Supporting Information

Screening and Modulation of Protein-Protein Interactions via Sulfo-Click Kinetic Target-Guided Synthesis

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General: All reagents and solvents were purchased from commercial sources and used without further purification. All reactions were run under an Argon atmosphere unless otherwise indicated. Prior to use of solvents in reactions, they were purified by passing the degassed solvents through a column of activated alumina and transferred by an oven-dried syringe or cannula. Thin layer chromatography was performed on Merck TLC plates (silica gel 60 F_{254}). ^{1}H NMR and ^{13}C NMR were recorded on a Varian Inova 400 (400 MHz) or a Bruker Avance DPX-250 (250 MHz) instrument. The purification of designated compounds was carried out using reverse phase HPLC system (Waters Prep LC 4000 system with Waters 996 photo-diode array detector, Agilent column Eclipse XDB-C18, 5 μm, 9.4 mm × 250 mm). Compounds were eluted using a gradient elution of A:B (80:20 to 0:100) over 40 min at a flow rate of 5.0 mL/min, where solvent A was H_2O (0.05% TFA) and solvent B was CH_3CN (0.05% TFA). The HRMS data were measured on an Agilent 1100 Series MSD/TOF with electrospray ionization. The LC/MS data were measured on an Agilent 1100 LC/MSD-VL with electrospray ionization.

The gradient used for LC/MS-SIM analysis is shown below:

Gradient System 1:

Time	% B*	Flow rate	Time	% B*	Flow rate
0.00	10%	0.7 mL min^{-1}	11.50	100%	1.0 mL min^{-1}
2.00	10%	0.7 mL min^{-1}	11.51	10%	0.7 mL min^{-1}
10.00	100%	1.0 mL min^{-1}	13.50	10%	0.7 mL min^{-1}

* eluent A: H_2O (0.05% TFA); eluent B: CH_3CN (0.05% TFA)

Gradient System 2:

Time	% B*	Flow rate	Time	% B*	Flow rate
0.00	10%	0.7 mL min^{-1}	13.01	100%	1.5 mL min^{-1}
4.00	20%	0.7 mL min^{-1}	15.00	100%	1.5 mL min^{-1}
12.00	100%	0.7 mL min^{-1}	15.50	20%	0.7 mL min^{-1}
13.00	100%	0.7 mL min^{-1}	16.50	20%	0.7 mL min^{-1}

* eluent A: H_2O (0.05% TFA); eluent B: CH_3CN (0.05% TFA)

The sulfonyl azides, **SZ1-SZ6**, thio acids, **TA1-TA3** and the acylsulfonamides **SZ2TA1**, **SZ2TA2**, **SZ2TA3**, **SZ4TA1**, **SZ4TA2**, **SZ5TA1** and **SZ5TA2** have been previously reported.[1] The 4-acetamidobenzenesulfonamide was purchased from TCI America.

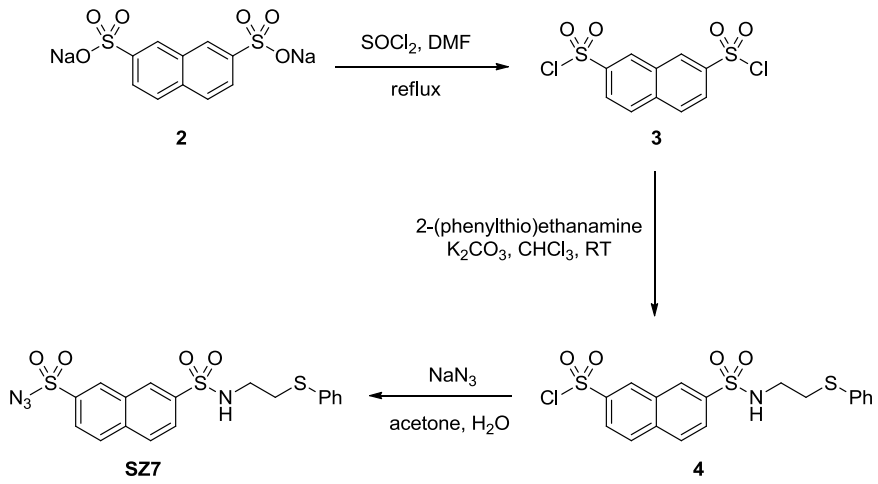
Expression and purification of wildtype and mutant Bcl-X_L fusion proteins. The protocols for the expression and purification of GST-tagged and His-tagged Bcl-X_L ΔTM fusion proteins have been previously reported.[1] The ^{F131A,D133A}Bcl-X_L ΔTM and ^{R139A}Bcl-X_L ΔTM mutants were generated by PCR mutagenesis using Bcl-X_L ΔTM cDNA as a template as described previously.[2]

General protocol for the control incubations of Bcl-X_L with reactive fragments and Bim BH3 peptides. For the Bcl-X_L containing incubation sample showing acylsulfonamide formation, control incubations with Bim peptides have been undertaken to demonstrate that the templation reaction occurs at the desired binding site. Thus, in a

96-well plate, one thio acid (1 μL of a 2 mM solution in methanol) and one sulfonyl azide (1 μL of a 2 mM solution in methanol) were added to a solution of Bcl-X_L (97 μL of a 2 μM Bcl-X_L solution in buffer). Finally, Bim BH3 peptide (1 μL of a 2 mM solution in DMSO) was added and the incubation sample in a sealed 96-well plate was incubated at 37 °C for six hours. Similar procedure was followed for the mutant Bim BH3 peptide incubation. These two incubation samples were then subjected to LC/MS-SIM analysis along with the wildtype Bcl-X_L containing sample without any of the Bim BH3 peptides.

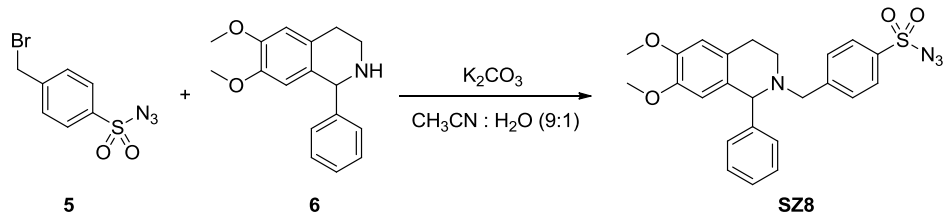
General protocol for the control incubations of mutants of Bcl-X_L with reactive fragments. Additional control experiments were carried out using the mutants of Bcl-X_L. In a 96-well plate, one thio acid (1 μL of a 2 mM solution in methanol) and one sulfonyl azide (1 μL of a 2 mM solution in methanol) were added to a solution of mutant Bcl-X_L (98 μL of a 2 μM mutant Bcl-X_L solution in buffer). This control sample was incubated along with the wildtype Bcl-X_L containing sample at 37 °C for six hours and subjected to LC/MS-SIM analysis.

Synthesis of Building Blocks:



Sulfonyl azide SZ7: The mixture of compound **2** (664 mg, 2 mmol), $SOCl_2$ (4 mL), and DMF (16 mL) was refluxed for 2 h. The reaction mixture was then treated with cold water (15 mL), extracted with DCM (15 mL × 3), and combined organic phases were dried over Na_2SO_4. A quick filtration through a pad of silica gel, evaporation, and vacuum drying gave the crude product **3** according to a similar procedure.[3] The sulfonyl chloride **3** obtained was used for the next step without further purification. A solution of sulfonyl chloride **3** (325 mg, 1 mmol), 2-(phenylthio)ethanamine (155 mg, 1 mmol) and potassium carbonate (200 mg, 1.44 mmol) in $CHCl_3$ (8 mL) was stirred at room temperature for 12 hours. The reaction mixture was then concentrated, treated with ethyl acetate (20 mL) and water (20 mL), and extracted with ethyl acetate (20 mL × 3). The combined organic layers were dried over Na_2SO_4 and concentrated. The crude product **4** obtained was dissolved in acetone and the solution of sodium azide (70 mg, 1 mmol) in water was added dropwise at 0 C. The mixture was stirred at 0 °C for 3 hours. Ethyl acetate (20 mL) and saturated aqueous potassium carbonate solution (20 mL) were added to the mixture and after extraction with ethyl acetate (20 mL × 3), the combined organic

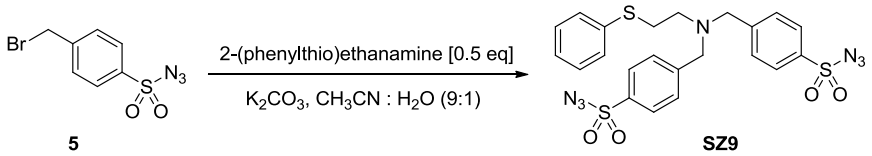
phases were dried over Na_2SO_4 and concentrated. The sulfonyl azide **SZ7** (315 mg, 70% over 3 steps) was obtained by flash chromatography (hexane : EtOAc = 4:1; R_f = 0.6 in hexane : EtOAc = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.56 (s, 1H), 8.49 (s, 1H), 8.11 – 8.01 (m, 4H), 7.19 – 7.10 (m, 5H), 5.37 (t, *J* = 6.0 Hz, 1H), 3.21 – 3.13 (m, 2H), 2.99 (t, *J* = 6.4 Hz, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 139.27, 137.05, 136.80, 133.49, 130.84, 130.25, 130.22, 130.15, 129.76, 129.44, 129.04, 126.93, 126.24, 124.59, 41.60, 33.85 ppm. HRMS (ESI) calcd for $C_{18}H_{16}N_4O_4S_3$ $[M+H]^+$: 449.04064, found: 449.04099



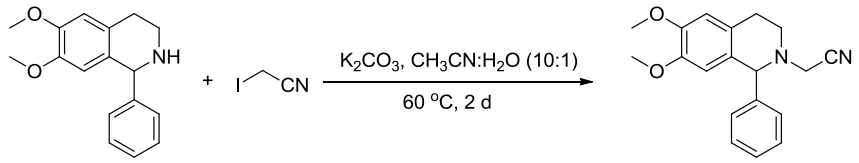
5 **6** **SZ8**

Sulfonyl Azide SZ8: A mixture of bromide **5**[1] (276 mg, 1 mmol), amine **6**[4] (276 mg, 1 mmol), and potassium carbonate (200 mg, 1.44 mmol) in acetonitrile and water (9:1; 6 mL), was stirred at room temperature for 12 hours. After treating with ethyl acetate (20 mL) and water (20 mL), the system was extracted with ethyl acetate (20 mL ×3). The combined organic layers were dried over anhydrous sodium sulfate and concentrated. Sulfonyl azide **SZ8** (404 mg, 87%) was obtained by flash chromatography (hexane : EtOAc = 6:1 with 0.1% triethylamine; R_f = 0.4 in hexane : EtOAc = 1:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.82 (d, *J* = 6.8 Hz, 2H), 7.54 (d, *J* = 7.3 Hz, 2H), 7.38 – 7.18 (m, 5H), 6.62 (s, 1H), 6.20 (s, 1H), 4.57 (s, 1H), 3.84 (d, *J* = 10.6 Hz, 1H), 3.80 (s, 3H), 3.56 (s, 3H), 3.39 (d, *J* = 14.5 Hz, 1H), 3.05 – 2.95 (m, 2H), 2.71 (d, *J* = 15.4 Hz, 1H), 2.58 – 2.48 (m, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 147.82, 147.18, 146.78, 143.40,

136.27, 129.48, 129.15, 129.08, 128.04, 127.14, 127.03, 126.22, 111.36, 110.59, 68.05, 57.90, 55.42, 47.32, 28.21 ppm. HRMS (ESI) calcd for $C_{24}H_{24}N_4O_4S$ $[M+H]^+$: 465.15965, found: 465.15970.

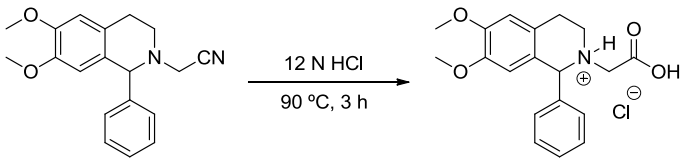


Sulfonyl azide SZ9: The sulfonyl azide **SZ9** was synthesized using a procedure described for the synthesis of **SZ8**, starting from 2-(phenylthio)ethanamine (72 mg, 0.47 mmol) and bromide **5** (260.4 mg, 0.94 mmol). The sulfonyl azide **SZ9** (154 mg, 60%) was obtained by flash chromatography (hexane : EtOAc = 6:1; R_f = 0.2 in hexane : EtOAc = 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.87 (d, *J* = 8.3 Hz, 4H), 7.6 (d, *J* = 8.1 Hz, 4H), 7.33 – 7.09 (m, 5H), 3.72 (s, 4H), 3.07 (t, *J* = 7.2 Hz, 2H), 2.76 (t, *J* = 6.9 Hz, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 146.61, 137.36, 129.63, 129.22, 128.97, 127.92, 127.65, 126.35, 57.91, 52.73, 31.48 ppm. HRMS (ESI) calcd for $C_{22}H_{21}N_7O_4S_3$ $[M+H]^+$: 544.08899, found: 544.08874.



Nitrile 7: To a solution of amine **6**[4] (1 g, 3.71 mmol) and iodoacetonitrile (620 mg, 3.71 mmol) in acetonitrile (30 mL) and water (3 mL), was added potassium carbonate (1.53 g, 11.13 mmol) and the resulting reaction mixture was stirred at 60 °C for 2 days. After cooling to room temperature, the solvent was removed under reduced pressure and

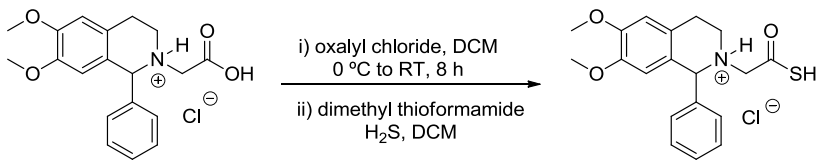
the crude was purified by flash chromatography (hexane : EtOAc = 6:1; R_f = 0.67 in hexane : EtOAc = 1:1) to obtain nitrile **7** with 79% yield (904 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.33 – 7.26 (m, 5H), 6.58 (s, 1H), 6.06 (s, 1H), 4.62 (s, 1H), 3.82 (s, 3H), 3.53 (s, 3H), 3.41 (d, *J* = 8.1 Hz, 2H), 3.27 – 3.16 (m, 1H), 3.09 – 2.94 (m, 2H), 2.74 (d, *J* = 15.7 Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 147.85, 147.47, 142.24, 129.53, 128.97, 128.38, 125.92, 115.05, 111.63, 110.89, 66.98, 56.01, 50.04, 44.00, 29.18 ppm. HRMS (ESI) calcd for $C_{19}H_{20}N_2O_2$ $[M+H]^+$: 309.15975, found: 309.15839.



7 8

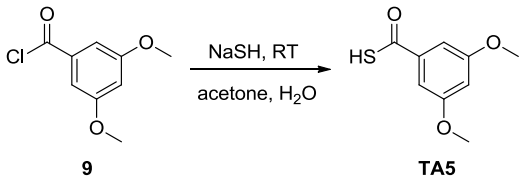
Acid 8: To a flask charged with nitrile **7** (100 mg, 0.32 mmol), was added 12 N HCl (1.5 mL) and the reaction mixture was stirred at 90 °C for 3 hours. The reaction mixture was then cooled to room temperature and treated with 2 N NaOH solution (pH = 5). The crashed out white solid was filtered, washed with cold MeOH and dried to obtain acid **8** as a hydrochloride salt (66%, 78 mg). The analytical sample was obtained by flash chromatography (MeOH : EtOAc = 2:1 with 0.2% acetic acid; R_f = 0.5 in MeOH : EtOAc = 3:1). ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.31 – 7.18 (m, 5H), 6.69 (s, 1H), 6.13 (s, 1H), 4.95 (s, 1H), 3.71 (s, 3H), 3.44 (s, 3H), 3.07 – 2.98 (m, 1H), 2.96 – 2.81 (m, 4H), 2.72 – 2.62 (m, 1H) ppm. ^{13}C NMR (101 MHz, DMSO-*d6*) δ 174.02, 147.02, 146.60, 144.42, 130.23, 129.29, 127.87, 126.85, 126.83, 111.98, 111.51, 64.97, 57.17, 55.44,

55.38, 47.30, 28.31 ppm. HRMS (ESI) calcd for $C_{19}H_{21}NO_4$ $[M+H]^+$: 328.15433, found: 328.15355.



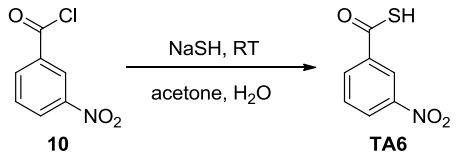
8 **TA4**

Thio acid TA4: The thio acid **TA4** was obtained starting from acid **8** (340 mg, 0.93 mmol) with 25% yield via the same procedure as previously reported for the thio acid **TA2**.[1] R_f = 0.6 in DCM : MeOH = 10:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35 – 7.23 (m, 5H), 6.66 (s, 1H), 6.27 (s, 1H), 5.57 (s, 1H), 3.83 (s, 3H), 3.63 (s, 3H), 3.50 – 3.39 (m, 2H), 3.37 (s, 2H), 3.24 – 3.01 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 204.67, 149.54, 148.69, 136.42, 130.45, 129.99, 129.30, 123.44, 121.74, 111.17, 110.88, 66.16, 63.53, 56.08, 45.27, 24.46 ppm. HRMS (ESI) calcd for $C_{19}H_{21}NO_3S$ $[M+H]^+$: 344.13149, found: 344.13149.



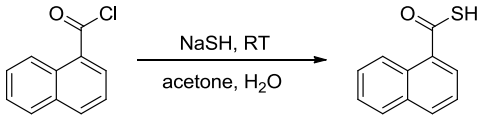
9 **TA5**

Thio acid TA5: The synthesis of thio acid **TA5** was accomplished starting from acid chloride **9** (400 mg, 1.99 mmol) via the same procedure as previously reported for thio acid **TA3**[1] with 15% yield. R_f = 0.17 in hexane : EtOAc = 2:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.00 (d, J = 2.1 Hz, 2H), 6.65 – 6.63 (m, 1H), 3.8 (s, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 190.10, 160.97, 138.57, 106.36, 105.69, 55.73 ppm. HRMS (ESI) calcd for $C_9H_{10}O_3S$ $[M-H]^-$: 197.02779, found: 197.02780.



10 **TA6**

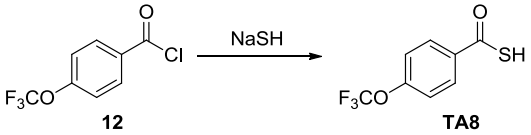
Thio acid TA6: To a solution of NaSH (90 mg, 1.6 mmol) in water (1mL) was added dropwise a solution of acid chloride **10** (200 mg, 1.07 mmol) in acetone (6 mL). The resulting mixture was stirred for 2 h. The solvent was removed under reduced pressure and resulting crude was basified using 10% NaOH solution (pH = 12). The reaction mixture was then extracted with ethyl acetate to remove organic impurities. The aqueous layer was slowly acidified using 2 N HCl solution (pH = 1). Corresponding thio acid **TA6** crashed out and was filtered, washed with deionized water and dried under vacuum to obtain pale yellow crystals of thio acid **TA6** with 25% yield. R_f = 0.26 in hexane : EtOAc = 1:3. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.75 – 8.72 (m, 1H), 8.50 – 8.44 (m, 1H), 8.22 (d, *J* = 7.8 Hz, 1H), 7.70 (t, *J* = 8.0 Hz, 1H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 188.19, 137.96, 133.42, 130.32, 128.32, 122.96 ppm. HRMS (ESI) calcd for $C_7H_5NO_3S$ $[M-H]^-$: 181.99174, found: 181.99167.



11 **TA7**

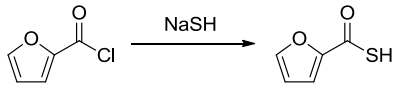
Thio acid TA7: To a solution of NaSH (90 mg, 1.6 mmol) in water (1mL) was added dropwise a solution of acid chloride **11** (204 mg, 1.07 mmol) in acetone (6 mL). The resulting mixture was stirred for 2 h. The solvent was removed under reduced pressure and resulting crude was basified using 10% NaOH solution (pH = 12). The reaction mixture was then extracted with ethyl acetate to remove organic impurities. The aqueous

layer was slowly acidified using 2 N HCl solution and the aqueous layer was extracted using ethyl acetate at various pH values starting from 6 to 2, collecting organic fractions for every unit change in the pH. Fractions collected between pH changing from 5 to 2 were combined and were subjected to preparative HPLC to obtain thio acid **TA7** with 27% yield. R_f = 0.24 in hexane : EtOAc = 1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.61 – 8.50 (m, 1H), 8.35 (d, *J* = 7.1 Hz, 1H), 8.13 – 7.99 (m, 1H), 7.94 – 7.84 (m, 1H), 7.68 – 7.53 (m, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 188.15, 134.29, 134.00, 133.43, 129.52, 129.09, 128.79, 128.65, 127.27, 125.41, 124.71 ppm. HRMS (ESI) calcd for $C_{11}H_8OS$ $[M-H]^-$: 187.02231, found: 187.02179.



12 **TA8**

Thio acid TA8: The acid chloride **12** (500 mg, 2.22 mmol) and NaSH (149 mg, 2.66 mmol) were stirred at 0 °C under solvent free conditions for 1 h and the thio acid **TA8** obtained, after filtering the salts, was used without further purification. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 7.93 – 7.85 (m, 2H), 7.32 – 7.17 (m, 2H) ppm. HRMS (ESI) calcd for $C_8H_5F_3O_2S$ $[M-H]^-$: 220.98896, found: 220.98860.



13 **TA9**

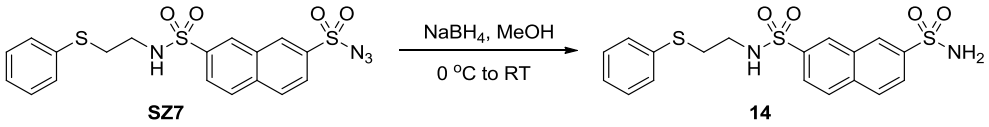
Thio acid TA9: The thio acid **TA9** was prepared following the same procedure as described for **TA8**. ^{1}H NMR (250 MHz, CD_3OD) δ: 7.92 (dd, *J* = 1.7, 0.8 Hz, 1H), 7.49

(dd, J = 3.7, 0.8 Hz, 1H), 6.73 (dd, J = 3.7, 1.7 Hz, 1H) ppm. HRMS (ESI) calcd for $C_5H_4O_2S$ $[M-H]^-$: 126.98592, found: 126.98631.

General procedure for the synthesis of acylsulfonamides (A): A solution of sulfonamide (1 eq), carboxylic acid (1 eq), EDCI (2 eq) and DMAP (0.2 eq) were stirred in dry DCM or THF, under inert atmosphere at room temperature overnight, quenched by adding water and the system was extracted with ethyl acetate. The combined organic layers were dried over anhydrous sodium sulfate and concentrated. The crude was then subjected to flash chromatography to obtain the corresponding acylsulfonamide.

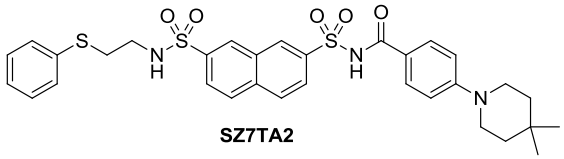
General procedure for the synthesis of acylsulfonamides (B): Synthesis of acylsulfonamide was accomplished by reacting selenocarboxylate (generated from corresponding carboxylic acid and selenating reagent, LiAlHSeH) with the sulfonyl azide according to a previously reported procedure.[5]

Synthesis of Kinetic TGS Hits:



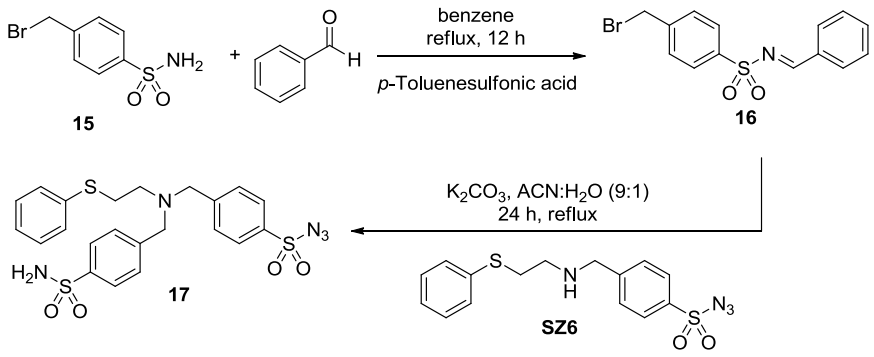
Sulfonamide 14: Sodium borohydride (60 mg, 1.5 mmol) was added slowly to the solution of **SZ7** (500 mg, 1.1 mmol) in methanol (6mL) at 0 °C. The reaction mixture was stirred for 30 min at room temperature, quenched using solid NH_4Cl and the solvent was removed under reduced pressure to afford the crude product. Sulfonamide **14** (418 mg, 90%) was obtained by flash chromatography. R_f = 0.64 in hexane : EtOAc = 1:2. ^1H NMR (250 MHz, Acetone-*d6*) δ: 8.67 (s, 1H), 8.60 (s, 1H), 8.21 – 8.12 (m, 3H), 8.02 (dd,

J = 8.7, 1.7 Hz, 1H), 7.28 – 7.10 (m, 5H), 6.97 (t, *J* = 5.8 Hz, 1H), 6.87 (bs, 2H), 3.30 – 3.18 (m, 2H), 3.15 – 3.06 (m, 2H) ppm. ^{13}C NMR (63 MHz, Acetone-*d6*) δ: 143.54, 140.22, 136.63, 135.93, 132.11, 130.57, 130.32, 130.03, 129.97, 129.74, 128.52, 127.20, 125.86, 125.83, 43.24, 33.73 ppm. HRMS (ESI) calcd for $C_{18}H_{18}N_2O_4S_3$ $[M+H]^+$: 423.05015, found: 423.04855.



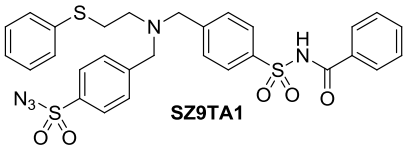
SZ7TA2

Acylsulfonamide SZ7TA2: The acylsulfonamide **SZ7TA2** was prepared following the general procedure **A**, starting from sulfonamide **14** and 4-(4,4-dimethylpiperidin-1-yl)benzoic acid[1] with 16% yield (102 mg) after purification using preparative HPLC system. R_f = 0.28 in EtOAc. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.77 (s, 1H), 8.46 (s, 1H), 8.23 (d, *J* = 8.2 Hz, 1H), 7.91 – 7.78 (m, 3H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.19 – 7.01 (m, 5H), 6.64 (d, *J* = 8.0 Hz, 2H), 5.65 (bs, 1H), 3.34 – 3.15 (m, 4H), 3.12 (d, *J* = 5.7 Hz, 2H), 2.96 (d, *J* = 5.6 Hz, 2H), 1.46 – 1.23 (m, 4H), 0.93 (s, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.05, 154.37, 138.41, 137.92, 136.46, 133.56, 131.23, 130.84, 130.17, 129.94, 129.51, 129.45, 129.02, 126.88, 126.18, 125.42, 117.85, 113.03, 43.71, 41.66, 37.76, 33.87, 28.58, 27.68 ppm. HRMS (ESI) calcd for $C_{32}H_{35}N_3O_5S_3$ $[M+H]^+$: 638.18116, found: 638.18097.



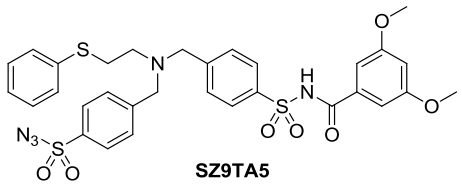
Sulfonamide 17: A solution of sulfonamide **15**[1] (900 mg, 3.6 mmol), benzaldehyde (381 mg, 3.6 mmol) and *p*-Toluenesulfonic acid (10 mg) in benzene was refluxed for 12 h using Dean-stark apparatus. The reaction mixture was cooled down to room temperature and extracted with ethyl acetate (20 mL × 3). The combined organic phases were dried over anhydrous sodium sulfate and concentrated to afford the product **16**, which was used without further purification. The mixture of **16** (1.22 g, 3.6 mmol), sulfonyl azide **SZ6** (1.25 g, 3.6 mmol) and potassium carbonate (1.0 g, 7.2 mmol) in acetonitrile and water (9:1, 20 mL), was refluxed for 24 hours. After cooling down to room temperature, the reaction mixture was treated with ethyl acetate (20 mL) and water (20 mL), extracted with ethyl acetate (20 mL × 3). The combined organic phases were dried over anhydrous sodium sulfate and concentrated. Interestingly, hydrolysis of the imine occurred smoothly under this basic condition. Sulfonamide **17** (930 mg, 50% over 2 steps) was thus obtained by flash chromatography (hexane : EtOAc = 2:1; R_f = 0.2 in hexane : EtOAc = 2:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.83 (d, *J* = 8.2 Hz, 4H), 7.56 (d, *J* = 8.2 Hz, 2H), 7.47 (d, *J* = 8.2 Hz, 2H), 7.24 – 7.14 (m, 5H), 5.00 (bs, 2H), 3.67 (d, *J* = 3.8 Hz, 4H), 3.06 (t, *J* = 6.8 Hz, 2H), 2.75 (t, *J* = 6.8 Hz, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 147.00, 144.11, 140.87, 137.06, 135.81, 129.61, 129.24, 129.08, 128.94,

127.50, 126.52, 126.19, 58.11, 57.99, 53.01, 31.56 ppm. HRMS (ESI) calcd for $C_{22}H_{23}N_5O_4S_3$ $[M+H]^+$: 518.09849, found: 518.09993.



SZ9TA1

Acylsulfonamide SZ9TA1: The acylsulfonamide **SZ9TA1** was prepared following the general procedure **A** starting from sulfonamide **17** and benzoic acid with 54% yield (65 mg). R_f = 0.77 in EtOAc. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, *J* = 8.0 Hz, 2H), 7.78 (d, *J* = 8.1 Hz, 2H), 7.77 (d, *J* = 7.6 Hz, 2H), 7.60 – 7.51 (m, 5H), 7.47 – 7.37 (m, 3H), 7.19 (d, *J* = 4.3 Hz, 3H), 7.14 – 7.08 (m, 1H), 3.67 (s, 4H), 3.04 (t, *J* = 7.2 Hz, 2H), 2.73 (t, *J* = 7.2 Hz, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 165.13, 147.07, 145.64, 137.64, 137.16, 135.85, 133.47, 131.42, 130.22, 129.70, 129.14, 129.03, 128.86, 128.73, 128.09, 127.64, 126.28, 58.00, 57.92, 52.84, 31.50 ppm. HRMS (ESI) calcd for $C_{29}H_{27}N_5O_5S_3$ $[M+H]^+$: 622.12471, found: 622.12402.

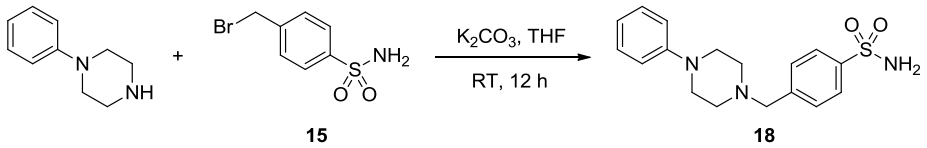


SZ9TA5

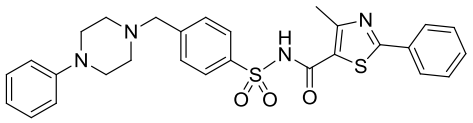
Acylsulfonamide SZ9TA5: was prepared following the general procedure **A** starting from sulfonamide **17** and 3,5-dimethoxybenzoic acid with 56% yield (110 mg). R_f = 0.28 in hexane : EtOAc = 1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (d, *J* = 6.8 Hz, 2H), 7.78 (d, *J* = 7.8 Hz, 2H), 7.47 (d, *J* = 7.6 Hz, 2H), 7.33 – 6.92 (m, 10H), 6.42 (s, 1H), 3.66 –

3.48 (m, 10H), 3.04 – 2.85 (m, 2H), 2.79 – 2.50 (m, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 160.67, 147.23, 137.21, 135.98, 129.81, 129.16, 129.00, 127.72, 126.37, 106.56, 105.27, 58.07, 57.91, 55.61, 52.89, 31.50 ppm. HRMS (ESI) calcd for $C_{31}H_{31}N_5O_7S_3$ $[M+H]^+$: 682.14584, found: 682.14395.

Synthesis of Additional Acylsulfonamides:

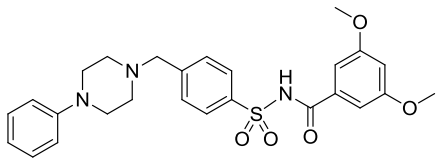


Sulfonamide 18: To a solution of 1-phenylpiperazine (285 mg, 1.76 mmol) and bromide **15** (400 mg, 1.59 mmol) in THF (8 mL), was added potassium carbonate (441 mg, 3.19 mmol) and the resulting solution was stirred at room temperature overnight. The reaction mixture was treated with 1N potassium carbonate solution (10 mL), extracted with ethyl acetate (20 mL × 3). The combined organic phases were dried over anhydrous sodium sulfate and concentrated. The sulfonamide **18** (461 mg, 87%) was thus obtained by flash chromatography (hexane : EtOAc = 2:1 with 0.1% triethylamine; R_f = 0.38 in hexane : EtOAc = 1:2). ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.80 – 7.75 (m, 2H), 7.49 (d, *J* = 8.1 Hz, 2H), 7.31 – 7.28 (m, 2H), 7.16 (t, *J* = 7.7 Hz, 2H), 6.88 (d, *J* = 8.1 Hz, 2H), 6.73 (t, *J* = 7.2 Hz, 1H), 3.56 (s, 2H), 3.11 – 3.08 (m, 4H), 2.50 – 2.46 (m, 4H) ppm. ^{13}C NMR (101 MHz, DMSO-*d6*) δ 151.41, 143.24, 142.77, 129.59, 129.32, 126.07, 119.23, 115.81, 61.76, 52.98, 48.64 ppm. HRMS (ESI) calcd for $C_{17}H_{21}N_3O_2S$ $[M+H]^+$: 332.14272, found: 332.14250.



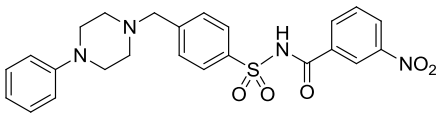
SZ1TA3

Acylsulfonamide SZ1TA3: was prepared following the general procedure **A** starting from sulfonamide **18** and 4-methyl-2-phenylthiazole-5-carboxylic acid with 58% yield (279 mg). R_f = 0.3 in EtOAc : MeOH = 20:1. ^{1}H NMR (400 MHz, CD_3OD) δ 8.16 (d, *J* = 7.0 Hz, 2H), 7.76 (t, *J* = 10.0 Hz, 4H), 7.39 – 7.29 (m, 3H), 7.13 (t, *J* = 6.8 Hz, 2H), 6.84 (d, *J* = 7.3 Hz, 2H), 6.79 (t, *J* = 6.6 Hz, 1H), 5.28 – 5.10 (m, 2H), 4.42 (s, 2H), 3.45 – 3.23 (m, 6H), 2.46 (s, 3H) ppm. ^{13}C NMR (101 MHz, CD_3OD) δ 169.70, 161.16, 160.43, 149.67, 141.85, 134.50, 132.22, 132.00, 131.40, 129.16, 129.12, 128.86, 126.68, 123.40, 121.18, 116.73, 59.25, 51.80, 46.63, 16.60 ppm. HRMS (ESI) calcd for $C_{28}H_{28}N_4O_3S_2$ $[M+H]^+$: 533.16756, found: 533.16680.



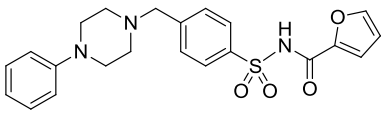
SZ1TA5

Acylsulfonamide SZ1TA5: was prepared following the general procedure **B** with 45% yield (67 mg). R_f = 0.44 in EtOAc. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 – 7.97 (m, 2H), 7.82 – 7.51 (m, 2H), 7.05 – 6.79 (m, 6H), 6.56 (s, 2H), 4.33 (s, 2H), 3.70 (s, 6H), 3.57 – 3.04 (m, 8H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.35, 161.11, 148.73, 140.80, 134.11, 133.02, 132.01, 129.77, 129.57, 122.78, 117.63, 106.30, 106.07, 60.10, 55.78, 51.89, 47.48 ppm. HRMS (ESI) calcd for $C_{26}H_{29}N_3O_5S$ $[M+H]^+$: 496.19007, found: 496.19151.



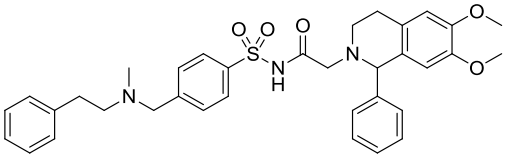
SZ1TA6

Acylsulfonamide SZ1TA6: was prepared following the general procedure **B** with 33% yield (48 mg). R_f = 0.54 in hexane : EtOAc = 1:1. ^{1}H NMR (400 MHz, CD_3OD) δ 8.58 – 8.55 (m, 1H), 8.40 – 8.34 (m, 1H), 8.18 (d, *J* = 8.3 Hz, 2H), 8.13 (d, *J* = 7.9 Hz, 1H), 7.77 (d, *J* = 8.4 Hz, 2H), 7.67 (t, *J* = 8.0 Hz, 1H), 7.20 (t, *J* = 8.0 Hz, 2H), 6.92 (d, *J* = 8.0 Hz, 2H), 6.85 (t, *J* = 7.3 Hz, 1H), 4.48 (s, 2H), 3.47 – 3.32 (m, 6H), 3.28 – 3.22 (m, 2H) ppm. ^{13}C NMR (101 MHz, CD_3OD) δ 164.63, 149.76, 148.45, 141.33, 134.81, 133.89, 133.77, 132.88, 131.95, 130.19, 129.10, 127.39, 122.99, 121.22, 116.79, 59.22, 51.88, 46.74 ppm. HRMS (ESI) calcd for $C_{24}H_{24}N_4O_5S$ $[M+H]^+$: 481.15402, found: 481.15510.



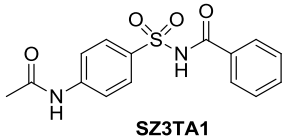
SZ1TA9

Acylsulfonamide SZ1TA9: was prepared following the general procedure **B** with 15% yield (19 mg). R_f = 0.47 in hexane : EtOAc = 1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.0 Hz, 2H), 7.66 (d, *J* = 8.1 Hz, 2H), 7.50 (s, 1H), 7.31 – 7.23 (m, 4H), 6.97 (t, *J* = 7.2 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 2H), 6.53 – 6.49 (m, 1H), 4.33 (s, 2H), 3.57 – 3.12 (m, 8H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.11, 149.12, 146.53, 145.08, 140.71, 134.43, 131.97, 129.74, 129.60, 122.43, 118.81, 117.51, 113.23, 59.99, 51.87, 47.32 ppm. HRMS (ESI) calcd for $C_{22}H_{23}N_3O_4S$ $[M+H]^+$: 426.14820, found: 426.14806.



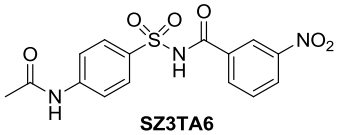
SZ2TA4

Acylsulfonamide SZ2TA4: was prepared following the general procedure **B** with 15% yield (55 mg). R_f = 0.56 in DCM : MeOH = 10:1. ^{1}H NMR (400 MHz, CD_3OD) δ 8.14 (d, *J* = 8.4 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.46 – 7.41 (m, 3H), 7.33 – 7.24 (m, 7H), 6.90 (s, 1H), 6.38 (s, 1H), 5.76 (s, 1H), 4.58 – 4.48 (m, 1H), 4.17 – 4.09 (m, 1H), 4.04 – 3.98 (m, 1H), 3.88 – 3.84 (m, 4H), 3.60 (s, 3H), 3.44 – 3.40 (m, 2H), 3.20 – 3.11 (m, 4H), 2.89 (s, 3H), 2.81 – 2.75 (m, 1H), 2.64 – 2.58 (m, 1H) ppm. ^{13}C NMR (101 MHz, CD_3OD) δ 167.91, 151.33, 150.33, 143.97, 137.46, 136.69, 136.11, 132.85, 132.11, 131.45, 130.38, 130.18, 129.96, 129.91, 128.52, 124.76, 122.31, 112.66, 112.51, 67.06, 60.19, 58.51, 56.62, 56.56, 56.01, 46.83, 40.46, 31.50, 27.98 ppm. HRMS (ESI) calcd for $C_{35}H_{39}N_3O_5S$ $[M+H]^+$: 614.26832, found: 614.26748.



SZ3TA1

Acylsulfonamide SZ3TA1: was prepared following the general procedure **B** with 11% yield (21 mg). R_f = 0.33 in EtOAc : MeOH = 20:1. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.91 – 7.83 (m, 4H), 7.75 (d, *J* = 8.3 Hz, 2H), 7.56 (t, *J* = 7.1 Hz, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 2.05 (s, 3H) ppm. ^{13}C NMR (126 MHz, DMSO-*d6*) δ 169.54, 166.17, 144.03, 133.86, 133.38, 132.66, 129.45, 128.94, 128.81, 118.76, 24.61 ppm. HRMS (ESI) calcd for $C_{15}H_{14}N_2O_4S$ $[M+H]^+$: 319.07470, found: 319.07444.



SZ3TA6

Acylsulfonamide SZ3TA6: was prepared following the general procedure **A** with 46 % yield (78 mg). R_f = 0.25 in EtOAc : MeOH = 20:1. ^{1}H NMR (250 MHz, Acetone-*d6*) δ: 8.61 (s, 1H), 8.32 (dd, *J* = 8.1, 1.5 Hz, 1H), 8.22 (d, *J* = 7.7 Hz, 1H), 7.91 (d, *J* = 8.7 Hz, 2H), 7.75 – 7.64 (m, 3H), 1.99 (s, 3H) ppm. ^{13}C NMR (63 MHz, Acetone-*d6*) δ: 169.69, 149.19, 145.17, 135.18, 135.04, 134.10, 131.13, 130.49, 128.09, 123.91, 119.11, 24.37 ppm. HRMS (ESI) calcd for $C_{15}H_{13}N_3O_6S$ $[M+H]^+$: 364.05978, found: 364.05879

SZ3TA7

Acylsulfonamide SZ3TA7: was prepared following the general procedure **B** with 14% yield (31 mg). R_f = 0.44 in hexane : EtOAc = 1:3. ^{1}H NMR (400 MHz, CD_3OD) δ 8.08 (d, *J* = 8.8 Hz, 2H), 8.01 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.91 – 7.87 (m, 1H), 7.84 (d, *J* = 8.8 Hz, 2H), 7.65 (d, *J* = 7.0 Hz, 1H), 7.51 – 7.46 (m, 3H), 2.17 (s, 3H) ppm. ^{13}C NMR (101 MHz, CD_3OD) δ 170.66, 168.03, 143.78, 133.64, 133.48, 131.69, 130.91, 129.74, 129.18, 128.14, 127.10, 126.25, 126.18, 124.26, 124.11, 118.72, 22.66 ppm. HRMS (ESI) calcd for $C_{19}H_{16}N_2O_4S$ $[M+H]^+$: 369.09035, found: 369.09041.

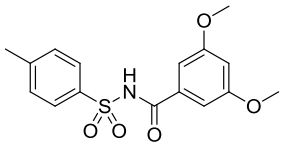
SZ3TA8

Acylsulfonamide SZ3TA8: was prepared following the general procedure **B** with 26% yield (63 mg). R_f = 0.63 in hexane : EtOAc = 1:3. ^{1}H NMR (400 MHz, CD_3OD) δ 8.01 –

7.98 (m, 2H), 7.91 – 7.87 (m, 2H), 7.78 – 7.74 (m, 2H), 7.36 – 7.32 (m, 2H), 2.13 (s, 3H) ppm. ^{13}C NMR (101 MHz, CD_3OD) δ 170.62, 164.89, 152.34, 143.69, 133.35, 130.74, 130.16, 129.22, 120.30, 118.62, 22.62 ppm. HRMS (ESI) calcd for $C_{16}H_{13}F_3N_2O_5S$ $[M+H]^+$: 403.05700, found: 403.05661.

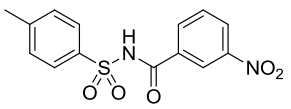
SZ3TA9

Acylsulfonamide SZ3TA9: was prepared following the general procedure **A** with 36% yield (52 mg). R_f = 0.23 in EtOAc. ^{1}H NMR (400 MHz, CD_3OD) δ: 7.97 (d, *J* = 8.8 Hz, 2H), 7.75 (d, *J* = 8.8 Hz, 2H), 7.70 (s, 1H), 7.25 (d, *J* = 3.5 Hz, 1H), 6.58 (dd, *J* = 3.4, 1.5 Hz, 1H), 2.13 (s, 3H) ppm. ^{13}C NMR (101 MHz, CD_3OD) δ: 170.87, 156.36, 147.08, 145.63, 143.91, 133.74, 129.33, 118.85, 117.76, 112.34, 22.87 ppm. HRMS (ESI) calcd for $C_{13}H_{12}N_2O_5S$ $[M+H]^+$: 309.05397, found: 309.05467.



