10
f1 (ppm)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7.7265
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7.6690
7.6484
7.5203
7.5165
7.5013
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7.4762
7.4711
7.4604
7.4557
7.4361
7.3749
7.3709
7.3562
7.3521
7.3368
7.3327
7.3182
7.3010
7.2973
7.2823
7.2787
7.2600
5.6520
5.6132
5.0239
4.9848
1.1259
O
N
N
Boc
3pa
CF3
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2.05
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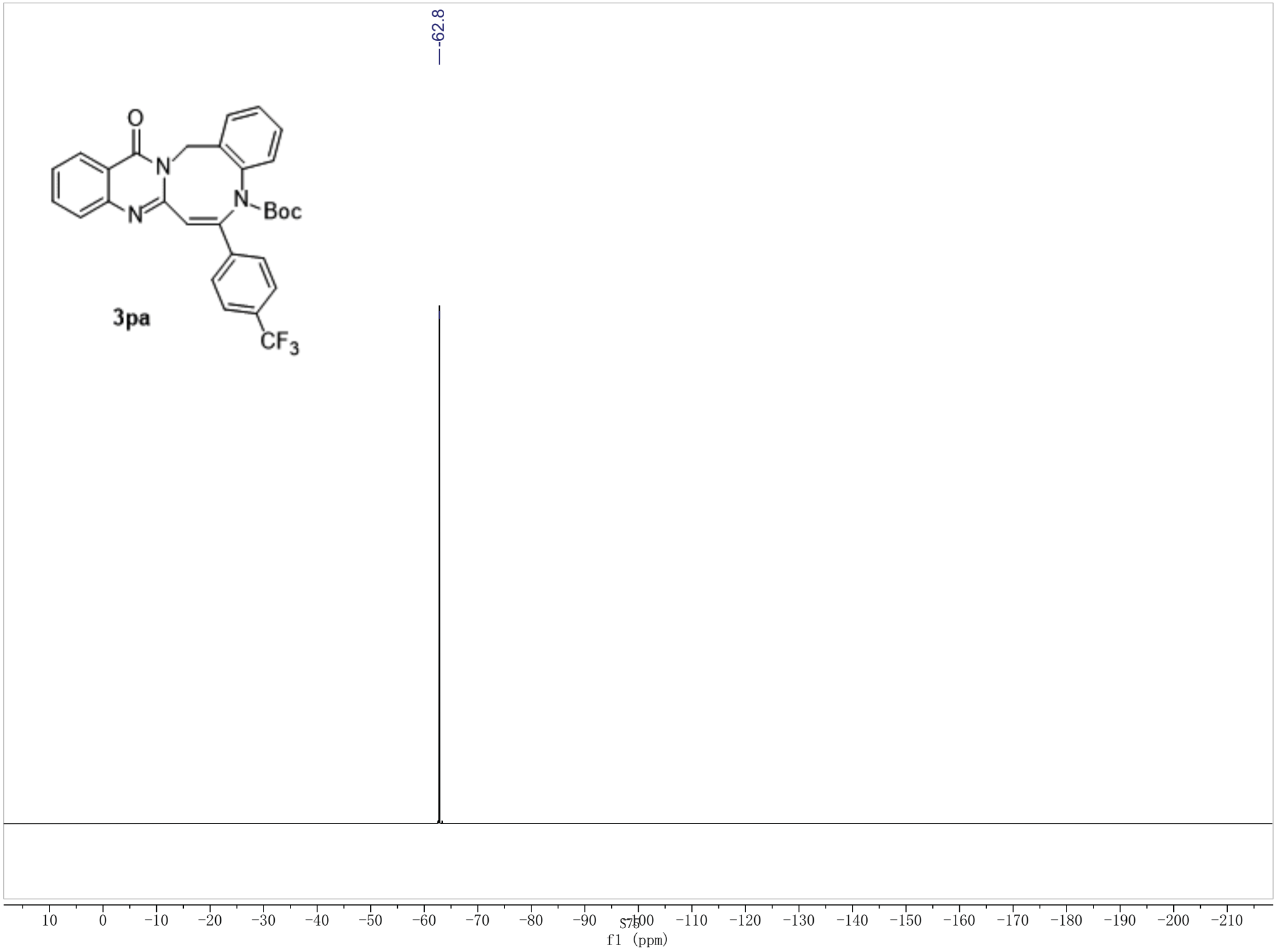
2.08
0.96
0.94
9.02
f1 (ppm)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-10
-20
-30
-40
-50
-60
-70
-80
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-100
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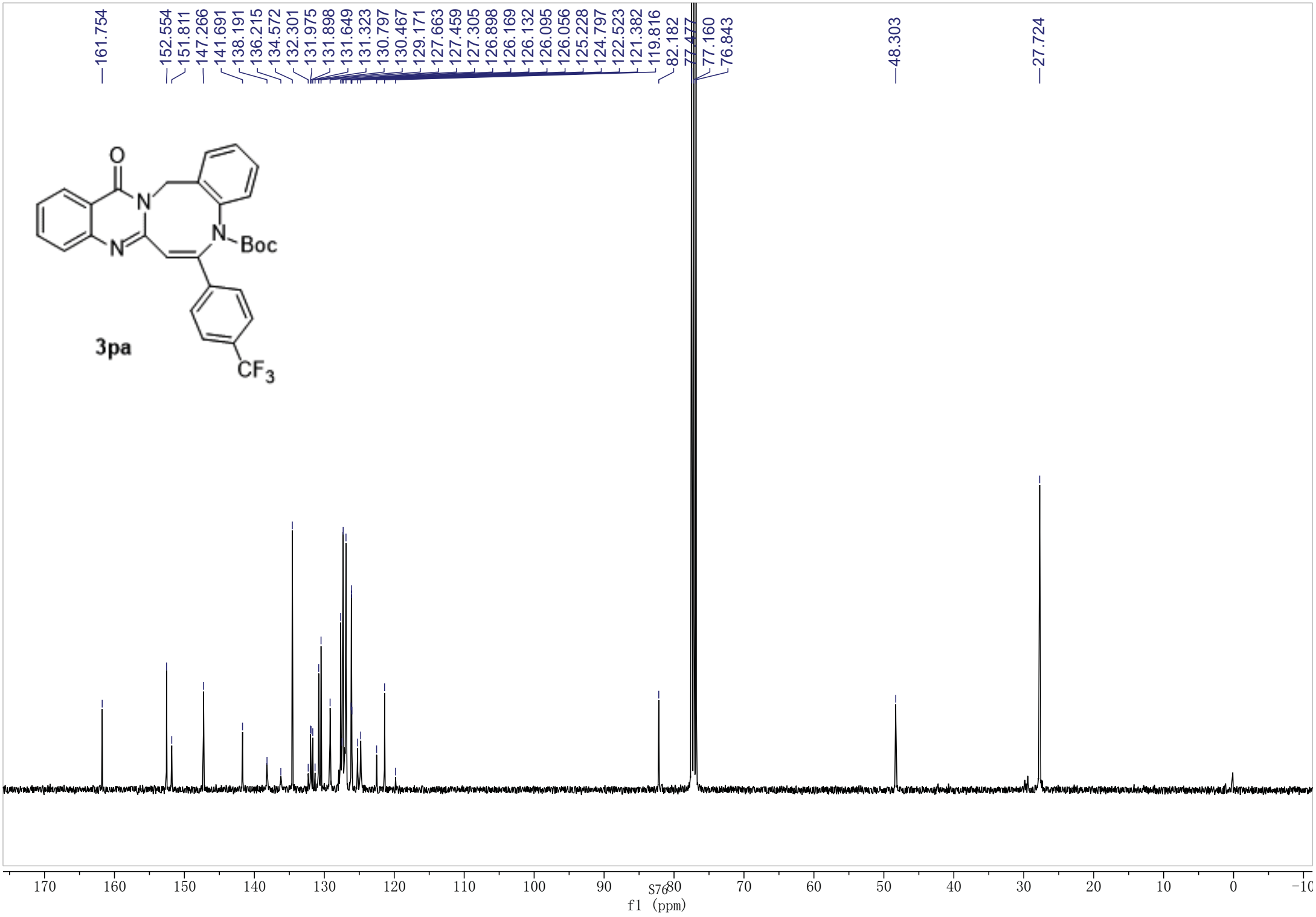
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)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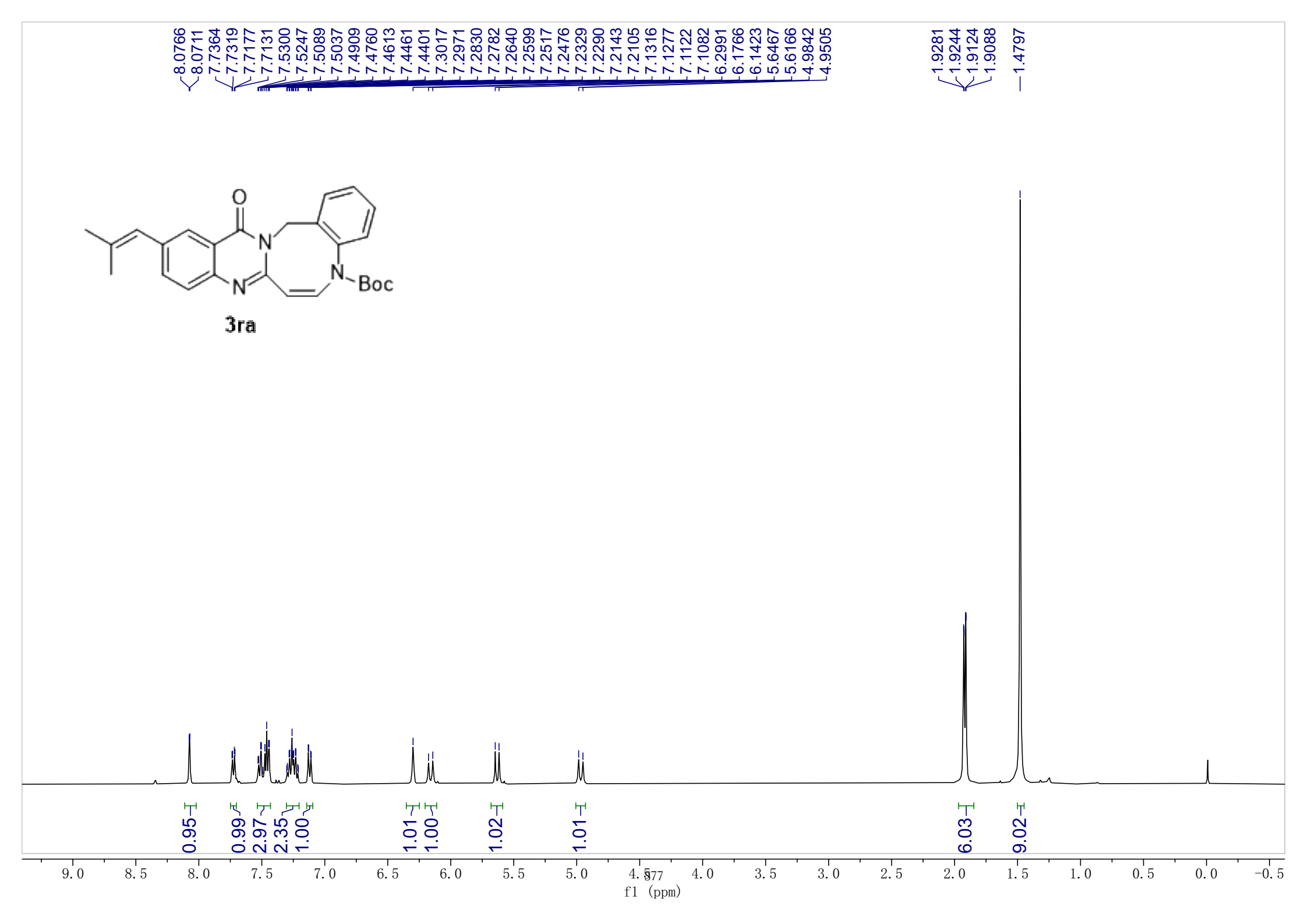
126.095
126.056
125.228
124.797
122.523
121.382
119.816
82.182
77.477
77.160
76.843
48.303
27.724
O
N
N
N
Boc
CF3
3pa
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.4760
7.4613
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7.4401
7.3017
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7.2830
7.2782
7.2640
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7.2517
7.2476
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7.2290
7.2143
7.2105
7.1316
7.1277
7.1122
7.1082
6.2991
6.1766
6.1423
5.6467
5.6166
4.9842
4.9505
1.9281
1.9244
1.9124
1.9088
1.4797
O
N
N
N
Boc
3ra
0.95
0.99
2.97
2.35
1.00
1.01
1.00
1.02
1.01
6.03
9.02
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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2.5
2.0
1.5
1.0
0.5
0.0
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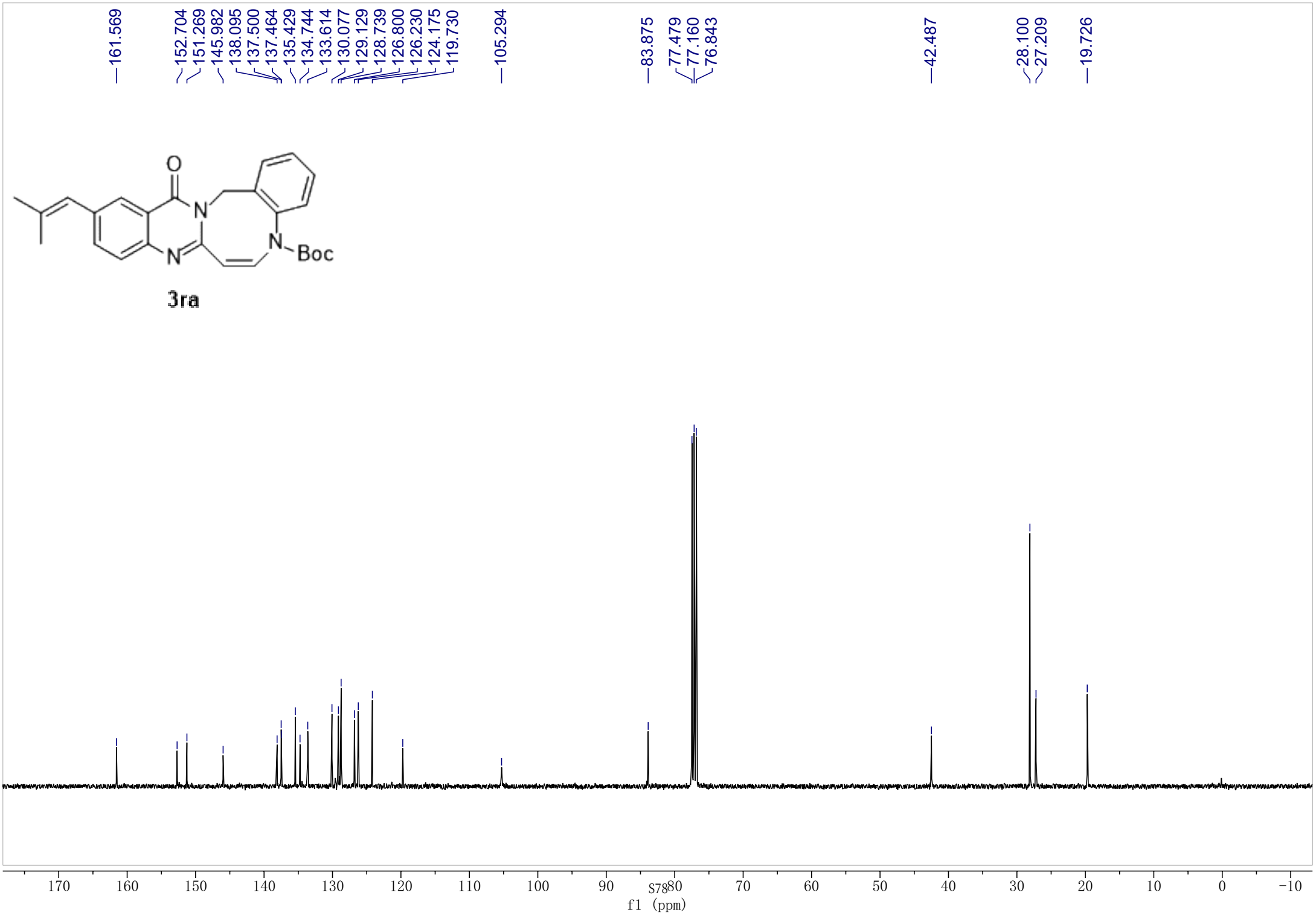
f1 (ppm)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76.843
42.487
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27.209
19.726
O
N
N
N
Boc
3ra
170
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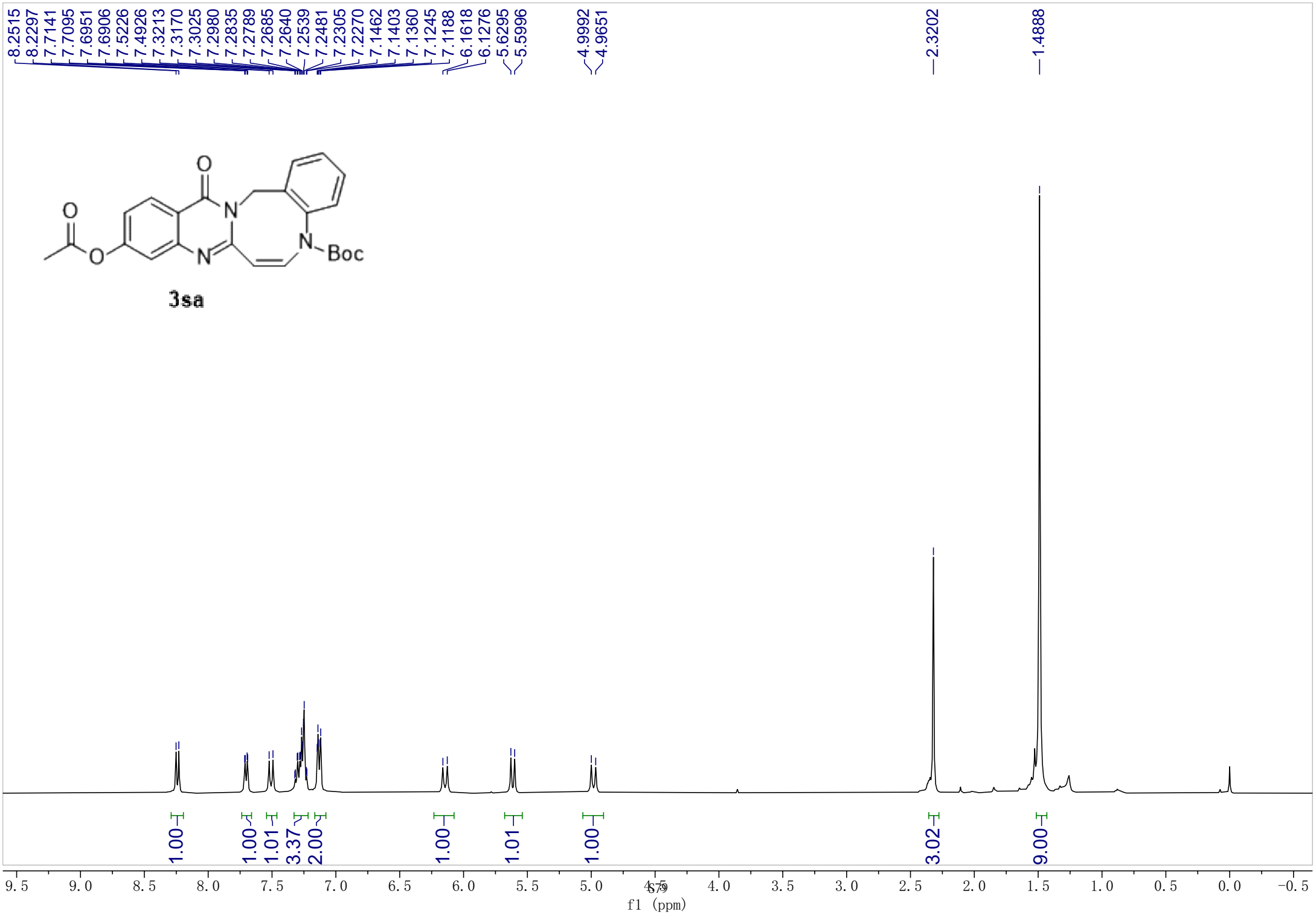
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)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7.3025
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7.2835
7.2789
7.2685
7.2640
7.2539
7.2481
7.2305
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7.1462
7.1403
7.1360
7.1245
7.1188
6.1618
6.1276
5.6295
5.5996
4.9992
4.9651
2.3202
1.4888
O
O
O
N
N
N
Boc
1.00
1.00
1.01
3.37
2.00
1.00
1.01
1.00
3.02
9.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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2.5
2.0
1.5
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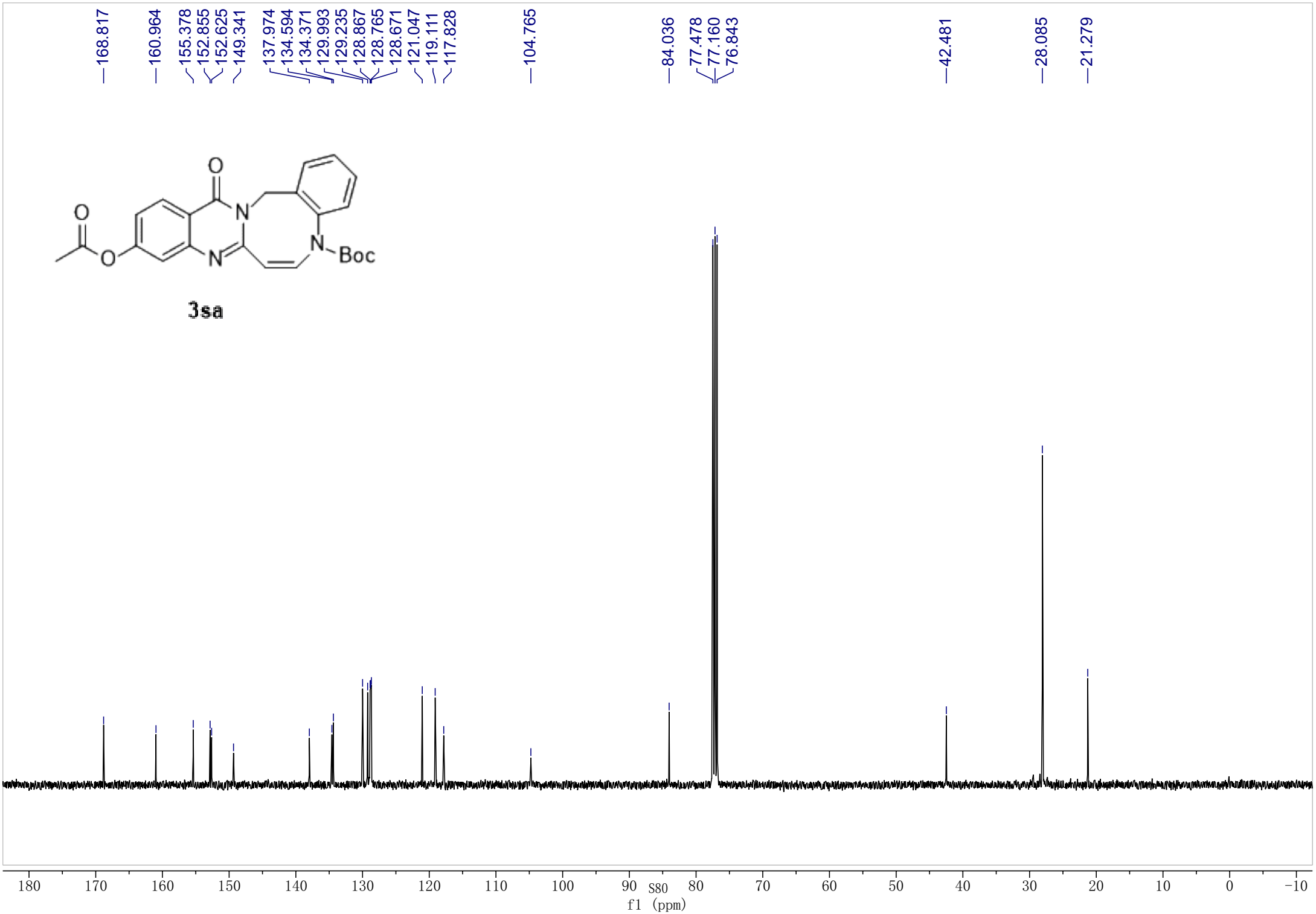
0.0
-0.5
f1 (ppm)

