Supporting Material for

Rapid access to a broad range of 6'-substituted firefly luciferin analogues reveals surprising emitters and inhibitors

*Deepak K. Sharma, Spencer T. Adams, Jr., Kate L. Liebmann, and Stephen C. Miller**

Department of Biochemistry and Molecular Pharmacology, University of Massachusetts Medical School, 364 Plantation St, Worcester, MA 01605

*Correspondence should be addressed to Stephen.miller@umassmed.edu

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General

All reactions were performed in well-dried round bottom flasks with rubber septa under argon atmosphere, unless otherwise noted. D-luciferin was purchased from Gold Bio. Chemical reagents and solvents were purchased from Aldrich, Frontier Scientific, Matrix, Oakwood, Synthonix, Toronto Chemical Research, Chem-Impex, or TCI and used as received. Flash column chromatography was carried out on a CombiFlash RF automated chromatography system using RediSep RF Gold silica columns. Thin-layer chromatography (TLC) was performed using silica gel (60 F-254) coated aluminum plates (EMD Millipore), and spots were visualized by exposure to ultraviolet light (UV). NMR spectra were acquired on Varian Mercury 400 MHz or Bruker Avance III HD 500 MHz NMR instruments. High-resolution mass spectra (HRMS) were recorded on a Thermo Scientific Orbitrap Velos Pro mass spectrometer coupled with a Thermo Scientific Accela 1250 UPLC and an autosampler using electrospray ionization (ESI) in the positive mode. UV absorbance was measured on a Varian Cary 50 Bio UV-Visible Spectrophotometer. Fluorescence data were recorded on a Horiba Scientific FluoroMax-4 using FluorEssence software. Solvents used for fluorescence spectra: PBS, 1X (Corning Cellgro), Methanol ≥ 99.9% pure (Sigma Aldrich), Dioxane 99+% pure (Acros Organic). Bioluminescence imaging assays were performed on a GloMax luminometer (Promega) or IVIS-100 (Xenogen, now Perkin-Elmer). GraphPad Prism ver. 7.0a (GraphPad Software, Inc.) was used to analyze data and generate graphs.

Luciferin Burst-Kinetics Assays

Wild-type and R218K mutant firefly luciferase were expressed and purified as previously described.[1,2] Using a GloMax Luminometer (Promega), 50 µl of enzyme buffer [20 mM Tris (pH 7.4), 0.1 mM EDTA, 0.8 mg/mL BSA, and 1 mM TCEP] containing firefly luciferase (2 nM) was rapidly injected into each well of a white 96-well plate (Costar 3912) containing luciferin analogue (500 µM) in substrate buffer [20 mM Tris (pH 7.4), 0.1 mM EDTA, 8 mM $MgSO_4$, and 4 mM ATP (AP Bio)], to a final enzyme concentration of 1 nM and luciferin analogue concentration of 250 µM. The peak emission occurring 0.5 s after injection was reported in Relative Light Units (RLU) and not corrected for the wavelength sensitivity of the

photomultiplier tube. To determine apparent Km values for emissive analogues, a two-fold dilution series of each substrate was prepared (final substrate concentrations ranging from 250 μM down to 0.122 μM). Peak emission occurring 0.5 s after injection of luciferase (0.1 nM final concentration) was fitted to a sigmoidal dose-response curve by non-linear regression in GraphPad Prism 7. All assays were performed in triplicate.

Luciferase Inhibition Assay

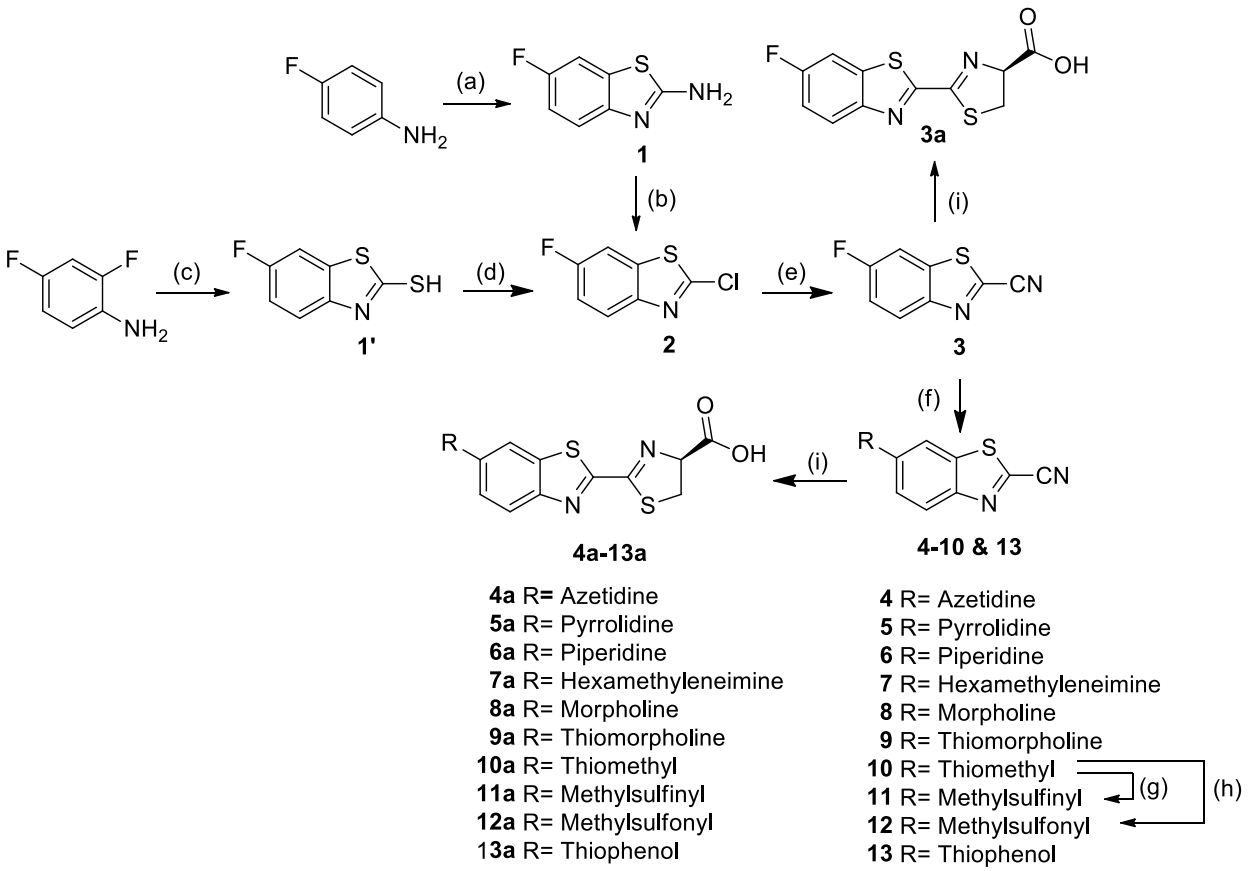
Fifty microliters of enzyme buffer [20 mM Tris (pH 7.4), 0.1 mM EDTA, 0.8 mg/mL BSA, and 1 mM TCEP] containing firefly luciferase (20 nM) was pipetted into each well of a 96-well plate containing 250 μM D-luciferin and 10 μM luciferin analogue in substrate buffer [20 mM Tris (pH 7.4), 0.1 mM EDTA, 8 mM $MgSO_4$, and 4 mM ATP (AP Bio)]. Luminescence measurements were taken one minute after substrate addition in an IVIS-100, in triplicate. The data was analyzed with Living Image Software ver. 4.3.1 and reported as total flux (p/s).

Cell Assays

Chinese hamster ovary (CHO) cells were maintained at 37°C and 5% CO_2 in F-12K medium (Gibco) containing 10% fetal bovine serum and 100 units/ml penicillin/streptomycin. Cells were seeded in black 96-well plates (Costar 3916) at 15,000 cells/ml. Twenty-four hours post-seeding, the cells were transiently transfected with pcDNA3.1 WT luc2 or R218K luc2, as previously reported, at 0.075 μg DNA/well using Lipofectamine 2000 (Invitrogen).[2] Assays were performed in triplicate 48 hours after transfection. Luciferin substrates were diluted in Hank's balanced salt solution (HBSS) to 100 μM, 10 μM, and 1 μM. Transfected CHO cells were washed with HBSS and incubated with 60 μl/well of 100, 10, or 1 μM substrate. Imaging was performed one minute after substrate addition in an IVIS-100. Data acquisition and analysis were performed with Living Image® software. Data are reported as total flux (p/s) for each ROI corresponding to each well of the 96-well plate, and plotted and analyzed with GraphPad Prism 7.0.

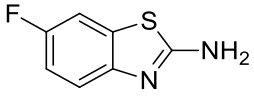
Relative Quantum Yield Measurement

Absorbance spectra were recorded at five different concentrations with absorbance between 0.01-0.10 for each sample. Fluorescence spectra were recorded on a Horiba Scientific FluoroMax-4. Relative quantum yields were calculated from plots of absorbance vs. integrated fluorescence and were referenced to that of 6'-aminoluciferin measured under the same conditions.

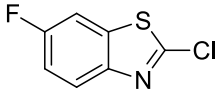


Scheme S1: (a) Bromine, potassium thiocyanate, acetic acid, rt, 21h then adjusted to pH 8 using NH_4OH; (b) t-butyl nitrite, $CuCl_2$, CH_3CN, rt, 2h, then 65°C for 1h; (c) potassium ethyl xanthogenate, DMF, 100°C, 4h; (d) SO_2Cl_2, rt, 2h; (e) *Method A:* KCN, DMSO, 90°C, 8h or

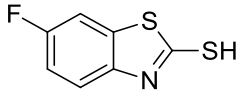
Method B: KCN, DABCO, DMSO:H_2O (9:1), rt, overnight; (f) Nucleophile, K_2CO_3, DMF, 60^{o}C, 4h; (g) mCPBA, DCM, rt, 12h; (h) Oxone, ethanol, 60^{o}C, 8h; (i) D-cysteine, aq. MeOH.



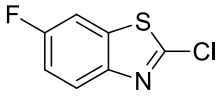
6-fluorobenzo[*d*]thiazol-2-amine (1): A solution of 4-fluoroaniline (1 g, 9.0 mmol) and potassium thiocyanate (3.5 g, 36 mmol) in AcOH (20 mL) was stirred at 20 ^{o}C for 10 min. Bromine (1.4 g, 9.0 mmol) was added dropwise over 20 min. The reaction mixture was stirred at room temperature for an additional 21 h. The reaction mixture was then poured onto crushed ice and the pH was adjusted to 8 using NH_4OH. The resulting precipitate was vacuum-filtered and dried to give **1** as yellow solid (1.4 g, 94%). ^{1}H NMR (500 MHz, CD_3OD) δ 7.27-7.21 (m, 2H), 6.90 (td, J = 9.0, 2.5 Hz, 1H). ^{13}C NMR (125 MHz, CD_3OD) δ 168.1, 158.3 (d, J= 237 Hz), 148.2, 131.5, 117.9 (d, J= 8.75 Hz), 112.7 (d, J= 24 Hz), 107.1 (d, J= 27.4 Hz). ^{19}F NMR (471 MHz, CD_3OD) δ -123.53 (td, J = 8.8, 4.7 Hz). HRMS (ESI$^+$) Calculated for $C_7H_6FN_2S$: 169.0230 and found: 169.0215.



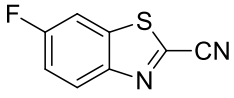
2-chloro-6-fluorobenzo[*d*]thiazole (**2)**: To a mixture of t-butyl nitrite (1.8 g, 17.85 mmol), cupric chloride (1.9 g, 14.28 mmol) and acetonitrile (50 mL) was added **1** (2 g, 11.90 mmol) in portions over 1h. The reaction mixture was stirred at room temperature for 2h, then heated to 65 ^{o}C for 1h. The mixture was cooled, filtered and the filtrate was poured into 6N HCl and extracted with ethyl acetate. After concentration the crude product was used for the next step without further purification (2.1 g, 95 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 8.8, 4.8 Hz, 1H), 7.40 (dd, J = 8.0, 2.4 Hz, 1H), 7.19 – 7.12 (m, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6 (d, J_{cf}= 246 Hz), 152.5 (d, J_{cf} = 3.0 Hz), 147.6, 137.0 (d, J_{cf} = 11.0 Hz), 124.0 (d, J_{cf} = 9.0 Hz), 115.3 (d, J_{cf}= 24 Hz), 107.6 (d, J_{cf}= 26 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.37 (td, J = 8.3, 4.5 Hz, 1F). HRMS (ESI$^+$) Calculated for C_7H_4ClFNS: 187.9732 and found: 187.9719.



6-fluorobenzo[*d*]thiazole-2-thiol (**1'**): A solution of 2,4-difluoroaniline (5.0 g, 38.7 mmol) and potassium ethyl xanthogenate (13.7 g, 85.3 mmol, 2.2 eq) in 50 mL anhydrous DMF was heated to 95 °C for 4 hours under argon. The reaction mixture was cooled to room temperature, then diluted with H_2O (50 mL) and 1 N HCl solution (100 mL) to induce precipitation. Stirring was continued for 1h. The solid precipitate was collected by filtration, and rinsed with water. The wet filter cake was dissolved in ethyl acetate, and dried over Na_2SO_4. Organic solvent was removed by rotary evaporation and the residue was dried in vacuo to afford **1'** as a colorless solid (6.9 g, 93%). ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.80 (s, 1H), 7.66 (dd, J = 8.5, 2.0 Hz, 1H), 7.31-724 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 190.4, 159.6 (d, J_{cf}= 238.7 Hz), 138.4, 131.2 (d, J_{cf} = 11.25 Hz), 115.2 (d, J_{cf} = 23.8 Hz), 113.8 (d, J_{cf} = 8.8 Hz), 109.3 (d, J_{cf} = 27.5 Hz). ^{19}F NMR (470 MHz, DMSO-d$_6$) δ -118.11 (m, 1F). HRMS (ESI$^+$) Calculated for $C_7H_5FNS_2$: 185.9842 and found: 185.9834.



2-chloro-6-fluorobenzo[*d*]thiazole (**2)**: To compound **1'** (1 g, 5.40 mmol) cooled in an ice-water bath, was slowly added 20 mL SO_2Cl_2 at below room temperature under nitrogen, and the suspension was stirred at room temperature for 2 hours. The reaction mixture was poured into ice water with stirring. Precipitation occurred, and stirring was continued for 2 hours. The solid precipitate was then collected by filtration, and rinsed with water. The solid was dried *in vacuo* to afford **2** as a colourless solid (0.95 g, 95 %).

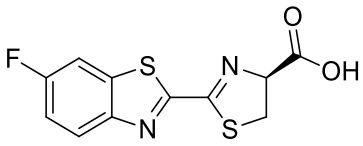


6-fluorobenzo[*d*]thiazole-2-carbonitrile (3):

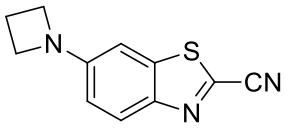
Method A: Potassium cyanide (0.63 g, 9.67 mmol) was added to a solution of **2** (1.5 g, 8.06 mmol) in DMSO (15 mL) and stirred for 6h at 80 °C. The reaction was then cooled to room temperature, poured into water and extracted with ethyl acetate (2 x 50 mL). The organic phase was evaporated to dryness and purified by flash chromatography using 10% ethyl acetate: hexane as eluent to yield **3** (269 mg, 27%) as a colourless solid.

Method B: Potassium cyanide (0.33g, 5.16 mmol) and DABCO (68 mg, 0.61 mmol) was added to a solution of **2** (0.8 g, 4.30 mmol) in DMSO: H_2O (9:1, 15 mL) and stirred for 12h at room temperature.[3] The reaction was poured into water and extracted with ethyl acetate (2 x 50 mL). The organic phase was evaporated to dryness and purified by flash chromatography using 10% ethyl acetate: hexane as eluent to yield **3** (613 mg, 81%) as a colourless solid.

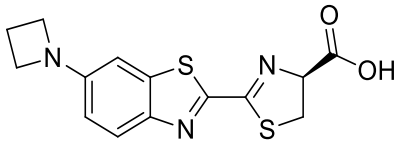
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, J = 9.2, 4.8 Hz, 1H), 7.40 (dd, J = 8.0, 2.4 Hz, 1H), 7.43-7.25 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5 (d, J_{cf} = 251 Hz), 148.9 (d, J_{cf} = 2.0 Hz), 136.6 (d, J_{cf}= 12.0 Hz), 136.2 (d, J_{cf} = 4.0 Hz), 126.6 (d, J_{cf} = 10.0 Hz), 117.4 (d, J_{cf} = 25 Hz), 112.6, 107.9 (d, J_{cf} = 28 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.31 (td, J = 8.3, 4.5 Hz, 1F). HRMS (ESI^+) Calculated for $C_8H_4FN_2S$: 179.0074 and found:179.0063.



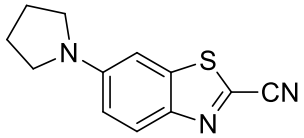
(*S*)-2-(6-fluorobenzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (3a): D-cysteine (8.14 mg, 0.067 mmol) was dissolved in 1 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **3** (10 mg, 0.056 mmol) in 1 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 10 mL). The solvent was removed by rotary evaporation to yield **4** as a colorless solid (13 mg, 81%). ^{1}H-NMR (400 MHz, $CDCl_3$ + 2 drops CD_3OD) δ 7.91 (ddd, J = 9.1, 4.8, 2.7 Hz, 1H), 7.47 (dt, J = 8.0, 2.2 Hz, 1H), 7.14-7.08 (m, 1H), 5.20 (td, J = 9.4, 2.3 Hz, 1H), 3.61 (qdd, J = 11.4, 9.4, 2.3 Hz, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$ + 2 drops CD_3OD) δ 171.6, 166.1, 161.5 (d, J_{cf}= 229.0 Hz), 160.3 (d, J_{cf}= 22.0 Hz), 149.4, 137.0 (d, J_{cf}= 11.0 Hz), 125.3 (d, J_{cf}= 9.0 Hz), 115.7 (d, J_{cf}= 25.0 Hz), 107.9 (d, J_{cf}= 26.0 Hz), 78.0, 34.0.^{19}F NMR (376 MHz, $CDCl_3$+ 2 drops CD_3OD) δ -112.38 (td, J = 8.6, 4.8 Hz, 1F). HRMS (ESI^+) Calculated for $C_{11}H_8FN_2O_2S_2$: 283.0006 and found: 283.0016.



6-(azetidin-1-yl)benzo[*d*]thiazole-2-carbonitrile (4): To a stirred solution of *azetidine* (153 mg, 2.69 mmol) in DMF (3 mL) was added **3** (400 mg, 2.24 mmol), potassium carbonate (92 mg, 0.67 mmol), and stirring continued at 60 °C for 6h. After the reaction mixture was cooled, the reaction mixture was diluted with ethyl acetate and washed with H_2O. The organic phase was evaporated to dryness and purified by flash chromatography using 10% ethyl acetate: hexane as eluent to yield **4** (8 mg, 2% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.5 Hz, 1H), 6.64-6.62 (m, 2H), 3.94 (t, *J* = 8.0 Hz, 4H), 2.42 (m, 2H). ^{13}C-NMR (125 MHz, $CDCl_3$) δ 151.7, 144.5, 138.3, 129.7, 125.5, 113.9, 113.6, 99.7, 52.1, 16.5. HRMS (ESI^+) Calculated for $C_{11}H_{10}N_3S$: 216.0590 and found: 216.0569.

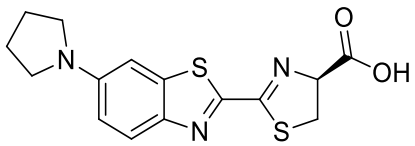


(*S*)-2-(6-(azetidin-1-yl)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (4a): D-cysteine (5 mg, 0.006 mmol) was dissolved in 1 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **4** (7 mg, 0.005 mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 10 mL). The solvent was removed by rotary evaporation to yield **4a** as red solid (7 mg, 50 %). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 9.0 Hz, 1H), 6.69 (d, *J* = 2.0 Hz, 1H), 6.58 (dd, *J* = 9.0, 2.5 Hz, 1H), 5.33 (t, *J* = 9.5 Hz, 1H), 3.93 (t, *J* = 7.5 Hz, 4H), 3.69 (d, J= 9.5 Hz, 2H), 2.39-2.34 (m, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$+ 2 drop of CD_3OD) δ 172.1, 166.5, 154.9, 151.4, 145.2, 138.2, 124.3, 112.7, 100.9, 77.9, 52.1, 34.7, 16.3. HRMS (ESI^+) Calculated for $C_{14}H_{14}N_3O_2S_2$: 320.0522 and found: 320.0512.

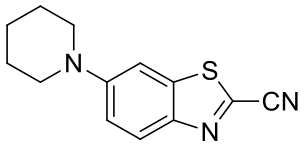


6-(pyrrolidin-1-yl)benzo[*d*]thiazole-2-carbonitrile (5): To a stirred solution of *pyrrolidine* (48 mg, 0.67 mmol) in DMF (3 mL) was added **3** (100 mg, 0.56 mmol),

potassium carbonate (92 mg, 0.67 mmol), and stirring continued at 60 °C for 6h. After the reaction mixture was cooled, the reaction mixture was diluted with ethyl acetate and washed with H_2O. The organic phase was evaporated to dryness and purified by flash chromatography using 10% ethyl acetate: hexane as eluent to yield **5** (22 mg, 17% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 9.2 Hz, 1H), 6.89 (dd, *J* = 9.2, 2.4 Hz, 1H), 6.84 (d, *J* = 2.4 Hz, 1H), 3.39 – 3.36 (m, 4H), 2.09-2.06 (m, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 148.1, 143.5, 138.8, 128.6, 125.3, 114.8, 114.1, 100.0, 48.0, 25.5. HRMS (ESI^+) Calculated for $C_{12}H_{12}N_3S$: 230.0746 and found: 230.0737.

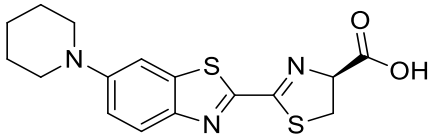


(*S*)-2-(6-(pyrrolidin-1-yl)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (5a): D-cysteine (6.4 mg, 0.052 mmol) was dissolved in 1 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **5** (10 mg, 0.043 mmol) in 1 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 10 mL). The solvent was removed by rotary evaporation to yield **5a** as red solid (10 mg, 67 %). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.5 Hz, 1H), 6.63-6.60 (m, 2H), 5.25 (bs, 1H), 3.63-3.59 (m, 2H), 3.17 (bs, 4H), 1.91 (bs, 4H). ^{13}C-NMR (125 MHz, $CDCl_3$+ DMSO-d_6) δ 172.5, 165.3, 153.8, 147.2, 144.3, 138.7, 124.6, 113.5, 101.0, 78.8, 47.8, 35.2, 25.5. HRMS (ESI^+) Calculated for $C_{15}H_{16}N_3O_2S_2$: 334.0678 and found: 334.0667.

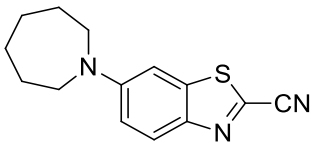


6-(piperidin-1-yl)benzo[*d*]thiazole-2-carbonitrile (6): To a stirred solution of *piperidine* (57 mg, 0.67 mmol) in DMF (3 mL) was added **3** (100 mg, 0.56 mmol), potassium carbonate (92 mg, 0.67 mmol), and stirring continued at 60 °C for 6h. After the reaction mixture was cooled, the reaction mixture was diluted with ethyl acetate and washed with H_2O. The organic phase was evaporated to dryness and purified by flash chromatography using 10% ethyl acetate: hexane as eluent to yield **6** (26 mg, 19% yield) as a yellow solid. ^{1}H NMR

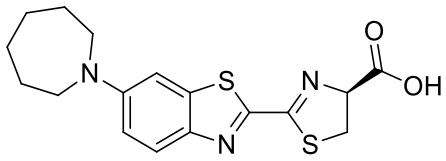
(400 MHz, $CDCl_3$) δ 7.98 (d, *J*= 9.2 Hz, 1H), 7.27-7.22 (m, 2H), 3.35-3.32 (m, 4H), 1.76-1.65 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 152.2, 145.1, 138.26, 131.0, 125.1, 118.5, 113.8, 104.3, 49.9, 25.5, 24.2. HRMS (ESI^+) Calculated for $C_{13}H_{14}N_3S$: 244.0903 and found: 244.0895.



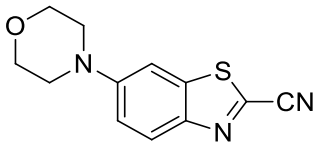
(*S*)-2-(6-(piperidin-1-yl)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (6a): D-cysteine (6 mg, 0.049 mmol) was dissolved in 1 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **6** (10 mg, 0.041 mmol) in 1 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 10 mL). The solvent was removed by rotary evaporation to yield **6a** as red solid (9 mg, 64 %). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 9.2 Hz, 1H), 7.31 (d, *J* = 2 Hz, 1H), 7.20 (dd, *J* = 9.2, 2.4 Hz, 1H), 5.41 (t, *J* = 9.6 Hz, 1H), 3.81-3.71 (m, 2H), 3.30(t, *J* = 9.6 Hz, 1H), 1.77-1.63 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 172.8, 167.5, 155.9, 151.1, 146.6, 138.4, 124.8, 117.9, 106.2, 77.9, 50.6, 34.9, 25.5, 24.1. HRMS (ESI^+) Calculated for $C_{16}H_{18}N_3O_2S_2$: 348.0835 and found: 348.0827.



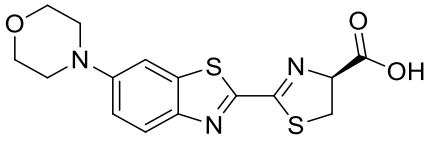
6-(azepan-1-yl)benzo[*d*]thiazole-2-carbonitrile (7): To a stirred solution of *hexamethyleneimine* (66 mg, 0.67 mmol) in DMF (3 mL) was added **3** (100 mg, 0.56 mmol), potassium carbonate (92 mg, 0.67 mmol), and stirring continued at 60 °C for 6h. After the reaction mixture was cooled, the reaction mixture was diluted with ethyl acetate and washed with H_2O. The organic phase was evaporated to dryness and purified by flash chromatography using 10% ethyl acetate: hexane as eluent to yield **7** (24 mg, 17% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J*= 9.6 Hz, 1H), 6.97 (dd, *J* = 9.2, 2.4 Hz, 1H), 6.92 (d, *J*= 2.4 Hz, 1H), 3.48 (t, *J*= 6 Hz, 4H), 1.79-1.74 (m, 4H), 1.52 – 1.48 (m, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 149.5, 143.4, 139.1, 125.4, 114.2, 114.1, 99.8, 49.8, 27.3, 26.8. HRMS (ESI^+) Calculated for $C_{14}H_{16}N_3S$: 258.1059 and found: 258.1049.



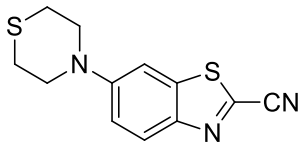
(*S*)-2-(6-(azepan-1-yl)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (7a): D-cysteine (5.6 mg, 0.046 mmol) was dissolved in 1 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **7** (10 mg, 0.039 mmol) in 1 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 10 mL). The solvent was removed by rotary evaporation to yield **7a** as a red solid (8 mg, 57 %). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 9.2 Hz, 1H), 6.94 (d, *J* = 2.4 Hz, 1H), 6.90 (dd, *J*= 9.2, 2.4 Hz, 1H), 5.34 (t, *J* = 9.6 Hz, 1H), 3.69 (dd, *J* = 10.0, 4.0 Hz, 2H), 3.48 (t, *J* = 6.0 Hz, 4H), 1.79-1.74 (bs, 4H), 1.52-1.49 (m, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$ + 2 drops CD_3OD) δ 172.2, 166.6, 153.9, 148.6, 144.1, 139.1, 124.6, 113.2, 100.6, 77.9, 49.7, 34.9, 27.4, 26.8. HRMS (ESI^+) Calculated for $C_{17}H_{20}N_3O_2S_2$: 362.0991and found: 362.0978.



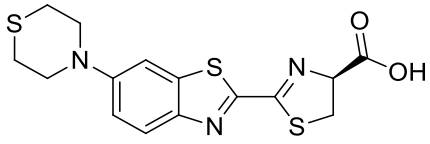
6-morpholinobenzo[*d*]thiazole-2-carbonitrile (8): To a stirred solution of *morpholine* (58 mg, 0.67 mmol) in DMF (3 mL) was added **3** (100 mg, 0.56 mmol), potassium carbonate (92 mg, 0.67 mmol), and stirring continued at 60 °C for 8h. After the reaction mixture was cooled, the reaction mixture was diluted with ethyl acetate and washed with H_2O. The organic phase was evaporated to dryness and purified by flash chromatography using 30% ethyl acetate: hexane as eluent to yield **8** (16 mg, 12% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 10.0 Hz, 1H), 7.27-7.24 (m, 2H), 3.89 (t, *J* = 4.8 Hz, 4H), 3.29 (t, *J* = 4.8 Hz, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 151.7, 145.9, 138.0, 132.1, 125.3, 117.9, 113.5, 104.5, 66.6, 48.7. HRMS (ESI^+) Calculated for $C_{12}H_{12}N_3OS$: 246.0696 and found: 246.0687.



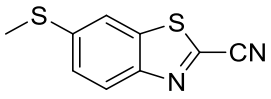
(*S*)-2-(6-morpholinobenzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (8a): D-cysteine (6 mg, 0.049 mmol) was dissolved in 1 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **8** (10 mg, 0.041 mmol) in 1 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 10 mL). The solvent was removed by rotary evaporation to yield **8a** as a yellow solid (7 mg, 50 %). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.97 (dd, *J* = 9.2, 0.8 Hz, 1H), 7.26 (d, *J* = 2 Hz, 1H), 7.16 (ddd, *J* = 9.2, 2.4, 0.8 Hz, 1H), 5.35 (ddd, *J* = 9.6, 8.8, 1.2 Hz, 1H), 3.87 (t, *J* = 4.8 Hz, 4H), 3.79-3.68 (m, 2H), 3.25 (t, *J* = 4.8 Hz, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$+ 2 drop of CD_3OD) 172.1, 166.6, 157.1, 150.6, 146.9, 138.1, 124.6, 117.1, 105.8, 78.0, 66.6, 49.1, 35.1. HRMS (ESI^+) Calculated for $C_{15}H_{16}N_3O_3S_2$: 350.0628 and found: 350.0619.



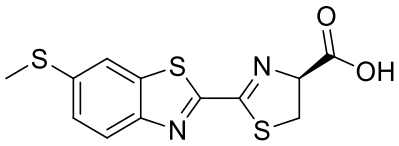
6-thiomorpholinobenzo[*d*]thiazole-2-carbonitrile (9): To a stirred solution of *thiomorpholine* (68 mg, 0.67 mmol) in DMF (3 mL) was added **3** (100 mg, 0.56 mmol), potassium carbonate (92 mg, 0.67 mmol), and stirring continued at 60 °C for 8h. After the reaction mixture was cooled, the reaction mixture was diluted with ethyl acetate and washed with H_2O. The organic phase was evaporated to dryness and purified by flash chromatography using 10% ethyl acetate: hexane as eluent to yield **9** (13 mg, 9% yield) as a brownish yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 9.2 Hz, 1H), 7.20-7.14 (m, 2H), 3.70-3.67 (m, 4H), 2.72-2.70 (m, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 138.2, 125.6, 118.7, 113.5, 105.3, 51.7, 26.2. HRMS (ESI^+) Calculated for $C_{12}H_{12}N_3S_2$: 262.0467 and found: 262.0458.



(*S*)-2-(6-thiomorpholinobenzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (9a): D-cysteine (5.6 mg, 0.046 mmol) was dissolved in 1 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **9** (10 mg, 0.038 mmol) in 1 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 10 mL). The solvent was removed by rotary evaporation to yield **9a** as a red solid (6.8 mg, 48 %). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 9.2 Hz, 1H), 7.24 (bs, 1H), 7.10 (d, *J* = 9.2, 1H), 5.36 (t, *J* = 9.6 Hz, 1H), 3.72 (d, *J* = 9.6 Hz, 2H), 3.64 (t, *J* = 4.8 Hz, 4H), 2.73 (bs, 4H). ^{13}C-NMR (100 MHz, $CDCl_3$ + 2 drop of CD_3OD) δ 172.0, 166.5, 157.1, 150.1, 146.6, 138.2, 124.7, 118.2, 106.9, 78.0, 52.1, 35.0, 26.3. HRMS (ESI^+) Calculated for $C_{15}H_{16}N_3O_2S_3$: 366.0399 and found: 366.0387.

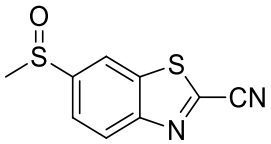


6-(methylthio)benzo[*d*]thiazole-2-carbonitrile (10): To a stirred solution of *sodium thiomethoxide* (47 mg, 0.67 mmol) in DMF (3 mL) was added **3** (100 mg, 0.56 mmol) and stirring continued at 60 °C for 8h. After the reaction mixture was cooled, the reaction mixture was diluted with ethyl acetate and washed with H_2O. The organic phase was evaporated to dryness and purified by flash chromatography using 10% ethyl acetate: hexane as eluent to yield **10** (55 mg, 48% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, *J* = 8.8, 0.4 Hz, 1H), 7.71 (d, *J* = 2.0 Hz, 1H), 7.49 (dd, J = 8.8, 2.0 Hz, 1H), 2.59 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 149.8, 141.6, 136.7, 134.7, 126.7, 124.9, 116.7, 113.1, 15.6. HRMS (ESI^+) Calculated for $C_9H_7N_2S_2$: 207.0045 and found: 207.0026.

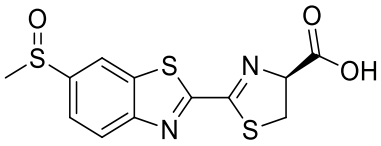


(*S*)-2-(6-(methylthio)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (10a): D-cysteine (14 mg, 0.12mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **10** (20 mg, 0.10mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h,

and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **10a** as yellow solid (15 mg, 50 %). ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.93 (d, *J* = 8.8 Hz, 1H), 7.65 (d, J = 2.0 Hz, 1H), 7.34 (dd, *J* = 8.8, 2.0 Hz, 1H), 5.30 (t, J = 8.8 Hz, 1H), 3.76-3.64 (m, 2H), 2.50 (s, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$+ 2 drop of CD_3OD) δ 171.9, 166.5, 159.2, 150.6, 139.1, 137.1, 125.8, 124.2, 117.7, 78.1, 35.1, 15.7. HRMS (ESI^+) Calculated for $C_{12}H_{11}N_2O_2S_3$: 310.9977 and found: 310.9948.

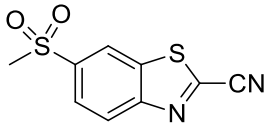


6-(methylsulfinyl)benzo[*d*]thiazole-2-carbonitrile (11): To a solution of **10** (33 mg, 0.16 mmol) in ethanol (5.0 mL) was added Oxone (49 mg, 0.08 mmol), and the mixture was stirred at 60 °C for 8 h. The mixture was cooled to room temperature and water was added (10 mL), then extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 50% ethyl acetate: hexane as eluent to yield **11** (25 mg, 71% yield) as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48-8.38 (d, *J*= 1.6Hz, 2H), 8.34 (d, *J* = 8.8 Hz, 2H), 7.74 (dd, *J* = 8.8, 1.6 Hz, 2H), 2.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 146.9, 138.8, 136.3, 126.1, 122.7, 117.8, 112.5, 44.2. HRMS (ESI^+) Calculated for $C_9H_7N_2OS_2$: 222.9994 and found: 222.9974.

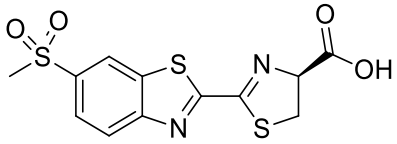


(4*S*)-2-(6-(methylsulfinyl)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (11a): D-cysteine (13 mg, 0.11 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **11** (20 mg, 0.09 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **11a** as an off-white solid (16 mg, 53 %). ^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD) δ 8.26 (d, *J* = 1.6 Hz, 1H), 8.19 (d, *J* = 8.8 Hz, 1H), 7.63

(ddd, J = 8.8, 1.6, 0.4 Hz, 1H), 5.32 (dd, J = 9.8, 9.0 Hz, 1H), 3.79-3.67 (m, 2H), 2.76 (s, 3H). ^{13}C NMR (100MHz, $CDCl_3$+CD_3OD) δ 171.6, 166.1, 163.3, 154.6, 143.6, 136.8, 125.3, 121.6, 118.1, 78.2, 43.6, 35.2. HRMS (ESI^+) Calculated for $C_{12}H_{11}N_2O_3S_3$: 326.9926 and found: 326.9897.

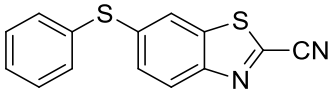


6-(methylsulfonyl)benzo[*d*]thiazole-2-carbonitrile (12): To a solution of **10** (50 mg, 0.24 mmol) in CH_2Cl_2 was added *m*-chloroperbenzoic acid (50 mg, 0.29 mmol). The resultant mixture was stirred for 12 h, after which the mixture was diluted with additional CH_2Cl_2. This mixture was then washed with saturated solution of sodium bicarbonate. After drying over Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 30% ethyl acetate: hexane as eluent to yield **12** (35 mg, 61% yield) as an off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$+ DMSO-d_6) δ 8.60 (d, J = 2.0 Hz, 1H), 8.28 (d, J = 8.4 Hz, 1H), 8.04 (dd, J = 8.8, 2.0 Hz, 1H), 3.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 154.6, 141.0, 140.3, 135.6, 126.2, 126.2, 122.9, 112.2, 44.5. HRMS (ESI^+) Calculated for $C_9H_7N_2O_2S_2$: 238.9943 and found: 238.9944.

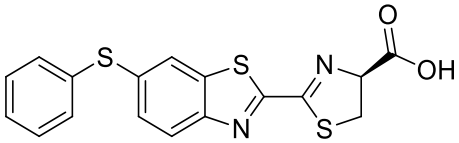


(*S*)-2-(6-(methylsulfonyl)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (12a): D-cysteine (12 mg, 0.09 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **12** (20 mg, 0.08 mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **12a** as an off-white solid (14 mg, 50 %). ^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD) δ 8.53 (dd, J = 2.0, 0.4 Hz, 1H), 8.25 (dd, J = 8.4, 0.4 Hz, 1H), 8.00 (dd, J = 8.4, 1.6 Hz, 1H), 5.35 (dd, J = 10.0, 9.2 Hz, 1H), 3.83-3.69 (m, 2H), 3.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD) δ 170.6, 165.1, 164.4, 154.9, 137.6, 135.5, 124.5,

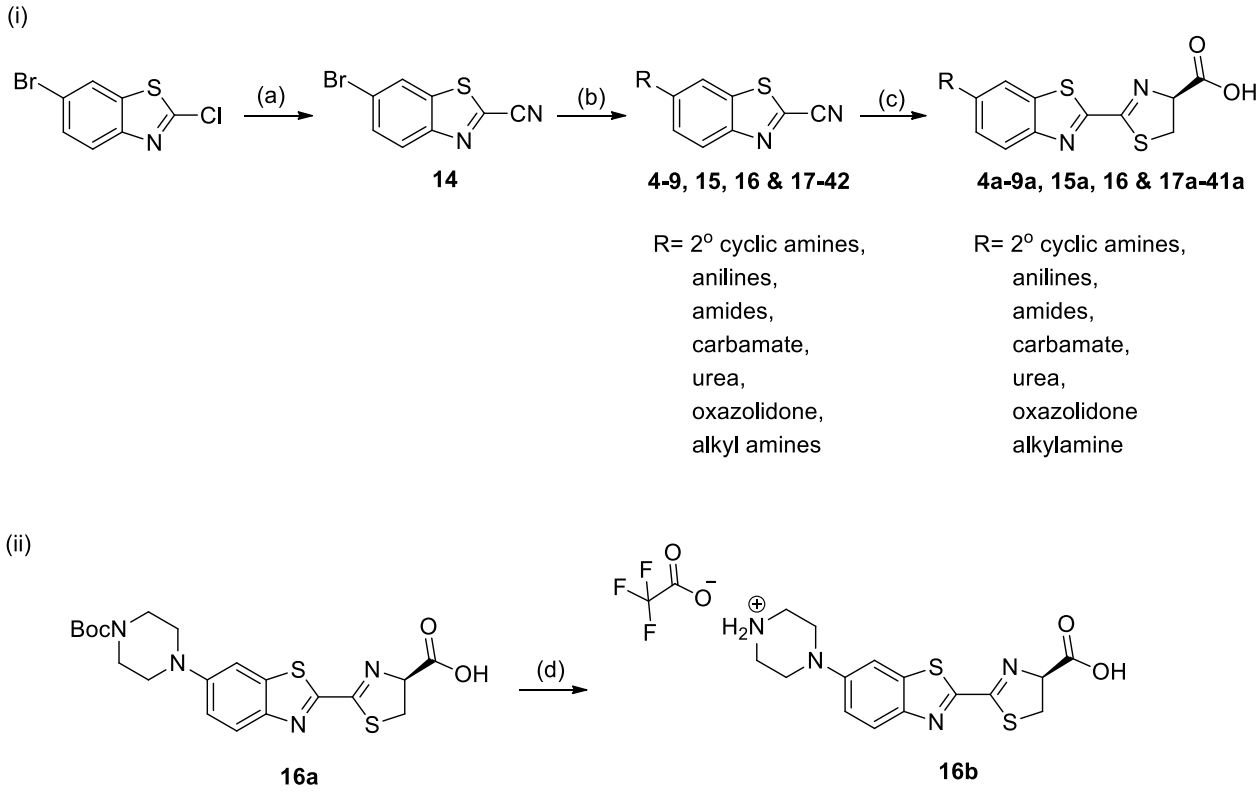
124.3, 121.7, 77.4, 43.7, 34.4. HRMS (ESI^+) Calculated for $C_{12}H_{11}N_2O_4S_3$: 342.9875 and found: 342.9845.



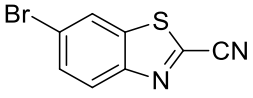
6-(phenylthio)benzo[*d*]thiazole-2-carbonitrile (13): To a stirred solution of *thiophenol* (74 mg, 0.67 mmol) in DMF (3 mL) was added **3** (100 mg, 0.56 mmol), potassium carbonate (92 mg, 0.67 mmol), and stirring continued at 60 °C for 8h. After the reaction mixture was cooled, the reaction mixture was diluted with ethyl acetate and washed with H_2O. The organic phase was evaporated to dryness and purified by flash chromatography using 10% ethyl acetate: hexane as eluent **13** (20 mg, 13% yield) as an off-white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.8 Hz, 1H), 7.58 (d, *J* = 1.6 Hz, 1H), 7.45-7.33 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ150.5, 140.5, 136.5, 135.6, 133.7, 132.3, 129.9, 129.0, 128.6, 125.2, 120.1, 112.9. HRMS (ESI^+) Calculated for $C_{14}H_9N_2S_2$: 269.0202 and found: 269.0194.



(*S*)-2-(6-(phenylthio)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (13a): D-cysteine (5.4 mg, 0.045 mmol) was dissolved in 1 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **13** (10 mg, 0.037 mmol) in 1 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 10 mL). The solvent was removed by rotary evaporation to yield **13a** as a yellow solid (8 mg, 57 %). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.96-7.94 (m, 1H), 7.68 (d, *J* = 1.2 Hz, 1H), 7.39 – 7.30 (m, 6H), 5.33-5.28(m, 1H), 3.81 – 3.68 (m, 2H). ^{13}C-NMR (125 MHz, DMSO-d_6) δ 171.5, 164.9, 161.43, 151.9, 137.0, 135.9, 133.9, 132.4, 130.3, 129.2, 128.7, 125.1, 123.9, 78.6, 35.3. HRMS (ESI^+) Calculated for $C_{17}H_{13}N_2O_2S_3$: 373.0134 and found: 373.0124.



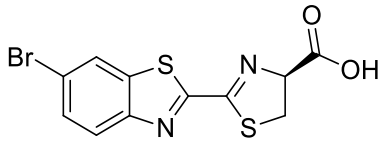
Scheme S2. (i) (a) *Method A:* KCN, DMSO, 90°C, 8h; *Method B:* KCN, DABCO, DMSO: H_2O (9:1), rt, overnight. (b) nucleophile, Pd_2dba_3, xantphos, Cs_2CO_3, dioxane, 95-100°C. (c) D-cysteine, pH 8 buffer. (**ii**) (d) dichloromethane: trifluoroacetic acid (3:1), rt, 2h.



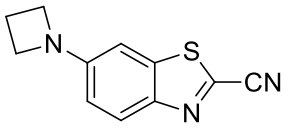
6-bromobenzo[*d*]thiazole-2-carbonitrile (**14**):

Method A: Potassium cyanide (203 mg, 3.13 mmol) was added to a solution of *6-bromo-2-chlorobenzo[d]thiazole* (650 mg, 2.61 mmol) in DMSO (15 mL) and stirred for 6h at 80°C. The reaction was cooled to room temperature, poured into water and extracted with ethyl acetate (2 x 50 mL). The organic phase was evaporated to dryness and purified by flash chromatography using 10% ethyl acetate: hexane as eluent to yield **14** (250 mg, 40%).

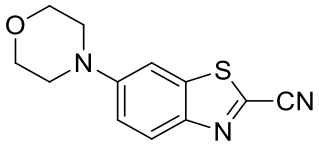
Method B: Potassium cyanide (2.22 g, 34.14 mmol) and DABCO (455 mg, 4.1 mmol) was added to a solution of *6-bromo-2-chlorobenzo[d]thiazole* (7 g, 28.45 mmol) in DMSO: H_2O (9:1, 50 mL) and stirred for 12h at room temperature.[3] The reaction was poured into water and extracted with ethyl acetate (2 x 50 mL). The organic phase was evaporated to dryness and purified by flash chromatography using 10% ethyl acetate: hexane as eluent to yield **14** (5 g, 74%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 2.0, 0.8 Hz, 1H), 8.08 (dd, *J* = 8.8, 0.8 Hz, 1H), 7.76 (dd, *J* = 8.8, 2.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.0, 136.9, 136.8, 131.8, 126.3, 124.3, 123.1, 112.6. HRMS (ESI^+) Calculated for $C_8H_4BrN_2S$: 240.9253 and found: 240.9252.



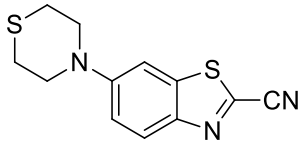
(*S*)-2-(6-bromobenzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (14a): D-cysteine (12 mg, 0.07 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **14** (20 mg, 0.08 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **14a** as colourless solid (22 mg, 71 %). ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.52 (s, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.76 (d, J = 8.5 Hz, 1H), 5.40 (t, *J* = 9.0 Hz, 1H), 3.80-3.70 (m, 2H). ^{13}C NMR (125MHz, DMSO-d_6) δ 171.7, 164.2, 162.2, 152.1, 137.6, 130.8, 126.0, 125.9, 120.7, 79.4, 35.6. HRMS (ESI^+) Calculated for $C_{11}H_8BrN_2O_2S_2$: 342.9205 & 344.9185 and found: 342.9206 & 344.9180.



6-(azetidin-1-yl)benzo[*d*]thiazole-2-carbonitrile (4): A sealed round bottom flask was charged with **14** (33 mg, 0.14 mmol), *azetidine* (10 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 50% ethyl acetate: hexane as eluent to yield **4** (10 mg, 33% yield) as a yellow solid.

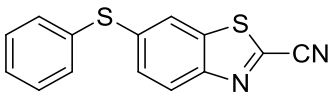


6-morpholinobenzo[*d*]thiazole-2-carbonitrile (8): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *morpholine* (14.4 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 50% ethyl acetate: hexane as eluent to yield **8** (24 mg, 71% yield) as a yellow solid.

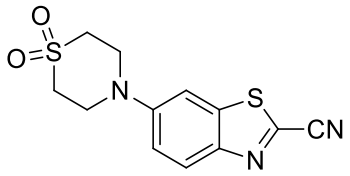


6-thiomorpholinobenzo[*d*]thiazole-2-carbonitrile (9): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *thiomorpholine* (17.5 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to

room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 30% ethyl acetate: hexane as eluent to yield **9** (20 mg, 55% yield) as a yellow solid.

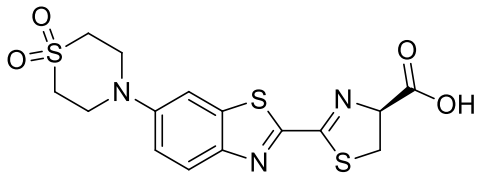


6-(phenylthio)benzo[*d*]thiazole-2-carbonitrile (13): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *thiophenol* (18.7 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 10% ethyl acetate: hexane as eluent to yield **10** (18 mg, 48% yield) as a colorless solid.

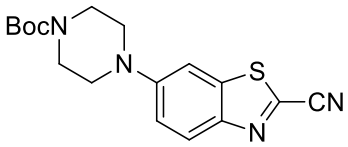


6-(1,1-dioxidothiomorpholino)benzo[*d*]thiazole-2-carbonitrile (15): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), thiomorpholinedioxide (29 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 50% ethyl acetate: hexane as eluent to yield **15** (30 mg, 74% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$+ CD_3OD) δ 7.97 (d, J = 9.2 Hz, 1H), 7.32 (d, J = 2.4 Hz, 1H), 7.20 (dd, J = 9.2, 2.8 Hz, 3H), 3.90 (t, J = 5.2 Hz, 4H), 3.07 (t, J = 5.2 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$ + CD_3OD) δ 148.2, 146.1, 138.1,

133.1, 125.9, 118.2, 113.1, 105.9, 50.5, 47.4. HRMS (ESI^+) Calculated for $C_{12}H_{12}N_3O_2S_2$: 294.0365 and found: 294.0340.

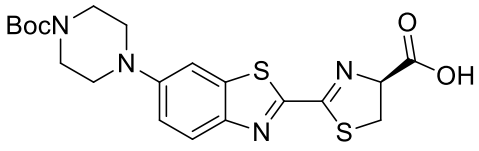


(*S*)-2-(6-(1,1-dioxidothiomorpholino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (15a): D-cysteine (9 mg, 0.07 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **15** (15 mg, 0.06 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **15a** as a red solid (14 mg, 70 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 9.2 Hz, 1H), 7.20 (d, J = 2.4 Hz, 1H), 6.98 (dd, *J* = 9.2, 2.4 Hz, 1H), 5.14 (dd, *J* = 9.6, 8.8 Hz, 1H), 3.75 (t, *J*= 5.2 Hz, 4H), 3.59-3.48 (m, 2H), 2.96 (t, *J*= 5.2 Hz, 4H). ^{13}C NMR (100MHz, $CDCl_3$ + DMSO-d_6) δ 171.7 165.5, 157.9, 147.1, 146.9, 138.1, 125.1, 116.9, 106.8, 78.3, 50.5, 47.5, 35.1. HRMS (ESI^+) Calculated for $C_{15}H_{16}N_3O_4S_3$: 398.0297 and found: 398.0260.

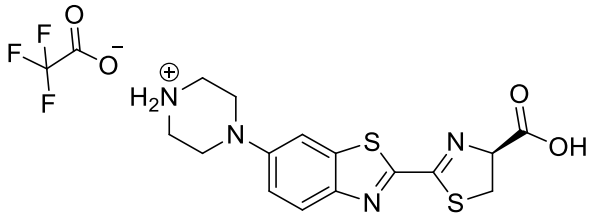


***tert*-butyl-4-(2-cyanobenzo[*d*]thiazol-6-yl)piperazine-1-carboxylate (16):** A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *tert-butyl-1-piperazinecarboxylate* (31 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 3h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 30% ethyl acetate: hexane as eluent to yield **16** (36 mg, 75% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 10.0 Hz, 1H), 7.26-7.24 (m, 2H), 3.61 (t, *J*= 5.2 Hz, 4H), 3.29 (t, *J*= 5.2Hz, 4H), 1.48

(s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 151.5, 145.9, 137.9, 132.1, 125.3, 118.6, 113.5, 105.1, 80.2, 48.7, 28.4. HRMS (ESI^+) Calculated for $C_{17}H_{21}N_4O_2S$: 345.1380 and found: 345.1379.

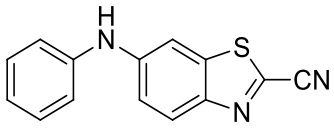


(*S*)-2-(6-(4-(tert-butoxycarbonyl)piperazin-1-yl)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (16a): D-cysteine (13.0 mg, 0.11 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **16** (30 mg, 0.09 mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **16a** as a red solid (36 mg, 92%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J*=9.2 Hz, 1H), 7.27 (s, 1H), 7.17 (dd, *J*= 9.2, 2.4Hz, 1H), 5.41 (t, *J*= 9.6 Hz, 1H), 3.82-3.72 (m, 2H), 3.61(t, *J*= 5.2 Hz, 4H), 3.26 (t, *J*= 4.4 Hz, 4H), 1.48 (s, 9H). ^{13}C NMR (100MHz, $CDCl_3$) δ 172.8, 167.2, 156.7, 154.8, 150.5, 147.1, 138.2, 124.8, 117.8, 106.4, 80.4, 77.8, 49.1, 34.9, 28.4. HRMS (ESI^+) Calculated for $C_{20}H_{25}N_4O_4S_2$: 449.1312 and found: 449.1307.



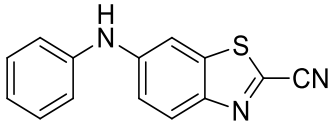
Trifluoroacetic acid salt of (S)-2-(6-(piperazin-1-yl)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (16b): Compound **16a** (32 mg, 0.07 mmol) was dissolved in 2 ml of dichloromethane: trifluoroacetic acid (3:1) and stirred for 2 hr under argon. The solvents were removed in vacuo, and the crude was re-dissolved in dichloromethane and concentrated in vacuo. This process was repeated three times to provide the product **16b** as a red solid (29 mg, 88%). ^{1}H NMR (500 MHz, CD_3OD) δ 7.96 (d, *J*= 9.0 Hz, 1H), 7.56 (d, *J*= 2.5 Hz, 1H), 7.34 (dd, *J*= 9.0, 2.5 Hz, 1H), 5.41(t, *J*= 9.0 Hz, 1H), 3.82-3.74 (m, 2H), 3.56 (t, *J*= 5.0 Hz, 4H), 3.43 (t, *J*= 5.0 Hz, 4H). ^{13}C NMR (125 MHz, CD_3OD) δ 171.9, 166.2, 158.0, 149.8, 147.4, 137.8, 124.2, 118.0, 107.1, 78.1, 46.3, 43.2, 34.5. ^{19}F NMR (470

MHz, CD_3OD) δ -77.03 (s, 3F). HRMS (ESI^+) Calculated for $C_{15}H_{17}N_4O_2S_2$: 349.0787 and found: 349.0775.

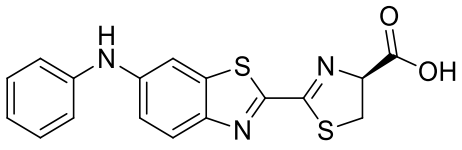


6-(phenylamino)benzo[*d*]thiazole-2-carbonitrile (**17**): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *aniline* (11.6 mg, 0.13 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 30% ethyl acetate: hexane as eluent to yield **17** (23 mg, 66% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 9.2 Hz, 1H), 7.48 (d, *J* = 2.0 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 7.22 – 7.20 (m, 3H), 7.12 (td, J = 7.6, 0.8 Hz, 1H), 6.13 (bs, 1H).^{13}C NMR (100 MHz, $CDCl_3$) δ 146.3, 145.2, 140.6, 138.1, 131.8, 129.7, 125.8, 123.7, 120.7, 118.9, 113.5, 104.3, 77.3, 77.0, 76.7. HRMS (ESI^+) Calculated for $C_{14}H_{10}N_3S$: 252.0590 and found: 252.0567.

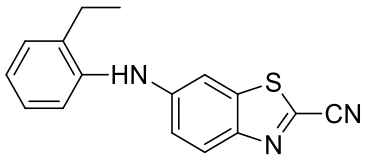
<u>On 1 mmol scale:</u>



6-(phenylamino)benzo[*d*]thiazole-2-carbonitrile (**17**): A round bottom flask was charged with **14** (239 mg, 1 mmol), aniline (84 mg, 0.9 mmol), tris(dibenzylideneacetone)palladium (46 mg, 0.051 mmol), xantphos (59 mg, 0.102 mmol), caesium carbonate (651 mg, 2 mmol) and dioxane (4.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL), and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 30% ethyl acetate: hexane as eluent to yield **17** (160 mg, 64% yield) as a yellow solid. NMR was identical to above.

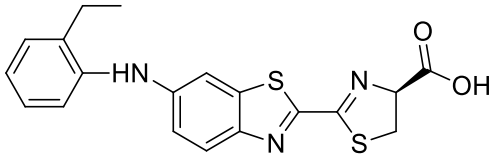


(*S*)-2-(6-(phenylamino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (17a): D-cysteine (11.5 mg, 0.09 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **17** (20 mg, 0.07 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **17a** as brown solid (16 mg, 57 %). ^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD) δ 7.88 (d, *J* = 9.2 Hz, 1H), 7.46 (d, *J* = 2.0 Hz, 1H), 7.29 -7.25 (m, 2H), 7.13 – 7.11 (m, 3H), 6.97 (t, *J* = 7.2 Hz, 1H), 5.28 (dd, *J* = 9.6, 8.8 Hz, 1H), 3.74-3.63 (m, 2H). ^{13}C NMR (100MHz, $CDCl_3$+CD_3OD) δ 172.1, 166.5, 156.5, 147.0, 143.8, 141.6, 138.1, 129.4, 124.9, 122.3, 119.4, 117.9, 105.6, 78.0, 35.03. HRMS (ESI^+) Calculated for $C_{17}H_{14}N_3O_2S_2$: 356.0522 and found: 356.0491.

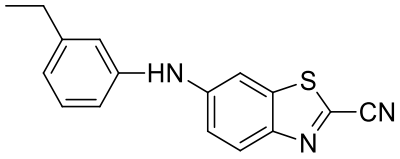


6-((2-ethylphenyl)amino)benzo[*d*]thiazole-2-carbonitrile (18): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *2-ethylaniline* (17 mg, 0.13 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 25% ethyl acetate: hexane as eluent to yield **18** (30 mg, 75% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (d, J= 9.0 Hz, 1H), 7.36-7.23 (m, 4H), 7.16-7.13 (m, 2H), 5.84 (s, 1H), 2.65 (q, J= 7.5 Hz, 2H), 1.24 (t, J= 7.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.1, 145.9, 138.5, 138.3, 138.1, 131.2, 129.7, 127.2, 125.8, 125.7,

124.4, 118.2, 113.7, 103.3, 24.5, 14.4. HRMS (ESI^+) Calculated for $C_{16}H_{14}N_3S$: 280.0903 and found: 280.0900.

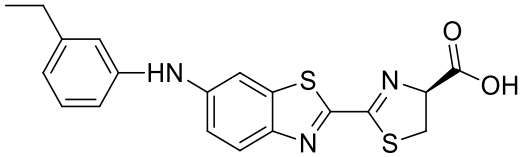


(*S*)-2-(6-((2-ethylphenyl)amino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (18a): D-cysteine (11 mg, 0.09 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **18** (20 mg, 0.07 mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **18a** as a red solid (17 mg, 62%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.5 Hz, 1H), 7.24-7.05 (m, 5H), 6.96 (dd, J= 9.0, 2.0Hz 1H), 5.34 (t, J= 8.5 Hz, 1H), 3.72-3.64 (m, 2H), 2.55 (q, J= 7.5 Hz, 2H), 1.14 (t, J= 7.5Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3, 167.7, 155.6, 147.0, 145.5, 138.8, 138.6, 137.5, 129.5, 127.0, 125.4, 124.9, 123.3, 117.4, 104.9, 77.8, 34.9, 24.4, 14.2. HRMS (ESI^+) Calculated for $C_{19}H_{18}N_3O_2S_2$: 384.0835 and found: 384.0834.

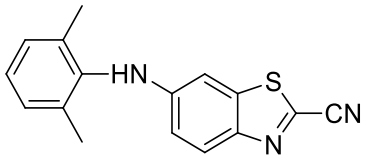


6-((3-ethylphenyl)amino)benzo[*d*]thiazole-2-carbonitrile (19): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *3-ethylaniline* (17 mg, 0.13 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 25% ethyl acetate: hexane as eluent to yield **19** (25 mg, 64% yield) as a yellow solid. ^1H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 9.0 Hz, 1H),

7.37 (d, J= 2.0 Hz, 1H), 7.23-7.20(m, 1H), 7.12 (dd, J= 9.0, 2.0 Hz, 1H), 6.98-6.95 (m,2H), 6.89 (d, J= 7.5 Hz, 1H), 5.99 (s, 1H), 2.58 (q, J= 7.5 Hz, 2H), 1.18(t, J= 7.5Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.3, 146.2, 145.5, 140.6, 138.1, 131.7, 129.6, 125.9, 123.5, 120.4, 118.9, 118.1, 113.6, 104.3, 28.8, 15.5. HRMS (ESI^+) Calculated for $C_{16}H_{14}N_3S$: 280.0903 and found: 280.0903.

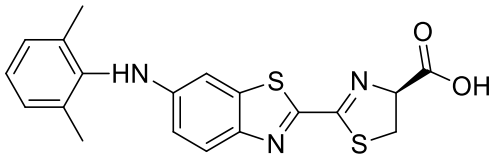


(*S*)-2-(6-((3-ethylphenyl)amino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (19a): D-cysteine (11 mg, 0.09 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **19** (20 mg, 0.07 mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **19a** as a red solid (15 mg, 54%). ^{1}H NMR (500 MHz, CD_3OD) δ 7.77 (d, *J* = 9.0 Hz, 1H), 7.46 (s, 1H), 7.15-7.10 (m, 2H), 6.94 (m, 2H), 6.73 (d, J= 7.5 Hz,1H), 5.26 (t, J= 9.0 Hz, 1H), 3.69-3.61 (m, 2H), 2.52 (q, J= 7.5 Hz, 2H), 1.14 (t, J= 7.5Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2, 166.2, 156.0, 146.5, 145.5, 144.9, 142.2, 138.1, 128.9, 124.2, 121.3, 118.6, 117.6, 116.3, 104.8, 78.2, 34.5, 28.5, 14.8. HRMS (ESI^+) Calculated for $C_{19}H_{18}N_3O_2S_2$: 384.0835 and found: 384.0832.

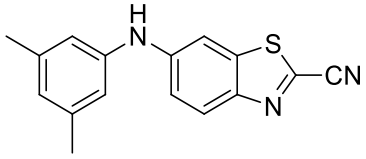


6-((2,6-dimethylphenyl)amino)benzo[*d*]thiazole-2-carbonitrile (20): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *2,6-dimethylaniline* (17 mg, 0.13 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with

ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 25% ethyl acetate: hexane as eluent to yield **20** (20 mg, 50% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 9.0 Hz, 1H), 7.11-7.09 (m, 3H), 6.88 (dd, J= 9.0, 2.0 Hz, 1H), 6.59 (d, J= 2.0 Hz, 1H), 5.54 (s,1H), 2.15 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.6, 145.4, 138.6, 136.6, 136.5, 130.5, 128.9, 127.2, 125.9, 116.8, 113.7, 101.3, 18.3. HRMS (ESI^+) Calculated for $C_{16}H_{14}N_3S$: 280.0903 and found: 280.0904.

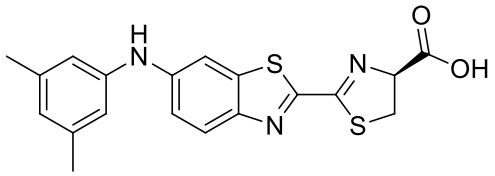


(*S*)-2-(6-((2,6-dimethylphenyl)amino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (20a): D-cysteine (10 mg, 0.08 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **20** (20 mg, 0.07 mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **20a** as a yellow solid (18 mg, 64%). ^{1}H NMR (500 MHz, CD_3OD) δ 7.85 (d, *J* = 8.5 Hz, 1H), 7.09 (s, 3H), 6.78 (dd, J= 9.0, 2.0 Hz, 1H), 6.64 (s, 1H), 5.33 (t, J= 9.5 Hz,1H), 3.72-3.65 (m, 2H), 2.15 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 167.9, 154.7, 146.5, 146.4, 138.9, 136.9, 136.5, 128.8, 126.8, 125.5, 115.7, 102.4, 77.7, 34.8, 18.3. HRMS (ESI^+) Calculated for $C_{19}H_{18}N_3O_2S_2$: 384.0835 and found: 384.0834.

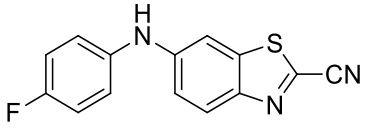


6-((3,5-dimethylphenyl)amino)benzo[*d*]thiazole-2-carbonitrile (21): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *3,5-dimethylaniline* (17 mg, 0.13 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The

resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 25% ethyl acetate: hexane as eluent to yield **21** (22 mg, 67% yield) as a red solid. ^{1}H NMR (500 MHz, CD_3OD) δ 7.81 (d, *J* = 9.0 Hz, 1H), 7.43 (d, J= 2.0 Hz, 1H), 7.17 (dd, J= 9.0, 2.0 Hz, 1H), 6.74 (s, 2H), 6.58 (s,1H), 2.18 (s, 6H). ^{13}C NMR (125 MHz, CD_3OD) δ 146.5, 145.3, 141.2, 138.8, 138.2, 130.5, 124.8, 1224.3, 118.7, 117.7, 113.3, 103.3, 20.4. HRMS (ESI^+) Calculated for $C_{16}H_{14}N_3S$: 280.0903 and found: 280.0888.

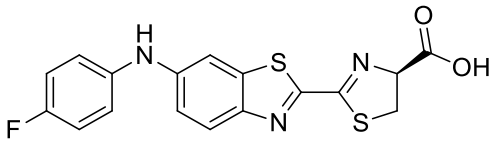


(*S*)-2-(6-((3,5-dimethylphenyl)amino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (21a): D-cysteine (9 mg, 0.07 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **21** (15 mg, 0.06 mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **21a** as a yellowish brown solid (14 mg, 68%). ^{1}H NMR (500 MHz, CD_3OD): δ 7.76 (d, *J* = 9.0 Hz, 1H), 7.44 (d, J= 2.0 Hz, 1H), 7.12 (dd, J= 9.0, 2.0 Hz, 1H), 6.73 (s, 2H), 6.55 (s, 1H), 5.27(t, J= 9.0Hz,1H), 3.68-3.61 (m, 2H), 2.18 (s, 6H). ^{13}C NMR (125 MHz, CD_3OD + $CDCl_3$) δ 172.0, 166.4, 155.8, 146.4, 144.9, 141.9, 138.7, 138.1, 124.2, 123.5, 117.7, 116.9, 104.8, 78.01, 34.5, 20.3. HRMS (ESI^+) Calculated for $C_{19}H_{18}N_3O_2S_2$: 384.0835 and found: 384.0817.

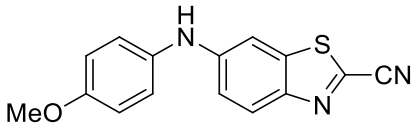


6-((4-fluorophenyl)amino)benzo[*d*]thiazole-2-carbonitrile (22): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *4-fluoroaniline* (14.4 mg, 0.13

mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 30% ethyl acetate: hexane as eluent to yield **22** (21 mg, 57% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (dd, J = 8.8, 0.4 Hz, 1H), 7.20-7.06 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD) δ 159.0 (J_{cf} = 241 Hz), 146.5, 145.5, 138.2, 136.8, 130.8, 125.5, 123.0(d, J_{cf} = 8 Hz), 118.4, 116.2 (d, J_{cf} = 23 Hz), 113.5, 102.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.47 (m, 1F). HRMS (ESI$^+$) Calculated for $C_{14}H_9FN_3S$: 270.0496 and found: 270.0471.

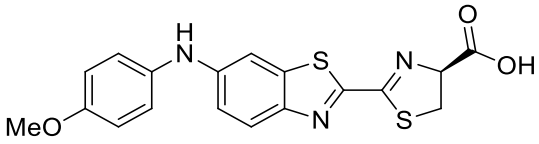


(*S*)-2-(6-((4-fluorophenyl)amino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (22a): D-cysteine (8.7 mg, 0.07 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **22** (15 mg, 0.06 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **22a** as a red solid (11 mg, 52 %). ^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD) δ 7.86 (d, J = 8.8 Hz, 1H), 7.32 (d, J = 8.8 Hz, 1H), 7.88 (d, J = 2.0 Hz, 1H), 7.11 – 6.95 (m, 5H), 5.28 (t, J = 9.2 Hz, 1H), 3.74-3.63 (m, 2H). ^{13}C NMR (100MHz, $CDCl_3$+CD_3OD) δ 172.0, 166.5, 158.5 (d, J_{cf} = 241Hz), 156.2, 146.6, 144.7, 138.2, 137.6, 124.8, 122.0 (d, J_{cf}= 8Hz), 117.3, 115.9 (d, J_{cf} = 22Hz), 104.6, 77.9, 34.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -120.56 (m, 1F). HRMS (ESI$^+$) Calculated for $C_{17}H_{13}FN_3O_2S_2$: 374.0428 and found: 374.0396.

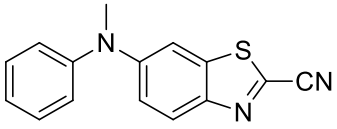


6-((4-methoxyphenyl)amino)benzo[*d*]thiazole-2-carbonitrile (23): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *4-methoxyaniline* (16 mg,

0.13 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 3h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 30% ethyl acetate: hexane as eluent to yield **23** (27 mg, 69% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 9.2 Hz, 1H), 7.22 (d, *J* = 2.0 Hz, 1H), 7.17-7.08 (m, 3H), 6.87 (d, *J* = 8.8 Hz, 1H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD) δ 156.3, 147.5, 145.1, 138.3, 133.6, 130.0, 125.3, 124.1, 118.1, 114.8, 113.6, 101.9, 55.38. HRMS (ESI^+) Calculated for $C_{15}H_{12}N_3OS$: 282.0696 and found: 282.0671.

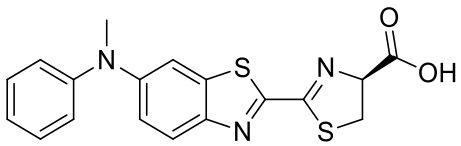


(*S*)-2-(6-((4-methoxyphenyl)amino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (23a): D-cysteine (10 mg, 0.08 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **23** (20 mg, 0.07 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **23a** as a red solid (18 mg, 66 %). ^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD) δ 7.89 (d, *J* = 8.8 Hz, 1H), 7.25-6.90 (m, 4H), 6.89 (d, *J* = 8.8 Hz, 2H), 5.32 (t, *J* = 9.2 Hz, 1H), 3.80 (s, 3H), 3.77-3.65 (m, 2H). ^{13}C NMR (100MHz, $CDCl_3$+CD_3OD) δ 172.1, 166.6, 155.8, 155.5, 146.2, 145.9, 138.4, 134.4, 124.7, 123.4, 116.9, 114.7, 103.5, 77.9, 55.4, 34.9. HRMS (ESI^+) Calculated for $C_{18}H_{16}N_3O_3S_2$: 386.0628 and found: 386.0596.

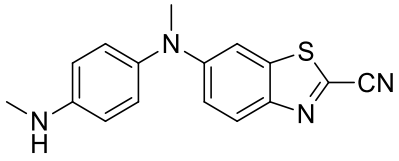


6-(methyl(phenyl)amino)benzo[*d*]thiazole-2-carbonitrile (24): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *N-methylaniline* (14 mg, 0.13

mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 30% ethyl acetate: hexane as eluent to yield **24** (22 mg, 59% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 9.2 Hz, 1H), 7.44-7.40 (m, 2H), 7.26-7.17 (m, 4H), 7.09 (dd, *J* = 9.2, 2.4 Hz, 1H), 3.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.8, 147.5, 145.2, 138.1, 130.9, 130.0, 125.7, 125.6, 125.0, 118.1, 113.7, 104.2, 40.7. HRMS (ESI$^+$) Calculated for $C_{15}H_{12}N_3S$: 266.0746 and found: 266.0722.

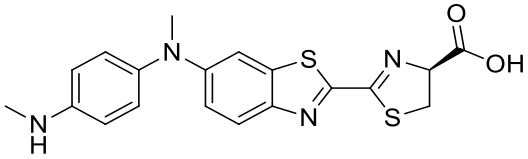


(*S*)-2-(6-(methyl(phenyl)amino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (24a): D-cysteine (9 mg, 0.07 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **24** (15 mg, 0.06 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **24a** as a red solid (12 mg, 60 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 9.6 Hz, 1H), 7.34-7.30 (m, 2H), 7.19-7.00 (m, 4H),6.98 (d, *J* = 2.4 Hz, 1H), 5.35 (t, *J* = 9.2 Hz, 1H), 3.72-3.69 (m, 2H),3.34 (s, 3H). ^{13}C NMR (100MHz, $CDCl_3$) δ 172.8, 167.7, 155.5, 148.8, 148.0, 146.6, 138.4, 129.7, 124.7, 124.7, 124.6, 118.0, 106.4, 77.7, 40.7, 34.8. HRMS (ESI$^+$) Calculated for $C_{18}H_{16}N_3O_3S_2$: 370.0678 and found: 370.0648.

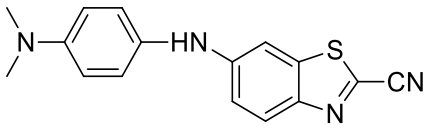


6-(methyl(4-(methylamino)phenyl)amino)benzo[*d*]thiazole-2-carbonitrile (25): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *alarmine* (17.7 mg, 0.13 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1

mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 20% ethyl acetate: hexane as eluent to yield **25** (25 mg, 63% yield) as a red solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, J = 9.2, 0.4 Hz, 1H), 7.05-6.96 (m, 4H), 6.66 (d, J = 8.4 Hz, 2H), 3.33 (s, 3H), 2.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 147.9, 144.3, 138.4, 136.9, 129.7, 128.1, 124.8, 116.6, 113.9, 113.4, 101.8, 40.9, 30.8. HRMS (ESI^+) Calculated for $C_{16}H_{15}N_4S$:295.1012 and found: 295.1006.

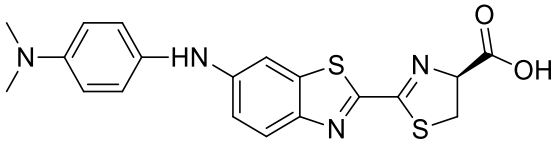


(*S*)-2-(6-(methyl(4-(methylamino)phenyl)amino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (25a): D-cysteine (10.2 mg, 0.08 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **25** (20 mg, 0.07 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **25a** as red solid (15 mg, 54 %). ^{1}H NMR (400 MHz, $CDCl_3$+ CD_3OD) δ7.84 (d, J = 9.2 Hz, 1H), 7.06-7.04 (d, J = 8.4 Hz, 3H), 6.90 (dd, J = 9.2, 2.4 Hz, 1H), 6.68 (d, J = 8.4 Hz, 2H), 5.39 (t, J = 9.6 Hz, 1H), 3.76 (d, J = 9.6 Hz, 2H), 3.32 (s, 3H), 2.88 (s, 3H). ^{13}C NMR (100MHz, $CDCl_3$+CD_3OD) δ 172.3, 166.6, 155.3, 149.4, 145.5, 145.3, 145.2, 138.3, 126.9, 124.2, 116.5, 114.8, 104.2, 77.9, 40.75, 34.9, 31.6. HRMS (ESI^+) Calculated for $C_{19}H_{19}N_4O_2S_2$: 399.0944 and found: 399.0941.

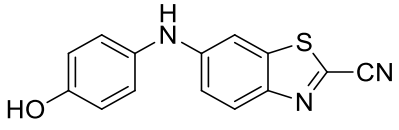


6-((4-(dimethylamino)phenyl)amino)benzo[*d*]thiazole-2-carbonitrile (26): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *4-(Dimethylamino)aniline* (17 mg, 0.13 mmol), tris(dibenzylideneacetone)palladium (6.4 mg,

0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 25% ethyl acetate: hexane as eluent to yield **26** (22 mg, 54% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 9.0 Hz, 1H), 7.06-7.04 (m, 3H), 6.96 (dd, *J* = 9.0, 2.0 Hz, 1H), 6.69 (d, *J* = 8.5 Hz 4H), 5.77 (s, 1H), 2.90 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.6, 148.1, 145.4, 138.5, 130.4, 129.2, 125.7, 125.6, 117.6, 113.8, 113.5, 101.9, 40.8. HRMS (ESI^+) Calculated for $C_{16}H_{15}N_4S$: 295.1012 and found: 295.1012.

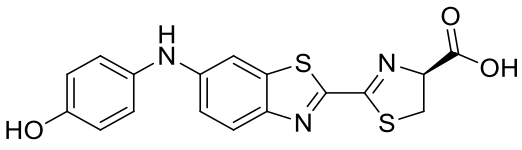


(*S*)-2-(6-((4-(dimethylamino)phenyl)amino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (26a): D-cysteine (10 mg, 0.08 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **26** (20 mg, 0.07 mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **26a** as a red solid (24 mg, 88%). ^{1}H NMR (500 MHz, CD_3OD) δ 7.71 (d, *J* = 9.0 Hz, 1H), 7.24 (s, 1H), 7.04-6.99 (m, 3H), 6.81 (d, J= 8.0 Hz, 2H), 5.23 (t, J= 9.0 Hz,1H), 3.67-3.60 (m, 2H), 2.87 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.4, 166.5, 155.3, 147.0, 146.5, 146.0, 138.4, 132.3, 124.6, 123.5, 116.8, 114.8, 103.2, 78.1, 41.4, 35.0. HRMS (ESI^+) Calculated for $C_{19}H_{19}N_4O_2S_2$: 399.0944 and found: 399.0930.

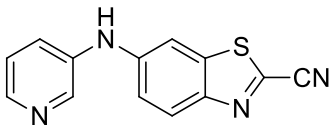


6-((4-hydroxyphenyl)amino)benzo[*d*]thiazole-2-carbonitrile (27): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *4-aminophenol* (14.2 mg,

0.13 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 30% ethyl acetate: hexane as eluent to yield **27** (27 mg, 73% yield) as a red solid. ^{1}H NMR (400 MHz, $CDCl_3$+ CD_3OD) δ 7.86 (d, *J* = 9.2 Hz, 1H), 7.14 (d, *J*= 2.4Hz, 1H), 7.05-7.01 (m, 3H), 6.82-6.78 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$+ CD_3OD) δ 153.9, 147.7, 145.1, 138.3, 132.2, 130.2, 125.4, 124.9, 117.8, 116.2, 113.6, 101.9. HRMS (ESI$^+$) Calculated for $C_{14}H_{10}N_3OS$: 268.0539 and found: 268.0540.

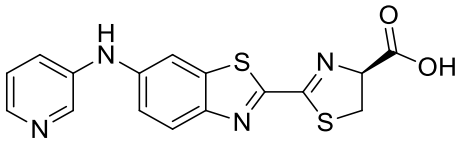


(*S*)-2-(6-((4-hydroxyphenyl)amino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (27a): D-cysteine (10.9 mg, 0.09 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **27** (20 mg, 0.07 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **27a** as a red solid (24 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$+ CD_3OD) δ 7.85 (d, *J* = 8.8 Hz, 1H), 7.19 (d, *J* = 2.4 Hz, 1H), 7.04 (dd, *J*= 10.0, 2.0 Hz, 2H), 6.97 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.80 (dd, *J*= 10.0, 2.0 Hz, 2H), 5.29 (t, *J* = 9.2 Hz, 1H), 3.76-3.63 (m, 2H). ^{13}C NMR (100MHz, $CDCl_3$+ CD_3OD) δ 173.4, 165.9, 155.3, 153.1, 146.3, 145.8, 138.2, 133.2, 124.5, 123.9, 116.6, 115.9, 103.0, 78.7, 35.1. HRMS (ESI$^+$) Calculated for $C_{17}H_{14}N_3O_3S_2$: 372.0471 and found: 372.0469.

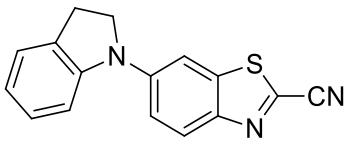


6-(pyridin-3-ylamino)benzo[*d*]thiazole-2-carbonitrile (28): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *3-aminopyridine* (16 mg, 0.17mmol),

tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 50% ethyl acetate: hexane as eluent to yield **28** (24 mg, 69% yield) as a red solid. ^{1}H NMR (500 MHz, CD_3OD+$CDCl_3$) δ 8.32 (d, J= 2.5 Hz, 1H), 8.05 (d, J= 4.0 Hz, 1H), 7.92 (d, J= 9.0 Hz, 1H), 7.65-7.60 (m, 2H), 7.29-7.26 (m, 2H). ^{13}C NMR (125 MHz, CD_3OD+$CDCl_3$) δ 146.5, 144.5, 141.7, 140.2, 139.4, 138.0, 132.3, 125.8, 125.3, 124.3, 119.3, 113.1, 105.2. HRMS (ESI$^+$) Calculated for $C_{13}H_9N_4S$: 253.0542 and found: 253.0526.

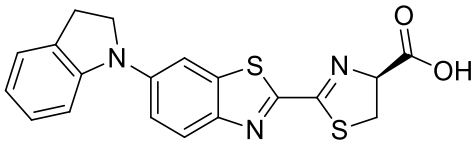


(*S*)-2-(6-(pyridin-3-ylamino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (28a): D-cysteine (7 mg, 0.06 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **28** (12 mg, 0.05 mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **28a** as a reddish yellow solid (12 mg, 60%). ^{1}H NMR (500 MHz, DMSO-d_6) δ8.87 (s, 1H), 8.47 (d, J= 2.5 Hz, 1H), 8.15 (d, J= 4.5 Hz, 1H), 8.01 (d, J= 8.5 Hz, 1H), 7.82 (d, J= 2.0 Hz, 1H), 7.65 (d, J= 8.0 Hz, 1H), 7.34-7.27 (m, 2H), 5.40 (t, J= 9.0 Hz, 1H), 3.78-3.65 (m, 2H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 171.7, 164.8, 157.1, 147.2, 143.3, 142.4, 140.9, 139.3, 138.1, 125.3, 124.7, 124.4, 106.6, 78.6, 35.1. HRMS (ESI$^+$) Calculated for $C_{16}H_{13}N_4O_2S_2$: 357.0474 and found: 357.0459.

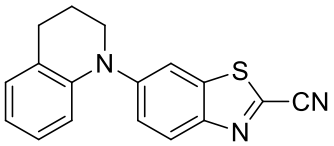


6-(indolin-1-yl)benzo[*d*]thiazole-2-carbonitrile (29): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *indoline* (15.5 mg, 0.13 mmol),

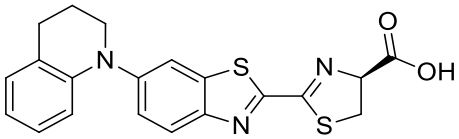
tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 20% ethyl acetate: hexane as eluent to yield **29** (24 mg, 62% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 9.6 Hz, 1H), 7.60-7.56(m, 2H), 7.27 (dd, *J* = 19.2, 7.2 Hz, 2H), 7.15 (t, *J* = 7.2 Hz, 1H), 6.88 (t, *J* = 7.2 Hz, 1H), 4.06 (t, *J* = 8.4 Hz, 2H), 3.21 (t, *J* = 8.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2, 145.2, 144.8, 137.8, 132.1, 131.9, 127.2, 125.5, 125.4, 120.7, 118.7, 113.5, 109.1, 106.4, 77.3, 77.2, 77.0, 76.7, 52.4, 28.1. HRMS (ESI$^+$) Calculated for $C_{16}H_{12}N_3S$: 278.0746 and found: 278.0737.



(*S*)-2-(6-(indolin-1-yl)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (29a): D-cysteine (10.2 mg, 0.08 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **29** (20 mg, 0.07 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **29a** as red solid (18 mg, 65 %). ^{1}H NMR (400 MHz, $CDCl_3$+ CD_3OD) δ 7.97 (d, *J* = 9.2 Hz, 1H), 7.54 (d, *J* = 2.0 Hz, 1H), 7.42 (dd, *J* = 9.2, 2.0 Hz, 1H), 7.19 (d, *J* = 8 Hz, 1H), 7.19 (d, *J* = 8 Hz, 1H), 7.14 (d, *J* = 7.2 Hz, 1H) 7.06 (t, *J* = 7.6 Hz, 1H), 6.75 (t, *J* = 7.2 Hz, 1H), 5.29 (t, *J* = 9.2 Hz, 1H), 3.98 (t, *J* = 8.4 Hz, 2H), 3.75-3.62 (m, 2H), 3.11 (t, *J* = 8.4 Hz, 2H). ^{13}C NMR (100MHz, $CDCl_3$+ CD_3OD) δ 172.1, 166.6, 157.1, 147.2, 145.7, 143.6, 138.0, 131.7, 127.1, 125.2, 124.6, 120.0, 117.8, 108.8, 107.6, 78.1, 52.4, 35.1, 28.1. HRMS (ESI$^+$) Calculated for $C_{19}H_{16}N_3O_2S_2$: 382.0678 and found: 382.0670.

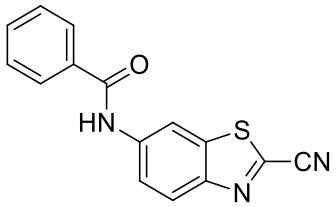


6-(3,4-dihydroquinolin-1(*2H*)-yl)benzo[*d*]thiazole-2-carbonitrile (30): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *1,2,3,4-tetrahydroquinoline* (17 mg, 0.13 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 20% ethyl acetate: hexane as eluent to yield **30** (35 mg, 87% yield) as a yellow solid. ^{1}H NMR (500 MHz, CD_3OD) δ 7.96 (d, *J* = 9.0 Hz, 1H), 7.54 (d, J= 2.5 Hz, 1H), 7.47 (dd, J= 9.0, 2.5 Hz, 1H), 7.06 (d, J= 7.5 Hz, 1H), 6.99-6.96 (m, 2H), 6.83-6.80 (m, 1H), 3.65 (t, J= 6.0 Hz, 2H), 2.75 (t, J= 6.5 Hz, 2H), 2.01-1.96 (m, 2H). ^{13}C NMR (125 MHz, CD_3OD) δ 149.3, 147.3, 142.3, 137.5, 133.1, 129.5, 128.4, 126.5, 125.2, 123.2, 121.3,118.5, 113.5, 111.6, 50.1, 27.4, 23.4. HRMS (ESI^+) Calculated for $C_{17}H_{14}N_3S$: 292.0903 and found: 292.0884.

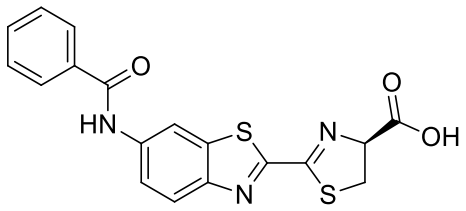


(*S*)-2-(6-(3,4-dihydroquinolin-1(*2H*)-yl)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (30a): D-cysteine (10 mg, 0.08 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **30** (20 mg, 0.07 mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **30a** as a red solid (18 mg, 67%). ^{1}H NMR (500 MHz, CD_3OD) δ 7.84 (d, *J*= 9.0 Hz, 1H), 7.65 (d, J= 1.5Hz, 1H), 7.36 (dd, J= 9.0, 1.5 Hz, 1H), 6.98 (d, J= 7.5Hz, 1H), 6.86 (t, J=7.5Hz, 1H), 6.80 (d, J= 8.0 Hz, 1H), 6.69 (t, J= 7.5 Hz, 1H), 5.29 (t, J= 9.0 Hz, 1H), 3.66 (dd, J= 9.0, 4.0 Hz, 2H), 3.62 (t, 6.0 Hz, 2H), 2.71 (t, J= 6.0 Hz, 2H), 1.94 (p, J= 6.0 Hz, 2H). ^{13}C NMR (125 MHz, CD_3OD) δ 171.9, 166.2, 158.4, 148.4,

148.3, 143.0, 137.6, 128.9, 127.3, 126.0, 123.9, 122.7, 120.1, 117.5, 113.6, 78.2, 50.2, 34.5, 27.1, 22.9. HRMS (ESI^+) Calculated for $C_{20}H_{18}N_3O_2S_2$: 396.0809 and found: 396.0835.

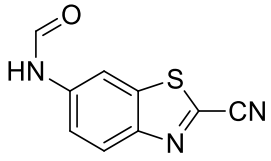


N-(2-cyanobenzo[d]thiazol-6-yl)benzamide (31): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *benzamide* (21 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 40% ethyl acetate: hexane as eluent to yield **31** (24 mg, 62% yield) as a yellow solid. ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.73 (s, 1H), 8.93 (s, 1H), 8.25 (d, J= 9.0 Hz, 1H), 8.01-7.97 (m, 3H), 7.65-7.56 (m, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 166.6, 148.3, 140.2, 137.0, 135.7, 134.9, 132.4, 128.9, 128.3, 125.1, 122.3, 114.1, 112.9. HRMS (ESI^+) Calculated for $C_{15}H_{10}N_3OS$: 280.0539 and found: 280.0540.

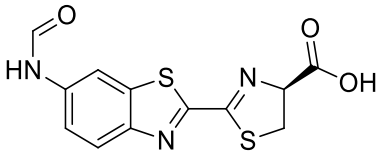


(*S*)-2-(6-benzamidobenzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (31a): D-cysteine (6 mg, 0.05 mmol) was dissolved in 1 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **31** (10 mg, 0.04 mmol) in 1 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **31a** as a yellow solid (9 mg, 66%). yellow

colour solid. ^{1}H NMR (500 MHz, CD_3OD) δ 8.59 (s, 1H), 8.04 (d, J= 9.0 Hz, 1H), 7.97 (d, J= 7.0 Hz, 2H), 7.81(d, J= 9.0 Hz, 1H), 7.60-7.52 (m, 3H), 5.42 (t, J= 9.0 Hz, 1H), 3.78 (d, J= 9.0Hz, 2H). ^{13}C NMR (100 MHz, CD_3OD) δ 171.8, 167.5, 166.1, 159.8, 149.5, 138.2, 136.7, 134.6, 131.7, 1228.3, 127.3, 123.8, 120.6, 112.7, 78.2, 34.5. HRMS (ESI^+) Calculated for $C_{18}H_{14}N_3O_3S_2$: 384.0471 and found: 384.0474.

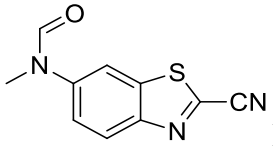


N-(2-cyanobenzo[*d*]thiazol-6-yl)formamide (32): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *formamide* (7.65 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 50% ethyl acetate: hexane as eluent to yield **32** (15 mg, 58% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, *J* = 2.0 Hz, 1H), 8.43 (d, *J* = 1.0 Hz, 1H), 8.08 (d, *J* = 9.0 Hz, 1H), 7.36 (dd, J= 9.0, 2.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$+ CD_3OD) δ 160.3, 148.4, 138.2, 136.6, 135.2, 125.1, 120.6, 112.8, 111.6. HRMS (ESI^+) Calculated for $C_9H_6N_3OS$: 204.0226 and found: 204.0227.

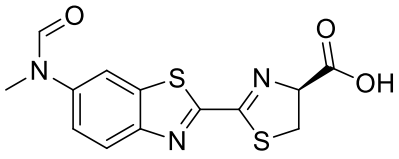


(*S*)-2-(6-formamidobenzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (32a): D-cysteine (7.1 mg, 0.06 mmol) was dissolved in 1 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **32** (10 mg, 0.05 mmol) in 1 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent

was removed by rotary evaporation to yield **32a** as an off-white solid (9 mg, 60%). ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 10.81(s, 1H), 8.54(s, 1H), 8.38 (s, 1H), 8.05(d, J= 9.0 Hz), 7.65(d, J= 9.0Hz, 1H), 4.98 (t, J= 9.0 Hz, 1H), 3.78-3.74 (m, 1H), 3.53 (t, J= 10.0 Hz, 1H). ^{13}C NMR (100MHz, $CDCl_3$+DMSO-d$_6$) δ 171.3, 164.8, 159.9, 159.4, 149.1, 137.7, 136.6, 124.4, 119.6, 111.8, 78.5, 34.9. HRMS (ESI$^+$) Calculated for $C_{12}H_{10}N_3O_3S_2$: 308.0158 and found: 308.0158.

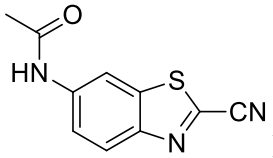


N-(2-cyanobenzo[*d*]thiazol-6-yl)-N-methylformamide (33): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *N-methylformamide* (10 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 25% ethyl acetate: hexane as eluent to yield **33** (23 mg, 77% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.27 (d, *J* = 9.0 Hz, 1H), 7.78 (s, 1H), 7.53 (d, J= 9.0 Hz, 1H), 3.45 (s, 3H).^{13}C NMR (125 MHz, $CDCl_3$) δ 161.9, 150.2, 142.7, 136.8, 136.7, 126.3, 122.5, 114.1, 112.7, 32.3. HRMS (ESI$^+$) Calculated for $C_{10}H_8N_3OS$: 218.0383 and found: 218.0377.

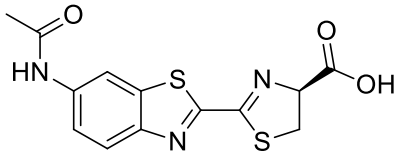


(*S*)-2-(6-(N-methylformamido)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (33a): D-cysteine (13.3 mg, 0.11 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **33** (20 mg, 0.09 mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL).

The solvent was removed by rotary evaporation to yield **33a** as a colourless solid (23 mg, 77%). ^{1}H NMR (500 MHz, CD_3OD) δ 8.62 (s, 1H), 8.14 (d, J= 9.0 Hz, 1H), 8.04(s, 1H), 7.57 (d, J= 8.5 Hz, 1H), 5.34 (t, J= 9.0 Hz, 1H), 3.79 (d, J= 9.0 Hz, 2H), 3.41 (s, 3H). ^{13}C NMR (125 MHz, CD_3OD) δ 173.8, 164.8, 163.2, 161.9, 151.2, 141.2, 1337.1, 124.5, 121.6, 115.4, 80.1, 35.3, 31.2. HRMS (ESI^+) Calculated for $C_{13}H_{12}N_3O_3S_2$: 322.0315 and found: 322.0306.

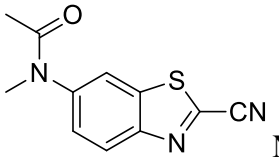


N-(2-cyanobenzo[*d*]thiazol-6-yl)acetamide (**34**): A round bottom flask was chargedwith **14** (33 mg, 0.14 mmol), *acetamide* (10 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 50% ethyl acetate: hexane as eluent to yield **34** (25 mg, 82% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$+ CD_3OD) δ 8.57 (d, *J* = 2.0 Hz, 1H), 7.96 (d, J= 9.2 Hz, 1H), 7.42 (dd, *J* = 9.2, 2.0 Hz, 1H), 7.44 (dd, J= 9.2, 2.0 Hz, 1H), 2.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$+ CD_3OD) δ170.3, 148.1, 139.3, 136.6, 134.7, 124.8, 120.6, 112.9, 110.9, 23.78. HRMS (ESI^+) Calculated for $C_{10}H_8N_3OS$: 218.0383 and found: 218.0384.

