Supporting Information

Novel 2-(5-Aryl-4,5-dihydropyrazol-1-yl)thiazol-4-one as EGFR Inhibitors: Synthesis, Biological Assessment and Molecular Docking Insights

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1. Anti-proliferative action toward cancer cell lines

The two examined lung cancer cell line A549 and the breast cancer cell line T-47D have been obtained from American Type Culture Collection (ATCC). Cells lines were maintained as monolayers in Dulbecco's Modified Eagle's Medium (DMEM) supplemented with 10% FBS, 2 mM L-glutamine, 100 U/ml penicillin and 100µg/ml streptomycin sulfate. Cells were sub-cultured with trypsine /EDTA solution, counted with haemocytometer and plated onto 96-well plates (5000 cells/well) and left overnight to form a semi-confluent monolayer. Cell monolayers were treated in quadrates with vehicle (DMSO, 0.1% v/v), test samples (thiazolyl-pyrazolines **7a-o**) or Staurosporine as positive control for an exposure time of 48 h. At the end of exposure, MTT solution in PBS (5 mg/ml) was then added to all well including no cell blank and left to incubate for 90 min. The formation of formazan crystals were visually confirmed using phase contract microscopy. DMSO (100 µl/well) was added to dissolve the formazan crystals with shaking for 10 min after which the absorbance was read at 590 nm against no cell blanks on a FLuo Star Optima microplate reader (BMG technologies, Germany). Cell proliferation was calculated comparing the OD values of the DMSO control wells and those of the samples represented as % proliferation to the control. Dose-response experiment was performed on samples producing > or =50% loss of cell proliferation using five serial 2-fold dilutions (50, 25, 12.5, 6.25 and 3.125 µM) of the sample. IC_{50} values (concentration of sample causing 50% loss of cell proliferation of the vehicle control) were calculated using non-linear regression curve fitting of the dose response plots on GraphPad Prism V.6.0 software.

2. Cell Cycle Analysis

Breast cancer T-47D cells were treated with thiazolyl-pyrazolines **7g** and **7m** for 24 h (at their IC_{50} concentration), and then cells were washed twice with ice-cold phosphate buffered saline (PBS). Subsequently, the treated cells were collected by centrifugation, fixed in ice-cold 70% (*v*/*v*) ethanol, washed with PBS, re-suspended with 100 µg/mL RNase, stained with 40 µg/mL PI, and analyzed by flow cytometry using FACS Calibur (Becton Dickinson, BD, Franklin Lakes, NJ, USA). The cell cycle distributions were calculated using CellQuest software 5.1 (Becton Dickinson).

3. Annexin V-FITC Apoptosis Assay

Phosphatidylserine externalization was assayed using Annexin V-FITC/PI apoptosis detection kit (BD Biosciences, USA) according to the manufacturer's instructions. Breast cancer T-47D cells were cultured to a monolayer then treated with thiazolyl-pyrazolines **7g** and **7m** at their IC_{50} concentration. Briefly, cells were then harvested *via* trypsinization, and rinsed twice in PBS followed by binding buffer. Moreover, cells were re-suspended in 100 µL of binding buffer with the addition of 1 µL of FITC-Annexin V followed by an incubation period of 30 min at 4 °C. Cells were then rinsed in binding buffer and resuspended in 150 µL of binding buffer with the addition of 1 µL of DAPI (1 µg/µL in PBS). Cells were then analyzed using the flow cytometer BD FACS Canto II and the results were interpreted with FlowJo7.6.4 software (Tree Star, Ashland, OR, USA).

4. EGFR Kinase Inhibitory Activity

Thiazolyl-pyrazolines **7b, 7g, 7l and 7m** were tested in vitro for inhibition of EGFR tyrosine kinase using ADP-Glo™ Kinase Assay (Promega, Catalogue No. V3831) which is a luminescent kinase assay that measures ADP formed from a kinase reaction. ADP is converted into ATP which is converted into light by Ultra-Glo™ Luciferase. The luminescent signal positively correlates with ADP amount and kinase activity.

Protocol: first dilute enzyme, substrate, ATP and inhibitors in Tyrosine Kinase Buffer (40 mM Tris,7.5; 20 mM $MgCl_2$; 0.1 mg/ml BSA (bovine serum albumin); 2 mM $MnCl_2$; 50µM DTT), then add to the wells of 384 low volume plate: 1 µl of inhibitor or (5% DMSO), 2 µl of enzyme and 2 µl of substrate/ATP mix. Incubate at room temperature for 60 minutes, add 5 µl of ADP-Glo™ Reagent, incubate at room temperature for 40 minutes, add 10 µl of Kinase Detection reagent, incubate at room temperature for 30 minutes and finally record luminescence (Integration time 0.5-1second).

6. Molecular Docking Study

All the molecular modeling studies were carried out using Molecular Operating Environment (MOE, 2020.0901) software. All minimizations were performed with MOE until an RMSD gradient of 0.05 kcal·mol^{-1}Å^{-1} with MMFF94x force field and the partial charges were automatically calculated. The X-ray crystallographic structure of Epidermal Growth Factor Receptor (EGFR) co-crystallized with the 4-anilinoquinazoline inhibitor Erlotinib (PDB ID: 1M17) was downloaded from the protein data bank. Water molecules and ligands that are not involved in binding were removed. Then, the protein was prepared for docking study using *Protonate 3D* protocol in MOE with default options. The co-crystalized ligand was used to define the binding site for docking. Triangle Matcher placement method and London dG scoring function were used for docking. Docking setup was first validated by self-docking of the co-crystallized ligand (Erlotinib) in the vicinity of the binding site of the enzyme with energy score (S) = −10.86 kcal/mol and RMSD of 1.46 Å. The ability of the docking protocol to reproduce all the key interactions accomplished by the co-crystallized ligand (Erlotinib) with the key amino acids in the binding site indicated the suitability of the adopted docking protocol for the intended docking study. These interactions include H-bonding with Met769, through water mediated H-bonding with Thr766 and cation-π interaction with Lys721 (Figure S1 and S2). The validated setup was then used for predicting the ligand-target interactions of the compounds of interest.

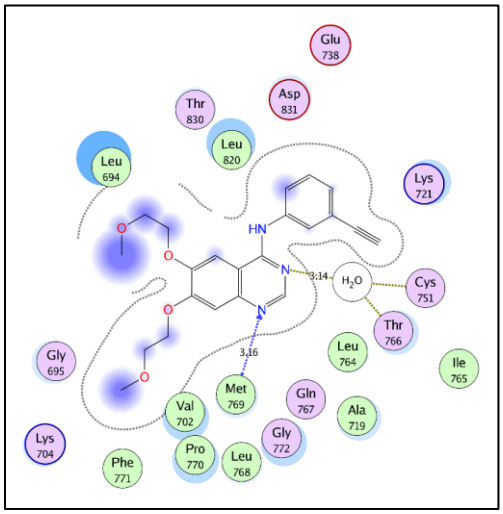
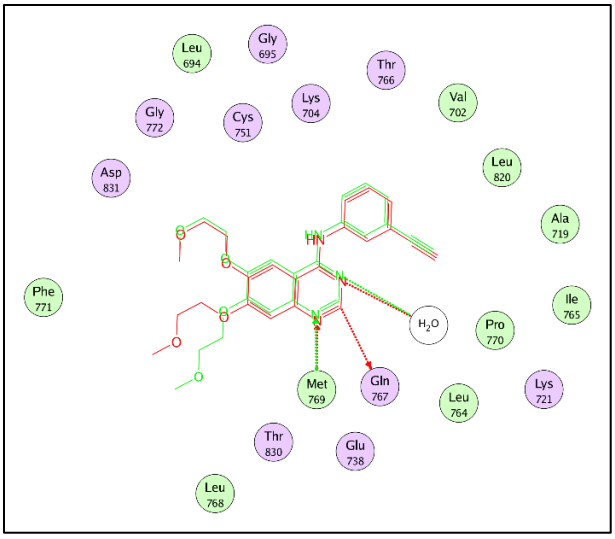
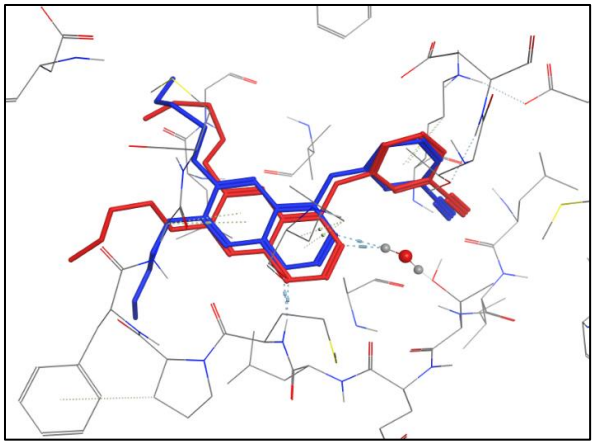


Figure S1. 2D interaction diagram showing Erlotinib docking pose interactions with the key amino acids in the EGFR binding site.



(A)



(**B)**

Figure S2. A) 2D representation and **B)** 3D representation of the superimposition of the co-crystallized (red) and the docking pose (blue) of Erlotinib in the EGFR binding site with RMSD of 1.46Å. (Ligand Hydrogen atoms were removed for clarity)

6. Cells distribution of Cell cycle

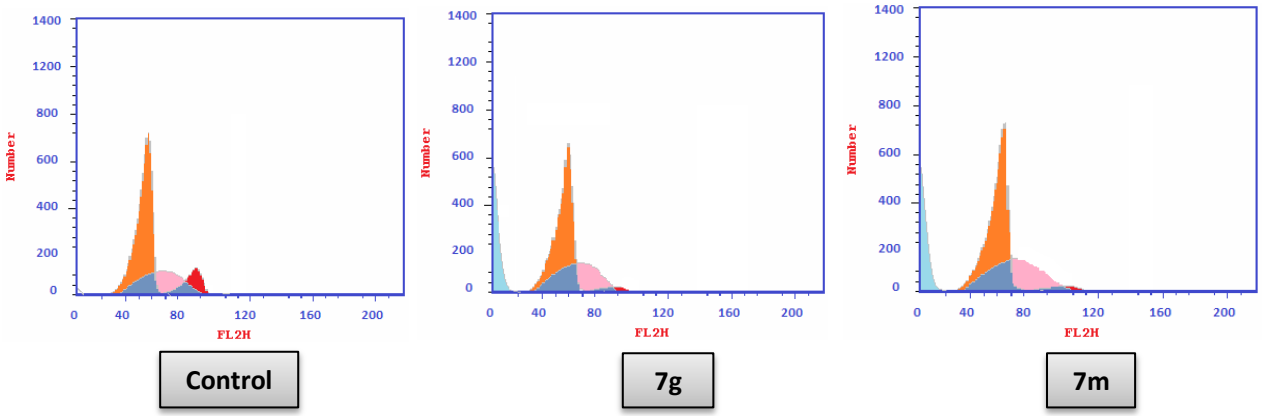


Figure S3. Effect of thiazolyl pyrazolines **7g** and **7m** on the phases of cell cycle of T-47D cells

7. Characterisation of the key intermediate (5c) and the target compounds (7a-o)

2-(5-(4-Fluorophenyl)-3-(thiophen-2-yl)-4,5-dihydro-1H-pyrazol-1-yl)thiazol-4(5H)-one 5c

White crystals (yield 89%), m.p. 191-193 °C; ^{1}H NMR δ *ppm*: 3.40 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 3.6 Hz, 18.0 Hz), 3.90 (s, 2H, CH_2 of thiazolidenone moiety), 4.11 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 4.8 Hz, 18.0 Hz), 5.87 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 3.6 Hz, 10.8 Hz), 7.14-7.18 (m, 3H, Aromatic protons), 7.28-7.30 (m, 2H, Aromatic protons), 7.58 (s, 1H, Aromatic protons), 7.80-7.84 (m, 1H, Aromatic protons); ^{13}C NMR *δ ppm*: 44.47, 60.53, 63.58, 116.32, 128.33, 128.97, 132.19, 132.91, 133.07, 136.85, 156.56, 175.36, 177.64, 187.39; Anal. Calcd. for $C_{16}H_{12}FN_3OS_2$: C, 55.64; H, 3.50; N, 12.17; found C, 55.81; H, 3.48; N, 12.22;

5-Benzylidene-2-(5-(4-fluorophenyl)-3-(p-tolyl)-4,5-dihydro-1H-pyrazol-1-yl)thiazol-4(5H)-one (7a).

White crystals (yield 85%), m.p. 247-249 °C; IR (KBr, *v* cm^{-1}) 1707 (C=O); ^{1}H NMR δ *ppm*: 2.39 (s, 3H, CH_3), 3.46 (dd, 1H, H_A of pyrazoline methylene C-4 protons , *J*= 4.4 Hz, 18.4 Hz), 4.12 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.2 Hz, 18.4 Hz), 5.90 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.4

Hz, 11.2 Hz), 7.20-7.24 (m, 2H, Aromatic protons), 7.33-7.37 (m, 4H, Aromatic protons), 7.45 (t, 1H, Aromatic protons, *J*= 7.2 Hz), 7.53-7.57 (m, 2H, Aromatic protons), 7.65-7.67 (m, 3H, Aromatic protons), 7.79 (d, 2H, Aromatic protons, *J*= 8.0 Hz); ^{13}C NMR *δ ppm*: 21.63 (CH_3), 43.98 (CH_2), 63.51(CH), 116.14, 116.35, 127.21, 128.00, 128.43, 128.53, 128.61, 129.76, 130.08, 130.14, 130.41, 131.42, 134.28, 136.70, 136.73, 142.57, 160.94, 162.01, 163.37 (Aromatic carbons), 170.73 (C=O); Anal. Calcd. for $C_{26}H_{20}FN_3OS$: C, 70.73; H, 4.57; N, 9.52; found C, 70.91; H, 4.53; N, 9.56.

2-(5-(4-Fluorophenyl)-3-(p-tolyl)-4,5-dihydro-1H-pyrazol-1-yl)-5-(4-hydroxybenzylidene)thiazol-4(5H)-one (7b).

White crystals (yield 78%), m.p. > 300 °C; IR (KBr, *v* cm^{-1}) 3215 (OH) and 1701 (C=O); ^{1}H NMR *δ ppm*: 2.37 (s, 3H, CH_3), 3.43 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.0 Hz, 18.4 Hz), 4.10 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.2 Hz, 18.4 Hz), 5.87 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.0 Hz, 11.2 Hz), 6.92-6.96 (m, 2H, Aromatic protons), 7.18-7.24 (m, 2H, Aromatic protons), 7.30-7.36 (m, 4H, Aromatic protons), 7.50 (d, 2H, Aromatic protons, *J*= 8.0 Hz), 7.56 (s, 1H, Aromatic protons), 7.78 (d, 2H, Aromatic protons, *J*= 8.0 Hz), 10.10 (s, 1H, OH); ^{13}C NMR *δ ppm*: 21.63 (CH_3), 43.94 (CH_2), 63.39 (CH), 116.12, 116.33, 116.74, 124.28, 125.16, 127.33, 127.94, 128.49, 128.57, 130.06, 131.95, 132.37, 136.86, 136.89, 142.41, 159.90, 160.91, 161.45, 163.34 (Aromatic carbons), 170.66 (C=O); Anal. Calcd. for $C_{26}H_{20}FN_3O_2S$: C, 68.26; H, 4.41; N, 9.18; found C, 68.07; H, 4.44; N, 9.14.

2-(5-(4-Fluorophenyl)-3-(p-tolyl)-4,5-dihydro-1H-pyrazol-1-yl)-5-(4-methoxybenzylidene)thiazol-4(5H)-one (7c).

