A Robust Protocol for Pd(II)-catalyzed C-3 Arylation of (*1H*) Indazoles and Pyrazoles: Total Synthesis of Nigellidine Hydrobromide

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SUPPORTING INFORMATION

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General Information:

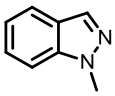
Unless otherwise noted, all reactions were run under air and were heated on hot plates with oil baths calibrated to an external thermometer. Prior to starting experiments, the hot plate was turned on, and the oil bath was allowed to equilibrate to the desired temperature over 30 minutes. All materials were used as received from commercial sources without further purification and all reagents were handled in air. ^{1}H and ^{13}C NMR spectra were recorded on Varian-Inova and Bruker AV (400 MHz and 100 MHz, respectively) instrument internally referenced to $SiMe_4$ or chloroform signals. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet. High resolution mass spectra were recorded at the Center for Mass Spectrometry, The Scripps Research Institute.

Experimental:

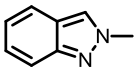
1. General Procedure for Substrate Synthesis:

(1) General Procedure for 1-Me-, Bn-, and SEM-indazole[1]:

To a suspended solution of NaH (6 mmol, 1.5 eq) in DMF (5 mL) and DMSO (2.5 mL), was added substituted indazole (4 mmol, 1.0 eq) in DMF (5 mL) at 0 °C under N_2 atmosphere. Then the reaction mixture was warmed to rt and stirred for 15 minutes. The solution was cooled back to 0 °C whereupon alkyl halide (6.4 mmol, 1.6 eq) was added dropwise to the stirred solution. Upon complete addition, the solution was stirred at rt overnight. The reaction was then quenched with saturated NH_4Cl and extracted with Et_2O. The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The resulting residue was purified by silica gel column using hexane:ethyl acetate (4:1 to 1:1) as the eluent to give the corresponding protected 1H-indazole and 2H-indazole (the ratio is about 2:1 to 3:1).

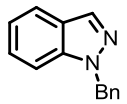


1-Methyl-1H-indazole[2]: white solid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.39 (d, *J* = 3.6 Hz, 2H), 7.15 (dt, *J* = 7.9, 3.8 Hz, 1H), 4.07 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.77, 132.60, 126.10, 123.91, 120.96, 120.32, 108.80, 35.40.

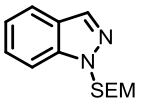


2-Methyl-2H-indazole[3]: white solid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.69 (d, *J* = 8.7 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.26 (t, *J* = 8.0 Hz, 1H), 7.05 (t, *J* = 8.0 Hz, 1H), 4.13 (s,

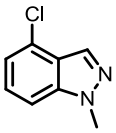
3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.87, 125.67, 123.36, 121.92, 121.43, 119.81, 117.02, 40.08.



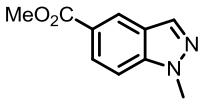
1-Benzyl-1H-indazole[4]: white solid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.36 – 7.20 (m, 5H), 7.18 (d, *J* = 6.7 Hz, 2H), 7.14 – 7.10 (m, 1H), 5.58 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.49, 136.84, 133.32, 128.65, 127.67, 127.10, 126.32, 124.31, 121.09, 120.58, 109.23, 52.90.



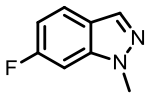
1-((2-(Trimethylsilyl)ethoxy)methyl)-1H-indazole[5]: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.42 (t, *J* = 7.7 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 5.75 (s, 2H), 3.55 (t, *J* = 8.0 Hz, 2H), 0.89 (t, *J* = 8.0 Hz, 2H), -0.07 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.69, 133.98, 126.68, 124.74, 121.22, 120.99, 109.93, 109.61, 77.61, 66.31, 17.70, -1.53.



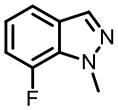
4-Chloro-1-methyl-1H-indazole[6]: yellow oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.29 – 7.24 (m, 2H), 7.12 – 7.07 (m, 1H), 4.05 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 140.70, 131.33, 126.70, 126.51, 123.18, 120.01, 107.47, 35.78



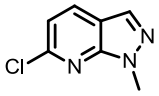
Methyl 1-methyl-1H-indazole-5-carboxylate: brown solid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.07 (s, 1H), 8.06 (d, *J* = 8.0 Hz, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 4.09 (s, 3H), 3.94 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.28, 141.53, 134.47, 127.04, 124.57, 123.63, 122.77, 108.61, 52.05, 35.68; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{10}H_{11}N_2O_2$ $[M+H]^+$ 191.0815, found 191.0820.



6-Fluoro-1-methyl-1H-indazole: white solid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.64 (dd, *J* = 8.8, 5.1 Hz, 1H), 7.00 (d, *J* = 9.2 Hz, 1H), 6.90 (td, *J* = 9.0, 2.1 Hz, 1H), 4.00 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.06 (d, *J* = 243 Hz), 140.11 (d, *J* = 12.0 Hz), 132.91, 122.34 (d, *J* = 11.0 Hz), 120.77, 110.34 (d, *J* = 25.0 Hz), 94.50 (d, *J* = 26.0 Hz), 35.49; **HRMS** (ESI-TOF) *m/z* Calcd for $C_8H_8FN_2$ $[M+H]^+$ 151.0666, found 151.0668.

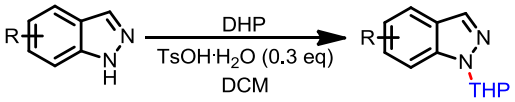


7-Fluoro-1-methyl-1H-indazole: yellow oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 2.3 Hz, 1H), 7.46 – 6.91 (m, 1H), 7.06 – 6.91 (m, 2H), 4.23 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.51(d, *J* = 246 Hz), 133.03 (d, *J* = 1.0 Hz), 129.37 (d, *J* = 12.0 Hz), 127.98 (d, *J* = 4.0 Hz), 120.78 (d, *J* = 5.0 Hz), 116.61 (d, *J* = 4.0 Hz), 110.58 (d, *J* = 17.0 Hz), 38.11 (d, *J* = 4.0 Hz); **HRMS** (ESI-TOF) *m/z* Calcd for $C_8H_8FN_2$ $[M+H]^+$ 151.0666, found 151.0665.

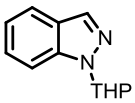


6-Chloro-1-methyl-1H-pyrazolo[3,4-b]pyridine: yellow solid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.0 Hz, 1H), 8.01 (s, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 4.17 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.55, 149.61, 132.14, 132.04, 117.31, 114.08, 34.18; **HRMS** (ESI-TOF) *m/z* Calcd for $C_7H_7ClN_3$ $[M+H]^+$ 168.0328, found 168.0330.

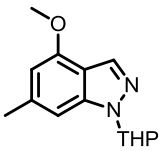
(2) General Procedure for 1-THP-indazole[7]:



To a solution of substituted indazole (10 mmol, 1.0 eq) in DCM (40 mL), was added *p*-toluenesulfonic acid (571 mg, 3 mmol, 0.3 eq), and dihydropyran (DHP, 30 mmol, 3.0 eq). The solution was then stirred at rt until TLC showed a complete conversion of starting material. The solution was further diluted with DCM, washed with saturated $NaHCO_3$. The separated organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The resulting residue was purified by silica gel column using hexane:ethyl acetate (6:1) as the eluent to give the sole 1-THP-1H-indazole.



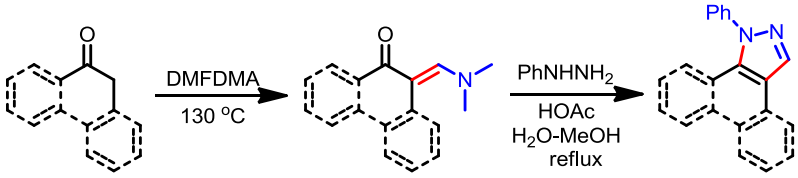
1-(Tetrahydro-2H-pyran-2-yl)-1H-indazole[7]: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.39 (t, *J* = 8.0 Hz, 1H), 7.17 (t, *J* = 8.0 Hz, 1H), 5.73 (dd, *J* = 9.5, 2.7 Hz, 1H), 4.06-4.01 (m, 1H), 3.78 – 3.72 (m, 1H), 2.65 – 2.55 (m, 1H), 2.18 – 2.06 (m, 2H), 1.79 – 1.63 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.42, 133.86, 126.42, 124.62, 121.11, 120.95, 109.90, 85.18, 67.43, 29.36, 25.07, 22.60.



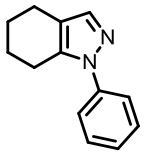
4-Methoxy-6-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole 7: white solid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 6.94 (s, 1H), 6.32 (s, 1H), 5.63 (dd, *J* = 9.5, 2.7 Hz, 1H), 4.07

– 4.01 (m, 1H), 3.93 (s, 3H), 3.79 – 3.68 (m, 1H), 2.61 – 2.52 (m, 1H), 2.47 (s, 3H), 2.22 – 2.10 (m, 1H), 2.10 – 1.99 (m, 1H), 1.81 – 1.57 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 153.18, 141.71, 138.47, 131.60, 114.76, 102.37, 102.25, 85.16, 67.49, 55.27, 29.35, 25.11, 22.70, 22.47; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{14}H_{19}N_2O_2$ $[M+H]^+$ 247.1441, found 247.1450.

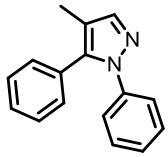
(3) General Procedure for Pyrazole Synthesis[8,9]:



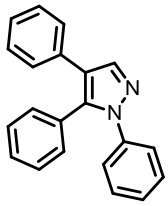
To a 35 mL sealed tube, were added N,N-dimethylformamide dimethyl acetal (DMFDMA) (1.0 mL, 7.5 mmol, 1.5 eq), and corresponding ketone (5 mmol, 1.0 eq) under N_2 atmosphere. The tube was capped and stirred at 130 °C overnight. The reaction mixture was cooled to rt and evaporated in *vacuo*. The residue was diluted with MeOH (13 mL) and transferred to a 50 mL flask, then HOAc (3.0 mL), H_2O (26 mL) and $PhNHNH_2$ (0.74 mL, 7.5 mmol) were added. The resulting mixture was heated to reflux overnight. After cooling, the mixture was evaporated to half volume in *vacuo*, and H_2O (20 mL) was added. The solution was extracted with DCM and the combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated in *vacuo*. The resulting residue was purified by silica gel column using hexane:ethyl acetate (10:1) as the eluent to give the product.



1-Phenyl-4,5,6,7-tetrahydro-1H-indazole[10]: brown oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 – 7.38 (m, 5H), 7.33 – 7.27 (m, 1H), 2.74 – 2.71 (m, 2H), 2.64 – 2.51 (m, 2H), 1.82– 1.77 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 140.04, 138.73, 138.10, 128.94, 126.49, 122.92, 117.66, 23.62, 23.10, 22.73, 20.67.

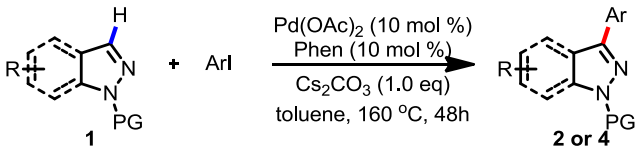


4-Methyl-1,5-diphenyl-1H-pyrazole[11]: white solid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.63 (s, 1H), 7.41 – 7.32 (m, 3H), 7.32 – 7.16 (m, 7H), 2.15 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 141.12, 140.27, 139.78, 130.56, 129.79, 128.64, 128.39, 127.94, 126.71, 124.59, 116.35, 9.17.

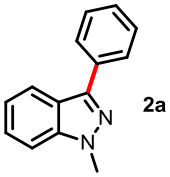


1,4,5-Triphenyl-1H-pyrazole[12]: white solid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.35 – 7.18 (m, 13H), 7.15 (dt, *J* = 6.6, 1.7 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 139.95, 139.75, 139.20, 132.78, 130.44, 130.22, 128.69, 128.59, 128.44, 128.41, 127.96, 127.19, 126.37, 125.16, 122.42.

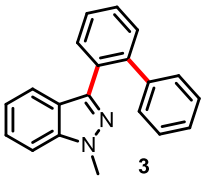
2. General Procedure for C-3 Arylation



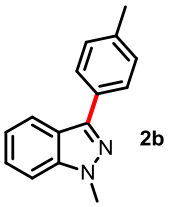
To a 35 mL sealed tube, were added $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), 1,10-phenanthroline (4.5 mg, 0.025 mmol), Cs_2CO_3 (82 mg, 0.25 mmol), aryl halide (0.25 mmol), indazole derivative (0.25 mmol), and toluene (1 mL). The tube was capped and stirred at 160 °C for 48-72 h. The reaction mixture was cooled to room temperature and diluted with EtOAc, filtered through a short pad of Celite, washed with EtOAc, and concentrated in *vacuo*. The resulting residue was purified by PTLC using hexanes:EtOAc (10:1 to 6:1, depending on different substrates) as the eluent.



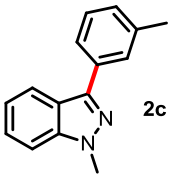
1-Methyl-3-phenyl-1H-indazole[13]: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 (dd, *J* = 8.2, 0.9 Hz, 1H), 7.99 (d, *J* = 7.6 Hz, 2H), 7.52 (t, *J* = 7.6 Hz, 2H), 7.47 – 7.37 (m, 3H), 7.25 – 7.20 (m, 1H), 4.13 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.65, 141.38, 133.65, 128.75, 127.75, 127.32, 126.20, 121.56, 121.29, 120.85, 109.14, 35.48.



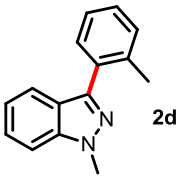
3-([1,1'-Biphenyl]-2-yl)-1-methyl-1H-indazole: white solid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 7.3, 2.0 Hz, 1H), 7.98 – 7.94 (m, 2H), 7.56 – 7.45 (m, 8H), 7.44 – 7.39 (m, 1H), 7.28 – 7.21 (m, 1H), 3.68 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.86, 139.29, 138.77, 133.54, 129.89, 128.79, 128.14, 128.04, 127.85, 127.75, 127.61, 126.20, 122.66, 120.82, 120.42, 39.23; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{20}H_{17}N_2$ $[M+H]^+$ 285.1386, found 285.1390.



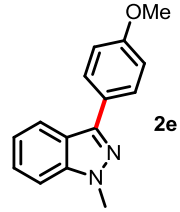
1-Methyl-3-(*p*-tolyl)-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.2 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 2H), 7.45 – 7.39 (m, 2H), 7.33 (dd, *J* = 7.9, 0.7 Hz, 2H), 7.23 – 7.19 (m, 1H), 4.12 (s, 3H), 2.44 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.74, 141.36, 137.54, 130.78, 129.46, 127.21, 126.15, 121.56, 121.37, 120.69, 109.08, 35.44, 21.29; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{15}H_{15}N_2$ $[M+H]^+$ 223.1230, found 223.1239.



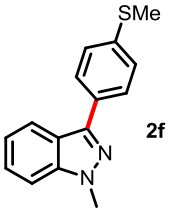
1-Methyl-3-(*m*-tolyl)-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.2 Hz, 1H), 7.80 (s, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.46 – 7.38 (m, 3H), 7.24 – 7.20 (m, 1H), 4.13 (s, 3H), 2.47 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.83, 141.37, 138.43, 133.52, 128.64, 128.58, 127.95, 126.20, 124.50, 121.61, 121.39, 120.78, 109.12, 35.48, 21.52; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{15}H_{15}N_2$ $[M+H]^+$ 223.1230, found 223.1238.



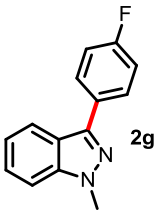
1-Methyl-3-(*o*-tolyl)-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.2 Hz, 1H), 7.56 – 7.51 (m, 1H), 7.46 – 7.40 (m, 2H), 7.38 – 7.29 (m, 3H), 7.19 – 7.15 (m, 1H), 4.15 (s, 3H), 2.42 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.44, 140.61, 137.15, 132.35, 130.64, 130.47, 128.03, 126.13, 125.61, 122.97, 121.37, 120.42, 108.94, 35.46, 20.50; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{15}H_{15}N_2$ $[M+H]^+$ 223.1230, found 223.1237.



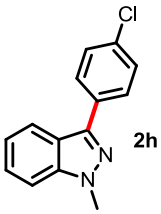
3-(4-Methoxyphenyl)-1-methyl-1H-indazole[13]: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.2 Hz, 1H), 7.93 – 7.87 (m, 2H), 7.45 – 7.37 (m, 2H), 7.22 – 7.18 (m, 1H), 7.08 – 7.02 (m, 2H), 4.11 (s, 3H), 3.88 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.37, 143.54, 141.35, 128.53, 126.32, 126.15, 121.46, 121.31, 120.61, 114.21, 109.06, 55.30, 35.40.



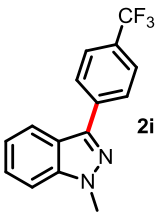
1-Methyl-3-(4-(methylthio)phenyl)-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 8.2, 1.0 Hz, 1H), 7.90 (d, *J* = 7.9 Hz, 2H), 7.46 – 7.36 (m, 4H), 7.24 – 7.18 (m, 1H), 4.12 (s, 3H), 2.54 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.11, 141.39, 138.00, 130.55, 127.60, 126.83, 126.23, 121.48, 121.20, 120.86, 109.18, 35.49, 15.83; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{15}H_{15}N_2S$ $[M+H]^+$ 255.0950, found 255.0958.



3-(4-Fluorophenyl)-1-methyl-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.3 Hz, 1H), 7.94 – 7.89 (m, 2H), 7.47 – 7.40 (m, 2H), 7.25 – 7.16 (m, 3H), 4.13 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.62 (d, *J* = 246 Hz), 142.09 (d, *J* = 146 Hz), 129.56 (d, *J* = 3.0 Hz), 129.07, 128.99, 126.54, 121.34, 121.11 (d, *J* = 1.0 Hz), 115.89, 115.68, 109.26, 35.47; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{14}H_{12}FN_2$ $[M+H]^+$ 227.0979, found 227.0979.

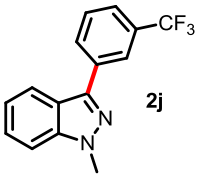


3-(4-Chlorophenyl)-1-methyl-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 (dt, *J* = 8.2, 1.0 Hz, 1H), 7.93 – 7.88 (m, 2H), 7.50 – 7.45 (m, 2H), 7.45 – 7.41 (m, 2H), 7.25 – 7.21 (m, 1H), 4.12 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.46, 141.42, 133.57, 132.19, 128.95, 128.46, 126.36, 121.40, 121.13, 121.01, 109.29, 35.56; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{14}H_{12}ClN_2$ $[M+H]^+$ 243.0683, found 243.0683.



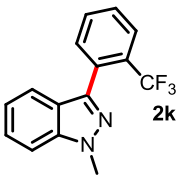
1-Methyl-3-(4-(trifluoromethyl)phenyl)-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.8 Hz, 2H), 8.01 (d, *J* = 8.3 Hz, 1H), 7.75 (d, *J* = 8.5 Hz, 2H), 7.49 – 7.42 (m, 2H), 7.28 – 7.24 (m, 1H), 4.14 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.02, 141.48, 137.24 (q, *J* = 2.0 Hz), 129.47 (q, *J* = 32.0 Hz), 127.29, 126.46, 125.68 (d, *J* = 4.0 Hz), 122.92,

121.51, 121.47, 120.88, 109.43, 35.64; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{15}H_{12}F_3N_2$ $[M+H]^+$ 277.0947, found 277.0952.



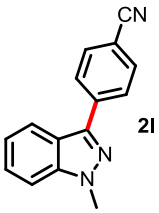
2j

1-Methyl-3-(3-(trifluoromethyl)phenyl)-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 8.16 (d, *J* = 7.3 Hz, 1H), 8.00 (d, *J* = 8.2 Hz, 1H), 7.68 – 7.58 (m, 2H), 7.46 – 7.44 (m, 2H), 7.29 – 7.23 (m, 1H), 4.14 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.06, 141.47, 134.55, 131.19 (q, *J* = 32.0 Hz), 129.21, 126.46, 125.54, 124.31 (q, *J* = 4.0 Hz), 124.00 (q, *J* = 4.0 Hz), 122.83, 121.41, 121.39, 120.81, 109.40, 35.62; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{15}H_{12}F_3N_2$ $[M+H]^+$ 277.0947, found 277.0952.



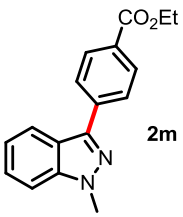
2k

1-Methyl-3-(2-(trifluoromethyl)phenyl)-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.87 – 7.83 (m, 1H), 7.67 – 7.53 (m, 4H), 7.47 – 7.40 (m, 2H), 7.18 – 7.14 (m, 1H), 4.14 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.10, 140.42, 132.74, 131.84 (q, *J* = 2.0 Hz), 131.37, 129.91 (q, *J* = 31.0 Hz), 128.42, 126.60 (q, *J* = 4.0 Hz), 126.34, 125.30, 123.38, 120.82, 120.73, 108.92, 35.59; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{15}H_{12}F_3N_2$ $[M+H]^+$ 277.0947, found 277.0957.



2l

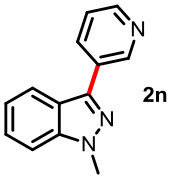
4-(1-Methyl-1H-indazol-3-yl)benzonitrile[13]: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.3 Hz, 2H), 7.99 (d, *J* = 8.3 Hz, 1H), 7.75 (d, *J* = 8.2 Hz, 2H), 7.50 – 7.42 (m, 2H), 7.29 – 7.25 (m, 1H), 4.15 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 141.52, 141.35, 138.25, 132.53, 127.37, 126.57, 121.78, 121.44, 120.71, 119.01, 110.83, 109.58, 35.76.



2m

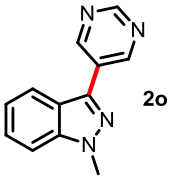
Ethyl 4-(1-methyl-1H-indazol-3-yl)benzoate: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 – 8.14 (m, 2H), 8.08 – 8.03 (m, 2H), 8.02 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.47 – 7.39 (m, 2H), 7.29 – 7.18 (m, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.13 (s, 3H), 1.43 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (100

MHz, $CDCl_3$) δ 166.45, 142.36, 141.43, 138.02, 130.00, 129.36, 126.84, 126.37, 121.58, 121.39, 121.04, 109.35, 60.92, 35.62, 14.32; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{17}H_{17}N_2O_2$ $[M+H]^+$ 281.1284, found 281.1290.



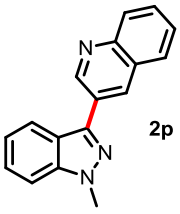
2n

1-Methyl-3-(pyridin-3-yl)-1H-indazole[13]: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.24 (dd, *J* = 2.3, 0.9 Hz, 1H), 8.64 (dd, *J* = 4.8, 1.7 Hz, 1H), 8.26 (ddd, *J* = 7.9, 2.3, 1.7 Hz, 1H), 7.99 (dt, *J* = 8.3, 1.0 Hz, 1H), 7.50 – 7.39 (m, 3H), 7.30 – 7.22 (m, 1H), 4.15 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.70, 148.26, 141.34, 140.45, 134.27, 129.72, 126.47, 123.63, 121.41, 120.74, 109.36, 35.61.



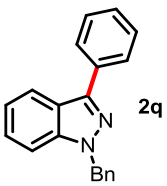
2o

1-Methyl-3-(pyrimidin-5-yl)-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.32 (s, 2H), 9.21 (s, 1H), 7.94 (d, *J* = 8.3 Hz, 1H), 7.52 – 7.42 (m, 2H), 7.31 – 7.25 (m, 1H), 4.15 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 157.43, 154.66, 141.37, 137.20, 128.07, 126.79, 122.00, 121.45, 120.29, 109.66, 35.83; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{12}H_{11}N_4$ $[M+H]^+$ 211.0978, found 211.0986.



2p

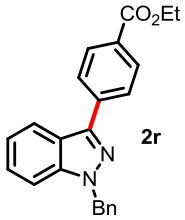
3-(1-Methyl-1H-indazol-3-yl)quinoline: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.58 (d, *J* = 2.2 Hz, 1H), 8.66 (s, 1H), 8.16 (d, *J* = 8.5 Hz, 1H), 8.08 (d, *J* = 8.2 Hz, 1H), 7.91 (d, *J* = 8.6 Hz, 1H), 7.77 – 7.67 (m, 1H), 7.62 – 7.55 (m, 1H), 7.47 – 7.45 (m, 2H), 7.31 – 7.24 (m, 1H), 4.17 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.81, 147.44, 141.42, 140.61, 132.96, 129.34, 129.32, 128.04, 128.00, 126.97, 126.94, 126.55, 121.74, 121.53, 120.83, 109.46, 35.70; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{17}H_{14}N_3$ $[M+H]^+$ 260.1182, found 260.1185.



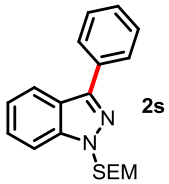
2q

1-Benzyl-3-phenyl-1H-indazole[13]: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.04 – 8.01 (m, 1H), 8.01 – 7.97 (m, 2H), 7.54 – 7.46 (m, 2H), 7.42 – 7.35 (m, 1H), 7.35 – 7.31 (m, 2H), 7.31 – 7.21 (m, 5H), 7.18 (dt, *J* = 8.0, 3.9 Hz, 1H), 5.64 (s, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.13,

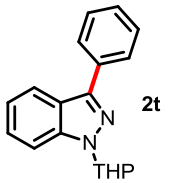
141.03, 136.84, 133.63, 128.76, 128.65, 127.85, 127.65, 127.49, 127.09, 126.33, 122.06, 121.38, 121.06, 109.60, 53.03.



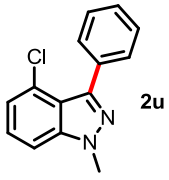
Ethyl 4-(1-benzyl-1H-indazol-3-yl)benzoate (Drug YD-3): colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.20 – 8.14 (m, 2H), 8.12 – 8.06 (m, 2H), 8.03 (d, *J* = 8.3 Hz, 1H), 7.38 – 7.32 (m, 2H), 7.32 – 7.19 (m, 6H), 5.65 (s, 2H), 4.41 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.46, 142.87, 141.08, 138.02, 136.53, 130.00, 129.46, 128.69, 127.76, 127.09, 127.03, 126.50, 122.07, 121.57, 121.14, 109.80, 60.93, 53.17, 14.33; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{23}H_{21}N_2O_2$ $[M+H]^+$ 357.1597, found 357.1581.



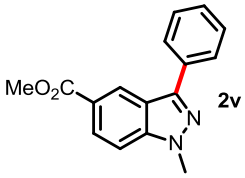
3-Phenyl-1-((2-(trimethylsilyl)ethoxy)methyl)-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.07 (dt, *J* = 8.1, 1.0 Hz, 1H), 8.04 – 7.99 (m, 2H), 7.66 (dt, *J* = 8.5, 0.9 Hz, 1H), 7.59 – 7.52 (m, 2H), 7.52 – 7.42 (m, 2H), 7.33 – 7.25 (m, 1H), 5.84 (s, 2H), 3.77 – 3.59 (m, 2H), 1.06 – 0.89 (m, 2H), -0.01 (s, 9H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.81, 141.25, 133.37, 128.76, 128.07, 127.58, 126.69, 122.57, 121.64, 121.31, 109.92, 77.72, 66.40, 17.73, -1.47; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{19}H_{25}N_2OSi$ $[M+H]^+$ 325.1731, found 325.1740.



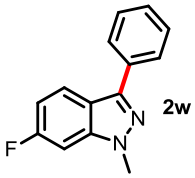
3-Phenyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.06 – 7.97 (m, 3H), 7.69 – 7.62 (m, 1H), 7.53 – 7.49 (m, 2H), 7.47 – 7.37 (m, 2H), 7.28 – 7.20 (m, 1H), 5.80 (dd, *J* = 9.3, 2.8 Hz, 1H), 4.15 – 4.04 (m, 1H), 3.81 – 3.75 (m, 1H), 2.72 – 2.67 (m, 1H), 2.31 – 2.07 (m, 2H), 1.86 – 1.60 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.52, 140.92, 133.57, 128.65, 127.91, 127.65, 126.41, 122.50, 121.54, 121.28, 110.37, 85.52, 67.43, 29.36, 25.13, 22.60; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{18}H_{19}N_2O$ $[M+H]^+$ 279.1492, found 279.1504.



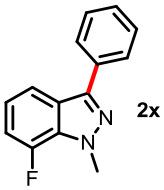
4-Chloro-1-methyl-3-phenyl-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 – 7.71 (m, 2H), 7.51 – 7.44 (m, 3H), 7.35 (s, 1H), 7.34 (d, *J* = 3.0 Hz, 1H), 7.18 (dd, *J* = 5.6, 2.6 Hz, 1H), 4.14 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.72, 142.27, 133.00, 130.56, 128.04, 127.64, 127.28, 126.82, 121.52, 119.59, 107.81, 35.76; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{14}H_{12}ClN_2$ $[M+H]^+$ 243.0683, found 243.0685.



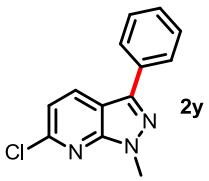
Methyl 1-methyl-3-phenyl-1H-indazole-5-carboxylate: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.75 (dd, *J* = 1.5, 0.8 Hz, 1H), 8.09 (dd, *J* = 8.9, 1.5 Hz, 1H), 8.00 – 7.93 (m, 2H), 7.53 (ddt, *J* = 8.8, 7.0, 0.8 Hz, 2H), 7.46 – 7.42 (m, 1H), 7.39 (dd, *J* = 8.8, 0.8 Hz, 1H), 4.12 (s, 3H), 3.96 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 167.26, 145.51, 143.03, 132.75, 128.88, 128.30, 127.48, 127.09, 124.84, 123.07, 121.30, 108.86, 52.07, 35.67; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{16}H_{15}N_2O_2$ $[M+H]^+$ 267.1128, found 267.1129.



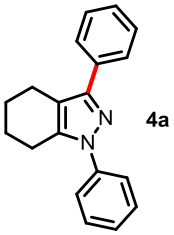
6-Fluoro-1-methyl-3-phenyl-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.96 – 7.89 (m, 3H), 7.53 – 7.50 (m, 2H), 7.44 – 7.38 (m, 1H), 7.04 (dd, *J* = 9.1, 2.2 Hz, 1H), 6.97 (dt, *J* = 9.0, 2.2 Hz, 1H), 4.06 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.11 (d, *J* = 244 Hz), 144.06, 141.76 (d, *J* = 12.0 Hz), 133.11, 128.82, 128.06, 127.33, 122.79 (d, *J* = 10.9 Hz), 118.51, 110.71 (d, *J* = 25.7 Hz), 94.77 (d, *J* = 25.9 Hz), 35.57; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{14}H_{12}FN_2$ $[M+H]^+$ 227.0979, found 227.0988.



7-Fluoro-1-methyl-3-phenyl-1H-indazole: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.97 – 7.90 (m, 2H), 7.78 – 7.72 (m, 1H), 7.55 – 7.47 (m, 2H), 7.45 – 7.38 (m, 1H), 7.12 – 7.02 (m, 2H), 4.31 (d, *J* = 1.1 Hz, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.59 (d, *J* = 246 Hz), 144.34 (d, *J* = 1.5 Hz), 133.07, 130.95 (d, *J* = 12.4 Hz), 128.80, 128.05, 127.42, 125.63 (d, *J* = 4.2 Hz), 121.25 (d, *J* = 5.44 Hz), 117.00 (d, *J* = 4.3 Hz), 110.77 (d, *J* = 16.9 Hz), 38.31 (d, *J* = 4.5 Hz); **HRMS** (ESI-TOF) *m/z* Calcd for $C_{14}H_{12}FN_2$ $[M+H]^+$ 227.0979, found 227.0990.

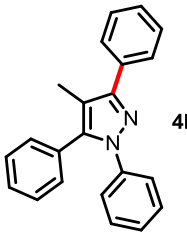


6-Chloro-1-methyl-3-phenyl-1H-pyrazolo[3,4-b]pyridine: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.30 (d, *J* = 8.0 Hz, 1H), 7.96 – 7.94 (m, 2H), 7.56 – 7.52 (m, 2H), 7.48 – 7.43 (m, 1H), 7.21 (d, *J* = 8.0 Hz, 1H), 4.21 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.51, 150.34, 143.00, 132.68, 132.11, 128.75, 128.60, 126.73, 117.35, 111.89, 33.55; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{13}H_{11}ClN_3$ $[M+H]^+$ 244.0642, found 244.0647.



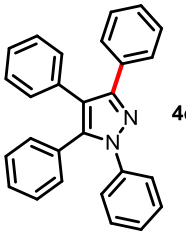
4a

1,3-Diphenyl-4,5,6,7-tetrahydro-1H-indazole: yellow oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 – 7.78 (m, 2H), 7.62 – 7.53 (m, 2H), 7.48 – 7.40 (m, 4H), 7.34 – 7.30 (m, 2H), 2.93 – 2.70 (m, 4H), 1.87 – 1.84 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.04, 140.02, 139.67, 134.10, 129.02, 128.40, 127.31, 126.92, 126.69, 123.39, 115.51, 23.94, 23.10, 22.75, 22.56; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{19}H_{19}N_2$ $[M+H]^+$ 275.1543, found 275.1542.



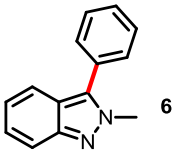
4b

4-Methyl-1,3,5-triphenyl-1H-pyrazole: white solid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 – 7.79 (m, 2H), 7.52 – 7.48 (m, 2H), 7.43 – 7.38 (m, 4H), 7.37 – 7.22 (m, 7H), 2.29 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.20, 141.41, 140.15, 133.83, 130.69, 130.04, 128.63, 128.43, 128.38, 128.10, 127.85, 127.54, 126.69, 124.69, 114.12, 10.19; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{22}H_{19}N_2$ $[M+H]^+$ 311.1543, found 311.1547.



4c

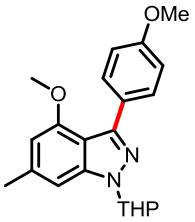
1,3,4,5-Tetraphenyl-1H-pyrazole: white solid, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.58 – 7.55 (m, 2H), 7.41 – 7.19 (m, 14H), 7.18 – 7.06 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.17, 141.33, 139.93, 133.10, 130.67, 130.40, 130.04, 128.72, 128.36, 128.22, 128.15, 128.10, 127.58, 127.17, 126.61, 125.28, 120.67; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{27}H_{21}N_2$ $[M+H]^+$ 373.1699, found 373.1703.



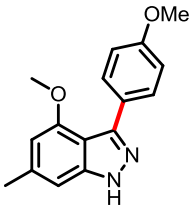
6

2-Methyl-3-phenyl-2H-indazole[14]: colorless oil, **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 8.7 Hz, 1H), 7.59 (d, *J* = 8.7 Hz, 1H), 7.59 – 7.50 (m, 4H), 7.53 – 7.44 (m, 1H), 7.34 – 7.30 (m, 1H), 7.13 – 7.04 (m, 1H), 4.19 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 147.99, 135.96, 129.63, 129.50, 128.93, 128.64, 126.19, 121.73, 121.11, 120.05, 116.92, 38.47.

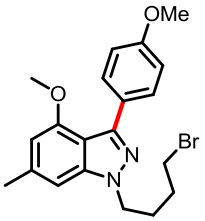
3. Total Synthesis of Nigellidine



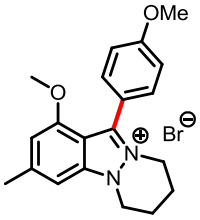
4-Methoxy-3-(4-methoxyphenyl)-6-methyl-1-(tetrahydro-2H-pyran-2-yl)-1H-indazole 8: To a 100 mL sealed tube, were added $Pd(OAc)_2$ (74.8 mg, 0.333 mmol, 0.1 eq), 1,10-phenanthroline (180 mg, 1.0 mmol, 0.3 eq), Cs_2CO_3 (3.25 g, 10 mmol, 3.0 eq), 4-bromoanisole (1.7 mL, 13.32 mmol, 4.0 eq), indazole **7** (820 mg, 3.33 mmol), and toluene (13 mL). The tube was capped and stirred at 160 °C for 72 h. The reaction mixture was cooled to room temperature and diluted with EtOAc, filtered through a short pad of Celite, washed with EtOAc, and concentrated in *vacuo*. The resulting residue was purified by silica gel column using hexanes:EtOAc (6:1) as the eluent to give a white solid, 634 mg (54% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 – 7.86 (m, 2H), 7.01 – 6.94 (m, 3H), 6.36 (s, 1H), 5.68 (dd, *J* = 9.5, 2.8 Hz, 1H), 4.13 – 4.02 (m, 1H), 3.87 (s, 6H), 3.82 – 3.70 (m, 1H), 3.70 – 3.60 (m, 1H), 2.50 (s, 3H), 2.24 – 2.13 (m, 1H), 2.12 – 2.02 (m, 1H), 1.84 – 1.59 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.24, 153.90, 144.67, 143.31, 138.29, 130.82, 126.66, 113.10, 111.73, 102.60, 102.36, 85.31, 67.45, 55.20, 55.07, 29.23, 25.11, 22.68, 22.30; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{21}H_{25}N_2O_3$ $[M+H]^+$ 353.1860, found 353.1862.



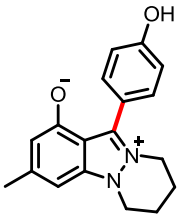
4-Methoxy-3-(4-methoxyphenyl)-6-methyl-1H-indazole 9: To a solution of compound **8** (0.46 g, 1.3 mmol, 1.0 eq) in MeOH (20 mL), was added AcCl (2.8 mL, 39 mmol, 30 eq) dropwise at 0 °C. The solution was heated to 55 °C for 2 h, then cooled to rt and evaporated in *vacuo*. The residue was diluted with EtOAc, washed with saturated $NaHCO_3$, and brine, dried over Na_2SO_4, filtered, and evaporated to give nearly pure product, white solid, 304 mg (87% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95 – 7.86 (m, 2H), 7.05 – 6.97 (m, 2H), 6.46 – 6.37 (m, 1H), 6.30 (s, 1H), 3.89 (s, 3H), 3.87 (s, 3H), 2.39 (s, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.41, 153.88, 145.59, 144.17, 138.42, 130.94, 126.74, 113.38, 110.41, 102.42, 102.06, 55.25, 55.10, 22.08; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{16}H_{17}N_2O_2$ $[M+H]^+$ 269.1284, found 269.1285.



1-(4-Bromobutyl)-4-methoxy-3-(4-methoxyphenyl)-6-methyl-1H-indazole 10: To a suspended solution of NaH (60% in mineral oil, 86 mg, 2.14 mmol, 2.0 eq) in DMF (2 mL) and DMSO (1 mL), was added compound **9** (287 mg, 1.07 mmol, 1.0 eq) in DMF (2 mL) at 0 °C under N_2 atmosphere. The mixture was stirred at rt for 20 min, then cooled back to 0 °C, and 1,4-dibromobutane (0.38 mL, 3.21 mmol, 3.0 eq) was added. The resulting mixture was stirred at rt overnight, quenched by saturated NH_4Cl, extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, evaporated in *vacuo*. The residue was purified by silica gel column using hexanes:EtOAc (6:1) as the eluent to give a colorless oil, 321 mg (74% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88 – 7.79 (m, 2H), 7.01 – 6.93 (m, 2H), 6.76 (s, 1H), 6.32 (s, 1H), 4.36 (t, *J* = 6.8 Hz, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 3.42 (t, *J* = 6.6 Hz, 2H), 2.49 (s, 3H), 2.16 – 2.05 (m, 2H), 1.97 – 1.84 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 159.20, 154.12, 144.12, 143.26, 138.12, 130.65, 126.67, 113.25, 111.00, 101.86, 101.23, 55.26, 55.11, 47.71, 33.15, 29.85, 28.27, 22.36; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{20}H_{24}BrN_2O_2$ $[M+H]^+$ 403.1016, found 403.1012.



1-Methoxy-11-(4-methoxyphenyl)-3-methyl-6,7,8,9-tetrahydropyridazino[1,2-a]indazol-10-ium Bromide 11: To a 35 mL sealed tube, were added compound **10** (310 mg, 0.77 mmol, 1.0 eq) and acetonitrile (5 mL). The tube was capped and stirred at 110 °C overnight. The reaction mixture was cooled to room temperature and concentrated in *vacuo*. The resulting residue was recrystallized with DCM/Hexane to give a white solid, 250 mg (81% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 – 7.60 (m, 2H), 7.11 – 7.02 (m, 2H), 6.98 (s, 1H), 6.45 (s, 1H), 4.77 – 4.61 (m, 4H), 3.88 (s, 3H), 3.75 (s, 3H), 2.52 (s, 3H), 2.52 – 2.47 (m, 2H), 2.37 – 2.24 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.58, 154.68, 147.03, 143.21, 142.06, 132.35, 116.52, 113.97, 109.84, 105.65, 101.41, 55.67, 55.40, 48.81, 46.99, 23.05, 20.28, 19.36; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{20}H_{24}BrN_2O_2$ $[M+H]^+$ 403.1016, found 403.1023.



Nigellidine Hydrobromide 12:[15] To a solution of compound **11** (40.3 mg, 0.1 mmol, 1.0 eq) in DCM (6 mL), was added BBr_3 (1M in DCM, 0.6 mL, 0.6 mmol, 6.0 eq) dropwise at rt. The solution was stirred at rt for 4h, then quenched with slow addition of MeOH (2 mL), and anhydrous K_2CO_3 (1.0 g) with vigorous stirring. The solution was then filtered through a pad of Celite and washed with DCM. The e filtrate was concentrated in *vacuo* and the resulting residue was purified by column (DCM/MeOH = 4/1) to give a pale yellow solid, 28 mg (74% yield). The solid was dissolved in hot methanol, then kept in an open flask at room temperature until the crystals were formed. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.59 – 7.43 (m, 2H), 7.09 (s, 1H), 7.06 – 6.91 (m, 2H), 6.71 – 6.55 (m, 1H), 4.48 (t, *J* = 6.1 Hz, 2H), 4.39 (t, *J* = 5.8 Hz, 2H), 2.44 (s, 3H), 2.23 – 2.17 (m, 2H), 2.12 – 2.07 (m, 2H); **^{13}C NMR** (151 MHz, DMSO) δ 160.73, 154.48, 146.78, 143.94, 143.23, 133.39, 116.14, 116.10, 109.97, 109.89, 100.53, 49.16, 47.51, 23.24, 20.73, 20.08; **HRMS** (ESI-TOF) *m/z* Calcd for $C_{18}H_{19}N_2O_2$ $[M\text{-}Br]^+$ 295.1441, found 295.1447.

