Supplemental File

Microwave-Assisted, Catalyst and Solvent Free Synthesis of Tryptanthrin Derivatives and Their *in-vitro* Cytotoxic Activity on Prostate DU145 Cancer Cell Lines

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General Information

Melting points were measured with a Buchi B-540 melting point apparatus and are uncorrected. IR spectra were recorded on Elmer FT-IR-2000 spectrometer on a thin film using chloroform. NMR spectra were recorded on Bruker Avance III 500 MHz FT-NMR spectrometer using tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on Trace DSQ GCMS instrument. All the commercially available regents were used as received. All experiments were monitored by thin layer chromatography (TLC). TLC was performed on pre-coated silica gel plates (Merck). Column chromatography was performed on silica gel (100-200 mesh, Merck). All MW reactions were carried out in a Synthos 3000 (Anton Paar) microwave reactor.

Microwave Instrumentation

All microwave reactions were carried out in a Synthos 3000 (Anton Paar) microwave reactor. The multitude microwave has a twin magnetron (2.45 GHz) with maximum output power of 1400 W. The output power can be controlled in unpulsed control mode over whole power which is adjustable in 1 W increment. A Motorola 68xxx series microprocessor system control is used to measure power, pressure, time and temperature during the reaction. The temperature and pressure were monitored throughout the reaction by an infrared detector. The temperature can be measured from 0 to 280 ^{o}C with uncertainty ± 1%. The temperature during the MW reaction was monitored by an externally calibrated IR sensor. The pressure can be measured from 0 to 86 bar with uncertainty ± 0.2 bar. The MW power is initially set at 700 W and the reaction is run. However, during the course of the reaction, once the set temperature and pressure limit is reached, the reactor automatically adjusts the power by lowering it.

General procedure for the synthesis of tryptanthrin derivatives (3): A finely pulverized mixture of isatoic anhydride (**1**, 1.0 mmol) and isatin (**2**, 1.0 mmol) was irradiated in a closed vessel in a Synthos 3000 microwave reactor at 700 Watt (120 ^{o}C and 14 bar) for 15 minutes. After completion of the reaction, the crude product was directly loaded on silica gel column and purified using EtOAc/hexane as the eluent to afford tryptanthrin derivatives **3**.

*Indolo[2,1-b]quinazoline-6,12-dione (**3aa**)*[1,2,3]: Yellow solid (96%); m.p. 270 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.63 (d, *J* = 8.0 Hz, 1H), 8.44 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J* = 7.5 Hz, 1H), 7.85 (t, *J* = 8.0 Hz, 1H), 7.80 (t, *J* = 7.7 Hz, 1H), 7.68 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 182.5, 158.0, 146.5, 146.2, 144.2, 138.2, 135.0, 130.6, 130.2, 127.44, 127.1, 125.31, 123.6, 121.8, 117.9. IR (film, cm^{-1}): 1732, 1681, 1591, 1471, 1338, 1309, 1131, 1022, 921, 761, 673; MS (EI): 248. CHN estimated for $C_{15}H_8N_2O_2$ is C, 72.58; H, 3.25; N, 11.28 and obtained C, 72.51; H, 3.13; N, 11.01.

*8-Methylindolo[2,1-b]quinazoline-6,12-dione (**3ab**)*[2]: Yellow solid (92%); m.p. 283 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.46 (d, *J* = 8.2 Hz, 1H), 8.41 (d, *J* = 8.0 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.83 (t, *J* = 7.5 Hz, 1H), 7.69 (s, 1H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.56 (d, *J* = 8.2, 1H), 2.45 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 182.5, 157.8, 146.52, 144.5, 144.2, 138.8, 137.3, 134.9, 130.5, 130.0, 127.3, 125.4, 123.7, 121.9, 117.5, 21.0. IR (film, cm^{-1}): 1721, 1677, 1576, 1477, 1353, 1301, 1133, 1049, 819, 777. MS (EI): 262.0. CHN estimated for $C_{16}H_{10}N_2O_2$ is C, 73.27; H, 3.84; N, 10.68 and found C, 73.21; H, 3.91; N, 10.53.

*8,10-Dimethyl-indolo[2,1-b]quinazoline-6,12-dione (**3ac**)*: Yellow solid (91%); m.p. 208 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.37 (d, *J* = 7.9 Hz, 1H), 7.99 (d, *J* = 8.1 Hz, 1H), 7.82 (t, *J* = 7.6 Hz, 1H), 7.64 (t, *J* = 7.6 Hz, 1H), 7.58 (s, 1H), 7.41 (s, 1H), 2.74 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 183.1, 157.5, 146.2, 145.4, 143.7, 142.9, 137.6, 134.7, 129.9, 129.9, 128.7, 128.0, 127.6, 124.2, 123.4, 23.1, 20.5. IR (film, cm^{-1}): 3043, 2934, 1726, 1630, 1056, 832, 771. MS (EI): 276. CHN estimated for $C_{17}H_{12}N_2O_2$ is C, 73.90; H, 4.38; N, 10.14; and found C, 73.59; H, 4.43; N, 10.01.

*8-Methoxyindolo[2,1-b]quinazoline-6,12-dione (**3ad**)*: Yellow solid (87%); m.p. 268 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.50 (d, *J* = 8.8 Hz, 1H), 8.41 (d, *J* = 7.9 Hz, 1H), 8.01 (d, *J* = 8.1 Hz, 1H), 7.83 (t, *J* = 7.6 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.37 (d, *J* = 2.7 Hz, 1H), 7.29 (dd, *J* = 8.8 Hz, 2.8 Hz, 1H), 3.89 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 182.5, 158.6, 157.6, 146.5, 144.6, 140.3, 134.8, 130.6, 130.1, 127.3, 124.90, 123.8, 122.8, 119.0, 108.3, 55.9. IR (film, cm^{-1}): 1745, 1695, 1591, 1487, 1279, 825, 776. MS (EI): 278.0. CHN estimated for $C_{16}H_{10}N_2O_3$ is C, 69.06; H, 3.62; N, 10.07 and found C, 69.17; H, 3.51; N, 10.15.

*8-Fluoroindolo[2,1-b]quinazoline-6,12-dione (**3ae**)*[2,3]: Yellow solid (82%); m.p. 275 °C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.63 (dd, *J* = 8.8 Hz, 4.0 Hz, 1H), 8.43 (d, *J* = 7.8 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.86 (t, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.5 Hz, 1H), 7.58 (dd, *J* = 6.5 Hz, 2.7 Hz, 1H), 7.48 (dt, *J* = 8.6 Hz, 2.7 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ

181.6, 162.0, 160.0, 157.7, 146.4, 142.4, 135.1, 130.7, 130.4, 127.4, 124.7 (d, *J* = 23.8 Hz), 123.6, 123.2 (d, *J* = 8.8 Hz), 119.6 (d, *J* = 7.5 Hz), 112.0 (d, *J* = 23.8 Hz). IR (film, cm^{-1}): 3045, 1711, 1665, 1578, 1451, 838, 771. MS (EI): 266. CHN estimated for $C_{15}H_7FN_2O_2$ is C, 67.67; H, 2.65; N, 10.52 and found C, 67.58; H, 2.78; N, 10.41.

*8-Chloroindolo[2,1-b]quinazoline-6,12-dione (**3af**)*[2]: Yellow solid (83%); m.p. 295 ^{o}C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.60 (d, *J* = 8.5 Hz, 1H), 8.44 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 8.2 Hz, 1H), 7.91–7.84 (m, 2H), 7.74 (dd, *J* = 8.5 Hz, 2.5 Hz, 1H), 7.70 (t, *J* = 7.7 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 181.3, 157.8, 146.4, 144.4, 137.6, 135.2, 133.2, 130.8, 130.5, 128.0, 127.5, 125.1, 123.5, 123.0, 119.1. IR (film, cm^{-1}): 1725, 1669, 1461, 1328, 847, 776. MS (EI): 282.0. CHN estimated for $C_{15}H_7ClN_2O_2$ is C, 63.73; H, 2.50; N, 9.91 and found C, 63.65; H, 2.58; N, 10.15.

*8-Bromoindolo[2,1-b]quinazoline-6,12-dione (**3ag**)*[2]: Yellow solid (79%); m.p. 290 ^{o}C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.52 (d, *J* = 8.5 Hz, 1H), 8.42 (d, *J* = 8.0 Hz, 1H), 8.06–7.99 (m, 2H), 7.91–7.84 (m, 2H), 7.69 (t, *J* = 7.6 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 181.2, 157.8, 146.4, 144.8, 143.6, 140.5, 135.2, 130.8, 130.4, 128.1, 127.5, 123.5, 123.3, 120.6, 119.4. IR (film, cm^{-1}): 2927, 1721, 1685, 1588, 1445, 1284, 1172, 837, 776. MS (EI): 326.0. CHN estimated for $C_{15}H_7BrN_2O_2$ is C, 55.07; H, 2.16; N, 8.56 and found C, 55.17; H, 2.09; N, 8.48.

*8-Trifluoromethoxyindolo[2,1-b]quinazoline-6,12-dione (**3ah**)*: Yellow solid (81%); m.p. 239 ^{o}C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.66 (d, *J* = 8.7 Hz, 1H), 8.40 (d, *J* = 7.9 Hz, 1H), 8.01 (d, *J* = 8.0 Hz, 1H), 7.86 (t, *J* = 7.6 Hz, 1H), 7.75 (s, 1H), 7.68 (t, *J* = 7.6 Hz, 1H), 7.62 (d, *J* = 8.8 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 181.3, 157.7, 147.6, 146.3, 144.2, 144.0, 135.3, 130.8, 130.5, 130.4, 127.5, 123.4, 123.0, 121.2, 119.3, 117.5. IR (film, cm^{-1}): 2920, 1737, 1680, 1594, 1211, 1188, 1169, 773. MS (EI): 332.0. CHN estimated for $C_{16}H_7F_3N_2O_3$ is C, 57.84; H, 2.12; N, 8.43 and found C, 57.78; H, 2.23; N, 8.36.

*3-chloroindolo[2,1-b]quinazoline-6,12-dione (**3ba**)*: Yellow solid (78%); m.p. 269 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60 (d, *J* = 8.1 Hz, 1H), 8.36 (d, *J* = 8.5 Hz, 1H), 8.00 (s, 1H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.80 (t, *J* = 7.8 Hz, 1H), 7.62 (dd, *J* = 8.5 Hz, 2.0 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 182.1, 157.4, 147.4, 146.0, 145.1, 141.4, 138.4, 130.5, 129.7, 128.6, 127.9, 127.4, 125.4, 121.9, 117.8. IR (film, cm^{-1}): 2921, 1726, 1675, 1586, 1349, 1316, 756. MS (EI): 282. CHN estimated for $C_{15}H_7ClN_2O_2$ is C, 63.73; H, 2.50; N, 9.91 and found C, 63.77; H, 2.53; N, 9.87.

*2-chloroindolo[2,1-b]quinazoline-6,12-dione (**3ca**)*: Yellow solid (81%); m.p. 316 ^{o}C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.62 (d, *J* = 8.1 Hz, 1H), 8.41 (s, 1H), 7.97 (d, *J* = 9.0 Hz, 1H), 7.93 (d, *J* = 7.5 Hz, 1H), 7.85-7.76 (m, 2H), 7.45 (t, *J* = 7.5 Hz, 1H). ^{13}C NMR (125

MHz, DMSO-d_6) δ 182.5, 157.1, 146.1, 145.6, 138.2, 135.6, 134.7, 132.3, 129.7, 127.5, 126.4, 125.2, 123.8, 122.6, 117.4. IR (film, cm^{-1}): 2923, 1727, 1685, 1591, 1463, 1354, 1314, 1112, 756. MS (EI): 282. CHN estimated for $C_{15}H_7ClN_2O_2$ is C, 63.73; H, 2.50; N, 9.91 and found C, 63.61; H, 2.55; N, 9.83.

*2-bromoindolo[2,1-b]quinazoline-6,12-dione (**3da**)*: Yellow solid (74%); m.p. 307 ^oC. ^1H NMR (500 MHz, Chloroform-*d*) δ 8.61 (d, *J* = 8.5 Hz, 1H), 8.57 (s, 1H), 7.96-7.87 (m, 3H), 7.81 (t, *J* = 7.7 Hz, 1H), 7.45 (t, *J* = 7.7 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 182.1, 156.7, 145.9, 145.3, 138.3, 138.2, 132.0, 130.2, 127.4, 125.4, 125.0, 124.6, 121.8, 117.9. IR (film, cm^{-1}): 2922, 1726, 1684, 1589, 1461, 1314, 1108, 756. MS (EI): 326. CHN estimated for $C_{15}H_7BrN_2O_2$ is C, 55.07; H, 2.16; N, 8.56 and found C, 55.21; H, 2.12; N, 8.59.

*3-chloro-8-methylindolo[2,1-b]quinazoline-6,12-dione (**3bb**)*: Yellow solid (78%); m.p. 265 ^oC. ^1H NMR (500 MHz, Chloroform-*d*) δ 8.44 (d, *J* = 8.2 Hz, 1H), 8.34 (d, *J* = 8.5 Hz, 1H), 7.98 (s, 1H), 7.70 (s, 1H), 7.63–7.56 (m, 2H), 2.46 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 182.2, 157.2, 147.6, 145.4, 141.2, 138.9, 137.7, 130.4, 129.9, 128.6, 125.6, 122.1, 121.8, 117.6, 21.0. IR (film, cm^{-1}): 2923, 1729, 1687, 1589, 1487, 1311, 1224, 1072, 776. MS (EI): 296. CHN estimated for $C_{16}H_9ClN_2O_2$ is C, 64.77; H, 3.06; N, 9.44 and found C, 64.79; H, 3.12; N, 9.39.

*8-bromo-3-chloroindolo[2,1-b]quinazoline-6,12-dione (**3bg**):* Yellow solid (81%); m.p. 280 ^oC. ^1H NMR (500 MHz, Chloroform-*d*) δ 8.51 (d, *J* = 8.6 Hz, 1H), 8.36 (d, *J* = 8.5 Hz, 1H), 8.02 (d, *J* = 11.5 Hz, 2H), 7.90 (dd, *J* = 8.5 Hz, 2.0 Hz, 1H), 7.64 (dd, *J* = 8.5 Hz, 1.9 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 180.9, 157.2, 147.5, 144.7, 144.6, 141.6, 140.7, 130.9, 130.2, 128.8, 128.2, 123.1, 121.9, 120.9, 119.4. IR (film, cm^{-1}): 2923, 1734, 1675, 1585, 1456, 1182, 1072, 777. MS (EI): 360. CHN estimated for $C_{15}H_6BrClN_2O_2$ is C, 49.83; H, 1.67; N, 7.75 and found C, 49.76; H, 1.61; N, 7.71.

*3-chloro-8-nitroindolo[2,1-b]quinazoline-6,12-dione (**3bi**)* : Yellow solid (74%); m.p. 281 ^oC. ^1H NMR (500 MHz, Chloroform-*d*) δ 8.84 (d, *J* = 8.8 Hz, 1H), 8.76 (d, *J* = 2.3 Hz, 1H), 8.70 (dd, *J* = 8.8 Hz, 2.3 Hz, 1H), 8.40 (d, *J* = 8.5 Hz, 1H), 8.04 (d, *J* = 2.0 Hz, 1H), 7.69 (dd, *J* = 8.5 Hz, 2.0 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 180.9, 157.7, 149.3, 147.7, 146.7, 146.1, 140.7, 133.0, 130.7, 129.6, 129.4, 123.4, 122.0, 120.0, 118.1. IR (film, cm^{-1}): 2921, 1730, 1701, 1585, 1527, 1351, 1313, 850, 780. MS (EI): 327. CHN estimated for $C_{15}H_6ClN_3O_4$ is C, 54.98; H, 1.85; N, 12.82 and found C, 54.91; H, 1.88; N, 12.78.

*2,8-Dimethylindolo[2,1-b]quinazoline-6,12-dione (**3eb**)*[2]: Yellow solid (90%); m.p. 251 ^oC. ^1H NMR (500 MHz, Chloroform-*d*) δ 8.44 (d, *J* = 8.5 Hz, 1H), 8.18 (s, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.67 (s, 1H), 7.63 (dd, *J* = 8.2 Hz, 2.0 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 1H), 2.54 (s,

3H), 2.44 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 182.6, 157.8, 144.4, 144.1, 143.9, 141.0, 138.6, 137.2, 136.1, 130.4, 127.1, 125.3, 123.4, 122.0, 117.5, 21.5, 21.0. IR (film, cm^{-1}): 3041, 2909, 1731, 1670, 1606, 1476, 1339, 1312, 1211, 1055, 827, 781. MS (EI): 276. CHN estimated for $C_{17}H_{12}N_2O_2$ is C, 73.90; H, 4.38; N, 10.14 and found C, 73.89; H, 4.42; N, 10.23.

*2,8-Dimethoxyindolo[2,1-b]quinazoline-6,12-dione (**3fd**)*[2,3]: Yellow solid (89%); m.p. 285 ^{o}C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.49 (d, *J* = 8.8 Hz, 1H), 7.92 (d, *J* = 8.8 Hz, 1H), 7.80 (d, *J* = 2.9 Hz, 1H), 7.40–7.35 (m, 2H), 7.31-7.27 (m, 1H), 3.98 (s, 3H), 3.89 (s, 3H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 182.4, 161.2, 158.6, 157.4, 142.9, 140.7, 140.1, 132.2, 125.2, 124.7, 124.0, 123.2, 119.0, 108.1, 107.9, 56.0, 55.9. IR (film, cm^{-1}): 2920, 1730, 1669, 1602, 1488, 1287, 1078, 1020. MS (EI): 308.0. CHN estimated for $C_{17}H_{12}N_2O_4$ is C, 66.23; H, 3.92; N, 9.09 and found C, 66.21; H, 3.98; N, 9.16.

*2,8-Bis-trifluoromethoxyindolo[2,1-b]quinazoline-6,12-dione(**3gh**)*: Yellow solid (82%); m.p. 230 ^{o}C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.69 (d, *J* = 8.5 Hz, 1H), 8.26 (s, 1H), 8.10 (d, *J* = 8.8 Hz, 1H), 7.78 (s, 1H), 7.73–7.62 (m, 2H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 180.9, 156.8, 147.8, 144.6, 144.2, 143.9, 132.8, 130.6, 128.0, 127.8, 127.5, 124.9, 123.0, 121.2, 119.4, 118.5, 117.7. IR (film, cm^{-1}): 2922, 1742, 1683, 1177, 1166, 863, 779. MS (EI): 416.0. CHN estimated for $C_{17}H_6F_6N_2O_4$ is C, 49.05; H, 1.45; N, 6.73 and found C, 49.17; H, 1.48; N, 6.61.

*2,8-Difluoroindolo[2,1-b]quinazoline-6,12-dione (**3he**)*: Yellow solid (76%); m.p. 295 ^{o}C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.63 (dd, *J* = 8.8 Hz, 4.1 Hz, 1H), 8.11-8.02 (m, 2H), 7.61-7.55 (m, 2H), 7.50 (dt, *J* = 8.6 Hz, 2.7 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 181.3, 164.2, 162.1, 160.1, 156.9, 143.0, 142.10, 133.2 (d, *J* = 8.7 Hz), 127.8 (d, *J* = 56.6 Hz), 125.5, 124.8 (d, *J* = 23.8 Hz), 123.4 (d, *J* = 23.8 Hz), 119.6 (d, *J* = 8.8 Hz), 113.2 (d, *J* = 25.0 Hz), 112.1 (d, *J* = 23.8 Hz). IR (film, cm^{-1}): 2911, 2845, 1731, 1684, 1487, 1305, 1277, 1143, 1043 cm^{-1}. MS (EI): 284. CHN estimated for $C_{15}H_6F_2N_2O_2$ is C, 63.39; H, 2.13; N, 9.86 and found C, 63.43; H, 2.17; N, 9.72.

*2,8-Dichloroindolo[2,1-b]quinazoline-6,12-dione (**3cf**)*[2]: Yellow solid (87%); m.p. 290 ^{o}C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.58 (d, *J* = 8.5 Hz, 1H), 8.39 (d, *J* = 2.5 Hz, 1H), 7.97 (d, *J* = 8.5 Hz, 1H), 7.88 (d, *J* = 2.5 Hz, 1H), 7.80 (dd, *J* = 8.5 Hz, 2.5 Hz, 1H), 7.76 (dd, *J* = 8.6 Hz, 2.2 Hz, 1H). ^{13}C NMR (125 MHz, Chloroform-*d*) δ 181.0, 156.7, 144.9, 144.1, 137.7, 136.87, 135.6, 133.5, 132.1, 127.1, 125.2, 124.7, 123.0, 119.2. IR (film, cm^{-1}): 2927, 1745, 1691, 1587, 1469, 1289, 1181, 1035. MS (EI): 315. CHN estimated for $C_{15}H_6Cl_2N_2O_2$ is C, 56.81; H, 1.91; N, 8.83 and found C, 56.68; H, 1.96; N, 8.76.

*3,9-dichloroindolo[2,1-b]quinazoline-6,12-dione (**3bj**)*: Yellow solid (87%); m.p. 267 ^{o}C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.67 (d, *J* = 1.7 Hz, 1H), 8.37 (d, *J* = 8.5 Hz, 1H), 8.01 (d, *J* = 2.0 Hz, 1H), 7.86 (d, *J* = 8.1 Hz, 1H), 7.65 (dd, *J* = 8.5 Hz, 2.0 Hz, 1H), 7.43 (dd, *J* = 8.1 Hz, 1.7 Hz, 1H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 181.3, 157.6, 147.9, 142.0, 140.3, 130.5, 129.5, 129.2, 127.5, 126.7, 122.2, 121.5, 117.5. IR (film, cm^{-1}): 2920, 1718, 1685, 1580, 1352, 1113, 887, 778. MS (EI): 315. CHN estimated for $C_{15}H_6Cl_2N_2O_2$ is C, 56.81; H, 1.91; N, 8.83 and found C, 56.85; H, 1.87; N, 8.86.

*2,8-Dibromoindolo[2,1-b]quinazoline-6,12-dione (**3dg**)*: Yellow solid (73%), m.p. 328 ^{o}C. ^{1}H NMR (500 MHz, Chloroform-*d*) δ 8.56 (s, 1H), 8.51 (d, *J* = 8.5 Hz, 1H), 8.03 (s, 1H), 7.97–7.87 (m, 3H). IR (film, cm^{-1}): 2931, 1721, 1671, 1592, 1456, 1291, 1171, 851, 771. MS (EI): 403.9. CHN estimated for $C_{15}H_6Br_2N_2O_2$ is C, 44.37; H, 1.49; N, 6.90 and found C, 44.44; H, 1.58; N, 6.79.

Reagents for biology:

Minimum Essential Medium, penicillin-streptomycin, fetal bovine serum (FBS), 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) were purchased from Himedia. Keratinocyte Serum Free Medium (K-SFM) was purchased from Invitrogen.

Cell culture:

Prostate cancer cell lines (DU145) and normal prostate epithelial RWPE-1 cells were purchased from the National Centre for Cell sciences (NCCS), Pune, India and American Type Culture Collection (ATCC) respectively. These cell lines were grown and maintained using appropriate culture medium supplemented with 10 % fetal bovine serum, and 1 % penicillin streptomycin antibiotic solution at 37 ºC in 5 % CO_2 incubator. Cells at a concentration of 5,000 cells/well were seeded separately in 96 well microlitre plates and exposed to various concentrations of those compounds (disolved in DMSO). Cell survival fraction was determined using MTT assay. After treatment for 24 h, 48 h and 72 h, MTT (5 mg/ml) was added into each well and incubated for 4 h at 37 °C. The formazan crystals formed were dissolved with DMSO. The intensity of coloured formazan formed was determined by measuring the absorbance at 570 nm using ELISA reader (Dynex MRX, USA). The cytotoxic effect of those compounds on DU145 and RWPE-1 cells were determined by measuring the concentration that inhibits 50 % of the cancer cell population in comparison with the untreated control. The percentage of cell viability was obtained by dividing the absorbance value of the samples treated with different concentrations of compounds with the absorbance value of control and then multiplied by 100 % as previously

described. Dose - response curves of % cell viability versus compound concentration were constructed and IC_{50} determined from the plots by interpolation.