White crystals (yield 82%), m.p. 189-200 °C; IR (KBr, *v* cm^{-1}) 1705 (C=O); ^{1}H NMR *δ ppm*: 2.38 (s, 3H, CH_3), 3.43 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.4 Hz, 18.4 Hz), 3.82 (s, 3H, OCH_3), 4.09 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.2 Hz, 18.4 Hz), 5.86 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.0 Hz, 11.2 Hz), 7.08 (d, 2H, Aromatic protons, *J*= 8.8 Hz), 7.19-7.24 (m, 2H, Aromatic protons), 7.31-7.35 (m, 4H, Aromatic protons), 7.58-7.62 (m, 3H, Aromatic protons), 7.77 (d, 2H, Aromatic protons, *J*= 8.8 Hz); ^{13}C NMR *δ ppm*: 21.60 (CH_3), 43.93 (CH_2), 55.84 (OCH_3), 63.41 (CH), 115.25, 115.30, 116.11, 116.32, 125.48, 126.70, 127.23, 127.89, 127.94, 128.47, 128.55, 130.04, 131.45, 132.06, 136.76, 136.79,

142.46, 160.92, 161.05, 161.52, 161.63, 163.35 (Aromatic carbons), 170.66 (C=O); Anal. Calcd. for $C_{27}H_{22}FN_3O_2S$: C, 68.77; H, 4.70; N, 8.91; found C, 68.67; H, 4.75; N, 8.95.

5-(4-(Dimethylamino)benzylidene)-2-(5-(4-fluorophenyl)-3-(p-tolyl)-4,5-dihydro-1H-pyrazol-1-yl)thiazol-4(5H)-one (7d).

White crystals (yield 84%), m.p. 285-287 °C; IR (KBr, *v* cm^{-1}) 1717 (C=O); ^{1}H NMR δ *ppm*: 2.39 (s, 3H, CH_3), 3.01 (s, 6H, $N(CH_3)_2$), 3.42 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.4 Hz, 18.8 Hz), 4.09 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.2 Hz, 18.4 Hz), 5.86 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.4 Hz, 11.2 Hz), 6.82 (d, 2H, Aromatic protons, *J*= 8.0 Hz), 7.19-7.24 (m, 2H, Aromatic protons), 7.31-7.37 (m, 4H, Aromatic protons), 7.47 (d, 2H, Aromatic protons, *J*= 8.4 Hz), 7.53 (s, 1H, Aromatic protons), 7.78 (d, 2H, Aromatic protons, *J*= 8.0 Hz); Anal. Calcd. for $C_{28}H_{25}FN_4OS$: C, 69.40; H, 5.20; N, 11.56; found C, 69.31; H, 5.16; N, 11.53.

5-(4-Chlorobenzylidene)-2-(5-(4-fluorophenyl)-3-(p-tolyl)-4,5-dihydro-1H-pyrazol-1-yl)thiazol-4(5H)-one (7e).

White crystals (yield 80%), m.p. 256-258 °C; IR (KBr, *v* cm^{-1}) 1709 (C=O); ^{1}H NMR δ *ppm*: 2.40 (s, 3H, CH_3), 3.48 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.4 Hz, 18.4 Hz), 4.13 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.6 Hz, 18.4 Hz), 5.90 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.4 Hz, 11.2 Hz), 7.20-7.25 (m, 2H, Aromatic protons), 7.31-7.38 (m, 4H, Aromatic protons), 7.59-7.65 (m, 3H, Aromatic protons), 7.67-7.72 (m, 2H, Aromatic protons), 7.79 (d, 2H, Aromatic protons, *J*= 8.8 Hz); MS *m/z* [%]: 475.93 [M^+, 60.89], 271.20 [100]; Anal. Calcd. for $C_{26}H_{19}ClFN_3OS$: C, 65.61; H, 4.02; N, 8.83; found C, 65.83; H, 4.07; N, 8.75.

5-Benzylidene-2-(5-(4-fluorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)thiazol-4(5H)-one (7f).

White crystals (yield 88%), m.p. 236-238 °C; IR (KBr, *v* cm^{-1}) 1705 (C=O); ^{1}H NMR δ *ppm*: 3.42 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.0 Hz, 18.0 Hz), 3.82 (2s, 3H, OCH_3), 4.07 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.2 Hz, 18.0 Hz), 5.85 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.4 Hz, 11.2 Hz), 7.06-7.10 (m, 3H, Aromatic protons), 7.18-7.23 (m, 3H, Aromatic protons), 7.31-7.34 (m, 3H,

Aromatic protons), 7.58-7.60 (m, 3H, Aromatic protons), 7.81 (d, 2H, Aromatic protons, *J*= 8.8 Hz); Anal. Calcd. for $C_{26}H_{20}FN_3O_2S$: C, 68.26; H, 4.41; N, 9.18; found C, 68.15; H, 4.38; N, 9.15.

2-(5-(4-Fluorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-5-(4-hydroxybenzylidene)thiazol-4(5H)-one (7g) 7f.

White crystals (yield 90%), m.p. > 300 °C; IR (KBr, *v* cm^{-1}) 3210 (OH) and 1702 (C=O); ^{1}H NMR δ *ppm*: 3.41 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.0 Hz, 17.6 Hz), 3.83 (s, 3H, OCH_3), 4.06 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.6 Hz, 18.8 Hz), 5.85 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.0 Hz, 11.2 Hz), 6.93 (d, 2H, Aromatic protons, *J*= 8.8 Hz), 7.05 (d, 2H, Aromatic protons, *J*= 8.8 Hz), 7.18-7.22 (m, 2H, Aromatic protons), 7.31-7.34 (m, 2H, Aromatic protons), 7.50 (d, 2H, Aromatic protons, *J*= 8.4 Hz), 7.56 (s, 1H, Aromatic protons), 7.81 (d, 2H, Aromatic protons, *J*= 8.8 Hz), 10.21 (s, 1H, OH); Anal. Calcd. for $C_{26}H_{20}FN_3O_3S$: C, 65.95; H, 4.26; N, 8.87; found C, 66.13; H, 4.21; N, 8.83.

2-(5-(4-Fluorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)-5-(4-methoxybenzylidene)thiazol-4(5H)-one (7h).

White crystals (yield 83%), m.p. 221-223 °C; IR (KBr, *v* cm^{-1}) 1711 (C=O); ^{1}H NMR δ *ppm*: 3.42 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.0 Hz, 18.0 Hz), 3.82, 3.83 (2s, 6H, 2 (OCH_3)), 4.07 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.2 Hz, 18.0 Hz), 5.85 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.4 Hz, 11.2 Hz), 7.06-7.10 (m, 4H, Aromatic protons), 7.18-7.23 (m, 2H, Aromatic protons), 7.31-7.34 (m, 2H, Aromatic protons), 7.58-7.60 (m, 3H, Aromatic protons), 7.81 (d, 2H, Aromatic protons, *J*= 8.8 Hz); Anal. Calcd. for $C_{27}H_{22}FN_3O_3S$: C, 66.52; H, 4.55; N, 8.62; found C, 66.74; H, 4.52; N, 8.66.

5-(4-(Dimethylamino)benzylidene)-2-(5-(4-fluorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)thiazol-4(5H)-one (7i).

White crystals (yield 90%), m.p. 283-285 °C; IR (KBr, *v* cm^{-1}) 1710 (C=O); ^{1}H NMR δ *ppm*: 2.99 (s, 6H, $N(CH_3)_2$), 3.44 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.4 Hz, 18.0 Hz), 3.83 (s, 3H, OCH_3), 4.05 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 10.8 Hz, 18.0 Hz), 5.83 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.4 Hz, 11.2 Hz), 6.79 (d, 2H, Aromatic protons, *J*= 8.8 Hz), 7.05 (d, 2H, Aromatic protons, *J*= 8.8 Hz), 7.18-7.23 (m, 2H, Aromatic protons), 7.30-7.34 (m, 2H, Aromatic protons), 7.45 (d, 2H, Aromatic

protons, *J*= 8.8 Hz), 7.52 (s, 1H, Aromatic protons), 7.81 (d, 2H, Aromatic protons, *J*= 8.8 Hz); ^{13}C NMR *δ ppm*: 43.94 (CH_2), 56.52($N(CH_3)_2$), 59.73 (OCH_3), 67.46 (CH), 112.58, 114.96, 116.33, 121.14, 121.64, 122.57, 124.47, 125.62, 127.67, 128.43, 129.78, 132.07, 134.13, 135.43, 135.79, 137.30, 140.27, 151.65, 160.82 (Aromatic carbons), 170.15 (C=O); Anal. Calcd. for $C_{28}H_{25}FN_4O_2S$: C, 67.18; H, 5.03; N, 11.19; found C, 67.08; H, 5.09; N, 11.12.

5-(4-Chlorobenzylidene)-2-(5-(4-fluorophenyl)-3-(4-methoxyphenyl)-4,5-dihydro-1H-pyrazol-1-yl)thiazol-4(5H)-one (7j).

White crystals (yield 80%), m.p. 240-243 °C; IR (KBr, *v* cm^{-1}) 1712 (C=O); ^{1}H NMR *δ ppm*: 3.46 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.0 Hz, 18.0 Hz), 3.84 (s, 3H, OCH_3), 4.10 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.2 Hz, 18.4 Hz), 5.88 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.0 Hz, 11.2 Hz), 7.08 (d, 2H, Aromatic protons, *J*= 8.8 Hz), 7.19-7.23 (m, 2H, Aromatic protons), 7.32-7.35 (m, 2H, Aromatic protons), 7.58-7.62 (m, 3H, Aromatic protons), 7.65 (d, 2H, *J*= 8.8 Hz), 7.83 (d, 2H, *J*= 8.8 Hz); ^{13}C NMR *δ ppm*: 44.00 (CH_2), 55.99 (OCH_3), 63.52 (CH), 114.95, 116.13, 116.35, 122.33, 128.52, 128.60, 129.27, 129.76, 129.84, 129.91, 131.75, 133.24, 134.83, 136.68, 136.71, 160.94, 161.84, 162.64, 163.37 (Aromatic carbons), 170.13 (C=O); MS *m/z* [%]: 392.97 [M^+, 21.59], 391.98 [100]; Anal. Calcd. for $C_{26}H_{19}ClFN_3O_2S$: C, 63.48; H, 3.89; N, 8.54; found C, 63.21; H, 3.82; N, 8.60.

5-Benzylidene-2-(5-(4-fluorophenyl)-3-(thiophen-2-yl)-4,5-dihydro-1H-pyrazol-1-yl)thiazol-4(5H)-one (7k).

White crystals (yield 84%), m.p. 266-268 °C; IR (KBr, *v* cm^{-1}) 1709 (C=O); ^{1}H NMR *δ ppm*: 3.41 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.4 Hz, 18.0 Hz), 4.14 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.2 Hz, 18.0 Hz), 5.91 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.4 Hz, 11.2 Hz), 7.20-7.25 (m, 3H, Aromatic protons), 7.34-7.37 (m, 2H, Aromatic protons), 7.42-7.56 (m, 4H, Aromatic protons), 7.61-7.67 (m, 3H, Aromatic protons), 7.90-7.93 (m, 1H, Aromatic protons); ^{13}C NMR *δ ppm*: 44.54 (CH_2), 63.68 (CH), 116.18, 116.39, 128.35, 128.51, 128.60, 129.02, 129.79, 130.14, 130.43, 131.56, 132.58, 132.68, 133.54, 134.25, 136.54, 157.47, 160.97 (Aromatic carbons), 170.42 (C=O); Anal. Calcd. for $C_{23}H_{16}FN_3OS_2$: C, 63.72; H, 3.72; N, 9.69; found C, 63.64; H, 3.76; N, 9.65.

2-(5-(4-Fluorophenyl)-3-(thiophen-2-yl)-4,5-dihydro-1H-pyrazol-1-yl)-5-(4-hydroxybenzylidene)thiazol-4(5H)-one (7l).

White crystals (yield 79%), m.p. 218-220 °C; IR (KBr, *v* cm^{-1}) 3224 (OH) and 1714 (C=O); ^{1}H NMR δ *ppm*: 3.47 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.0 Hz, 18.0 Hz), 4.14 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.2 Hz, 18.0 Hz), 5.90 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.0 Hz, 11.2 Hz), 6.93 (d, 2H, Aromatic protons, *J*= 8.0 Hz), 7.19-7.25 (m, 3H, Aromatic protons), 7.31-7.36 (m, 2H, Aromatic protons), 7.48 (d, 2H, Aromatic protons, *J*= 8.0 Hz), 7.57 (s, 1H, Aromatic protons), 7.65 (d, 1H, Aromatic protons, *J*= 8.4 Hz), 7.91 (d, 1H, Aromatic protons, *J*= 8.0 Hz), 10.15 (s, 1H, OH); ^{13}C NMR *δ ppm*: 44.50 (CH_2), 63.56 (CH), 116.16, 116.38, 116.82, 124.04, 124.99, 128.46, 128.55, 128.99, 132.16, 132.40, 132.80, 133.36, 136.71, 156.98, 160.12, 160.94 (Aromatic carbons), 170.32 (C=O); Anal. Calcd. for $C_{23}H_{16}FN_3O_2S_2$: C, 61.46; H, 3.59; N, 9.35; found C, 61.68; H, 3.62; N, 9.32.

2-(5-(4-Fluorophenyl)-3-(thiophen-2-yl)-4,5-dihydro-1H-pyrazol-1-yl)-5-(4-methoxybenzylidene)thiazol-4(5H)-one (7m).

White crystals (yield 82%), m.p. 260-262 °C; IR (KBr, *v* cm^{-1}) 1700 (C=O); ^{1}H NMR δ *ppm*: 3.48 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.0 Hz, 18.0 Hz), 3.83 (s, 3H, OCH_3), 4.14 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.2 Hz, 18.4 Hz), 5.90 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.0 Hz, 11.2 Hz), 7.10 (d, 2H, Aromatic protons, *J*= 7.2 Hz), 7.20-7.25 (m, 3H, Aromatic protons), 7.32-7.36 (m, 2H, Aromatic protons), 7.59-7.66 (m, 4H, Aromatic protons), 7.91 (d, 1H, Aromatic protons, *J*= 5.2 Hz); Anal. Calcd. for $C_{24}H_{18}FN_3O_2S_2$: C, 62.19; H, 3.91; N, 9.07; found C, 61.96; H, 3.96; N, 9.03.

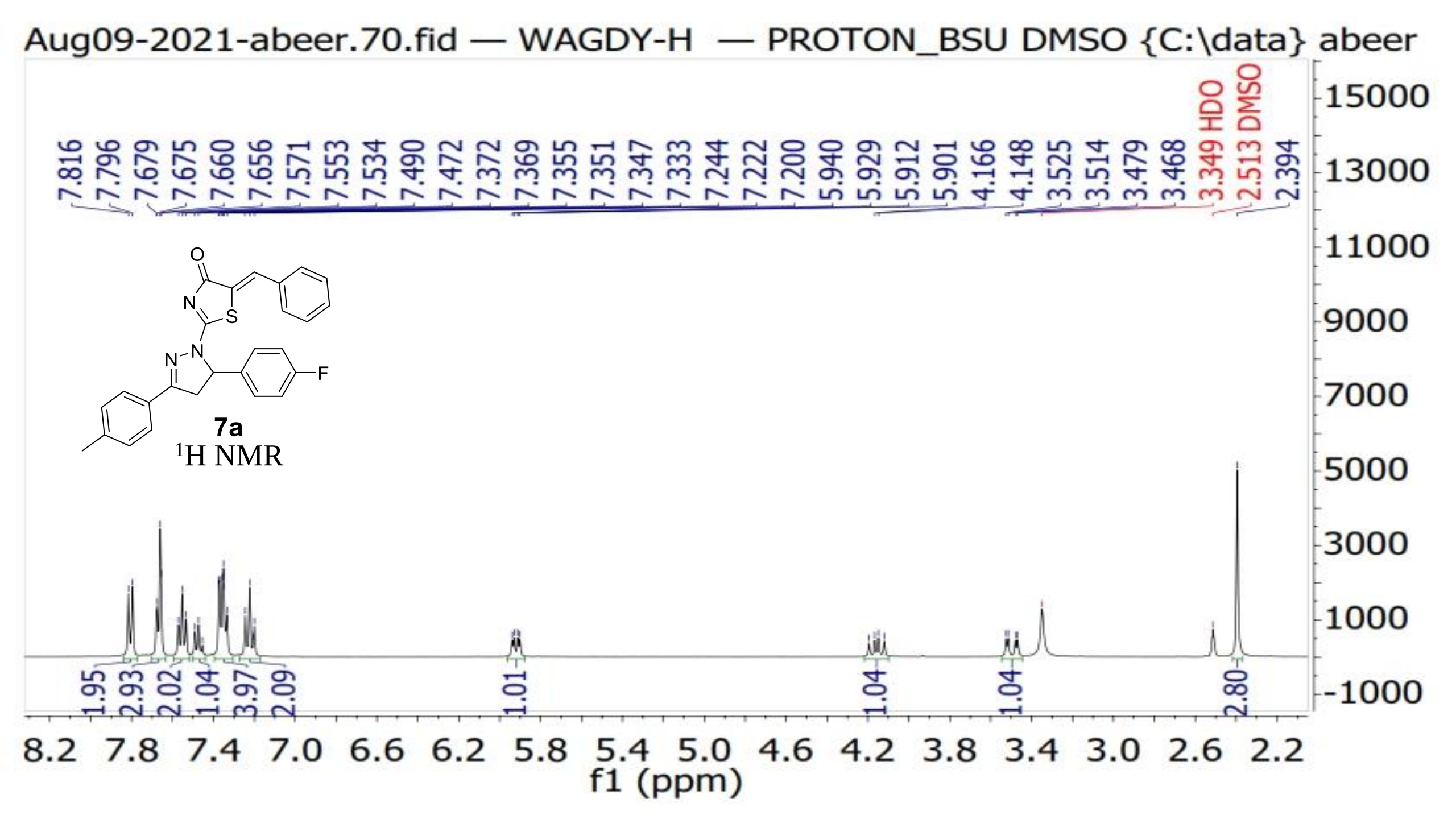
5-(4-(Dimethylamino)benzylidene)-2-(5-(4-fluorophenyl)-3-(thiophen-2-yl)-4,5-dihydro-1H-pyrazol-1-yl)thiazol-4(5H)-one (7n).