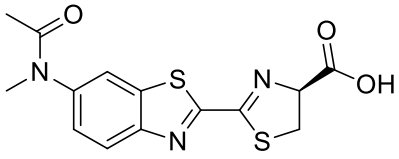


(*S*)-2-(6-acetamidobenzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (34a): D-cysteine (13.3 mg, 0.11 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **34** (20 mg, 0.09 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was

removed by rotary evaporation to yield **34a** as an off-white solid (14 mg, 48%). ^{1}H NMR (500 MHz, DMSO-d$_6$) δ 10.35 (s, 1H), 8.60 (s, 1H), 8.06 (d, J= 9.0 Hz, 1H), 7.59 (d, J= 9.0 Hz, 1H), 5.32 (t, J= 9.0 Hz, 1H), 3.74-3.67 (m, 2H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d$_6$) δ 171.6, 169.3, 164.8, 159.3, 148.9, 139.1, 136.8, 124.6, 119.9, 111.5, 78.7, 35.2, 24.6. HRMS (ESI$^+$) Calculated for $C_{13}H_{12}N_3O_3S_2$: 322.0315 and Found: 322.0316.

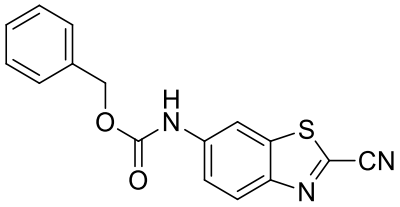


N-(2-cyanobenzo[*d*]thiazol-6-yl)-N-methylacetamide (35): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *N-Methylacetamide* (12.4 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 50% ethyl acetate: hexane as eluent to yield **35** (19.8 mg, 62 % yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.8 Hz, 1H), 7.85 (s, 1H), 7.50 (dd, *J* = 8.8, 2.0 Hz, 1H), 3.36 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 151.1, 144.8, 137.6, 136.3, 127.5, 126.3, 120.2, 112.6, 37.6, 22.7. HRMS (ESI$^+$) Calculated for $C_{11}H_{10}N_3OS$: 232.0539 and found: 232.0540.

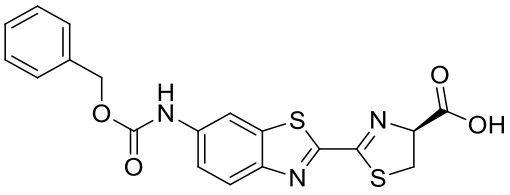


(*S*)-2-(6-(N-methylacetamido)benzo[d]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (35a): D-cysteine (9.6 mg, 0.08 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **35** (15 mg, 0.06 mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL).

The solvent was removed by rotary evaporation to yield **35a** as a yellow solid (12 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J= 8.4 Hz, 1H), 7.80 (d, J= 1.6 Hz, 1H), 7.37 (dd, J= 8.4, 2.0 Hz, 1H), 5.46 (t, J= 9.6 Hz, 1H), 3.88-3.77 (m, 2H), 3.34 (s, 3H), 1.94 (s, 3H). ^{13}C NMR (100MHz, $CDCl_3$) δ 172.4, 171.5, 166.7, 161.9, 152.2, 142.9, 136.9 126.2, 125.7, 120.5, 78.1, 37.7, 35.2, 22.5. HRMS (ESI^+) Calculated for $C_{14}H_{14}N_3O_3S_2$: 336.0471 and found: 336.0472.

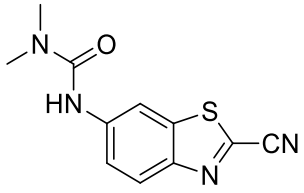


benzyl (2-cyanobenzo[*d*]thiazol-6-yl)carbamate (36): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *benzyl carbamate* (26 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 30% ethyl acetate: hexane as eluent to yield **36** (16.5 mg, 38% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (s, 1H), 8.11 (dd, *J* = 9.0, 2.0 Hz, 1H), 7.45-7.28 (m, 5H), 7.09 (s, 1H), 5.27 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.0, 148.3, 138.6, 137.2, 135.5, 134.9, 128.7, 128.6, 128.5, 125.5, 119.7, 113.1, 109.7, 67.6. HRMS (ESI^+) Calculated for $C_{16}H_{12}N_3O_2S$: 310.0645 and found: 310.0645.

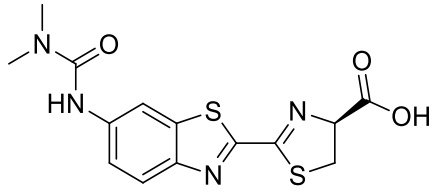


(S)-2-(6(((benzyloxy)carbonyl)amino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (36a): D-cysteine (9 mg, 0.06 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **36** (15 mg, 0.05 mmol) in 2 mL of degassed acetonitrile. The reaction

was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **36a** as a yellow solid (13 mg, 67%). ^{1}H NMR (500 MHz, CD_3OD) δ 8.02 (s, 1H), 7.88 (d, J= 9.0 Hz, 1H), 7.42 (dd, J= 9.0, 2.0 Hz, 1H), 7.33 (d, J= 7.5Hz, 2H), 7.27 (t, J= 7.5 Hz, 2H), 7.25 (t, J= 7.5 Hz, 1H), 5.30 (t, J= 9.0 Hz, 1H), 5.13 (s, 2H), 3.68 (d, J= 9.0 Hz, 2H). ^{13}C NMR (125MHz, CD_3OD) δ 171.9, 166.4, 158.9, 154.2, 148.6, 138.6, 137.1, 136.3, 128.2, 127.9, 127.8, 123.9, 118.8, 110.0, 78.1, 66.6, 34.7. HRMS (ESI^+) Calculated for $C_{19}H_{16}N_3O_4S_2$: 414.0577 and found: 414.0579.

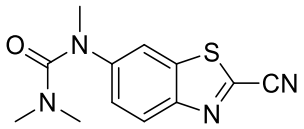


3-(2-cyanobenzo[*d*]thiazol-6-yl)-1,1-dimethylurea (37): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *1,1-dimethylurea* (15 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 3h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 50% ethyl acetate: hexane as eluent to yield **37** (15 mg, 45% yield) as an off-white solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (d, *J* = 2.0 Hz, 1H), 7.98 (d, *J* = 9.0 Hz, 1H), 7.26 (dd, J= 9.0, 2.5Hz, 1H), 6.57 (s, 1H), 3.01 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.9, 147.8, 140.0, 137.2, 134.4, 125.1, 120.5, 113.2, 110.4, 36.6. HRMS (ESI^+) Calculated for $C_{11}H_{11}N_4OS$: 247.0648 and found: 247.0639.

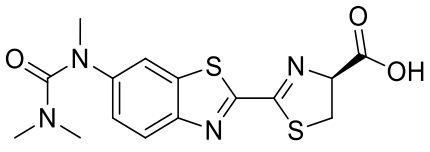


(S)-2-(6-(3,3-dimethylureido)benzo[d]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (37a): D-cysteine (9 mg, 0.07 mmol) was dissolved in 2 mL

of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **37** (15 mg, 0.06 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **37a** as a yellow solid (13 mg, 61%). ^{1}H NMR (500 MHz, CD_3OD) δ 8.04 (d, J= 2.0 Hz, 1H), 7.84 (d, J= 9.0 Hz, 1H), 7.46 (dd, J= 9.0, 2.0Hz, 1H), 5.29 (t, J= 9.0 Hz, 1H), 3.70-3.62 (m, 2H), 2.94 (s, 6H). ^{13}C NMR (125 MHz, CD_3OD) δ 171.9, 166.2, 158.7, 156.9, 148.6, 139.7, 136.7, 123.5, 120.7, 111.9, 78.1, 35.4, 34.5. HRMS (ESI^+) Calculated for $C_{14}H_{15}N_4O_3S_2$: 351.0580 and found: 351.0568.

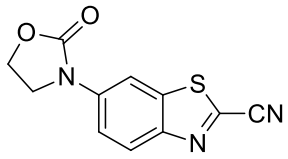


1-(2-cyanobenzo[d]thiazol-6-yl)-1,3,3-trimethylurea (38): A round bottom flask was charged with **16** (33 mg, 0.14 mmol), *N,N,N'-trimethylurea* (21 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 50% ethyl acetate: hexane as eluent to yield **38** (13 mg, 36% yield) as a yellow solid. ^{1}H NMR (500 MHz, CD_3OD): δ 8.04 (d, J= 9.0 Hz, 1H), 7.72 (d, J= 2.0 Hz, 1H), 7.33 (dd, J= 9.0, 2.0 Hz, 1H), 3.19 (s, 3H), 2.69 (s, 6H). ^{13}C NMR (125 MHz, CD_3OD): δ 161.7, 148.3, 146.9, 137.2, 135.6, 125.1, 123.1, 113.6, 112.6, 37.7, 36.8. HRMS (ESI^+) Calculated for $C_{12}H_{13}N_4OS$: 261.0805 and found: 261.0803.

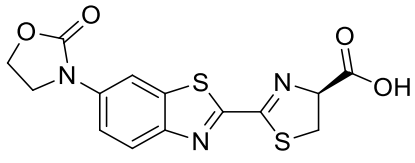


(S)-2-(6-(1,3,3-trimethylureido)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (38a): D-cysteine (5.6 mg, 0.05mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution

was added to **38** (10 mg, 0.04 mmol) in 2 mL of degassed acetonitrile. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **38a** as a yellow solid (8 mg, 57%). ^{1}H NMR (500 MHz, CD_3OD) δ 7.95 (d, J= 8.5Hz, 1H), 7.67 (d, J= 2.0 Hz, 1H), 7.23 (dd, J= 9.0, 2.0 Hz, 1H), 5.31 (t, J= 9.0 Hz, 1H), 3.71-3.64 (m, 2H), 3.17 (s, 3H), 2.65 (s, 6H). ^{13}C NMR (125 MHz, CD_3OD) δ 171.8, 166.1, 162.1, 160.3, 149.5, 145.8, 137.3, 124.5, 122.7, 115.1, 78.2, 38.3, 36.8, 34.5. HRMS (ESI^+) Calculated for $C_{15}H_{17}N_4O_3S_2$: 365.0737 and found: 365.0721.

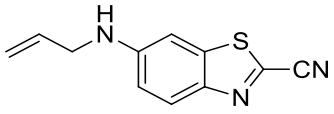


6-(2-oxooxazolidin-3-yl)benzo[*d*]thiazole-2-carbonitrile (39): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), 2-oxazolidone (14 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 30% ethyl acetate: hexane as eluent to yield **39** (25 mg, 73% yield) as a colourless solid. ^{1}H NMR (400 MHz, $CDCl_3$+ CD_3OD) δ 8.31 (d, *J* = 2.4 Hz, 1H), 8.13 (dd, *J*= 8.8, 0.4Hz, 1H), 7.70 (dd, *J*= 9.2, 2.4 Hz, 1H), 4.54-4.51 (m, 2H), 4.17-4.13 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$+ CD_3OD) δ 155.3, 148.3, 138.7, 136.7, 135.5, 125.3, 118.7, 112.8, 110.1, 61.5, 45.3. HRMS (ESI^+) Calculated for $C_{11}H_8N_3O_2S$: 246.0332 and found: 246.0333.



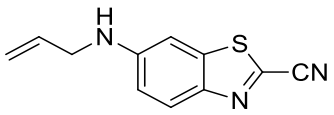
(*S*)-2-(6-(2-oxooxazolidin-3-yl)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (39a): D-cysteine (12.0 mg, 0.10 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution

was added to **39** (20 mg, 0.08 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **39a** as a yellow solid (24 mg, 84 %). ^{1}H NMR (400 MHz, $CDCl_3$ + CD_3OD) δ 8.03 (d, *J*=2.4Hz, 1H), 7.93 (d, *J*= 9.2 Hz, 1H), 7.56 (dd, *J*= 9.2, 2.4Hz, 1H), 5.23-5.19 (m, 1H), 4.42-4.38 (m, 2H), 4.05-4.03 (m, 2H), 3.67-3.57 (m, 2H). ^{13}C NMR (100MHz, $CDCl_3$ + CD_3OD): δ 171.8, 166.3, 160.0, 155.7, 149.2, 137.2, 136.9, 124.3, 117.9, 110.7, 78.0, 61.6, 45.4, 34.9. HRMS (ESI^+) Calculated for $C_{14}H_{12}N_3O_4S_2$: 350.0264 and found: 350.0263.



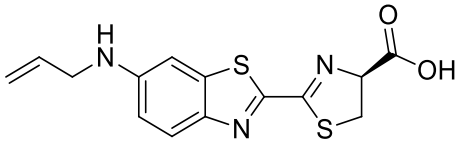
6-(allylamino)benzo[*d*]thiazole-2-carbonitrile (40): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), allylamine (7.4 mg, 0.13 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 20% ethyl acetate: hexane as eluent to yield **40** (12 mg, 40% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.8 Hz, 1H), 6.93-6.88 (m, 2H), 5.94 (ddd, *J* = 22.3, 10.4, 5.2 Hz, 1H), 5.32 (dd, *J* = 17.2, 1.2 Hz, 1H), 5.24 (dd, *J* = 10.4, 1.2 Hz, 1H), 4.40 (s, 1H, -NH), 3.87 (t, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$ + CD_3OD) δ 148.7, 144.8, 138.6, 133.8, 130.0, 125.5, 117.1, 117.0, 113.8, 100.2, 46.2. HRMS (ESI^+) Calculated for $C_{11}H_{10}N_3S$: 216.0590 and found: 216.0585.

<u>On 1 mmol scale:</u>

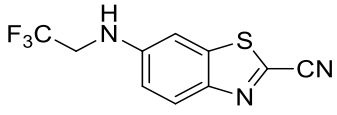


6-(allylamino)benzo[*d*]thiazole-2-carbonitrile (40): A screw-cap vial was charged with **14** (239 mg, 1 mmol), allylamine (57 mg, 1 mmol),

tris(dibenzylideneacetone)palladium (46 mg, 0.051 mmol), xantphos (59 mg, 0.102 mmol), caesium carbonate (651 mg, 2 mmol) and dioxane (4.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature, then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 20% ethyl acetate: hexane as eluent to yield **40** (82 mg, 38% yield) as a yellow solid. NMR was identical to above.

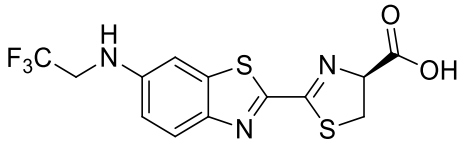


(*S*)-2-(6-(allylamino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (40a): D-cysteine (7 mg, 0.06 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **40** (10 mg, 0.05 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **40a** as a red solid (8 mg, 53 %). ^{1}H NMR (400 MHz, $CDCl_3$+ DMSO-d_6) δ 7.82 (d, J = 9.2 Hz, 1H), 6.87 (s, 1H), 6.84 (dd, J = 8.8, 2.0 Hz, 1H), 5.94-5.84 (m, 1H), 5.29-5.23 (m, 2H), 5.17 – 5.15 (m, 1H), 3.79 (d, J = 5.6 Hz, 2H), 3.73 – 3.62 (m, 2H). ^{13}C NMR (100MHz, $CDCl_3$): δ 171.7 166.6, 154.8, 147.7, 145.6, 138.7, 134.3, 124.8, 116.7, 115.7, 101.3, 78.0, 46.2, 35.0. HRMS (ESI^+) Calculated for $C_{14}H_{14}N_3O_2S_2$: 320.0522 and found: 320.0512.

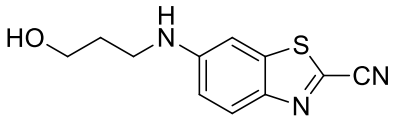


6-((2,2,2-trifluoroethyl)amino)benzo[*d*]thiazole-2-carbonitrile (41): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), 2,2,2-trifluoroethylamine (13 mg, 0.13 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg, 0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was

allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 20% ethyl acetate: hexane as eluent to yield **41** (6 mg, 17% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (d, *J* = 9.0 Hz, 1H), 7.03 (d, *J* = 2.0 Hz, 1H), 6.92 (dd, *J* = 9.0, 2.5 Hz, 1H), 4.41 (t, *J* = 6.5 Hz, 1H,-NH), 3.84-3.78 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.1, 145.9, 138.3, 131.7, 125.9,124.6 (q, *J* = 280.2 Hz), 121.3, 116.8, 113.4, 101.3, 45.7 (q, *J* = 34.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -71.97 (t, *J* = 8.6 Hz, 3F). HRMS (ESI^+) Calculated for $C_{10}H_7F_3N_3S$: 258.0307 and found: 258.0302.



(*S*)-2-(6-((2,2,2-trifluoroethyl)amino)benzo[*d*]thiazol-2-yl)-4,5-dihydrothiazole-4-carboxylic acid (41a): D-cysteine (3 mg, 0.02 mmol) was dissolved in 2 mL of 50 mM aqueous sodium phosphate buffer, pH 8 and degassed under argon. This solution was added to **41** (5 mg, 0.02 mmol) in 2 mL of degassed methanol. The reaction was stirred for 1h, and then diluted with sodium phosphate buffer and washed with ethyl acetate. The aqueous phase was acidified to pH 4 with 1M HCl and extracted with ethyl acetate (2 x 20 mL). The solvent was removed by rotary evaporation to yield **41a** as yellowish red solid (4 mg, 57 %). ^{1}H NMR (500 MHz, CD_3OD) δ 7.71 (d, *J* = 9.0 Hz, 1H), 7.13 (d, *J* = 2.5 Hz, 1H), 6.89 (dd, *J* = 9.0, 2.5 Hz, 1H), 5.26 (t, *J* = 9.0 Hz, 1H), 3.83 (q, *J* = 9.5 Hz, 2H), 3.67-3.60 (m, 2H). ^{13}C NMR (125 MHz, CD_3OD) δ 172.1, 166.2, 155.4, 147.8, 145.6, 138.4, 125.5 (q, *J*= 279.2 Hz), 124.2, 115.3, 101.2, 78.0, 44.5 (q, *J* = 33.9 Hz), 34.4. ^{19}F NMR (470 MHz, $CDCl_3$) δ -73.68 (t, *J* = 9.4 Hz, 3F). HRMS (ESI^+) Calculated for $C_{13}H_{11}F_3N_3O_2S_2$: 362.0239 and found: 362.0236.



6-((3-hydroxypropyl)amino)benzo[*d*]thiazole-2-carbonitrile (42): A round bottom flask was charged with **14** (33 mg, 0.14 mmol), *3-Amino-1-propanol* (13 mg, 0.17 mmol), tris(dibenzylideneacetone)palladium (6.4 mg, 0.007 mmol), xantphos (8.1 mg,

0.014 mmol), caesium carbonate (91 mg, 0.28 mmol) and dioxane (2.0 mL) under argon. The resulting solution was heated at 100 °C with rapid stirring for 6h. The reaction mixture was allowed to cool to room temperature and then diluted with water (10 mL) and extracted with ethyl acetate (25 mL × 3). After drying with anhydrous Na_2SO_4, the organic phase was evaporated to dryness and purified by flash chromatography using 70% ethyl acetate: hexane as eluent to yield **40** (16 mg, 49% yield) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 (d, *J* = 9.0 Hz, 1H), 6.87 (d, *J*= 2.0 Hz, 1H), 6.81 (dd, *J*= 9.0, 2.0 Hz, 1H), 3.79 (t, *J*= 5.5 Hz, 2H), 3.29 (t, *J*= 6.0 Hz, 2H), 1.88 (p, *J*= 6.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.2, 144.7, 138.8, 129.7, 125.5, 117.1, 113.8, 99.7, 61.4, 41.8, 31.3. ^{1}H NMR is consistent with the literature report.[4]

	Peak Wavelength (nm)	
Substrate	WT Firefly Luciferase	R218K Firefly Luciferase
D-luciferin	551	560
Azetidine (**4a**)	612	626
Pyrolidine (**5a**)	604	624
Piperidine (**6a**)	612	634
Azepane (**7a**)	607	ND
Morpholine (**8a**)	604	ND
Thiomorpholine (**9a**)	ND	614
TMPDO (**15a**)	557	ND
Boc-PIPE (**16a**)	547	587
Piperazine (**16b**)	554	596
2,6 DMAN (**20a**)	575	590
1,1 DMU (**37a**)	594	ND
ALL (**40a**)	602	606
TRIFET (**41a**)	559	572

Table S1. Peak bioluminescence emission wavelengths for selected luciferins.

Measurements were performed as previously described.[1,2] ND = not determined.

Compound	PBS			Methanol			Dioxane		
	Abs. (nm)	Em. (nm)	RQY	Abs. (nm)	Em. (nm)	RQY	Abs. (nm)	Em. (nm)	RQY
4a	369	554	0.40	380	516	0.78	383	464	1.24
7a [a]	414	550	0.13	402	517	0.76			
8a	346	546	0.22	363	518	0.73			
9a	354	533	0.47	366	512	0.75			
10a	344	494	0.29	342	465	0.33	340	405	0.82
11a	300	-	0	299	-	0			
12a	291	-	0	286	-	0			
15a	359	515	1.02	358	488	1.00	364	445	1.14
17a	384	-	0	389	-	0	384	469	1.12
6'-amino-luciferin	351	517	1	360	487	1	362	441	1

Table S2. Fluorescence properties of selected luciferin analogues.

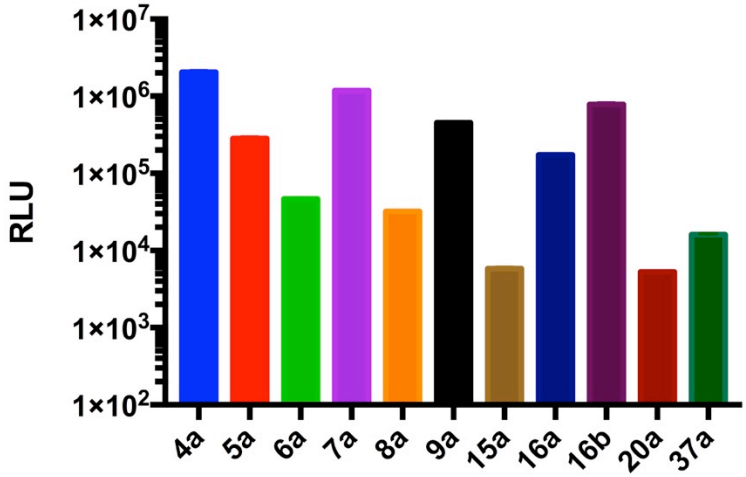
Excitation wavelength was 351 nm in PBS and dioxane, 359 nm in methanol. An observed lack of fluorescence is indicated by a QY of 0 and "-" for emission wavelength. Grayed out boxes indicate no measurements were carried out.

[a]Excitation wavelength was 384 nm in PBS and methanol

	Wild Type Luciferase		R218K Luciferase	
Substrate	**Apparent Km**	**R-squared**	**Apparent Km**	**R-squared**
D-luciferin	7.5±0.86	0.9679	120±4.9	0.9978
Azetidine (4a)	0.534±0.079	0.8971	0.15±0.053	0.4778
Thiomorpholine (9a)	0.52±0.081	0.876	0.30±0.069	0.7413
Azepane (7a)	1.7±0.29	0.8861	9.0±0.97	0.9671
Morpholine (8a)	0.93±0.093	0.9587	1.6±0.18	0.9584
Piperazine (16b)	19±1.9	0.9787	53±2.2	0.9969
Boc-PIPE (16a)	7.9±0.73	0.9788	48±2.4	0.9955
TMPDO (15a)	3.5±0.61	0.9176	12±1.2	0.9785
Piperidine (6a)	1.3±0.21	0.9155	0.67±0.13	0.8532
Pyrrolidine (5a)	3.7±0.79	0.8756	1.3±0.23	0.8882
2ETHAN (18a)	nd	nd	0.36±0.095	0.6604
IND (29a)	nd	nd	4.2±0.42	0.9691
1,1 DMU (37a)	0.95±0.37	0.6294	9.1±1.2	0.9617
2,6 DMAN (20a)	nd	nd	1.9±0.23	0.9491
ALL (40a)	0.56±0.076	0.9099	0.53±0.083	0.8865
TRIFET (41a)	0.89±0.086	0.9698	1.1±0.10	0.9631

Table S3. Apparent Km values for selected luciferin analogues.

A)



B)

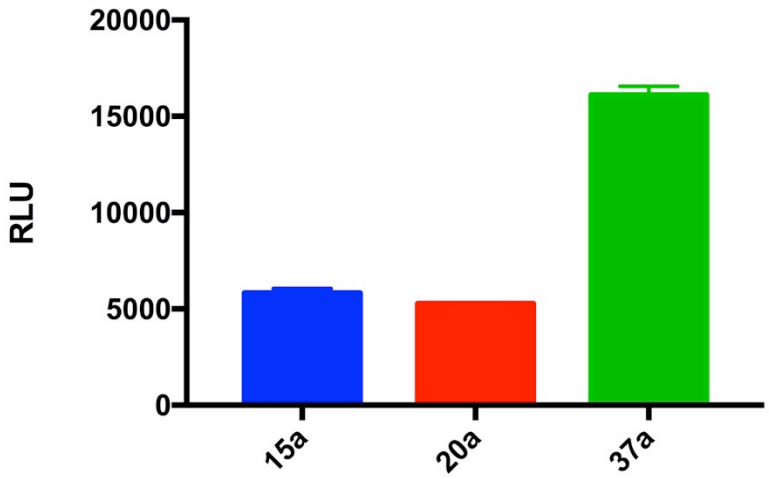
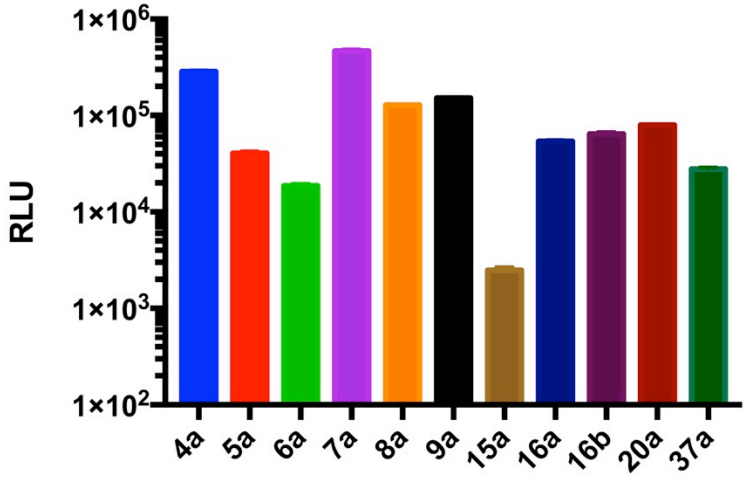


Figure S1. Burst bioluminescence emission from WT firefly luciferase with luciferin analogues. A) Log scale shows dramatically lower emission from thiomorpholine dioxide **15a** compared to other cyclic amines. B) Non-canonical luciferin analogues **20a** and **37a** compared to **15a** on a linear scale.

A)



B)

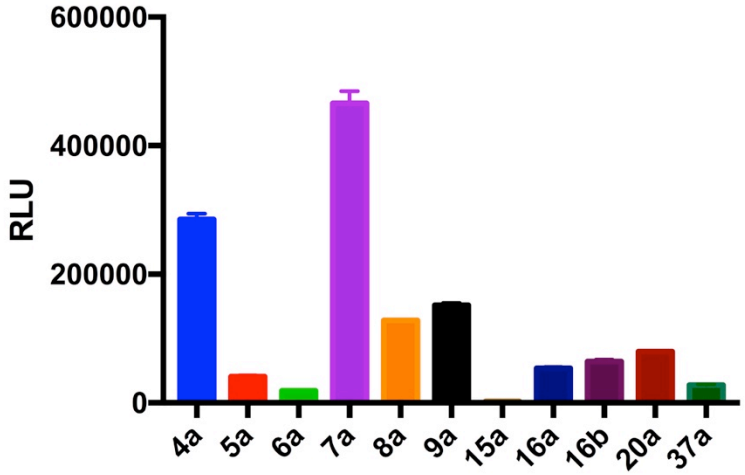


Figure S2. Burst bioluminescence emission from R218K mutant firefly luciferase with luciferin analogues on A) log scale and B) linear scale. The mutant enzyme improved emission from **8a** and non-canonical luciferin analogues **20a** and **37a**.

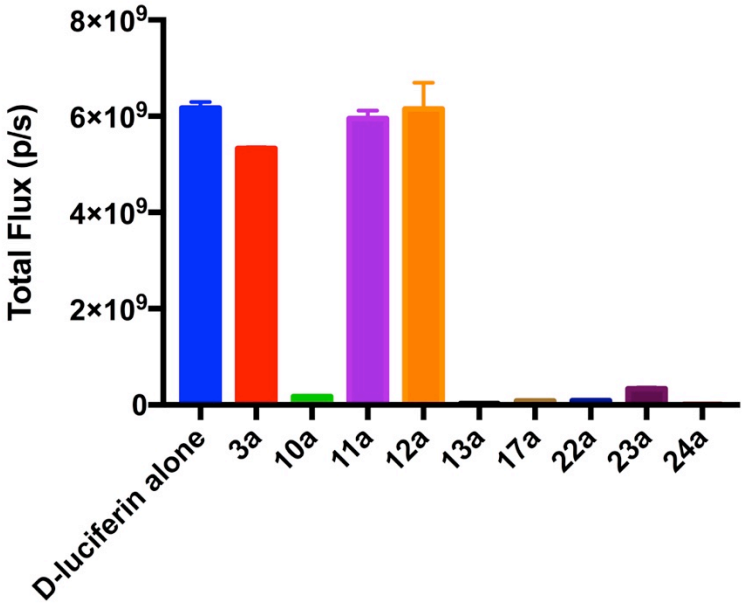


Figure S3. Inhibition of firefly luciferase by luciferin analogues. Purified firefly luciferase (10 nM) was treated with D-luciferin (250 μM) in the presence of the indicated luciferin analogue (10 μM). Thioethers and anilines were strongly inhibitory.

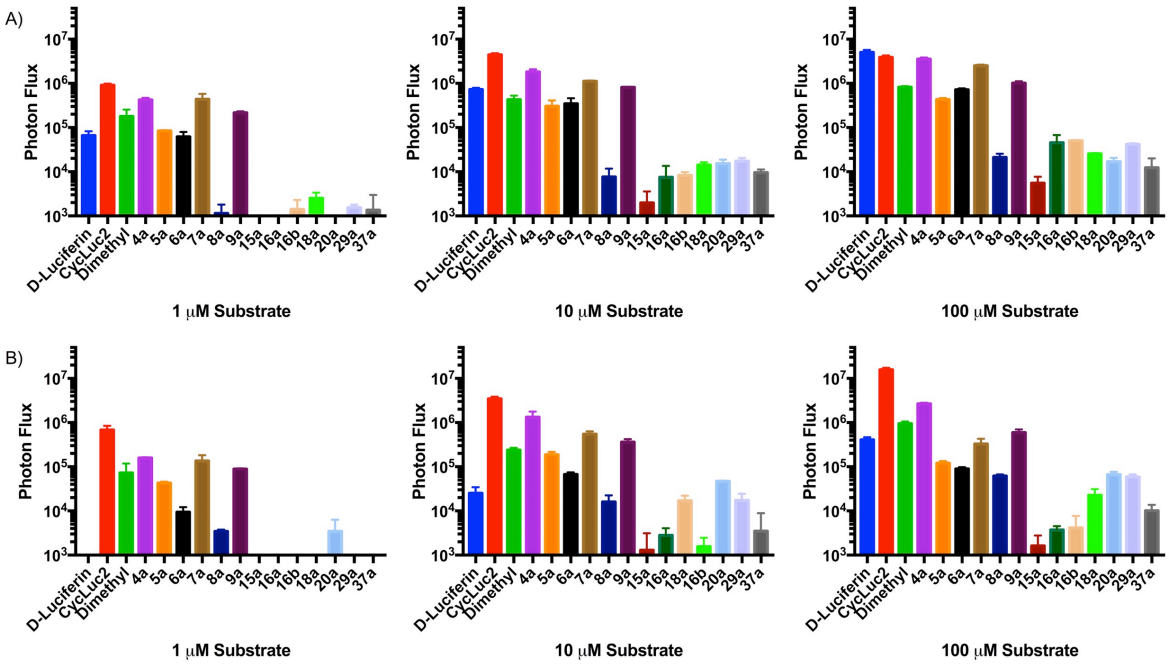


Figure S4. Comparison of bioluminescence from selected luciferin analogues. Live CHO cells expressing A) wild-type firefly luciferase or B) R218K mutant luciferase were incubated with 1, 10, or 100 μM of the indicated substrate.

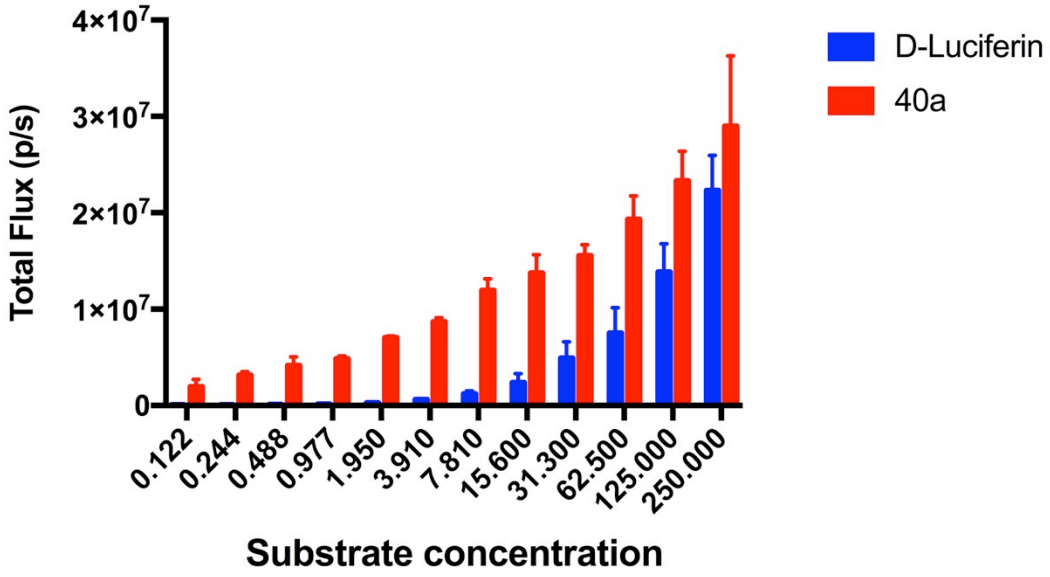
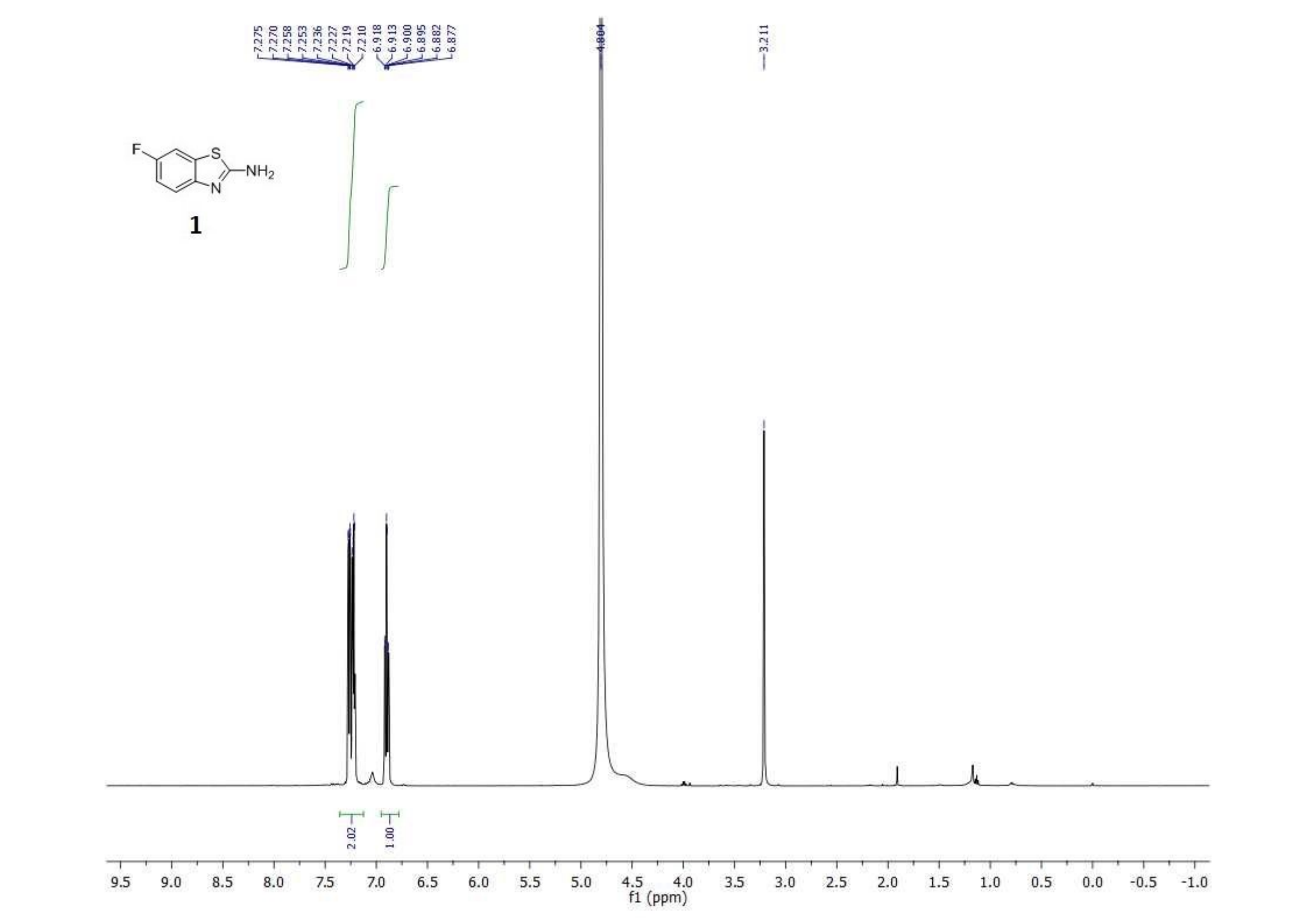


Figure S5. Live CHO cells expressing WT firefly luciferase treated with D-luciferin or allyl amine 40a. Substrate concentration ranging from 0.122-250 μM.

Supplementary References:

(1) Harwood, K. R.; Mofford, D. M.; Reddy, G. R.; Miller, S. C. *Chem. Biol.* **2011**, *18*, 1649.
(2) Mofford, D. M.; Reddy, G. R.; Miller, S. C. *J. Am. Chem. Soc.* **2014**, *136*, 13277.
(3) Hauser, J. R.; Beard, H. A.; Bayana, M. E.; Jolley, K. E.; Warriner, S. L.; Bon, R. S. *Beilstein J. Org. Chem.* **2016**, *12*, 2019.
(4) Woodroofe, C. C.; Shultz, J. W.; Wood, M. G.; Osterman, J.; Cali, J. J.; Daily, W. J.; Meisenheimer, P. L.; Klaubert, D. H. *Biochemistry* **2008**, *47*, 10383.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7.210
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6.882
6.877
4.804
3.211
F
S
NH2
N
1
2.02
1.00
9.5
9.0
8.5
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7.0
6.5
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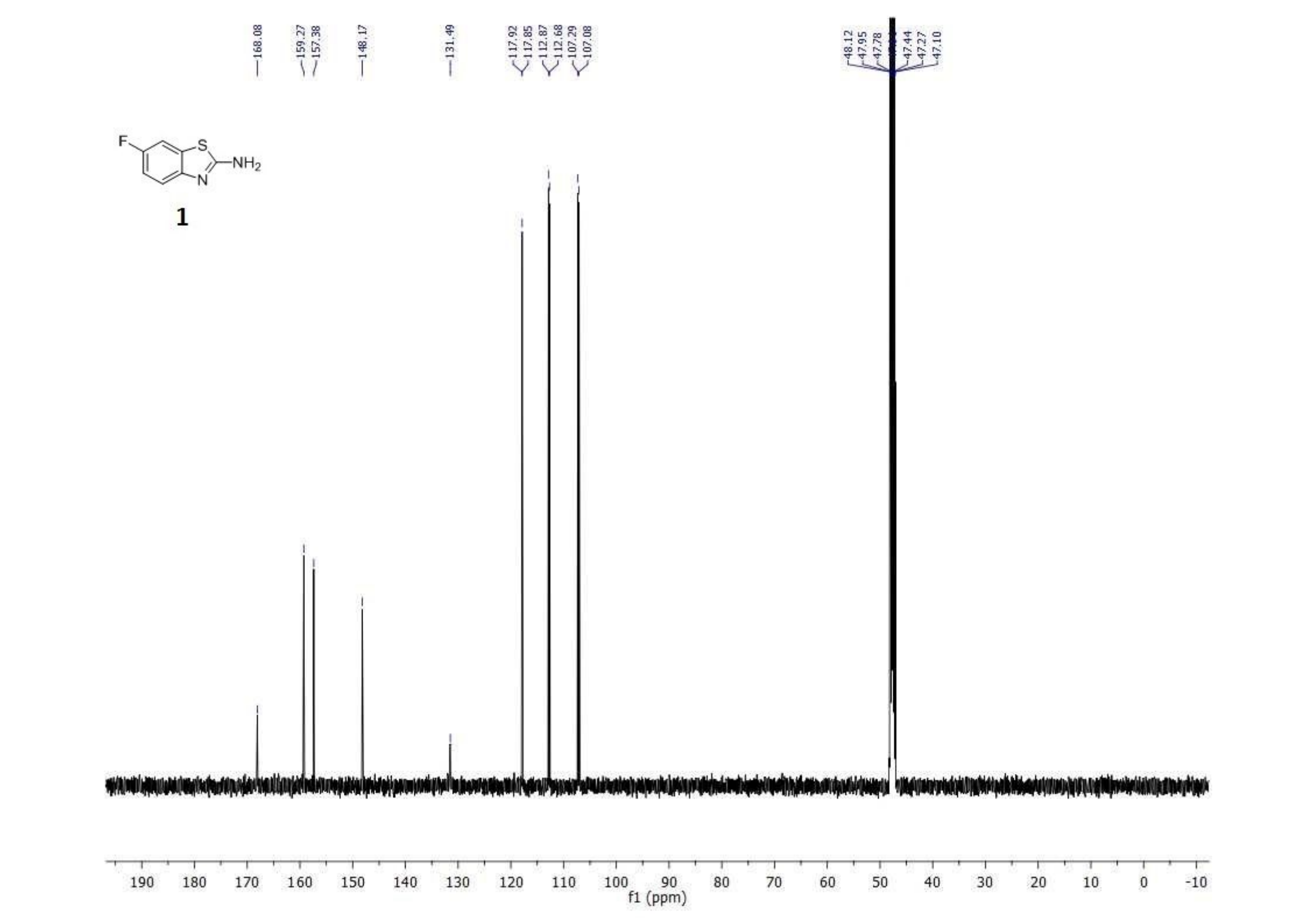
-0.5
-1.0
f1 (ppm)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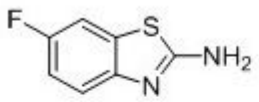
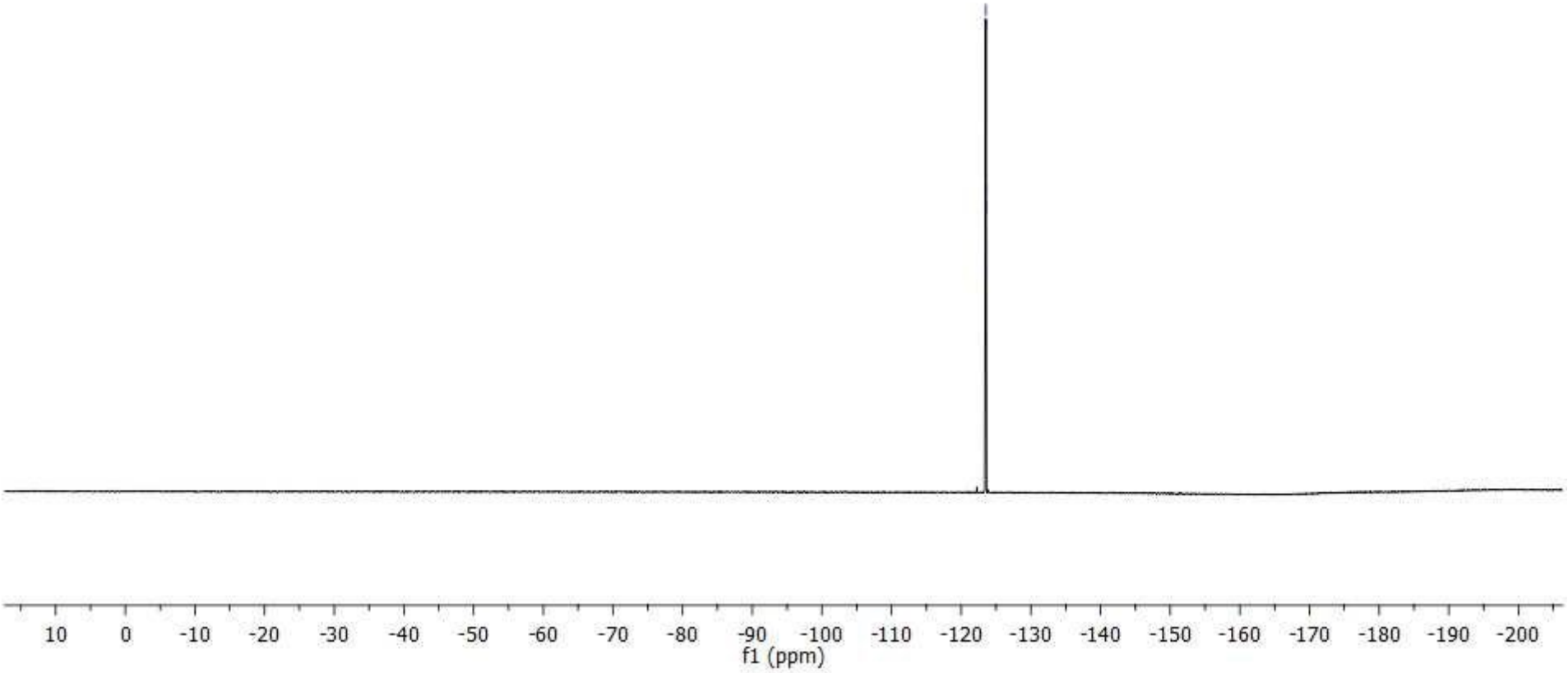
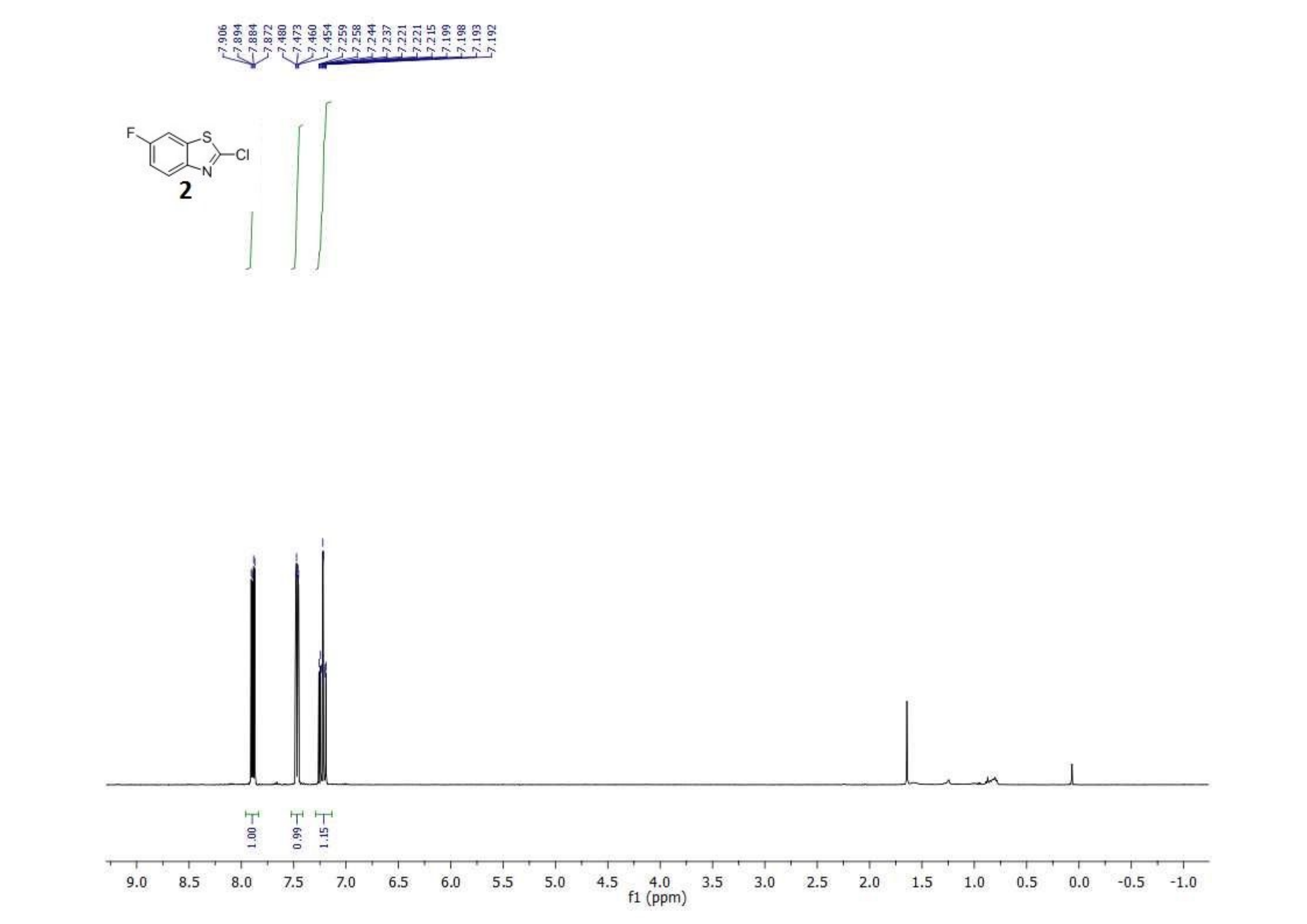
47.78
47.44
47.27
47.10
F
S
NH2
N
1
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

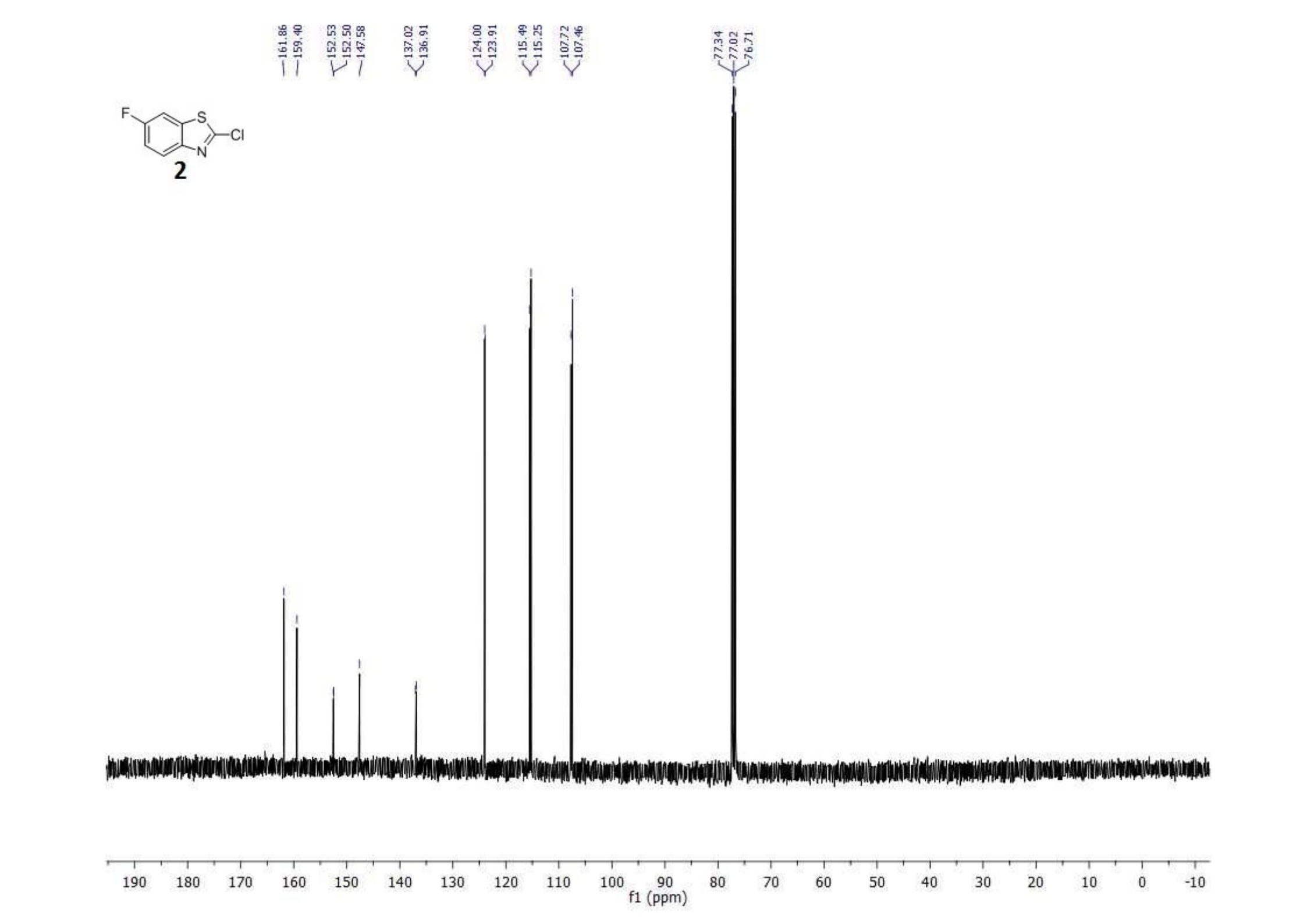


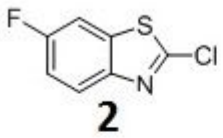
1

123.509
123.519
123.527
123.537
123.546
123.556



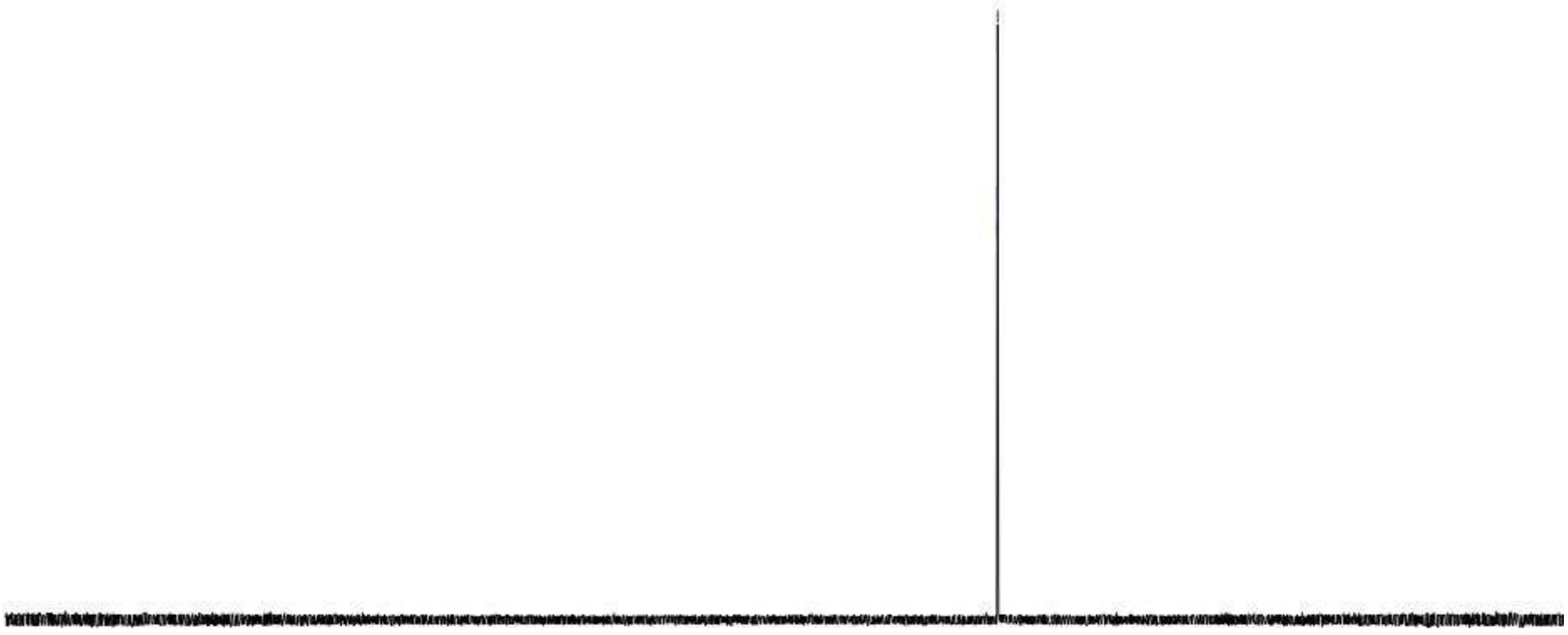

7.906
7.894
7.884
7.872
7.480
7.473
7.460
7.454
7.259
7.258
7.244
7.237
7.221
7.221
7.215
7.199
7.198
7.193
7.192
F
S
Cl
N
2
1.00
0.99
1.15
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

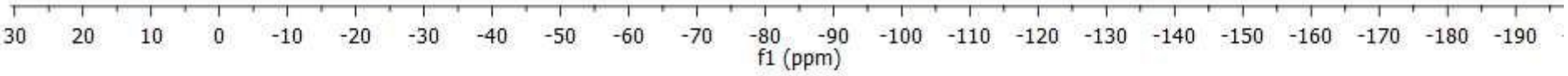

161.86
159.40
152.53
152.50
147.58
137.02
136.91
124.00
123.91
115.49
115.25
107.72
107.46
77.34
77.02
76.71
F
S
Cl
N
2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

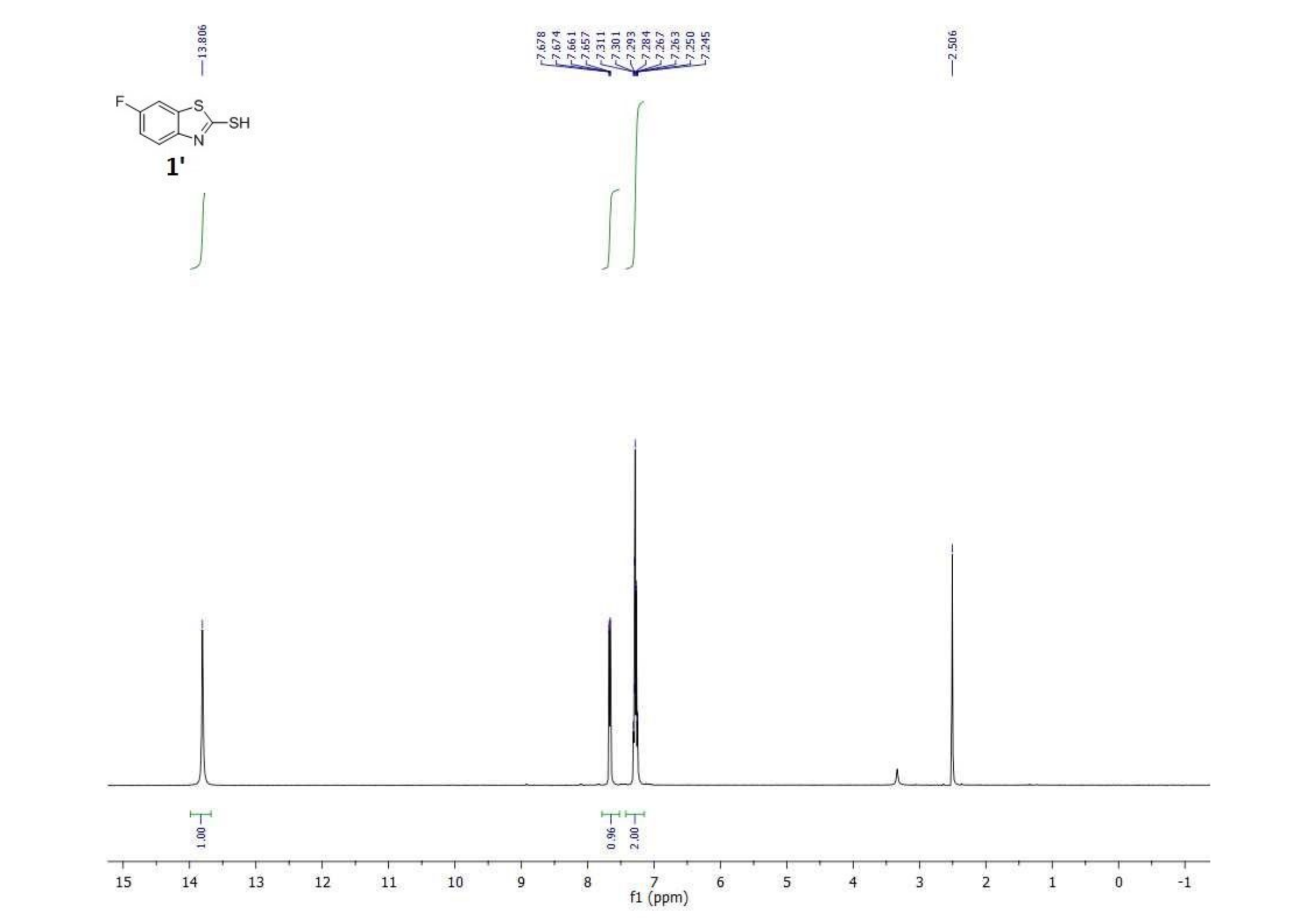

F
S
Cl
N

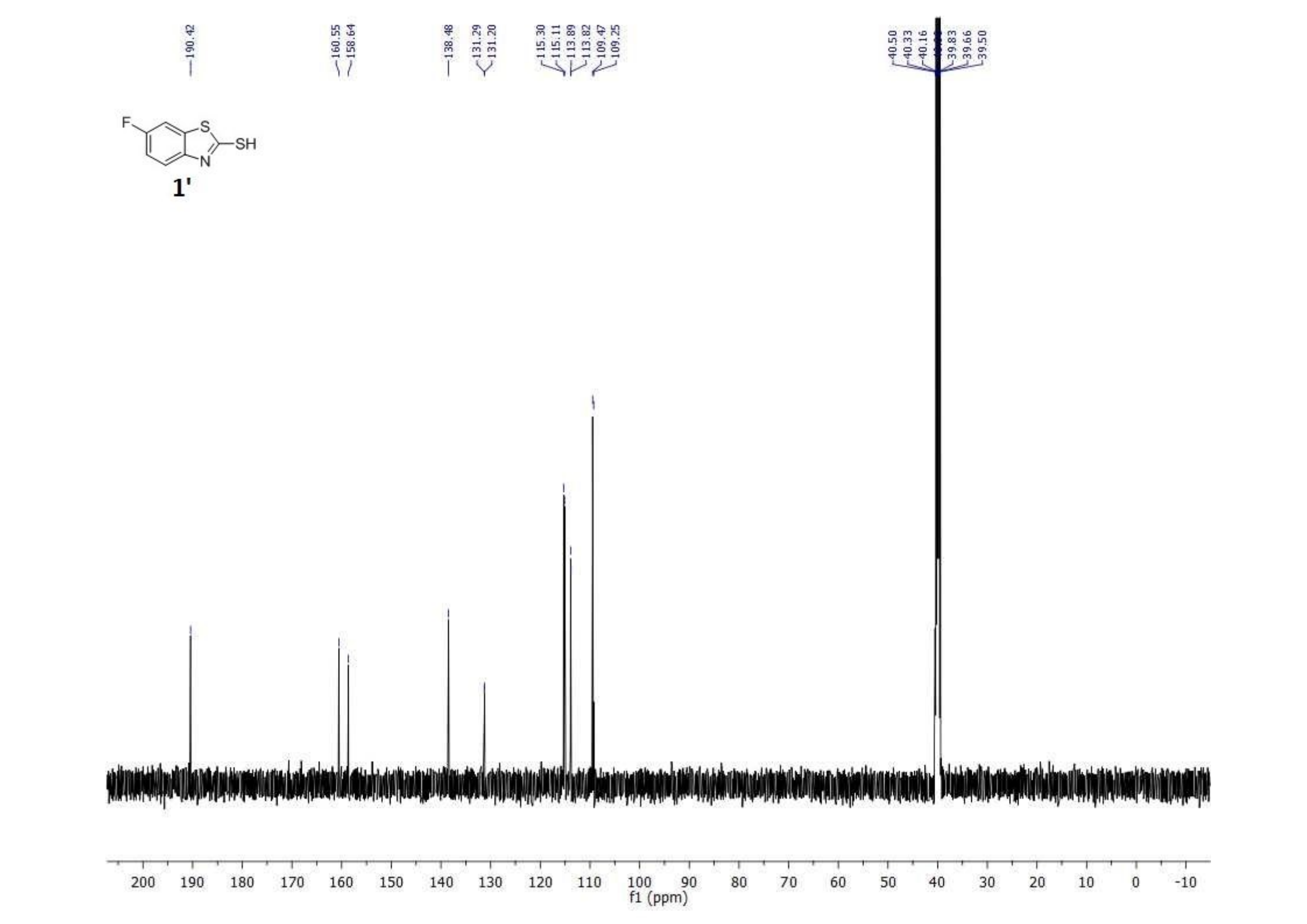
2

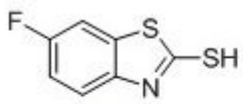

114.343
114.356
114.366
114.378
114.388
114.396
114.400




30
20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

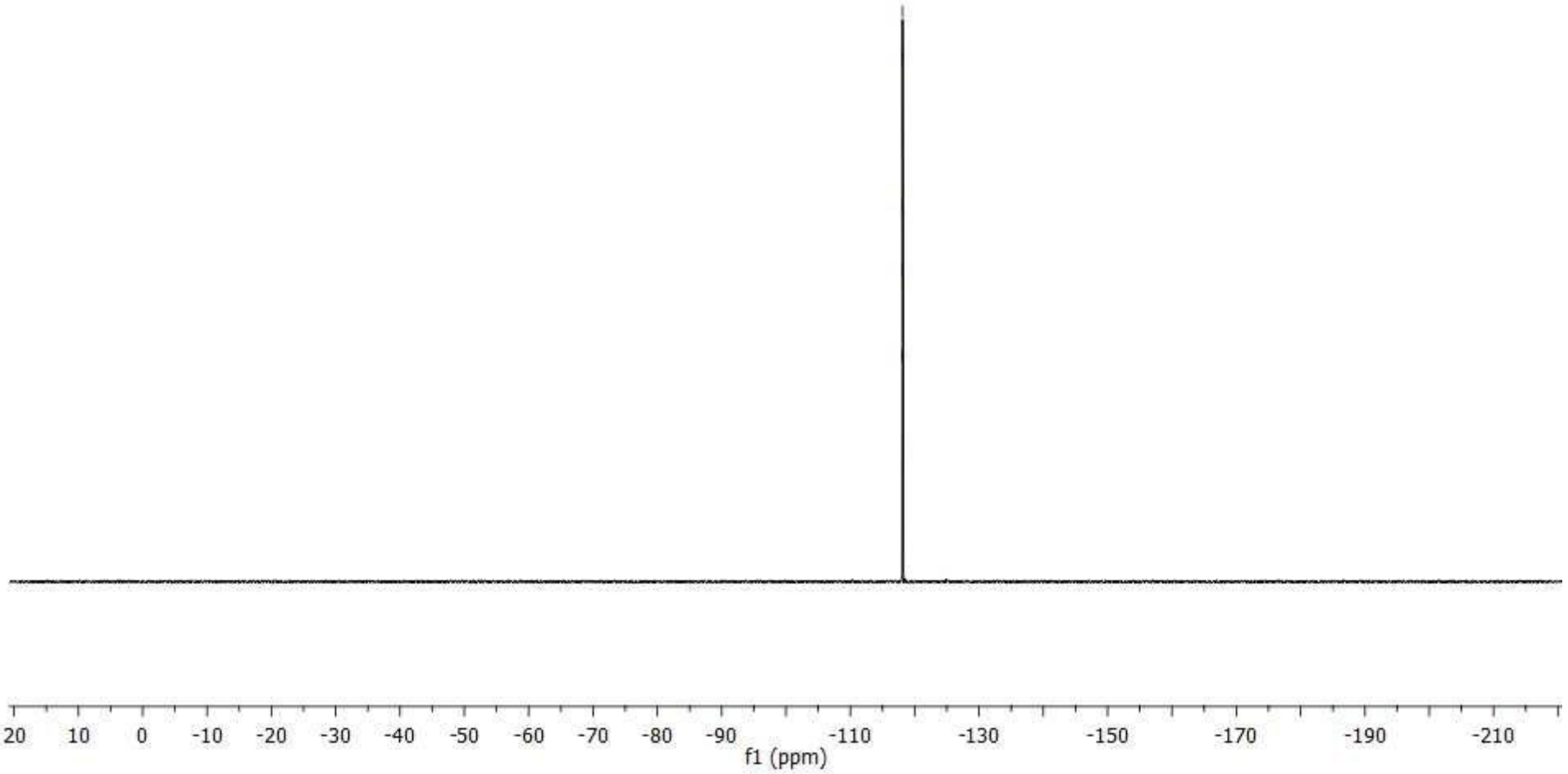

13.806
7.678
7.674
7.661
7.657
7.311
7.301
7.293
7.284
7.267
7.263
7.250
7.245
2.506
F
S
SH
N
1'
1.00
0.96
2.00
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)


190.42
160.55
158.64
138.48
131.29
131.20
115.30
115.11
113.89
113.82
109.47
109.25
40.50
40.33
40.16
39.83
39.66
39.50
F
S
SH
N
1'
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

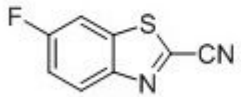

F
S
SH
N

1'

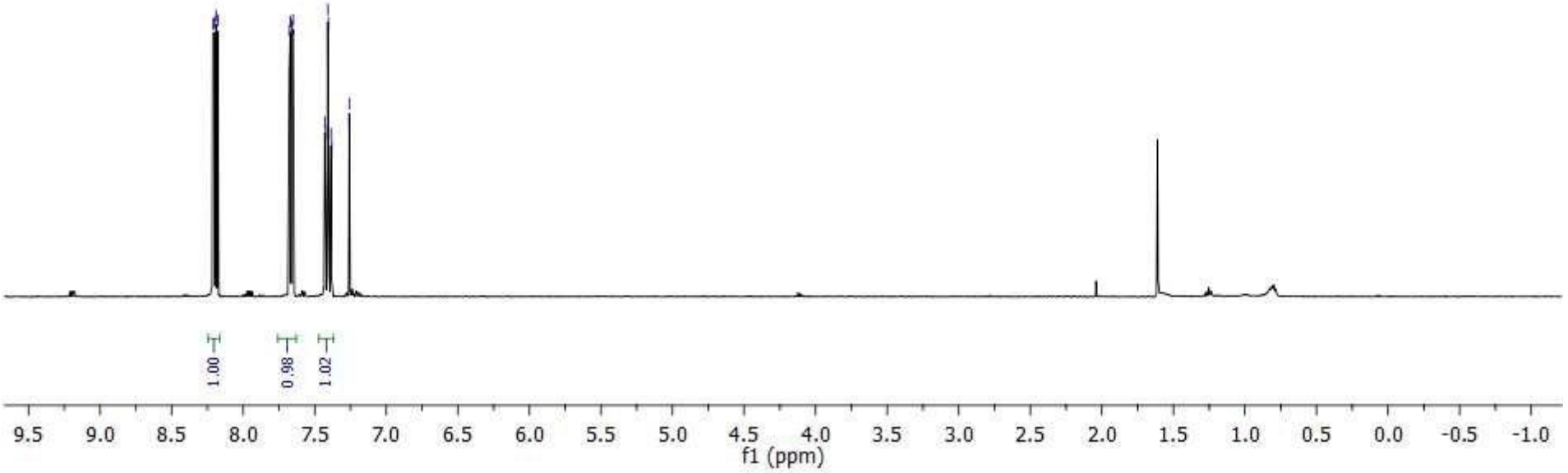

118.091
118.110
118.120
118.127
118.138

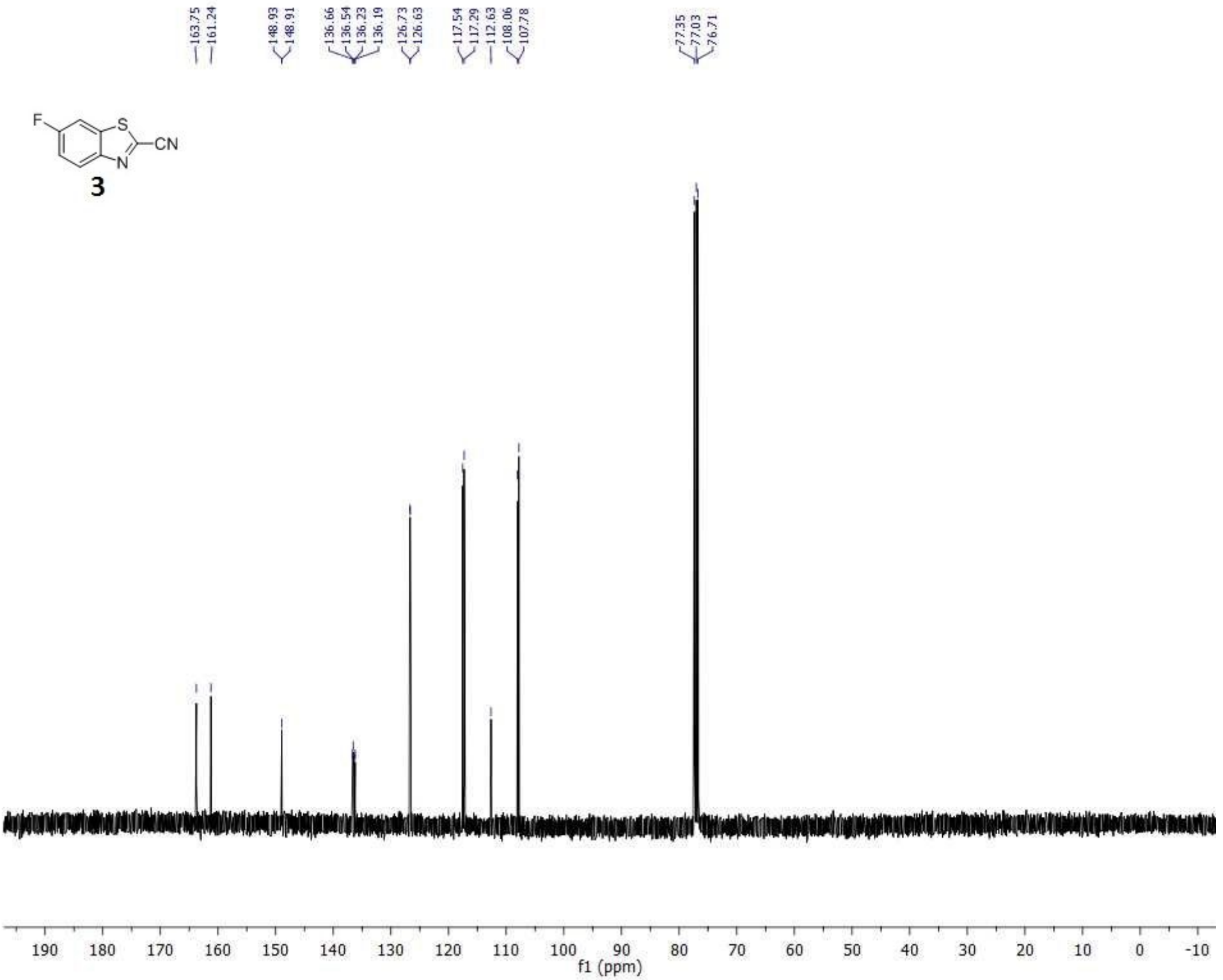

20
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-110
-130
-150
-170
-190
-210
f1 (ppm)

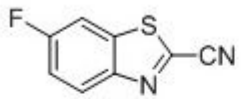

8.212
8.200
8.189
8.177
7.677
7.670
7.657
7.651
7.431
7.424
7.409
7.402
7.386
7.380
7.259
7.258


F
S
CN
N

3

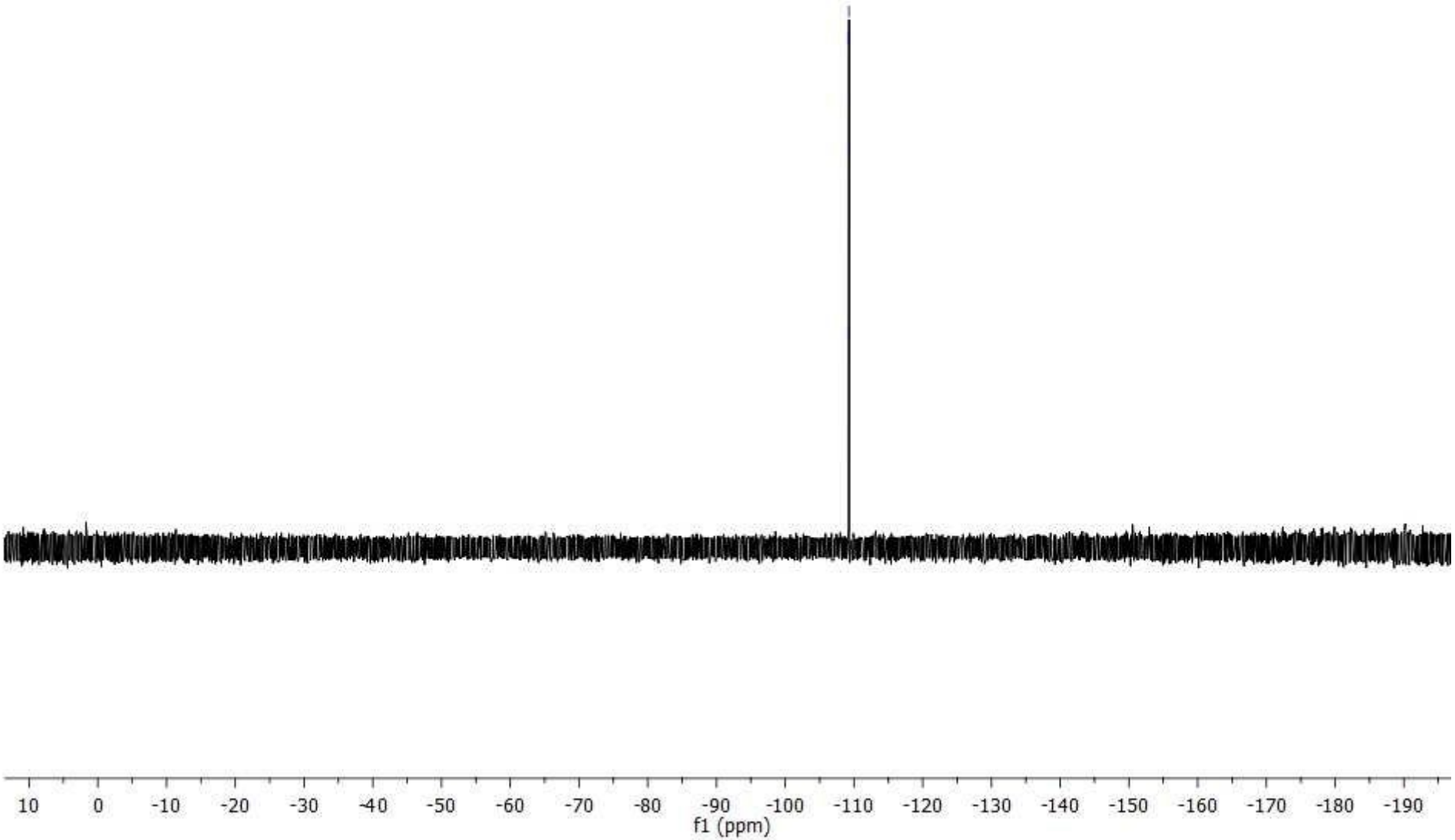

1.00
0.98
1.02
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

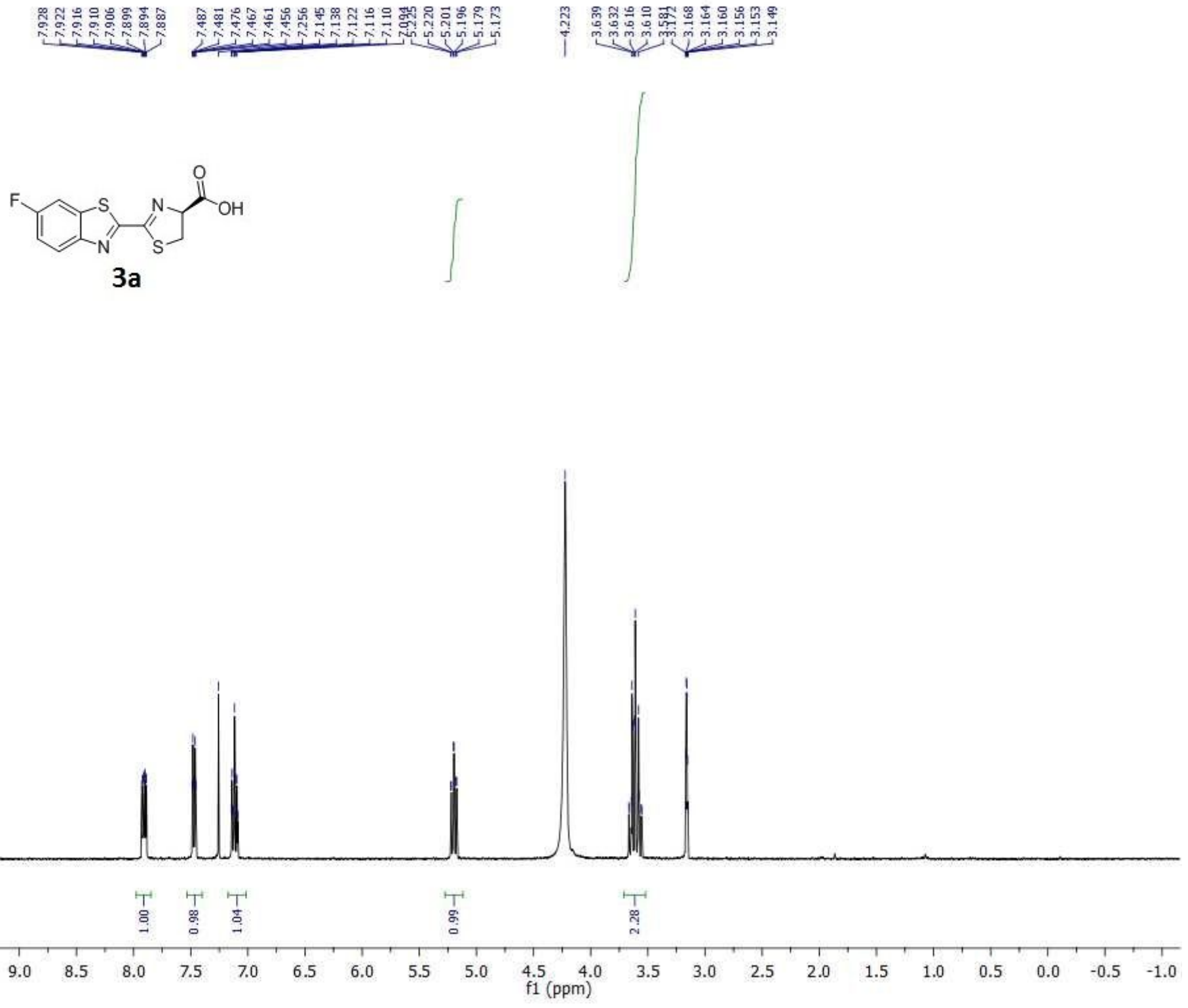

163.75
161.24
148.93
148.91
136.66
136.54
136.23
136.19
126.73
126.63
117.54
117.29
112.63
108.06
107.78
77.35
77.03
76.71
F
S
CN
N
3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

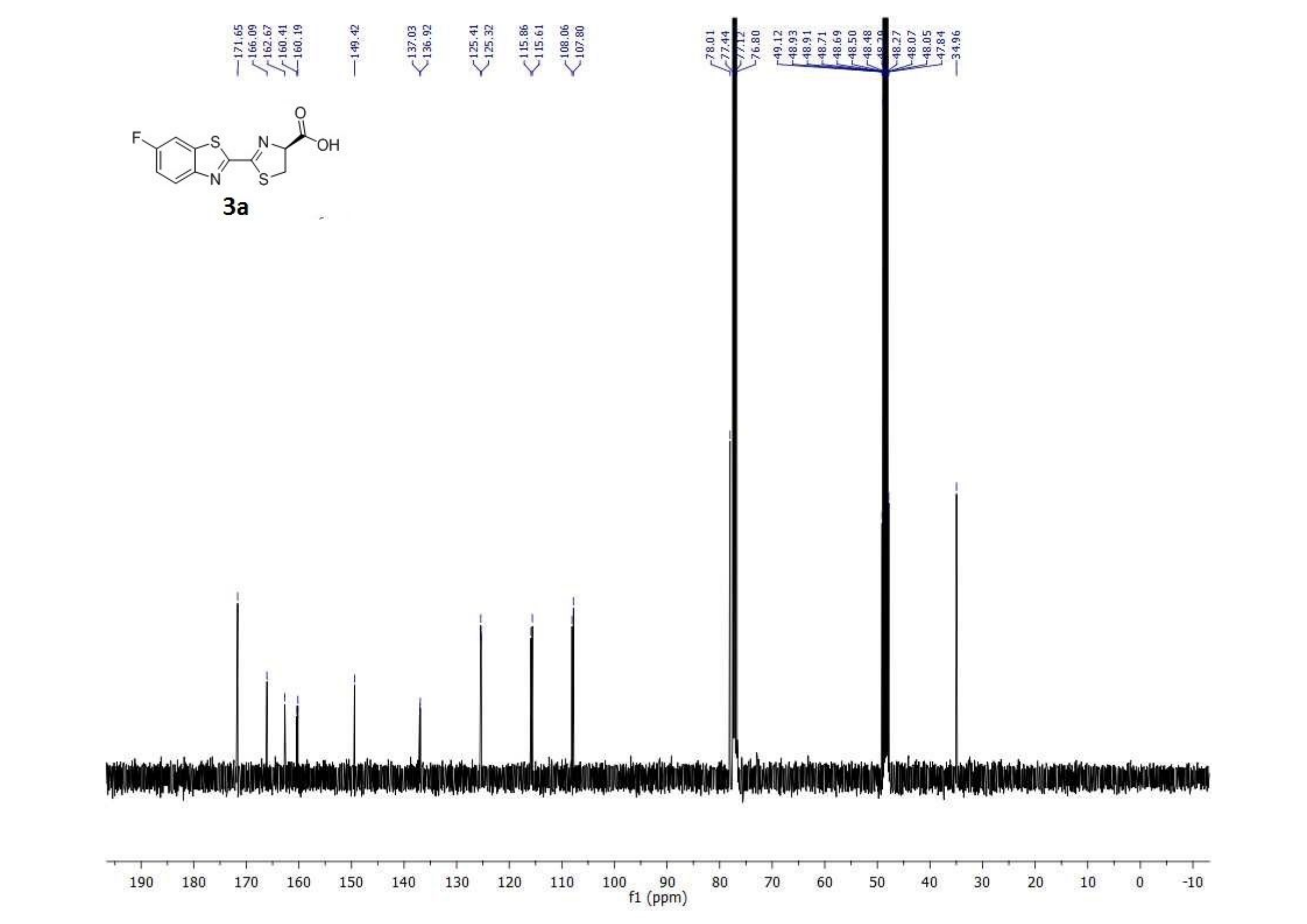

F
S
CN
N

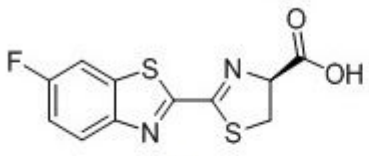
3


109.278
109.290
109.300
109.306
109.312
109.321
109.334


10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

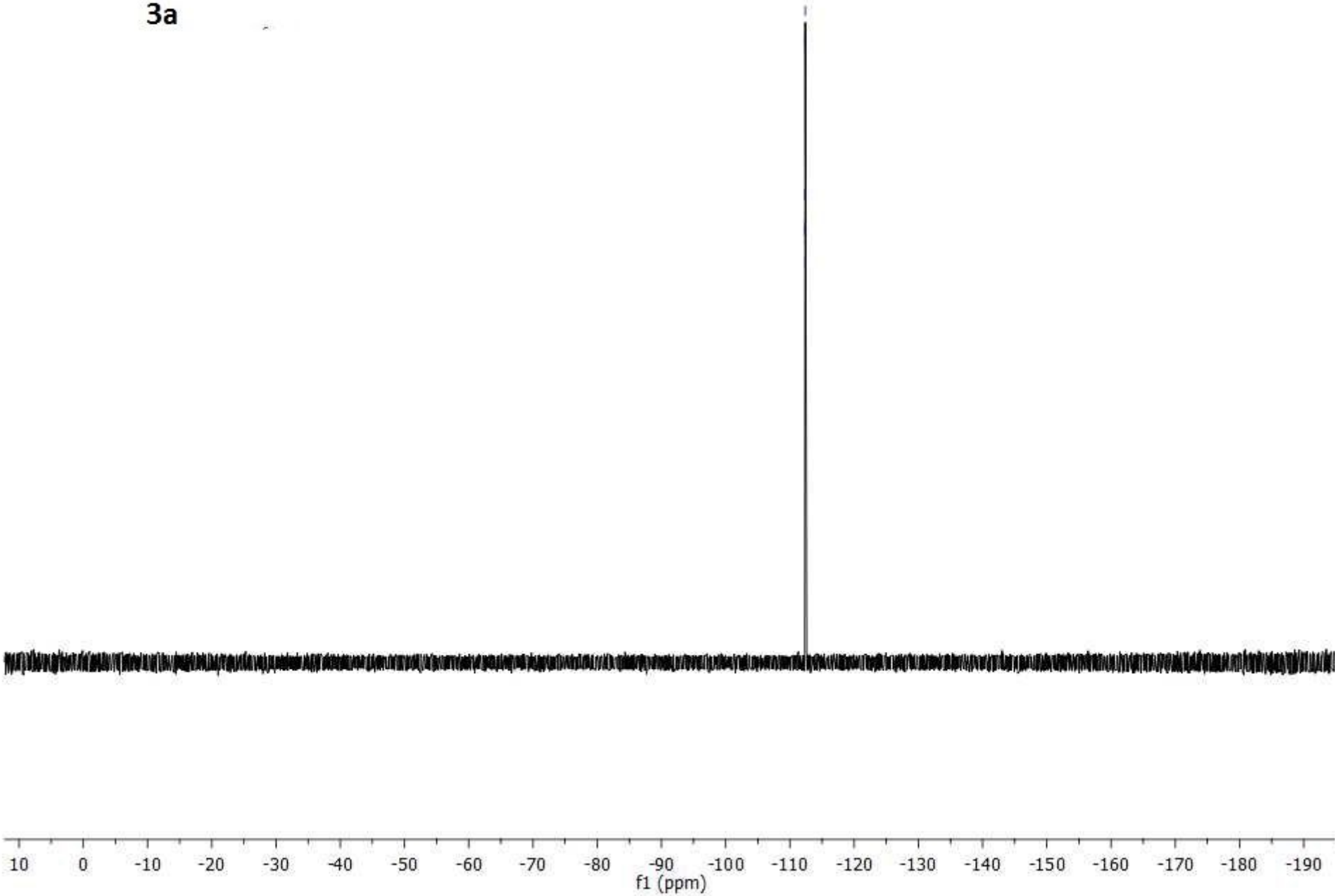

7.928
7.922
7.916
7.910
7.906
7.899
7.894
7.887
7.487
7.481
7.476
7.467
7.461
7.456
7.256
7.145
7.138
7.122
7.116
7.110
5.225
5.220
5.201
5.196
5.179
5.173
4.223
3.639
3.632
3.616
3.610
3.581
3.172
3.168
3.164
3.160
3.156
3.153
3.149
F
S
N
O
OH
N
S
3a
1.00
0.98
1.04
0.99
2.28
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

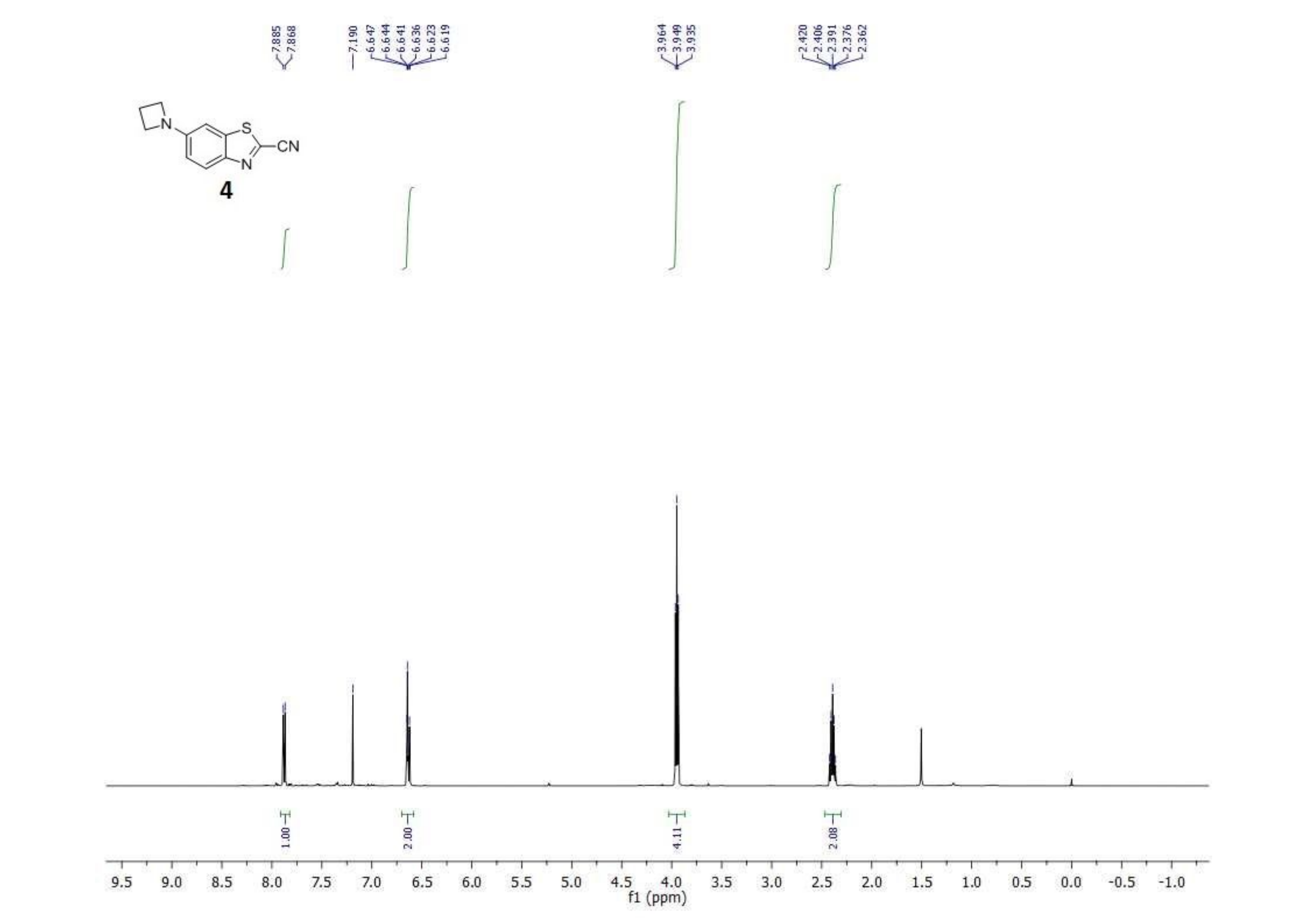

171.65
166.09
162.67
160.41
160.19
149.42
137.03
136.92
125.41
125.32
115.86
115.61
108.06
107.80
78.01
77.44
77.12
76.80
49.12
48.93
48.91
48.71
48.69
48.50
48.48
48.27
48.07
48.05
47.84
34.96
F
S
N
O
OH
N
S
3a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