3sa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119.111
117.828
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84.036
77.478
77.160
76.843
42.481
28.085
21.279
O
O
O
N
N
N
Boc
3sa
180
170
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140
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120
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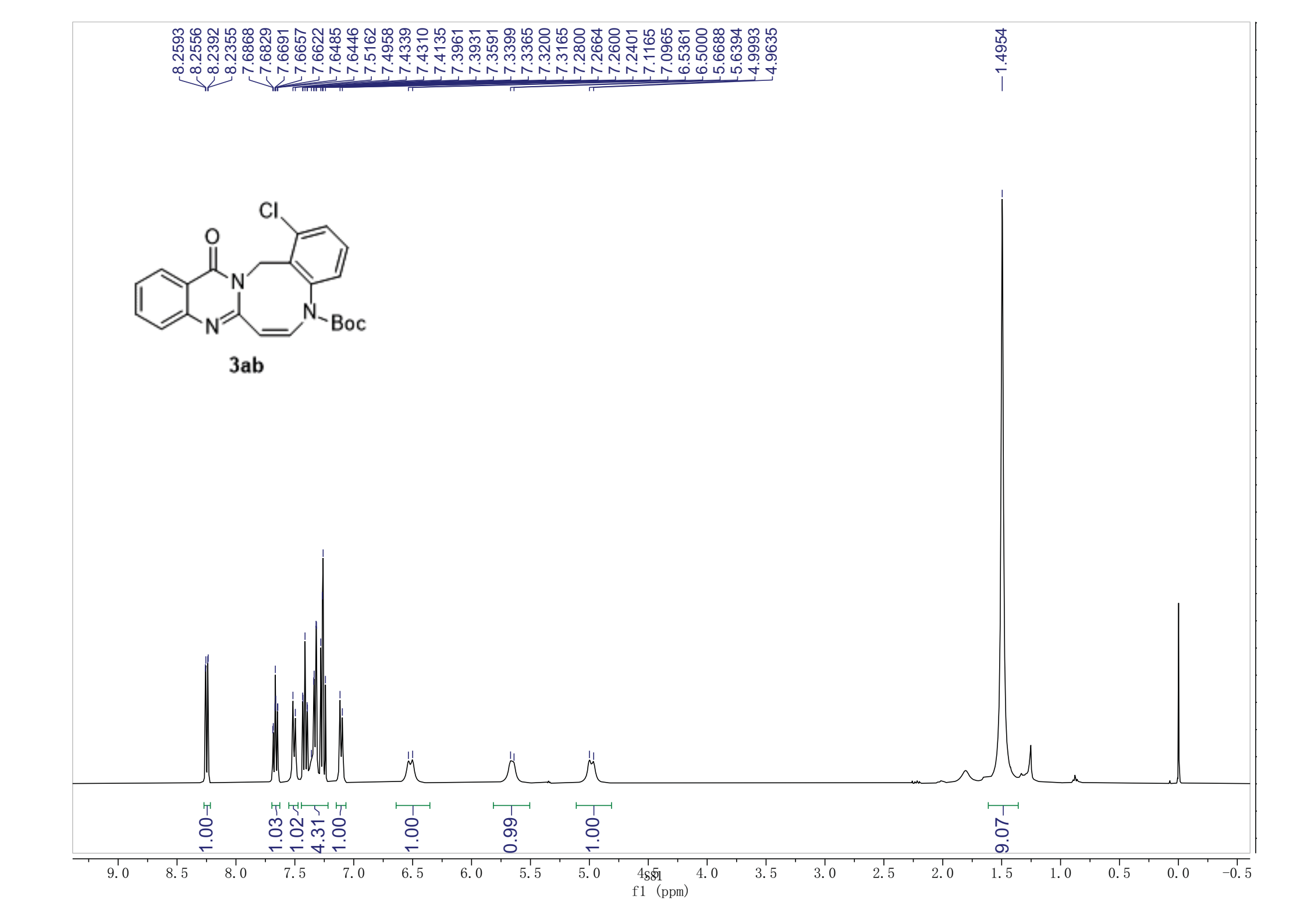
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.5162
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7.3399
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7.3200
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1.4954
Cl
O
N
N
N
Boc
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1.03
1.02
4.31
1.00
1.00
0.99
1.00
9.07
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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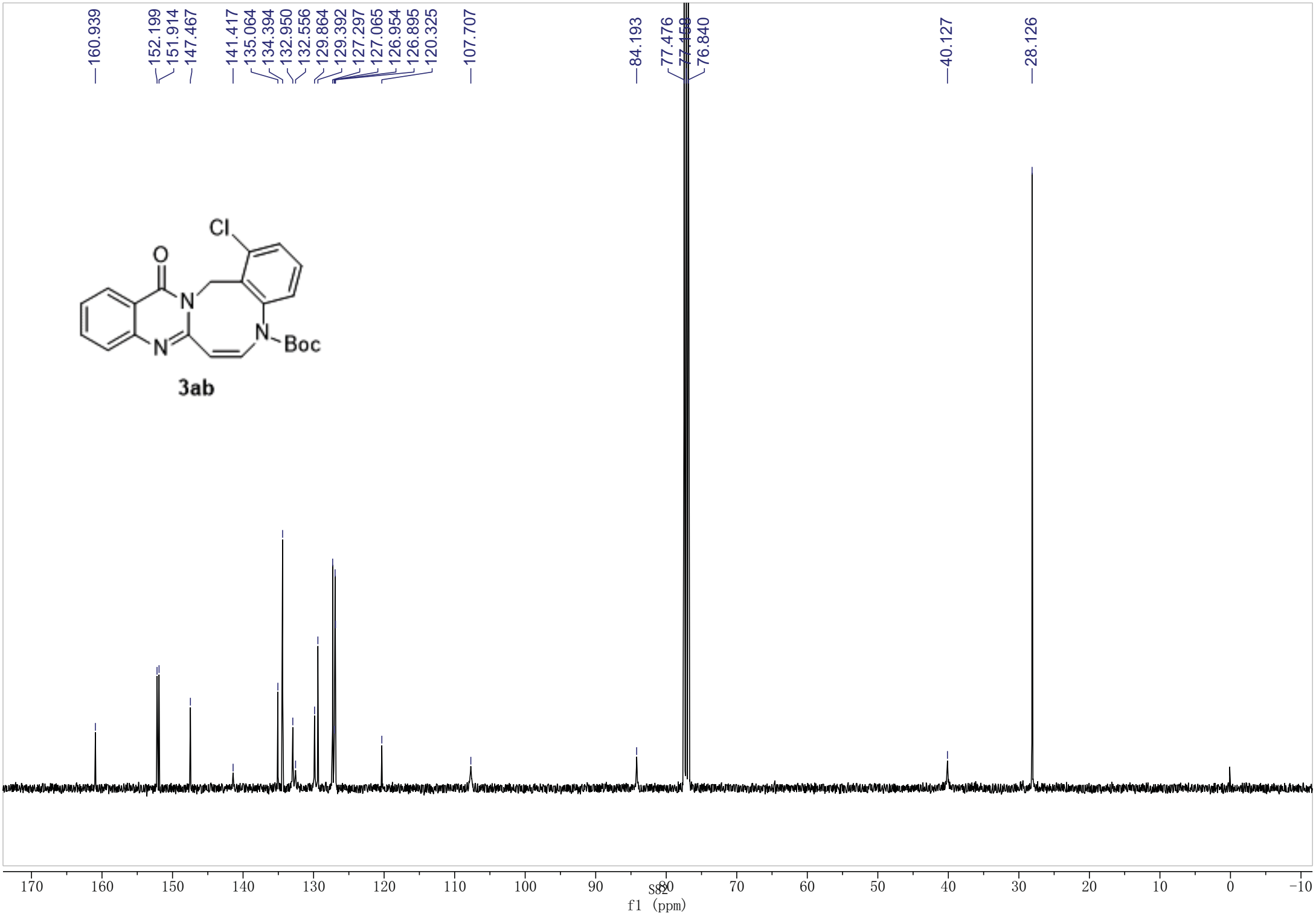
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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126.954
126.895
120.325
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84.193
77.476
77.159
76.840
40.127
28.126
Cl
O
N
N
N
Boc
3ab
170
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100
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80
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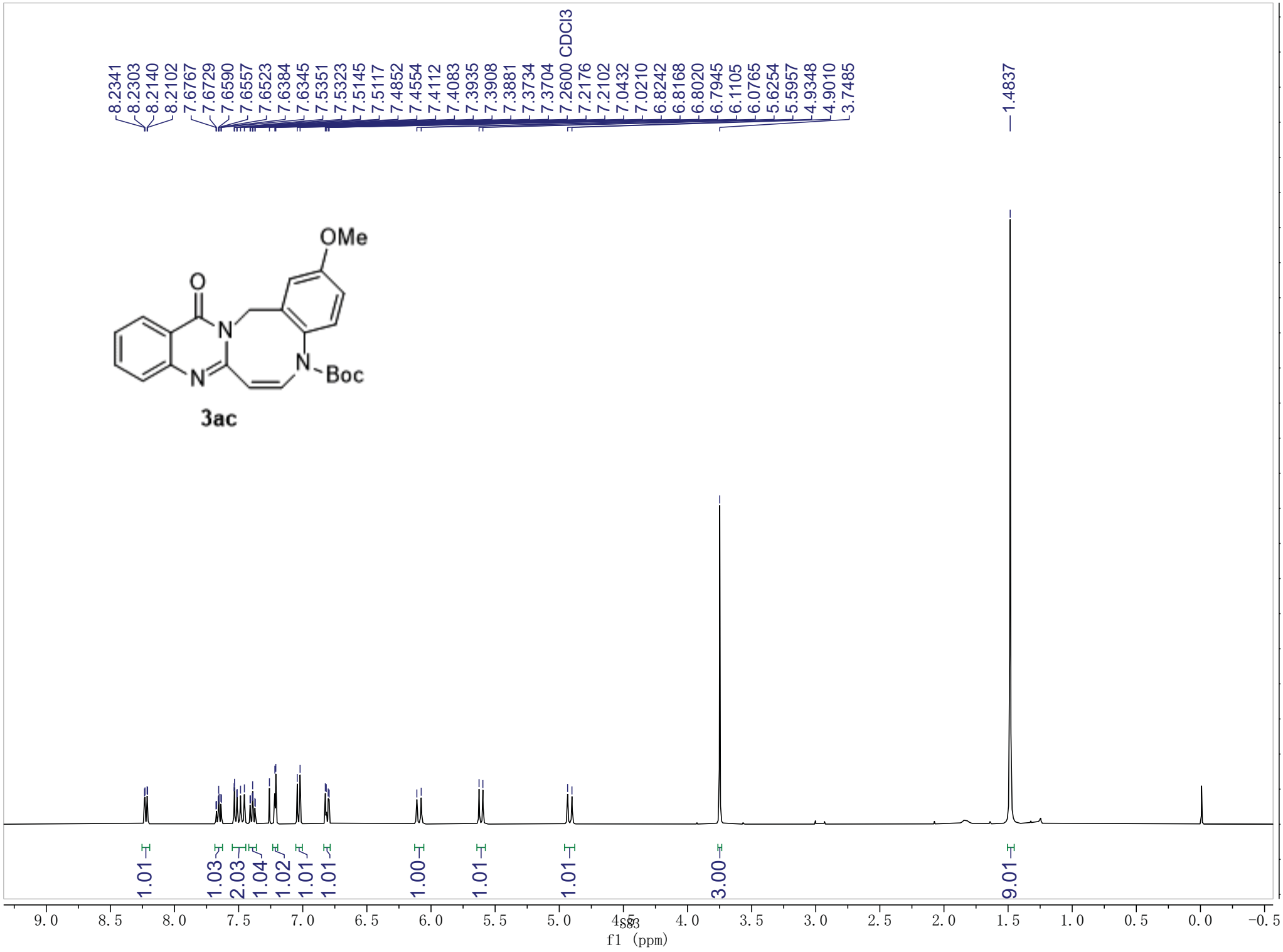
50
40
30
20
10
0
-10
f1 (ppm)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7.6729
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7.5351
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7.3881
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1.4837
OMe
O
N
N
N
Boc
3ac
1.01
1.03
2.03
1.04
1.02
1.01
1.01
1.00
1.01
1.01
3.00
9.01
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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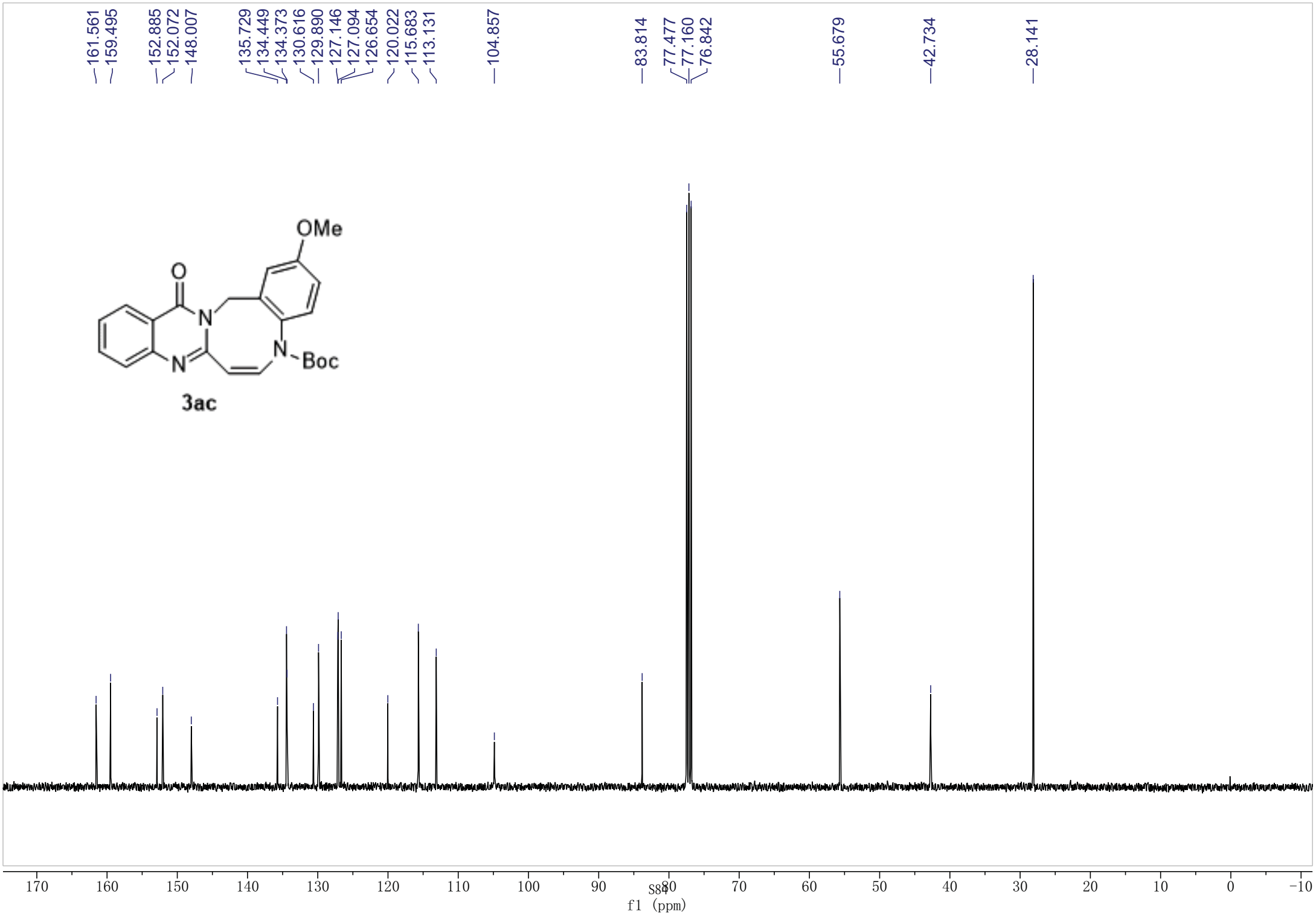
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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134.373
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126.654
120.022
115.683
113.131
104.857
83.814
77.477
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76.842
55.679
42.734
28.141
OMe
O
N
N
N
Boc
3ac
170
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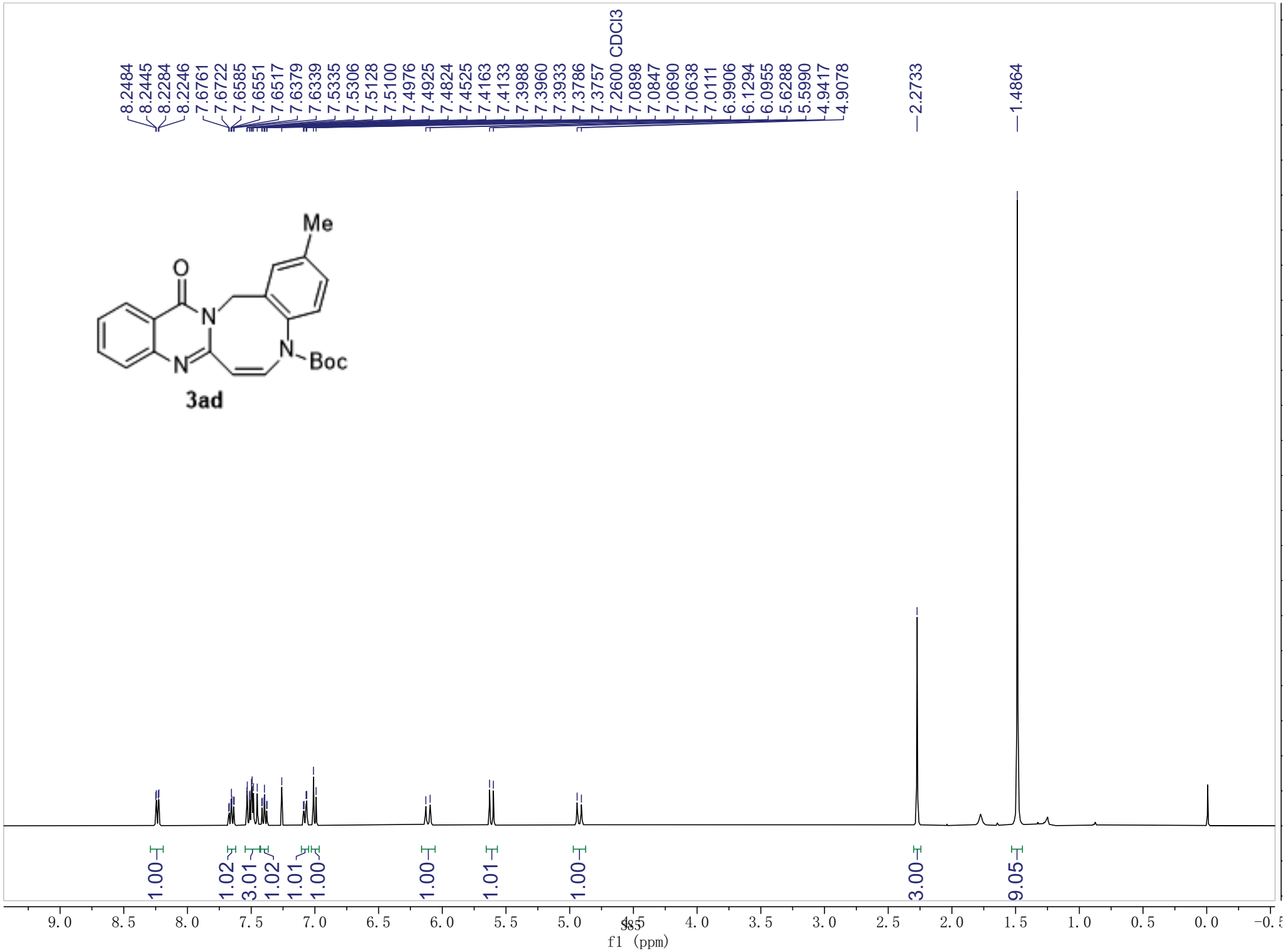
f1 (ppm)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7.6551
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7.6339
7.5335
7.5306
7.5128
7.5100
7.4976
7.4925
7.4824
7.4525
7.4163
7.4133
7.3988
7.3960
7.3933
7.3786
7.3757
7.2600
CDCl3
7.0898
7.0847
7.0690
7.0638
7.0111
6.9906
6.1294
6.0955
5.6288
5.5990
4.9417
4.9078
2.2733
1.4864
Me
O
N
N
N
Boc
3ad
1.00
1.02
3.01
1.02
1.01
1.00
1.00
1.01
1.00
3.00
9.05
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.0
2.5
2.0
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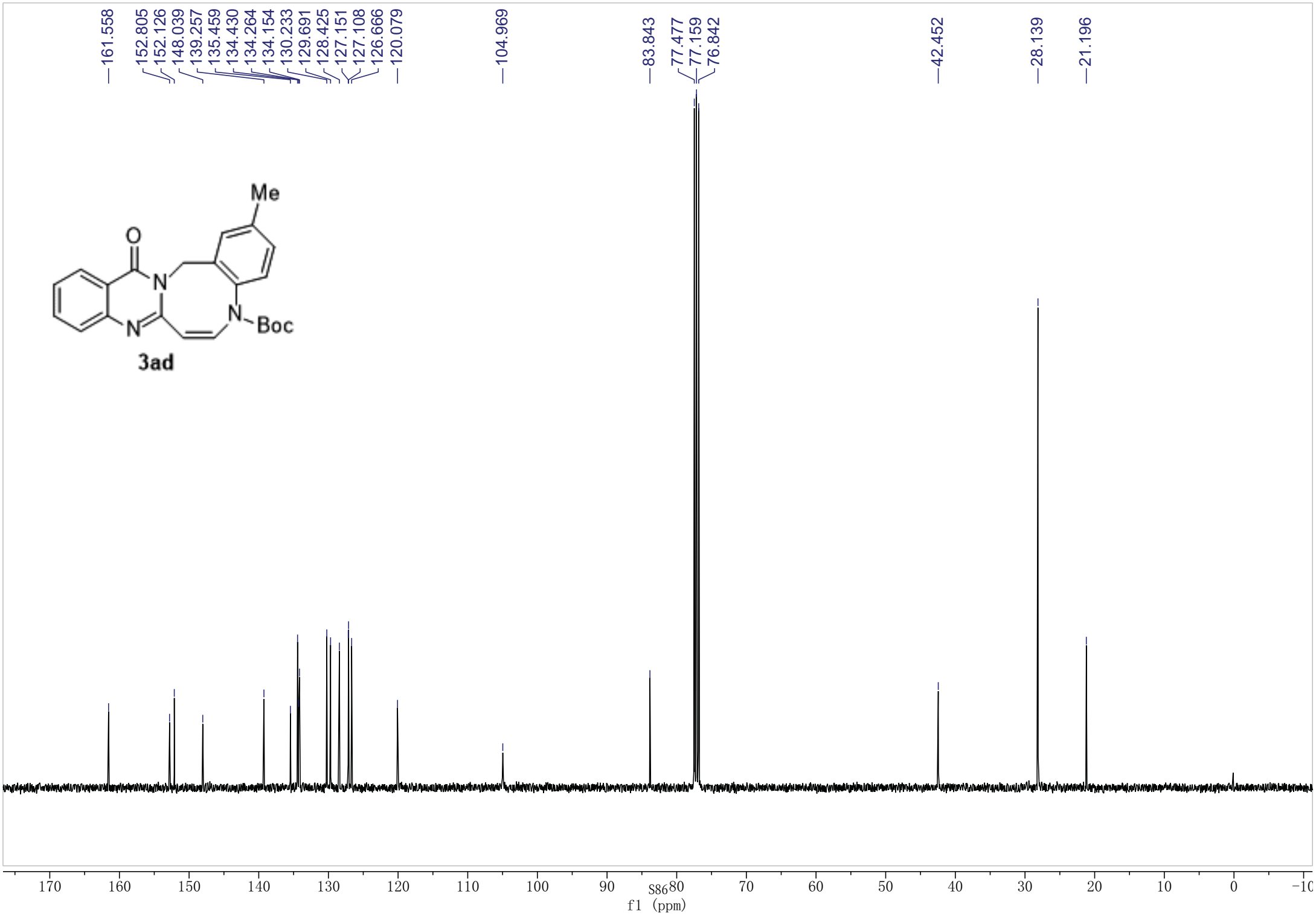
0.0
f1 (ppm)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134.264
134.154
130.233
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127.151
127.108
126.666
120.079
104.969
83.843
77.477
77.159
76.842
42.452
28.139
21.196
Me
O
N
N
N
Boc
3ad
170
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140
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120
110
100
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80
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60
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40
30
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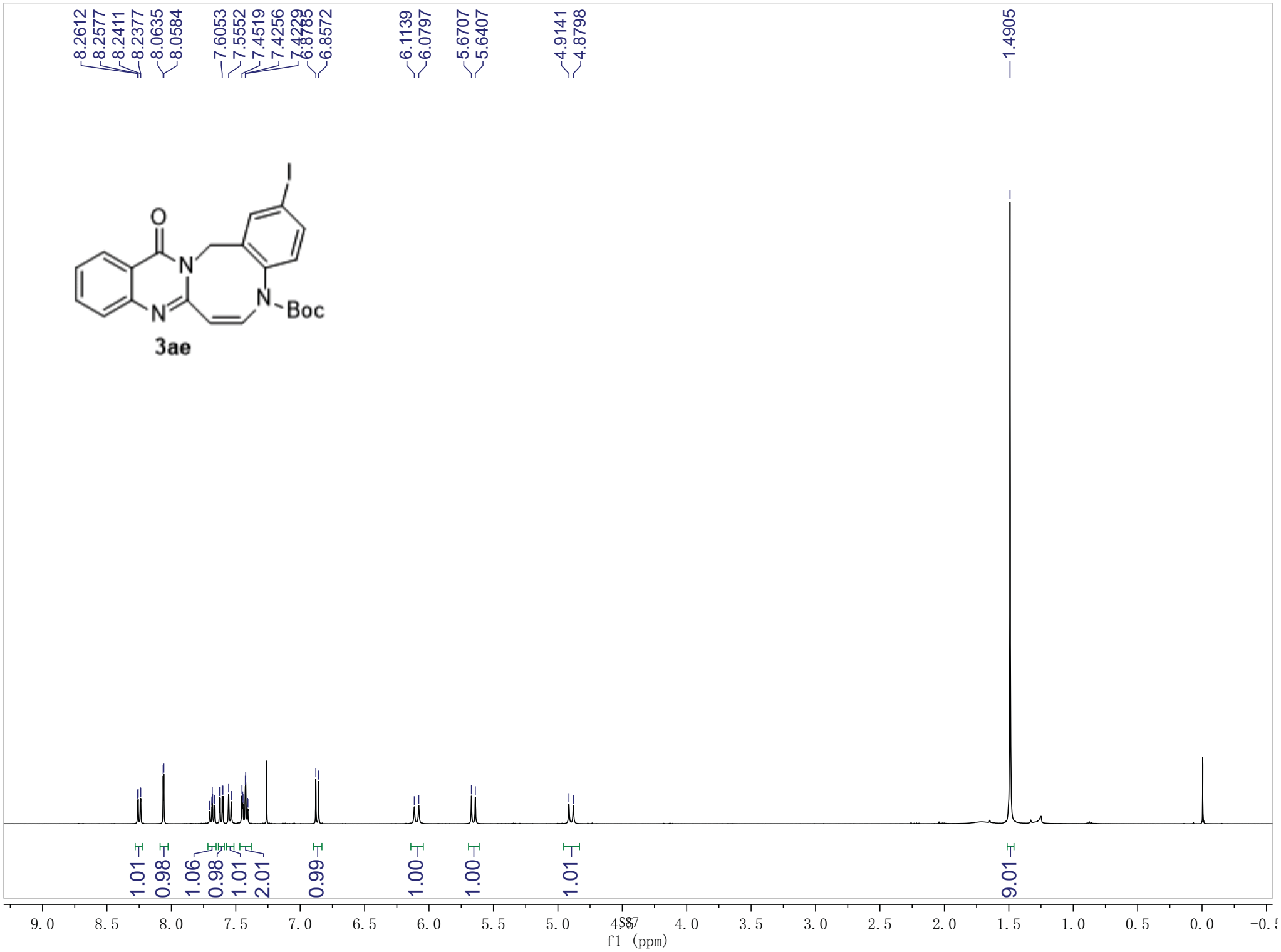
-10
f1 (ppm)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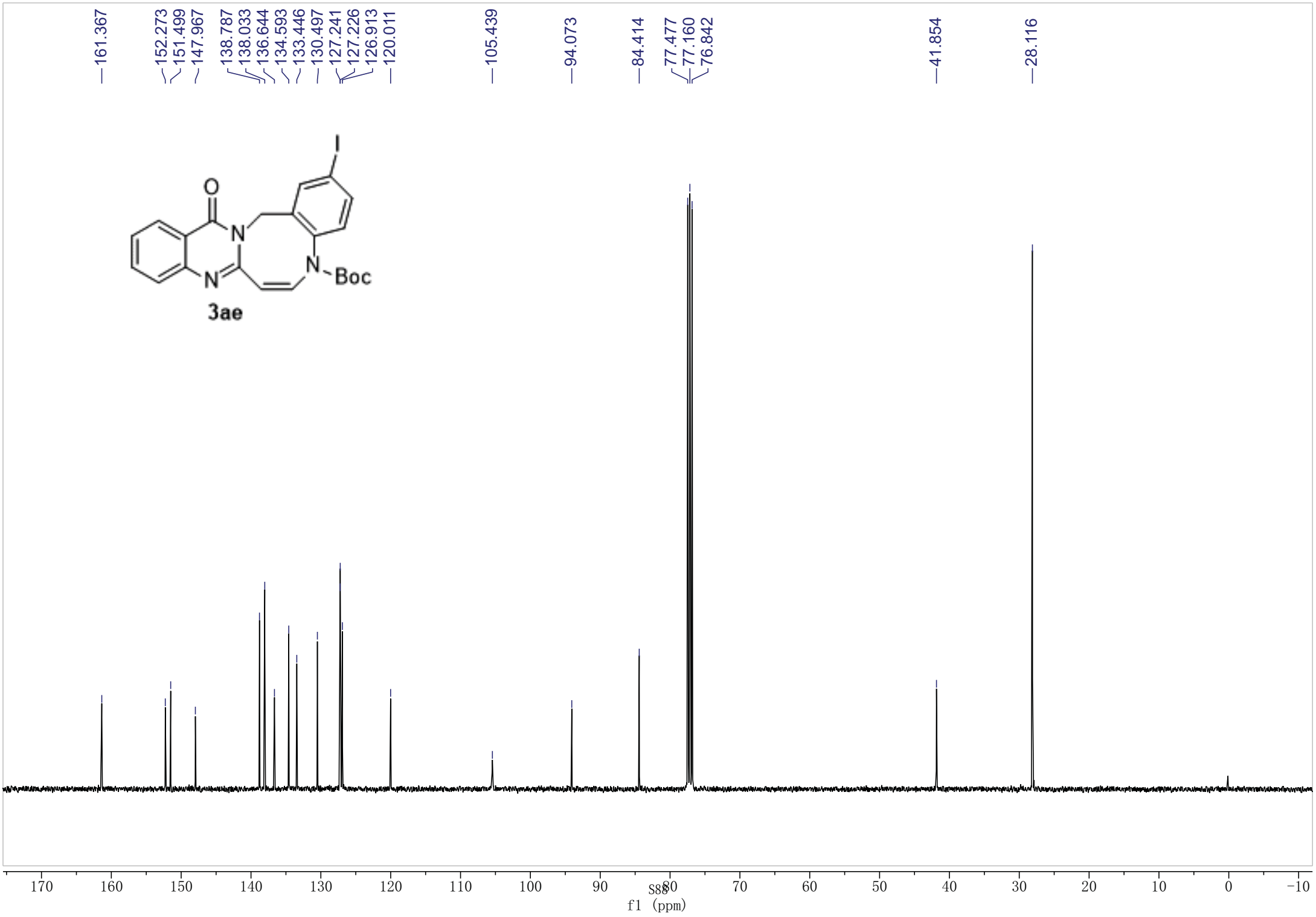
8.2377
8.0635
8.0584
7.6053
7.5552
7.4519
7.4256
7.4229
6.8785
6.8572
6.1139
6.0797
5.6707
5.6407
4.9141
4.8798
1.4905
I
O
N
N
N
Boc
3ae
1.01
0.98
1.06
0.98
1.01
2.01
0.99
1.00
1.00
1.01
9.01
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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134.593
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127.241
127.226
126.913
120.011
105.439
94.073
84.414
77.477
77.160
76.842
41.854
28.116
I
O
N
N
N
Boc
3ae
170
160
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120
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100
90
80
70
60
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40
30
20
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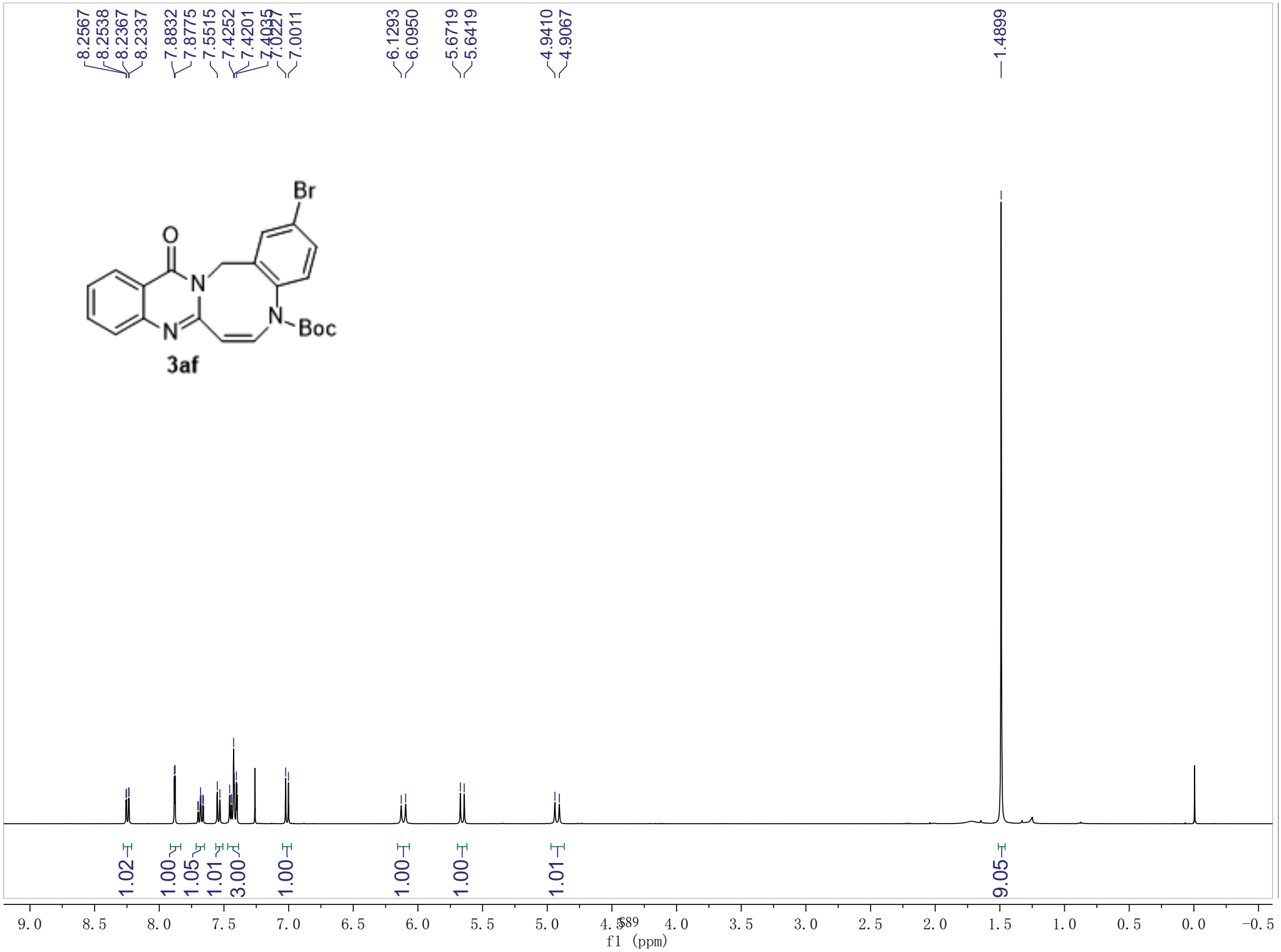
f1 (ppm)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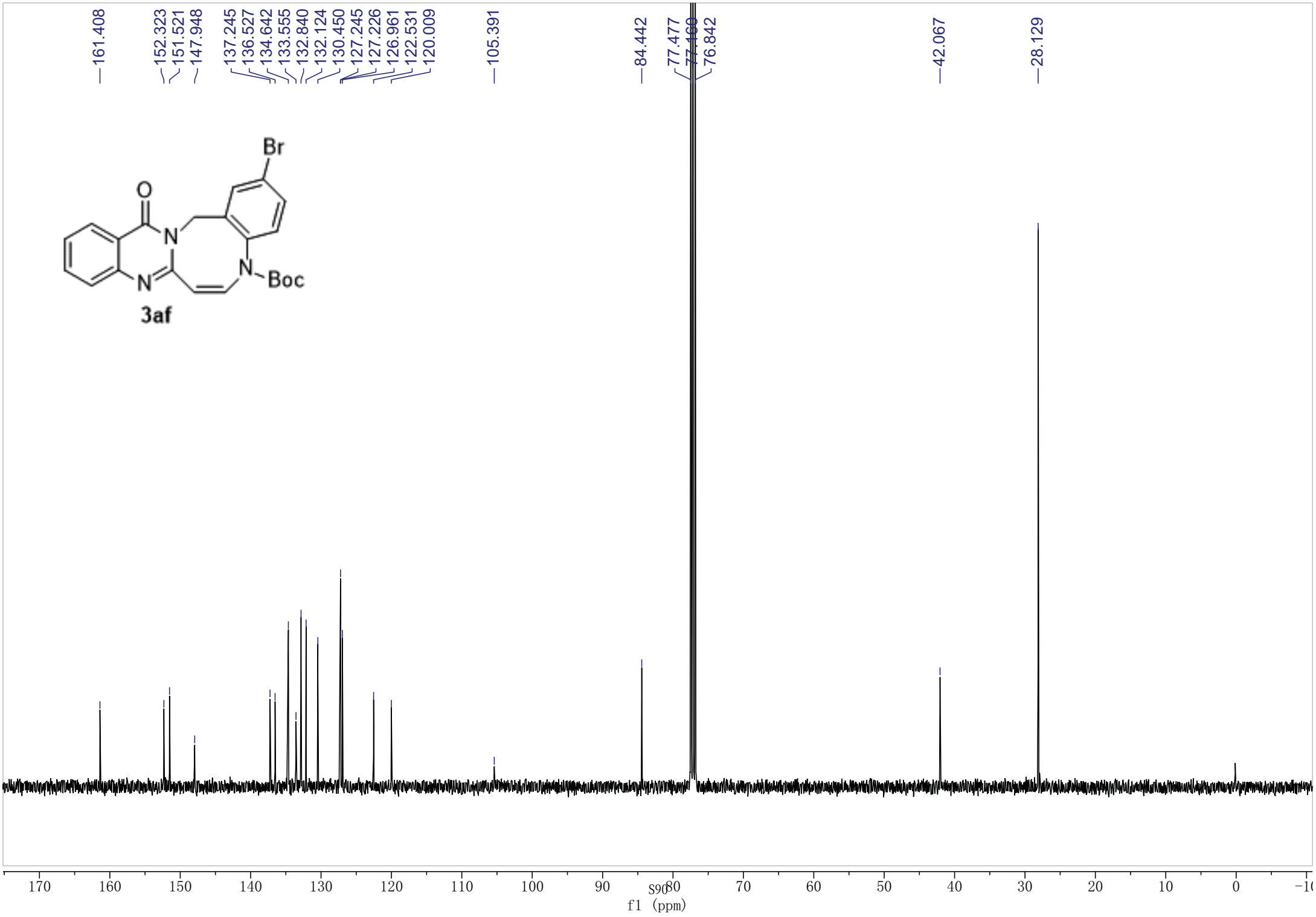
8.2337
7.8832
7.8775
7.5515
7.4252
7.4201
7.4035
7.0227
7.0011
6.1293
6.0950
5.6719
5.6419
4.9410
4.9067
1.4899
Br
O
N
N
N
Boc
3af
1.02
1.00
1.05
1.01
3.00
1.00
1.00
1.00
1.01
9.05
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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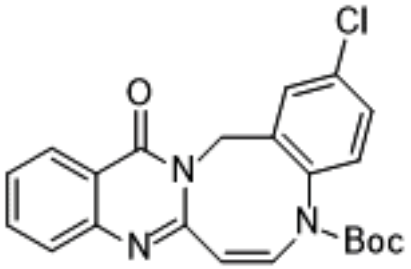
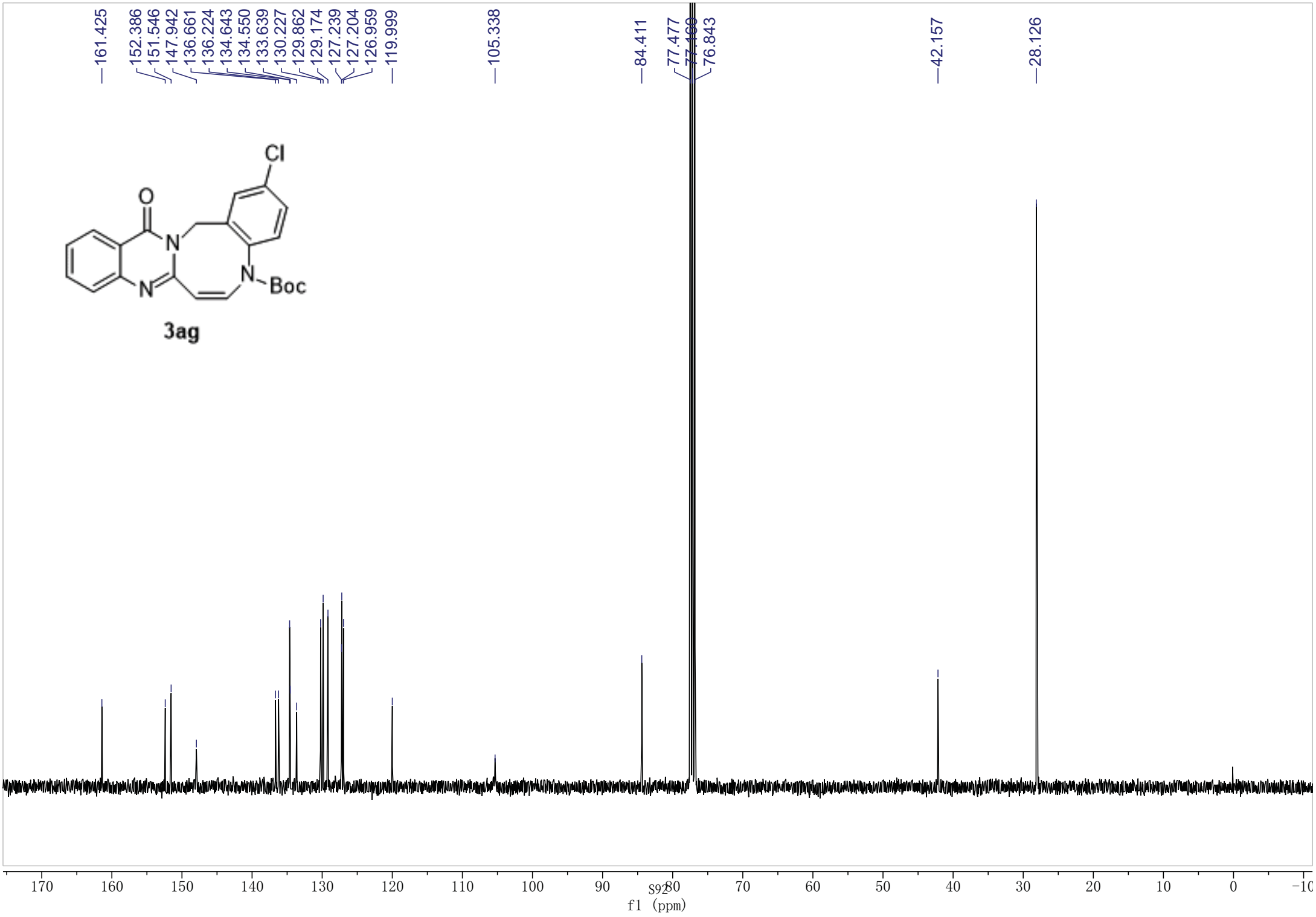
136.527
134.642
133.555
132.840
132.124
130.450
127.245
127.226
126.961
122.531
120.009
105.391
84.442
77.477
77.160
76.842
42.067
28.129
Br
O
N
N
N
Boc
3af
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



3ag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134.550
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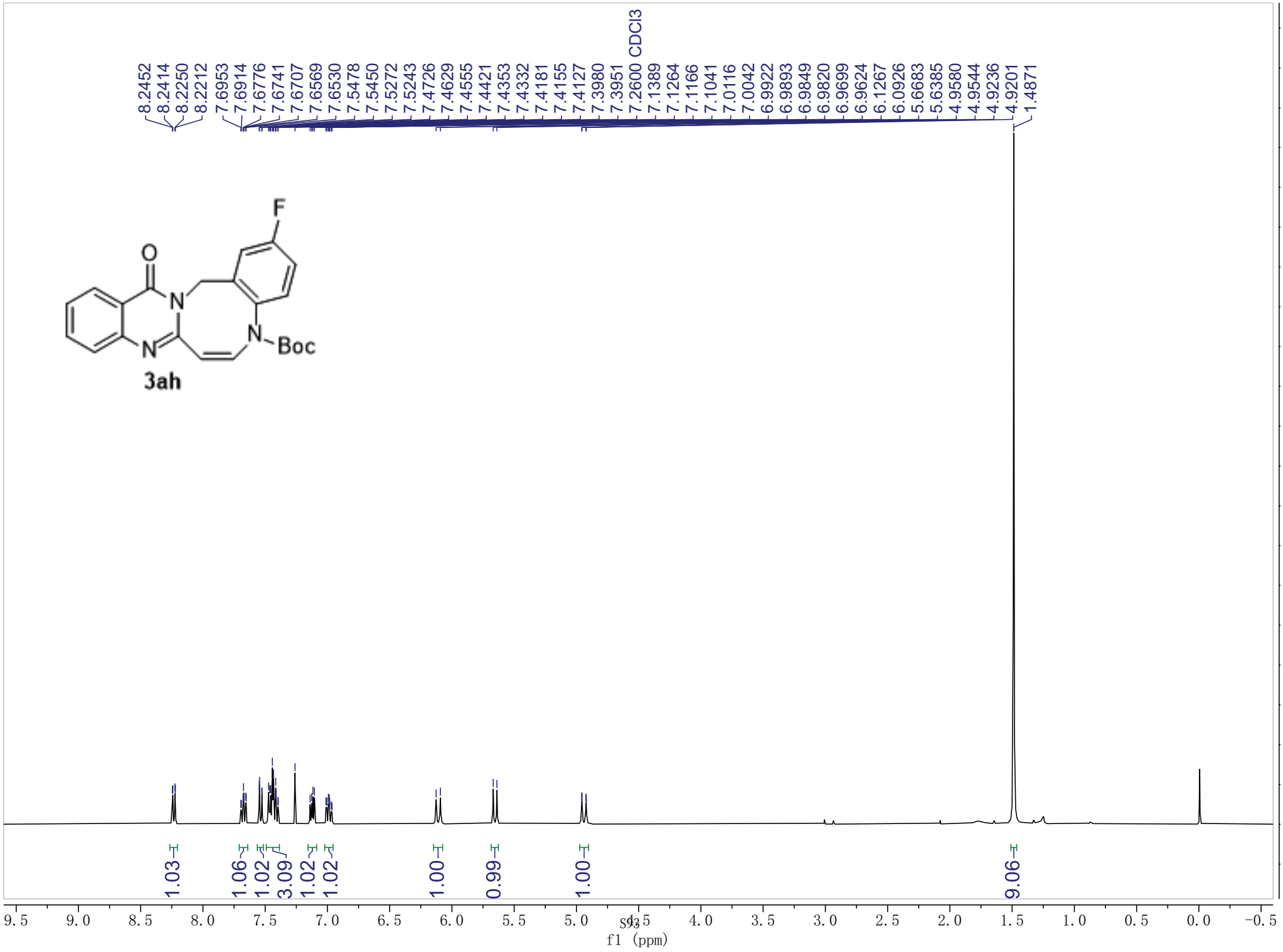
127.239
127.204
126.959
119.999
105.338
84.411
77.477
77.160
76.843
42.157
28.126
Cl
O
N
N
N
Boc
3ag
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.6914
7.6776
7.6741
7.6707
7.6569
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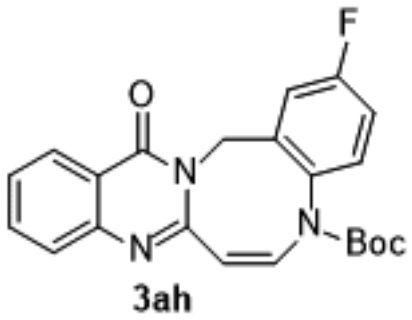
7.5478
7.5450
7.5272
7.5243
7.4726
7.4629
7.4555
7.4421
7.4353
7.4332
7.4181
7.4155
7.4127
7.3980
7.3951
7.2600 CDCl3
7.1389
7.1264
7.1166
7.1041
7.0116
7.0042
6.9922
6.9893
6.9849
6.9820
6.9699
6.9624
6.1267
6.0926
5.6683
5.6385
4.9580
4.9544
4.9236
4.9201
1.4871
F
O
N
N
N
Boc
3ah
1.03
1.06
1.02
3.09
1.02
1.02
1.00
0.99
1.00
9.06
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

