Chemistry informer libraries: a chemoinformatics enabled approach to evaluate and advance synthetic methods

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Electronic Supplementary Information

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I. General Information Section 1- General Experimental Procedures

All reagents were used as purchased from commercial suppliers. Solvents were purchased from Aldrich, anhydrous, sure-seal quality, and used with no further purification. The reagents and catalysts were purchased from commercial sources and stored in the glovebox. All reactions, including parallel synthesis, were performed inside an MBraun glovebox operating with a constant N_2-purge (oxygen typically < 5 ppm) unless otherwise noted. Reaction experimental design was aided by the use of Accelrys Library Studio. Reactions run at 10 μmol scale for the limiting reagent were carried out in 1 mL glass vials (Analytical Sales, Cat. No. 84001, 8 x 30 mm, 1mL, flat bottom) equipped with magnetic tumble stir bars (V&P Scientific, Cat. No. 7111D-1 and 716-1 for microvials) in 24-well reaction plates (Analytical-Sales, Cat. No. 24249). Reactions run at 2.5 μmol scale for the limiting reagent were carried out in 250 μL microvials (Analytical Sales, Cat. No. 10421) in 24-well reaction microplates (Analytical-Sales, Cat. No. 24250). Liquid handling was done using single and multi-channel Eppendorf pipettors (10, 100, 200, and 1000 μL). On completion of solution dosing the plates were covered by a perfluoroalkoxy alkane (PFA) mat (Analytical-Sales, Cat. No. 96967 and 24261), followed by two silicon rubber mats (Analytical-Sales, Cat. No. 96965 and 24262), and an aluminum cover which was tightly and evenly sealed by 9 screws. The scale-up reactions described below were typically run prior to identification of optimal conditions, and no attempt was made to optimize the isolated yield of material. The goal in these experiments was to isolate pure material for characterization and to provide a standard for quantitative LC analysis. Quantitative analysis was accomplished by reverse phase UPLC (Waters X-Bridge™ BEH 2.5 micron, RP C-18, 2.1 x 50 mm column, eluents: MeCN-H_2O containing 0.05% TFA) using an internal standard (either 4,4-di-tert-butyl biphenyl, or 1,3,5-trimethoxybenzene as noted in the experiment). Extinction coefficients for LC analysis were determined by first measuring the molar ratio of a mixture of desired product with internal standard by ^{1}H-NMR analysis, then determining the UV absorption for this mixture by running the same mixture on the UPLC method used for analysis. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 500 (500 MHz) as noted, and are internally referenced to residual protio solvent signals. Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration and coupling constant (Hz). Data for ^{13}C NMR are reported in terms of chemical shift. Mass spectra were obtained from an Agilent LC/MSD TOF model G1969A.

II. General Information Section 2- Creation of Small-Molecule Drug Principal Component Analysis.

Selection of Compounds for Analysis. To obtain a set of drugs, FDA approved drugs were downloaded from DrugBank (accessed September 29th, 2015), and filtered for MW < 650, Number of atoms >6, Number of aromatic rings >0, Number of hydrogen bond acceptors ≤10, and number of hydrogen bond donors ≤5, resulting in 1,040 unique compounds. To obtains sets of literature compounds, the products reported for the Suzuki (1981, seminal),[1] Suzuki (2004-2013, evolved)[2,3,4,5,6,7,8] cyanation,[9,10,11,12,13,14] and aryl amine coupling[15,16,17,18,19,20] were obtained either from SciFinder or generated by hand. For the aryl amine coupling products, we required the coupling of an aryl group with a secondary amine. This resulted in sets of 10 (seminal Suzuki), 227 (evolved Suzuki), 108 (cyanation), and 75 (aryl amine coupling) for literature products. To obtain the informer products sets of 24 (Suzuki), 24 (cyanation), and 18 (aryl amine coupling) products were generated based on the product of the informer library substrate with the corresponding reactant. An SD file containing all drugs, literature products, and informer library products is included as supplementary information.

PCA Training: Fourteen physical chemical properties that are often used to assess the drug-like nature of small molecules were computed for each compound: molecular weight, molecular polar surface area, number of atoms, number of positive atoms, number of negative atoms, number of rotatable bonds, number of rings, number of aromatic rings, number of ring assemblies, number of stereo atoms, number of hydrogen bond acceptors, number of hydrogen bond donors, fraction sp^3, and AlogP. The principle components were calculated in Pipeline Pilot, using the above physical properties to describe each compound. Prior to training the PCA, properties were centered (subtract mean) and scaled (divide by variance). The principle components that captured the most variance were then visualized in Spotfire. The cumulative total variance explained by the principle components were as follows: 37% (PC1), 58% (PC2), 71% (PC3), and 78% (PC4). The first two principle components were visualized in the main text (Fig 2), and the third and fourth components are visualized below (Fig S1). The loadings of the physical properties used to generate the PCA were assessed to assist in the interpretation of the PCA (Fig S2).

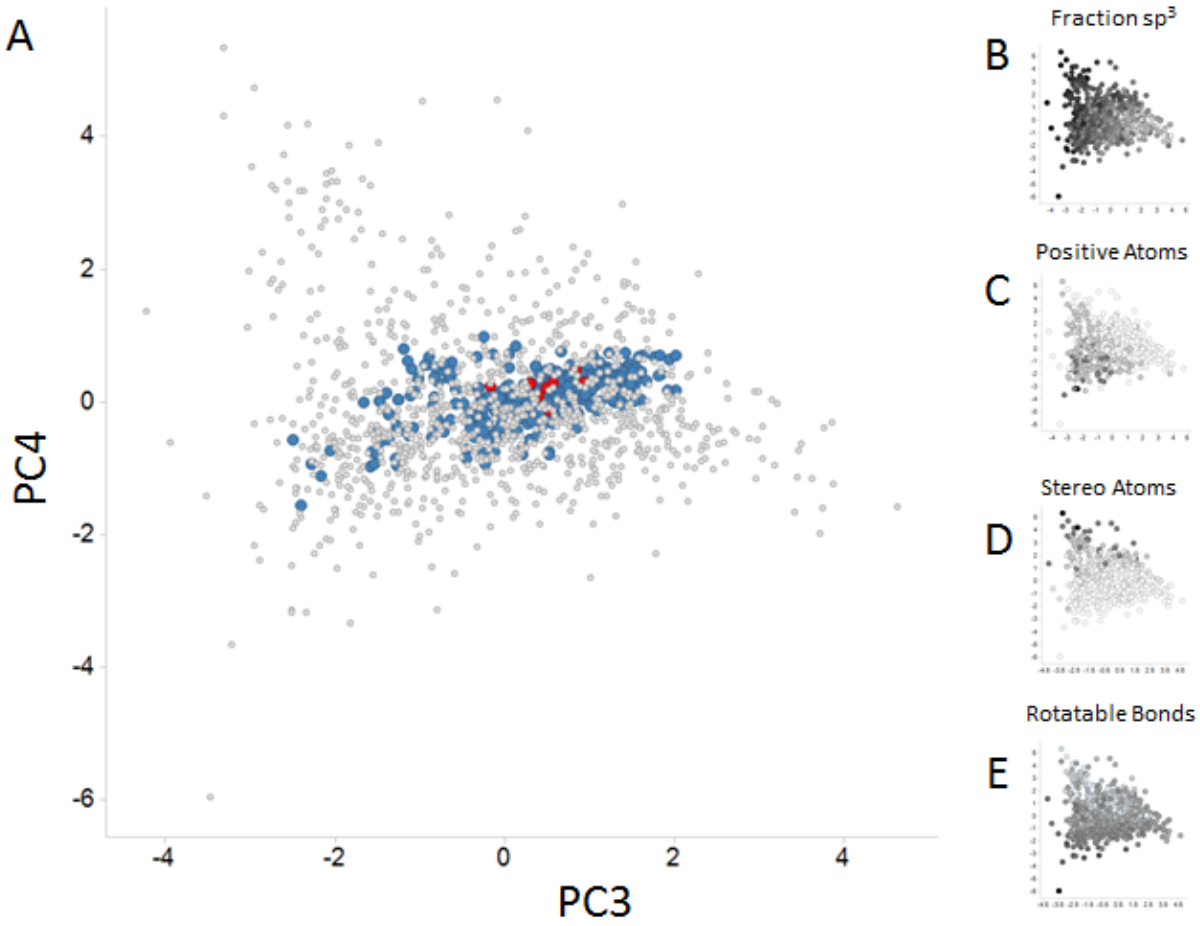


Figure S1. Principal component analysis (PCA) comparing small molecule drugs with products described in synthetic literature reports. Figure S1A shows a principle component analysis (PC4 vs PC3) used to visualize the physicochemical space occupied by marketed small molecule drugs compounds (grey) and products described in literature reports for several reaction types evaluated in this work: in red are compounds that were prepared in the seminal Suzuki-Miyaura paper, in blue are the products formed in leading literature Suzuki-Miyaura reports, recent methods reported for the conversion of aryl pinacol boronates into aryl nitriles and recent Buchwald-Hartwig C-N coupling methods. Representative structures from both the small molecule drugs collection and literature reports are highlighted. Figures S1B-E depict how properties with the greatest contribution to PC3 and PC4 are mapped by the PCA, with black representing the highest values for each parameter.

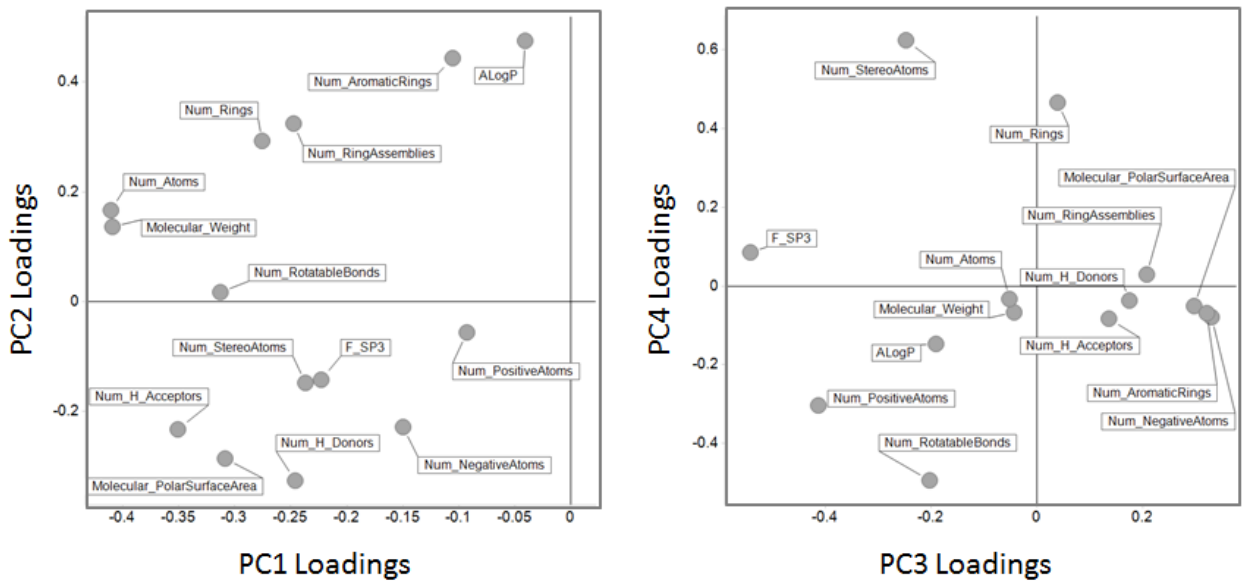


Figure S2. The loadings for PC1-PC4 were visualized to help interpret the PCA. We see that by inspecting the magnitudes of the loadings size (molecular weight, number of atoms) and number of hydrogen bond donors contribute the greatest to PC1, while hydrophobicity (ALogP and number of aromatic rings) contribute the greates to PC2. The greatest contributions for PC3 are fractions sp3 and number of positive atoms while the greatest contributions to PC4 are from the number of stereo atoms and the number of rotatable bonds.

III. Experimental Section 1 – Comparison of Suzuki-Miyaura Cross Coupling Methods using the Aryl Pinacol Boronate Informer Library

Experimental Procedure for Figure 3D, Entry 1. In a nitrogen filled glovebox to 1 mL reaction vials containing aryl pinacol boronates (10 µmol), along with 4,4'-di-tert-butyl biphenyl (10 µmol) internal standard and magnetic stir bars, was added 36.6 µl of a solution of 6- bromo-1H-indole (0.41 M in DME, 15 µmol, 1.5 equiv.) then 10 µl of tetrakis(triphenylphosphine)palladium (0.05 M in DME, 0.50 µmol, 5 mol%) was added, followed by 20 µl of Na_2CO_3 (1.0 M aquoeus, 20 µmol, 2 equiv.). The reaction vials were sealed and stirred at 85 °C for 24 hrs. The rxn vials were then cooled to r.t. and diluted with 500 µL of DMSO and were stirred vigorously for 5 min. A 10 µL aliquot was removed from each vial and diluted with 700 µl of MeCN and quantitative UPLC-MS analysis was performed to determine the solution yield.

Experimental Procedure for Figure 3D, Entry 2. In a nitrogen filled glovebox to 1 mL reaction vials containing aryl pinacol boronates (10 µmol), along with 4,4'-di-tert-butyl biphenyl (10 µmol) internal standard and magnetic stir bars, was added 36.6 µl of a solution of 6- bromo-1H-indole (0.41 M in DME, 15 µmol, 1.5 equiv.) then 10 µl of [1,1′-Bis(diphenylphosphino)ferrocene]dichloropalladium(II), complex with dichloromethane, (0.05M in DME, 0.50 µmol, 5 mol%), followed by 20 µl of Na_2CO_3 (1.0

M aqueous, 20 µmol, 2 equiv.). The reaction vials were sealed and stirred at 85 °C for 24 hrs. The rxn vials were then cooled to r.t. and diluted with 500 µL of DMSO and were stirred vigorously for 5 min. A 10 µL aliquot was removed from each vial and diluted with 700 µL of MeCN and quantitative UPLC-MS analysis was performed to determine the solution yield.

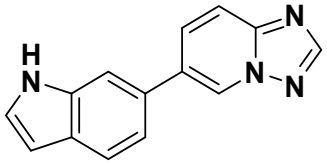
Experimental Procedure for Figure 3D, Entries 3-5. In a nitrogen filled glovebox to 1 mL reaction vials containing aryl pinacol boronates (10 µmol), along with 4,4'-di-tert-butyl biphenyl (10 µmol) internal standard and magnetic stir bars, was added 36.6 µl of a solution of 6- chloro-1H-indole (0.41 M in THF, 15 µmol, 1.5 equiv.) then 10 µl of palladium XPhos G2 precatalyst (0.05 M in THF, 0.50 µmol, 5 mol%) was added, followed by 20 µl of K_3PO_4 (1.0 M aqueous, 20 µmol, 2 equiv.). The reaction vials were sealed and stirred at the desired temperature (as noted in Table 1) for 24 hrs. The rxn vials were then cooled to r.t. and diluted with 500 µL of DMSO and were stirred vigorously for 5 min. A 10 µL aliquot was removed from each vial and diluted with 700 µL of MeCN and quantitative UPLC-MS analysis was performed to determine the solution yield.

General Procedure A for Suzuki-Miyaura Scale-up Reactions. In a nitrogen filled glovebox, aryl pinacol boronates (0.10 mmol) and 6-chloro-1H-indole (15.2 mg, 0.10 mmol, 1 equiv.) were combined with palladium XPhos G2 precatalyst (16 mg, 0.020 mmol, 5 mol %) in anhydrous THF (0.10 M overall conc.). To these mixtures, 150 µl (0.30 mmol) of aq. K_2CO_3 (2.0 M aqueous solution, 0.3 mmol, 3 equiv.) was added and the mixtures were stirred at 60 °C overnight. The mixtures were cooled to r.t., diluted with ethyl acetate (1 mL), washed with aqueous sodium bicarbonate (saturated, 1x1 mL). The organic phase was dried (Na_2SO_4), filtered and the solvent was evaporated under reduced pressure. The crude mixtures were diluted with 0.8 ml of DMSO, then filter through a filter plate (0.45 micron) and purified by RP HPLC (Waters Sunfire™ 5 micron RP C-18, 30x 100 mm column, eluents: MeCN-H2O containing 0.05% TFA). No attempt was made to obtain optimal yield on these experiments, rather to obtain high purity samples for quantitative UPLC analysis.

General Procedure B for Suzuki-Miyaura Scale-up Reactions. In a nitrogen filled glovebox, aryl pinacol boronates (0.10 mmol) and 6-bromo-1H-indole (22.7 mg, 0.15 mmol) were combined with [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) complex with dichloromethane (4.1 mg, 0.005 mmol, 5 mol%) in anhydrous DME (0.10 M overall conc.). To these mixtures, 200 uL of Na_2CO_3 (2.0 M aqueous solution 0.20 mmol, 2 equiv.) was added and the mixtures were stirred at 85°C overnight. The mixtures were cooled to r.t., diluted with 0.8 ml of DMSO then filter through a filter plate (0.45 micron) and purified by RP HPLC (Waters X-bridge™ 5 micron RP C-18, 30x 100 mm column, eluents: MeCN-

H2O containing 0.1% NH_4OH). No attempt was made to obtain optimal yield on these experiments, rather to obtain high purity samples for quantitative UPLC analysis.

6-(1H-indol-6-yl)-[1,2,4]triazolo[1,5-a]pyridine



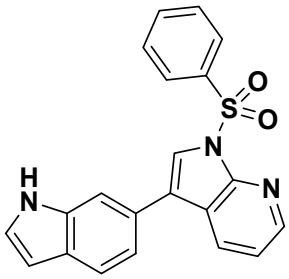
Scale-up Method A: obtained 6.1 mg white solid (26% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.28 (s, 1H), 9.24 (d, J = 1.7 Hz, 1H), 8.52 (d, J = 1.9 Hz, 1H), 8.06 (dd, J = 9.4, 1.9 Hz, 1H), 7.92 (d, J = 9.1 Hz, 1H), 7.77 (d, J = 1.5 Hz, 1H), 7.67 (d, J = 8.1 Hz, 1H), 7.45 – 7.39 (m, 2H), 6.51 – 6.46 (m, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 154.41 , 136.84 , 131.14 , 129.60 , 128.94 , 128.17 , 127.22 , 126.05 , 121.21 , 118.79 , 116.33 , 110.50 , 101.54 , 40.67.

MS ESI $[M+H]^+$ calculated for $C_{14}H_{10}N_4$ 234.09, found 235.23.

3-(1H-indol-6-yl)-1-(phenylsulfonyl)-1H-pyrrolo[2,3-b]pyridine



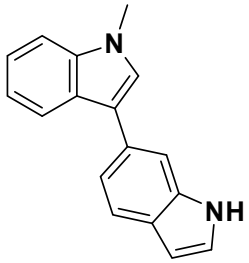
Scale-up Method A: obtained 27 mg white solid (72% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.16 (s, 1H), 8.45 (dd, J = 4.8, 1.6 Hz, 1H), 8.31 (dd, J = 7.9, 1.7 Hz, 1H), 8.19 (dd, J = 7.6, 1.9 Hz, 2H), 8.12 (s, 1H), 7.77 – 7.70 (m, 2H), 7.72 – 7.61 (m, 3H), 7.41 (s, 1H), 7.44 – 7.35 (m, 2H), 6.49 (t, J = 2.5 Hz, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 147.59 , 145.39 , 138.03 , 136.73 , 135.19 , 130.06 , 129.83 , 128.07 , 127.83 , 126.79 , 125.06 , 122.57 , 121.69 , 121.65 , 121.12 , 120.16 , 119.25 , 110.71 , 101.62 , 39.59 .

MS ESI $[M+H]^+$ calculated for $C_{21}H_{15}N_3O_2S$ 373.09, found 374.31.

1-methyl-1H,1'H-3,6'-biindole

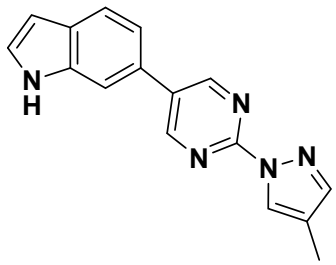


Scale-up Method A: obtained 16.2 mg white solid (65% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.02 (s, 1H), 7.91 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 1.2 Hz, 1H), 7.63 – 7.56 (m, 2H), 7.50 (d, J = 8.2 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.26 – 7.19 (m, 1H), 7.14 (ddd, J = 8.2, 6.9, 1.3 Hz, 1H), 6.43 (s, 1H), 3.86 (s, 2H).^{13}C NMR (126 MHz, DMSO-d_6) δ 137.70 , 137.11 , 128.84 , 127.40 , 126.27 , 126.13 , 125.53 , 121.83 , 120.75 , 119.88 , 119.71 , 119.33 , 116.78 , 110.57 , 109.53 , 101.45 , 32.96.

MS ESI $[M+H]^+$ calculated for $C_{17}H_{14}N_2$ 246.12, found 246.25.

6-(2-(4-methyl-1H-pyrazol-1-yl)pyrimidin-5-yl)-1H-indole



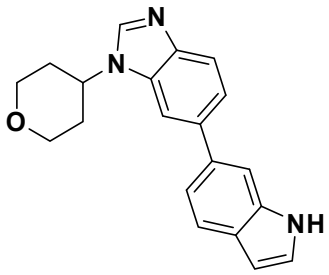
Scale-up Method A: obtained 15.6 mg of a white solid (10.7 % yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.34 (s, 5H), 9.17 (s, 7H), 8.48 (t, J = 1.2 Hz, 5H), 7.88 – 7.80 (m, 5H), 7.71 (d, J = 8.7 Hz, 10H), 7.48 – 7.42 (m, 8H), 6.51 (d, J = 5.2 Hz, 2H), 6.51 (s, 3H), 3.39 (d, J = 20.0 Hz, 6H), 3.30 (s, 4H), 3.29 (s, 1H), 2.57 (dp, J = 20.0, 1.8 Hz, 4H), 2.15 (d, J = 0.9 Hz, 14H), 1.92 (s, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 156.89 , 144.73 , 132.46 , 127.81 , 127.13 , 126.50 , 121.41 , 119.14 , 118.24 , 110.08 , 101.63 , 40.51 , 9.17.

MS ESI $[M+H]^+$ calculated for $C_{16}H_{13}N_5$ 275.12 found 276.30.

6-(1H-indol-6-yl)-1-(tetrahydro-2H-pyran-4-yl)-1H-benzo[d]imidazole



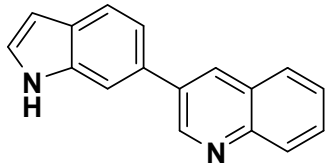
Scale-up Method A: obtained 29.8 mg of a white solid as a TFA salt (69% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.24 (s, 1H), 9.51 (s, 1H), 8.35 (s, 1H), 7.94 – 7.83 (m, 2H), 7.77 (d, J = 1.6 Hz, 1H), 7.69 (d, J = 8.3 Hz, 1H), 7.50 – 7.41 (m, 2H), 6.50 (t, J = 2.6 Hz, 1H), 5.15 – 5.04 (m, 1H), 4.08 (dd, J = 11.1, 4.1 Hz, 2H), 3.83 (s, 1H), 3.67 – 3.59 (m, 2H), 2.23 – 2.07 (m, 5H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 140.79 , 136.94 , 133.10 , 132.38 , 127.07 , 120.97 , 119.39 , 116.44 , 110.94 , 110.68 , 101.50 , 66.52 , 53.47 , 32.79.

MS ESI $[M+H]^+$ calculated for $C_{20}H_{19}N_{3O}$ 317.15, found 318.38.

3-(1H-indol-6-yl)quinolone



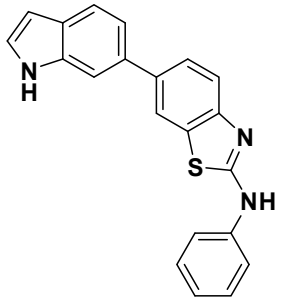
Scale-up Method A: obtained 11.9 mg of a off white solid as a TFA salt (33% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.35 (s, 1H), 9.42 (d, J = 2.3 Hz, 1H), 8.86 (d, J = 2.4 Hz, 1H), 8.17 (dd, J = 8.3, 1.4 Hz, 1H), 8.12 (d, J = 8.5 Hz, 1H), 7.91 (d, J = 1.6 Hz, 1H), 7.85 (ddd, J = 8.3, 6.8, 1.5 Hz, 1H), 7.74 (t, J = 7.7 Hz, 2H), 7.56 (dd, J = 8.2, 1.7 Hz, 1H), 7.50 – 7.45 (m, 1H), 6.53 (t, J = 2.2 Hz, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 149.05 , 136.98 , 135.05 , 129.00 , 128.63 , 128.42 , 128.11 , 127.52 , 121.39 , 118.94 , 110.70 , 101.63 .

MS ESI $[M+H]^+$ calculated for $C_{17}H_{12}N_2$ 244.10, found 245.28.

6-(1H-indol-6-yl)-N-phenylbenzo[d]thiazol-2-amine



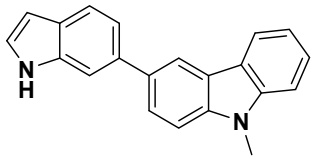
Scale-up Method A: obtained 10.6 mg of a white solid as a TFA salt (23% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.15 (s, 2H), 10.55 (s, 3H), 7.93 – 7.80 (m, 9H), 7.77 – 7.58 (m, 17H), 7.40 – 7.29 (m, 10H), 7.18 (td, J = 7.8, 1.6 Hz, 3H), 6.45 (t, J = 2.4 Hz, 3H), 2.55 (p, J = 1.8 Hz, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 157.33 , 156.40 , 137.02 , 135.22 , 133.49 , 128.22 , 127.18 , 126.34 , 121.39 , 120.80 , 118.51 , 115.53 , 109.34 , 101.35 , 67.53 , 66.83 , 49.38 , 40.67 , 39.59 , 31.21. MS ESI

$[M+H]^+$ calculated for $C_{21}H_{15}N_3S$ 341.10 found, 342.31.

3-(1H-indol-6-yl)-9-methyl-9H-carbazole



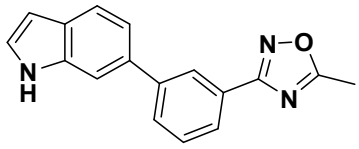
Scale-up Method A: obtained 15.6 mg of a white solid as a TFA salt (38 % yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.12 (s, 1H), 8.46 (d, J = 1.9 Hz, 1H), 8.28 (d, J = 7.4 Hz, 1H), 7.81 (dd, J = 8.5, 1.8 Hz, 1H), 7.74 (d, J = 1.5 Hz, 1H), 7.70 – 7.58 (m, 4H), 7.53 – 7.42 (m, 2H), 7.40 – 7.35 (m, 1H), 7.23 (t, J = 7.3 Hz, 1H), 6.49 – 6.44 (m, 1H), 3.92 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 141.55 , 140.23 , 137.19 , 134.98 , 133.31 , 126.97 , 126.24 , 126.18 , 125.48 , 123.10 , 122.71 , 120.93 , 120.78 , 119.18 , 118.64 , 109.89 , 109.81 , 109.65 , 101.36 , 29.55.

MS ESI $[M+H]^+$ calculated for $C_{21}H_{16}N_2$ 296.13, found 296.18.

3-(1H-indol-6-yl)phenyl)-5-methyl-1,2,4-oxadiazole

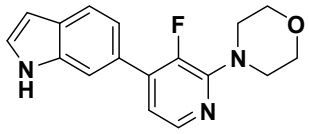


Scale-up Method B: obtained 15.6 mg of a white solid (33.7 % yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.21 (s, 3H), 8.27 (s, 2H), 8.27 (d, J = 3.6 Hz, 1H), 7.93 (ddt, J = 19.5, 7.9, 1.6 Hz, 6H), 7.75 – 7.69 (m, 3H), 7.71 – 7.59 (m, 7H), 7.43 (t, J = 2.7 Hz, 3H), 7.38 (dd, J = 8.2, 1.7 Hz, 3H), 6.49 (s, 2H), 6.49 (d, J = 5.6 Hz, 1H), 2.71 (s, 7H).
^{13}C NMR (126 MHz, DMSO-d_6) δ 177.99 , 168.17 , 142.99 , 136.99 , 132.68 , 130.38 , 130.14 , 128.02 , 127.36 , 127.05 , 125.41 , 125.38 , 121.13 , 118.58 , 110.01 , 101.48 , 40.67 , 12.54.

MS ESI $[M+H]^+$ calculated for $C_{17}H_{13}N_3O$ 275.11, found 276.23.

4-(4-fluoro-5-(1H-indol-6-yl)pyridin-3-yl)morpholine



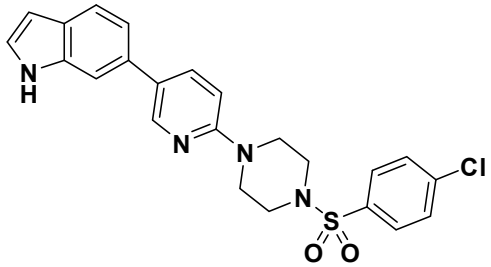
Scale-up Method A: obtained 26 mg of a white solid as a TFA salt (72% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.29 (s, 1H), 8.06 (d, J = 5.1 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.47 (t, J = 2.8 Hz, 1H), 7.24 (dt, J = 8.2, 1.8 Hz, 1H), 7.09 (t, J = 5.1 Hz, 1H), 6.53 – 6.48 (m, 1H), 3.81 – 3.73 (m, 4H), 3.43 – 3.37 (m, 4H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 142.84 , 136.26 , 128.55 , 127.61 , 126.08 , 120.65 , 120.22 , 118.09 , 112.58 , 112.55 , 101.59 , 66.56 , 48.90 , 48.86 , 40.67 , 39.59 . ^{19}F NMR (470 MHz, DMSO-d_6) δ -137.

MS ESI $[M+H]^+$ calculated for $C_{17}H_{16}FN_3O$ 297.13 found 298.32.

6-(6-(4-((4-chlorophenyl)sulfonyl)piperazin-1-yl)pyridin-3-yl)-1H-indole

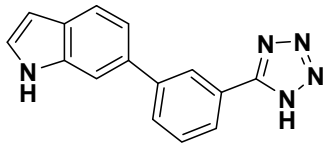


Scale-up Method B: obtained 26 mg of a white solid (26% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.11 (s, 1H), 8.43 (d, J = 2.6 Hz, 1H), 7.89 – 7.71 (m, 5H), 7.61 – 7.53 (m, 2H), 7.38 – 7.32 (m, 1H), 7.23 (dd, J = 8.2, 1.7 Hz, 1H), 6.92 (d, J = 8.8 Hz, 1H), 6.43 (s, 1H), 3.68 – 3.62 (m, 4H), 3.04 (t, J = 5.1 Hz, 4H).
^{13}C NMR (126 MHz, DMSO-d_6) δ 157.57 , 145.70 , 138.84 , 137.01 , 136.52 , 134.29 , 130.14 , 129.97 , 127.23 , 126.37 , 120.95 , 118.08 , 108.91 , 108.00 , 101.40 , 46.00 , 44.72 , 40.67.

MS ESI $[M+H]^+$ calculated for $C_{23}H_{21}ClN_4O_2S$ 452.11, found 453.38.

6-(3-(1H-tetrazol-5-yl)phenyl)-1H-indole



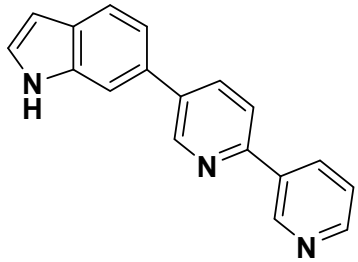
Scale-up Method A: obtained 26 mg of a white solid (33.5% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.25 (s, 3H), 8.35 (d, J = 3.8 Hz, 1H), 8.35 (s, 2H), 7.98 (dt, J = 7.9, 1.5 Hz, 3H), 7.80 (dt, J = 7.9, 1.5 Hz, 3H), 7.73 (d, J = 1.5 Hz, 3H), 7.67 (d, J = 8.3 Hz, 3H), 7.62 (t, J = 7.7 Hz, 3H), 7.45 – 7.37 (m, 6H), 6.49 (d, J = 2.6 Hz, 2H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 157.46 , 142.84 , 136.98 , 133.08 , 130.15 , 128.57 , 127.93 , 127.78 , 126.94 , 125.25 , 125.13 , 121.04 , 118.69 , 109.97 , 101.48 , 40.66 , 39.58.

MS ESI $[M+H]^+$ calculated for $C_{15}H_{11}N_5$ 261.103, found 262.22.

5-([2,3'-bipyridin]-5-yl)-1H-indole



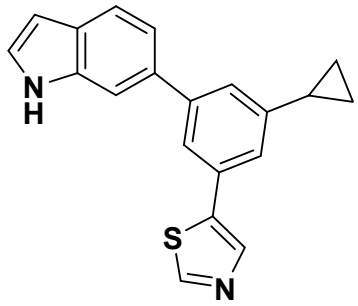
Scale-up Method A: obtained 8 mg of a white solid as a TFA salt (29% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.30 (s, 1H), 9.43 (d, J = 2.2 Hz, 1H), 9.10 (d, J = 2.4 Hz, 1H), 8.80 – 8.74 (m, 2H), 8.29 (dd, J = 8.3, 2.4 Hz, 1H), 8.22 (d, J = 8.3 Hz, 1H), 7.83 – 7.73 (m, 2H), 7.71 (d, J = 8.3 Hz, 1H), 7.49 – 7.43 (m, 2H), 6.53 – 6.48 (m, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 158.73 , 148.32 , 137.34 , 136.94 , 135.72 , 135.37 , 129.66 , 128.41 , 127.40 , 125.46 , 121.48 , 121.30 , 118.59 , 110.25 , 101.60.

MS ESI $[M+H]^+$ calculated for $C_{18}H_{13}N_3$ 271.11, found 272.30.

5-(3-cyclopropyl-5-(1H-indol-6-yl)phenyl)thiazole



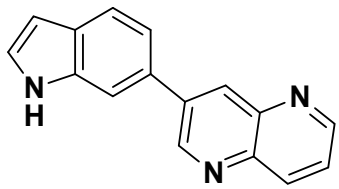
Scale-up Method A: obtained 13.3 mg of a white solid as a TFA salt (42% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.30 (s, 1H), 9.43 (d, J = 2.2 Hz, 1H), 9.10 (d, J = 2.4 Hz, 1H), 8.80 – 8.74 (m, 2H), 8.29 (dd, J = 8.3, 2.4 Hz, 1H), 8.22 (d, J = 8.3 Hz, 1H), 7.83 – 7.73 (m, 2H), 7.71 (d, J = 8.3 Hz, 1H), 7.49 – 7.43 (m, 2H), 6.53 – 6.48 (m, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 158.73 , 148.32 , 137.34 , 136.94 , 135.72 , 135.37 , 129.66 , 128.41 , 127.40 , 125.46 , 121.48 , 121.30 , 118.59 , 110.25 , 101.60.

MS ESI $[M+H]^+$ calcd for $C_{20}H_{16}N_2S$ 316.10, found 317.31.

3-(1H-indol-6-yl)-1,5-naphthyridine



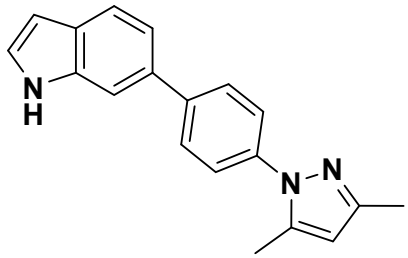
Scale-up Method A: obtained 17.6 mg of a white solid as a TFA salt (72% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.35 (s, 1H), 9.44 (d, J = 2.3 Hz, 1H), 9.07 (dd, J = 4.2, 1.8 Hz, 1H), 8.63 (d, J = 2.3 Hz, 1H), 8.50 (dd, J = 8.5, 1.8 Hz, 1H), 7.95 (d, J = 1.6 Hz, 1H), 7.81 (dd, J = 8.5, 4.2 Hz, 1H), 7.75 (d, J = 8.1 Hz, 1H), 7.59 (dd, J = 8.3, 1.8 Hz, 1H), 7.48 (t, J = 2.8 Hz, 1H), 6.56 – 6.51 (m, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 152.05 , 151.28 , 143.63 , 142.12 , 138.42 , 137.32 , 136.99 , 132.73 , 129.45 , 128.61 , 127.67 , 124.76 , 121.46 , 119.09 , 111.01 , 101.64 , 39.59.

MS ESI $[M+H]^+$ calculated for $C_{16}H_{11}N_3$ 245.10, found 246.28.

6-(4-(3,5-dimethyl-1H-pyrazol-1-yl)phenyl)-1H-indole



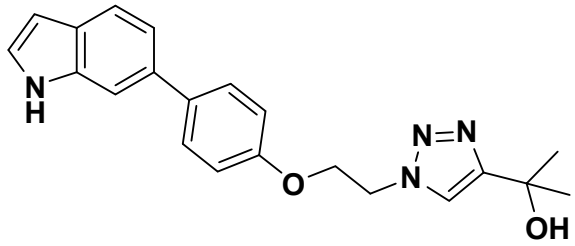
Scale-up Method A: obtained 19.7 mg of a white solid as a TFA salt (69% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.21 (s, 2H), 7.84 – 7.76 (m, 4H), 7.76 – 7.63 (m, 5H), 7.63 – 7.49 (m, 5H), 7.45 – 7.34 (m, 4H), 6.47 (s, 2H), 6.10 (s, 2H), 2.36 (s, 6H), 2.34 (d, J = 1.4 Hz, 1H), 2.21 (s, 7H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 148.27 , 139.60 , 138.63 , 136.99 , 132.82 , 127.58 , 126.84 , 124.80 , 120.99 , 118.66 , 109.89 , 107.63 , 101.45 , 40.67 , 13.81 , 12.73.

MS ESI $[M+H]^+$ calculated for $C_{19}H_{17}N_3$ 287.14, found 288.35.

2-(1-(2-(4-(1H-indol-6-yl)phenoxy)ethyl)-1H-1,2,3-triazol-4-yl)propan-2-ol



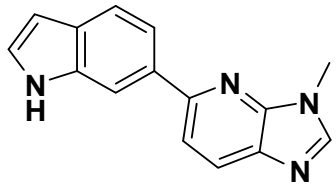
Scale-up Method A: obtained 21.2 mg of a white solid as a TFA salt (59% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.10 (s, 1H), 7.96 (s, 1H), 7.64 – 7.54 (m, 4H), 7.38 – 7.33 (m, 1H), 7.25 (dd, J = 8.0, 1.6 Hz, 1H), 7.07 – 6.99 (m, 2H), 6.43 (t, J = 2.5 Hz, 1H), 5.10 (s, 1H), 4.75 (t, J = 5.2 Hz, 2H), 4.45 (t, J = 5.2 Hz, 2H), 3.29 (d, J = 7.8 Hz, 8H), 1.47 (s, 6H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 157.33 , 156.40 , 137.02 , 135.22 , 133.49 , 128.22 , 127.18 , 126.34 , 121.39 , 120.80 , 118.51 , 115.53 , 109.34 , 101.35 , 67.53 , 66.83 , 49.38 , 40.67 , 39.59 , 31.21. MS ESI

$[M+H]^+$ calculated for $C_{21}H_{22}N_4O_2$ 362.17, found 363.42.

5-(1H-indol-6-yl)-3-methyl-3H-imidazo[4,5-b]pyridine

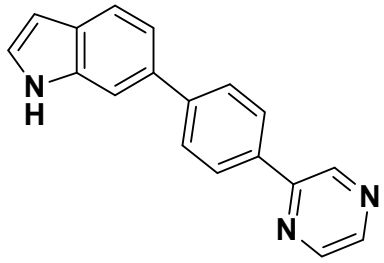


Scale-up Method A: obtained 11 mg of a white solid as a TFA salt (44% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.24 (s, 1H), 8.83 – 8.78 (m, 2H), 8.36 (d, J = 2.1 Hz, 1H), 7.75 – 7.65 (m, 2H), 7.45 – 7.37 (m, 2H), 6.49 (t, J = 2.4 Hz, 1H), 3.95 (s, 3H).
^{13}C NMR (126 MHz, DMSO-d_6) δ 146.27 , 144.38 , 137.00 , 133.97, 131.15, 127.76 , 126.91 , 124.51 , 121.16 , 119.30 , 110.65 , 101.45 , 39.58 , 30.49.

MS ESI $[M+H]^+$ calculated for $C_{15}H_{12}N_4$ 248.11, found 249.28.

6-(4-(pyrazin-2-yl)phenyl)-1H-indole



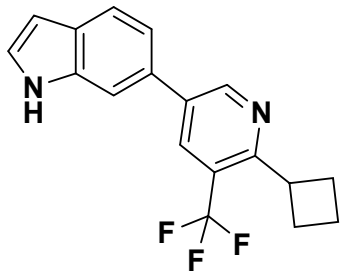
Scale-up Method A: obtained 5.6 mg of a white solid (20.6% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.23 (s, 0H), 9.32 (d, J = 1.8 Hz, 1H), 8.83 – 8.71 (m, 0H), 8.67 – 8.59 (m, 0H), 8.29 – 8.22 (m, 1H), 7.92 – 7.84 (m, 1H), 7.75 (s, 0H), 7.66 (d, J = 8.2 Hz, 0H), 7.45 – 7.36 (m, 1H), 6.52 – 6.45 (m, 0H), 3.35 – 3.30 (m, 29H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 151.73 , 144.80 , 143.69 , 143.58 , 142.37 , 136.99 , 134.34 , 132.80 , 128.04 , 127.69 , 127.65 , 127.04 , 121.02 , 118.67 , 109.99 , 101.51 , 39.58 .

MS ESI $[M+H]^+$ calculated for C18H13N3 271.11, found 272.37.

6-(6-cyclobutyl-5-(trifluoromethyl)pyridin-3-yl)-1H-indole



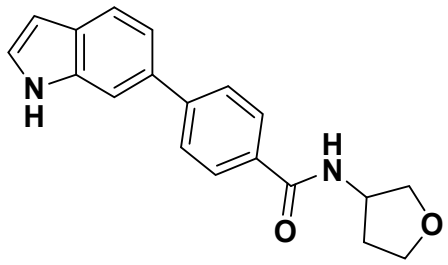
Scale-up Method A: obtained 22.4 mg of a white solid as a TFA salt (70.8% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.28 (s, 1H), 9.19 (d, J = 2.2 Hz, 1H), 8.24 (d, J = 2.3 Hz, 1H), 7.82 – 7.72 (m, 1H), 7.69 (d, J = 8.3 Hz, 1H), 7.48 – 7.38 (m, 2H), 6.50 (s, 1H), 3.97 (p, J = 8.6 Hz, 1H), 3.38 (d, J = 19.4 Hz, 0H), 2.60 – 2.52 (m, 2H), 2.26 (qt, J = 8.5, 2.8 Hz, 2H), 2.14 – 2.01 (m, 1H), 1.95 – 1.85 (m, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 158.79 , 150.80 , 136.87 , 135.14 , 131.98 , 128.81 , 128.45 , 127.47 , 121.32 , 118.65 , 110.49 , 101.58 , 40.67 , 38.47 , 28.12 , 17.95 . ^{19}F NMR (470 MHz, DMSO-d_6) δ -58.

MS ESI $[M+H]^+$ calculated for $C_{18}H_{15}F_3N_2$ 316.12, found 317.33.

4-(1H-indol-6-yl)-N-(tetrahydrofuran-3-yl)benzamide



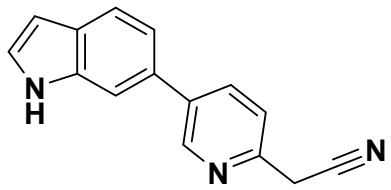
Scale-up Method A: obtained 8.4 mg of a white solid (27.4 % yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.21 (s, 1H), 8.54 (d, J = 6.6 Hz, 1H), 7.99 – 7.93 (m, 2H), 7.81 – 7.75 (m, 2H), 7.71 (d, J = 1.3 Hz, 1H), 7.65 (d, J = 8.1 Hz, 1H), 7.45 – 7.35 (m, 2H), 6.47 (s, 1H), 4.54 – 4.44 (m, 1H), 3.88 (td, J = 8.4, 6.5 Hz, 2H), 3.74 (td, J = 8.1, 5.9 Hz, 1H), 3.61 (dd, J = 8.9, 4.4 Hz, 1H), 2.18 (dtd, J = 12.7, 7.9, 6.7 Hz, 1H), 2.01 – 1.91 (m, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 166.69 , 144.76 , 136.94 , 132.61 , 128.49 , 128.07 , 127.09 , 126.73 , 120.99 , 118.75 , 110.13 , 101.49 , 72.81 , 67.01 , 50.75 , 40.67 , 32.35 .

MS ESI $[M+H]^+$ calculated for C19H18N2O2 306.14, found 307.37.

2-(5-(1H-indol-6-yl)pyridin-2-yl)acetonitrile



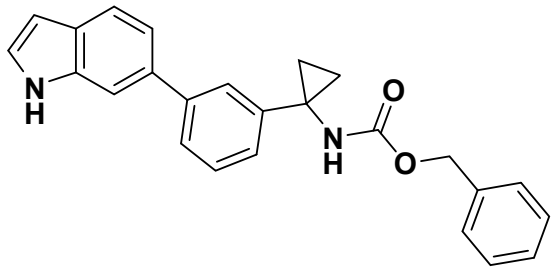
Scale-up Method A: obtained 9.6 mg of a white solid as a TFA salt (23.4% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.26 (s, 1H), 8.90 (d, J = 2.2 Hz, 1H), 8.13 (dd, J = 8.2, 2.4 Hz, 1H), 7.74 – 7.64 (m, 2H), 7.50 (d, J = 8.2 Hz, 1H), 7.46 – 7.41 (m, 1H), 7.36 (dd, J = 8.3, 1.9 Hz, 1H), 6.51 – 6.46 (m, 1H), 4.25 (s, 2H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 149.62 , 147.96 , 136.91 , 136.63 , 135.72 , 129.87 , 128.19 , 127.20 , 123.21 , 121.23 , 118.87 , 110.18 , 101.53 , 40.84 , 25.72.

MS ESI $[M+H]^+$ calculated for $C_{15}H_{11}N_3$ 233.10, found 234.28.

benzyl (1-(3-(1H-indol-6-yl)phenyl)cyclopropyl)carbamate



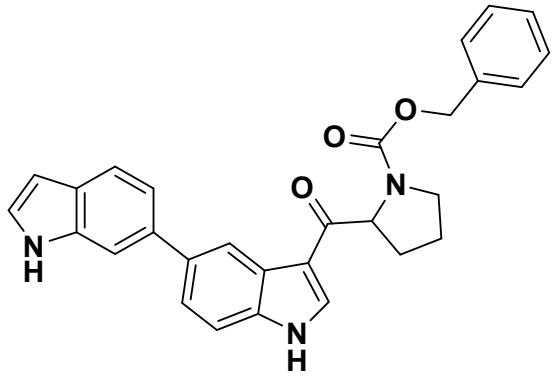
Scale-up Method A: obtained 3.3 mg of a white solid (8.6% yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.16 (s, 1H), 8.22 (s, 1H), 7.62 (d, J = 8.6 Hz, 2H), 7.53 – 7.42 (m, 2H), 7.42 – 7.22 (m, 7H), 7.10 (dt, J = 7.5, 1.2 Hz, 1H), 5.04 (s, 2H), 1.29 – 1.18 (m, 4H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 156.56 , 142.02 , 137.66 , 136.97 , 134.14 , 129.09 , 128.82 , 128.22 , 128.12 , 127.59 , 126.62 , 124.76 , 124.02 , 123.36 , 120.84 , 118.82 , 109.93 , 101.41 , 65.62 , 35.26 , 18.39.

MS ESI $[M+H]^+$ calculated for $C_{25}H_{22}N_2O_2$ 382.17, found 383.43.

benzyl 2-(1H,1'H-[5,6'-biindole]-3-carbonyl)pyrrolidine-1-carboxylate



Scale-up Method A: obtained 13.6 mg of a white solid (20.3 % yield).

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.11 (d, J = 5.1 Hz, 3H), 8.59 – 8.43 (m, 8H), 8.11 (d, J = 7.9 Hz, 1H), 7.69 – 7.55 (m, 14H), 7.49 (d, J = 8.0 Hz, 1H), 7.44 – 7.29 (m, 16H), 7.19 – 7.04 (m, 7H), 7.01 (q, J = 7.5, 7.0 Hz, 4H), 6.45 (d, J = 2.5 Hz, 3H), 5.25 (ddd, J = 21.0, 8.4, 3.3 Hz, 4H), 5.16 – 4.96 (m, 6H),

4.93 (d, J = 13.2 Hz, 2H), 3.60 – 3.48 (m, 15H), 2.49 – 2.32 (m, 4H), 2.01 – 1.94 (m, 2H), 1.91 (qd, J = 8.5, 7.7, 3.0 Hz, 9H).

^{13}C NMR (126 MHz, DMSO-d6) δ 194.22 , 193.83 , 154.26 , 137.65 , 137.35 , 137.15 , 135.09 , 134.77 , 128.88 , 128.33 , 128.22 , 127.91 , 127.72 , 127.20 , 127.11 , 126.98 , 126.89 , 126.26 , 122.96 , 120.79 , 120.59 , 119.75 , 119.07 , 114.28 , 112.91 , 109.85 , 101.35 , 66.24 , 66.10 , 62.45 , 62.05 , 47.76 , 47.08 , 32.33 , 31.26 , 24.46 , 23.67.

MS ESI $[M+H]^+$ calculated for $C_{29}H_{25}N_3O_3$ 463.19, found 464.47.

Experimental Section 2 – Comparison of Aryl Pinacol Boronate Cyanation Methods using the Aryl Pinacol Boronate Informer Library

Experimental Procedure for Figure 3D, Entry 6. In a fume-hood under air, to 1 mL reaction vials containing aryl pinacol boronates (10 µmol) equipped with magnetic stir bars and containing potassium carbonate (4.2 mg, 30.0 µmol, 3 equiv.) was added 100 uL of a solution of CuCN (0.1 M in DMF, 10.0 µmol, 1 equiv.). The mixture was stirred at 60 °C for 2 hours, then was cooled to room temperature and quenched with 600 ml quench solution 1:1:1 of DMF/MeOH/DCE. 4,4'-di-tert-butyl-1,1'-biphenyl internal standard (0.1 M in DCE, 10.0 µmol, 1 equiv.) was then added to each well, and this was stirred at RT for 2 two hours. 10 µL from each reaction was diluted in 1400 µL in ACN and quantitative UPLC-MS analysis was performed to determine the solution yield.

Experimental Procedure for Figure 3D, Entry 7. In a fume-hood under air, to 1 mL reaction vials containing aryl pinacol boronates (10 µmol) equipped with magnetic stir bars was added a solution of CuI (0.15M in DMA, 15.0 µmol, 1.5 equiv.). The mixture was stirred at 130 °C for 20 hours, then was cooled to room temperature and quenched with 600 ml quench solution 1:1:1 of DMF/MeOH/DCE. 4,4'-di-tert-butyl-1,1'-biphenyl internal standard (0.1 M in DCE, 10.0 µmol, 1 equiv.) was then added to each well, and this was stirred at RT for 2 two hours. 10 µL from each reaction was diluted in 1400 µL in ACN and quantitative UPLC-MS analysis was performed to determine the solution yield.

Experimental Procedure for Figure 3D, Entry 8. In a fume-hood under air, to 1 mL reaction vials containing aryl pinacol boronates (10 µmol) equipped with magnetic stir bars was added a mixture of $Cu(NO_3)_2$ (0.2 M, 20.0 µmol, 2 equiv.), CsF (0.1 M, 10.0 µmol, 1 equiv.) and $Zn(CN)_2$ (0.3 M, 30.0 µmol, 3 equiv) in MeOH/ water (7:3 ratio). The mixture was stirred at 100 °C for 4 hours, then was cooled to room temperature and quenched with 600 ml quench solution 1:1:1 of DMF/MeOH/DCE. 4,4'-di-tert-butyl-1,1'-biphenyl internal standard (0.1 M in DCE, 10.0 µmol, 1 equiv.) was then added to each

well, and this was stirred at RT for 2 two hours. 10 µL from each reaction was diluted in 1400 µL in ACN and quantitative UPLC-MS analysis was performed to determine the solution yield.

Experimental Procedure for Figure 3D, Entry 9. In a fume-hood under air, to 1 mL reaction vials containing aryl pinacol boronates (10 µmol) equipped with magnetic stir bars was added a mixture of $Cu(NO_3)_2$ (0.2 M, 20.0 µmol, 2 equiv.), CsF (0.1 M, 10.0 µmol, 1 equiv.) and $Zn(CN)_2$ (0.3 M, 30.0 µmol, 3 equiv) in MeOH/ water (7:3 ratio). The mixture was stirred at 70 °C for 20 hours, then was cooled to room temperature and quenched with 600 ml quench solution 1:1:1 of DMF/MeOH/DCE. 4,4'-di-tert-butyl-1,1'-biphenyl internal standard (0.1 M in DCE, 10.0 µmol, 1 equiv.) was then added to each well, and this was stirred at RT for 2 two hours. 10 µL from each reaction was diluted in 1400 µL in ACN and quantitative UPLC-MS analysis was performed to determine the solution yield.

Experimental Procedure for Figure 3D, Entry 10. In a fume-hood under air, to 1 mL reaction vials containing aryl pinacol boronates (10 µmol) equipped with magnetic stir bars was added a mixture of $Cu(NO_3)_2$ (0.2 M, 20.0 µmol, 2 equiv.), CsF (0.1 M, 10.0 µmol, 1 equiv.) and $Zn(CN)_2$ (0.3 M, 30.0 µmol, 3 equiv) in MeOH/ water (7:3 ratio). The mixture was stirred at 40 °C for 20 hours, then was cooled to room temperature and quenched with 600 ml quench solution 1:1:1 of DMF/MeOH/DCE. 4,4'-di-tert-butyl-1,1'-biphenyl internal standard (0.1 M in DCE, 10.0 µmol, 1 equiv.) was then added to each well, and this was stirred at RT for 2 two hours. 10 µL from each reaction was diluted in 1400 µL in ACN and quantitative UPLC-MS analysis was performed to determine the solution yield.

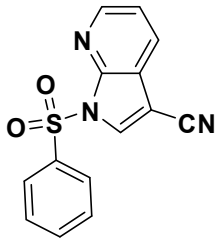
Experimental Procedure for Figure 3D, Entry 11. In a fume-hood under air, to 1 mL reaction vials containing aryl pinacol boronates (10 µmol) equipped with magnetic stir bars was added a mixture of $Cu(NO_3)_2$ (0.2 M, 20.0 µmol, 2 equiv.), CsF (0.1 M, 10.0 µmol, 1 equiv.) and $Zn(CN)_2$ (0.3 M, 30.0 µmol, 3 equiv) in DMF/ MeOH/ water (20:4:1 ratio). The mixture was stirred at 70 °C for 20 hours, then was cooled to room temperature and quenched with 600 ml quench solution 1:1:1 of DMF/MeOH/DCE. 4,4'-di-tert-butyl-1,1'-biphenyl internal standard (0.1 M in DCE, 10.0 µmol, 1 equiv.) was then added to each well, and this was stirred at RT for 2 two hours. 10 µL from each reaction was diluted in 1400 µL in ACN and quantitative UPLC-MS analysis was performed to determine the solution yield.

Experimental Procedure for Figure 3D, Entry 12. In a fume-hood under air, to 1 mL reaction vials containing aryl pinacol boronates (10 µmol) equipped with magnetic stir bars was added a mixture of $Cu(NO_3)_2$ (0.2 M, 20.0 µmol, 2 equiv.), CsF (0.1 M, 10.0 µmol, 1 equiv.) and $Zn(CN)_2$ (0.3 M, 30.0 µmol, 3 equiv) in in DMF/ MeOH/ water (20:4:1 ratio). The mixture was stirred at 40 °C for 20 hours, then was cooled to room temperature and quenched with 600 ml quench solution 1:1:1 of DMF/MeOH/DCE. 4,4'-di-tert-butyl-1,1'-biphenyl internal standard (0.1 M in DCE, 10.0 µmol, 1 equiv.)

was then added to each well, and this was stirred at RT for 2 two hours. 10 µL from each reaction was diluted in 1400 µL in ACN and quantitative UPLC-MS analysis was performed to determine the solution yield.

General Procedure for Boronate Cyanation Scale-up Reactions. Aryl pinacol boronate (0.015 g, 0.1 mmol) was added to a stirred, cooled room temperature mixture of CsF (0.015 g, 0.100 mmol), $Zn(CN)_2$ (0.035 g, 0.300 mmol) and $Cu(NO_3)_2$ (0.048 g, 0.200 mmol) in DMF (1.0 ml), water (0.04 ml) and methanol (0.16 ml) and then the mixture was stirred at 70 °C for overnight. The mixture was cooled, diluted with ethyl acetate (2 mL), washed with water (1 x 2 mL), and the solvent was evaporated under reduced pressure. The reactions were then diluted with 0.8 ml DMSO, filtered through filter plate (0.45 micron) and submit to High Througput Purifcation group (HTP) for mass triggered reverse phase HPLC purification.

1-(phenylsulfonyl)-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile:



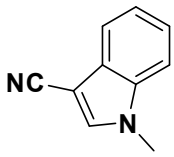
Scale-up Isolated yield: 14.5%

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.01 (s, 1H), 8.54 (dd, J = 4.8, 1.5 Hz, 1H), 8.30 – 8.11 (m, 3H), 7.80 (t, J = 7.4 Hz, 1H), 7.69 (t, J = 7.8 Hz, 2H), 7.50 (dd, J = 8.1, 4.8 Hz, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 147.29 , 145.55 , 136.80 , 136.29 , 136.07 , 130.34 , 129.77 , 128.62 , 121.34 , 120.84 , 113.70 , 90.18.

$[M+H]^+$ calculated for 283.0415476; found 283.04

1-methyl-1H-indole-3-carbonitrile:



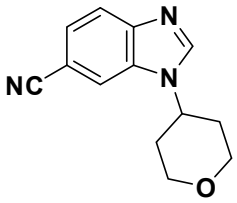
Scale-up Isolated yield: 21.8%

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.25 (s, 1H), 7.76 – 7.59 (m, 2H), 7.45 – 7.33 (m, 1H), 7.34 – 7.24 (m, 1H), 3.88 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 125.40 , 121.32 , 120.33 , 116.95 , 104.62 , 99.99 , 66.76, 33.04.

[M+H]+ calculated for 156.0687483; found 156.07

1-(tetrahydro-2H-pyran-4-yl)-1H-benzo[d]imidazole-6-carbonitrile:



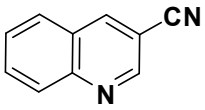
Scale-up Isolated yield: 29.9%

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.79 (s, 1H), 8.47 (s, 1H), 7.86 (s, 1H), 7.61 (d, J = 5.7 Hz, 1H), 4.78 (tt, J = 11.7, 4.3 Hz, 1H), 4.03 (dd, J = 11.3, 4.1 Hz, 2H), 3.56 (td, J = 11.5, 2.1 Hz, 2H), 2.17 – 2.00 (m, 4H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 125.40 , 121.32 , 120.33 , 116.95 , 104.62 , 99.99 , 66.76 , 52.42, 33.04.

[M+H]+ calculated for 227.1058621; found 227.11.

Quinoline-3-carbonitrile:



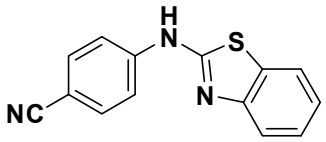
Scale-up Isolated yield: 12.3%

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.18 (d, J = 2.1 Hz, 1H), 9.11 (d, J = 2.1 Hz, 1H), 8.24 – 8.06 (m, 2H), 8.00 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.80 (t, J = 7.5 Hz, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 150.53 , 148.53 , 142.98 , 133.51 , 129.55 , 129.35 , 128.88 , 126.38 , 117.92 , 106.30.

[M+H]+ calculated for 154.0530982; found 154.05.

4-(benzo[d]thiazol-2-ylamino)benzonitrile:



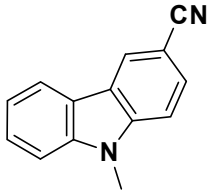
Scale-up Isolated yield: 29.9%

^{1}H NMR (500 MHz, DMSO-d_6) δ 11.02 (s, 1H), 8.02 – 7.95 (m, 2H), 7.89 (dd, J = 7.7, 1.2 Hz, 1H), 7.87 – 7.78 (m, 2H), 7.70 (d, J = 7.6 Hz, 1H), 7.39 (td, J = 7.8, 1.3 Hz, 1H), 7.27 – 7.20 (m, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 161.31 , 152.06 , 144.92 , 133.99 , 130.65 , 126.60 , 123.52 , 121.79 , 120.33 , 119.84 , 118.11 , 103.67.

[M+H]+ calculated for 251.0517183; found 251.05.

9-methyl-9H-carbazole-3-carbonitrile:



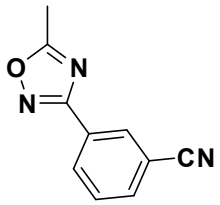
Scale-up Isolated yield: 45.1%

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.74 (d, J = 1.6 Hz, 1H), 8.39 – 8.17 (m, 1H), 7.94 – 7.74 (m, 2H), 7.70 (d, J = 8.4 Hz, 1H), 7.66 – 7.52 (m, 1H), 7.46 – 7.21 (m, 1H), 3.95 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 142.80 , 141.75 , 129.24 , 127.59 , 125.93 , 122.68 , 121.69 , 120.95 , 120.62 , 110.83 , 110.36 , 100.80.

[M+H]+ calculated for 206.0843983; found 206.08.

3-(5-methyl-1,2,4-oxadiazol-3-yl)benzonitrile:



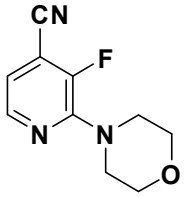
Scale-up Isolated yield: 45.9%

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.42 – 8.25 (m, 2H), 8.08 (dd, J = 7.7, 1.5 Hz, 1H), 7.80 (t, J = 8.0 Hz, 1H), 2.71 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 178.60 , 166.79 , 135.50 , 131.93 , 131.18 , 130.79 , 128.02 , 118.44 , 113.03 , 12.55.

[M+H]+ calculated for 185.0589119; found 185.06.

3-fluoro-2-morpholinoisonicotinonitrile:



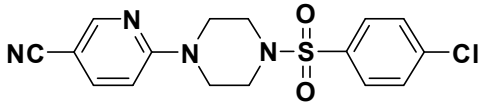
Scale-up Isolated yield: 25.1%

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.19 (d, J = 4.8 Hz, 1H), 7.25 (dd, J = 5.0, 3.6 Hz, 1H), 3.81 – 3.64 (m, 4H), 3.57 – 3.44 (m, 4H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 144.41, 116.54 , 116.50 , 113.25 , 108.87 , 108.77 , 66.31, 47.76.

[M+H]+ calculated for 207.0807902; found 207.08.

6-(4-((4-chlorophenyl)sulfonyl)piperazin-1-yl)nicotinonitrile:



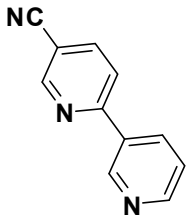
Scale-up Isolated yield: 44.7%

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.47 (d, J = 2.3 Hz, 1H), 7.86 (dd, J = 9.1, 2.4 Hz, 1H), 7.84 – 7.74 (m, 2H), 7.77 – 7.69 (m, 2H), 6.92 (d, J = 9.1 Hz, 1H), 3.84 – 3.74 (m, 4H), 3.02 (t, J = 5.1 Hz, 4H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 159.16 , 152.83 , 140.63 , 138.87 , 134.27 , 130.14 , 129.94 , 118.93 , 107.23 , 96.34 , 45.87 , 43.78.

[M+H]+ calculated for 362.0604245; found 362.06.

[2,3'-bipyridine]-5-carbonitrile:



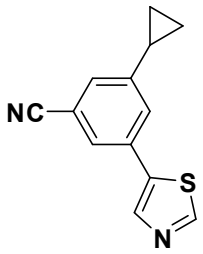
Scale-up Isolated yield: 19.9%

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.37 (d, J = 2.5 Hz, 1H), 9.17 (d, J = 2.0 Hz, 1H), 8.75 (dd, J = 4.9, 1.8 Hz, 1H), 8.58 (dt, J = 8.0, 2.1 Hz, 1H), 8.48 (dd, J = 8.3, 2.0 Hz, 1H), 8.33 (d, J = 8.3 Hz, 1H), 7.64 (dd, J = 8.0, 4.8 Hz, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 157.34 , 153.22 , 151.16 , 148.41 , 141.74 , 135.69 , 133.20 , 124.68 , 121.24 , 117.54 , 108.70.

[M+H]+ calculated for 181.0639973; found 181.06.

3-cyclopropyl-5-(thiazol-5-yl)benzonitrile:



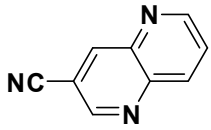
Scale-up Isolated yield: 23.4%

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.16 (s, 1H), 8.48 (s, 1H), 7.97 (t, J = 1.6 Hz, 1H), 7.73 (t, J = 1.7 Hz, 1H), 7.52 (t, J = 1.6 Hz, 1H), 2.08 (tt, J = 8.4, 5.1 Hz, 1H), 1.08 – 0.98 (m, 2H), 0.91 – 0.82 (m, 2H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 155.19 , 141.47 , 137.06 , 128.99 , 128.62 , 127.25 , 118.95 , 112.94 , 15.32 , 10.60 .

[M+H]+ calculated for 226.0564693; found 226.06.