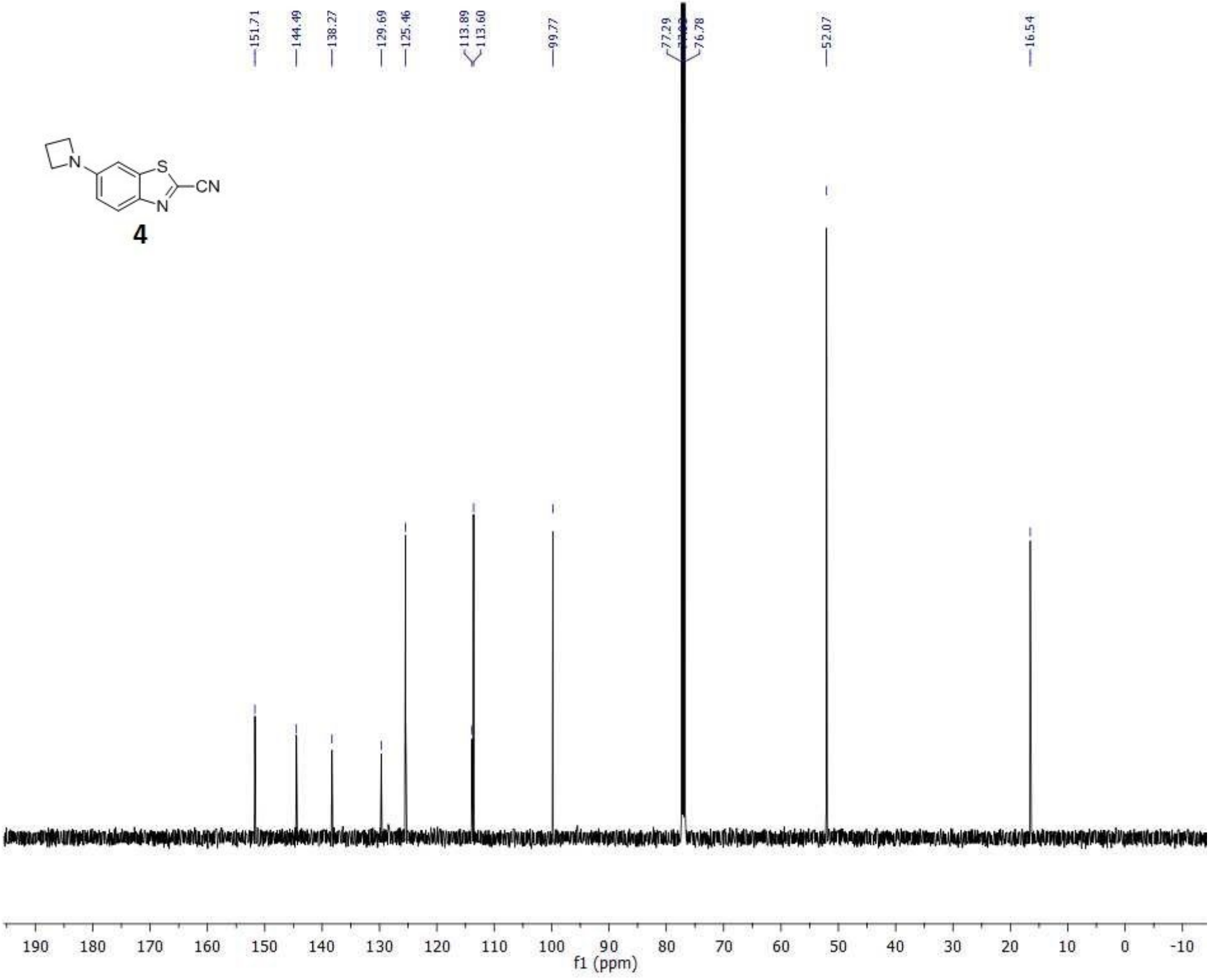

F
S
N
O
OH
N
S

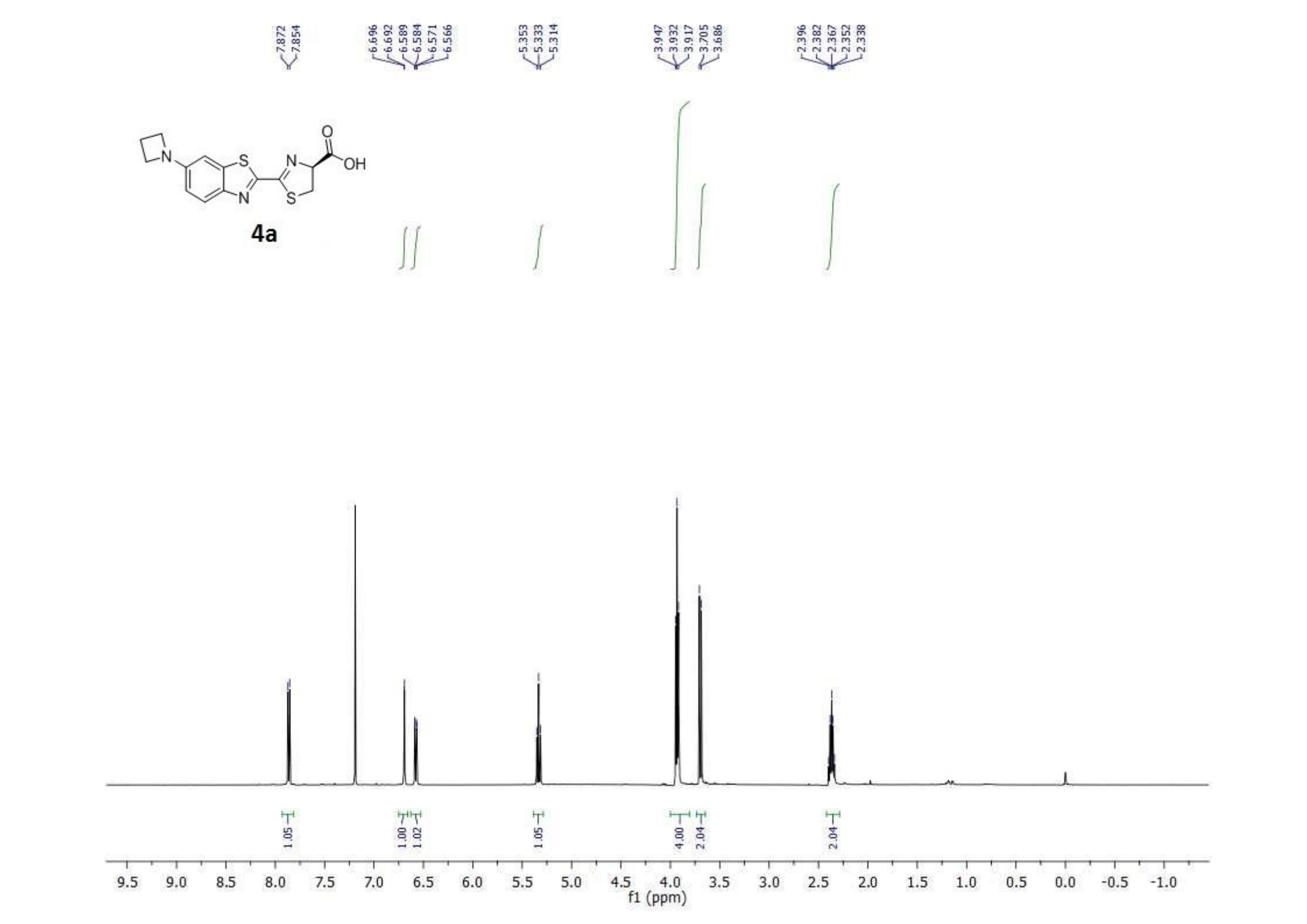
3a

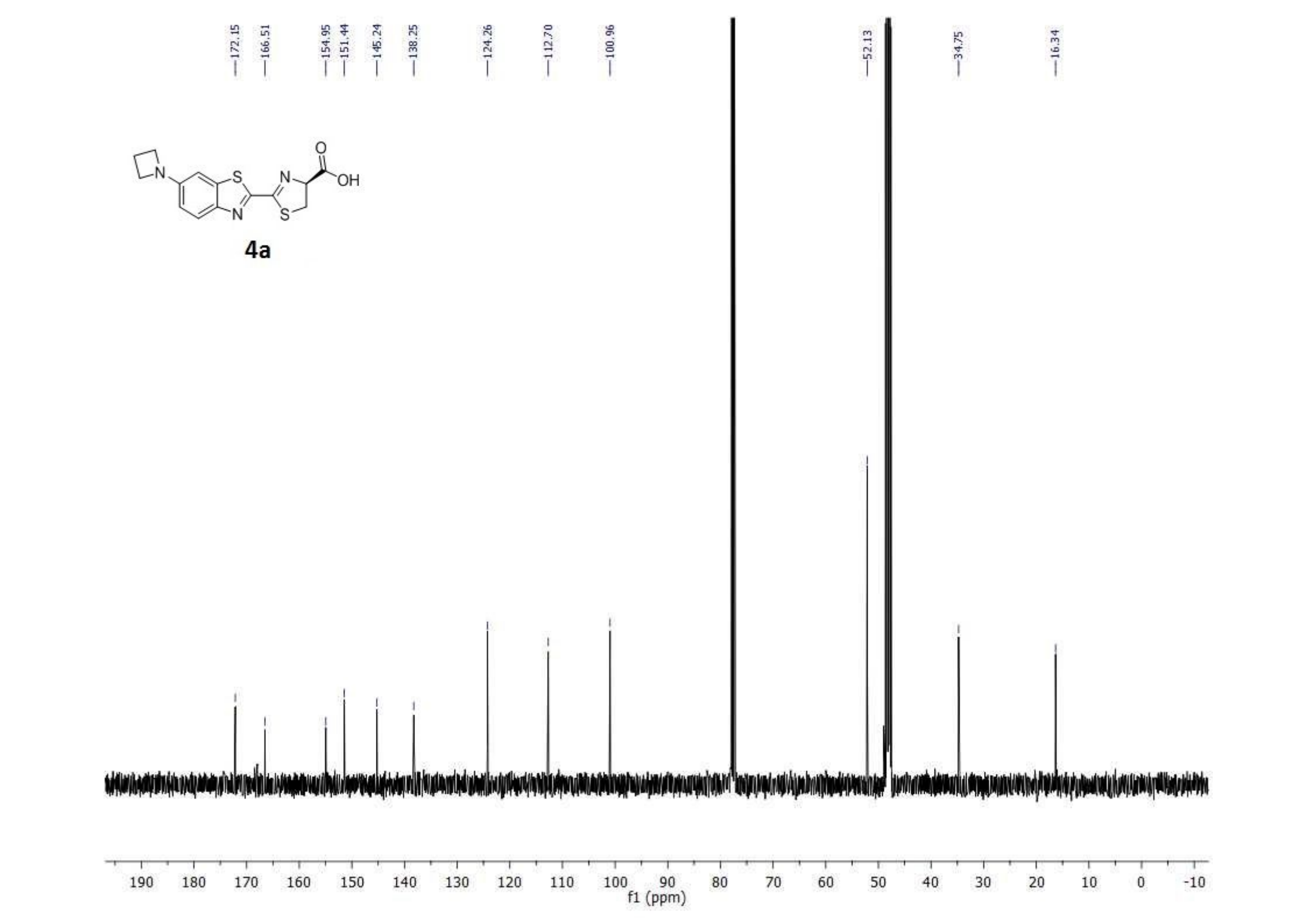

112.349
112.362
112.372
112.384
112.394
112.407


10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

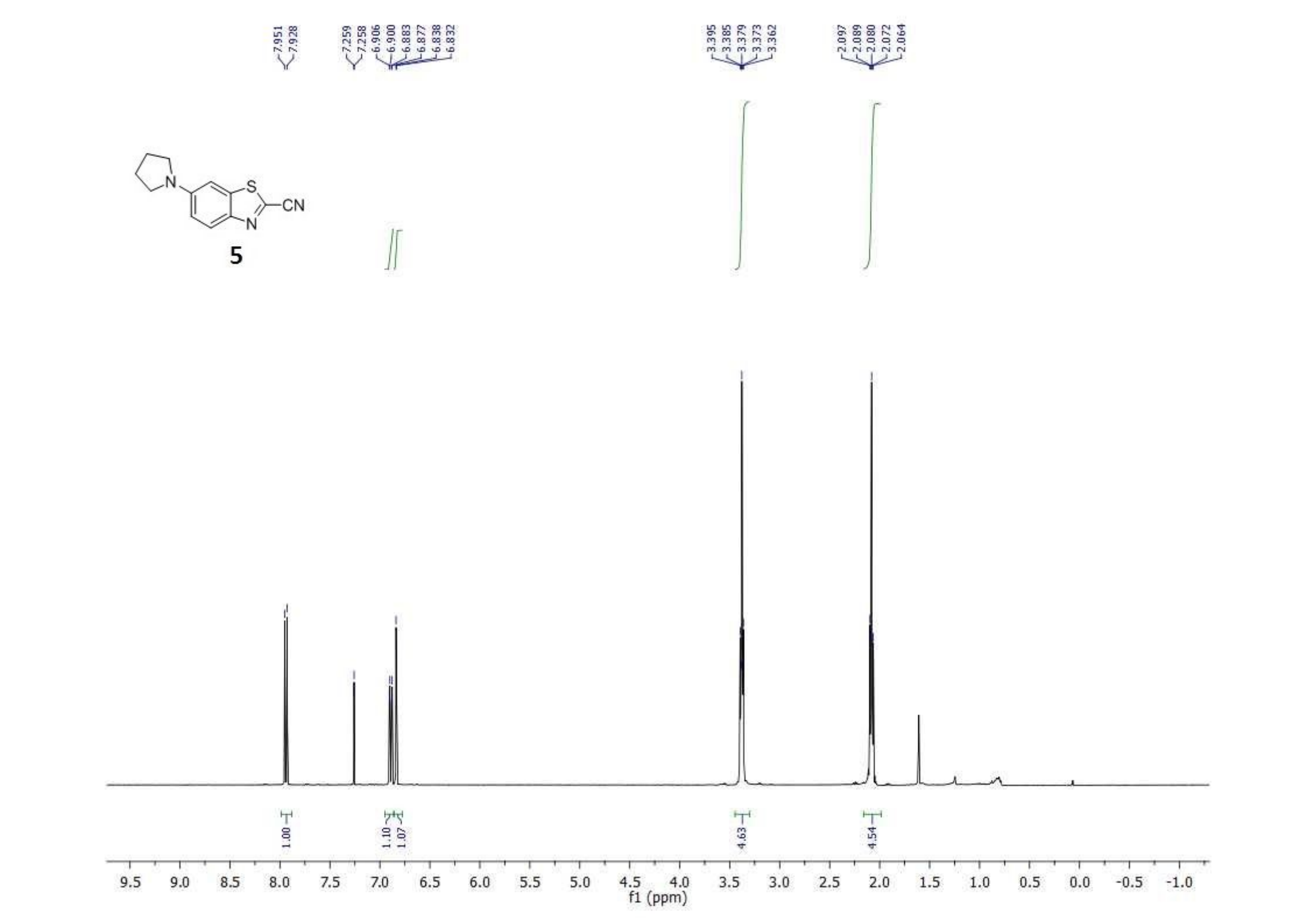

7.885
7.868
7.190
6.647
6.644
6.641
6.636
6.623
6.619
3.964
3.949
3.935
2.420
2.406
2.391
2.376
2.362
N
S
CN
N
4
1.00
2.00
4.11
2.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

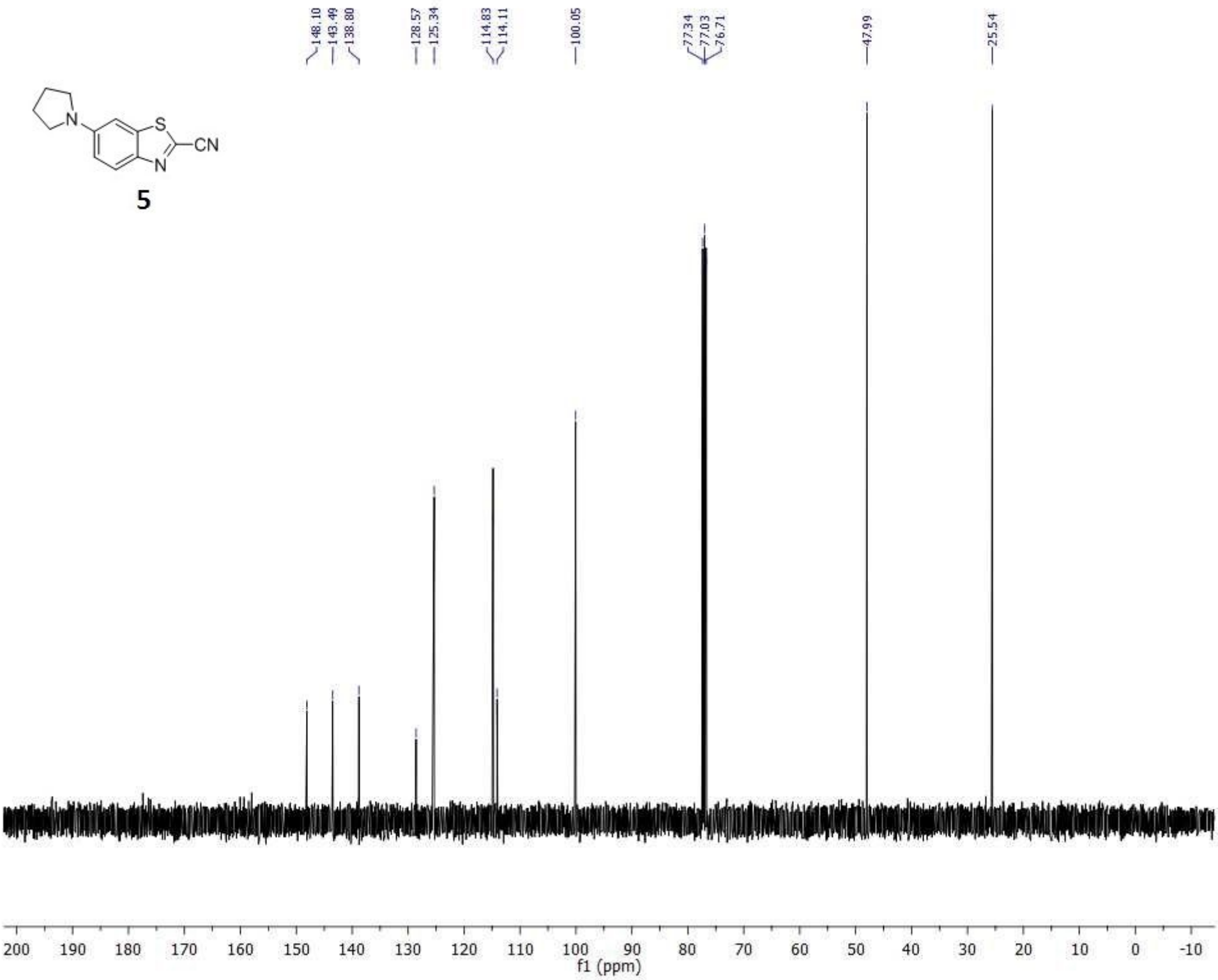

151.71
144.49
138.27
129.69
125.46
113.89
113.60
99.77
77.29
76.78
52.07
16.54
N
S
CN
N
4
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

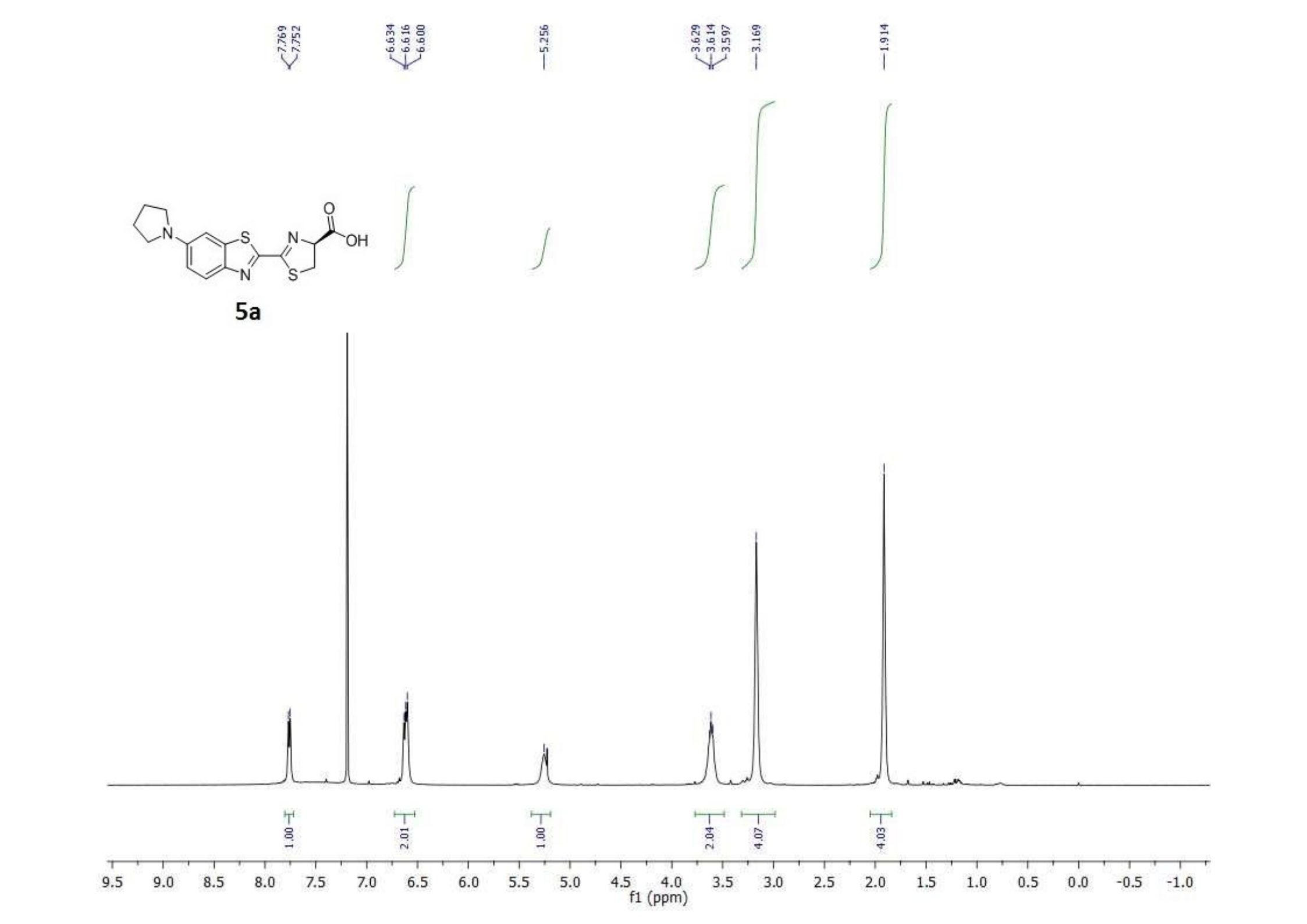

7.872
7.854
6.696
6.692
6.589
6.584
6.571
6.566
5.353
5.333
5.314
3.947
3.932
3.917
3.705
3.686
2.396
2.382
2.367
2.352
2.338
O
OH
N
S
N
N
S
4a
1.05
1.00
1.02
1.05
4.00
2.04
2.04
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

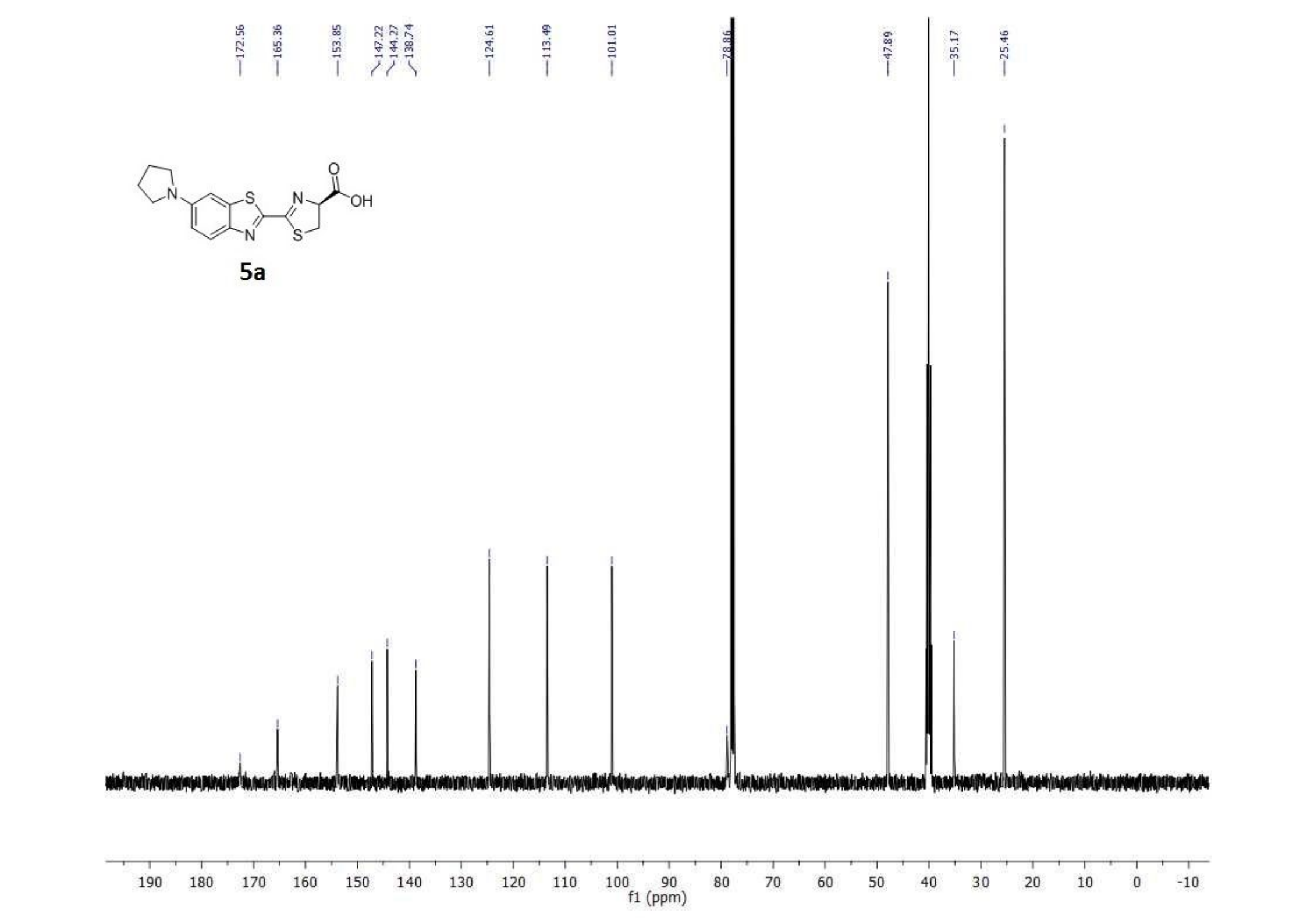

172.15
166.51
154.95
151.44
145.24
138.25
124.26
112.70
100.96
52.13
34.75
16.34
N
S
N
O
OH
N
S
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

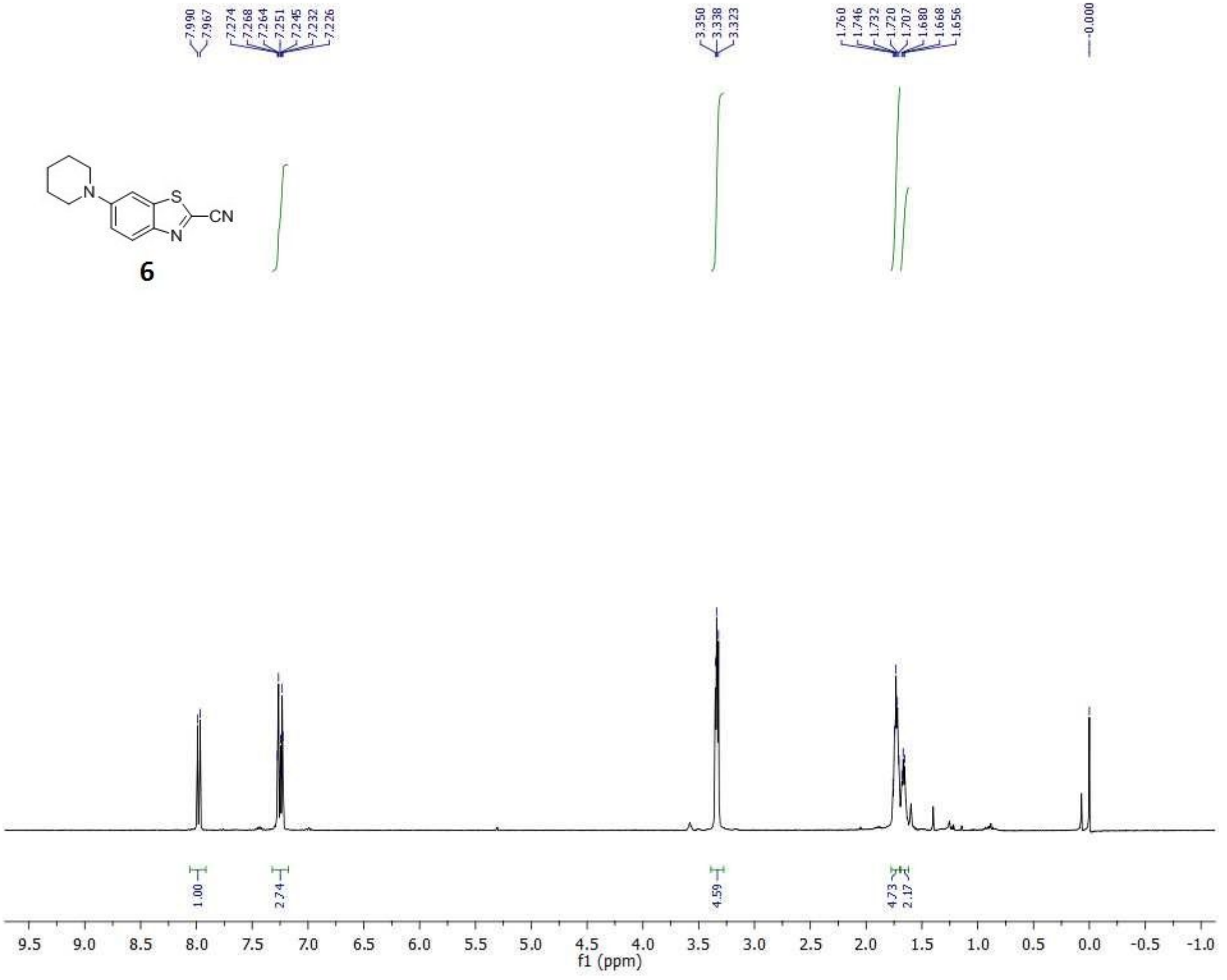
4a

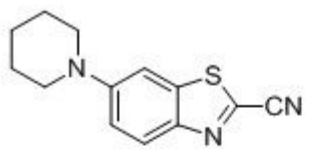

7.951
7.928
7.259
7.258
6.906
6.900
6.883
6.877
6.838
6.832
3.395
3.385
3.379
3.373
3.362
2.097
2.089
2.080
2.072
2.064
N
S
CN
N
5
1.00
1.10
1.07
4.63
4.54
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


148.10
143.49
138.80
128.57
125.34
114.83
114.11
100.05
77.34
77.03
76.71
47.99
25.54
N
S
CN
N
5
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.769
7.752
6.634
6.616
6.600
5.256
3.629
3.614
3.597
3.169
1.914
N
S
N
O
OH
N
S
5a
1.00
2.01
1.00
2.04
4.07
4.03
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

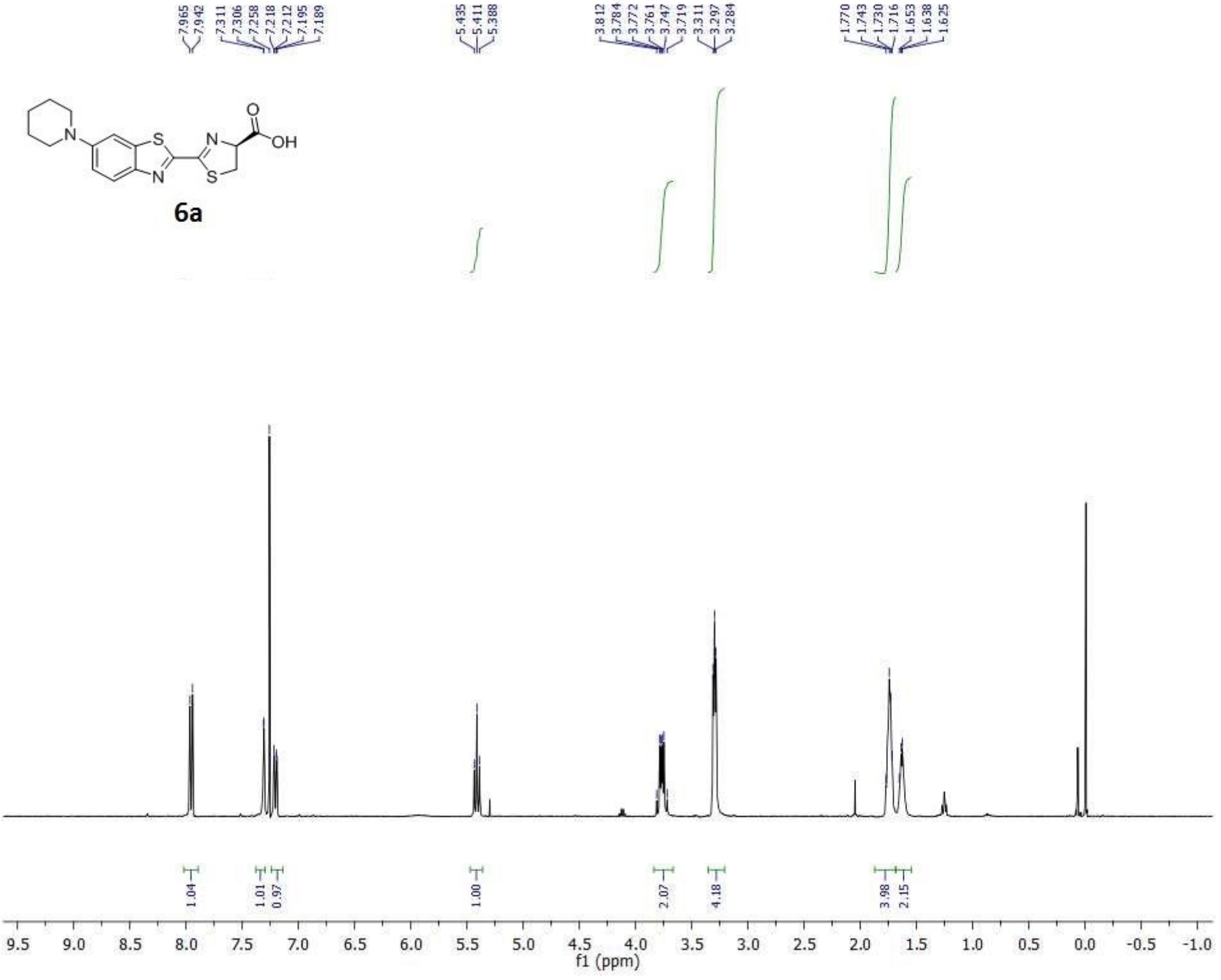

172.56
165.36
153.85
147.22
144.27
138.74
124.61
113.49
101.01
78.86
47.89
35.17
25.46
N
S
N
O
OH
N
S
5a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.990
7.967
7.274
7.268
7.264
7.251
7.245
7.232
7.226
3.350
3.338
3.323
1.760
1.746
1.732
1.720
1.707
1.680
1.668
1.656
0.000
N
S
CN
N
6
1.00
2.74
4.59
4.73
2.17
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


N
S
CN
N

6

152.16
145.07
138.26
131.01
125.13
118.50
113.76
104.30
77.33
77.02
76.70
49.94
25.47
24.17
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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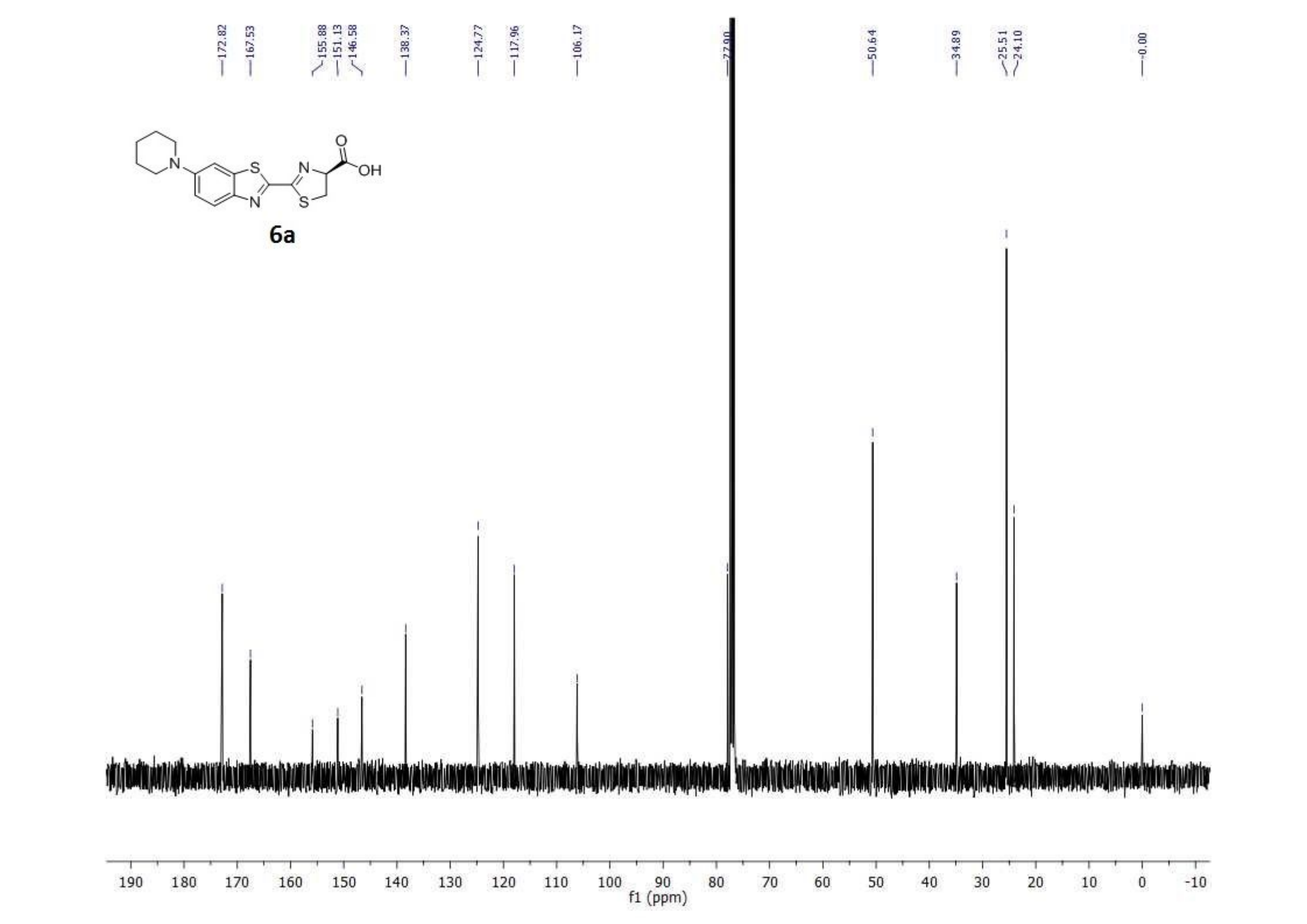
7.942
7.311
7.306
7.258
7.218
7.212
7.195
7.189
5.435
5.411
5.388
3.812
3.784
3.772
3.761
3.747
3.719
3.311
3.297
3.284
1.770
1.743
1.730
1.716
1.653
1.638
1.625
N
S
N
N
S
O
OH
6a
1.04
1.01
0.97
1.00
2.07
4.18
3.98
2.15
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)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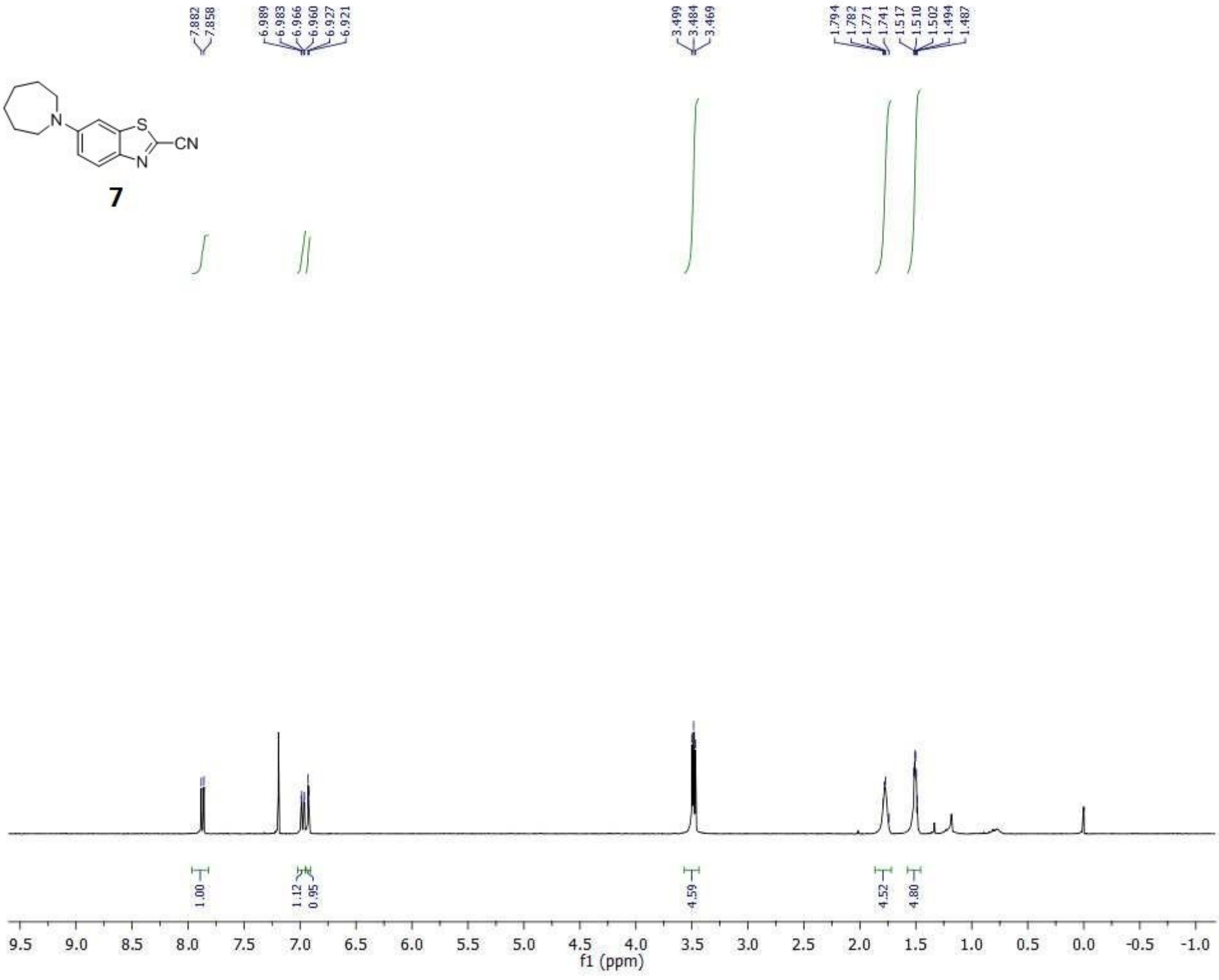
167.53
155.88
151.13
146.58
138.37
124.77
117.96
106.17
77.00
50.64
34.89
25.51
24.10
0.00
O
OH
N
S
N
N
S
6a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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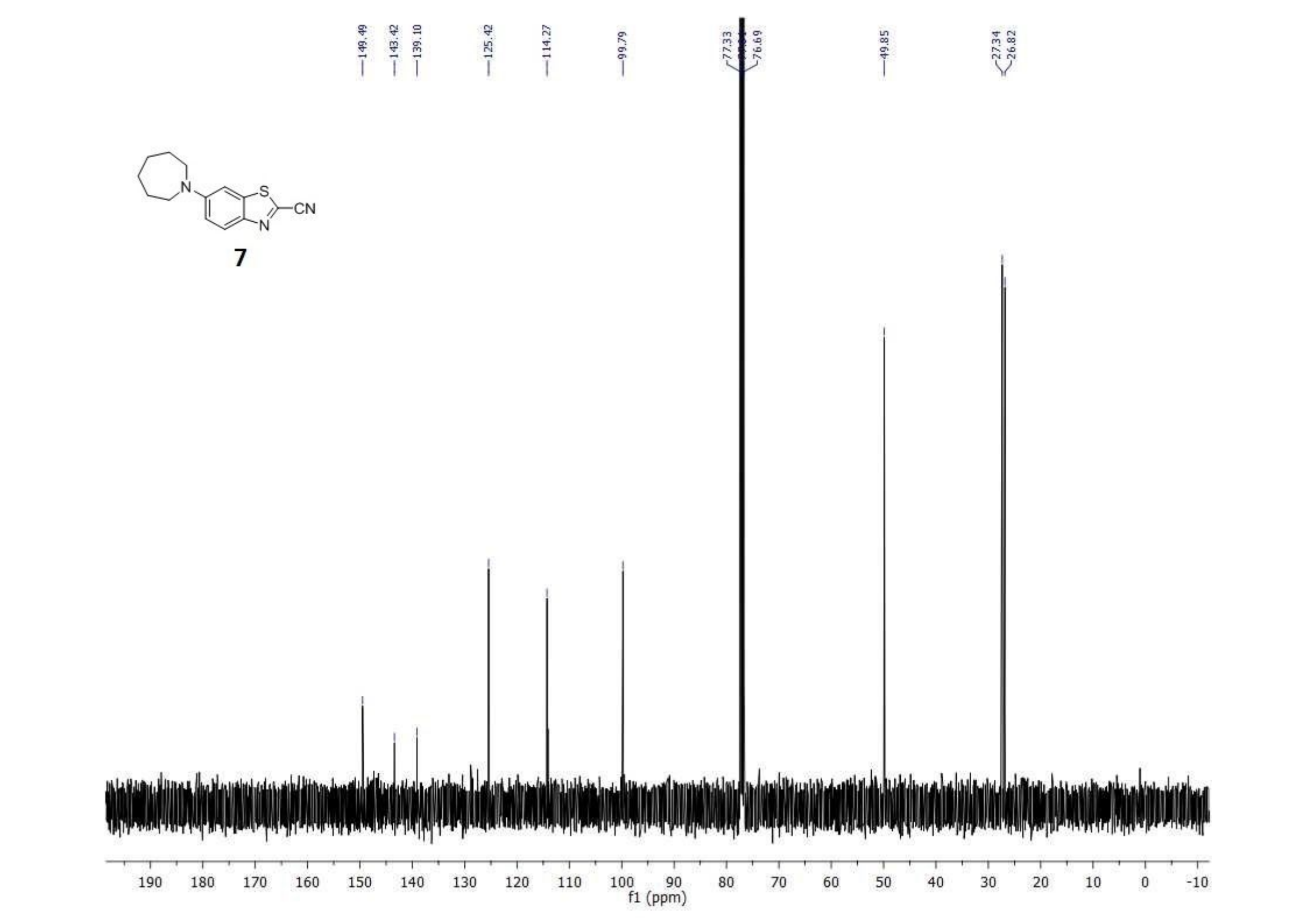
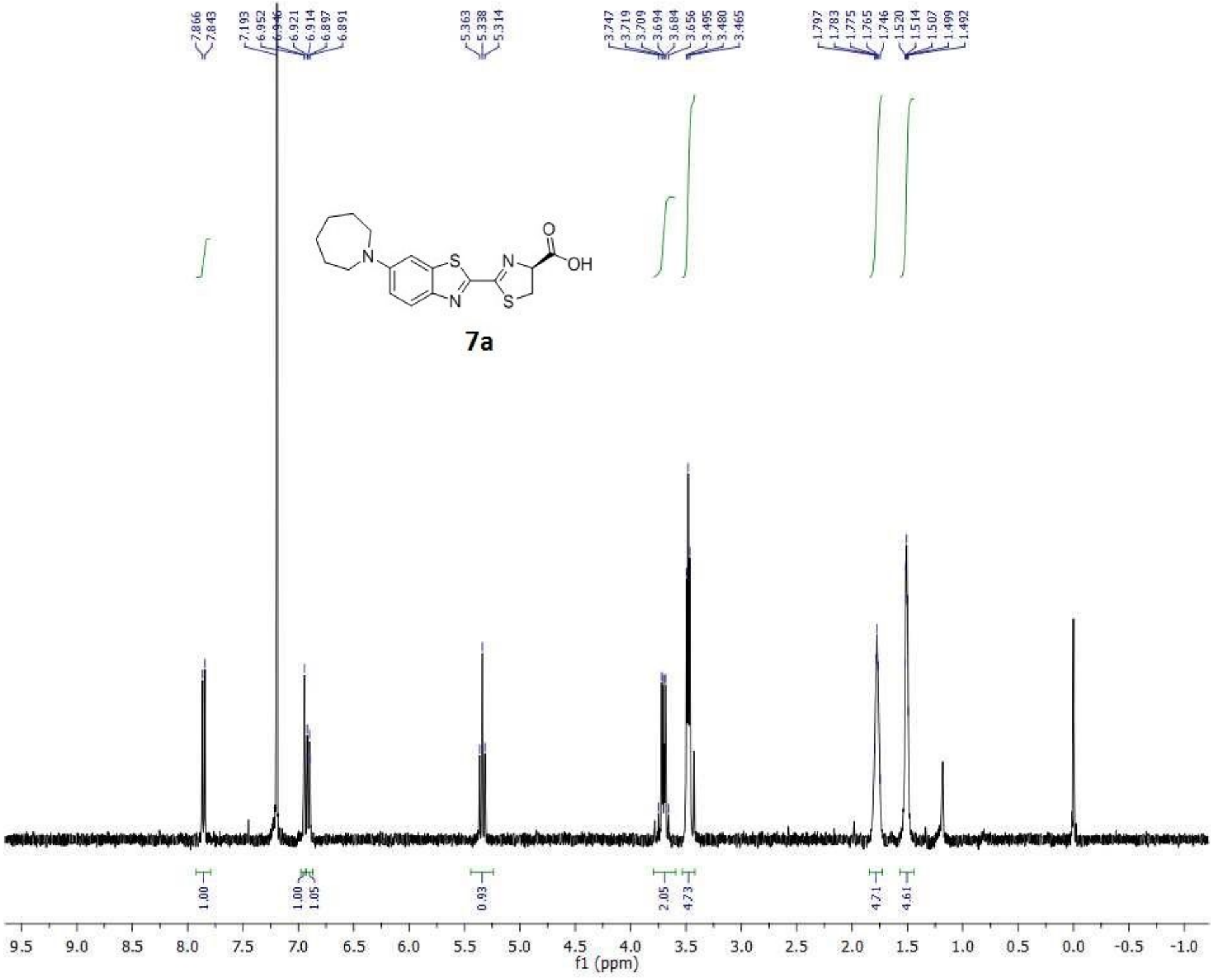
7.858
6.989
6.983
6.966
6.960
6.927
6.921
3.499
3.484
3.469
1.794
1.782
1.771
1.741
1.517
1.510
1.502
1.494
1.487
N
S
CN
N
7
1.00
1.12
0.95
4.59
4.52
4.80
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


149.49
143.42
139.10
125.42
114.27
99.79
77.33
76.69
49.85
27.34
26.82
N
S
CN
N
7
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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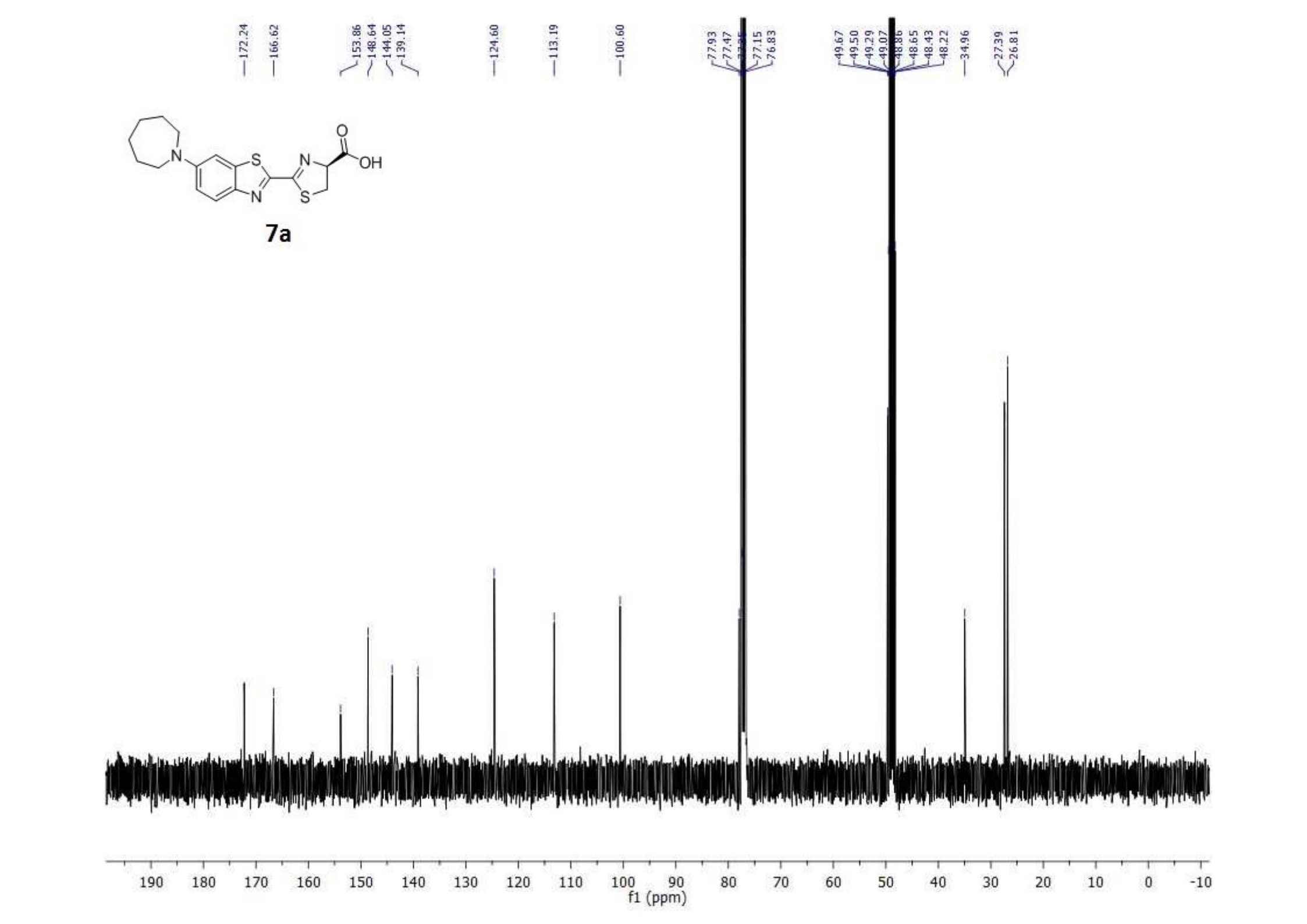
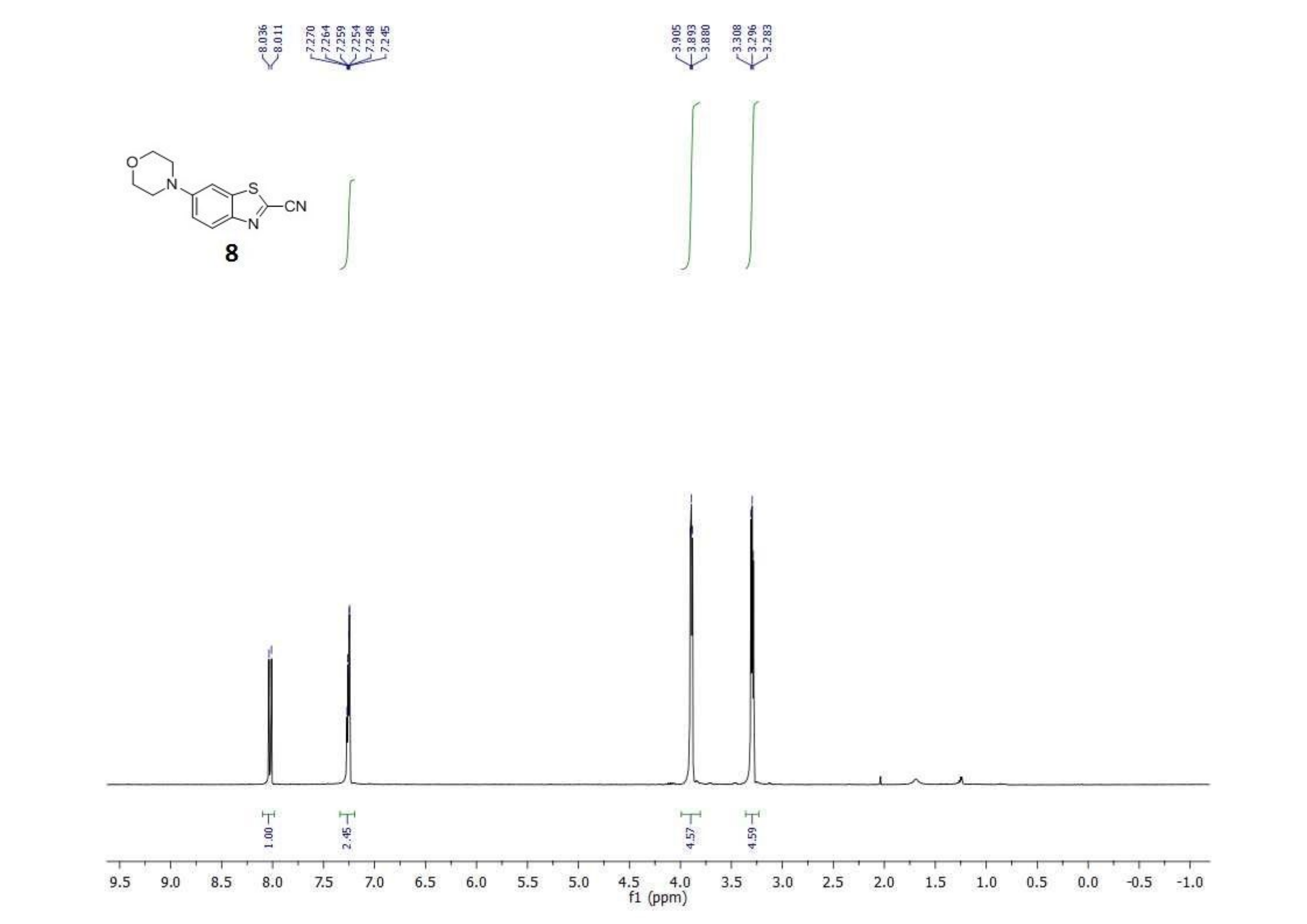
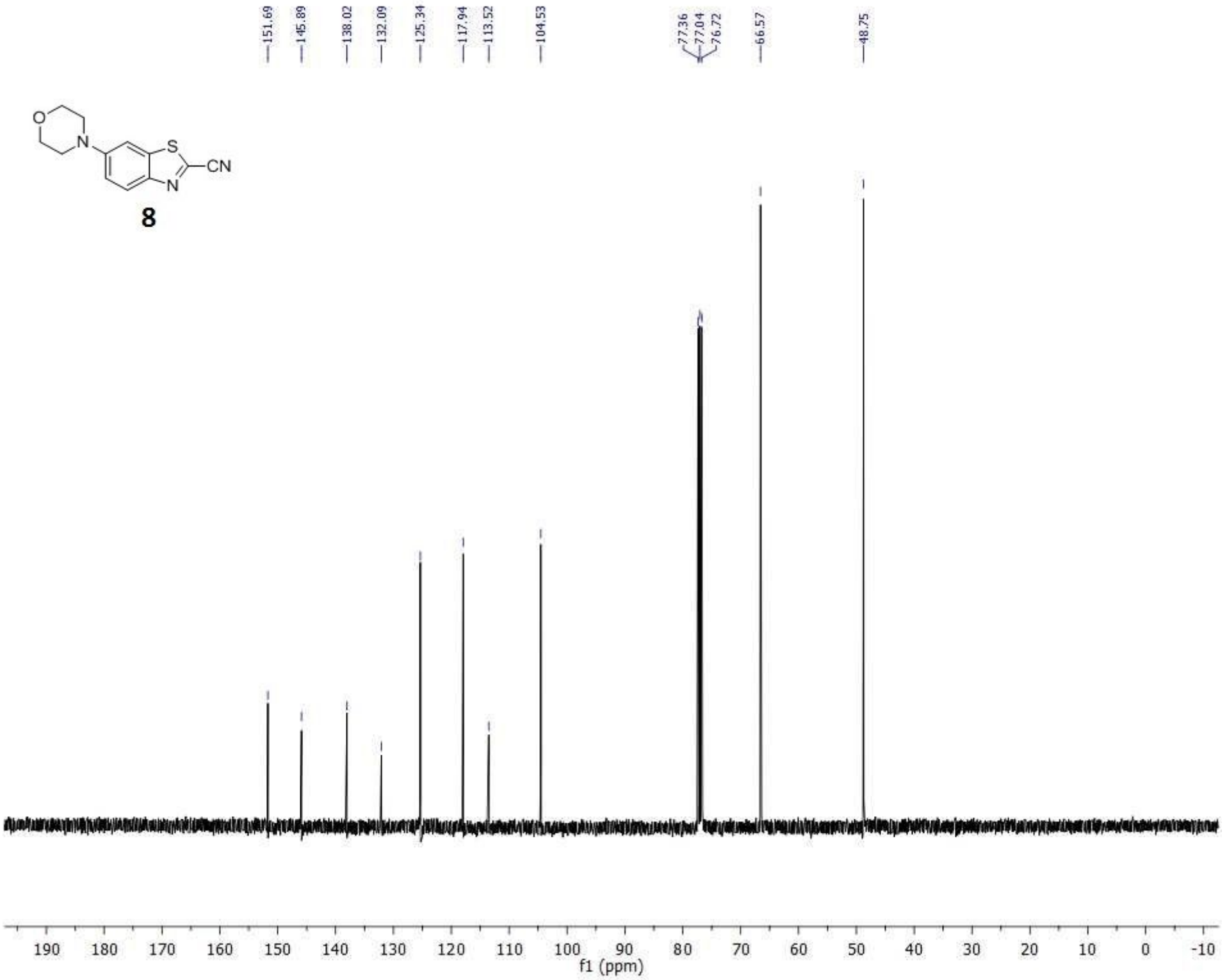
7.843
7.193
6.952
6.946
6.921
6.914
6.897
6.891
5.363
5.338
5.314
3.747
3.719
3.709
3.694
3.684
3.656
3.495
3.480
3.465
1.797
1.783
1.775
1.765
1.746
1.520
1.514
1.507
1.499
1.492
N
S
N
S
N
O
OH
1.00
1.00
1.05
0.93
2.05
4.73
4.71
4.61
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

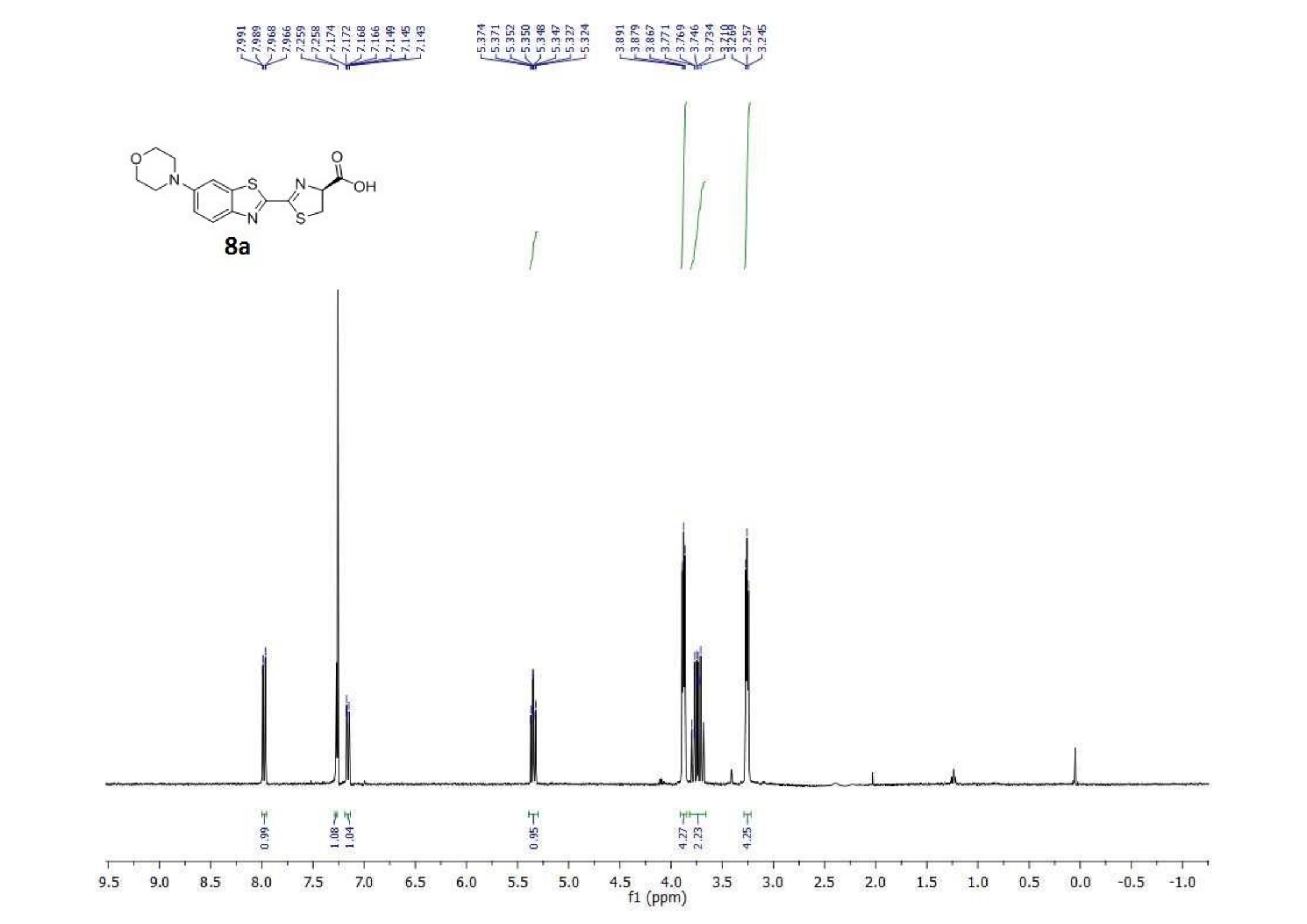
7a


172.24
166.62
153.86
148.64
144.05
139.14
124.60
113.19
100.60
77.93
77.47
77.15
76.83
49.67
49.50
49.29
49.07
48.86
48.65
48.43
48.22
34.96
27.39
26.81
N
S
N
O
OH
N
S
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

7a


8.036
8.011
7.270
7.264
7.259
7.254
7.248
7.245
3.905
3.893
3.880
3.308
3.296
3.283
O
N
S
CN
N
8
1.00
2.45
4.57
4.59
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


151.69
145.89
138.02
132.09
125.34
117.94
113.52
104.53
77.36
77.04
76.72
66.57
48.75
O
N
S
CN
N
8
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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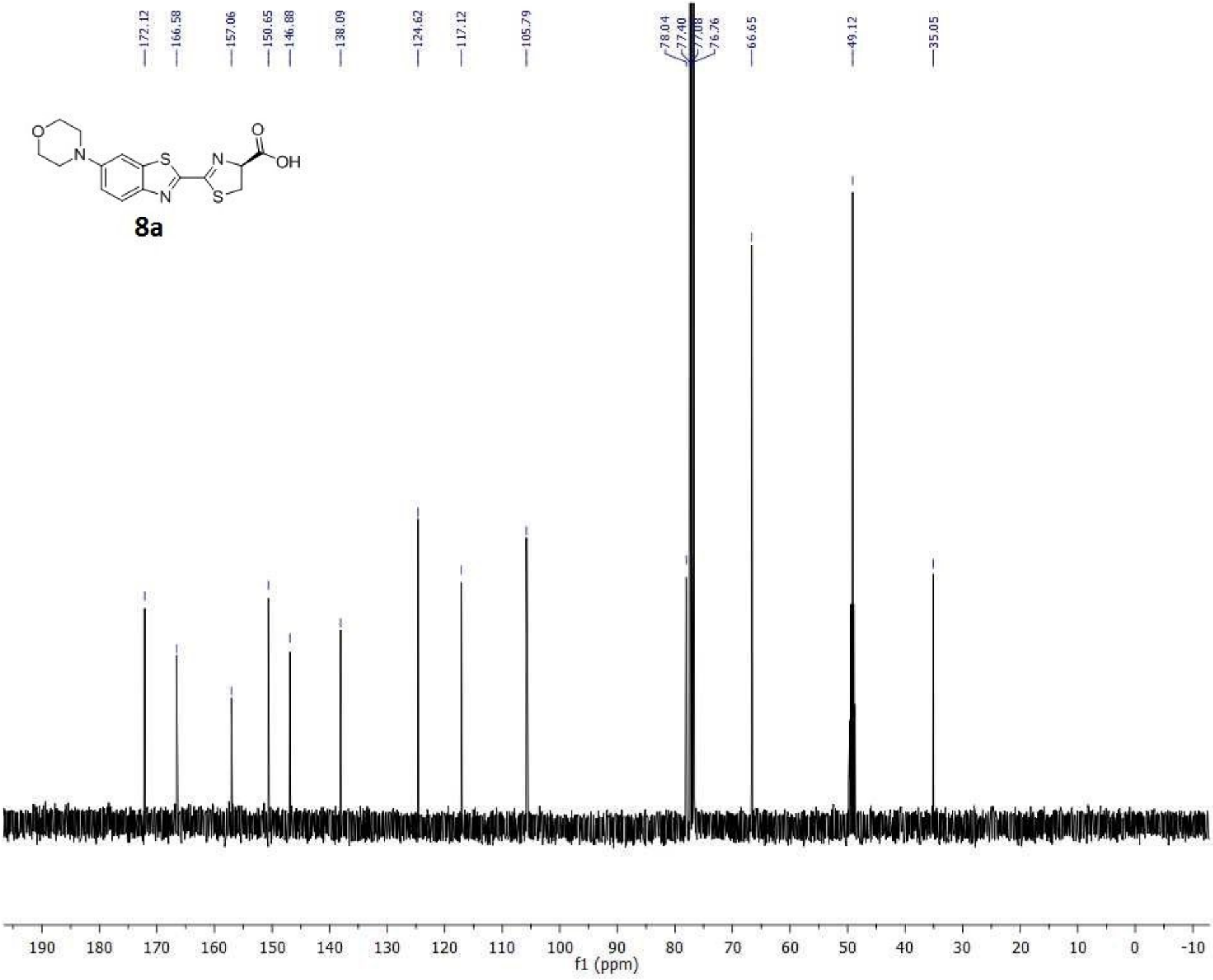
7.989
7.968
7.966
7.259
7.258
7.174
7.172
7.168
7.166
7.149
7.145
7.143
5.374
5.371
5.352
5.350
5.348
5.347
5.327
5.324
3.891
3.879
3.867
3.771
3.769
3.746
3.734
3.257
3.245
O
N
S
N
O
OH
S
8a
0.99
1.08
1.04
0.95
4.27
2.23
4.25
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)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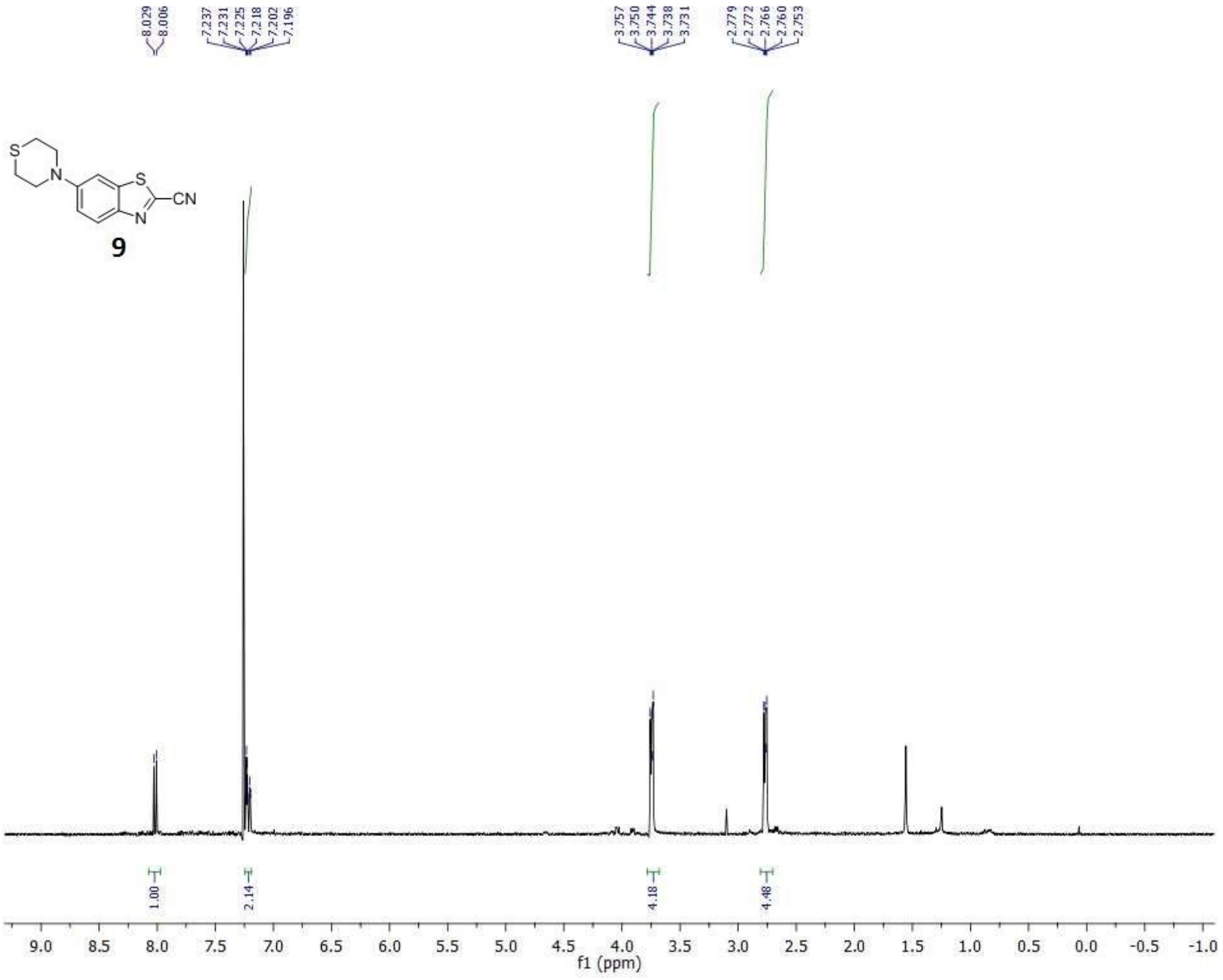
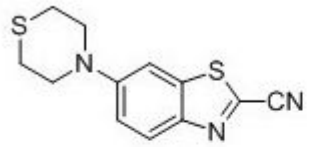
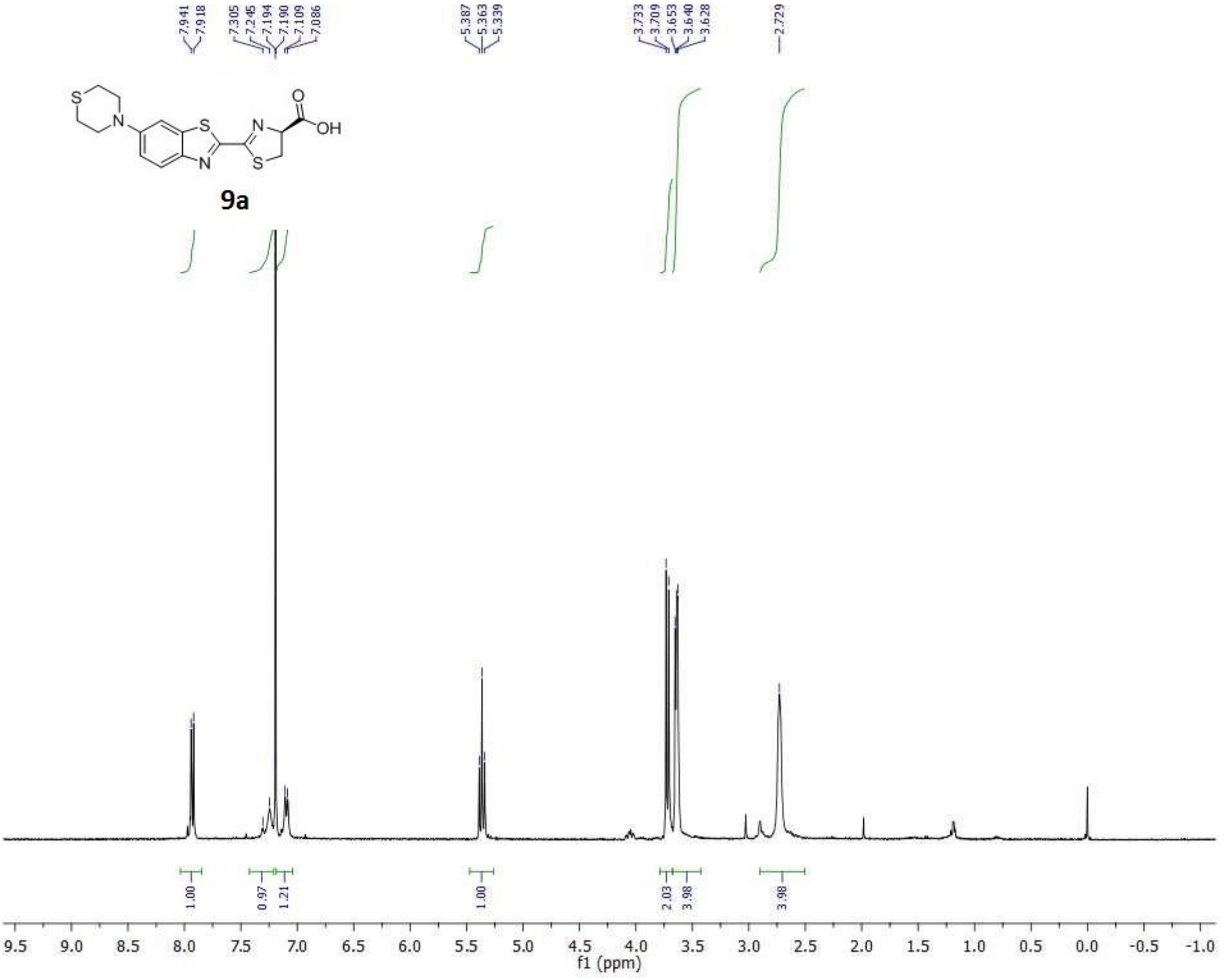
166.58
157.06
150.65
146.88
138.09
124.62
117.12
105.79
78.04
77.40
77.08
76.76
66.65
49.12
35.05
O
N
S
N
O
OH
N
S
8a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.029
8.006
7.237
7.231
7.225
7.218
7.202
7.196
3.757
3.750
3.744
3.738
3.731
2.779
2.772
2.766
2.760
2.753
S
N
S
CN
N
9
1.00
2.14
4.18
4.48
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


S
N
S
CN
N

9

138.22
125.58
118.75
113.53
105.35
51.69
26.27
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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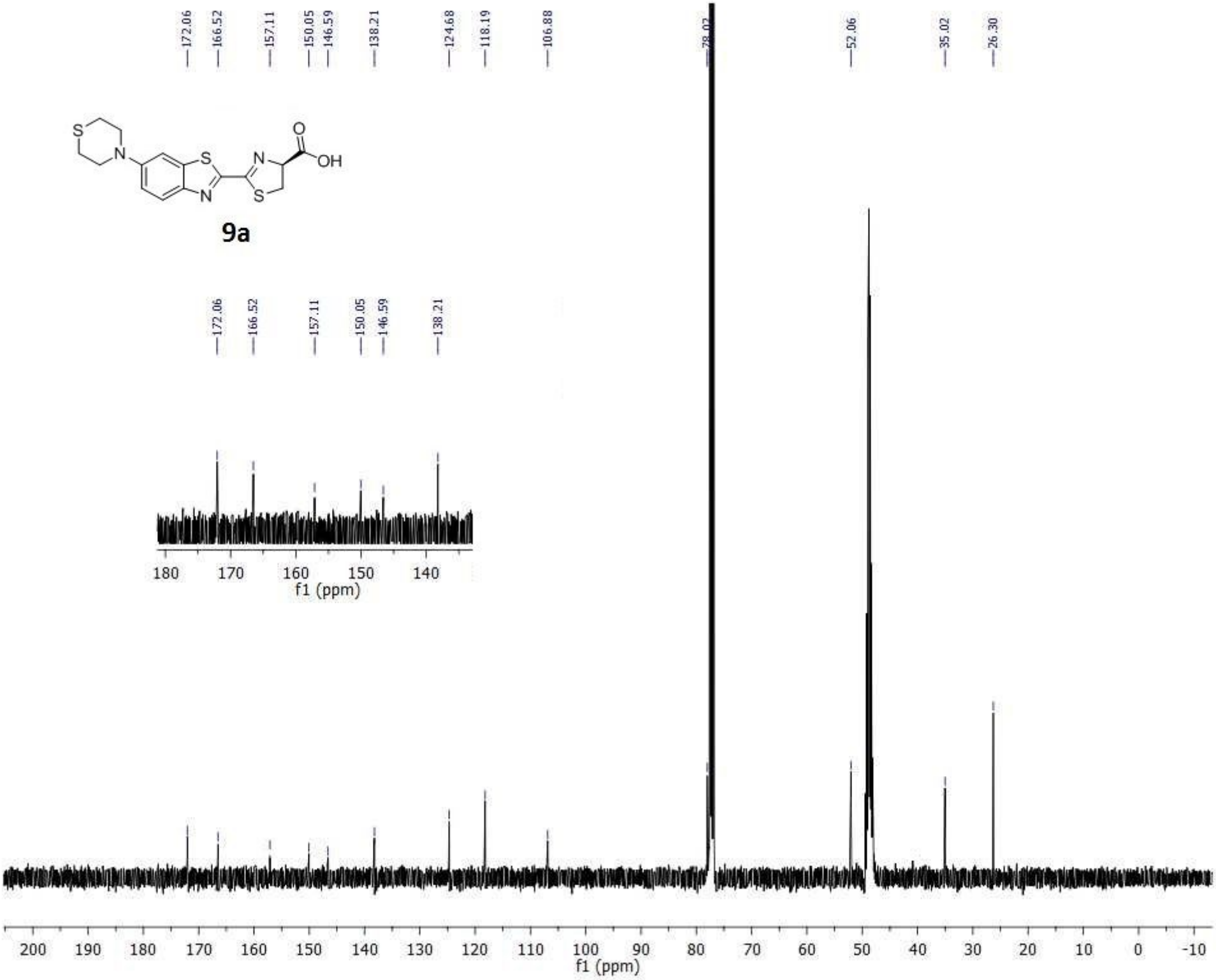
7.918
7.305
7.245
7.194
7.190
7.109
7.086
5.387
5.363
5.339
3.733
3.709
3.653
3.640
3.628
2.729
S
N
S
N
S
O
OH
9a
1.00
0.97
1.21
1.00
2.03
3.98
3.98
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)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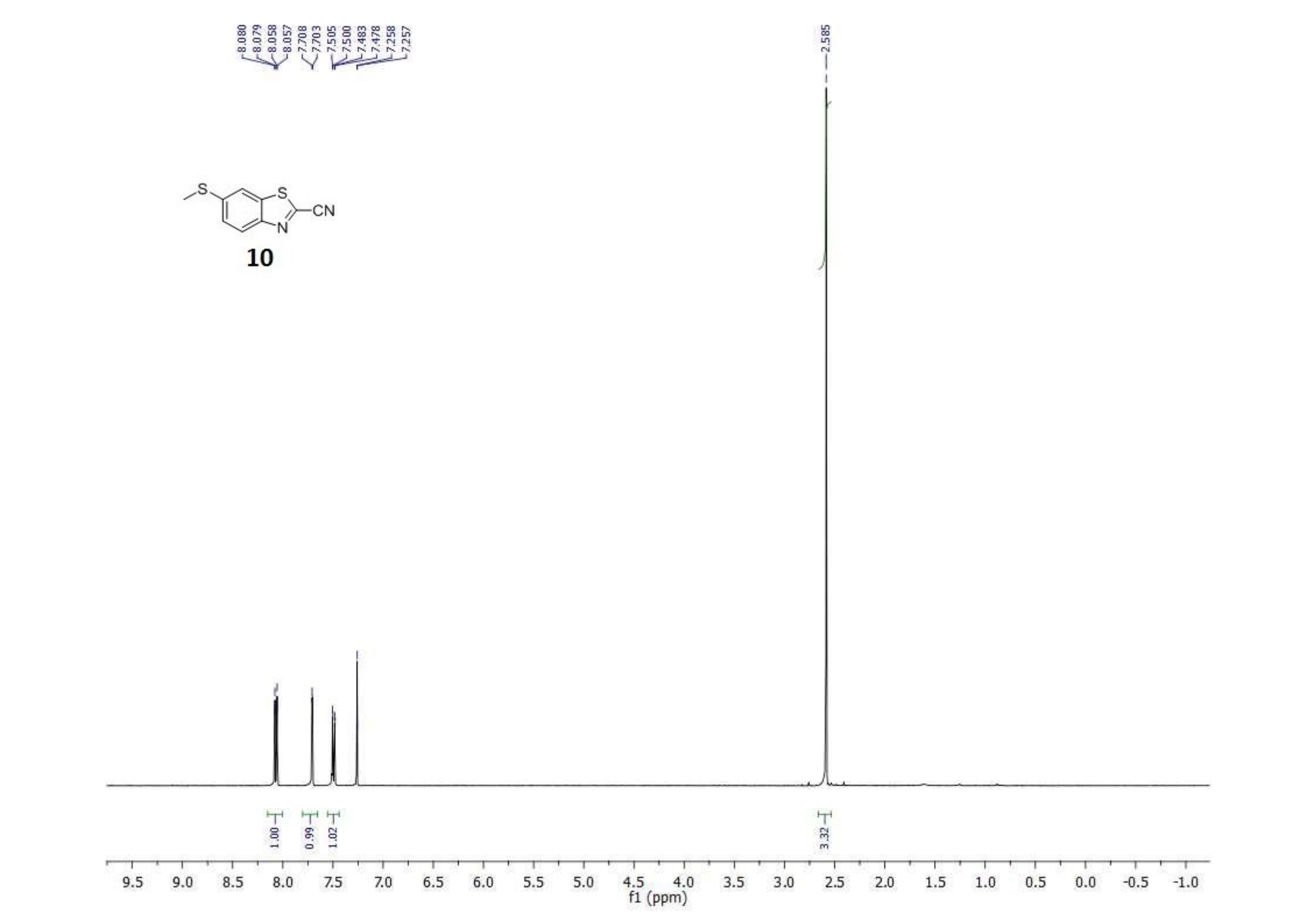
166.52
157.11
150.05
146.59
138.21
124.68
118.19
106.88
78.02
52.06
35.02
26.30
S
N
S
N
S
O
OH
9a
172.06
166.52
157.11
150.05
146.59
138.21
180
170
160
150
140
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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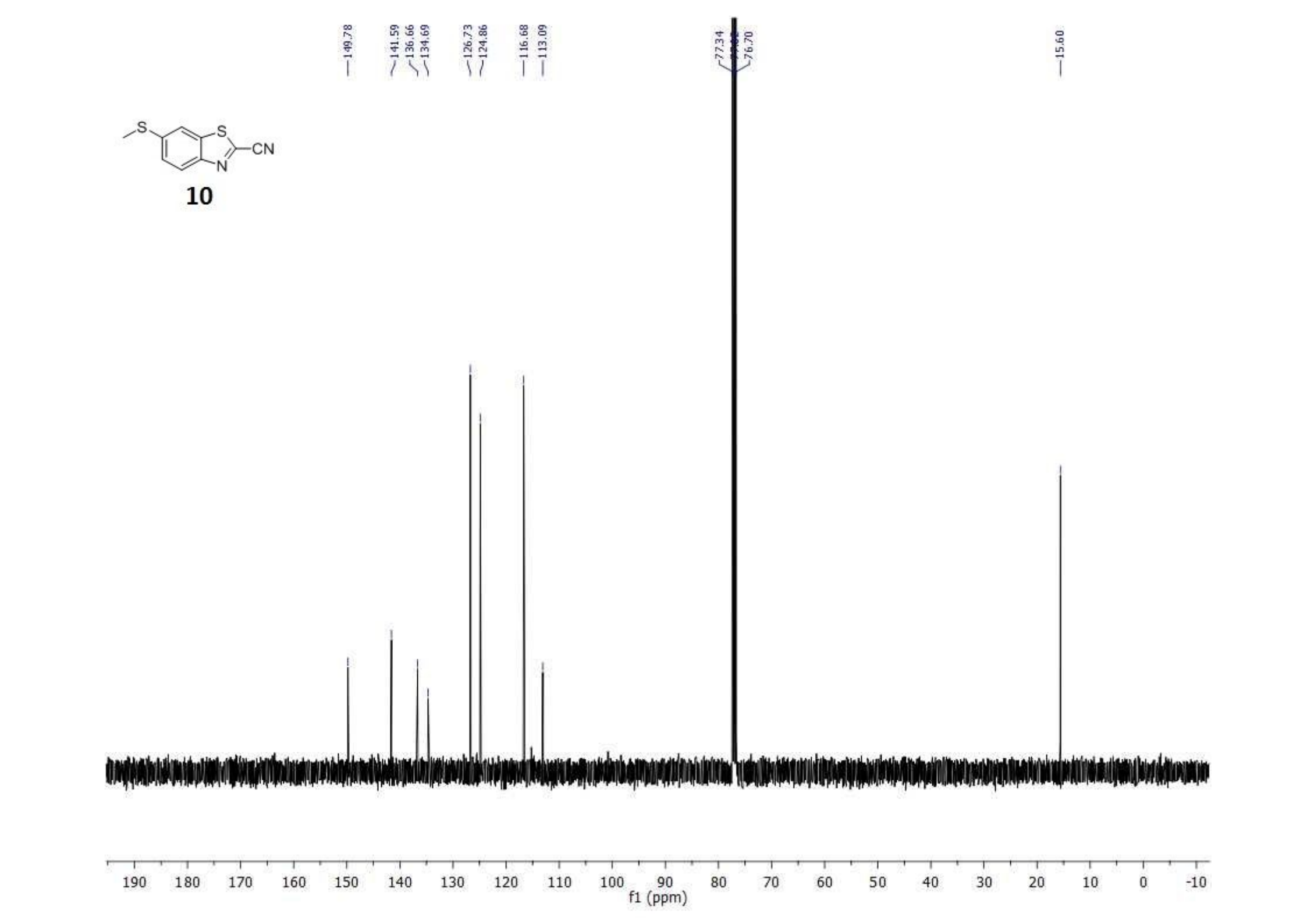
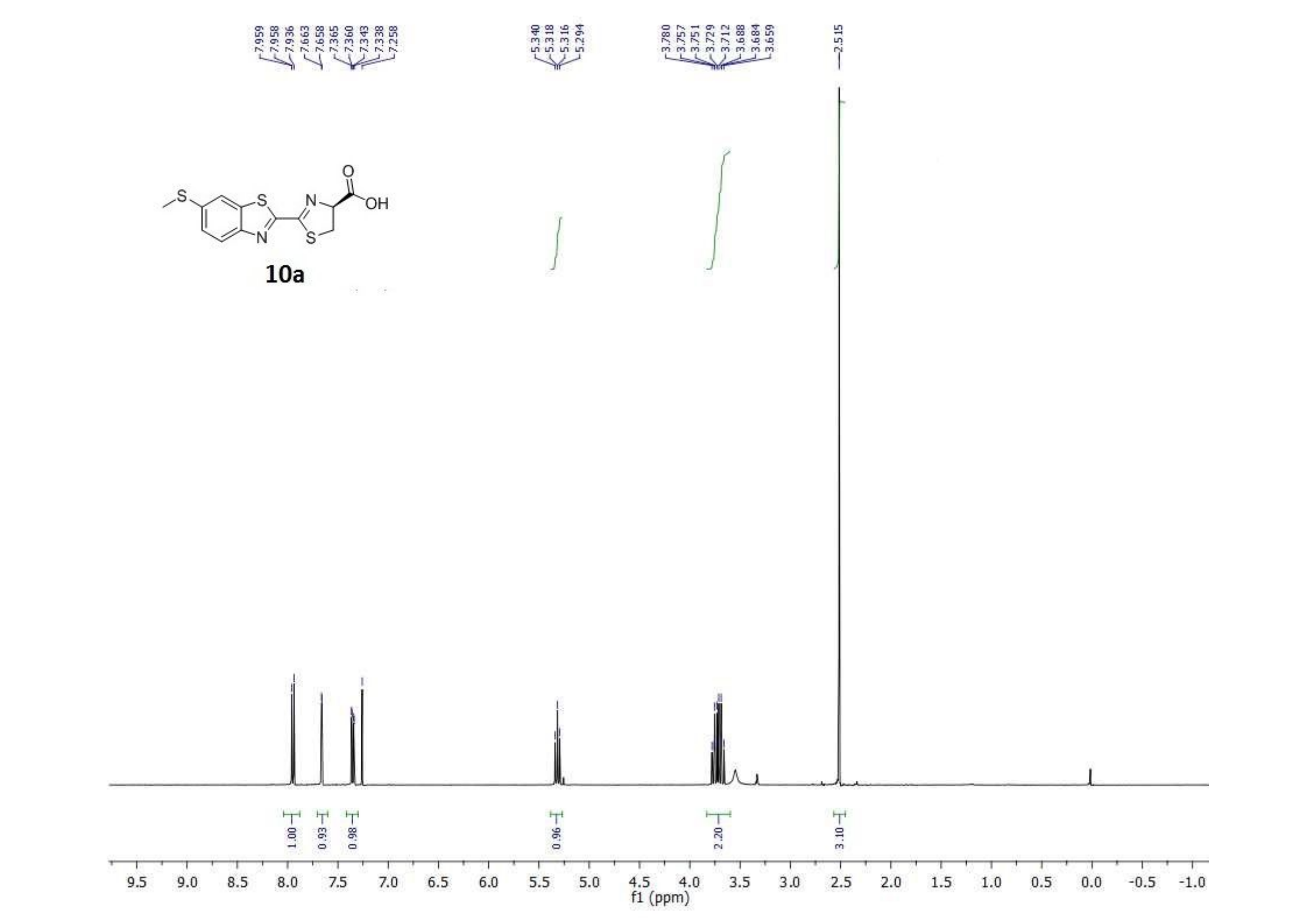
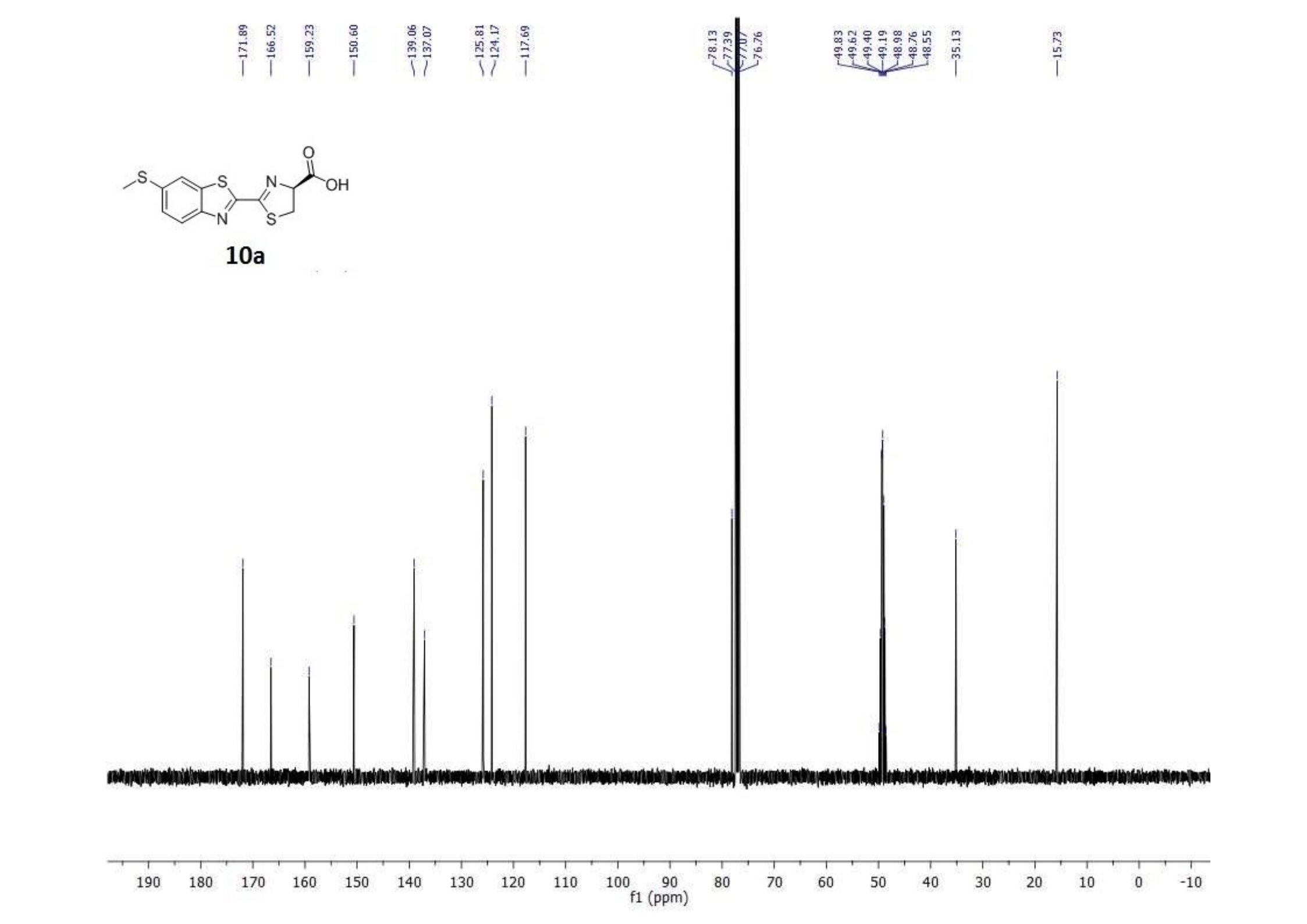
8.079
8.058
8.057
7.708
7.703
7.505
7.500
7.483
7.478
7.258
7.257
2.585
S
S
CN
N
10
1.00
0.99
1.02
3.32
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