The percentage cell viability was calculated by following formula:

% Cell Viability = (Mean OD of Test/Mean OD of control) x 100

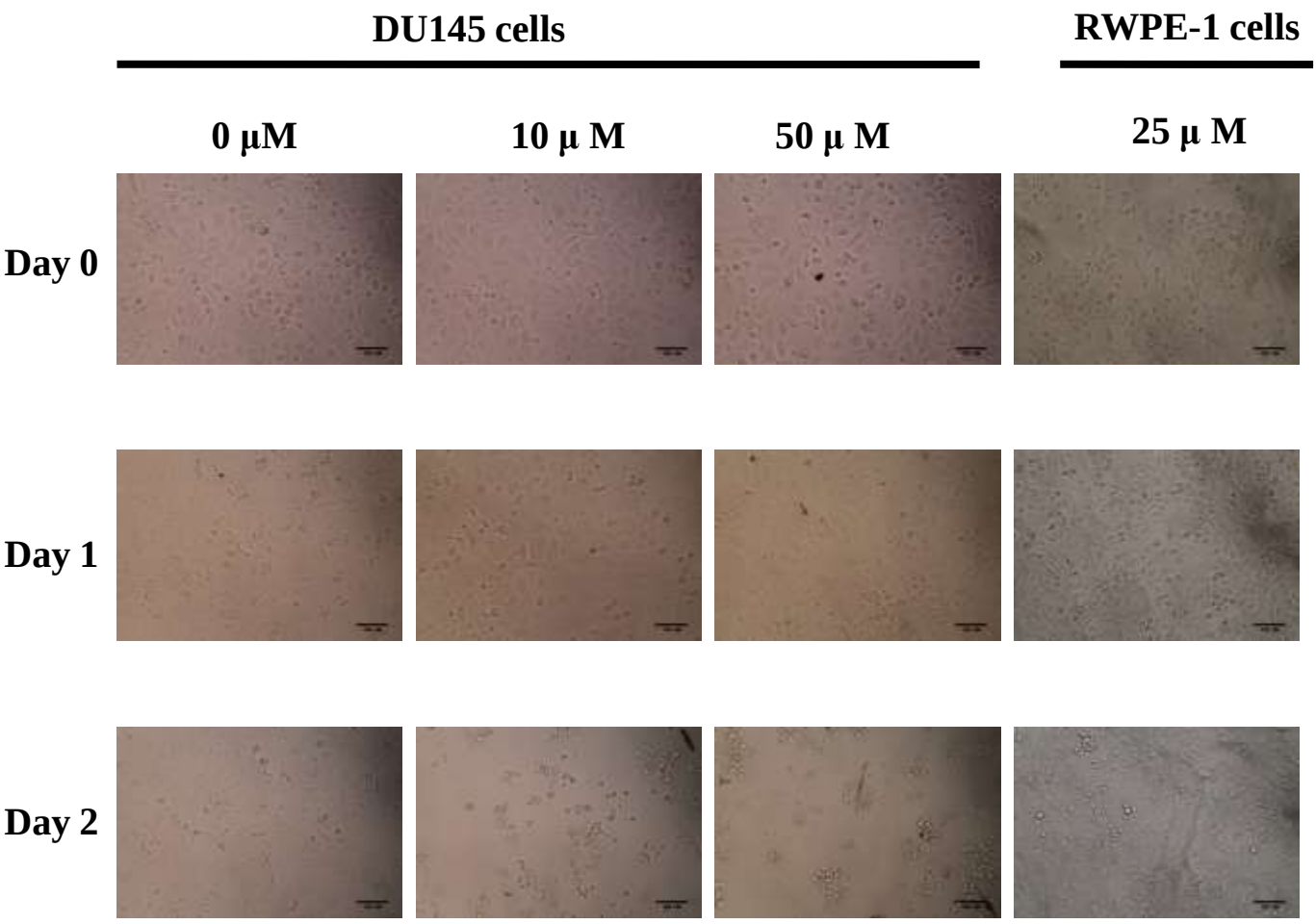


Figure 1. Representative phage contrast microscopic images of cytotoxic effect of **KR-T1** on prostate cancer DU145 cells at 0, 10 and 50 µM concentrations after treatment at on Day 0, Day 1 and Day 2.

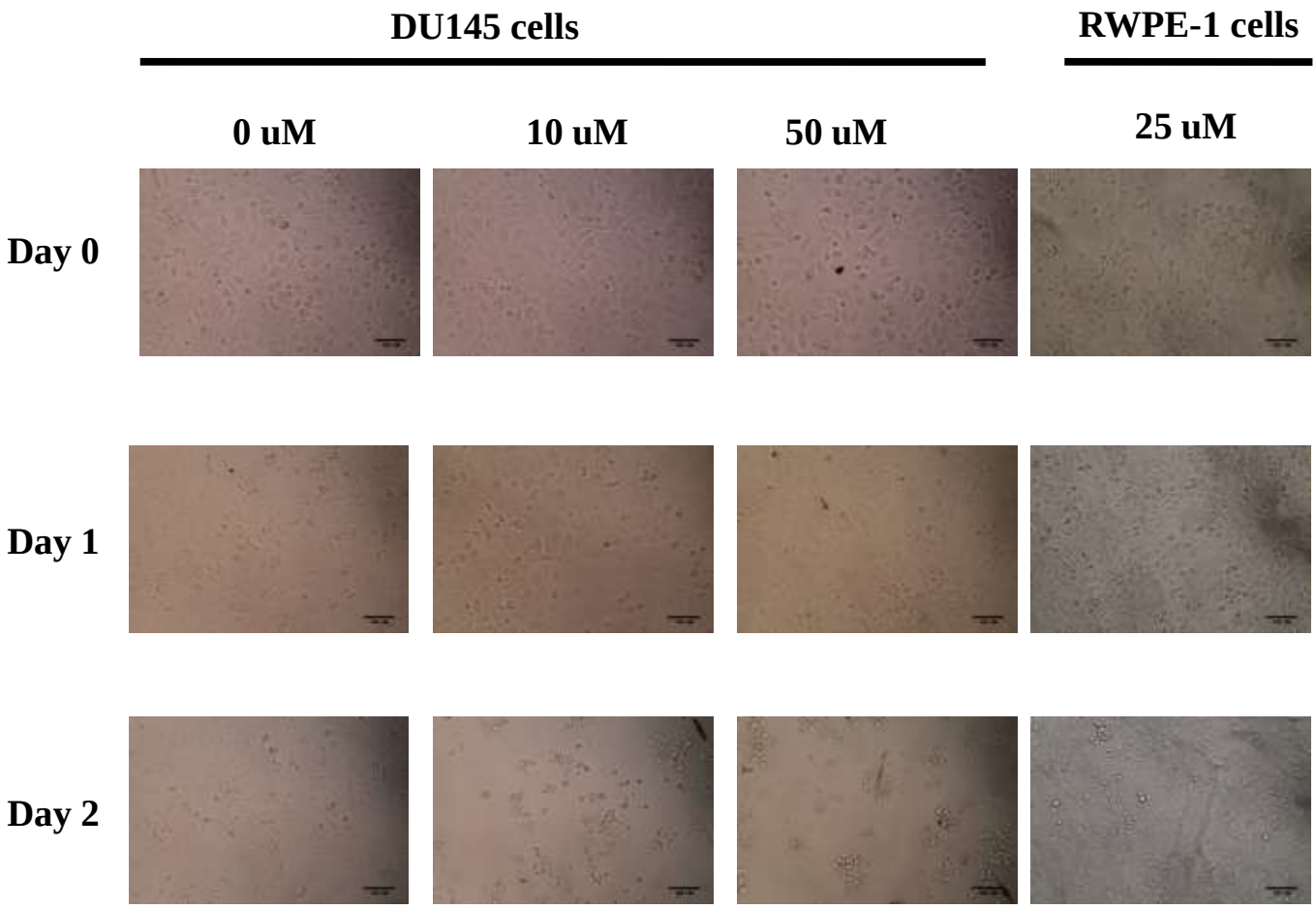
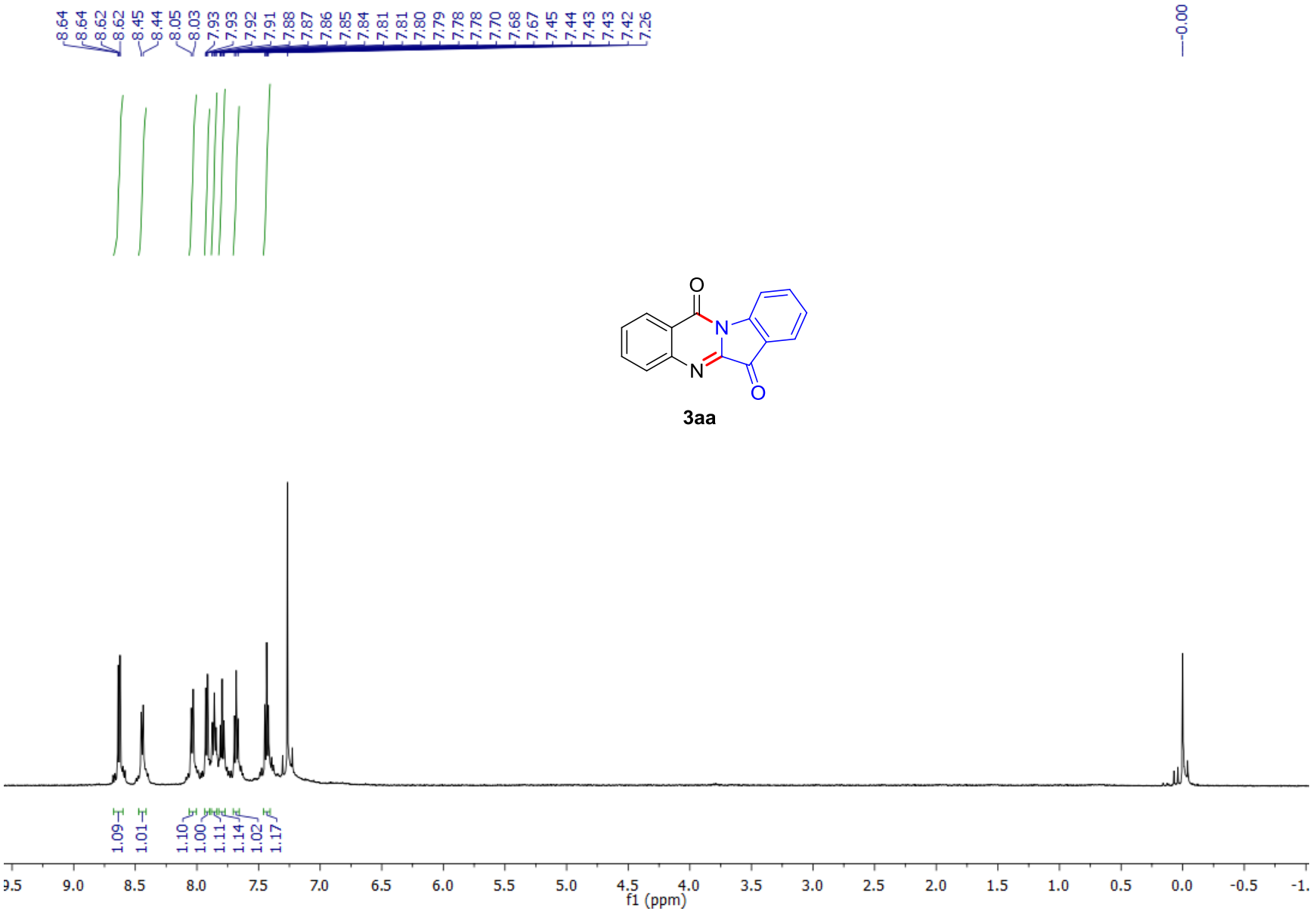


Figure 2. Representative phage contrast microscopic images of cytotoxic effect of **SB-34** on prostate cancer DU145 cells at 0, 10 and 50 μM concentrations after treatmentat on Day 0, Day 1 and Day 2.

References:

1. A. Kumar, V. D. Tripathi and P. Kumar, *Green Chem.*, 2011, **13**, 51-54.
2. M. A. E. A. A. Ali El-Remaily and O. M. Elhady, *Tetrahedron Lett.*, 2016, **57**, 435-437
3. S. Yang, X. Li, F. Hu, Y. Li, Y. Yang, J. Yan, C. Kuang, and Q. Yang, *J. Med. Chem.*, 2013, **56**, 8321-8331.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7.78
7.70
7.68
7.67
7.45
7.44
7.43
7.43
7.42
7.26
-0.00
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1.00
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1.14
1.02
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f1 (ppm)