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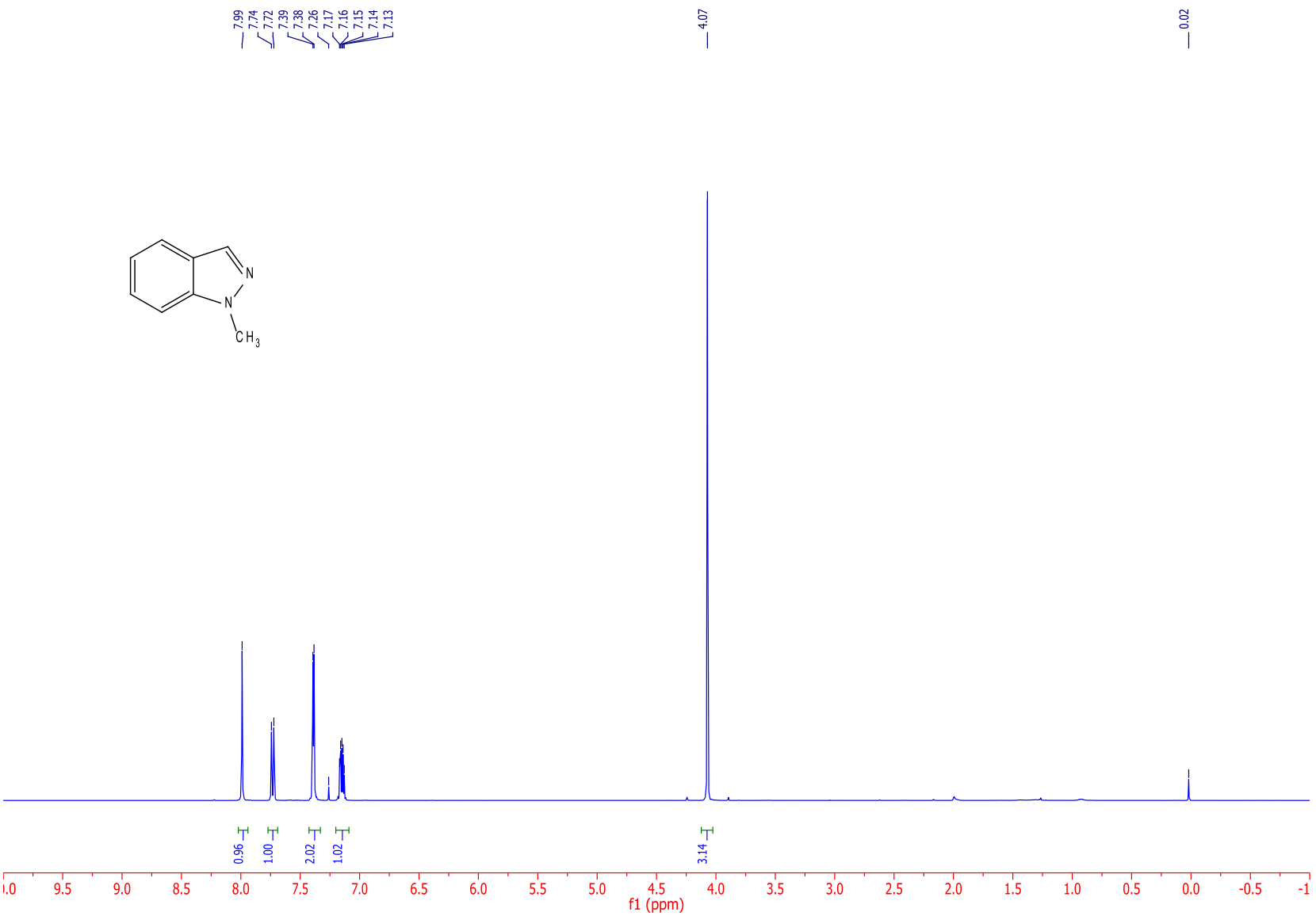
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7.39
7.38
7.26
7.17
7.16
7.15
7.14
7.13
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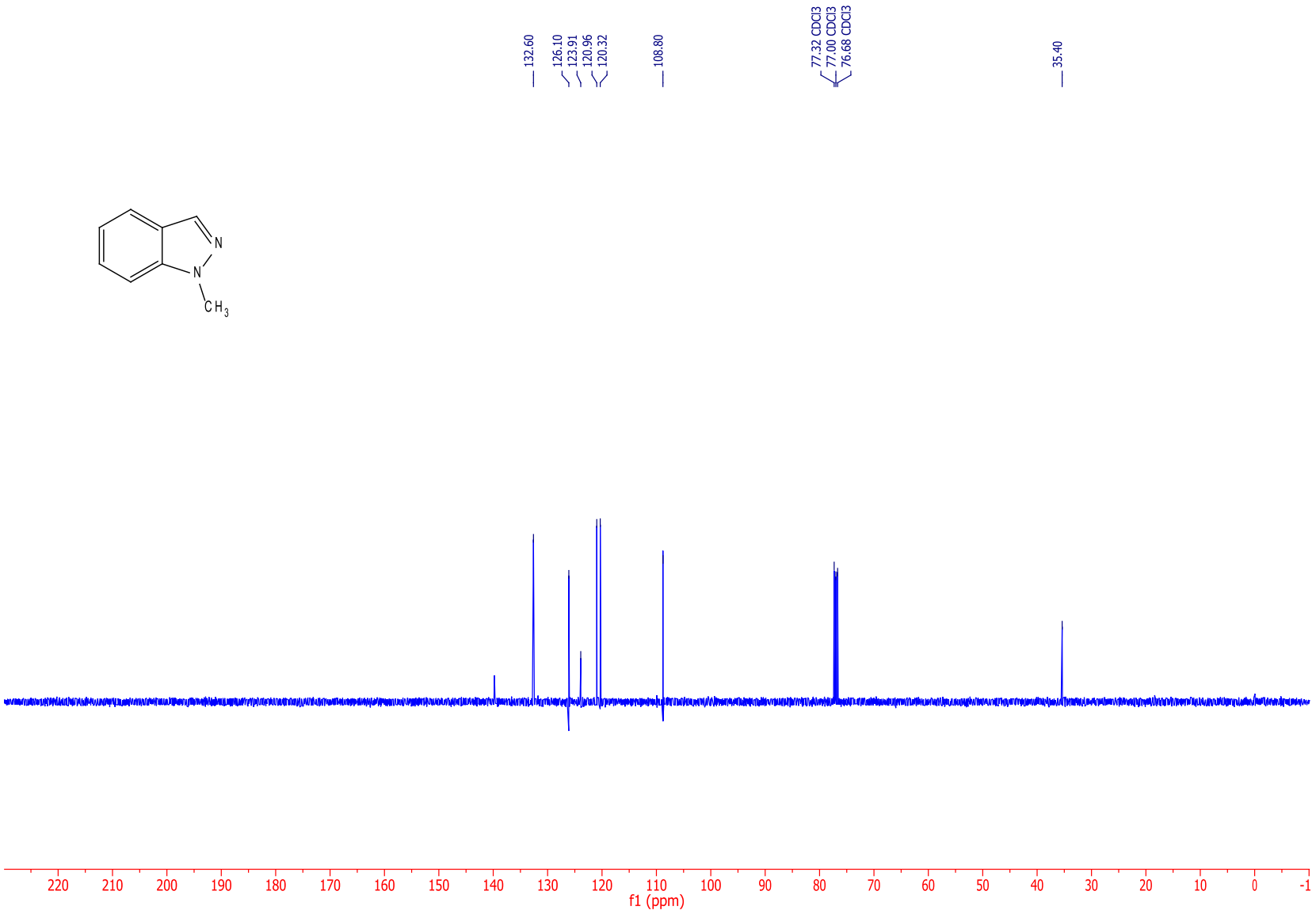
N
N
CH3
0.96
1.00
2.02
1.02
3.14
f1 (ppm)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120.96
120.32
108.80
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77.00 CDCl3
76.68 CDCl3
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CH3
220
210
200
190
180
170
160
150
140
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120
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40
30
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10
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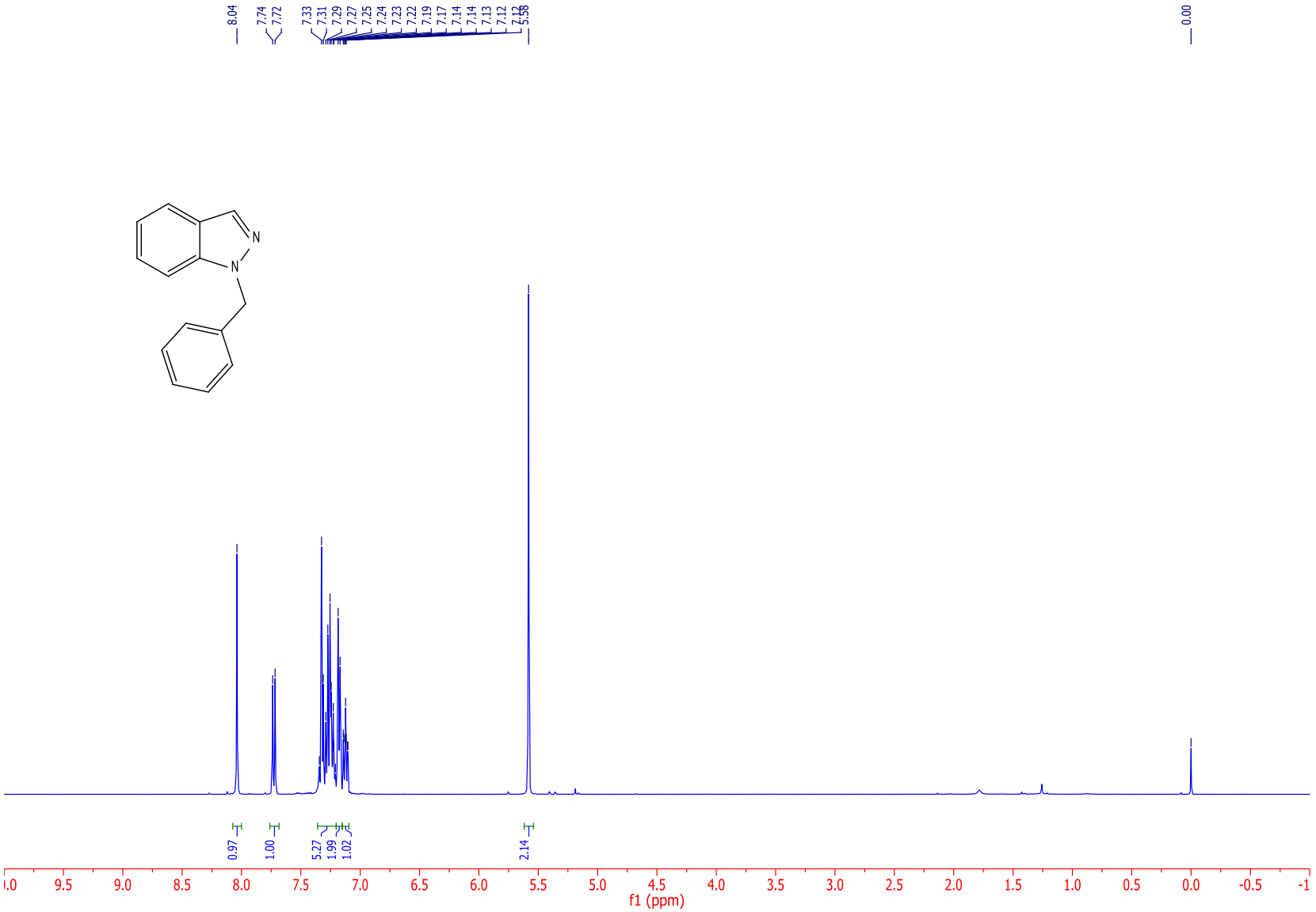
-1
f1 (ppm)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7.14
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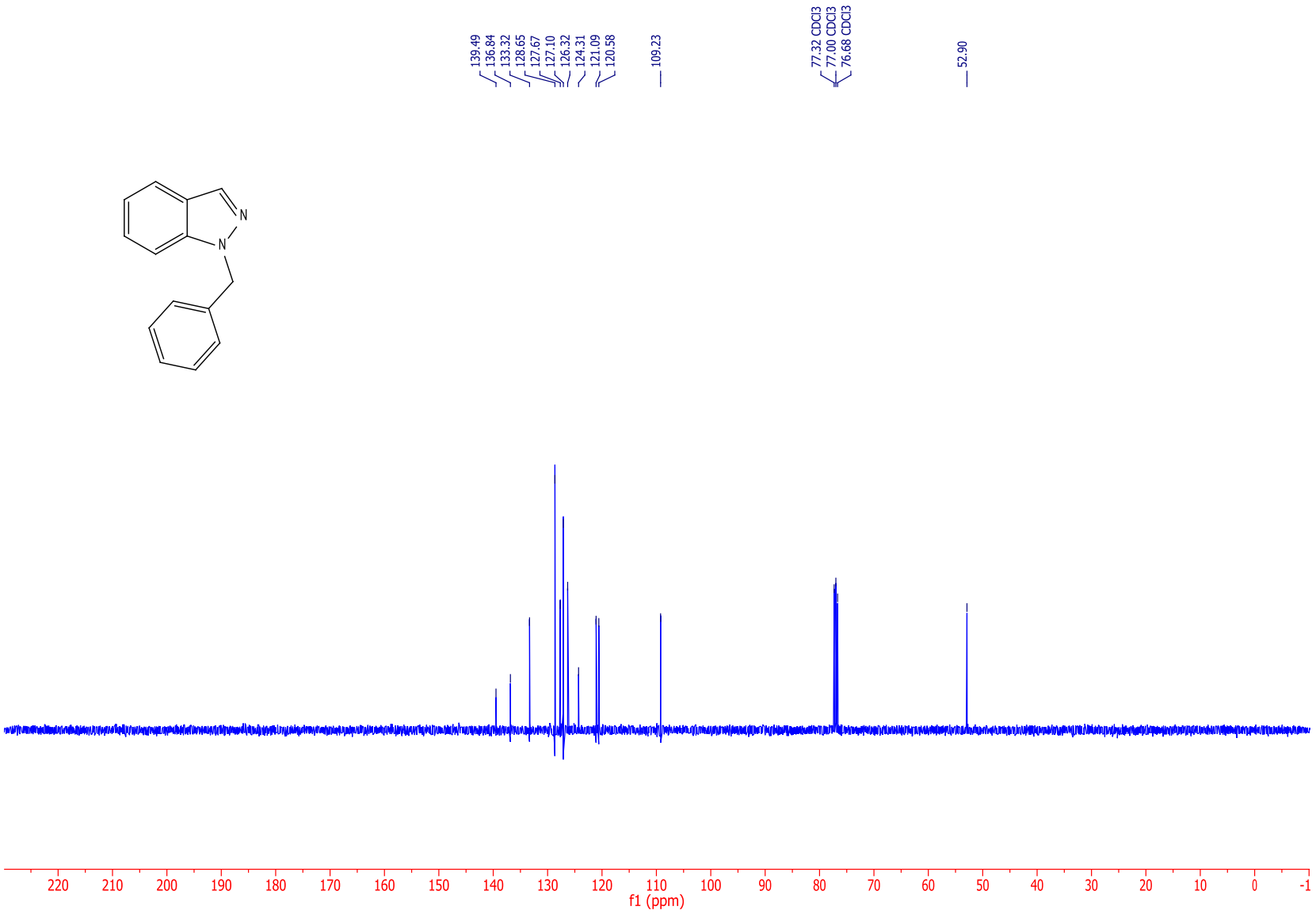
2.14
f1 (ppm)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190
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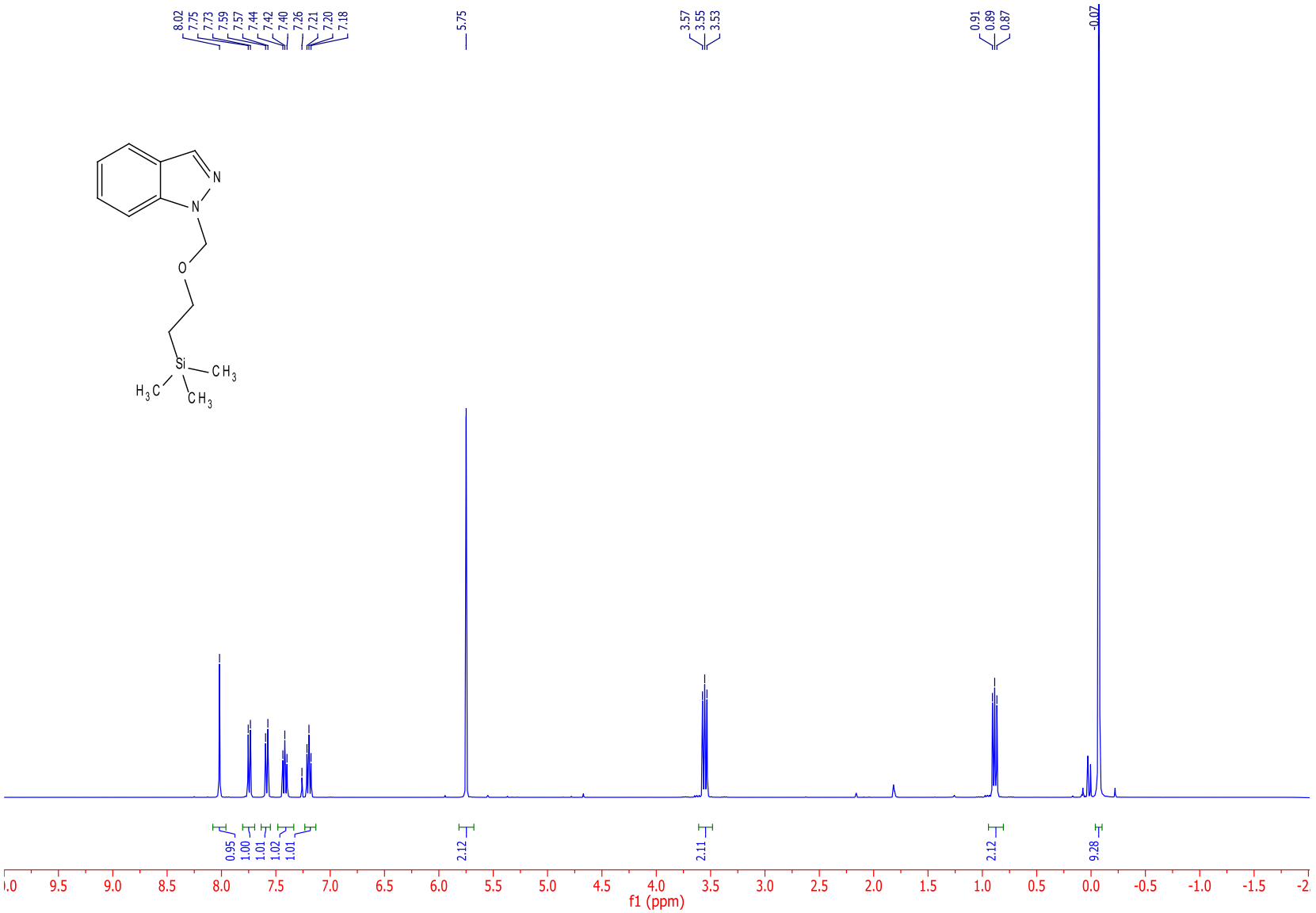
f1 (ppm)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0.91
0.89
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N
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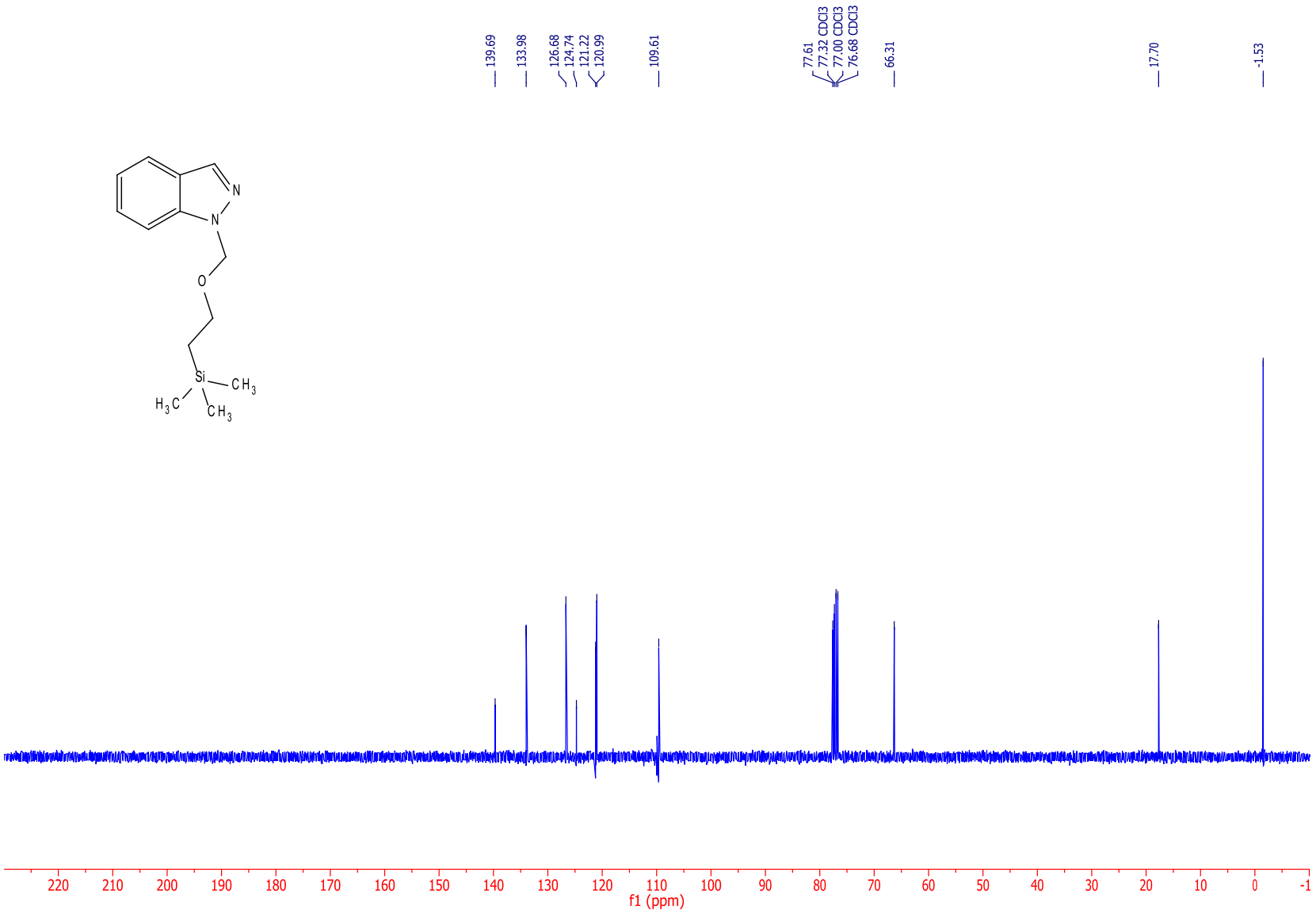
CH3
0.95
1.00
1.01
1.02
1.01
2.12
2.11
2.12
9.28
f1 (ppm)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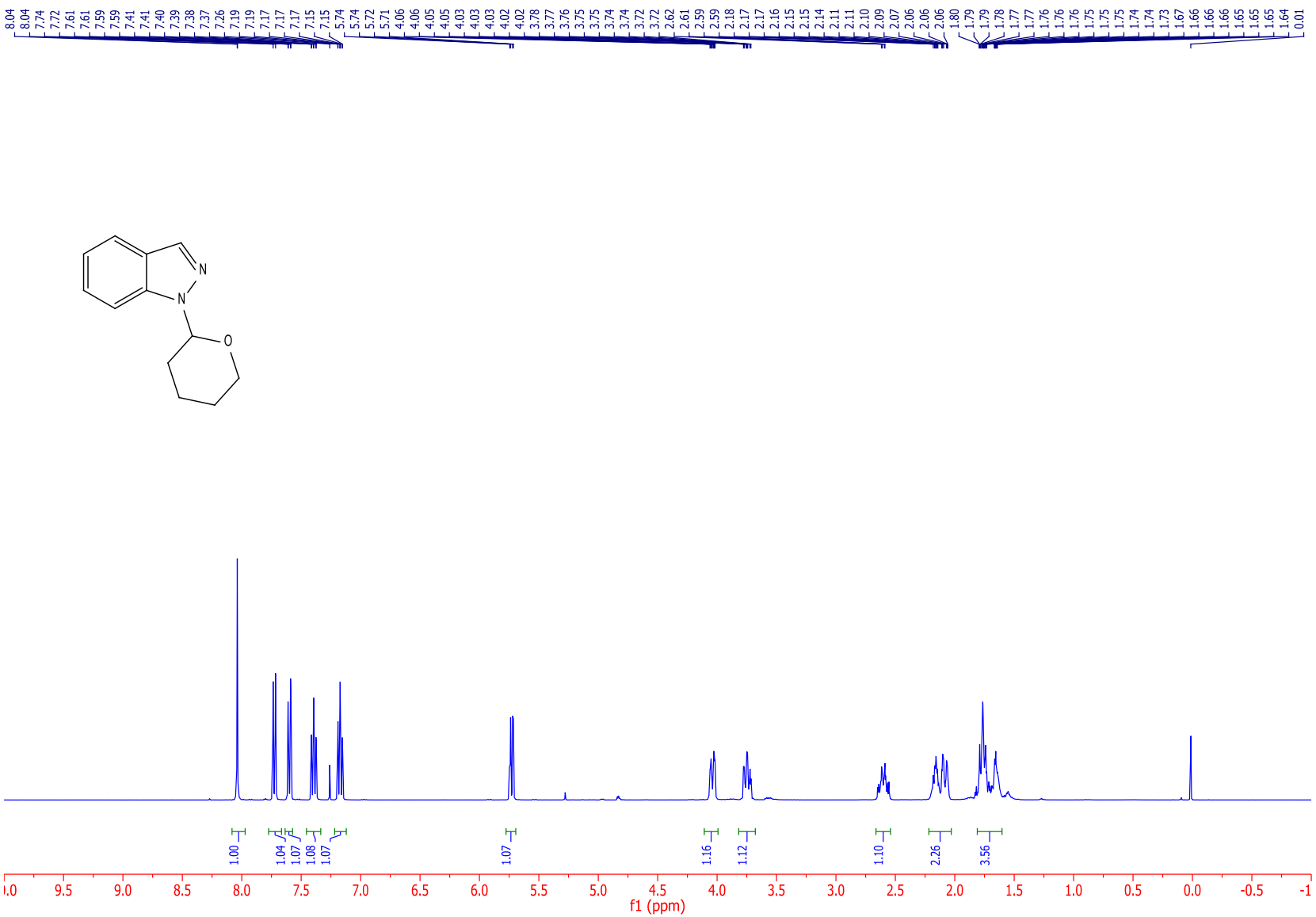
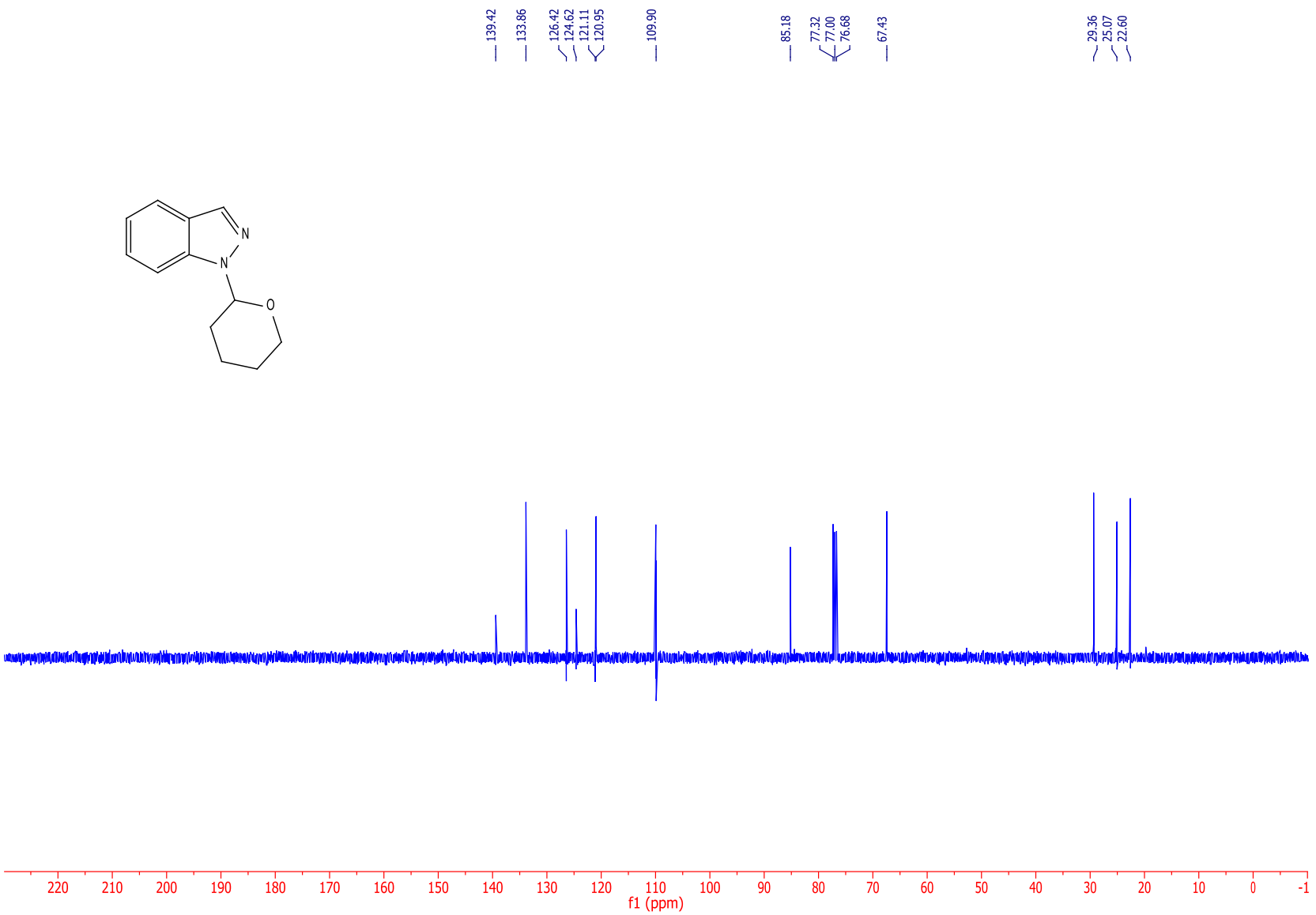
133.98
126.68
124.74
121.22
120.99
109.61
77.61
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
66.31
17.70
-1.53
N
N
O
Si
CH3
H3C
CH3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


8.04 8.04 7.74 7.72 7.61 7.61 7.59 7.59 7.41 7.40 7.39 7.38 7.37 7.26 7.19 7.19 7.17 7.17 7.17 7.15 7.15 5.74 5.74 5.72 5.71 4.06 4.06 4.05 4.05 4.03 4.03 4.02 4.02 3.78 3.77 3.76 3.75 3.75 3.74 3.74 3.72 3.72 2.62 2.61 2.59 2.59 2.18 2.17 2.17 2.16 2.15 2.15 2.14 2.11 2.11 2.10 2.09 2.07 2.06 2.06 2.06 1.80 1.79 1.79 1.78 1.77 1.77 1.76 1.76 1.76 1.75 1.75 1.75 1.74 1.74 1.73 1.67 1.66 1.66 1.66 1.65 1.65 1.65 1.64 0.01
N
N
O
1.00
1.04
1.07
1.08
1.07
1.07
1.16
1.12
1.10
2.26
3.56
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
f1 (ppm)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126.42
124.62
121.11
120.95
109.90
85.18
77.32
77.00
76.68
67.43
29.36
25.07
22.60
N
N
O
220
210
200
190
180
170
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120
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100
90
80
70
60
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40
30
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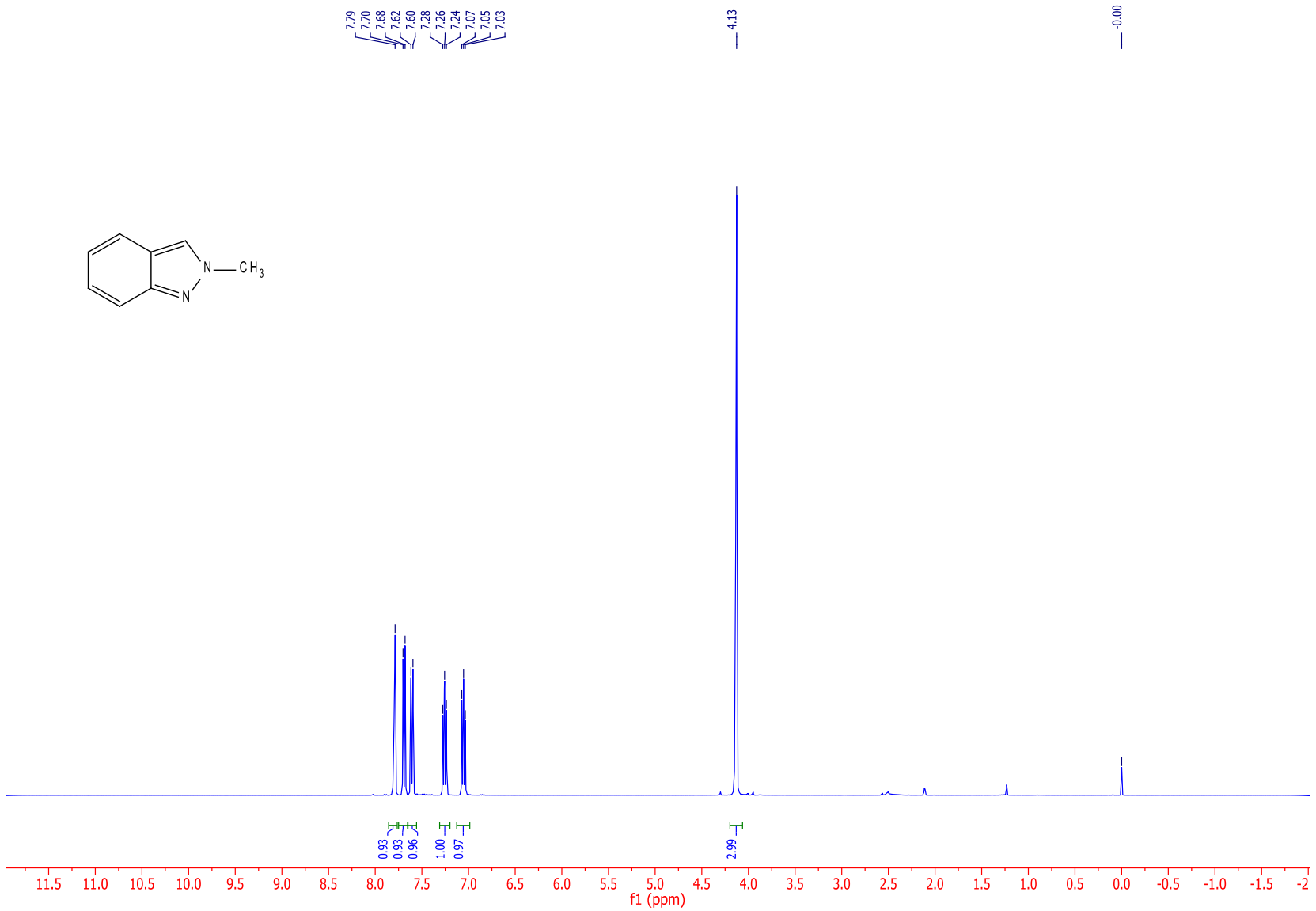
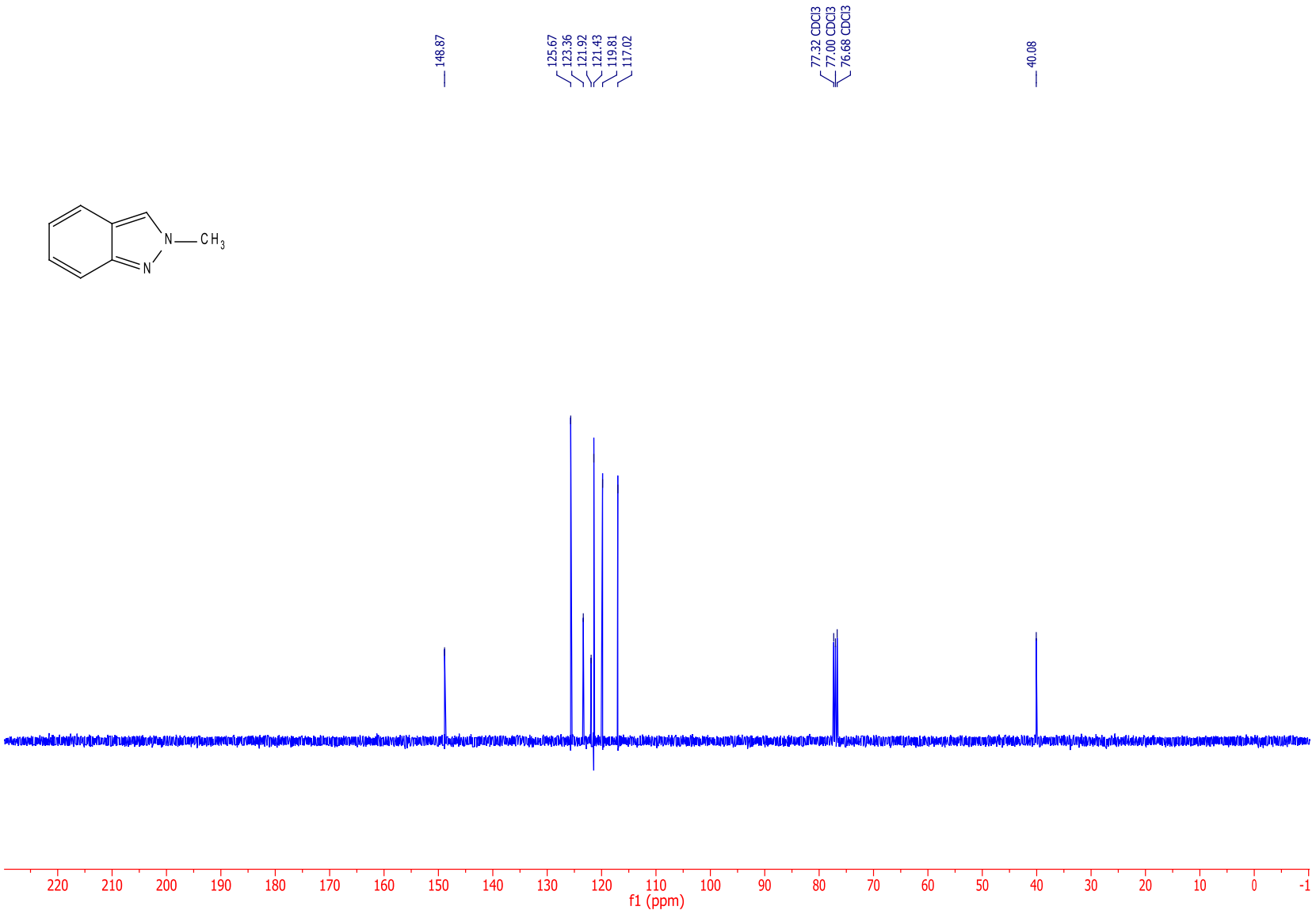
0
-1
f1 (ppm)


7.79
7.70
7.68
7.62
7.60
7.28
7.26
7.24
7.07
7.05
7.03
4.13
-0.00
N
CH3
N
0.93
0.93
0.96
1.00
0.97
2.99
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 -1.0 -1.5
f1 (ppm)


148.87
125.67
123.36
121.92
121.43
119.81
117.02
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
40.08
N
CH3
N
220
210
200
190
180
170
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140
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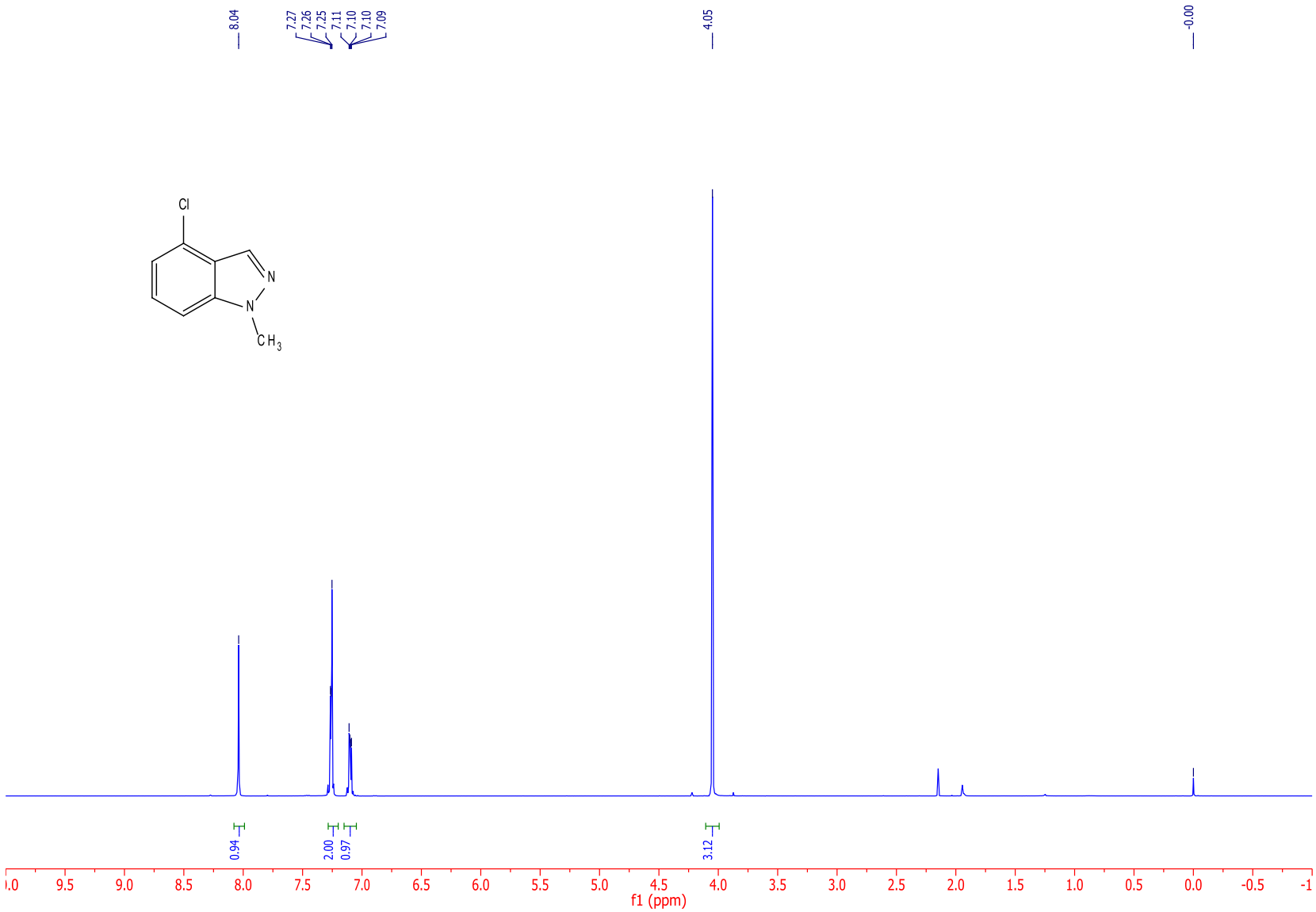
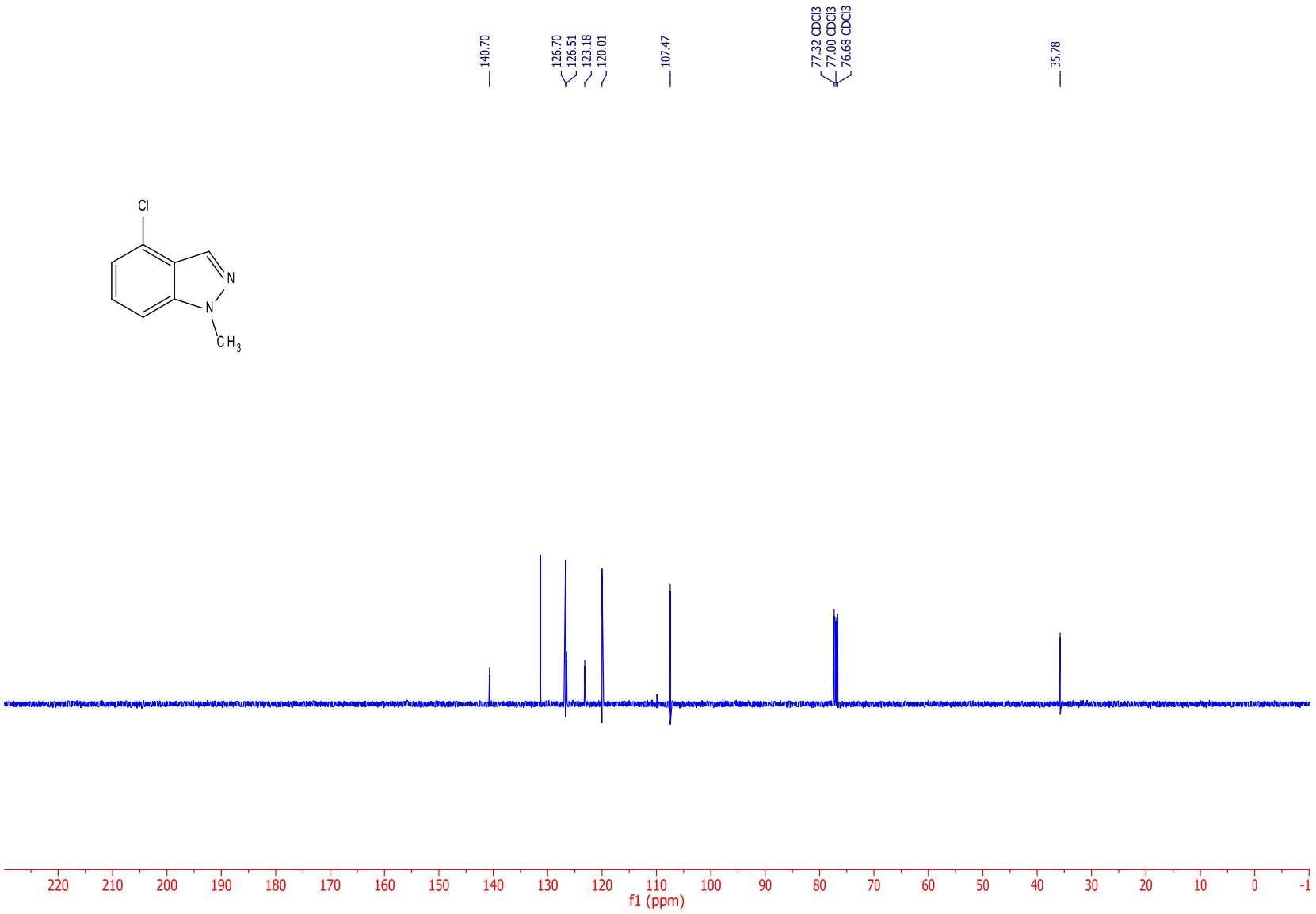
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


8.04
7.27
7.26
7.25
7.11
7.10
7.10
7.09
4.05
-0.00
Cl
N
N
CH3
0.94
2.00
0.97
3.12
f1 (ppm)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126.70
126.51
123.18
120.01
107.47
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
35.78
Cl
N
N
CH3
220
210
200
190
180
170
160
150
140
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120
110
100
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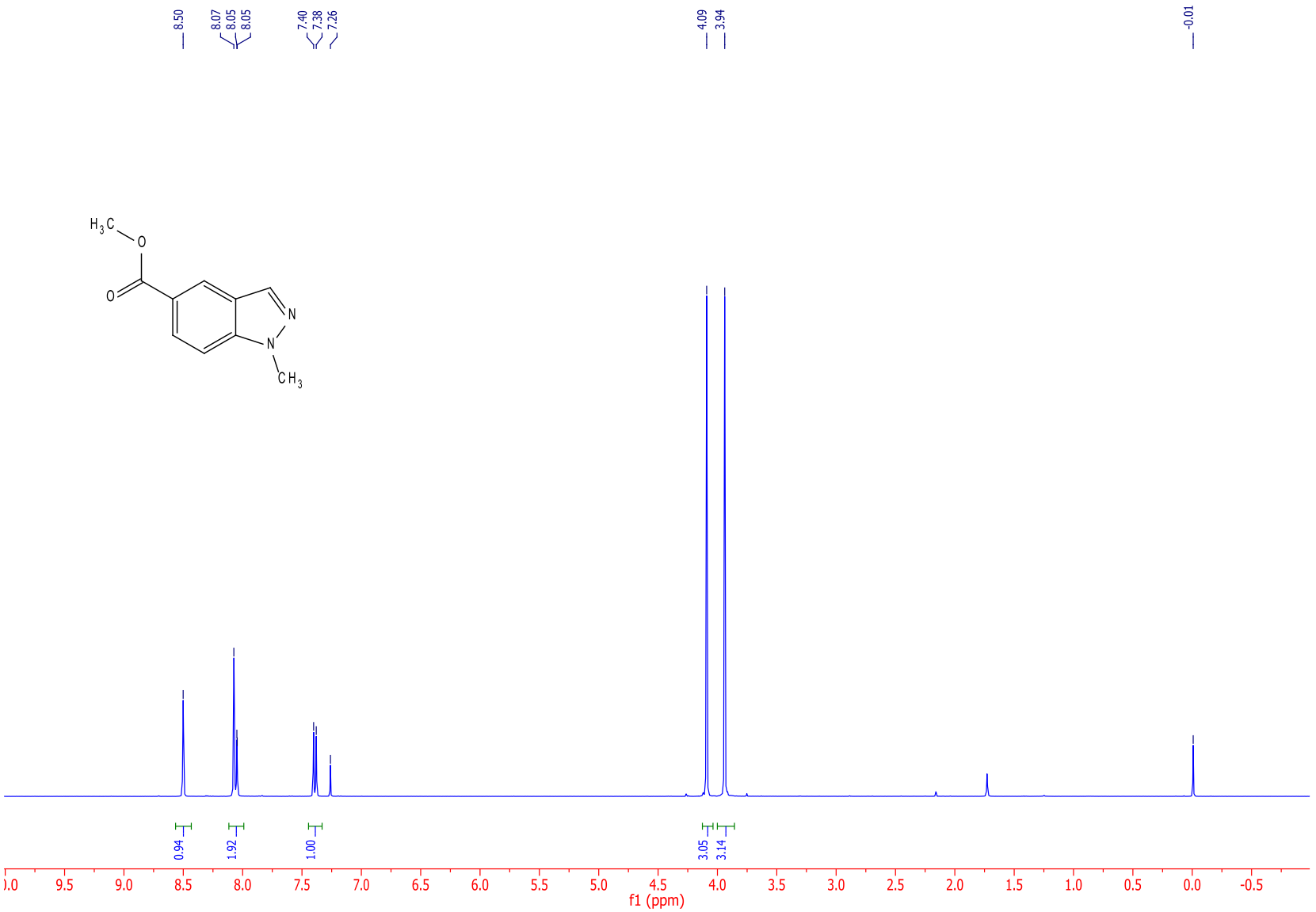
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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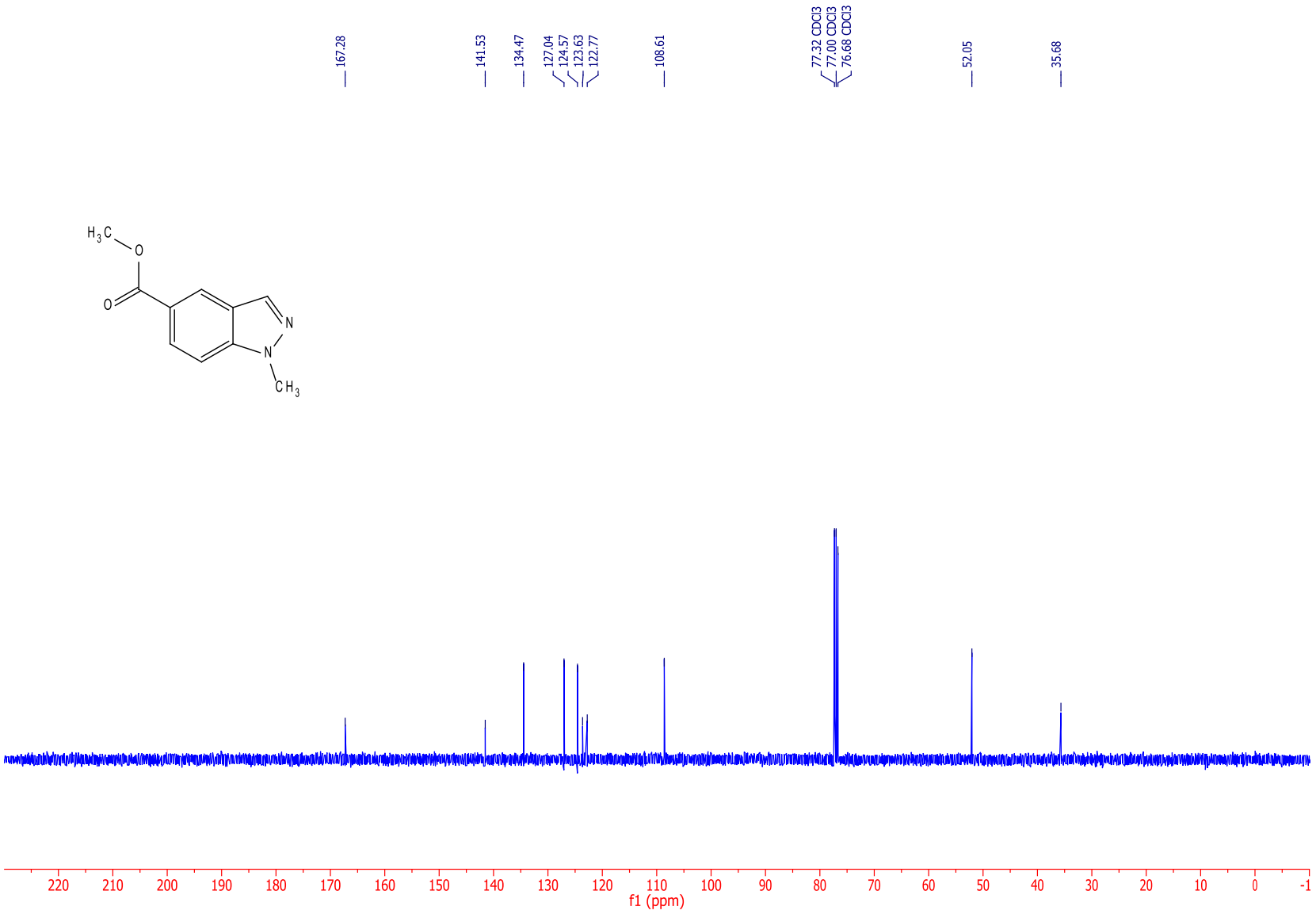
8.07
8.05
8.05
7.40
7.38
7.26
4.09
3.94
-0.01
H3C
O
O
N
N
CH3
0.94
1.92
1.00
3.05
3.14
f1 (ppm)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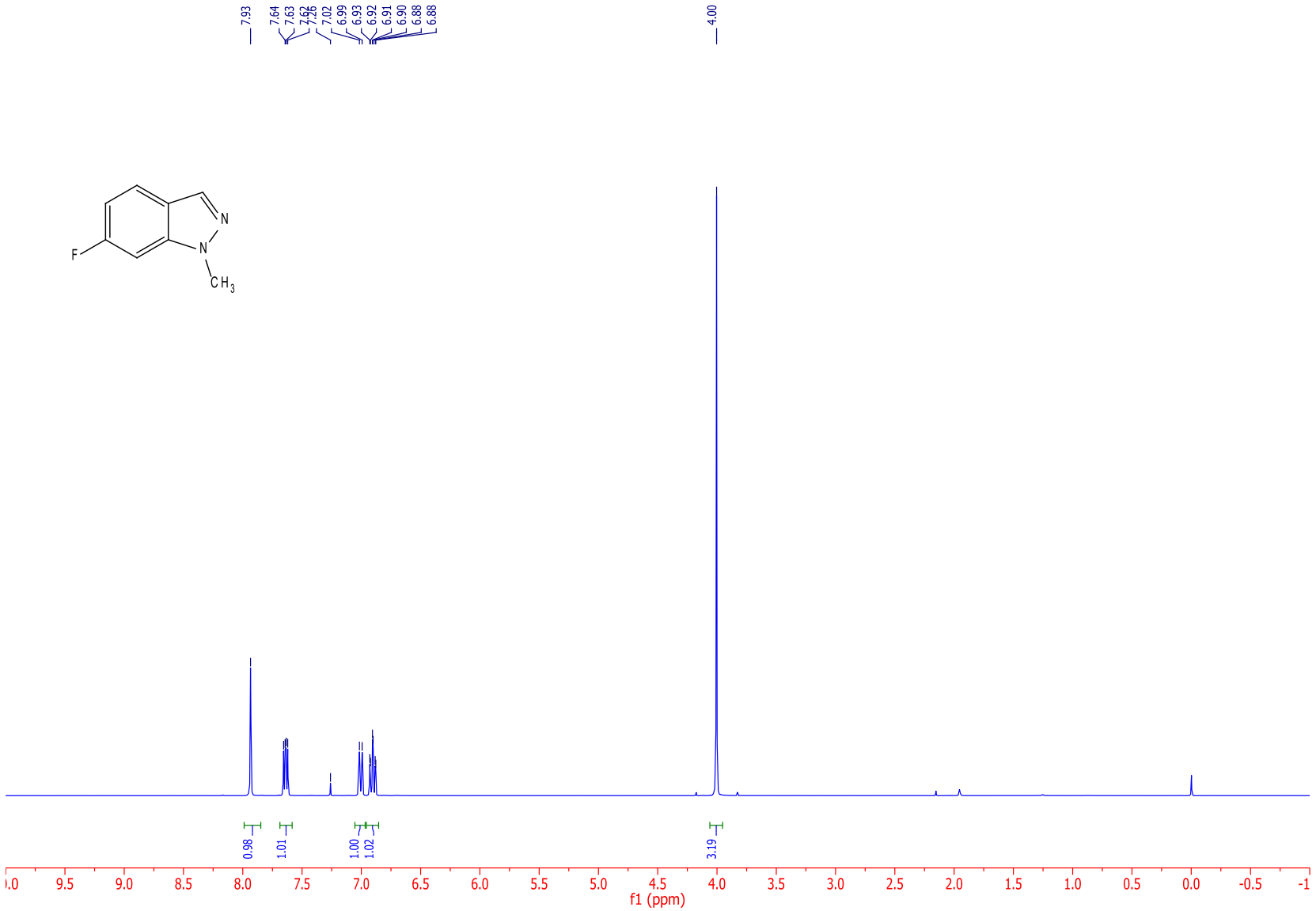
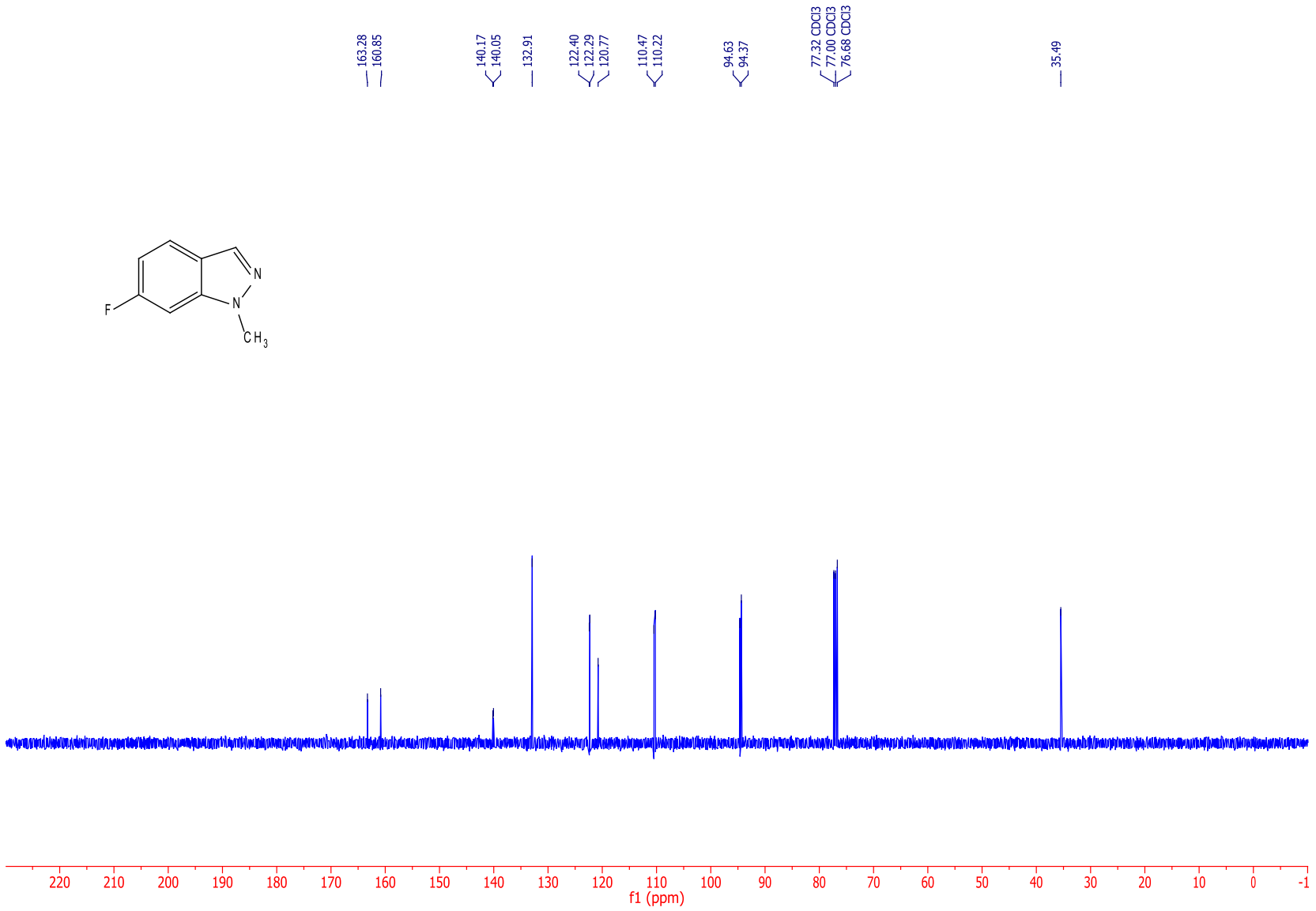
141.53
134.47
127.04
124.57
123.63
122.77
108.61
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
52.05
35.68
H3C
O
O
N
N
CH3
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


7.93
7.64
7.63
7.62
7.26
7.02
6.99
6.93
6.92
6.91
6.90
6.88
6.88
4.00
F
N
N
CH3
0.98
1.01
1.00
1.02
3.19
f1 (ppm)