149.78
141.59
136.66
134.69
126.73
124.86
116.68
113.09
77.34
76.70
15.60
S
S
CN
N
10
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.959
7.958
7.936
7.663
7.658
7.365
7.360
7.343
7.338
7.258
5.340
5.318
5.316
5.294
3.780
3.757
3.751
3.729
3.712
3.688
3.684
3.659
2.515
S
S
N
O
OH
N
S
10a
1.00
0.93
0.98
0.96
2.20
3.10
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)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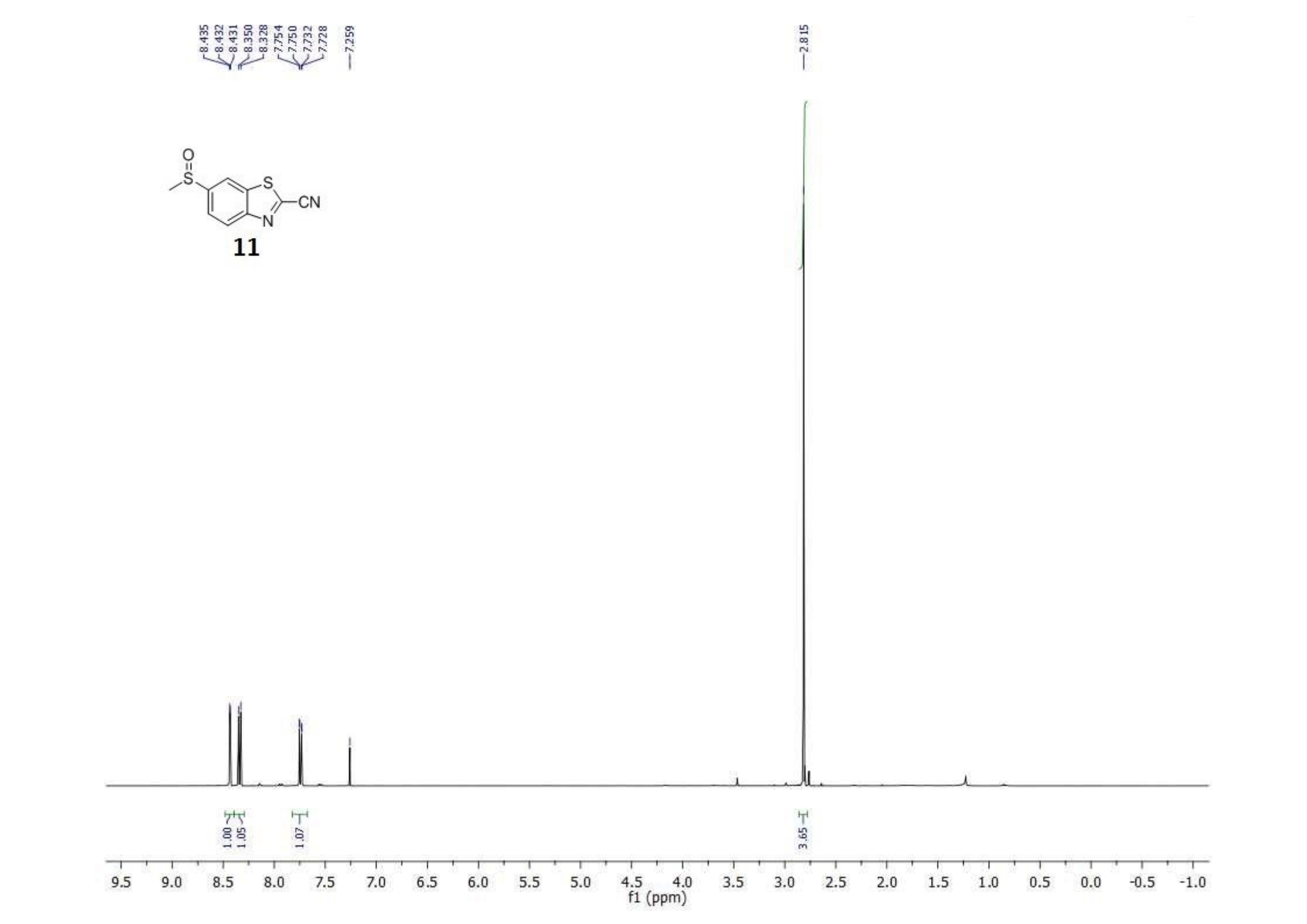
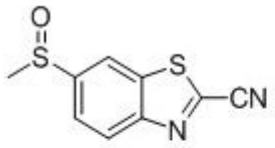
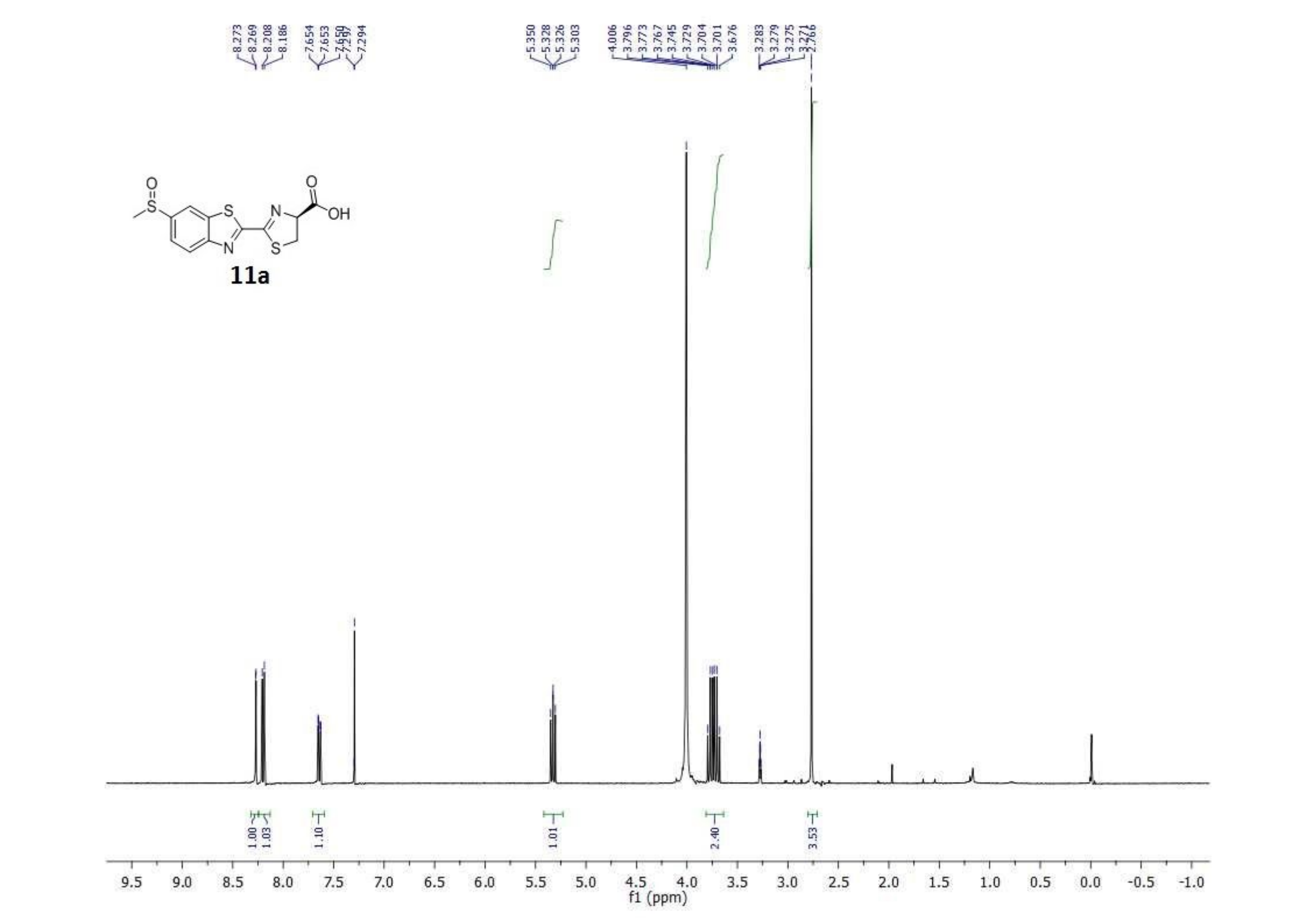
150.60
139.06
137.07
125.81
124.17
117.69
78.13
77.39
77.07
76.76
49.83
49.62
49.40
49.19
48.98
48.76
48.55
35.13
15.73
S
S
N
O
OH
N
S
10a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

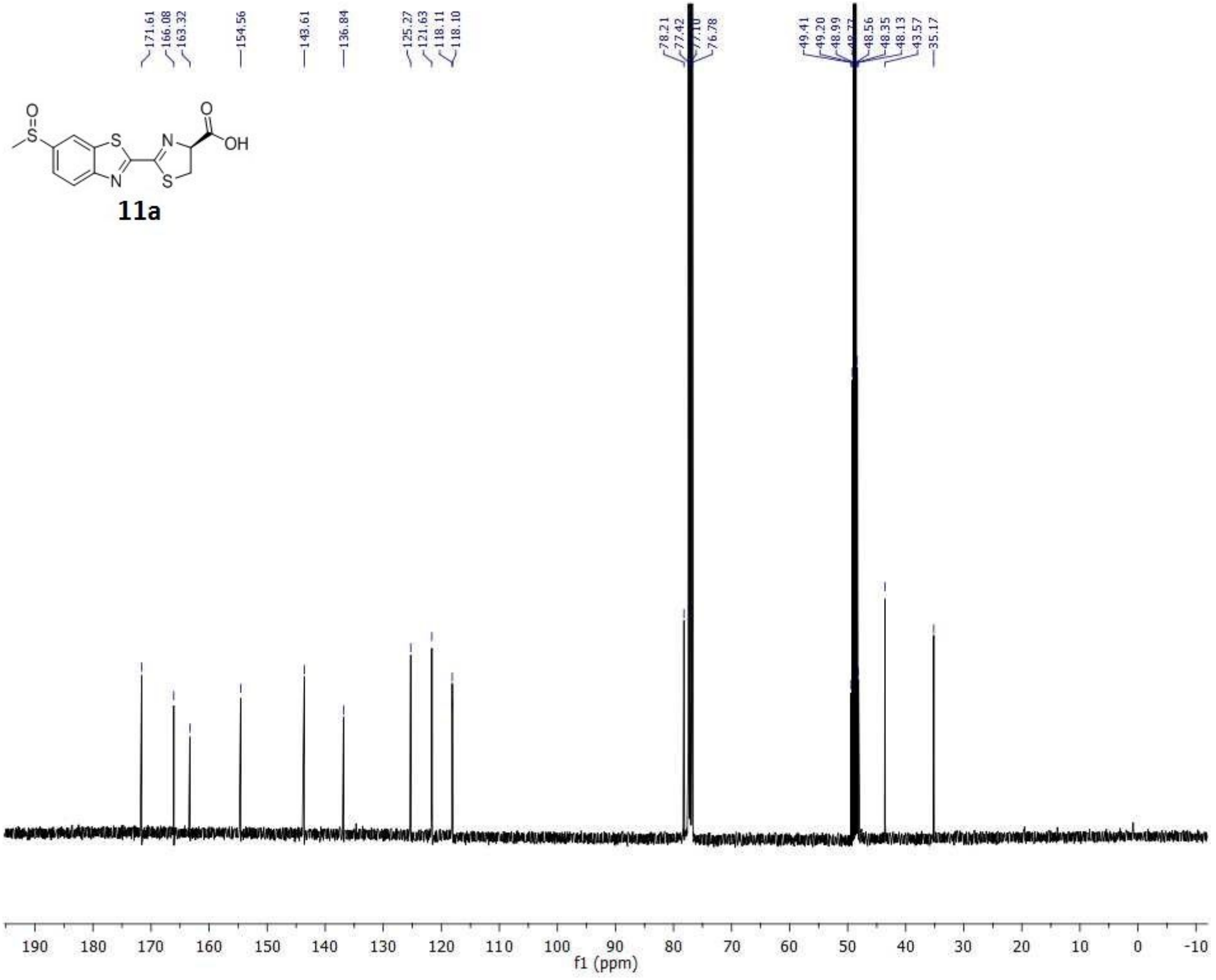

8.435
8.432
8.431
8.350
8.328
7.754
7.750
7.732
7.728
7.259
2.815
O
S
S
CN
N
11
1.00
1.05
1.07
3.65
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

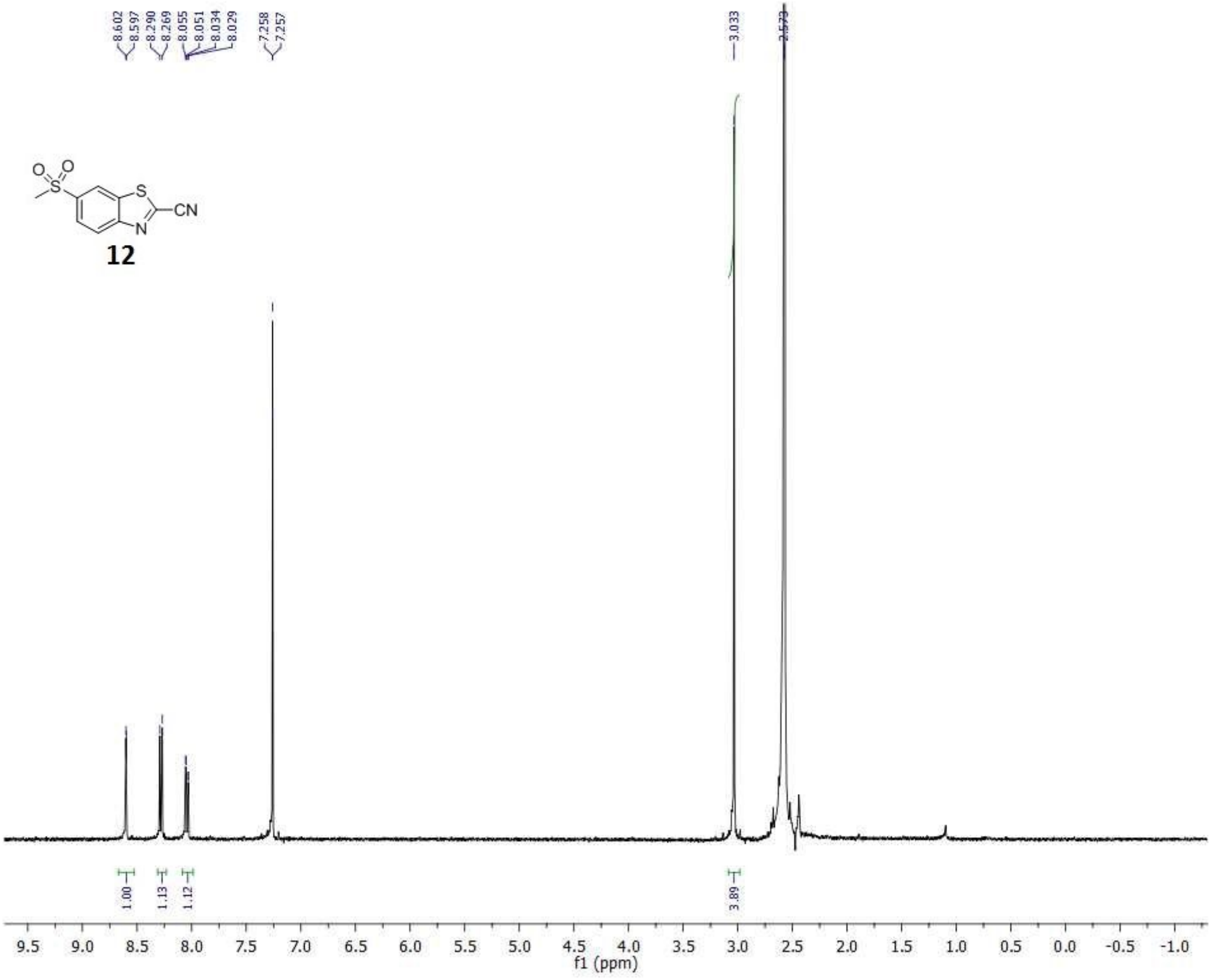

O
S
S
CN
N

11

153.57
146.98
138.83
136.33
126.09
122.74
117.88
112.48
77.37
77.05
76.74
44.19
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.273
8.269
8.208
8.186
7.654
7.653
7.650
7.297
7.294
5.350
5.328
5.326
5.303
4.006
3.796
3.773
3.767
3.745
3.729
3.704
3.701
3.676
3.283
3.279
3.275
3.271
2.766
O
S
O
S
N
OH
N
S
11a
1.00
1.03
1.10
1.01
2.40
3.53
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


171.61
166.08
163.32
154.56
143.61
136.84
125.27
121.63
118.11
118.10
78.21
77.42
76.78
49.41
49.20
48.99
48.56
48.35
48.13
43.57
35.17
O
S
S
N
N
S
O
OH
11a
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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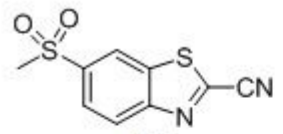
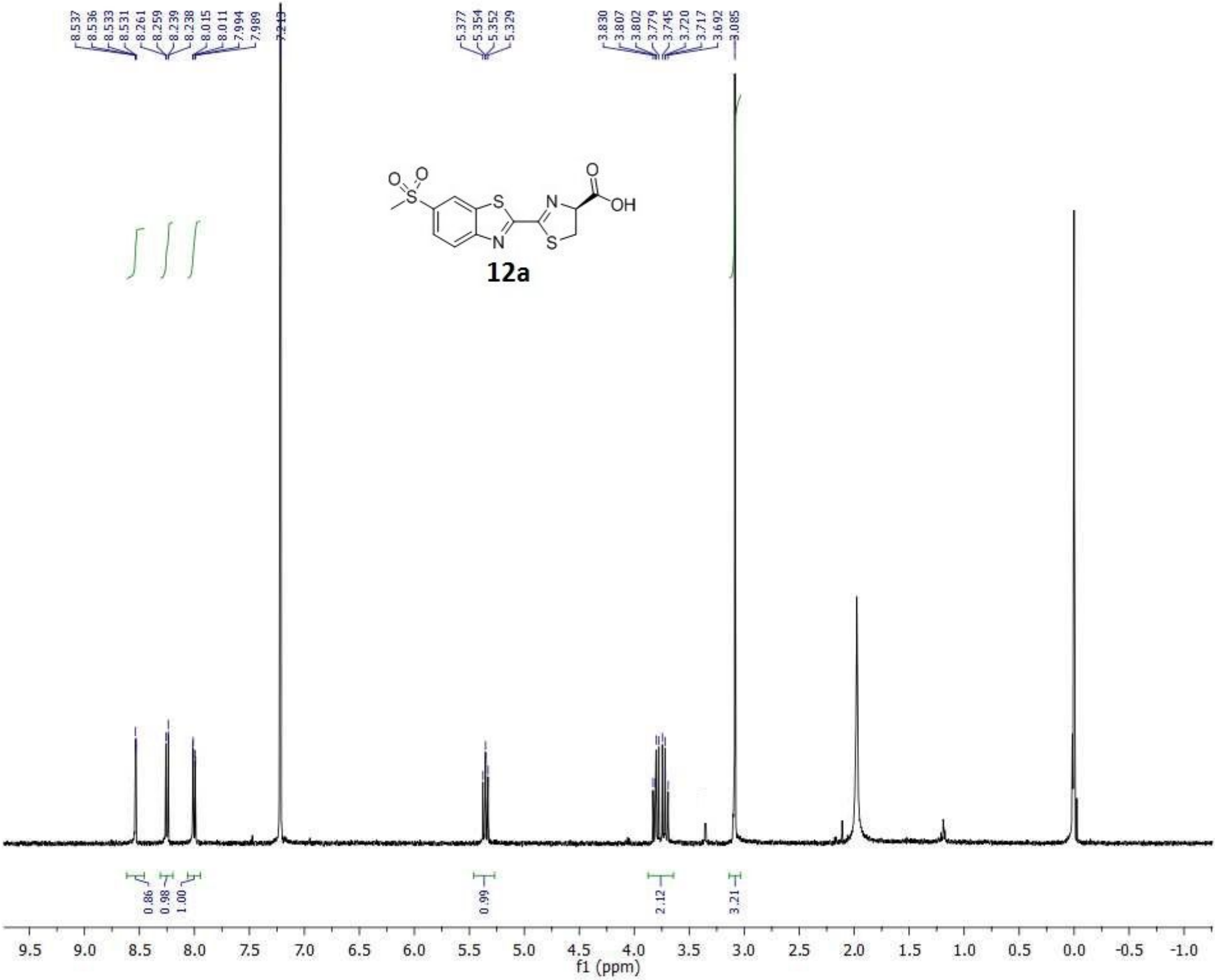
8.290
8.269
8.055
8.051
8.034
8.029
7.258
7.257
3.033
2.573
O
O
S
S
CN
N
12
1.00
1.13
1.12
3.89
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


O
O
S
S
CN
N

12

154.64
141.02
140.32
135.64
126.23
126.19
122.86
112.17
77.59
77.37
76.95
44.53
40.58
40.37
40.16
39.95
39.74
39.54
39.32
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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8.259
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8.238
8.015
8.011
7.994
7.989
7.213
5.377
5.354
5.352
5.329
3.830
3.807
3.802
3.779
3.745
3.720
3.717
3.692
3.085
O
O
S
S
N
N
S
O
OH
12a
0.86
0.98
1.00
0.99
2.12
3.21
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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2.5
2.0
1.5
1.0
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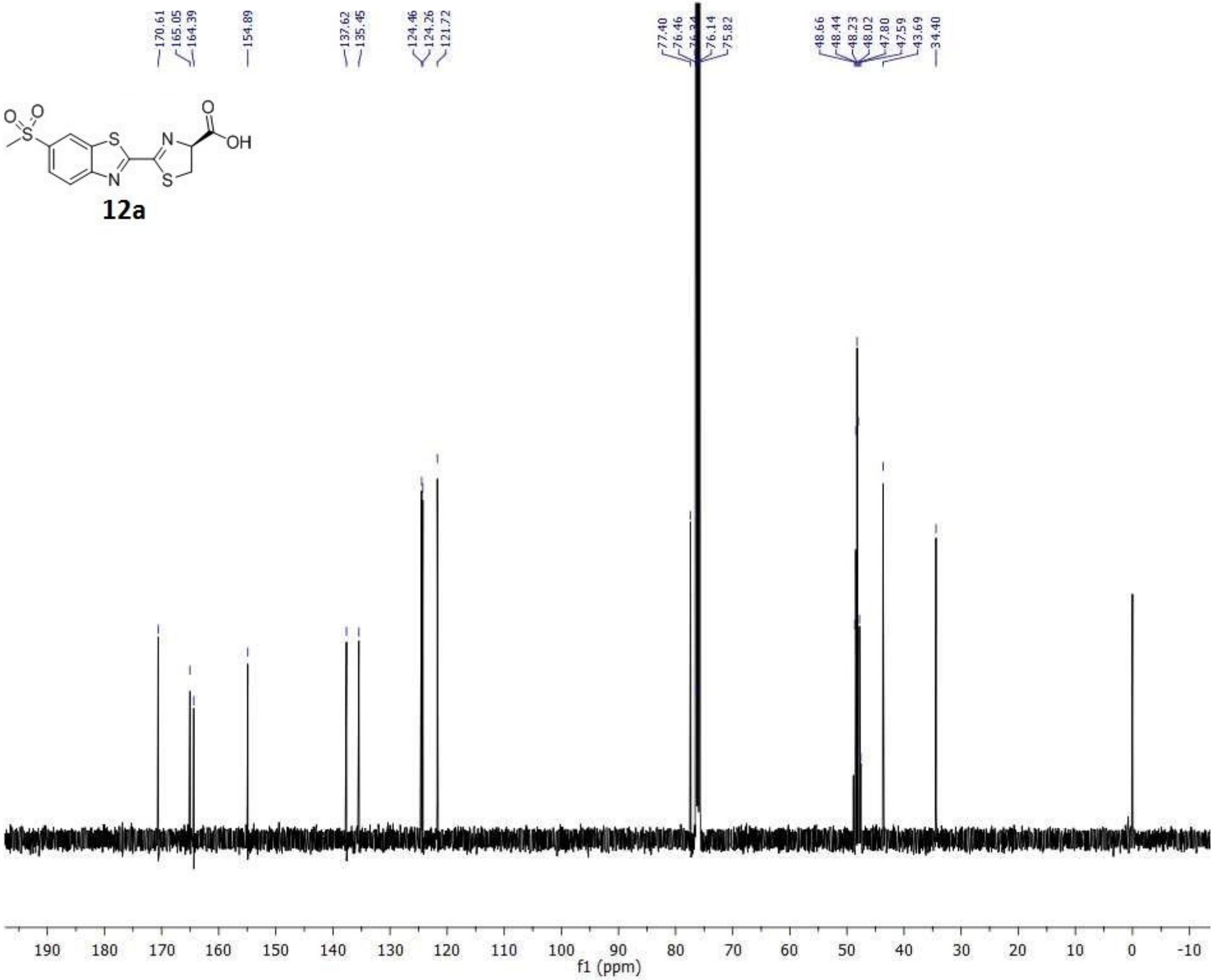
0.0
-0.5
-1.0
f1 (ppm)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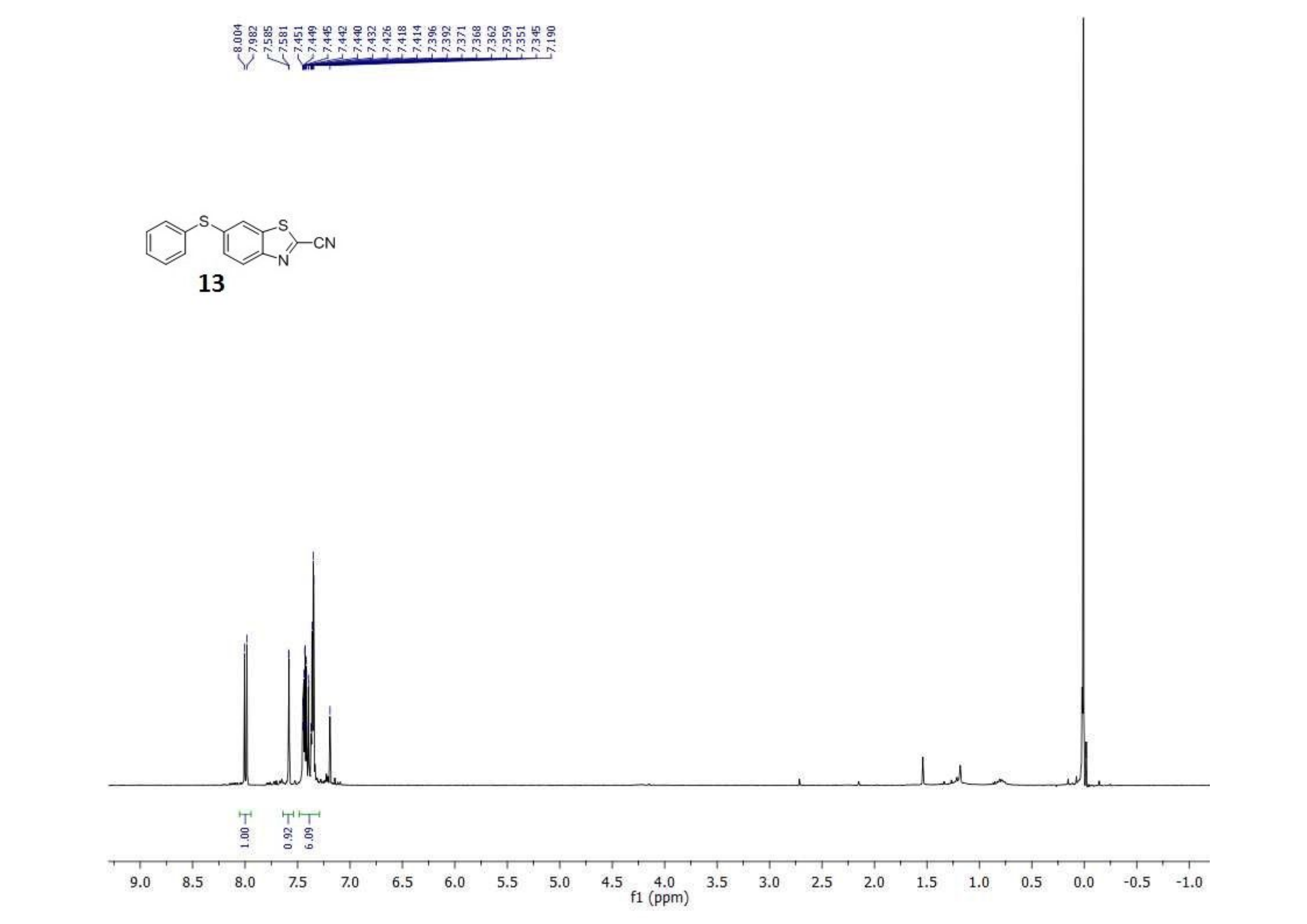
165.05
164.39
154.89
137.62
135.45
124.46
124.26
121.72
77.40
76.46
76.14
75.82
48.66
48.44
48.23
48.02
47.80
47.59
43.69
34.40
O
O
S
S
N
N
O
OH
12a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.982
7.585
7.581
7.451
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7.442
7.440
7.432
7.426
7.418
7.414
7.396
7.392
7.371
7.368
7.362
7.359
7.351
7.345
7.190
S
S
CN
N
13
1.00
0.92
6.09
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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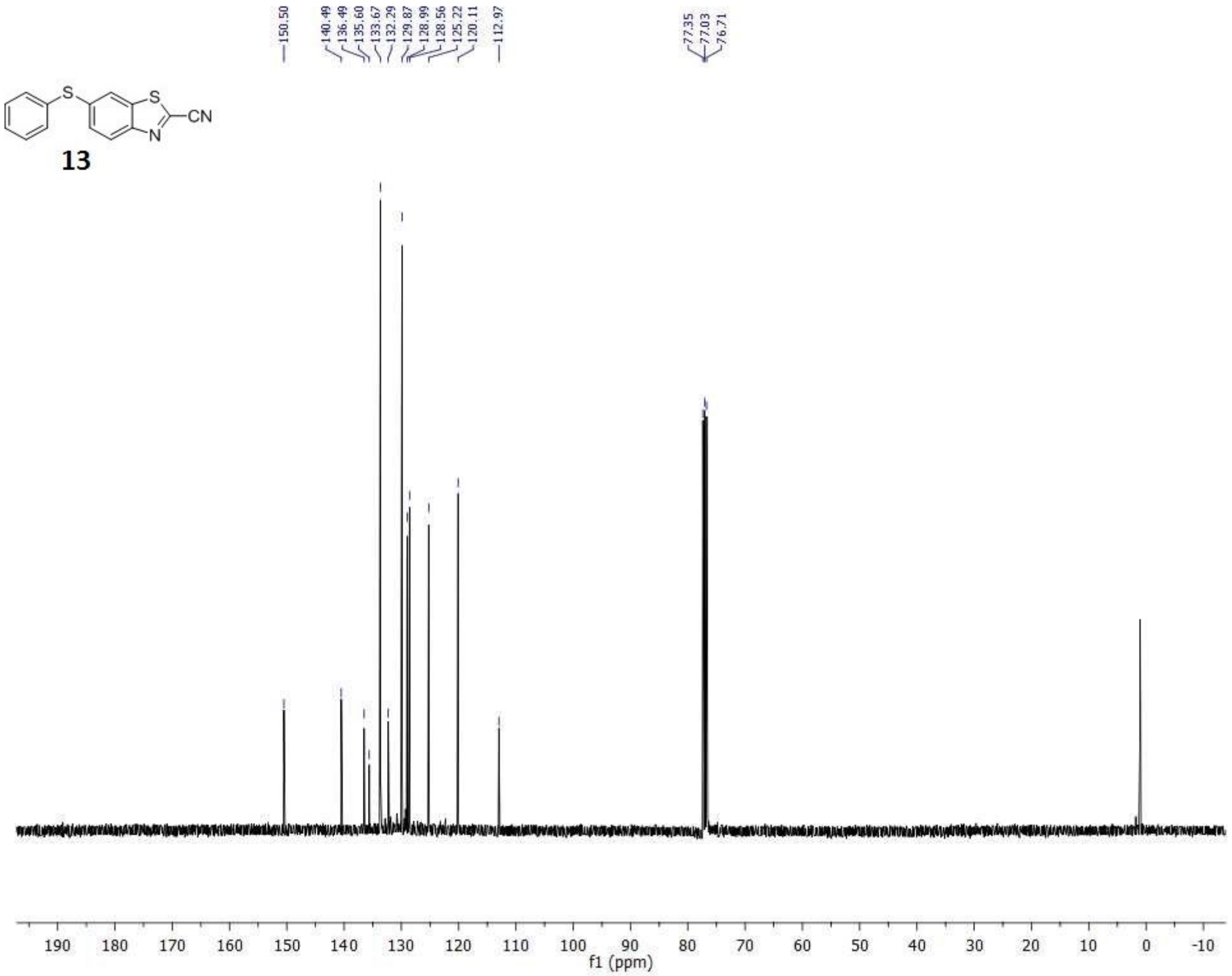
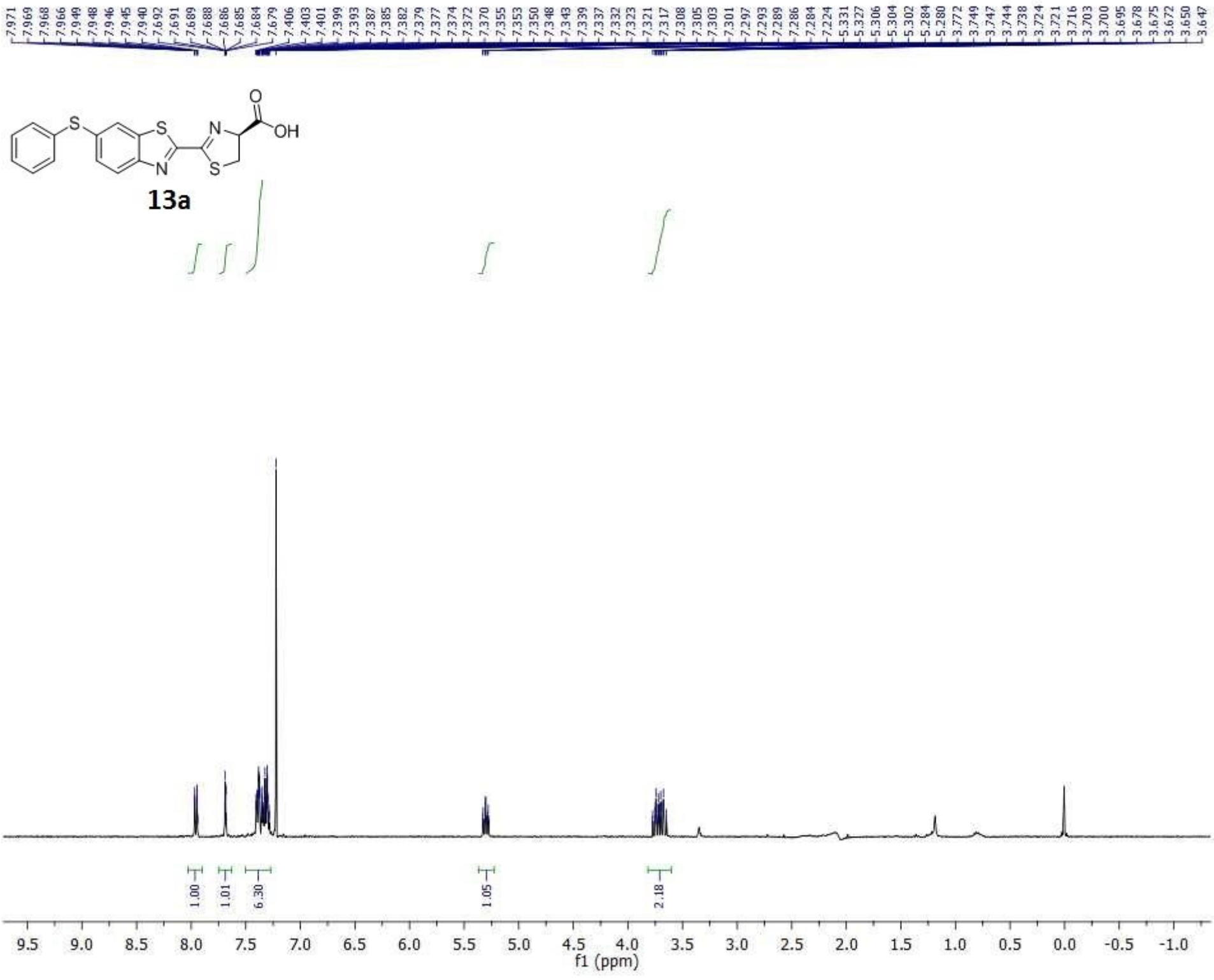
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


150.50
140.49
136.49
135.60
133.67
132.29
129.87
128.99
128.56
125.22
120.11
112.97
77.35
77.03
76.71
S
S
CN
N
13
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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7.969
7.968
7.966
7.949
7.948
7.946
7.945
7.940
7.692
7.691
7.689
7.688
7.686
7.685
7.684
7.679
7.406
7.403
7.401
7.399
7.393
7.387
7.385
7.382
7.379
7.377
7.374
7.372
7.370
7.355
7.353
7.350
7.348
7.343
7.339
7.337
7.332
7.323
7.321
7.317
7.308
7.305
7.303
7.301
7.297
7.293
7.289
7.286
7.284
7.224
5.331
5.327
5.306
5.304
5.302
5.284
5.280
3.772
3.749
3.747
3.744
3.738
3.724
3.721
3.716
3.703
3.700
3.695
3.678
3.675
3.672
3.650
3.647
O
OH
N
S
S
N
S
13a
1.00
1.01
6.30
1.05
2.18
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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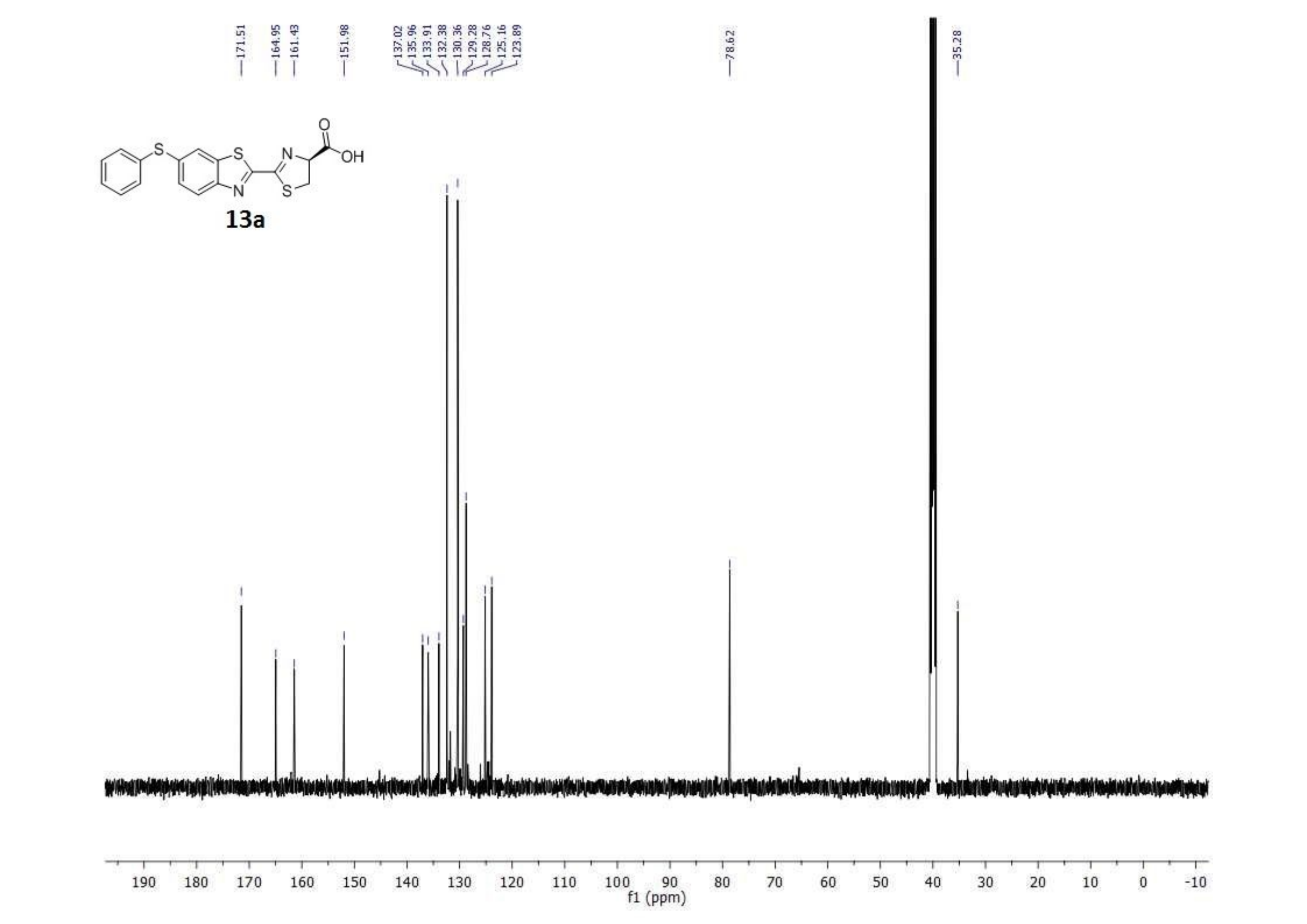
0.0
-0.5
-1.0
f1 (ppm)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161.43
151.98
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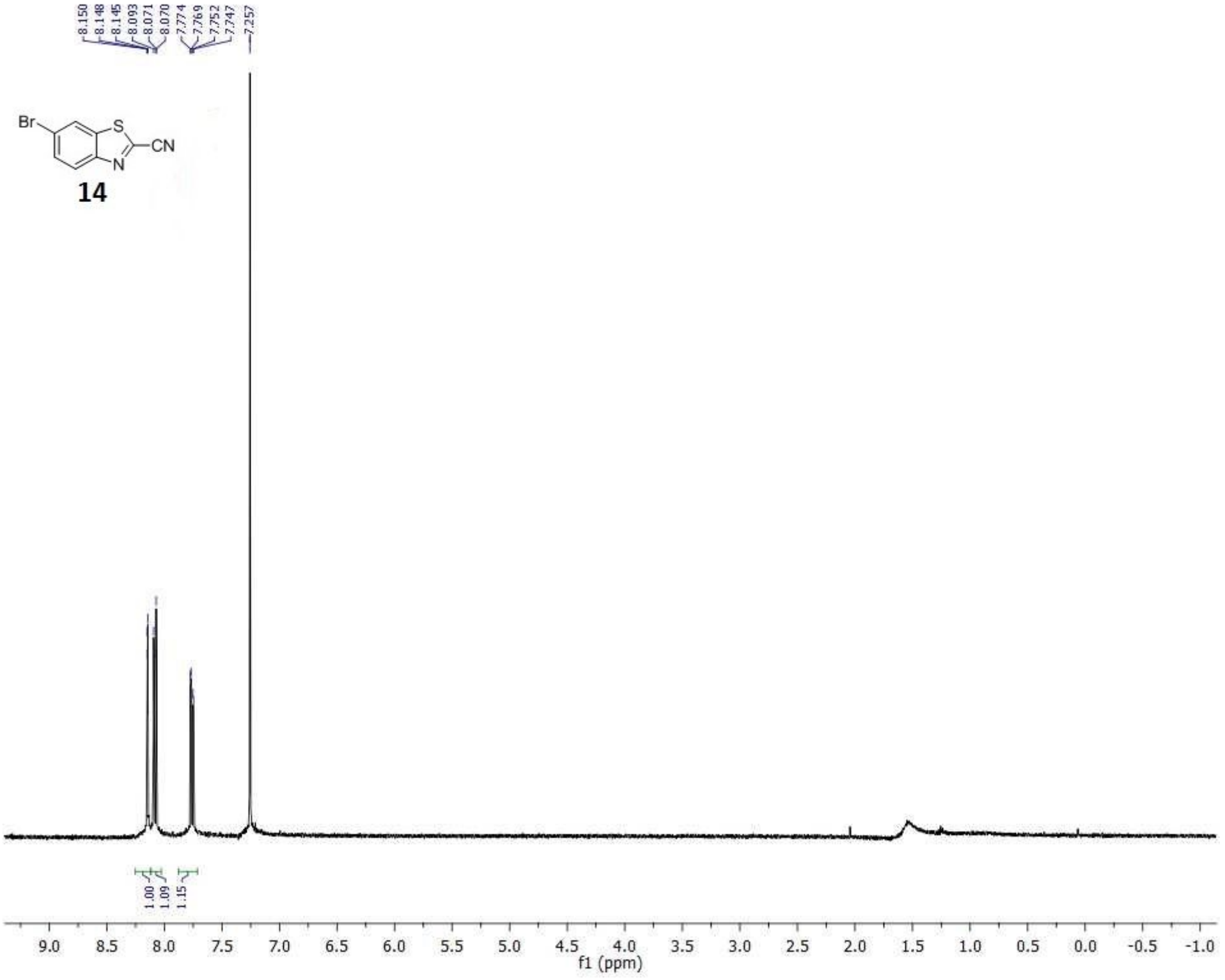
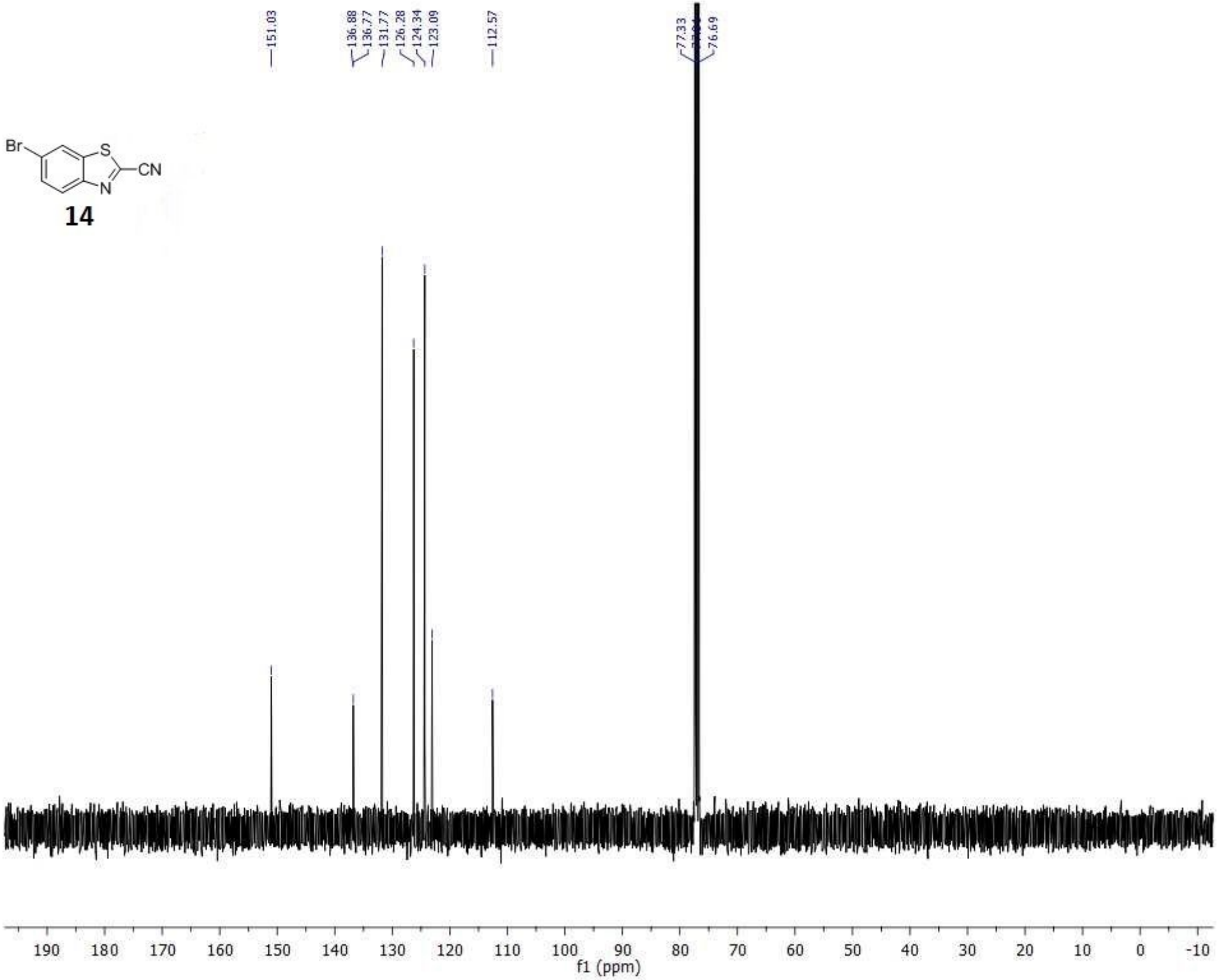
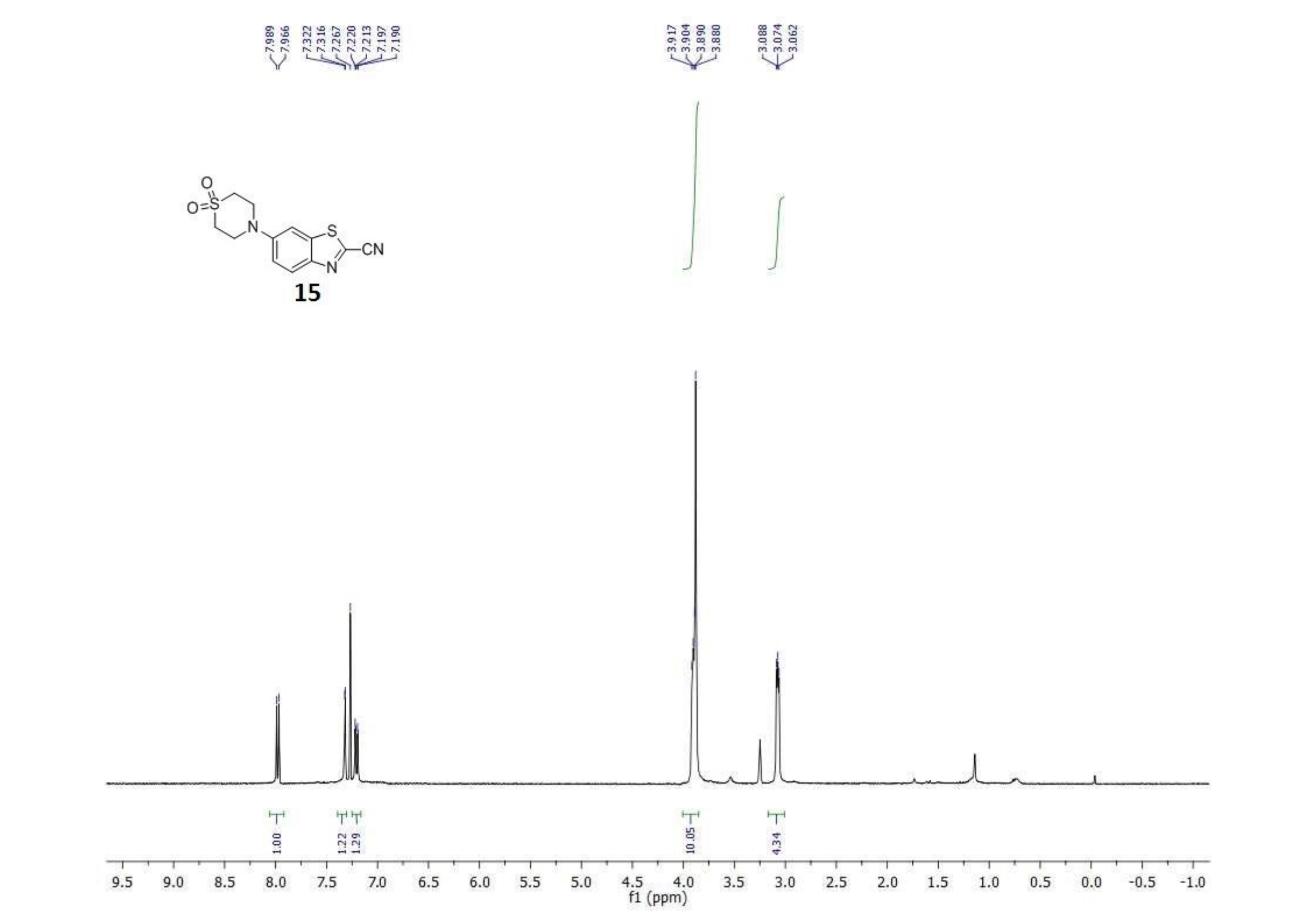
135.96
133.91
132.38
130.36
129.28
128.76
125.16
123.89
78.62
35.28
S
S
N
O
OH
N
S
13a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.150
8.148
8.145
8.093
8.071
8.070
7.774
7.769
7.752
7.747
7.257
Br
S
CN
N
14
1.00
1.09
1.15
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


151.03
136.88
136.77
131.77
126.28
124.34
123.09
112.57
77.33
76.69
Br
S
CN
N
14
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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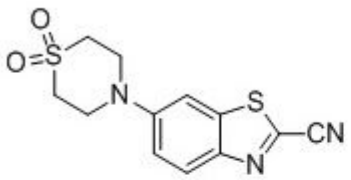
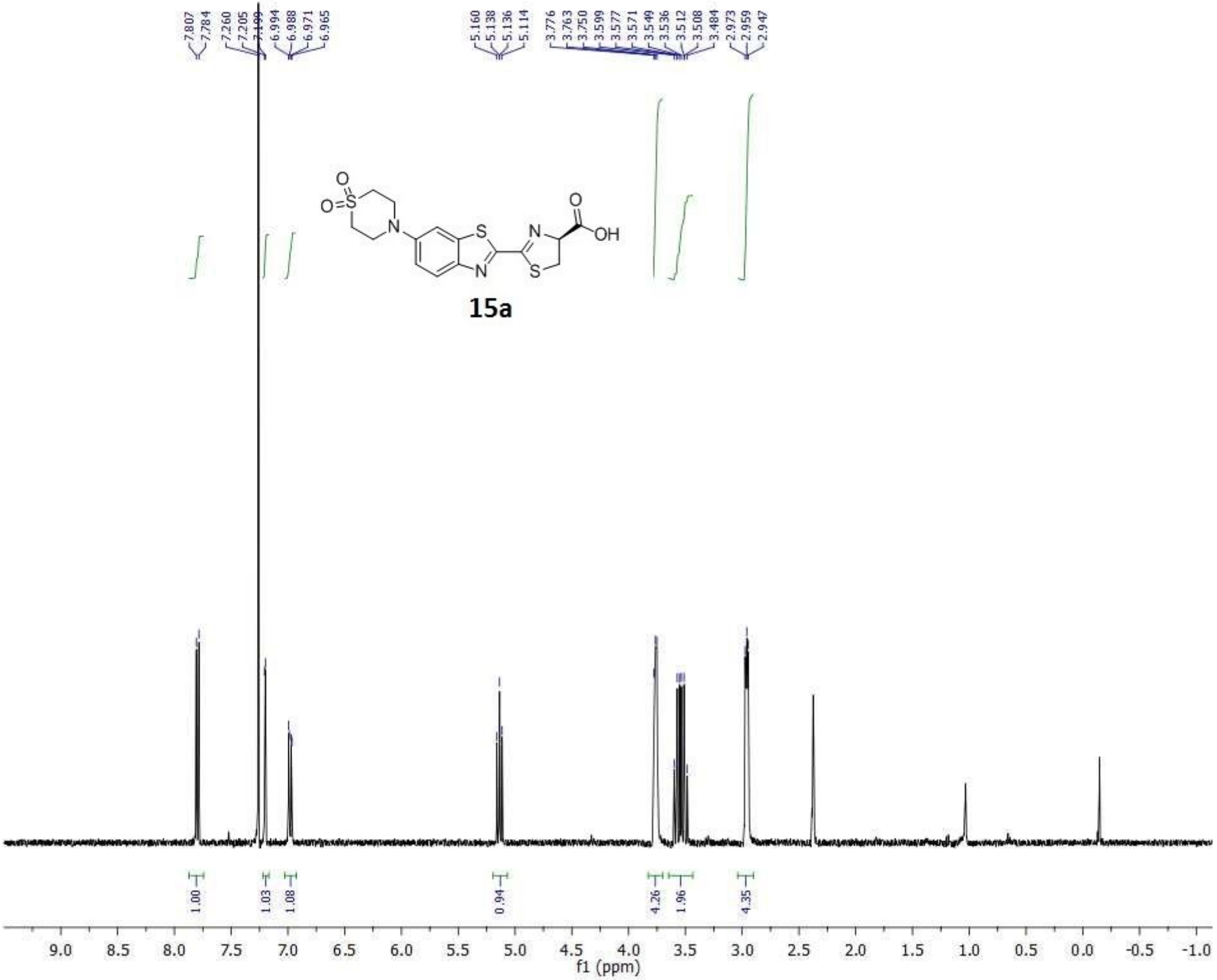
7.267
7.220
7.213
7.197
7.190
3.917
3.904
3.890
3.880
3.088
3.074
3.062
O
O
S
N
S
CN
N
15
1.00
1.22
1.29
10.05
4.34
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


O
O
S
N
S
CN
N

15

148.18
146.14
138.11
133.13
125.94
118.16
113.10
105.86
50.48
47.38
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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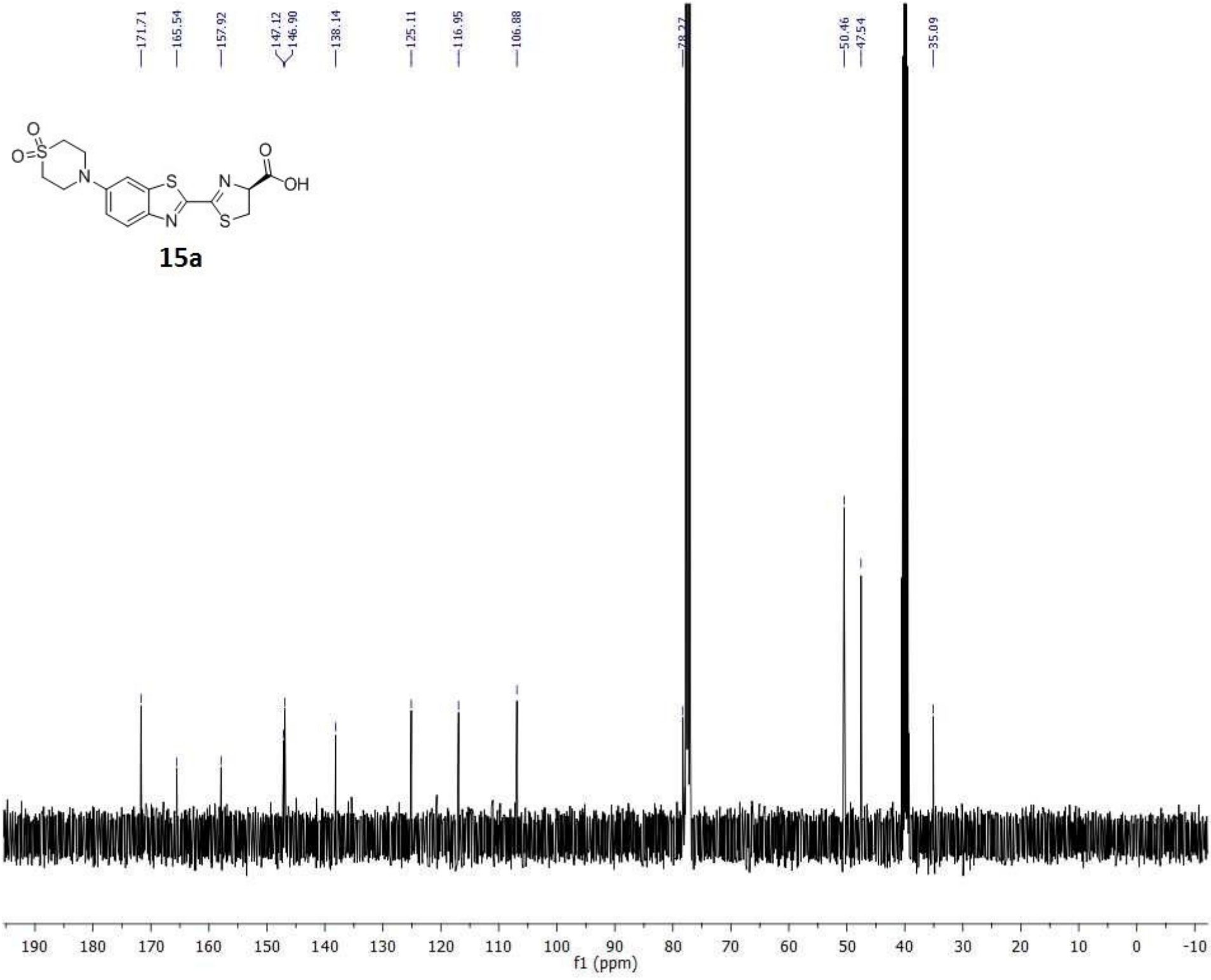
7.260
7.205
7.199
6.994
6.988
6.971
6.965
5.160
5.138
5.136
5.114
3.776
3.763
3.750
3.599
3.577
3.571
3.549
3.536
3.512
3.508
3.484
2.973
2.959
2.947
O
O=S
N
S
N
S
O
OH
1.00
1.03
1.08
0.94
4.26
1.96
4.35
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

15a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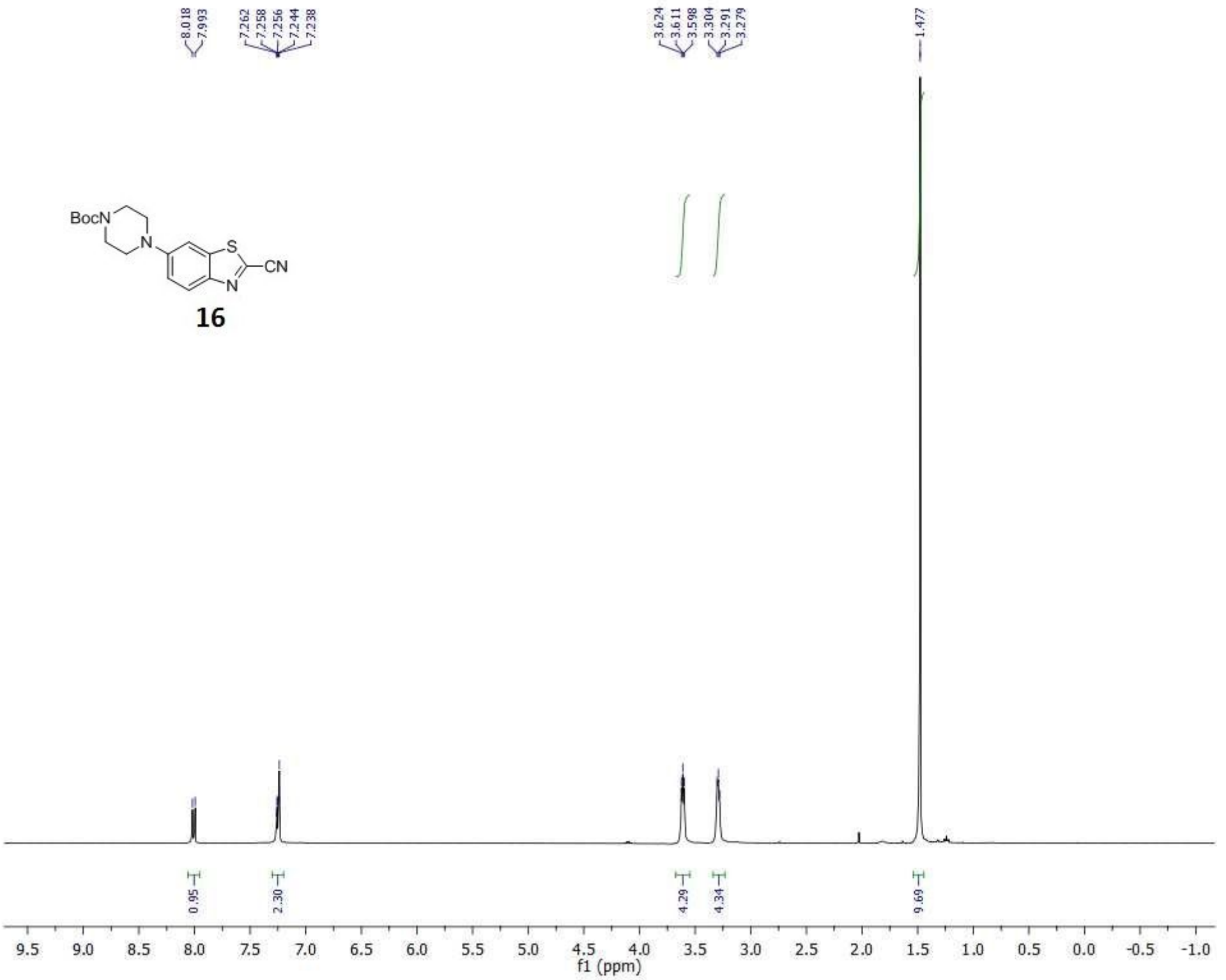
165.54
157.92
147.12
146.90
138.14
125.11
116.95
106.88
78.27
50.46
47.54
35.09
O
O=S
N
S
N
S
O
OH
15a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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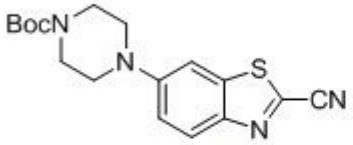
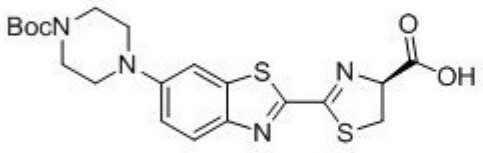
7.262
7.258
7.256
7.244
7.238
3.624
3.611
3.598
3.304
3.291
3.279
1.477
BocN
N
S
CN
N
16
0.95
2.30
4.29
4.34
9.69
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


BocN
N
S
CN
N

16

154.59
151.54
145.86
137.98
132.09
125.35
118.63
113.51
105.08
80.26
77.37
77.06
76.74
48.69
28.39
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


BocN
N
S
N
O
OH
N
S

16a

7.996
7.973
7.278
7.265
7.264
7.258
7.186
7.180
7.163
7.157
5.437
5.413
5.389
3.821
3.798
3.793
3.779
3.770
3.754
3.726
3.626
3.614
3.601
3.274
3.262
1.487
1.00
1.11
1.05
0.95
2.42
4.64
4.53
9.63
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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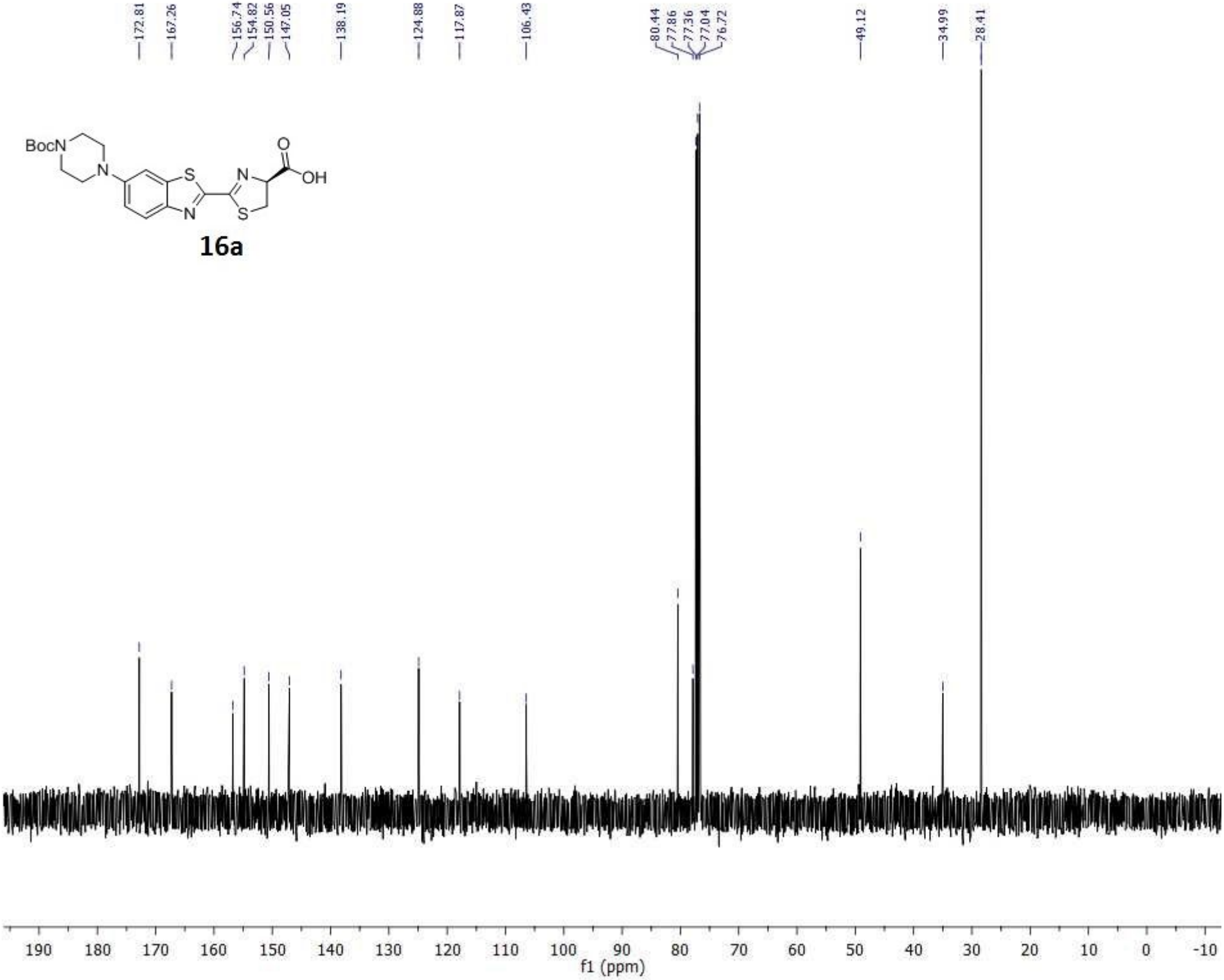
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)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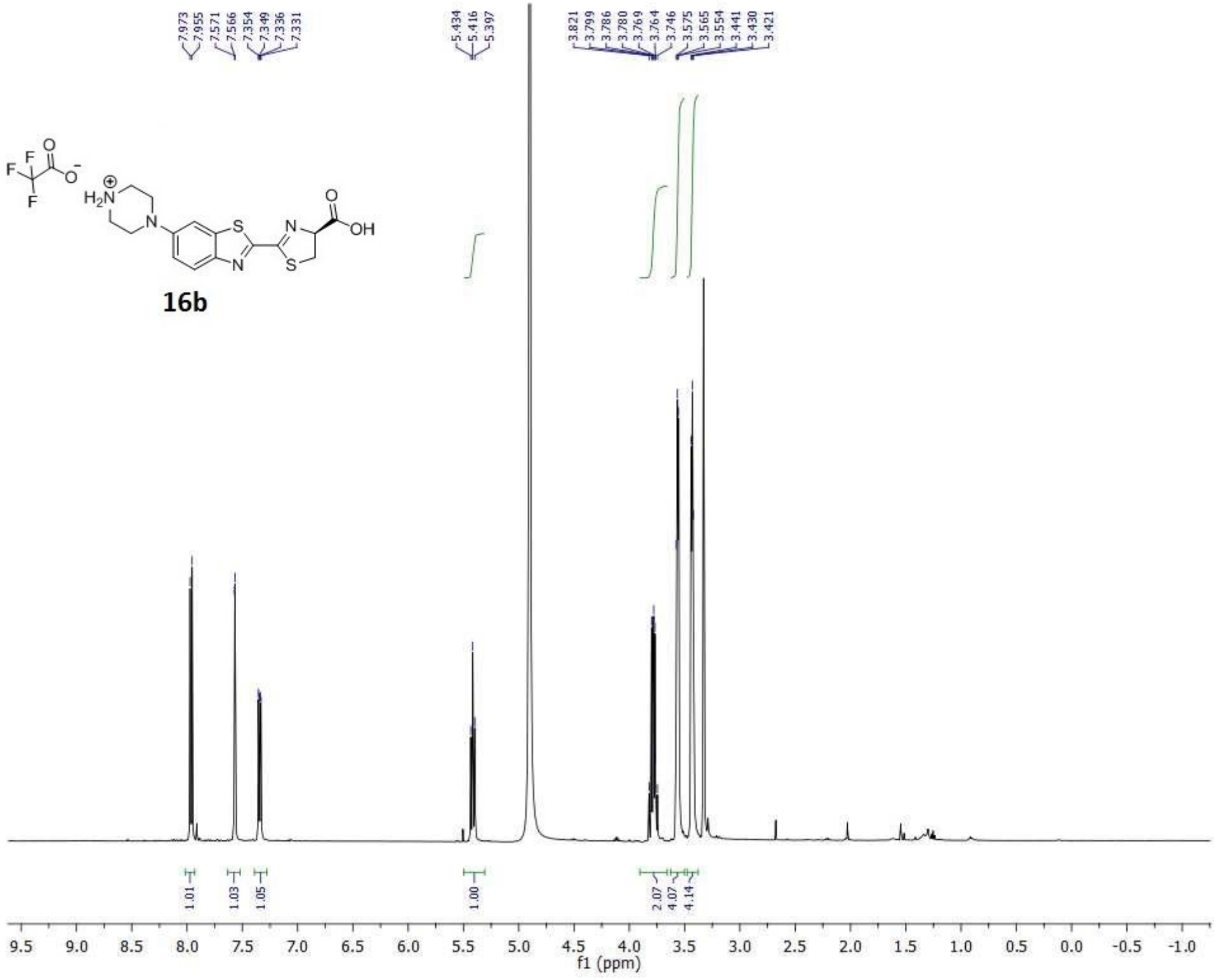
167.26
156.74
154.82
150.56
147.05
138.19
124.88
117.87
106.43
80.44
77.86
77.36
77.04
76.72
49.12
34.99
28.41
BocN
N
S
N
O
OH
N
S
16a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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7.349
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5.416
5.397
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3.799
3.786
3.780
3.769
3.764
3.746
3.575
3.565
3.554
3.441
3.430
3.421
16b
1.01
1.03
1.05
1.00
2.07
4.07
4.14
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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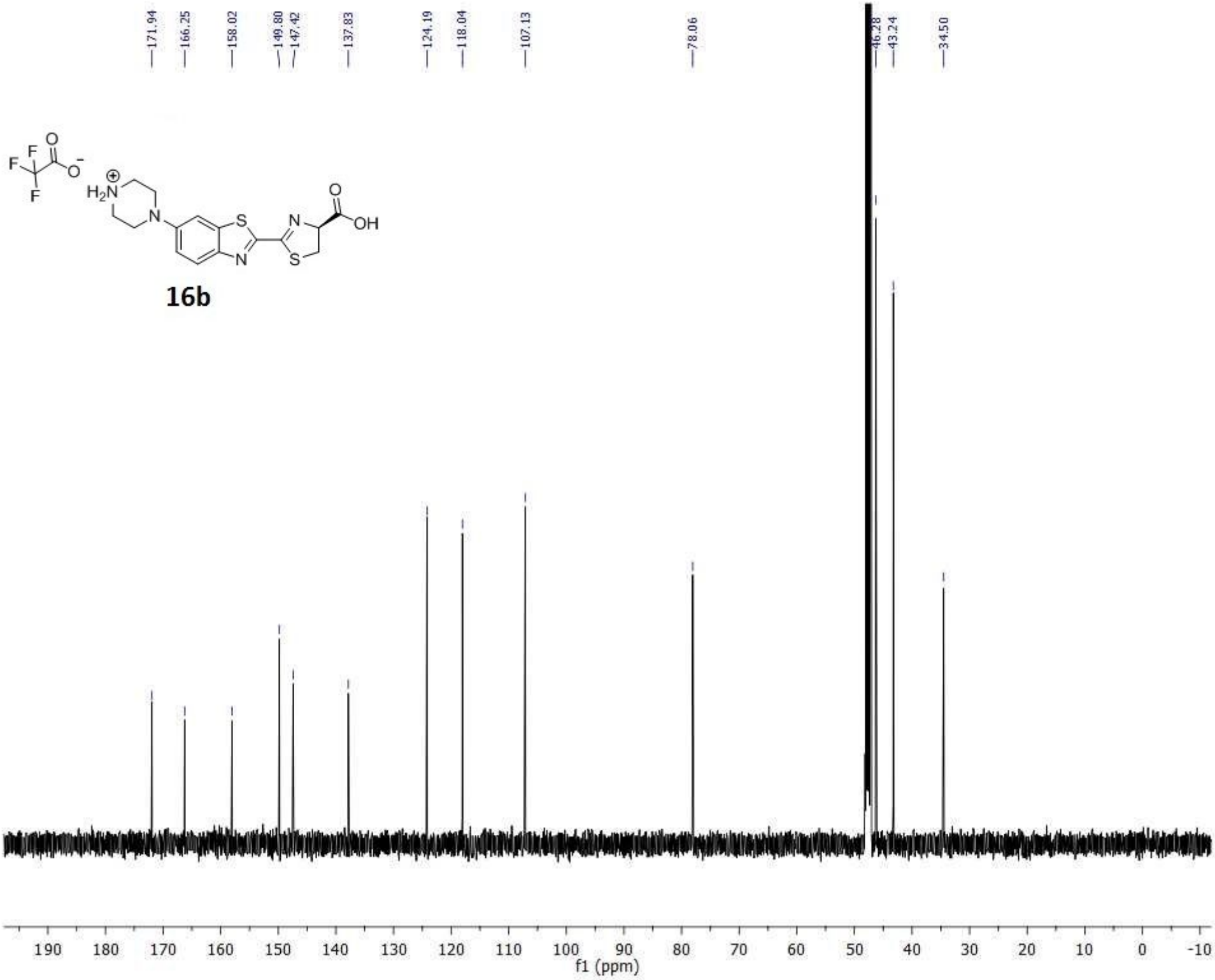
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)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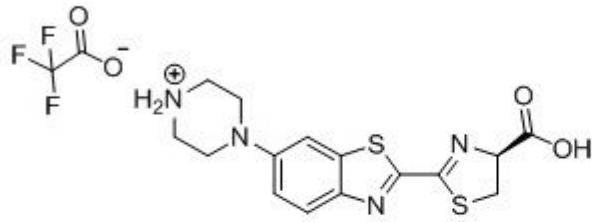
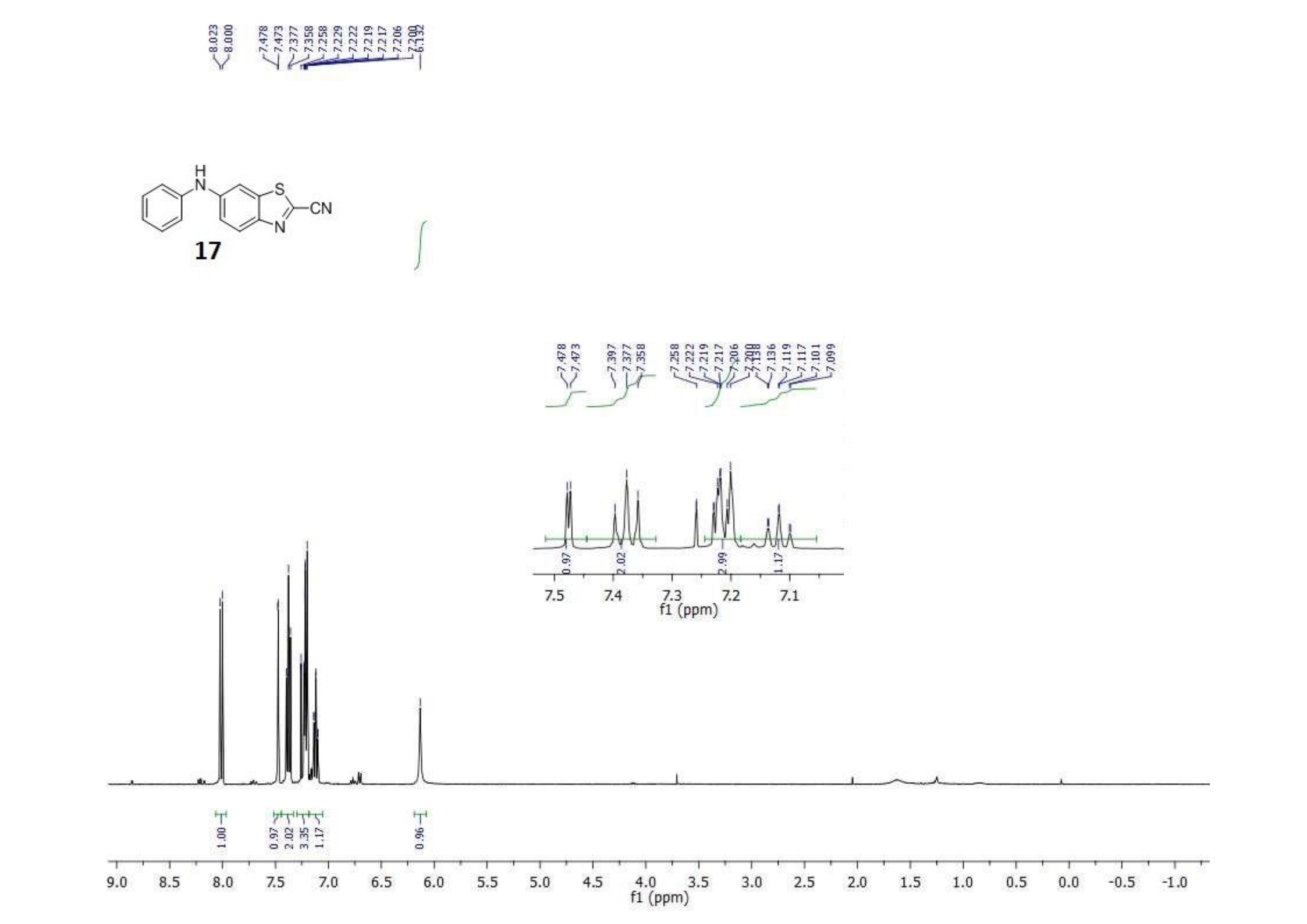
166.25
158.02
149.80
147.42
137.83
124.19
118.04
107.13
78.06
46.28
43.24
34.50
F
F
F
O
O
H2N
N
S
N
N
S
O
OH
16b
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



16b

-77.027
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)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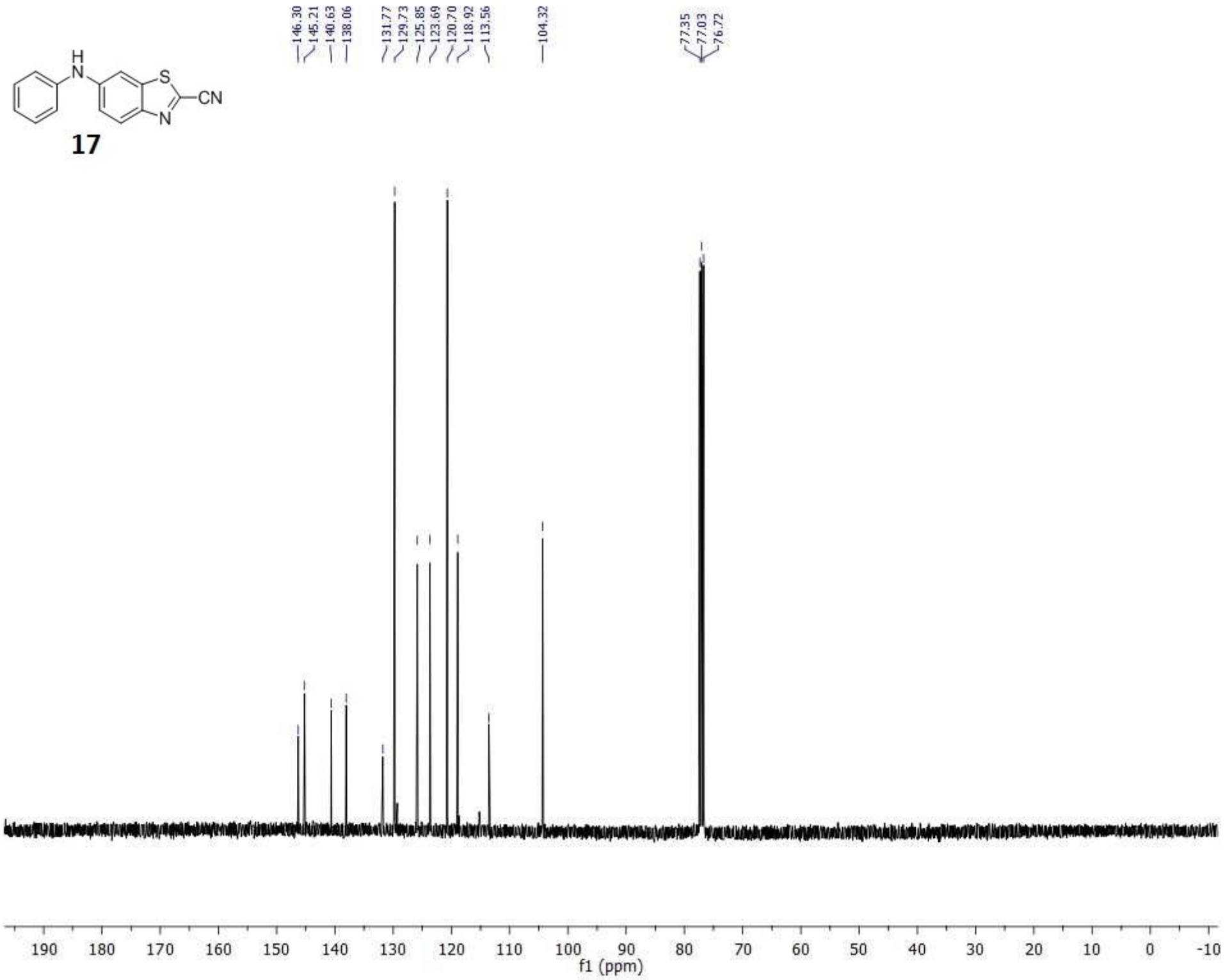
7.377
7.358
7.258
7.229
7.222
7.219
7.217
7.206
7.200
6.132
H
N
S
CN
N
17
7.478
7.473
7.397
7.377
7.358
7.258
7.222
7.219
7.217
7.206
7.136
7.119
7.117
7.101
7.099
0.97
2.02
2.99
1.17
7.5
7.4
7.3
7.2
7.1
f1 (ppm)
1.00
0.97
2.02
3.35
1.17
0.96
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)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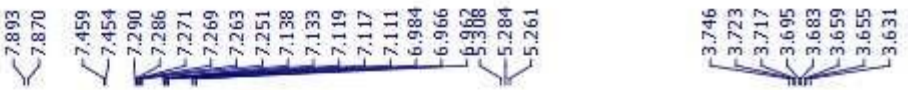
145.21
140.63
138.06
131.77
129.73
125.85
123.69
120.70
118.92
113.56
104.32
77.35
77.03
76.72
H
N
S
CN
N
17
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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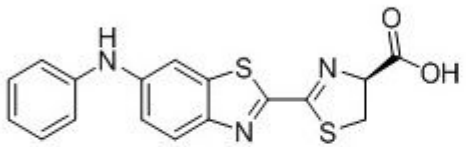
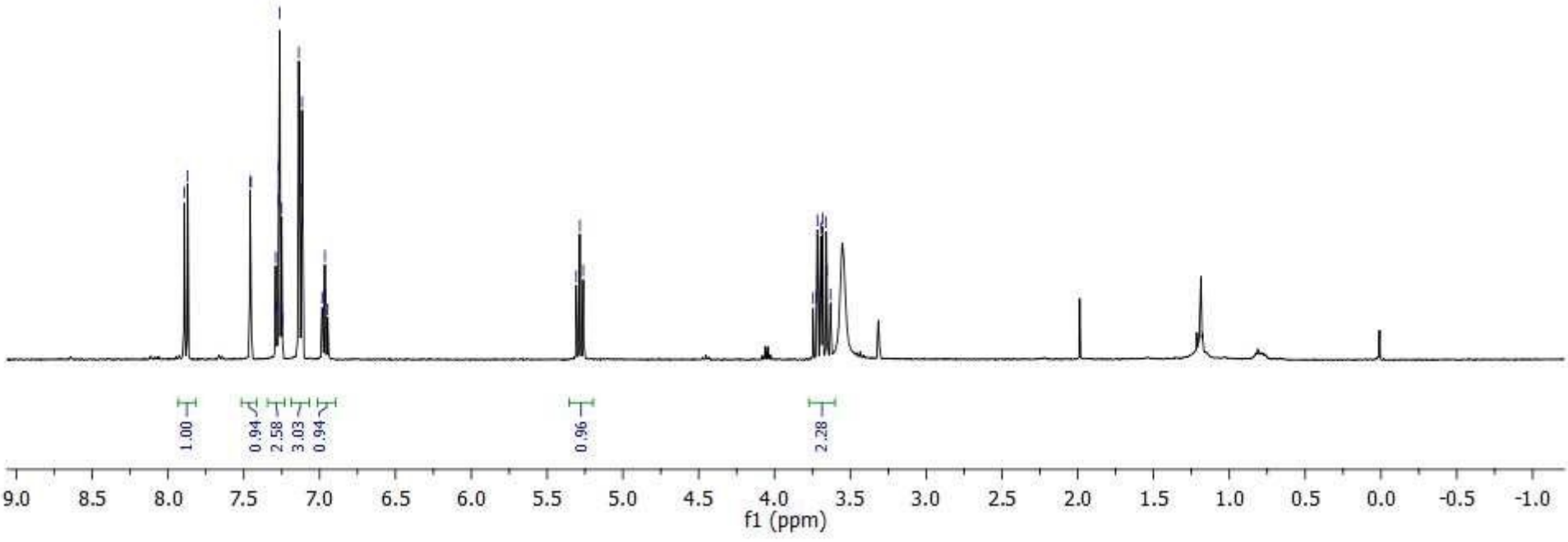
7.870
7.459
7.454
7.290
7.286
7.271
7.269
7.263
7.251
7.138
7.133
7.119
7.117
7.111
6.984
6.966
5.284
5.261
3.746
3.723
3.717
3.695
3.683
3.659
3.655
3.631


