Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information for:

One-pot radioiodination of aryl amines via stable diazonium salts: preparation of ^{125}I-imaging agents

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1. General Experimental

All reagents and starting materials were obtained from commercial sources and used as received unless otherwise stated. Dry solvents (dichloromethane) were purified using a PureSolv 500 MD solvent purification system. All reactions were performed open to air unless otherwise stated. Brine is defined as a saturated aqueous solution of sodium chloride. Room temperature refers to 20–25 °C. Flash column chromatography was carried out using Fisher Matrix silica 60. Macherey-Nagel aluminium-backed plates, pre-coated with silica gel 60 (UV254) were used for thin layer chromatography and were visualised using UV light (254/365 nm) then potassium permanganate solution. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 400 (^{1}H: 400 MHz; ^{13}C: 101 MHz) spectrometer or a Bruker 500 (^{1}H: 500 MHz; ^{13}C: 126 MHz) spectrometer with chemical shift values reported in ppm relative to a residual solvent peak and in the solvent stated. Assignment of ^{1}H NMR signals is based on COSY experiments. Assignment of ^{13}C NMR signals is based on HSQC and/or DEPT experiments. All coupling constants, *J*, are quoted in Hz. Infrared spectra were recorded using Golden Gate apparatus on a JASCO FTIR 410 spectrometer directly as either a solid or liquid. Mass spectra were obtained using a JEOL JMS-700 spectrometer. Melting points were determined on a Gallenkamp melting point apparatus. For use as a standard for HPLC analysis, 4-chloro-2-iodonitrobenzene was purchased from a commercial supplier. All other standards were prepared using the one-pot diazotisation-iodination procedure (see below). Ethyl 7-nitro-5,6-dihydro-5-methyl-6-oxo-4H-imidazo[1,5-a][1,4]benzodiazepine-3-carboxylate (**3c**) was supplied from GE Healthcare Ltd. *N*-Methyl-*N*-(3-nitrophenyl)cyanamide, required for the preparation of CN1261, was prepared as previously reported.[1] Ethyl 4-(2'-nitrophenyl)quinoline-2-carboxylate, required for the preparation of the TSPO agent, was prepared as previously reported.[2] 4-[4'-Fluoro-3'-(piperazine-1''-carbonyl)benzyl]-2*H*-phthalazin-1-one, for the preparation of the PARP-1 imaging agent, was prepared as previously reported.[3]

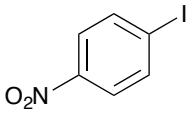
2. Experimental Procedures and Spectroscopic Data for all Compounds

General Procedure for Preparation of Polymer-Supported Nitrite[4]

The polymer-supported nitrite reagent was prepared by the addition of Amberlyst® A26 hydroxide form resin (1.00 g, 4.00 mmol) to a solution of $NaNO_2$ (0.55 g, 8.00 mmol) in water (20 mL). The mixture was stirred at room temperature for 0.5 h. The

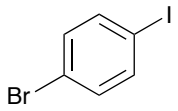
polymer-supported nitrite was filtered and washed with water until the pH of the filtrate became neutral. The content of the polymer-supported nitrite was 3.5 mmol of NO_2/g.[4]

General Procedure for One-Pot Diazotisation and Iodination: 4-Iodonitrobenzene[5]



To a solution of *p*-toluenesulfonic acid monohydrate (0.27 g, 1.1 mmol) in acetonitrile (2 mL) was added 4-nitroaniline (0.050 g, 0.36 mmol). The solution was cooled in a water bath to 10–15 °C. Polymer-supported nitrite (0.31 g, containing 1.1 mmol of NO_2) was added, followed by sodium iodide (0.11 g, 0.54 mmol) in water (0.2 mL). The reaction mixture was stirred for 1 h then warmed to room temperature and stirred for 2 h in total. The mixture was filtered from the resin and the resin was washed with diethyl ether (50 mL). The reaction mixture and diethyl ether washings were combined and washed with water (50 mL). The aqueous layer was then extracted with diethyl ether (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified using flash column chromatography eluting with 20% ethyl acetate in petroleum ether (40–60) to give 4-iodonitrobenzene as a pale yellow solid (0.080 g, 86%). Mp 170–172 °C (lit.[5] 169–171 °C); δ_H (400 MHz, $CDCl_3$) 7.91 (2H, d, *J* 8.0 Hz, 3-H and 5-H), 7.94 (2H, d, *J* 8.0 Hz, 2-H and 6-H); δ_C (101 MHz, $CDCl_3$) 102.8 (C), 125.0 (2 × CH), 138.8 (2 × CH), 148.0 (C); *m/z* (CI) 250 (MH^+, 60%), 209 (12), 193 (15), 124 (30), 113 (22), 85 (78), 69 (100).

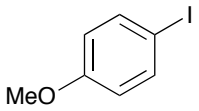
4-Iodobromobenzene[6]



The reaction was carried out according to the previously described general procedure for 4-iodonitrobenzene using 4-bromoaniline (0.050 g, 0.28 mmol), *p*-toluenesulfonic acid monohydrate (0.17 g, 0.87 mmol), polymer-supported nitrite

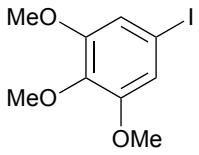
(0.25 g, containing 0.87 mmol of NO_2) and sodium iodide (0.090 g, 0.58 mmol). Purification by flash column chromatography eluting with 5% diethyl ether in petroleum ether (40–60) gave 4-iodobromobenzene as a white solid (0.063 g, 77%). Mp 91–92 °C (lit.[6] 90 °C); δ_H (400 MHz, $CDCl_3$) 7.23 (2H, d, *J* 8.6 Hz, 3-H and 5-H), 7.54 (2H, d, *J* 8.6 Hz, 2-H and 6-H); δ_C (101 MHz, $CDCl_3$) 92.2 (C), 122.4 (C), 133.6 (2 × CH), 139.2 (2 × CH); *m/z* (EI) 282 (M^+, 48%), 155 (32), 84 (100), 49 (48).

4-Iodoanisole[7]



The reaction was carried out according to the previously described general procedure for 4-iodonitrobenzene using 4-methoxyaniline (0.050 g, 0.40 mmol), *p*-toluenesulfonic acid monohydrate (0.23 g, 1.2 mmol), polymer-supported nitrite (0.34 g, containing 1.2 mmol of NO_2) and sodium iodide (0.12 g, 0.80 mmol). The crude material was purified using flash column chromatography eluting with 5% ethyl acetate in petroleum ether (40–60) to give 4-iodoanisole as a white solid (0.070 g, 71%). Mp 47–48 °C (lit.[7] 49–50 °C); δ_H (400 MHz, $CDCl_3$) 3.78 (1H, s, OCH_3), 6.68 (2H, d, *J* 9.0 Hz, 2-H and 6-H), 7.56 (2H, d, *J* 9.0 Hz, 3-H and 5-H); δ_C (101 MHz, $CDCl_3$) 55.5 (CH_3), 82.9 (C), 116.5 (2 × CH), 138.4 (2 × CH), 159.6 (C); *m/z* (EI) 234 (M^+. 100%), 219 (22), 191 (11), 92 (14).

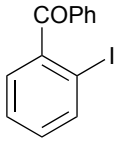
3,4,5-Trimethoxyiodobenzene[8]



The reaction was carried out according to the previously described general procedure for 4-iodonitrobenzene using 3,4,5-trimethoxyaniline (0.050 g, 0.29 mmol), *p*-toluenesulfonic acid monohydrate (0.16 g, 0.82 mmol), polymer-supported nitrite (0.23 g, containing 0.82 mmol of NO_2) and sodium iodide (0.080 g, 0.55 mmol). The crude material was purified using flash column chromatography eluting with 20%

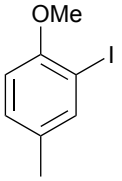
diethyl ether in petroleum ether (40–60) to give 3,4,5-trimethoxyiodobenzene as a yellow solid (0.060 g, 73%). Mp 84–86 °C (lit.[8] 83–85 °C); δ_H (400 MHz, $CDCl_3$) 3.80 (3H, s, OCH_3), 3.82 (6H, s, 2 × OCH_3), 6.87 (2H, s, 2 × ArH); δ_C (101 MHz, $CDCl_3$) 56.5 (2 × CH_3), 61.0 (CH_3), 86.2 (C), 115.1 (2 × CH), 138.4 (C), 154.1 (2 × C); *m/z* (EI) 294 (M^+, 100%), 279 (58), 251 (19), 236 (18), 124 (21), 109 (12), 84 (70).

2-Iodobenzophenone[9]



The reaction was carried out according to the previously described general procedure for 4-iodonitrobenzene using 2-aminobenzophenone (0.050 g, 0.25 mmol), *p*-toluenesulfonic acid monohydrate (0.14 g, 0.76 mmol), polymer-supported nitrite (0.22 g, containing 0.76 mmol of NO_2) and sodium iodide (0.080 g, 0.51 mmol). The crude material was purified using flash column chromatography eluting with 5% diethyl ether in petroleum ether (40–60) to give 2-iodobenzophenone as an orange solid (0.060 g, 79%). Mp 30–31 °C (lit.[9] 31–32 °C); δ_H (400 MHz, $CDCl_3$) 7.15–7.21 (1H, m, ArH), 7.30 (1H, dd, *J* 7.6, 1.5 Hz, ArH), 7.42–7.49 (3H, m, 3 × ArH), 7.58–7.63 (1H, m, ArH), 7.79–7.83 (2H, m, 2 × ArH), 7.93 (1H, dd, *J* 8.0, 0.8 Hz, ArH); δ_C (101 MHz, $CDCl_3$) 92.3 (C), 127.9 (CH), 128.6 (CH), 128.8 (CH), 130.6 (2 × CH), 131.2 (2 × CH), 133.8 (CH), 135.7 (C), 139.8 (CH), 144.5 (C), 197.3 (C); *m/z* (ESI) 331 (MNa^+. 100%).

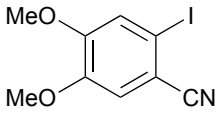
2-Iodo-4-methylanisole[10]



The reaction was carried out according to the previously described general procedure for 4-iodonitrobenzene using 2-methoxy-5-methylaniline (0.050 g, 0.36

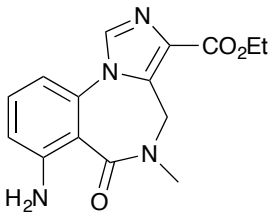
mmol), *p*-toluenesulfonic acid monohydrate (0.21 g, 1.1 mmol), polymer-supported nitrite (0.31 g, containing 1.1 mmol of NO_2) and sodium iodide (0.11 g, 0.73 mmol). The crude material was purified using flash column chromatography eluting with 20% ethyl acetate in petroleum ether (40–60) to give 2-iodo-4-methylanisole as a white solid (0.070 g, 82%). Mp 28–29 °C (lit.[10] 30 °C); δ_H (500 MHz, $CDCl_3$) 2.26 (3H, s, 4-CH_3), 3.85 (3H, s, OCH_3), 6.72 (1H, d, *J* 8.3 Hz, 6-H), 7.10 (1H, dd, *J* 8.3, 1.6 Hz, 5-H), 7.60 (1H, d, *J* 1.6 Hz, 3-H); δ_C (126 MHz, $CDCl_3$) 20.1 (CH_3), 56.6 (CH_3), 85.9 (C), 110.9 (CH), 130.1 (CH), 132.2 (C), 140.0 (CH), 156.2 (C); *m/z* (EI) 248 (M^+. 100%), 233 (28), 121 (11), 84 (28), 78 (17).

4,5-Dimethoxy-2-iodobenzonitrile[7]



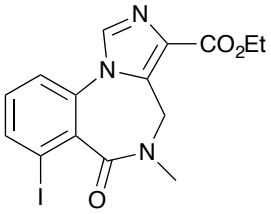
The reaction was carried out according to the previously described general procedure for 4-iodonitrobenzene using 2-amino-4,5-dimethoxybenzonitrile (0.050 g, 0.28 mmol), *p*-toluenesulfonic acid monohydrate (0.16 g, 0.84 mmol), polymer-supported nitrite (0.24 g, containing 0.84 mmol of NO_2) and sodium iodide (0.080 g, 0.56 mmol). Purification by flash column chromatography eluting with 20% ethyl acetate in petroleum ether (40–60) gave 4,5-dimethoxy-2-iodobenzonitrile as an orange solid (0.070 g, 86%). Mp 98–99 °C (lit.[7] 103–104 °C); δ_H (400 MHz, $CDCl_3$) 3.87 (3H, s, OCH_3), 3.91 (3H, s, OCH_3), 7.02 (1H, s, 3-H), 7.24 (1H, s, 6-H); δ_C (101 MHz, $CDCl_3$) 56.4 (CH_3), 56.6 (CH_3), 88.8 (C), 112.3 (C), 115.9 (CH), 119.9 (C), 121.7 (CH), 149.5 (C), 153.0 (C); *m/z* (ESI) 312 (MNa^+. 100%).

Ethyl 7-amino-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate



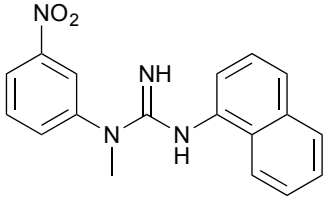
Ethyl 7-nitro-5,6-dihydro-5-methyl-6-oxo-4H-imidazo[1,5-a][1,4]benzodiazepine-3-carboxylate (0.030 g, 0.090 mmol) was dissolved in ethanol (1 mL) before addition of tin(II) chloride dihydrate (0.10 g, 0.45 mmol). The reaction mixture was stirred under reflux for 16 h. After cooling to room temperature, the reaction was quenched by addition of a saturated aqueous solution of sodium hydrogen carbonate and the product was extracted with ethyl acetate (3 × 5 mL). The organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude material was purified using flash column chromatography eluting with 1% methanol in dichloromethane to give give ethyl 7-amino-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate as a white solid (0.019 g, 71%). Mp 218−220 °C; ν_{max}/cm^{-1} (neat) 3460 (NH), 3313 (NH), 2926 (CH), 1696 (C=O), 1646 (C=O), 1614, 1582, 1493, 1377, 1317, 1284, 1222, 1195, 1142, 1096, 942, 800, 761, 704; δ_H (400 MHz, $CDCl_3$) 1.43 (3H, t, *J* 7.1 Hz, $CO_2CH_2CH_3$), 3.20 (3H, s, NCH_3), 4.34–4.50 (3H, m, $CO_2CH_2CH_3$ and 4-*H*H), 5.07 (1H, d, *J* 15.5 Hz, 4-H*H*), 5.29 (2H, br s, NH_2), 6.65 (1H, dd, *J* 8.0, 1.0 Hz, 8-H), 6.76 (1H, dd, *J* 8.0, 1.0 Hz, 10-H), 7.27 (1H, t, *J* 8.0 Hz, 9-H), 7.81 (1H, s, 1-H); δ_C (126 MHz, $CDCl_3$) 14.5 (CH_3), 35.3 (CH_3), 42.4 (CH_2), 61.0 (CH_2), 111.4 (CH), 112.2 (C), 116.6 (CH), 128.4 (C), 132.2 (CH), 133.7 (C), 135.5 (CH), 136.1 (C), 150.0 (C), 163.3 (C), 166.8 (C); *m/z* (ESI) 323.1101 (MNa^+. $C_{15}H_{16}N_4NaO_3$ requires 323.1115).

Ethyl 7-iodo-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate (Iomazenil)



The reaction was carried out according to the previously described general procedure for 4-iodonitrobenzene using ethyl 7-amino-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate (0.020 g, 0.070 mmol), *p*-toluenesulfonic acid monohydrate (0.040 g, 0.21 mmol), polymer-supported nitrite (0.060 g, containing 0.21 mmol of NO_2) and sodium iodide (0.020 g, 0.14 mmol). The reaction mixture was heated to 60 °C and stirred for 16 h. The crude material was purified using flash column chromatography eluting with 5% methanol in dichloromethane to give ethyl 7-iodo-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate as a white solid (0.020 g, 72%). Mp 232−234 °C; ν_{max}/cm^{-1} (neat) 3091, 2924 (CH), 1694 (C=O), 1647(C=O), 1577, 1486, 1390, 1372, 1348, 1303, 1281, 1240, 1198, 1070, 1050, 938, 799, 772, 705, 664; δ_H (400 MHz, $CDCl_3$) 1.44 (3H, t, *J* 7.1 Hz, $CO_2CH_2C\mathit{H}_3$), 3.20 (3H, s, NCH_3), 4.33–4.51 (3H, m, $CO_2C\mathit{H}_2CH_3$ and 4-*H*H), 5.14 (1H, d, *J* 15.8 Hz, 4-H*H*), 7.25 (1H, t, *J* 8.0 Hz, 9-H), 7.37 (1H, dd, *J* 8.0, 0.7 Hz, 10-H), 7.89 (1H, s, 1-H), 8.06 (1H, dd, *J* 8.0, 0.7 Hz, 8-H); δ_C (126 MHz, $CDCl_3$) 14.5 (CH_3), 35.1 (CH_3), 42.7 (CH_2), 61.2 (CH_2), 97.4 (C), 122.4 (CH), 129.4 (C), 132.4 (CH), 132.5 (C), 134.0 (C), 135.1 (CH), 136.0 (C), 141.2 (CH), 163.0 (C), 166.1 (C); *m/z* (ESI) 433.9963 (MNa^+. $C_{15}H_{14}IN_3NaO_3$ requires 433.9972).

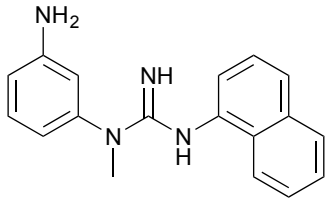
***N*-(1-Naphthyl)-*N'*-(3-nitrophenyl)-*N'*-methylguanidine**



1-Naphthylamine (0.13 g, 0.75 mmol) was dissolved in diethyl ether (1 mL) and converted to its hydrochloride salt by dropwise addition of aqueous hydrochloric acid

(1 M) in diethyl ether (1 mL) to give a pink precipitate. This was filtered and dried. This was added to *N*-methyl-*N*-(3-nitrophenyl)cyanamide (0.13 g, 0.75 mmol) under argon and the reaction mixture was stirred at 160 °C neat for 3 h. After cooling to room temperature, the reaction mixture was diluted with dichloromethane (10 mL) and washed with 0.1 M NaOH (10 mL). The aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude material was purified using flash column chromatography eluting with 1% methanol and 1% triethylamine in dichloromethane to give *N*-(1-naphthyl)-*N′*-(3-nitrophenyl)-*N′*-methylguanidine as a viscous oil (0.20 g, 84%). ν_{max}/cm^{-1} (neat) 3485 (NH), 3386 (NH), 2924 (CH), 1631, 1567, 1522 (NO), 1482, 1379, 1345 (NO), 1234, 960, 854, 783, 771, 732, 684; δ_H (400 MHz, $CDCl_3$) 3.60 (3H, s, NCH_3), 7.02 (1H, dd, *J* 7.2, 1.0 Hz, 2'-H), 7.39–7.58 (5H, m, 5 × ArH), 7.72 (1H, ddd, *J* 8.1, 2.1, 1.0 Hz, 6-H), 7.79–7.86 (1H, m, ArH), 8.03 (1H, ddd, *J* 8.1, 2.1, 1.0 Hz, 4-H), 8.07–8.13 (1H, m, ArH), 8.23 (1H, t, *J* 2.1 Hz, 2-H); δ_C (101 MHz, $CDCl_3$) 39.0 (CH_3), 117.5 (CH), 120.1 (CH), 120.6 (CH), 122.8 (CH), 124.0 (CH), 125.4 (CH), 126.2 (CH), 126.5 (CH), 128.1 (CH), 128.6 (C), 130.2 (CH), 131.9 (CH), 134.9 (C), 145.9 (C), 146.5 (C), 149.1 (C), 150.1 (C); *m/z* (ESI) 321.1333 (MH^+. $C_{18}H_{17}N_4O_2$ requires 321.1346).

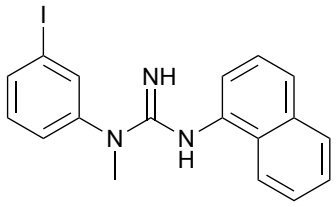
_N_-(1-Naphthyl)-_N′_-(3-aminophenyl)-_N′_-methylguanidine



The reaction was carried out according to the previously described procedure for ethyl 7-amino-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate using *N*-(1-naphthyl)-*N′*-(3-nitrophenyl)-*N′*-methylguanidine (0.23 g, 0.73 mmol) and tin(II) chloride dihydrate (0.82 g, 3.6 mmol) in ethanol (10 mL). The reaction mixture was stirred under reflux for 16 h to give *N*-(1-naphthyl)-*N′*-(3-aminophenyl)-*N′*-methylguanidine as a brown solid (0.12 g, 95%). Mp 96−98 °C; ν_{max}/cm^{-1} (neat) 3322 (NH), 3200 (NH), 3051, 1618, 1599, 1580, 1560, 1491, 1383, 1275, 1227, 970, 781, 750; δ_H (400 MHz, $CDCl_3$) 3.50 (3H, s, NCH_3), 6.53 (1H, ddd,

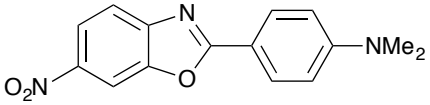
J 7.9, 2.2, 0.9 Hz, 4-H), 6.63 (1H, t, *J* 2.2 Hz, 2-H), 6.70 (1H, ddd, *J* 7.9, 2.2, 0.9 Hz, 6-H), 7.05 (1H, dd, *J* 7.4, 1.1 Hz, 2'-H), 7.15 (1H, t, *J* 7.9 Hz, 5-H), 7.40 (1H, dd, *J* 8.4, 7.4 Hz, 3'-H), 7.43–7.49 (2H, m, 2 × ArH), 7.52 (1H, br d, *J* 8.4 Hz, 4'-H), 7.78–7.84 (1H, m, ArH), 8.13–8.19 (1H, m, ArH); δ_C (101 MHz, $CDCl_3$) 39.0 (CH_3), 113.4 (CH), 113.5 (CH), 116.7 (CH), 118.4 (CH), 122.5 (CH), 124.1 (CH), 125.2 (CH), 126.0 (CH), 126.4 (CH), 128.0 (CH), 129.2 (C), 130.6 (CH), 134.9 (C), 145.5 (C), 145.7 (C), 148.0 (C), 151.2 (C); *m/z* (EI) 290.1528 (M^+. $C_{18}H_{18}N_4$ requires 290.1531), 247 (11%), 234 (10), 168 (22), 122 (56), 93 (8).

_N_-(1-Naphthyl)-_N′_-(3-iodophenyl)-_N′_-methylguanidine (CNS1261)



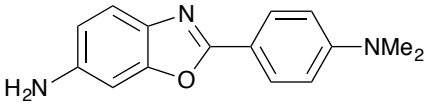
The reaction was carried out according to the previously described general procedure for 4-iodonitrobenzene using *N*-(1-naphthyl)-*N′*-(3-aminophenyl)-*N′*-methylguanidine (0.061 g, 0.21 mmol), *p*-toluenesulfonic acid monohydrate (0.12 g, 0.62 mmol), polymer-supported nitrite (0.18 g, containing 0.62 mmol of NO_2) and sodium iodide (0.062 g, 0.41 mmol). The reaction mixture was stirred at room temperature for 16 h. Purification by flash column chromatography eluting with 60−100% ethyl acetate in petroleum ether gave *N*-(1-naphthyl)-*N′*-(3-iodophenyl)-*N′*-methylguanidine as a viscous oil (0.049 g, 58%). ν_{max}/cm^{-1} (neat) 3482 (NH), 3385 (NH), 3053, 2924 (CH), 1624, 1557, 1474, 1376, 1266, 1233, 943, 782, 693; δ_H (400 MHz, $CDCl_3$) 3.53 (3H, s, NCH_3), 7.03 (1H, dd, *J* 7.2, 1.1 Hz, 2'-H), 7.13 (1H, t, *J* 8.0 Hz, 5-H), 7.35 (1H, ddd, *J* 8.0, 2.0, 0.9 Hz, 6-H), 7.41 (1H, dd, *J* 8.1, 7.2, Hz, 3'-H), 7.44–7.49 (2H, m, 2 × ArH), 7.52 (1H, br d, *J* 8.1 Hz, 4'-H), 7.58 (1H, ddd, *J* 8.0, 2.0, 0.9 Hz, 4-H), 7.73 (1H, t, *J* 2.0 Hz, 2-H), 7.79–7.85 (1H, m, ArH), 8.09–8.16 (1H, m, ArH); δ_C (101 MHz, $CDCl_3$) 39.2 (CH_3), 94.6 (C), 117.9 (CH), 122.6 (CH), 124.1 (CH), 125.3 (CH), 126.1 (CH), 126.2 (CH), 126.5 (CH), 128.1 (CH), 129.0 (C), 131.1 (CH), 134.9 (C), 135.5 (CH), 135.9 (CH), 145.9 (C), 146.2 (C), 150.5 (C); *m/z* (ESI) 402.0445 (MH^+. $C_{18}H_{17}IN_3$ requires 402.0462).

2-(4'-Dimethylaminophenyl)-6-nitrobenzoxazole



4-(Dimethylamino)benzoic acid (0.530 g, 3.25 mmol), 5-nitro-2-aminophenol (0.500 g, 3.25 mmol) and boric acid (0.200 g, 3.25 mmol) in *p*-xylene (50 mL) were stirred under Dean-Stark conditions for 72 h. After cooling to room temperature, the reaction mixture was filtered and washed with xylene before concentrating *in vacuo*. Water was added to the residue (20 mL) and the mixture made basic with 1 M sodium hydroxide solution. The aqueous layer was extracted with dichloromethane (3 × 20 mL) and the organic layers combined, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude material was purified using flash column chromatography eluting with 40% ethyl acetate in petroleum ether (40–60) to give 2-(4'-dimethylaminophenyl)-6-nitrobenzoxazole as an orange solid (0.485 g, 54%). Mp 215−217 °C; ν_{max}/cm^{-1} (neat) 3422, 3315, 2924 (CH), 1615 (C=C), 1510, 1491, 1357, 822; δ_H (500 MHz, $CDCl_3$) 3.10 (6H, s, 2 × NCH_3), 6.75 (2H, d, *J* 9.1 Hz, 3'-H and 5'-H), 7.69 (1H, d, *J* 8.7 Hz, 4-H), 8.10 (2H, d, *J* 9.1 Hz, 2'-H and 6'-H), 8.26 (1H, dd, *J* 8.7, 2.1 Hz, 5-H), 8.37 (1H, d, *J* 2.1 Hz, 7-H); δ_C (126 MHz, $CDCl_3$) 40.2 (2 × CH_3), 106.7 (CH), 111.7 (2 × CH), 112.5 (C), 118.5 (CH), 120.9 (CH), 130.1 (2 × CH), 144.2 (C), 148.6 (C), 149.9 (C), 153.3 (C), 168.9 (C); *m/z* (EI) 283.0956 (M^+. $C_{15}H_{13}N_3O_3$ requires 283.0957), 253 (31%), 209 (48), 145 (11).

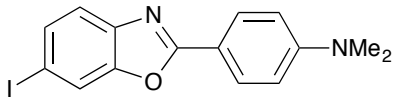
2-(4'-Dimethylaminophenyl)-6-aminobenzoxazole



The reaction was carried out according to the previously described procedure for ethyl 7-amino-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate using 2-(4'-dimethylaminophenyl)-6-nitrobenzoxazole (0.12 g, 0.42 mmol) and tin(II) chloride dihydrate (0.48 g, 2.1 mmol) in ethanol (10 mL). The reaction mixture was stirred under reflux for 16 h. The crude material was purified using flash column chromatography eluting with 1−5% methanol in dichloromethane to give 2-(4'-dimethylaminophenyl)-6-aminobenzoxazole as an orange solid (0.089 g, 83%). Mp 186−187 °C; ν_{max}/cm^{-1} (neat) 3430 (NH), 3314 (NH), 2916 (CH), 1613

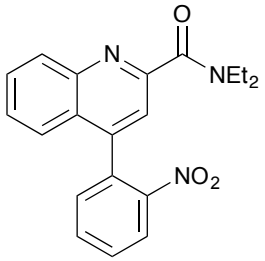
(C=C), 1508, 1489, 1356, 1126, 949, 820; δ_H (500 MHz, $CDCl_3$) 3.05 (6H, s, 2 × NCH_3), 6.65 (1H, dd, *J* 8.4, 2.1 Hz, 5-H), 6.75 (2H, d, *J* 9.0 Hz, 3'-H and 5'-H), 6.84 (1H, d, *J* 2.1 Hz, 7-H), 7.45 (1H, d, *J* 8.4 Hz, 4-H), 8.03 (2H, d, *J* 9.0 Hz, 2'-H and 6'-H); δ_C (126 MHz, $CDCl_3$) 40.3 (2 × CH_3), 96.8 (CH), 111.8 (2 × CH), 112.8 (CH), 115.0 (C), 119.4 (CH), 128.6 (2 × CH), 135.3 (C), 144.1 (C), 151.9 (C), 152.1 (C), 162.6 (C); *m/z* (CI) 254.1289 (MH^+. $C_{15}H_{16}N_3O$ requires 254.1293), 165 (3%), 113 (4), 69 (12).