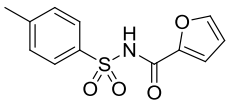
SZ5TA5

Acylsulfonamide SZ5TA5: was prepared following the general procedure **B** with 46% yield (46 mg). R_f = 0.72 in EtOAc. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 6.94 (d, *J* = 2.0 Hz, 2H), 6.61 – 6.59 (m, 1H), 3.75 (s, 6H), 2.44 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.37, 161.20, 145.50, 135.56, 133.22, 129.85, 128.83, 106.53, 105.59, 55.85, 21.91 ppm. HRMS (ESI) calcd for $C_{16}H_{17}NO_5S$ $[M+H]^+$: 336.09002, found: 336.09043.



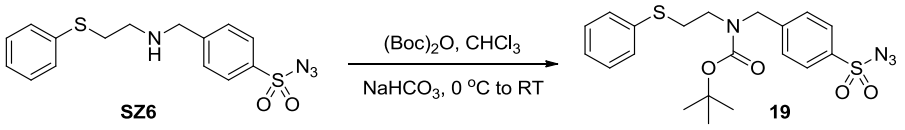
SZ5TA6

Acylsulfonamide SZ5TA6: was prepared following the general procedure **B** with 10% yield (10 mg). R_f = 0.29 in EtOAc. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.41 (d, *J* = 7.9 Hz, 1H), 8.17 (d, *J* = 7.6 Hz, 1H), 8.06 (d, *J* = 8.0 Hz, 2H), 7.66 (t, *J* = 7.9 Hz, 1H), 7.38 (d, *J* = 7.9 Hz, 2H), 2.45 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.46, 148.54, 145.97, 135.11, 133.80, 133.21, 130.46, 129.96, 128.98, 127.93, 123.11, 21.95 ppm. HRMS (ESI) calcd for $C_{14}H_{12}N_2O_5S$ $[M+H]^+$: 321.05397, found: 321.05334.



SZ5TA9

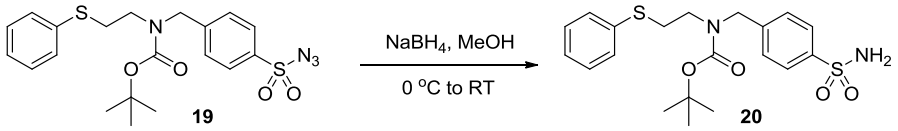
Acylsulfonamide SZ5TA9: was prepared following the general procedure **B** with 40% yield (32 mg). R_f = 0.4 in EtOAc. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84 (s, 1H), 8.03 (d, *J* = 8.2 Hz, 2H), 7.50 (s, 1H), 7.34 (d, *J* = 8.1 Hz, 2H), 7.22 (d, *J* = 3.4 Hz, 1H), 6.53 (d, *J* = 1.8 Hz, 1H), 2.43 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.53, 145.97, 145.50, 145.40, 135.71, 129.80, 128.82, 118.30, 113.26, 21.89 ppm. HRMS (ESI) calcd for $C_{12}H_{11}NO_4S$ $[M+H]^+$: 266.04815, found: 266.04812.



SZ6 19

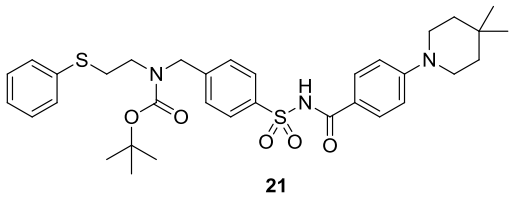
Sulfonyl Azide 19: To a solution of sulfonyl azide **SZ6**[1] (600 mg, 1.72 mmol) and $NaHCO_3$ (145 mg, 1.72 mmol) in $CHCl_3$ (6.5 mL) was added $(Boc)_2O$ (376 mg, 1.72 mmol) at 0 °C. The reaction mixture was then slowly warmed to room temperature and

monitored using TLC until **SZ6** was completely consumed. The reaction mixture was then treated with 1N $NaHCO_3$ solution (20 mL) and extracted with $CHCl_3$ (15 mL × 3). The combined organic phases were dried over anhydrous sodium sulfate and concentrated. The crude obtained was subjected to flash chromatography (hexane : EtOAc = 8:1; R_f = 0.54 in hexane : EtOAc = 2:1) to obtain the corresponding sulfonyl azide **19** with 93% yield (717 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.2 Hz, 2H), 7.38 – 7.16 (m, 7H), 4.51 (s, 2H), 3.39 – 3.29 (m, 2H), 3.01 – 2.95 (m, 2H), 1.45 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.50, 146.12, 137.21, 129.52, 129.07, 128.52, 127.99, 127.78, 126.52, 80.82, 50.48, 47.04, 31.80, 28.32 ppm. HRMS (ESI) calcd for $C_{20}H_{24}N_4O_4S_2$ $[M+Na]^+$: 471.11312, found: 471.11266.



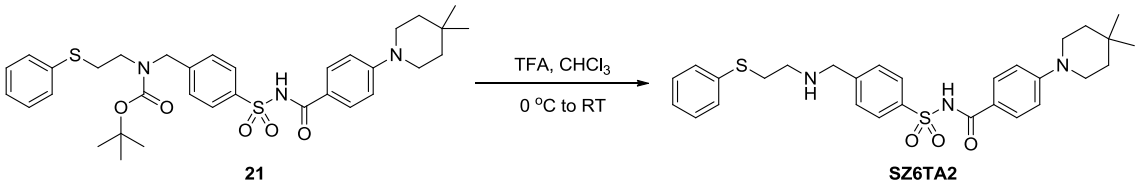
19 20

Sulfonamide 20: The sulfonamide **20** was prepared starting from sulfonyl azide **19** (600 mg, 1.54 mmol) following the procedure described for synthesis of sulfonamide **14** with 92% yield (600 mg). R_f = 0.42 in hexane : EtOAc = 1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.3 Hz, 2H), 7.30 – 7.13 (m, 7H), 5.16 (s, 2H), 4.45 (s, 2H), 3.34 – 3.27 (m, 2H), 3.00 – 2.89 (m, 2H), 1.43 (s, 9H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.57, 143.41, 140.98, 135.12, 129.44, 129.05, 128.08, 127.53, 126.68, 80.73, 50.37, 46.90, 31.66, 28.34 ppm. HRMS (ESI) calcd for $C_{20}H_{26}N_2O_4S_2$ $[M+Na]^+$: 445.12262, found: 445.12185.



21

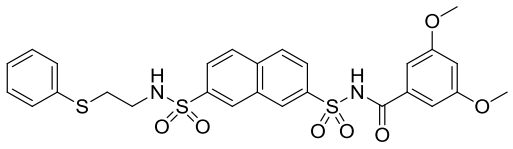
Acylsulfonamide 21: was prepared following the general procedure **A** with 85% yield (576 mg). R_f = 0.54 in hexane : EtOAc = 1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, *J* = 8.1 Hz, 2H), 7.71 (d, *J* = 8.9 Hz, 2H), 7.31 – 7.06 (m, 9H), 4.47 (s, 2H), 3.38 – 3.30 (m, 6H), 3.01 – 2.90 (m, 2H), 1.59 (t, *J* = 5.4 Hz, 4H), 1.41 (s, 9H), 1.00 (s, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.91, 155.80, 150.97, 137.88, 135.29, 130.25, 129.72, 129.26, 129.09, 127.97, 127.56, 126.68, 126.38, 116.78, 80.99, 50.62, 47.71, 47.23, 37.11, 31.93, 28.52, 28.28, 27.72 ppm. HRMS (ESI) calcd for $C_{34}H_{43}N_3O_5S_2$ $[M+H]^+$: 638.27169, found: 638.26931.



21 SZ6TA2

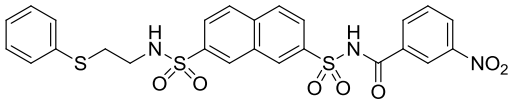
Acylsulfonamide SZ6TA2: To a solution of acylsulfonamide **21** (437 mg, 0.68 mmol) in $CHCl_3$ (5 mL) cooled to 0 °C, was added TFA (1.2 mL) dropwise. The reaction mixture was then slowly warmed to room temperature and monitored using TLC until acylsulfonamide **21** was completely consumed. The reaction was then treated with saturated K_2CO_3 solution (pH = 7) and extracted with $CHCl_3$ (20 mL × 3). The combined organic phases were dried over anhydrous sodium sulfate and concentrated. The crude obtained was purified using preparative HPLC to afford the acylsulfonamide **SZ6TA2** with 90% yield (330 mg). R_f = 0.69 in EtOAc : MeOH = 20:1. ^{1}H NMR (400 MHz, CD_3OD) δ 8.21 (d, *J* = 8.4 Hz, 2H), 7.77 (dd, *J* = 17.2, 8.7 Hz, 4H), 7.49 (d, *J* = 7.7 Hz,

2H), 7.40 (t, *J* = 7.5 Hz, 2H), 7.32 (t, *J* = 7.3 Hz, 1H), 7.08 (d, *J* = 9.1 Hz, 2H), 4.40 (s, 2H), 3.53 – 3.44 (m, 4H), 3.41 – 3.38 (m, 3H), 1.63 – 1.52 (m, 4H), 1.37 (s, 1H), 1.10 (s, 6H) ppm. ^{13}C NMR (101 MHz, CD_3OD) δ 165.85, 154.02, 141.32, 136.66, 133.42, 130.61, 130.22, 130.07, 129.29, 128.91, 127.38, 120.11, 113.83, 50.10, 46.32, 44.57, 37.67, 29.35, 28.26, 26.87 ppm. HRMS (ESI) calcd for $C_{29}H_{35}N_3O_3S_2$ $[M+H]^+$: 538.21926, found: 538.21798.



SZ7TA5

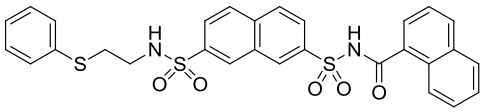
Acylsulfonamide SZ7TA5: was prepared following the general procedure **B** with 28% yield (49 mg). R_f = 0.31 in EtOAc. ^{1}H NMR (400 MHz, CD_3OD) δ 8.80 (s, 1H), 8.50 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 8.18 – 8.05 (m, 2H), 7.98 (d, *J* = 8.2 Hz, 1H), 7.17 – 7.01 (m, 5H), 6.97 (s, 2H), 6.67 (s, 1H), 3.77 (s, 6H), 3.07 (t, *J* = 6.1 Hz, 2H), 2.94 (t, *J* = 6.2 Hz, 2H). ^{13}C NMR (101 MHz, CD_3OD) δ 166.26, 161.22, 139.44, 138.34, 136.65, 134.86, 133.71, 131.15, 131.02, 129.52, 129.10, 128.74, 126.28, 125.57, 105.83, 105.28, 54.86, 41.97, 32.93 ppm. HRMS (ESI) calcd for $C_{27}H_{26}N_2O_7S_3$ $[M+H]^+$: 609.07943, found: 609.07718.



SZ7TA6

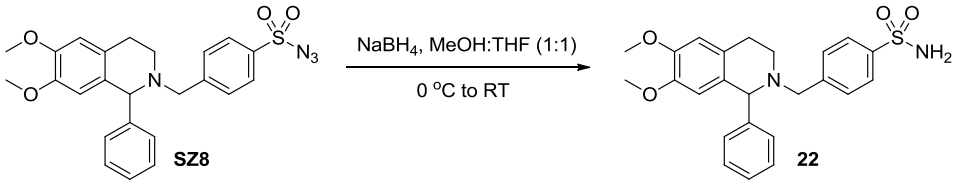
Acylsulfonamide SZ7TA6: was prepared following the general procedure **B** with 46% yield (79 mg). R_f = 0.5 in EtOAc. ^{1}H NMR (400 MHz, CD_3OD) δ 8.79 (s, 1H), 8.61 (s, 1H), 8.47 (s, 1H), 8.37 (d, *J* = 7.4 Hz, 1H), 8.23 – 8.03 (m, 4H), 7.94 (d, *J* = 8.0 Hz, 1H),

7.67 (t, *J* = 8.0 Hz, 1H), 7.15 – 6.95 (m, 6H), 3.04 (t, *J* = 7.0 Hz, 2H), 2.91 (t, *J* = 7.0 Hz, 2H) ppm. ^{13}C NMR (101 MHz, CD_3OD) δ 164.42, 148.39, 139.47, 138.06, 136.70, 134.89, 133.95, 133.63, 131.31, 131.01, 130.13, 129.54, 129.46, 129.22, 129.12, 128.74, 127.36, 126.24, 125.61, 123.00, 41.99, 32.94 ppm. HRMS (ESI) calcd for $C_{25}H_{21}N_3O_7S_3$ $[M+H]^+$: 572.06144, found: 572.05968.



SZ7TA7

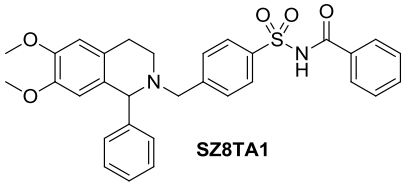
Acylsulfonamide SZ7TA7: was prepared following the general procedure **B** with 42% yield (145 mg). R_f = 0.48 in EtOAc : MeOH = 20:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 8.45 (s, 1H), 8.27 (d, *J* = 8.7 Hz, 1H), 8.09 (d, *J* = 8.3 Hz, 1H), 7.98 (d, *J* = 8.7 Hz, 1H), 7.95 – 7.83 (m, 4H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 7.1 Hz, 1H), 7.43 – 7.29 (m, 4H), 7.14 – 7.05 (m, 5H), 3.11 (m, 2H), 2.93 (t, *J* = 6.4 Hz, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.50, 138.81, 137.55, 136.87, 133.78, 133.36, 131.85, 131.09, 130.43, 130.10, 129.80, 129.53, 129.29, 128.71, 128.18, 127.25, 127.17, 127.02, 126.17, 125.88, 124.85, 124.55, 41.86, 34.12 ppm. HRMS (ESI) calcd for $C_{29}H_{24}N_2O_5S_3$ $[M+H]^+$: 577.09201, found: 577.09051.



SZ8 **22**

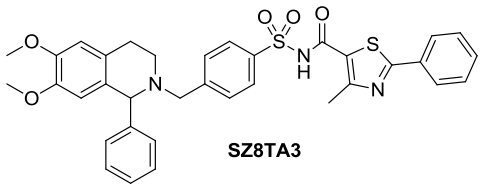
Sulfonamide 22: The sulfonamide **22** was obtained starting from sulfonyl azide **SZ8** (290 mg, 0.62 mmol) following the procedure described for synthesis of sulfonamide **14** with 89% yield (243 mg). R_f = 0.33 in hexane : EtOAc = 1:1. ^{1}H NMR (250 MHz,

$CDCl_3$) δ: 7.59 (d, *J* = 7.6 Hz, 2H), 7.22 – 7.00 (m, 7H), 6.39 (s, 1H), 5.99 (s, 1H), 5.28 (bs, 2H), 4.34 (s, 1H), 3.62 – 3.51 (m, 4H), 3.34 (s, 3H), 3.11 (d, *J* = 13.9 Hz, 1H), 2.85 – 2.67 (m, 2H), 2.55 – 2.42 (m, 1H), 2.36 – 2.21 (m, 1H) ppm. ^{13}C NMR (63 MHz, $CDCl_3$) δ 147.44, 147.06, 144.95, 143.84, 140.81, 129.97, 129.51, 129.10, 128.45, 127.52, 126.78, 126.30, 111.75, 111.03, 68.20, 58.26, 55.80, 55.74, 47.26, 28.47 ppm. HRMS (ESI) calcd for $C_{24}H_{26}N_2O_4S$ $[M+H]^+$: 439.16860, found: 439.16821.



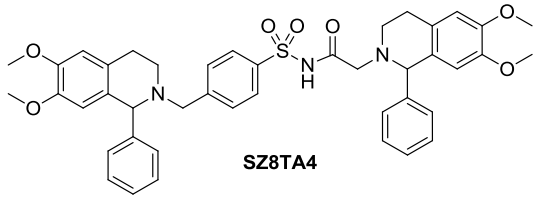
SZ8TA1

Acylsulfonamide SZ8TA1: was prepared following the general procedure **B** with 50% yield (163 mg). R_f = 0.4 in hexane : EtOAc = 1:1. ^{1}H NMR (400 MHz, CD_3OD) δ: 8.17 (d, *J* = 8.3 Hz, 2H), 7.77 (d, *J* = 7.8 Hz, 2H), 7.67 (d, *J* = 8.3 Hz, 2H), 7.63 – 7.55 (m, 1H), 7.51 – 7.42 (m, 5H), 7.29 (s, 2H), 6.89 (s, 1H), 6.35 (s, 1H), 5.71 (s, 1H), 4.57 (d, *J* = 12.7 Hz, 1H), 4.35 (bs, 1H), 3.83 (s, 3H), 3.71 – 3.60 (m, 1H), 3.57 (s, 3H), 3.49 – 3.37 (m, 2H), 3.23 (d, *J* = 5.4 Hz, 2H) ppm. ^{13}C NMR (101 MHz, CD_3OD) δ 166.83, 149.85, 148.85, 141.35, 136.04, 135.70, 133.27, 132.08, 131.45, 130.70, 130.04, 129.21, 128.99, 128.62, 128.09, 123.76, 111.17, 66.85, 56.59, 55.27, 55.19, 45.22, 23.57 ppm. HRMS (ESI) calcd for $C_{31}H_{30}N_2O_5S$ $[M+H]^+$: 543.19482, found: 543.19360.



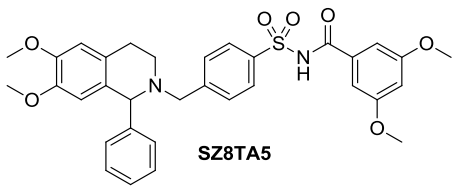
SZ8TA3

Acylsulfonamide SZ8TA3: was prepared following the general procedure **A** with 14% yield (20 mg). R_f = 0.35 in EtOAc. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (bs, 2H), 7.82 (d, *J* = 7.2 Hz, 2H), 7.63 (bs, 2H), 7.47 – 7.34 (m, 6H), 7.24 (bs, 2H), 6.67 (s, 1H), 6.25 (s, 1H), 4.51 (d, *J* = 10.1 Hz, 1H), 3.82 (s, 3H), 3.65 (s, 3H), 3.58 – 3.34 (m, 3H), 3.33 – 3.06 (m, 3H), 2.60 (s, 3H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 169.52, 161.45, 159.66, 149.51, 148.72, 140.63, 135.02, 133.97, 132.17, 131.55, 131.41, 130.99, 130.28, 129.72, 129.22, 129.12, 126.89, 126.61, 122.50, 122.22, 110.54, 65.52, 55.88, 43.00, 23.67, 17.73 ppm. HRMS (ESI) calcd for $C_{35}H_{33}N_3O_5S_2$ $[M+H]^+$: 640.19399, found: 640.19350.



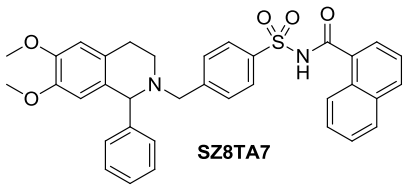
SZ8TA4

Acylsulfonamide SZ8TA4: was prepared following the general procedure **A** with 18% yield (31 mg). R_f = 0.45 in EtOAc. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.58 (bs, 1H), 7.98 (bs, 2H), 7.56 (bs, 2H), 7.39 – 7.18 (m, 11H), 6.65 (s, 2H), 6.20 (s, 2H), 5.68 (s, 1H), 4.45 – 4.25 (m, 2H), 4.07 – 3.96 (m, 3H), 3.84 (s, 3H), 3.83 (s, 3H), 3.60 (s, 6H), 3.38 (bs, 3H), 3.13 – 3.03 (m, 4H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 165.34, 149.47, 148.56, 140.50, 134.64, 131.67, 130.80, 130.16, 129.71, 129.25, 129.13, 128.63, 127.99, 122.76, 121.64, 120.84, 110.84, 110.63, 66.50, 65.95, 56.20, 55.85, 54.09, 45.50, 23.51 ppm. HRMS (ESI) calcd for $C_{43}H_{45}N_3O_7S$ $[M+H]^+$: 748.30565, found: 748.30620.



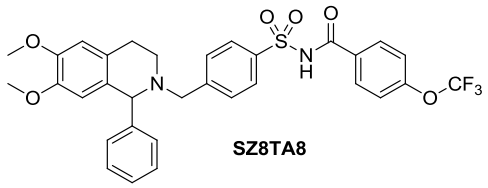
SZ8TA5

Acylsulfonamide SZ8TA5: was prepared following the general procedure **B** with 42% yield (152 mg). R_f = 0.58 in hexane : EtOAc = 1:3. ^{1}H NMR (400 MHz, CD_3OD) δ: 8.21 – 8.12 (m, 2H), 7.69 – 7.63 (m, 2H), 7.49 – 7.43 (m, 3H), 7.30 – 7.25 (m, 2H), 6.94 – 6.85 (m, 3H), 6.69 – 6.65 (m, 1H), 6.33 (s, 1H), 5.64 (s, 1H), 4.50 (d, *J* = 13.1 Hz, 1H), 3.83 (s, 3H), 3.76 (s, 6H), 3.67 – 3.60 (m, 1H), 3.57 (s, 3H), 3.46 – 3.34 (m, 1H), 3.31 – 3.26 (m, 1H), 3.23 – 3.15 (m, 2H) ppm. ^{13}C NMR (101 MHz, CD_3OD) δ: 166.18, 161.04, 149.68, 148.67, 141.13, 135.56, 133.58, 131.29, 130.51, 129.89, 129.20, 129.02, 128.84, 123.41, 110.95, 110.88, 105.64, 104.85, 66.54, 56.29, 55.03, 54.95, 54.65, 23.20 ppm. HRMS (ESI) calcd for $C_{33}H_{34}N_2O_7S$ $[M+H]^+$: 603.21595, found: 603.21454.



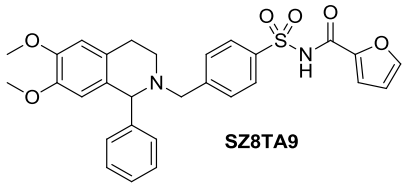
SZ8TA7

Acylsulfonamide SZ8TA7: was prepared following the general procedure **A** with 48% yield (97 mg). R_f = 0.41 in hexane : EtOAc = 1:1. ^{1}H NMR (400 MHz, CD_3OD) δ 8.24 (d, *J* = 8.1 Hz, 2H), 8.07 – 7.86 (m, 4H), 7.77 – 7.66 (m, 4H), 7.54 – 7.45 (m, 5H), 7.32 – 7.26 (m, 1H), 6.90 (s, 1H), 6.34 (s, 1H), 5.68 (s, 1H), 4.58 (d, *J* = 12.9 Hz, 1H), 3.84 (s, 3H), 3.70 – 3.62 (m, 1H), 3.55 (s, 3H), 3.48 – 3.40 (m, 1H), 3.35 – 3.30 (m, 1H), 3.26 – 3.19 (m, 2H) ppm. ^{13}C NMR (101 MHz, CD_3OD) δ 168.17, 150.02, 148.99, 141.41, 135.69, 135.18, 133.95, 133.65, 132.18, 131.79, 130.80, 130.52, 130.26, 129.33, 129.16, 128.53, 127.42, 126.92, 126.55, 124.52, 124.28, 123.53, 121.83, 111.22, 111.08, 66.62, 56.41, 55.29, 55.19, 45.10, 23.25 ppm. HRMS (ESI) calcd for $C_{35}H_{32}N_2O_5S$ $[M+H]^+$: 593.21047, found: 593.20940.



SZ8TA8

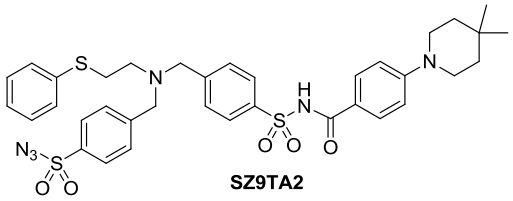
Acylsulfonamide SZ8TA8: was prepared following the general procedure **A** with 44% yield (50 mg). R_f = 0.63 in EtOAc : MeOH = 20:1. ^{1}H NMR (400 MHz, CD_3OD) δ 7.98 (d, *J* = 8.2 Hz, 2H), 7.71 (d, *J* = 8.7 Hz, 2H), 7.54 (d, *J* = 8.2 Hz, 2H), 7.30 – 7.23 (m, 3H), 7.14 (d, *J* = 8.2 Hz, 4H), 6.69 (s, 1H), 6.17 (s, 1H), 5.57 (s, 1H), 4.40 (d, *J* = 13.3 Hz, 1H), 4.20 (s, 1H), 3.63 (s, 3H), 3.53 – 3.44 (m, 1H), 3.36 (s, 3H), 3.15 – 3.02 (m, 3H) ppm. ^{13}C NMR (101 MHz, CD_3OD) δ 165.65, 152.66, 149.86, 148.82, 141.39, 135.45, 135.11, 131.81, 130.89, 130.55, 130.20, 129.29, 128.99, 123.64, 122.17, 120.53, 120.49 (q, *J* = 259.81 Hz), 111.22, 111.14, 66.88, 56.53, 55.29, 55.22, 45.14, 23.42 ppm. HRMS (ESI) calcd for $C_{32}H_{29}F_3N_2O_6S$ $[M+H]^+$: 627.17712, found: 627.17851.



SZ8TA9

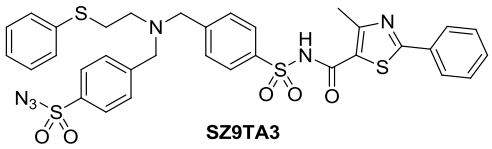
Acylsulfonamide SZ8TA9: was prepared following the general procedure **A** with 49% yield (47 mg). R_f = 0.52 in EtOAc : MeOH = 20:1. ^{1}H NMR (400 MHz, CD_3OD) δ 8.13 (d, *J* = 7.8 Hz, 2H), 7.73 – 7.65 (m, 3H), 7.44 (s, 3H), 7.31 (s, 2H), 7.25 (d, *J* = 3.2 Hz, 1H), 6.88 (s, 1H), 6.58 (d, *J* = 2.0 Hz, 1H), 6.35 (s, 1H), 5.73 (s, 1H), 4.57 (d, *J* = 12.9 Hz, 1H), 4.36 (s, 1H), 3.82 (s, 3H), 3.70 – 3.60 (m, 1H), 3.56 (s, 3H), 3.49 – 3.40 (m, 1H), 3.23 (s, 2H) ppm. ^{13}C NMR (101 MHz, CD_3OD) δ 156.66, 149.87, 148.83, 147.32, 145.55, 141.36, 135.47, 135.06, 131.77, 130.84, 130.19, 129.27, 128.89, 123.58, 122.05,

118.06, 112.46, 111.18, 111.09, 66.81, 56.51, 55.29, 55.21, 45.10, 23.34 ppm. HRMS (ESI) calcd for $C_{29}H_{28}N_2O_6S$ $[M+H]^+$: 533.17408, found: 533.17347.



SZ9TA2

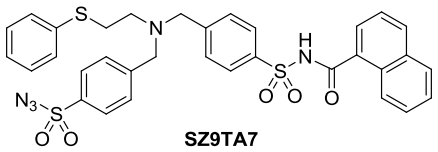
Acylsulfonamide SZ9TA2: was prepared following the general procedure **A** with 60% yield (169 mg). R_f = 0.56 in hexane : EtOAc = 1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (d, *J* = 8.4 Hz, 2H), 7.85 (d, *J* = 8.0 Hz, 2H), 7.63 (d, *J* = 8.6 Hz, 2H), 7.56 (d, *J* = 8.4 Hz, 2H), 7.51 (d, *J* = 8.0 Hz, 2H), 7.22 – 7.12 (m, 5H), 6.86 (d, *J* = 9.2 Hz, 2H), 3.77 (d, *J* = 4.8 Hz, 4H), 3.32 (t, *J* = 5.8 Hz, 4H), 3.06 (t, *J* = 7.2 Hz, 2H), 2.79 (t, *J* = 7.2 Hz, 2H), 1.47 (t, *J* = 5.6 Hz, 4H), 0.98 (s, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 154.12, 147.00, 136.96, 135.69, 130.03, 129.54, 128.96, 128.87, 128.72, 128.30, 127.46, 126.11, 113.06, 57.87, 57.69, 52.65, 43.87, 37.79, 31.29, 28.53, 27.70, 27.59 ppm. HRMS (ESI) calcd for $C_{36}H_{40}N_6O_5S_3$ $[M+H]^+$: 733.22951, found: 733.22965.



SZ9TA3

Acylsulfonamide SZ9TA3: was prepared following the general procedure **A** with 45% yield (62 mg). R_f = 0.66 in EtOAc : MeOH = 20:1. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 8.01 – 7.95 (m, 4H), 7.95 – 7.91 (m, 2H), 7.76 (d, *J* = 8.4, 2H), 7.66 (d, *J* = 8.2, 2H), 7.53 – 7.49 (m, 3H), 7.19 – 7.15 (m, 4H), 7.09 – 7.04 (m, 1H), 3.91 (s, 4H), 3.21 (t, *J* = 7.1 Hz, 2H), 2.73 (s, 2H), 2.55 (s, 3H) ppm. ^{13}C NMR (101 MHz, DMSO-*d6*) δ 168.41, 161.13, 159.47, 145.80, 143.06, 139.86, 136.90, 135.55, 132.49, 131.71, 130.99, 129.91,

129.77, 129.33, 128.55, 128.21, 127.80, 126.85, 126.15, 124.67, 57.27, 57.14, 52.14, 29.03, 17.81 ppm. HRMS (ESI) calcd for $C_{33}H_{30}N_6O_5S_4$ $[M+H]^+$: 719.12333, found: 719.12280.

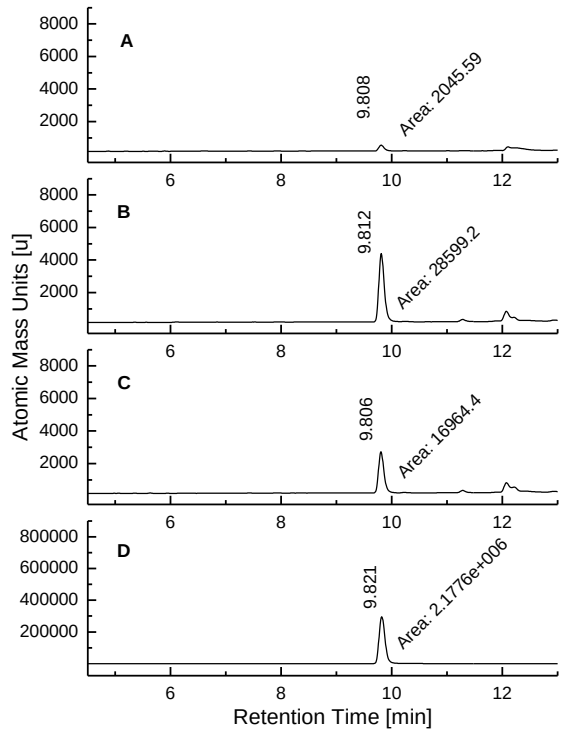


SZ9TA7

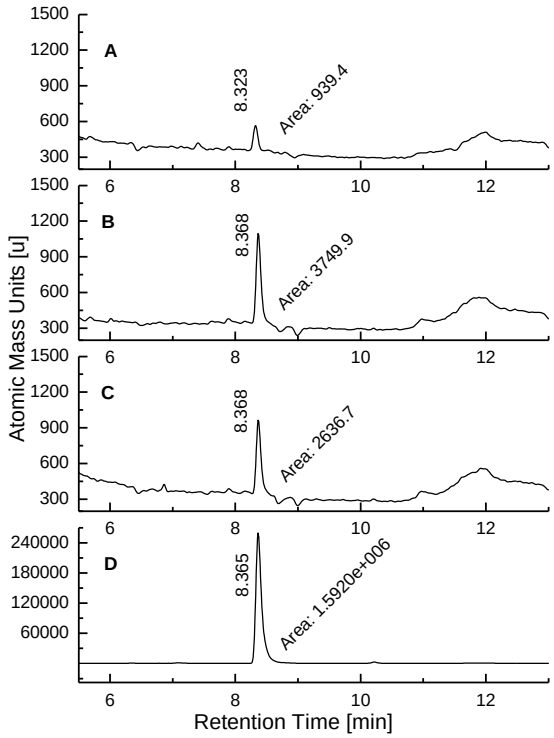
Acylsulfonamide SZ9TA7: was prepared following the general procedure **A** with 69% yield (45 mg). R_f = 0.44 in hexane : EtOAc = 1:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.44 (s, 1H), 7.96 (d, *J* = 8.0 Hz, 2H), 7.74 – 7.68 (m, 3H), 7.60 – 7.51 (m, 3H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.18 – 6.93 (m, 10H), 3.37 (s, 2H), 3.31 (s, 2H), 2.86 (t, *J* = 6.4 Hz, 2H), 2.50 (bs, 2H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$) δ: 146.99, 143.43, 140.01, 136.83, 135.75, 133.39, 131.40, 130.42, 129.47, 128.86, 128.82, 128.66, 127.93, 127.66, 127.36, 127.12, 126.86, 126.06, 125.73, 124.34, 57.60, 57.39, 52.47, 31.14 ppm. HRMS (ESI) calcd for $C_{33}H_{29}N_5O_5S_3$ $[M+H]^+$: 672.14036, found: 672.14091.

LC/MS-SIM Analysis:

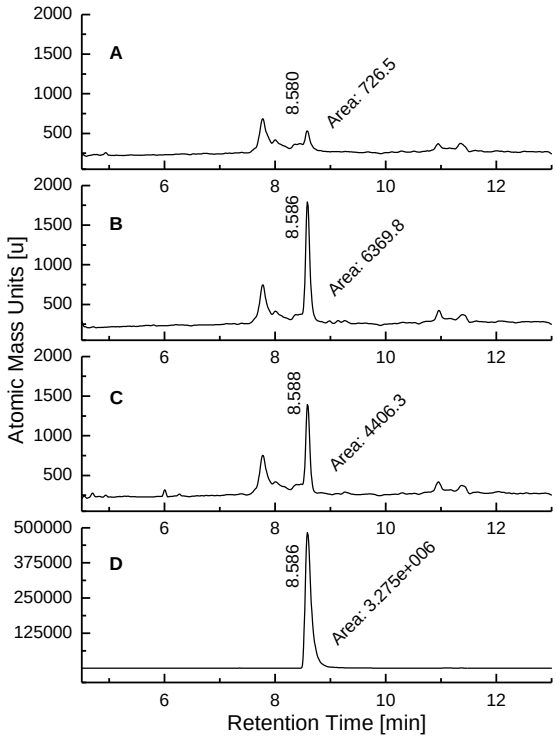
A. Mutant Bcl-X_L (^{R139A}Bcl-X_L) experiments:



Bcl-X_L and mutant Bcl-X_L templated incubations with SZ7 and TA2. The samples were incubated for six hours at 37 °C and subjected to LC/MS-SIM analysis with gradient system 1. A) Incubation of **SZ7** and **TA2** without Bcl-X_L B) Incubation of **SZ7** and **TA2** with 2 μM Bcl-X_L C) Incubation of **SZ7** and **TA2** with 2 μM mutant Bcl-X_L D) Synthetic **SZ7TA2** as the reference.

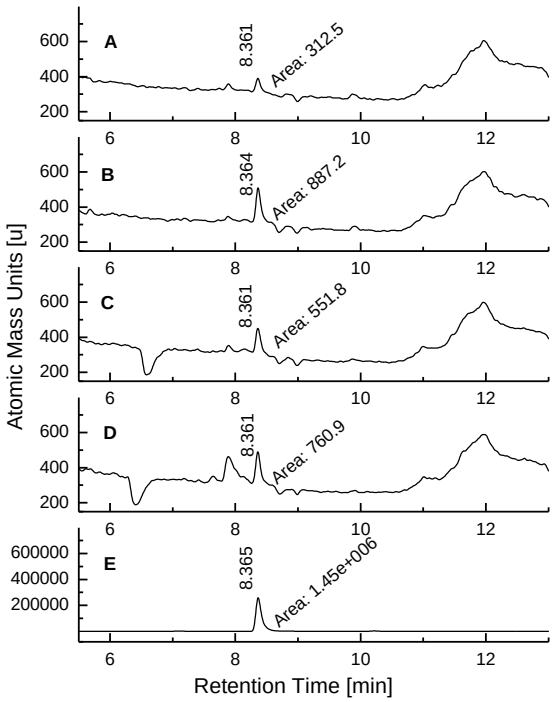


Bcl-X_L and mutant Bcl-X_L templated incubations with SZ9 and TA1. The samples were incubated for six hours at 37 °C and subjected to LC/MS-SIM analysis with gradient system 1. A) Incubation of **SZ9** and **TA1** without Bcl-X_L B) Incubation of **SZ9** and **TA1** with 2 μM Bcl-X_L C) Incubation of **SZ9** and **TA1** with 2 μM mutant Bcl-X_L D) Synthetic **SZ9TA1** as the reference.

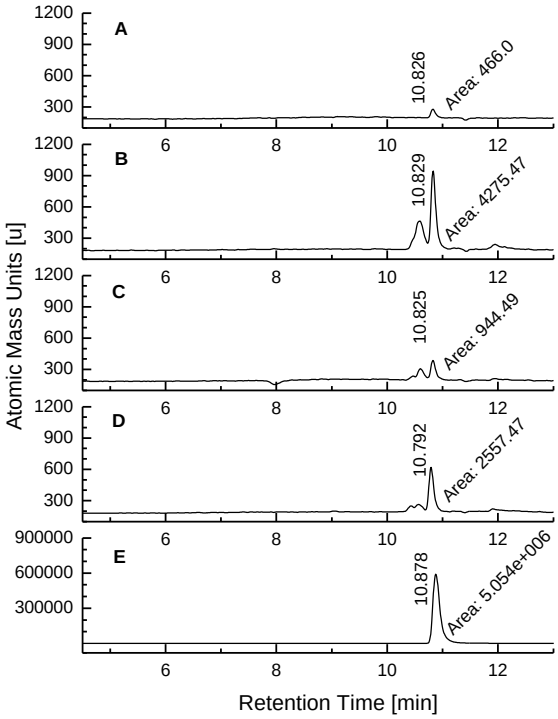


Bcl-X_L and mutant Bcl-X_L templated incubations with SZ9 and TA5. The samples were incubated for six hours at 37 °C and subjected to LC/MS-SIM analysis with gradient system 1. A) Incubation of **SZ9** and **TA5** without Bcl-X_L B) Incubation of **SZ9** and **TA5** with 2 μM Bcl-X_L C) Incubation of **SZ9** and **TA5** with 2 μM mutant Bcl-X_L D) Synthetic **SZ9TA5** as the reference.

B. Peptide control experiments:



Incubation of SZ9 and TA1 and suppressing Bcl-X_L-templated incubations with Bim and mutant Bim. The samples were incubated for six hours at 37 °C and subjected to LC/MS-SIM analysis with gradient system 1. A) Incubation of **SZ9** and **TA1** without Bcl-X_L B) Incubation of **SZ9** and **TA1** with 2 μM Bcl-X_L C) Incubation of **SZ9** and **TA1** with 2 μM Bcl-X_L and 20 μM Bim D) Incubation of **SZ9** and **TA1** with 2 μM Bcl-X_L and 20 μM mutant Bim E) Synthetic **SZ9TA1** as the reference.



Incubation of SZ9 and TA5 and suppressing Bcl-X_L-templated incubations with Bim and mutant Bim. The samples were incubated for six hours at 37 °C and subjected to LC/MS-SIM analysis with gradient system 2. A) Incubation of **SZ9** and **TA5** without Bcl-X_L B) Incubation of **SZ9** and **TA5** with 2 μM Bcl-X_L C) Incubation of **SZ9** and **TA5** with 2 μM Bcl-X_L and 20 μM Bim D) Incubation of **SZ9** and **TA5** with 2 μM Bcl-X_L and 20 μM mutant Bim E) Synthetic **SZ9TA5** as the reference.

References:

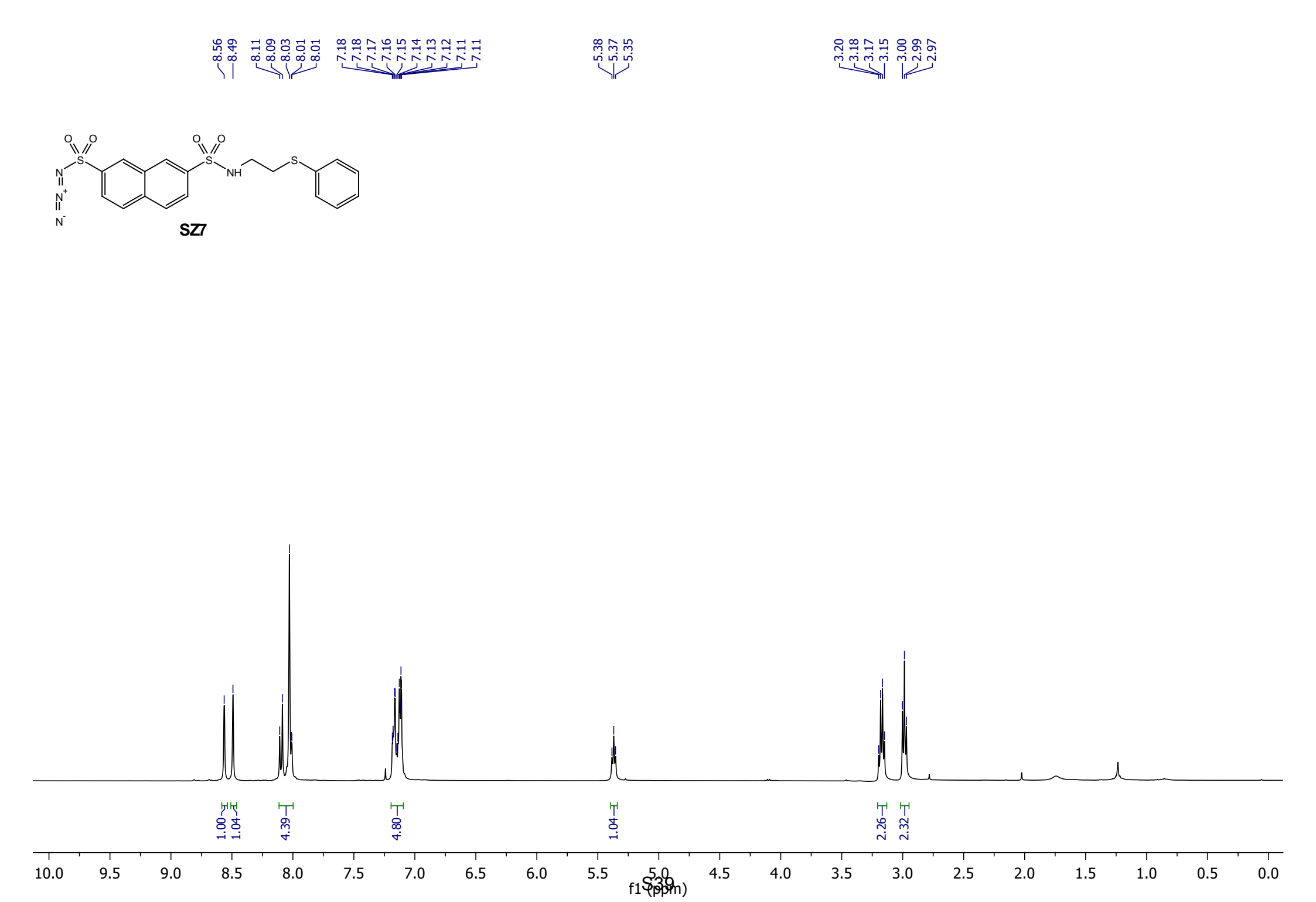
1. Hu, X., Sun, J., Wang, H.-G., and Manetsch, R. (2008) Bcl-XL-Templated Assembly of Its Own Protein-Protein Interaction Modulator from Fragments Decorated with Thio Acids and Sulfonyl Azides, *Journal of the American Chemical Society 130*, 13820–13821.

2. Yamaguchi, H., and Wang, H.-G. (2002) Bcl-XL protects BimEL-induced Bax conformational change and cytochrome c release independent of interacting with Bax or BimEL, *Journal of Biological Chemistry 277*, 41604–41612.

3. Paruch, K., Vyklicky, L., Katz, T. J., Incarvito, C. D., and Rheingold, A. L. (2000) Expeditious procedure to synthesize ethers and esters of tri- and tetrahydroxy[6]helicenebisquinones from the dye-intermediates disodium 4-hydroxy- and 4,5-dihydroxynaphthalene-2,7-disulfonates, *J Org Chem 65*, 8774–8782.

