Supporting Information

Discovery of [1,2,3]Triazolo[4,5-d]pyrimidine Derivatives as Novel LSD1 Inhibitors

Zhong-Hua Li[#], Xue-Qi Liu[#], Peng-Fei Geng, Feng-Zhi Suo, Jin-Lian Ma, Bin Yu, Tao-Qian Zhao, Zhao-Qing Zhou, Chen-Xi Huang, Yi-Chao Zheng, Hong-Min Liu**

Key Laboratory of Technology of Drug Preparation (Zhengzhou University), Ministry of Education; Key Laboratory of Henan Province for Drug Quality and Evaluation; Collaborative Innovation Center of New Drug Research and Safety Evaluation, Henan Province; Institute of Drug Discovery and Development, Zhengzhou University, 100 Kexue Avenue, Zhengzhou, Henan 450001, China.

Corresponding Author:

Prof. Hong-Min Liu (liuhm@zzu.edu.cn)

Contents:

1. Biological assay

1.1 Inhibitory evaluation of compound 27 against LSD1, MAO-A and MAO-B

Inhibitory effects of the candidate compounds against LSD1 were evaluated according to our previously reported methods.[1] Full length LSD1 cDNA encoding LSD1 was obtained by RT-PCR and cloned into pET-28b (pET-28b-LSD1). Then the plasmid pET-28b-LSD1 was transfected into BL21 (DE). The recombinant was induced with 0.25 mM IPTG at 20 ^{o}C and purified following affinity chromatography, ion exchange chromatography and gel filtration. Then the compounds were incubated with the recombinant and H3K4me2. After that, the fluorescence was measured at excitation wavelength 530 nm and emission wavelength 590 nm as reported in order to evaluate the inhibition rate of the candidate compounds. Inhibitory effects of compound **27** toward MAO-A and MAO-B were evaluated with enzyme from Sigma and a commercialized kit from Promega.

1.2 Cell viability analysis

The human gastric carcinoma cell lines MGC-803 were supplied by the Cell Bank of Shanghai Institute of Cell Biology, Chinese Academy of Sciences. Exponentially growing cells were seeded at 5×10^3 cells per well into 96-well plates. After 24 h incubation at 37 ^{o}C, the culture medium was removed and replaced with fresh medium containing the candidate compounds in different concentrations. The cells were incubated for another 5 days. Then, 20 μL of 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) solution (5 mg/mL) was added to each well and incubated for 4 h at 37 ^{o}C. The medium containing MTT was discarded, then 150 mL of dimethyl sulfoxide (DMSO) was added to each well and the plates agitated until the dark blue crystals (formazan) had completely dissolved. The absorbance was measured using a microplate reader at a wavelength of 570 nm. Each concentration was analyzed in triplicate and the experiment was repeated three times.

1.3 Reversibility analysis

The dilution assay was done as published.[2] Briefly, an amount of 2.5 μg of LSD1 recombinant was incubated with 312.5 μM compound **27**, 600 μM GSK2879552, or DMSO. At 1 h later, 1.25 μg aliquots were removed from all samples and diluted into

HRP-assay solution containing substrate and coupling reagents to a final volume of 100 μL. This represents an 80-fold dilution of the inhibitor concentration, which is expected to yield the same inhibition rate for an irreversible inhibitor or significant difference for a reversible inhibitor.

1.4 Western blot

MGC-803 cells were treated with indicated concentrations of compound **27**, the cells were collected, lysed in RIPA buffer containing a protease inhibitor cocktail for 30 min, followed by centrifugation at 12,000 rpm for 10 min at 4 ^{o}C. After the collection of supernatant, the protein concentration was detected using a bicinchonininc acid assay kit (Beyotmie Biotechnology, Haimen, China). After addition with loading buffer, cell lyses were boiled for 10 min at 100 ^{o}C for SDS-polyacrylamide gel electrophoresis (PAGE). Proteins were transferred to nitrocellulose (NC) membranes. Then the membranes were blocked with 5% skim milk at room temperature for 2 h, and then incubated overnight at 4 ^{o}C with primary antibodies. After washing the membrane with the secondary antibody (1:5000) at room temperature for 2 h,the blots were washed with PBS containing 0.05% Tween-20 (PBST). The antibody-reactive bands were revealed by enhanced chemiluminescence (ECL) and exposed on Kodak radiographic film.

Antibodies used were against histone H3K4me1 (Abcam no. ab176877), H3K4me2 (Abcam no. ab32356), H3K4me3 (Abcam no. ab8580), H3K9me1 (Abcam no. ab9045), H3K9me2 (Abcam no. ab1220), E-Cadherin (Cell Signaling no. 3195S), N-Cadherin (Cell Signaling no. 13116S), and GAPDH (GoodHere no. AB-M-M 001).

1.5 Transwell

For the migration assay, MGC-803 cells were seeding into Corning® Costar®Transwell® cell culture chamber with porous membrance (8.0 μM pore size). The upper chamber was placed into a 24-well plate (lower chamber). 100 uL medium containing 1% FBS, different concentrations of compound **27** and 10,000 cells were added to each upper chamber. In the lower chamber, 500 μL medium with 20% FBS was used as chemoattractant. After incubation for 24 h, both chambers were washed by PBS for three times. Non-migrated cells were removed from the upper surface of

the membrane byscrubbing with cotton tipped swab, and the migrated cells were fixed with methanol for 15 min. Then the chambers were stained with Hoechest 33258 (10 μg/mL) for 15 min, migrated cells were detected and numbered using high content screening system (ArrayScan XTI, Thermo Fisher Scientific, MA).

2. Molecular docking

The Molecular Operating Environment (MOE, Version 2015) was used for docking studies. The crystal structure of LSD1 in complex with an H3K4 peptide (PDB code 2V1D) was downloaded from PDB database and prepared using the default parameters. Hydrogen atoms and the partial charges for all atoms were added by using the protonate 3D module, the H3K4 peptide ligand and all water molecules were deleted, FAD was retained in the protein structure for docking, and the protein was energy-minimized using Amber 10 : EHT forcefield. The docking site was generated using MOE-site Finder. The 3D structures of compounds **18** and **20** were built and energy-minimized using Amber 10 : EHT forcefield. The default Triangle Matcher placement method was used for docking. GBVI/WSA dGscoring function which estimates the free energy of binding of the ligand from a giver pose was used to rank the final poses.

3. Chemistry

General

Reagents and solvents were purchased from commercial sources and were used without further purification. All reaction were monitored by thin-layer chromatography and visualized with UV light. Melting points were determined on an X-5 micromelting apparatus and are uncorrected. ^{1}HNMR and ^{13}CNMR spectra were recorded on a Bruker 400 MHz and 100 MHz spectrometer respectively. High resolution mass spectra (HRMS) were recorded on a Waters Micromass Q-T of Micromass spectrometer by electrospray ionization (ESI). Final products were of >95% purity as analyzed by HPLC analysis (Phenomenex column, C-18, 5.0 μm, 4.6 mm × 150 mm) on Dionex UltiMate 3000 UHPLC instrument from ThermoFisher. The signal was monitored at 254 nm with a UV dector. A flow rate of 1.0 mL/min was used with a mobile phase of methanol in H_2O (80:20, v/v). The intermediates **1a-c** and

1f-h were previously reported.[3]

***General procedure for the synthesis of intermediates* 1d and 1e**

7-Chloro-3-cyclopentyl-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidine (1d)

The intermediate **1d** was prepared following our previously reported procedure.[3] The mixture of 4,6-dichloro-2-(propylthio)pyrimidin-5-amine (1 eq), cyclopentylamine (1 eq) and triethylamine (1.2 eq) in N,N-dimethylformamide was heated to 100 ^{o}C for 20 h and monitored by TLC (PE/EA = 5:1). After completion of the reaction, the mixture was cooled to room temperature and acetic acid (1/2 volume of DMF) was added. The mixture was cooled in an ice bath and sodium nitrite (1 eq in small amount of water) was added dropwise to keep the reaction temperature below 15 ^{o}C. After the addition, the reaction mixture was stirred for 30 min at 10~15 ^{o}C. TLC indicated completion of the reaction. The solution was diluted with double volume of ethyl acetate and washed with water for 3 times, then neutralized with saturated sodium bicarbonate. The organic layer was concentrated under reduced pressure to give the crude product **1d**, which was used to the next step without further purification. Small amount of the crude product was purified by flash column chromatography for structure identification. Yellow waxy solid. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm): δ 5.26-5.33 (m, 1H), 3.19-3.23 (m, 2H), 2.28-2.33 (m, 4H), 2.03-2.08 (m, 2H), 1.78-1.87 (m, 4H), 1.07-1.11 (t, J = 7.4 Hz, 3H). HR-MS (ESI): Calcd. $C_{12}H_{16}ClN_5S$, $[M+Na]^+$ m/z: 320.0713, found: 320.0712.

7-Chloro-3-isobutyl-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidine (1e)

The intermediate **1e** was prepared from isobutylamine and 4,6-dichloro-2-(propylthio)pyrimidin-5-amine using a procedure similar to the synthesis of **1d**. Yellow oil. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm) : δ 4.42-4.44 (d, J = 7.2 Hz, 2H), 3.19-3.22 (t, J = 7.2 Hz, 2H), 2.39-2.47 (m, 1H), 1.77-1.85 (m, 2H), 1.07-1.11 (t, J = 7.2 Hz, 3H), 0.98-1.00 (d, J = 6.4 Hz, 6H). HR-MS (ESI): Calcd. $C_{11}H_{16}ClN_5S$, $[M+Na]^+$ m/z: 308.0713, found: 308.0715.

***General procedure for the synthesis of compounds* 3-27**

2-(7-((4-Chlorophenyl)amino)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl)ethan-1-ol (3)

The mixture of **1b** (100 mg, 1 eq), 4-chloroaniline (47 mg, 1 eq) and triethylamine (45 mg, 1.2 eq) in 20 ml of ethanol was refluxed overtime and monitored by TLC (PE/EA, 1:1). After completion of the reaction, the mixture was concentrated under reduced pressure. The residue was dissolved in ethyl acetate and washed with water successively. The pure product was obtained by flash column chromatography on silica gel using PE/EA (1:1) to afford compound **3** (83 mg, yield 62%**)** as a white solid. Mp 156~157 ^{o}C. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ 11.01 (s, 1H), 7.92-7.94 (d, J = 8.8 Hz, 2H), 7.44-7.46 (d, J = 8.8 Hz, 2H), 4.97-5.00 (t, J = 5.8 Hz, 1H), 4.55-4.58 (t, J = 5.4 Hz, 2H), 3.91-3.95 (q, 2H), 3.09-3.13 (t, J = 7.2 Hz, 2H), 1.68-1.74 (m, 2H), 0.96-1.00 (t, J = 7.2 Hz, 3H). ^{13}CNMR (100 MHz, DMSO-d_6, ppm): δ 169.70, 151.41, 150.48, 137.84, 128.92, 128.25, 123.70, 123.39, 59.27, 49.72, 32.94, 22.96, 13.76. HR-MS (ESI): Calcd. $C_{15}H_{17}ClN_6OS$, $[M+H]^+$ m/z: 365.0951, found: 365.0953.

2-(7-((4-Bromophenyl)amino)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl)ethan-1-ol (4)

Compound **4** was prepared from **1b** (100 mg, 1 eq), 4-bromoaniline (63 mg, 1 eq) and triethylamine (45 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **4** (75 mg, yield 50%) as a yellow solid. Mp 149~151 ^{o}C. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ 11.00(s,1H)，7.87-7.89 (d, J = 8.8 Hz, 2H), 7.57-7.60 (m, 2H), 4.55-4.58 (t, J = 5.6 Hz, 2H), 3.91-3.94 (t, J = 5.6 Hz, 2H), 3.09-3.13 (t, J = 7.1 Hz, 2H), 1.68-1.74 (m, 2H), 0.96-1.00 (t, J = 7.4 Hz, 3H). ^{13}CNMR (100 MHz, DMSO-d_6, ppm): δ 169.70, 151.39, 150.49, 138.27, 131.83, 124.06, 123.41, 116.37, 59.27, 49.72, 32.94, 22.96, 13.76. HR-MS (ESI): Calcd. $C_{15}H_{17}BrN_6OS$, $[M+H]^+$ m/z: 409.0446, found: 409.0444.

2-(7-((4-Fluorophenyl)amino)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl)ethan-1-ol (5)

Compound **5** was prepared from **1b** (100 mg, 1 eq), 4-fluoroaniline (41 mg, 1 eq) and triethylamine (45 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **5** (67 mg, yield 53%) as a light yellow

solid. Mp 140~141 °C. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ 10.92 (s, 1H)，7.87-7.90 (m, 2H), 7.23-7.27 (m, 2H), 4.98-5.00 (t, J = 5.6 Hz, 2H), 4.54-4.57 (t, J = 5.6 Hz, 2H), 3.91-3.95 (q, 2H), 3.08-3.11 (t, J = 7.0 Hz, 2H), 1.65-1.74 (m, 2H), 0.95-0.99 (t, J = 7.4 Hz, 3H). ^{13}CNMR (100 MHz, DMSO-d_6, ppm): δ 169.68, 151.53, 150.44, 135.10, 124.25, 123.30, 115.78, 115.57, 59.27, 49.68, 32.91, 23.01, 13.75. HR-MS (ESI): Calcd. $C_{15}H_{17}FN_6OS$, $[M+Na]^+$ m/z: 371.1066, found: 371.1072.

2-(5-(Propylthio)-7-((3,4,5-trimethoxyphenyl)amino)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl)ethan-1-ol (6)

Compound **6** was prepared from **1b** (100 mg, 1 eq), 3,4,5-trimethoxyaniline (67 mg, 1 eq) and triethylamine (45 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **6** (110 mg, yield 72%) as a white solid. Mp 163~165 °C. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm): δ 8.34 (s, 1H)，7.13 (s, 2H), 4.72-4.75 (t, J = 4.8 Hz, 2H), 4.38-4.42 (t, J = 6.8 Hz, 1H), 4.25-4.27 (q, 2H), 3.90 (s, 6H), 3.85 (s, 3H), 3.08-3.12 (t, J = 7.2 Hz, 2H), 1.73-1.78 (q, 2H), 1.03-1.06 (t, J = 7.2 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm): δ 171.52, 153.24, 150.62, 149.64, 134.89, 133.58, 123.33, 98.59, 61.00, 60.70, 56.18, 50.94, 33.24, 22.30, 13.50. HR-MS (ESI): Calcd. $C_{18}H_{24}N_6O_4S$, $[M+Na]^+$ m/z: 443.1477, found: 443.1479.

2-(7-(Benzylamino)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl)ethan-1-ol (7)

Compound **7** was prepared from **1b** (100 mg, 1 eq), benzylamine (40 mg, 1 eq) and triethylamine (45 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **7** (98 mg, yield 78%) as a white solid. Mp 139~140 °C. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm): δ 7.31-7.41 (m, 5H), 7.14-7.15 (m, 1H), 4.88-4.90 (d, J = 6 Hz, 2H), 4.68-4.70 (t, J = 4.6 Hz, 2H), 4.45 (m, 1H), 4.16 (m, 2H), 3.10-3.13 (t, J = 7.4 Hz, 2H), 1.73-1.82 (m, 2H), 1.03-1.07 (t, J = 7.2 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm): δ 171.42, 153.23, 149.55, 137.44, 128.79, 127.89, 127.79, 123.30, 60.85, 51.17, 44.68, 33.36, 22.71, 13.51. HR-MS (ESI): Calcd. $C_{16}H_{20}N_6OS$, $[M+Na]^+$ m/z: 367.1317, found: 367.1319.

2-(7-((4-Methylbenzyl)amino)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-

3-yl)ethan-1-ol (8)

Compound **8** was prepared from **1b** (100 mg, 1 eq), 4-methylbenzylamine (44 mg, 1 eq) and triethylamine (45 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **8** (88 mg, yield 67%) as a white solid. Mp 154~155 ^{o}C. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm): δ 7.28-7.30 (d, J = 8.0 Hz, 2H), 7.16-7.18 (d, J = 7.9 Hz, 2H), 4.83-4.85 (d, J = 5.6 Hz, 2H), 4.68-4.70 (t, J = 4.6 Hz, 2H), 4.47-4.50 (t, J = 6.4 Hz, 1H), 4.14-4.17 (m, 2H), 3.121-3.14 (t, J = 7.2 Hz, 2H), 2.36 (s, 3H), 1.79-1.82 (m, 2H), 1.06 (t, J = 7.4 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm): δ 171.39, 153.18, 149.51, 137.55, 134.37, 129.44, 127.94, 123.31, 60.85, 51.21, 44.46, 33.36, 22.72, 21.14, 13.52. HR-MS (ESI): Calcd. $C_{17}H_{22}N_6OS$, $[M+Na]^+$ m/z: 381.1473, found: 381.1475.

2-(7-((4-Methoxybenzyl)amino)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl)ethan-1-ol (9)

Compound **9** was prepared from **1b** (100 mg, 1 eq), 4-methoxybenzylamine (50 mg, 1 eq) and triethylamine (45 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **9** (110 mg, yield 81%) as a white solid. Mp 148~149 ^{o}C. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ 9.45-9.48 (t, J = 6 Hz, 1H), 7.27-7.29 (d, J = 8.8 Hz, 2H), 6.88-6.90 (d, J = 8.8 Hz, 2H), 4.94-4.97 (t, J = 5.8 Hz, 1H), 4.64-4.66 (d, J = 6.0 Hz, 2H), 4.48-4.50 (t, J = 5.4 Hz, 2H), 3.86-3.91 (q, 2H), 3.72 (s, 3H), 3.04-3.07 (t, J = 7.2 Hz, 2H), 1.61-1.72 (m, 2H), 0.92-0.96 (t, J = 7.4 Hz, 3H). ^{13}CNMR (100 MHz, DMSO-d_6, ppm): δ 169.59, 158.74, 153.42, 150.05, 131.35, 129.04, 123.22, 114.28, 114.18, 59.28, 55.51, 49.52, 43.11, 32.90, 23.08, 13.78. HR-MS (ESI): Calcd. $C_{17}H_{22}N_6O_2S$, $[M+H]^+$ m/z: 375.1603, found: 375.1608.

4-(((3-(2-Hydroxyethyl)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-7-yl)amino)methyl)phenol (10)

Compound **10** was prepared from **1b** (100 mg, 1 eq), 4-hydroxybenzylamine (45 mg, 1 eq) and triethylamine (45 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **10** (99 mg, yield 75%) as a white solid. Mp 198~199 ^{o}C. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ 9.40-9.43 (t, J = 6.0 Hz, 1H), 9.31 (s, 1H), 7.15-7.17 (d, J = 8.4 Hz, 2H), 6.70-6.72 (d, J = 8.4 Hz,

2H), 4.94-4.97 (t, *J* = 5.8 Hz, 1H), 4.60-4.62 (d, *J* = 6 Hz, 2H), 4.48-4.50 (d, *J* = 5.4 Hz, 2H), 3.86-3.91 (m, 2H), 3.05-3.08 (t, *J* = 7.2 Hz, 2H), 1.62-1.70 (m, 2H), 0.93-0.97 (t, *J* = 7.4 Hz, 3H). ^{13}CNMR (100 MHz, DMSO-d_6, ppm): δ 169.58, 156.81, 153.40, 150.04, 129.57, 129.08, 123.21, 115.50, 59.29, 49.51, 43.20, 32.90, 23.09, 13.78. HR-MS (ESI): Calcd. $C_{16}H_{20}N_6O_2S$, $[M+H]^+$ m/z: 361.1447, found: 361.1448.

2-(7-(4-Benzylpiperazin-1-yl)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl)ethan-1-ol (11)

Compound **11** was prepared from **1b** (100 mg, 1 eq), benzylpiperazine (65 mg, 1 eq) and triethylamine (45 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **11** (116 mg, yield 77%) as a yellow solid. Mp 115~116 ^{o}C. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm): δ 7.36-7.37(m, 4H), 7.31-7.33 (m, 1H), 4.70-4.72 (t, *J* = 4.6 Hz, 2H), 4.66 (m, 2H), 4.51 (br, 1H), 4.09-4.15 (m, 4H), 3.60 (s, 2H), 3.07-3.11 (t, *J* = 7.2 Hz, 2H), 2.58-2.67 (m, 4H), 1.76-1.81 (m, 2H), 1.05-1.08 (t, *J* = 7.4 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm): δ 170.07, 152.29, 150.86, 137.48, 129.20, 128.39, 127.37, 123.85, 62.93, 61.10, 53.23, 52.67, 51.28, 47.35, 43.69, 33.21, 22.69, 13.51. HR-MS (ESI): Calcd. $C_{20}H_{27}N_7OS$, $[M+H]^+$ m/z: 414.2076, found: 414.2078.

3-Benzyl-7-(4-benzylpiperazin-1-yl)-5-(prop-2-yn-1-ylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidine (12)

Compound **12** was prepared from **1c** (100 mg, 1 eq), benzylpiperazine (56 mg, 1 eq) and triethylamine (39 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **12** (85 mg, yield 77%) as a yellow solid. Mp 103~104 ^{o}C. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm): δ 7.43-7.45 (m, 2H), 7.32-7.34 (m, 4H), 7.28-7.30 (m, 4H), 5.65 (s, 2H), 4.64 (s, 2H), 4.06 (s, 2H), 3.89-3.90 (d, *J* = 2.4 Hz, 2H), 3.56 (s, 2H), 2.55-2.62 (m, 4H), 2.16 (t, *J* = 2.6 Hz, 1H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm): δ 167.84, 152.49, 150.76, 137.48, 135.06, 129.18, 128.75, 128.54, 128.35, 128.31, 127.32, 123.82, 80.22, 70.15, 62.91, 53.19, 52.70, 50.16, 47.27, 43.70, 19.73. HR-MS (ESI): Calcd. $C_{25}H_{25}N_7S$, $[M+H]^+$m/z:456.1970, found: 456.1971.

Tert-butyl4-(3-benzyl-5-(prop-2-yn-1-ylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-

7-yl)piperazine-1-carboxylate (13)

Compound **13** was prepared from **1c** (100 mg, 1 eq), 1-boc-piperazine (59 mg, 1 eq) and triethylamine (39 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **13** (121 mg, yield 82%) as a yellow solid. Mp 128~129 ^{o}C. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm): δ 7.44-7.46 (m, 2H), 7.29-7.34 (m, 3H), 5.67 (s, 1H), 4.61 (s, 2H), 4.04 (s, 2H), 3.90-3.91 (d, J = 2.8 Hz, 2H), 3.56-3.60 (m, 4H), 2.17-2.18 (t, J = 2.8 Hz, 1H), 1.49 (s, 9H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm): δ 168.00, 154.58, 152.69, 150.81, 134.95, 128.78, 128.58, 128.38, 123.79, 80.41, 80.15, 70.21, 50.26, 47.13, 43.52, 28.40, 19.78. HR-MS (ESI): Calcd. $C_{23}H_{27}N_7O_2S$, $[M+H]^+$ m/z: 466.2025, found: 466.2026.

2-(7-(3-Chlorophenoxy)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl)ethan-1-ol (14)

The mixture of **1b** (100 mg, 1 eq), 3-chlorophenol (47 mg, 1 eq) and K_2CO_3 (60 mg, 1.2 eq) in 20 ml of ethanol was refluxed for 3 h and monitored by TLC (PE/EA, 1:1). After completion of the reaction, the reaction mixture was concentrated under reduced pressure. The residue was dissolved in ethyl acetate and washed with water successively. The pure product was obtained by flash column chromatography on silica gel using PE/EA (1:1) to afford compound **14** (114 mg, yield 85%) as a white solid. Mp 143~144 ^{o}C. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm): δ 7.38-7.42 (t, J = 8.0 Hz, 1H), 7.31-7.33 (m, 2H), 7.18-7.21 (m, 1H), 4.77-4.80 (t, J = 4.8 Hz, 2H), 4.19-4.23 (m, 2H), 3.20-3.23 (t, J = 6.6 Hz, 1H), 2.89-2.93 (t, J = 7.4 Hz, 1H), 1.58-1.63 (m, 2H), 0.88-0.92 (t, J = 7.4 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm): δ 171.57, 159.37, 152.75, 152.03, 134.84, 130.35, 126.65, 123.62, 122.57, 120.22, 60.78, 50.69, 33.62, 22.67, 13.30. HR-MS (ESI): Calcd. $C_{15}H_{16}ClN_5O_2S$, $[M+Na]^+$ m/z: 388.0611, found: 388.0612.

2-(7-(4-Chlorophenoxy)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl)ethan-1-ol (15)

Compound **15** was prepared from **1b** (100 mg, 1 eq), 4-chlorophenol (47 mg, 1 eq) and K_2CO_3 (60 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **14** to afford compound **15** (106 mg, yield 79%) as a white

solid. Mp 153~155 ^{o}C. ^{1}HNMR (400 MHz, DMSO-d_6, ppm): δ 7.59-7.61 (d, J = 8.8 Hz, 2H), 7.45-7.48 (d, J = 8.8 Hz, 2H), 4.97-4.50 (t, J = 5.8 Hz, 1H), 4.64-4.66 (t, J = 5.4 Hz, 2H), 3.92-3.96 (m, 2H), 2.89-2.93 (t, J = 7.2 Hz, 1H), 1.51-1.57 (m, 2H), 0.80-0.84 (t, J = 7.2 Hz, 3H). ^{13}CNMR (100 MHz, DMSO-d_6, ppm): δ 169.26, 159.20, 152.64, 150.17, 130.56, 129.69, 123.90, 123.07, 58.79, 49.67, 32.67, 22.38, 13.08. HR-MS (ESI): Calcd. $C_{15}H_{16}ClN_5O_2S$, $[M+Na]^+$ m/z:388.0611, found: 388.0612.

2-(7-(Naphthalen-1-yloxy)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl)ethan-1-ol (16)

Compound **16** was prepared from **1b** (100 mg, 1 eq), 1-naphthol (53 mg, 1 eq) and K_2CO_3 (60 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **14** to afford compound **16** (94 mg, yield 67%) as a white solid. Mp 124~125 ^{o}C. ^{1}HNMR (400 MHz, Chloroform-d, ppm): δ 7.83-7.93 (m, 3H), 7.51-7.56 (m, 2H), 7.44-7.48 (m, 1H), 7.39-7.41 (d, J = 7.2 Hz, 1H), 4.79-4.81 (t, J = 5.0 Hz, 2H), 4.20-4.24 (m, 2H), 3.31-3.34 (t, J = 6.4 Hz, 1H), 2.55-2.59 (t, J = 7.4 Hz, 2H), 1.19-1.28 (m, 2H), 0.56-0.60 (t, J = 7.4 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-d, ppm): δ 171.66, 160.28, 152.85, 147.89, 134.79, 128.05, 126.89, 126.68, 126.64, 126.58, 125.38, 123.71, 121.51, 118.22, 60.84, 50.73, 33.47, 22.60, 13.09. HR-MS (ESI): Calcd. $C_{19}H_{19}N_5O_2S$, $[M+Na]^+$ m/z: 404.1157, found: 404.1155.

2-(7-(naphthalen-2-yloxy)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl) ethan-1-ol (17)

Compound **17** was prepared from **1b** (100 mg, 1 eq), 2-naphthol (53 mg, 1 eq) and K_2CO_3 (60 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **14** to afford compound **17** (102 mg, yield 73%) as a white solid. Mp 127~128 ^{o}C. ^{1}HNMR (400 MHz, Chloroform-d, ppm): δ 7.89-7.94 (m, 2H), 7.84-7.86 (m, 1H), 7.73-7.74 (d, J = 2.0 Hz, 1H), 7.52-7.54 (m, 2H), 7.39-7.42 (m, 1H), 4.79-4.81 (t, J = 4.8 Hz, 2H), 4.20-4.24 (m, 2H), 3.33-3.36 (t, J = 6.5 Hz, 1H), 2.79-2.83 (t, J = 7.4 Hz, 2H), 1.47-1.53 (m, 2H), 0.66-0.70 (t, J = 7.4 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-d, ppm): δ 171.62, 159.97, 152.67, 149.35, 133.81, 131.70, 129.51, 127.86, 127.75, 126.76, 126.04, 123.87, 121.22, 118.80, 60.83, 50.76,

33.54, 22.67, 13.11. HR-MS (ESI): Calcd. $C_{19}H_{19}N_5O_2S$, $[M+Na]^+$ m/z: 404.1157, found: 404.1155.

2-(5-(Propylthio)-7-(p-tolylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl)ethan-1-ol (18)

Compound **18** was prepared from **1b** (100 mg, 1 eq), 4-toluenethiol (45 mg, 1 eq) and triethylamine (45 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **18** (95 mg, yield 72%) as a orange solid. Mp 107~108 ^oC. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm): δ 7.50-7.52 (d, J = 8.4 Hz, 2H), 7.27-7.29 (d, J = 8.0 Hz, 2H), 4.72-4.74 (t, J = 4.8 Hz, 2H), 4.14-4.18 (m, 2H), 3.34-3.37 (t, J = 6.6 Hz, 1H), 2.75-2.79 (t, J = 7.2 Hz, 2H), 2.43 (s, 3H), 1.43-1.49 (m, 2H), 0.82-0.86 (t, J = 7.4 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm): δ 170.34, 165.08, 148.66, 140.43, 135.96, 131.63, 130.15, 122.00, 60.81, 50.58, 33.44, 22.53, 21.43, 13.28. HR-MS (ESI): Calcd. $C_{16}H_{19}N_5OS_2$, $[M+Na]^+$ m/z: 384.0929, found: 384.0931.

2-(7-((4-Chlorophenyl)thio)-5-(propylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl)ethan-1-ol (19)

Compound **19** was prepared from **1b** (100 mg, 1 eq), 4-chlorothiophenol (53 mg, 1 eq) and triethylamine (45 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **19** (96 mg, yield 69%) as a white solid. Mp 114~115 ^oC. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm): δ 7.56-7.58 (d, J = 8.4 Hz, 2H), 7.45-7.47 (d, J = 8.8 Hz, 2H), 4.73-4.75 (t, J = 5.0 Hz, 2H), 4.15-4.19 (m, 2H), 3.18-3.22 (t, J = 6.4 Hz, 1H), 2.78-2.82 (t, J = 7.4 Hz, 2H), 1.47-1.53 (m, 2H), 0.88-0.91 (t, J = 7.2 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm): δ 170.55, 164.02, 148.77, 137.32, 136.73, 131.54, 129.63, 124.05, 60.79, 50.57, 33.50, 22.41, 13.31. HR-MS (ESI): Calcd. $C_{15}H_{16}ClN_5OS_2$, $[M+Na]^+$ m/z: 404.0382, found: 404.0381.

2-(5-(Propylthio)-7-(pyridin-2-ylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-3-yl)ethan-1-ol (20)

Compound **20** was prepared from **1b** (100 mg, 1 eq), 2-mercaptopyridine (41 mg, 1 eq) and triethylamine (45 mg, 1.2 eq) according to the procedure described above for

the synthesis of compound **3** to afford compound **20** (102 mg, yield 81%) as yellow sticky oil. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm): δ 8.68-8.69 (m, 1H), 7.80-7.82 (m, 2H), 7.38-7.42 (m, 1H), 4.71-4.74 (t, J = 5.0 Hz, 2H), 4.16-4.18 (t, J = 5.0 Hz, 2H), 2.84-2.87 (t, J = 7.2 Hz, 2H), 1.52-1.61 (m, 2H), 0.90-0.93 (t, J = 7.2 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm): δ 170.48, 163.72, 150.80, 150.02, 148.92, 137.34, 131.72, 131.38, 124.17, 60.68, 50.43, 33.42, 22.28, 13.34. HR-MS (ESI): Calcd. $C_{14}H_{16}N_6OS_2$, $[M+H]^+$ m/z: 349.0905, found: 349.0902.