2-(4'-Dimethylaminophenyl)-6-iodobenzoxazole (IBOX, 5e)[11]



The reaction was carried out according to the previously described general procedure for 4-iodonitrobenzene using 2-(4'-dimethylaminophenyl)-6-aminobenzoxazole (0.050 g, 0.20 mmol), *p*-toluenesulfonic acid monohydrate (0.11 g, 0.60 mmol), polymer-supported nitrite (0.17 g, containing 0.60 mmol of NO_2) and sodium iodide (0.060 g, 0.40 mmol). The reaction mixture was heated to 60 °C and stirred for 16 h. Purification by flash column chromatography eluting with 20% ethyl acetate in petroleum ether (40–60) gave 2-(4'-dimethylaminophenyl)-6-iodobenzoxazole as a yellow solid (0.040 g, 59%). Mp 183−184 °C; δ_H (400 MHz, $CDCl_3$) 3.08 (6H, s, 2 × NCH_3), 6.77 (2H, d, *J* 9.0 Hz, 3'-H and 5'-H), 7.43 (1H, d, *J* 8.4 Hz, 4-H), 7.60 (1H, dd, *J* 8.4, 1.4 Hz, 5-H), 7.86 (1H, d, *J* 1.4 Hz, 7-H), 8.08 (2H, d, *J* 9.0 Hz, 2'-H and 6'-H); δ_C (101 MHz, $CDCl_3$) 40.3 (2 × CH_3), 86.5 (C), 111.9 (2 × CH), 113.8 (C), 119.5 (CH), 120.7 (CH), 129.5 (2 × CH), 133.5 (CH), 142.7 (C), 151.5 (C), 152.7 (C), 164.6 (C); *m/z* (ESI) 387 (MNa^+. 100%). Spectroscopic data was in agreement with previously published data.[11]

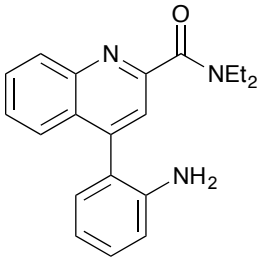
4-(2'-Nitrophenyl)-*N,N*-diethylquinoline-2-carboxamide



Ethyl 4-(2'-nitrophenyl)quinoline-2-carboxylate (0.380 g, 1.18 mmol) was dissolved in 50% aqueous ethanol (20 mL) before addition of ground sodium hydroxide (0.190 g, 4.72 mmol). The mixture was stirred under reflux for 16 h. After cooling to room temperature, the ethanol was removed *in vacuo* and the water layer acidified (pH 4) with 1 M hydrochloric acid solution. The product was extracted with dichloromethane (3 × 50 mL), washed with water (2 × 50 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give 4-(2'-nitrophenyl)quinoline-2-carboxylic acid as a brown solid (0.320 g, 92%), which was used without further purification. 4-(2'-Nitrophenyl)quinoline-2-carboxylic acid (0.090 g, 0.30 mmol) was dissolved in *N,N'*-dimethylformamide (10 mL), before addition of triethylamine (61 μL, 0.44 mmol) and *N,N,N',N'*-tetramethyl-*O*-(1*H*-benzotriazol-1-yl)uronium hexafluorophosphate (0.12 g, 0.32 mmol). The mixture was stirred at room temperature for 1 h and then heated to 50 °C, with the addition of diethylamine (30 μL, 0.44 mmol). The reaction mixture was stirred at 50 °C for 16 h. Water was added and the mixture stirred for an additional 1 h. After cooling to room temperature, the reaction mixture was diluted in ethyl acetate (20 mL) and washed with a 5% aqueous solution of lithium chloride (3 × 20 mL), followed by brine (20 mL). The organic layer was dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude material was purified using flash column chromatography eluting with 60% ethyl acetate in petroleum ether (40–60) to give 4-(2'-nitrophenyl)-*N,N*-diethylquinoline-2-carboxamide as a colourless oil (0.055 g, 54%). ν_{max}/cm^{-1} (neat) 2974 (CH), 1630 (C=O), 1528, 1346, 1275, 1098, 766; δ_H (400 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.2 Hz, NCH_2CH_3), 1.32 (3H, t, *J* 7.2 Hz, NCH_2CH_3), 3.40–3.72 (4H, m, 2 × NCH_2CH_3), 7.42 (1H, dd, *J* 8.4, 1.2 Hz, ArH), 7.47–7.53 (2H, m, 2 × ArH), 7.55 (1H, s, 3-H), 7.66–7.80 (3H, m, 3 × ArH), 8.16–8.24 (2H, m, 2 × ArH); δ_C (101 MHz, $CDCl_3$) 13.1 (CH_3), 14.6 (CH_3), 40.7 (CH_2), 43.7 (CH_2), 119.9 (CH), 124.6 (CH), 124.9 (CH), 126.4 (C), 128.1 (CH), 129.9 (CH), 130.2 (CH), 130.5

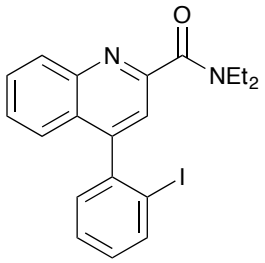
(CH), 132.5 (CH), 132.9 (C), 133.5 (CH), 145.9 (C), 146.9 (C), 148.8 (C), 154.4 (C), 168.5 (C); *m/z* (ESI) 372.1303 (MNa^+. $C_{20}H_{19}N_3O_3Na$ requires 372.1319).

4-(2'-Aminophenyl)-*N,N*-diethylquinoline-2-carboxamide



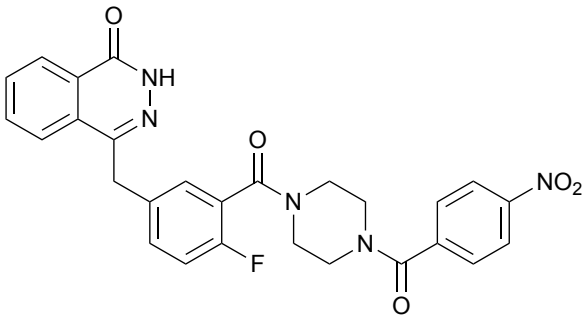
4-(2'-Nitrophenyl)-*N,N*-diethylquinoline-2-carboxamide (0.050 g, 0.15 mmol) was dissolved in ethanol (2 mL) before addition of tin(II) chloride dihydrate (0.18 g, 0.77 mmol). The solution was stirred under reflux for 16 h. After cooling to room temperature, the reaction was quenched by addition of a saturated aqueous solution of sodium hydrogen carbonate and the product was extracted with ethyl acetate (3 × 5 mL). The organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The crude material was purified using flash column chromatography eluting with 1% methanol in dichloromethane to give 4-(2'-aminophenyl)-*N,N*-diethylquinoline-2-carboxyamide as a colourless oil (0.045 g, 91%). ν_{max}/cm^{-1} (neat) 3348 (NH), 2973 (CH), 1620 (C=O), 1486, 1451, 1275, 1099, 750; δ_H (500 MHz, $CDCl_3$) 1.27 (3H, t, *J* 7.2 Hz, NCH_2CH_3), 1.32 (3H, t, *J* 7.2 Hz, NCH_2CH_3), 3.42–3.67 (6H, m, 2 × NCH_2CH_3 and NH_2), 6.83 (1H, dd, *J* 8.2, 1.2 Hz, ArH), 6.88 (1H, td, *J* 8.2, 1.2 Hz, ArH), 7.14 (1H, dd, *J* 8.2, 1.2 Hz, ArH), 7.28 (1H, td, *J* 8.2, 1.2 Hz, ArH), 7.53 (1H, ddd, *J* 8.2, 7.2, 1.2 Hz, ArH), 7.64 (1H, s, 3-H), 7.71–7.78 (2H, m, 2 × ArH), 8.17 (1H, d, *J* 8.2 Hz, ArH); δ_C (126 MHz, $CDCl_3$) 13.1 (CH_3), 14.6 (CH_3), 40.5 (CH_2), 43.6 (CH_2), 115.9 (CH), 118.6 (CH), 121.4 (CH), 122.7 (C), 126.2 (CH), 126.7 (C), 127.6 (CH), 129.9 (CH), 130.2 (CH), 130.4 (CH), 130.8 (CH), 143.9 (C), 147.3 (C), 147.4 (C), 155.0 (C), 168.8 (C); *m/z* (ESI) 320.1743 (MH^+. $C_{20}H_{22}N_3O$ requires 320.1757).

4-(2-Iodophenyl)-*N,N*-diethylquinoline-2-carboxamide[2]



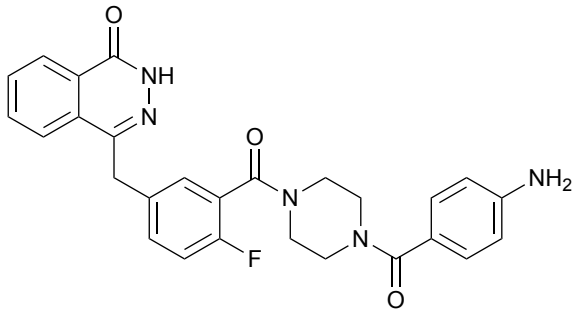
The reaction was carried out according to the previously described general procedure for 4-iodonitrobenzene using 4-(2-aminophenyl)-*N,N*-diethylquinoline-2-carboxamide (0.040 g, 0.12 mmol), *p*-toluenesulfonic acid monohydrate (0.070 g, 0.38 mmol), polymer-supported nitrite (0.11 g, containing 0.38 mmol of NO_2) and sodium iodide (0.038 g, 0.25 mmol). The reaction mixture was heated to 60 °C and stirred for 16 h. The crude material was purified using flash column chromatography eluting with 40% ethyl acetate in petroleum ether (40–60) to give 4-(2-iodophenyl)-*N,N*-diethylquinoline-2-carboxamide as a pale yellow solid (0.037 g, 67%). Mp 58−59 °C (lit.[2] 64−66 °C); δ_H (500 MHz, $CDCl_3$) 1.25 (3H, t, *J* 7.1 Hz, NCH_2CH_3), 1.33 (3H, t, *J* 7.1 Hz, NCH_2CH_3), 3.38–3.60 (2H, m, NCH_2CH_3), 3.63 (2H, q, *J* 7.1 Hz, NCH_2CH_3), 7.18 (1H, td, *J* 7.8, 1.6 Hz, 4'-H), 7.33 (1H, dd, *J* 7.8, 1.6 Hz, 5-H), 7.44–7.55 (4H, m, 3-H, 6-H, 5'-H and 6'-H), 7.75 (1H, ddd, *J* 8.4, 7.8, 1.6 Hz, 7-H), 8.01 (1H, dd, *J* 7.8, 1.6 Hz, 3'-H), 8.19 (1H, d, *J* 8.4 Hz, 8-H); δ_C (126 MHz, $CDCl_3$) 13.1 (CH_3), 14.7 (CH_3), 40.6 (CH_2), 43.6 (CH_2), 98.5 (C), 120.8 (CH), 125.9 (CH), 126.5 (C), 127.6 (CH), 128.3 (CH), 130.1 (CH), 130.1 (CH), 130.2 (CH), 130.3 (CH), 139.5 (CH), 142.6 (C), 147.2 (C), 151.3 (C), 154.5 (C), 168.7 (C); *m/z* (EI) 430.0543 (M^+. $C_{20}H_{19}IN_2O$ requires 430.0542), 359 (84%), 331 (91), 294 (23), 203 (100), 176 (26), 149 (26), 72 (78), 69 (31).

4-[3'-[4''-(4'''-Nitrobenzoyl)piperazine-1''-carbonyl]-4'-fluorobenzyl]-2*H*-phthalazin-1-one



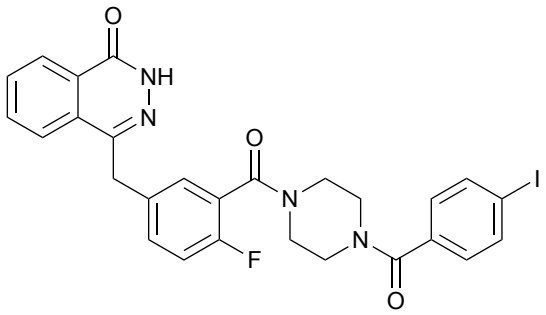
To a solution of 4-nitrobenzoic acid (92.0 mg, 0.550 mmol) in *N,N'*-dimethylformamide (6 mL) was added triethylamine (119 µL, 0.880 mmol), followed by *O*-benzotriazole-*N*,*N*,*N*',*N*'-tetramethyluroniumhexafluorophosphate (231 mg, 0.610 mmol) and the mixture was stirred at room temperature for 2 h. 4-[4'-Fluoro-3'-(piperazine-1''-carbonyl)benzyl]-2*H*-phthalazin-1-one (200 mg, 0.550 mmol) was added and the mixture was stirred at room temperature for a further 48 h. Water (12 mL) was then added, followed by 1 h of stirring, after which the mixture was cooled to 0 °C. The resulting precipitate was collected by vacuum filtration, washed with water (4 × 20 mL) and dried *in vacuo* to yield 4-[3'-[4''-(4'''-nitrobenzoyl)piperazine-1''-carbonyl]-4'-fluorobenzyl]-2*H*-phthalazin-1-one (239.0 mg, 84%) as an orange foam. NMR spectra showed a 60:40 mixture of rotamers. Only data for the major rotamer were recorded. ν_{max}/cm^{-1} (neat) 3167 (NH), 3012 (CH), 2905 (CH), 1638 (CO), 1599 (C=C), 1346, 1433, 1265, 1005, 766, 735; δ_H (400 MHz, d_6-DMSO) 3.22 (2H, br s, N-CH_2), 3.38 (2H, br s, NCH_2), 3.57–3.86 (4H, m, NCH_2), 4.39 (2H, d, *J* 18.6 Hz, 7'-*H*H and 7'-H*H*), 7.21–7.53 (3H, m, 2'-H, 5'-H and 6'-H), 7.69–8.05 (5H, m, 5-H, 6-H, 7-H, 2'''-H and 6'''-H), 8.25–8.38 (3H, m, 8-H, 3'''-H and 5'''-H), 12.65 (1H, br s, NH); δ_c (101 MHz, d_6-DMSO) 37.5 (CH_2), 41.8 (2 × CH_2), 46.6 (2 × CH_2), 116.0 (d, *J* 18.2 Hz, CH), 123.5 (d, *J* 18.0 Hz, C), 123.9 (2 × CH), 125.5 (CH), 126.2 (CH), 127.9 (C), 128.5 (2 × CH), 129.0 (CH), 129.1 (C), 131.7 (CH), 131.9 (d, *J* 8.8 Hz, CH), 133.6 (CH), 134.9 (d, *J* 3.4 Hz, C), 141.9 (C), 145.0 (C), 148.0 (C), 156.5 (d, *J* 245.7 Hz, C), 159.5 (C), 164.2 (C), 167.5 (C); *m/z* (ESI) 538.1488 (MNa^+. $C_{27}H_{22}FN_5NaO_5$ requires 538.1497).

4-[3'-[4''-(4'''-Aminobenzoyl)piperazine-1''-carbonyl]-4'-fluorobenzyl]-2*H*-phthalazin-1-one



The reaction was carried out according to the previously described procedure for ethyl 7-amino-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate using 4-[3'-[4''-(4'''-nitrobenzoyl)piperazine-1''-carbonyl]-4'-fluorobenzyl]-2*H*-phthalazin-1-one (55.0 mg, 0.107 mmol) and tin(II) chloride dihydrate (120 mg, 0.533 mmol) in ethanol (10 mL). The suspension was stirred under reflux for 16 h after which the mixture was cooled to ambient temperature and a saturated solution of sodium hydrogen carbonate (12 mL) was added. The product was extracted into ethyl acetate (3 × 10 mL), dried ($MgSO_4$), filtered and concentrated *in vacuo* to give 4-[3'-[4''-(4'''-aminobenzoyl)piperazine-1''-carbonyl]-4'-fluorobenzyl]-2*H*-phthalazin-1-one (45.0 mg, 87%) as an orange foam. ν_{max}/cm^{-1} (neat) 3347 (NH), 2924 (CH), 1605 (CO), 1424, 1256, 1177, 1003, 748, 729; δ_H (400 MHz, $CDCl_3$) 3.30 (2H, br s, NCH_2), 3.49–4.16 (8H, m, 3 × NCH_2, and 4'''-NH_2), 4.27 (2H, s, 7'-H_2), 6.61 (2H, d, *J* 8.4 Hz, 3'''-H and 5'''-H), 7.01 (1H, t, *J* 8.7 Hz, 5'-H), 7.22 (2H, d, *J* 8.4 Hz, 2'''-H and 6'''-H), 7.28–7.36 (2H, m, 2'-H and 6'-H), 7.66–7.77 (3H, m, 5-H, 6-H and 7-H), 8.42–8.48 (1H, m, 8-H), 11.61 (1H, s, NH); δ_c (101 MHz, $CDCl_3$) 37.5 (CH_2), 42.1 (2 × CH_2), 47.0 (2 × CH_2), 114.0 (2 × CH), 116.0 (d, *J* 22.0 Hz, CH), 123.6 (d, *J* 17.9 Hz, C), 123.9 (C), 124.9 (CH), 127.0 (CH), 128.1 (C), 129.1 (d, *J* 3.6 Hz, CH), 129.3 (2 × CH), 129.4 (C), 131.5 (CH), 131.6 (d, *J* 8.1 Hz, CH), 133.5 (CH), 134.3 (d, *J* 3.5 Hz, C), 145.4 (C), 148.6 (C), 156.8 (d, *J* 247.6 Hz, C), 160.7 (C), 165.1 (C), 171.1 (C); *m/z* (ESI) 508.1912 (MNa^+. $C_{27}H_{24}FN_5NaO_3$ requires 508.1902).

4-[3'-[4''-(4'''-Iodobenzoyl)piperazine-1''-carbonyl]-4'-fluorobenzyl]-2*H*-phthalazin-1-one[3]



The reaction was carried out according to the previously described general procedure for 4-iodonitrobenzene using 4-[3'-[4''-(4'''-aminobenzoyl)piperazine-1''-carbonyl]-4'-fluorobenzyl]-2*H*-phthalazin-1-one (30.0 mg, 0.035 mmol), *p*-toluenesulfonic acid monohydrate (20.0 mg, 0.105 mmol), polymer-supported nitrite (30.0 mg, containing 0.105 mmol of NO_2) and sodium iodide (10.5 mg, 0.070 mmol). The reaction mixture was stirred at room temperature for 1 h. Purification by flash column chromatography, using 4% methanol in dichloromethane gave 4-[3'-[4''-(4'''-iodobenzoyl)piperazine-1''-carbonyl]-4'-fluorobenzyl]-2*H*-phthalazin-1-one (28.0 mg, 67%) as a white foam. ν_{max}/cm^{-1} (neat) 3198 (NH), 2899 (CH), 1628 (CO), 1587 (C=C), 1427, 1254, 1225, 1001, 747; δ_H (400 MHz, $CDCl_3$) 3.14–4.02 (8H, m, 4 × NCH_2), 4.29 (2H, s, 7'-H_2), 7.03 (1H, t, *J* 7.8 Hz, 5'-H), 7.14 (2H, d, *J* 8.0 Hz, 3'''-H and 5'''-H), 7.29–7.37 (2H, m, 2'-H and 6'-H), 7.67–7.84 (5H, m, ArH), 8.42–8.51 (1H, m, 8-H), 10.96 (1H, br s, NH); δ_c (101 MHz, $CDCl_3$) 37.8 (CH_2), 42.2 (2 × CH_2), 47.3 (2 × CH_2), 96.6 (C), 116.3 (d, *J* 21.7 Hz, CH), 123.6 (d, *J* 17.7 Hz, C), 125.1 (CH), 127.3 (CH), 128.4 (C), 128.9 (2 × CH), 129.4 (d, *J* 3.6 Hz, CH), 129.6 (C), 131.8 (CH), 131.9 (d, *J* 8.0 Hz, CH), 133.8 (CH), 134.5 (C), 134.6 (d, *J* 3.7 Hz, C), 138.0 (2 × CH), 145.6 (C), 157.1 (d, *J* 247.1 Hz, C), 160.7 (C), 165.3 (C), 169.8 (C); *m/z* (ESI) 619.0597 (MNa^+. $C_{27}H_{22}FIN_4NaO_3$ requires 619.0613).

3. Radiochemistry Methodology

General Experimental for Radioiodination of Anilines with [^{125}I]NaI

Reductant free [^{125}I]NaI was purchased from Perkin Elmer (product number NEZ033H005MC) with a concentration of 12.95 GBq/mL and specific radioactivity of 643.8 GBq/mg in 0.1 M NaOH (pH 12–14) aqueous solution. All radiochemical yields were determined by radio-HPLC analysis of the crude product.

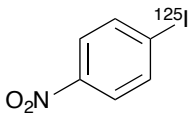
Analytical Radio-HPLC Method for determination of Radioiodide incorporation

Analytical HPLC was performed with a Dionex Ultimate 3000 HPLC system equipped with a Flowstar LB 513 NaI scintillation detector and a DAD-3000 UV detector using a Synergi 4 µm Hydro-RP 80 Å column (150 × 4.6 mm) with 10 mm guard cartridge, UV 254 nm and flow 1 mL/min. The mobile phase for the analysis of substrates was water:acetonitrile. Analysis of the reaction mixture (to assess radioiodide incorporation) used a gradient profile of water and acetonitrile, as shown below.

Time (mins)	%MeCN
0–20	10–95
20–24	95
24–25	95–10
25–30	10

Co-elution with the UV signal from the ^{127}I-compound was used to confirm identity of the ^{125}I-product from each reaction described.

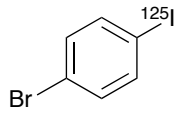
General Method for Radiodination: 4-[^{125}I]Iodonitrobenzene (2a)



To a solution of *p*-toluenesulfonic acid monohydrate (2.1 mg, 11.0 µmol) in acetonitrile (0.2 mL) was added 4-nitroaniline (0.50 mg, 3.6 µmol). The solution was cooled in a water bath to 10–15 °C. Polymer-supported nitrite (3.2 mg, containing 11.0 µmol of NO_2) was added and the reaction mixture was stirred for 0.25 h. A 4–6

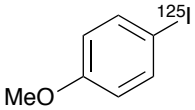
MBq solution of [^{125}I]NaI in water (0.01 mL) was added and the reaction mixture warmed to 20 °C and stirred for 2 h. The mixture was removed from the resin by syringe and diluted by the addition of water (0.2 mL). Analysis of this solution by analytical radio-HPLC showed a radiochemical yield of 93%.

4-[^{125}I]Iodobromobenzene (2b)



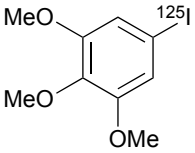
The reaction was done using 4-bromoaniline (1.0 mg, 5.8 μmol) in acetonitrile (0.2 mL) as described in the general method except for the following: six equivalents of both polymer-supported nitrite and *p*-toluenesulfonic acid monohydrate were used. Analysis by radio-HPLC gave a radiochemical yield of 73%.

4-[^{125}I]Iodoanisole (2c)



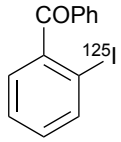
The reaction was done using 4-methoxyaniline (0.50 mg, 4.1 μmol) as described in the general method except for the following: six equivalents of both polymer-supported nitrite and *p*-toluenesulfonic acid monohydrate were used and the reaction was performed at 40 °C. Analysis by radio-HPLC gave a radiochemical yield of 97%.

3,4,5-Trimethoxy-[^{125}I]iodobenzene (2d)



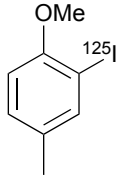
The reaction was done using 3,4,5-trimethoxyaniline (1.0 mg, 5.5 μmol) in acetonitrile (0.2 mL) as described in the general method except for the following: six equivalents of both polymer-supported nitrite and *p*-toluenesulfonic acid monohydrate were used. Analysis by radio-HPLC gave a radiochemical yield of 94%.

2-[^{125}I]Iodobenzophenone (2e)



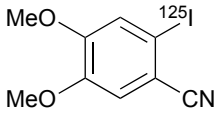
The reaction was done using 2-aminobenzophenone (0.5 mg, 2.5 μmol) in acetonitrile (0.2 mL) as described in the general method except for the following: six equivalents of both polymer-supported nitrite and *p*-toluenesulfonic acid monohydrate were used and the reaction required 4 h. Analysis by radio-HPLC gave a radiochemical yield of 94%.

2-[^{125}I]Iodo-4-methylanisole (2f)



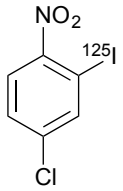
The reaction was performed using 2-methoxy-5-methylaniline (0.50 mg, 3.6 μmol) in acetonitrile (0.2 mL) as described in the general method except for the following: one equivalent of both polymer-supported nitrite and *p*-toluenesulfonic acid monohydrate were used. Analysis by radio-HPLC gave a radiochemical yield of 83%.

4,5-Dimethoxy-2-[^{125}I]iodobenzonitrile (2g)



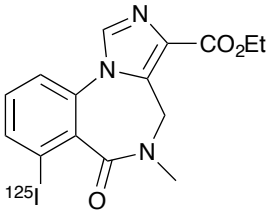
The reaction was performed using 2-amino-4,5-dimethoxybenzonitrile (1.0 mg, 5.6 μmol) in acetonitrile (0.2 mL) as described in the general method except for the following: six equivalents of both polymer-supported nitrite and *p*-toluenesulfonic acid monohydrate were used. Analysis by radio-HPLC gave a radiochemical yield of 61%.

4-Chloro-2-[^{125}I]iodonitrobenzene (2h)



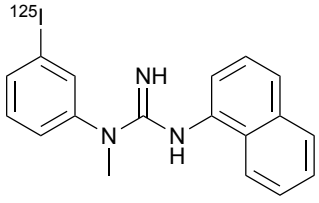
The reaction was done using 2-nitro-5-chloroaniline (0.50 mg, 2.9 μmol) in acetonitrile (0.2 mL) as described in the general method except for the following: one equivalent of both polymer-supported nitrite and *p*-toluenesulfonic acid monohydrate were used. Analysis by radio-HPLC gave a radiochemical yield of 64%.

Ethyl 7-[^{125}I]iodo-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate (2i)



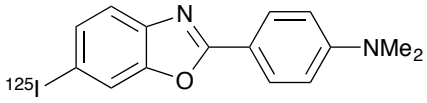
The reaction was performed using ethyl 7-amino-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate (0.50 mg, 1.7 μmol) as described in the general method except for the following: six equivalents of both polymer-supported nitrite and *p*-toluenesulfonic acid monohydrate were used and the reaction was performed at 60 °C. Analysis by radio-HPLC gave a radiochemical yield of 92%.

***N*-(1-Naphthyl)-*N′*-(3-[^{125}I]iodophenyl)-*N′*-methylguanidine (2j)**



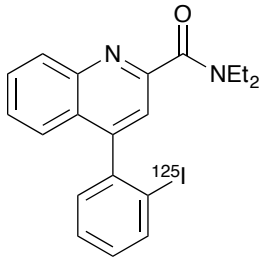
The reaction was performed using *N*-(1-naphthyl)-*N′*-(3-aminophenyl)-*N′*-methylguanidine (1.0 mg, 3.4 μmol) as described in the general method except for the following: six equivalents of both polymer-supported nitrite and *p*-toluenesulfonic acid monohydrate were used and the reaction was performed at 60 °C. Analysis by radio-HPLC gave a radiochemical yield of 64%.

2-(4'-Dimethylaminophenyl)-6-[^{125}I]iodobenzoxazole (2k)



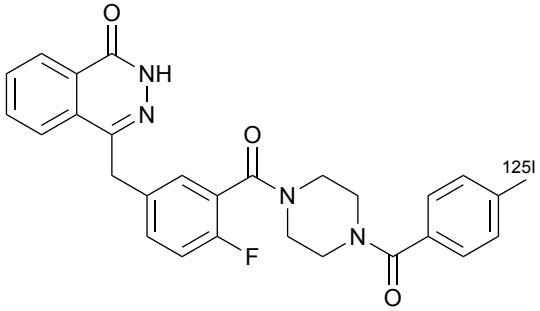
The reaction was performed using 2-(4'-dimethylaminophenyl)-6-aminobenzoxazole (1.0 mg, 4.0 µmol) as described in the general method except for the following: six equivalents of both polymer-supported nitrite and *p*-toluenesulfonic acid monohydrate were used. Analysis by radio-HPLC gave a radiochemical yield of 47%.

4-(2-[^{125}I]Iodophenyl)-*N,N*-diethylquinoline-2-carboxamide (2l)



The reaction was performed using 4-(2-aminophenyl)-*N,N*-diethylquinoline-2-carboxamide (0.50 mg, 1.6 µmol) as described in the general method except for the following: six equivalents of both polymer-supported nitrite and *p*-toluenesulfonic acid monohydrate were used and the reaction was performed at 60 °C. Analysis by radio-HPLC gave a radiochemical yield of 50%.

4-{3'-[4"-(4'"-[^{125}I]iodobenzoyl)piperazine-1"-carbonyl]-4'-fluorobenzyl}-2*H*-phthalazin-1-one (2m)

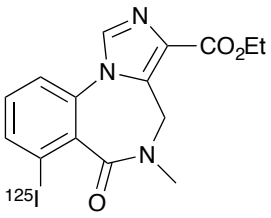


The reaction was performed using 4-{3'-[4"-(4'"-aminobenzoyl)piperazine-1"-carbonyl]-4'-fluorobenzyl}-2*H*-phthalazin-1-one (0.50 mg, 1.0 µmol) in acetonitrile (0.2 mL) as described in the general method except for the following: six equivalents of both polymer-supported nitrite and *p*-toluenesulfonic acid monohydrate were used. Analysis by radio-HPLC gave a radiochemical yield of 59%.

Semi-Preparative Radio-HPLC Method for Purification of Ethyl 7-[^{125}I]iodo-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate (2i): Semi-preparative HPLC was performed with a Dionex Ultimate 3000 HPLC system equipped with a Knauer Advanced Scientific Instruments Smartline UV Detector 2500 and a photomultiplier tube (PMT) connected to a Lab Logic Flow-Count radiodetector and using a Synergi 4 µm Hydro-RP 80 Å column (150 × 10 mm) with 10 mm guard cartridge, UV 254 nm and flow 3 mL/min. A gradient profile of water and acetonitrile was used, as shown below.