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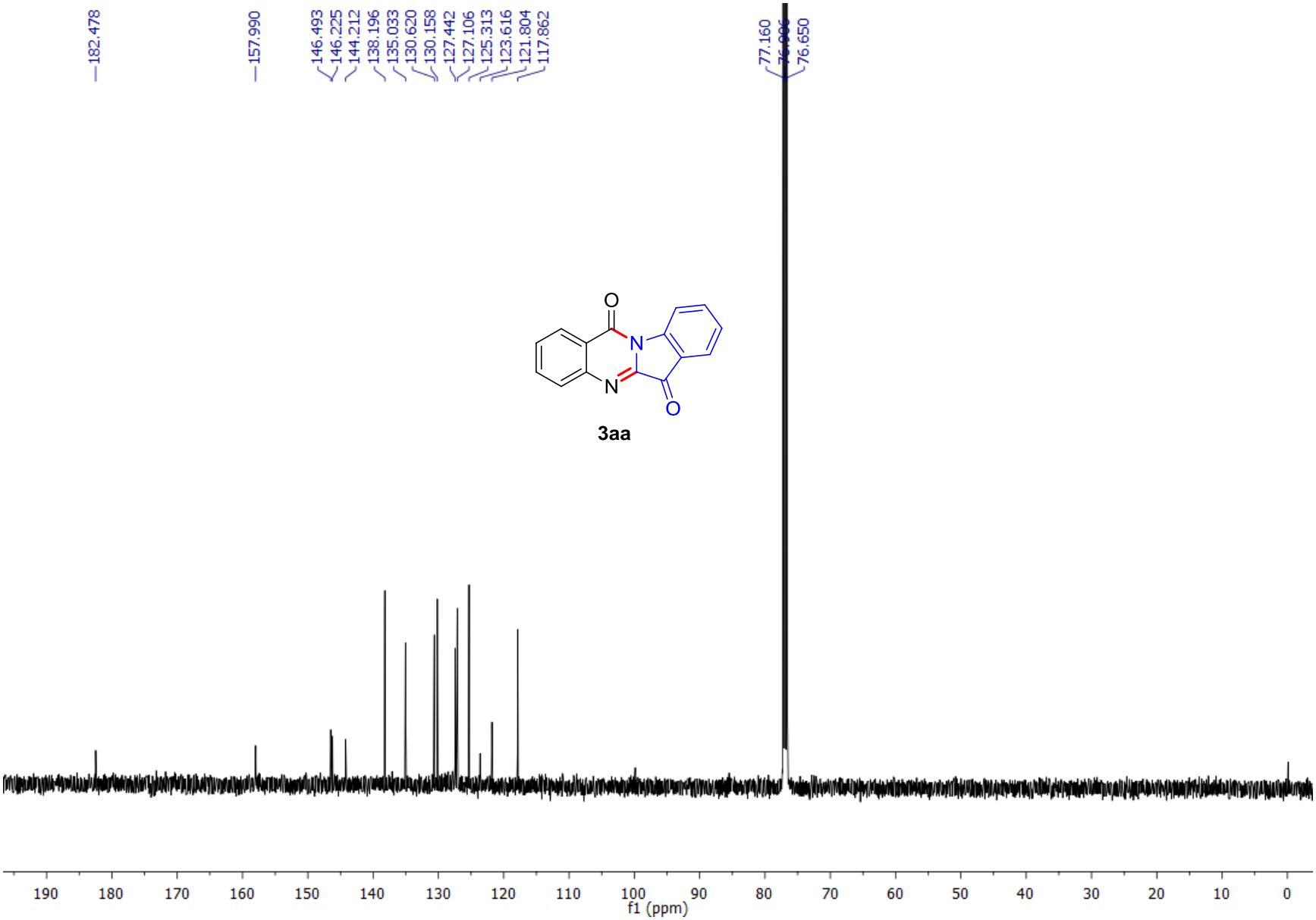
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N
N
O
3aa
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180
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10
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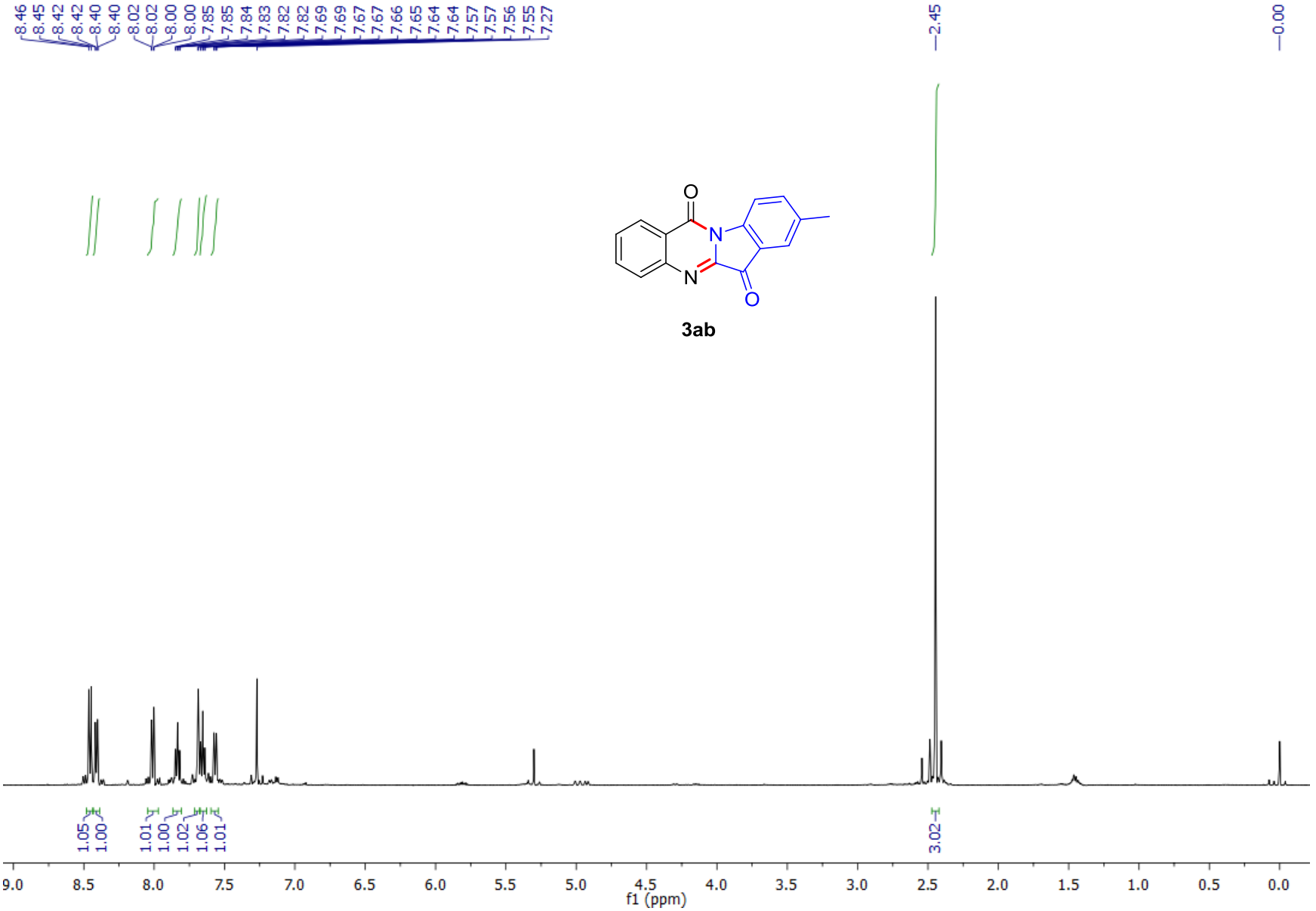
f1 (ppm)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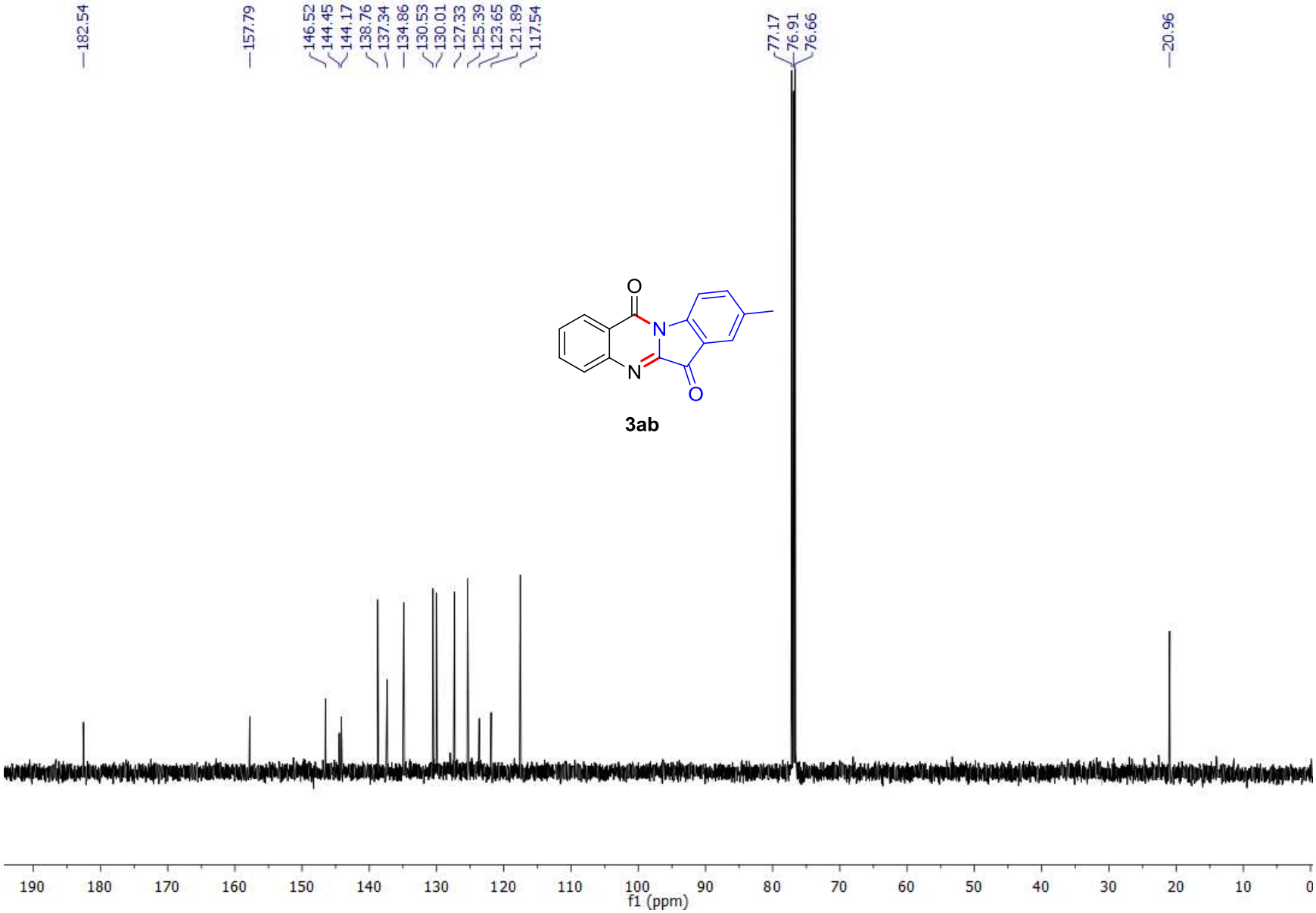
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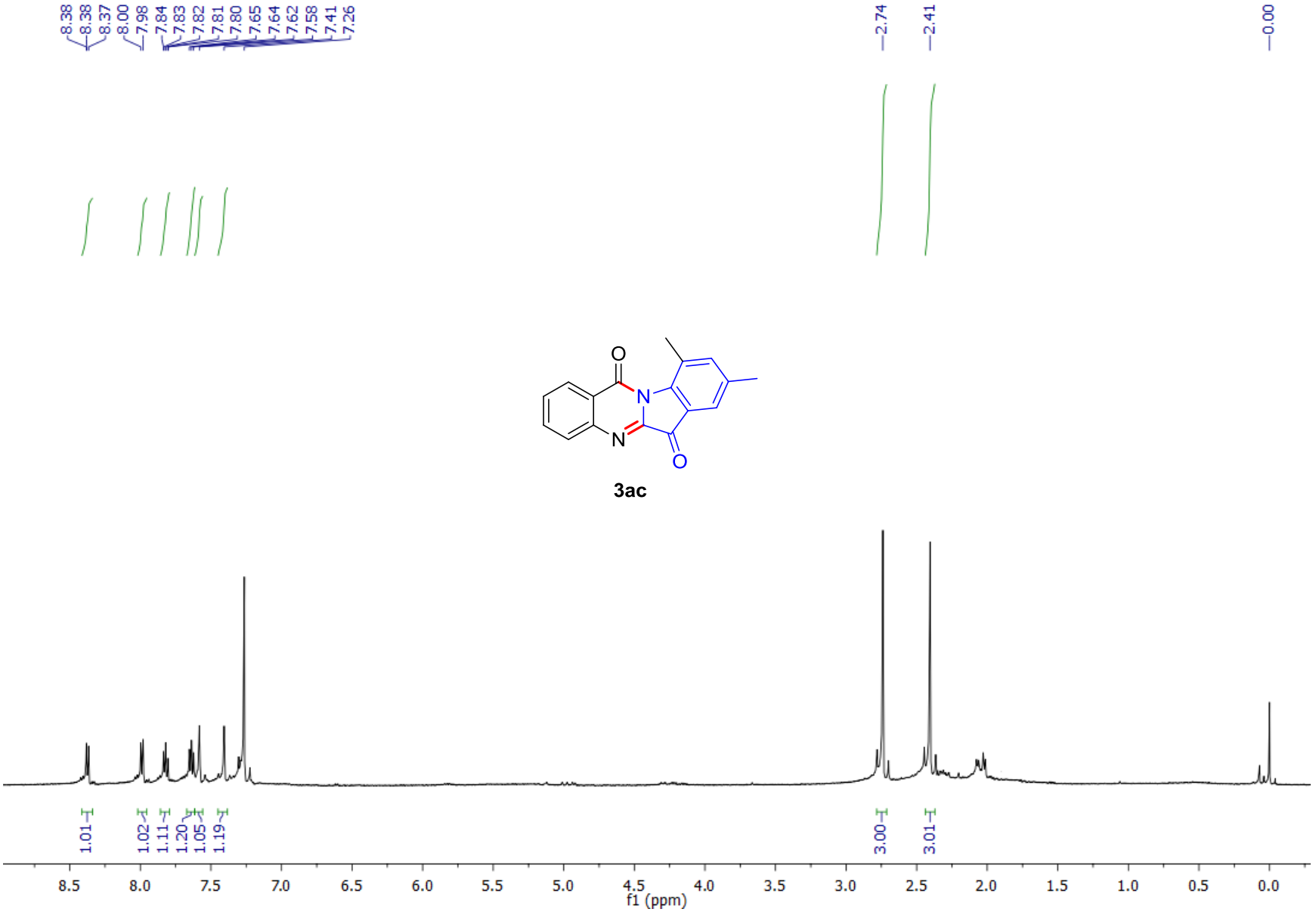
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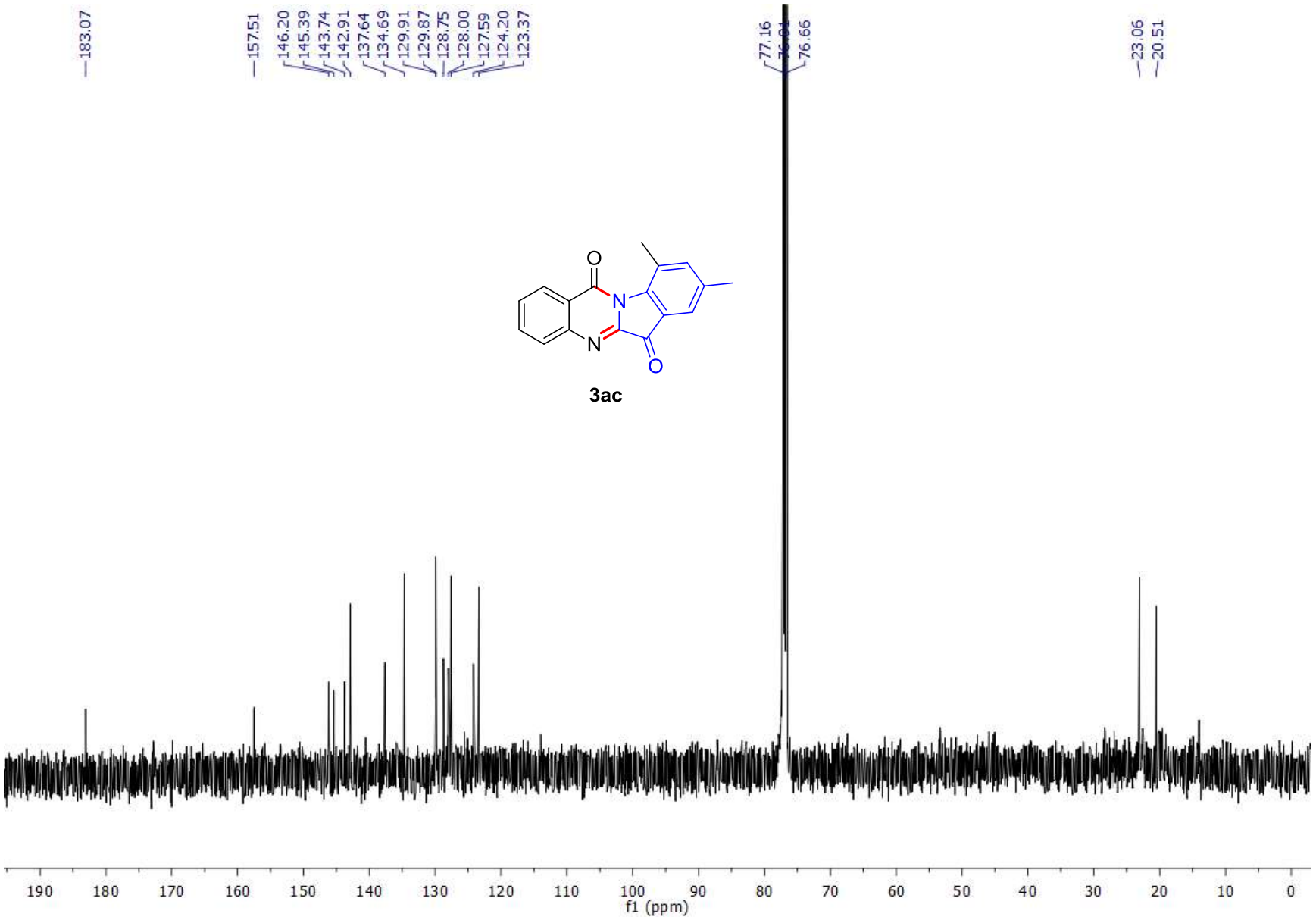
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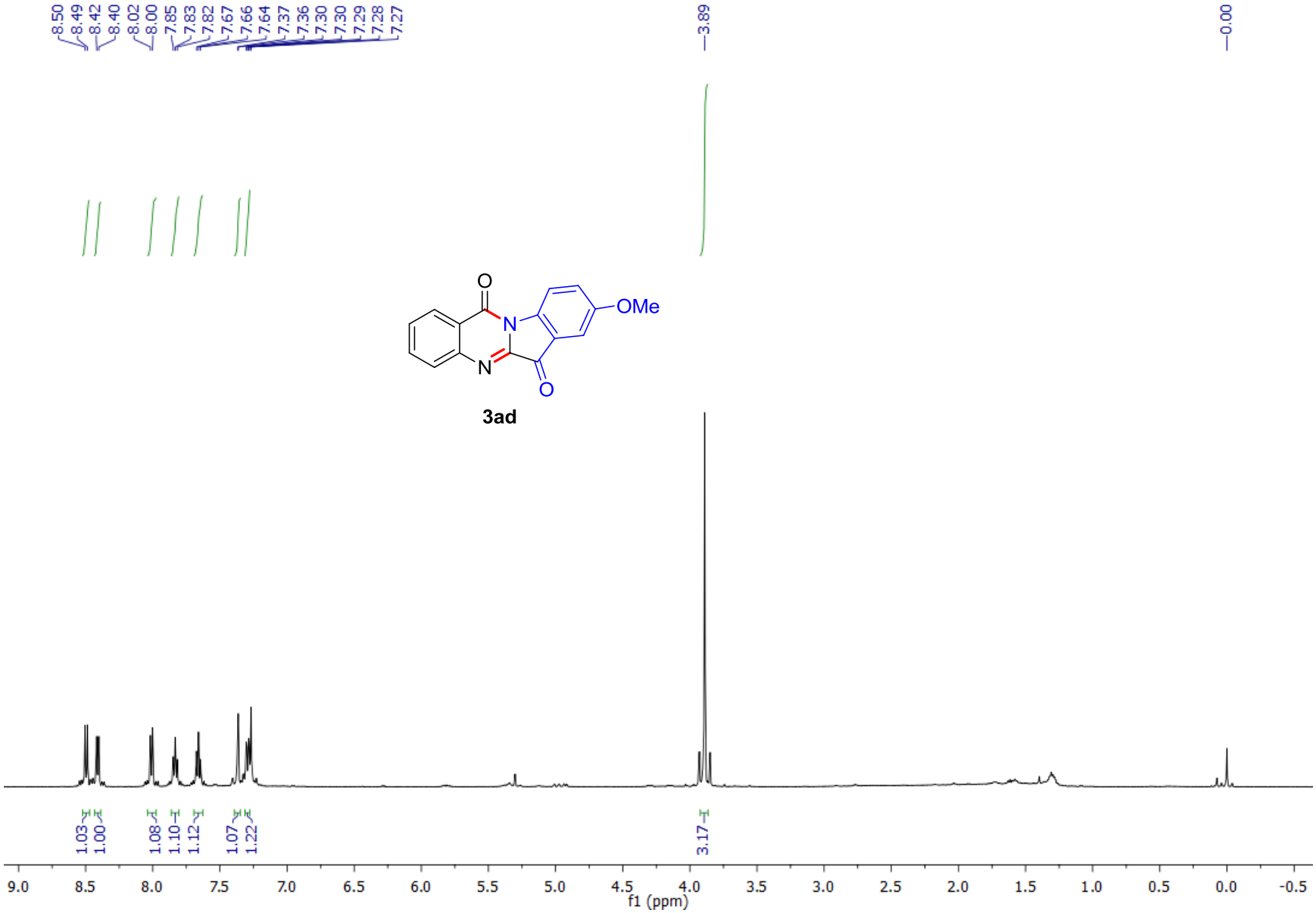
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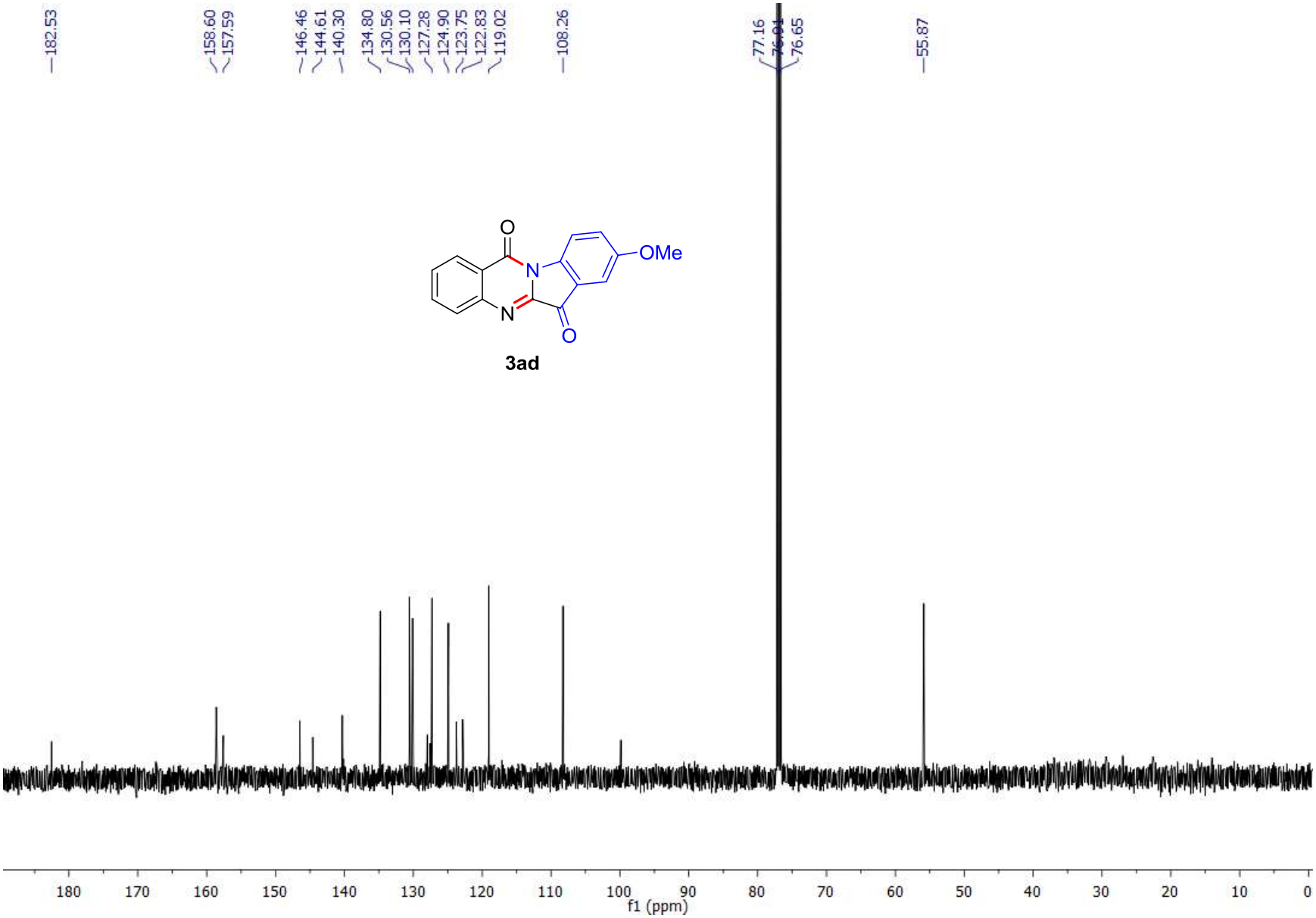
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O
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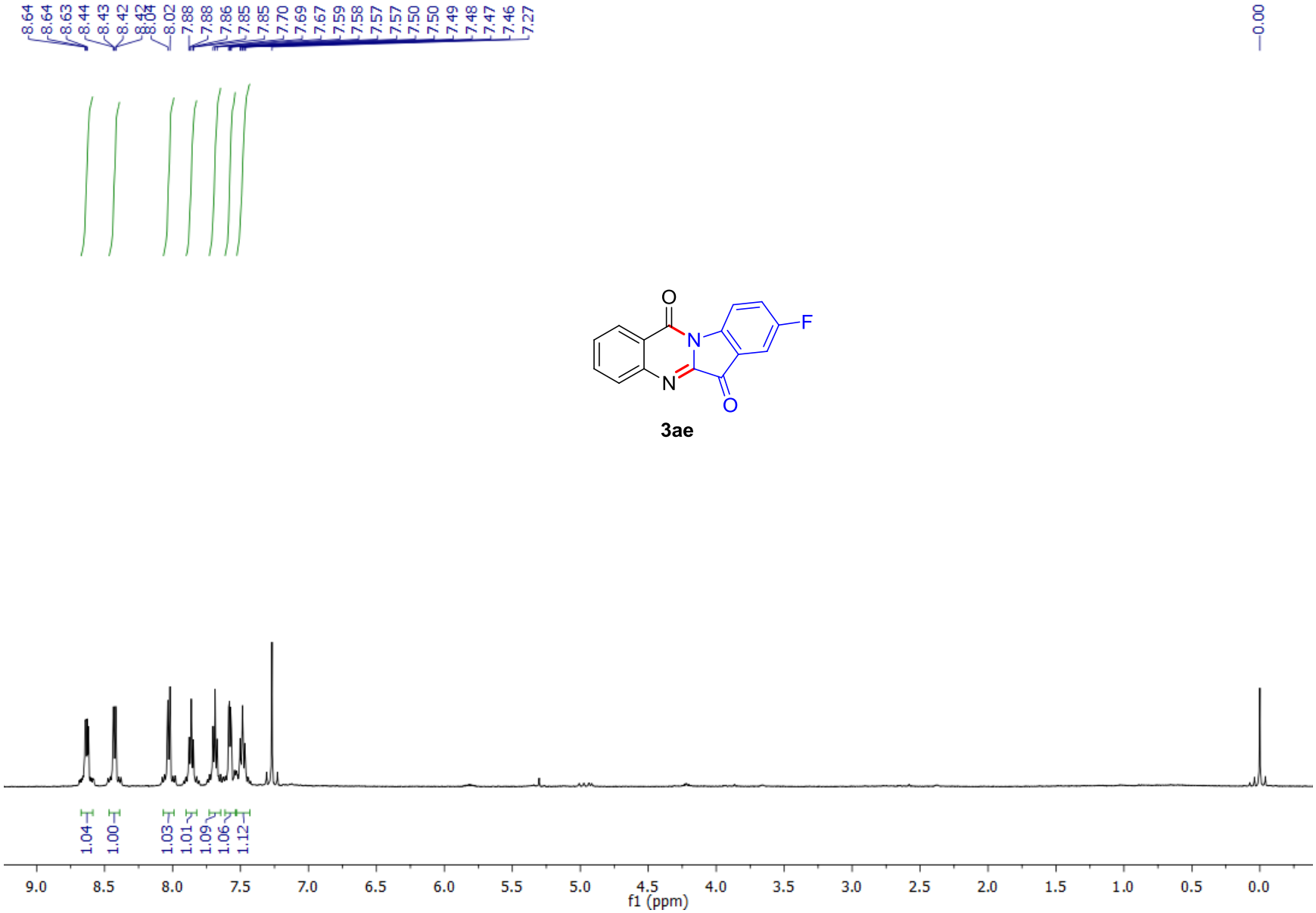
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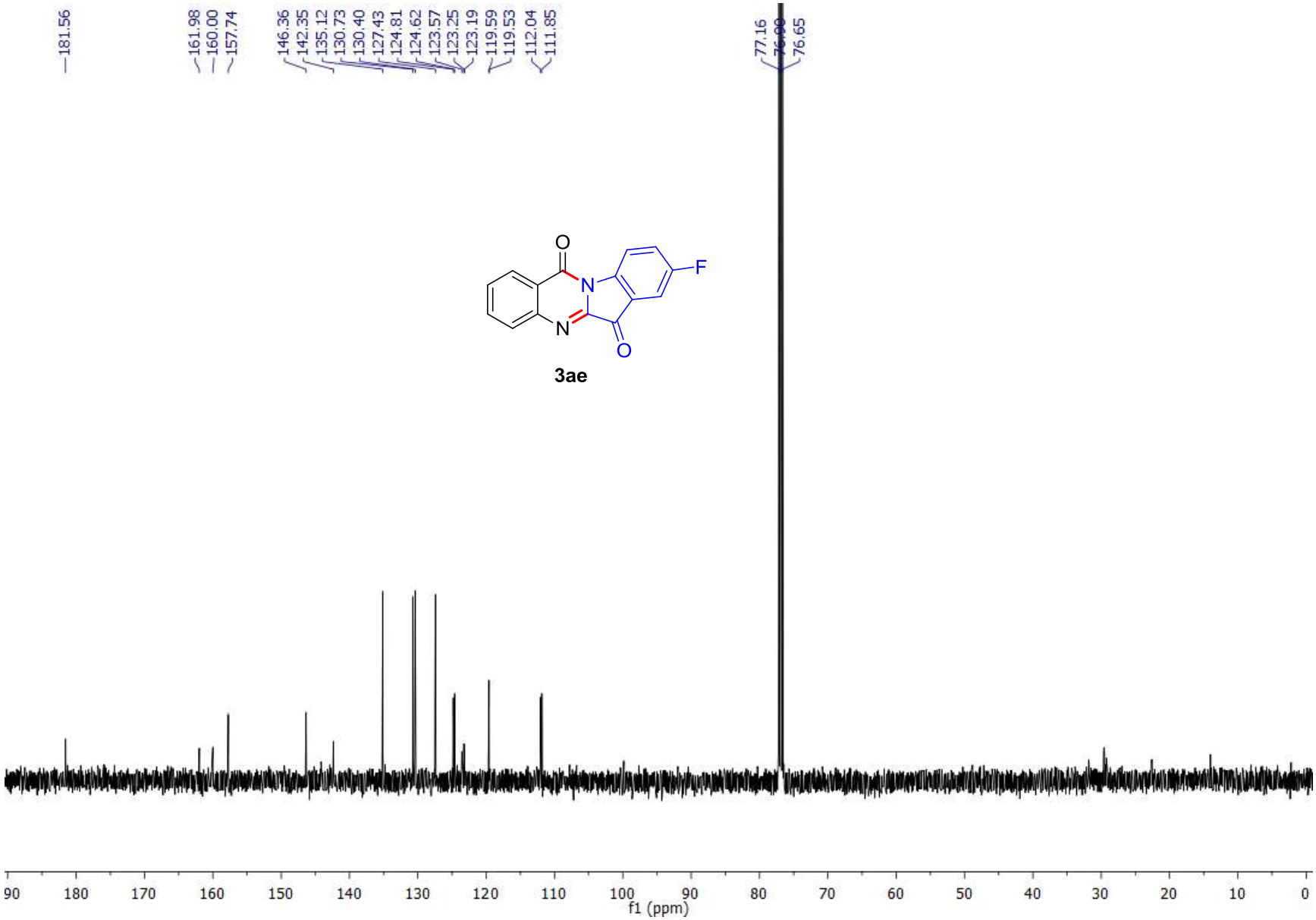
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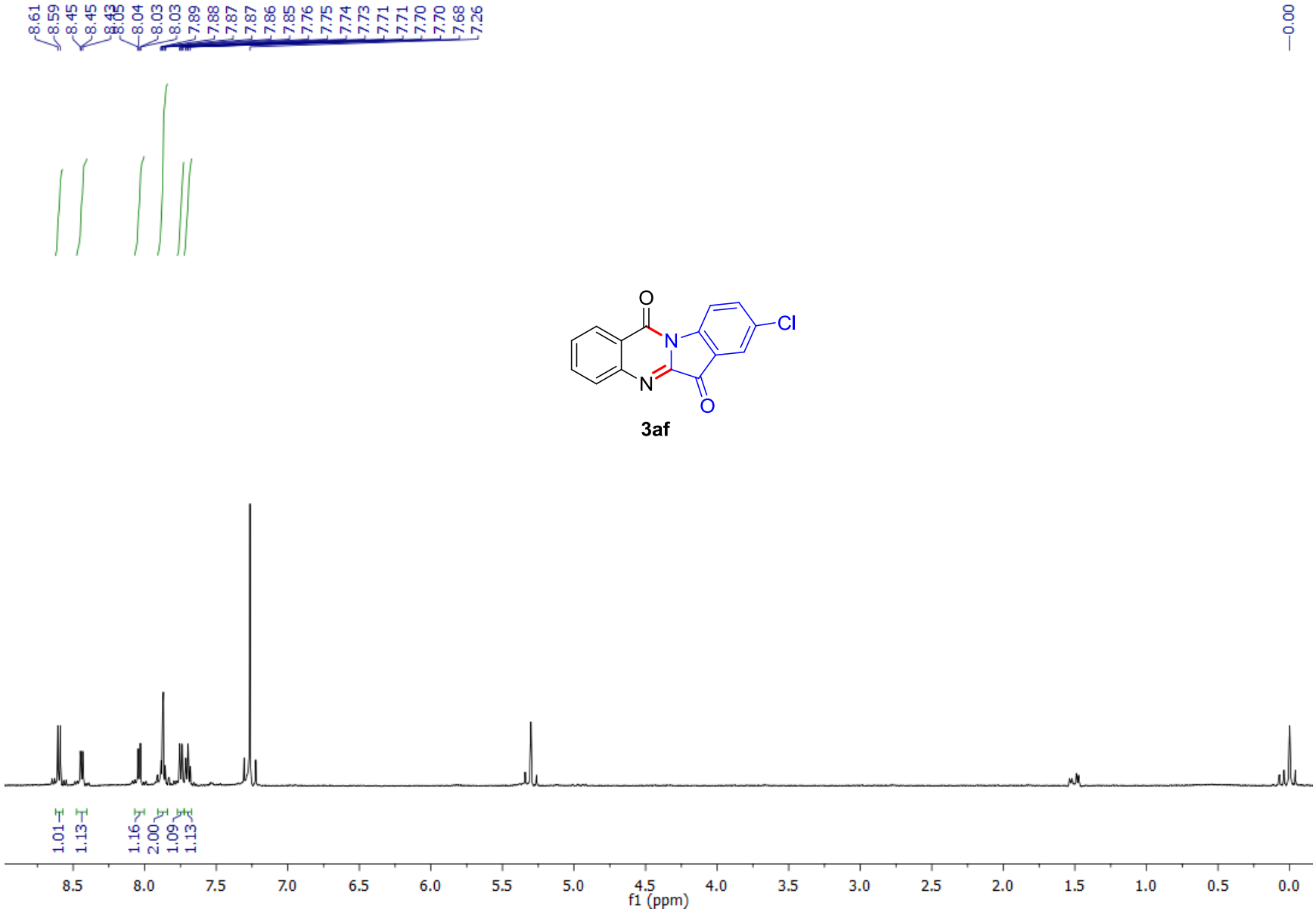