3-(Furan-2-ylmethyl)-5-(propylthio)-7-(pyridin-2-ylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidine (21)

Compound **21** was prepared from **1h** (100 mg, 1 eq), 2-mercaptopyridine (36 mg, 1 eq) and triethylamine (45 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **21** (103 mg, yield 83%) as yellow semi-solid. ^{1}HNMR (400 MHz, Chloroform-*d*) δ 8.68-8.69 (m, 1H), 7.77-7.82 (m, 2H), 7.37-7.40 (m, 1H), 7.35 (m, 1H), 6.45-6.46 (d, J = 3.3 Hz, 1H), 6.33-6.34 (m, 1H), 5.71 (s, 2H), 2.88-2.91 (t, J = 7.2 Hz, 2H), 1.56-1.62 (m, 2H), 0.92-0.95 (t, J = 7.4 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm): δ 170.54, 163.39, 150.78, 150.15, 148.62, 147.30, 143.26, 137.29, 131.56, 131.28, 124.10, 110.70, 110.07, 43.13, 33.41, 22.37, 13.44. HR-MS (ESI): Calcd. $C_{17}H_{16}N_6OS_2$, $[M+H]^+$ m/z: 385.0905, found: 385.0901.

3-Isobutyl-5-(propylthio)-7-(pyridin-2-ylthio)-3H-[1,2,3]triazolo[4,5-d]-pyrimidine (22)

Compound **22** was prepared from **1e** (100 mg, 1 eq), 2-mercaptopyridine (39 mg, 1 eq) and triethylamine (42 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **22** (91 mg, yield 72%) as yellow oil. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm) δ 8.69-8.71 (m, 1H), 7.79-7.85 (m, 2H), 7.38-7.42 (m, 1H), 4.36-4.38 (d, J = 7.2 Hz, 2H), 2.85-2.89 (t, J = 7.2 Hz, 2H), 2.38-2.45 (m, 1H), 1.54-1.60 (m, 2H), 0.95-0.96 (d, J = 6.8 Hz, 6H), 0.90-0.94 (t, J = 7.4 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm): δ 170.03, 163.18, 150.77, 150.18, 148.99, 137.27, 131.50, 131.35, 124.07, 53.94, 33.37, 29.00, 22.41, 19.96, 13.41. HR-MS (ESI): Calcd. $C_{16}H_{20}N_6S_2$, $[M+H]^+$ m/z:361.1269, found: 361.1268.

3-Cyclopentyl-5-(propylthio)-7-(pyridin-2-ylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidine (23)

Compound **23** was prepared from **1d** (100 mg, 1 eq), 2-mercaptopyridine (37 mg, 1 eq) and triethylamine (41 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **23** (86 mg, yield 69%) as yellow sticky oil. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm) δ 8.68– 8.70 (m, 1H), 7.78-7.84 (m, 2H), 7.37-7.41 (m, 1H), 5.21-5.28 (m, 1H), 2.87-2.91 (t, *J* = 7.2 Hz, 2H), 2.23-2.28 (m, 4H), 2.00-2.04 (m, 2H), 1.75-1.80 (m, 2H), 1.56-1.62 (m, 2H), 0.91-0.95 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, Chloroform-*d*, ppm): *δ* 169.51, 163.12, 150.72, 150.35, 148.43, 137.24, 132.00, 131.23, 124.02, 59.25, 33.37, 32.46, 24.55, 22.43, 13.41. HR-MS (ESI): Calcd. $C_{17}H_{20}N_6S_2$, $[M+H]^+$ m/z: 373.1269, found: 373.1271.

5-(Propylthio)-7-(pyridin-2-ylthio)-3-(2-(thiophen-2-yl)ethyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidine (24)

Compound **24** was prepared from **1g** (100 mg, 1 eq), 2-mercaptopyridine (33 mg, 1 eq) and triethylamine (36 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **24** (92 mg, yield 75%) as yellow sticky oil. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm): *δ* 8.69-8.70 (m, 1H), 7.78-7.84 (m, 2H), 7.38-7.41 (m, 1H), 7.12-7.14 (m, 1H), 6.86-6.89 (m, 1H), 6.76-6.77 (d, *J* = 3.4 Hz, 1H), 4.79-4.83 (t, *J* = 7.3 Hz, 2H), 3.53-3.57 (t, *J* = 7.3 Hz, 2H), 2.84-2.88 (t, *J* = 7.2 Hz, 2H), 1.54-1.59 (m, 2H), 0.91-0.95 (t, *J* = 7.3 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm): *δ* 170.23, 163.23, 150.75, 150.06, 148.78, 138.64, 137.29, 131.52, 131.34, 127.06, 125.94, 124.48, 124.10, 48.05, 33.36, 29.59, 22.37, 13.44. HR-MS (ESI): Calcd. $C_{18}H_{18}N_6S_3$, $[M+H]^+$m/z: 415.0833, found: 415.0832.

3-Benzyl-5-(propylthio)-7-(pyridin-2-ylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidine (25)

Compound **25** was prepared from **1b** (100 mg, 1 eq), 2-mercaptopyridine (35 mg, 1 eq) and triethylamine (38 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **25** (101 mg, yield 82%) as yellow oil. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm) *δ* 8.67-8.68 (m, 1H), 7.76-7.82 (m, 2H),

7.36-7.41 (m, 3H), 7.30-7.34 (m, 3H), 5.71 (s, 2H), 2.87-2.91 (t, *J* = 7.2 Hz, 2H), 1.55-1.61 (m, 2H), 0.91-0.95 (t, *J* = 7.3 Hz, 3H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm) *δ* 170.37, 163.33, 150.74, 150.18, 148.63, 137.26, 134.48, 131.66, 131.21, 128.84, 128.53, 128.41, 124.05, 50.52, 33.37, 22.37, 13.45. HR-MS (ESI): Calcd. $C_{19}H_{18}N_6S_2$, $[M+H]^+$ m/z: 395.1113, found: 395.1111.

3-Benzyl-5-(prop-2-yn-1-ylthio)-7-(pyridin-2-ylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidine (26)

Compound **26** was prepared from **1c** (100 mg, 1 eq), 2-mercaptopyridine (35 mg, 1 eq) and triethylamine (38 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **26** (100 mg, yield 82%) as yellow semi-solid. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm) δ 8.67-8.69 (m, 1H), 7.78-7.84 (m, 2H), 7.38-7.44(m, 3H), 7.29-7.35 (m, 3H), 5.73 (s, 2H), 3.67 (d, *J* = 2.6 Hz, 2H), 2.13-2.14 (t, *J* = 2.7 Hz, 1H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm) δ 168.06, 163.90, 150.80, 149.83, 148.52, 137.37, 134.32, 131.80, 131.37, 128.88, 128.60, 128.53, 124.20, 79.25, 70.76, 50.67, 19.84. HR-MS (ESI): Calcd. $C_{19}H_{14}N_6S_2$, $[M+Na]^+$ m/z: 413.0619, found: 413.0619.

3-Benzyl-5-(benzylthio)-7-(pyridin-2-ylthio)-3H-[1,2,3]triazolo[4,5-d]pyrimidine (27)

Compound **27** was prepared from **1a** (100 mg, 1 eq), 2-mercaptopyridine (30 mg, 1 eq) and triethylamine (33 mg, 1.2 eq) according to the procedure described above for the synthesis of compound **3** to afford compound **27** (102 mg, yield 85%) as a white solid. Mp 114~116 ^{o}C. ^{1}HNMR (400 MHz, Chloroform-*d*, ppm) *δ* 8.62-8.64 (m, 1H), 7.78-7.80 (m, 1H), 7.68-7.73 (m, 1H), 7.36-7.38 (m, 2H), 7.30-7.33 (m, 4H), 7.25-7.26 (m, 5H), 5.72 (s, 2H), 4.20 (s, 2H). ^{13}CNMR (100 MHz, Chloroform-*d*, ppm) *δ* 169.66, 163.64, 150.72, 150.04, 148.59, 137.24, 136.99, 134.44, 131.75, 131.18, 128.90, 128.78, 128.55, 128.50, 128.34, 127.29, 124.10, 50.53, 35.66. HR-MS (ESI): Calcd. $C_{23}H_{18}N_6S_2$, $[M+H]^+$ m/z: 443.1113, found: 443.1115.

References

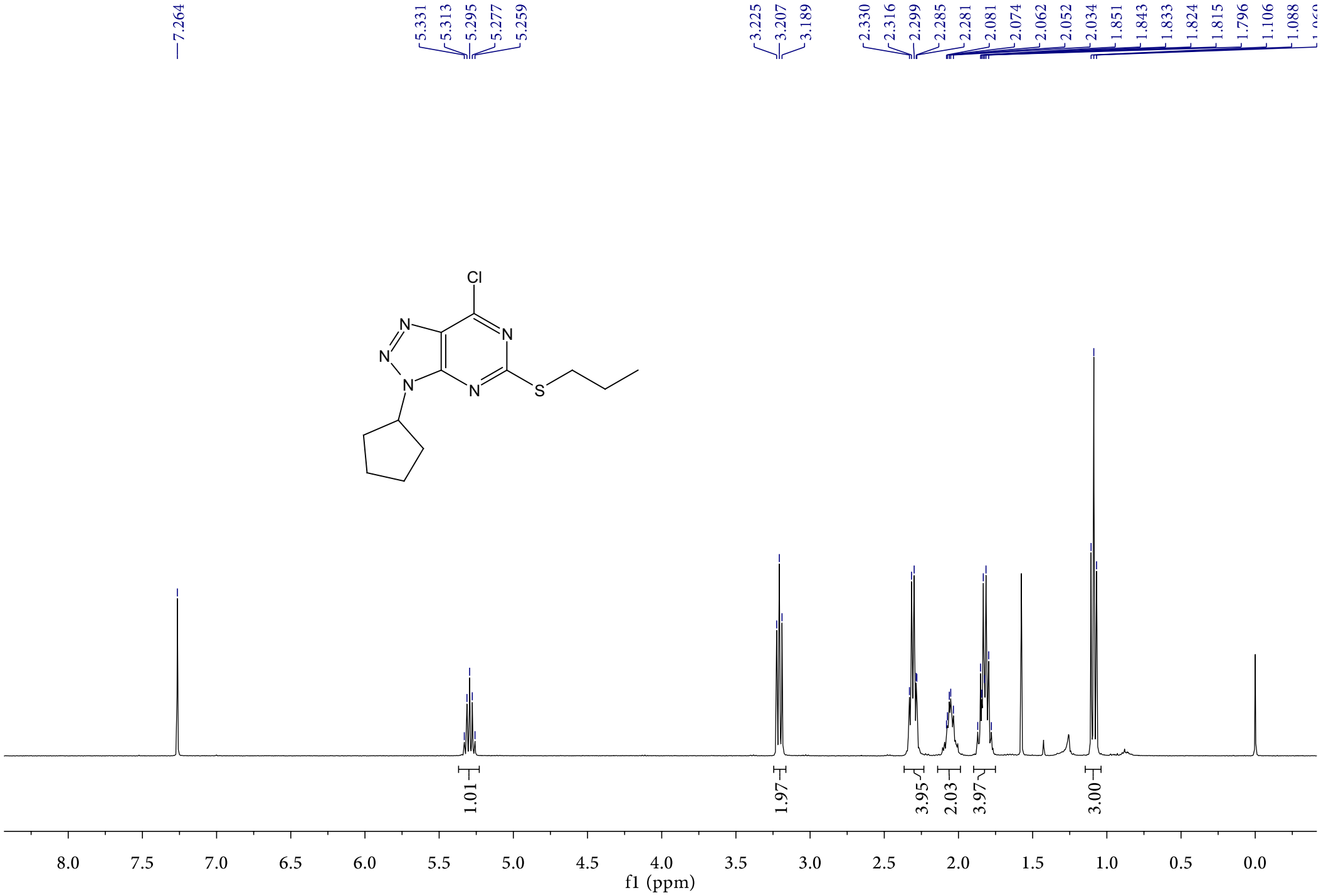
(1) Zheng, Y. C.; Duan, Y. C.; Ma, J. L.; Xu, R. M.; Zi, X.; Lv, W. L.; Wang, M. M.; Ye, X. W.; Zhu, S.;

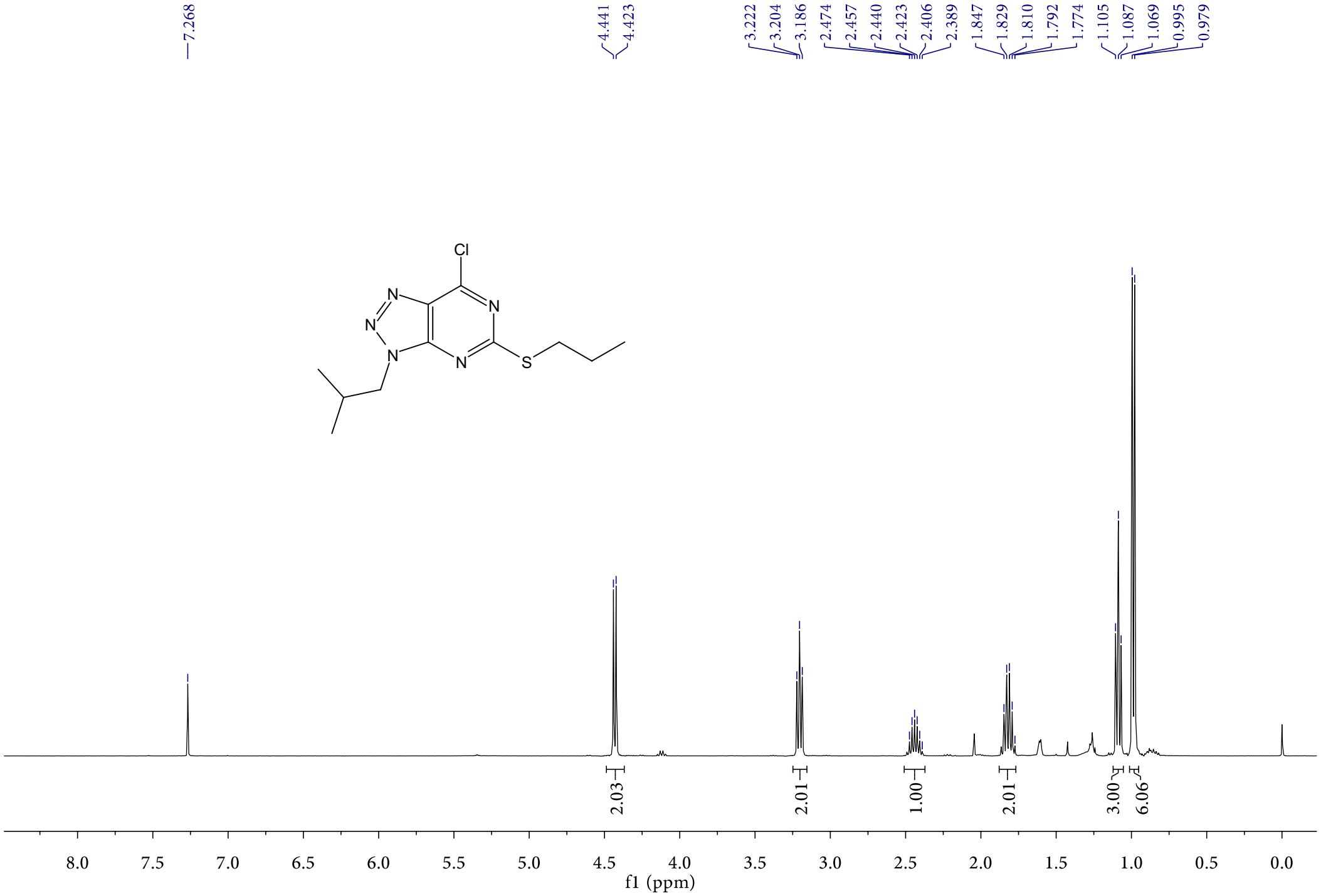
Mobley, D.; Zhu, Y. Y.; Wang, J. W.; Li, J. F.; Wang, Z. R.; Zhao, W.; Liu, H. M. Triazole-dithiocarbamate based selective lysine specific demethylase 1 (LSD1) inactivators inhibit gastric cancer cell growth, invasion, and migration. *J Med Chem* 2013, 56, 8543-60.

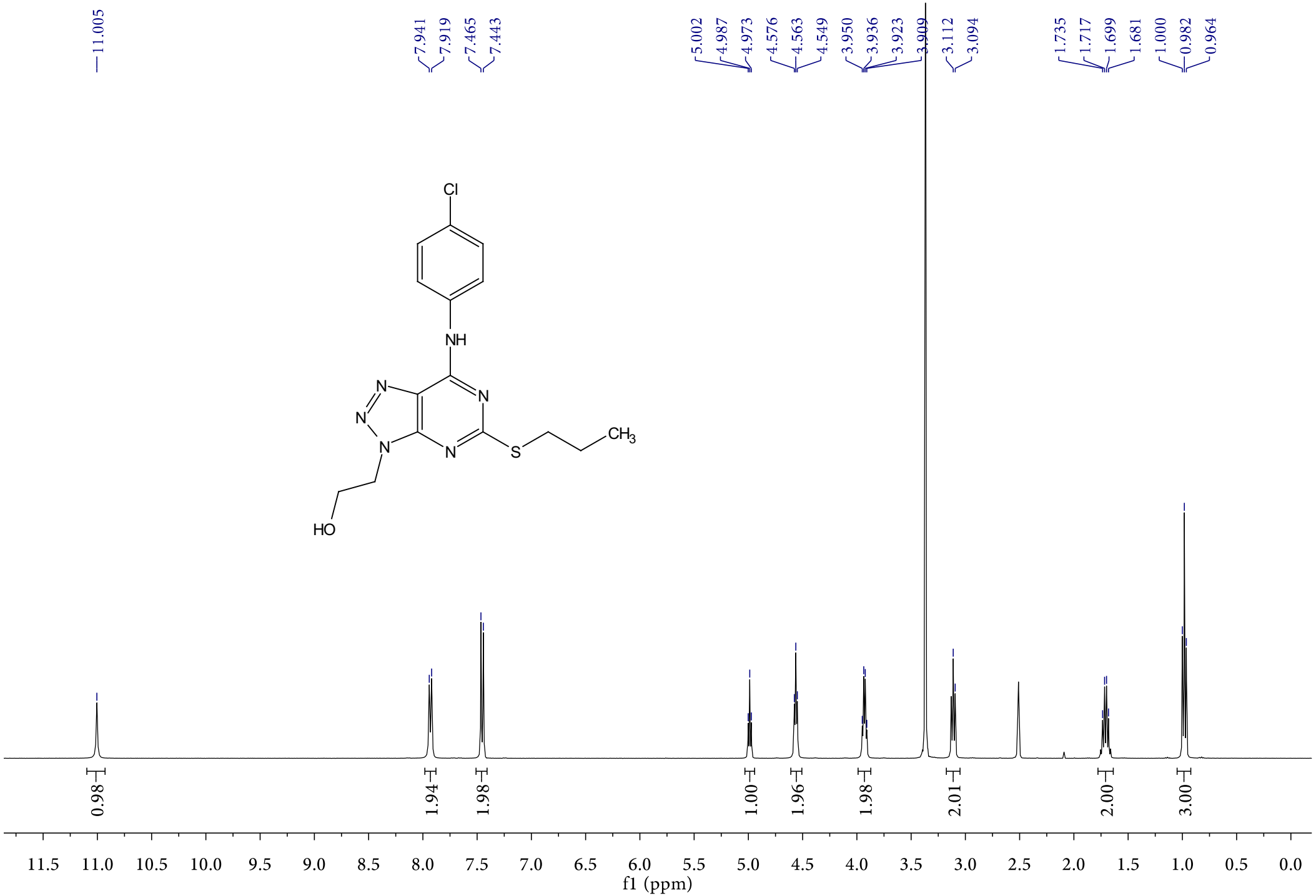
(2) Willmann, D.; Lim, S.; Wetzel, S.; Metzger, E.; Jandausch, A.; Wilk, W.; Jung, M.; Forne, I.; Imhof, A.; Janzer, A.; Kirfel, J.; Waldmann, H.; Schule, R.; Buettner, R. Impairment of prostate cancer cell growth by a selective and reversible LSD1 inhibitor. Int. J. Cancer 2012, 131, 2704-2709.

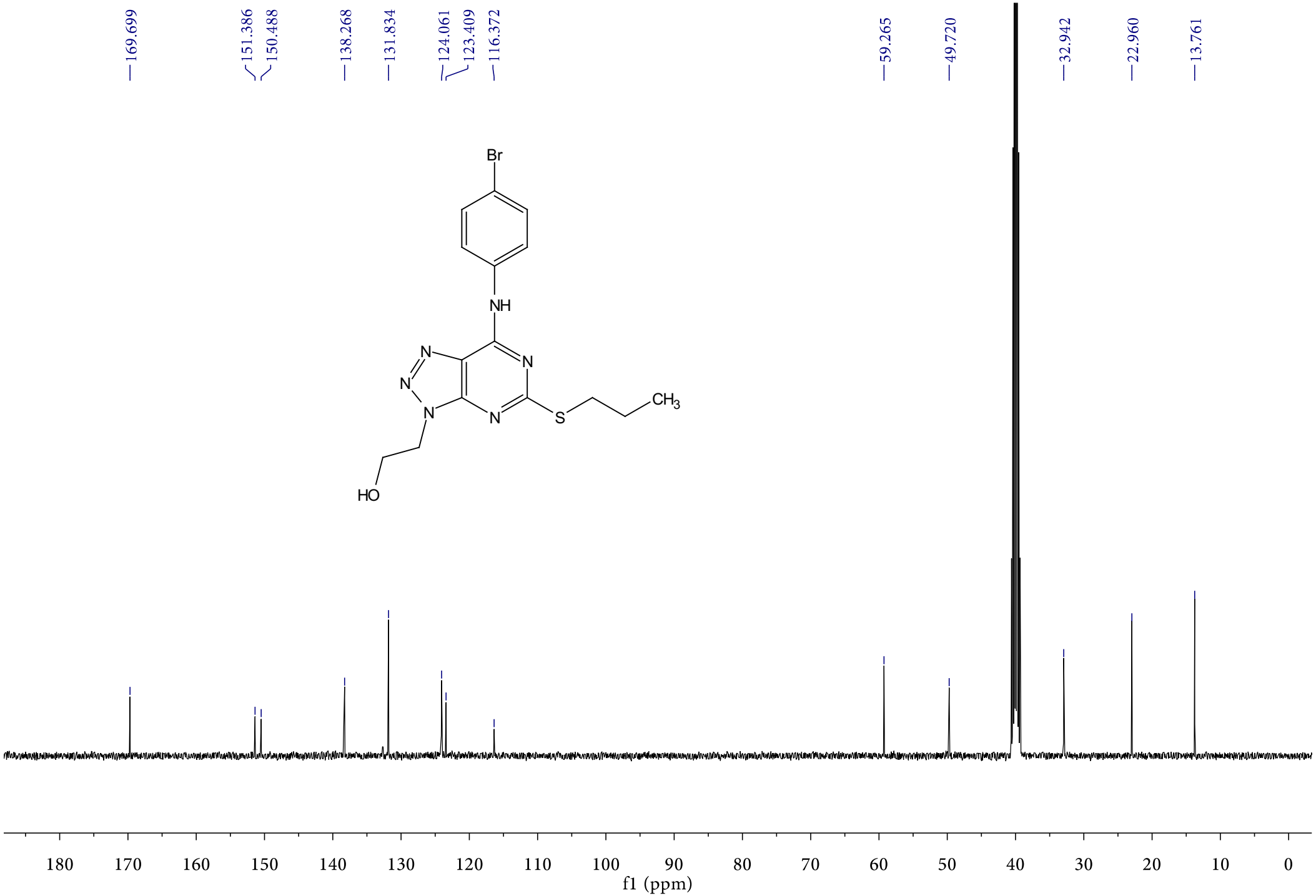
(3) Li, Z. H.; Yang, D. X.; Geng, P. F.; Zhang, J.; Wei, H. M.; Hu, B.; Guo, Q.; Zhang, X. H.; Guo, W. G.; Zhao, B.; Yu, B.; Ma, L. Y.; Liu, H. M. Design, synthesis and biological evaluation of [1,2,3]triazolo[4,5-d]pyrimidine derivatives possessing a hydrazone moiety as antiproliferative agents. *Eur J Med Chem* 2016, 124, 967-980.

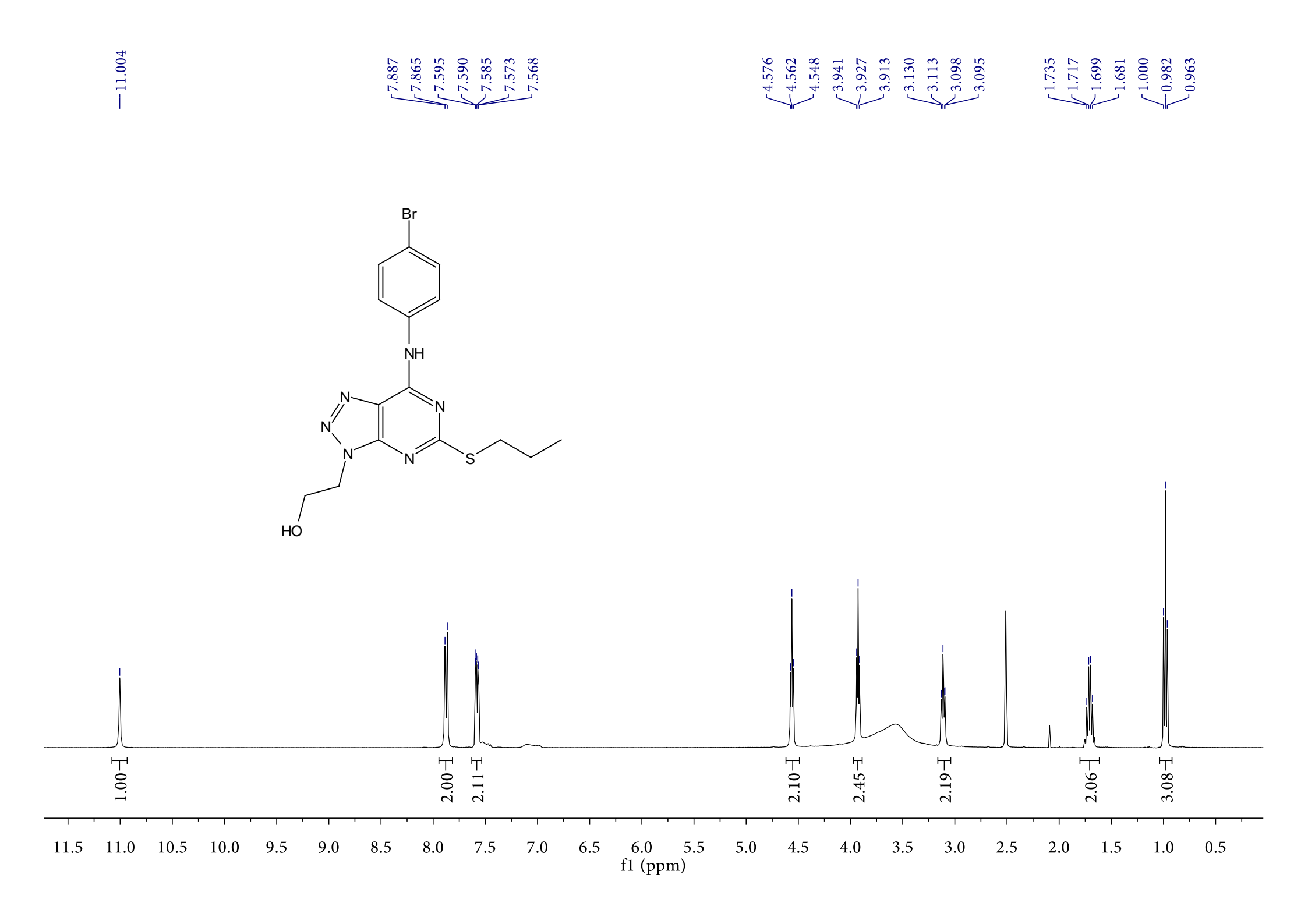
The NMR spectra of compounds **1d-e** and **3-27**

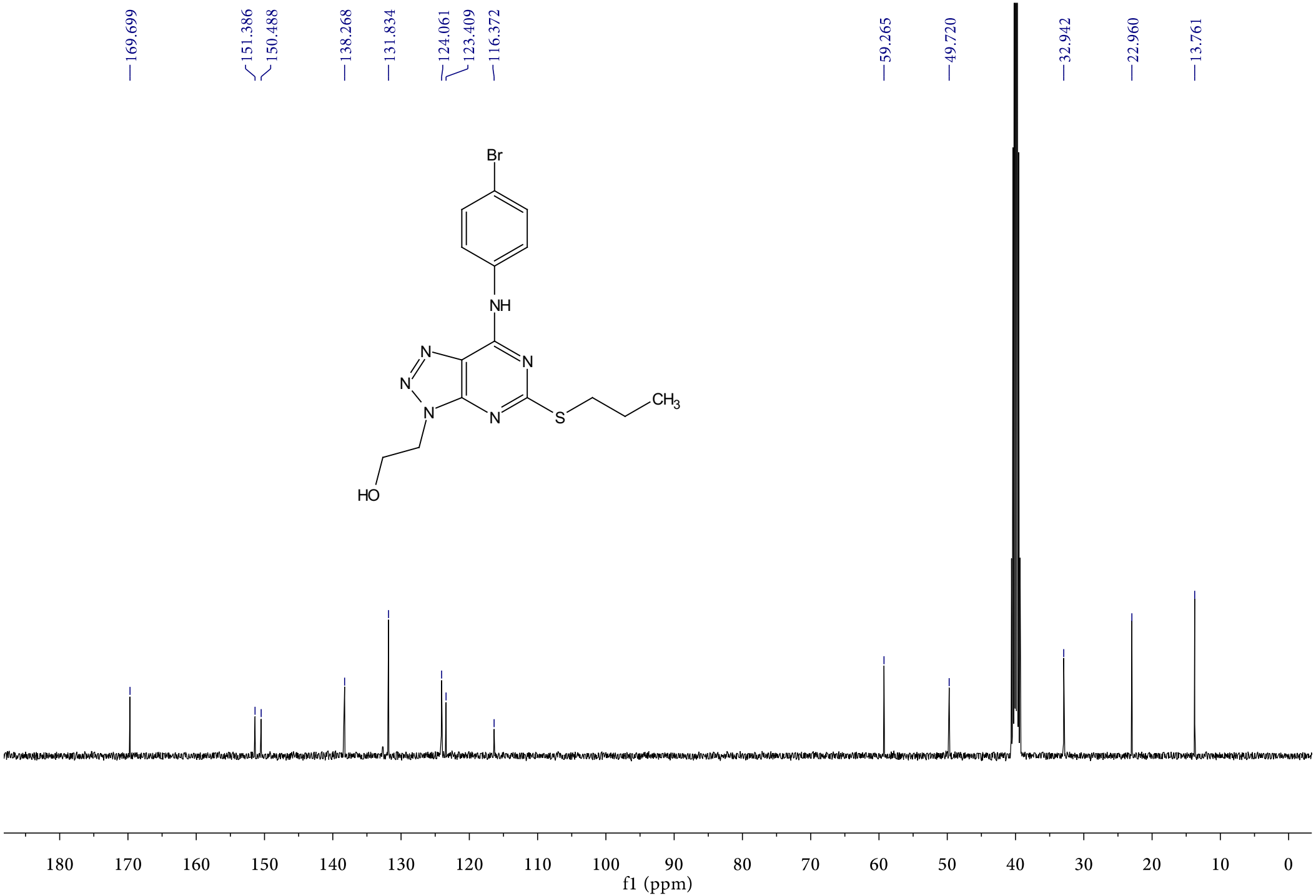

7.264
5.331
5.313
5.295
5.277
5.259
3.225
3.207
3.189
2.330
2.316
2.299
2.285
2.281
2.081
2.074
2.062
2.052
2.034
1.851
1.843
1.833
1.824
1.815
1.796
1.106
1.088
Cl
N
N
N
N
N
S
1.01
1.97
3.95
2.03
3.97
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