White crystals (yield 80%), m.p. 281-283 °C; IR (KBr, *v* cm^{-1}) 1700 (C=O); ^{1}H NMR δ *ppm*: 3.01 (s, 6H, $N(CH_3)_2$), 3.46 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.0 Hz, 18.0 Hz), 4.08 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.2 Hz, 18.4 Hz), 5.89 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.0 Hz, 11.2 Hz), 6.83-6.78 (m, 2H, Aromatic protons), 7.18-7.25 (m, 3H, Aromatic protons), 7.32-7.37 (m, 2H, Aromatic protons), 7.46-7.49 (m, 2H, Aromatic protons), 7.54 (s, 1H, Aromatic protons), 7.64-7.66 (m, 1H,

Aromatic protons), 7.87-7.92 (m, 1H, Aromatic protons); Anal. Calcd. for $C_{25}H_{21}FN_4OS_2$: C, 63.01; H, 4.44; N, 11.76; found C, 62.83; H, 4.40; N, 11.72.

5-(4-Chlorobenzylidene)-2-(5-(4-fluorophenyl)-3-(thiophen-2-yl)-4,5-dihydro-1H-pyrazol-1-yl)thiazol-4(5H)-one (7o).

White crystals (yield 87%), m.p. 264-266 °C; IR (KBr, *v* cm^{-1}) 1701 (C=O); ^{1}H NMR δ *ppm*: 3.50 (dd, 1H, H_A of pyrazoline methylene C-4 protons, *J*= 4.0 Hz, 18.0 Hz), 4.16 (dd, 1H, H_B of pyrazoline methylene C-4 protons, *J*= 11.2 Hz, 18.4 Hz), 5.92 (dd, 1H, H_X of pyrazoline C-5 proton, *J*= 4.4 Hz, 11.2 Hz), 7.20-7.26 (m, 3H, Aromatic protons), 7.33-7.37 (m, 2H, Aromatic protons), 7.60-7.63 (m, 3H, Aromatic protons), 7.67-7.69 (m, 3H, Aromatic protons), 7.93 (d, 1H, *J*= 5.2 Hz); ^{13}C NMR δ *ppm*: 44.47 (CH_2), 63.73 (CH), 116.19, 116.41, 128.18, 128.52, 128.60, 129.11, 129.86, 130.22, 131.81, 132.69, 133.18, 133.66, 134.93, 135.25, 136.48, 143.17, 155.28, 157.68, 158.44, 164.76 (Aromatic carbons), 170.15 (C=O); MS *m/z* [%]: 491.69 [M^+, 21.23]; Anal. Calcd. for $C_{23}H_{15}ClFN_3OS_2$: C, 59.03; H, 3.23; N, 8.98; found C, 58.85; H, 3.22; N, 9.06.


Aug09-2021-abeer.70.fid — WAGDY-H — PROTON_BSU DMSO {C:\data} abeer
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7.571
7.553
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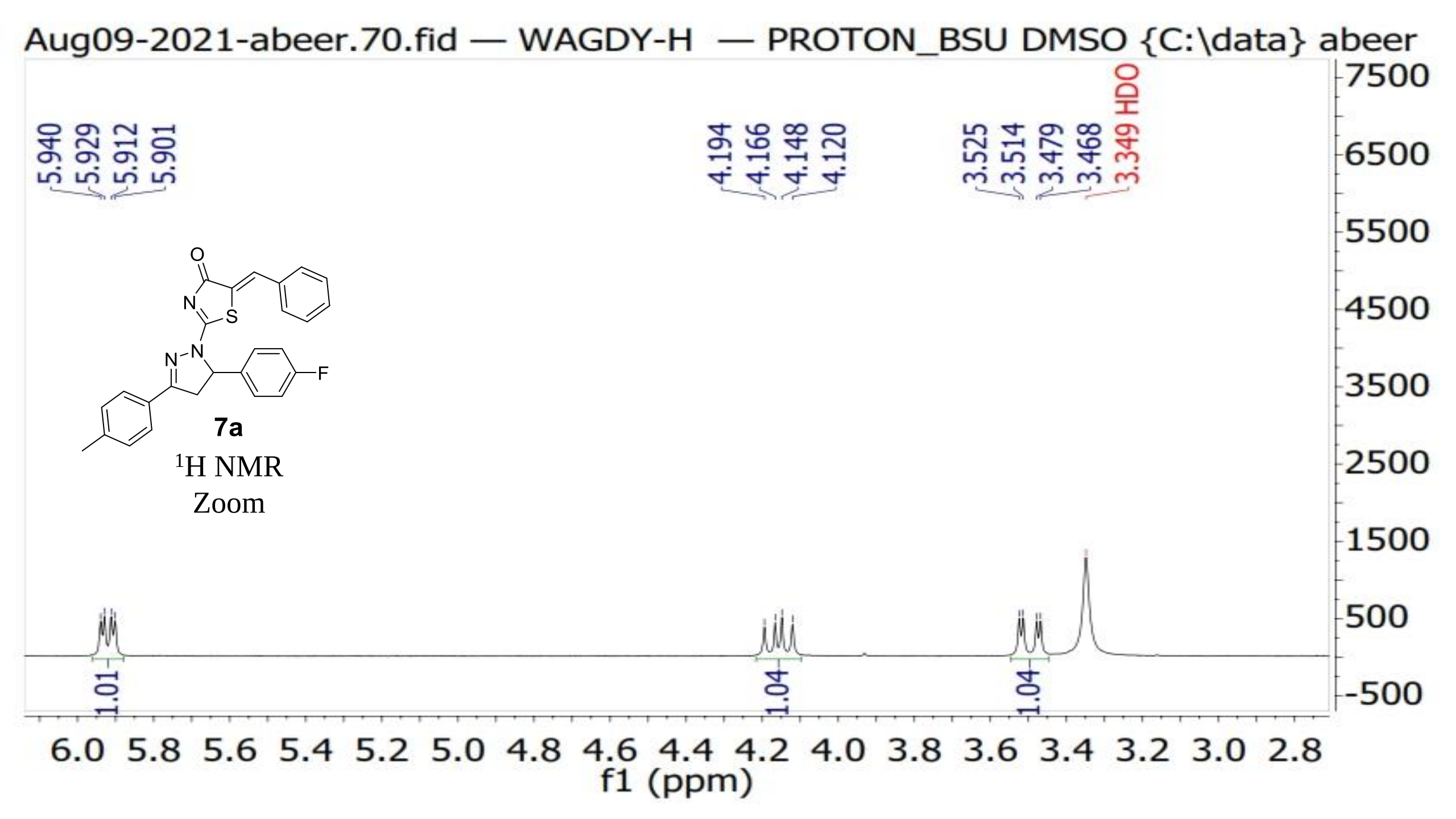
7.472
7.372
7.369
7.355
7.351
7.347
7.333
7.244
7.222
7.200
5.940
5.929
5.912
5.901
4.166
4.148
3.525
3.514
3.479
3.468
3.349 HDO
2.513 DMSO
2.394
O
N
S
N
N
F
7a
1H NMR
1.95
2.93
2.02
1.04
3.97
2.09
1.01
1.04
1.04
2.80
15000
13000
11000
9000
7000
5000
3000
1000
-1000
8.2
7.8
7.4
7.0
6.6
6.2
5.8
5.4
5.0
4.6
4.2
3.8
3.4
3.0
2.6
2.2
f1 (ppm)


Aug09-2021-abeer.70.fid — WAGDY-H — PROTON_BSU DMSO {C:\data} abeer
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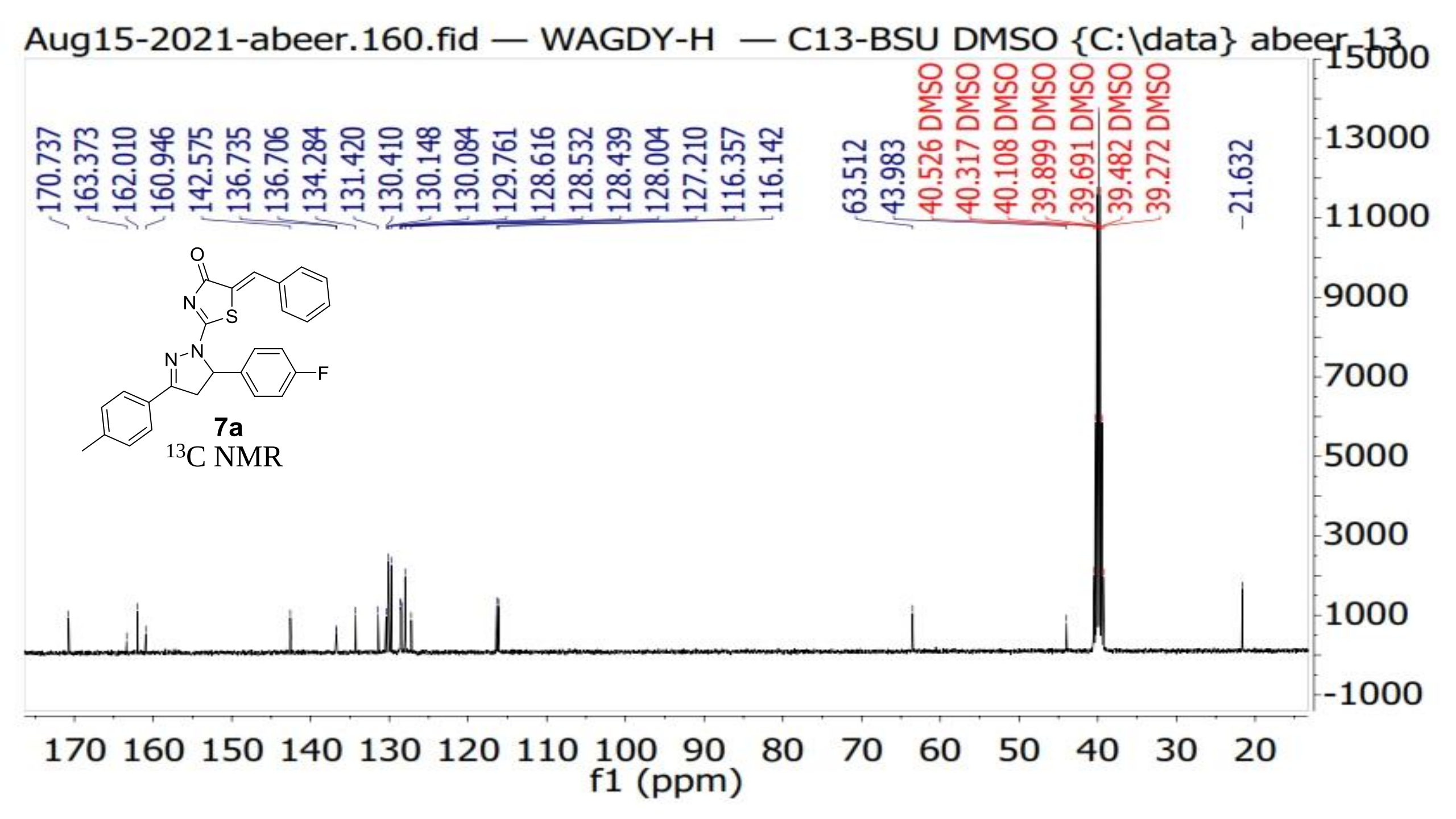
5.912
5.901
4.194
4.166
4.148
4.120
3.525
3.514
3.479
3.468
3.349 HDO
O
N
S
N
N
F
7a
1H NMR
Zoom
1.01
1.04
1.04
7500
6500
5500
4500
3500
2500
1500
500
-500
6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8
f1 (ppm)


Aug15-2021-abeer.160.fid — WAGDY-H — C13-BSU DMSO {C:\data} abeer 13
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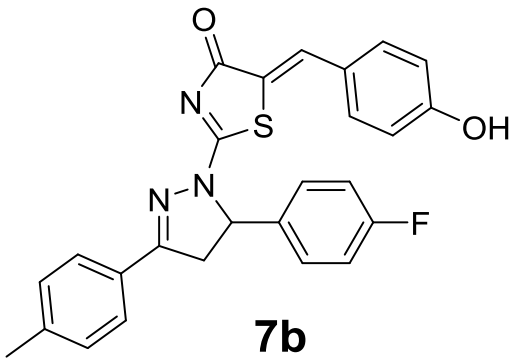
162.010
160.946
142.575
136.735
136.706
134.284
131.420
130.410
130.148
130.084
129.761
128.616
128.532
128.439
128.004
127.210
116.357
116.142
63.512
43.983
40.526 DMSO
40.317 DMSO
40.108 DMSO
39.899 DMSO
39.691 DMSO
39.482 DMSO
39.272 DMSO
21.632
O
N
S
N
N
F
7a
13C NMR
15000
13000
11000
9000
7000
5000
3000
1000
-1000
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)

PROTON_BSU DMSO {C:\data} abeer 11



7b

BRUKER

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NAME      Aug08-2021-abeer
EXPNO                   40
PROCNO                   1

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FIDRES           0.122266 Hz
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RG                  147.93
DW                  62.400 usec
DE                   6.50 usec
TE                  298.8 K
D1             1.00000000 sec
TD0                     1

