**Supporting Information**

# Discovery and Evaluation of Novel Angular Fused Pyridoquinazolinonecarboxamides as RNA Polymerase I Inhibitors

Tony E. Dorado,[‡] Pablo de León,[§] Asma Begum,[¶] Hester Liu,[¶] Daming Chen,[§] N.V. Rajeshkumar,[¶] Romain Rey-Rodriguez,[#] Coralie Hoareau-Aveilla,[⊥] Chantal Alcouffe,[#] Marikki Laiho,[¶]* and James C. Barrow[§||]*

[‡]Department of Chemistry, Johns Hopkins University, Baltimore, MD 21218, USA

[§]Lieber Institute for Brain Development, Baltimore, MD 21205, USA

[¶]Department of Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins University School of Medicine, Baltimore, MD 21287, USA

[#]Department of Chemistry, Evotec, 31036 Toulouse, France

[⊥]Department of In vitro Biology, Evotec, 31036 Toulouse, France

[||]Department of Pharmacology, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA

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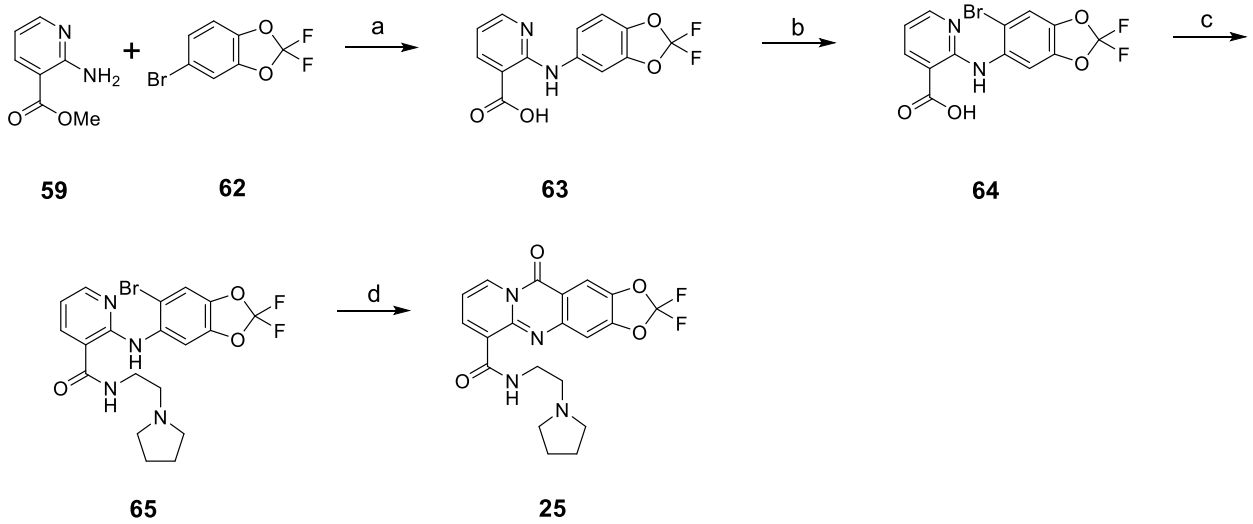
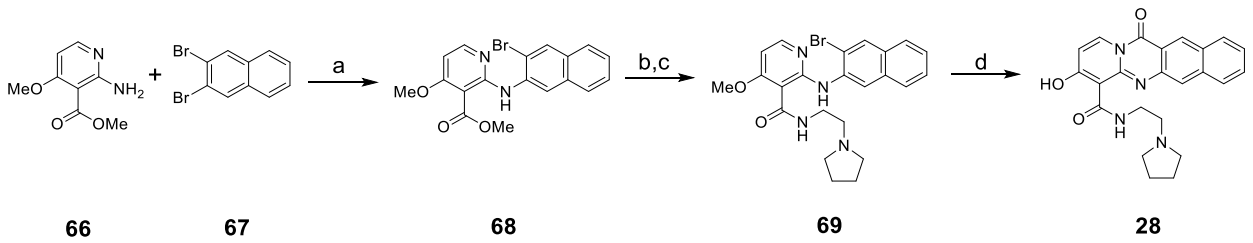
**Scheme S1. Synthesis of compound 25[a]**



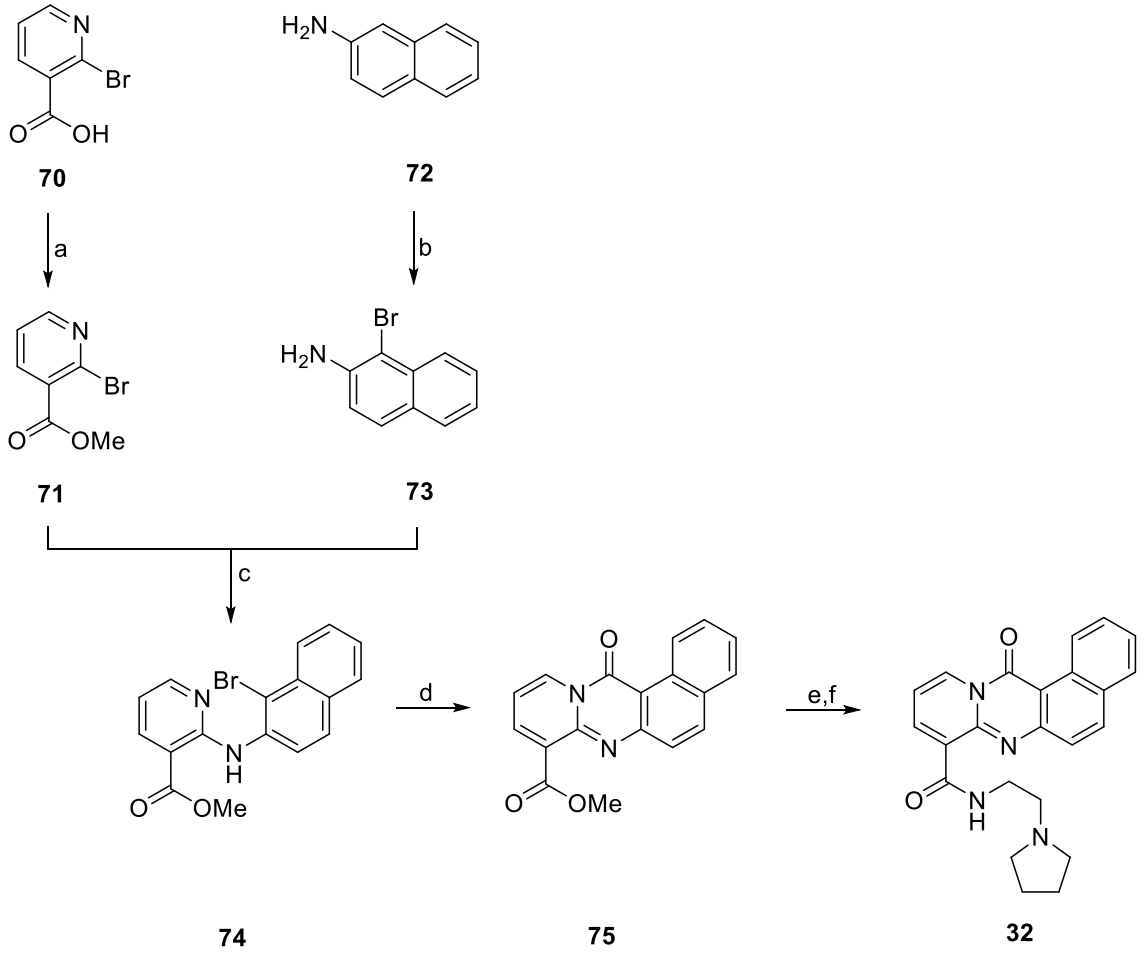

[a]Reagents and conditions: (a) $Pd_2(dba)_3$ (5 mol %), Xantphos (10 mol %), NaOtBu, 1,4-dioxane, 90°C. (b) [$NBnMe_3$•$Br_3$], 2:1 DCM/MeOH. (c) 2-pyrrolidin-1-ylethanamine, TBTU, DIPEA, DMF, rt. (d) $Pd(OAc)_2$ (5 mol %), Xantphos (15 mol %), Xantphos Pd G3 (5 mol %), $K_3PO_4$, CO(g) (saturating), toluene, 100°C.

**Scheme S2. Synthesis of compound 28[a]**



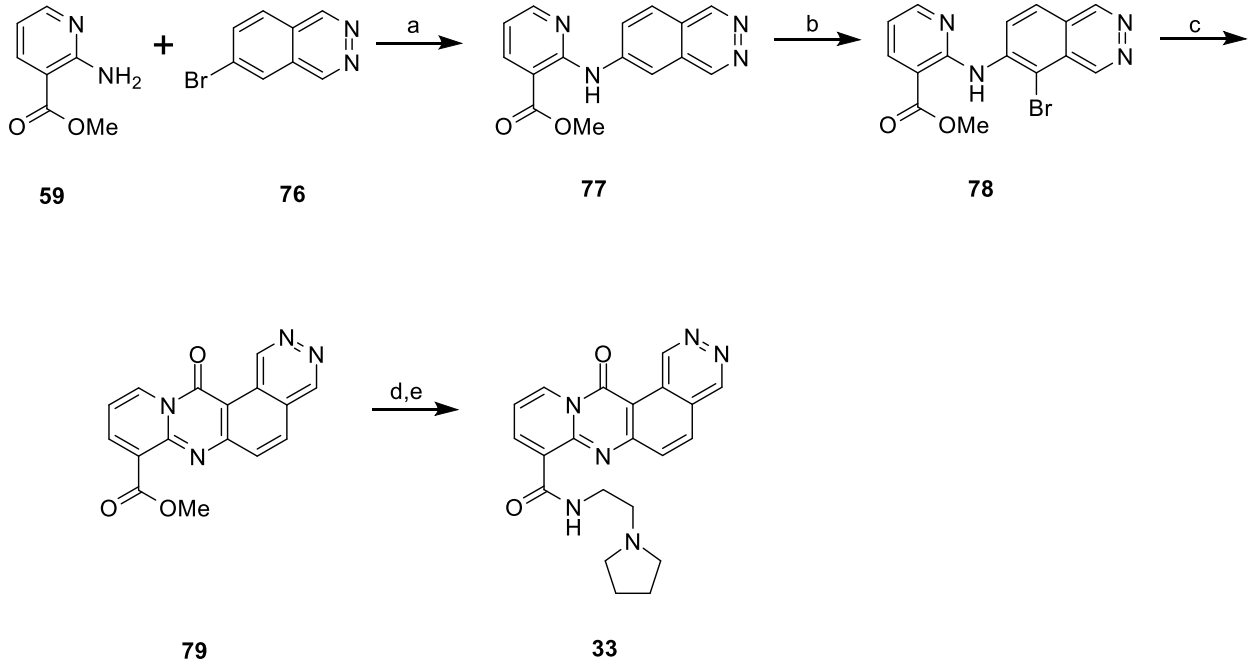

[a]Reagents and conditions: (a) $Pd(OAc)_2$ (10 mol %), Xantphos (15 mol %), $Cs_2CO_3$, toluene, 130°C. (b) 1M NaOH, MeOH, rt. (c) 2-pyrrolidin-1-ylethanamine, TBTU, DIPEA, DMF, rt. (d) $Pd(OAc)_2$ (10 mol %), Xantphos (15 mol %), Xantphos Pd G3 (5 mol %), $K_3PO_4$, CO(g) (saturating), toluene, 115°C.

**Scheme S3. Synthesis of compound 32[a]**




[a]Reagents and conditions: (a) DEAD, $PPh_3$, MeOH, diethyl ether, rt. (b) NBS, DMF, rt. (c) Rac-BINAP-Pd-G3 (10 mol %), 1,4-dioxane, 100°C. (d) $Pd(OAc)_2$ (0.5 eq), Xantphos (1 eq.), $K_3PO_4$, CO(g) (saturating), 1,4-dioxane, 100°C. (e) 2M NaOH, MeOH, rt. (f) 2-pyrrolidin-1-ylethanamine, TBTU, DIPEA, DMF, rt.

**Scheme S4. Synthesis of compound 33**[a]




[a]Reagents and conditions: (a) $Pd(OAc)_2$ (10 mol %), Xantphos (15 mol %), $Cs_2CO_3$, toluene, 130°C. (b) [$BnNMe_3 \bullet Br_3$], 2:1 DCM:MeOH, rt. (c) $Pd(OAc)_2$ (10 mol %), Xantphos (15 mol %), Xantphos Pd G3 (5 mol %), $K_3PO_4$, $Mo(CO)_6$, toluene, 115°C. (d) 1M NaOH, MeOH, rt. (e) 2-pyrrolidin-1-ylethanamine, TBTU, DIPEA, DMF, rt.

**EXPERIMENTAL SECTION**

**Synthesis.** *General Methods*. All commercially available reagents and solvents were used without further purification unless otherwise stated. Automated flash chromatography was performed on an ISCO CombiFlash Rf or Biotage Isolera using Biotage Flash cartridges with peak detection at 254 nm. Reverse phase purification was accomplished using a Gilson 215 liquid handler equipped with a Phenomenex C18 column (150 mm x 20 mm i.d., 5 µm). Peak collection was triggered by UV detection at 214 or 254 nm. $^1$H NMR spectra were recorded on a Bruker 400 instrument operating at 400 MHz with tetramethylsilane or residual protonated solvent used as a reference. Analytical LC/MS was performed using an Agilent 1260 equipped with autosampler (Agilent Poroshell 120 C18 column (50 mm x 4.6 mm i.d., 3.5 µm); 0.05% TFA in water/acetonitrile gradient; UV detection at 215 and 254 nm) and electrospray ionization. All final compounds showed purity greater than 95% at 215 and 254 nm using this method.

*12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxylic acid (**50**)*. This compound was synthesized as described by *J. Med. Chem.* **2014**, *57*, 4950-4961.

*N-(2-(dimethylamino)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide (**1**)*. This compound was synthesized as described by *J. Med. Chem.* **2014**, *57*, 4950-4961.

*12-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide (**2**)*. This compound was synthesized as described by *J. Med. Chem.* **2014**, *57*, 4950-4961.

*12-oxo-N-(2-(piperidin-1-yl)ethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide (**3**)*. This compound was synthesized as described by *J. Med. Chem.* **2014**, *57*, 4950-4961.

*12-oxo-N-(pyrrolidin-2-ylmethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide trifluoroacetate (**4**).* In a 20 mL vial charged with a magnetic stir bar was added **50** (100 mg, 0.34 mmol), TBTU (123.41 mg, 0.38 mmol), DMF (1.5 mL), and DIPEA (0.19 mL, 1.05 mmol). The resulting mixture was stirred for 15 minutes at room temperature before adding pyrrolidin-2-ylmethanamine (**49a**) (52.76 mg, 0.53 mmol). The reaction mixture was stirred for 1.5 hours at room temperature, poured into 100 mL of cold water with stirring, and the solid was collected by vacuum filtration. The solid was taken up in a solution of 4M HCl in 1,4-dioxane, stirred for 1 hour at room temperature, and concentrated in vacuo. The solid was dissolved in a minimal amount of DMSO and purified via automated reverse phase liquid chromatography on a 50 x 21.2 mm Luna 10 µm C18(2) 100 Å column with 10-50% ACN/water (0.05 % TFA buffer) to give 12-oxo-N-(pyrrolidin-2-ylmethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide trifluoroacetate (7 mg, 0.014 mmol, 4% yield) as a red solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.36 – 11.28 (m, 1H), 9.13 (s, 1H), 8.96 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.83 – 8.64 (m, 1H), 8.60 – 8.51 (m, 1H), 8.32 (d, *J* = 8.5 Hz, 1H), 8.12 (d, *J* = 8.5 Hz, 1H), 7.77 – 7.69 (m, 1H), 7.65 – 7.59 (m, 1H), 7.08 (t, *J* = 7.1 Hz, 1H), 4.42 (obs.), 3.82 (d, *J* = 5.4 Hz, 2H), 3.36 – 3.16 (m, 2H), 2.27 – 2.10 (m, 1H), 2.06 – 1.87 (m, 1H), 1.86 – 1.72 (m, 1H). LCMS (ESI): *m/z* calcd for $C_{22}H_{20}N_4O_2$, 372.2; found 373.0 $[M+H]^+$.

*12-oxo-N-(piperidin-2-ylmethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**5**)*. In a 20 mL vial charged with a magnetic stir bar was added **50** (100 mg, 0.34 mmol), TBTU (123.41 mg, 0.38 mmol), DMF (1.5 mL), and DIPEA (0.19 mL, 1.05 mmol). The resulting mixture was stirred for 15 minutes at room temperature before adding piperidin-2-ylmethanamine (60.15 mg, 0.53 mmol). The reaction was stirred for 1 hour at room temperature, poured into 100 mL of cold water with stirring, and

the solid was collected by vacuum filtration. The solid was dissolved in ~1 mL of 1M HCl and stirred for 3 hours at room temperature then concentrated to dryness to give 12-oxo-N-(piperidin-2-ylmethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (102 mg, 0.24 mmol, 70% yield) as a yellow-orange solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.29 (t, *J* = 6.2 Hz, 1H), 9.15 (s, 1H), 8.97 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.78 – 8.68 (m, 1H), 8.62 (d, *J* = 11.2 Hz, 1H), 8.57 (dd, *J* = 6.9, 1.7 Hz, 1H), 8.54 (s, 1H), 8.33 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.79 – 7.70 (m, 1H), 7.66 – 7.58 (m, 1H), 7.10 (t, *J* = 7.1 Hz, 1H), 3.87 – 3.75 (m, 1H), 3.75 – 3.65 (m, 1H), 3.27 (d, *J* = 12.4 Hz, 1H), 2.96 – 2.83 (m, 1H), 2.01 (d, *J* = 11.5 Hz, 1H), 1.89 – 1.79 (m, 1H), 1.74 (d, *J* = 13.1 Hz, 1H), 1.67 – 1.48 (m, 2H). LCMS (ESI): *m/*z calcd for $C_{23}H_{22}N_4O_2$, 386.2; found 387.0 $[M+H]^+$.

*12-oxo-N-(1-(piperidin-2-yl)ethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**6**)*. To a 4 mL vial charged with a magnetic stir bar was added **50** (75 mg, 0.26 mmol), TBTU (92.56 mg, 0.29 mmol), DMF (0.92 mL), and DIPEA (0.14 mL, 0.79 mmol). The resulting mixture was stirred for 15 minutes at room temperature before adding (1-piperidin-2-ylethyl)amine (50.66 mg, 0.40 mmol). The reaction mixture was stirred for 3 hours at room temperature then poured into 100 mL of cold water and stirred overnight at room temperature. The solid was removed by vacuum filtration. The filtrate was transferred to a separatory funnel and extracted with DCM (4 x 5 mL). Combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo to give an orange liquid. This material was taken up in a solution of 4M HCl in 1,4-dioxane, stirred overnight at room temperature, and concentrated in vacuo to give 12-oxo-N-(1-(piperidin-2-yl)ethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (25.3 mg, 0.058 mmol, 22% yield, mixture of diastereomers) as an orange solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.34 (d, *J* = 8.5 Hz, 1H), 11.22 (d, *J* = 8.4 Hz, 1H), 9.14 (s, 1H), 9.04 – 8.93 (m, 2H), 8.71 (s, 2H), 8.58 (dd, *J* = 6.9, 1.8 Hz, 1H), 8.55 (dd, *J* = 7.0, 1.7 Hz, 1H), 8.47 (s, 1H), 8.37 (s, 1H), 8.32 (d, *J* = 8.4 Hz, 2H), 8.22 – 8.15 (m, 2H), 7.78 – 7.71 (m, 2H), 7.67 – 7.57 (m, 2H), 7.11 (td, *J* = 7.1, 2.6 Hz, 2H), 4.55 (d, *J* = 10.2 Hz, 1H), 4.42 – 4.33 (obs.), 3.34 (s, 2H), 3.26 (d, *J* = 12.4 Hz, 2H), 2.91 (s, 2H), 2.68 (s, 1H), 2.21 (d, *J* = 2.1 Hz, 1H), 2.02 (d, *J* = 12.3 Hz, 1H), 1.87 (s, 2H), 1.72 (s, 2H), 1.56 (s, 1H), 1.46 (dd, *J* = 9.3, 6.9 Hz, 6H). LCMS (ESI): *m/z* calcd for $C_{24}H_{24}N_4O_2$, 400.2; found 401.0 $[M+H]^+$.

*Method A: Synthesis of amide analogs with commercially available amine and formation of the hydrochloride salt*. *N-((4-methylmorpholin-3-yl)methyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**7**)*. In a 4 mL vial charged with a magnetic stir bar was added **50** (25 mg, 0.086 mmol), TBTU (30.85 mg, 0.096 mmol), DMF (0.5 mL), and DIPEA (0.05 mL, 0.28 mmol). The resulting mixture was stirred for 15 minutes at room temperature before adding (4-methylmorpholin-3-yl)methanamine (17.14 mg, 0.13 mmol). The reaction mixture was stirred overnight at room temperature, then poured into 50 mL of cold water with stirring. The solid was collected by filtration and dried under vacuum. The solid was taken up in a solution of 4M HCl in 1,4-dioxane, stirred overnight at room temperature, and concentrated in vacuo to give N-((4-methylmorpholin-3-yl)methyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (32.9 mg, 0.075 mmol, 87% yield) as a light orange solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.26 – 11.16 (m, 1H), 9.15 (s, 1H), 8.97 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.57 – 8.50 (m, 2H), 8.34 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 8.4 Hz, 1H), 7.81 – 7.72 (m, 1H), 7.66 – 7.58 (m, 1H), 7.09 (t, *J* = 7.1 Hz, 1H), 4.30 (d, *J* = 12.5 Hz, 1H), 3.95 – 3.86 (m, 1H), 3.74 – 3.62 (m, 1H), 3.47 – 3.44 (obs.) 3.09 (d, *J* = 4.2 Hz, 2H). LCMS (ESI): *m/*z calcd for $C_{23}H_{22}N_4O_3$, 402.2; found 403.0 $[M+H]^+$.

*N-((6-(hydroxymethyl)piperidin-2-yl)methyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**8**)*. This compound was synthesized from **50** (25 mg, 0.086 mmol) and [6-

(aminomethyl)piperidin-2-yl]methanol (18.99 mg, 0.13 mmol) according to method A to give N-((6-(hydroxymethyl)piperidin-2-yl)methyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (28.5 mg, 0.063 mmol, 73% yield, mixture of diastereomers) as a yellow solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.14 (t, *J* = 6.1 Hz, 1H), 9.14 (s, 1H), 8.96 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.75 (d, *J* = 10.9 Hz, 1H), 8.54 (dd, *J* = 6.9, 1.8 Hz, 1H), 8.48 (s, 1H), 8.33 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.4 Hz, 1H), 7.78 – 7.71 (m, 1H), 7.66 – 7.59 (m, 1H), 7.09 (t, *J* = 7.1 Hz, 1H), 3.97 – 3.84 (m, 1H), 3.80 – 3.68 (m, 1H), 3.64 (dd, *J* = 11.4, 4.4 Hz, 1H), 3.42 (s, 1H), 3.17 (s, 1H), 2.05 (d, *J* = 9.7 Hz, 1H), 1.88 (d, *J* = 7.3 Hz, 1H), 1.82 – 1.73 (m, 1H), 1.66 – 1.46 (m, 3H). LCMS (ESI): *m/*z calcd for $C_{24}H_{24}N_4O_3$, 416.2; found 417.0 $[M+H]^+$.

*N-((1-methylpyrrolidin-2-yl)methyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**9**)*. This compound was synthesized from **50** (25 mg, 0.086 mmol) and (1-methylpyrrolidin-2-yl)methanamine (15.04 mg, 0.13 mmol) according to method A to give N-((1-methylpyrrolidin-2-yl)methyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (28.7 mg, 0.068 mmol, 79% yield) as an orange solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.34 – 11.28 (m, 1H), 10.26 (s, 1H), 9.13 (s, 1H), 8.98 – 8.93 (m, 1H), 8.69 (s, 1H), 8.55 (dd, *J* = 6.9, 1.7 Hz, 1H), 8.32 (d, *J* = 8.5 Hz, 1H), 8.12 (d, *J* = 8.5 Hz, 1H), 7.78 – 7.70 (m, 1H), 7.65 – 7.58 (m, 1H), 7.08 (t, *J* = 7.1 Hz, 1H), 3.94 (q, *J* = 6.1 Hz, 2H), 3.77 – 3.69 (obs.), 3.49 – 3.06 (obs.), 3.18 – 3.06 (m, 1H), 2.96 (d, *J* = 4.9 Hz, 3H), 2.34 – 2.30 (m, 1H), 2.05 (s, 1H), 2.00 – 1.88 (m, 1H). LCMS (ESI): *m/z* calcd for $C_{23}H_{22}N_4O_2$, 386.2; found 387.0 $[M+H]^+$.

*N-((1-ethylpiperidin-2-yl)methyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**10**)*. This compound was synthesized from **50** (33.38 mg, 0.12 mmol) and (1-ethylpiperidin-2-yl)methanamine (25 mg, 0.18 mmol) according to method A to give N-((1-ethylpiperidin-2-yl)methyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (29.1 mg, 0.064 mmol, 56% yield) as an orange solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.27 – 11.20 (m, 1H), 9.77 (s, 1H), 9.14 (s, 1H), 8.96 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.54 (dd, *J* = 7.0, 1.7 Hz, 1H), 8.48 (d, *J* = 12.0 Hz, 1H), 8.33 (d, *J* = 8.5 Hz, 1H), 8.15 (d, *J* = 8.7 Hz, 1H), 7.78 – 7.71 (m, 1H), 7.67 – 7.58 (m, 1H), 7.13 – 7.04 (m, 1H), 3.97 – 3.90 (obs.), 3.69 – 3.64 (obs.), 3.53 – 3.34 (m, 3H), 3.34 – 3.21 (m, 1H), 3.08 (d, *J* = 11.9 Hz, 1H), 2.21 (d, *J* = 13.9 Hz, 1H), 1.89 – 1.70 (m, 3H), 1.31 (t, *J* = 7.2 Hz, 3H). LCMS (ESI): *m/z* calcd for $C_{25}H_{26}N_4O_2$, 414.2; found 415.0 $[M+H]^+$.

*N-((1-isopropylpiperidin-2-yl)methyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**11**)*. This compound was synthesized from **50** (25 mg, 0.086 mmol) and (1-propan-2-ylpiperidin-2-yl)methanamine (20.58 mg, 0.13 mmol) according to method A to give N-((1-isopropylpiperidin-2-yl)methyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (29.7 mg, 0.064 mmol, 74% yield) as a yellow solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.24 – 11.18 (m, 1H), 9.62 (s, 1H), 9.14 (s, 1H), 8.97 – 8.94 (m, 1H), 8.53 (dd, *J* = 6.9, 1.7 Hz, 1H), 8.46 (s, 1H), 8.33 (d, *J* = 8.5 Hz, 1H), 8.15 (d, *J* = 8.6 Hz, 1H), 7.78 – 7.71 (m, 1H), 7.66 – 7.59 (m, 1H), 7.08 (t, *J* = 7.1 Hz, 1H), 4.27 – 4.15 (m, 1H), 4.07 – 3.98 (obs.), 3.81 – 3.74 (obs.), 2.90 (d, *J* = 11.5 Hz, 1H), 2.21 (d, *J* = 14.1 Hz, 1H), 1.91 (d, *J* = 13.2 Hz, 1H), 1.86 – 1.77 (m, 3H), 1.38 (d, *J* = 6.5 Hz, 3H), 1.27 (d, *J* = 6.6 Hz, 3H). LCMS (ESI): *m/z* calcd for $C_{26}H_{28}N_4O_2$, 428.2; found 429.0 $[M+H]^+$.