H
N
S
N
N
S
O
OH

17a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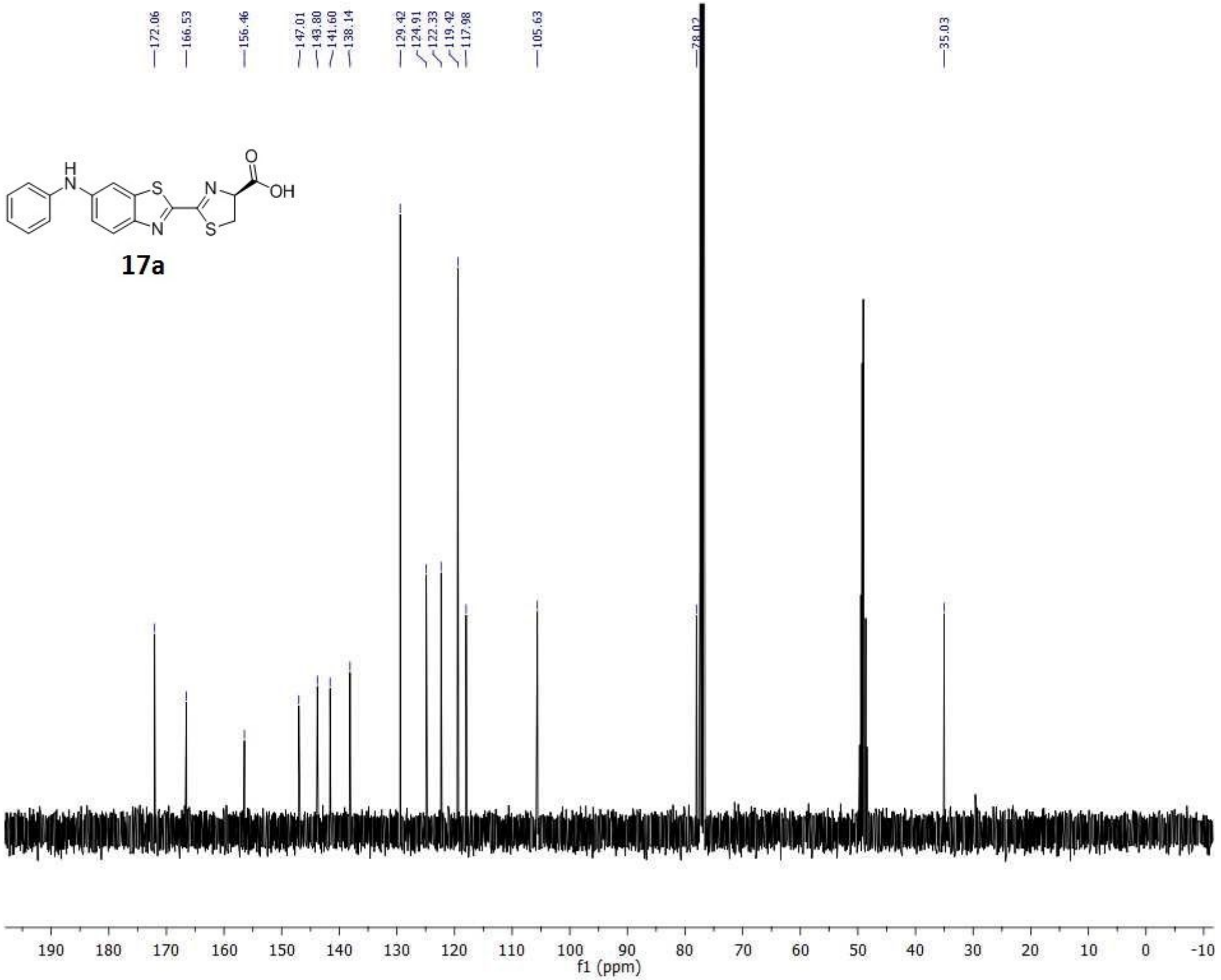
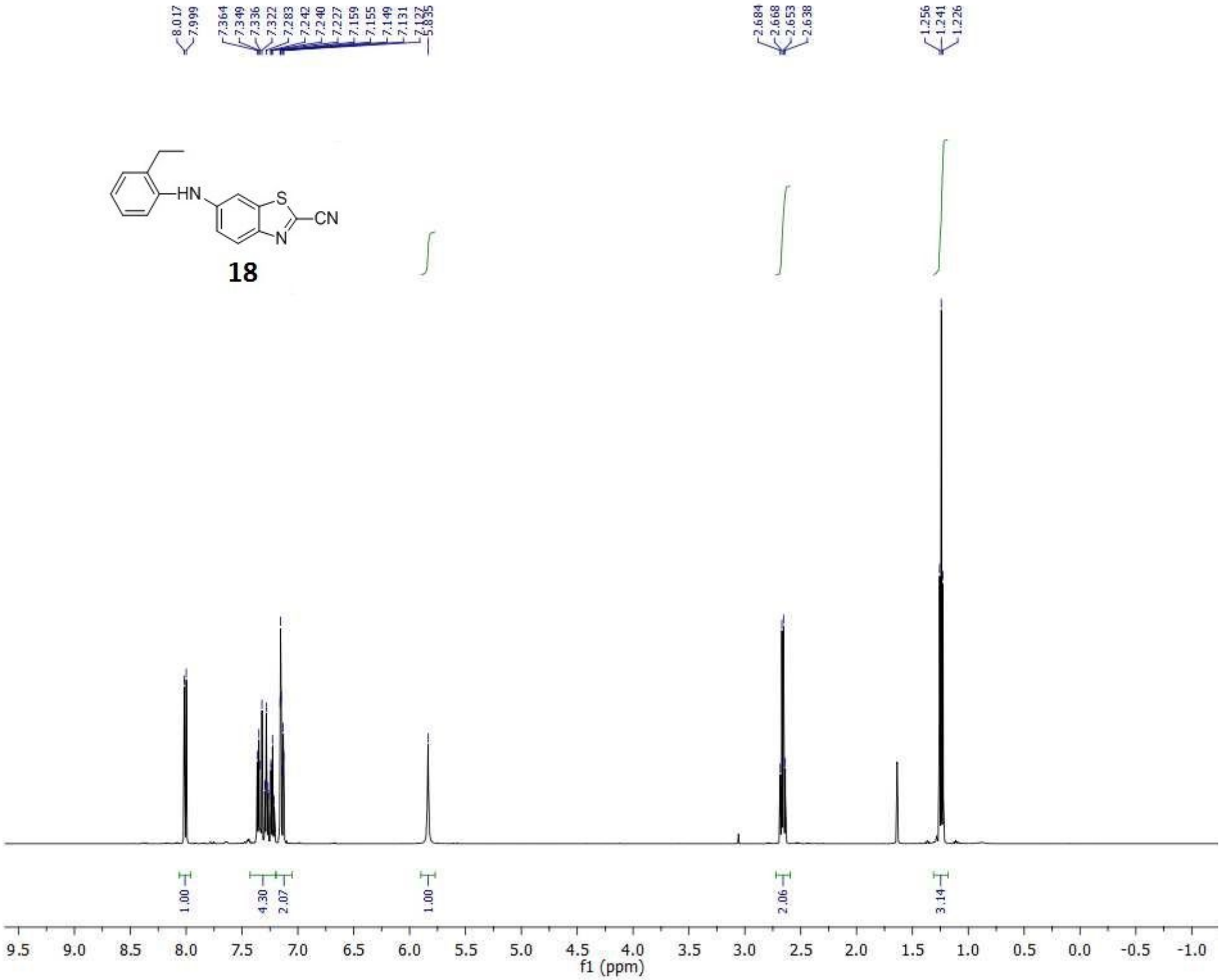
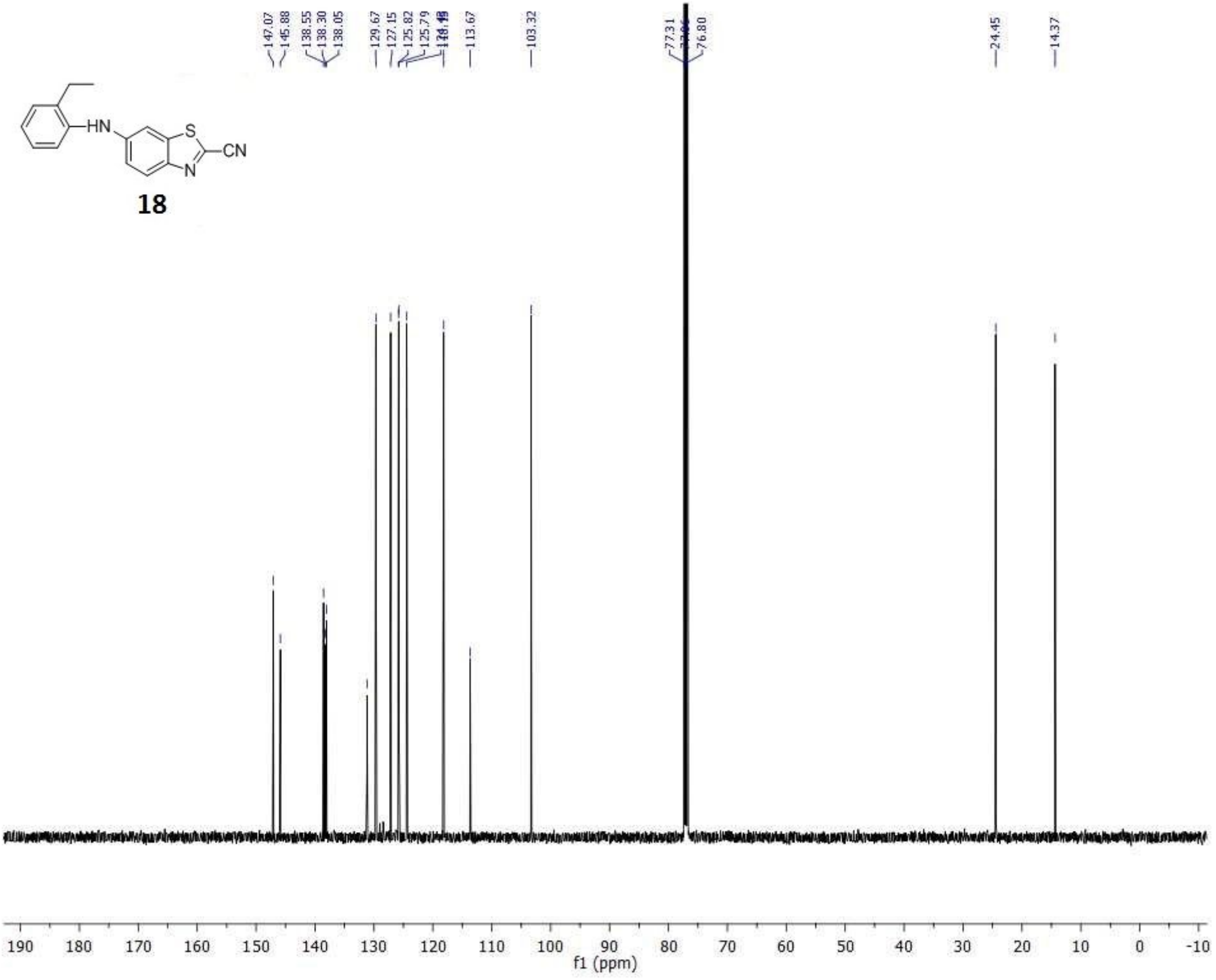
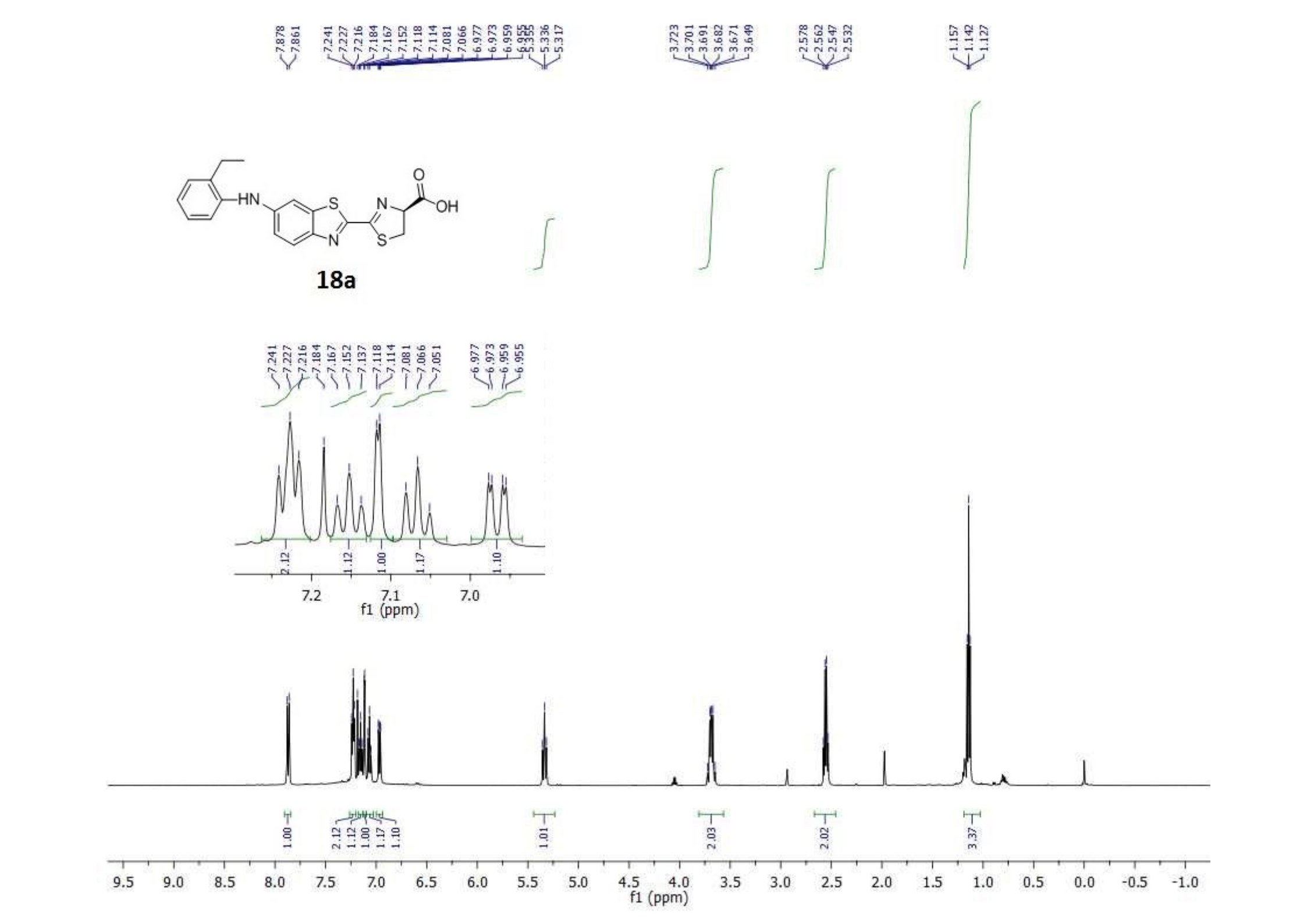
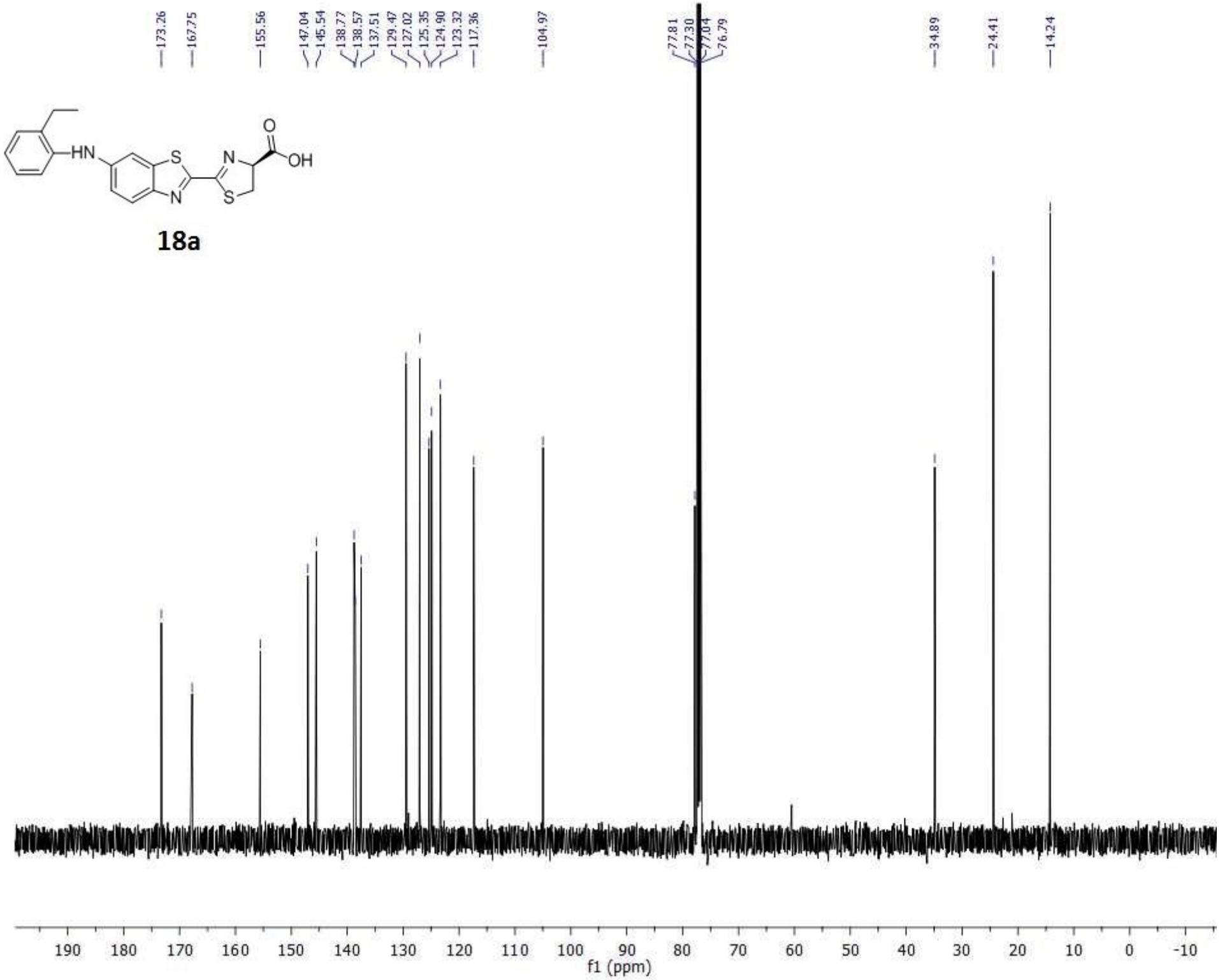
0.94
2.58
3.03
0.94
0.96
2.28
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

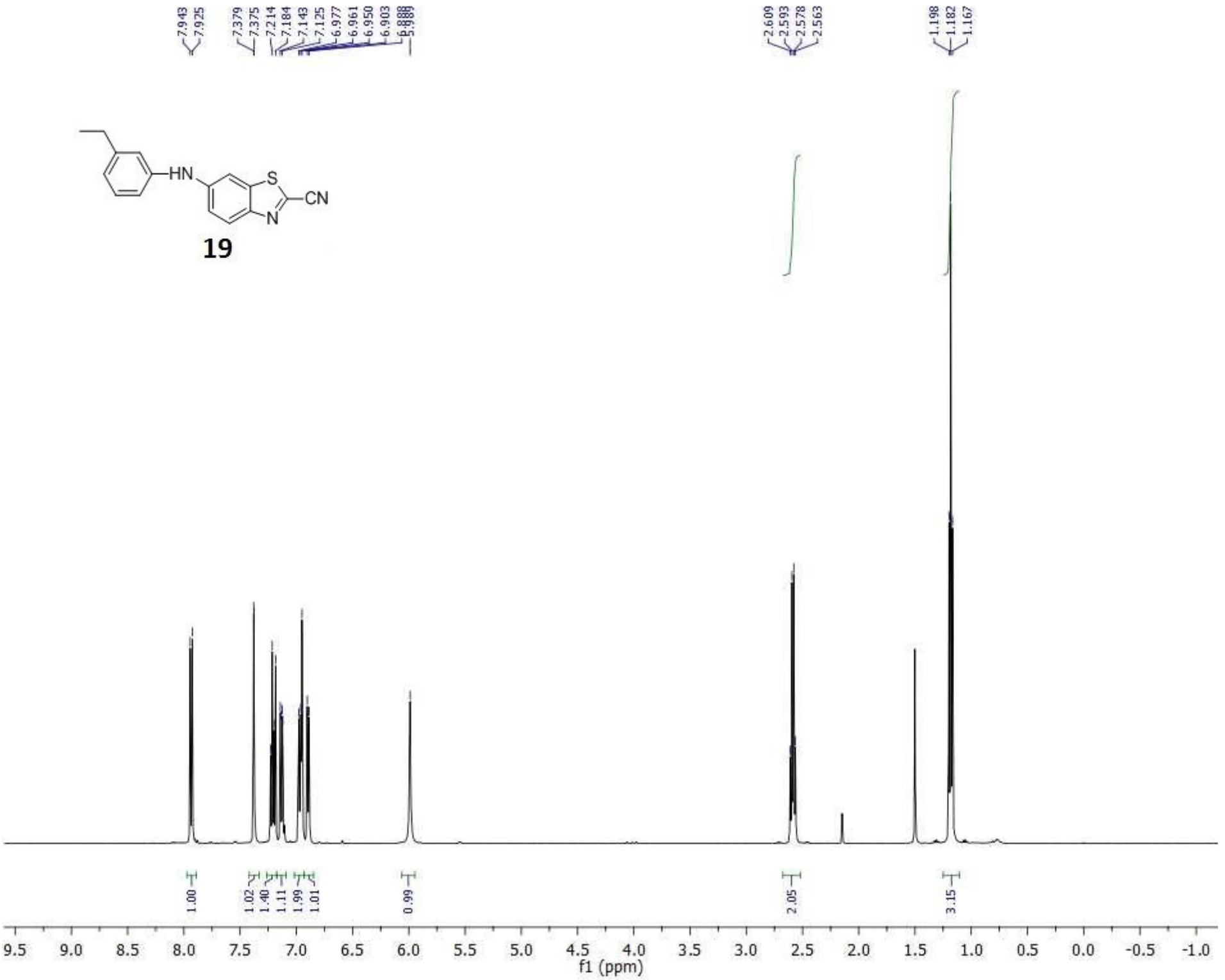

172.06
166.53
156.46
147.01
143.80
141.60
138.14
129.42
124.91
122.33
119.42
117.98
105.63
28.02
35.03
H
N
S
N
S
N
O
OH
17a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

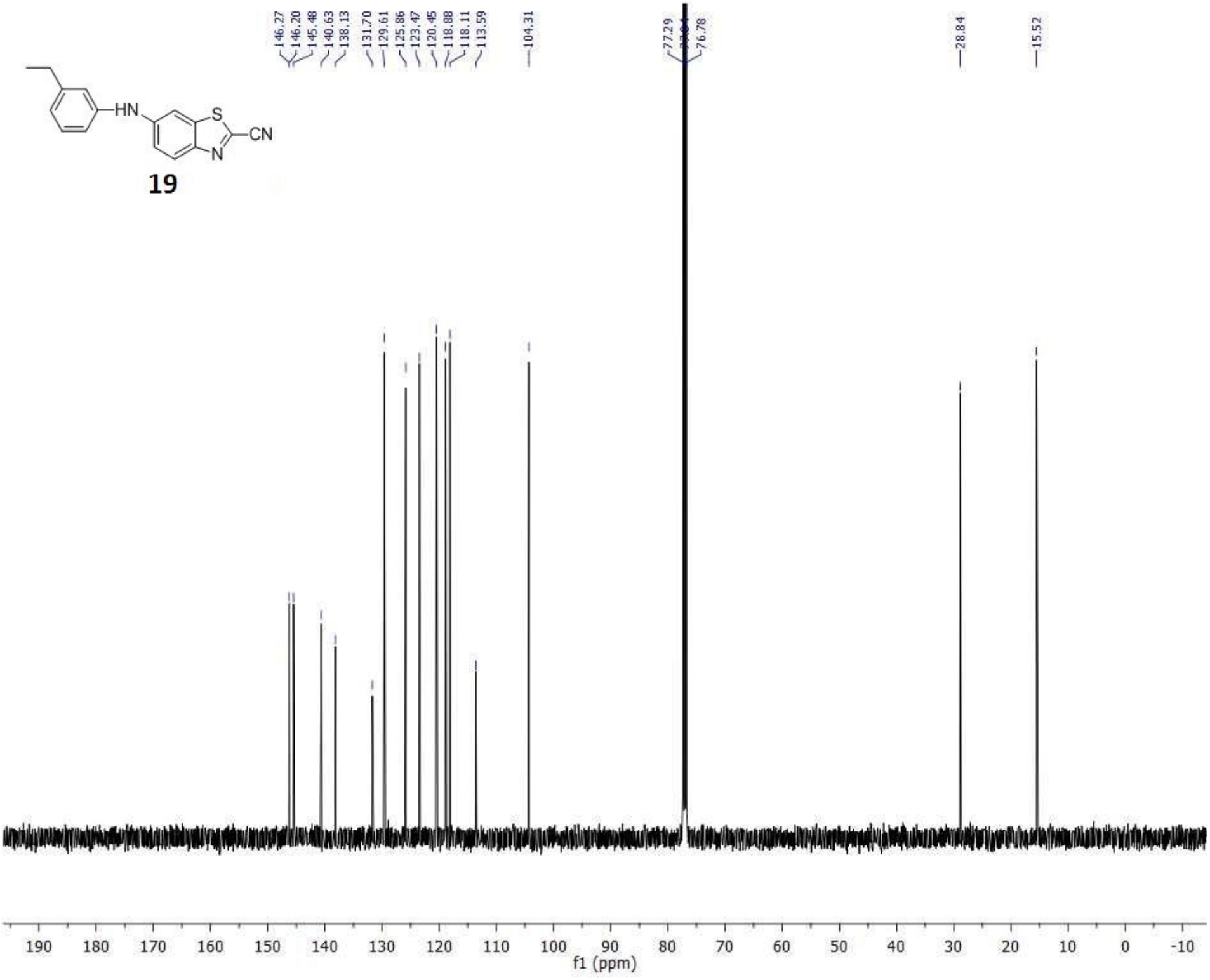

8.017
7.999
7.364
7.349
7.336
7.322
7.283
7.242
7.240
7.227
7.159
7.155
7.149
7.131
7.127
5.835
2.684
2.668
2.653
2.638
1.256
1.241
1.226
HN
S
CN
N
18
1.00
4.30
2.07
1.00
2.06
3.14
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

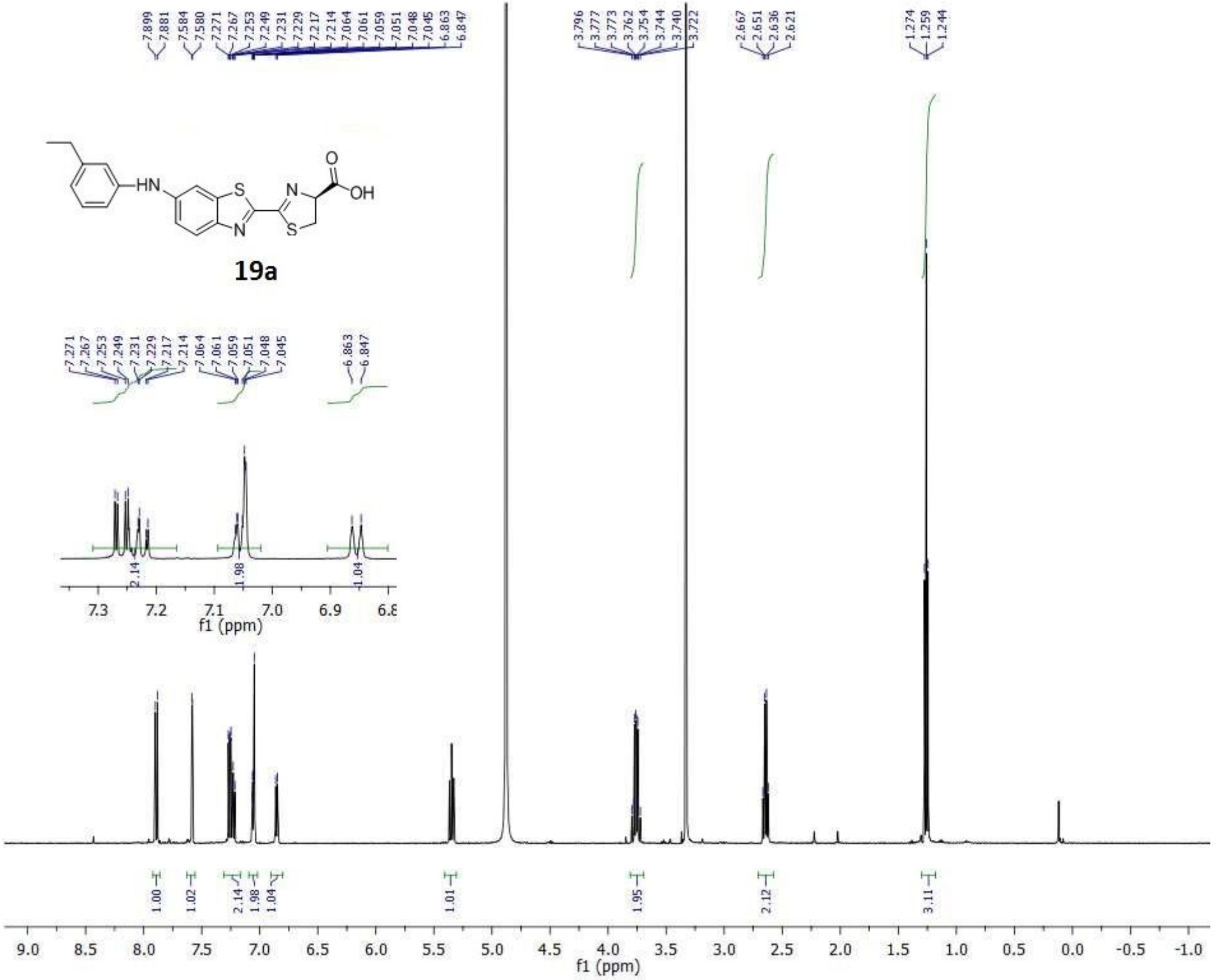

147.07
145.88
138.55
138.30
138.05
129.67
127.15
125.82
125.79
113.67
103.32
77.31
76.80
24.45
14.37
HN
S
CN
N
18
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

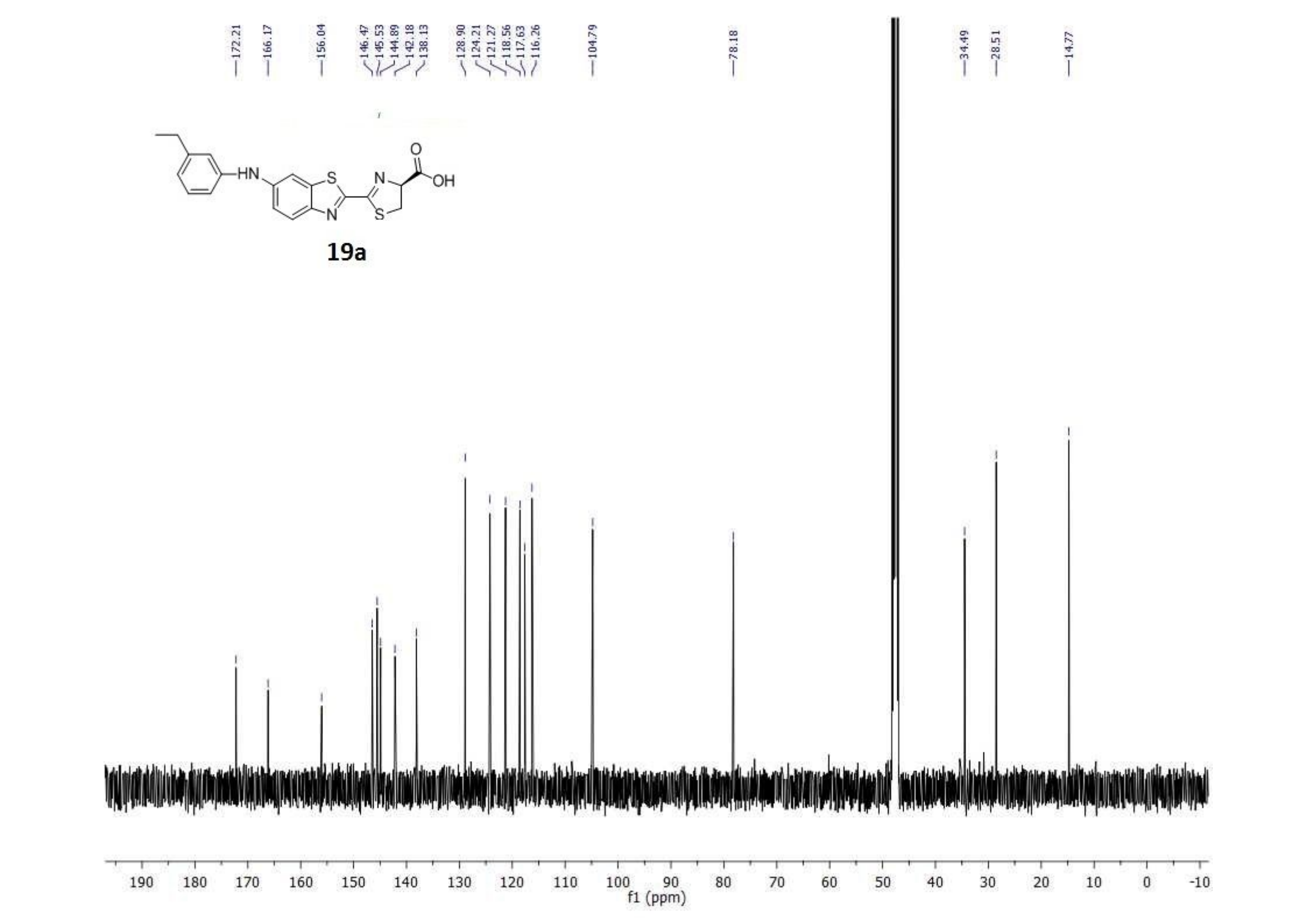

7.878
7.861
7.241
7.227
7.216
7.184
7.167
7.152
7.118
7.114
7.081
7.066
6.977
6.973
6.959
6.955
5.355
5.336
5.317
3.723
3.701
3.691
3.682
3.671
3.649
2.578
2.562
2.547
2.532
1.157
1.142
1.127
HN
S
N
N
S
O
OH
18a
7.241
7.227
7.216
7.184
7.167
7.152
7.137
7.118
7.114
7.081
7.066
7.051
6.977
6.973
6.959
6.955
2.12
1.12
1.00
1.17
1.10
7.2
7.1
7.0
f1 (ppm)
1.00
2.12
1.12
1.00
1.17
1.10
1.01
2.03
2.02
3.37
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

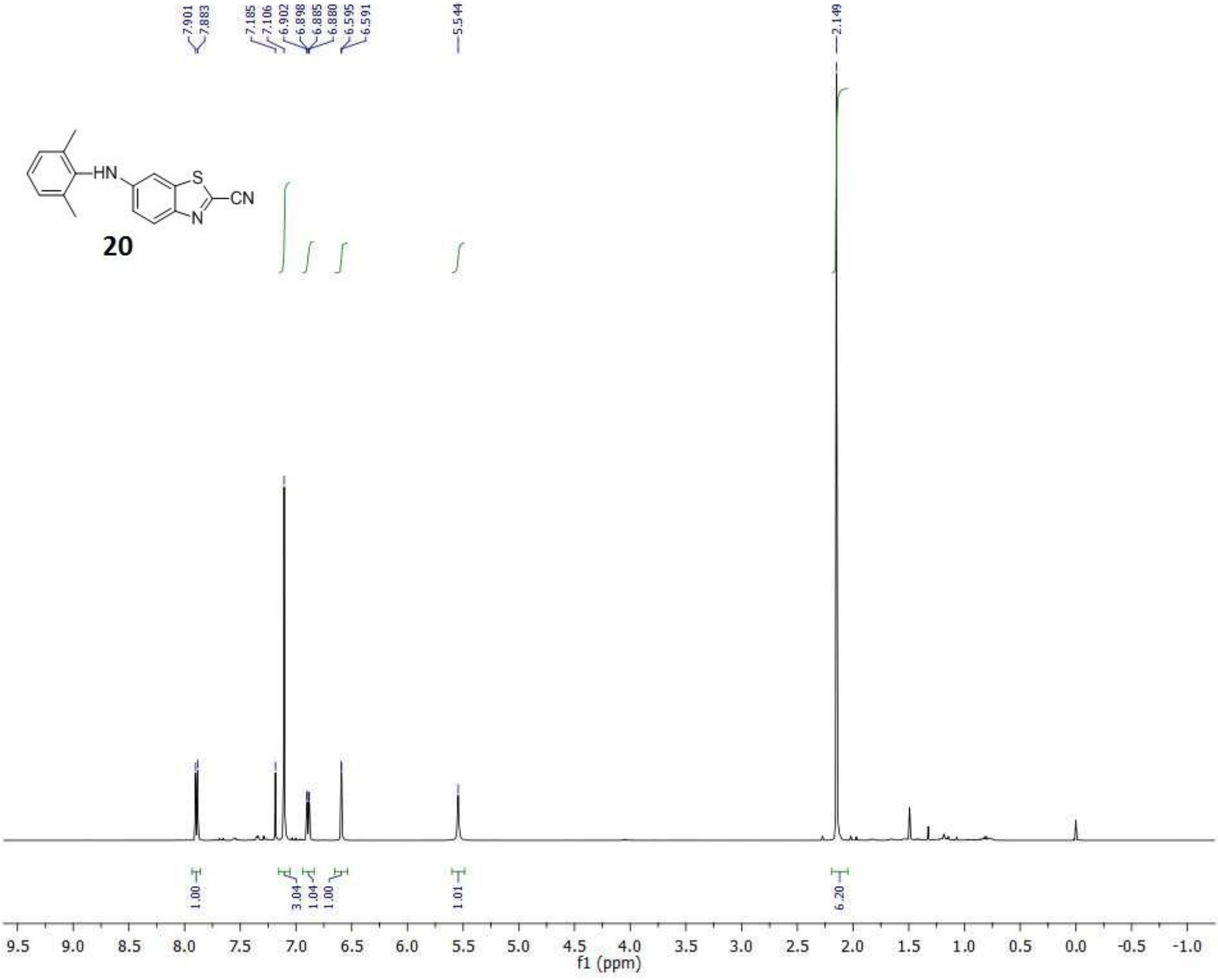

173.26
167.75
155.56
147.04
145.54
138.77
138.57
137.51
129.47
127.02
125.35
124.90
123.32
117.36
104.97
77.81
77.30
77.04
76.79
34.89
24.41
14.24
HN
S
N
O
OH
N
S
18a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.943
7.925
7.379
7.375
7.214
7.184
7.143
7.125
6.977
6.961
6.950
6.903
2.609
2.593
2.578
2.563
1.198
1.182
1.167
HN
S
CN
N
19
1.00
1.02
1.40
1.11
1.99
1.01
0.99
2.05
3.15
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


146.27
146.20
145.48
140.63
138.13
131.70
129.61
125.86
123.47
120.45
118.88
118.11
113.59
104.31
77.29
76.78
28.84
15.52
HN
S
CN
N
19
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.899
7.881
7.584
7.580
7.271
7.267
7.253
7.249
7.231
7.229
7.217
7.214
7.064
7.061
7.059
7.051
7.048
7.045
6.863
6.847
3.796
3.777
3.773
3.762
3.754
3.744
3.740
3.722
2.667
2.651
2.636
2.621
1.274
1.259
1.244
HN
S
N
O
OH
N
S
19a
2.14
1.98
1.04
7.3
7.2
7.1
7.0
6.9
f1 (ppm)
1.00
1.02
2.14
1.98
1.04
1.01
1.95
2.12
3.11
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


172.21
166.17
156.04
146.47
145.53
144.89
142.18
138.13
128.90
124.21
121.27
118.56
117.63
116.26
104.79
78.18
34.49
28.51
14.77
HN
S
N
O
OH
N
S
19a
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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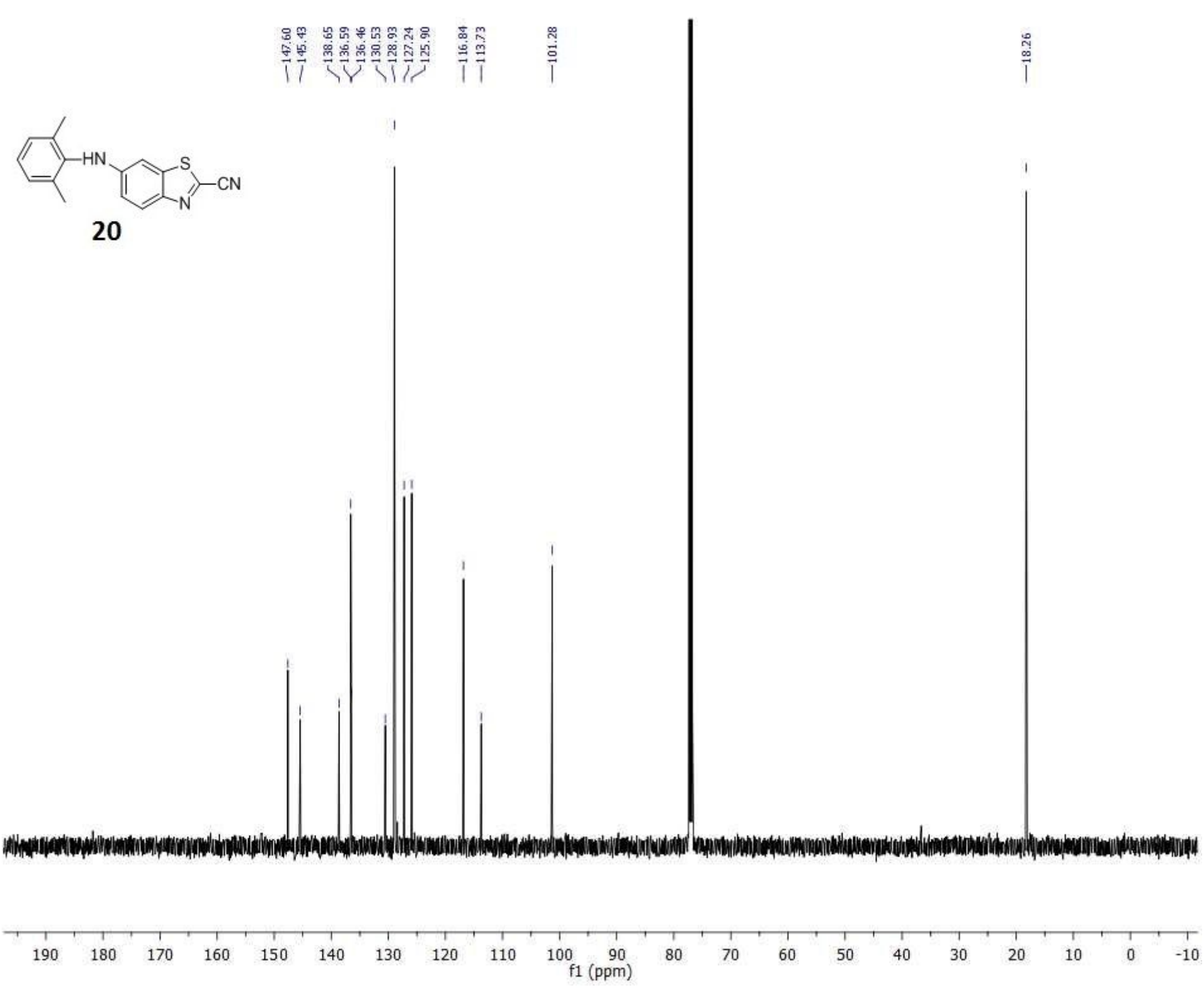
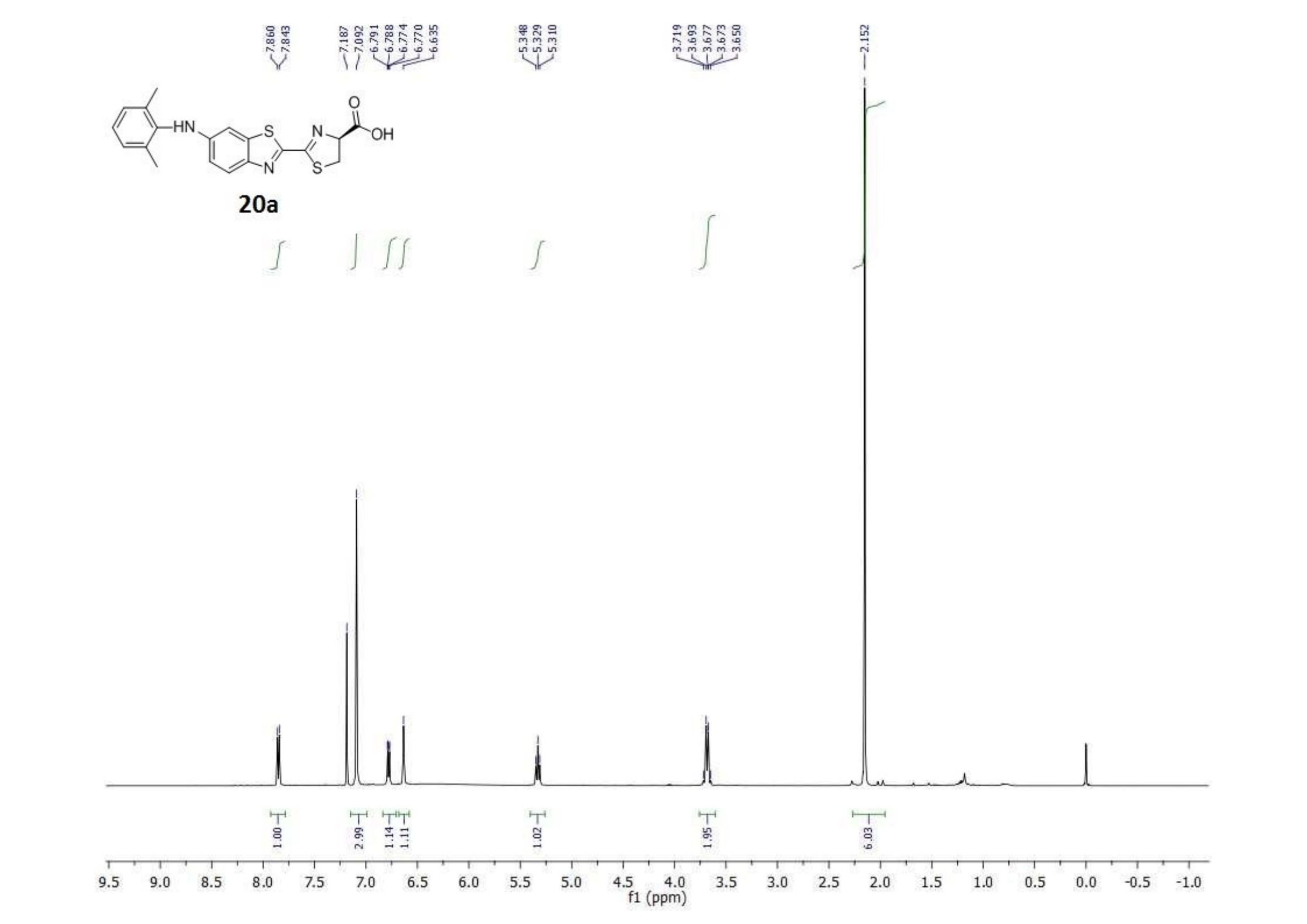
7.883
7.185
7.106
6.902
6.898
6.885
6.880
6.595
6.591
5.544
2.149
HN
S
CN
N
20
1.00
3.04
1.04
1.00
1.01
6.20
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


147.60
145.43
138.65
136.59
136.46
130.53
128.93
127.24
125.90
116.84
113.73
101.28
18.26
HN
S
CN
N
20
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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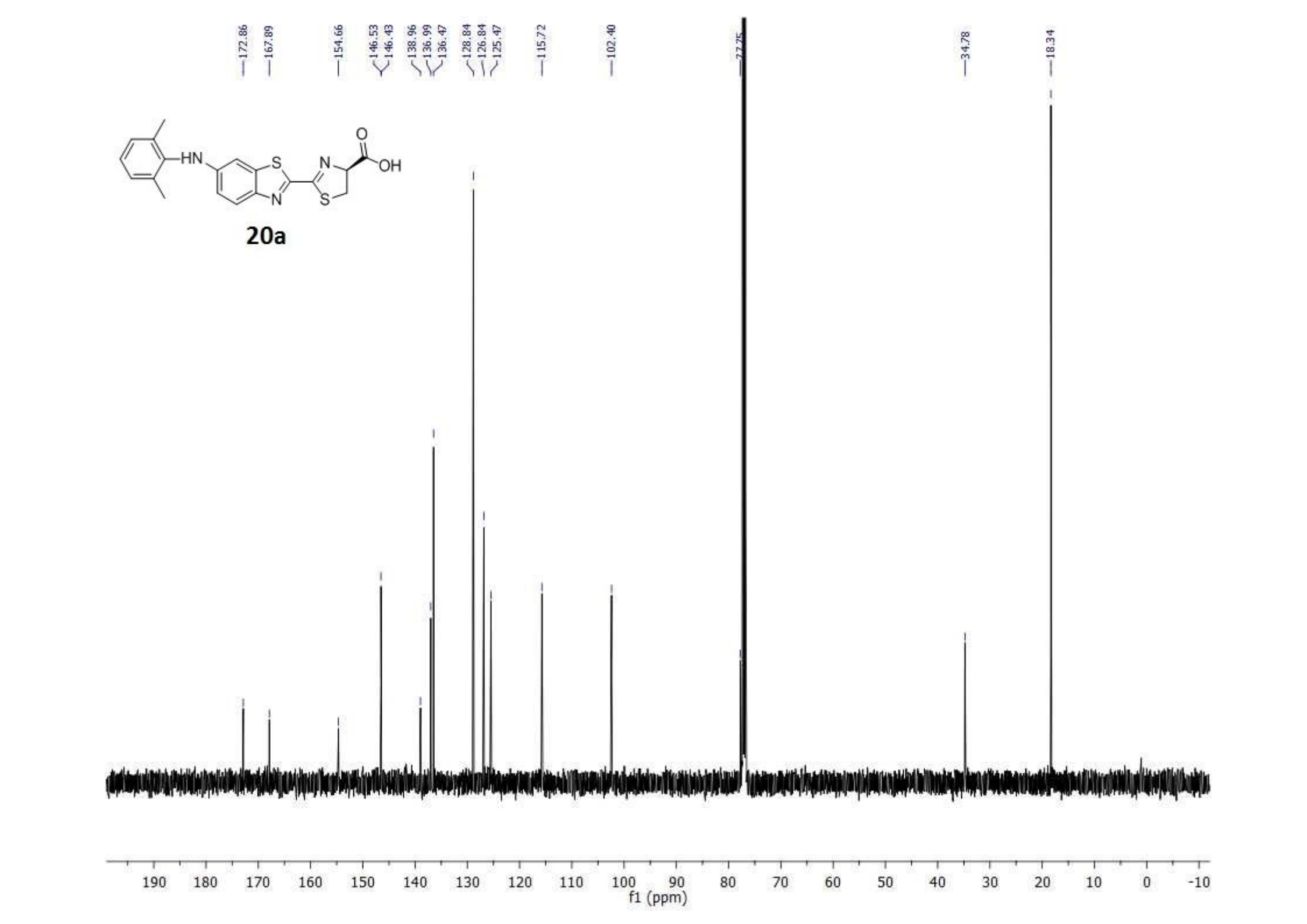
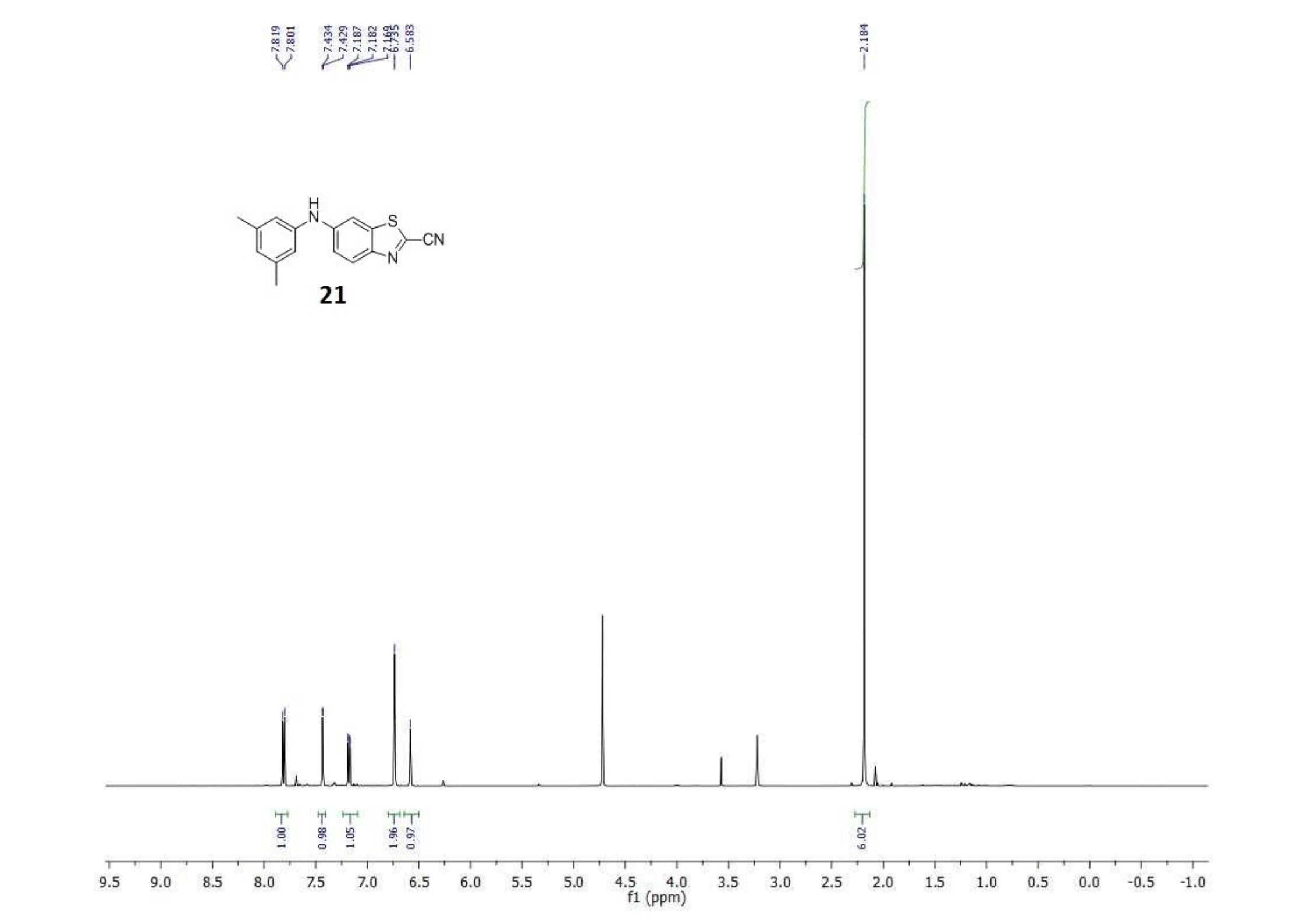
7.187
7.092
6.791
6.788
6.774
6.770
6.635
5.348
5.329
5.310
3.719
3.693
3.677
3.673
3.650
2.152
HN
S
N
O
OH
N
S
20a
1.00
2.99
1.14
1.11
1.02
1.95
6.03
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


172.86
167.89
154.66
146.53
146.43
138.96
136.99
136.47
128.84
126.84
125.47
115.72
102.40
77.25
34.78
18.34
HN
S
N
O
OH
N
S
20a
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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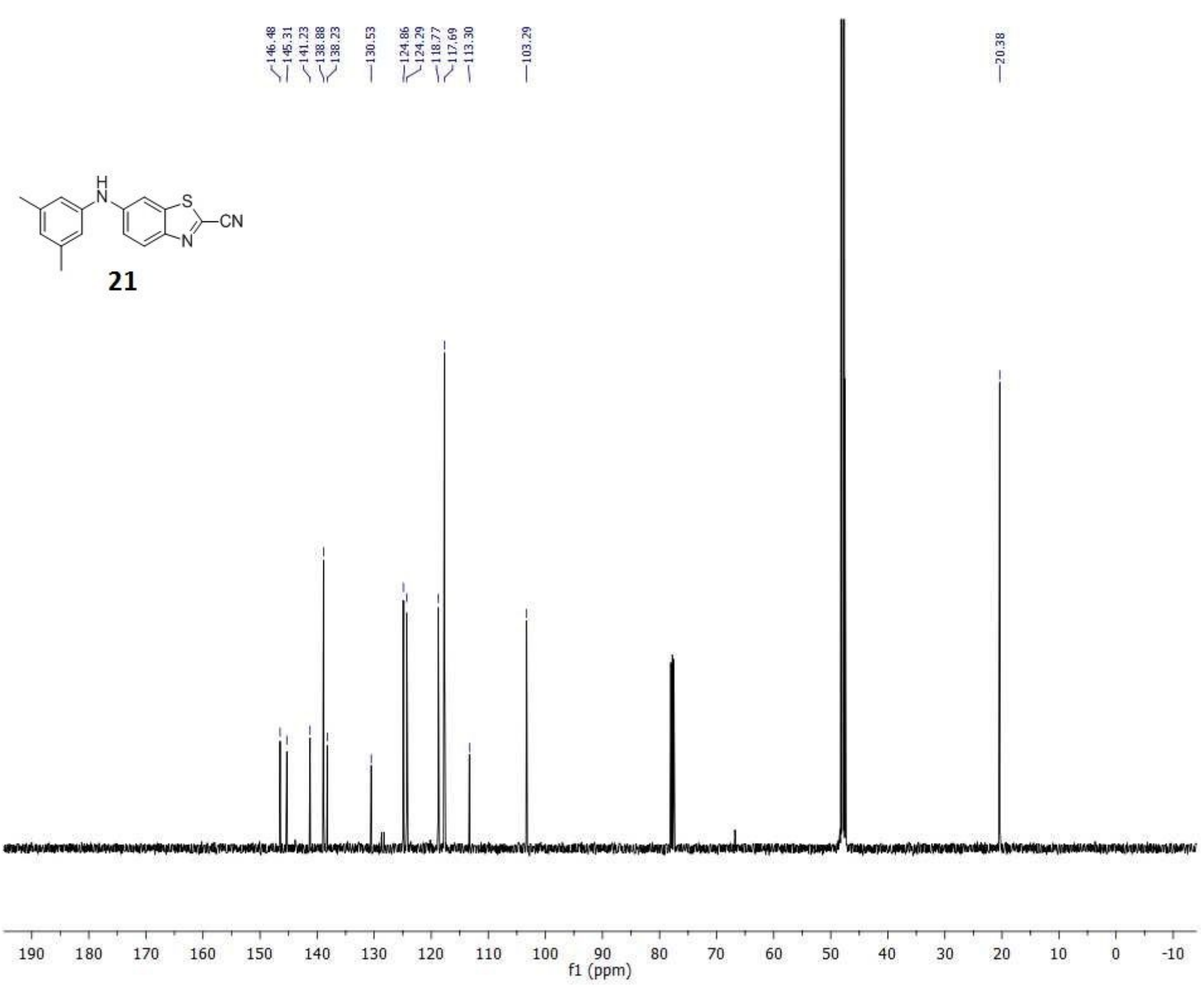
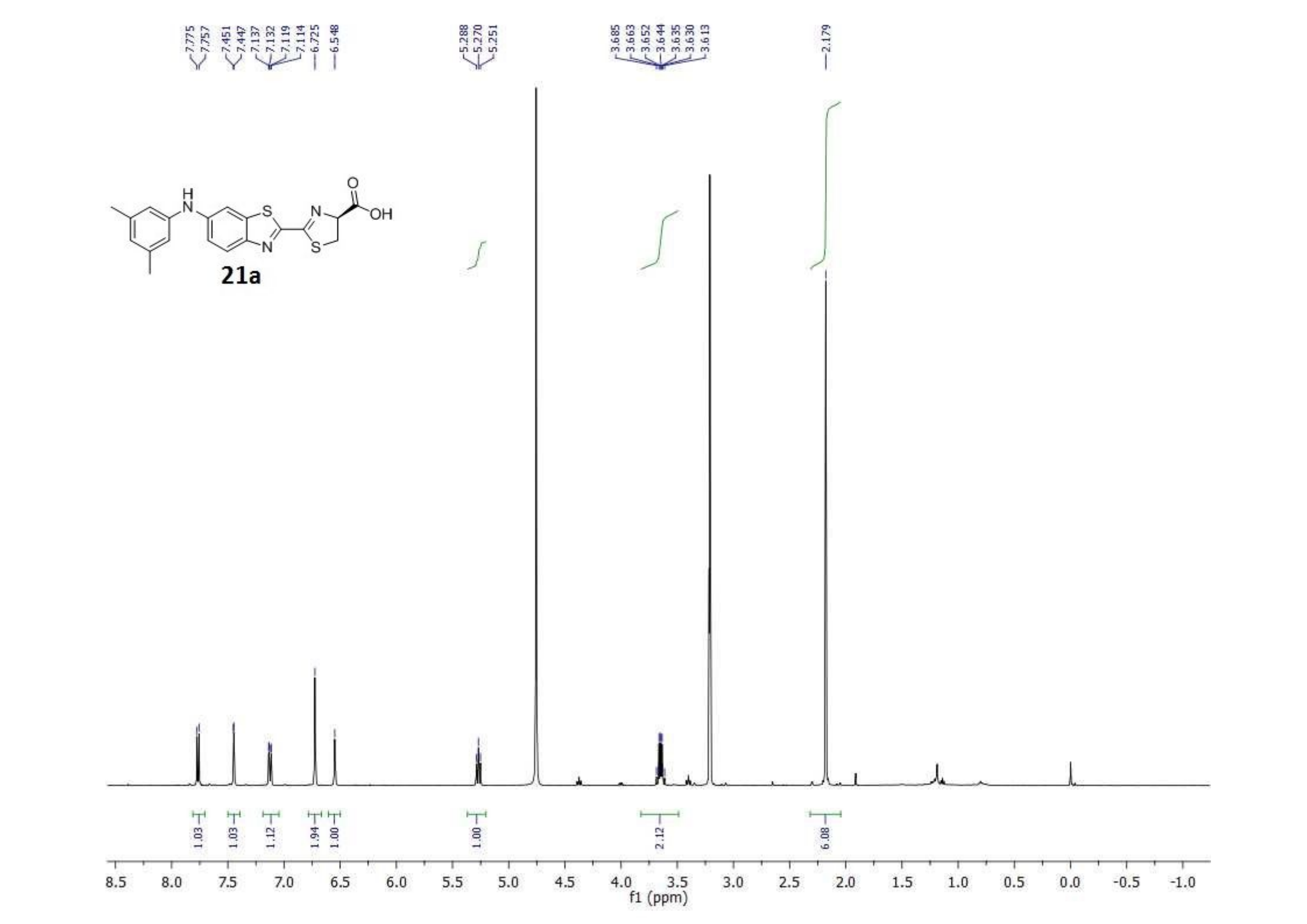
7.434
7.429
7.187
7.182
6.583
2.184
H
N
S
CN
N
21
1.00
0.98
1.05
1.96
0.97
6.02
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


146.48
145.31
141.23
138.88
138.23
130.53
124.86
124.29
118.77
117.69
113.30
103.29
20.38
H
N
S
CN
N
21
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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7.757
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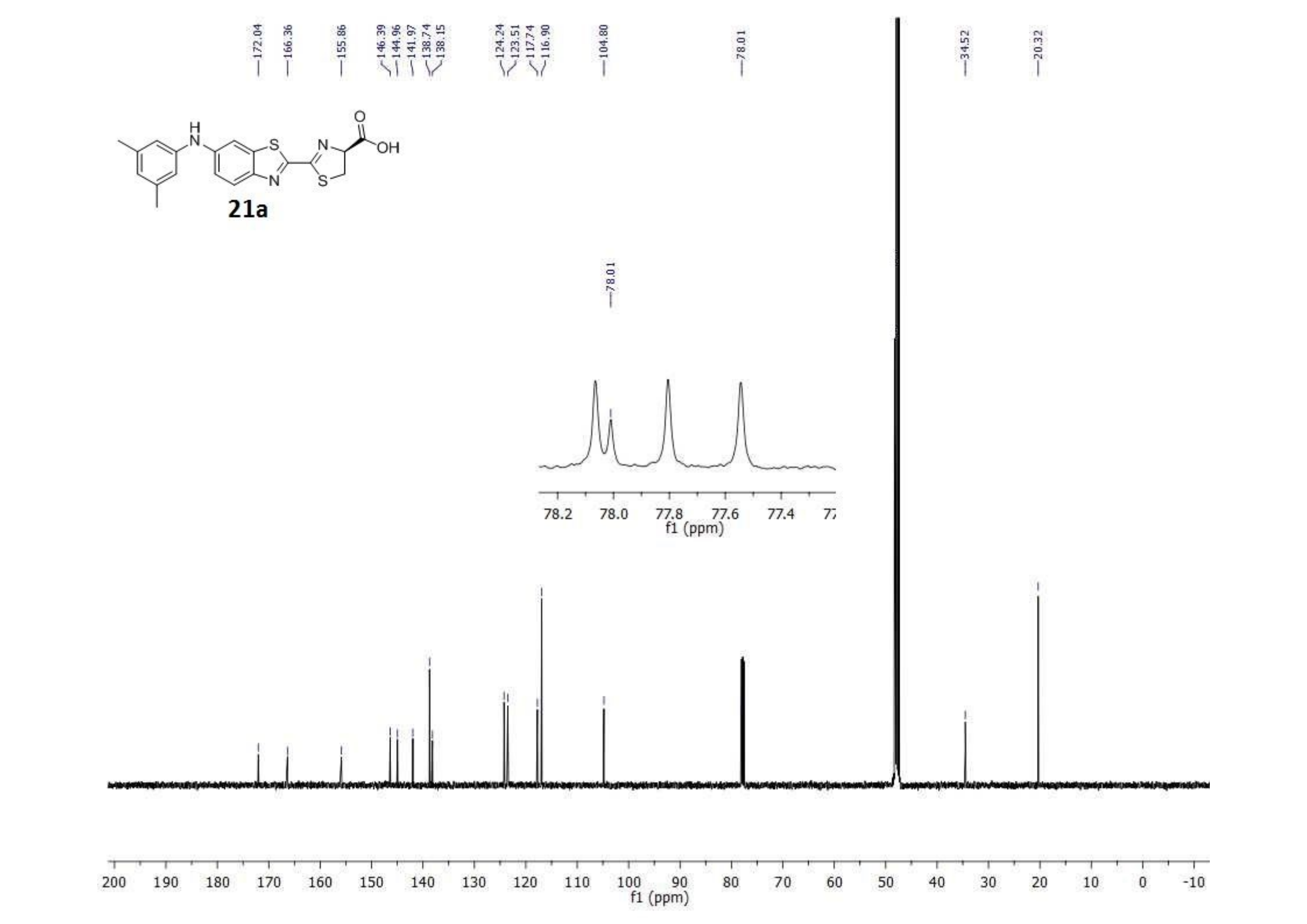
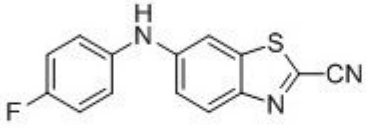
7.447
7.137
7.132
7.119
7.114
6.725
6.548
5.288
5.270
5.251
3.685
3.663
3.652
3.644
3.635
3.630
3.613
2.179
H
N
S
N
S
N
O
OH
21a
1.03
1.03
1.12
1.94
1.00
1.00
2.12
6.08
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

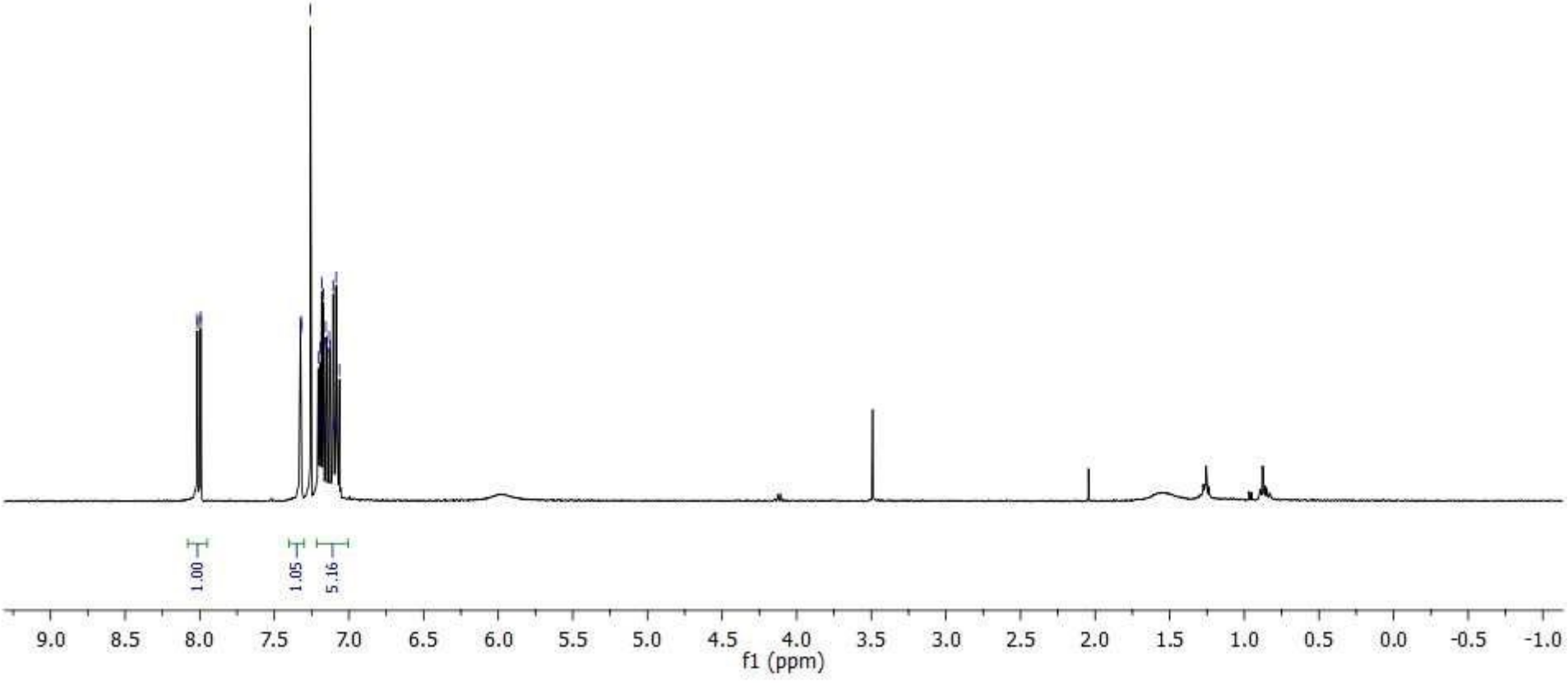

172.04
166.36
155.86
146.39
144.96
141.97
138.74
138.15
124.24
123.51
117.74
116.90
104.80
78.01
34.52
20.32
78.01
78.2
78.0
77.8
77.6
77.4
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

21a


8.016
8.015
7.994
7.993
7.326
7.325
7.320
7.319
7.258
7.206
7.200
7.194
7.189
7.183
7.178
7.175
7.172
7.155
7.149
7.133
7.127
7.107
7.101
7.090
7.087
7.085
7.081
7.064


H
N
S
CN
N
F

22


1.00
1.05
5.16
9.0
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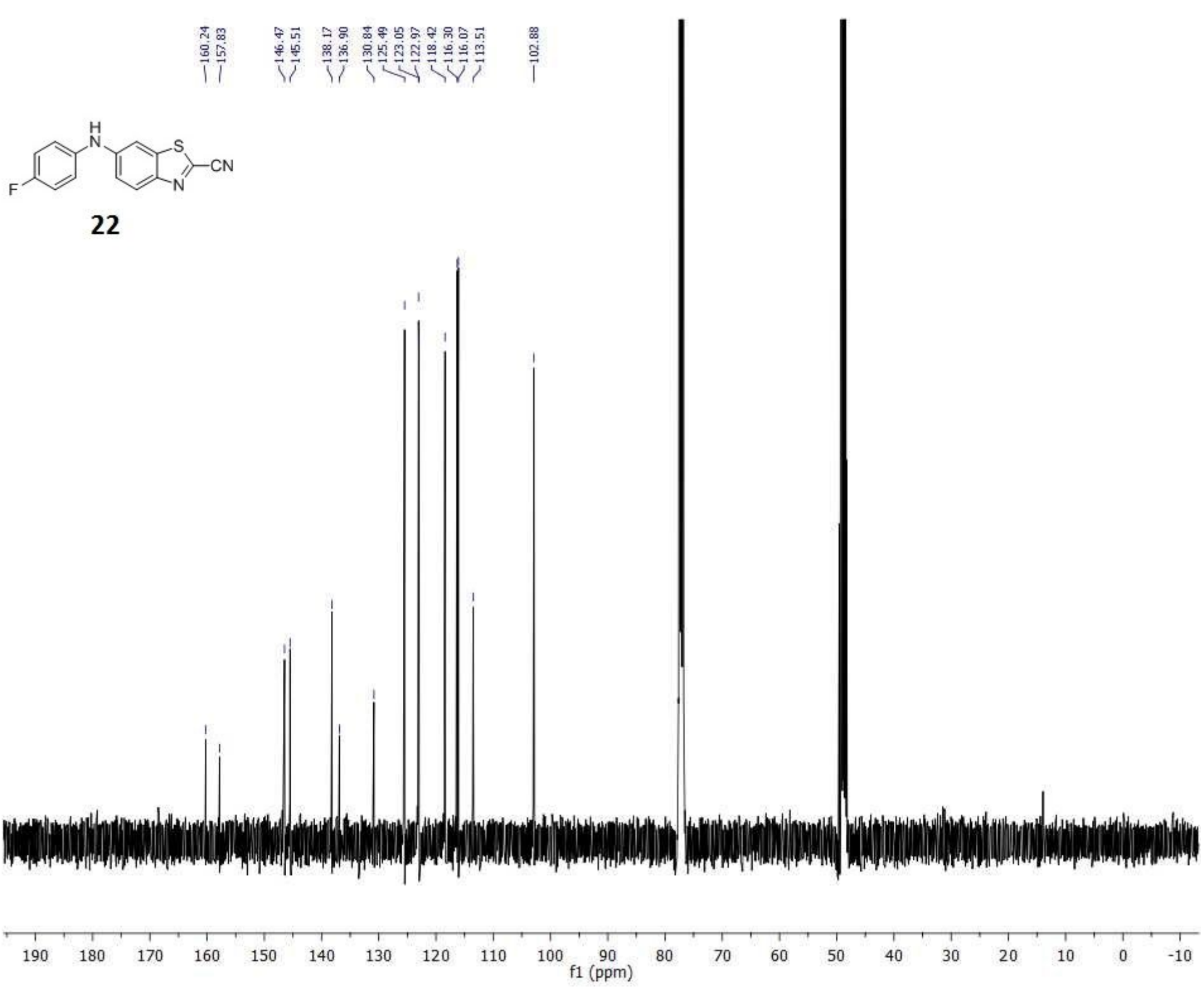
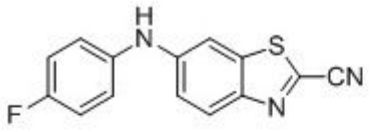
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

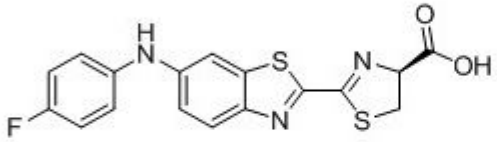

160.24
157.83
146.47
145.51
138.17
136.90
130.84
125.49
123.05
122.97
118.42
116.30
116.07
113.51
102.88
H
N
S
CN
N
F
22
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


H
N
S
CN
F
N

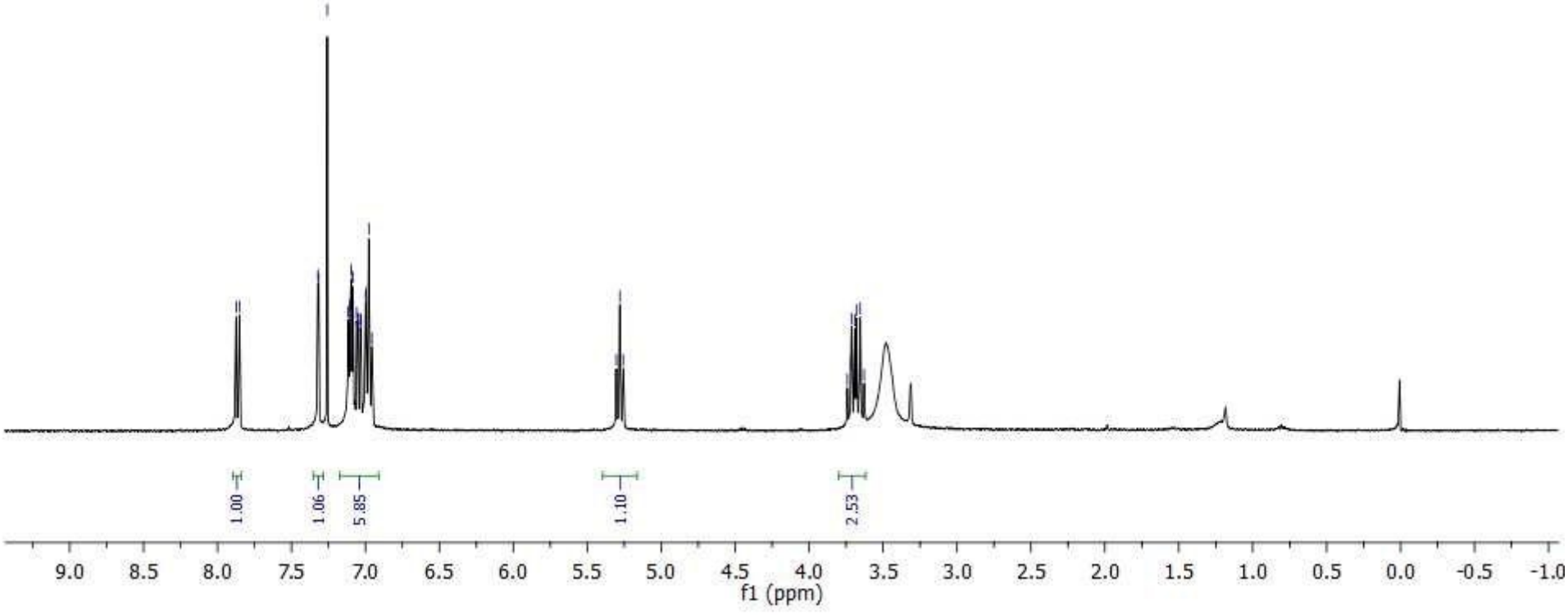
22

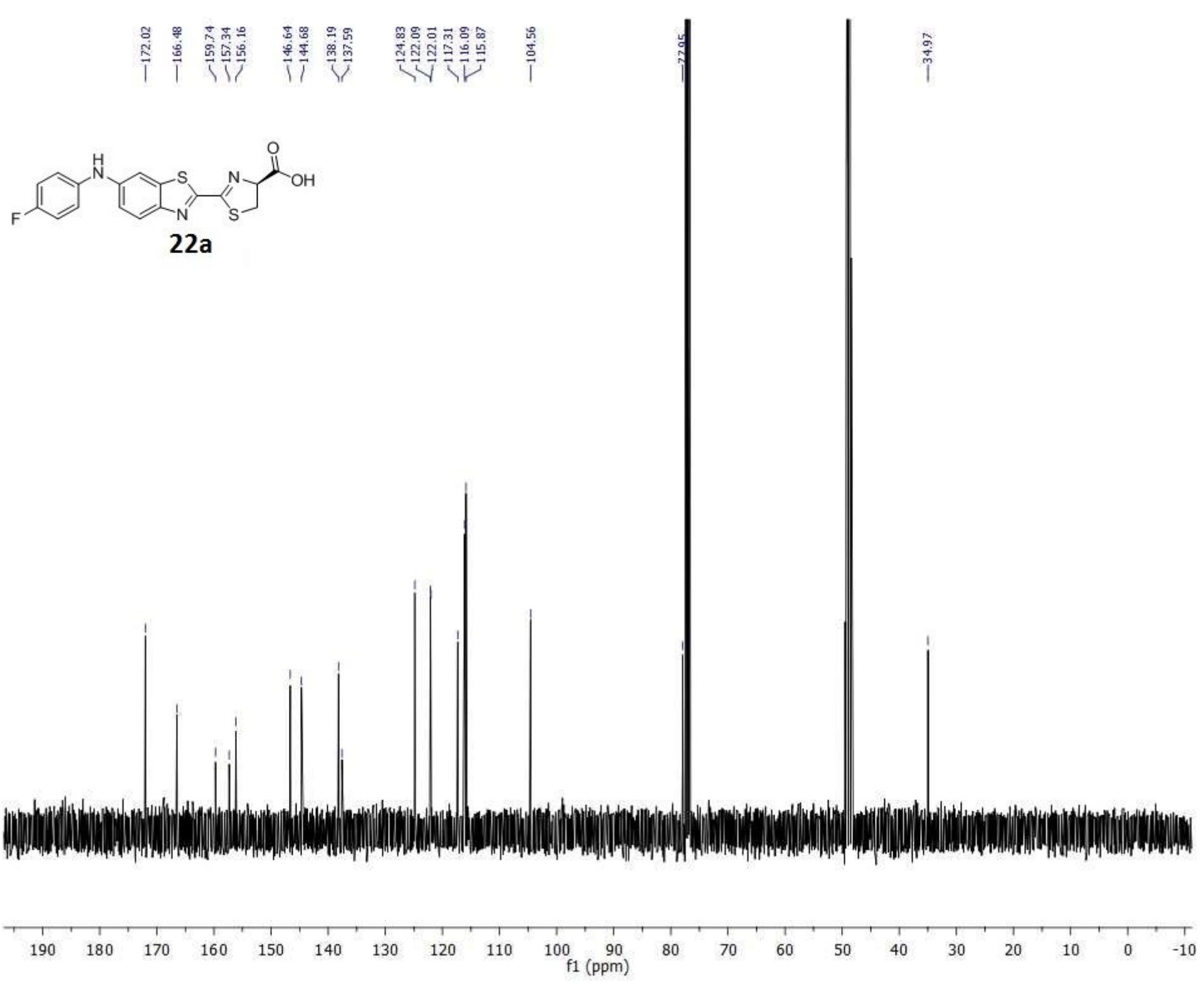
-119.475
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)

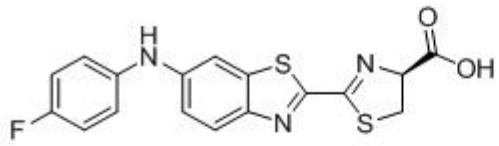

7.874
7.852
7.321
7.316
7.258
7.117
7.105
7.096
7.084
7.058
7.053
7.036
7.035
7.030
6.999
6.997
6.977
5.304
5.280
5.257
3.741
3.717
3.713
3.691
3.680
3.654
3.628


H
N
S
N
O
OH
F
N
S

22a

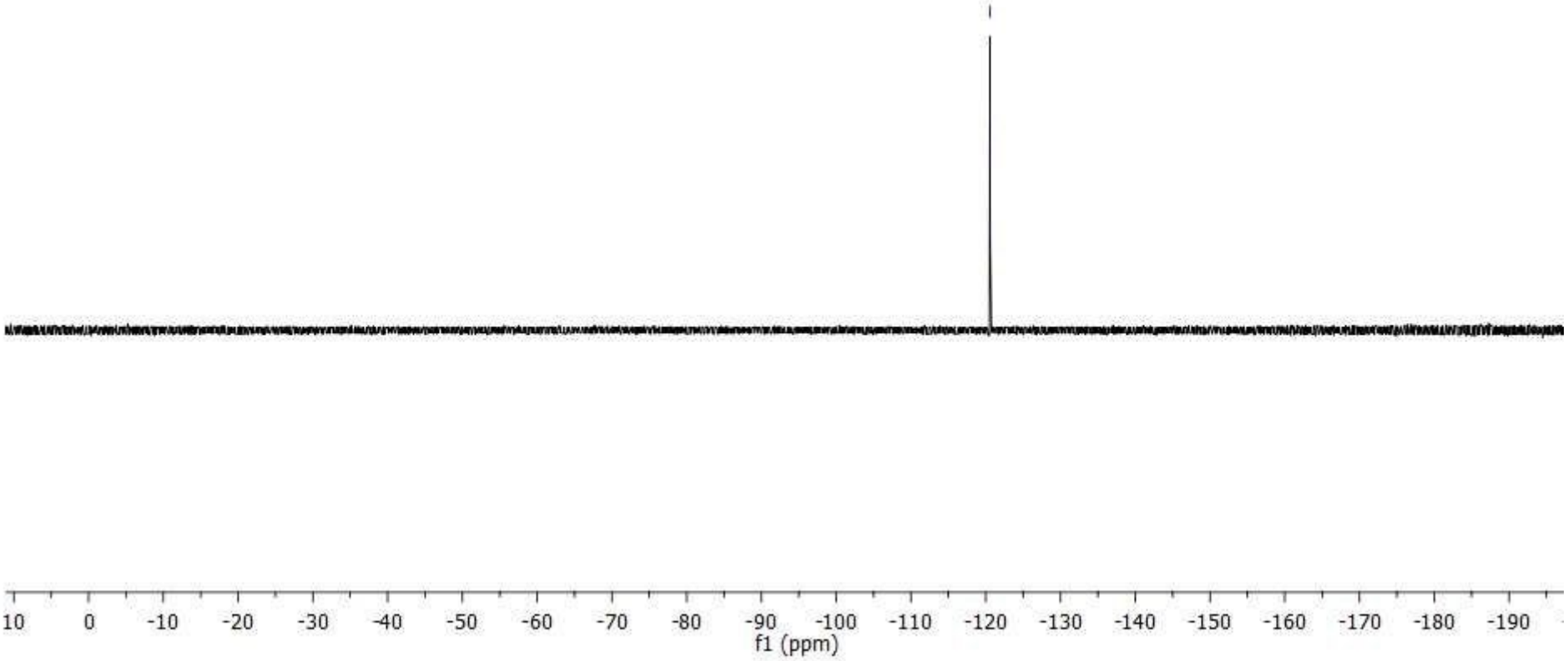

1.00
1.06
5.85
1.10
2.53
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

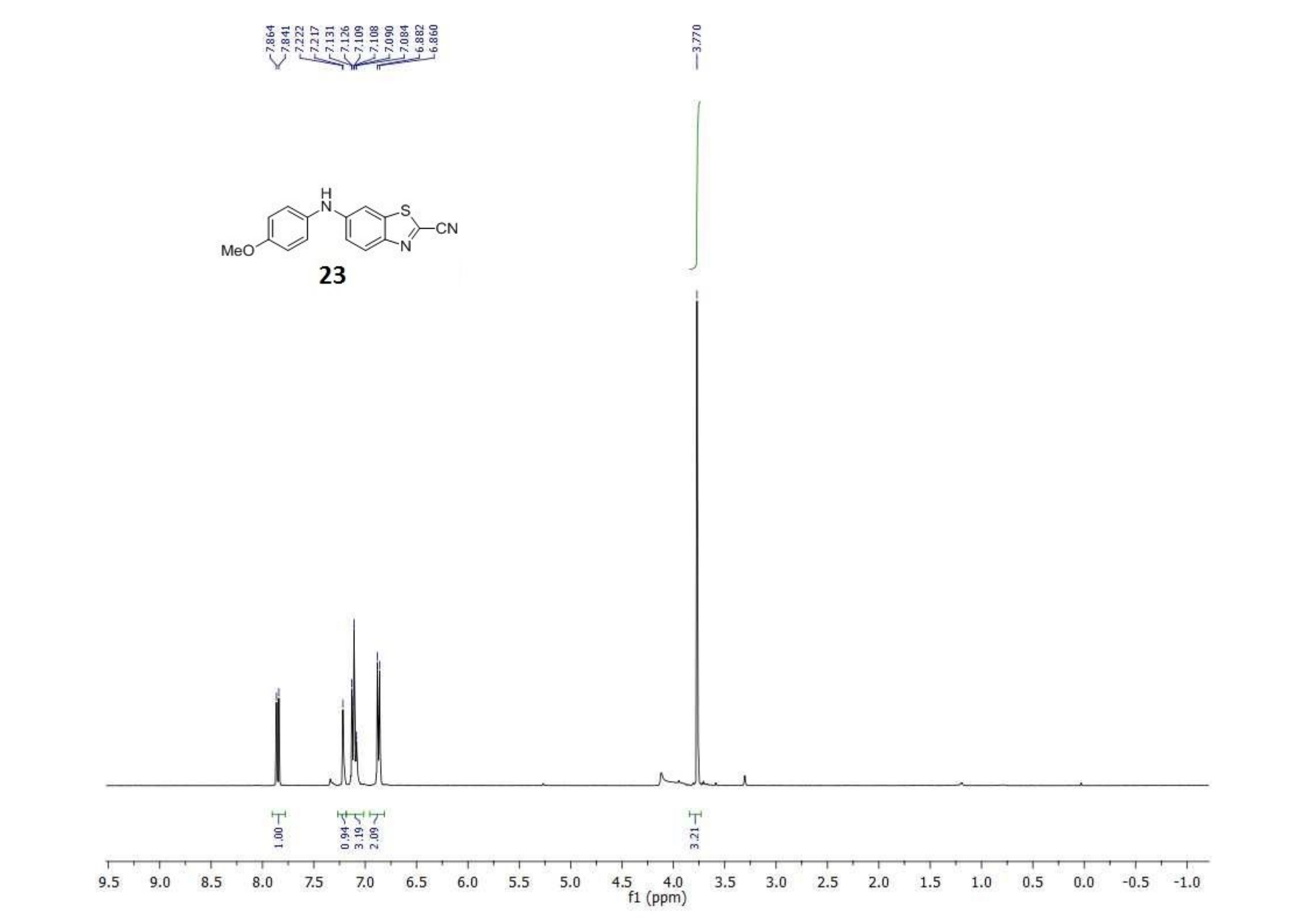

172.02
166.48
159.74
157.34
156.16
146.64
144.68
138.19
137.59
124.83
122.09
122.01
117.31
116.09
115.87
104.56
77.05
34.97
H
N
S
N
O
OH
F
N
S
22a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

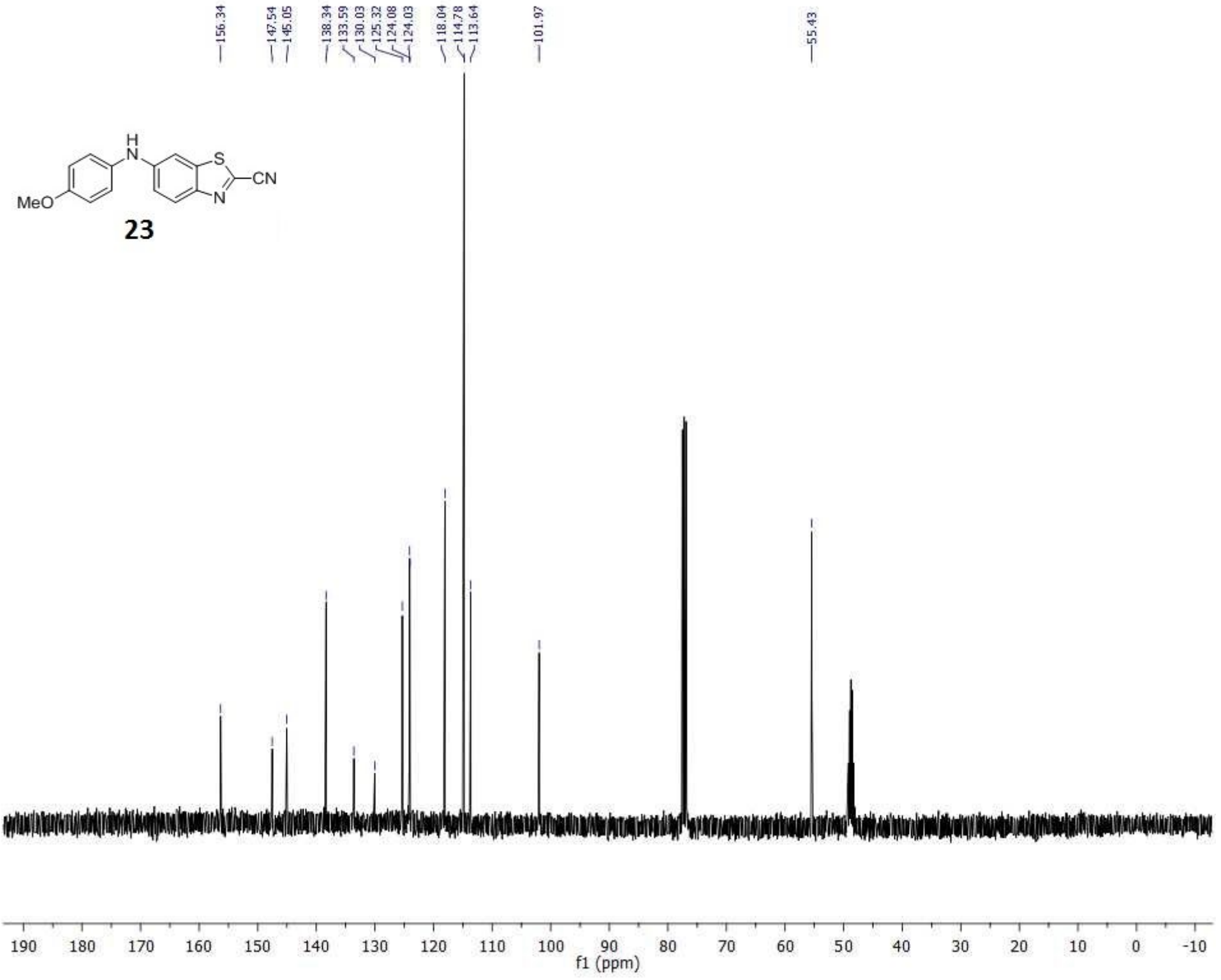

H
N
S
N
O
OH
F
N
S

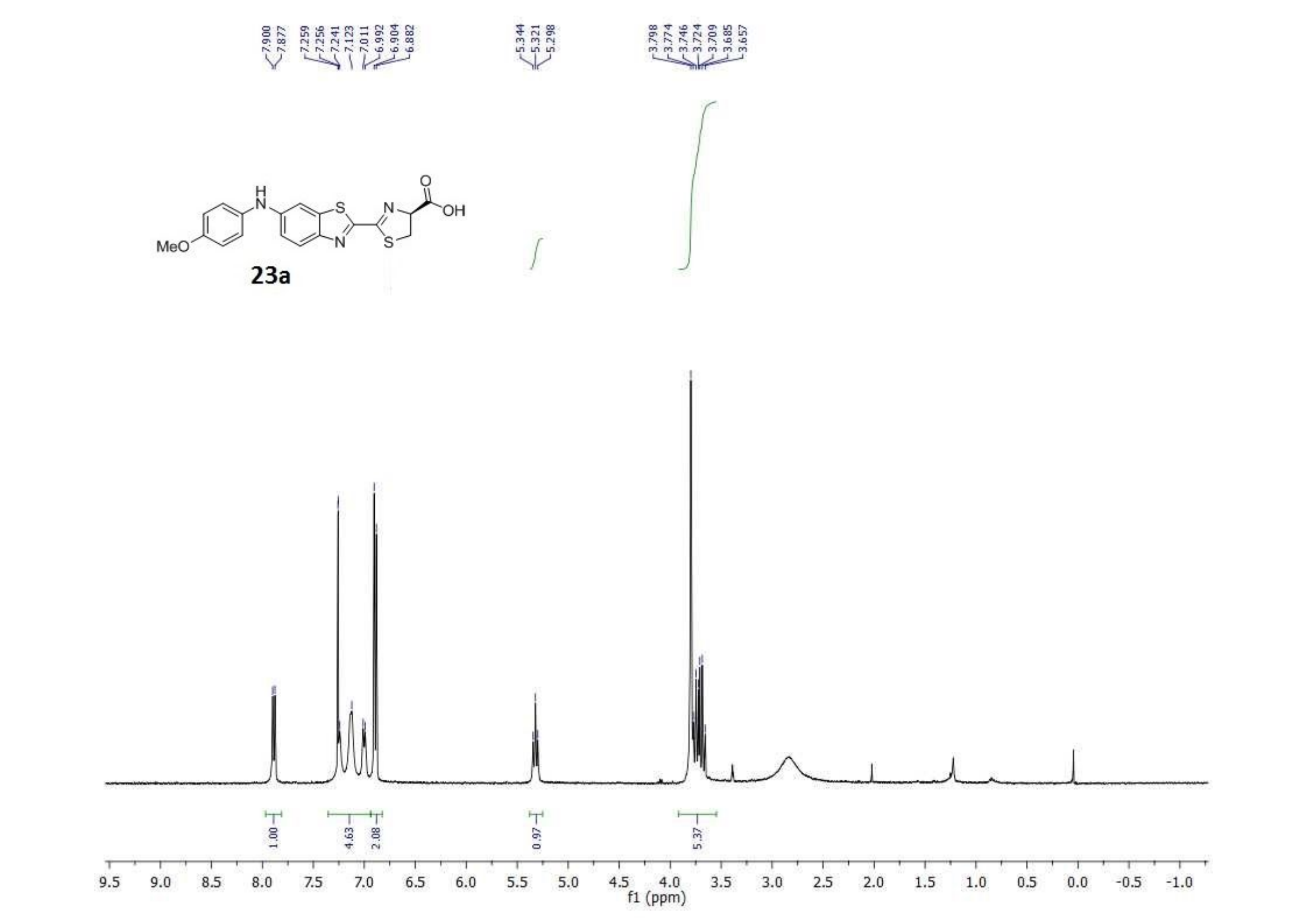
22a

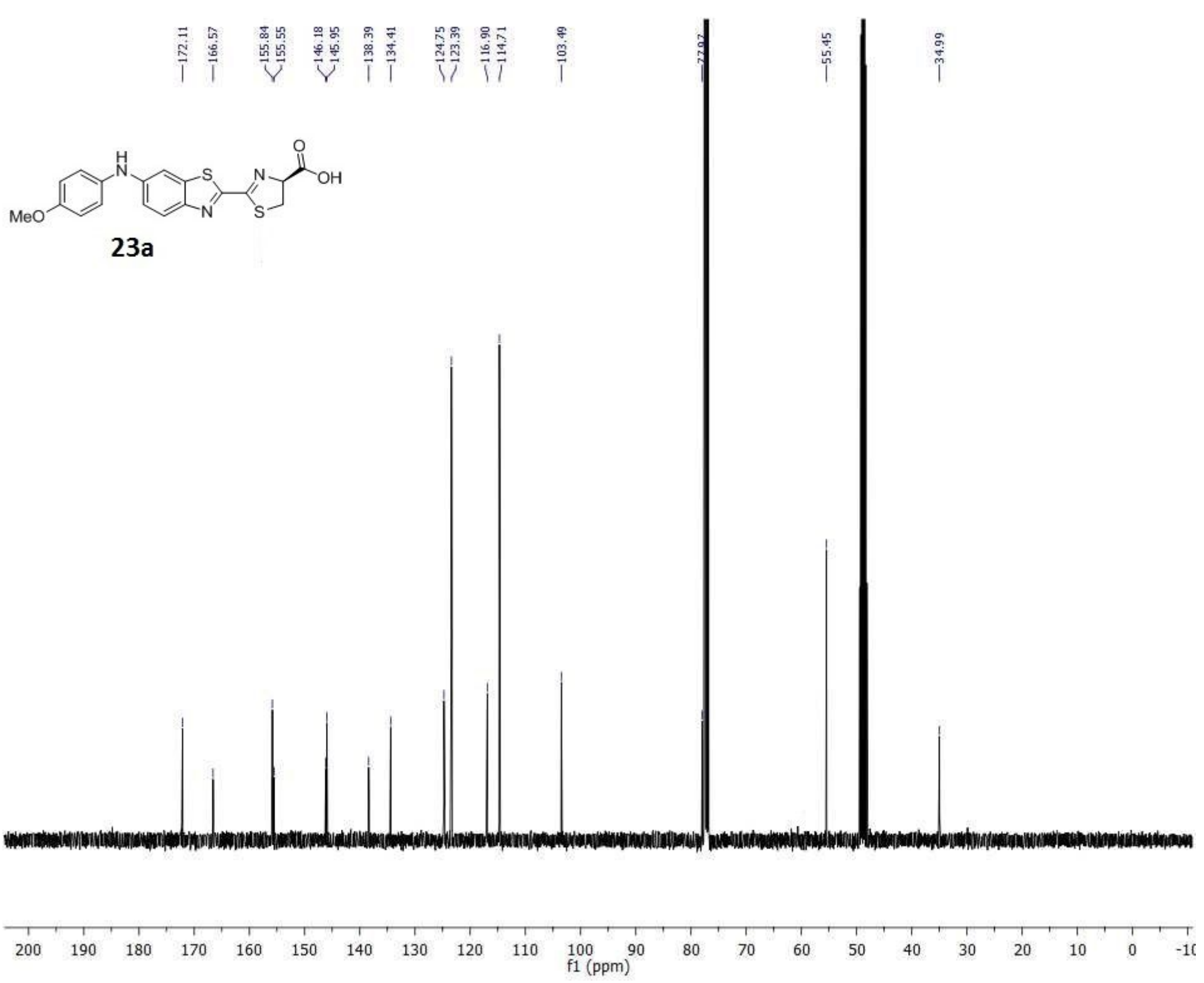

120.523
120.535
120.545
120.557
120.569
120.579
120.592

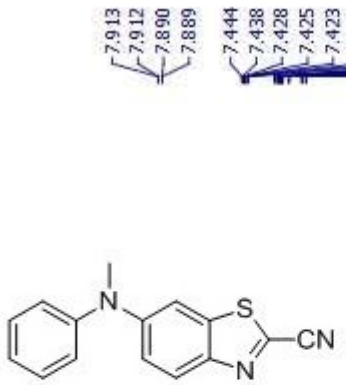

10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


7.864
7.841
7.222
7.217
7.131
7.126
7.109
7.108
7.090
7.084
6.882
6.860
3.770
H
N
S
CN
N
MeO
23
1.00
0.94
3.19
2.09
3.21
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