Time (mins)	%MeCN
0–20	10–95
20–24	95
24–25	95–10
25–30	10

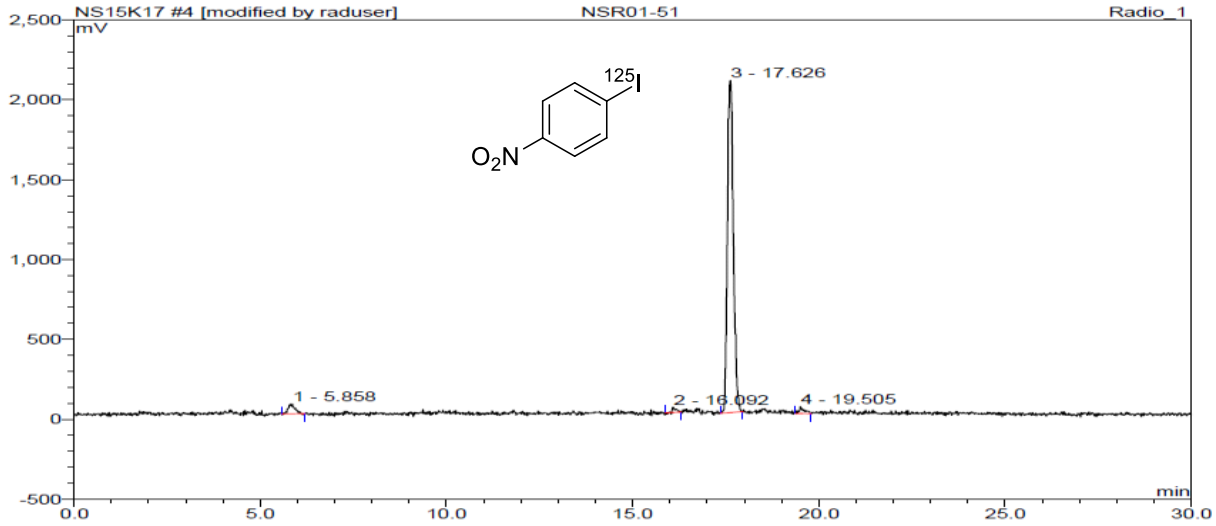
Synthesis and Purification of Ethyl 7-[^{125}I]iodo-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate (2i)

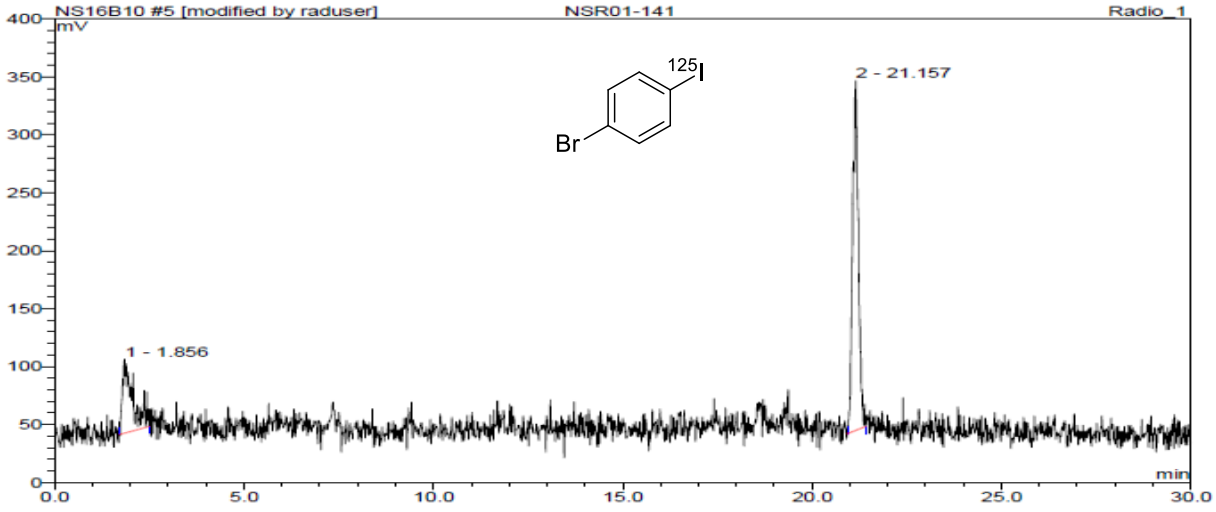


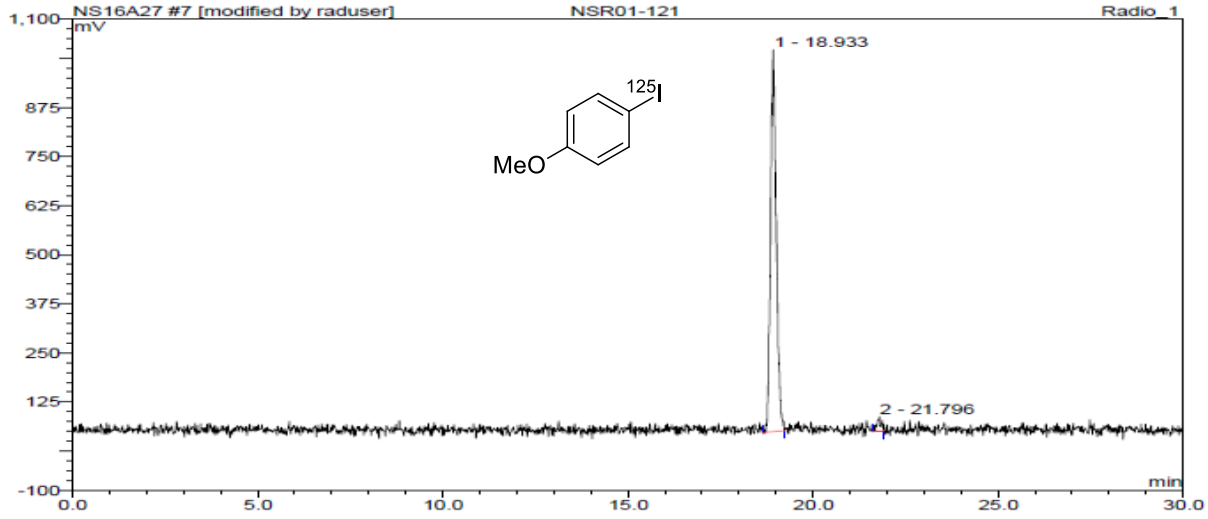
To a solution of *p*-toluenesulfonic acid monohydrate (2.1 mg, 11.0 µmol) in acetonitrile (0.2 mL) was added ethyl 7-amino-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate (0.50 mg, 1.7 µmol). The solution was cooled in a water bath to 10–15 °C. Polymer-supported nitrite (3.2 mg, containing 11.0 µmol of NO_2) was added and the reaction mixture was stirred for 0.25 h. A 4–6 MBq solution of [^{125}I]NaI in water (0.01 mL) was added and the reaction mixture warmed to 60 °C and stirred for 2 h. The mixture was removed from the resin by syringe and diluted by the addition of water (0.2 mL). The crude product was purified by semi-preparative HPLC. The fraction containing ethyl 7-[^{125}I]iodo-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate (**2i**) was evaporated to dryness, then reconstituted in 10.0% ethanol in 0.9% saline to afford ethyl 7-[^{125}I]iodo-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-

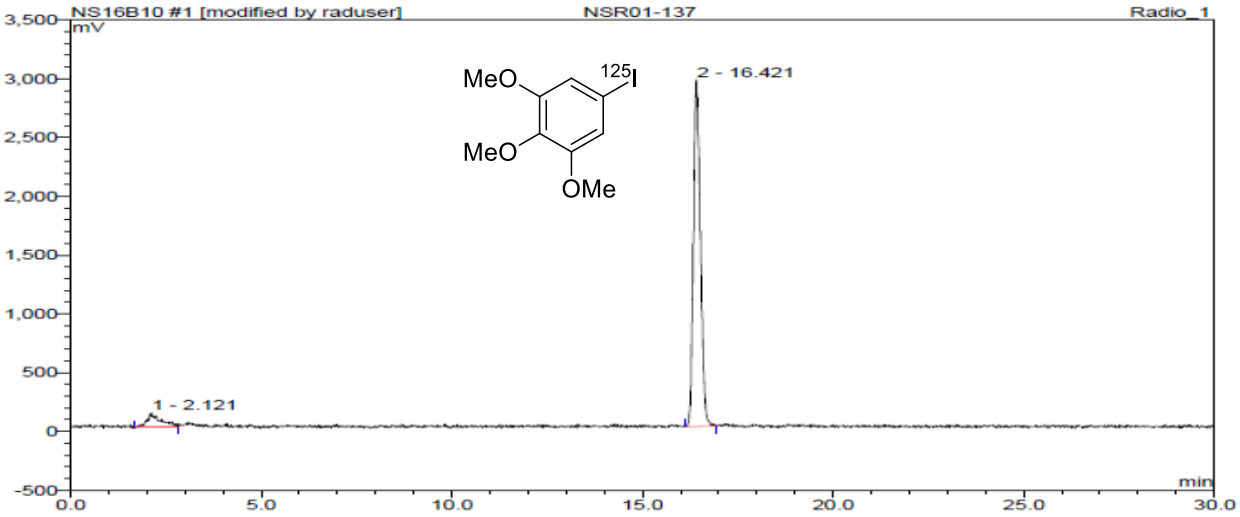
a][1,4]diazepine-3-carboxylate (**2i**) in 75 ± 9.9% radioactivity yield (estimated using the measured radioactivity of the isolated product), with molar activity of 16.2 ± 1.22 GBq μmol^{-1} (n=2). The radiochemical purity of the final product was determined by analytical HPLC and was >99% (n=2). The identity of the product was confirmed by comparing the retention time of the ethyl 7-[^{125}I]iodo-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate (**2i**) against the retention time of ethyl 7-[^{127}I]iodo-5,6-dihydro-5-methyl-6-oxo-4*H*-benzo[*f*]imidazo[1,5-*a*][1,4]diazepine-3-carboxylate.

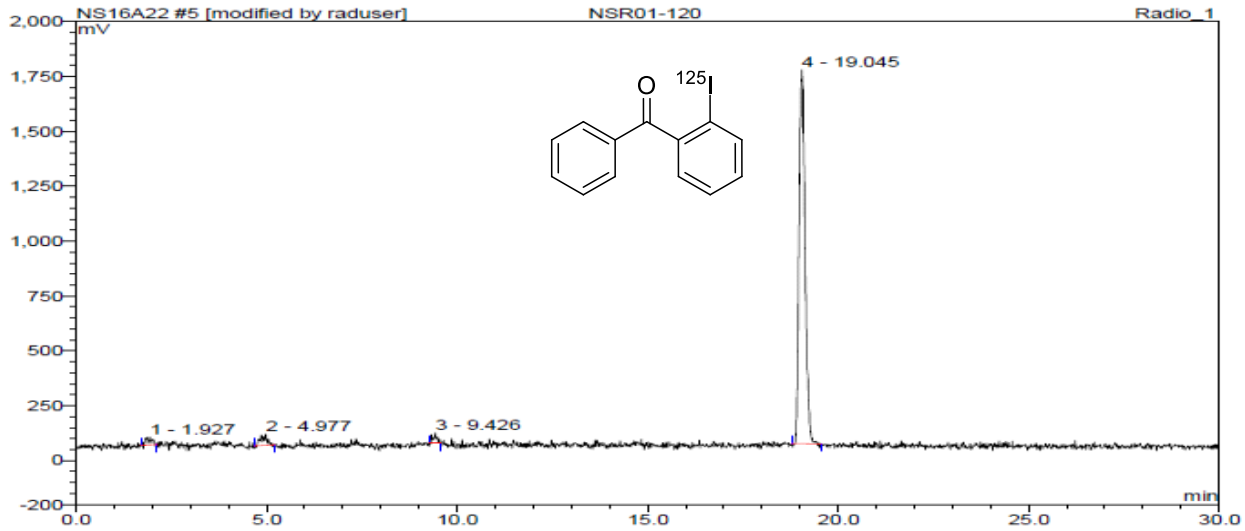
4. Radio-HPLC Chromatograms for all Compounds

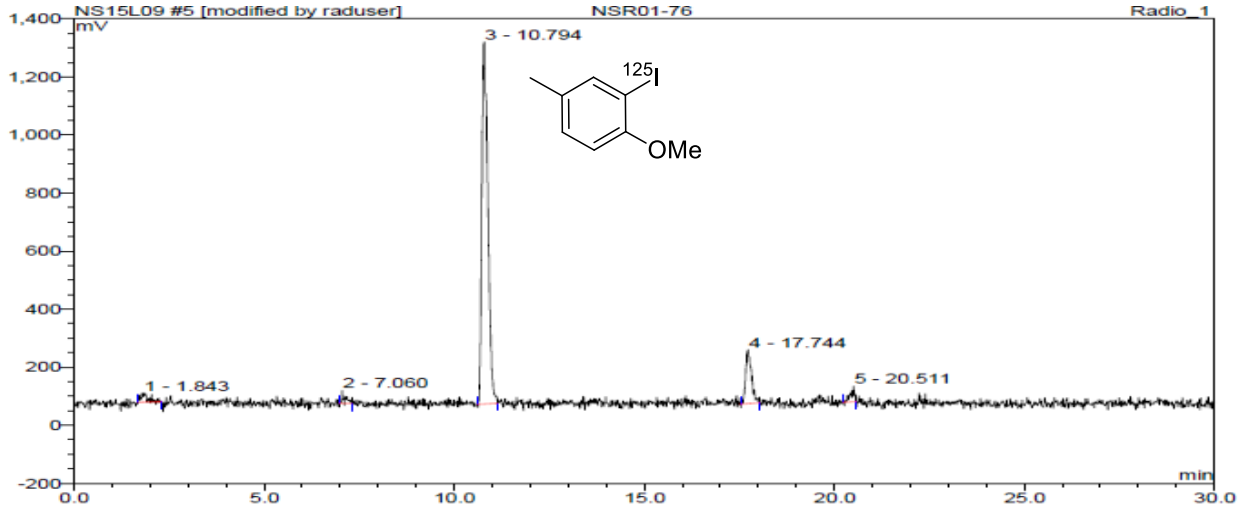


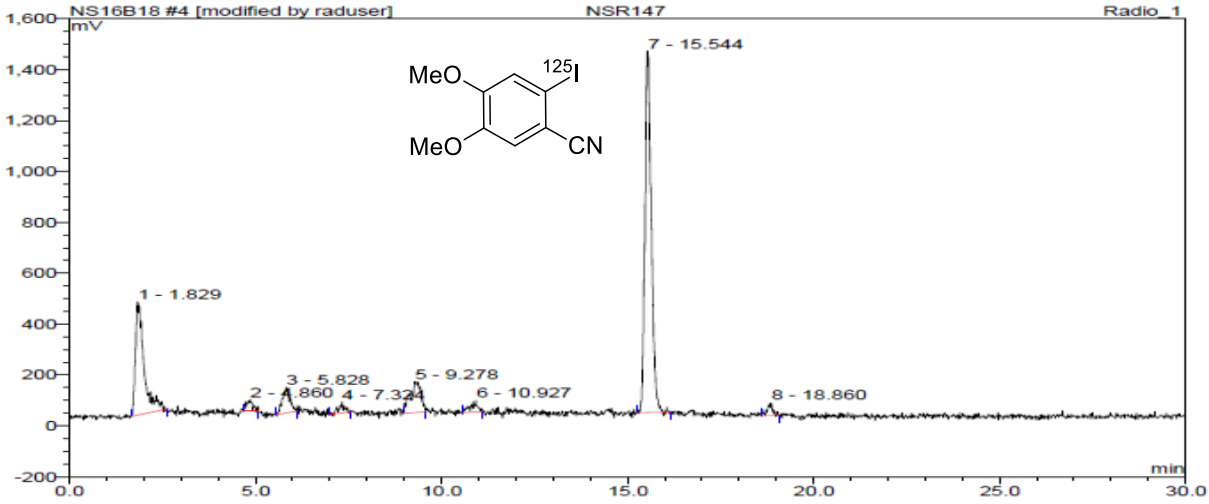


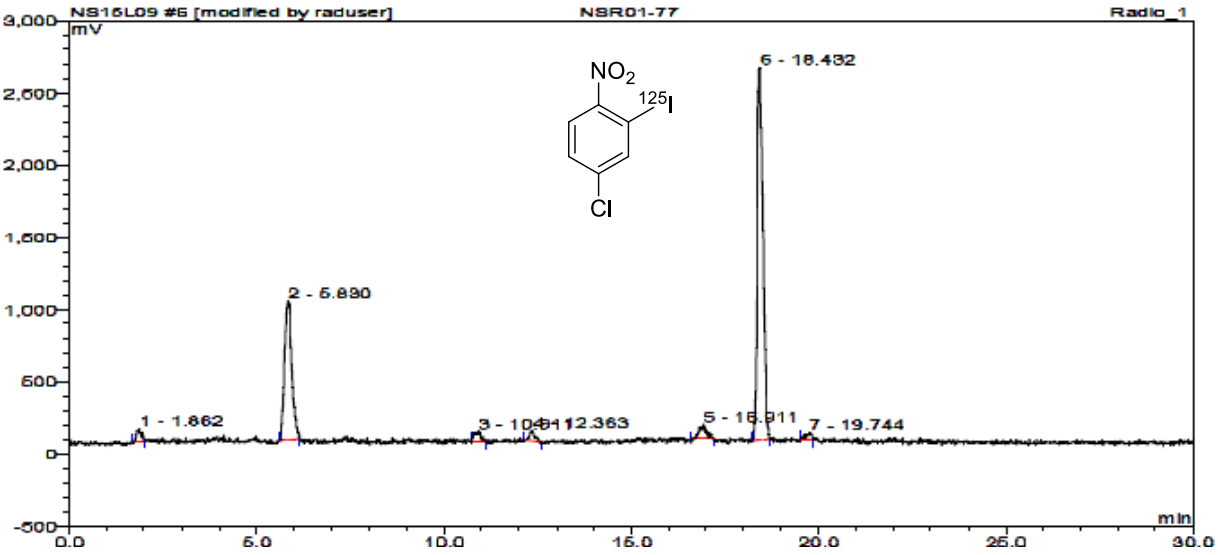



NS16B10 #1 [modified by raduser]
NSR01-137
Radio_1
mV
MeO
MeO
OMe
125
I
2 - 16.421
1 - 2.121
min

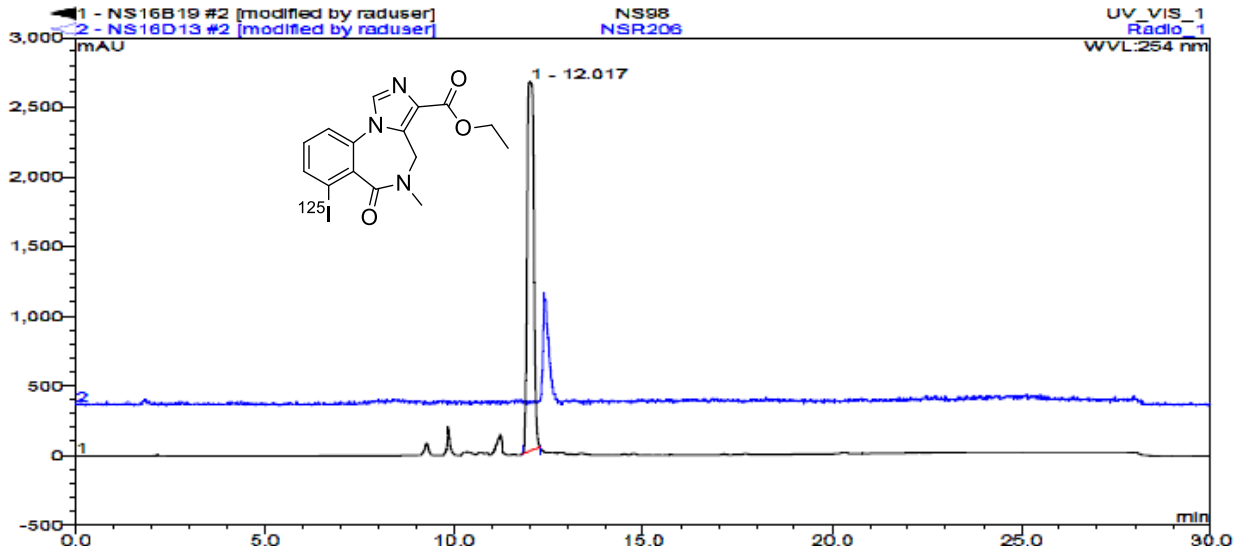

NS16A22 #5 [modified by raduser]
NSR01-120
Radio_1
mV
O
125
I
4 - 19.045
1 - 1.927
2 - 4.977
3 - 9.426
min

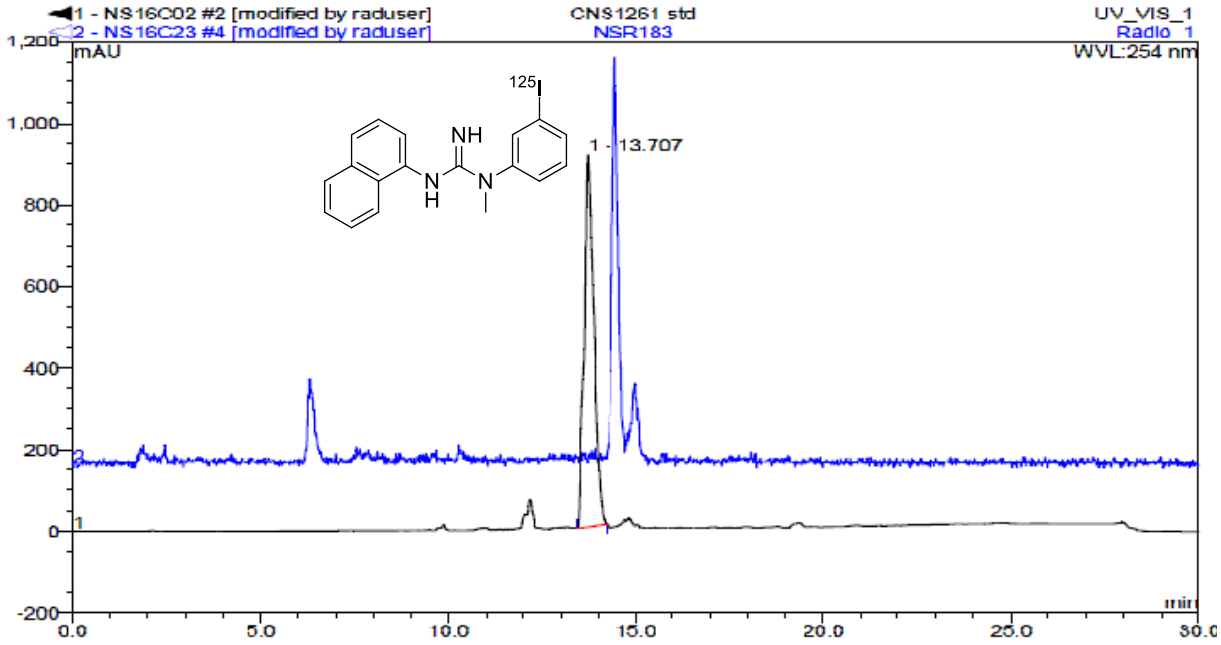

NS15L09 #5 [modified by raduser]
NSR01-76
Radio_1
mV
3 - 10.794
125
I
OMe
4 - 17.744
1 - 1.843
2 - 7.060
5 - 20.511
min

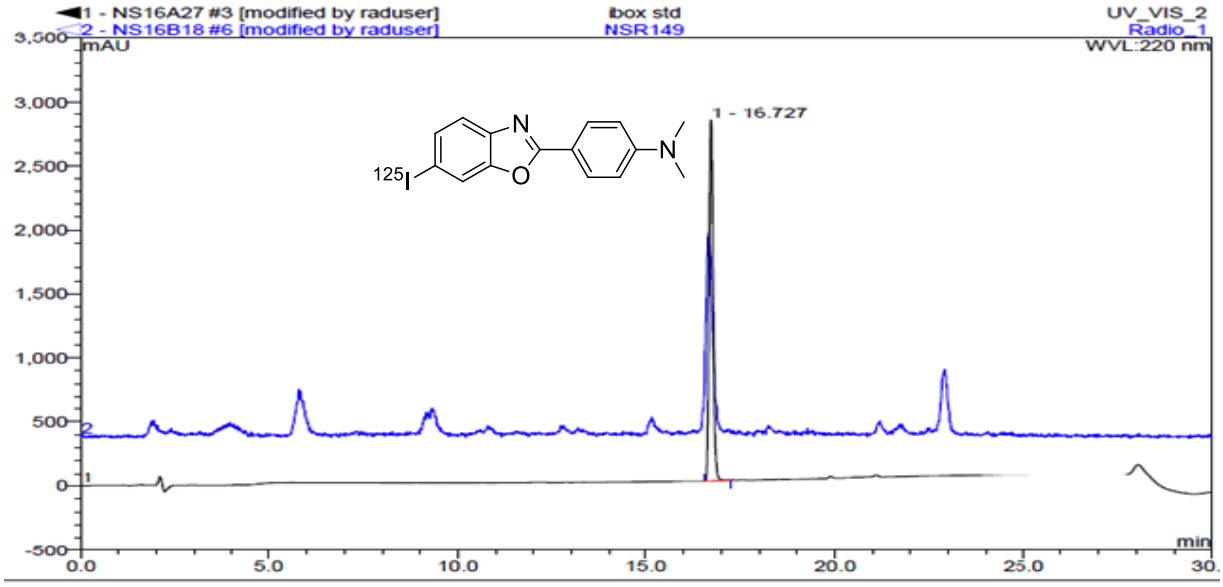

NS16B18 #4 [modified by raduser]
NSR147
Radio_1
mV
MeO
MeO
125I
CN
1 - 1.829
2 - 4.860
3 - 5.828
4 - 7.324
5 - 9.278
6 - 10.927
7 - 15.544
8 - 18.860
min

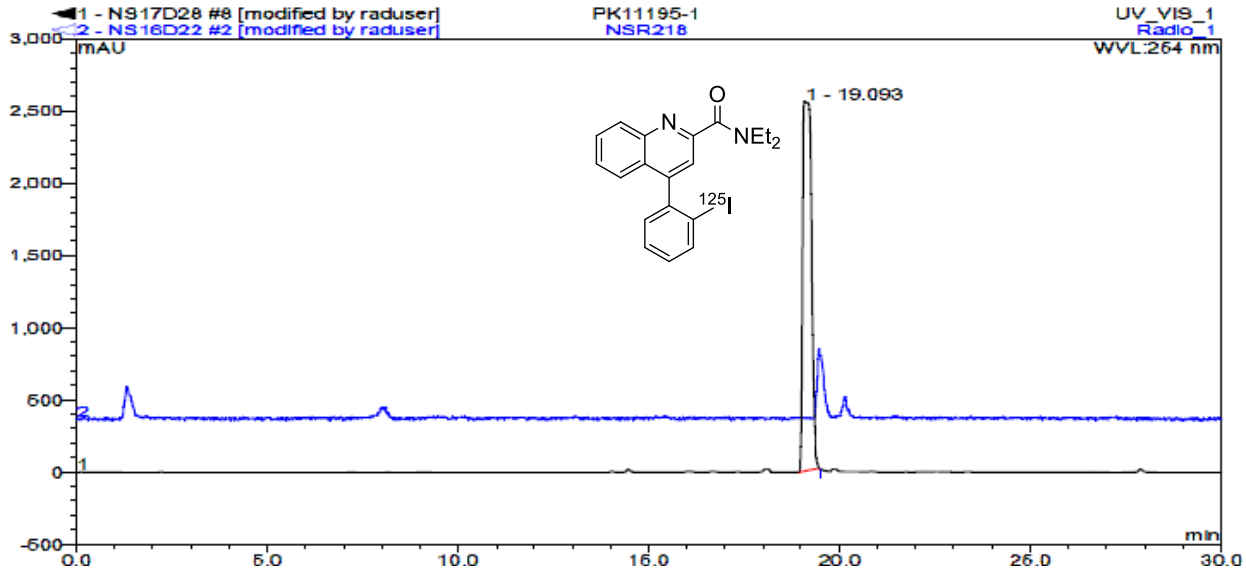

NS16L09 #6 [modified by raduser]
NSR01-77
Radio_1
mV
NO2
125I
Cl
1 - 1.862
2 - 5.890
3 - 10.411
12.363
5 - 15.911
6 - 18.432
7 - 19.744
min

For target compounds, an overlay of the UV-Vis HPLC trace (in black) is provided along with the radio-HPLC trace (in blue):






1 - NS16A27 #3 [modified by raduser]
2 - NS16B18 #6 [modified by raduser]
ibox std
NSR149
UV_VIS_2
Radio_1
WVL:220 nm
mAU
1 - 16.727
min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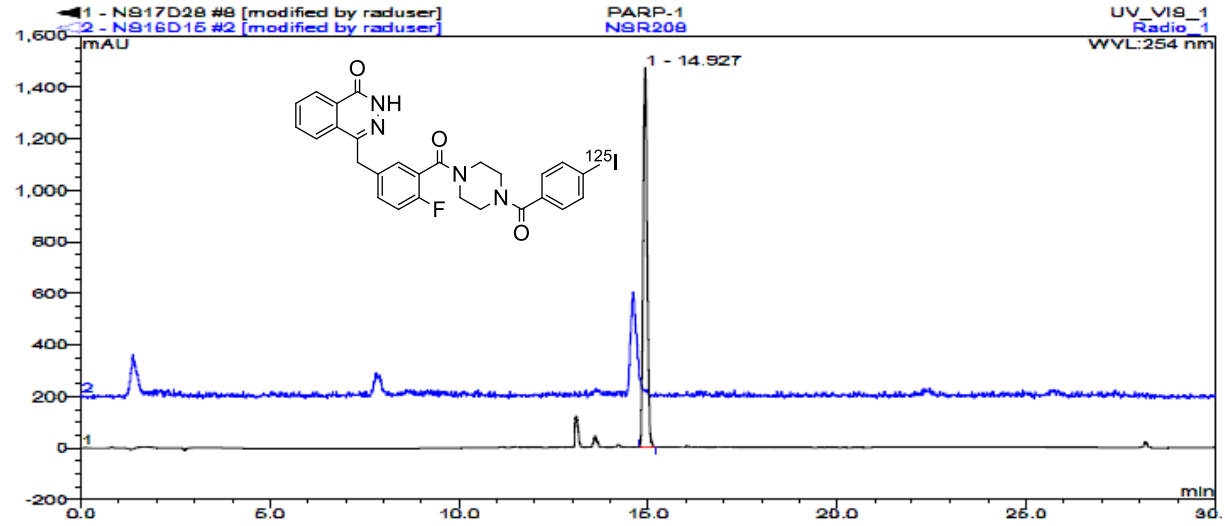
2 - NS16D22 #2 [modified by raduser]
PK11195-1
NSR218
UV_VIS_1
Radio_1
WVL:264 nm
mAU
1 - 19.093
min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2 - NS16D16 #2 [modified by raduser]
PARP-1
NSR208
UV_VIS_1
Radio_1
WVL:254 nm
mAU
1 - 14.927
min