*Method B: Synthesis of amide analogs with synthesized amines and formation of the hydrochloride salt.*
*N-(2-(3-fluoropyrrolidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**12**)*. To a 20 mL vial charged with a magnetic stir bar was added 3-fluoropyrrolidine

hydrochloride (**48a**) (280.17 mg, 2.23 mmol), ACN (5.6 mL), tert-butyl N-(2-bromoethyl)carbamate (**47**) (250 mg, 1.12 mmol), and DIPEA (0.6 mL, 3.35 mmol). The resulting mixture was stirred overnight at room temperature. The reaction was concentrated in vacuo, the residue was taken up in DCM, and was washed 1x with water. The aqueous layer was extracted with DCM (3 x 20 mL). Combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was taken up in 1,4-dioxane (2.6 mL) and a solution of 4M HCl in 1,4-dioxane (0.78 mL, 3.10 mmol) was added. The resulting mixture was stirred overnight at room temperature then concentrated in vacuo. A portion of this material, 2-(3-fluoropyrrolidin-1-yl)ethanamine hydrochloride (**49a**) (100.22 mg, 0.59 mmol) was dissolved in DMF (4 mL) and DIPEA (0.21 mL, 1.19 mmol) was added. The mixture was stirred at room temperature until all solid dissolved and then was added dropwise to a 20 mL vial containing **50** (115 mg, 0.40 mmol), TBTU (190.81, 0.59 mmol), DMF (4 mL), and DIPEA (0.21 mL, 1.19 mmol). The resulting mixture was stirred overnight at room temperature then poured into 100 mL of cold water with stirring. The solid was vacuum filtered and washed with cold water. The crude material was purified via automated normal phase liquid chromatography using a 12 g silica cartridge with 1-10% MeOH/DCM. This material was taken up in a solution of 4M HCl in 1,4-dioxane, stirred for 4.5 hours at room temperature, and concentrated in vacuo to give N-(2-(3-fluoropyrrolidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (59.9 mg, 0.14 mmol, 34% yield) as a yellow-brown solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.25 – 11.07 (m, 1H), 10.80 (s, 1H), 9.12 (s, 1H), 8.96 (d, *J* = 7.2 Hz, 1H), 8.65 (d, *J* = 12.1 Hz, 1H), 8.58 – 8.54 (m, 1H), 8.32 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 8.5 Hz, 1H), 7.74 (t, *J* = 7.6 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.09 (t, *J* = 7.1 Hz, 1H), 5.47 (d, *J* = 56.9 Hz, 1H), 3.97 – 3.77 (m, 2H), 3.33 (s, 1H), 2.24 – 2.04 (m, 3H). LCMS (ESI): *m/z* calcd for $C_{23}H_{21}FN_4O_2$, 404.2; found 405.0 $[M+H]^+$.

*Method C: Alternate synthesis of amide analogs with synthesized amines and formation of the hydrochloride salt*. *N-(2-(3,3-difluoropyrrolidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**13**).* In a 20 mL vial charged with a magnetic stir bar was added tert-butyl N-(2-bromoethyl)carbamate (**47**) (836.98 mg, 3.73 mmol), ACN (9.3 mL), 3,3-difluoropyrrolidine (**48b**) (200 mg, 1.87 mmol), and DIPEA (1 mL, 5.6 mmol). The resulting mixture was stirred for 2 days at room temperature. The reaction mixture was poured into water and extracted with DCM (3 x 20 mL). Combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting residue was taken up in DCM (13.6 mL) and TFA (0.57 mL, 7.47 mmol) was added. The resulting mixture was stirred for 2 days at room temperature then concentrated in vacuo. A portion of this material, 2-(3,3-difluoropyrrolidin-1-yl)ethanamine trifluoroacetate (**49b**) (493.35 mg, 1.87 mmol) was dissolved in DMF (3 mL) and DIPEA (0.65 mL, 3.66 mmol) was added. This solution was added dropwise to a 20 mL vial containing **50** (354.51 mg, 1.22 mmol), TBTU (437.49 mg, 1.36 mmol), DMF (3 mL), and DIPEA (0.65 mL, 3.66 mmol). The resulting mixture was stirred overnight at room temperature then poured into 100 mL of cold water with stirring. The solid was vacuum filtered and washed with cold water. The crude material was purified via automated normal phase liquid chromatography using a 12 g silica cartridge with 0-4% MeOH/DCM. Mixed fractions were subjected to another purification via automated normal phase liquid chromatography using a 12 g silica cartridge with 1-10%, hold 10% for ~3 column volumes, then 10-25% acetone/DCM. This material was taken up in a solution of 4M HCl in 1,4-dioxane, stirred overnight at room temperature, and concentrated in vacuo to give N-(2-(3,3-difluoropyrrolidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (27.7 mg, 0.060 mmol, 4% yield) as a yellow solid. $^1$H NMR (500 MHz, MeOD) δ ppm 9.33 – 9.25 (m, 1H), 9.18 (s, 1H), 8.95 – 8.87 (m, 1H), 8.43 (s, 1H), 8.25 (d, *J* = 8.4 Hz, 1H), 8.13 (d, *J* = 8.5 Hz, 1H), 7.80 (t, *J* = 7.6 Hz, 1H),

7.69 (t, *J* = 7.6 Hz, 1H), 7.46 (s, 1H), 3.97 (t, *J* = 5.5 Hz, 2H), 3.72 (t, *J* = 5.6 Hz, 2H), 2.83 – 2.69 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{23}H_{20}F_2N_4O_2$, 422.2; found 423.2 $[M+H]^+$.

*N-(2-(3-fluoropiperidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**14**)*. This compound was synthesized using 3-fluoropiperidine (**48c**) (498 mg, 3.57 mmol) according to method B. A portion of deprotected diamine, 2-(3-fluoro-1-piperidyl)ethanaminechydrochloride (**49c**) (94.4 mg, 0.52 mmol) was coupled with **50** (100 mg, 0.34 mmol) to give N-(2-(3-fluoropiperidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (60.5 mg, 0.13 mmol, 39% yield) as a yellow solid. $^1$H NMR (400 MHz, DMSO) δ ppm 11.27 – 11.12 (m, 1H), 9.87 (s, 1H), 9.13 (d, *J* = 2.7 Hz, 1H), 8.96 (dd, *J* = 7.2, 1.4 Hz, 1H), 8.58 (s, 1H), 8.56 (dd, *J* = 6.9, 1.8 Hz, 1H), 8.33 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.79 – 7.71 (m, 1H), 7.65 – 7.59 (m, 1H), 7.08 (t, *J* = 7.1 Hz, 1H), 5.17 (d, *J* = 45.3 Hz, 1H), 4.01 – 3.86 (m, 2H), 3.66 – 3.59 (m, 1H), 3.48 – 3.38 (m, 1H), 3.18 – 3.04 (m, 1H), 2.53 – 2.51 (obs.), 2.46 – 2.43 (obs.), 2.06 – 1.93 (m, 1H), 1.86 – 1.73 (m, 1H). LCMS (ESI): *m/z* calcd for $C_{24}H_{23}FN_4O_2$, 418.2; found 419.0 $[M+H]^+$.

*N-(2-(3,3-difluoropiperidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**15**)*. This compound was synthesized using 3,3-difluoropiperidine hydrochloride (**48d**) (506.31 mg, 3.21 mmol) according to method B. A portion of deprotected diamine, 2-(3,3-difluoro-1-piperidyl)ethanamine hydrochloride (**49d**) (103.69 mg, 0.52 mmol) was coupled with **50** (100 mg, 0.34 mmol) to give N-(2-(3,3-difluoropiperidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (23.7 mg, 0.050 mmol, 14% yield) as an orange solid. $^1$H NMR (500 MHz, MeOD) δ ppm 9.10 – 9.01 (m, 1H), 8.71 – 8.62 (m, 1H), 8.39 (s, 1H), 8.17 (d, *J* = 8.4 Hz, 1H), 8.05 (d, *J* = 8.4 Hz, 1H), 7.71 (t, *J* = 7.6 Hz, 1H), 7.60 (t, *J* = 7.6 Hz, 1H), 7.16 – 7.04 (m, 1H), 4.05 (t, *J* = 5.7 Hz, 2H), 4.00 – 3.83 (m, 5H), 3.66 (t, *J* = 5.8 Hz, 2H), 3.62 – 3.47 (m, 2H), 2.32 – 2.19 (m, 3H), 2.19 – 2.10 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{24}H_{22}F_2N_4O_2$, 436.2; found 437.0 $[M+H]^+$.

*N-(2-(4,4-difluoropiperidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**16**)*. This compound was synthesized using 4,4-difluoropiperidine (270 mg, 2.23 mmol) (**48e**) according to method C. Deprotected diamine, 2-(4,4-difluoropiperidin-1-yl)ethan-1-amine trifluoroacetate (**49e**) (109.1 mg, 0.39 mmol) was coupled with **50** (75 mg, 0.26 mmol) to give N-(2-(4,4-difluoropiperidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (59.7 mg, 0.126 mmol, 49% yield). $^1$H NMR (400 MHz, DMSO) δ ppm 11.23 (t, *J* = 5.9 Hz, 1H), 10.97 (s, 1H), 9.12 (s, 1H), 8.95 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.66 (s, 1H), 8.55 (dd, *J* = 6.9, 1.7 Hz, 1H), 8.32 (d, *J* = 8.4 Hz, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.79 – 7.71 (m, 1H), 7.65 – 7.59 (m, 1H), 7.08 (t, *J* = 7.1 Hz, 1H), 4.03 – 3.86 (m, 8H), 3.86 – 3.75 (m, 2H), 3.55 – 3.47 (m, 2H), 3.39 – 3.23 (m, 2H), 2.44 – 2.33 (m, 3H). LCMS (ESI): *m/z* calcd for $C_{24}H_{22}F_2N_4O_2$, 436.2; found 437.0 $[M+H]^+$.

*N-(2-(4-fluoropiperidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**17**)*. This compound was synthesized using 4-fluoropiperidine hydrochloride (**48f**) (311.47 mg, 2.23 mmol) according to method B. Deprotected diamine, 2-(4-fluoro-1-piperidyl)ethanamine hydrochloride (**49f**) (70.8 mg, 0.39 mmol) was coupled with **50** (75 mg, 0.26 mmol) to give N-(2-(4-fluoropiperidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (64.3 mg, 0.14 mmol, 54% yield) as a yellow solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.24 – 11.14 (m, 1H), 10.53 (s, 1H), 9.12 (s, 1H), 8.96 (d, *J* = 7.3 Hz, 1H), 8.65 (s, 1H), 8.56 (d, *J* = 6.9 Hz, 1H), 8.32 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 7.75 (t, *J* = 7.6 Hz, 1H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.08 (t, *J* = 7.1 Hz, 1H), 5.01

(d, *J* = 47.8 Hz, 1H), 4.0 – 3.90 (m, 2H), 3.75 – 3.65 (m, 1H), 3.49 – 3.36 (m, 2H), 3.31 – 3.10 (m, 2H), 2.29 – 2.16 (m, 1H), 2.16 – 2.05 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{24}H_{23}FN_4O_2$, 418.2; found 419.0 $[M+H]^+$.

*N-(2-(4,4-dihydroxypiperidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**18**)*. This compound was synthesized using piperidine-4,4-diol hydrochloride (**48g**) (200 mg, 1.30 mmol) according to method B. A portion of deprotected diamine, 1-(2-aminoethyl)piperidine-4,4-diol hydrochloride (**49g**) (101.64 mg, 0.52 mmol) was coupled with **50** (100 mg, 0.34 mmol) to give N-(2-(4,4-dihydroxypiperidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (48.7 mg, 0.10 mmol, 30% yield) as a yellow-orange solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.27 (t, *J* = 5.9 Hz, 1H), 10.63 (s, 1H), 9.14 (s, 1H), 8.96 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.63 (s, 1H), 8.57 (dd, *J* = 7.0, 1.8 Hz, 1H), 8.33 (d, *J* = 8.3 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.78 – 7.72 (m, 1H), 7.65 – 7.59 (m, 1H), 7.08 (t, *J* = 7.1 Hz, 1H), 4.02 – 3.96 (m, 1H), 3.94 – 3.87 (m, 1H), 2.93 – 2.76 (m, 1H), 2.57 (d, *J* = 14.7 Hz, 2H). LCMS (ESI): *m/z* calcd for $C_{24}H_{24}N_4O_4$, 432.2; found 433.2 $[M+H]^+$.

*N-(2-(4-cyanopiperidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**19**)*. This compound was synthesized using piperidine-4-carbonitrile (**48h**) (0.20 mL, 1.82 mmol) according to method C. A portion of deprotected diamine, 1-(2-aminoethyl)piperidine-4-carbonitrile trifluoroacetate (**49h**) (138.1 mg, 0.52 mmol) was coupled with **50** (100 mg, 0.34 mmol) and purified via automated normal phase liquid chromatography using a 12 g silica cartridge with 1-10% MeOH/DCM to give N-(2-(4-cyanopiperidin-1-yl)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (109.9 mg, 0.24 mmol, 69% yield) as an orange solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.27 – 11.15 (m, 1H), 10.59 (s, 1H), 9.13 (s, 1H), 8.96 (d, *J* = 7.3 Hz, 1H), 8.65 (s, 1H), 8.56 (d, *J* = 6.8 Hz, 1H), 8.32 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 8.5 Hz, 1H), 7.75 (t, *J* = 7.5 Hz, 1H), 7.66 – 7.58 (m, 1H), 7.08 (t, *J* = 7.0 Hz, 1H), 4.00 – 3.86 (m, 2H), 3.78 – 3.64 (m, 3H), 3.55 – 3.45 (m, 1H), 3.43 – 3.33 (m, 1H), 3.13 – 3.01 (m, 2H), 2.32 – 2.22 (m, 1H), 2.20 – 2.05 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{25}H_{23}N_5O_2$, 425.2; found 426.2 $[M+H]^+$.

*12-oxo-N-(2-thiomorpholinoethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**20**)*. This compound was synthesized using thiomorpholine (**48i**) (0.19 mL, 1.94 mmol) according to method B. A portion of deprotected diamine, 2-thiomorpholinoethanamine hydrochloride (**49i**) (94.42 mg, 0.52 mmol) was coupled with **50** (100 mg, 0.34 mmol) to give 12-oxo-N-(2-thiomorpholinoethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (90.7 mg, 0.20 mmol, 58% yield) as a yellow solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.23 (t, *J* = 5.9 Hz, 1H), 10.29 (s, 1H), 9.13 (s, 1H), 8.96 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.63 (s, 1H), 8.56 (dd, *J* = 6.9, 1.7 Hz, 1H), 8.33 (d, *J* = 8.3 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.78 – 7.71 (m, 1H), 7.65 – 7.59 (m, 1H), 7.08 (t, *J* = 7.1 Hz, 1H), 4.03 – 3.80 (m, 3H), 3.50 – 3.42 (m, 2H), 3.30 (q, *J* = 11.0, 10.6 Hz, 2H), 3.13 (t, *J* = 13.0 Hz, 2H), 2.89 (d, *J* = 14.5 Hz, 2H). LCMS (ESI): *m/z* calcd for $C_{23}H_{22}N_4O_2S$, 418.2; found 419.0 $[M+H]^+$.

*N-(2-(1,1-dioxidothiomorpholino)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**21**)*. This compound was synthesized using thiomorpholine-1,1-dioxide (**48j**) (200 mg, 1.48 mmol) according to method B. A portion of deprotected diamine, 2-(1,1-dioxo-1,4-thiazinan-4-yl)ethanamine hydrochloride (**49j**) (110.95 mg, 0.52 mmol) was coupled with **50** (100 mg, 0.34 mmol) and purified via automated normal phase liquid chromatography using a 12 g silica cartridge with 1-10% MeOH/DCM followed by a second column using a 12 g silica cartridge with 6-50% Acetone/DCM to give N-(2-(1,1-dioxidothiomorpholino)ethyl)-12-oxo-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (44 mg, 0.090 mmol, 26% yield) as a yellow solid. $^1$H NMR (400 MHz, DMSO) δ ppm 11.25

– 11.18 (m, 1H), 9.13 (s, 1H), 8.95 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.62 (s, 1H), 8.56 (dd, *J* = 6.9, 1.8 Hz, 1H), 8.32 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 8.4 Hz, 1H), 7.79 – 7.70 (m, 1H), 7.66 – 7.57 (m, 1H), 7.08 (t, *J* = 7.1 Hz, 1H), 3.96 – 3.87 (obs.), 3.71 – 3.59 (obs.), 3.54 – 3.44 (obs.), 2.53 – 2.52 (obs.). LCMS (ESI): *m/z* calcd for $C_{23}H_{22}N_4O_4S$, 450.1; found 451.0 $[M+H]^+$.

*Method D: Synthesis of alternate cores. 12-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-2,3-dihydro-12H-[1,4]dioxino[2,3-g]pyrido[2,1-b]quinazoline-7-carboxamide hydrochloride (**22**).* To a solution of 7-amino-2,3-dihydrobenzo[b][1,4]dioxine-6-carboxylic acid (**52a**) (1.00 g, 5.12 mmol) and 2-chloronicotinic acid (**51**) (807 mg, 5.12 mmol) in EtOH (20 mL) was added hydrochloric acid (37%, 505 mg, 5.12 mmol). The mixture was stirred for 12 hours at 90°C. Upon completion, the reaction mixture was concentrated under reduced pressure to give a residue and was purified by prep-HPLC (TFA condition; column: Phenomenex luna C18 250*50mm*10 µm;mobile phase: [water (0.1% TFA)- ACN]; B%: 10%-35%, 18min.) to give ethyl 12-oxo-2,3-dihydro-12H-[1,4]dioxino[2,3-g]pyrido[2,1-b]quinazoline-7-carboxylate (**53a**) (1.25 g, 3.83 mmol, 75% yield) as yellow oil. Ethyl 12-oxo-2,3-dihydro-12H-[1,4]dioxino[2,3-g]pyrido[2,1-b]quinazoline-7-carboxylate (**53a**) (500 mg, 1.53 mmol) was added to HCl aq. (2 M, 20 mL) in $H_2O$ (20 mL). The mixture was stirred for 12 hours at 100°C. Upon completion, the reaction mixture was concentrated under reduced pressure to give 12-oxo-2,3-dihydro-12H-[1,4]dioxino[2,3-g]pyrido[2,1-b]quinazoline-7-carboxylic acid (0.31 g, crude) as a yellow solid, used without further purification. To a solution of 12-oxo-2,3-dihydro-12H-[1,4]dioxino[2,3-g]pyrido[2,1-b]quinazoline-7-carboxylic acid (70.0 mg, 0.24 mmol) in DMF (3.0 mL) was added TBTU (90 mg, 0.28 mmol) and DIPEA (91.0 mg, 0.70 mmol). The mixture was added to 2-pyrrolidin-1-ylethanamine (40 mg, 0.35 mmol) in THF (1.0 mL). The mixture was stirred for 12 hours at 25°C. Upon completion, the reaction mixture was concentrated under reduced pressure and purified by prep-HPLC (HCl condition; column: Luna C18 100*30 5u;mobile phase: [water (0.04% HCl)-ACN]; B%: 1%-30%, 15min) to give 12-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-2,3-dihydro-12H-[1,4]dioxino[2,3-g]pyrido[2,1-b]quinazoline-7-carboxamide hydrochloride (62 mg, 0.16 mmol, 67% yield) as a yellow solid. $^1$H NMR (400 MHz, MeOD) δ ppm 9.38 (d, *J* = 6.4 Hz, 1H), 9.03 (d, *J* = 7.2 Hz, 1H), 7.89 (s, 1H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.49 (s, 1H), 4.55-4.45 (m, 4H), 3.95-3.90 (m, 4H),3.59 (t, *J* = 5.6 Hz, 2H), 3.25-3.21 (m, 2H), 2.23-2.09 (m, 4H). LCMS (ESI): *m/z* calcd for $C_{21}H_{22}N_4O_4$, 394.2; found 395.1 $[M+H]^+$.

*12-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-7,9,10,12-tetrahydro-8H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**23**).* This compound was synthesized using 3-amino-5,6,7,8-tetrahydronaphthalene-2-carboxylic acid (**52b**), 2-chloronicotinic acid (**51**), and 2-(pyrrolidine-1-yl)ethan-1-amine according to method D to give 14.6 mg, 0.034 mmol. $^1$H NMR (400 MHz, MeOD) δ ppm 9.30 (d, *J* = 6.4 Hz, 1H), 8.90 (d, *J* = 7.2 Hz, 1H), 8.20 (s, 1H), 7.70 (s, 1H), 7.48 (b.s., 1H), 3.97-3.88 (m, 4H), 3.58 (t, *J* = 6 Hz, 2H), 3.24 (b. s, 2H) 3.08-3.04 (m, 4H), 2.22-2.11 (m, 4H), 1.94-1.93 (m, 4H). LCMS (ESI): *m/z* calcd for $C_{23}H_{26}N_4O_2$, 390.2; found 391.1 $[M+H]^+$.

*11-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-11H-[1,3]dioxolo[4,5-g]pyrido[2,1-b]quinazoline-6-carboxamide hydrochloride (**24**).* This compound was synthesized using 6-aminobenzo[d][1,3]dioxole-5-carboxylic acid (**52c**), 2-chloronicotinic acid (**51**), and 2-pyrrolidin-1-ylethan-1-amine according to method D to give 1.3 mg, 0.0031 mmol. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.31 (s, 1H), 8.96 (m, 1H), 8.58 (m, 1H), 7.70-7.56 (m, 2H) 7.20 (s, 1H), 6.28 (s, 2H), 3.54 (s, 2H), 2.70-2.50 (m, 6H), 1.81 (b.s., 4H). LCMS (ESI): *m/z* calcd for $C_{20}H_{20}N_4O_4$, 380.2; found 381.1 $[M+H]^+$.

*2,2-difluoro-11-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-11H-[1,3]dioxolo[4,5-g]pyrido[2,1-b]quinazoline-6-carboxamide hydrochloride (**25**).* To a 10-20 mL microwave vial charged with a magnetic stir bar, 5-bromo-2,2-difluoro-1,3-benzodioxole (**62**) (500 mg, 2.1 mmol), methyl 2-aminopyridine-3-carboxylate (**59**) (320 mg, 2.1 mmol), tris(dibenzylideneacetone)dipalladium(0) (97 mg, 0.10 mmol), and Xantphos (120 mg, 0.21 mmol) was added 1,4-dioxane (11 mL) [deoxygenated by bubbling nitrogen for 5 min prior to initiation]. To this reaction mixture was added sodium t-butoxide (510 mg, 5.3 mmol). Sealed reaction with teflon cap. Heated for 2 hours at 90°C using microwaves. Upon completion, desired mass of hydrolyzed product [M+1=295] is observed. Poured into brine, extracted with EtOAc, dried over $Na_2SO_4$, filtered off solids, concentrated under reduced pressure. Purified by automated normal phase chromatography (0-100% EtOAC/heptane) to give 2-((2,2-difluorobenzo[d][1,3]dioxol-5-yl)amino)nicotinic acid (**63**) (350 mg, 1.19 mmol, 56% yield). $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 6.91 (dd, *J* = 7.71, 4.80 Hz, 1 H) 7.28 - 7.37 (m, 2 H) 8.04 (d, *J* = 1.96 Hz, 1 H) 8.26 (dd, *J* = 7.74, 1.99 Hz, 1 H) 8.39 (dd, *J* = 4.77, 1.99 Hz, 1 H) 10.47 (s, 1 H).

Benzyltrimethylammonium tribromide (230 mg, 0.59 mmol, 0.5 equivalents) was added to a solution of 2-((2,2-difluorobenzo[d][1,3]dioxol-5-yl)amino)nicotinic acid (**63**) (350 mg, 1.2 mmol) in 2:1 DCM (8 mL)/MeOH (4 mL) at room temperature. Stirred for 5 minutes. The reaction was monitored by LCMS. The expected mass for mono-brominated product is observed [M + 1] = 373, unreacted starting material remains. Added another 0.45 equivalents for a total of 0.95 equivalents. Upon completion, the crude reaction was poured into water, acidified to pH 1 using 1N HCl aq., extracted with EtOAc, dried over $Na_2SO_4$, filtered off solids, and concentrated under reduced pressure. Purified by automated reverse phase liquid chromatography (5-95% ACN/water; 0.05 % TFA buffer). The product-containing fractions were combined. Concentrated under reduced pressure to give 2-((6-bromo-2,2-difluorobenzo[d][1,3]dioxol-5-yl) amino)nicotinic acid (**64**) (320 mg, 0.86 mmol, 72% yield). $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 6.99 (dd, *J* = 7.74, 4.77 Hz, 1 H) 7.89 (s, 1 H) 8.31 (dd, *J* = 7.77, 1.96 Hz, 1 H) 8.42 (dd, *J* = 4.83, 2.05 Hz, 1 H) 8.58 (s, 1 H) 10.68 (s, 1 H).

To a 20 mL scintillated vial charged with a magnetic stir bar, 2-((6-bromo-2,2-difluorobenzo[d][1,3]dioxol-5-yl) amino)nicotinic acid (**64**) (50 mg, 0.13 mmol) was taken up in DMF (1.0 mL). To this solution was added DIPEA (72 µL, 0.40 mmol), followed by TBTU (65 mg, 0.20 mmol) and 2-pyrrolidin-1-ylethanamine (28 µL, 0.20 mmol). The reaction was stirred for 24 hours at room temperature and monitored by LCMS. Upon completion, the crude reaction was diluted with EtOAc, poured into water. The organic phase was washed with water, followed by brine, dried over sodium sulfate, filtered off solids, and concentrated under reduced pressure. Purified by automated reverse phase chromatography (5-95% ACN/water; 0.05 % TFA buffer). The product-containing fractions were combined. Concentrated under reduced pressure. To a 10-20 mL microwave vial with a septum were added of 2-[(6-bromo-2,2-difluoro-1,3-benzodioxol-5-yl)amino]-N-(2-pyrrolidin-1-ylethyl)pyridine-3-carboxamide (**65**) (135 mg, 0.29 mmol) and degassed toluene (6 mL). palladium(II) acetate (3.2 mg, 0.01 mmol), Xantphos (25 mg, 0.04 mmol), Xantphos Pd G3 (13.6 mg, 0.01 mmol) and $K_3PO_4$ (177 mg, 0.83 mmol) were added while the solution was degassed with $N_2$. The septum was replaced by the seal, and the mixture was degassed with CO for 5 min. The mixture was heated for 18 hours at 100°C, then cooled to room temperature. The mixture was concentrated under reduced pressure. The material was purified by prep-HPLC using ACN and 10 mM AmBic pH 10. The product-containing fractions were combined. The material was taken in DCM (5 mL) and HCl (4 N in dioxane, 0.15 mL, 0.58 mmol) was added. The mixture was concentrated under reduced pressure and lyophilized to provide title compound (28 mg, 0.067

mmol, 22%) as a yellow solid. $^1$H NMR (400 MHz, $CD_3OD$) δ ppm 9.14 (dd, *J* = 7.3, 1.7 Hz, 1H), 8.78 (dd, *J* = 7.1, 1.7 Hz, 1H), 8.11 (s, 1H), 7.86 (s, 1H), 7.24 (t, *J* = 7.2 Hz, 1H), 3.97 (t, *J* = 5.9 Hz, 2H), 3.88 – 3.81 (m, 2H), 3.57 (t, *J* = 5.9 Hz, 2H), 3.25 – 3.17 (m, 2H), 2.26 – 2.15 (m, 2H), 2.10 – 2.00 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{20}H_{18}F_2N_4O_4$, 416.1; found 416.2 $[M+H]^+$.

*2,3-dimethyl-11-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-11H-pyrido[2,1-b]quinazoline-6-carboxamide hydrochloride (**26**).* This compound was synthesized using 2-amino-4,5-dimethylbenzoic acid (**52d**), 2-chloronicotinic acid (**51**), and 2-(pyrrolidine-1-yl)ethan-1-amine according to method D to give 23.9 mg, 0.060 mmol. $^1$H NMR (400 MHz, MeOD) δ ppm 8.95 (d, *J* = 6.8 Hz, 1H), 8.58 (d, *J* = 6.8 Hz, 1H), 8.28 (b.s., 1H), 7.97 (s, 1H), 7.55 (s, 1H), 7.06 (t, *J* = 6.8 Hz, 1H), 3.95 (m, 2H), 3.94-3.52 (m, 6H), 2.42 (d, 6H), 2.12 (s, 4H). LCMS (ESI): *m/z* calcd for $C_{21}H_{24}N_4O_2$, 364.2; found 365.2 $[M+H]^+$.

*2,3-dimethoxy-11-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-11H-pyrido[2,1-b]quinazoline-6-carboxamide hydrochloride (**27**).* This compound was synthesized using 2-amino-4,5-dimethoxybenzoic acid (**52e**), 2-chloronicotinic acid (**51**), and 2-(pyrrolidine-1-yl)ethan-1-amine according to method D to give 4.7 mg, 0.011 mmol. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 11.05-11.04 (m, 1H), 9.02 (dd, *J* = 7.2, 1.6 Hz, 1H), 8.59 (dd, *J* = 7.2, 1.6 Hz, 1H), 7.60 (s, 1H), 7.24 (s, 1H), 7.19 (t, *J* = 6.8 Hz, 1H), 4.01 (s, 3H), 3.95 (s, 3H), 3.58 (obs.), 2.76 (t, *J* = 6.0 Hz, 2H), 2.63 (b.s., 4H), 1.75 (b.s., 4H). LCMS (ESI): *m/z* calcd for $C_{21}H_{24}N_4O_4$, 396.2; found 397.1 $[M+H]^+$.