156.34
147.54
145.05
138.34
133.59
130.03
125.32
124.08
124.03
118.04
114.78
113.64
101.97
55.43
H
N
S
CN
N
MeO
23
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

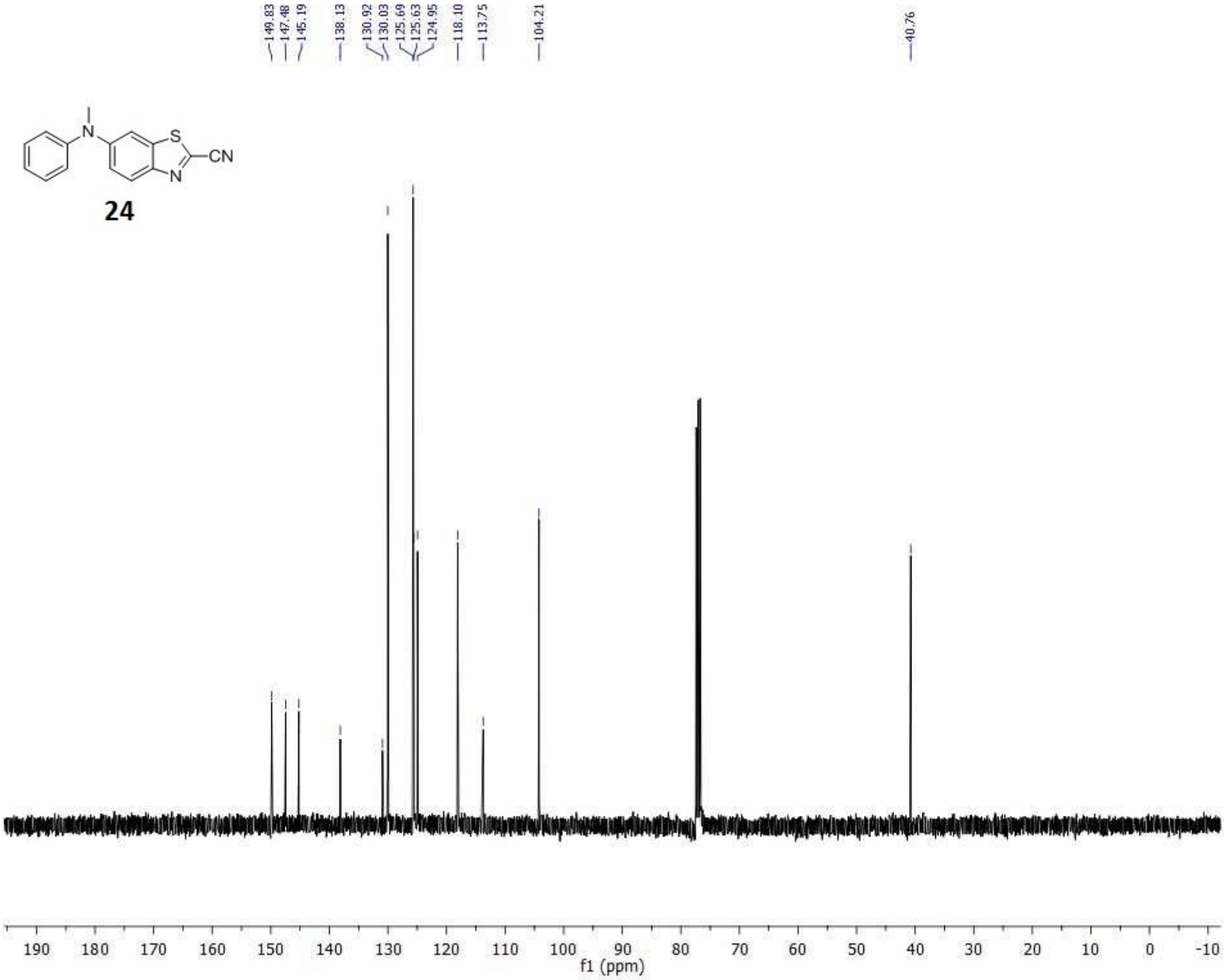

7.900
7.877
7.259
7.256
7.241
7.123
7.011
6.992
6.904
6.882
5.344
5.321
5.298
3.798
3.774
3.746
3.724
3.709
3.685
3.657
MeO
H
N
S
N
S
N
O
OH
23a
1.00
4.63
2.08
0.97
5.37
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

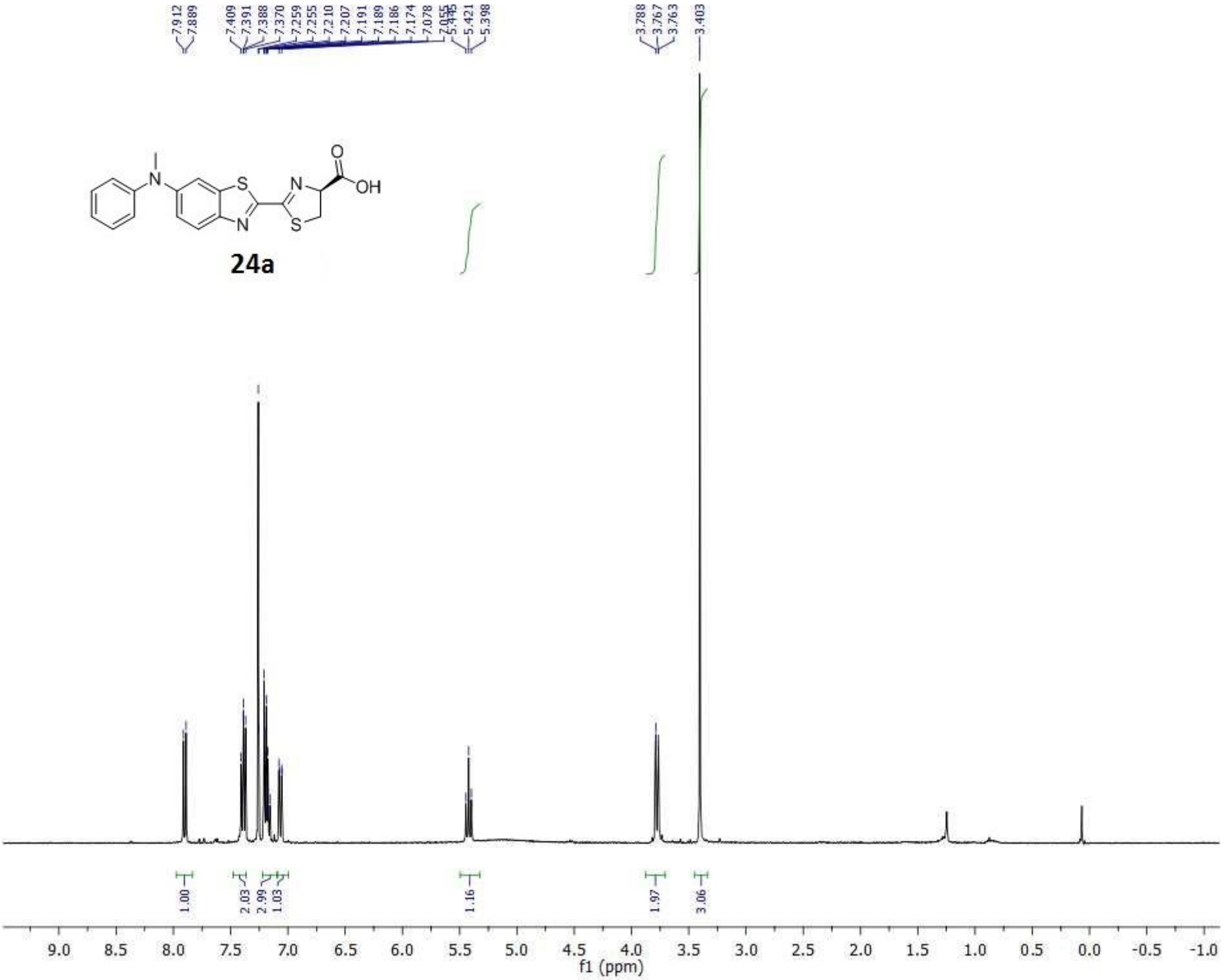

172.11
166.57
155.84
155.55
146.18
145.95
138.39
134.41
124.75
123.39
116.90
114.71
103.49
77.02
55.45
34.99
MeO
H
N
S
N
S
N
O
OH
23a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


N
S
CN
N

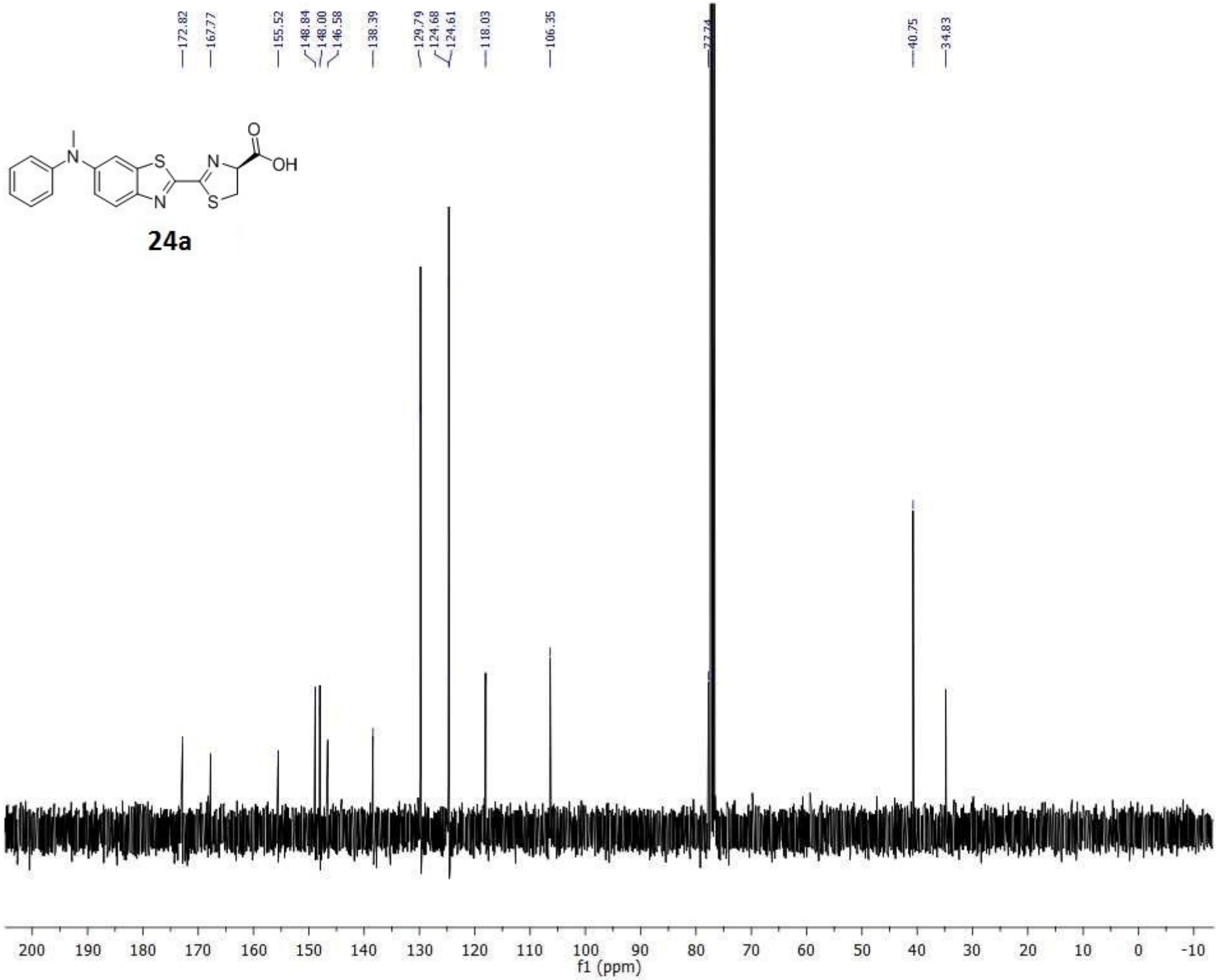
24

7.913
7.912
7.890
7.889
7.444
7.438
7.428
7.425
7.423
7.420
7.409
7.404
7.258
7.256
7.244
7.241
7.239
7.235
7.232
7.230
7.227
7.225
7.222
7.219
7.216
7.214
7.211
7.181
7.175
7.109
7.103
7.086
3.512
1.00
2.11
4.47
1.23
3.53
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

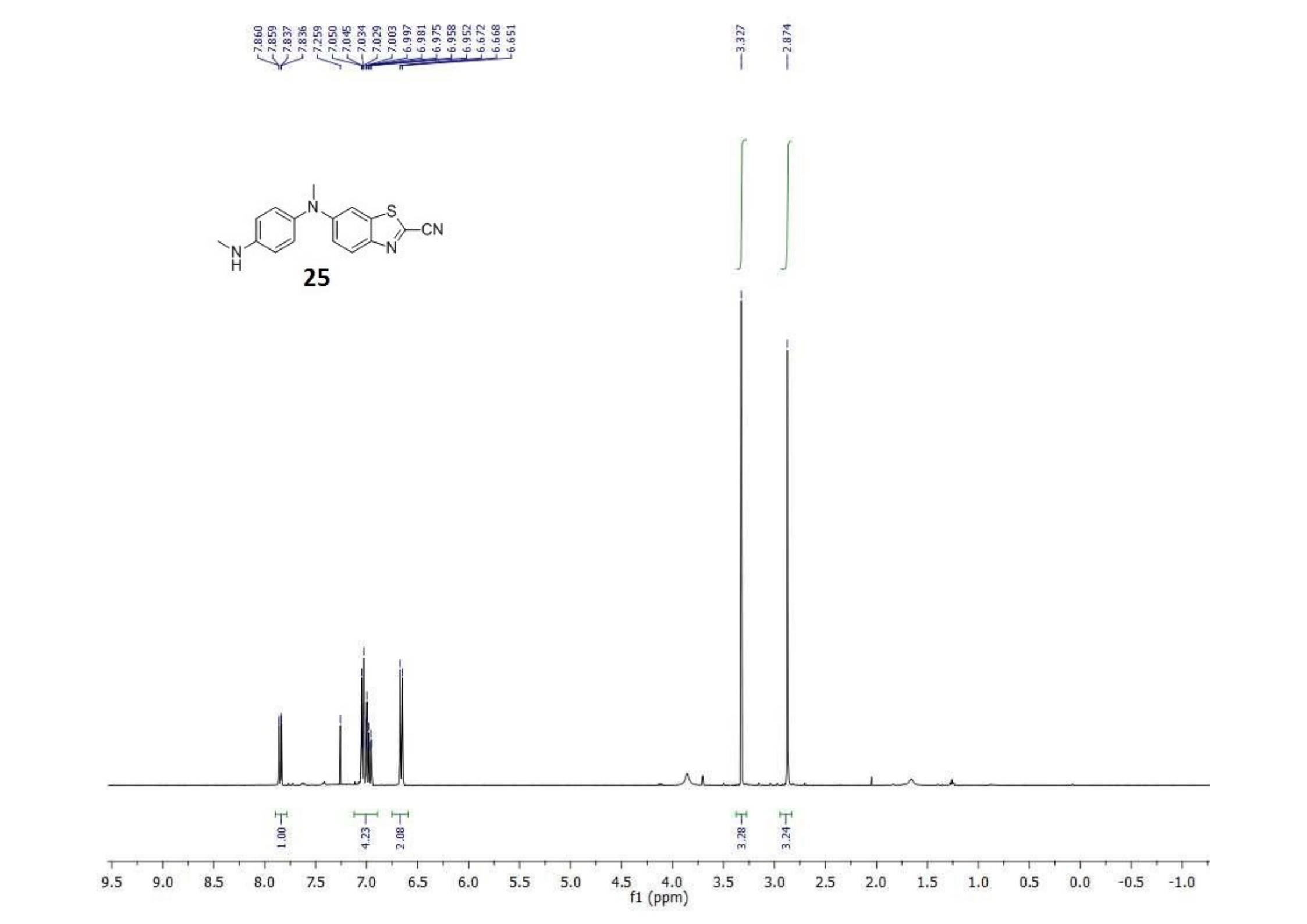

149.83
147.48
145.19
138.13
130.92
130.03
125.69
125.63
124.95
118.10
113.75
104.21
40.76
N
S
CN
N
24
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

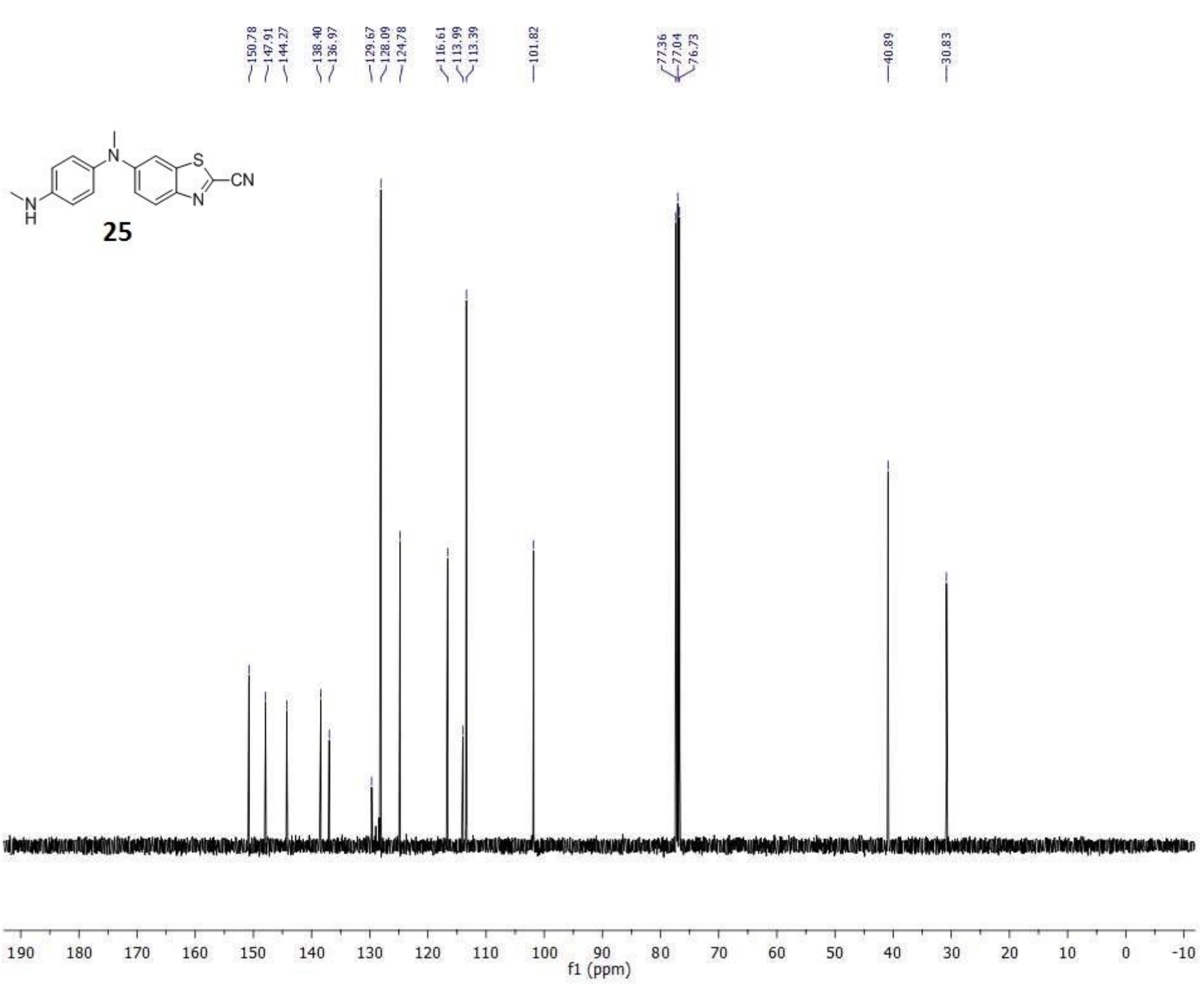

7.912
7.889
7.409
7.391
7.388
7.370
7.259
7.255
7.210
7.207
7.191
7.189
7.186
7.174
7.078
5.421
5.398
3.788
3.767
3.763
3.403
N
S
N
S
O
OH
1.00
2.03
2.99
1.03
1.16
1.97
3.06
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

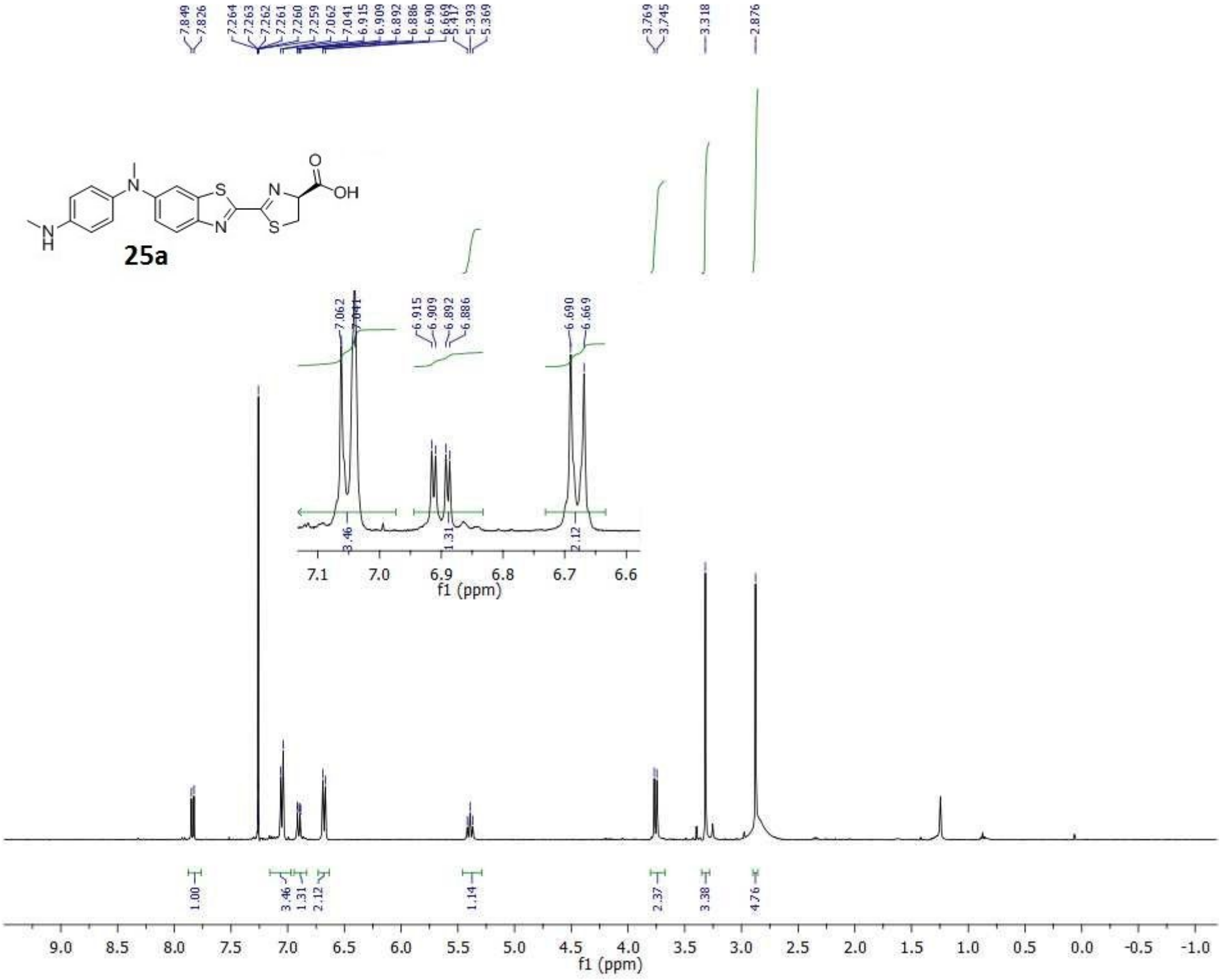
24a

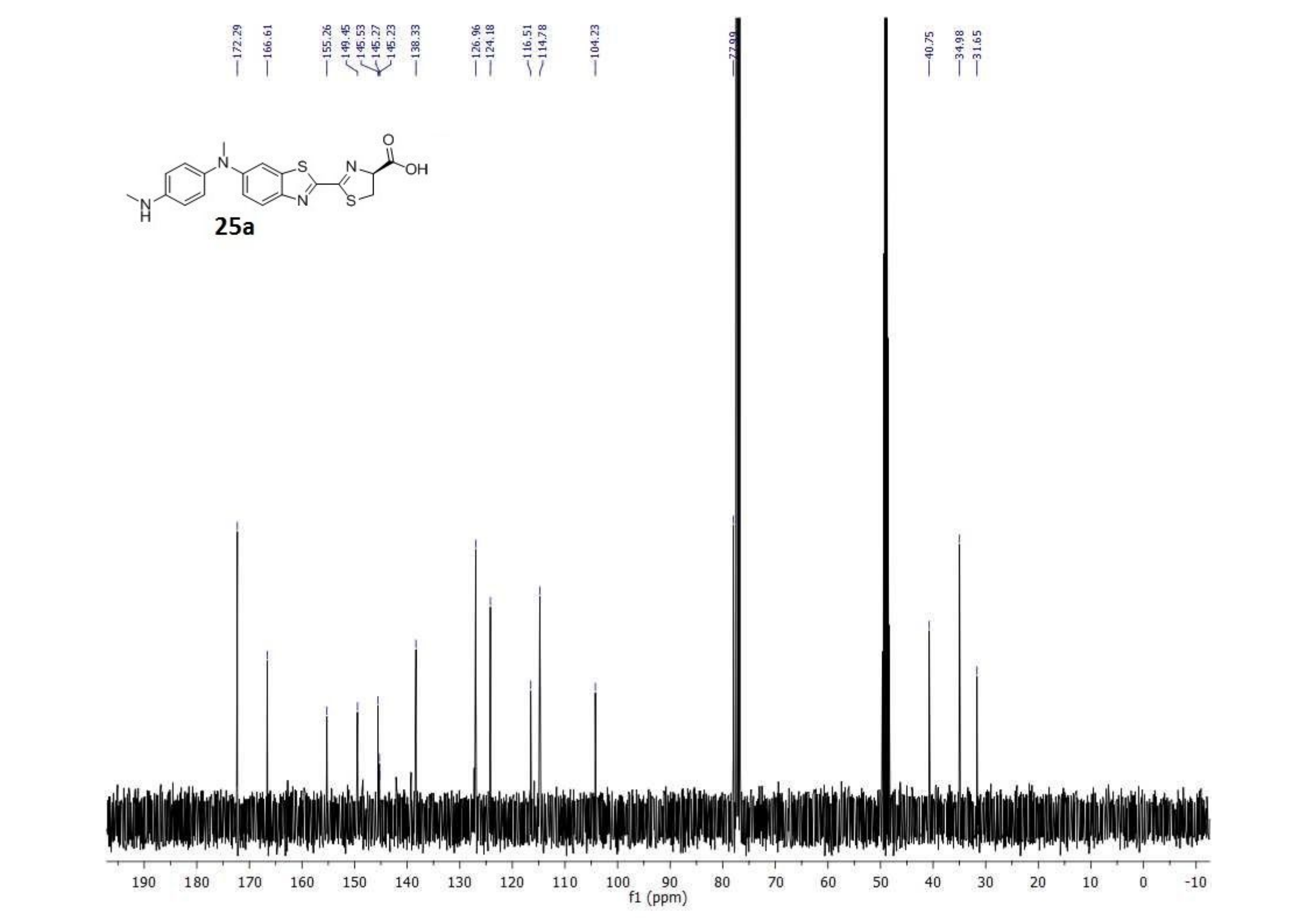

172.82
167.77
155.52
148.84
148.00
146.58
138.39
129.79
124.68
124.61
118.03
106.35
77.24
40.75
34.83
N
S
N
S
O
OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

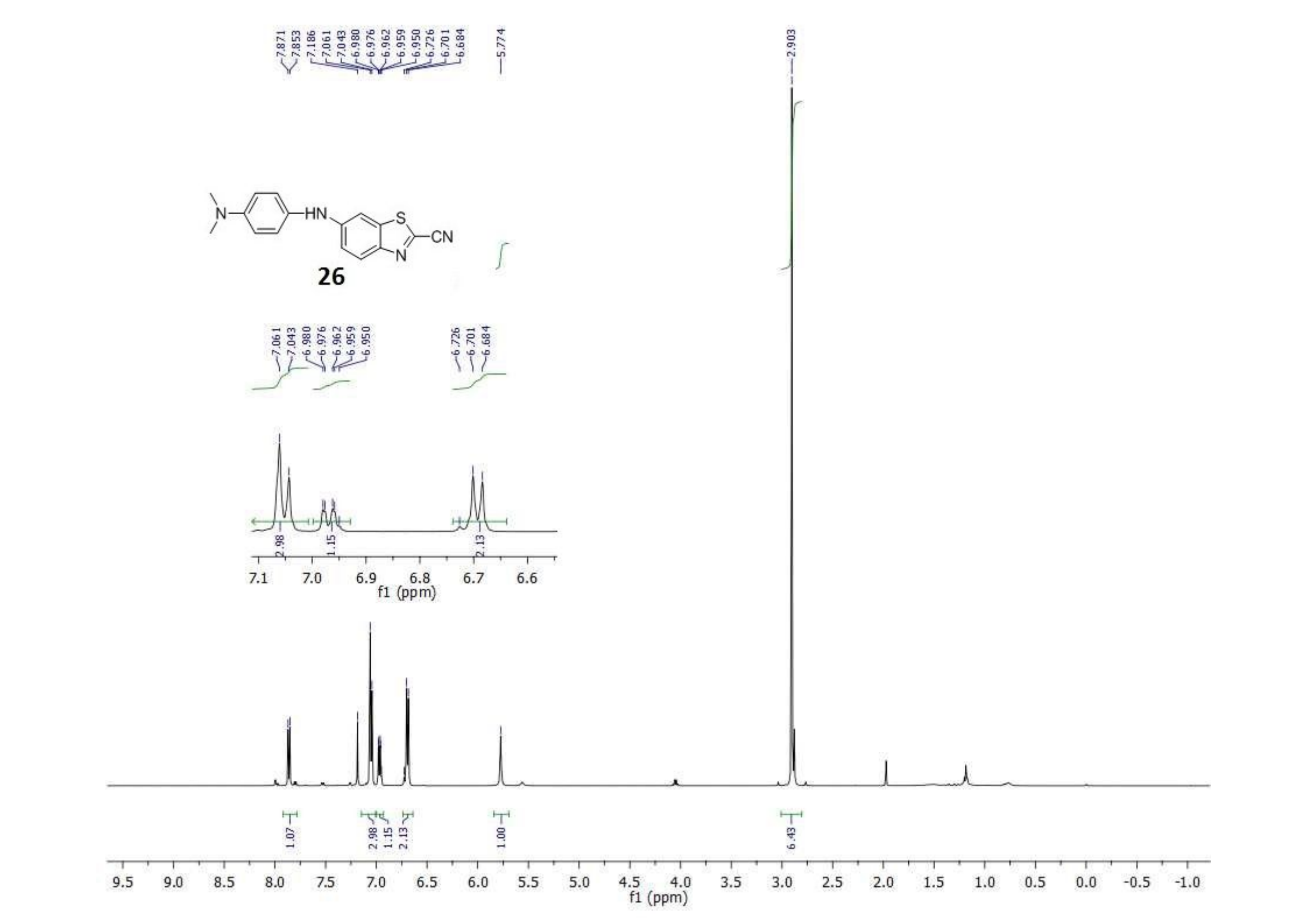
24a

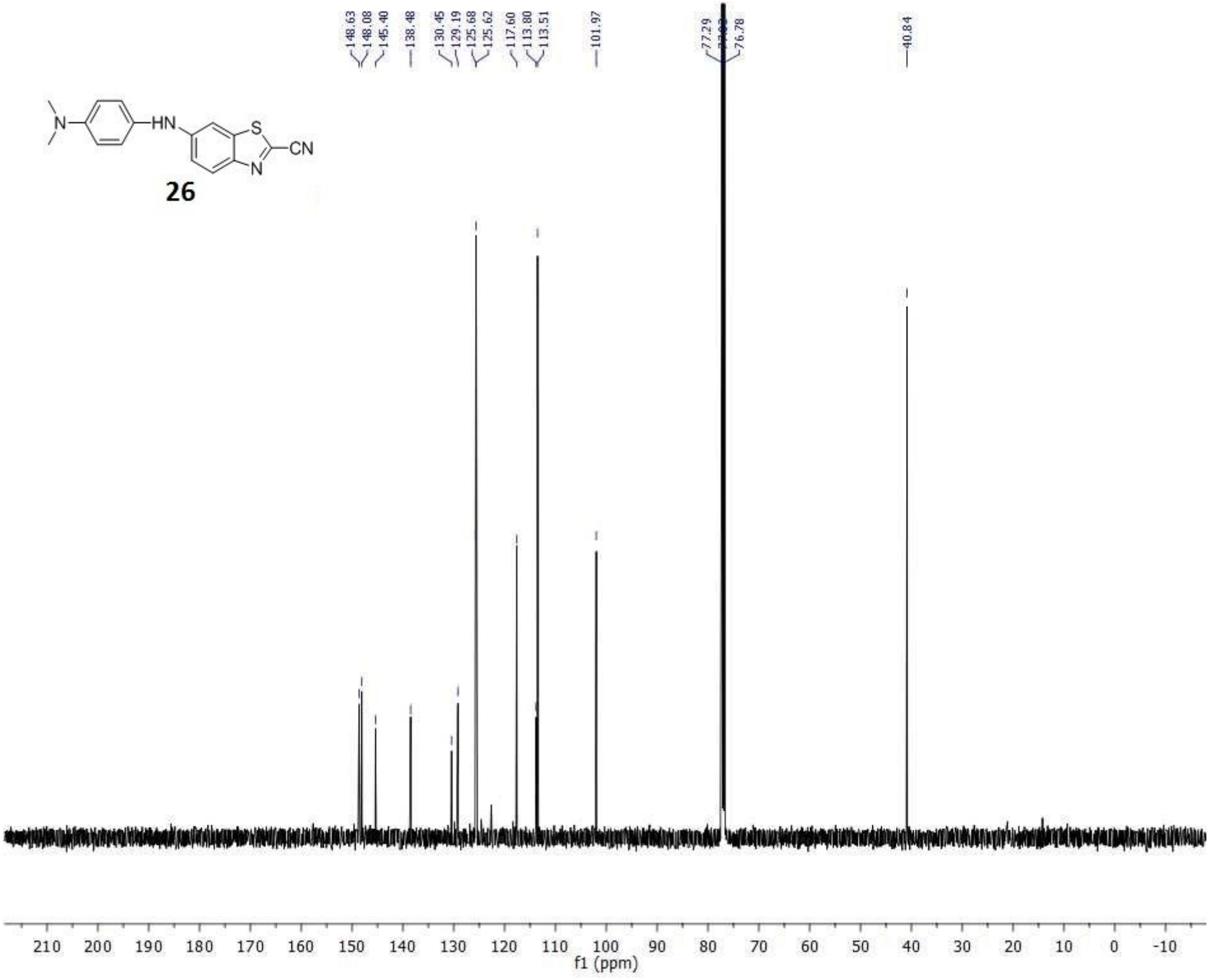

7.860
7.859
7.837
7.836
7.259
7.050
7.045
7.034
7.029
7.003
6.997
6.981
6.975
6.958
6.952
6.672
6.668
6.651
3.327
2.874
N
S
CN
N
N
H
25
1.00
4.23
2.08
3.28
3.24
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

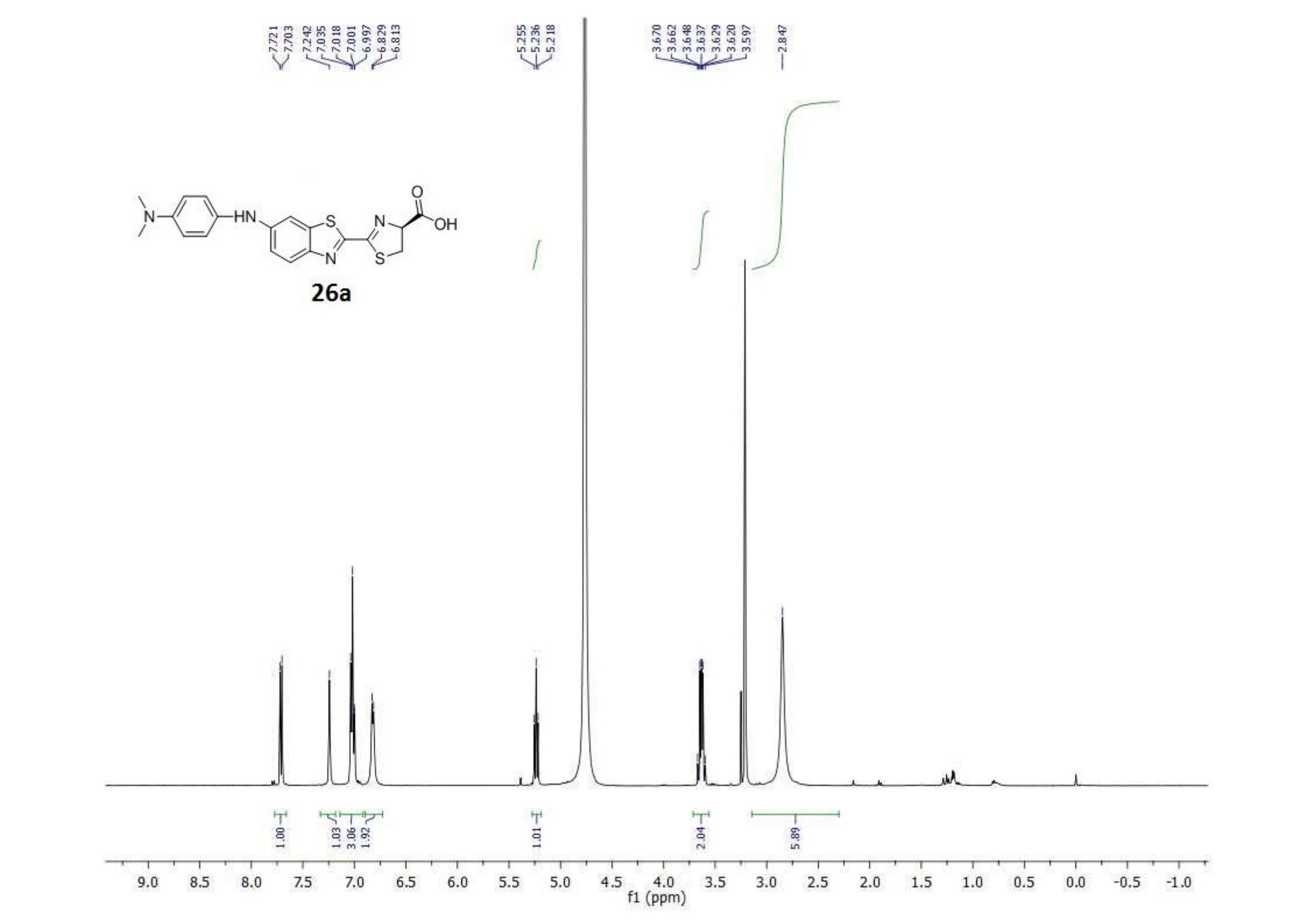

150.78
147.91
144.27
138.40
136.97
129.67
128.09
124.78
116.61
113.99
113.39
101.82
77.36
77.04
76.73
40.89
30.83
N
S
CN
N
N
H
25
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

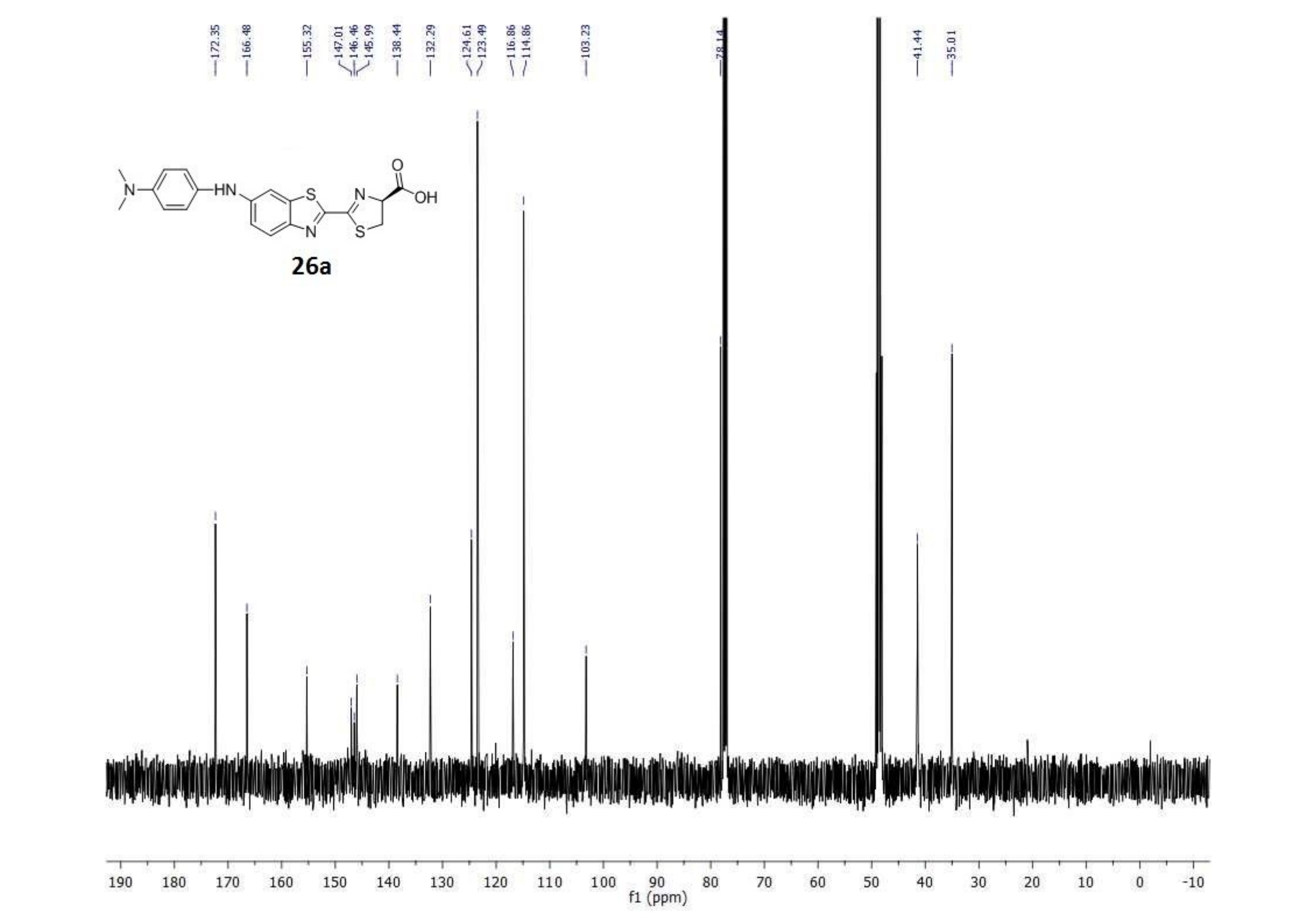

7.849
7.826
7.264
7.263
7.262
7.261
7.260
7.259
7.062
7.041
6.915
6.909
6.892
6.886
6.690
6.669
5.417
5.393
5.369
3.769
3.745
3.318
2.876
25a
7.062
7.041
6.915
6.909
6.892
6.886
6.690
6.669
3.46
1.31
2.12
7.1
7.0
6.9
6.8
6.7
6.6
f1 (ppm)
1.00
3.46
1.31
2.12
1.14
2.37
3.38
4.76
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

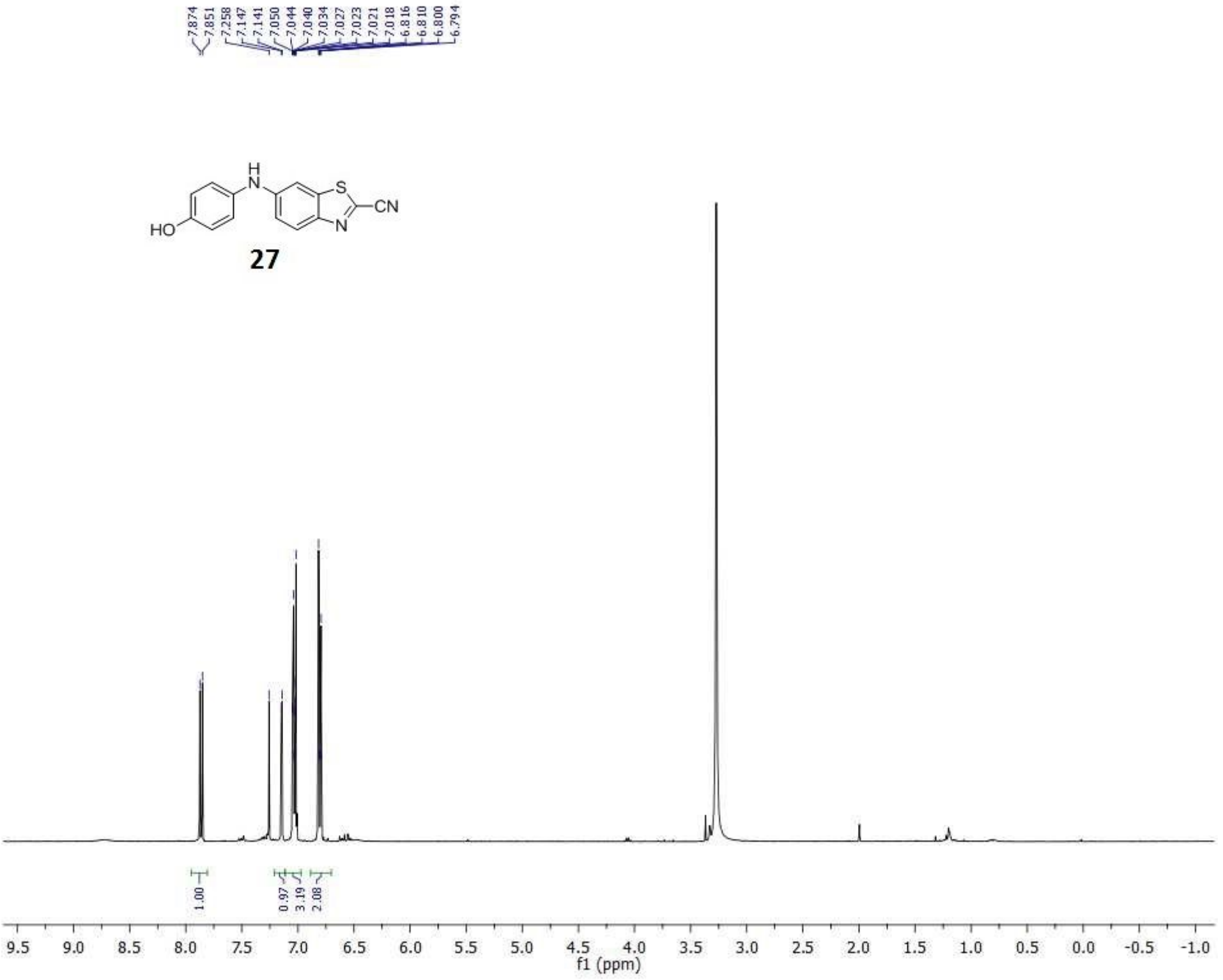

172.29
166.61
155.26
149.45
145.53
145.27
145.23
138.33
126.96
124.18
116.51
114.78
104.23
77.99
40.75
34.98
31.65
O
OH
N
S
N
S
N
H
25a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

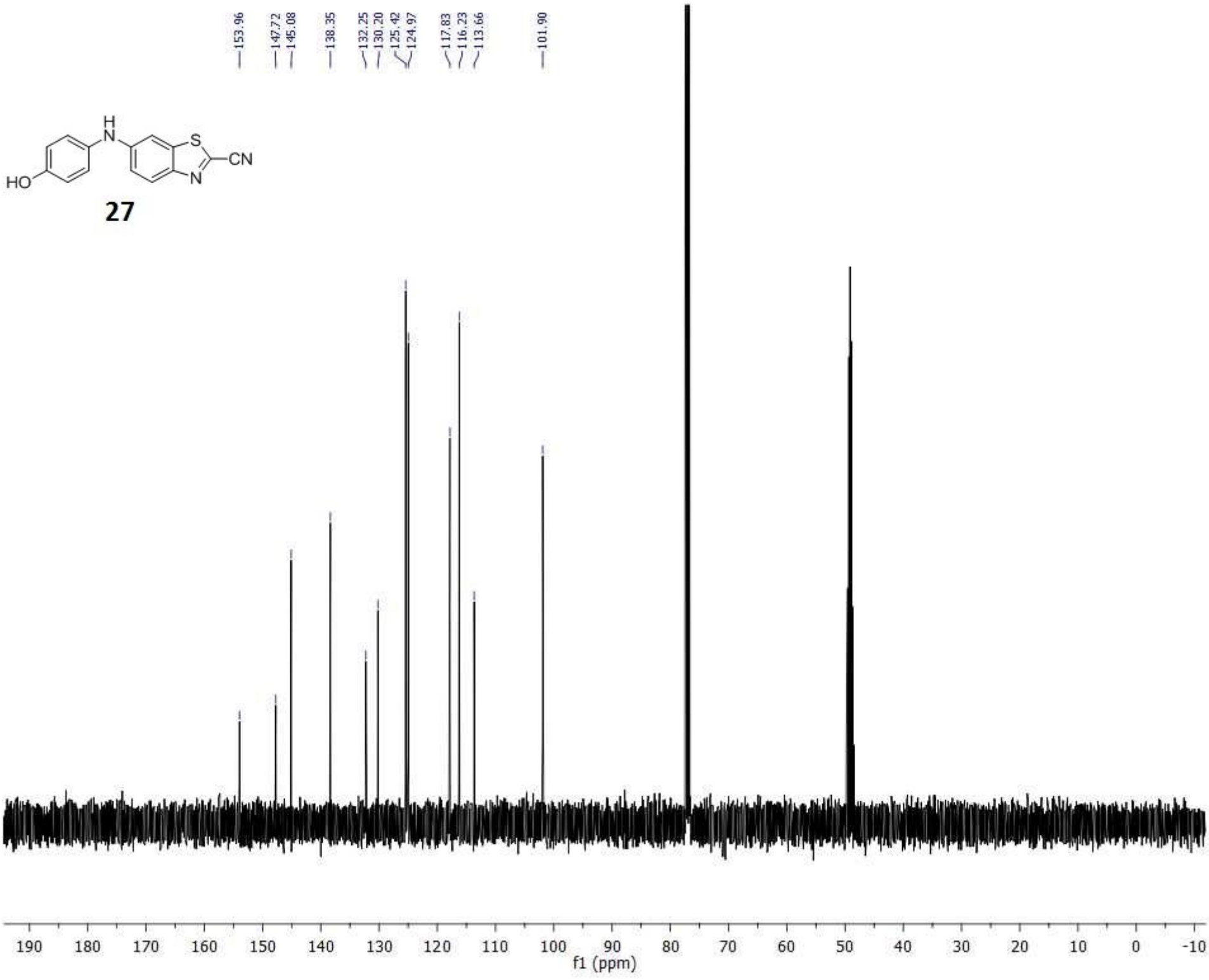

7.871
7.853
7.186
7.061
7.043
6.980
6.976
6.962
6.959
6.950
6.726
6.701
6.684
5.774
2.903
N
HN
S
CN
N
26
7.061
7.043
6.980
6.976
6.962
6.959
6.950
6.726
6.701
6.684
2.98
1.15
2.13
7.1
7.0
6.9
6.8
6.7
6.6
f1 (ppm)
1.07
2.98
1.15
2.13
1.00
6.43
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

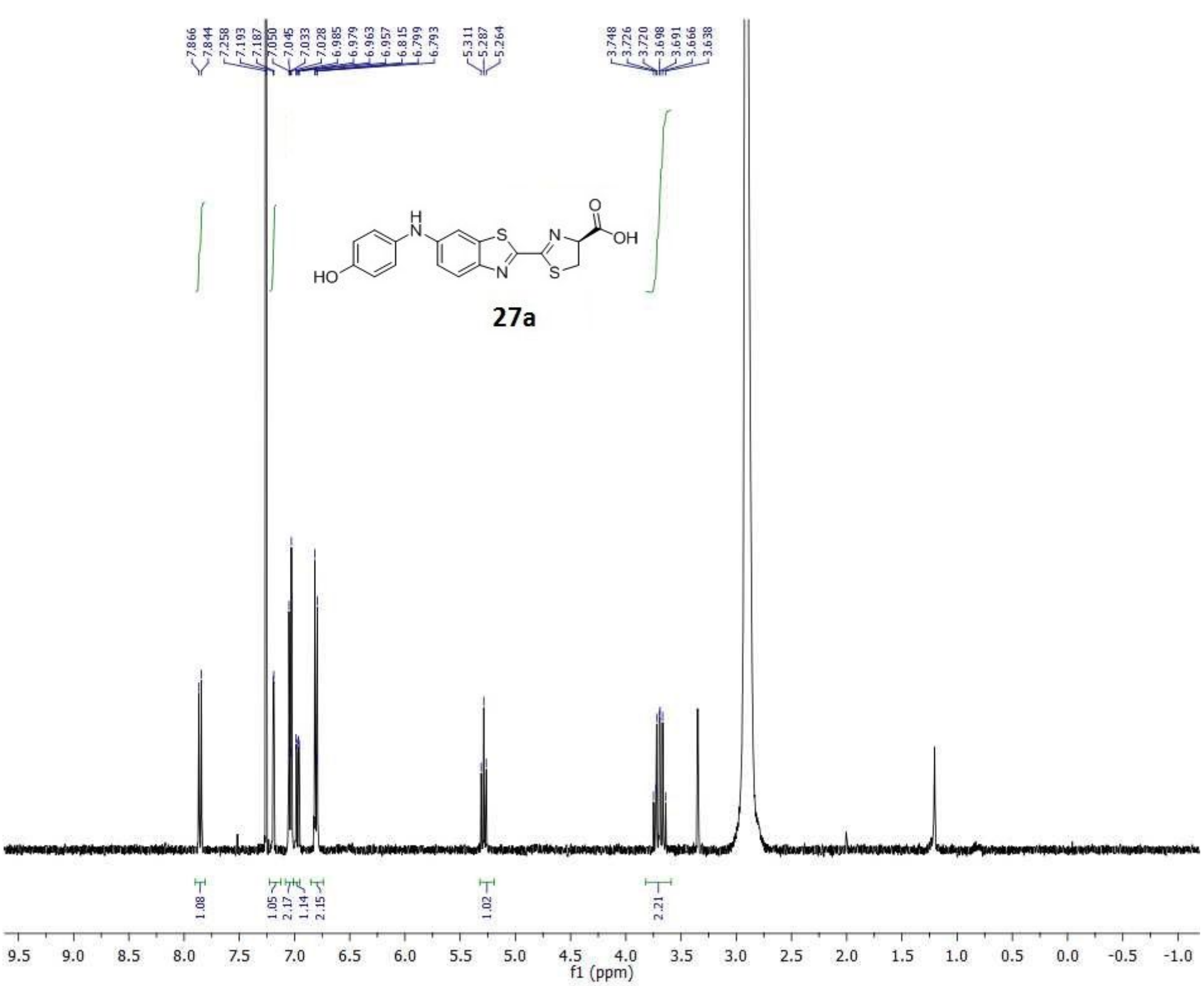

148.63
148.08
145.40
138.48
130.45
129.19
125.68
125.62
117.60
113.80
113.51
101.97
77.29
76.78
40.84
N
HN
S
CN
N
26
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.721
7.703
7.242
7.035
7.018
7.001
6.997
6.829
6.813
5.255
5.236
5.218
3.670
3.662
3.648
3.637
3.629
3.620
3.597
2.847
N
HN
S
N
N
S
O
OH
26a
1.00
1.03
3.06
1.92
1.01
2.04
5.89
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


172.35
166.48
155.32
147.01
146.46
145.99
138.44
132.29
124.61
123.49
116.86
114.86
103.23
78.14
41.44
35.01
N
HN
S
N
N
S
O
OH
26a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.874
7.851
7.258
7.147
7.141
7.050
7.044
7.040
7.034
7.027
7.023
7.021
7.018
6.816
6.810
6.800
6.794
H
N
S
CN
N
HO
27
1.00
0.97
3.19
2.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


153.96
147.72
145.08
138.35
132.25
130.20
125.42
124.97
117.83
116.23
113.66
101.90
HO
N
H
S
CN
N
27
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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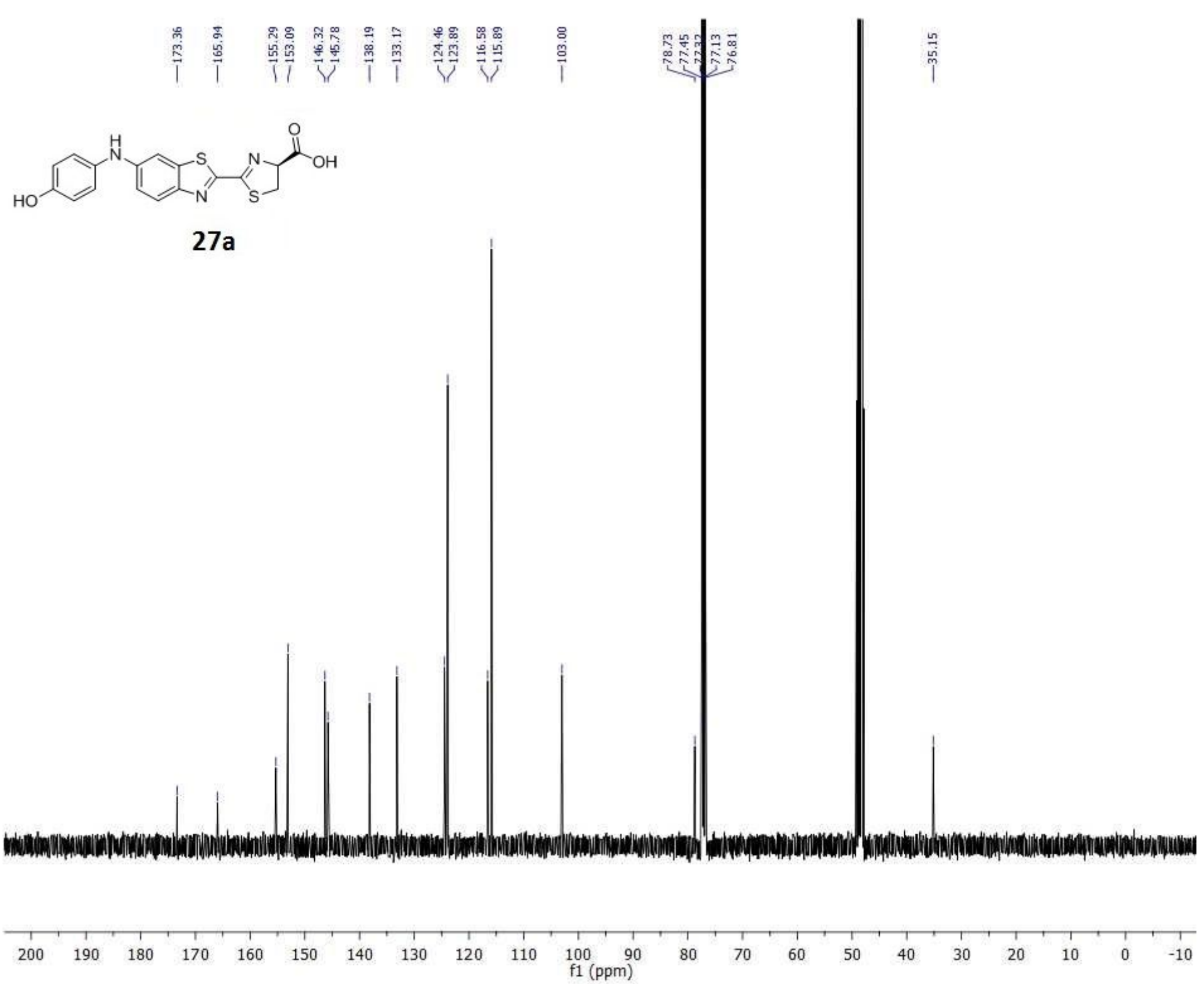
7.844
7.258
7.193
7.187
7.050
7.045
7.033
7.028
6.985
6.979
6.963
6.957
6.815
6.799
6.793
5.311
5.287
5.264
3.748
3.726
3.720
3.698
3.691
3.666
3.638
HO
H
N
S
N
S
N
O
OH
1.08
1.05
2.17
1.14
2.15
1.02
2.21
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

27a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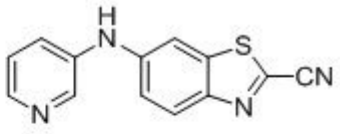
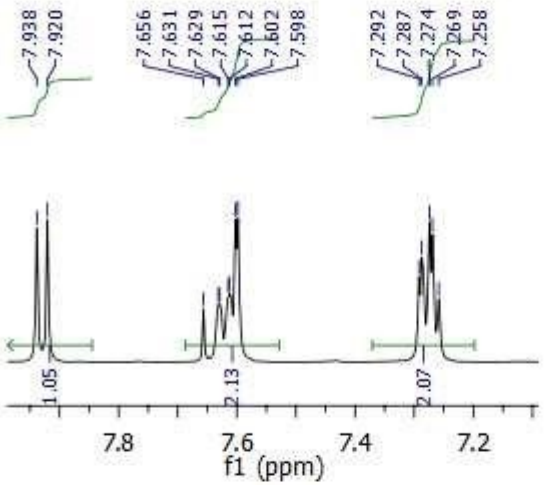
165.94
155.29
153.09
146.32
145.78
138.19
133.17
124.46
123.89
116.58
115.89
103.00
78.73
77.45
77.32
77.13
76.81
35.15
HO
H
N
S
N
S
N
O
OH
27a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

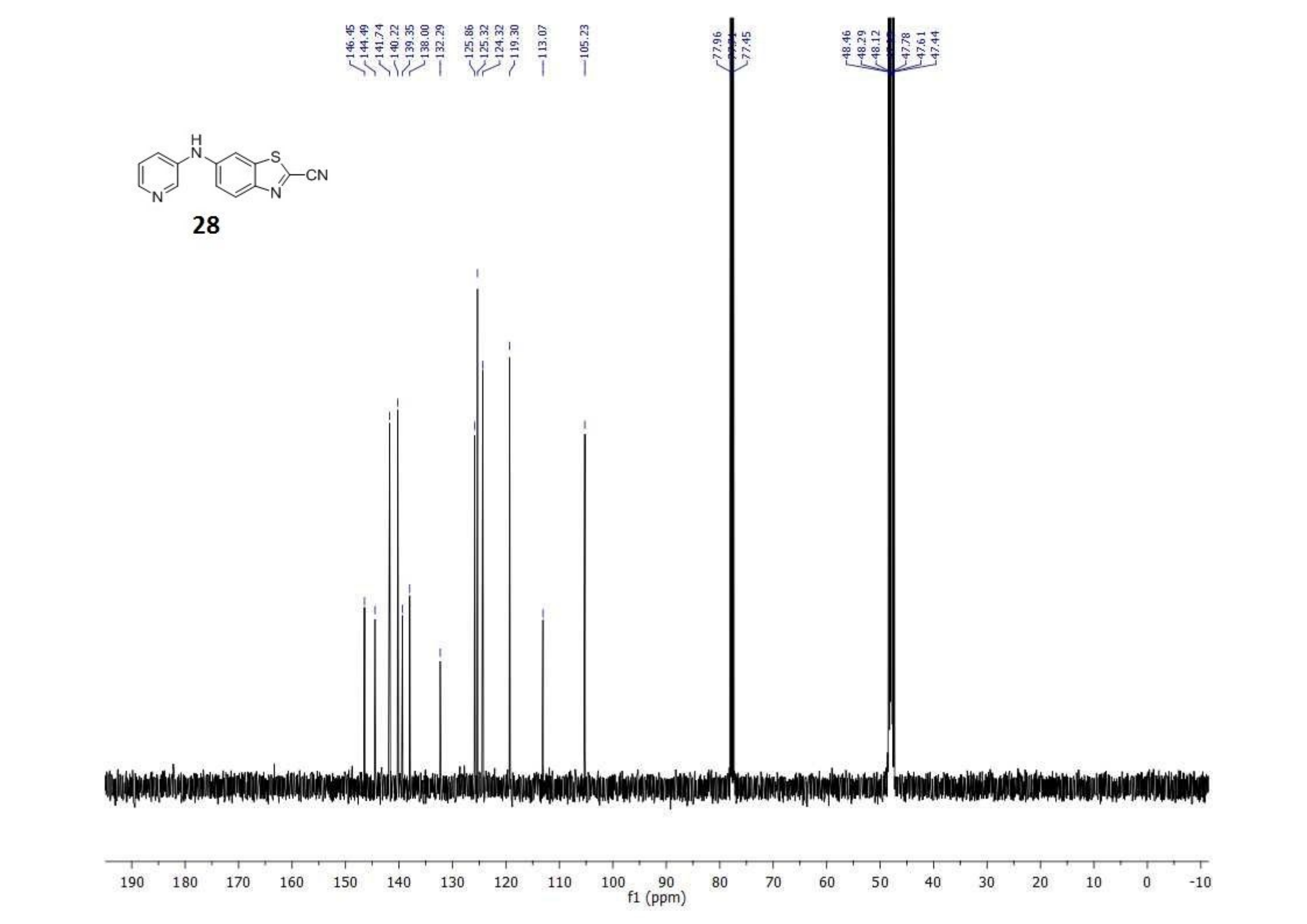

8.331
8.326
8.059
8.051
7.938
7.920
7.656
7.631
7.629
7.615
7.612
7.602
7.598
7.292
7.287
7.274
7.269
7.258

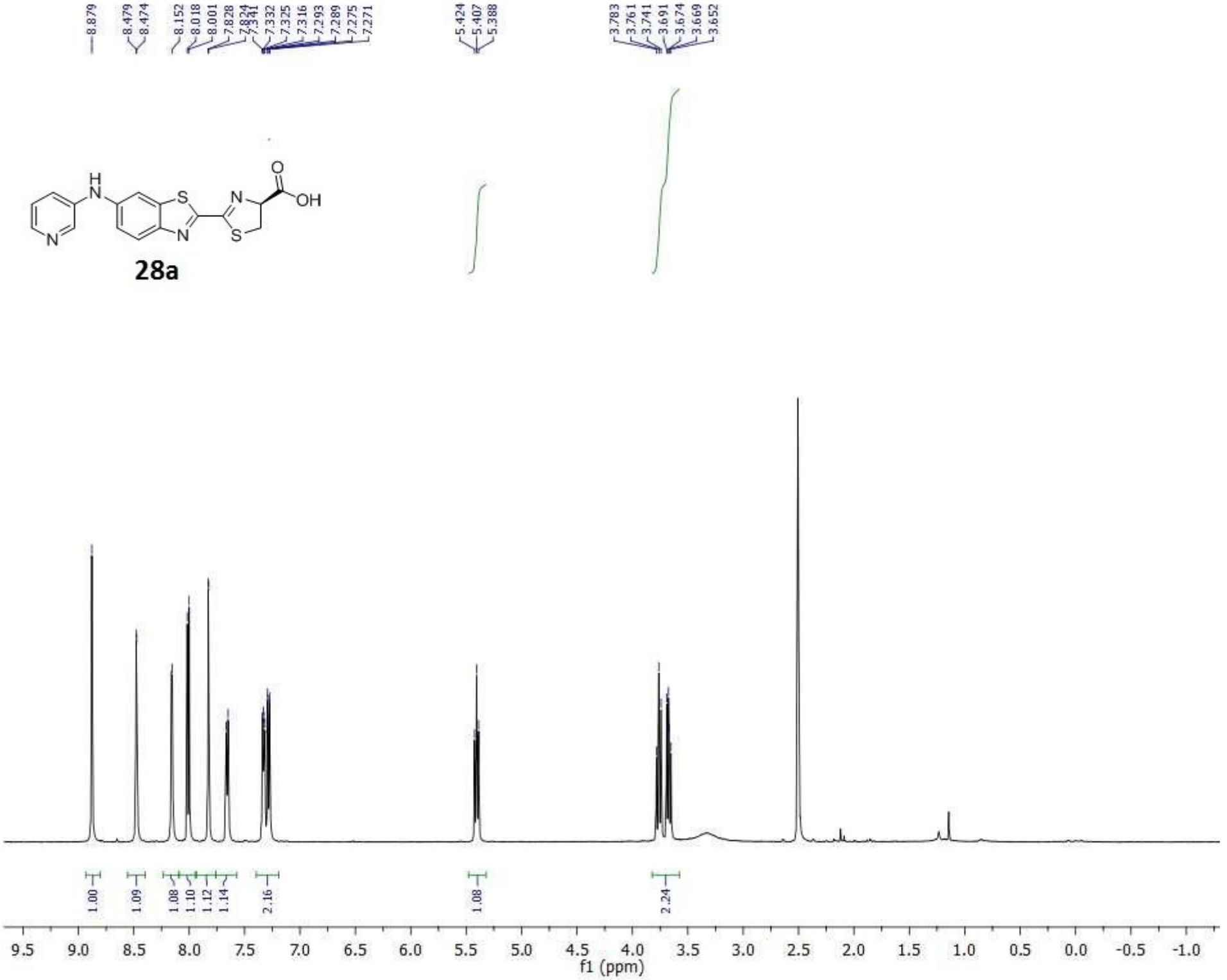

H
N
S
CN
N
N

28


7.938
7.920
7.656
7.631
7.629
7.615
7.612
7.602
7.598
7.292
7.287
7.274
7.269
7.258
1.05
2.13
2.07
7.8
7.6
7.4
7.2
f1 (ppm)

1.00
1.02
1.05
2.13
2.07
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


146.45
144.49
141.74
140.22
139.35
138.00
132.29
125.86
125.32
124.32
119.30
113.07
105.23
77.96
77.45
48.46
48.29
48.12
47.78
47.61
47.44
H
N
S
CN
N
N
28
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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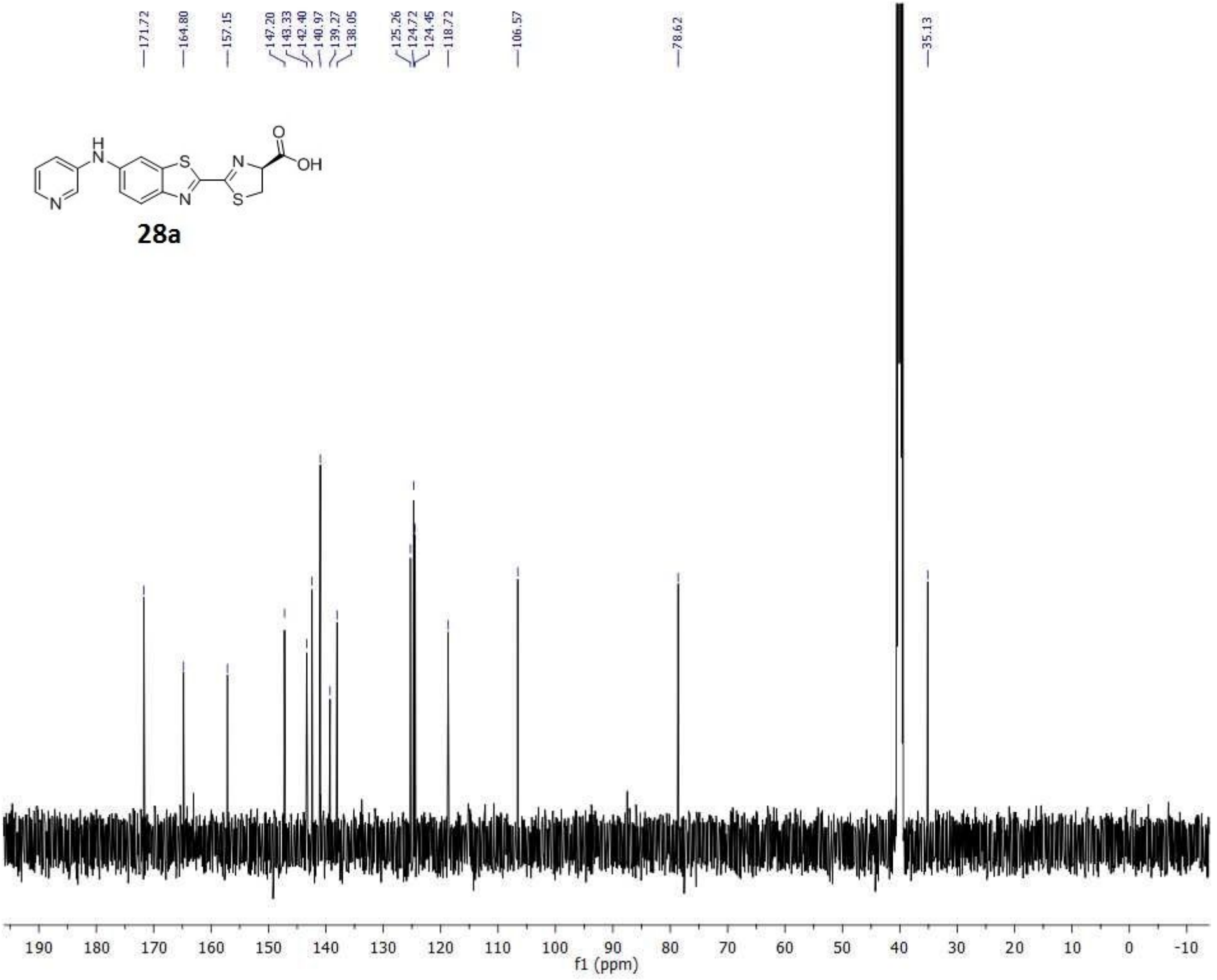
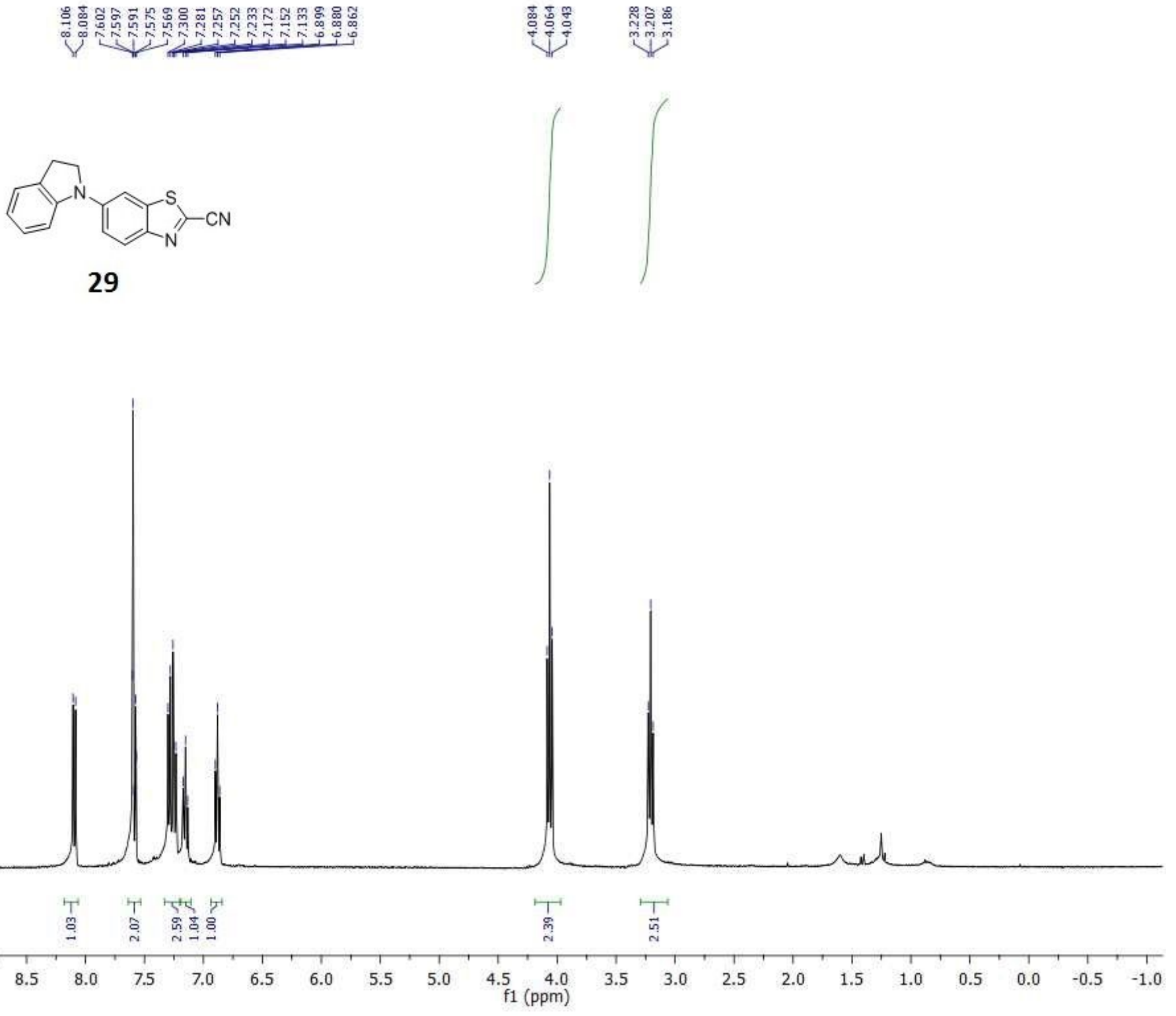
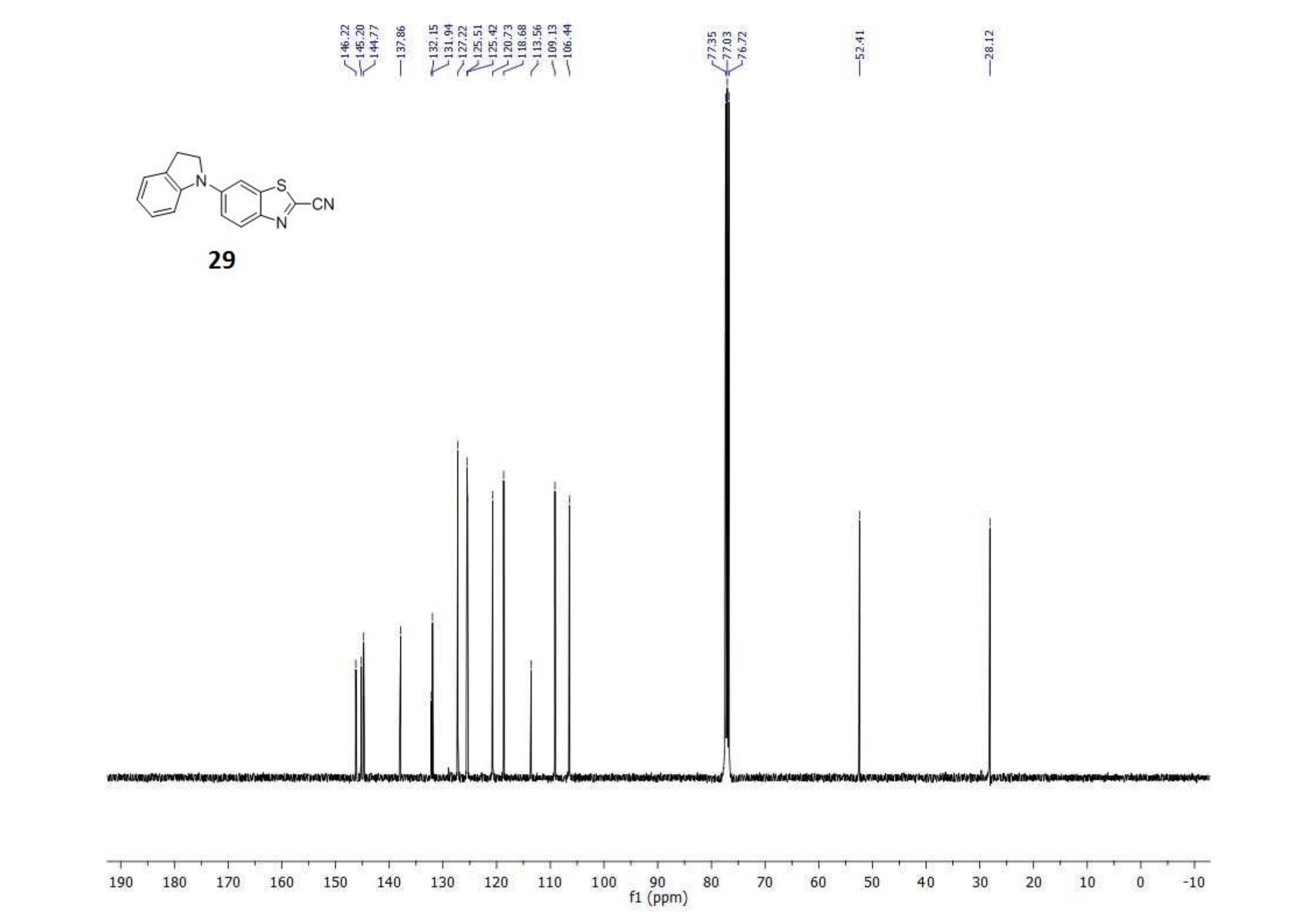
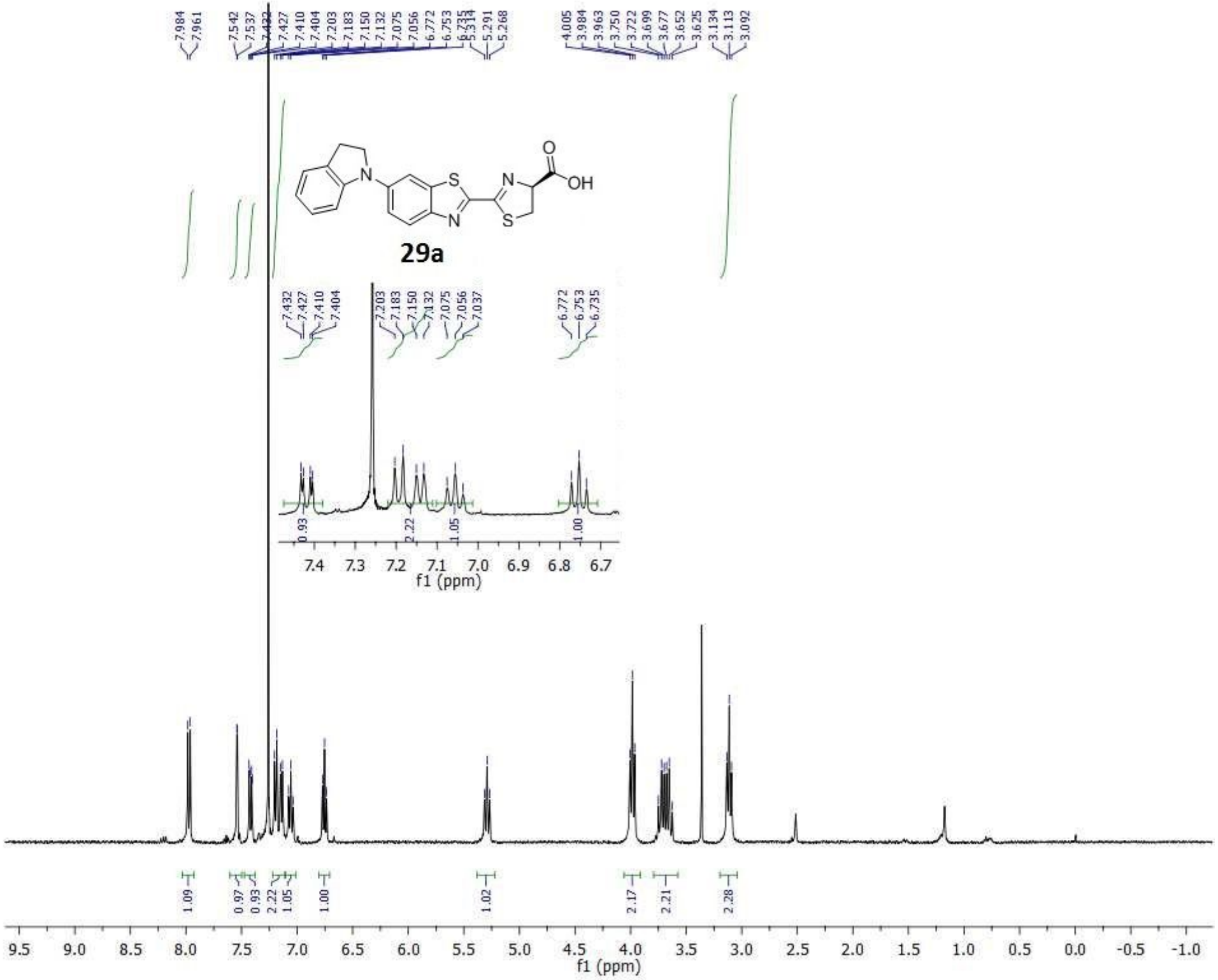
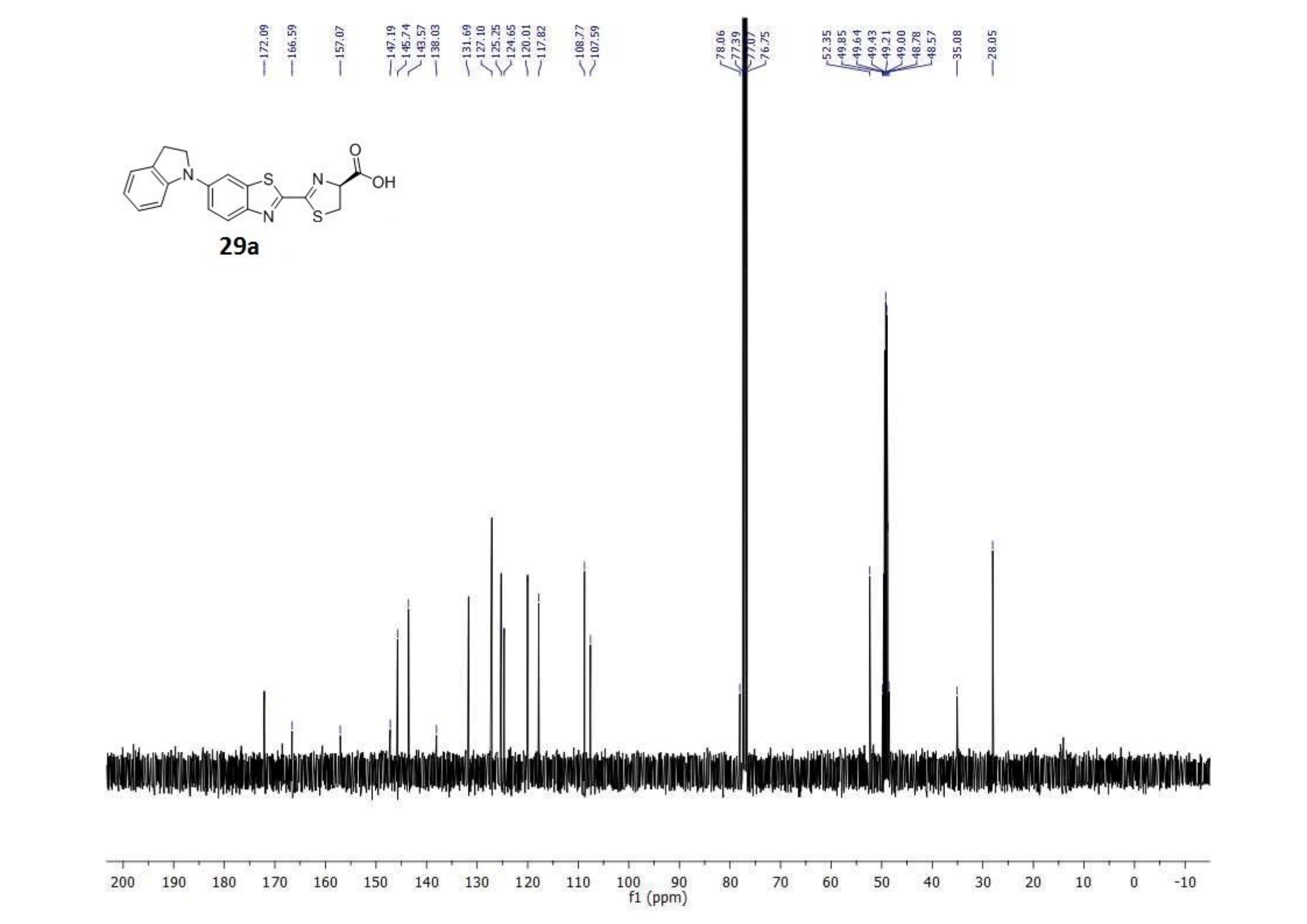
8.479
8.474
8.152
8.018
8.001
7.828
7.824
7.341
7.332
7.325
7.316
7.293
7.289
7.275
7.271
5.424
5.407
5.388
3.783
3.761
3.741
3.691
3.674
3.669
3.652
H
N
S
N
N
S
O
OH
28a
1.00
1.09
1.08
1.10
1.12
1.14
2.16
1.08
2.24
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


171.72
164.80
157.15
147.20
143.33
142.40
140.97
139.27
138.05
125.26
124.72
124.45
118.72
106.57
78.62
35.13
H
N
S
N
O
OH
N
N
S
28a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.106
8.084
7.602
7.597
7.591
7.575
7.569
7.300
7.281
7.257
7.252
7.233
7.172
7.152
7.133
6.899
6.880
6.862
4.084
4.064
4.043
3.228
3.207
3.186
N
S
CN
N
29
1.03
2.07
2.59
1.04
1.00
2.39
2.51
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