5. References

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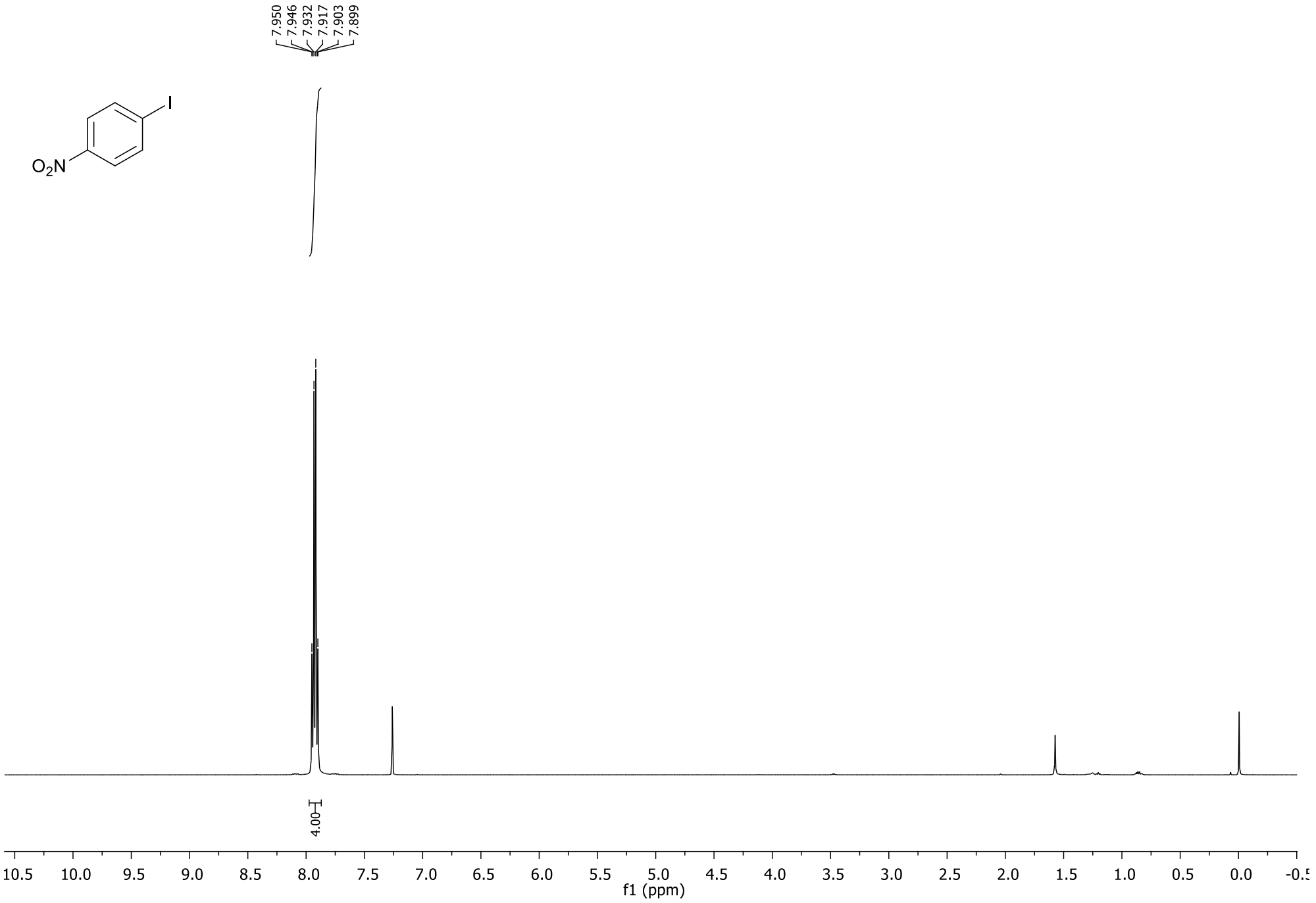
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7.899
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O2N
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10.5
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9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.5
3.0
2.5
2.0
1.5
1.0
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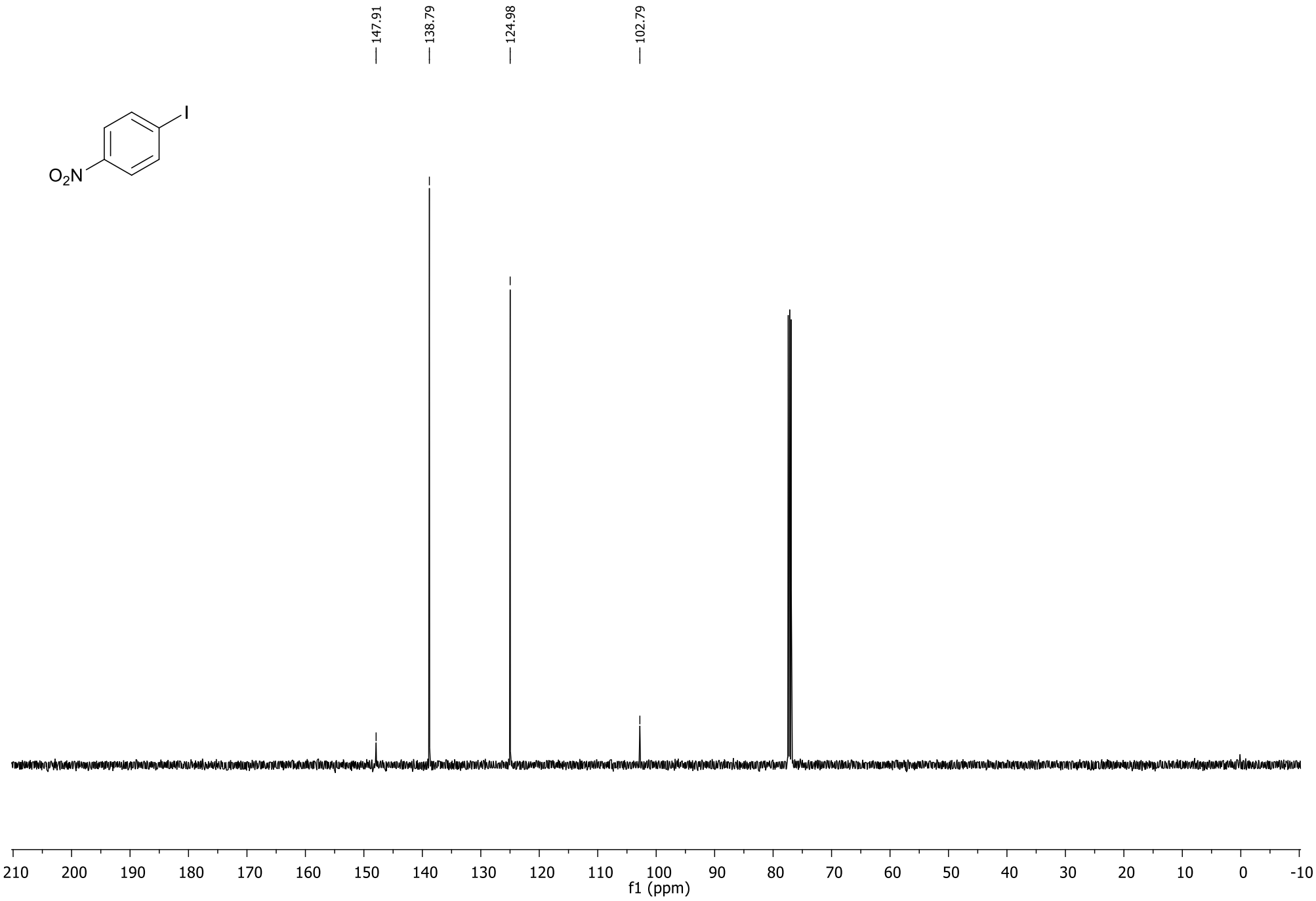
0.0
f1 (ppm)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138.79
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O_2N
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200
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100
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80
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60
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40
30
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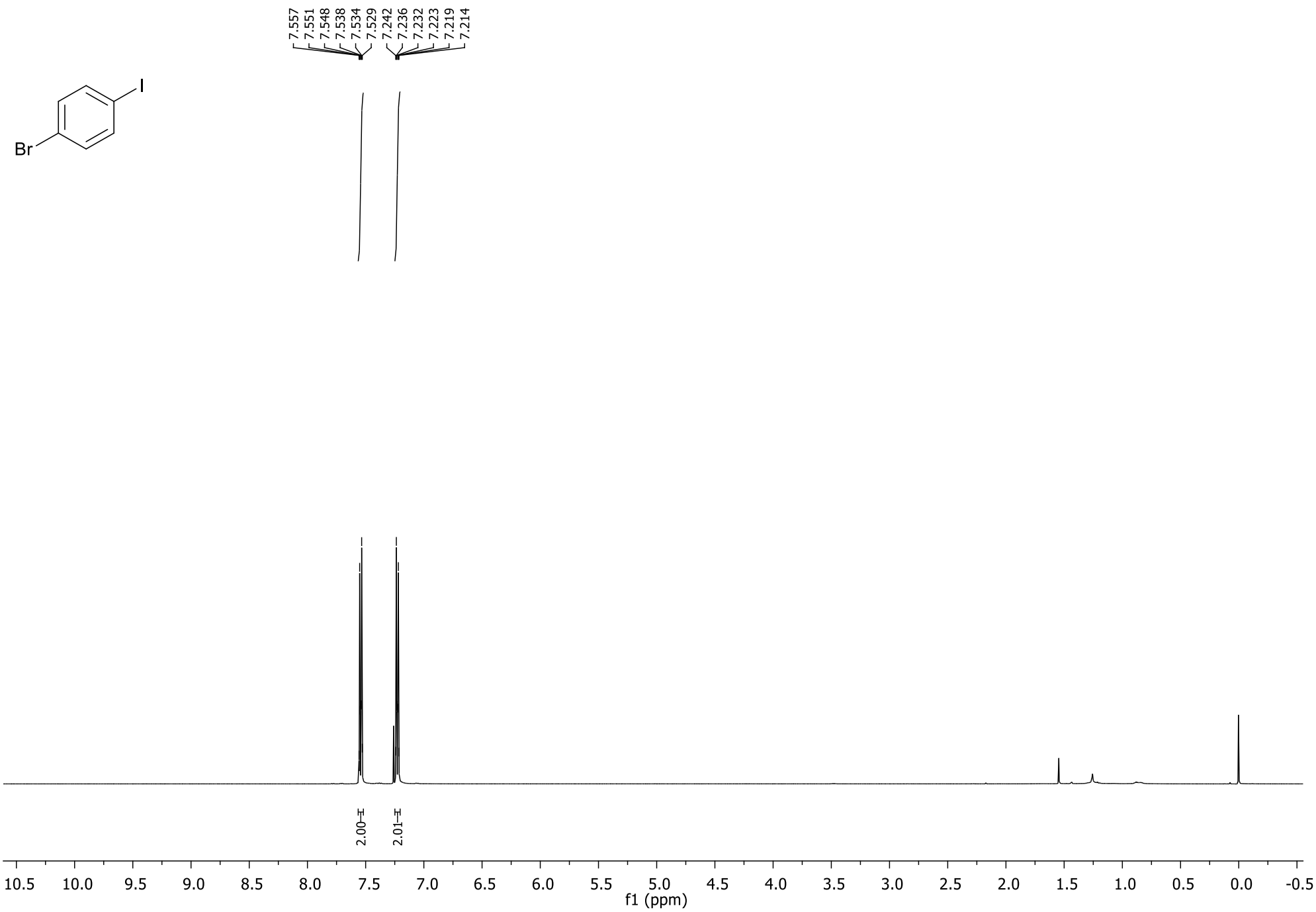
f1 (ppm)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7.223
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7.214
I
Br
2.00
2.01
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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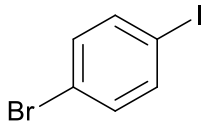
f1 (ppm)


I
Br

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133.58
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92.16
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200
190
180
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160
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140
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120
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100
90
80
70
60
50
40
30
20
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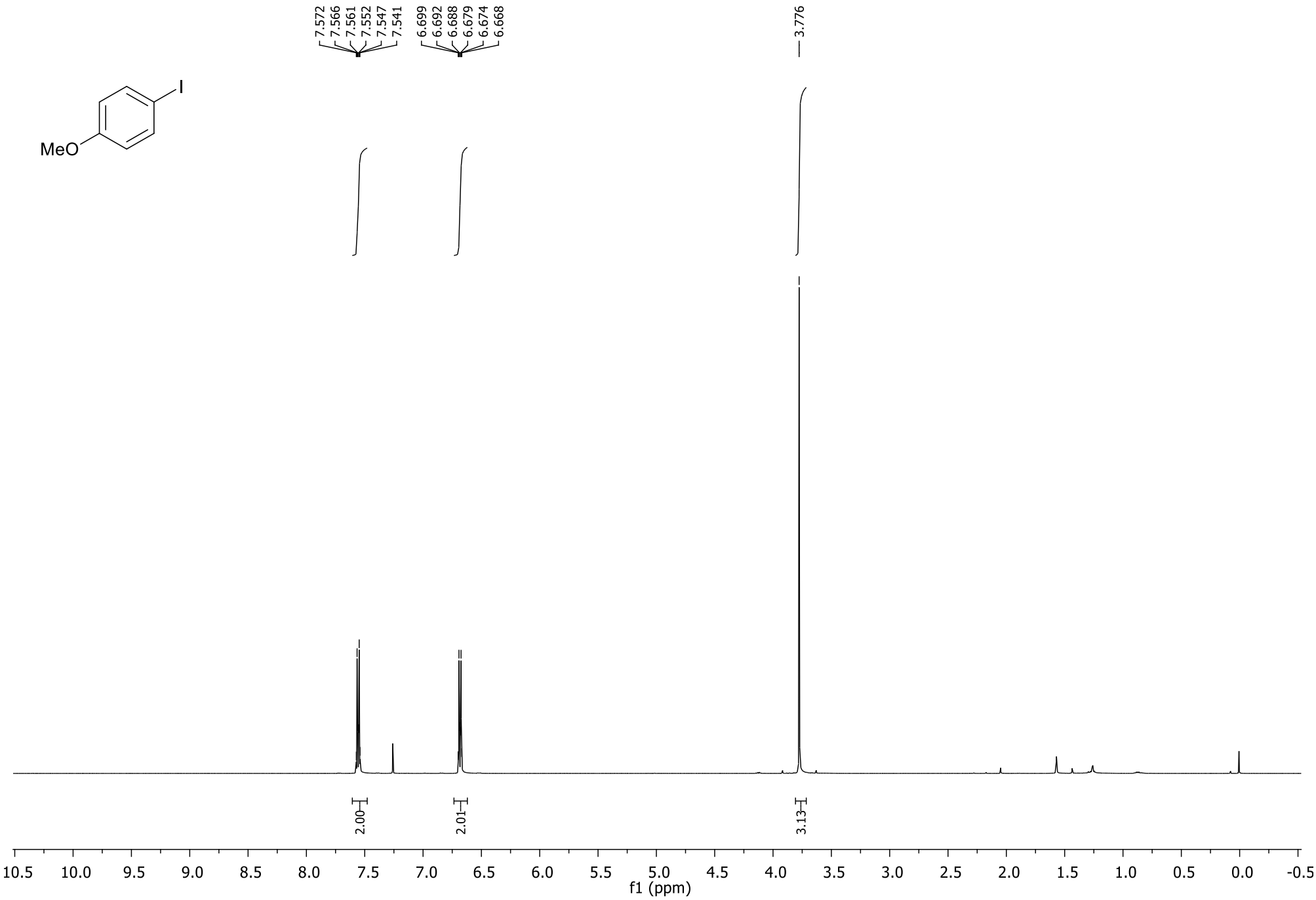
0
-10
f1 (ppm)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I
MeO
2.00
2.01
3.13
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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3.0
2.5
2.0
1.5
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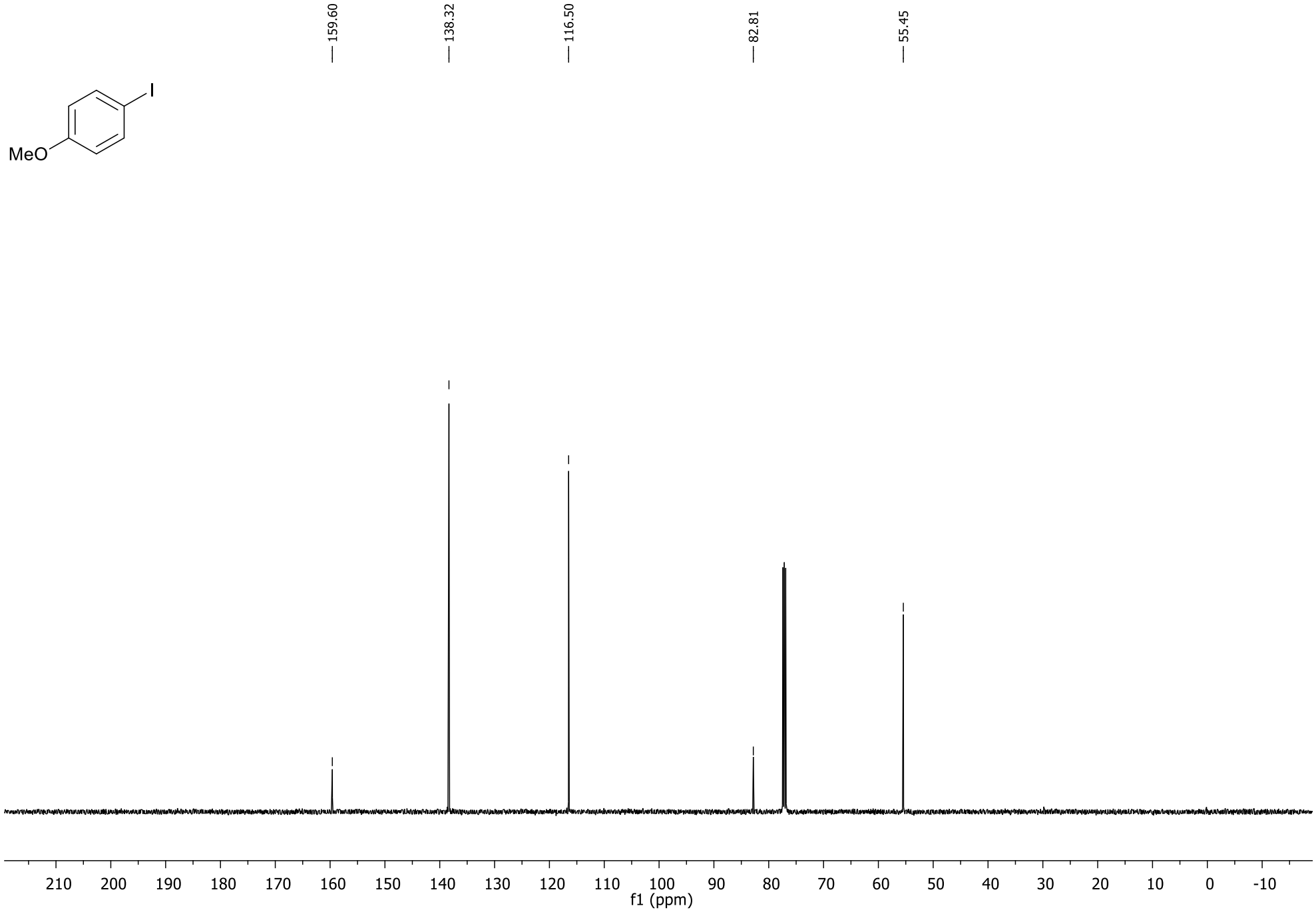
0.0
-0.5
f1 (ppm)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120
110
100
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80
70
60
50
40
30
20
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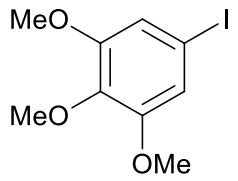
-10
f1 (ppm)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I
MeO
OMe