4. Aubry, S., Pellet-Rostaing, S., Faure, R., and Lemaire, M. (2006) Racemic and diastereoselective synthesis of aryl and heteroaryl tetrahydroisoquinolines via the Pictet-Spengler reaction, *Journal of Heterocyclic Chemistry 43*, 139–148.

5. Wu, X. H., and Hu, L. Q. (2007) Efficient amidation from carboxylic acids and azides via selenocarboxylates: Application to the coupling of amino acids and peptides with azides, *Journal of Organic Chemistry 72*, 765–774.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8.01
8.01
7.18
7.18
7.17
7.16
7.15
7.14
7.13
7.12
7.11
7.11
5.38
5.37
5.35
3.20
3.18
3.17
3.15
3.00
2.99
2.97
SZ7
1.00
1.04
4.39
4.80
1.04
2.26
2.32
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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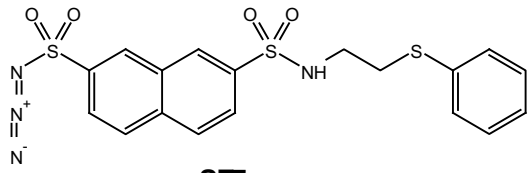
f1 (ppm)



SZ7

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130.22
130.15
129.76
129.44
129.04
126.93
126.24
124.59
77.31
77.00
76.68
41.60
33.85
190
180
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90
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70
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50
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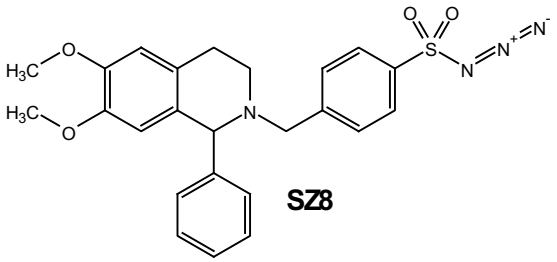
f1 (ppm)


SZ8

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2.69
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2.51
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0.89
0.90
0.72
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2.70
0.91
1.73
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9.0
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8.0
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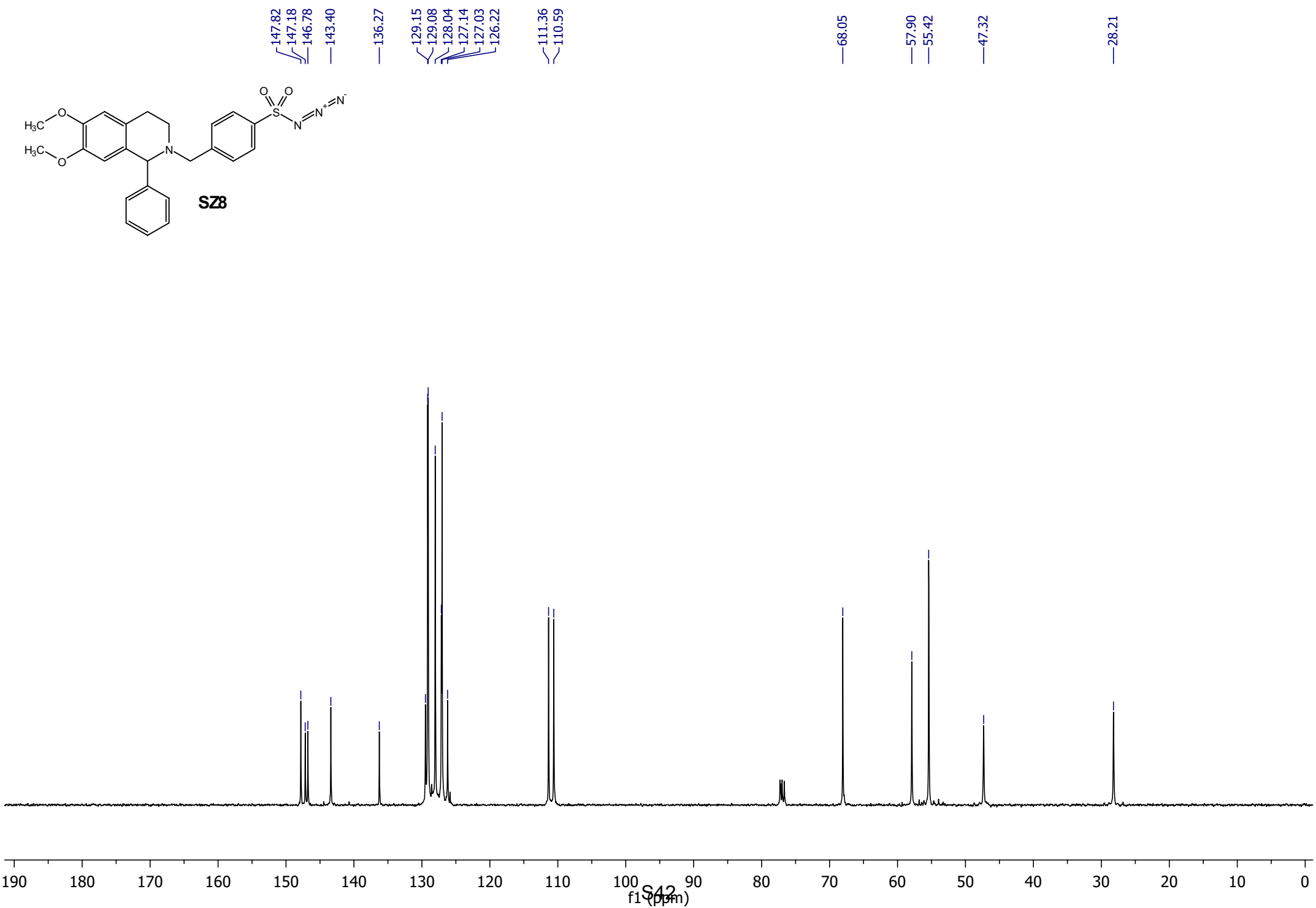
f1 (ppm)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128.04
127.14
127.03
126.22
111.36
110.59
68.05
57.90
55.42
47.32
28.21
SZ8
190
180
170
160
150
140
130
120
110
100
90
80
70
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50
40
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10
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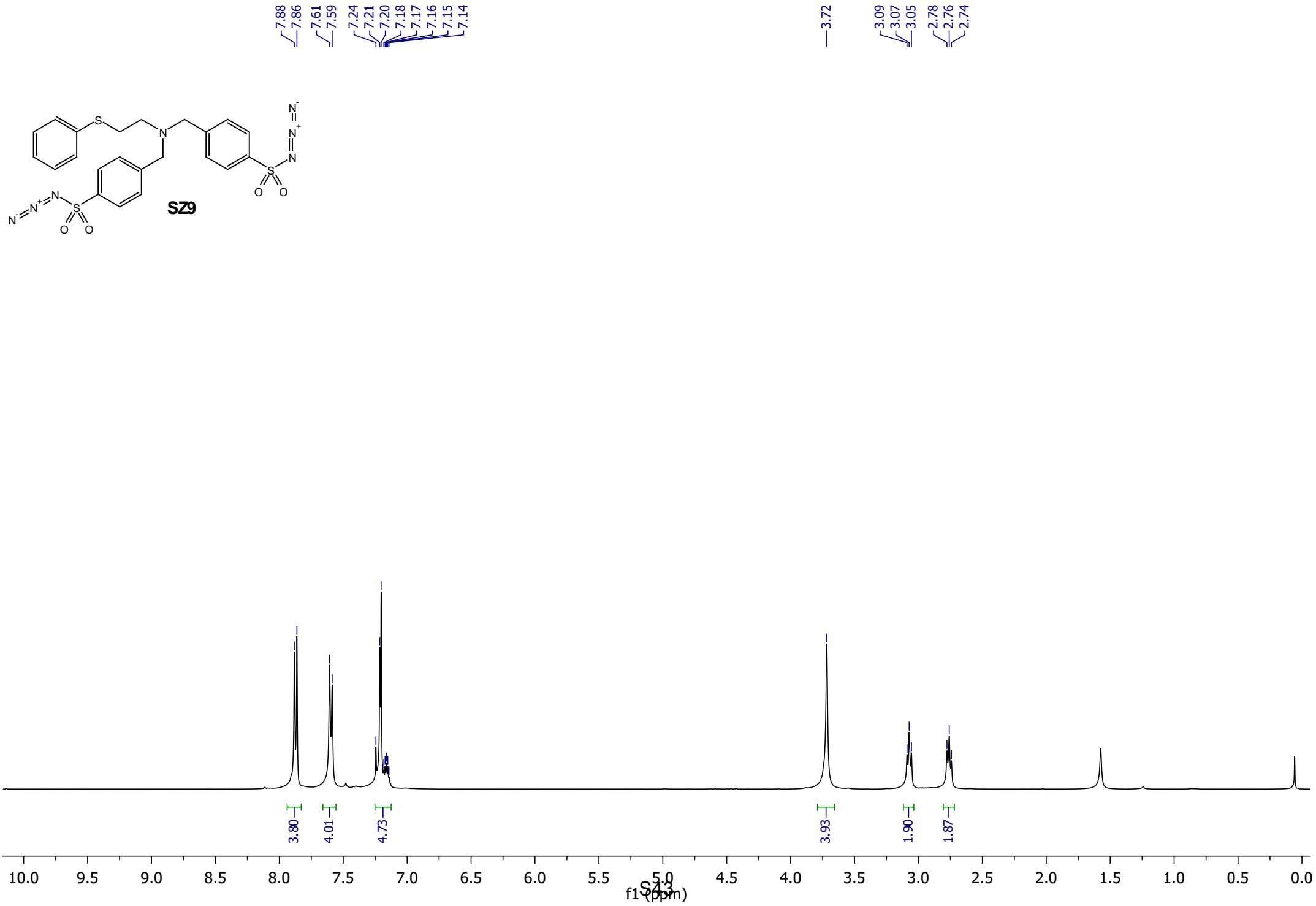
f1 (ppm)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3.07
3.05
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2.76
2.74
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4.73
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8.0
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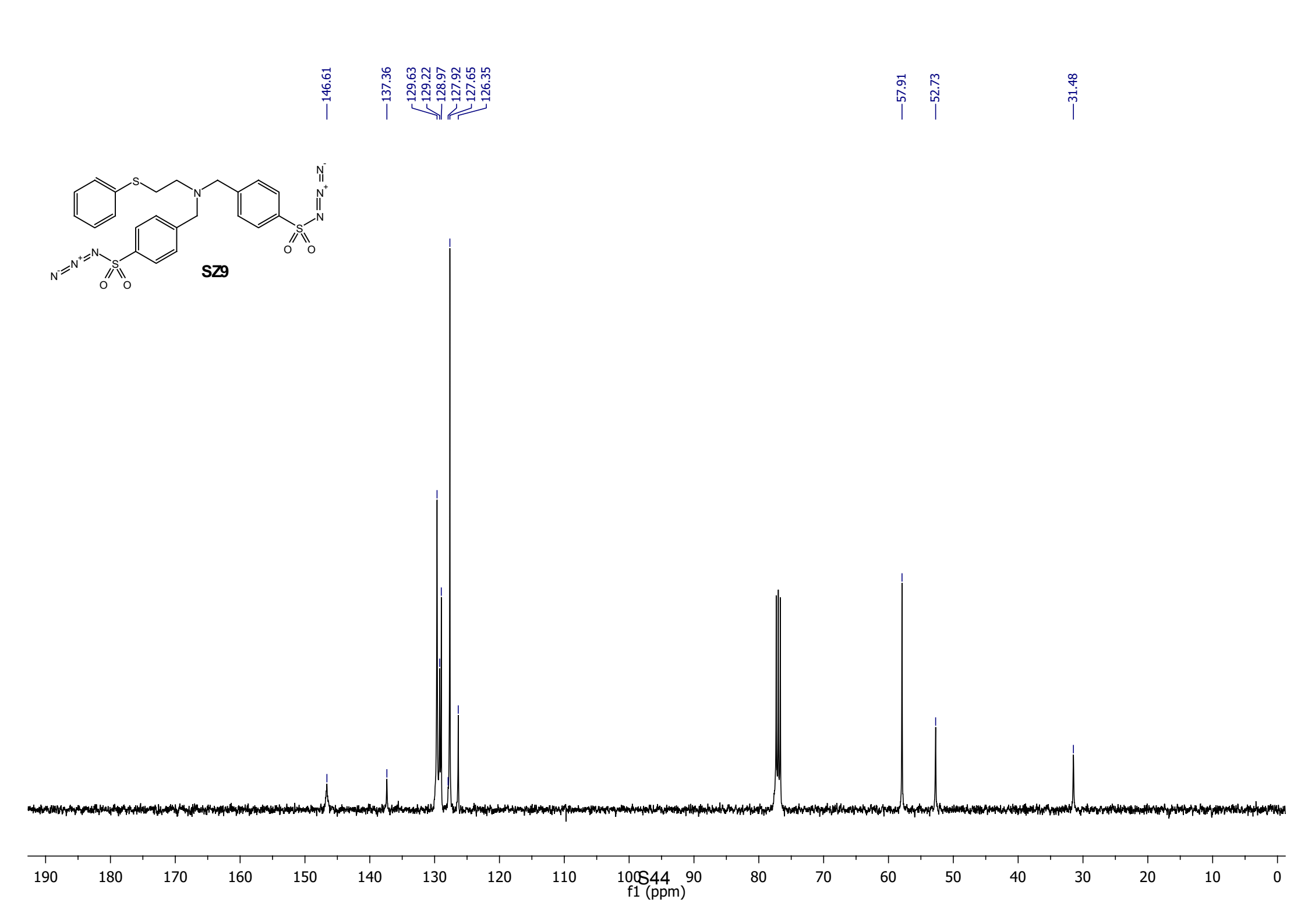
f1 (ppm)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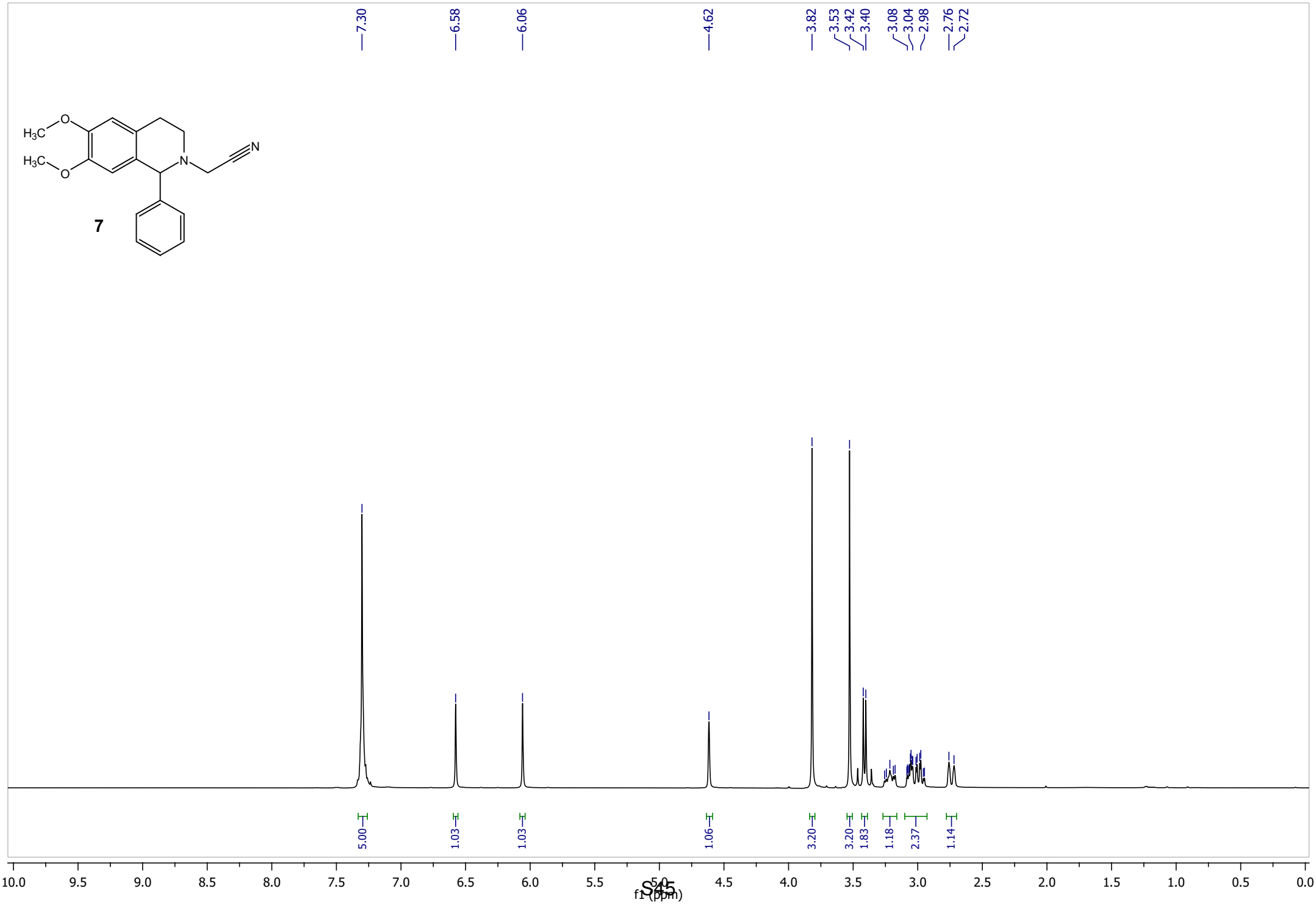
f1 (ppm)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H3C
O
N
N
7
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1.03
1.03
1.06
3.20
3.20
1.83
1.18
2.37
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6.5
6.0
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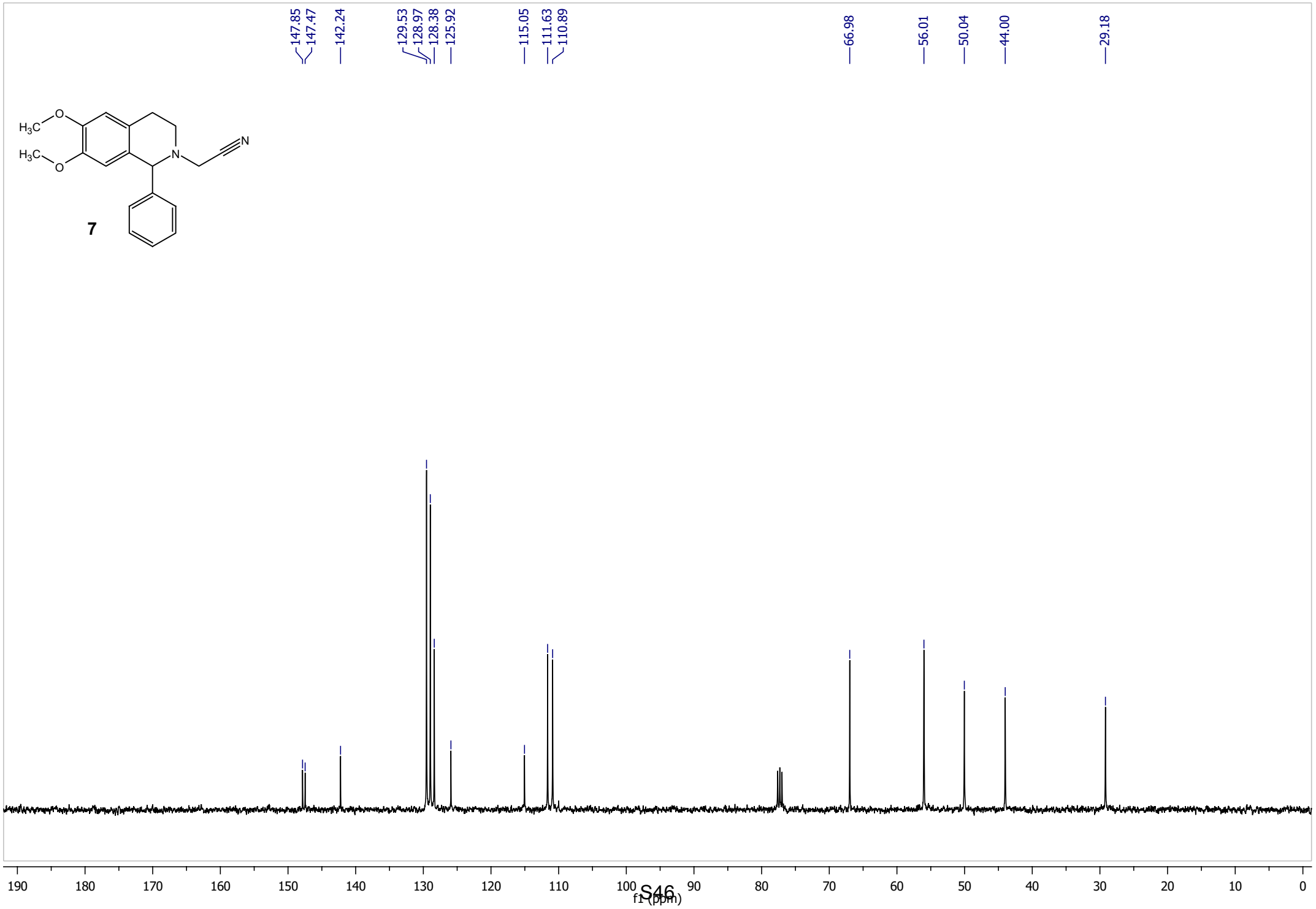
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H3C
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7
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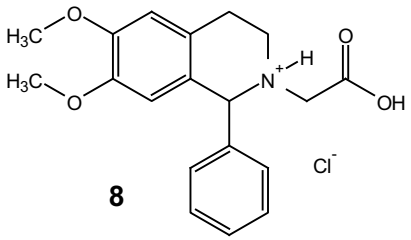
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O
H3C
O
N+
H
O
OH
Cl-

8

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7.20
6.69
6.13
4.95
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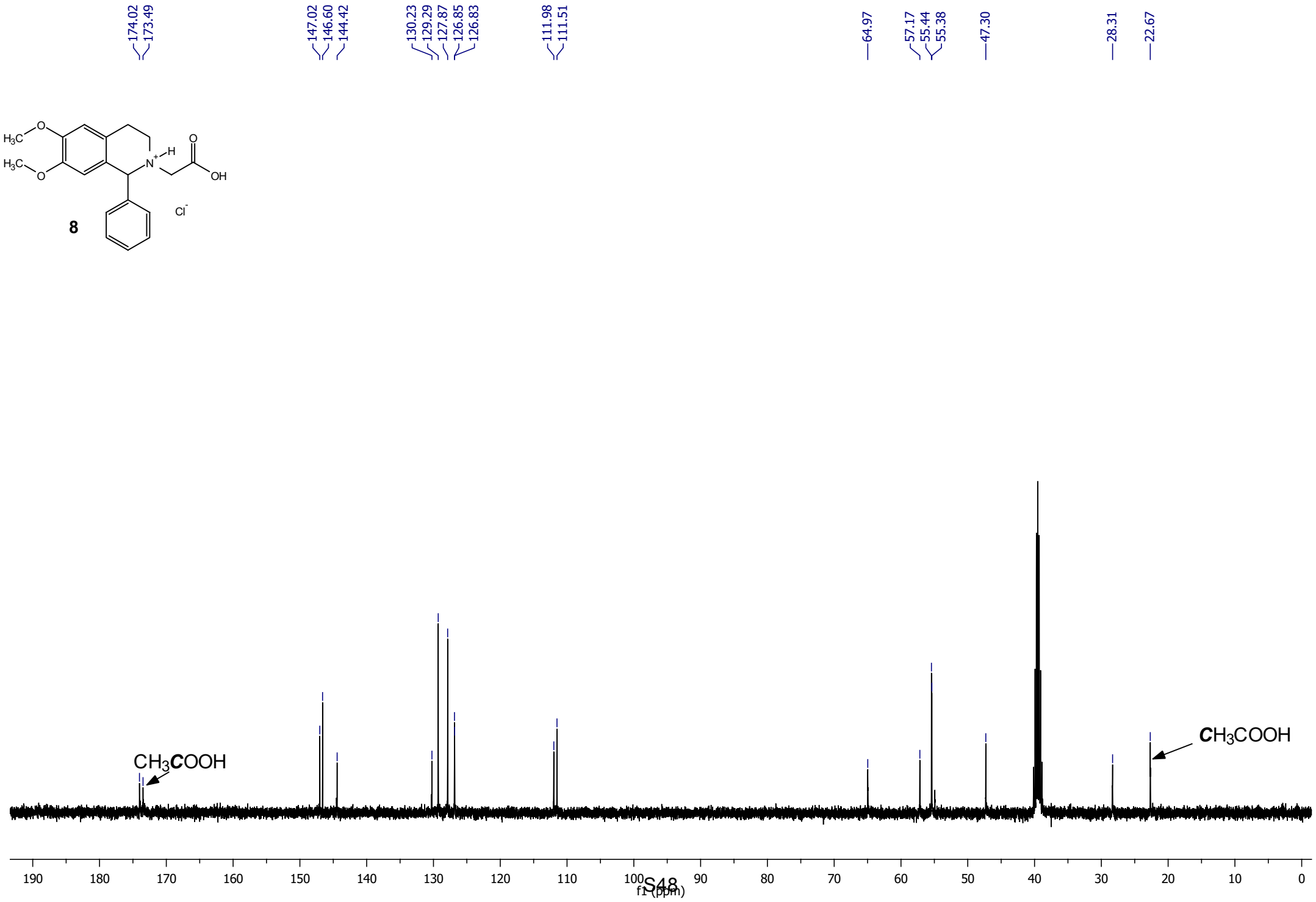
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CH3COOH
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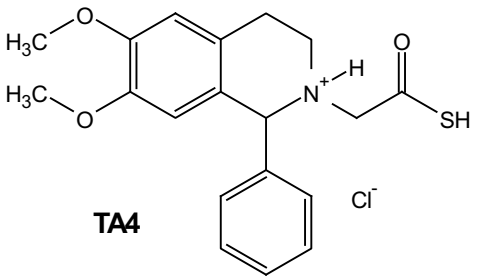
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Cl-

TA4

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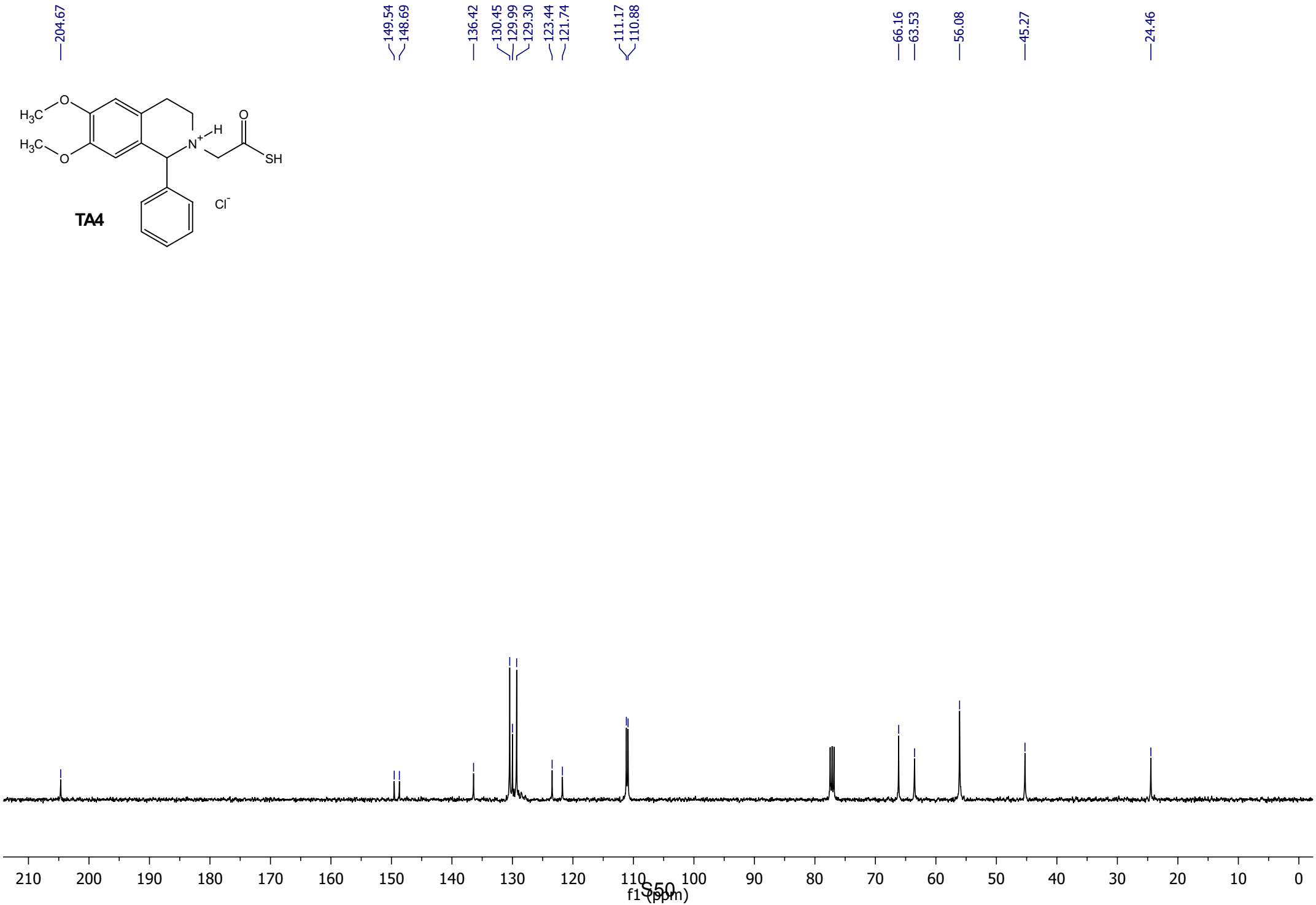
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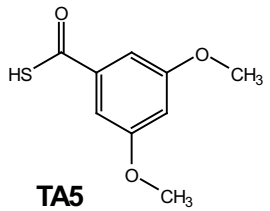
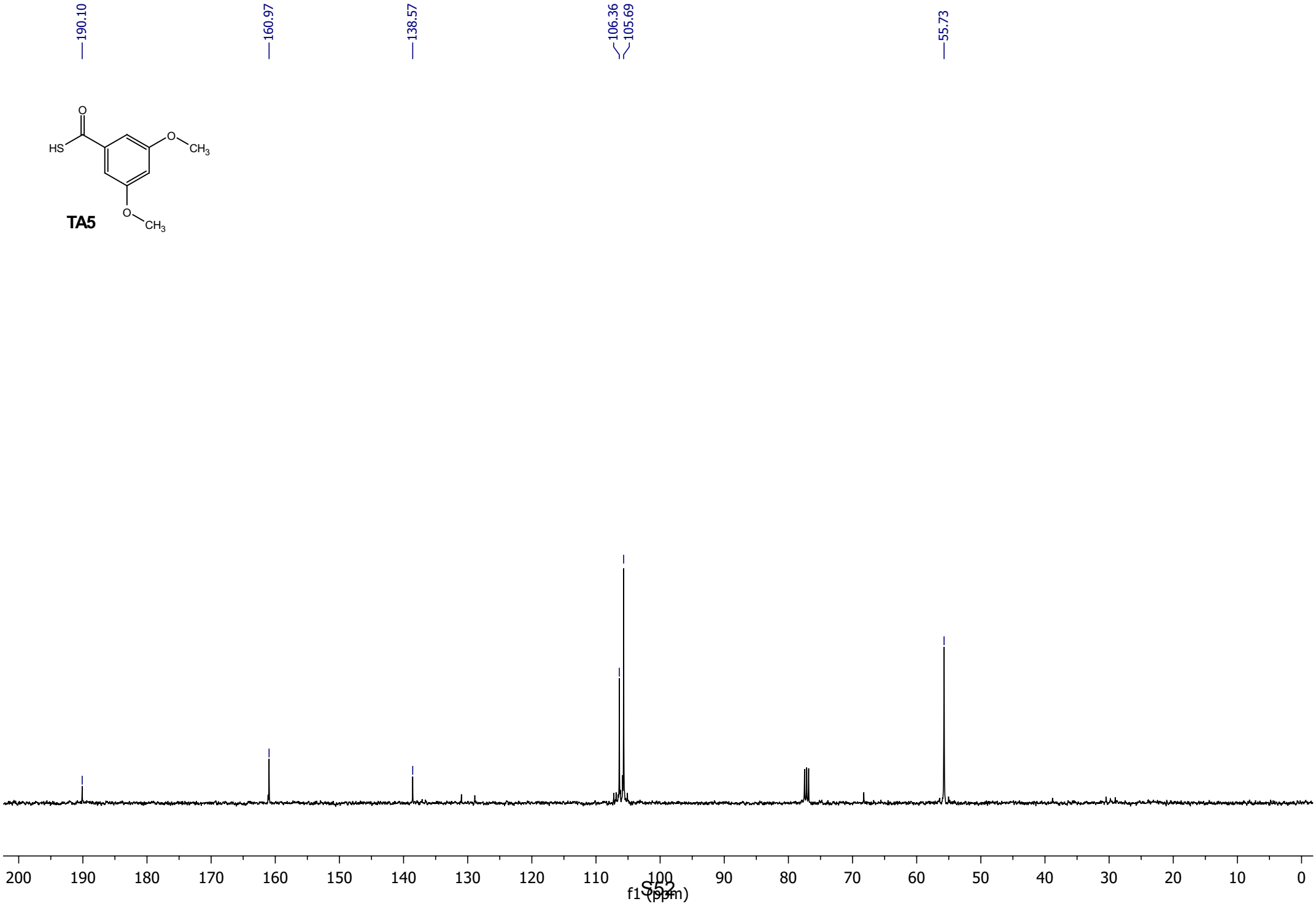
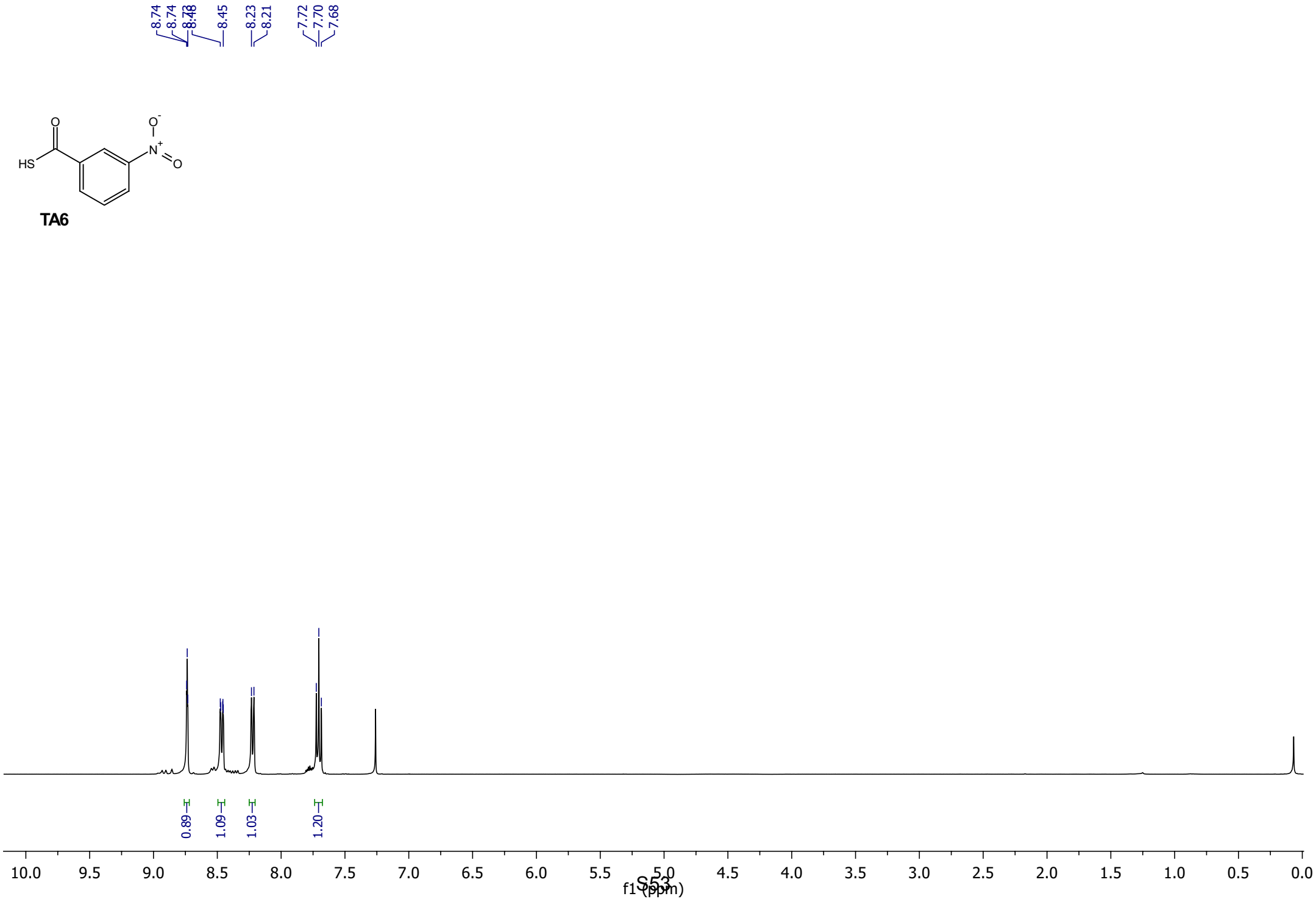
30
20
10
0
f1 (ppm)

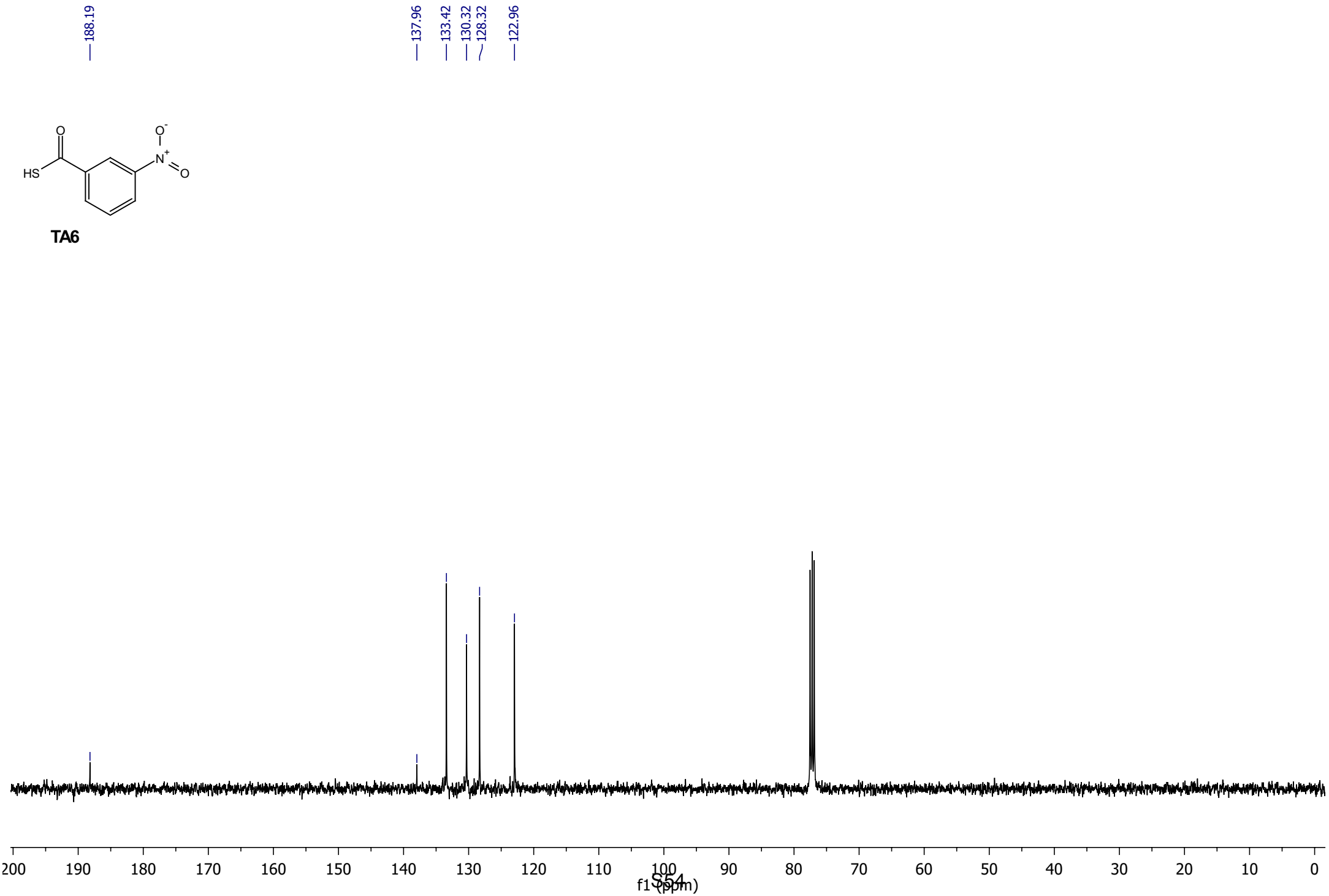

O
HS
O
CH3
O
CH3

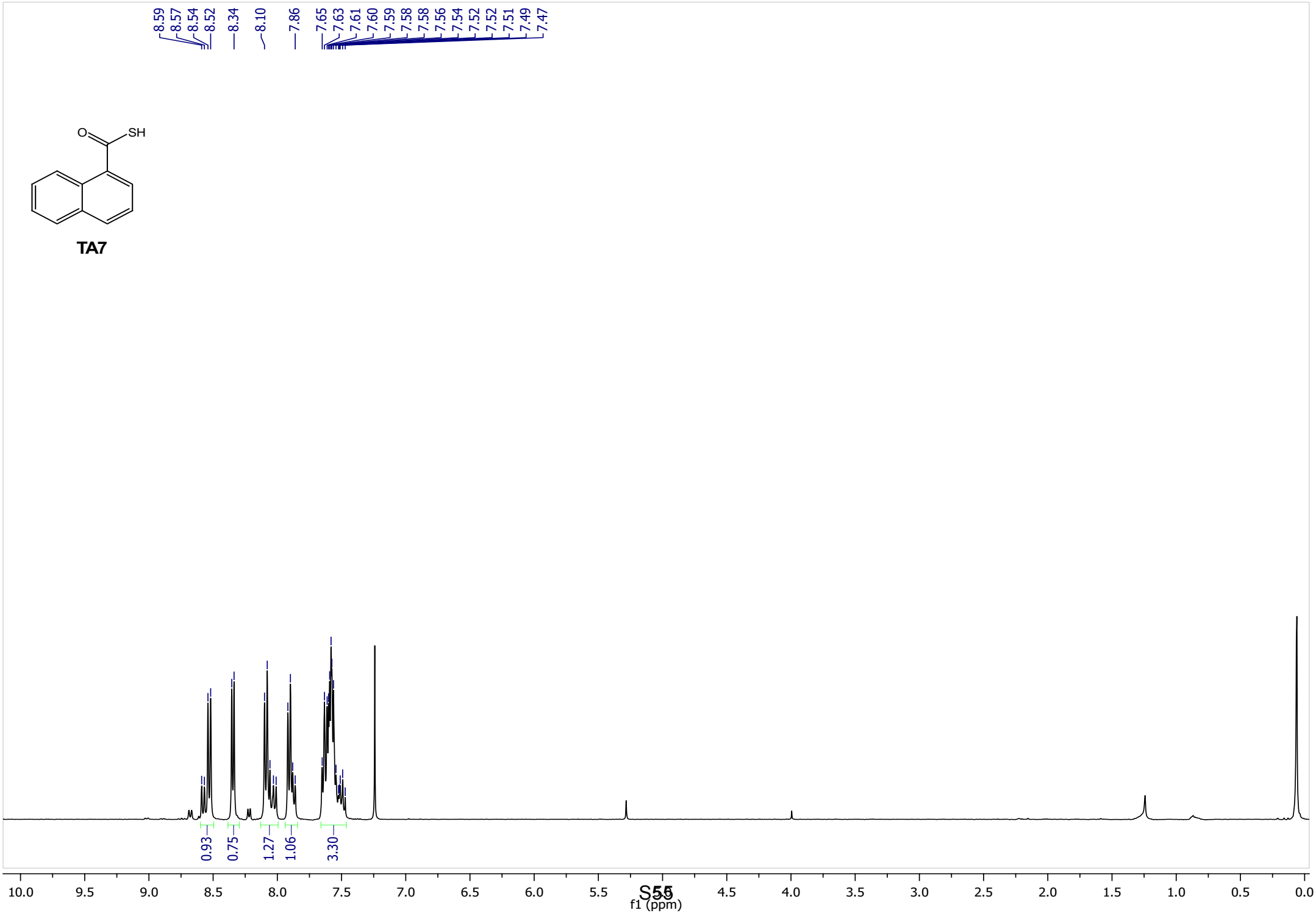
TA5

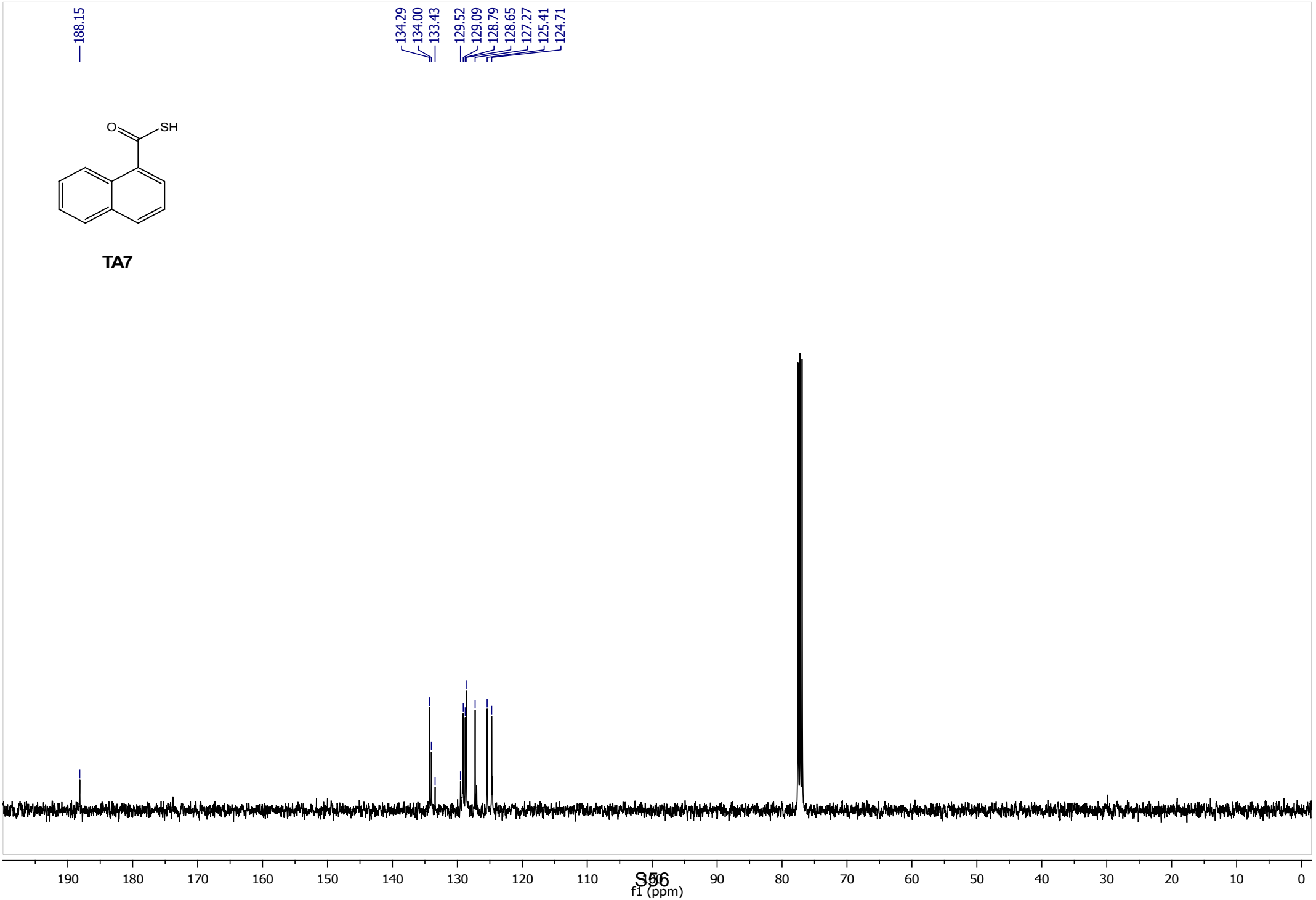
7.00
7.00
6.65
3.80
1.80
0.94
6.18
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