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NUC1                   1H
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F2 - Processing parameters
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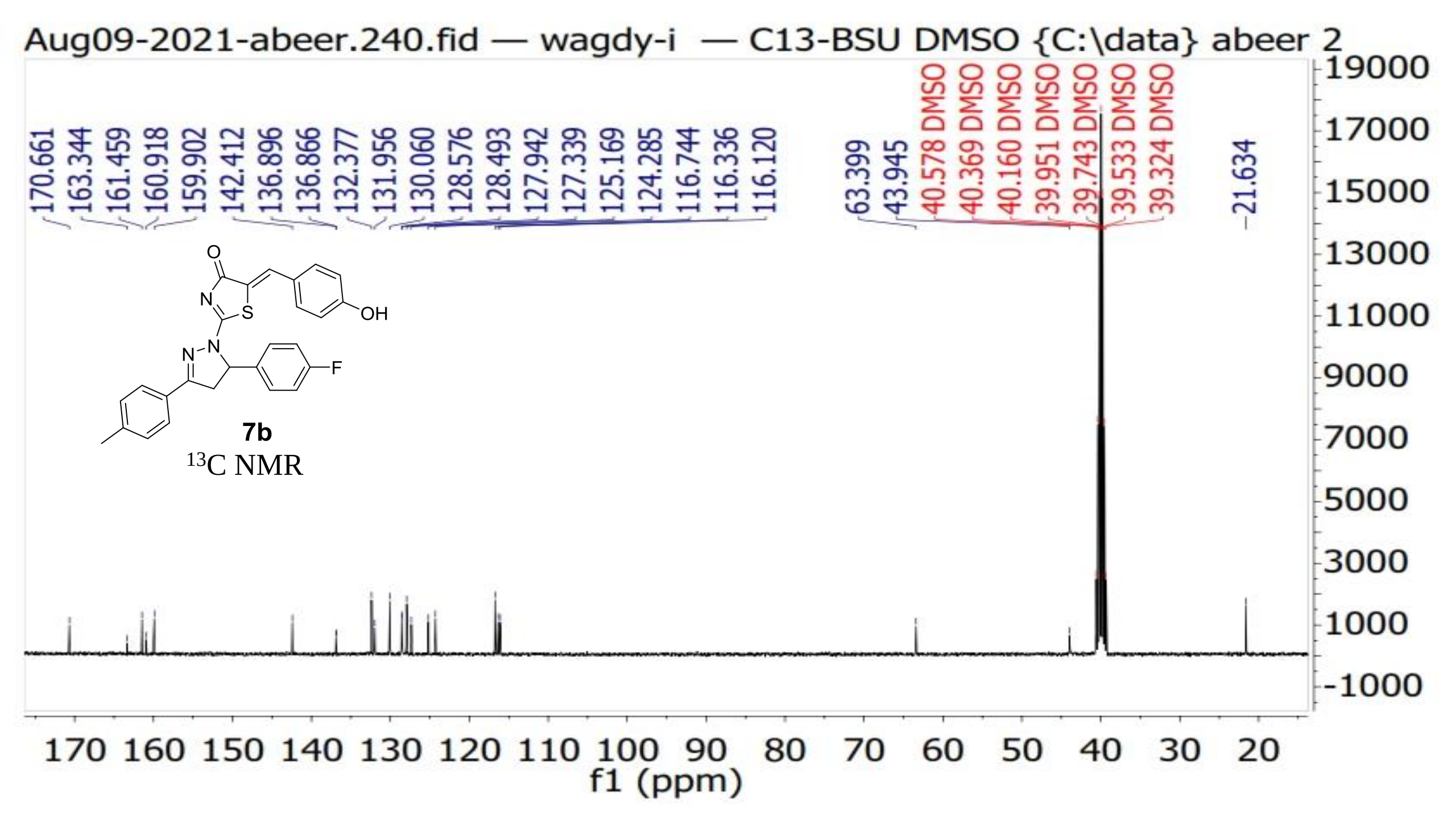
Aug09-2021-abeer.240.fid — wagdy-i — C13-BSU DMSO {C:\data} abeer 2
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160.918
159.902
142.412
136.896
136.866
132.377
131.956
130.060
128.576
128.493
127.942
127.339
125.169
124.285
116.744
116.336
116.120
63.399
43.945
40.578 DMSO
40.369 DMSO
40.160 DMSO
39.951 DMSO
39.743 DMSO
39.533 DMSO
39.324 DMSO
21.634
O
N
S
OH
N
N
F
7b
13C NMR
19000
17000
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11000
9000
7000
5000
3000
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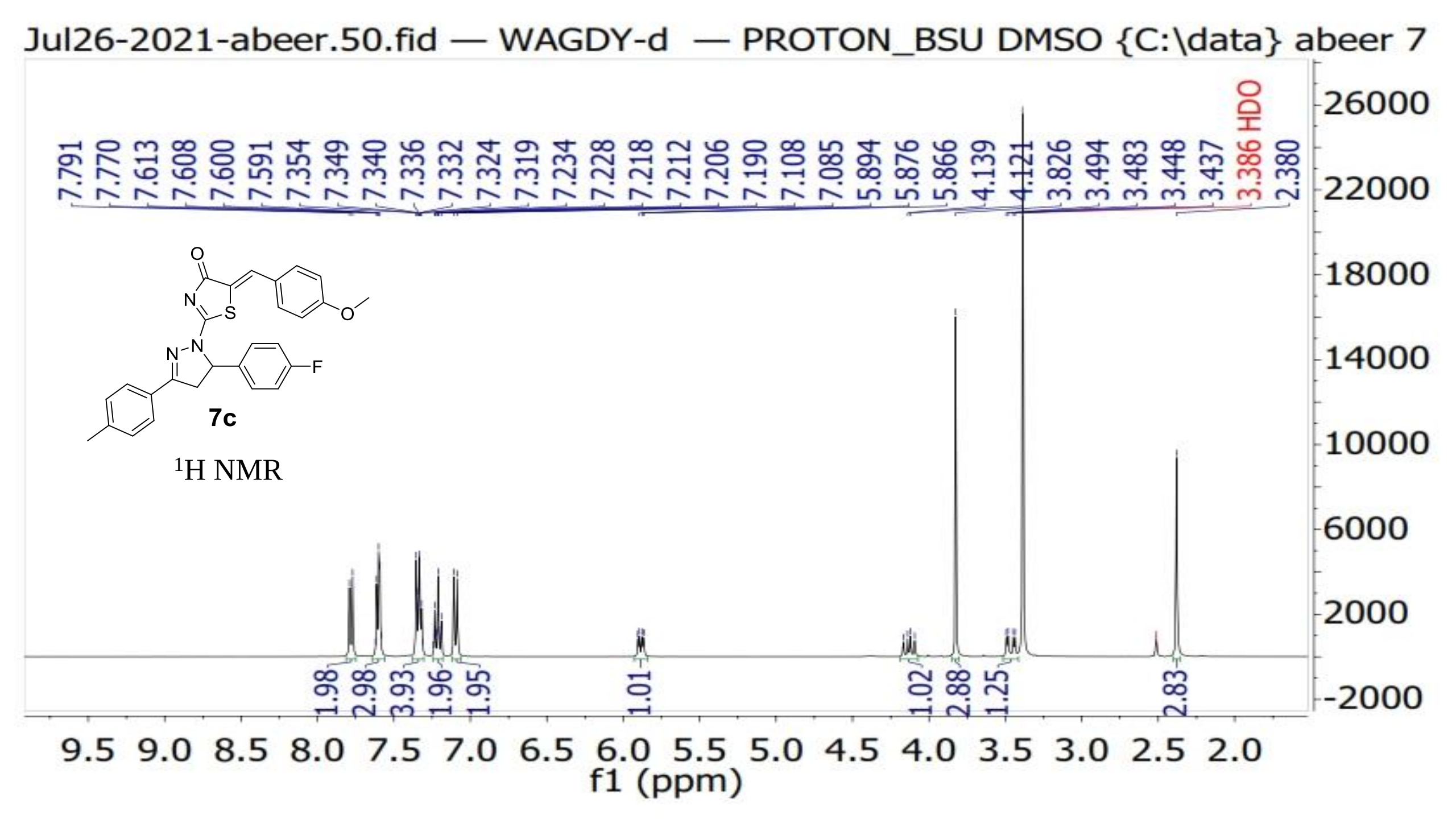
-1000
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)


Jul26-2021-abeer.50.fid — WAGDY-d — PROTON_BSU DMSO {C:\data} abeer 7
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7.613
7.608
7.600
7.591
7.354
7.349
7.340
7.336
7.332
7.324
7.319
7.234
7.228
7.218
7.212
7.206
7.190
7.108
7.085
5.894
5.876
5.866
4.139
4.121
3.826
3.494
3.483
3.448
3.437
3.386 HDO
2.380
O
N
S
O
N
N
F
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3.93
1.96
1.95
1.01
1.02
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1.25
2.83
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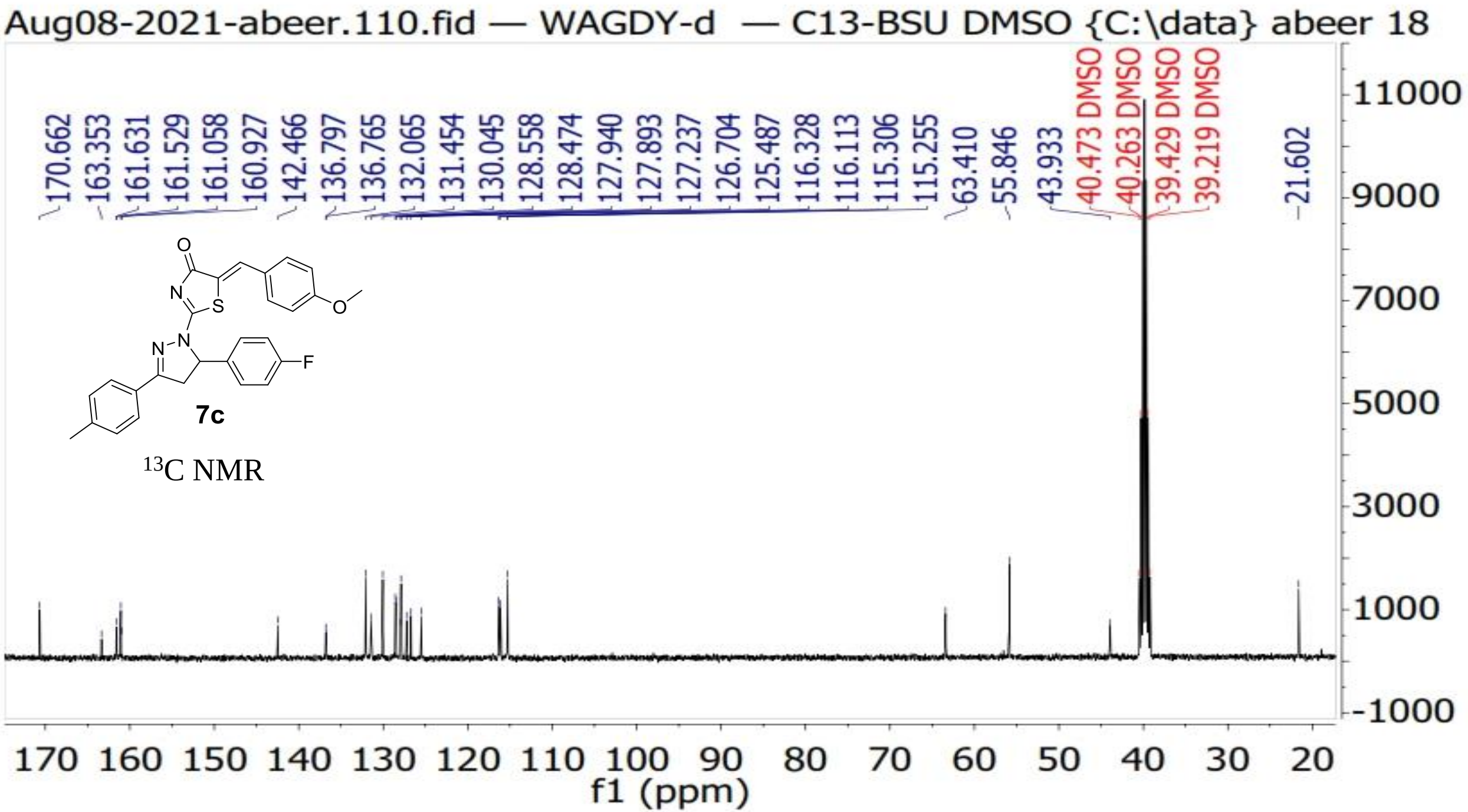
f1 (ppm)


Aug08-2021-abeer.110.fid — WAGDY-d — C13-BSU DMSO {C:\data} abeer 18
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161.529
161.058
160.927
142.466
136.797
136.765
132.065
131.454
130.045
128.558
128.474
127.940
127.893
127.237
126.704
125.487
116.328
116.113
115.306
115.255
63.410
55.846
43.933
40.473 DMSO
40.263 DMSO
39.429 DMSO
39.219 DMSO
21.602
O
N
S
O
N
N
F
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7000
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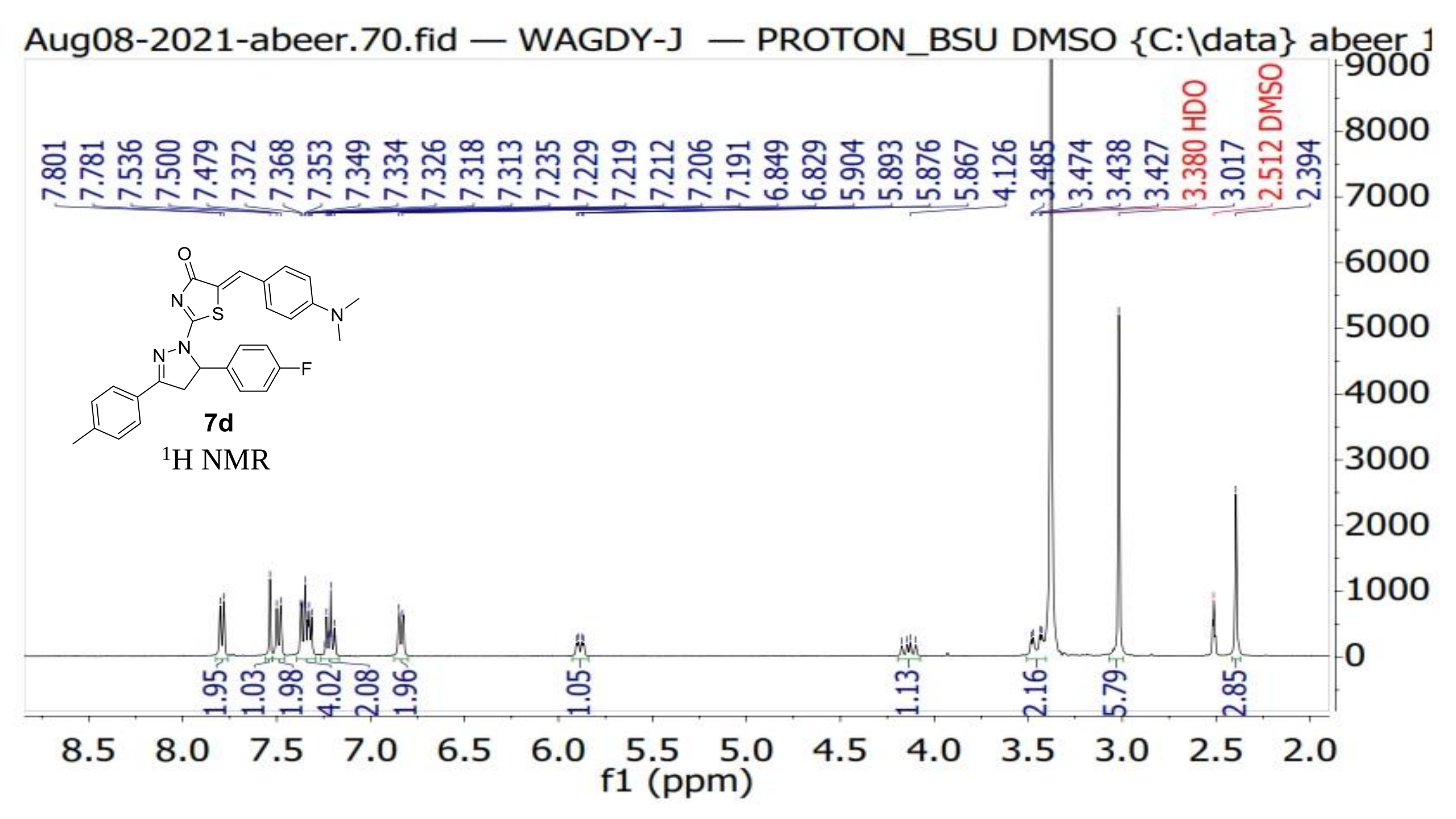
-1000
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)


Aug08-2021-abeer.70.fid — WAGDY-J — PROTON_BSU DMSO {C:\data} abeer 1
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7.536
7.500
7.479
7.372
7.368
7.353
7.349
7.334
7.326
7.318
7.313
7.235
7.229
7.219
7.212
7.206
7.191
6.849
6.829
5.904
5.893
5.876
5.867
4.126
3.485
3.474
3.438
3.427
3.380 HDO
3.017
2.512 DMSO
2.394
O
N
S
N
N
N
F
7d
1H NMR
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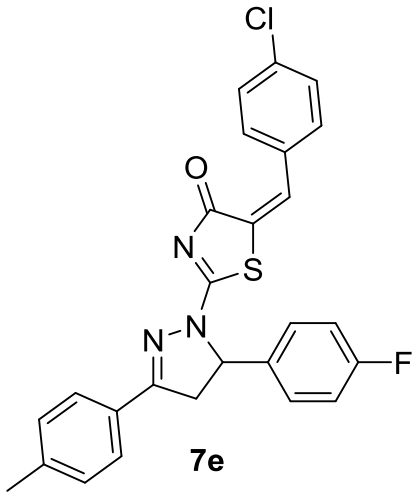
2.08
1.96
1.05
1.13
2.16
5.79
2.85
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)