*3-hydroxy-12-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (**28**).* To a 10-20 mL microwave vial charged with a magnetic stir bar was dissolved methyl 2-amino-4-methoxypyridine-3-carboxylate (**66**) (400 mg, 2.20 mmol) in anhydrous toluene (14 mL). Argon was bubbled through the solution. 2,3-dibromonapthalene (**67**) (731 mg, 2.43 mmol), cesium carbonate (1 g, 3.07 mmol), Xantphos (191 mg, 0.329 mmol), and palladium(II) acetate (50 mg, 0.220 mmol) were added and the vial was sealed. The mixture was heated for 2 hours at 130°C using microwaves. The reaction mixture was cooled to room temperature and diluted with water. The aqueous layer was extracted 2x with EtOAc. Combined organic layers were washed 1x with water, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. Purified via automated normal phase liquid chromatography: silica gel, Merck 70 g, 15-40 µm, dry loading, eluent: heptane/DCM to give methyl 2-[(3-bromo-2-napthyl)amino]-4-methoxy-pyridine-3-carboxylate (**68**) (391 mg, 1.01 mmol, 46% yield) as a white solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 9.58 (s, 1H), 8.77 (s, 1H), 8.32 (s, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 7.84 (t, *J* = 8.0 Hz, 2H), 7.51 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.43 (dd, *J* = 10.0, 8.0 Hz, 1H), 6.80 (d, *J* = 4.0 Hz, 1H), 3.91 (s, 3H), 3.89 (s, 3H). LCMS (ESI): *m/z* calcd for $C_{18}H_{15}BrN_2O_3$, 386.0; found 387.2 $[M+H]^+$.

To a suspension of methyl 2-[(3-bromo-2-napthyl)amino]-4-methoxypyridine-3-carboxylate (**68**) (391 mg, 1.01 mmol) in MeOH (7 mL) was added 1M NaOH (2.1 mL, 2.12 mmol). The mixture was stirred overnight at 59°C then for 3 hours at 65°C. The reaction mixture was cooled to room temperature and the solvent concentrated in vacuo. The residue was acidified to pH ~ 4 with 1N citric acid. The precipitate that formed was filtered, washed with a minimum amount of water, and dried on vacuo at 35°C to give 2-[(3-bromo-2-napthyl)amino]-4-methoxy-pyridine-3-carboxylic acid (386 mg, 1.03 mmol) as an off-white solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 10.21 (s, 1H), 8.92 (s, 1H), 8.29 (s, 1H), 8.25 (d, *J* = 4.0 Hz, 1H), 7.81 (t, *J* = 8.0 Hz, 2H), 7.49 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.39 (dd, *J* = 8.0, 8.0 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 3.88 (s, 3H). LCMS (ESI): *m/z* calcd for $C_{17}H_{13}BrN_2O_3$, 372.0; found 373.1 $[M+H]^+$.

To a 2-5 mL microwave vial charged with a magnetic stir bar was dissolved 2-[(3-bromo-2-napthyl)amino]-4-methoxypyridine-3-carboxylic acid (224 mg, 0.600 mmol), TBTU (275 mg, 0.840

mmol), N-(2-aminoethyl)pyrrolidine (109 µL, 0.840 mmol), and DIPEA (314 µL, 1.80 mmol) successively in anhydrous DCM (5 mL). The vial was sealed and heated overnight at 45°C. The reaction mixture was cooled to room temperature and quenched with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with DCM (3 x 50 mL). Combined organic layers were washed with water, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. Purified via automated normal phase liquid chromatography on a 30 g SI60 15-40 µm column with DCM/MeOH 0-10% to give 2-[(3-bromo-2-napthyl)amino]-4-methoxy-N-(2-pyrrolidin-1-ylethyl)pyridine-3-carboxamide (**69**) (226 mg, 0.481 mmol, 80% yield). $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 10.86 (s, 1H), 8.87 (s, 1H), 8.60 (t, *J* = 4.0 Hz, 1H), 8.29 (s, 1H), 8.26 (d, *J* = 4.0 Hz, 1H), 7.49 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.41 (dd, *J* = 8.0, 4.0 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 3.95 (s, 3H), 3.49 (q, *J* = 8.0 Hz, 2H), 2.75-2.66 (m, 6H), 1.72 (s, 4H). LCMS (ESI): *m/z* calcd for $C_{23}H_{25}BrN_4O_2$, 468.1; found 469.1 $[M+H]^+$.

To a 2-5 mL microwave vial charged with a magnetic stir bar was added anhydrous toluene (3 mL). Carbon monoxide was bubbled to saturate the solvent. Then 2-[(3-bromo-2-napthyl)amino]-4-methoxy-N-(2-pyrrolidin-1-ylethyl)pyridine-3-carboxamide (50 mg, 0.107 mmol), palladium(II) acetate (2.4 mg, 0.011 mmol), Xantphos (9.2 mg, 0.016 mmol), Xantphos Pd G3 (5.3 mg, 0.006 mmol), and $K_3PO_4$ (69 mg, 0.320 mmol) were added successively. The mixture was bubbled again with carbon monoxide for 5 minutes then sealed. The mixture was heated for 2 hours at 130°C using microwaves. By LCMS, the hydroxyl byproduct looked to form instead of the methoxy product. The reaction mixture was cooled to room temperature and filtered on Talc. Rinsed with EtOAc and the filtrate was concentrated in vacuo. Purified via automated normal phase liquid chromatography on a 15 g SI60 15-40 µm column with DCM/MeOH 0-10% to give 3-hydroxy-12-oxo-N-(2-pyrrolidin-1-ylethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide (6 mg, 0.015 mmol, 14% yield). LCMS (ESI): *m/z* calcd for $C_{23}H_{22}N_4O_3$, 402.2; found 403.2 $[M+H]^+$.

To a 50 mL round-bottom flask charged with a magnetic stir bar was dissolved 3-hydroxy-12-oxo-N-(2-pyrrolidin-1-ylethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide (6 mg, 0.015 mmol) in a 1:1 mixture of DCM/MeOH (1 mL). A solution of 4M HCl in 1,4-dioxane (11 µL, 0.045 mmol) was added dropwise and the mixture was stirred for 1 hour at room temperature. Diethyl ether was then added (10-20 mL) until precipitation of a yellow solid. The solid was collected by filtration and dried on vacuo overnight to give 3-hydroxy-12-oxo-N-(2-pyrrolidin-1-ylethyl)-12H-benzo[g]pyrido[2,1-b]quinazoline-4-carboxamide hydrochloride (5.7 mg, 0.013 mmol, 87% yield). $^1$H NMR (600 MHz, DMSO-$d_6$) δ ppm 11.18 (t, *J* = 6 Hz, 1H), 9.86 (b.s., 1H), 9.00 (s, 1H), 8.62 (d, *J* = 8.4 Hz, 1H), 8.25 (d, *J* = 8.4 Hz, 1H), 8.09 (s, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.73 (dd, *J* = 9.6, 6.6 Hz, 1H), 7.57 (dd, *J* = 8.4, 6.0 Hz, 1H), 6.49 (d, *J* = 8.4 Hz, 1H), 3.76 (q, *J* = 6.0 Hz, 2H), 3.64-3.62 (m, 2H), 3.40 (q, *J* = 6.6 Hz, 2H), 3.10-3.07 (m, 2H), 2.04-2.01 (m, 2H), 1.91-1.87 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{23}H_{22}N_4O_3$, 402.2; found 403.3 $[M+H]^+$.

*N-(2-(pyrrolidin-1-yl)ethyl)naphtho[2',3':4,5]imidazo[1,2-a]pyridine-4-carboxamide hydrochloride (**29**).* To a 2-5 mL microwave vial charged with a magnetic stir bar was dissolved methyl 2-chloropyridine-3-carboxylate (**54**) (100 mg, 0.58 mmol) in anhydrous toluene (3 mL). The mixture was purged three times with argon, then 2-bromonapthalen-1-amine (**55**) (163 mg, 0.70 mmol), palladium(II) acetate (13 mg, 0.06 mmol), Xantphos (51 mg, 0.09 mmol), and cesium carbonate (266 mg, 0.82 mmol) were added. The mixture was purged again three times with argon, sealed, and heated for 2 hours at 130°C using microwaves. The reaction mixture was cooled to room temperature and diluted with water. The aqueous layer was extracted with EtOAc (3 x 50 mL). Combined organic layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated under reduced pressure. Purified via automated normal

phase liquid chromatography on a 30 g SI60 15-40 µm column with EtOAc/Heptane (0-50%) to give methyl naphtho[1',2':4,5]imidazo[1,2-a]pyridine-11-carboxylate (**58**) (30 mg, 0.11 mmol, 18% yield) as an off-white solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 9.47-9.41 (m, 1H), 8.71 (d, *J* = 8.1 Hz, 1H), 8.44 (d, *J* = 8.9 Hz, 1H), 8.22-8.17 (m, 1H), 8.14 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.9 Hz, 1H), 7.75 (t, *J* = 7.4 Hz, 1H), 7.63 (m, 1H), 7.24 (t, *J* = 6.9 Hz, 1H), 4.01 (s, 3H). LCMS (ESI): *m/z* calcd for $C_{17}H_{12}N_2O_2$, 276.1; found 277.2 $[M+H]^+$.

To a 50 mL round-bottom flask charged with a magnetic stir bar was dissolved methyl naphtho[1',2':4,5]imidazo[1,2-a]pyridine-11-carboxylate (**58**) (25 mg, 0.09 mmol) in MeOH (2 mL). A solution of 1M NaOH (190 µL, 0.19 mmol) was added dropwise and the mixture was stirred overnight at room temperature. The mixture was acidified to pH ~ 3-4 with 1N HCl. A solid precipitated but some of the product was still soluble, so MeOH was evaporated under reduced pressure and water was added to the mixture. The precipitate was filtered, washed with water, and dried overnight in vacuo to give naphtho[1',2':4,5]imidazo[1,2-a]pyridine-11-carboxylic acid (21 mg, 0.08 mmol, 88% yield) as an off-white solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 9.62 (s, 1H), 8.90 (s, 1H), 8.54 (d, *J* = 7.8 Hz, 1H), 8.45 (s, 1H), 8.20 (d, *J* = 6.2 Hz, 1H), 8.05 (d, *J* = 7.9 Hz, 1H), 7.81 (s, 1H), 7.74 (s, 1H), 7.50 (s, 1H). LCMS (ESI): *m/z* calcd for $C_{16}H_{10}N_2O_2$, 262.1; found 263.2 $[M+H]^+$.

To a 5 mL vial charged with a magnetic stir bar was added naphtho[1',2':4,5]imidazo[1,2-a]pyridine-11-carboxylic acid (18 mg, 0.07 mmol), TBTU (31 mg, 0.10 mmol), and DIPEA (48 µL, 0.28 mmol) in DMF (1 mL). The resulting mixture was stirred for 5 minutes at room temperature before adding N-(2-aminoethyl)pyrrolidine (22 µL, 0.14 mmol). The vial was sealed and the reaction was stirred overnight at room temperature. The reaction was quenched with a saturated solution of $NaHCO_3$ then the organic layer was extracted with EtOAc (3 x 30 mL). Combined organic layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. Purified via automated normal phase liquid chromatography on a 15 g SI60 15-40 µm column with MeOH/DCM (0-10%) to give N-(2-(pyrrolidin-1-yl)ethyl)naphtho[1',2':4,5]imidazo[1,2-a]pyridine-11-carboxamide (17 mg, 0.05 mmol, 68% yield) as an off-white solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 10.86 (d, *J* = 4.9 Hz, 1H), 9.41 (dd, *J* = 6.8, 1.3 Hz, 1H), 8.77 (d, *J* = 7.8 Hz, 1H), 8.47 (d, *J* = 8.9 Hz, 1H), 8.35 (dd, *J* = 7.1, 1.3 Hz, 1H), 8.16 (d, *J* = 7.7 Hz, 1H), 7.93 (d, *J* = 8.9 Hz, 1H), 7.79-7.65 (m, 2H), 7.32 (t, *J* = 6.9 Hz, 1H), 3.69 (d, *J* = 5.6 Hz, 2H), 2.80 (s, 2H), 2.69 (s, 4H), 1.87 (s, 4H). LCMS (ESI): *m/z* calcd for $C_{22}H_{22}N_4O$, 358.2; found 359.4 $[M+H]^+$.

To a 50 mL round-bottom flask was dissolved N-(2-(pyrrolidin-1-yl)ethyl)naphtho[1',2':4,5]imidazo[1,2-a]pyridine-11-carboxamide (17 mg, 0.05 mmol) in a DCM/MeOH 1:1 mixture (3 mL). A solution of 4M HCl in 1,4-dioxane (36 µL, 0.14 mmol) was added dropwise, and the reaction was stirred for 1 hour at room temperature. Diethyl ether was then added (10-20 mL) until precipitation of a yellow solid. A solid precipitated but was too thin to be filtered so solvents were removed under vacuo to give N-(2-(pyrrolidin-1-yl)ethyl)naphtho[1',2':4,5]imidazo[1,2-a]pyridine-11-carboxamide hydrochloride (17.7 mg, 0.04 mmol, 95% yield) as a yellow solid. $^1$H NMR (500 MHz, DMSO-$d_6$) δ ppm 10.65 (s, 1H), 10.35 (s, 1H), 9.49 (d, *J* = 10.0 Hz, 1H), 8.95 (d, *J* = 10.0 Hz, 1H), 8.50 (d, *J* = 10.0 Hz, 1H), 8.41 (d, *J* = 5.0 Hz, 1H), 8.17 (d, *J* = 10.0 Hz, 1H), 7.97 (d, *J* = 10.0 Hz, 1H), 7.75 (dt, *J* = 35.0, 7.5 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 1H), 3.99-3.96 (obs.), 3.75-3.70 (obs.), 3.53 (q, *J* = 7.5, 2H), 3.18-3.11 (m, 2H), 2.05-2.00 (m, 2H), 1.92-1.88 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{22}H_{22}N_4O$, 358.2; found 359.1 $[M+H]^+$.

*N-(2-(pyrrolidin-1-yl)ethyl)pyrido[2',1':2,3]imidazo[4,5-b]quinoline-10-carboxamide hydrochloride (**30**)*. To a 10-20 mL microwave vial charged with a magnetic stir bar was added 3-bromoquinoline (**60**) (301

mg, 1.42 mmol) in toluene (12 mL). The mixture was bubbled with argon, then methyl 2-aminopyridine-3-carboxylate (**59**) (200 mg, 1.29 mmol), cesium carbonate (591 mg, 1.80 mmol), Xantphos (112 mg, 0.19 mmol), and palladium(II) acetate (29 mg, 0.29 mmol) were added. The vial was sealed and heated for 2 hours at 130°C using microwaves. The reaction was cooled to room temperature and quenched with water. The aqueous layer was extracted 2x with EtOAc. Combined organic layers were washed 1x with water, 1x with sat. brine, dried over $Na_2SO_4$, filtered over a pad of talc, and evaporated to dryness to give a brown solid. The crude was taken up with EtOAc to give a suspension that was filtered. The residue was collected and dried on vacuum at 35°C to give 210 mg of a beige solid. The filtrate was evaporated to dryness and the process repeated to give an additional 36 mg. The residues were combined to give methyl 2-(quinolin-3-ylamino)nicotinate (**61**) (246 mg, 0.88 mmol, 68% yield) as a beige solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 10.36 (s, 1H), 9.02 (d, *J* = 2.6 Hz, 1H), 8.88 (d, *J* = 2.5 Hz, 1H), 8.53 (dd, *J* = 4.8, 1.9 Hz, 1H), 8.34 (dd, *J* = 7.8, 2.0 Hz, 1H), 8.00-7.88 (m, 2H), 7.67-7.53 (m, 2H), 7.02 (dd, *J* = 7.8, 4.8 Hz, 1H), 3.96 (s, 3H). LCMS (ESI): *m/z* calcd for $C_{16}H_{13}N_3O_2$, 279.1; found 280.3 $[M+H]^+$.

To a suspension of methyl 2-(quinolin-3-ylamino)nicotinate (**61**) (138 mg, 0.49 mmol) in DCM (4.6 mL) was added N-bromosuccinimide (97 mg, 0.54 mmol) and the reaction was stirred overnight at room temperature. The reaction mixture was quenched with water and the aqueous layer was extracted 2x with DCM. Combined organic layers were washed 1x with water, 1x with sat. brine, dried over $Na_2SO_4$, filtered, and evaporated to dryness to give a yellow solid. Purified by flash chromatography: RediSep Gold 24 g, 30 µm spheric, eluent: MeOH/DCM, liquid loading to give methyl pyrido[2',1':2,3]imidazo[4,5-b]quinoline-10-carboxylate (**62**) (65 mg, 0.23 mmol, 47% yield) as a yellow solid. $^1$H NMR (600 MHz, DMSO-$d_6$) δ ppm 9.30 (d, *J* = 6.0 Hz, 1H), 8.92 (s, 1H), 8.39 (d, *J* = 6.0 Hz, 1H), 8.26 (dd, *J* = 21.3, 8.1 Hz, 2H), 7.82 (dd, *J* = 8.4, 5.4 Hz, 1H), 7.67 (dd, *J* = 8.4, 5.4 Hz, 1H), 7.15 (t, *J* = 3.6 Hz, 1H), 3.98 (s, 3H). LCMS (ESI): *m/z* calcd for $C_{16}H_{11}N_3O_2$, 277.1; found 278.2 $[M+H]^+$.

To a suspension of methyl pyrido[2',1':2,3]imidazo[4,5-b]quinoline-10-carboxylate (**62**) (78 mg, 0.28 mmol) in MeOH (5 mL) was added 1M NaOH (0.70 mL, 0.70 mmol) and the reaction mixture was stirred overnight at room temperature. The solvent was evaporated and the residue was taken up with water and extracted with DCM. The aqueous layer was collected and acidified with 1N HCl to give a suspension that was filtered. The residue was collected and dried on vacuum at 35°C to give pyrido[2',1':2,3]imidazo[4,5-b]quinoline-10-carboxylic acid (63 mg, 0.24 mmol, 84% yield) as a yellow solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 14 (m, 1H), 9.73 (d, *J* = 6.5 Hz, 1H), 8.97 (s, 1H), 8.88 (d, *J* = 7.3 Hz, 1H), 8.44 (d, *J* = 8.0 Hz, 1H), 8.33 (d, *J* = 8.5 Hz, 1H), 8.02-7.93 (m, 1H), 7.83 (t, *J* = 7.6 Hz, 1H), 7.70 (t, *J* = 7.1 Hz, 1H). LCMS (ESI): *m/z* calcd for $C_{15}H_9N_3O_2$, 263.1; found 264.2 $[M+H]^+$.

To a suspension of pyrido[2',1':2,3]imidazo[4,5-b]quinoline-10-carboxylic acid (63 mg, 0.24 mmol) in DMF (2 mL) was added TBTU (110 mg, 0.34 mmol) and DIPEA (0.17 mL, 0.96 mmol) to give a red solution. Then, N-(2-aminoethyl)pyrrolidine (0.043 mL, 0.34 mmol) was added and the reaction mixture was stirred for 2 hours at room temperature. The reaction mixture was quenched with water and extracted 2x with EtOAc. Combined organic layers were washed 1x with water, 1x with sat. brine, dried over $Na_2SO_4$, filtered and evaporated to dryness to give a red solid. Purified by flash chromatography: silica gel, RediSep Gold 12 g, 30 µm spheric, eluent: MeOH/DCM, liquid loading to give N-(2-(pyrrolidin-1-yl)ethyl)pyrido[2',1':2,3]imidazo[4,5-b]quinoline-10-carboxamide (47 mg, 0.13 mmol, 55% yield) as a yellow solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 10.31 (s, 1H), 9.29 (dd, *J* = 6.7, 1.4 Hz, 1H), 8.88 (s, 1H), 8.54 (dd, *J* = 7.1, 1.4 Hz, 1H), 8.32 (d, *J* = 7.4 Hz, 1H), 8.26 (d, *J* = 8.8 Hz, 1H), 7.89-7.80 (m, 1H), 7.69 (t, *J* =

7.0 Hz, 1H), 7.26 (t, *J* = 6.9 Hz, 1H), 3.64 (q, *J* = 6.0 Hz, 2H), 2.75 (d, *J* = 6.3 Hz, 2H), 2.55 (s, 4H), 1.79 (s, 4H). LCMS (ESI): *m/z* calcd for $C_{21}H_{21}N_5O$, 359.2; found 360.3 $[M+H]^+$.

To a solution of N-(2-(pyrrolidin-1-yl)ethyl)pyrido[2',1':2,3]imidazo[4,5-b]quinoline-10-carboxamide (47 mg, 0.13 mmol) in 1:1 MeOH/DCM (4 mL) was added 4M HCl in 1,4-dioxane (0.098 mL, 0.39 mmol). The reaction mixture was stirred for 1 hour at room temperature. Diethyl ether was added and a suspension formed. The precipitate was filtered, washed with diethyl ether, and dried on vacuo at 35°C to give N-(2-(pyrrolidin-1-yl)ethyl)pyrido[2',1':2,3]imidazo[4,5-b]quinoline-10-carboxamide hydrochloride (57.1 mg, 0.14 mmol) as a yellow solid. $^1$H NMR (500 MHz, DMSO-$d_6$) δ ppm 10.40 (b.s., 1H), 10.21-10.19 (m, 1H), 9.40 (d, *J* = 7.8 Hz, 1H), 8.92 (s, 1H), 8.67-8.66 (m, 1H), 8.34 (d, *J* = 8.0 Hz, 1H), 8.27 (d, *J* = 8.5 Hz, 1H), 7.87 (t, *J* = 7.0 Hz, 1H), 7.72 (t, *J* = 7.0 Hz, 1H), 7.39-7.37 (m, 1H), 3.91 (q, *J* = 6.0 Hz, 2H), 3.68-3.64 (m, 2H), 3.47 (q, *J* = 6.0 Hz, 2H), 3.15-3.08 (m, 2H), 2.06-1.99 (m, 2H), 1.93-1.89 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{21}H_{21}N_5O$, 359.2; found 360.4 $[M+H]^+$.

*7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxylic acid (**57**).* To a 10-20 mL microwave vial charged with a magnetic stir bar, methyl 2-chloropyridine-3-carboxylate (**54**) (1 g, 5.83 mmol) was dissolved in anhydrous toluene (15 mL). The mixture was purged three times with argon. Then, 2-bromonapthalen-1-amine (**55**) (1499 mg, 6.41 mmol), palladium(II) acetate (53 mg, 0.233 mmol), rac-BINAP (218 mg, 0.350 mmol), and cesium carbonate (2659 mg, 8.16 mmol) were successively added. The mixture was purged again three times with argon before the vial was sealed. The reaction was heated for 2 hours at 130°C using microwaves. The reaction mixture was cooled to room temperature, water was added, and the mixture was extracted with EtOAc. Combined organic layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The crude material was washed with diethyl ether until purity >90% to give methyl 2-((2-bromonaphthalen-1-yl)amino)nicotinate (**56**) (810 mg, 2.27 mmol, 34% yield) as a grey solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 9.64 (s, 1H), 8.28 (dd, *J* = 7.8, 1.9 Hz, 1H), 8.09 (dd, *J* = 4.7, 1.9 Hz, 1H), 8.01 (d, *J* = 7.7 Hz, 1H), 7.87 (d, *J* = 8.8 Hz, 1H), 7.85 – 7.76 (m, 1H), 7.55 (m, 1H), 6.81 (dd, *J* = 7.8, 4.7 Hz, 1H), 3.96 (s, 2H). LCMS (ESI): *m/z* calcd for $C_{17}H_{13}BrN_2O_2$, 356.0; found 356.9 $[M+H]^+$.

To a 40 mL vial charged with a magnetic stir bar was dissolved methyl 2-((2-bromonaphthalen-1-yl)amino)nicotinate (**56**) (1 g, 2.80 mmol) in anhydrous toluene (15 mL). The mixture was purged three times with argon then palladium(II) acetate (63 mg, 0.28 mmol), Xantphos (243 mg, 0.42 mmol), Xantphos-Pd-G3 (140 mg, 0.14 mmol), and $K_3PO_4$ (1808 mg, 8.40 mmol) were added. The mixture was purged again three times before adding hexakis(oxomethylidene)molybdenum (739 mg, 2.80 mmol). The vial was sealed and stirred overnight at 115°C. The mixture was cooled to room temperature, filtered over a pad of talc, and rinsed with EtOAc. The filtrate was concentrated in vacuo. Purified via automated normal phase liquid chromatography using a 90 g SI60 15-40 µm column (0-75% EtOAc/heptane) to give methyl 7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxylate (310 mg, 1.02 mmol, 30% yield) as a yellow solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 9.08 (dd, *J* = 7.3, 1.6 Hz, 2H), 9.00 (s, 1H), 8.24 – 8.15 (m, 3H), 8.09 (d, *J* = 7.2 Hz, 2H), 7.94 (d, *J* = 8.8 Hz, 2H), 7.90 – 7.76 (m, 4H), 7.69 – 7.58 (m, 1H), 7.41 – 7.24 (m, 4H), 4.05 (s, 5H), 1.65 (d, *J* = 21.6 Hz, 1H). LCMS (ESI): *m/z* calcd for $C_{18}H_{12}N_2O_3$, 304.1; found 305.2 $[M+H]^+$.

To a 50 mL round-bottom flask charged with a magnetic stir bar was dissolved methyl 7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxylate (310 mg, 1.02 mmol) in MeOH (10 mL). A solution of 1M NaOH (2.14 mL, 2.14 mmol) was added dropwise and the mixture was stirred overnight at room

temperature. The mixture was acidified using 1N HCl until pH ~ 2-3, then the product precipitated as a yellow solid. The solid was filtered and dried in vacuo to give 7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxylic acid (250 mg, 0.86 mmol, 84% yield) as a yellow solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ ppm 16.81 (m, 1H), 9.22 (d, *J* = 7.4 Hz, 1H), 8.75 – 8.65 (m, 2H), 8.28 – 8.15 (m, 2H), 8.03 (d, *J* = 8.9 Hz, 1H), 7.92 (dd, *J* = 6.1, 3.2 Hz, 2H), 7.45 (t, *J* = 7.1 Hz, 1H). LCMS (ESI): *m/z* calcd for $C_{17}H_{10}N_2O_3$, 290.1; found 291.1 $[M+H]^+$.n

*Method E: Synthesis of amide analogs with commercially available amine. N-(2-(dimethylamino)ethyl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide (**37 free base**).* To a 10 mL vial charged with a magnetic stir bar was added **57** (14 mg, 0.048 mmol), TBTU (22 mg, 0.068 mmol), and DIPEA (25.3 µL, 0.145 mmol) in anhydrous DMF (0.4 mL). The resulting mixture was stirred overnight at room temperature then quenched with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with EtOAc and DCM. Combined organic layers were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. Purified via automated normal phase liquid chromatography using a 12 g SI60 15-40 µm column (10% MeOH/DCM) to give N-(2-(dimethylamino)ethyl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide (10 mg, 0.028 mmol, 55% yield) as a yellow solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.67 (d, *J* = 5.2 Hz, 1H), 9.18 (d, *J* = 7.2 Hz, 1H), 9.10 (d, *J* = 7.7 Hz, 1H), 8.74 (d, *J* = 7.0 Hz, 1H), 8.22 (d, *J* = 8.8 Hz, 1H), 8.12 (d, *J* = 7.4 Hz, 1H), 7.96 (d, *J* = 8.8 Hz, 1H), 7.86 (p, *J* = 6.4 Hz, 2H), 7.37 (t, *J* = 7.1 Hz, 1H), 3.70 (q, *J* = 5.7 Hz, 2H), 2.62 (t, *J* = 5.9 Hz, 2H), 2.32 (s, 6H). LCMS (ESI): *m/z* calcd for $C_{21}H_{20}N_4O_2$, 360.2; found 361.4 $[M+1]^+$.

*Method F: Synthesis of hydrochloride analogs. N-(2-(dimethylamino)ethyl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (**37**).* To a 100 mL round bottom flask charged with a magnetic stir bar, N-(2-(dimethylamino)ethyl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide (8.5 mg, 0.024 mmol) was dissolved in a 1:1 mixture of DCM/MeOH (2 mL). A solution of 4M HCl in 1,4-dioxane (18 µL, 0.071 mmol) was added dropwise and the reaction mixture was stirred for 1 hour at room temperature. Diethyl ether was then added (50-100 mL) until precipitation of a yellow solid. The solid was filtered and dried in vacuo overnight to give N-(2-(dimethylamino)ethyl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (8 mg, 0.020 mmol, 85% yield) as a yellow solid. $^1$H NMR (400 MHz, DMSO-$d_6$) δ 10.66 (s, 1H), 10.10 (s, 1H), 9.19 (d, *J* = 6.2 Hz, 1H), 8.84 (s, 1H), 8.61 (d, *J* = 6.7 Hz, 1H), 8.23 (d, *J* = 8.5 Hz, 1H), 8.14 (s, 1H), 7.98 (d, *J* = 9.1 Hz, 1H), 7.90 (s, 2H), 7.39 (s, 1H), 4.04 – 3.98 (m, 2H), 2.90 (s, 6H). LCMS (ESI): *m/z* calcd for $C_{21}H_{20}N_4O_2$, 360.2; found 361.5 $[M+1]^+$.