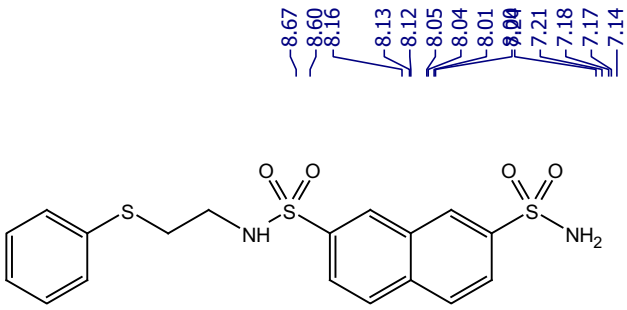

190.10
160.97
138.57
106.36
105.69
55.73
HS
O
O
CH3
O
CH3
TA5
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.74
8.74
8.45
8.23
8.21
7.72
7.70
7.68
HS
O
O
N
O
TA6
0.89
1.09
1.03
1.20
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


188.19
137.96
133.42
130.32
128.32
122.96
O
O-
N+
O
HS
TA6
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

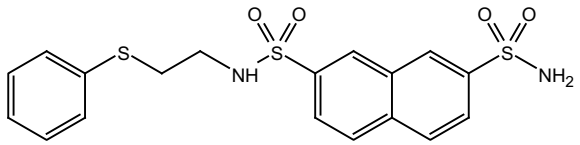

8.59
8.57
8.54
8.52
8.34
8.10
7.86
7.65
7.63
7.61
7.60
7.59
7.58
7.58
7.56
7.54
7.52
7.52
7.51
7.49
7.47
O
SH
TA7
0.93
0.75
1.27
1.06
3.30
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


188.15
134.29
134.00
133.43
129.52
129.09
128.79
128.65
127.27
125.41
124.71
O
SH
TA7
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O
O
S
NH
S
O
O
S
NH2

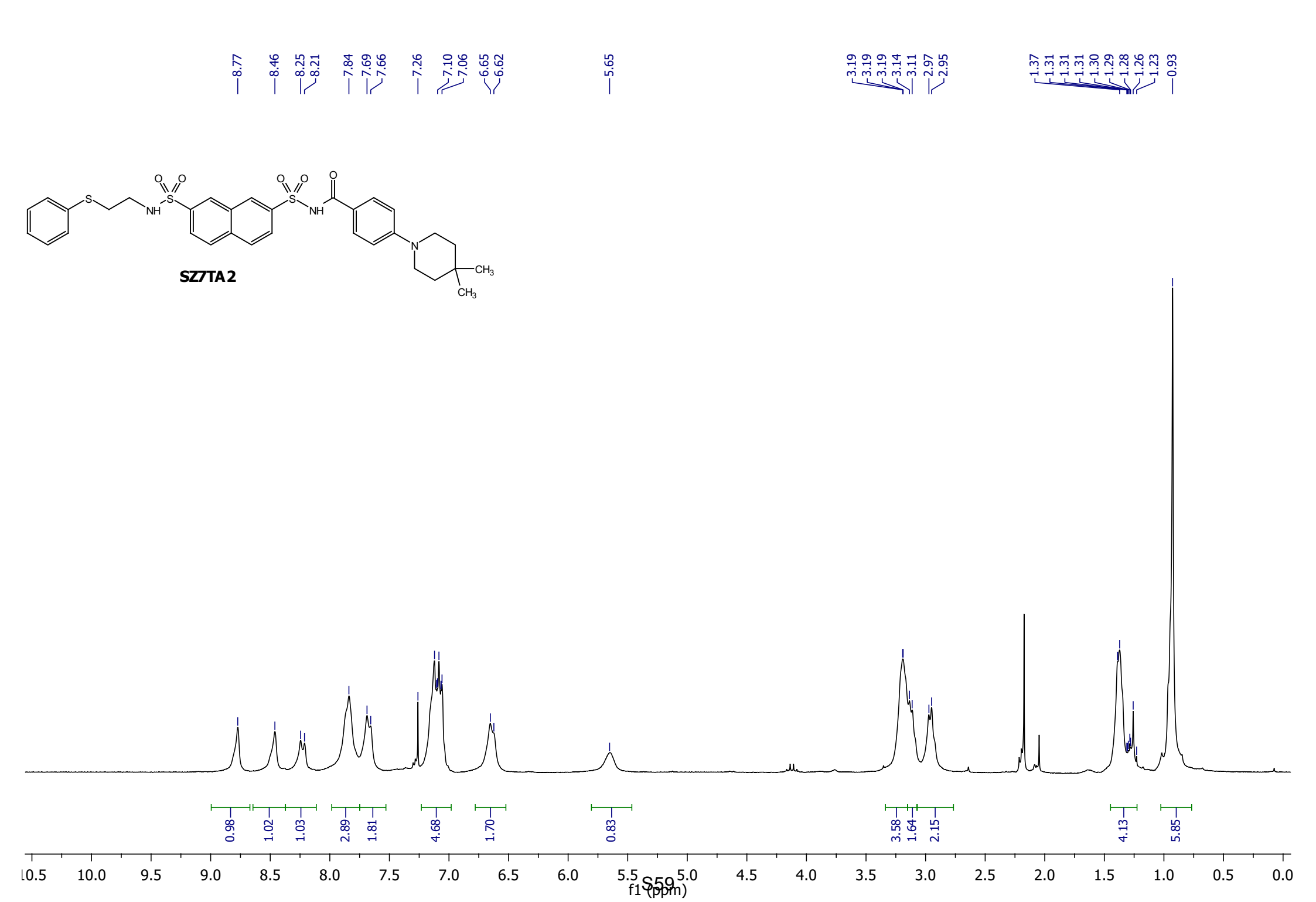
14

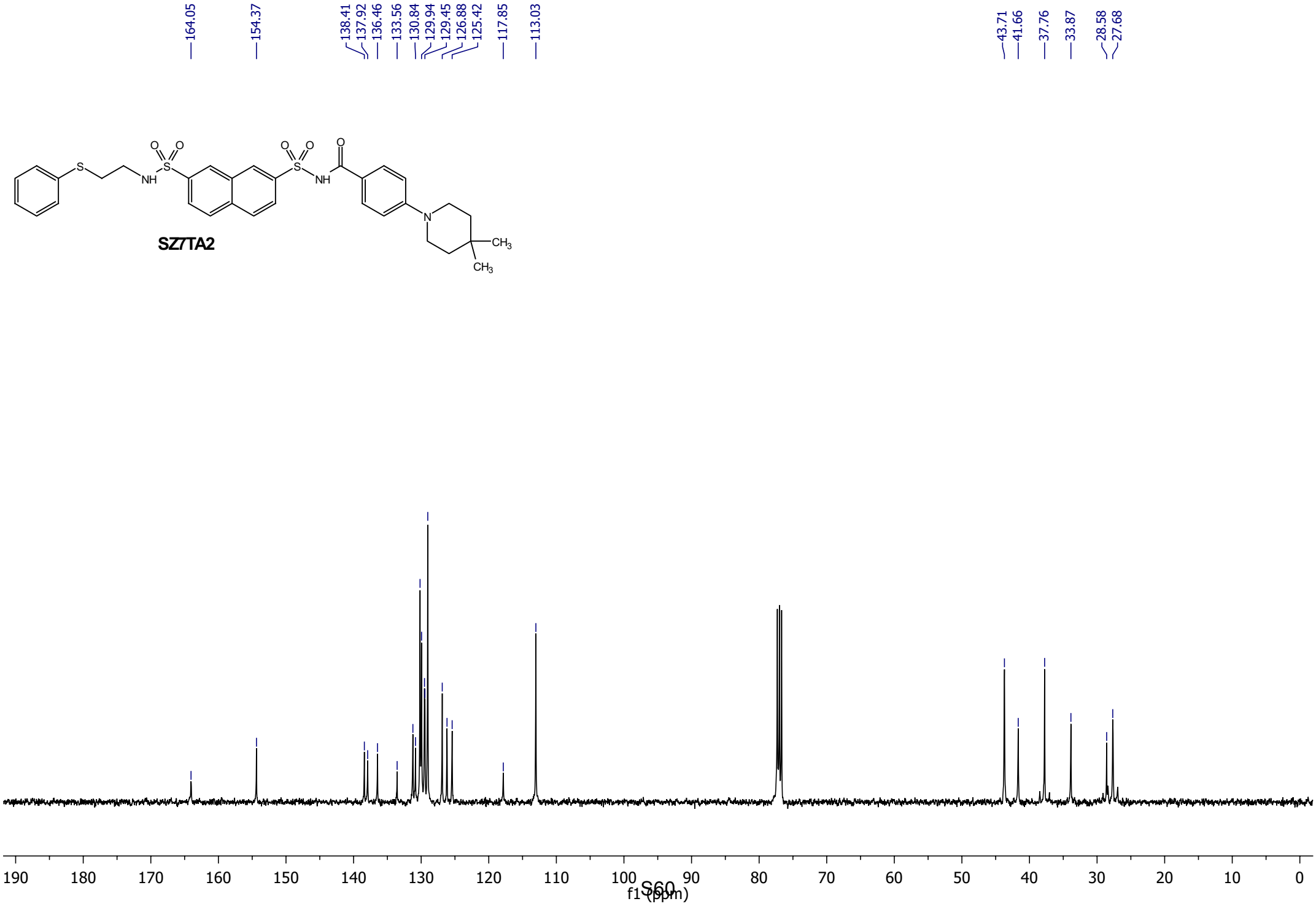
8.67
8.60
8.16
8.13
8.12
8.05
8.04
8.01
7.21
7.18
7.17
7.14
6.99
6.97
6.94
6.87
3.29
3.28
3.27
3.25
3.24
3.22
3.19
3.13
3.11
3.10
3.08
3.07
0.90
0.93
2.76
0.91
4.78
0.92
1.73
2.20
1.85
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

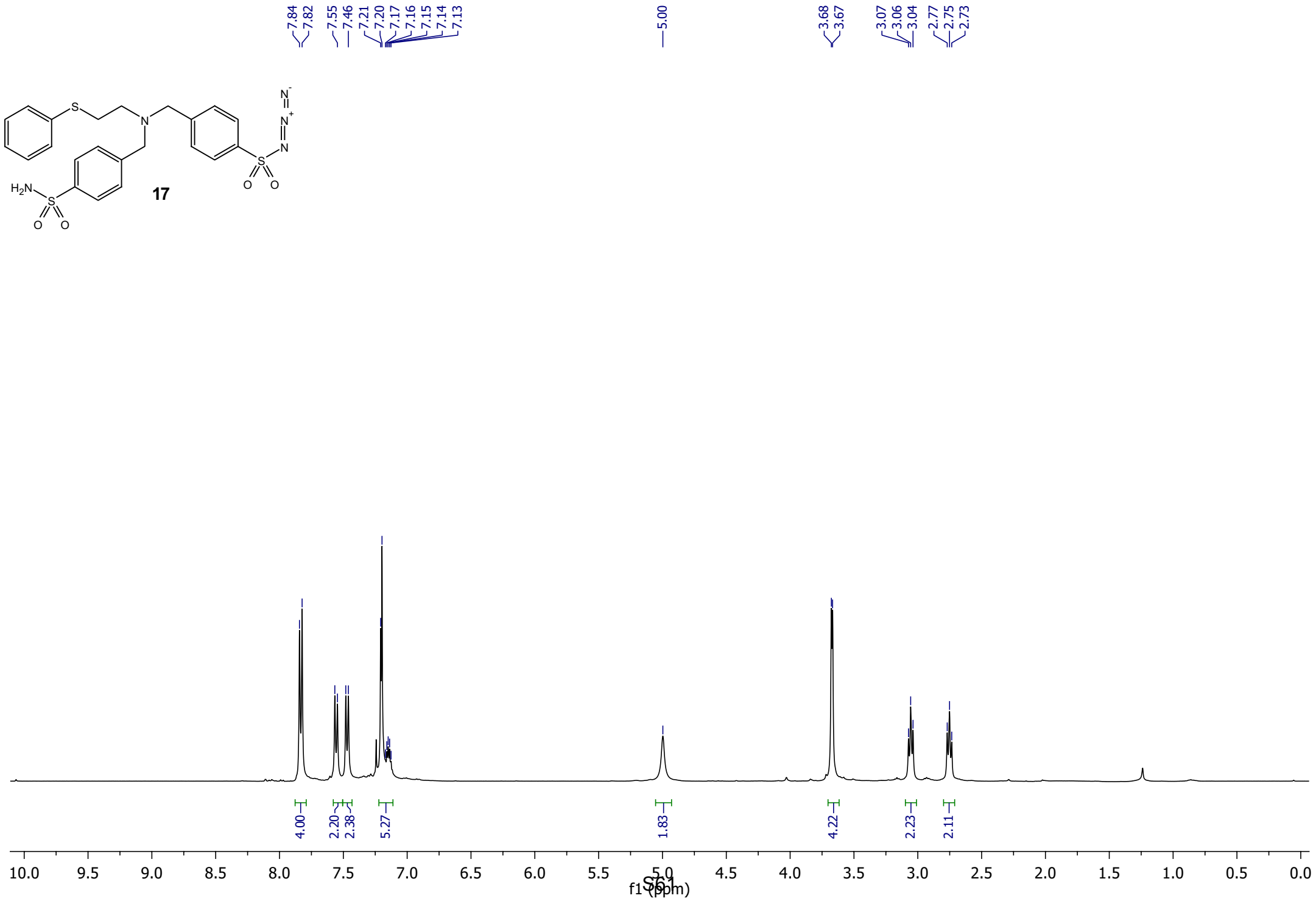

O
O
S
NH
S
O
O
S
NH2

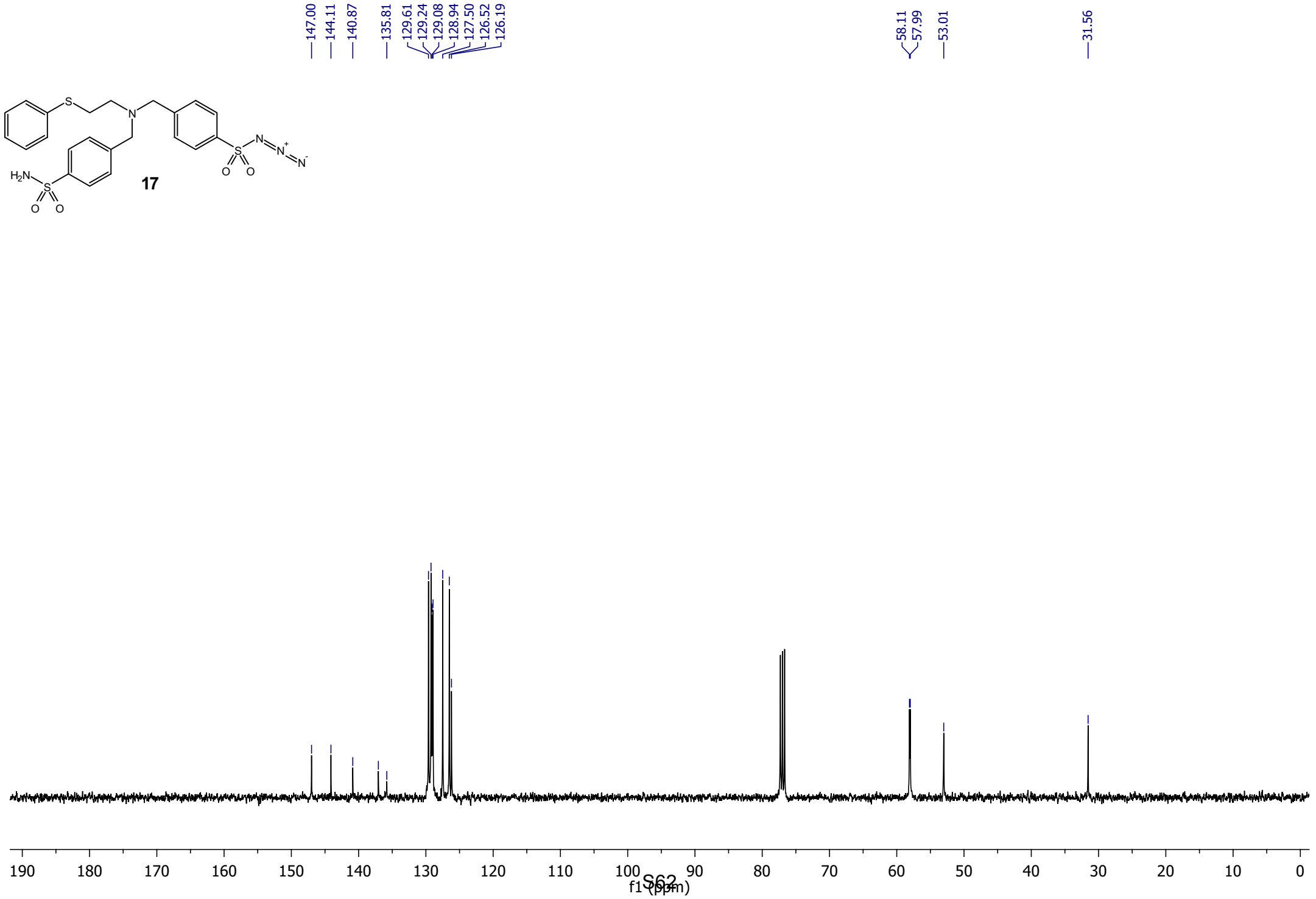
14

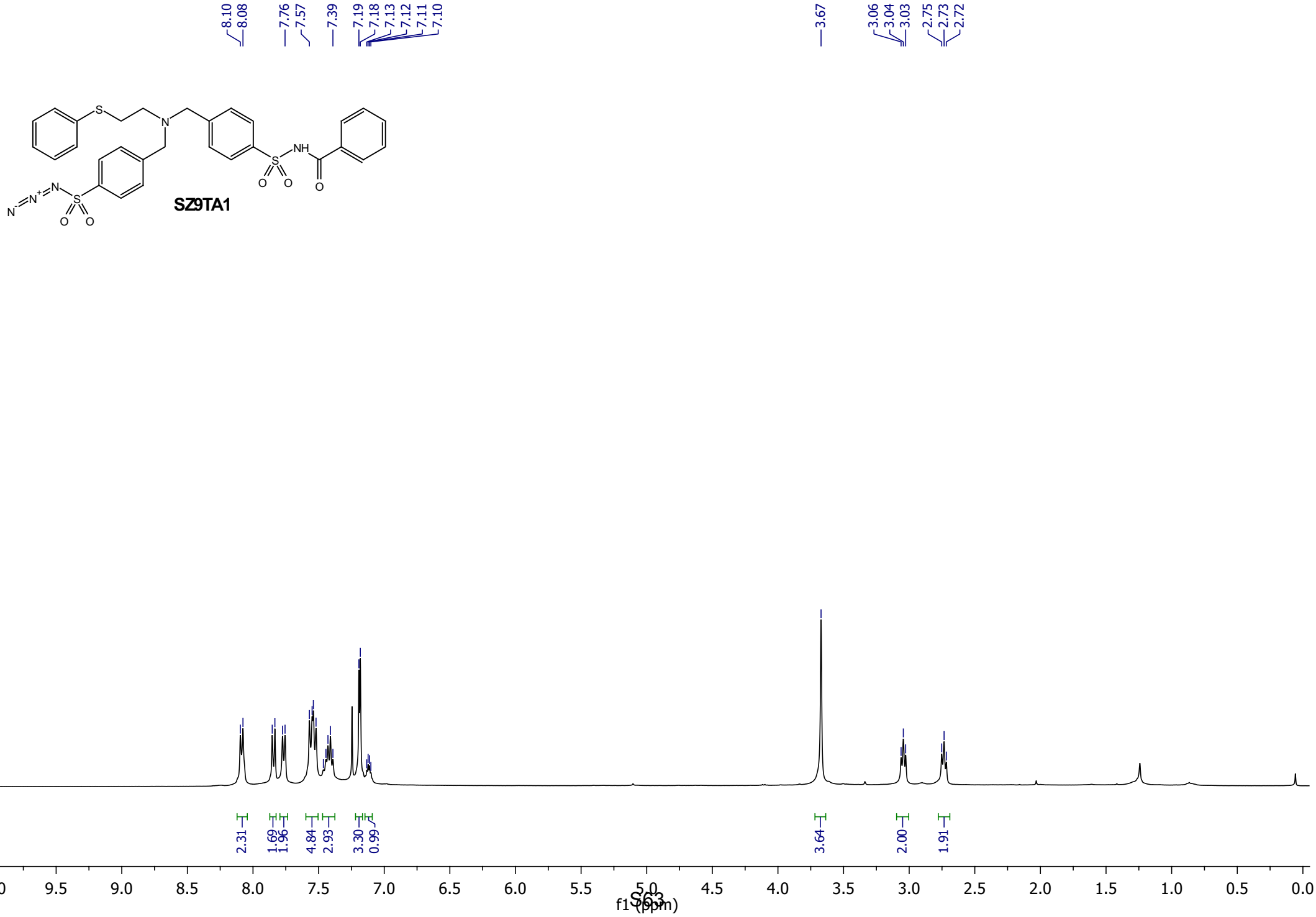
143.54
140.22
135.93
132.11
130.57
130.32
130.03
129.97
129.74
128.52
127.20
125.86
125.83
43.24
33.73
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

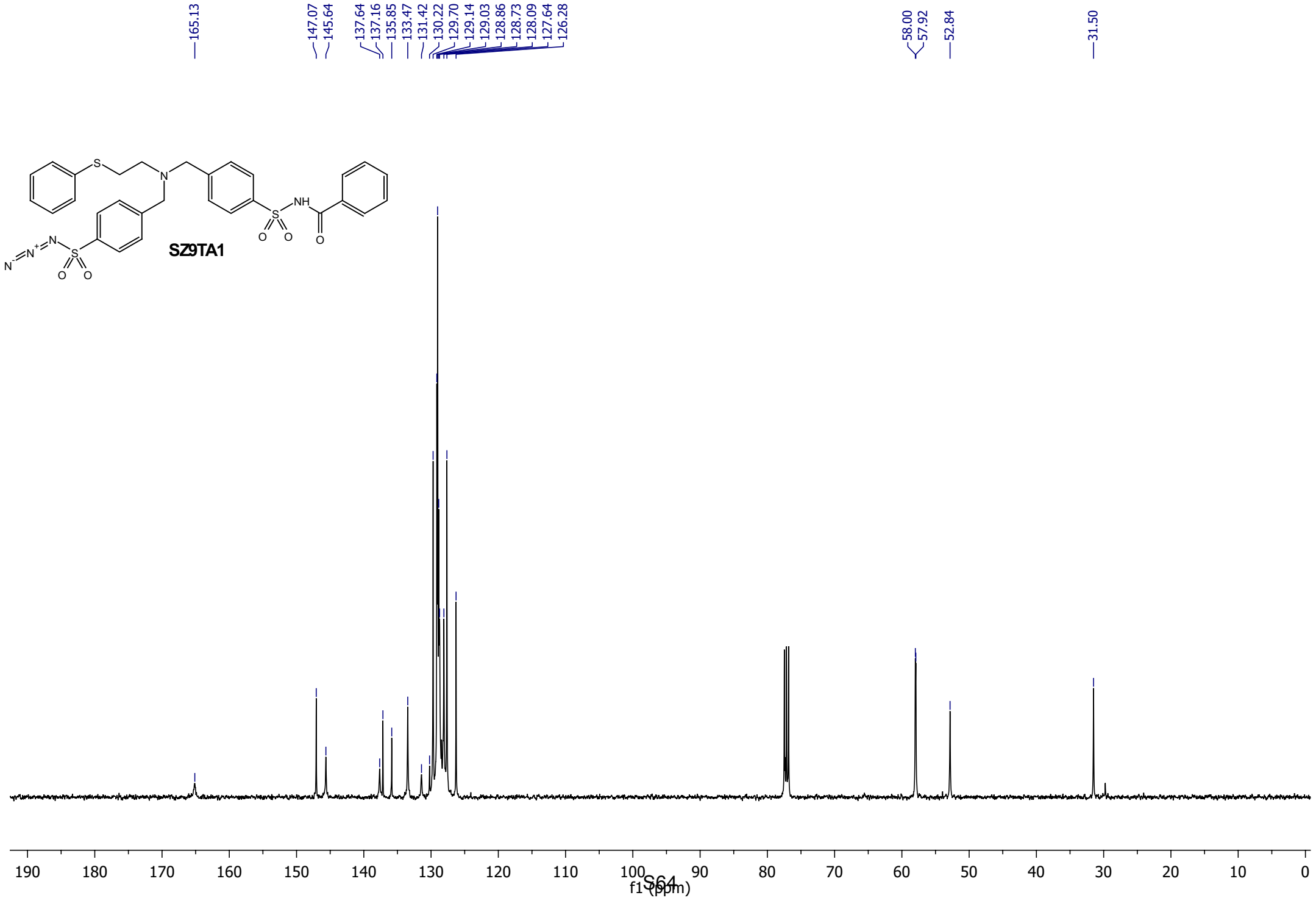

8.77
8.46
8.25
8.21
7.84
7.69
7.66
7.26
7.10
7.06
6.65
6.62
5.65
3.19
3.19
3.19
3.14
3.11
2.97
2.95
1.37
1.31
1.31
1.31
1.30
1.29
1.28
1.26
1.23
0.93
SZ7TA2
0.98
1.02
1.03
2.89
1.81
4.68
1.70
0.83
3.58
1.64
2.15
4.13
5.85
f1 (ppm)

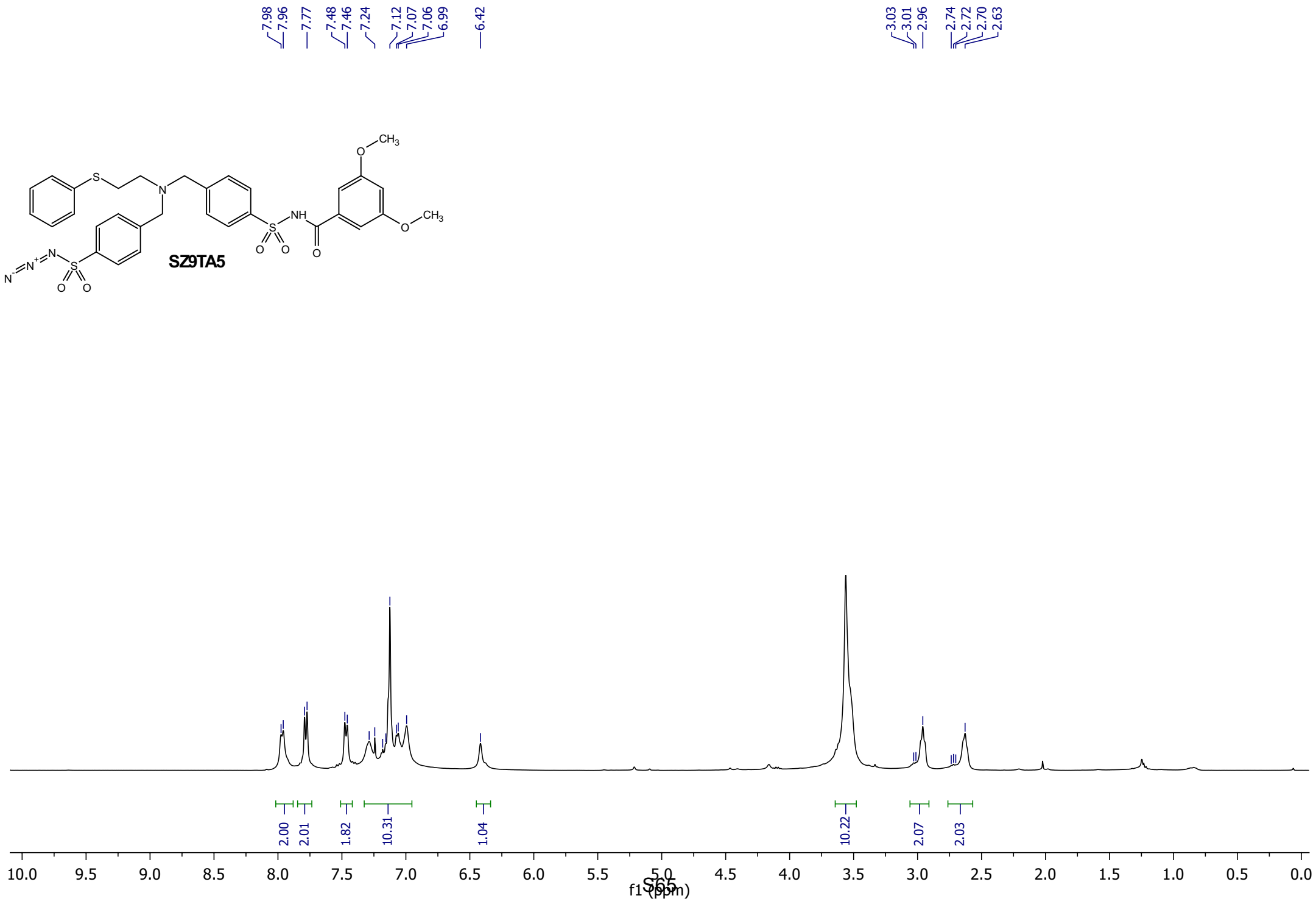

164.05
154.37
138.41
137.92
136.46
133.56
130.84
129.94
129.45
126.88
125.42
117.85
113.03
43.71
41.66
37.76
33.87
28.58
27.68
SZ7TA2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.84
7.82
7.55
7.46
7.21
7.20
7.17
7.16
7.15
7.14
7.13
5.00
3.68
3.67
3.07
3.06
3.04
2.77
2.75
2.73
17
4.00
2.20
2.38
5.27
1.83
4.22
2.23
2.11
f1 (ppm)


147.00
144.11
140.87
135.81
129.61
129.24
129.08
128.94
127.50
126.52
126.19
58.11
57.99
53.01
31.56
17
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.10
8.08
7.76
7.57
7.39
7.19
7.18
7.13
7.12
7.11
7.10
3.67
3.06
3.04
3.03
2.75
2.73
2.72
SZ9TA1
2.31
1.69
1.96
4.84
2.93
3.30
0.99
3.64
2.00
1.91
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


165.13
147.07
145.64
137.64
137.16
135.85
133.47
131.42
130.22
129.70
129.14
129.03
128.86
128.73
128.09
127.64
126.28
58.00
57.92
52.84
31.50
SZ9TA1
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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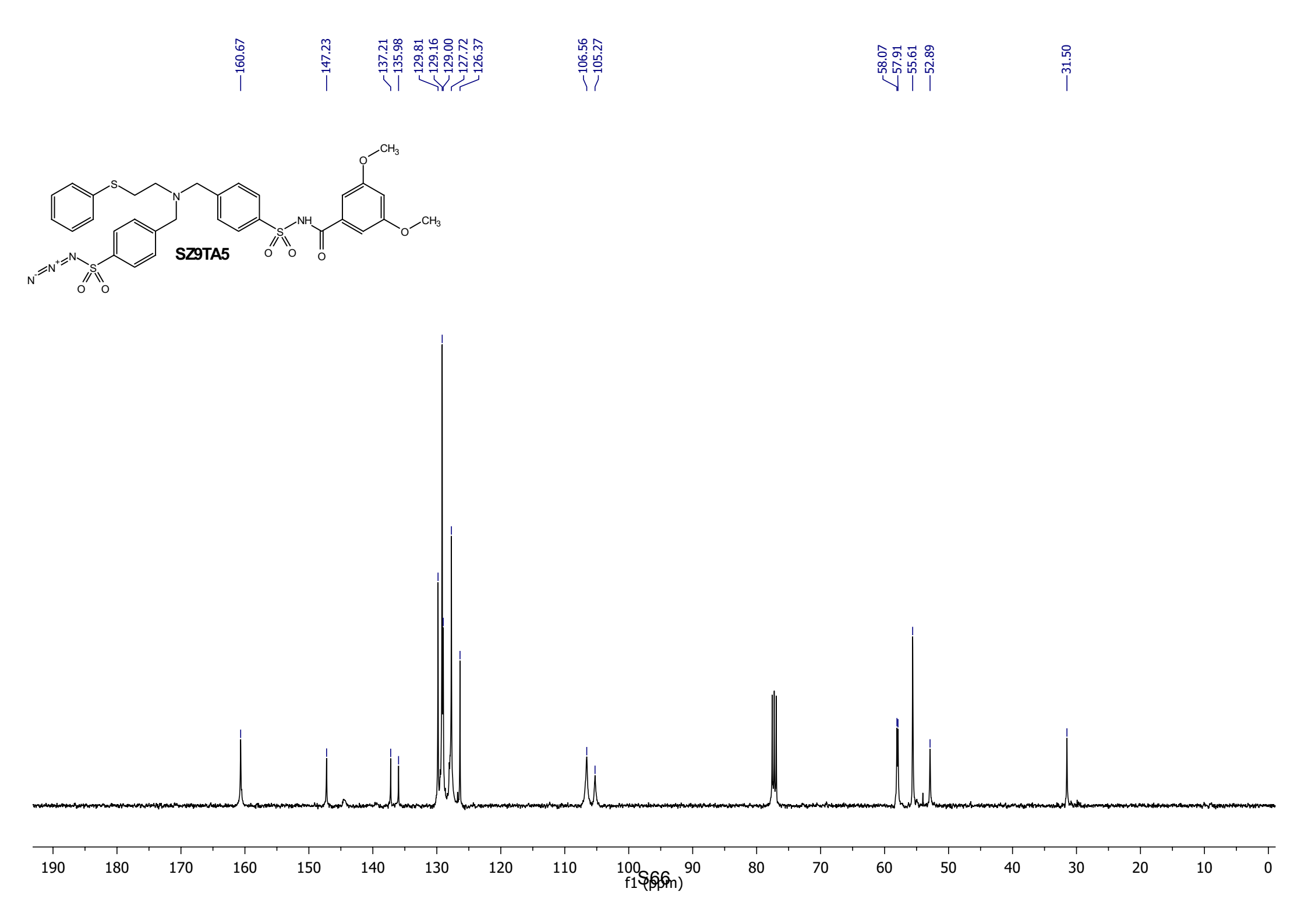
7.96
7.77
7.48
7.46
7.24
7.12
7.07
7.06
6.99
6.42
3.03
3.01
2.96
2.74
2.72
2.70
2.63
SZ9TA5
2.00
2.01
1.82
10.31
1.04
10.22
2.07
2.03
f1 (ppm)


160.67
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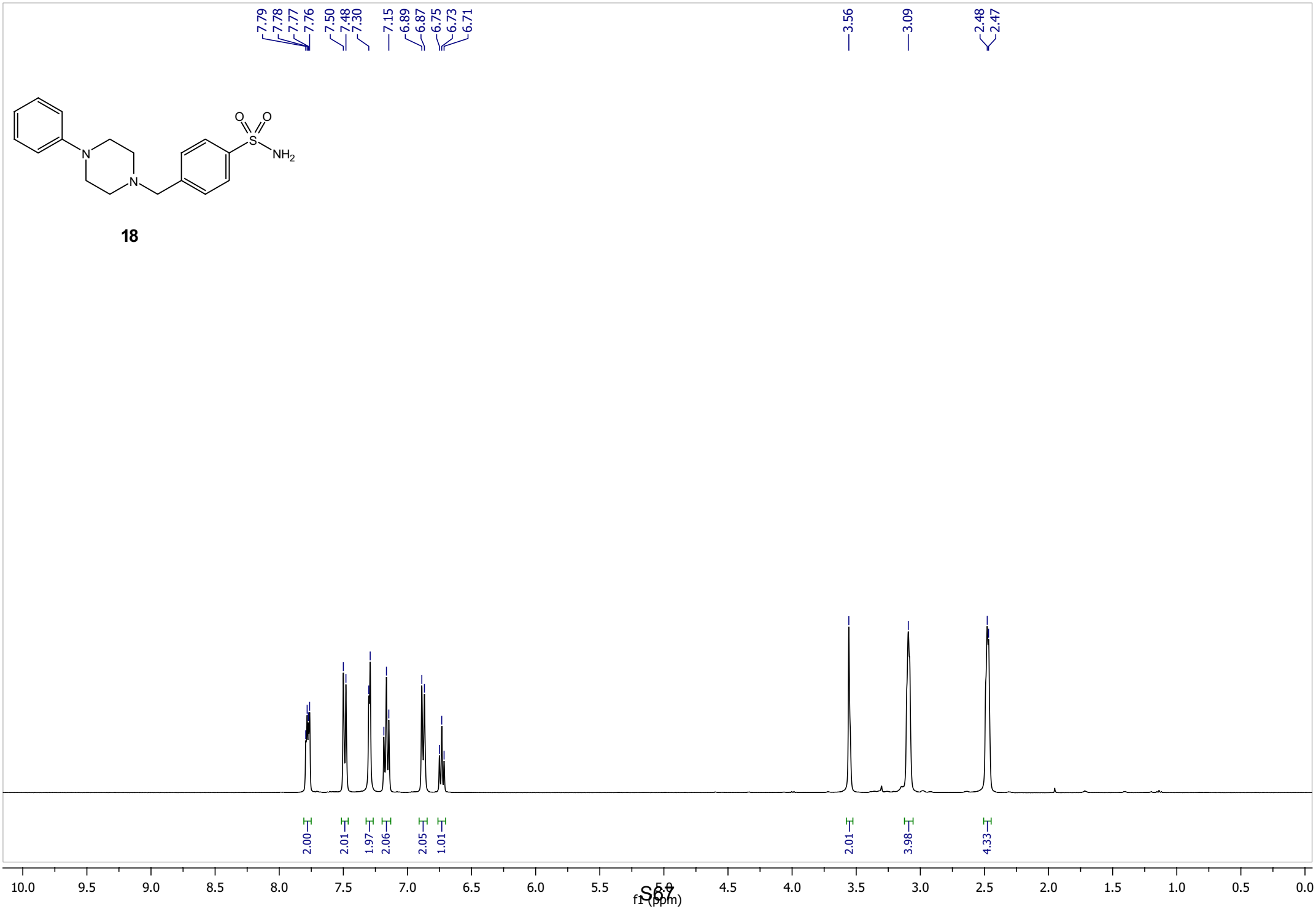
137.21
135.98
129.81
129.16
129.00
127.72
126.37
106.56
105.27
58.07
57.91
55.61
52.89
31.50
SZ9TA5
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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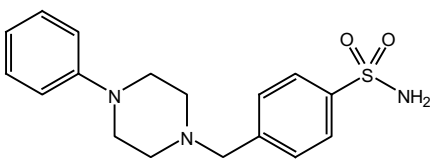
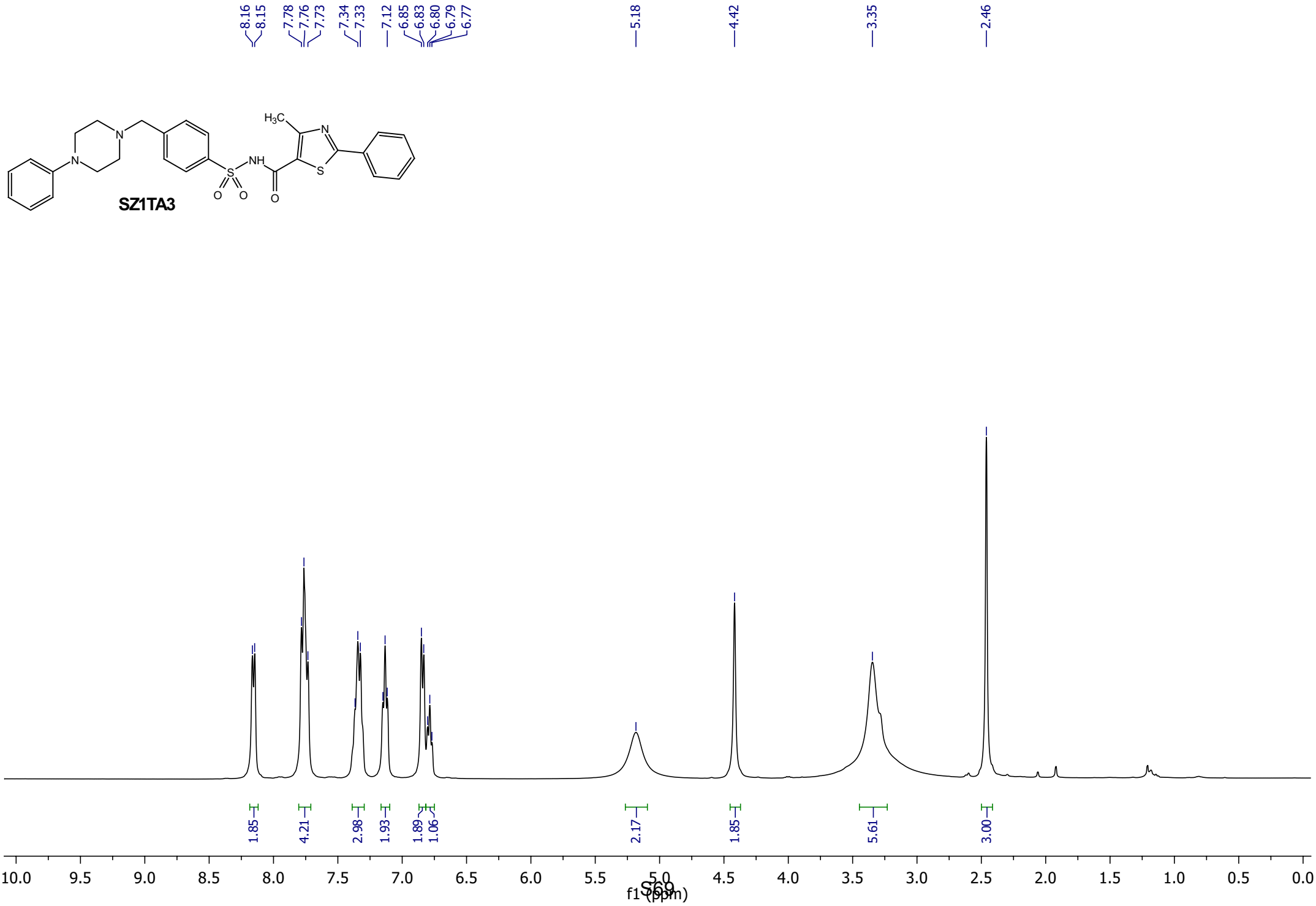
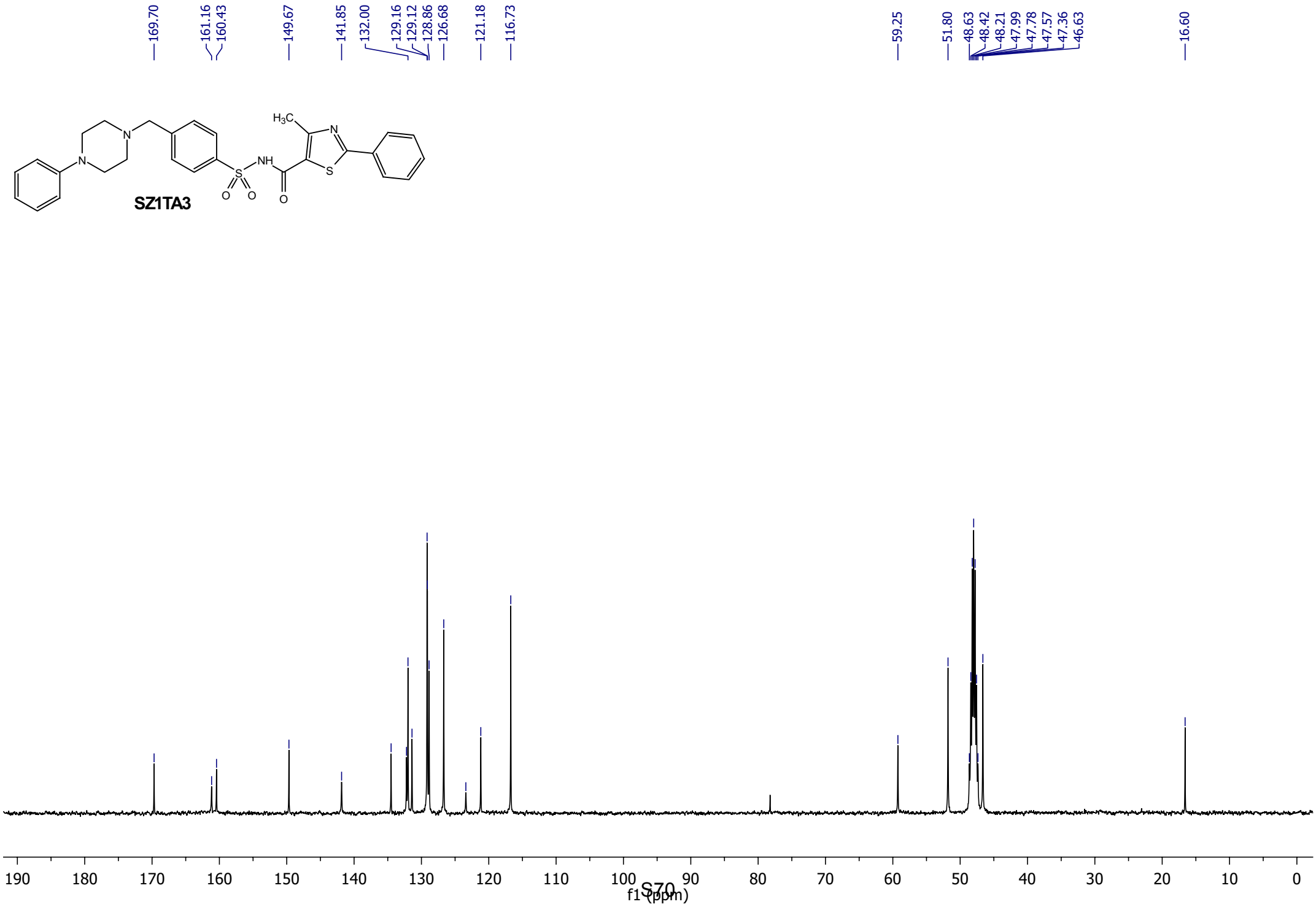
7.78
7.77
7.76
7.50
7.48
7.30
7.15
6.89
6.87
6.75
6.73
6.71
3.56
3.09
2.48
2.47
O
O
S
NH2
N
N
18
2.00
2.01
1.97
2.06
2.05
1.01
2.01
3.98
4.33
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