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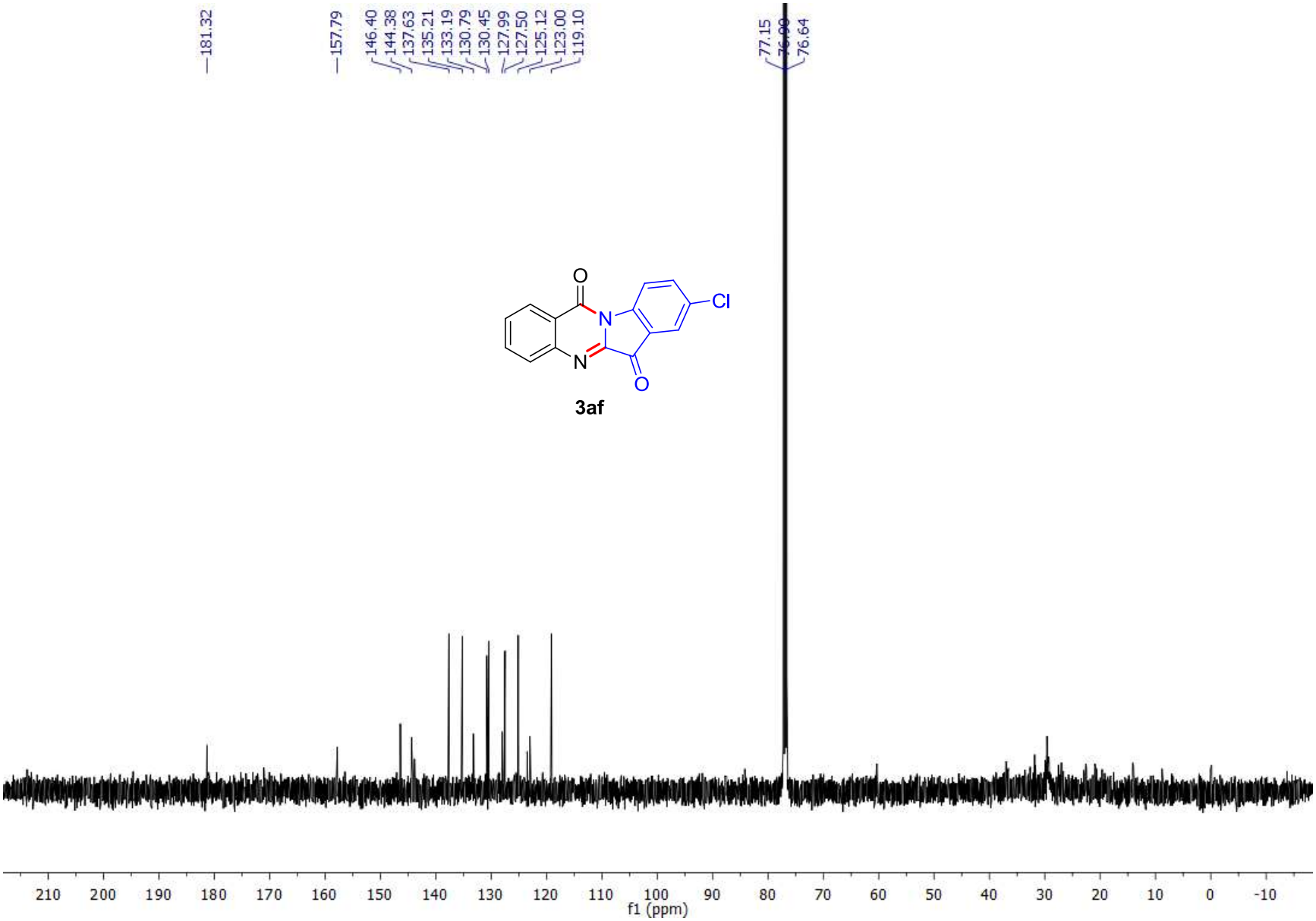
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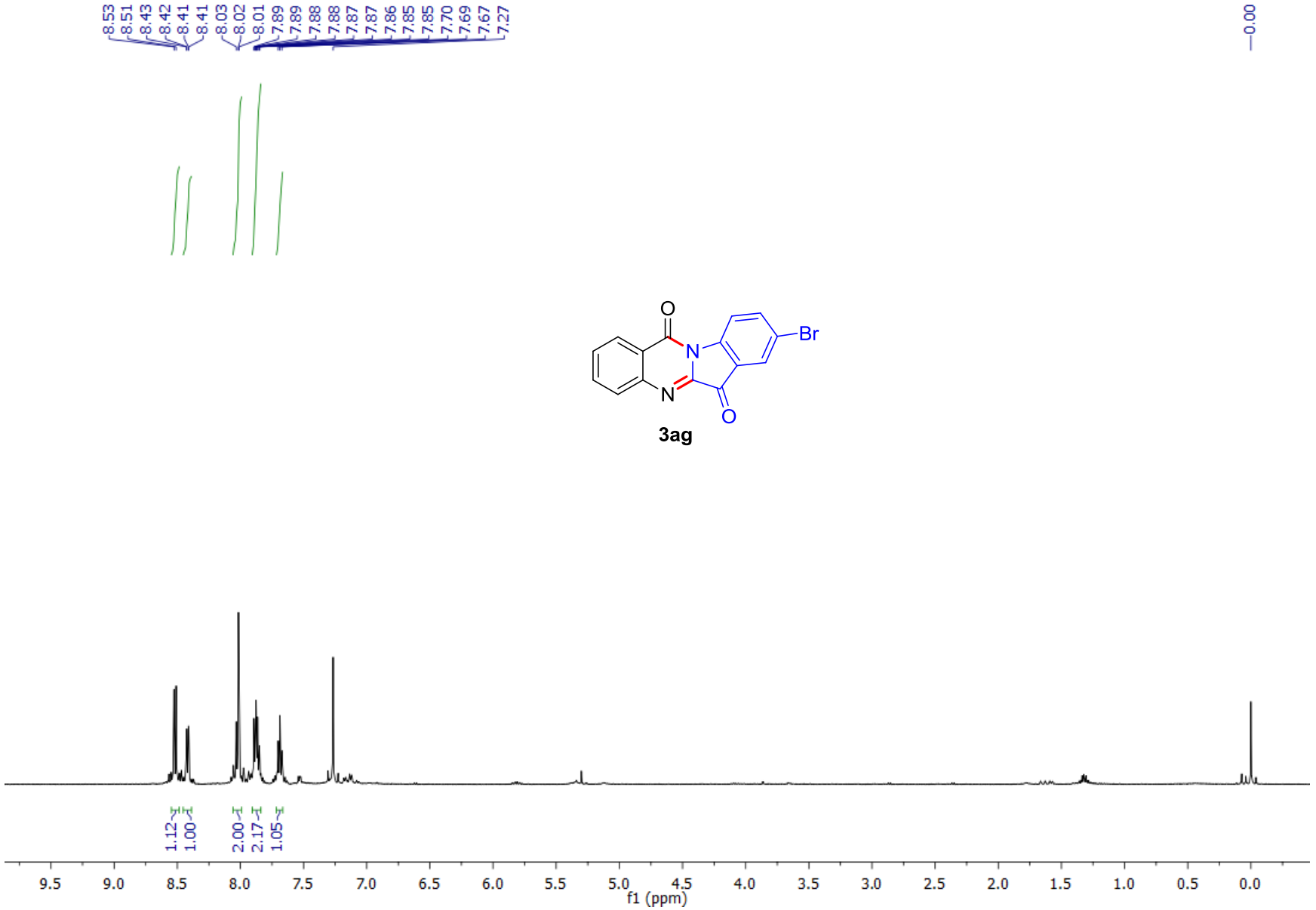
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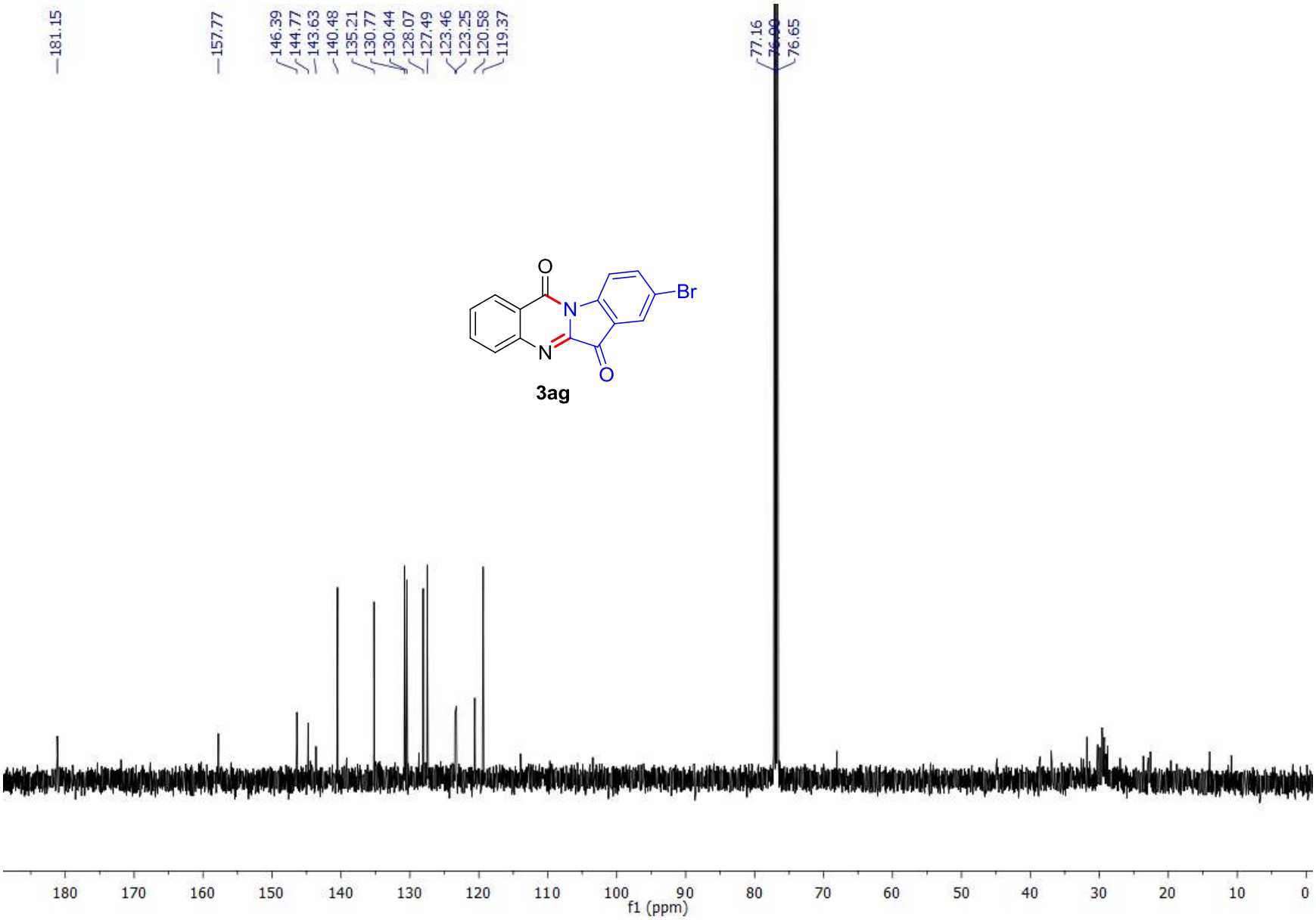
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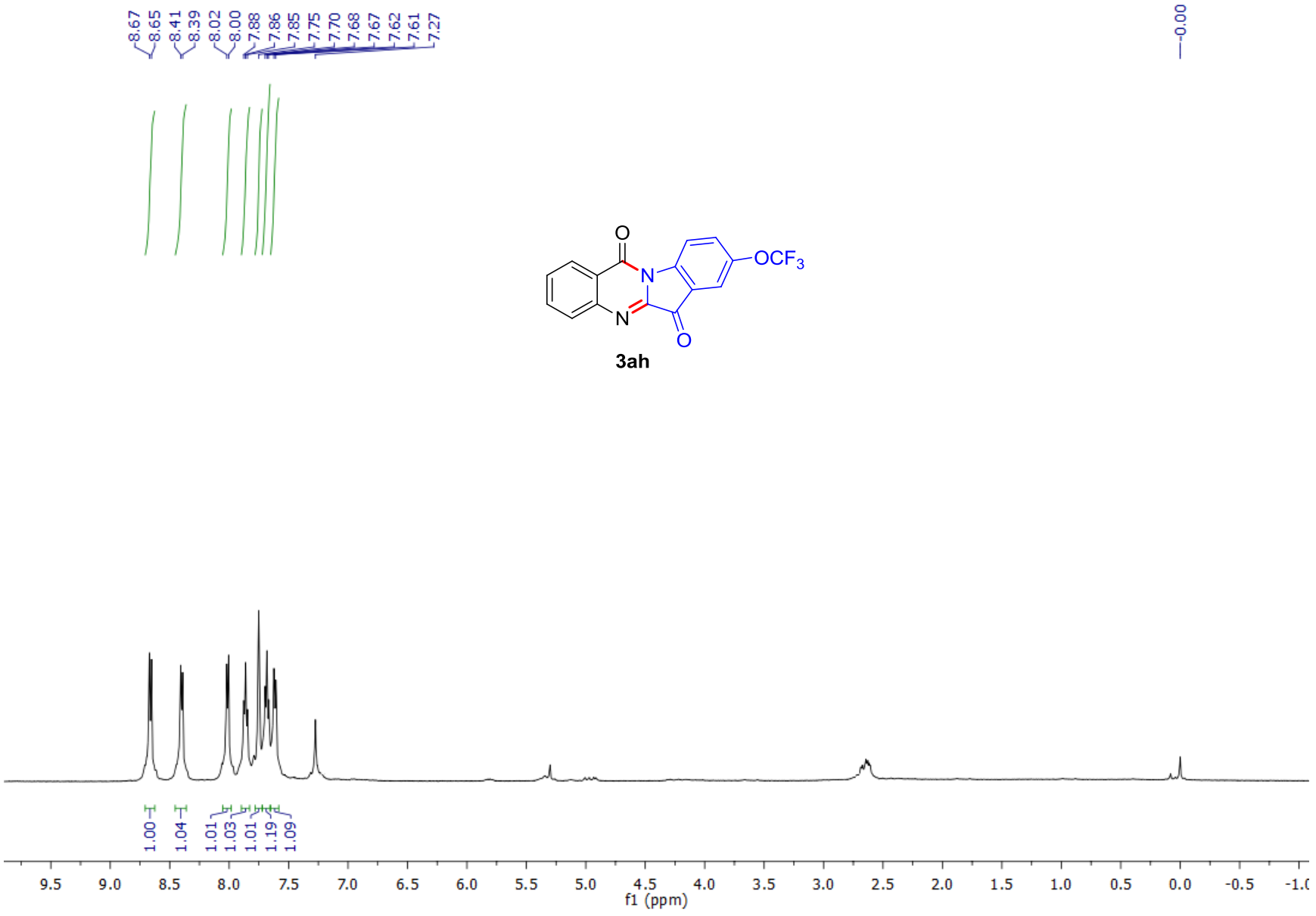
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1.03
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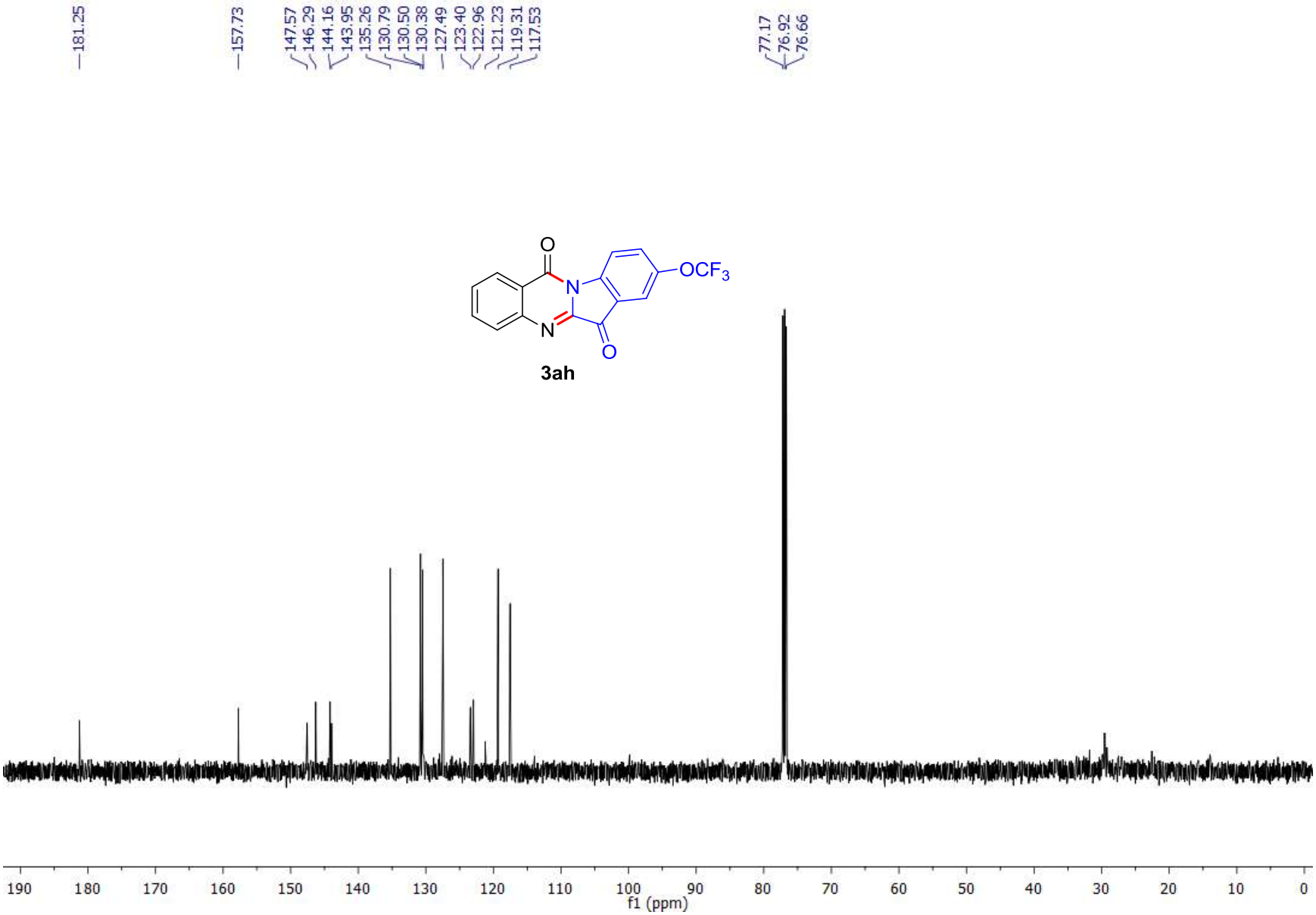
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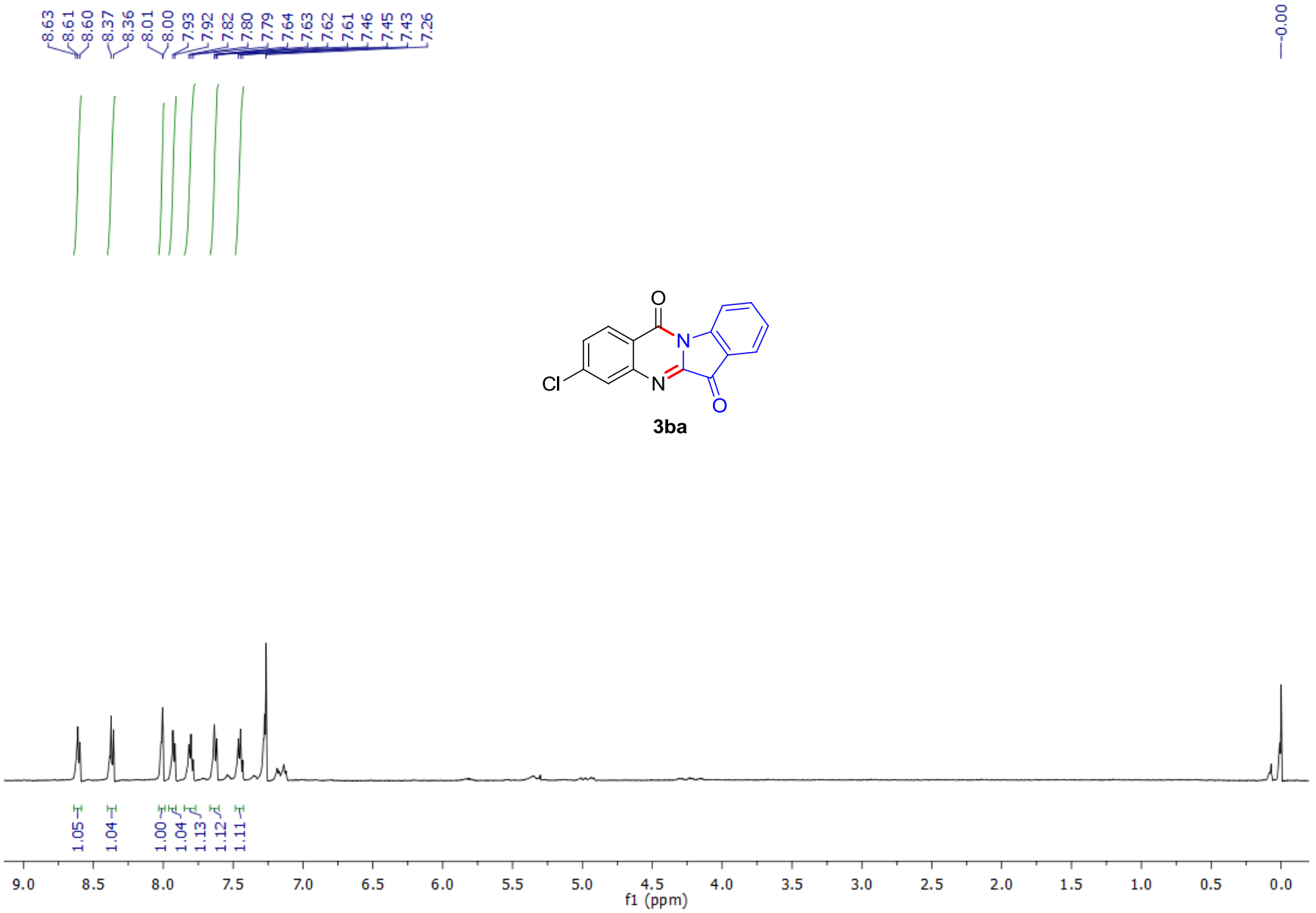
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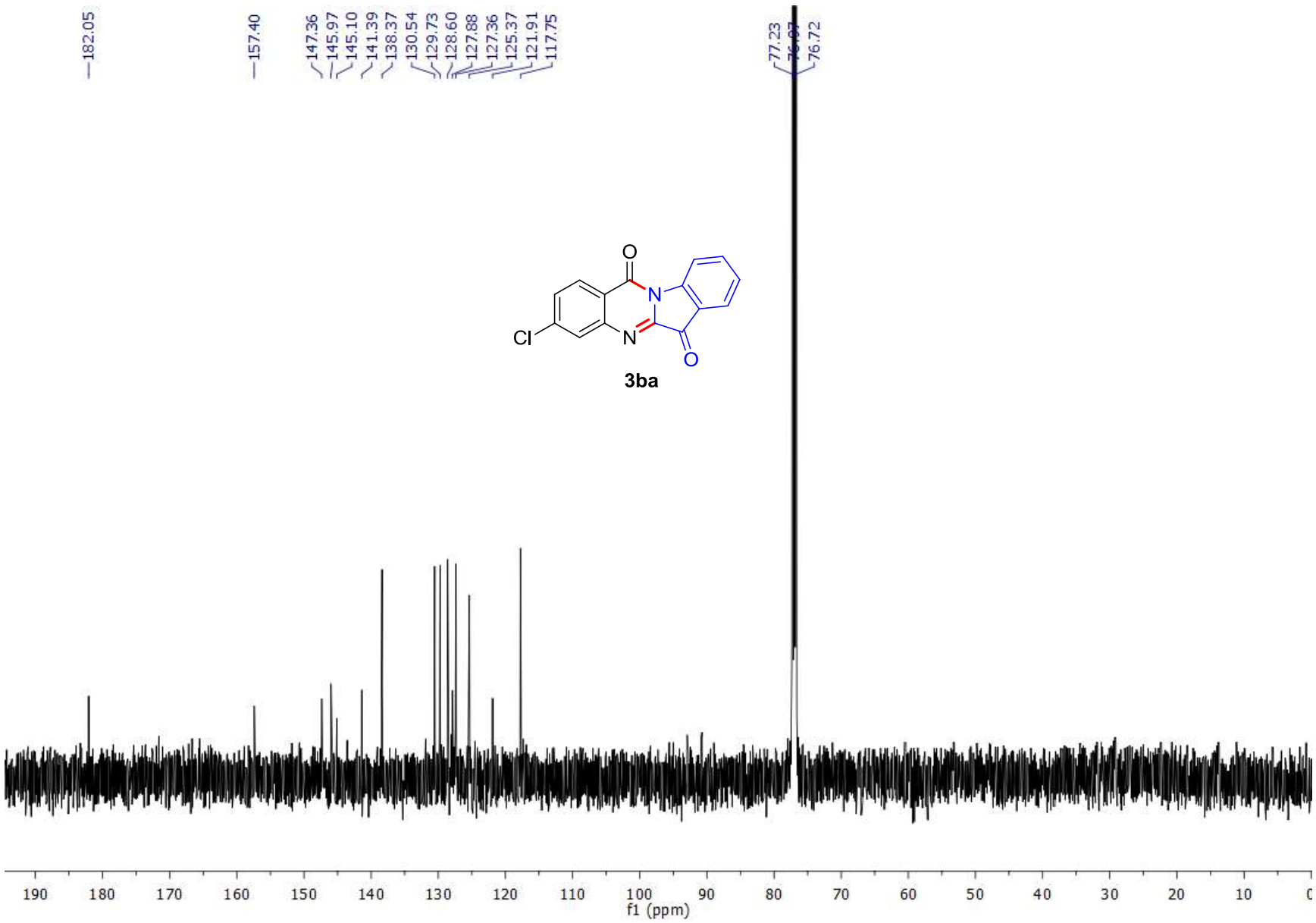
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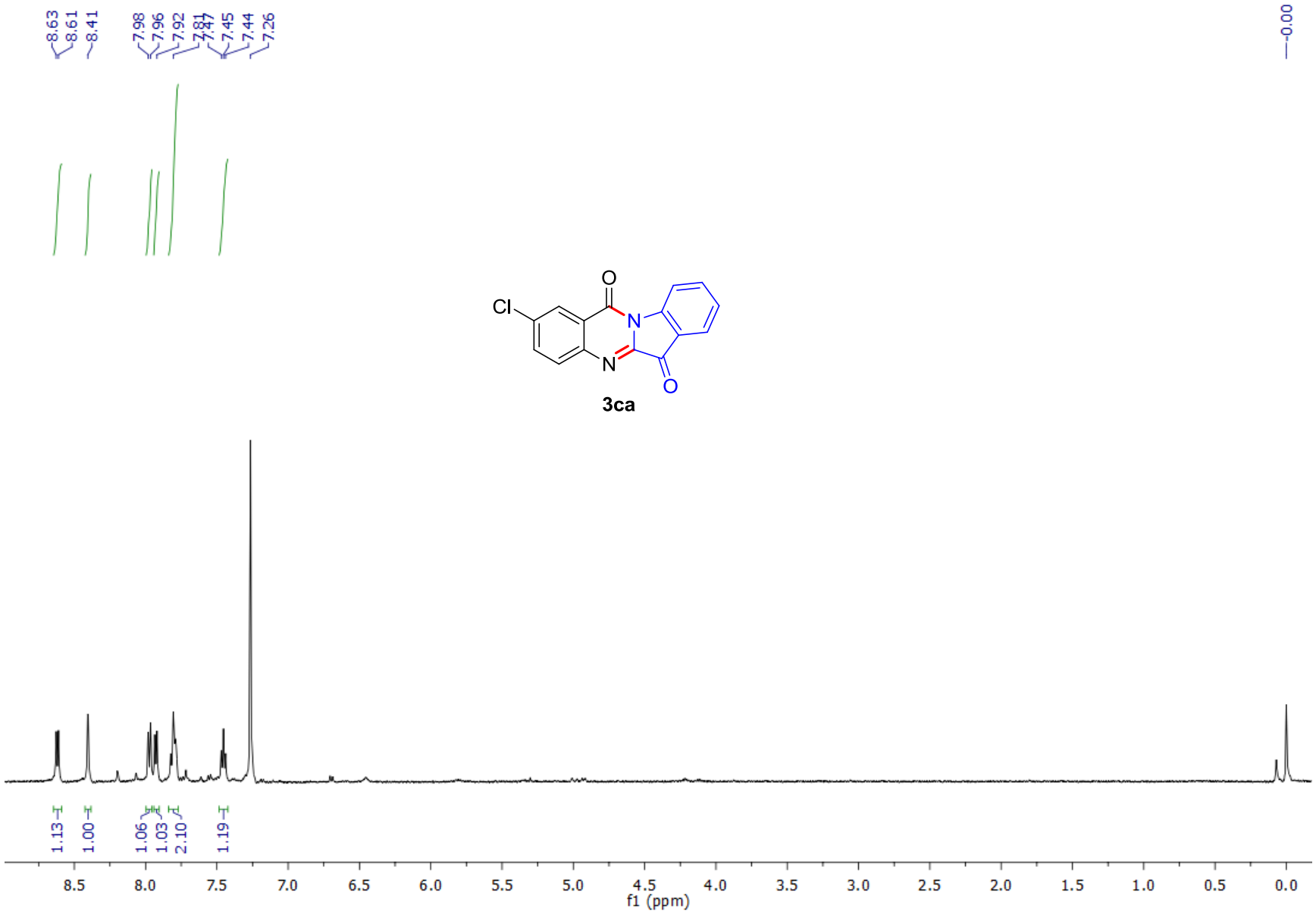
f1 (ppm)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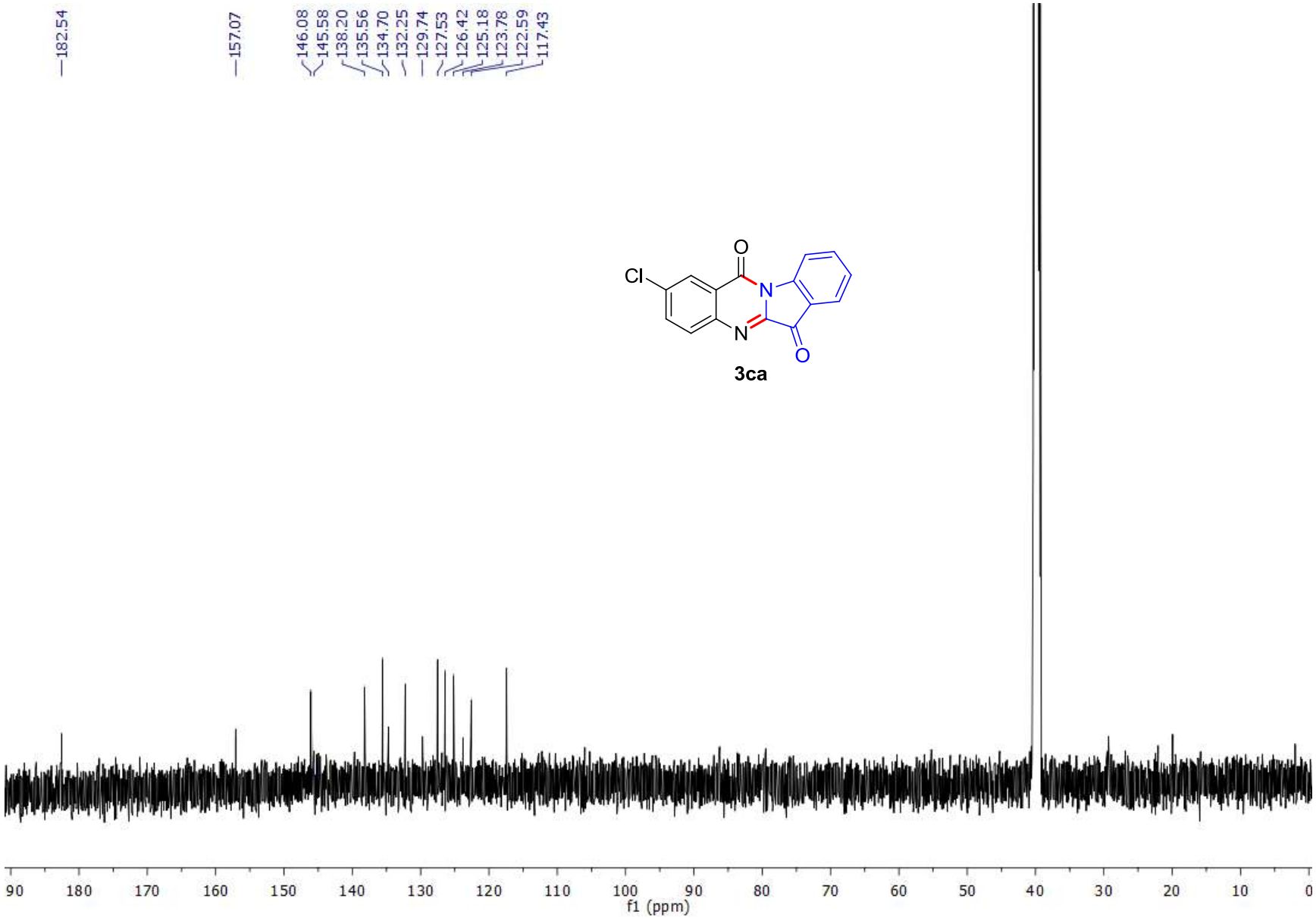
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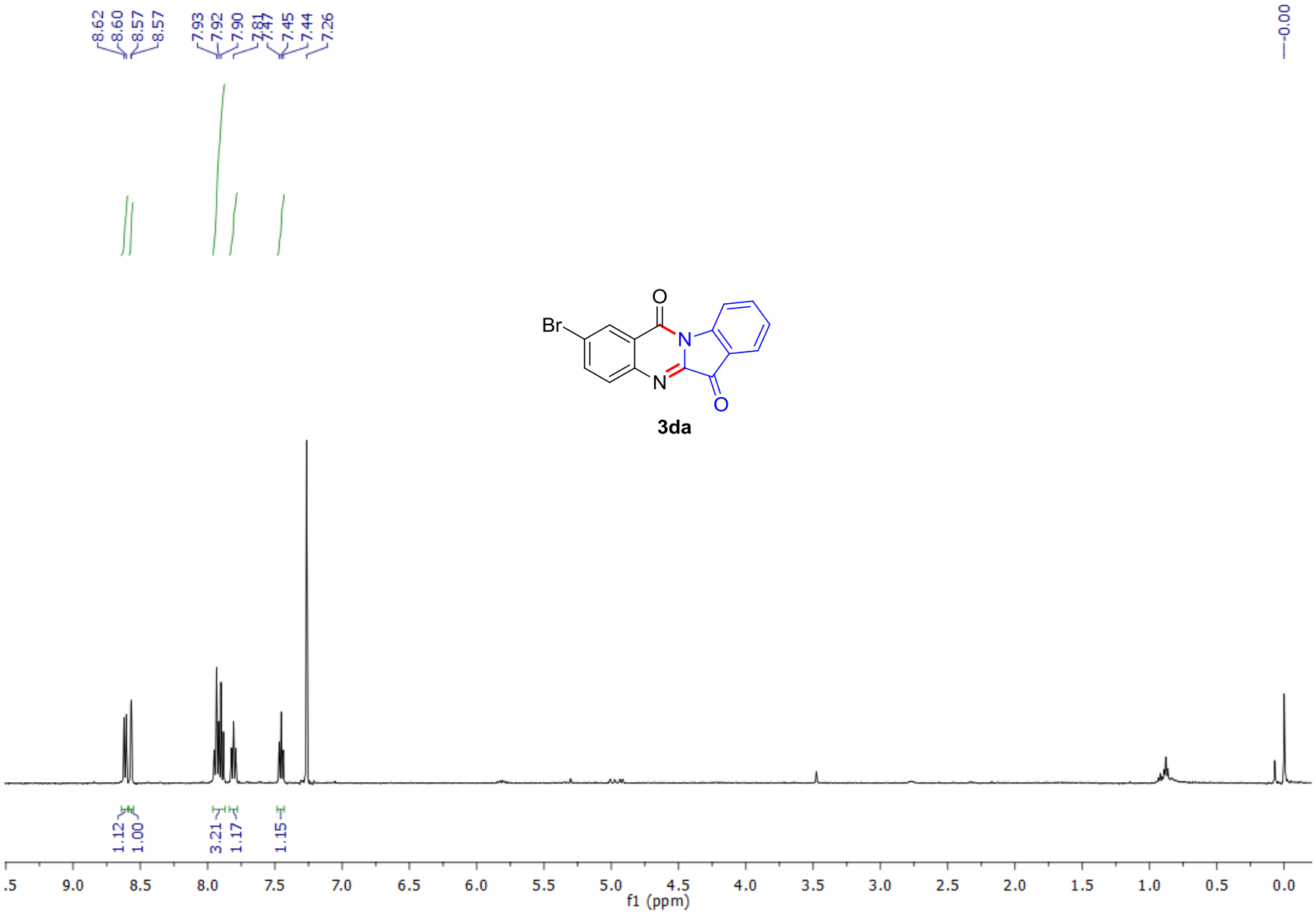
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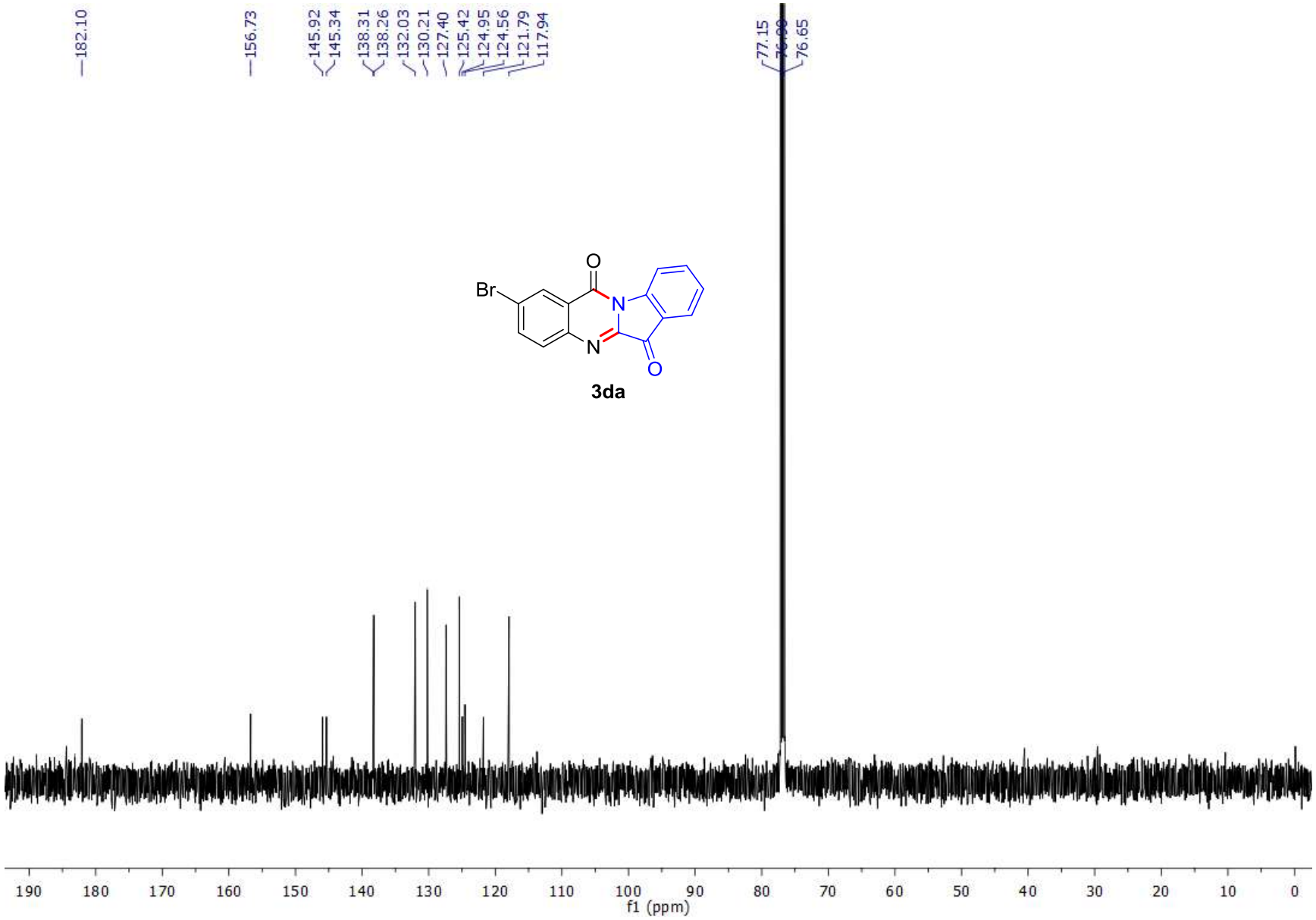
1.15