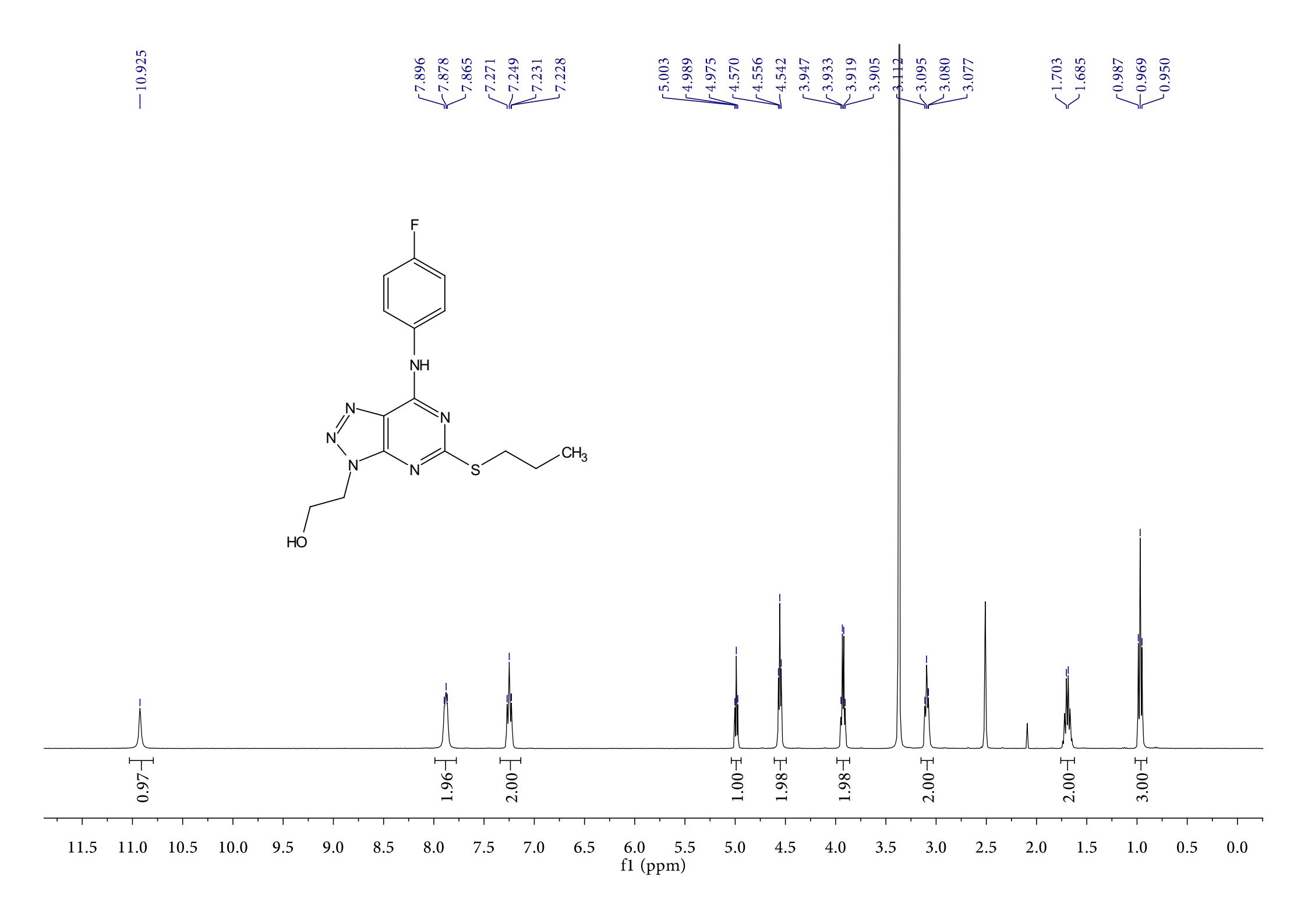

7.268
4.441
4.423
3.222
3.204
3.186
2.474
2.457
2.440
2.423
2.406
2.389
1.847
1.829
1.810
1.792
1.774
1.105
1.087
1.069
0.995
0.979
Cl
N
N
N
N
S
2.03
2.01
1.00
2.01
3.00
6.06
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

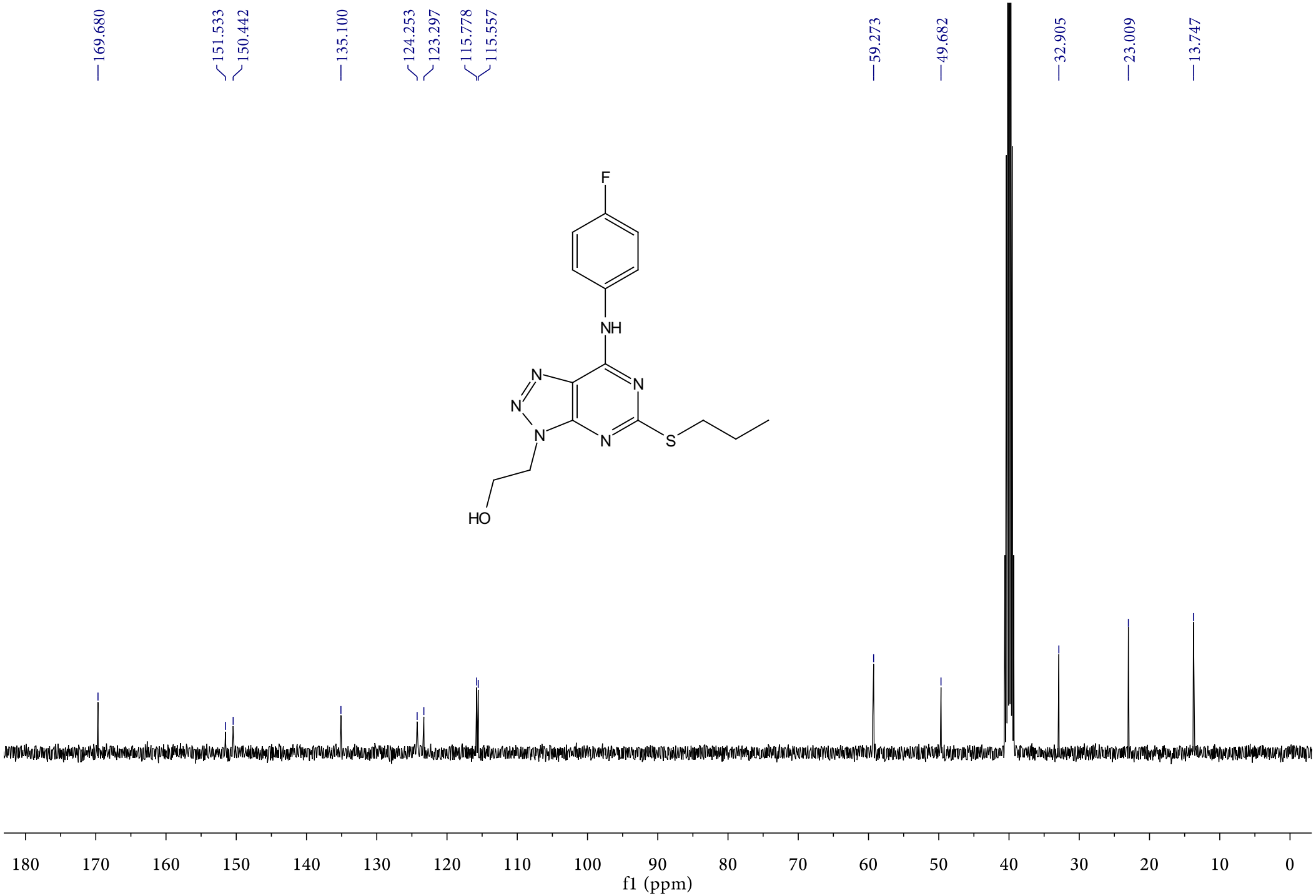

11.005
7.941
7.919
7.465
7.443
5.002
4.987
4.973
4.576
4.563
4.549
3.950
3.936
3.923
3.909
3.112
3.094
1.735
1.717
1.699
1.681
1.000
0.982
0.964
Cl
NH
N
N
N
N
N
S
CH3
HO
0.98
1.94
1.98
1.00
1.96
1.98
2.01
2.00
3.00
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

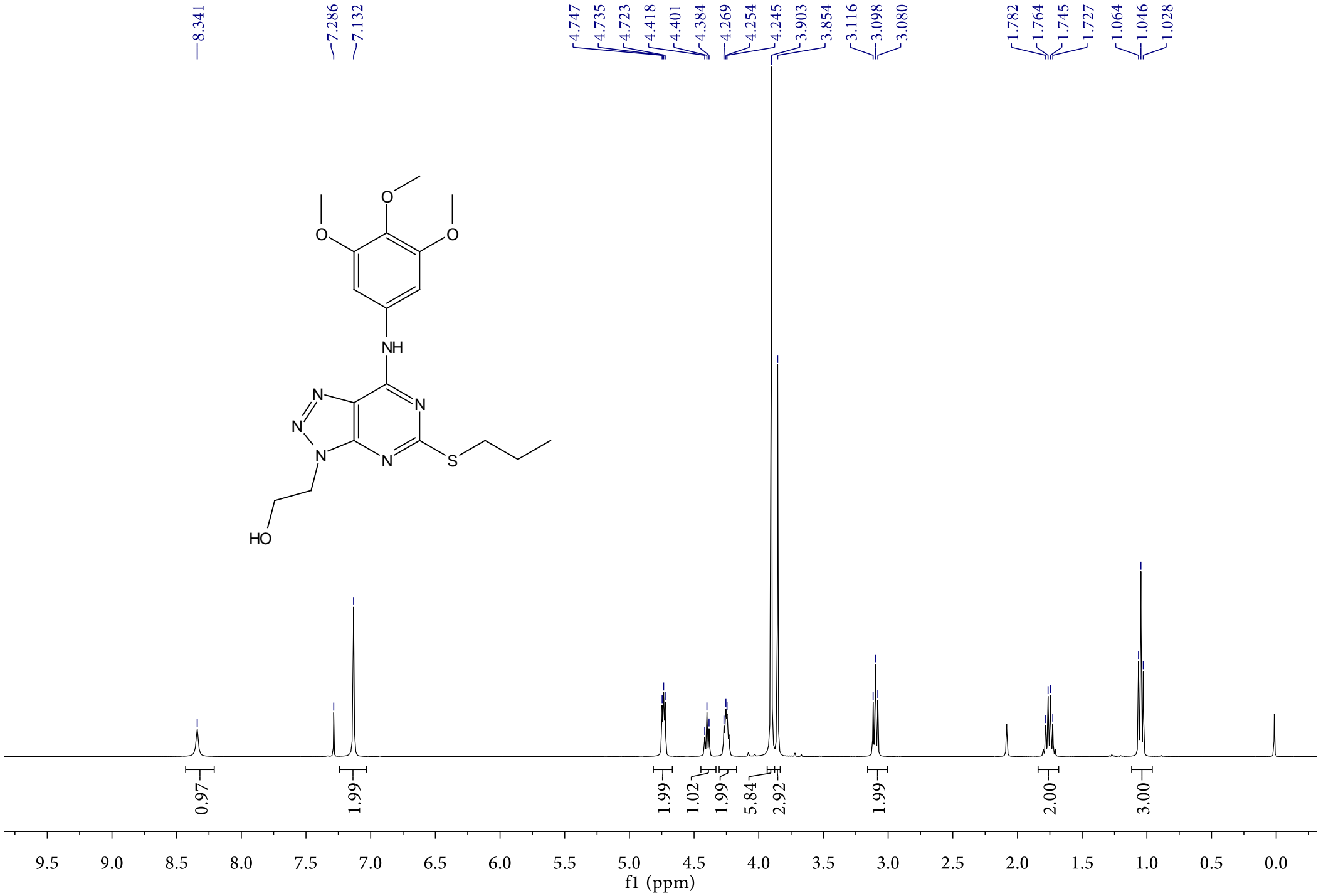

169.699
151.386
150.488
138.268
131.834
124.061
123.409
116.372
59.265
49.720
32.942
22.960
13.761
Br
NH
N
N
N
N
N
S
CH3
HO
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

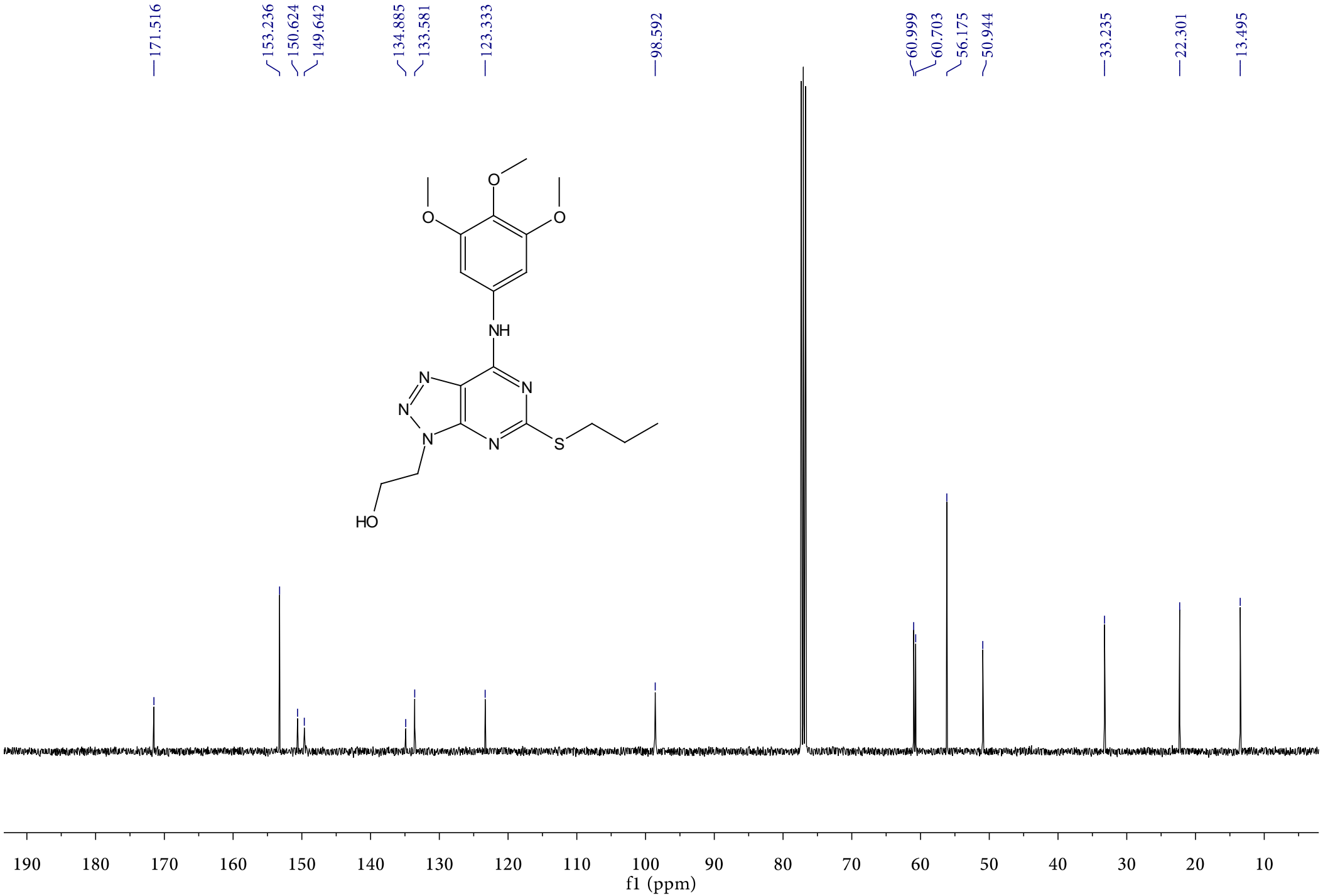

11.004
7.887
7.865
7.595
7.590
7.585
7.573
7.568
4.576
4.562
4.548
3.941
3.927
3.913
3.130
3.113
3.098
3.095
1.735
1.717
1.699
1.681
1.000
0.982
0.963
Br
NH
N
N
N
N
N
S
HO
1.00
2.00
2.11
2.10
2.45
2.19
2.06
3.08
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

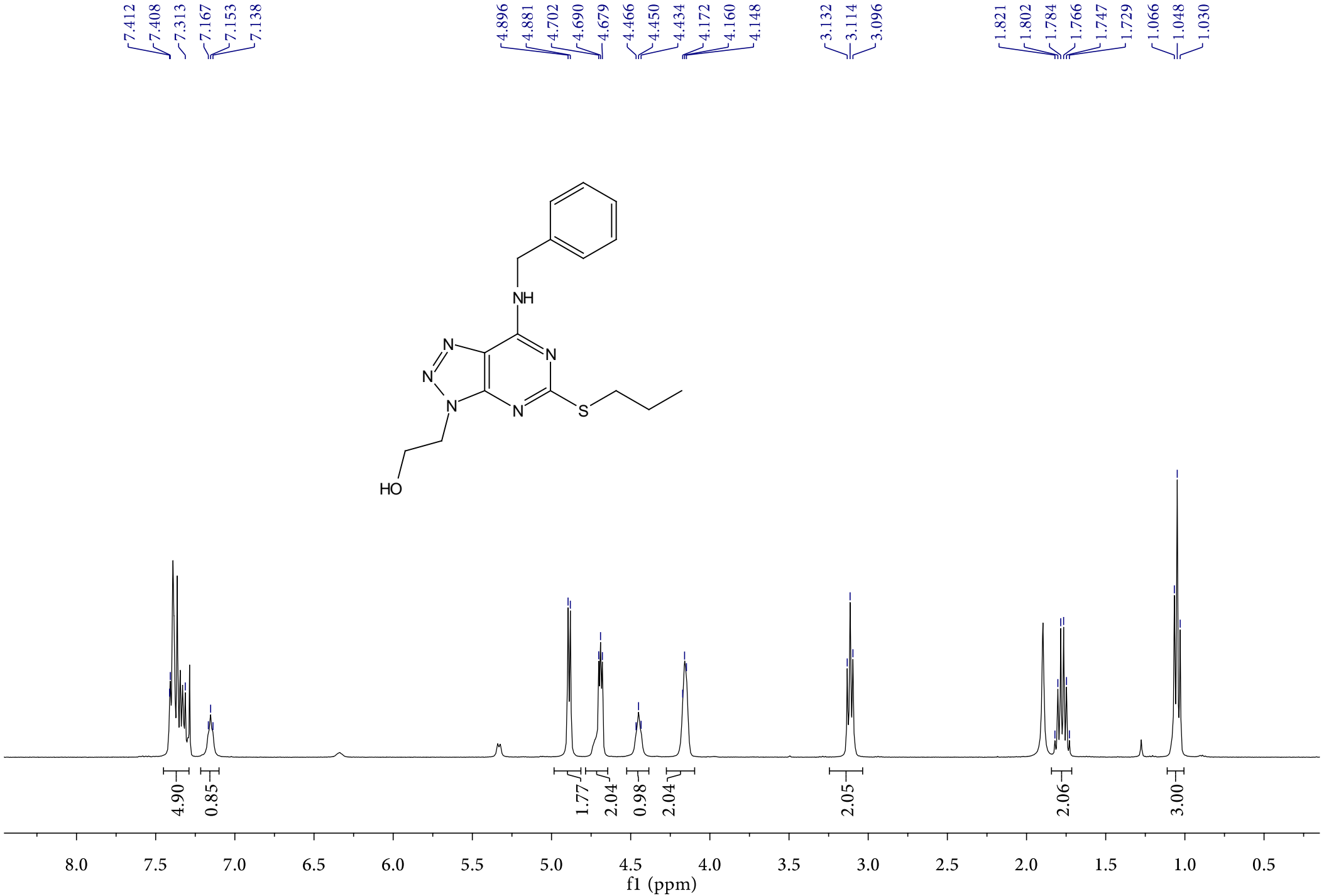

169.699
151.386
150.488
138.268
131.834
124.061
123.409
116.372
59.265
49.720
32.942
22.960
13.761
Br
NH
N
N
N
N
N
S
CH3
HO
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

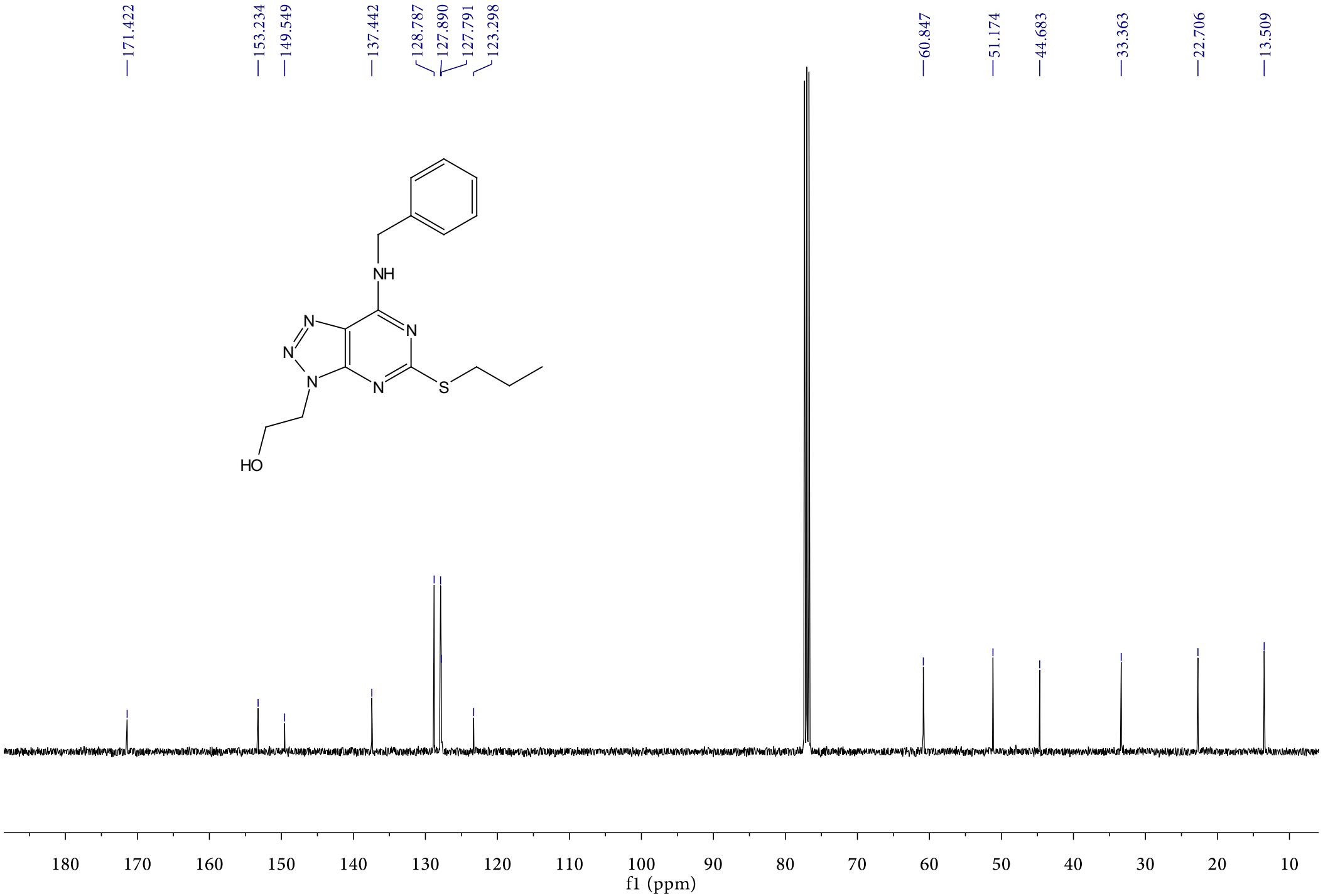

10.925
7.896
7.878
7.865
7.271
7.249
7.231
7.228
5.003
4.989
4.975
4.570
4.556
4.542
3.947
3.933
3.919
3.905
3.112
3.095
3.080
3.077
1.703
1.685
0.987
0.969
0.950
F
NH
N
N
N
N
N
S
CH3
HO
0.97
1.96
2.00
1.00
1.98
1.98
2.00
2.00
3.00
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

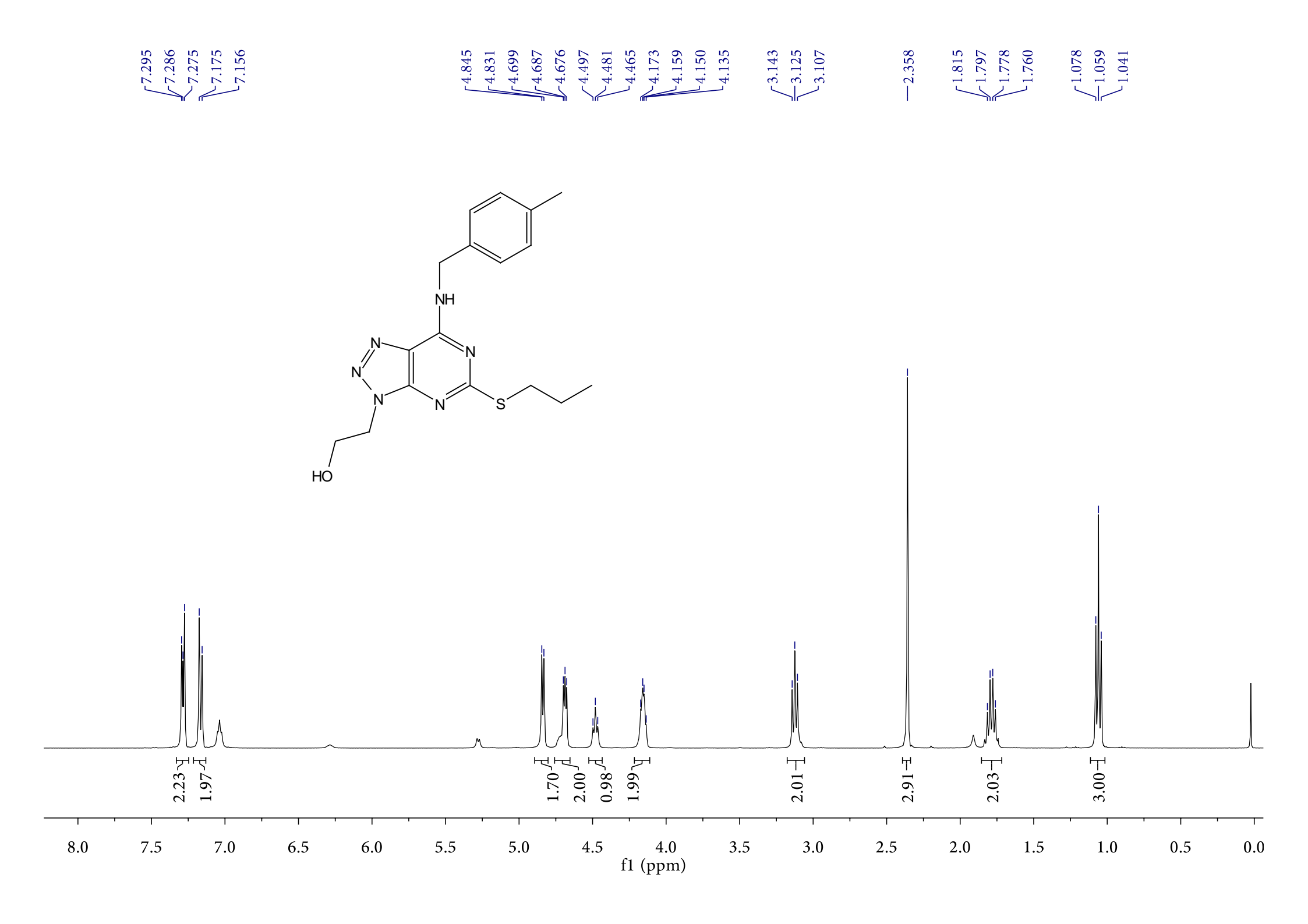

169.680
151.533
150.442
135.100
124.253
123.297
115.778
115.557
59.273
49.682
32.905
23.009
13.747
F
NH
N
N
N
N
N
S
HO
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

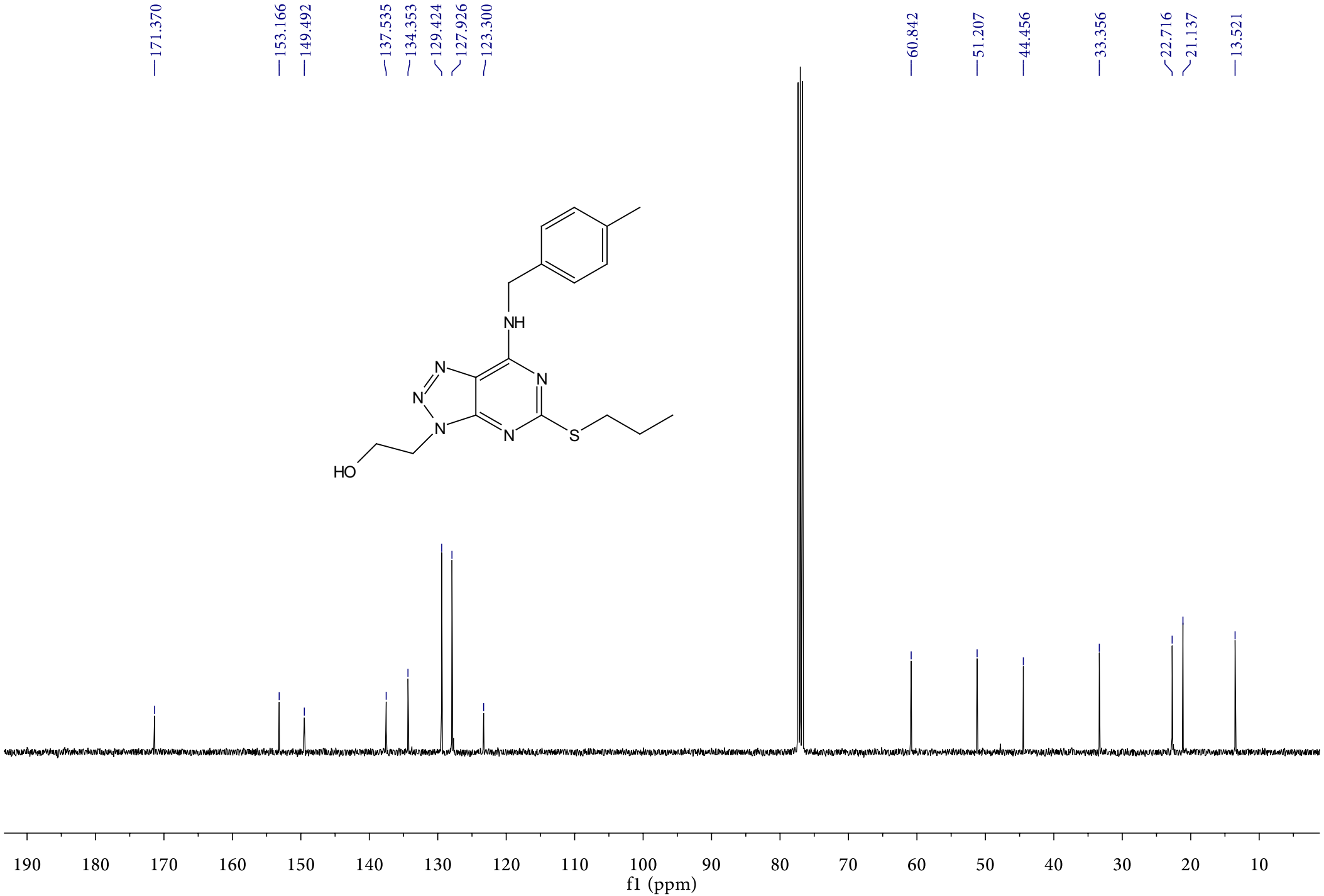

8.341
7.286
7.132
4.747
4.735
4.723
4.418
4.401
4.384
4.269
4.254
4.245
3.903
3.854
3.116
3.098
3.080
1.782
1.764
1.745
1.727
1.064
1.046
1.028
O
O
O
NH
N
N
N
N
N
S
HO
0.97
1.99
1.99
1.02
1.99
5.84
2.92
1.99
2.00
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