1,5-naphthyridine-3-carbonitrile



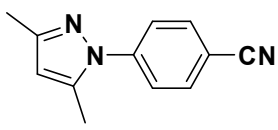
Scale-up Isolated yield: 16.1%

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.31 (d, J = 2.0 Hz, 1H), 9.26 – 9.10 (m, 2H), 8.67 – 8.49 (m, 1H), 7.99 (dd, J = 8.6, 4.2 Hz, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 153.88 , 151.50 , 145.32 , 143.30 , 141.60 , 137.57 , 127.95 , 117.19 , 109.72 .

[M+H]+ calculated for 155.0483472; found 155.05.

4-(3,5-dimethyl-1H-pyrazol-1-yl)benzonitrile:



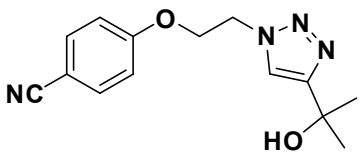
Scale-up Isolated yield: 28.4%

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.08 – 7.89 (m, 2H), 7.85 – 7.69 (m, 2H), 6.16 (s, 1H), 2.40 (s, 3H), 2.20 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 149.86 , 143.61 , 140.48 , 133.90 , 124.08 , 118.97 , 109.30 , 109.26 , 13.76 , 13.05.

[M+H]+ calculated for 197.0952974; found 197.10.

4-(2-(4-(2-hydroxypropan-2-yl)-1H-1,2,3-triazol-1-yl)ethoxy)benzonitrile:



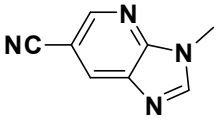
Scale-up Isolated yield: 12.9%

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.94 (s, 1H), 7.86 – 7.66 (m, 2H), 7.20 – 7.01 (m, 2H), 5.08 (s, 1H), 4.75 (t, J = 5.1 Hz, 2H), 4.52 (t, J = 5.1 Hz, 2H), 1.45 (s, 6H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 161.80 , 156.42 , 134.71 , 121.43 , 119.47 , 116.16 , 103.83 , 67.50 , 67.12 , 49.07, 31.55.

[M+H]+ calculated for 272.1273258; found 272.10.

3-methyl-3H-imidazo[4,5-b]pyridine-6-carbonitrile:



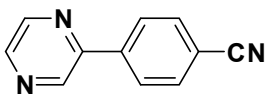
Scale-up Isolated yield: 45.6%

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.82 (d, J = 1.9 Hz, 1H), 8.72 – 8.66 (m, 2H), 3.89 (s, 3H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 149.67, 149.48 , 147.43 , 134.32 , 131.85 , 118.61 , 102.77 , 30.23 .

[M+H]+ calculated for 158.0592462; found 158.06.

4-(pyrazin-2-yl)benzonitrile:



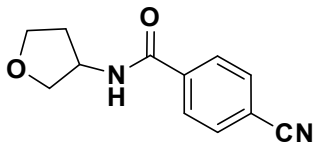
Scale-up Isolated yield: 37.0%

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.38 (d, J = 1.6 Hz, 1H), 8.80 (dd, J = 2.6, 1.4 Hz, 1H), 8.72 (d, J = 2.4 Hz, 1H), 8.38 – 8.33 (m, 2H), 8.03 (d, J = 8.6 Hz, 2H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 150.09 , 145.10 , 145.06 , 143.24 , 140.66 , 133.45 , 127.98 , 119.06 , 112.82.

[M+H]+ calculated for 181.0639973; found 181.06.

4-cyano-N-(tetrahydrofuran-3-yl)benzamide:



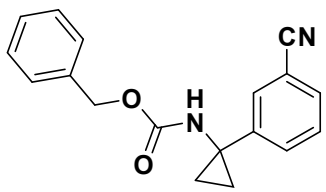
Scale-up Isolated yield: 15.3%

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.79 (d, J = 6.4 Hz, 1H), 8.09 – 7.99 (m, 2H), 8.02 – 7.90 (m, 2H), 4.47 (dtt, J = 8.2, 6.4, 4.3 Hz, 1H), 3.91 – 3.79 (m, 2H), 3.73 (td, J = 8.2, 5.9 Hz, 1H), 3.61 (dd, J = 9.0, 4.2 Hz, 1H), 2.23 – 2.12 (m, 1H), 1.98 – 1.88 (m, 1H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 165.51 , 138.76 , 132.80 , 128.72 , 118.82 , 114.03 , 72.66 , 66.97 , 50.97 , 32.27.

[M+H]+ calculated for 216.0898776; found 216.09.

Benzyl (1-(3-cyanophenyl)cyclopropyl)carbamate:



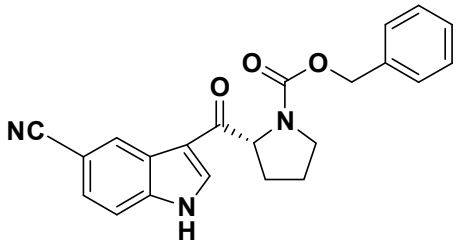
Scale-up Isolated yield: 44.2%

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.24 (s, 1H), 7.71 – 7.58 (m, 1H), 7.59 – 7.45 (m, 4H), 7.37 (hept, J = 7.4, 6.9 Hz, 4H), 5.04 (s, 2H), 1.40 – 1.11 (m, 4H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 156.58 , 146.11 , 137.51 , 130.07 , 129.97 , 129.88 , 128.86 , 128.58 , 128.32 , 128.18 , 119.40 , 111.69 , 65.86 , 34.93 , 18.98.

[M+H]+ calculated for 292.1211778; found 292.12.

Benzyl (R)-2-(5-cyano-1H-indole-3-carbonyl)pyrrolidine-1-carboxylate:



Scale-up Isolated yield: 41.3%

^{1}H NMR (500 MHz, DMSO-d_6) δ 12.54 (s, 2H), 8.69 (s, 1H), 8.64 (s, 1H), 8.57 – 8.52 (m, 2H), 7.69 (dd, J = 8.4, 4.0 Hz, 2H), 7.63 (ddd, J = 8.4, 3.9, 1.6 Hz, 2H), 7.39 (s, 2H), 7.46 – 7.29 (m, 3H), 7.15 – 6.97 (m, 6H), 5.23 (ddd, J = 16.9, 8.6, 3.5 Hz, 2H), 5.13 – 5.03 (m, 2H), 4.99 (d, J = 13.1 Hz, 1H), 4.89 (d, J = 13.1 Hz, 1H), 3.54 (dddd, J = 17.7, 10.3, 6.9, 3.8 Hz, 4H), 2.50 – 2.29 (m, 2H), 1.90 (dh, J = 17.6, 5.9 Hz, 7H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 154.14 , 138.91 , 137.21 , 136.68 , 136.60 , 128.88 , 128.27 , 128.23 , 127.90 , 127.78 , 127.28 , 126.83 , 126.38 , 120.57 , 114.30 , 114.22 , 104.58 , 66.30 , 66.16 , 62.51 , 62.10 , 47.71 , 47.07 , 32.07 , 31.02 , 24.49 , 23.68 .

$[M+H]^+$ calculated for: 373.1426415; found 373.14.

V. Experimental Section 3 – Comparison of Aryl Halide C-N coupling Methods using the Aryl Halide Informer Library

Experimental Procedure for Figure 4D, Entry 1. In a nitrogen filled glovebox, to the collection of 18 high-complexity aryl halides[21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38] (2.5 µmol/ reaction) in 250 uL microvials equipped with magnetic stir bars, 10 µl of $(o\text{-Tol})_3P)_2PdCl_2$ (0.025M in toluene, 0.25 µmol, 10 mol%) was added. Then a 15 µL mixture of piperidine (0.25M, 3.75 µmol, 1.5 equiv.) and NaOtBu (0.5M, 7.5 µmol, 3 equiv.) in toluene was added to the reaction vials. The reaction vials were sealed and stirred at 100 °C for 16 hrs. The reaction vials were then cooled to r.t. and diluted with 100 µL of 5% AcOH in DMSO containing 1,3,5-trimethoxybenzene (0.005M) and were shaken vigorously. A 25 µL aliquot was removed from each vial, and diluted with 700 µl of MeCN and quantitative UPLC analysis was performed to determine the solution yield.

Experimental Procedure for Figure 4D, Entry 2. In a nitrogen filled glovebox, to the collection of 18 high-complexity aryl halides (2.5 µmol/ reaction) in 250 uL microvials equipped with magnetic stir bars, 10 µl of J-009 ligand (0.025M in DME, 0.25 µmol, 10 mol%) and 10 µL $Pd(OAc)_2$ (0.025M in DME, 0.25 µmol, 10 mol%) was added. Then a 15 µL mixture of of piperidine (0.25M, 3.75 µmol, 1.5 equiv.) and NaOtBu (0.5M, 7.5 µmol, 3 equiv.) in DME was added to the reaction vials. The reaction vials were sealed and stirred at 80 °C for 16 hrs. The reaction vials were then cooled to r.t. and diluted

with 100 µL of 5% AcOH in DMSO containing 1,3,5-trimethoxybenzene (0.005M) and were shaken vigorously. A 25 µL aliquot was removed from each vial, and diluted with 700 µl of MeCN and quantitative UPLC analysis was performed to determine the solution yield.

Experimental Procedure for Figure 4D, Entry 3. In a nitrogen filled glovebox, to the collection of 18 high-complexity aryl halides (2.5 µmol/ reaction) in 250 uL microvials equipped with magnetic stir bars, 10 µl of [1,3-Bis(2,6-di-isopropylphenyl)-4,5-dihydroimidazol-2-ylidene]chloro][3-phenylallyl] palladium(II) (0.025M in DME, 0.25 µmol, 10 mol%) was added. Then a 15 µL mixture of piperidine (0.25M, 3.75 µmol, 1.5 equiv.) and KOtBu (0.5M, 7.5 µmol, 3 equiv.) in DME was added to the reaction vials. The reaction vials were sealed and stirred at room temperature for 16 hrs. The reaction vials were then diluted with 100 µL of 5% AcOH in DMSO containing 1,3,5-trimethoxybenzene (0.005M) and were shaken vigorously. A 25 µL aliquot was removed from each vial, and diluted with 700 µl of MeCN and quantitative UPLC analysis was performed to determine the solution yield.

Experimental Procedure for Figure 4D, Entry 4. In a nitrogen filled glovebox, to the collection of 18 high-complexity aryl halides (2.5 µmol/ reaction) in 250 uL microvials equipped with magnetic stir bars, 12.5 µl of RuPHOS G2 biaryl Pd precatalyst (0.02M in dioxane, 0.25 µmol, 10 mol%) was added. Then a solution of 12.5 µL of piperidine (0.3M, 3.75 µmol, 1.5 equiv.) and LiHMDS (0.6M, 7.5 µmol, 3 equiv.) in dioxane was added to the reaction vials. The reaction vials were sealed and stirred at 80 °C for 16 hrs. The reaction vials were then diluted with 100 µL of 5% AcOH in DMSO containing 1,3,5-trimethoxybenzene (0.005M) and were shaken vigorously. A 25 µL aliquot was removed from each vial, and diluted with 700 µl of MeCN and quantitative UPLC analysis was performed to determine the solution yield.

Experimental Procedure for Figure 4D, Entry 5. In a nitrogen filled glovebox, to the collection of 18 high-complexity aryl halides (2.5 µmol/ reaction) in 250 uL microvials equipped with magnetic stir bars, 12.5 µl of RuPHOS G2 biaryl Pd precatalyst (0.02M in tBuOH, 0.25 µmol, 10 mol%) was added. Then a mixture of 12.5 µL of piperidine (0.3M, 3.75 µmol, 1.5 equiv.) and K_2CO_3 (0.6M, 7.5 µmol, 3 equiv.) in tBuOH was added to the reaction vials. The reaction vials were sealed and stirred at 80 °C for 16 hrs. The reaction vials were then diluted with 100 µL of 5% AcOH in DMSO containing 1,3,5-trimethoxybenzene (0.005M) and were shaken vigorously. A 25 µL aliquot was removed from each vial, and diluted with 700 µl of MeCN and quantitative UPLC analysis was performed to determine the solution yield.

Experimental Procedure for Figure 4D, Entry 6. In a nitrogen filled glovebox, to the collection of 18 high-complexity aryl halides (2.5 µmol/ reaction) in 250 uL microvials equipped with magnetic stir

bars, 12.5 µl of RuPHOS G2 biaryl Pd precatalyst (0.02M in dioxane, 0.25 µmol, 10 mol%) was added. Then a mixture of 12.5 µL of piperidine (0.3M, 3.75 µmol, 1.5 equiv.) and Cs_2CO_3 (0.6M, 7.5 µmol, 3 equiv.) in dioxane was added to the reaction vials. The reaction vials were sealed and stirred at 80 °C for 16 hrs. The reaction vials were then diluted with 100 µL of 5% AcOH in DMSO containing 1,3,5-trimethoxybenzene (0.005M) and were shaken vigorously. A 25 µL aliquot was removed from each vial, and diluted with 700 µl of MeCN and quantitative UPLC analysis was performed to determine the solution yield.

Experimental Procedure for Figure 4D, Entries 7 and 8. In a nitrogen filled glovebox, to the collection of 18 high-complexity aryl halides (2.5 µmol/ reaction) in 250 uL microvials equipped with magnetic stir bars, 10 µl of a DMSO solution of tBuXPHOS G3 biaryl Pd precatalyst (0.02M, 0.25 µmol, 10 mol%) was added. Then a mixture of 15 µL of piperidine (0.25M, 3.75 µmol, 1.5 equiv.) and P2Et phosphazene (0.33M, 5 µmol, 2 equiv.) in dioxane was added to the reaction vials. The reaction vials were sealed and stirred room temperature or 60 °C as described in Table 3 for 16 hrs. The reaction vials were then diluted with 100 µL of 5% AcOH in DMSO containing 1,3,5-trimethoxybenzene (0.005M) and were shaken vigorously. A 25 µL aliquot was removed from each vial, and diluted with 700 µl of MeCN and quantitative UPLC analysis was performed to determine the solution yield.

Experimental Procedure for Figure 4D, Entry 9. In a nitrogen filled glovebox, to the collection of 18 high-complexity aryl halides (2.5 µmol/ reaction) in 250 uL microvials equipped with magnetic stir bars, 10 µl of CuI (0.25M in DMF, 2.5 µmol, 100 mol%) was added. Then a mixture of 15 µL of piperidine (0.25M, 3.75 µmol, 1.5 equiv.) and Cs_2CO_3 (0.5M, 7.5 µmol, 3 equiv.) in DMF was added to the reaction vials. The reaction vials were sealed and stirred at 100 °C for 16 hrs. The reaction vials were then diluted with 100 µL of 5% AcOH in DMSO containing 1,3,5-trimethoxybenzene (0.005M) and were shaken vigorously. A 25 µL aliquot was removed from each vial, and diluted with 700 µl of MeCN and quantitative UPLC analysis was performed to determine the solution yield.

Experimental Procedure for Figure 4D, Entry 10. In a nitrogen filled glovebox, to the collection of 18 high-complexity aryl halides (2.5 µmol/ reaction) in 250 uL microvials equipped with magnetic stir bars, 25 µl of a mixture containing CuI (0.01M, 0.25 µmol, 10 mol%), 2-Isobutyrylcyclohexanone (0.04M, 1 µmol, 40 mol%), piperidine (0.15M, 3.75 µmol, 1.5 equiv.) and Cs_2CO_3 (0.3M, 7.5 µmol, 3 equiv.) in DMF was added. The reaction vials were sealed and stirred at 100 °C for 16 hrs. The reaction vials were then diluted with 100 µL of 5% AcOH in DMSO containing 1,3,5-trimethoxybenzene (0.005M) and were shaken vigorously. A 25 µL aliquot was removed from each vial, and diluted with 700 µl of MeCN and quantitative UPLC analysis was performed to determine the solution yield.

Experimental Procedure for Figure 4D, Entries 11-15. In a nitrogen filled glovebox, to the collection of 18 high-complexity aryl halides (2.5 µmol/ reaction) in 250 uL microvials equipped with magnetic stir bars, 12.5 µl of a mixture of K_3PO_4 (0.6M, 7.5 µmol, 3 equiv.), CuI (0.02M, 0.25 µmol, 10 mol%) and piperidine (0.3 M, 3.75 µmol, 1.5 equiv.) in DMSO was added. Then a solution of 12.5 µL of the appropriate oxamate ligand (0.04M, 0.5 µmol, 20 mol%) in DMSO was added to the reaciton vials. The reaction vials were sealed and stirred at 80 °C for 16 hrs. The reaction vials were then cooled to r.t. and diluted with 100 µL of 5% AcOH in DMSO, containing 1,3,5-trimethoxybenzene (0.005M) and were shaken vigorously. A 25 µL aliquot was removed from each vial, and diluted with 700 µl of MeCN and quantitative UPLC analysis was performed to determine the solution yield.

Experimental Procedure for Figure 4D, Entries 16-18. In a nitrogen filled glovebox, to the collection of 18 high-complexity aryl halides (2.5 µmol/ reaction) in 250 uL microvials equipped with magnetic stir bars, 12.5 µl of a mixture of K_3PO_4 (0.6M, 7.5 µmol, 3 equiv.), CuI (0.05M, 0.625 µmol, 25 mol%) and piperidine (0.3 M, 3.75 µmol, 1.5 equiv.) in DMSO was added. Then a solution of 12.5 µL of the appropriate oxamate ligand **L2- L6**[39] (0.1M, 1.25 µmol, 50 mol%) in DMSO was added to the reaciton vials. The reaction vials were sealed and stirred at 100 or 120 °C as noted in Table 3 for 16 hrs. The reaction vials were then cooled to r.t. and diluted with 100 µL of 5% AcOH in DMSO, containing 1,3,5-trimethoxybenzene (0.005M) and were shaken vigorously. A 25 µL aliquot was removed from each vial, and diluted with 700 µl of MeCN and quantitative UPLC analysis was performed to determine the solution yield.

General Procedure A Scale-up Reactions for C-N Coupling of X1 with piperidine. In a nitrogen filled glovebox, 100 mg of aryl halide was charged to a 4-mL vial with stirbar. Then CuI (20 mol%), K_3PO_4 (3 equiv.), DMSO (1 mL), piperidine (2 equiv.) and finally oxamate ligand **L5** (40 mol%) were added, in that order. The reactions were then capped and heated at 80 °C for 16h. The reactions were then cooled to room temperature, filtered and submitted directly for MS-directed purification. No attempt was made to obtain optimal yield on these experiments, rather to obtain high purity samples for quantitative UPLC analysis. Isolated yields for the compound using this method is noted below.

General Procedure B Scale-up Reactions for C-N Couplings of X2, X3, X4, X6, X8, X9, X12, X14 and X15 with piperidine. In a nitrogen filled glovebox, 100 mg of aryl halide was charged to a 4-mL vial with stirbar. Then CuI (20 mol%), K_3PO_4 (3 equiv.), DMSO (1 mL), piperidine (2 equiv.) and finally oxamate ligand **L4** (40 mol%) were added, in that order. The reactions were then capped and heated at 80 °C for 16h. The reactions were then cooled to room temperature, filtered and submitted directly for MS-directed purification. No attempt was made to obtain highest yield on these experiments, rather to obtain

high purity samples for quantitative UPLC analysis. Isolated yields for compounds using this method are noted below.

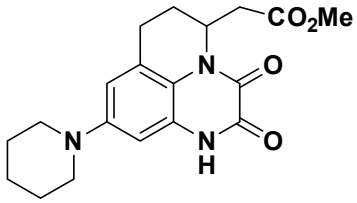
General Procedure C Scale-up Reactions for C-N Couplings of X5, X13 and X15 with piperidine. In a nitrogen filled glovebox, 100 mg of aryl halide was charged to a 4-mL vial with stirbar. Then tBuXPHOS G3 pre-catalyst (10 mol%), DMSO (0.2M concentration relative to aryl halide), piperidine (2 equiv.) and finally P2Et phosphazene (2 equiv.) were added, in that order. The reactions were then capped and heated at 60 °C for 16h. The reactions were then cooled to room temperature, and 2MeTHF solvent was added (4 mL) followed by NH_4Cl (4 mL). The aqueous layer was cut, the organic layer was stripped and the resulting residue was dissolved in DMSO (1 mL) and purified by MS-directed durification. No attempt was made to obtain highest yield on these experiments, rather to obtain high purity samples for quantitative UPLC analysis. Isolated yields for compounds using this method are noted below.

General Procedure D Scale-up Reactions for C-N Coupling of X10 with piperidine In a nitrogen filled glovebox, 100 mg of aryl halide was charged to a 4-mL vial with stirbar. Then [1,3-Bis(2,6-di-isopropylphenyl)-4,5-dihydroimidazol-2-ylidene]chloro][3-phenylallyl]palladium(II) (10 mol%), DME (0.2M concentration relative to aryl halide), piperidine (2 equiv.) and finally KOtBu (2 equiv.) were added, in that order. The reaction was then capped and stirred at room temperature for 16h. The reaction was then cooled to room temperature, and 2MeTHF solvent was added (4 mL) followed by NH_4Cl (4 mL). The aqueous layer was cut, the organic layer was stripped and the resulting residue was dissolved in DMSO (1 mL) and purified by MS-directed durification. No attempt was made to obtain highest yield on these experiments, rather to obtain high purity samples for quantitative UPLC analysis. Isolated yields for the compound using this method is noted below.

General Procedure E Scale-up Reactions for C-N Coupling of X16 with piperidine. In a nitrogen filled glovebox, 100 mg of aryl halide was charged to a 4-mL vial with stirbar. Then RuPhos G2 biaryl precatalyst (10 mol%), LiHMDS (2 equiv.), dioxane (0.2M concentration relative to aryl halide), and finally piperidine (2 equiv.) were added, in that order. The reaction was then capped and stirred at 80 °C for 16h. The reaction was then cooled to room temperature, and 2MeTHF solvent was added (4 mL) followed by NH_4Cl (4 mL). The aqueous layer was cut, the organic layer was stripped and the resulting residue was dissolved in DMSO (1 mL) and purified by MS-directed durification. No attempt was made to obtain highest yield on these experiments, rather to obtain high purity samples for quantitative UPLC analysis. Isolated yields for the compound using this method is noted below.

General Procedure F Scale-up Reactions for C-N Coupling of X18 with piperidine. In a nitrogen filled glovebox, 100 mg of aryl halide was charged to a 4-mL vial with stirbar. Then RuPhos G2 biaryl precatalyst (10 mol%), Cs_2CO_3 (2 equiv.), dioxane (0.2M concentration relative to aryl halide), and finally piperidine (2 equiv.) were added, in that order. The reaction was then capped and stirred at 80 °C for 16h. The reaction was then cooled to room temperature, and 2MeTHF solvent was added (4 mL) followed by NH_4Cl (4 mL). The aqueous layer was cut, the organic layer was stripped and the resulting residue was dissolved in DMSO (1 mL) and purified by MS-directed durification. No attempt was made to obtain highest yield on these experiments, rather to obtain high purity samples for quantitative UPLC analysis. Isolated yields for compounds using this method are noted below.

*Product of **X1** + piperidine*



Scale-up Method A: 23 mg (26% yield).

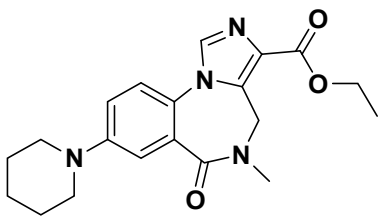
Methyl 2-(2,3-dioxo-9-(piperidin-1-yl)-2,3,6,7-tetrahydro-1H,5H-pyrido[1,2,3-de]quinoxalin-5-yl)acetate

^{1}H NMR (500 MHz, DMSO-d_6) δ 6.65 (d, J = 2.5 Hz, 1H), 6.55 (d, J = 2.6 Hz, 1H), 5.10 – 5.03 (m, 1H), 3.62 (s, 3H), 3.07 (t, J = 5.3 Hz, 4H), 2.88 (m, 1H), 2.76 – 2.67 (m, 1H), 2.63 – 2.56 (om, 2H), 2.08 (m, 1H), 1.89 (tt, J = 13.9, 4.8 Hz, 1H), 1.60 (m, 4H), 1.53 (m, 2H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 171.21, 154.43, 153.83, 148.12, 126.73, 125.43, 115.45, 112.19, 100.75, 52.13, 50.24, 47.38, 35.37, 25.60, 24.28, 23.51, 21.80.

LRMS-ESI m/z calcd. for $C_{19}H_{23}N_3O_4$: 357.17, found 358.3 $[M+H]^+$

*Product of **X2** + piperidine*



Scale-up Method B: 13.7 mg (15% yield).

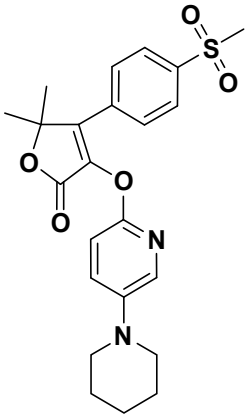
Ethyl 5-methyl-6-oxo-8-(piperidin-1-yl)-5,6-dihydro-4H-benzo[f]imidazo[1,5-a][1,4]diazepine-3-carboxylate

^{1}H NMR (500 MHz, Acetic Acid-d_4) δ 8.34 (bs, 1H), 7.73 (d, J = 2.8 Hz, 1H), 7.59 (d, J = 8.9 Hz, 1H), 7.47 (dd, J = 8.9, 2.9 Hz, 1H), 4.44 (bm, 2H), 3.50 – 3.36 (m, 4H), 3.29 (s, 3H), 1.82 (m, 4H), 1.70 (m, 2H), 1.44 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, Acetic-*d4*) δ 167.79, 162.42, 150.02, 136.16, 135.23, 128.86, 126.70, 124.75, 123.60, 121.30, 118.90, 60.97, 50.61, 42.35, 35.48, 24.73, 23.41, 13.32.

LRMS-ESI m/z calcd. for $C_{20}H_{24}N_4O_3$: 368.18, found 369.3 $[M+H]^+$

*Product of **X3** + piperidine*



Scale-up Method B: 18 mg (16% yield).

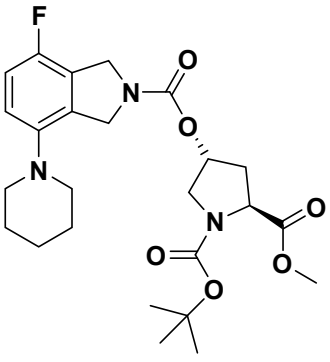
5,5-dimethyl-4-(4-(methylsulfonyl)phenyl)-3-((5-(piperidin-1-yl)pyridin-2-yl)oxy)furan-2(5H)-one

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.01 (d, J = 8.8 Hz, 1H), 7.86 (d, J = 8.8 Hz, 1H), 7.75 (dd, J = 3.1, 0.7 Hz, 1H), 7.50 (dd, J = 9.0, 3.1 Hz, 1H), 7.00 (dd, J = 9.0, 0.6 Hz, 1H), 3.24 (s, 3H), 3.14 – 2.98 (m, 4H), 1.70 (s, 6H), 1.61 (m, 4H), 1.51 (m, 2H).

^{13}C NMR (126 MHz, DMSO) δ 165.91, 154.30, 148.44, 145.58, 141.92, 137.52, 134.45, 134.24, 129.33, 127.99, 111.17, 84.74, 50.23, 43.74, 26.38, 25.54, 24.00.

LRMS-ESI m/z calcd. for $C_{23}H_{26}N_2O_5S$: 442.16, found 443.2 $[M+H]^+$

*Product of **X4** + piperidine*



Scale-up Method B: 16.3 mg (13% yield).

1-(tert-butyl) 2-methyl (2S,4R)-4-((4-fluoro-7-(piperidin-1-yl)isoindoline-2-carbonyl)oxy) pyrrolidine-1,2-dicarboxylate

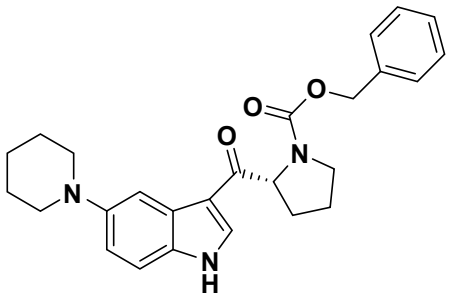
^{1}H NMR (500 MHz, DMSO-d_6) δ 7.11 (m, 2H), 5.27 – 5.09 (m, 1H), 4.64 (m, 4H), 4.35 (m, 1H), 3.69 (s, 3H), 3.65 – 3.47 (m, 1H), 3.09 – 2.85 (m, 4H), 2.49 – 2.37 (m, 1H), 2.18 (m, 1H), 1.68 (m, 4H), 1.60 – 1.48 (m, 2H), 1.37 (m, 9H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 173.27, 172.85, 154.83, 154.15, 153.69, 153.46, 152.91, 133.60, 132.96, 124.54, 120.09, 115.41, 115.25, 115.18, 80.03, 80.00, 79.92, 73.84, 73.28, 58.00, 57.66, 53.42, 53.37, 52.72, 52.56, 52.47, 51.94, 51.29, 49.74, 49.30, 36.50, 35.58, 28.42, 28.25, 25.90, 25.87, 23.52.

The sample is a mixture of diastereomers

LRMS-ESI m/z calcd. for $C_{25}H_{34}FN_3O_6$: 491.24, found 492.4 $[M+H]^+$

*Product of **X5** + piperidine*



Scale-up Method C: 10.1 mg (10% yield).

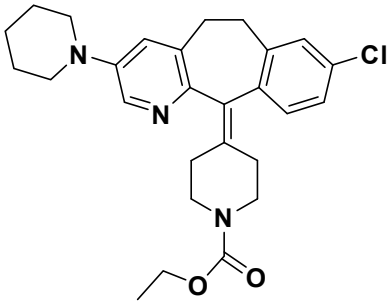
Benzyl (R)-2-(5-(piperidin-1-yl)-1H-indole-3-carbonyl)pyrrolidine-1-carboxylate

^{1}H NMR (500 MHz, DMSO-d_6) δ 12.40 (d, J = 10.4 Hz, 1H), 8.58 (d, J = 13.8 Hz, 1H), 8.48 (bs, 1H), 7.70 (d, J = 8.9 Hz, 1H), 7.57 (dd, J = 7.7, 7.0 Hz, 1H), 7.35 (om, 2H), 7.15 – 6.92 (om, 3H), 5.30 – 5.11 (m, 1H), 5.05 (s, 1H), 4.98 – 4.83 (m, 1H), 3.59 (om, 4H), 2.46 – 2.27 (m, 1H), 1.93 (m, 4H), 1.90 – 1.77 (om, 5H), 1.69 (bs, 2H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 194.62, 194.18, 154.46, 154.34, 137.93, 137.86, 137.44, 136.96, 136.63, 136.60, 136.50, 128.91, 128.36, 128.29, 127.83, 127.80, 127.15, 126.13, 126.07, 116.29, 114.55, 114.48, 114.42, 66.30, 66.27, 62.51, 62.08, 57.34, 57.30, 47.71, 47.12, 32.10, 31.10, 24.45, 23.88, 23.64, 20.98.

Resonances are doubled; likely due to rotamers

*Product of **X6** + piperidine*



Scale-up Method B: 8.0 mg (7% yield).

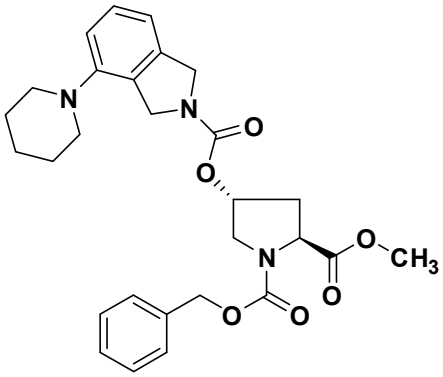
Ethyl 4-(8-chloro-3-(piperidin-1-yl)-5,6-dihydro-11H-benzo[5,6]cyclohepta[1,2-b]pyridin-11-ylidene)piperidine-1-carboxylate

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.03 (d, J = 2.7 Hz, 1H), 7.30 (d, J = 2.2 Hz, 1H), 7.19 (dd, J = 8.1, 2.3 Hz, 1H), 7.09 – 7.00 (om, 2H), 4.03 (q, J = 7.1 Hz, 2H), 3.60 (dt, J = 12.6, 5.2 Hz, 2H), 3.33 – 3.05 (om, 8H), 2.83 – 2.68 (m, 2H), 2.35 (m, 1H), 2.30 – 2.17 (m, 2H), 2.13 (m, 1H), 1.62 – 1.54 (m, 4H), 1.51 (m, 2H), 1.17 (t, J = 7.1 Hz, 3H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 155.06, 146.46, 146.42, 140.96, 139.50, 136.02, 134.93, 133.82, 133.29, 131.72, 130.65, 128.96, 126.03, 123.80, 61.16, 49.20, 44.90, 44.87, 31.70, 31.27, 30.83, 30.61, 25.42, 24.16, 15.05.

LRMS-ESI m/z calcd. for $C_{27}H_{32}ClN_3O_2$: 465.22, found 466.4 $[M+H]^+$

*Product of **X8** + piperidine*



Scale-up Method B: 24.5 mg (19.3% yield).

8. 1-benzyl 2-methyl (2S,4R)-4-((4-(piperidin-1-yl)isoindoline-2-carbonyl)oxy)pyrrolidine-1,2-dicarboxylate

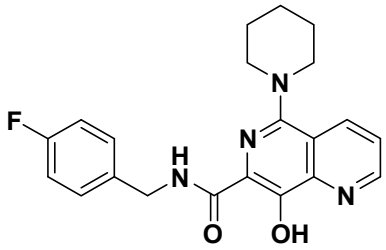
^{1}H NMR (500 MHz, DMSO-d_6) δ 7.42 – 7.25 (om, 6H), 7.19 (m, 1H), 7.09 (m, 1H), 5.28 – 5.16 (m, 1H), 5.16 – 4.97 (om, 2H), 4.71 (bs, 1H), 4.64 – 4.45 (m, 4H), 3.82 – 3.72 (m, 1H), 3.68 (om, 3H), 3.53 (d, J = 12.2 Hz, 1H), 3.23 – 3.11 (m, 2H), 3.04 (m, 2H), 2.67 – 2.51 (m, 1H), 2.24 (td, J = 15.1, 6.2 Hz, 1H), 1.74 (om, 4H), 1.65 – 1.51 (m, 2H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 172.53, 172.43, 172.20, 172.11, 154.38, 154.16, 153.64, 153.61, 139.34, 138.61, 137.19, 137.09, 130.15, 129.67, 129.52, 129.40, 128.88, 128.77, 128.74, 128.38, 128.35, 128.21, 128.06, 128.01, 127.72, 127.69, 120.06, 119.98, 118.96, 118.80, 118.46, 118.04, 117.99, 74.26, 74.04, 73.24, 73.03, 66.71, 66.63, 58.24, 58.17, 57.80, 53.92, 53.57, 53.35, 53.27, 53.13, 52.92, 52.56, 52.44, 51.90, 51.43, 50.87, 36.54, 35.57, 25.69, 25.64, 25.17, 23.43, 22.88.

The sample is a mixture of diastereomers; some resonances are doubled due to rotamers

LRMS-ESI m/z calcd. for $C_{28}H_{33}N_3O_6$: 507.24, found 508.2 $[M+H]^+$

*Product of **X10** + piperidine*



Scale-up Method D: 39.4 mg (40% yield)

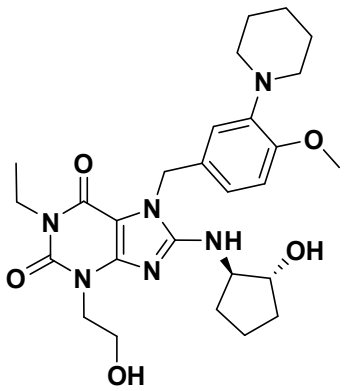
N-(4-fluorobenzyl)-8-hydroxy-5-(piperidin-1-yl)-1,6-naphthyridine-7-carboxamide

^{1}H NMR (500 MHz, DMSO-d_6) δ 13.03 (bs, 1H), 9.26 (t, J = 6.5 Hz, 1H), 9.08 (dd, J = 4.3, 1.6 Hz, 1H), 8.44 (dd, J = 8.5, 1.7 Hz, 1H), 7.74 (dd, J = 8.5, 4.2 Hz, 1H), 7.46 – 7.36 (m, 2H), 7.21 – 7.13 (m, 2H), 4.56 (d, J = 6.5 Hz, 2H), 3.20 (t, J = 5.2 Hz, 4H), 1.75 (m, 4H), 1.60 (m, 2H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 170.13, 161.70 (d, J = 242.5 Hz), 153.72, 153.58, 150.81, 144.77, 135.67 (d, J = 3.0 Hz), 134.63, 129.88 (d, J = 8.1 Hz), 124.28, 122.21, 120.97, 115.55 (d, J = 21.2 Hz), 52.92, 41.96, 26.00, 24.61

LRMS-ESI m/z calcd. for $C_{21}H_{21}FN_4O_2$: 380.16, found 381.3 $[M+H]^+$

*Product of **X12** + piperidine*



Scale-up Method B: 17.8 mg (13.5% yield).

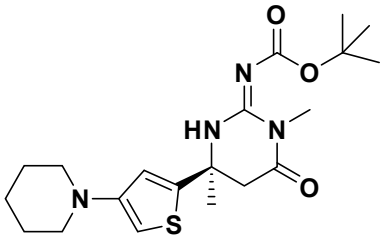
1-Ethyl-8-(((1R,2R)-2-hydroxycyclopentyl)amino)-3-(2-hydroxyethyl)-7-(4-methoxy-3-(piperidin-1-yl)benzyl)-3,7-dihydro-1H-purine-2,6-dione

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.02 (m, 1H), 6.97 (m, 1H), 6.90 (m, 1H), 6.82 (m, 1H), 5.20 (s, 1H), 4.83 (bs, 2H), 4.05 – 3.95 (m, 3H), 3.95 – 3.82 (m, 3H), 3.72 (s, 3H), 3.67 – 3.57 (m, 2H), 2.84 (m, 4H), 2.06 (m, 1H), 1.86 (m, 1H), 1.73 – 1.55 (m, 6H), 1.49 (m, 4H), 1.09 (t, J = 7.0, 3H).

^{13}C NMR (126 MHz, DMSO) δ 153.92, 153.05, 151.90, 150.89, 149.17, 142.58, 142.55, 129.84, 121.84, 118.74, 112.13, 101.74, 101.66, 76.72, 70.73, 61.91, 58.28, 55.83, 51.92, 45.42, 45.06, 35.62, 32.89, 30.40, 26.25, 24.47, 21.07, 13.73.

LRMS-ESI m/z calcd. for $C_{27}H_{38}N_6O_5$: 526.29, found 527.4 $[M+H]^+$

*Product of **X13** + piperidine*



Scale-up Method C: 17.9 mg (18 % yield)

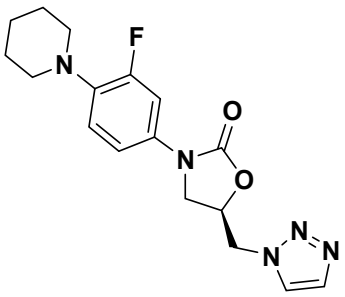
tert-butyl (S,Z)-(1,4-dimethyl-6-oxo-4-(4-(piperidin-1-yl)thiophen-2-yl)tetrahydropyrimidin-2(1H)-ylidene)carbamate

^{1}H NMR (500 MHz, DMSO-d_6) δ 9.97 (s, 1H), 6.94 (d, J = 1.8 Hz, 1H), 6.15 (d, J = 1.8 Hz, 1H), 3.18 (dd, J = 16.1, 1.5 Hz, 1H), 3.09 (d, J = 16.1 Hz, 1H), 3.03 (s, 3H), 2.97 – 2.92 (m, 4H), 1.65 (s, 3H), 1.61 – 1.54 (m, 4H), 1.51 – 1.44 (m, 2H), 1.43 (s, 9H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 168.20, 163.55, 157.35, 153.02, 147.73, 118.32, 98.50, 79.16, 53.50, 50.89, 44.58, 29.91, 28.38, 28.35, 25.51, 24.01.

LRMS-ESI m/z calcd. for $C_{20}H_{30}N_4O_3S$: 406.20, found 407.3 $[M+H]^+$

*Product of **X14**+ piperidine*



Scale-up Method B: 50.0 mg (57.9% yield).

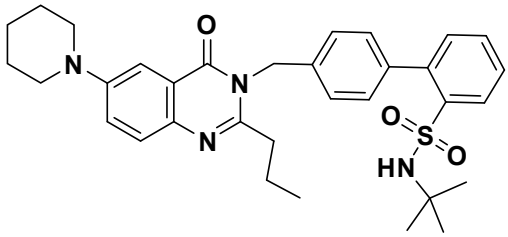
(R)-5-((1H-1,2,3-triazol-1-yl)methyl)-3-(3-fluoro-4-(piperidin-1-yl)phenyl)oxazolidin-2-one

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.16 (d, J = 1.0 Hz, 1H), 7.77 (d, J = 1.0 Hz, 1H), 7.36 (dd, J = 14.8, 2.5 Hz, 1H), 7.09 (ddd, J = 8.8, 2.6, 0.7 Hz, 1H), 7.03 (dd, J = 9.7, 8.8 Hz, 1H), 5.12 (m, 1H), 4.83 (s, 1H), 4.82 (d, J = 1.1 Hz, 1H), 4.20 (t, J = 9.2 Hz, 1H), 3.85 (dd, J = 9.3, 5.7 Hz, 1H), 2.97 – 2.84 (m, 5H), 1.64 (m, 5H), 1.51 (m, 2H).

^{13}C NMR (126 MHz, DMSO) δ 155.03 (d, J = 243.7 Hz), 153.97, 137.49 (d, J = 8.9 Hz), 133.85, 132.96 (d, J = 10.5 Hz), 126.32, 120.01 (d, J = 4.3 Hz), 114.78 (d, J = 3.1 Hz), 107.24 (d, J = 26.1 Hz), 71.21, 52.20, 52.11 (d, J = 2.8 Hz), 47.59, 26.12, 24.14.

LRMS-ESI m/z calcd. for $C_{17}H_{20}FN_5O_2$: 345.16, found 346.2 $[M+H]^+$

*Product of **X15** + piperidine*



Scale-up Method B: 28.2 mg (19.7% yield).

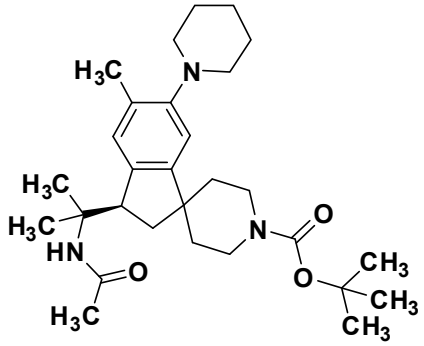
N-(tert-butyl)-4'-((4-oxo-6-(piperidin-1-yl)-2-propylquinazolin-3(4H)-yl)methyl)-[1,1'-biphenyl]-2-sulfonamide

^{1}H NMR (500 MHz, Acetic Acid-d_4) δ 8.19 (dd, J = 8.0, 1.4 Hz, 1H), 8.06 (d, J = 2.4 Hz, 1H), 7.89 – 7.82 (om, 2H), 7.63 (td, J = 7.5, 1.4 Hz, 1H), 7.55 (td, J = 8.1, 1.8 Hz, 1H), 7.52 (d, J = 8.2 Hz, 2H), 7.38 – 7.31 (om, 3H), 5.60 (s, 2H), 3.51 (t, J = 5.5 Hz, 4H), 1.91 (m, 4H), 1.82 (q, J = 7.4 Hz, 2H), 1.73 (m, 2H), 1.05 (t, J = 7.4 Hz, 3H), 1.04 (s, 9H).

^{13}C NMR (126 MHz, Acetic Acid-d_4) δ 162.30, 158.15, 147.44, 141.77, 141.17, 139.90, 139.23, 135.77, 132.36, 131.91, 130.20, 128.41, 127.78, 126.84, 126.62, 125.91, 120.42, 113.62, 53.89, 52.57, 46.81, 28.88, 24.39, 22.80, 21.00, 12.95.

LRMS-ESI m/z calcd. for $C_{33}H_{40}N_4O_3S$: 572.28, found 573.4 $[M+H]^+$

*Product of **X16** + piperidine*



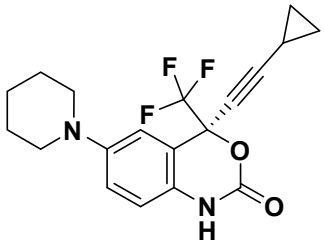
Scale-up Method E: 80.0 mg (66.2% yield).

tert-butyl (R)-3-(2-acetamidopropan-2-yl)-5-methyl-6-(piperidin-1-yl)-2,3-dihydrospiro[indene-1,4'-piperidine]-1'-carboxylate

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.83 (s, 1H), 7.10 (s, 1H), 6.72 (s, 1H), 4.06 (om, 4H), 2.86 (bs, 2H), 2.71 (bs, 4H), 2.33 – 2.04 (om, 4H), 1.86 (bs, 4H), 1.59 (m, 4H), 1.48 (bs, 2H), 1.40 (s, 9H), 1.28 (om, 6H), 1.07 (s, 3H).

LRMS-ESI m/z calcd. for $C_{29}H_{45}N_3O_3$: 483.35, found 484.5 $[M+H]^+$

*Product of **X17** + piperidine*



Scale-up Method C: 11 mg (10% yield)

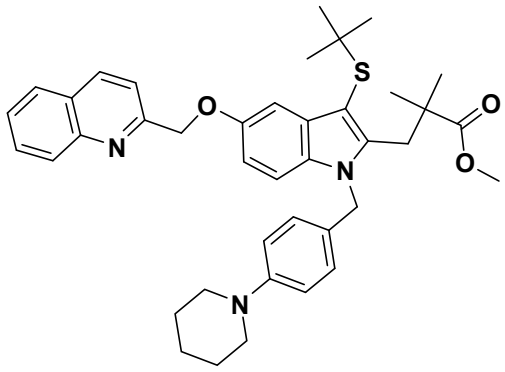
(S)-4-(cyclopropylethynyl)-6-(piperidin-1-yl)-4-(trifluoromethyl)-1,4-dihydro-2H-benzo[d][1,3]oxazin-2-one

^{1}H NMR (500 MHz, DMSO-d_6) δ 7.09 (dd, J = 8.8, 2.7 Hz, 1H), 6.87 (d, J = 2.6 Hz, 1H), 6.84 (d, J = 8.8 Hz, 1H), 6.08 (s, 1H), 3.10 – 3.00 (m, 4H), 1.61 (m, 4H), 1.56 (m, 1H), 1.51 (m, 2H), 0.99 – 0.90 (m, 2H), 0.73 (m, 2H).

^{13}C NMR (126 MHz, DMSO-d_6) δ 148.48, 147.33, 127.71, 124.17, 123.03 (q, J = 287.2 Hz), 121.89, 120.72, 116.15, 114.30, 113.34, 95.40, 67.15, 50.54, 25.53, 24.05, 9.00, 8.98, -0.84.

LRMS-ESI m/z calcd. for $C_{19}H_{19}F_3N_2O_2$: 364.14, found 365.5 $[M+H]^+$

*Product of **X18** + piperidine*



Scale-up Method F: 35.0 mg (21.5% yield).

Methyl 3-(3-(tert-butylthio)-1-(4-(piperidin-1-yl)benzyl)-5-(quinolin-2-ylmethoxy)-1H-indol-2-yl)-2,2-dimethylpropanoate

^{1}H NMR (500 MHz, Acetic Acid-d_4) δ 8.55 (d, J = 8.6 Hz, 1H), 8.34 (d, J = 8.5 Hz, 1H), 8.03 (dd, J = 8.2, 1.4 Hz, 1H), 7.95 – 7.88 (om, 2H), 7.72 (ddd, J = 8.1, 6.9, 1.1 Hz, 1H), 7.59 (d, J = 8.7 Hz, 2H), 7.38 (d, J = 2.5 Hz, 1H), 7.18 (d, J = 8.9 Hz, 1H), 7.02 (d, J = 8.4 Hz, 2H), 6.98 (dd, J = 8.9, 2.5 Hz, 1H), 5.64 (s, 2H), 5.52 (s, 2H), 3.66 (s, 3H), 3.55 (m, 4H), 3.36 (bs, 2H), 2.01 (m, 4H), 1.71 (m, 2H), 1.25 (s, 6H), 1.18 (s, 9H).

^{13}C NMR (126 MHz, Acetic) δ 178.37, 158.32, 153.30, 144.14, 143.75, 142.41, 140.49, 139.52, 132.49, 132.28, 131.48, 128.07, 127.91, 127.53, 127.33, 125.51, 121.50, 119.64, 112.71, 111.23, 105.09, 104.13, 56.54, 51.86, 47.53, 46.88, 44.03, 33.93, 30.47, 24.76, 23.37, 21.05.

LRMS-ESI m/z calcd. for $C_{40}H_{47}N_3O_3S$: 649.33, found 650.3 $[M+H]^+$

VI. Experimental Section 4- Comparison of Informer Library Approach with Fragment-based Robustness Test

Experimental Procedure Figure 6– 10 umol Microscale Fragment Additive Reactions for Suzuki Miyaura Couplings. In a nitrogen filled glovebox, into 5 x 1 mL vials containing stirbars, THF solutions of 20 uL of phenylpinacolboronate (0.75 M, 15.0 umol, 1 equiv), 20 uL of chlorobenzene (0.75M, 15.0 umol, 1 equiv), and XPhos G3 biaryl precatalyst (0.0375M, 0.75 umol, 5 mol%) were combined. Then in the appropriate vials were added the following:

Vial 1: 40 uL THF

Vial 2: 40 uL indole **F1** (0.375 M in THF, 15.0 umol, 1 equiv)

Vial 3: 40 uL oxadiazole **F2** (0.375 M in THF, 15.0 umol, 1 equiv)

Vial 4: 40 uL chlorosulfonamide **F3** (0.375 M in THF, 15.0 umol, 1 equiv)

Vial 5: 40 uL tetrazole **F4** (0.375 M in THF, 15.0 umol, 1 equiv)

Finally, 30 uL of aqueous K_3PO_4 (1 M, 30 umol, 2 equiv) was added to each reaction. The reactions were then sealed and heated at 100 °C for 16h, then cooled to room temperature. The reacitons were diluted with 500 uL of acetonitrile, mixed thoroughly, then 20 uL of these reactions were added to 700 uL of ACN. UPLC analysis of the reactions revealed the area counts of product and fragment remaining for each reaction. The performance of vials 2-5 was compared to the performance of vial 1. The amount of fragment remaining was determined by comparison of reactions 2-5 with UPLC analysis of solutions of unreacted fragments **F1**-**F4** of the same overall concentration.

Results from this test are presented graphically in the bar graph below, with the LC area counts of product and the fragments remaining depicted.

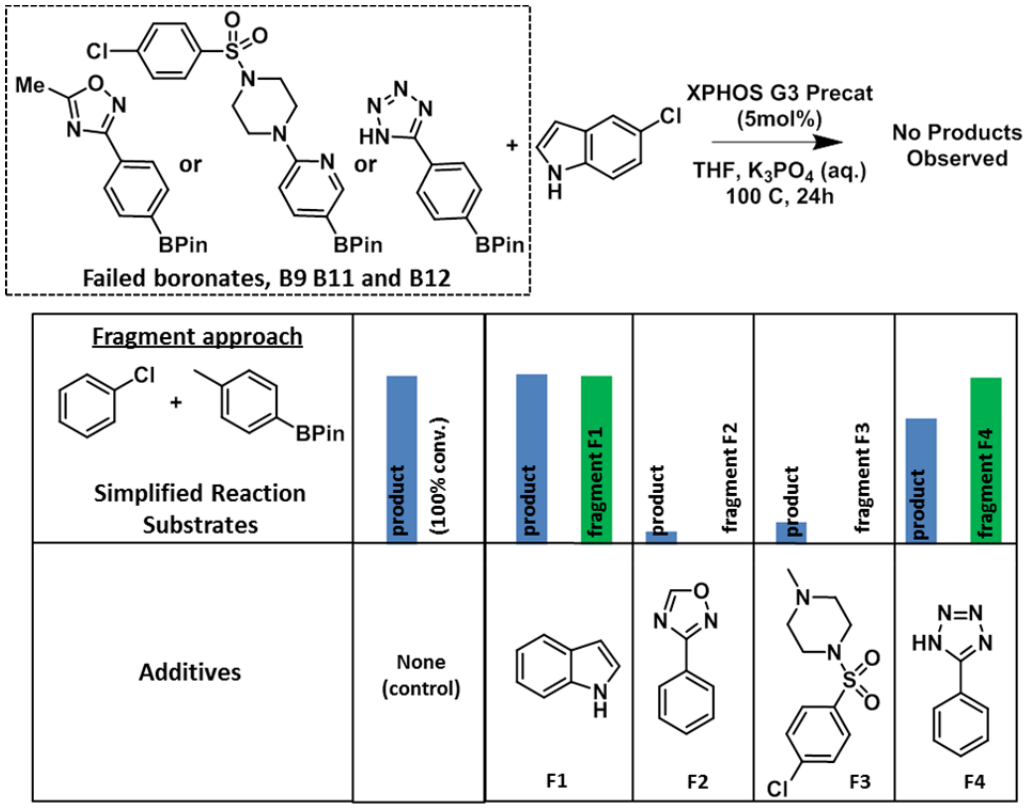


Figure S3

Experimental Procedure Figure 6– 10 umol Microscale Fragment Additive Reactions for Cu C-N Couplings. In a nitrogen filled glovebox, into 5 x 1 mL vials containing stirbars, was added 20 uL of a DMSO solution of bromobenzene (0.5 M, 10 umol), followed by 30 uL of a DMSO mixture containing copper idodie (0.083 M, 25

mol%), K_3PO_4 (1.0 M, 30 umol, 3 equiv.) and piperidine (0.5 M, 15 umol, 1.5 equiv.). Then in the appropriate vials were added the following:

Vial 1: 30 uL DMSO

Vial 2: 10 uL 4-n-butylchlorobenzene **F5** (1.0 M in DMSO, 10.0 umol, 1 equiv) + 20 uL DMSO

Vial 3: 10 uL N-benzylindole **F6** (1.0 M in DMSO, 10.0 umol, 1 equiv) + 20 uL DMSO

Vial 4: 10 uL 3-phenylbutanoic acid **F7** (1.0 M in DMSO, 10.0 umol, 1 equiv) + 20 uL DMSO

Vial 5: 10 uL 4-n-butylchlorobenzene **F5** (1.0 M in DMSO, 10.0 umol, 1 equiv), 10 uL N-benzylindole **F6** (1.0 M in DMSO, 10.0 umol, 1 equiv.), 10 uL 3-phenylbutanoic acid **F7** (1.0 M in DMSO, 10.0 umol, 1 equiv)

Finally, a DMSO solution of oxamate ligand **L4** (0.25 M, 50 mol%) was added to each vial. The reactions were then sealed and heated at 100 °C for 16h, then cooled to room temperature. The reacitons were diluted with 500 uL of acetonitrile, mixed thoroughly, then 20 uL of these reactions were added to 700 uL of ACN. UPLC analysis of the reactions revealed the area counts of product and fragment remaining for each reaction. The performance of vials 2-5 was compared to the performance of vial 1. The amount of fragment remaining was determined by comparison of reactions 2-5 with UPLC analysis of solutions of unreacted fragments **F5**-**F7** of the same overall concentration.

Results from this test are presented graphically in the bar graph below, with the LC area counts of product and the fragments remaining depicted.

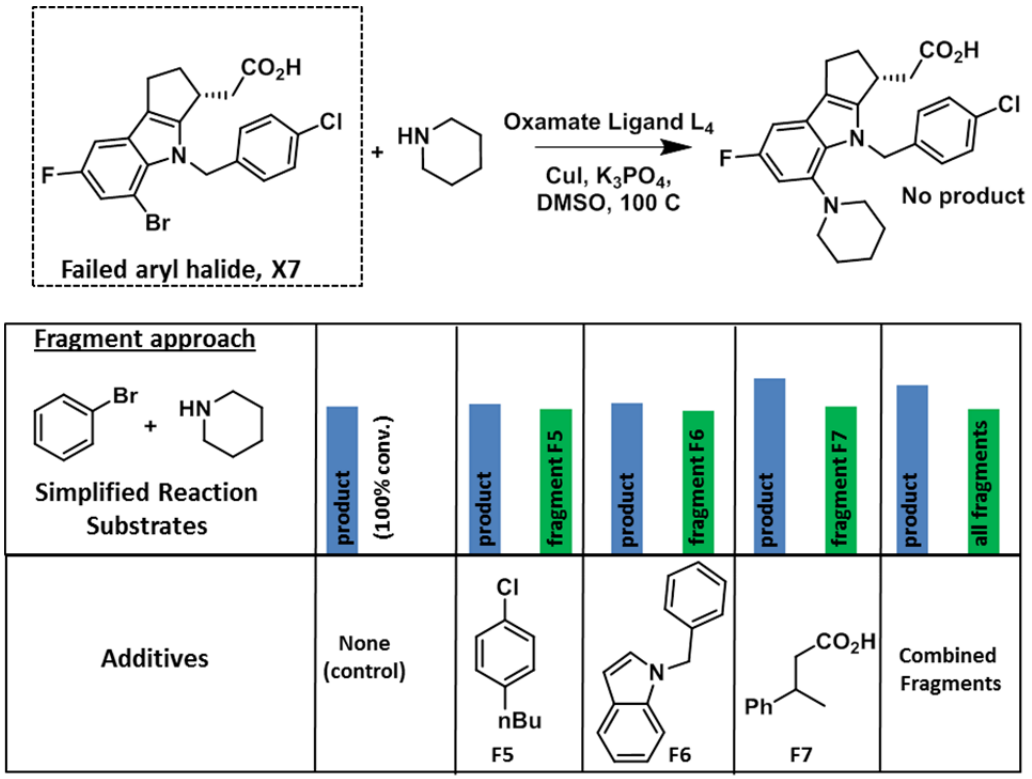


Figure S4

Experimental Procedure Figure 6– 10 umol Microscale Fragment Additive Reactions for Cu C-N Couplings. In a nitrogen filled glovebox, into 4 x 1 mL vials containing stirbars, was added 20 uL of a DMSO solution of bromobenzene (0.5 M, 10 umol), followed by 30 uL of a DMSO mixture containing copper idodie (0.083 M, 25 mol%), K_3PO_4 (1.0 M, 30 umol, 3 equiv.) and piperidine (0.5 M, 15 umol, 1.5 equiv.). Then in the appropriate vials were added the following:

Vial 1: 30 uL DMSO

Vial 2: 10 uL 4-n-butylchlorobenzene **F5** (1.0 M in DMSO, 10.0 umol, 1 equiv) + 20 uL DMSO

Vial 3: 10 uL 3-phenylbutanoic acid **F7** (1.0 M in DMSO, 10.0 umol, 1 equiv) + 20 uL DMSO

Vial 4: 10 uL 4-n-butylchlorobenzene **F5** (1.0 M in DMSO, 10.0 umol, 1 equiv), 10 uL 3-phenylbutanoic acid **F7** (1.0 M in DMSO, 10.0 umol, 1 equiv) + 10 uL DMSO

Finally, a DMSO solution of oxamate ligand **L4** (0.25 M, 50 mol%) was added to each vial. The reactions were then sealed and heated at 100 °C for 16h, then cooled to room temperature. The reacitons were diluted with 500 uL of acetonitrile, mixed thoroughly, then 20 uL of these reactions were added to 700 uL of ACN. UPLC analysis of the reactions revealed the area counts of product and fragment remaining for each reaction. The performance of vials 2-5 was compared to the performance of vial 1. The amount of fragment remaining was determined by comparison of reactions 2-5 with UPLC analysis of solutions of unreacted fragments **F5** and **F7** of the same overall concentration.

Results from this test are presented graphically in the bar graph below, with the LC area counts of product and the fragments remaining depicted.