163.28
160.85
140.17
140.05
132.91
122.40
122.29
120.77
110.47
110.22
94.63
94.37
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
35.49
F
N
N
CH3
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210
200
190
180
170
160
150
140
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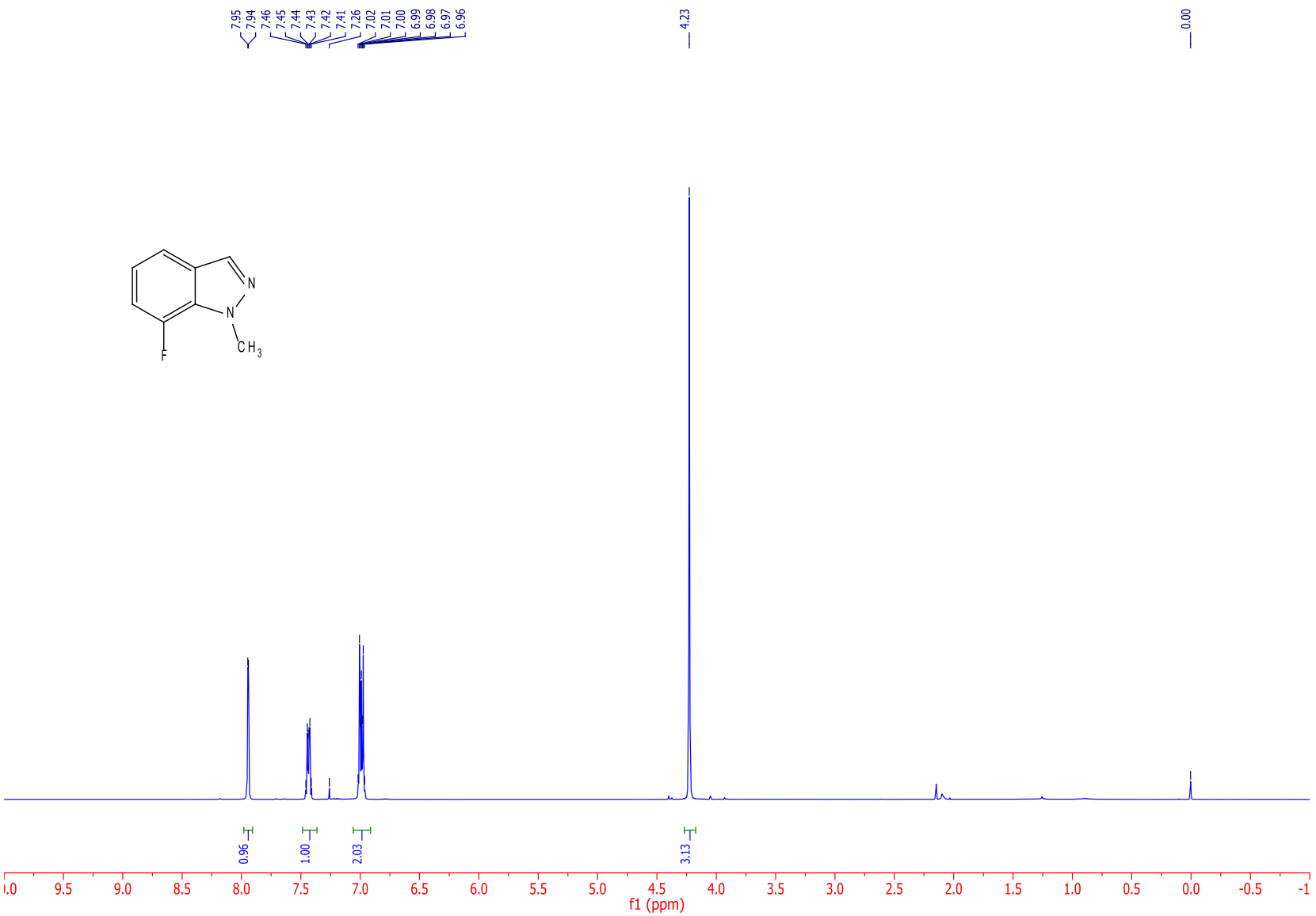
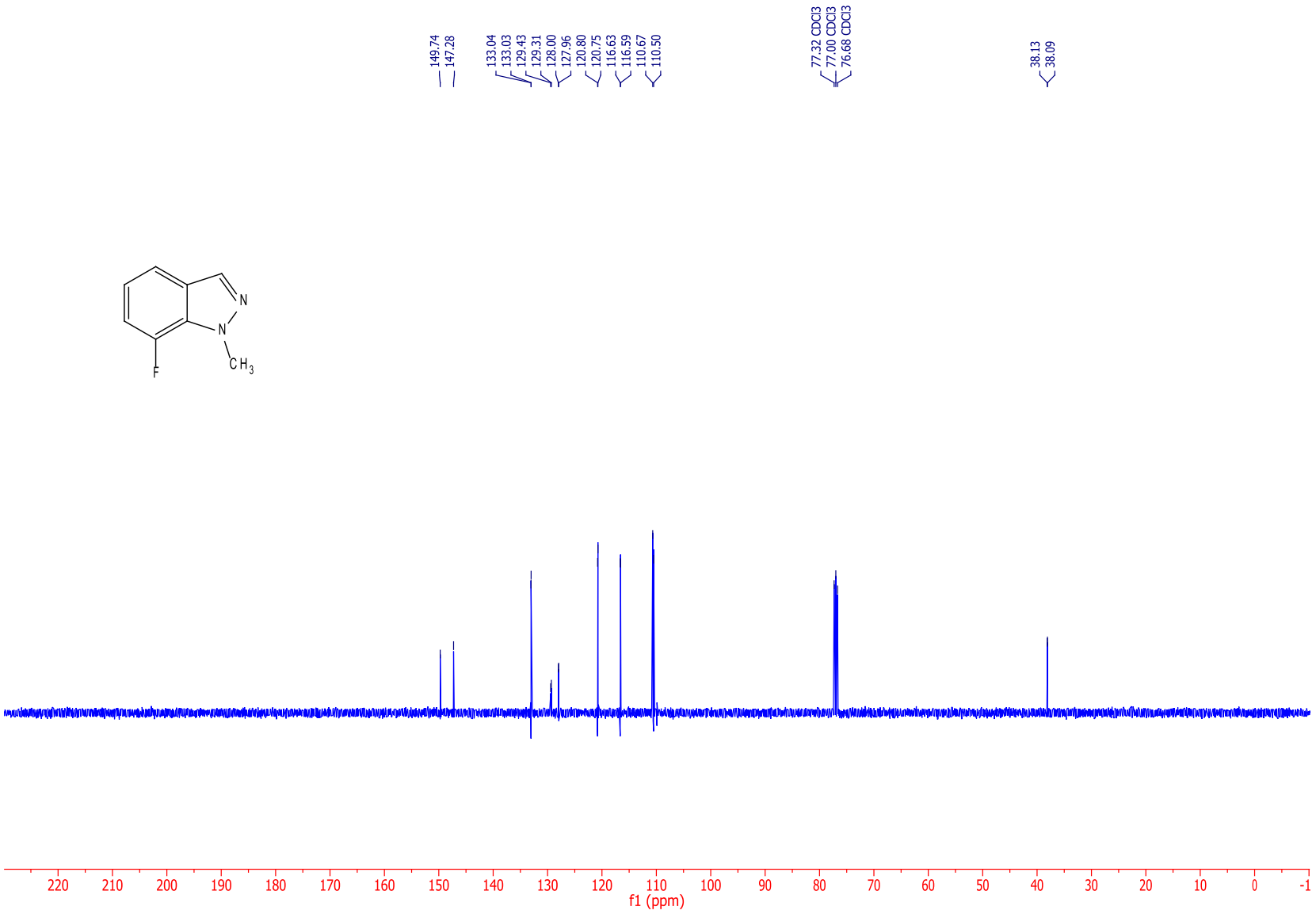
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


7.95
7.94
7.46
7.45
7.44
7.43
7.42
7.41
7.26
7.02
7.01
7.00
6.99
6.98
6.97
6.96
4.23
0.00
N
N
CH3
F
0.96
1.00
2.03
3.13
f1 (ppm)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147.28
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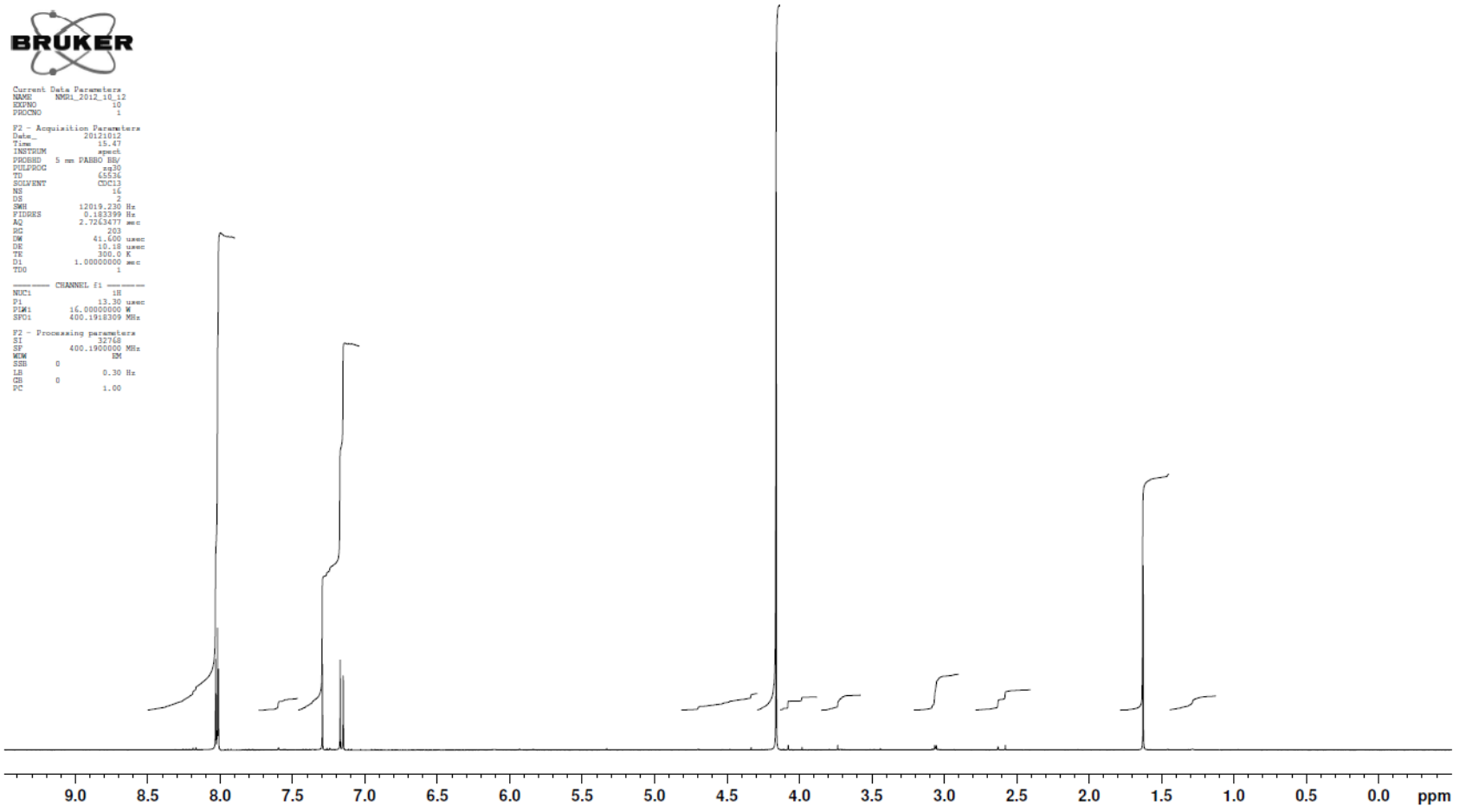
133.03
129.43
129.31
128.00
127.96
120.80
120.75
116.63
116.59
110.67
110.50
77.32 CDCl3
77.00 CDCl3
76.68 CDCl3
38.13
38.09
N
N
CH3
F
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


BRUKER
Current Data Parameters
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EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121012
Time 15.47
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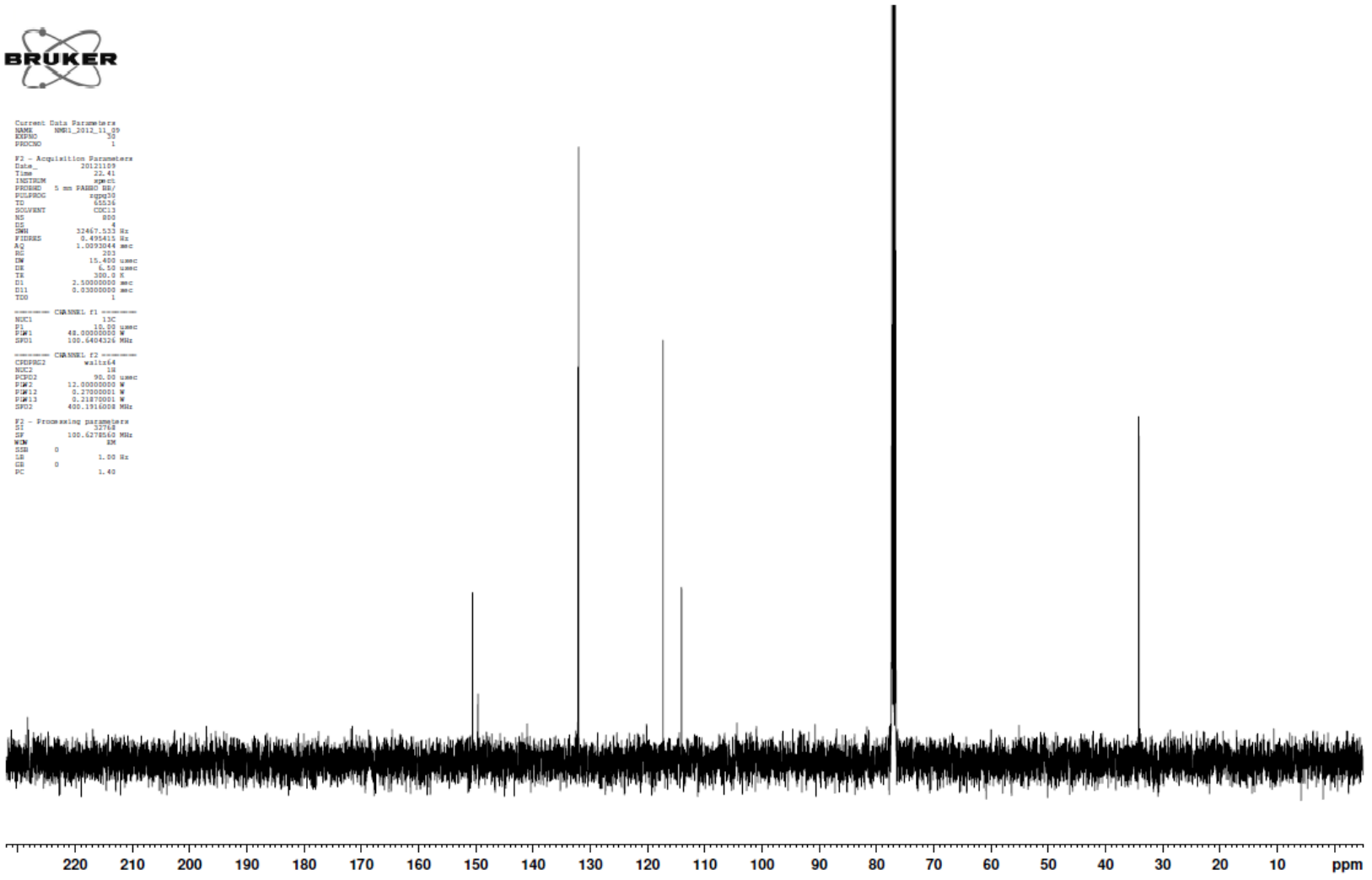
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 12019.230 Hz
FIDRES 0.183399 Hz
AQ 2.7263477 sec
RG 203
DW 41.600 usec
DE 10.18 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 13.30 usec
PLW1 16.00000000 W
SFO1 400.1918309 MHz
F2 - Processing parameters
SI 32768
SF 400.1900000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
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 ppm

1y


BRUKER
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EXPNO 35
PROCNO 1
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Time 22.41
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PROBHD 5 mm PABBO BB/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 800
DS 4
SWH 32467.533 Hz
FIDRES 0.495415 Hz
AQ 1.0093044 sec
RG 203
DW 15.400 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
CHANNEL f1
NUC1 13C
P1 10.00 usec
PLW1 48.00000000 W
SFO1 100.6404326 MHz
CHANNEL f2
CPDPRG2 waltz64
NUC2 1H
PCPD2 90.00 usec
PLW2 12.00000000 W
PLW12 0.27000001 W
PLW13 0.21870001 W
SFO2 400.1916008 MHz
F2 - Processing parameters
SI 32768
SF 100.6278560 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
220
210
200
190
180
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100
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80
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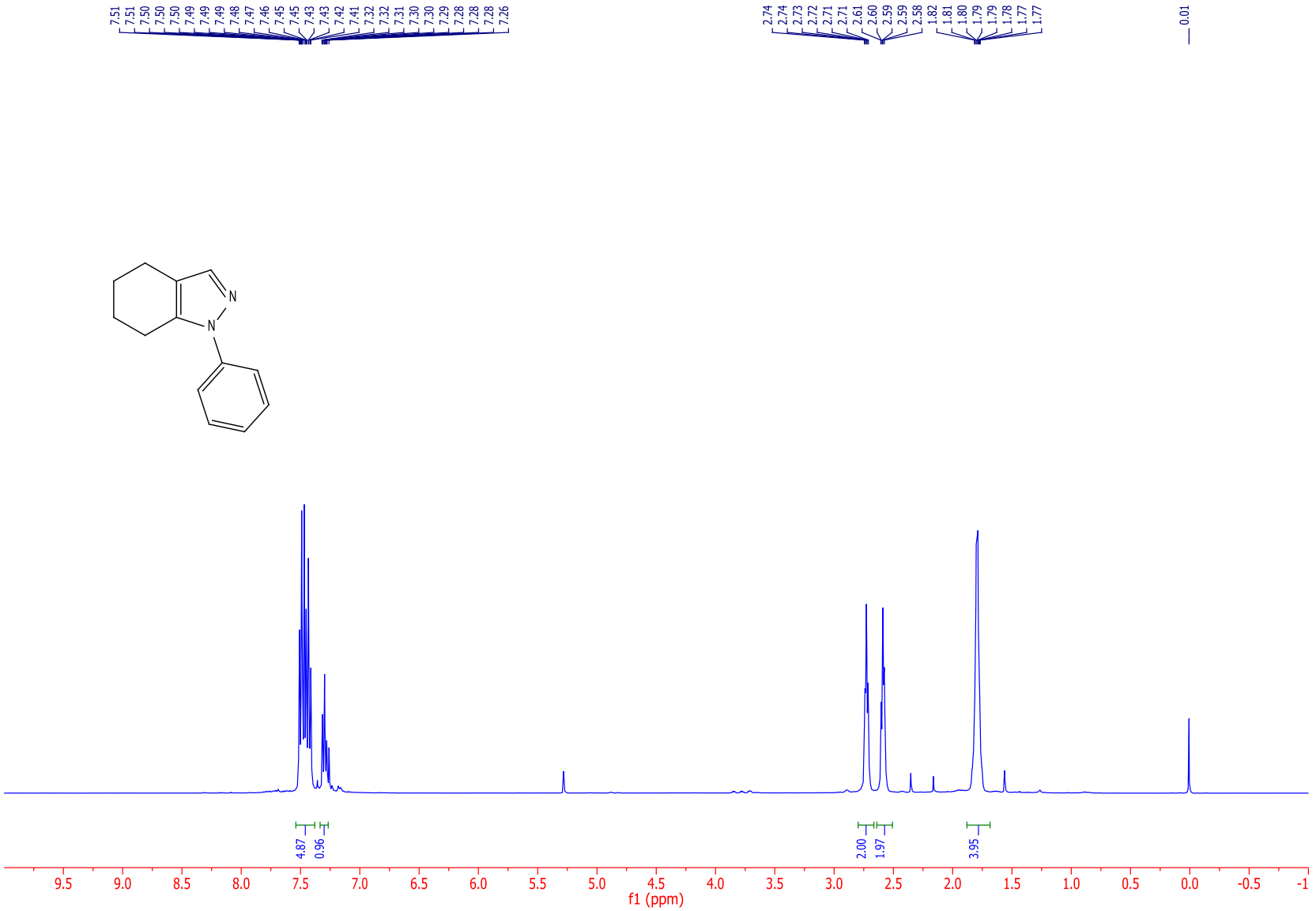
60
50
40
30
20
10
ppm

1y


7.51
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7.49
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7.47
7.46
7.45
7.45
7.43
7.43
7.42
7.41
7.32
7.32
7.31
7.30
7.30
7.29
7.28
7.28
7.28
7.26
2.74
2.74
2.73
2.72
2.71
2.71
2.61
2.60
2.59
2.59
2.58
1.82
1.81
1.80
1.79
1.79
1.78
1.77
1.77
0.01
N
N
4.87
0.96
2.00
1.97
3.95
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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2.0
1.5
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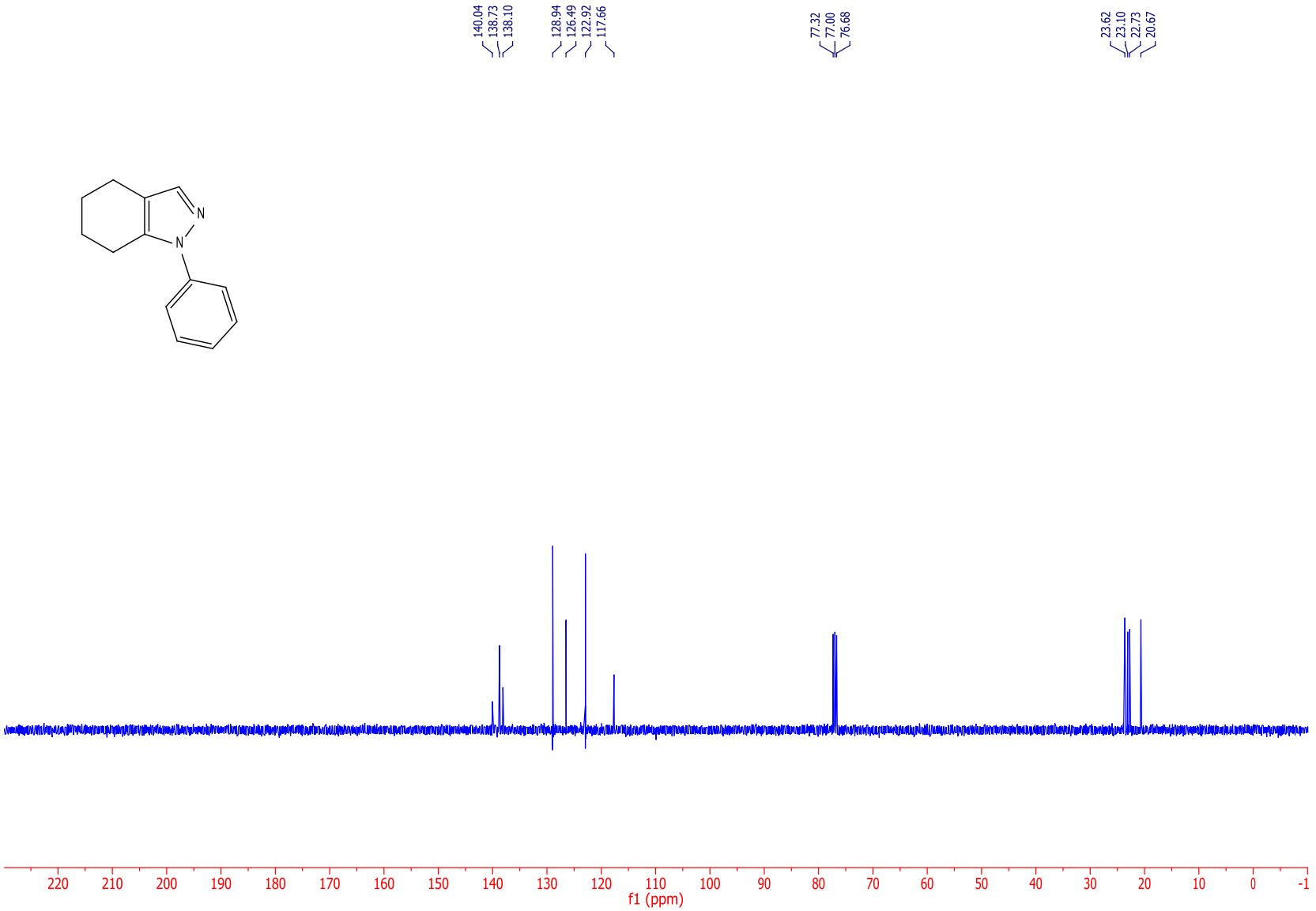
0.0
-0.5
-1
f1 (ppm)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138.10
128.94
126.49
122.92
117.66
77.32
77.00
76.68
23.62
23.10
22.73
20.67
N
N
220
210
200
190
180
170
160
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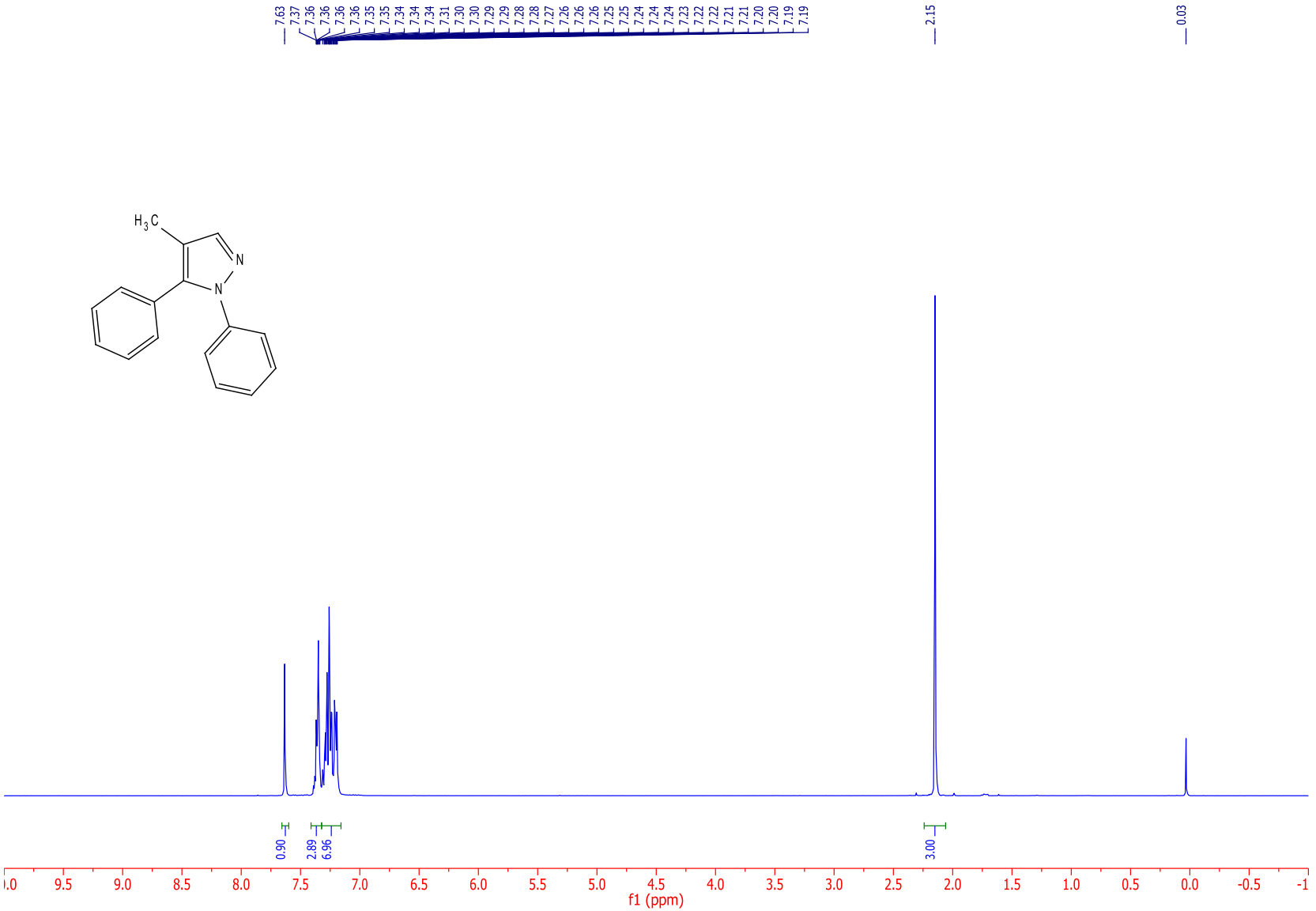
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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7.35
7.35
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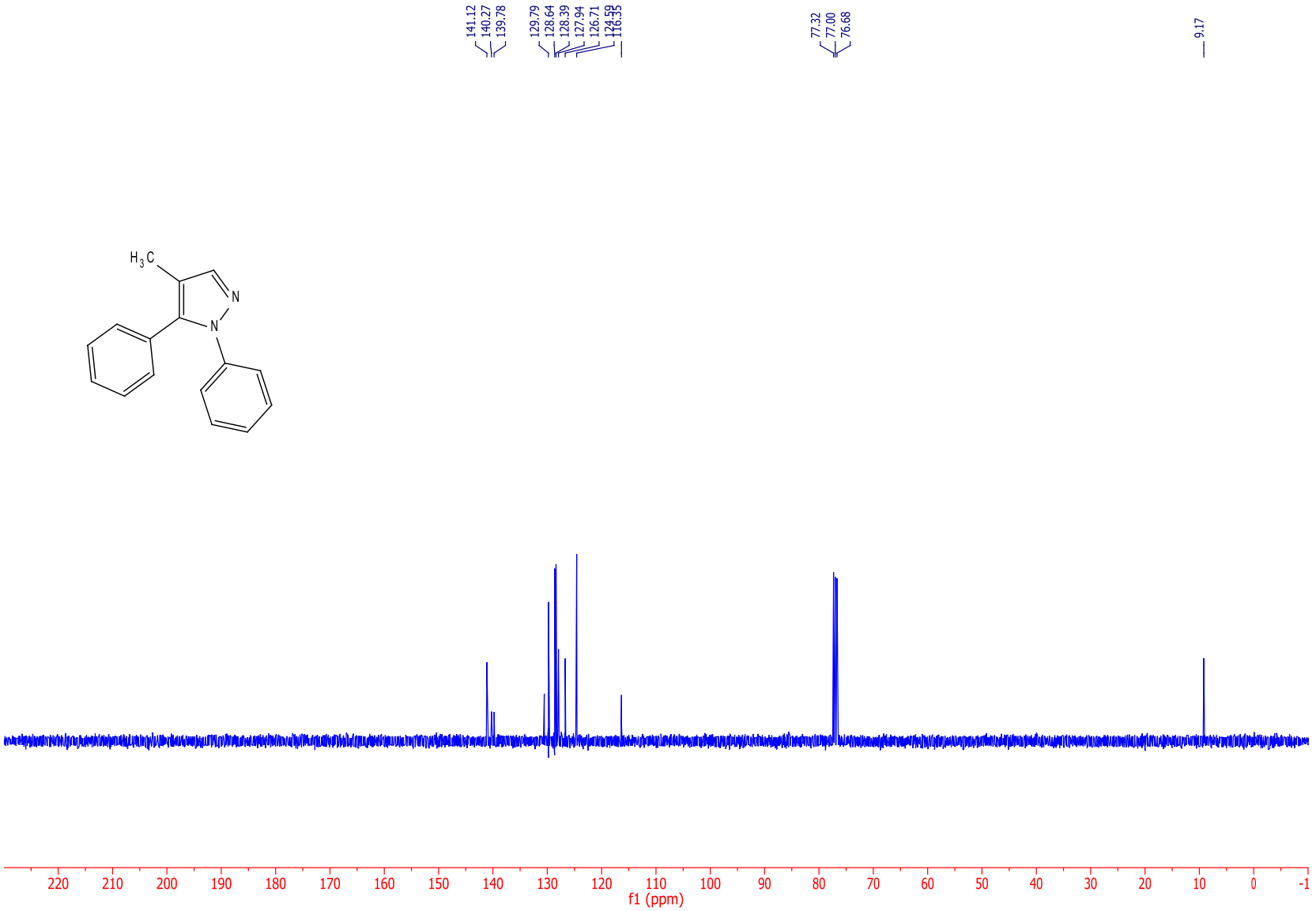
7.31
7.30
7.30
7.29
7.29
7.28
7.28
7.27
7.26
7.26
7.26
7.25
7.25
7.24
7.24
7.24
7.23
7.22
7.22
7.21
7.21
7.20
7.20
7.19
7.19
2.15
0.03
H3C
N
N
0.90
2.89
6.96
3.00
f1 (ppm)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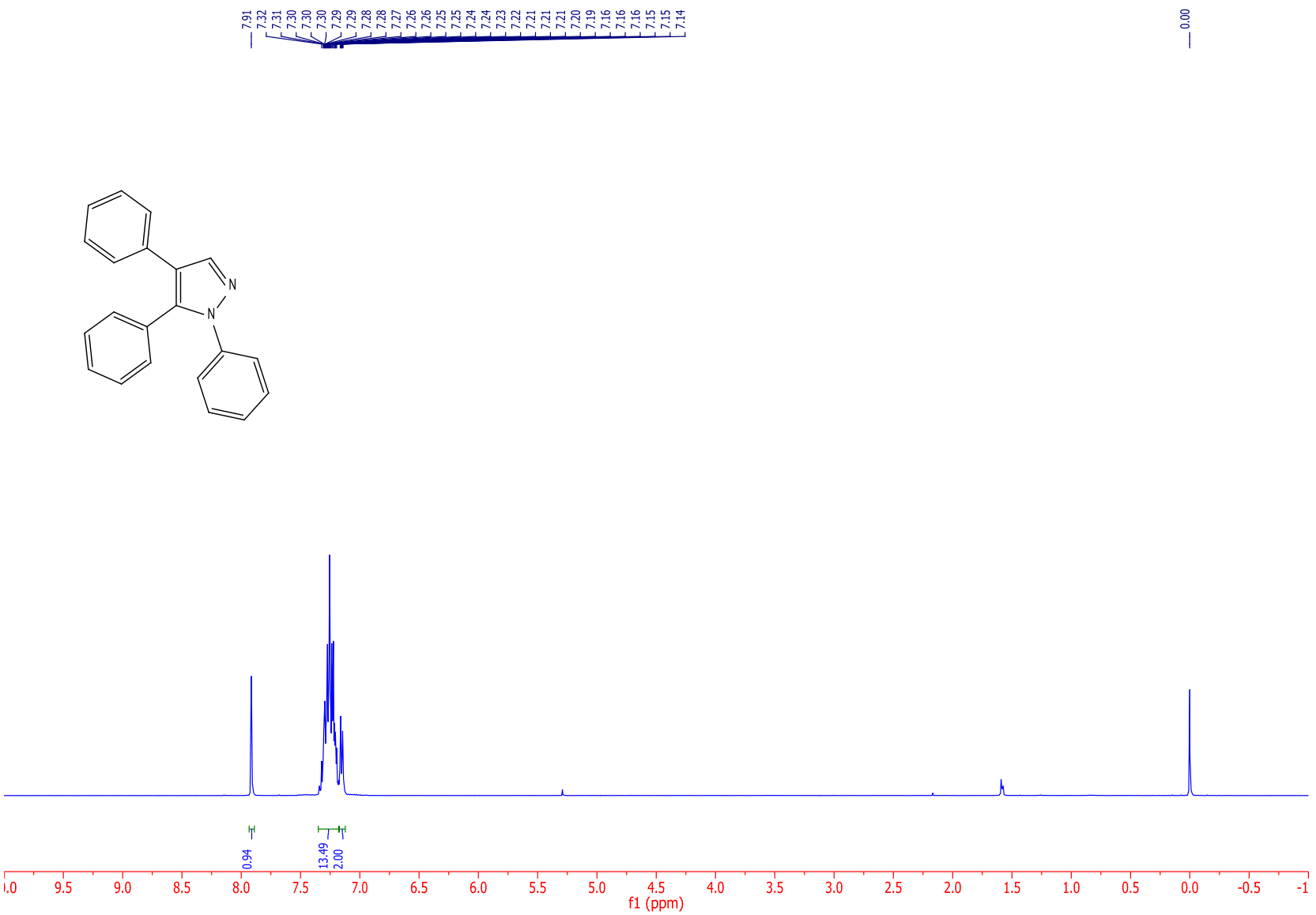
140.27
139.78
129.79
128.64
128.39
127.94
126.71
124.59
116.35
77.32
77.00
76.68
9.17
H3C
N
N
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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7.30
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7.29
7.29
7.28
7.28
7.27
7.26
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7.25
7.25
7.24
7.24
7.23
7.22
7.21
7.21
7.21
7.20
7.19
7.16
7.16
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7.15
7.15
7.14
0.00
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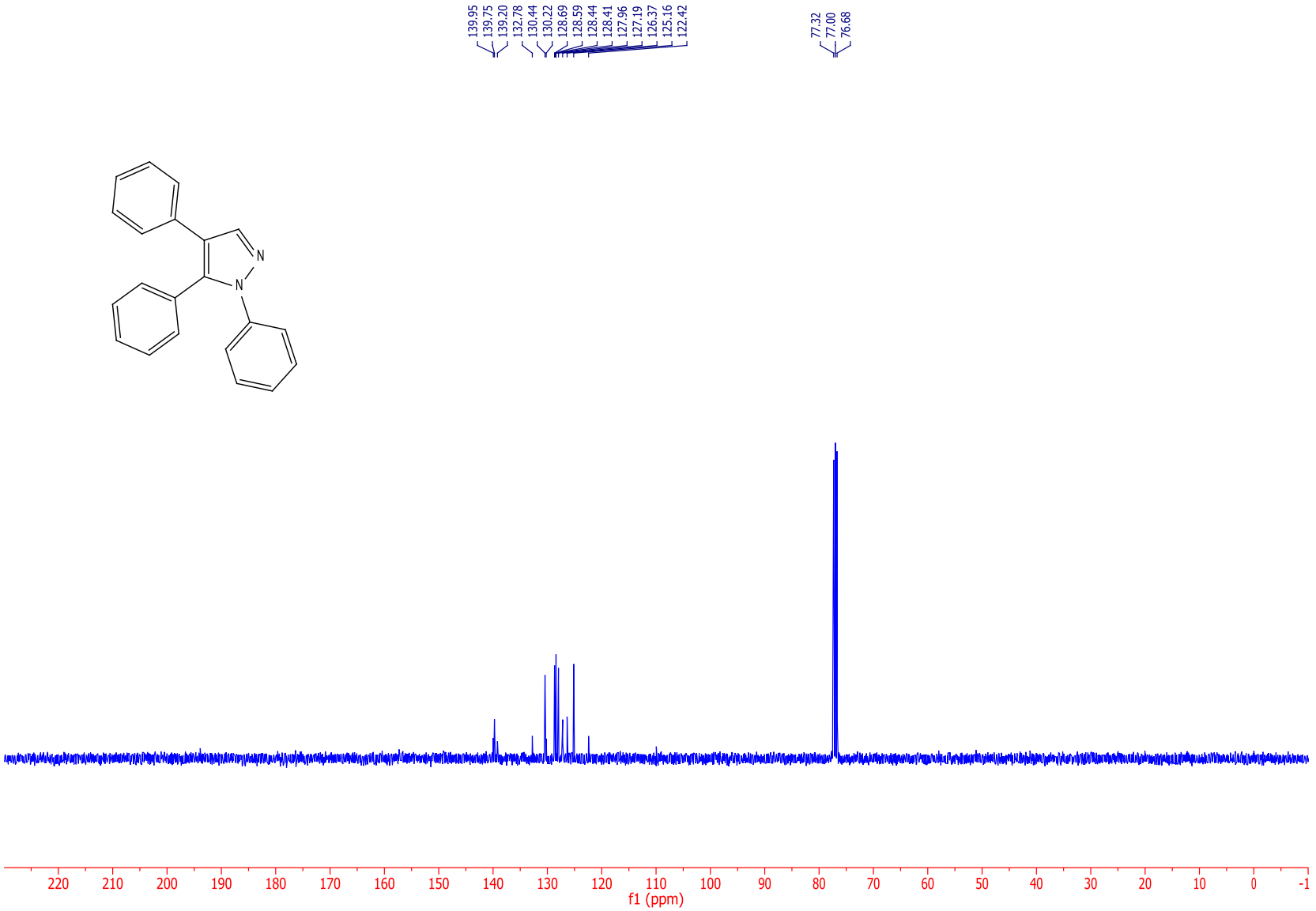
N
0.94
13.49
2.00
f1 (ppm)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130.22
128.69
128.59
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127.96
127.19
126.37
125.16
122.42
77.32
77.00
76.68
N
N
220
210
200
190
180
170
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120
110
100
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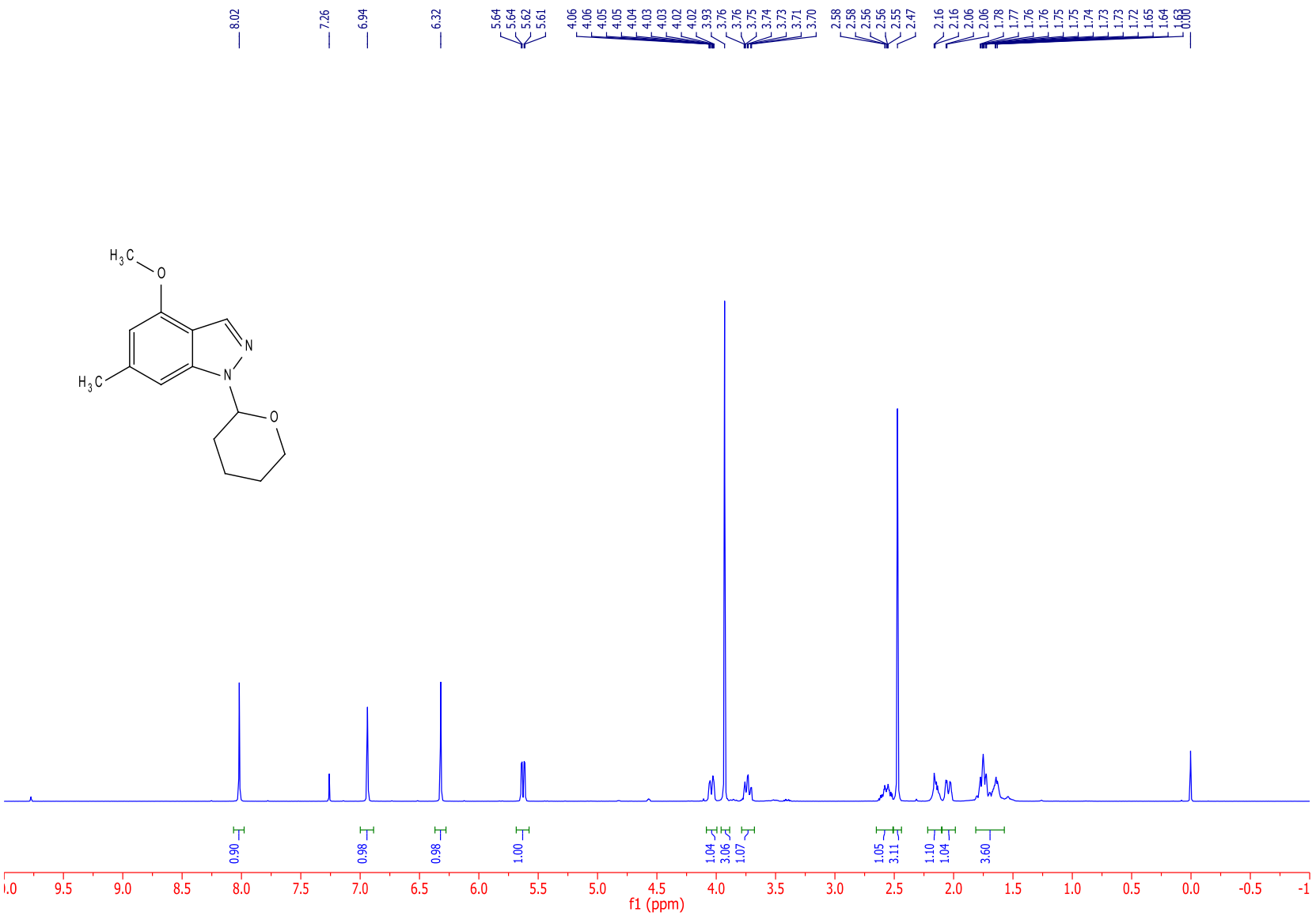
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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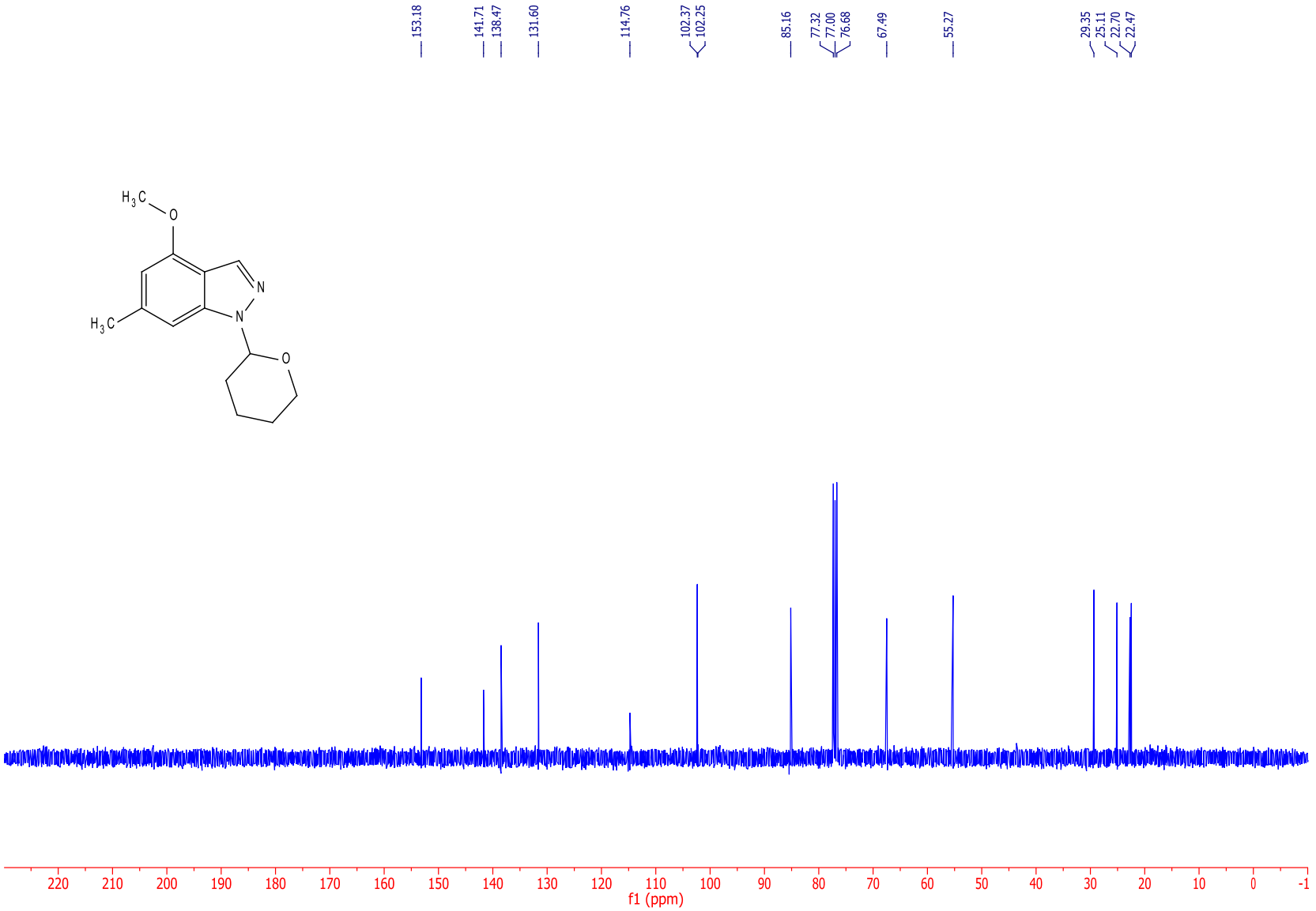
7.26
6.94
6.32
5.64
5.64
5.62
5.61
4.06
4.06
4.05
4.05
4.04
4.03
4.03
4.02
4.02
3.93
3.76
3.76
3.75
3.74
3.73
3.71
3.70
2.58
2.58
2.56
2.56
2.55
2.47
2.16
2.16
2.06
2.06
1.78
1.77
1.76
1.76
1.75
1.75
1.74
1.73
1.73
1.72
1.65
1.64
1.63
0.00
H3C
O
N
N
H3C
O
0.90
0.98
0.98
1.00
1.04
3.06
1.07
1.05
3.11
1.10
1.04
3.60
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
f1 (ppm)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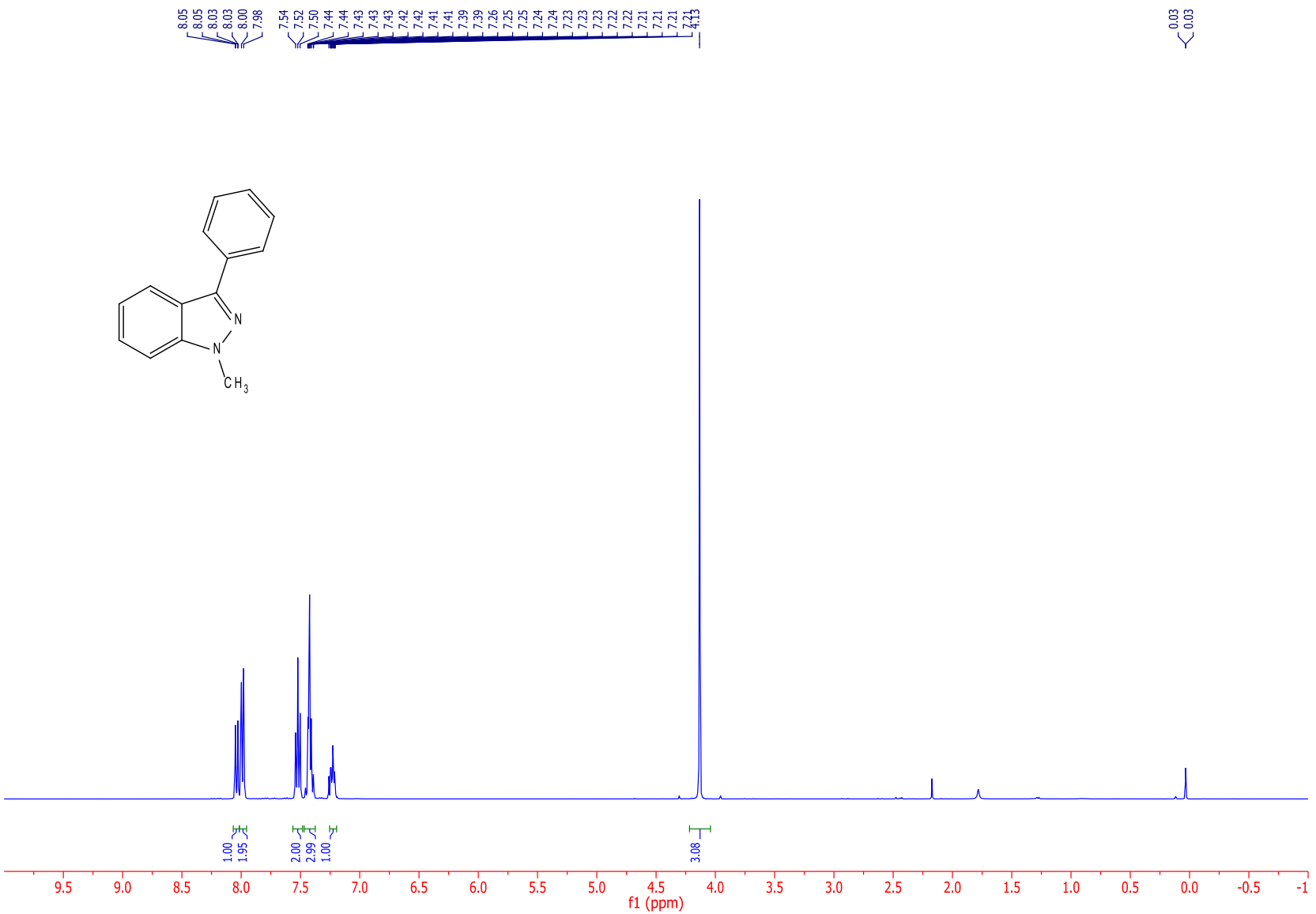
102.37
102.25
85.16
77.32
77.00
76.68
67.49
55.27
29.35
25.11
22.70
22.47
H3C
O
N
N
H3C
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