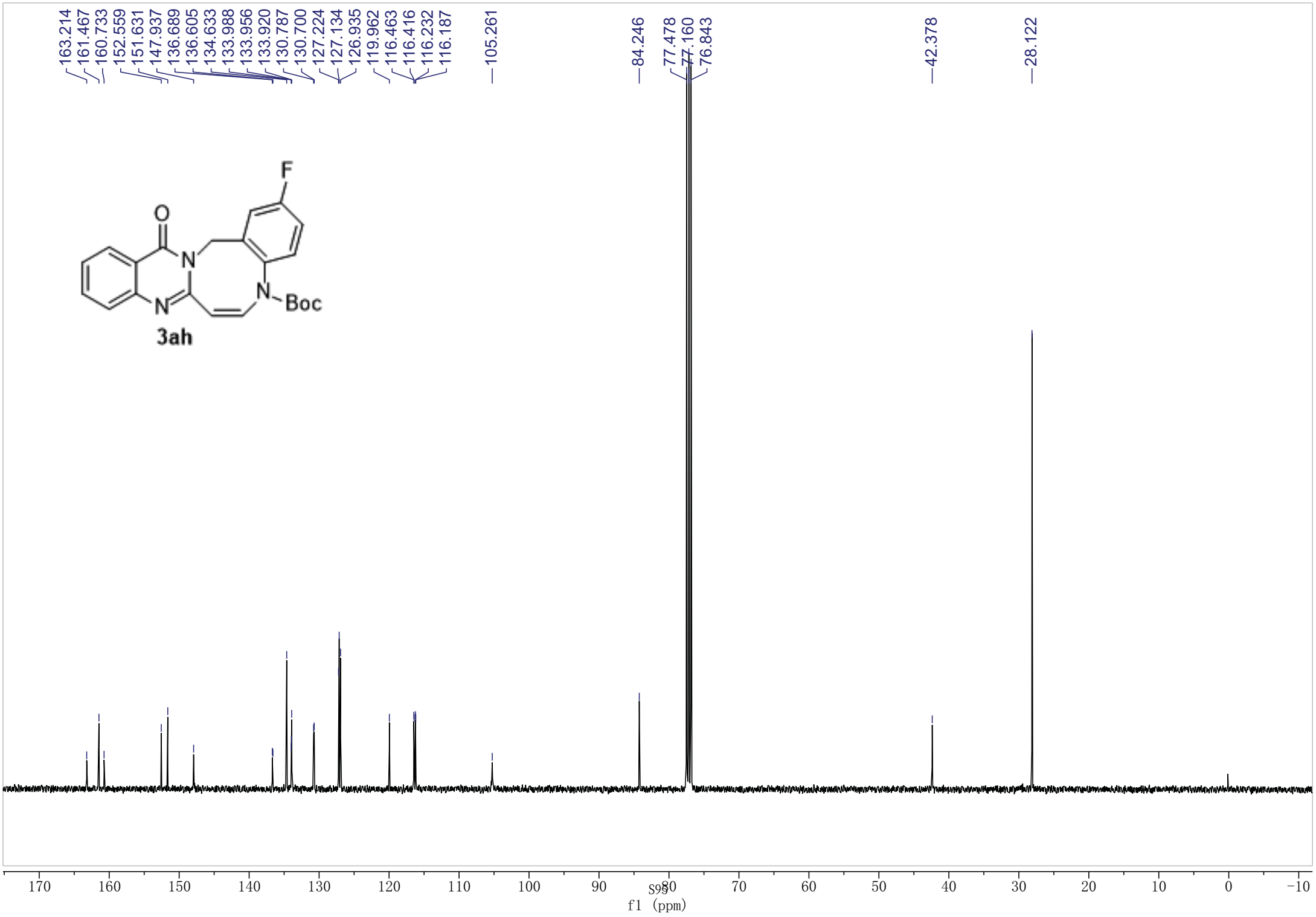


3ah

-111.0

10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

f1 (ppm)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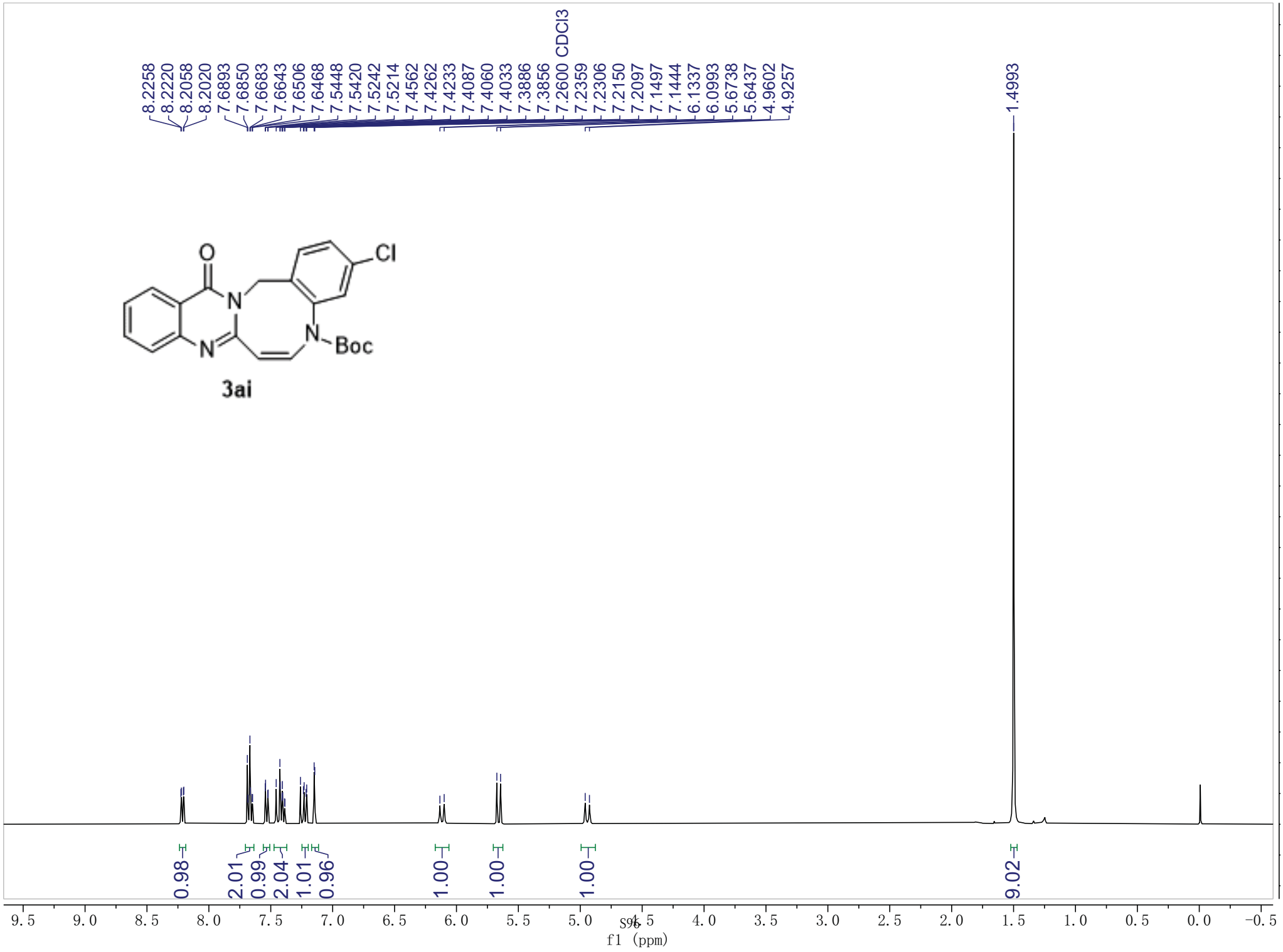
133.988
133.956
133.920
130.787
130.700
127.224
127.134
126.935
119.962
116.463
116.416
116.232
116.187
105.261
84.246
77.478
77.160
76.843
42.378
28.122
F
O
N
N
N
Boc
3ah
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)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8.2058
8.2020
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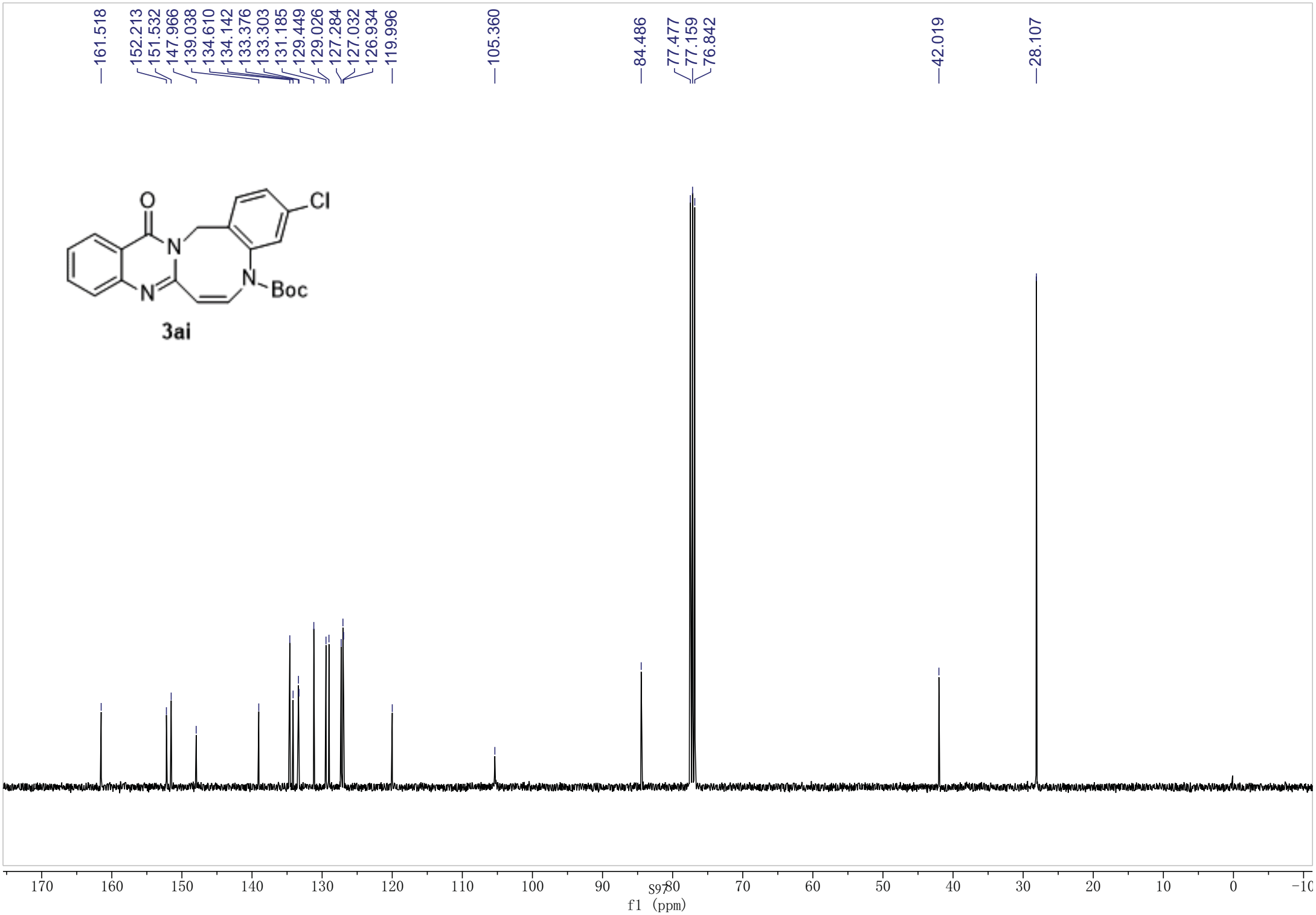
7.6850
7.6683
7.6643
7.6506
7.6468
7.5448
7.5420
7.5242
7.5214
7.4562
7.4262
7.4233
7.4087
7.4060
7.4033
7.3886
7.3856
7.2600 CDCl3
7.2359
7.2306
7.2150
7.2097
7.1497
7.1444
6.1337
6.0993
5.6738
5.6437
4.9602
4.9257
1.4993
O
N
N
N
Boc
Cl
3ai
0.98
2.01
0.99
2.04
1.01
0.96
1.00
1.00
1.00
9.02
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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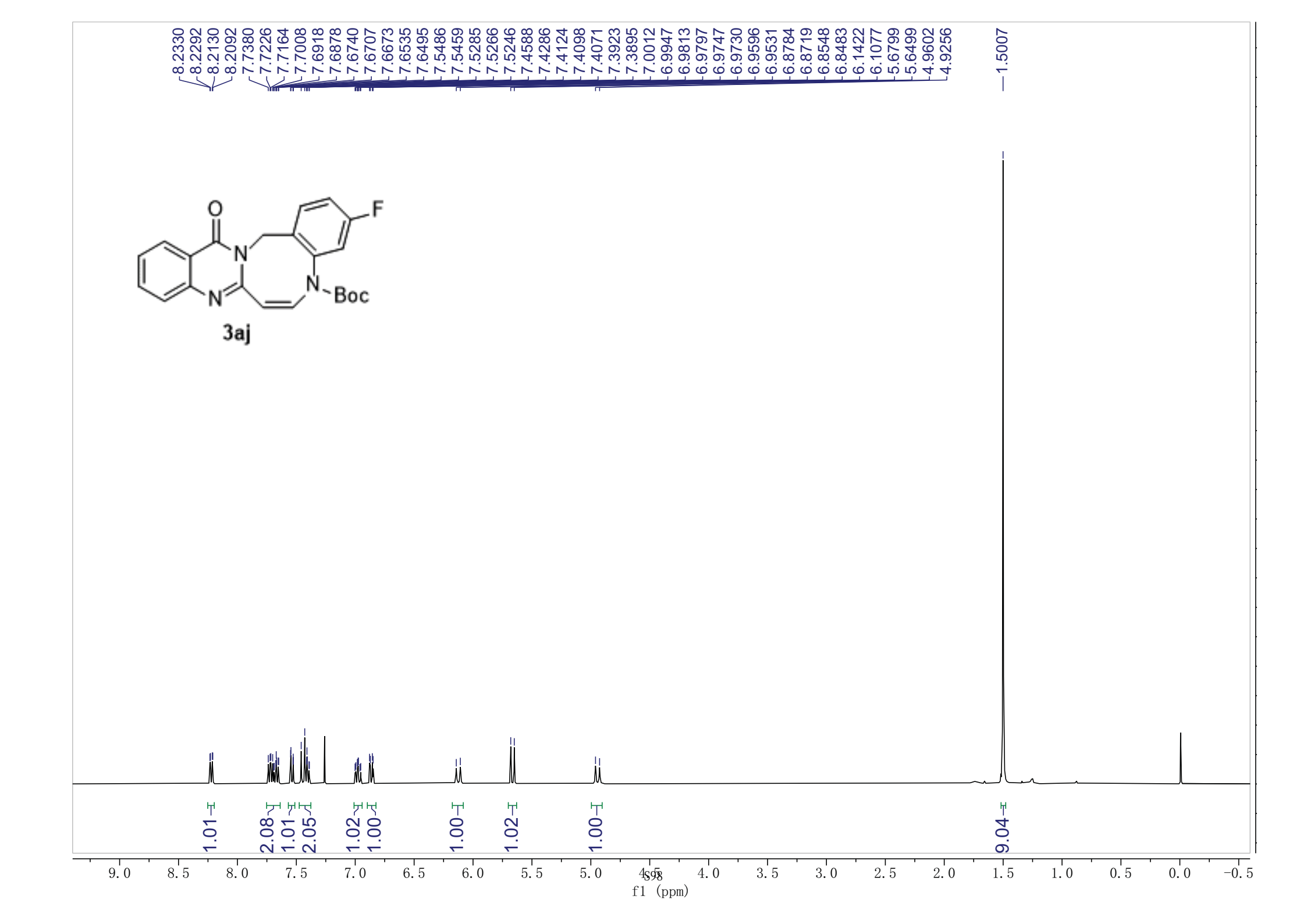
131.185
129.449
129.026
127.284
127.032
126.934
119.996
105.360
84.486
77.477
77.159
76.842
42.019
28.107
O
N
N
N
Boc
Cl
3ai
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.6673
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7.6495
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7.5266
7.5246
7.4588
7.4286
7.4124
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7.4071
7.3923
7.3895
7.0012
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6.9813
6.9797
6.9747
6.9730
6.9596
6.9531
6.8784
6.8719
6.8548
6.8483
6.1422
6.1077
5.6799
5.6499
4.9602
4.9256
1.5007
O
N
N
N
Boc
F
3aj
1.01
2.08
1.01
2.05
1.02
1.00
1.00
1.02
1.00
9.04
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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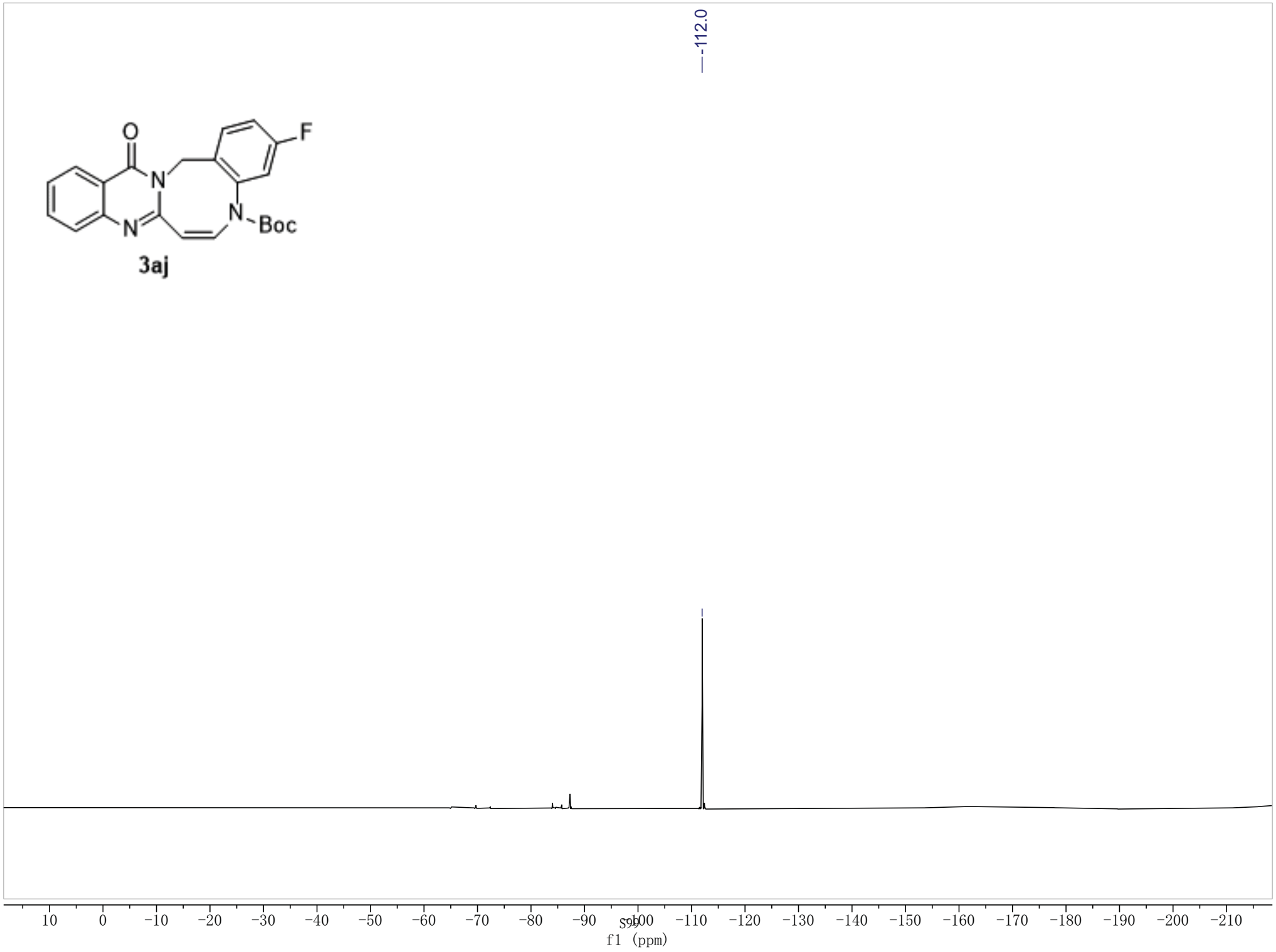
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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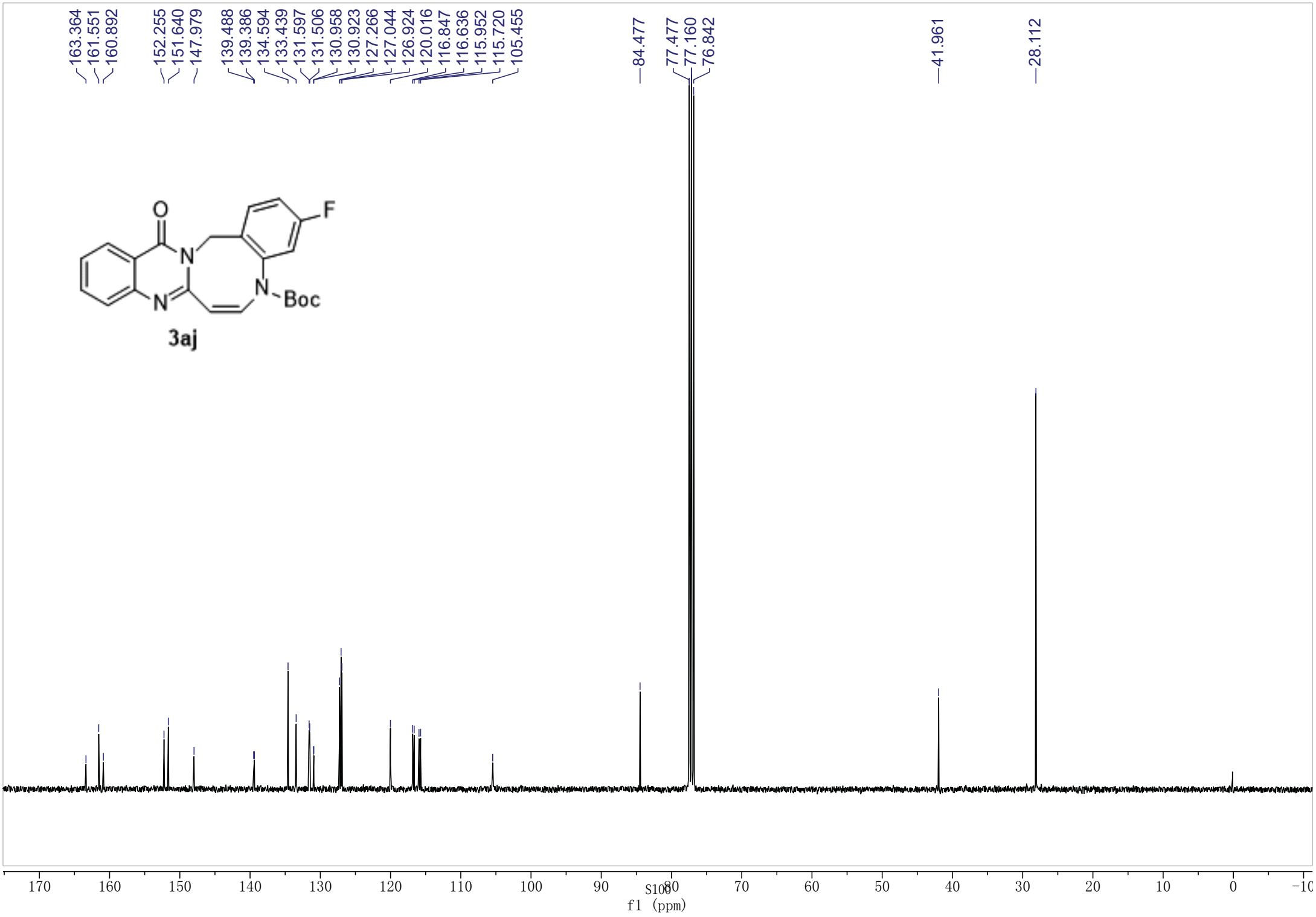
F
N
N
N
Boc
3aj
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)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139.386
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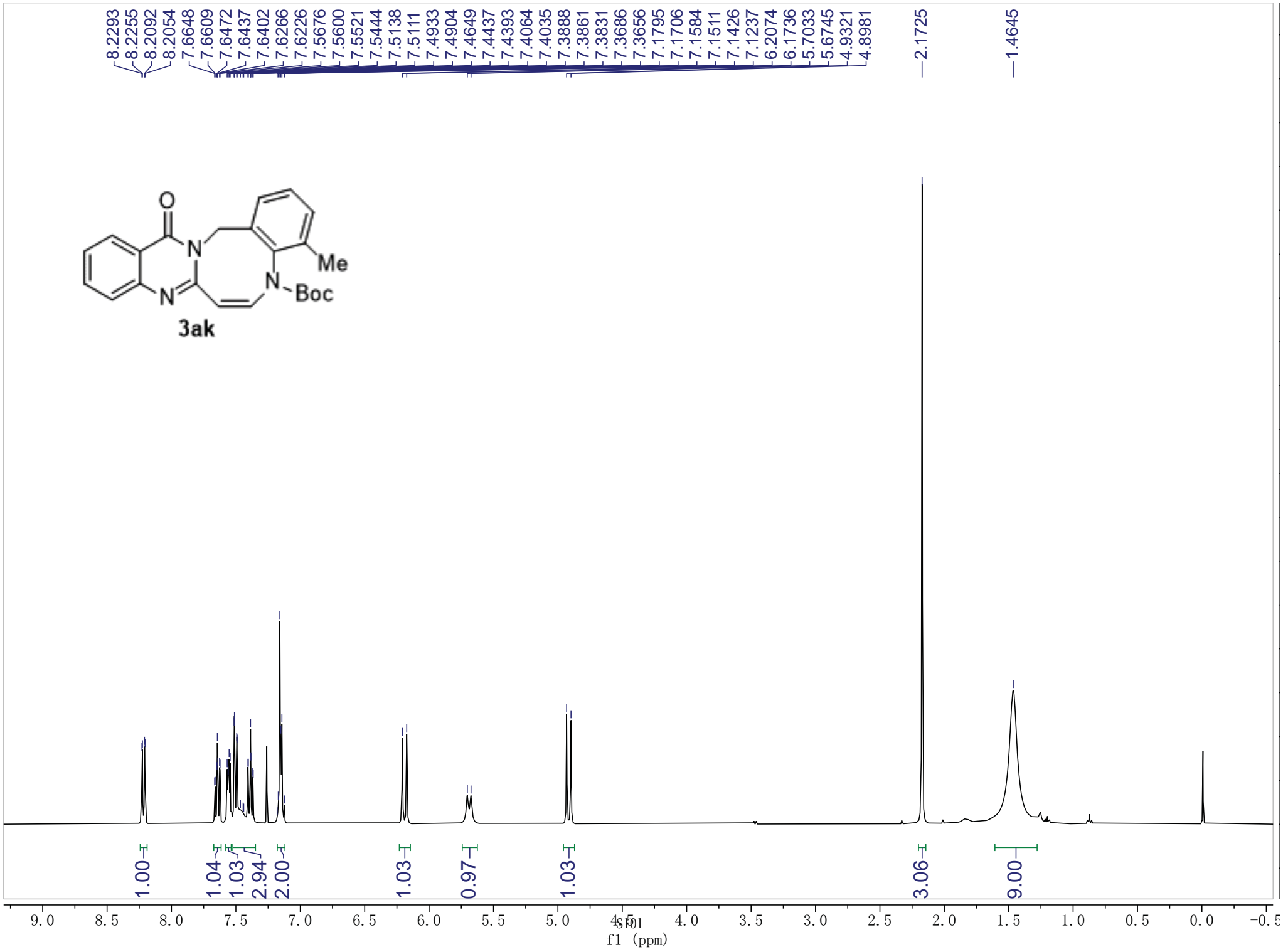
133.439
131.597
131.506
130.958
130.923
127.266
127.044
126.924
120.016
116.847
116.636
115.952
115.720
105.455
84.477
77.477
77.160
76.842
41.961
28.112
O
F
N
N
N
Boc
3aj
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.6402
7.6266
7.6226
7.5676
7.5600
7.5521
7.5444
7.5138
7.5111
7.4933
7.4904
7.4649
7.4437
7.4393
7.4064
7.4035
7.3888
7.3861
7.3831
7.3686
7.3656
7.1795
7.1706
7.1584
7.1511
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7.1237
6.2074
6.1736
5.7033
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4.8981
2.1725
1.4645
O
N
N
Me
N
Boc
3ak
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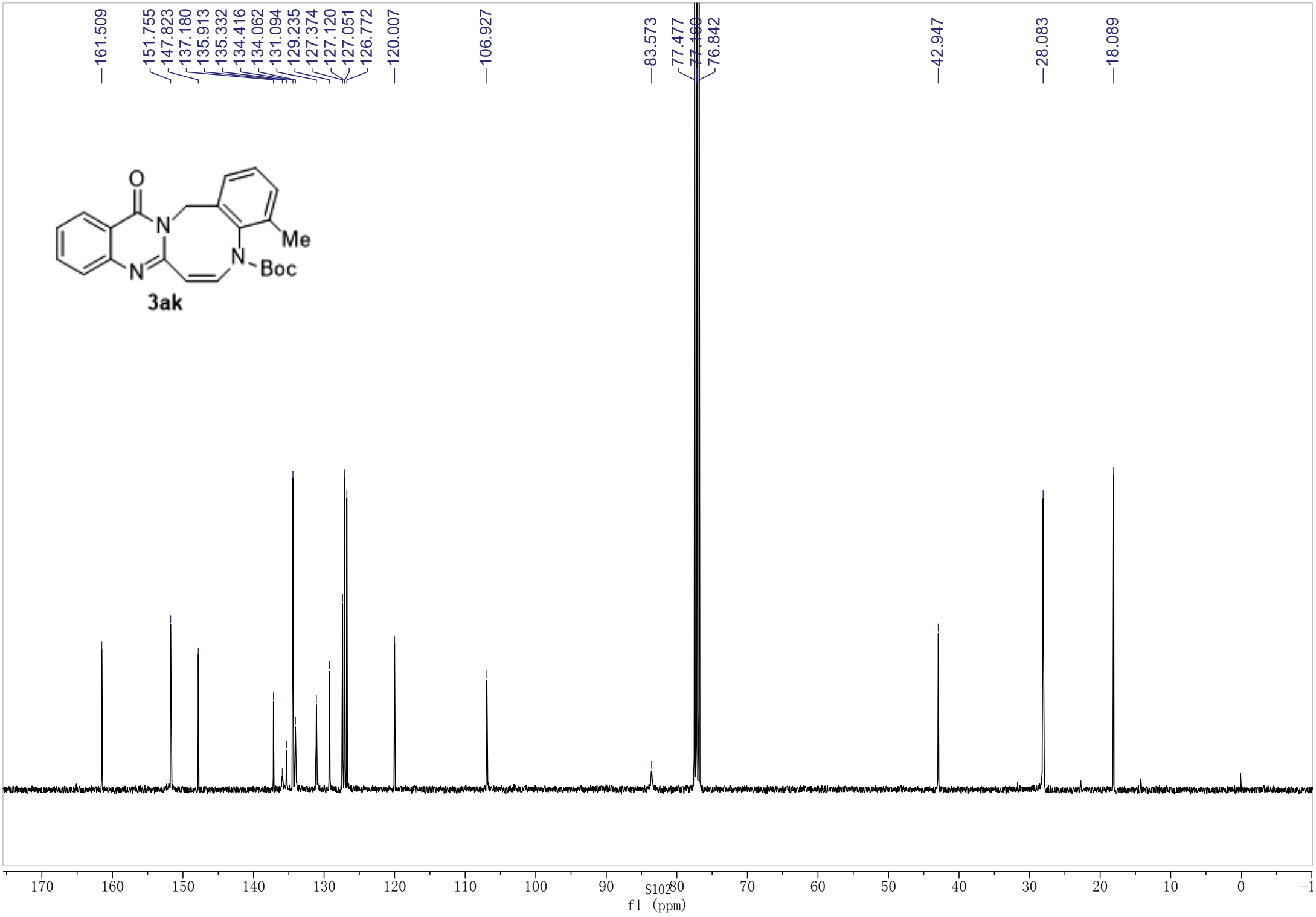
1.04
1.03
2.94
2.00
1.03
0.97
1.03
3.06
9.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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134.062
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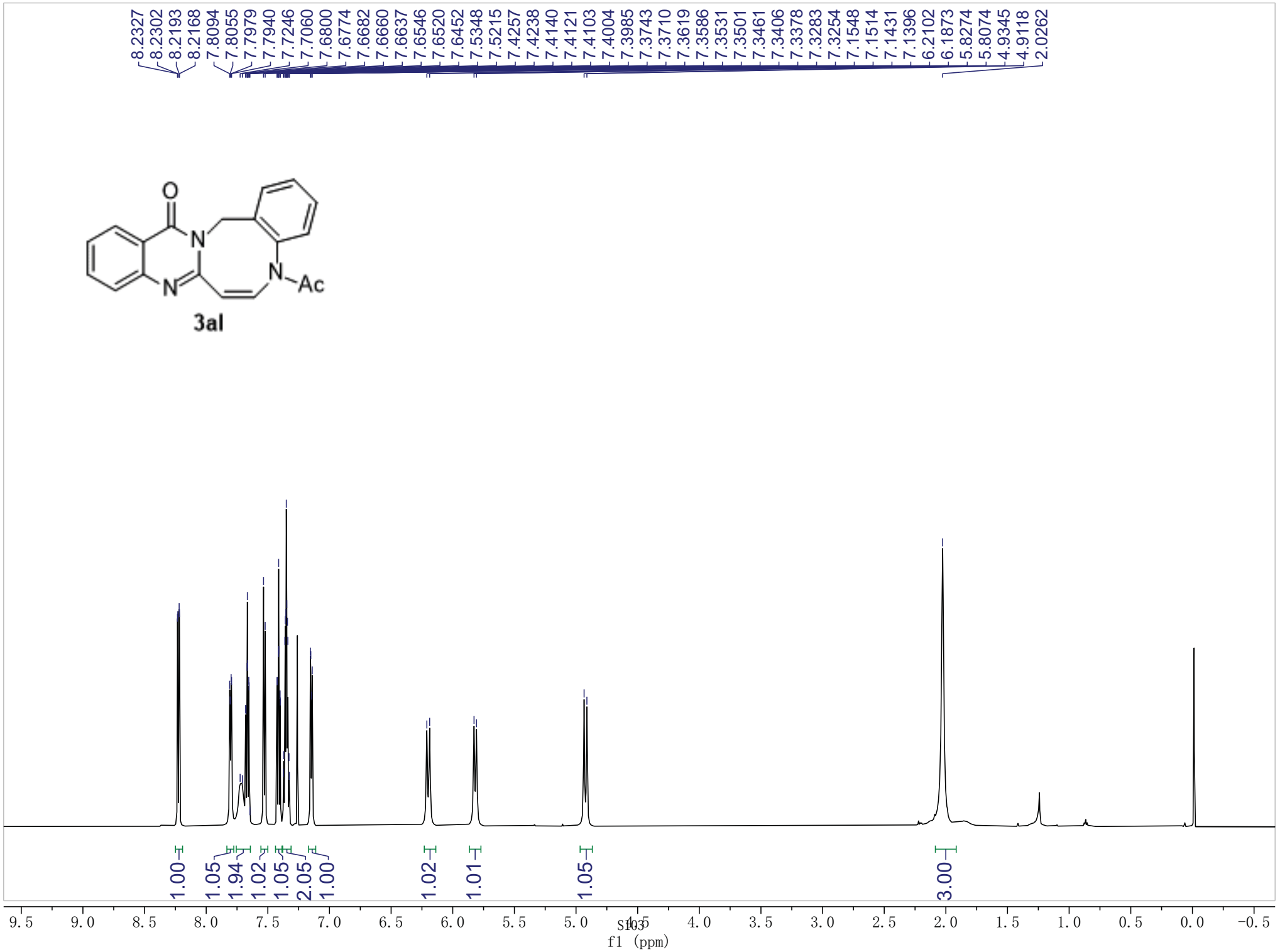
129.235
127.374
127.120
127.051
126.772
120.007
106.927
83.573
77.477
77.160
76.842
42.947
28.083
18.089
O
N
N
N
Me
Boc
3ak
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)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7.6774
7.6682
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7.6637
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7.6520
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7.5348
7.5215
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7.3461
7.3406
7.3378
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7.1431
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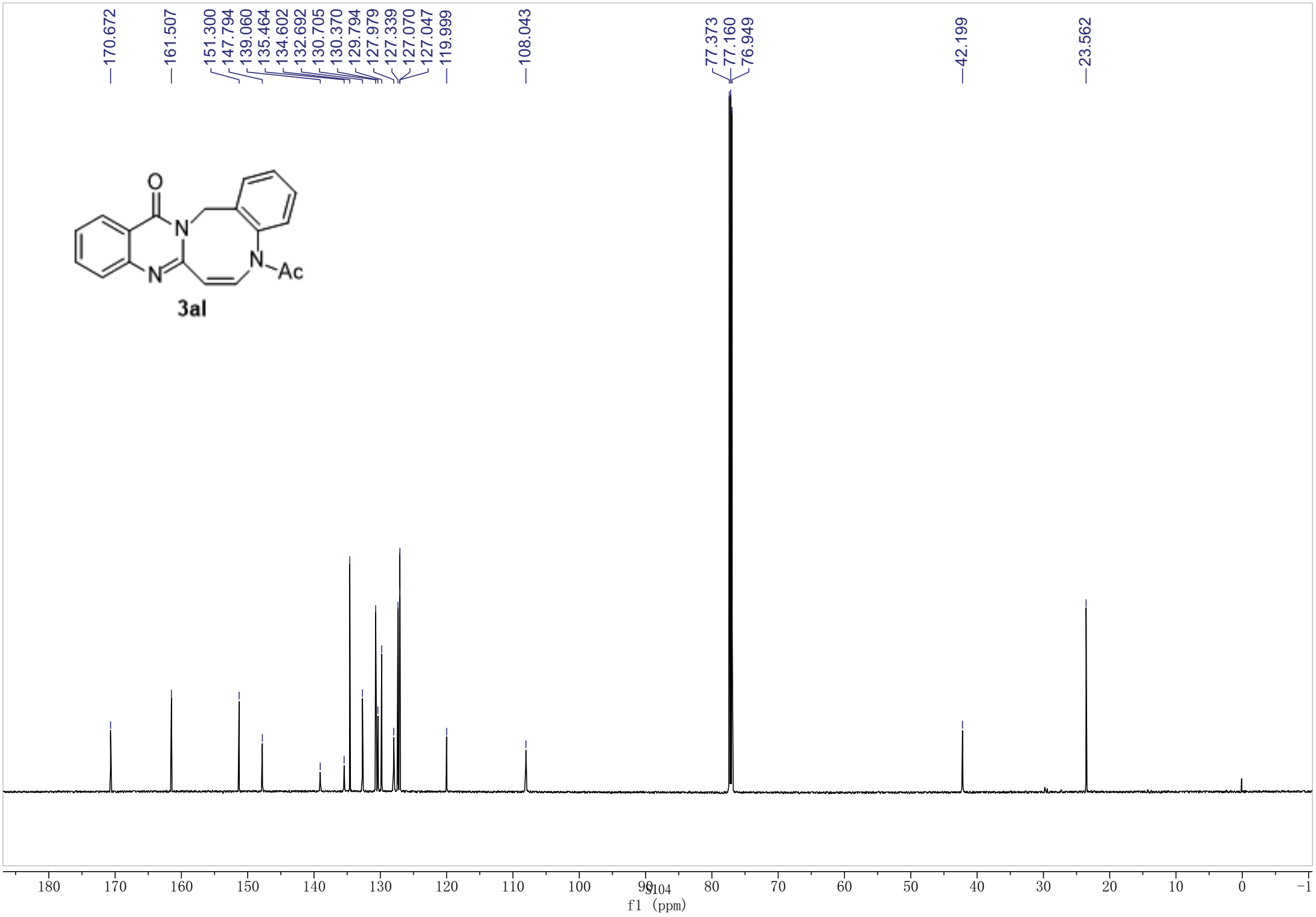
4.9118
2.0262
O
N
N
N
Ac
3al
1.00
1.05
1.94
1.02
1.05
2.05
1.00
1.02
1.01
1.05
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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129.794
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127.070
127.047
119.999
108.043
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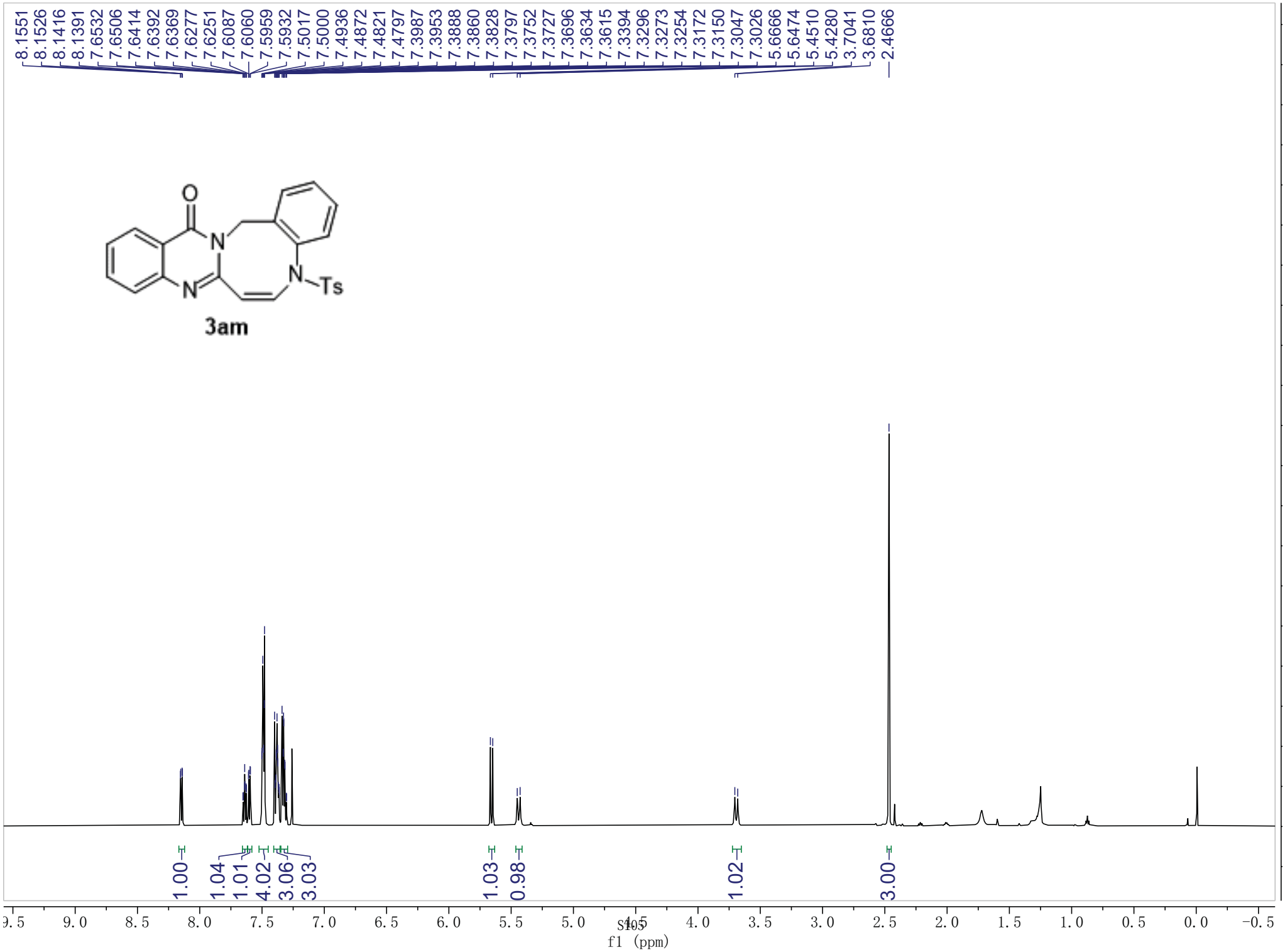
77.160
76.949
42.199
23.562
O
N
N
N
Ac
3al
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−1
f1 (ppm)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7.6251
7.6087
7.6060
7.5959
7.5932
7.5017
7.5000
7.4936
7.4872
7.4821
7.4797
7.3987
7.3953
7.3888
7.3860
7.3828
7.3797
7.3752
7.3727
7.3696
7.3634
7.3615
7.3394
7.3296
7.3273
7.3254
7.3172
7.3150
7.3047
7.3026
5.6666
5.6474
5.4510
5.4280
3.7041
3.6810
2.4666
O
N
N
N
Ts
3am
1.00
1.04
1.01
4.02
3.06
3.03
1.03
0.98
1.02
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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3.0
2.5
2.0
1.5
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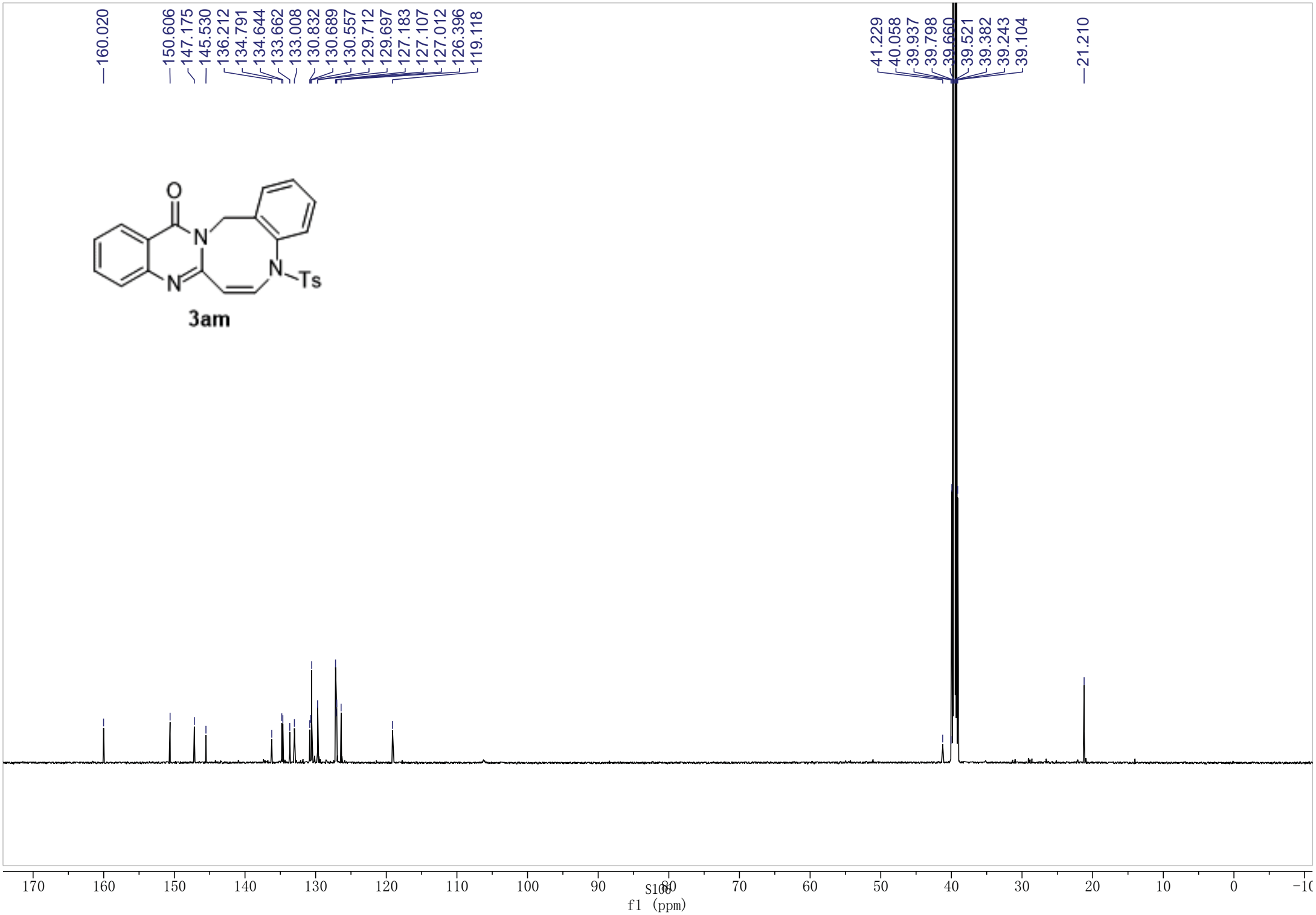
0.5
0.0
-0.5
f1 (ppm)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127.183
127.107
127.012
126.396
119.118
41.229
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39.937
39.798
39.660
39.521
39.382
39.243
39.104
21.210
O
N
N
N
Ts
3am
170
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120
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100
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80
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30