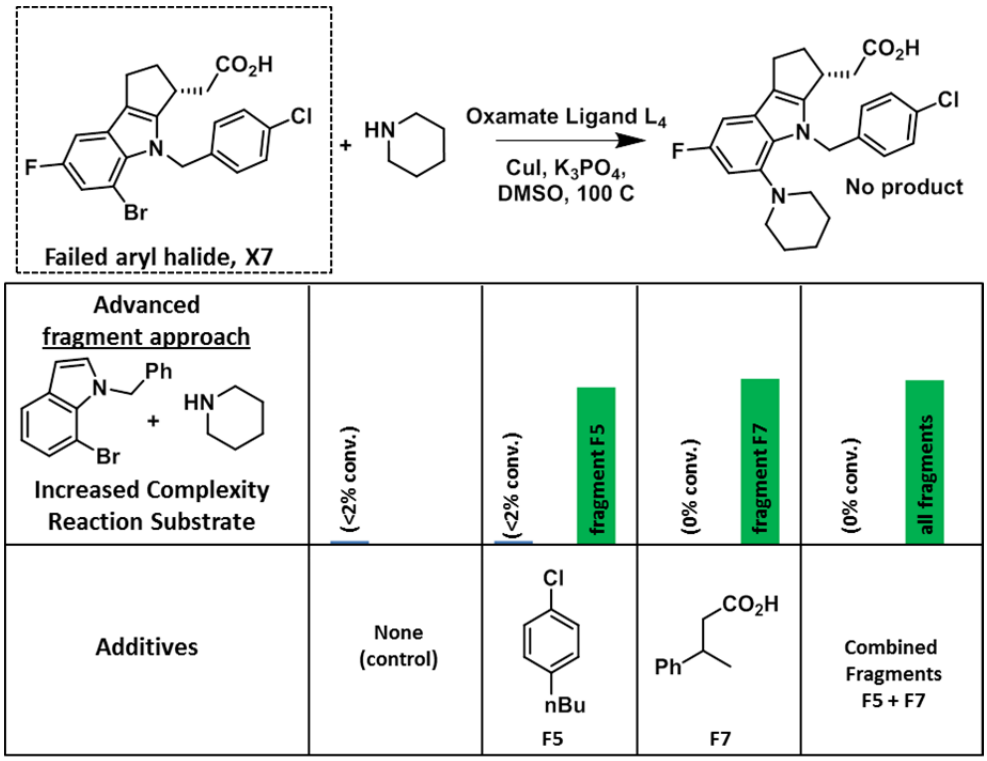
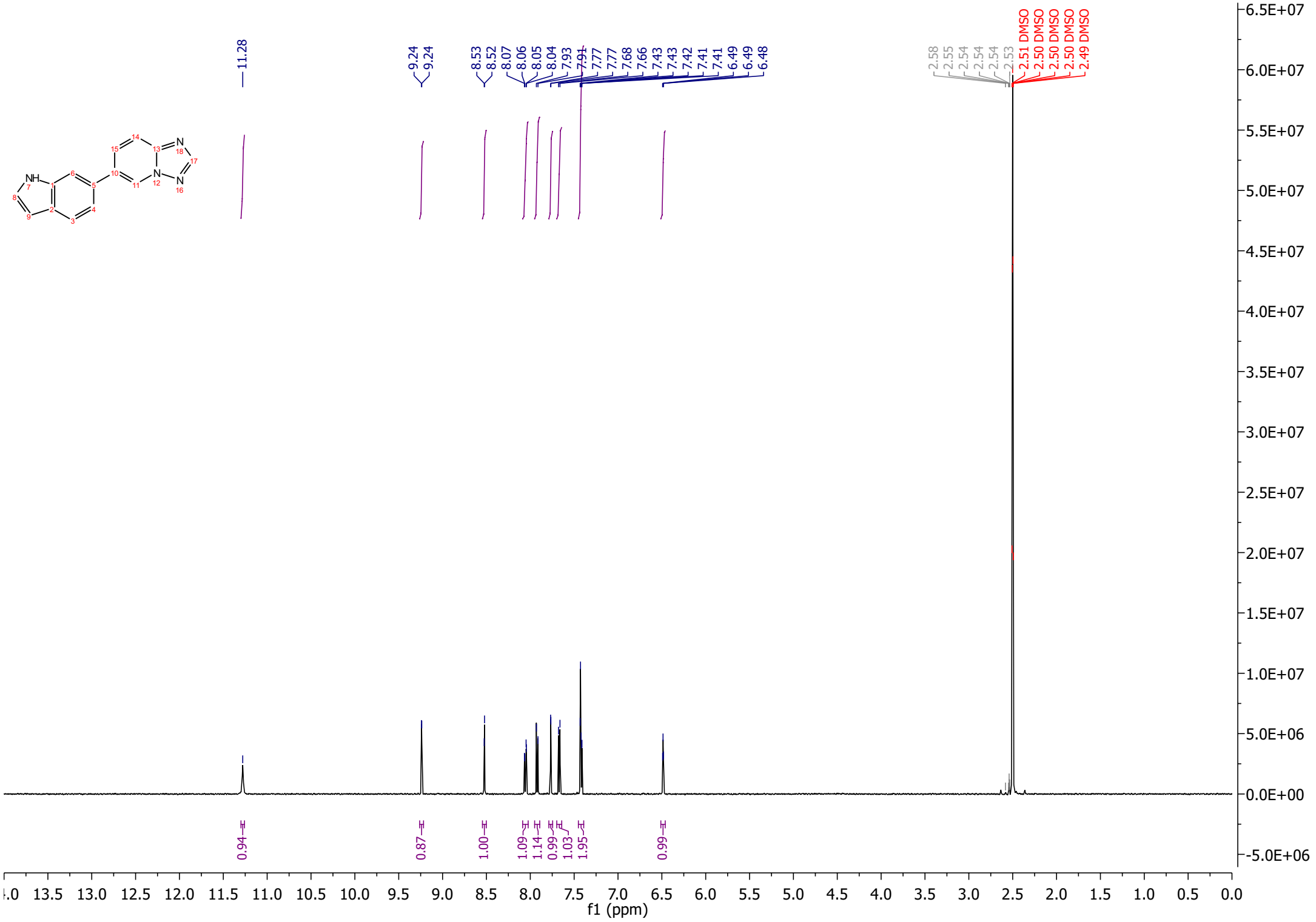


Figure S5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9.24
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8.52
8.07
8.06
8.05
8.04
7.93
7.91
7.77
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7.68
7.66
7.43
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7.41
7.41
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2.55
2.54
2.54
2.54
2.53
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.50 DMSO
2.49 DMSO
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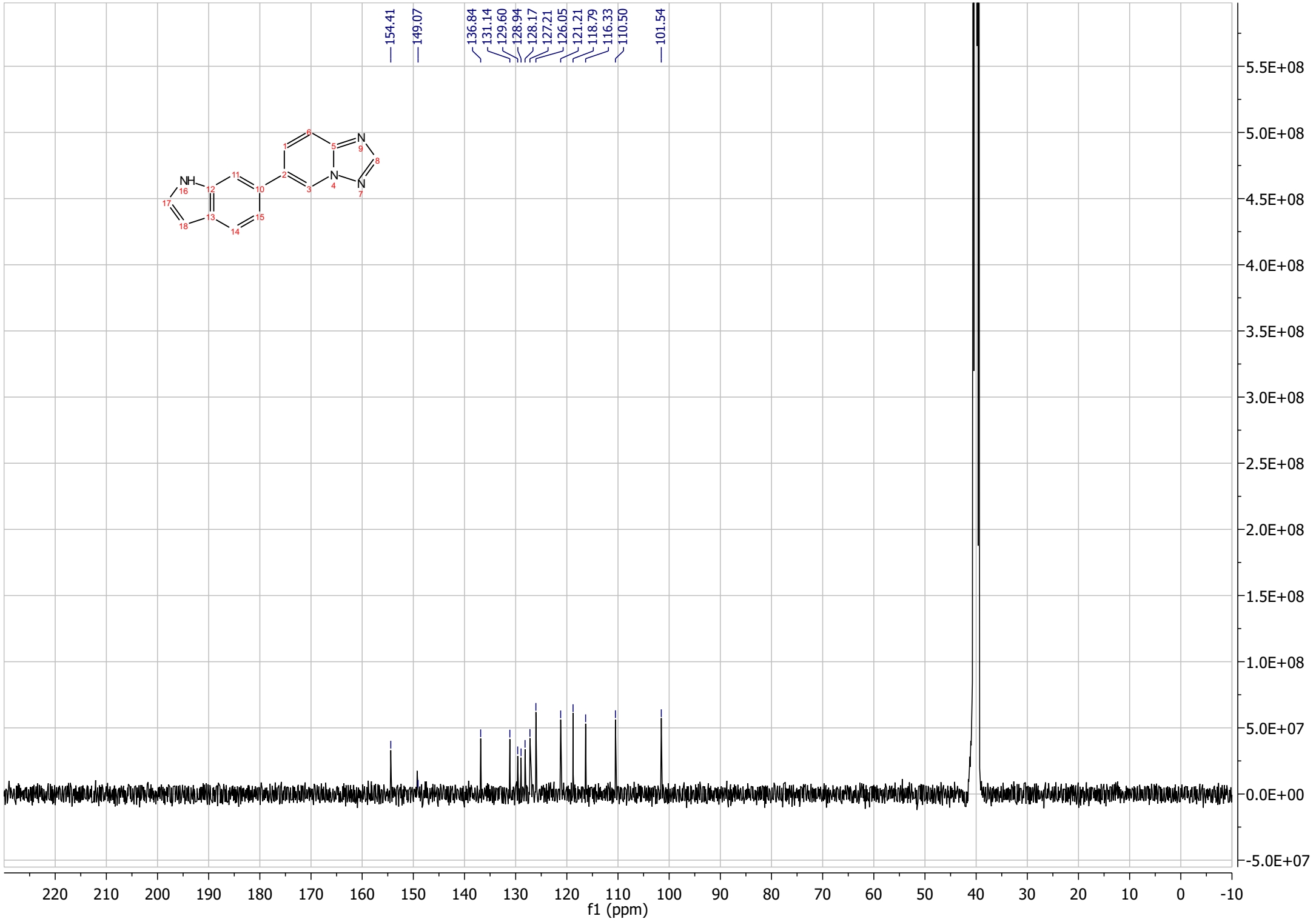
0.87
1.00
1.09
1.14
0.99
1.03
1.95
0.99
f1 (ppm)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3.0E+08
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2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
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220
210
200
190
180
170
160
150
140
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100
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30
20
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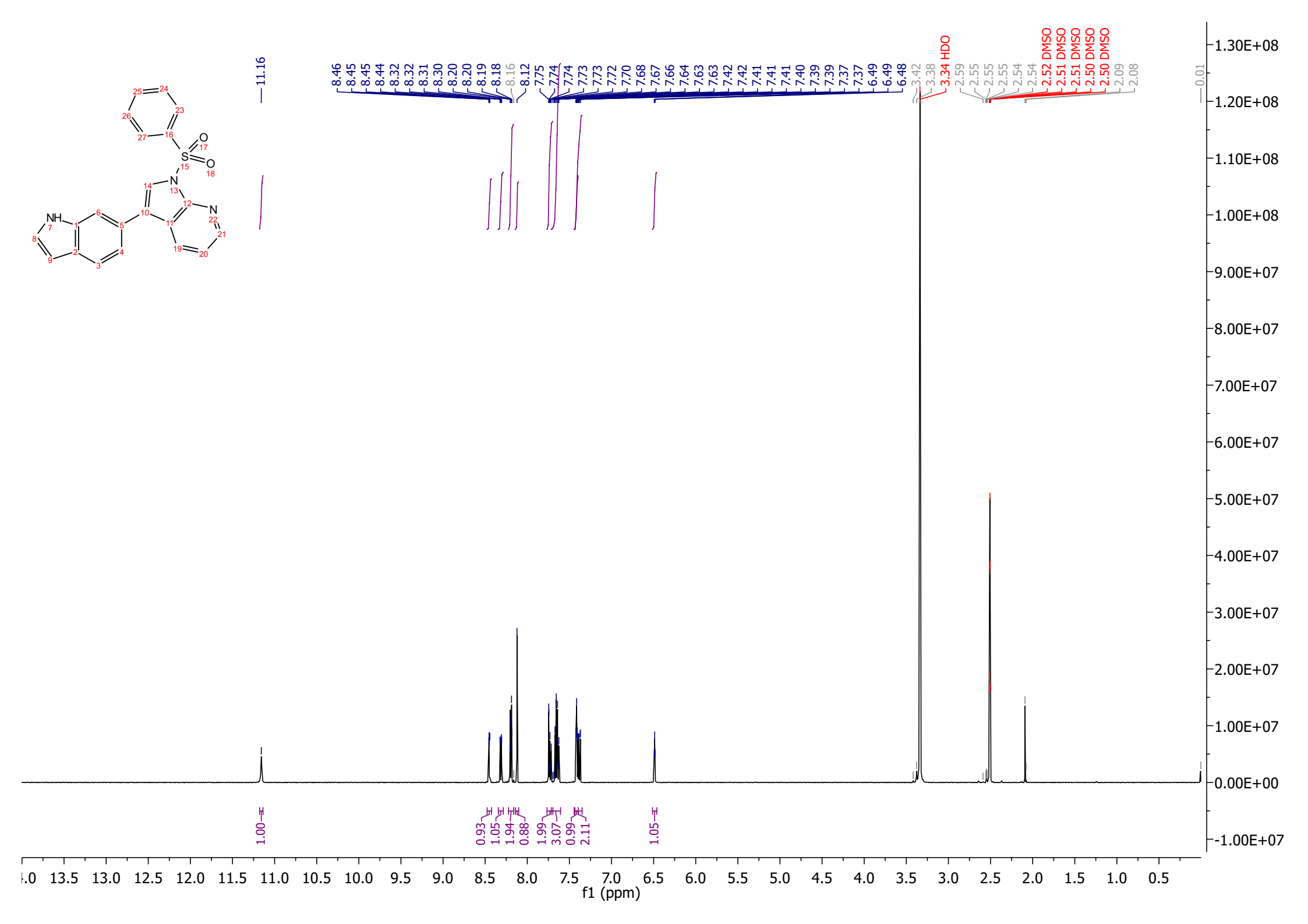
0
-10
f1 (ppm)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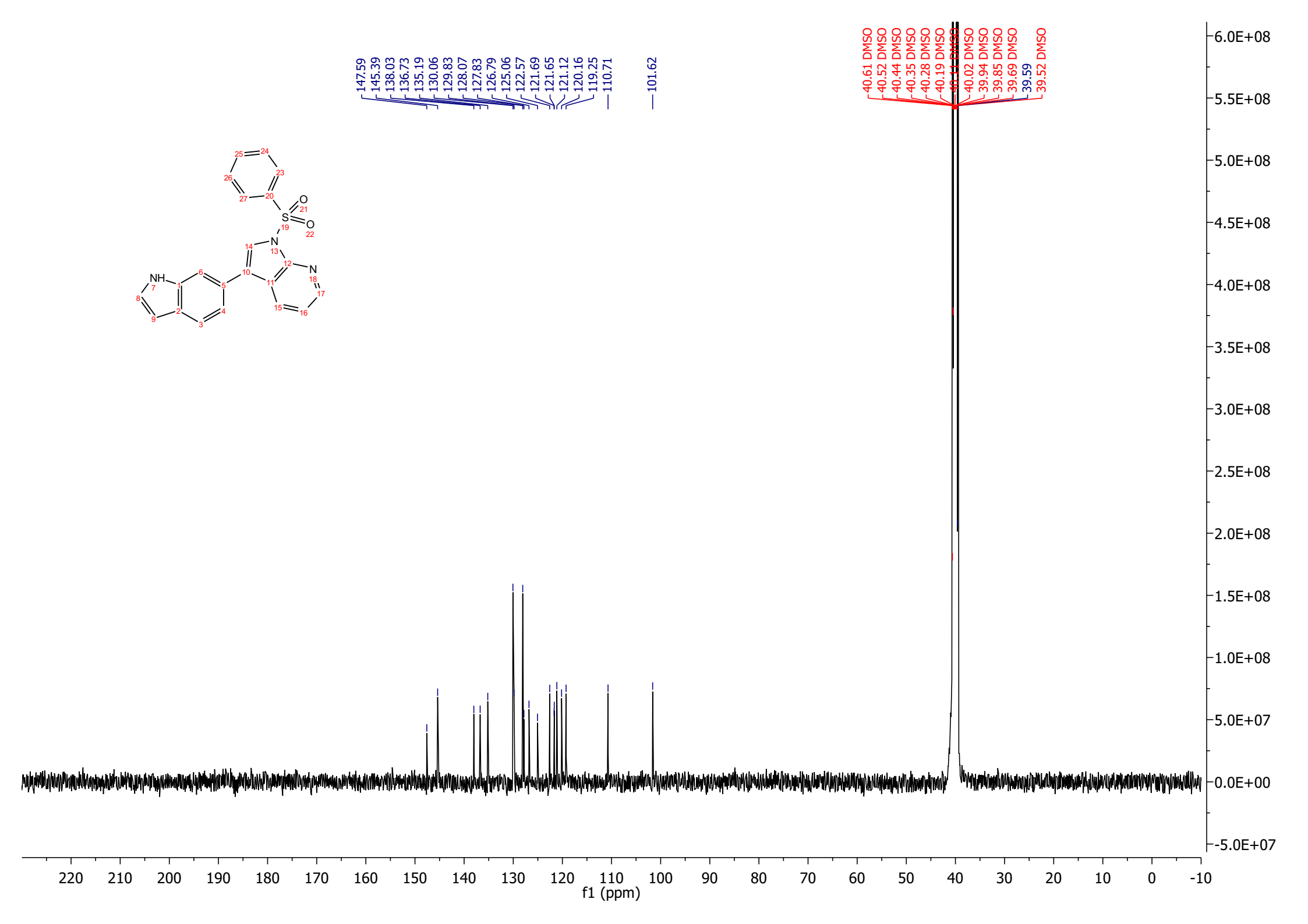
2.55
2.55
2.55
2.54
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.09
2.08
0.01
1.00
0.93
1.05
1.94
0.88
1.99
3.07
0.99
2.11
1.05
f1 (ppm)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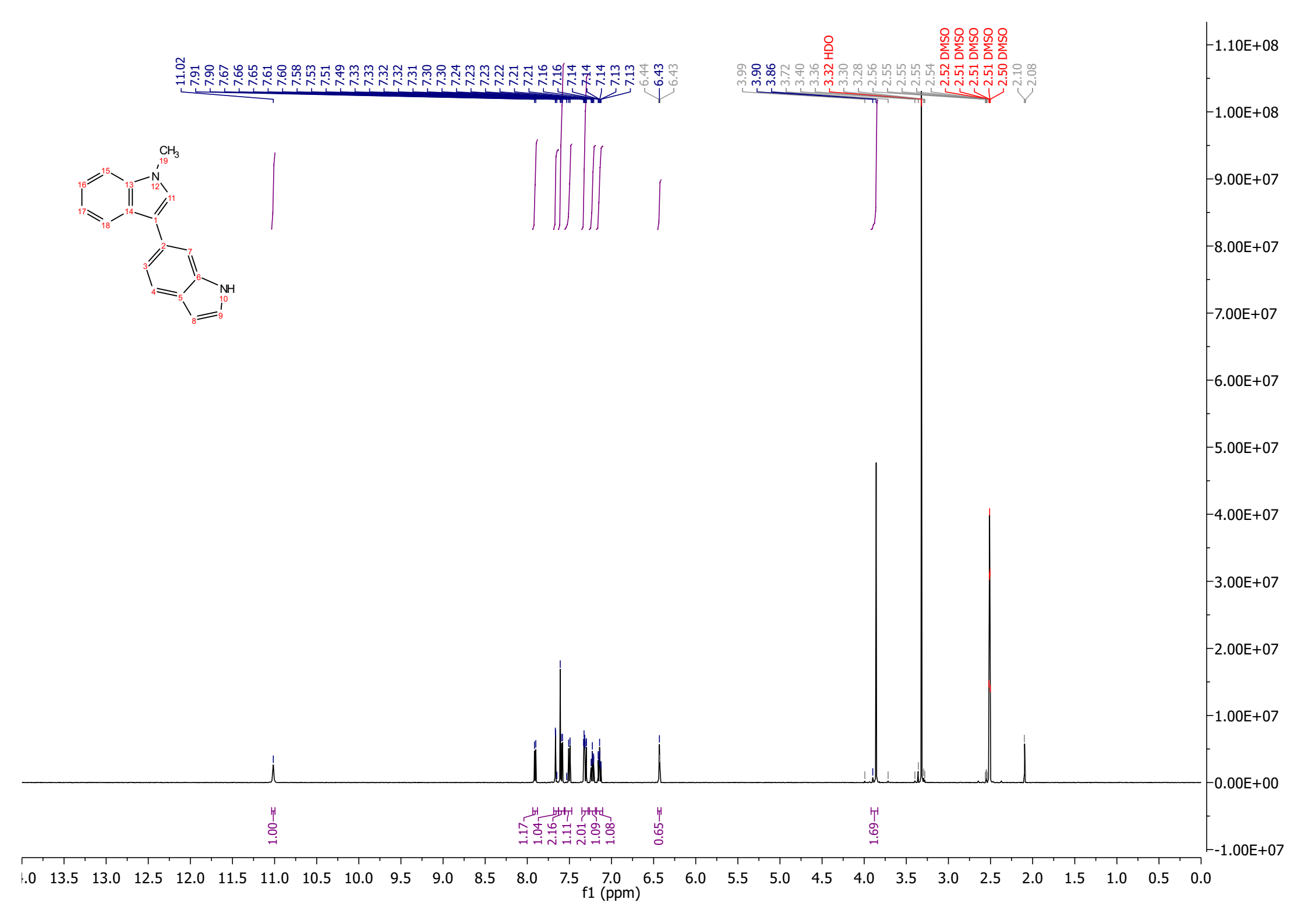
138.03
136.73
135.19
130.06
129.83
128.07
127.83
126.79
125.06
122.57
121.69
121.65
121.12
120.16
119.25
110.71
101.62
40.61 DMSO
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.69 DMSO
39.59
39.52 DMSO
NH
N
N
S
O
O
6.0E+08
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
220
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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7.65
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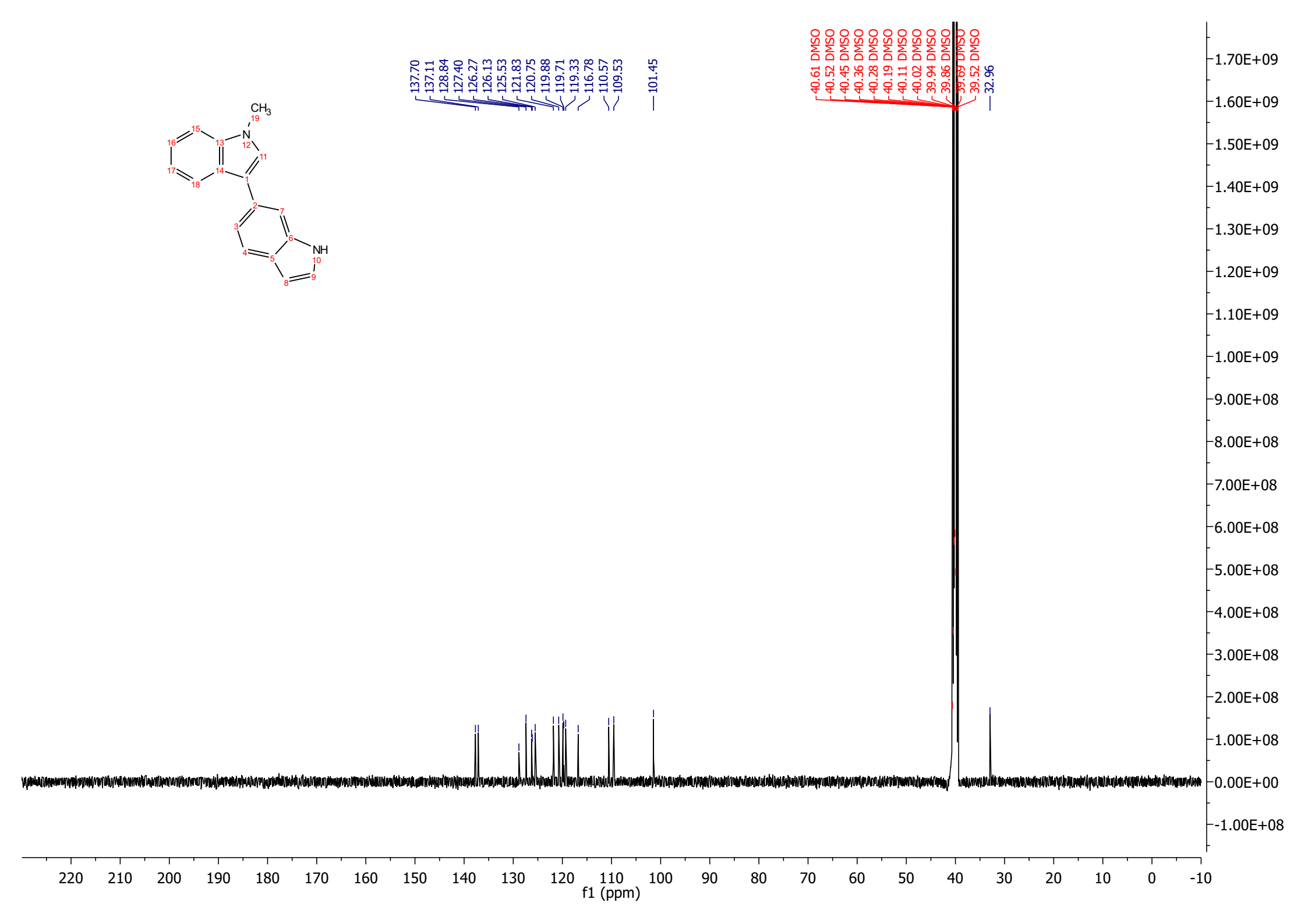
7.60
7.58
7.53
7.51
7.49
7.33
7.33
7.32
7.32
7.31
7.30
7.30
7.24
7.23
7.23
7.22
7.21
7.21
7.16
7.16
7.14
7.14
7.14
7.13
7.13
6.44
6.43
6.43
3.99
3.90
3.86
3.72
3.40
3.36
3.32 HDO
3.30
3.28
2.56
2.55
2.55
2.55
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.10
2.08
CH3
19
N
12
15
16
13
11
17
14
1
18
2
7
3
6
NH
10
4
5
8
9
1.00
1.17
1.04
2.16
1.11
2.01
1.09
1.08
0.65
1.69
1.10E+08
1.00E+08
9.00E+07
8.00E+07
7.00E+07
6.00E+07
5.00E+07
4.00E+07
3.00E+07
2.00E+07
1.00E+07
0.00E+00
-1.00E+07
13.5
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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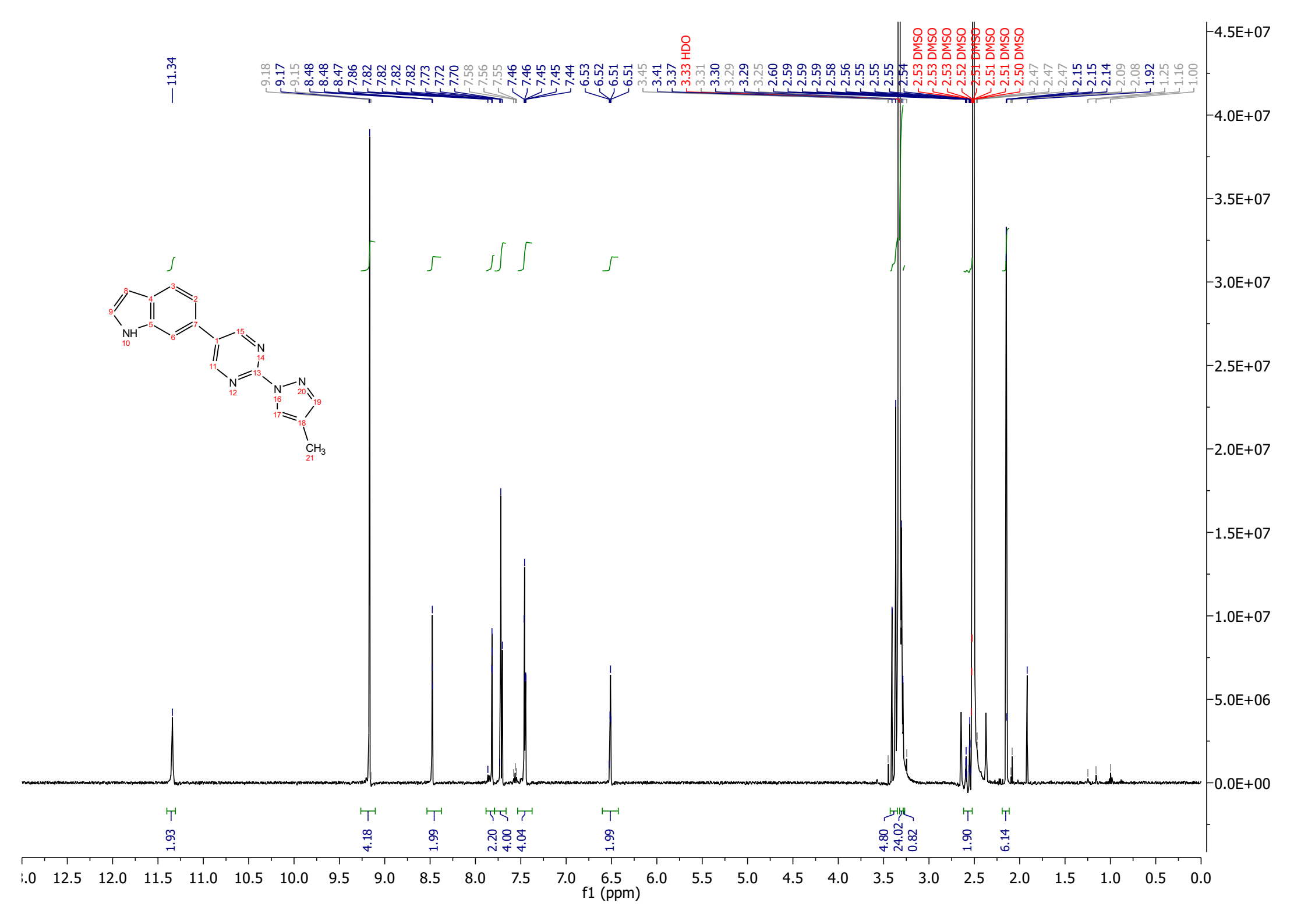
137.11
128.84
127.40
126.27
126.13
125.53
121.83
120.75
119.88
119.71
119.33
116.78
110.57
109.53
101.45
40.61 DMSO
40.52 DMSO
40.45 DMSO
40.36 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.86 DMSO
39.69 DMSO
39.52 DMSO
32.96
CH3
19
N
12
NH
10
1.70E+09
1.60E+09
1.50E+09
1.40E+09
1.30E+09
1.20E+09
1.10E+09
1.00E+09
9.00E+08
8.00E+08
7.00E+08
6.00E+08
5.00E+08
4.00E+08
3.00E+08
2.00E+08
1.00E+08
0.00E+00
-1.00E+08
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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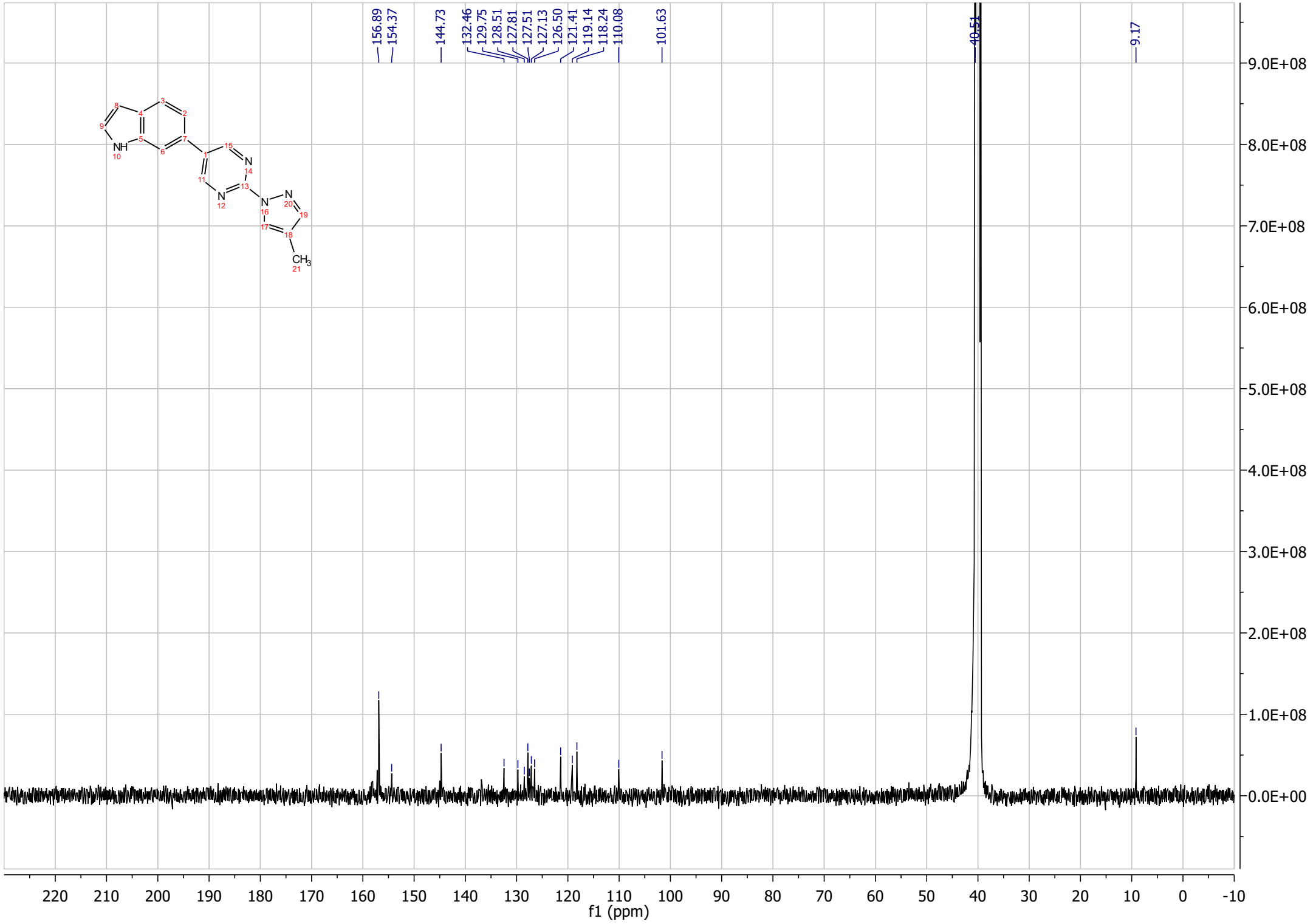
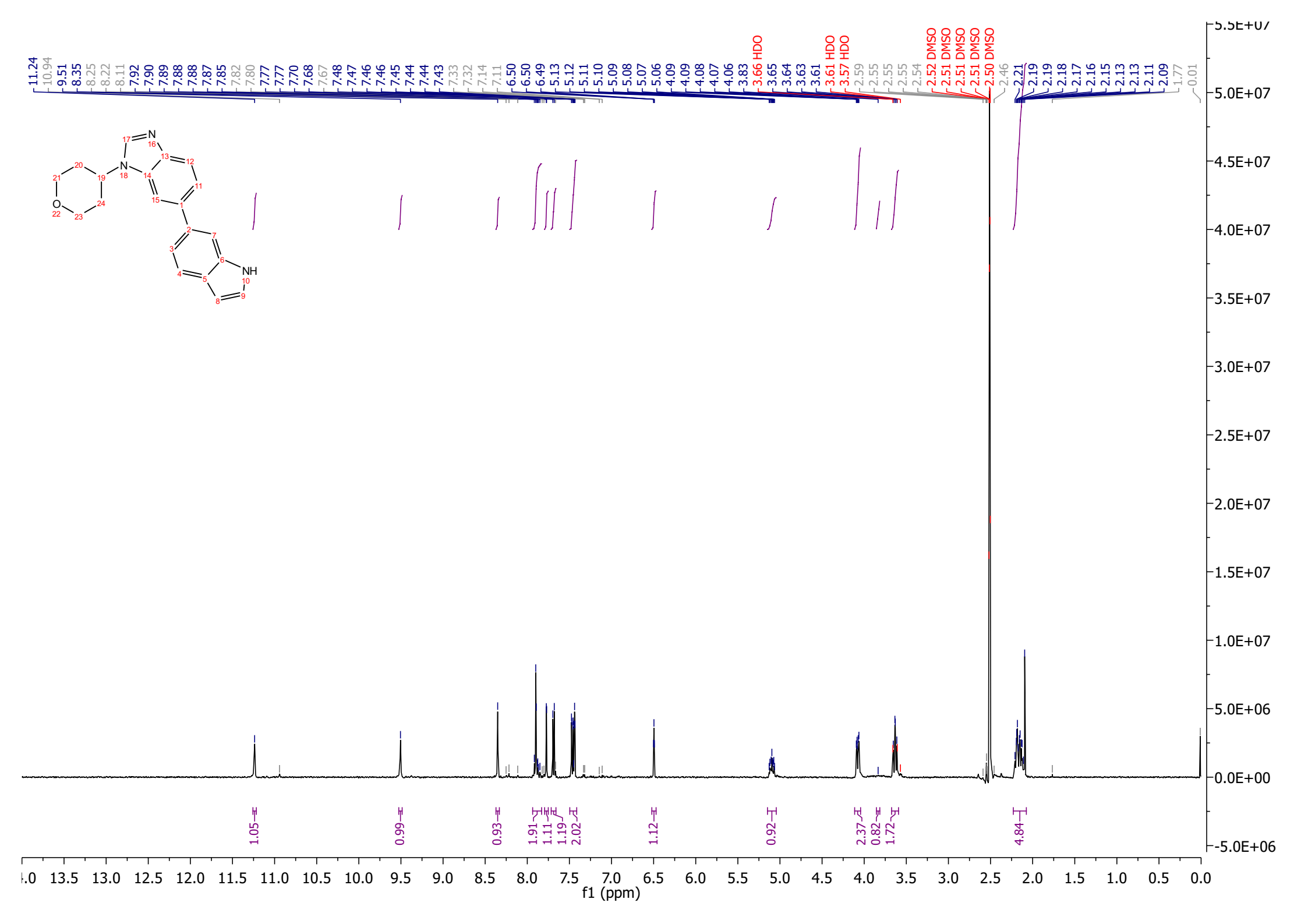
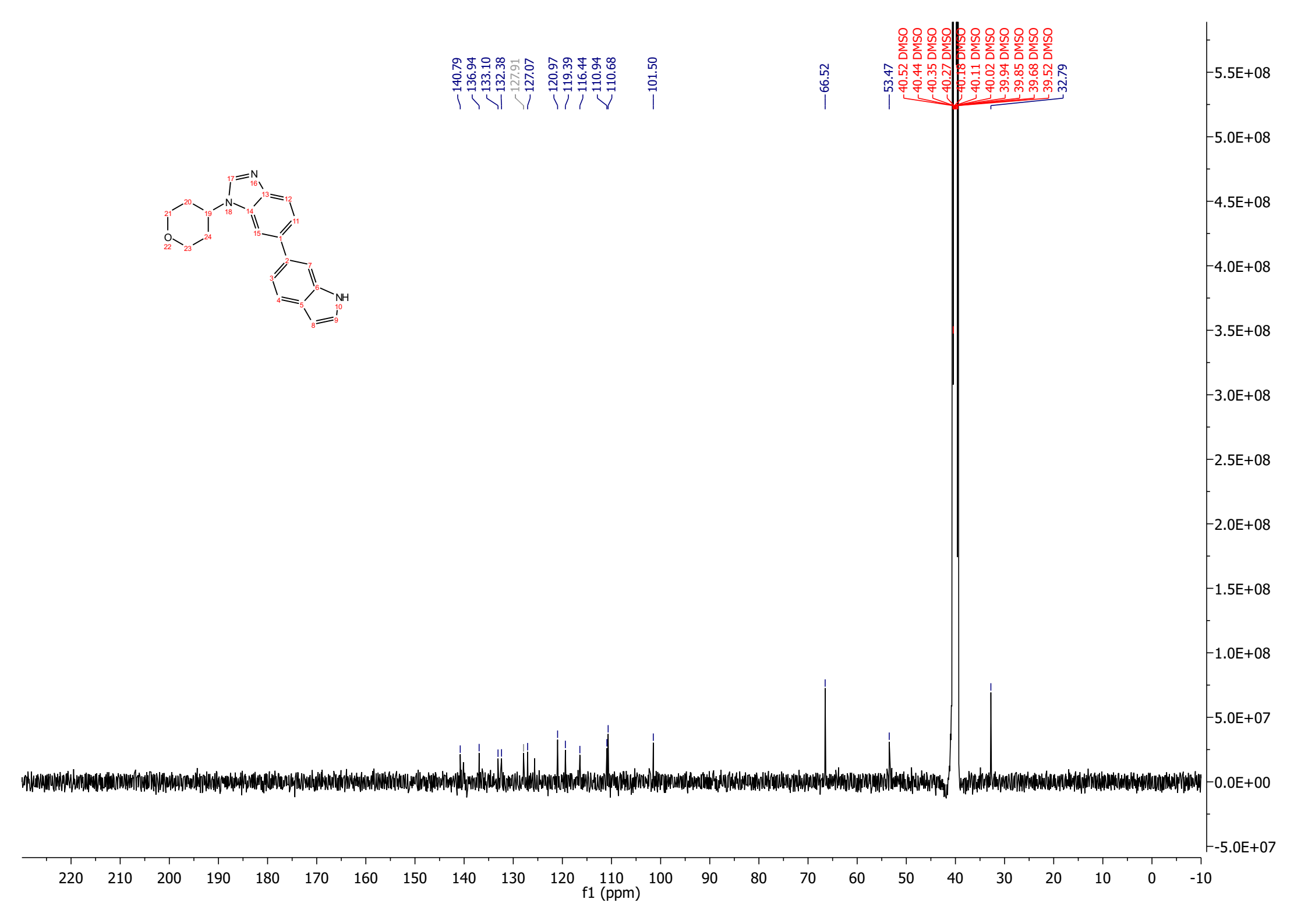
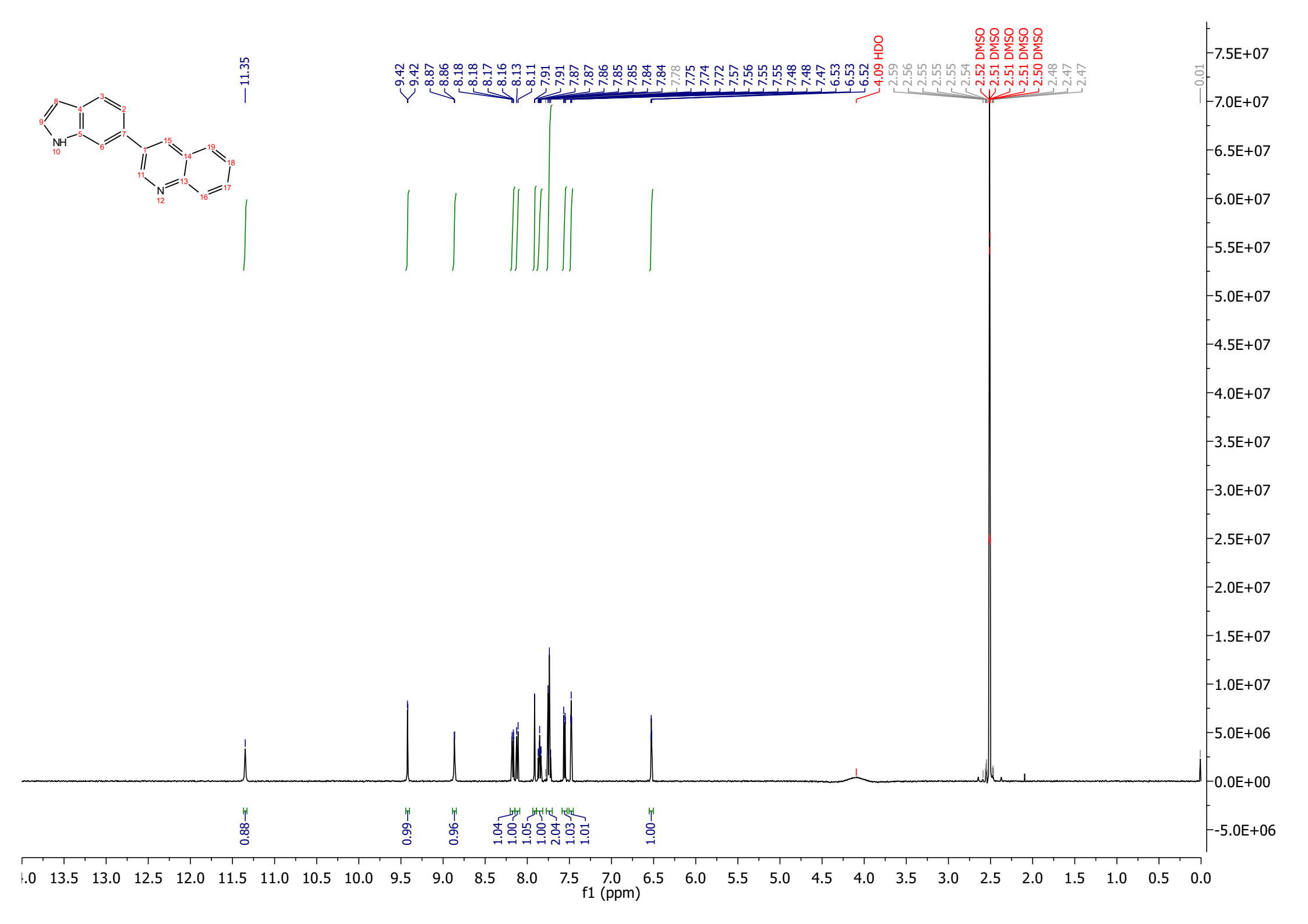
8.48
8.47
7.86
7.82
7.82
7.82
7.73
7.72
7.70
7.58
7.56
7.55
7.46
7.46
7.45
7.45
7.44
6.53
6.52
6.51
6.51
3.45
3.41
3.37
3.33 HDO
3.31
3.30
3.29
3.29
3.25
2.60
2.59
2.59
2.59
2.58
2.56
2.55
2.55
2.55
2.54
2.53 DMSO
2.53 DMSO
2.53 DMSO
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.47
2.47
2.47
2.15
2.15
2.14
2.09
2.08
1.92
1.25
1.16
1.00
NH
N
N
N
N
CH3
1.93
4.18
1.99
2.20
4.00
4.04
1.99
4.80
24.02
0.82
1.90
6.14
f1 (ppm)


156.89
154.37
144.73
132.46
129.75
128.51
127.81
127.51
127.13
126.50
121.41
119.14
118.24
110.08
101.63
40.51
9.17
NH
N
CH3
9.0E+08
8.0E+08
7.0E+08
6.0E+08
5.0E+08
4.0E+08
3.0E+08
2.0E+08
1.0E+08
0.0E+00
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


11.24
10.94
9.51
8.35
8.25
8.22
8.11
7.92
7.90
7.89
7.88
7.88
7.87
7.85
7.82
7.80
7.77
7.77
7.70
7.68
7.67
7.48
7.47
7.46
7.46
7.45
7.44
7.44
7.43
7.33
7.32
7.14
7.11
6.50
6.50
6.49
5.13
5.12
5.11
5.10
5.09
5.08
5.07
5.06
4.09
4.09
4.08
4.07
4.06
3.83
3.66 HDO
3.65
3.64
3.63
3.61
3.61 HDO
3.57 HDO
2.59
2.55
2.55
2.55
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.46
2.21
2.19
2.19
2.18
2.17
2.16
2.15
2.13
2.13
2.11
2.09
1.77
0.01
1.05
0.99
0.93
1.91
1.11
1.19
2.02
1.12
0.92
2.37
0.82
1.72
4.84
f1 (ppm)


140.79
136.94
133.10
132.38
127.91
127.07
120.97
119.39
116.44
110.94
110.68
101.50
66.52
53.47
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.27 DMSO
40.18 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.68 DMSO
39.52 DMSO
32.79
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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9.42
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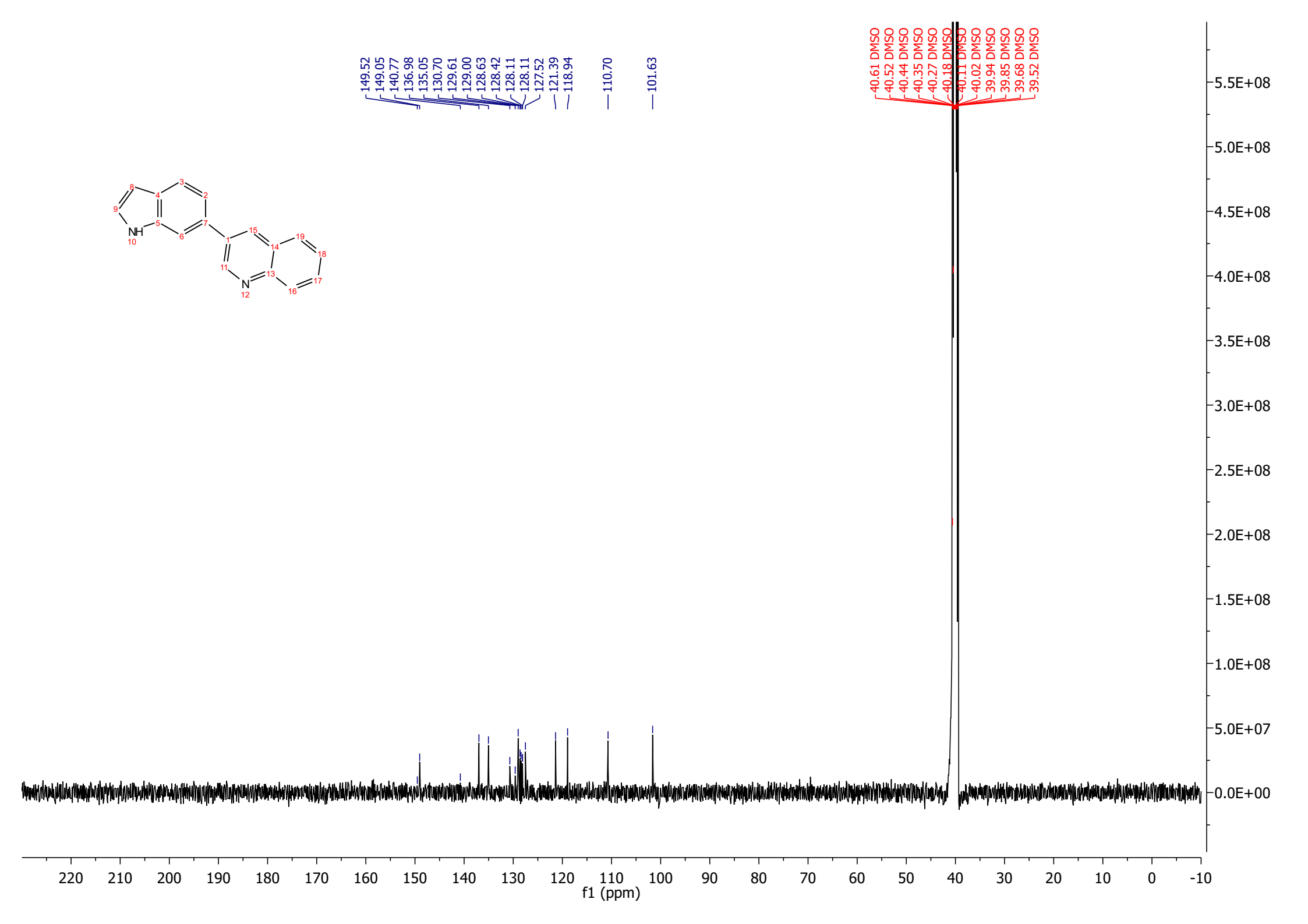
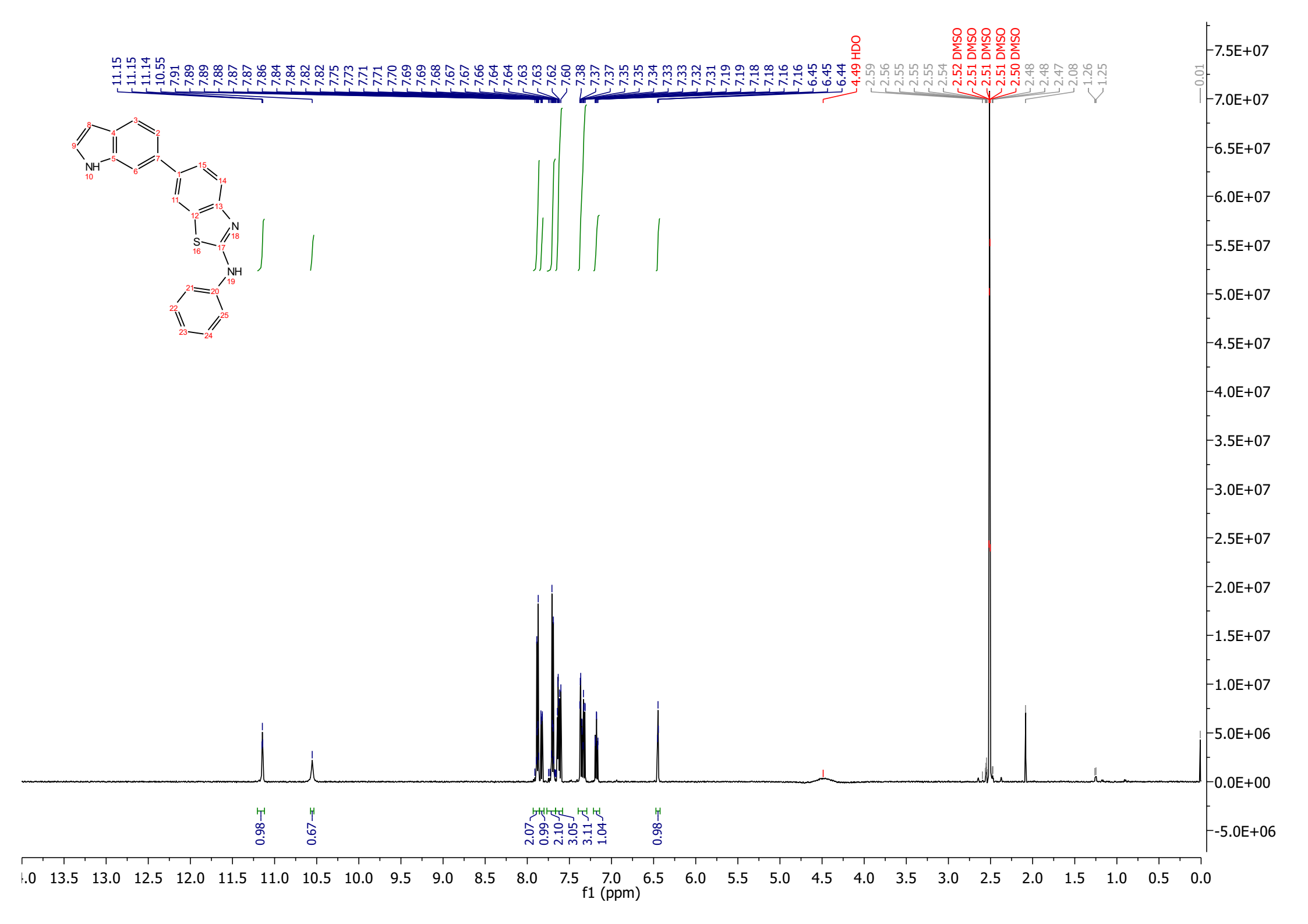
8.86
8.18
8.18
8.17
8.16
8.13
8.11
7.91
7.91
7.87
7.87
7.86
7.85
7.85
7.84
7.84
7.78
7.75
7.74
7.72
7.57
7.56
7.55
7.55
7.48
7.48
7.47
6.53
6.52
4.09 HDO
2.59
2.56
2.55
2.55
2.55
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.48
2.47
2.47
0.01
NH
10
N
12
0.88
0.99
0.96
1.04
1.00
1.05
1.00
2.04
1.03
1.01
1.00
f1 (ppm)


149.52
149.05
140.77
136.98
135.05
130.70
129.61
129.00
128.63
128.42
128.11
128.11
127.52
121.39
118.94
110.70
101.63
40.61 DMSO
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.27 DMSO
40.18 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.68 DMSO
39.52 DMSO
NH
N
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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11.15
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7.89
7.89
7.88
7.87
7.87
7.86
7.84
7.84
7.82
7.82
7.75
7.73
7.71
7.71
7.70
7.69
7.69
7.68
7.67
7.67
7.66
7.64
7.64
7.63
7.63
7.62
7.60
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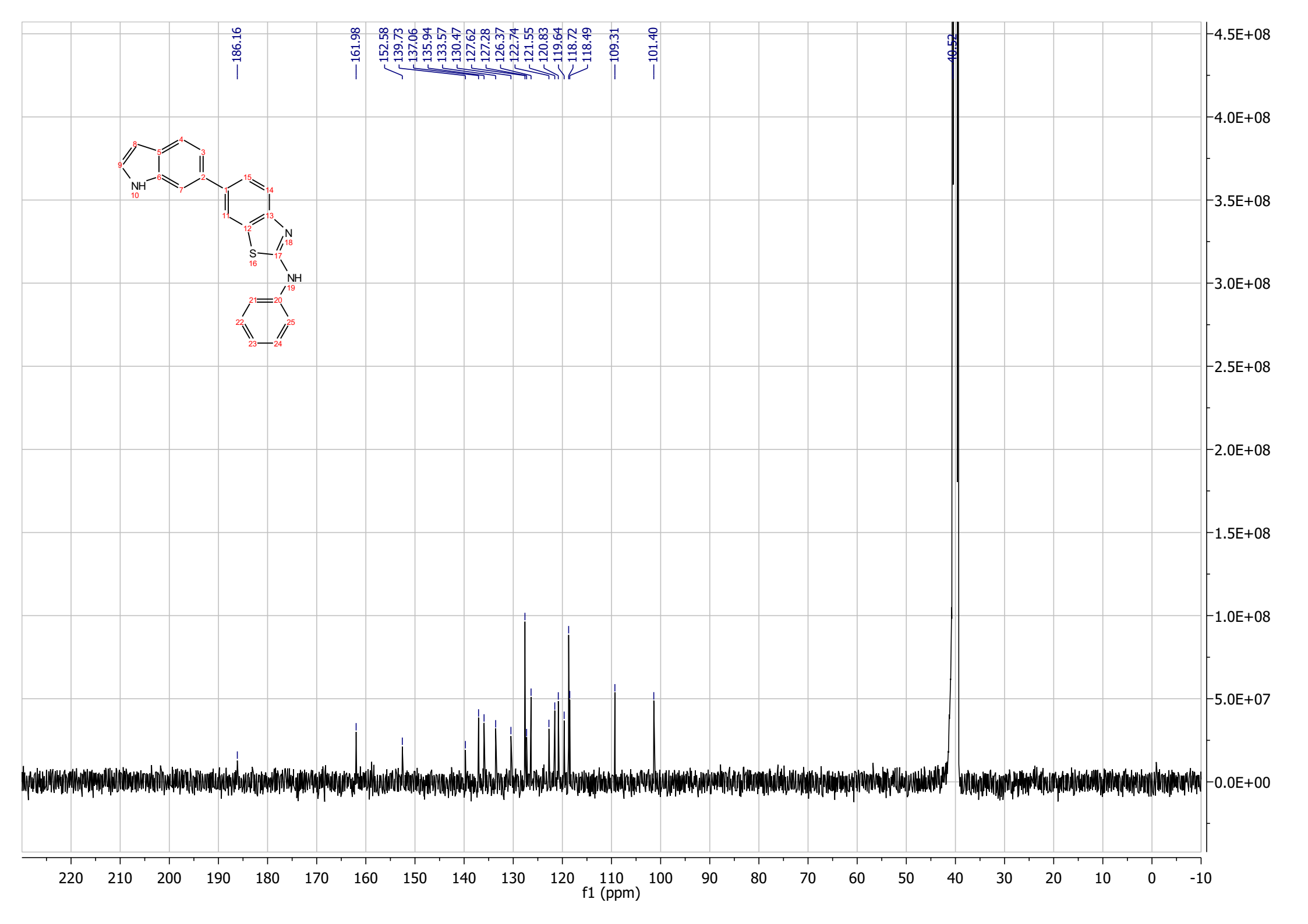
7.37
7.37
7.35
7.35
7.34
7.33
7.33
7.32
7.31
7.19
7.19
7.18
7.18
7.16
7.16
6.45
6.45
6.44
4.49 HDO
2.59
2.56
2.55
2.55
2.55
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.48
2.48
2.47
2.08
1.26
1.25
0.01
NH
10
N
18
S
16
NH
19
0.98
0.67
2.07
0.99
2.10
3.05
3.11
1.04
0.98
7.5E+07
7.0E+07
6.5E+07
6.0E+07
5.5E+07
5.0E+07
4.5E+07
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
-5.0E+06
13.5
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


186.16
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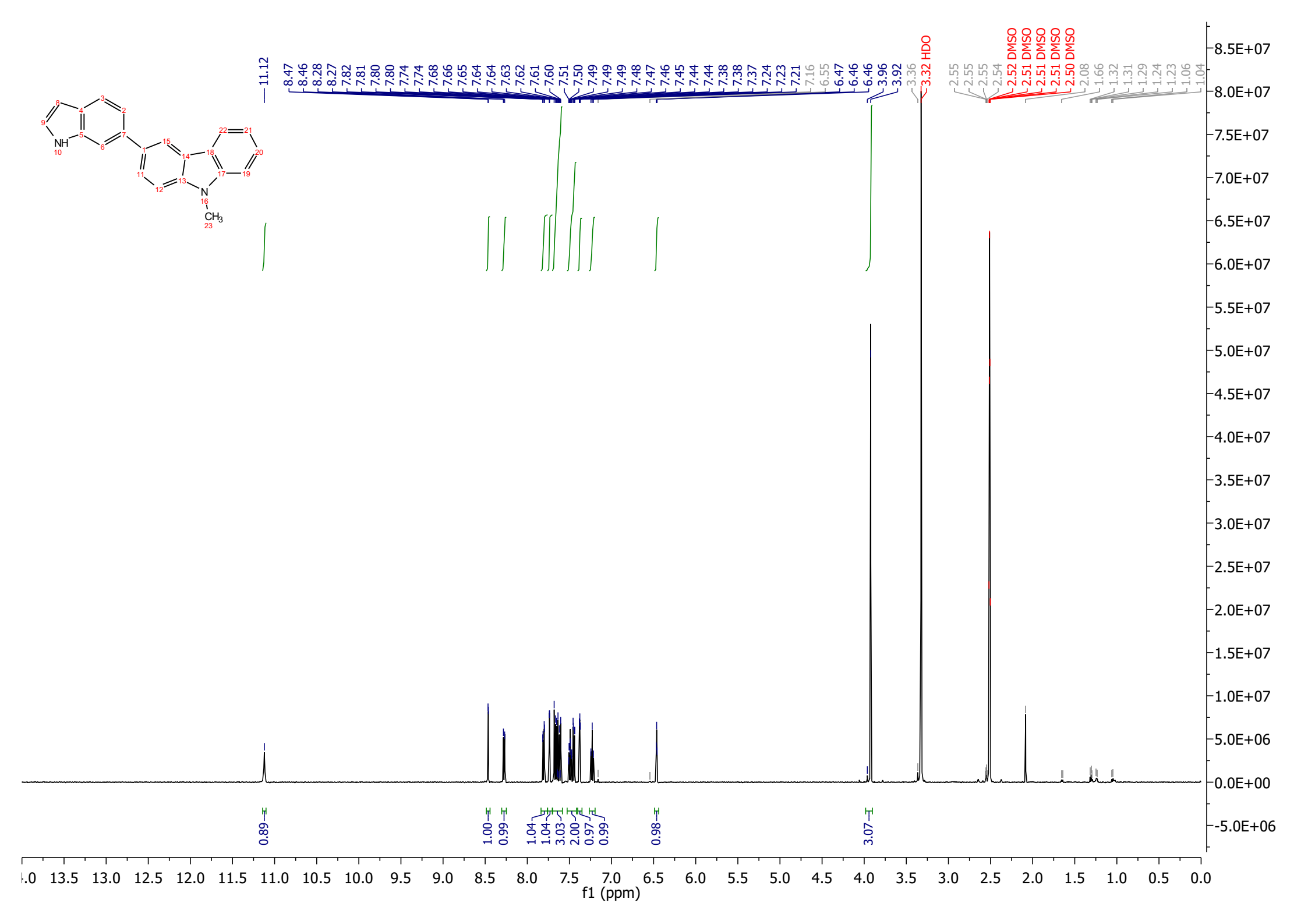
137.06
135.94
133.57
130.47
127.62
127.28
126.37
122.74
121.55
120.83
119.64
118.72
118.49
109.31
101.40
40.52
NH
10
N
18
S
16
17
NH
19
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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8.46
8.28
8.27
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7.81
7.80
7.80
7.74
7.74
7.68
7.66
7.65
7.64
7.64
7.63
7.62
7.61
7.60
7.51
7.50
7.49
7.49
7.48
7.47
7.46
7.45
7.44
7.44
7.38
7.38
7.37
7.24
7.23
7.21
7.16
6.55
6.47
6.46
6.46
3.96
3.92
3.36
3.32 HDO
2.55
2.55
2.55
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.08
1.66
1.32
1.31
1.29
1.24
1.23
1.06
1.04
NH
10
N
16
CH3
23
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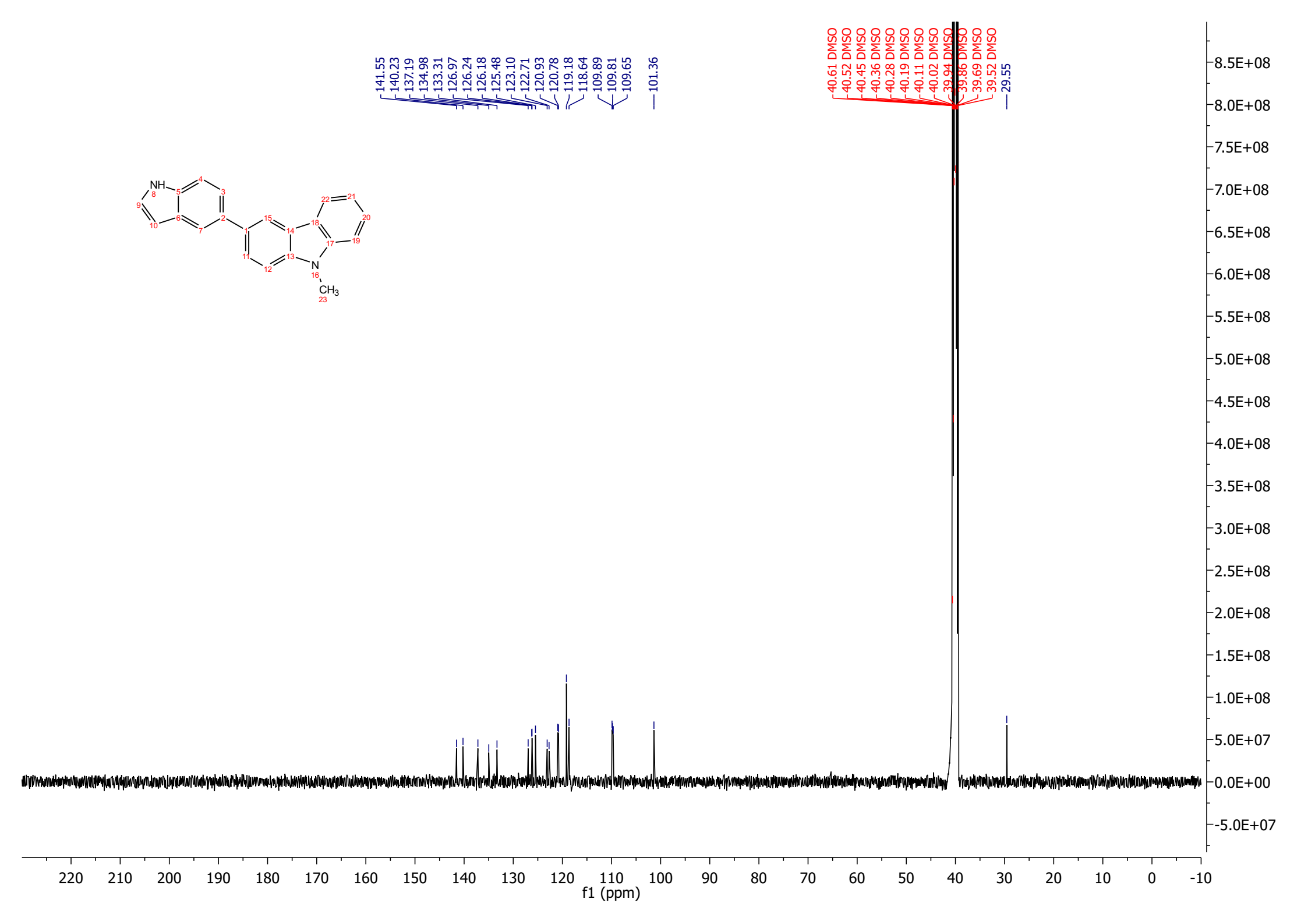
1.04
1.04
3.03
2.00
0.97
0.99
0.98
3.07
f1 (ppm)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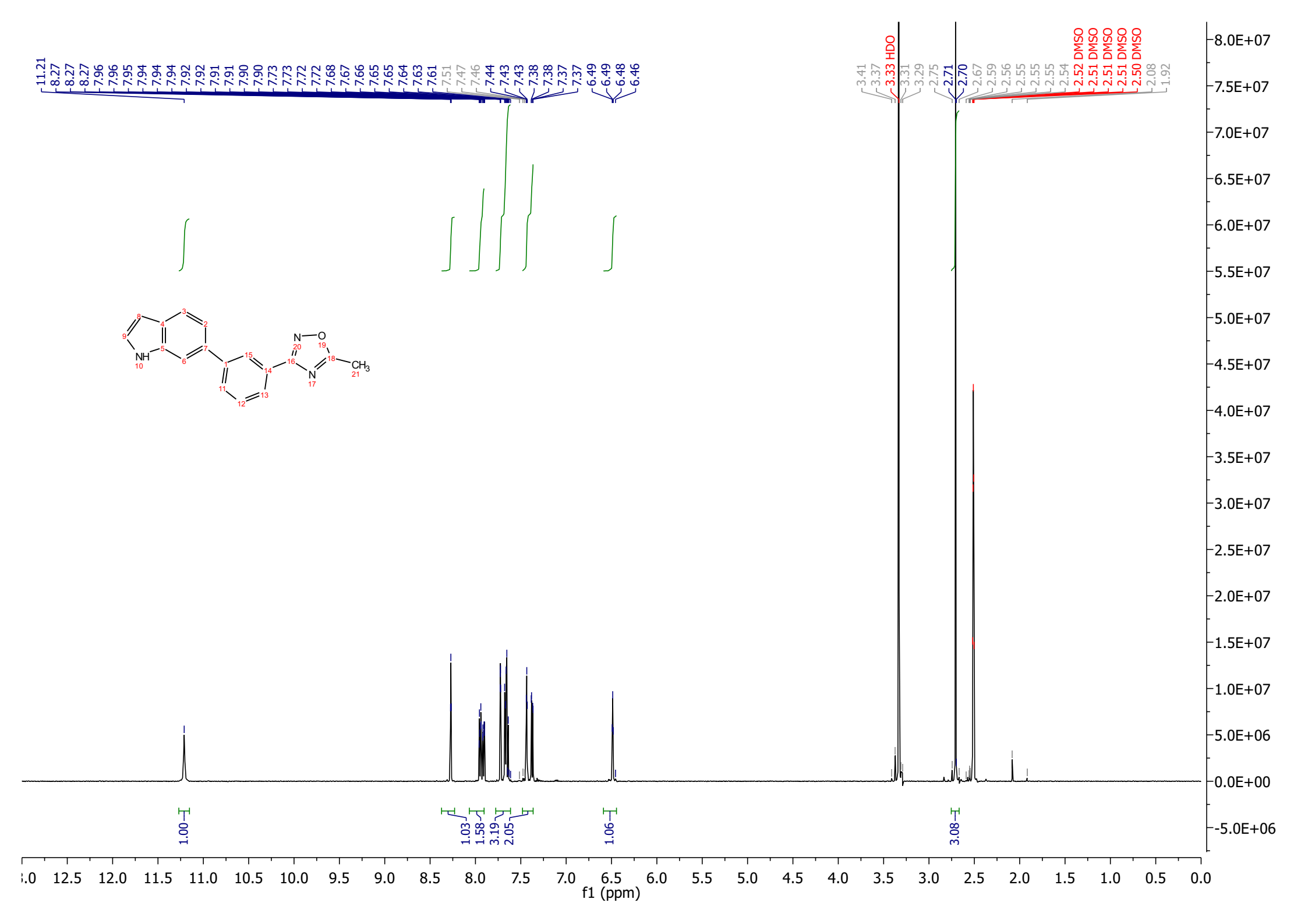
126.97
126.24
126.18
125.48
123.10
122.71
120.93
120.78
119.18
118.64
109.89
109.81
109.65
101.36
40.61 DMSO
40.52 DMSO
40.45 DMSO
40.36 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.86 DMSO
39.69 DMSO
39.52 DMSO
29.55
NH
N
CH3
8.5E+08
8.0E+08
7.5E+08
7.0E+08
6.5E+08
6.0E+08
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