WAGDY-e
PROTON_BSU DMSO {C:\data} abeer 16



7e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PROCNO                   1

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TE                299.0 K
D1           1.00000000 sec
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======== CHANNEL f1 ========
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NUC1                 1H
P1                10.00 usec
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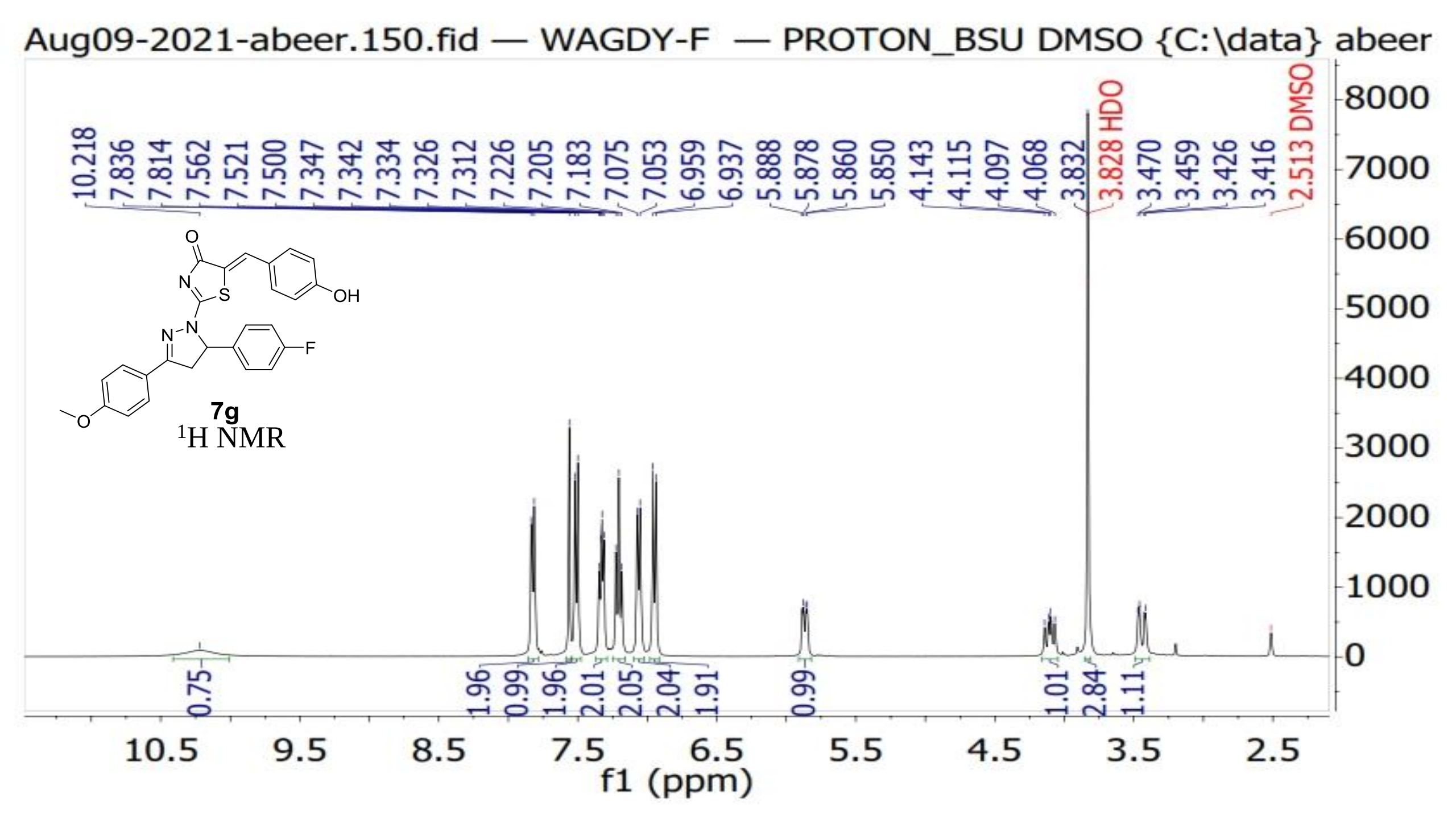
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7.814
7.562
7.521
7.500
7.347
7.342
7.334
7.326
7.312
7.226
7.205
7.183
7.075
7.053
6.959
6.937
5.888
5.878
5.860
5.850
4.143
4.115
4.097
4.068
3.832
3.828 HDO
3.470
3.459
3.426
3.416
2.513 DMSO
O
N
S
OH
N
N
F
O
7g
1H NMR
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1.96
0.99
1.96
2.01
2.05
2.04
1.91
0.99
1.01
2.84
1.11
8000
7000
6000
5000
4000
3000
2000
1000
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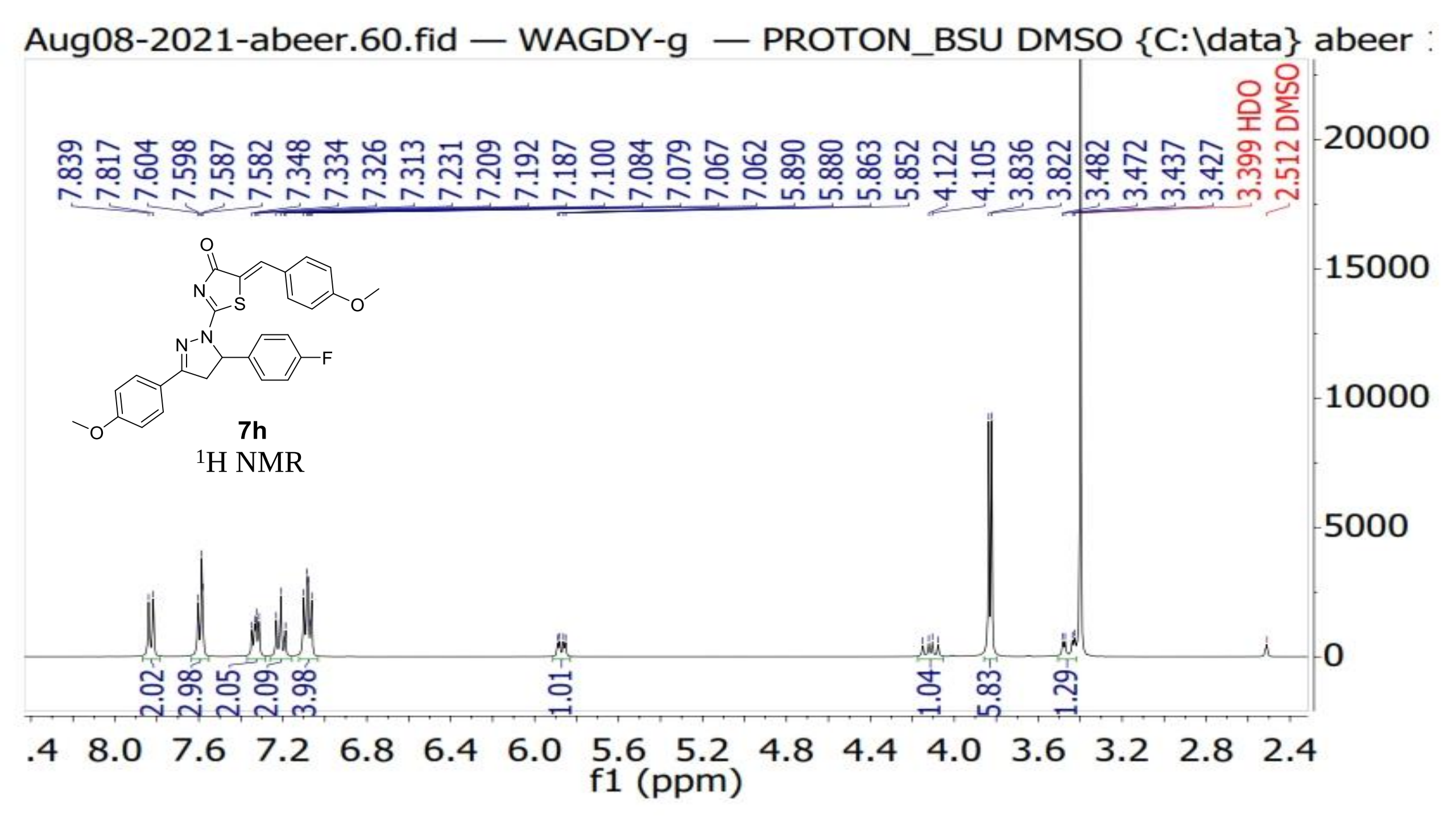
7.5
6.5
5.5
4.5
3.5
2.5
f1 (ppm)