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10
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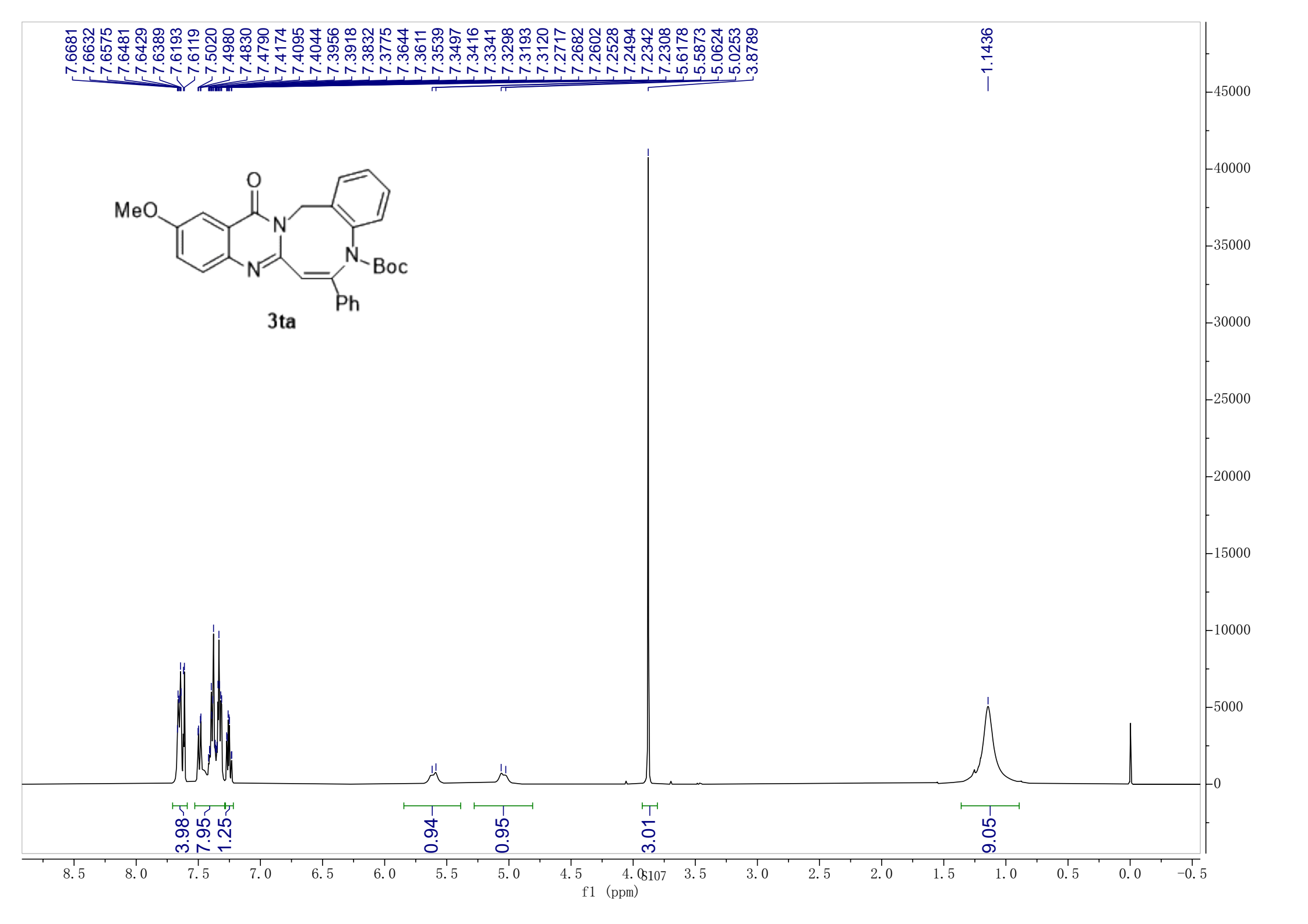
-10
f1 (ppm)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7.5020
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7.4830
7.4790
7.4174
7.4095
7.4044
7.3956
7.3918
7.3832
7.3775
7.3644
7.3611
7.3539
7.3497
7.3416
7.3341
7.3298
7.3193
7.3120
7.2717
7.2682
7.2602
7.2528
7.2494
7.2342
7.2308
5.6178
5.5873
5.0624
5.0253
3.8789
1.1436
MeO
O
N
N
N
Boc
Ph
3ta
3.98
7.95
1.25
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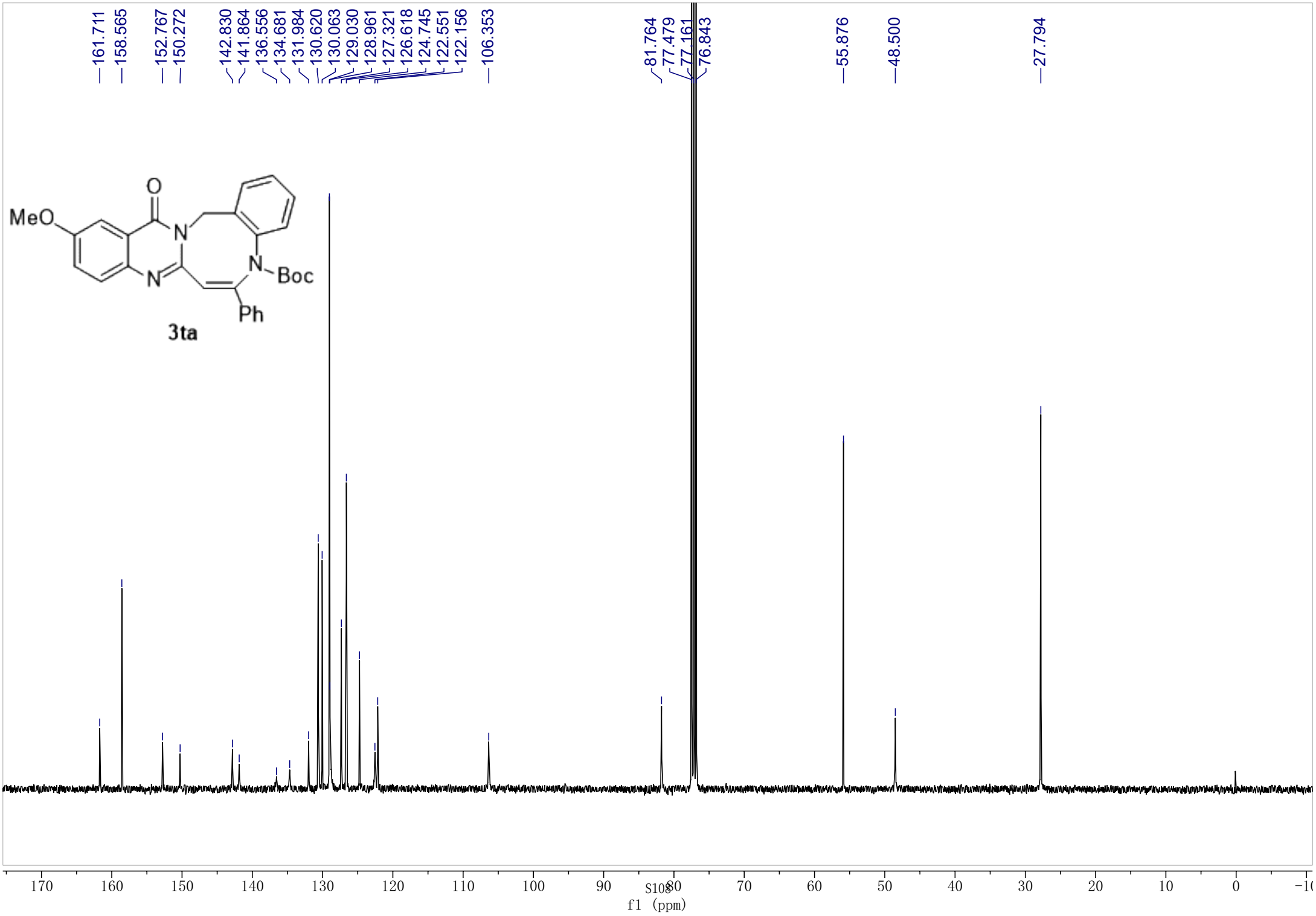
0.95
3.01
9.05
f1 (ppm)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126.618
124.745
122.551
122.156
106.353
81.764
77.479
77.161
76.843
55.876
48.500
27.794
MeO
O
N
N
N
Boc
Ph
3ta
170
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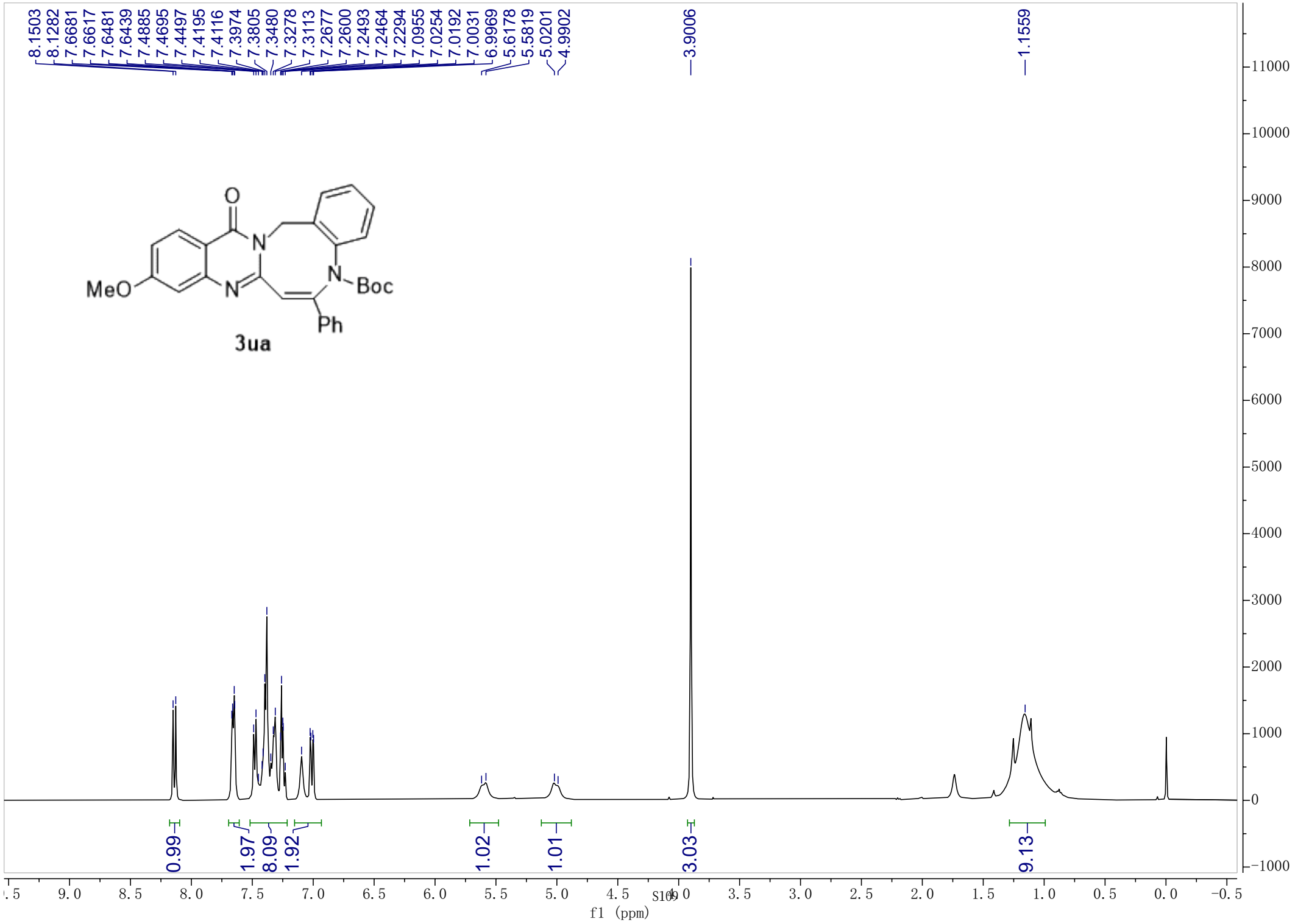
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.4116
7.3974
7.3805
7.3480
7.3278
7.3113
7.2677
7.2600
7.2493
7.2464
7.2294
7.0955
7.0254
7.0192
7.0031
6.9969
5.6178
5.5819
5.0201
4.9902
3.9006
1.1559
MeO
N
O
N
Boc
Ph
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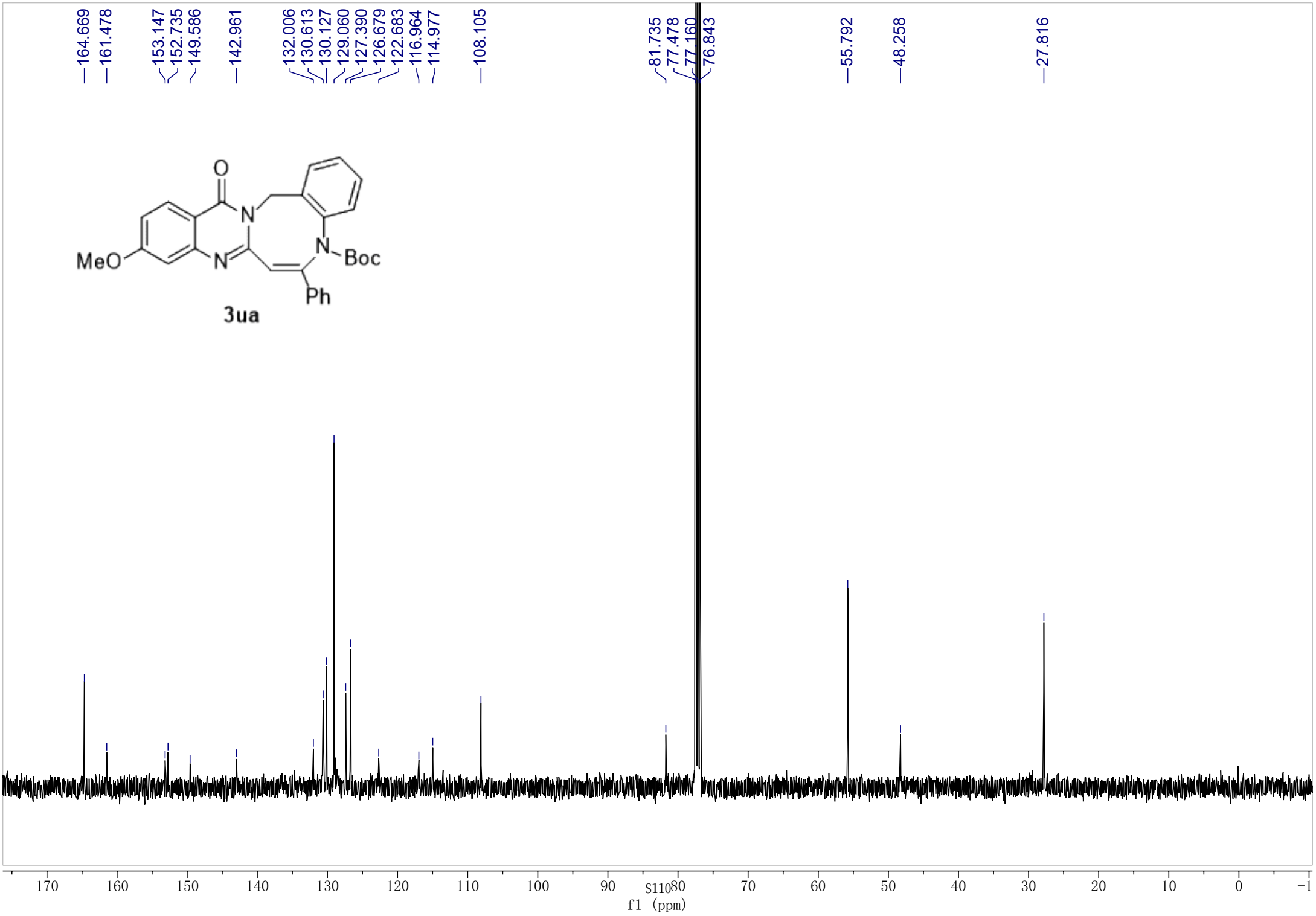
1.97
8.09
1.92
1.02
1.01
3.03
9.13
f1 (ppm)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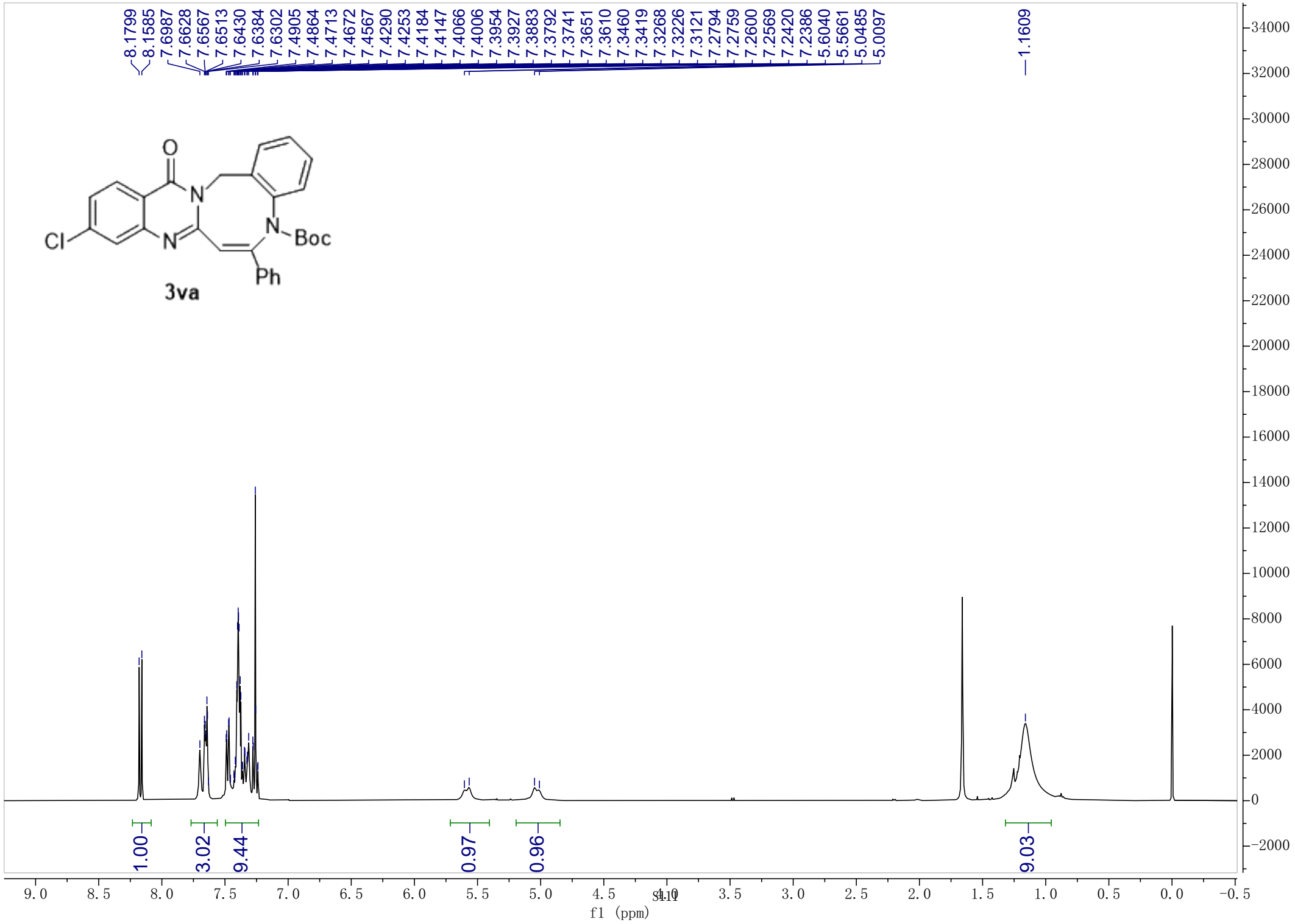
142.961
132.006
130.613
130.127
129.060
127.390
126.679
122.683
116.964
114.977
108.105
81.735
77.478
77.160
76.843
55.792
48.258
27.816
O
N
N
Boc
MeO
N
Ph
3ua
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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7.6430
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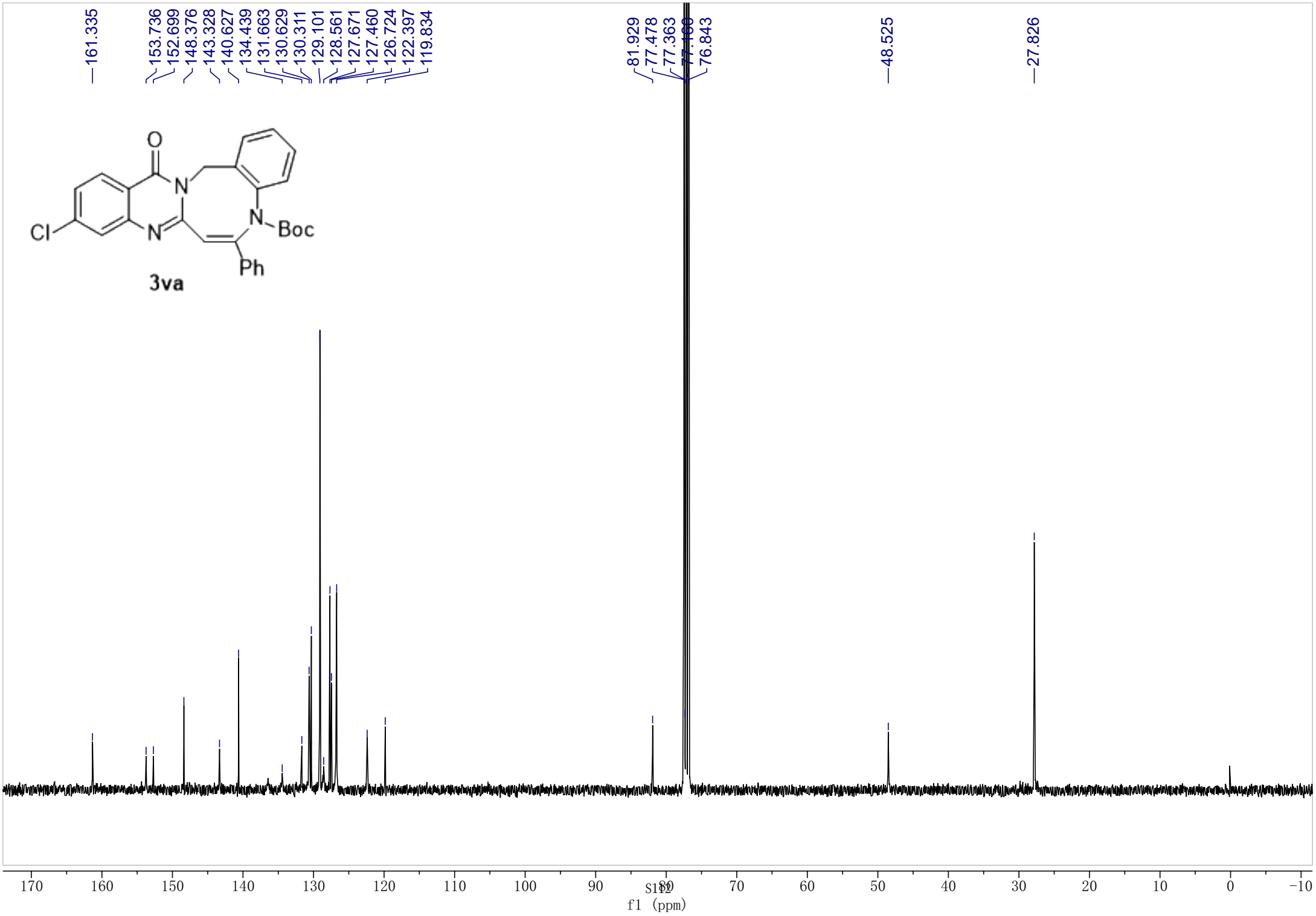
7.6302
7.4905
7.4864
7.4713
7.4672
7.4567
7.4290
7.4253
7.4184
7.4147
7.4066
7.4006
7.3954
7.3927
7.3883
7.3792
7.3741
7.3651
7.3610
7.3460
7.3419
7.3268
7.3226
7.3121
7.2794
7.2759
7.2600
7.2569
7.2420
7.2386
5.6040
5.5661
5.0485
5.0097
1.1609
O
N
N
N
Boc
Cl
Ph
3va
1.00
3.02
9.44
0.97
0.96
9.03
f1 (ppm)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131.663
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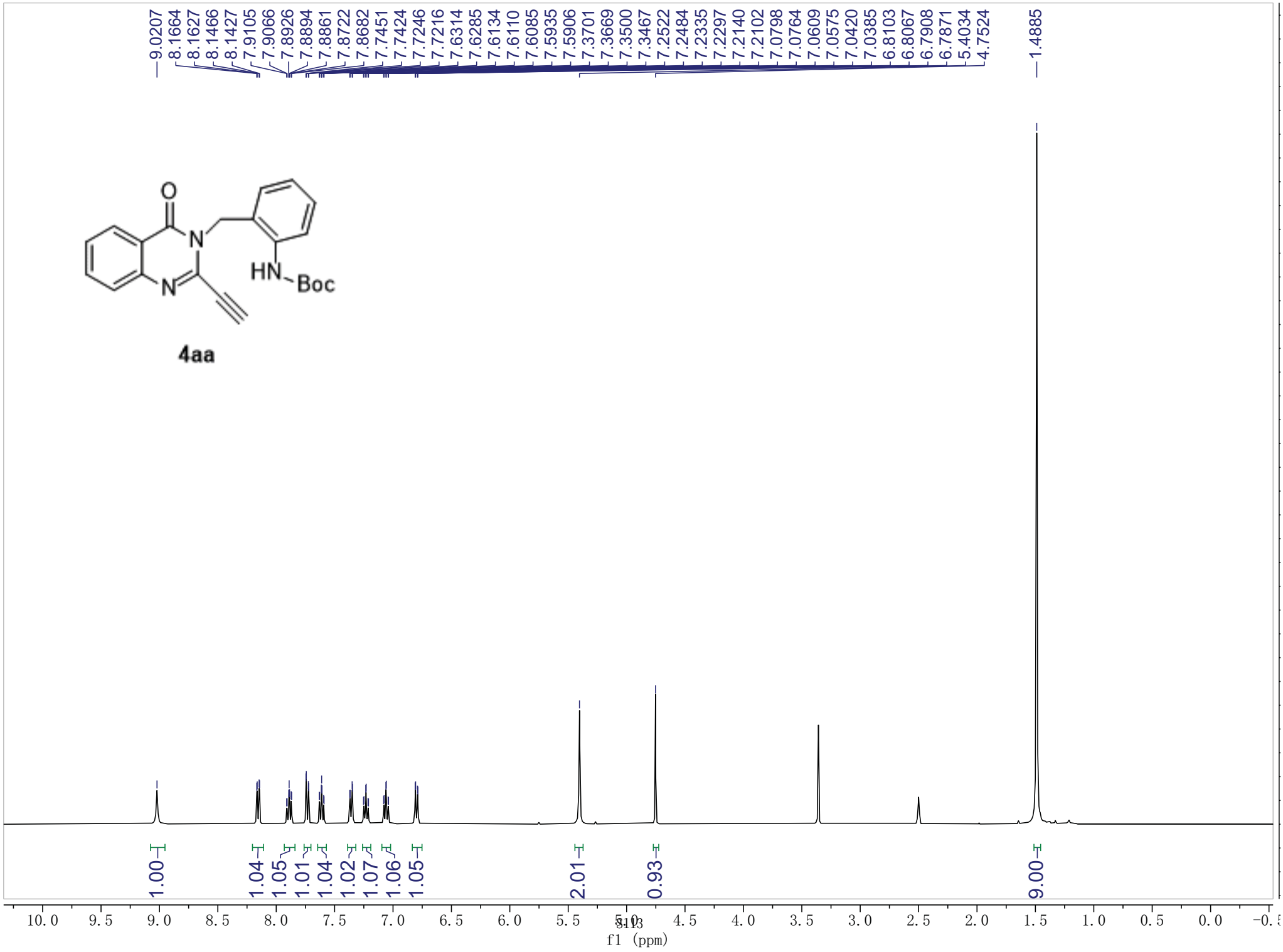
129.101
128.561
127.671
127.460
126.724
122.397
119.834
81.929
77.478
77.363
77.160
76.843
48.525
27.826
O
N
N
N
Boc
Cl
Ph
3va
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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8.1427
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7.9066
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7.8894
7.8861
7.8722
7.8682
7.7451
7.7424
7.7246
7.7216
7.6314
7.6285
7.6134
7.6110
7.6085
7.5935
7.5906
7.3701
7.3669
7.3500
7.3467
7.2522
7.2484
7.2335
7.2297
7.2140
7.2102
7.0798
7.0764
7.0609
7.0575
7.0420
7.0385
6.8103
6.8067
6.7908
6.7871
5.4034
4.7524
1.4885
O
N
N
HN
Boc
4aa
1.00
1.04
1.05
1.01
1.04
1.02
1.07
1.06
1.05
2.01
0.93
9.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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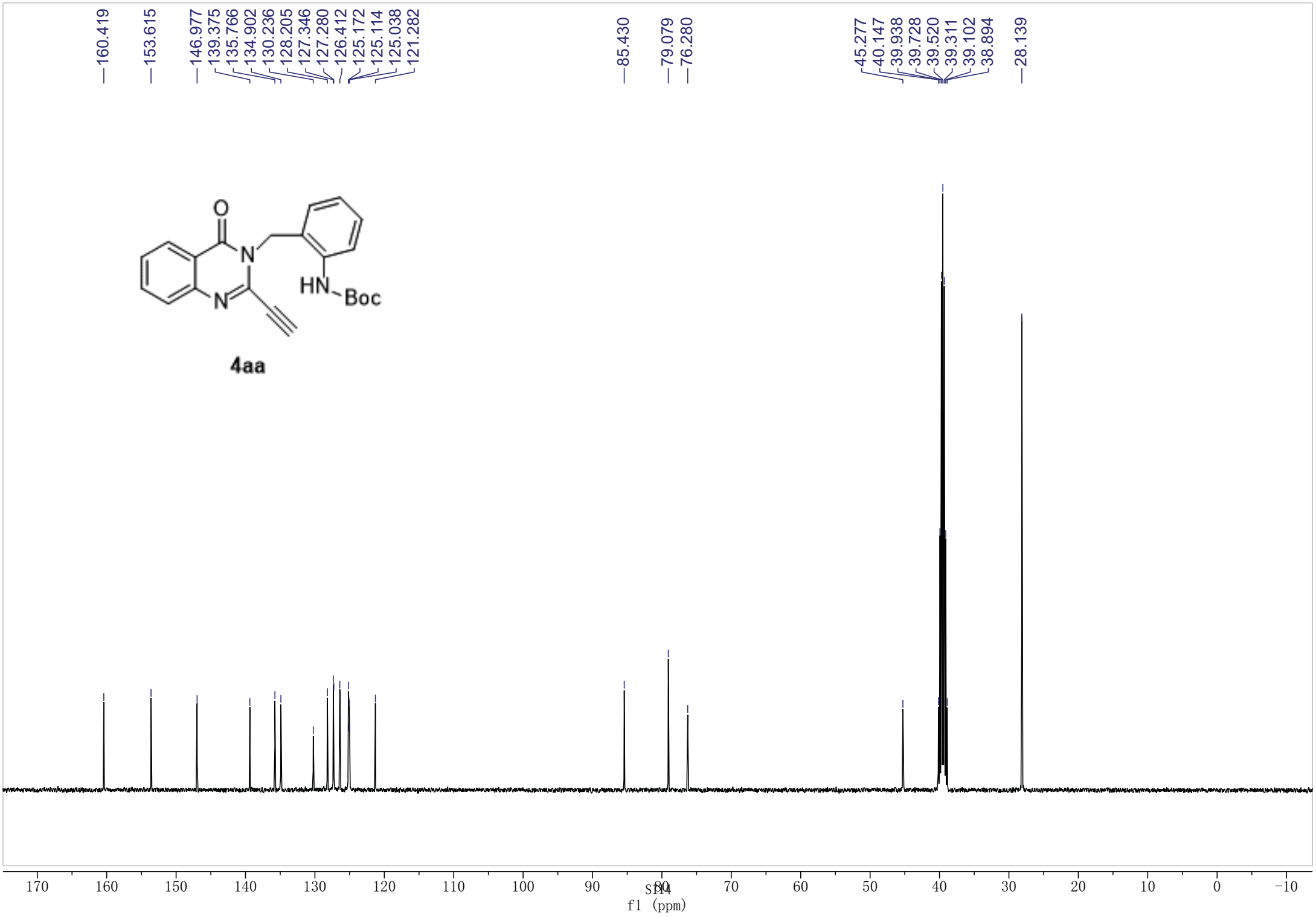
0.0
f1 (ppm)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125.114
125.038
121.282
85.430
79.079
76.280
45.277
40.147
39.938
39.728
39.520
39.311
39.102
38.894
28.139
O
N
N
HN
Boc
4aa
170
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140
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100
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80
70
60
50
40
30
20
10
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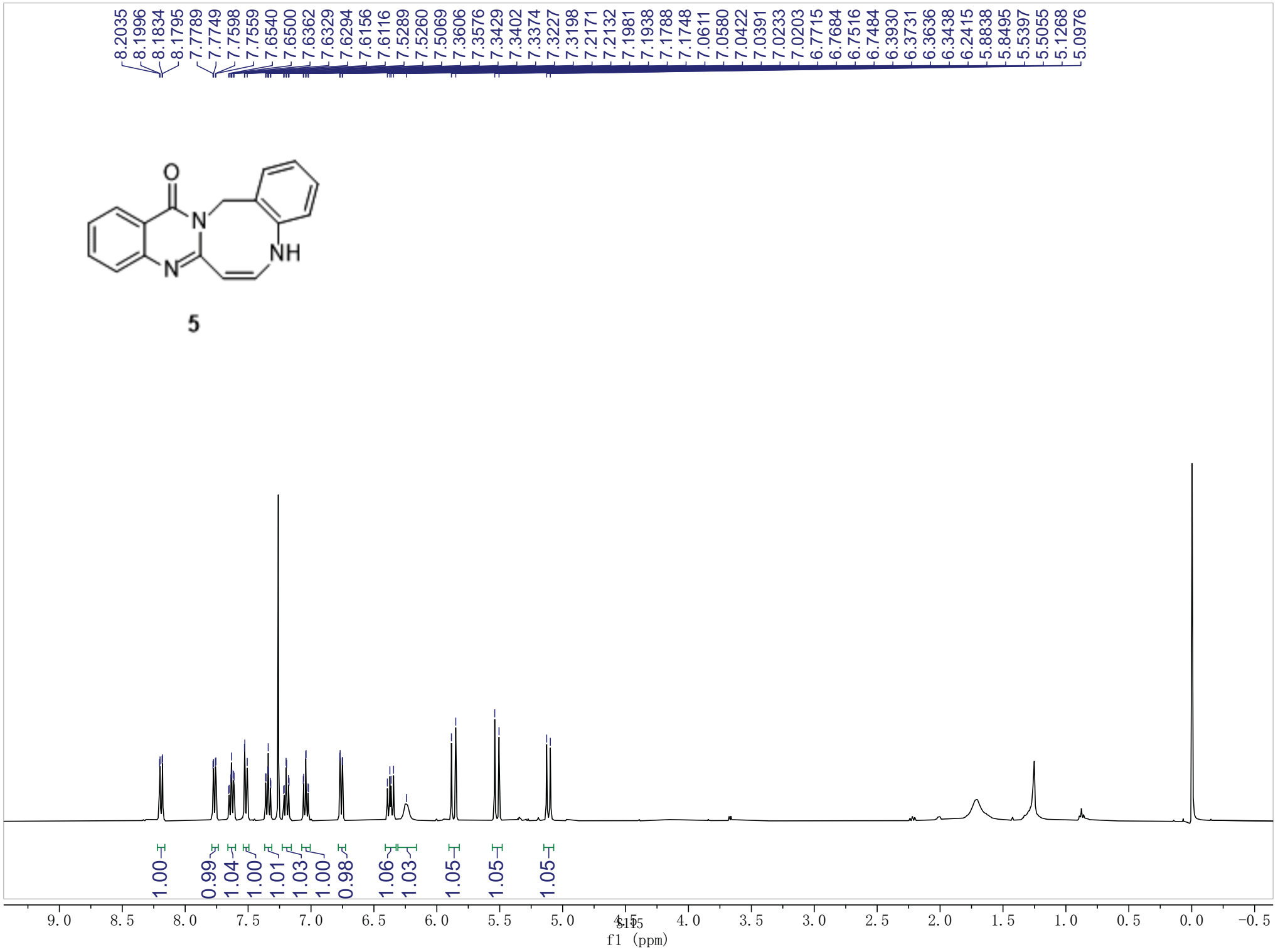
-10
f1 (ppm)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7.6362
7.6329
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7.6156
7.6116
7.5289
7.5260
7.5069
7.3606
7.3576
7.3429
7.3402
7.3374
7.3227
7.3198
7.2171
7.2132
7.1981
7.1938
7.1788
7.1748
7.0611
7.0580
7.0422
7.0391
7.0233
7.0203
6.7715
6.7684
6.7516
6.7484
6.3930
6.3731
6.3636
6.3438
6.2415
5.8838
5.8495
5.5397
5.5055
5.1268
5.0976
O
N
NH
N
5
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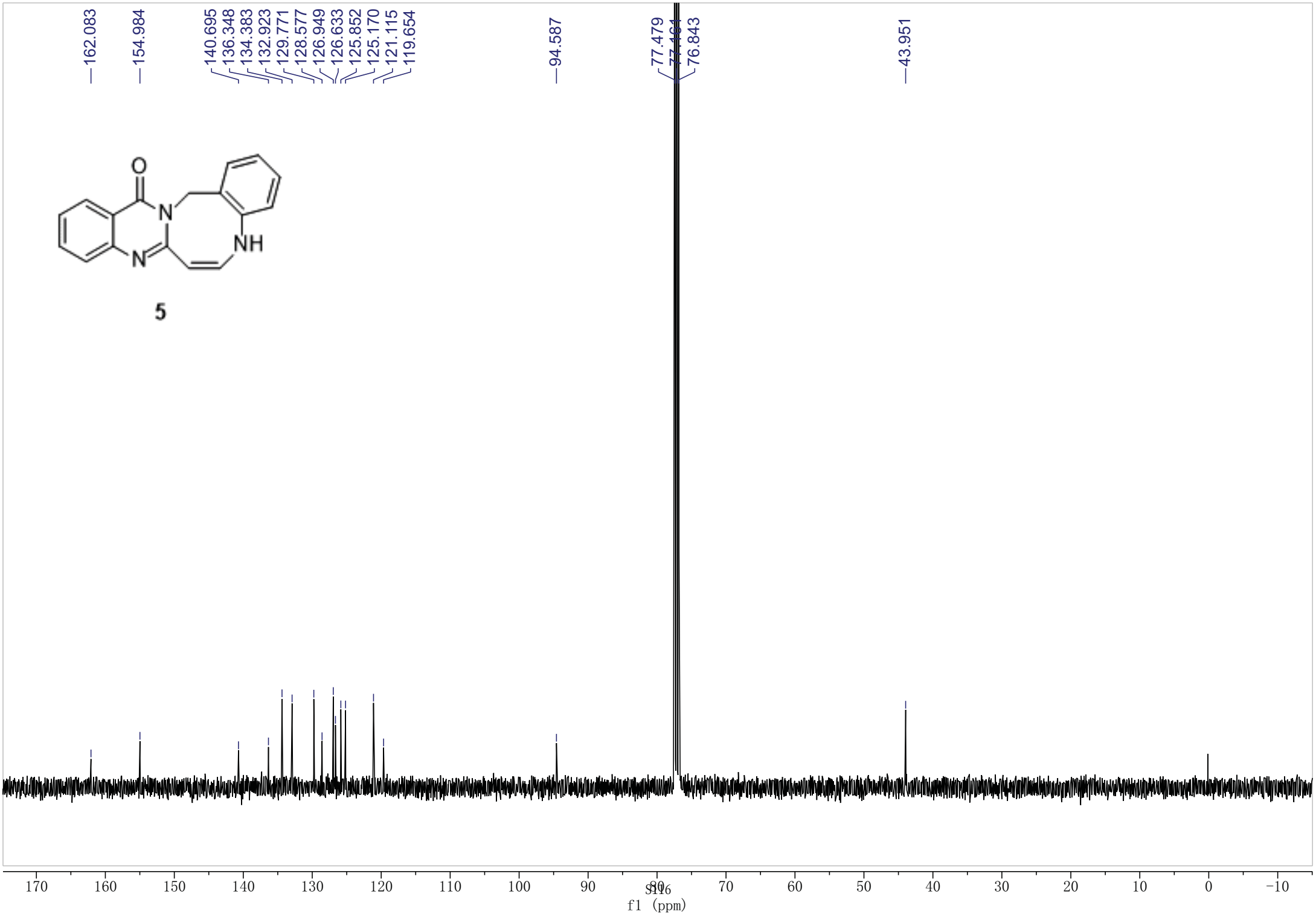
0.99
1.04
1.00
1.01
1.03
1.00
0.98
1.06
1.03
1.05
1.05
1.05
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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121.115
119.654
94.587
77.479
77.161
76.843
43.951
O
N
N
NH
5
170
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140
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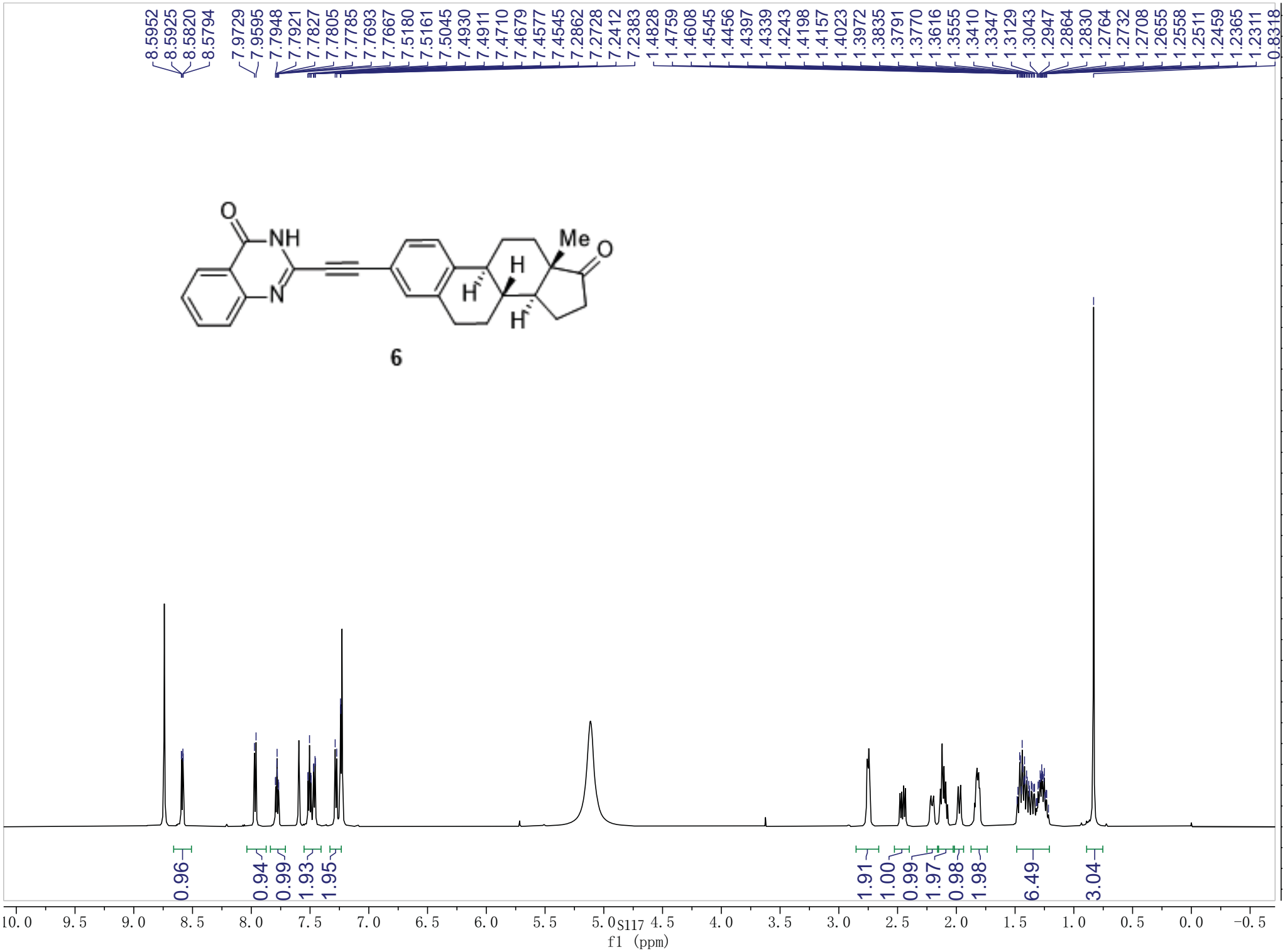
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.7948
7.7921
7.7827
7.7805
7.7785
7.7693
7.7667
7.5180
7.5161
7.5045
7.4930
7.4911
7.4710
7.4679
7.4577
7.4545
7.2862
7.2728
7.2412
7.2383
1.4828
1.4759
1.4608
1.4545
1.4456
1.4397
1.4339
1.4243
1.4198
1.4157
1.4023
1.3972
1.3835
1.3791
1.3770
1.3616
1.3555
1.3410
1.3347
1.3129
1.3043
1.2947
1.2864
1.2830
1.2764
1.2732
1.2708
1.2655
1.2558
1.2511
1.2459
1.2365
1.2311
0.8318
O
NH
N
Me
O
H
H
H
6
0.96
0.94
0.99
1.93
1.95
1.91
1.00
0.99
1.97
0.98
1.98
6.49
3.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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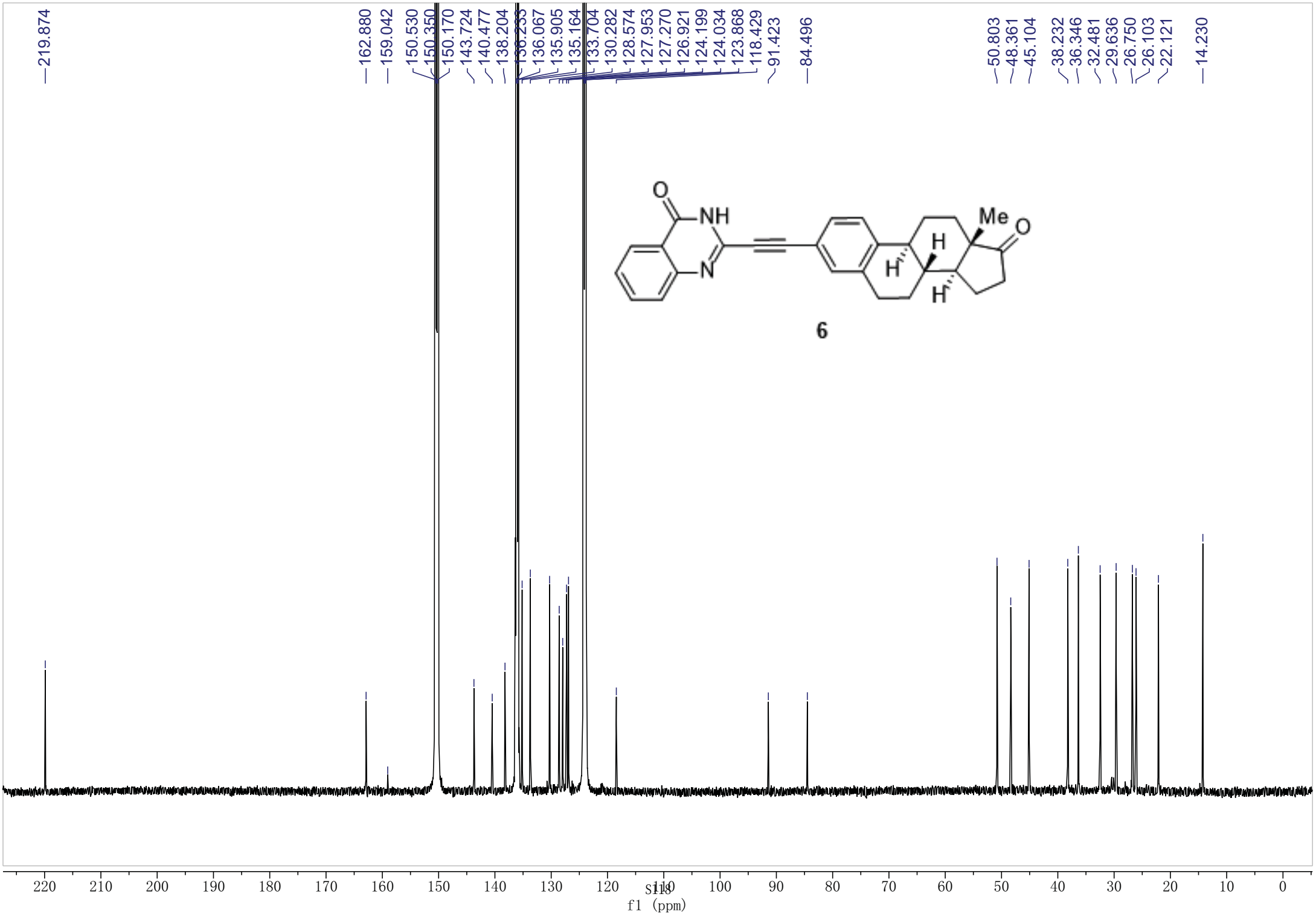
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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133.704
130.282
128.574
127.953
127.270
126.921
124.199
124.034
123.868
118.429
91.423
84.496
50.803
48.361
45.104
38.232
36.346
32.481
29.636
26.750
26.103
22.121
14.230
O
NH
N
Me