*13-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-13H-benzo[f]pyrido[2,1-b]quinazoline-8-carboxamide hydrochloride (**32**).* To a 100 mL round-bottom flask charged with a magnetic stir bar was added 2-bromonicotinic acid (**70**) (2 g, 9.9 mmol), diethyl ether (11 mL), MeOH (0.63 mL, 15.64 mmol), and DEAD (1.61 mL, 10.2 mmol). A pressure-equalized addition funnel was fitted and a solution of triphenylphosphine (2.67 g, 10.2 mmol) in diethyl ether (11 mL) was added dropwise over a period of 15 minutes at room temperature. Stirring continued for 17 hours at room temperature. The reaction mixture was vacuum filtered and the precipitate was washed with diethyl ether. The filtrate was concentrated to give a yellow solid. Purified via automated normal phase liquid chromatography using an 80 g silica cartridge (10-40% EtOAc/heptane) to give methyl 2-bromonicotinate (**71**) (1.74 g, 8.05 mmol, 81% yield) as a clear colorless oil. $^1$H NMR (400 MHz, $CDCl_3$) δ ppm 8.52 – 8.46 (m, 1H), 8.12 – 8.05 (m, 1H), 7.39 – 7.32 (m, 1H), 3.96 (s, 3H). LCMS (ESI): *m/z* calcd for $C_7H_6BrNO_2$, 215.0; found 215.9 $[M+H]^+$.

To a 250 mL round-bottom flask was added napthalen-2-amine (**72**) (2 g, 13.97 mmol) and DMF (28 mL). The resulting mixture was cooled to 0°C. Freshly recrystallized N-bromosuccinimide (2.61 g, 14.67 mmol) was added at 0°C and the reaction mixture was allowed to warm to room temperature. Stirred for 5 minutes at room temperature. Diluted with EtOAc and washed 1x with sat. $NaHCO_3$. The aqueous layer was extracted 4x with additional EtOAc. Combined organic layers were washed 1x with 10% LiCl, 1x with water, 1x with sat. brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. Purified via automated normal phase liquid chromatography using a 120 g silica cartridge (6-50% EtOAc/heptane) to give 1-bromonaphthalen-2-amine (**73**) (2.34 g, 10.54 mmol, 75% yield) as a peach-colored solid. $^1$H NMR (400 MHz, DMSO) δ ppm 7.83 (d, *J* = 8.5 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.66 (d, *J* = 8.8 Hz, 1H), 7.51 – 7.44 (m, 1H), 7.25 – 7.19 (m, 1H), 7.12 (d, *J* = 8.8 Hz, 1H). LCMS (ESI): *m/z* calcd for $C_{10}H_8BrN$, 221.0; found 222.0 $[M+H]^+$.

To a 10-20 mL microwave vial charged with a magnetic stir bar was added methyl 2-bromonicotinate (**71**) (500 mg, 2.31 mmol), 1-bromonaphthalen-2-amine (**73**) (616.8 mg, 2.78 mmol), rac-BINAP-Pd-G3 (229.69 mg, 0.23 mmol), cesium carbonate (1.51 g, 4.63 mmol), and 1,4-dioxane (15 mL). The resulting mixture was capped, sealed, and bubbled with nitrogen for 10 min, then heated for 45 minutes at 100°C. The reaction was allowed to cool to room temperature, diluted with DCM, and poured into sat. brine. The aqueous layer was extracted 3x with additional DCM. Combined organic layers were washed 1x with sat. brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. Purified via automated normal phase liquid chromatography using a 120 g silica cartridge (6-50% EtOAc/heptane). Clean fractions were collected and set aside. Mixed fractions were subjected to another automated normal phase column using an 80 g silica cartridge (6-50% EtOAc/heptane). Clean fractions were combined to give methyl 2-((1-bromonaphthalen-2-yl)amino)nicotinate (**74**) (431.9 mg, 1.21 mmol, 52% yield) as an off-white solid. $^1$H NMR (400 MHz, DMSO) δ ppm 10.60 (s, 1H), 8.55 (d, *J* = 9.0 Hz, 1H), 8.45 (dd, *J* = 4.7, 2.0 Hz, 1H), 8.35 (dd, *J* = 7.8, 1.9 Hz, 1H), 8.14 (dd, *J* = 8.5, 1.0 Hz, 1H), 7.95 (dd, *J* = 8.9, 2.5 Hz, 2H), 7.68 – 7.63 (m, 1H), 7.55 – 7.49 (m, 1H), 7.02 (dd, *J* = 7.8, 4.8 Hz, 1H), 3.95 (s, 3H). LCMS (ESI): *m/z* calcd for $C_{17}H_{13}BrN_2O_2$, 356.0; found 358.0 $[M+2]^+$.

To a 10-20 mL microwave vial charged with a magnetic stir bar was added methyl 2-((1-bromonaphthalen-2-yl)amino)nicotinate (300 mg, 0.84 mmol), palladium(II) acetate (94.28 mg, 0.42 mmol), Xantphos (485.96 mg, 0.84 mmol), $K_3PO_4$ (534.83 mg, 2.52 mmol) and 1,4-dioxane (6 mL). The resulting mixture was capped, sealed, and bubbled with carbon monoxide for 10 min, then heated for 3 hours at 100°C. The reaction was allowed to cool to room temperature, then was diluted with EtOAc and filtered through a pad of celite. The filtrate was washed 1x with sat. brine. The aqueous layer was extracted 3x with additional EtOAc. Combined organic layers were washed 1x with sat. brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. Purified via automated normal phase liquid chromatography using a 40g silica cartridge (6-50% EtOAc/heptane) to give methyl 13-oxo-13H-benzo[f]pyrido[2,1-b]quinazoline-8-carboxylate (**75**) (220.2 mg, 0.72 mmol, 86% yield) as a yellow solid. $^1$H NMR (400 MHz, DMSO) δ ppm 9.87 (d, *J* = 8.4 Hz, 1H), 9.23 (dd, *J* = 7.3, 1.6 Hz, 1H), 8.36 (d, *J* = 9.0 Hz, 1H), 8.17 (dd, *J* = 6.8, 1.5 Hz, 1H), 8.12 (d, *J* = 7.9 Hz, 1H), 7.88 – 7.81 (m, 1H), 7.74 – 7.68 (m, 2H), 7.31 (t, *J* = 7.1 Hz, 1H), 3.97 (s, 3H). LCMS (ESI): *m/z* calcd for $C_{18}H_{12}N_2O_3$, 304.1; found 305.0 $[M+H]^+$.

To a 20 mL vial charged with a magnetic stir bar was added methyl 13-oxo-13H-benzo[f]pyrido[2,1-b]quinazoline-8-carboxylate (100 mg, 0.33 mmol), MeOH (7 mL), and 2N NaOH (0.33 mL, 0.66 mmol). The resulting mixture was stirred for 2 days at room temperature. Concentrated to dryness to give 13-oxo-13H-benzo[f]pyrido[2,1-b]quinazoline-8-carboxylic acid (125.2 mg, 0.43 mmol) as

an off-white solid, used without further purification. $^1$H NMR (400 MHz, DMSO) δ ppm 9.90 (d, *J* = 8.8 Hz, 1H), 9.01 (dd, *J* = 7.2, 1.6 Hz, 1H), 8.28 (d, *J* = 9.0 Hz, 1H), 8.09 – 8.03 (m, 1H), 7.84 – 7.76 (m, 1H), 7.70 (d, *J* = 9.0 Hz, 1H), 7.68 – 7.63 (m, 1H), 7.48 (dd, *J* = 6.6, 1.6 Hz, 1H), 7.23 – 7.17 (m, 1H). LCMS (ESI): *m/z* calcd for $C_{17}H_{10}N_2O_3$, 290.1; found 291.0 $[M+H]^+$.

To a 20 mL vial charged with a magnetic stir bar was added 13-oxo-13H-benzo[f]pyrido[2,1-b]quinazoline-8-carboxylic acid (115 mg, 0.40 mmol), TBTU (190.81 mg, 0.59 mmol), DMF (3 mL), DIPEA (0.21 mL, 1.19 mmol), and 2-(pyrrolidin-1-yl)ethan-1-amine (0.08 mL, 0.59 mmol). The resulting mixture was stirred for 16 hours at room temperature. An additional 1.5 equivalents of TBTU and 1.5 equivalents of 2-(pyrrolidin-1-yl)ethan-1-amine were added to push the reaction forward. Stirring continued for 3 days at room temperature. At this time, another 1.5 equivalents of TBTU and 1.5 equivalents of 2-(pyrrolidin-1-yl)ethan-1-amine were added and stirring continued for 3 hours at room temperature. The reaction mixture was diluted with water and the formed precipitate was vacuum filtered and washed with additional water. Purified via automated reverse phase liquid chromatography using a 30x75 LUNA column (10-60% ACN/water) to give 13-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-13H-benzo[f]pyrido[2,1-b]quinazoline-8-carboxamide trifluoroacetate (34.9 mg, 0.0697 mmol, 18% yield) as an orange-brown oil. $^1$H NMR (500 MHz, DMSO) δ ppm 11.16 (t, *J* = 6.0 Hz, 1H), 9.83 (d, *J* = 8.6 Hz, 1H), 9.64 (s, 1H), 9.36 (d, *J* = 7.2 Hz, 1H), 8.77 (d, *J* = 7.7 Hz, 1H), 8.45 (d, *J* = 8.9 Hz, 1H), 8.15 (d, *J* = 8.0 Hz, 1H), 8.11 (d, *J* = 8.9 Hz, 1H), 7.87 (t, *J* = 7.8 Hz, 1H), 7.73 (t, *J* = 7.5 Hz, 1H), 7.44 (t, *J* = 7.1 Hz, 1H), 3.89 (q, *J* = 6.2 Hz, 2H), 3.75 – 3.67 (m, 2H), 3.50 (q, *J* = 6.1 Hz, 2H), 3.18 – 3.10 (m, 2H), 2.09 – 1.99 (m, 2H), 1.91 – 1.83 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{23}H_{22}N_4O_2$, 386.2; found 387.0 $[M+H]^+$.

13-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-13H-benzo[f]pyrido[2,1-b]quinazoline-8-carboxamide trifluoroacetate (34 mg, 0.0679 mmol) was taken up in DCM (6 mL) and washed 1x with sat. $NaHCO_3$. The aqueous layer was extracted 3x with DCM. Combined organic layers were concentrated in vacuo and taken back up in 1,4-dioxane (2 mL). 4M HCl in 1,4-dioxane (0.03 mL, 0.11 mmol) was added and the resulting mixture was stirred for 3 hours at room temperature. The resulting suspension was concentrated to dryness to give 13-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-13H-benzo[f]pyrido[2,1-b]quinazoline-8-carboxamide hydrochloride (23.1, 0.055 mmol, 97% yield) as a yellow solid. $^1$H NMR (500 MHz, DMSO) δ ppm 11.15 (t, *J* = 5.8 Hz, 1H), 9.97 (s, 1H), 9.84 (d, *J* = 8.5 Hz, 1H), 9.38 – 9.33 (m, 1H), 8.80 – 8.75 (m, 1H), 8.45 (d, *J* = 9.0 Hz, 1H), 8.18 – 8.11 (m, 2H), 7.87 (t, *J* = 7.7 Hz, 1H), 7.73 (t, *J* = 7.4 Hz, 1H), 7.44 (t, *J* = 7.1 Hz, 1H), 3.90 (q, *J* = 6.1 Hz, 2H), 3.73 – 3.66 (m, 2H), 3.53 – 3.46 (m, 2H), 3.18 – 3.07 (m, 2H), 2.07 – 1.99 (m, 2H), 1.92 – 1.81 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{23}H_{22}N_4O_2$, 386.2; found 387.0 $[M+H]^+$.

*13-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-13H-pyridazino[4,5-f]pyrido[2,1-b]quinazoline-8-carboxamide hydrochloride (**33**).* To a 2-5 mL microwave vial charged with a magnetic stir bar and fitted with a Teflon cap was dissolved 6-bromopthalazine (**76**) (100 mg, 0.48 mmol) in anhydrous toluene (3 mL). Under argon atmosphere, methyl 2-aminopyridine-3-carboxylate (**59**) (74 mg, 0.48 mmol), cesium carbonate (218 mg, 0.67 mmol), Xantphos (42 mg, 0.072 mmol), and palladium(II) acetate (11 mg, 0.048 mmol) were added and the vial was sealed with a Teflon cap before heating for 2 hours at 130°C using microwaves. The reaction mixture was cooled to room temperature, diluted with water, and the aqueous layer was extracted with EtOAc. Combined organic layers were washed with brine, dried over $Na_2SO_4$, and concentrated in vacuo. Purified via automated normal phase liquid chromatography using a 12 g silica cartridge (0-50% EtOAc/heptane). The column was then rinsed with 10% MeOH/DCM to give

methyl 2-(phthalazin-6-ylamino)nicotinate (**77**) (74 mg, 0.18 mmol) as a pale brown solid, used directly in the next step. LCMS (ESI): *m/z* calcd for $C_{15}H_{12}N_4O_2$, 280.1; found 281.1 $[M+H]^+$.

To a solution of methyl 2-(phthalazin-6-ylamino)nicotinate (**77**) (74 mg, 0.26 mmol) in a 2:1 mixture of DCM/MeOH (6 mL), benzyltrimethylammonium tribromide (37 mg, 0.093 mmol) was added and the reaction mixture was stirred for 1.5 hours at room temperature. An additional 0.25 equivalents benzyltrimethylammonium tribromide was added and the reaction was stirred for 2.5 hours at room temperature. Water was added and the mixture was acidified to pH ~ 1 using 1N HCl. The mixture was then extracted with EtOAc. Combined organic layers were washed with water and brine, dried over $Na_2SO_4$, and concentrated under reduced pressure. Purified via automated normal phase liquid chromatography using a 4 g silica cartridge (10% MeOH/DCM) to give methyl 2-((5-bromophthalazin-6-yl)amino)nicotinate (**78**) (30.9 mg, 0.09 mmol) as a pale orange solid, used directly in the next step, contains residual benzyltrimethylammonia. $^1$H NMR (400 MHz, DMSO) δ ppm 8.19 (d, *J* = 8.0 Hz, 2H), 7.98-7.94 (m, 3H), 7.80 (d, *J* = 12.0 Hz, 2H), 1.06 (t, *J* = 8.0 Hz, 3H). LCMS (ESI): *m/z* calcd for $C_{15}H_{11}BrN_4O_2$, 358.0; found 359.9 $[M+2]^+$.

To a 10-20 mL microwave vial charged with a magnetic stir bar was dissolved methyl 2-((5-bromophthalazin-6-yl)amino)nicotinate (**78**) (31 mg, 0.086 mmol) in anhydrous toluene (1 mL). The mixture was purged 3 times with argon, then palladium(II) acetate (1.9 mg, 0.0086 mmol), Xantphos (7.5 mg, 0.013 mmol), Xantphos Pd G3 (4.3 mg, 0.0043 mmol), and $K_3PO_4$ (56 mg, 0.258 mmol) were added. The mixture was again purged 3 times with argon before adding hexakis(oxomethylene)molybdenum (23 mg, 0.086 mmol). The vial was sealed and heated overnight at 115°C. The mixture was cooled to room temperature, filtered over a pad of talc, and rinsed with EtOAc. The filtrate was evaporated to give crude product. Purified via automated normal phase liquid chromatography using a 4 g silica cartridge (0-60% EtOAc/heptane) to give methyl 13-oxo-13H-pyridazino[4,5-f]pyrido[2,1-b]quinazoline-8-carboxylate (**79**) (1.6 mg, 0.01 mmol, 6% yield) as an orange solid. $^1$H NMR (400 MHz, $CDCl_3$) δ ppm 11.62, 11.42, 11.13, 9.74, 9.37-9.36, 8.26-8.21, 4.11. LCMS (ESI): *m/z* calcd for $C_{16}H_{10}N_4O_3$, 306.1; found 307.1 $[M+H]^+$.

To a 10 mL vial charged with a magnetic stir bar was added methyl 13-oxo-13H-pyridazino[4,5-f]pyrido[2,1-b]quinazoline-8-carboxylate (5 mg, 0.0163 mmol) in MeOH (1 mL), and 1M NaOH (0.034 mL, 0.0343 mmol). The resulting mixture was stirred for 2 days at room temperature. The mixture was acidified to pH ~ 3-4 with conc. HCl. The yellow solid that formed was triturated with MeOH, filtered, washed with MeOH, and dried under vacuum to give 13-oxo-13H-pyridazino[4,5-f]pyrido[2,1-b]quinazoline-8-carboxylic acid (11.5 mg, 0.04 mmol) as a yellow solid, used without further purification. LCMS (ESI): *m/z* calcd for $C_{15}H_8N_4O_3$, 292.1; found 293.2 $[M+H]^+$.

To a 10 mL vial charged with a magnetic stir bar and fitted with a Teflon cap was added 13-oxo-13H-pyridazino[4,5-f]pyrido[2,1-b]quinazoline-8-carboxylic acid (11.5 mg, 0.04 mmol), TBTU (9 mg, 0.0275 mmol), DIPEA (0.010 mL, 0.059 mmol), and anhydrous DMF (0.21 mL). The resulting mixture was stirred for 15 minutes at room temperature. before addition of 2-(pyrrolidin-1-yl)ethan-1-amine (0.036 mL, 0.0275 mmol). The resulting mixture was stirred overnight at 45°C. The reaction mixture was hydrolyzed with sat. $NaHCO_3$ and extracted 3x with EtOAc and DCM. Combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. Purified via automated normal phase liquid chromatography using a 4 g silica cartridge (10% MeOH/DCM). The column was rinsed with 15% MeOH/DCM + 1% $Et_3N$ and the solvent was evaporated under vacuum to give 13-oxo-N-

(2-(pyrrolidin-1-yl)ethyl)-13H-pyridazino[4,5-f]pyrido[2,1-b]quinazoline-8-carboxamide (4.6 mg, 0.01 mmol, 60% yield) as a yellow solid. $^1$H NMR (400 MHz, DMSO) δ ppm 11.17 (s, 1H), 9.84 (s, 1H), 9.37 (d, *J* = 8.0 Hz, 1H), 8.89 (d, *J* = 8.0 Hz, 1H), 8.61 (d, *J* = 8.0 Hz, 1H), 8.26 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 3.62-3.61 (m, 2H), 2.77-2.76 (m, 2H), 2.64 (m, 3H), 1.85 (m, 3H).

13-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-13H-pyridazino[4,5-f]pyrido[2,1-b]quinazoline-8-carboxamide (4.6 mg, 0.0118 mmol) was dissolved in a 1:1 mixture of DCM/MeOH (2 mL) and 4M HCl in 1,4-dioxane (0.089 mL, 0.0355 mmol) was added. The resulting mixture was stirred for 1.5 hours at room temperature. Diethyl ether was added and the solid was filtered and dried under vacuum overnight to give 13-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-13H-pyridazino[4,5-f]pyrido[2,1-b]quinazoline-8-carboxamide hydrochloride (2 mg, 0.0047 mmol, 36% yield) as a yellow solid. $^1$H NMR (600 MHz, DMSO) δ ppm 11.20 (s, 1H), 10.90-10.88 (m, 1H), 9.85 (s, 1H), 9.68 (b.s., 1H), 9.41 (d, *J* = 6.0 Hz, 1H), 8.88 (d, *J* = 6.0 Hz, 1H), 8.58 (dd, *J* = 24.0, 12.0 Hz, 2H), 7.56 (t, *J* = 9.0 Hz, 1H), 3.89 (q, *J* = 6.0 Hz, 2H), 3.69-3.67 (m, 3H), 3.50 (q, *J* = 6.0 Hz, 2H), 3.14-3.13 (obs.), 2.04-2.03 (m, 2H), 1.89-1.87 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{21}H_{20}N_6O_2$, 388.2; found 389.2 $[M+H]^+$.

*7-oxo-N-(2-(pyrrolidin-1-yl)ethyl)-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (**31**).* This compound was synthesized from **57** (172 mg, 0.593 mmol) and N-(2-aminoethyl)pyrrolidine (98 µL, 0.773 mmol) according to method E followed by method F to give 82 mg, 0.19 mmol, 84 % yield. $^1$H NMR (500 MHz, DMSO-$d_6$) δ ppm 10.67 (t, *J* = 5.9 Hz, 1H), 9.17 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.83 (d, *J* = 8.0 Hz, 1H), 8.60 (dd, *J* = 7.0, 1.7 Hz, 1H), 8.21 (d, *J* = 8.8 Hz, 1H), 8.15 – 8.10 (m, 1H), 7.99 – 7.85 (m, 3H), 7.38 (t, *J* = 7.1 Hz, 1H), 3.99 (q, *J* = 6.3 Hz, 2H), 3.64 (s, 2H), 3.50 (s, 2H), 3.11 (s, 2H), 2.05 – 1.79 (m, 4H). LCMS (ESI): *m/z* calcd for $C_{23}H_{22}N_4O_2$, 386.2; found 387.3 $[M+H]^+$.

*N-(2-hydroxyethyl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (**34**).* This compound was synthesized from **57** (28 mg, 0.096 mmol) and 2-aminoethan-1-ol (7.28 µL, 0.122 mmol) according to method E followed by method F to give 7 mg, 0.019 mmol, 20% yield. $^1$H NMR (600 MHz, DMSO-$d_6$) δ ppm 11.00-10.98 (m, 1H), 9.19-9.16 (m, 2H), 8.74 (d, *J* = 7.2 Hz, 1H), 8.21 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 7.96 (d, *J* = 9.0 Hz, 1H), 7.87 (dd, *J* = 7.8, 6.0 Hz, 1H), 7.80 (dd, *J* = 8.1, 5.7 Hz, 1H), 7.38 (t, *J* = 6.9 Hz, 1H), 3.78-3.76 (obs.), 3.69-3.66 (obs.). LCMS (ESI): *m/z* calcd for $C_{19}H_{15}N_3O_3$, 333.1; found 334.2 $[M+H]^+$.

*N-(2-aminoethyl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (**35**)*. This compound was synthesized from **57** (40 mg, 0.138 mmol) and tert-butyl N-(2-aminoethyl)carbamate (31.5 mg, 0.193 mmol) according to method E followed by method F to give 20 mg, 0.050 mmol, 36% yield. $^1$H NMR (500 MHz, DMSO-$d_6$) δ ppm 10.64 (t, *J* = 5.8 Hz, 1H), 9.25 – 9.16 (m, 1H), 8.85 – 8.79 (m, 1H), 8.62 (dd, *J* = 7.0, 1.7 Hz, 1H), 8.27 – 8.21 (m, 1H), 8.15 (dd, *J* = 9.8, 8.2 Hz, 1H), 8.01 (dd, *J* = 21.4, 8.8 Hz, 3H), 7.94 – 7.84 (m, 2H), 7.39 (t, *J* = 7.1 Hz, 1H), 5.75 (s, 1H), 3.86 (d, *J* = 12.5 Hz, 7H), 3.17 (s, 3H). LCMS (ESI): *m/z* calcd for $C_{19}H_{16}N_4O_2$, 332.1; found 333.0 $[M+H]^+$.

*N-(2-(methylamino)ethyl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (**36**).* This compound was synthesized from **57** (40 mg, 0.138 mmol) and tert-butyl (2-aminoethyl)methylcarbamate (33.6 mg, 0.193 mmol) according to method E followed by method F to give 9.3 mg, 0.024 mmol, 17% yield. $^1$H NMR (500 MHz, DMSO-$d_6$) δ ppm 10.70 (t, *J* = 5.9 Hz, 1H), 9.18 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.86 (s, 2H), 8.82 – 8.78 (m, 1H), 8.63 (dd, *J* = 7.0, 1.7 Hz, 1H), 8.22 (d, *J* = 8.8 Hz, 1H), 8.15 – 8.09 (m, 1H), 7.97 (d, *J* = 8.8 Hz, 1H), 7.93 – 7.85 (m, 2H), 7.39 (t, *J* = 7.1 Hz, 1H), 3.92 (q, *J* =

6.2 Hz, 2H), 3.30 – 3.24 (m, 2H), 2.64 (t, *J* = 5.0 Hz, 3H). LCMS (ESI): *m/z* calcd for $C_{20}H_{18}N_4O_2$, 346.1; found 347.0 $[M+H]^+$.

*N-(2-(diethylamino)ethyl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (**38**).* This compound was synthesized from **57** (40 mg, 0.138 mmol) and N,N-diethylethylenediamine (22.4 mg, 0.193 mmol) according to method E followed by method F to give 26 mg, 0.059 mmol, 43% yield. $^1$H NMR (500 MHz, DMSO-$d_6$) δ ppm 10.60 (t, *J* = 5.9 Hz, 1H), 10.12 (s, 1H), 9.18 (dd, *J* = 7.2, 1.6 Hz, 1H), 8.88 – 8.83 (m, 1H), 8.58 (dd, *J* = 7.0, 1.6 Hz, 1H), 8.23 (d, *J* = 8.8 Hz, 1H), 8.16 – 8.11 (m, 1H), 7.98 (d, *J* = 8.8 Hz, 1H), 7.93 – 7.86 (m, 2H), 7.38 (t, *J* = 7.1 Hz, 1H), 4.00 (q, *J* = 6.5 Hz, 2H), 3.41 (dq, *J* = 14.1, 6.9 Hz, 2H), 3.33 – 3.21 (m, 4H), 1.27 (t, *J* = 7.3 Hz, 6H). LCMS (ESI): *m/z* calcd for $C_{23}H_{24}N_4O_2$, 388.2; found 389.0 $[M+H]^+$.

*7-oxo-N-(2-(piperidin-1-yl)ethyl)-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (**39**).* This compound was synthesized from **57** (40 mg, 0.138 mmol) and 2-(1-piperidyl)ethanamine (24.7 mg, 0.193 mmol) according to method E followed by method F to give 18 mg, 0.038 mmol, 28% yield). $^1$H NMR (500 MHz, DMSO-$d_6$) δ ppm 10.65 (t, *J* = 5.9 Hz, 1H), 9.19 (dd, *J* = 7.2, 1.7 Hz, 1H), 8.87 – 8.82 (m, 1H), 8.60 (dd, *J* = 7.0, 1.7 Hz, 1H), 8.23 (d, *J* = 8.8 Hz, 1H), 8.17 – 8.11 (m, 1H), 8.05 – 7.96 (m, 1H), 7.94 – 7.86 (m, 2H), 7.39 (t, *J* = 7.1 Hz, 1H), 4.02 (q, *J* = 6.4 Hz, 2H), 3.61 (d, *J* = 11.7 Hz, 2H), 3.42 (q, *J* = 6.5 Hz, 2H), 3.03 (q, *J* = 8.9 Hz, 2H), 1.83 (d, *J* = 14.3 Hz, 2H), 1.70 (d, *J* = 12.6 Hz, 2H). LCMS (ESI): *m/z* calcd for $C_{24}H_{24}N_4O_2$, 400.2; found 401.0 $[M+H]^+$.

*N-(2-(4-methylpiperazin-1-yl)ethyl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (**40**).* This compound was synthesized from **57** (40 mg, 0.138 mmol) and 2-(4-methylpiperazin-1-yl)ethanamine (27.6 mg, 0.193 mmol) according to method E followed by method F to give 19 mg, 0.042 mmol, 30% yield. $^1$H NMR (600 MHz, DMSO-$d_6$) δ ppm 11.60 (b.s., 1H), 10.65 (s, 1H), 9.17 (d, *J* = 6.0 Hz, 1H), 8.85 (d, *J* = 6.0 Hz, 1H), 8.61 (d, *J* = 12.0 Hz, 1H), 8.22 (d, *J* = 6.0 Hz, 1H), 8.13 (d, *J* = 6.0 Hz, 1H), 7.97 (d, *J* = 12.0 Hz, 1H), 7.94-7.87 (m, 2H), 7.38 (t, *J* = 6.0 Hz, 1H), 4.09-4.02 (obs.), 3.56-3.37 (obs.), 2.82 (s, 3H). LCMS (ESI): *m/z* calcd for $C_{24}H_{25}N_5O_2$, 415.2; found 416.2 $[M+H]^+$.

(*S)-N-(2-(3-fluoropyrrolidin-1-yl)ethyl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (**41**)*. This compound was synthesized from **57** (40 mg, 0.138 mmol) and (S)-2-(3-fluoropyrrolidin-1-yl)ethan-1-amine hydrochloride (74.9 mg, 0.444 mmol, prepared according to method B) according to method E followed by method F to give 5 mg, 0.011 mmol, 8% yield). $^1$H NMR (500 MHz, DMSO-$d_6$) δ ppm 10.70 (t, *J* = 6.0 Hz, 1H), 1 0.56 (s, 1H), 9.19 (d, *J* = 7.1 Hz, 1H), 8.86–8.81 (m, 1H), 8.65–8.59 (m, 1H), 8.23 (d, *J* = 8.8 Hz, 1H), 8.16–8.12 (m, 1H), 7.98 (d, *J* = 8.8 Hz, 1H), 7.89 (dd, *J* = 6.1, 2.9 Hz, 2H), 7.39 (t, *J* = 7.1 Hz, 1H), 5.48 (dd, J = 53.5, 23.7 Hz, 1H), 4.00 (q, *J* = 6.3 Hz, 3H), 3.83 (d, *J* = 7.9 Hz, 1H), 3.63–3.55 (obs.), 2.24–2.06 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{23}H_{21}FN_4O_2$, 404.2; found 405.1 $[M+H]^+$.