8.05
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8.03
8.00
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7.52
7.50
7.44
7.43
7.43
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7.42
7.42
7.41
7.41
7.39
7.39
7.26
7.25
7.25
7.24
7.24
7.23
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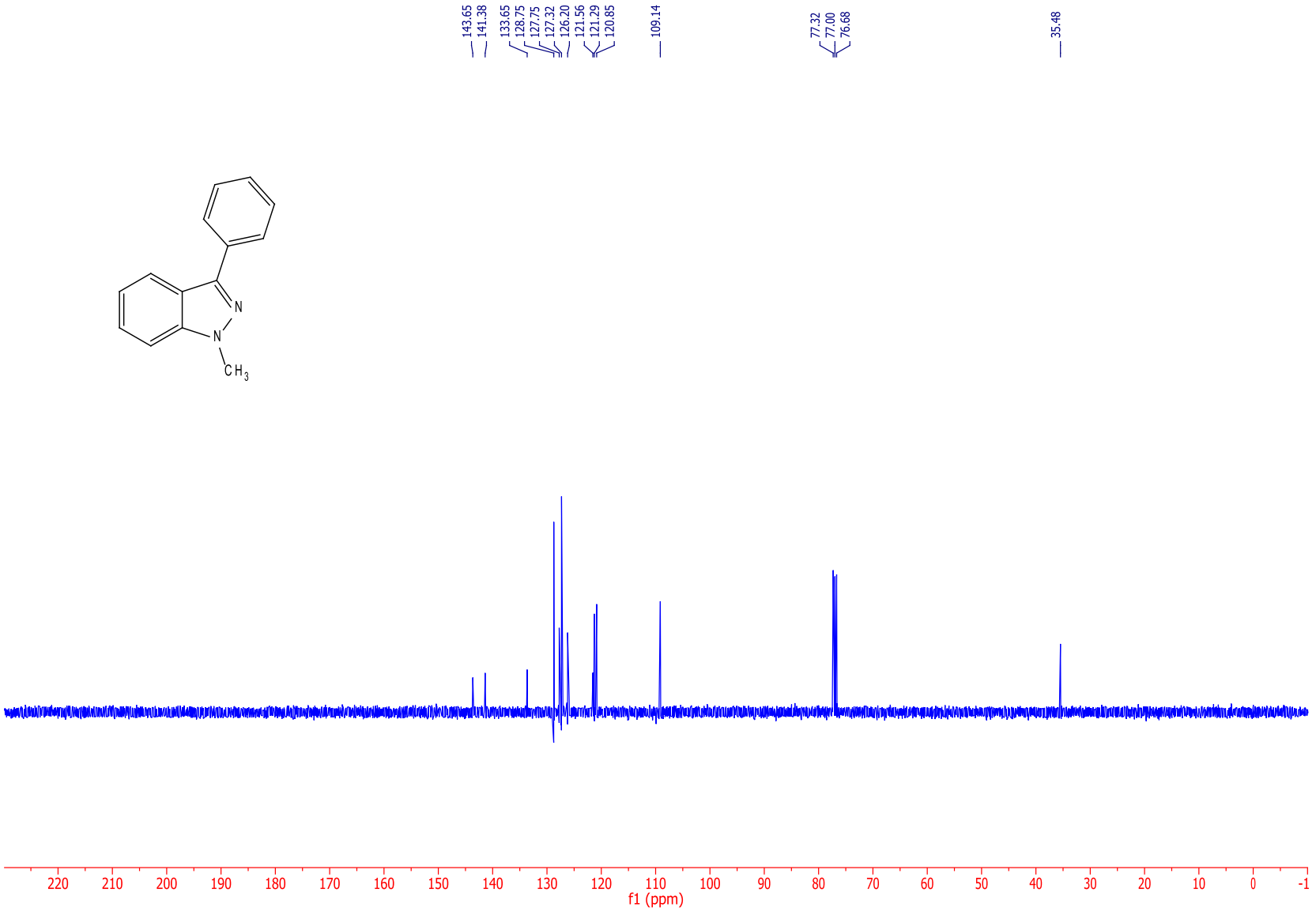
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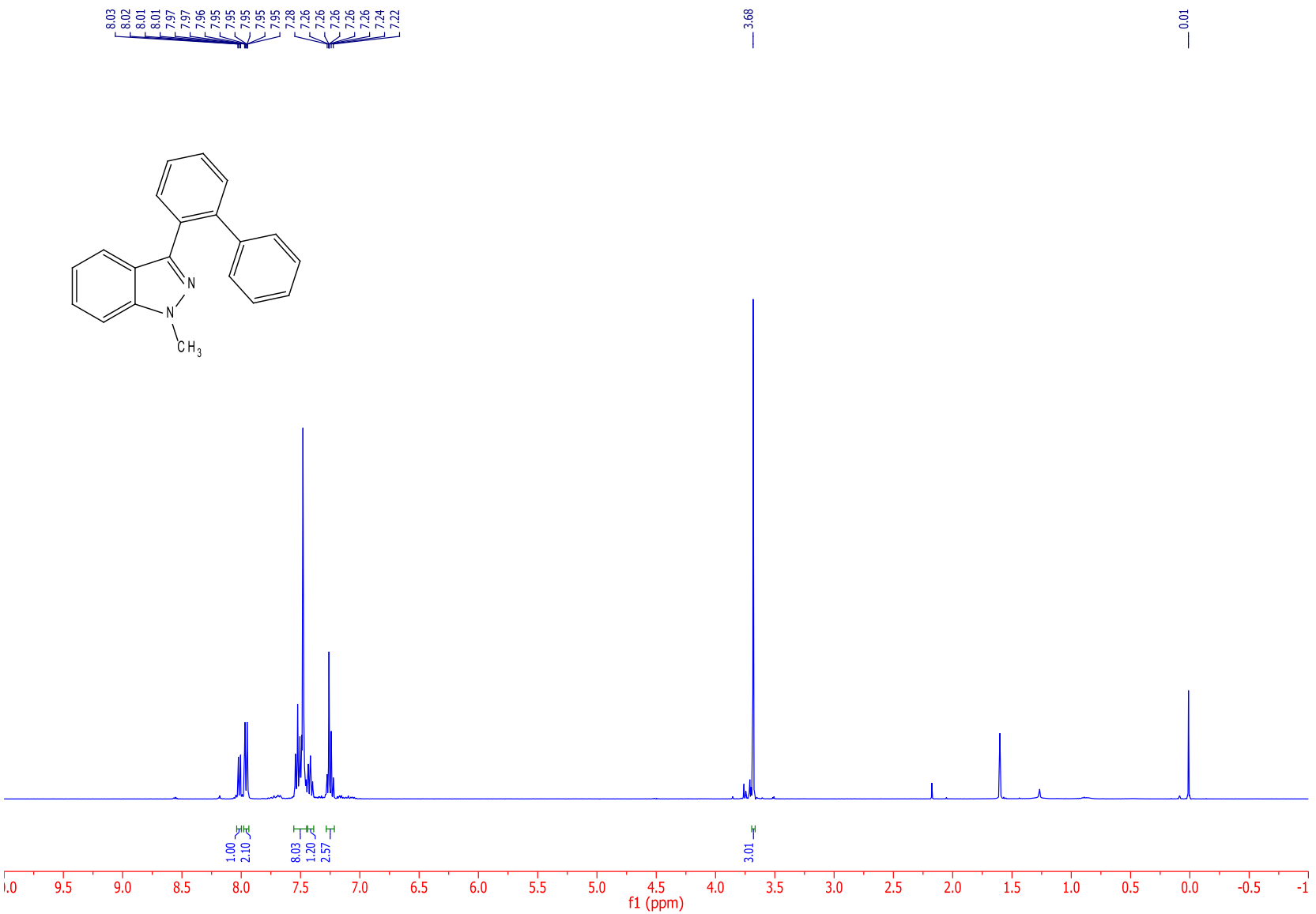
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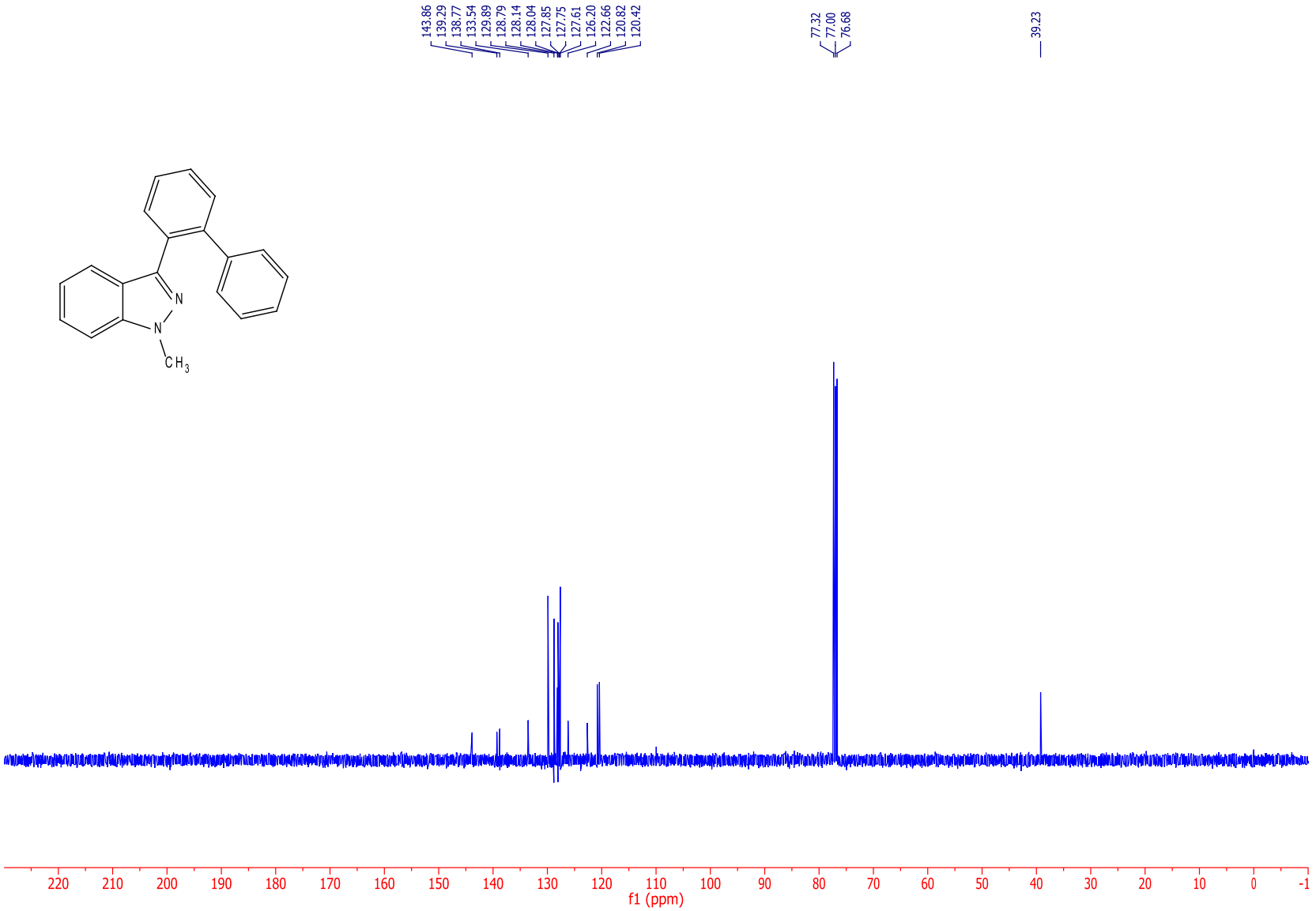
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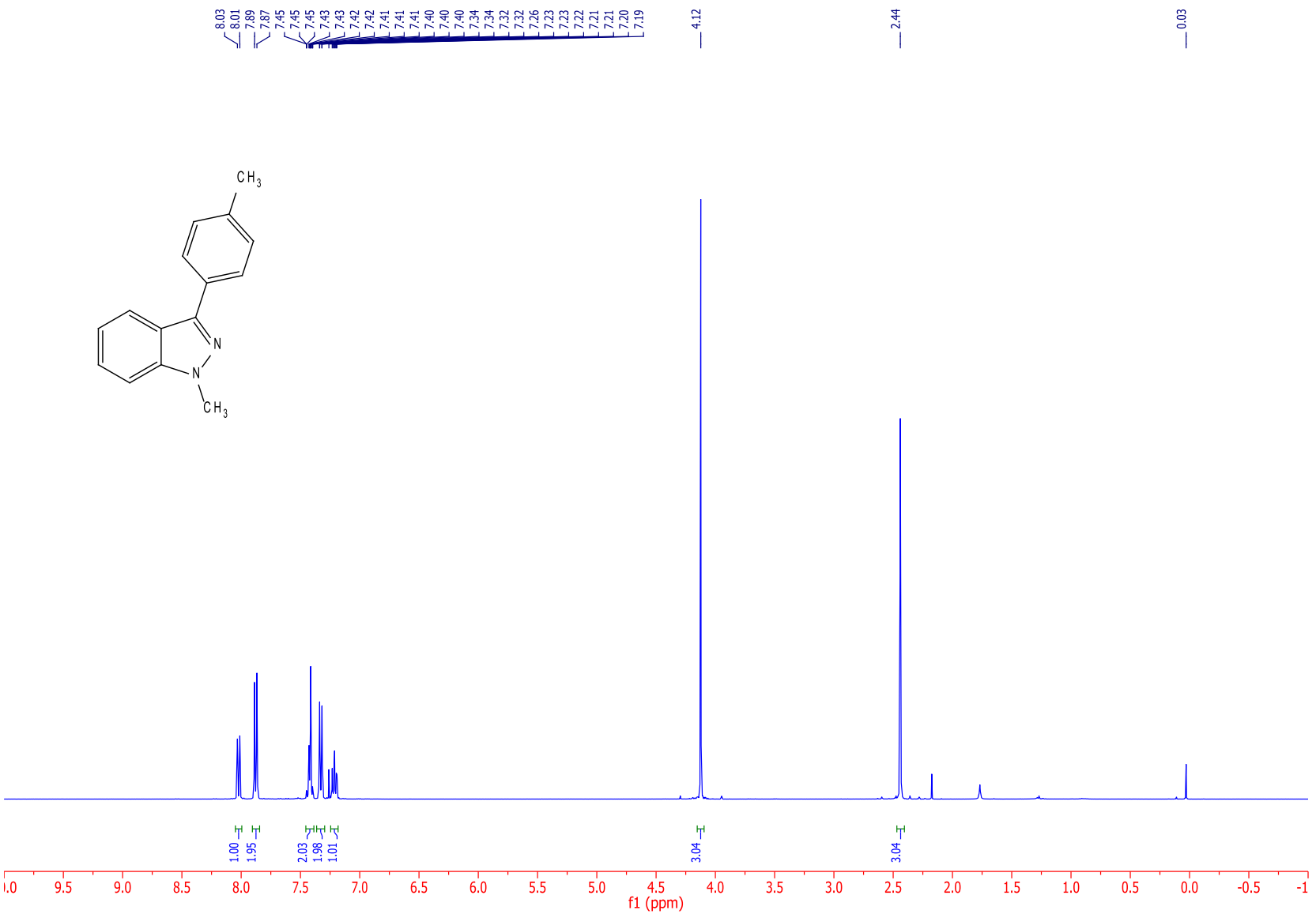
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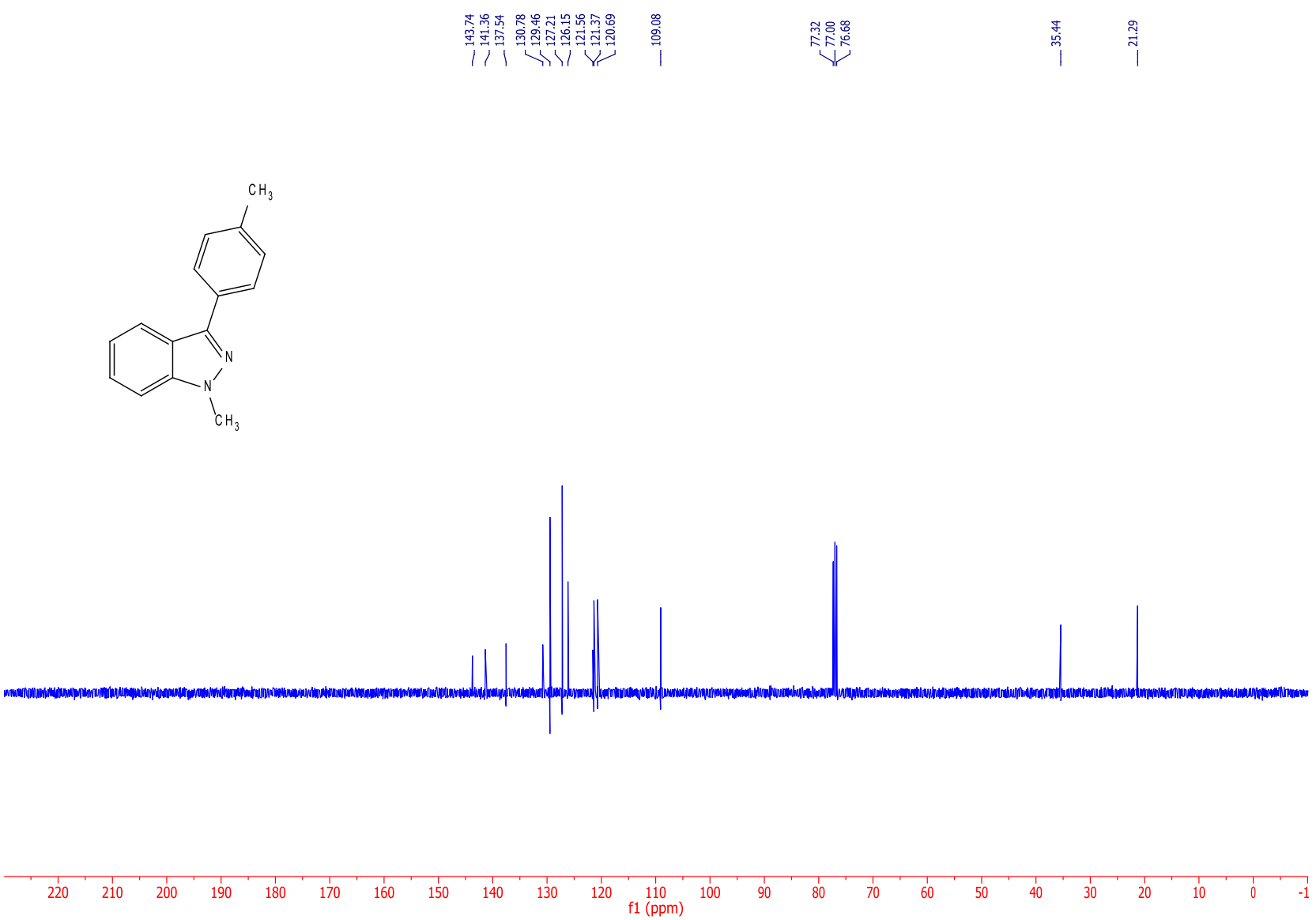
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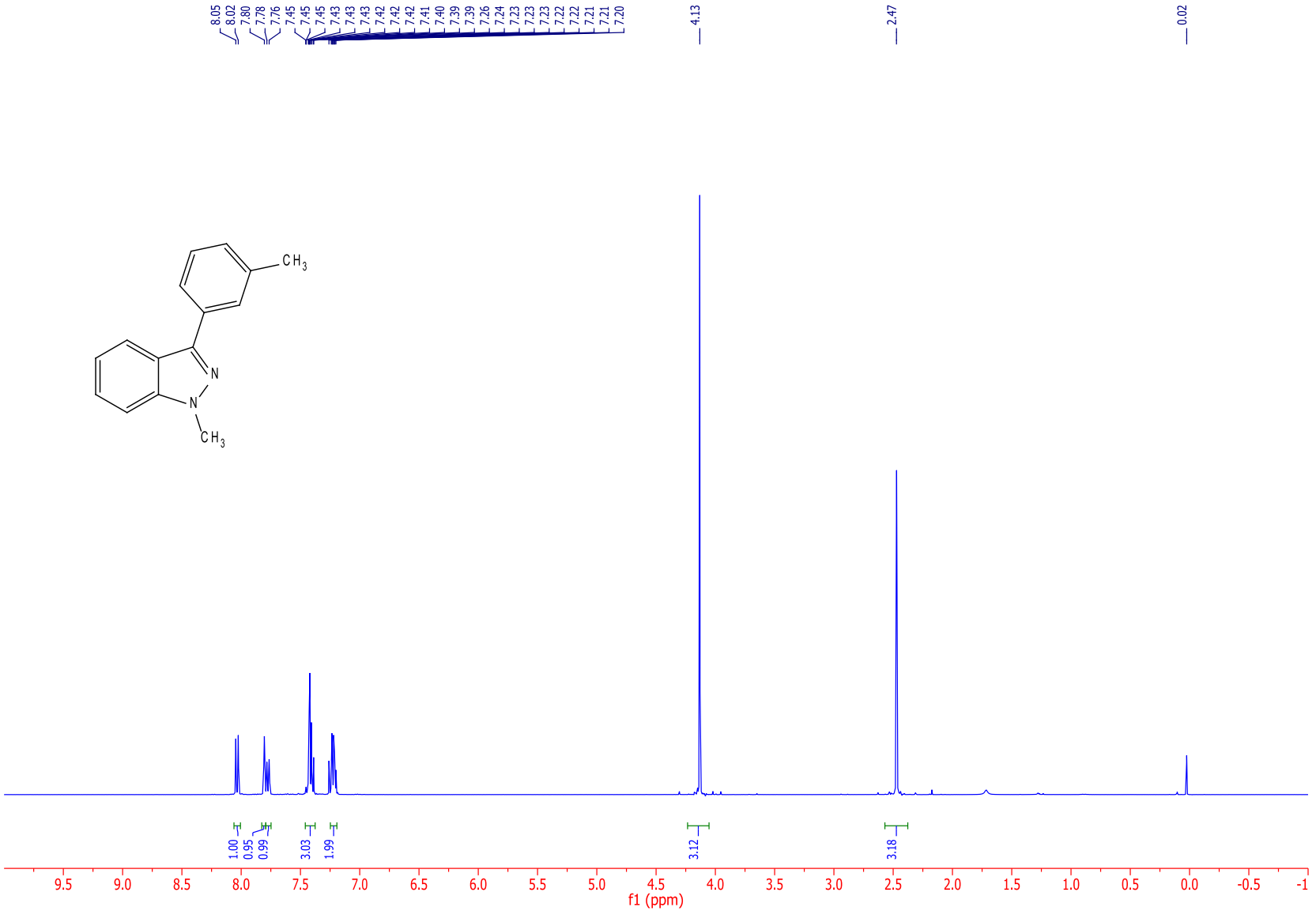
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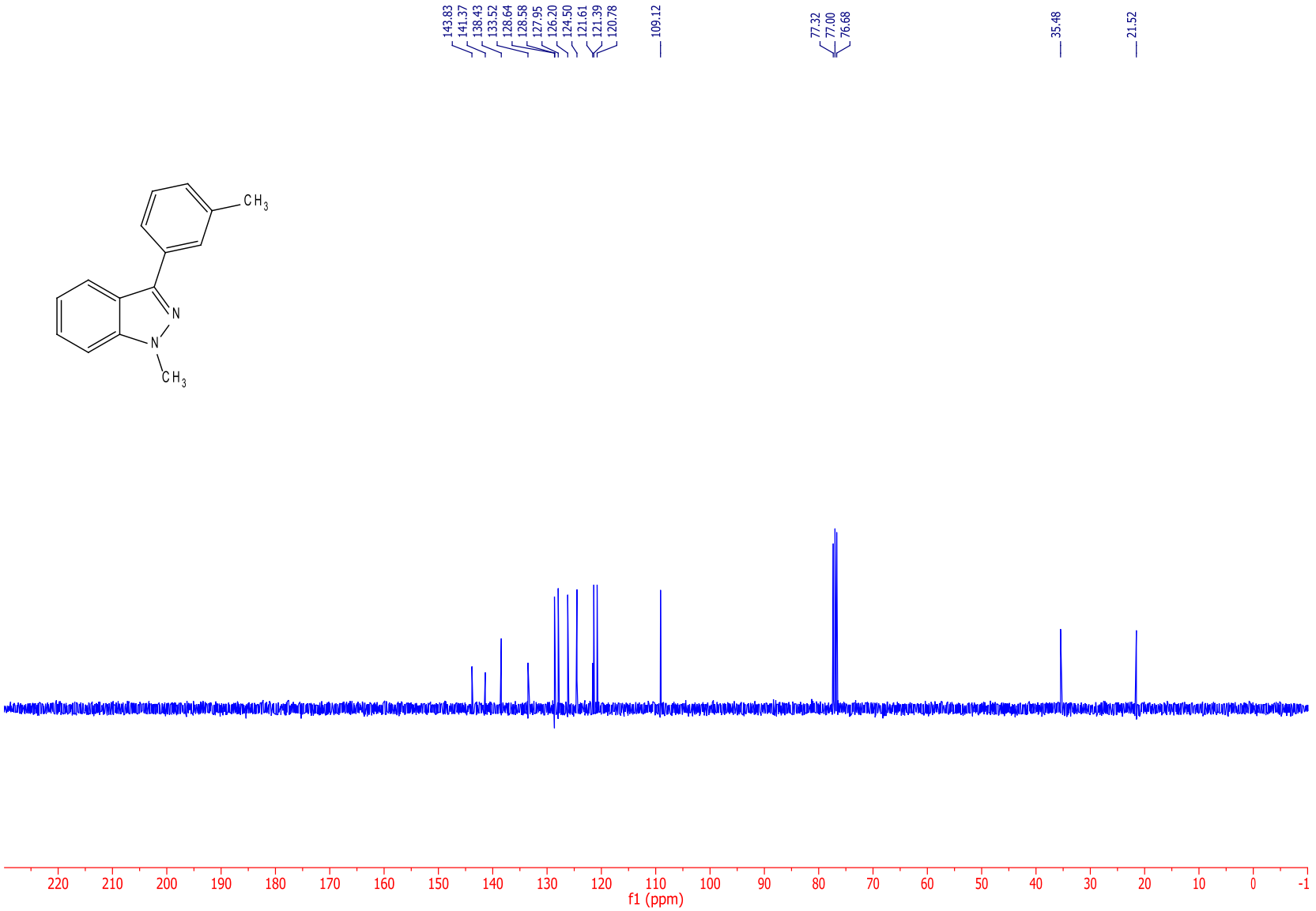
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77.00
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35.48
21.52
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CH3
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180
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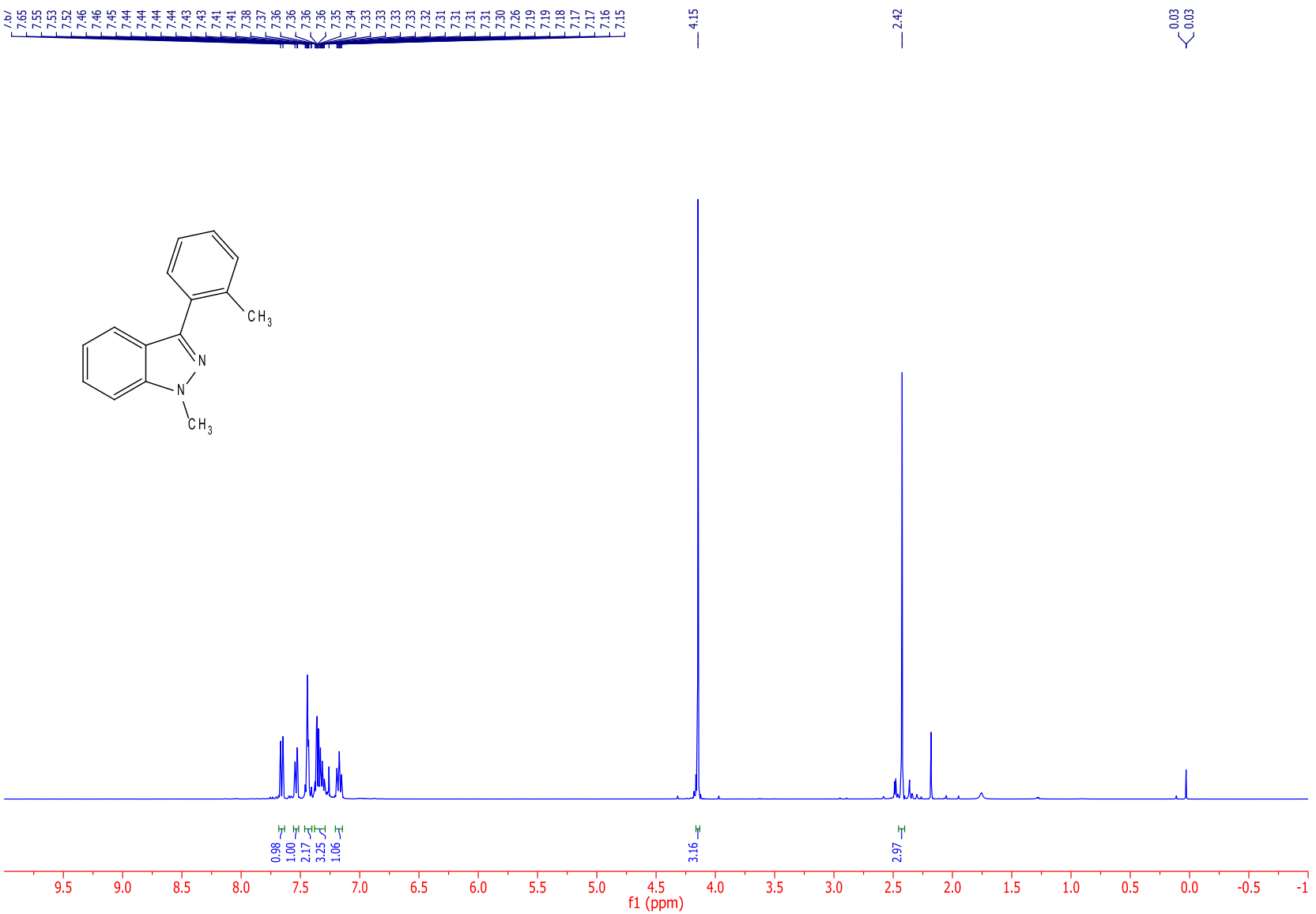
f1 (ppm)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7.19
7.18
7.17
7.17
7.16
7.15
4.15
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0.03
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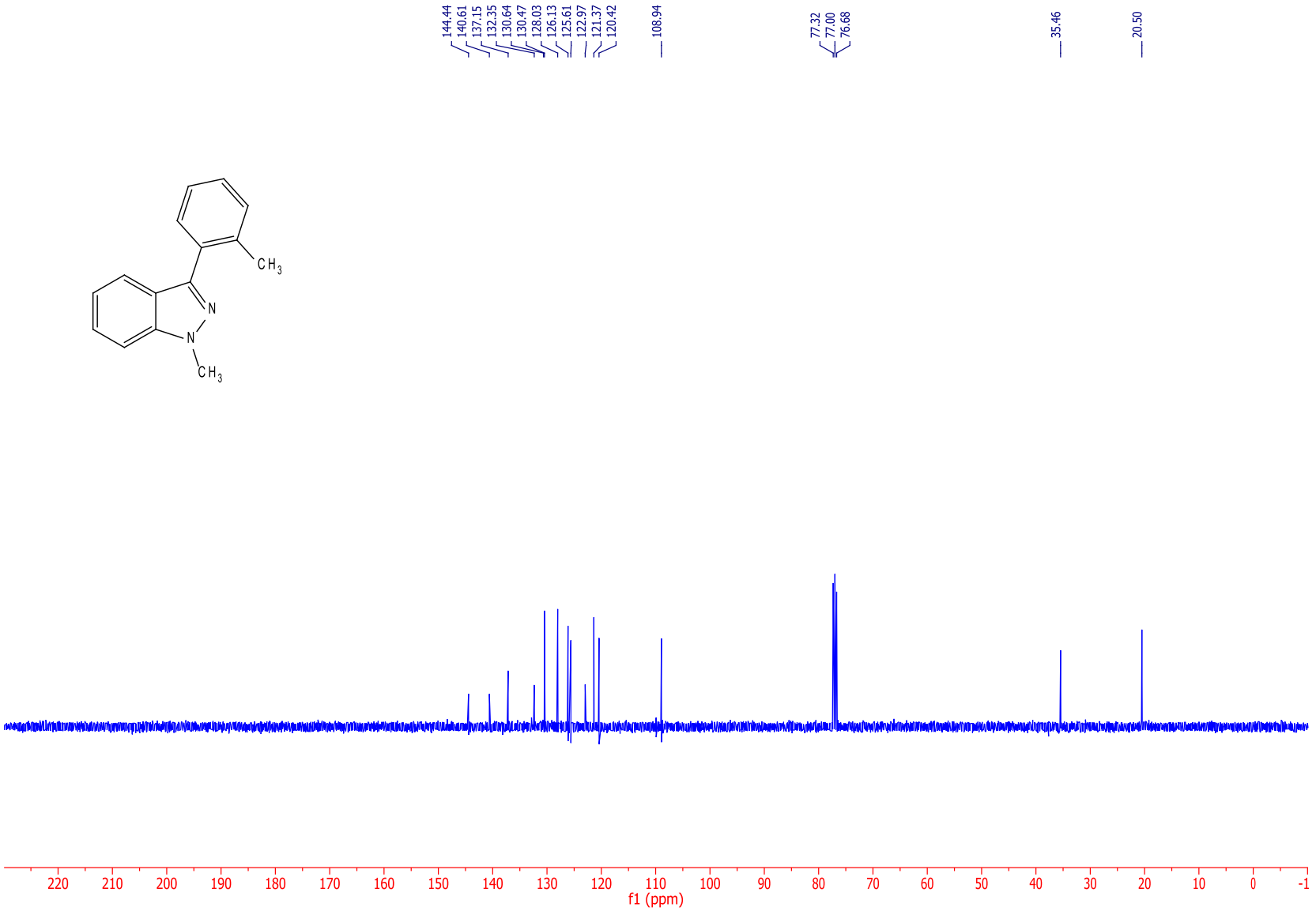
f1 (ppm)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77.00
76.68
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CH3
N
N
CH3
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180
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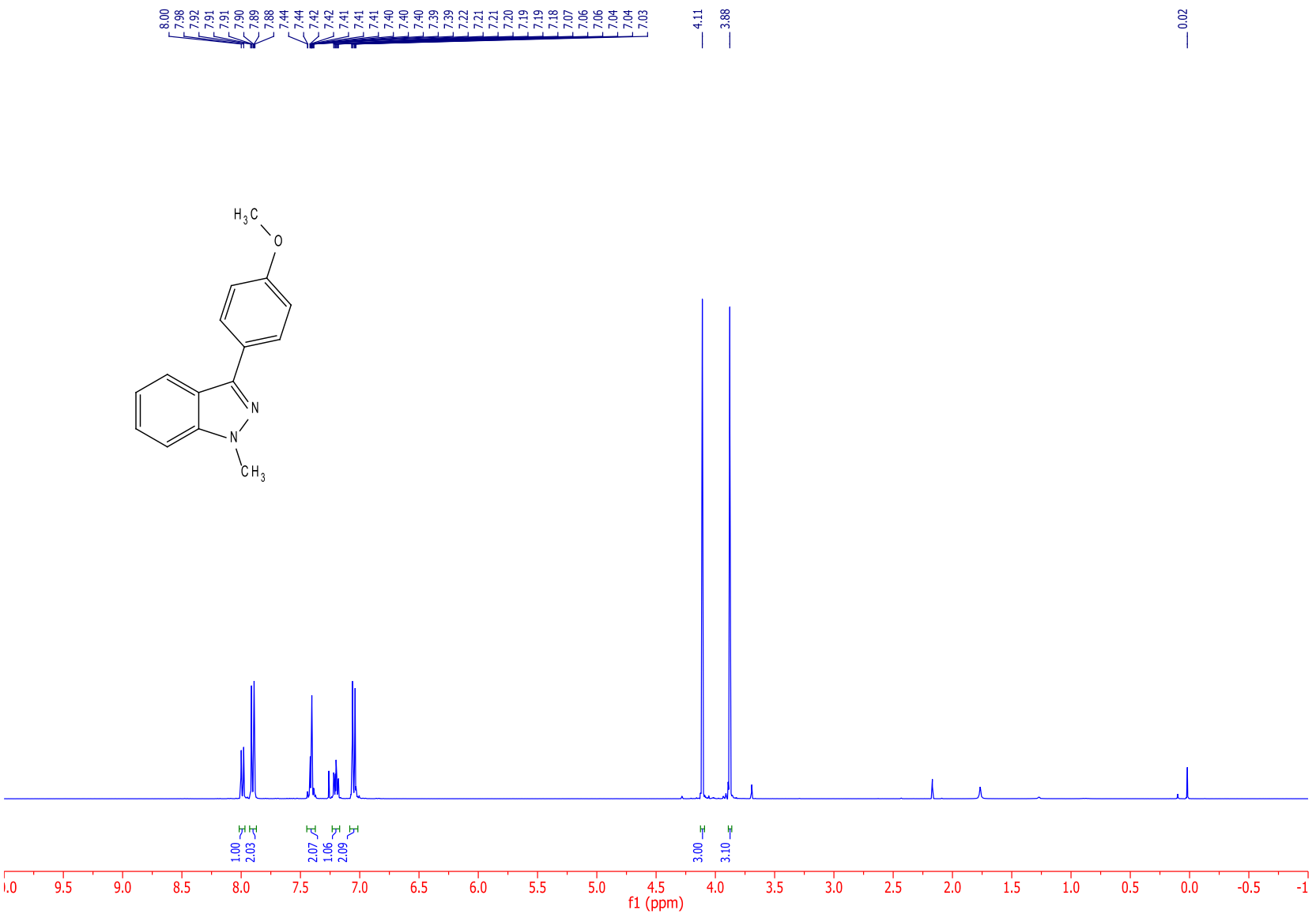
f1 (ppm)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7.19
7.19
7.18
7.07
7.06
7.06
7.04
7.04
7.03
4.11
3.88
0.02
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N
CH3
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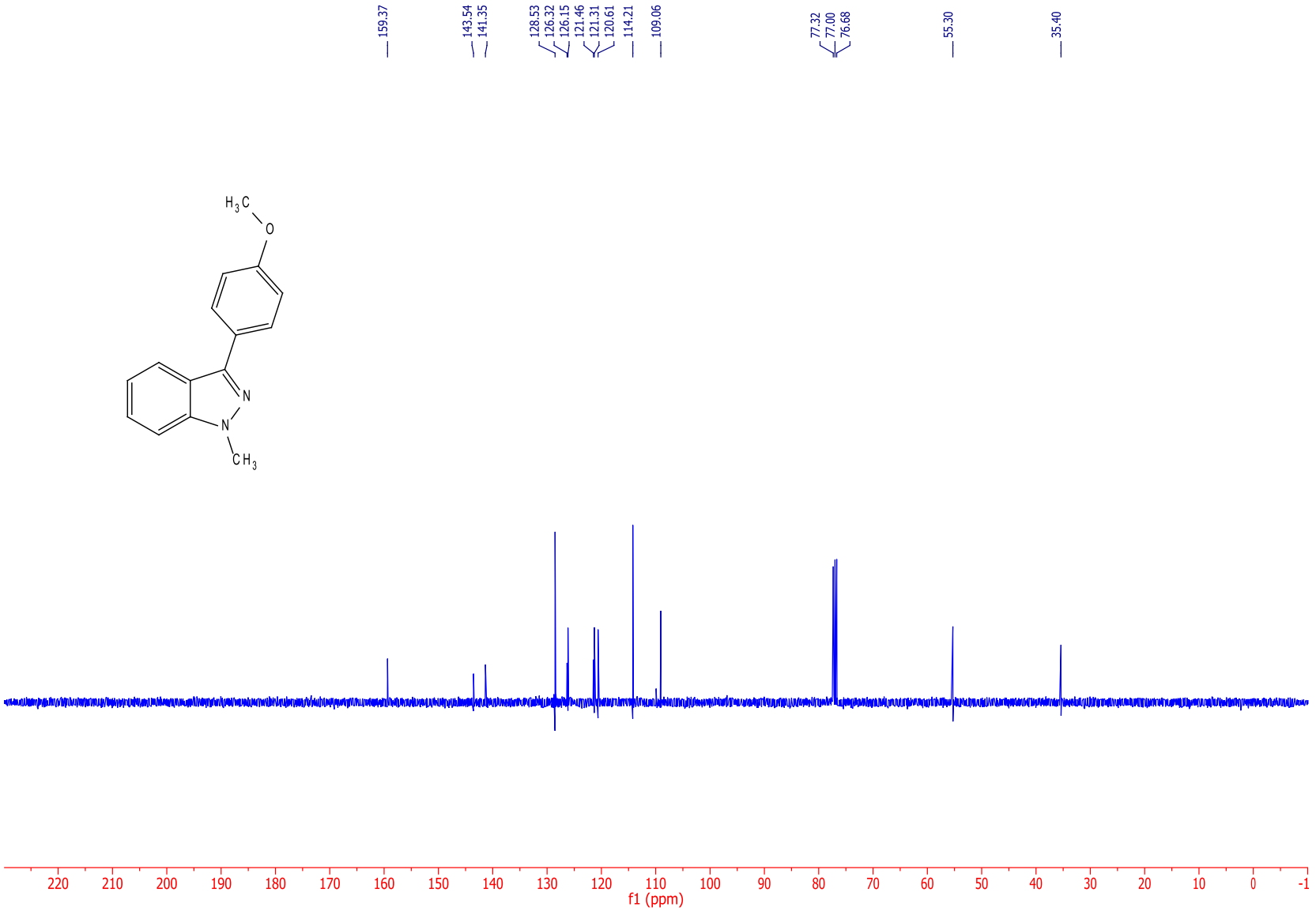
2.07
1.06
2.09
3.00
3.10
f1 (ppm)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H3C
O
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N
CH3
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200
190
180
170
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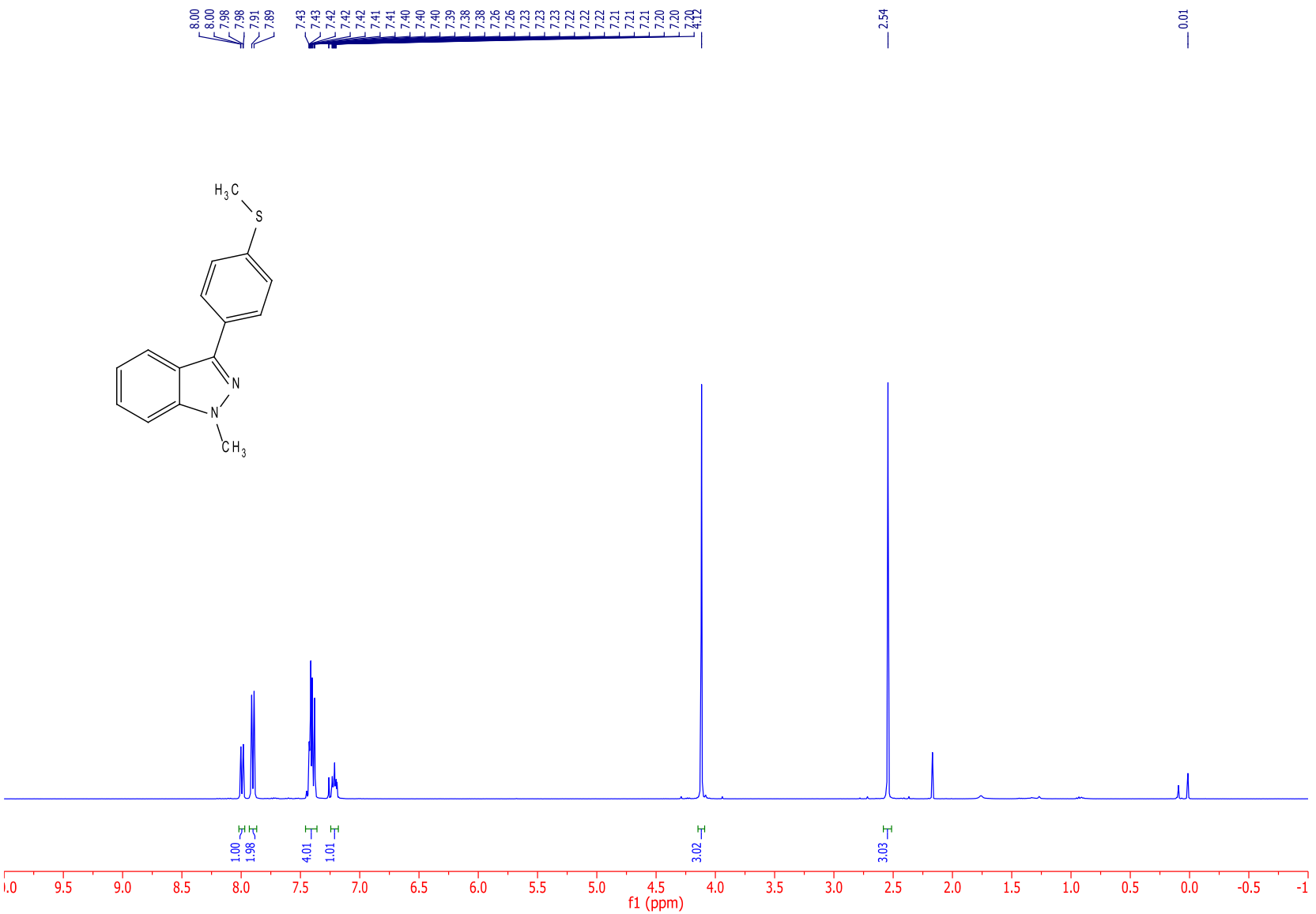
f1 (ppm)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7.21
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7.20
7.20
4.12
2.54
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S
N
N
CH3
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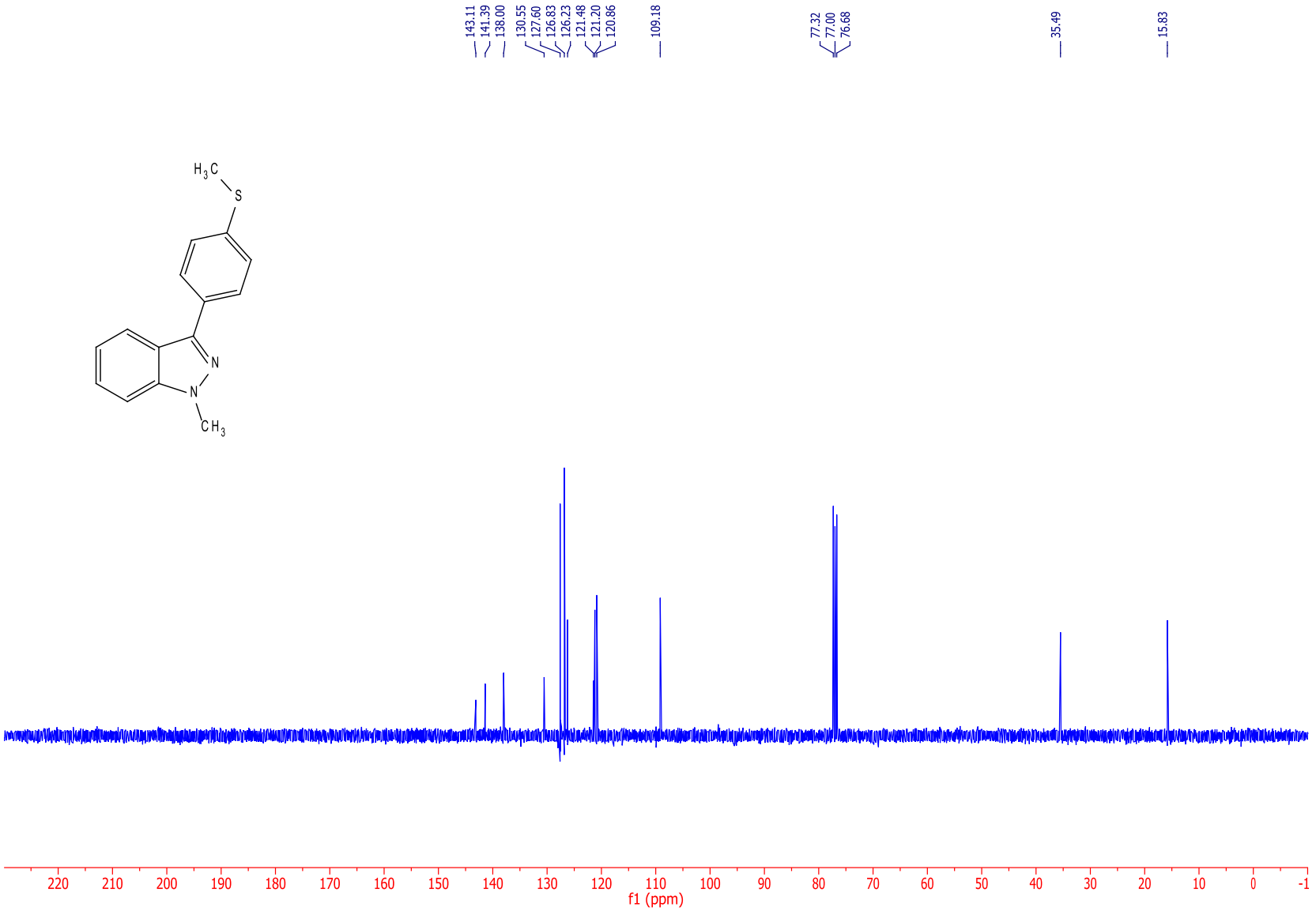
1.01
3.02
3.03
f1 (ppm)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35.49
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H3C
S
N
N
CH3
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200
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180
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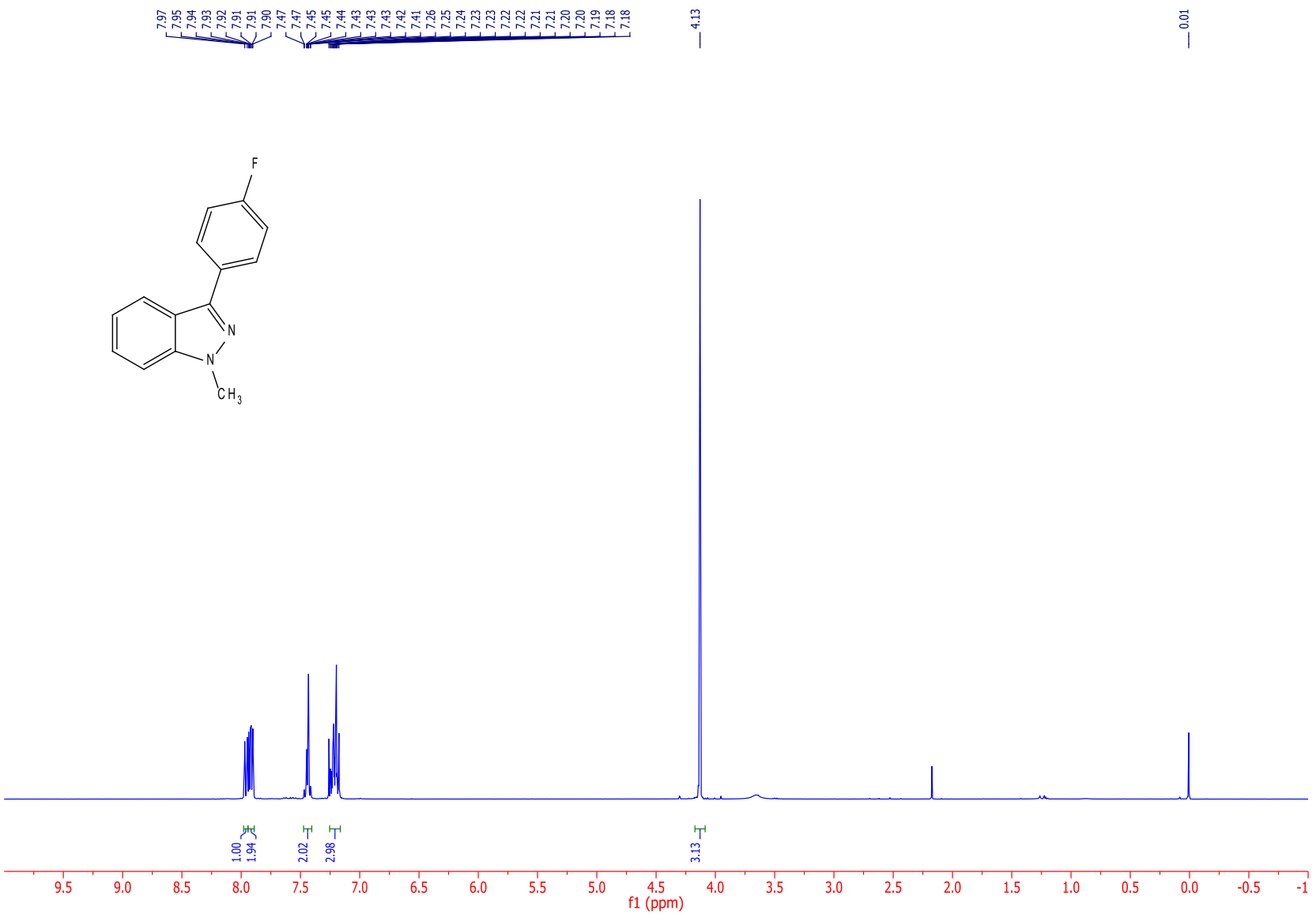
f1 (ppm)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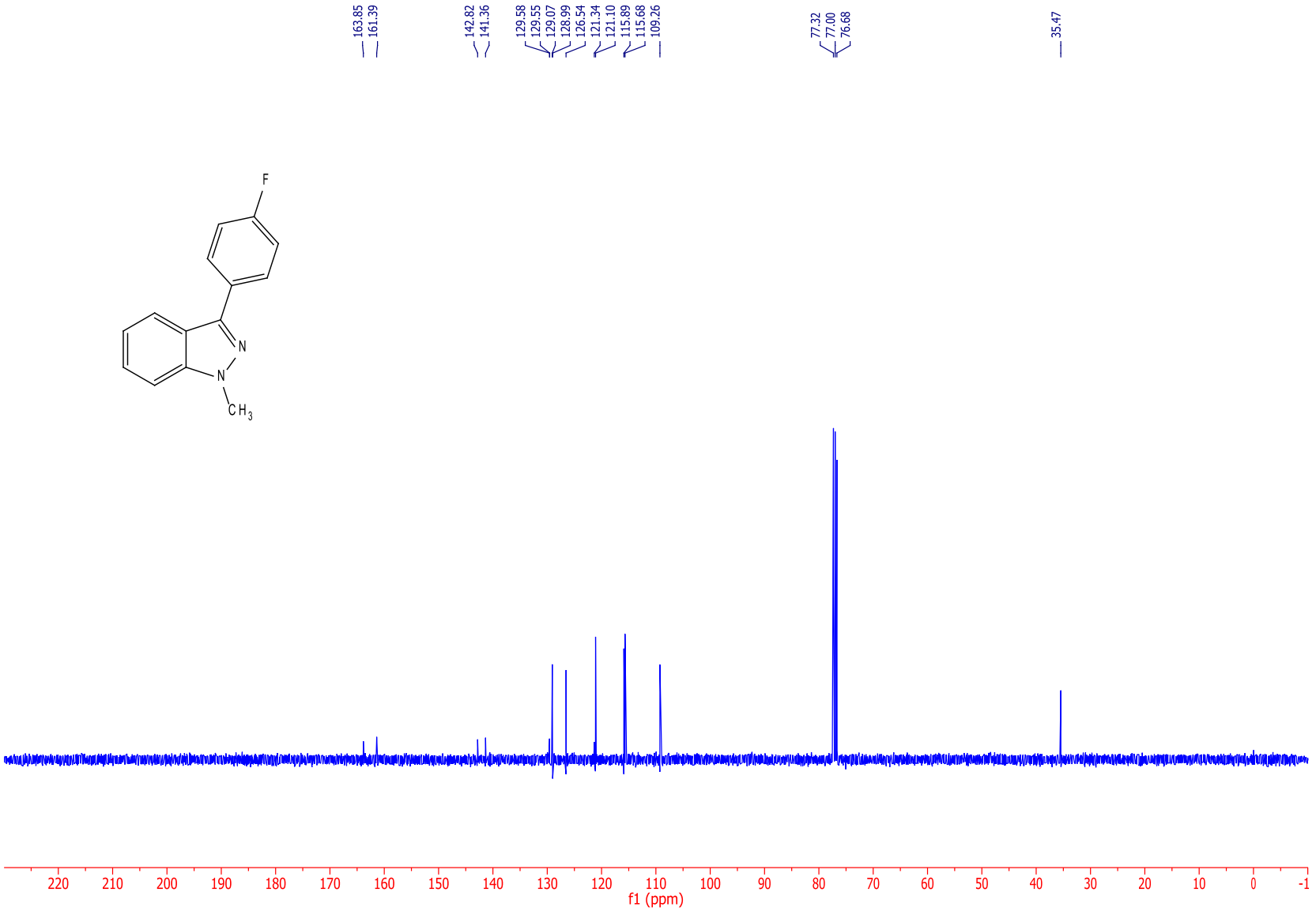
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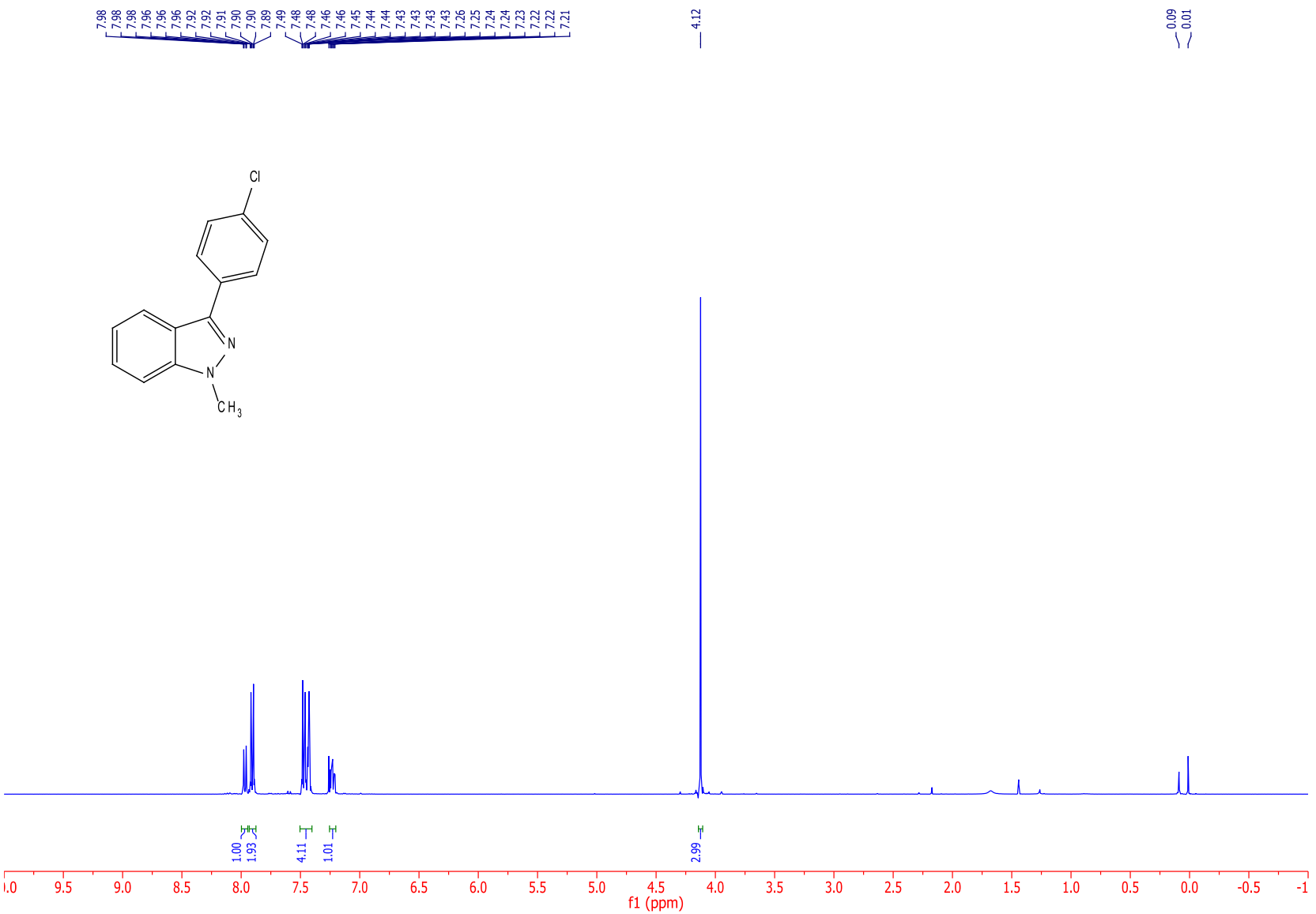
f1 (ppm)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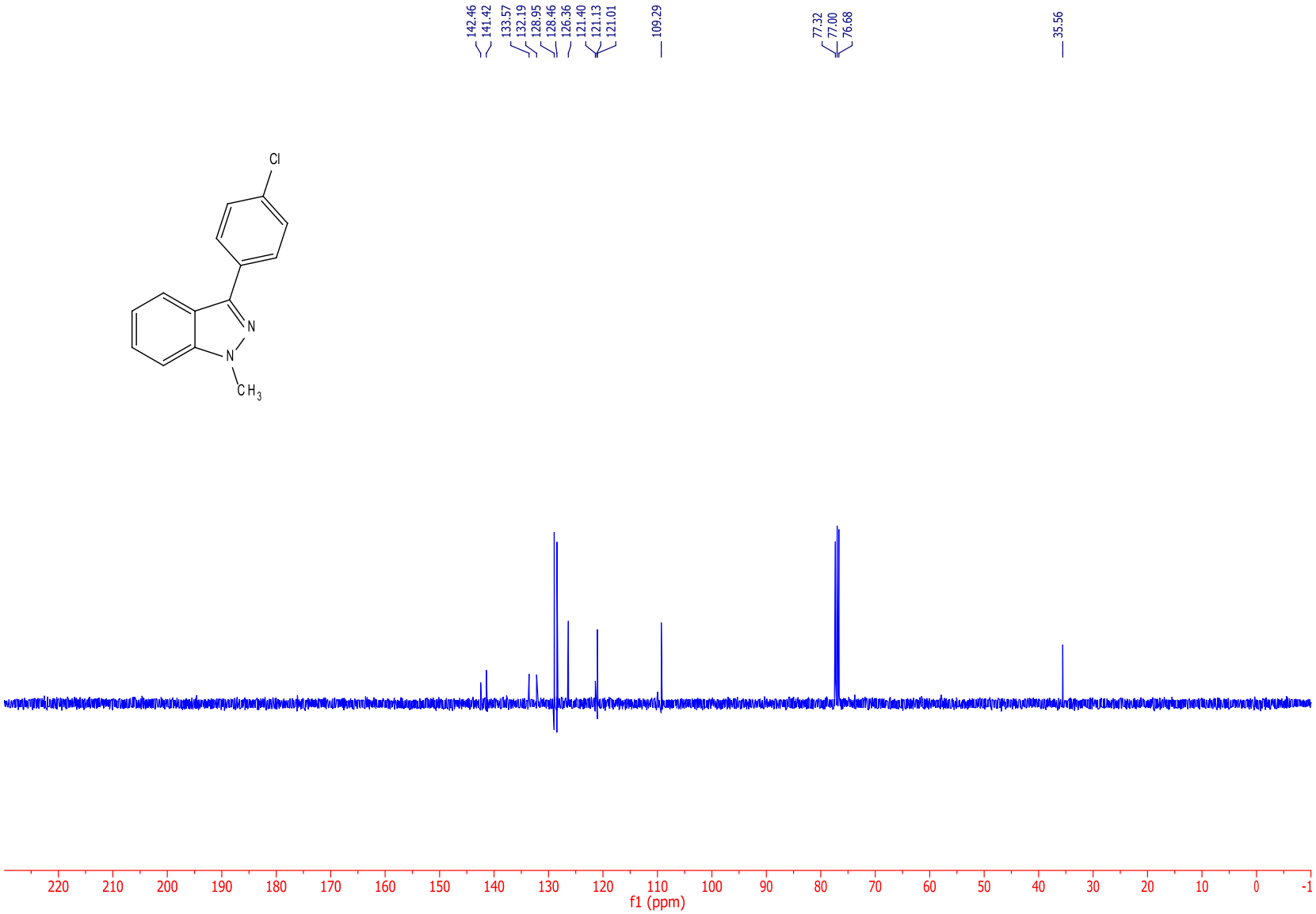
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CH3
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200
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180
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100
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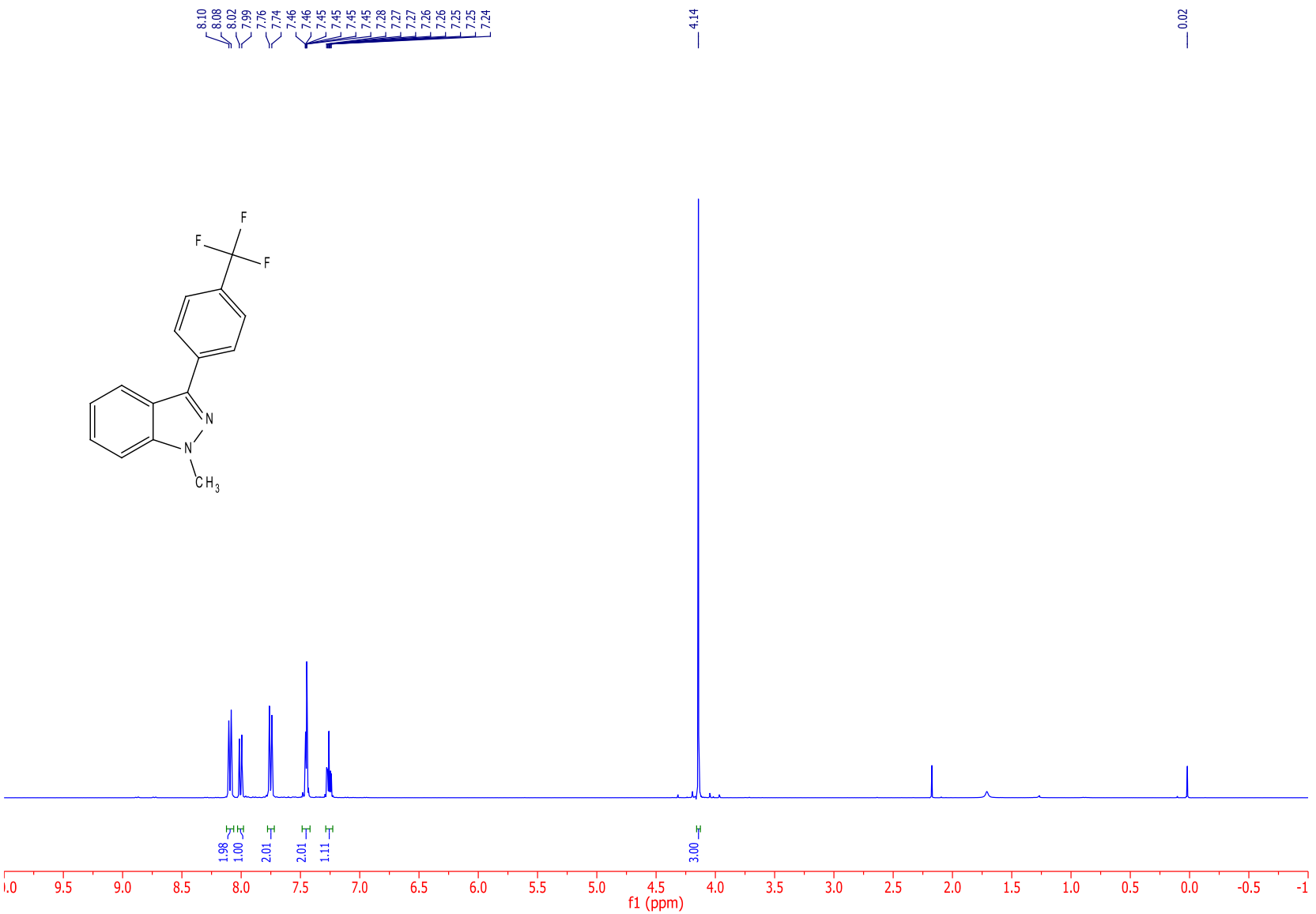
f1 (ppm)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7.26
7.26
7.25
7.25
7.24
4.14
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N
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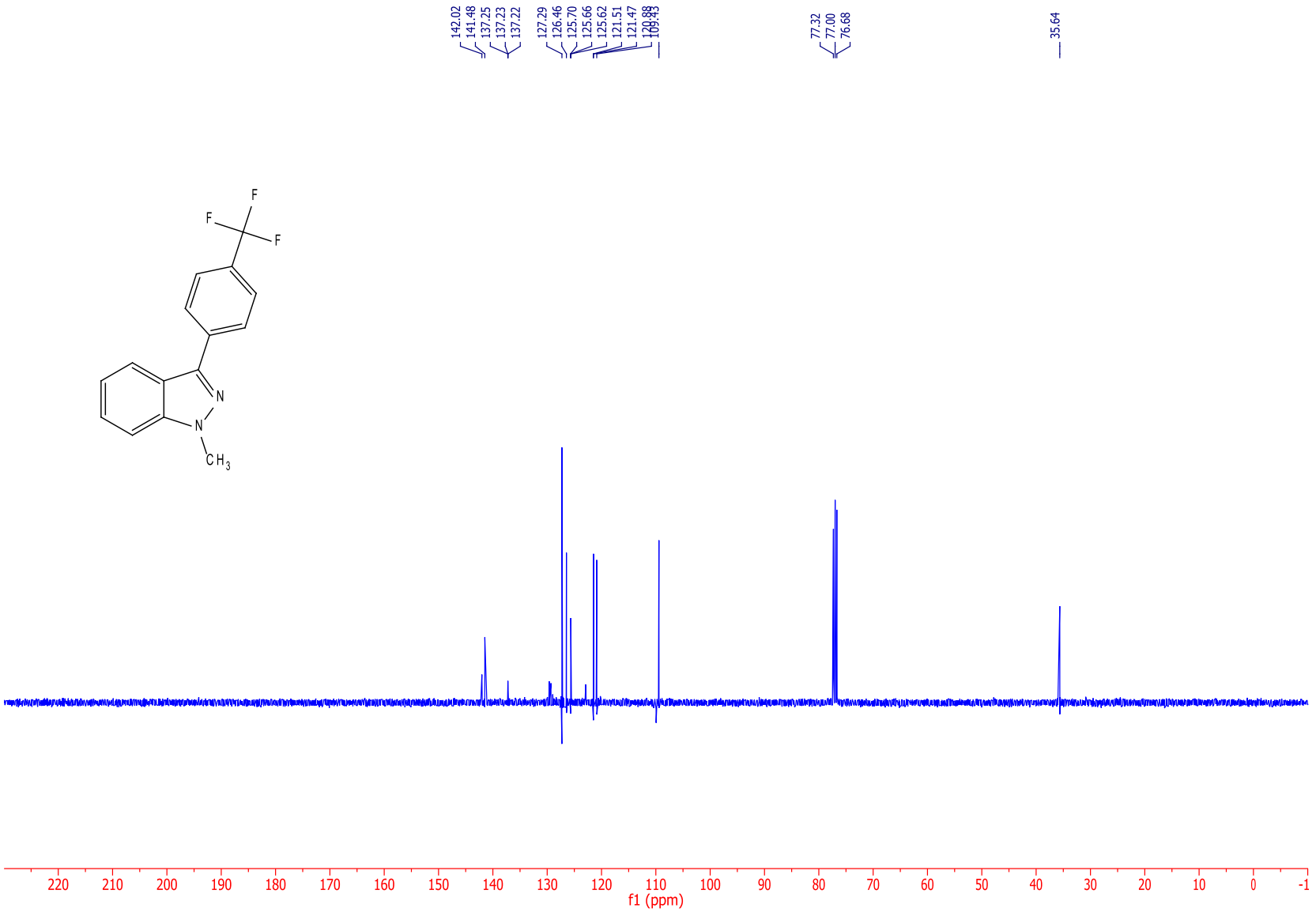
2.01
1.11
3.00
f1 (ppm)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77.00
76.68
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F
F
F
N
N
CH3
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180
170
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80
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30
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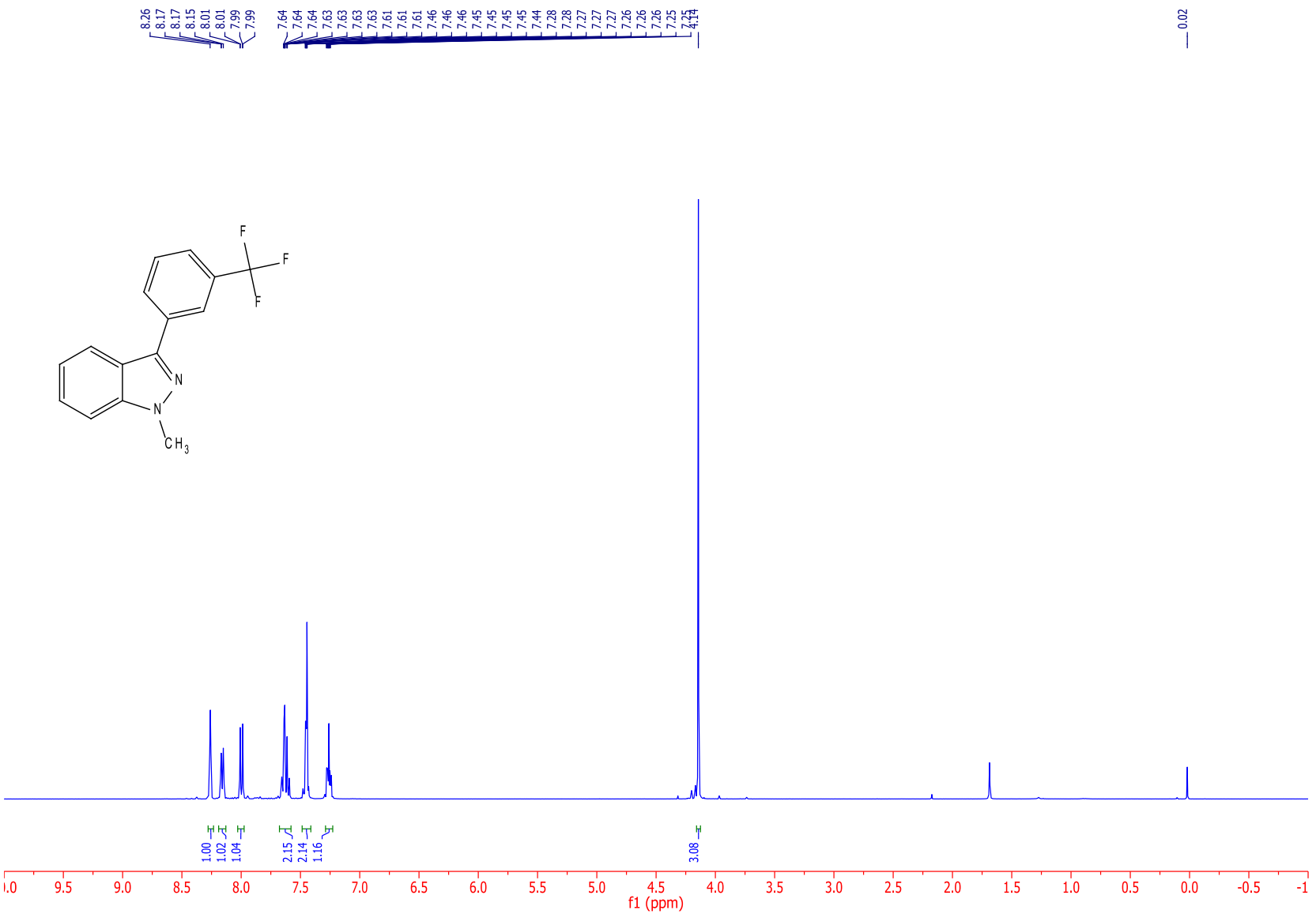
f1 (ppm)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7.26
7.26
7.25
4.14
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2.14
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3.08
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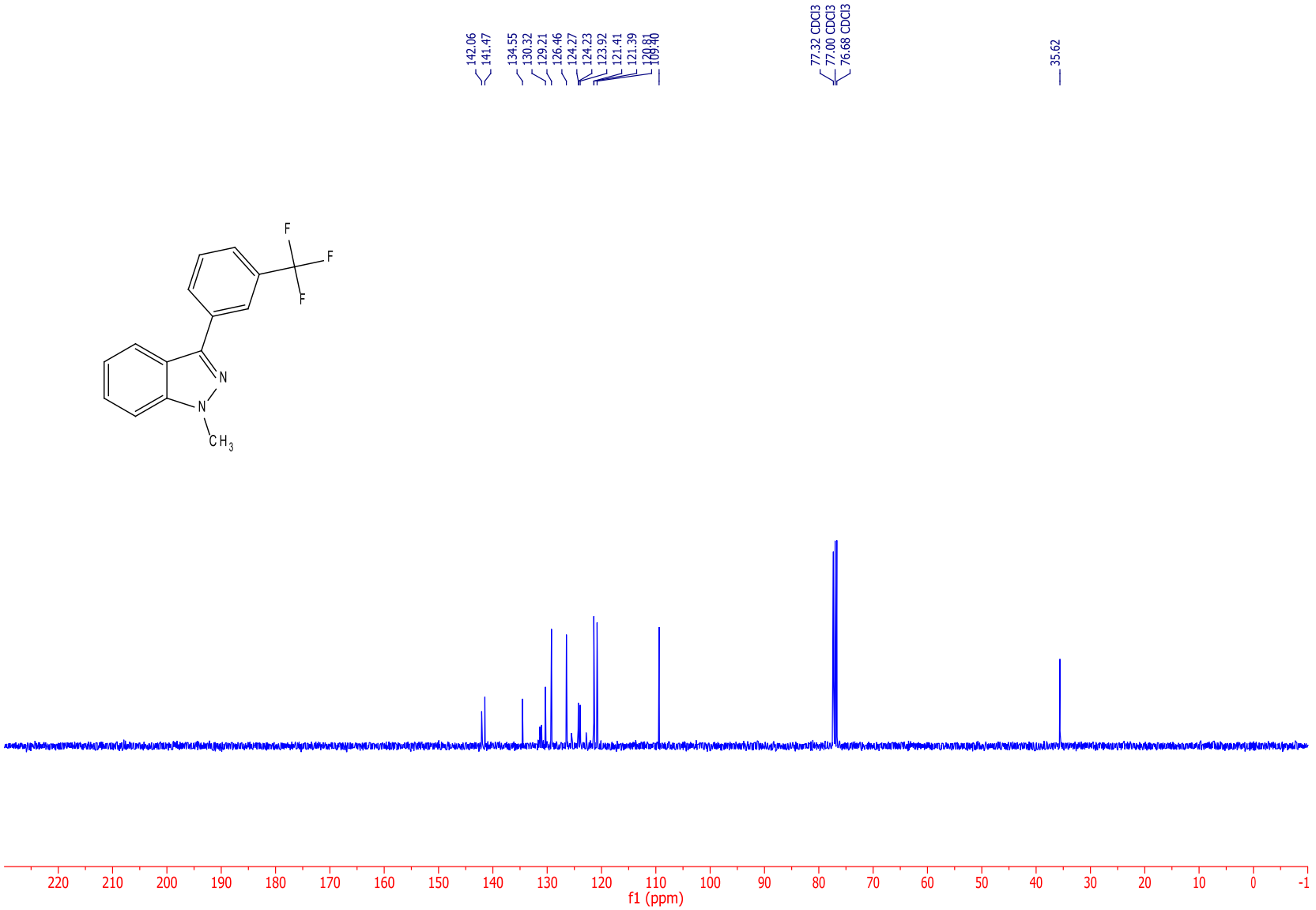
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109.40
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77.00 CDCl3
76.68 CDCl3
35.62
F
F
F
N
N
CH3
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180
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100
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80
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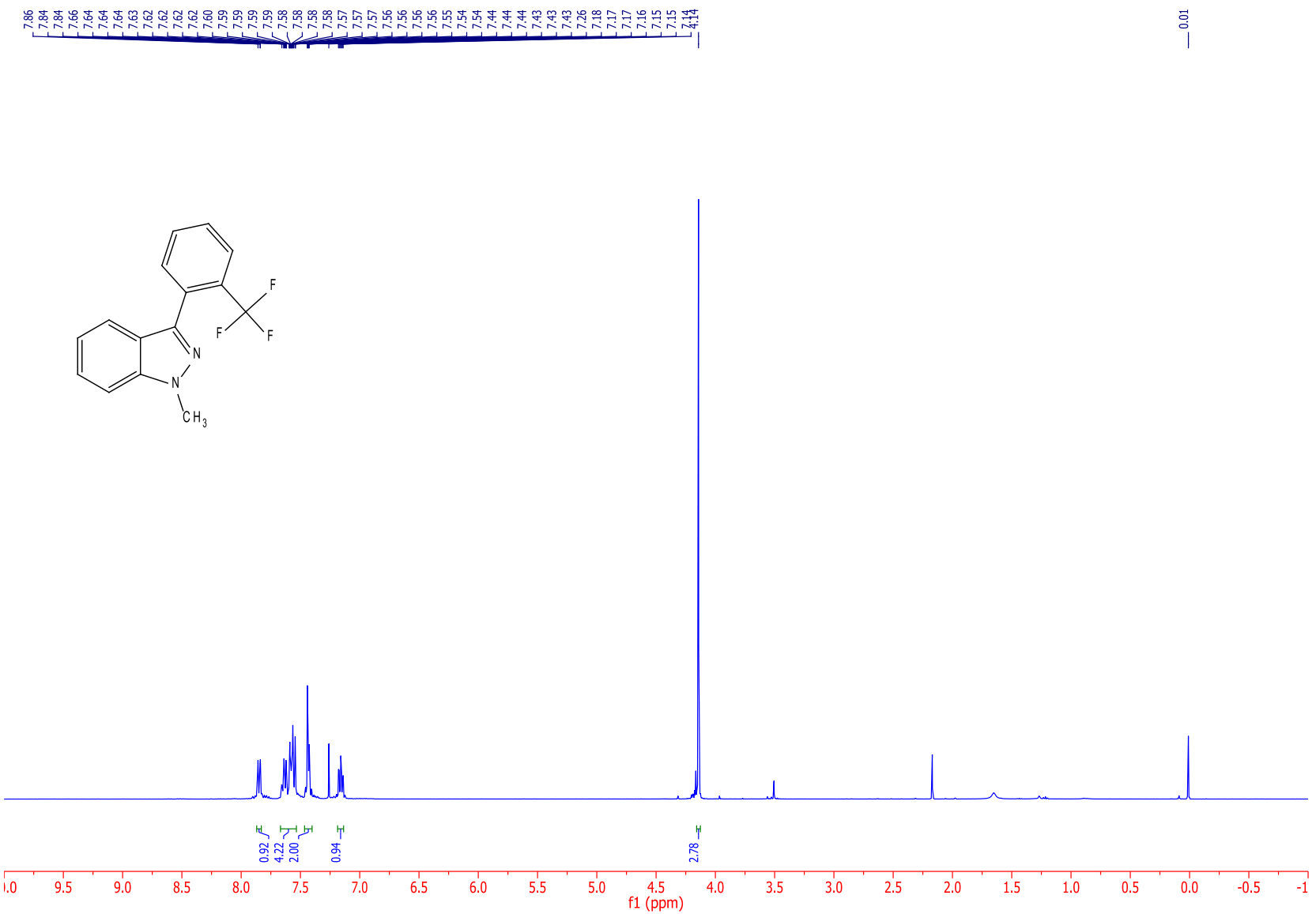
f1 (ppm)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F