f1 (ppm)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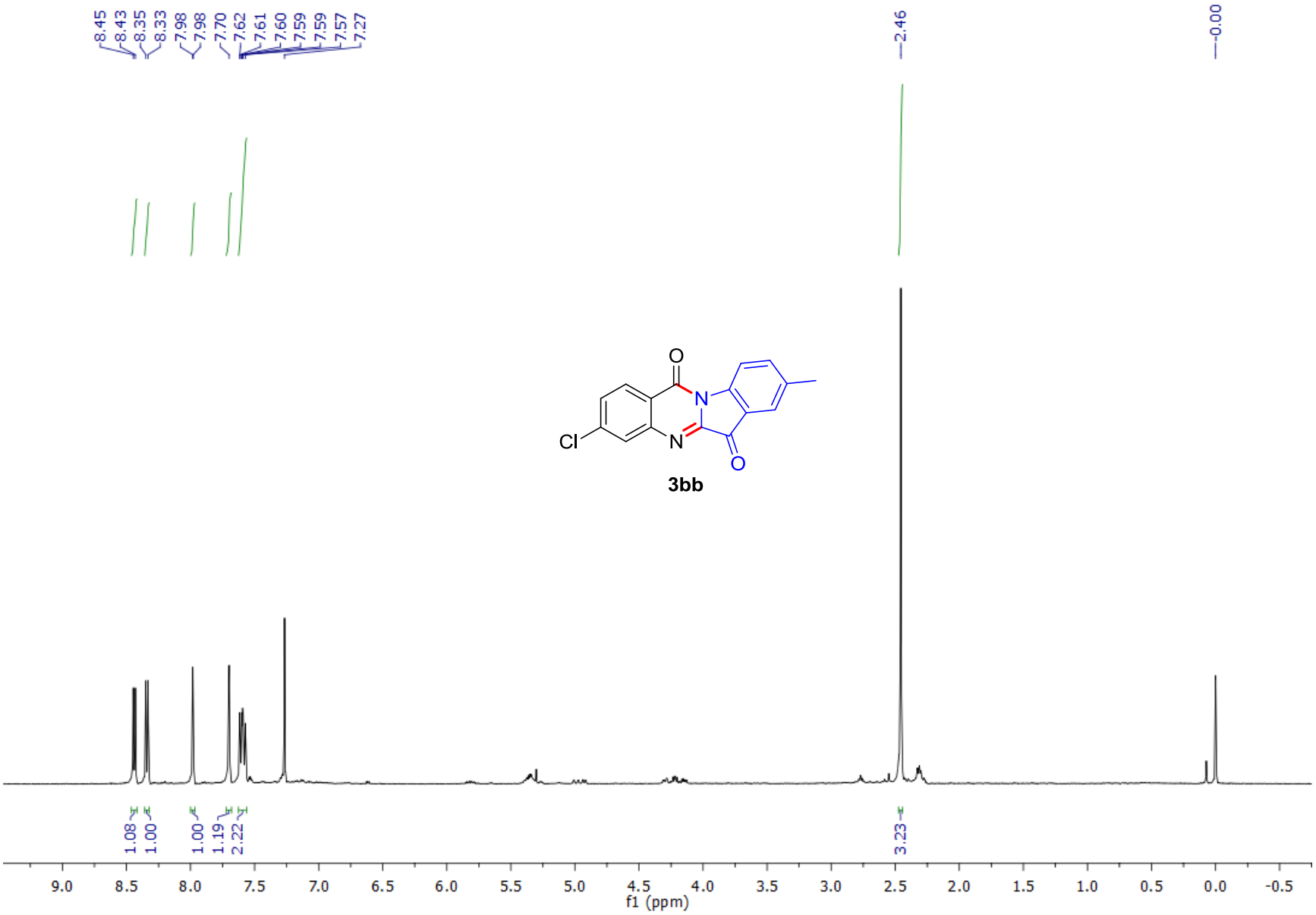
145.92
145.34
138.31
138.26
132.03
130.21
127.40
125.42
124.95
124.56
121.79
117.94
77.15
76.65
Br
O
N
N
O
3da
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.43
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8.33
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7.98
7.70
7.62
7.61
7.60
7.59
7.59
7.57
7.27
2.46
0.00
O
N
N
O
Cl
3bb
1.08
1.00
1.00
1.19
2.22
3.23
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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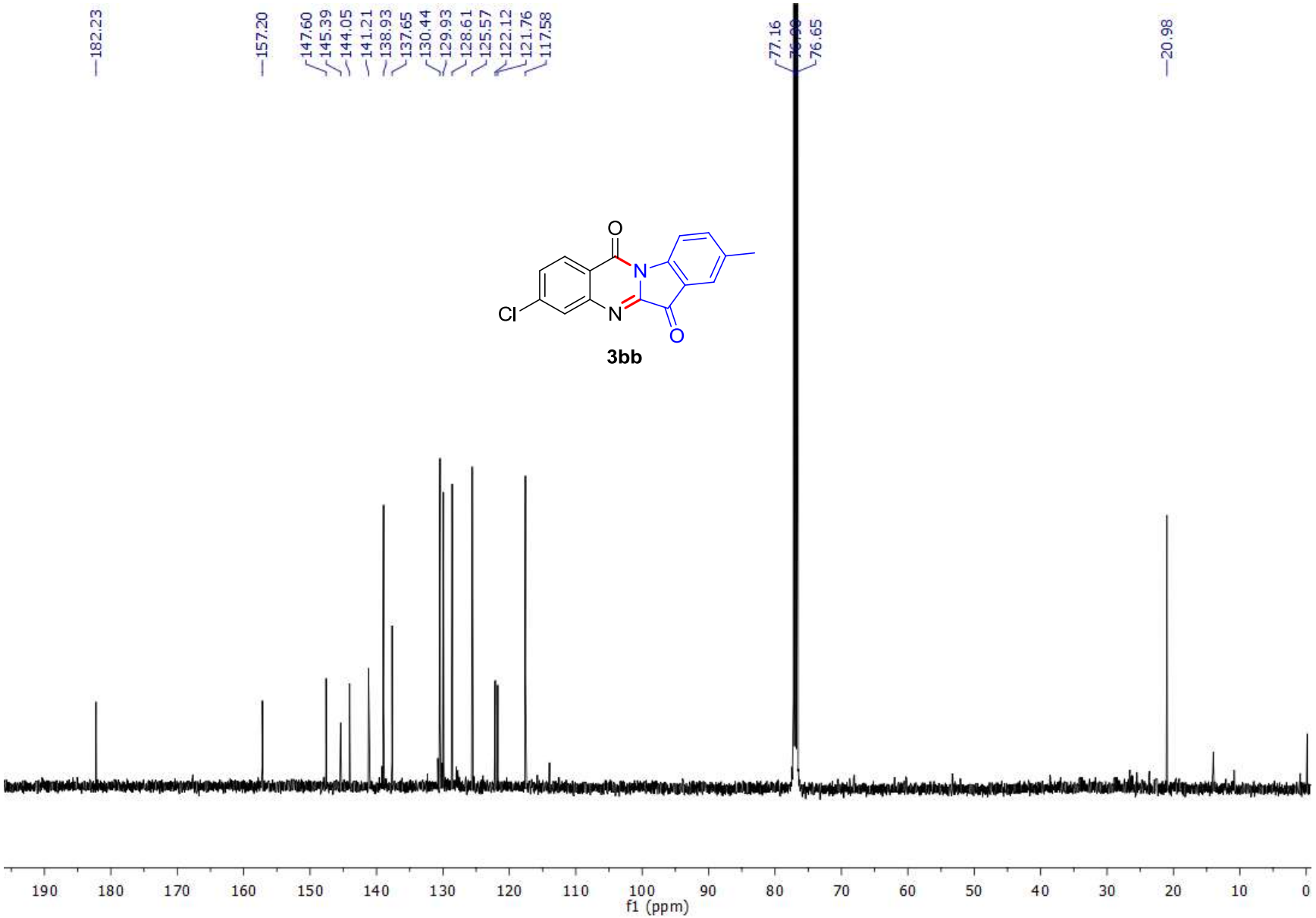
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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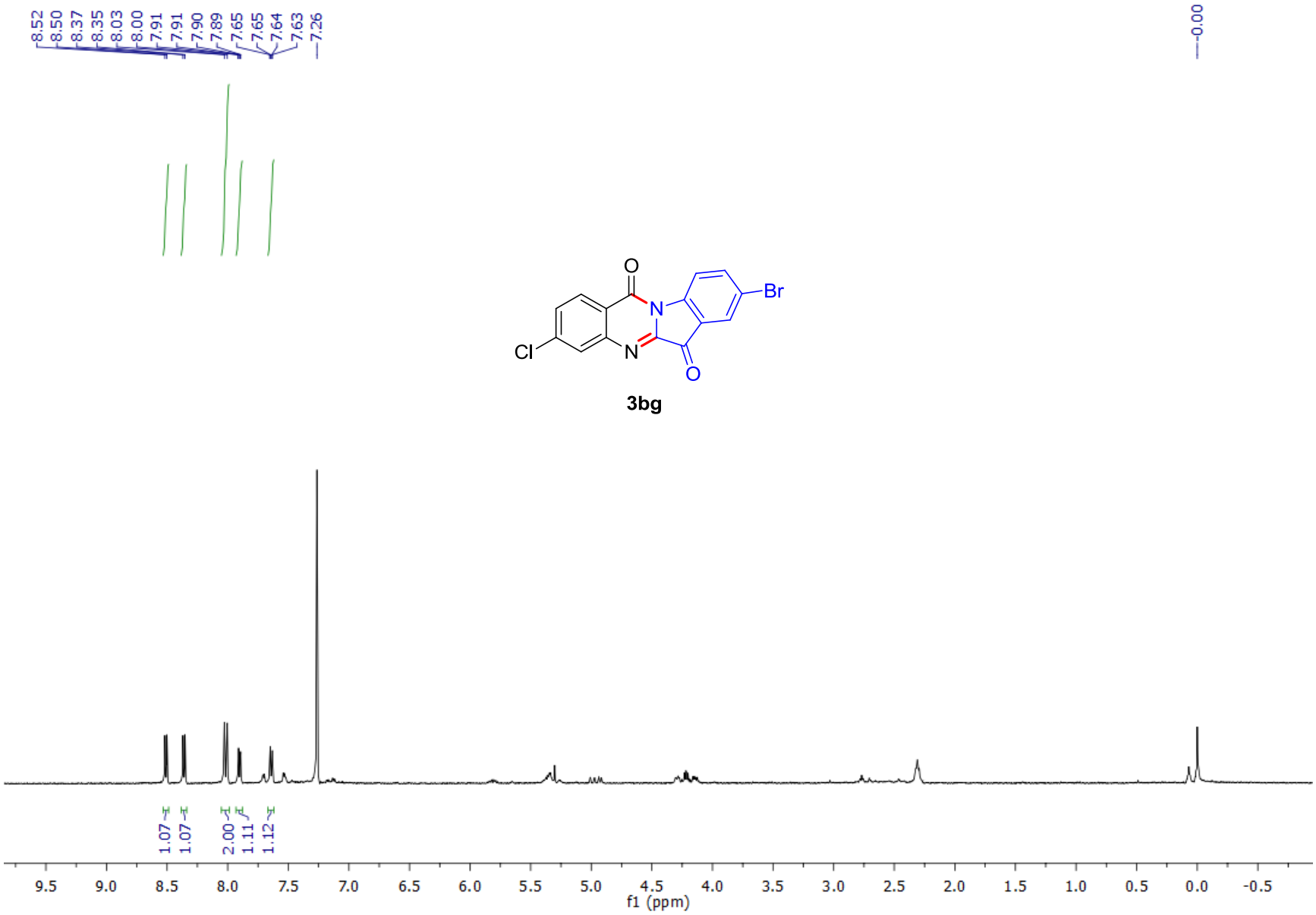
141.21
138.93
137.65
130.44
129.93
128.61
125.57
122.12
121.76
117.58
77.16
76.65
20.98
O
N
Cl
N
O
3bb
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.37
8.35
8.03
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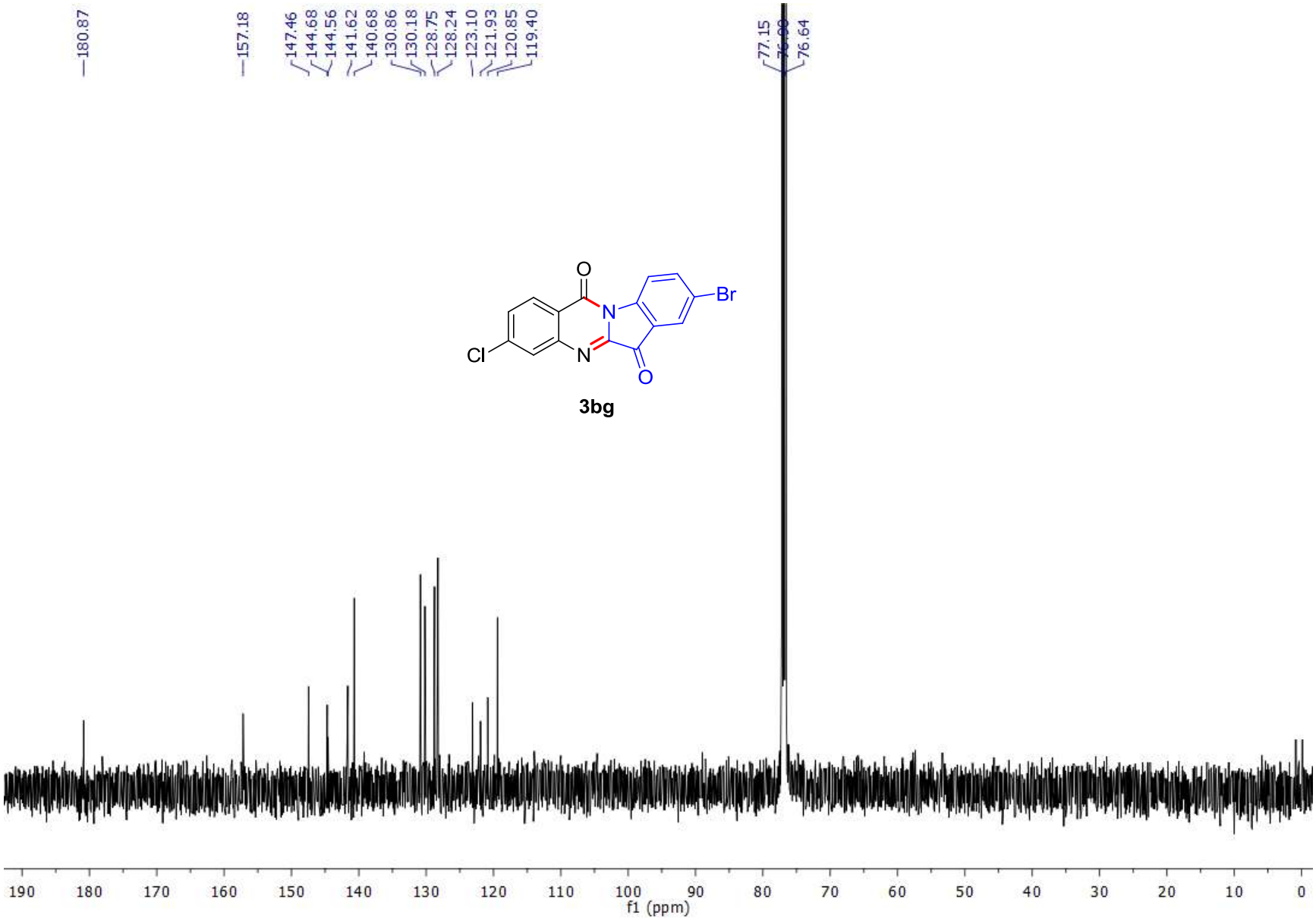
7.91
7.91
7.90
7.89
7.65
7.65
7.64
7.63
7.26
0.00
O
N
Br
Cl
N
O
1.07
1.07
2.00
1.11
1.12
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