*(R)-N-(2-(3-fluoropyrrolidin-1-yl)ethyl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide (**42**)*. This compound was synthesized from **57** (50 mg, 0.172 mmol) and (R)-2-(3-fluoropyrrolidin-1-yl)ethan-1-amine (74.9 mg, 0.444 mmol, prepared according to method B) according to method E followed by method F to give 1 mg, 0.002 mmol. $^1$H NMR (600 MHz, DMSO-$d_6$) δ ppm 10.69 (d, *J* = 5.7 Hz, 1H), 10.46 (s, 1H), 9.19 (dd, *J* = 7.1, 1.7 Hz, 1H), 8.86 – 8.82 (m, 1H), 8.65 – 8.59 (m, 1H), 8.23 (d, *J* = 8.8 Hz, 1H), 8.14 (d, *J* = 7.0 Hz, 1H), 7.99 (d, *J* = 8.8 Hz, 1H), 7.93 – 7.86 (m, 2H), 7.40 (t, *J* = 7.0 Hz, 1H), 5.56 – 5.33 (m, 1H), 4.00 (p, *J* = 6.4 Hz, 2H), 3.88 – 3.73 (m, 1H), 3.63 – 3.57 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{23}H_{21}FN_4O_2$, 404.2; found 405.0 $[M+H]^+$.

*N-(3-(dimethylamino)propyl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (**43**).* This compound was synthesized from **57** (40 mg, 0.138 mmol) and *N*,*N*-dimethylpropane-1,3-diamine (20.8 mg, 0.204 mmol) according to method E followed by method F to give 34 mg, 0.083 mmol, 60% yield. $^1$H NMR (600 MHz, DMSO-$d_6$) δ ppm 10.58 (t, *J* = 5.7 Hz, 1H), 9.87 (s, 1H), 9.17 (dd, *J* = 7.1, 1.6 Hz, 1H), 8.81 (d, *J* = 7.9 Hz, 1H), 8.60 (dd, *J* = 7.0, 1.7 Hz, 1H), 8.23 (d, *J* = 8.8 Hz, 1H), 8.14 (d, *J* = 8.6 Hz, 1H), 7.98 (d, *J* = 8.8 Hz, 1H), 7.94 – 7.86 (m, 2H), 7.38 (t, *J* = 7.0 Hz, 1H), 3.67 (q, *J* = 6.9 Hz, 2H), 3.22 (dt, *J* = 10.6, 5.5 Hz, 2H), 2.79 (d, *J* = 4.9 Hz, 6H), 2.13 (p, *J* = 7.3 Hz, 2H). LCMS (ESI): *m/z* calcd for $C_{22}H_{22}N_4O_2$, 374.2; found 375.0 $[M+H]^+$.

*7-oxo-N-(3-(pyrrolidin-1-yl)propyl)-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (**44**).* This compound was synthesized from **57** (40 mg, 0.138 mmol) and 3-(pyrrolidin-1-yl)propan-1-amine (18.2 mg, 0.142 mmol) according to method E followed by method F to give 35.5 mg, 0.081 mmol, 59% yield. $^1$H NMR (500 MHz, DMSO-$d_6$) δ ppm 10.58 (t, *J* = 5.0 Hz, 1H), 10.50 (b.s., 1H), 9.17 (d, *J* = 5.0 Hz, 1H), 8.81 (d, *J* = 10.0 Hz, 1H), 8.60 (d, *J* = 7.5 Hz, 1H), 8.22 (d, *J* = 10.0 Hz, 1H), 8.14 (d, *J* = 5.0 Hz, 1H), 7.98-7.94 (m, 2H), 7.90-7.87 (m, 1H), 7.38 (t, *J* = 7.5 Hz, 1H), 3.68 (q, *J* = 5.0 Hz, 2H), 3.57-3.54 (m, 2H), 3.31-3.27 (m, 2H), 3.02-2.98 m, 2H), 2.18-2.15 (m, 2H), 2.00-1.97 (m, 2H), 1.90-1.87 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{24}H_{24}N_4O_2$, 400.2; found 401.1 $[M+H]^+$.

*N-(azetidin-3-yl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (**45**).* This compound was synthesized from **57** (40 mg, 0.138 mmol) and tert-butyl 3-aminoazetidine-1-carboxylate (56 µL, 0.355 mmol) according to method E followed by method F to give 35 mg, 0.082 mmol, 59% yield. $^1$H NMR (500 MHz, DMSO-$d_6$) δ ppm 10.76 (d, *J* = 6.5 Hz, 2H), 9.17 (dd, *J* = 7.2, 1.7 Hz, 2H), 8.86 – 8.81 (m, 2H), 8.54 (dd, *J* = 7.0, 1.6 Hz, 2H), 8.22 (d, *J* = 8.8 Hz, 2H), 8.17 – 8.11 (m, 2H), 7.98 (d, *J* = 8.9 Hz, 2H), 7.94 – 7.86 (m, 4H), 7.38 (t, *J* = 7.1 Hz, 2H), 5.75 (s, 1H), 5.04 (h, *J* = 7.8 Hz, 2H), 4.38 (s, 4H), 4.27 (d, *J* = 7.1 Hz, 3H). LCMS (ESI): *m/z* calcd for $C_{20}H_{16}N_4O_2$, 344.1; found 345.0 $[M+H]^+$.

*N-(1-methylpiperidin-4-yl)-7-oxo-7H-benzo[h]pyrido[2,1-b]quinazoline-12-carboxamide hydrochloride (**46**).* This compound was synthesized from **57** (40 mg, 0.138 mmol) and 1-methylpiperidin-4-amine (22 mg, 0.193 mmol) according to method E followed by method F to give 42.2 mg, 0.1 mmol, 72% yield as a yellow solid. $^1$H NMR (500 MHz, DMSO-$d_6$) δ ppm 10.66 (m, 2H), 9.17 (d, *J* = 7.0 Hz, 1H), 8.78 (d, *J* = 8.5 Hz, 1H), 8.63 (d, *J* = 7.0 Hz, 1H), 8.22 (d, *J* = 9.0 Hz, 1H), 8.15-8.12 (m, 2H), 7.97 (d, *J* = 9.0 Hz, 1H), 7.89 (t, *J* = 7.0 Hz, 1H), 7.37 (t, *J* = 7.3 Hz, 1H), 4.30-4.25 (obs.), 3.23-3.20 (m, 2H), 2.80 (d, *J* = 5.0 Hz, 3H), 2.32-2.30 (m, 2H), 2.12 (m, 2H). LCMS (ESI): *m/z* calcd for $C_{23}H_{22}N_4O_2$, 386.2; found 387.1 $[M+H]^+$.

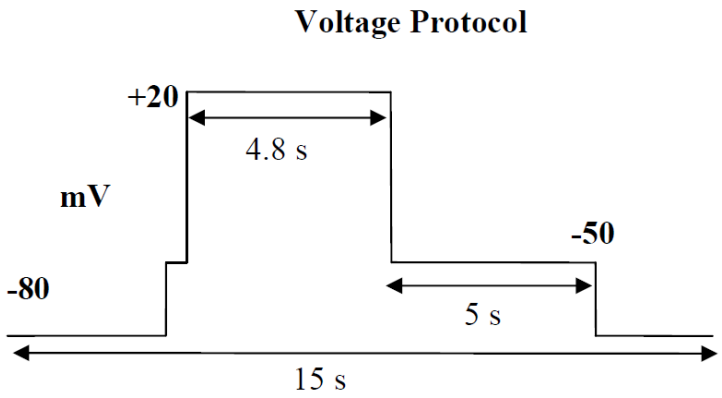
**Cell culture.** A375 melanoma cells were maintained at 37°C in a humidified atmosphere containing 5% $CO_2$. A375 cells were cultured in DMEM supplemented with 10% fetal bovine serum (FBS) and 4 mM glutamine.

**RPA194 Degradation Assay.** A375 cells were seeded on 96-well plates (PerkinElmer ViewPlate-96 Black, catalog # 6005182) and treated with the compounds at 0.01, 0.03, 0.1, 0.3, 1, 3, 10, and 30 µM or treated with vehicle (DMSO) for 4 h. After treatment, cells were washed with phosphate-buffered saline (PBS), fixed in 3.5-4% paraformaldehyde, permeabilized with 0.1-0.5% NP-40, and blocked with 1-3% bovine serum albumin (BSA). Cells were incubated with primary antibody, anti-RPA194 (C1) [sc-48385, Santa Cruz Biotechnology], for 2 h at 37°C and washed three times with PBS. Cells were incubated with secondary antibody, Alexa 594-conjugated anti-mouse (A11005, Invitrogen) or Alexa 488-conjugated anti-mouse (A11001, Thermo Fisher), for 1 h at 37°C, washed three times with PBS, and DNA was stained with Hoechst 33342 (H-21492, Invitrogen). Images were acquired using a Molecular Devices

ImageXpress Micro XLS High Content Imager (20X objective, 9 fields/well) and processed using MetaXpress High Content Software-6. The fold change to control was determined. $IC_{50}$ was determined using GraphPad Prism for Windows (version 6.01) using a three or four-parameter fit.

**hERG Inhibition Assay.** hERG inhibition analysis was performed at Evotec. Studies were performed using HEK293 cells stably transfected with hERG cDNA. QPatch was primed with appropriate extracellular (bath) and intracellular (pipette) solutions prior to conducting a study. The composition of the extracellular solution was: NaCl (137 mM), KCl (4 mM), $CaCl_2$ (1.8 mM), $MgCl_2$ (1 mM), glucose (10 mM), HEPES (10 mM), pH 7.4 with NaOH. The composition of the intracellular solution was: KCl (130 mM), $MgCl_2$ (1 mM), EGTA (5 mM), Mg-ATP (5 mM), HEPES (10 mM), pH 7.2 with KOH. Extracellular and intracellular solutions were filtered through a 0.2 µm polycarbonate membrane filter upon formulation. A 48-well plate (QPlate, Sophion Biosciences A/S), used for the QPatch was loaded into the system and primed before preparing cells suspension in the bath solution. Test substances were formulated in DMSO. Stock solutions were diluted in extracellular solutions to final perfusion concentrations (0.01, 0.1, 1, 10, and 30 µM).

A schematic diagram of the voltage protocol used is indicated. The standard voltage profile will be as follows: step from -80 mV to -50 mV for 200 ms, +20 mV for 4.8 s, step to -50 mV for 5 s then step to the holding potential of -80 mV. The step from -80 mV to the test command (+20 mV) results in an outward current (i.e. current flows out of the cell) and the step from the test command (+20 mV) to -50 mV results in the tail current (the tail current represents deactivation of the current over time).



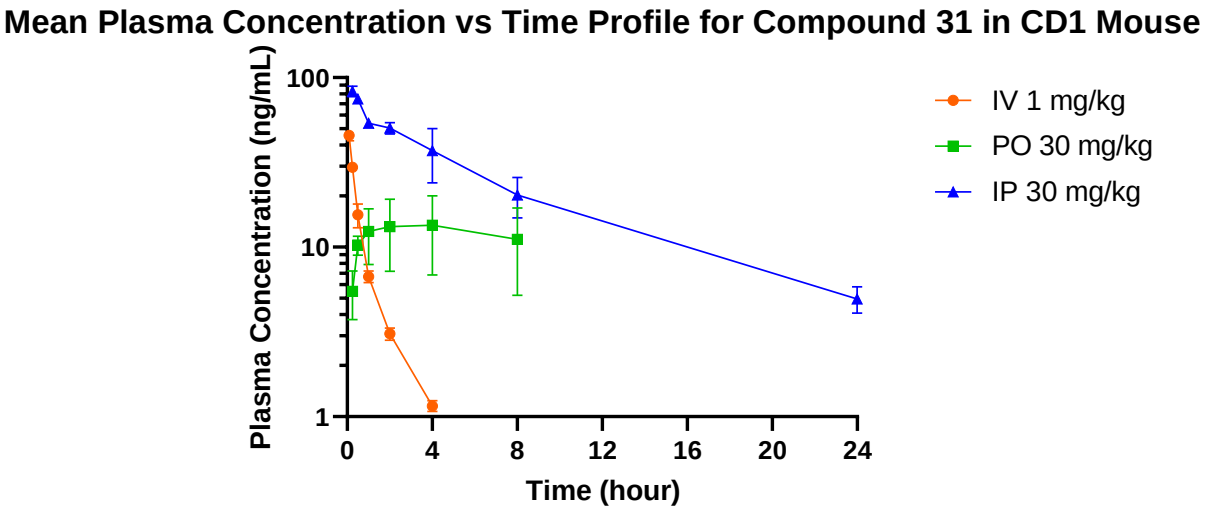

The voltage protocol was run and recorded continuously during the experiment. The stability of recording was assessed through initial wash with bath solution alone. The vehicle (extracellular solution + 0.3% DMSO and 0.05% Pluronic F-68) was then applied for 3 minutes followed by the test substance. The test substance was applied in triplicate to ensure adequate mixing. The standard combined exposure time was 5 minutes. If the quality of the recording deteriorates, then the experiment may be finished at that point and cell data was not analyzed and reported. Each test substance was tested in at least 2 cells. Finally, to verify and confirm assay quality, the hERG pharmacological standard E-4031 was tested at 5 concentrations (0.003, 0.011, 0.033, 0.1, and 0.3 µM) at least in duplicate, as a positive control.

The average of tail current amplitude values recorded from 4 sequential voltage pulses will be used to calculate for each cell the effect of the test substance by calculating the residual current (% control) compared with vehicle pre-treatment. The data was plotted and an $IC_{50}$ value was estimated from the

concentration-response relationship, if appropriate. If a test compound blocks less than 50% at the maximum concentration, only percentage of block for each tested concentration is reported, rather than an extrapolated $IC_{50}$ value. The computer systems used on this study to acquire and quantify data include QPatch assay software v5.6 (Sophion Biosciences), GraphPad (Prism), and Excel 2010 (Microsoft Office).

**CYP1A2 Inhibition Assay.** CYP1A2 inhibition analysis was performed at Evotec. Recombinant human hepatic CYP450s (baculovirus-insect-cell expression system) expressing the isoform 1A2 were obtained from BD GenTest Corp. Test compounds were received in DMSO at a concentration of 10 mM. Probe substrate was formulated in DMF. 3-cyano-7-ethoxycoumarin (CEC) was used as a probe substrate. Furafylline was used as a control inhibitor. The following buffers were prepared: 0.5 M filtered potassium phosphate and 1 M magnesium chloride. Test compounds were pre-dissolved in 10% DMSO and aliquots transferred to individual wells containing phosphate buffer (0.1 M final concentration) and probe substrate. Final concentration of DMSO in the incubations was < 1%. A source of reducing equivalents was added containing glucose-6-phosphate dehydrogenase (1 unit/mL), glucose-6-phoshate (7.9 mM), and NADP (3mM). Magnesium chloride was added to each well to a final concentration of 7.5 mM. CEC was added to a final concentration of 0.01 mM. Protein concentration for CYP1A2 was 26 µg/mL. For the determination of $IC_{50}$, the final concentrations of test compounds ranged from 0.023 to 50 µM (3-fold dilution, 8-concentration ranges). Control incubations contained furafylline in place of test compounds. Positive and negative controls representing minimum and maximum probe substrate degradation contained known inhibitor at high concentration or 10% DMSO, respectively. After a 5 minute pre-incubation, the reactions were initiated by addition of protein. After the appropriate incubation time, fluorescence was measured using a plate reader at the following wavelengths: excitation – 390 nm, emission – 455 nm. Fluorescence values obtained at each concentration of test compound were converted to percent inhibition based on positive and negative controls. Calculation of $IC_{50}$, where required, was from fitting a 4-parameter logistic equation. Where $IC_{50}$ is greater than that of top concentration (50 µM), data is reported as > 50 µM. $IC_{50}$ determined for control inhibitors were compared with historic and literature values to ensure assay functionality. Control compounds were compared with historic and literature values to ensure assay functionality.

**In Vivo Pharmacokinetic Study.** Pharmacokinetic analysis was performed at Pharmaron. Male CD1 mice were treated with a single dose administered intravenously (1 mg/kg, n = 3), orally (30 mg/kg, n = 3), or intraperitoneally (30 mg/kg, n = 3) and blood samples were taken at timepoints 0, 0.083, 0.25, 0.5, 1, 2, 4, 8, and 24 h for IV; 0, 0.25, 0.5, 1, 2, 4, 8, and 24 h for PO and IP. IV compound was formulated in 30% dimethylacetamide (DMA) + 10% polyethylene glycol 200 (PEG200) + 5% Kolliphor ELP in Milli-Q water. PO and IP compound was formulated in 0.2 M phosphate buffer, pH 6.8.




**Microsomal Stability Assay.** A mixture of mouse liver microsomes (0.5 mg/mL protein) and test compound (1 µM) was preincubated at 37°C for 5 min, then NADPH was added to the mixture. The time course (0 to 45 min) concentration of the test compound was determined by LC-MS/MS. Time (minutes) is plotted against the natural logarithm of the percent compound remaining to determine the slope. Apparent intrinsic clearance was determined from the slope ($min^{-1}$), the volume of incubation (mL), and the amount of protein (mg). Apparent intrinsic clearance values are expressed as µL/min/mg protein.

$$t_{\frac{1}{2}} = \frac{Ln(2)}{Slope} \quad (1)$$

$$Cl_{int,app} = \frac{Ln(2)}{t_{\frac{1}{2}}} \times \frac{Vol.incubation}{Amount\ of\ protein} \quad (2)$$

**Hepatocyte Stability Assay.** A mixture of cryopreserved rat hepatocytes (1 million cells/mL) and test compound (1 µM) was incubated at 37°C for 2 h. The time course (0 to 2 h) concentration of the test compound was determined by LC-MS/MS. Time (minutes) is plotted against the natural logarithm of the percent compound remaining to determine the slope. Apparent intrinsic clearance was determined from the slope ($min^{-1}$), the volume of incubation (mL), and the number of cells (million cells). Apparent intrinsic clearance values are expressed as µL/min/million cells. A scaling factor of 6.5 was applied to apparent intrinsic clearance values to provide scaled intrinsic clearance. Scaled intrinsic clearance values are expressed as mL/min/kg.

$$t_{\frac{1}{2}} = \frac{Ln(2)}{Slope} \quad (1)$$

$$Cl_{int,app} = \frac{Ln(2)}{t_{\frac{1}{2}}} \times \frac{Vol.incubation}{Number\ of\ cells} \quad (3)$$

**Cell Viability Assay.** Cell viability analysis was performed at Evotec. A375 cells were plated in 384-well plates at a density of 800 cells/well and incubated for 3 days with the compounds at 37 °C in 5% $CO_2$.

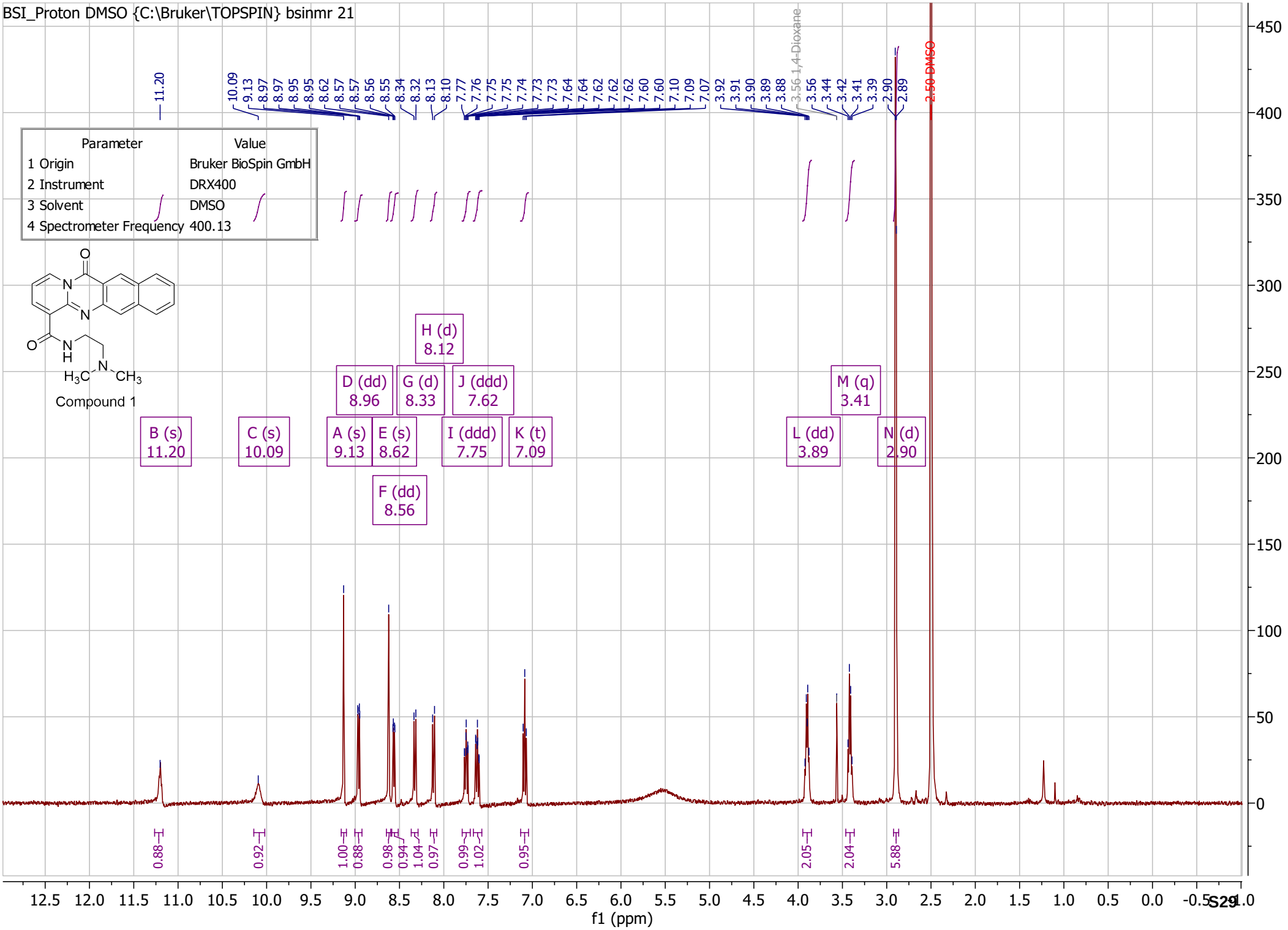
Viability was determined using CellTiter-Glo® Luminescent Cell Viability Assay (Promega). Experiment was reperformed to provide at least 3 replicates.

**RNA Isolation and qPCR.** A375 cells were treated with the compounds (1 µM) for 6 hours, collected by scraping, and pelleted by centrifugation. RNA was isolated using Qiagen RNeasy kit. Total RNA (4 µg) was reverse transcribed and used to perform qPCR in triplicate with SYBR GREEN master mix (Fisher Scientific) on ABI QuantStudio 12K Flex System using primer pairs:

| GENE | F= forward; R = Reverse | Primer sequence 5' – 3' |
|---|---|---|
| GAPDH | F | ACCCAGAAGACTGTGGATGG |
| | R | TTCAGCTCAGGGATGACCTT |
| 5'ETS851 | F | GAACGGTGGTGTGTCGTT |
| | R | GCGTCTCGTCTCGTCTCACT |
| DHFR | F | GCTGCTGTCATGGTTGGTTC |
| | R | AGAGGTTGTGGTCATTCTCTGG |
| tRNA Valine | F | TCCGTAGTGTAGTGGTTATCACG |
| | R | GTTTCGAACCGGGGACCT |

Transcript quantification was measured by ΔΔCt method. All results were normalized against GAPDH, and coefficient of variation was calculated. The experiment was conducted using three biological repeats in triplicate.

**Statistical Analysis**. Values were calculated and statistical significance was assessed using ordinary one-way ANOVA in GraphPad Prism 9.3.1.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I (ddd) 7.75
J (ddd) 7.62
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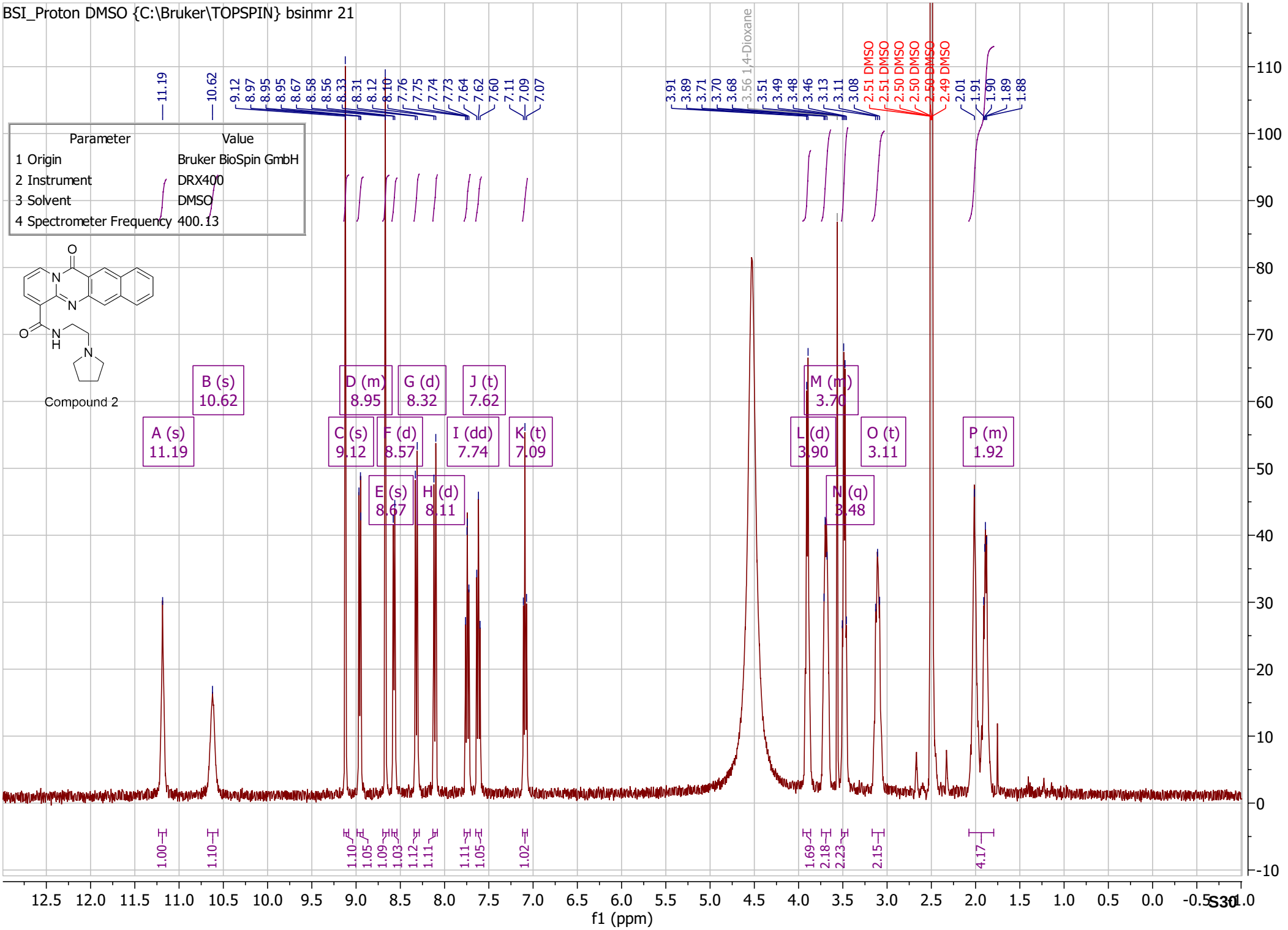
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C (s) 9.12
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E (s) 8.67
F (d) 8.57
G (d) 8.32
H (d) 8.11
I (dd) 7.74
J (t) 7.62
K (t) 7.09
L (d) 3.90
M (m) 3.70
N (q) 3.48
O (t) 3.11
P (m) 1.92
1.4-Dioxane
DMSO
f1 (ppm)
S30