O
O
S
NH2
N
N

18

151.41
143.24
142.77
129.59
129.32
126.07
119.23
115.81
61.76
52.98
48.64
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.16
8.15
7.78
7.76
7.73
7.34
7.33
7.12
6.85
6.83
6.80
6.79
6.77
5.18
4.42
3.35
2.46
H3C
N
N
NH
S
S
O
O
O
SZ1TA3
1.85
4.21
2.98
1.93
1.89
1.06
2.17
1.85
5.61
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


169.70
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132.00
129.16
129.12
128.86
126.68
121.18
116.73
59.25
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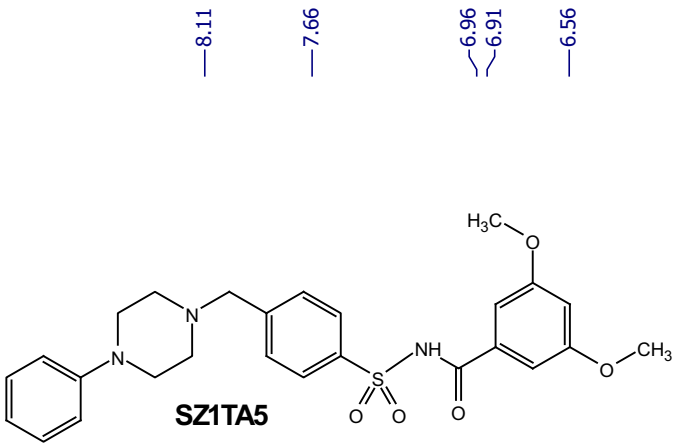
48.42
48.21
47.99
47.78
47.57
47.36
46.63
16.60
SZ1TA3
f1 (ppm)


SZ1TA5

8.11
7.66
6.96
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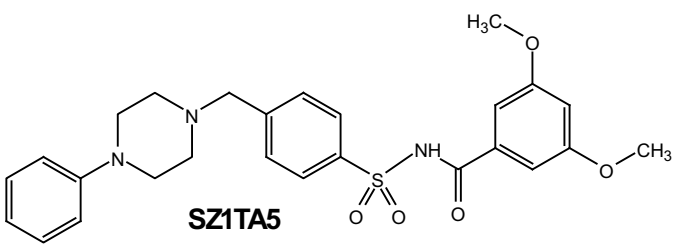
6.56
4.33
3.70
3.46
2.16
2.17
6.18
1.59
2.01
6.11
8.07
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


SZ1TA5

165.35
161.11
148.73
140.80
134.11
133.02
132.01
129.77
129.57
122.78
117.63
106.30
106.07
77.55
77.23
76.91
60.10
55.78
51.89
47.48
190
180
170
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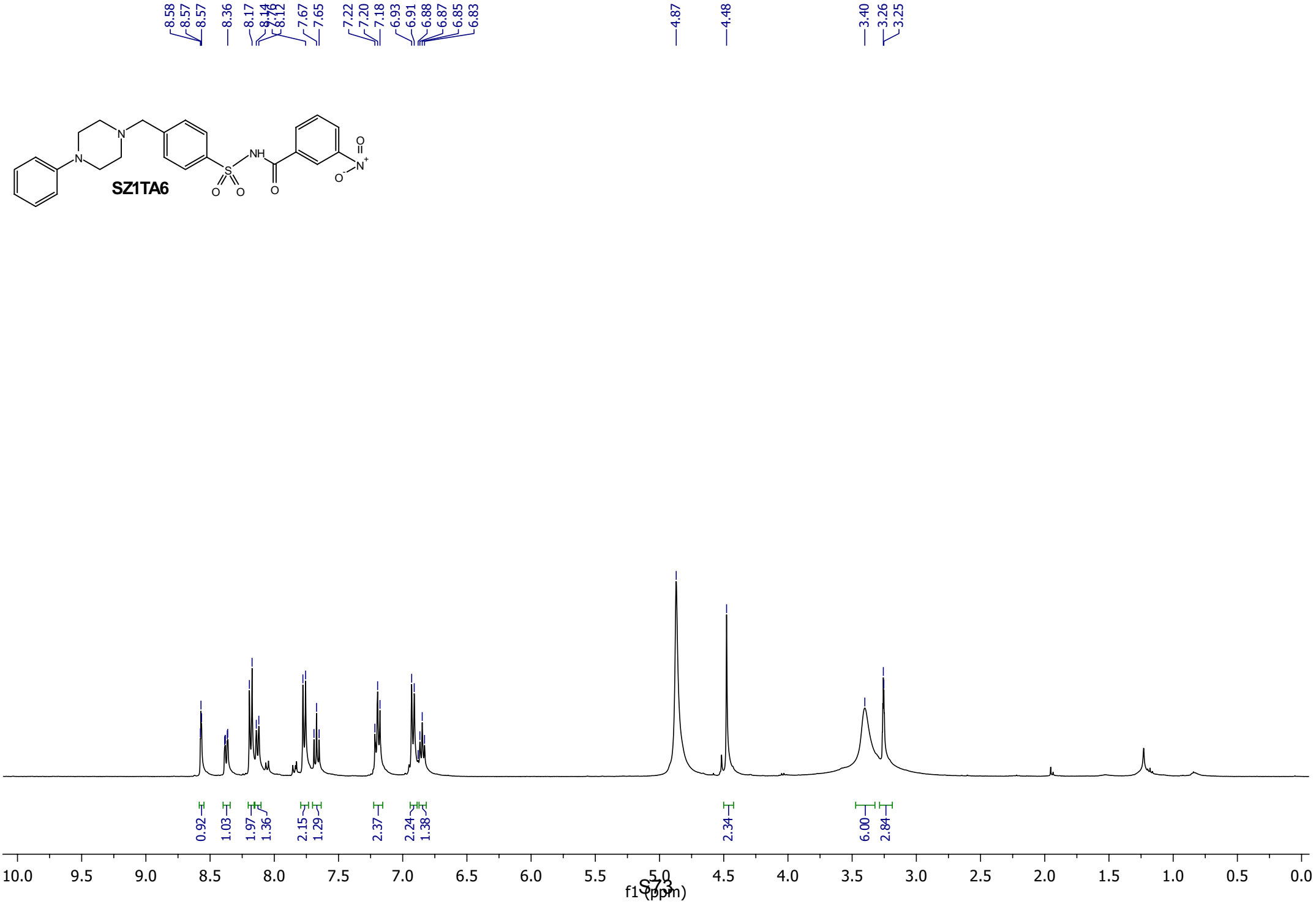
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.58
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8.57
8.36
8.17
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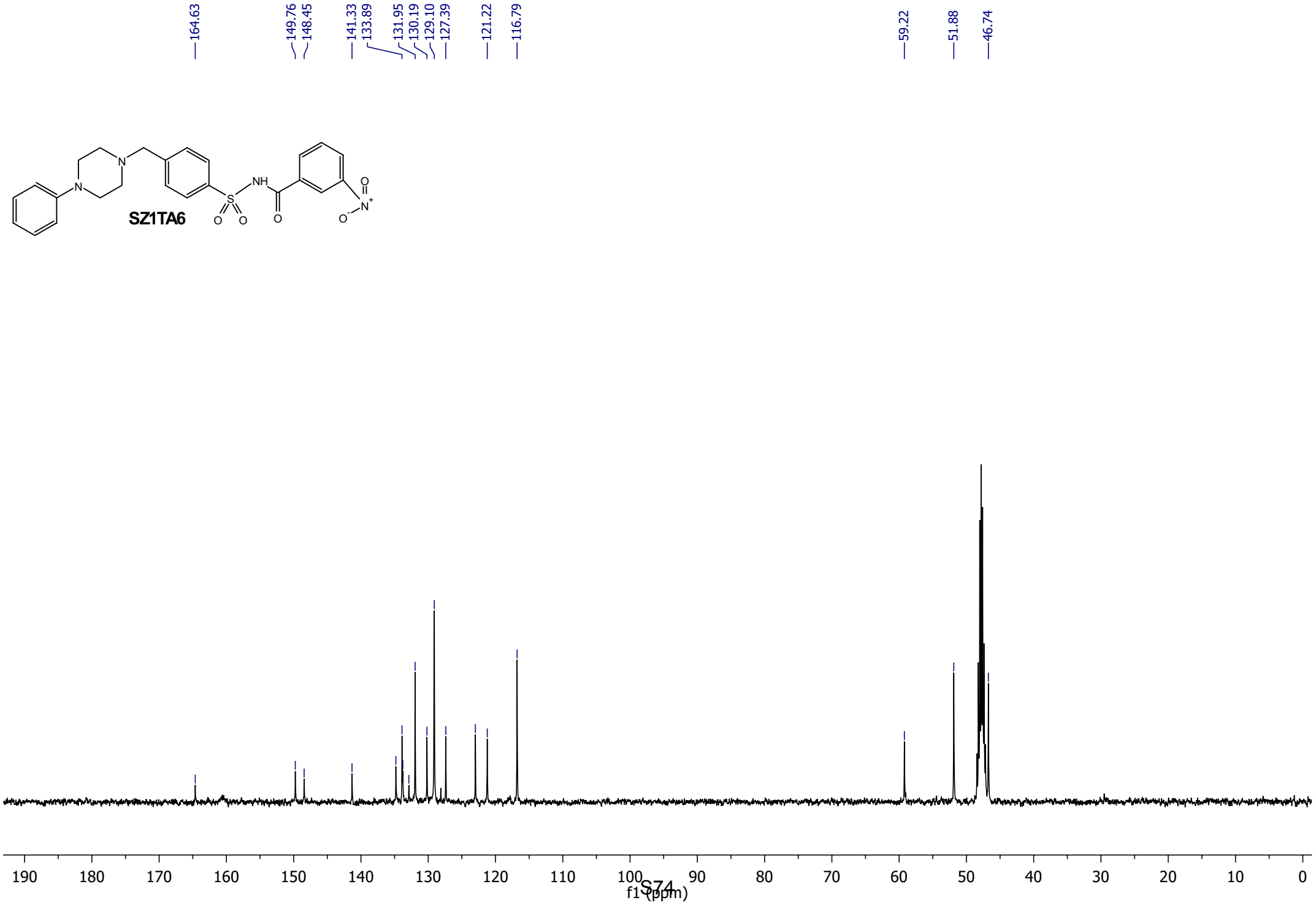
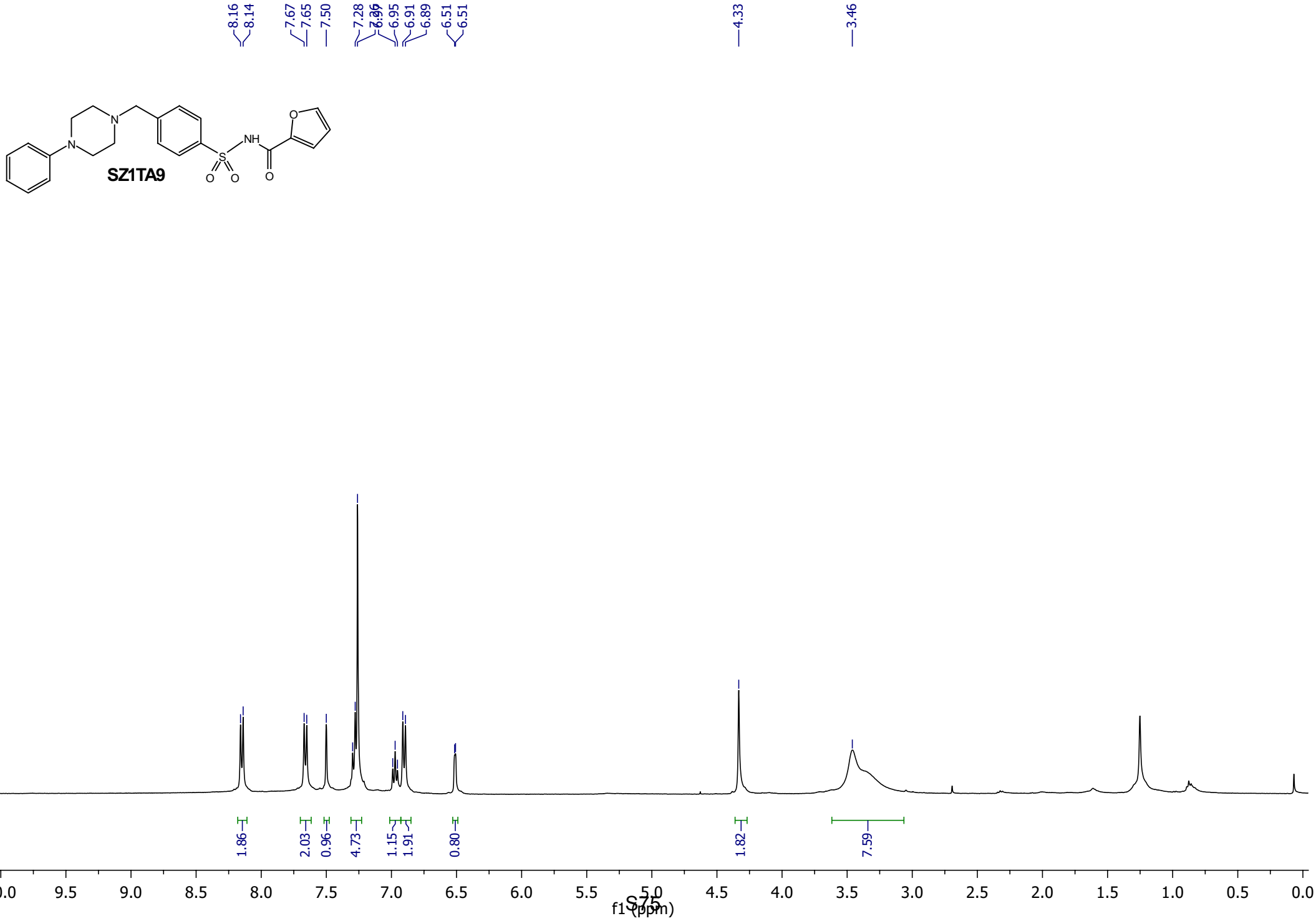
8.12
7.67
7.65
7.22
7.20
7.18
6.93
6.91
6.88
6.87
6.85
6.83
4.87
4.48
3.40
3.26
3.25
SZ1TA6
0.92
1.03
1.97
1.36
2.15
1.29
2.37
2.24
1.38
2.34
6.00
2.84
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


164.63
149.76
148.45
141.33
133.89
131.95
130.19
129.10
127.39
121.22
116.79
59.22
51.88
46.74
SZ1TA6
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.16
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7.28
6.95
6.91
6.89
6.51
6.51
4.33
3.46
SZ1TA9
1.86
2.03
0.96
4.73
1.15
1.91
0.80
1.82
7.59
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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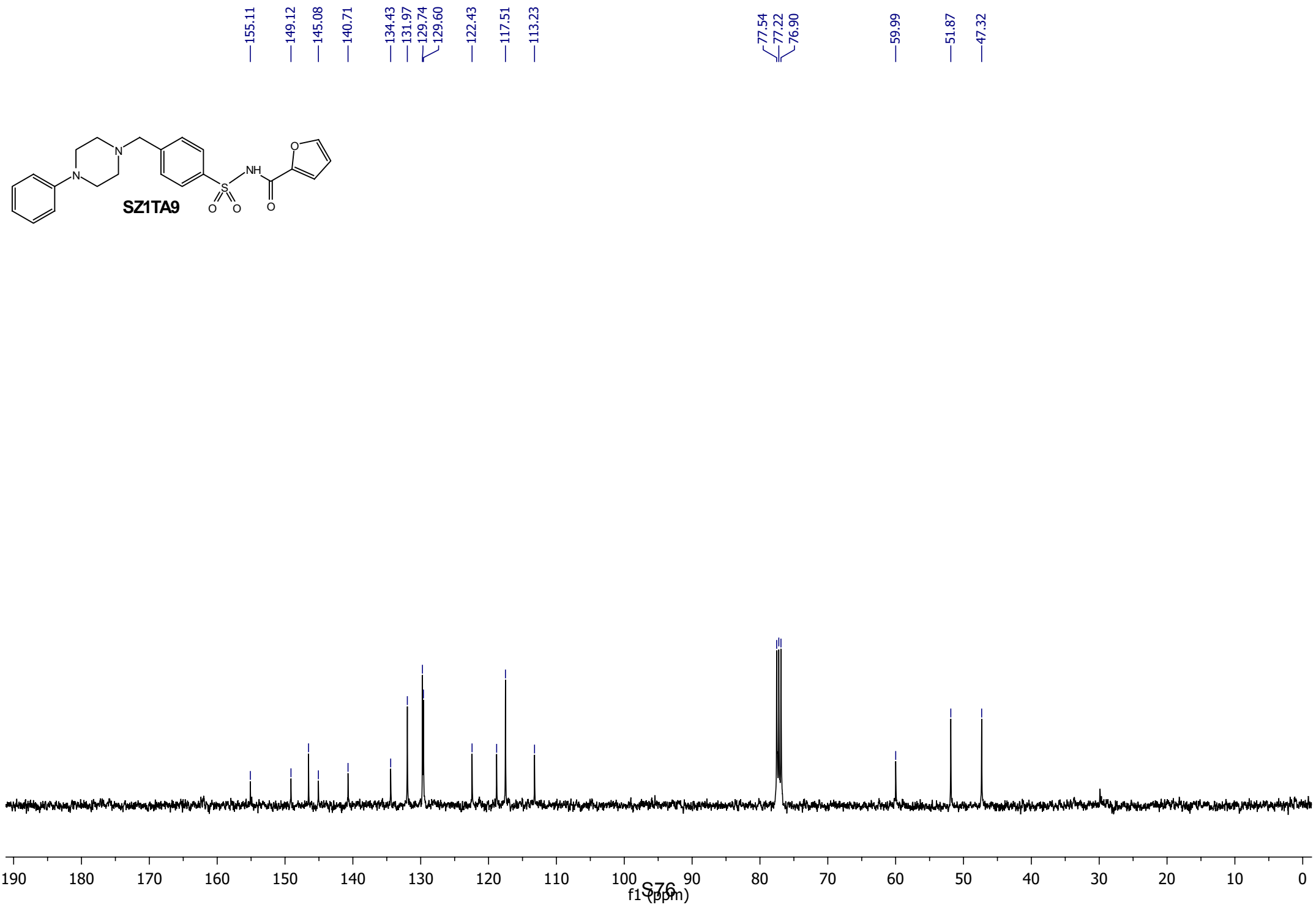
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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149.12
145.08
140.71
134.43
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129.74
129.60
122.43
117.51
113.23
77.54
77.22
76.90
59.99
51.87
47.32
SZ1TA9
190
180
170
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150
140
130
120
110
100
90
80
70
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50
40
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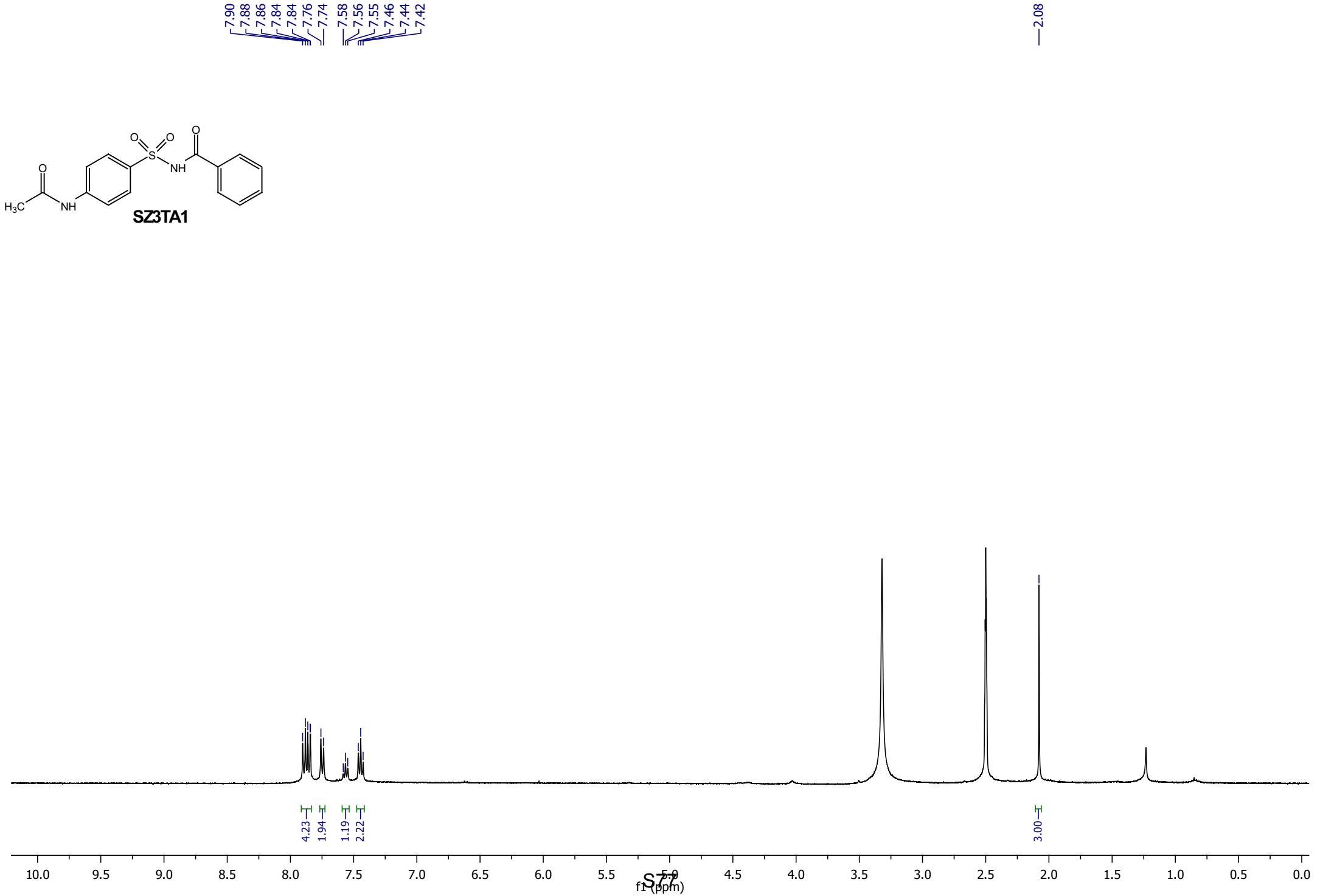
20
10
0
f1 (ppm)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7.84
7.84
7.76
7.74
7.58
7.56
7.55
7.46
7.44
7.42
2.08
O
O
S
O
NH
O
O
NH
H3C
SZ3TA1
4.23
1.94
1.19
2.22
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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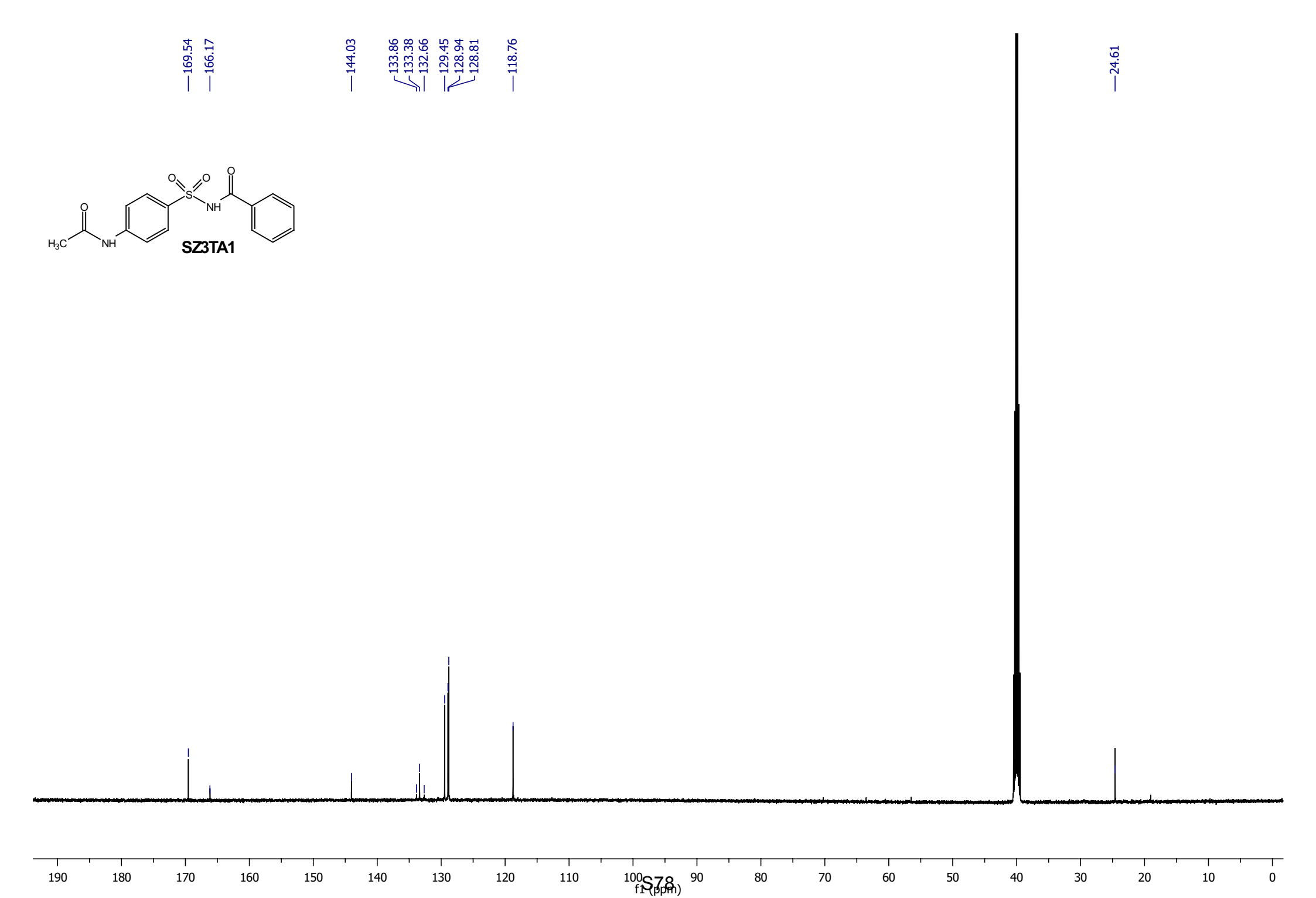
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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133.38
132.66
129.45
128.94
128.81
118.76
24.61
SZ3TA1
190
180
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130
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110
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90
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70
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50
40
30
20
10
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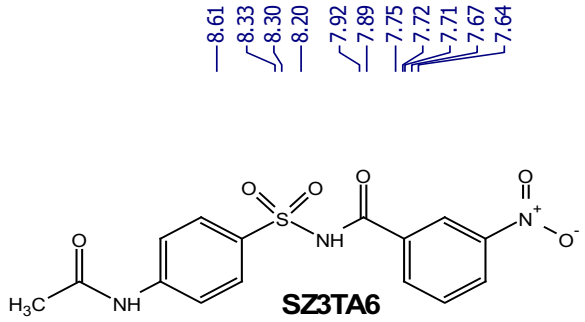
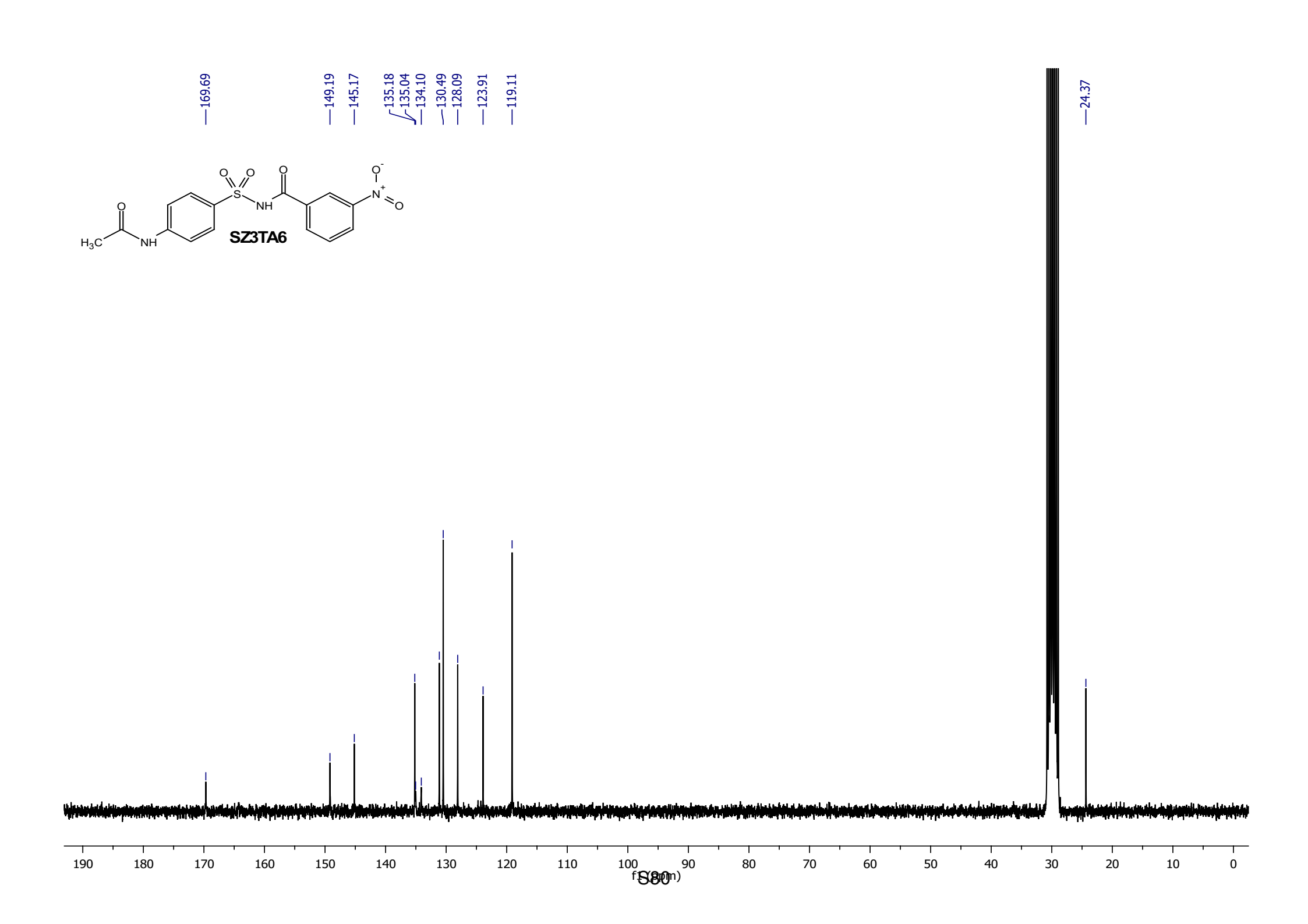
f1 (ppm)


SZ3TA6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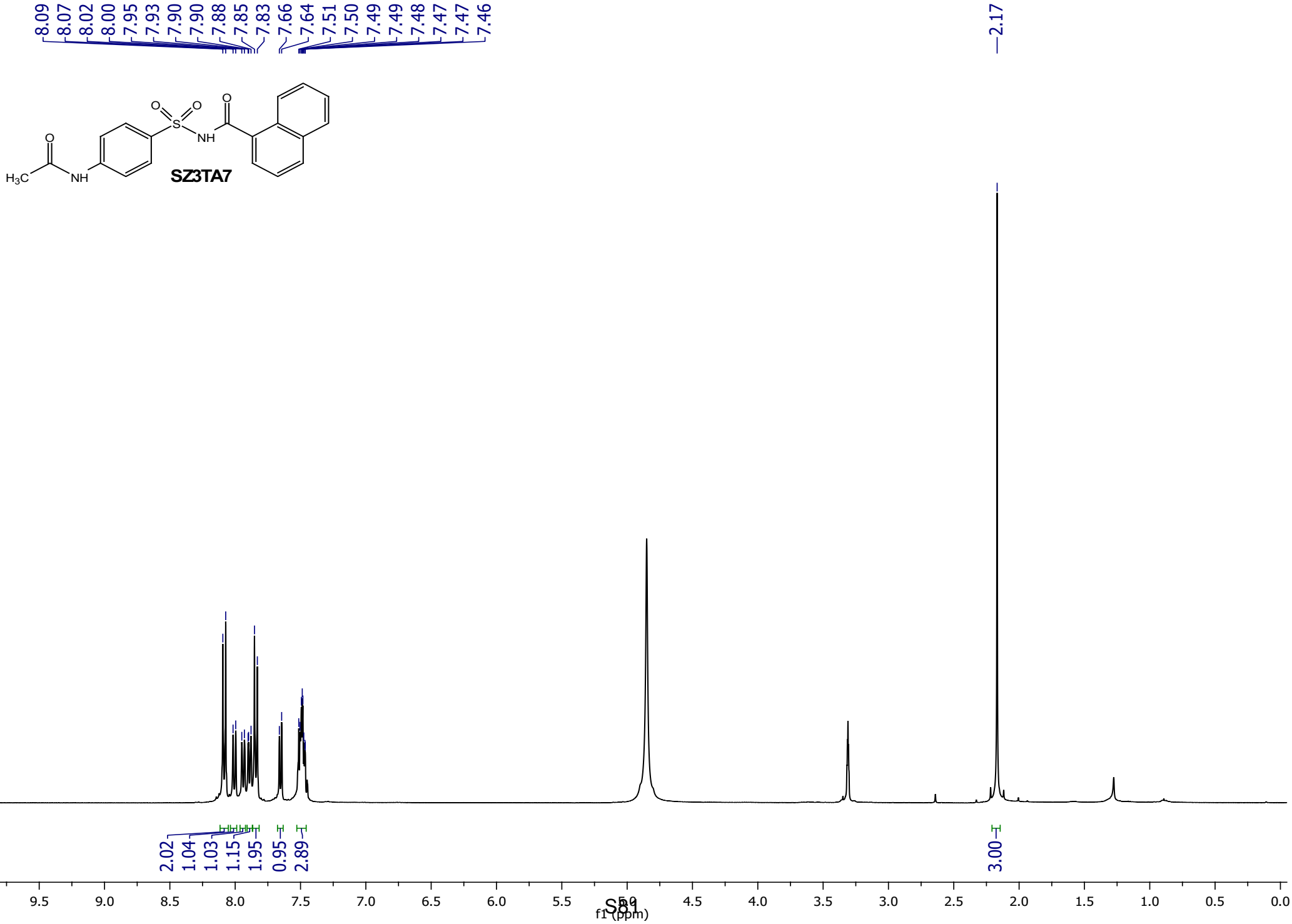
145.17
135.18
135.04
134.10
130.49
128.09
123.91
119.11
24.37
SZ3TA6
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.07
8.02
8.00
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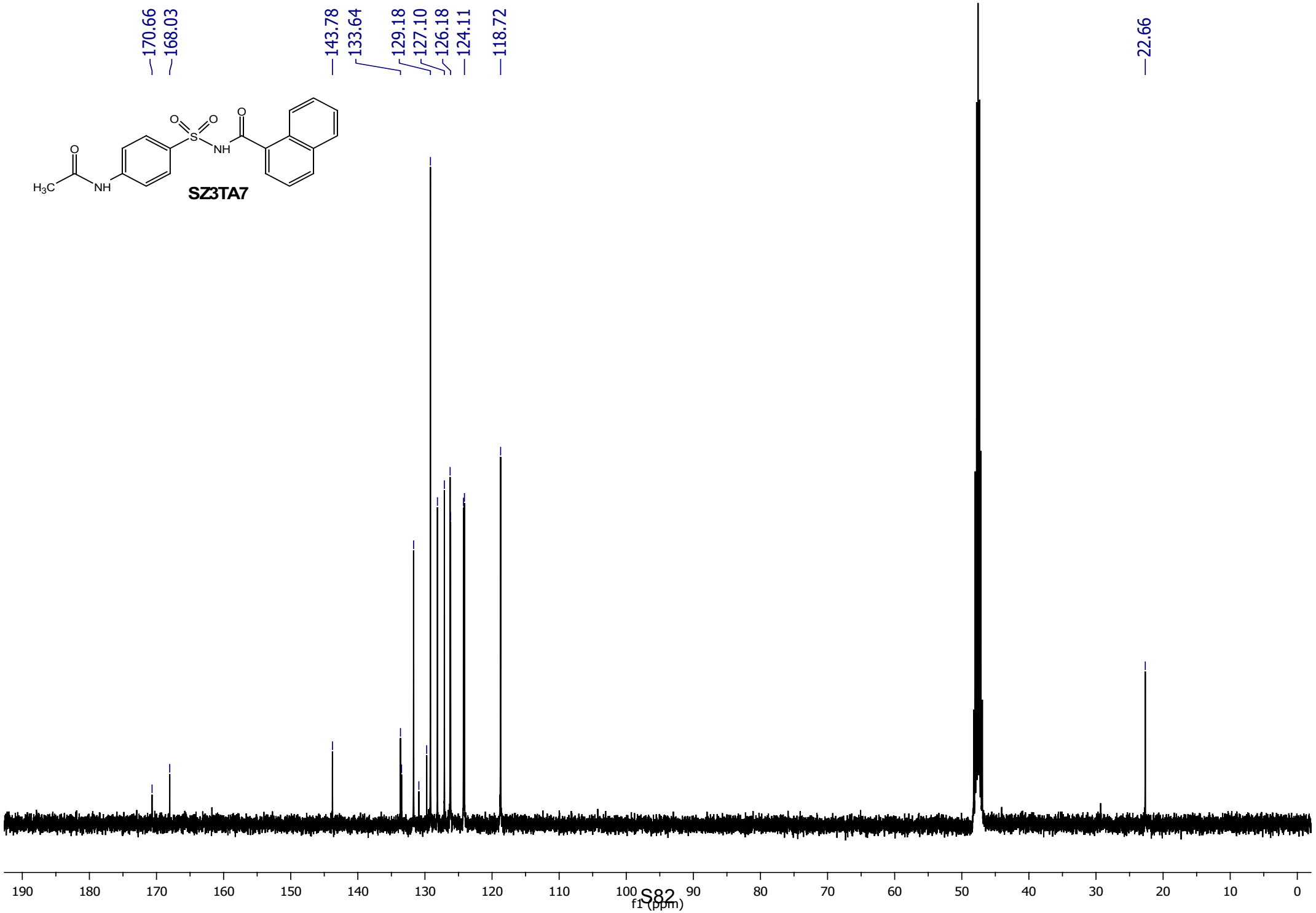
7.93
7.90
7.90
7.88
7.85
7.83
7.66
7.64
7.51
7.50
7.49
7.49
7.48
7.47
7.47
7.46
2.17
SZ3TA7
2.02
1.04
1.03
1.15
1.95
0.95
2.89
3.00
f1 (ppm)