F
N
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CH3
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2.78
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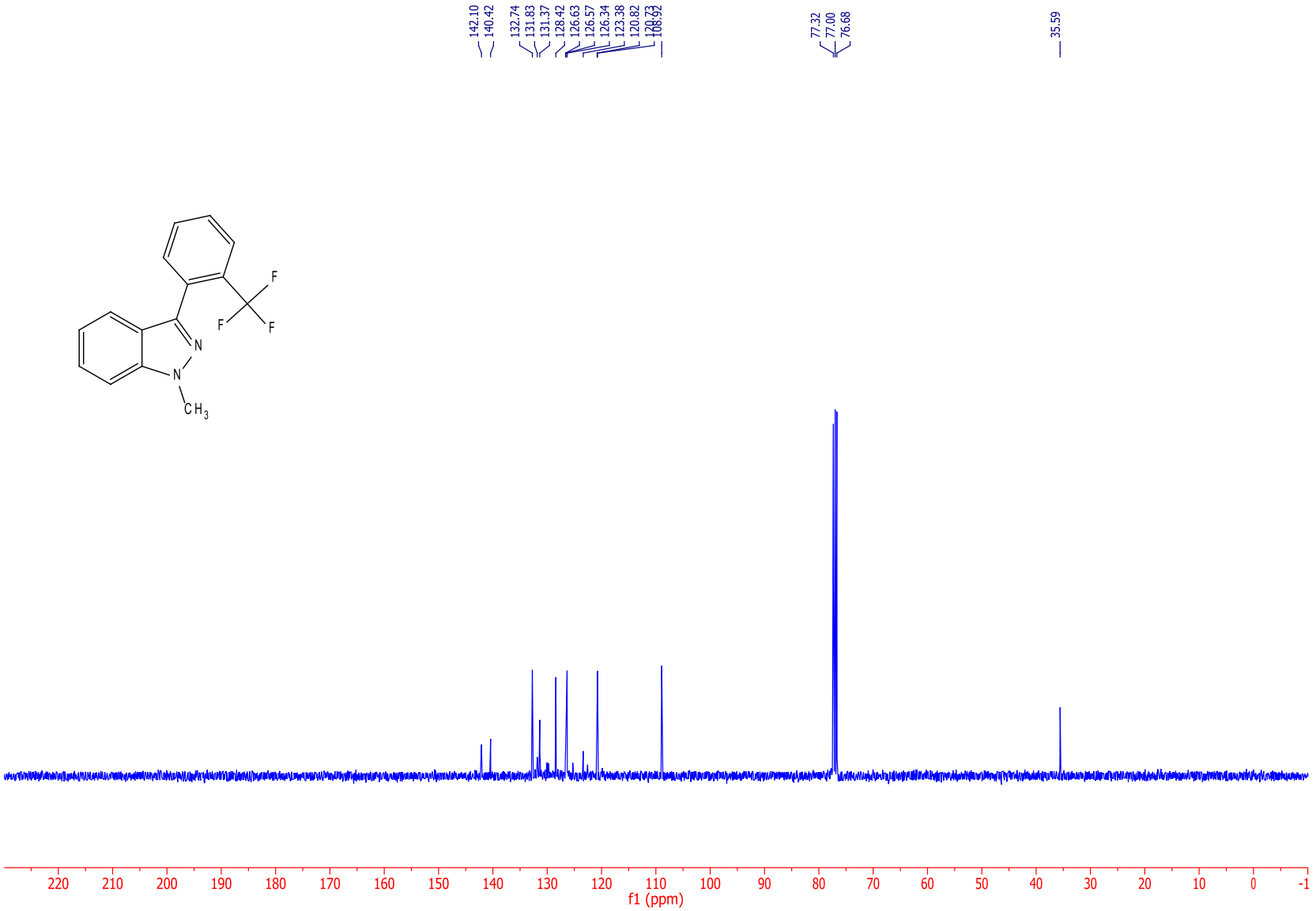
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70
60
50
40
30
20
10
0
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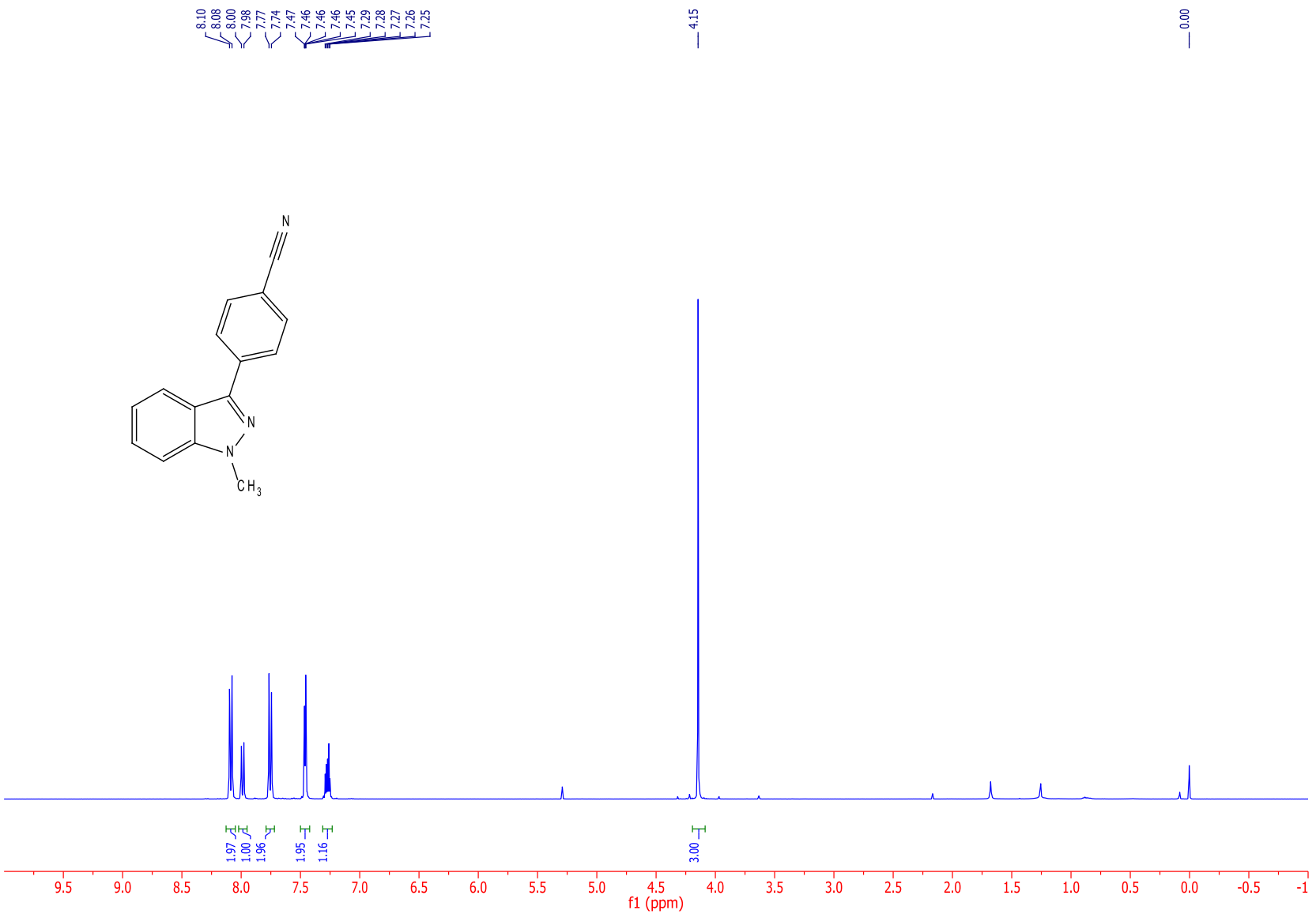
f1 (ppm)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7.25
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N
N
CH3
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1.00
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1.95
1.16
3.00
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6.0
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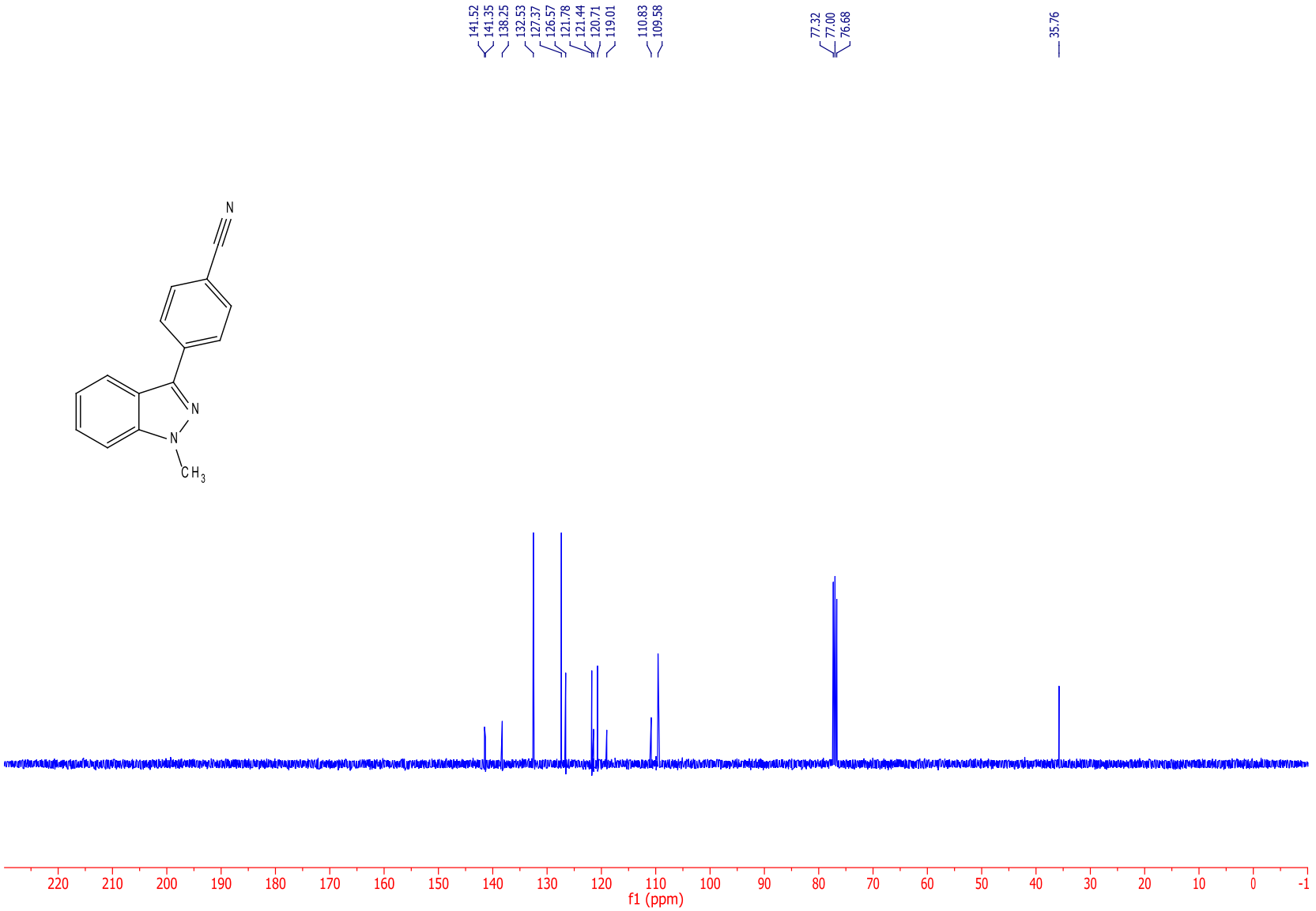
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180
170
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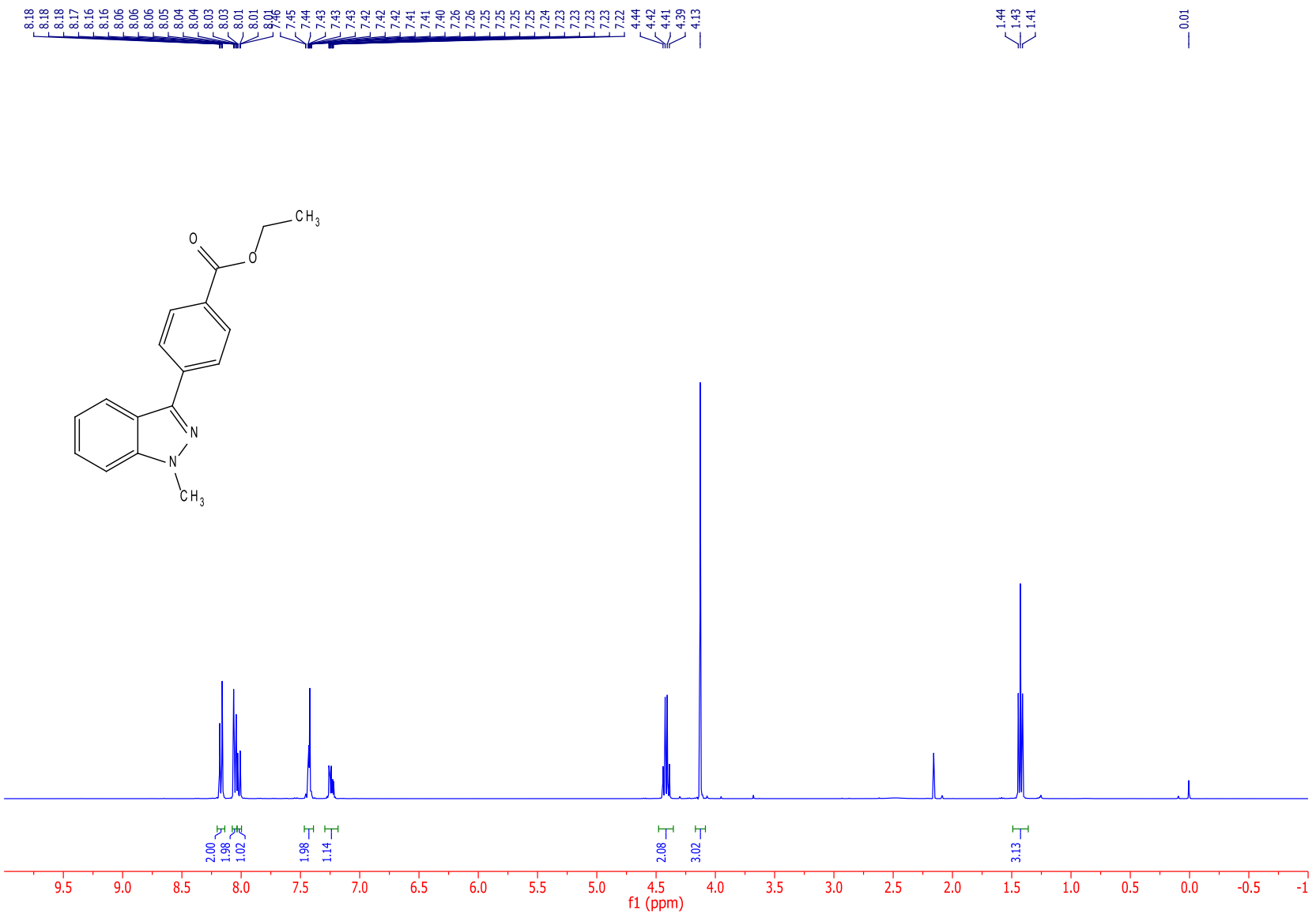
f1 (ppm)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1.44 1.43 1.41
0.01
O
O
CH3
N
N
CH3
2.00 1.98 1.02 1.98 1.14 2.08 3.02 3.13
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
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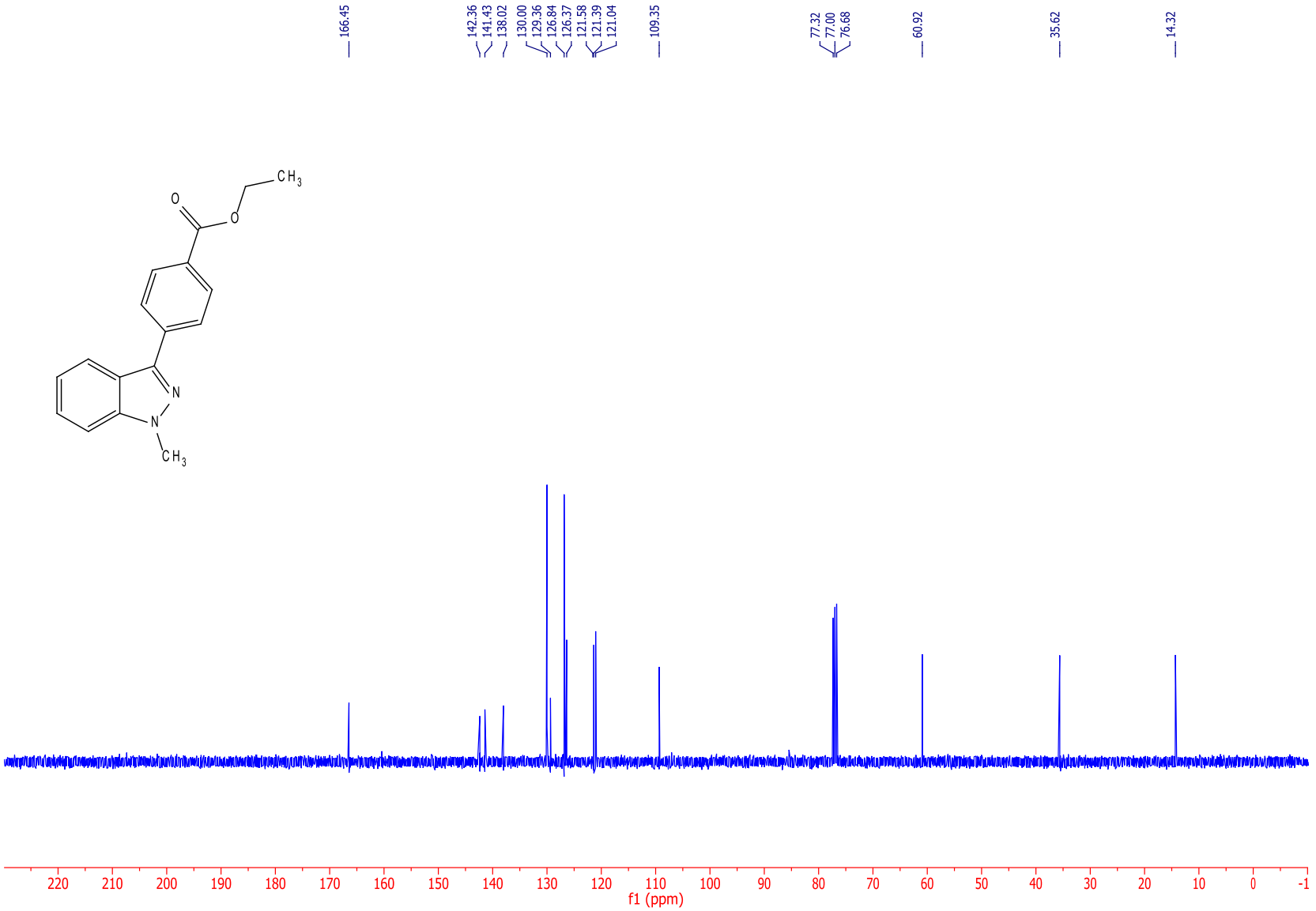
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O
CH3
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180
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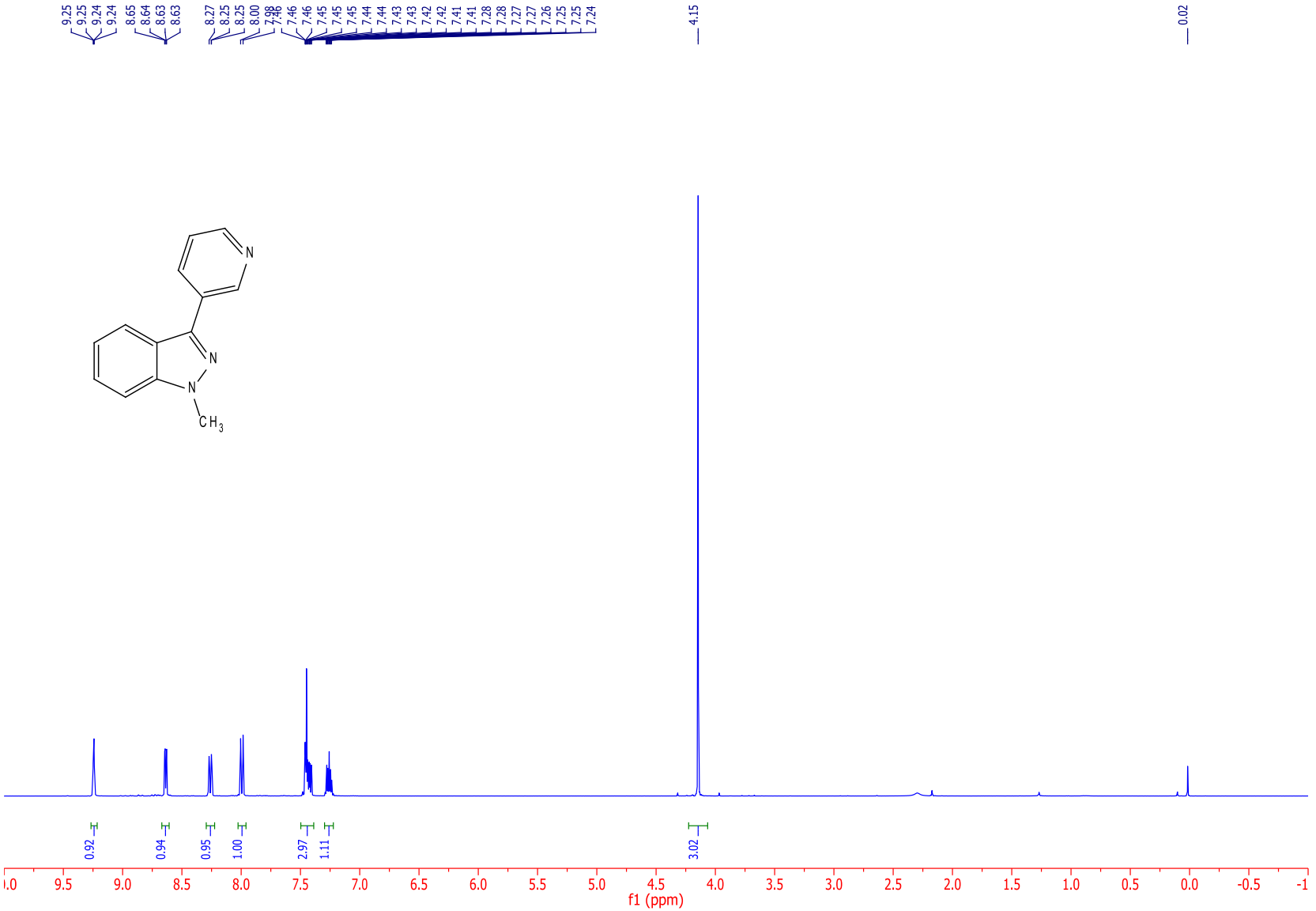
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7.27
7.26
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7.25
7.24
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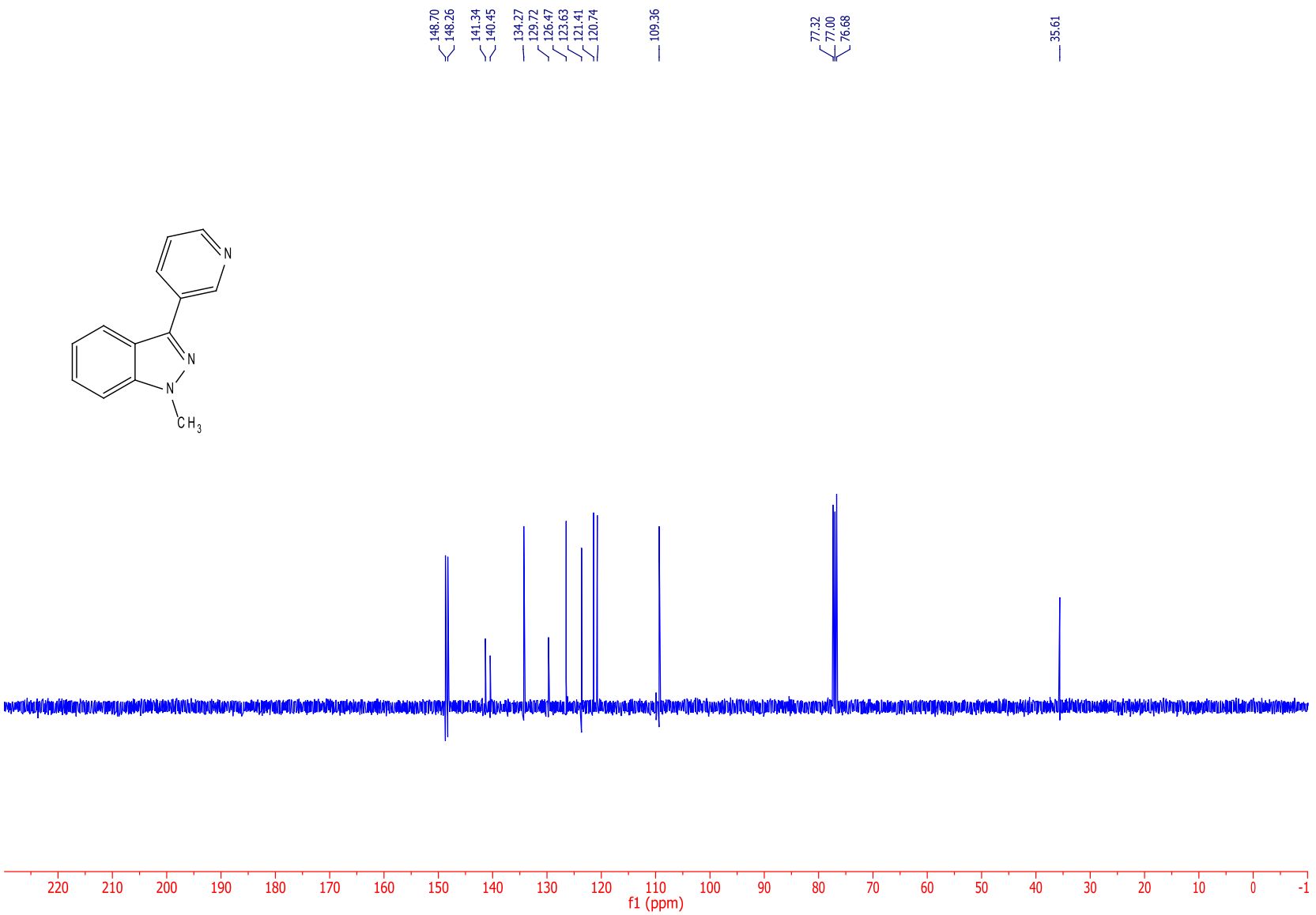
3.02
f1 (ppm)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77.00
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CH3
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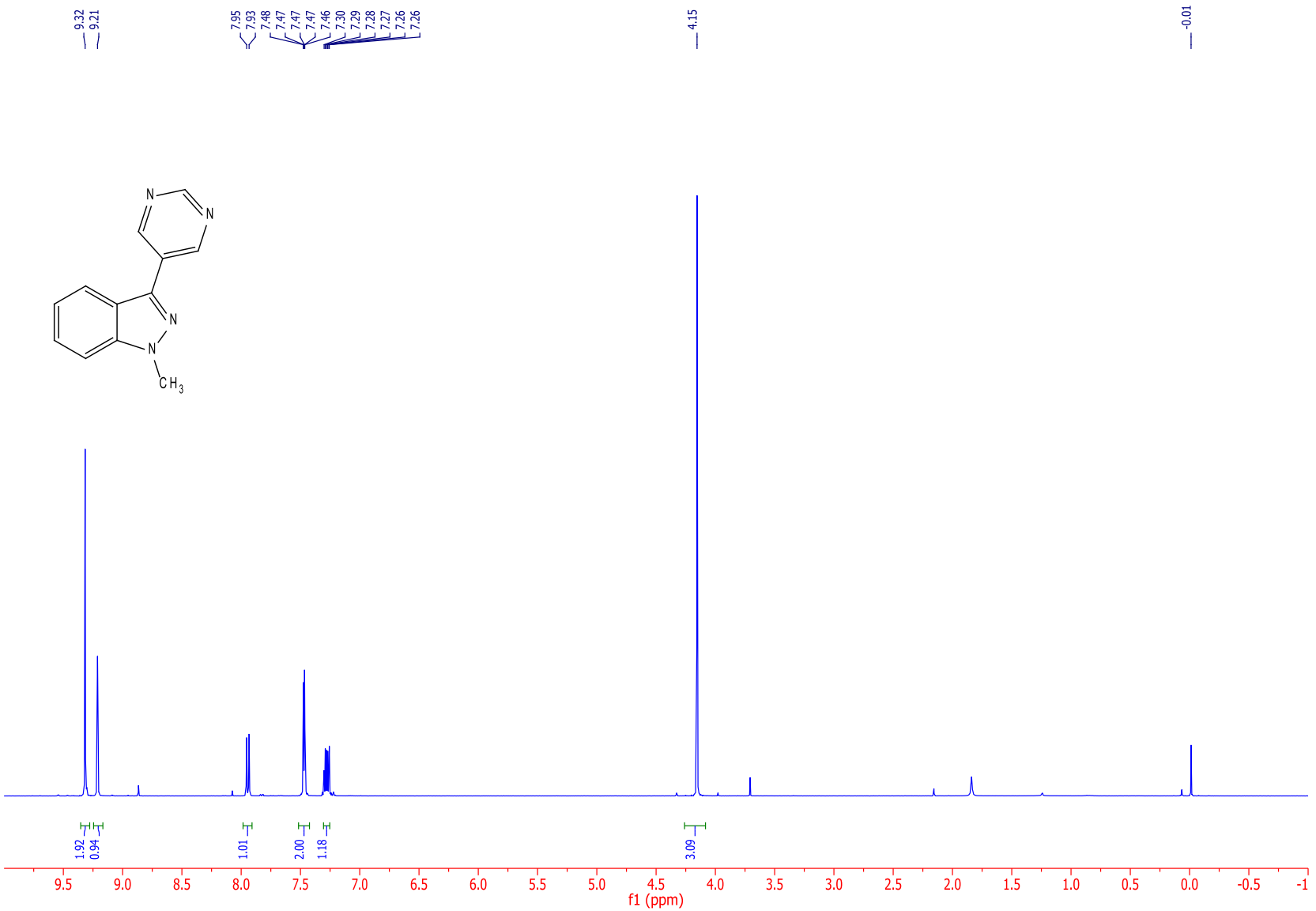
f1 (ppm)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7.27
7.26
7.26
4.15
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N
N
N
CH3
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2.00
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9.0
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8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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2.0
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0.0
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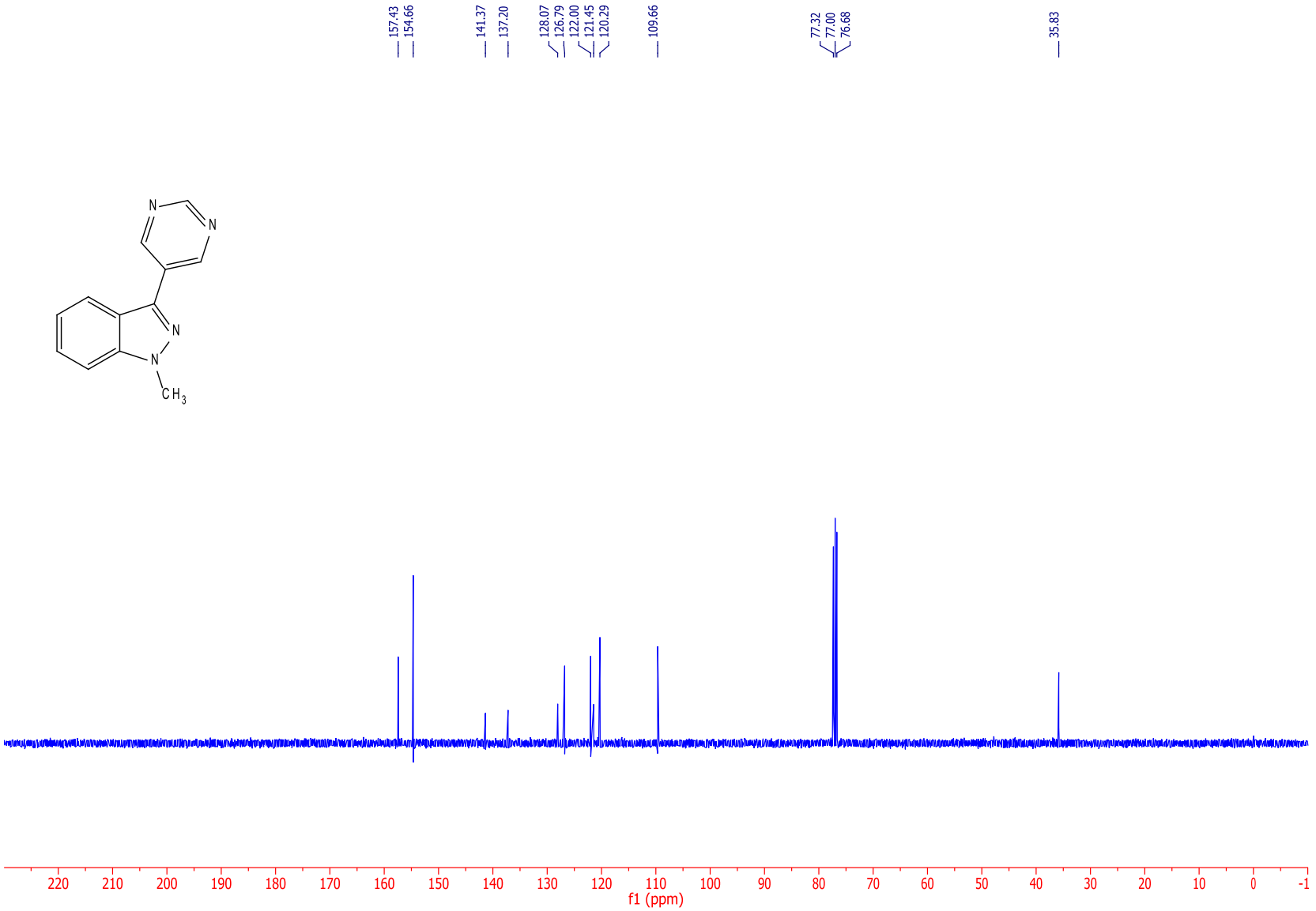
-1
f1 (ppm)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N
N
CH3
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200
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180
170
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100
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80
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30
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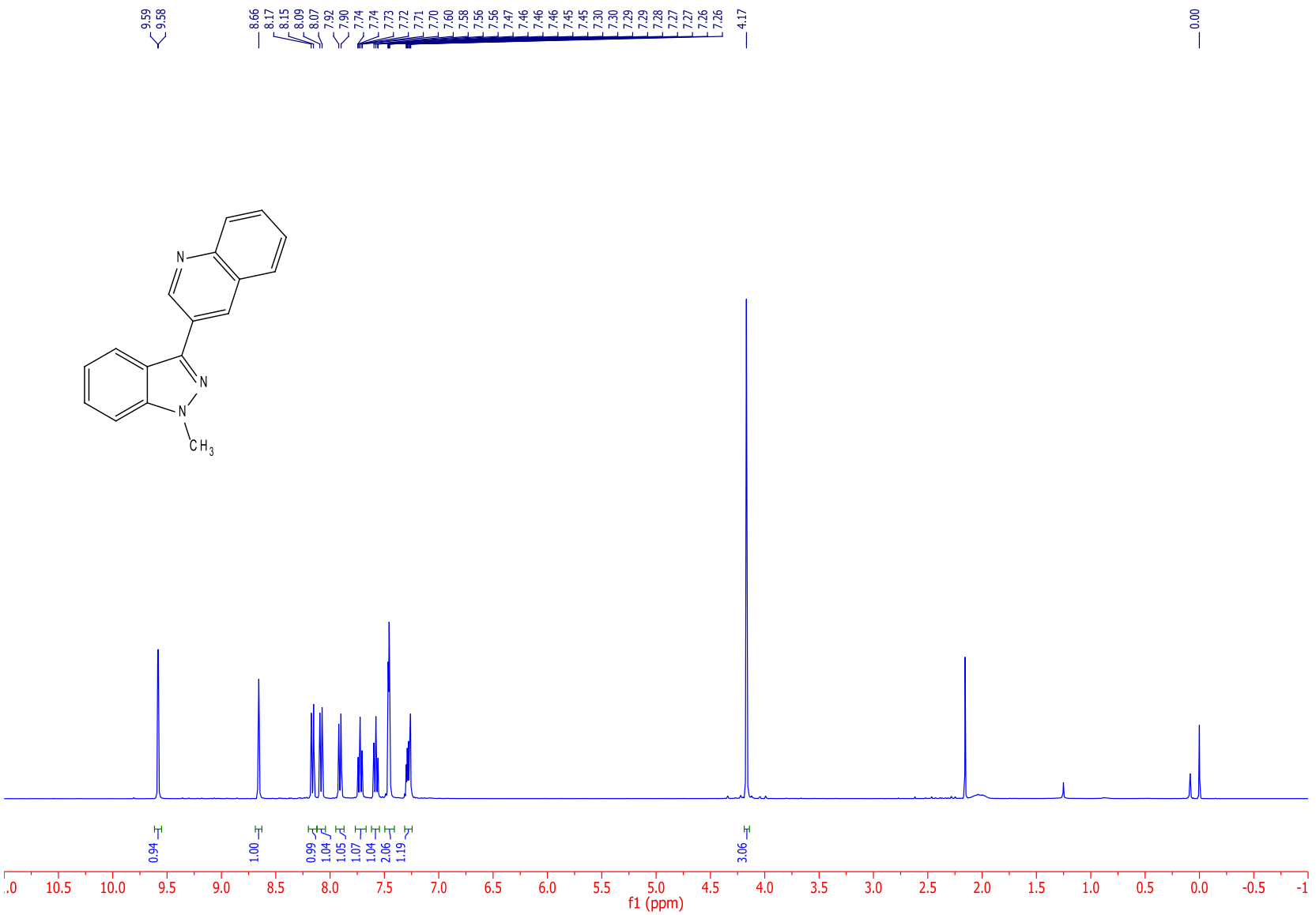
0
-1
f1 (ppm)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7.46
7.46
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7.29
7.29
7.28
7.27
7.27
7.26
7.26
4.17
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N
N
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1.05
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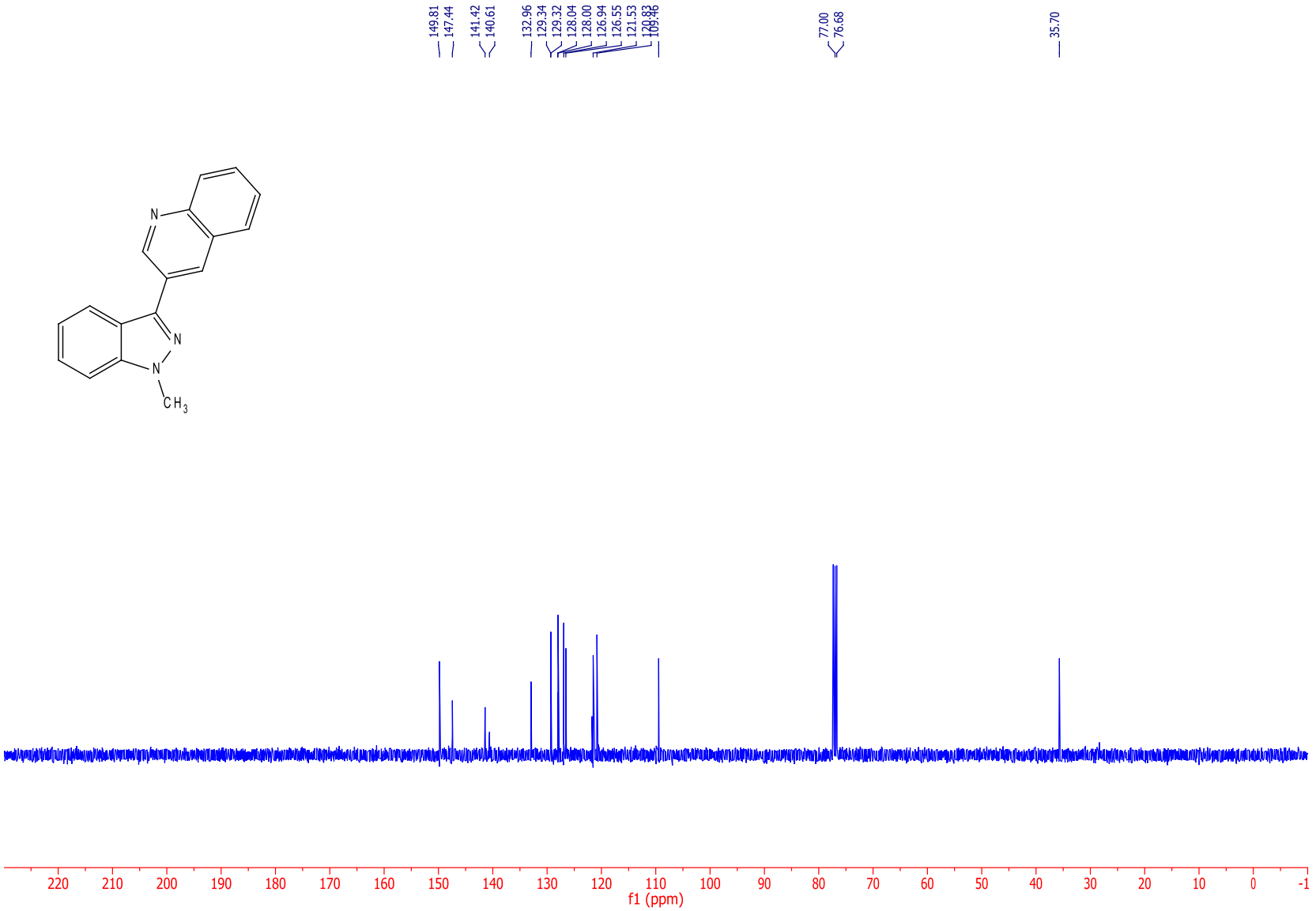
1.04
2.06
1.19
3.06
f1 (ppm)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76.68
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N
N
N
CH3
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210
200
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180
170
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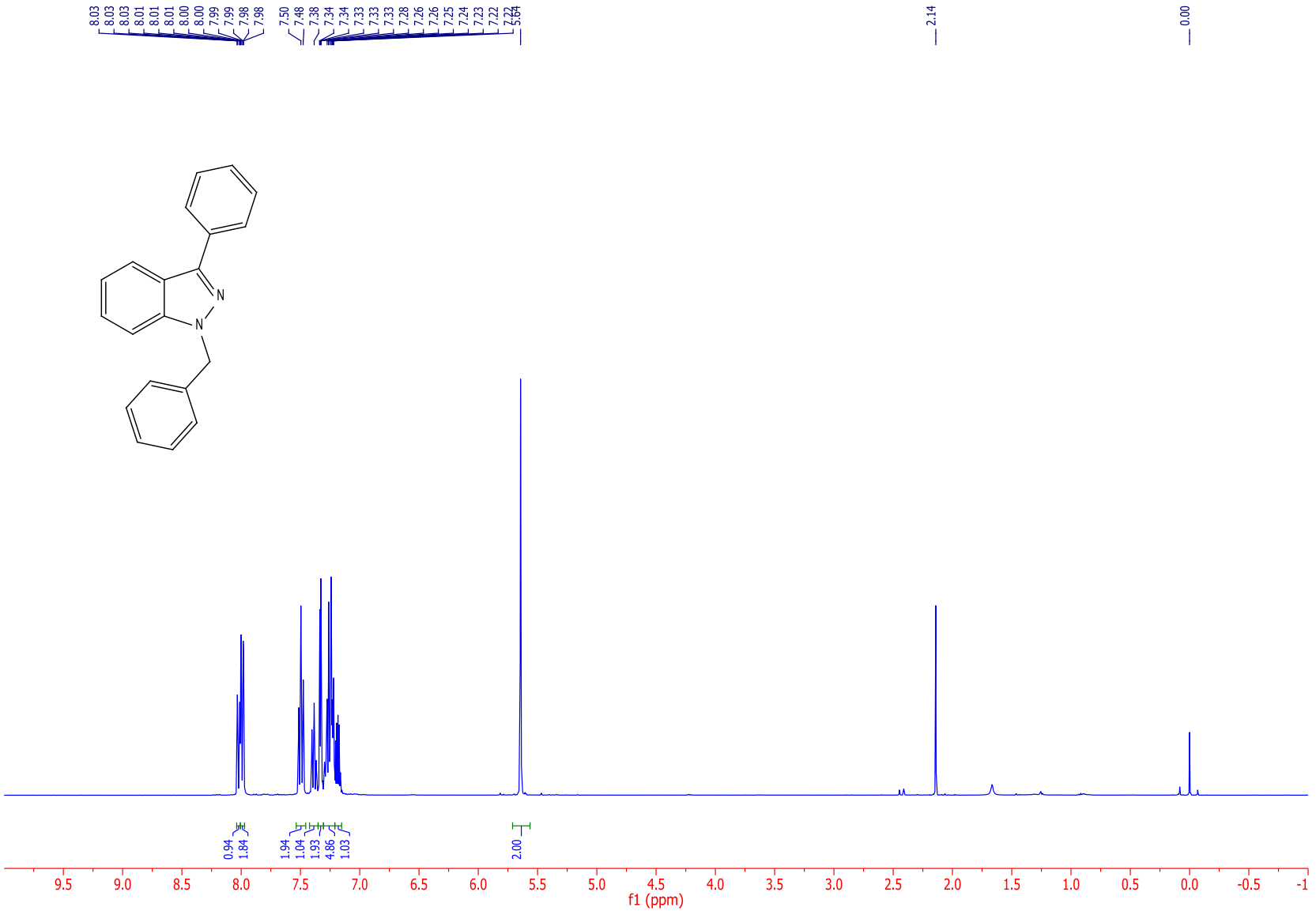
f1 (ppm)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7.26
7.25
7.24
7.23
7.22
7.22
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1.94
1.04
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4.86
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2.00
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7.5
7.0
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6.0
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5.0
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1.5
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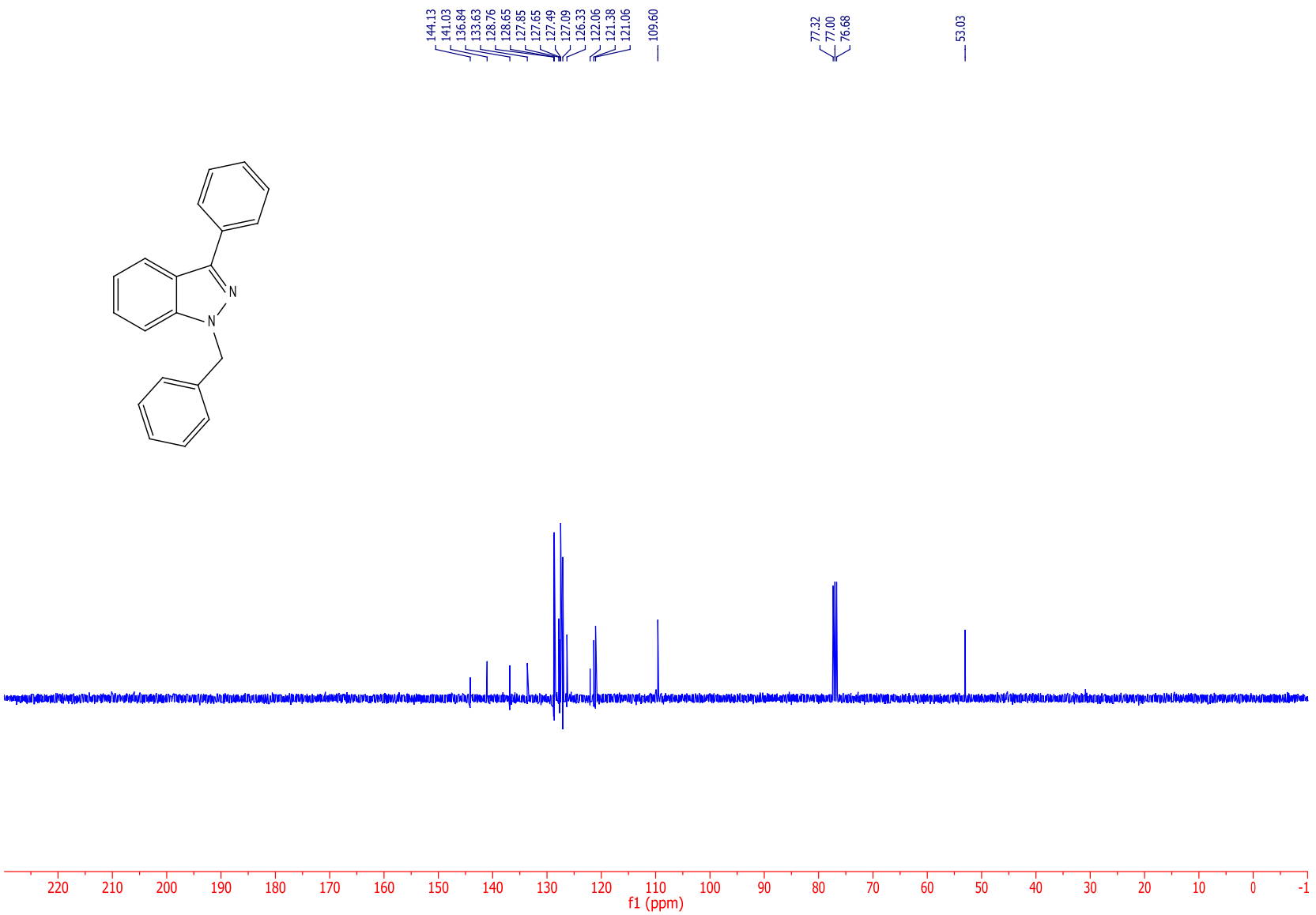
f1 (ppm)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200
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180
170
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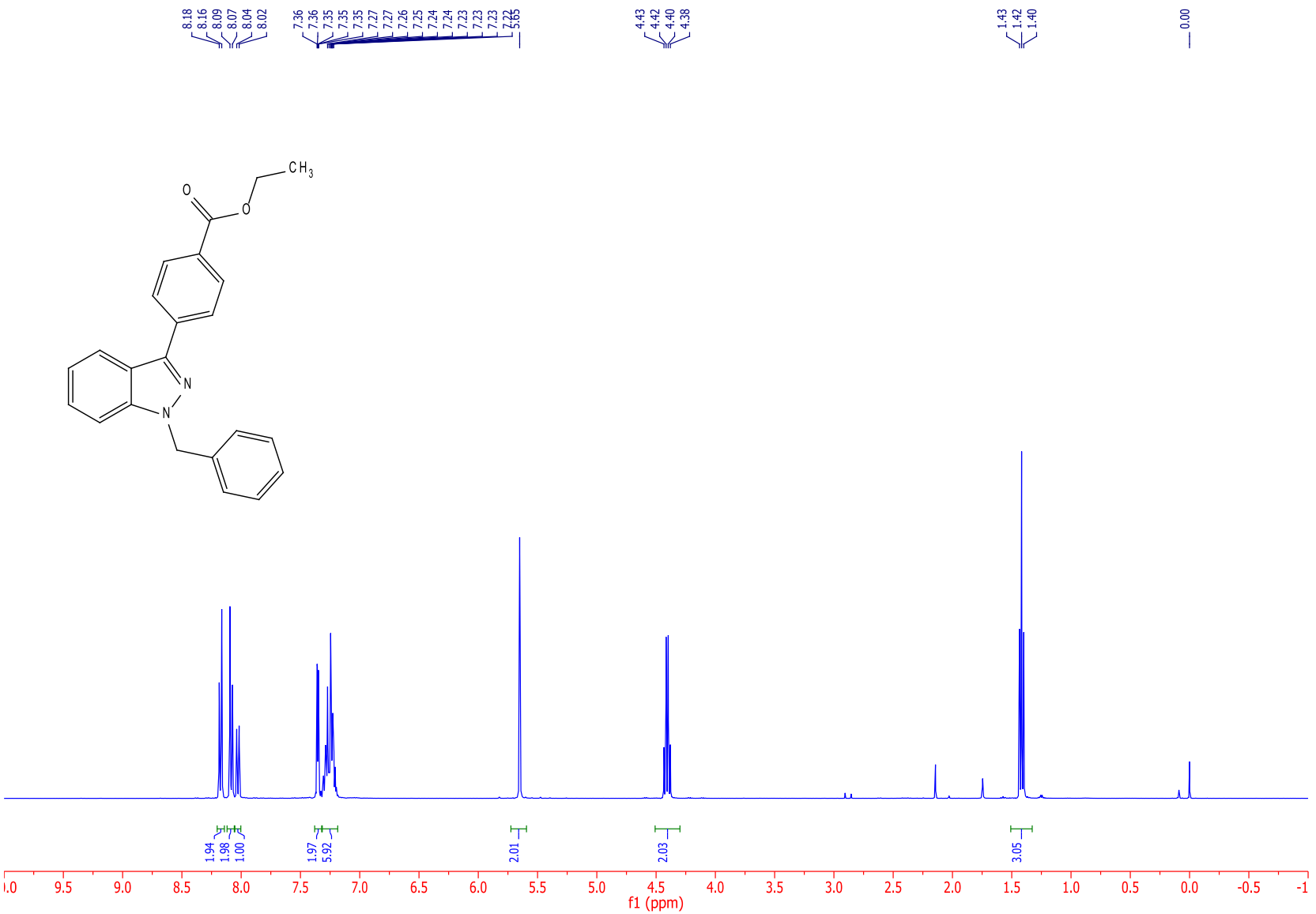
f1 (ppm)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7.23
7.23
7.23
7.22
5.65
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4.42
4.40
4.38
1.43
1.42
1.40
0.00
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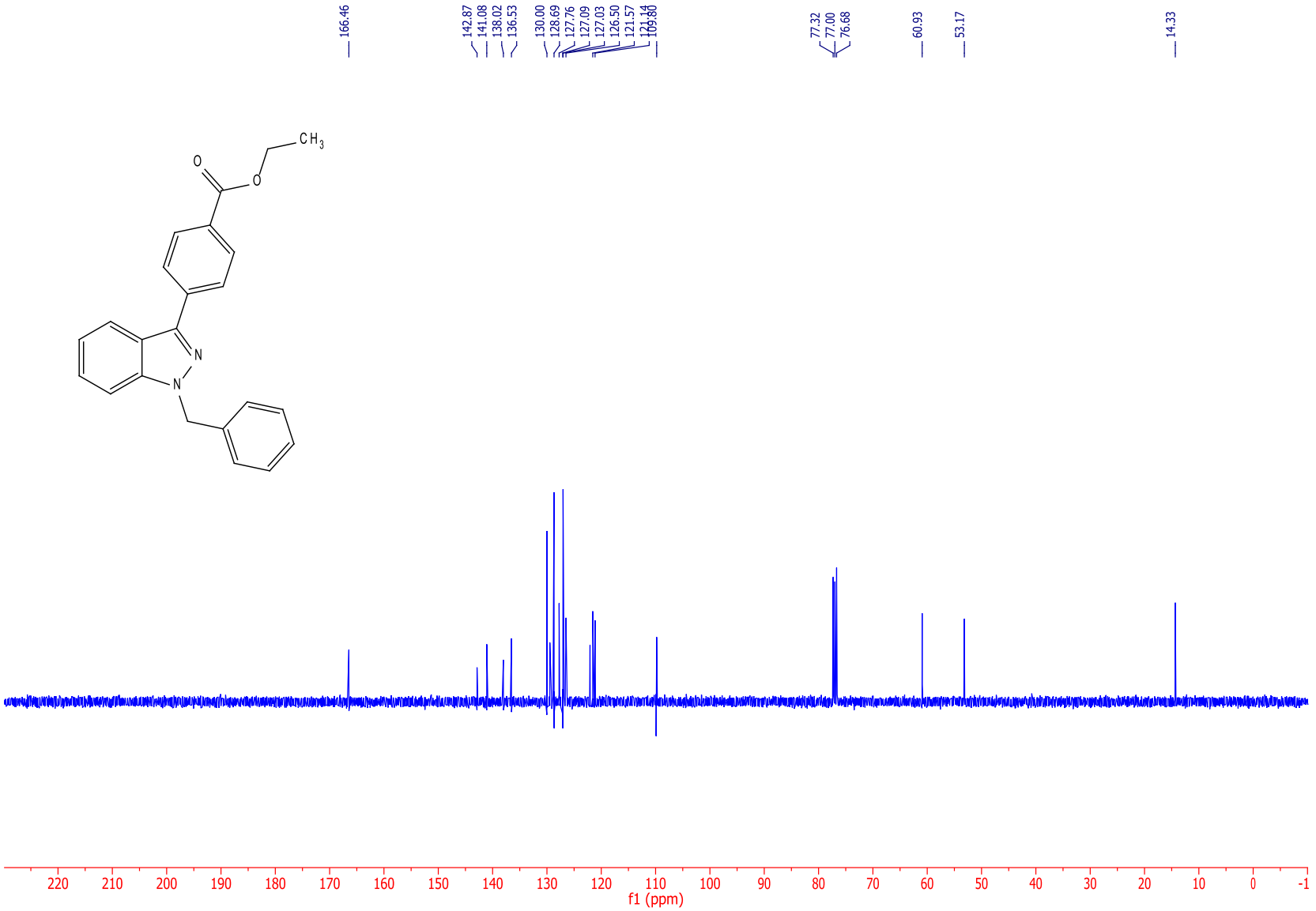
1.00
1.97
5.92
2.01
2.03
3.05
f1 (ppm)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77.00
76.68
60.93
53.17
14.33
CH3
O
O
N
N
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210
200
190
180
170
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100