11.21
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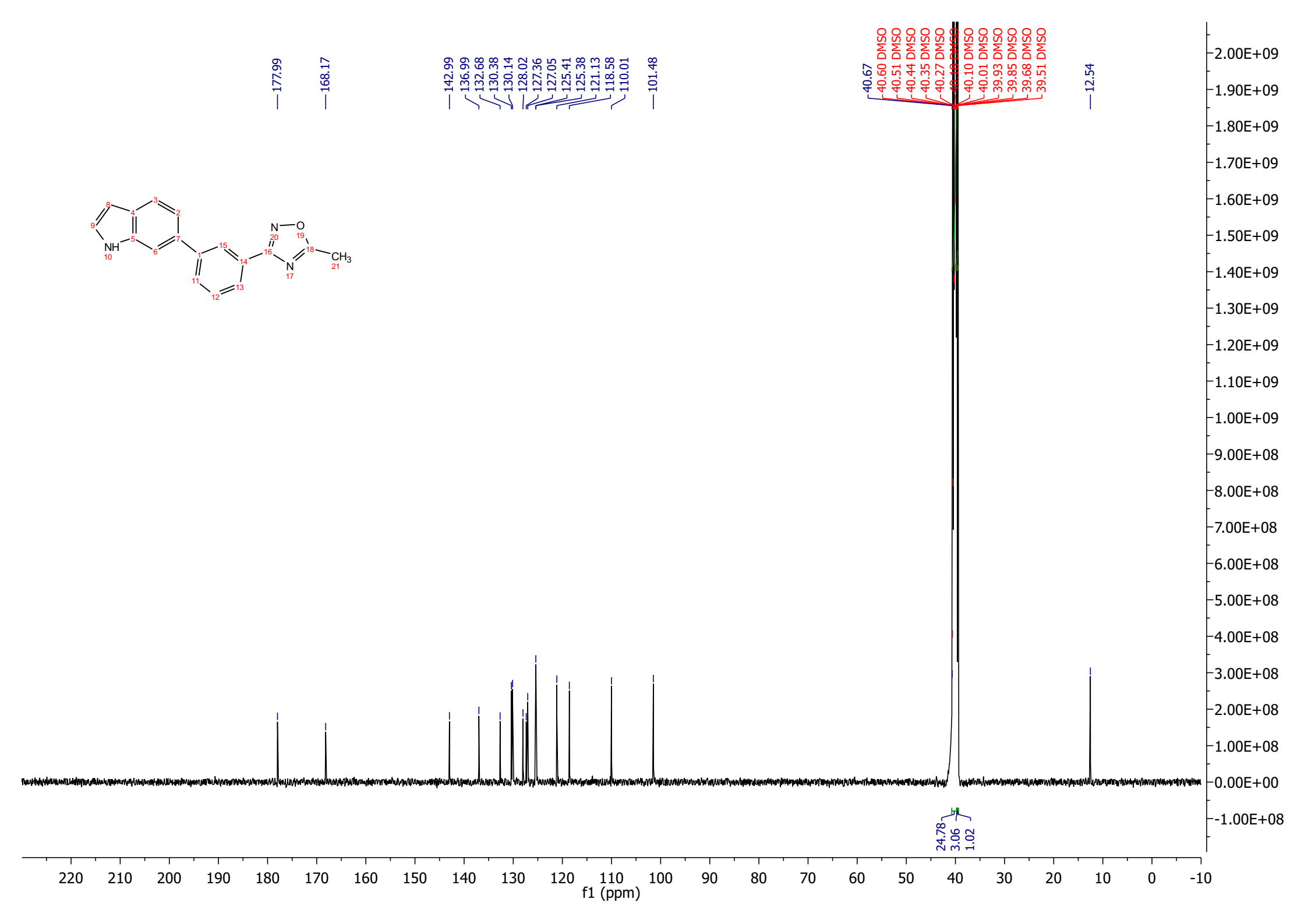
8.27
7.96
7.96
7.95
7.94
7.94
7.94
7.92
7.92
7.91
7.91
7.90
7.90
7.73
7.73
7.72
7.72
7.68
7.67
7.66
7.65
7.65
7.64
7.63
7.61
7.51
7.47
7.46
7.44
7.43
7.43
7.38
7.38
7.37
7.37
6.49
6.49
6.48
6.46
3.41
3.37
3.33 HDO
3.31
3.29
2.75
2.71
2.70
2.67
2.59
2.56
2.55
2.55
2.55
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.08
1.92
NH
N
O
CH3
1.00
1.03
1.58
3.19
2.05
1.06
3.08
f1 (ppm)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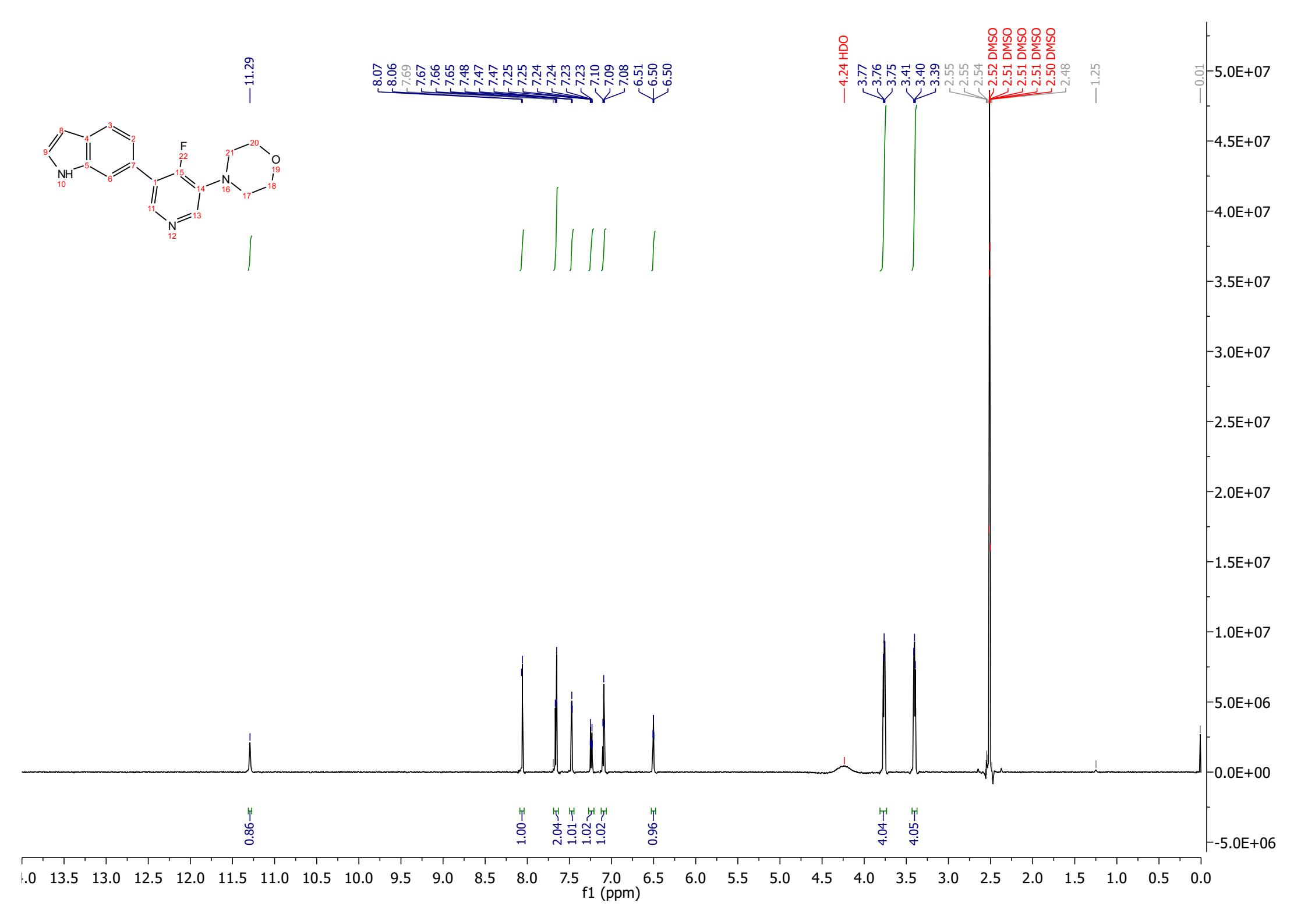
130.14
128.02
127.36
127.05
125.41
125.38
121.13
118.58
110.01
101.48
40.67
40.60 DMSO
40.51 DMSO
40.44 DMSO
40.35 DMSO
40.27 DMSO
40.10 DMSO
40.01 DMSO
39.93 DMSO
39.85 DMSO
39.68 DMSO
39.51 DMSO
12.54
24.78
3.06
1.02
f1 (ppm)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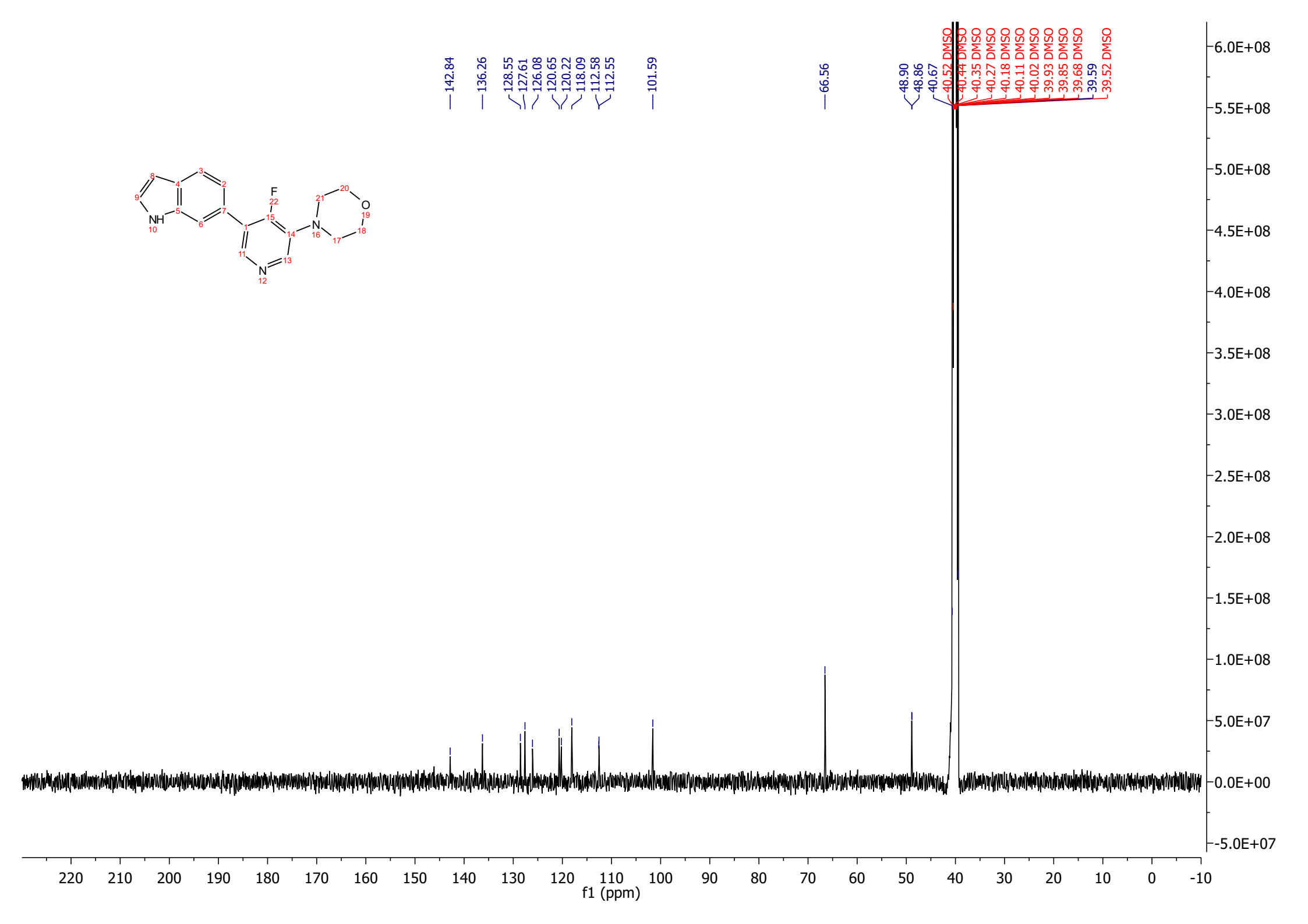
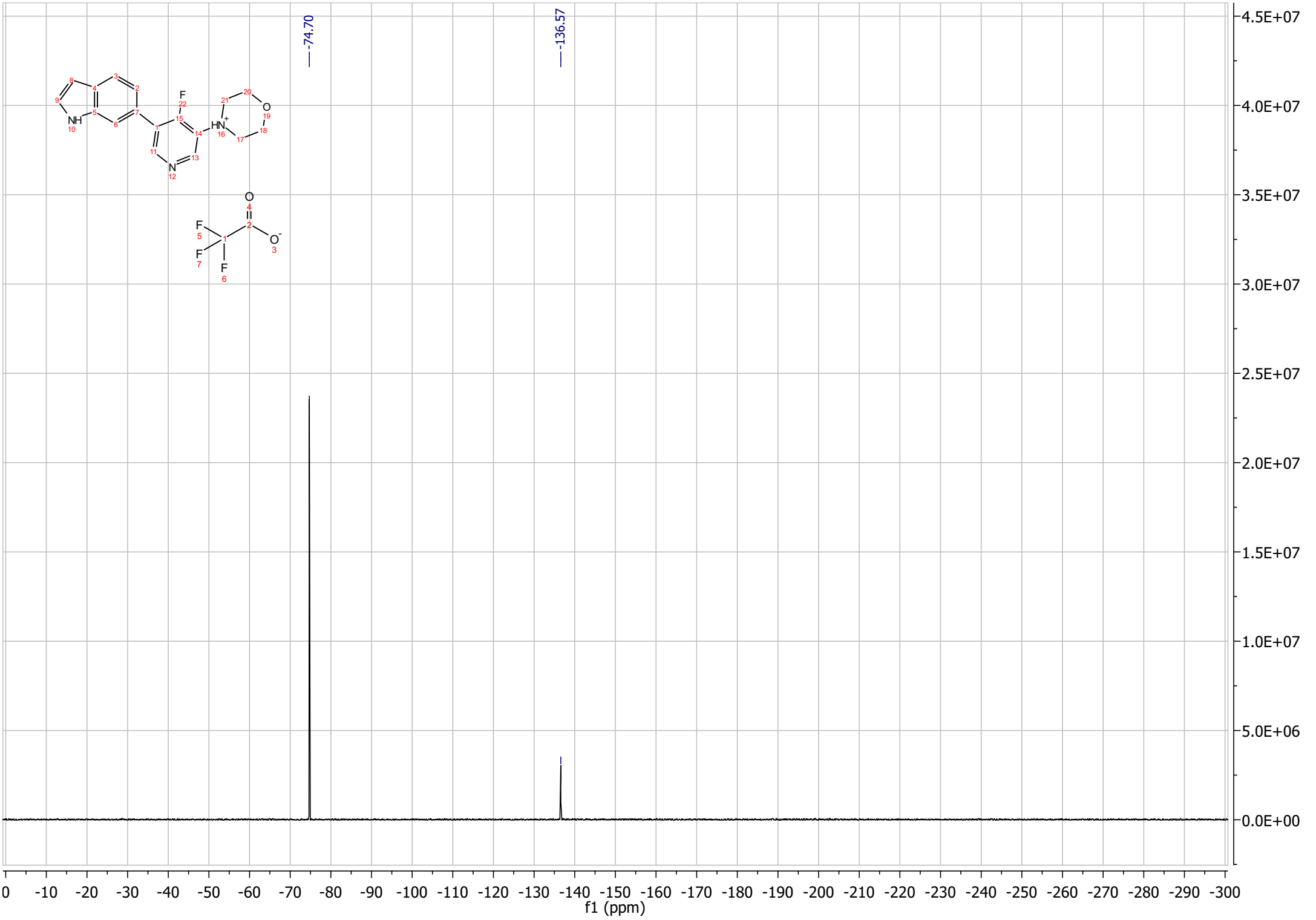
8.07
8.06
7.69
7.67
7.66
7.65
7.48
7.47
7.47
7.25
7.25
7.24
7.24
7.23
7.23
7.10
7.09
7.08
6.51
6.50
6.50
4.24 HDO
3.77
3.76
3.75
3.41
3.40
3.39
2.55
2.55
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.48
1.25
0.01
0.86
1.00
2.04
1.01
1.02
1.02
0.96
4.04
4.05
f1 (ppm)


142.84
136.26
128.55
127.61
126.08
120.65
120.22
118.09
112.58
112.55
101.59
66.56
48.90
48.86
40.67
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.27 DMSO
40.18 DMSO
40.11 DMSO
40.02 DMSO
39.93 DMSO
39.85 DMSO
39.68 DMSO
39.59
39.52 DMSO
F
NH
N
O
6.0E+08
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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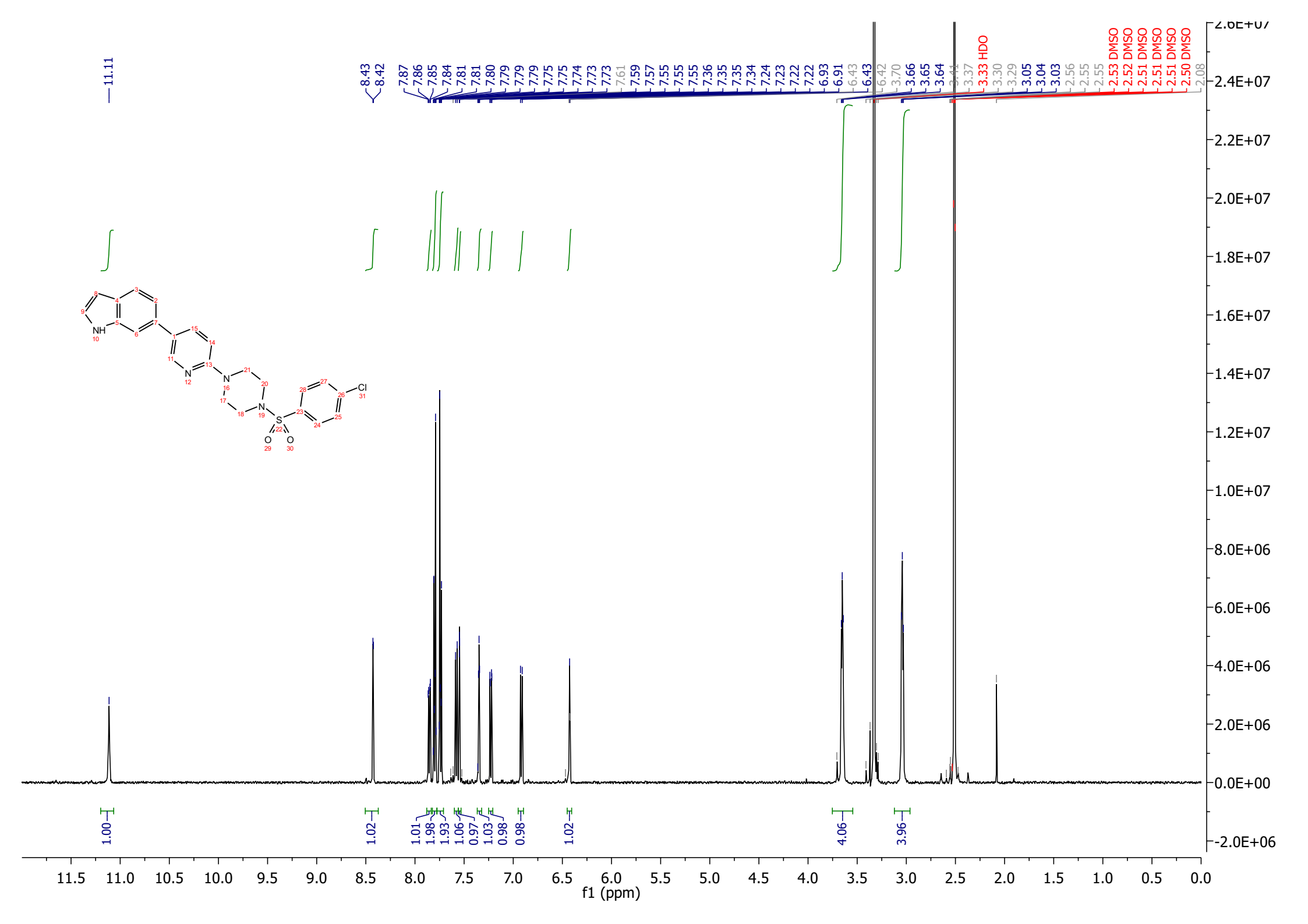
-136.57
4.5E+07
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -250 -260 -270 -280 -290 -300
f1 (ppm)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8.43
8.42
7.87
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7.84
7.81
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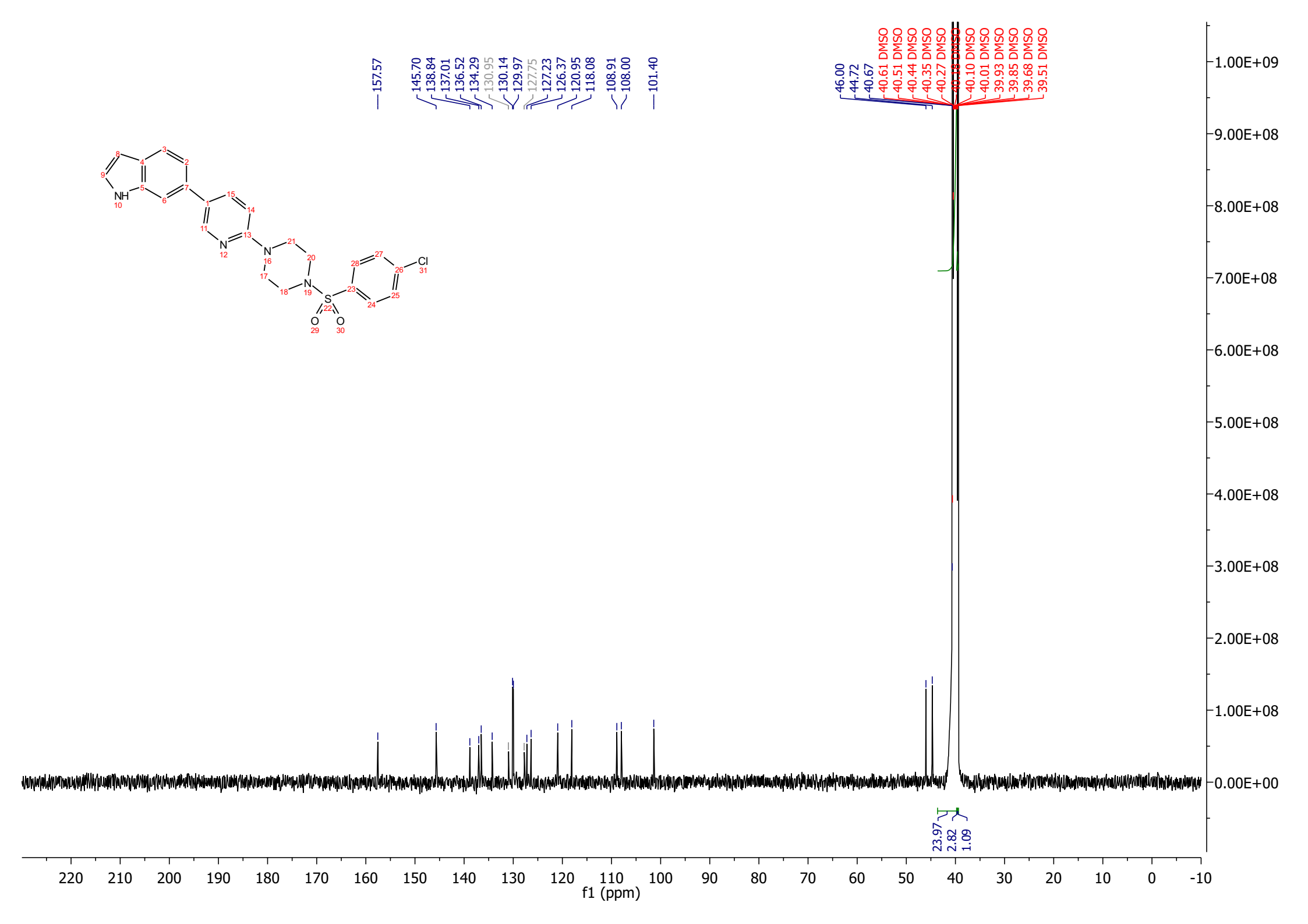
7.80
7.79
7.79
7.79
7.75
7.75
7.74
7.73
7.73
7.61
7.59
7.57
7.55
7.55
7.55
7.36
7.35
7.35
7.34
7.24
7.23
7.22
7.22
6.93
6.91
6.43
6.43
6.42
3.70
3.66
3.65
3.64
3.41
3.37
3.33 HDO
3.30
3.29
3.05
3.04
3.03
2.56
2.55
2.55
2.53 DMSO
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.08
NH
N
N
N
S
O
O
Cl
1.00
1.02
1.01
1.98
1.93
1.06
0.97
1.03
0.98
0.98
1.02
4.06
3.96
f1 (ppm)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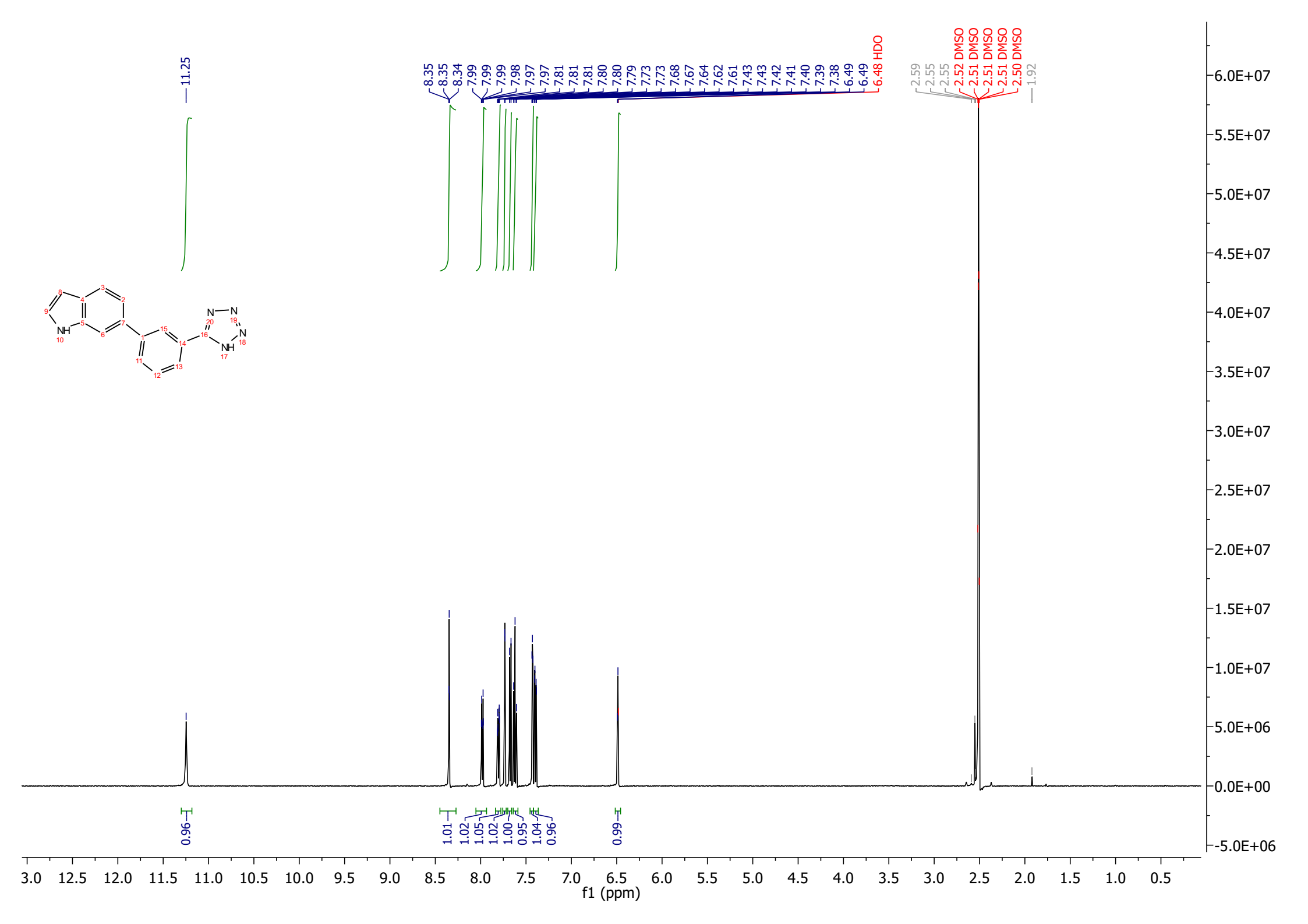
130.95
130.14
129.97
127.75
127.23
126.37
120.95
118.08
108.91
108.00
101.40
46.00
44.72
40.67
40.61 DMSO
40.51 DMSO
40.44 DMSO
40.35 DMSO
40.27 DMSO
40.18 DMSO
40.10 DMSO
40.01 DMSO
39.93 DMSO
39.85 DMSO
39.68 DMSO
39.51 DMSO
NH
N
N
N
S
O
O
Cl
23.97
2.82
1.09
1.00E+09
9.00E+08
8.00E+08
7.00E+08
6.00E+08
5.00E+08
4.00E+08
3.00E+08
2.00E+08
1.00E+08
0.00E+00
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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8.35
8.35
8.34
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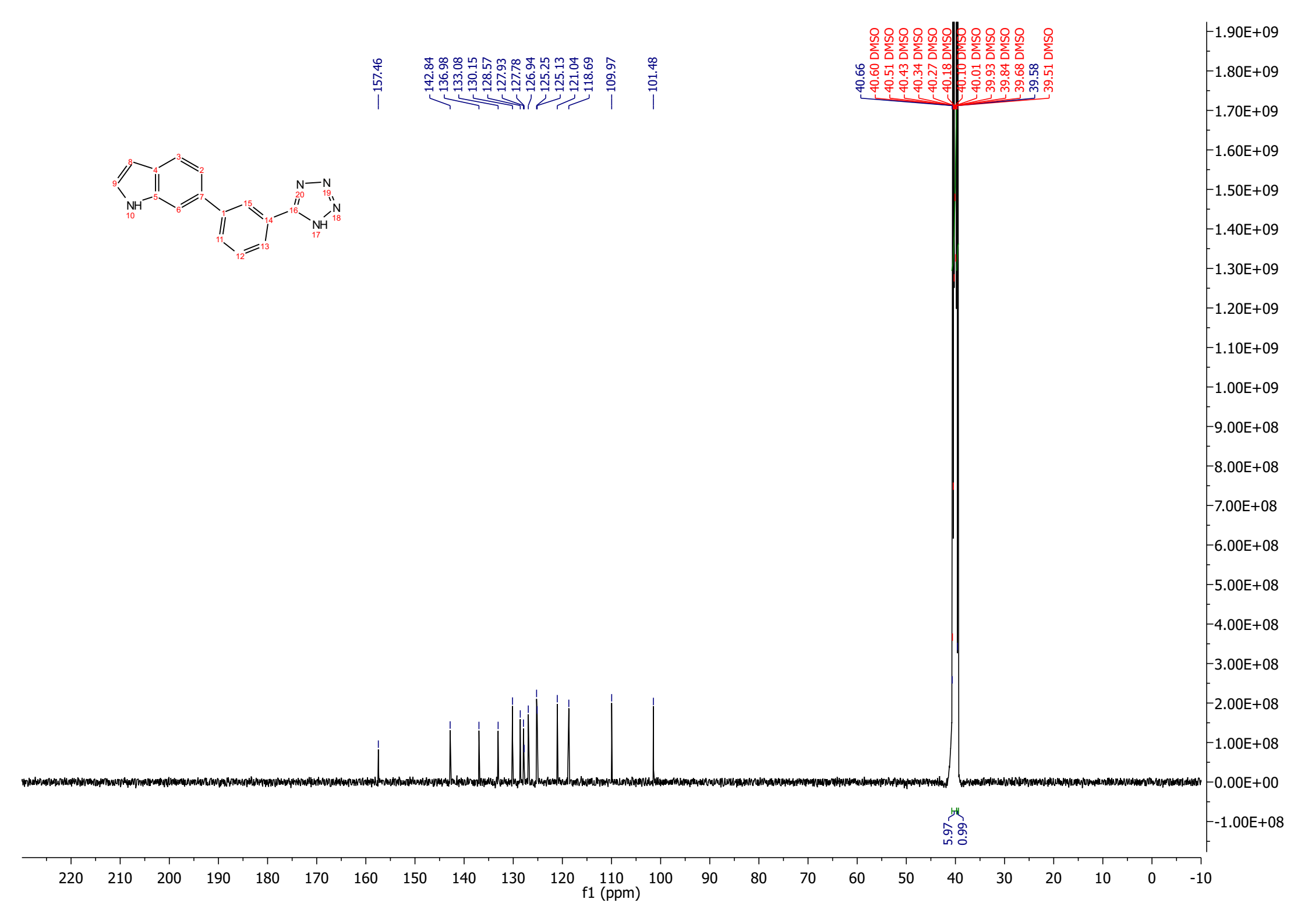
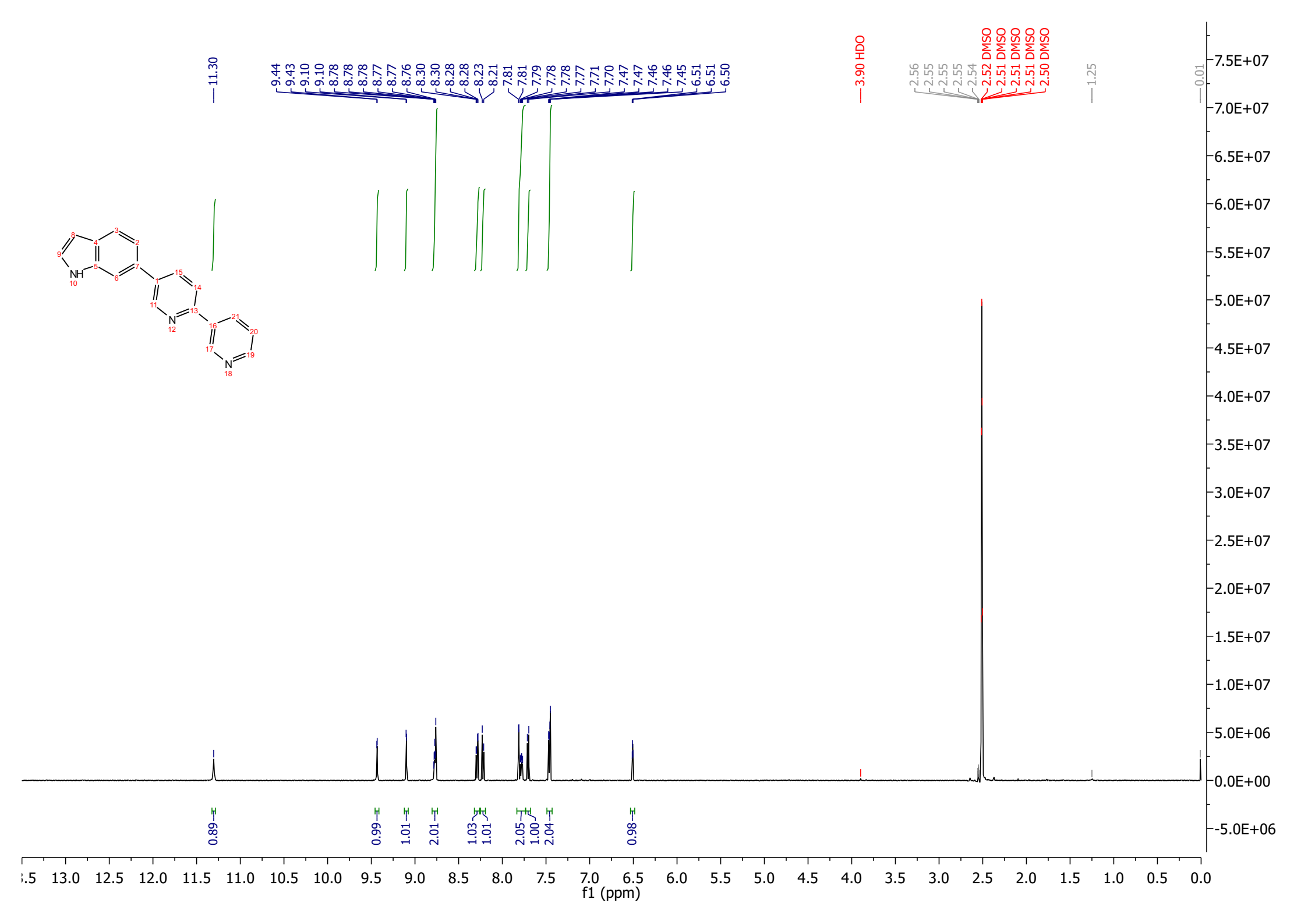
7.99
7.99
7.98
7.97
7.97
7.81
7.81
7.80
7.80
7.79
7.73
7.73
7.68
7.67
7.64
7.62
7.61
7.43
7.43
7.42
7.41
7.40
7.39
7.38
6.49
6.49
6.48 HDO
2.59
2.55
2.55
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
1.92
0.96
1.01
1.02
1.05
1.02
1.00
0.95
1.04
0.96
0.99
f1 (ppm)


157.46
142.84
136.98
133.08
130.15
128.57
127.93
127.78
126.94
125.25
125.13
121.04
118.69
109.97
101.48
40.66
40.60 DMSO
40.51 DMSO
40.43 DMSO
40.34 DMSO
40.27 DMSO
40.18 DMSO
40.10 DMSO
40.01 DMSO
39.93 DMSO
39.84 DMSO
39.68 DMSO
39.58
39.51 DMSO
5.97
0.99
f1 (ppm)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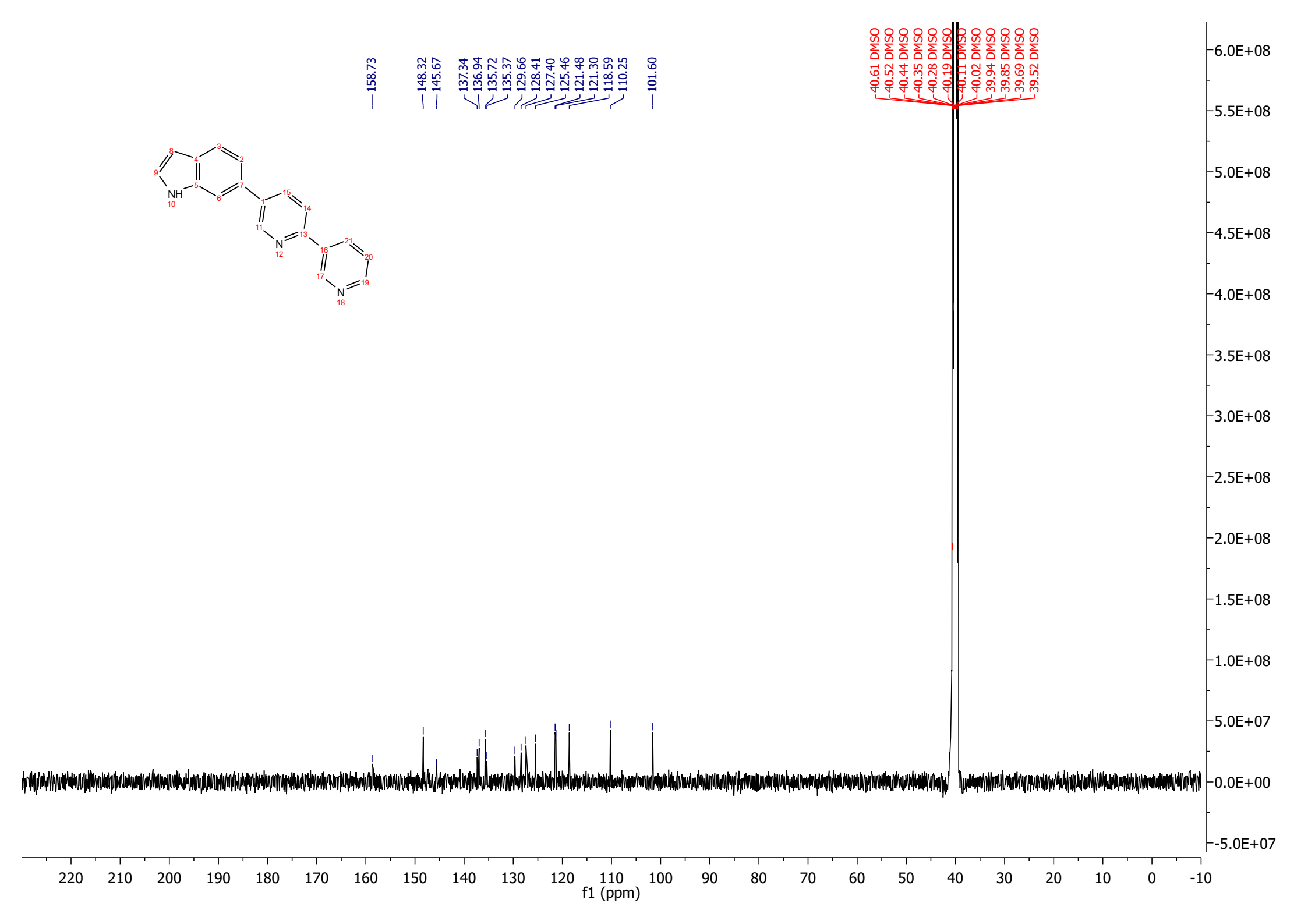
9.44
9.43
9.10
9.10
8.78
8.78
8.78
8.77
8.77
8.76
8.30
8.30
8.28
8.28
8.23
8.21
7.81
7.81
7.79
7.78
7.78
7.77
7.71
7.70
7.47
7.47
7.46
7.46
7.45
6.51
6.51
6.50
3.90 HDO
2.56
2.55
2.55
2.55
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
1.25
0.01
0.89
0.99
1.01
2.01
1.03
1.01
2.05
1.00
2.04
0.98
f1 (ppm)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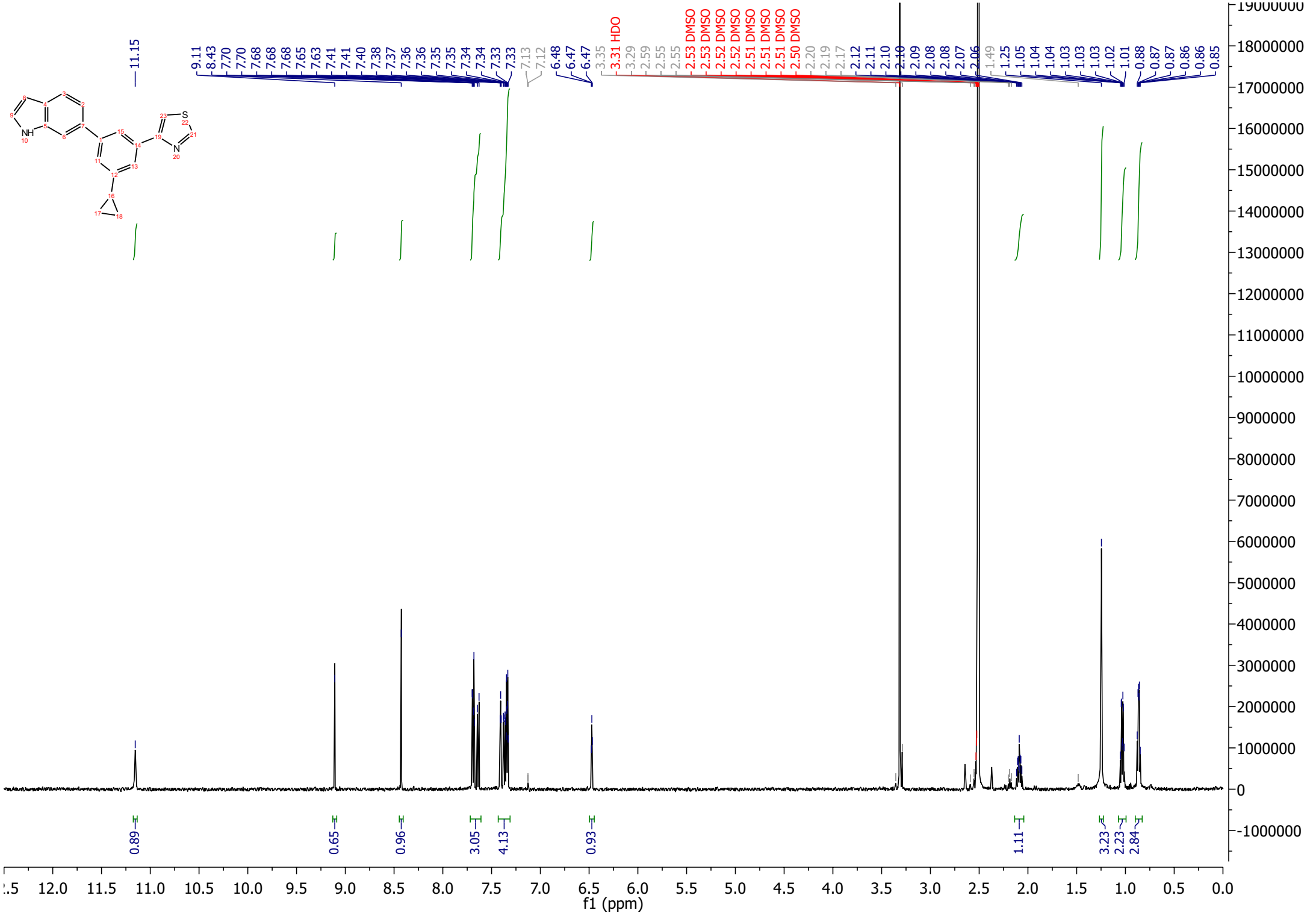
148.32
145.67
137.34
136.94
135.72
135.37
129.66
128.41
127.40
125.46
121.48
121.30
118.59
110.25
101.60
40.61 DMSO
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.69 DMSO
39.52 DMSO
NH
N
N
6.0E+08
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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9.11
8.43
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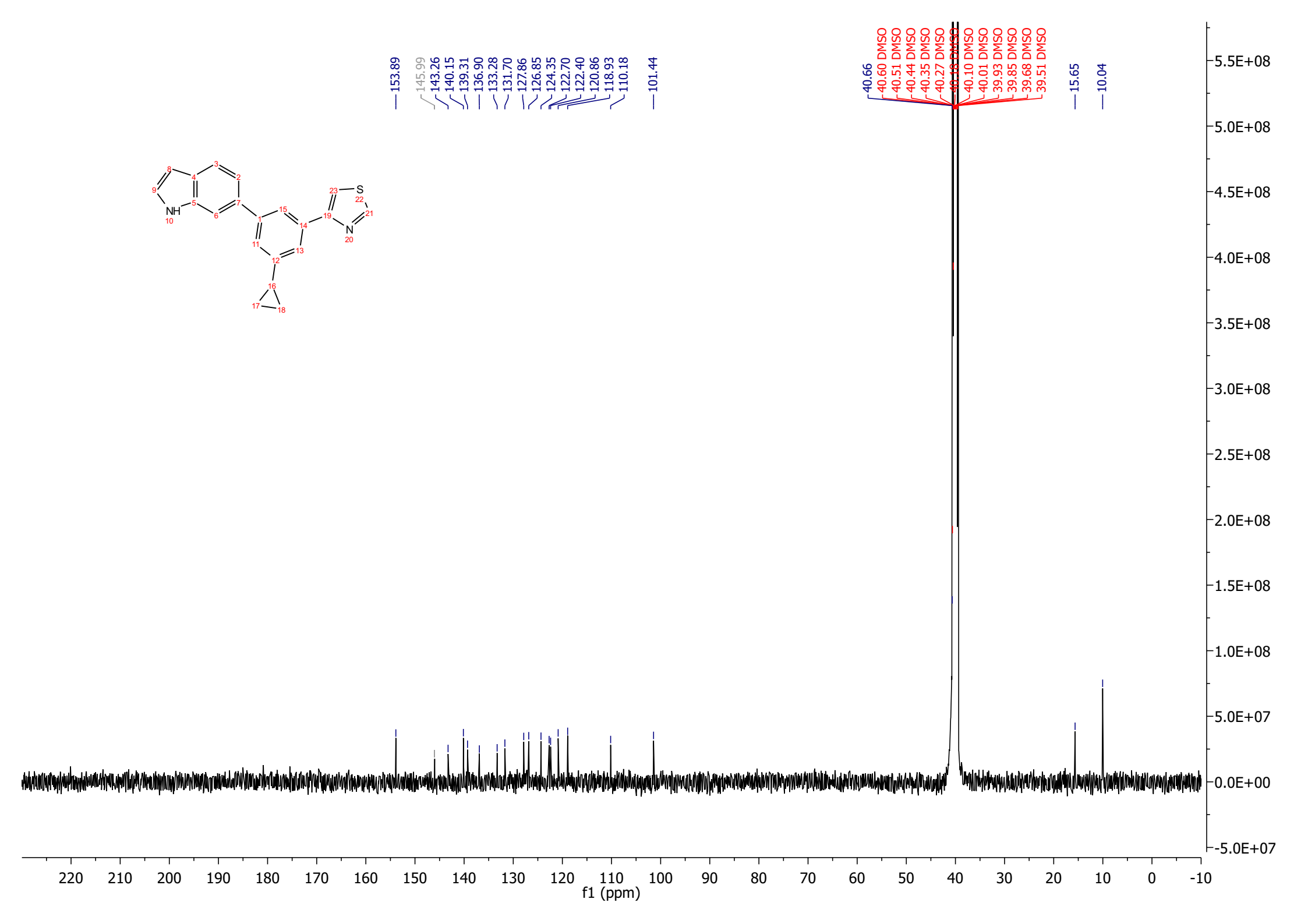
7.70
7.68
7.68
7.68
7.65
7.63
7.41
7.41
7.40
7.38
7.37
7.36
7.36
7.35
7.35
7.34
7.34
7.33
7.33
7.13
7.12
6.48
6.47
6.47
3.35
3.31 HDO
3.29
2.59
2.55
2.55
2.53 DMSO
2.53 DMSO
2.52 DMSO
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.20
2.19
2.17
2.12
2.11
2.10
2.10
2.09
2.08
2.08
2.07
2.06
1.49
1.25
1.05
1.04
1.04
1.03
1.03
1.03
1.02
1.01
0.88
0.87
0.87
0.86
0.86
0.85
NH
S
N
0.89
0.65
0.96
3.05
4.13
0.93
1.11
3.23
2.23
2.84
f1 (ppm)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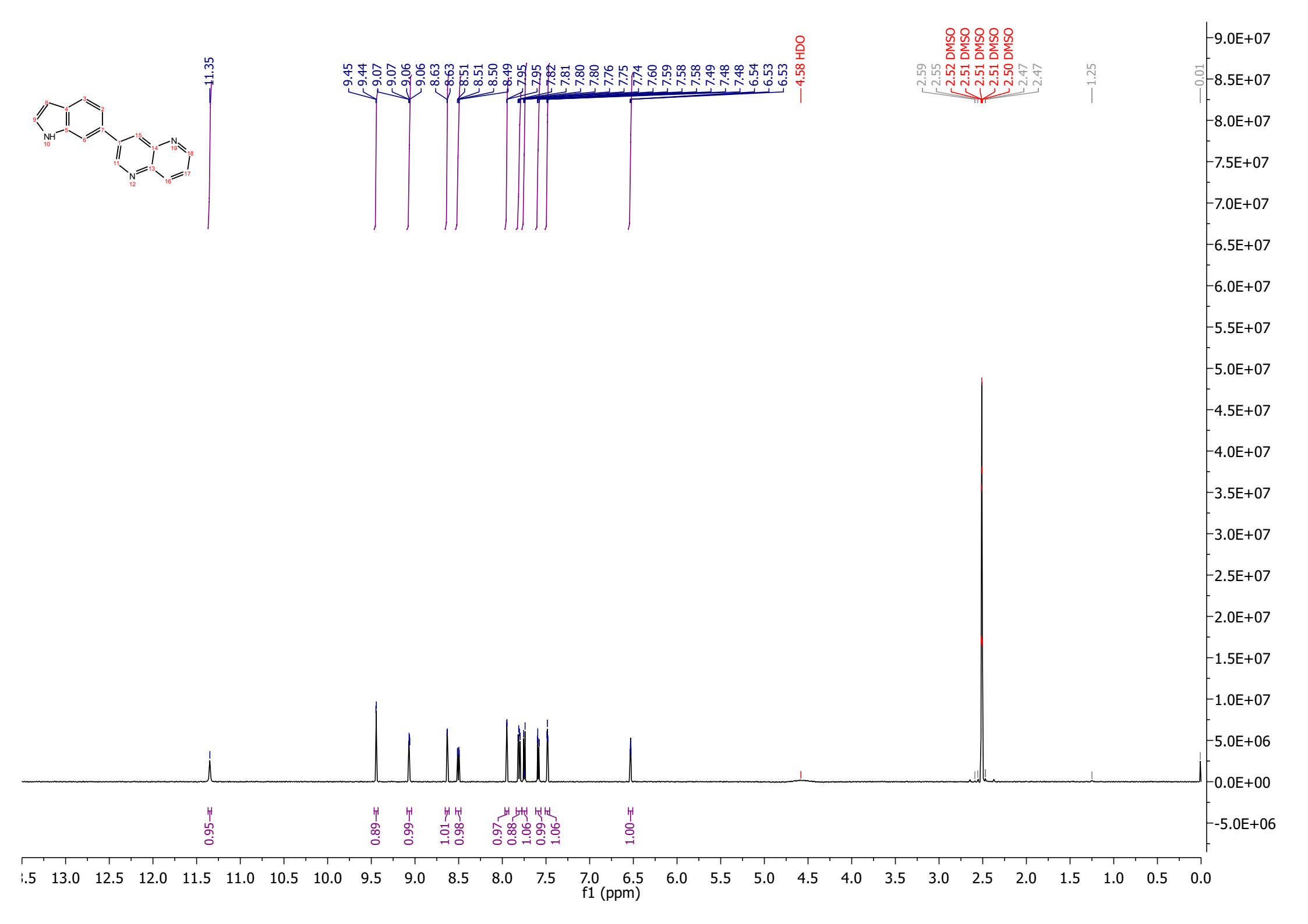
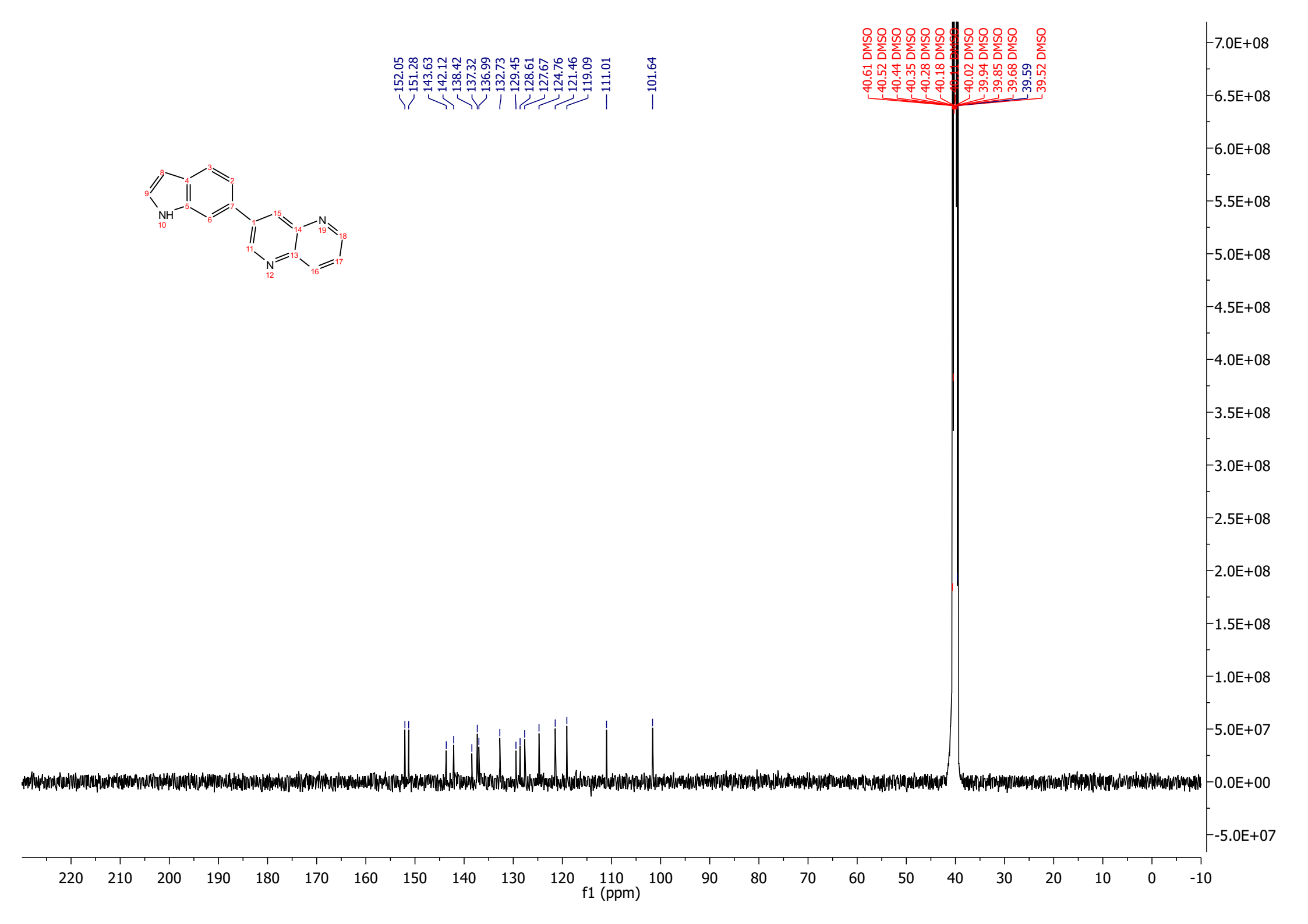
140.15
139.31
136.90
133.28
131.70
127.86
126.85
124.35
122.70
122.40
120.86
118.93
110.18
101.44
40.66
40.60 DMSO
40.51 DMSO
40.44 DMSO
40.35 DMSO
40.27 DMSO
40.18 DMSO
40.10 DMSO
40.01 DMSO
39.93 DMSO
39.85 DMSO
39.68 DMSO
39.51 DMSO
15.65
10.04
NH
S
N
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