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8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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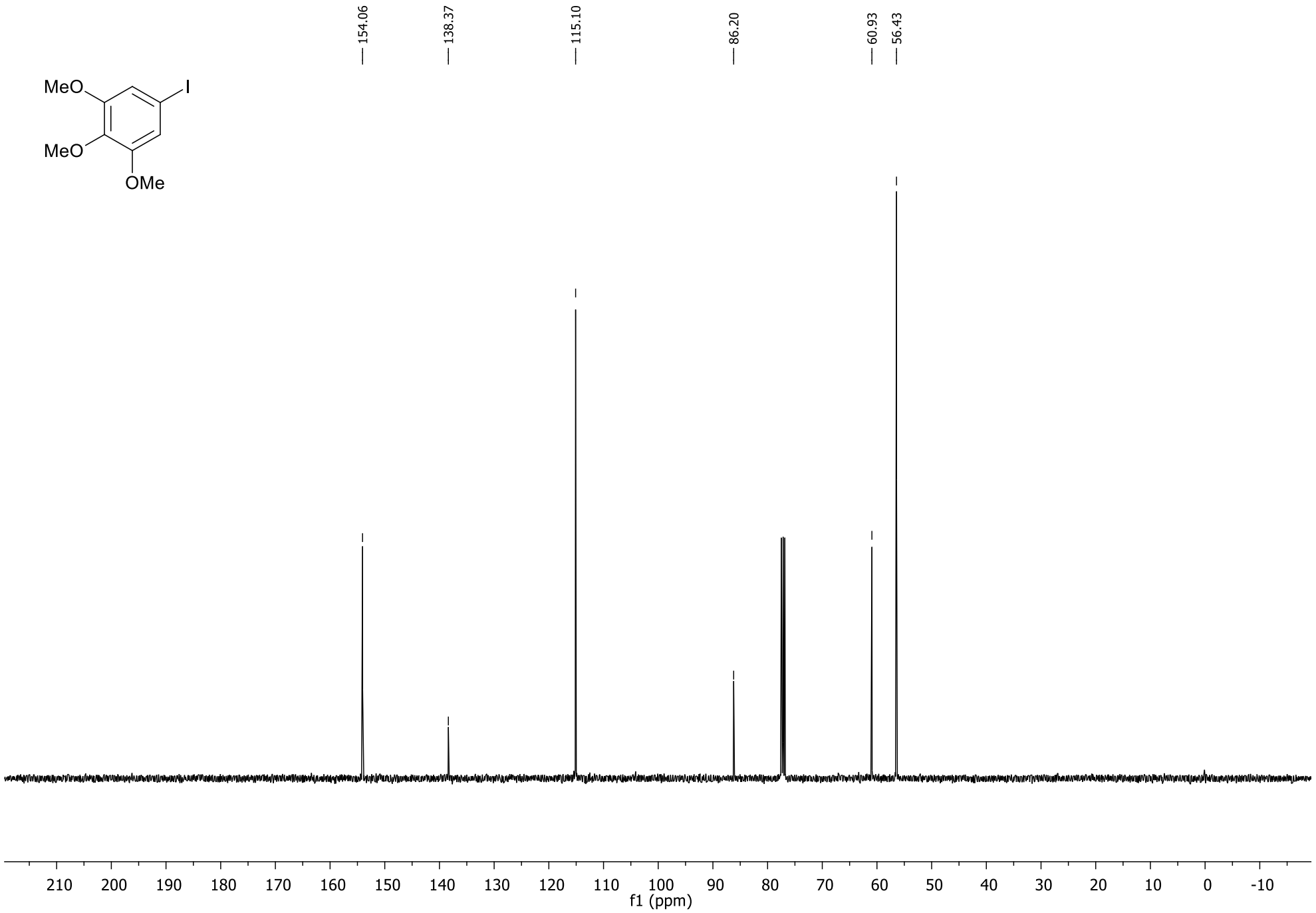
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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60.93
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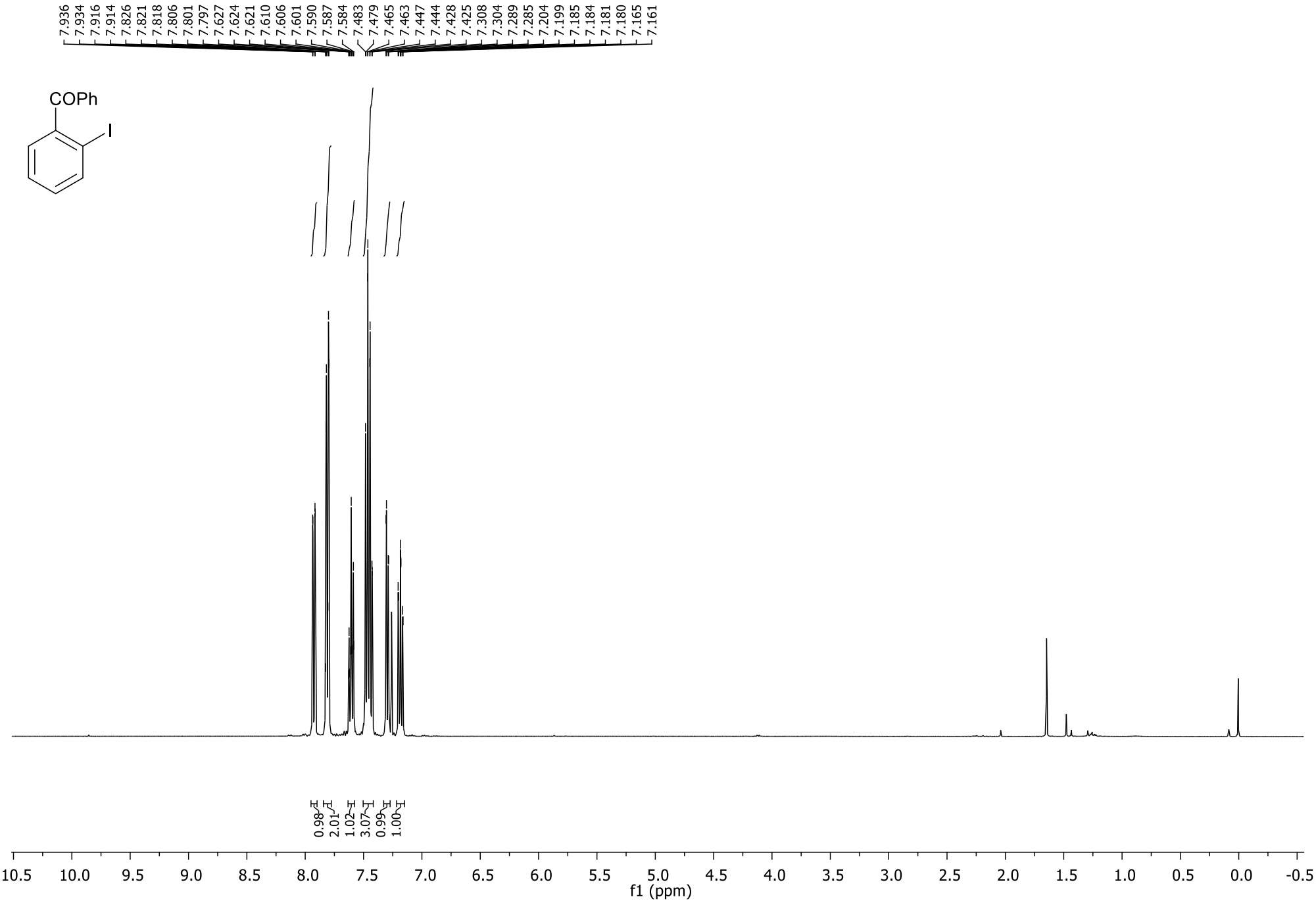
MeO
MeO
OMe
I
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.624
7.621
7.610
7.606
7.601
7.590
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7.479
7.465
7.463
7.447
7.444
7.428
7.425
7.308
7.304
7.289
7.285
7.204
7.199
7.185
7.184
7.181
7.180
7.165
7.161
COPh
I
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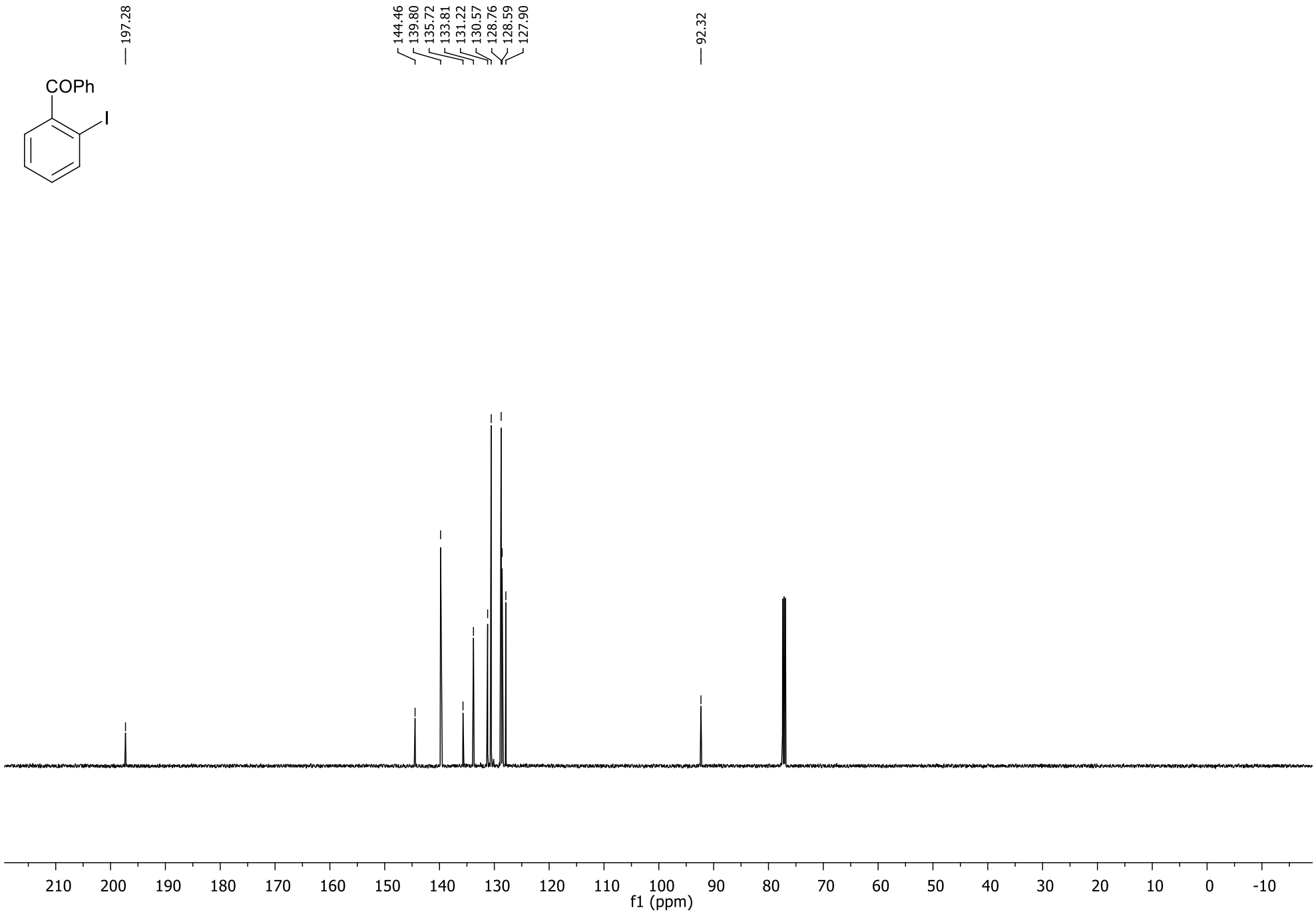
2.01
1.02
3.07
0.99
1.00
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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COPh
I
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200
190
180
170
160
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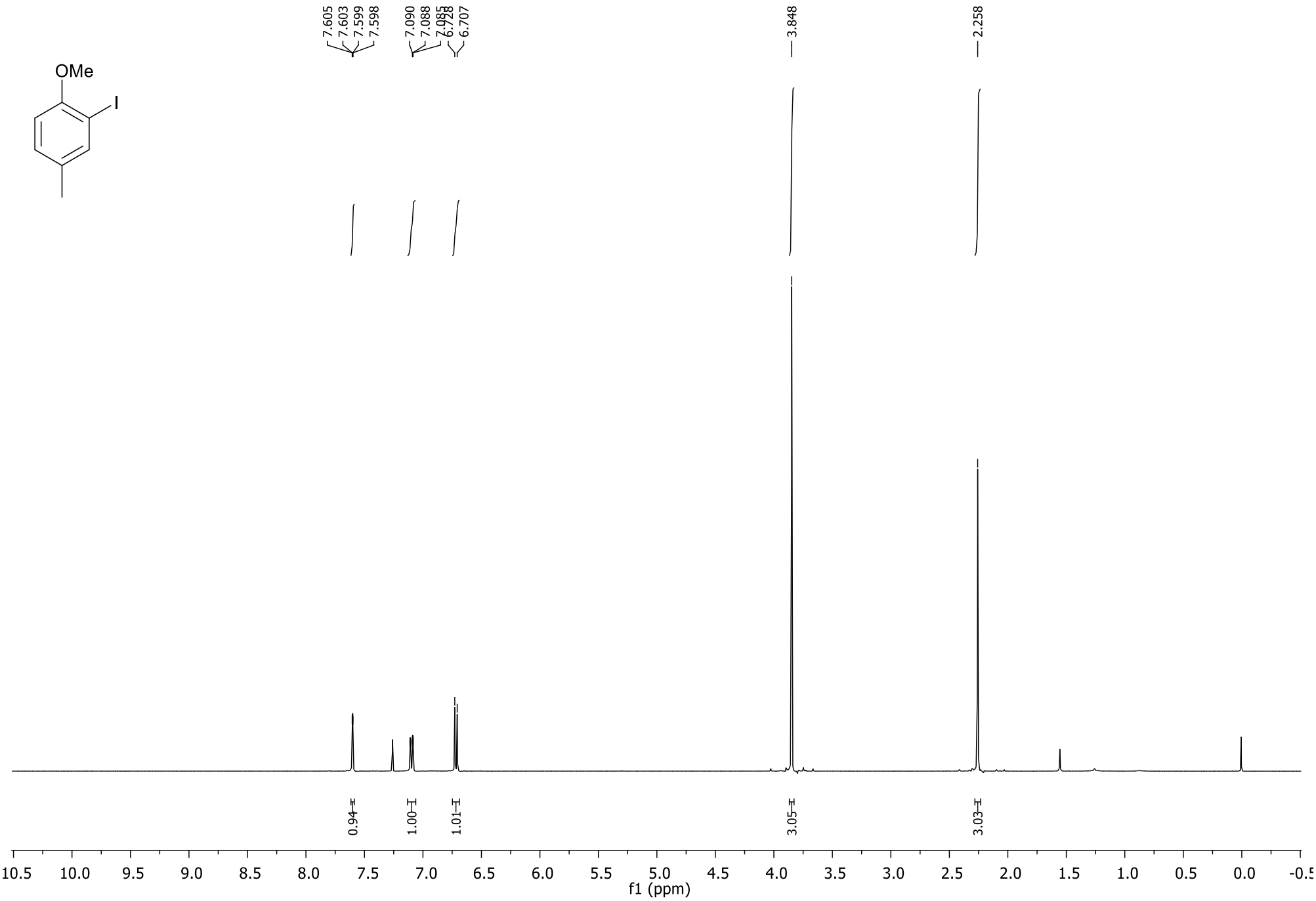
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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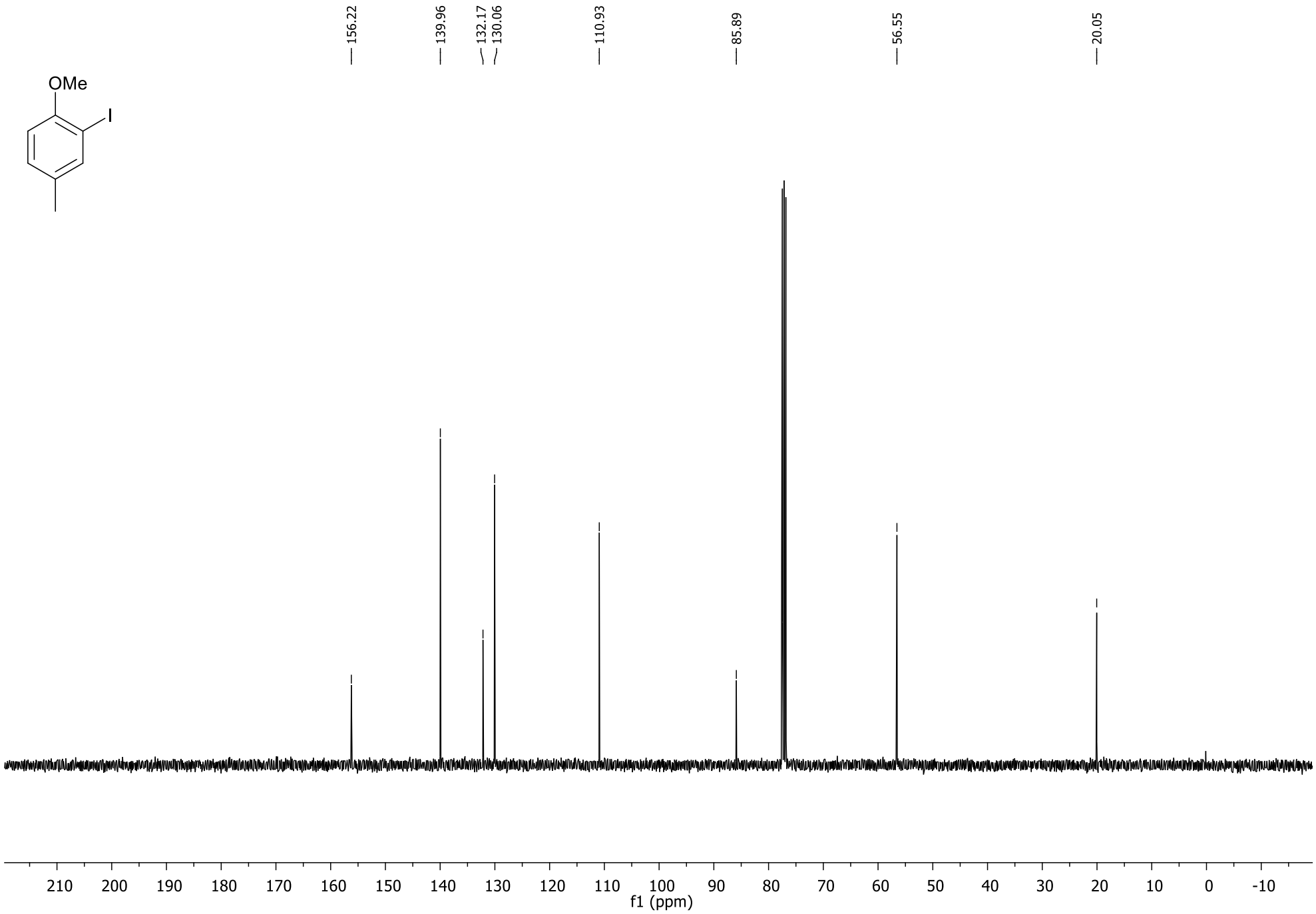
1.01
3.05
3.03
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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OMe
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180
170
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120
110
100
90
80
70
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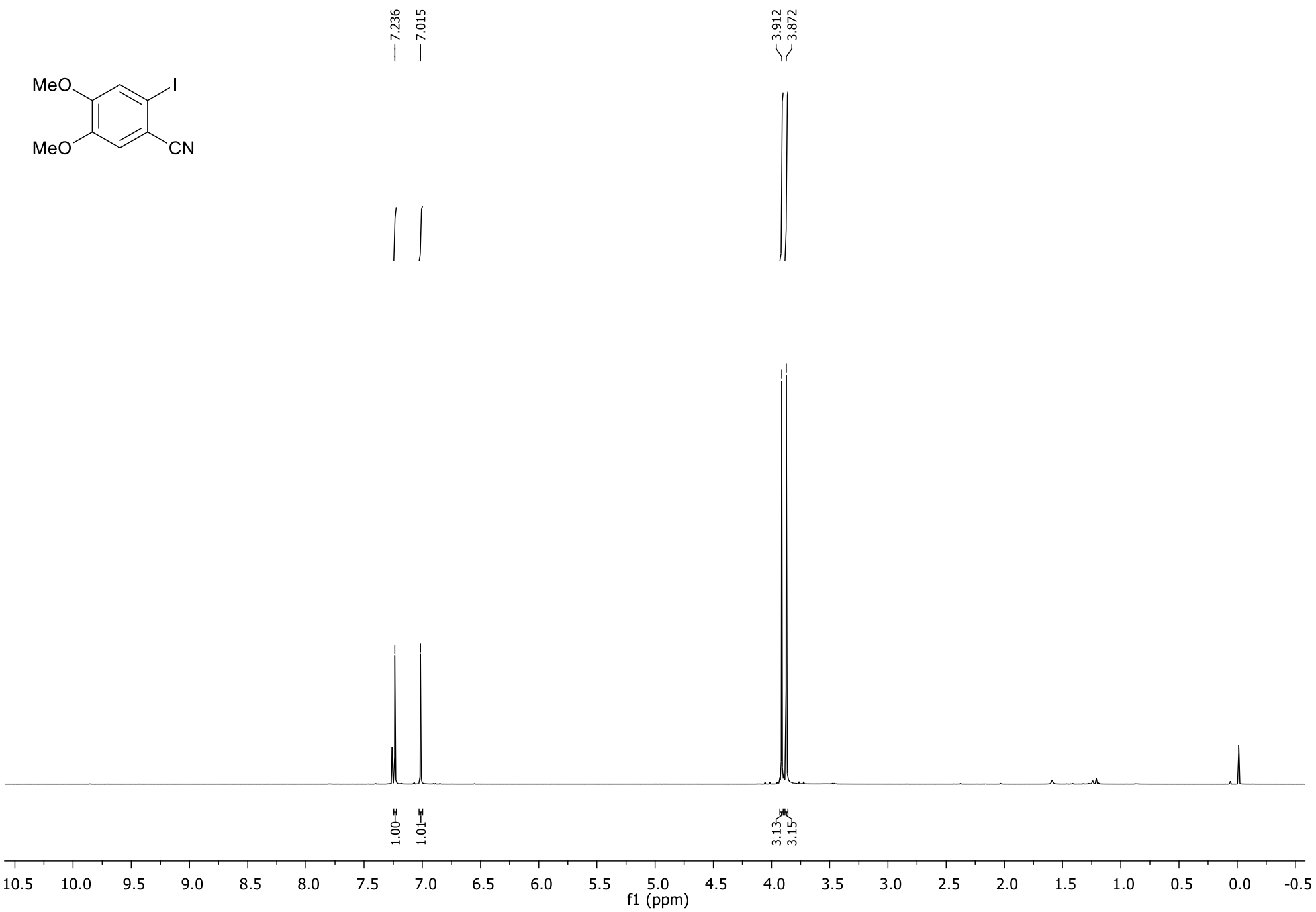
50
40
30
20
10
0
-10
f1 (ppm)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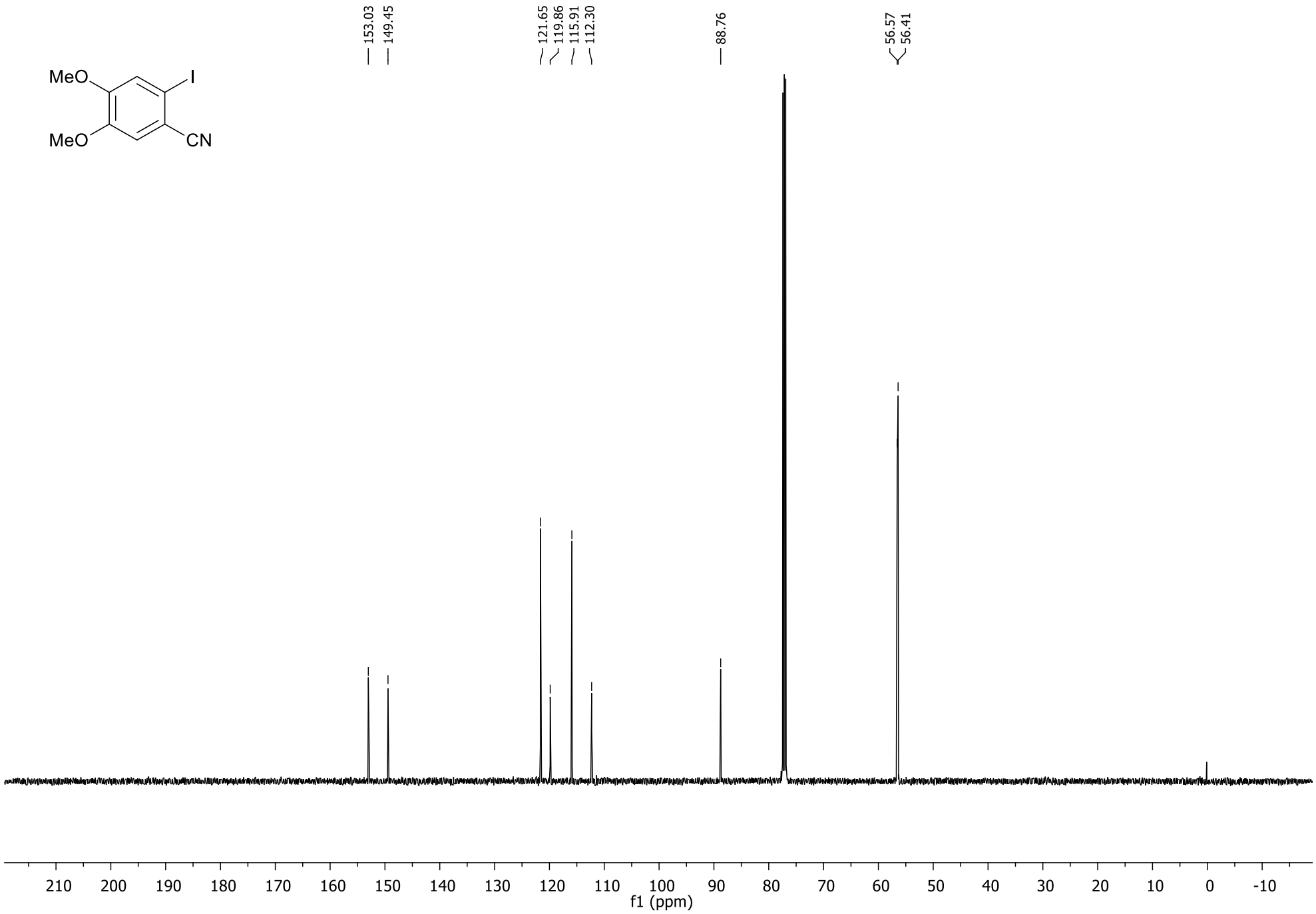
f1 (ppm)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56.41
MeO
I
MeO
CN
210
200
190
180
170
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100
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80
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40
30
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10
0
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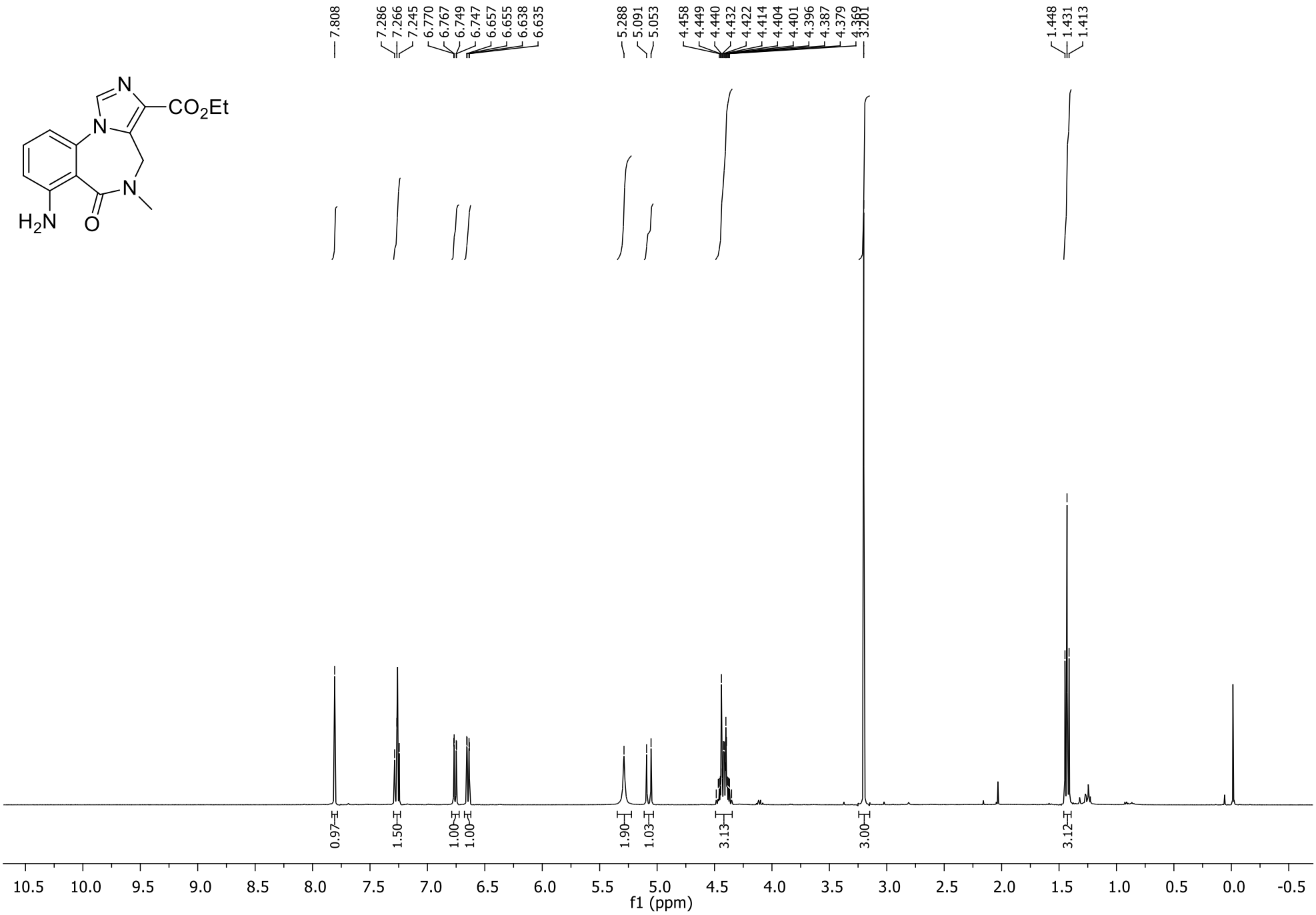
f1 (ppm)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6.747
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6.655
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5.053
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4.449
4.440
4.432
4.422
4.414
4.404
4.401
4.396
4.387
4.379
4.369
4.361
3.201
1.448
1.431
1.413
CO2Et
N
N
N
H2N
O
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1.00
1.00
1.90
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3.00
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6.0
5.5
5.0
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2.0
1.5
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0.5
0.0
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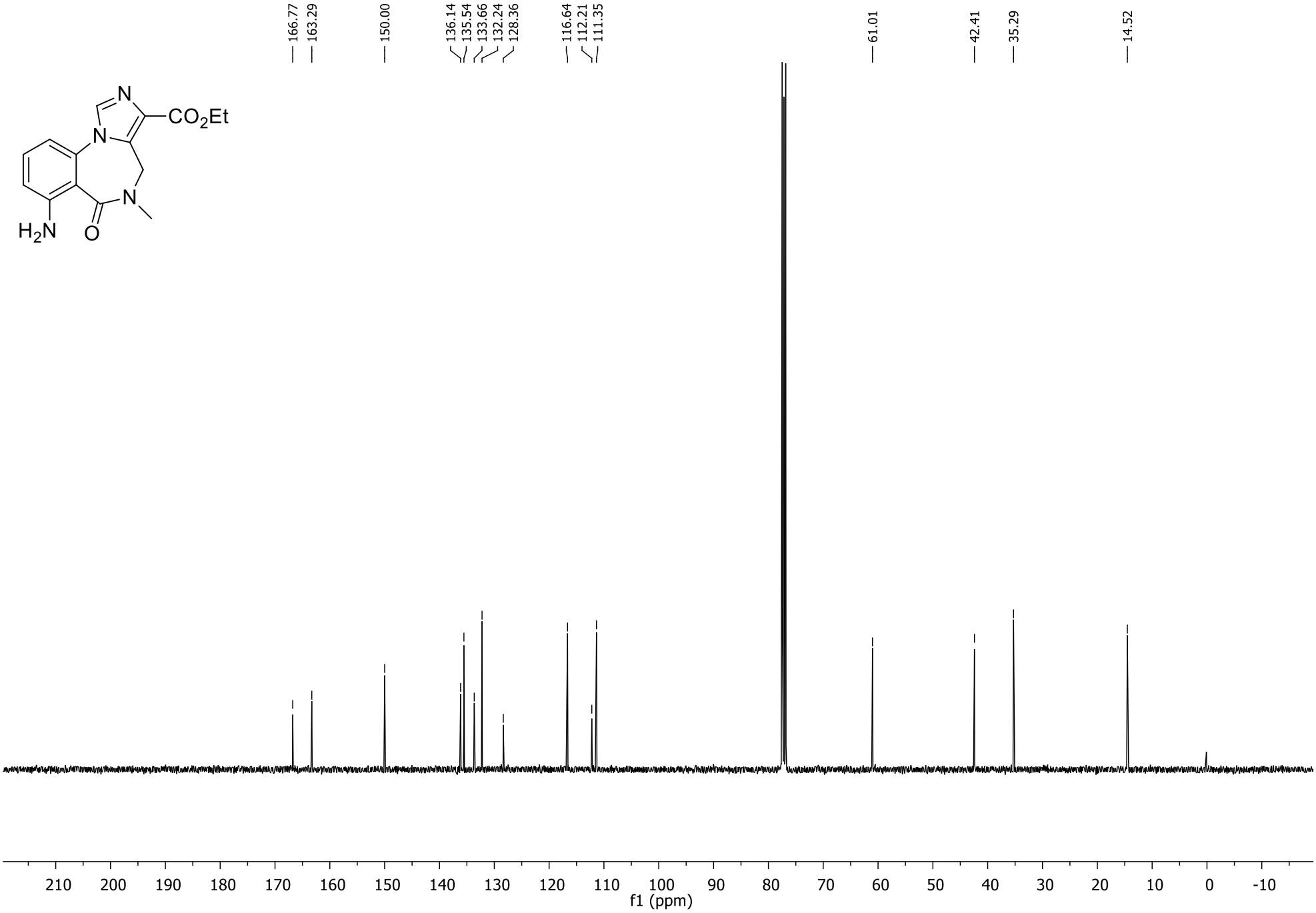
f1 (ppm)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42.41
35.29
14.52
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N
CO2Et
N
H2N
O
210
200
190
180
170
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120
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100
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80
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60
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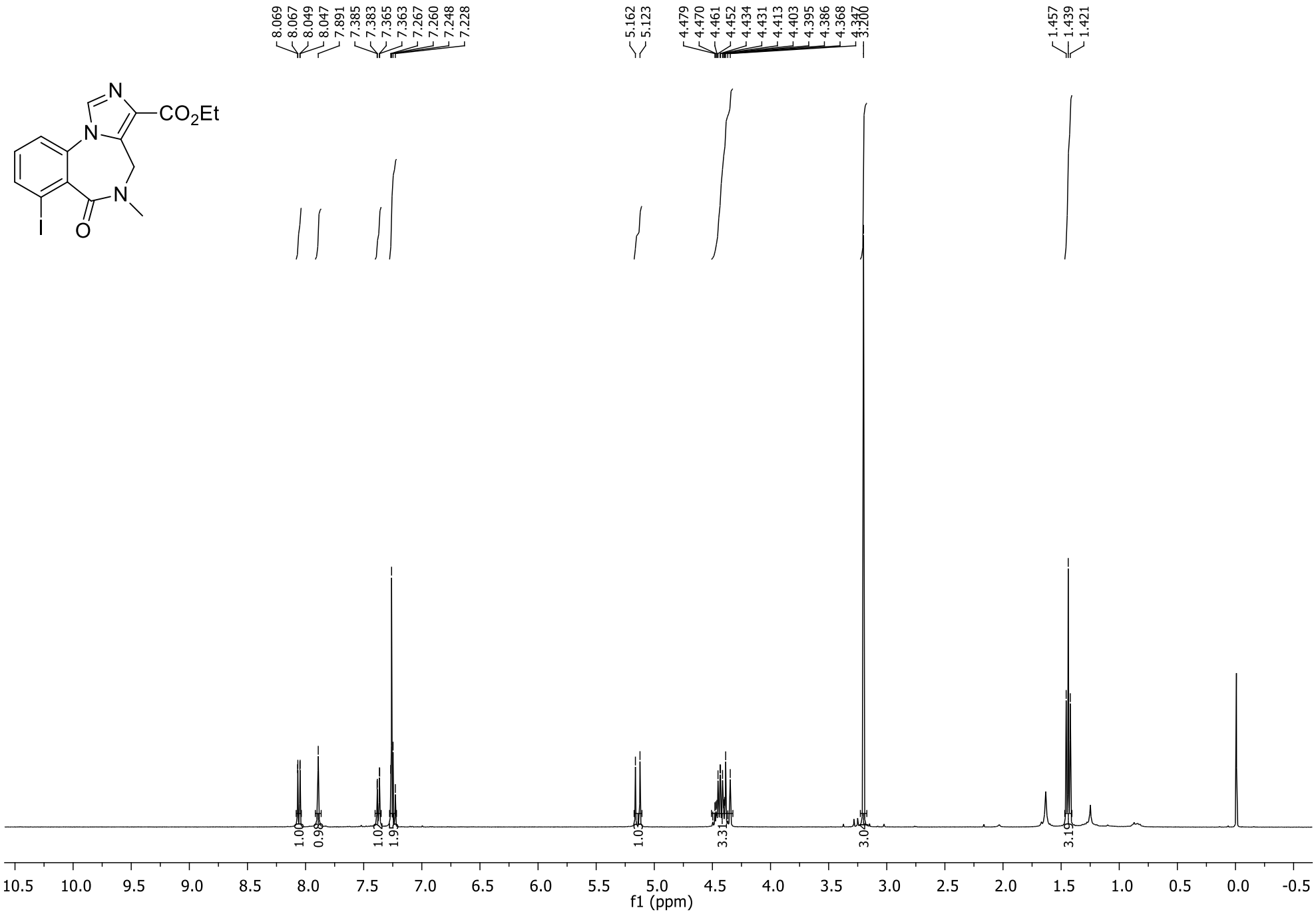
40
30
20
10
0
-10
f1 (ppm)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7.228
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5.123
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4.470
4.461
4.452
4.434
4.431
4.413
4.403
4.395
4.386
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1.439
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O
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1.93
1.03
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3.04
3.19
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9.5
9.0
8.5
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7.5
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6.5
6.0
5.5
5.0