146.22
145.20
144.77
137.86
132.15
131.94
127.22
125.51
125.42
120.73
118.68
113.56
109.13
106.44
77.35
77.03
76.72
52.41
28.12
N
S
CN
N
29
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.984
7.961
7.542
7.537
7.432
7.427
7.410
7.404
7.203
7.183
7.150
7.132
7.075
7.056
6.772
6.753
6.735
5.314
5.291
5.268
4.005
3.984
3.963
3.750
3.722
3.699
3.677
3.652
3.625
3.134
3.113
3.092
N
S
N
S
O
OH
29a
7.432
7.427
7.410
7.404
7.203
7.183
7.150
7.132
7.075
7.056
7.037
6.772
6.753
6.735
0.93
2.22
1.05
1.00
7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7
f1 (ppm)
1.09
0.97
0.93
2.22
1.05
1.00
1.02
2.17
2.21
2.28
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0
f1 (ppm)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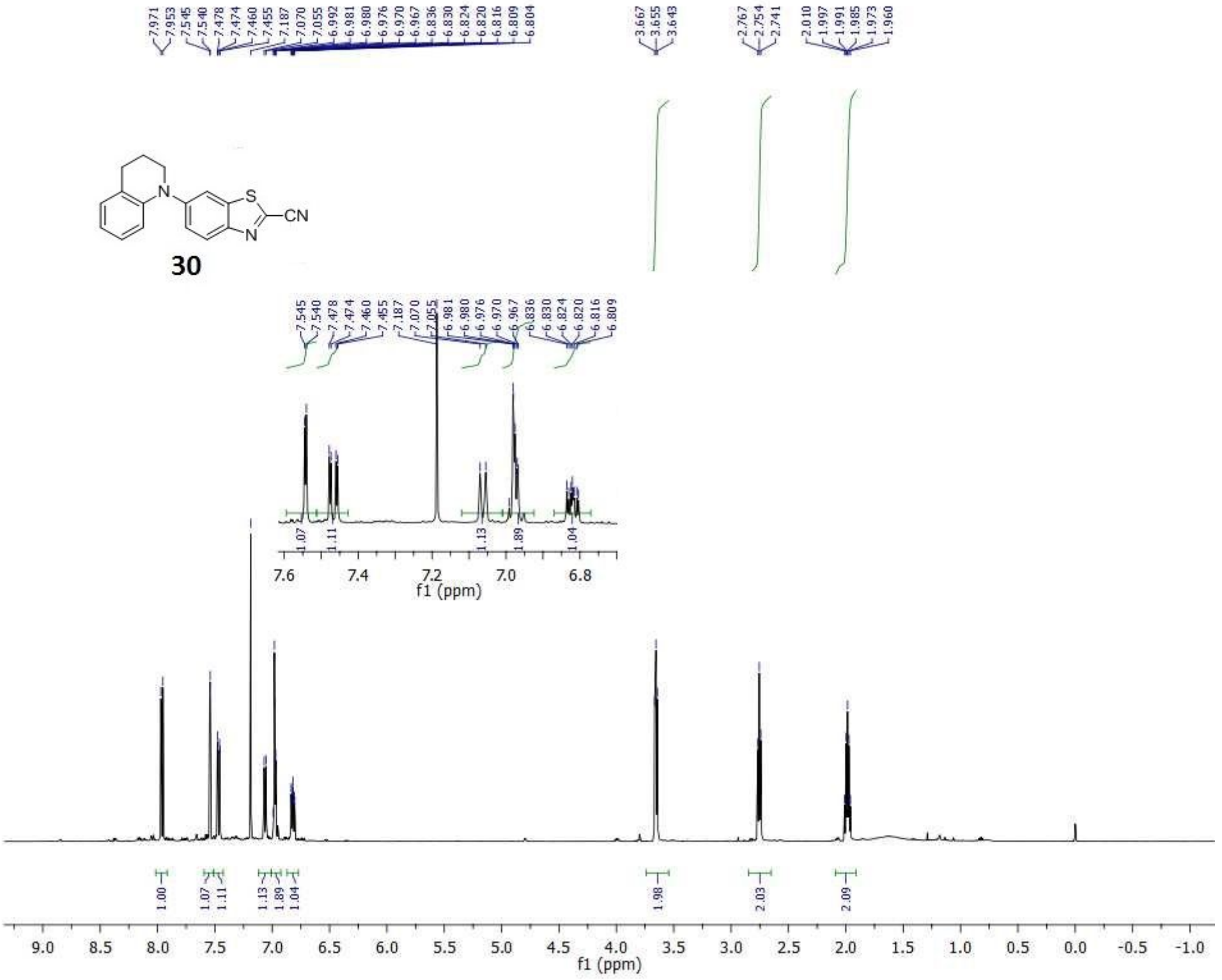
166.59
157.07
147.19
145.74
143.57
138.03
131.69
127.10
125.25
124.65
120.01
117.82
108.77
107.59
78.06
77.39
77.07
76.75
52.35
49.85
49.64
49.43
49.21
49.00
48.78
48.57
35.08
28.05
O
OH
N
S
N
N
S
29a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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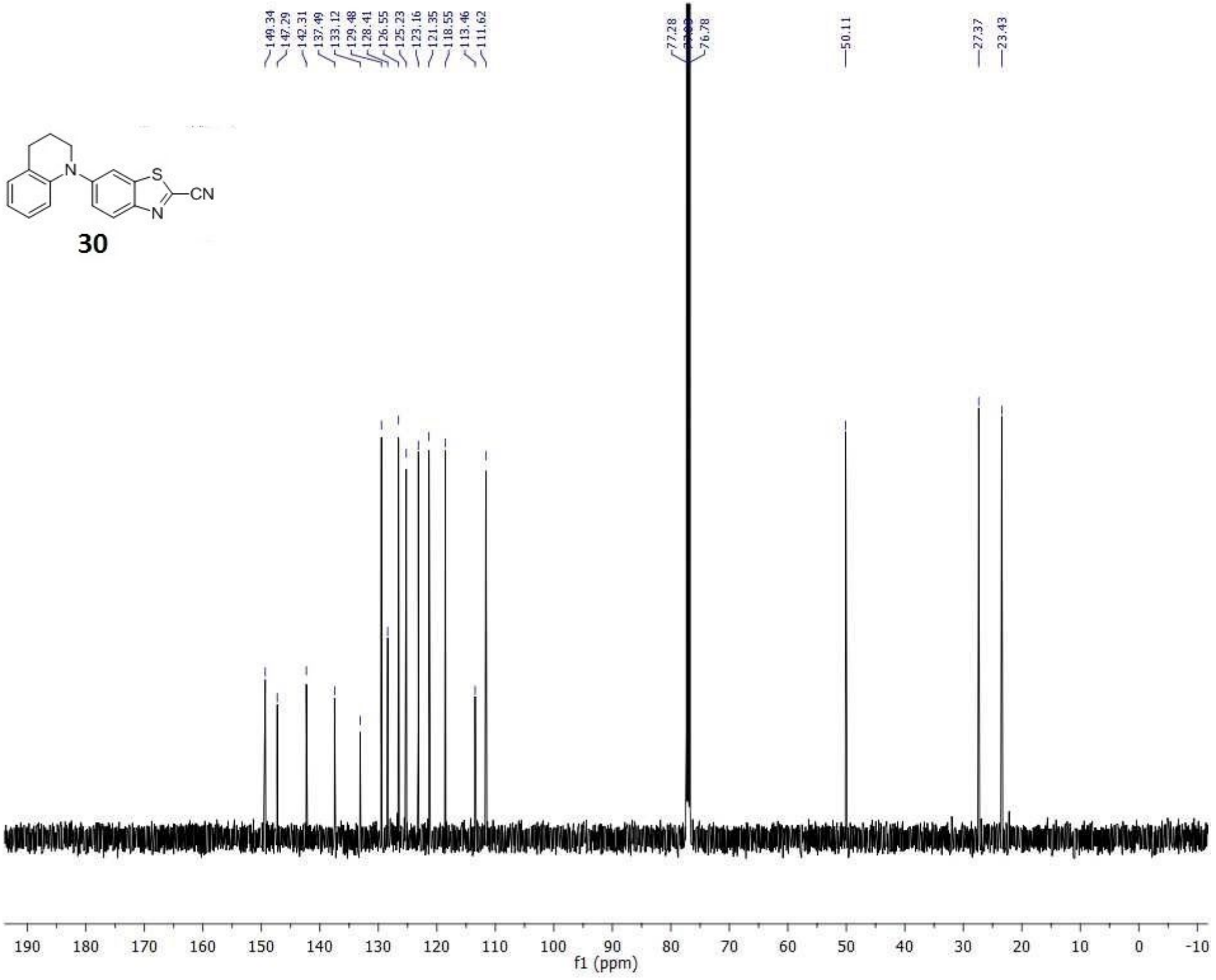
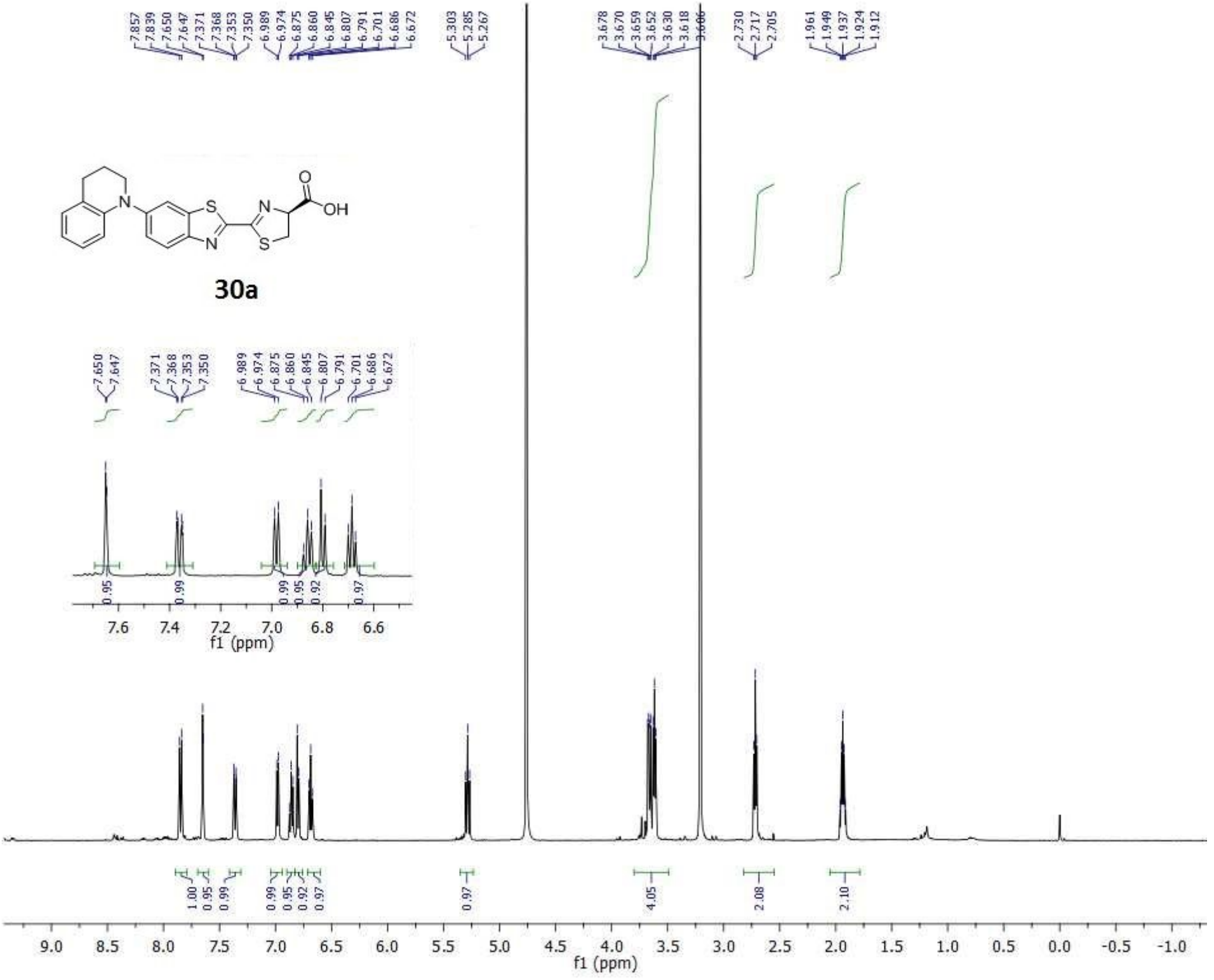
7.540
7.478
7.474
7.460
7.455
7.187
7.070
7.055
6.992
6.981
6.980
6.976
6.970
6.967
6.836
6.830
6.824
6.820
6.816
6.809
6.804
3.667
3.655
3.643
2.767
2.754
2.741
2.010
1.997
1.991
1.985
1.973
1.960
N
S
CN
N
30
1.07
1.11
1.13
1.89
1.04
7.6
7.4
7.2
7.0
6.8
f1 (ppm)
1.00
1.07
1.11
1.13
1.89
1.04
1.98
2.03
2.09
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


149.34
147.29
142.31
137.49
133.12
129.48
128.41
126.55
125.23
123.16
121.35
118.55
113.46
111.62
77.28
76.78
50.11
27.37
23.43
N
S
CN
N
30
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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7.650
7.647
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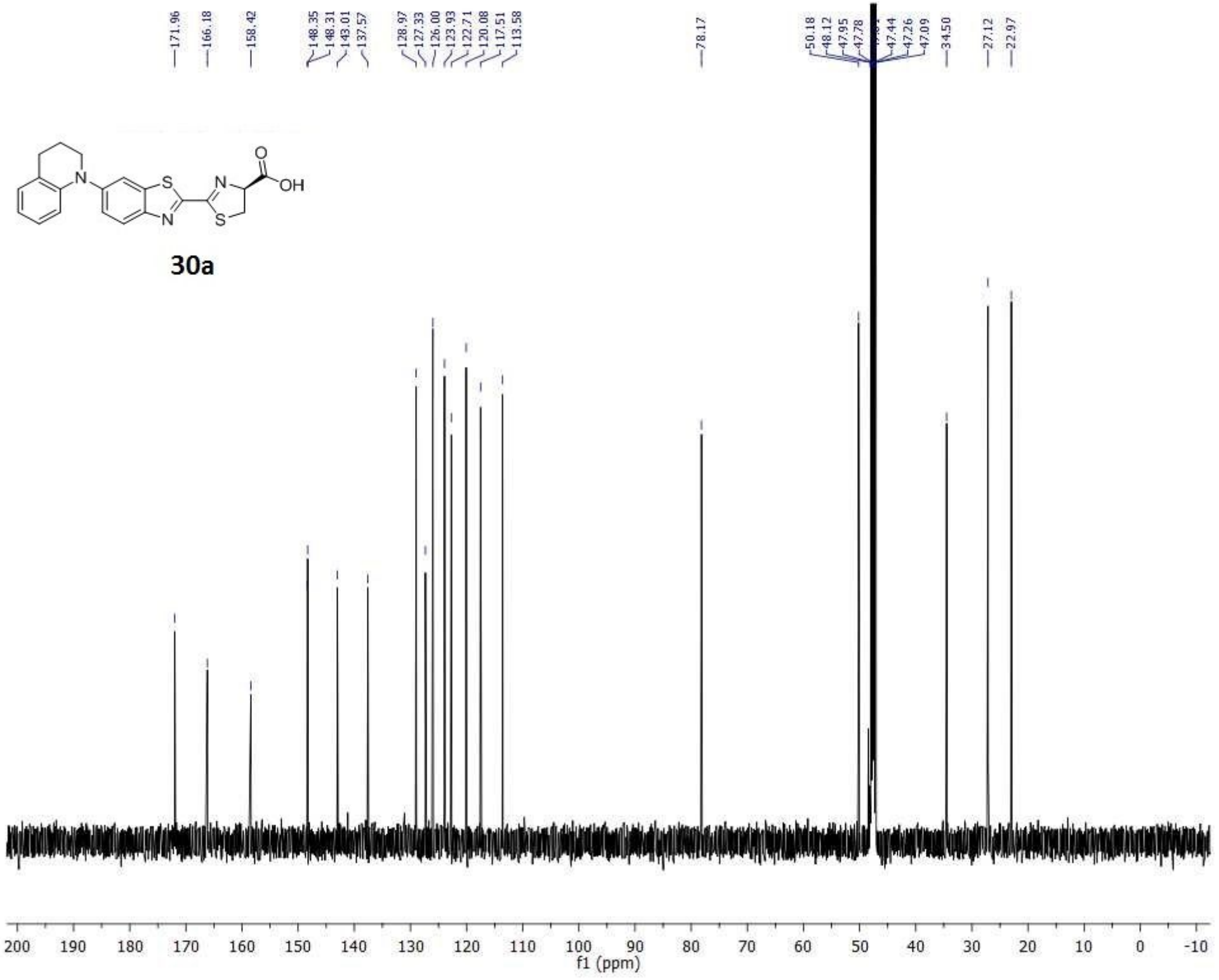
7.368
7.353
7.350
6.989
6.974
6.875
6.860
6.845
6.807
6.791
6.701
6.686
6.672
5.303
5.285
5.267
3.678
3.670
3.659
3.652
3.630
3.618
3.606
2.730
2.717
2.705
1.961
1.949
1.937
1.924
1.912
O
OH
N
S
N
N
S
30a
0.95
0.99
0.99
0.95
0.92
0.97
7.6
7.4
7.2
7.0
6.8
6.6
f1 (ppm)
1.00
0.95
0.99
0.99
0.95
0.92
0.97
0.97
4.05
2.08
2.10
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)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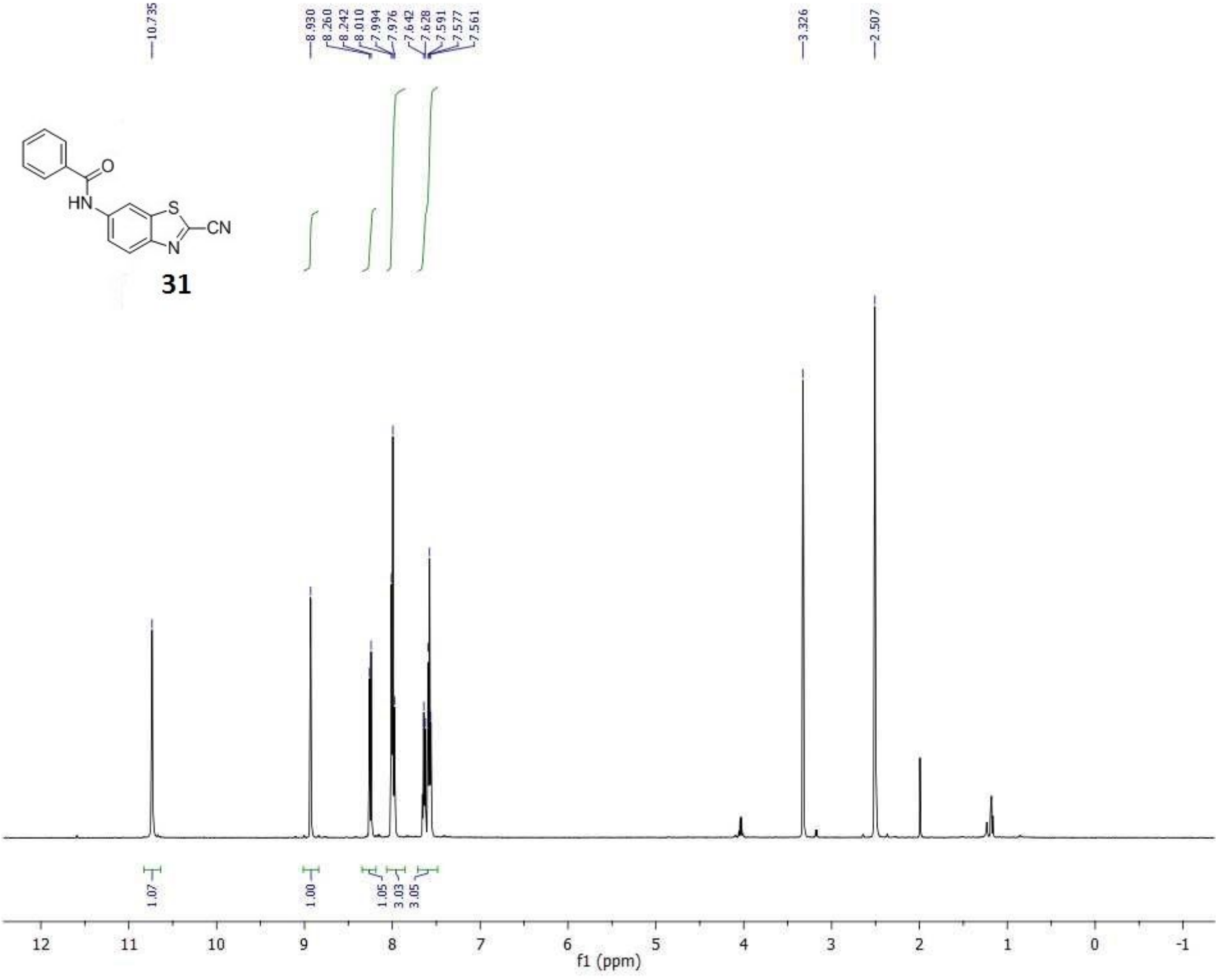
158.42
148.35
148.31
143.01
137.57
128.97
127.33
126.00
123.93
122.71
120.08
117.51
113.58
78.17
50.18
48.12
47.95
47.78
47.44
47.26
47.09
34.50
27.12
22.97
N
S
N
S
O
OH
30a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


10.735
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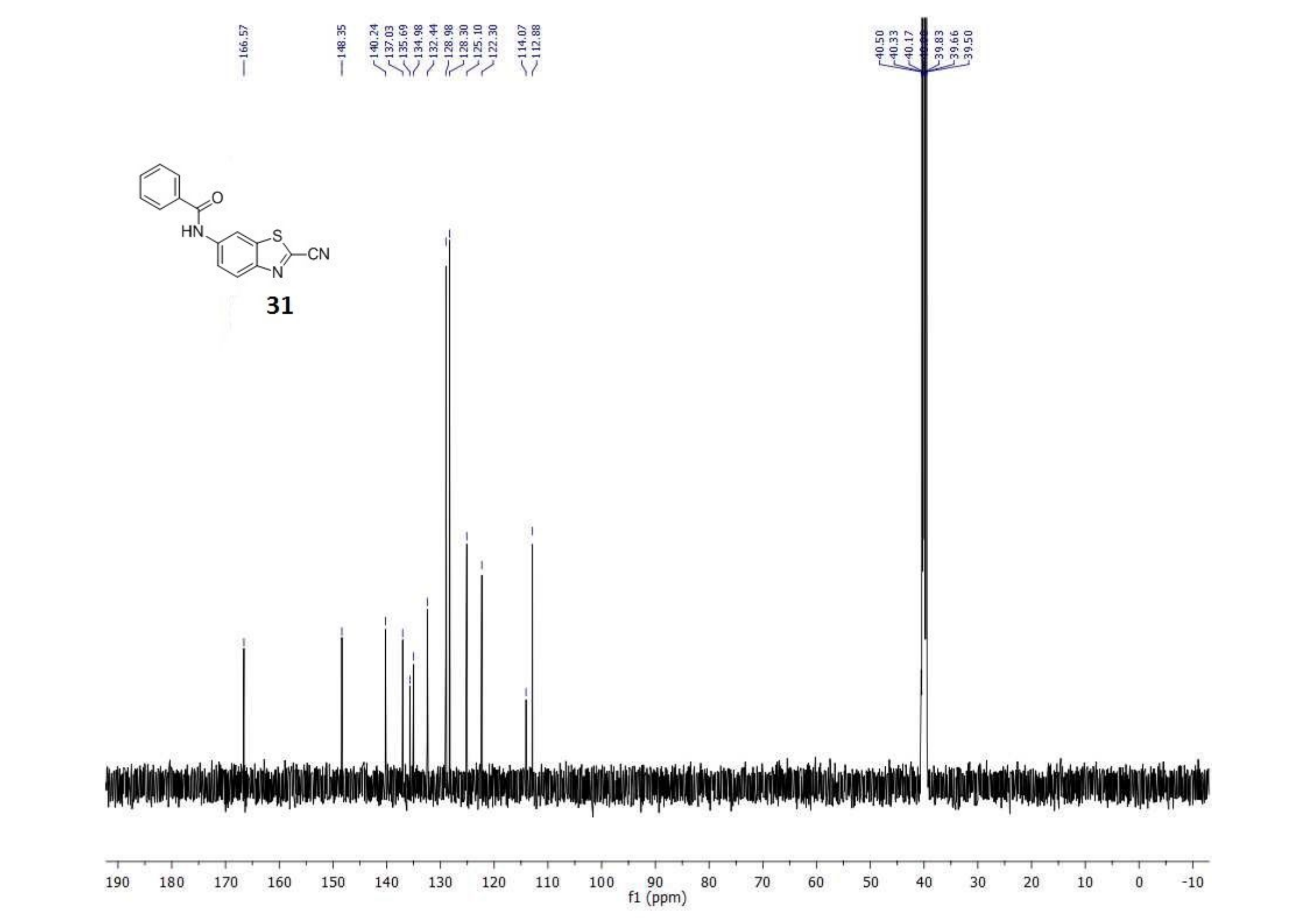
8.260
8.242
8.010
7.994
7.976
7.642
7.628
7.591
7.577
7.561
3.326
2.507
O
HN
S
CN
N
31
1.07
1.00
1.05
3.03
3.05
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)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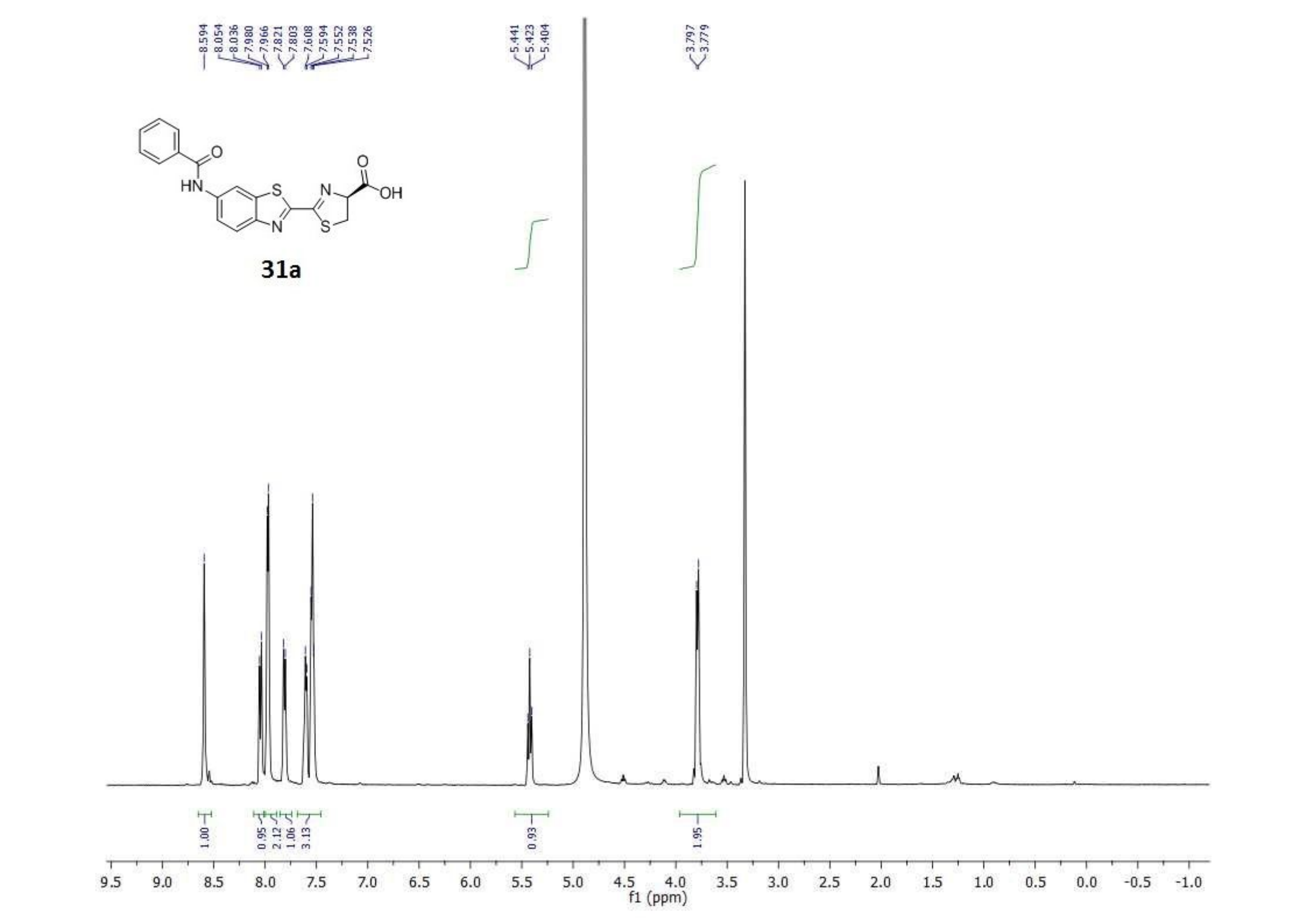
140.24
137.03
135.69
134.98
132.44
128.98
128.30
125.10
122.30
114.07
112.88
40.50
40.33
40.17
39.83
39.66
39.50
O
HN
S
CN
N
31
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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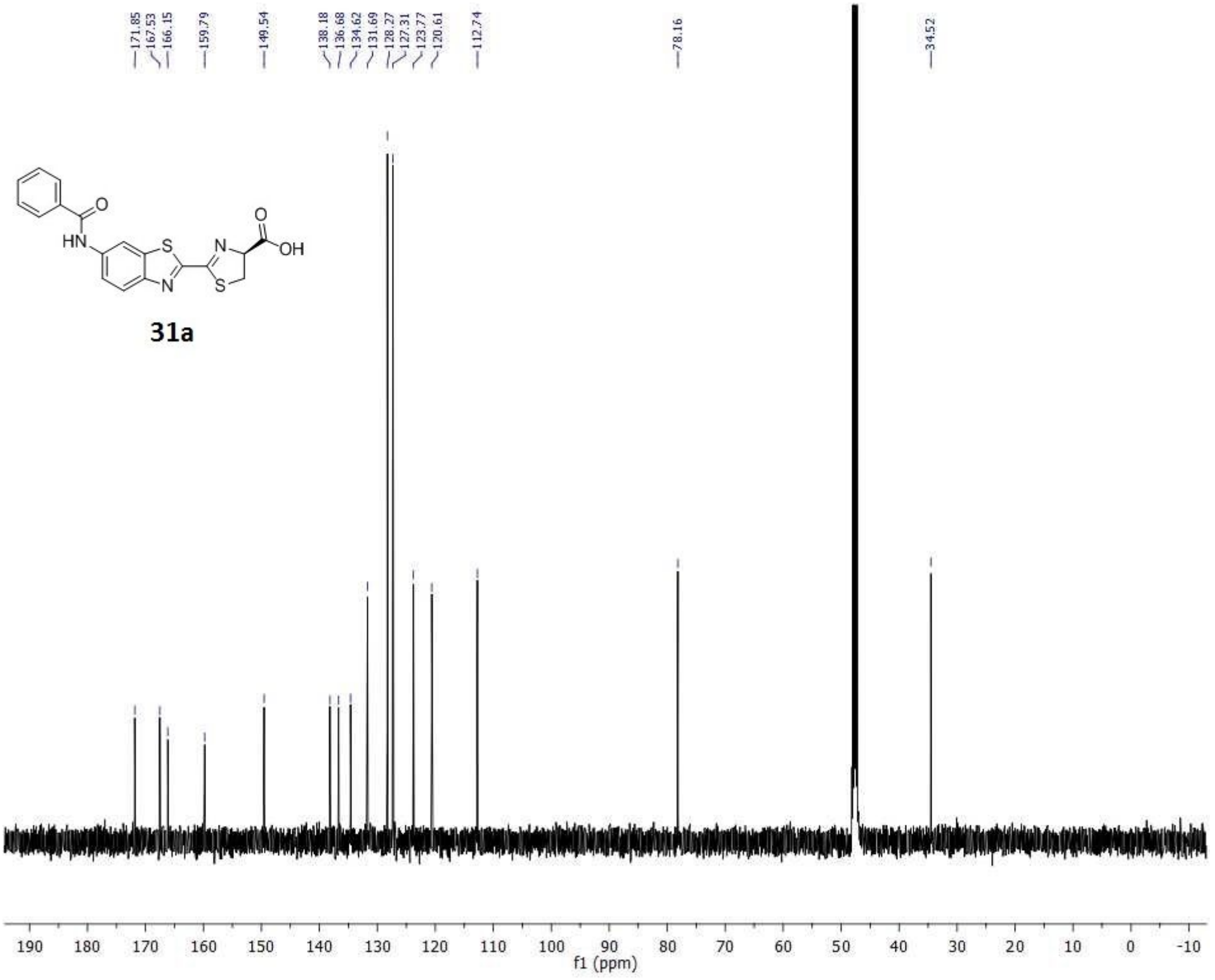
8.036
7.980
7.966
7.821
7.803
7.608
7.594
7.552
7.538
7.526
5.441
5.423
5.404
3.797
3.779
O
HN
S
N
O
OH
N
S
31a
1.00
0.95
2.12
1.06
3.13
0.93
1.95
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)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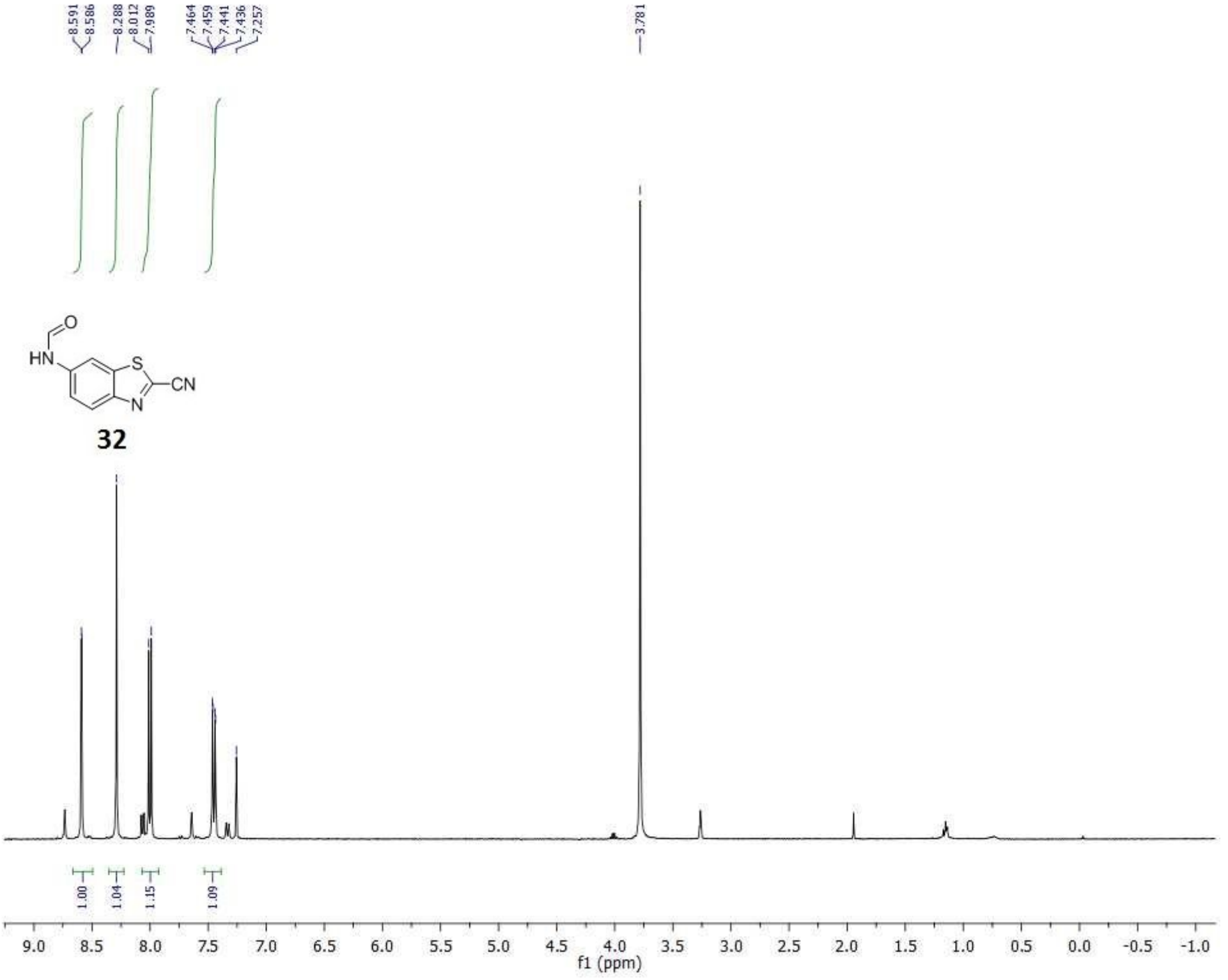
167.53
166.15
159.79
149.54
138.18
136.68
134.62
131.69
128.27
127.31
123.77
120.61
112.74
78.16
34.52
HN
O
S
N
O
OH
N
S
31a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.591
8.586
8.288
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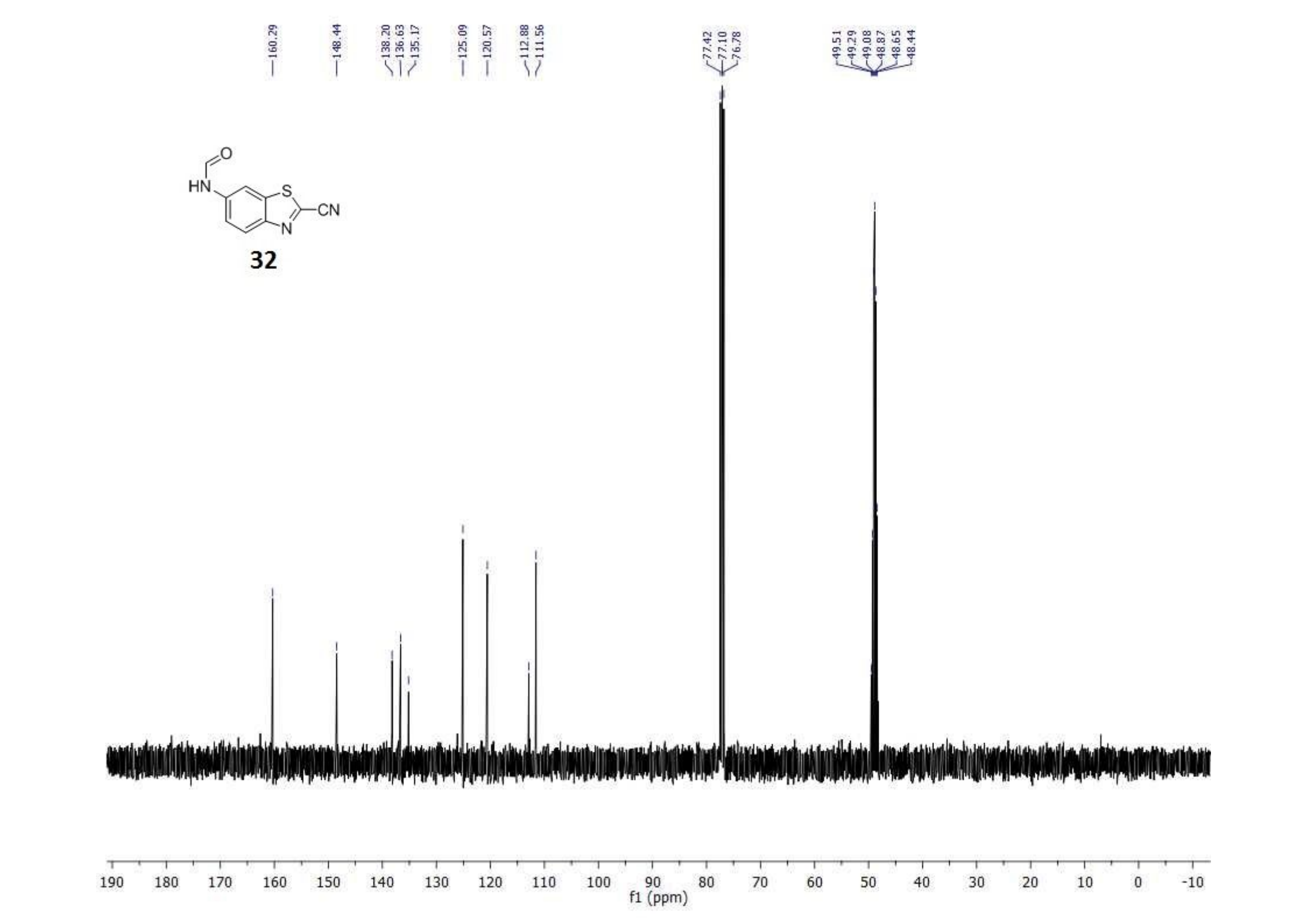
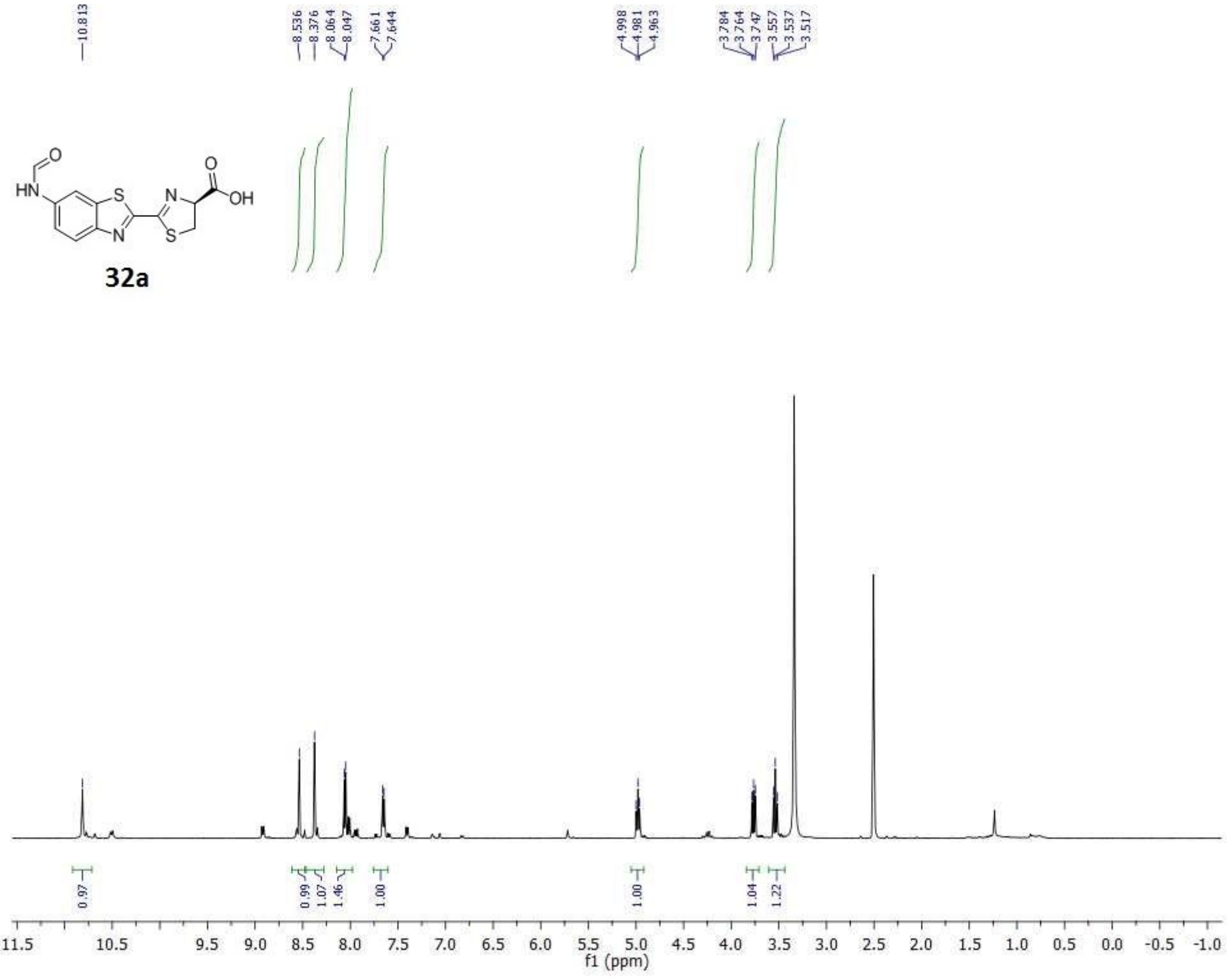
7.464
7.459
7.441
7.436
7.257
3.781
HN
O
S
CN
N
32
1.00
1.04
1.15
1.09
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


160.29
148.44
138.20
136.63
135.17
125.09
120.57
112.88
111.56
77.42
77.10
76.78
49.51
49.29
49.08
48.87
48.65
48.44
O
HN
S
CN
N
32
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


10.813
8.536
8.376
8.064
8.047
7.661
7.644
4.998
4.981
4.963
3.784
3.764
3.747
3.557
3.537
3.517
HN
O
S
N
O
OH
N
S
32a
0.97
0.99
1.07
1.46
1.00
1.00
1.04
1.22
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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2.5
2.0
1.5
1.0
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0.0
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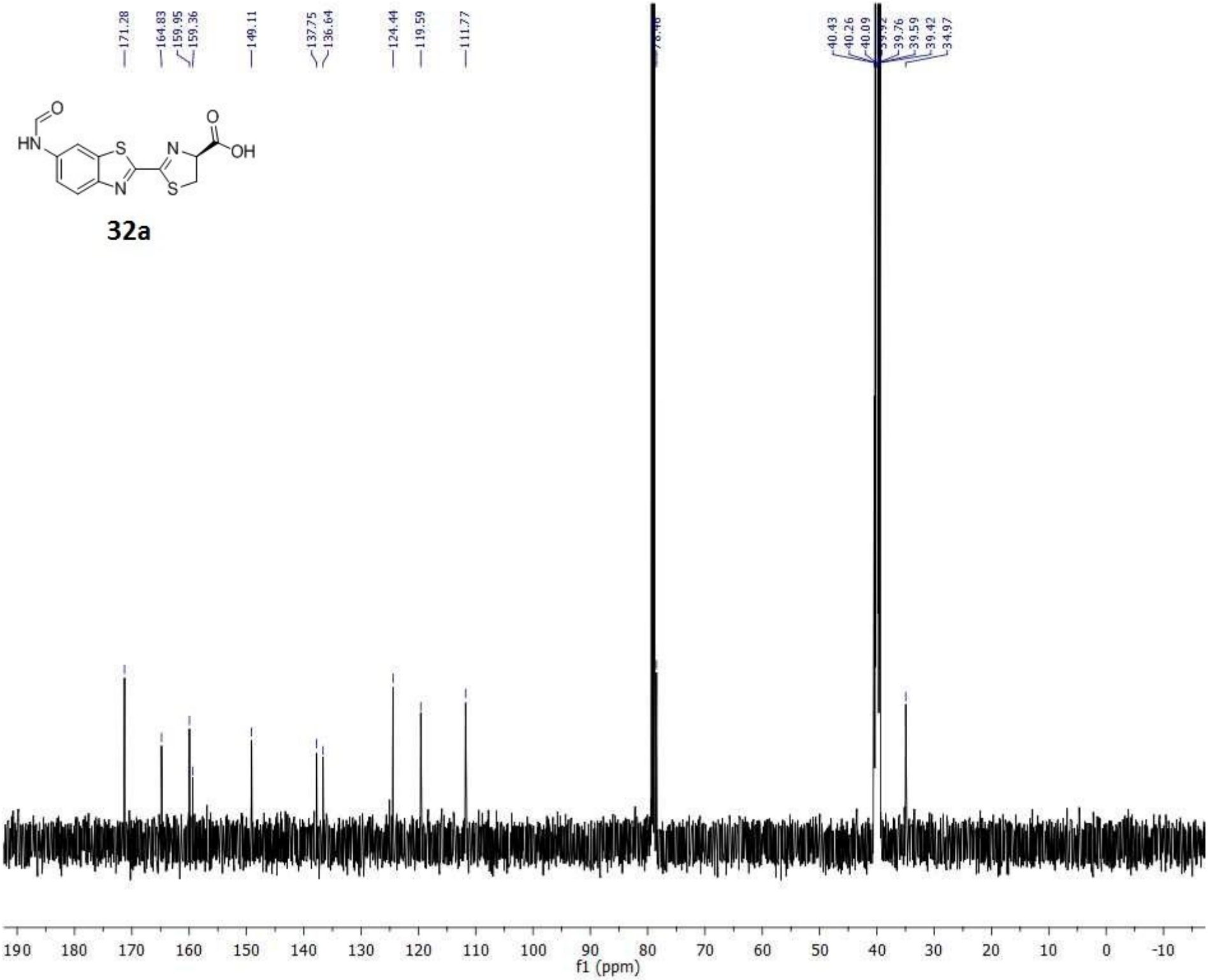
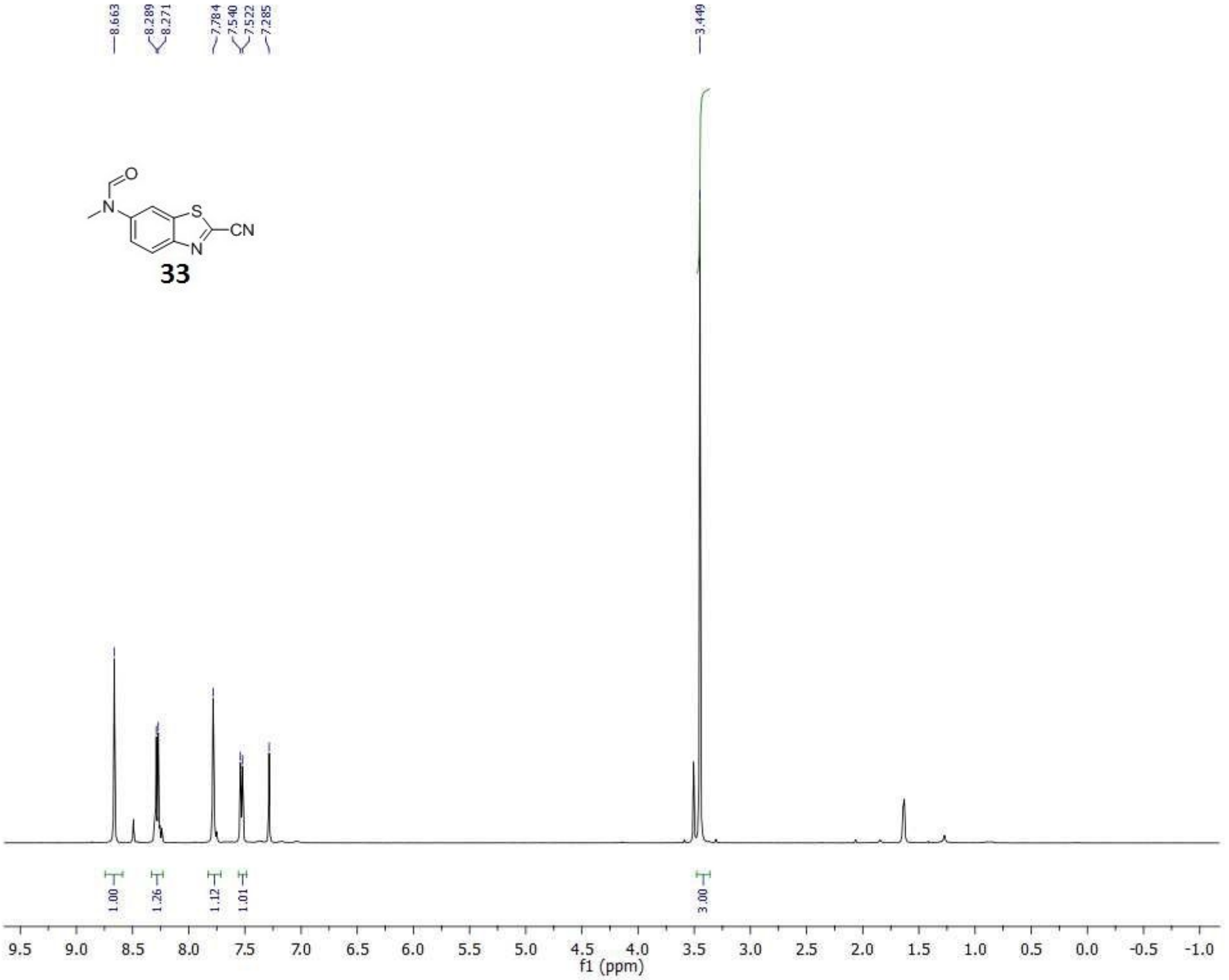
-1.0
f1 (ppm)


171.28
164.83
159.95
159.36
149.11
137.75
136.64
124.44
119.59
111.77
40.43
40.26
40.09
39.76
39.59
39.42
34.97
HN
O
S
N
O
OH
N
S
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

32a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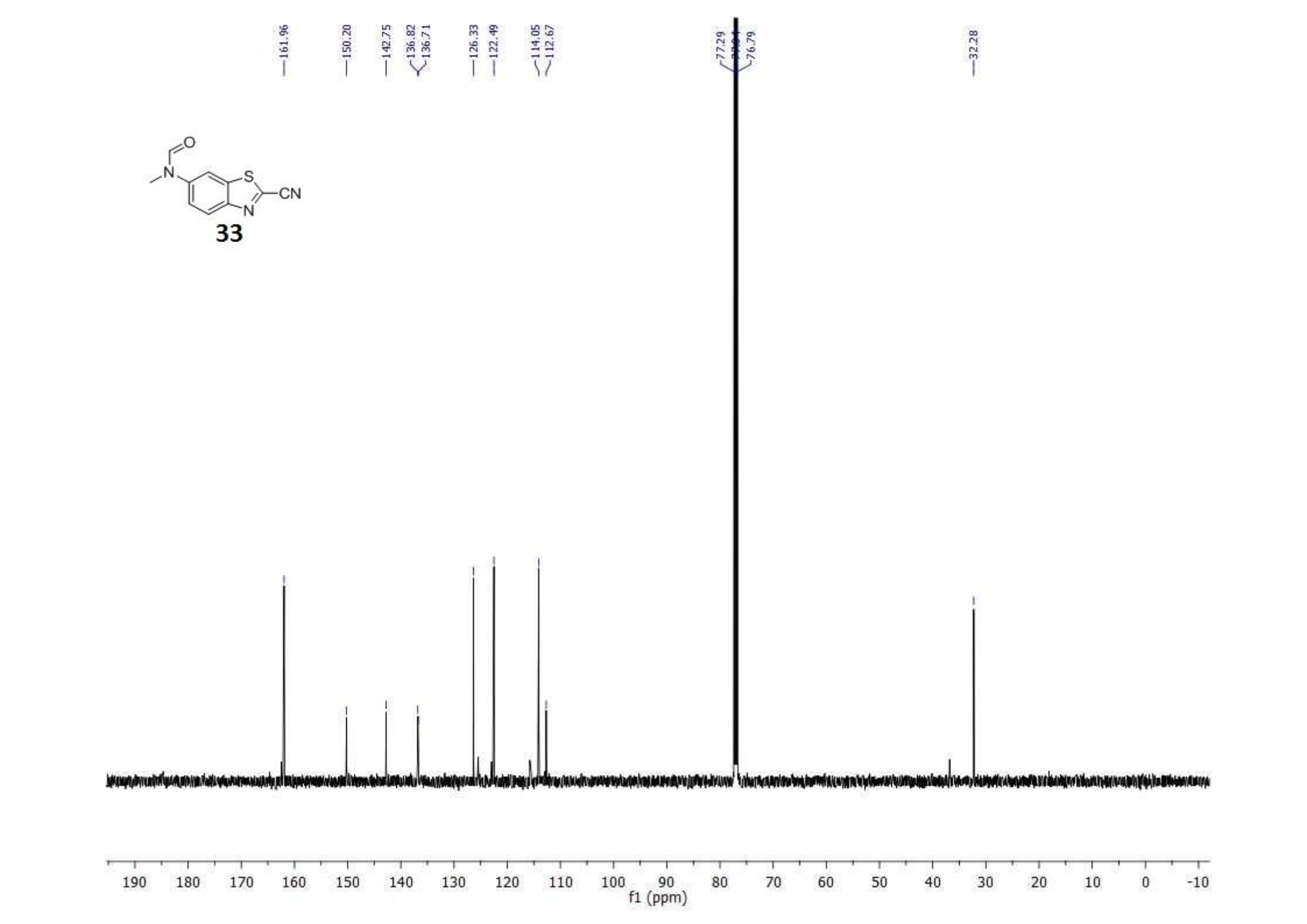
8.289
8.271
7.784
7.540
7.522
7.285
3.449
O
N
S
CN
N
33
1.00
1.26
1.12
1.01
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


161.96
150.20
142.75
136.82
136.71
126.33
122.49
114.05
112.67
77.29
76.79
32.28
O
N
S
CN
N
33
190
180
170
160
150
140
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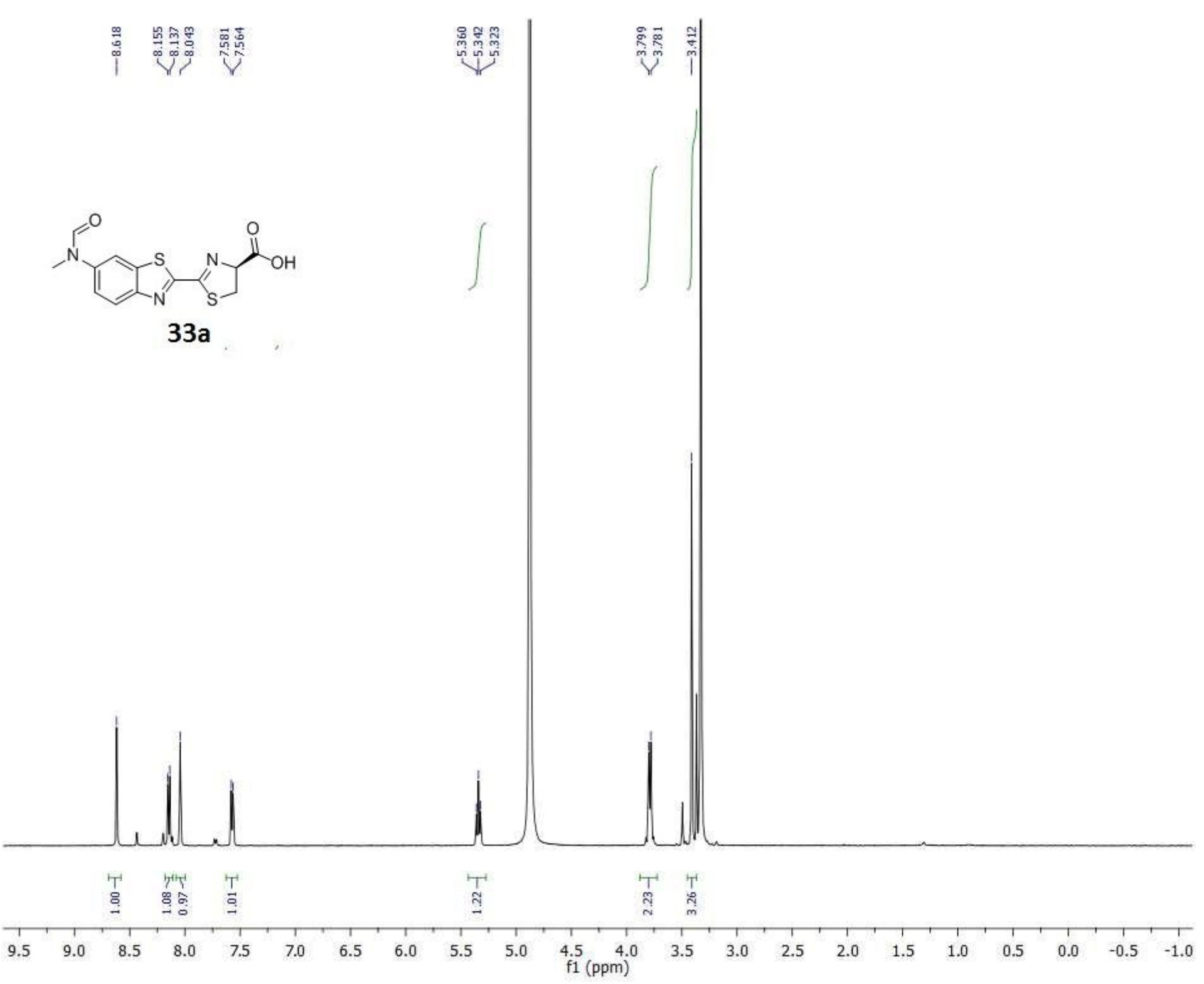
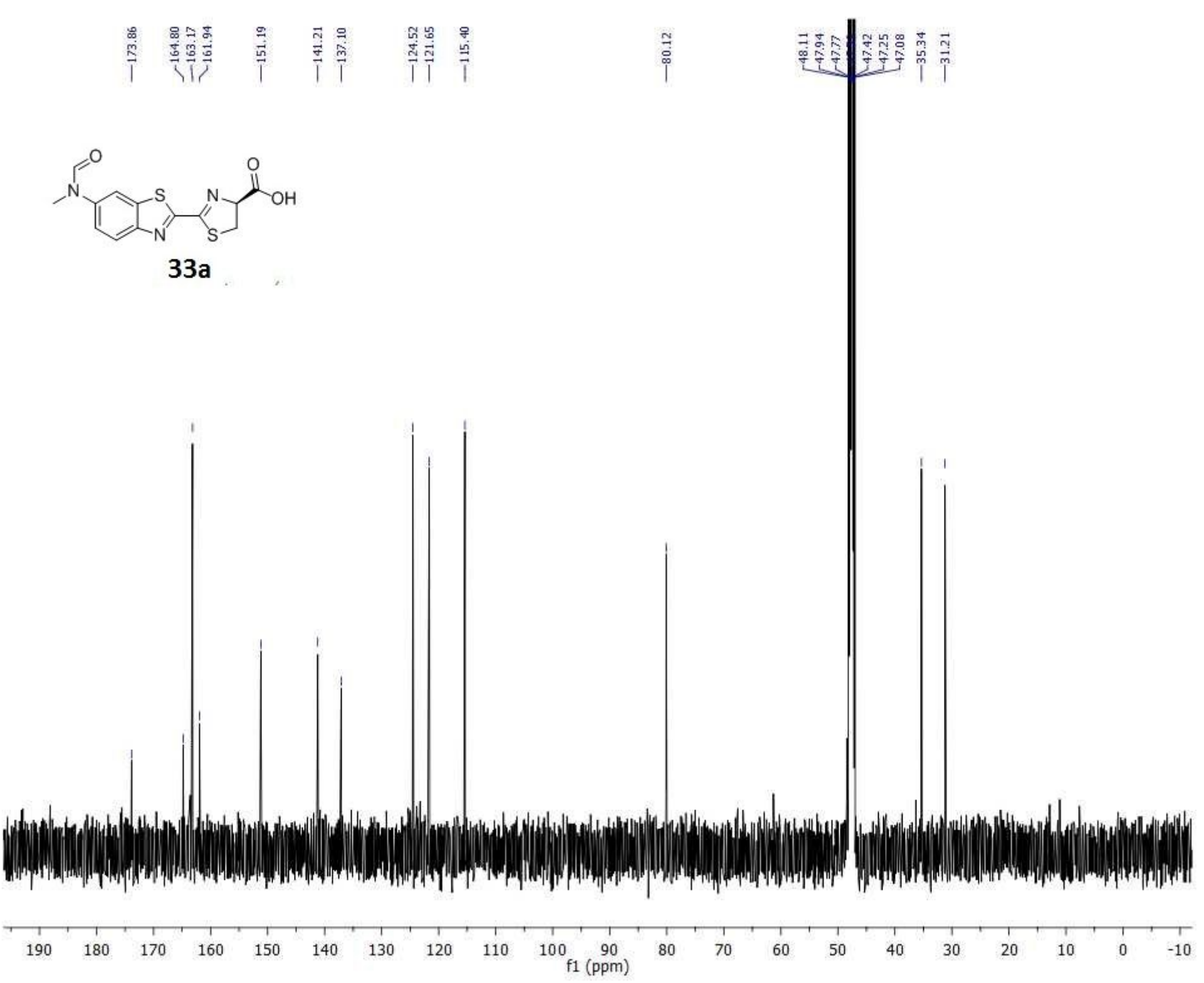
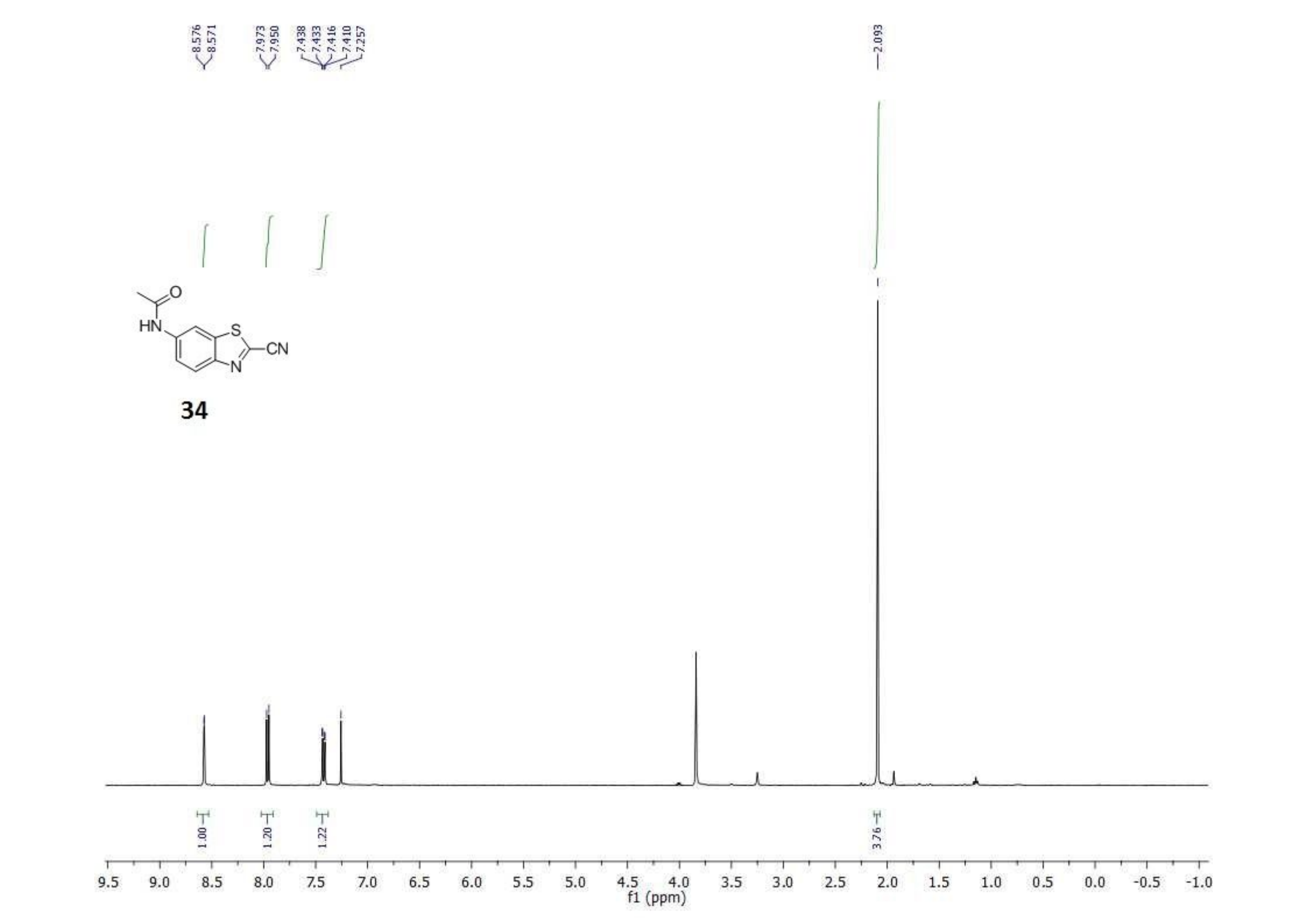
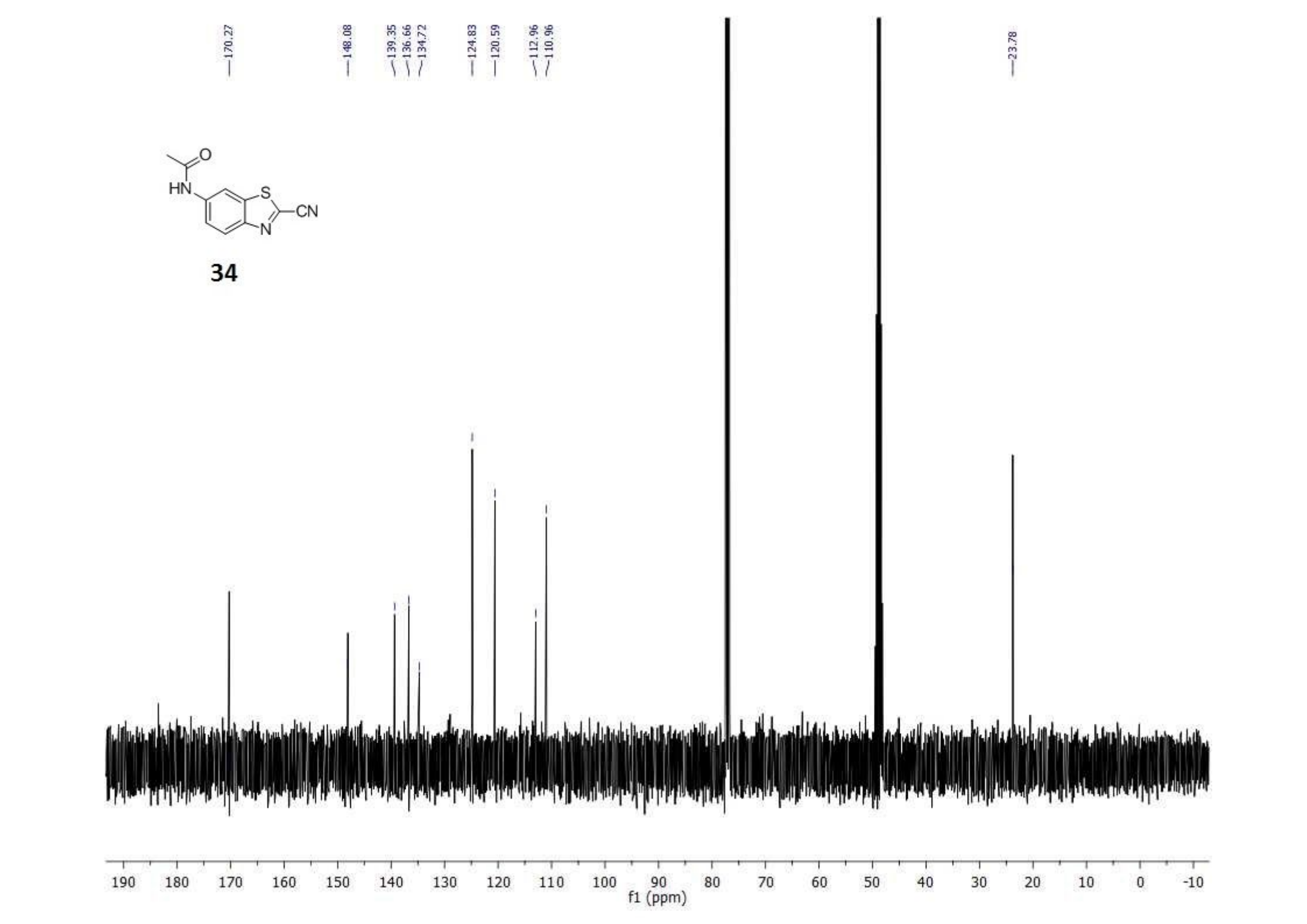
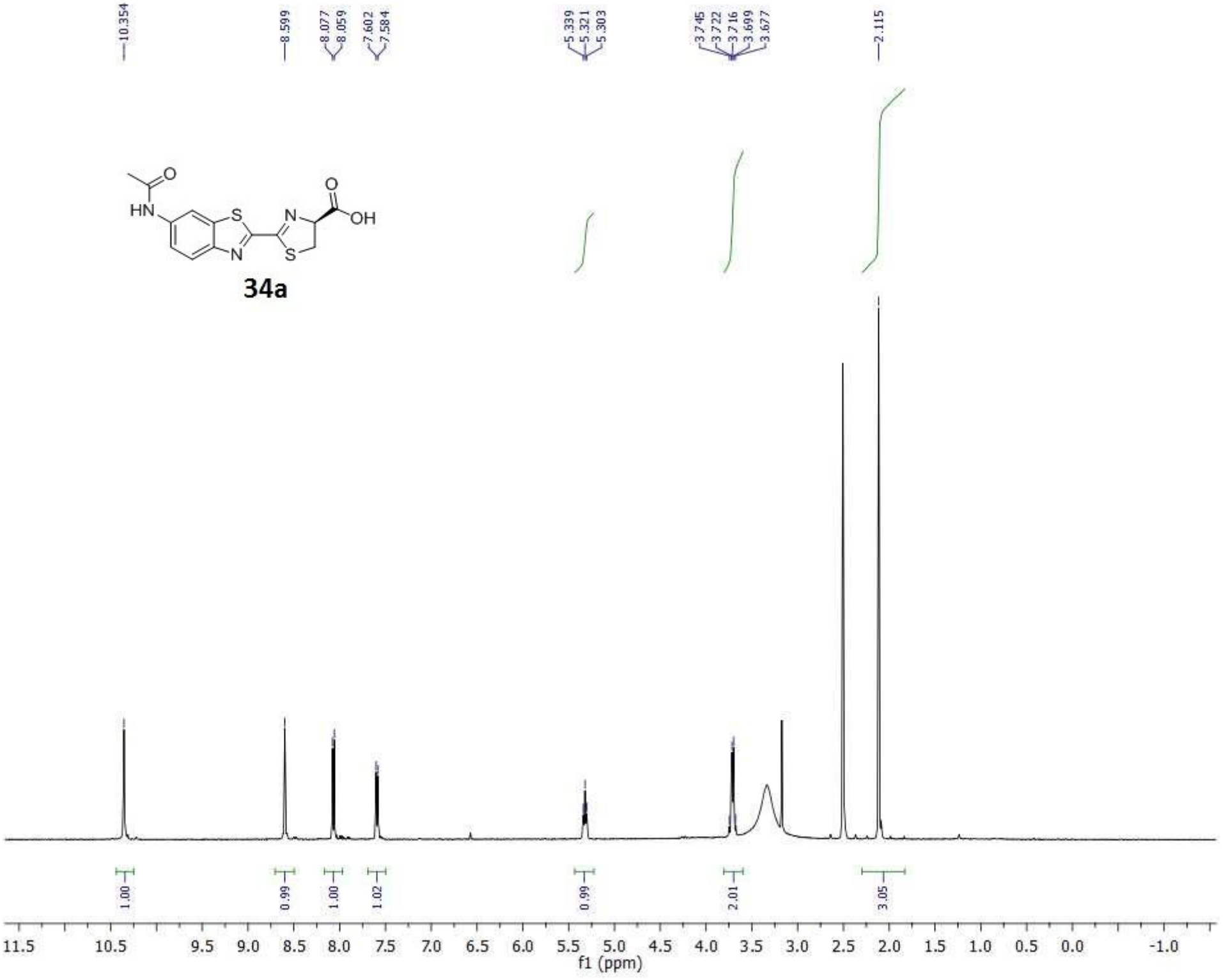
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

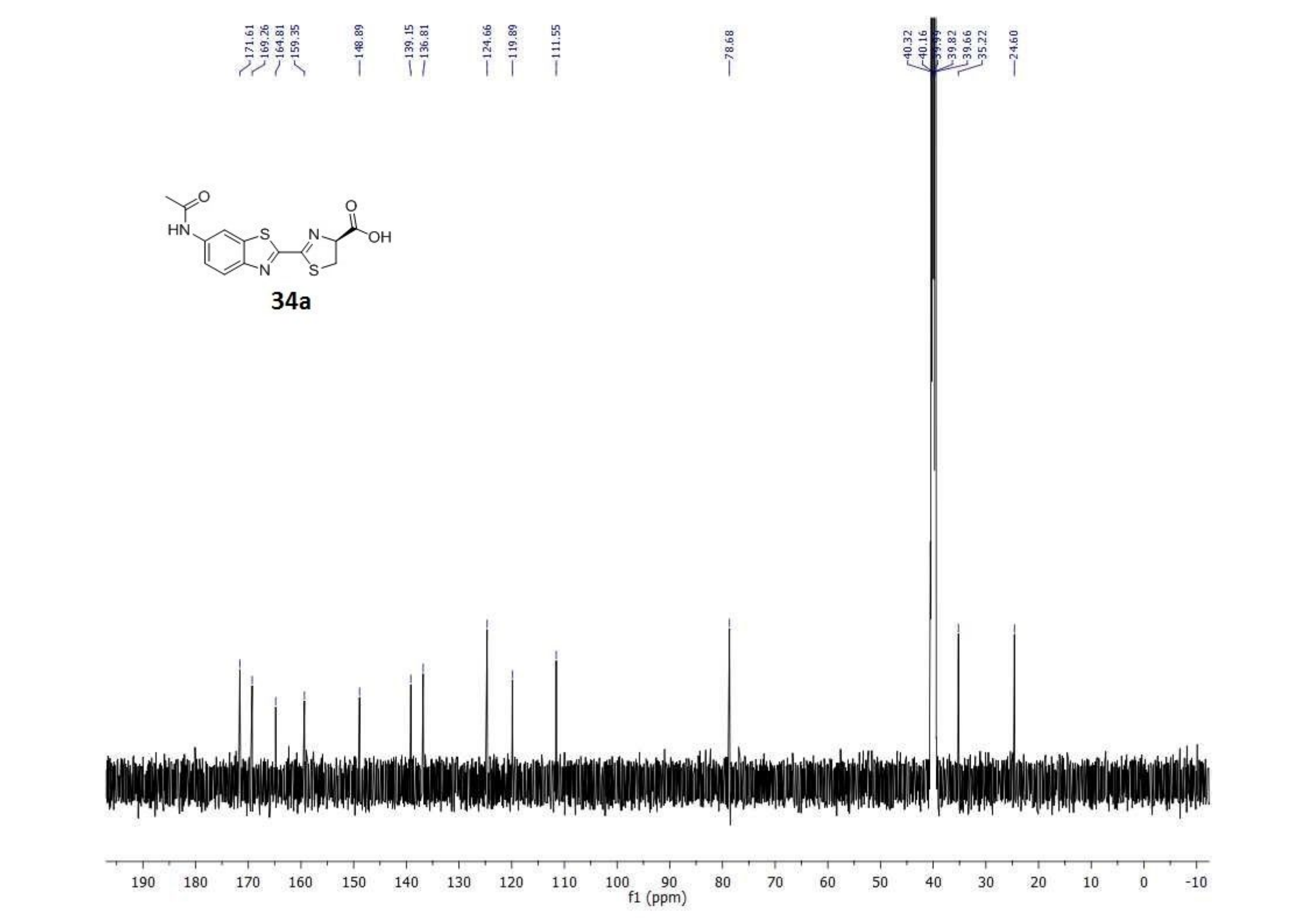

8.618
8.155
8.137
8.043
7.581
7.564
5.360
5.342
5.323
3.799
3.781
3.412
O
N
S
N
O
OH
N
S
33a
1.00
1.08
0.97
1.01
1.22
2.23
3.26
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

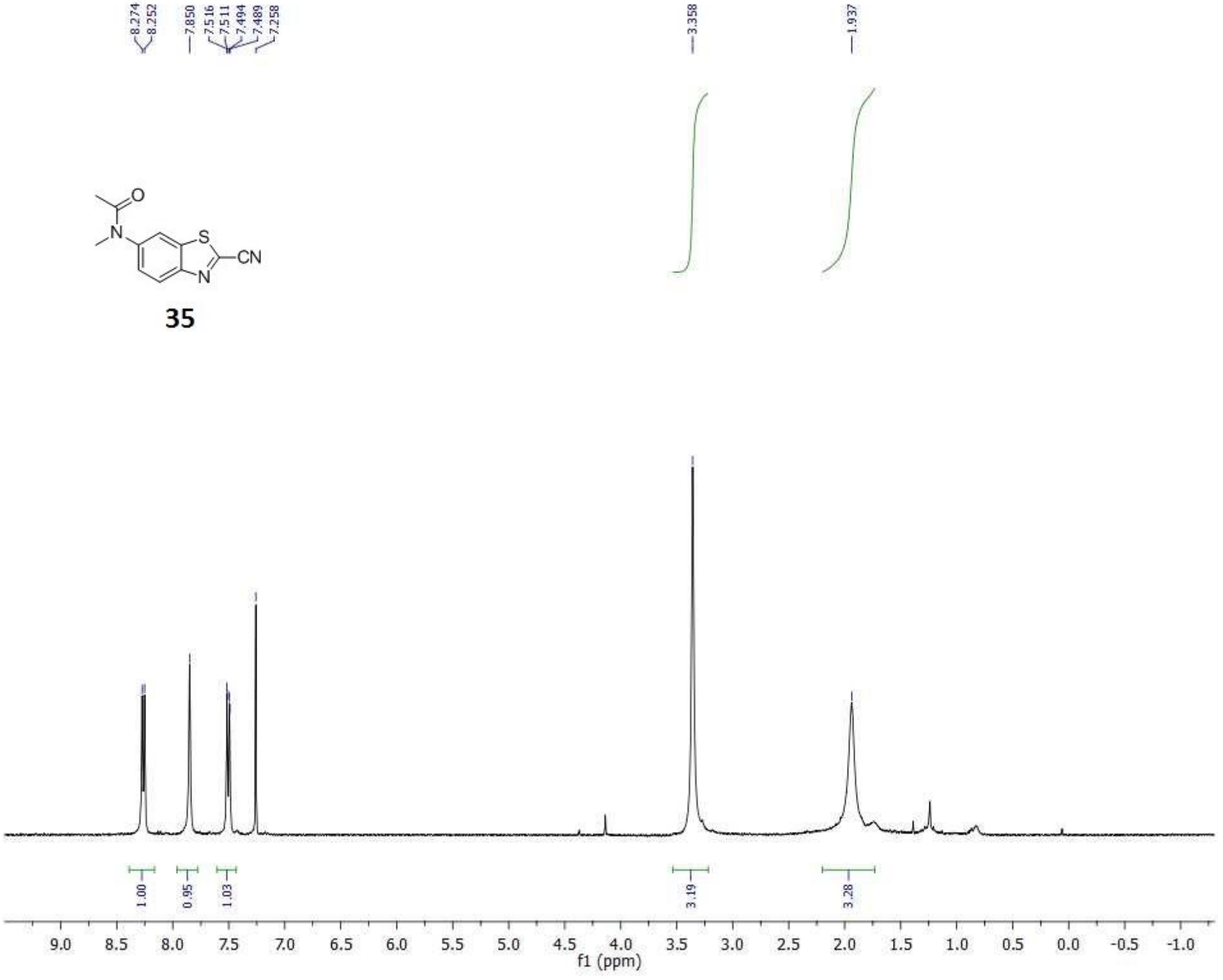

173.86
164.80
163.17
161.94
151.19
141.21
137.10
124.52
121.65
115.40
80.12
48.11
47.94
47.77
47.42
47.25
47.08
35.34
31.21
O
N
S
N
O
OH
N
S
33a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.576
8.571
7.973
7.950
7.438
7.433
7.416
7.410
7.257
2.093
HN
O
S
N
CN
34
1.00
1.20
1.22
3.76
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

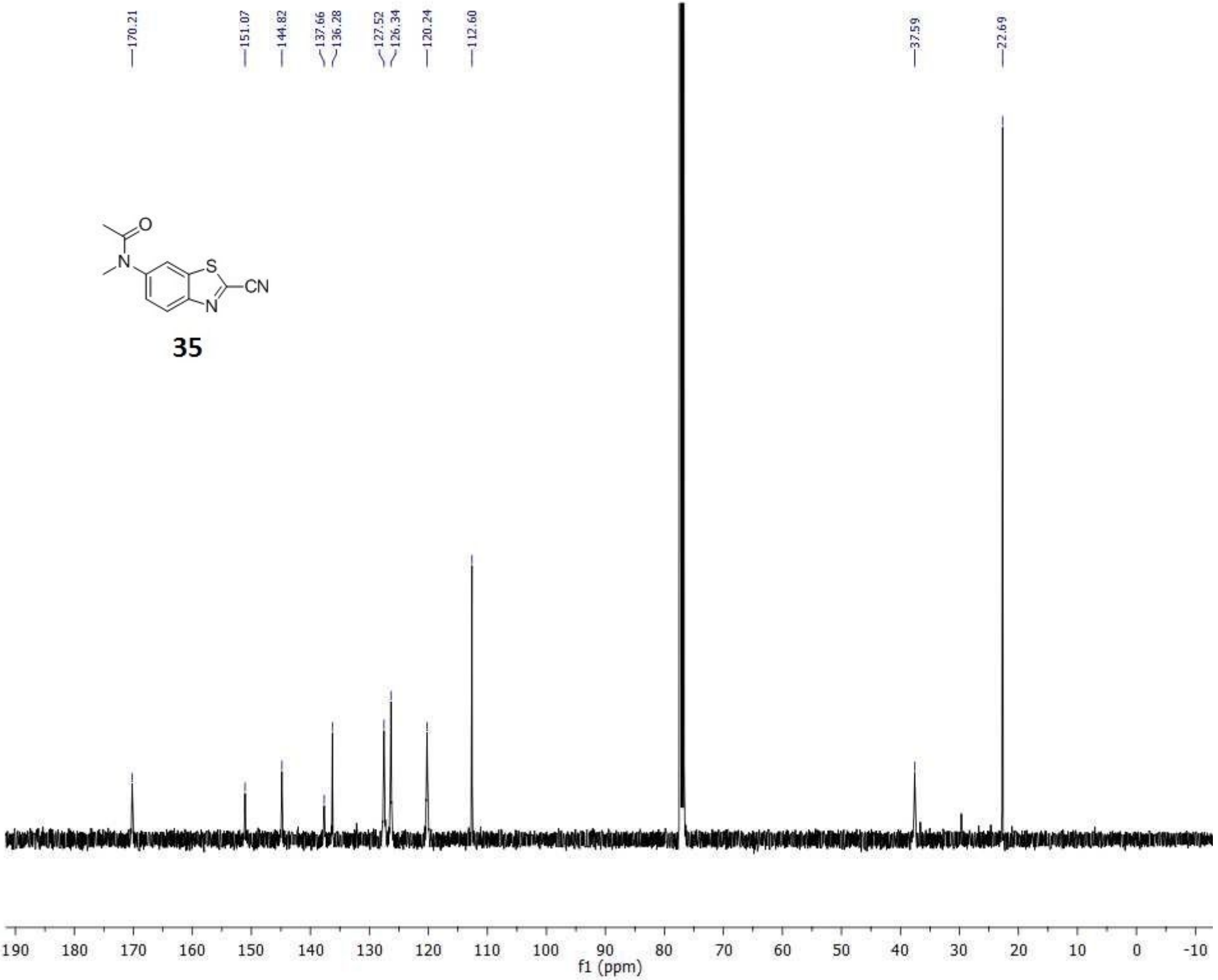

170.27
148.08
139.35
136.66
134.72
124.83
120.59
112.96
110.96
23.78
O
HN
S
CN
N
34
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

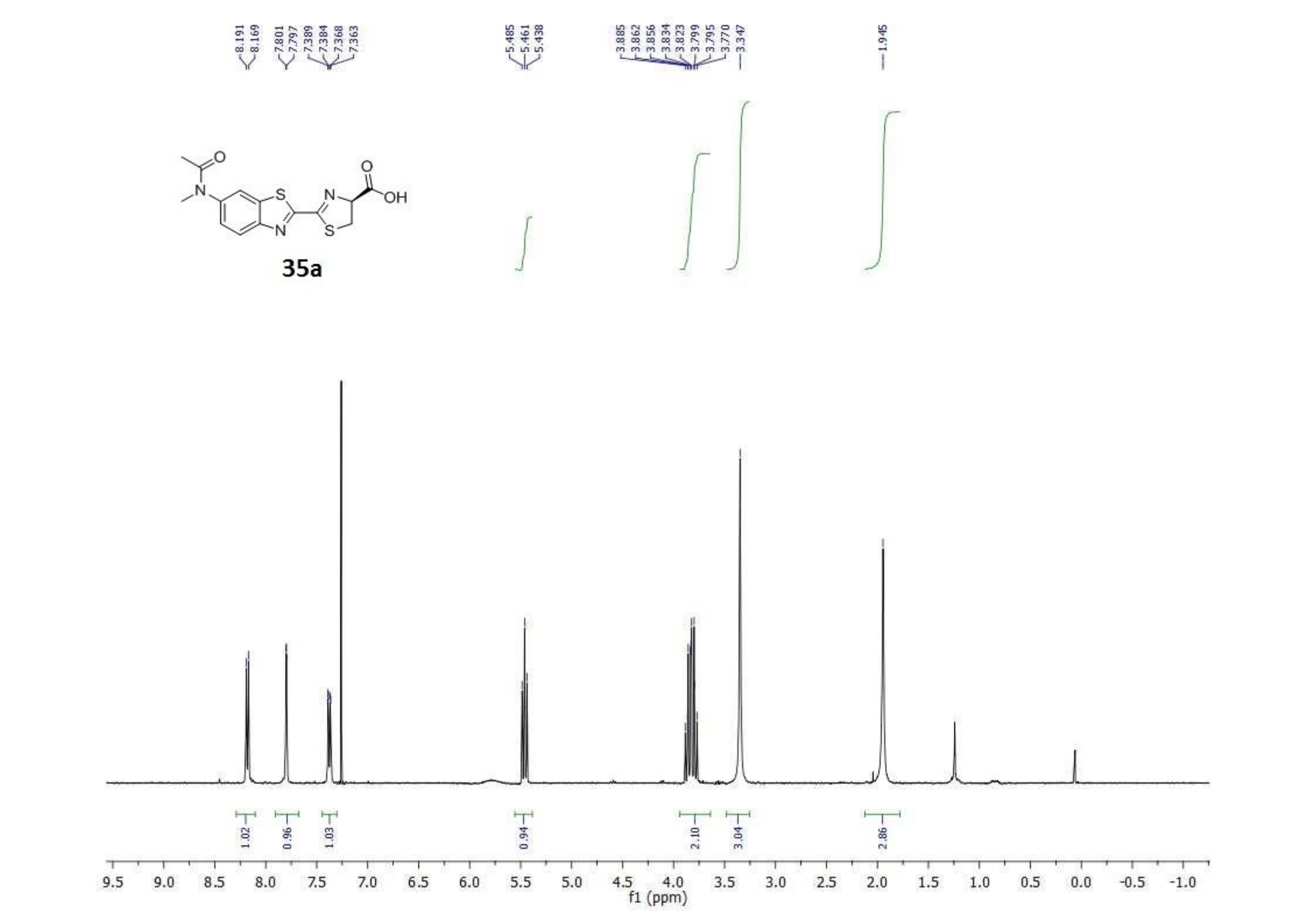

10.354
8.599
8.077
8.059
7.602
7.584
5.339
5.321
5.303
3.745
3.722
3.716
3.699
3.677
2.115
HN
O
S
N
O
OH
N
S
34a
1.00
0.99
1.00
1.02
0.99
2.01
3.05
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-1.0
f1 (ppm)


171.61
169.26
164.81
159.35
148.89
139.15
136.81
124.66
119.89
111.55
78.68
40.32
40.16
39.82
39.66
35.22
24.60
HN
O
S
N
N
S
O
OH
34a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.274
8.252
7.850
7.516
7.511
7.494
7.489
7.258
3.358
1.937
O
N
S
CN
N
1.00
0.95
1.03
3.19
3.28
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

35


170.21
151.07
144.82
137.66
136.28
127.52
126.34
120.24
112.60
37.59
22.69
O
N
S
CN
N
35
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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8.169
7.801
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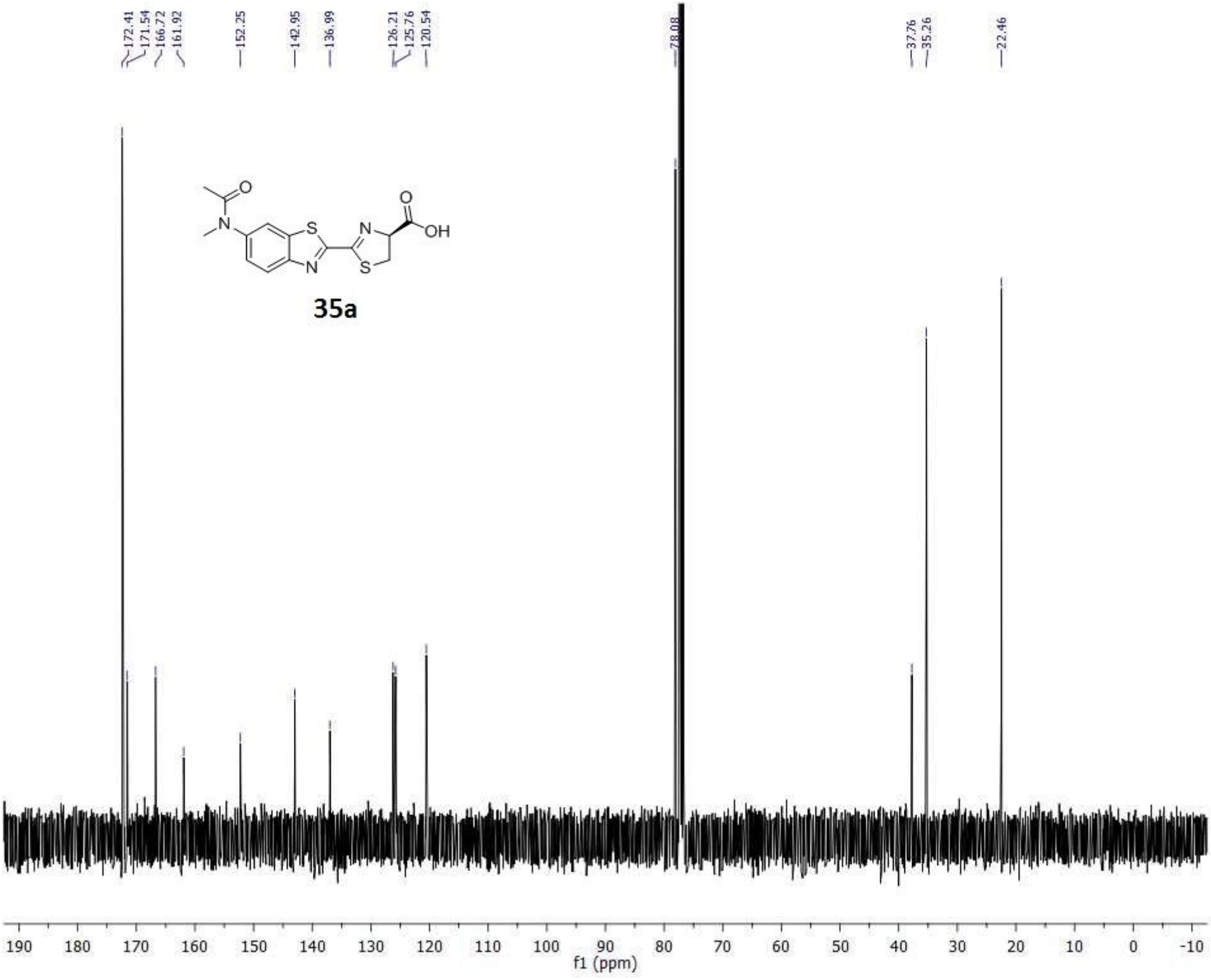
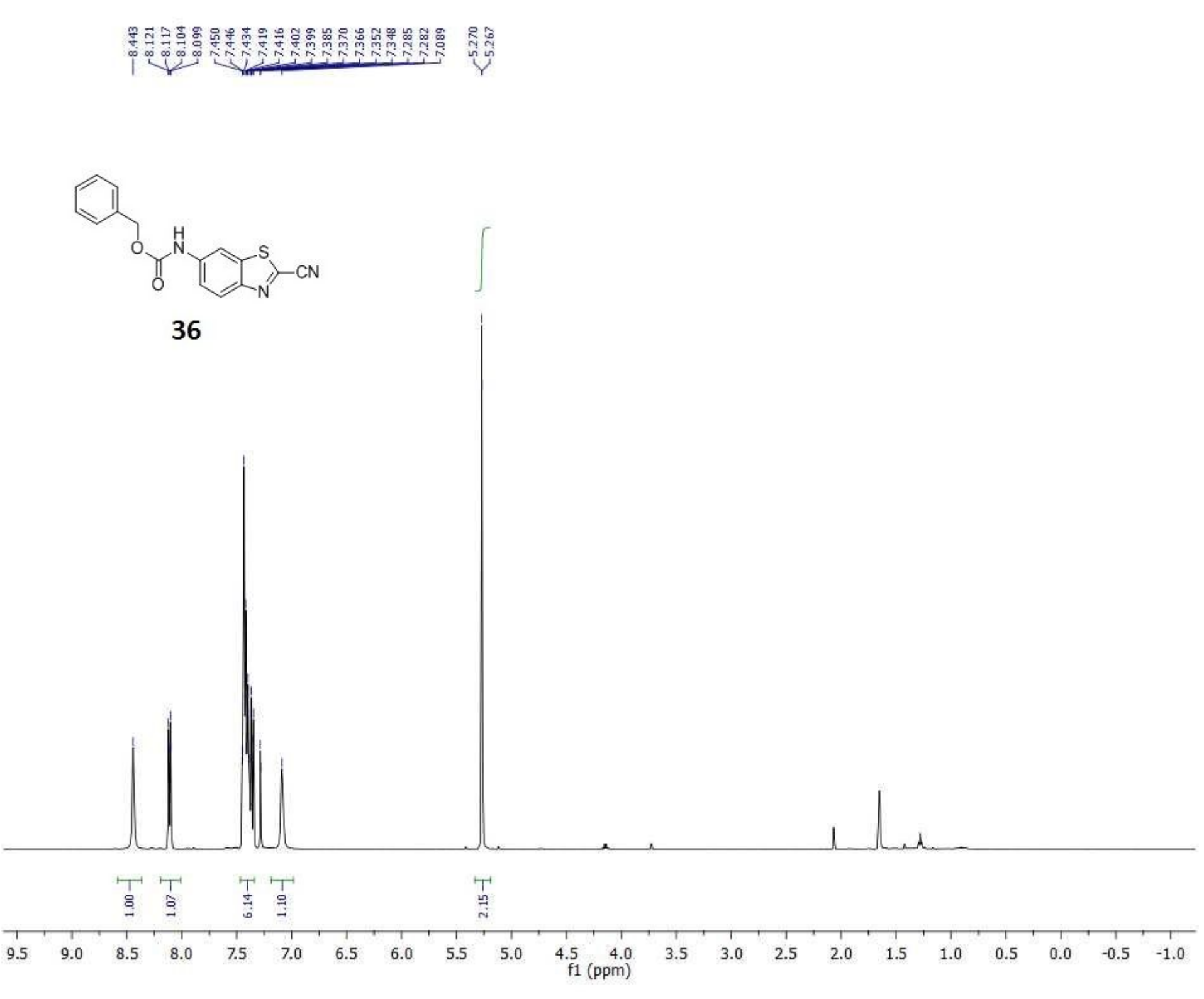
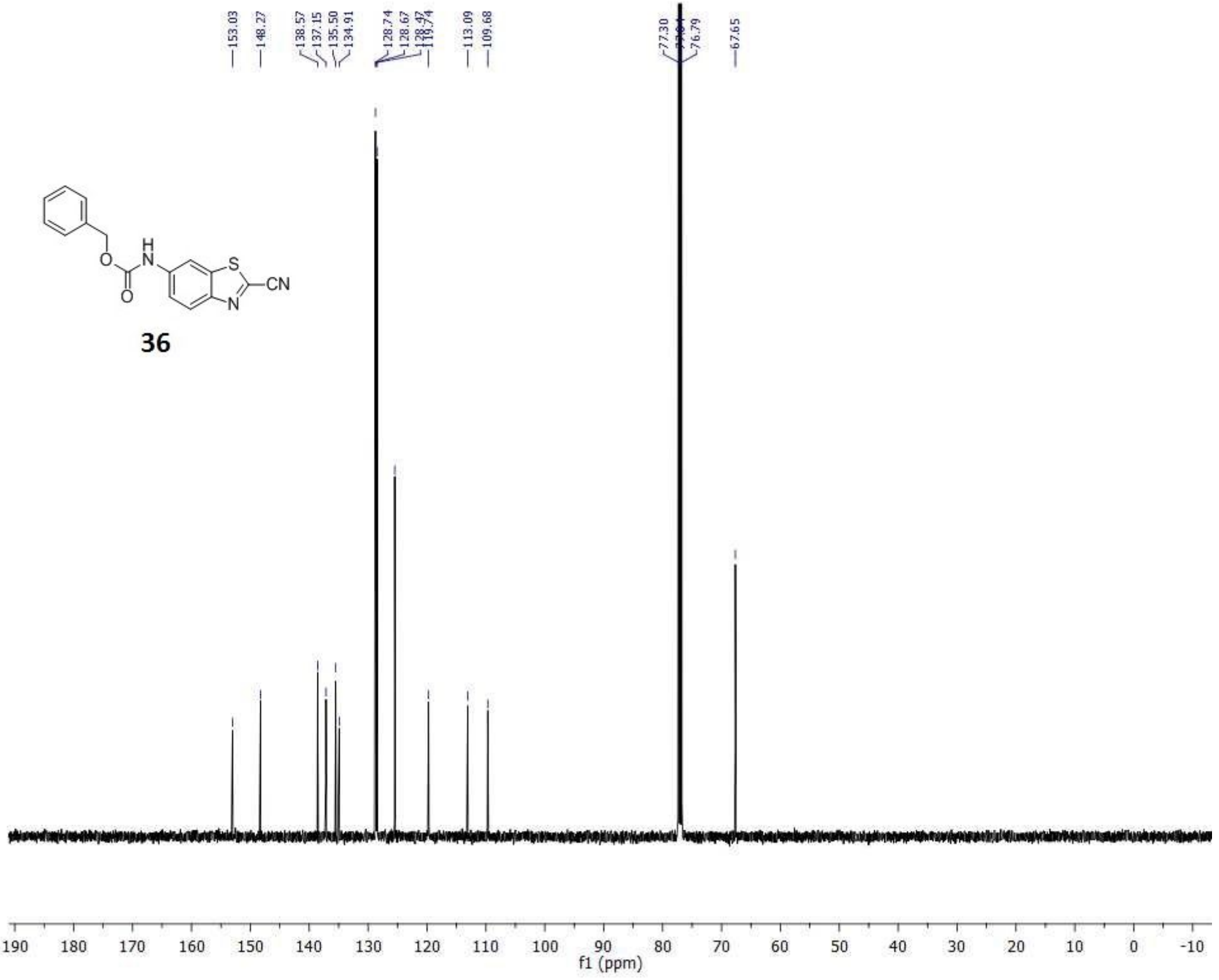
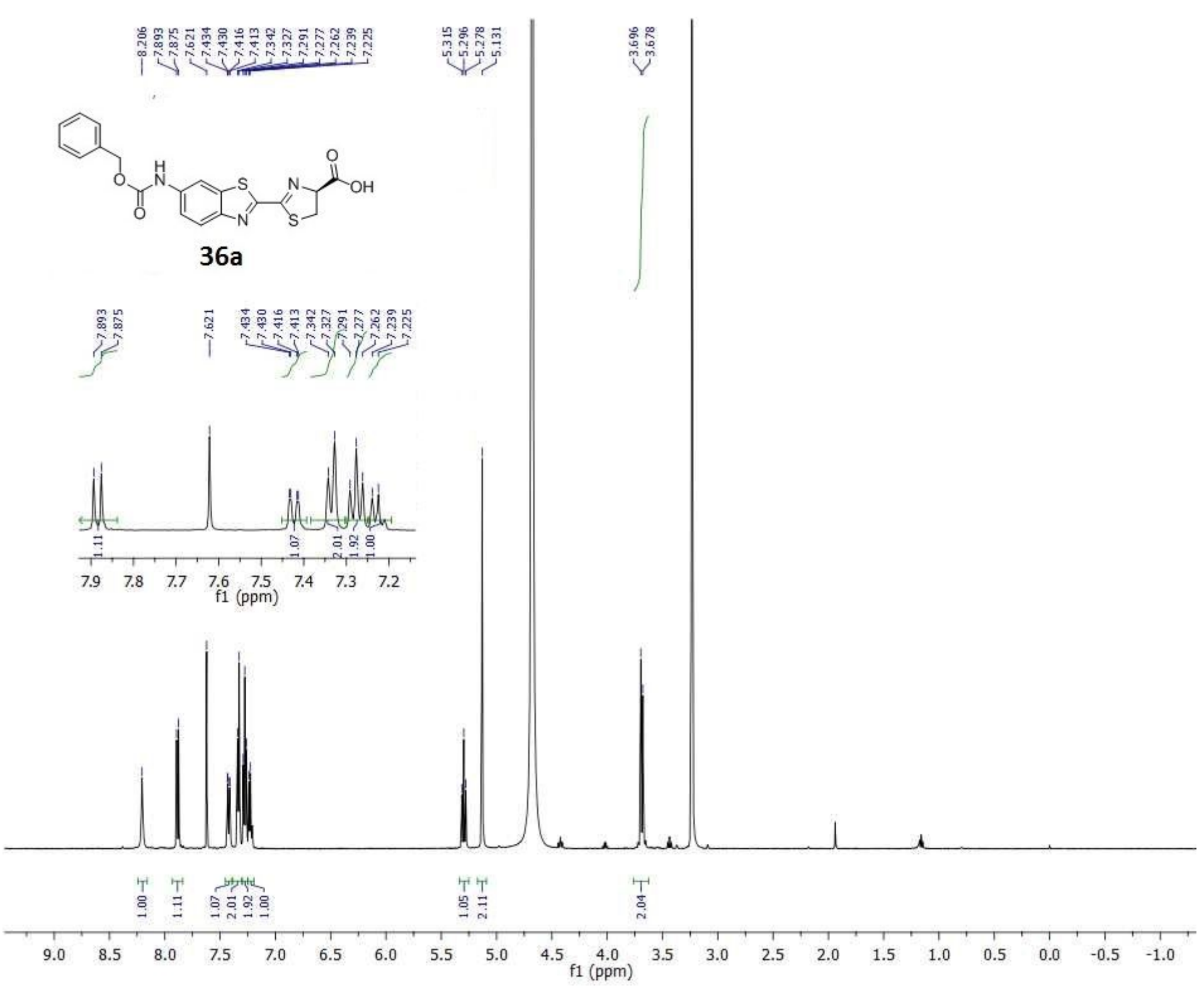
7.389
7.384
7.368
7.363
5.485
5.461
5.438
3.885
3.862
3.856
3.834
3.823
3.799
3.795
3.770
3.347
1.945
O
N
S
N
O
OH
N
S
35a
1.02
0.96
1.03
0.94
2.10
3.04
2.86
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