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80
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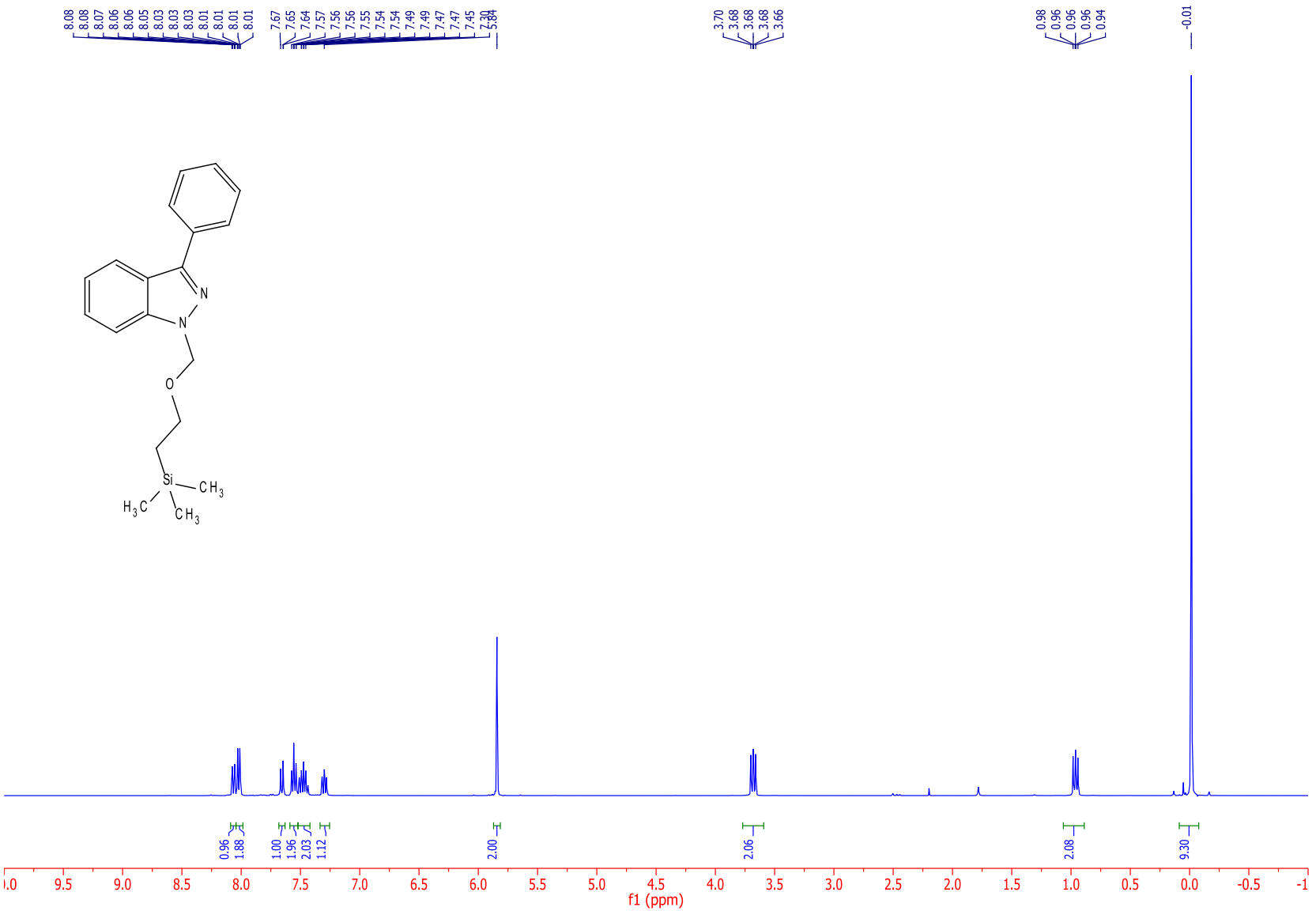
40
30
20
10
0
-1
f1 (ppm)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8.03
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8.01
8.01
8.01
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7.55
7.54
7.54
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7.45
7.39
7.38
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0.94
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CH3
H3C
CH3
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1.96
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1.12
2.00
2.06
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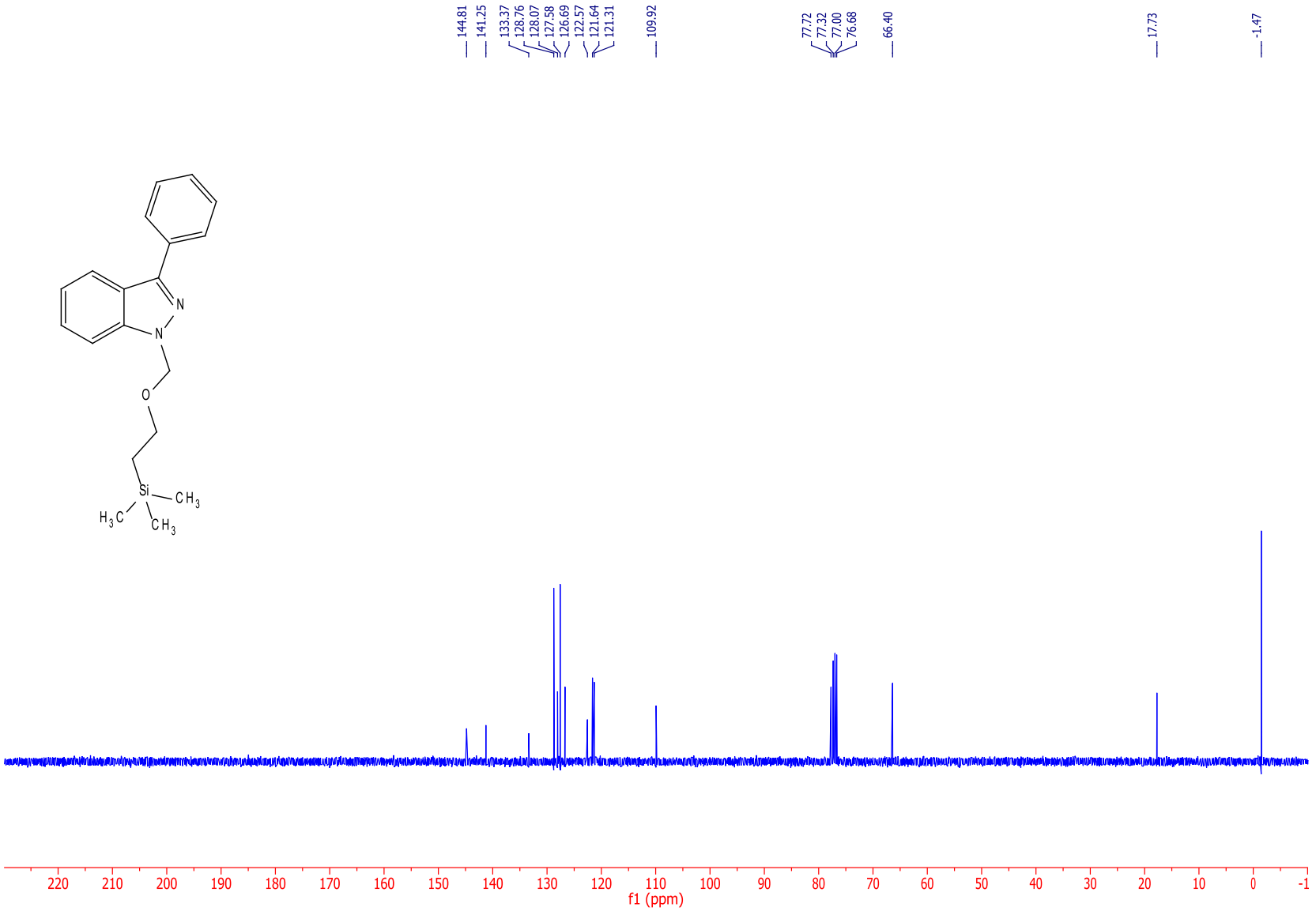
9.30
f1 (ppm)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O
Si
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H3C
CH3
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210
200
190
180
170
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100
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80
70
60
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40
30
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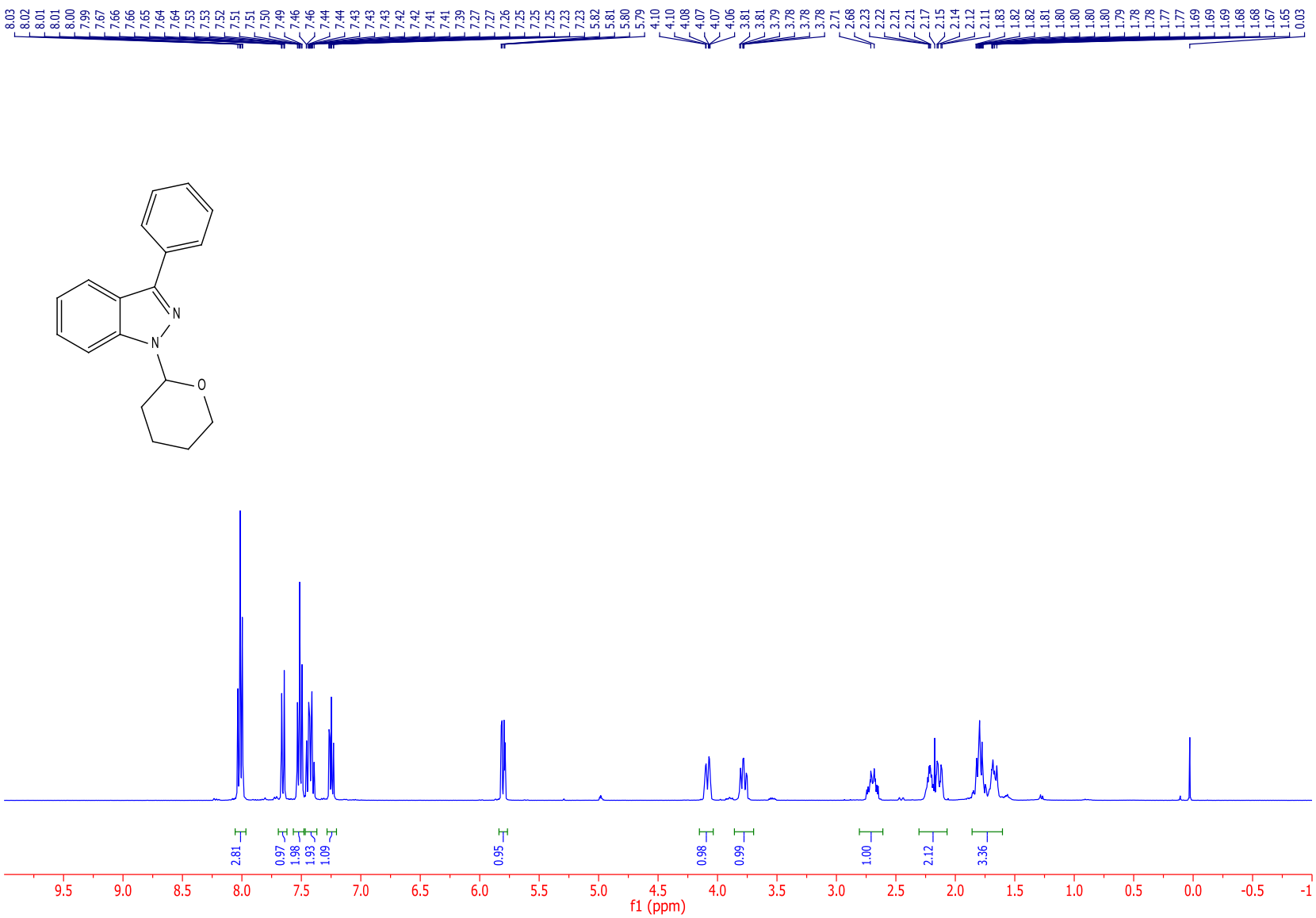
-1
f1 (ppm)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N
O
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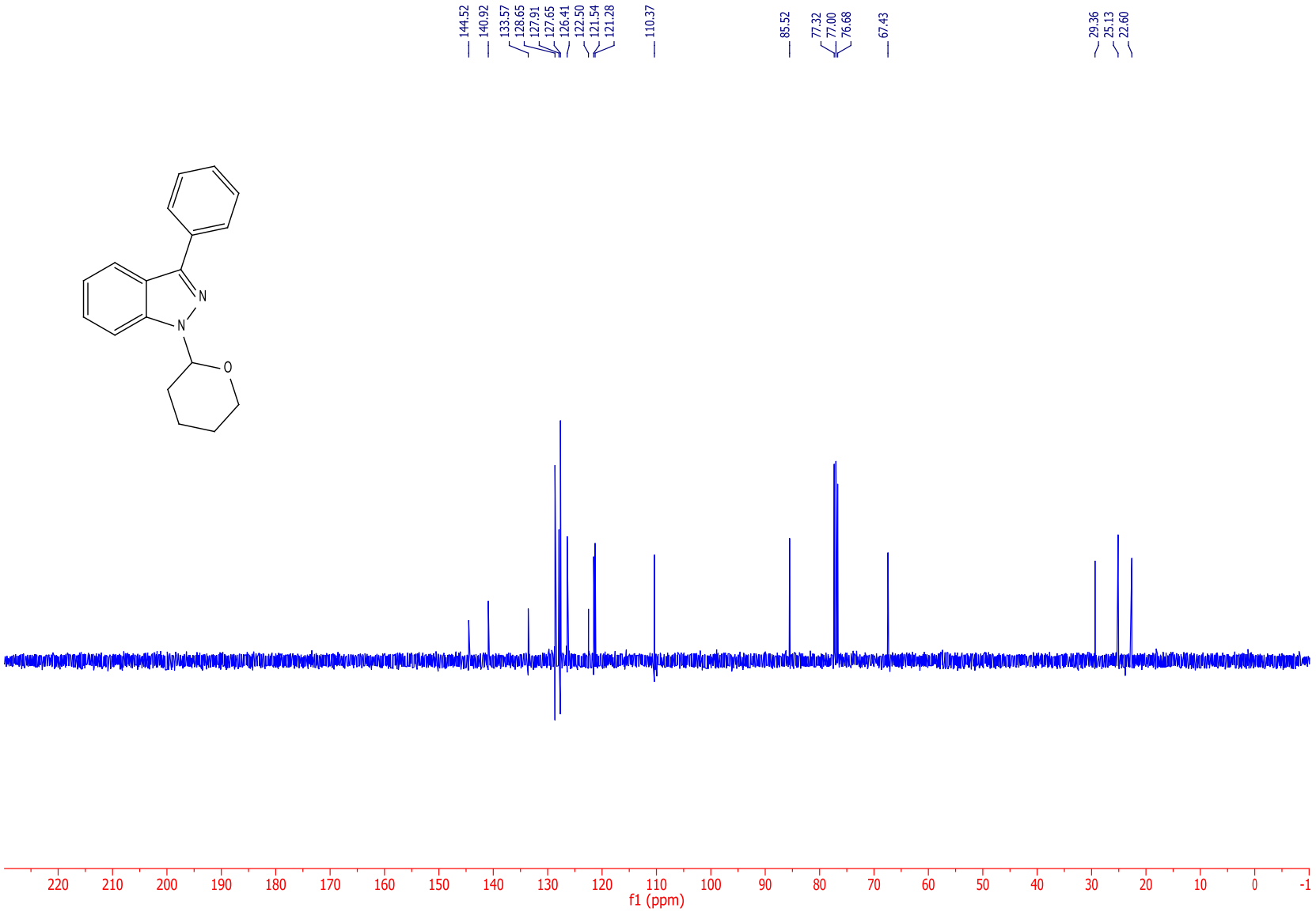
0.97
1.98
1.93
1.09
0.95
0.98
0.99
1.00
2.12
3.36
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1
f1 (ppm)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25.13
22.60
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O
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200
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180
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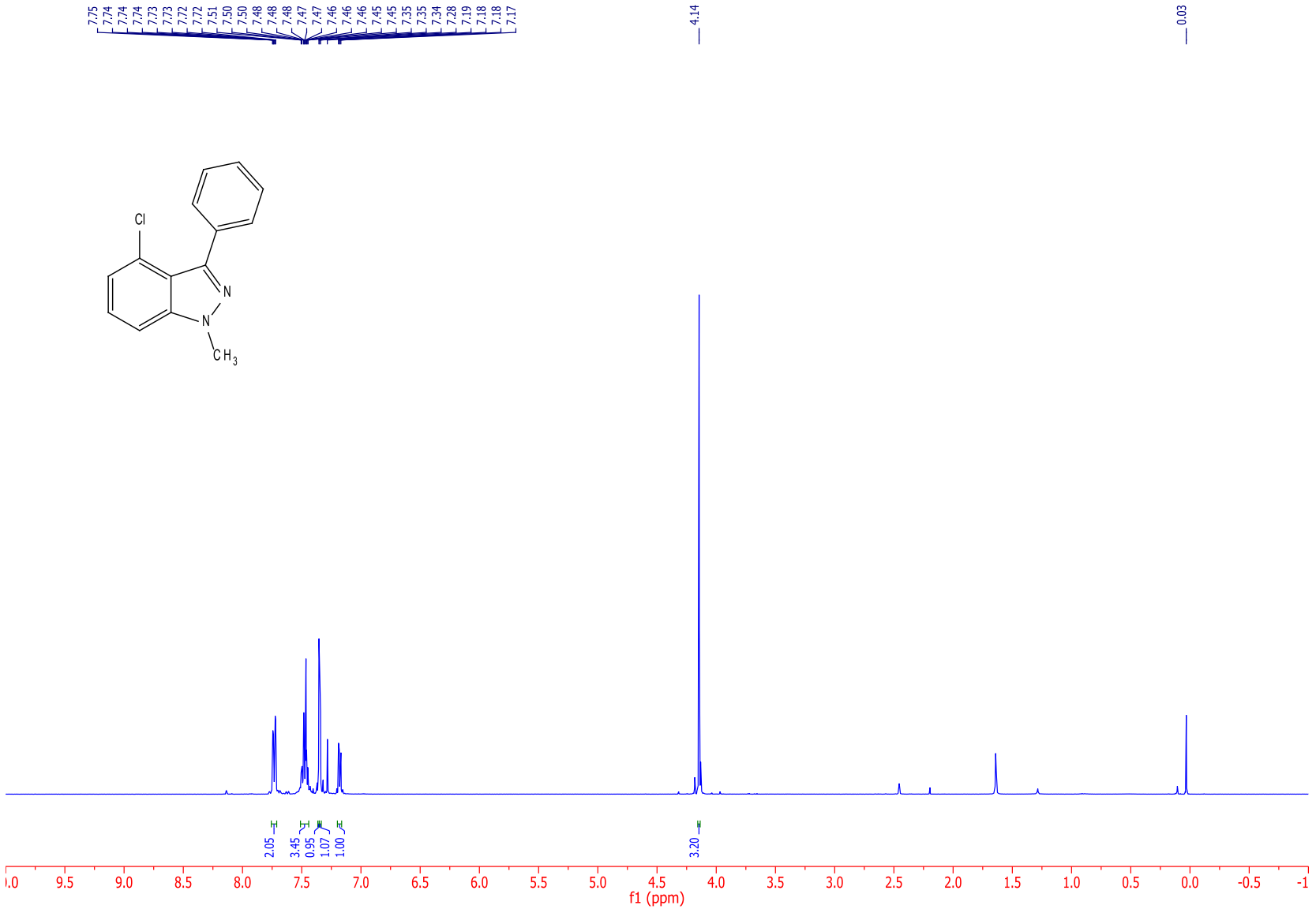
-1
f1 (ppm)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7.46
7.45
7.45
7.35
7.35
7.34
7.28
7.19
7.18
7.18
7.17
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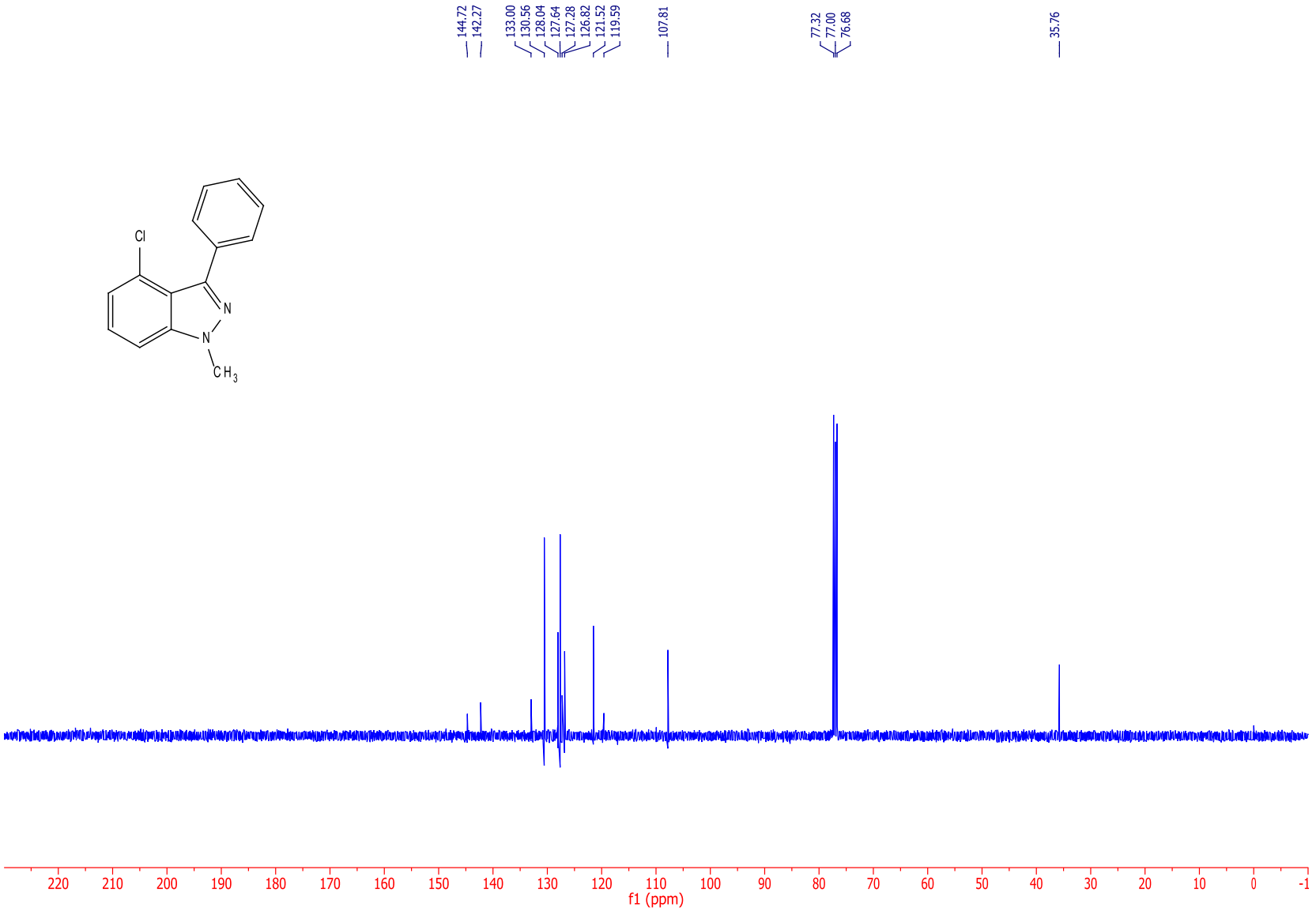
1.07
1.00
3.20
f1 (ppm)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200
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100
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80
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40
30
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0
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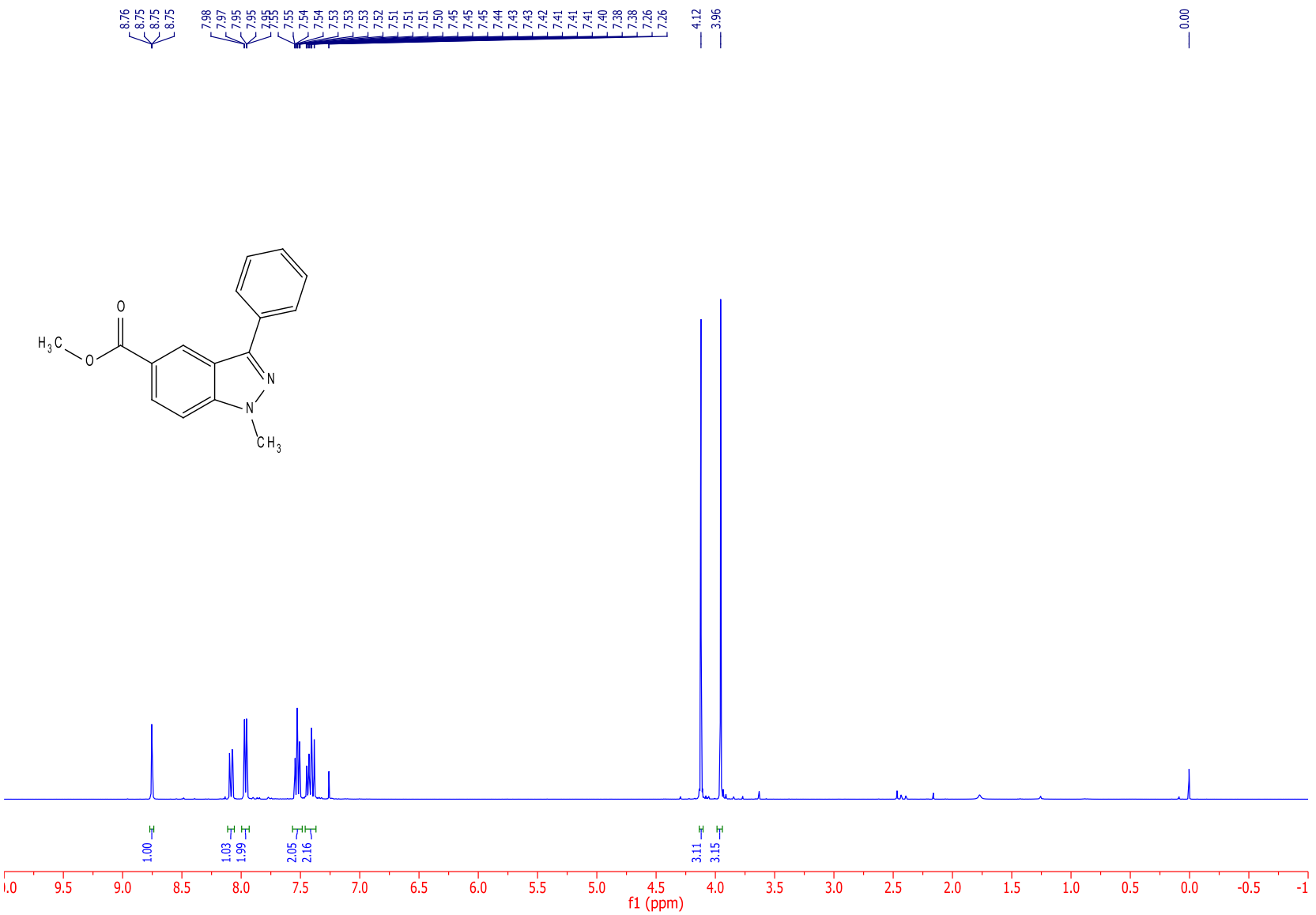
f1 (ppm)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7.41
7.40
7.38
7.26
7.26
4.12
3.96
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CH3
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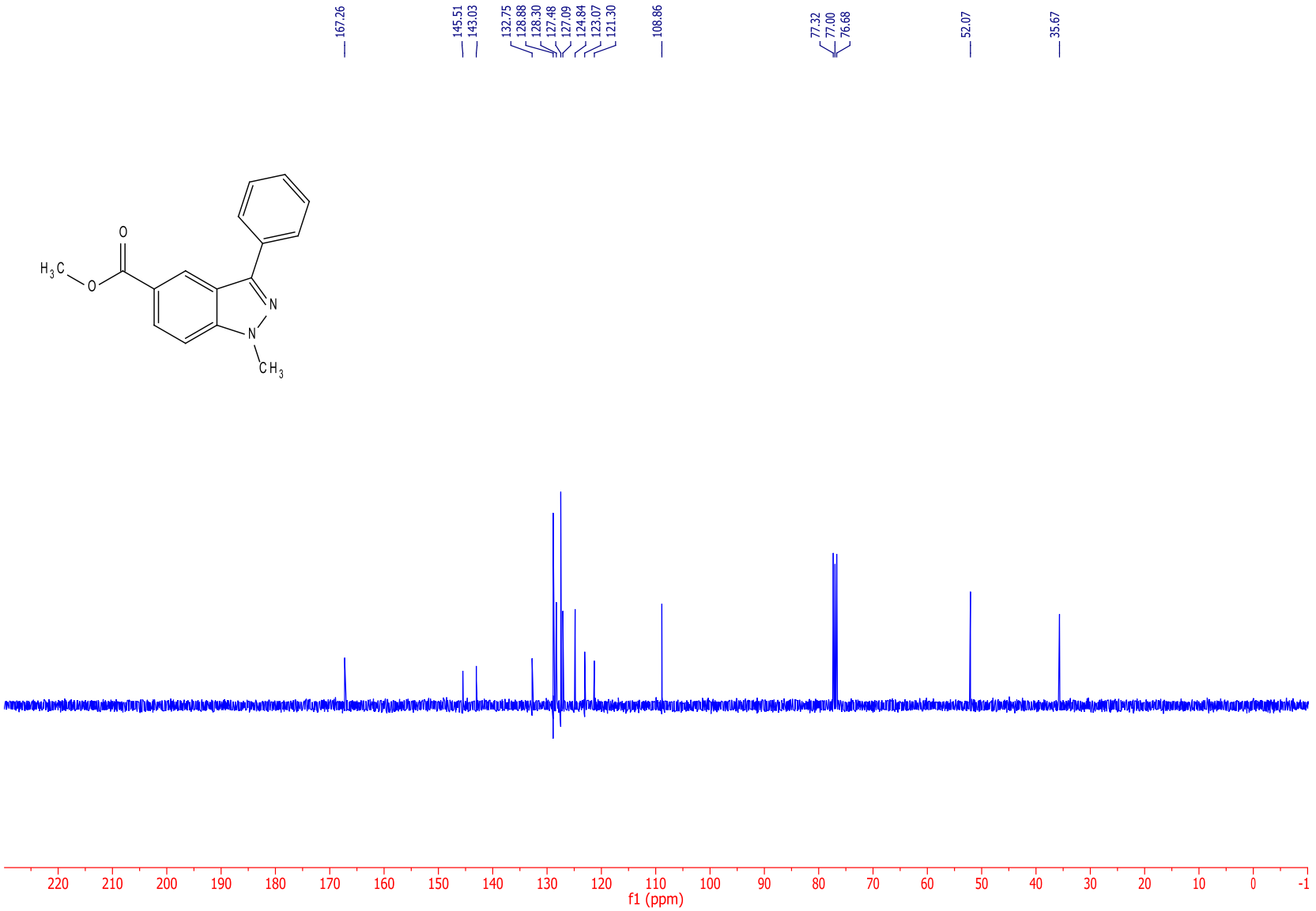
2.16
3.11
3.15
f1 (ppm)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35.67
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180
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80
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30
20
10
0
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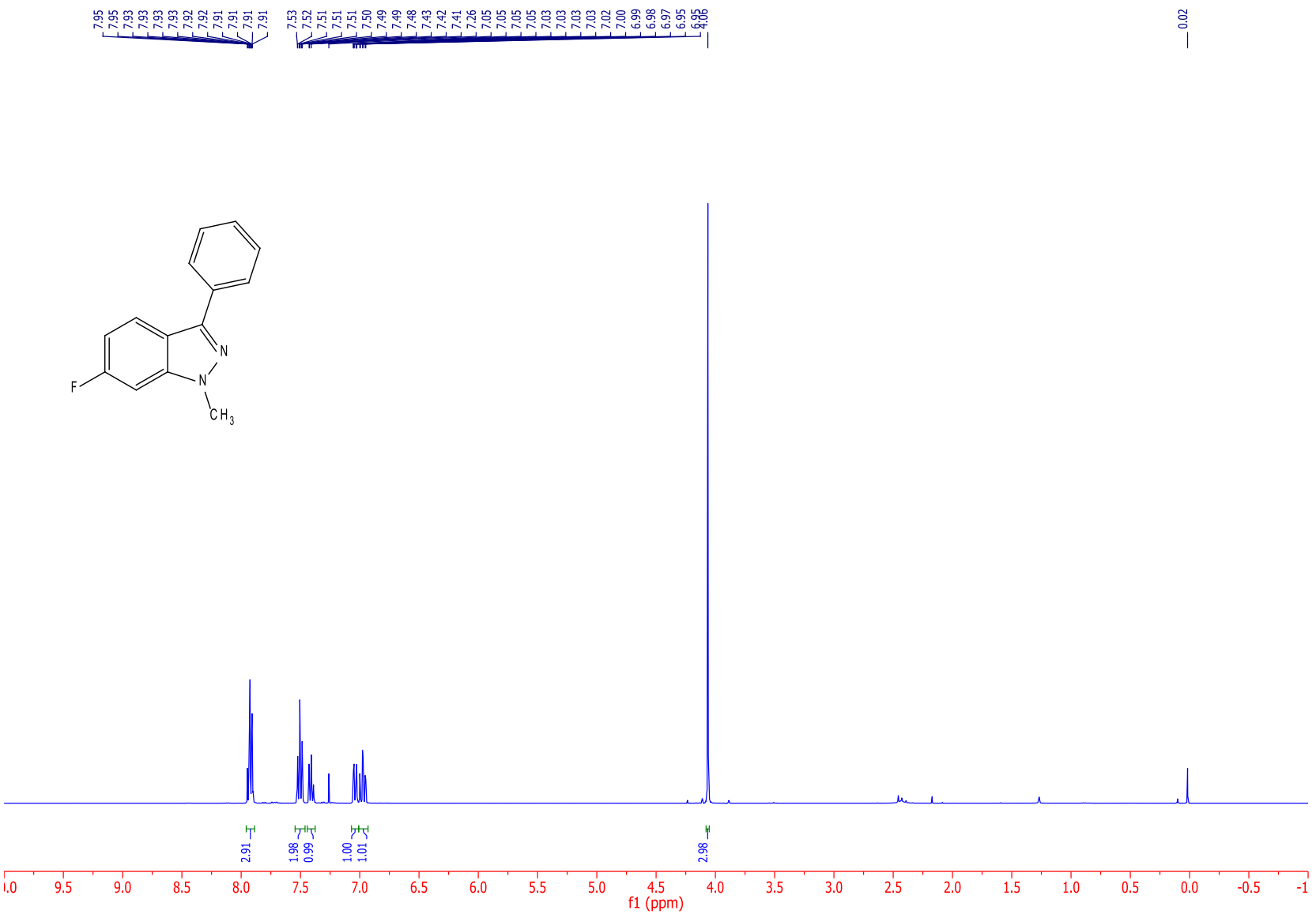
f1 (ppm)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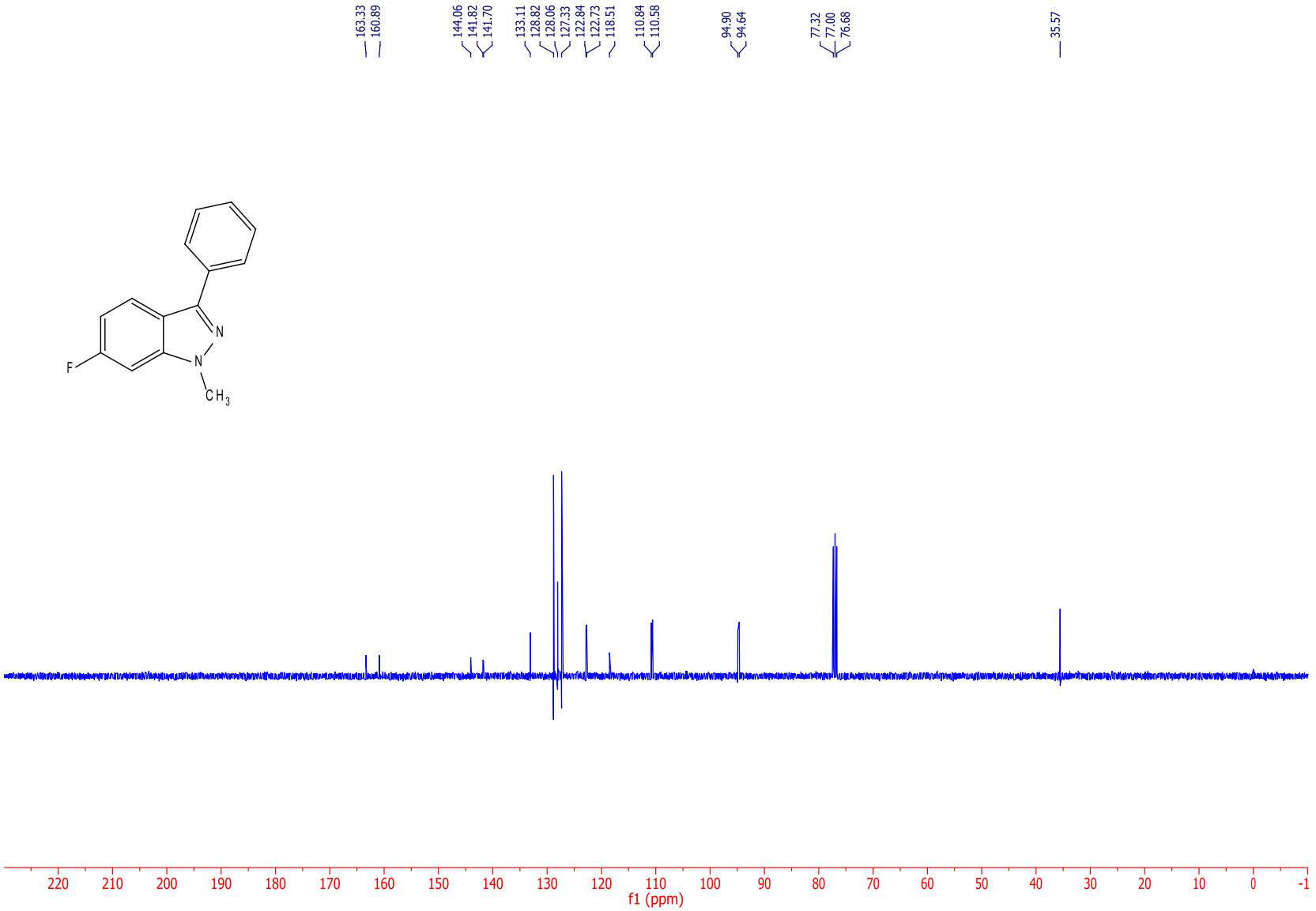
2.98
f1 (ppm)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122.84
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110.84
110.58
94.90
94.64
77.32
77.00
76.68
35.57
F
N
N
CH3
220
210
200
190
180
170
160
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30
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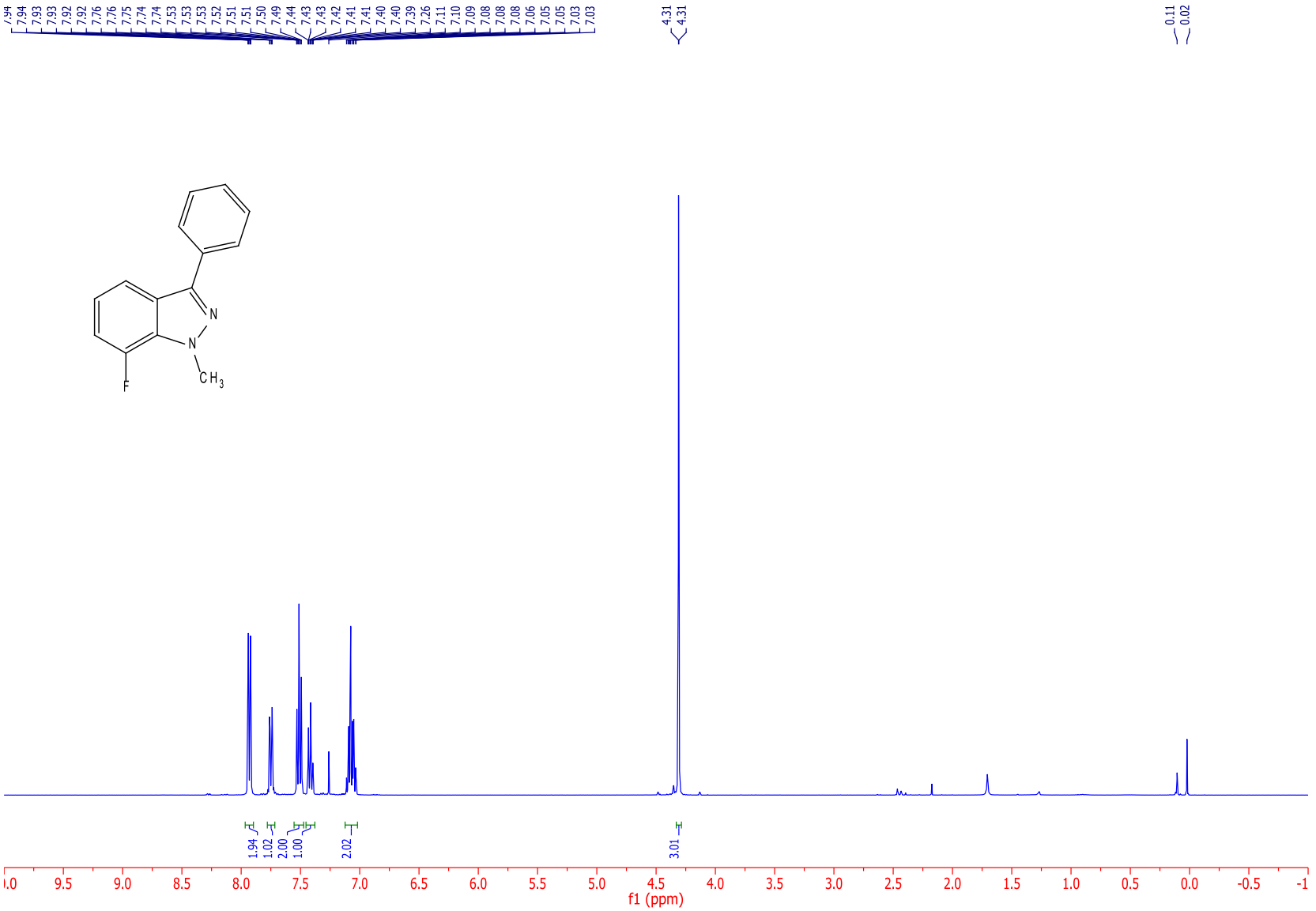
f1 (ppm)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7.94
7.93
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7.76
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7.74
7.74
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7.53
7.52
7.51
7.51
7.50
7.49
7.44
7.43
7.43
7.42
7.41
7.41
7.40
7.40
7.39
7.26
7.11
7.10
7.09
7.08
7.08
7.08
7.06
7.05
7.05
7.03
7.03
4.31
4.31
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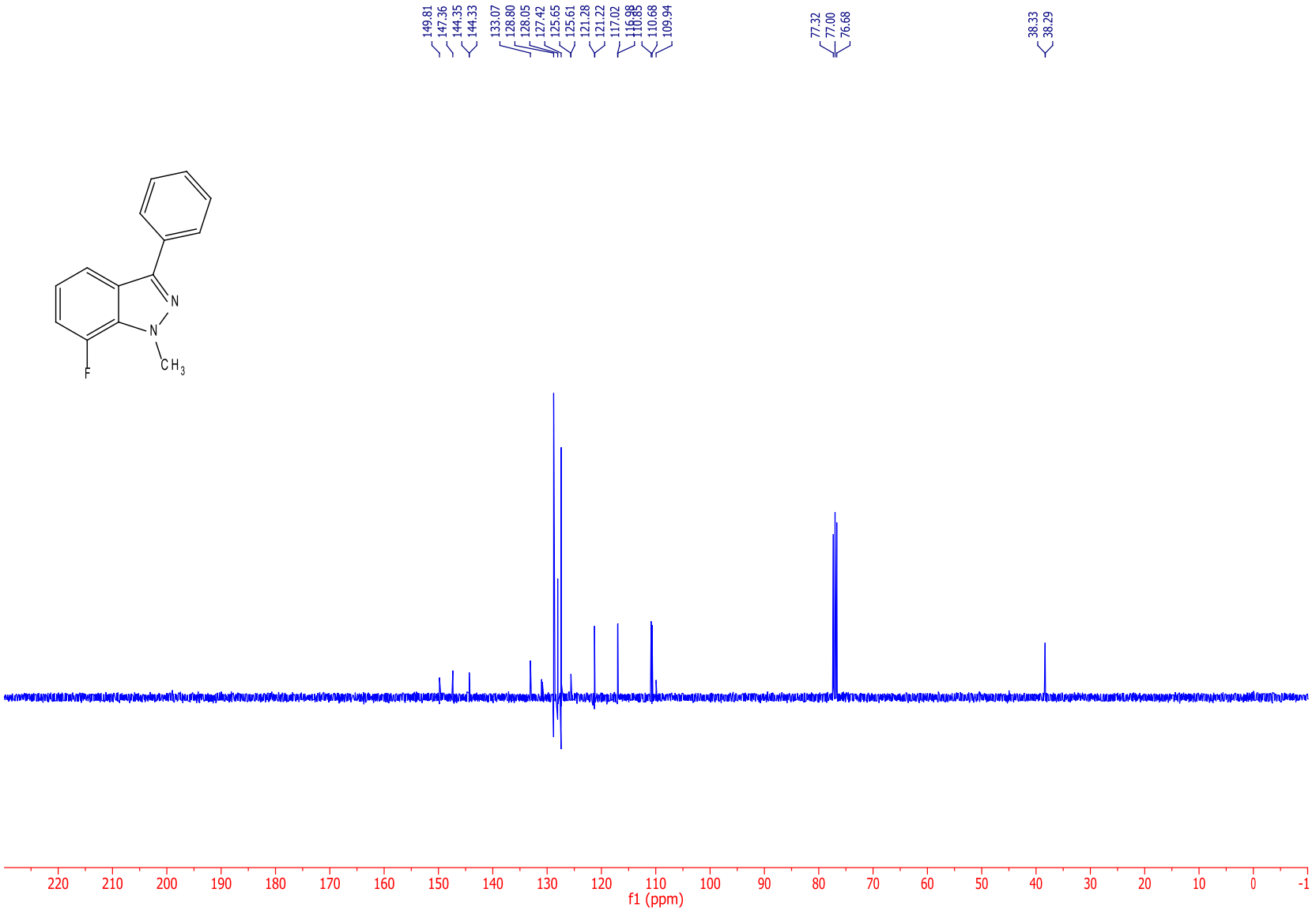
N
CH3
F
1.94
1.02
2.00
1.00
2.02
3.01
f1 (ppm)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125.61
121.28
121.22
117.02
110.68
109.94
77.32
77.00
76.68
38.33
38.29
N
N
CH3
F
220
210
200
190
180
170
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100
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80
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30
20
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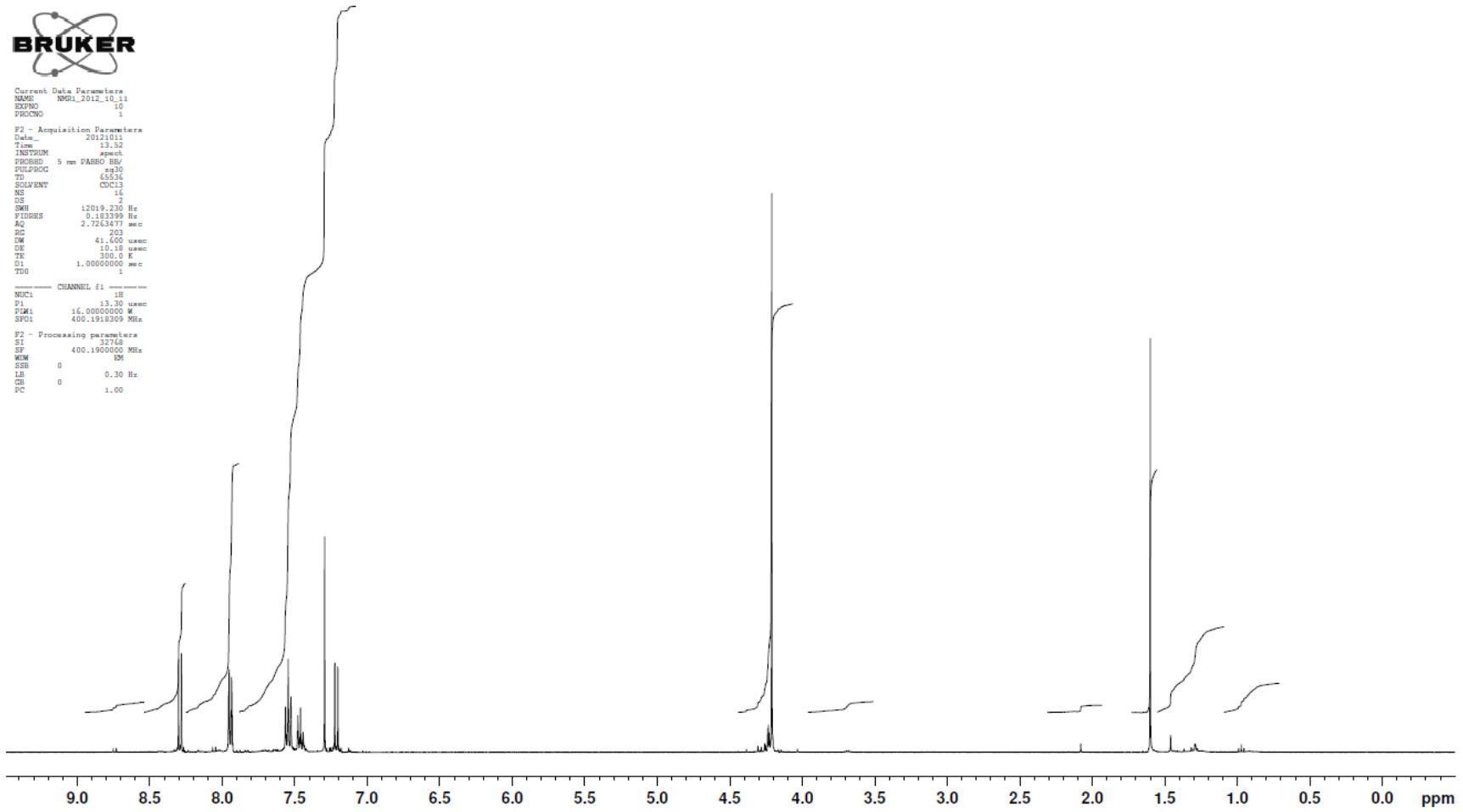
0
-1
f1 (ppm)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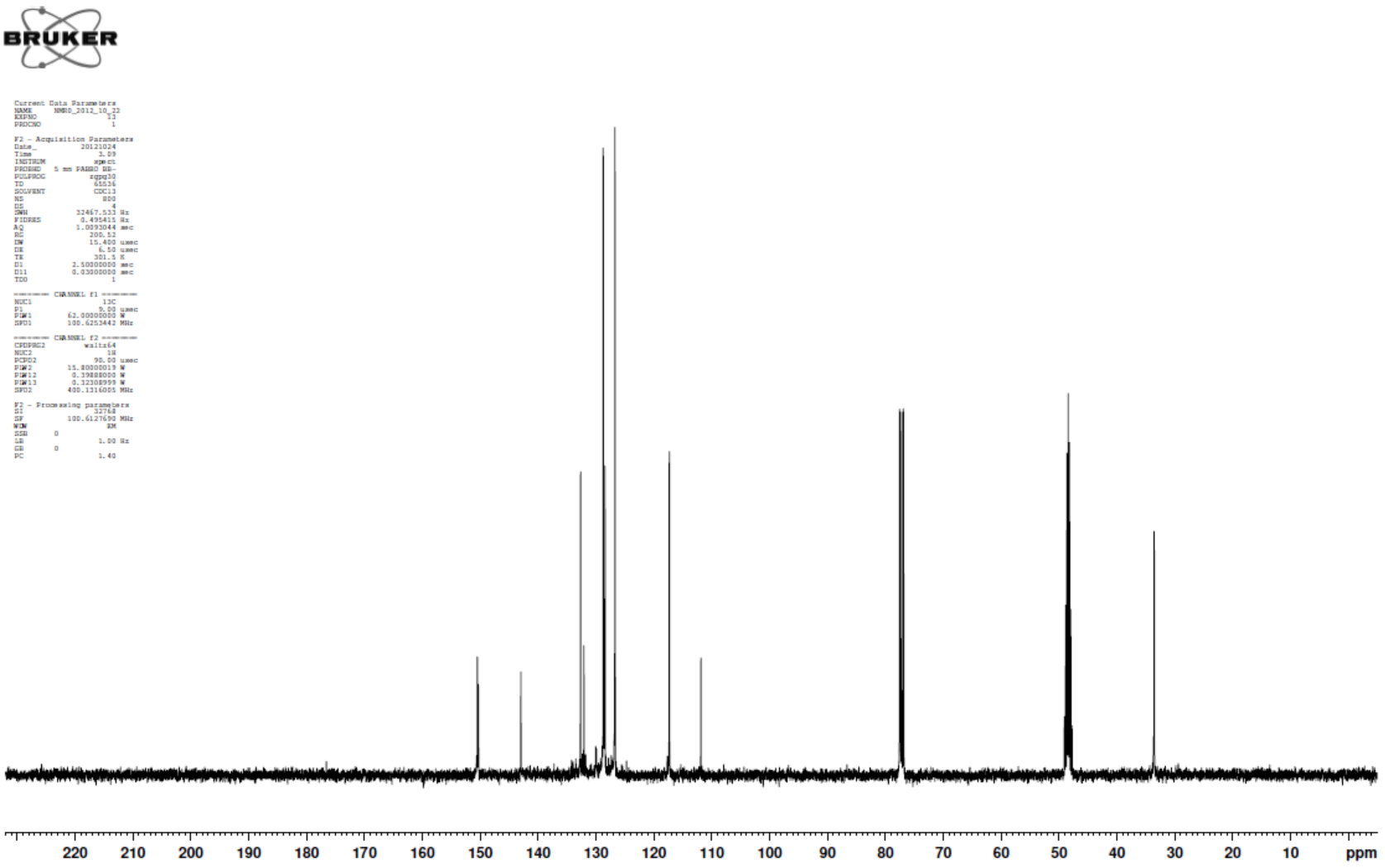
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20121011
Time 13.52
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 12019.230 Hz
FIDRES 0.183399 Hz
AQ 2.7263477 sec
RG 203
DW 41.600 usec
DE 10.18 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 13.30 usec
PLW1 16.00000000 W
SFO1 400.1918309 MHz
F2 - Processing parameters
SI 32768
SF 400.1900000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
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 ppm