Aug08-2021-abeer.60.fid — WAGDY-g — PROTON_BSU DMSO {C:\data} abeer
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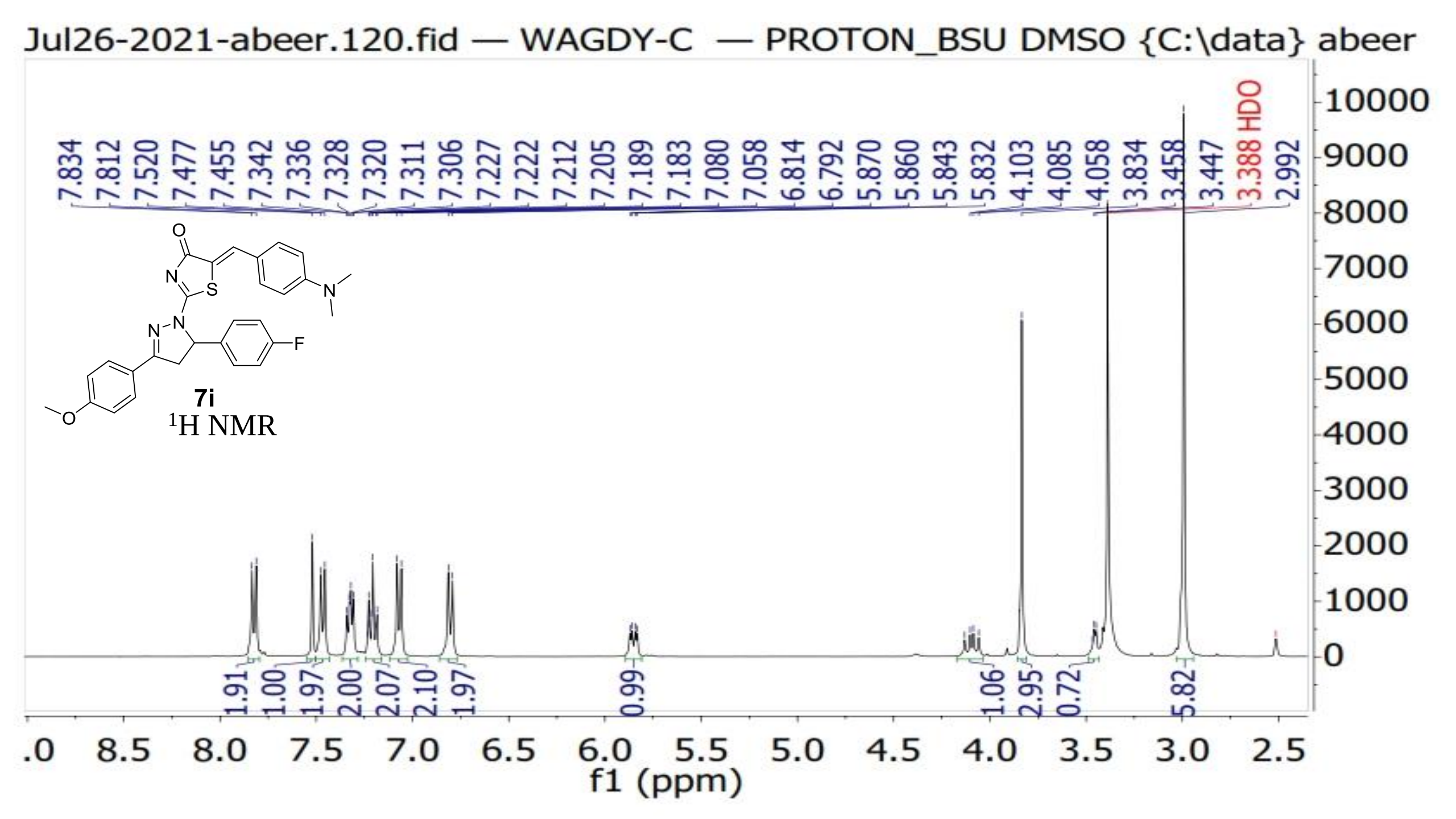
7.817
7.604
7.598
7.587
7.582
7.348
7.334
7.326
7.313
7.231
7.209
7.192
7.187
7.100
7.084
7.079
7.067
7.062
5.890
5.880
5.863
5.852
4.122
4.105
3.836
3.822
3.482
3.472
3.437
3.427
3.399 HDO
2.512 DMSO
O
N
S
O
N
N
F
O
7h
1H NMR
20000
15000
10000
5000
0
2.02
2.98
2.05
2.09
3.98
1.01
1.04
5.83
1.29
.4 8.0 7.6 7.2 6.8 6.4 6.0 5.6 5.2 4.8 4.4 4.0 3.6 3.2 2.8 2.4
f1 (ppm)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7.342
7.336
7.328
7.320
7.311
7.306
7.227
7.222
7.212
7.205
7.189
7.183
7.080
7.058
6.814
6.792
5.870
5.860
5.843
5.832
4.103
4.085
4.058
3.834
3.458
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7000
6000
5000
4000
3000
2000
1000
0
1.91
1.00
1.97
2.00
2.07
2.10
1.97
0.99
1.06
2.95
0.72
5.82
.0
8.5
8.0
7.5
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6.0
5.5
5.0
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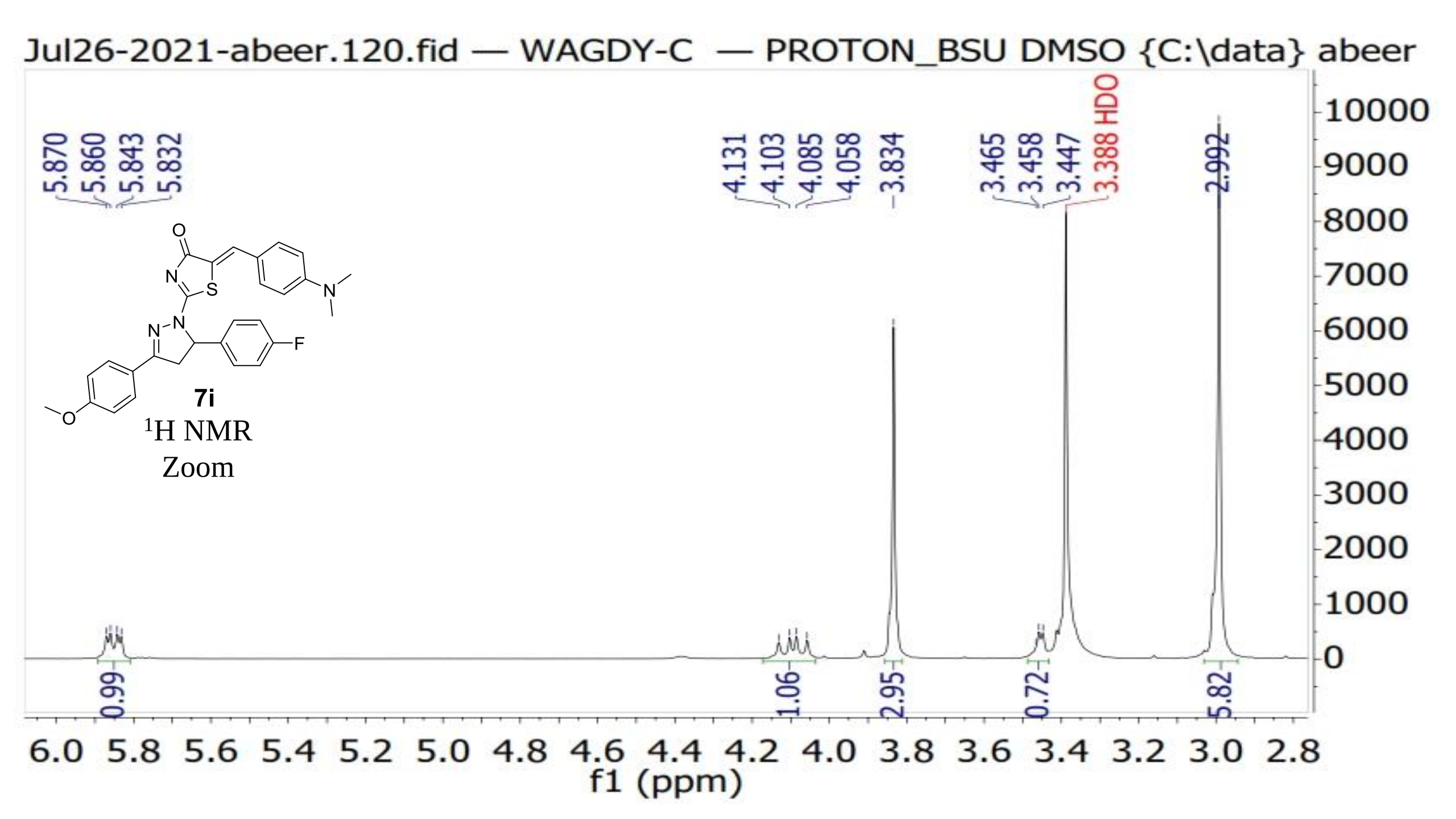
2.5
f1 (ppm)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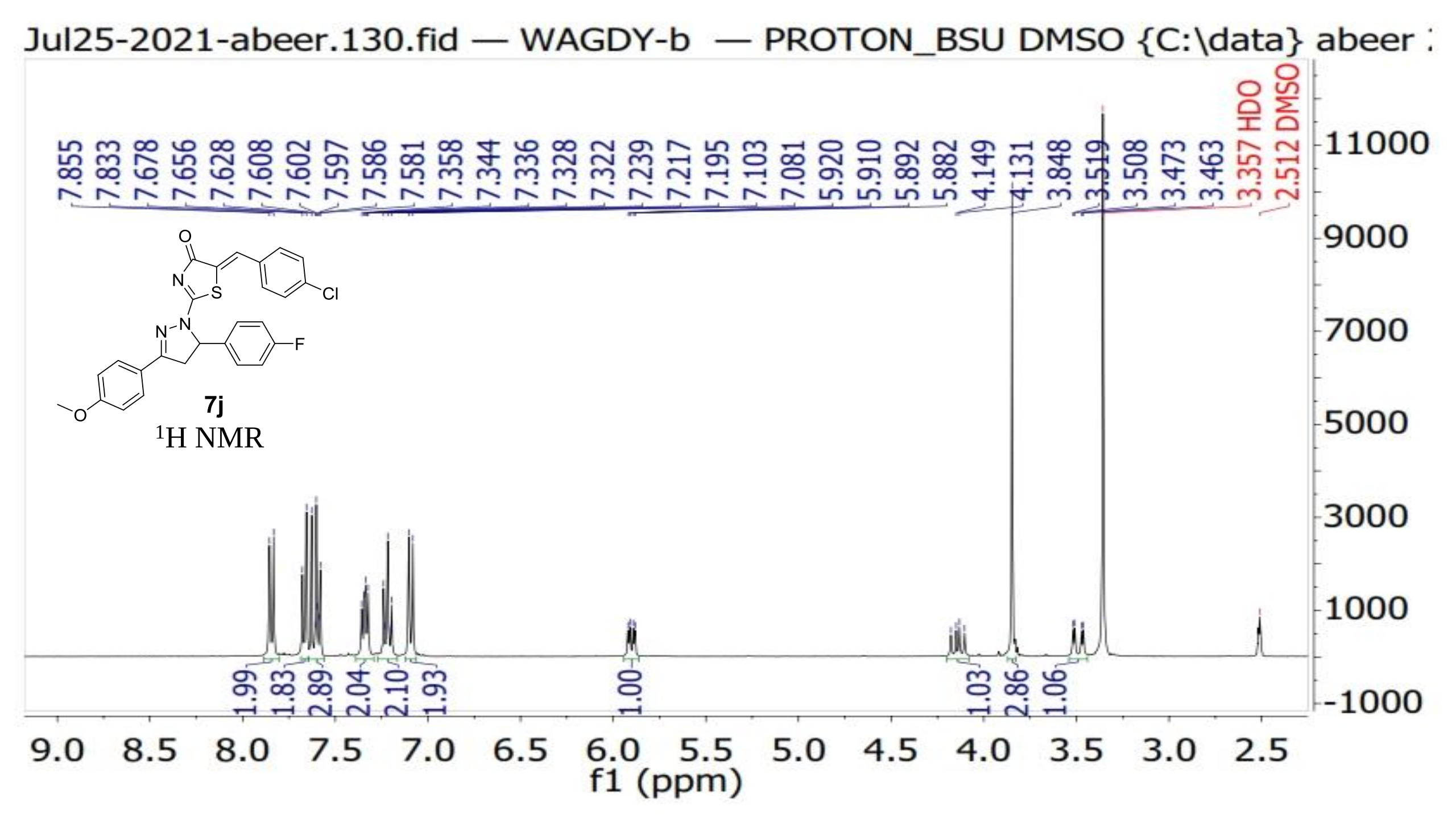
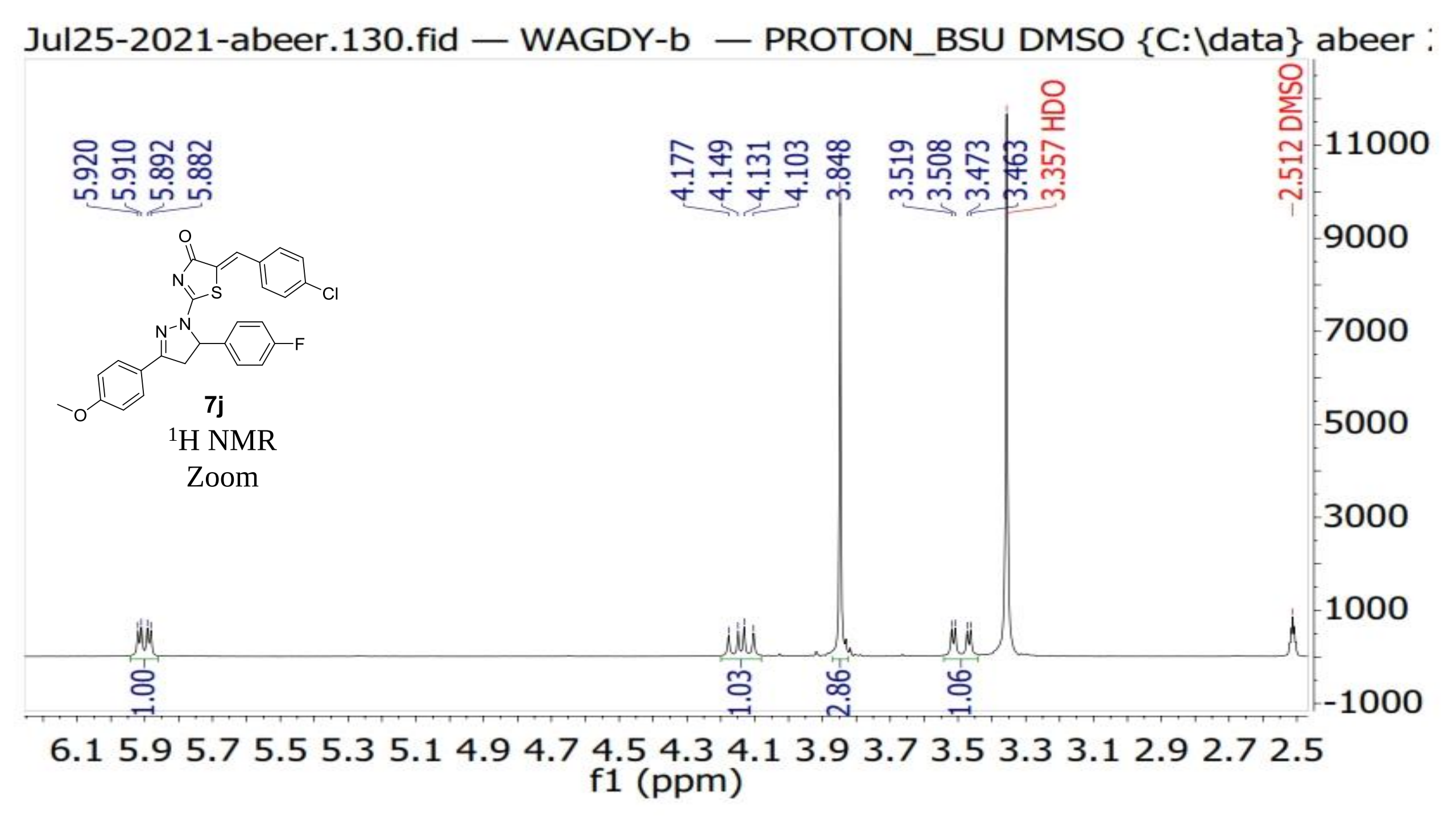
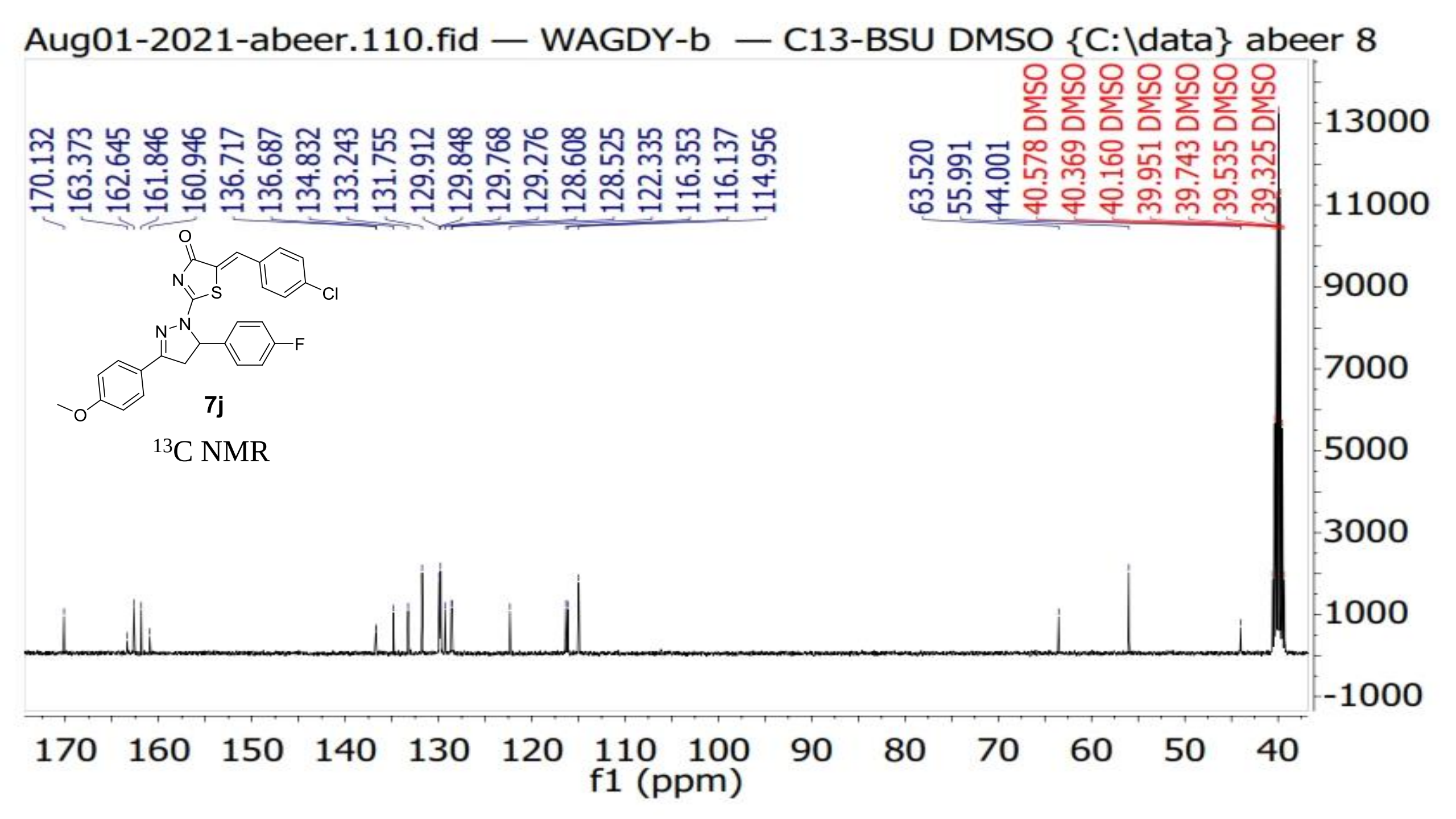
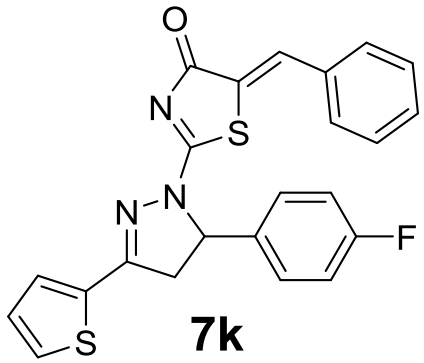
3.447
3.388 HDO
2.992
O
N
S
N
N
F
O
7i
1H NMR
Zoom
0.99
1.06
2.95
0.72
5.82
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8
f1 (ppm)


Jul25-2021-abeer.130.fid — WAGDY-b — PROTON_BSU DMSO {C:\data} abeer
7.855
7.833
7.678
7.656
7.628
7.608
7.602
7.597
7.586
7.581
7.358
7.344
7.336
7.328
7.322
7.239
7.217
7.195
7.103
7.081
5.920
5.910
5.892
5.882
4.149
4.131
3.848
3.519
3.508
3.473
3.463
3.357 HDO
2.512 DMSO
O
N
S
Cl
N
N
F
O
7j
1H NMR
1.99
1.83
2.89
2.04
2.10
1.93
1.00
1.03
2.86
1.06
11000
9000
7000
5000
3000
1000
-1000
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
f1 (ppm)


Jul25-2021-abeer.130.fid — WAGDY-b — PROTON_BSU DMSO {C:\data} abeer
5.920
5.910
5.892
5.882
4.177
4.149
4.131
4.103
3.848
3.519
3.508
3.473
3.463
3.357 HDO
2.512 DMSO
O
N
S
Cl
N
N
F
O
7j
1H NMR
Zoom
11000
9000
7000
5000
3000
1000
-1000
1.00
1.03
2.86
1.06
6.1 5.9 5.7 5.5 5.3 5.1 4.9 4.7 4.5 4.3 4.1 3.9 3.7 3.5 3.3 3.1 2.9 2.7 2.5
f1 (ppm)


Aug01-2021-abeer.110.fid — WAGDY-b — C13-BSU DMSO {C:\data} abeer 8
170.132
163.373
162.645
161.846
160.946
136.717
136.687
134.832
133.243
131.755
129.912
129.848
129.768
129.276
128.608
128.525
122.335
116.353
116.137
114.956
63.520
55.991
44.001
40.578 DMSO
40.369 DMSO
40.160 DMSO
39.951 DMSO
39.743 DMSO
39.535 DMSO
39.325 DMSO
O
N
S
Cl
N
N
F
O
7j
13C NMR
13000
11000
9000
7000
5000
3000
1000
-1000
170 160 150 140 130 120 110 100 90 80 70 60 50 40
f1 (ppm)