# LI-E02-150-1

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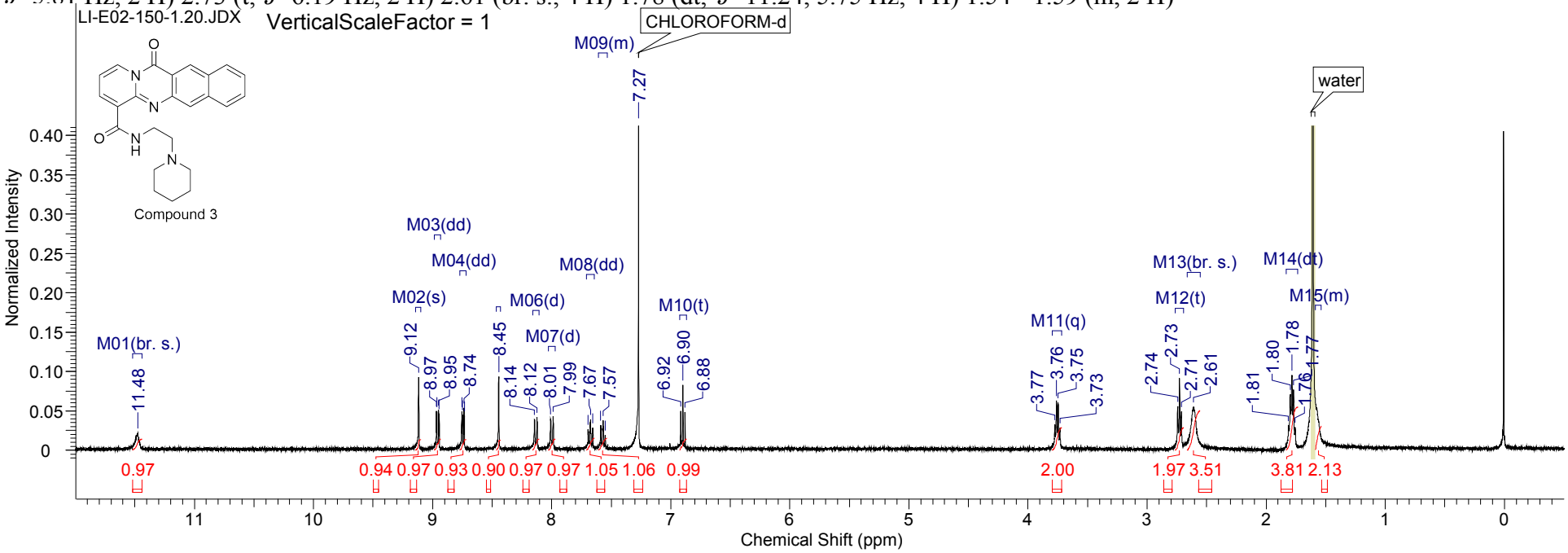
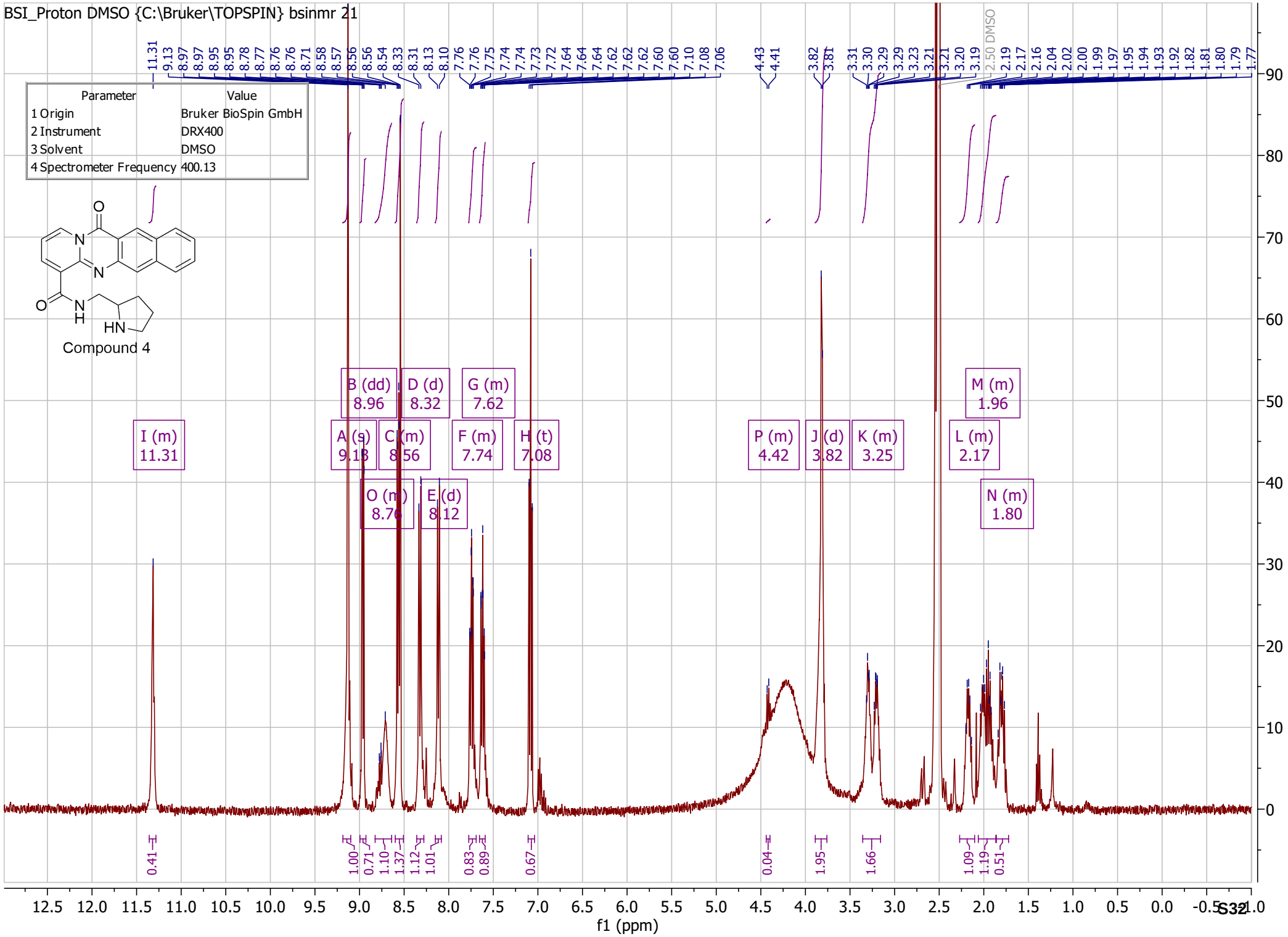
| ***Temperature (degree C)*** | 21.160 | | | | | | |

$^{1}$H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 11.48 (br. s., 1 H) 9.12 (s, 1 H) 8.96 (dd, *J*=7.33, 1.77 Hz, 1 H) 8.74 (dd, *J*=6.95, 1.64 Hz, 1 H) 8.44 (s, 1 H) 8.13 (d, *J*=8.34 Hz, 1 H) 8.00 (d, *J*=8.34 Hz, 1 H) 7.68 (dd, *J*=8.08, 7.07 Hz, 1 H) 7.53 - 7.61 (m, 1 H) 6.90 (t, *J*=7.07 Hz, 1 H) 3.75 (q, *J*=5.81 Hz, 2 H) 2.73 (t, *J*=6.19 Hz, 2 H) 2.61 (br. s., 4 H) 1.78 (dt, *J*=11.24, 5.75 Hz, 4 H) 1.54 - 1.59 (m, 2 H)

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G (m) 7.62
H (t) 7.08
O (m) 8.76
P (m) 4.42
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K (m) 3.25
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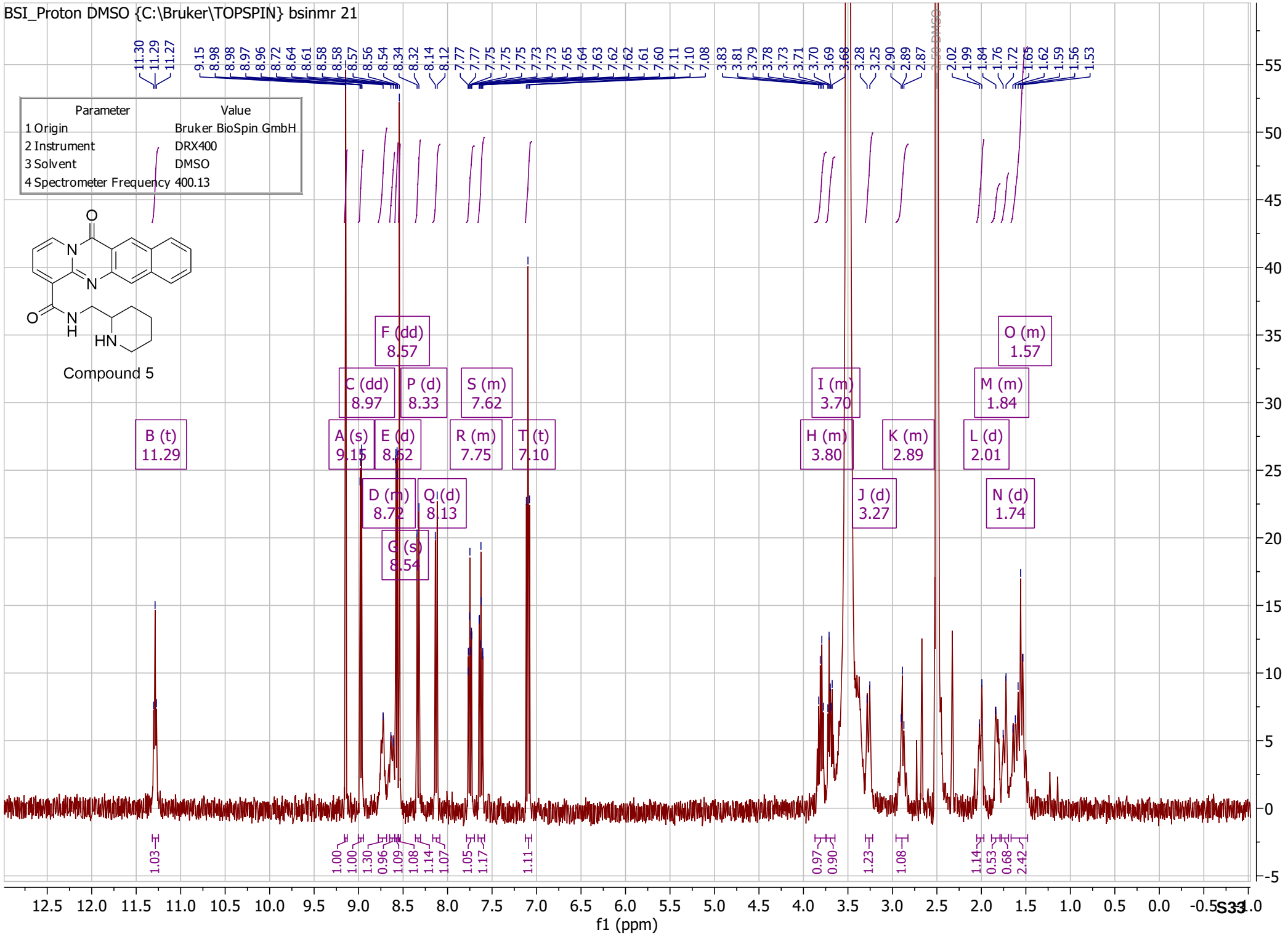
2.50 DMSO
f1 (ppm)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O (m) 1.57
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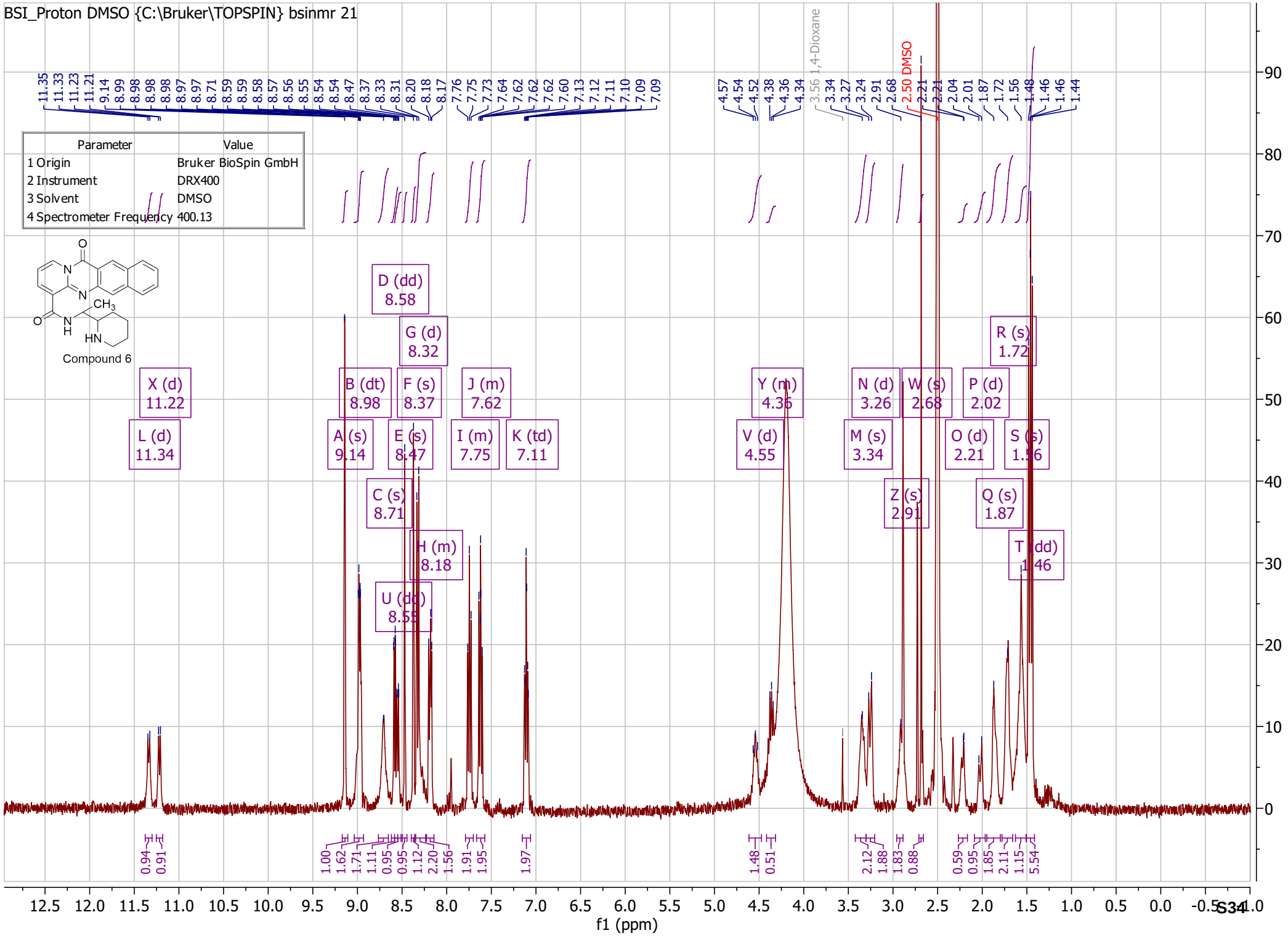
f1 (ppm)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K (td) 7.11
D (dd) 8.58
G (d) 8.32
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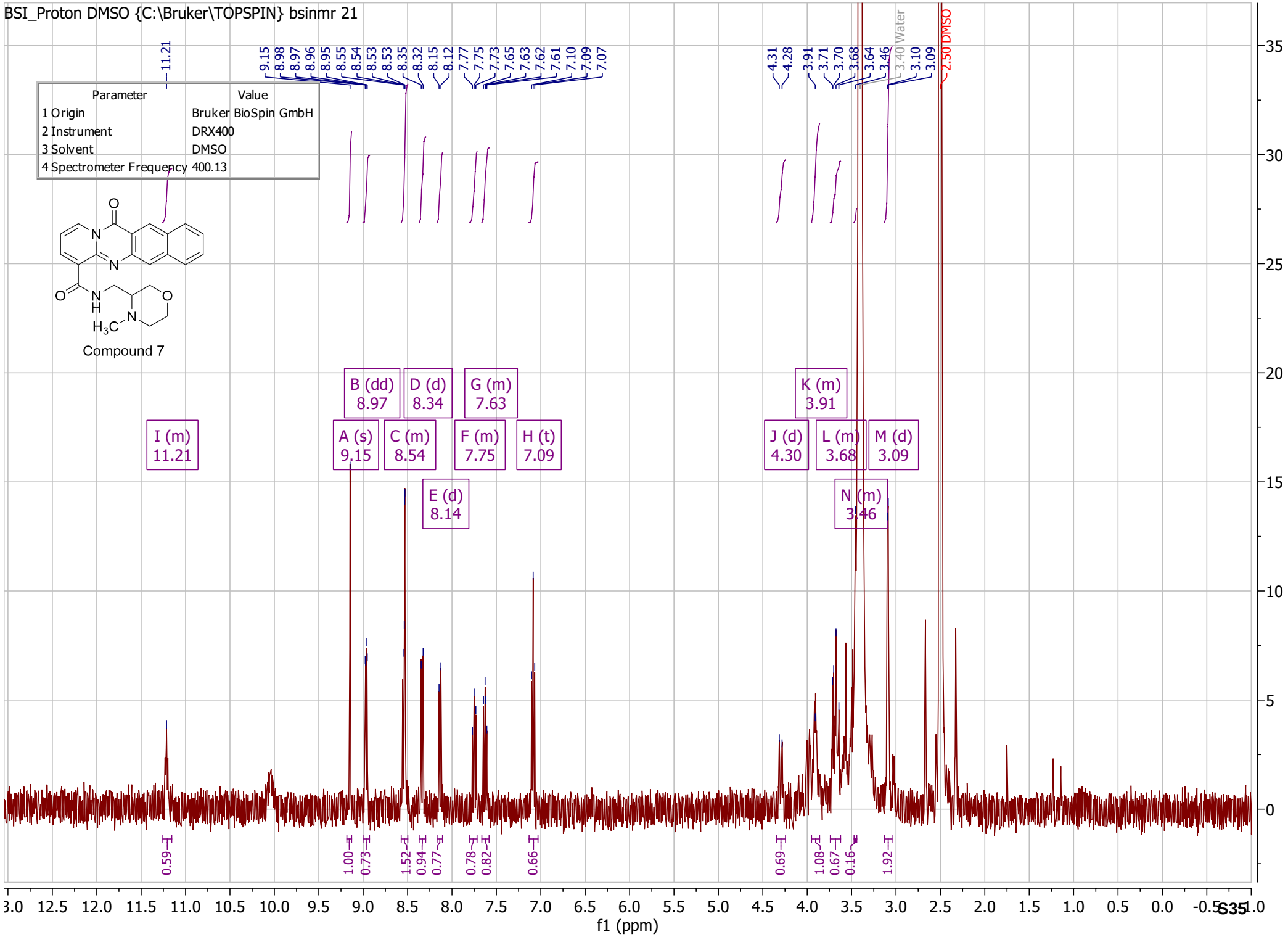
f1 (ppm)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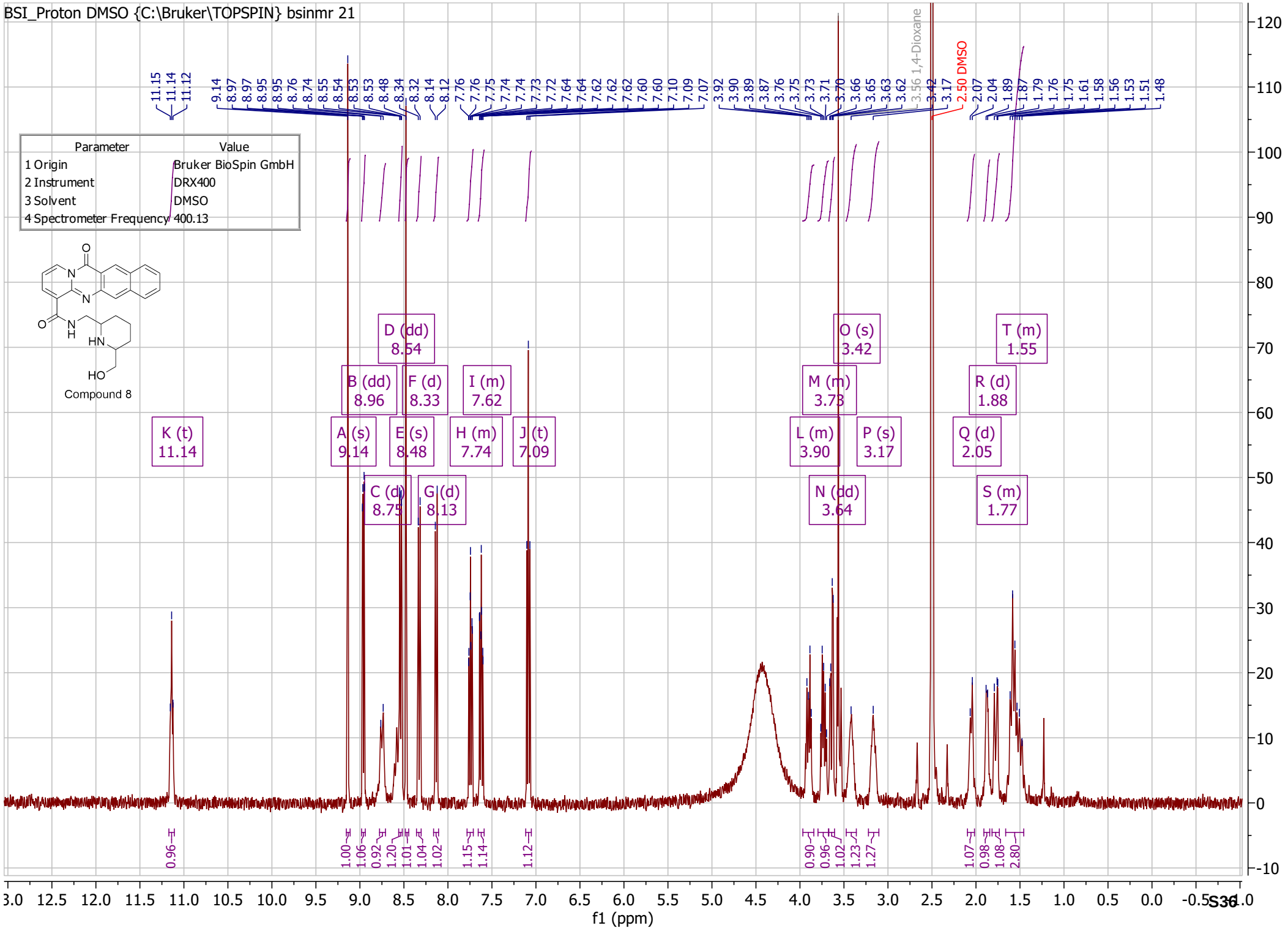
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DMSO
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D (dd) 8.54
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F (d) 8.33
G (d) 8.13
H (m) 7.74
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J (t) 7.09
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M (m) 3.73
N (dd) 3.64
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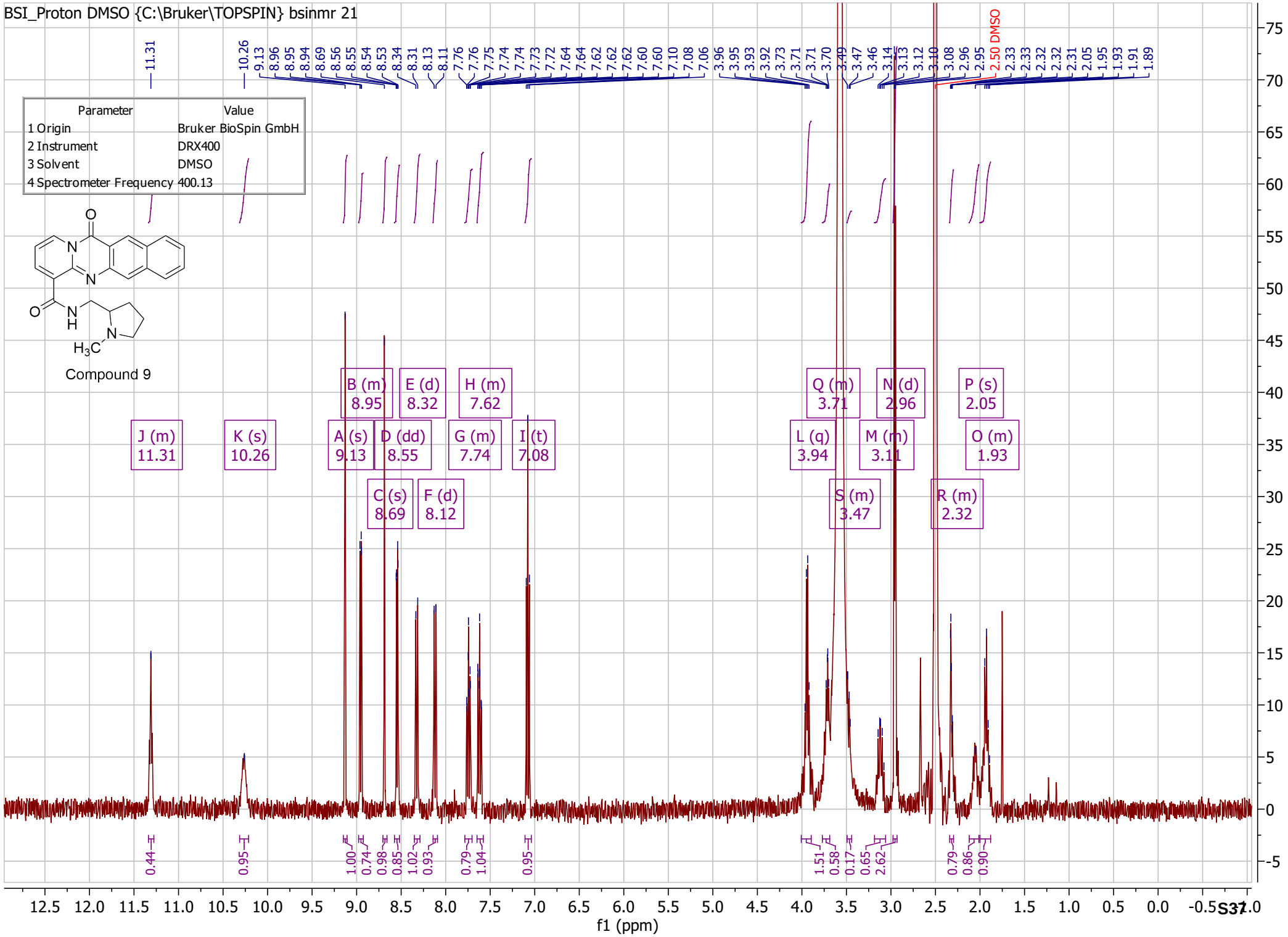
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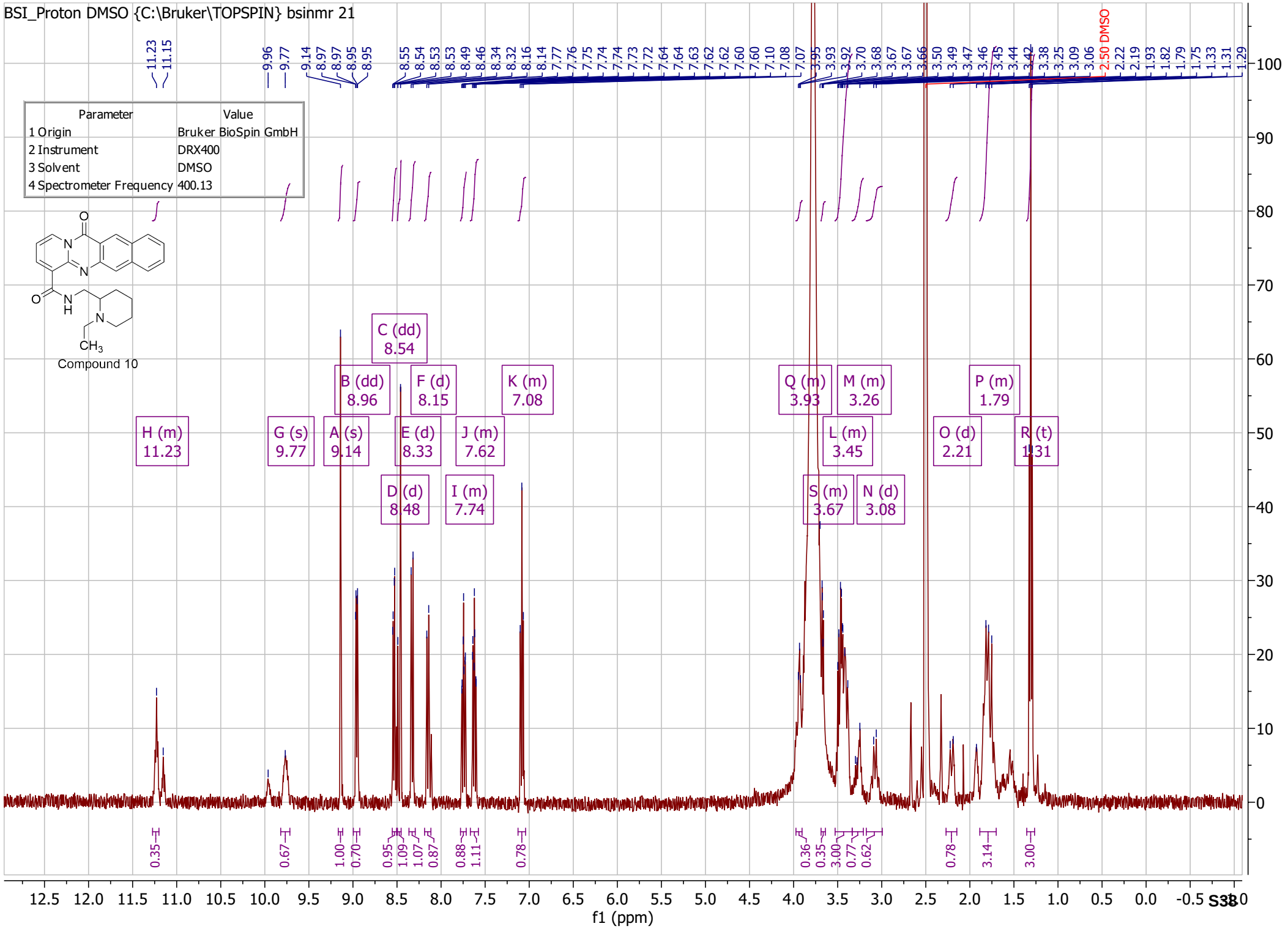
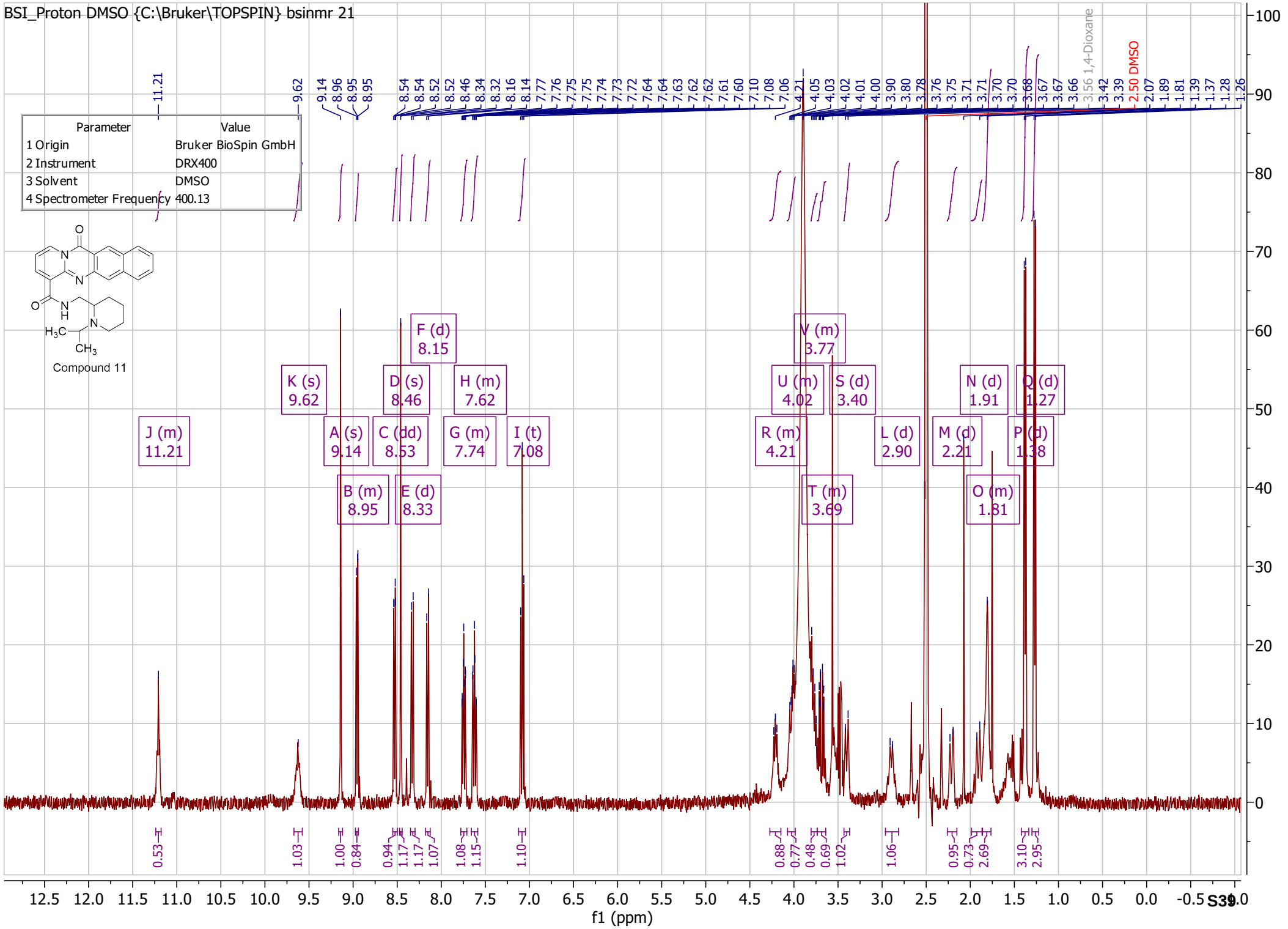
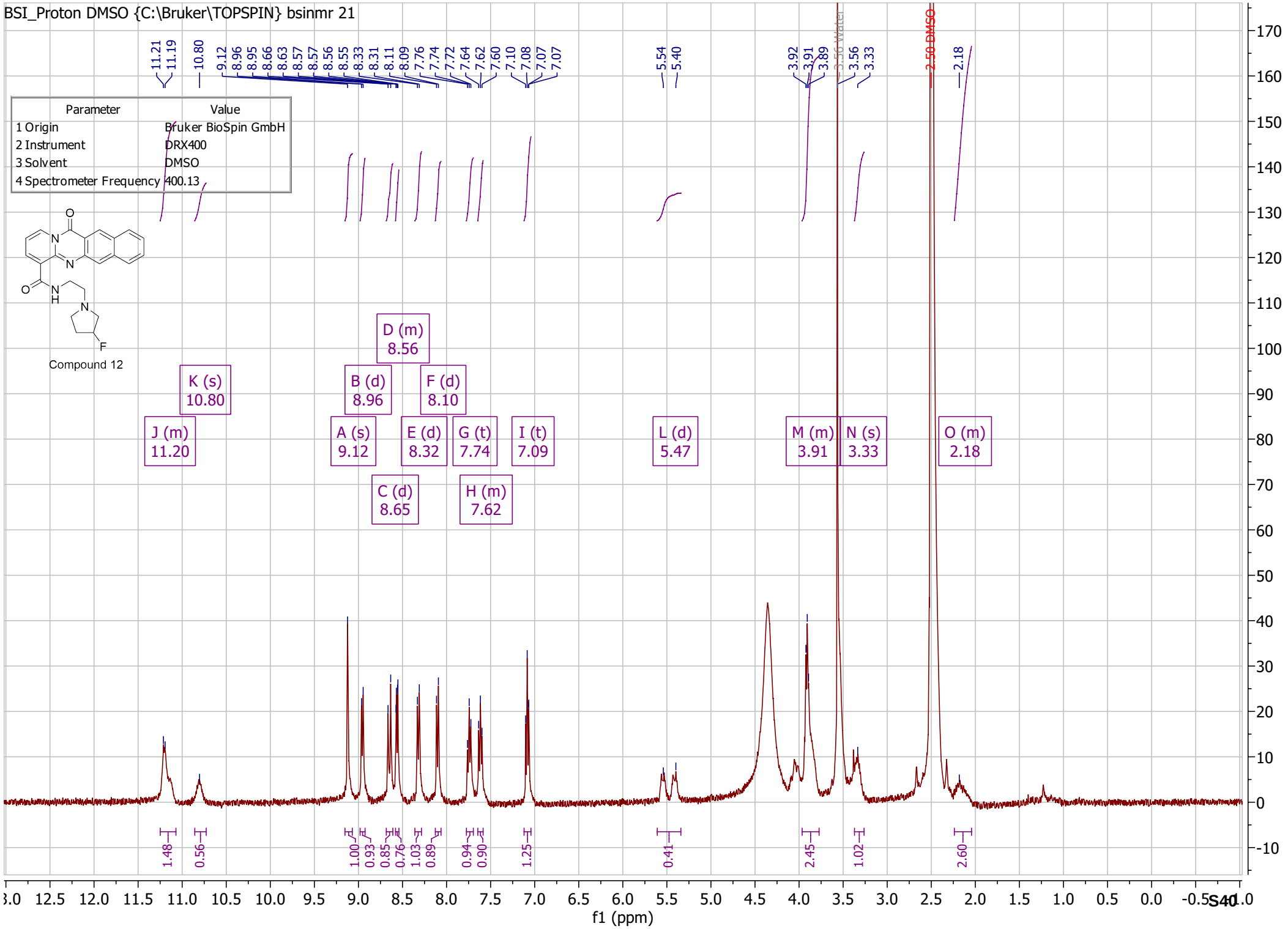
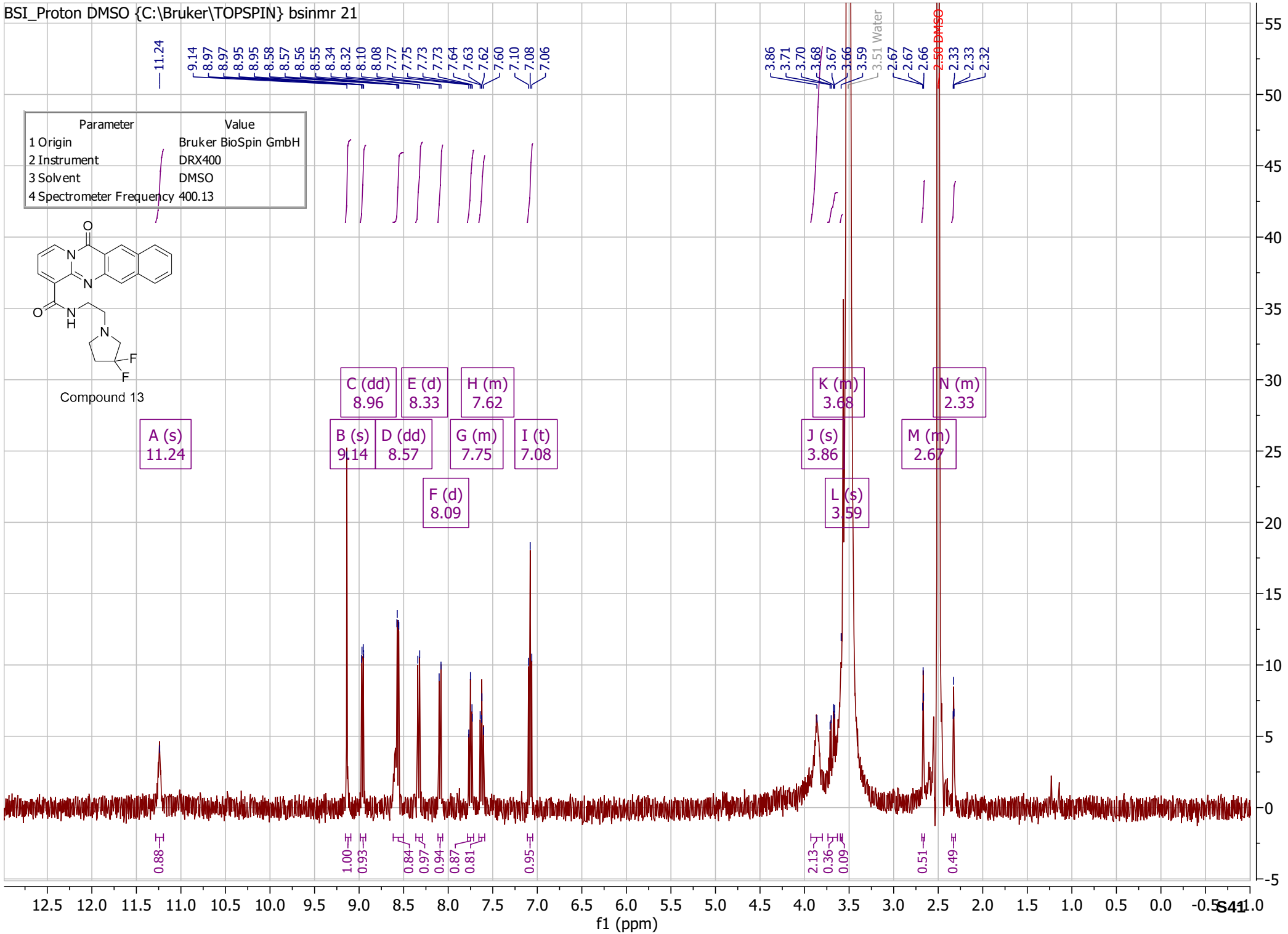
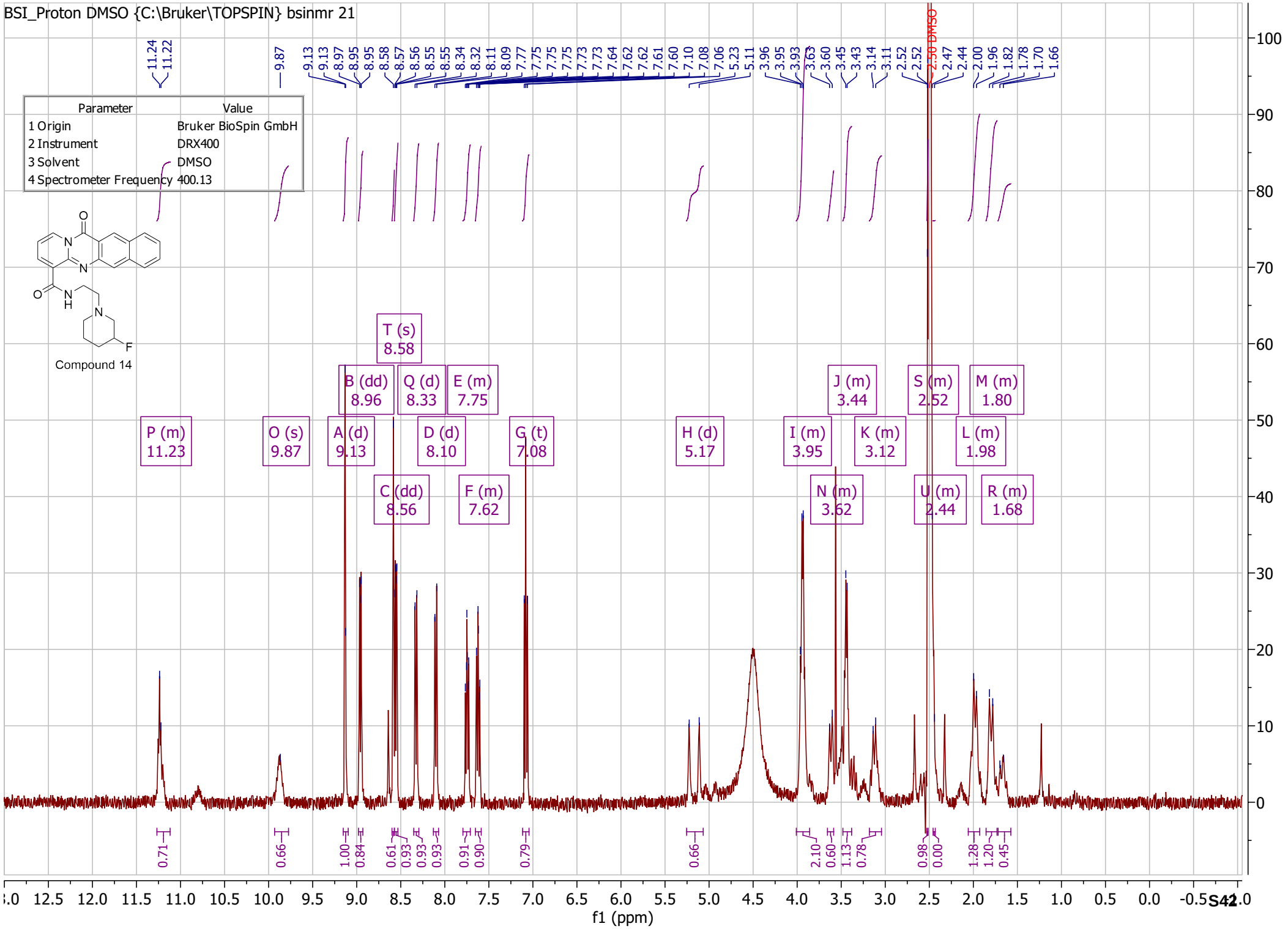
F (d) 8.12
G (m) 7.74
H (m) 7.62
I (t) 7.08
L (q) 3.94
M (m) 3.11
N (d) 2.96
O (m) 1.93
P (s) 2.05
Q (m) 3.71
R (m) 2.32
S (m) 3.47
2.50 DMSO
f1 (ppm)