2y


BRUKER
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EXPNO 13
PROCNO 1
F2 - Acquisition Parameters
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Time 3.09
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 800
DS 4
SWH 32467.533 Hz
FIDRES 0.495415 Hz
AQ 1.0093044 sec
RG 200.52
DW 15.400 usec
DE 6.50 usec
TE 301.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
CHANNEL f1
NUC1 13C
P1 5.00 usec
PW1 62.00000000 W
SFO1 100.6253442 MHz
CHANNEL f2
CPDPRG2 waltz64
NUC2 1H
PCPD2 90.00 usec
PW2 15.80000019 W
PW12 0.39888000 W
PW13 0.32308999 W
SFO2 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
220
210
200
190
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130
120
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100
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80
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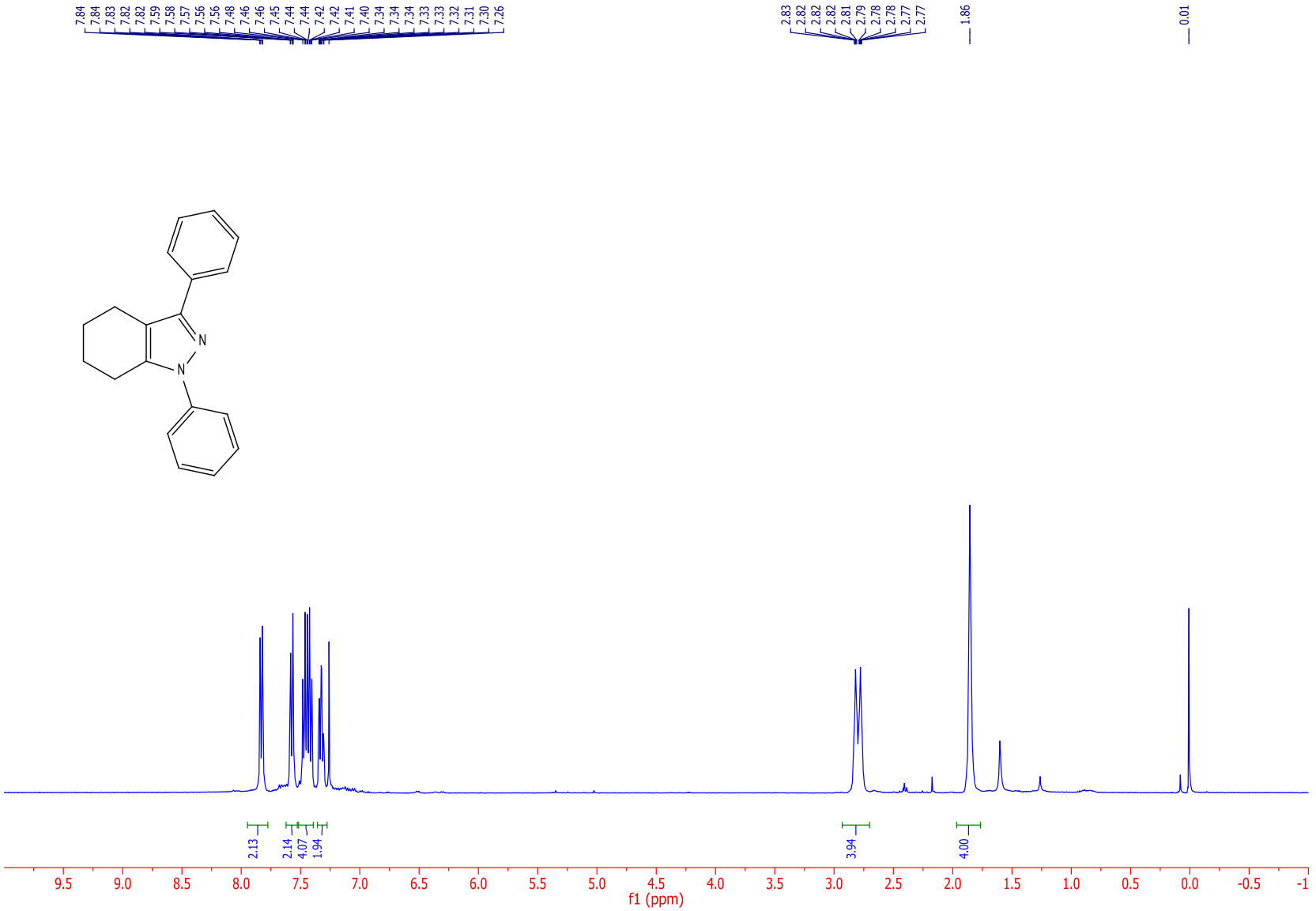
60
50
40
30
20
10
ppm