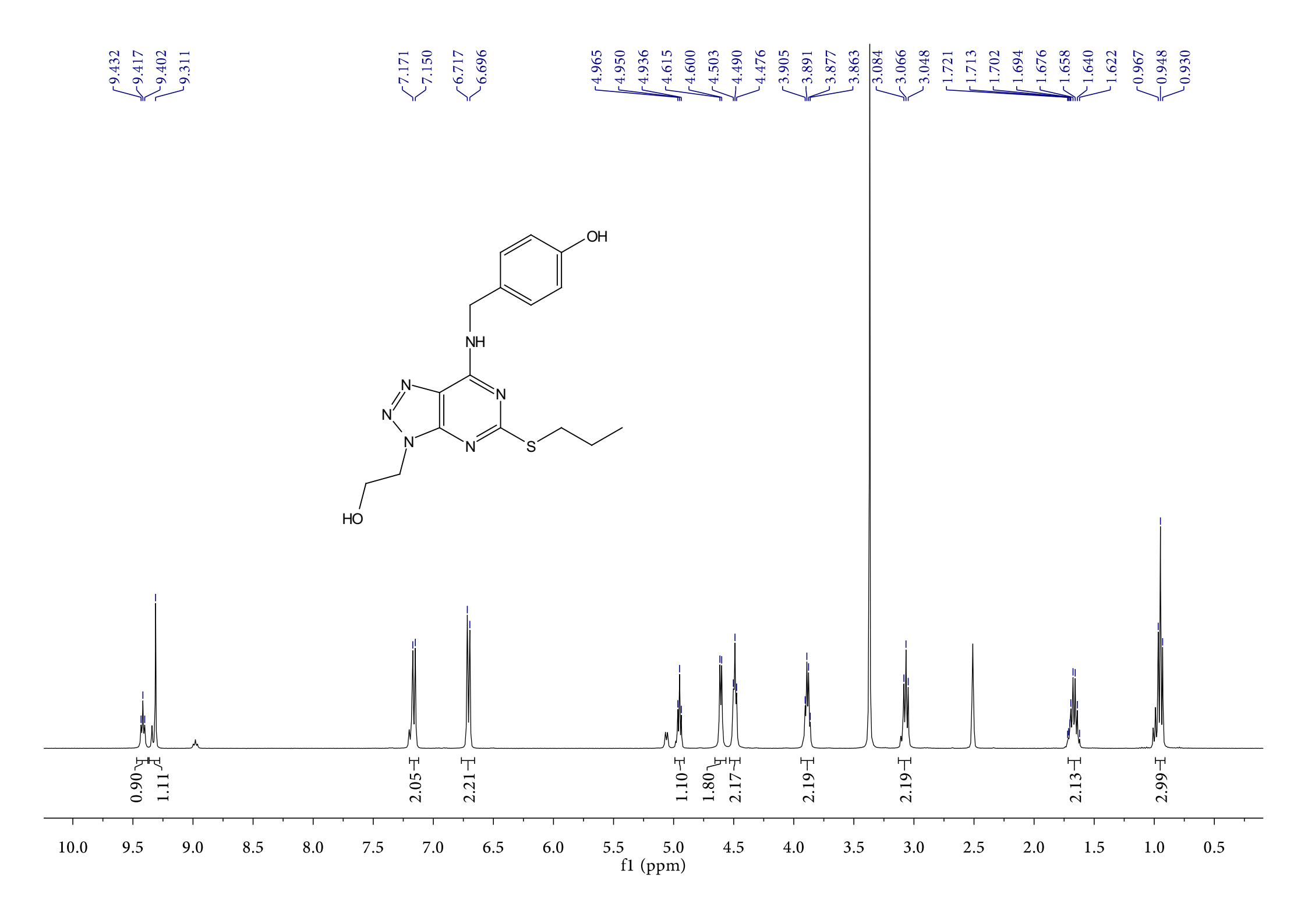

171.516
153.236
150.624
149.642
134.885
133.581
123.333
98.592
60.999
60.703
56.175
50.944
33.235
22.301
13.495
O
O
O
NH
N
N
N
N
N
S
HO
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

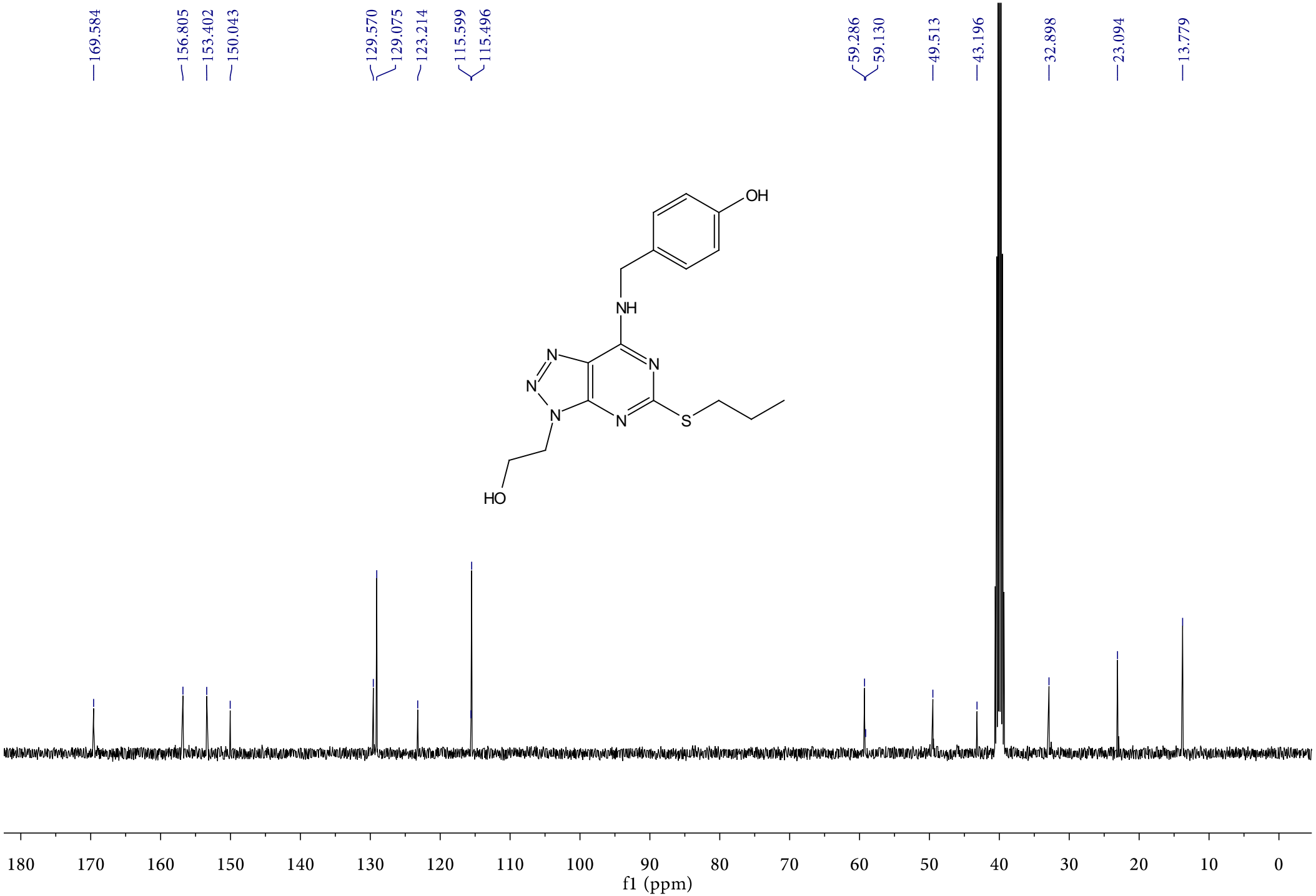

7.412
7.408
7.313
7.167
7.153
7.138
4.896
4.881
4.702
4.690
4.679
4.466
4.450
4.434
4.172
4.160
4.148
3.132
3.114
3.096
1.821
1.802
1.784
1.766
1.747
1.729
1.066
1.048
1.030
NH
N
N
N
N
S
HO
4.90
0.85
1.77
2.04
0.98
2.04
2.05
2.06
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

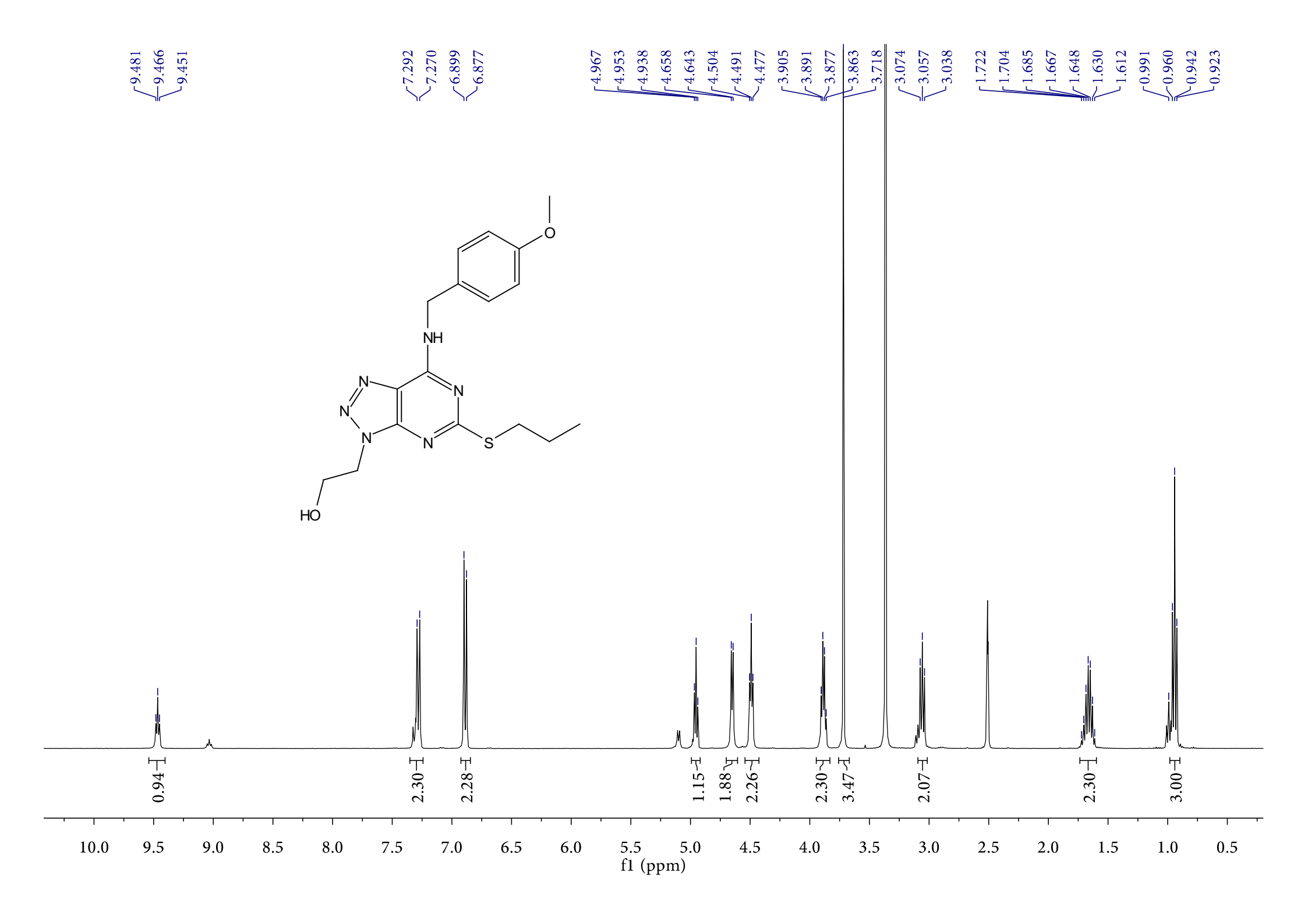

171.422
153.234
149.549
137.442
128.787
127.890
127.791
123.298
60.847
51.174
44.683
33.363
22.706
13.509
NH
N
N
N
N
N
S
HO
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

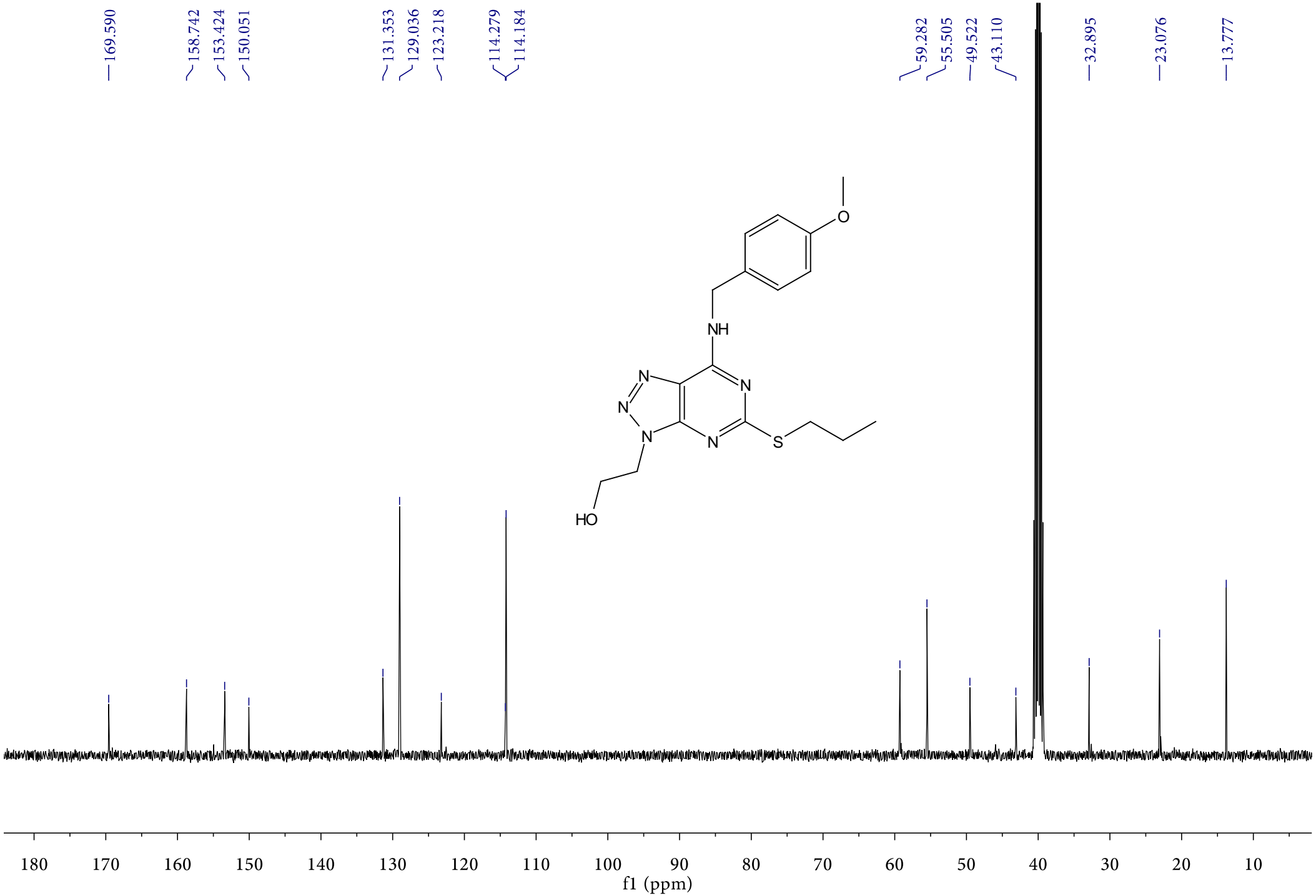

7.295
7.286
7.275
7.175
7.156
4.845
4.831
4.699
4.687
4.676
4.497
4.481
4.465
4.173
4.159
4.150
4.135
3.143
3.125
3.107
2.358
1.815
1.797
1.778
1.760
1.078
1.059
1.041
NH
N
N
N
N
N
S
HO
2.23
1.97
1.70
2.00
0.98
1.99
2.01
2.91
2.03
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

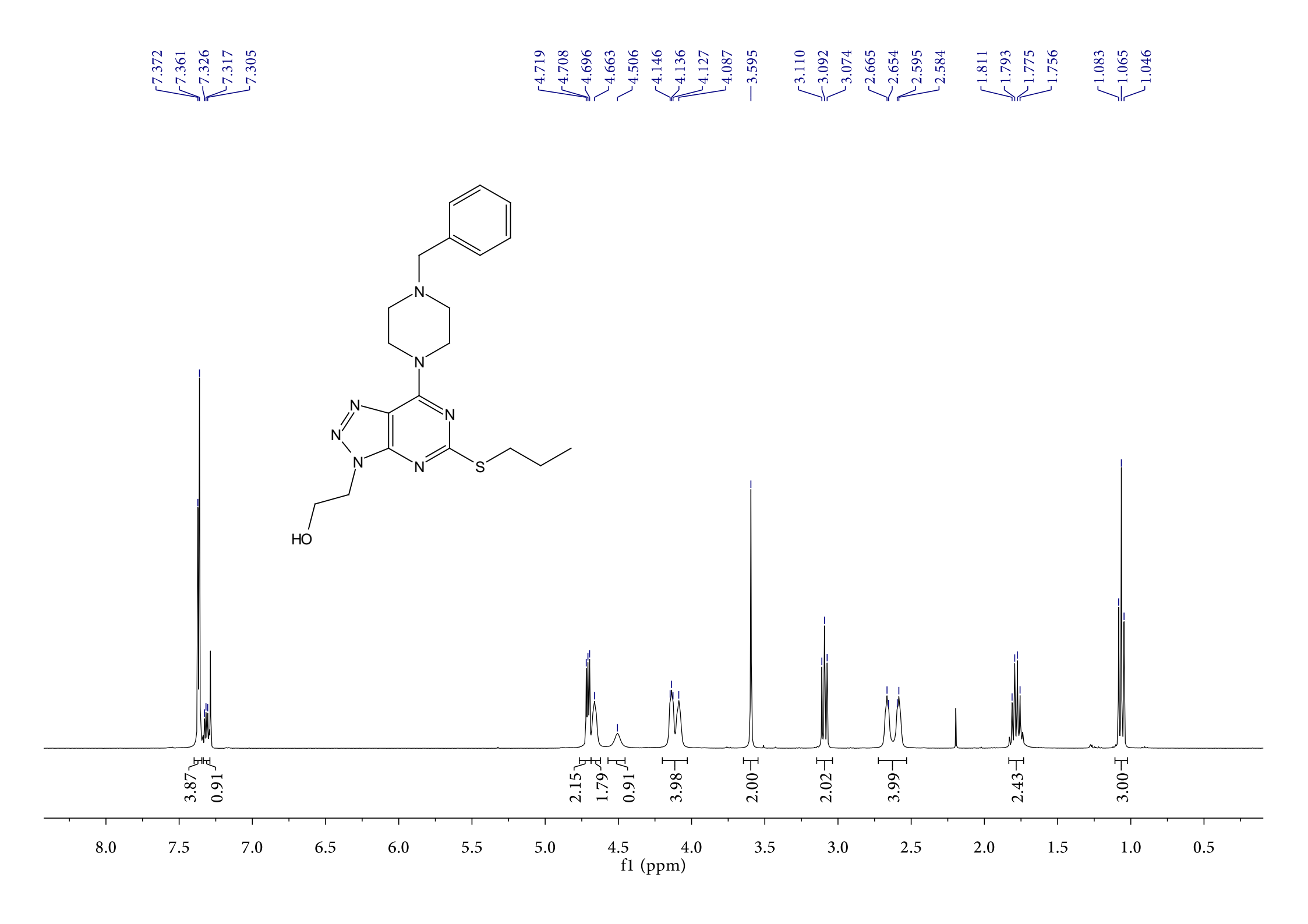

171.370
153.166
149.492
137.535
134.353
129.424
127.926
123.300
60.842
51.207
44.456
33.356
22.716
21.137
13.521
NH
N
N
N
N
N
S
HO
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

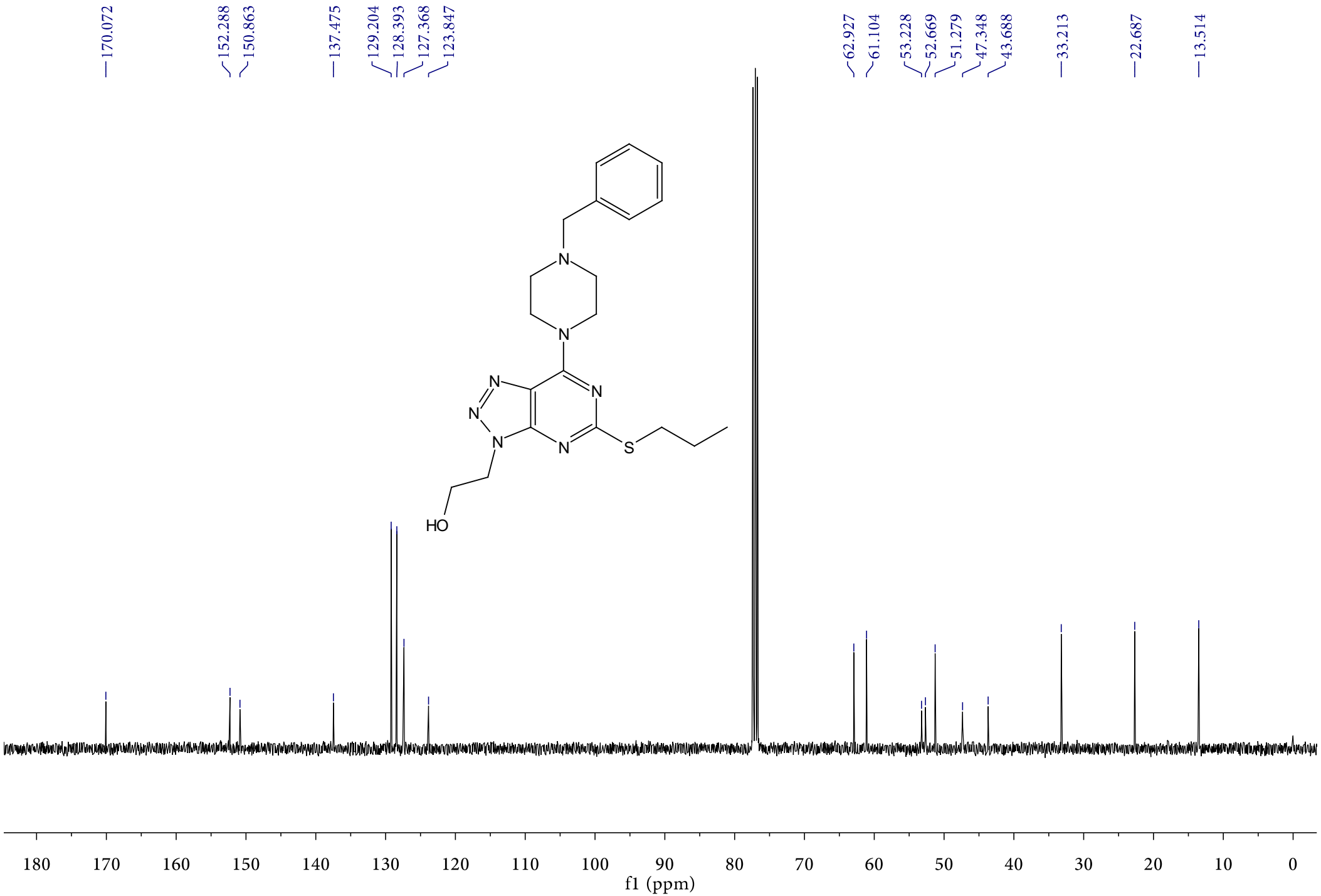

9.432
9.417
9.402
9.311
7.171
7.150
6.717
6.696
4.965
4.950
4.936
4.615
4.600
4.503
4.490
4.476
3.905
3.891
3.877
3.863
3.084
3.066
3.048
1.721
1.713
1.702
1.694
1.676
1.658
1.640
1.622
0.967
0.948
0.930
OH
NH
N
N
N
N
N
S
HO
0.90
1.11
2.05
2.21
1.10
1.80
2.17
2.19
2.19
2.13
2.99
10.0
9.5
9.0
8.5
8.0
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
f1 (ppm)

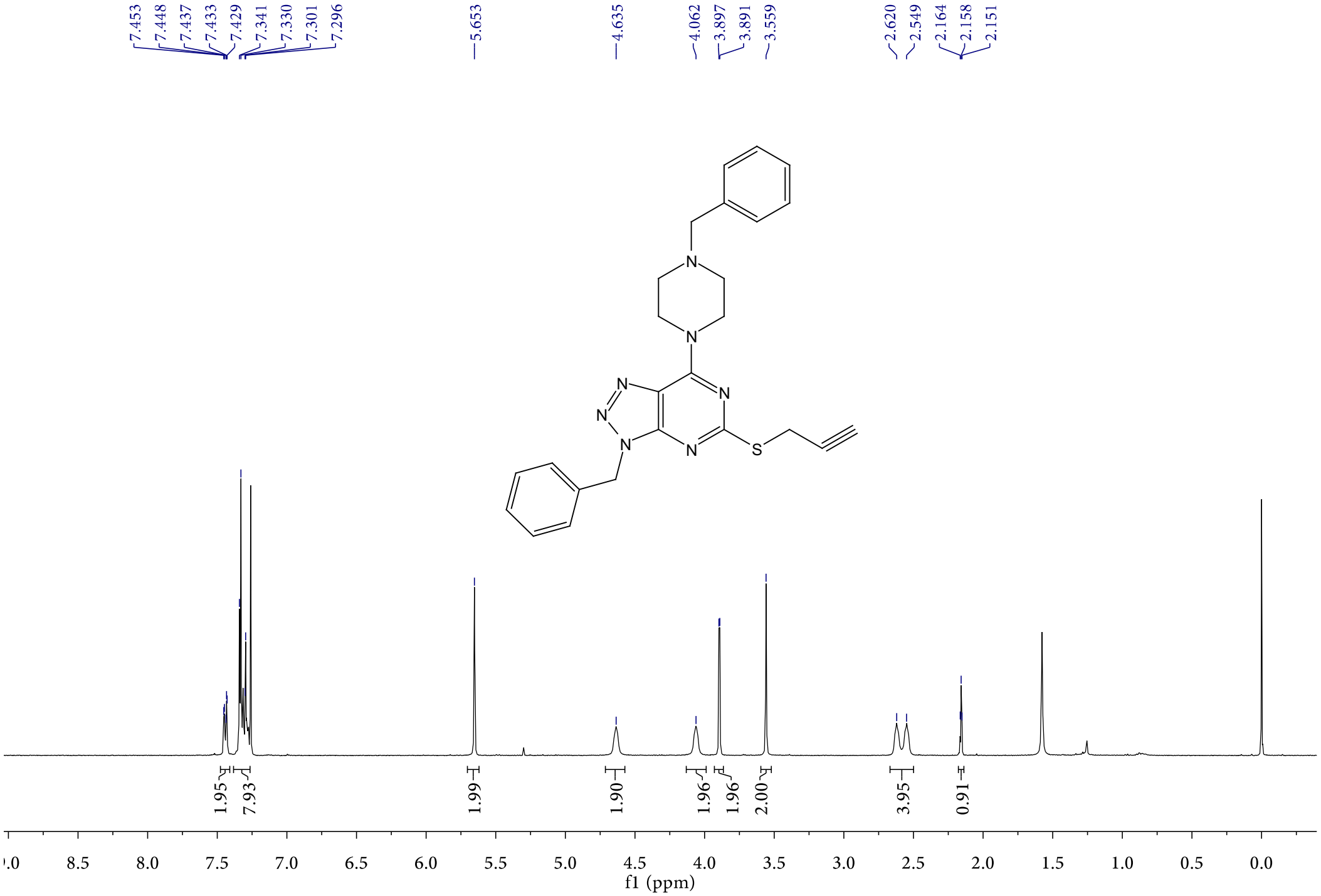

169.584
156.805
153.402
150.043
129.570
129.075
123.214
115.599
115.496
59.286
59.130
49.513
43.196
32.898
23.094
13.779
OH
NH
N
N
N
N
N
S
HO
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