O
H
H
H
6
220
210
200
190
180
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150
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130
120
110
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90
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70
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50
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30
20
10
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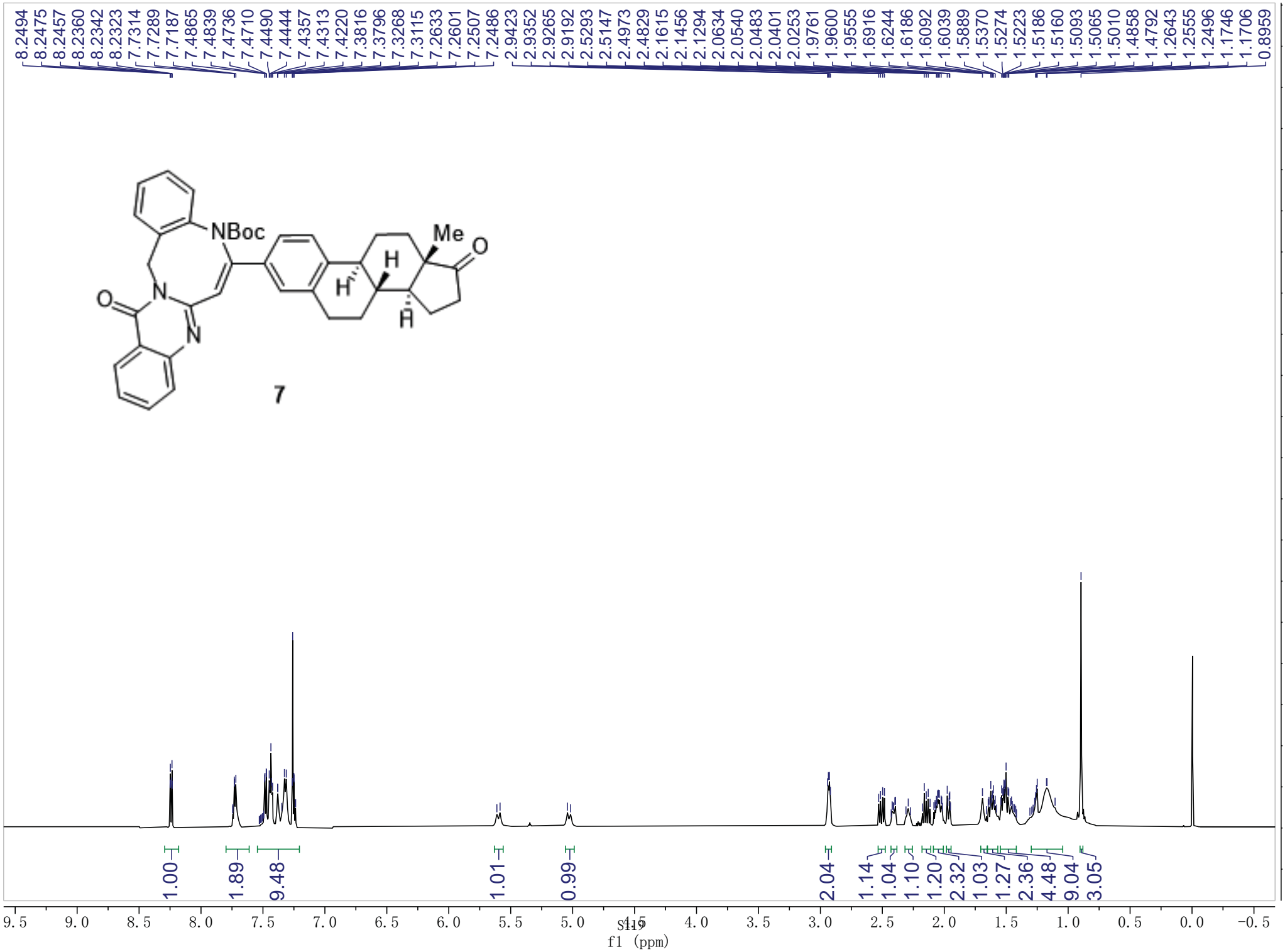
f1 (ppm)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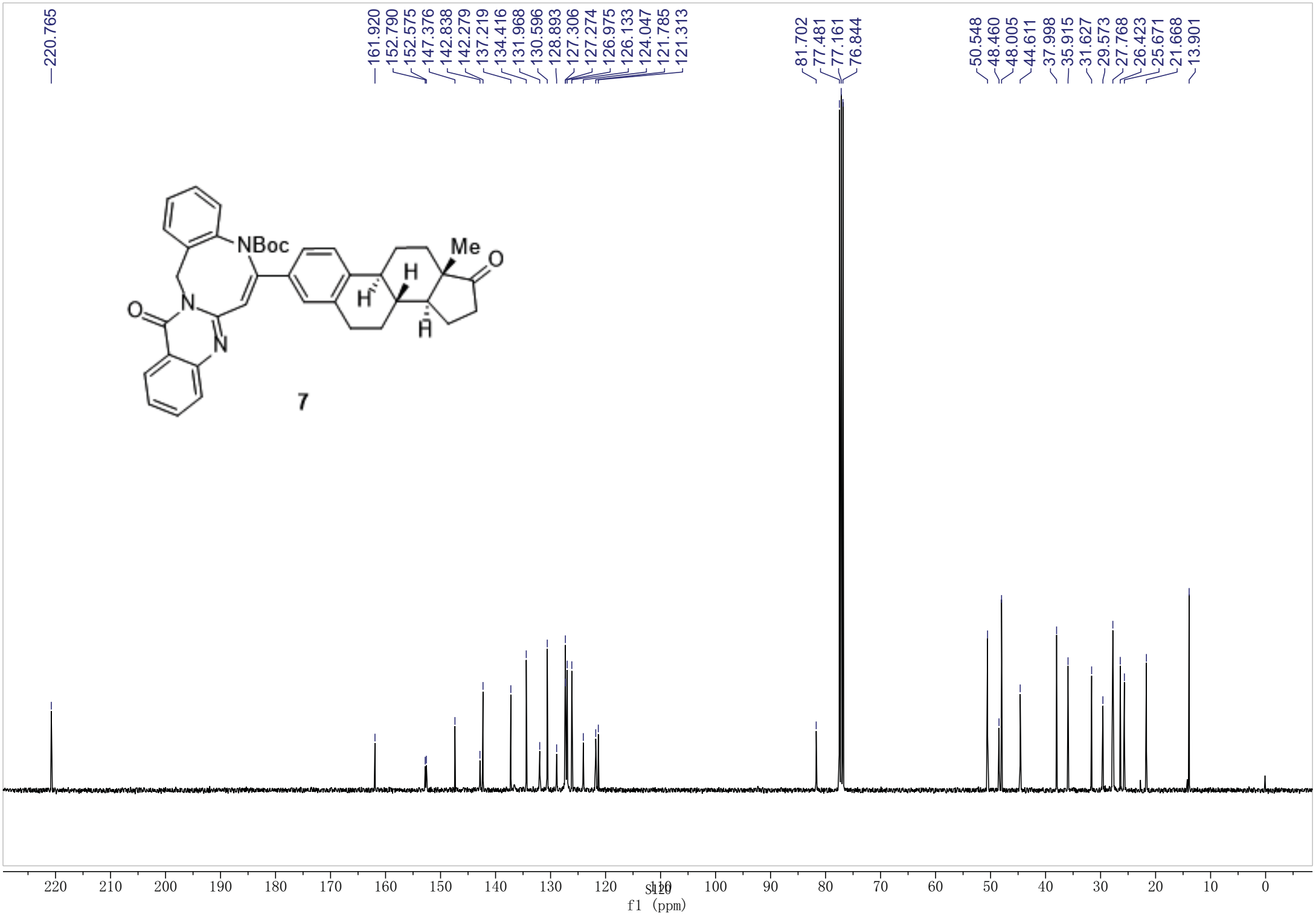
NBoc
Me
O
H
H
H
O
N
N
7
1.00 1.89 9.48 1.01 0.99 2.04 1.14 1.04 1.10 1.20 2.32 1.03 1.27 2.36 4.48 9.04 3.05
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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142.838
142.279
137.219
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128.893
127.306
127.274
126.975
126.133
124.047
121.785
121.313
81.702
77.481
77.161
76.844
50.548
48.460
48.005
44.611
37.998
35.915
31.627
29.573
27.768
26.423
25.671
21.668
13.901
NBoc
Me
O
O
N
N
H
H
H
7
220
210
200
190
180
170
160
150
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130
120
110
100
90
80
70
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50
40
30
20
10
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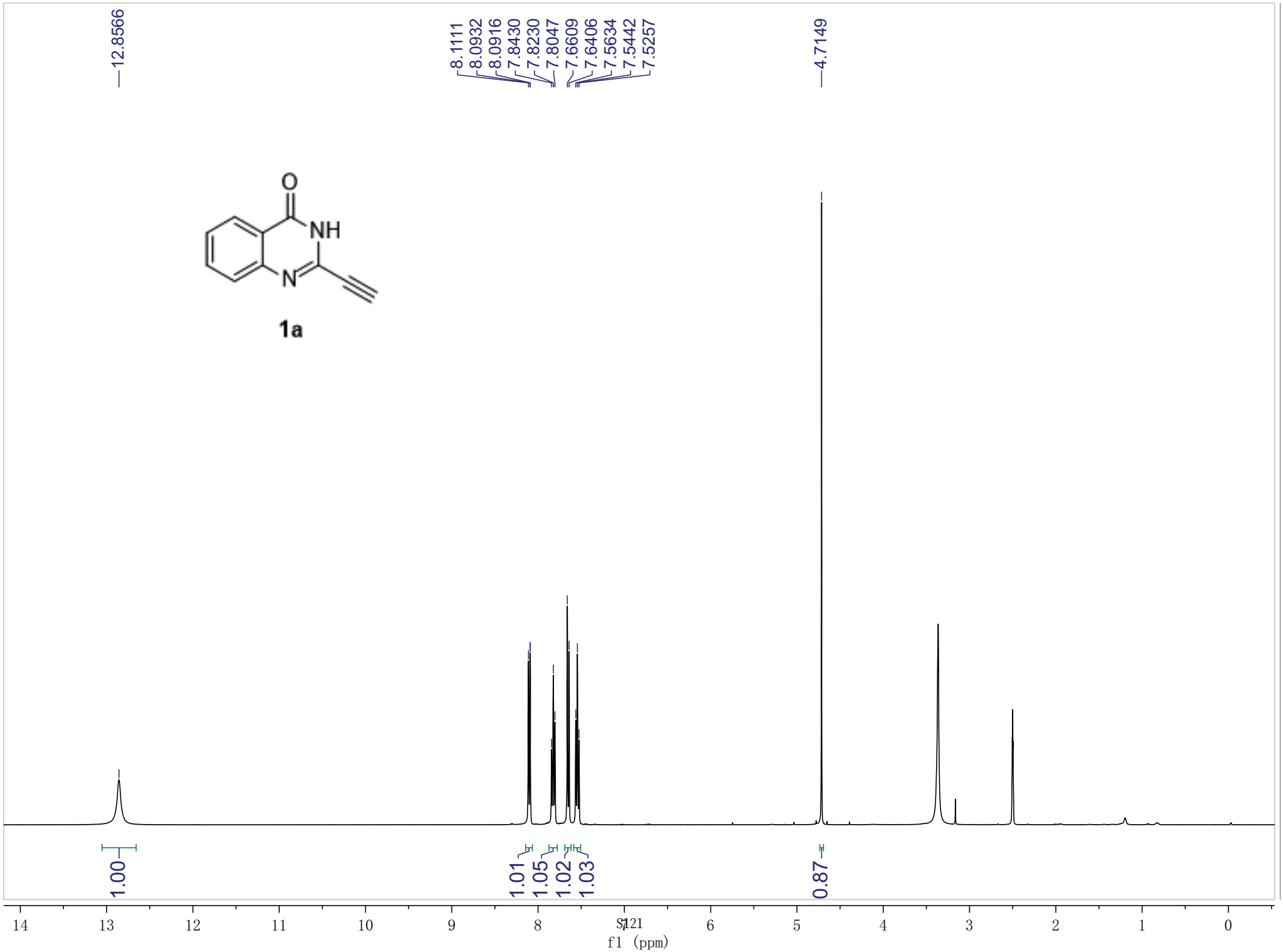
f1 (ppm)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7.8047
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7.6406
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7.5442
7.5257
4.7149
O
NH
N
1a
1.00
1.01
1.05
1.02
1.03
0.87
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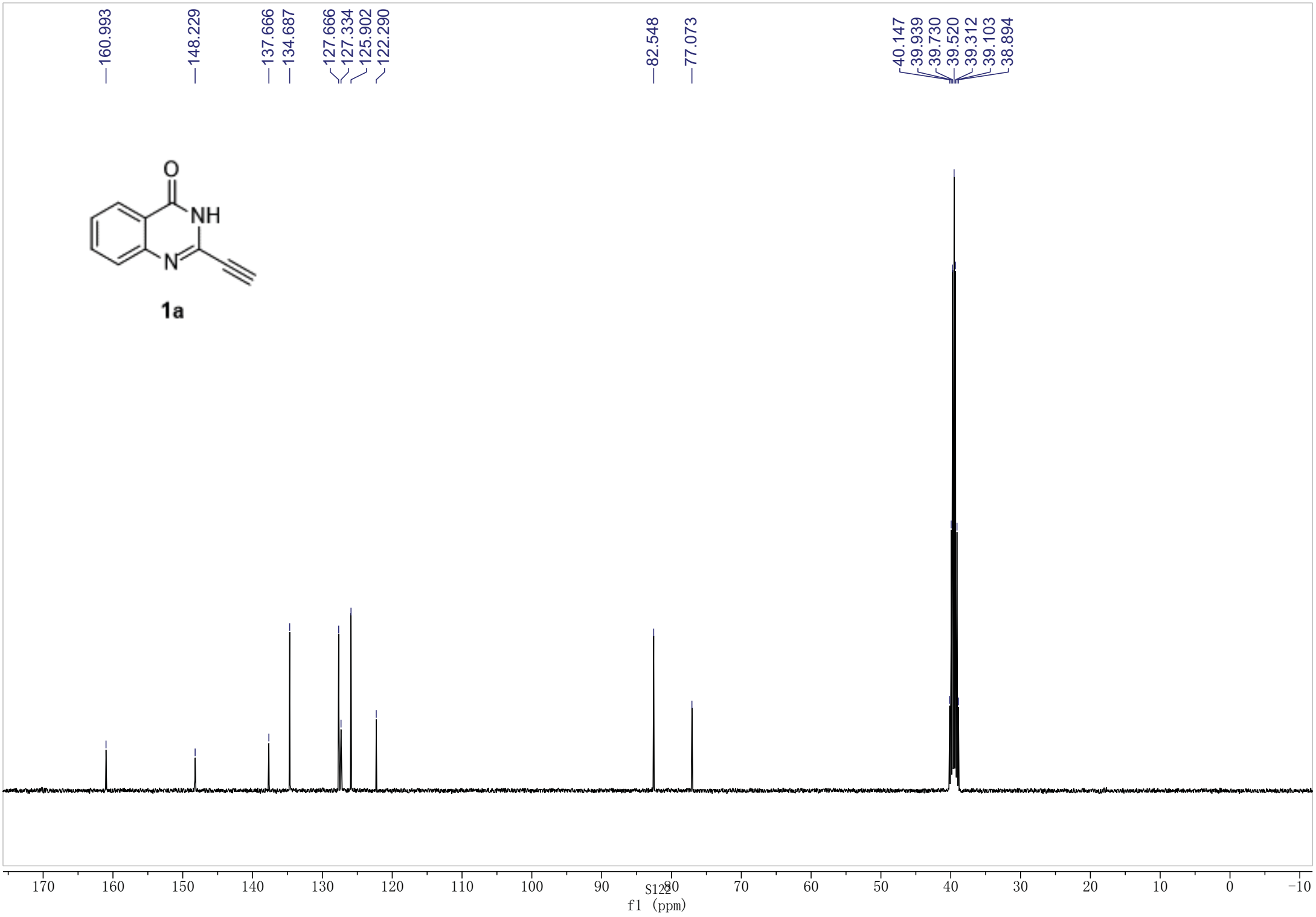
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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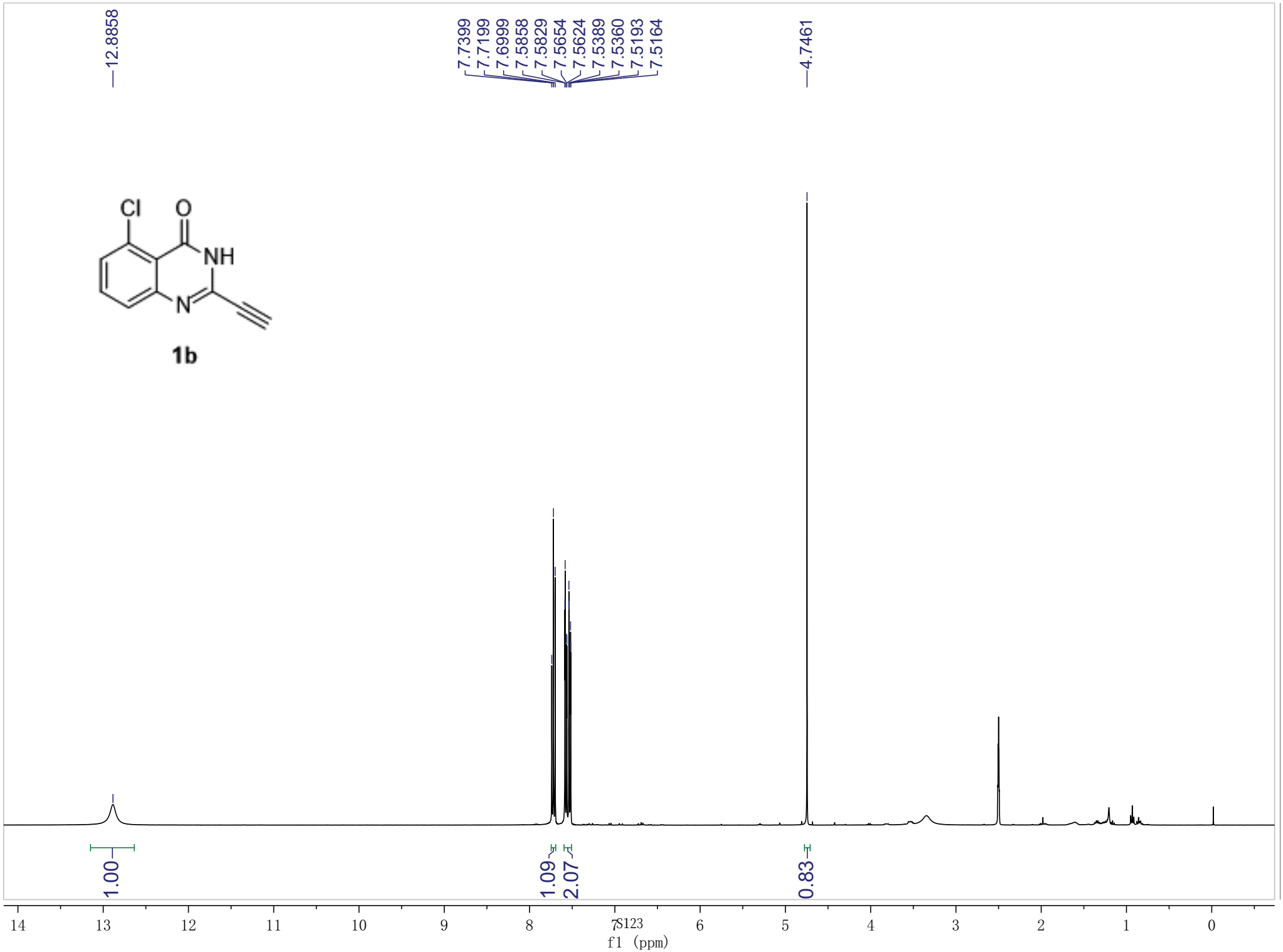
122.290
82.548
77.073
40.147
39.939
39.730
39.520
39.312
39.103
38.894
O
NH
N
1a
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.5193
7.5164
4.7461
Cl
O
NH
N
1b
1.00
1.09
2.07
0.83
14
13
12
11
10
9
8
7
6
5
4
3
2
1
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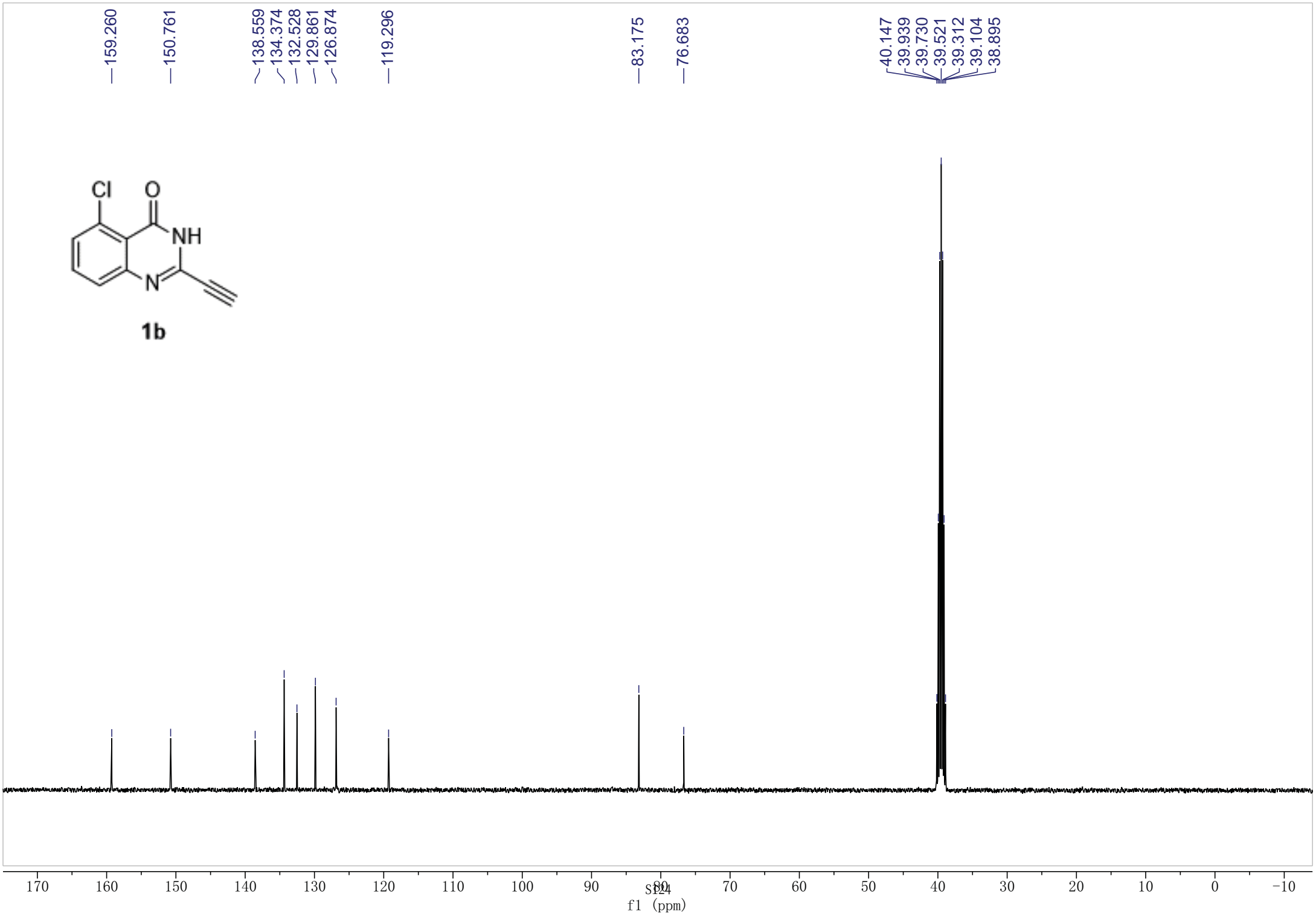
f1 (ppm)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119.296
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76.683
40.147
39.939
39.730
39.521
39.312
39.104
38.895
Cl
O
NH
N
1b
170
160
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140
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120
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100
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70
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30
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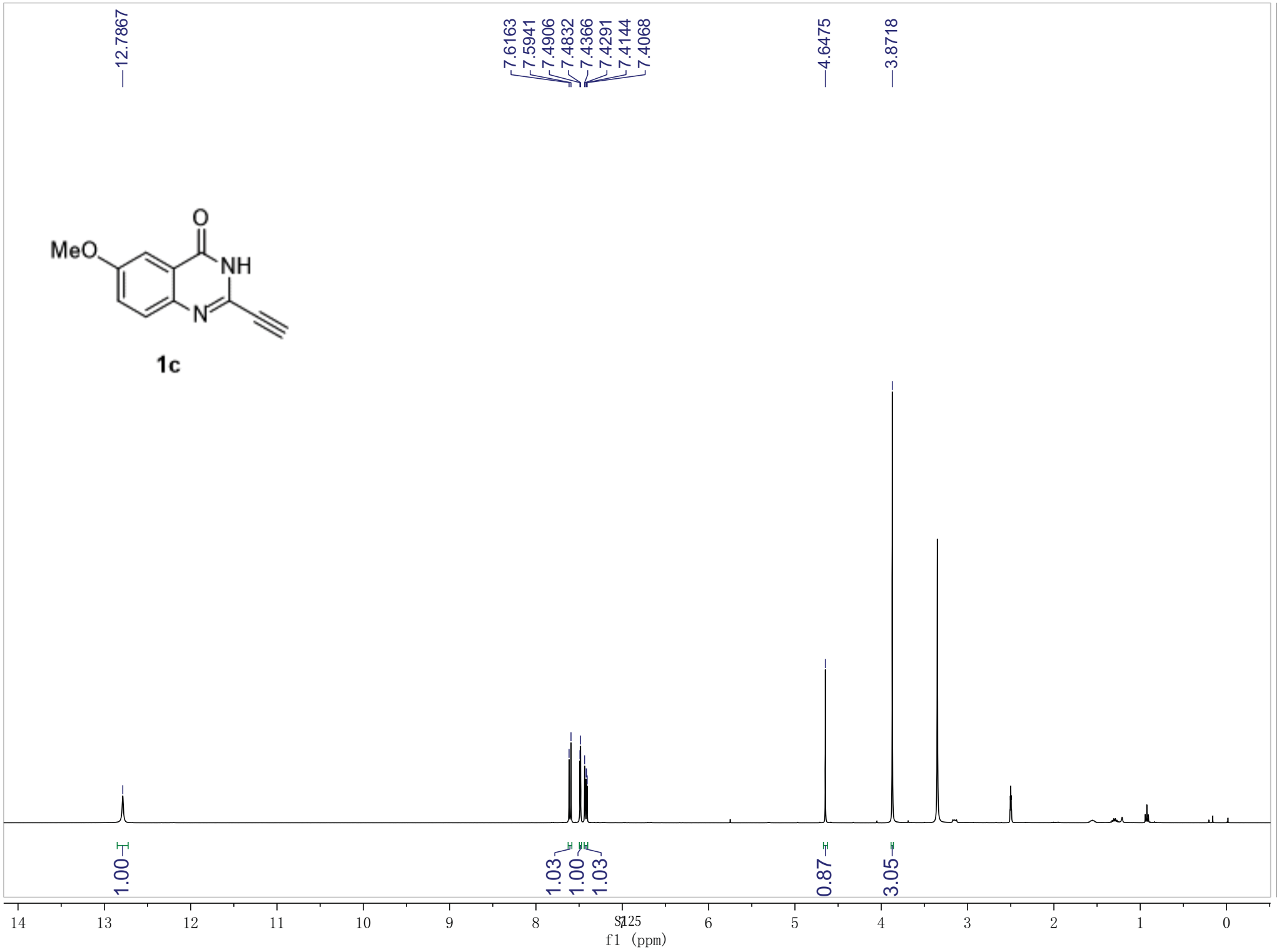
f1 (ppm)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7.5941
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7.4832
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7.4291
7.4144
7.4068
4.6475
3.8718
MeO
O
NH
N
1c
1.00
1.03
1.00
1.03
0.87
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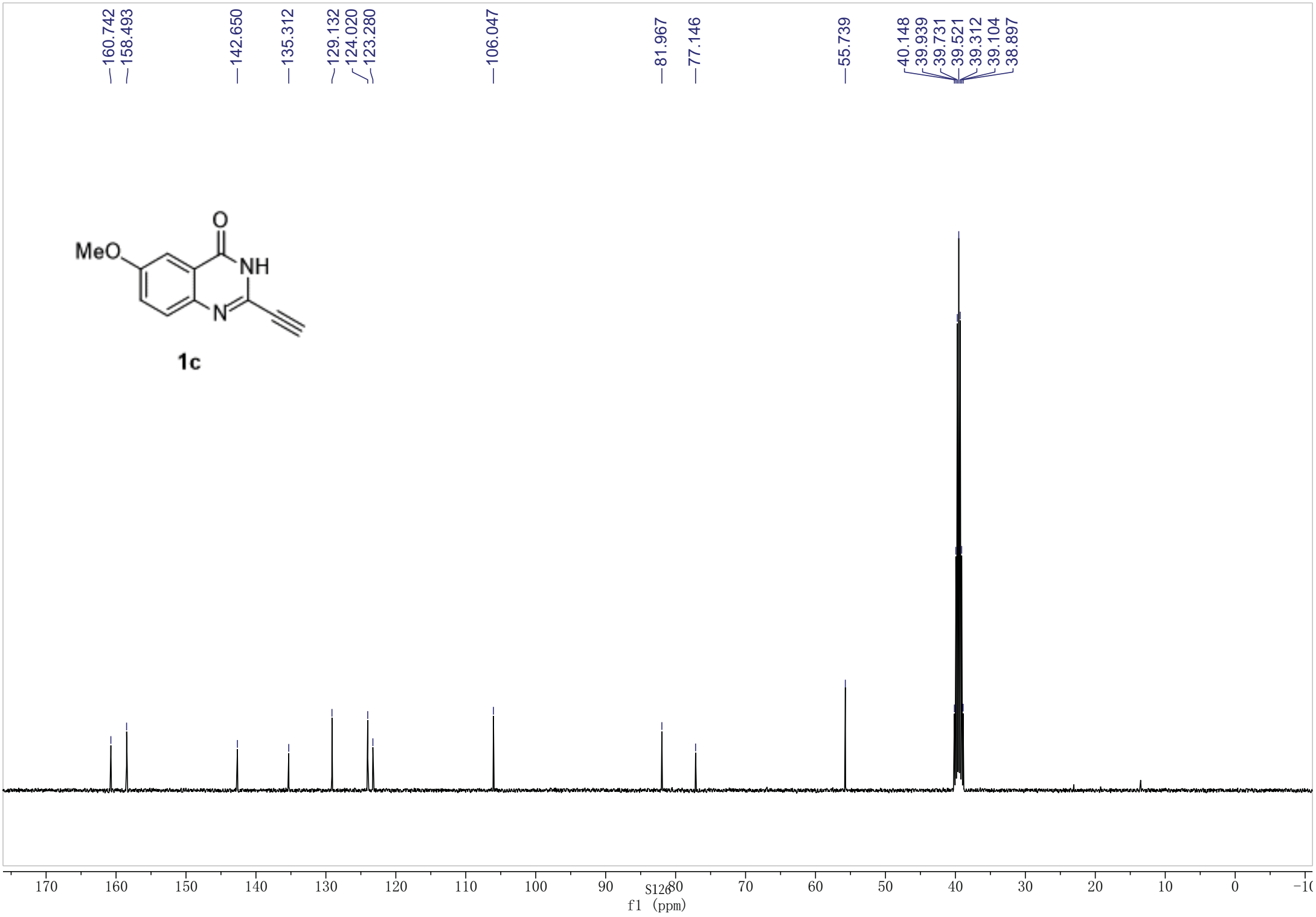
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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129.132
124.020
123.280
106.047
81.967
77.146
55.739
40.148
39.939
39.731
39.521
39.312
39.104
38.897
MeO
O
NH
N
1c
170
160
150
140
130
120
110
100
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80
70
60
50
40
30
20
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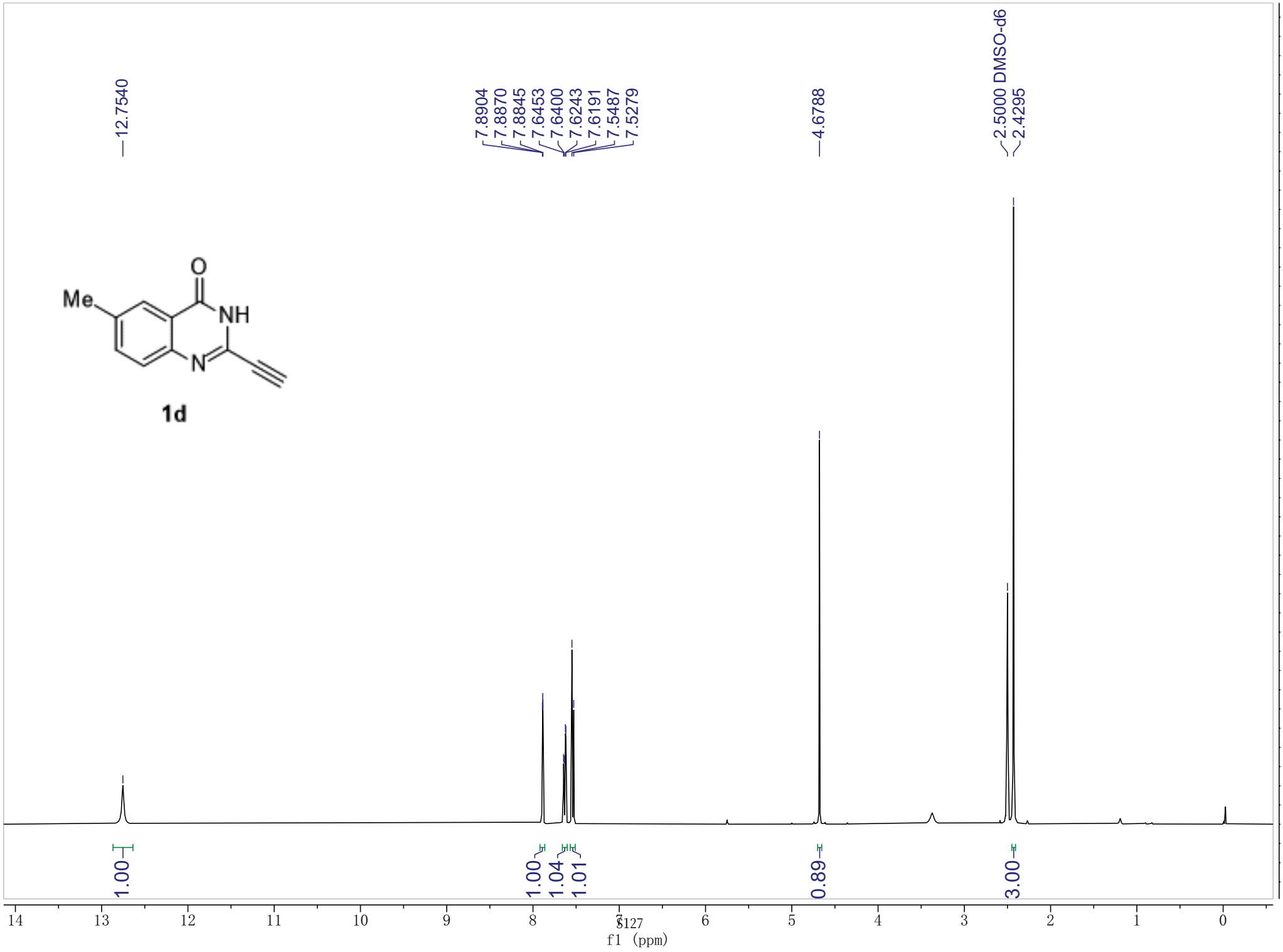
-10
f1 (ppm)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7.8870
7.8845
7.6453
7.6400
7.6243
7.6191
7.5487
7.5279
4.6788
2.5000 DMSO-d6
2.4295
O
Me
NH
N
1d
1.00
1.00
1.04
1.01
0.89
3.00
14
13
12
11
10
9
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7
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5
4
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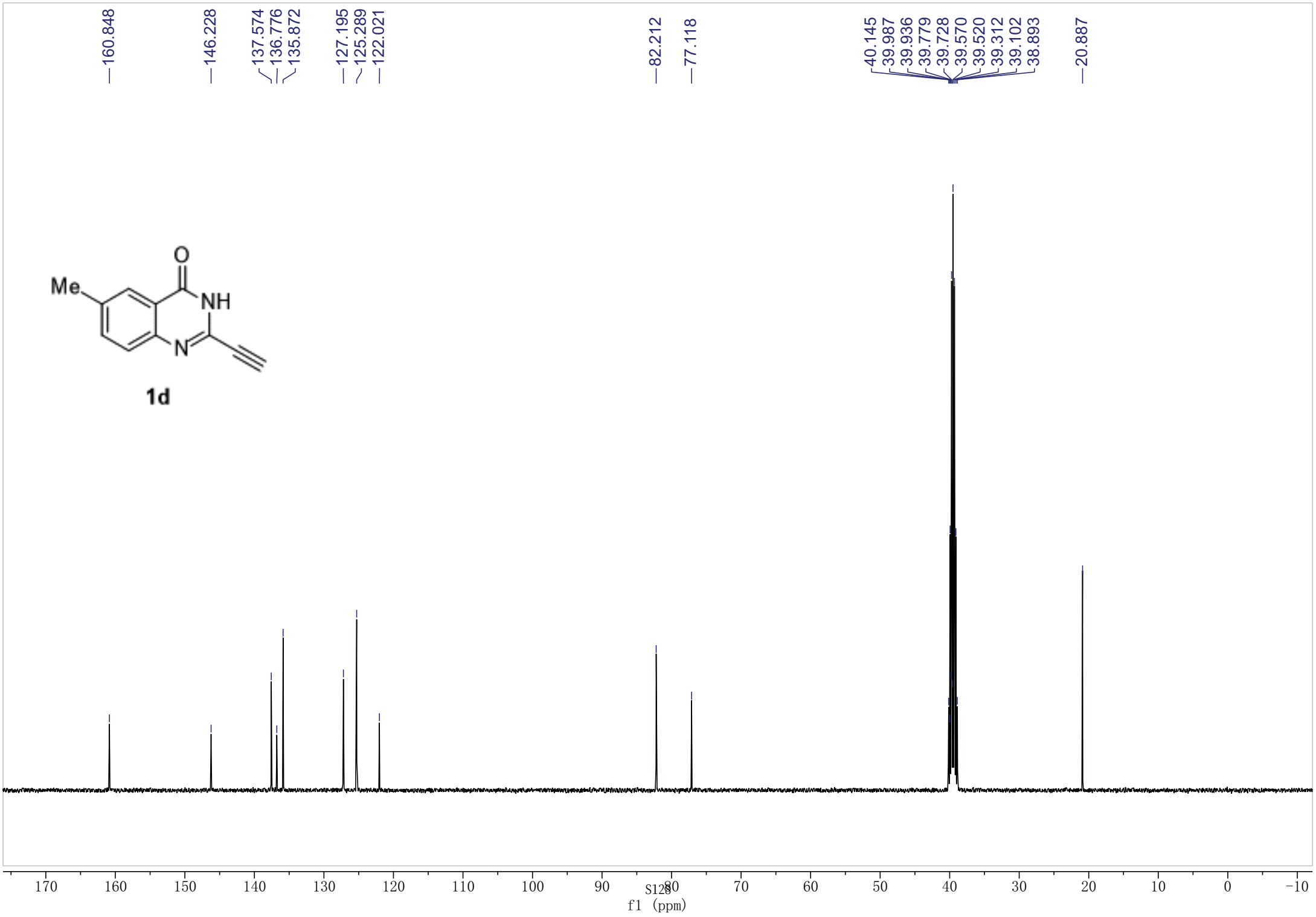
1
0
f1 (ppm)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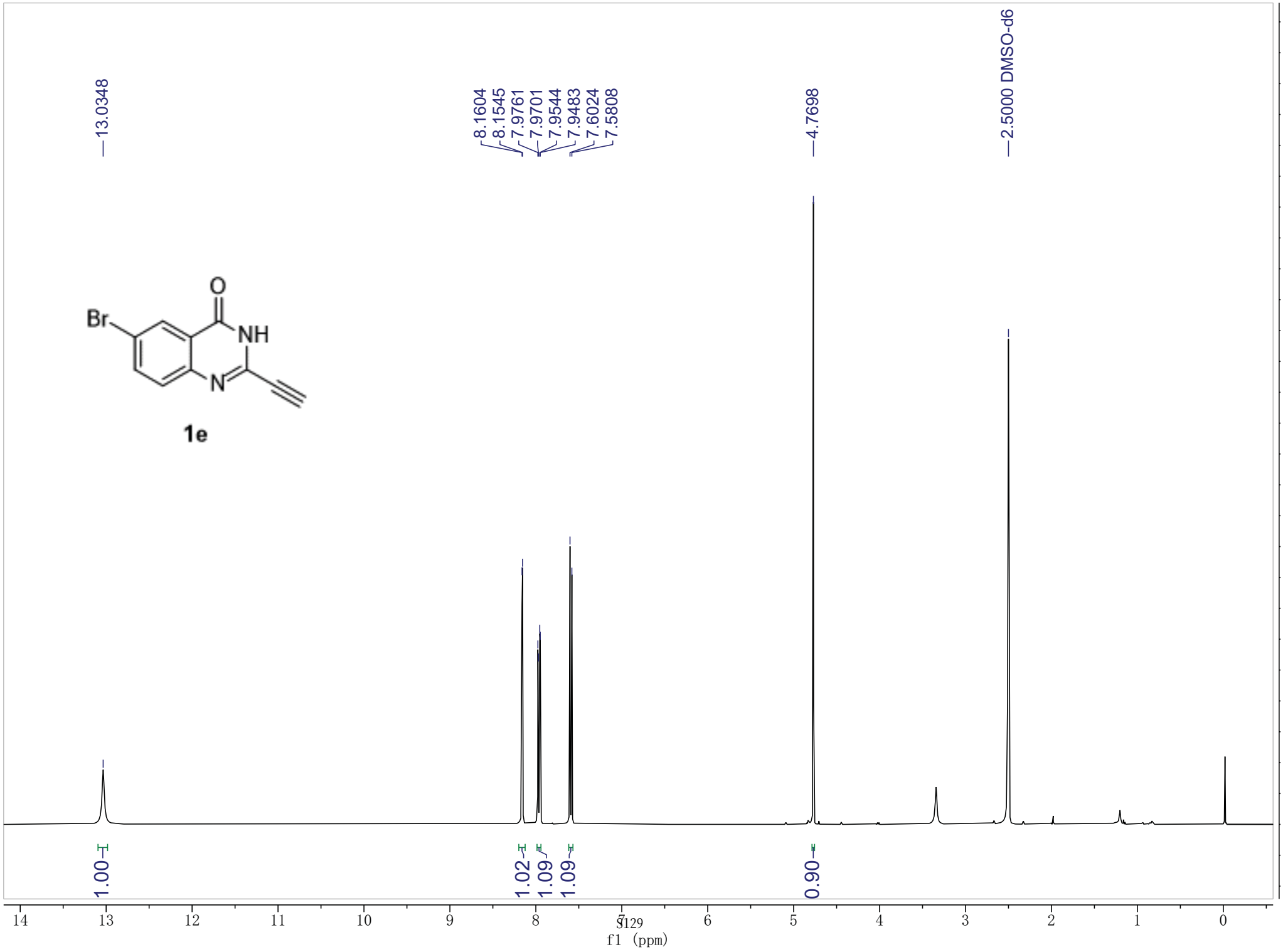
125.289
122.021
82.212
77.118
40.145
39.987
39.936
39.779
39.728
39.570
39.520
39.312
39.102
38.893
20.887
Me
O
NH
N
1d
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)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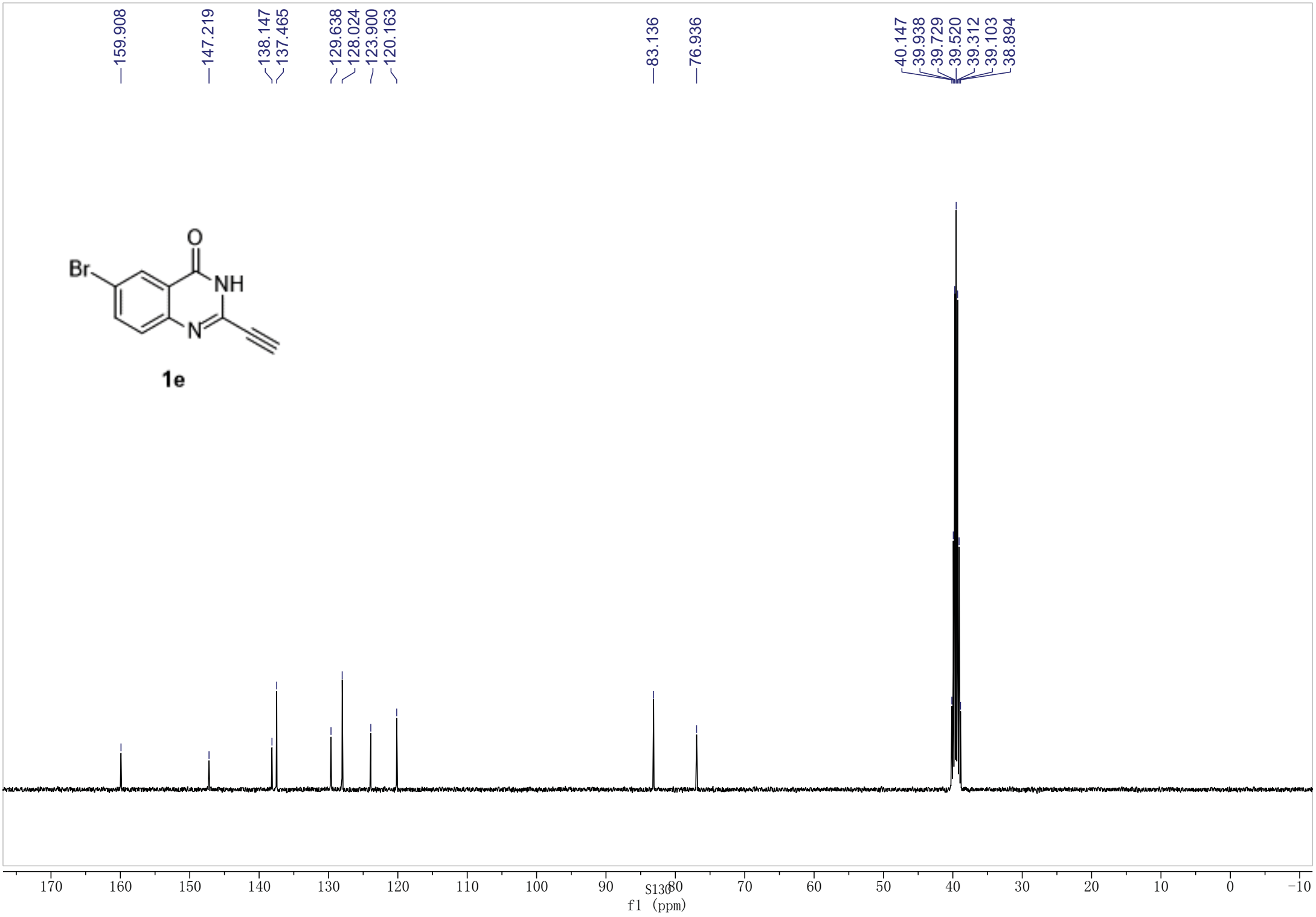
8.1604
8.1545
7.9761
7.9701
7.9544
7.9483
7.6024
7.5808
4.7698
2.5000 DMSO-d6
Br
O
NH
N
1e
1.00
1.02
1.09
1.09
0.90
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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138.147
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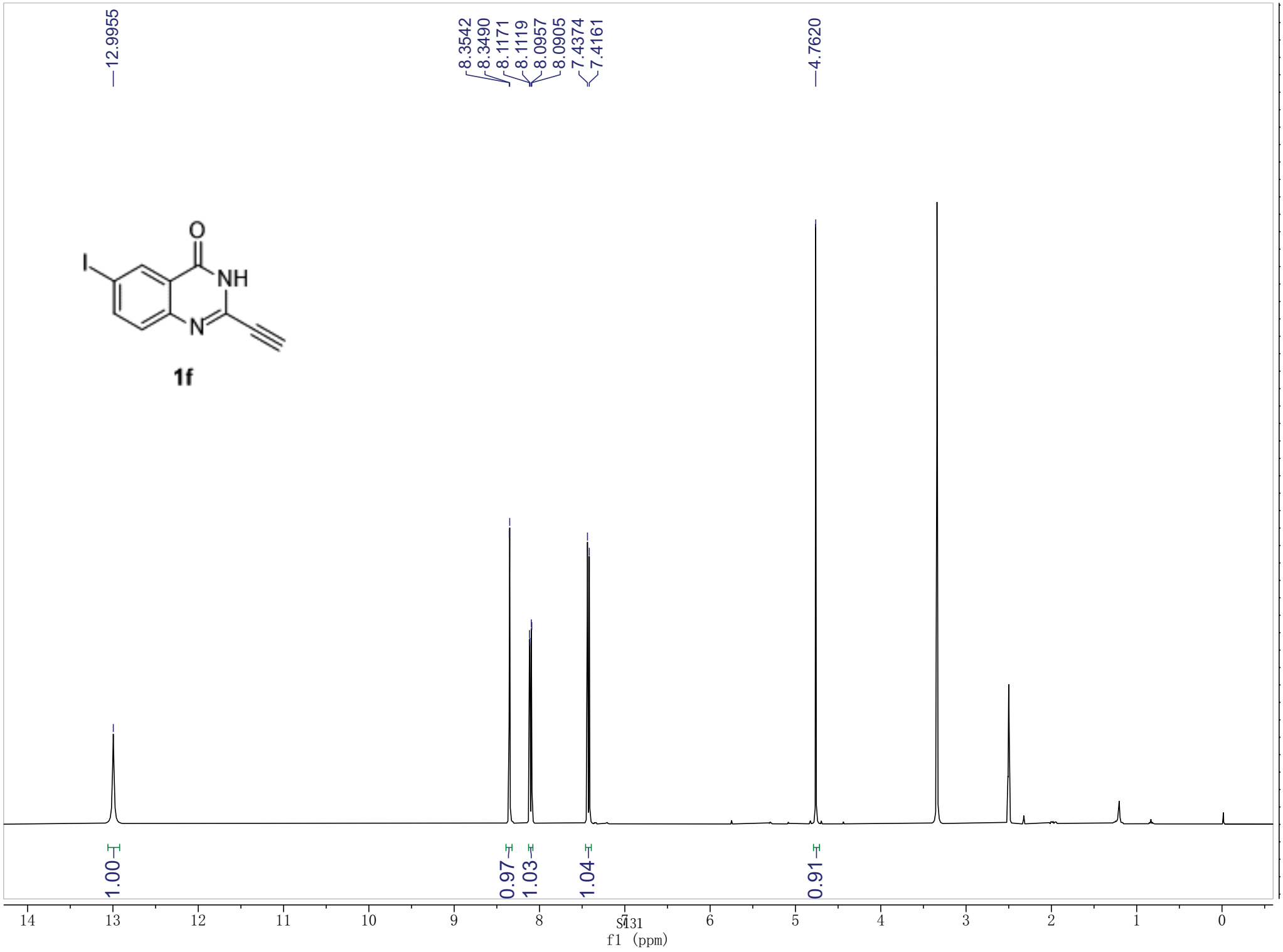
129.638
128.024
123.900
120.163
83.136
76.936
40.147
39.938
39.729
39.520
39.312
39.103
38.894
O
Br
NH
N
1e
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)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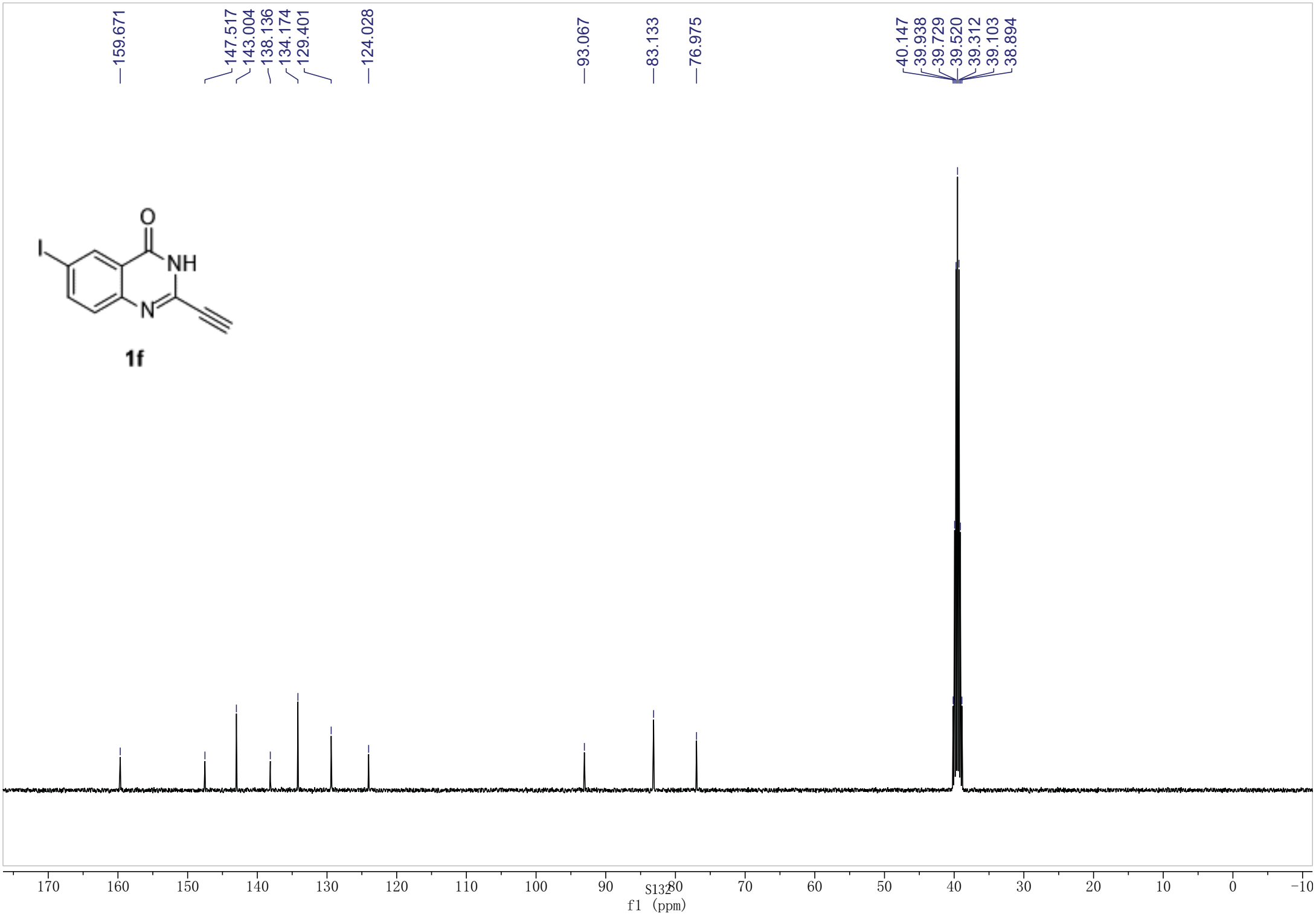
8.3542
8.3490
8.1171
8.1119
8.0957
8.0905
7.4374
7.4161
4.7620
O
NH
I
N
1f
1.00
0.97
1.03
1.04
0.91
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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147.517
143.004
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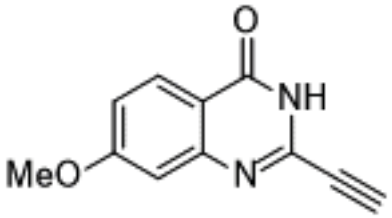
134.174
129.401
124.028
93.067
83.133
76.975
40.147
39.938
39.729
39.520
39.312
39.103
38.894
O
NH
N
I
1f
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