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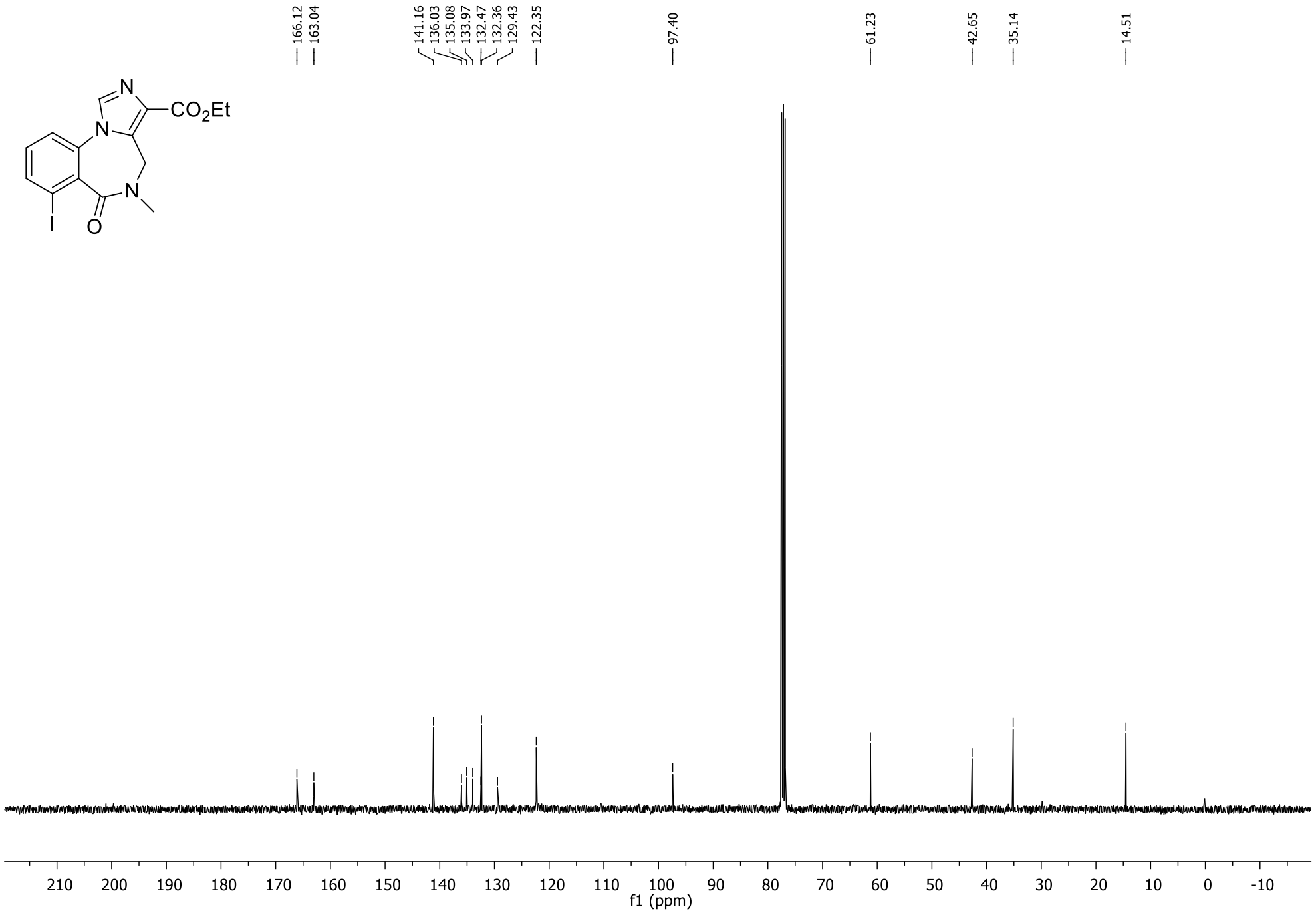
f1 (ppm)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35.14
14.51
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N
I
O
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200
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180
170
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80
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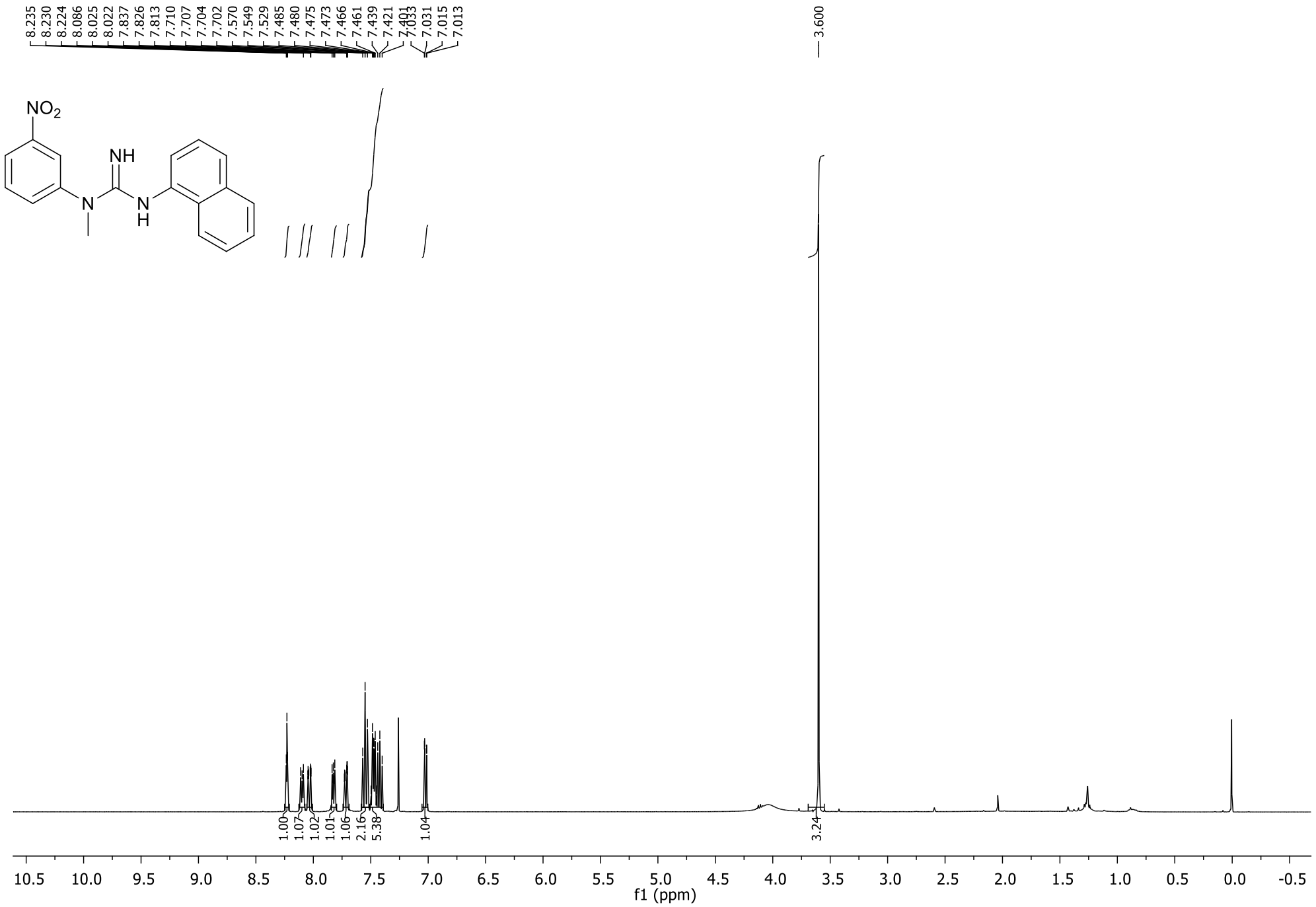
0
-10
f1 (ppm)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8.022
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7.826
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7.710
7.707
7.704
7.702
7.570
7.549
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7.480
7.475
7.473
7.466
7.461
7.439
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7.401
7.033
7.031
7.015
7.013
3.600
NO2
NH
N
N
H
1.00
1.07
1.02
1.01
1.06
2.16
5.38
1.04
3.24
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
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3.0
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0.5
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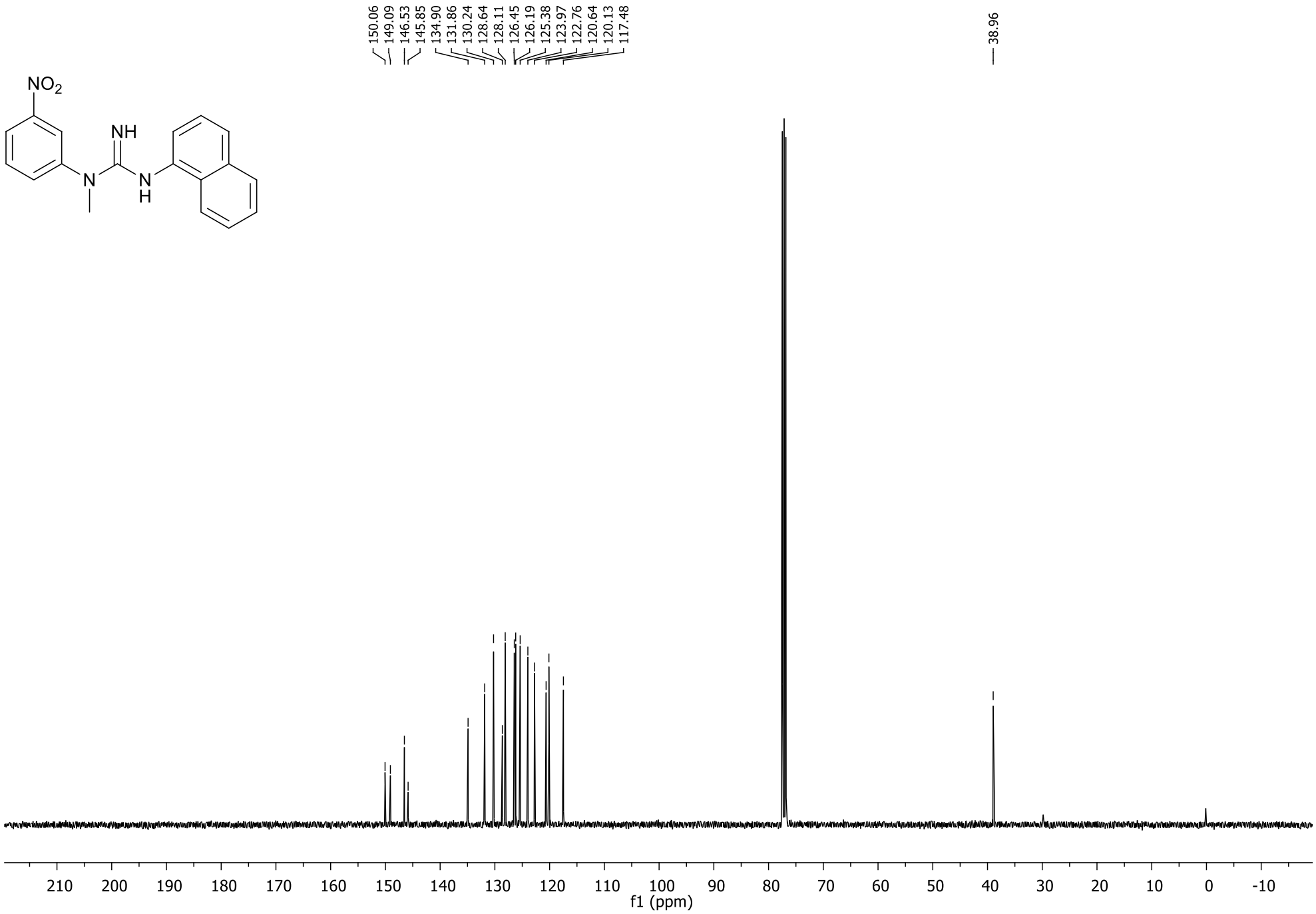
f1 (ppm)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126.19
125.38
123.97
122.76
120.64
120.13
117.48
38.96
NO2
NH
N
N
H
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200
190
180
170
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80
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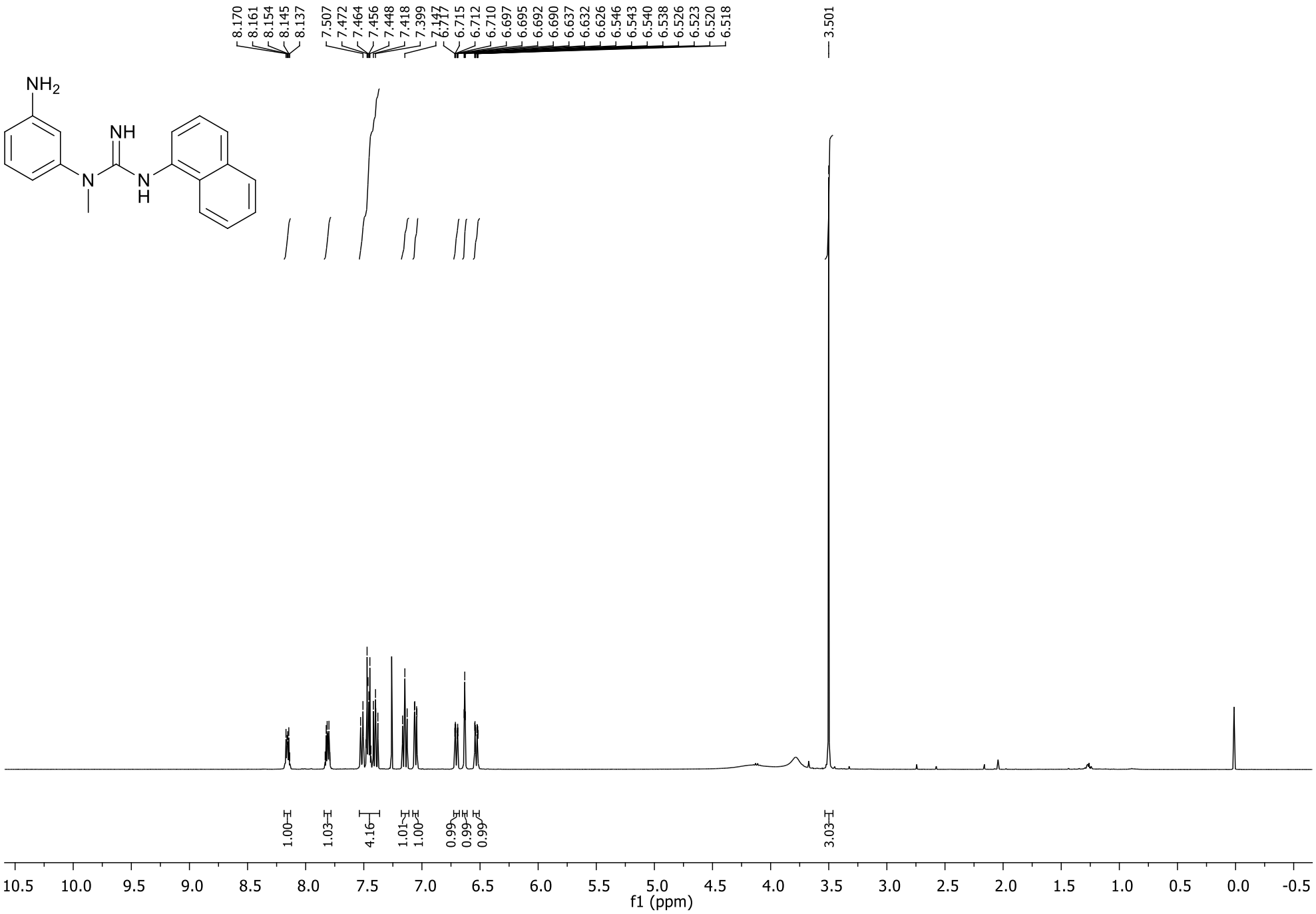
-10
f1 (ppm)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7.418
7.399
7.147
7.117
6.715
6.712
6.710
6.697
6.695
6.692
6.690
6.637
6.632
6.626
6.546
6.543
6.540
6.538
6.526
6.523
6.520
6.518
3.501
NH2
NH
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H
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4.16
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1.00
0.99
0.99
0.99
3.03
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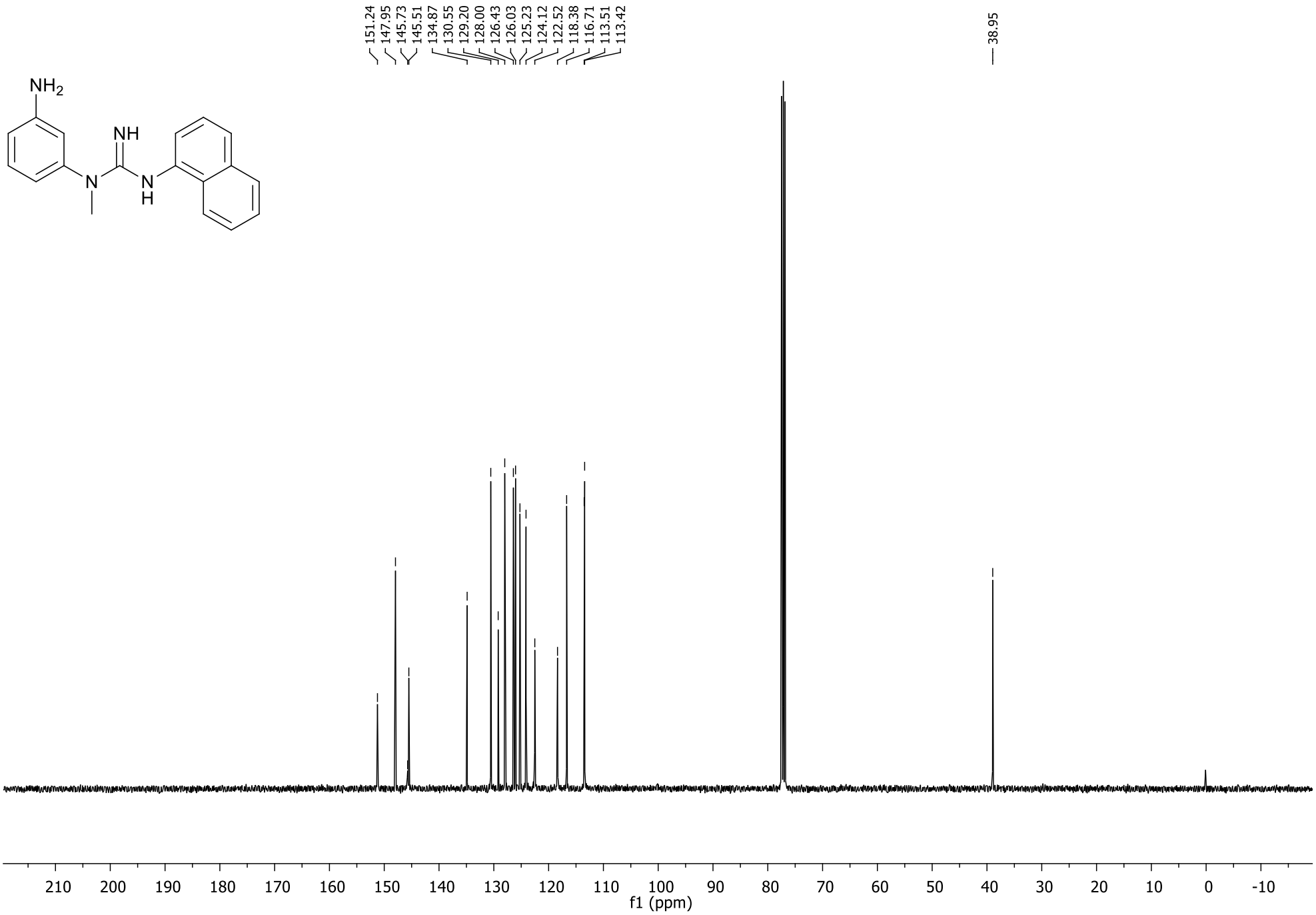
f1 (ppm)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128.00
126.43
126.03
125.23
124.12
122.52
118.38
116.71
113.51
113.42
38.95
NH2
NH
N
N
H
210
200
190
180
170
160
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120
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100
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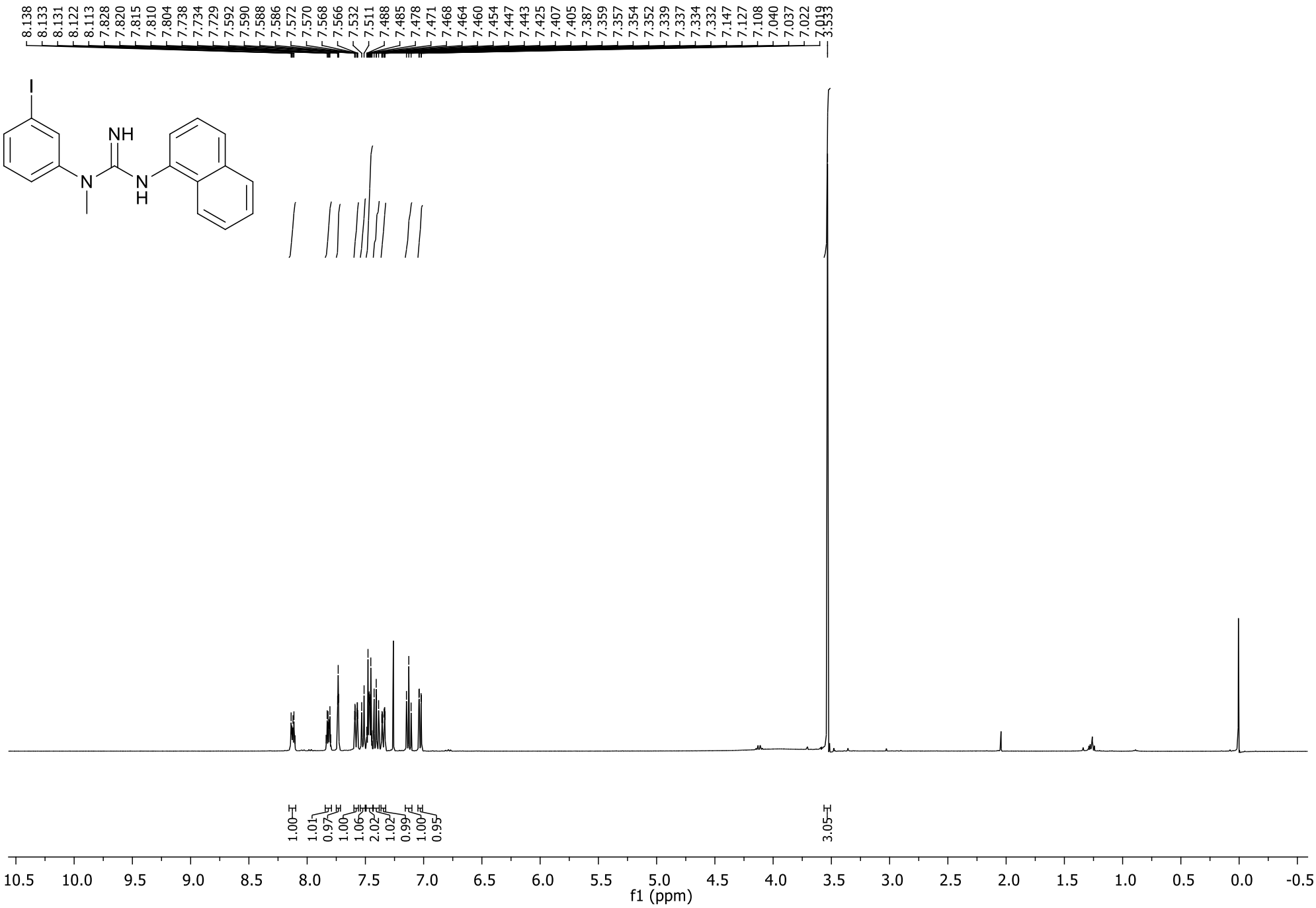
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.820
7.815
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7.572
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7.568
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7.460
7.454
7.447
7.443
7.425
7.407
7.405
7.387
7.359
7.357
7.354
7.352
7.339
7.337
7.334
7.332
7.147
7.127
7.108
7.040
7.037
7.022
7.019
3.533
I
NH
N
N
H
1.00
1.01
0.97
1.00
1.06
2.02
1.02
0.99
1.00
0.95
3.05
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
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2.0
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0.5
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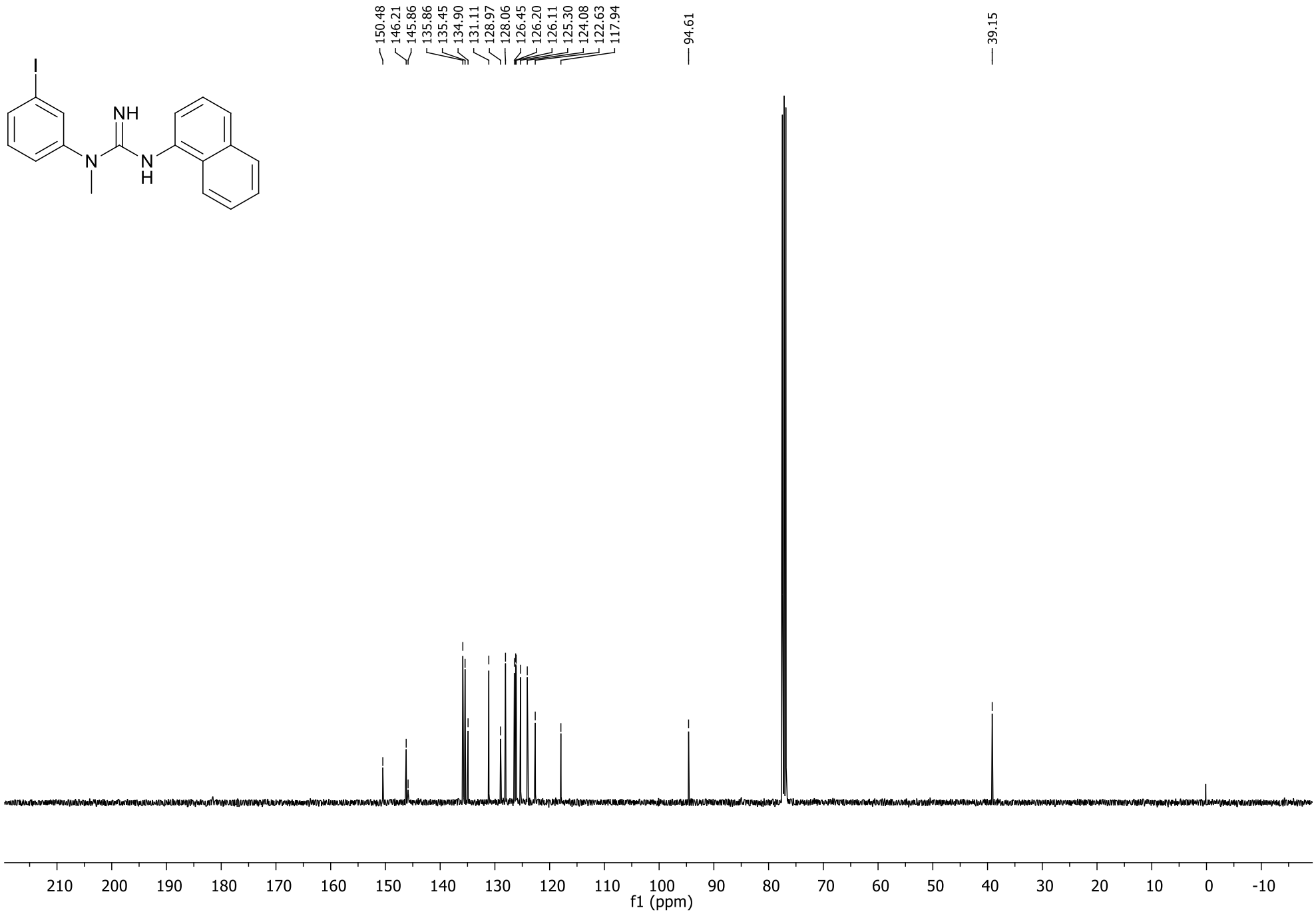
f1 (ppm)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145.86
135.86
135.45
134.90
131.11
128.97
128.06
126.45
126.20
126.11
125.30
124.08
122.63
117.94
94.61
39.15
I
NH
N
N
H
210
200
190
180
170
160
150
140
130
120
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100
90
80
70
60
50
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30
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10
0
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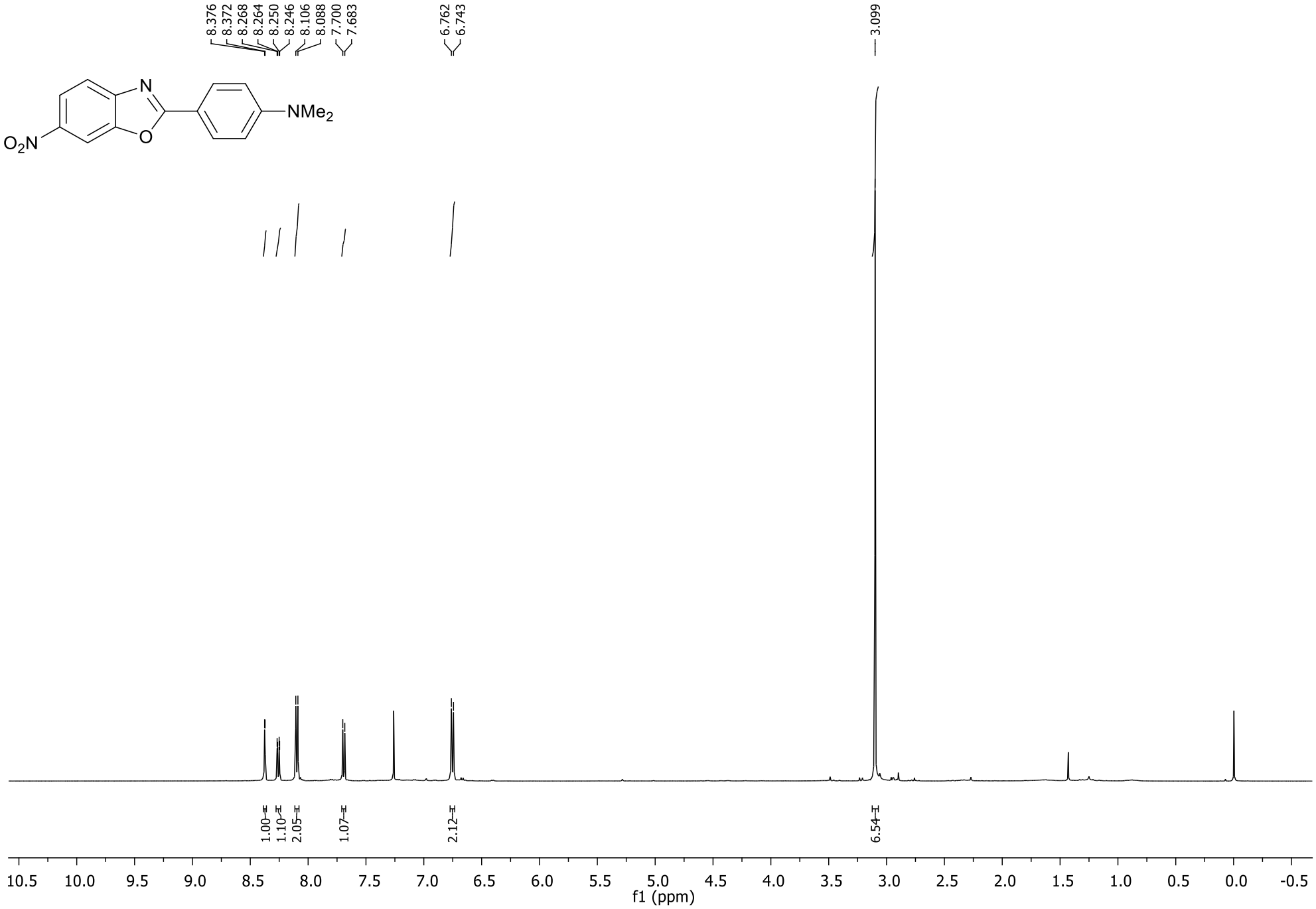
f1 (ppm)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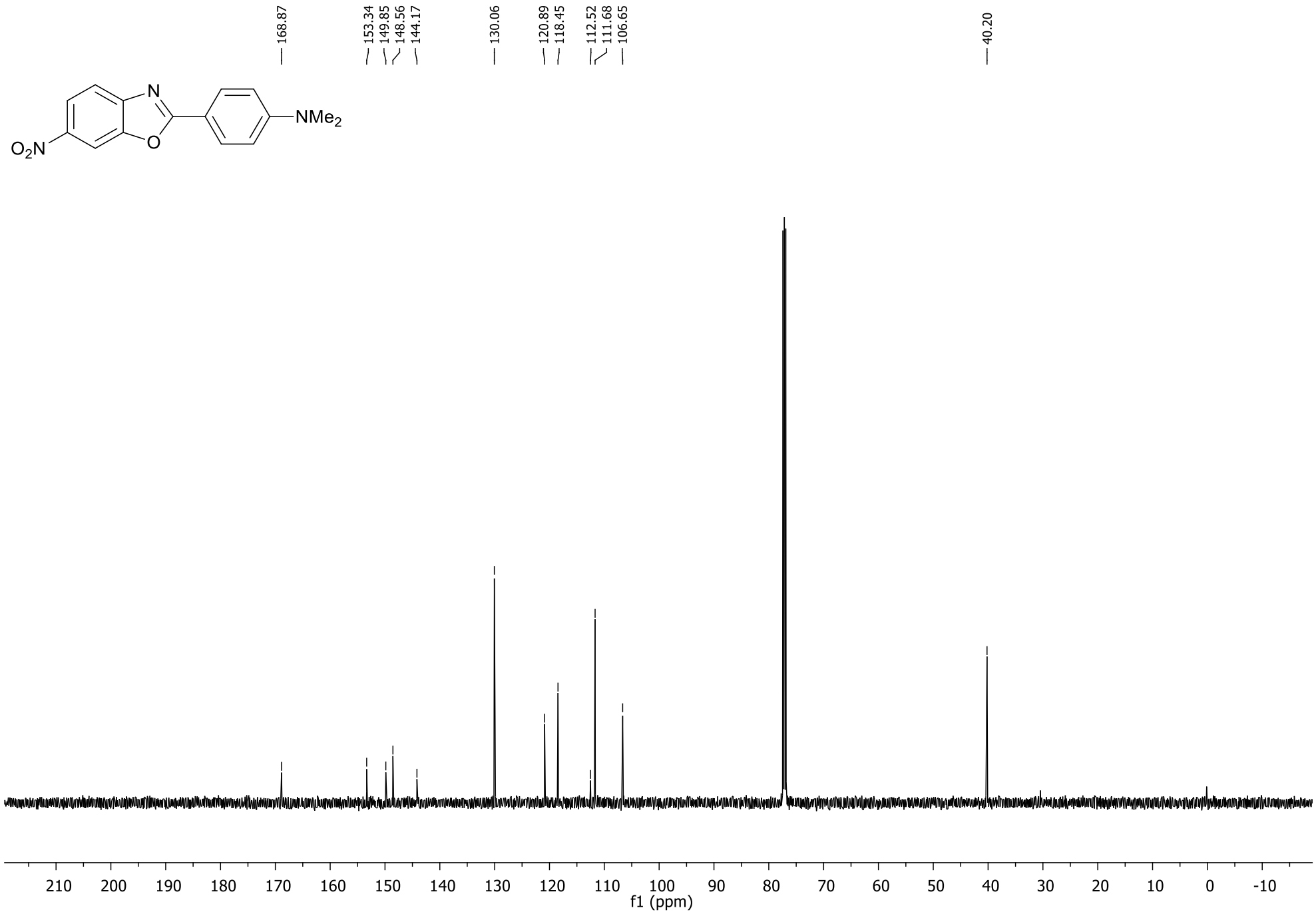
8.106
8.088
7.700
7.683
6.762
6.743
3.099
N
O
O_2N
NMe_2
1.00
1.10
2.05
1.07
2.12
6.54
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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149.85
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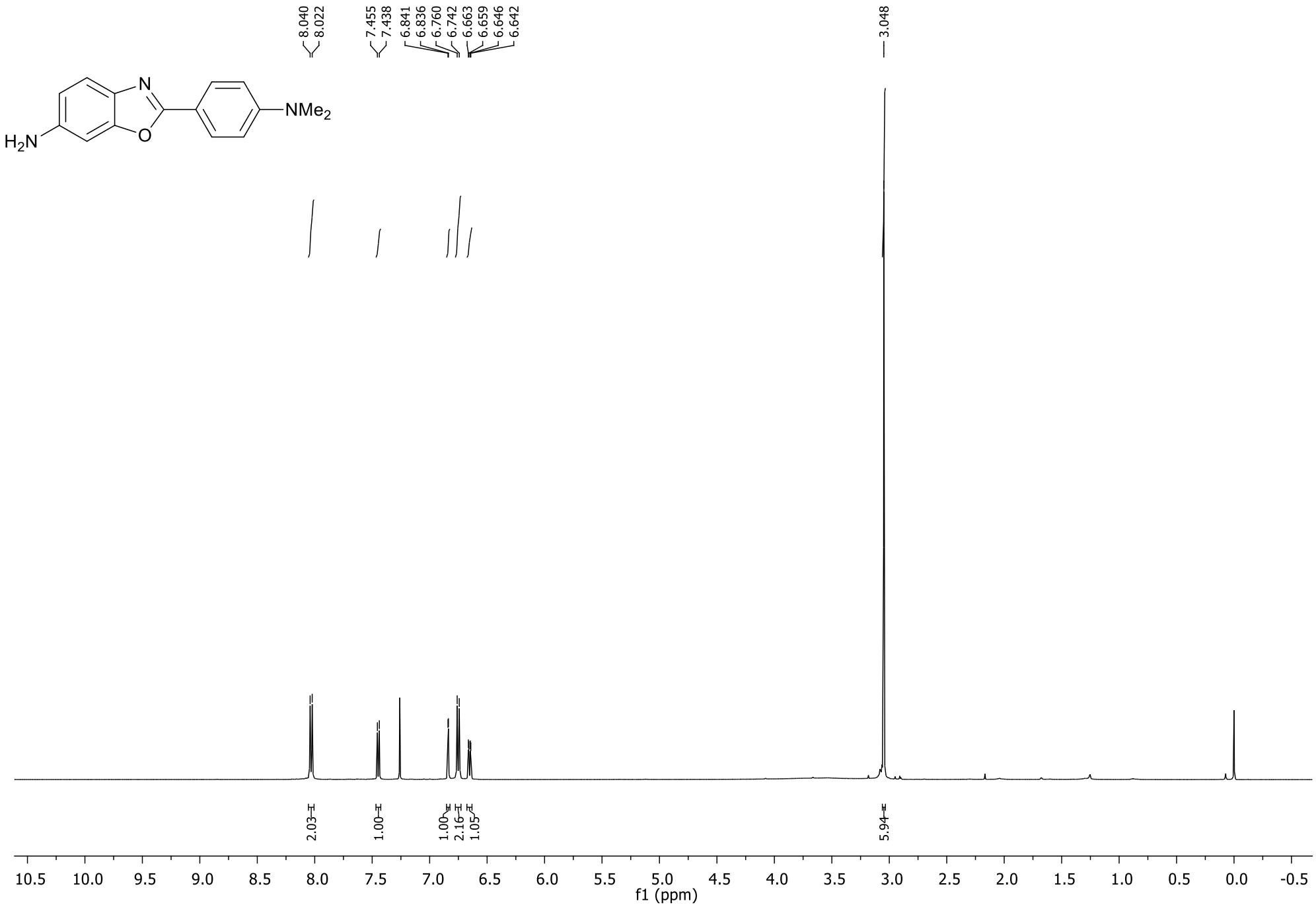
144.17
130.06
120.89
118.45
112.52
111.68
106.65
40.20
N
O