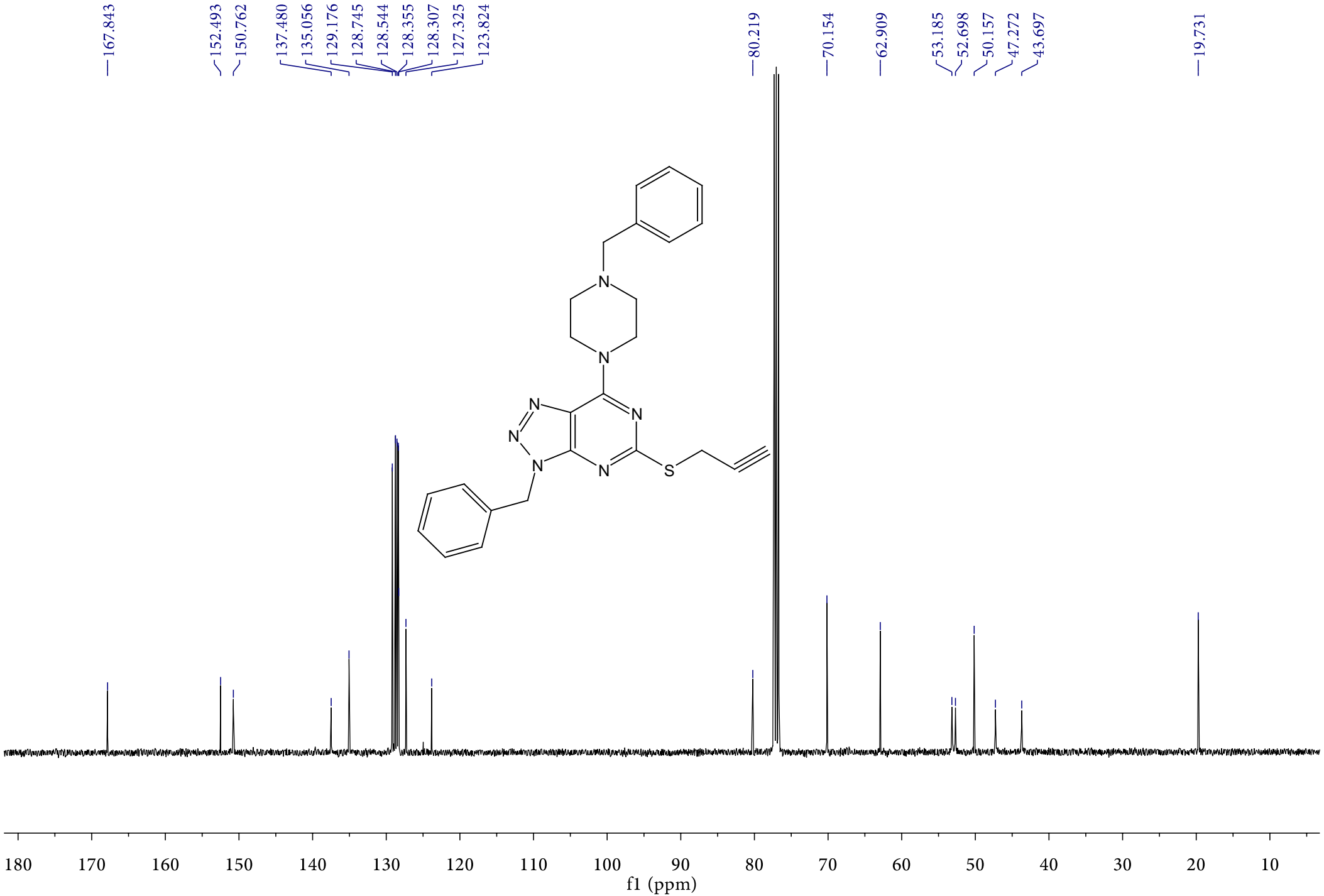

9.481
9.466
9.451
7.292
7.270
6.899
6.877
4.967
4.953
4.938
4.658
4.643
4.504
4.491
4.477
3.905
3.891
3.877
3.863
3.718
3.074
3.057
3.038
1.722
1.704
1.685
1.667
1.648
1.630
1.612
0.991
0.960
0.942
0.923
O
NH
N
N
N
N
N
S
HO
0.94
2.30
2.28
1.15
1.88
2.26
2.30
3.47
2.07
2.30
3.00
10.0
9.5
9.0
8.5
8.0
7.5
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
f1 (ppm)

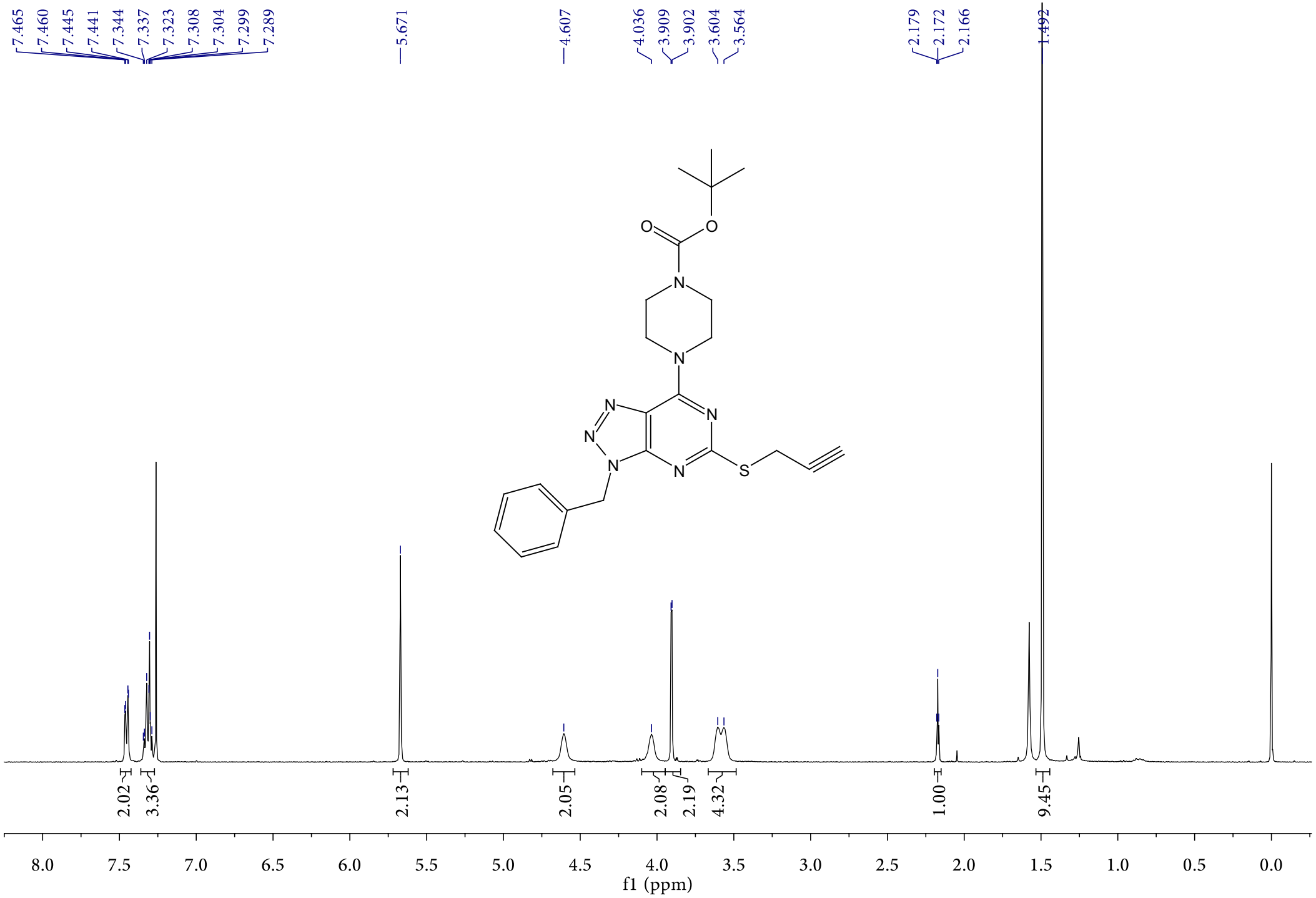

169.590
158.742
153.424
150.051
131.353
129.036
123.218
114.279
114.184
59.282
55.505
49.522
43.110
32.895
23.076
13.777
O
NH
N
N
N
N
N
S
HO
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

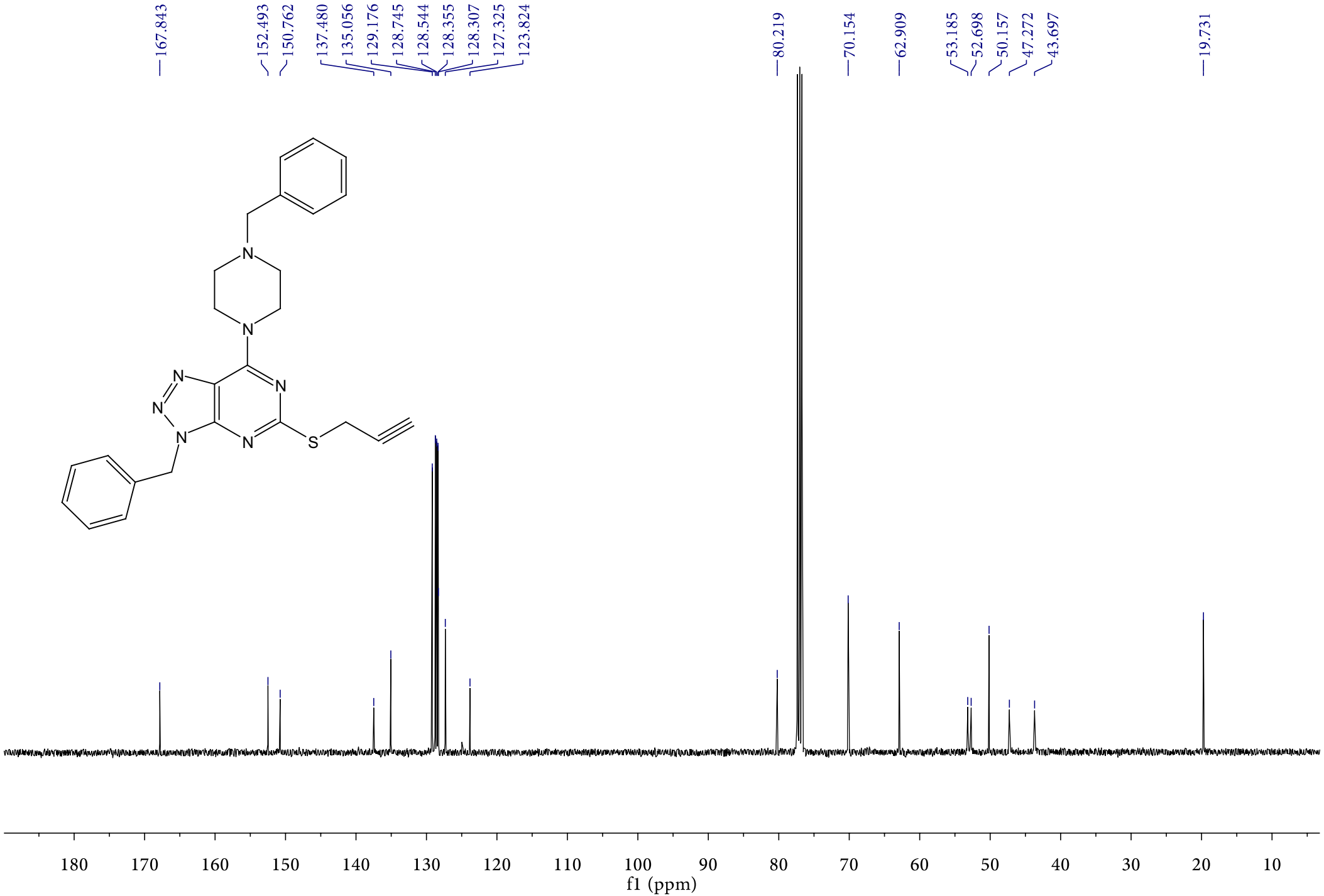

7.372
7.361
7.326
7.317
7.305
4.719
4.708
4.696
4.663
4.506
4.146
4.136
4.127
4.087
3.595
3.110
3.092
3.074
2.665
2.654
2.595
2.584
1.811
1.793
1.775
1.756
1.083
1.065
1.046
N
N
N
N
N
N
S
HO
3.87
0.91
2.15
1.79
0.91
3.98
2.00
2.02
3.99
2.43
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

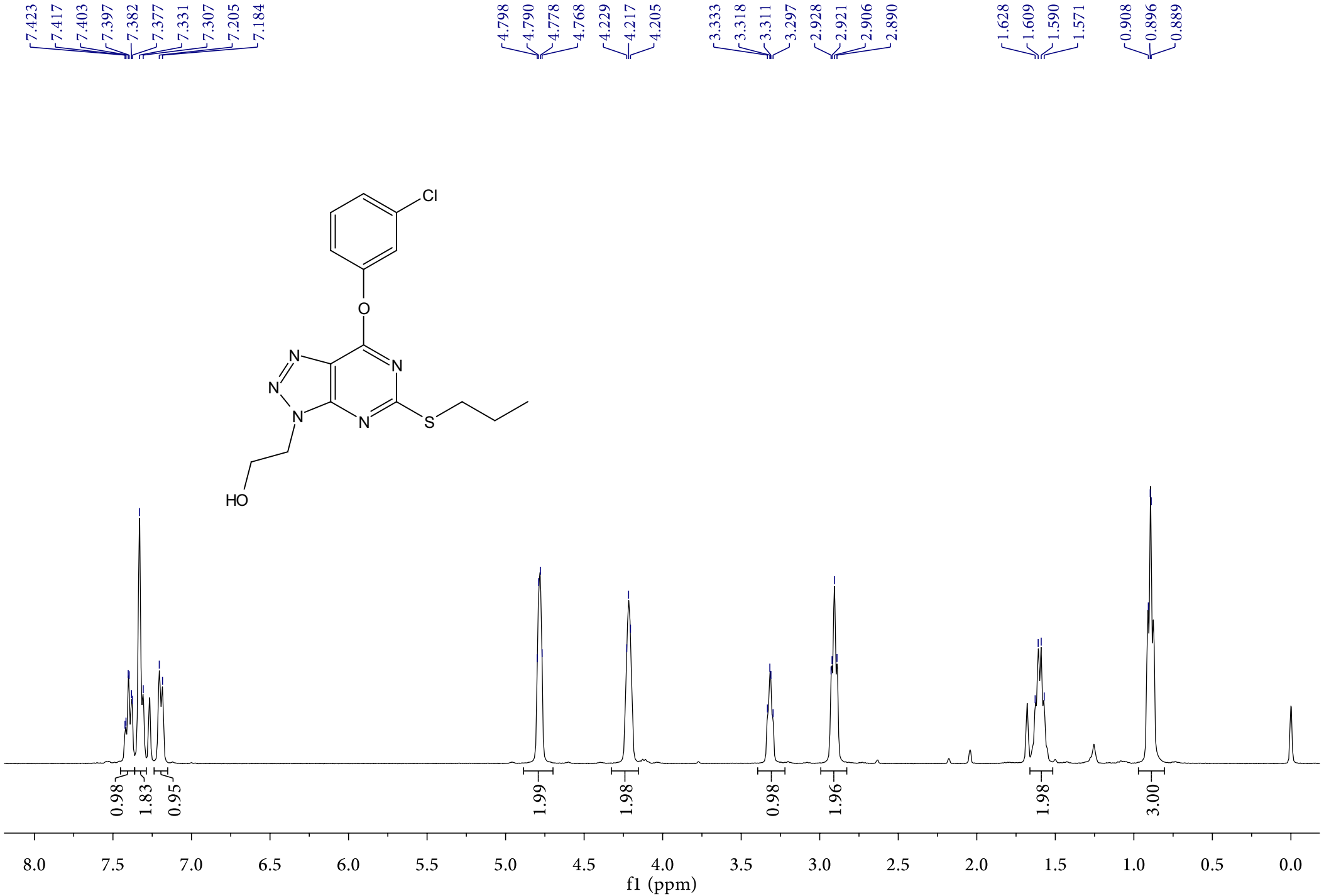

170.072
152.288
150.863
137.475
129.204
128.393
127.368
123.847
62.927
61.104
53.228
52.669
51.279
47.348
43.688
33.213
22.687
13.514
N
N
N
N
N
N
S
HO
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

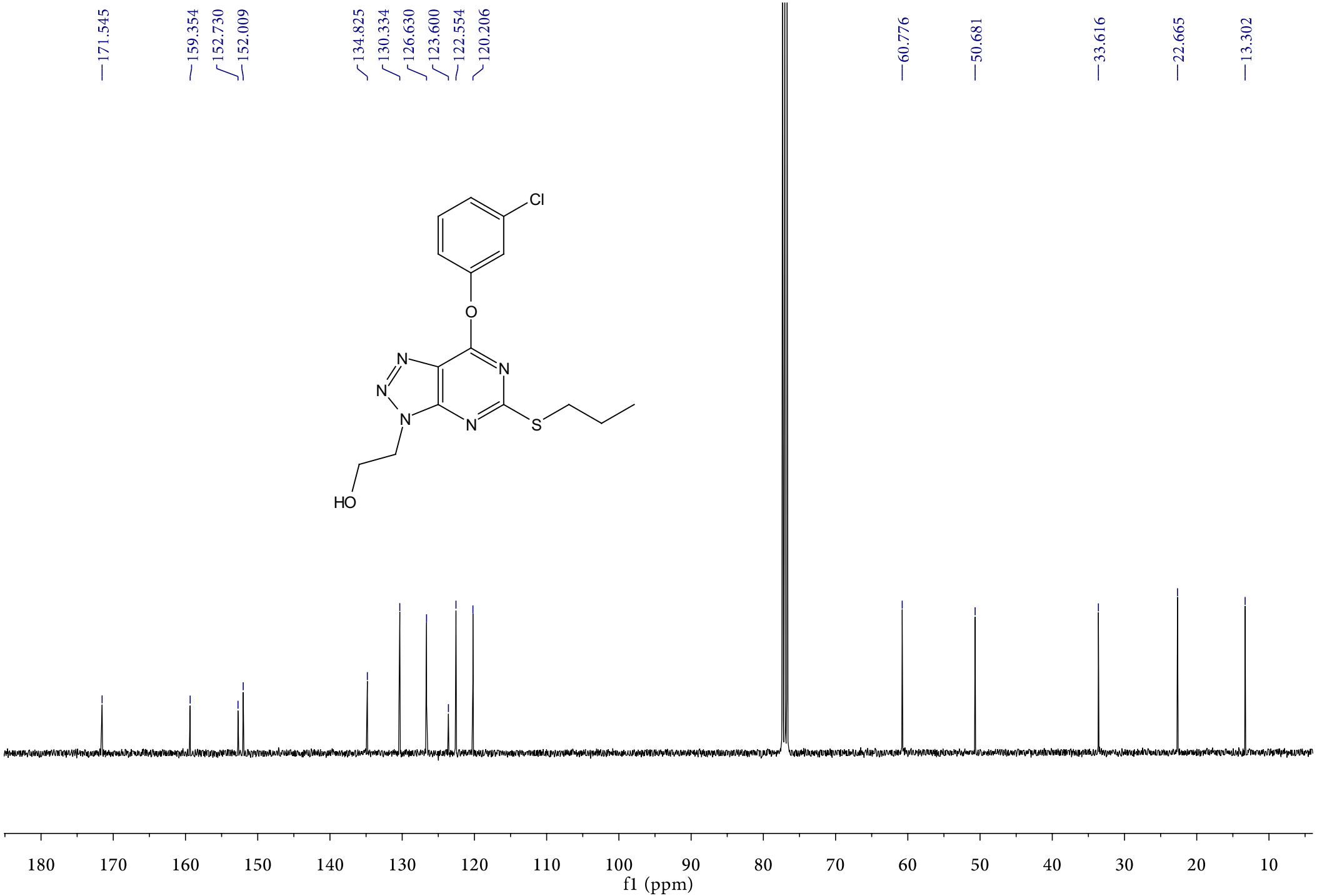

7.453
7.448
7.437
7.433
7.429
7.341
7.330
7.301
7.296
5.653
4.635
4.062
3.897
3.891
3.559
2.620
2.549
2.164
2.158
2.151
N
N
N
N
N
N
S
1.95
7.93
1.99
1.90
1.96
1.96
2.00
3.95
0.91
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

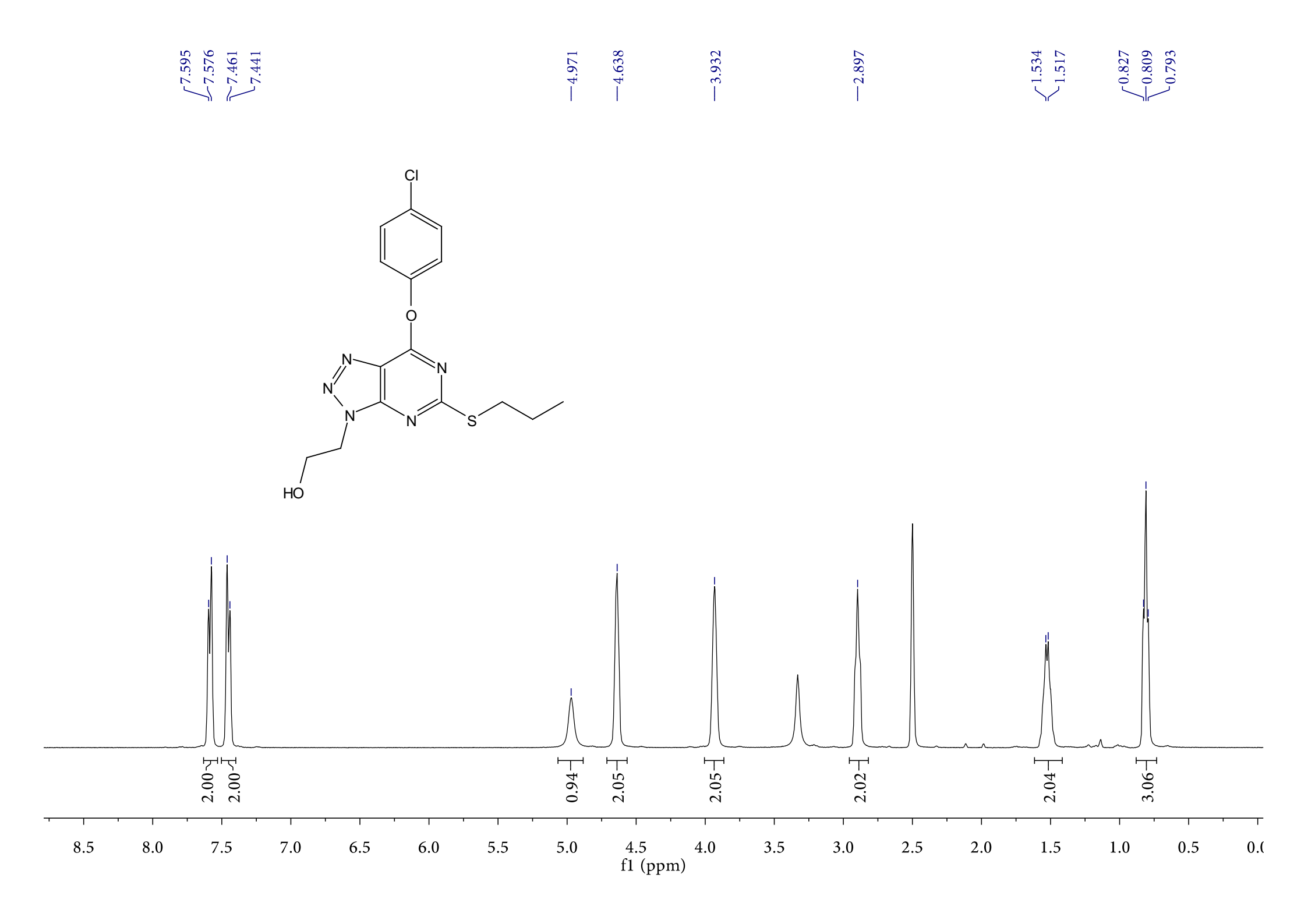

167.843
152.493
150.762
137.480
135.056
129.176
128.745
128.544
128.355
128.307
127.325
123.824
80.219
70.154
62.909
53.185
52.698
50.157
47.272
43.697
19.731
N
N
N
N
N
N
S
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

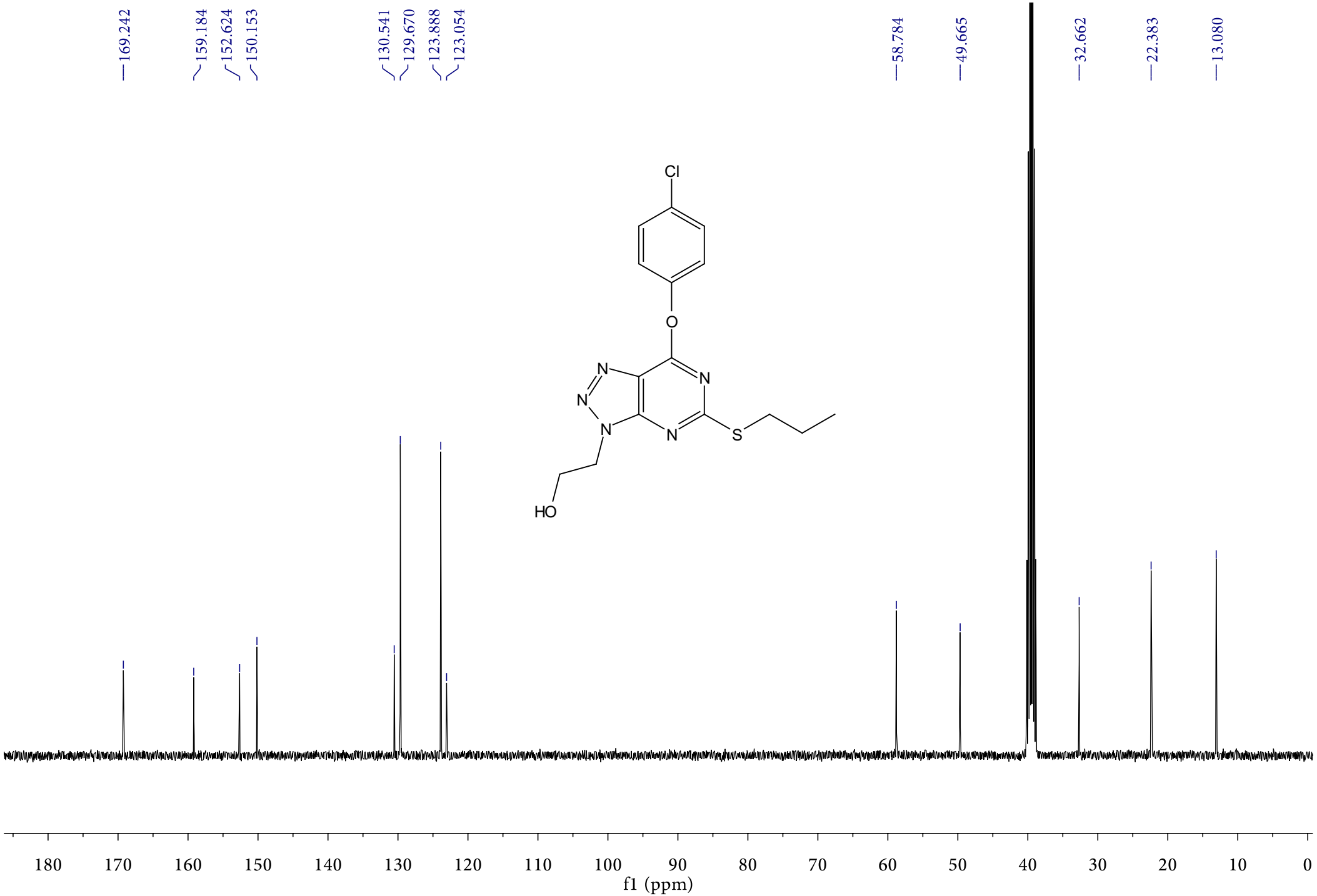

7.465
7.460
7.445
7.441
7.344
7.337
7.323
7.308
7.304
7.299
7.289
5.671
4.607
4.036
3.909
3.902
3.604
3.564
2.179
2.172
2.166
1.492
O
O
N
N
N
N
N
N
S
2.02
3.36
2.13
2.05
2.08
2.19
4.32
1.00
9.45
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

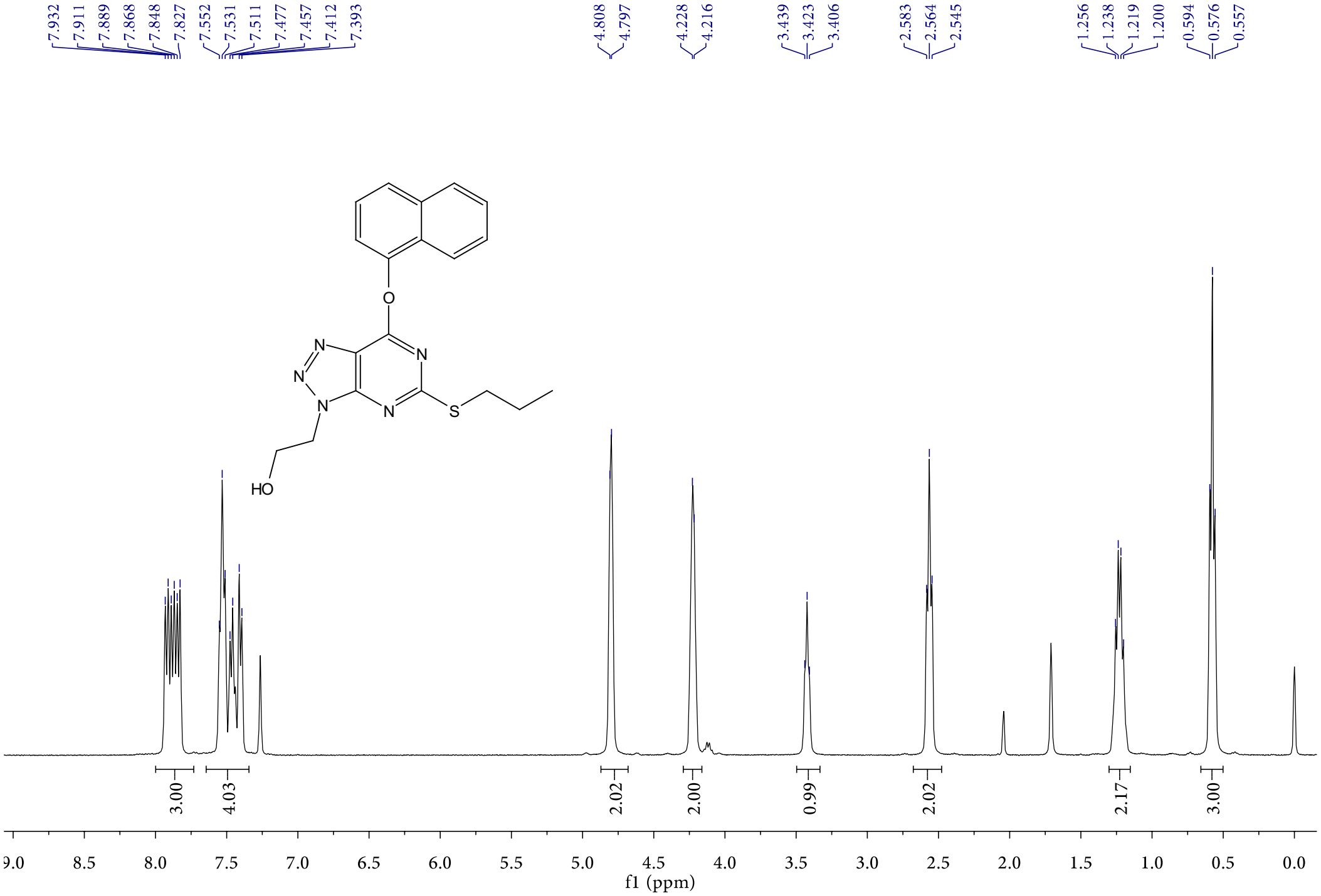

167.843
152.493
150.762
137.480
135.056
129.176
128.745
128.544
128.355
128.307
127.325
123.824
80.219
70.154
62.909
53.185
52.698
50.157
47.272
43.697
19.731
N
N
N
N
N
N
S
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