170.66
168.03
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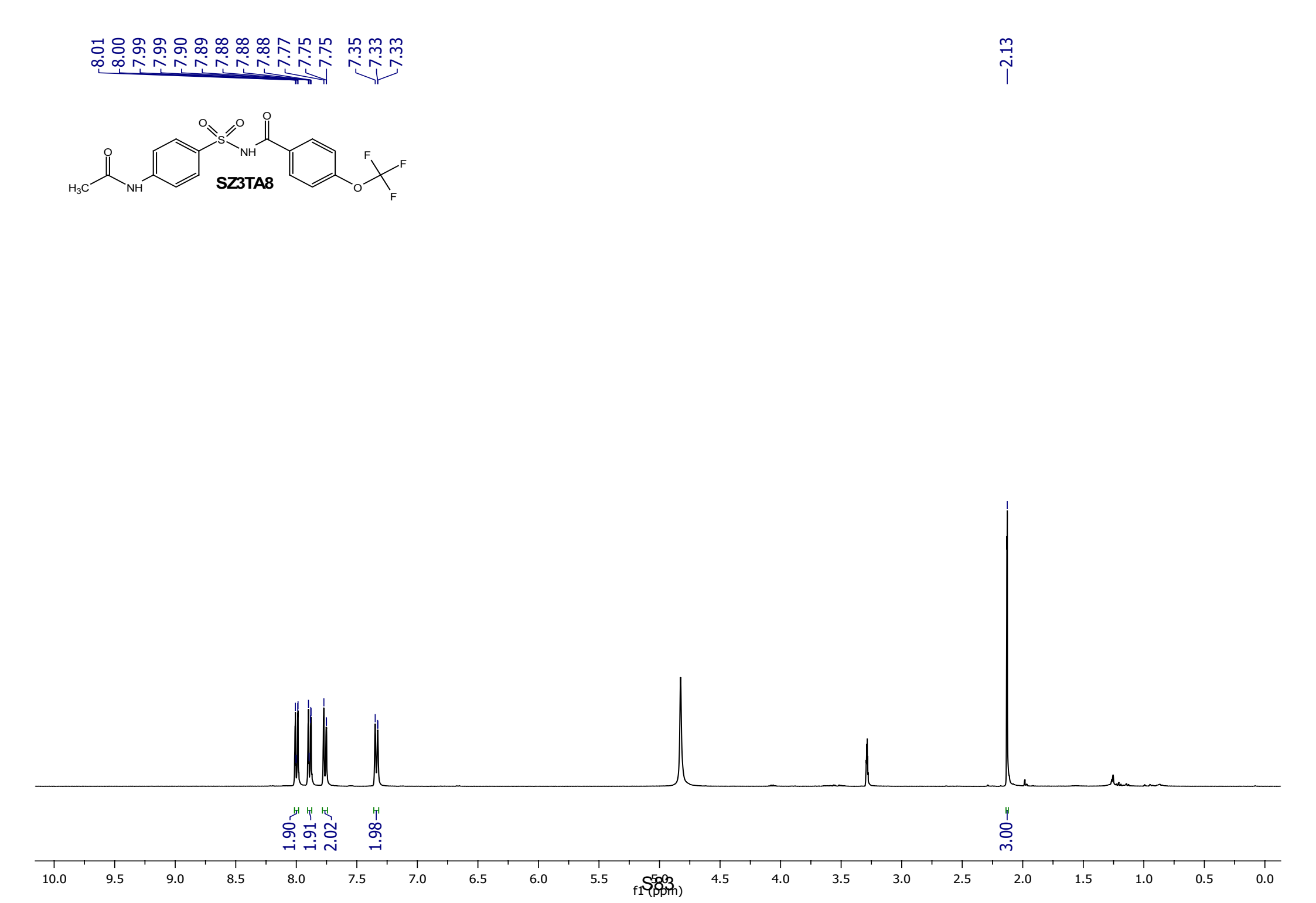
133.64
129.18
127.10
126.18
124.11
118.72
22.66
SZ3TA7
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.99
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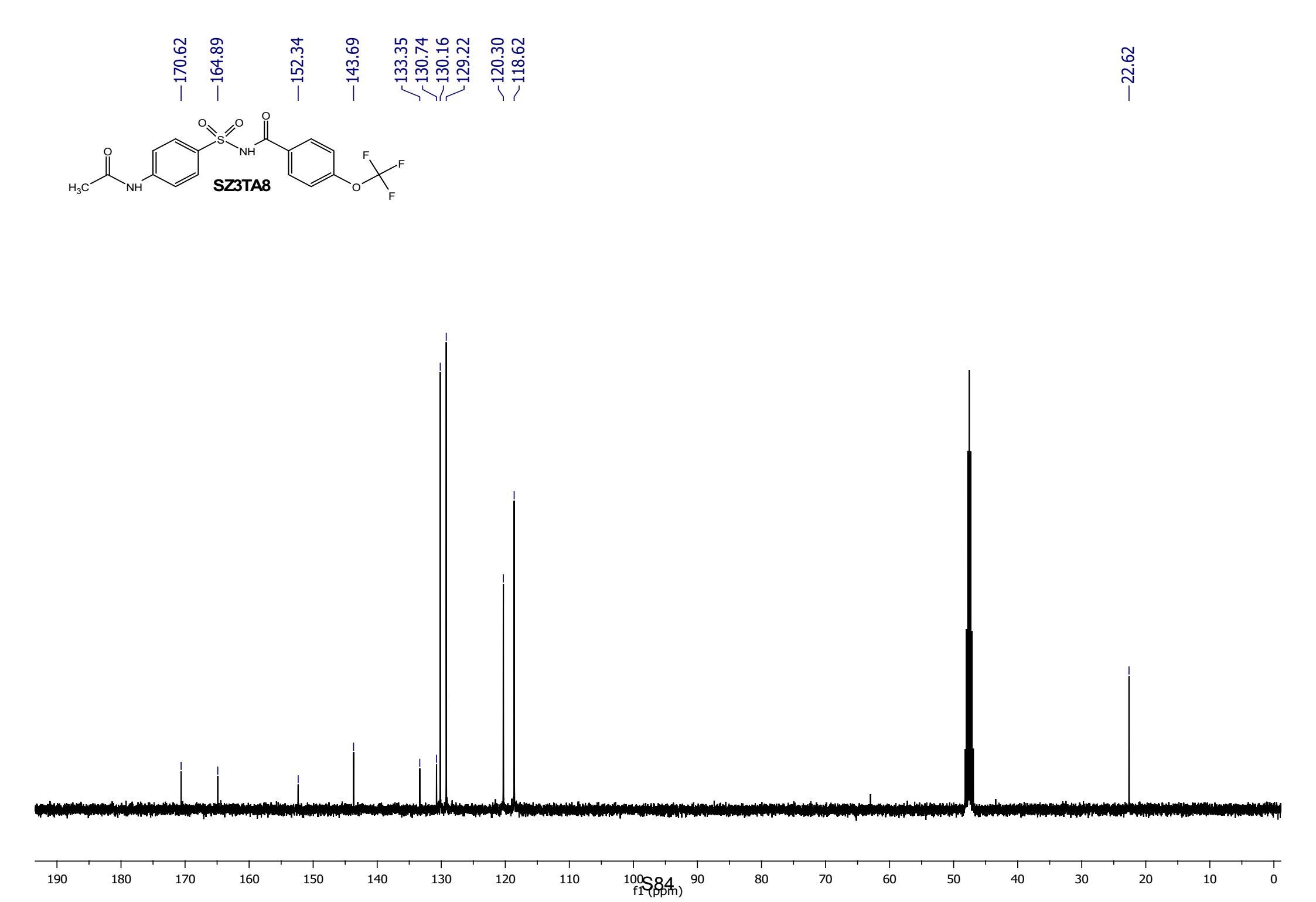
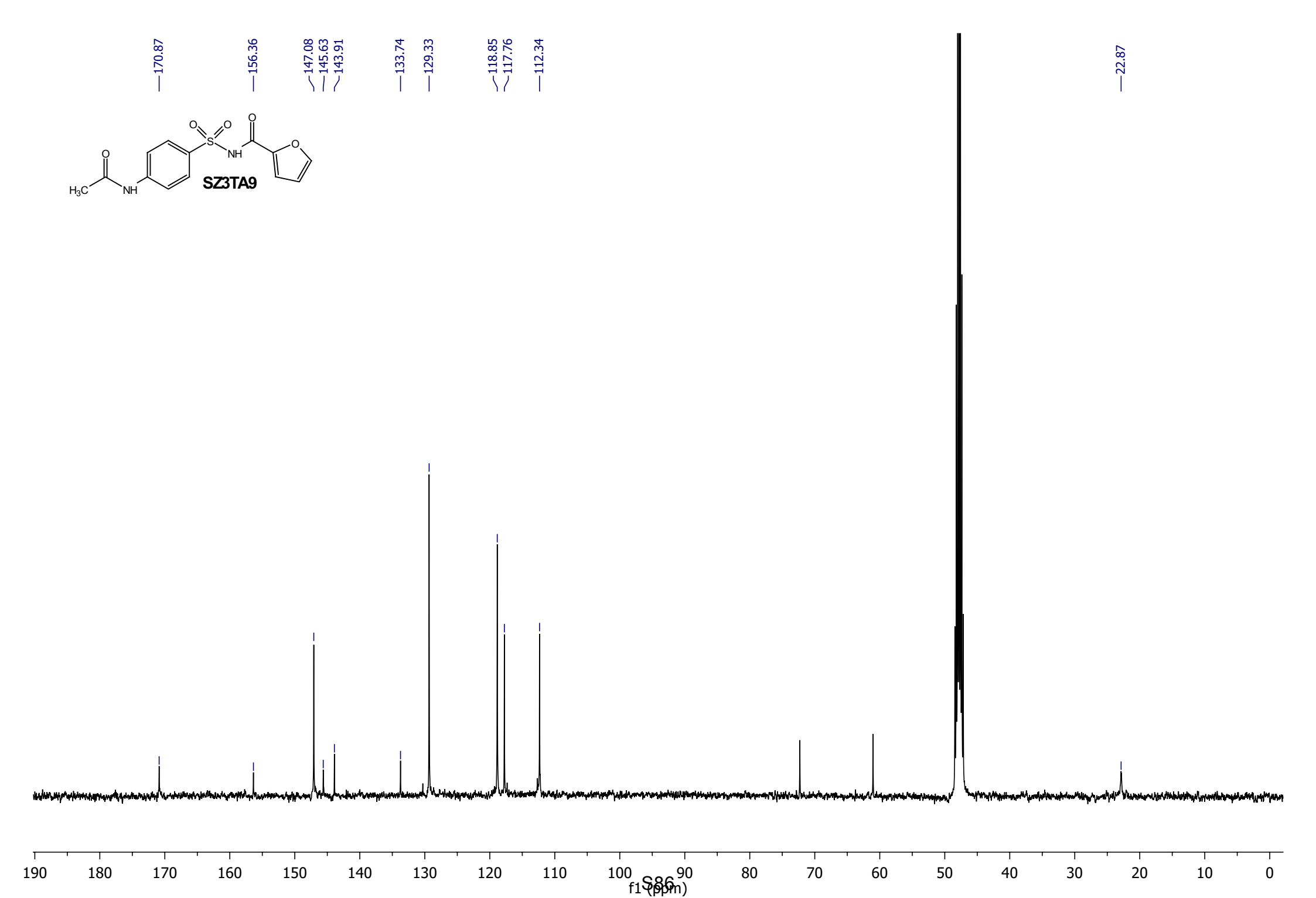
7.89
7.88
7.88
7.88
7.77
7.75
7.75
7.35
7.33
7.33
2.13
SZ3TA8
1.90
1.91
2.02
1.98
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


170.62
164.89
152.34
143.69
133.35
130.74
130.16
129.22
120.30
118.62
22.62
SZ3TA8
f1 (ppm)


O
O
S
NH
O
O
H3C
NH
O

SZ3TA9

7.99
7.97
7.77
7.74
7.70
7.25
7.25
6.58
6.58
6.58
6.57
2.13
1.75
1.71
0.86
0.80
0.86
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


170.87
156.36
147.08
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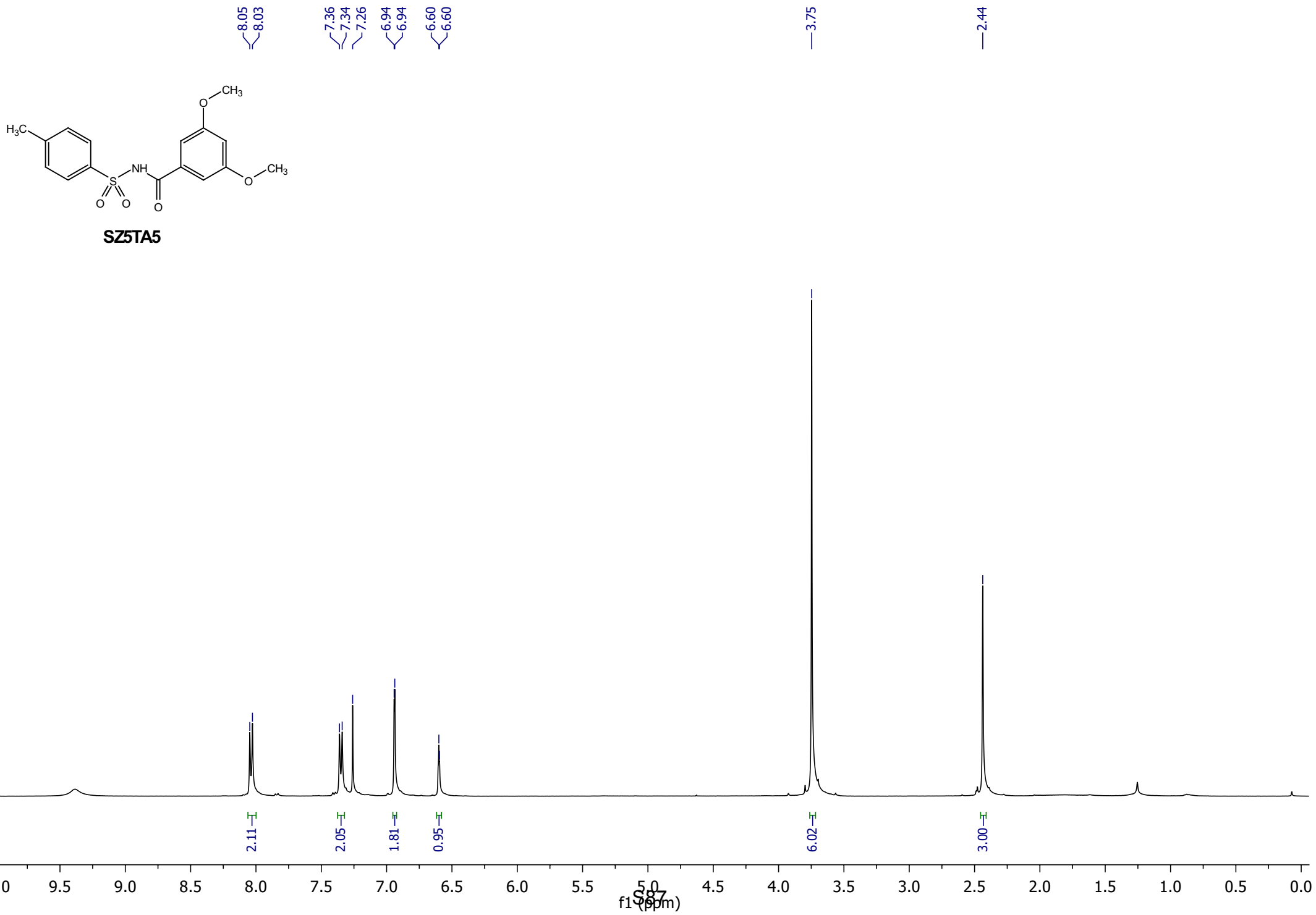
143.91
133.74
129.33
118.85
117.76
112.34
22.87
SZ3TA9
f1 (ppm)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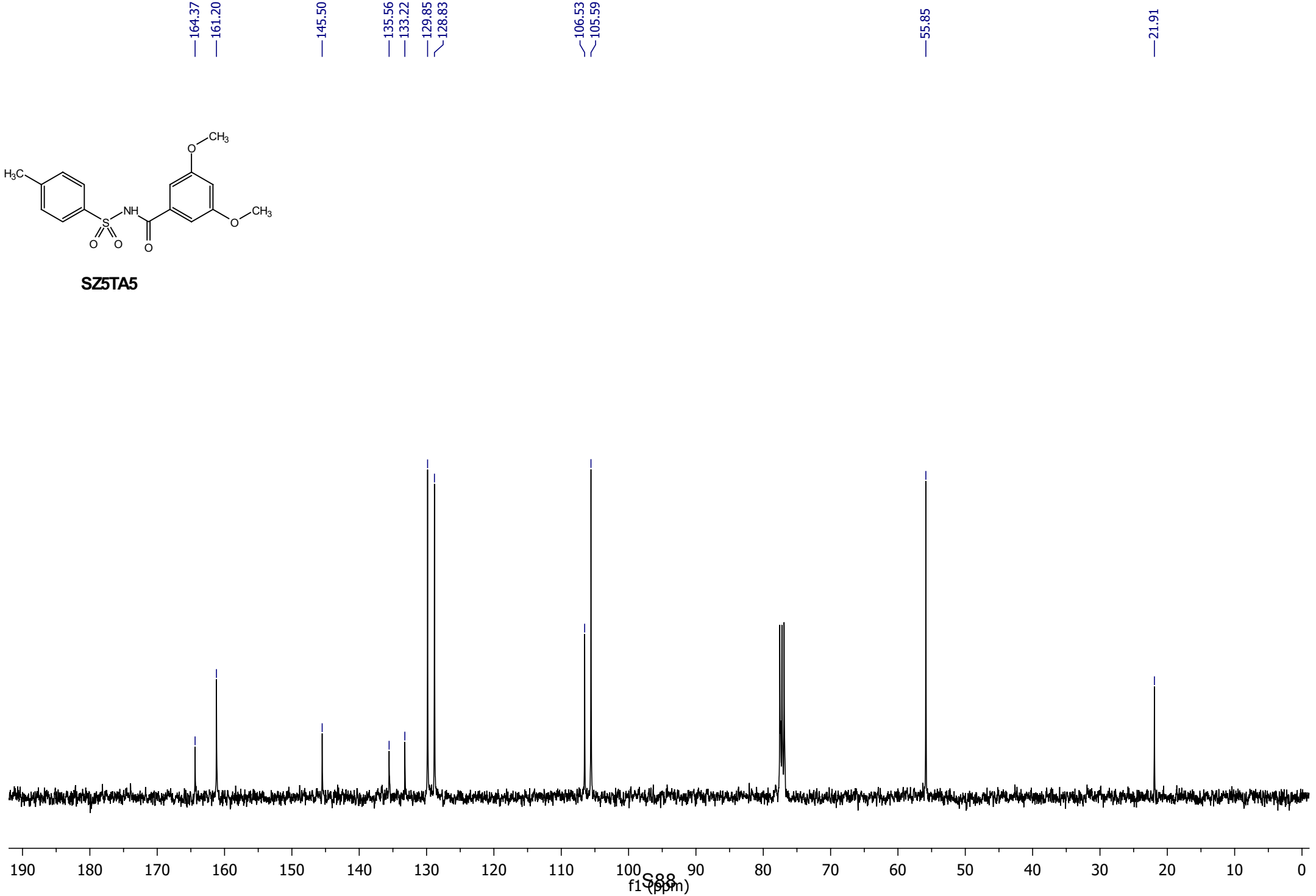
8.03
7.36
7.34
7.26
6.94
6.94
6.60
6.60
3.75
2.44
CH3
O
H3C
NH
S
O
O
O
CH3
O
SZ5TA5
2.11
2.05
1.81
0.95
6.02
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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145.50
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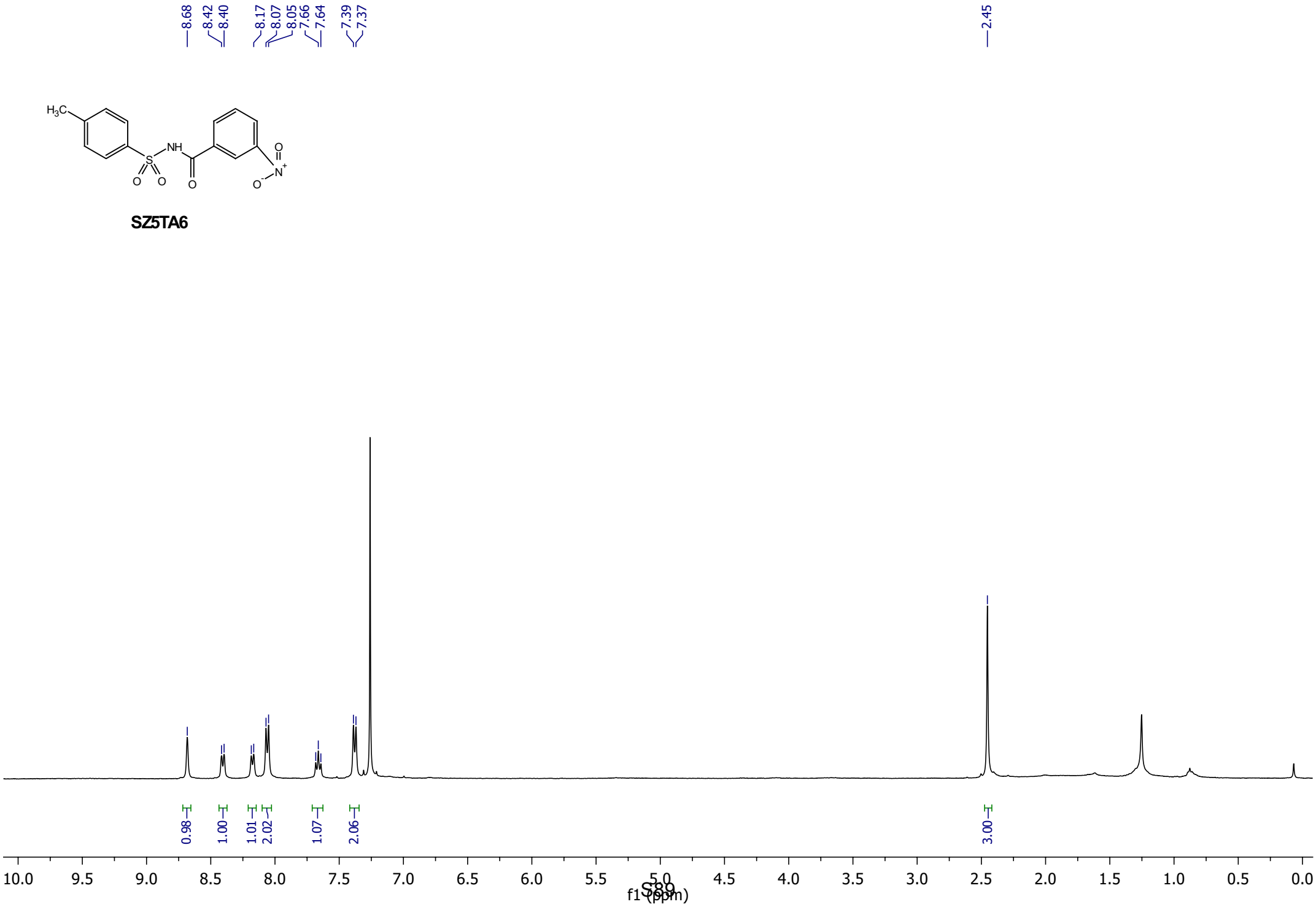
129.85
128.83
106.53
105.59
55.85
21.91
H3C
CH3
O
NH
S
O
O
O
O
CH3
SZ5TA5
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.42
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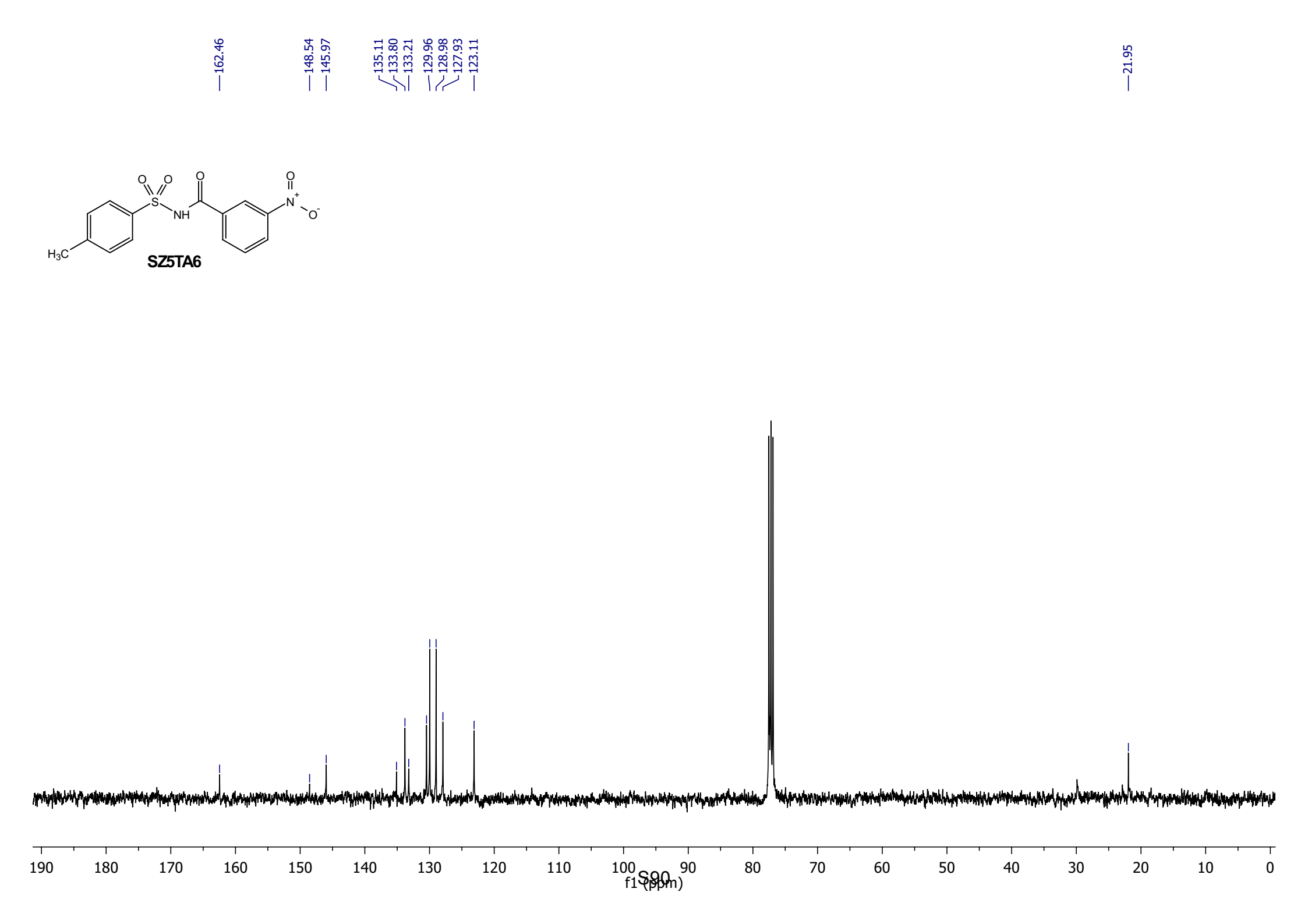
8.05
7.66
7.64
7.39
7.37
2.45
H3C
NH
S
O
O
O
O
N+
O-
SZ5TA6
0.98
1.00
1.01
2.02
1.07
2.06
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


162.46
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145.97
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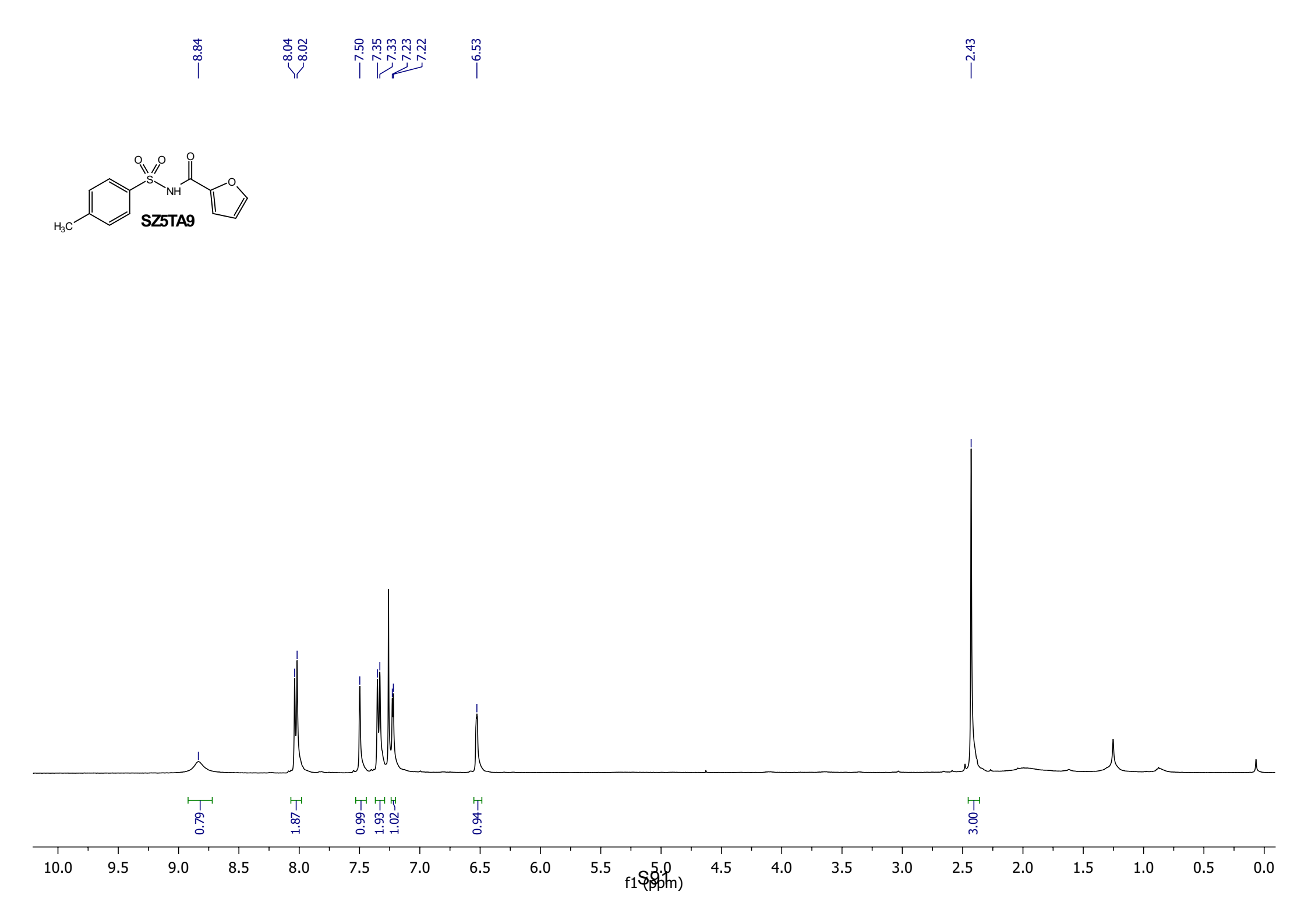
133.80
133.21
129.96
128.98
127.93
123.11
21.95
SZ5TA6
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.04
8.02
7.50
7.35
7.33
7.23
7.22
6.53
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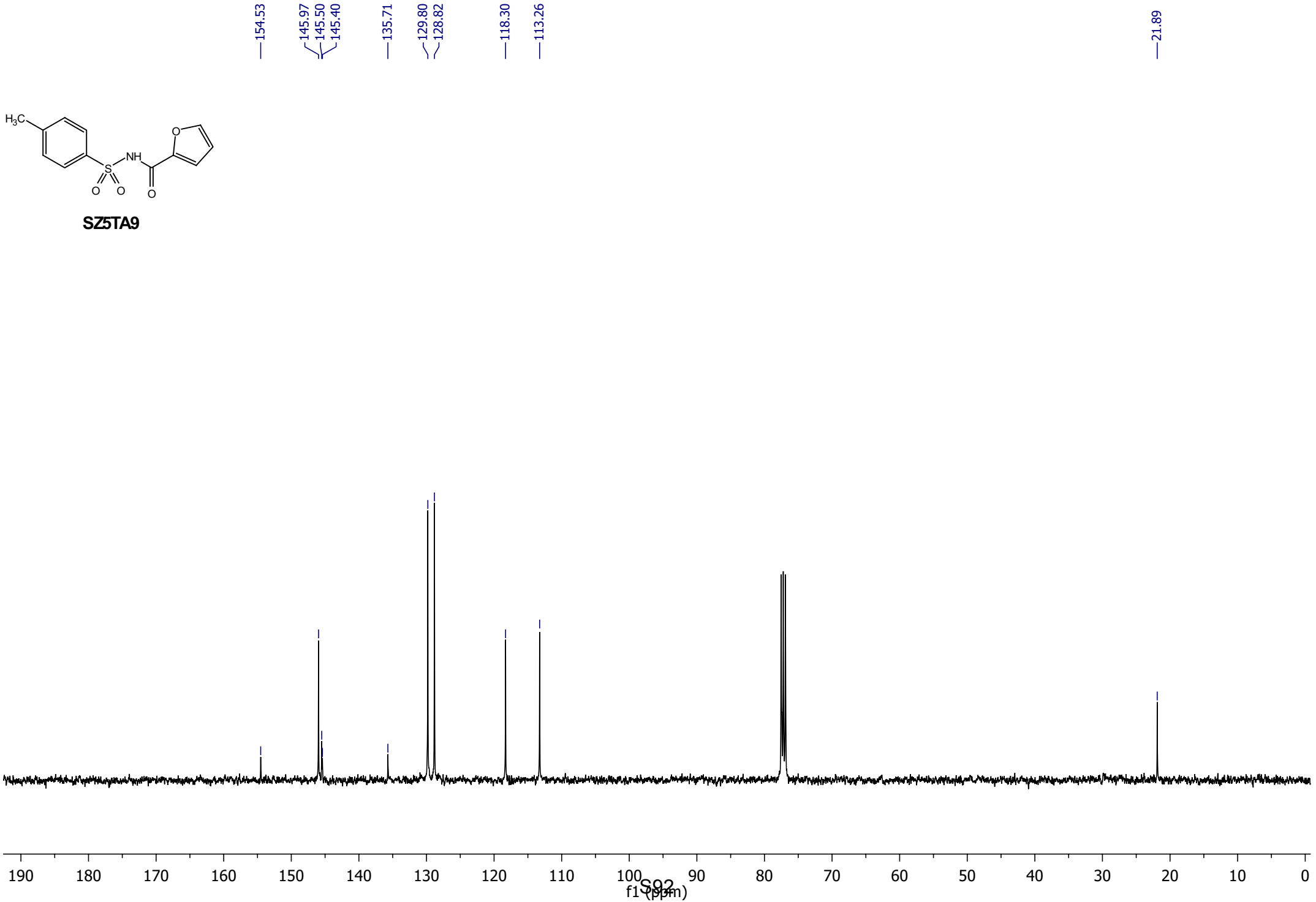
SZ5TA9
0.79
1.87
0.99
1.93
1.02
0.94
3.00
f1 (ppm)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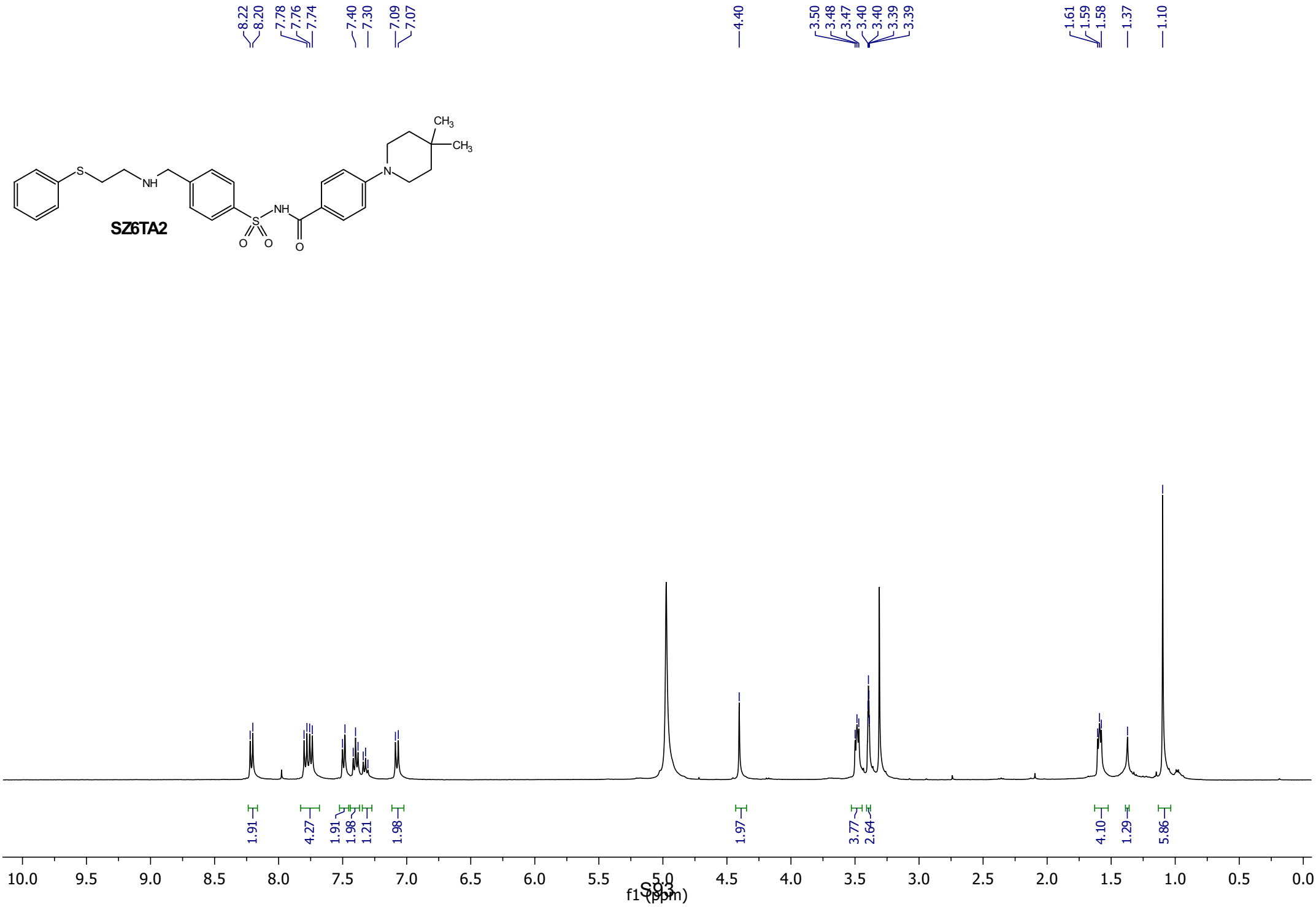
145.97
145.50
145.40
135.71
129.80
128.82
118.30
113.26
21.89
H3C
NH
O
S
O
O
O
SZ5TA9
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.74
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7.30
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7.07
4.40
3.50
3.48
3.47
3.40
3.40
3.39
3.39
1.61
1.59
1.58
1.37
1.10
CH3
CH3
S
NH
N
NH
S
O
O
O
SZ6TA2
1.91
4.27
1.91
1.98
1.21
1.98
1.97
3.77
2.64
4.10
1.29
5.86
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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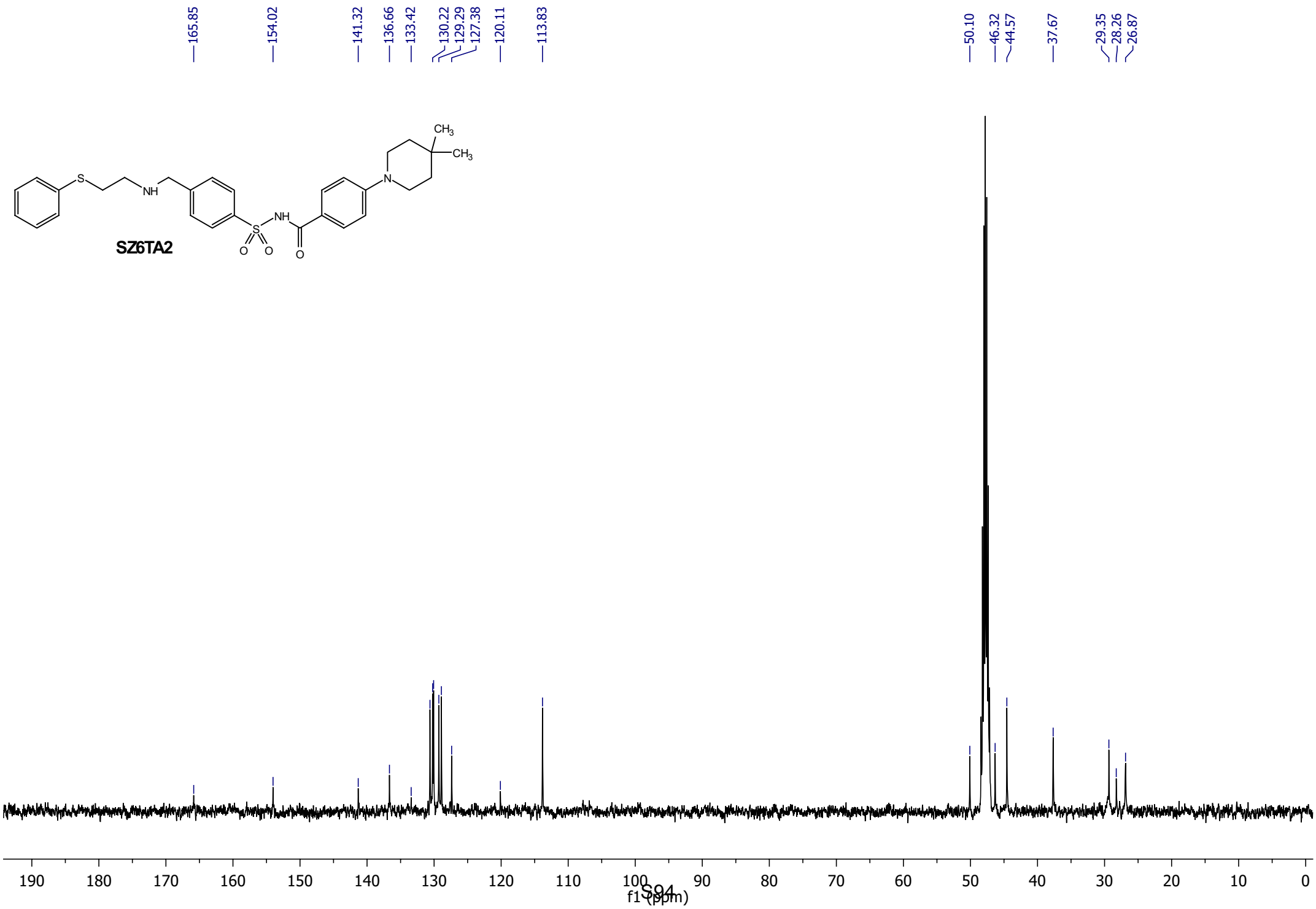
0.0
f1 (ppm)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154.02
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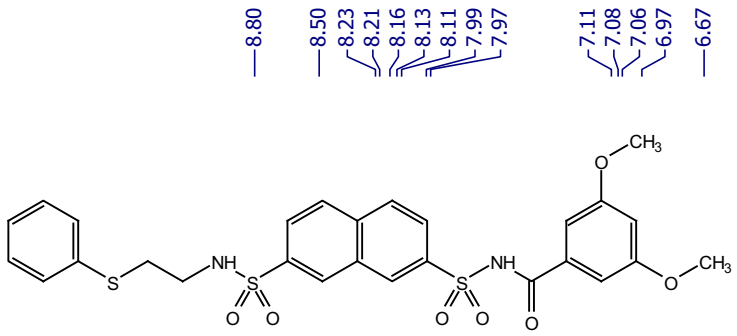
133.42
130.22
129.29
127.38
120.11
113.83
50.10
46.32
44.57
37.67
29.35
28.26
26.87
CH3
CH3
S
NH
NH
S
O
O
O
N
SZ6TA2
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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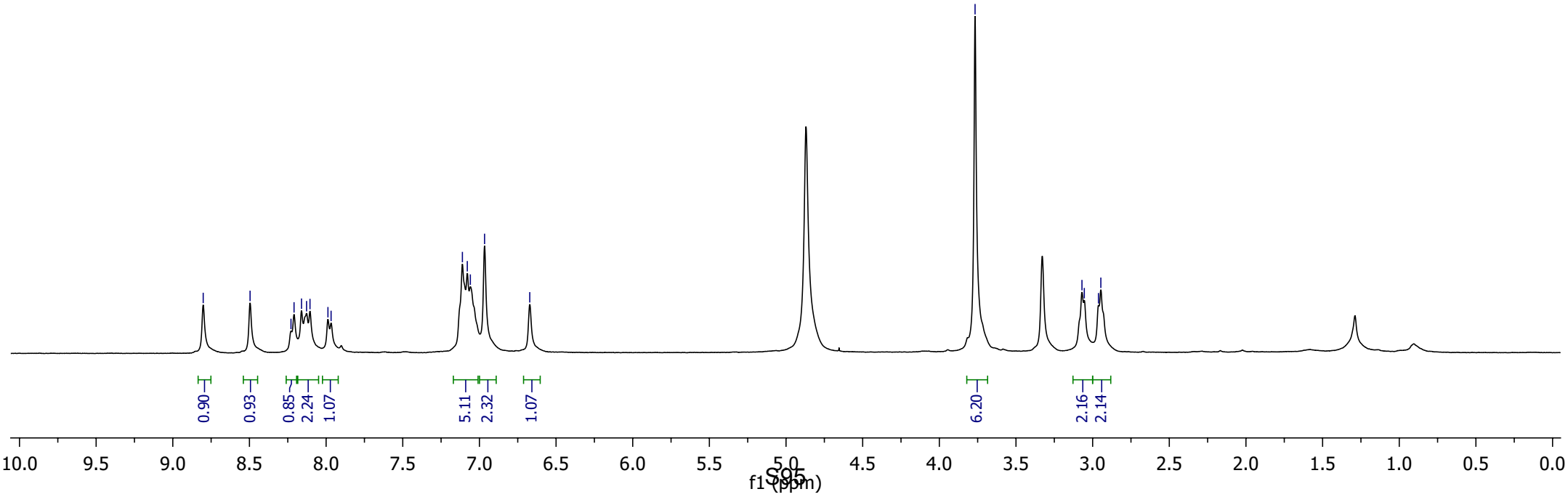
8.21
8.16
8.13
8.11
7.99
7.97
7.11
7.08
7.06
6.97
6.67
3.77
3.07
3.05
2.96
2.95
CH3
O
NH
S
O
O
NH
O
O
CH3
O
S
O
O