NMe2
O2N
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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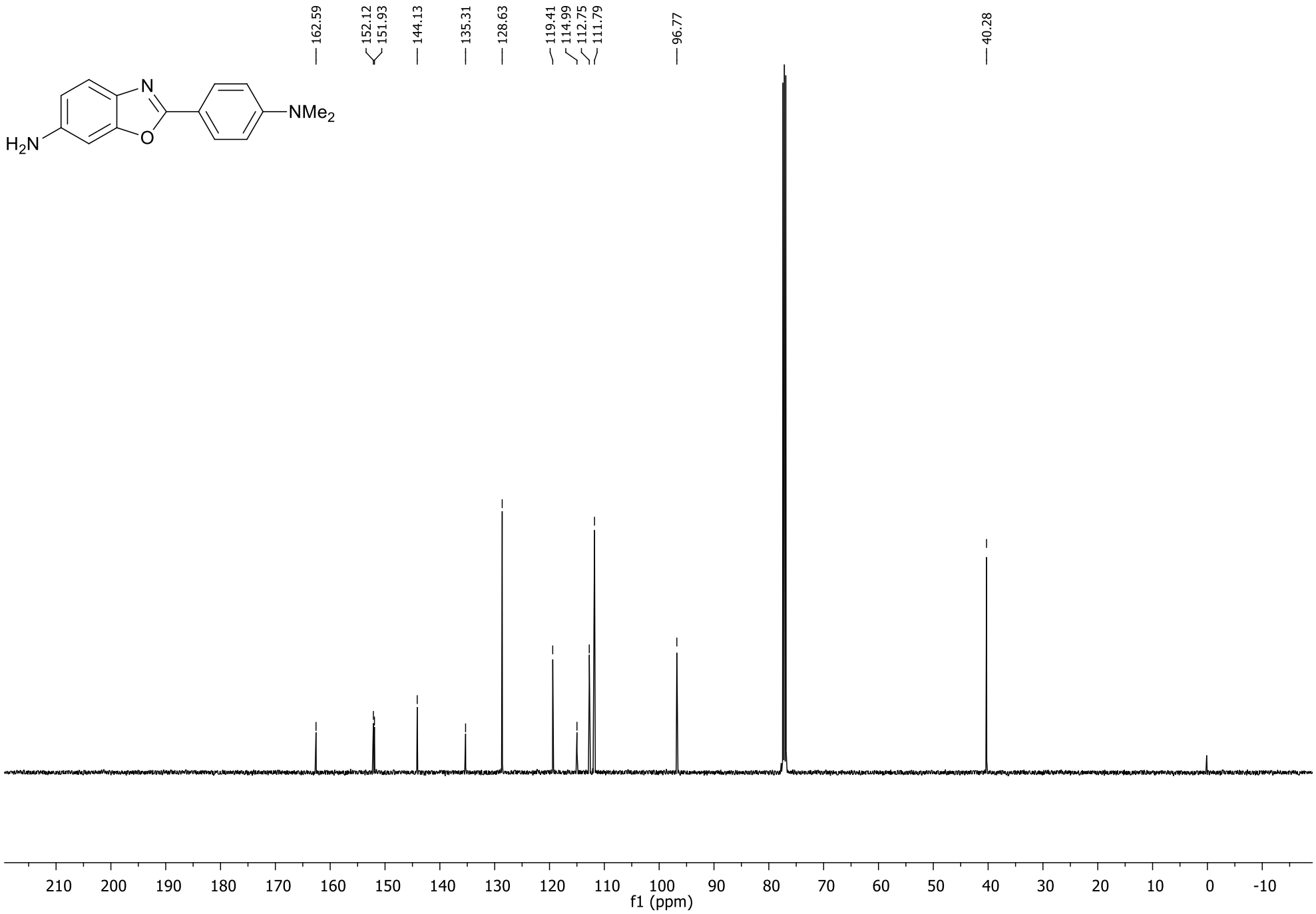
8.022
7.455
7.438
6.841
6.836
6.760
6.742
6.663
6.659
6.646
6.642
3.048
N
NMe2
H2N
O
2.03
1.00
1.00
2.16
1.05
5.94
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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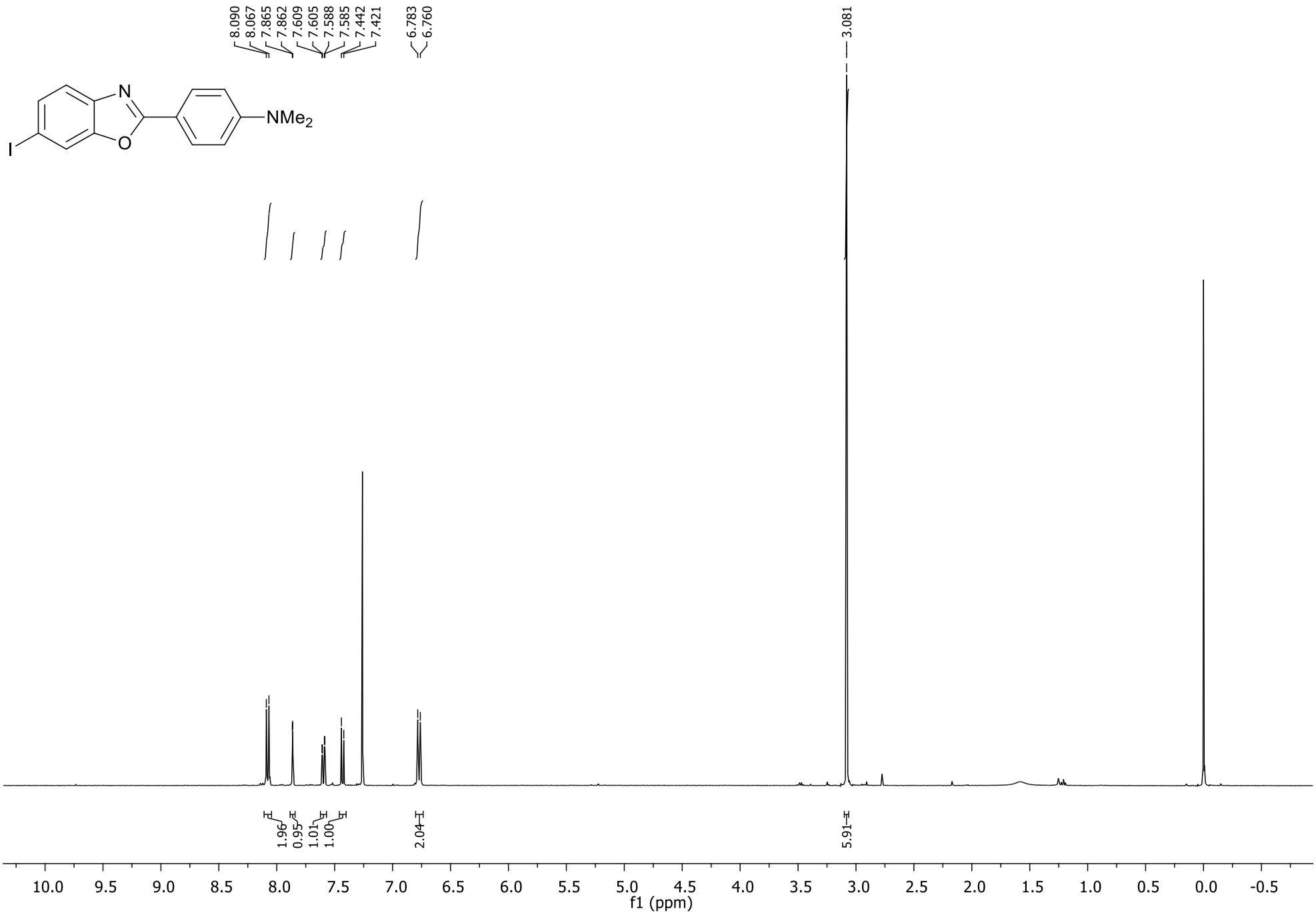
152.12
151.93
144.13
135.31
128.63
119.41
114.99
112.75
111.79
96.77
40.28
N
O
H2N
NMe2
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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8.067
7.865
7.862
7.609
7.605
7.588
7.585
7.442
7.421
6.783
6.760
3.081
N
O
I
NMe2
1.96
0.95
1.01
1.00
2.04
5.91
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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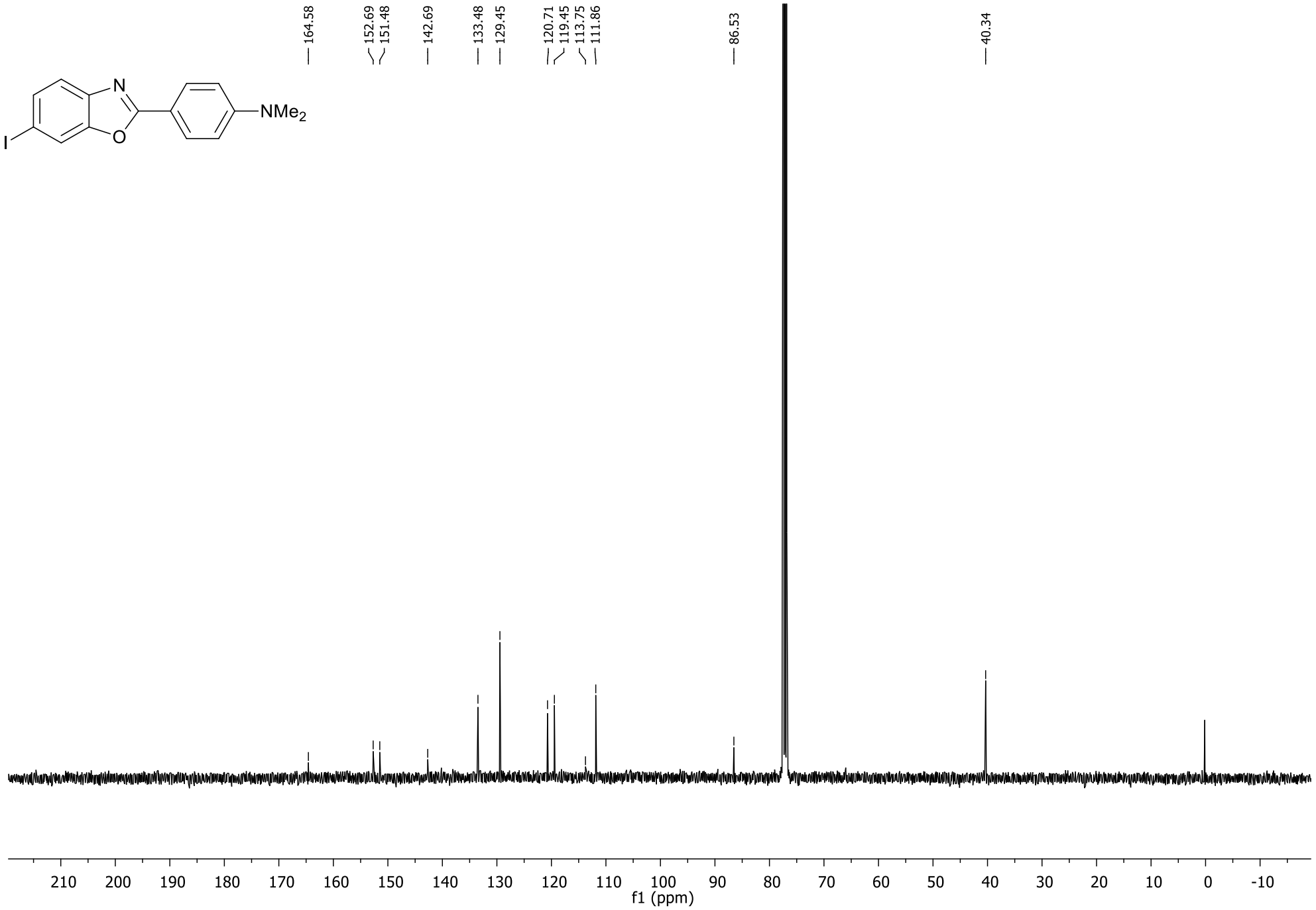
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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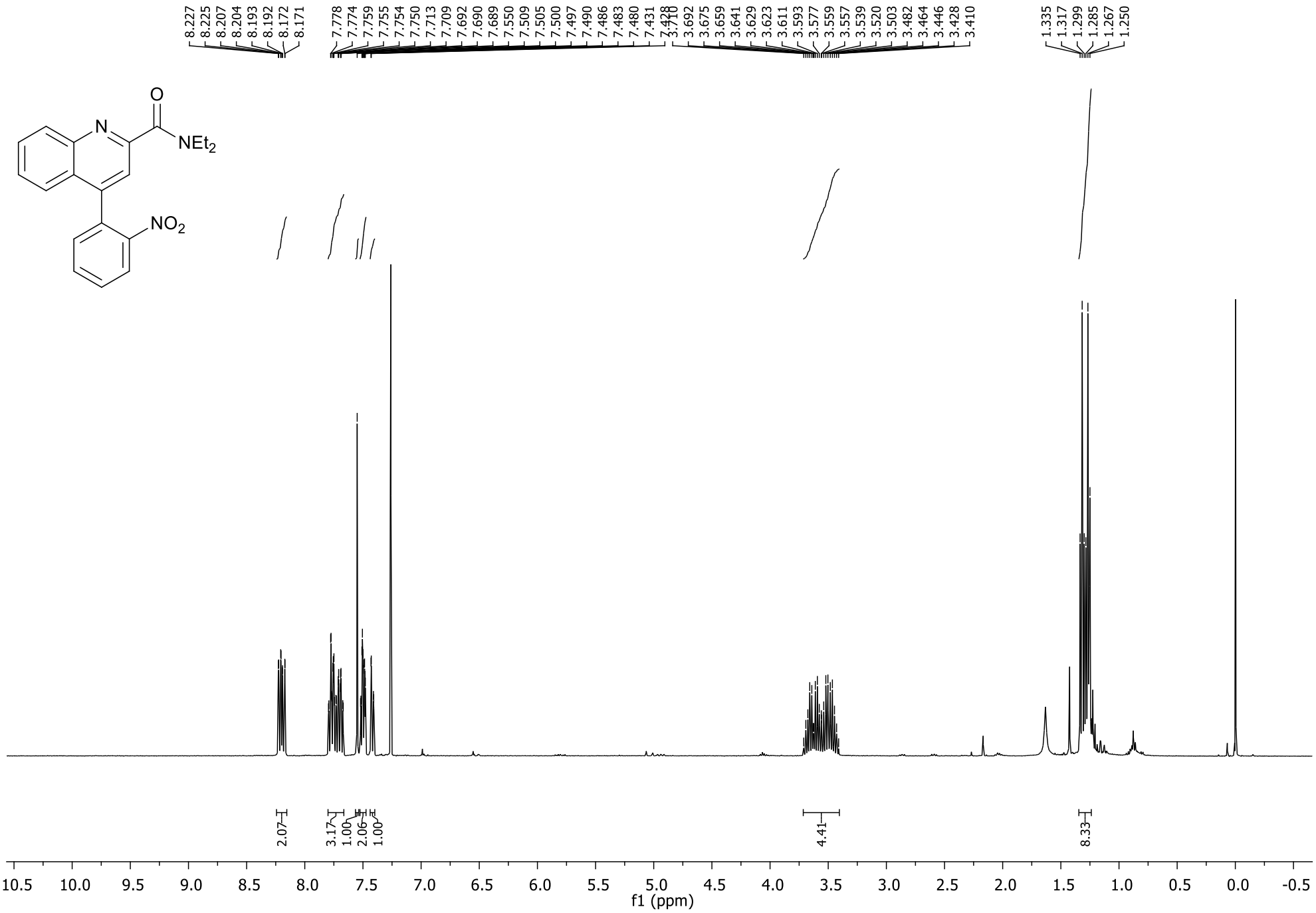
151.48
142.69
133.48
129.45
120.71
119.45
113.75
111.86
86.53
40.34
N
O
I
NMe2
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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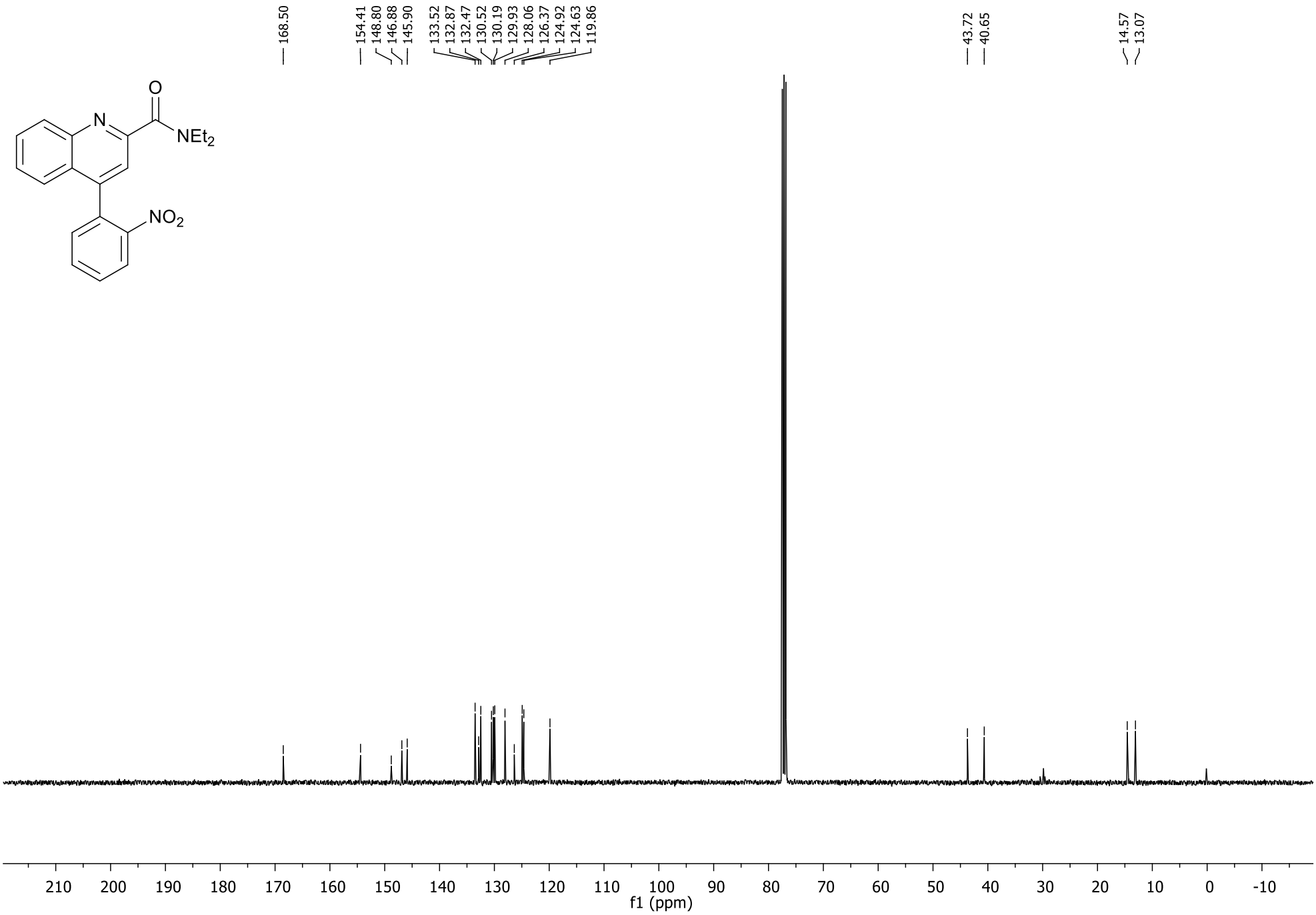
8.207
8.204
8.193
8.192
8.172
8.171
7.778
7.774
7.759
7.755
7.754
7.750
7.713
7.709
7.692
7.690
7.689
7.550
7.509
7.505
7.500
7.497
7.490
7.486
7.483
7.480
7.431
7.428
3.710
3.692
3.675
3.659
3.641
3.629
3.623
3.611
3.593
3.577
3.559
3.557
3.539
3.520
3.503
3.482
3.464
3.446
3.428
3.410
1.335
1.317
1.299
1.285
1.267
1.250
O
N
NEt2
NO2
2.07
3.17
1.00
2.06
1.00
4.41
8.33
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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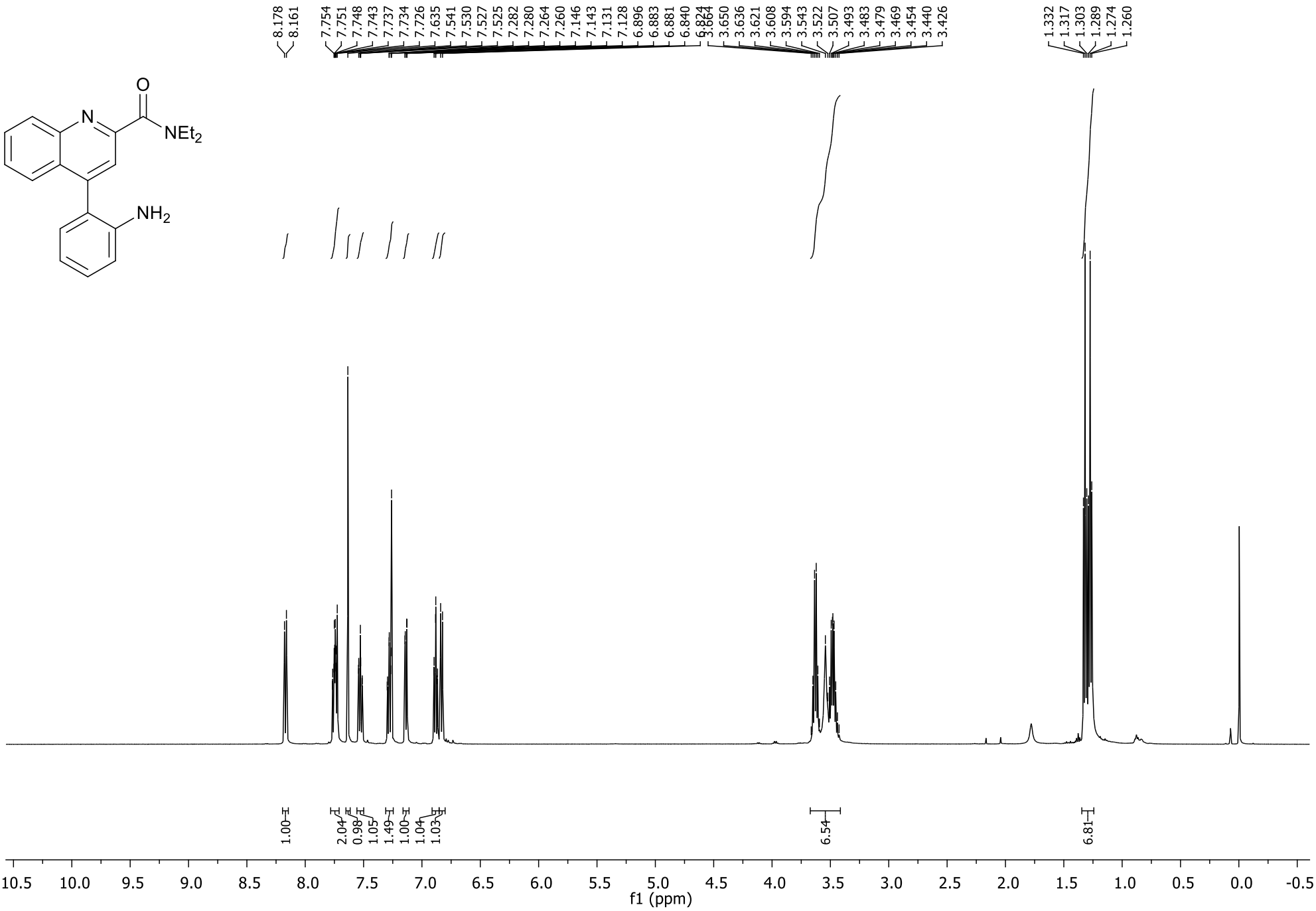
132.87
132.47
130.52
130.19
129.93
128.06
126.37
124.92
124.63
119.86
43.72
40.65
14.57
13.07
O
N
NEt2
NO2
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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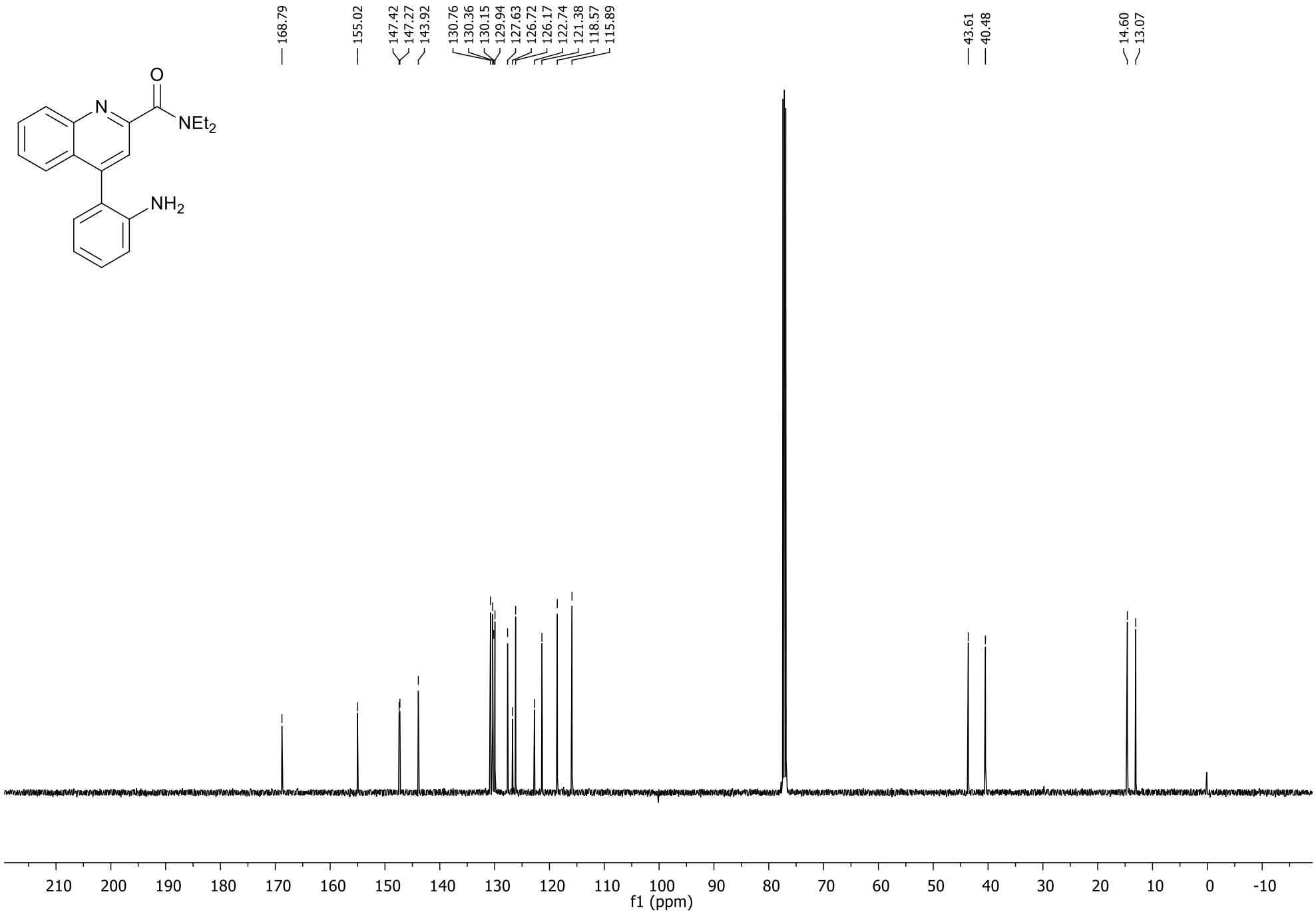
7.734
7.726
7.635
7.541
7.530
7.527
7.525
7.282
7.280
7.264
7.260
7.146
7.143
7.131
7.128
6.896
6.883
6.881
6.840
6.824
3.664
3.650
3.636
3.621
3.608
3.594
3.543
3.522
3.507
3.493
3.483
3.479
3.469
3.454
3.440
3.426
1.332
1.317
1.303
1.289
1.274
1.260
O
N
NEt2
NH2
1.00
2.04
0.98
1.05
1.49
1.00
1.04
1.03
6.54
6.81
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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143.92
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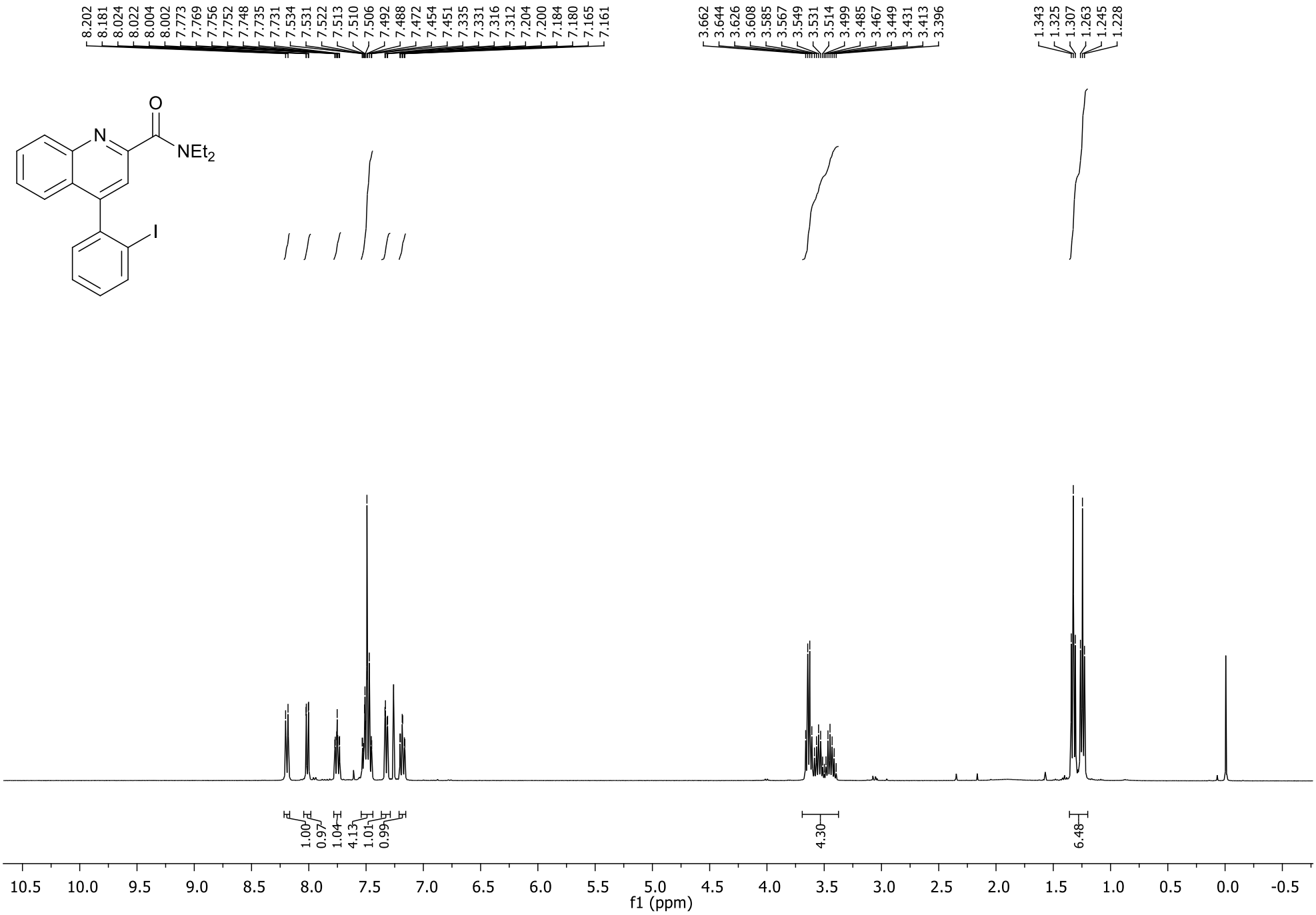
130.15
129.94
127.63
126.72
126.17
122.74
121.38
118.57
115.89
43.61
40.48
14.60
13.07
O
N
NEt2
NH2
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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8.002
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7.769
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7.752
7.748
7.735
7.731
7.534
7.531
7.522
7.513
7.510
7.506
7.492
7.488
7.472
7.454
7.451
7.335
7.331
7.316
7.312
7.204
7.200
7.184
7.180
7.165
7.161
3.662
3.644
3.626
3.608
3.585
3.567
3.549
3.531
3.514
3.499
3.485
3.467
3.449
3.431
3.413
3.396
1.343
1.325
1.307
1.263
1.245
1.228
O
N
NEt2
I
1.00
0.97
1.04
4.13
1.01
0.99
4.30
6.48
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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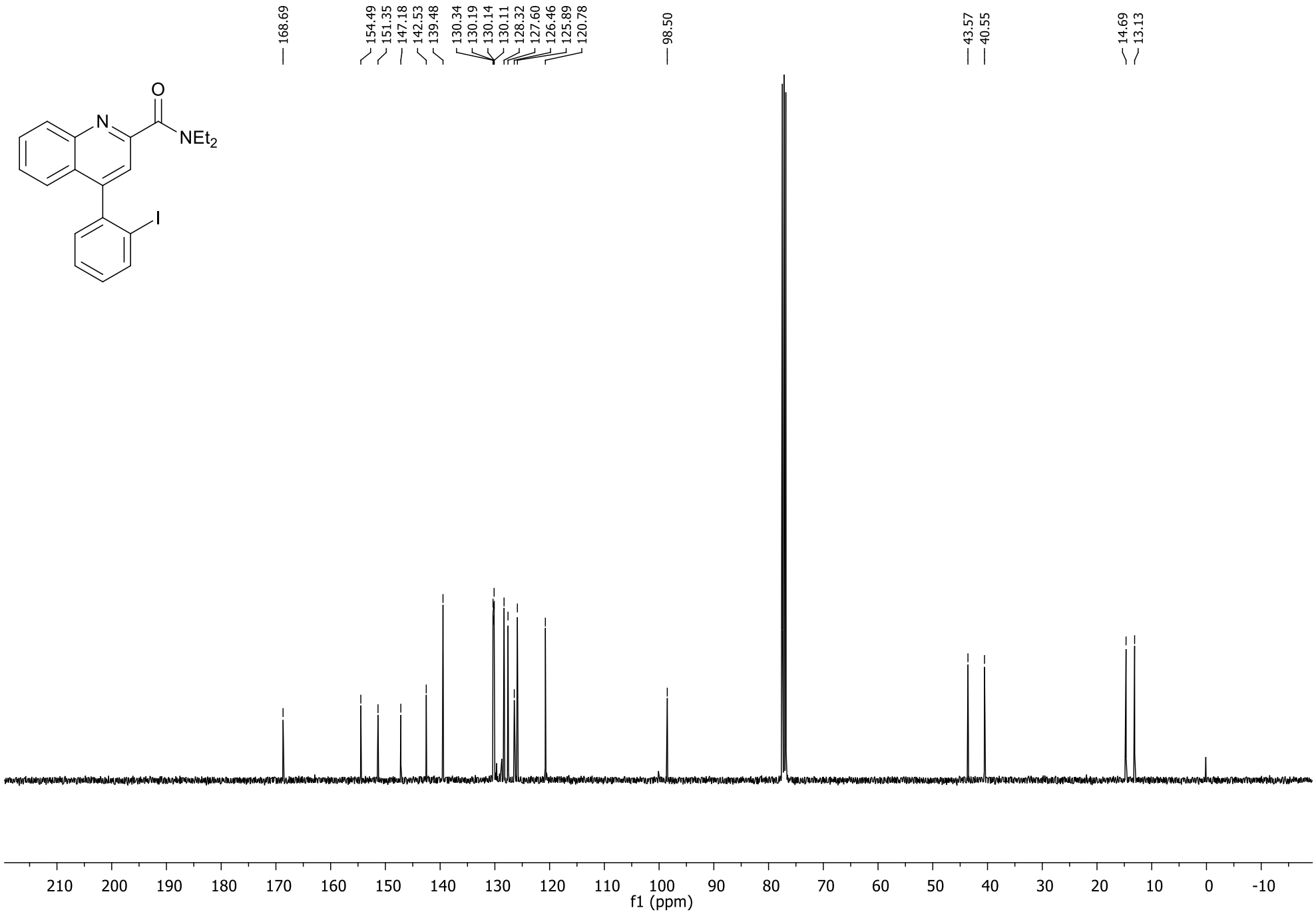
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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139.48
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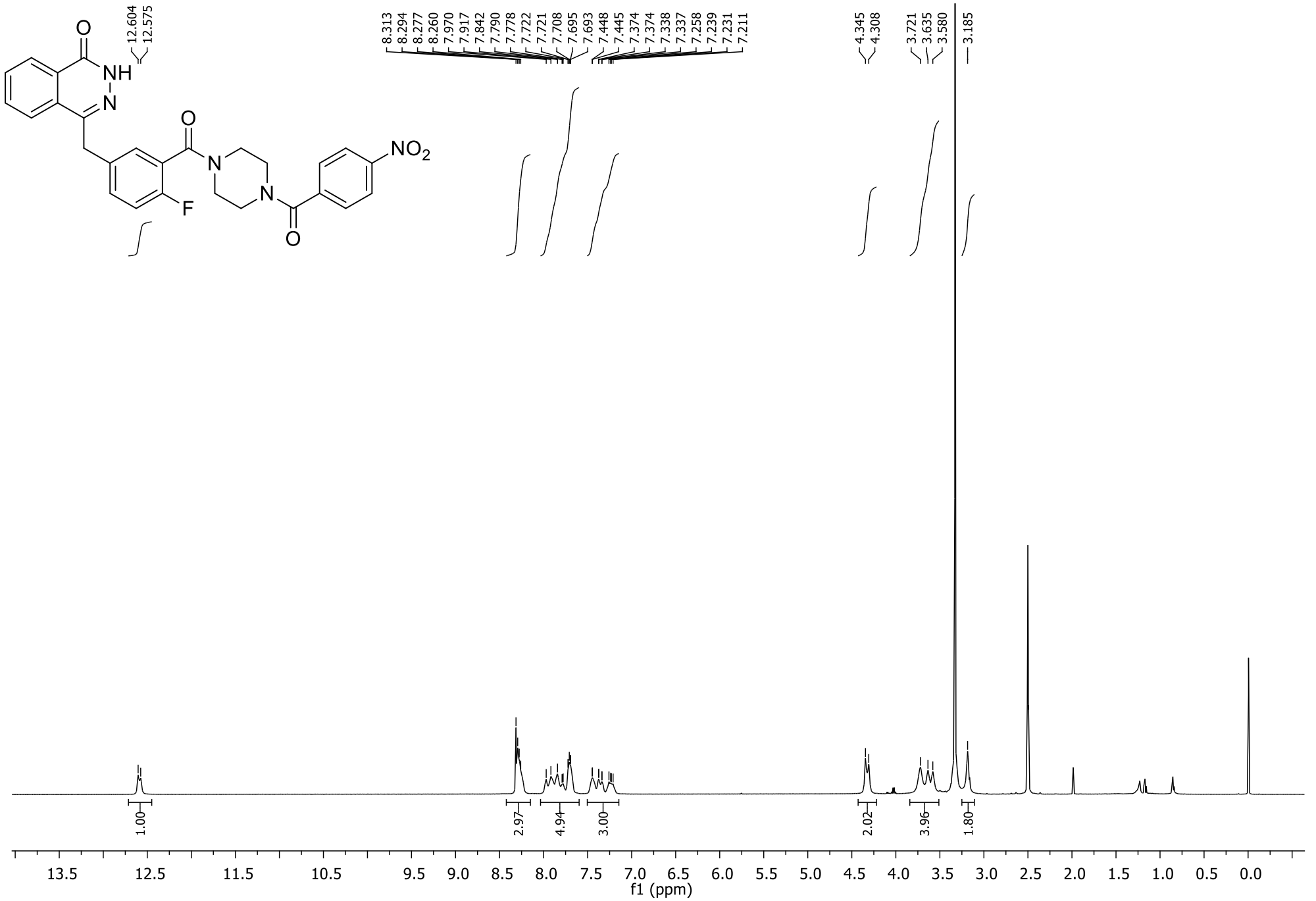
130.19
130.14
130.11
128.32
127.60
126.46
125.89
120.78
98.50
43.57
40.55
14.69
13.13
O
N
NEt2
I
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.917
7.842
7.790
7.778
7.722
7.721
7.708
7.695
7.693
7.448
7.445
7.374
7.374
7.338
7.337
7.258
7.239
7.231
7.211
4.345
4.308
3.721
3.635
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3.185
1.00
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4.94
3.00
2.02
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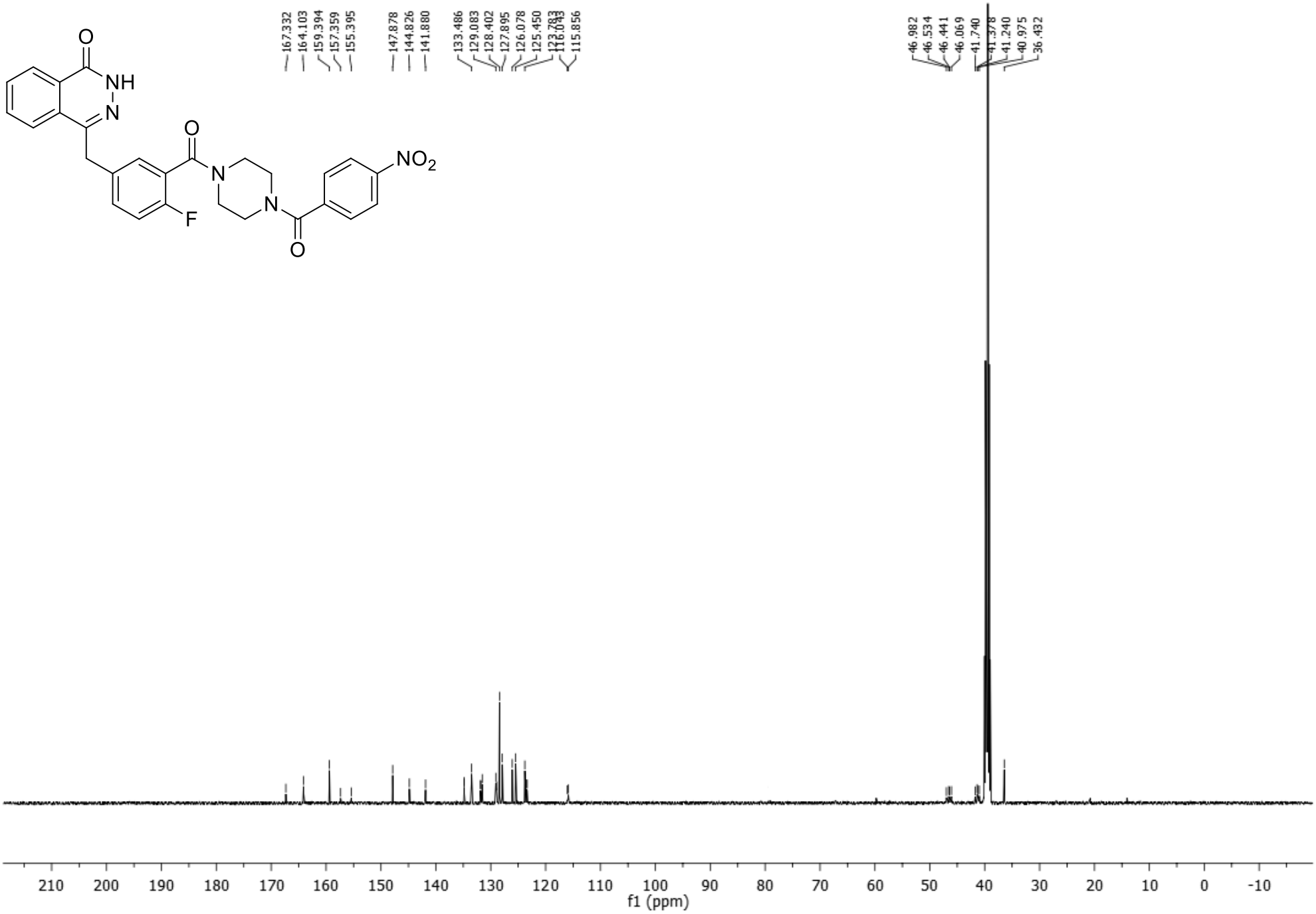
1.80
f1 (ppm)