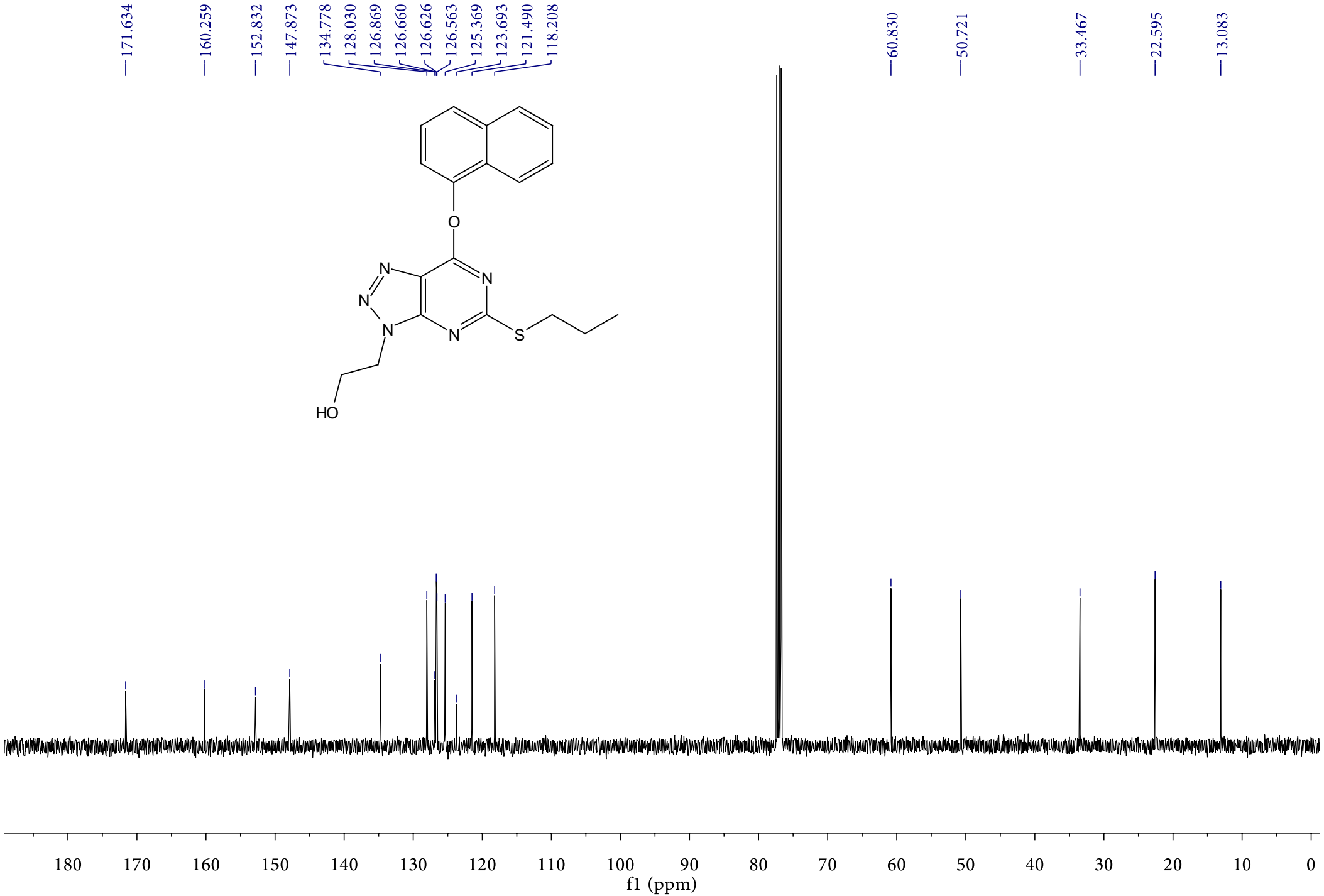

7.423
7.417
7.403
7.397
7.382
7.377
7.331
7.307
7.205
7.184
4.798
4.790
4.778
4.768
4.229
4.217
4.205
3.333
3.318
3.311
3.297
2.928
2.921
2.906
2.890
1.628
1.609
1.590
1.571
0.908
0.896
0.889
Cl
O
N
N
N
N
N
S
HO
0.98
1.83
0.95
1.99
1.98
0.98
1.96
1.98
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

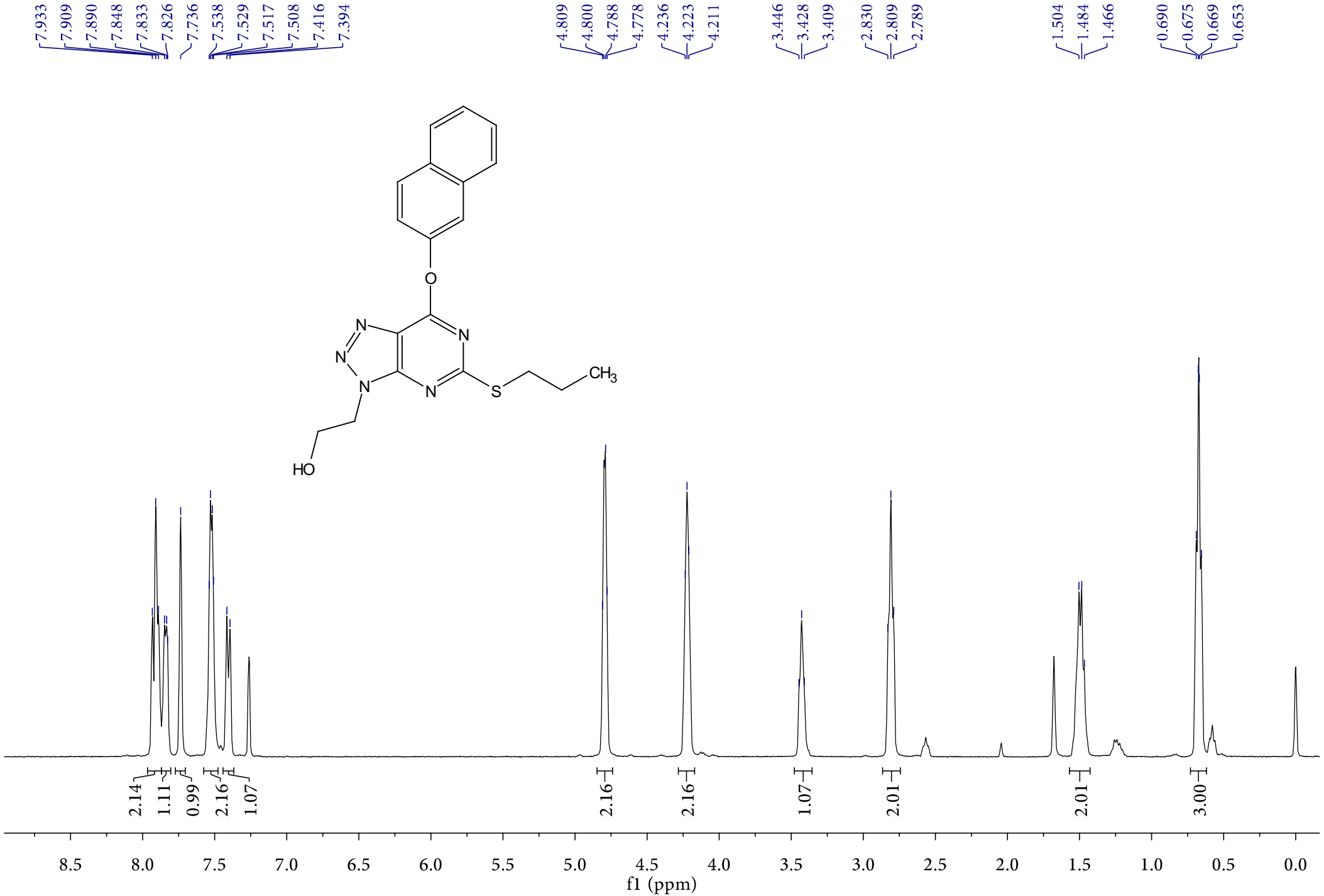

171.545
159.354
152.730
152.009
134.825
130.334
126.630
123.600
122.554
120.206
60.776
50.681
33.616
22.665
13.302
Cl
O
N
N
N
N
N
S
HO
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

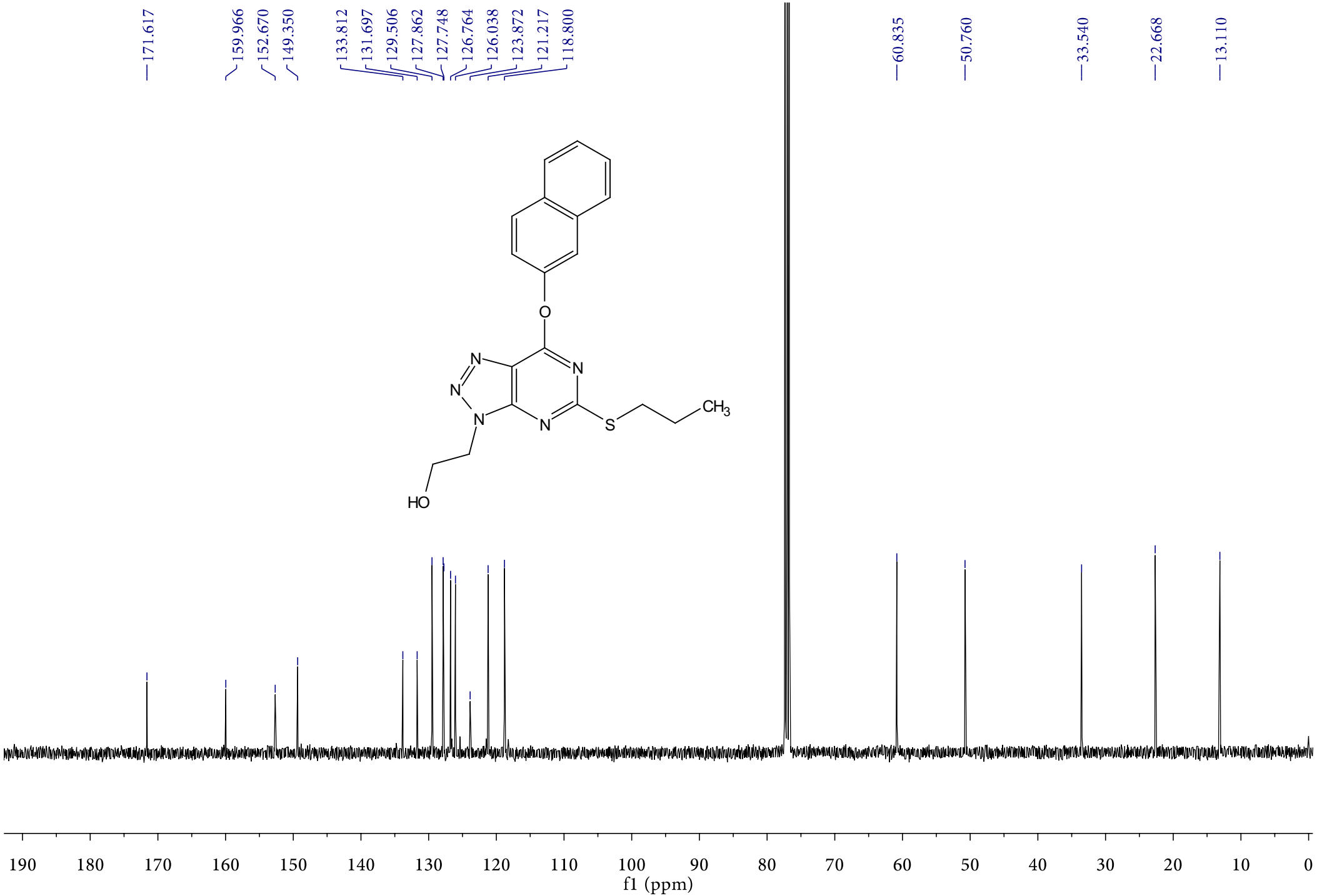

7.595
7.576
7.461
7.441
4.971
4.638
3.932
2.897
1.534
1.517
0.827
0.809
0.793
Cl
O
N
N
N
N
N
S
HO
2.00
2.00
0.94
2.05
2.05
2.02
2.04
3.06
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

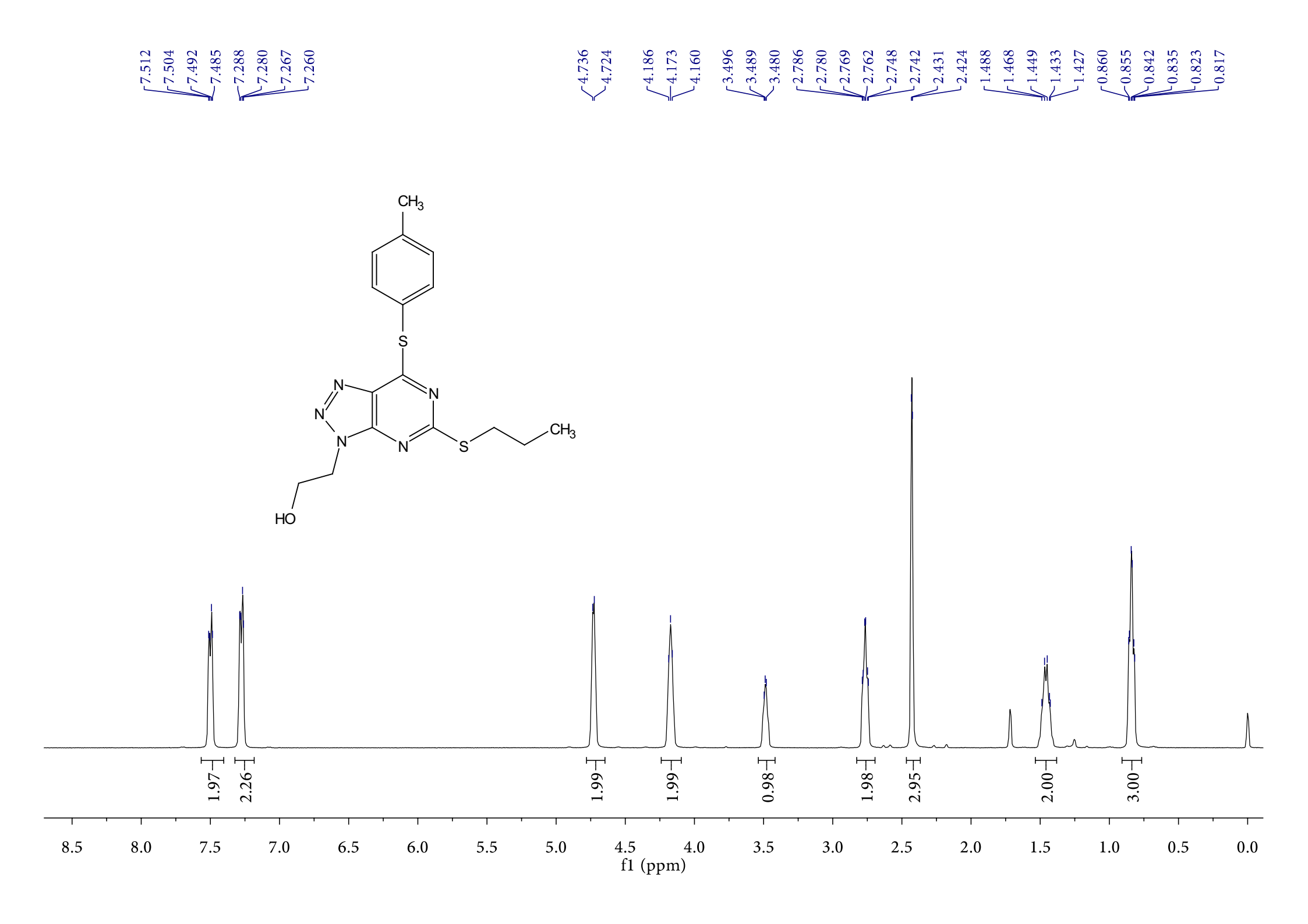

169.242
159.184
152.624
150.153
130.541
129.670
123.888
123.054
58.784
49.665
32.662
22.383
13.080
Cl
O
N
N
N
N
N
S
HO
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

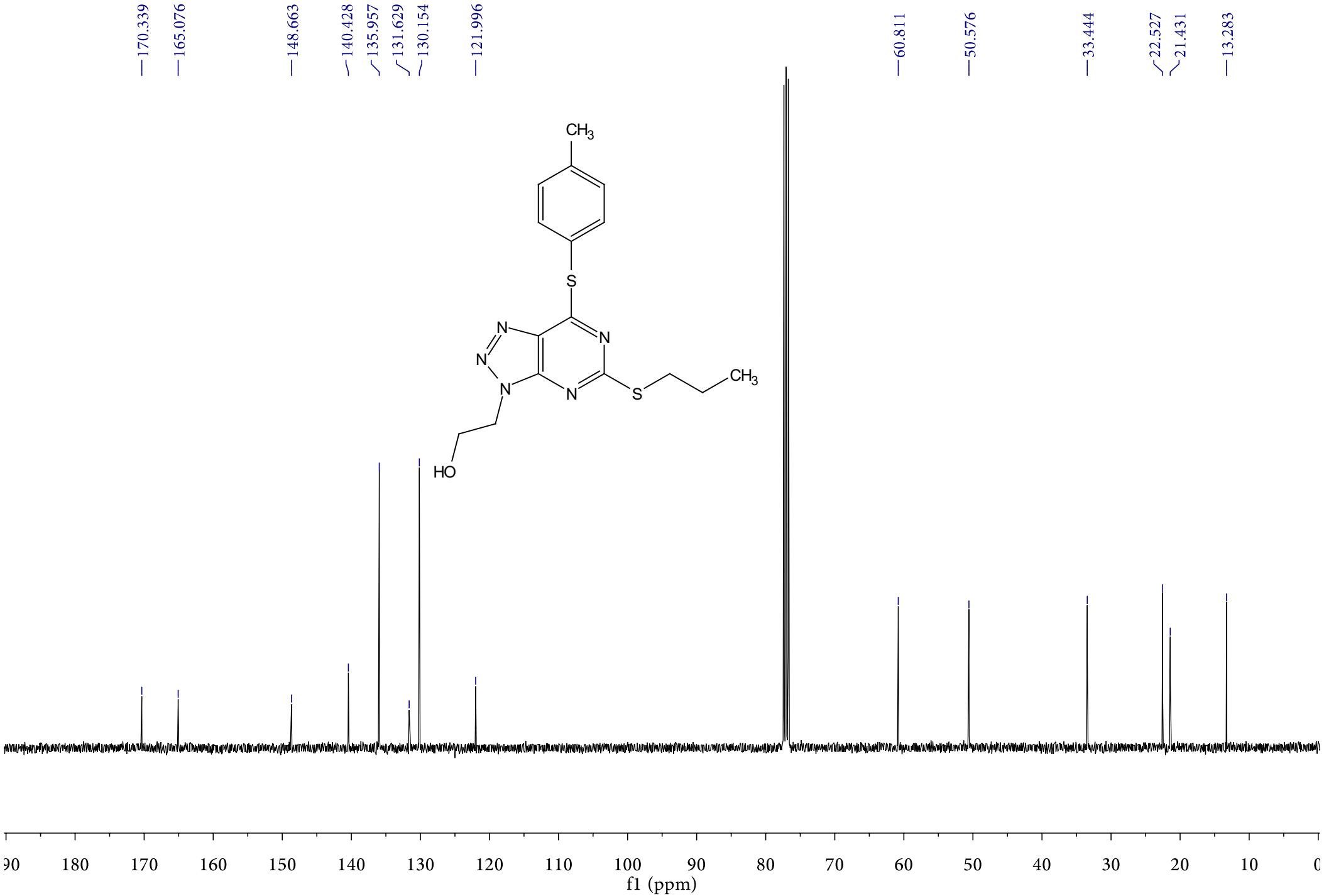

7.932
7.911
7.889
7.868
7.848
7.827
7.552
7.531
7.511
7.477
7.457
7.412
7.393
4.808
4.797
4.228
4.216
3.439
3.423
3.406
2.583
2.564
2.545
1.256
1.238
1.219
1.200
0.594
0.576
0.557
O
N
N
N
N
N
S
HO
3.00
4.03
2.02
2.00
0.99
2.02
2.17
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

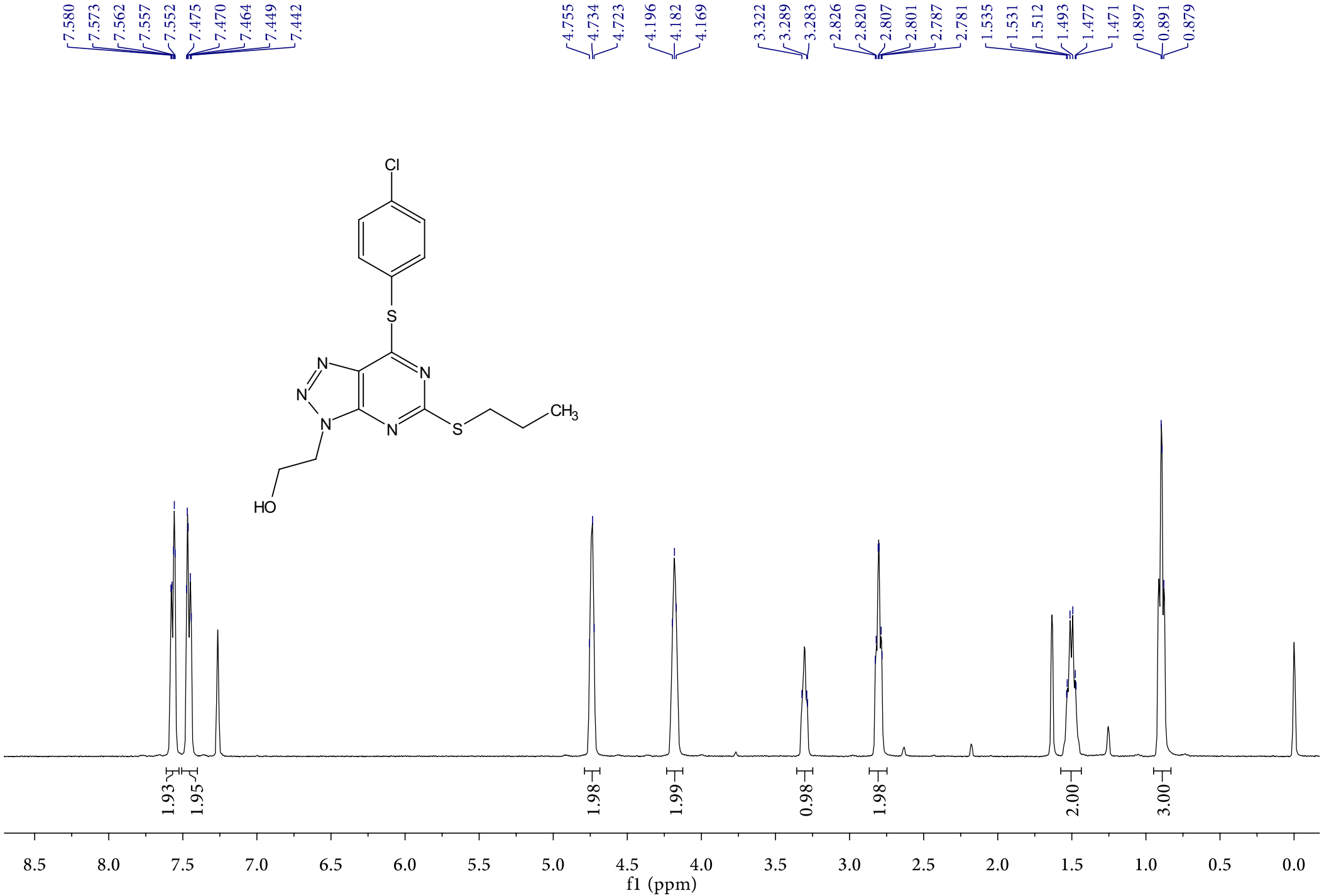

171.634
160.259
152.832
147.873
134.778
128.030
126.869
126.660
126.626
126.563
125.369
123.693
121.490
118.208
60.830
50.721
33.467
22.595
13.083
O
N
N
N
N
N
S
HO
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

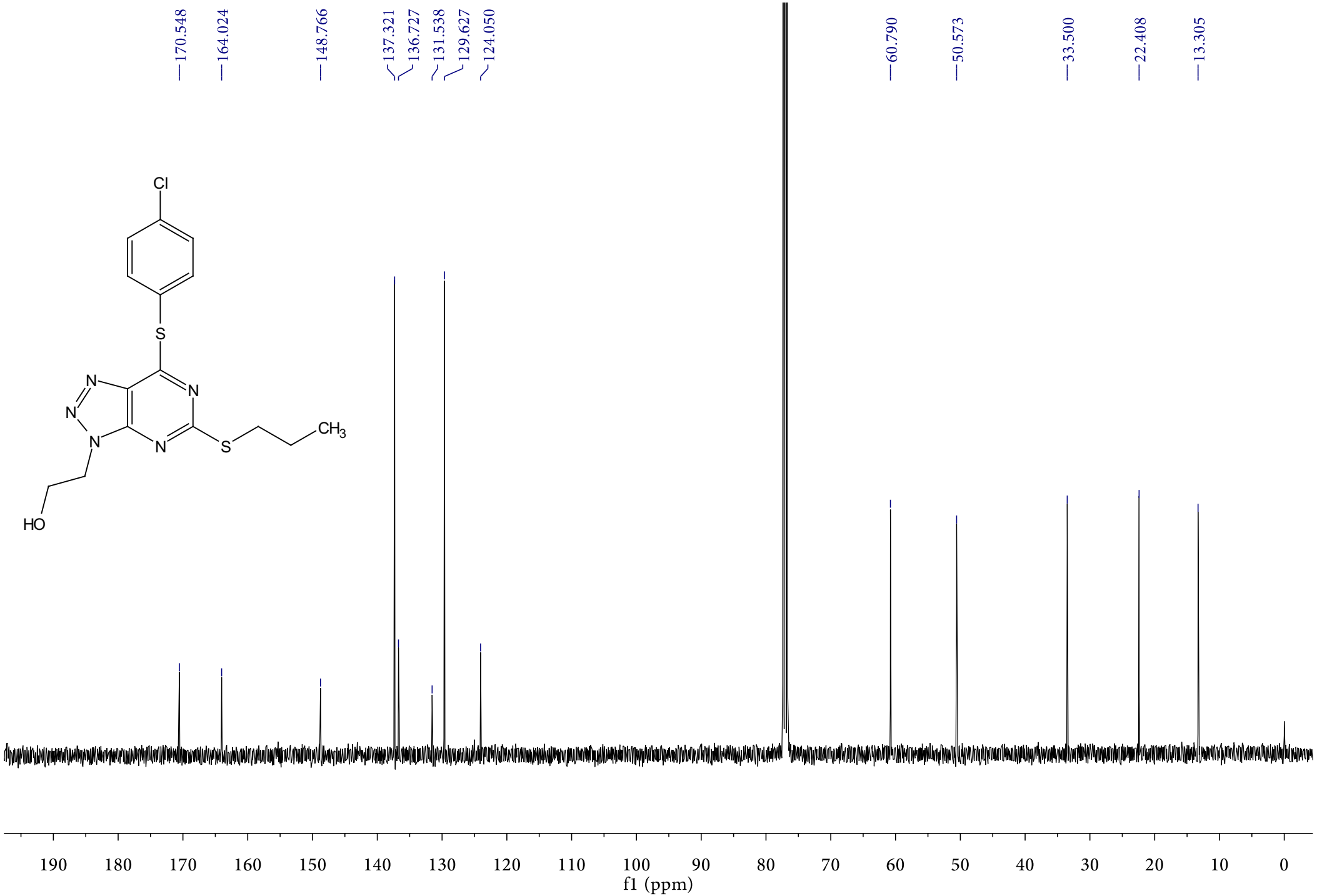

7.933
7.909
7.890
7.848
7.833
7.826
7.736
7.538
7.529
7.517
7.508
7.416
7.394
4.809
4.800
4.788
4.778
4.236
4.223
4.211
3.446
3.428
3.409
2.830
2.809
2.789
1.504
1.484
1.466
0.690
0.675
0.669
0.653
O
N
N
N
N
N
S
CH3
HO
2.14
1.11
0.99
2.16
1.07
2.16
2.16
1.07
2.01
2.01
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

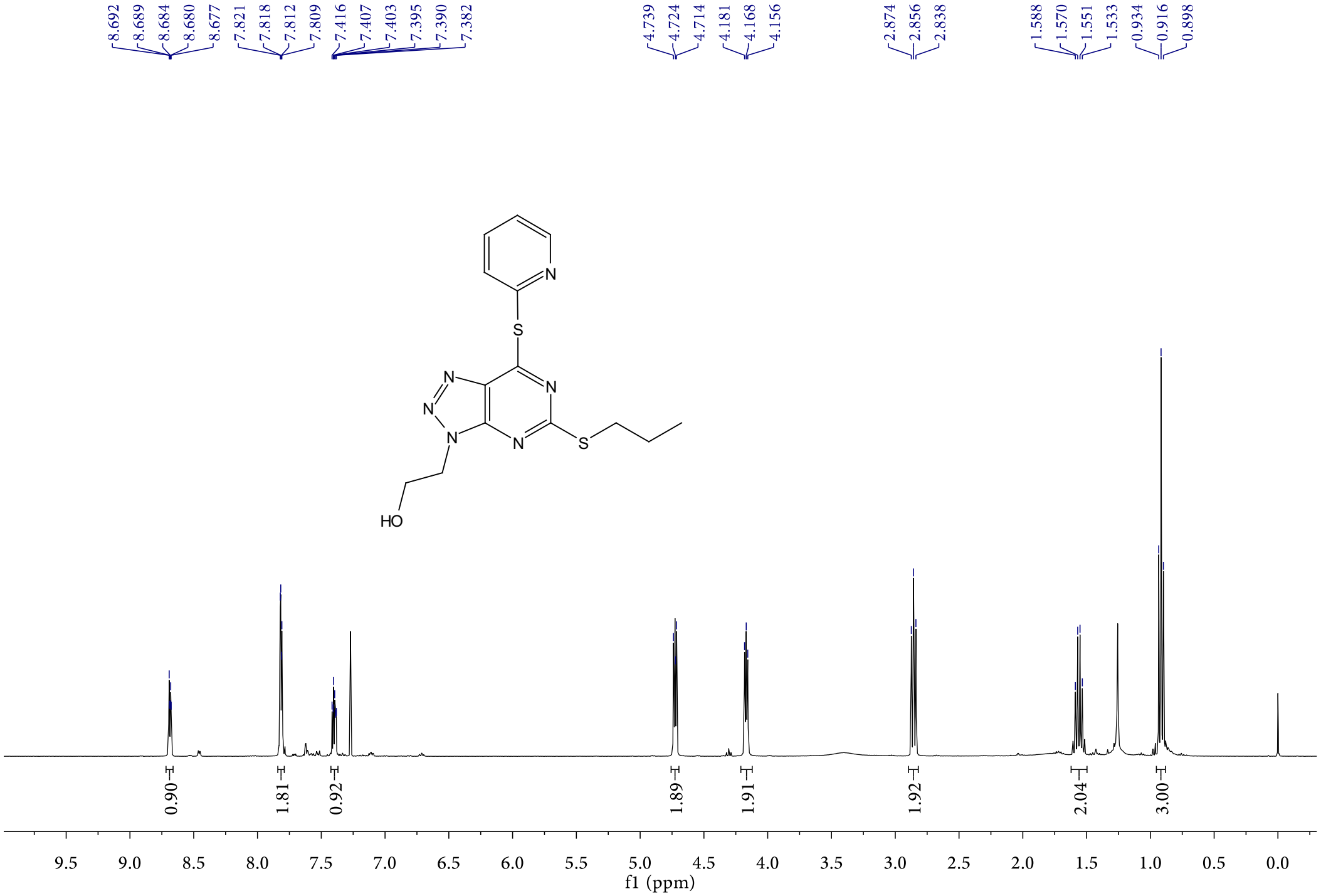

171.617
159.966
152.670
149.350
133.812
131.697
129.506
127.862
127.748
126.764
126.038
123.872
121.217
118.800
60.835
50.760
33.540
22.668
13.110
O
N
N
N
N
N
S
CH3
HO
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