P-W-16-1



1g

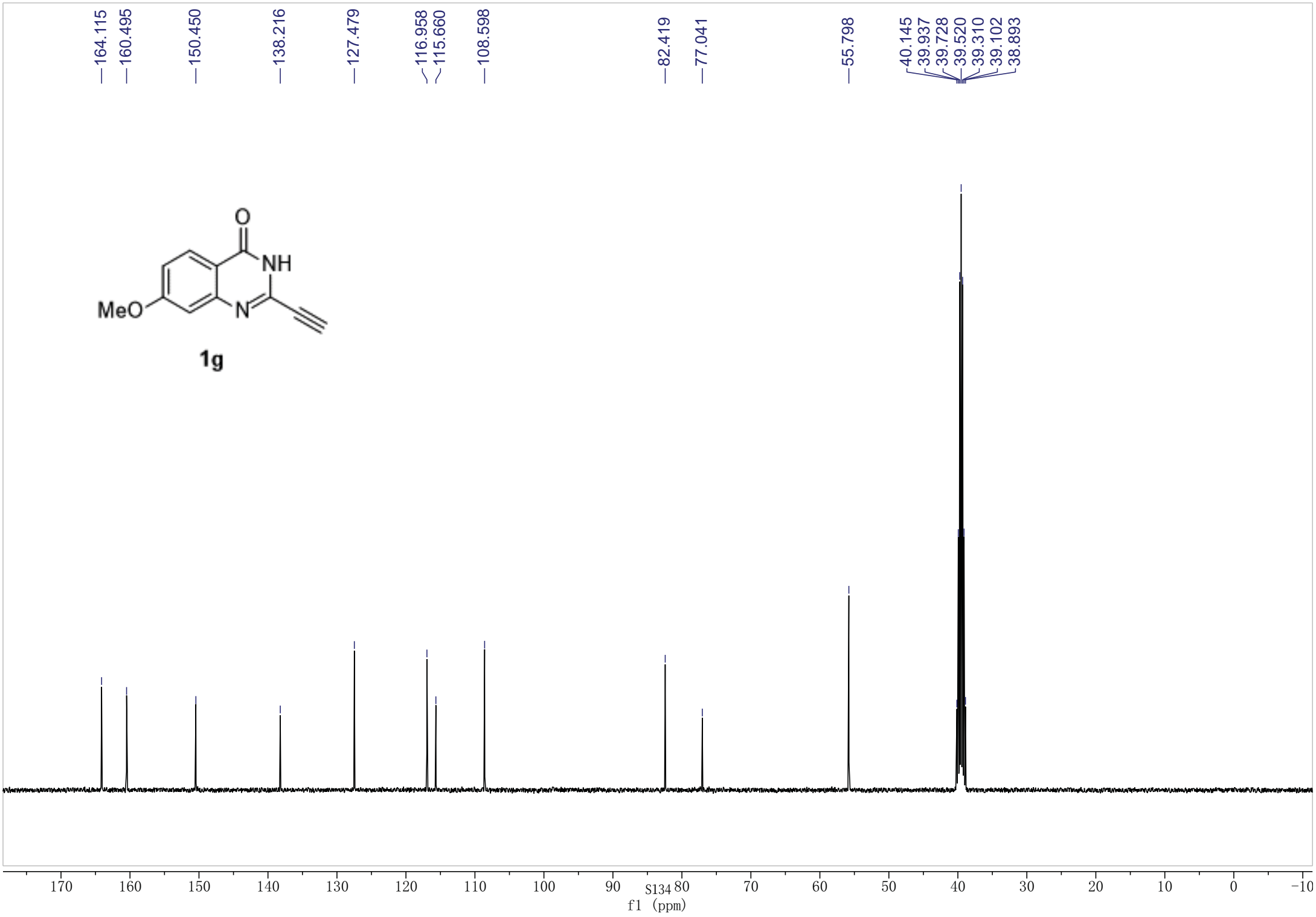
12.7151
8.0034
7.9961
7.9871
7.9797
7.1227
7.1164
7.1057
7.0992
7.0925
4.6980
3.8777

1.00
1.01
2.01
0.81
3.08

13 12 11 10 9 8 7 6 5 4 3 2 1 0

S133

f1 (ppm)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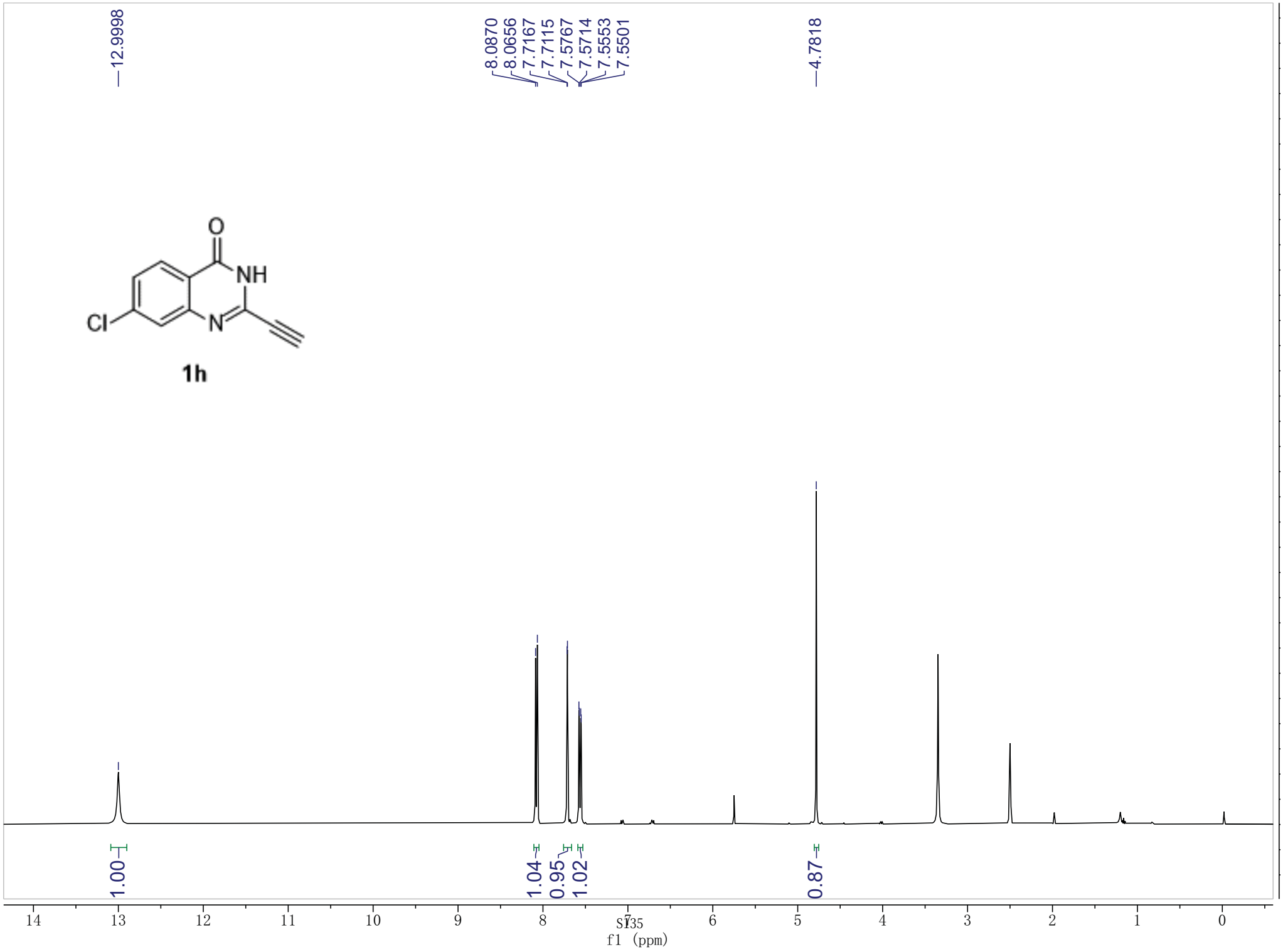
160.495
150.450
138.216
127.479
116.958
115.660
108.598
82.419
77.041
55.798
40.145
39.937
39.728
39.520
39.310
39.102
38.893
O
NH
MeO
N
1g
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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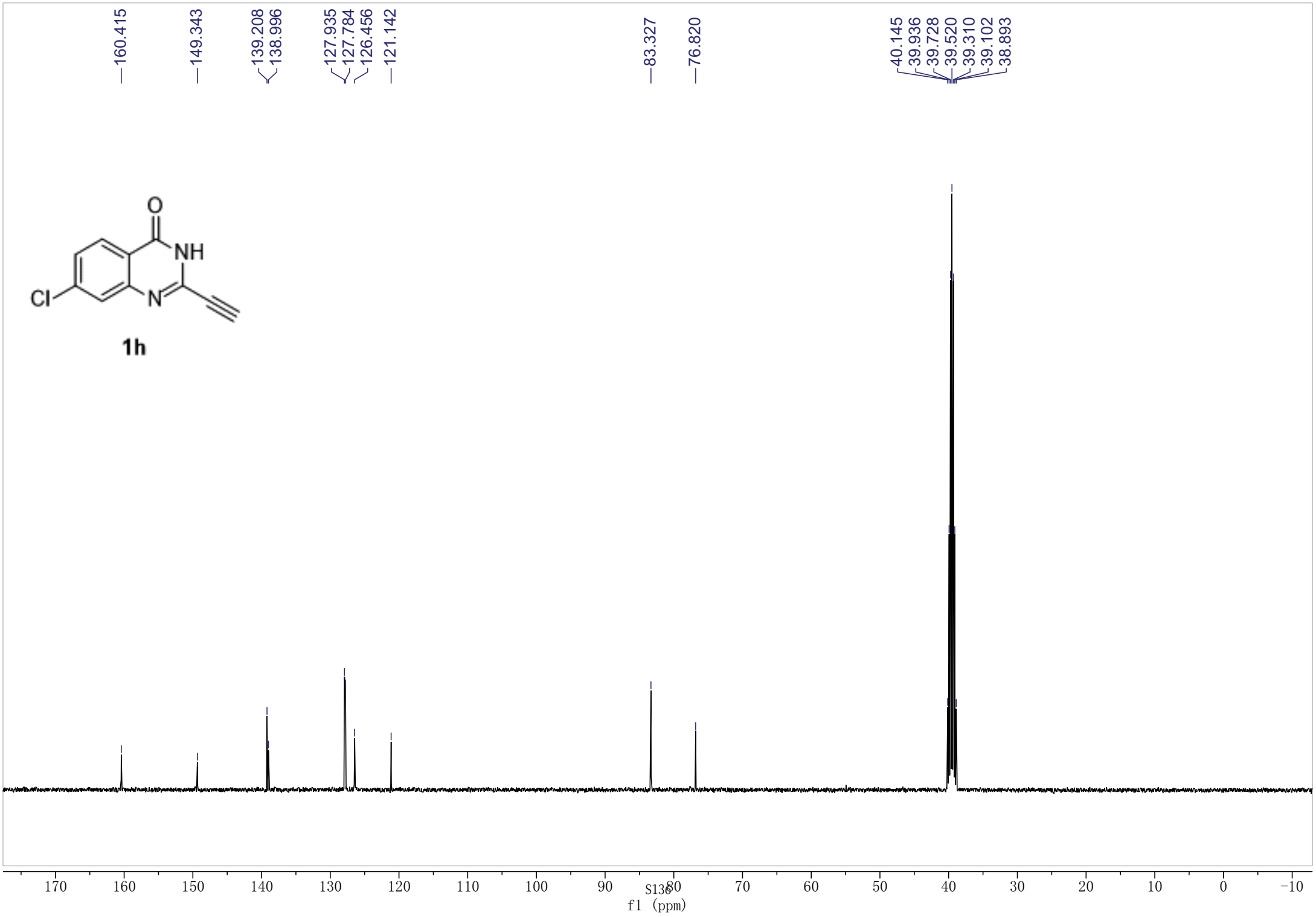
8.0656
7.7167
7.7115
7.5767
7.5714
7.5553
7.5501
4.7818
O
NH
Cl
N
1h
1.00
1.04
0.95
1.02
0.87
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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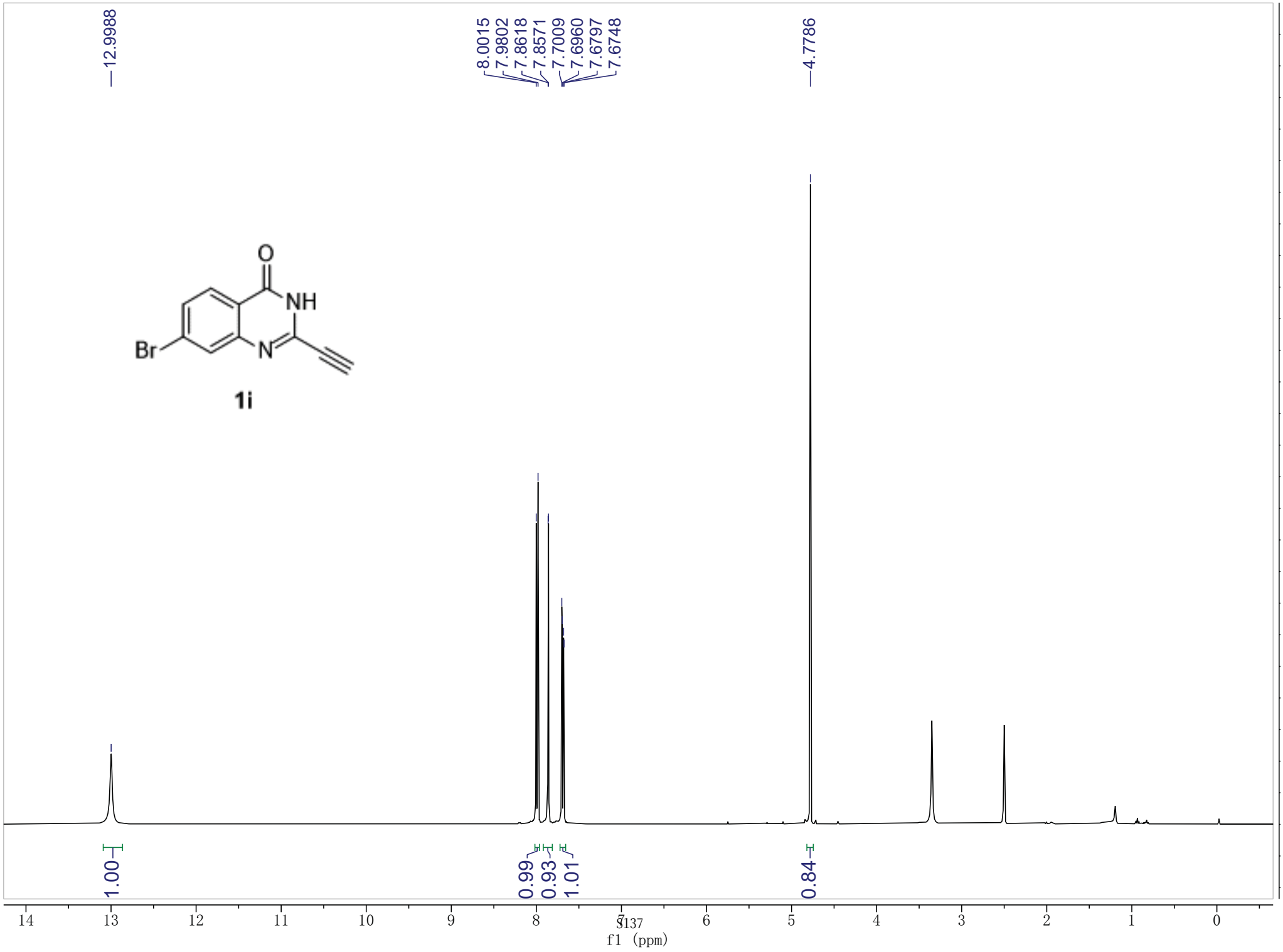
139.208
138.996
127.935
127.784
126.456
121.142
83.327
76.820
40.145
39.936
39.728
39.520
39.310
39.102
38.893
O
NH
Cl
N
1h
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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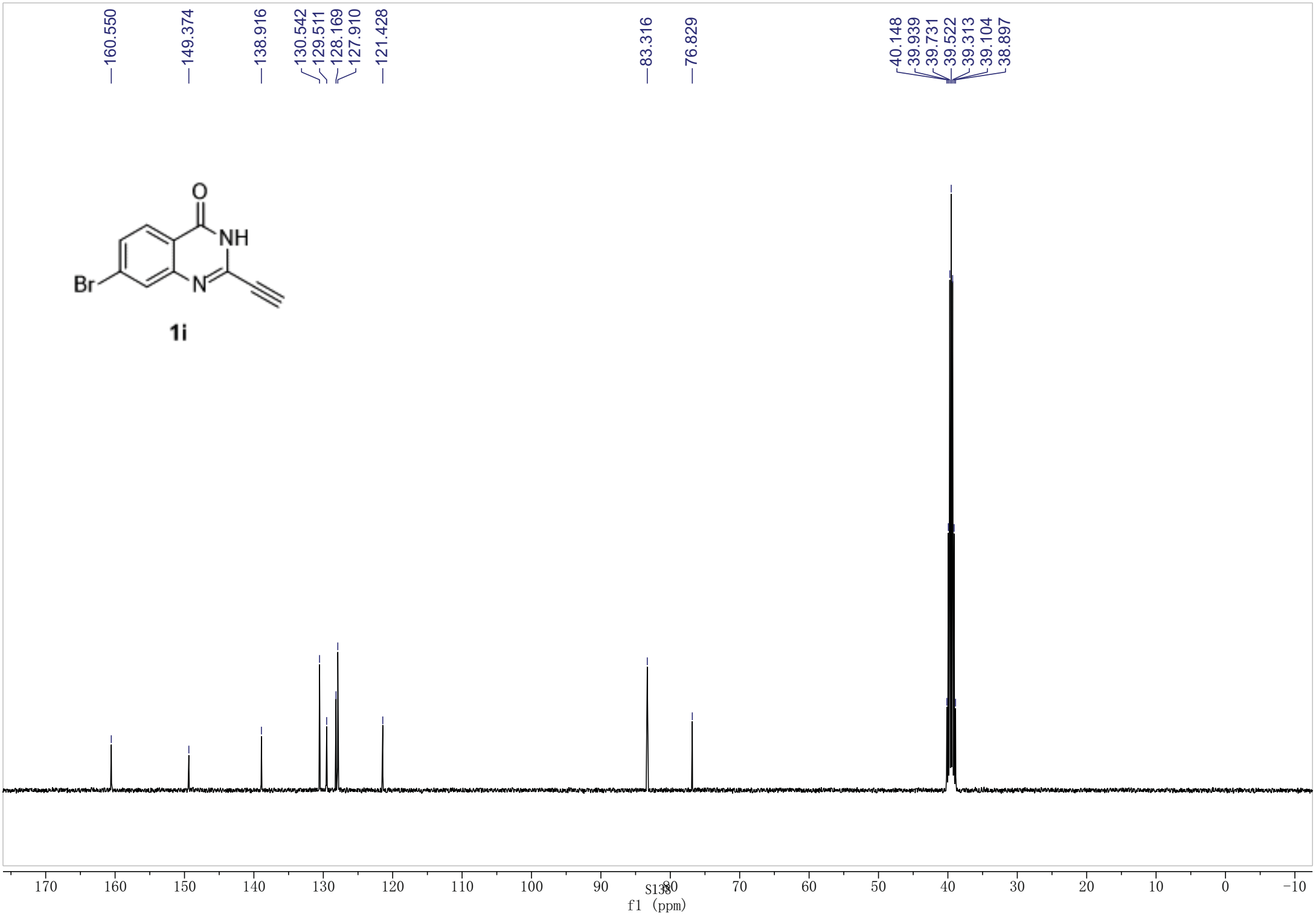
7.9802
7.8618
7.8571
7.7009
7.6960
7.6797
7.6748
4.7786
O
NH
Br
N
1i
1.00
0.99
0.93
1.01
0.84
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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138.916
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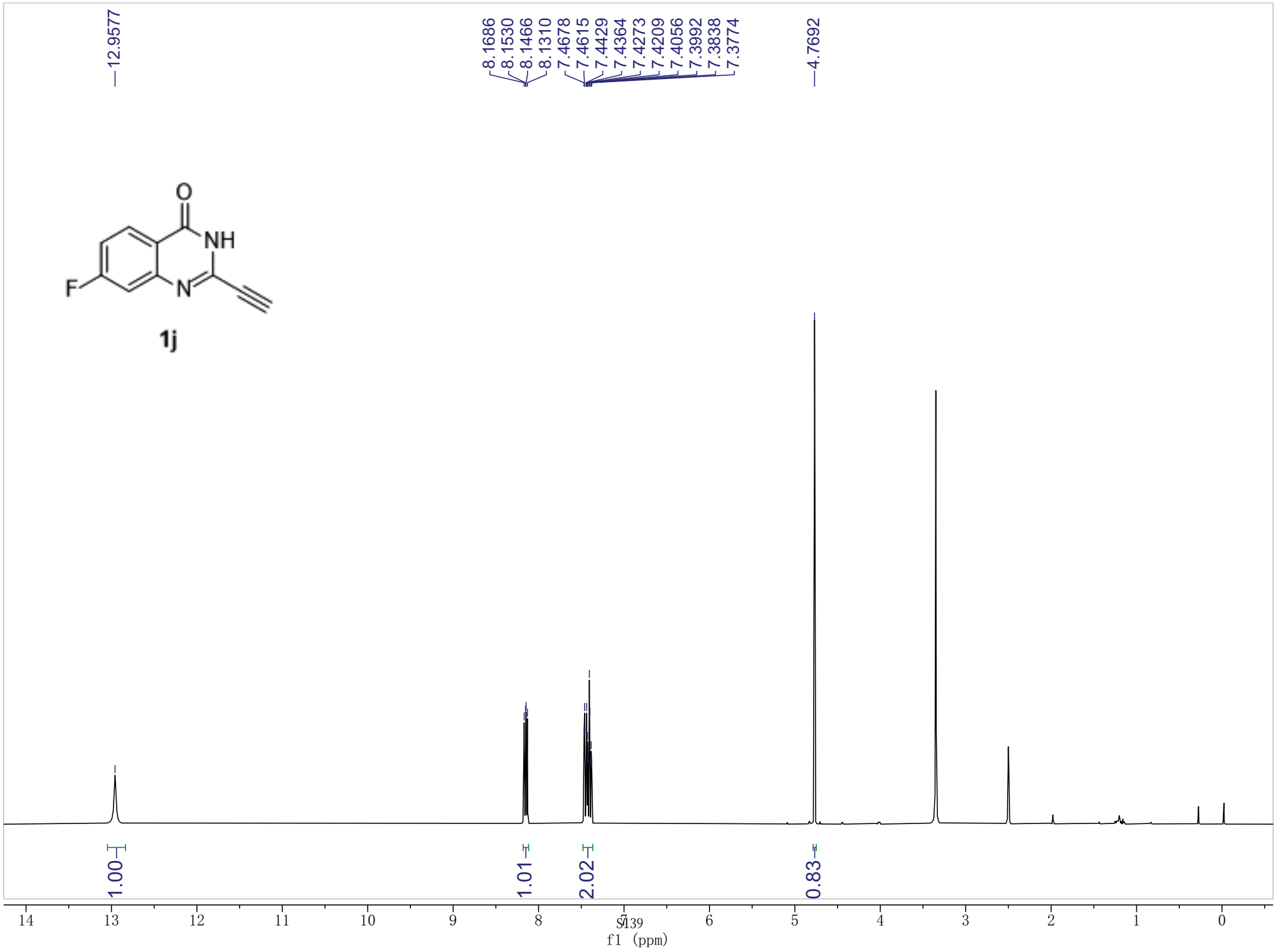
129.511
128.169
127.910
121.428
83.316
76.829
40.148
39.939
39.731
39.522
39.313
39.104
38.897
O
NH
Br
N
1i
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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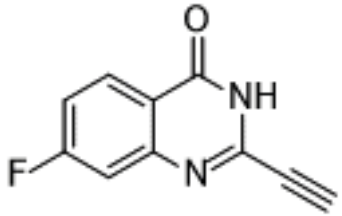
7.4678
7.4615
7.4429
7.4364
7.4273
7.4209
7.4056
7.3992
7.3838
7.3774
4.7692
O
NH
F
N
1j
1.00
1.01
2.02
0.83
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

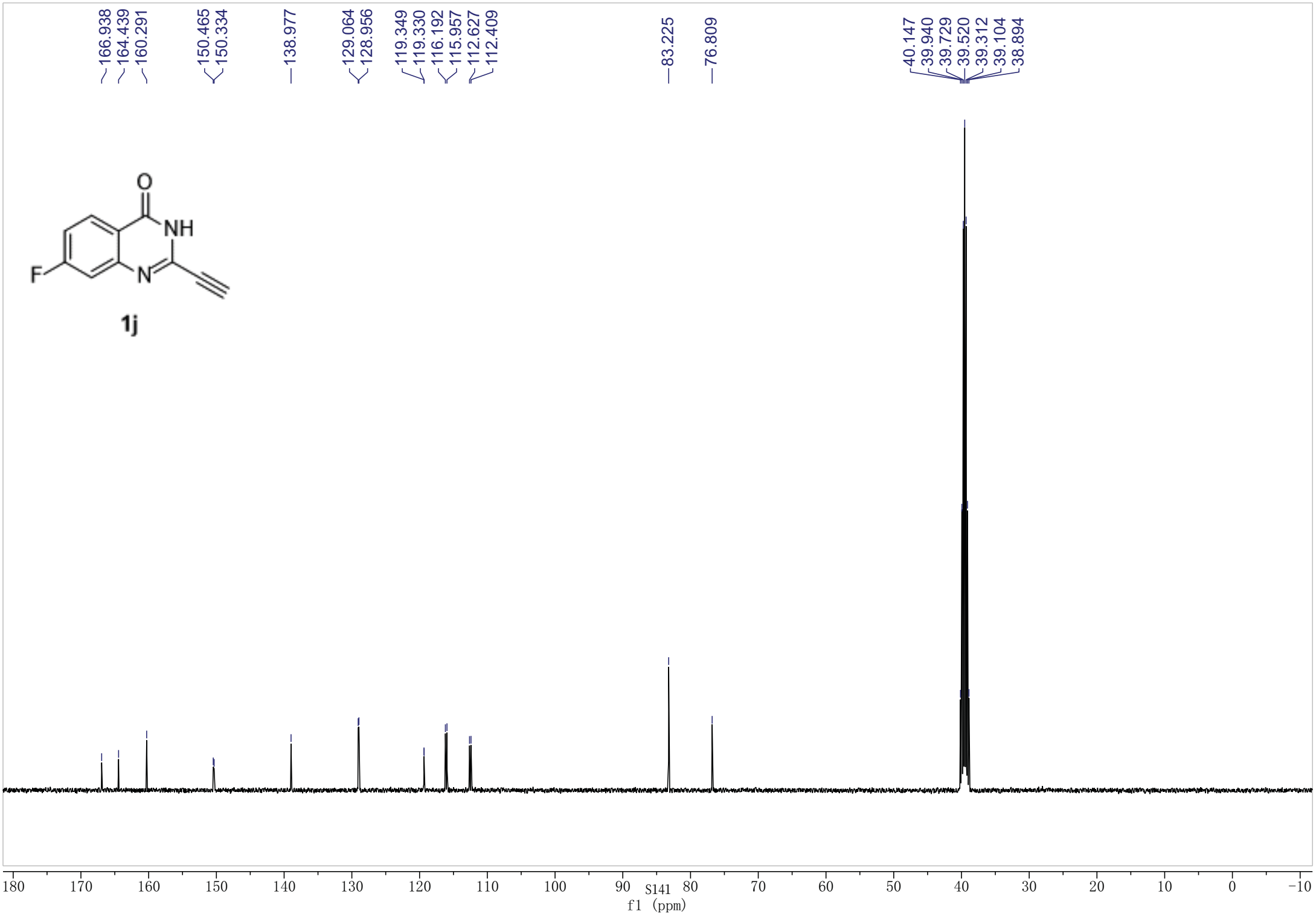


1j

-104.0

10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210

f1 (ppm)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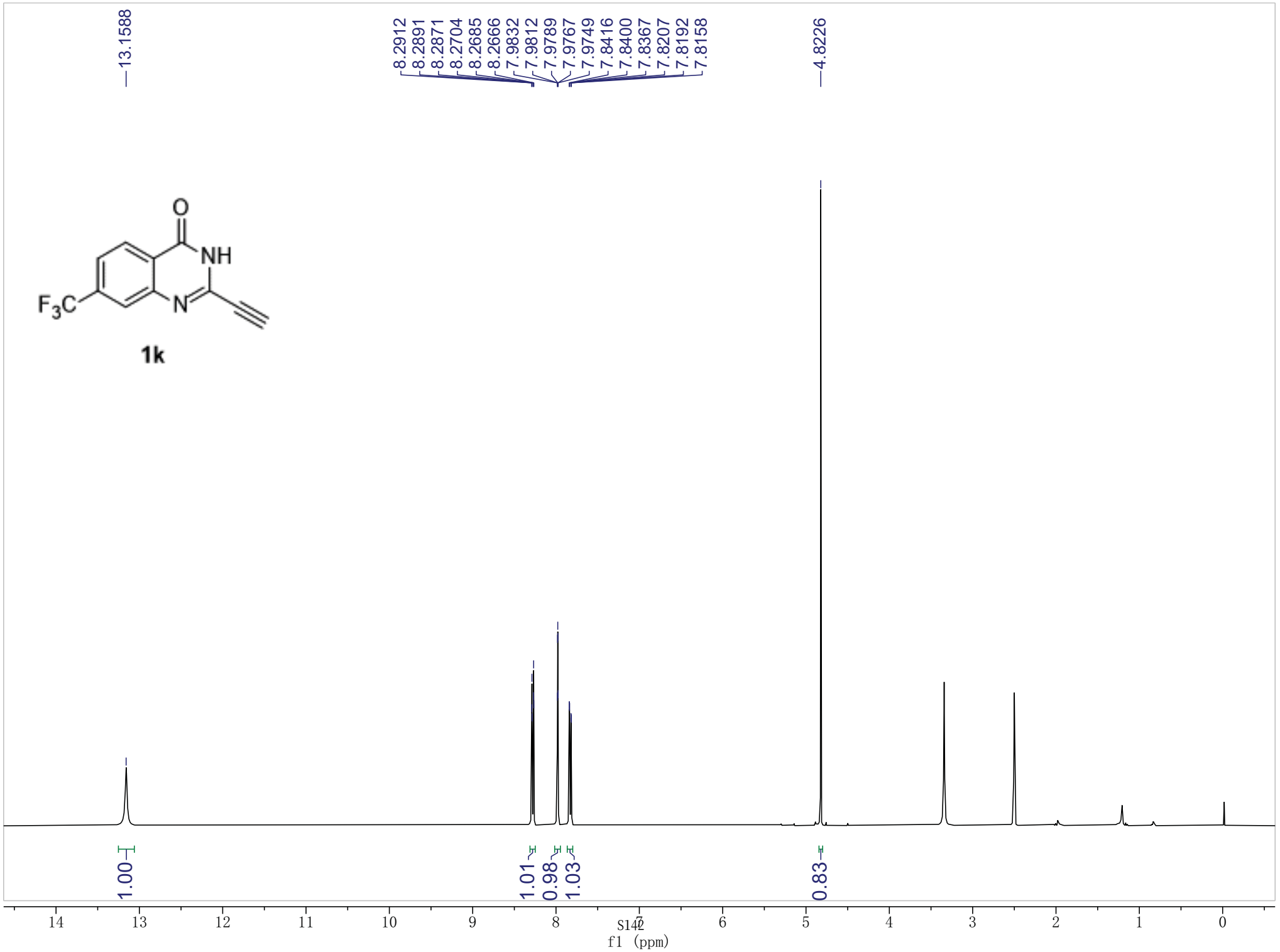
115.957
112.627
112.409
83.225
76.809
40.147
39.940
39.729
39.520
39.312
39.104
38.894
O
NH
F
N
1j
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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8.2871
8.2704
8.2685
8.2666
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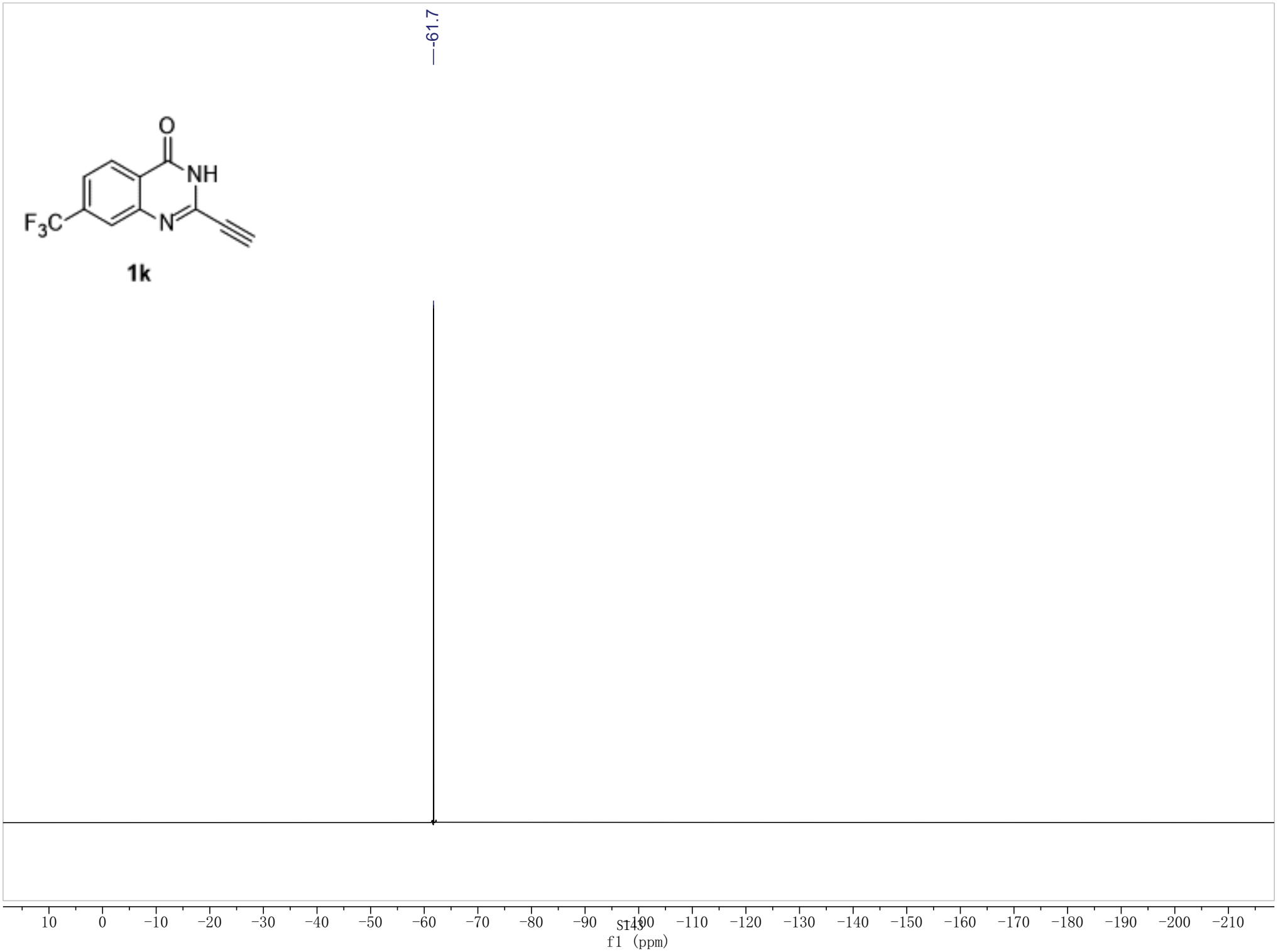
7.9812
7.9789
7.9767
7.9749
7.8416
7.8400
7.8367
7.8207
7.8192
7.8158
4.8226
O
NH
N
F3C
1k
1.00
1.01
0.98
1.03
0.83
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


-61.7
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N
F3C
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10
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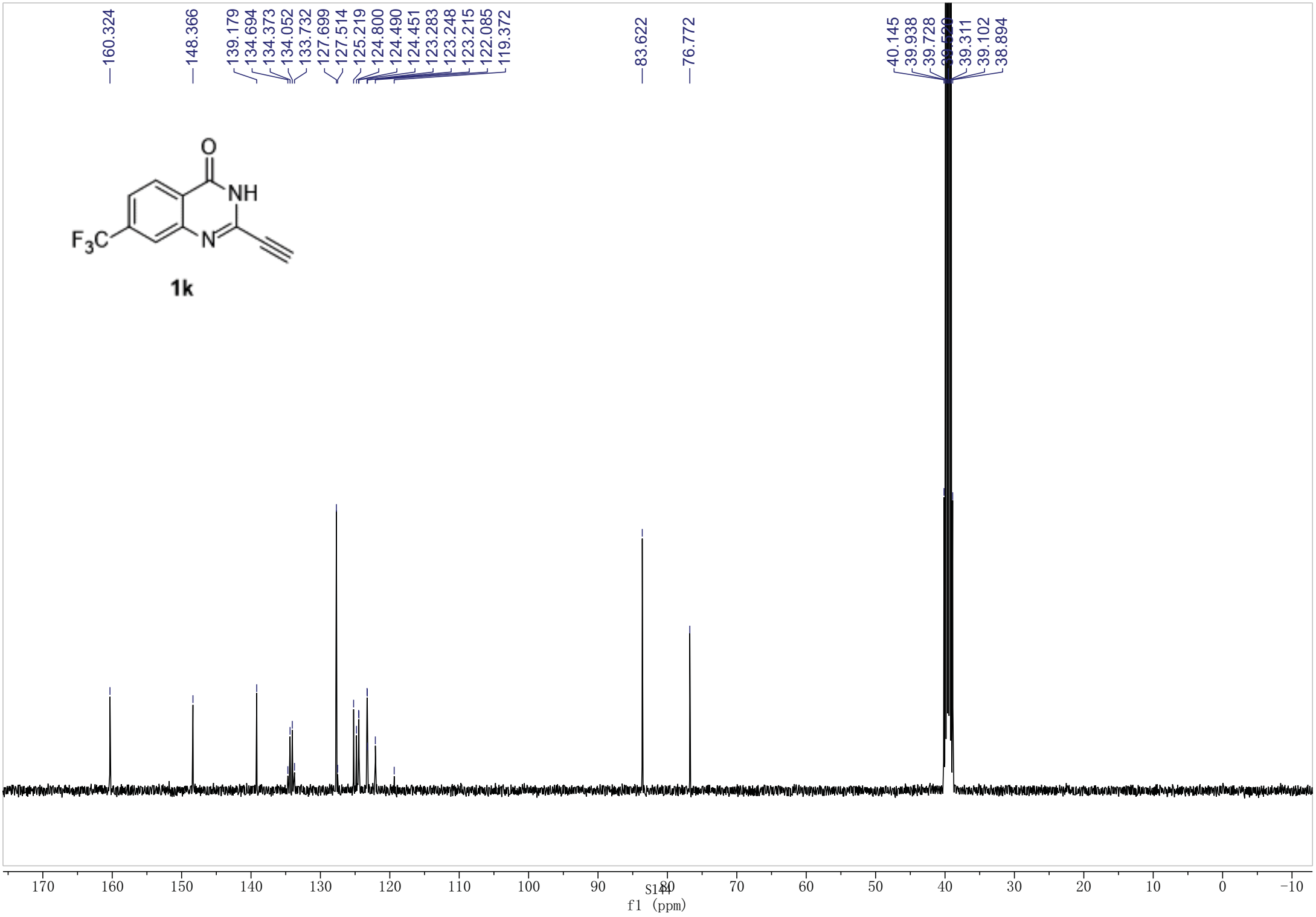
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)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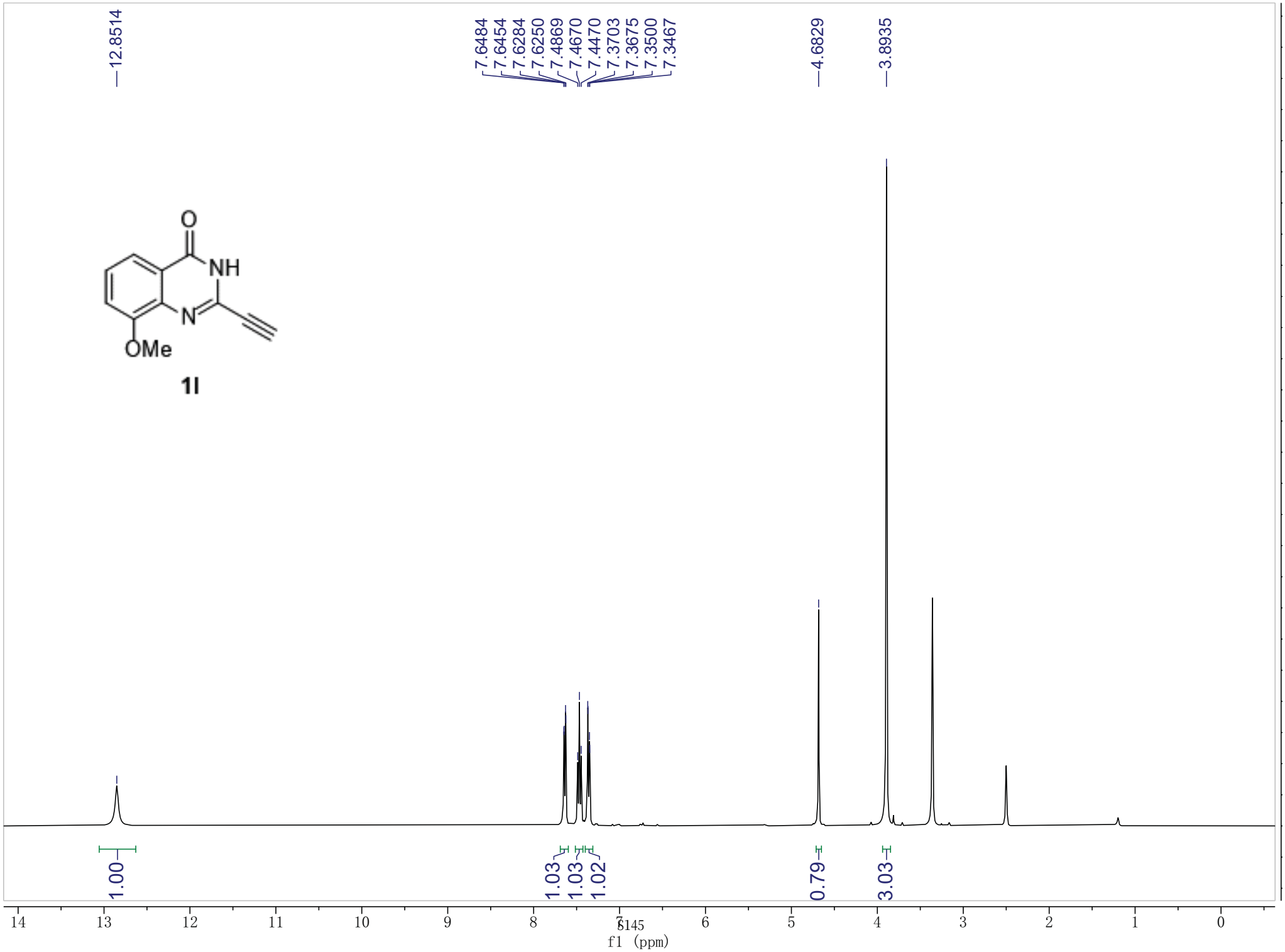
139.179
134.694
134.373
134.052
133.732
127.699
127.514
125.219
124.800
124.490
124.451
123.283
123.248
123.215
122.085
119.372
83.622
76.772
40.145
39.938
39.728
39.311
39.102
38.894
O
NH
N
F3C
1k
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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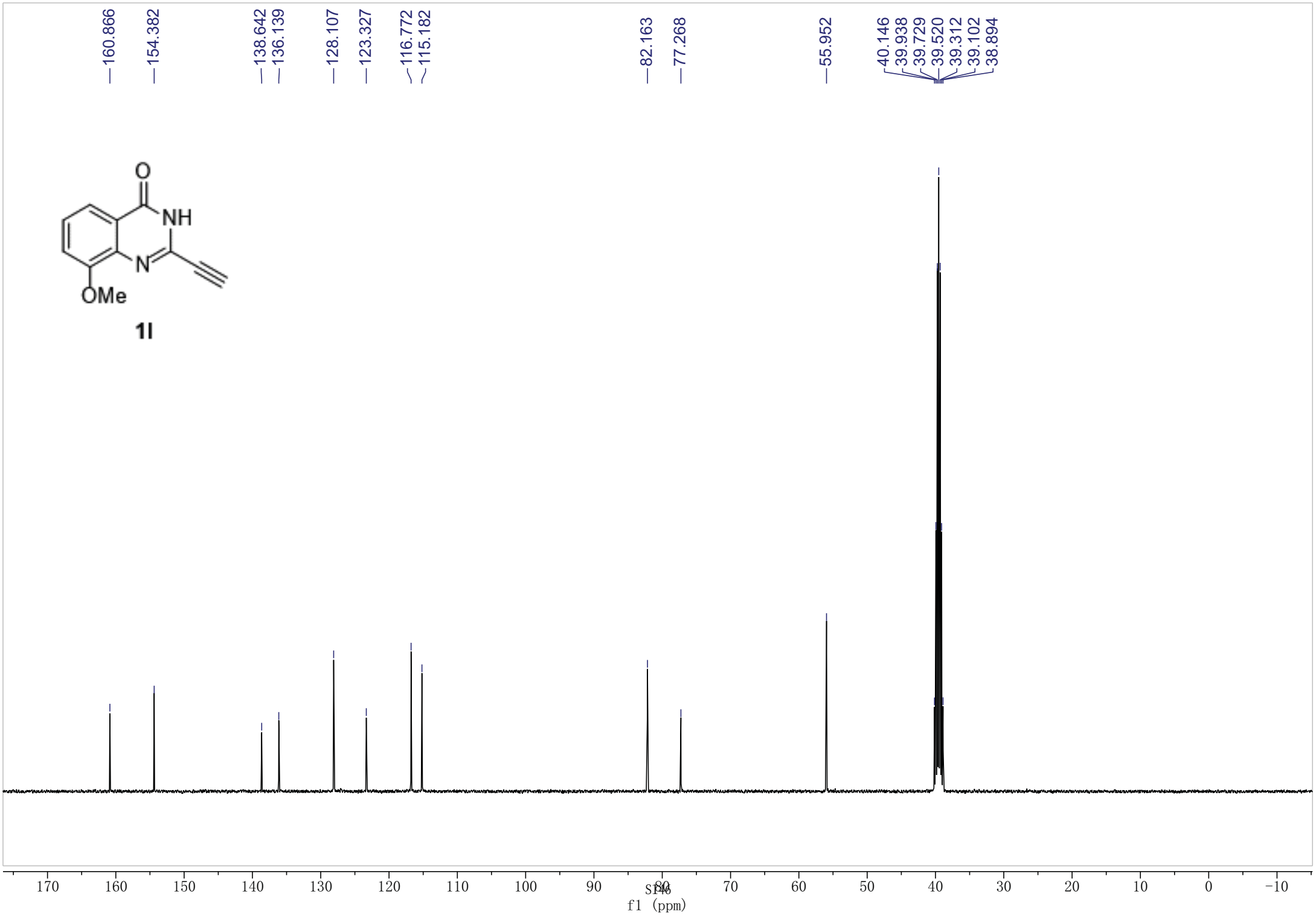
7.4670
7.4470
7.3703
7.3675
7.3500
7.3467
4.6829
3.8935
O
NH
N
OMe
1.00
1.03
1.03
1.02
0.79
3.03
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