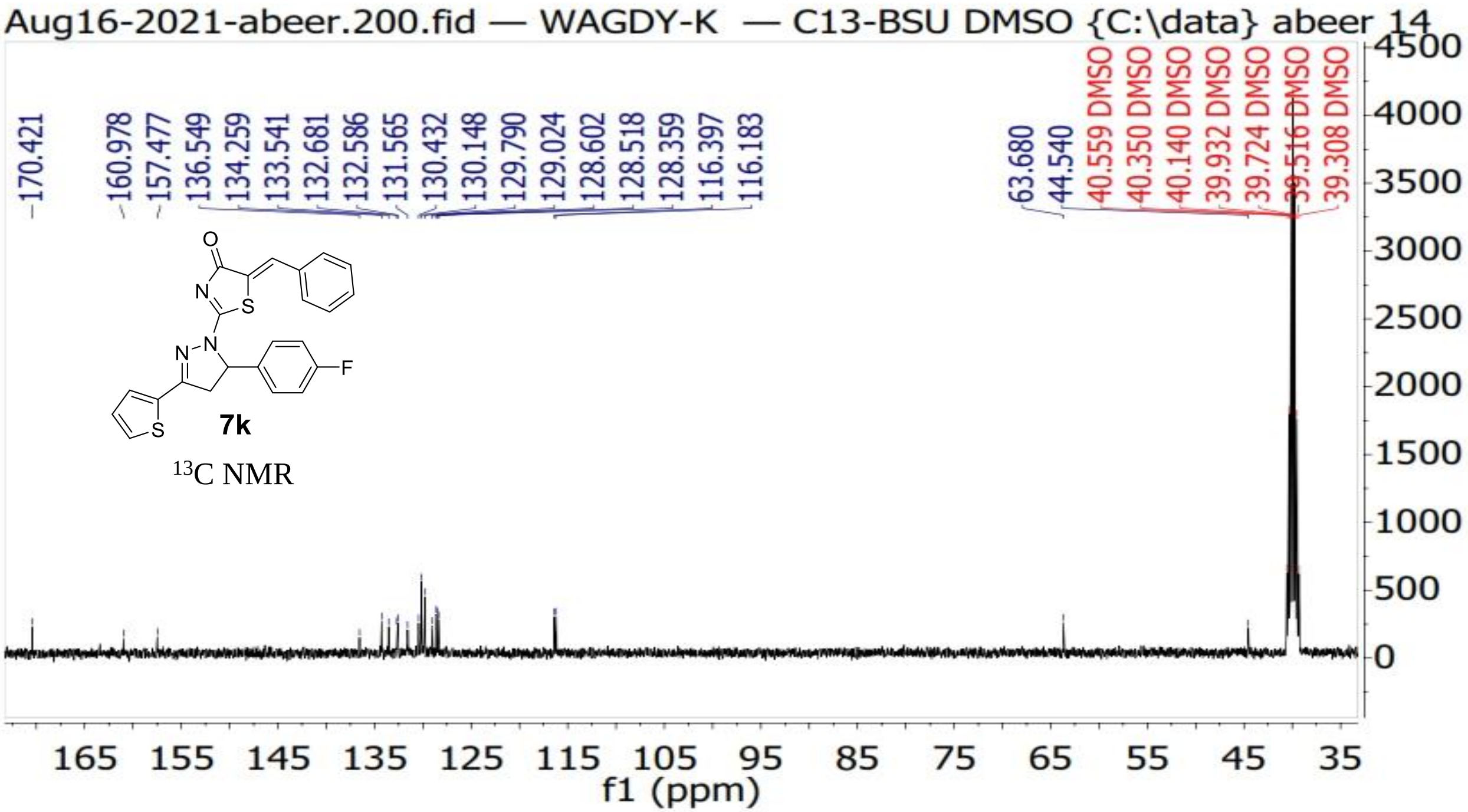
wagdy-k
PROTON_BSU DMSO (C:\data) abeer 16



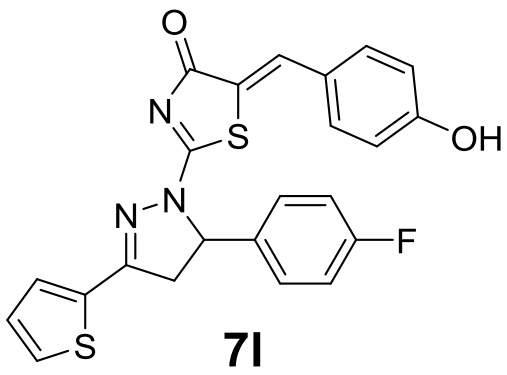
7k

BRUKER

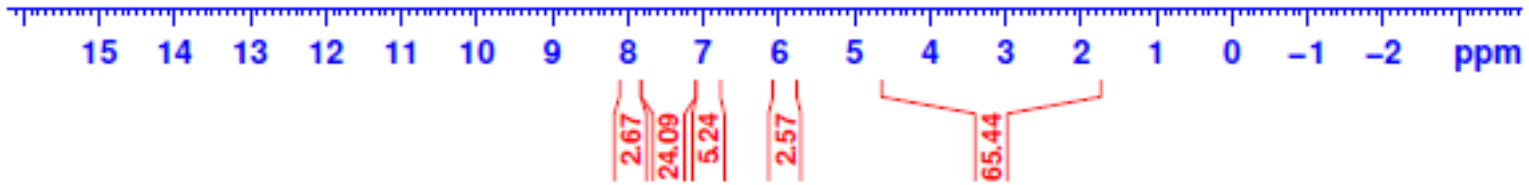
```
Current Data Parameters
NAME      Aug08-2021-abeer
EXPNO                   90
PROCNO                   1

F2 - Acquisition Parameters
Date_              20210808
Time                 11.08
INSTRUM              spect
PROBHD   5 mm PABBO BB/
PULPROG              zg30
TD                  65536
SOLVENT              DMSO
NS                     16
DS                      2
SWH              8012.820 Hz
FIDRES           0.122266 Hz
AQ               4.0894465 sec
RG                  147.93
DW                  62.400 usec
DE                   6.50 usec
TE                  299.0 K
D1             1.00000000 sec
TD0                     1

======== CHANNEL f1 =======
SFO1          400.1324710 MHz
NUC1                    1H
P1                  10.00 usec
PLW1          16.00000000 W

F2 - Processing parameters
SI                  65536
SF            400.1300000 MHz
WDW                    EM
SSB       0
LB                   0.10 Hz
GB        0
PC                   1.00
```


Aug16-2021-abeer.200.fid — WAGDY-K — C13-BSU DMSO {C:\data} abeer 14
170.421
160.978
157.477
136.549
134.259
133.541
132.681
132.586
131.565
130.432
130.148
129.790
129.024
128.602
128.518
128.359
116.397
116.183
63.680
44.540
40.559 DMSO
40.350 DMSO
40.140 DMSO
39.932 DMSO
39.724 DMSO
39.516 DMSO
39.308 DMSO
O
N
S
N
N
F
S
7k
13C NMR
4500
4000
3500
3000
2500
2000
1500
1000
500
0
165
155
145
135
125
115
105
95
85
75
65
55
45
35
f1 (ppm)

wagdy-1
PROTON_BSU DMSO (C:\data) abeer 8

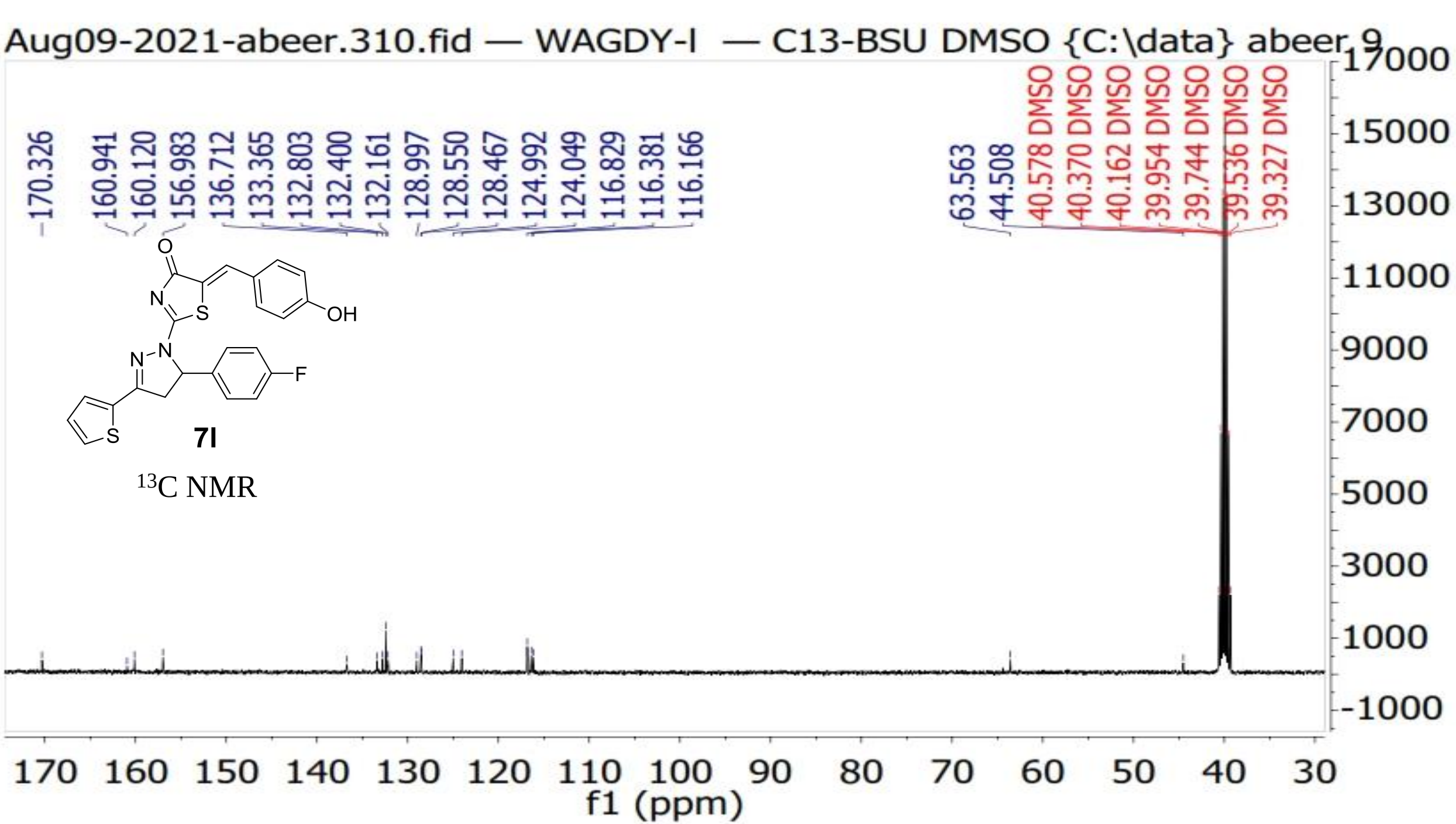


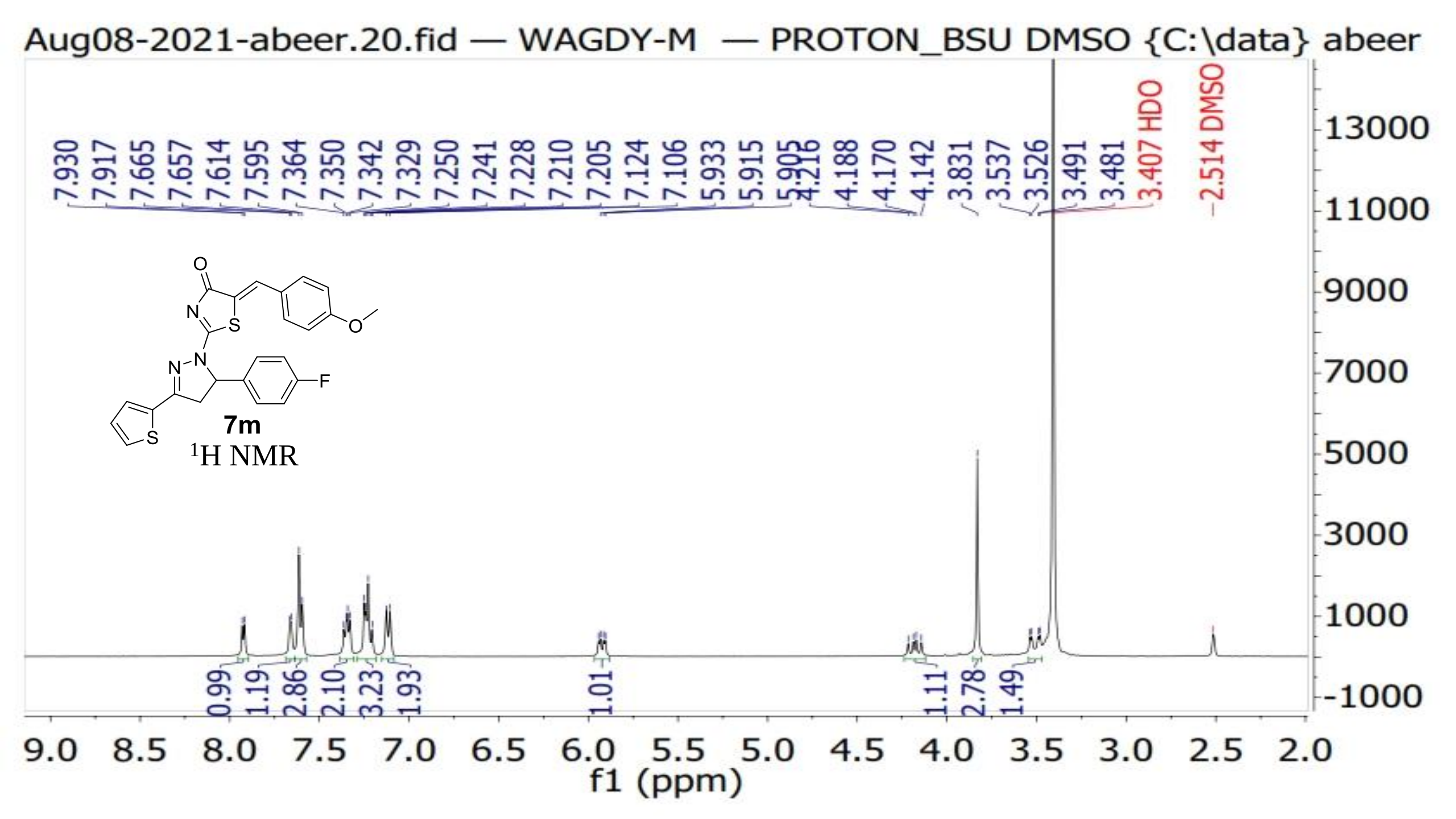
7l



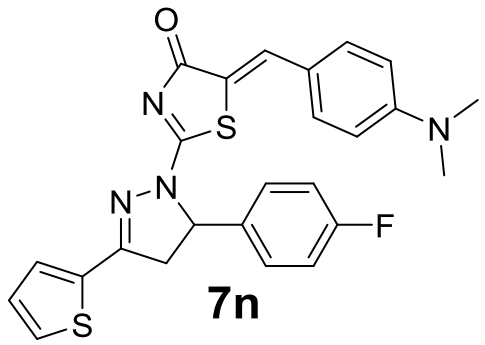
BRUKER

```
Current Data Parameters
NAME      Aug08-2021-abeer
EXPNO                   10
PROCNO                   1

F2 - Acquisition Parameters
Date_           20210808
Time              10.36
INSTRUM             spect
PROBHD   5 mm PABBO BB/
PULPROG             zg30
TD                 65536
SOLVENT             DMSO
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ              4.0894465 sec
RG                147.93
DW                62.400 usec
DE                 6.50 usec
TE                296.0 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         400.1324710 MHz
NUC1                   1H
P1                 10.00 usec
PLW1        16.00000000 W

F2 - Processing parameters
SI                 65536
SF          400.1300000 MHz
WDW                   EM
SSB       0
LB                 0.10 Hz
GB        0
PC                 1.00
```