11.35
9.45
9.44
9.07
9.07
9.06
9.06
8.63
8.63
8.51
8.51
8.50
8.49
7.95
7.95
7.82
7.81
7.80
7.80
7.76
7.75
7.74
7.60
7.59
7.58
7.58
7.49
7.48
7.48
6.54
6.53
6.53
4.58 HDO
2.59
2.55
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.47
2.47
1.25
0.01
0.95
0.89
0.99
1.01
0.98
0.97
0.88
1.06
0.99
1.06
1.00
f1 (ppm)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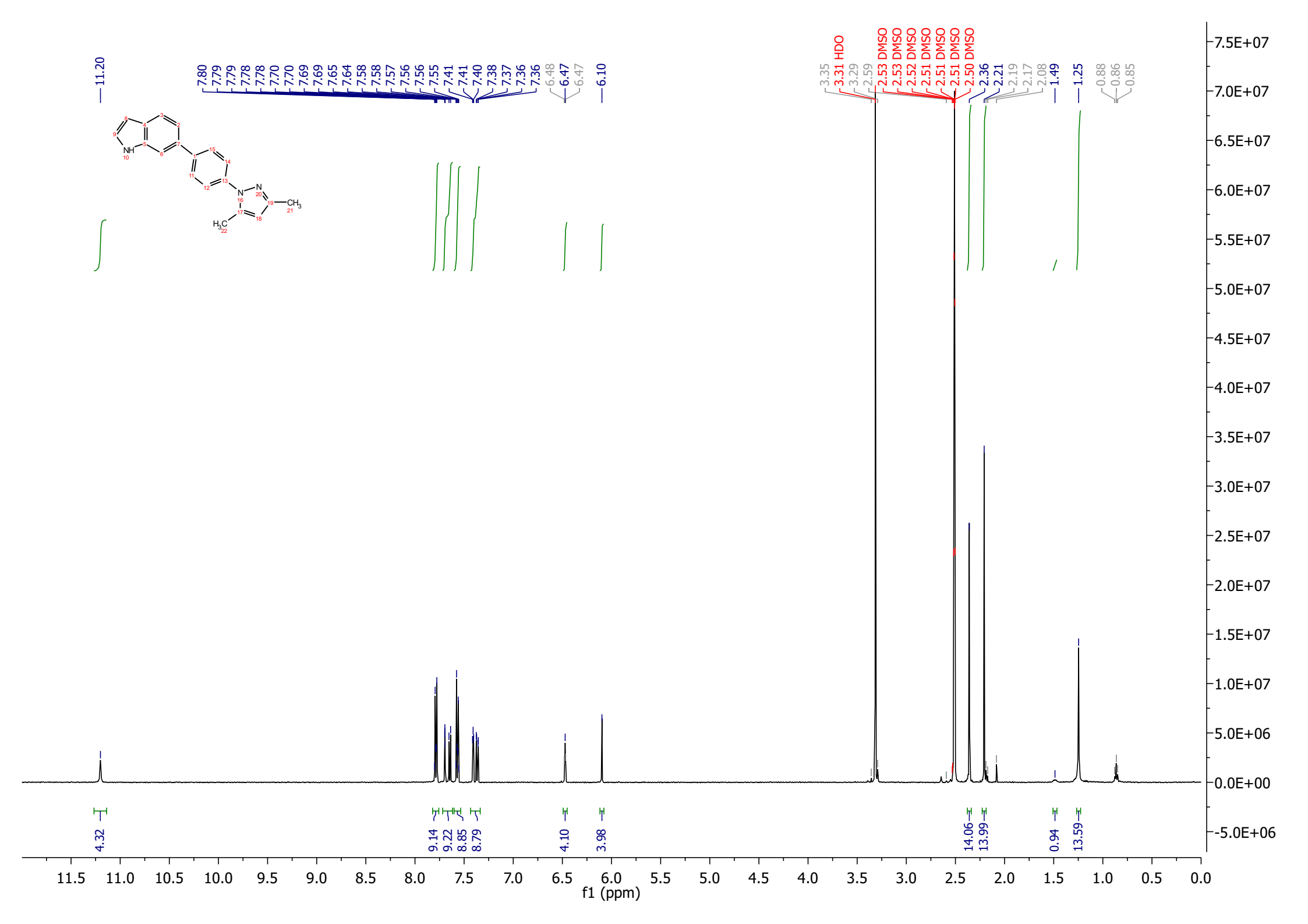
151.28
143.63
142.12
138.42
137.32
136.99
132.73
129.45
128.61
127.67
124.76
121.46
119.09
111.01
101.64
40.61 DMSO
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.28 DMSO
40.18 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.68 DMSO
39.59
39.52 DMSO
NH
N
N
f1 (ppm)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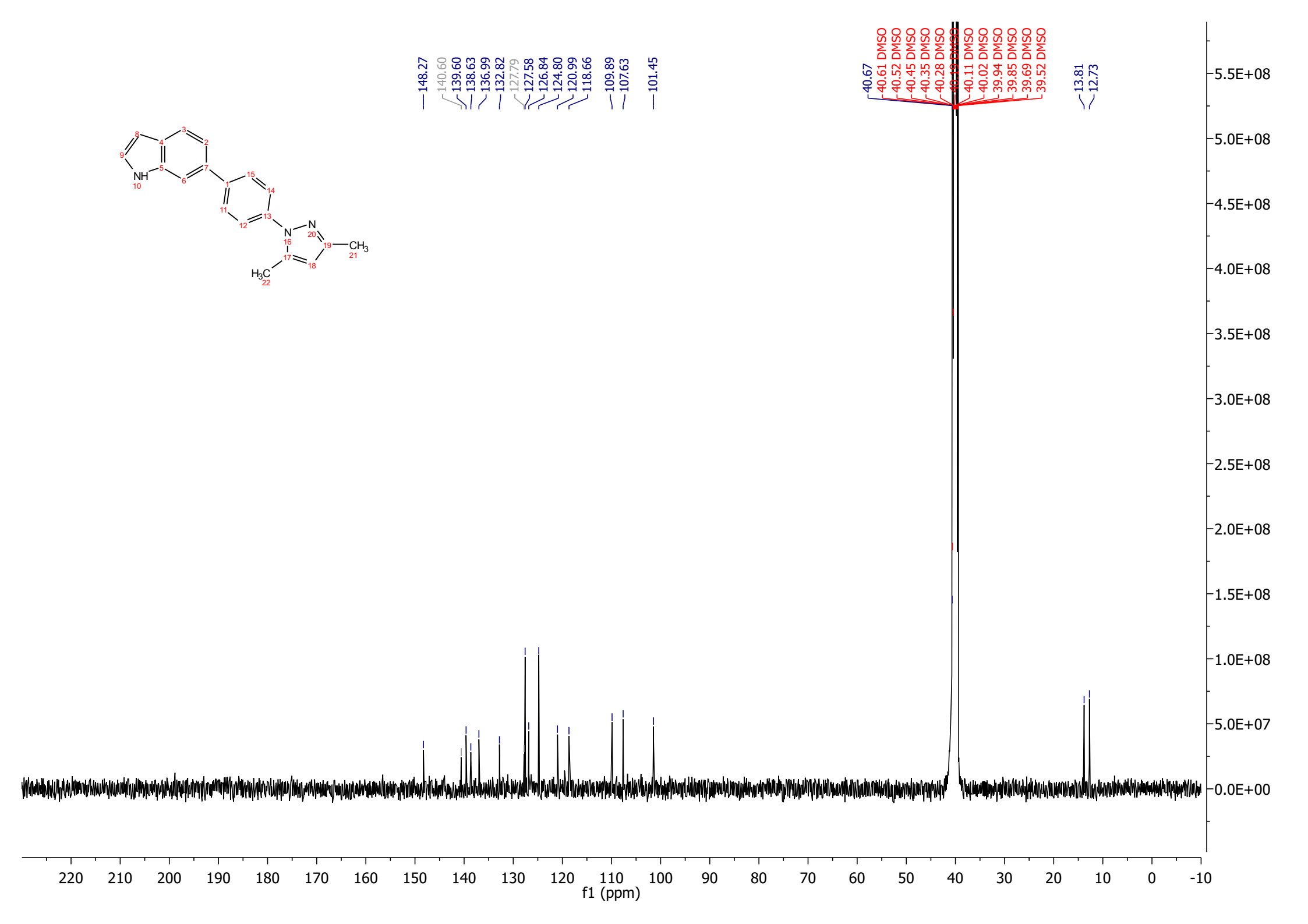
7.70
7.69
7.69
7.65
7.64
7.58
7.58
7.57
7.56
7.56
7.55
7.41
7.41
7.40
7.38
7.37
7.36
7.36
6.48
6.47
6.47
6.10
3.35
3.31 HDO
3.29
2.59
2.53 DMSO
2.53 DMSO
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.36
2.21
2.19
2.17
2.08
1.49
1.25
0.88
0.86
0.85
NH
N
N
CH3
H3C
4.32
9.14
9.22
8.85
8.79
4.10
3.98
14.06
13.99
0.94
13.59
f1 (ppm)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132.82
127.79
127.58
126.84
124.80
120.99
118.66
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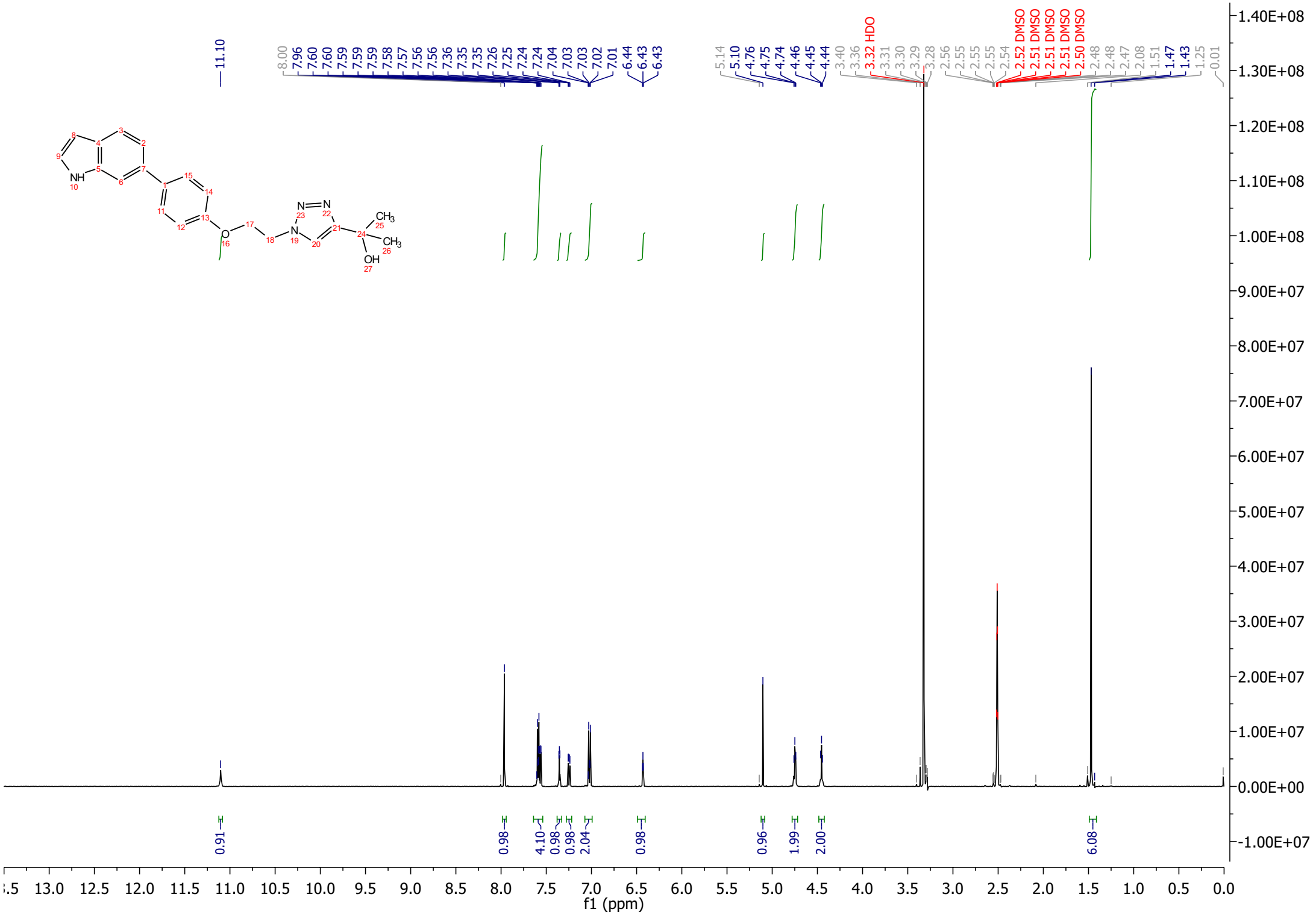
107.63
101.45
40.67
40.61 DMSO
40.52 DMSO
40.45 DMSO
40.35 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.69 DMSO
39.52 DMSO
13.81
12.73
NH
10
N
16
N
20
CH3
21
H3C
22
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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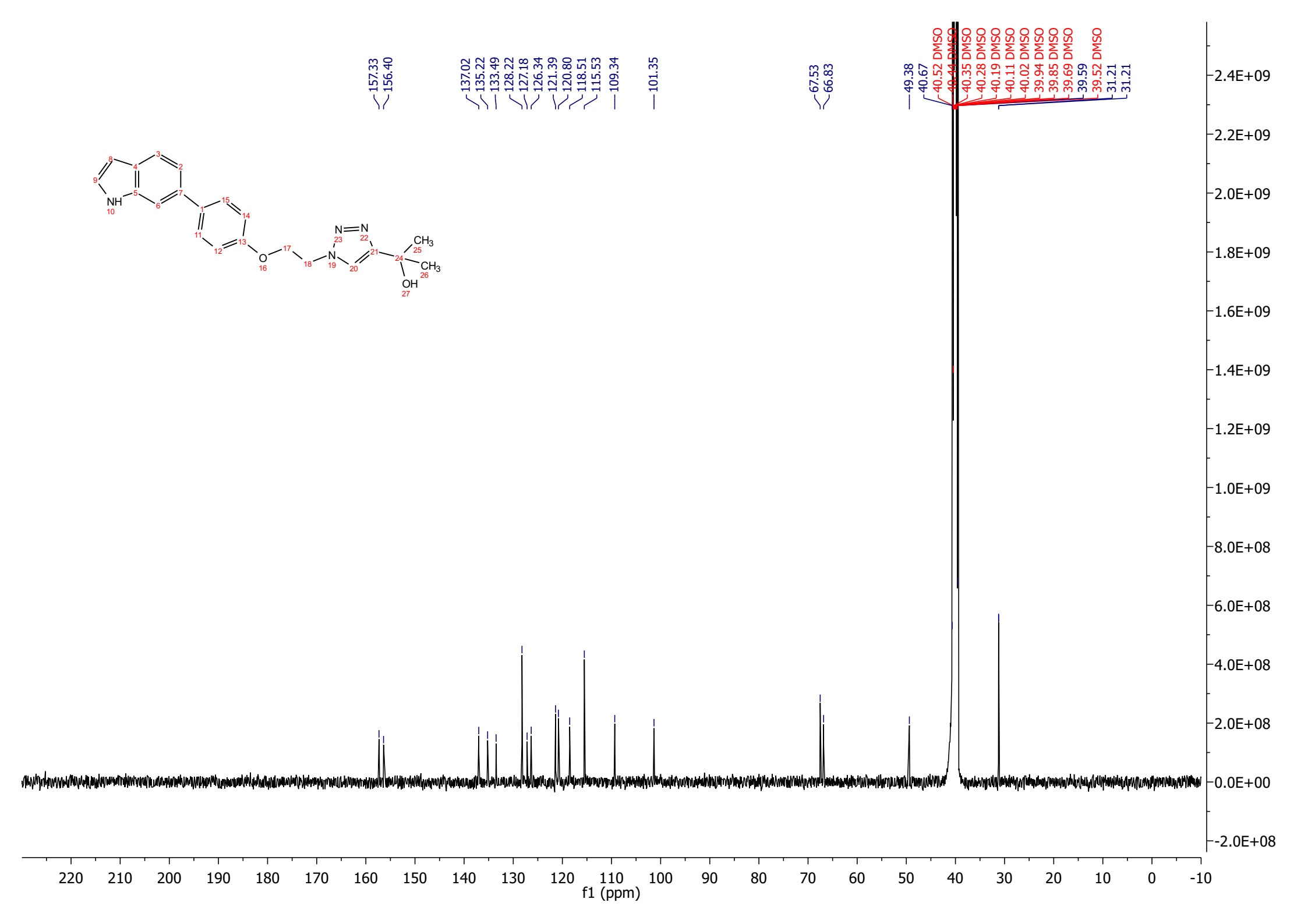
8.00
7.96
7.60
7.60
7.59
7.59
7.59
7.58
7.57
7.56
7.56
7.36
7.35
7.35
7.26
7.25
7.24
7.24
7.04
7.03
7.03
7.02
7.01
6.44
6.43
6.43
5.14
5.10
4.76
4.75
4.74
4.46
4.45
4.44
3.40
3.36
3.32 HDO
3.31
3.30
3.29
3.28
2.56
2.55
2.55
2.55
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.48
2.48
2.47
2.08
1.51
1.47
1.43
1.25
0.01
NH
10
O
16
N
19
N
23
N
22
CH3
25
CH3
26
OH
27
0.91
0.98
4.10
0.98
0.98
2.04
0.98
0.96
1.99
2.00
6.08
1.40E+08
1.30E+08
1.20E+08
1.10E+08
1.00E+08
9.00E+07
8.00E+07
7.00E+07
6.00E+07
5.00E+07
4.00E+07
3.00E+07
2.00E+07
1.00E+07
0.00E+00
-1.00E+07
13.0
12.5
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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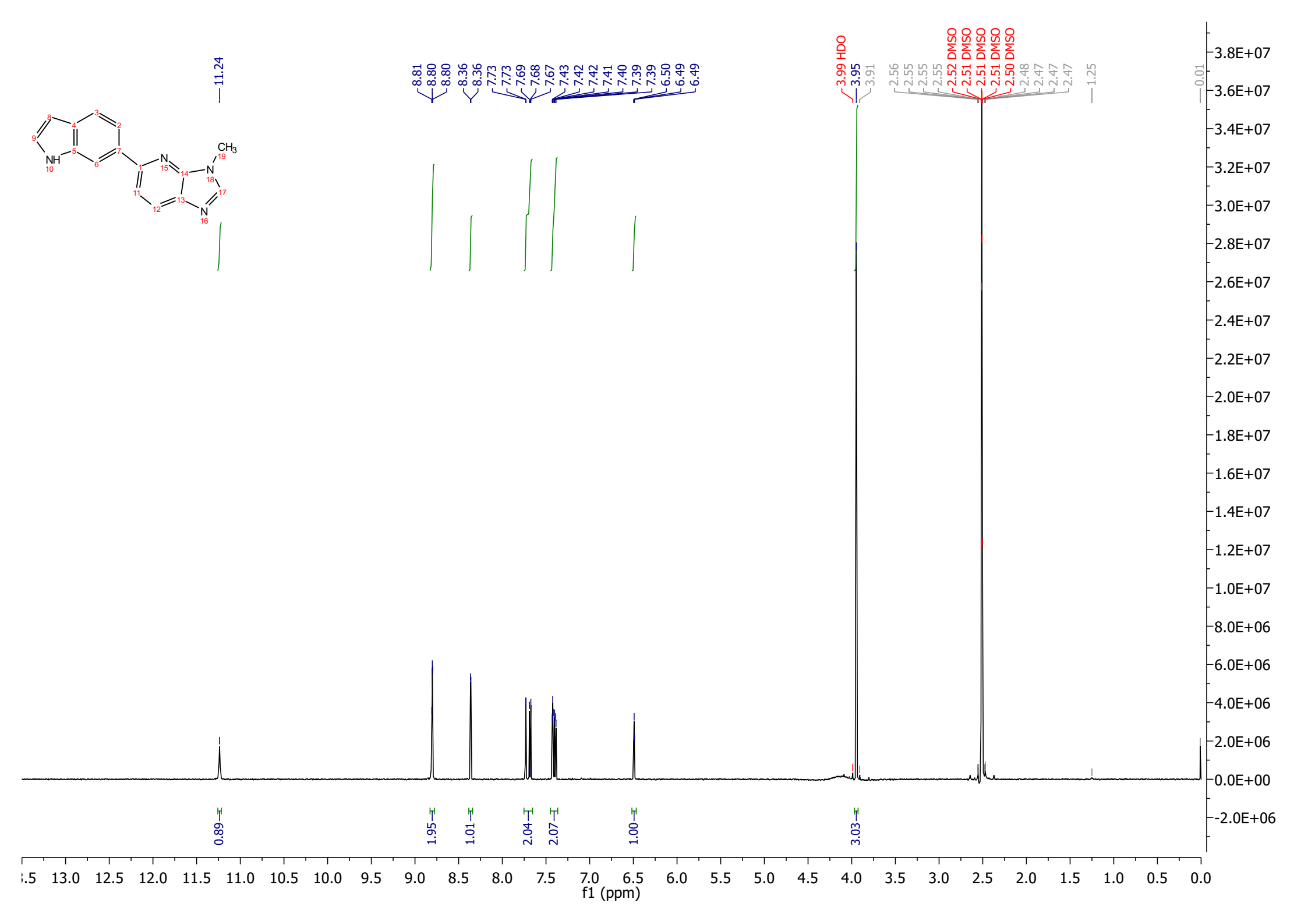
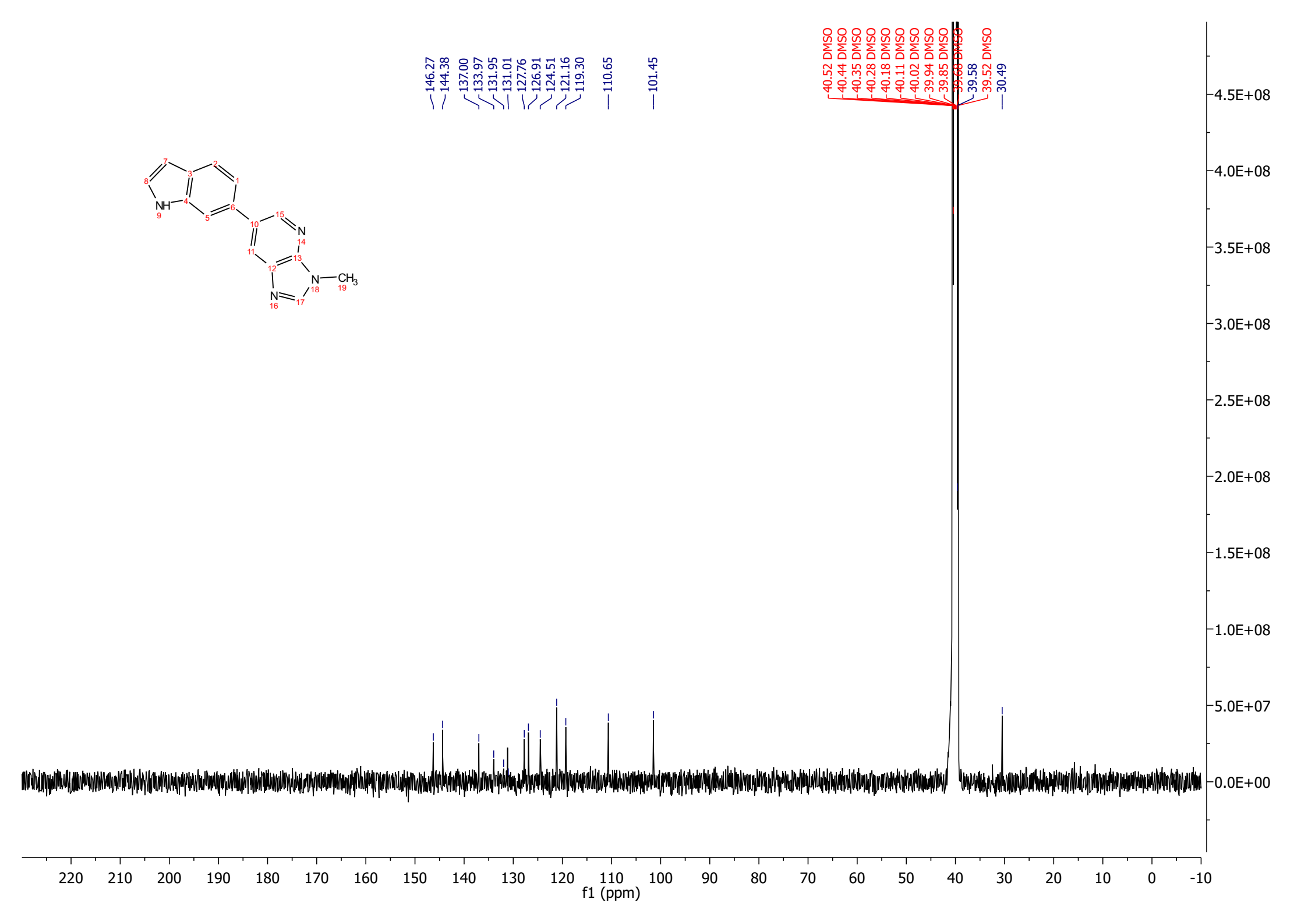
135.22
133.49
128.22
127.18
126.34
121.39
120.80
118.51
115.53
109.34
101.35
67.53
66.83
49.38
40.67
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.69 DMSO
39.59
39.52 DMSO
31.21
31.21
NH
10
O
16
N
19
N
23
N
22
CH3
25
CH3
26
OH
27
2.4E+09
2.2E+09
2.0E+09
1.8E+09
1.6E+09
1.4E+09
1.2E+09
1.0E+09
8.0E+08
6.0E+08
4.0E+08
2.0E+08
0.0E+00
-2.0E+08
220
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)


11.24
8.81
8.80
8.80
8.36
8.36
7.73
7.73
7.69
7.68
7.67
7.43
7.42
7.42
7.41
7.40
7.39
7.39
6.50
6.49
6.49
3.99 HDO
3.95
3.91
2.56
2.55
2.55
2.55
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.48
2.47
2.47
2.47
1.25
0.01
0.89
1.95
1.01
2.04
2.07
1.00
3.03
f1 (ppm)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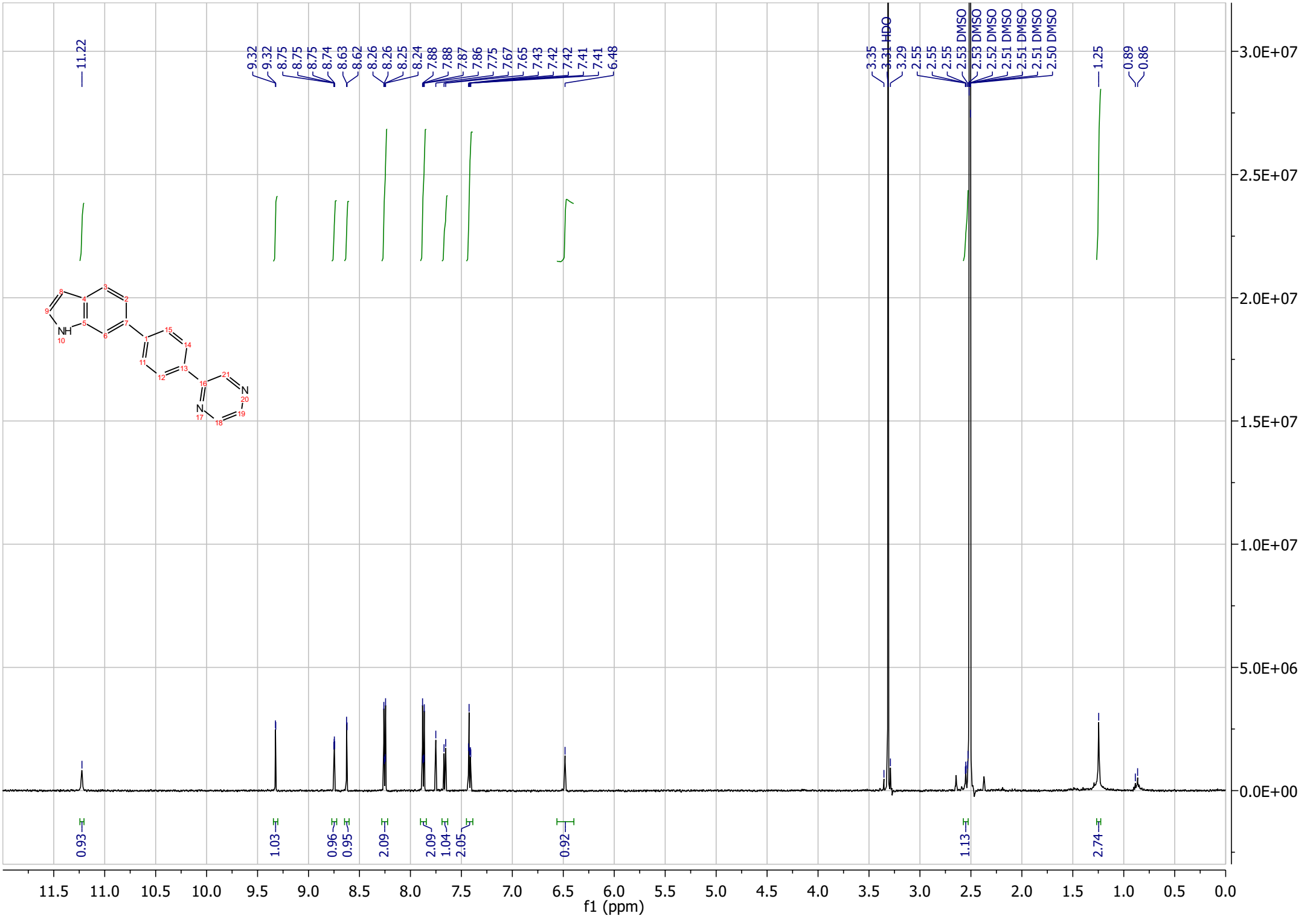
133.97
131.95
131.01
127.76
126.91
124.51
121.16
119.30
110.65
101.45
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.28 DMSO
40.18 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.68 DMSO
39.58
39.52 DMSO
30.49
NH
N
N
N
CH3
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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9.32
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8.75
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8.63
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8.26
8.25
8.24
7.88
7.88
7.87
7.86
7.75
7.67
7.65
7.43
7.42
7.42
7.41
7.41
6.48
3.35
3.31 HDO
3.29
2.55
2.55
2.55
2.53 DMSO
2.53 DMSO
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
1.25
0.89
0.86
NH
10
N
17
N
20
0.93
1.03
0.96
0.95
2.09
2.09
1.04
2.05
0.92
1.13
2.74
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
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
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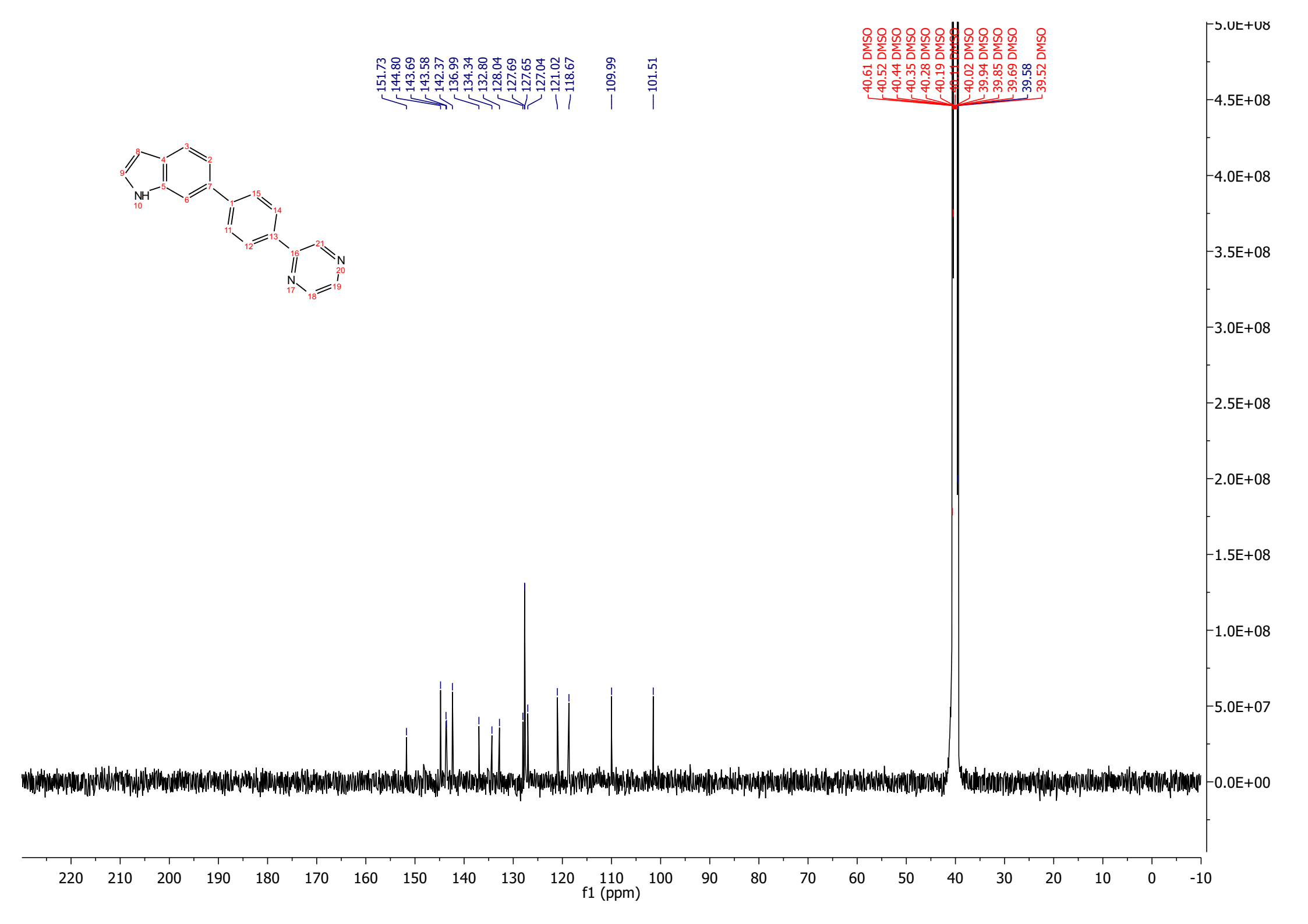
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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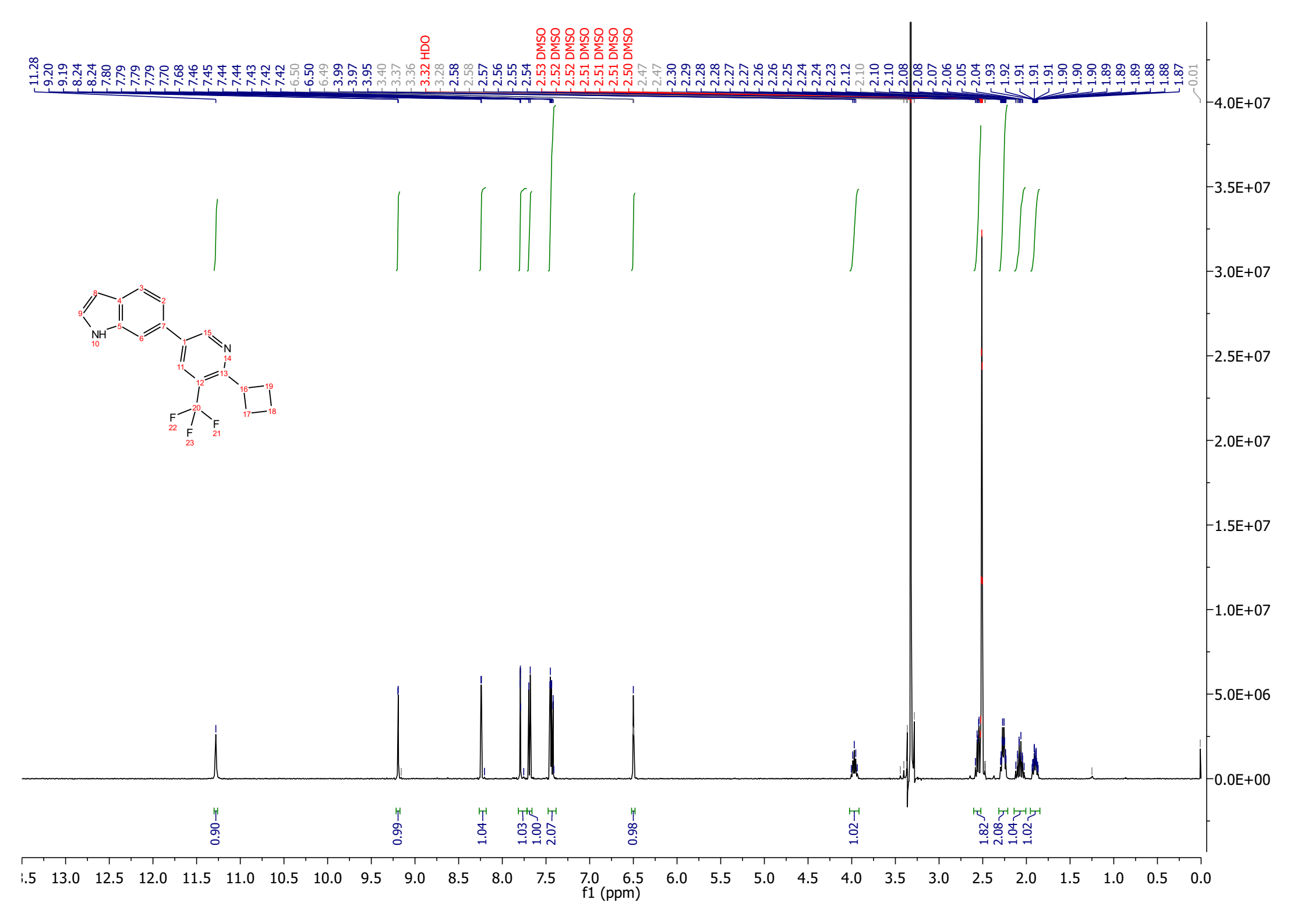
144.80
143.69
143.58
142.37
136.99
134.34
132.80
128.04
127.69
127.65
127.04
121.02
118.67
109.99
101.51
40.61 DMSO
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.69 DMSO
39.58
39.52 DMSO
NH
N
N
f1 (ppm)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7.79
7.79
7.70
7.68
7.46
7.45
7.44
7.44
7.43
7.42
7.42
6.50
6.50
6.49
3.99
3.97
3.95
3.40
3.37
3.36
3.32 HDO
3.28
2.58
2.58
2.57
2.56
2.55
2.54
2.53 DMSO
2.52 DMSO
2.52 DMSO
2.51 DMSO
2.51 DMSO
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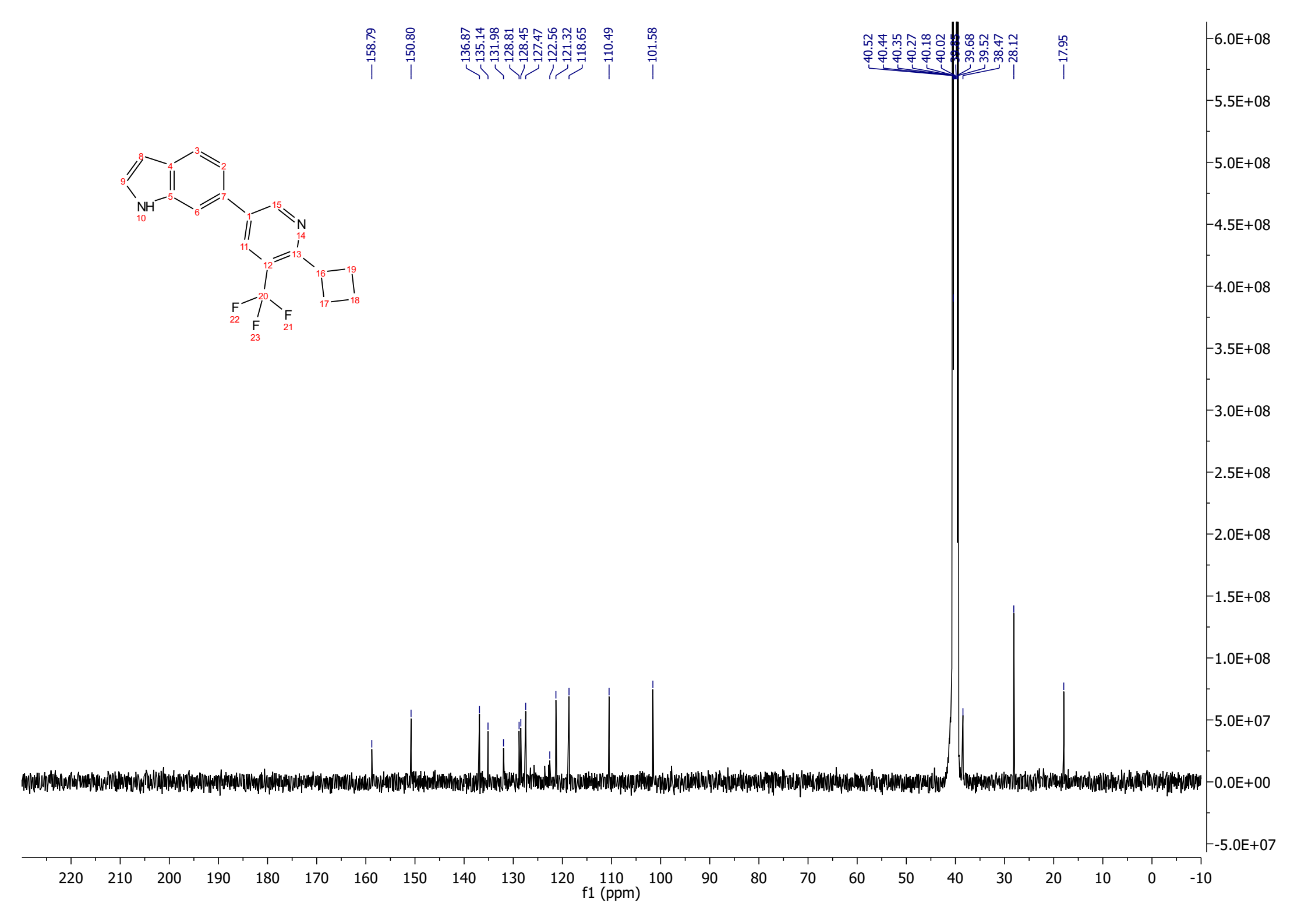
2.47
2.30
2.29
2.28
2.28
2.27
2.27
2.26
2.26
2.25
2.24
2.24
2.23
2.12
2.10
2.10
2.10
2.08
2.08
2.07
2.06
2.05
2.04
1.93
1.92
1.91
1.91
1.91
1.90
1.90
1.90
1.89
1.89
1.89
1.88
1.88
1.87
0.01
NH
N
F
F
F
0.90
0.99
1.04
1.03
1.00
2.07
0.98
1.02
1.82
2.08
1.04
1.02
f1 (ppm)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127.47
122.56
121.32
118.65
110.49
101.58
40.52
40.44
40.35
40.27
40.18
40.02
39.68
39.52
38.47
28.12
17.95
NH
N
F
F
F
6.0E+08
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
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60
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40
30
20
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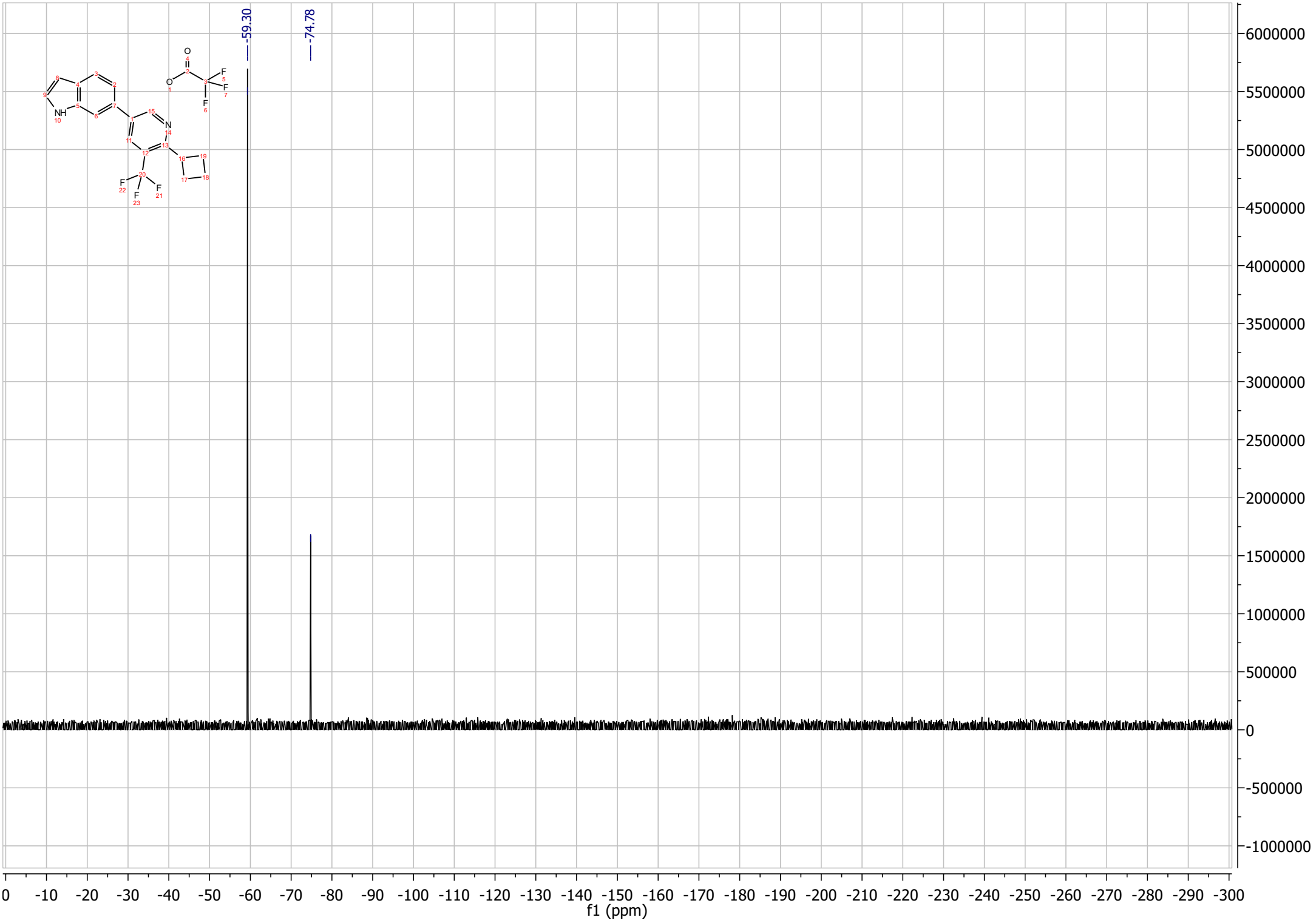
0
-10
f1 (ppm)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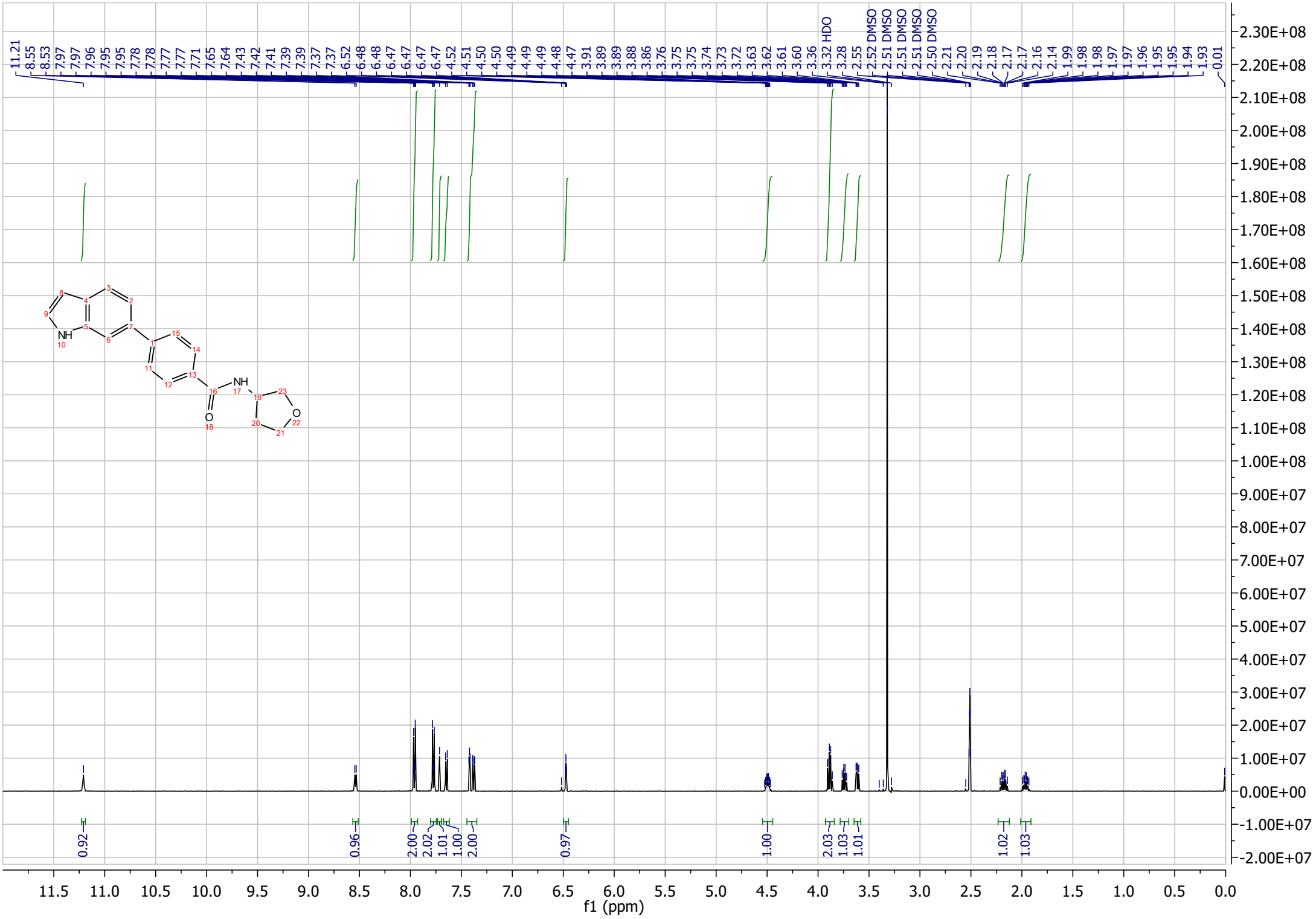
-74.78
6000000
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000
-1000000
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -250 -260 -270 -280 -290 -300
f1 (ppm)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8.55
8.53
7.97
7.97
7.96
7.95
7.95
7.78
7.78
7.77
7.77
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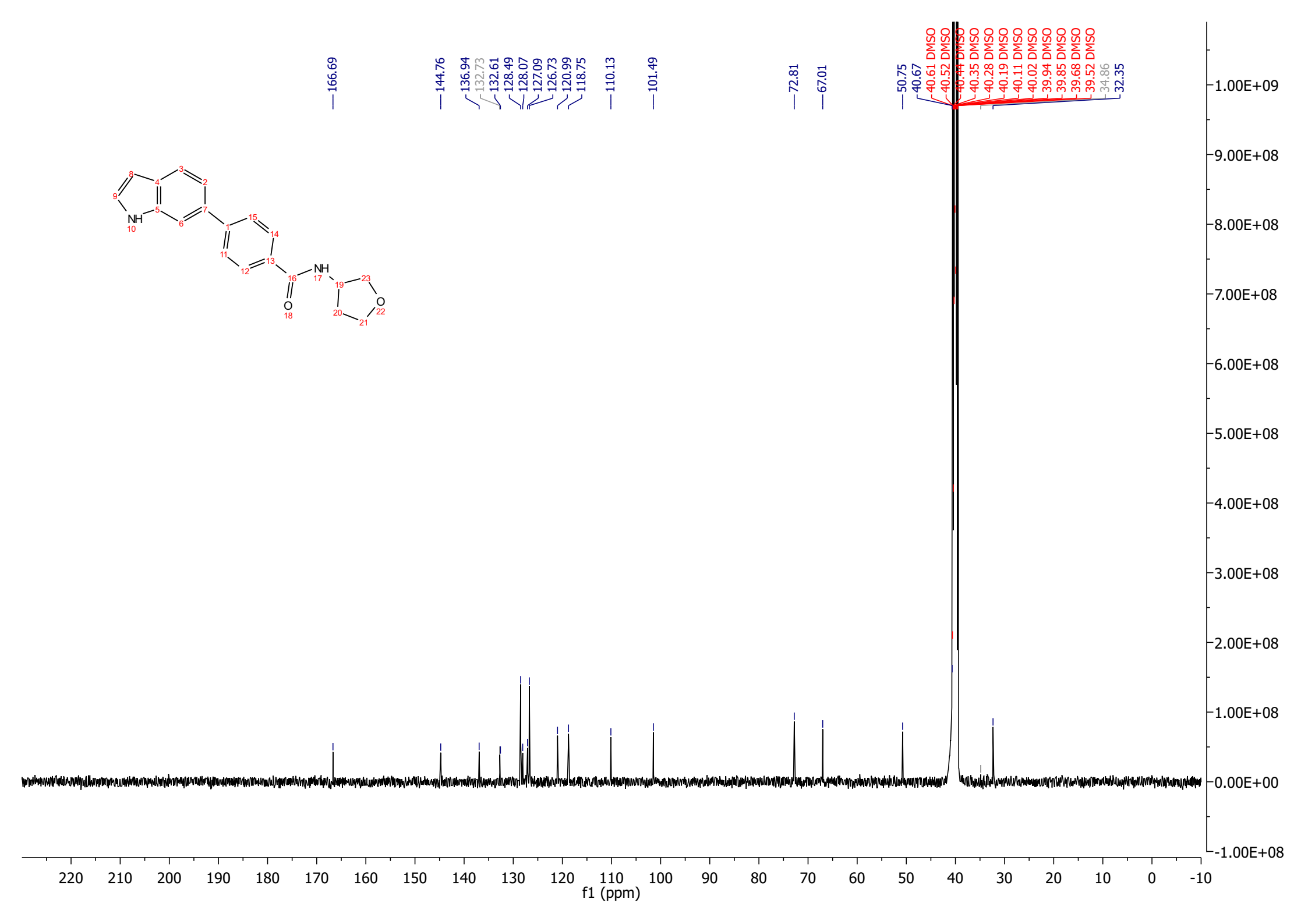
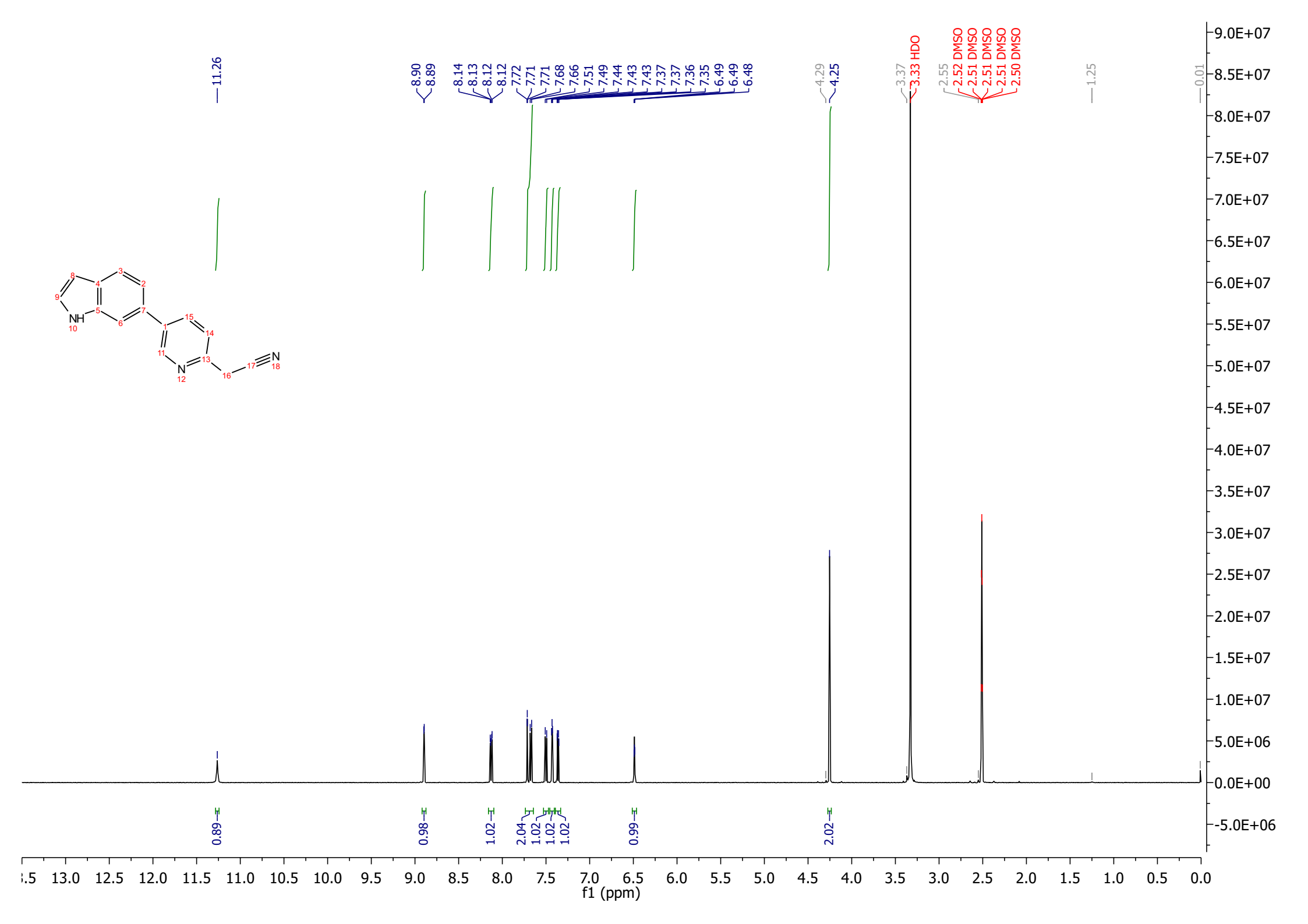
7.65
7.64
7.43
7.42
7.41
7.39
7.39
7.37
7.37
6.52
6.48
6.48
6.47
6.47
6.47
6.47
4.52
4.51
4.50
4.50
4.49
4.49
4.48
4.47
3.91
3.89
3.89
3.88
3.86
3.76
3.75
3.75
3.74
3.73
3.72
3.63
3.62
3.61
3.60
3.36
3.32 HDO
3.28
2.55
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.21
2.20
2.19
2.18
2.17
2.17
2.16
2.14
1.99
1.98
1.98
1.97
1.97
1.96
1.95
1.95
1.94
1.93
0.01
NH
NH
O
O
0.92
0.96
2.00
2.02
1.01
1.00
2.00
0.97
1.00
2.03
1.03
1.01
1.02
1.03
2.30E+08
2.20E+08
2.10E+08
2.00E+08
1.90E+08
1.80E+08
1.70E+08
1.60E+08
1.50E+08
1.40E+08
1.30E+08
1.20E+08
1.10E+08
1.00E+08
9.00E+07
8.00E+07
7.00E+07
6.00E+07
5.00E+07
4.00E+07
3.00E+07
2.00E+07
1.00E+07
0.00E+00
-1.00E+07
-2.00E+07
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
f1 (ppm)


166.69
144.76
136.94
132.73
132.61
128.49
128.07
127.09
126.73
120.99
118.75
110.13
101.49
72.81
67.01
50.75
40.67
40.61 DMSO
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.68 DMSO
39.52 DMSO
34.86
32.35
NH
10
NH
17
O
18
O
22
1.00E+09
9.00E+08
8.00E+08
7.00E+08
6.00E+08
5.00E+08
4.00E+08
3.00E+08
2.00E+08
1.00E+08
0.00E+00
-1.00E+08
220
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)


11.26
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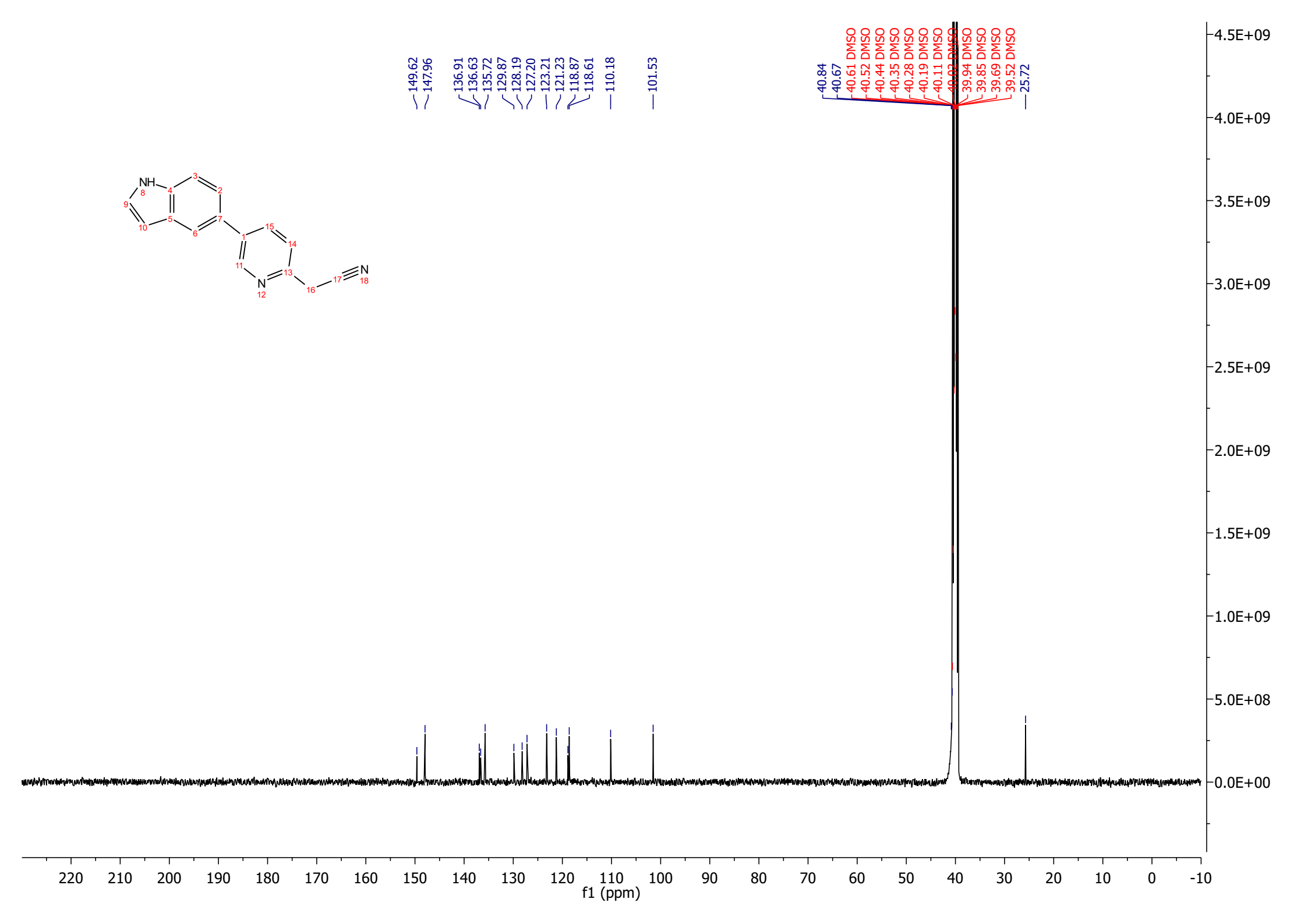
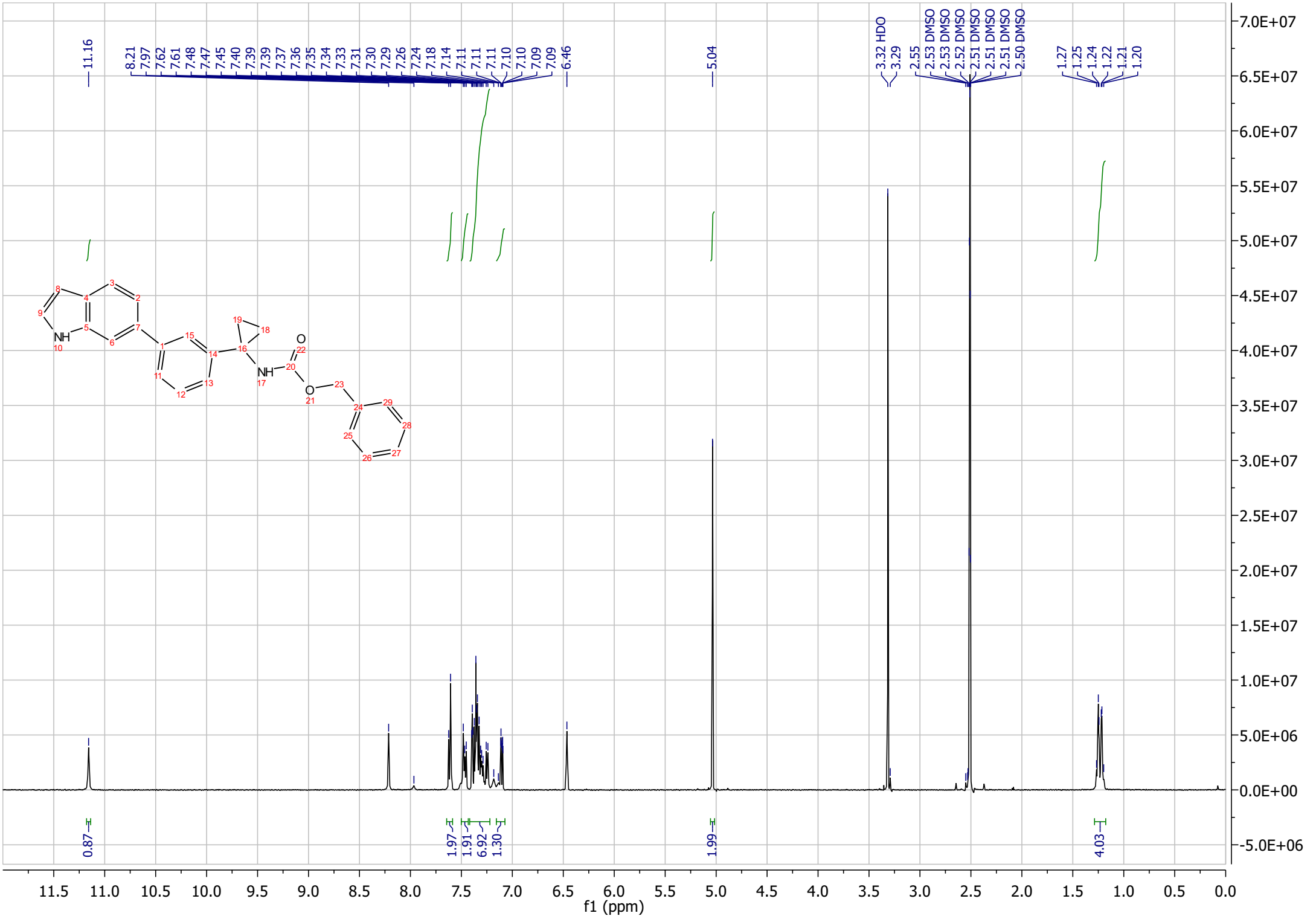
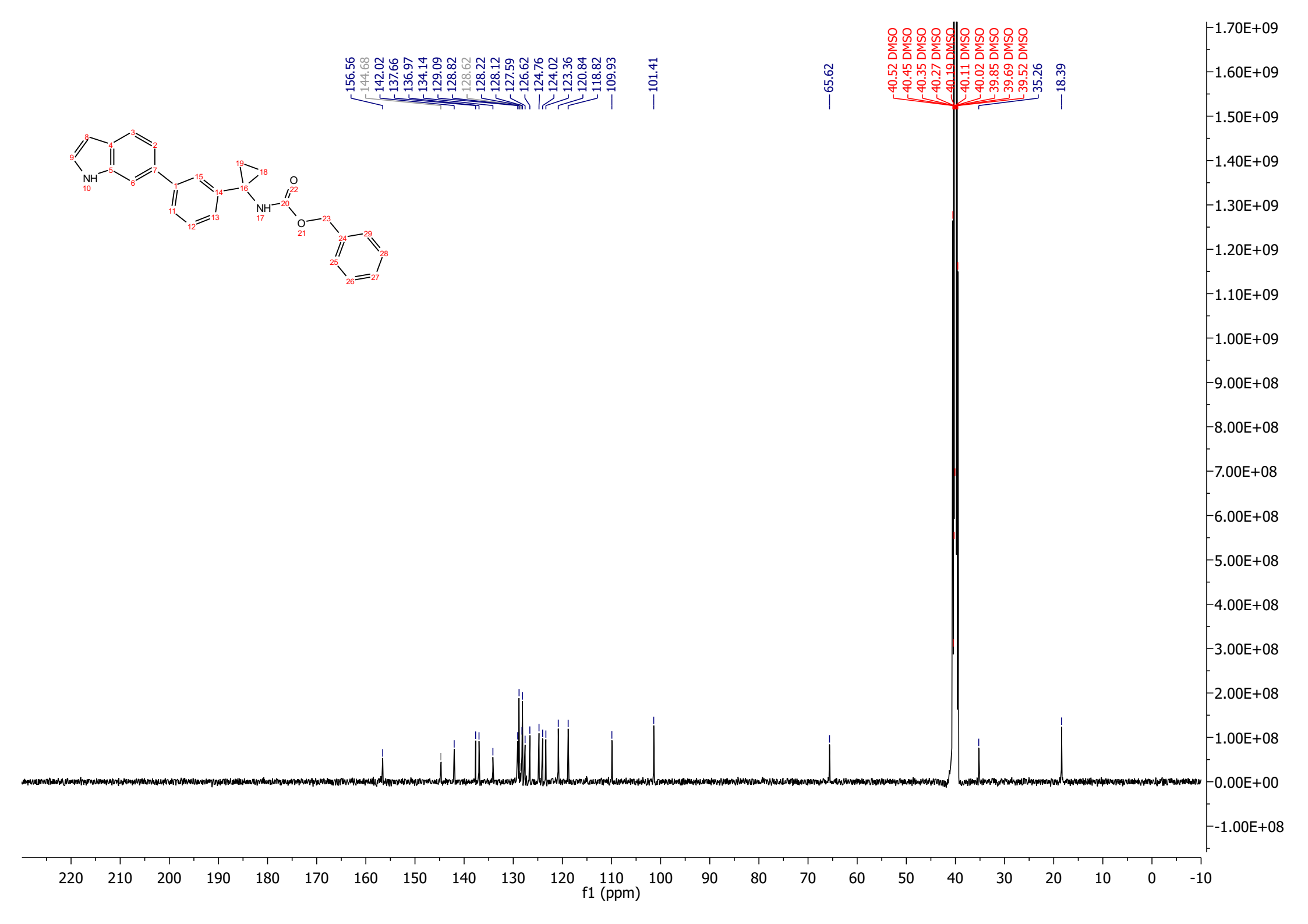
8.89
8.14
8.13
8.12
8.12
7.72
7.71
7.71
7.68
7.66
7.51
7.49
7.44
7.43
7.43
7.37
7.37
7.36
7.35
6.49
6.49
6.48
4.29
4.25
3.37
3.33 HDO
2.55
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
1.25
0.01
NH
N
0.89
0.98
1.02
2.04
1.02
1.02
1.02
0.99
2.02
f1 (ppm)