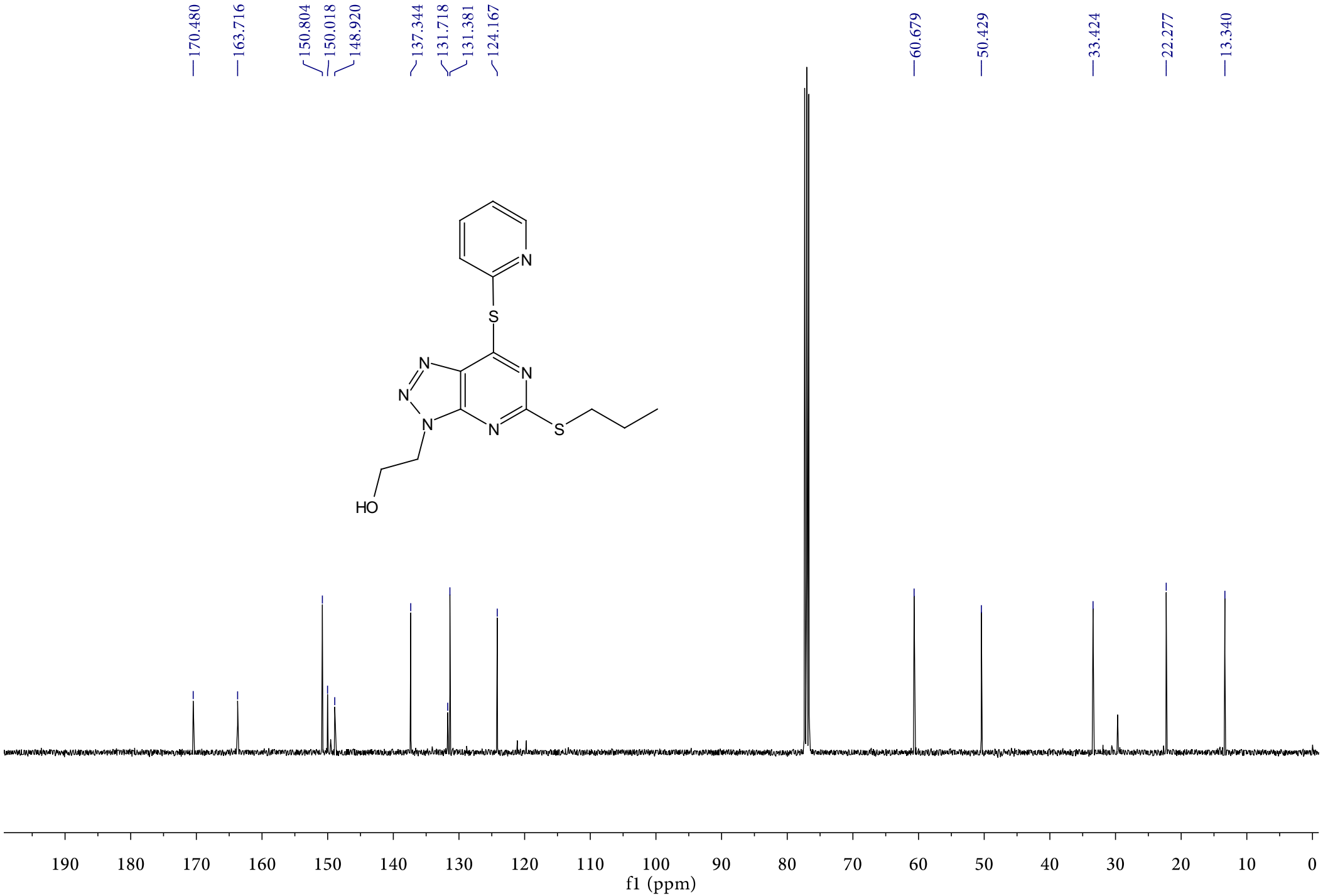

7.512
7.504
7.492
7.485
7.288
7.280
7.267
7.260
4.736
4.724
4.186
4.173
4.160
3.496
3.489
3.480
2.786
2.780
2.769
2.762
2.748
2.742
2.431
2.424
1.488
1.468
1.449
1.433
1.427
0.860
0.855
0.842
0.835
0.823
0.817
CH3
S
N
N
N
N
S
CH3
HO
1.97
2.26
1.99
1.99
0.98
1.98
2.95
2.00
3.00
8.5
8.0
7.5
7.0
6.5
6.0
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)

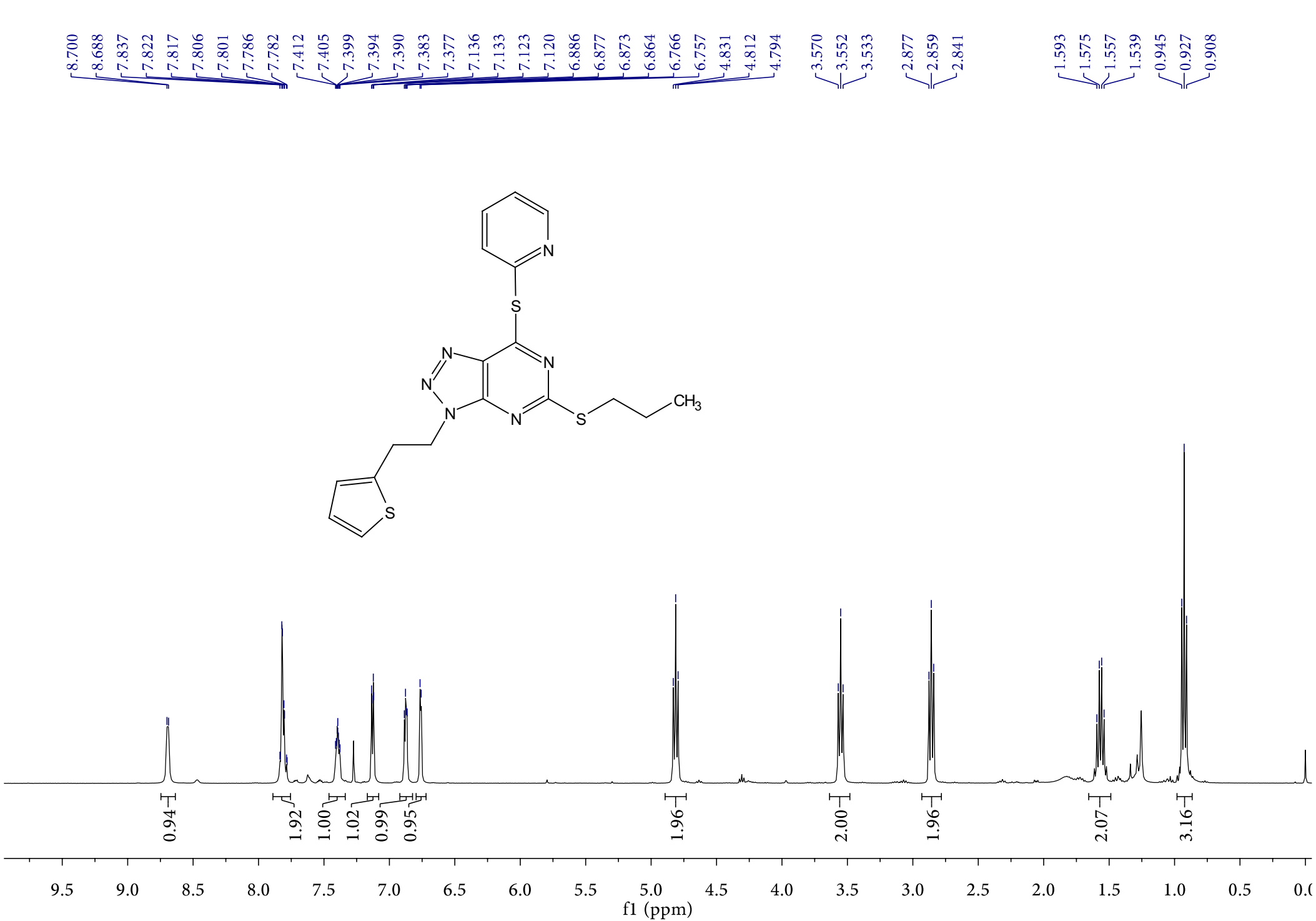

170.339
165.076
148.663
140.428
135.957
131.629
130.154
121.996
60.811
50.576
33.444
22.527
21.431
13.283
CH3
S
N
N
N
N
N
S
CH3
HO
f1 (ppm)

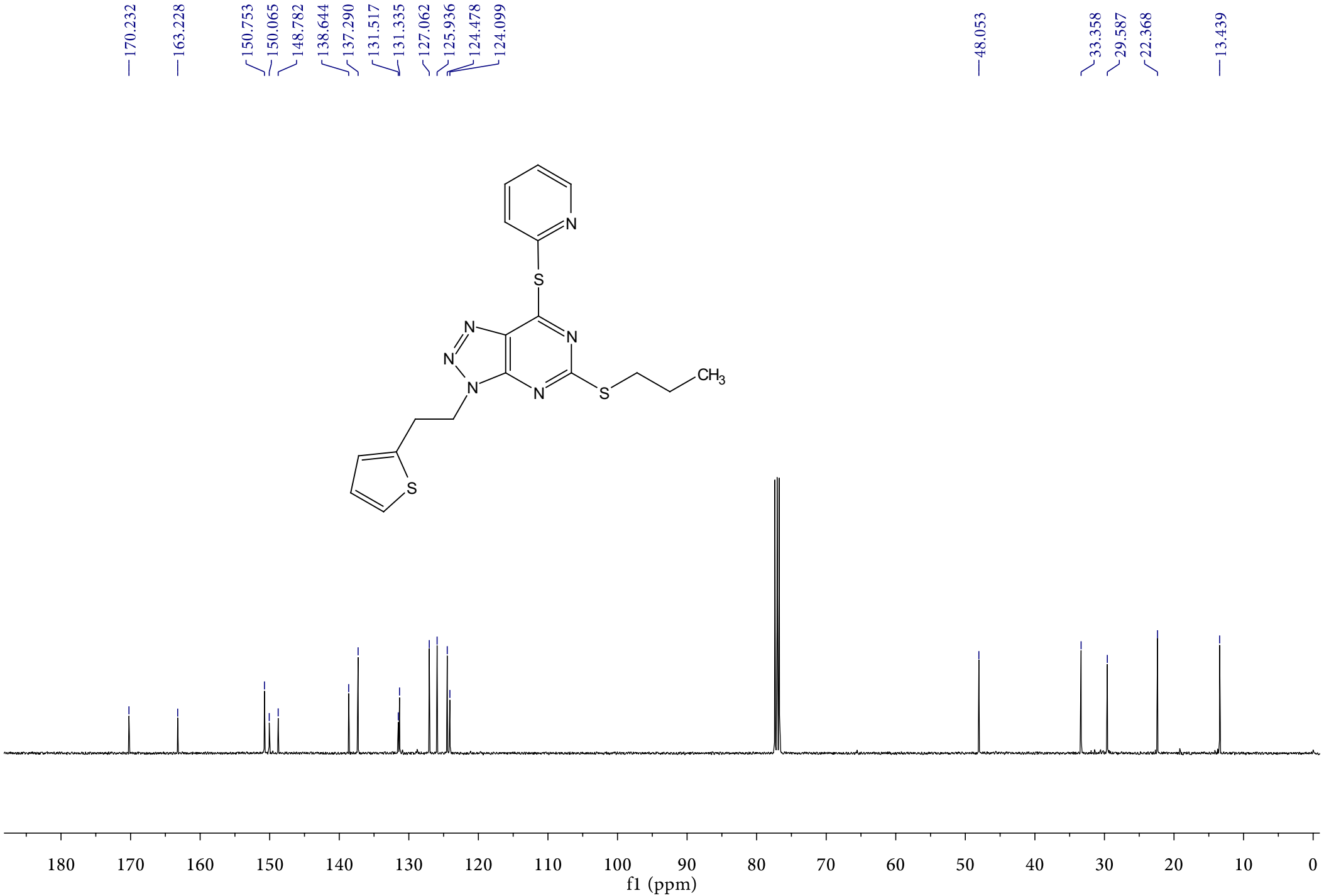

7.580
7.573
7.562
7.557
7.552
7.475
7.470
7.464
7.449
7.442
4.755
4.734
4.723
4.196
4.182
4.169
3.322
3.289
3.283
2.826
2.820
2.807
2.801
2.787
2.781
1.535
1.531
1.512
1.493
1.477
1.471
0.897
0.891
0.879
Cl
S
N
N
N
N
S
CH3
HO
1.93
1.95
1.98
1.99
0.98
1.98
2.00
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

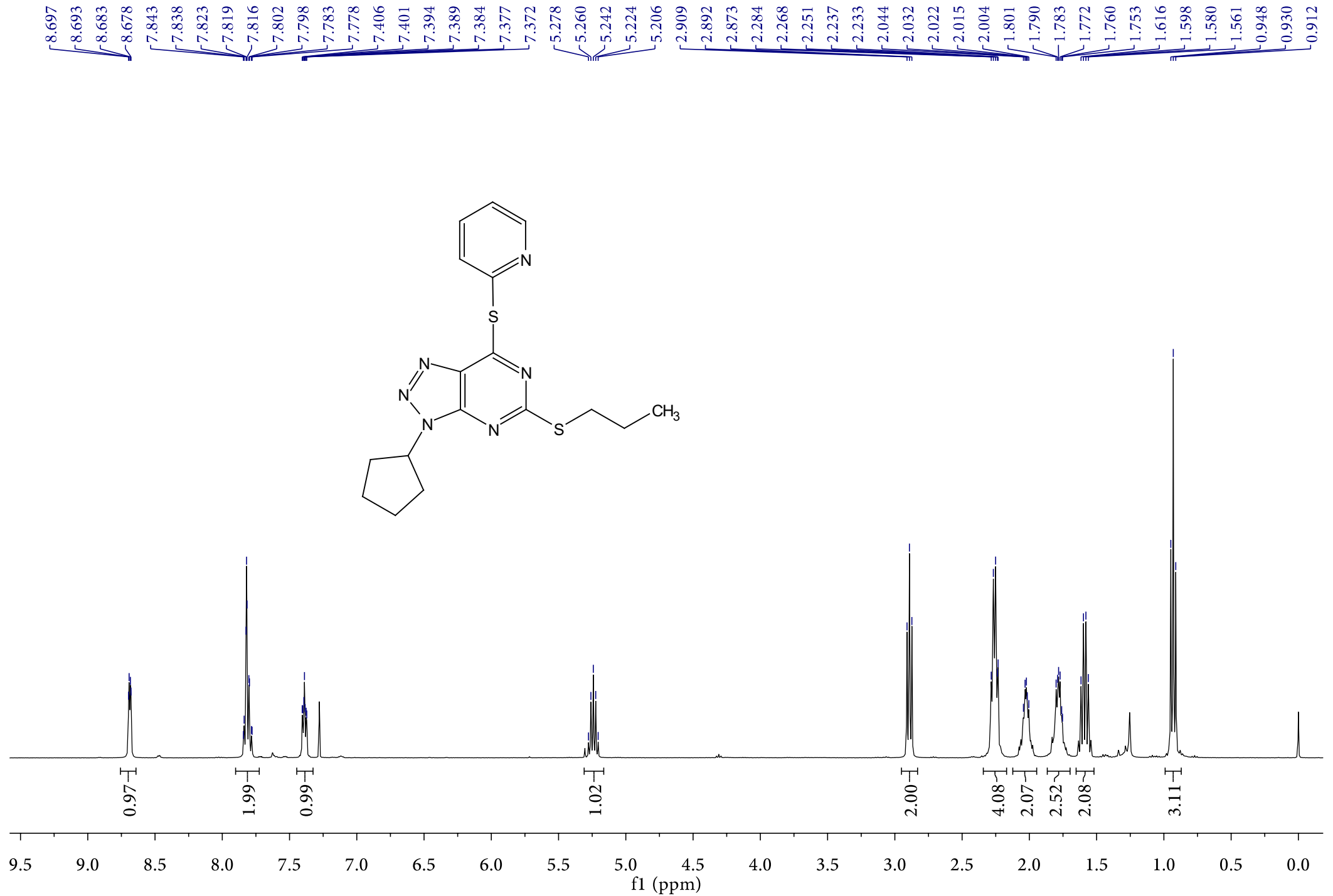

170.548
164.024
148.766
137.321
136.727
131.538
129.627
124.050
60.790
50.573
33.500
22.408
13.305
Cl
S
N
N
N
N
N
S
CH3
HO
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

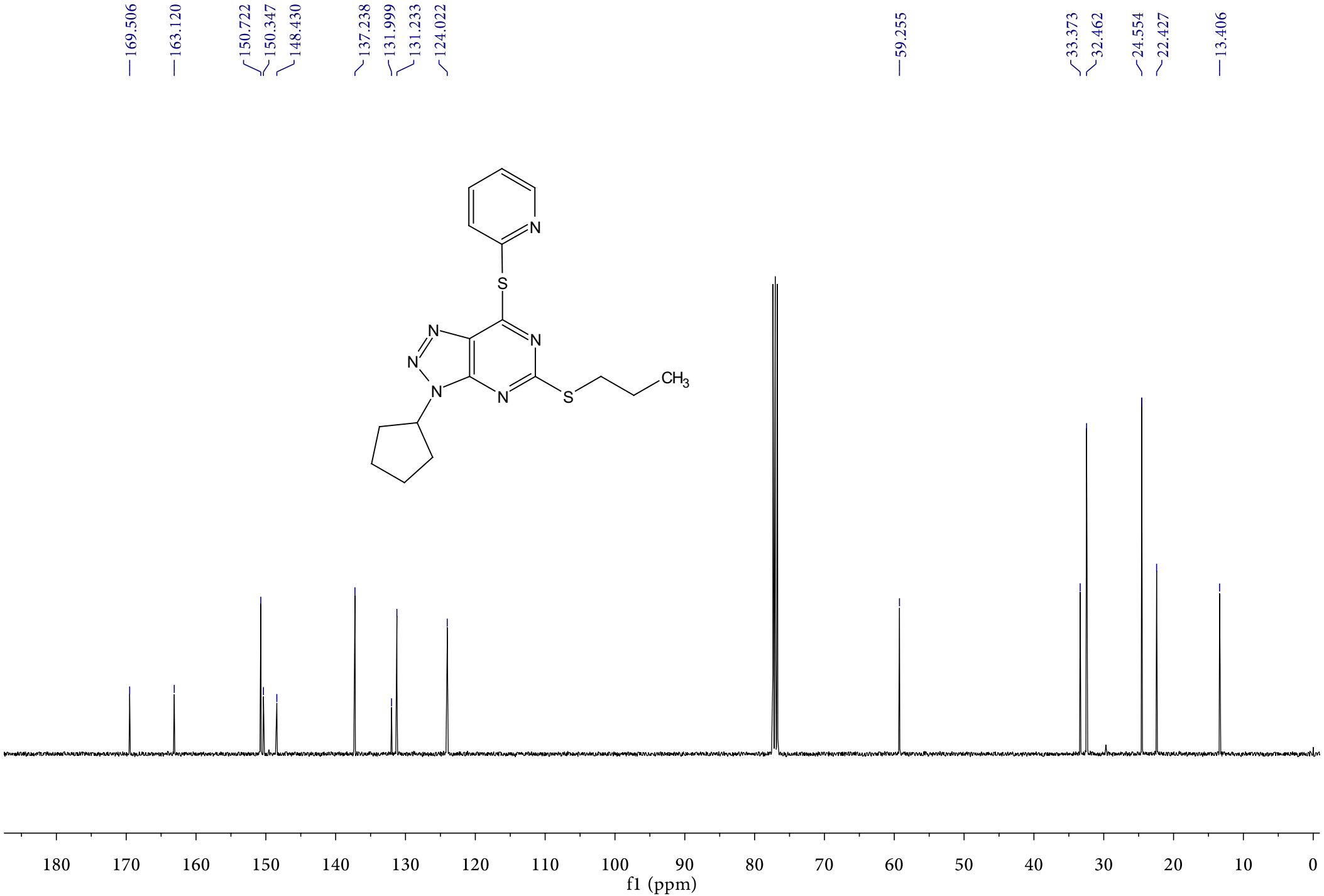

8.692
8.689
8.684
8.680
8.677
7.821
7.818
7.812
7.809
7.416
7.407
7.403
7.395
7.390
7.382
4.739
4.724
4.714
4.181
4.168
4.156
2.874
2.856
2.838
1.588
1.570
1.551
1.533
0.934
0.916
0.898
N
S
N
N
N
N
S
HO
0.90
1.81
0.92
1.89
1.91
1.92
2.04
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

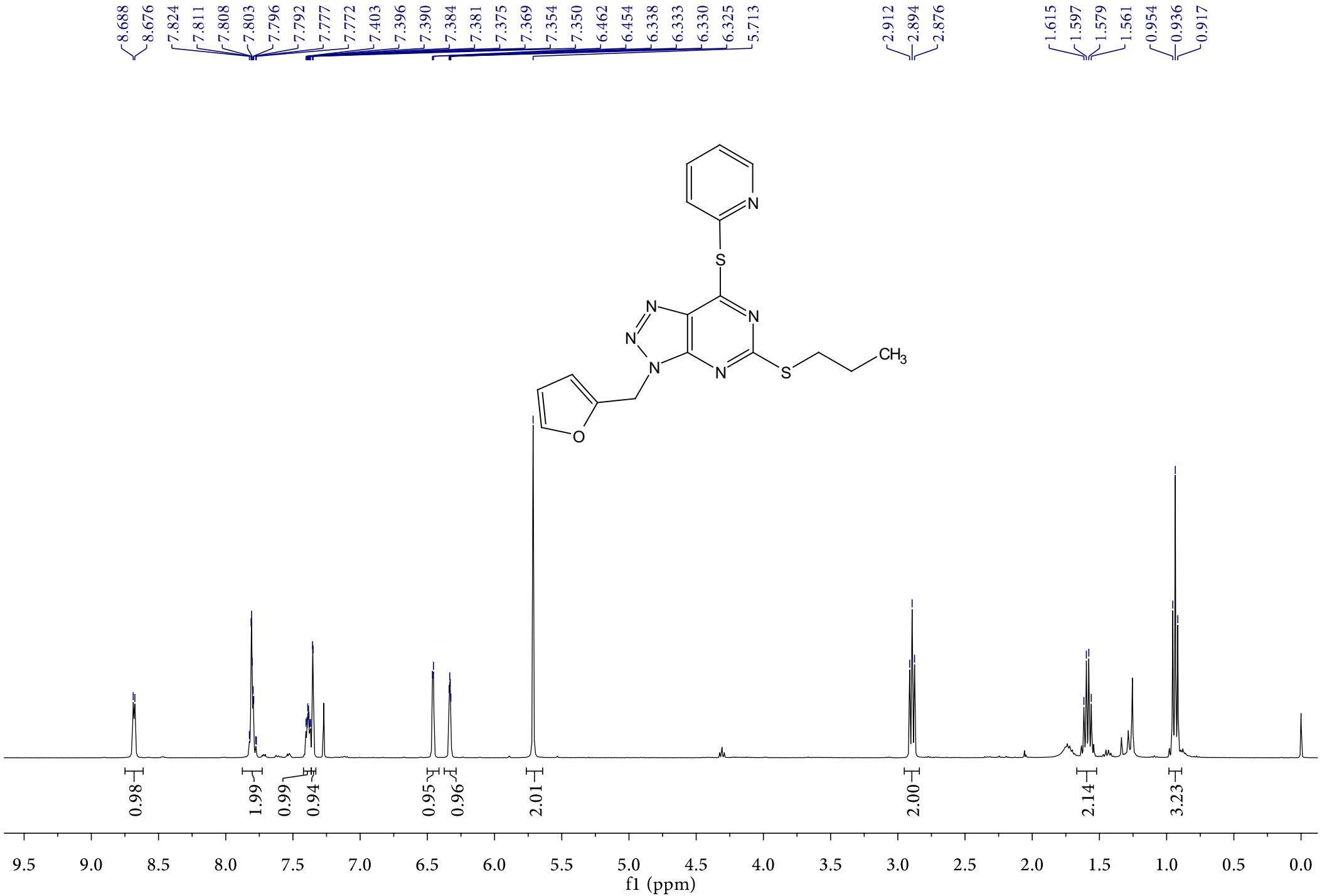

170.480
163.716
150.804
150.018
148.920
137.344
131.718
131.381
124.167
60.679
50.429
33.424
22.277
13.340
N
S
N
N
N
N
S
HO
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

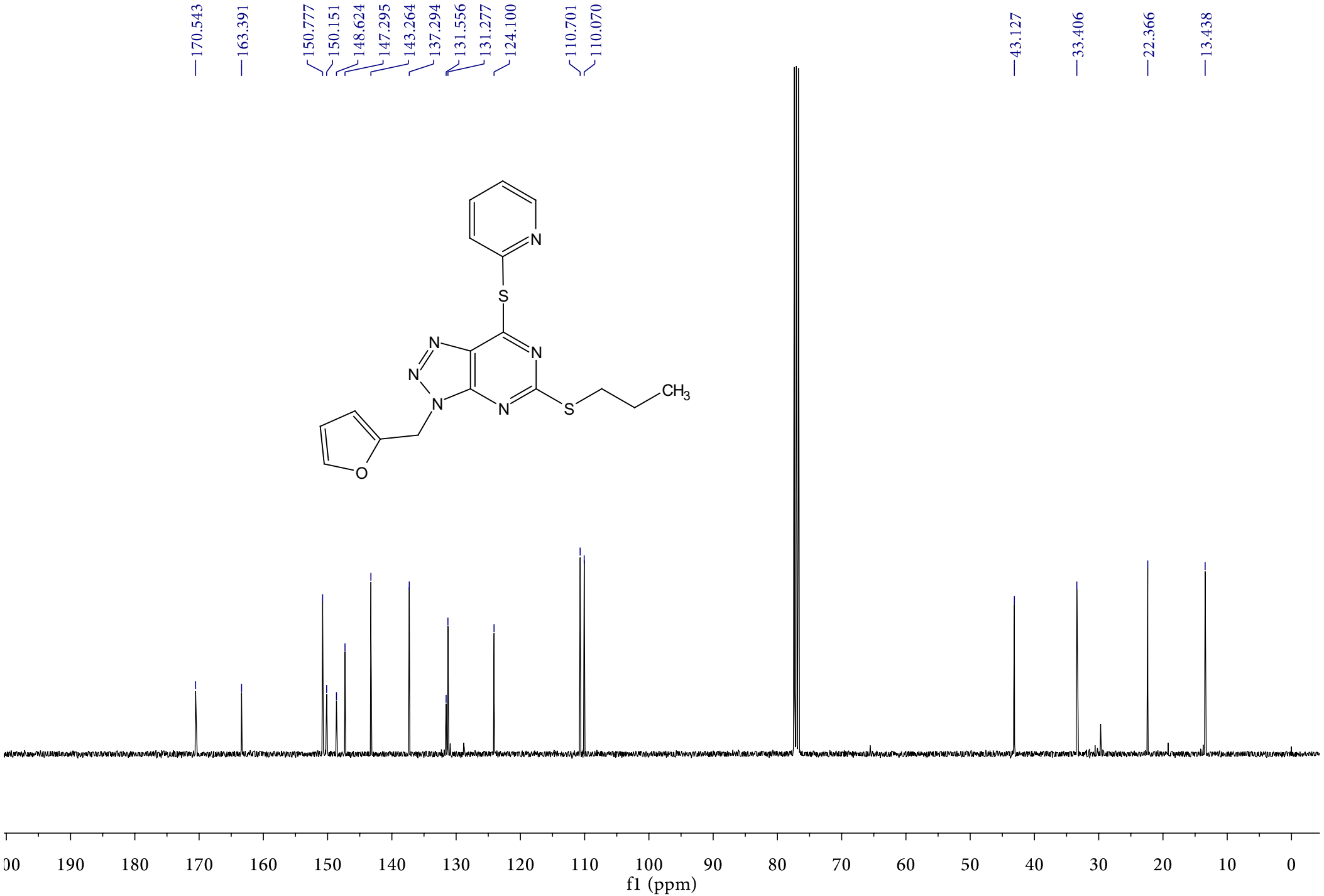

8.700
8.688
7.837
7.822
7.817
7.806
7.801
7.786
7.782
7.412
7.405
7.399
7.394
7.390
7.383
7.377
7.136
7.133
7.123
7.120
6.886
6.877
6.873
6.864
6.766
6.757
4.831
4.812
4.794
3.570
3.552
3.533
2.877
2.859
2.841
1.593
1.575
1.557
1.539
0.945
0.927
0.908
N
S
N
N
N
N
N
S
CH3
S
0.94
1.92
1.00
1.02
0.99
0.95
1.96
2.00
1.96
2.07
3.16
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
f1 (ppm)

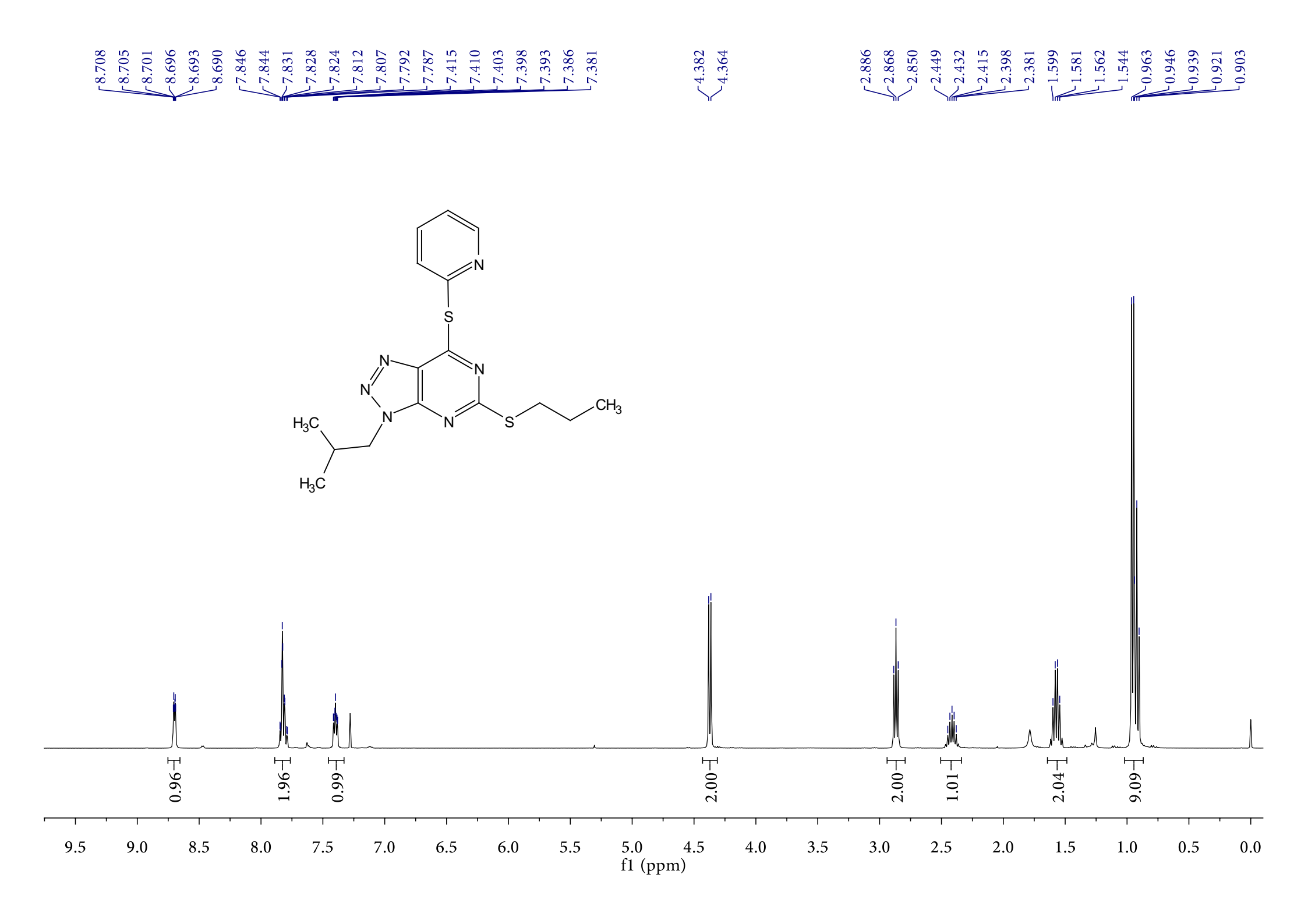

170.232
163.228
150.753
150.065
148.782
138.644
137.290
131.517
131.335
127.062
125.936
124.478
124.099
48.053
33.358
29.587
22.368
13.439
N
S
N
N
N
N
S
CH3
S
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