BSI_Proton DMSO {C:\Bruker\TOPSPIN} bsinmr 21
Parameter | Value
1 Origin | Bruker BioSpin GmbH
2 Instrument | DRX400
3 Solvent | DMSO
4 Spectrometer Frequency | 400.13
Compound 10
H (m) 11.23
G (s) 9.77
A (s) 9.14
B (dd) 8.96
C (dd) 8.54
D (d) 8.48
E (d) 8.33
F (d) 8.15
I (m) 7.74
J (m) 7.62
K (m) 7.08
Q (m) 3.93
S (m) 3.67
M (m) 3.26
L (m) 3.45
N (d) 3.08
O (d) 2.21
P (m) 1.79
R (t) 1.31
2.50 DMSO
f1 (ppm)

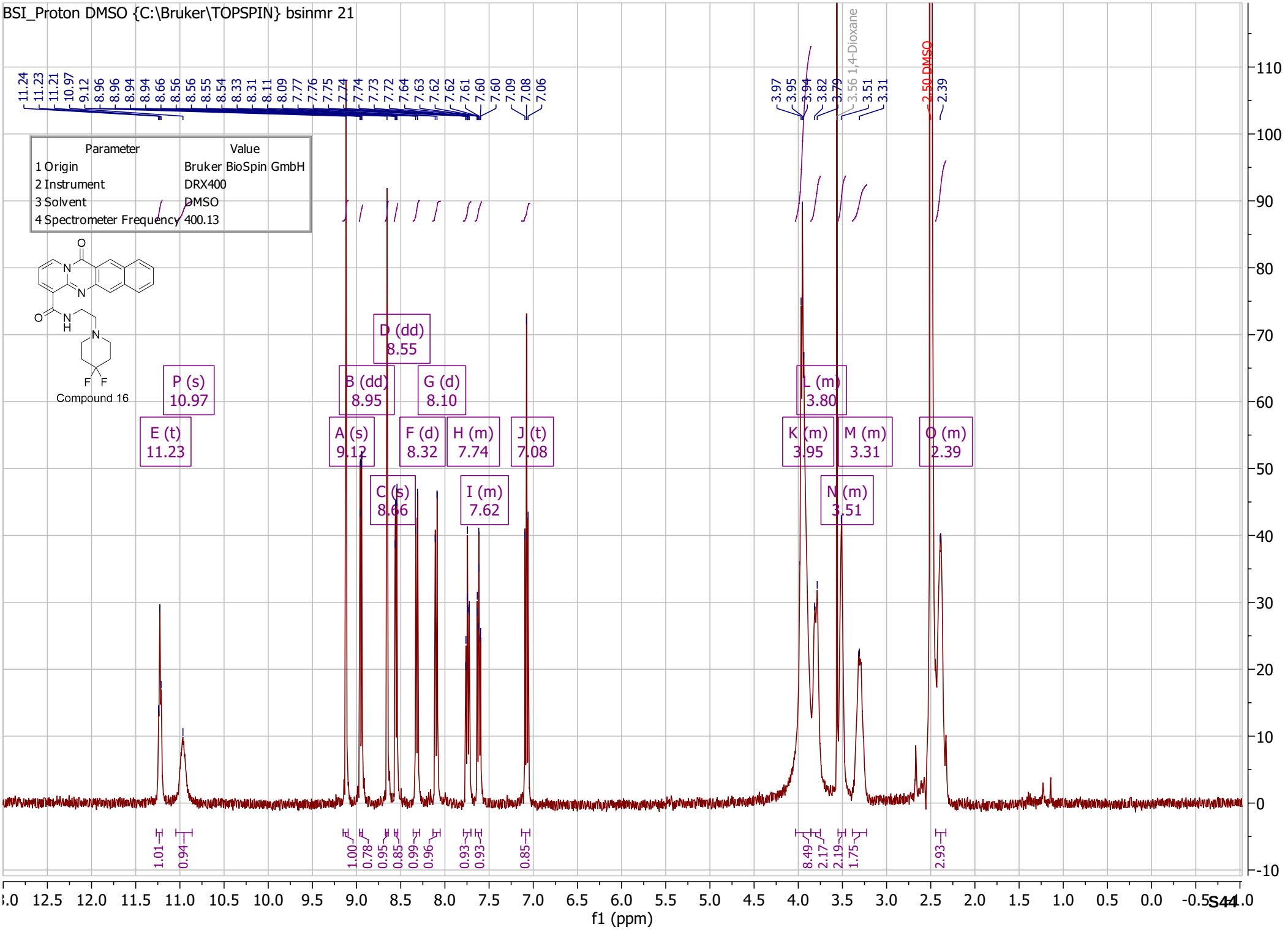

BSI_Proton DMSO {C:\Bruker\TOPSPIN} bsinmr 21
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Instrument DRX400
3 Solvent DMSO
4 Spectrometer Frequency 400.13
Compound 11
J (m) 11.21
K (s) 9.62
A (s) 9.14
B (m) 8.95
C (dd) 8.53
D (s) 8.46
E (d) 8.33
F (d) 8.15
G (m) 7.74
H (m) 7.62
I (t) 7.08
R (m) 4.21
V (m) 3.77
U (m) 4.02
S (d) 3.40
T (m) 3.69
L (d) 2.90
M (d) 2.21
O (m) 1.81
N (d) 1.91
P (d) 1.38
Q (d) 1.27
1,4-Dioxane
DMSO
f1 (ppm)

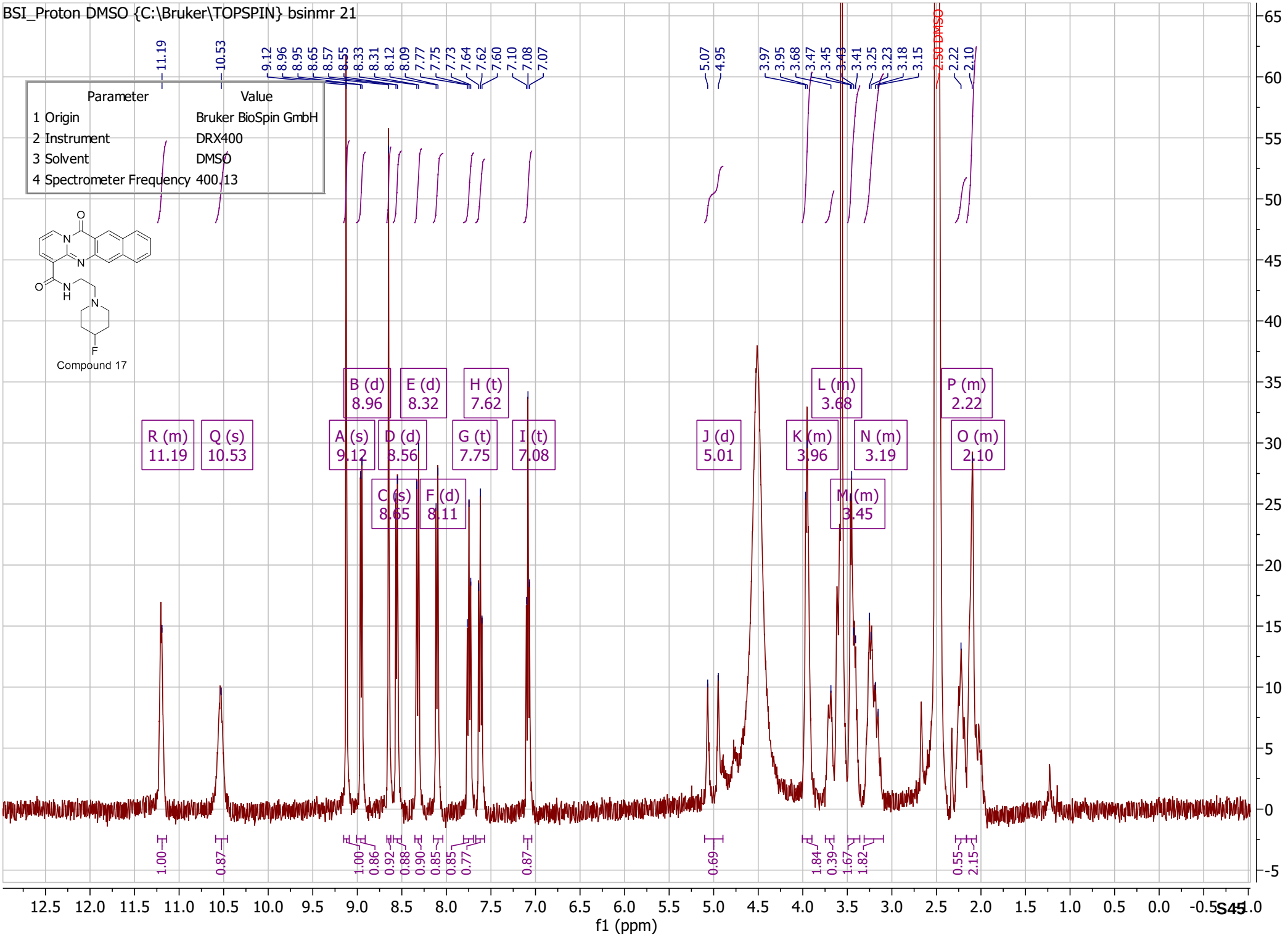

BSI_Proton DMSO {C:\Bruker\TOPSPIN} bsinmr 21
Parameter | Value
1 Origin | Bruker BioSpin GmbH
2 Instrument | DRX400
3 Solvent | DMSO
4 Spectrometer Frequency | 400.13
Compound 12
K (s) 10.80
J (m) 11.20
D (m) 8.56
B (d) 8.96
F (d) 8.10
A (s) 9.12
E (d) 8.32
G (t) 7.74
I (t) 7.09
C (d) 8.65
H (m) 7.62
L (d) 5.47
M (m) 3.91
N (s) 3.33
O (m) 2.18
2.50 DMSO
3.56 Water
f1 (ppm)

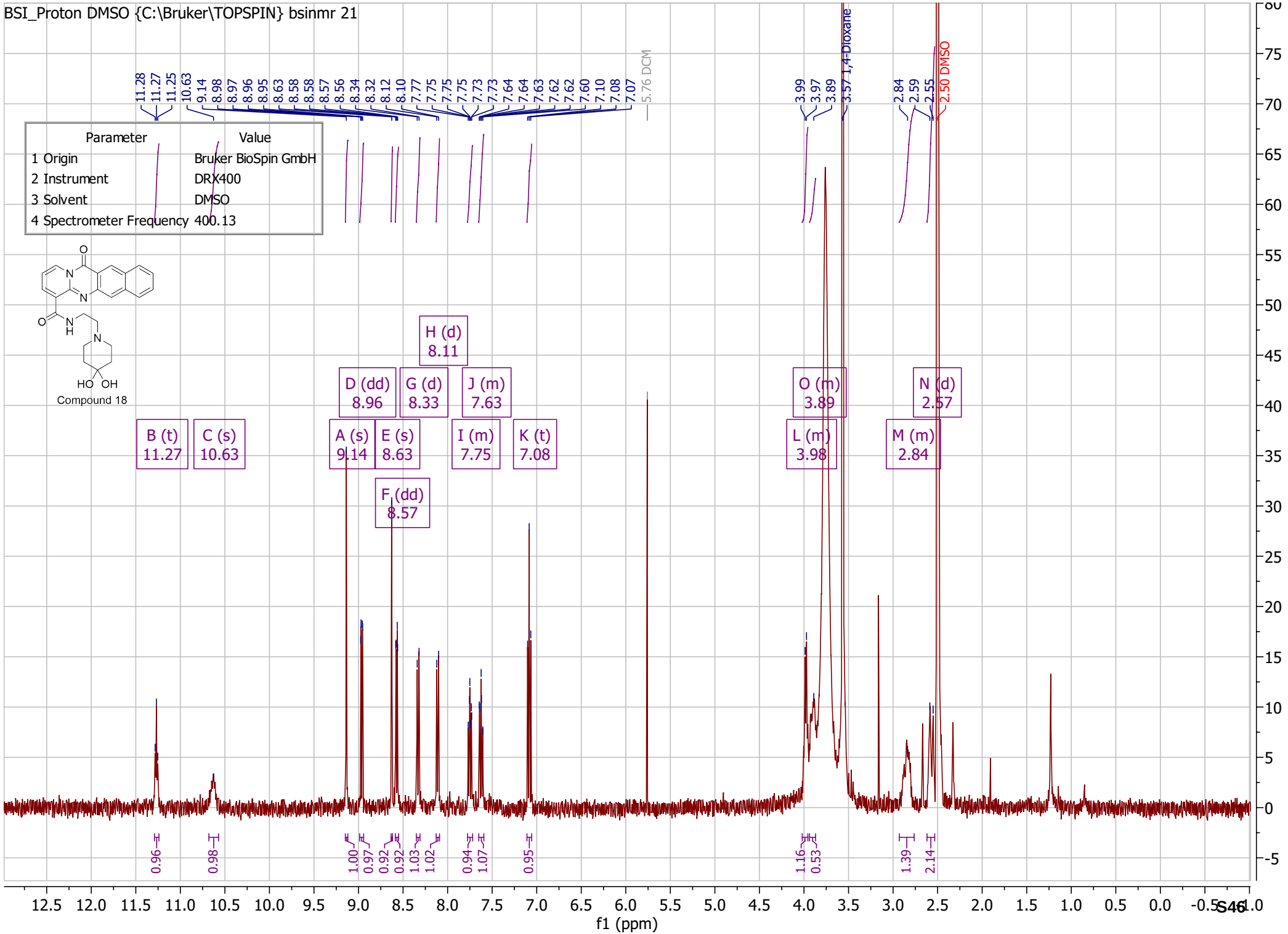

BSI_Proton DMSO {C:\Bruker\TOPSPIN} bsinmr 21
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Instrument DRX400
3 Solvent DMSO
4 Spectrometer Frequency 400.13
Compound 13
A (s) 11.24
B (s) 9.14
C (dd) 8.96
D (dd) 8.57
E (d) 8.33
F (d) 8.09
G (m) 7.75
H (m) 7.62
I (t) 7.08
J (s) 3.86
K (m) 3.68
L (s) 3.59
M (m) 2.67
N (m) 2.33
3.51 Water
2.50 DMSO
f1 (ppm)