1l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123.327
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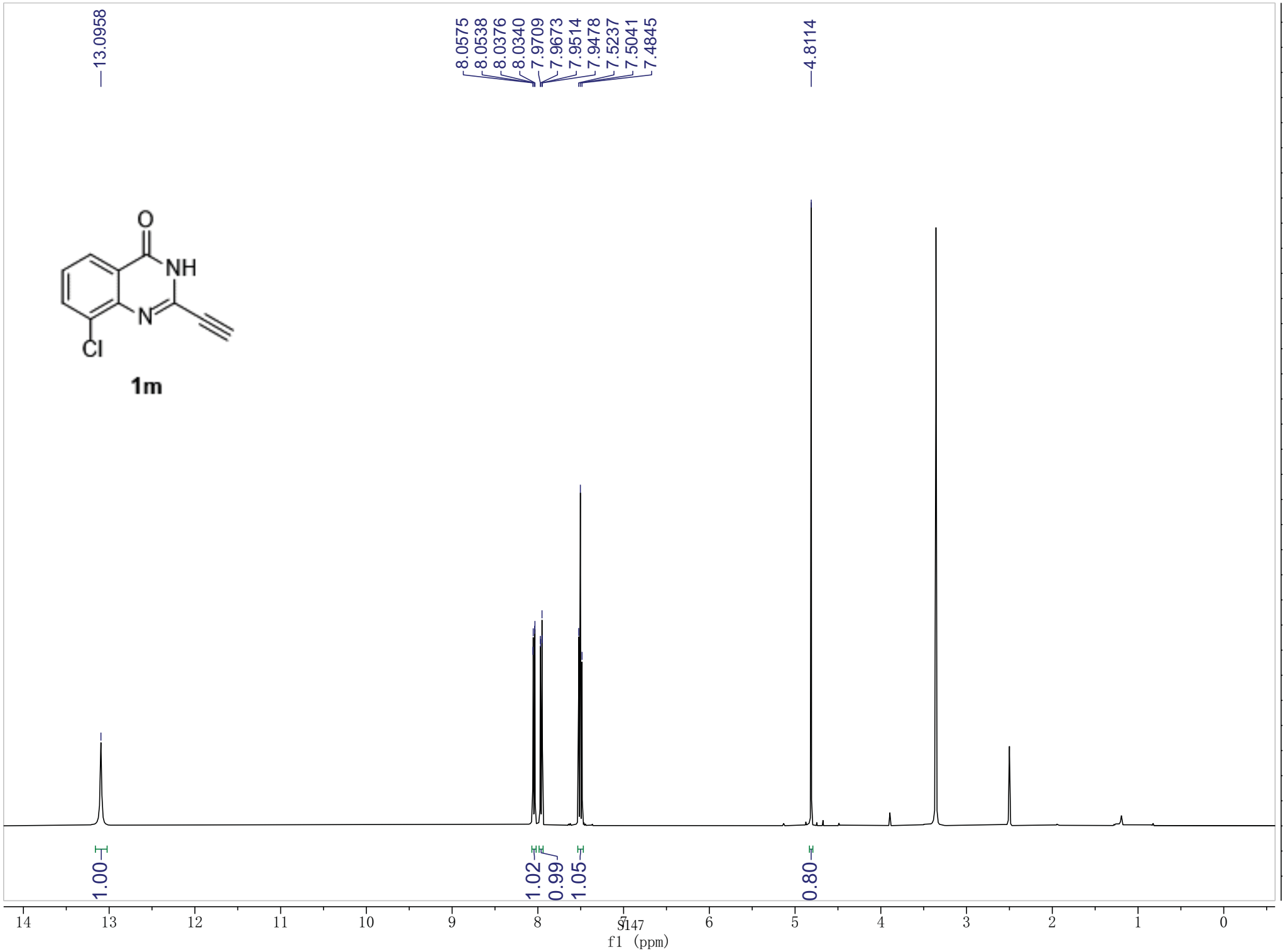
115.182
82.163
77.268
55.952
40.146
39.938
39.729
39.520
39.312
39.102
38.894
O
NH
N
OMe
1l
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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8.0376
8.0340
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7.9673
7.9514
7.9478
7.5237
7.5041
7.4845
4.8114
O
NH
N
Cl
1m
1.00
1.02
0.99
1.05
0.80
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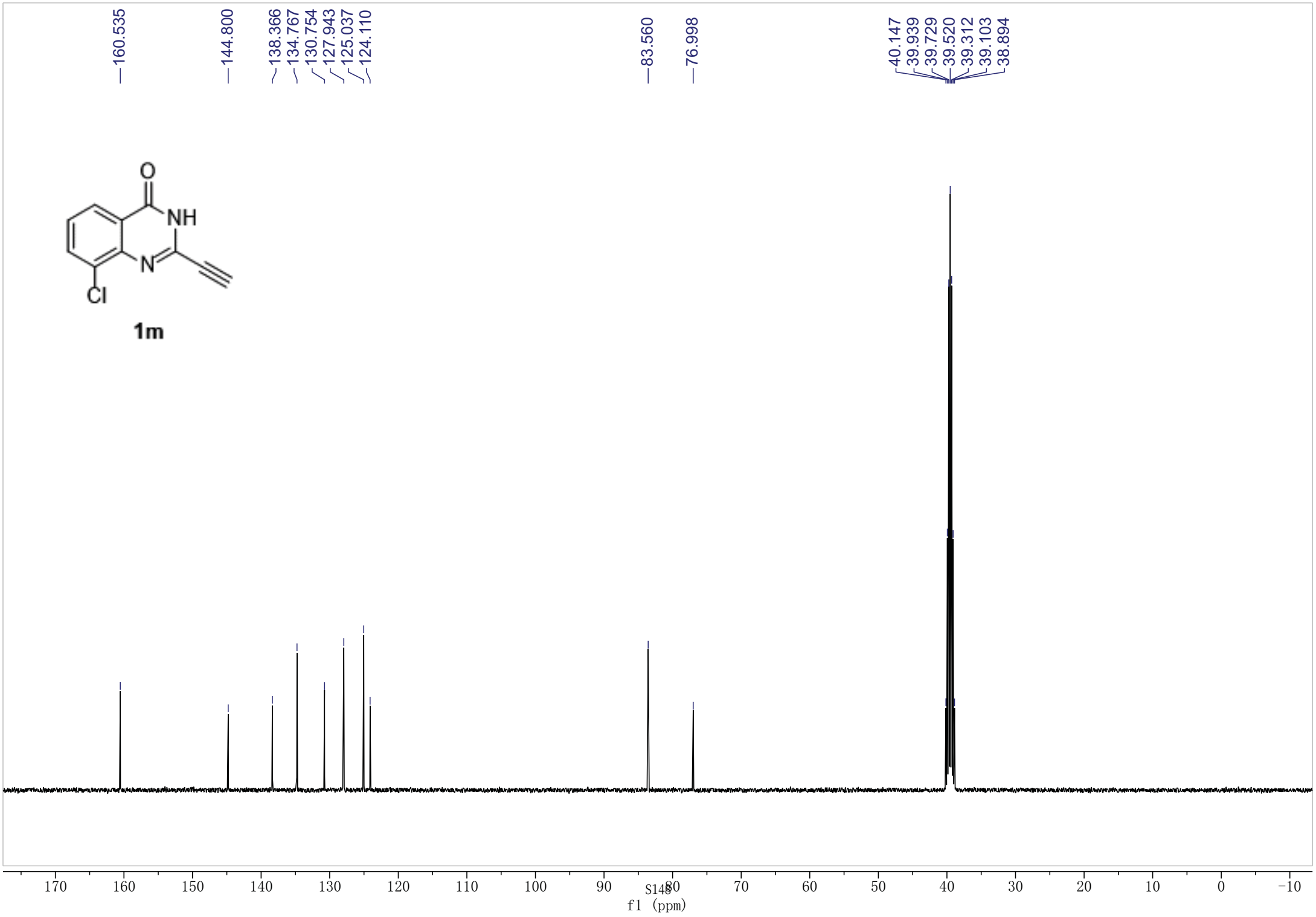
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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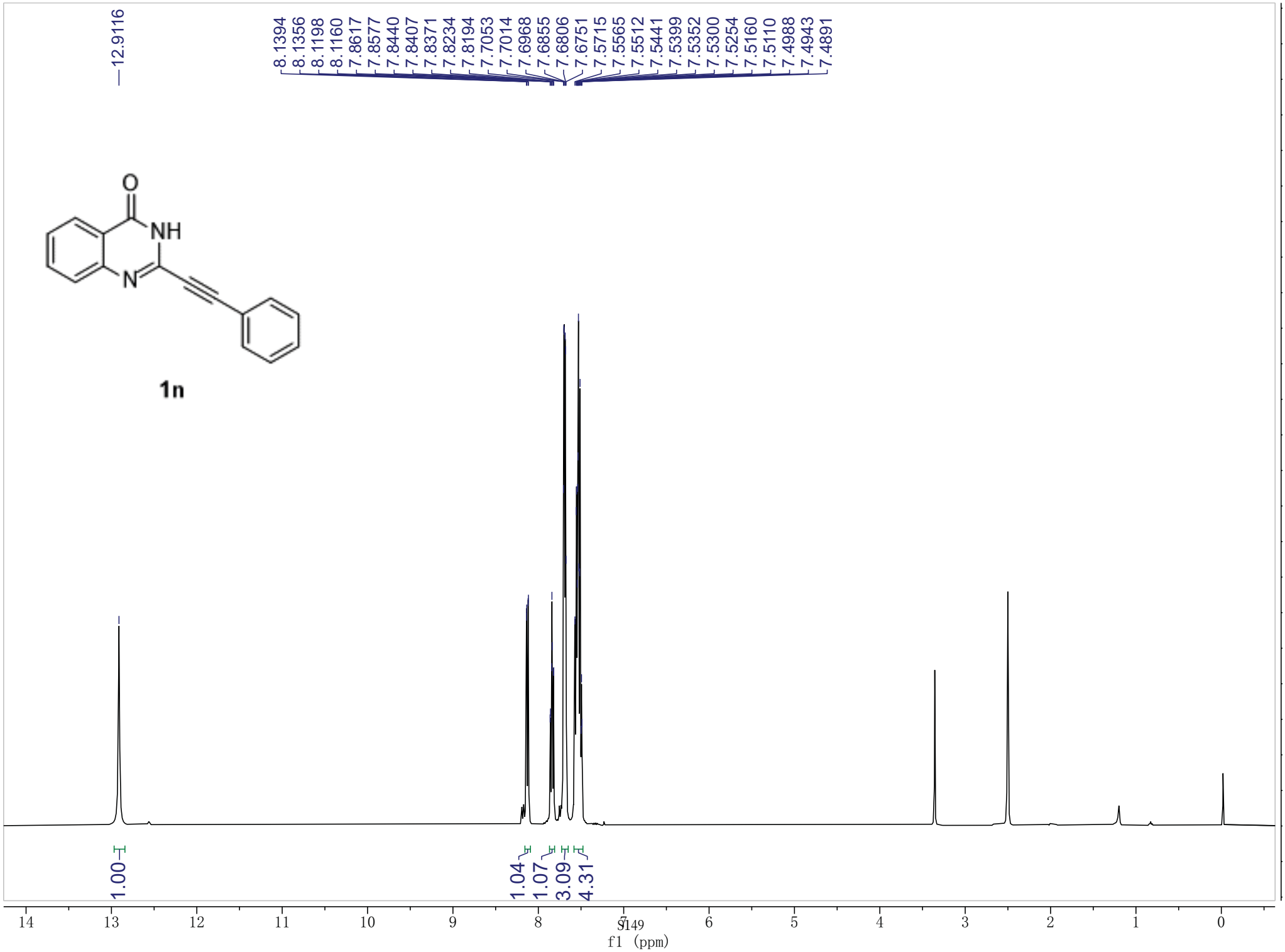
124.110
83.560
76.998
40.147
39.939
39.729
39.520
39.312
39.103
38.894
O
NH
N
Cl
1m
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)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7.8234
7.8194
7.7053
7.7014
7.6968
7.6855
7.6806
7.6751
7.5715
7.5565
7.5512
7.5441
7.5399
7.5352
7.5300
7.5254
7.5160
7.5110
7.4988
7.4943
7.4891
O
NH
N
1n
1.00
1.04
1.07
3.09
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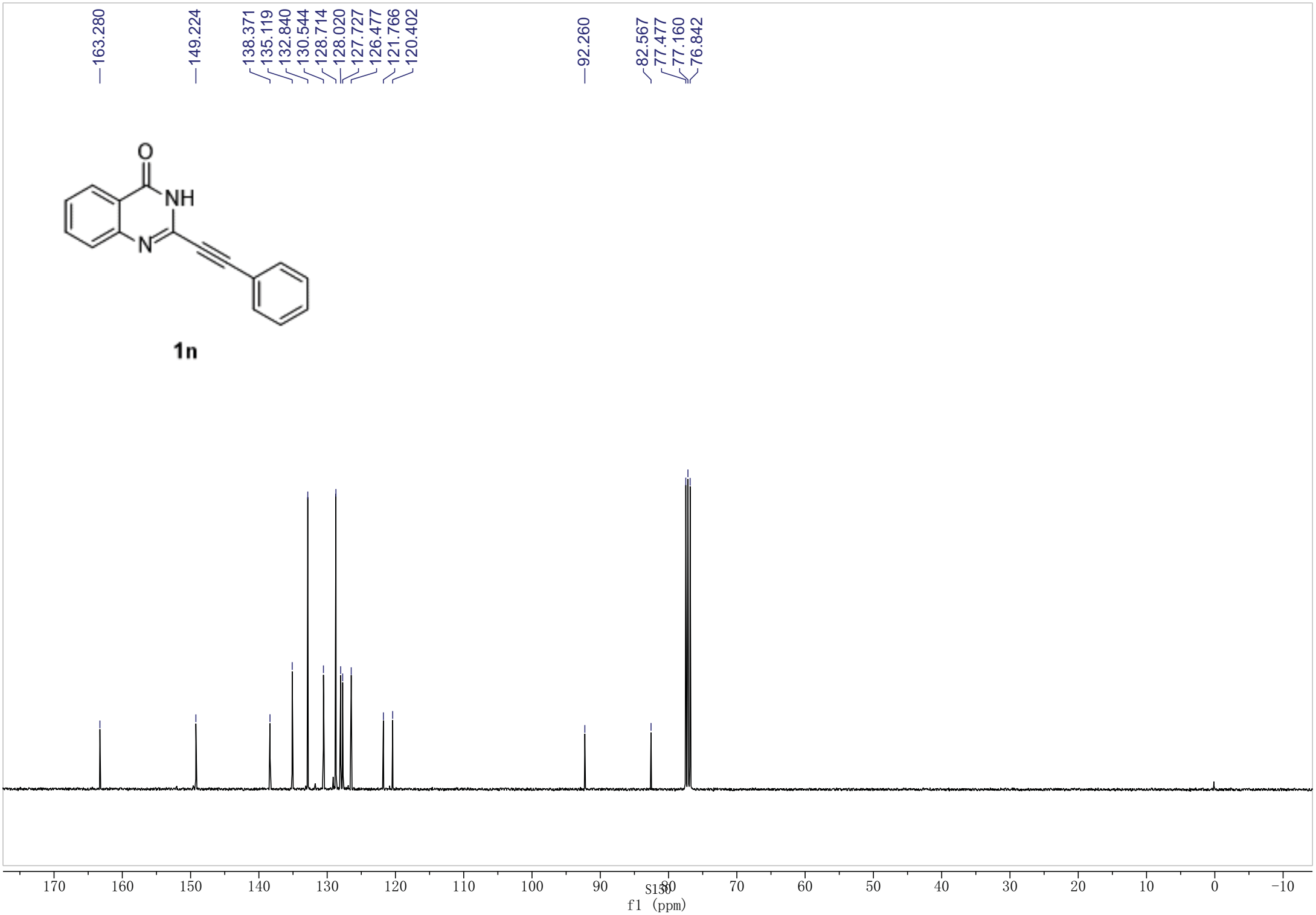
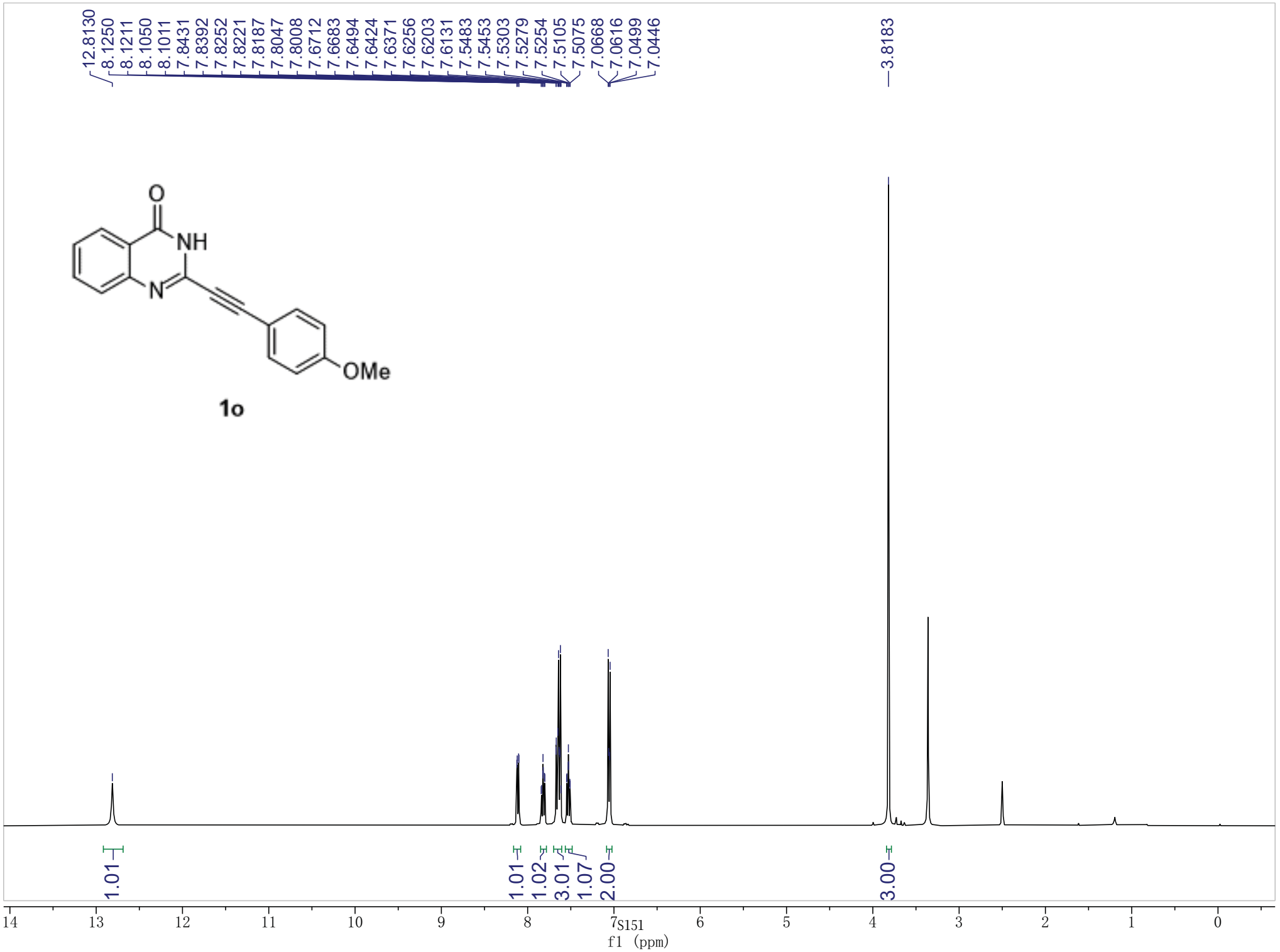
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)


163.280
149.224
138.371
135.119
132.840
130.544
128.714
128.020
127.727
126.477
121.766
120.402
92.260
82.567
77.477
77.160
76.842
O
NH
N
1n
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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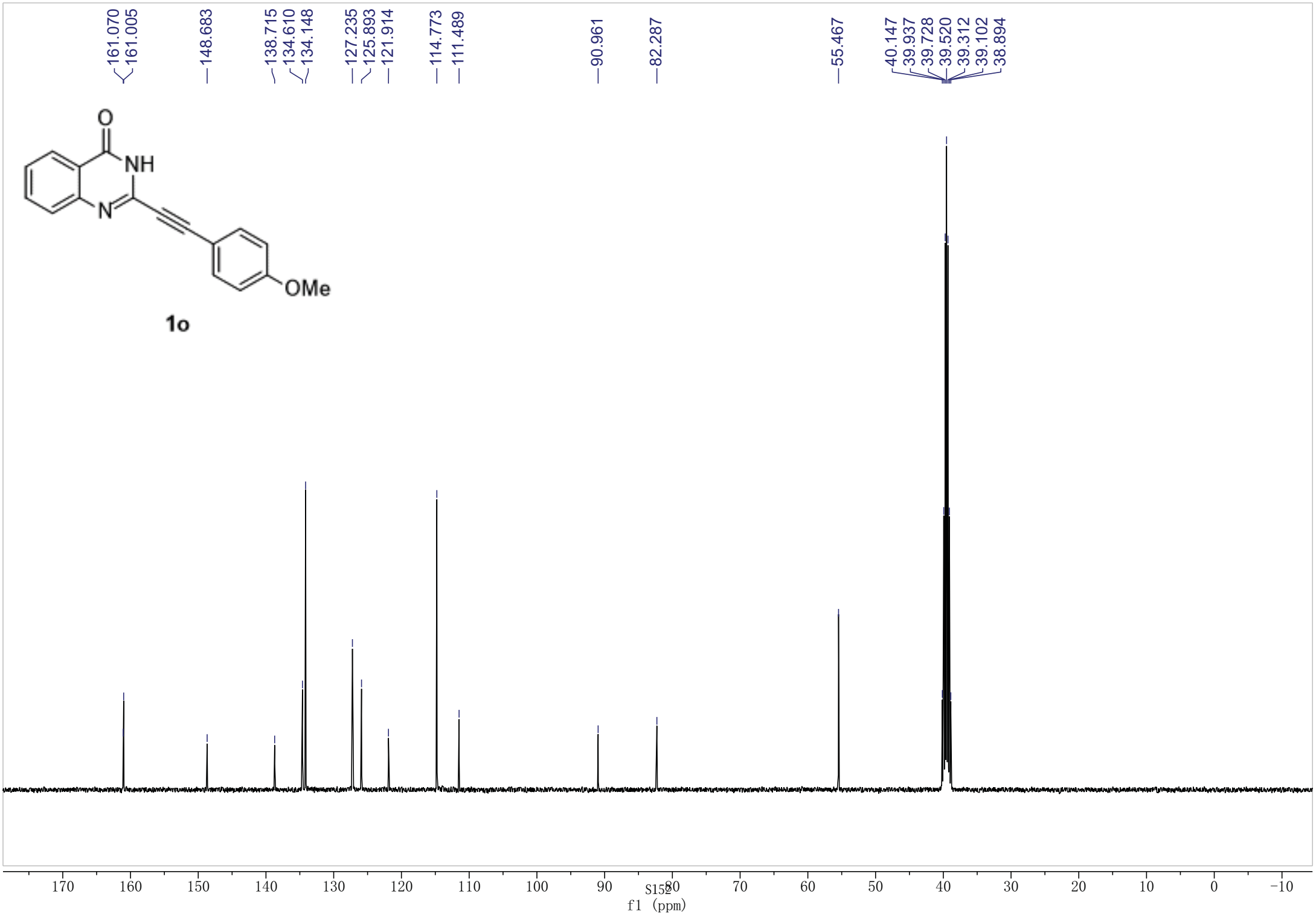
8.1211
8.1050
8.1011
7.8431
7.8392
7.8252
7.8221
7.8187
7.8047
7.8008
7.6712
7.6683
7.6494
7.6424
7.6371
7.6256
7.6203
7.6131
7.5483
7.5453
7.5303
7.5279
7.5254
7.5105
7.5075
7.0668
7.0616
7.0499
7.0446
3.8183
O
NH
N
OMe
1o
1.01
1.01
1.02
3.01
1.07
2.00
3.00
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)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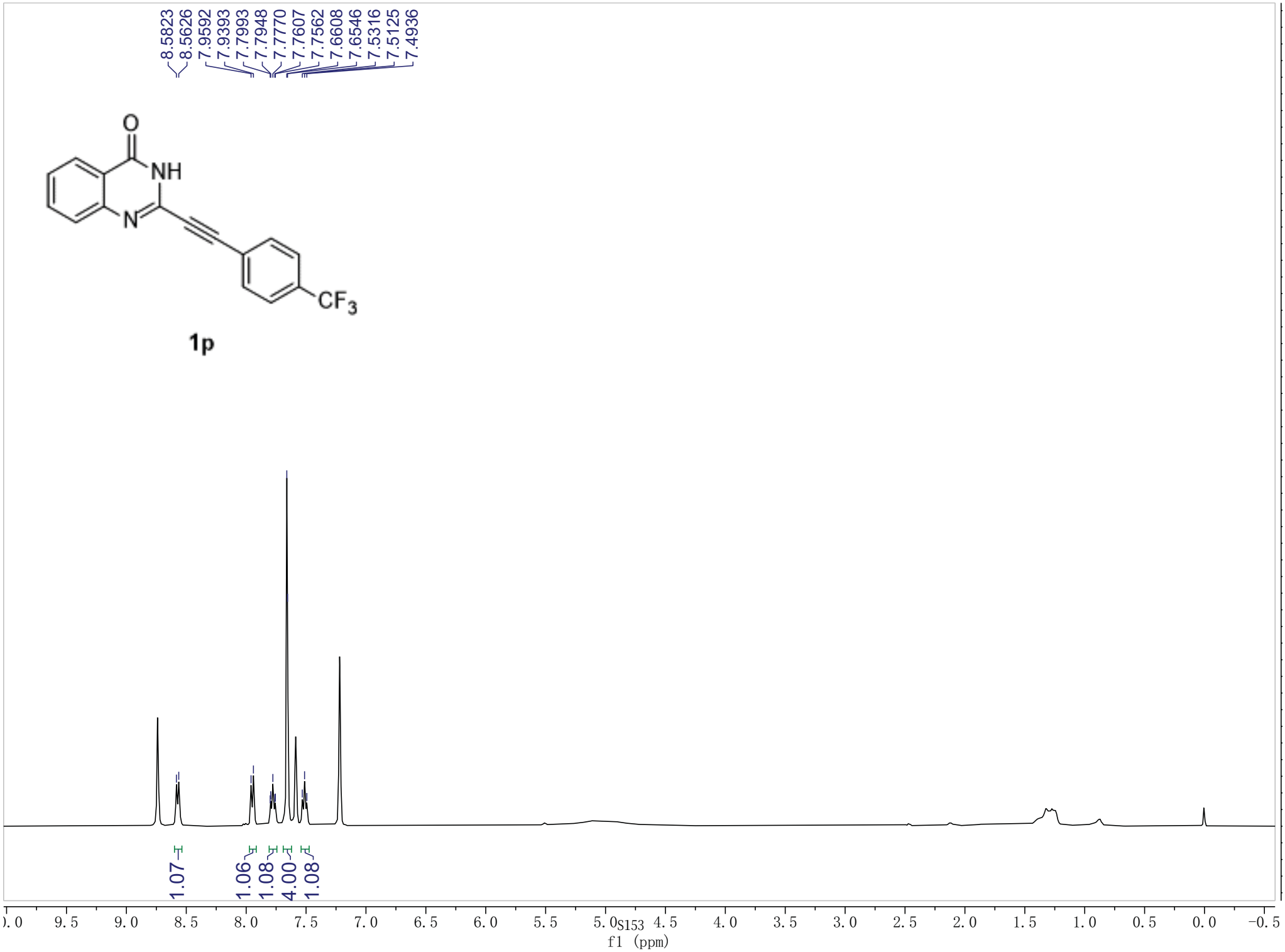
161.005
148.683
138.715
134.610
134.148
127.235
125.893
121.914
114.773
111.489
90.961
82.287
55.467
40.147
39.937
39.728
39.520
39.312
39.102
38.894
O
NH
N
OMe
1o
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)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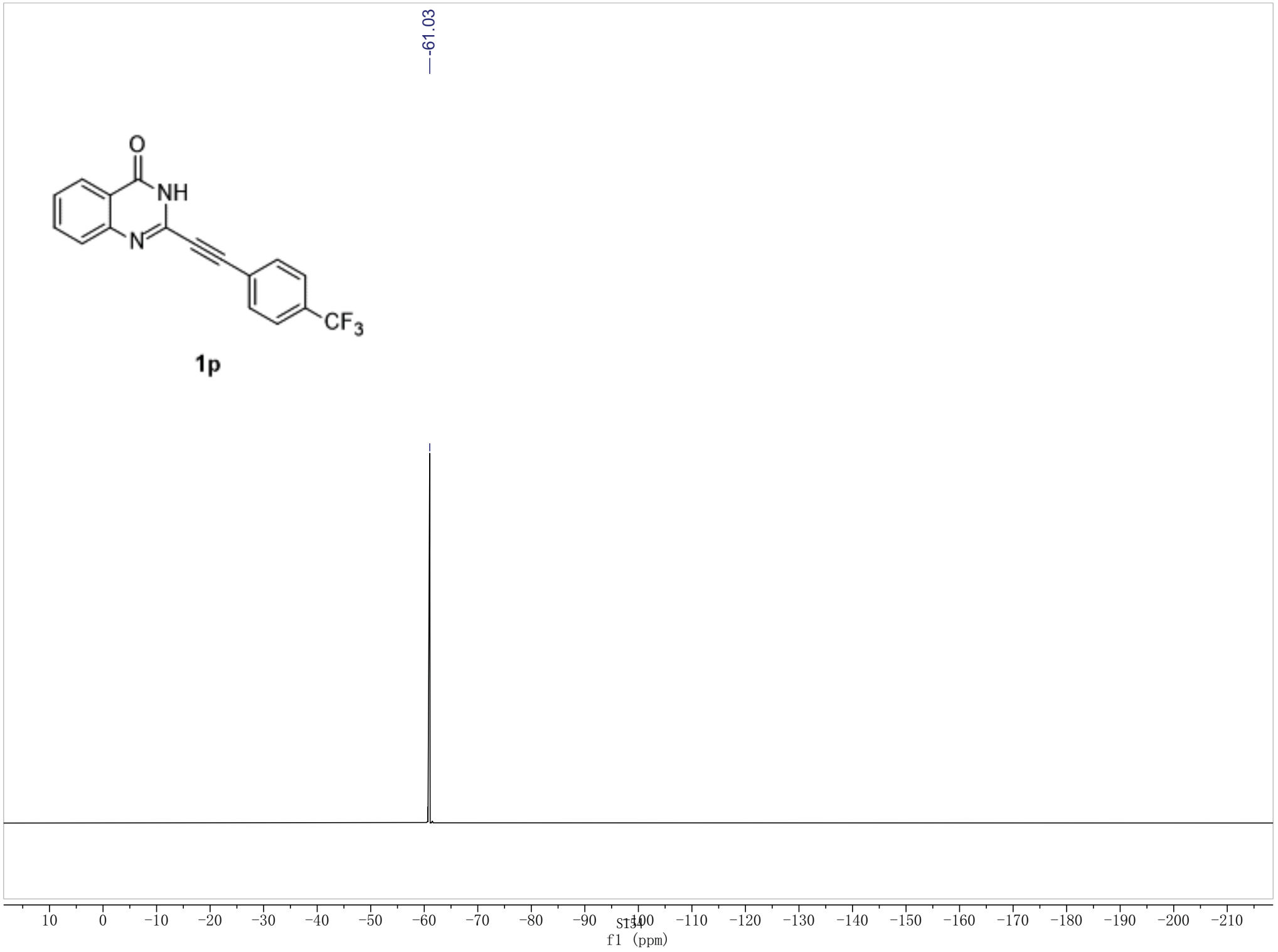
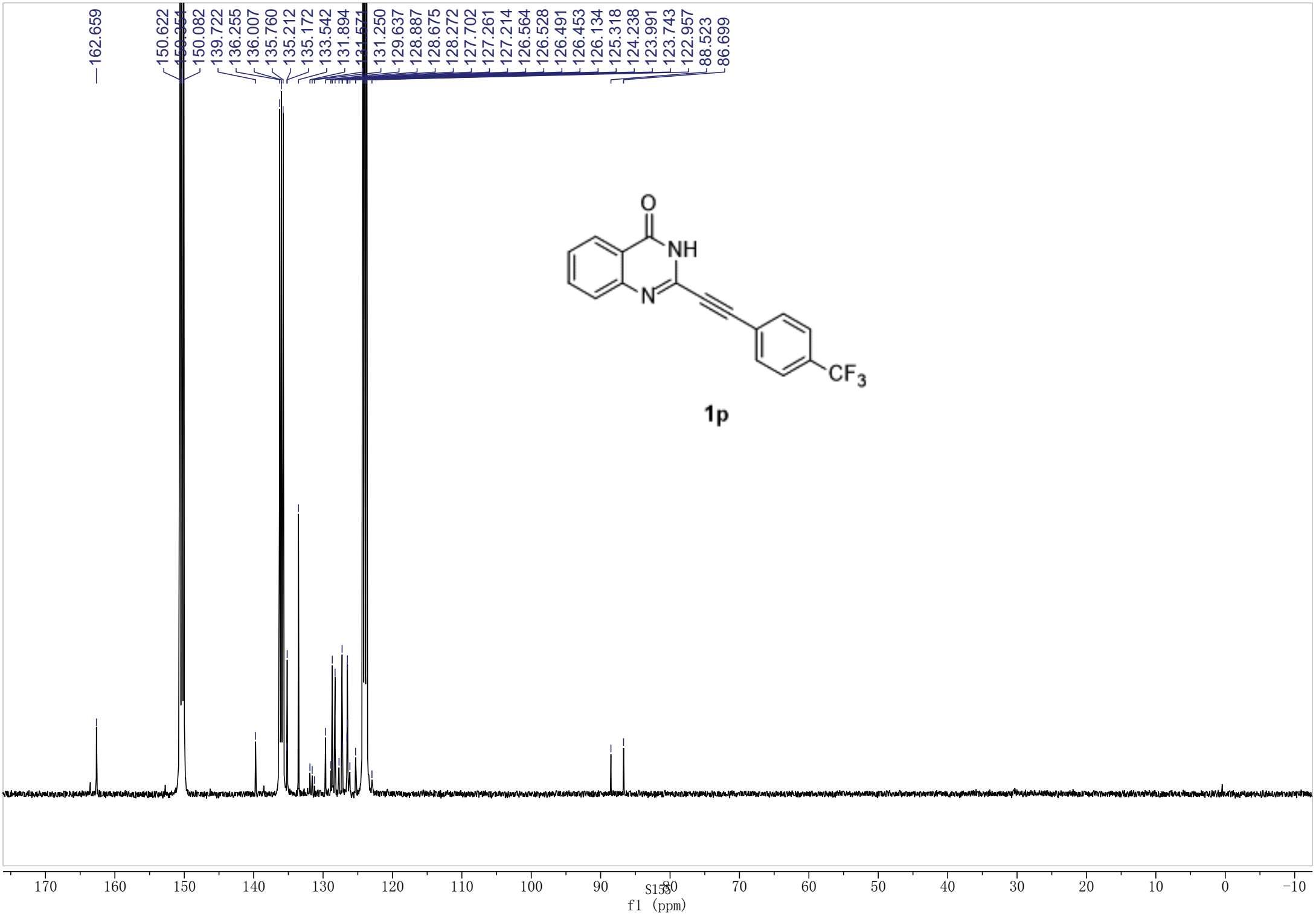
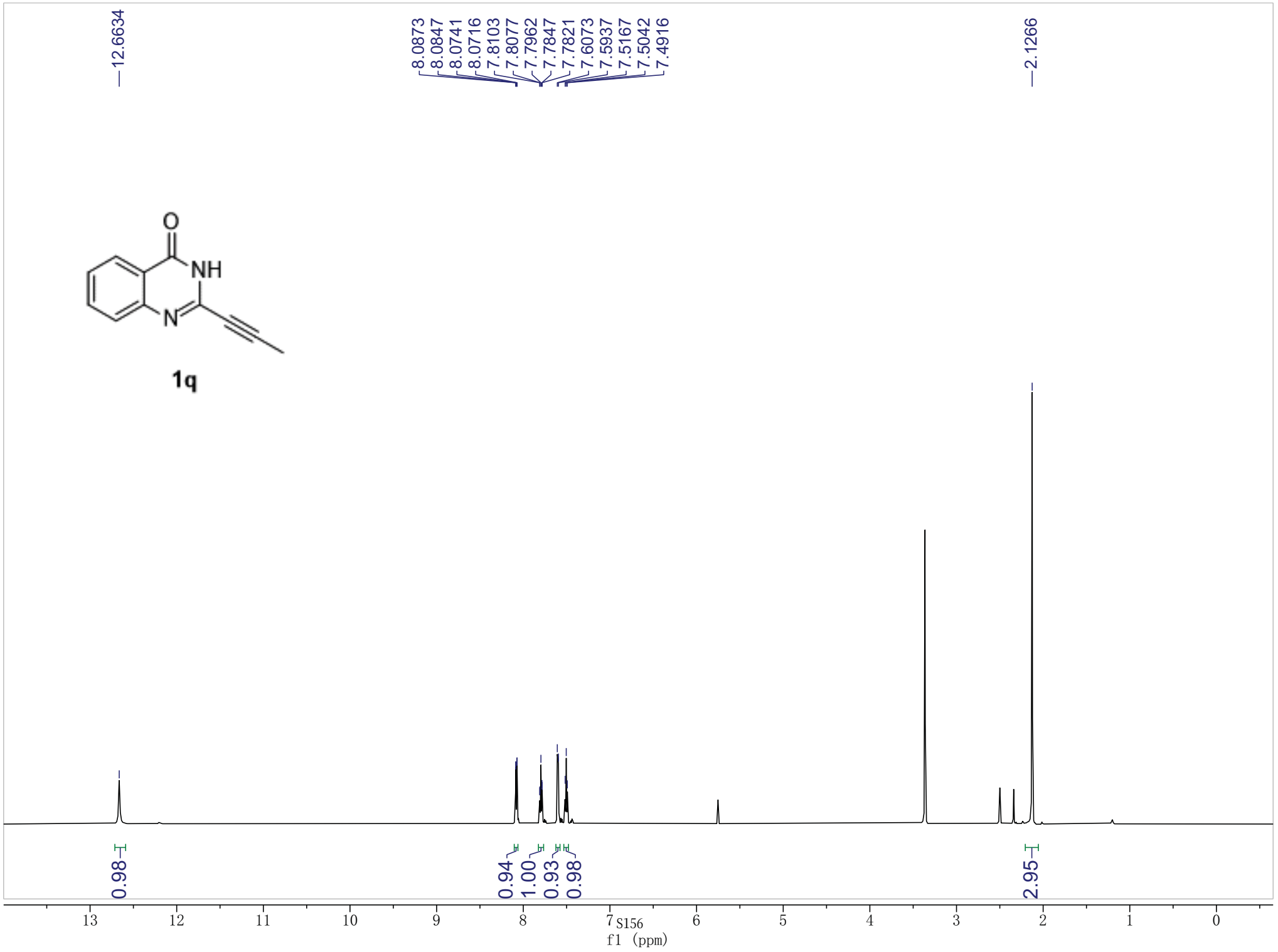
8.5626
7.9592
7.9393
7.7993
7.7948
7.7770
7.7607
7.7562
7.6608
7.6546
7.5316
7.5125
7.4936
O
NH
N
CF3
1p
1.07
1.06
1.08
4.00
1.08
f1 (ppm)