149.62
147.96
136.91
136.63
135.72
129.87
128.19
127.20
123.21
121.23
118.87
118.61
110.18
101.53
40.84
40.67
40.61 DMSO
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.03 DMSO
39.94 DMSO
39.85 DMSO
39.69 DMSO
39.52 DMSO
25.72
NH
N
N
f1 (ppm)


11.16
8.21
7.97
7.62
7.61
7.48
7.47
7.45
7.40
7.39
7.39
7.37
7.36
7.35
7.34
7.33
7.31
7.30
7.29
7.26
7.24
7.18
7.14
7.11
7.11
7.11
7.10
7.10
7.09
7.09
6.46
5.04
3.32 HDO
3.29
2.55
2.53 DMSO
2.53 DMSO
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
1.27
1.25
1.24
1.22
1.21
1.20
NH
10
NH
17
O
21
O
22
0.87
1.97
1.91
6.92
1.30
1.99
4.03
f1 (ppm)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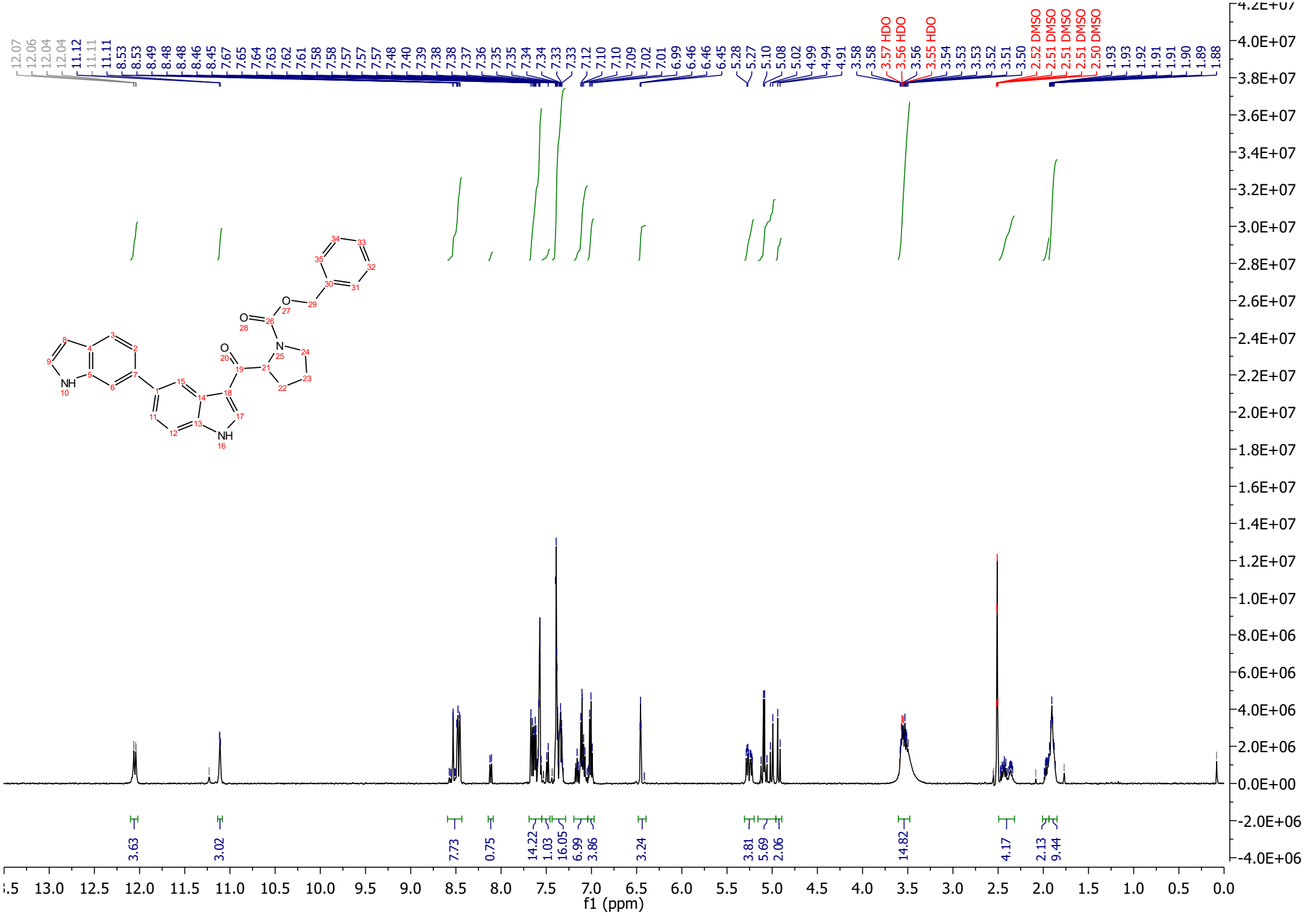
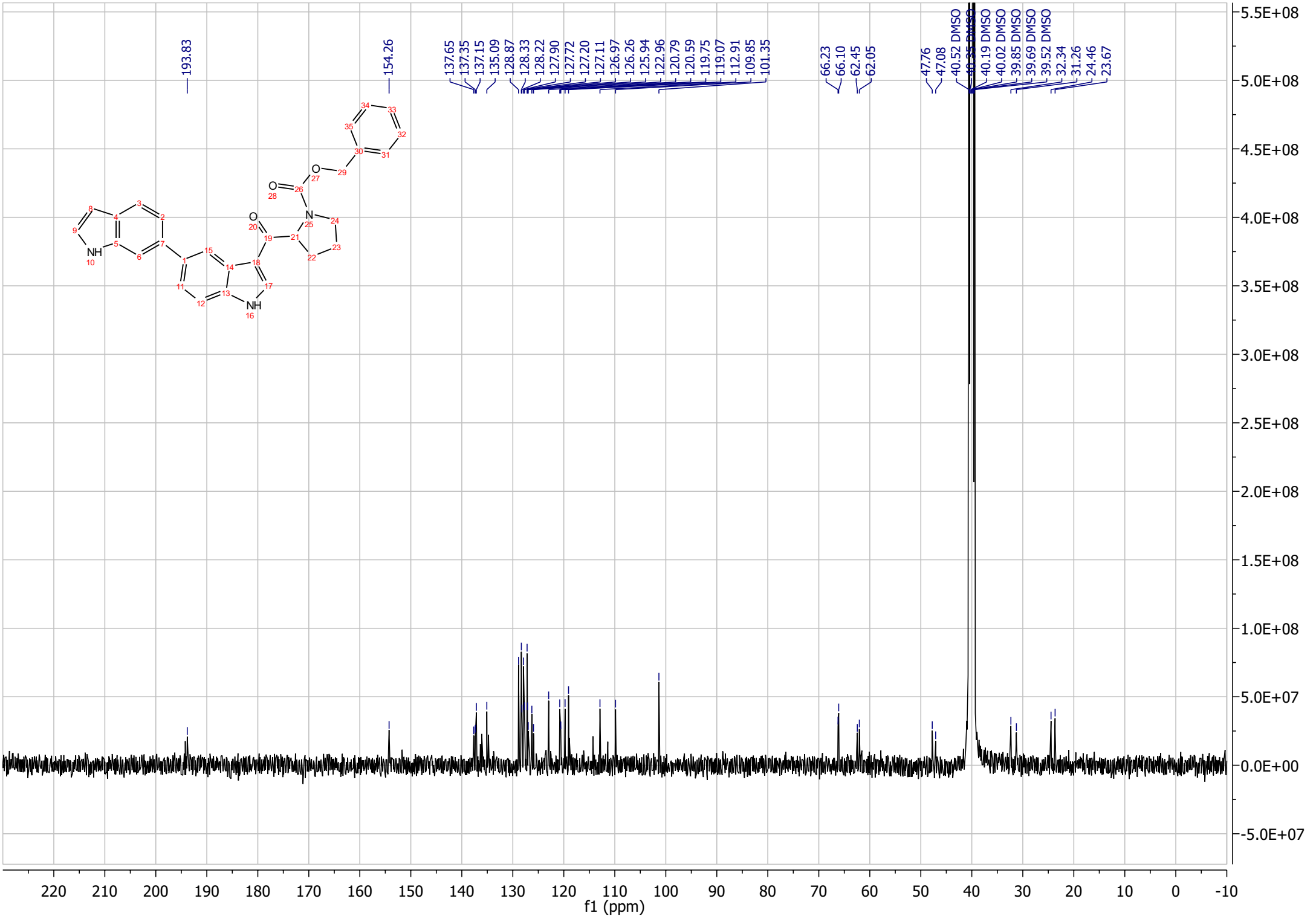
144.68
142.02
137.66
136.97
134.14
129.09
128.82
128.62
128.22
128.12
127.59
126.62
124.76
124.02
123.36
120.84
118.82
109.93
101.41
65.62
40.52 DMSO
40.45 DMSO
40.35 DMSO
40.27 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.85 DMSO
39.69 DMSO
39.52 DMSO
35.26
18.39
NH
10
NH
17
O
21
O
22
1.70E+09
1.60E+09
1.50E+09
1.40E+09
1.30E+09
1.20E+09
1.10E+09
1.00E+09
9.00E+08
8.00E+08
7.00E+08
6.00E+08
5.00E+08
4.00E+08
3.00E+08
2.00E+08
1.00E+08
0.00E+00
-1.00E+08
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


12.07 12.06 12.04 12.04 11.12 11.11 11.11 8.53 8.53 8.49 8.48 8.48 8.46 8.45 7.67 7.65 7.64 7.63 7.62 7.61 7.58 7.58 7.57 7.57 7.57 7.48 7.40 7.39 7.38 7.38 7.37 7.36 7.35 7.35 7.34 7.34 7.33 7.33 7.12 7.10 7.10 7.09 7.02 7.01 6.99 6.46 6.46 6.45 5.28 5.27 5.10 5.08 5.02 4.99 4.94 4.91 3.58 3.58 3.57 HDO 3.56 HDO 3.56 3.55 HDO 3.54 3.53 3.53 3.52 3.51 3.50 2.52 DMSO 2.51 DMSO 2.51 DMSO 2.51 DMSO 2.50 DMSO 1.93 1.93 1.92 1.91 1.91 1.90 1.89 1.88
NH 10
NH 16
O 20
O 27
O 28
N 25
3.63 3.02 7.73 0.75 14.22 1.03 16.05 6.99 3.86 3.24 3.81 5.69 2.06 14.82 4.17 2.13 9.44
f1 (ppm)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154.26
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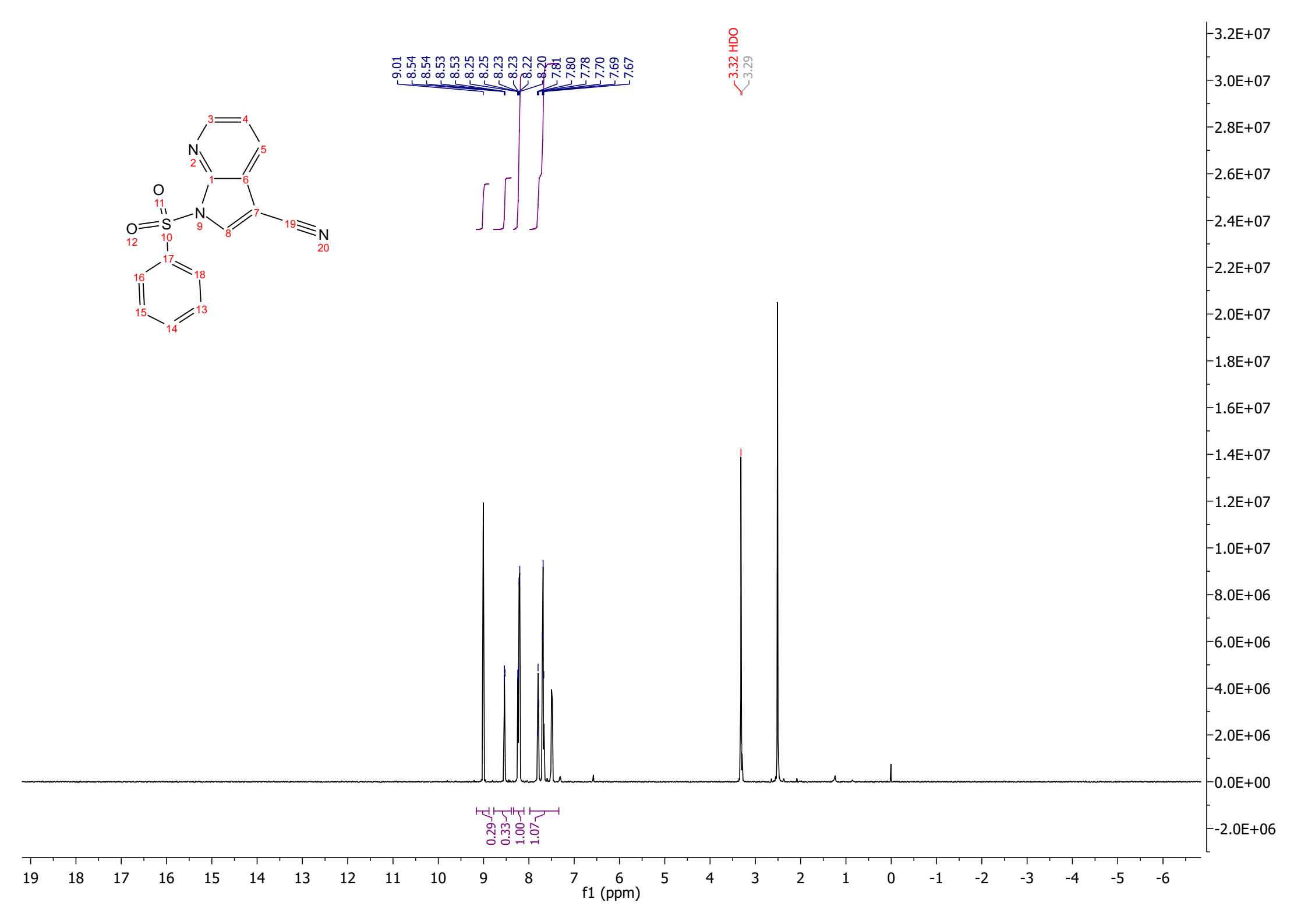
137.35
137.15
135.09
128.87
128.33
128.22
127.90
127.72
127.20
127.11
126.97
126.26
125.94
122.96
120.79
120.59
119.75
119.07
112.91
109.85
101.35
66.23
66.10
62.45
62.05
47.76
47.08
40.52 DMSO
40.35 DMSO
40.19 DMSO
40.02 DMSO
39.85 DMSO
39.69 DMSO
39.52 DMSO
32.34
31.26
24.46
23.67
5.5E+08
5.0E+08
4.5E+08
4.0E+08
3.5E+08
3.0E+08
2.5E+08
2.0E+08
1.5E+08
1.0E+08
5.0E+07
0.0E+00
-5.0E+07
220
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)


9.01
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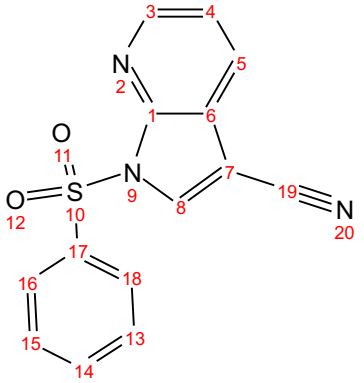
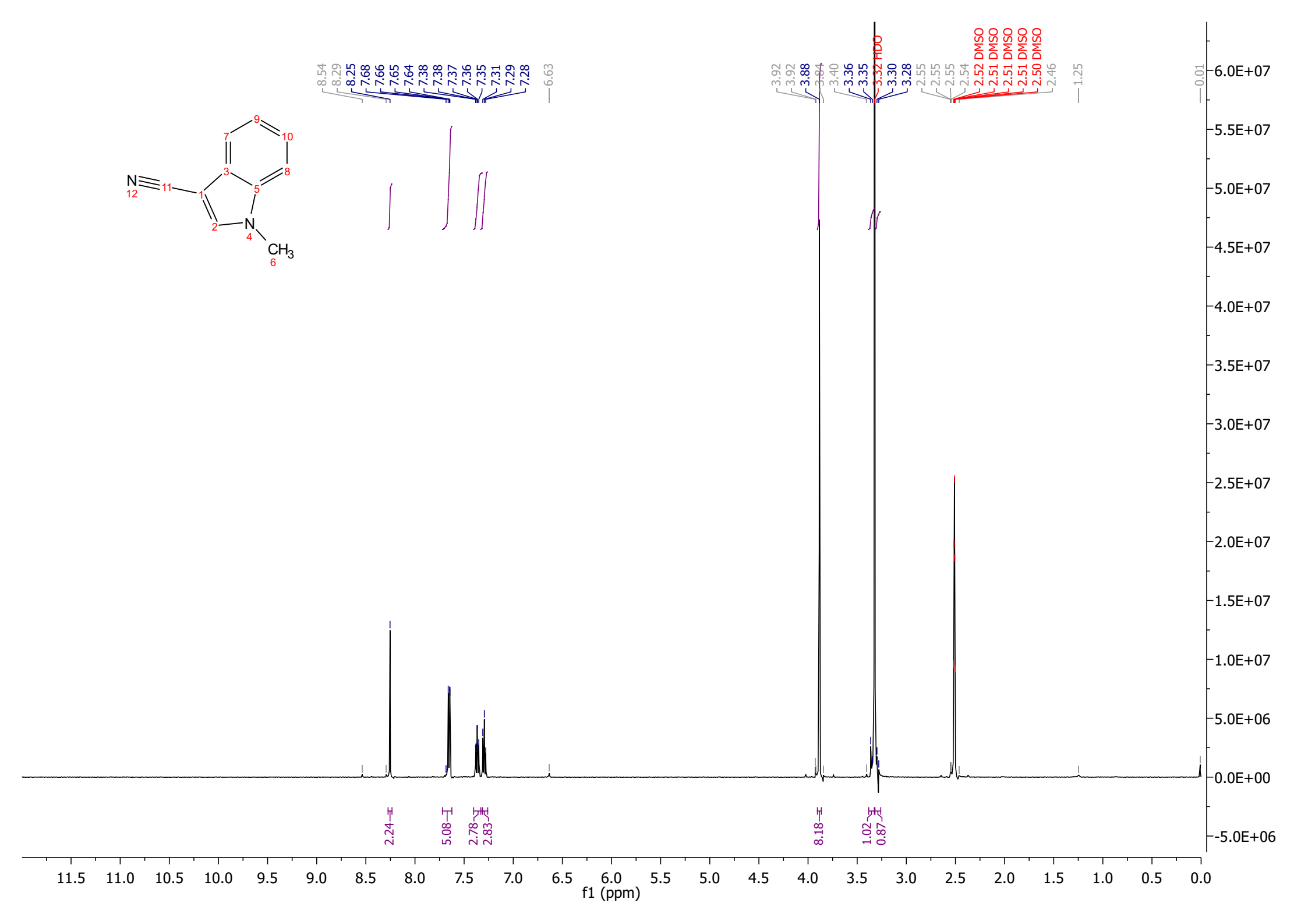
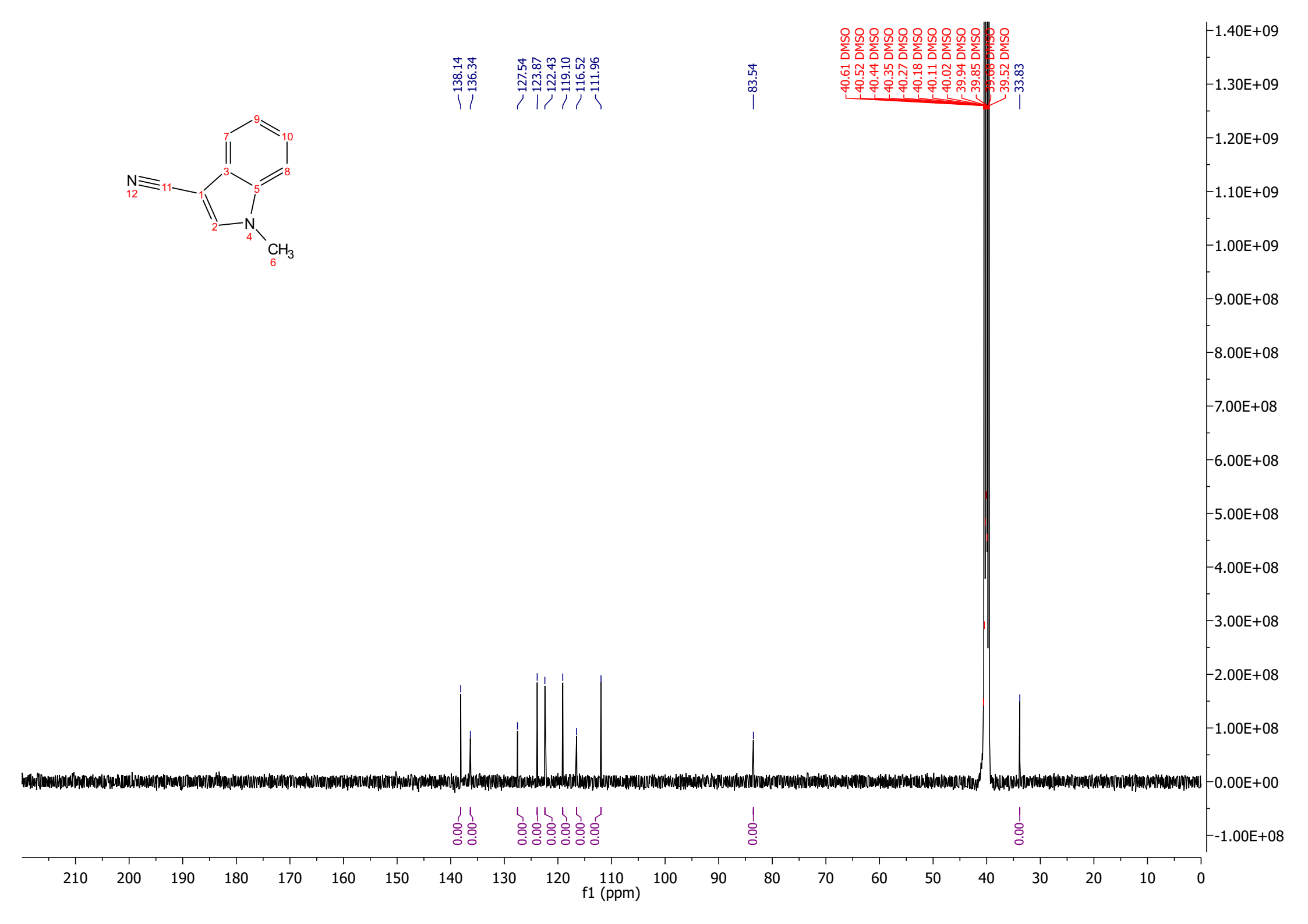
8.54
8.53
8.53
8.25
8.25
8.23
8.23
8.22
8.20
7.81
7.80
7.78
7.70
7.69
7.67
3.32 HDO
3.29
0.29
0.33
1.00
1.07
f1 (ppm)

1-(phenylsulfonyl)-1H-pyrrolo[2,3-b]pyridine-3-carbonitrile



A2


8.54
8.29
8.25
7.68
7.66
7.65
7.64
7.38
7.38
7.37
7.36
7.35
7.31
7.29
7.28
6.63
3.92
3.92
3.88
3.84
3.40
3.36
3.35
3.32 HDO
3.30
3.28
2.55
2.55
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.46
1.25
0.01
N
12
11
1
2
3
4
5
6
7
8
9
10
CH3
2.24
5.08
2.78
2.83
8.18
1.02
0.87
6.0E+07
5.5E+07
5.0E+07
4.5E+07
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
-5.0E+06
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
f1 (ppm)


138.14
136.34
127.54
123.87
122.43
119.10
116.52
111.96
83.54
40.61 DMSO
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.27 DMSO
40.18 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.77 DMSO
39.52 DMSO
33.83
N
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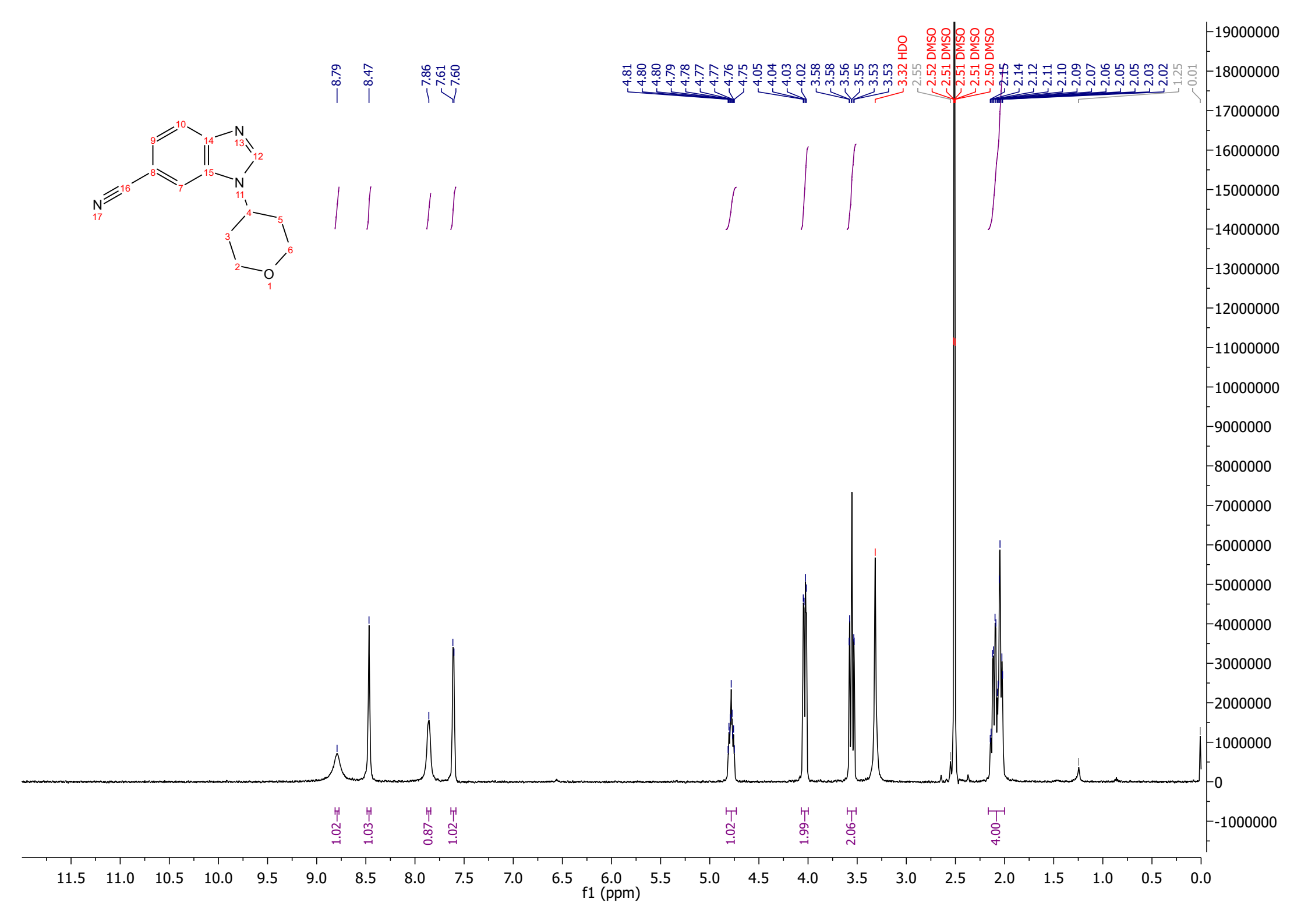
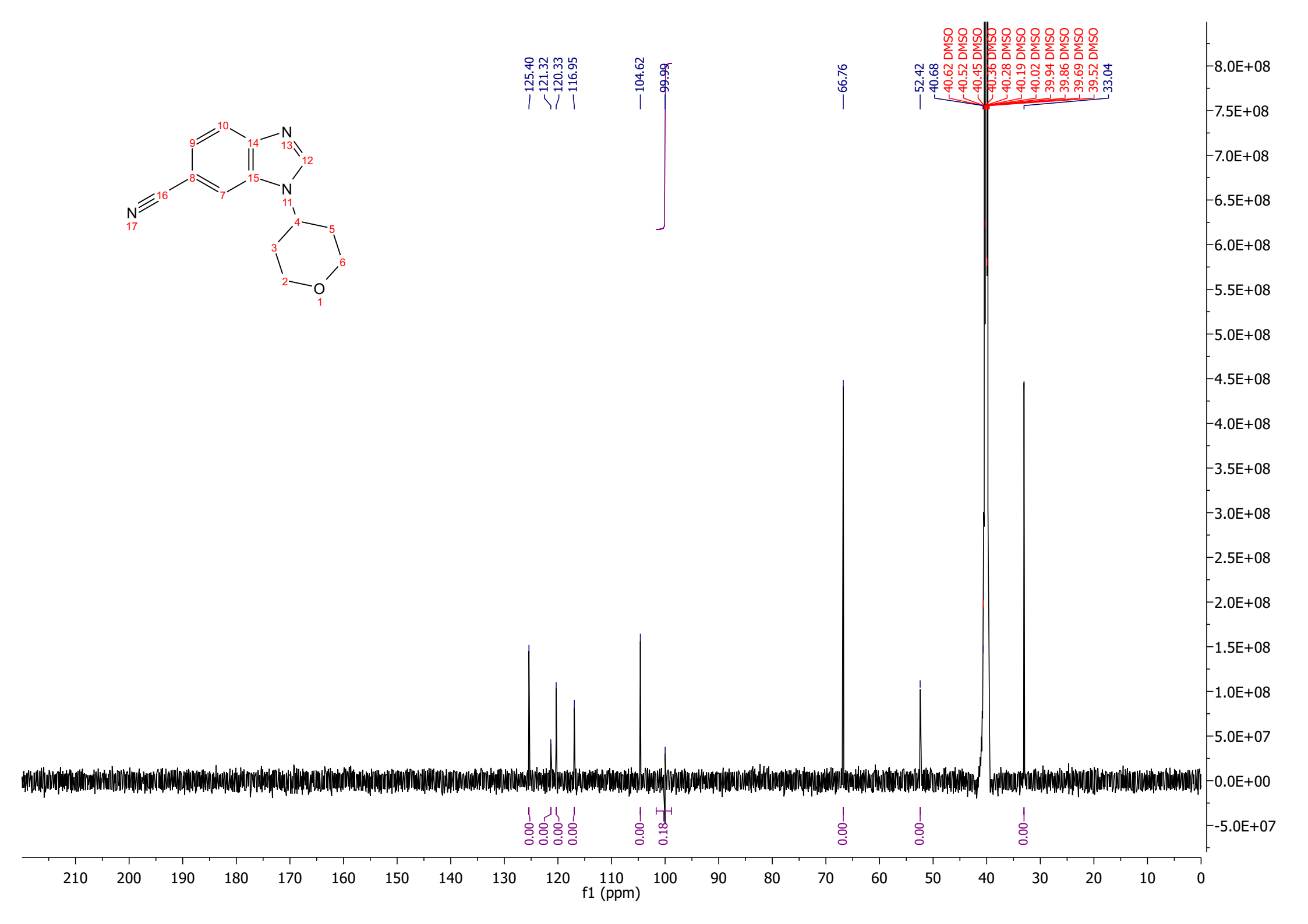
11
1
2
3
4
5
6
7
8
9
10
CH3
0.00
f1 (ppm)


8.79
8.47
7.86
7.61
7.60
4.81
4.80
4.80
4.79
4.78
4.77
4.77
4.76
4.75
4.05
4.04
4.03
4.02
3.58
3.58
3.56
3.55
3.53
3.53
3.32 HDO
2.55
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.15
2.14
2.12
2.11
2.10
2.09
2.07
2.06
2.05
2.05
2.03
2.02
1.25
0.01
1.02
1.03
0.87
1.02
1.02
1.99
2.06
4.00
f1 (ppm)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121.32
120.33
116.95
104.62
99.99
66.76
52.42
40.68
40.62 DMSO
40.52 DMSO
40.45 DMSO
40.36 DMSO
40.28 DMSO
40.19 DMSO
40.02 DMSO
39.94 DMSO
39.86 DMSO
39.69 DMSO
39.52 DMSO
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0.00
0.00
0.00
0.18
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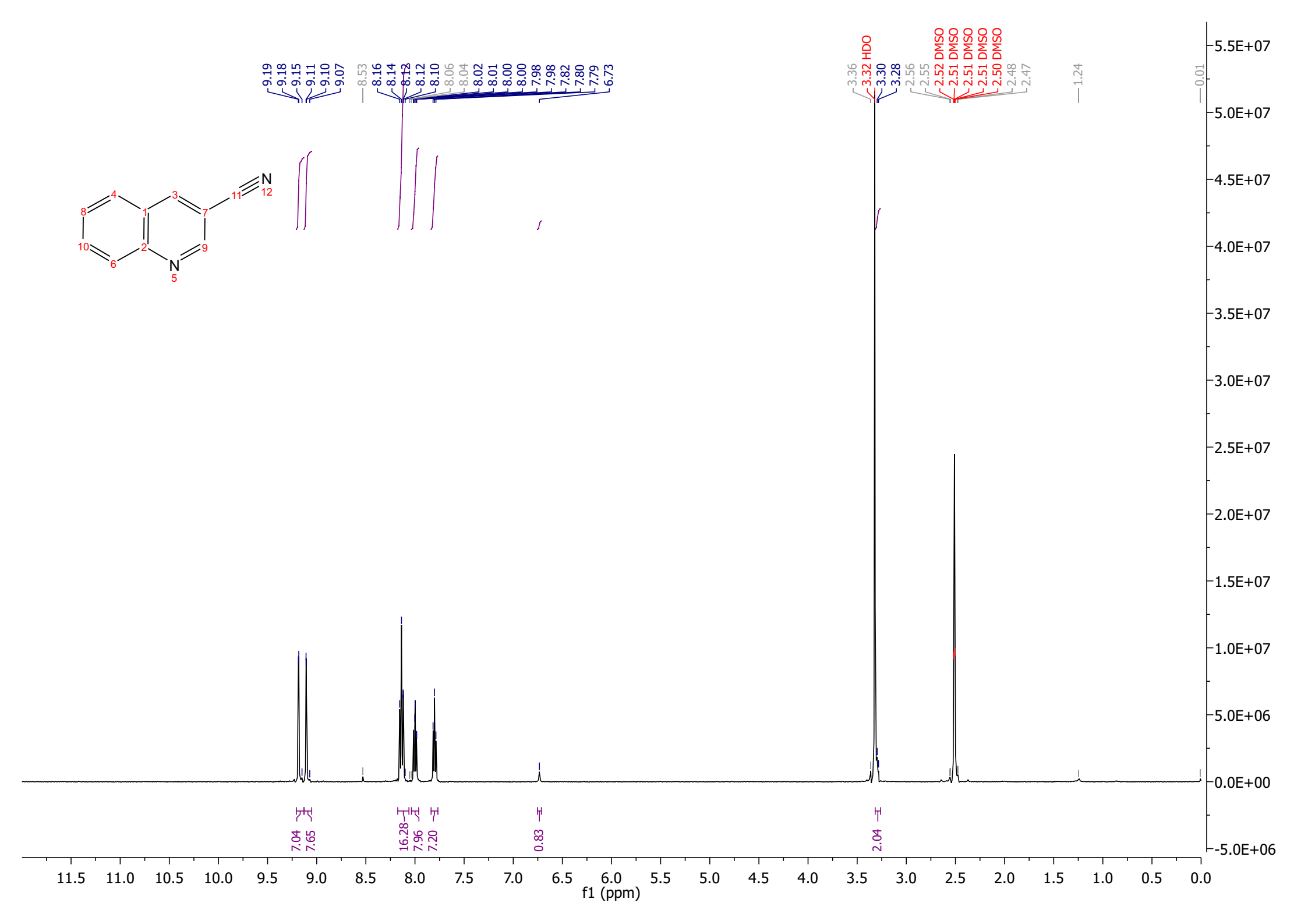
0.00
0.00
f1 (ppm)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8.16
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8.12
8.10
8.06
8.04
8.02
8.01
8.00
8.00
7.98
7.98
7.82
7.80
7.79
6.73
3.36
3.32 HDO
3.30
3.28
2.56
2.55
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.48
2.47
1.24
0.01
N
12
11
4
3
8
1
7
10
2
9
6
N
5
7.04
7.65
16.28
7.96
7.20
0.83
2.04
5.5E+07
5.0E+07
4.5E+07
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
-5.0E+06
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
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3.0
2.5
2.0
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1.0
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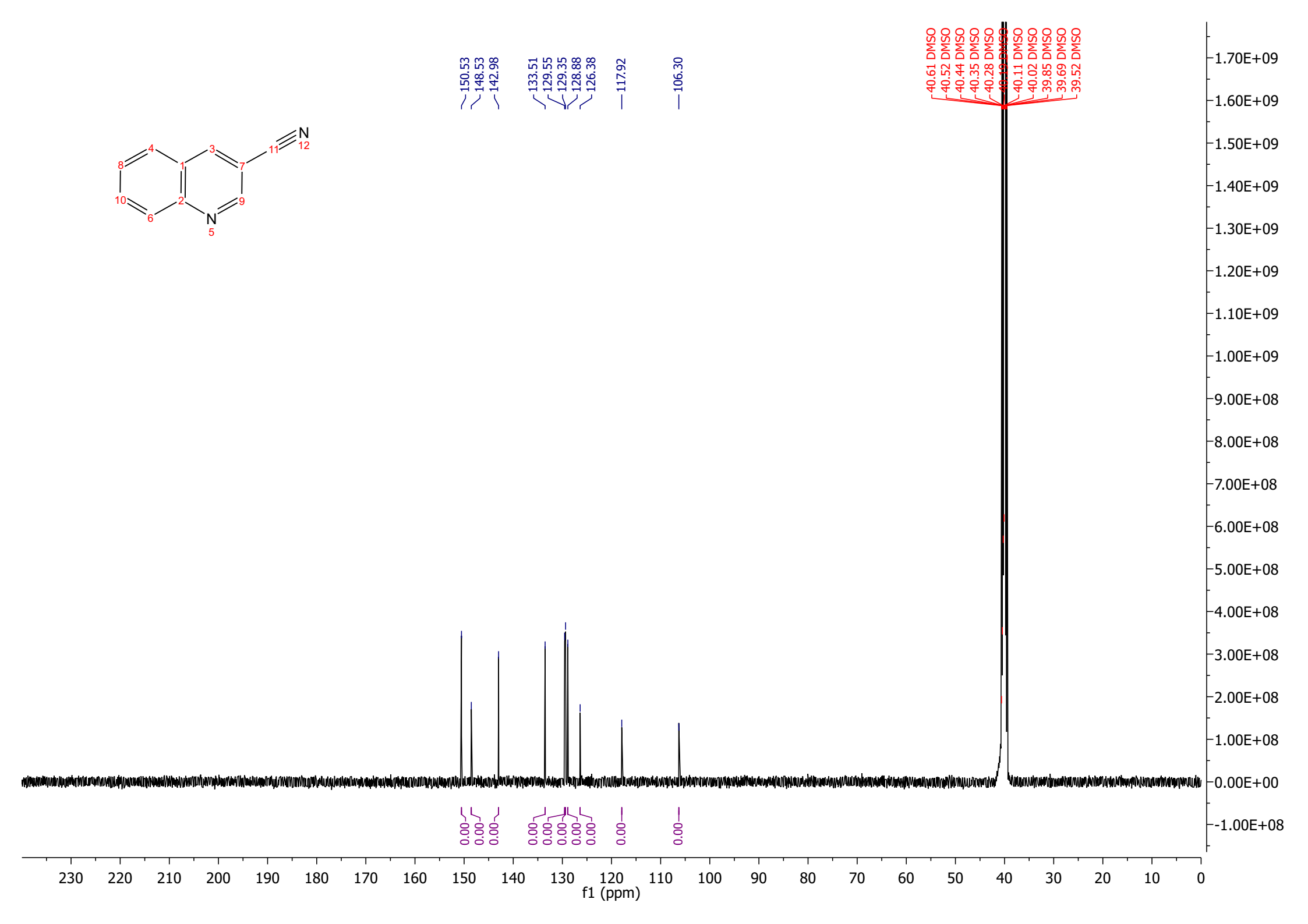
0.0
f1 (ppm)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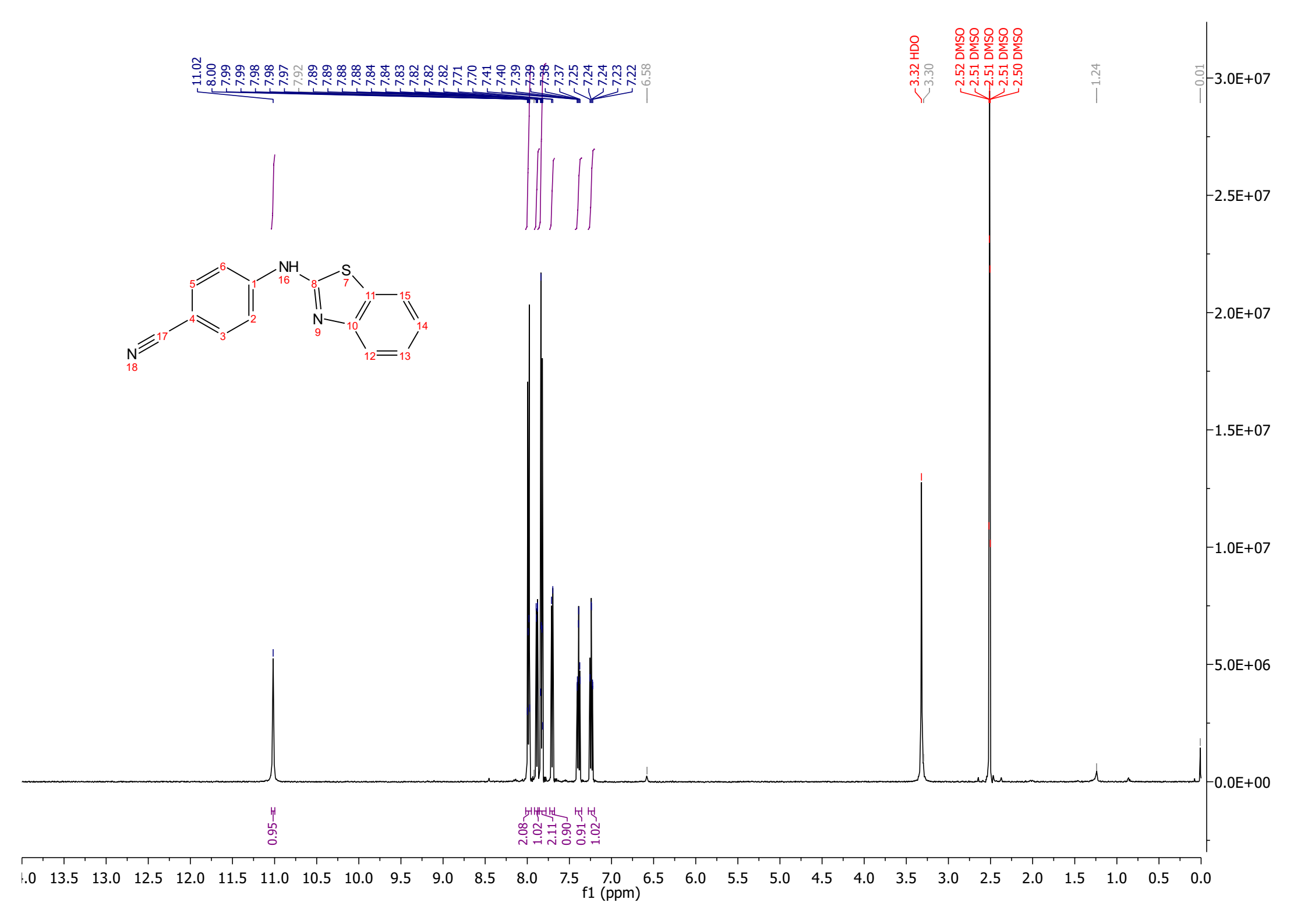
133.51
129.55
129.35
128.88
126.38
117.92
106.30
40.61 DMSO
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.85 DMSO
39.69 DMSO
39.52 DMSO
N
12
11
4
3
8
1
7
10
2
9
6
N
5
0.00
0.00
0.00
0.00
0.00
0.00
0.00
0.00
0.00
0.00
1.70E+09
1.60E+09
1.50E+09
1.40E+09
1.30E+09
1.20E+09
1.10E+09
1.00E+09
9.00E+08
8.00E+08
7.00E+08
6.00E+08
5.00E+08
4.00E+08
3.00E+08
2.00E+08
1.00E+08
0.00E+00
-1.00E+08
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.00
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7.98
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7.92
7.89
7.89
7.88
7.88
7.84
7.84
7.83
7.82
7.82
7.82
7.71
7.70
7.41
7.40
7.39
7.39
7.38
7.37
7.25
7.24
7.24
7.23
7.22
6.58
3.32 HDO
3.30
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
1.24
0.01
NH
16
S
7
N
9
N
18
0.95
2.08
1.02
2.11
0.90
0.91
1.02
3.0E+07
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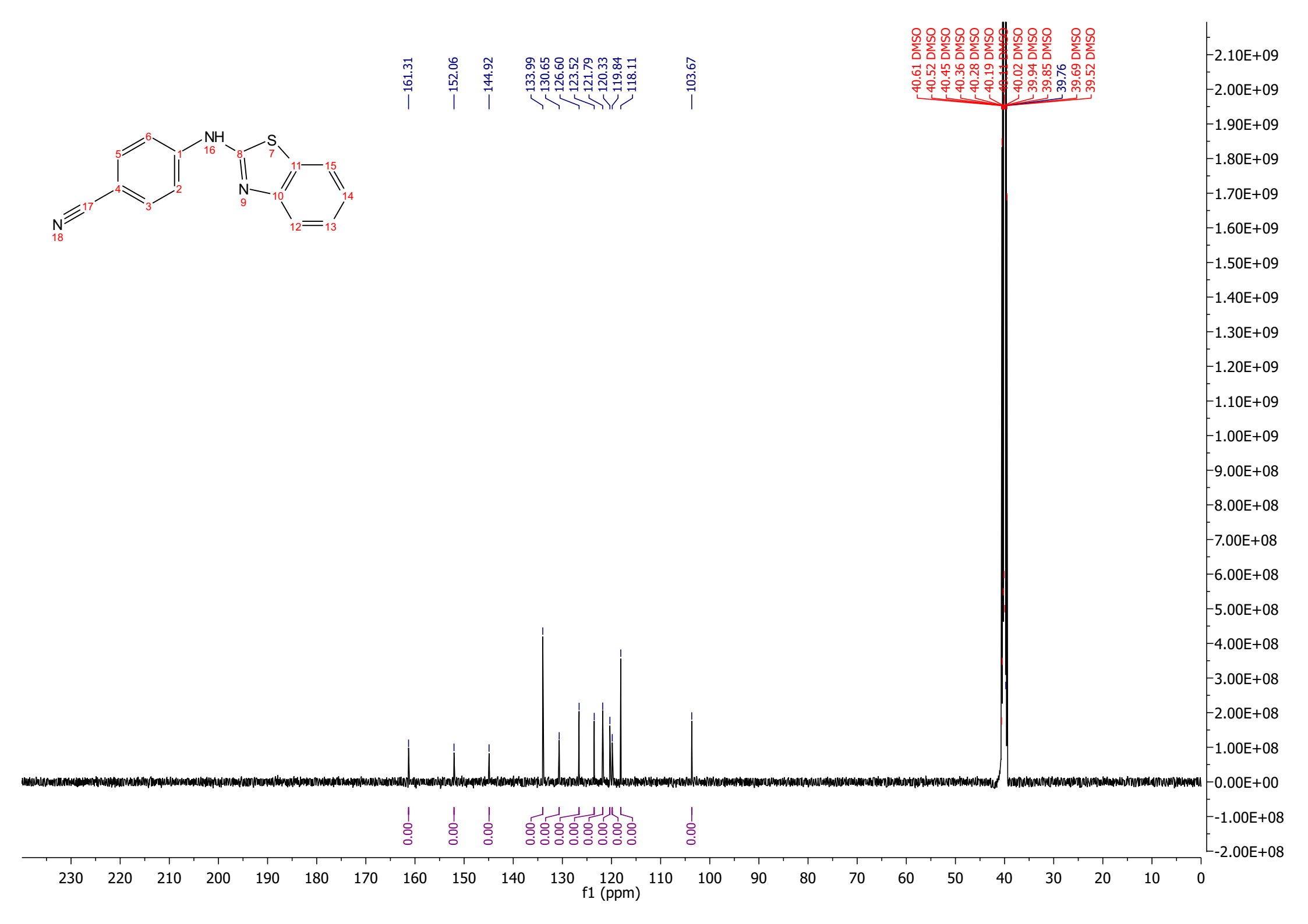
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
f1 (ppm)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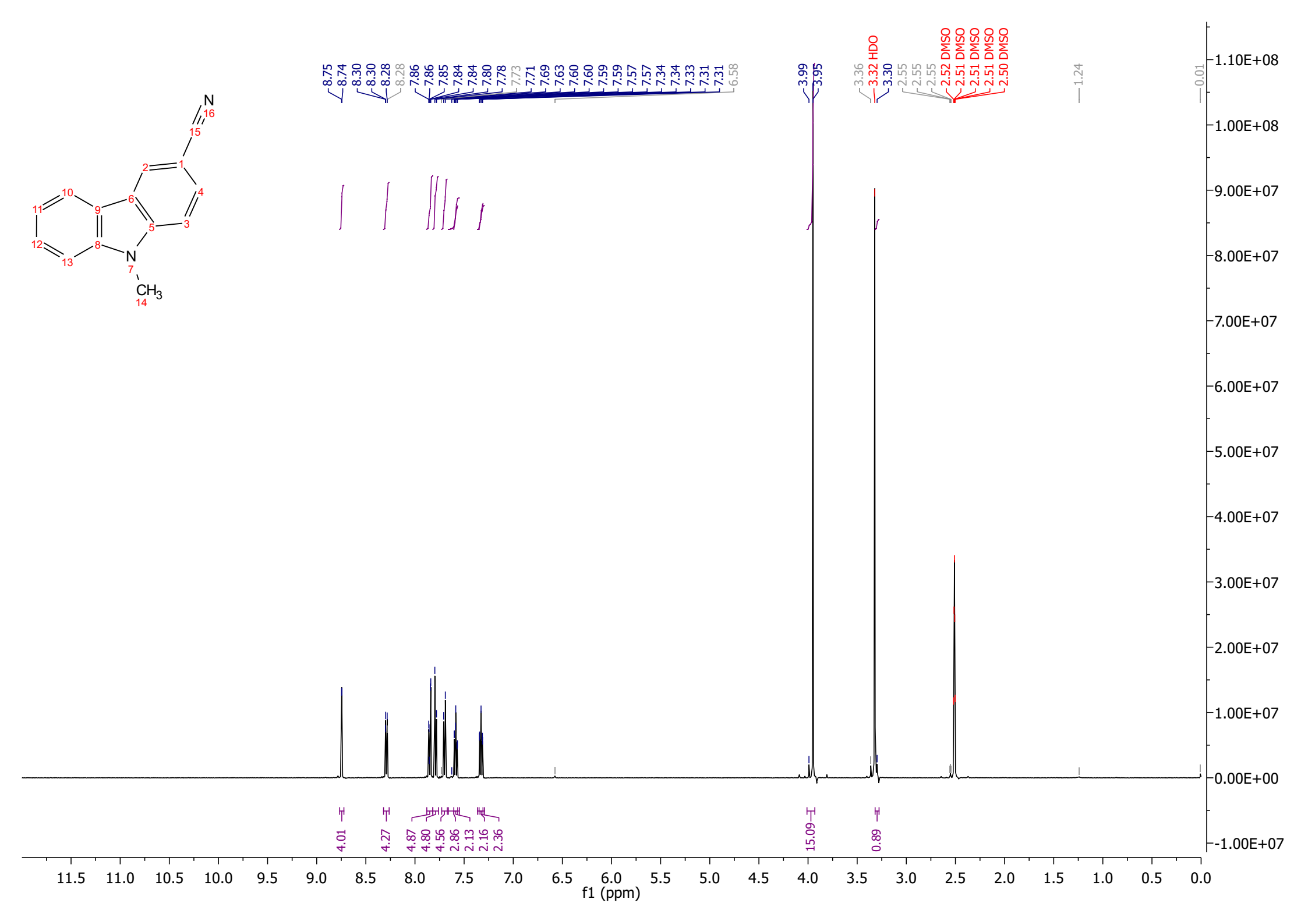
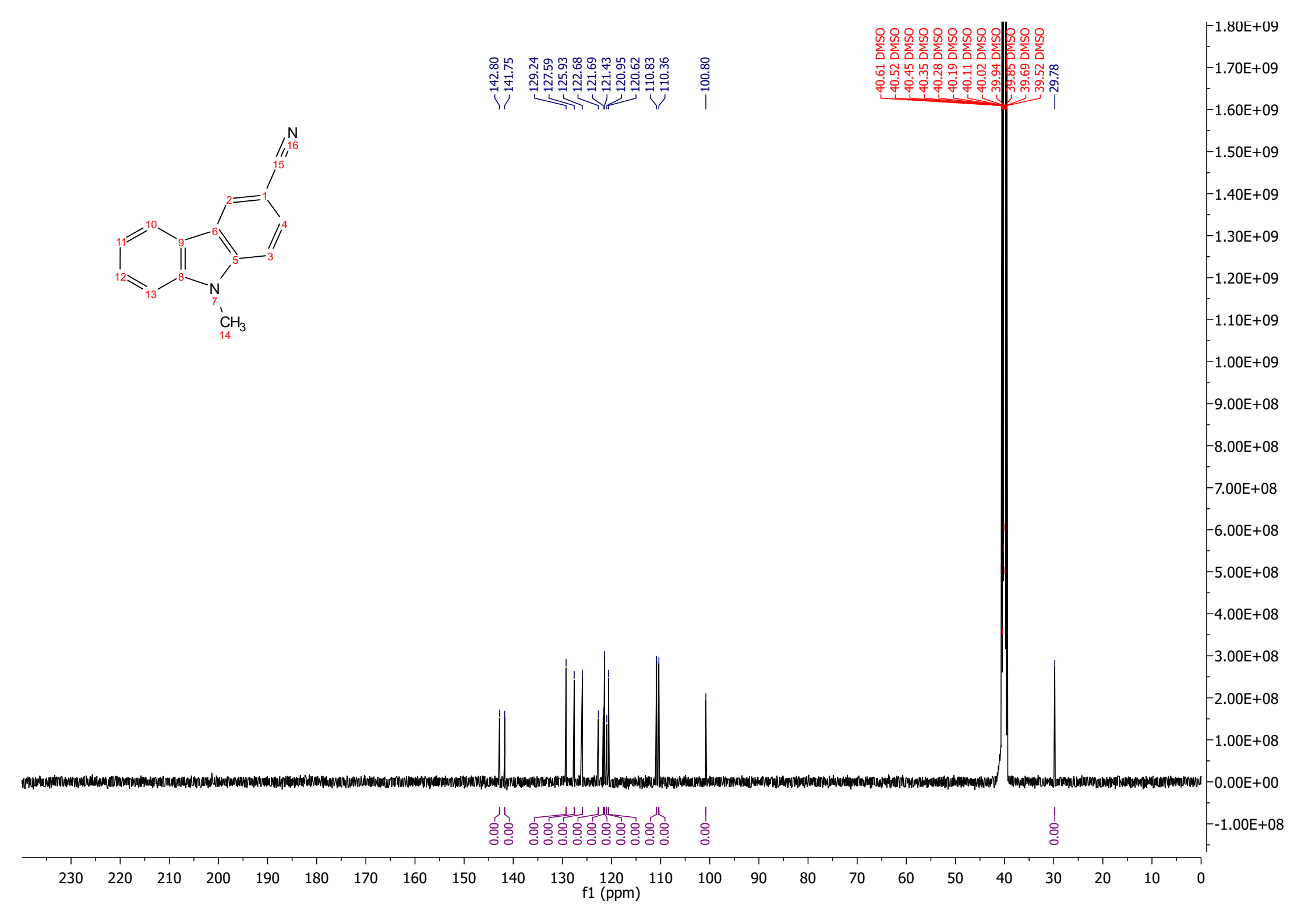
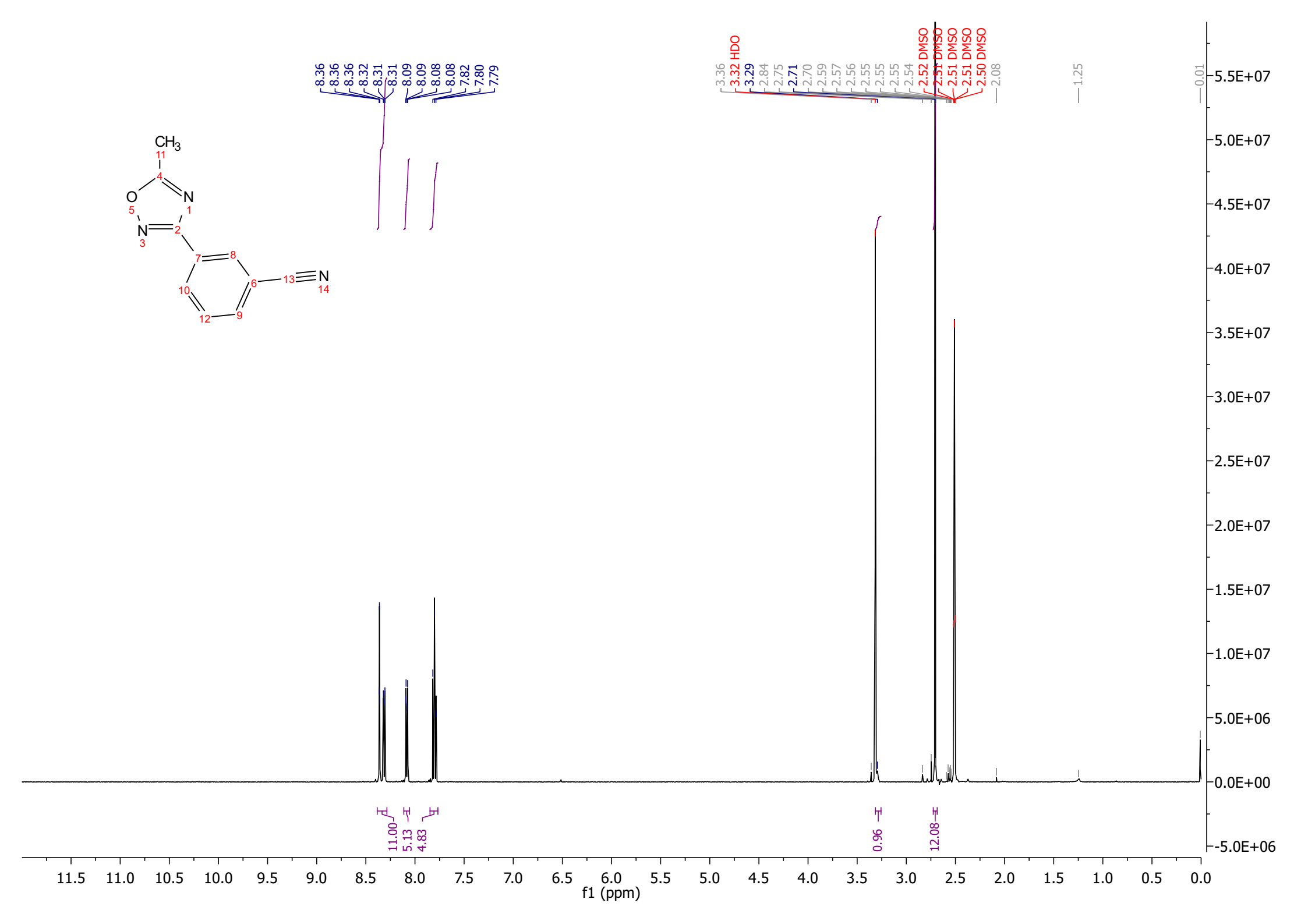
152.06
144.92
133.99
130.65
126.60
123.52
121.79
120.33
119.84
118.11
103.67
40.61 DMSO
40.52 DMSO
40.45 DMSO
40.36 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.76
39.69 DMSO
39.52 DMSO
NH
16
S
7
N
9
N
18
f1 (ppm)


8.75
8.74
8.30
8.30
8.28
8.28
7.86
7.86
7.85
7.84
7.84
7.80
7.78
7.73
7.71
7.69
7.63
7.60
7.60
7.59
7.59
7.57
7.57
7.34
7.34
7.33
7.31
7.31
6.58
3.99
3.95
3.36
3.32 HDO
3.30
2.55
2.55
2.55
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
1.24
0.01
N
16
15
1
2
4
3
5
6
9
10
11
12
13
8
N
7
CH3
14
4.01
4.27
4.87
4.80
4.56
2.86
2.13
2.16
2.36
15.09
0.89
1.10E+08
1.00E+08
9.00E+07
8.00E+07
7.00E+07
6.00E+07
5.00E+07
4.00E+07
3.00E+07
2.00E+07
1.00E+07
0.00E+00
-1.00E+07
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
f1 (ppm)