SZ7TA5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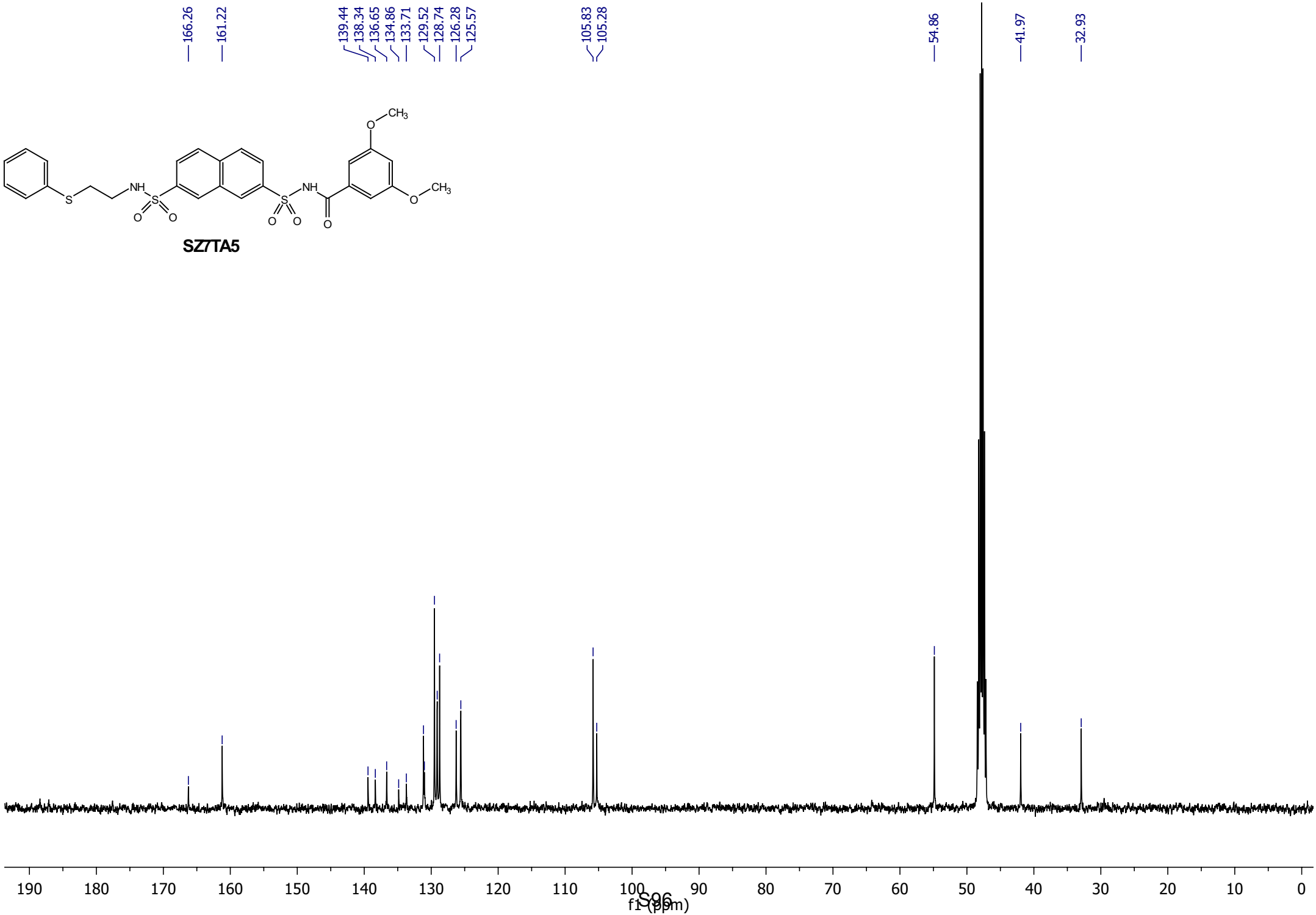
2.24
1.07
5.11
2.32
1.07
6.20
2.16
2.14
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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134.86
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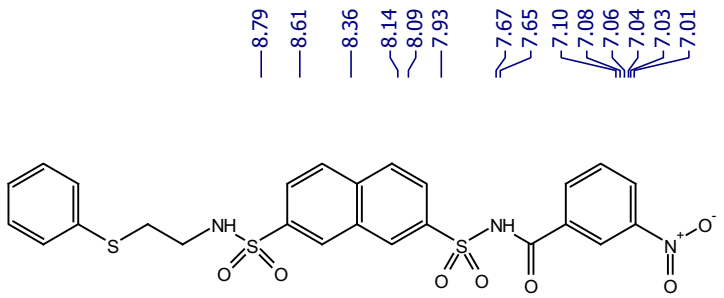
126.28
125.57
105.83
105.28
54.86
41.97
32.93
SZ7TA5
f1 (ppm)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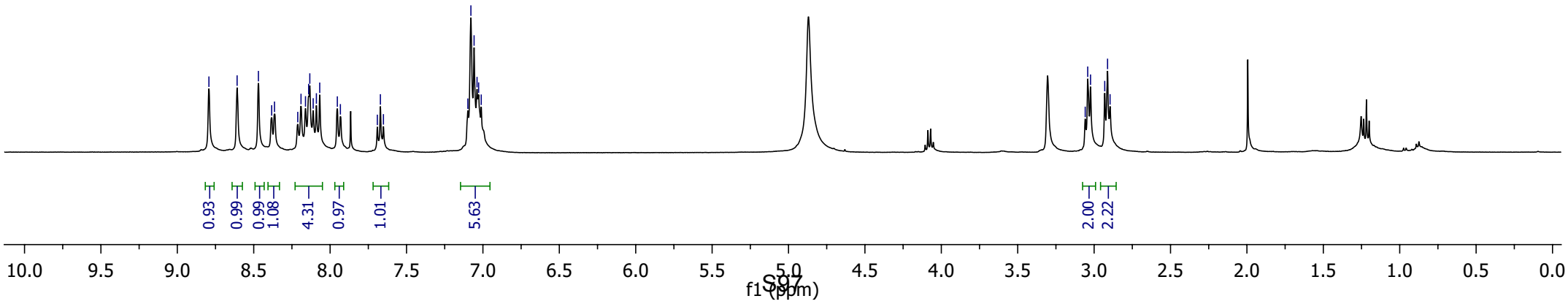
7.93
7.67
7.65
7.10
7.08
7.06
7.04
7.03
7.01
3.06
3.04
3.02
2.93
2.91
2.90
NH
S
O
O
NH
S
O
O
O
N+
O-
O