3bg


180.87
157.18
147.46
144.68
144.56
141.62
140.68
130.86
130.18
128.75
128.24
123.10
121.93
120.85
119.40
77.15
76.64
O
N
Br
Cl
N
O
3bg
190
180
170
160
150
140
130
120
110
100
90
80
70
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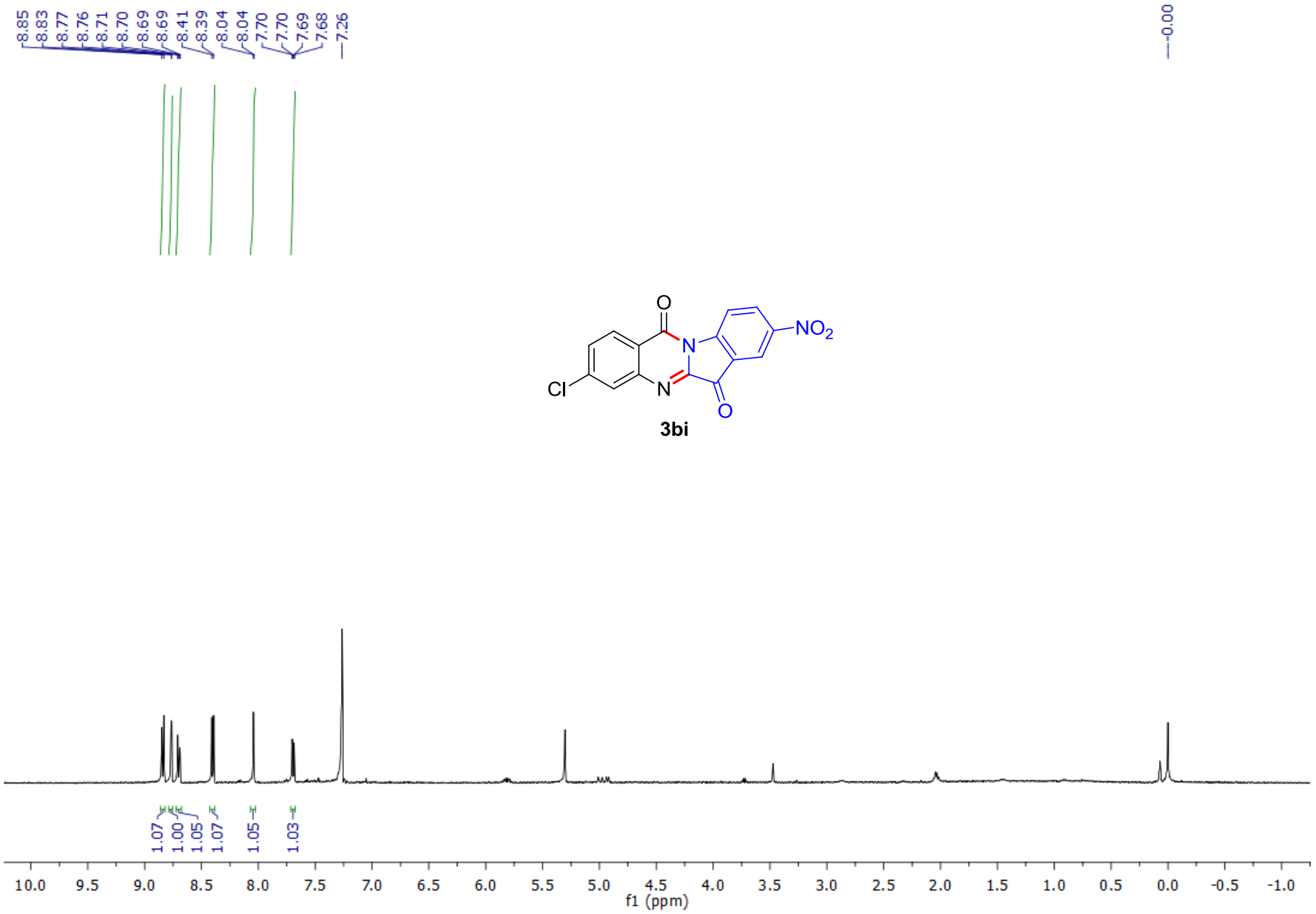
50
40
30
20
10
0
f1 (ppm)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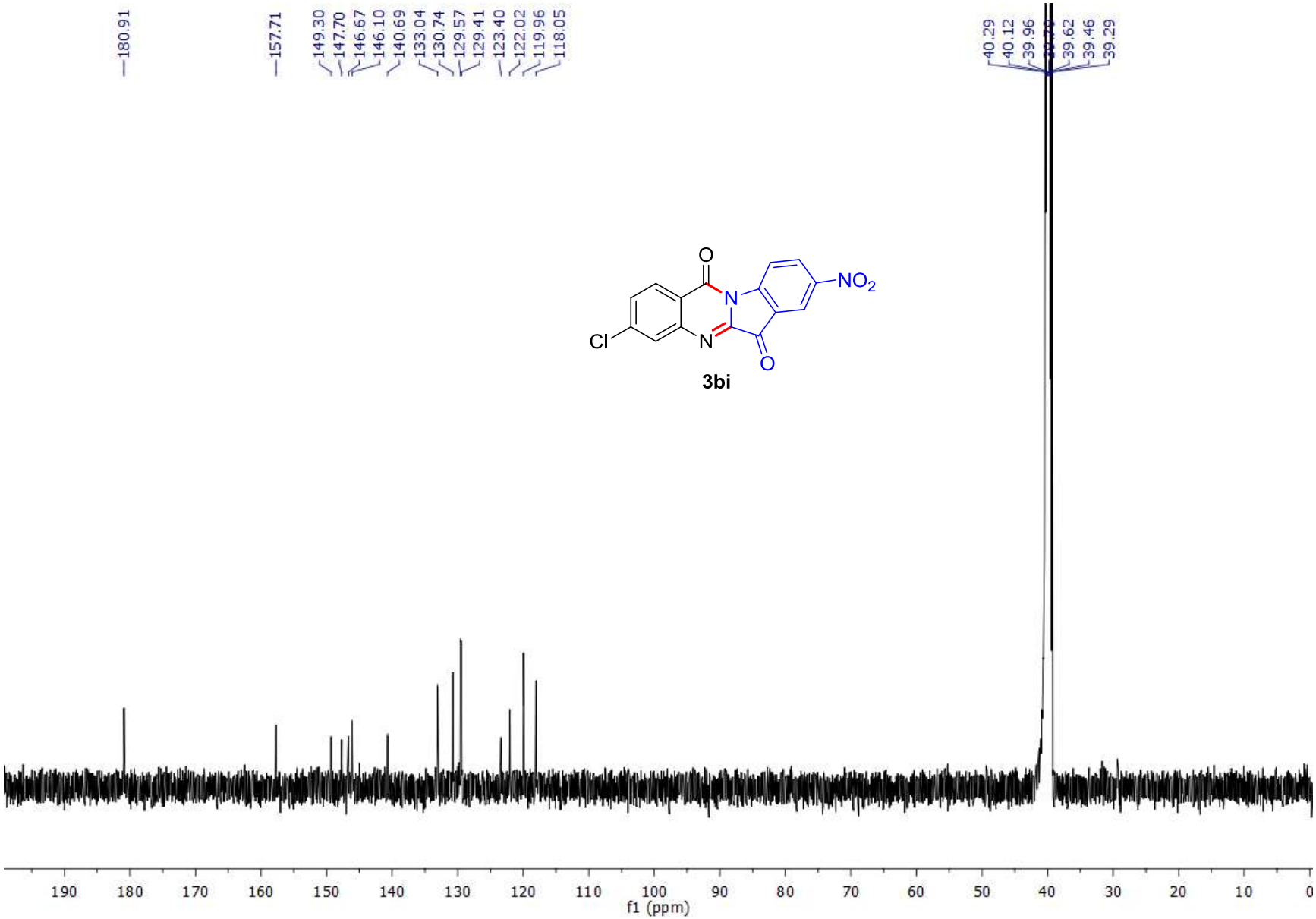
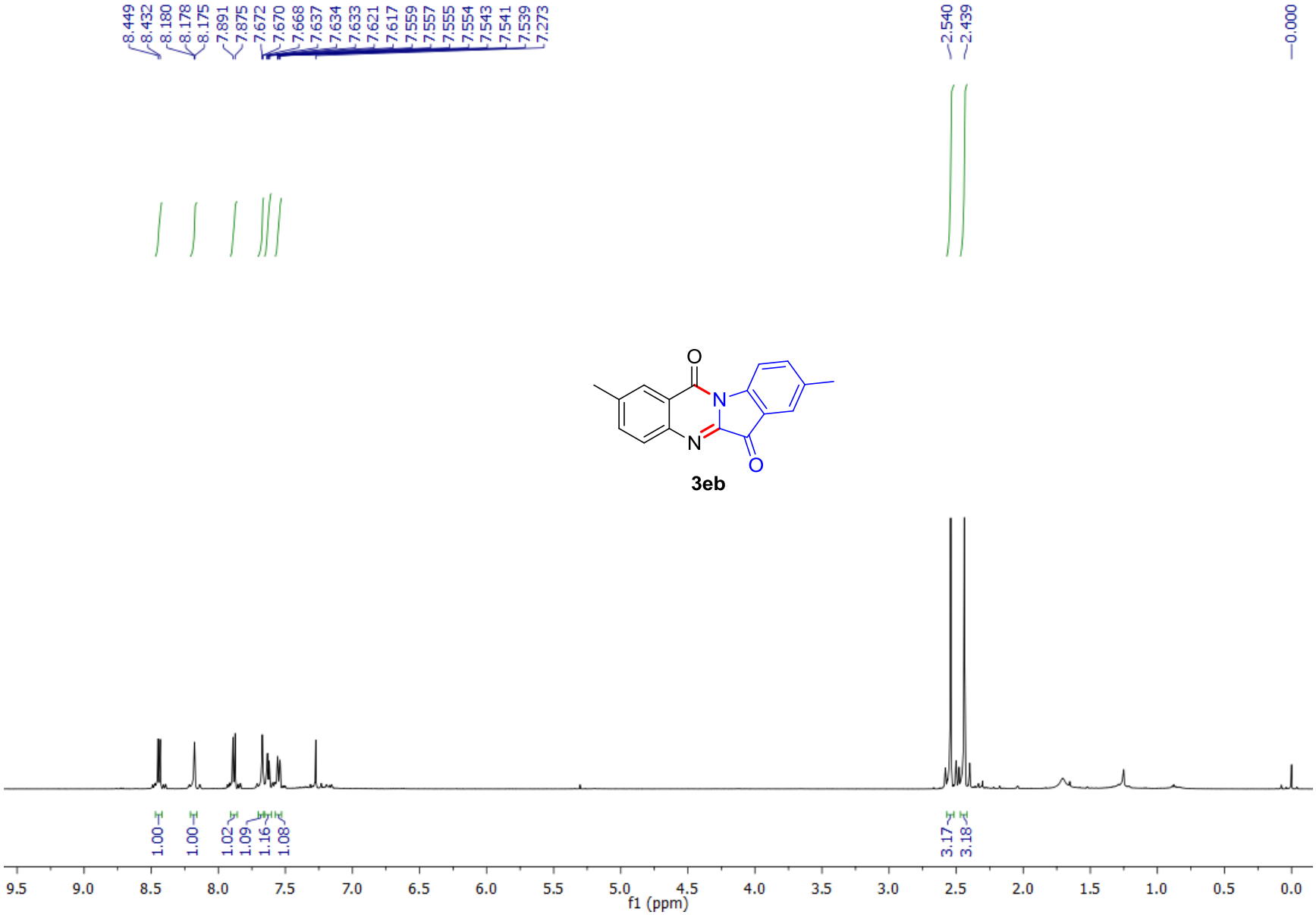
8.83
8.77
8.76
8.71
8.70
8.69
8.69
8.41
8.39
8.04
8.04
7.70
7.70
7.69
7.68
7.26
0.00
O
N
NO2
Cl
N
O
3bi
1.07
1.00
1.05
1.07
1.05
1.03
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