142.80
141.75
129.24
127.59
125.93
122.68
121.69
121.43
120.95
120.62
110.83
110.36
100.80
40.61 DMSO
40.52 DMSO
40.45 DMSO
40.35 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.69 DMSO
39.52 DMSO
29.78
N
16
15
1
2
4
3
6
5
10
9
11
12
8
13
N
7
CH3
14
0.00
f1 (ppm)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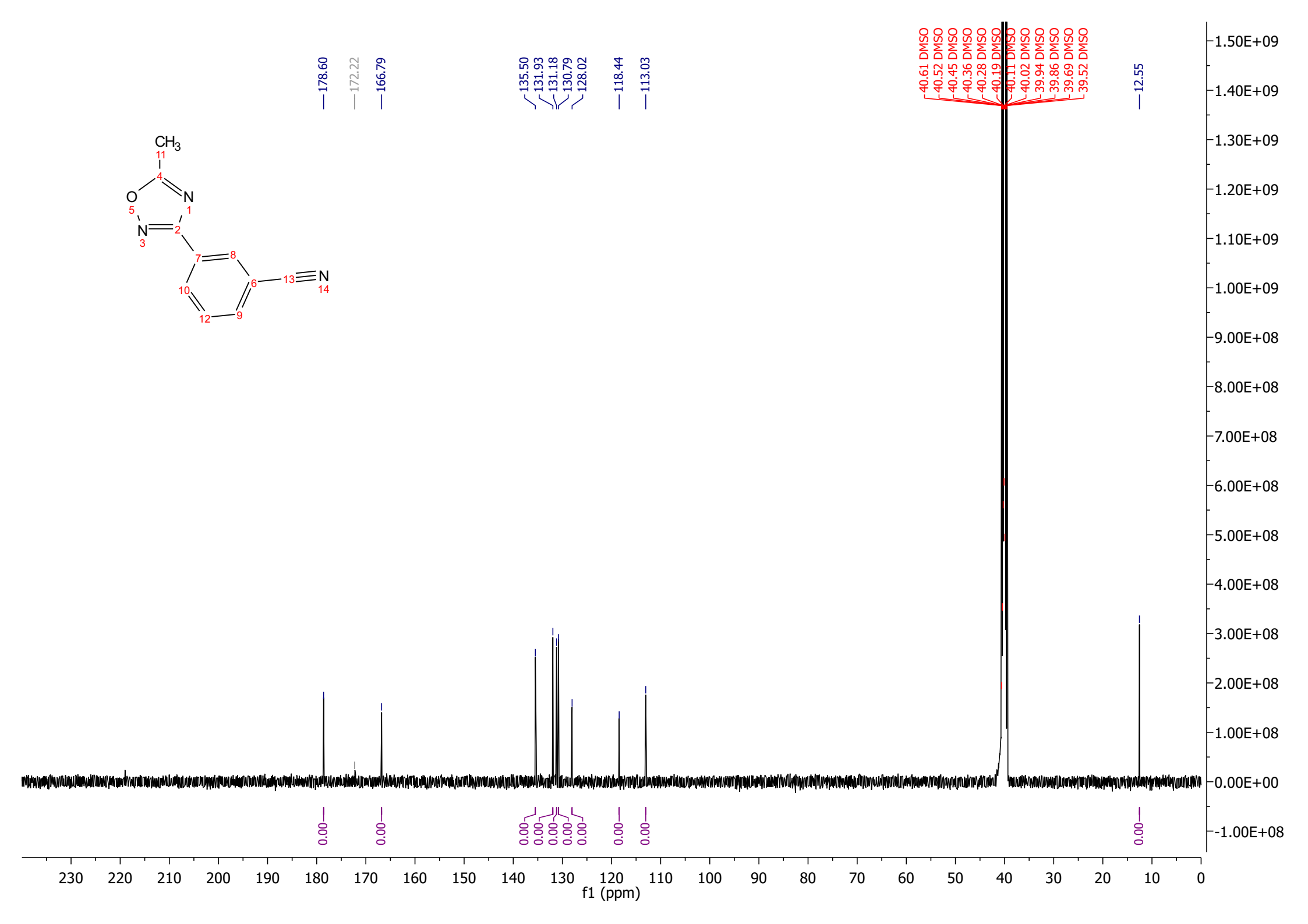
8.36
8.36
8.32
8.31
8.31
8.09
8.09
8.08
8.08
7.82
7.80
7.79
3.36
3.32 HDO
3.29
2.84
2.75
2.71
2.70
2.59
2.57
2.56
2.55
2.55
2.55
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.08
1.25
0.01
CH3
11
4
O
5
N
1
N
3
2
7
8
6
13
N
14
10
12
9
11.00
5.13
4.83
0.96
12.08
5.5E+07
5.0E+07
4.5E+07
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
-5.0E+06
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
f1 (ppm)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172.22
166.79
135.50
131.93
131.18
130.79
128.02
118.44
113.03
40.61 DMSO
40.52 DMSO
40.45 DMSO
40.36 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.86 DMSO
39.69 DMSO
39.52 DMSO
12.55
CH3
11
4
N
1
O
5
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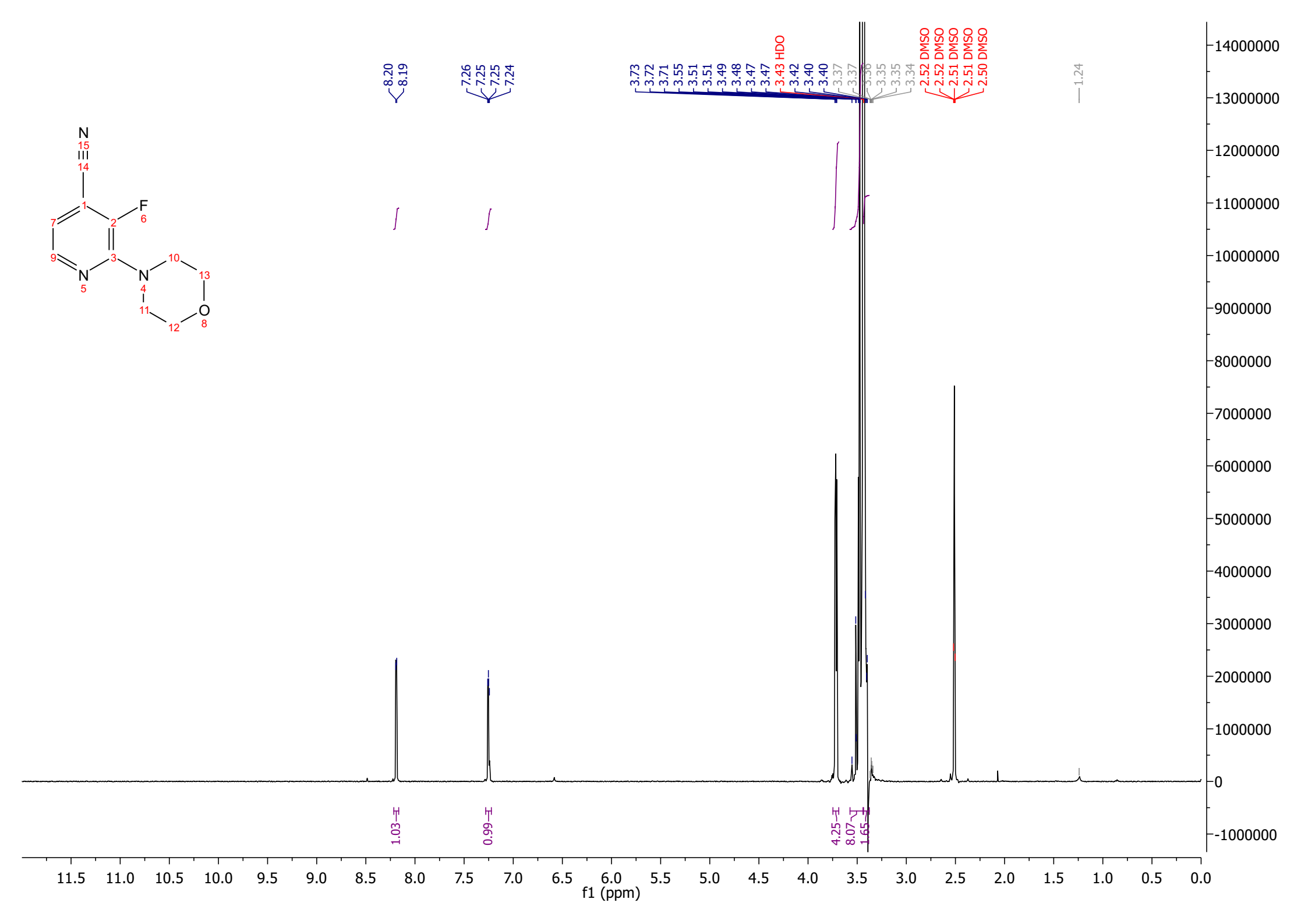
13
N
14
10
12
9
0.00
f1 (ppm)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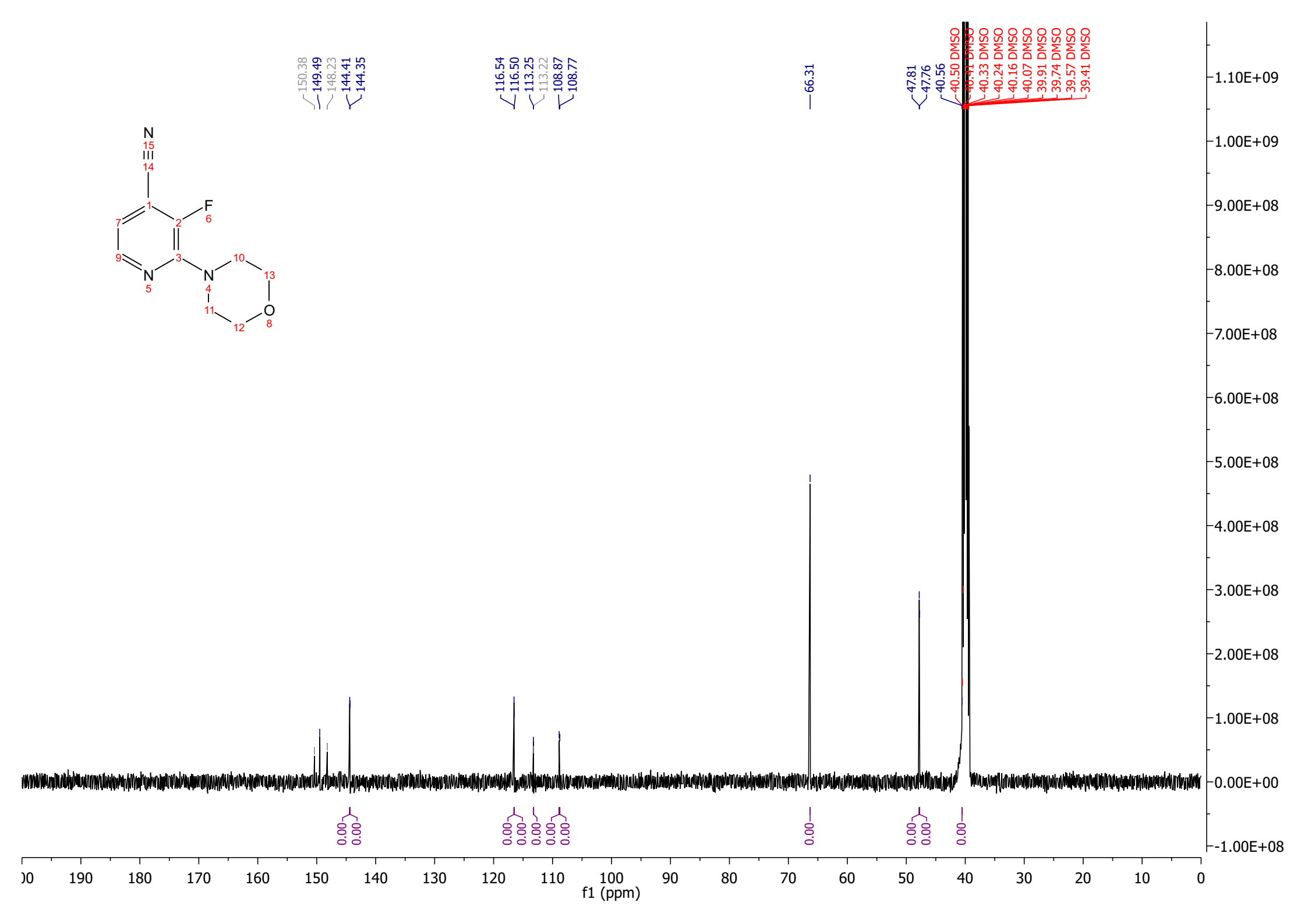
8.19
7.26
7.25
7.25
7.24
3.73
3.72
3.71
3.55
3.51
3.51
3.49
3.48
3.47
3.47
3.43 HDO
3.42
3.40
3.40
3.37
3.37
3.36
3.35
3.35
3.34
2.52 DMSO
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
1.24
1.03
0.99
4.25
8.07
1.65
f1 (ppm)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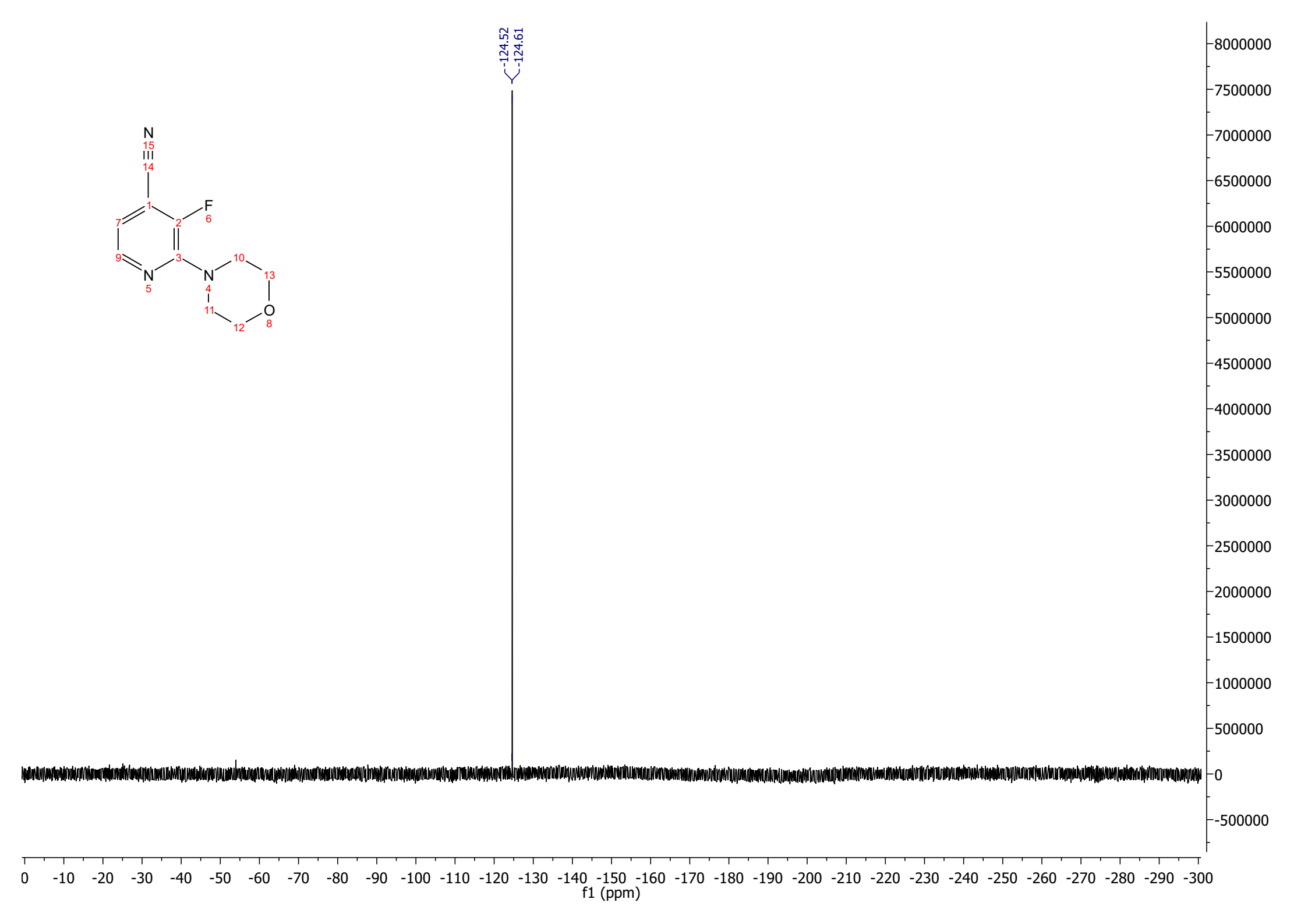
144.41
144.35
116.54
116.50
113.25
113.22
108.87
108.77
66.31
47.81
47.76
40.56
40.50 DMSO
40.41 DMSO
40.33 DMSO
40.24 DMSO
40.16 DMSO
40.07 DMSO
39.91 DMSO
39.74 DMSO
39.57 DMSO
39.41 DMSO
N
15
14
1
F
6
7
2
9
3
10
13
N
5
N
4
11
O
8
12
0.00
0.00
0.00
0.00
0.00
0.00
0.00
0.00
0.00
0.00
1.10E+09
1.00E+09
9.00E+08
8.00E+08
7.00E+08
6.00E+08
5.00E+08
4.00E+08
3.00E+08
2.00E+08
1.00E+08
0.00E+00
-1.00E+08
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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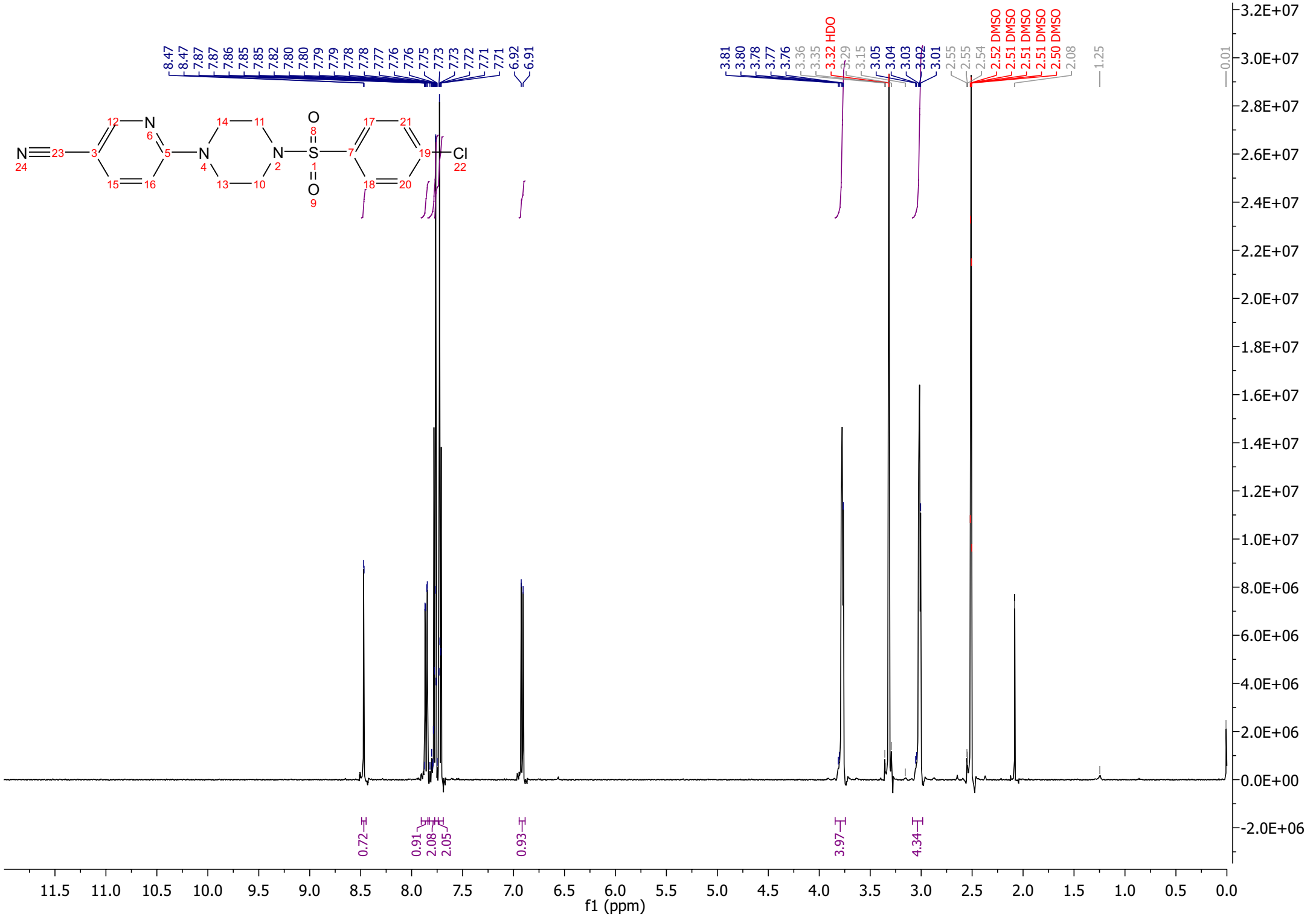
-124.61
N
15
14
1
F
6
7
2
9
3
10
13
N
5
N
4
11
12
O
8
8000000
7500000
7000000
6500000
6000000
5500000
5000000
4500000
4000000
3500000
3000000
2500000
2000000
1500000
1000000
500000
0
-500000
0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210 -220 -230 -240 -250 -260 -270 -280 -290 -300
f1 (ppm)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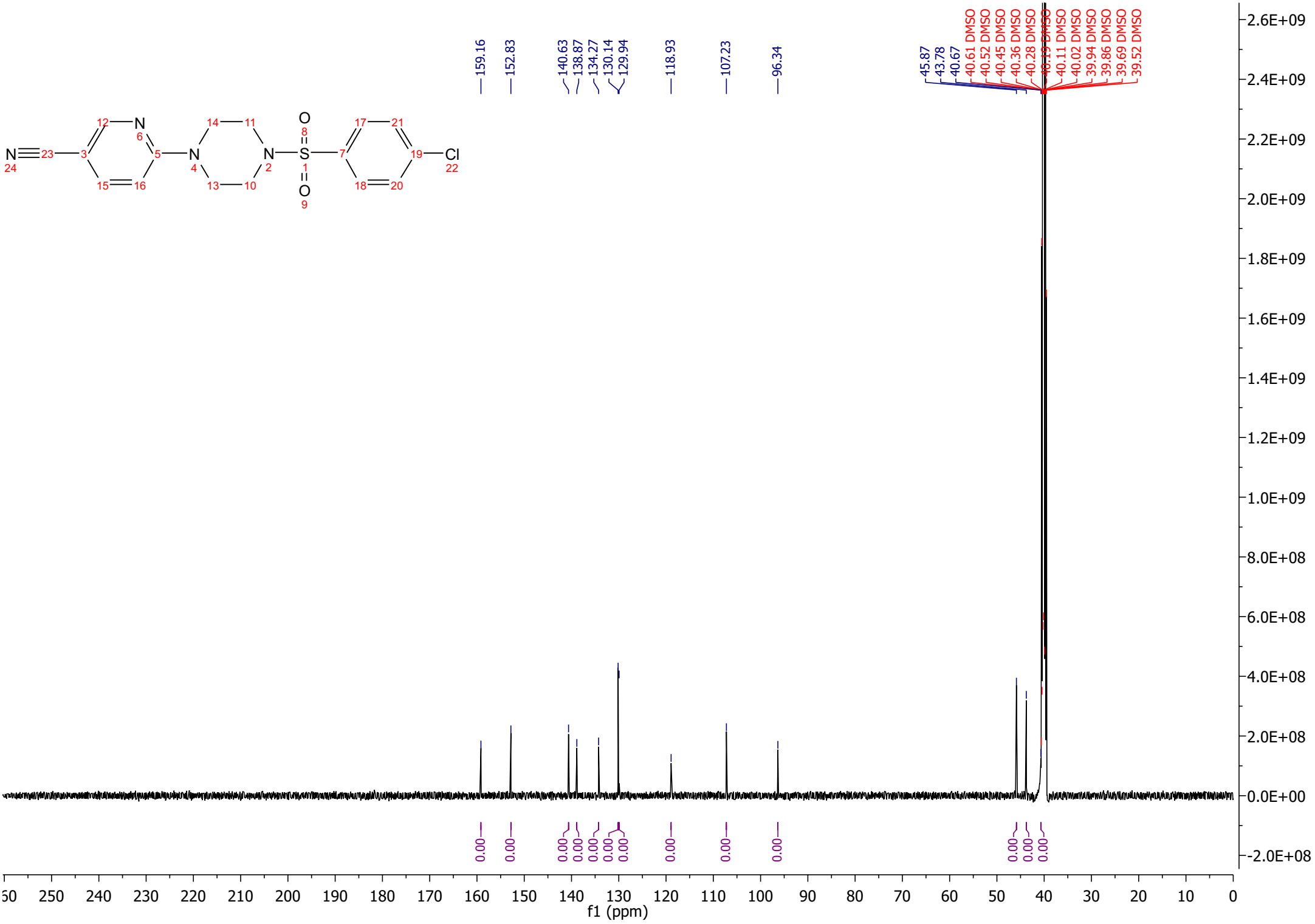
3.81 3.80 3.78 3.77 3.76 3.36 3.35 3.32 HDO 3.29 3.15 3.05 3.04 3.03 3.02 3.01 2.55 2.54 2.52 DMSO 2.51 DMSO 2.51 DMSO 2.51 DMSO 2.50 DMSO 2.08 1.25 0.01
0.72 0.91 2.08 2.05 0.93 3.97 4.34
f1 (ppm)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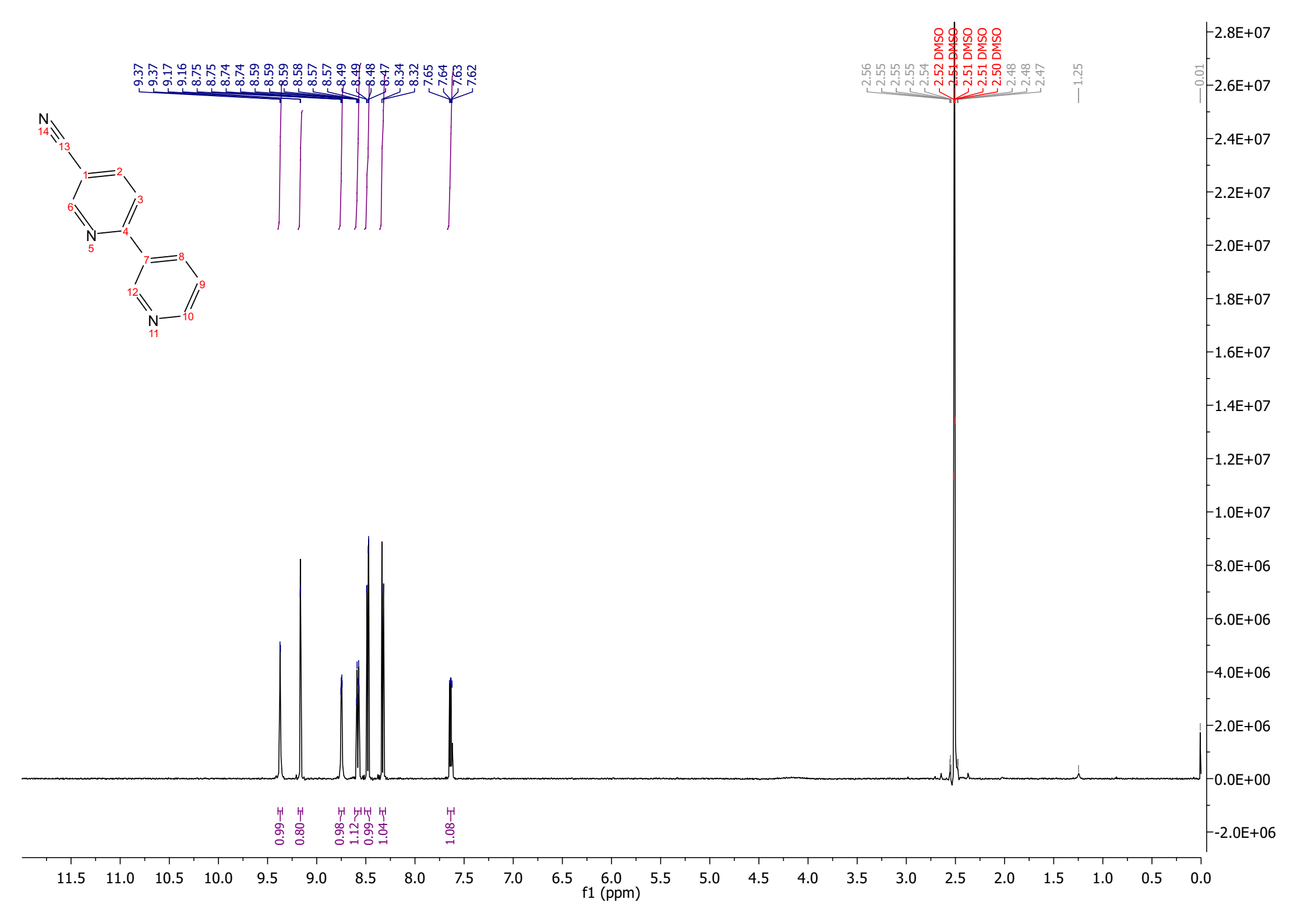
134.27
130.14
129.94
118.93
107.23
96.34
45.87
43.78
40.67
40.61 DMSO
40.52 DMSO
40.45 DMSO
40.36 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.86 DMSO
39.69 DMSO
39.52 DMSO
2.6E+09
2.4E+09
2.2E+09
2.0E+09
1.8E+09
1.6E+09
1.4E+09
1.2E+09
1.0E+09
8.0E+08
6.0E+08
4.0E+08
2.0E+08
0.0E+00
-2.0E+08
0.00
250
240
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.74
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8.59
8.59
8.58
8.57
8.57
8.49
8.49
8.48
8.47
8.34
8.32
7.65
7.64
7.63
7.62
2.56
2.55
2.55
2.55
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.48
2.48
2.47
1.25
0.01
N
14
13
1
2
3
4
5
6
7
8
9
10
11
12
0.99
0.80
0.98
1.12
0.99
1.04
1.08
2.8E+07
2.6E+07
2.4E+07
2.2E+07
2.0E+07
1.8E+07
1.6E+07
1.4E+07
1.2E+07
1.0E+07
8.0E+06
6.0E+06
4.0E+06
2.0E+06
0.0E+00
-2.0E+06
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
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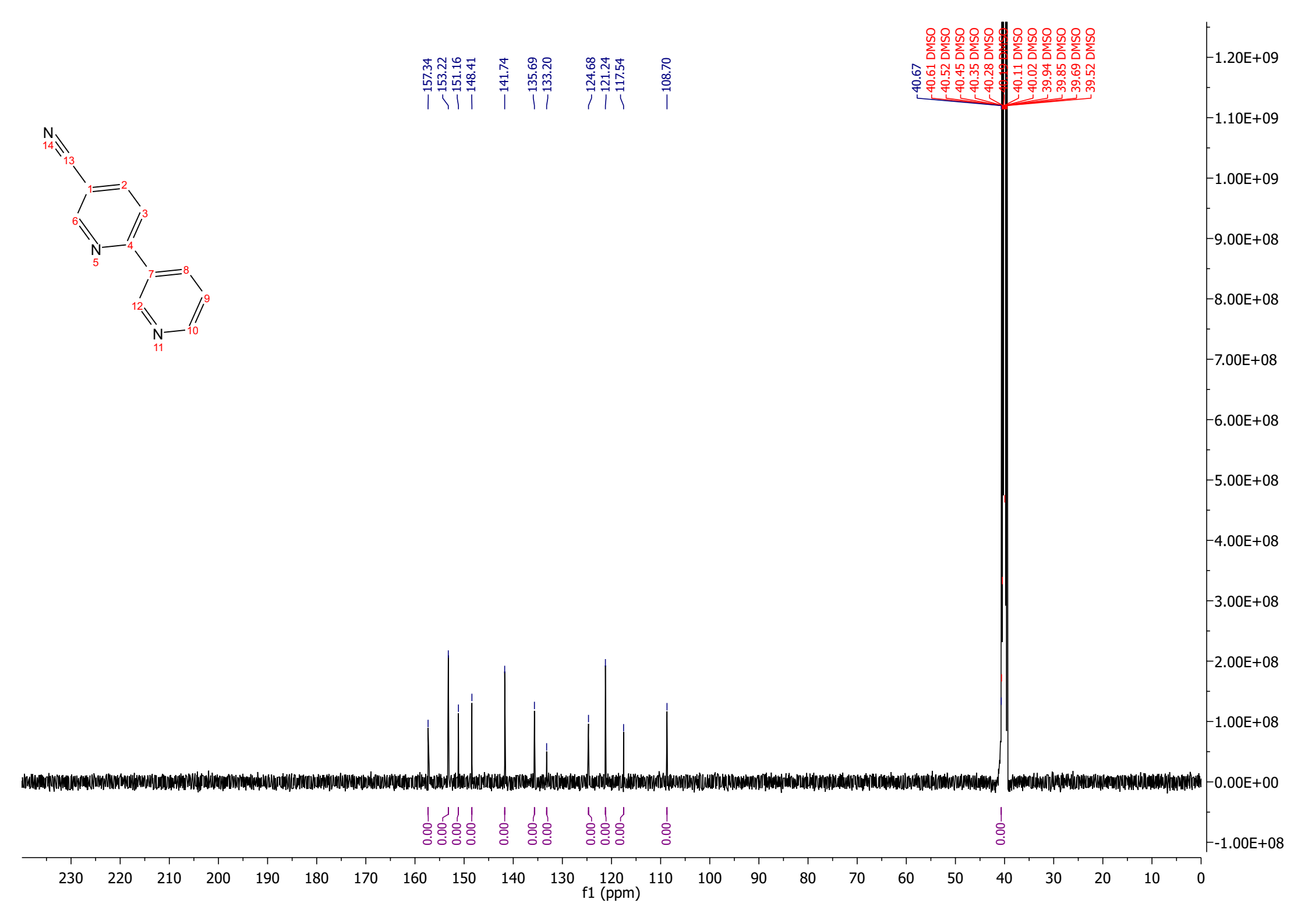
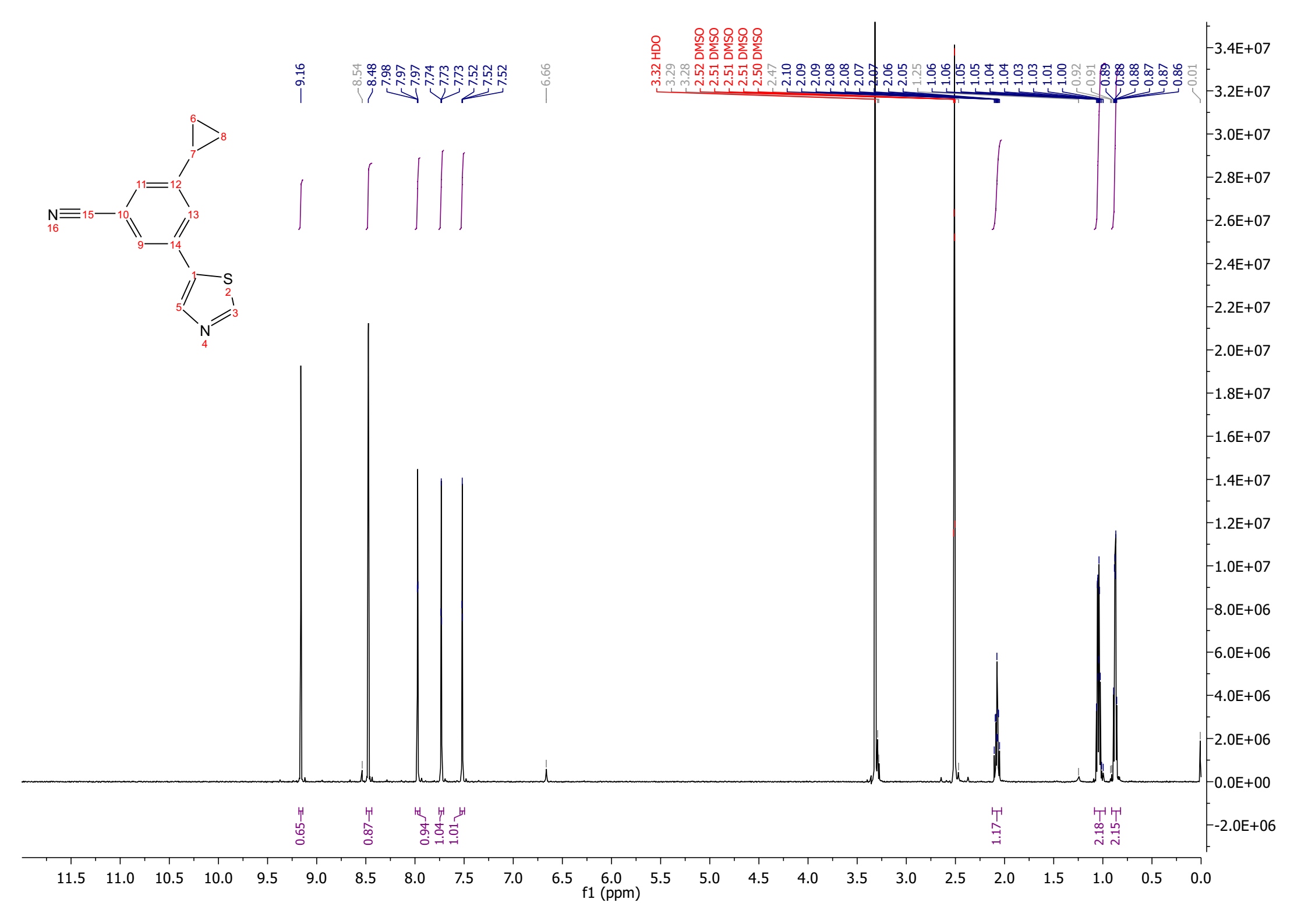
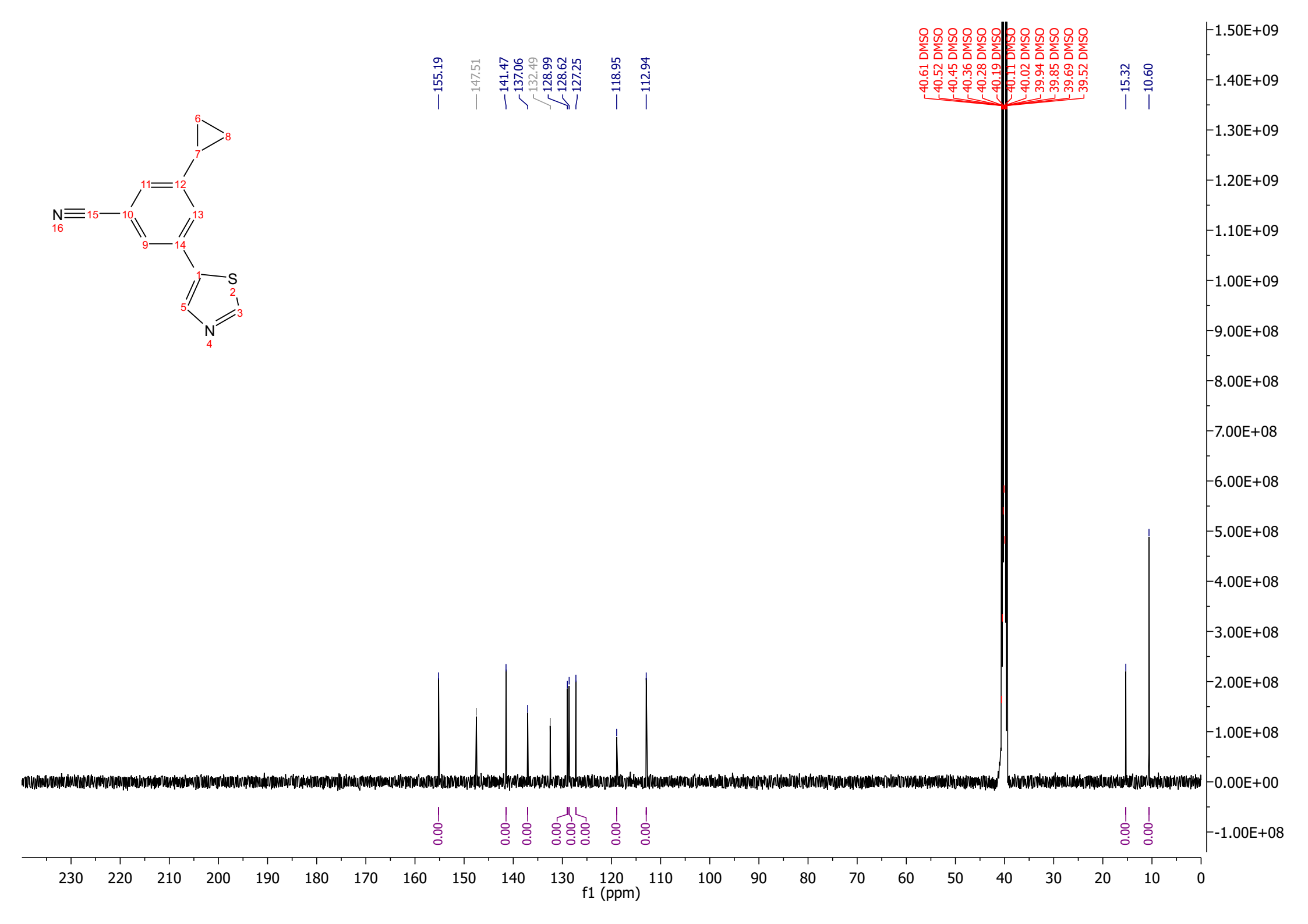
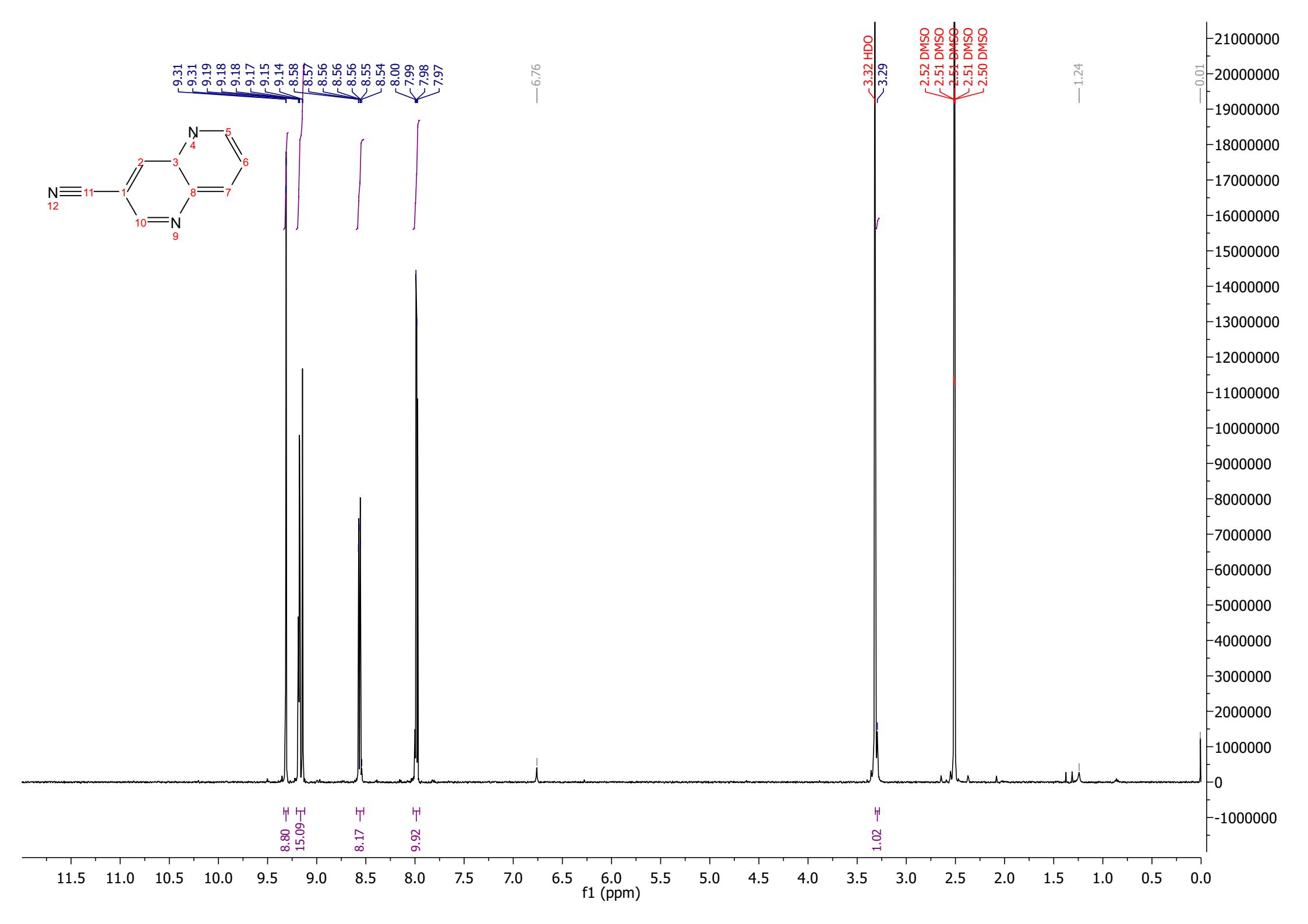
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


157.34
153.22
151.16
148.41
141.74
135.69
133.20
124.68
121.24
117.54
108.70
40.67
40.61 DMSO
40.52 DMSO
40.45 DMSO
40.35 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.69 DMSO
39.52 DMSO
N
14
13
1
2
3
6
N
5
4
7
8
9
12
N
11
10
0.00
1.20E+09
1.10E+09
1.00E+09
9.00E+08
8.00E+08
7.00E+08
6.00E+08
5.00E+08
4.00E+08
3.00E+08
2.00E+08
1.00E+08
0.00E+00
-1.00E+08
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9.16
8.54
8.48
7.98
7.97
7.97
7.74
7.73
7.73
7.52
7.52
7.52
6.66
3.32 HDO
3.29
3.28
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.47
2.10
2.09
2.09
2.08
2.08
2.07
2.07
2.06
2.05
1.25
1.06
1.06
1.05
1.05
1.04
1.04
1.03
1.03
1.01
1.00
0.92
0.91
0.89
0.88
0.88
0.87
0.87
0.86
0.01
0.65
0.87
0.94
1.04
1.01
1.17
2.18
2.15
f1 (ppm)


155.19
147.51
141.47
137.06
132.49
128.99
128.62
127.25
118.95
112.94
40.61 DMSO
40.52 DMSO
40.45 DMSO
40.36 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.69 DMSO
39.52 DMSO
15.32
10.60
0.00
f1 (ppm)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8.56
8.56
8.56
8.55
8.54
8.00
7.99
7.98
7.97
6.76
3.32 HDO
3.29
2.52 DMSO
2.51 DMSO
2.51 DMSO
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2.50 DMSO
1.24
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15.09
8.17
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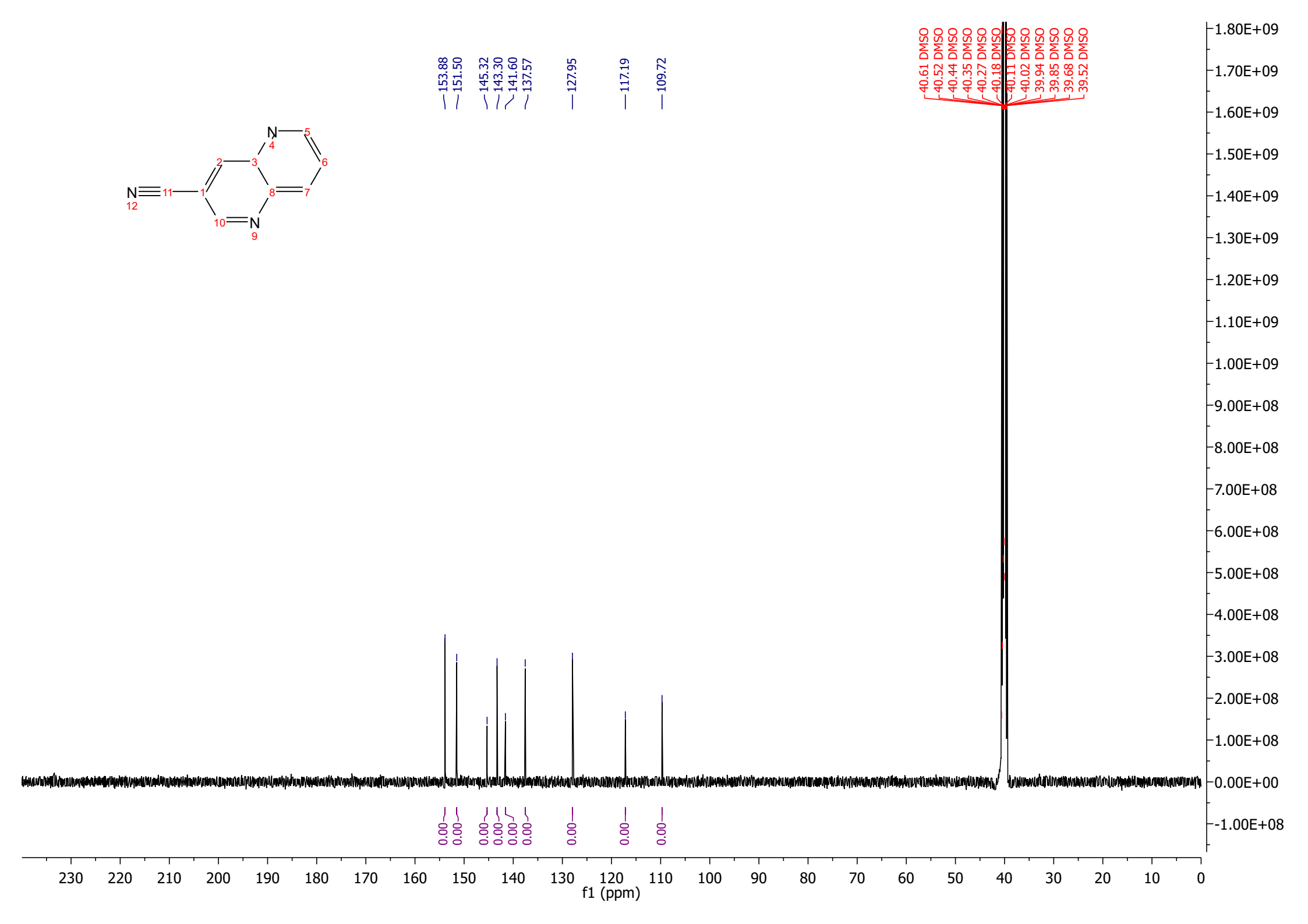
1.02
f1 (ppm)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145.32
143.30
141.60
137.57
127.95
117.19
109.72
40.61 DMSO
40.52 DMSO
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40.35 DMSO
40.27 DMSO
40.18 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.68 DMSO
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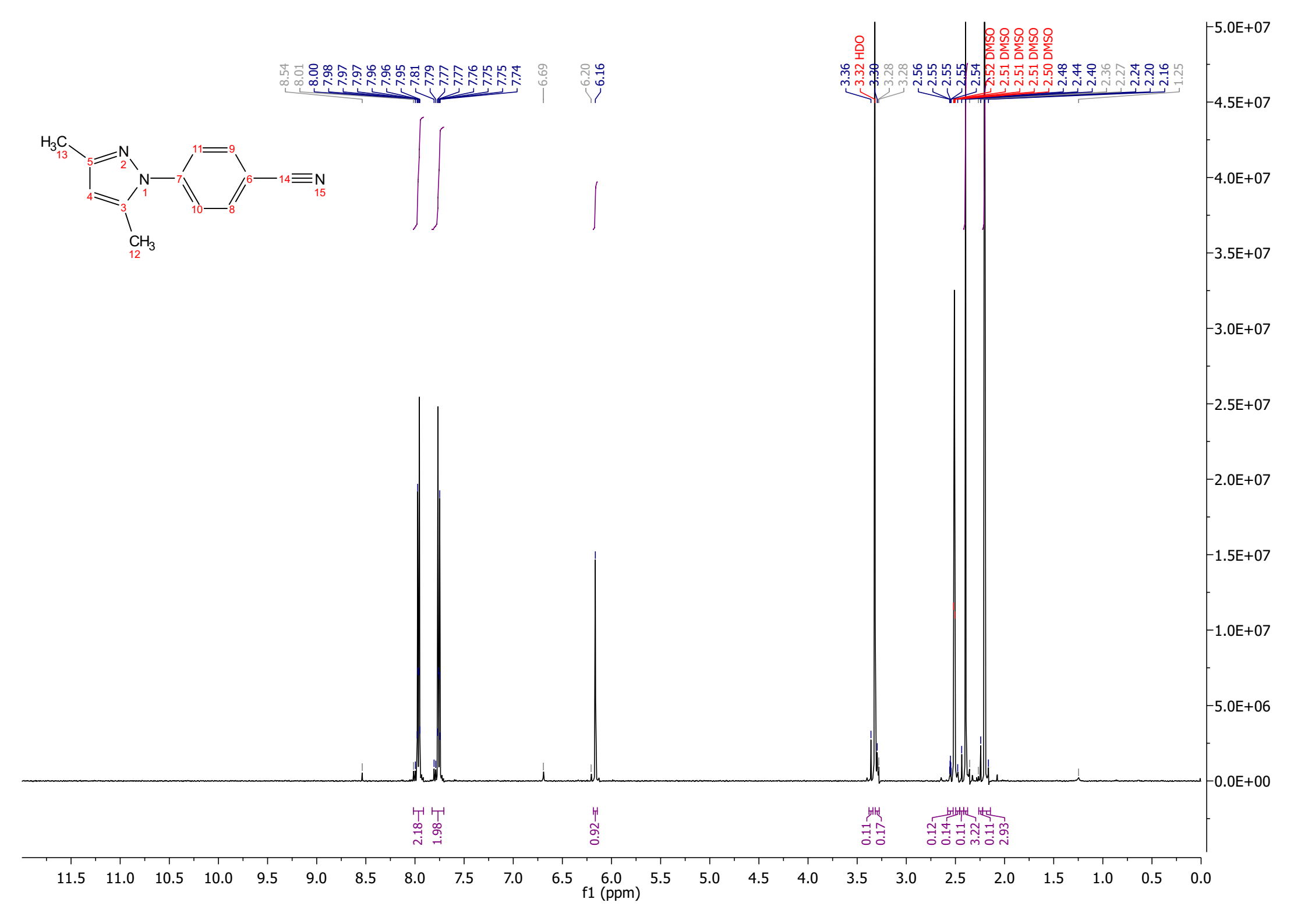
f1 (ppm)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7.96
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7.77
7.77
7.76
7.75
7.75
7.74
6.69
6.20
6.16
3.36
3.32 HDO
3.30
3.28
3.28
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2.55
2.55
2.55
2.54
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2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
2.48
2.44
2.40
2.36
2.27
2.24
2.20
2.16
1.25
H3C
13
N
2
5
4
3
N
1
7
11
9
6
14
N
15
10
8
CH3
12
2.18
1.98
0.92
0.11
0.17
0.12
0.14
0.11
3.22
0.11
2.93
5.0E+07
4.5E+07
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
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
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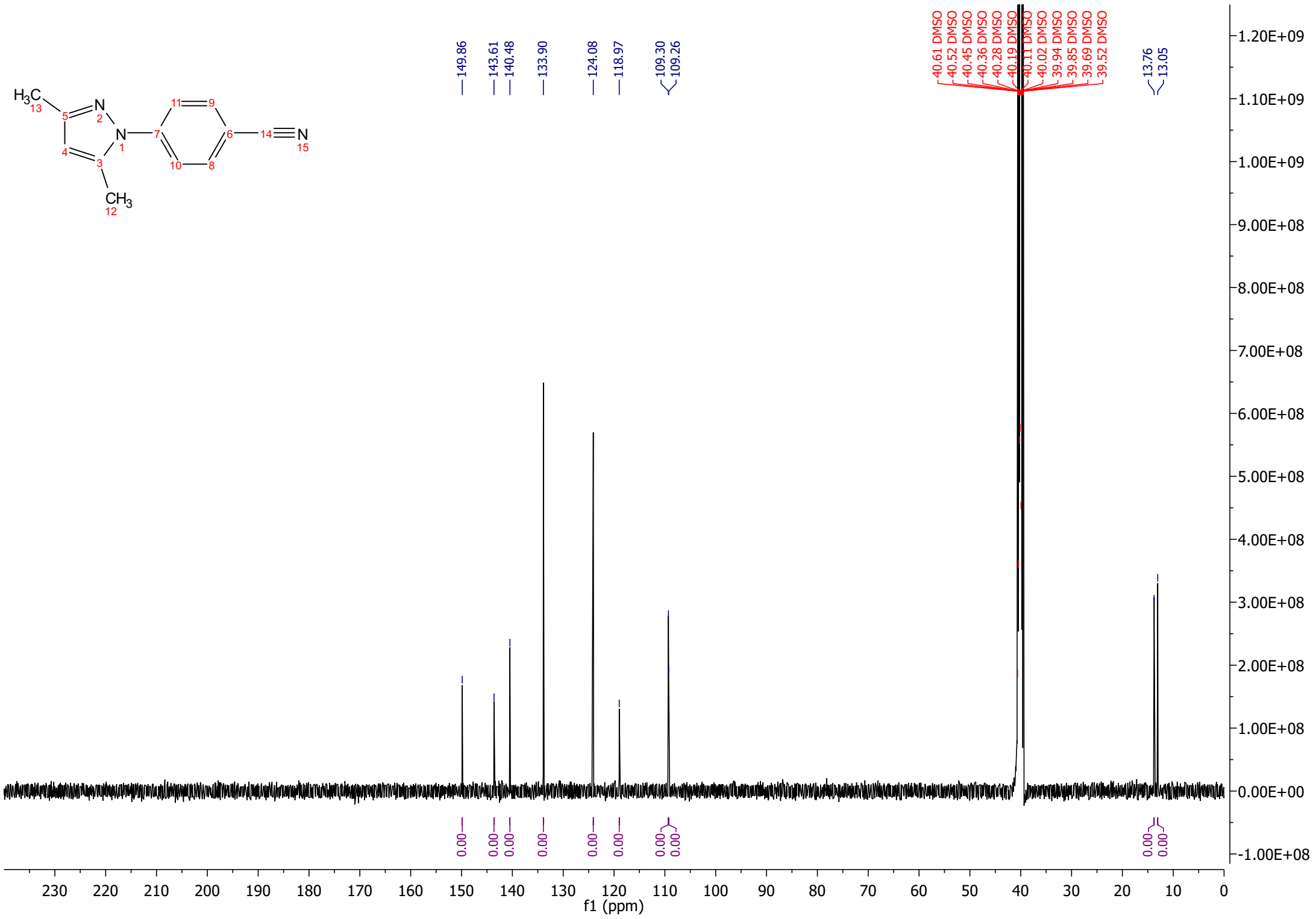
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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143.61
140.48
133.90
124.08
118.97
109.30
109.26
40.61 DMSO
40.52 DMSO
40.45 DMSO
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40.28 DMSO
40.19 DMSO
40.11 DMSO
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39.94 DMSO
39.85 DMSO
39.69 DMSO
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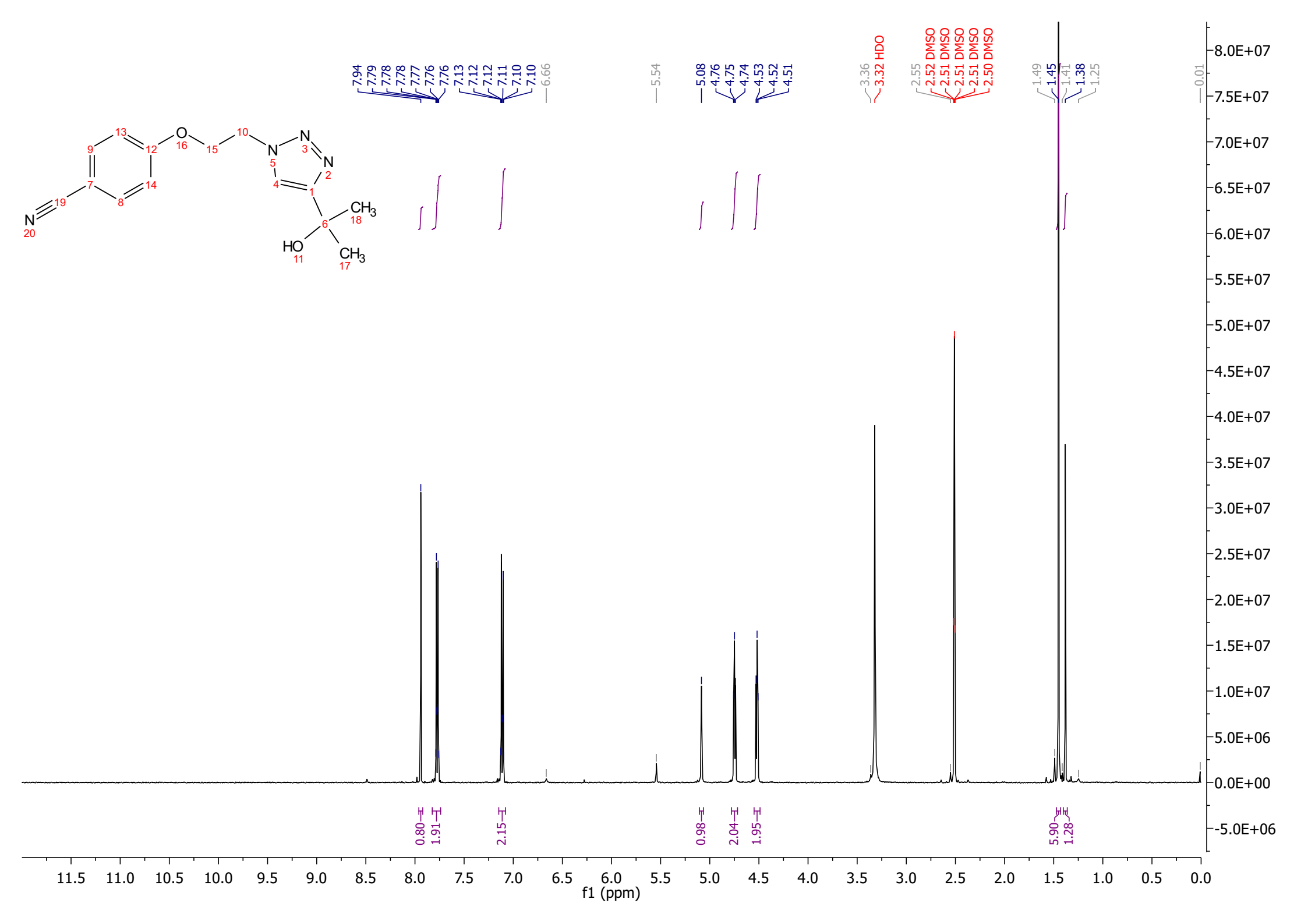
13.76
13.05
0.00
f1 (ppm)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7.78
7.78
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7.76
7.13
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7.12
7.11
7.10
7.10
6.66
5.54
5.08
4.76
4.75
4.74
4.53
4.52
4.51
3.36
3.32 HDO
2.55
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
1.49
1.45
1.41
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1.25
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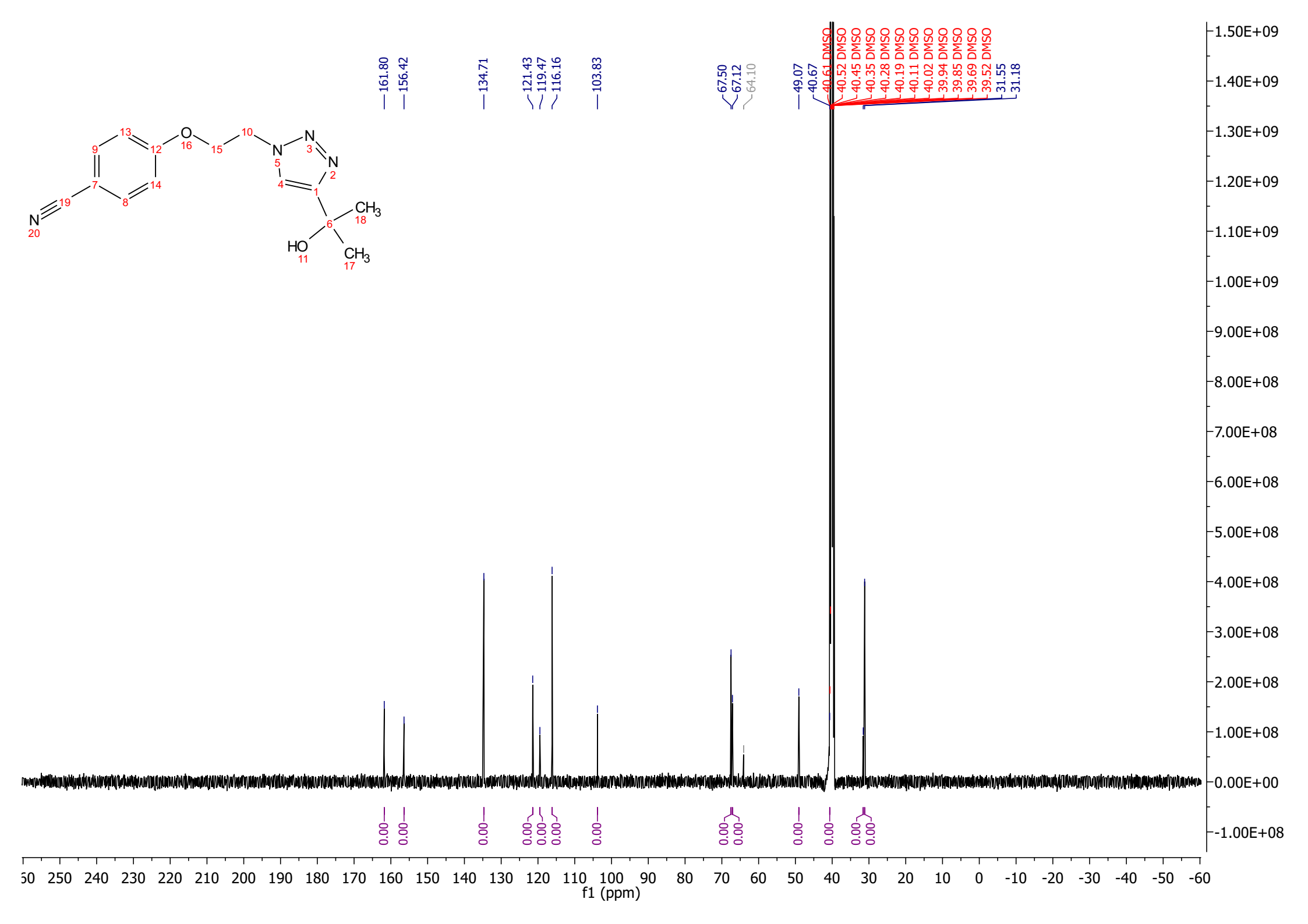
0.80
1.91
2.15
0.98
2.04
1.95
5.90
1.28
f1 (ppm)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134.71
121.43
119.47
116.16
103.83
67.50
67.12
64.10
49.07
40.67
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40.52 DMSO
40.45 DMSO
40.35 DMSO
40.28 DMSO
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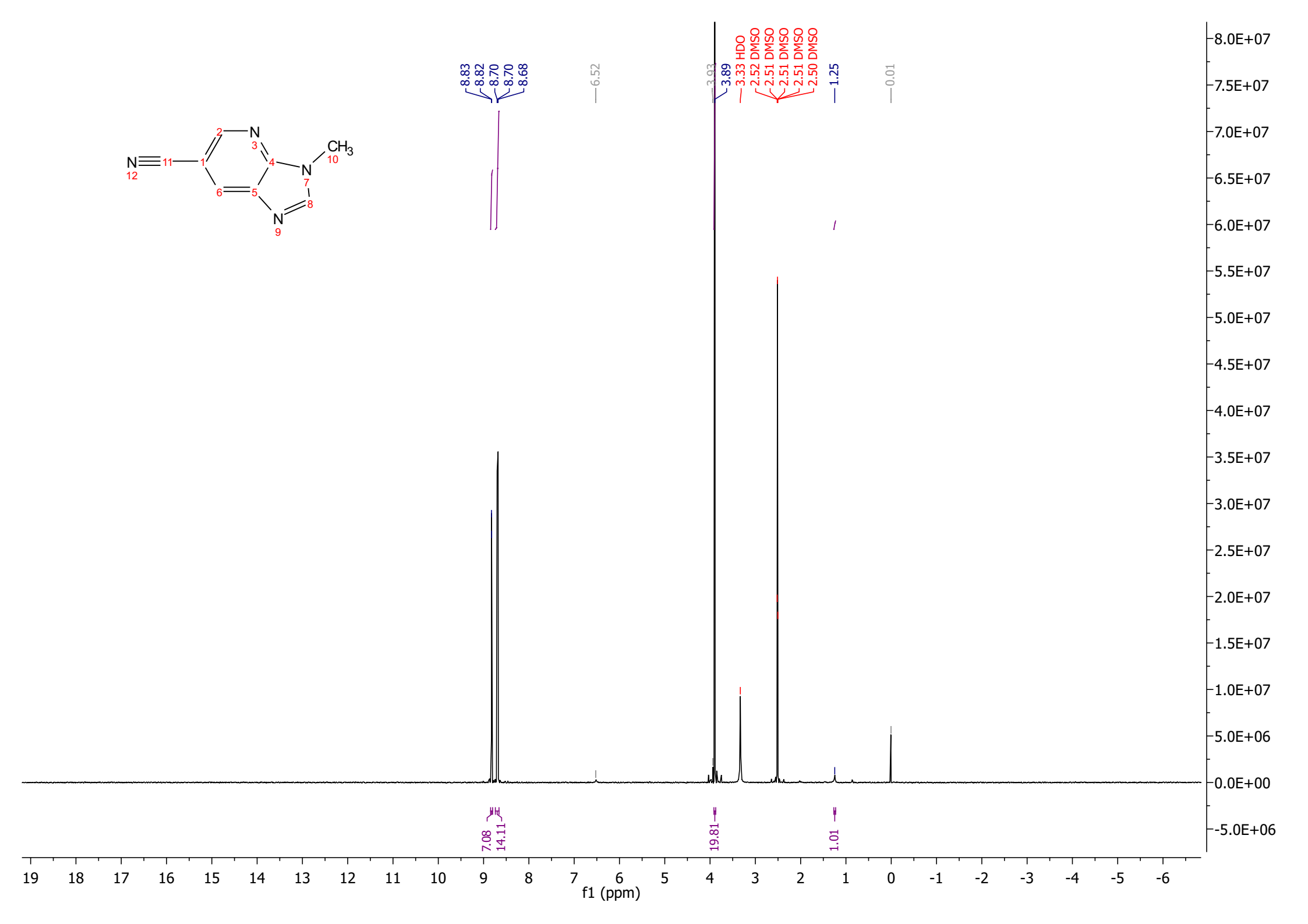
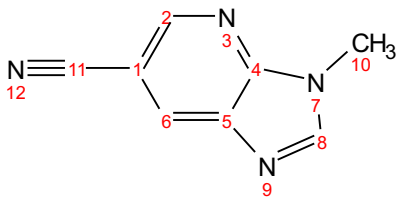
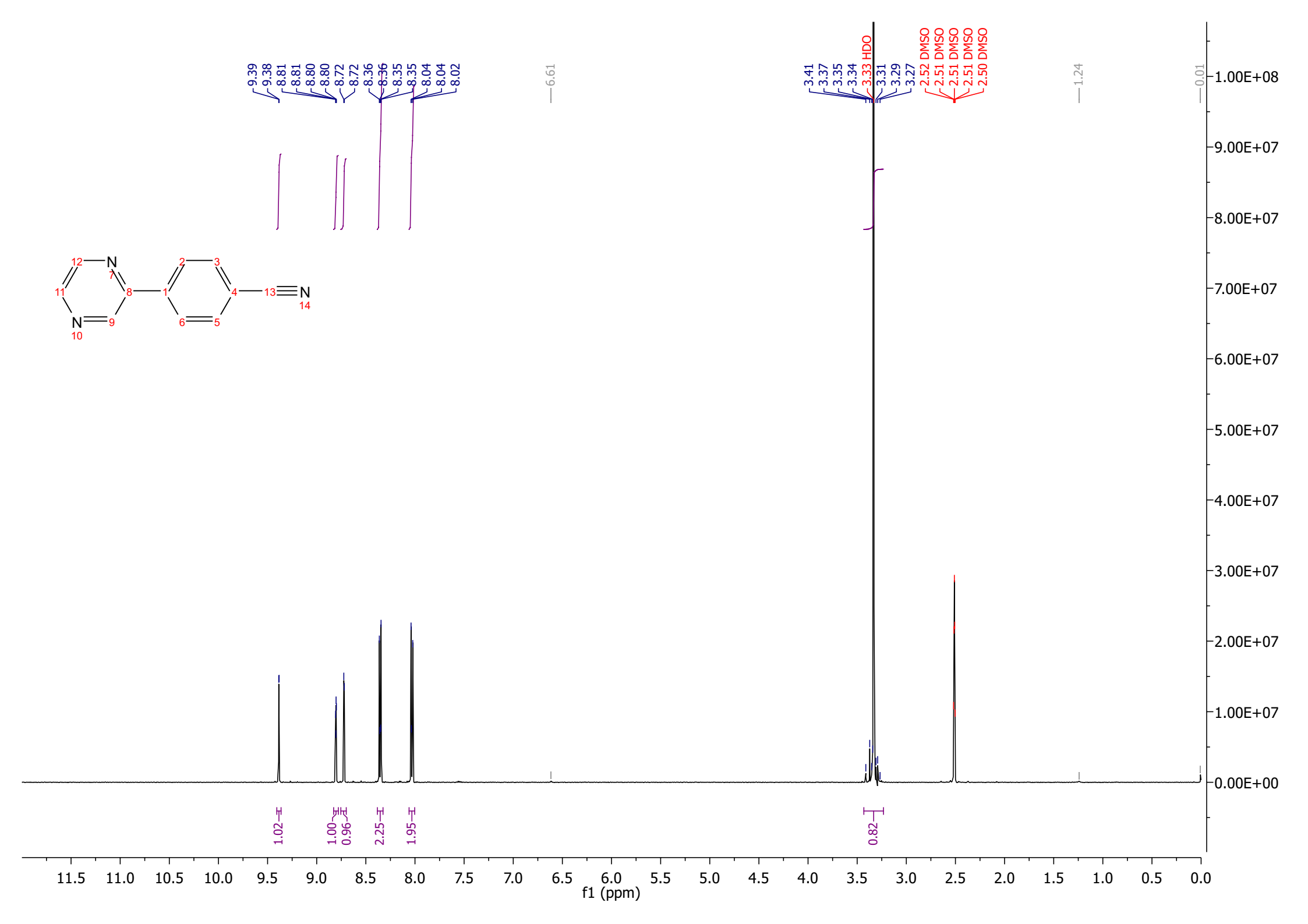
39.69 DMSO
39.52 DMSO
31.55
31.18
f1 (ppm)