O
NH
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O
N
N
O
F
NO2
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155.395
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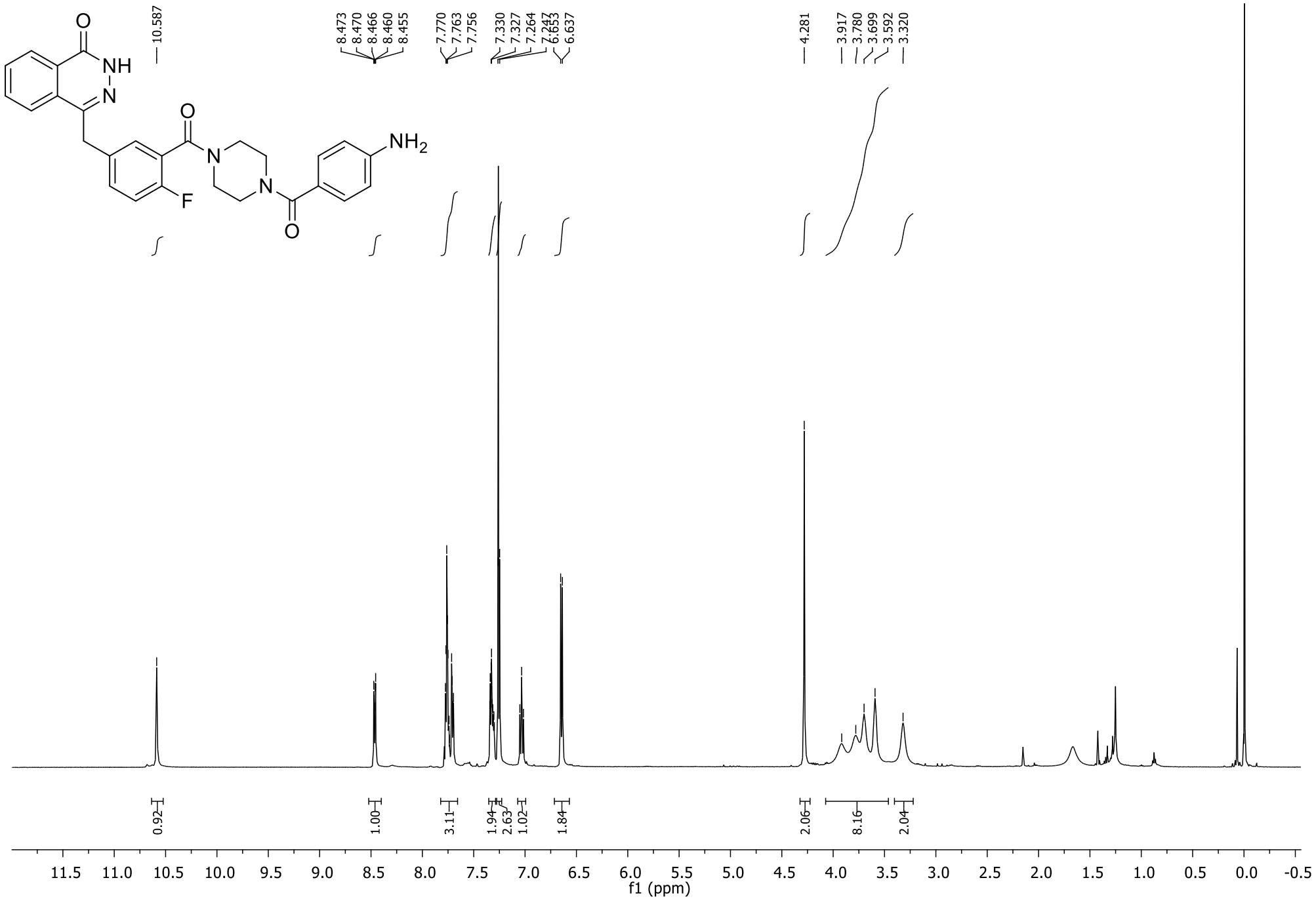
144.826
141.880
133.486
129.083
128.402
127.895
126.078
125.450
123.783
116.043
115.856
46.982
46.534
46.441
46.069
41.740
41.378
41.240
40.975
36.432
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.330
7.327
7.264
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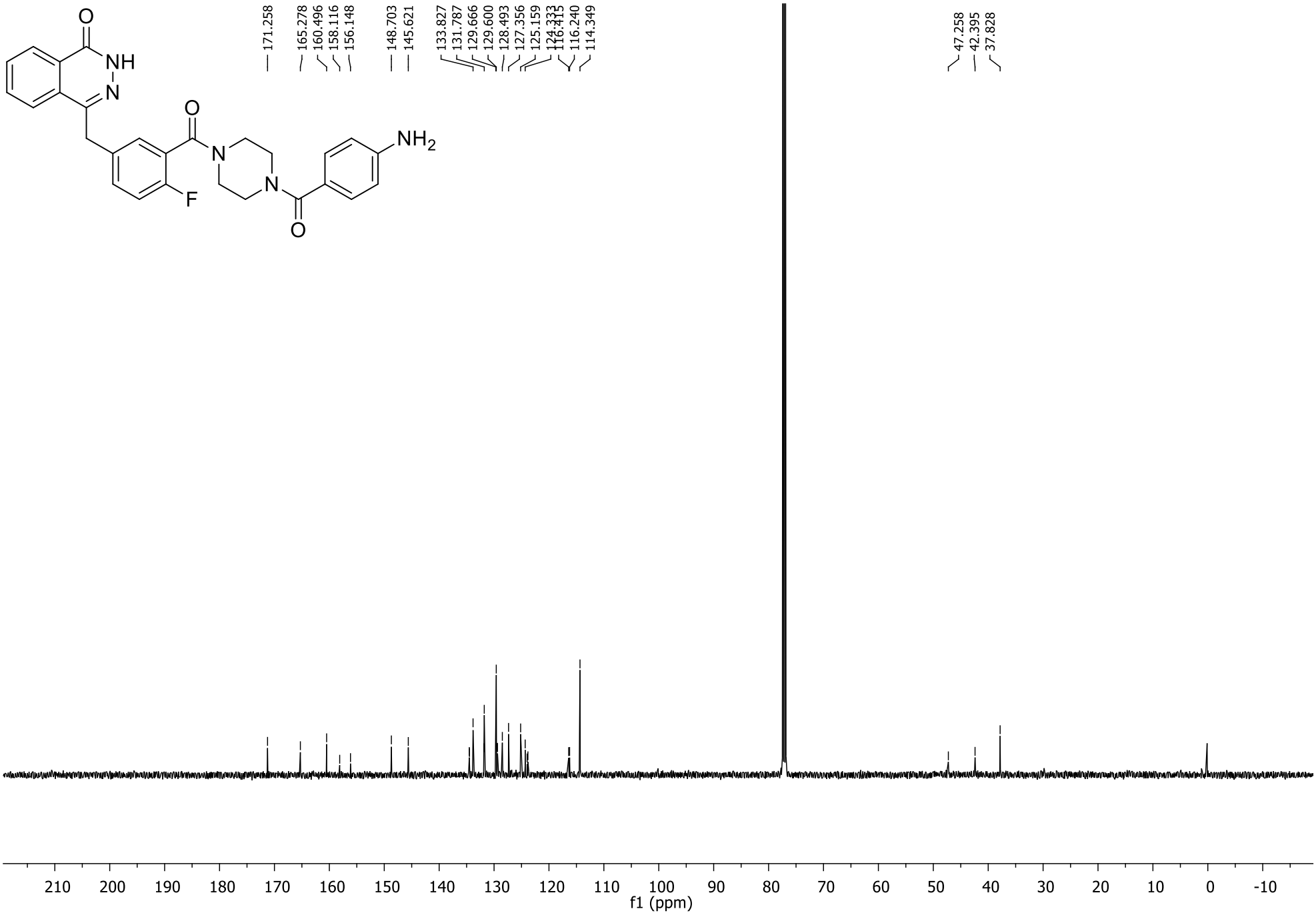
6.637
4.281
3.917
3.780
3.699
3.592
3.320
NH
N
O
O
N
N
O
F
NH2
0.92
1.00
3.11
1.94
2.63
1.02
1.84
2.06
8.16
2.04
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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133.827
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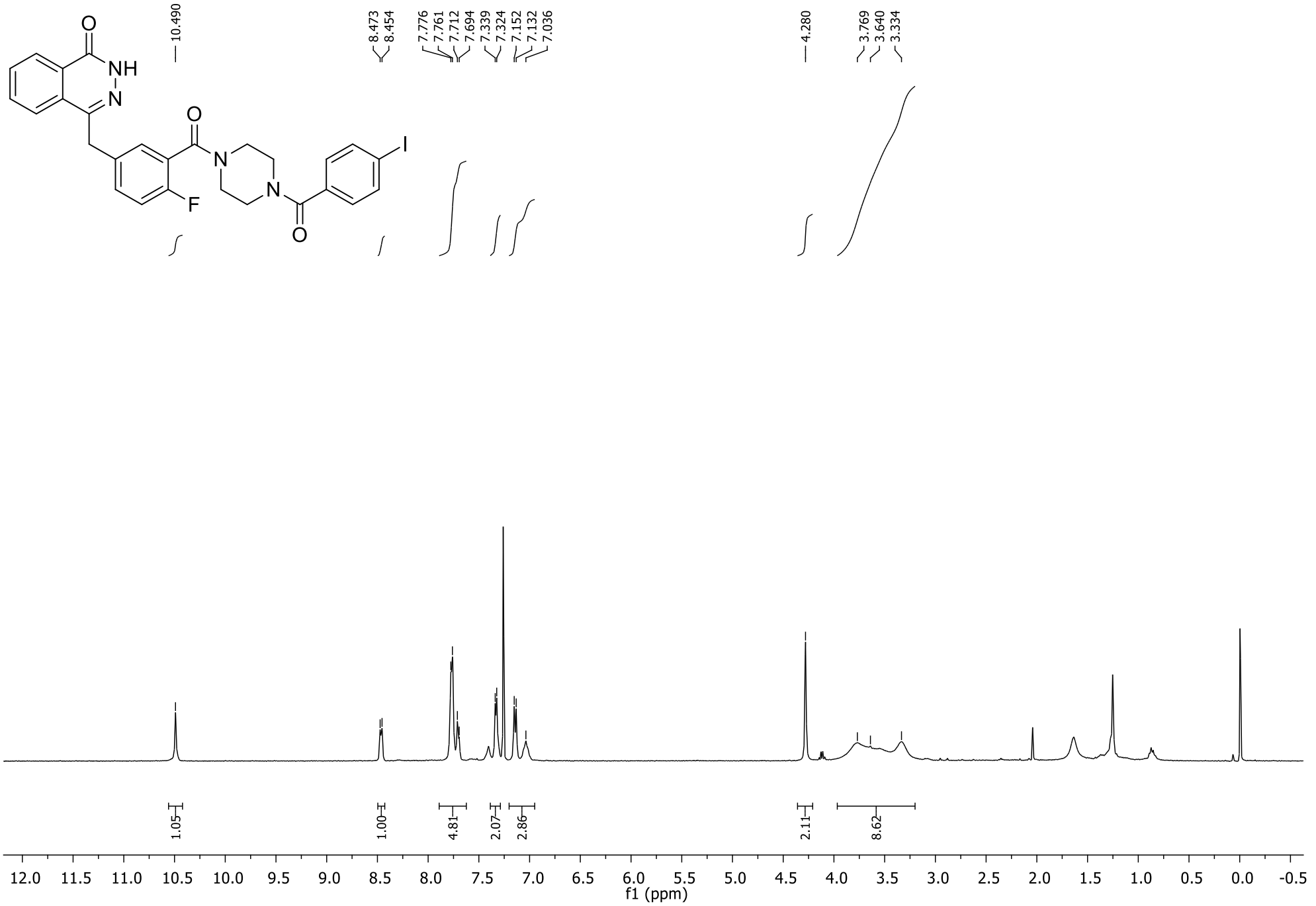
129.666
129.600
128.493
127.356
125.159
124.333
116.411
116.240
114.349
47.258
42.395
37.828
O
NH
N
O
N
N
O
F
NH2
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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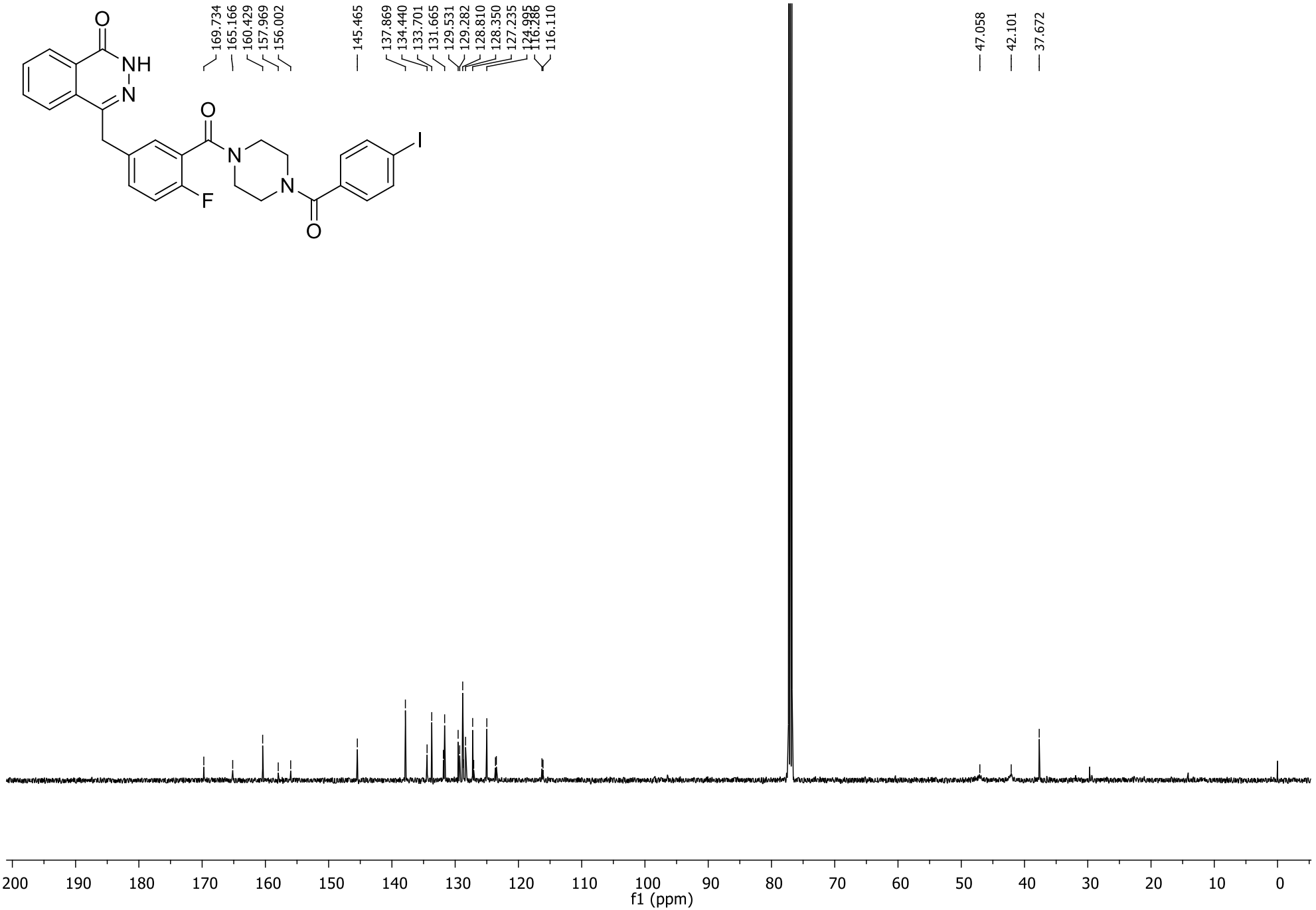
7.339
7.324
7.152
7.132
7.036
4.280
3.769
3.640
3.334
O
NH
N
O
N
N
I
F
O
1.05
1.00
4.81
2.07
2.86
2.11
8.62
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


O
NH
N
O
N
N
O
F
I
169.734
165.166
160.429
157.969
156.002
145.465
137.869
134.440
133.701
131.665
129.531
129.282
128.810
128.350
127.235
124.995
116.286
116.110
47.058
42.101
37.672
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)