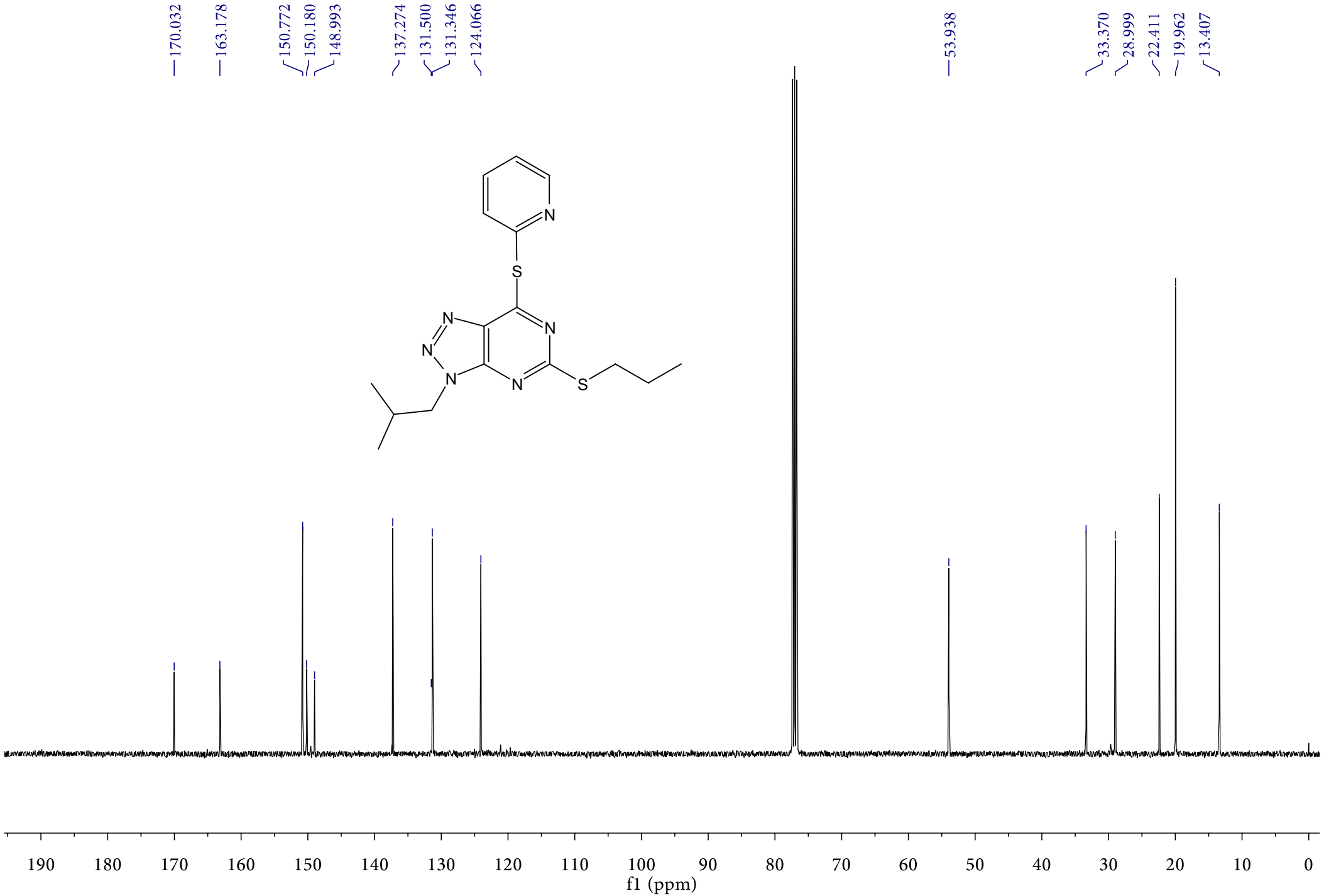

8.697
8.693
8.683
8.678
7.843
7.838
7.823
7.819
7.816
7.802
7.798
7.783
7.778
7.406
7.401
7.394
7.389
7.384
7.377
7.372
5.278
5.260
5.242
5.224
5.206
2.909
2.892
2.873
2.284
2.268
2.251
2.237
2.233
2.044
2.032
2.022
2.015
2.004
1.801
1.790
1.783
1.772
1.760
1.753
1.616
1.598
1.580
1.561
0.948
0.930
0.912
N
S
N
N
N
N
N
S
CH3
0.97
1.99
0.99
1.02
2.00
4.08
2.07
2.52
2.08
3.11
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)

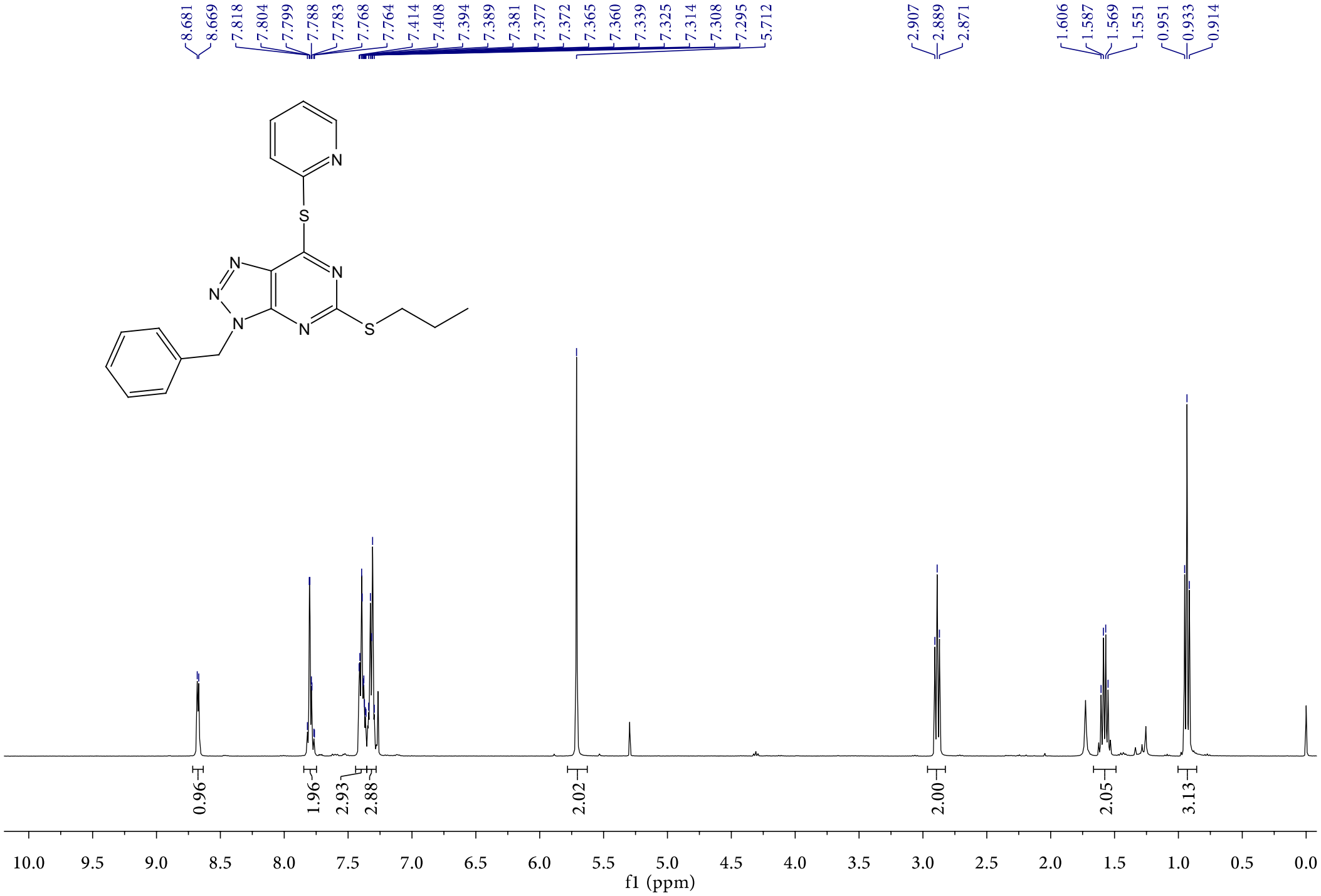

169.506
163.120
150.722
150.347
148.430
137.238
131.999
131.233
124.022
59.255
33.373
32.462
24.554
22.427
13.406
N
S
N
N
N
N
S
CH3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

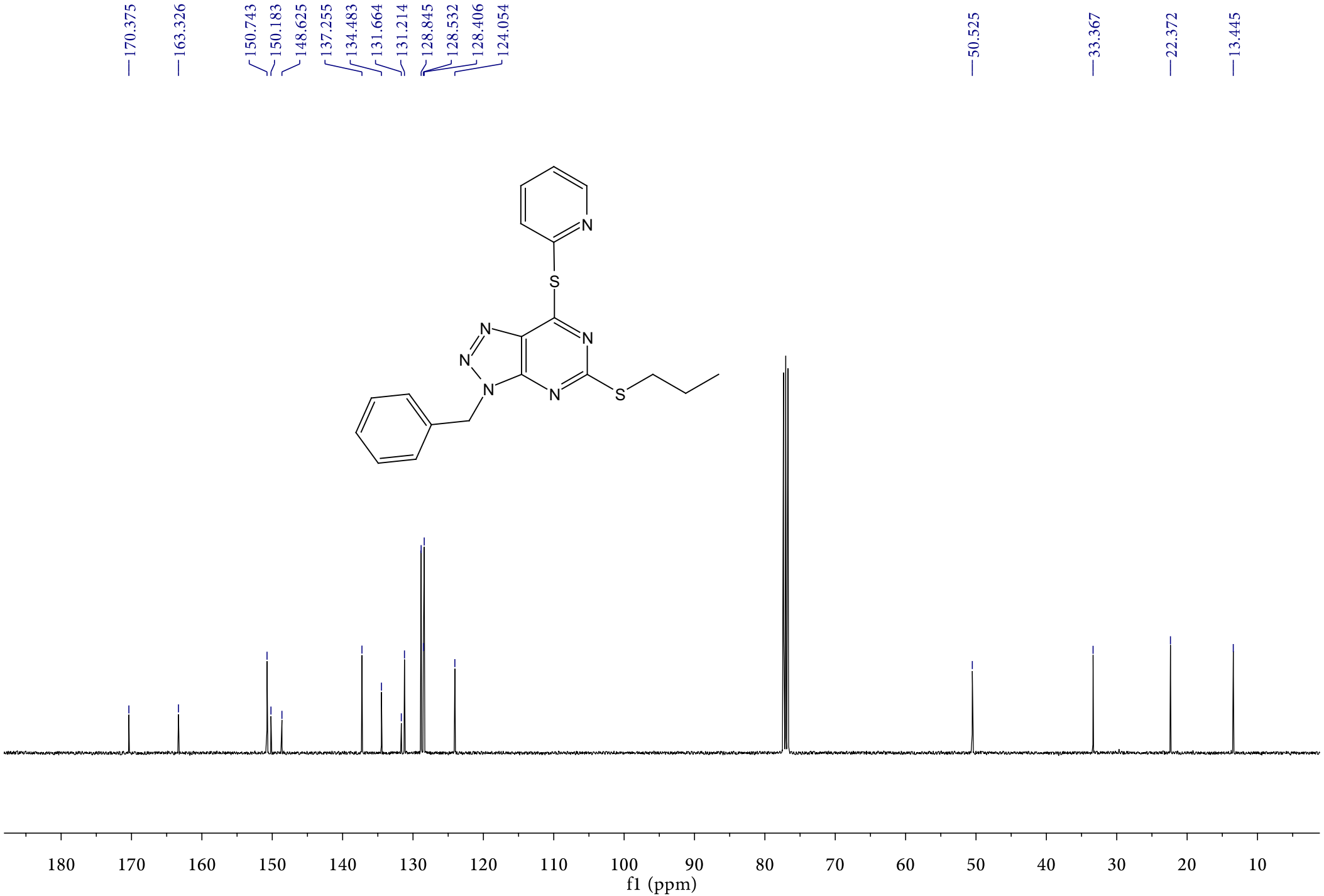

8.688
8.676
7.824
7.811
7.808
7.803
7.796
7.792
7.777
7.772
7.403
7.396
7.390
7.384
7.381
7.375
7.369
7.354
7.350
6.462
6.454
6.338
6.333
6.330
6.325
5.713
2.912
2.894
2.876
1.615
1.597
1.579
1.561
0.954
0.936
0.917
N
S
N
N
N
N
N
S
CH3
O
0.98
1.99
0.99
0.94
0.95
0.96
2.01
2.00
2.14
3.23
9.5
9.0
8.5
8.0
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)

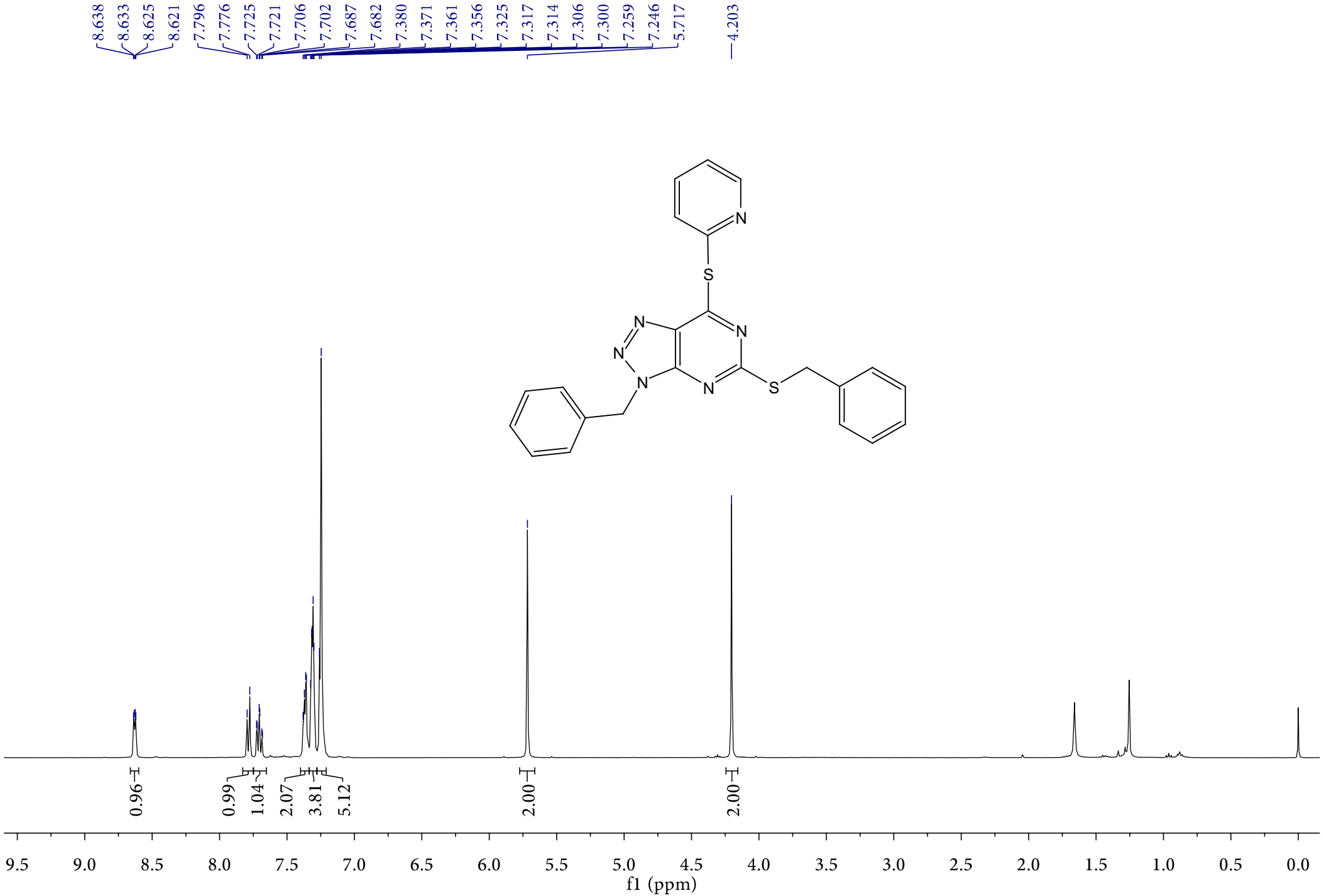

170.543
163.391
150.777
150.151
148.624
147.295
143.264
137.294
131.556
131.277
124.100
110.701
110.070
43.127
33.406
22.366
13.438
N
S
N
N
N
N
S
CH3
O
f1 (ppm)

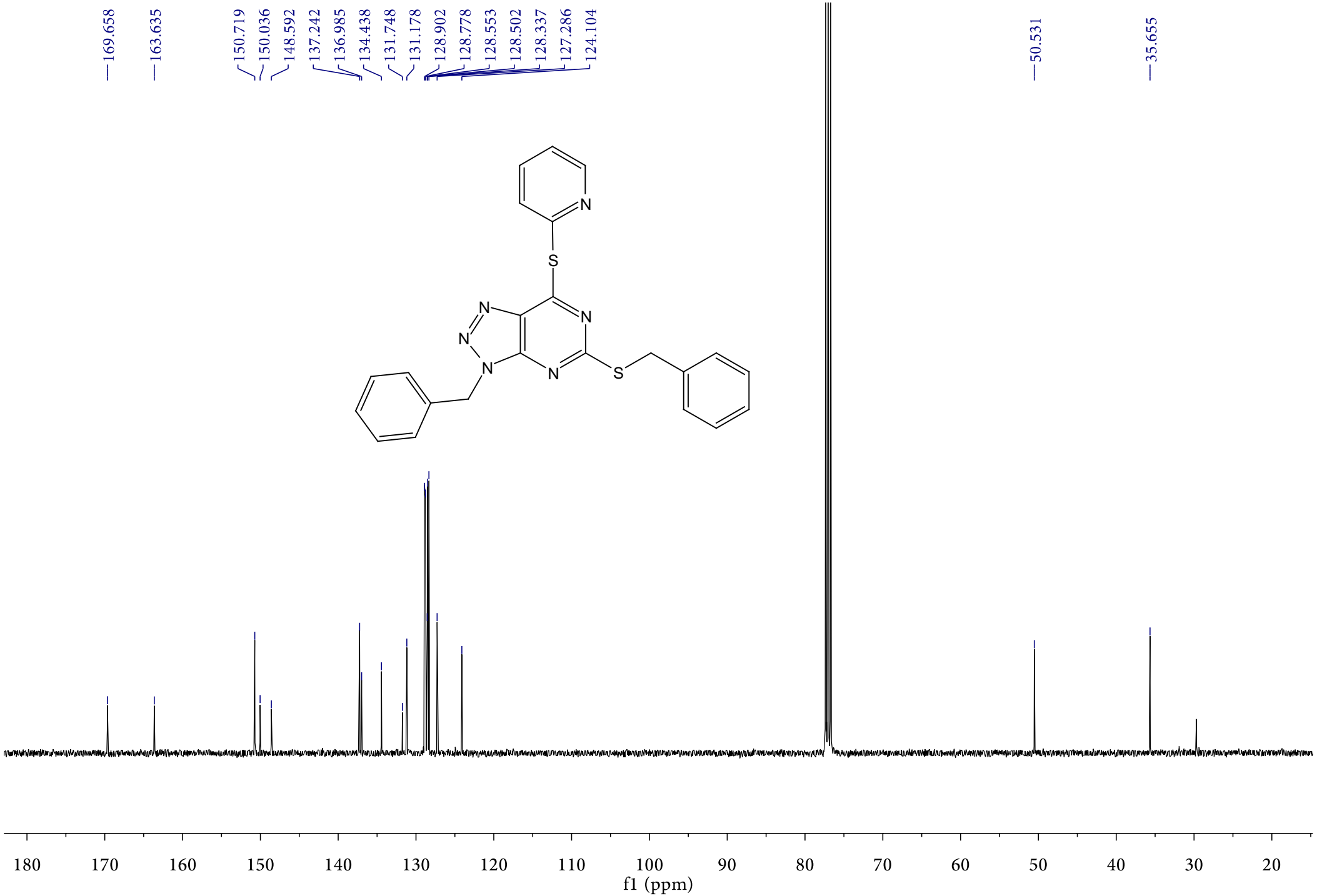

8.708
8.705
8.701
8.696
8.693
8.690
7.846
7.844
7.831
7.828
7.824
7.812
7.807
7.792
7.787
7.415
7.410
7.403
7.398
7.393
7.386
7.381
4.382
4.364
2.886
2.868
2.850
2.449
2.432
2.415
2.398
2.381
1.599
1.581
1.562
1.544
0.963
0.946
0.939
0.921
0.903
N
S
N
N
N
N
N
S
CH3
H3C
H3C
0.96
1.96
0.99
2.00
2.00
1.01
2.04
9.09
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

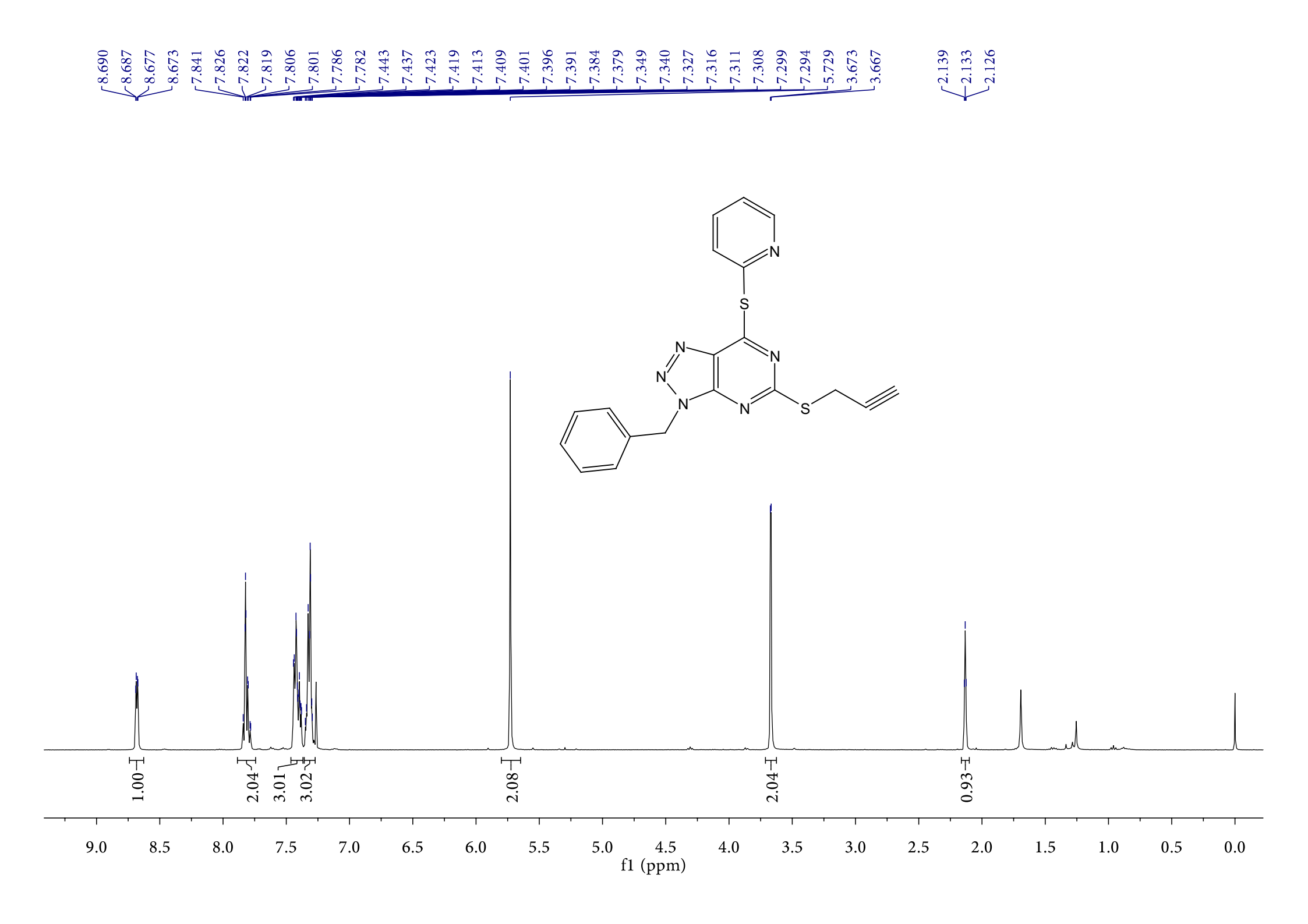

170.032
163.178
150.772
150.180
148.993
137.274
131.500
131.346
124.066
53.938
33.370
28.999
22.411
19.962
13.407
N
S
N
N
N
N
S
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

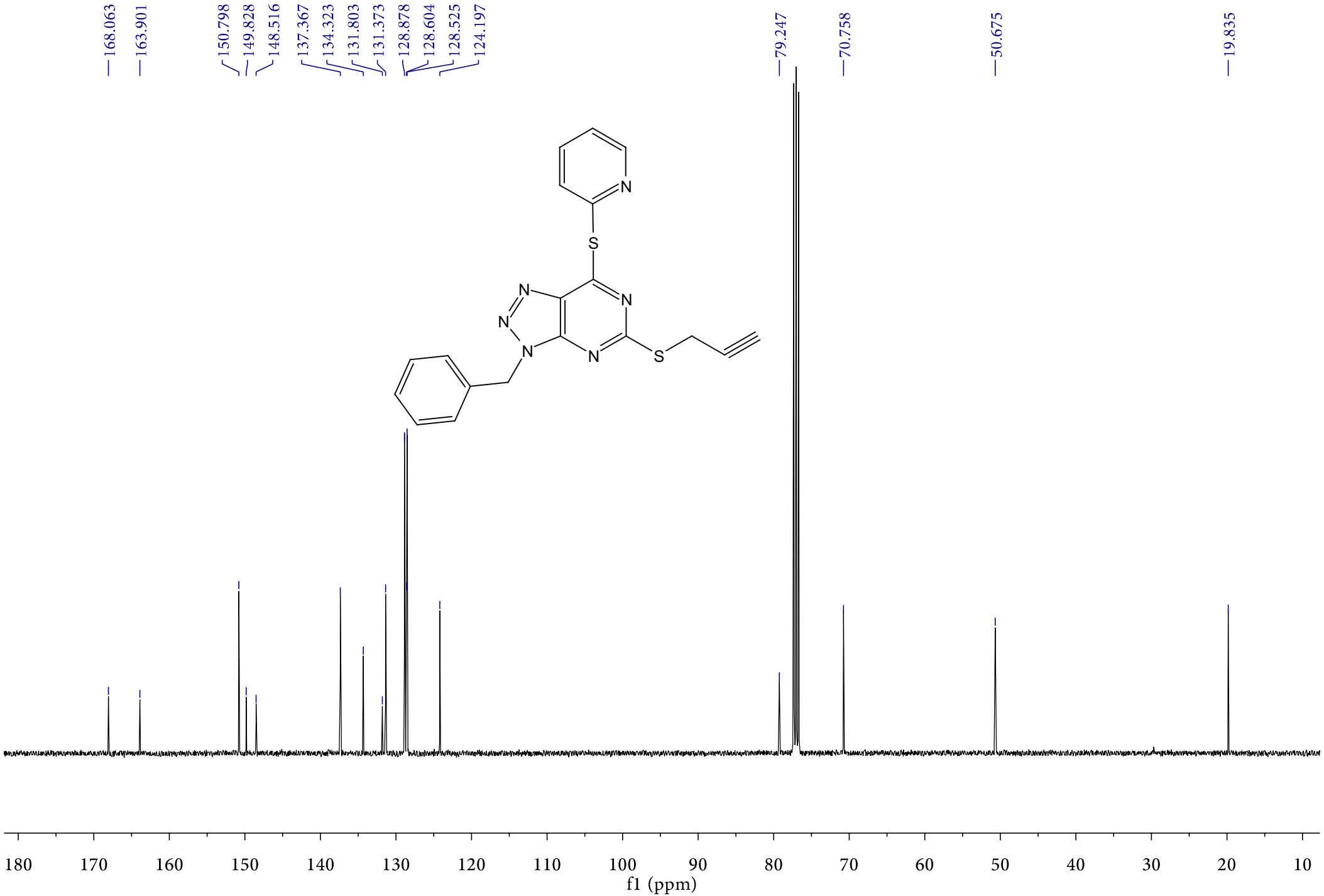

8.681
8.669
7.818
7.804
7.799
7.788
7.783
7.768
7.764
7.414
7.408
7.394
7.389
7.381
7.377
7.372
7.365
7.360
7.339
7.325
7.314
7.308
7.295
5.712
2.907
2.889
2.871
1.606
1.587
1.569
1.551
0.951
0.933
0.914
N
S
N
N
N
N
S
0.96
1.96
2.93
2.88
2.02
2.00
2.05
3.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


170.375
163.326
150.743
150.183
148.625
137.255
134.483
131.664
131.214
128.845
128.532
128.406
124.054
50.525
33.367
22.372
13.445
N
S
N
N
N
N
S
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


8.638
8.633
8.625
8.621
7.796
7.776
7.725
7.721
7.706
7.702
7.687
7.682
7.380
7.371
7.361
7.356
7.325
7.317
7.314
7.306
7.300
7.259
7.246
5.717
4.203
N
S
N
N
N
N
N
S
0.96
0.99
1.04
2.07
3.81
5.12
2.00
2.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


169.658
163.635
150.719
150.036
148.592
137.242
136.985
134.438
131.748
131.178
128.902
128.778
128.553
128.502
128.337
127.286
124.104
50.531
35.655
N
S
N
N
N
N
N
S
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


8.690
8.687
8.677
8.673
7.841
7.826
7.822
7.819
7.806
7.801
7.786
7.782
7.443
7.437
7.423
7.419
7.413
7.409
7.401
7.396
7.391
7.384
7.379
7.349
7.340
7.327
7.316
7.311
7.308
7.299
7.294
5.729
3.673
3.667
2.139
2.133
2.126
N
S
N
N
N
N
N
S
1.00
2.04
3.01
3.02
2.08
2.04
0.93
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)


168.063
163.901
150.798
149.828
148.516
137.367
134.323
131.803
131.373
128.878
128.604
128.525
124.197
79.247
70.758
50.675
19.835
N
S
N
N
N
N
N
S
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)