180.91
157.71
149.30
147.70
146.67
146.10
140.69
133.04
130.74
129.57
129.41
123.40
122.02
119.96
118.05
40.29
40.12
39.96
39.62
39.46
39.29
O
N
NO2
Cl
N
O
3bi
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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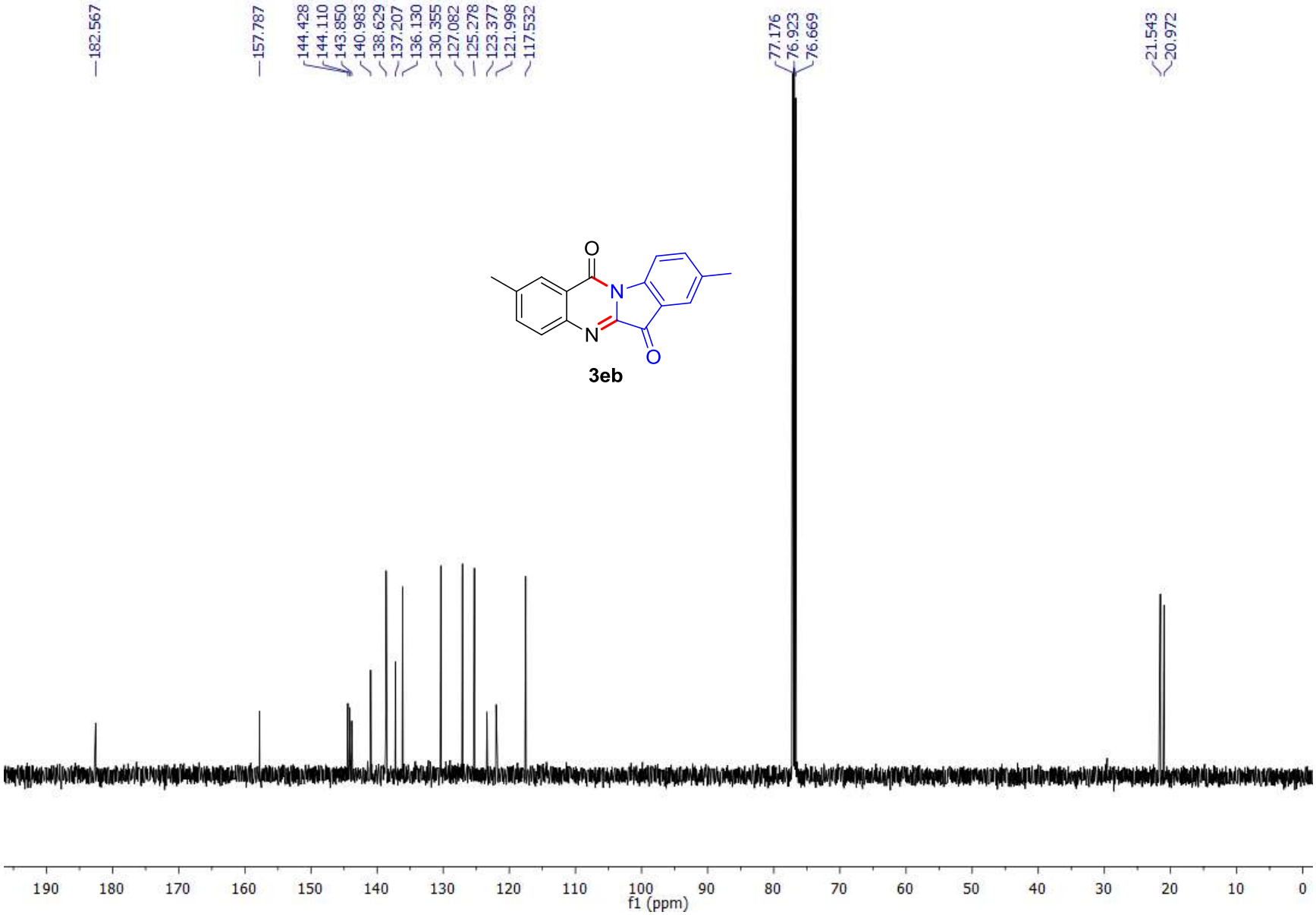
8.432
8.180
8.178
8.175
7.891
7.875
7.672
7.670
7.668
7.637
7.634
7.633
7.621
7.617
7.559
7.557
7.555
7.554
7.543
7.541
7.539
7.273
2.540
2.439
0.000
O
N
N
O
3eb
1.00
1.00
1.02
1.09
1.16
1.08
3.17
3.18
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


182.567
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144.428
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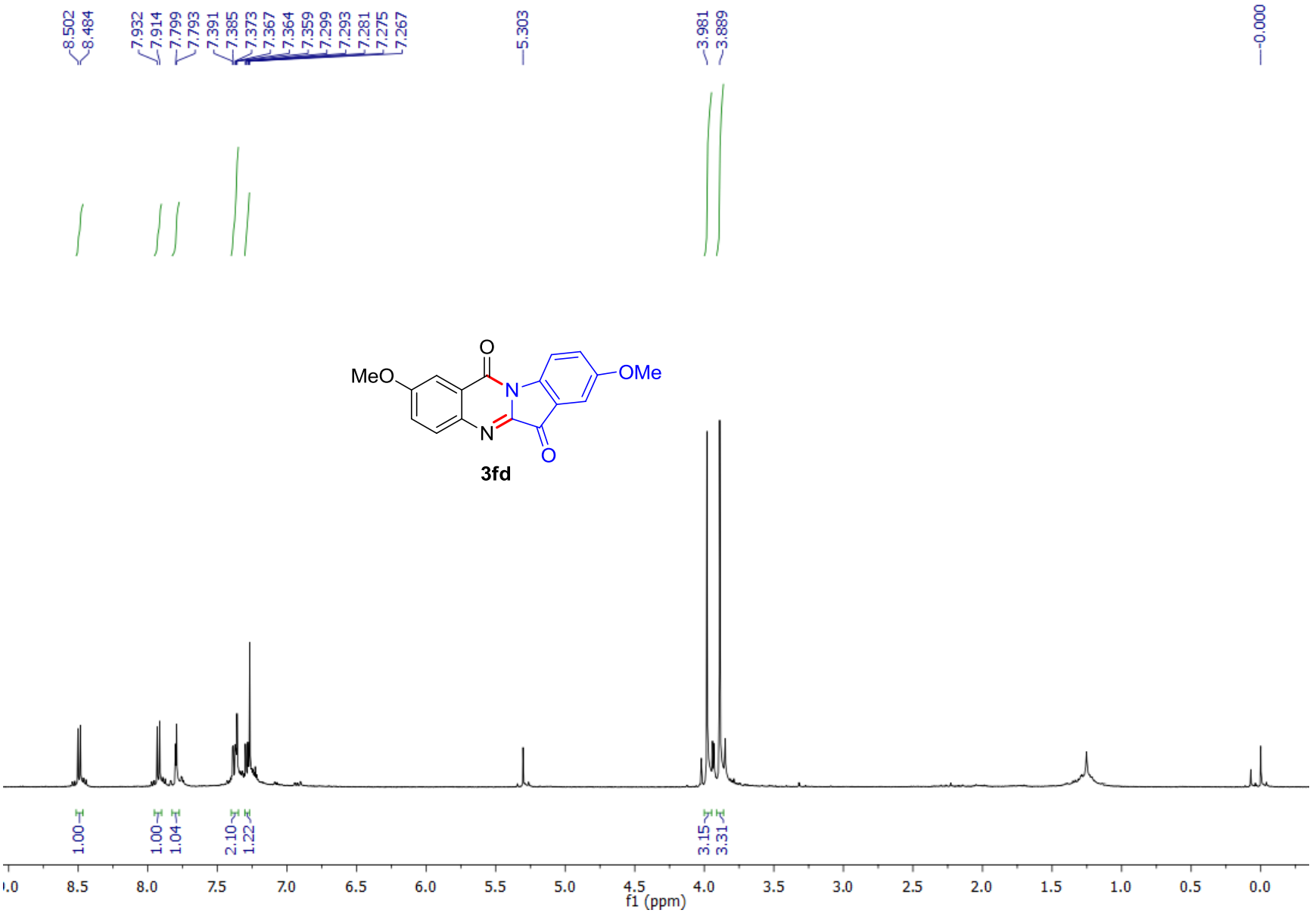
143.850
140.983
138.629
137.207
136.130
130.355
127.082
125.278
123.377
121.998
117.532
77.176
76.923
76.669
21.543
20.972
O
N
N
O
3eb
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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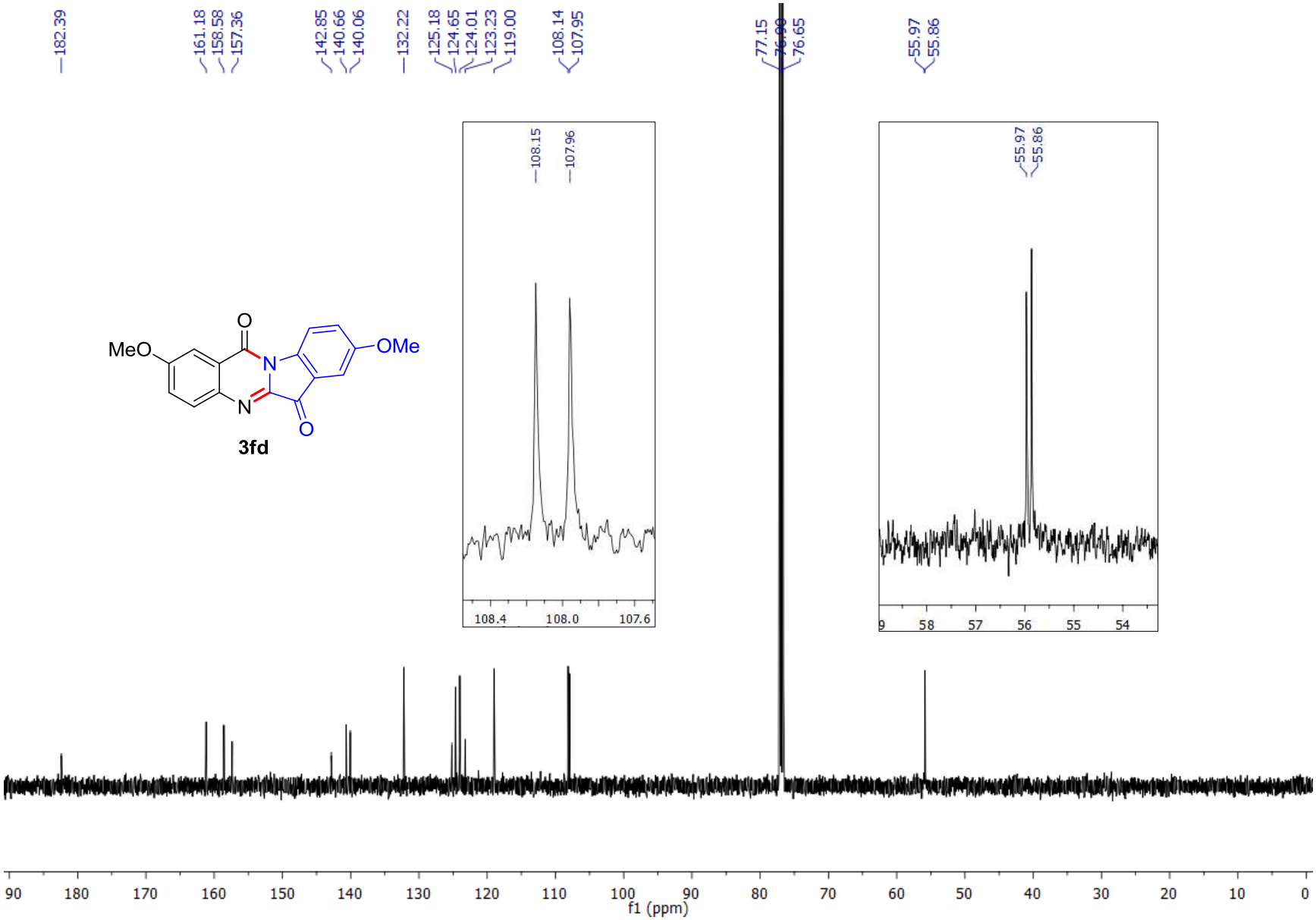
8.484
7.932
7.914
7.799
7.793
7.391
7.385
7.373
7.367
7.364
7.359
7.299
7.293
7.281
7.275
7.267
5.303
3.981
3.889
0.000
MeO
OMe
O
N
N
O
3fd
1.00
1.00
1.04
2.10
1.22
3.15
3.31
f1 (ppm)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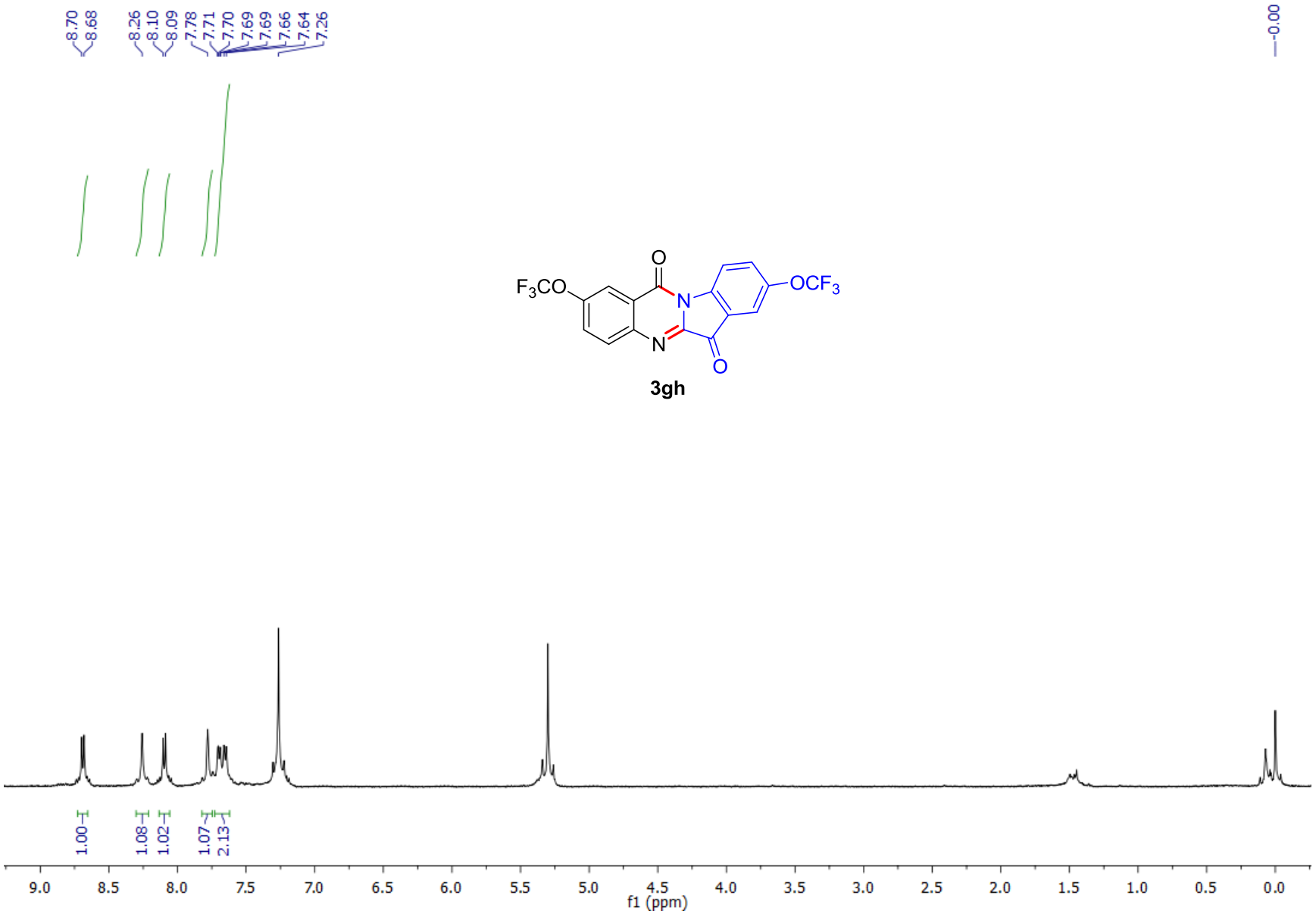
158.58
157.36
142.85
140.66
140.06
132.22
125.18
124.65
124.01
123.23
119.00
108.14
107.95
77.15
76.90
76.65
55.97
55.86
MeO
OMe
O
N
N
O
3fd
108.15
107.96
108.4
108.0
107.6
55.97
55.86
58
57
56
55
54
90
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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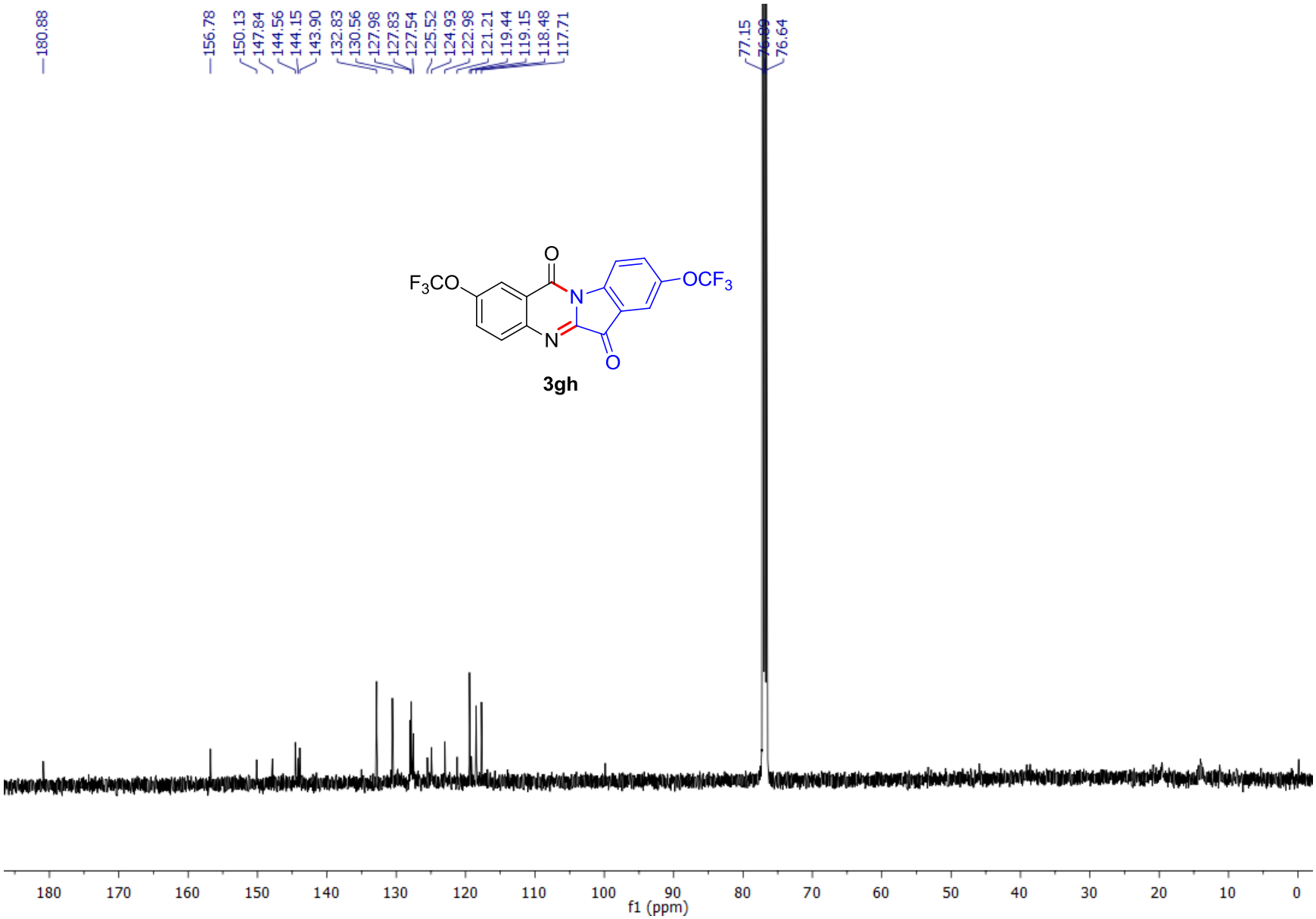
8.09
7.78
7.71
7.70
7.69
7.69
7.66
7.64
7.26
-0.00
O
F3CO
N
OCF3
N
O
3gh
1.00
1.08
1.02
1.07
2.13
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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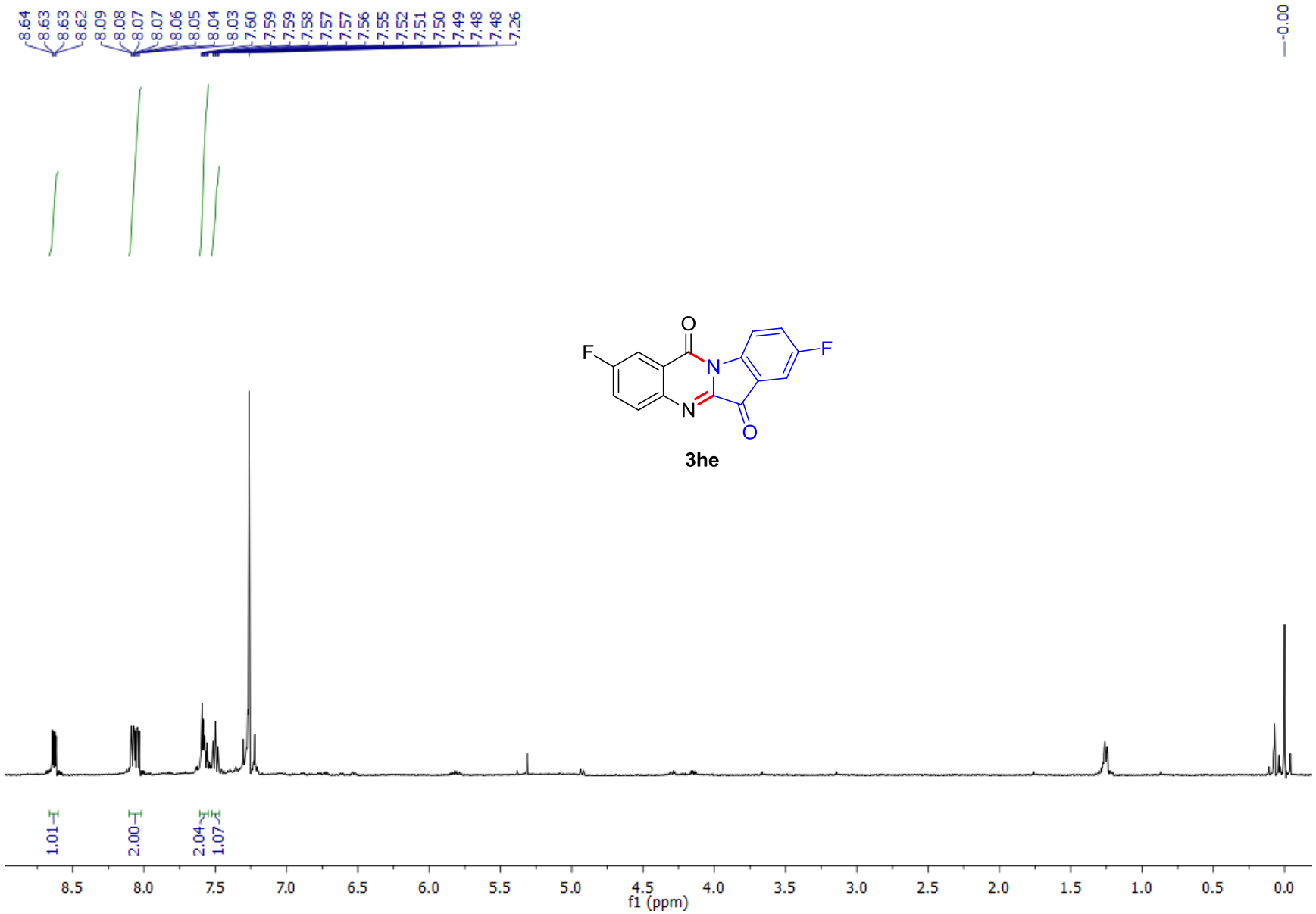
144.56
144.15
143.90
132.83
130.56
127.98
127.83
127.54
125.52
124.93
122.98
121.21
119.44
119.15
118.48
117.71
77.15
76.64
O
F3CO
N
N
OCF3
O
3gh
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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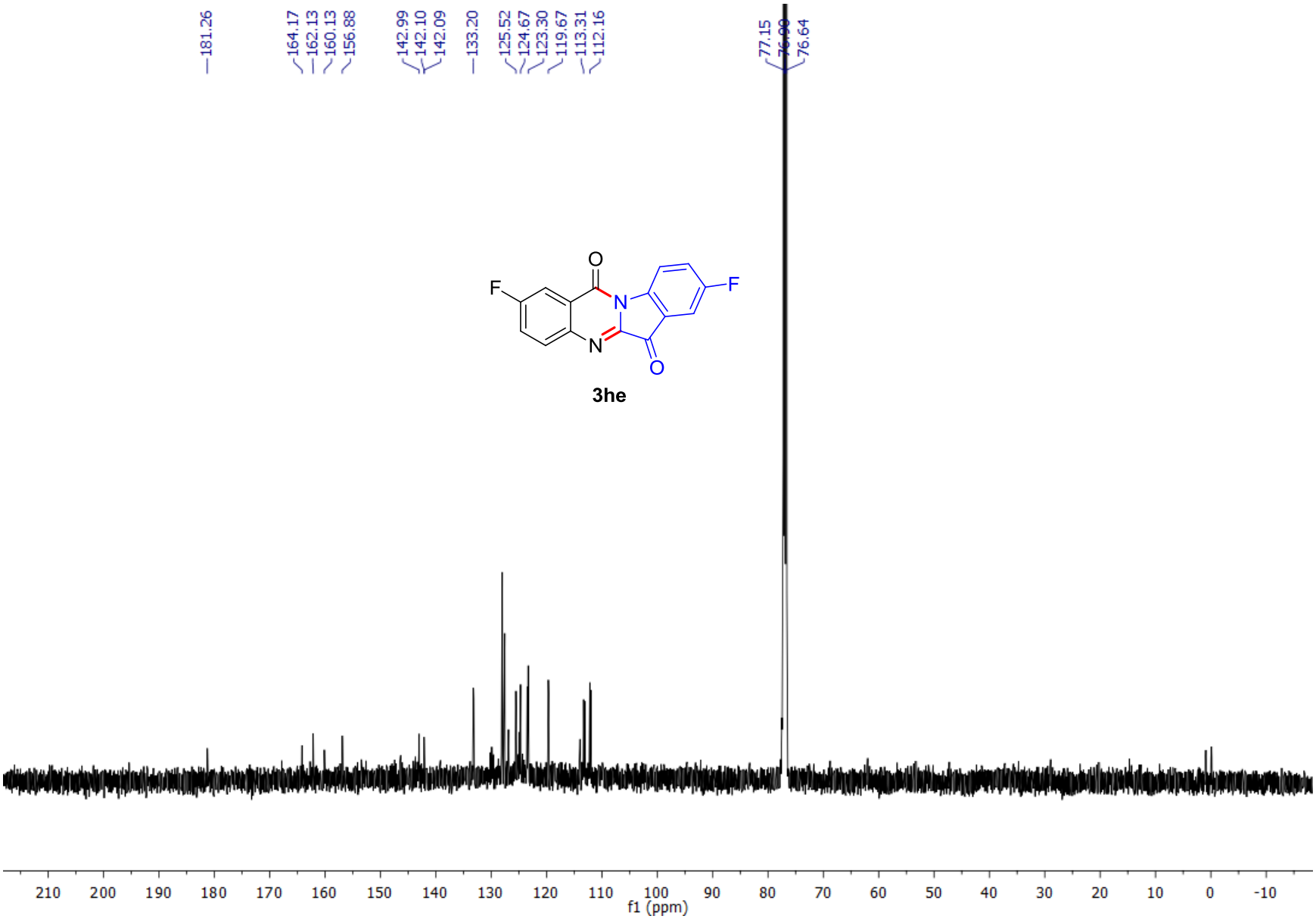
8.63
8.63
8.62
8.09
8.08
8.07
8.07
8.06
8.05
8.04
8.03
7.60
7.59
7.59
7.58
7.57
7.57
7.56
7.55
7.52
7.51
7.50
7.49
7.48
7.48
7.26
-0.00
O
F
N
N
F
O
1.01
2.00
2.04
1.07
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