-61.03
O
NH
N
CF3
1p
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


162.659
150.622
150.351
150.082
139.722
136.255
136.007
135.760
135.212
135.172
133.542
131.894
131.571
131.250
129.637
128.887
128.675
128.272
127.702
127.261
127.214
126.564
126.528
126.491
126.453
126.134
125.318
124.238
123.991
123.743
122.957
88.523
86.699
O
NH
N
CF3
1p
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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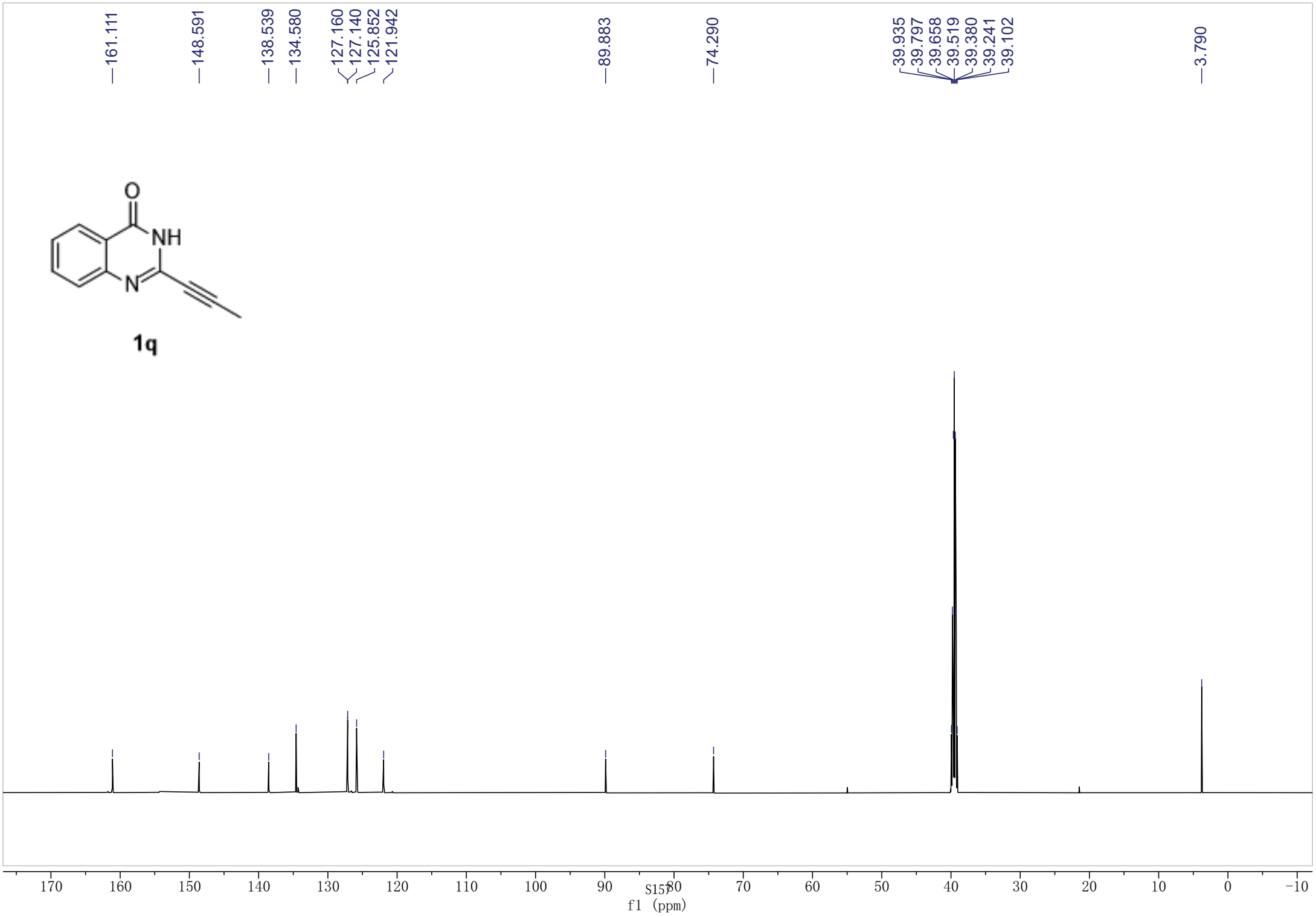
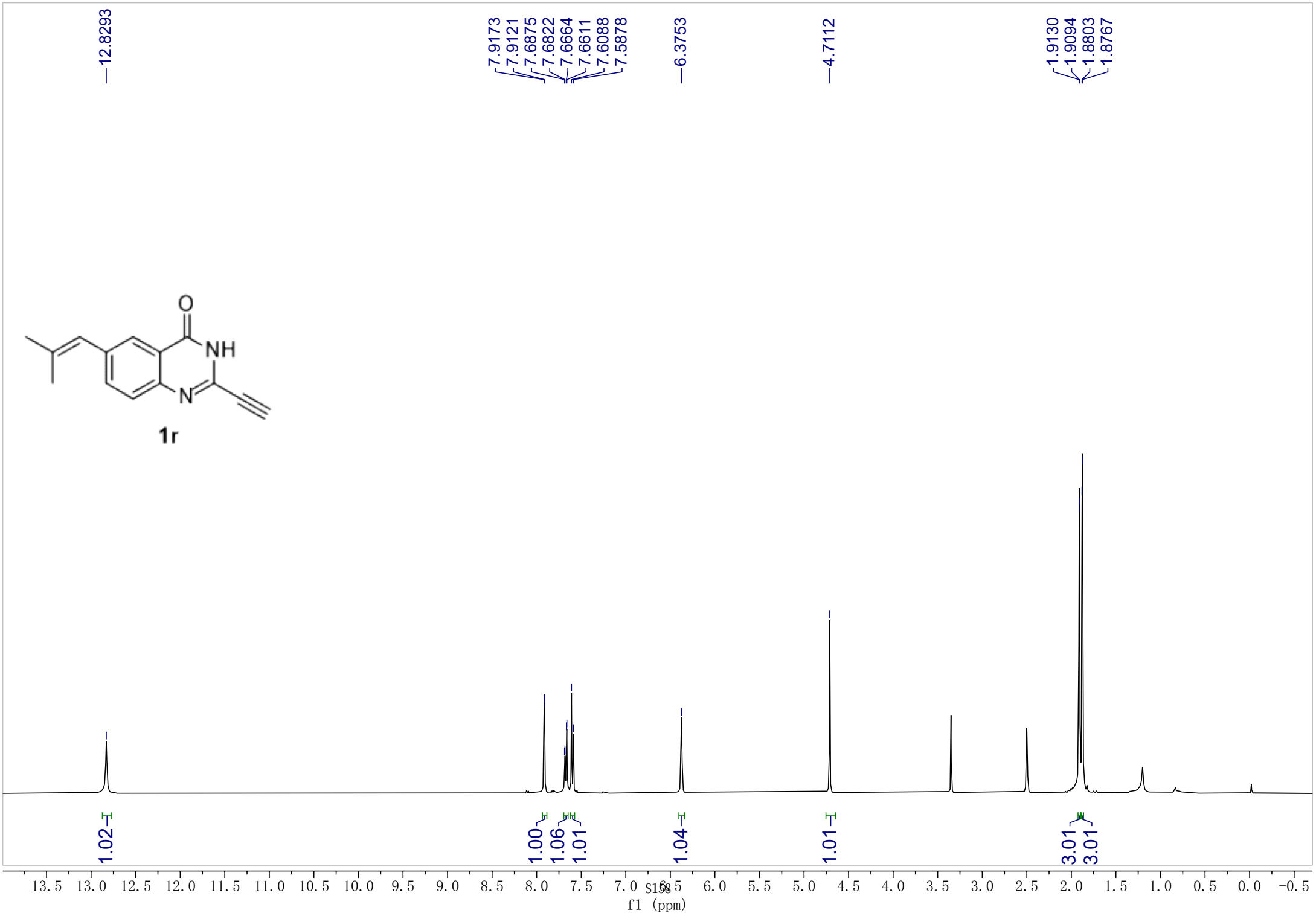
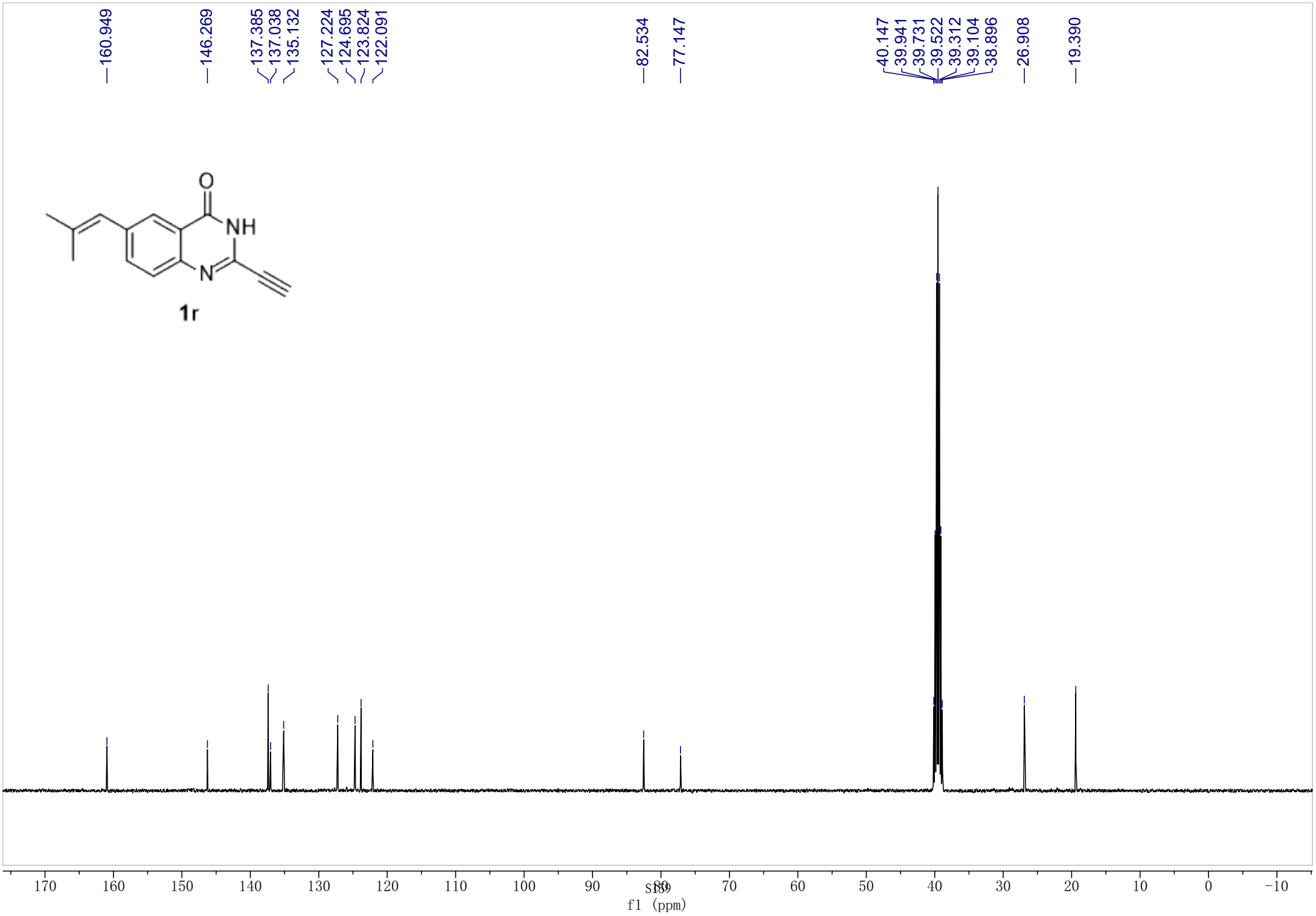
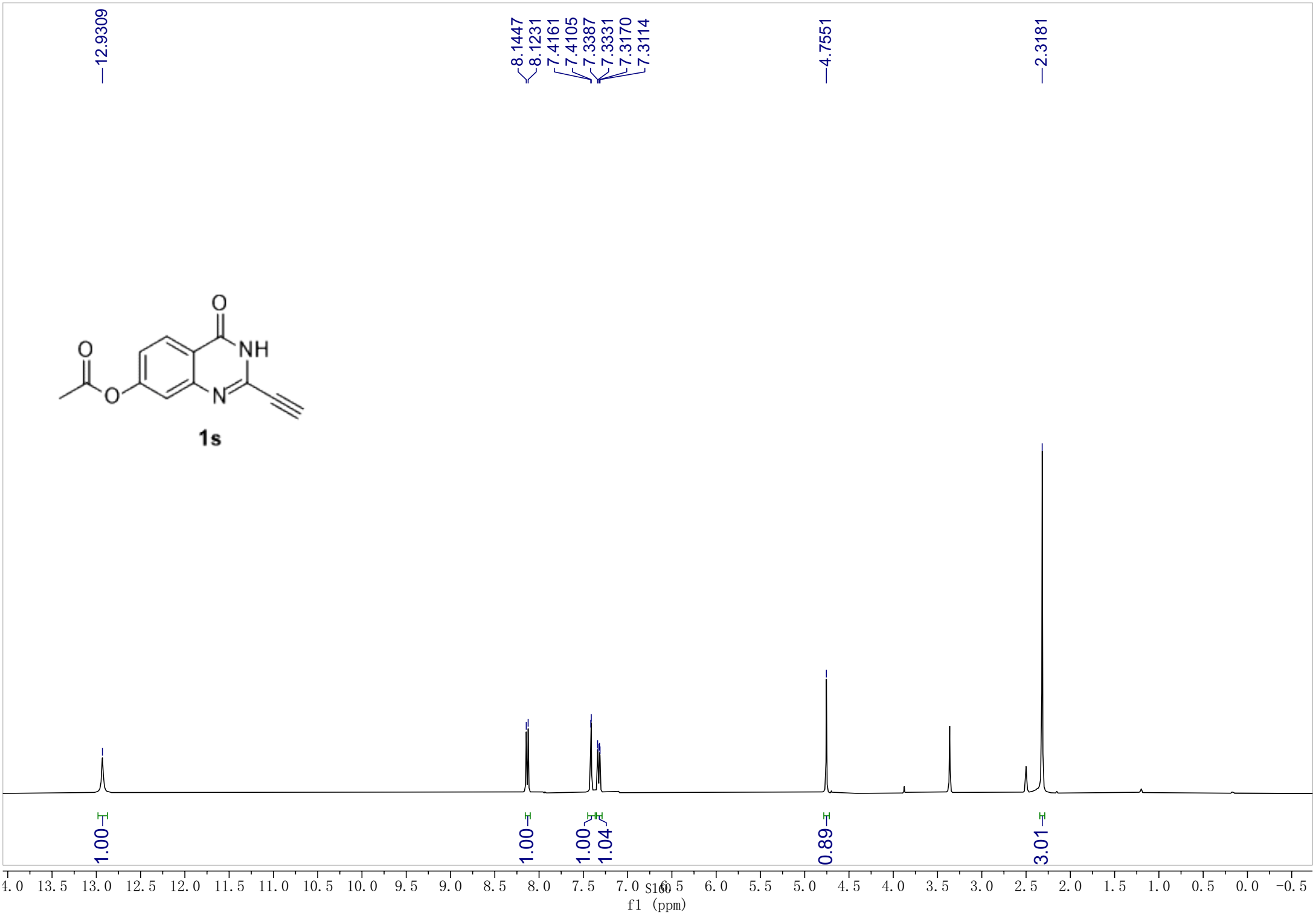
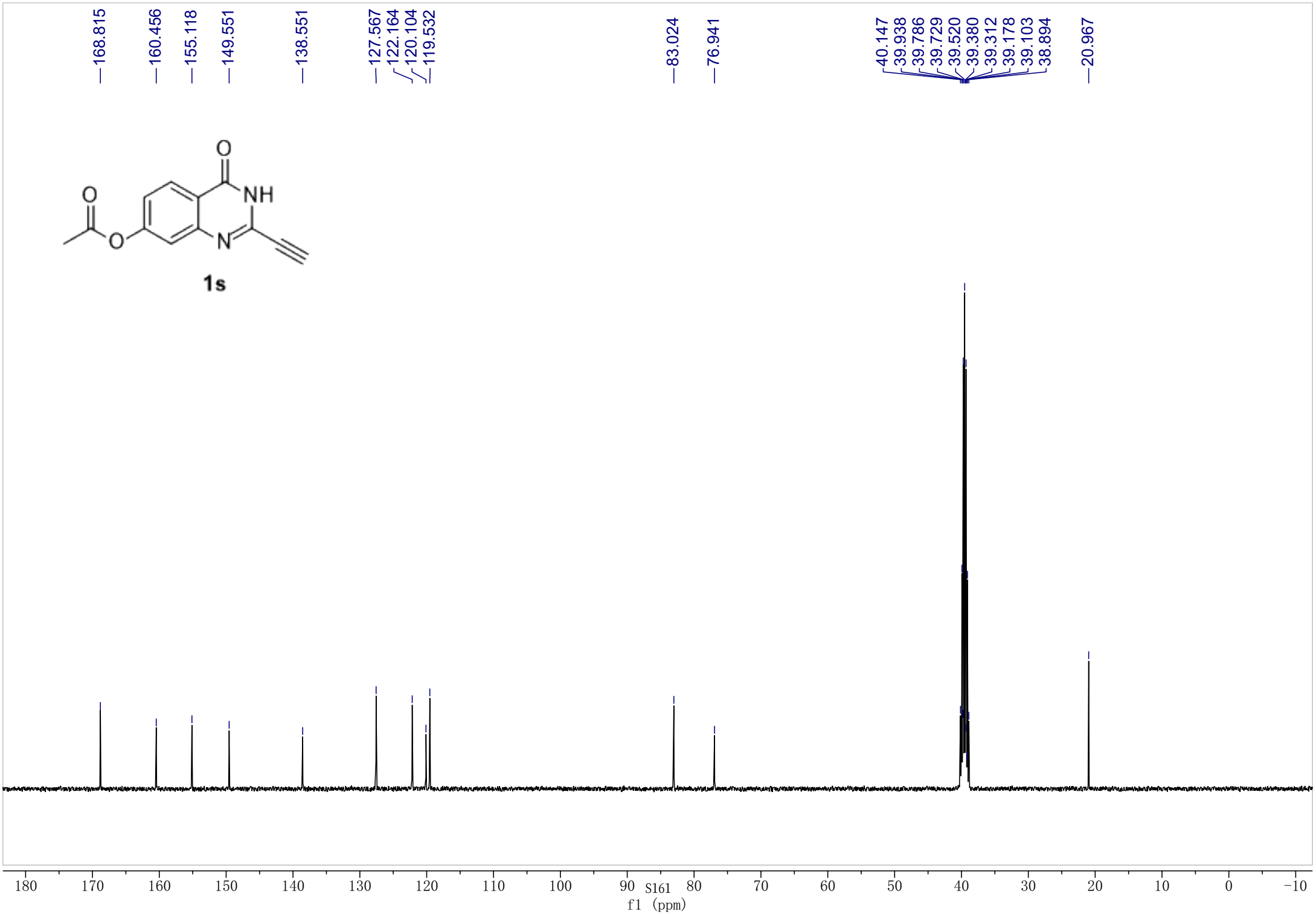
8.0873
8.0847
8.0741
8.0716
7.8103
7.8077
7.7962
7.7847
7.7821
7.6073
7.5937
7.5167
7.5042
7.4916
2.1266
O
NH
N
1q
0.98
0.94
1.00
0.93
0.98
2.95
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

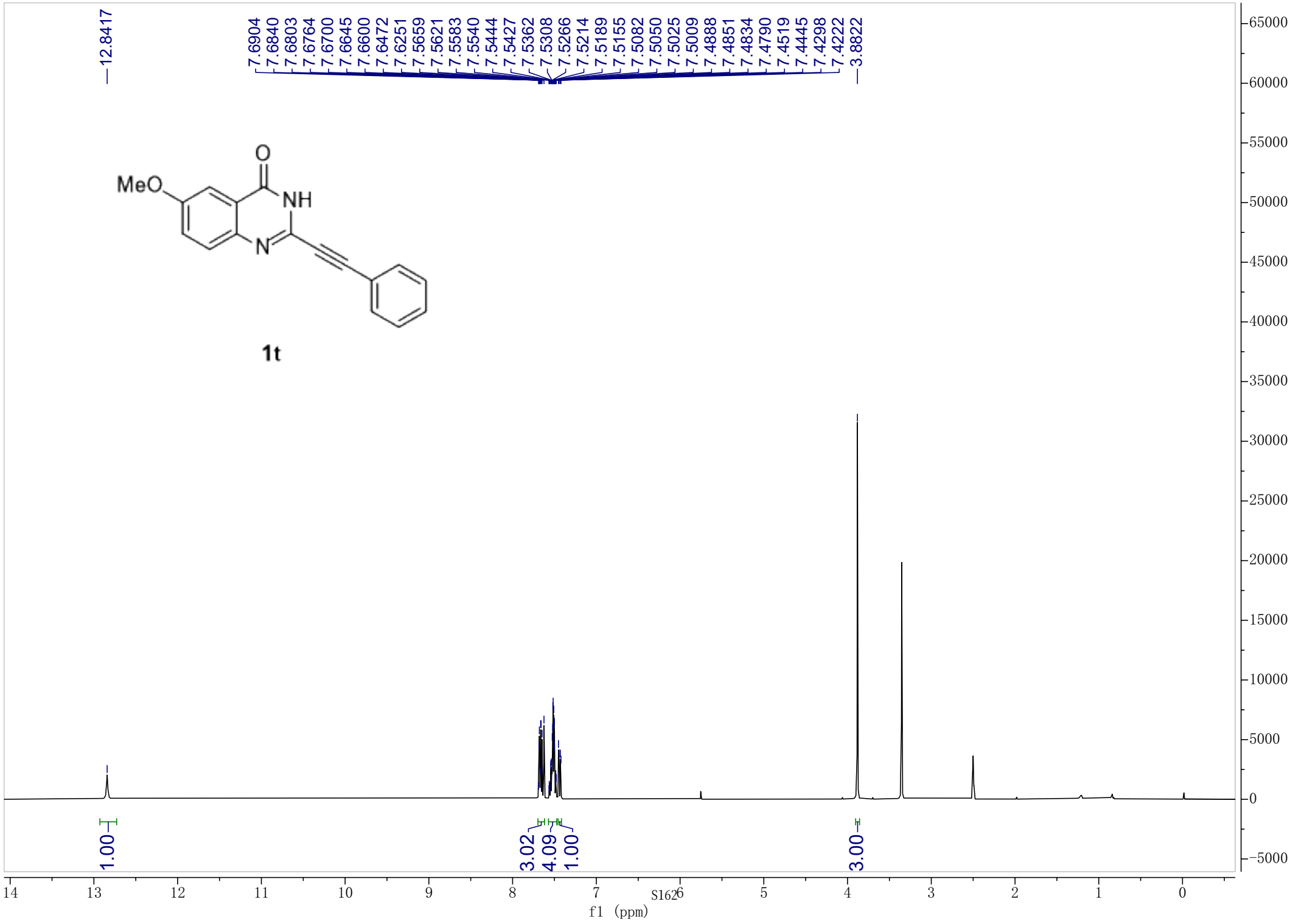

161.111
148.591
138.539
134.580
127.160
127.140
125.852
121.942
89.883
74.290
39.935
39.797
39.658
39.519
39.380
39.241
39.102
3.790
O
NH
N
1q
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

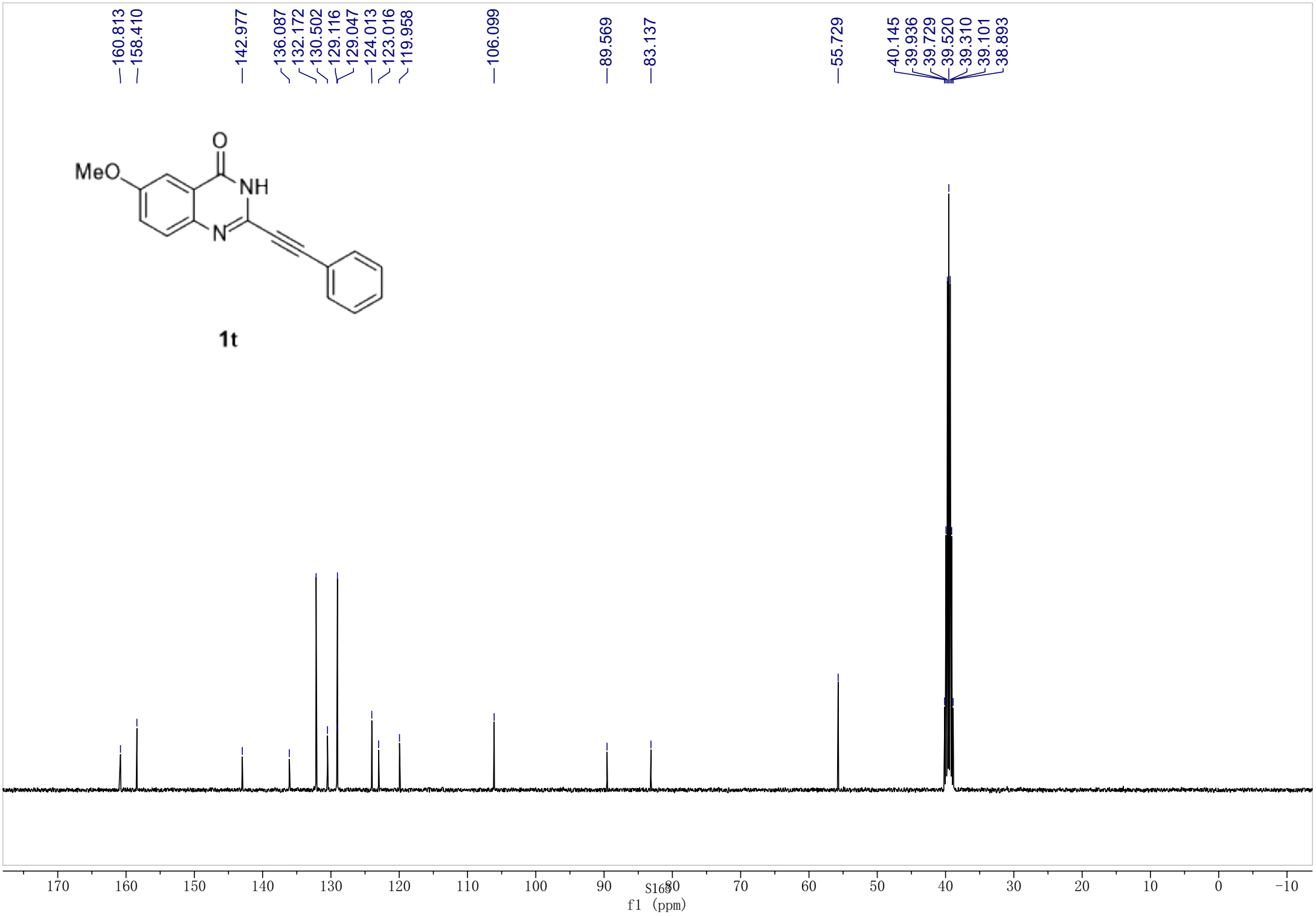

12.8293
7.9173
7.9121
7.6875
7.6822
7.6664
7.6611
7.6088
7.5878
6.3753
4.7112
1.9130
1.9094
1.8803
1.8767
O
NH
N
1r
1.02
1.00
1.06
1.01
1.04
1.01
3.01
3.01
13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

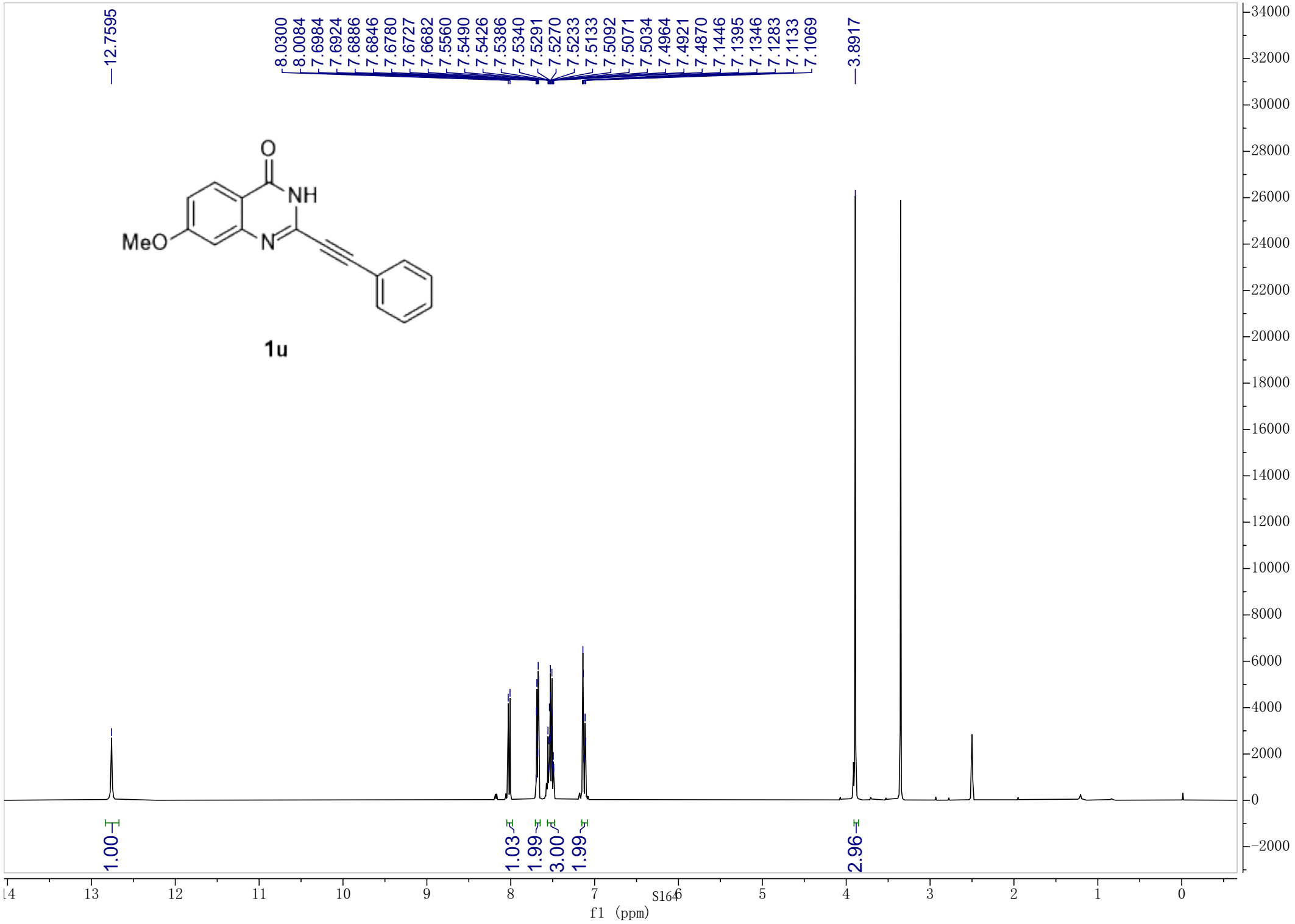

160.949
146.269
137.385
137.038
135.132
127.224
124.695
123.824
122.091
82.534
77.147
40.147
39.941
39.731
39.522
39.312
39.104
38.896
26.908
19.390
O
NH
N
1r
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


12.9309
8.1447
8.1231
7.4161
7.4105
7.3387
7.3331
7.3170
7.3114
4.7551
2.3181
O
NH
O
O
N
1s
1.00
1.00
1.00
1.04
0.89
3.01
f1 (ppm)


168.815
160.456
155.118
149.551
138.551
127.567
122.164
120.104
119.532
83.024
76.941
40.147
39.938
39.786
39.729
39.520
39.380
39.312
39.178
39.103
38.894
20.967
O
NH
O
O
N
1s
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


12.8417
7.6904
7.6840
7.6803
7.6764
7.6700
7.6645
7.6600
7.6472
7.6251
7.5659
7.5621
7.5583
7.5540
7.5444
7.5427
7.5362
7.5308
7.5266
7.5214
7.5189
7.5155
7.5082
7.5050
7.5025
7.5009
7.4888
7.4851
7.4834
7.4790
7.4519
7.4445
7.4298
7.4222
3.8822
MeO
O
NH
N
1t
1.00
3.02
4.09
1.00
3.00
f1 (ppm)


160.813
158.410
142.977
136.087
132.172
130.502
129.116
129.047
124.013
123.016
119.958
106.099
89.569
83.137
55.729
40.145
39.936
39.729
39.520
39.310
39.101
38.893
MeO
O
NH
N
1t
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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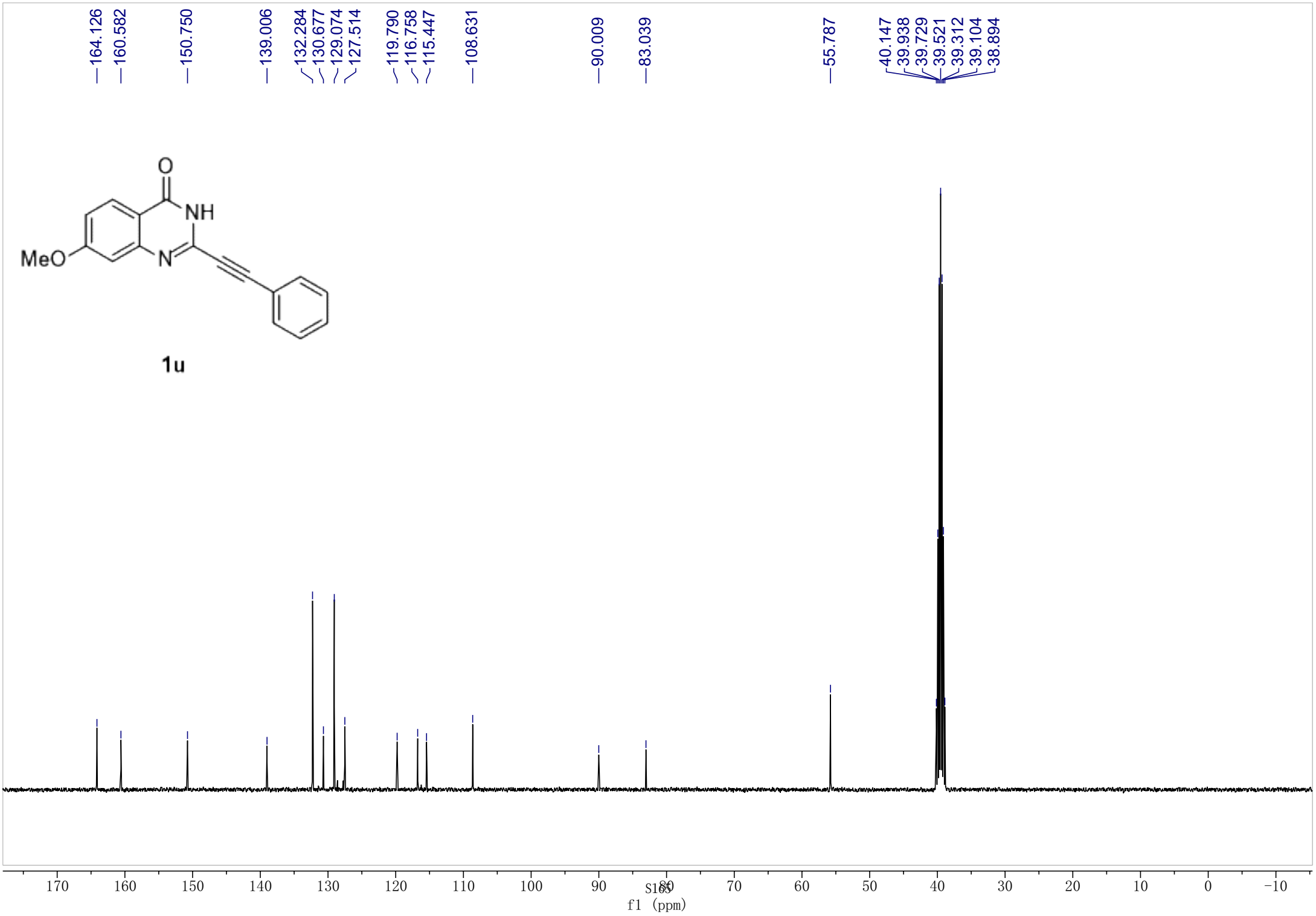
8.0084
7.6984
7.6924
7.6886
7.6846
7.6780
7.6727
7.6682
7.5560
7.5490
7.5426
7.5386
7.5340
7.5291
7.5270
7.5233
7.5133
7.5092
7.5071
7.5034
7.4964
7.4921
7.4870
7.1446
7.1395
7.1346
7.1283
7.1133
7.1069
3.8917
O
NH
MeO
N
1u
1.00
1.03
1.99
3.00
1.99
2.96
f1 (ppm)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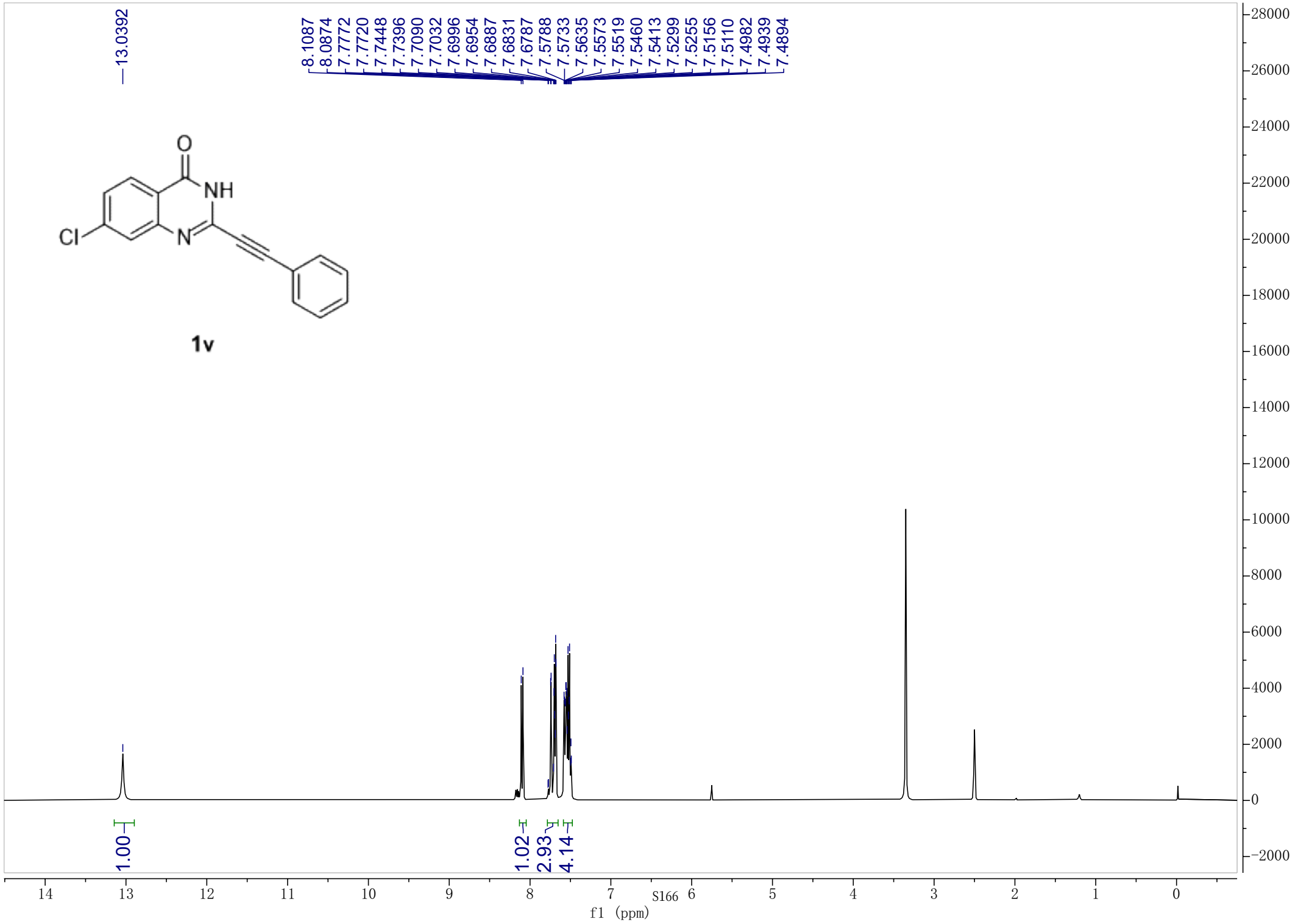
150.750
139.006
132.284
130.677
129.074
127.514
119.790
116.758
115.447
108.631
90.009
83.039
55.787
40.147
39.938
39.729
39.521
39.312
39.104
38.894
O
NH
MeO
N
1u
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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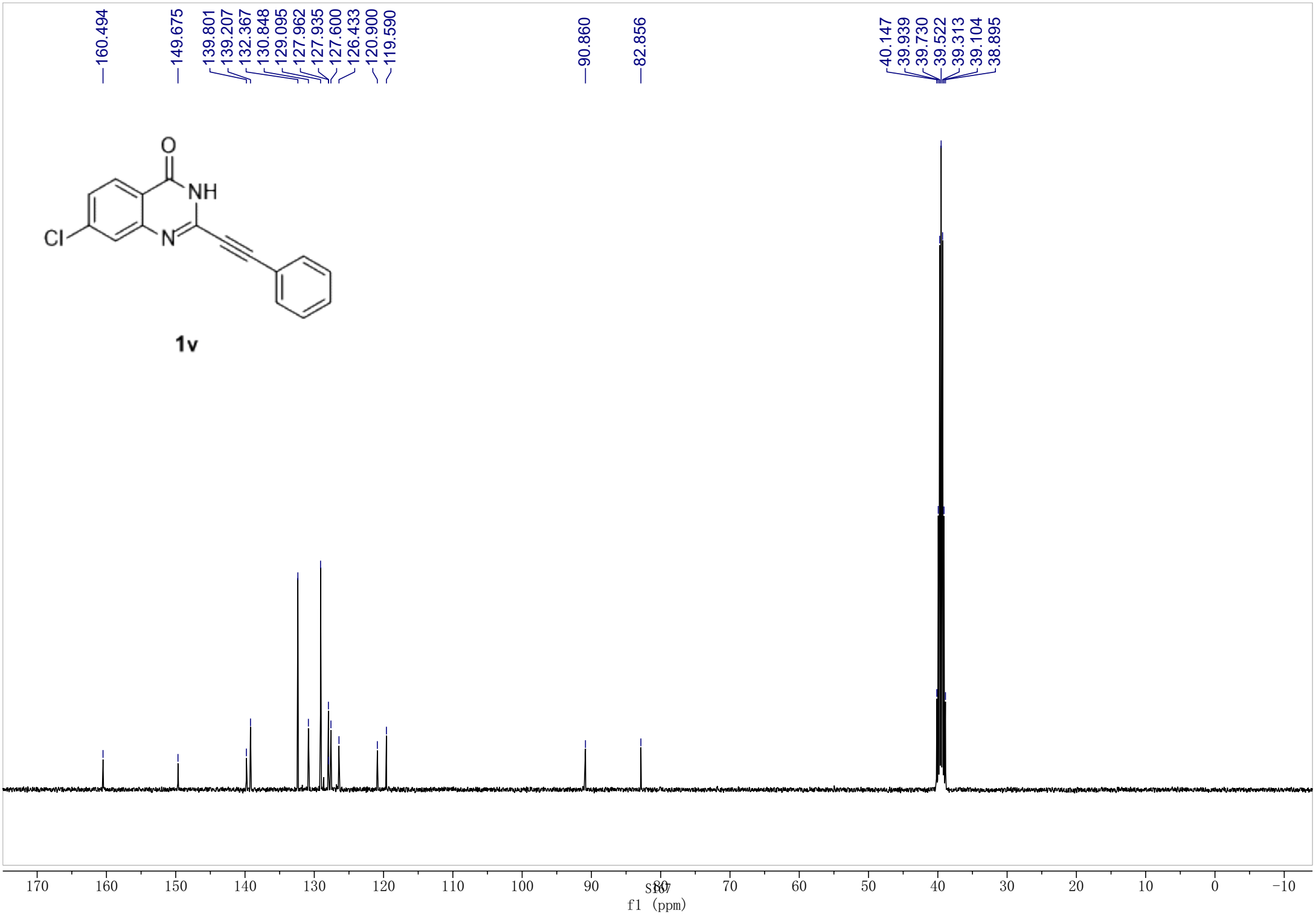
7.7720
7.7448
7.7396
7.7090
7.7032
7.6996
7.6954
7.6887
7.6831
7.6787
7.5788
7.5733
7.5635
7.5573
7.5519
7.5460
7.5413
7.5299
7.5255
7.5156
7.5110
7.4982
7.4939
7.4894
O
NH
Cl
N
1v
1.00
1.02
2.93
4.14
f1 (ppm)
S166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139.801
139.207
132.367
130.848
129.095
127.962
127.935
127.600
126.433
120.900
119.590
90.860
82.856
40.147
39.939
39.730
39.522
39.313
39.104
38.895
O
NH
N
Cl
1v
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)