SZ7TA6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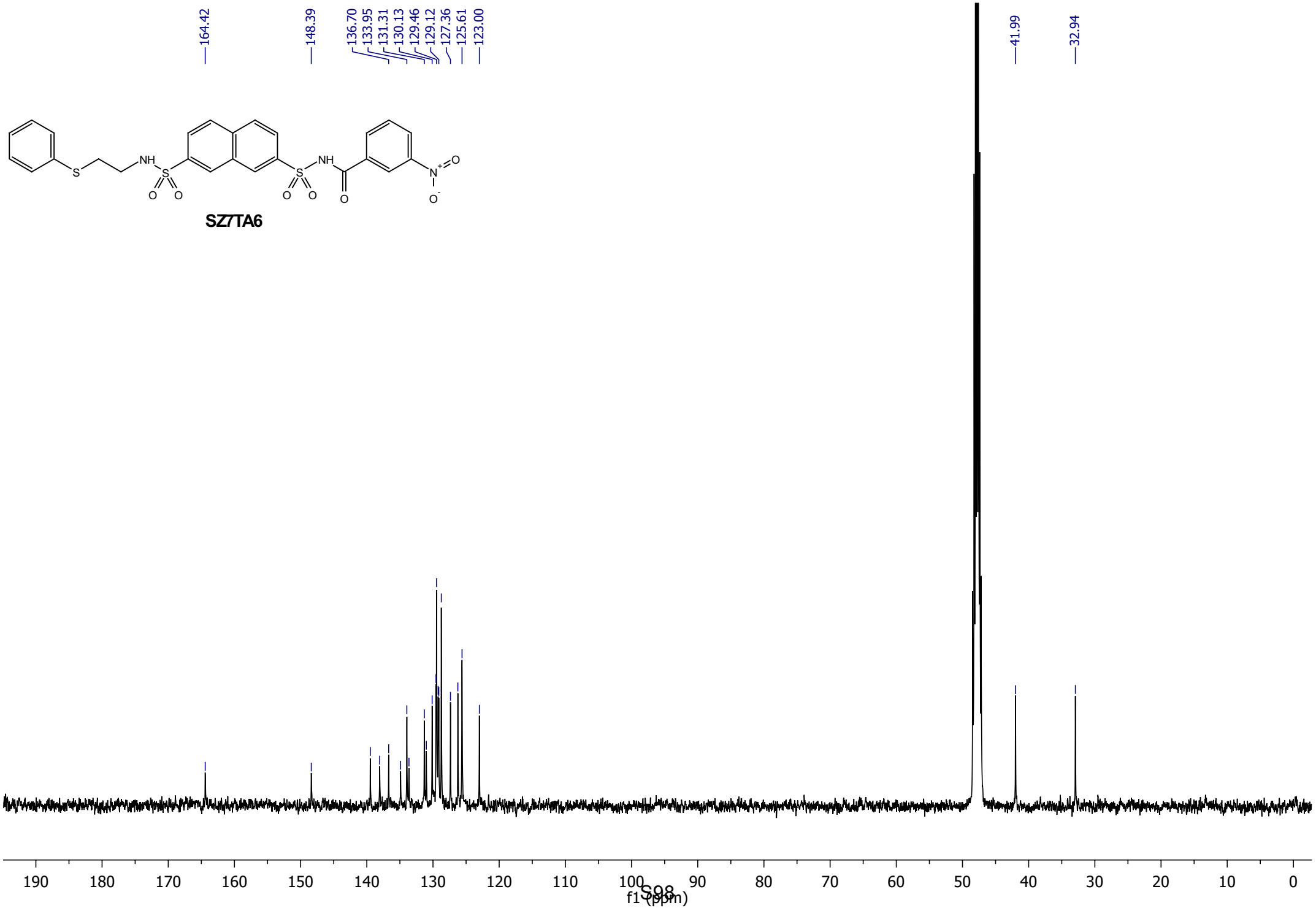
0.99
0.99
1.08
4.31
0.97
1.01
5.63
2.00
2.22
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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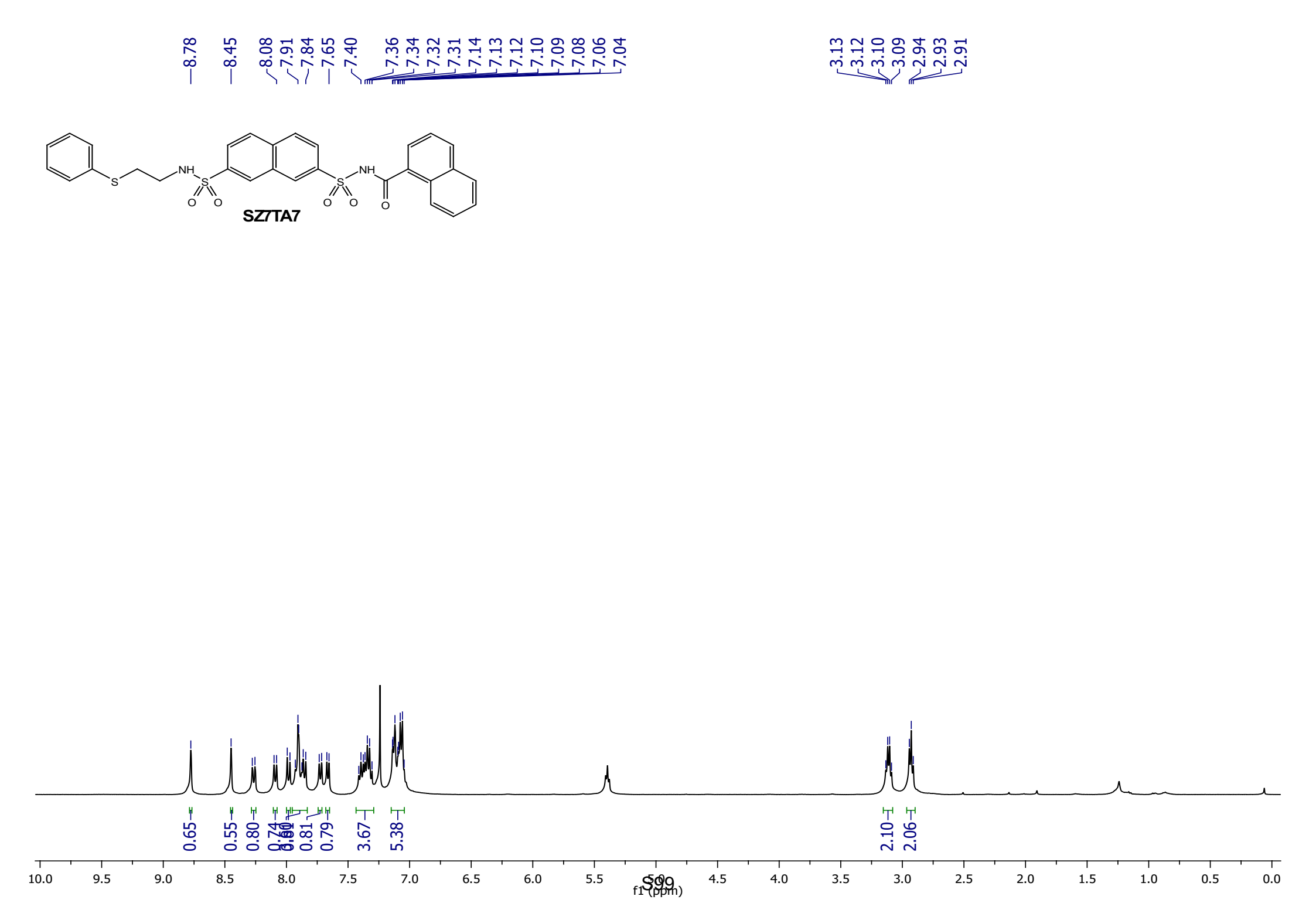
133.95
131.31
130.13
129.46
129.12
127.36
125.61
123.00
41.99
32.94
NH
S
O
NH
S
O
O
O
N+
O
O-
SZ7TA6
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.65
7.40
7.36
7.34
7.32
7.31
7.14
7.13
7.12
7.10
7.09
7.08
7.06
7.04
3.13
3.12
3.10
3.09
2.94
2.93
2.91
NH
S
O
O
S
O
O
NH
O
SZ7TA7
0.65
0.55
0.80
0.74
0.81
0.79
3.67
5.38
2.10
2.06
10.0
9.5
9.0
8.5
8.0
7.5
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6.5
6.0
5.5
5.0
4.5
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3.5
3.0
2.5
2.0
1.5
1.0
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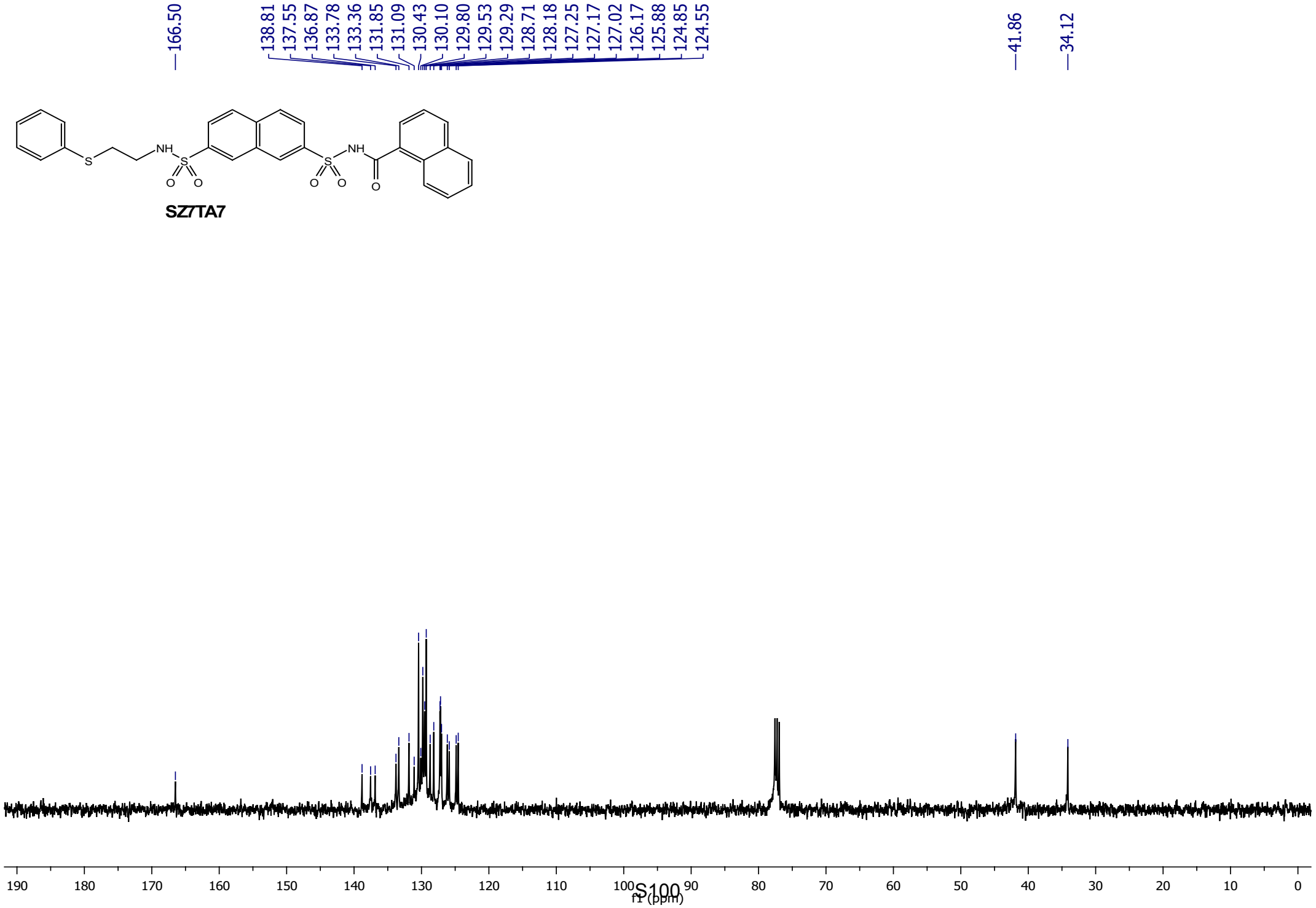
0.0
f1 (ppm)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133.36
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131.09
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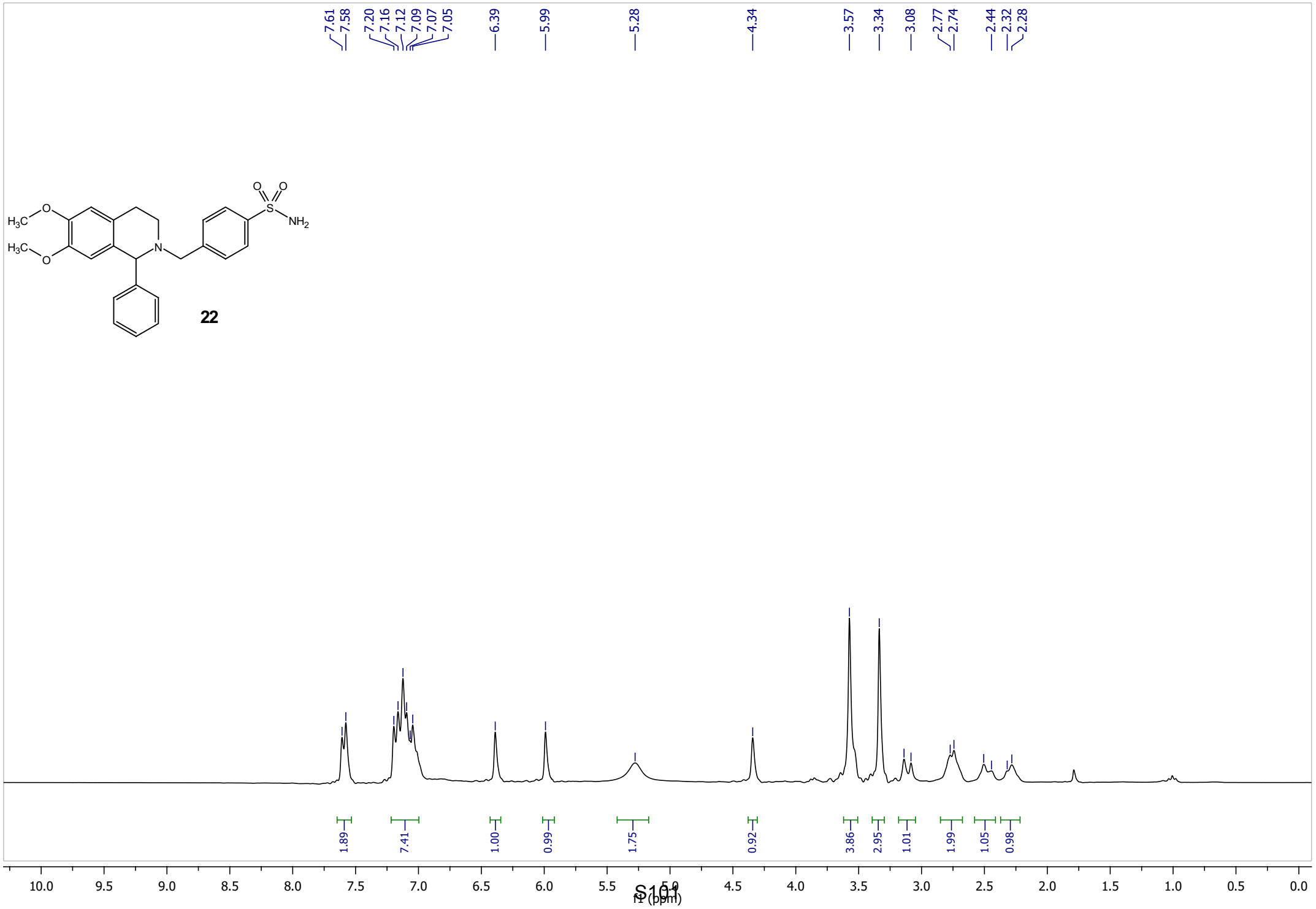
130.10
129.80
129.53
129.29
128.71
128.18
127.25
127.17
127.02
126.17
125.88
124.85
124.55
41.86
34.12
NH
S
O
O
NH
S
O
O
O
S
SZ7TA7
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.07
7.05
6.39
5.99
5.28
4.34
3.57
3.34
3.08
2.77
2.74
2.44
2.32
2.28
O
O
S
NH2
H3C
O
H3C
O
N
22
1.89
7.41
1.00
0.99
1.75
0.92
3.86
2.95
1.01
1.99
1.05
0.98
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.0
2.5
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1.0
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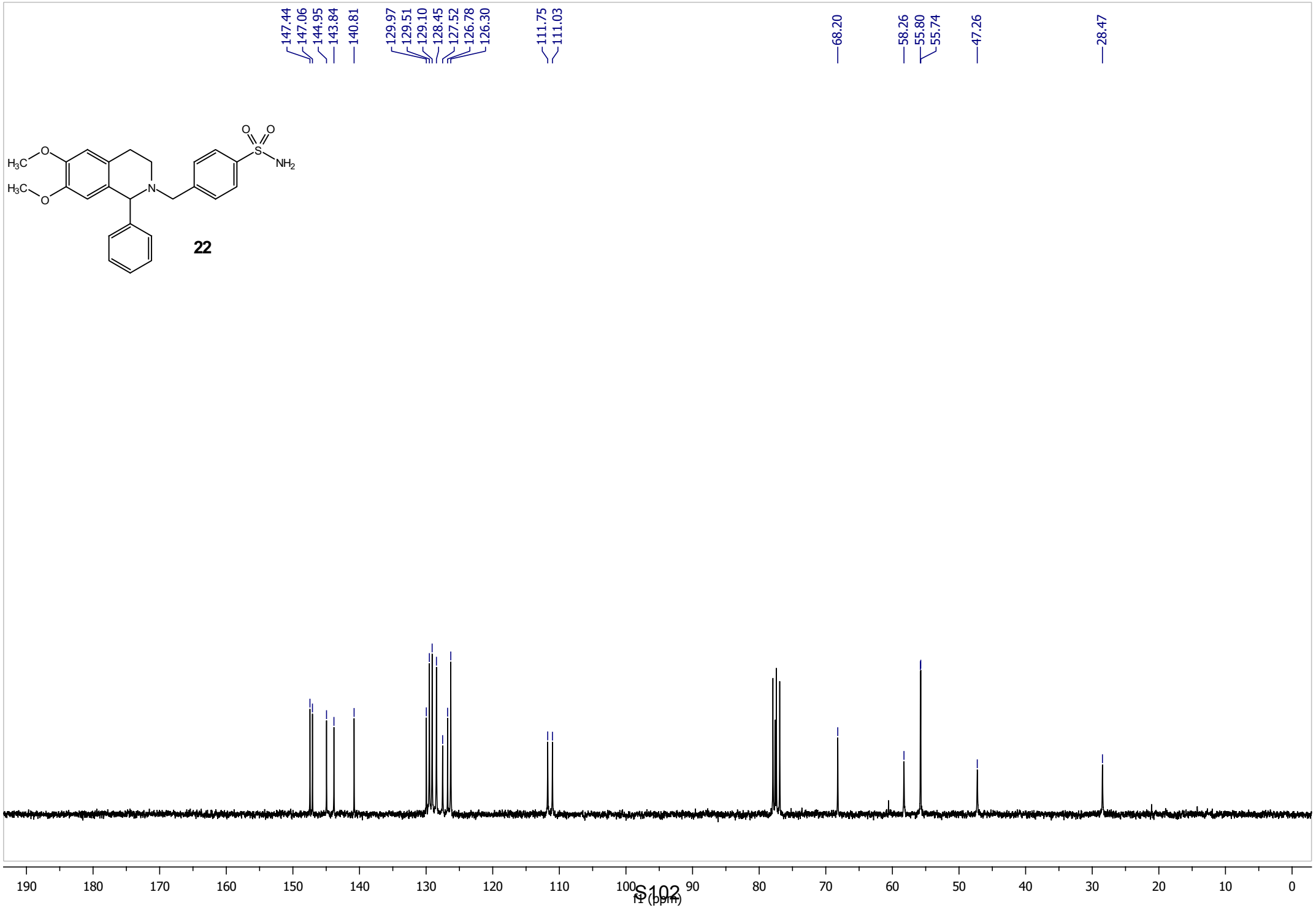
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129.10
128.45
127.52
126.78
126.30
111.75
111.03
68.20
58.26
55.80
55.74
47.26
28.47
O
O
S
NH2
H3C
O
H3C
O
N
22
190
180
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130
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110
100
90
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70
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50
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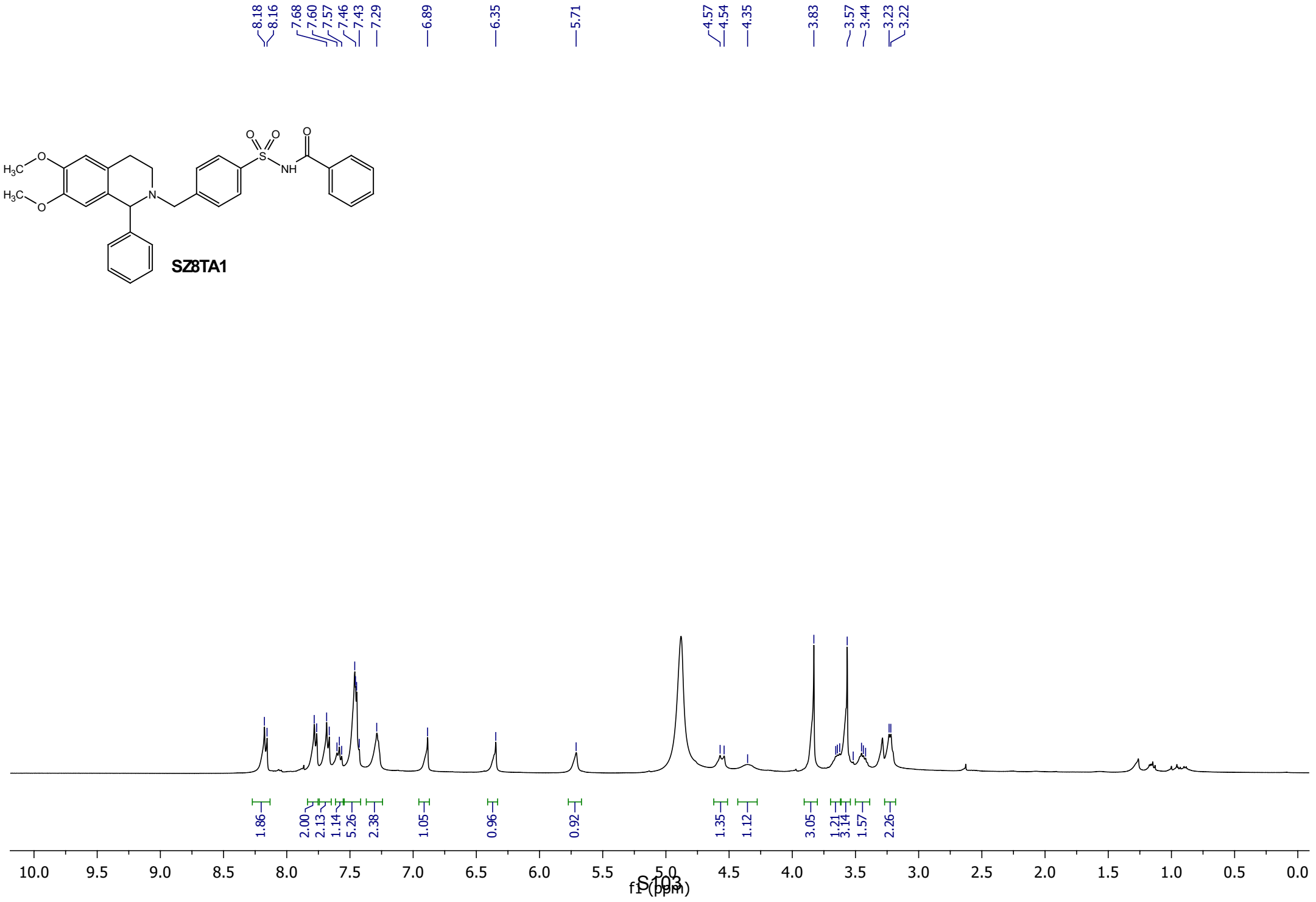
f1 (ppm)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7.29
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6.35
5.71
4.57
4.54
4.35
3.83
3.57
3.44
3.23
3.22
SZ8TA1
1.86
2.00
2.13
1.14
5.26
2.38
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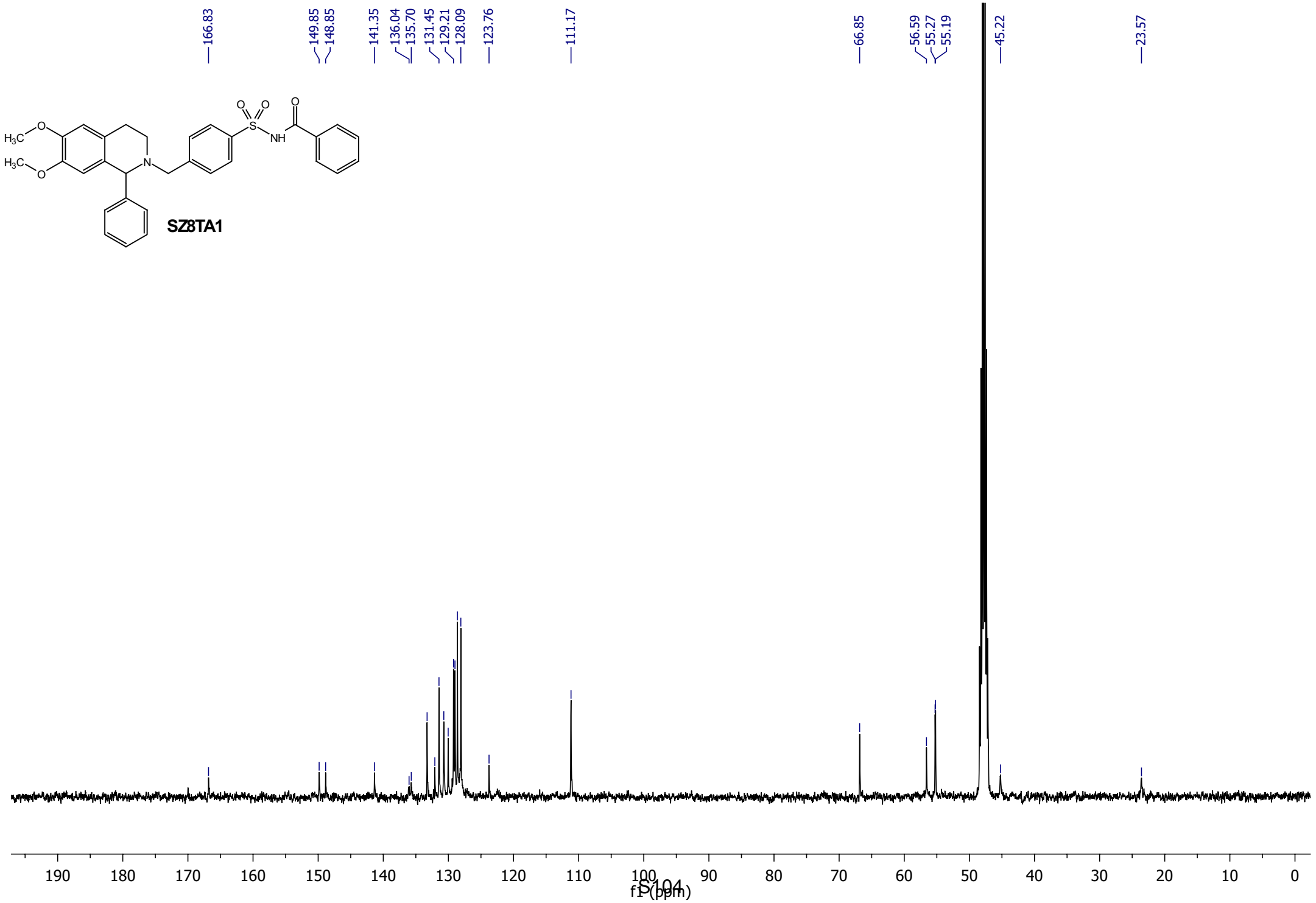
1.35
1.12
3.05
1.21
3.14
1.57
2.26
f1 (ppm)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131.45
129.21
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123.76
111.17
66.85
56.59
55.27
55.19
45.22
23.57
SZ8TA1
190
180
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90
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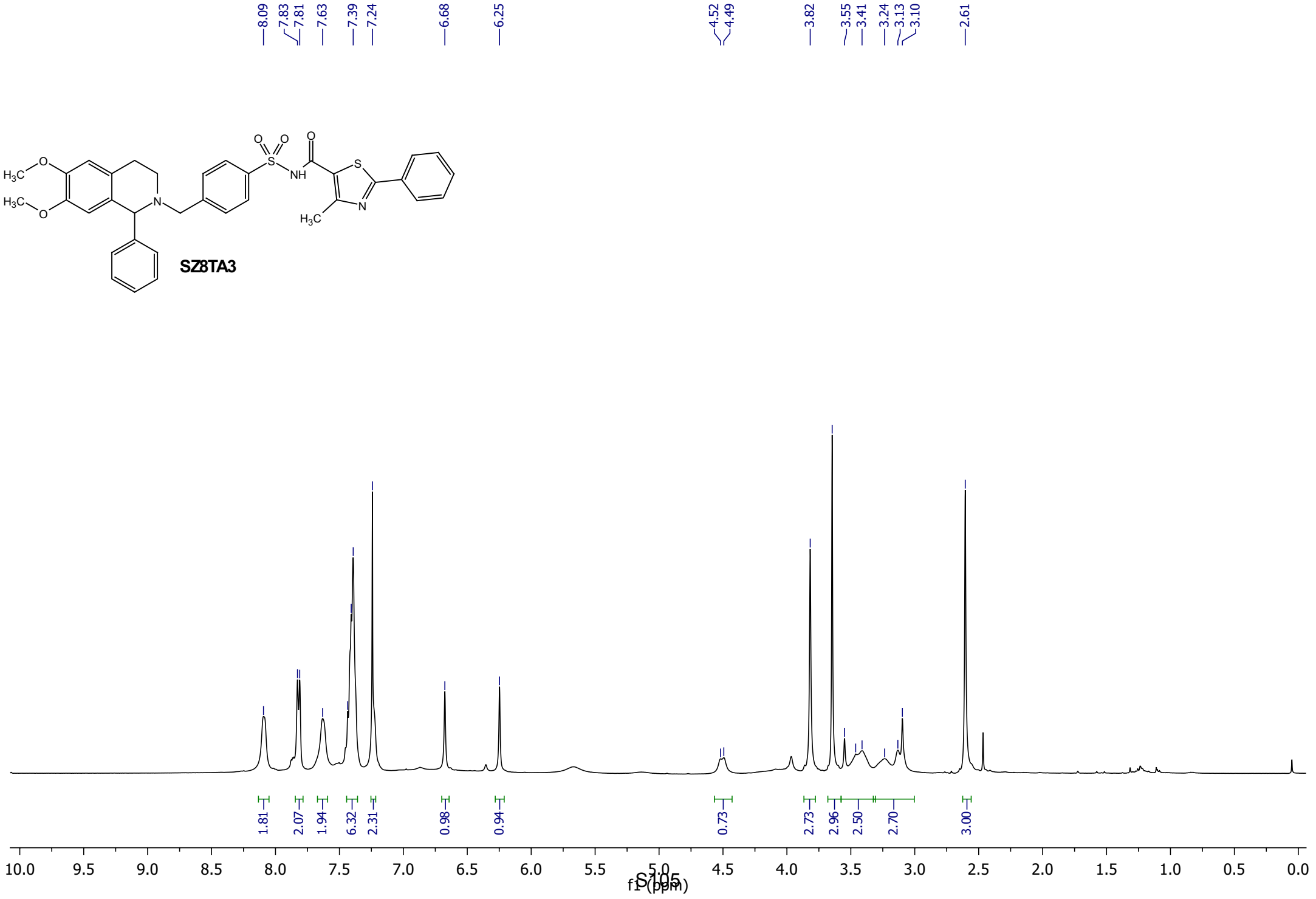
f1 (ppm)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6.25
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4.49
3.82
3.55
3.41
3.24
3.13
3.10
2.61
SZ8TA3
1.81
2.07
1.94
6.32
2.31
0.98
0.94
0.73
2.73
2.96
2.50
2.70
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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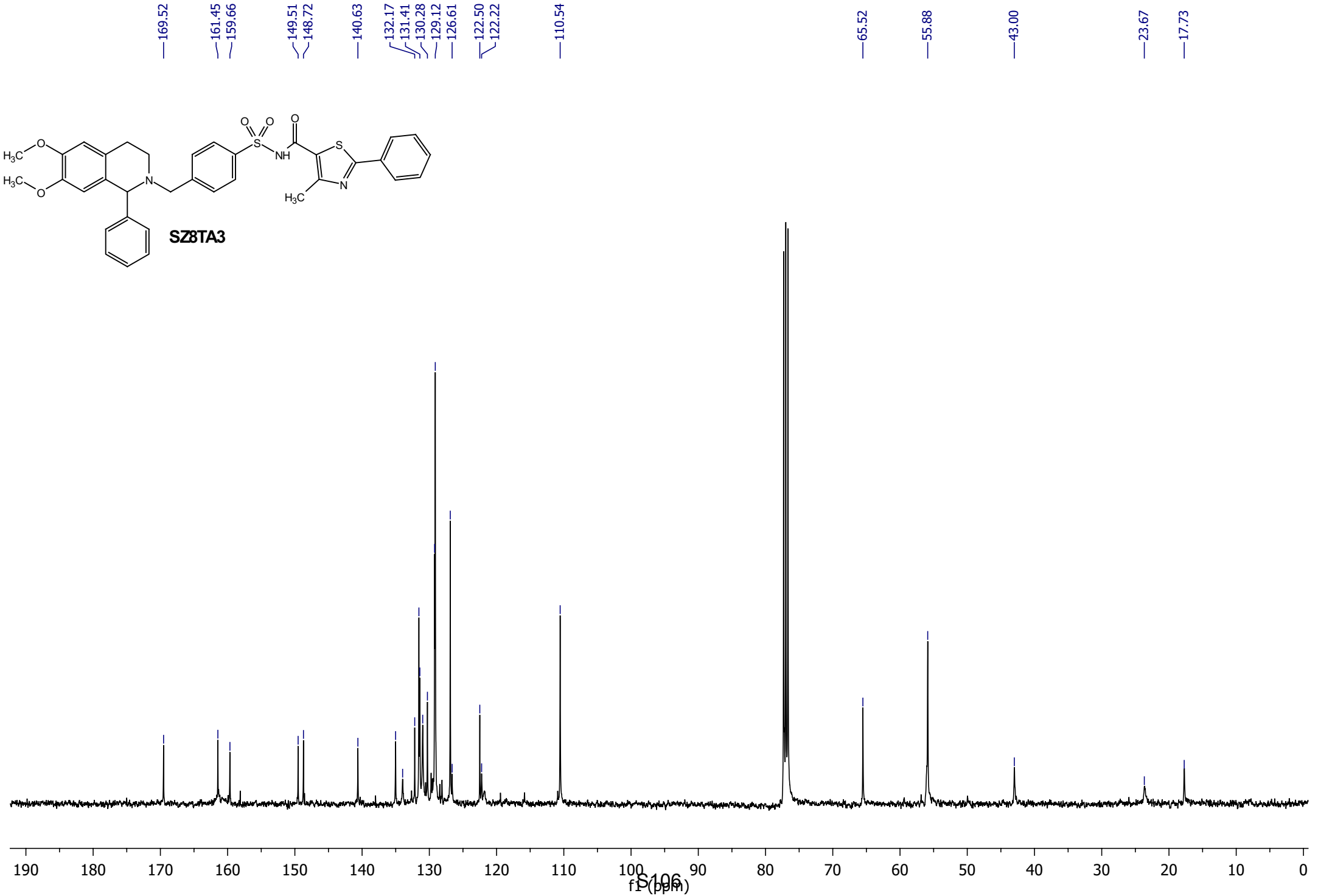
0.0
f1 (ppm)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129.12
126.61
122.50
122.22
110.54
65.52
55.88
43.00
23.67
17.73
SZ8TA3
190
180
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120
110
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90
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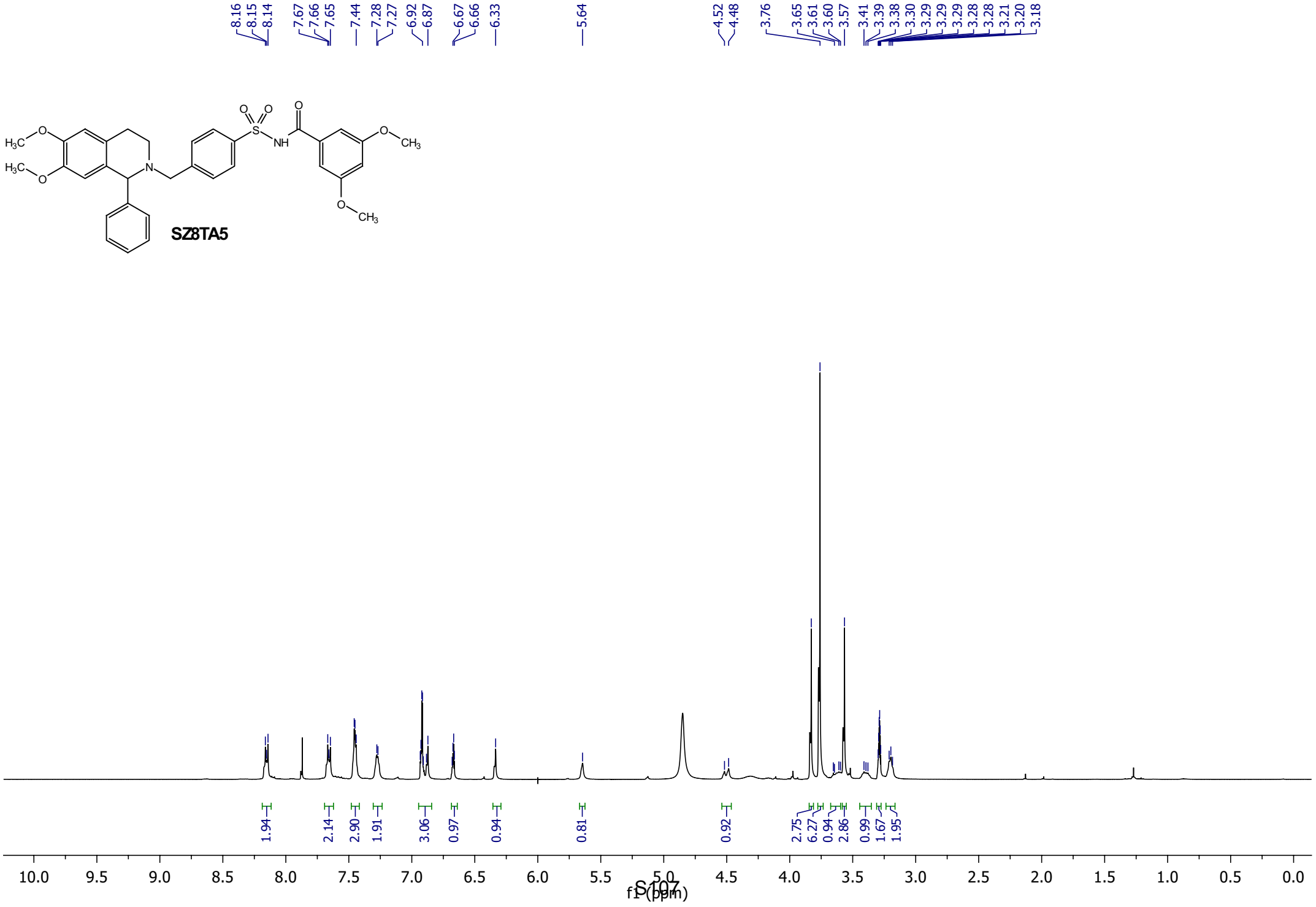
f1 (ppm)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7.28
7.27
6.92
6.87
6.67
6.66
6.33
5.64
4.52
4.48
3.76
3.65
3.61
3.60
3.57
3.41
3.39
3.38
3.30
3.29
3.29
3.29
3.28
3.28
3.21
3.20
3.18
SZ8TA5
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2.90
1.91
3.06
0.97
0.94
0.81
0.92
2.75
6.27
0.94
2.86
0.99
1.67
1.95
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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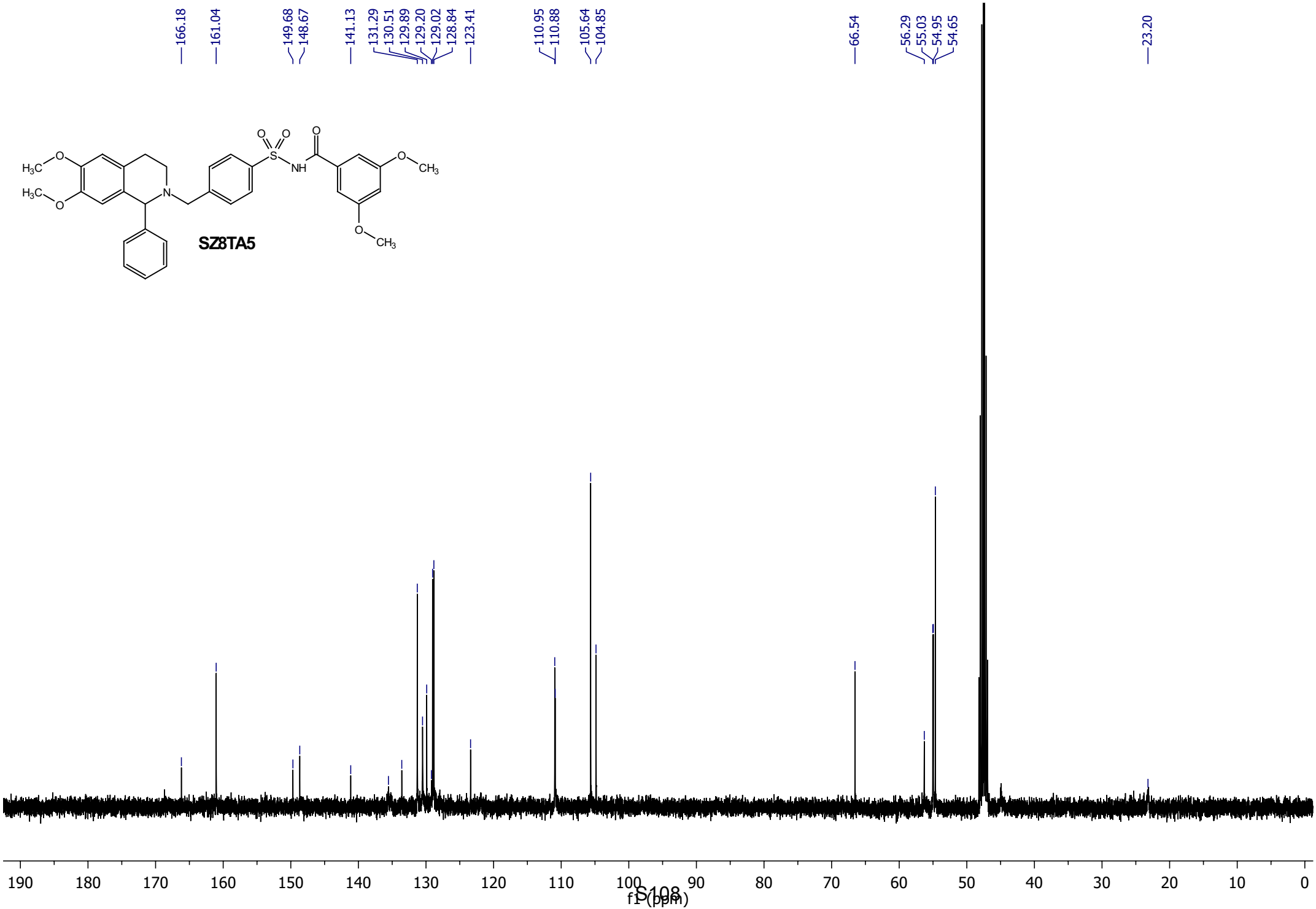
0.0
f1 (ppm)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128.84
123.41
110.95
110.88
105.64
104.85
66.54
56.29
55.03
54.95
54.65
23.20
SZ8TA5
190
180
170
160
150
140
130
120
110
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90
80
70
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50
40
30
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10
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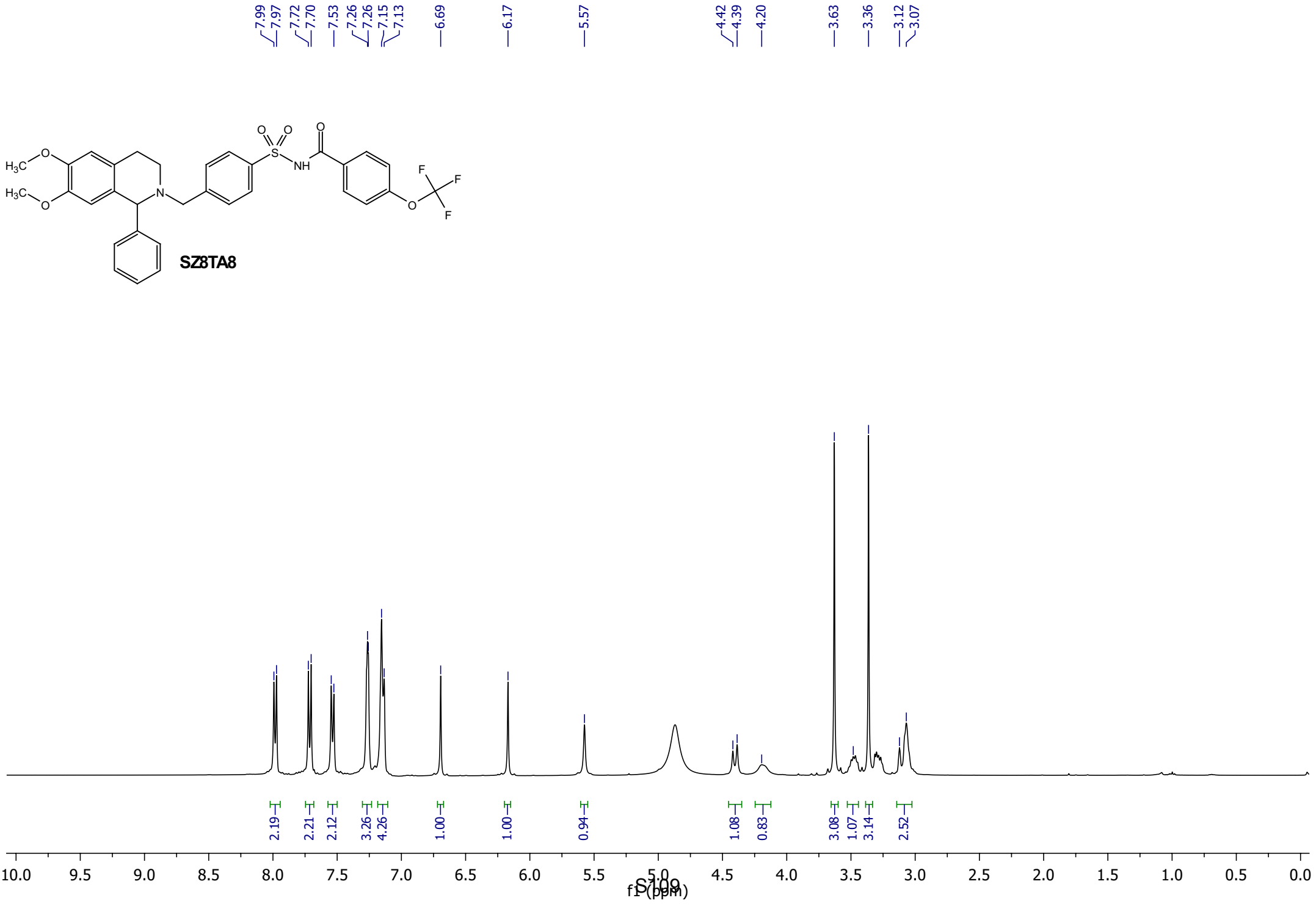
f1 (ppm)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7.15
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6.69
6.17
5.57
4.42
4.39
4.20
3.63
3.36
3.12
3.07
SZ8TA8
2.19
2.21
2.12
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1.00
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1.07
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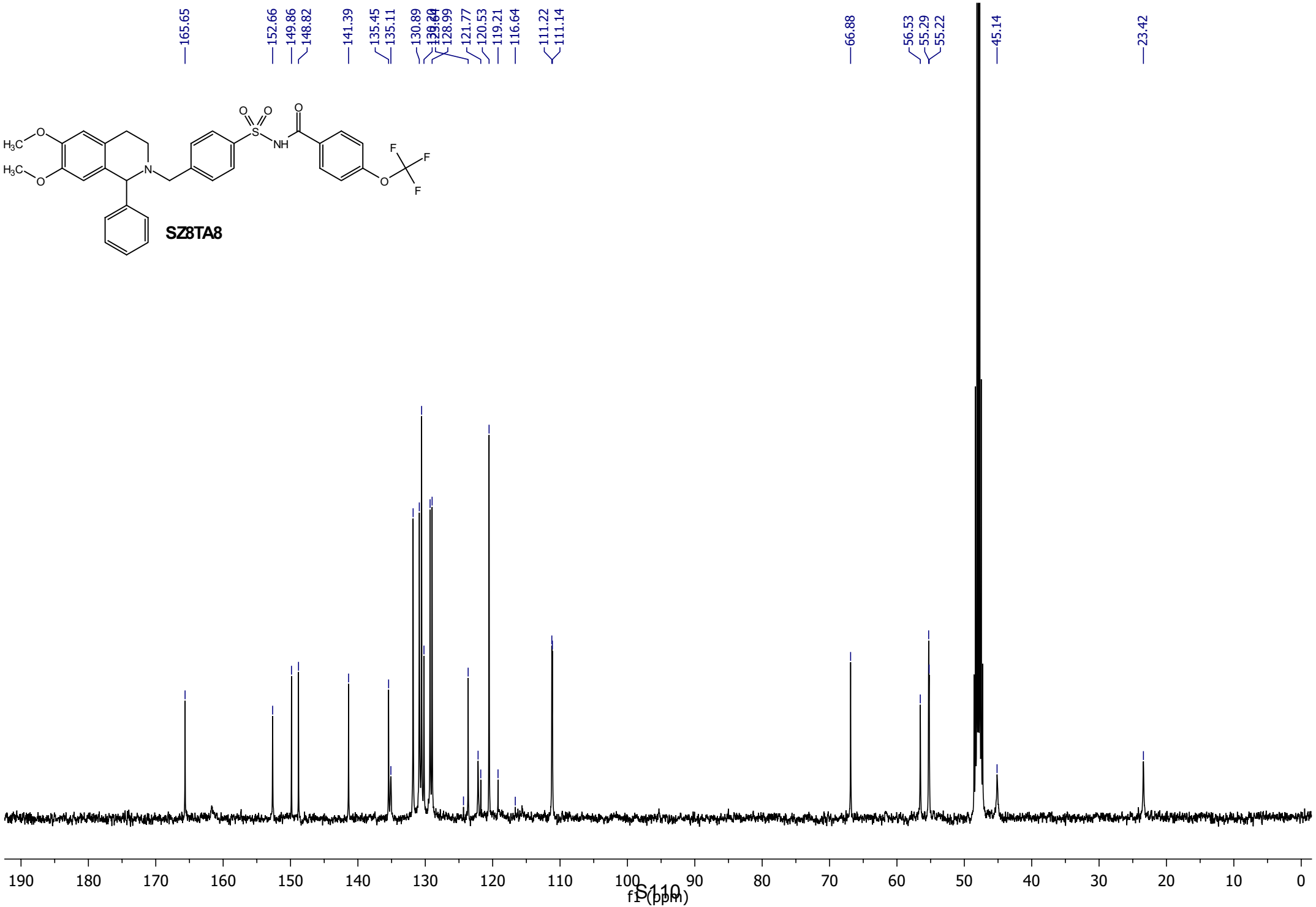
2.52
f1 (ppm)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111.14
66.88
56.53
55.29
55.22
45.14
23.42
SZ8TA8
190
180
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130
120
110
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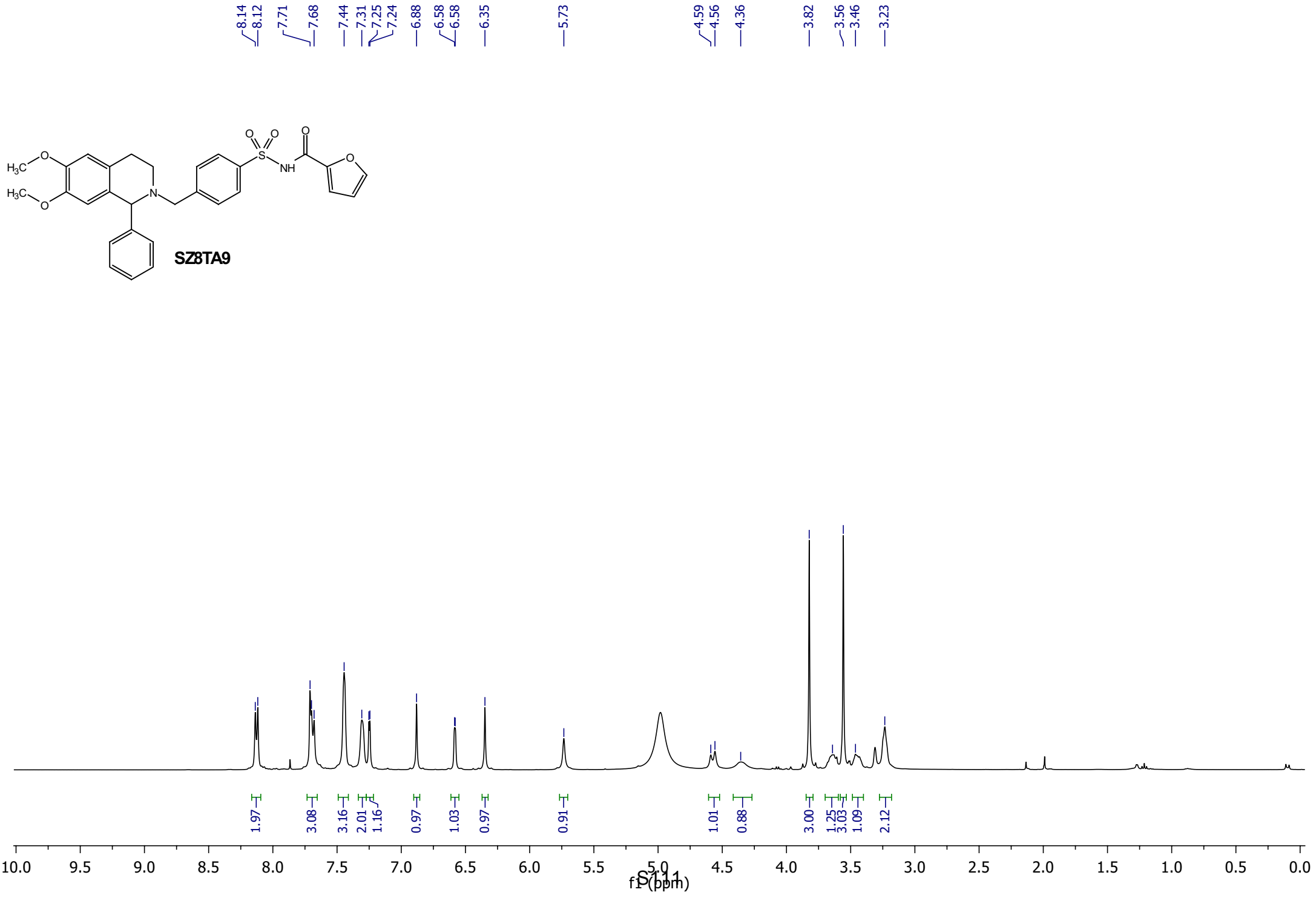
50
40
30
20
10
0
f1 (ppm)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6.58
6.58
6.35
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4.59
4.56
4.36
3.82
3.56
3.46
3.23
SZ8TA9
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3.08
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1.16
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0.91
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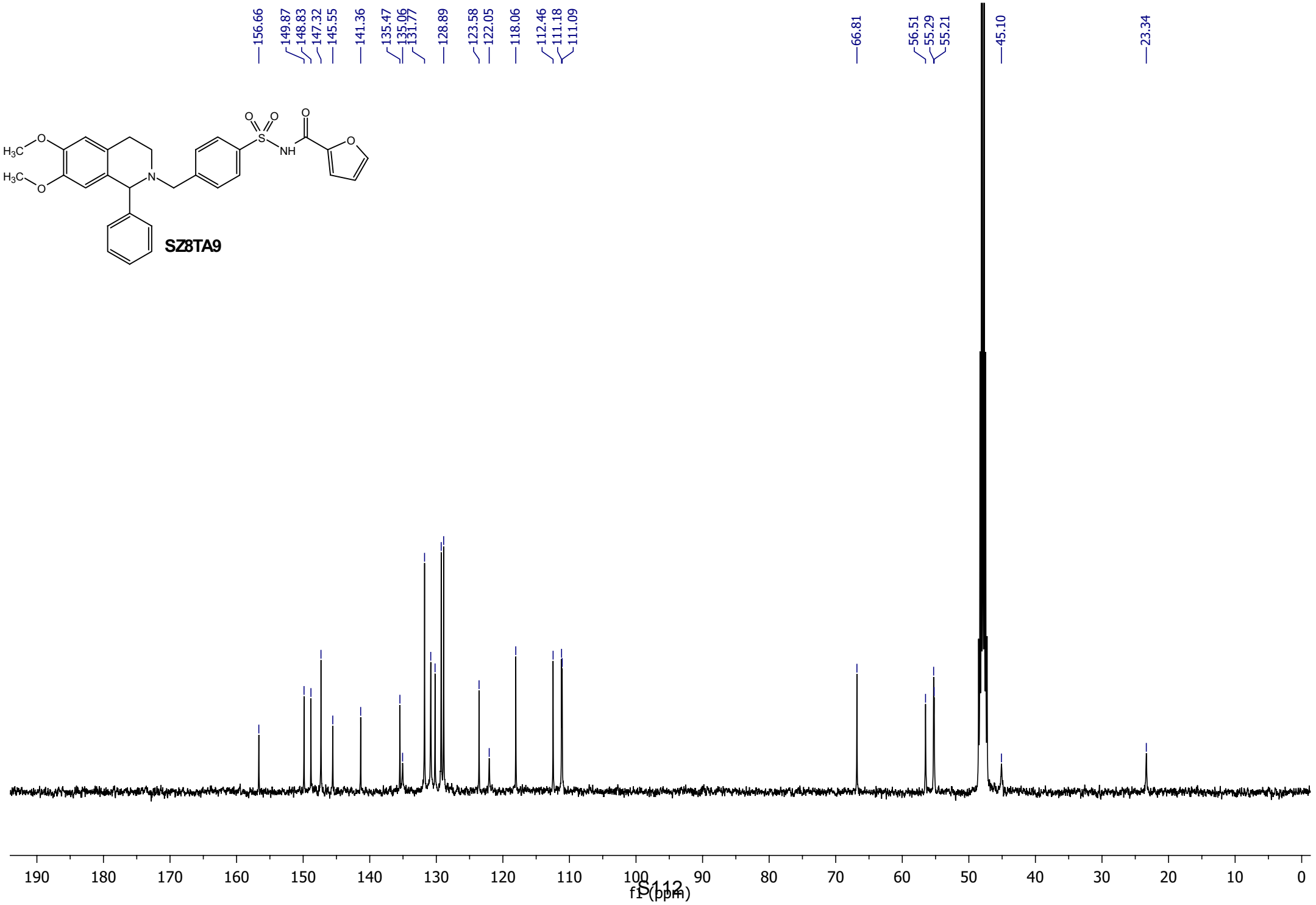
3.03
1.09
2.12
f1 (ppm)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190
180
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130
120
110
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90
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50
40
30
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10
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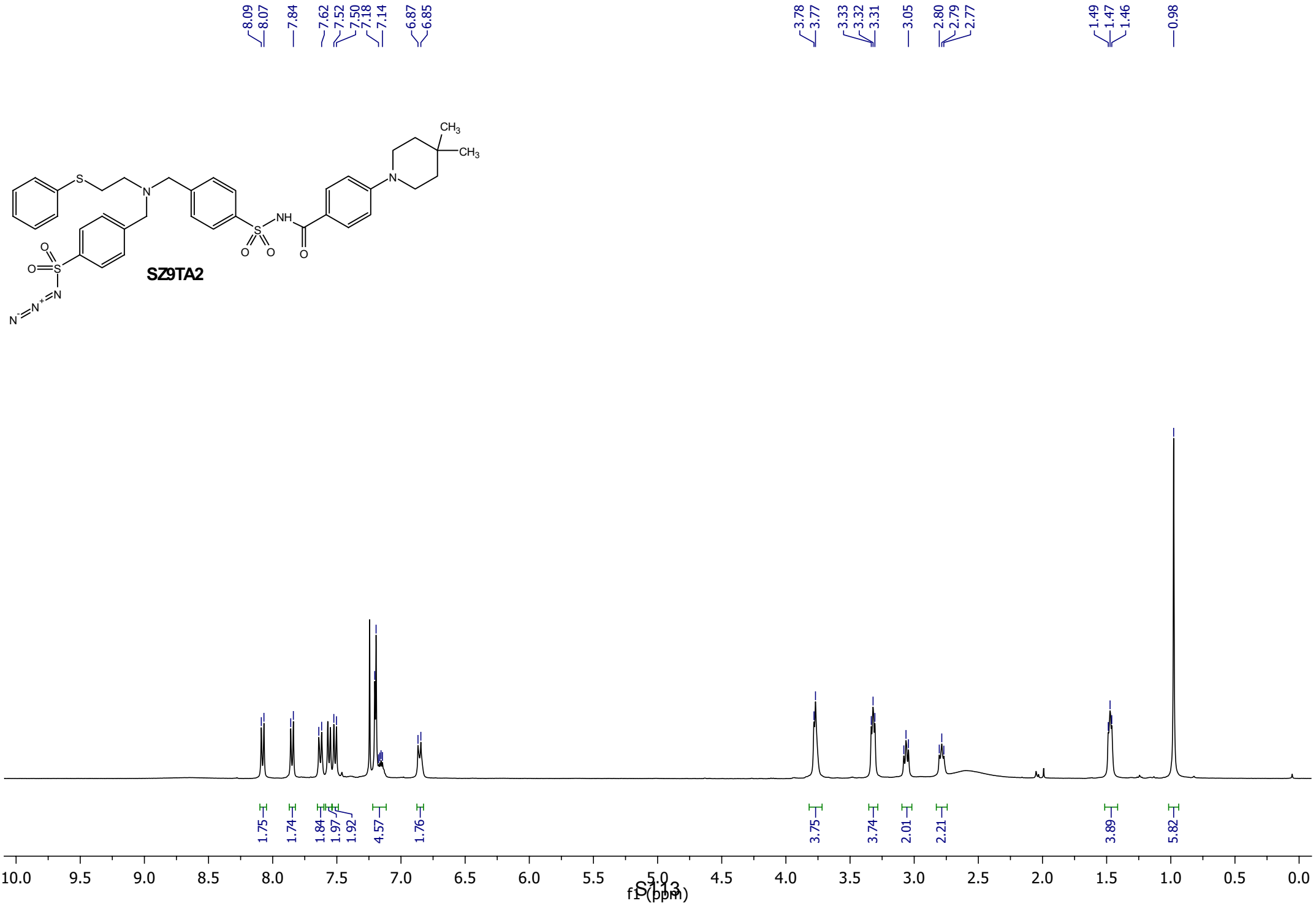
f1 (ppm)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3.32
3.31
3.05
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2.77
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1.47
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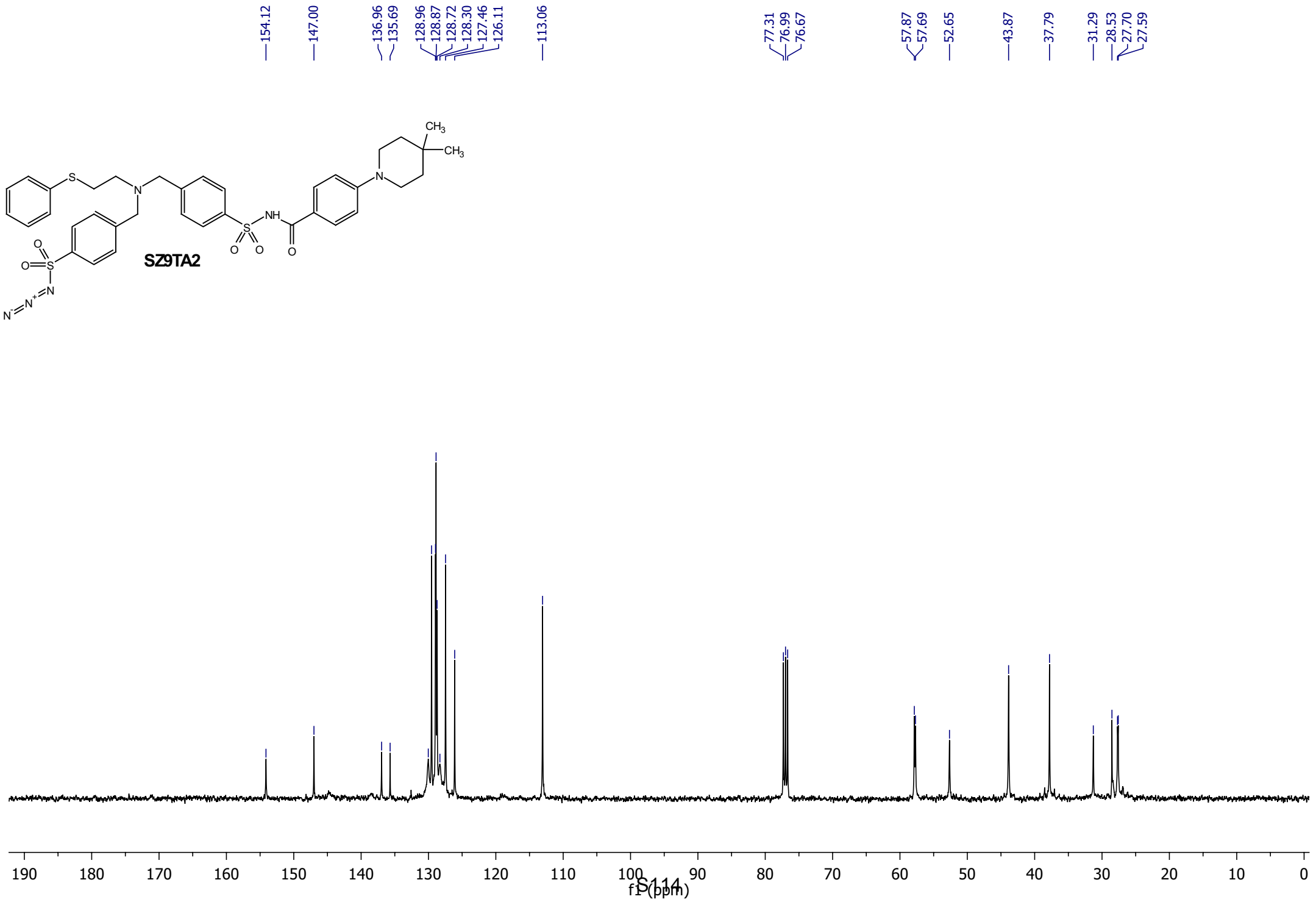
5.82
f1 (ppm)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113.06
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76.99
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27.70
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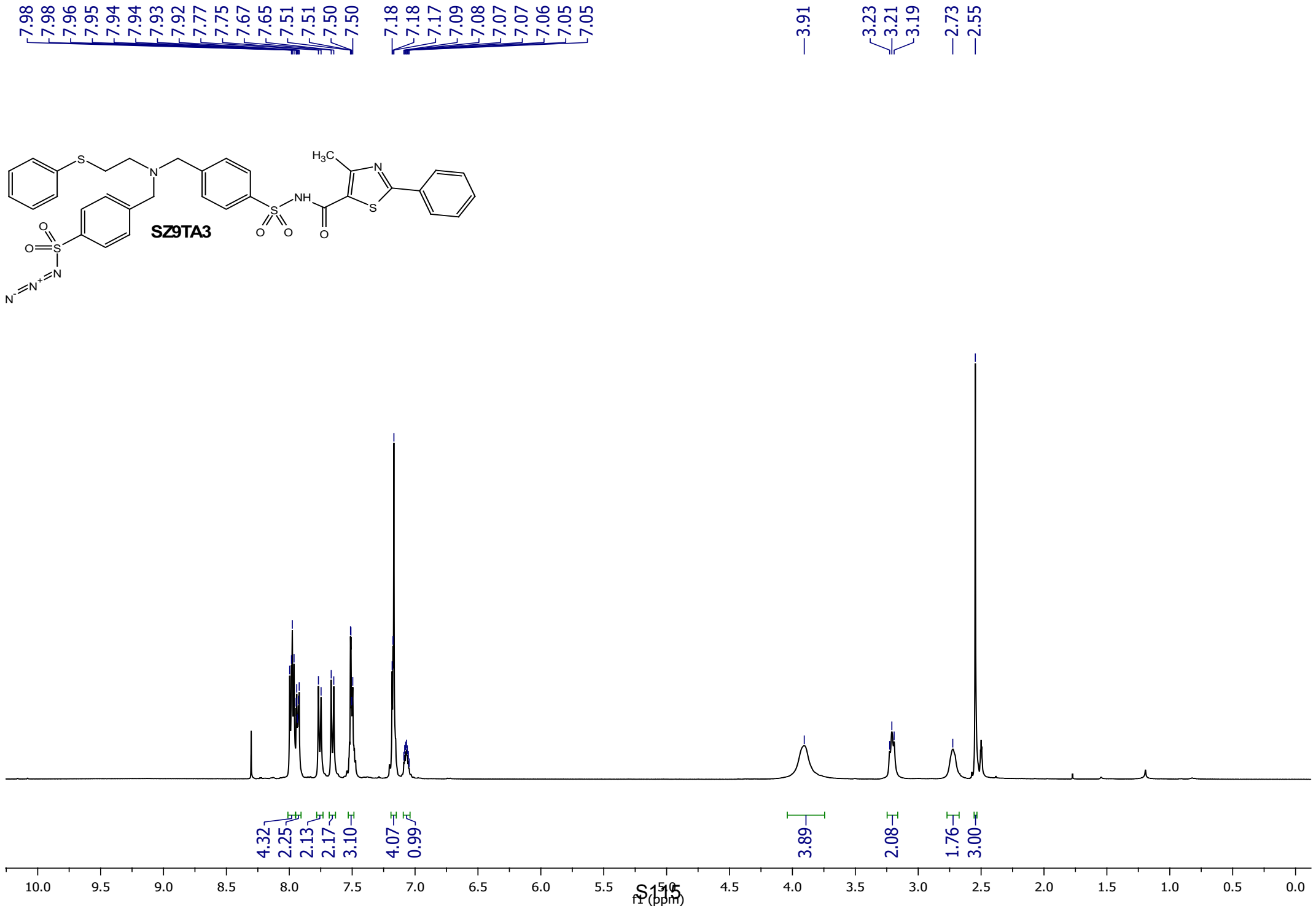
f1 (ppm)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7.67
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7.51
7.50
7.50
7.18
7.18
7.17
7.09
7.08
7.07
7.07
7.06
7.05
7.05
3.91
3.23
3.21
3.19
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SZ9TA3
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2.17
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2.08
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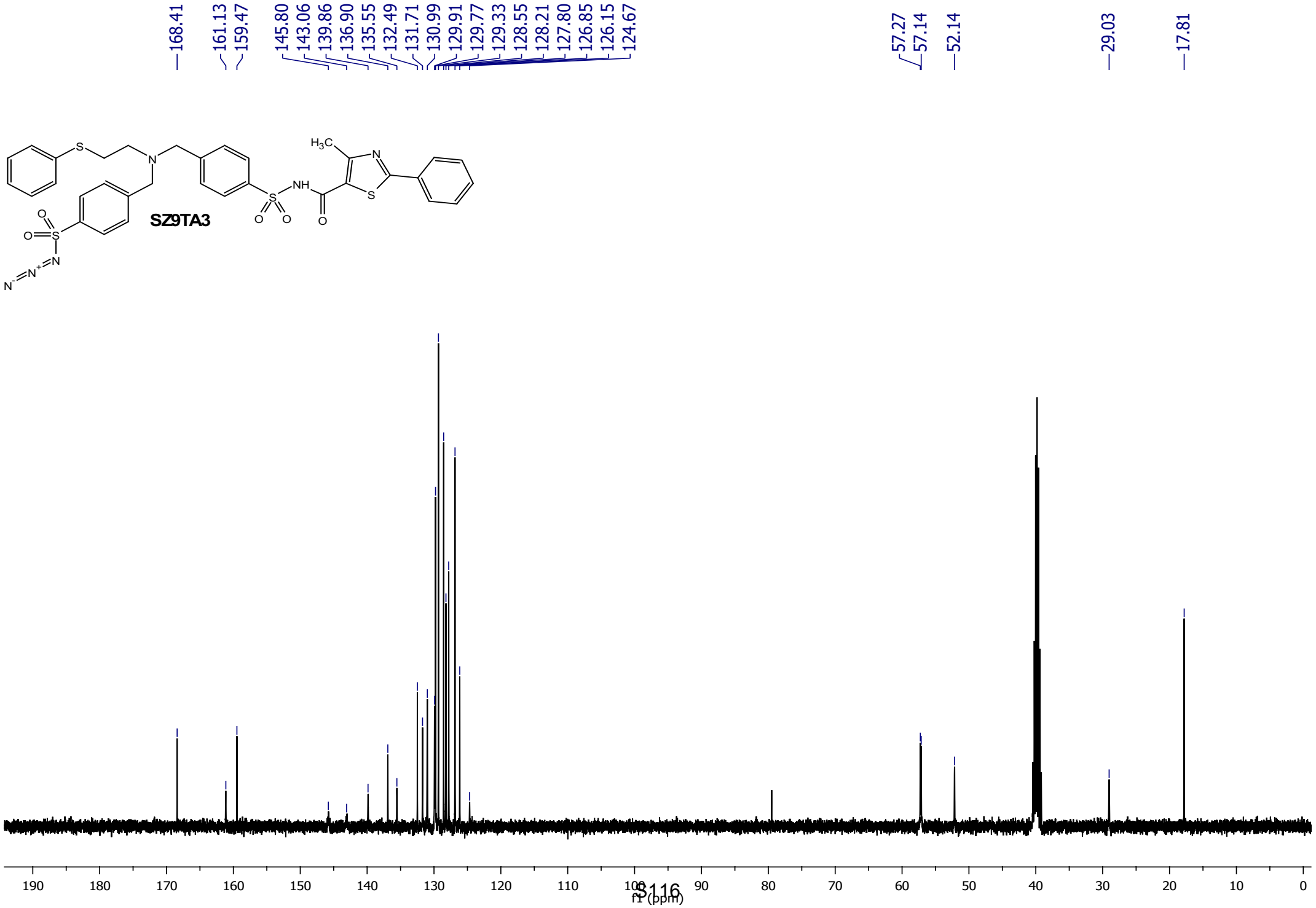
f1 (ppm)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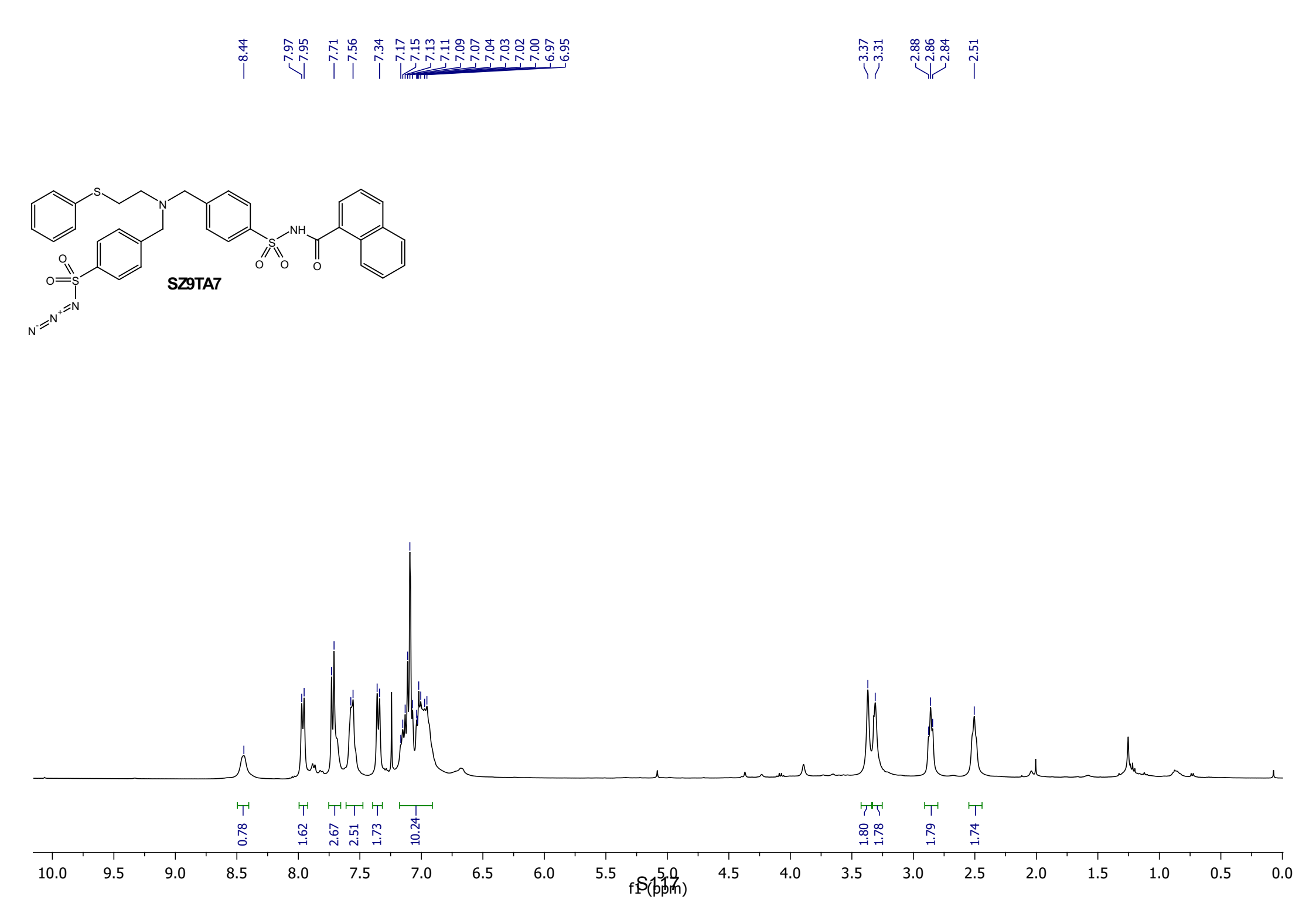
f1 (ppm)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7.03
7.02
7.00
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3.37
3.31
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2.84
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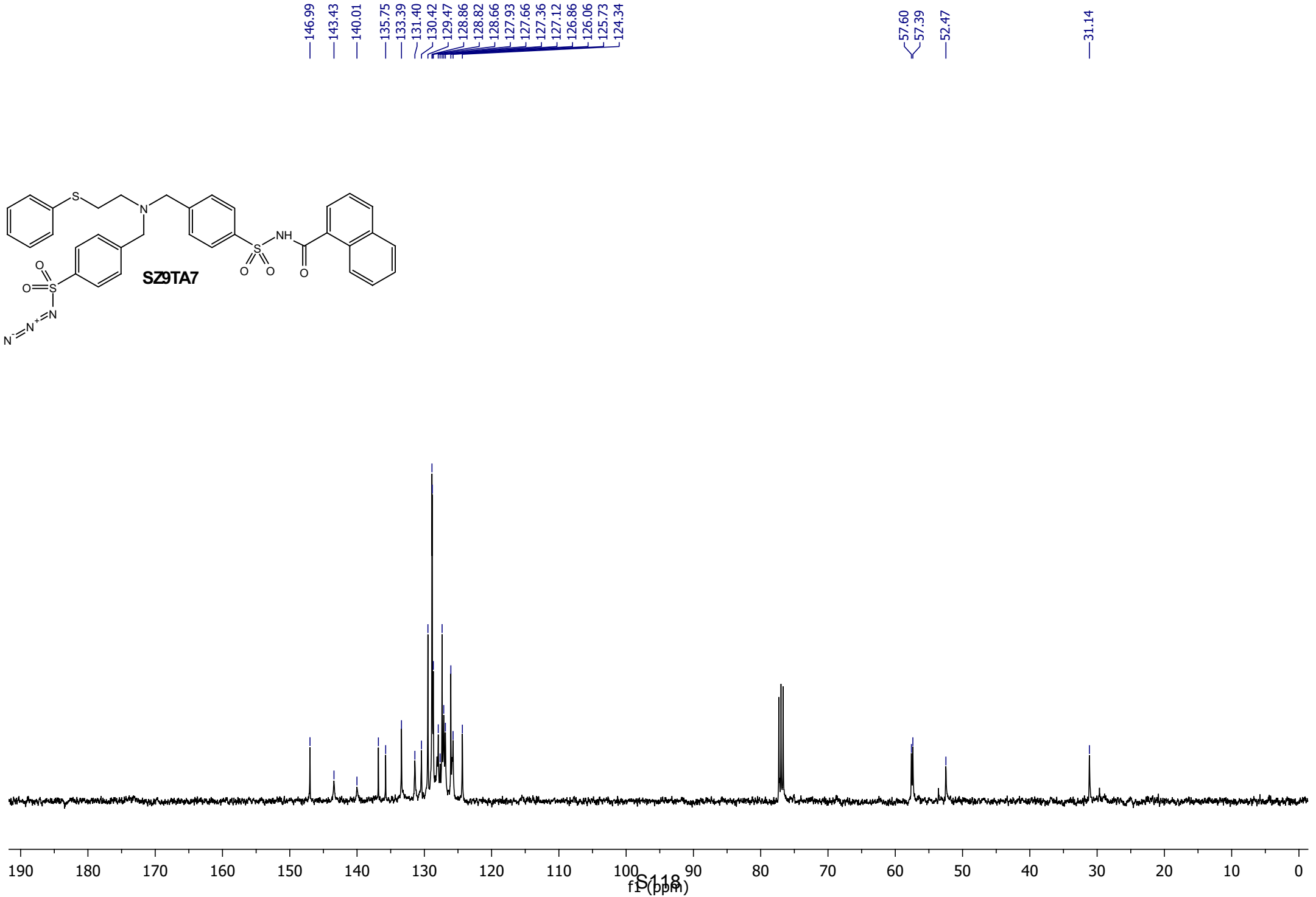
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126.06
125.73
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52.47
31.14
SZ9TA7
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180
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160
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10
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f1 (ppm)