3he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160.13
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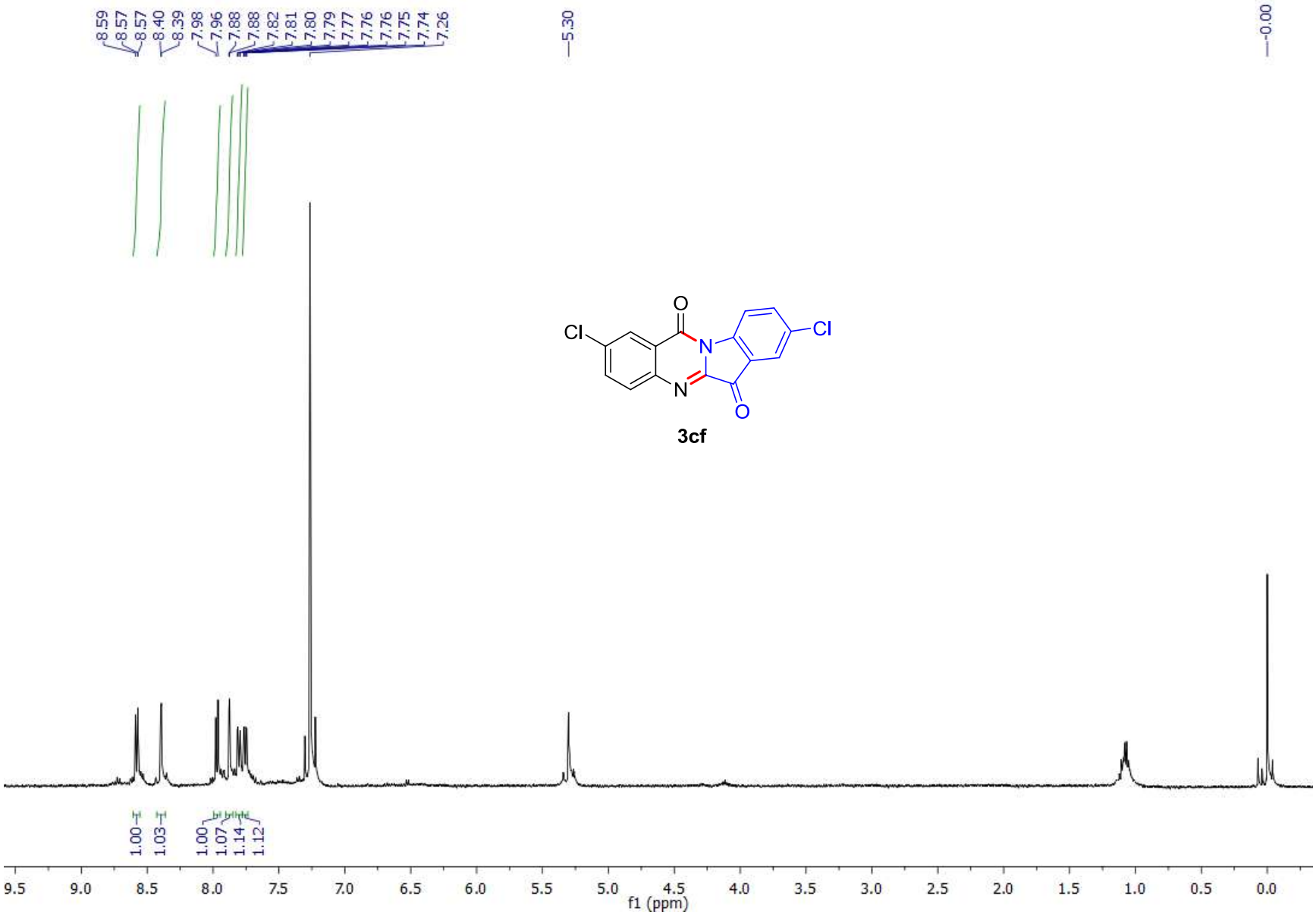
142.99
142.10
142.09
133.20
125.52
124.67
123.30
119.67
113.31
112.16
77.15
76.00
76.64
O
F
N
N
F
O
3he
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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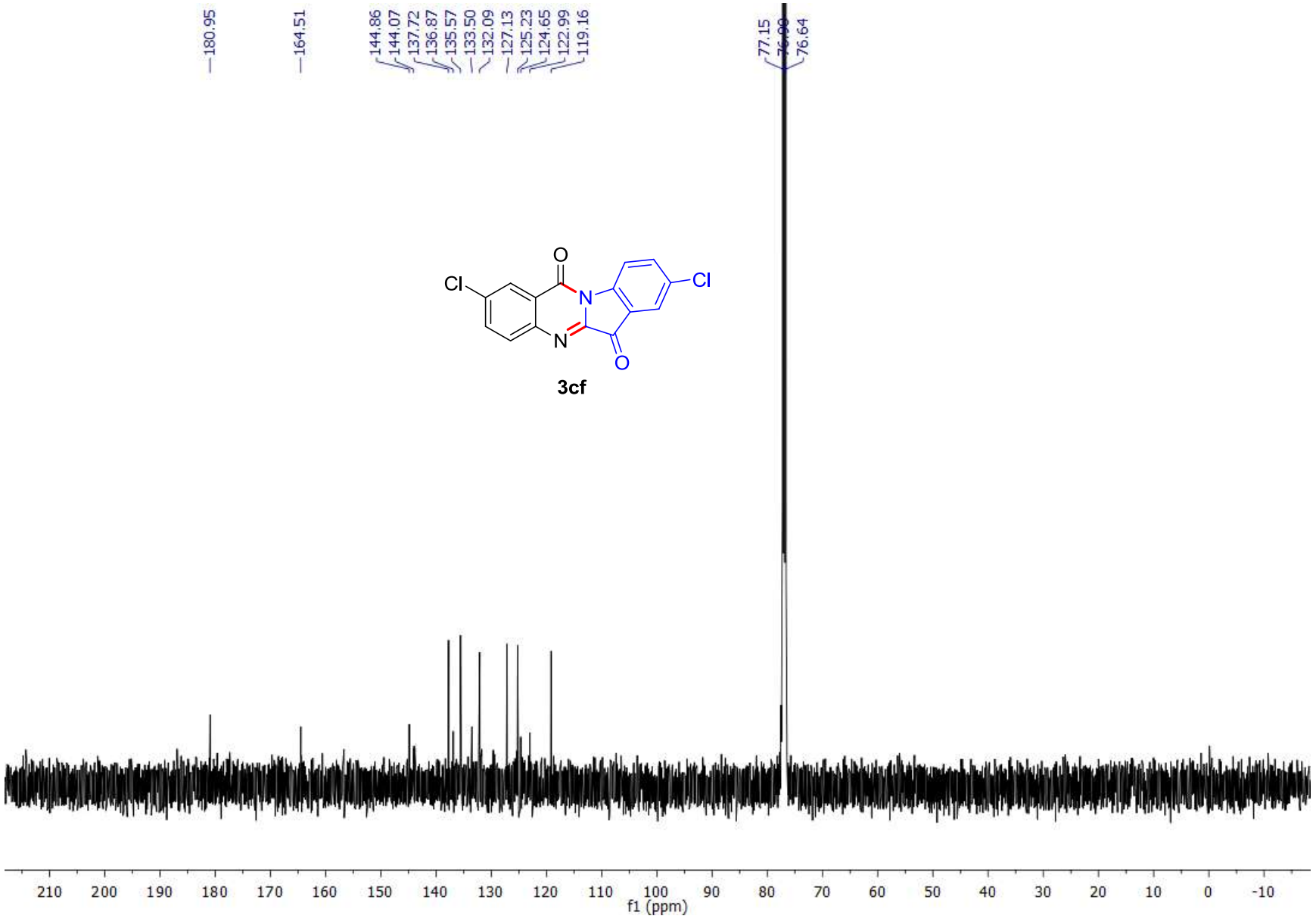
7.82
7.81
7.80
7.79
7.77
7.76
7.76
7.75
7.74
7.26
5.30
0.00
Cl
O
N
N
Cl
O
3cf
1.00
1.03
1.00
1.07
1.14
1.12
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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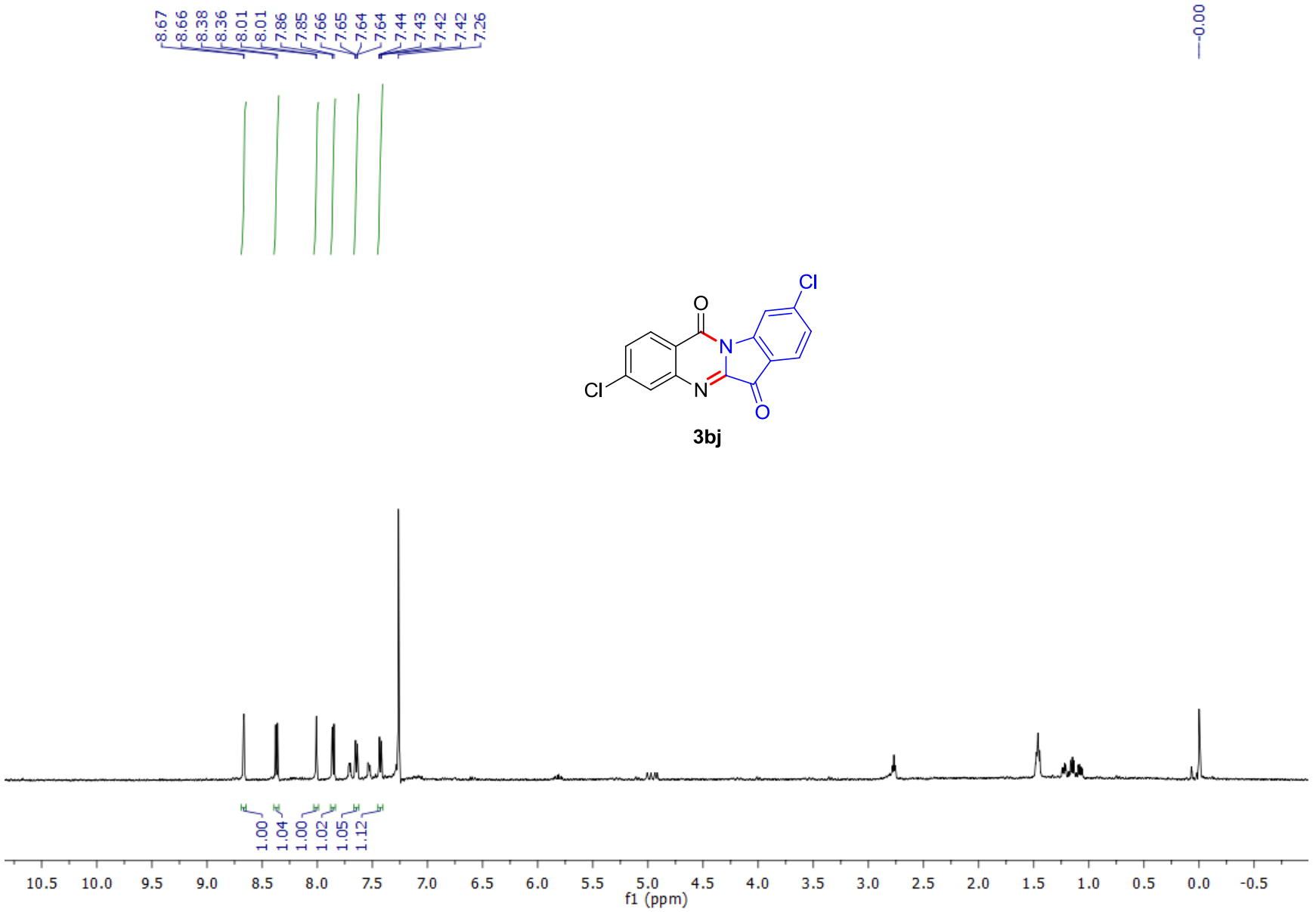
133.50
132.09
127.13
125.23
124.65
122.99
119.16
77.15
76.64
Cl
Cl
O
N
N
O
3cf
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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8.36
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8.01
7.86
7.85
7.66
7.65
7.64
7.64
7.44
7.43
7.42
7.42
7.26
-0.00
Cl
O
N
Cl
N
O
3bj
1.00
1.04
1.00
1.02
1.05
1.12
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
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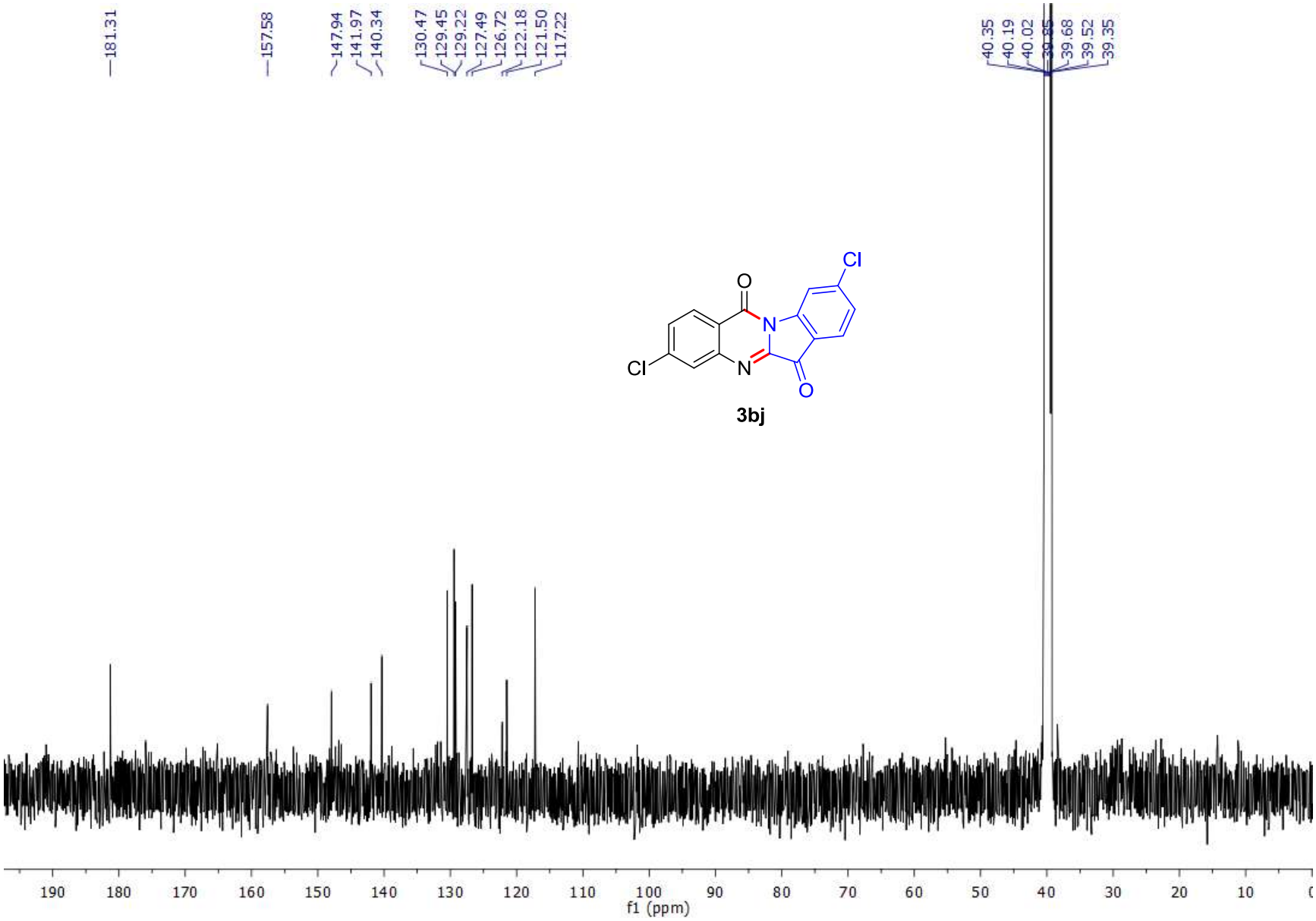
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


181.31
157.58
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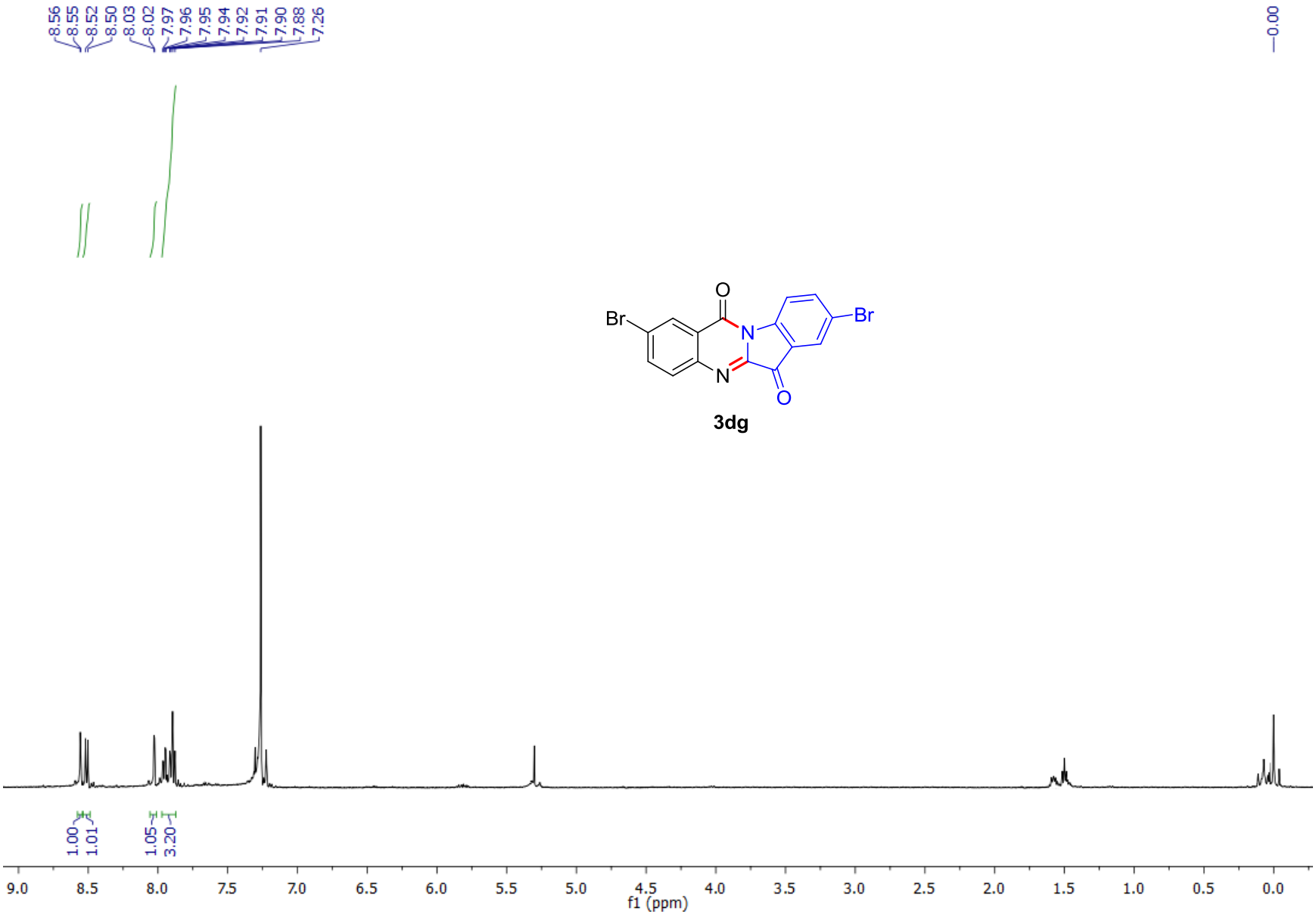
141.97
140.34
130.47
129.45
129.22
127.49
126.72
122.18
121.50
117.22
40.35
40.19
40.02
39.85
39.68
39.52
39.35
Cl
O
N
Cl
N
O
3bj
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)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8.02
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7.96
7.95
7.94
7.92
7.91
7.90
7.88
7.26
0.00
Br
O
N
N
Br
O
3dg
1.00
1.01
1.05
3.20
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)