172.41
171.54
166.72
161.92
152.25
142.95
136.99
126.21
125.76
120.54
78.08
37.76
35.26
22.46
O
N
S
N
O
OH
N
S
35a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.443
8.121
8.117
8.104
8.099
7.450
7.446
7.434
7.419
7.416
7.402
7.399
7.385
7.370
7.366
7.352
7.348
7.285
7.282
7.089
5.270
5.267
O
H
N
S
CN
O
N
36
1.00
1.07
6.14
1.10
2.15
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


153.03
148.27
138.57
137.15
135.50
134.91
128.74
128.67
113.09
109.68
77.30
76.79
67.65
O
H
N
O
S
N
CN
36
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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7.875
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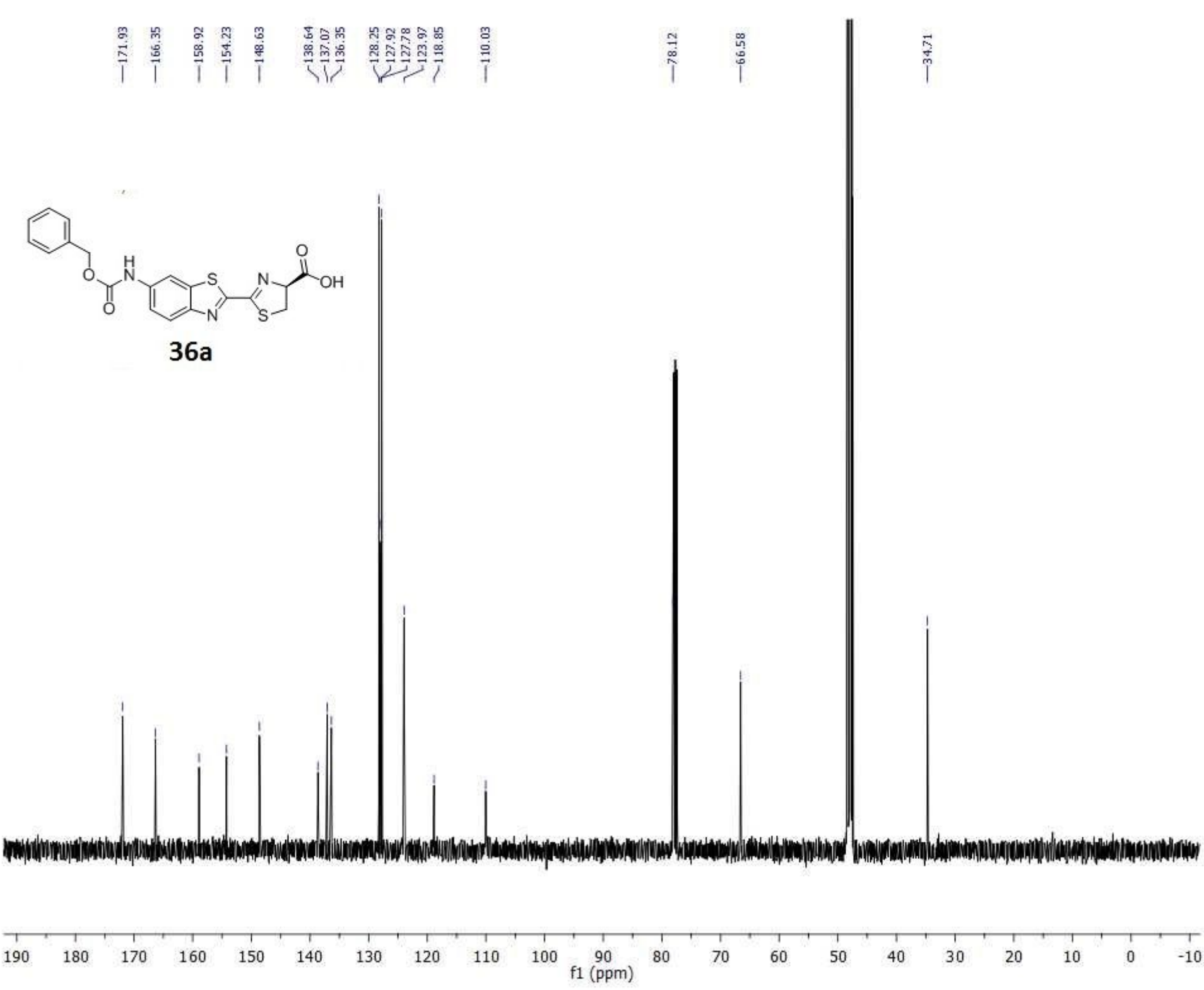
7.434
7.430
7.416
7.413
7.342
7.327
7.291
7.277
7.262
7.239
7.225
5.315
5.296
5.278
5.131
3.696
3.678
O
H
N
O
O
S
N
N
S
OH
36a
1.11
1.07
2.01
1.92
1.00
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
f1 (ppm)
1.00
1.11
1.07
2.01
1.92
1.00
1.05
2.11
2.04
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)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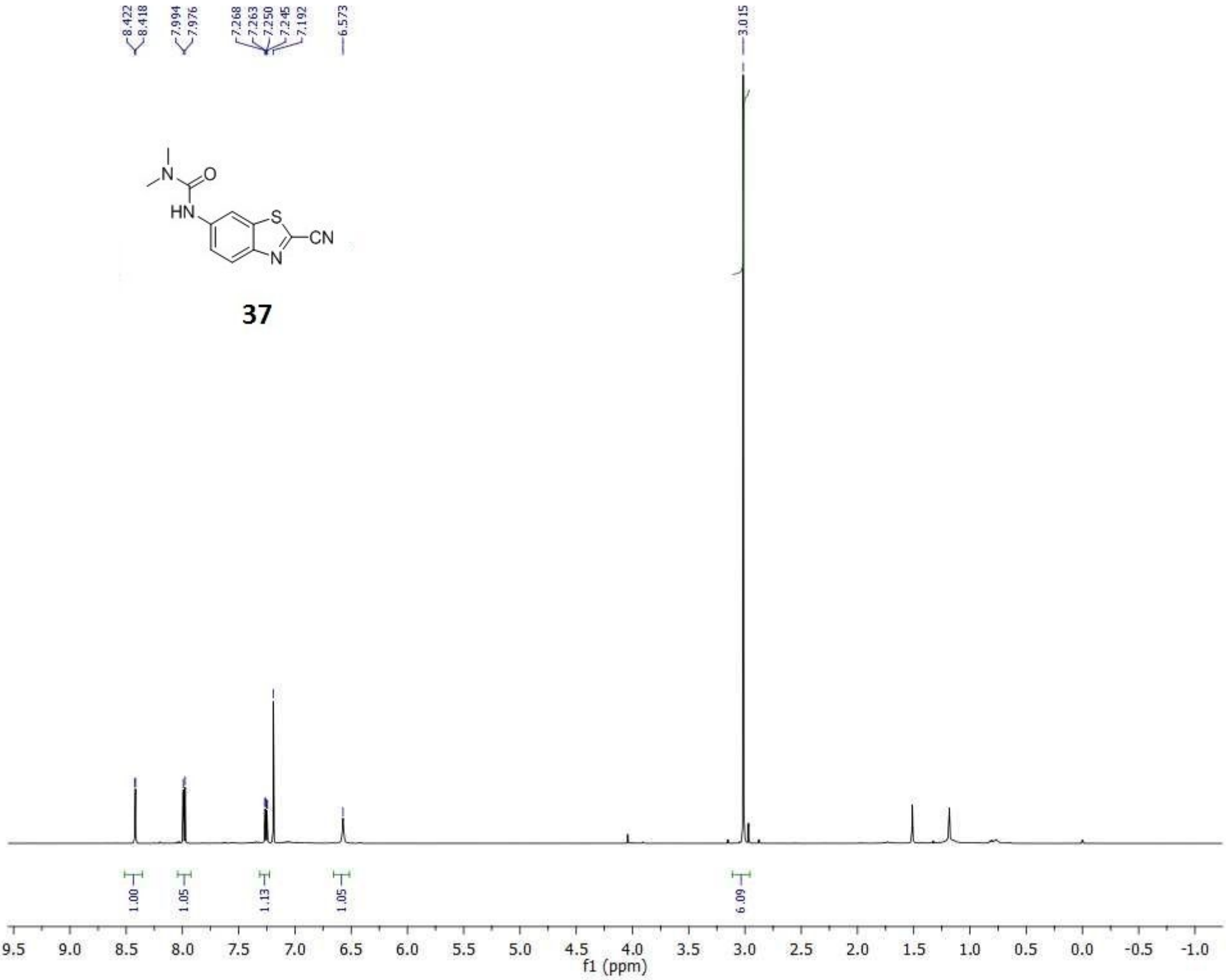
166.35
158.92
154.23
148.63
138.64
137.07
136.35
128.25
127.92
127.78
123.97
118.85
110.03
78.12
66.58
34.71
O
H
N
O
O
S
N
N
S
O
OH
36a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)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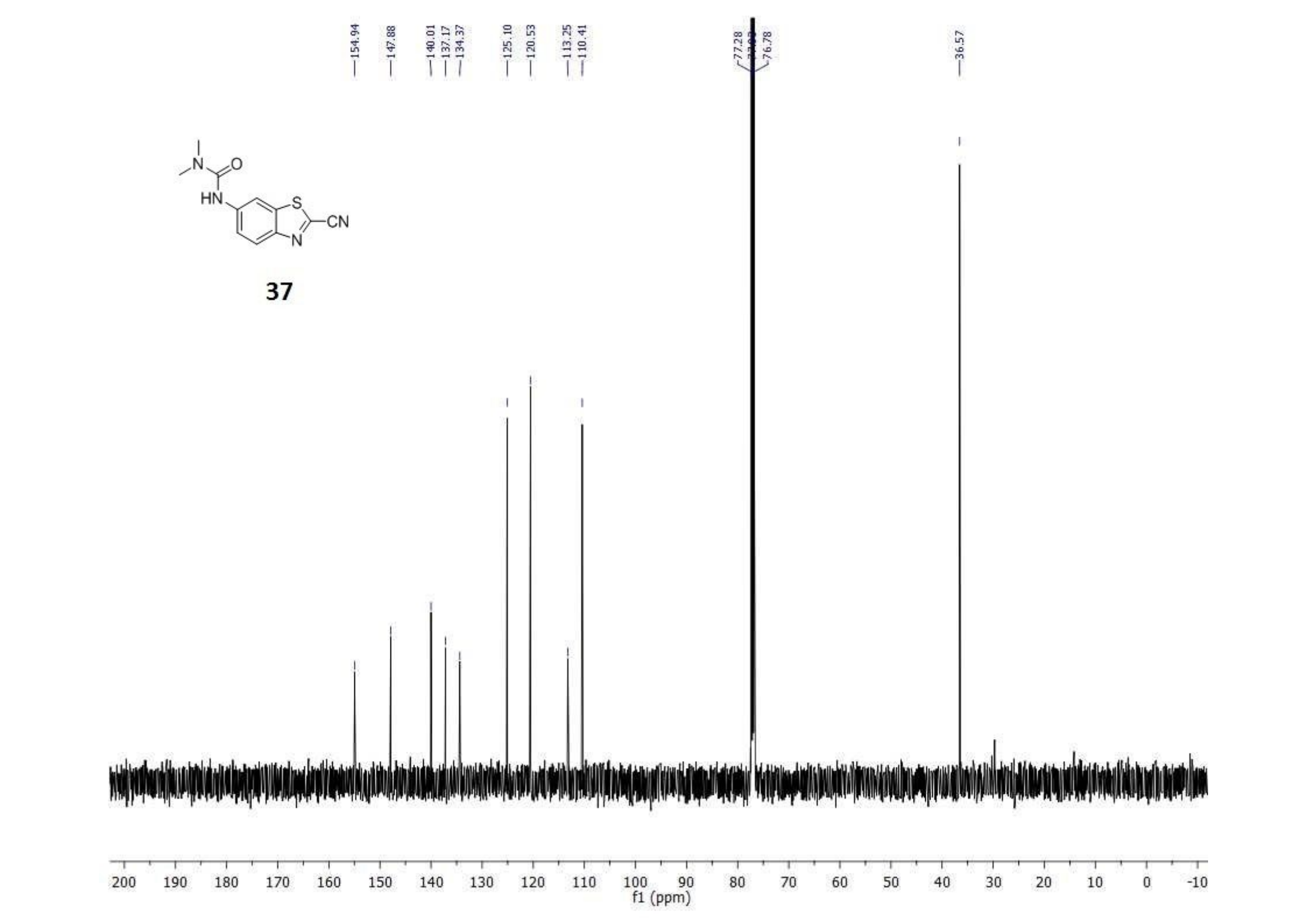
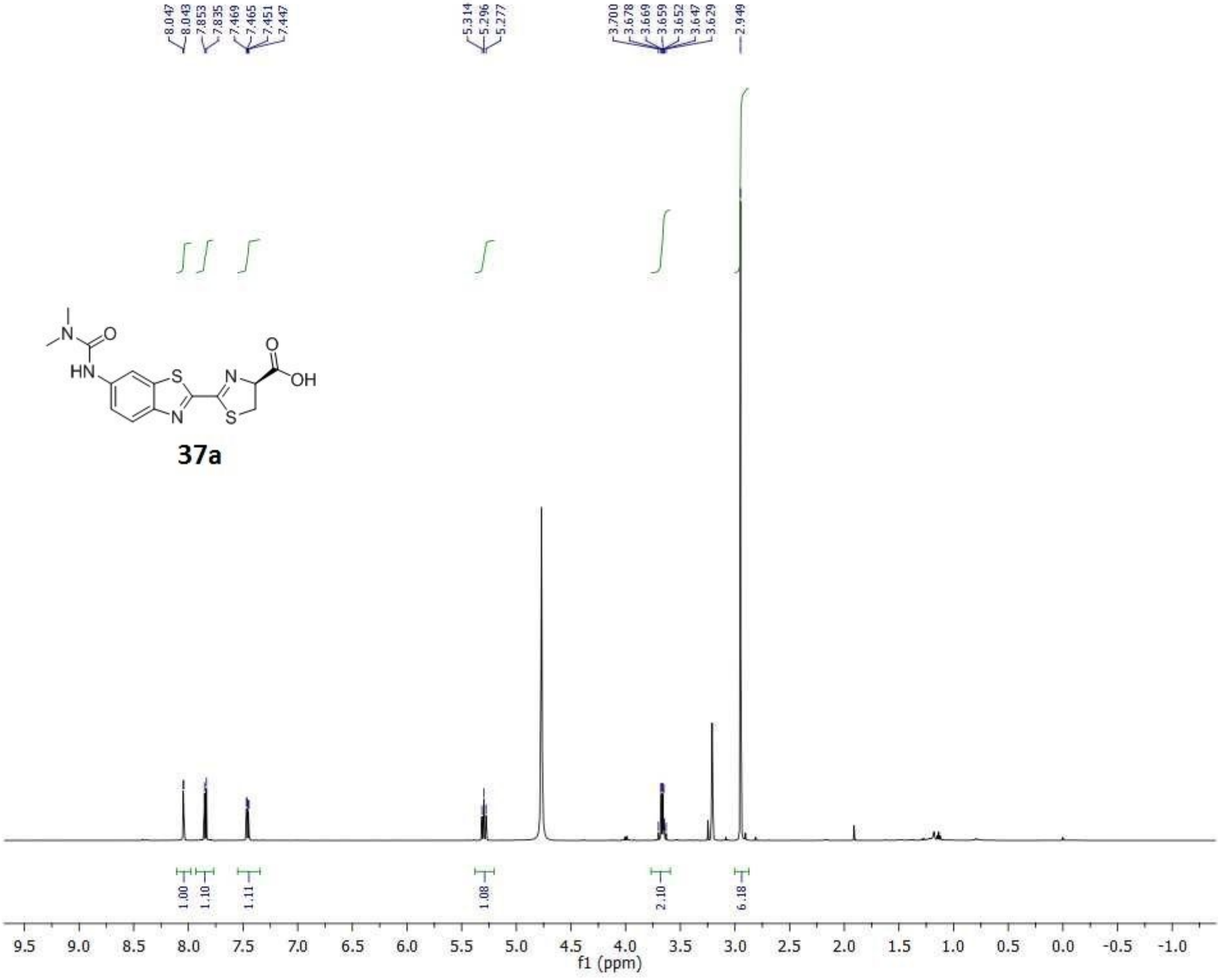
7.263
7.250
7.245
7.192
6.573
3.015
N
O
HN
S
CN
N
37
1.00
1.05
1.13
1.05
6.09
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


154.94
147.88
140.01
137.17
134.37
125.10
120.53
113.25
110.41
77.28
76.78
36.57
N
O
HN
S
CN
N
37
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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8.043
7.853
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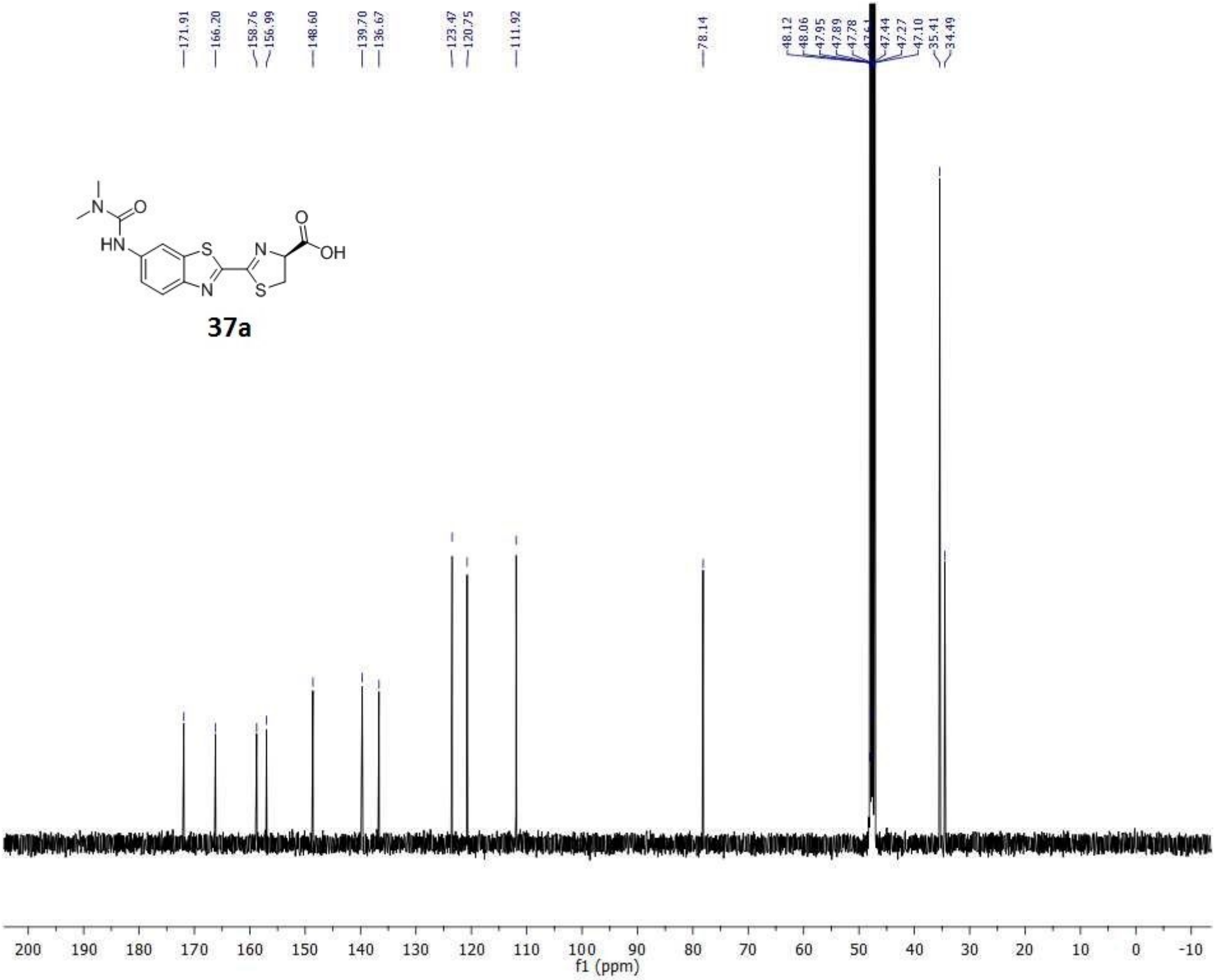
7.465
7.451
7.447
5.314
5.296
5.277
3.700
3.678
3.669
3.659
3.652
3.647
3.629
2.949
1.00
1.10
1.11
1.08
2.10
6.18
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

37a


171.91
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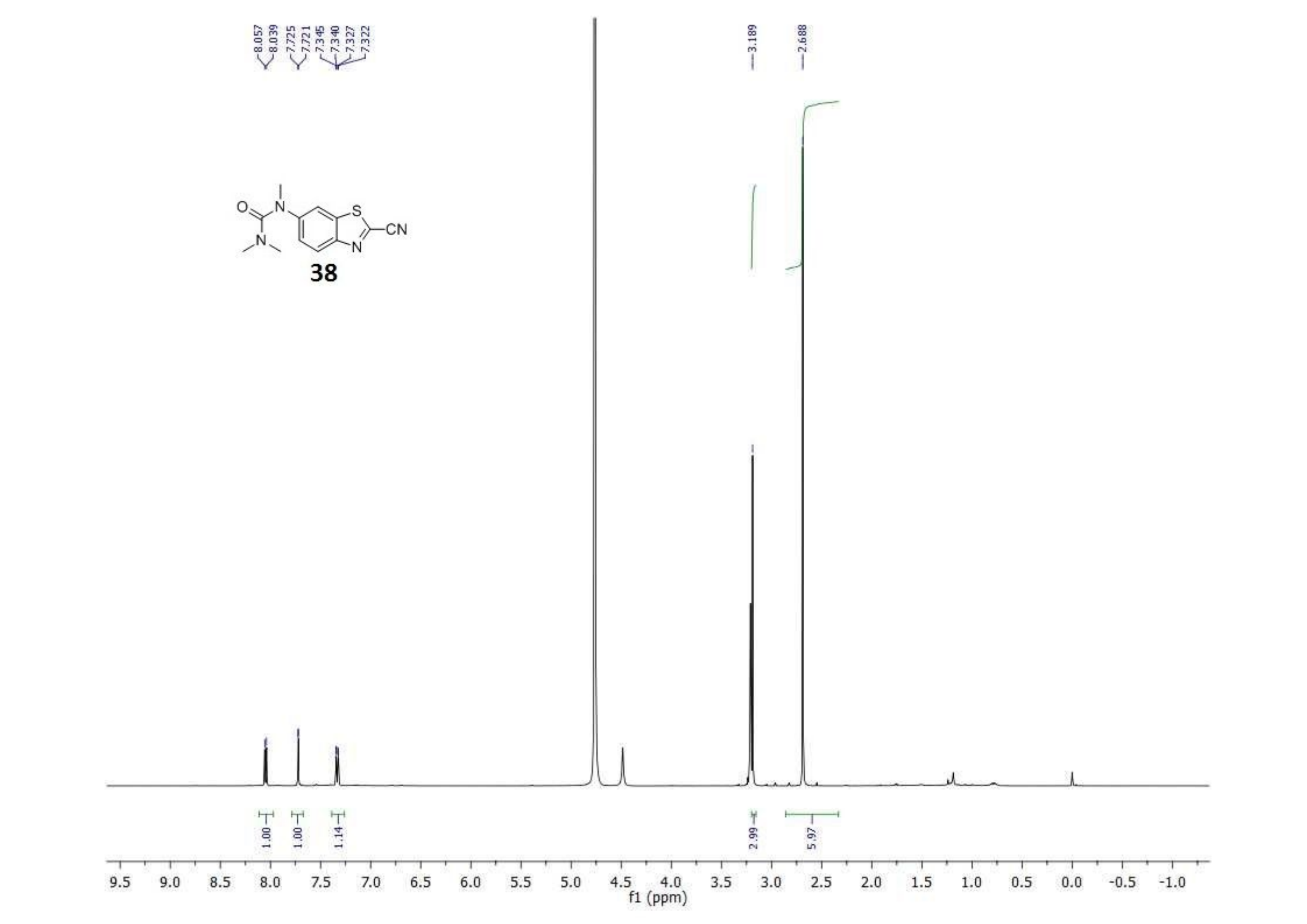
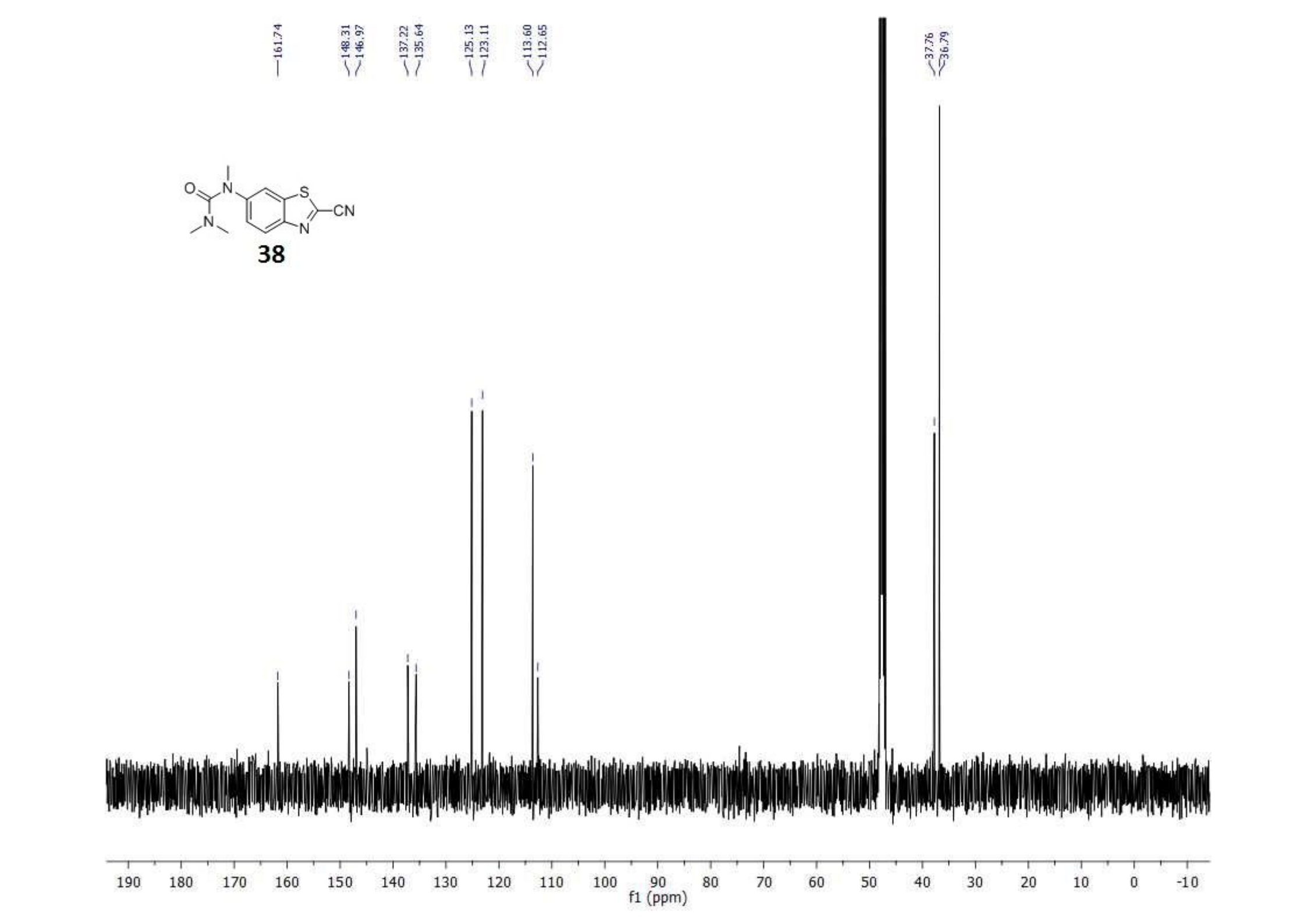
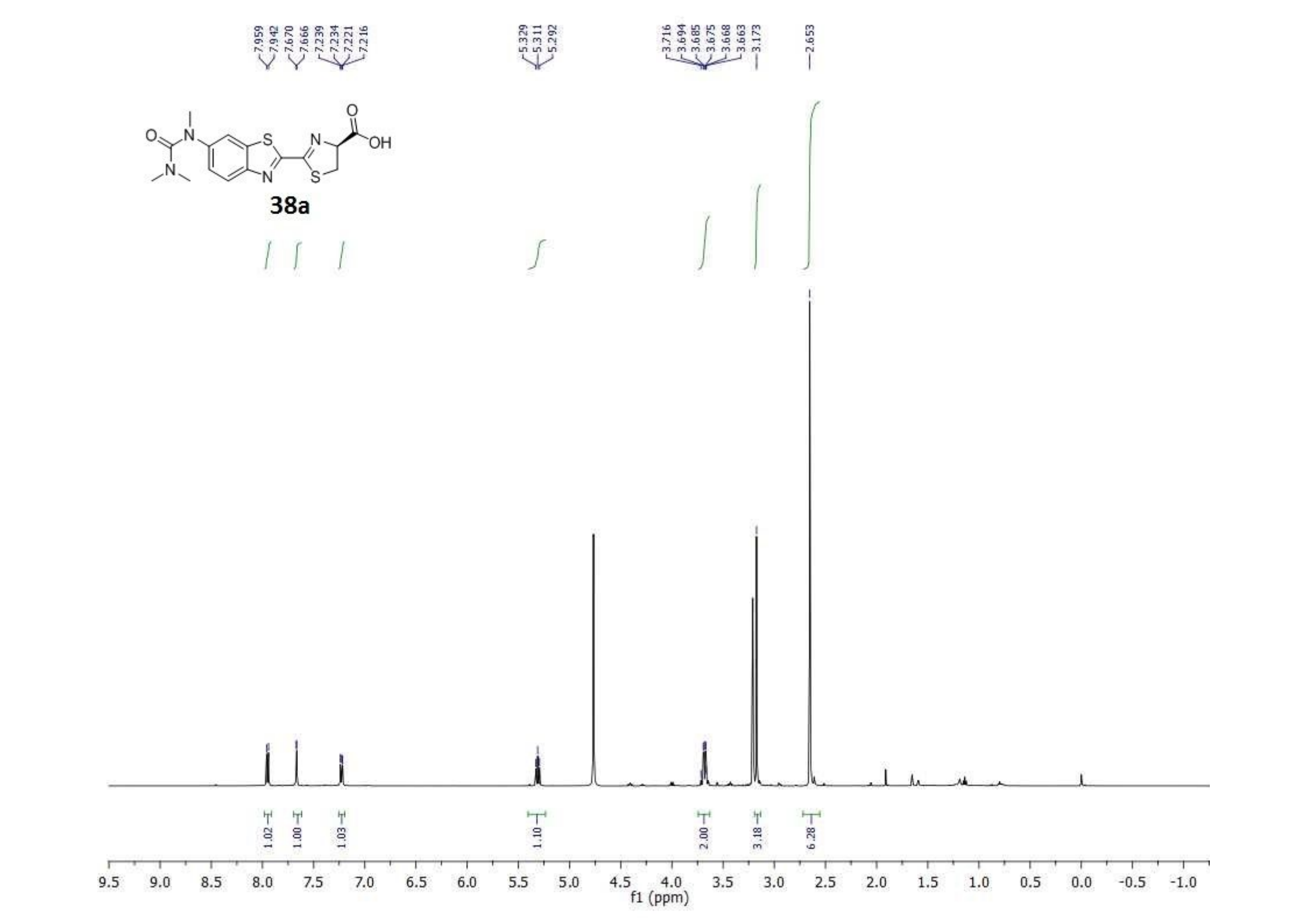
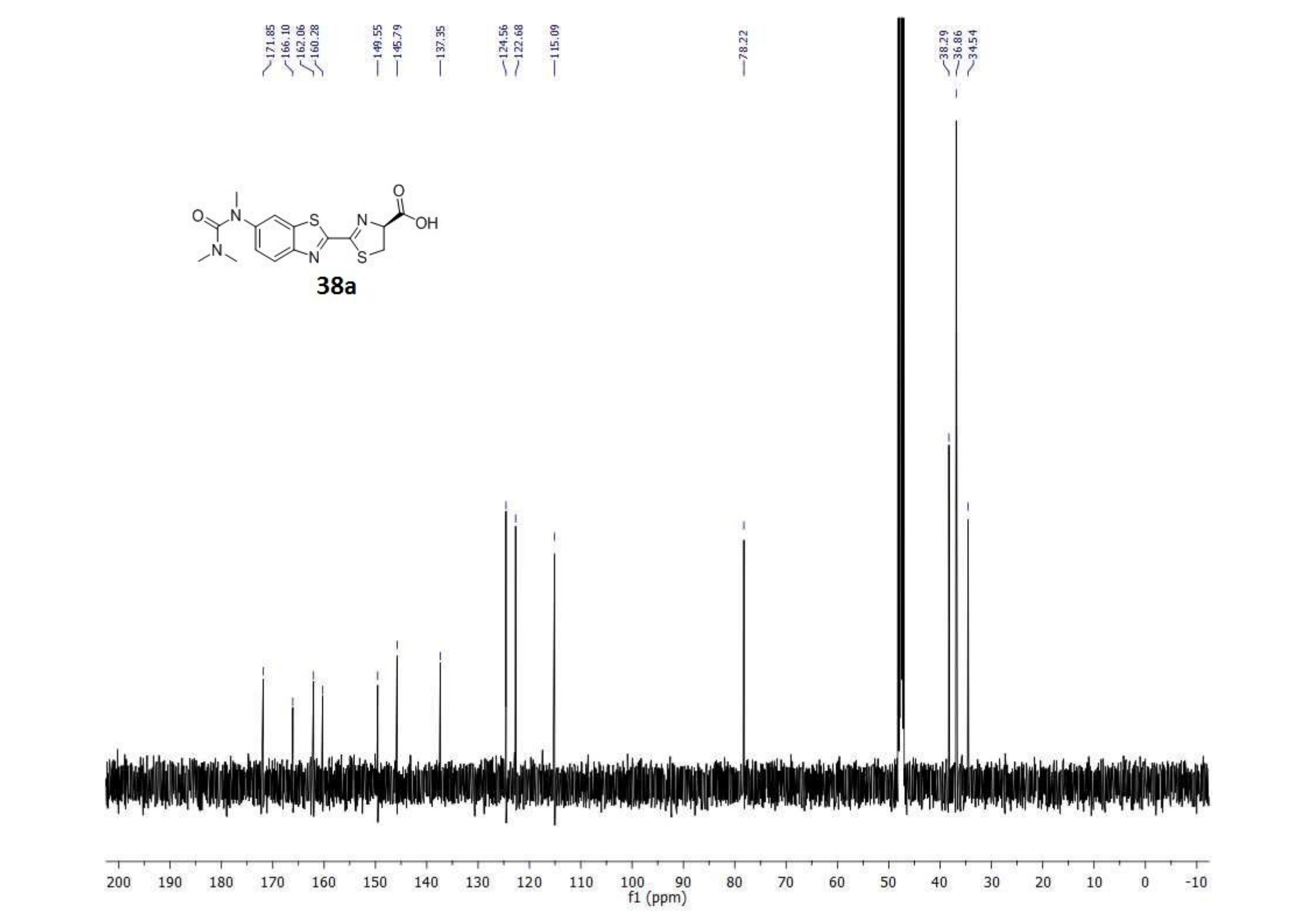
156.99
148.60
139.70
136.67
123.47
120.75
111.92
78.14
48.12
48.06
47.95
47.89
47.78
47.44
47.27
47.10
35.41
34.49
HN
N
O
S
N
O
OH
S
N
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

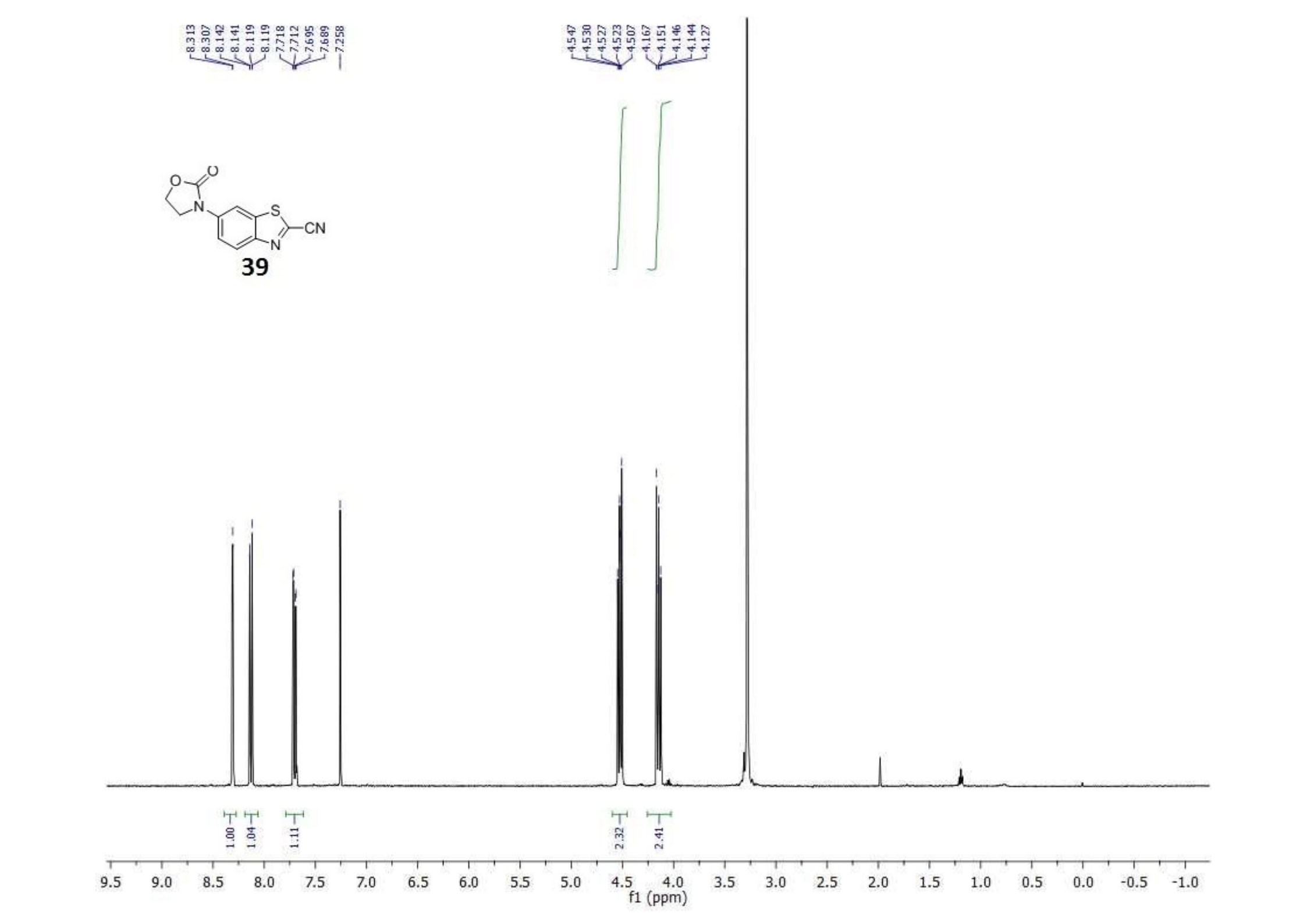
37a

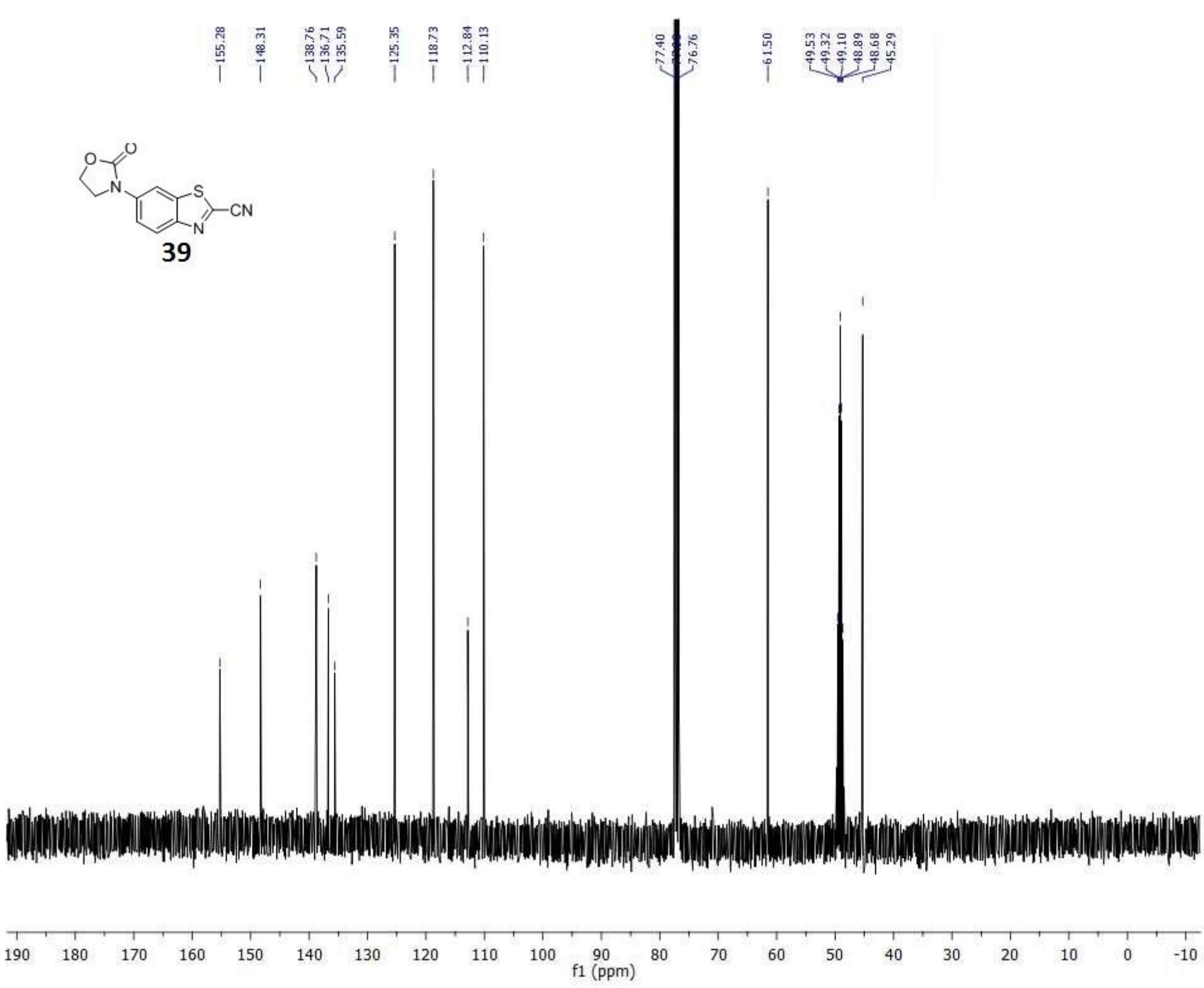

8.057
8.039
7.725
7.721
7.345
7.340
7.327
7.322
3.189
2.688
O
N
S
CN
N
N
38
1.00
1.00
1.14
2.99
5.97
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

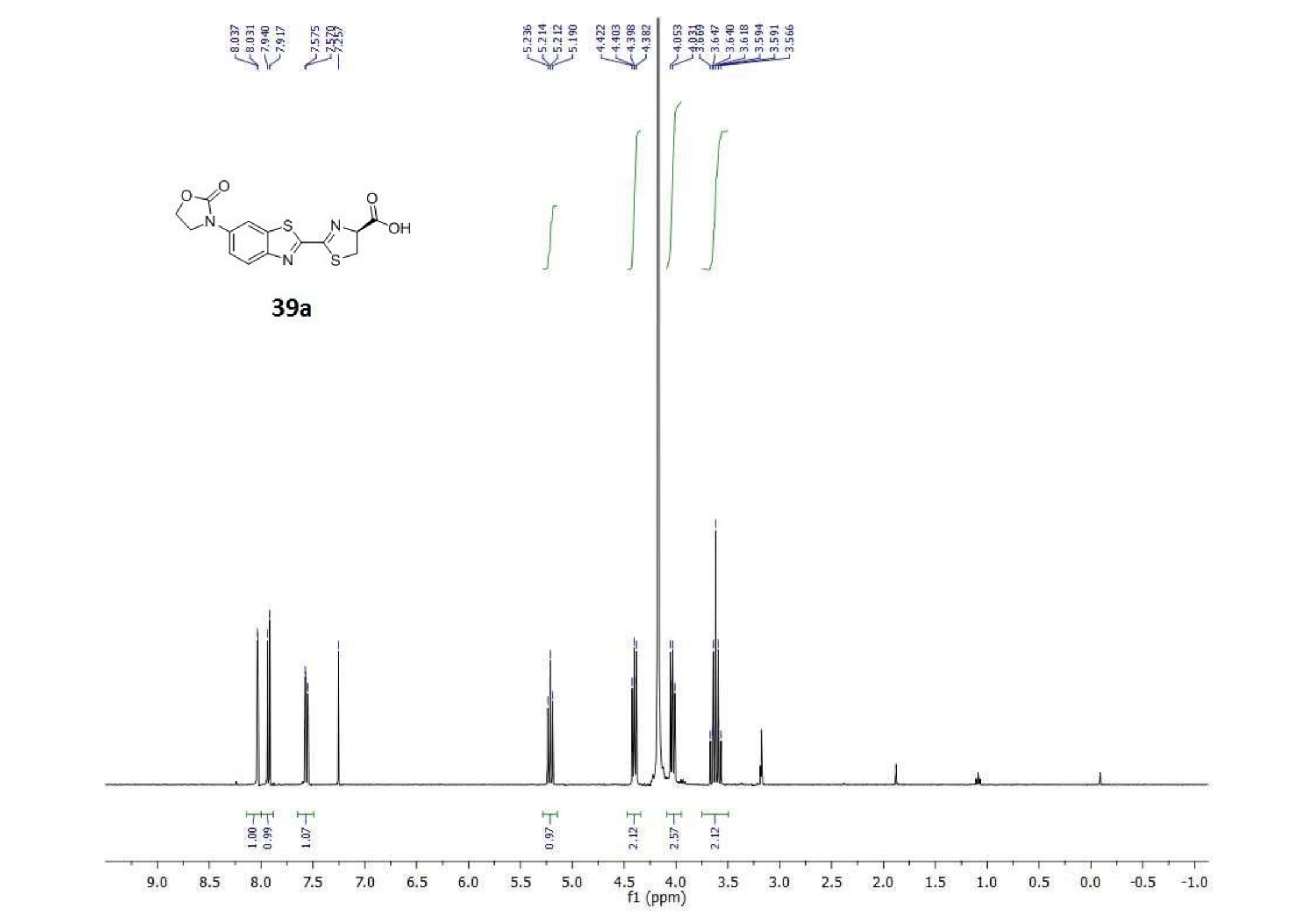

161.74
148.31
146.97
137.22
135.64
125.13
123.11
113.60
112.65
37.76
36.79
O
N
S
CN
N
N
38
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

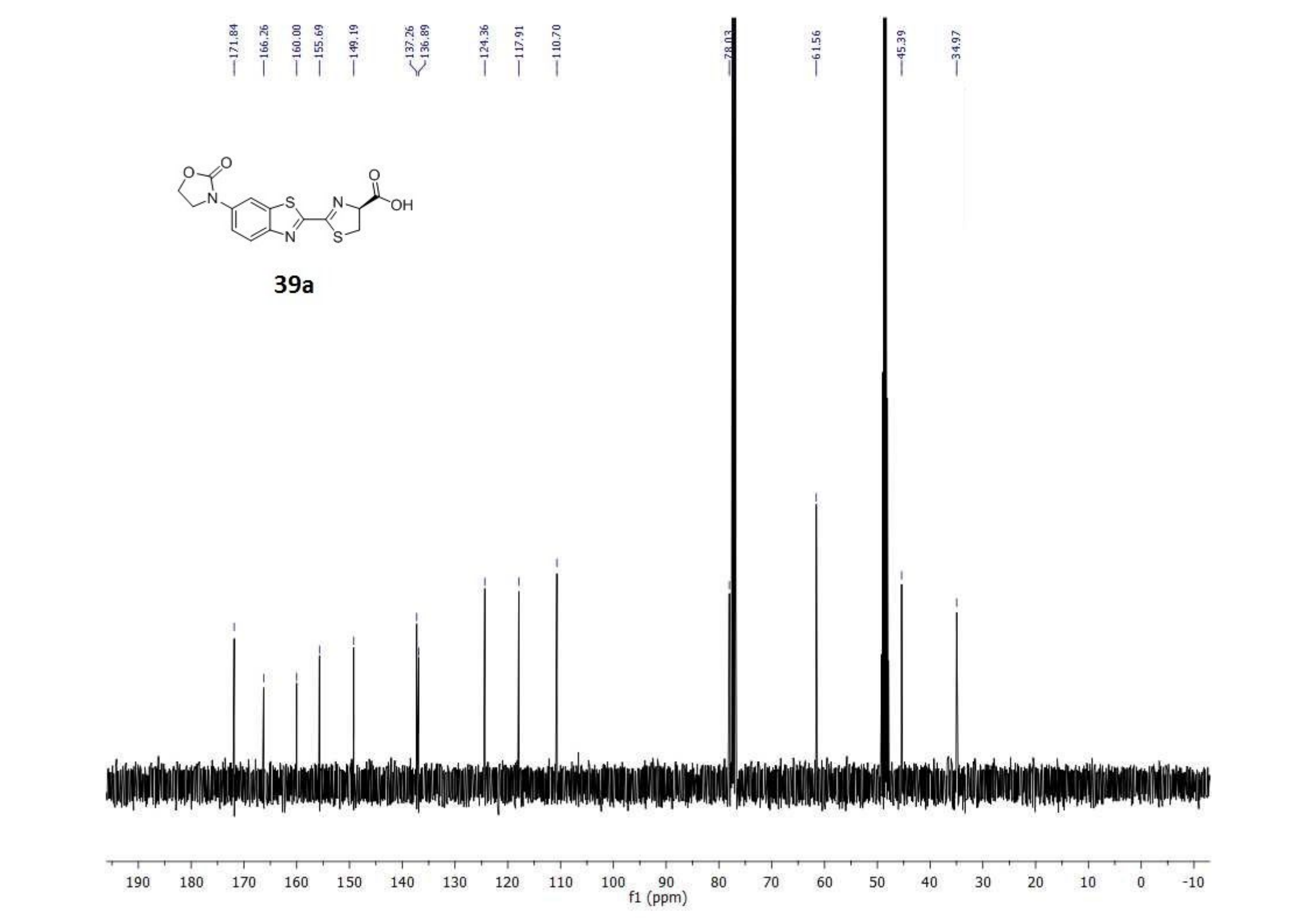

7.959
7.942
7.670
7.666
7.239
7.234
7.221
7.216
5.329
5.311
5.292
3.716
3.694
3.685
3.675
3.668
3.663
3.173
2.653
38a
1.02
1.00
1.03
1.10
2.00
3.18
6.28
f1 (ppm)

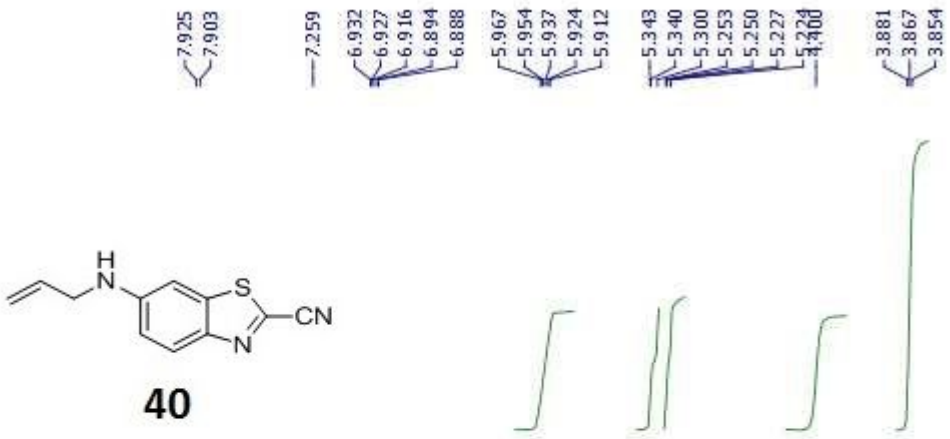

171.85
166.10
162.06
160.28
149.55
145.79
137.35
124.56
122.68
115.09
78.22
38.29
36.86
34.54
O
N
S
N
O
OH
N
S
N
38a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


8.313
8.307
8.142
8.141
8.119
8.119
7.718
7.712
7.695
7.689
7.258
4.547
4.530
4.527
4.523
4.507
4.167
4.151
4.146
4.144
4.127
O
O
N
S
CN
N
39
1.00
1.04
1.11
2.32
2.41
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

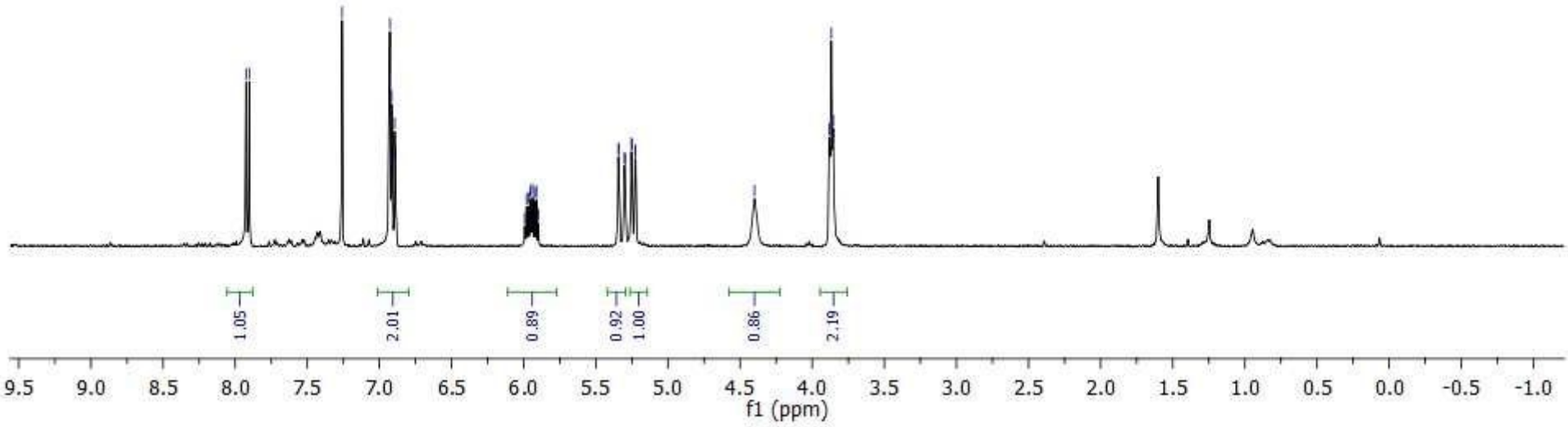

155.28
148.31
138.76
136.71
135.59
125.35
118.73
112.84
110.13
77.40
76.76
61.50
49.53
49.32
49.10
48.89
48.68
45.29
O
O
N
S
CN
N
39
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

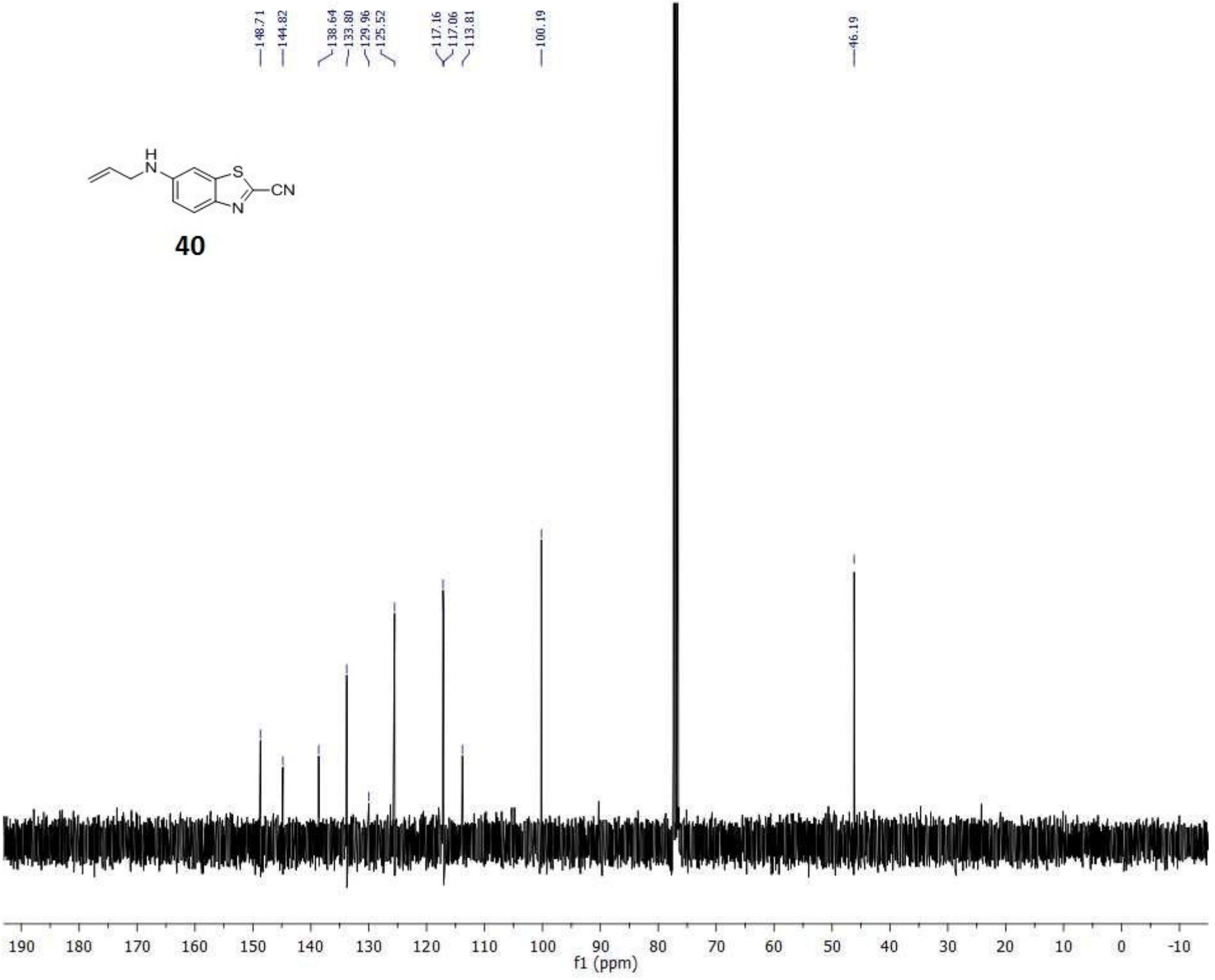

8.037
8.031
7.940
7.917
7.575
7.570
7.557
5.236
5.214
5.212
5.190
4.422
4.403
4.398
4.382
4.053
4.031
4.009
3.647
3.640
3.618
3.594
3.591
3.566
O
O
N
S
N
O
OH
S
N
39a
1.00
0.99
1.07
0.97
2.12
2.57
2.12
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

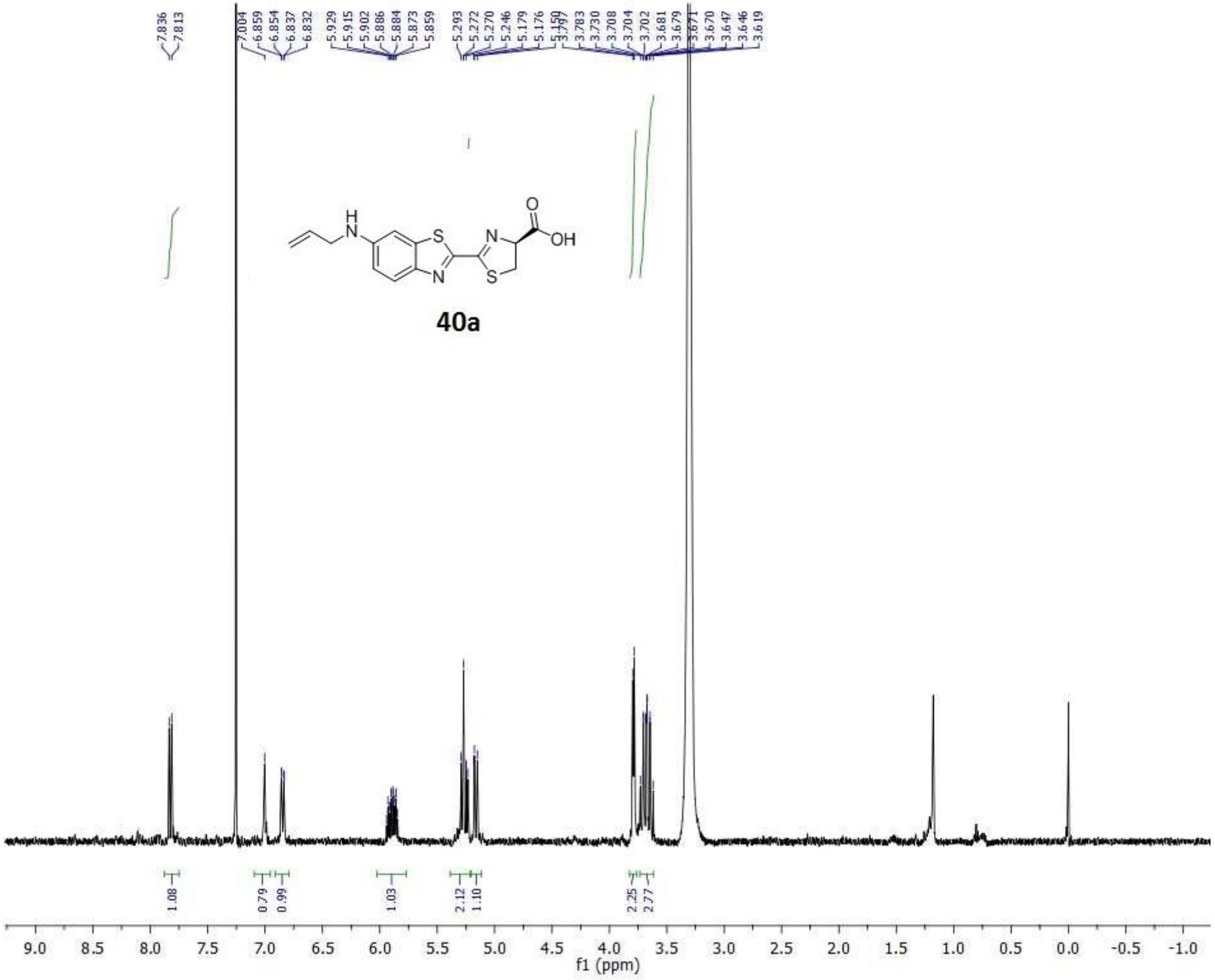

171.84
166.26
160.00
155.69
149.19
137.26
136.89
124.36
117.91
110.70
78.03
61.56
45.39
34.97
O
O
N
S
N
O
OH
N
S
39a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.925
7.903
7.259
6.932
6.927
6.916
6.894
6.888
5.967
5.954
5.937
5.924
5.912
5.343
5.340
5.300
5.253
5.250
5.227
5.224
3.881
3.867
3.854
H
N
S
CN
N

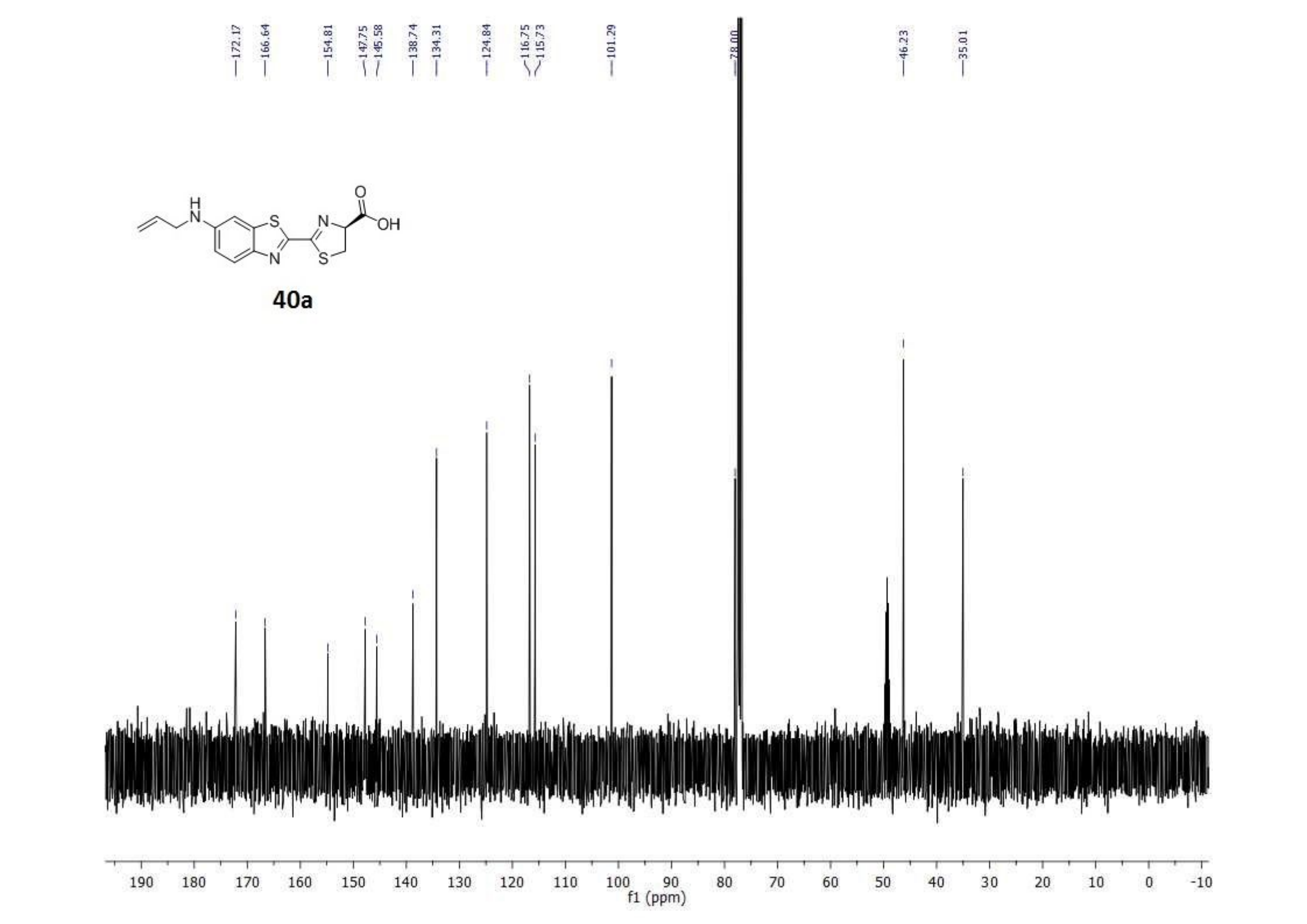
40

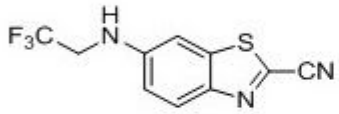

1.05
2.01
0.89
0.92
1.00
0.86
2.19
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


148.71
144.82
138.64
133.80
129.96
125.52
117.16
117.06
113.81
100.19
46.19
H
N
S
CN
N
40
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


7.836
7.813
7.004
6.859
6.854
6.837
6.832
5.929
5.915
5.902
5.886
5.884
5.873
5.859
5.293
5.272
5.270
5.246
5.179
5.176
5.150
3.797
3.783
3.730
3.708
3.704
3.702
3.681
3.679
3.671
3.670
3.647
3.646
3.619
H
N
S
N
N
S
O
OH
1.08
0.79
0.99
1.03
2.12
1.10
2.25
2.77
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

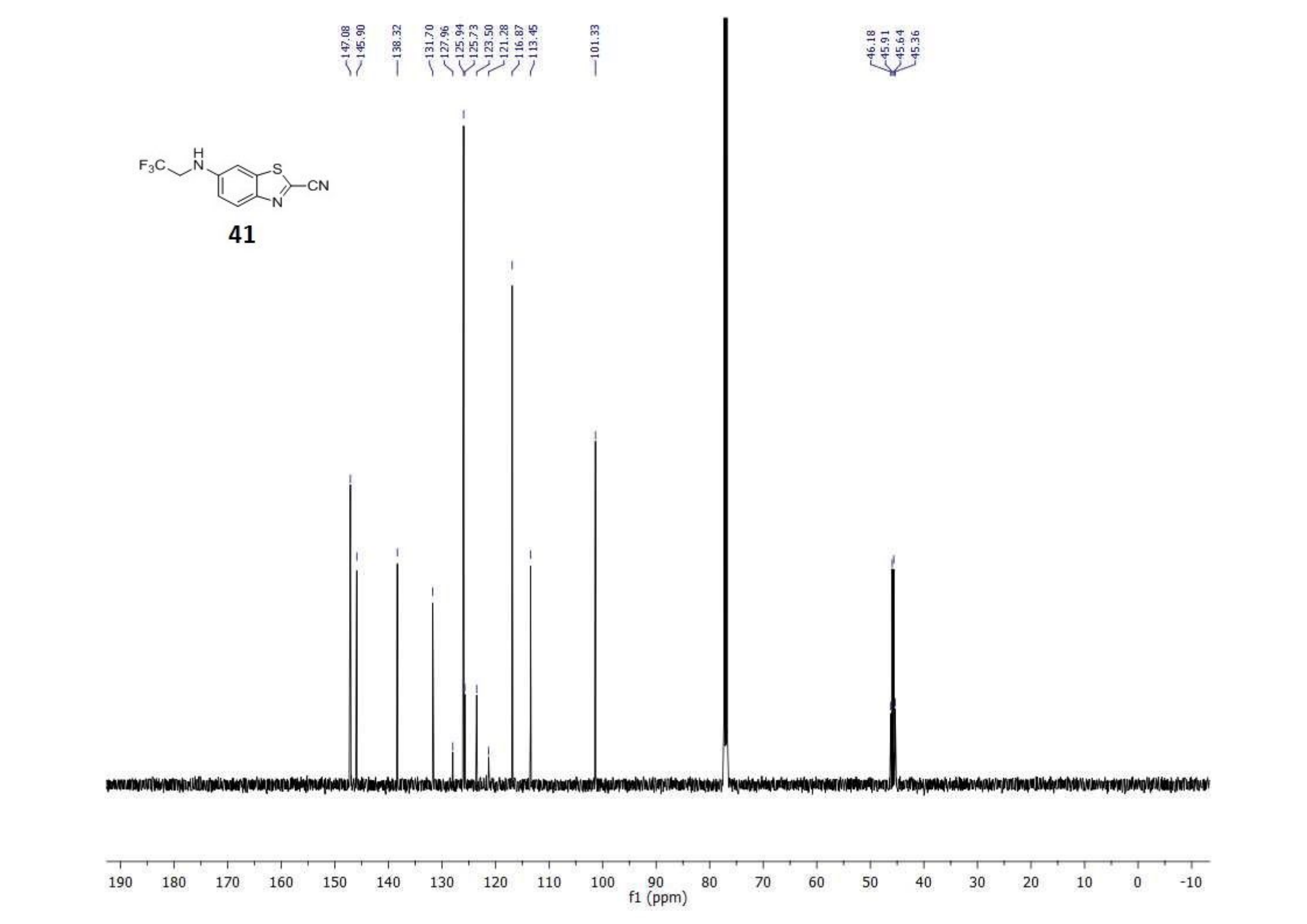
40a

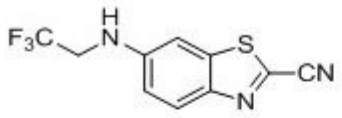

172.17
166.64
154.81
147.75
145.58
138.74
134.31
124.84
116.75
115.73
101.29
78.00
46.23
35.01
H
N
S
N
N
S
O
OH
40a
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


F3C
H
N
S
CN
N

41

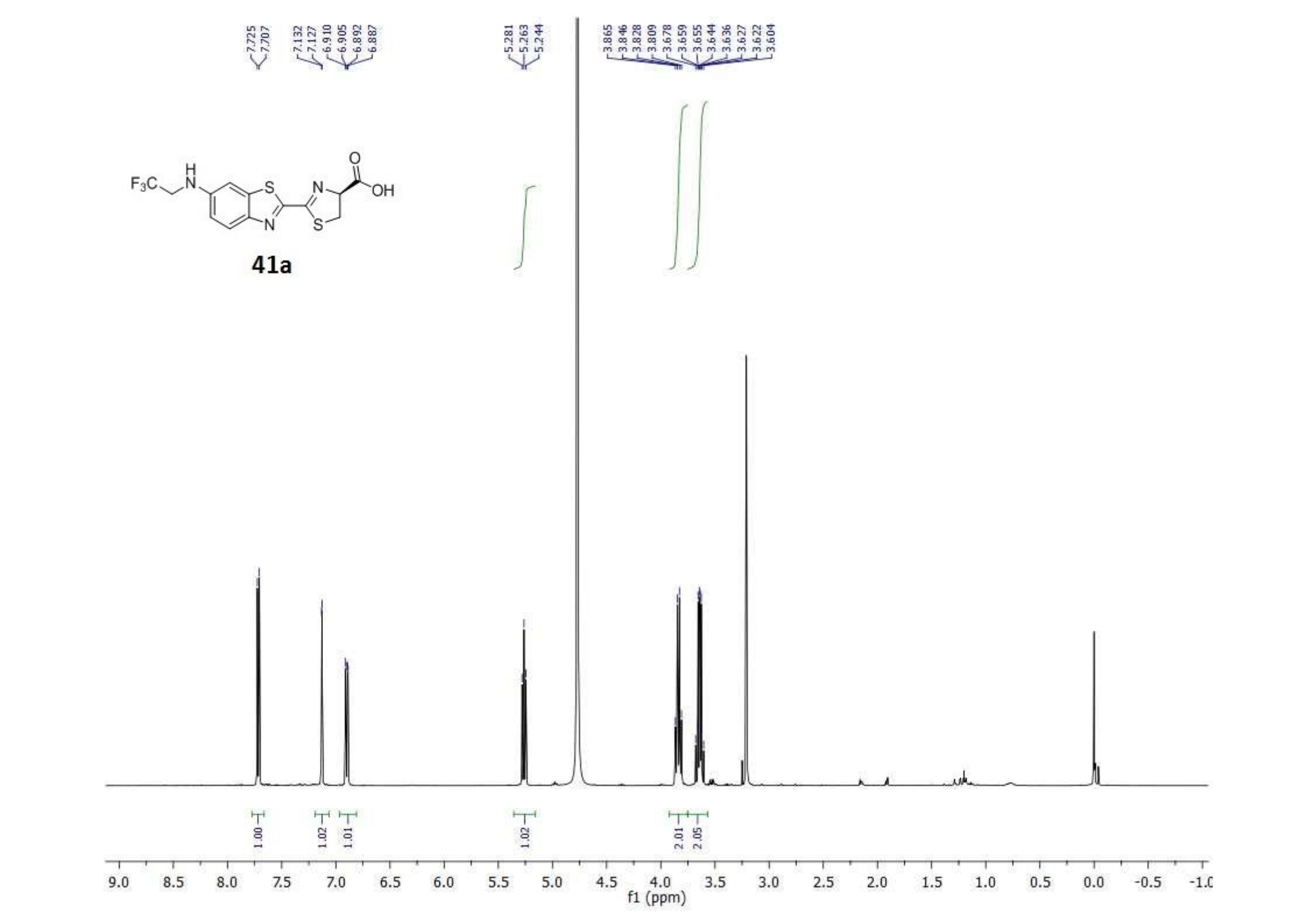
7.930
7.912
7.190
7.038
7.034
6.928
6.923
6.910
6.905
4.426
4.414
4.401
3.845
3.827
3.813
3.810
3.796
3.778
1.00
1.02
1.04
0.99
2.08
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


147.08
145.90
138.32
131.70
127.96
125.94
125.73
123.50
121.28
116.87
113.45
101.33
46.18
45.91
45.64
45.36
F3C
H
N
S
CN
N
41
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

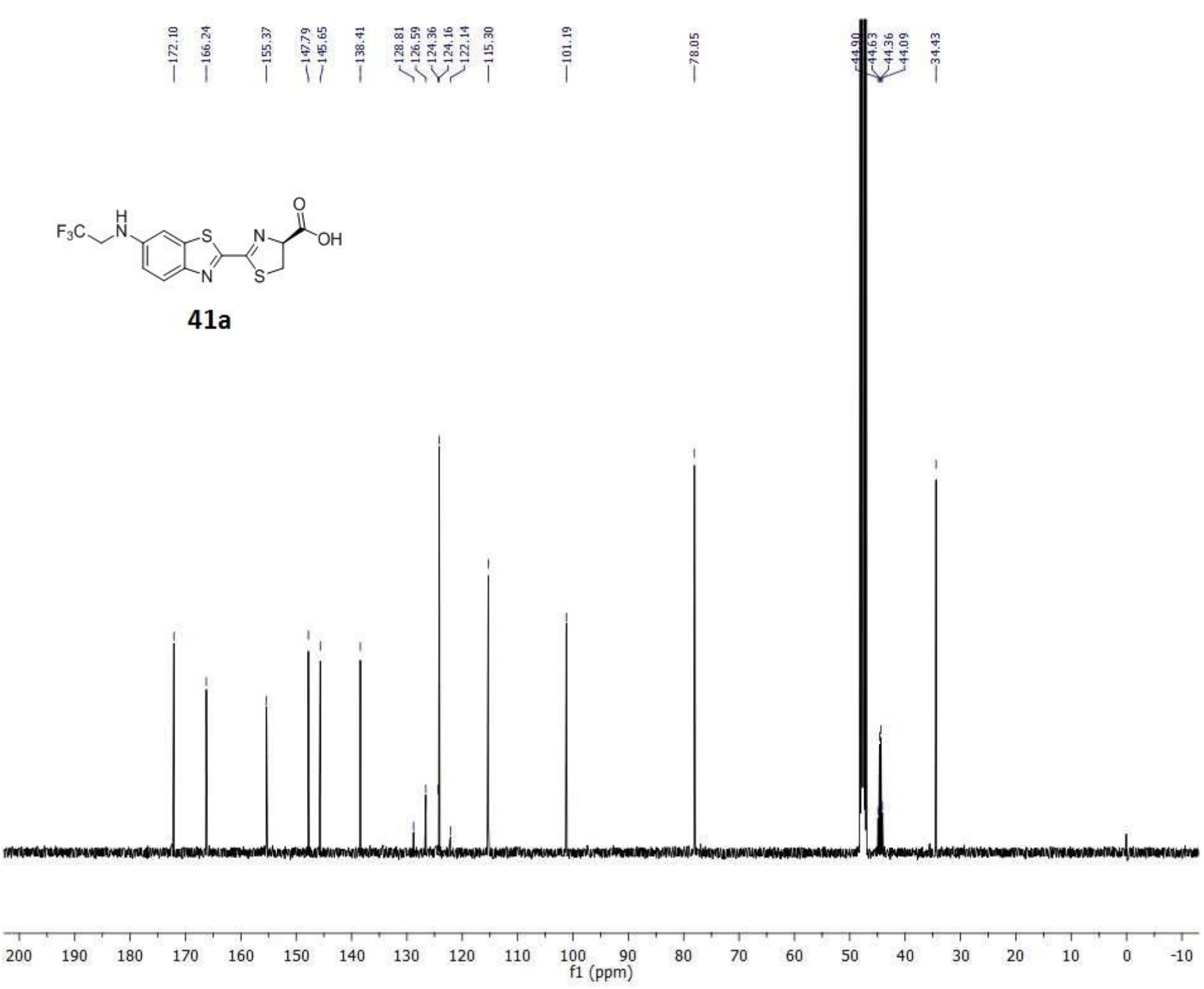

F3C
H
N
S
CN
N

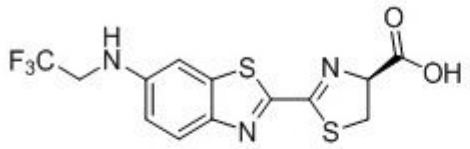
41

-71.947
-71.971
-71.994
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
f1 (ppm)


7.725
7.707
7.132
7.127
6.910
6.905
6.892
6.887
5.281
5.263
5.244
3.865
3.846
3.828
3.809
3.678
3.659
3.655
3.644
3.636
3.627
3.622
3.604
F3C
H
N
S
N
S
N
O
OH
1.00
1.02
1.01
1.02
2.01
2.05
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

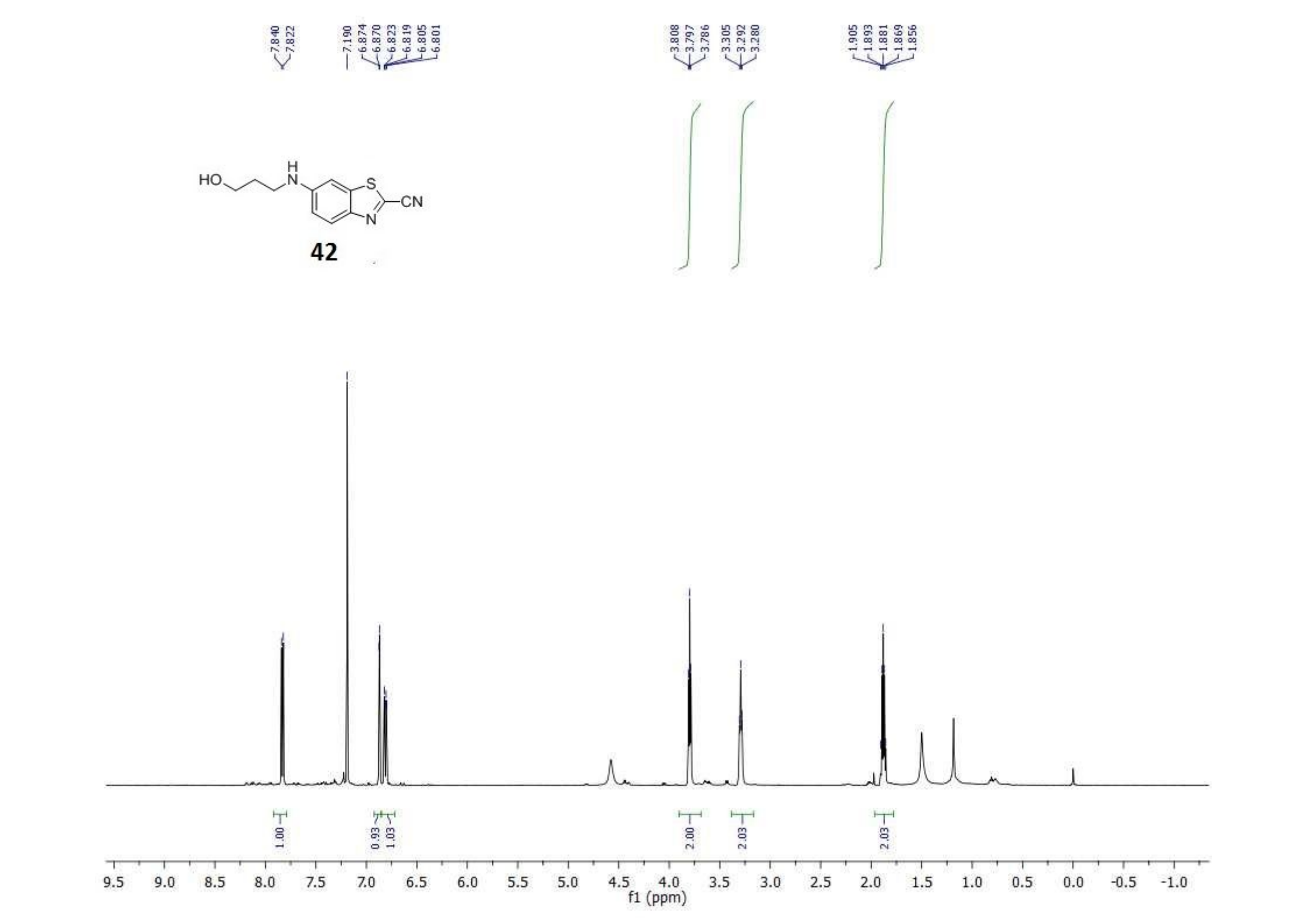
41a

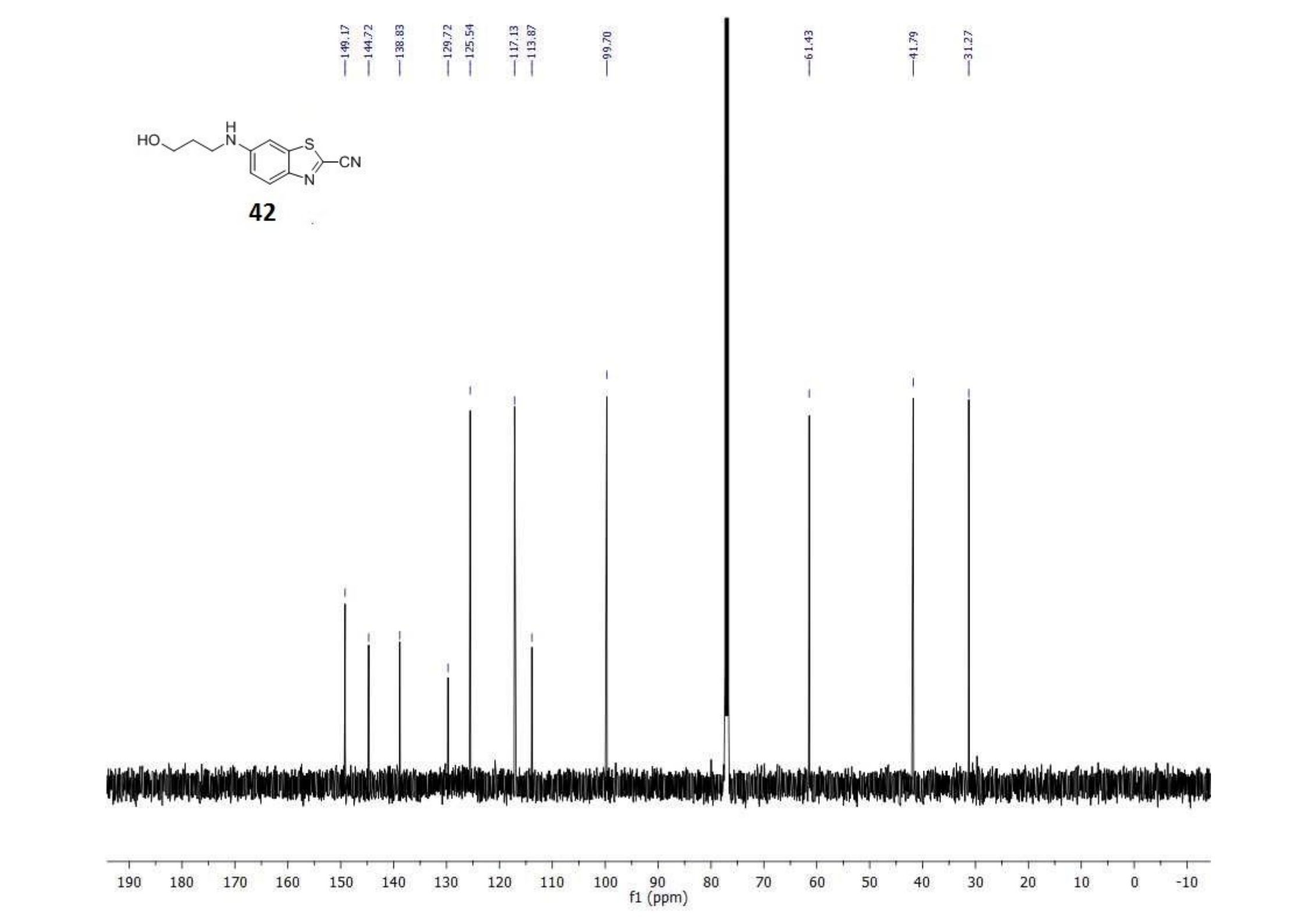

172.10
166.24
155.37
147.79
145.65
138.41
128.81
126.59
124.36
124.16
122.14
115.30
101.19
78.05
44.90
44.63
44.36
44.09
34.43
F3C
H
N
S
N
O
OH
N
S
41a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


F3C
H
N
S
N
S
N
O
OH

41a

-73.668
-73.688
-73.707
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
f1 (ppm)


7.840
7.822
7.190
6.874
6.870
6.823
6.819
6.805
6.801
3.808
3.797
3.786
3.305
3.292
3.280
1.905
1.893
1.881
1.869
1.856
HO
H
N
S
CN
N
42
1.00
0.93
1.03
2.00
2.03
2.03
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


149.17
144.72
138.83
129.72
125.54
117.13
113.87
99.70
61.43
41.79
31.27
HO
H
N
S
CN
N
42
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)