8.83
8.82
8.70
8.70
8.68
6.52
3.93
3.89
3.33 HDO
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
1.25
0.01
7.08
14.11
19.81
1.01
f1 (ppm)

3-methyl-3H-imidazo[4,5-b]pyridine-6-carbonitrile

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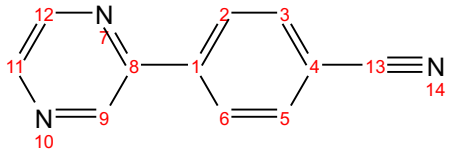
8.80
8.72
8.72
8.36
8.36
8.35
8.35
8.04
8.04
8.02
6.61
3.41
3.37
3.35
3.34
3.33 HDO
3.31
3.29
3.27
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
1.24
0.01
1.00E+08
9.00E+07
8.00E+07
7.00E+07
6.00E+07
5.00E+07
4.00E+07
3.00E+07
2.00E+07
1.00E+07
0.00E+00
1.02
1.00
0.96
2.25
1.95
0.82
11.5 11.0 10.5 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
f1 (ppm)



150.09
145.10
145.06
143.24
140.66
133.45
127.98
119.06
112.82

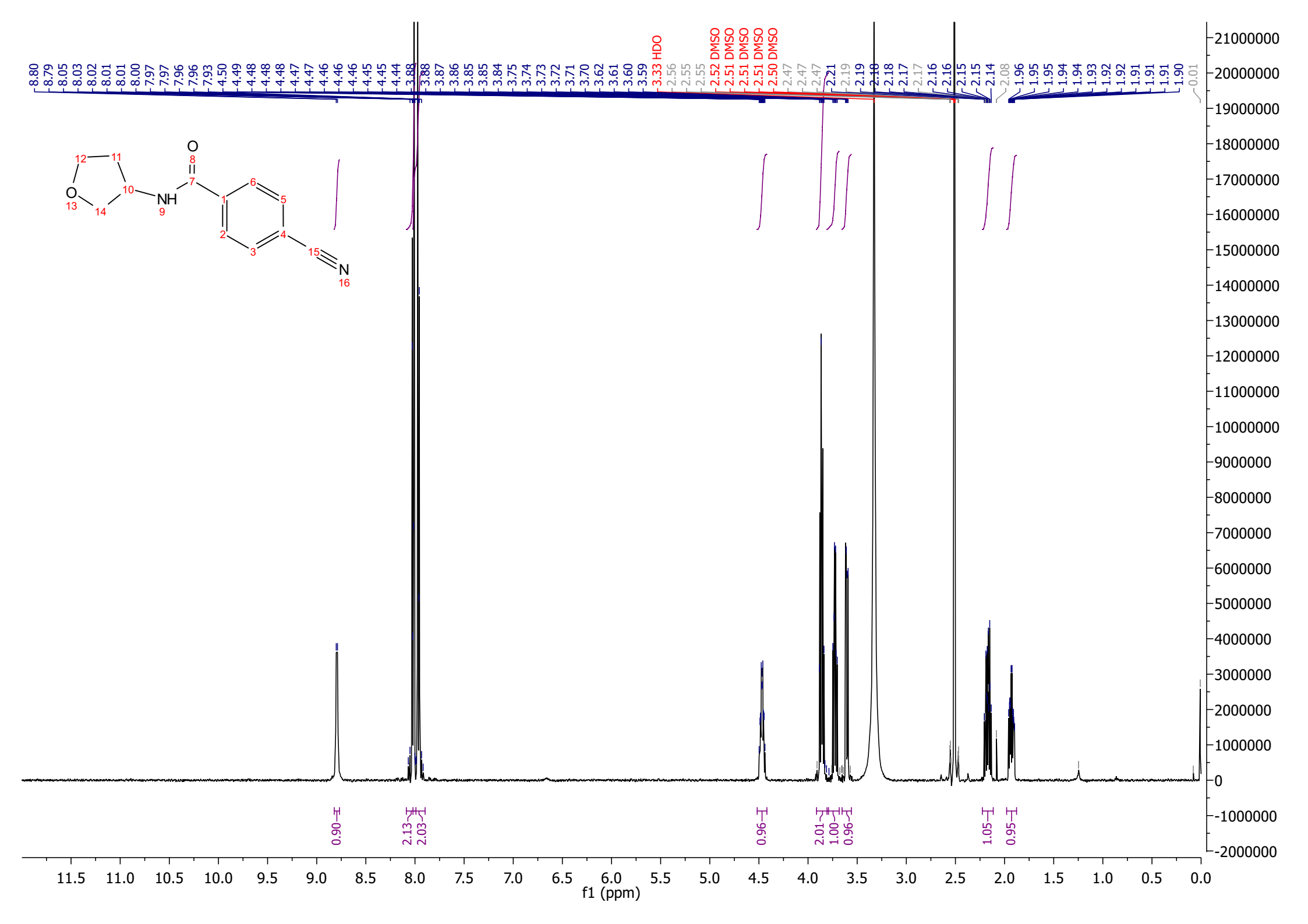
40.60 DMSO
40.51 DMSO
40.43 DMSO
40.34 DMSO
40.27 DMSO
40.18 DMSO
40.10 DMSO
40.01 DMSO
39.93 DMSO
39.84 DMSO
39.67 DMSO
39.51 DMSO

0.00
0.00
0.00
0.00
0.00
0.00
0.00
0.00
0.00

2.20E+09
2.10E+09
2.00E+09
1.90E+09
1.80E+09
1.70E+09
1.60E+09
1.50E+09
1.40E+09
1.30E+09
1.20E+09
1.10E+09
1.00E+09
9.00E+08
8.00E+08
7.00E+08
6.00E+08
5.00E+08
4.00E+08
3.00E+08
2.00E+08
1.00E+08
0.00E+00
-1.00E+08
-2.00E+08

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

f1 (ppm)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O
8
12
11
10
O
13
14
NH
9
7
1
6
5
2
4
3
15
N
16
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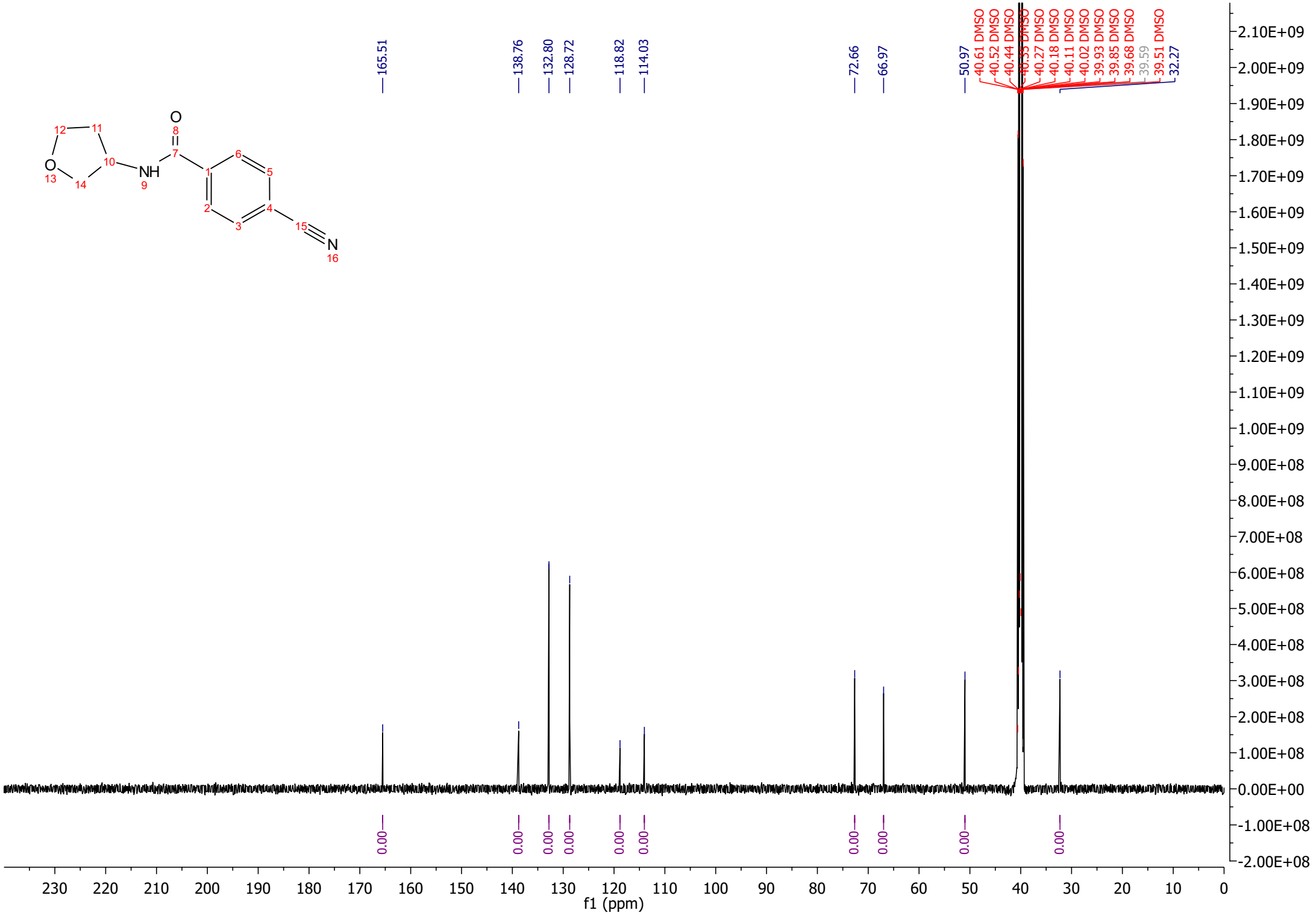
2.13
2.03
0.96
2.01
1.00
0.96
1.05
0.95
f1 (ppm)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128.72
118.82
114.03
72.66
66.97
50.97
40.61 DMSO
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.27 DMSO
40.18 DMSO
40.11 DMSO
40.02 DMSO
39.93 DMSO
39.85 DMSO
39.68 DMSO
39.59
39.51 DMSO
32.27
O
8
12
11
10
NH
9
O
13
14
7
6
1
5
2
4
3
15
N
16
2.10E+09
2.00E+09
1.90E+09
1.80E+09
1.70E+09
1.60E+09
1.50E+09
1.40E+09
1.30E+09
1.20E+09
1.10E+09
1.00E+09
9.00E+08
8.00E+08
7.00E+08
6.00E+08
5.00E+08
4.00E+08
3.00E+08
2.00E+08
1.00E+08
0.00E+00
-1.00E+08
-2.00E+08
0.00
230
220
210
200
190
180
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150
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50
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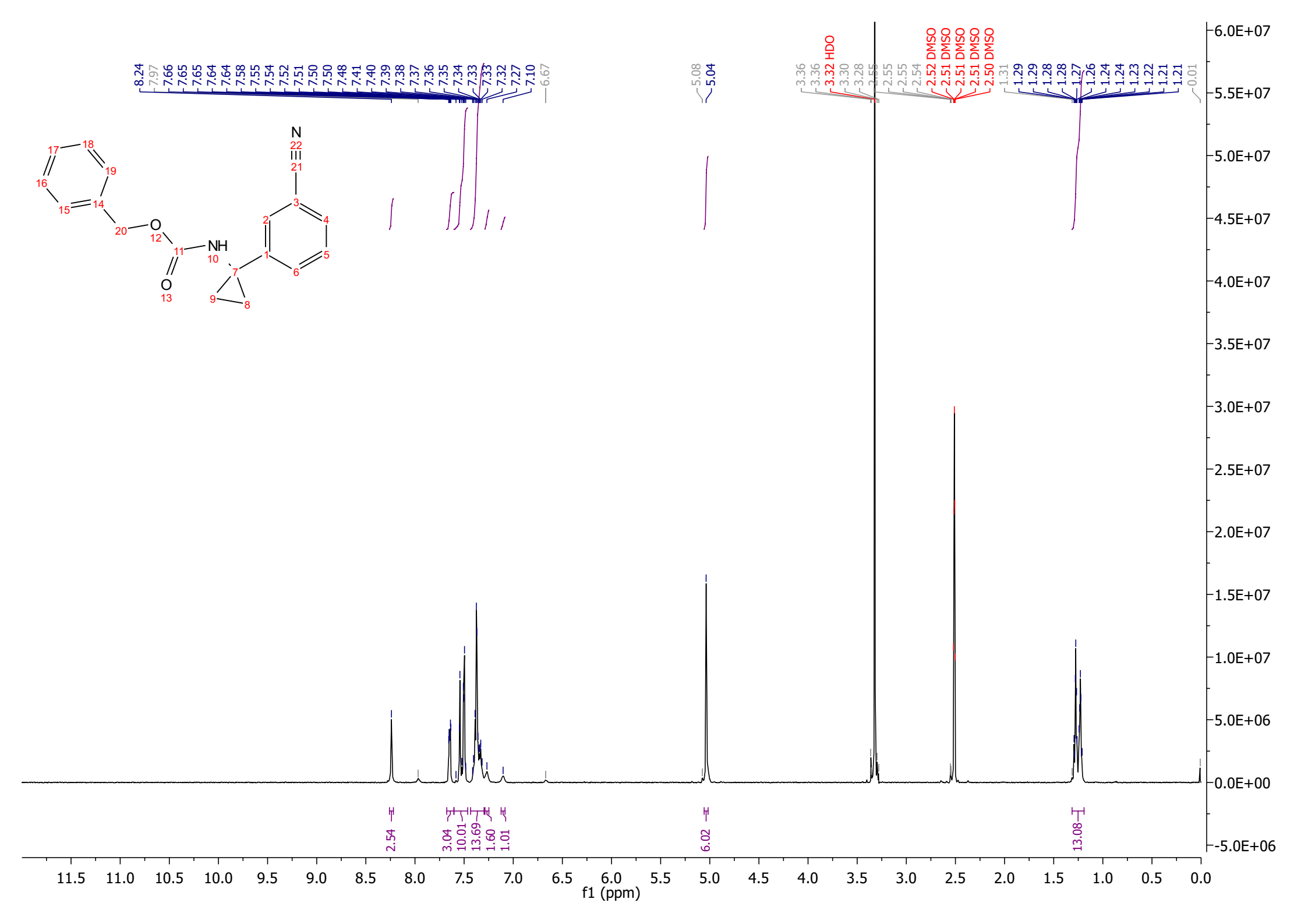
f1 (ppm)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7.54
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7.51
7.50
7.50
7.48
7.41
7.40
7.39
7.38
7.37
7.36
7.35
7.34
7.33
7.33
7.32
7.27
7.10
6.67
5.08
5.04
3.36
3.36
3.32 HDO
3.30
3.28
2.55
2.55
2.55
2.54
2.52 DMSO
2.51 DMSO
2.51 DMSO
2.51 DMSO
2.50 DMSO
1.31
1.29
1.29
1.28
1.28
1.27
1.26
1.24
1.24
1.23
1.22
1.21
1.21
0.01
N
22
21
18
17
19
16
15
14
20
O
12
11
NH
10
O
13
3
2
4
1
5
6
7
9
8
2.54
3.04
10.01
13.69
1.60
1.01
6.02
13.08
6.0E+07
5.5E+07
5.0E+07
4.5E+07
4.0E+07
3.5E+07
3.0E+07
2.5E+07
2.0E+07
1.5E+07
1.0E+07
5.0E+06
0.0E+00
-5.0E+06
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
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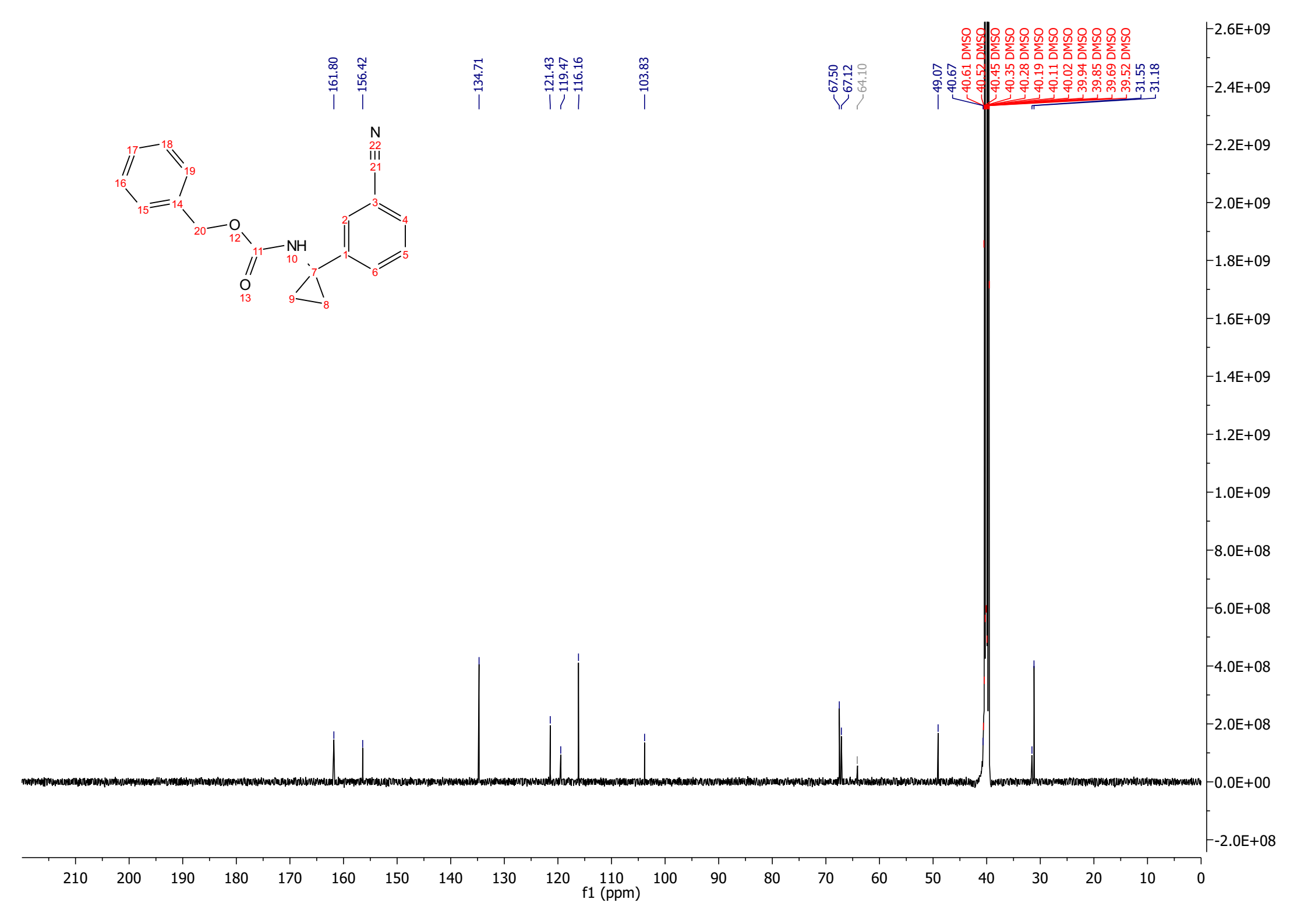
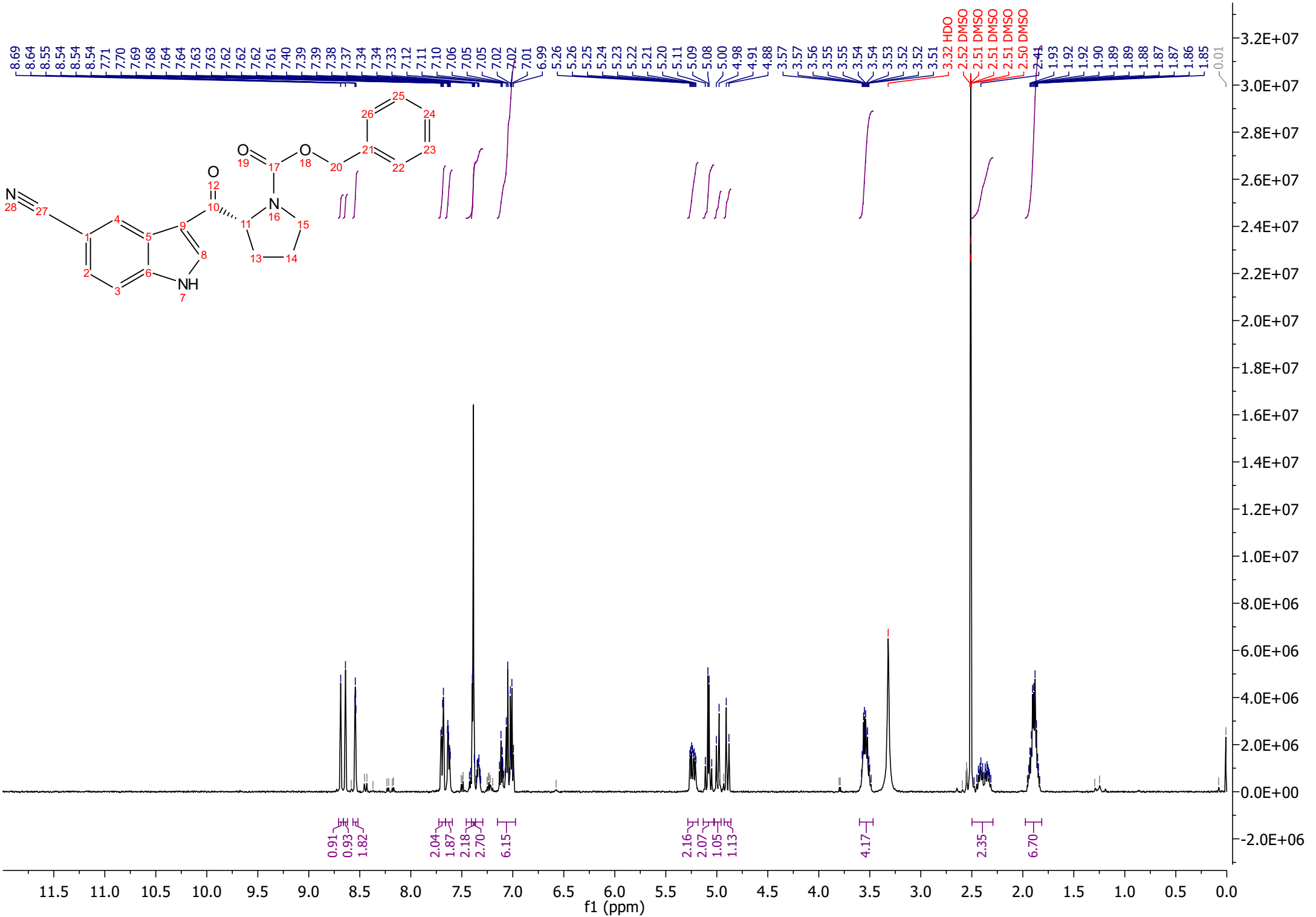
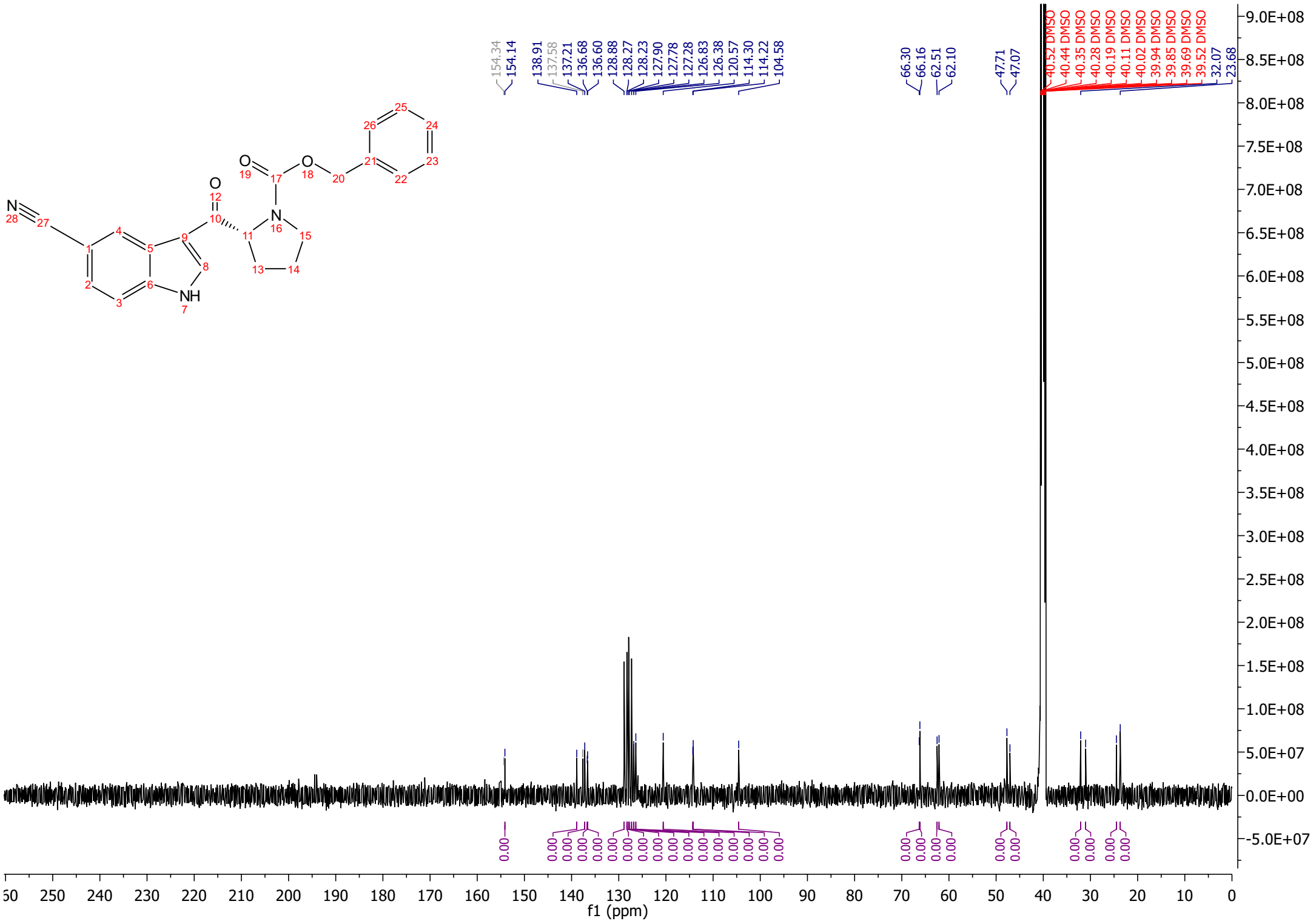
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


161.80
156.42
134.71
121.43
119.47
116.16
103.83
67.50
67.12
64.10
49.07
40.67
40.61 DMSO
40.52 DMSO
40.45 DMSO
40.35 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.69 DMSO
39.52 DMSO
31.55
31.18
N
22
21
NH
10
O
12
O
13
f1 (ppm)


8.69 8.64 8.55 8.54 8.54 8.54 7.71 7.70 7.69 7.68 7.64 7.64 7.63 7.63 7.62 7.62 7.62 7.61 7.40 7.39 7.39 7.38 7.37 7.34 7.34 7.33 7.12 7.11 7.10 7.06 7.05 7.05 7.02 7.02 7.01 6.99
5.26 5.26 5.25 5.24 5.23 5.22 5.21 5.20 5.11 5.09 5.08 5.00 4.98 4.91 4.88
3.57 3.57 3.56 3.55 3.55 3.54 3.54 3.53 3.52 3.52 3.51
3.32 HDO
2.52 DMSO 2.51 DMSO 2.51 DMSO 2.51 DMSO 2.50 DMSO
2.44 1.93 1.92 1.92 1.90 1.89 1.89 1.88 1.87 1.87 1.86 1.85
0.01
0.91 0.93 1.82 2.04 1.87 2.18 2.70 6.15 2.16 2.07 1.05 1.13 4.17 2.35 6.70
f1 (ppm)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137.58
137.21
136.68
136.60
128.88
128.27
128.23
127.90
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126.83
126.38
120.57
114.30
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104.58
66.30
66.16
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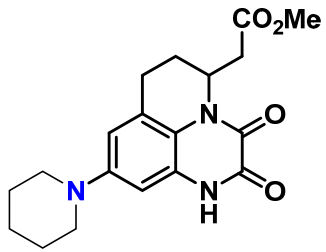
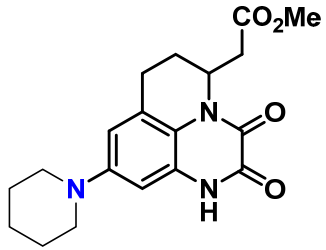
62.10
47.71
47.07
40.52 DMSO
40.44 DMSO
40.35 DMSO
40.28 DMSO
40.19 DMSO
40.11 DMSO
40.02 DMSO
39.94 DMSO
39.85 DMSO
39.69 DMSO
39.52 DMSO
32.07
23.68
f1 (ppm)

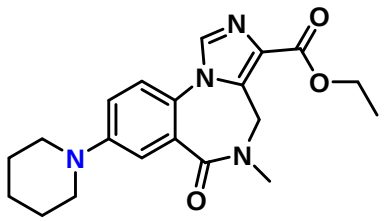
^{1}H NMR of Product of X1 + piperidine



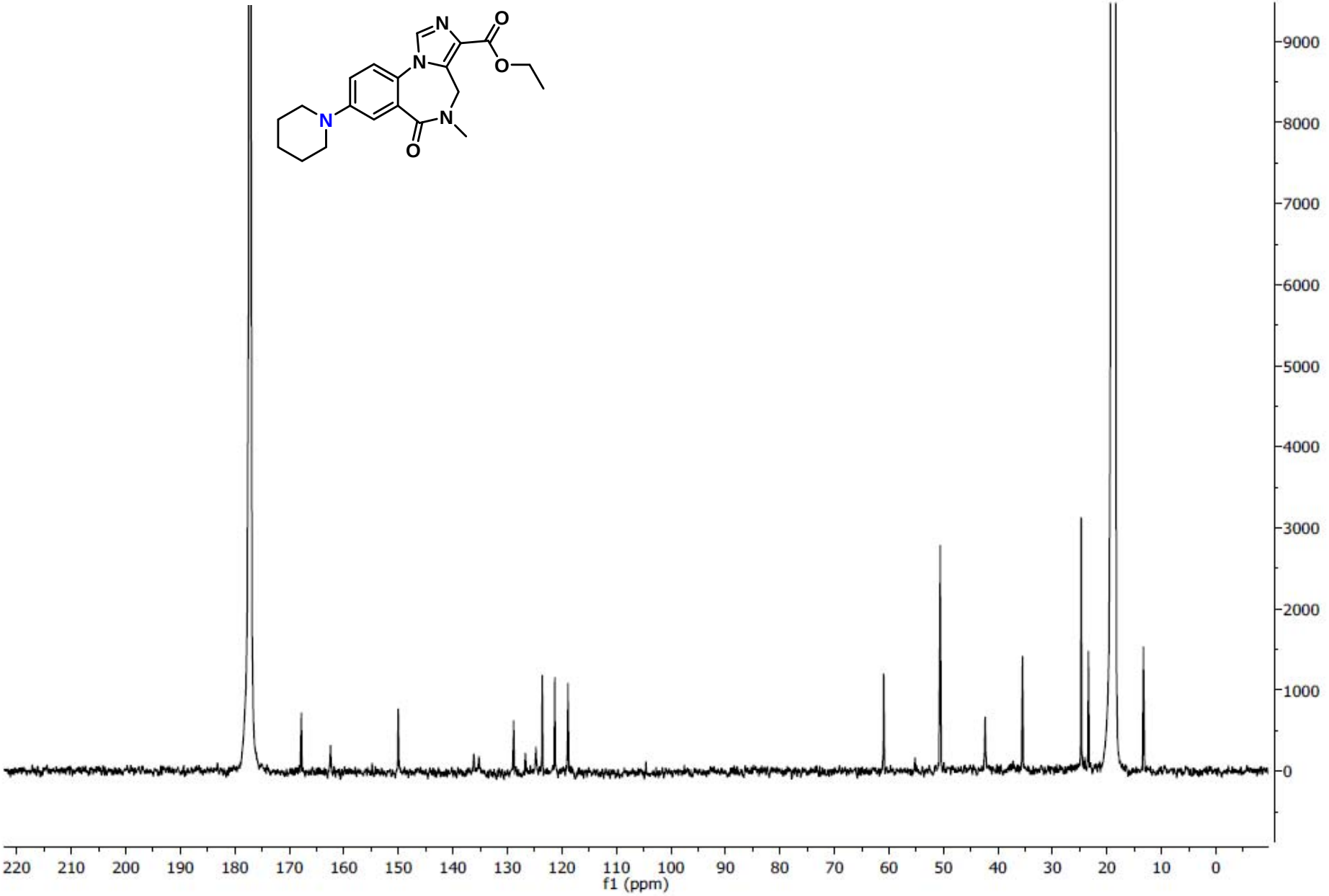
^{13}C NMR of Product of X1 + piperidine



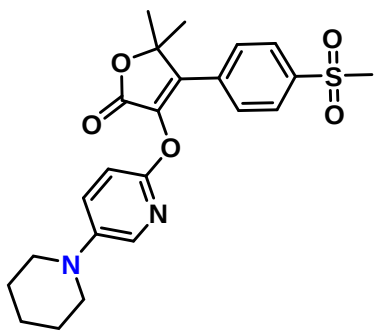
^{1}H NMR of Product of X2 + piperidine



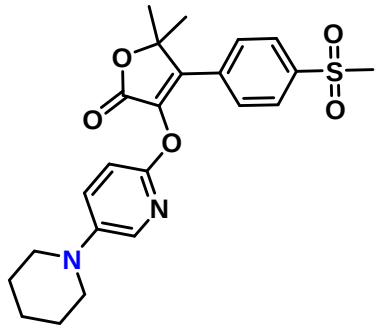
^{13}C NMR of Product of X2 + piperidine



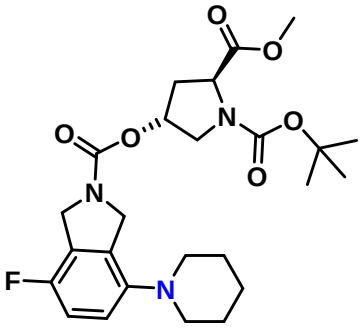
^{1}H NMR of Product of X3 + piperidine



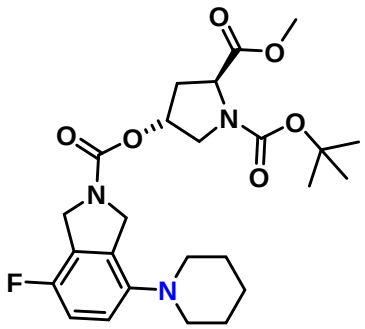
^{13}C NMR of Product of X3 + piperidine



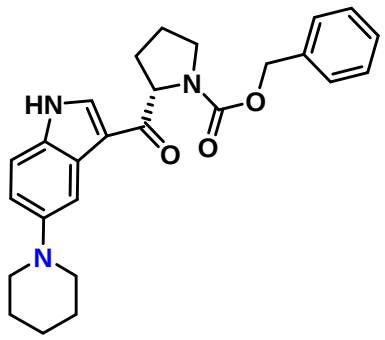
^{1}H NMR of Product of X4 + piperidine



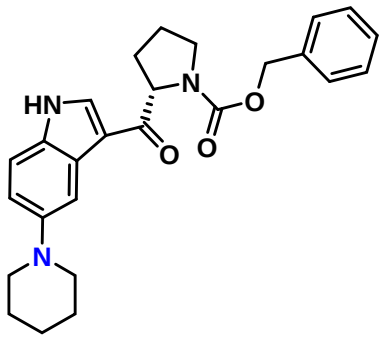
^{13}C NMR of Product of X4 + piperidine



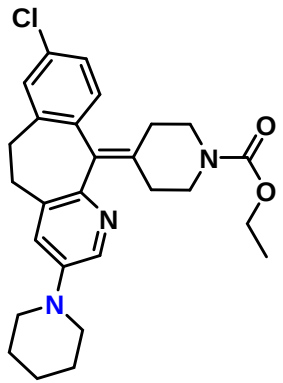
^{1}H NMR of Product of X5 + piperidine



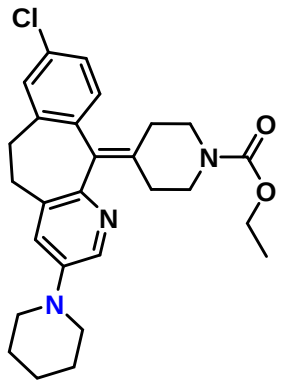
^{13}C NMR of Product of X5 + piperidine



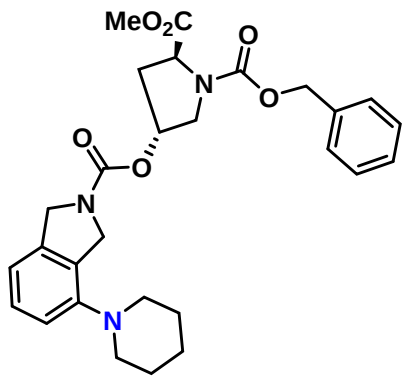
^{1}H NMR of Product of X6 + piperidine



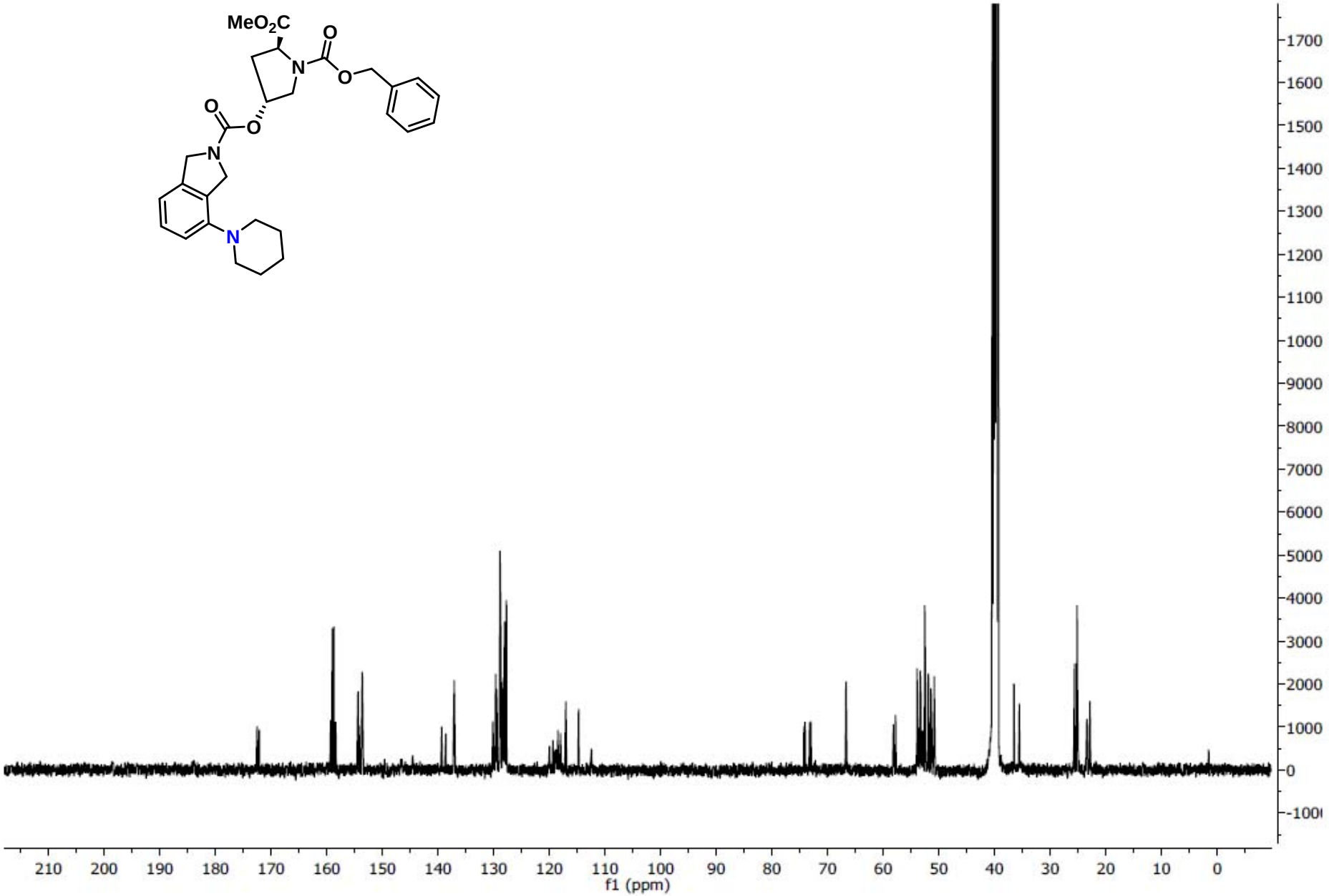
^{13}C NMR of Product of X6 + piperidine



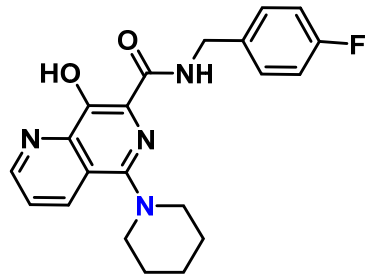
^{1}H NMR of Product of X8 + piperidine



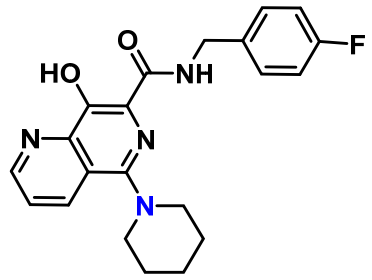
^{13}C NMR of Product of X8 + piperidine



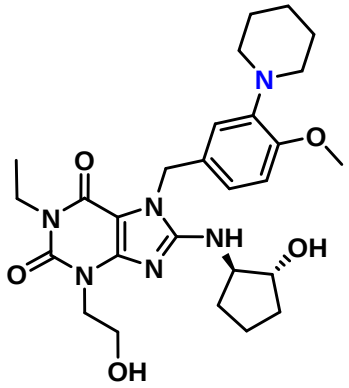
^{1}H NMR of Product of X10 + piperidine



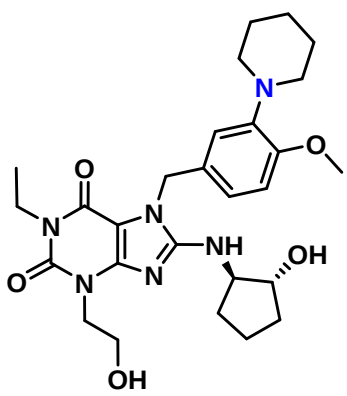
^{13}C NMR of Product of X10 + piperidine



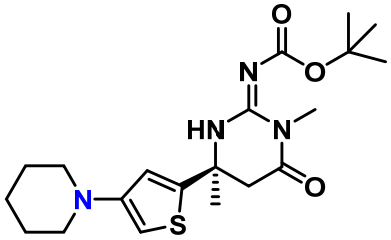
^{1}H NMR of Product of X12 + piperidine



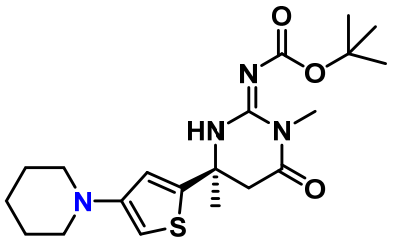
^{13}C NMR of Product of X12 + piperidine



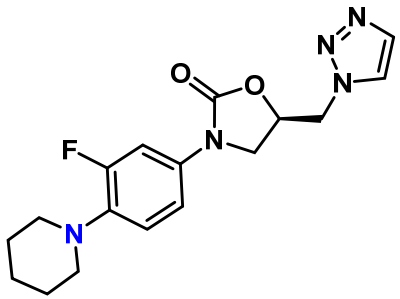
^{1}H NMR of Product of X13 + piperidine



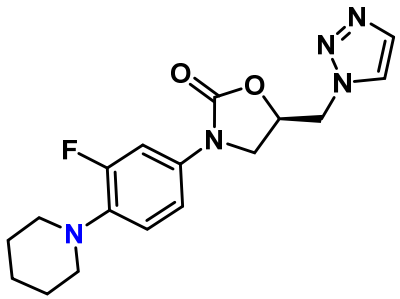
^{13}C NMR of Product of X13 + piperidine



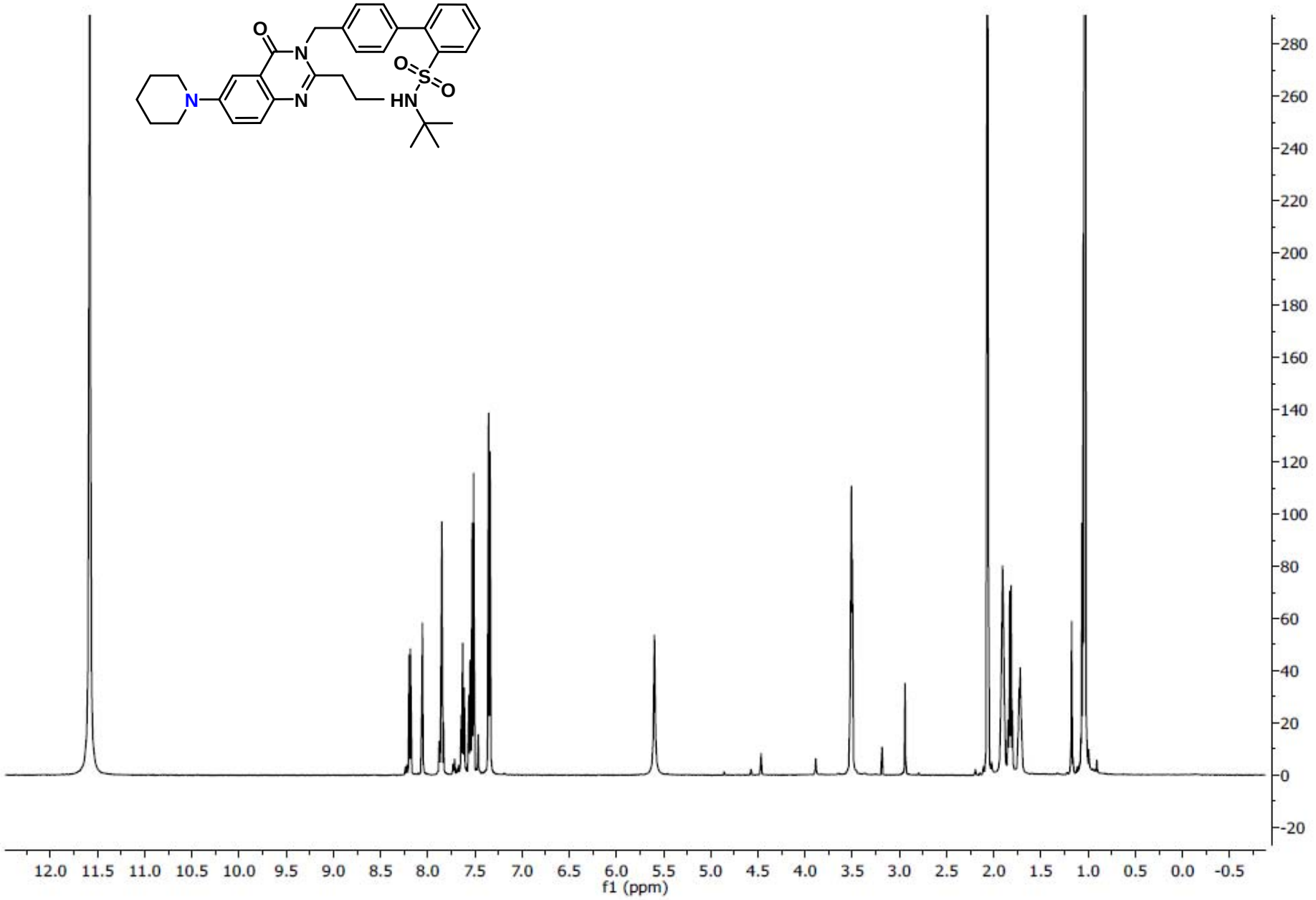
^{1}H NMR of Product of X14 + piperidine



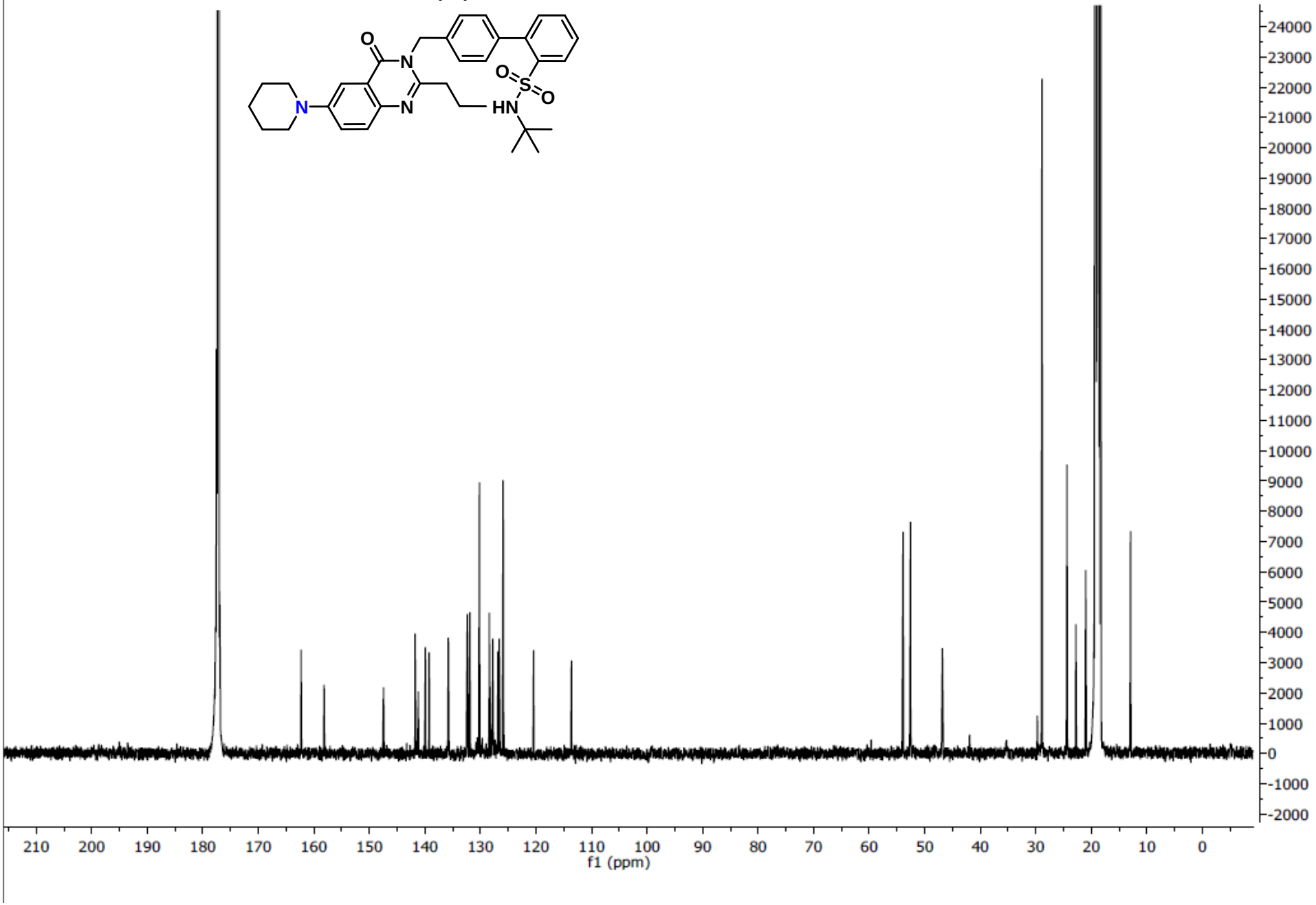
^{13}C NMR of Product of X14 + piperidine



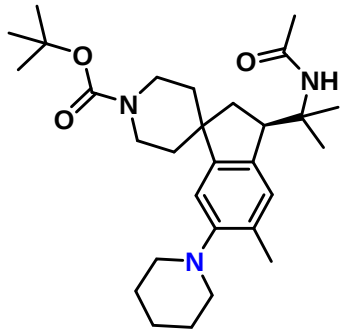
^{1}H NMR of Product of X15 + piperidine



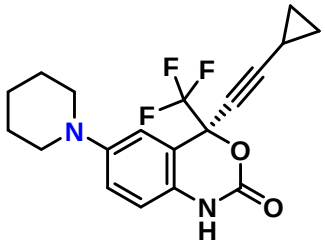
^{13}C NMR of Product of X15 + piperidine



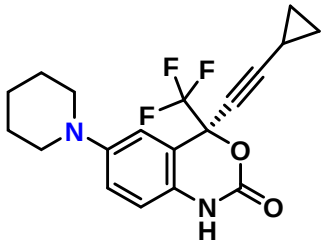
^{1}H NMR of Product of X16 + piperidine



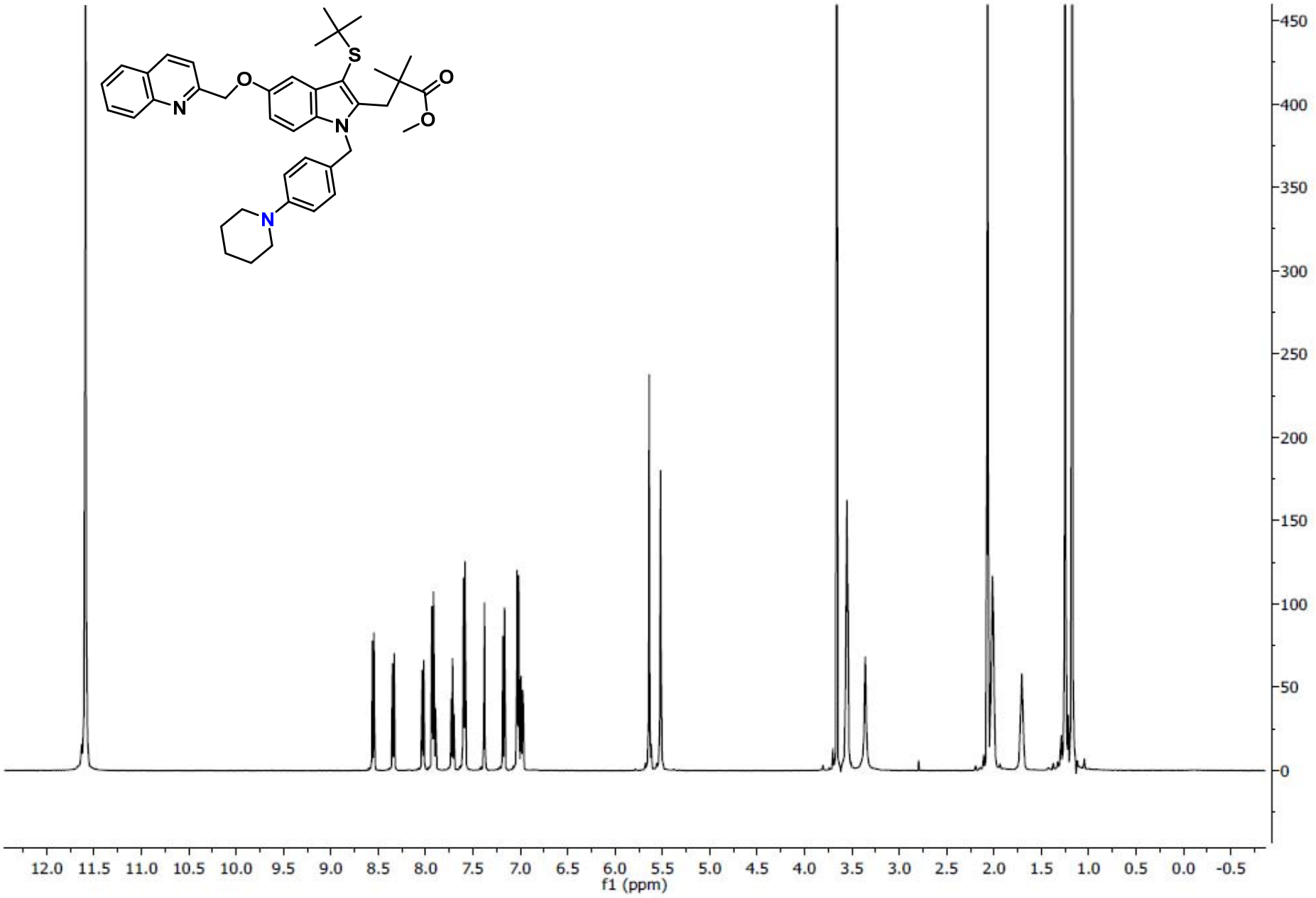
^{1}H NMR of Product of X17 + piperidine



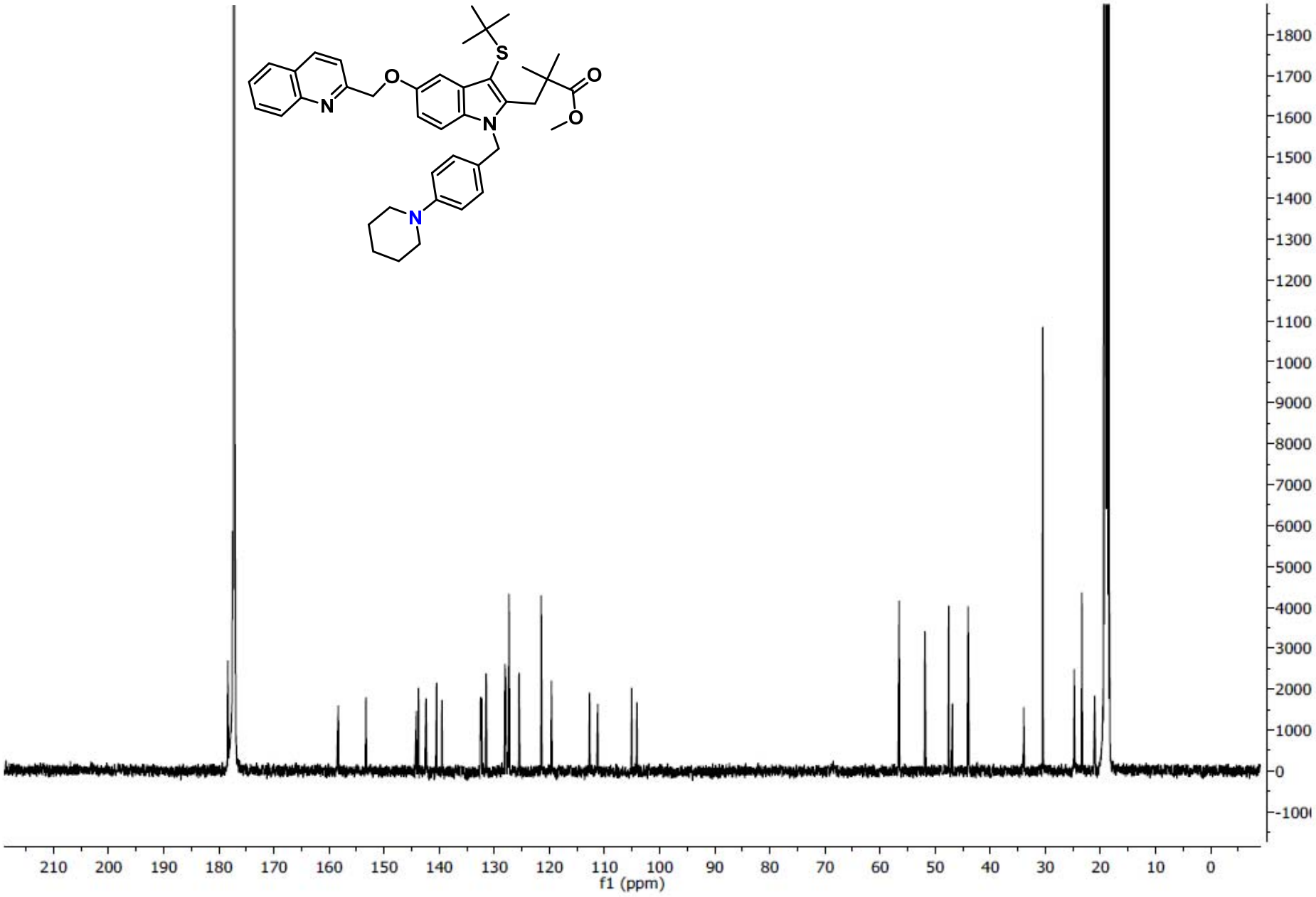
^{13}C NMR of Product of X17 + piperidine



^{1}H NMR of Product of X18 + piperidine



^{13}C NMR of Product of X18 + piperidine



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