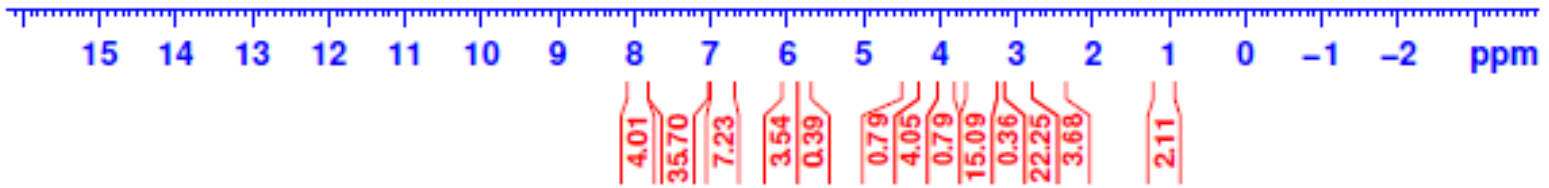

Aug09-2021-abeer.310.fid — WAGDY-I — C13-BSU DMSO {C:\data} abeer 9
170.326
160.941
160.120
156.983
136.712
133.365
132.803
132.400
132.161
128.997
128.550
128.467
124.992
124.049
116.829
116.381
116.166
63.563
44.508
40.578 DMSO
40.370 DMSO
40.162 DMSO
39.954 DMSO
39.744 DMSO
39.536 DMSO
39.327 DMSO
O
N
S
OH
N
N
F
S
7l
13C NMR
17000
15000
13000
11000
9000
7000
5000
3000
1000
-1000
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30
f1 (ppm)


Aug08-2021-abeer.20.fid — WAGDY-M — PROTON_BSU DMSO {C:\data} abeer
7.930
7.917
7.665
7.657
7.614
7.595
7.364
7.350
7.342
7.329
7.250
7.241
7.228
7.210
7.205
7.124
7.106
5.933
5.915
4.188
4.170
4.142
3.831
3.537
3.526
3.491
3.481
3.407 HDO
2.514 DMSO
O
N
S
O
N
N
F
S
7m
1H NMR
0.99
1.19
2.86
2.10
3.23
1.93
1.01
1.11
2.78
1.49
13000
11000
9000
7000
5000
3000
1000
-1000
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
f1 (ppm)

wagdy-N
PROTON_BSU DMSO (C:\data) abeer 22

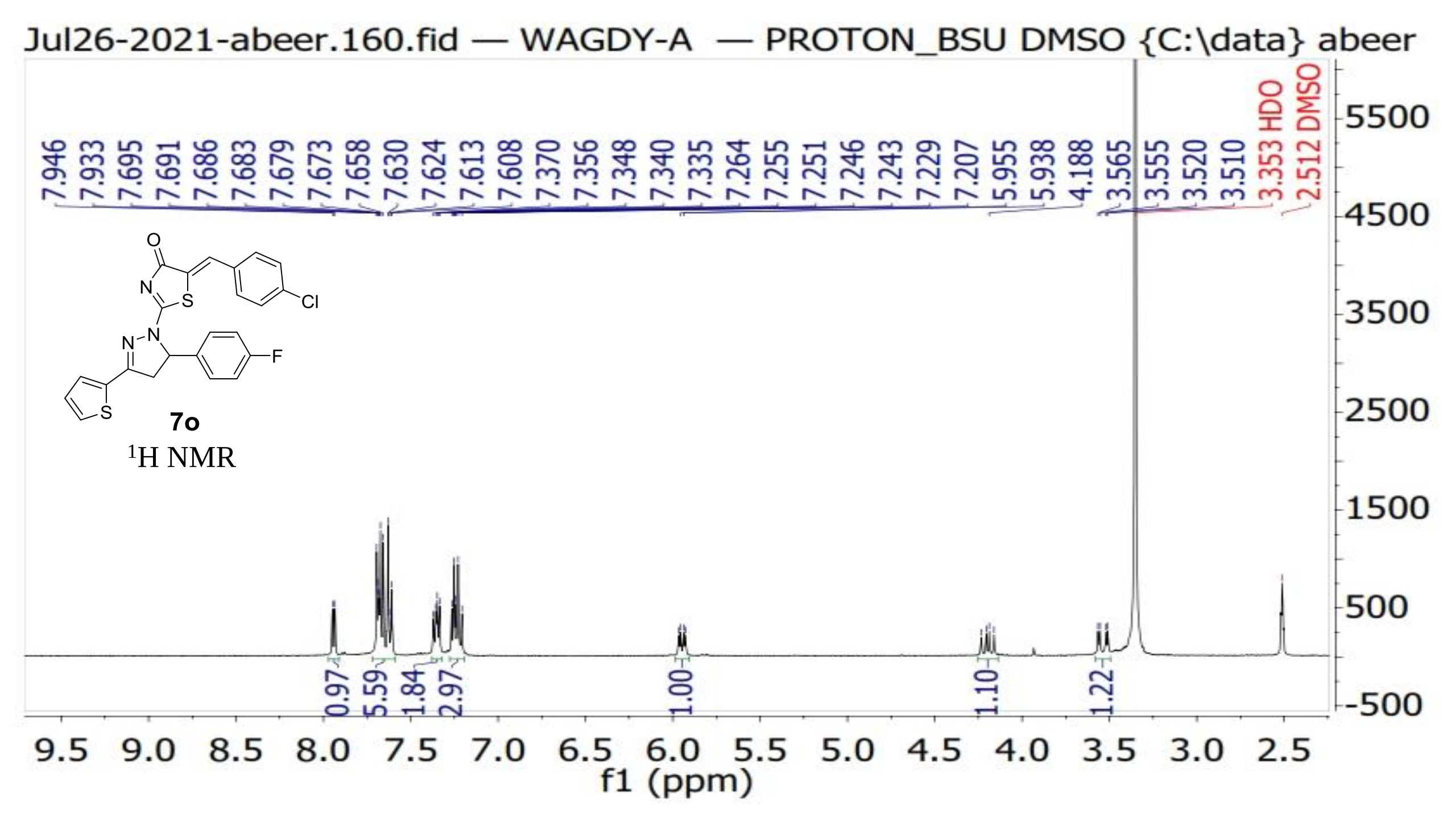


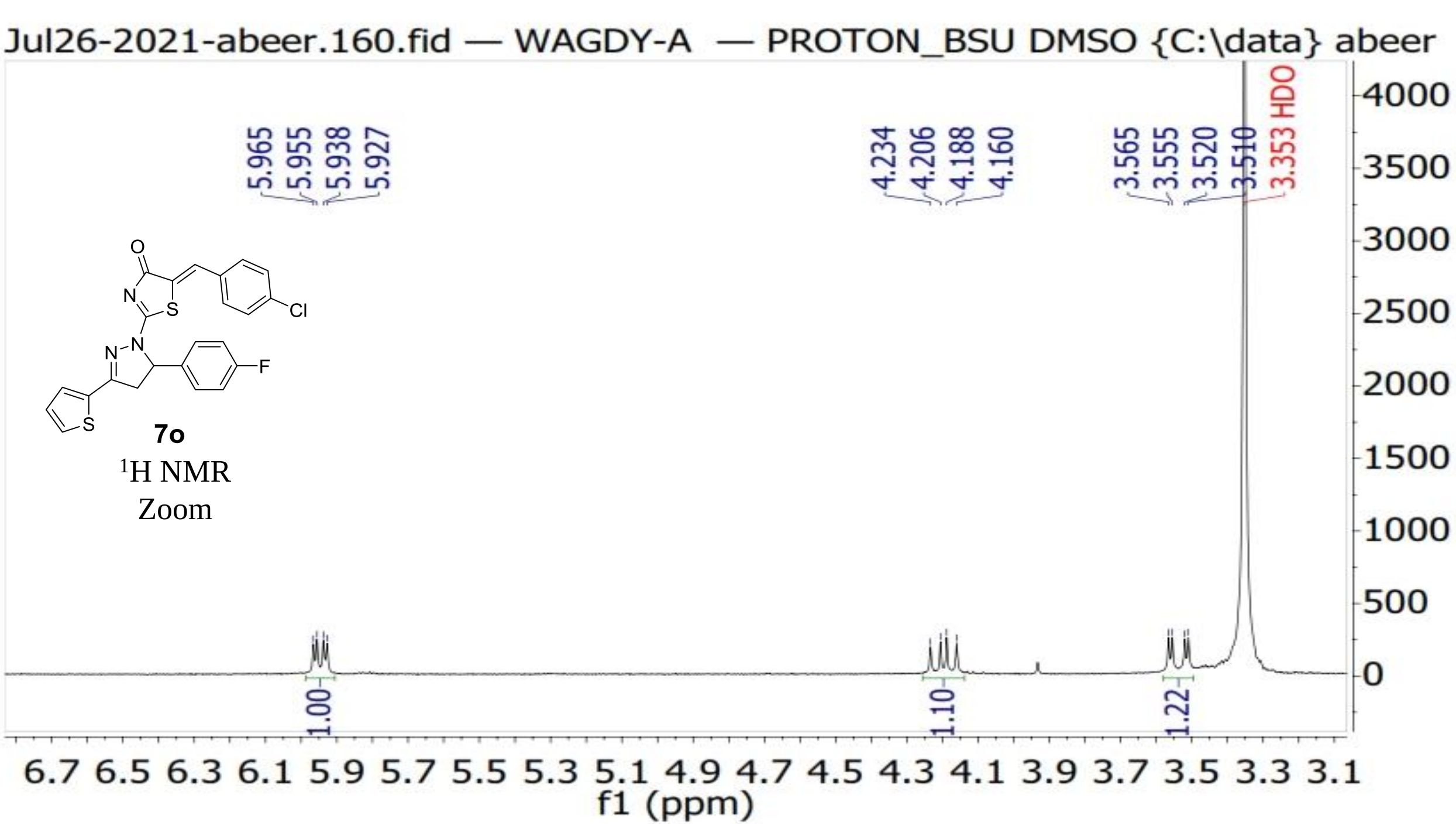
7n

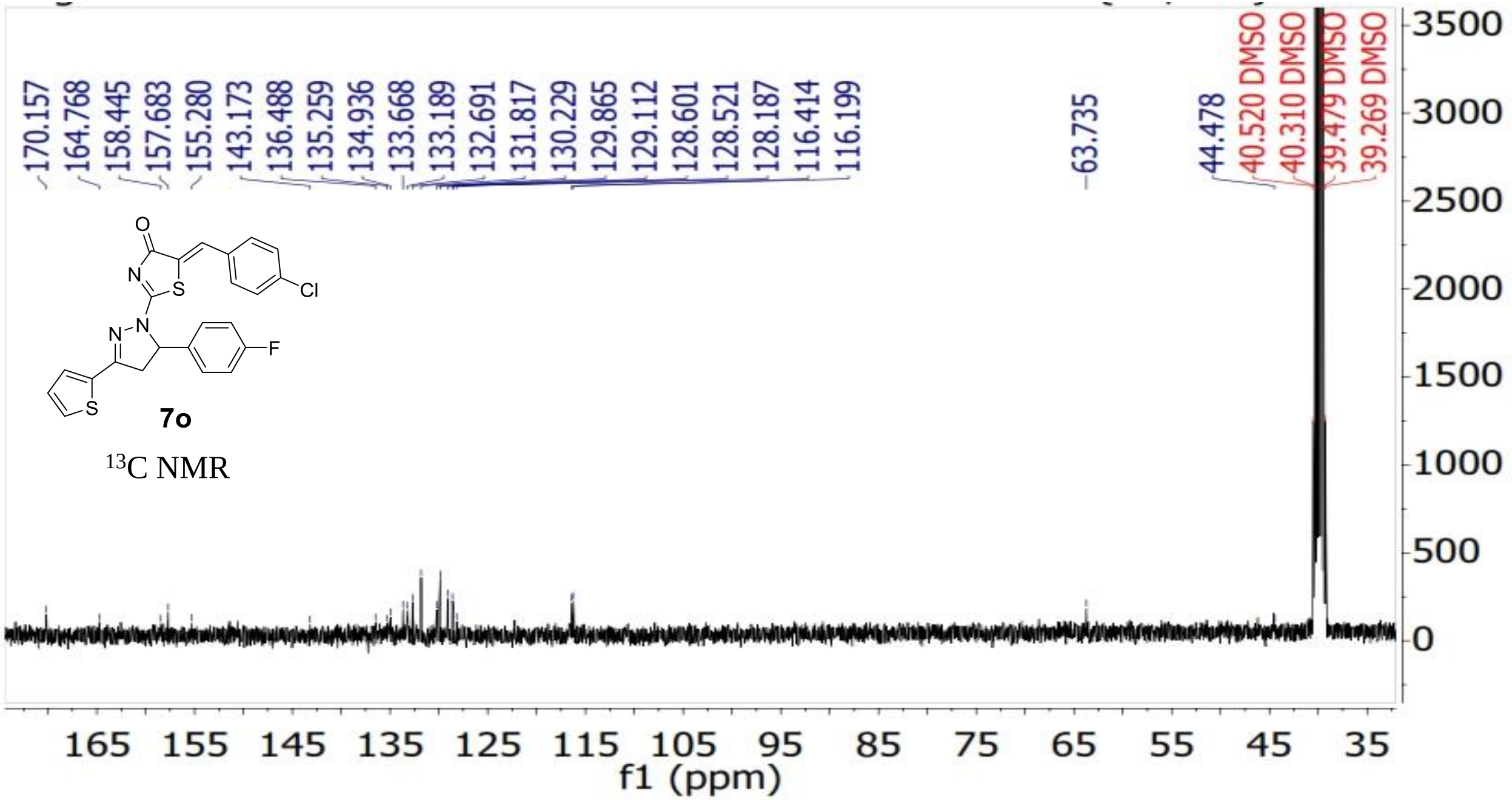


BRUKER

```
Current Data Parameters
NAME      Aug09-2021-abeer
EXPNO                  200
PROCNO                   1

F2 - Acquisition Parameters
Date_           20210809
Time              11.33
INSTRUM           spect
PROBHD   5 mm PABBO BB/
PULPROG            zg30
TD                65536
SOLVENT            DMSO
NS                   16
DS                    2
SWH            8012.820 Hz
FIDRES         0.122266 Hz
AQ             4.0894465 sec
RG               147.93
DW               62.400 usec
DE                6.50 usec
TE               299.0 K
D1            1.00000000 sec
TD0                  1

======== CHANNEL f1 =======
SFO1         400.1324710 MHz
NUC1               1H
P1               10.00 usec
PLW1         16.00000000 W

F2 - Processing parameters
SI                65536
SF           400.1300000 MHz
WDW                EM
SSB       0
LB               0.10 Hz
GB        0
PC               1.00
```


Jul26-2021-abeer.160.fid — WAGDY-A — PROTON_BSU DMSO {C:\data} abeer
7.946
7.933
7.695
7.691
7.686
7.683
7.679
7.673
7.658
7.630
7.624
7.613
7.608
7.370
7.356
7.348
7.340
7.335
7.264
7.255
7.251
7.246
7.243
7.229
7.207
5.955
5.938
4.188
3.565
3.555
3.520
3.510
3.353 HDO
2.512 DMSO
O
N
S
Cl
N
N
F
S
7o
1H NMR
0.97
5.59
1.84
2.97
1.00
1.10
1.22
5500
4500
3500
2500
1500
500
-500
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
f1 (ppm)


Jul26-2021-abeer.160.fid — WAGDY-A — PROTON_BSU DMSO {C:\data} abeer
5.965
5.955
5.938
5.927
4.234
4.206
4.188
4.160
3.565
3.555
3.520
3.510
3.353 HDO
O
N
S
Cl
N
N
F
S
7o
1H NMR
Zoom
1.00
1.10
1.22
4000
3500
3000
2500
2000
1500
1000
500
0
6.7 6.5 6.3 6.1 5.9 5.7 5.5 5.3 5.1 4.9 4.7 4.5 4.3 4.1 3.9 3.7 3.5 3.3 3.1
f1 (ppm)


170.157
164.768
158.445
157.683
155.280
143.173
136.488
135.259
134.936
133.668
133.189
132.691
131.817
130.229
129.865
129.112
128.601
128.521
128.187
116.414
116.199
63.735
44.478
40.520 DMSO
40.310 DMSO
39.479 DMSO
39.269 DMSO
O
N
S
Cl
N
N
F
S
7o
13C NMR
3500
3000
2500
2000
1500
1000
500
0
165 155 145 135 125 115 105 95 85 75 65 55 45 35
f1 (ppm)