2y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7.56
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7.46
7.46
7.45
7.44
7.44
7.42
7.42
7.41
7.40
7.34
7.34
7.34
7.33
7.33
7.32
7.31
7.30
7.26
2.83
2.82
2.82
2.82
2.81
2.79
2.78
2.78
2.77
2.77
1.86
0.01
N
N
2.13
2.14
4.07
1.94
3.94
4.00
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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2.5
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1.5
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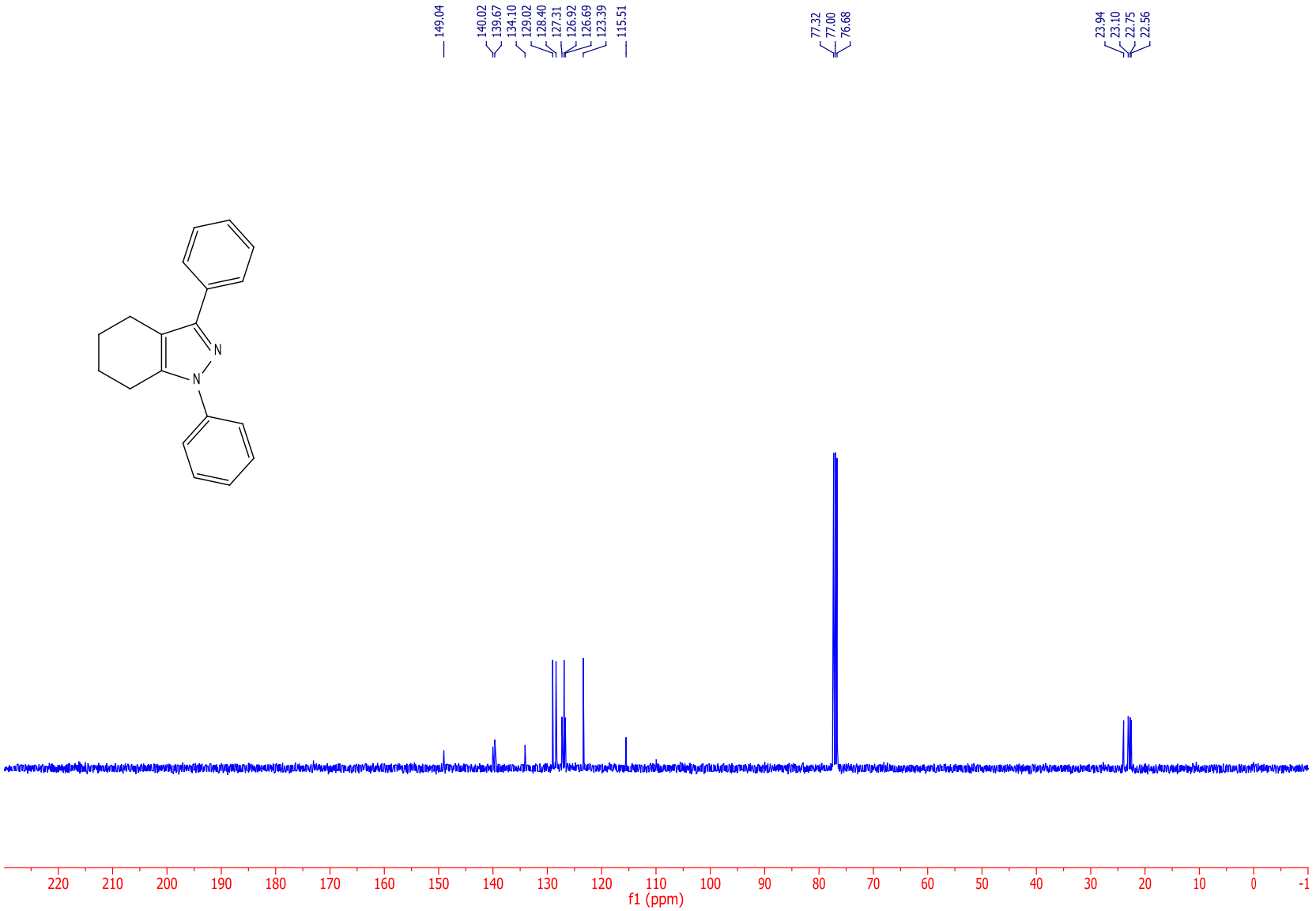
f1 (ppm)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140.02
139.67
134.10
129.02
128.40
127.31
126.92
126.69
123.39
115.51
77.32
77.00
76.68
23.94
23.10
22.75
22.56
N
N
220
210
200
190
180
170
160
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140
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120
110
100
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80
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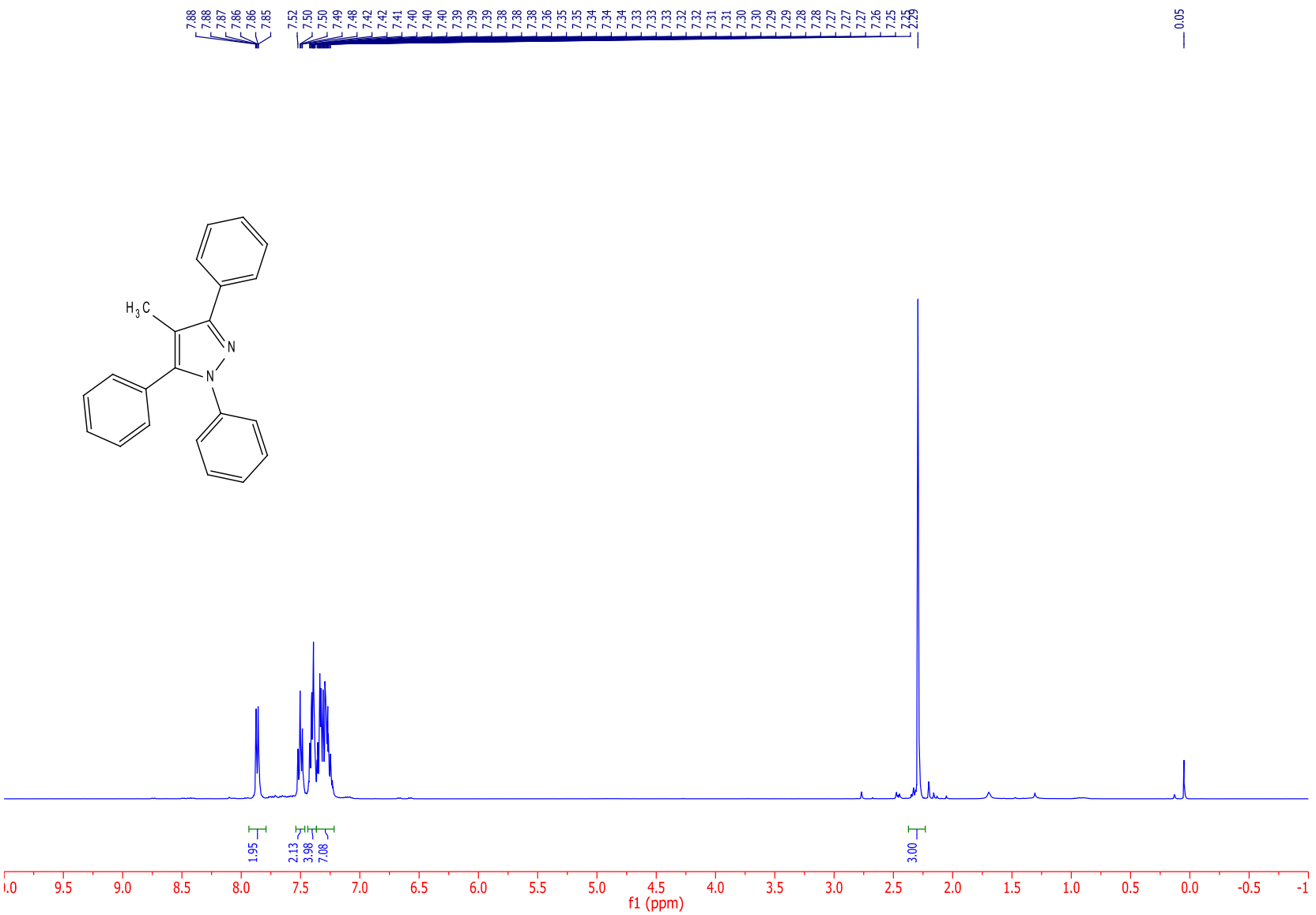
60
50
40
30
20
10
0
-1
f1 (ppm)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7.88
7.87
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7.86
7.85
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7.50
7.50
7.49
7.48
7.42
7.42
7.41
7.40
7.40
7.40
7.39
7.39
7.39
7.38
7.38
7.38
7.36
7.35
7.35
7.34
7.34
7.34
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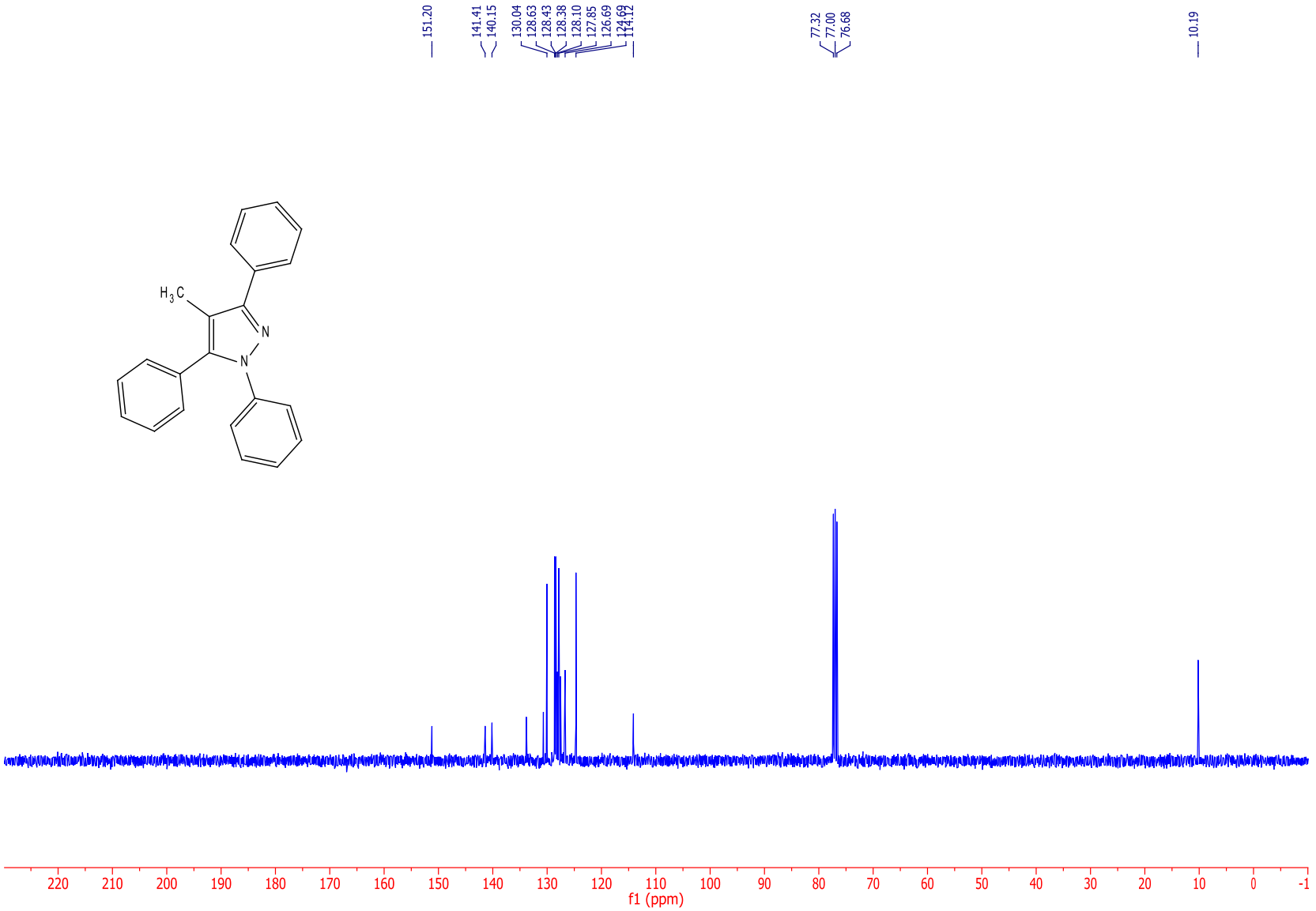
7.30
7.30
7.29
7.29
7.28
7.28
7.27
7.27
7.27
7.26
7.25
2.29
0.05
H3C
N
N
1.95
2.13
3.98
7.08
3.00
f1 (ppm)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128.43
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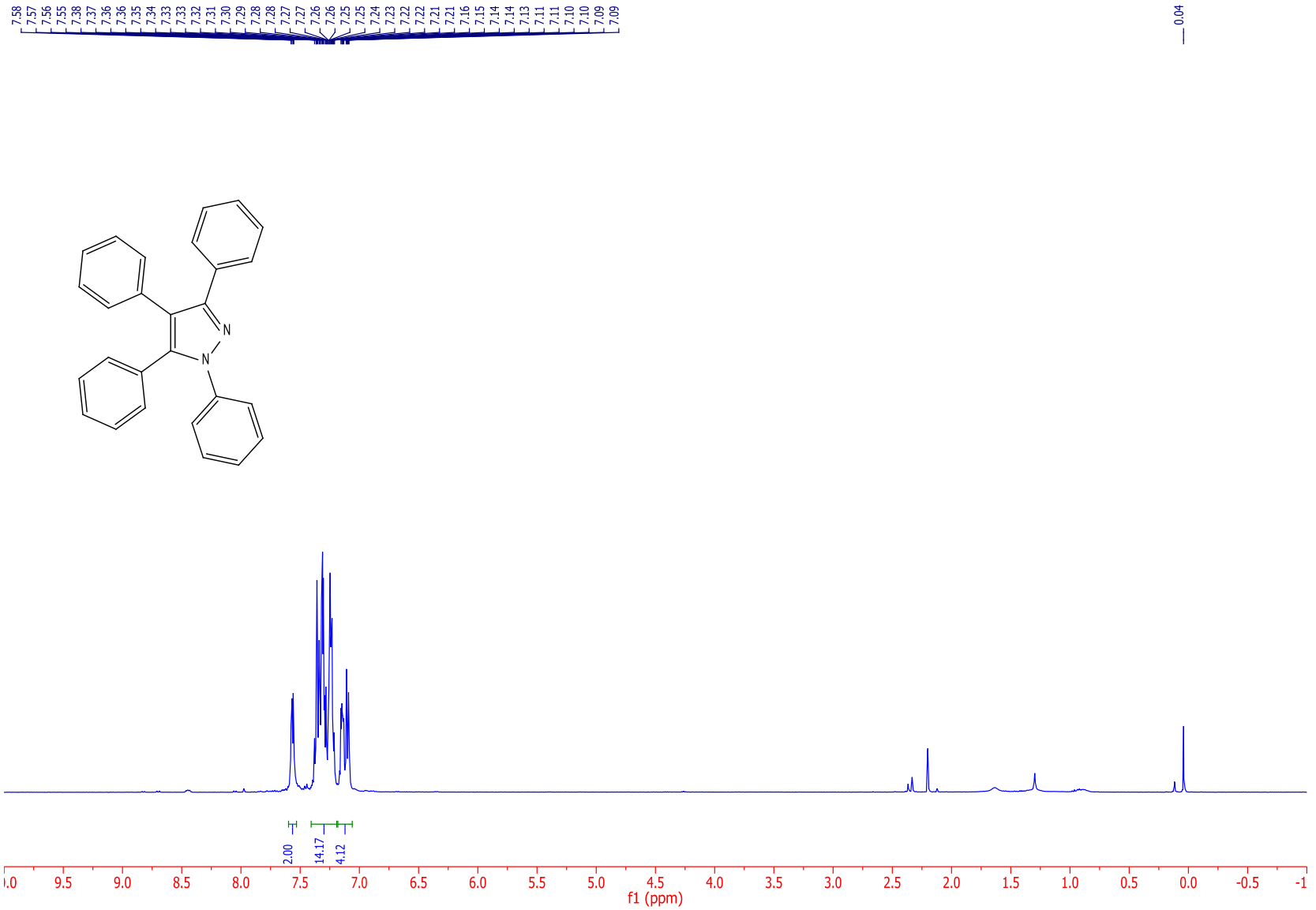
128.10
127.85
126.69
124.69
114.12
77.32
77.00
76.68
10.19
H3C
N
N
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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7.31
7.30
7.29
7.28
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7.27
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7.24
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7.22
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7.21
7.21
7.16
7.15
7.14
7.14
7.13
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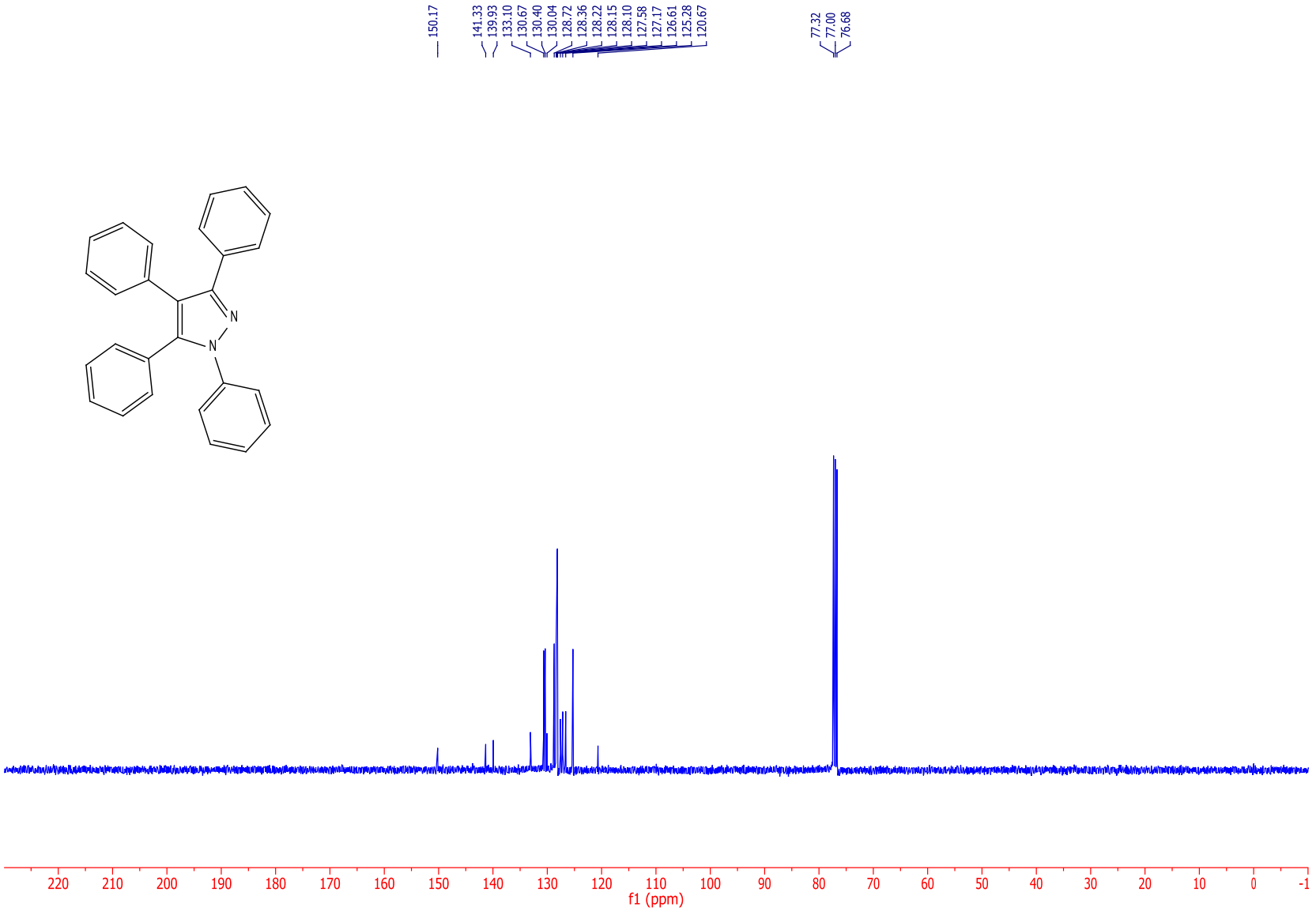
7.11
7.10
7.09
7.09
0.04
N
N
2.00
14.17
4.12
f1 (ppm)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141.33
139.93
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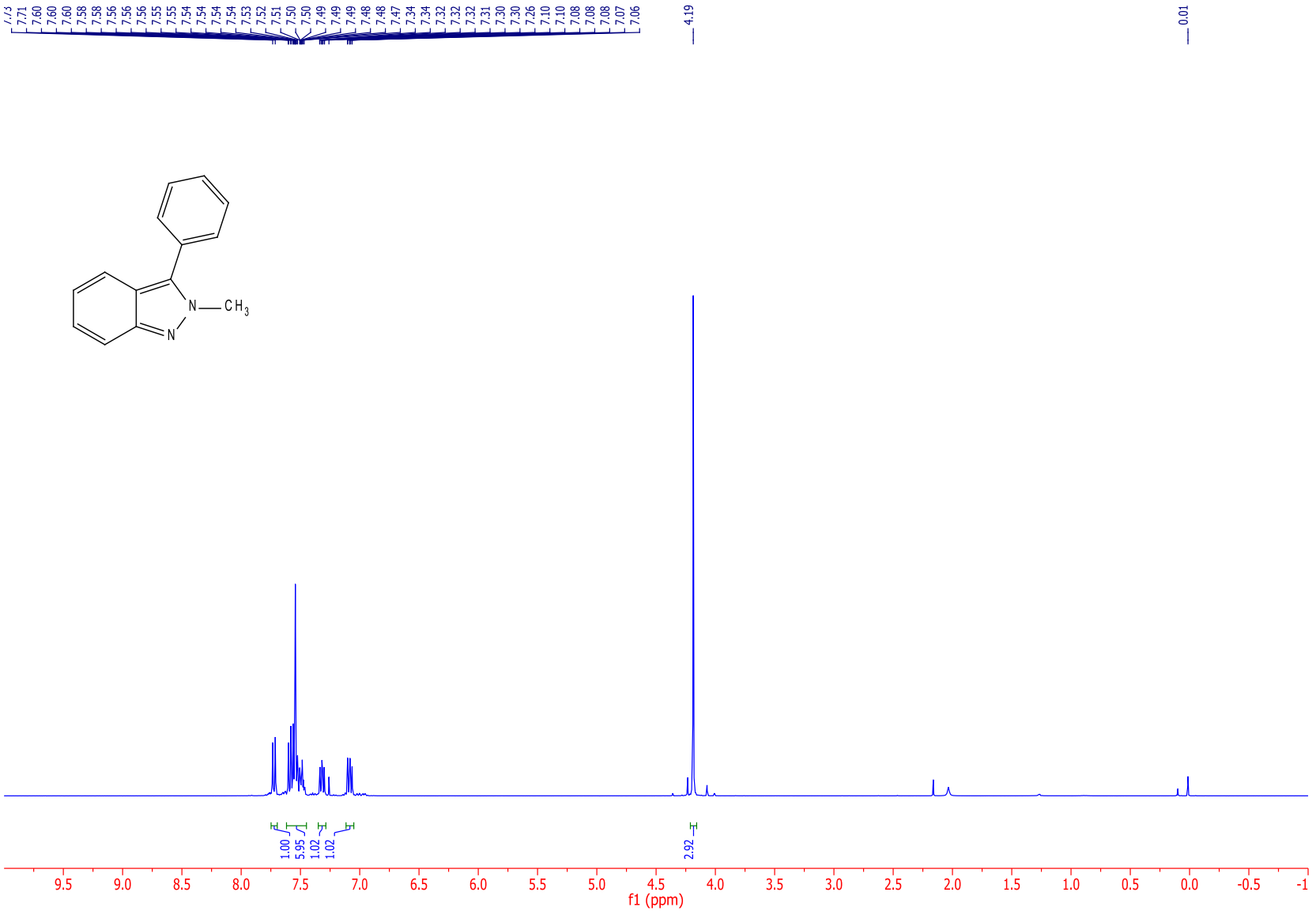
128.72
128.36
128.22
128.15
128.10
127.58
127.17
126.61
125.28
120.67
77.32
77.00
76.68
N
N
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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7.54
7.54
7.54
7.53
7.52
7.51
7.50
7.50
7.49
7.49
7.49
7.48
7.48
7.47
7.34
7.34
7.32
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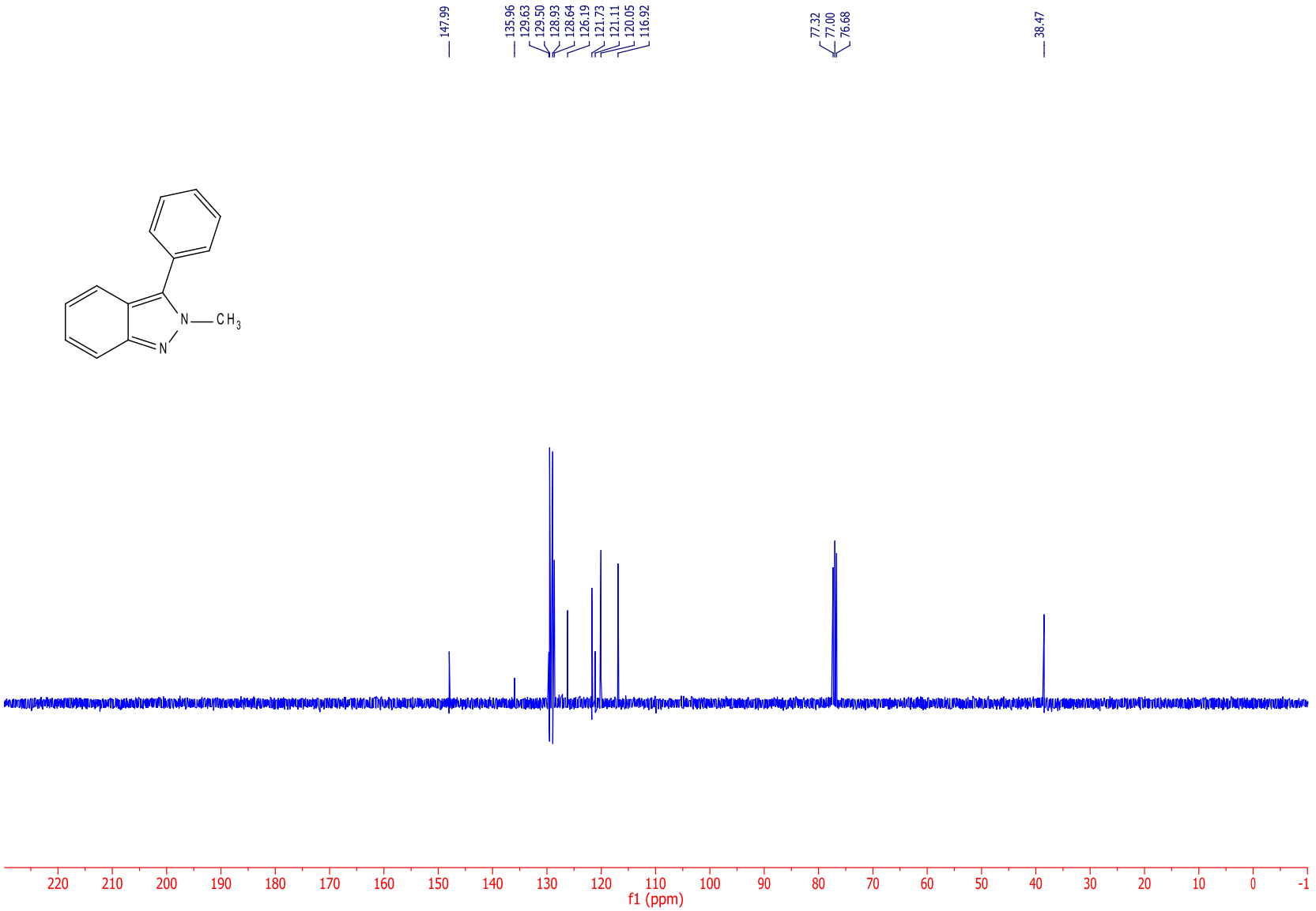
7.31
7.30
7.30
7.26
7.10
7.10
7.08
7.08
7.08
7.07
7.06
4.19
0.01
N
CH3
N
1.00
5.95
1.02
1.02
2.92
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)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121.73
121.11
120.05
116.92
77.32
77.00
76.68
38.47
N
CH3
N
220
210
200
190
180
170
160
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140
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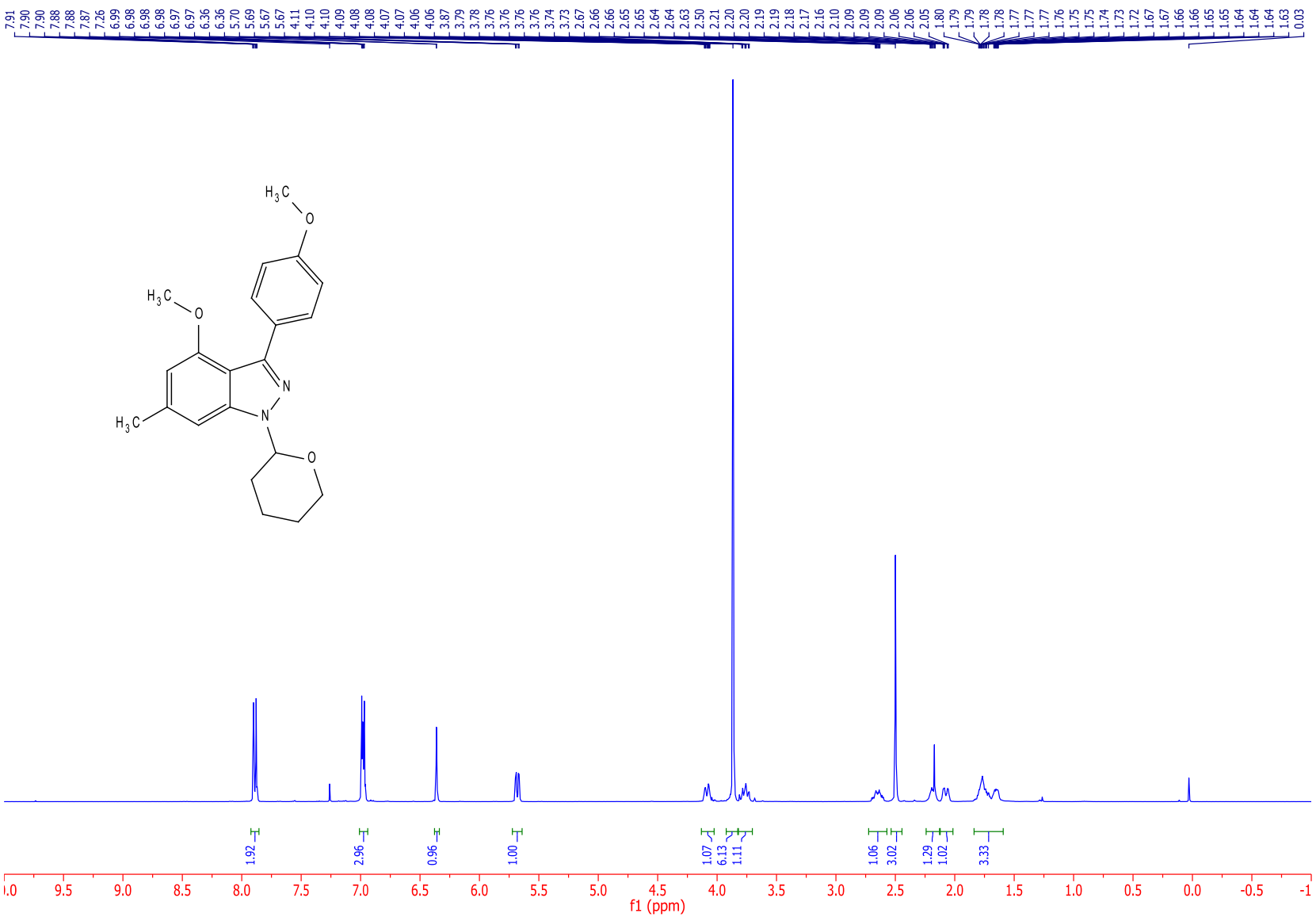
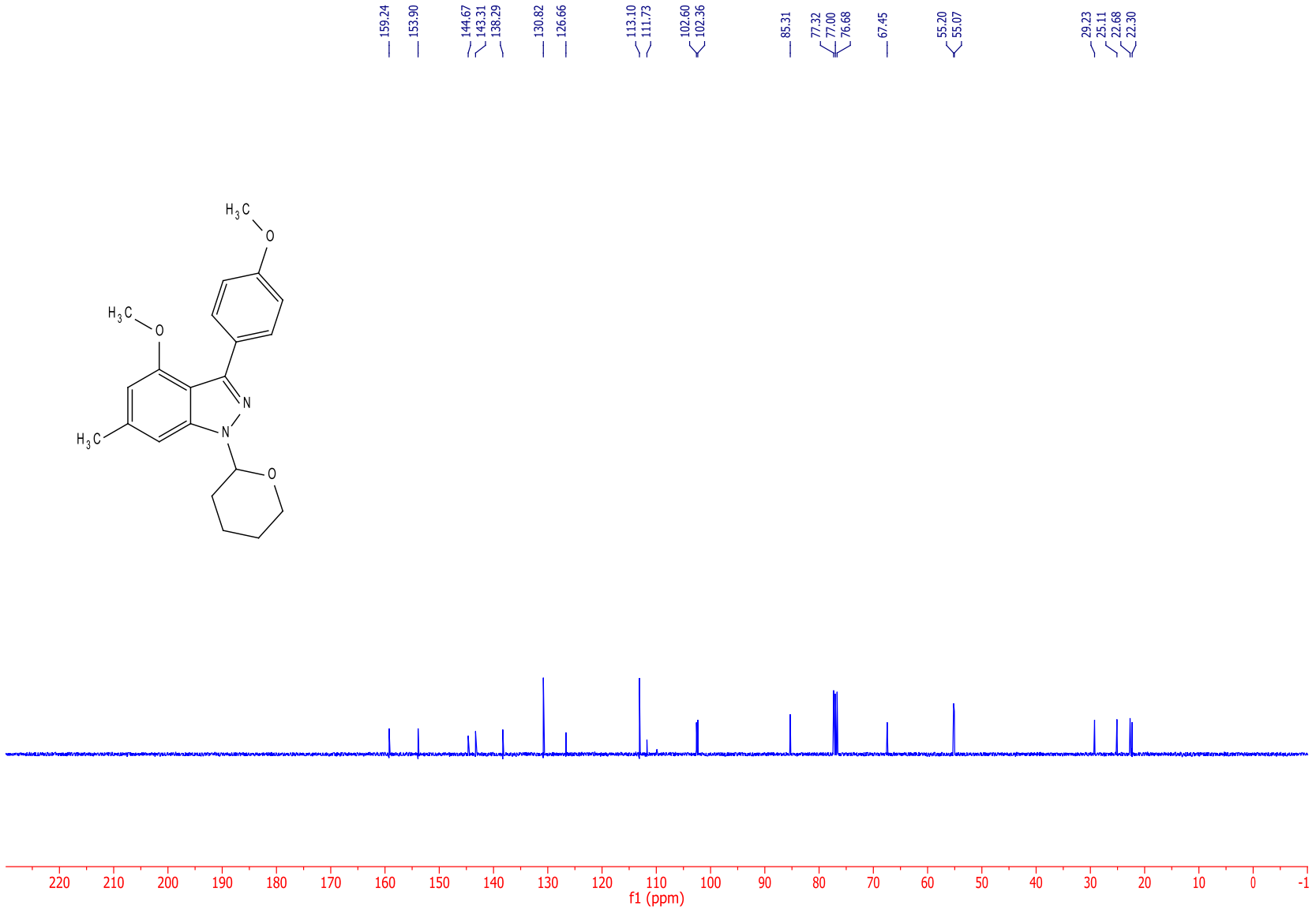
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


7.91 7.90 7.90 7.88 7.88 7.87 7.26 6.99 6.98 6.98 6.98 6.97 6.97 6.36 6.36 5.70 5.69 5.67 5.67 4.11 4.10 4.10 4.09 4.08 4.08 4.07 4.07 4.06 4.06 3.87 3.79 3.78 3.76 3.76 3.76 3.74 3.73 2.67 2.66 2.66 2.65 2.65 2.64 2.64 2.63 2.50 2.21 2.20 2.20 2.19 2.19 2.18 2.17 2.16 2.10 2.09 2.09 2.09 2.06 2.06 2.05 1.80 1.79 1.79 1.78 1.78 1.77 1.77 1.77 1.76 1.75 1.75 1.74 1.73 1.72 1.67 1.67 1.66 1.66 1.65 1.65 1.64 1.64 1.64 1.63 0.03
H3C
O
H3C
O
N
N
H3C
O
1.92
2.96
0.96
1.00
1.07
6.13
1.11
1.06
3.02
1.29
1.02
3.33
f1 (ppm)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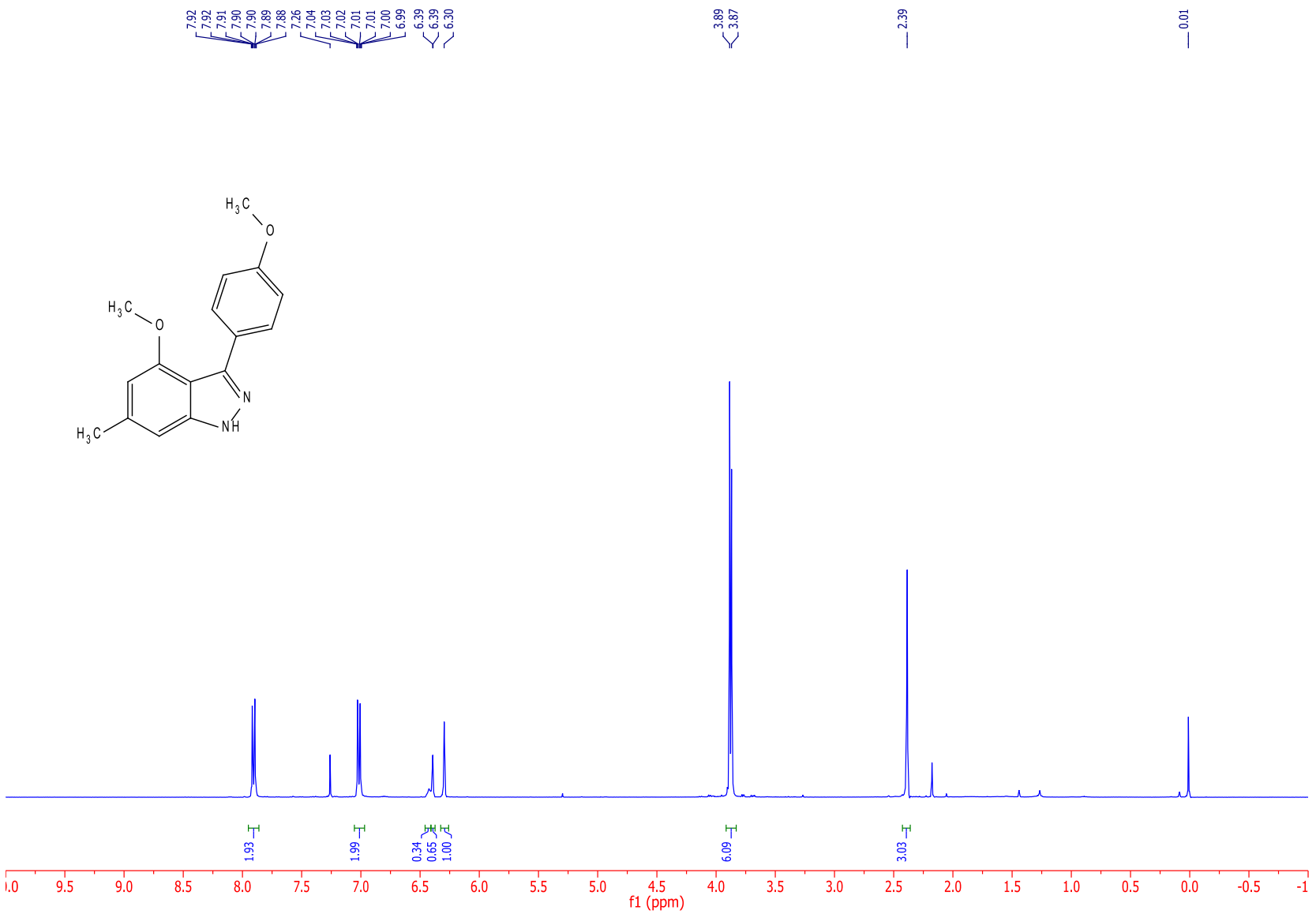
111.73
102.60
102.36
85.31
77.32
77.00
76.68
67.45
55.20
55.07
29.23
25.11
22.68
22.30
H3C
O
H3C
O
N
N
H3C
O
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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7.26
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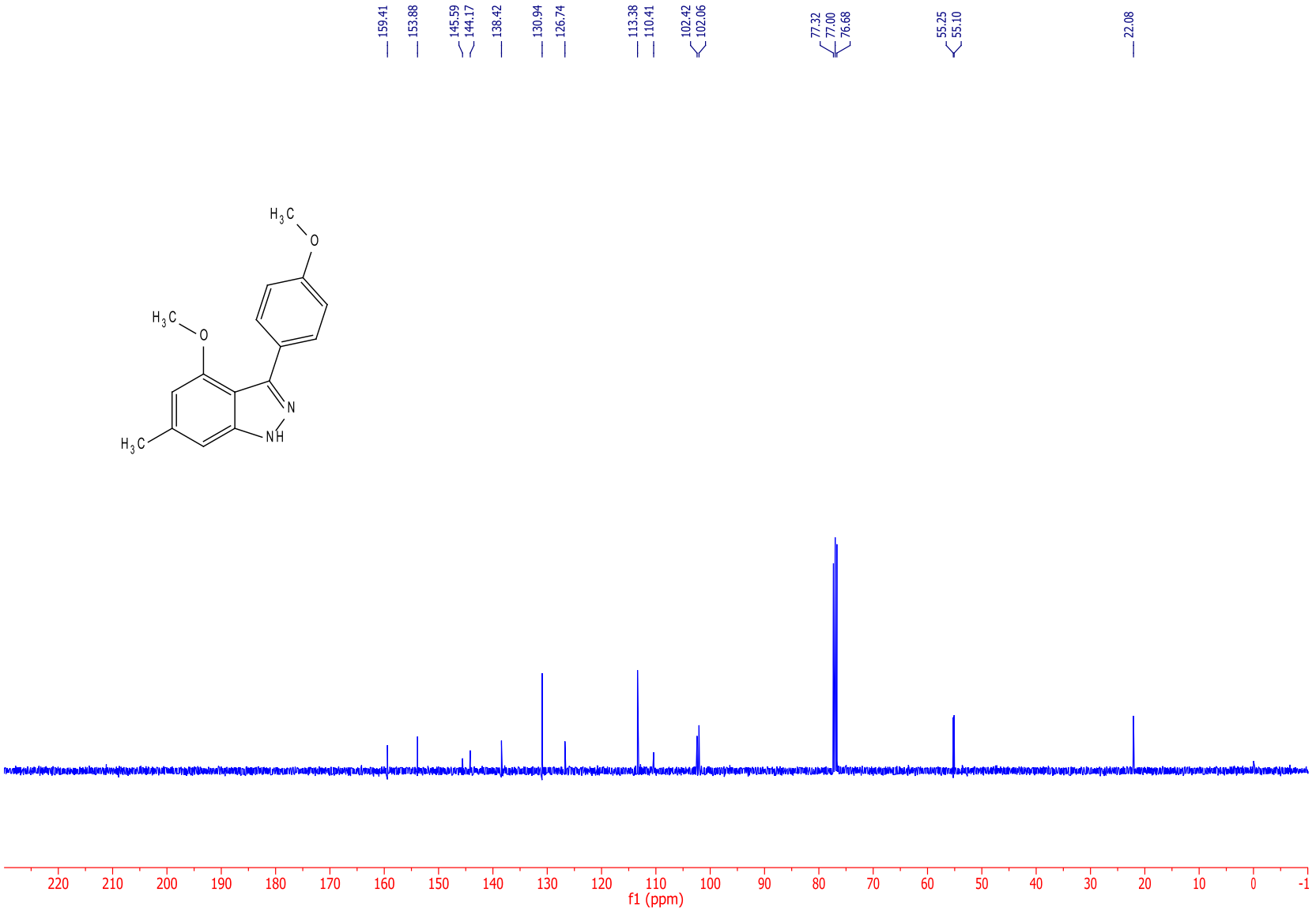
7.03
7.02
7.01
7.01
7.00
6.99
6.39
6.39
6.30
3.89
3.87
2.39
0.01
H3C
O
H3C
O
N
NH
H3C
1.93
1.99
0.34
0.65
1.00
6.09
3.03
f1 (ppm)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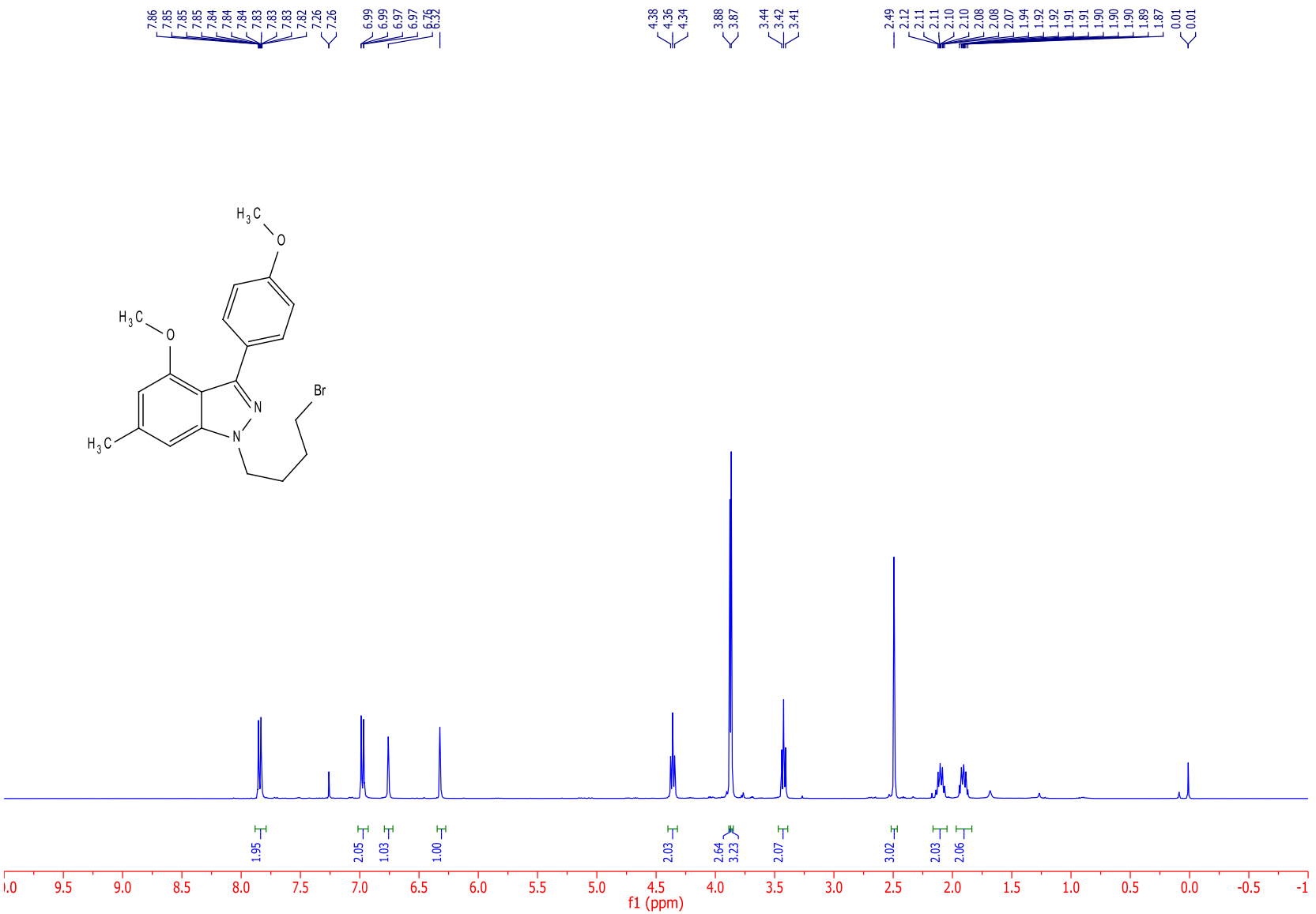
126.74
113.38
110.41
102.42
102.06
77.32
77.00
76.68
55.25
55.10
22.08
H3C
O
H3C
O
N
NH
H3C
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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7.84
7.84
7.83
7.83
7.83
7.82
7.26
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6.99
6.99
6.97
6.97
6.36
6.32
4.38
4.36
4.34
3.88
3.87
3.44
3.42
3.41
2.49
2.12
2.11
2.11
2.10
2.10
2.08
2.08
2.07
1.94
1.92
1.92
1.91
1.91
1.90
1.90
1.90
1.89
1.87
0.01
0.01
H3C
O
H3C
O
N
N
H3C
Br
1.95
2.05
1.03
1.00
2.03
2.64
3.23
2.07
3.02
2.03
2.06
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
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2.5
2.0
1.5
1.0
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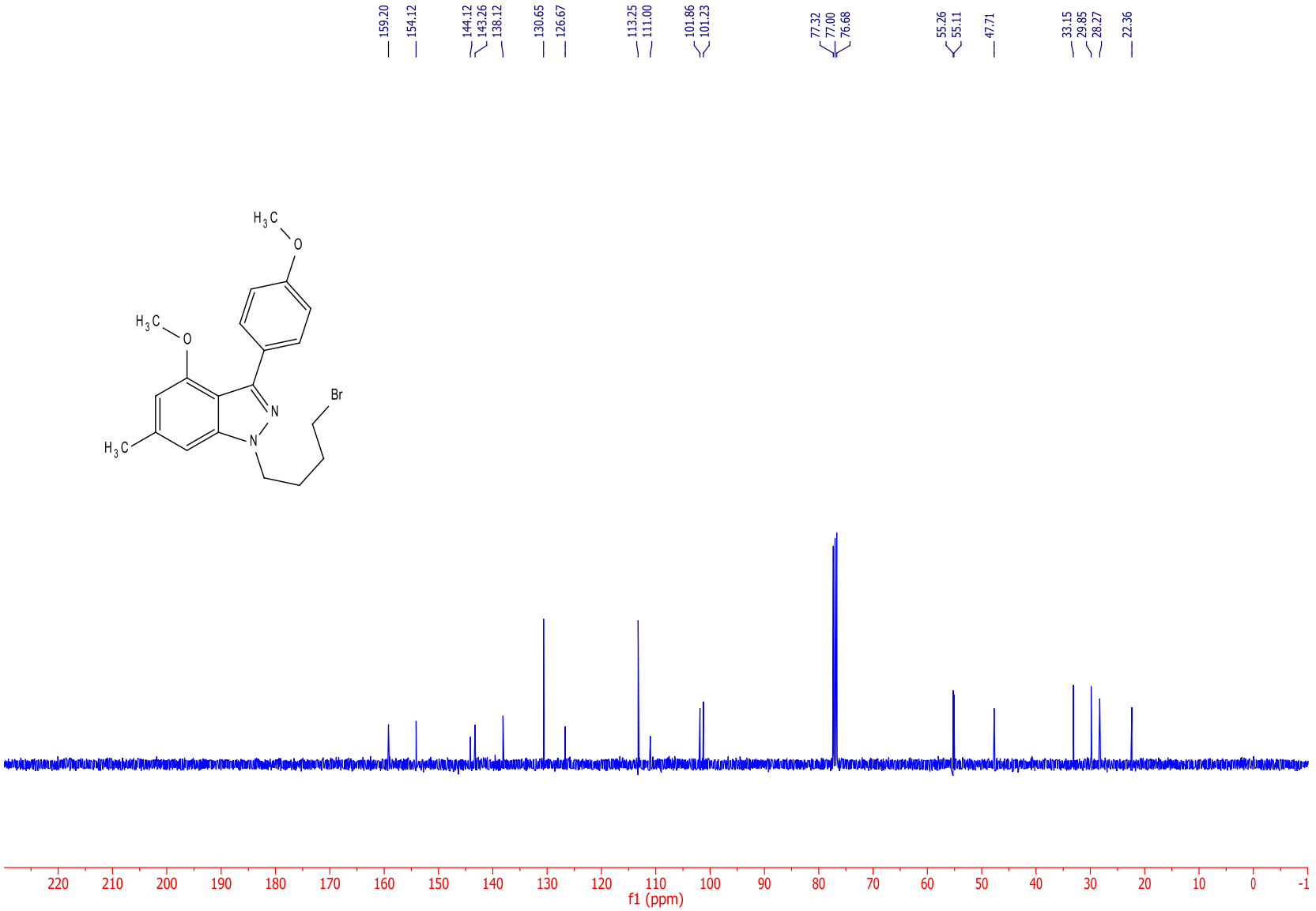
0.0
-0.5
-1
f1 (ppm)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113.25
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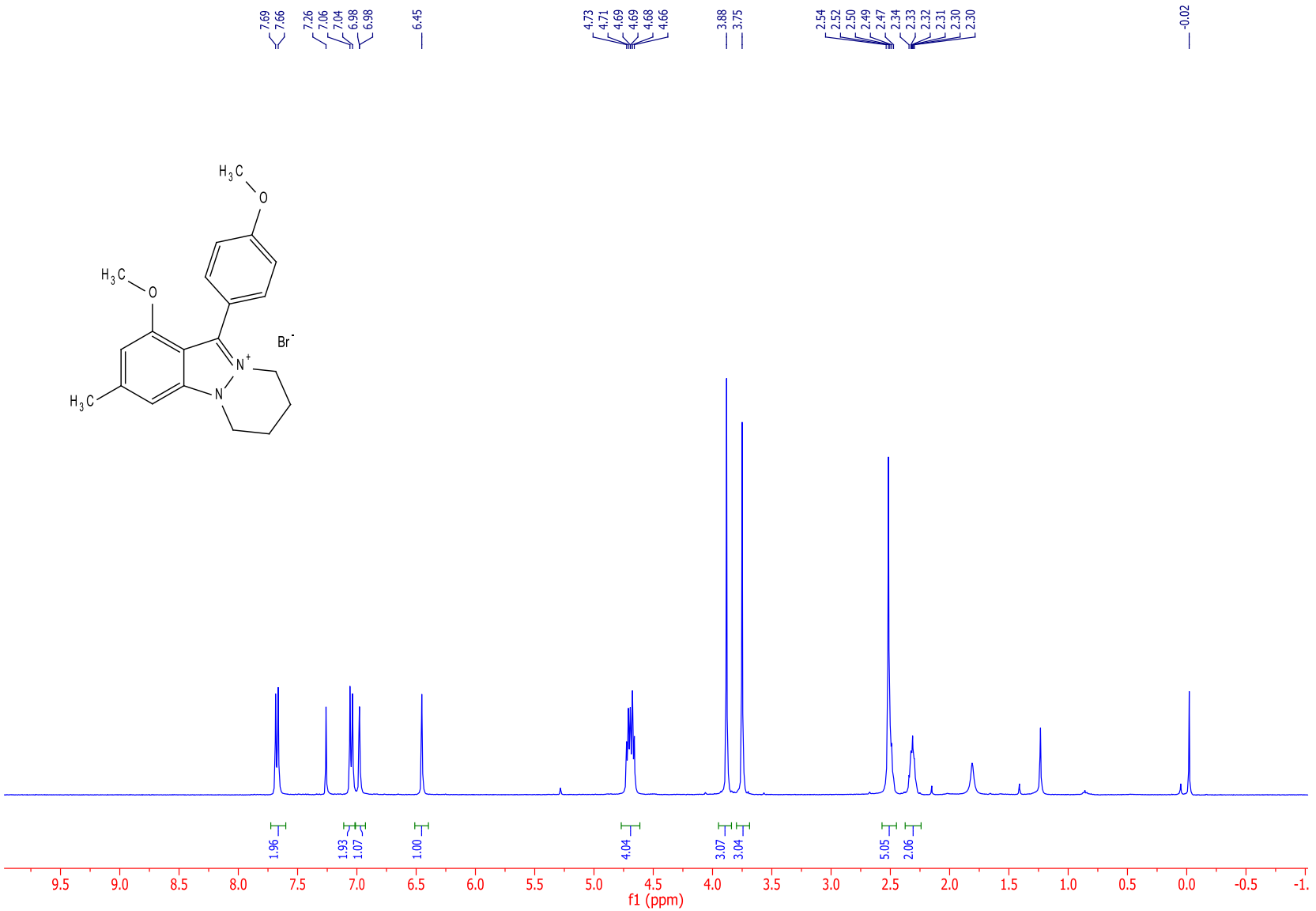
101.86
101.23
77.32
77.00
76.68
55.26
55.11
47.71
33.15
29.85
28.27
22.36
H3C
O
H3C
O
N
N
Br
H3C
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)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6.98
6.45
4.73
4.71
4.69
4.69
4.68
4.66
3.88
3.75
2.54
2.52
2.50
2.49
2.47
2.34
2.33
2.32
2.31
2.30
2.30
-0.02
H3C
O
H3C
O
Br-
N+
N
H3C
1.96
1.93
1.07
1.00
4.04
3.07
3.04
5.05
2.06
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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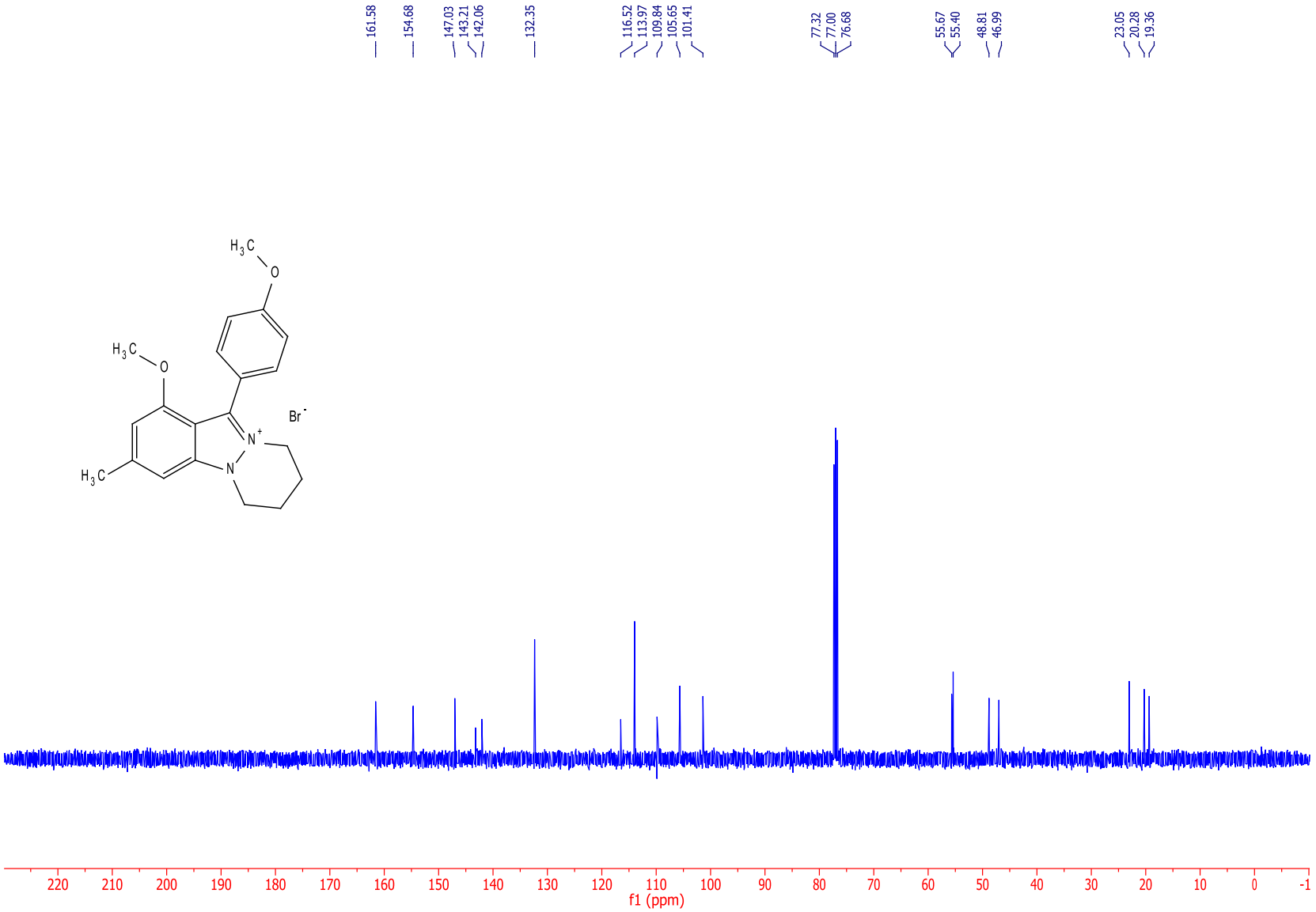
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)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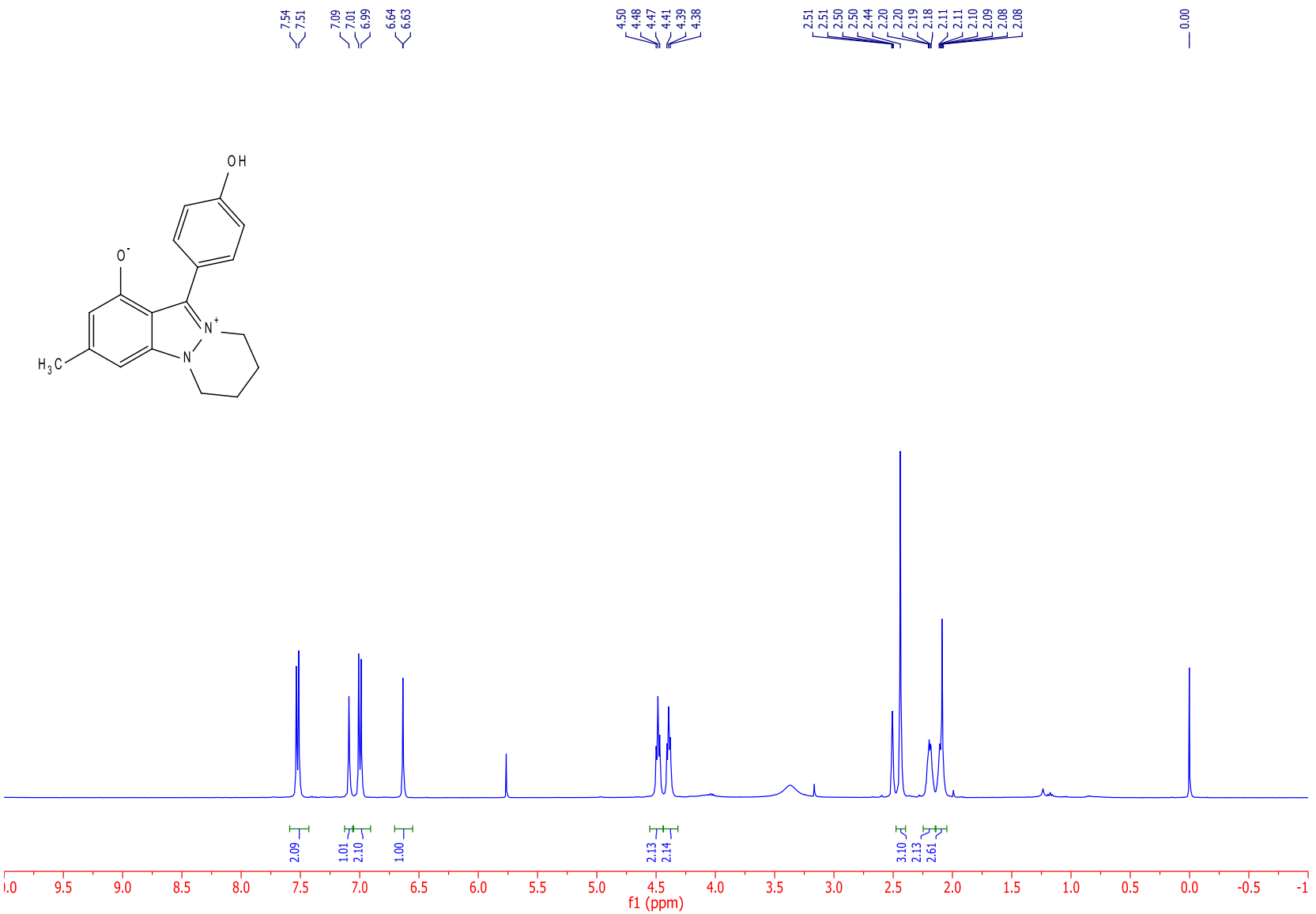
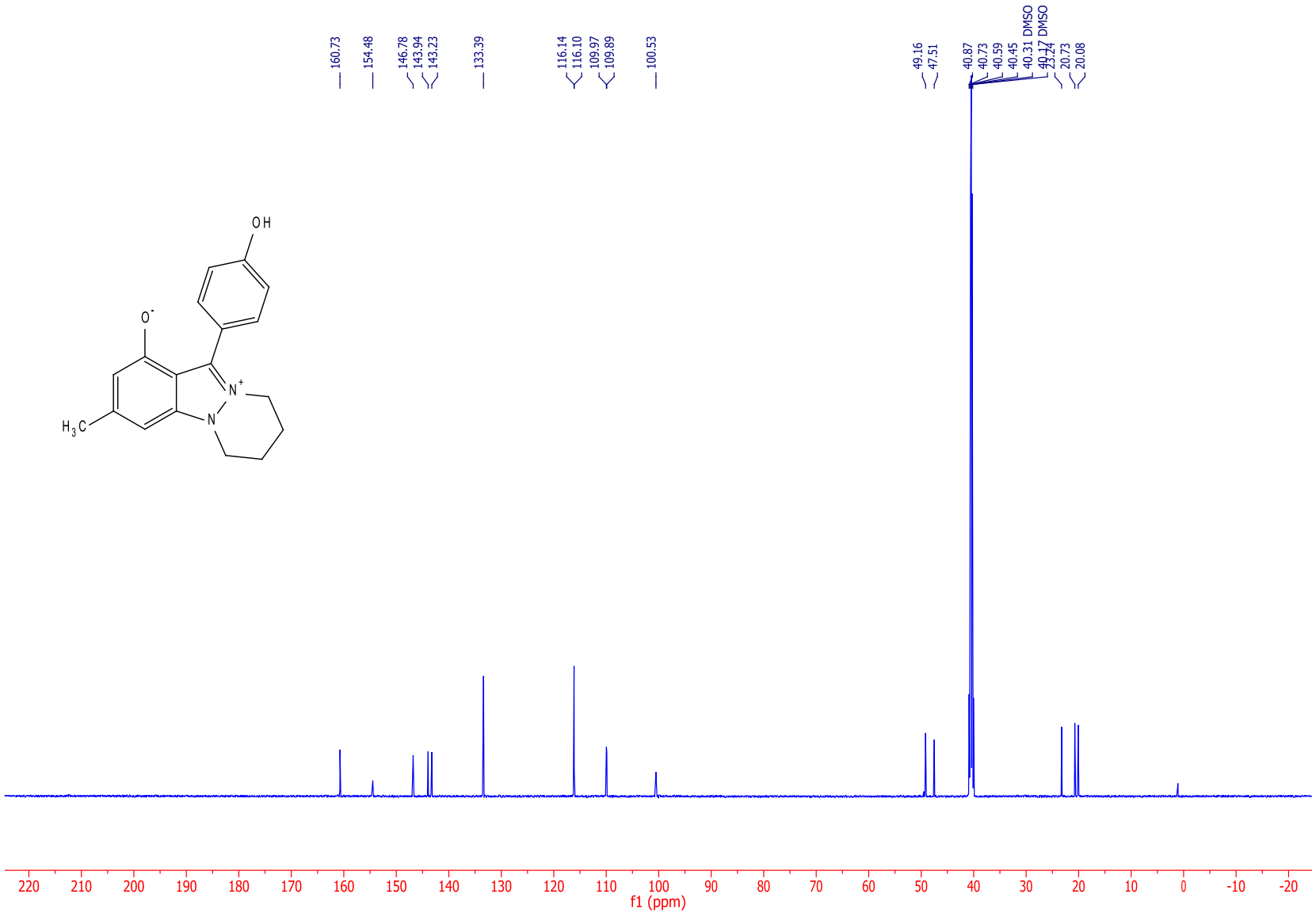
101.41
77.32
77.00
76.68
55.67
55.40
48.81
46.99
23.05
20.28
19.36
H3C
O
H3C
O
Br-
N+
N
H3C
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-1
f1 (ppm)


7.54
7.51
7.09
7.01
6.99
6.64
6.63
4.50
4.48
4.47
4.41
4.39
4.38
2.51
2.51
2.50
2.50
2.44
2.20
2.20
2.19
2.18
2.11
2.11
2.10
2.09
2.08
2.08
0.00
OH
O
N+
N
H3C
2.09
1.01
2.10
1.00
2.13
2.14
3.10
2.13
2.61
f1 (ppm)


160.73
154.48
146.78
143.94
143.23
133.39
116.14
116.10
109.97
109.89
100.53
49.16
47.51
40.87
40.73
40.59
40.45
40.31 DMSO
40.17 DMSO
20.74
20.73
20.08
OH
O-
N+
N
H3C
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)