BSI_Proton DMSO {C:\Bruker\TOPSPIN} bsinmr 21
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Instrument DRX400
3 Solvent DMSO
4 Spectrometer Frequency 400.13
Compound 14
P (m) 11.23
O (s) 9.87
A (d) 9.13
B (dd) 8.96
C (dd) 8.56
T (s) 8.58
Q (d) 8.33
D (d) 8.10
E (m) 7.75
F (m) 7.62
G (t) 7.08
H (d) 5.17
I (m) 3.95
J (m) 3.44
K (m) 3.12
N (m) 3.62
S (m) 2.52
U (m) 2.44
M (m) 1.80
L (m) 1.98
R (m) 1.68
f1 (ppm)

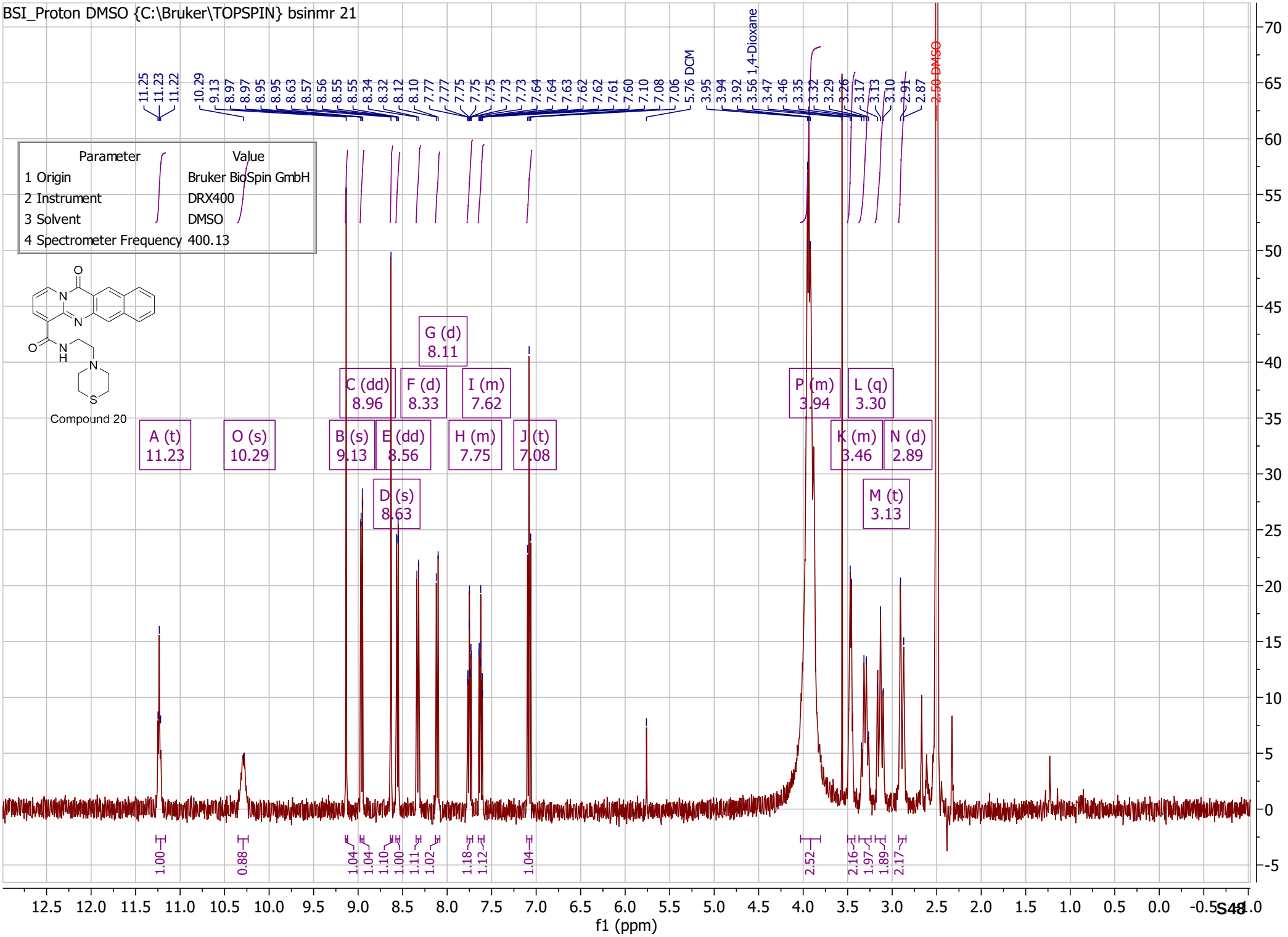

Parameter Value
1 Origin JCB_Tony
2 Instrument spect
3 Solvent MeOD
4 Spectrometer Frequency 499.80
Compound 15
9.07
8.67
8.39
8.18
8.16
8.06
8.04
7.72
7.71
7.69
7.62
7.60
7.59
7.09
4.87 Water
4.06
4.05
4.04
3.94
3.67
3.66
3.64
3.54
3.31 MeOD
2.25
2.16
2.15
2.14
G (m) 9.07
F (m) 8.67
A (s) 8.39
B (d) 8.17
C (d) 8.05
D (t) 7.71
E (t) 7.60
N (m) 7.09
H (t) 4.05
M (m) 3.94
L (m) 3.54
I (t) 3.66
K (m) 2.25
J (m) 2.15
1.07
0.92
1.00
0.99
1.00
1.04
1.08
1.06
2.17
4.97
2.11
2.44
2.88
2.17
f1 (ppm)

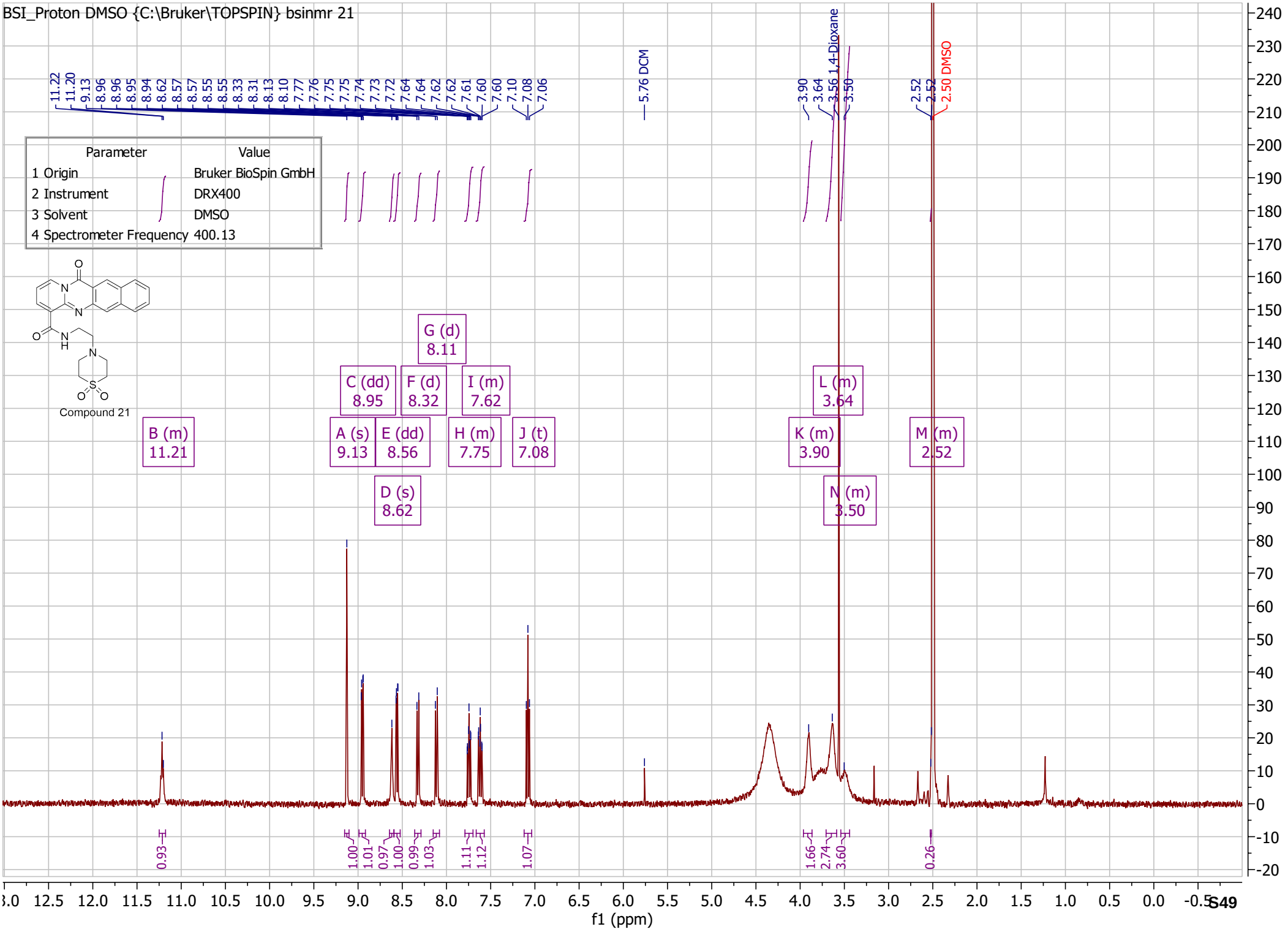

BSI_Proton DMSO {C:\Bruker\TOPSPIN} bsinmr 21
11.24
11.23
11.21
10.97
9.12
8.96
8.96
8.94
8.94
8.66
8.56
8.56
8.55
8.54
8.33
8.31
8.11
8.09
7.77
7.76
7.75
7.74
7.74
7.73
7.72
7.64
7.63
7.62
7.62
7.61
7.60
7.60
7.09
7.08
7.06
3.97
3.95
3.94
3.82
3.79
3.56 1,4-Dioxane
3.51
3.31
2.50 DMSO
2.39
Parameter
Value
1 Origin
Bruker BioSpin GmbH
2 Instrument
DRX400
3 Solvent
DMSO
4 Spectrometer Frequency
400.13
Compound 16
P (s)
10.97
E (t)
11.23
D (dd)
8.55
B (dd)
8.95
G (d)
8.10
A (s)
9.12
F (d)
8.32
H (m)
7.74
J (t)
7.08
C (s)
8.66
I (m)
7.62
L (m)
3.80
K (m)
3.95
M (m)
3.31
O (m)
2.39
N (m)
3.51
1.01
0.94
1.00
0.78
0.95
0.85
0.99
0.96
0.93
0.93
0.85
8.49
2.17
2.19
1.75
2.93
f1 (ppm)
S44


BSI_Proton DMSO {C:\Bruker\TOPSPIN} bsinmr 21
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Instrument DRX400
3 Solvent DMSO
4 Spectrometer Frequency 400.13
Compound 17
R (m) 11.19
Q (s) 10.53
A (s) 9.12
B (d) 8.96
C (s) 8.65
D (d) 8.56
E (d) 8.32
F (d) 8.11
G (t) 7.75
H (t) 7.62
I (t) 7.08
J (d) 5.01
K (m) 3.96
L (m) 3.68
M (m) 3.45
N (m) 3.19
O (m) 2.10
P (m) 2.22
f1 (ppm)


BSI_Proton DMSO {C:\Bruker\TOPSPIN} bsinmr 21
Parameter
Value
1 Origin
Bruker BioSpin GmbH
2 Instrument
DRX400
3 Solvent
DMSO
4 Spectrometer Frequency
400.13
Compound 18
B (t) 11.27
C (s) 10.63
A (s) 9.14
E (s) 8.63
F (dd) 8.57
D (dd) 8.96
G (d) 8.33
H (d) 8.11
I (m) 7.75
J (m) 7.63
K (t) 7.08
L (m) 3.98
O (m) 3.89
M (m) 2.84
N (d) 2.57
5.76 DCM
3.57 1,4-Dioxane
2.50 DMSO
f1 (ppm)

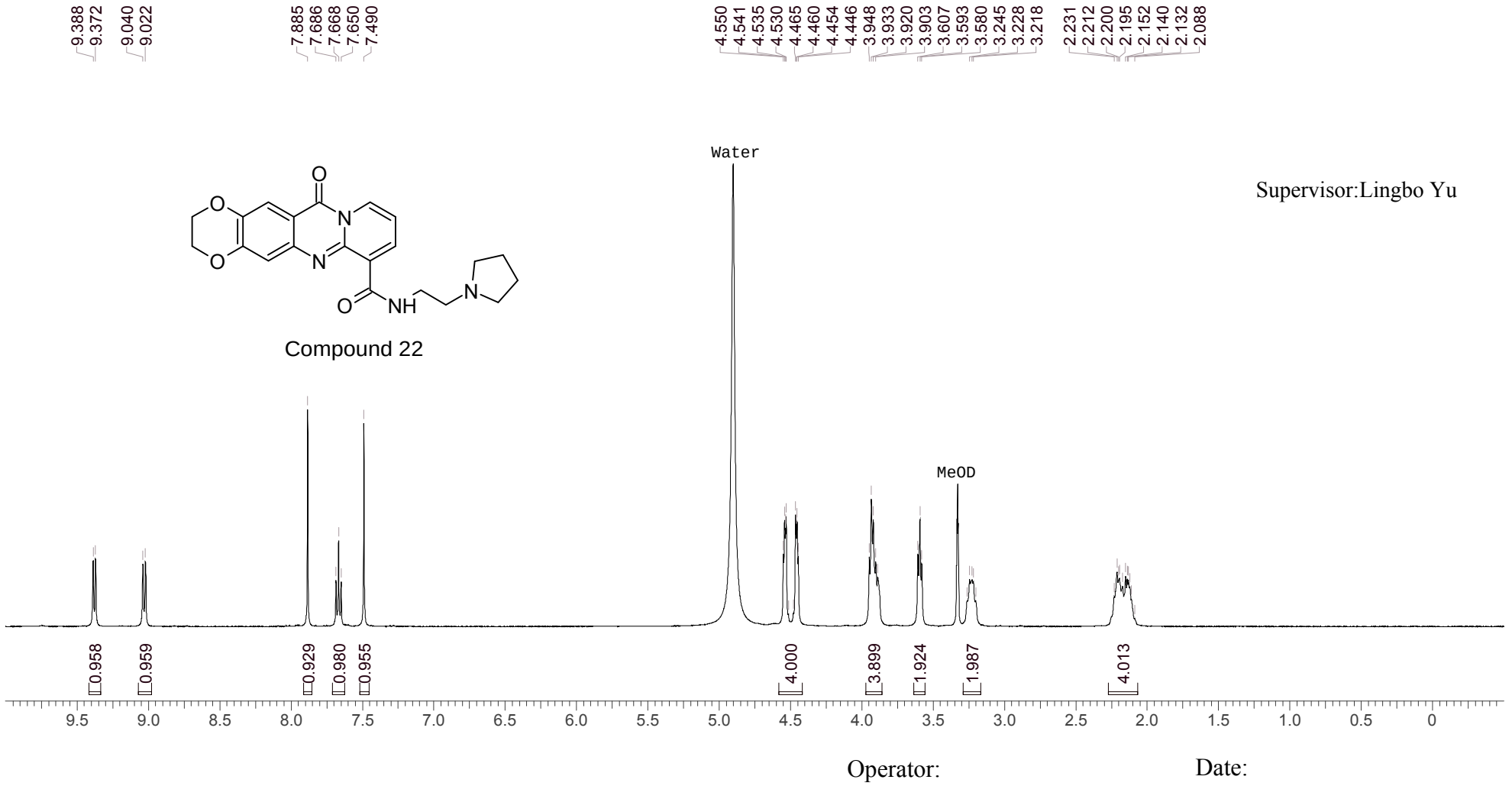

BSI_Proton DMSO {C:\Bruker\TOPSPIN} bsinmr 21
Parameter Value
1 Origin Bruker BioSpin GmbH
2 Instrument DRX400
3 Solvent DMSO
4 Spectrometer Frequency 400.13
Compound 19
J (m) 11.20
K (s) 10.59
A (s) 9.13
B (d) 8.96
C (s) 8.65
D (d) 8.56
E (d) 8.32
F (d) 8.11
G (t) 7.75
H (m) 7.62
I (t) 7.08
L (m) 3.94
M (m) 3.69
N (m) 3.39
O (m) 3.07
P (m) 2.13
Q (m) 2.27
R (m) 3.49
1,4-Dioxane
DCM
DMSO
f1 (ppm)


BSI_Proton DMSO {C:\Bruker\TOPSPIN} bsinmr 21
Parameter
Value
1 Origin
Bruker BioSpin GmbH
2 Instrument
DRX400
3 Solvent
DMSO
4 Spectrometer Frequency
400.13
Compound 20
A (t) 11.23
O (s) 10.29
B (s) 9.13
C (dd) 8.96
D (s) 8.63
E (dd) 8.56
F (d) 8.33
G (d) 8.11
H (m) 7.75
I (m) 7.62
J (t) 7.08
K (m) 3.46
L (q) 3.30
M (t) 3.13
N (d) 2.89
P (m) 3.94
1,4-Dioxane
DCM
DMSO
f1 (ppm)


BSI_Proton DMSO {C:\Bruker\TOPSPIN} bsinmr 21
11.22
11.20
9.13
8.96
8.96
8.95
8.94
8.62
8.57
8.57
8.55
8.55
8.33
8.31
8.13
8.10
7.77
7.76
7.75
7.75
7.74
7.73
7.72
7.64
7.64
7.62
7.62
7.61
7.60
7.60
7.10
7.08
7.06
5.76 DCM
3.90
3.64
3.56 1,4-Dioxane
3.50
2.52
2.52
2.50 DMSO
Parameter
Value
1 Origin
Bruker BioSpin GmbH
2 Instrument
DRX400
3 Solvent
DMSO
4 Spectrometer Frequency
400.13
Compound 21
B (m) 11.21
A (s) 9.13
E (dd) 8.56
D (s) 8.62
C (dd) 8.95
F (d) 8.32
G (d) 8.11
H (m) 7.75
I (m) 7.62
J (t) 7.08
K (m) 3.90
N (m) 3.50
L (m) 3.64
M (m) 2.52
0.93
1.00
1.01
0.97
1.00
0.99
1.03
1.11
1.12
1.07
1.66
2.74
3.60
0.26
f1 (ppm)

**Compound ID: JHU_3la4x**

**ET20498-13-P1A MeOD Bruker_F_400MHz**




Compound 22

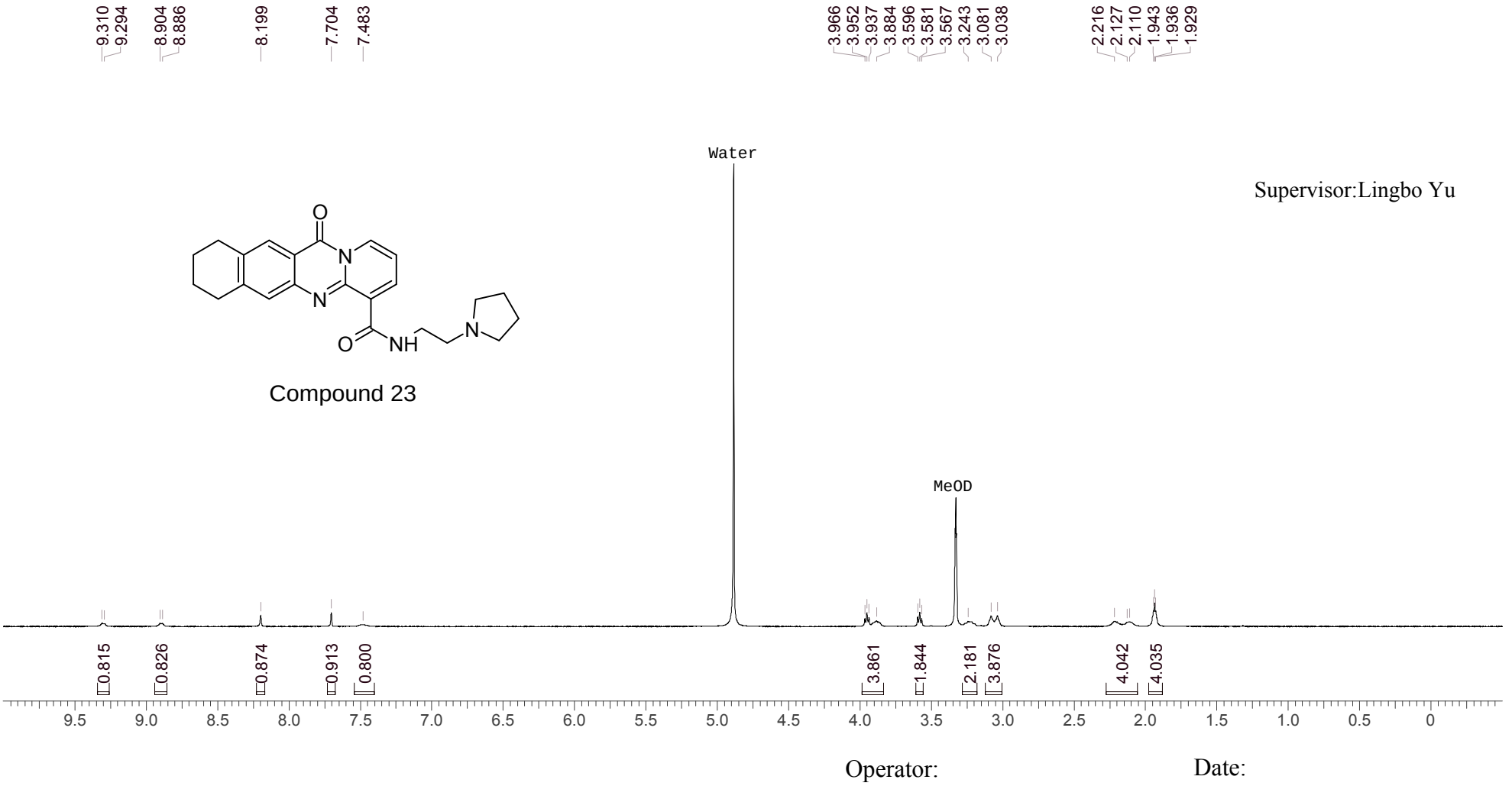
Supervisor:Lingbo Yu

Operator:

Date:

**Compound ID: JHU_3ma4x**

**ET20498-16-P1A MeOD Bruker_F_400MHz**







Compound 23

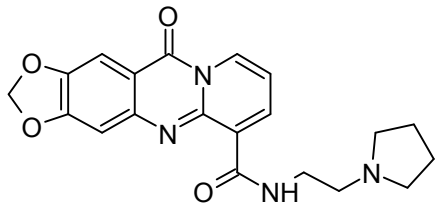
Supervisor:Lingbo Yu

Operator:

Date:

**Compound ID: JHU_3NA4X**

**ET20749-21-P1B DMSO Varian_S_400MHz**



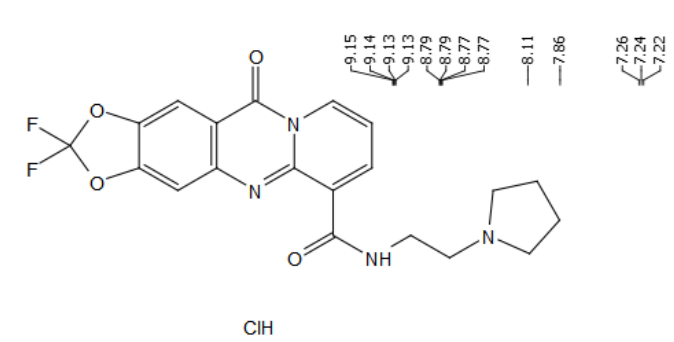
Compound 24




Supervisor:Lingbo Yu

Operator:

Date:

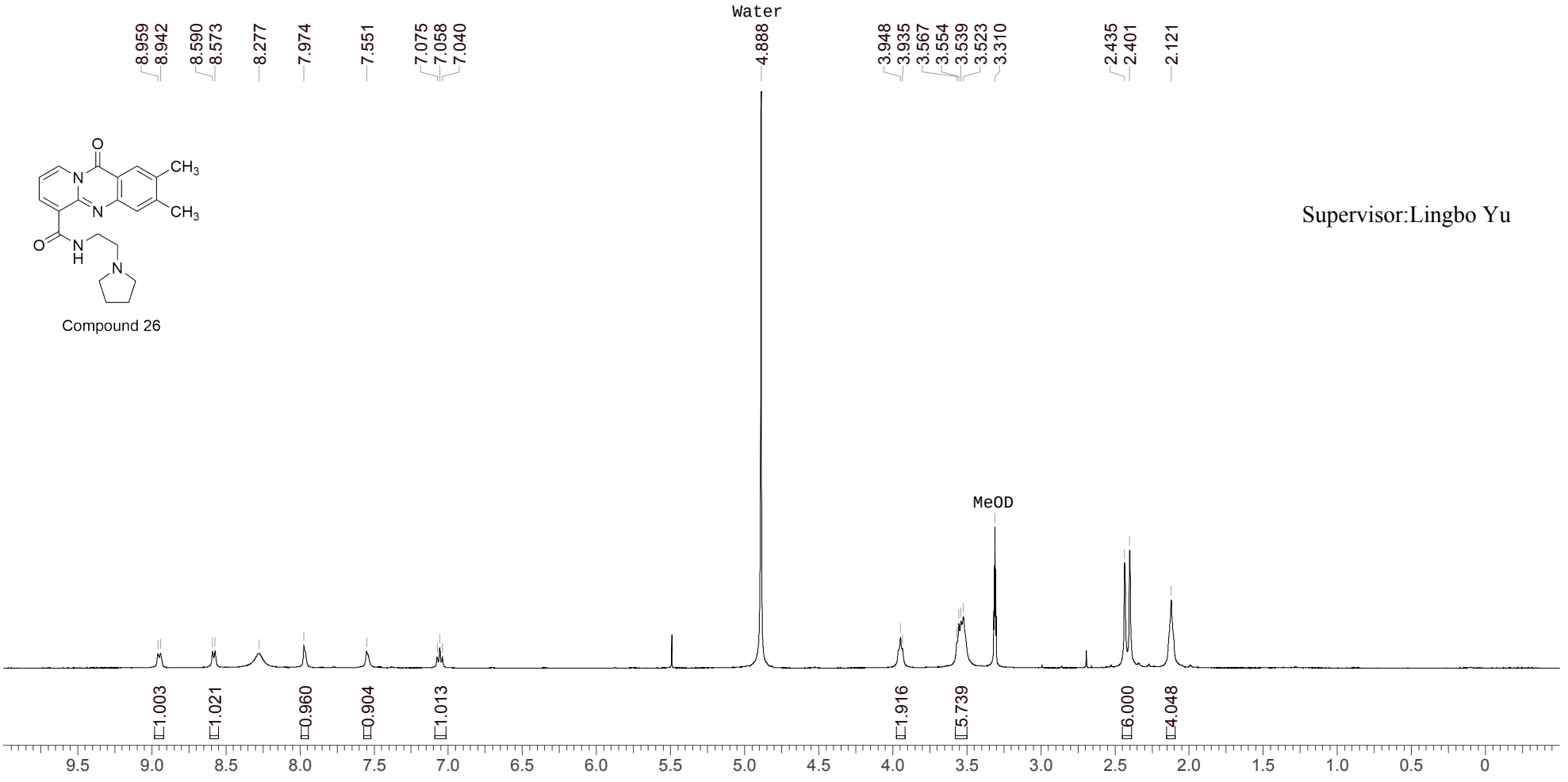



Compound 25

$^1$H NMR (400 MHz, $cd_3od$) δ 9.14 (dd, $J$ = 7.3, 1.7 Hz, 1H), 8.78 (dd, $J$ = 7.1, 1.7 Hz, 1H), 8.11 (s, 1H), 7.86 (s, 1H), 7.24 (t, $J$ = 7.2 Hz, 1H), 3.97 (t, $J$ = 5.9 Hz, 2H), 3.88 – 3.81 (m, 2H), 3.57 (t, $J$ = 5.9 Hz, 2H), 3.25 – 3.17 (m, 2H), 2.26 – 2.15 (m, 2H), 2.10 – 2.00 (m, 2H).

**Compound ID:JHU_3ia4x**

**ET19349-33-P1D1 MeOD Bruker_C_400MHz**




Compound 26

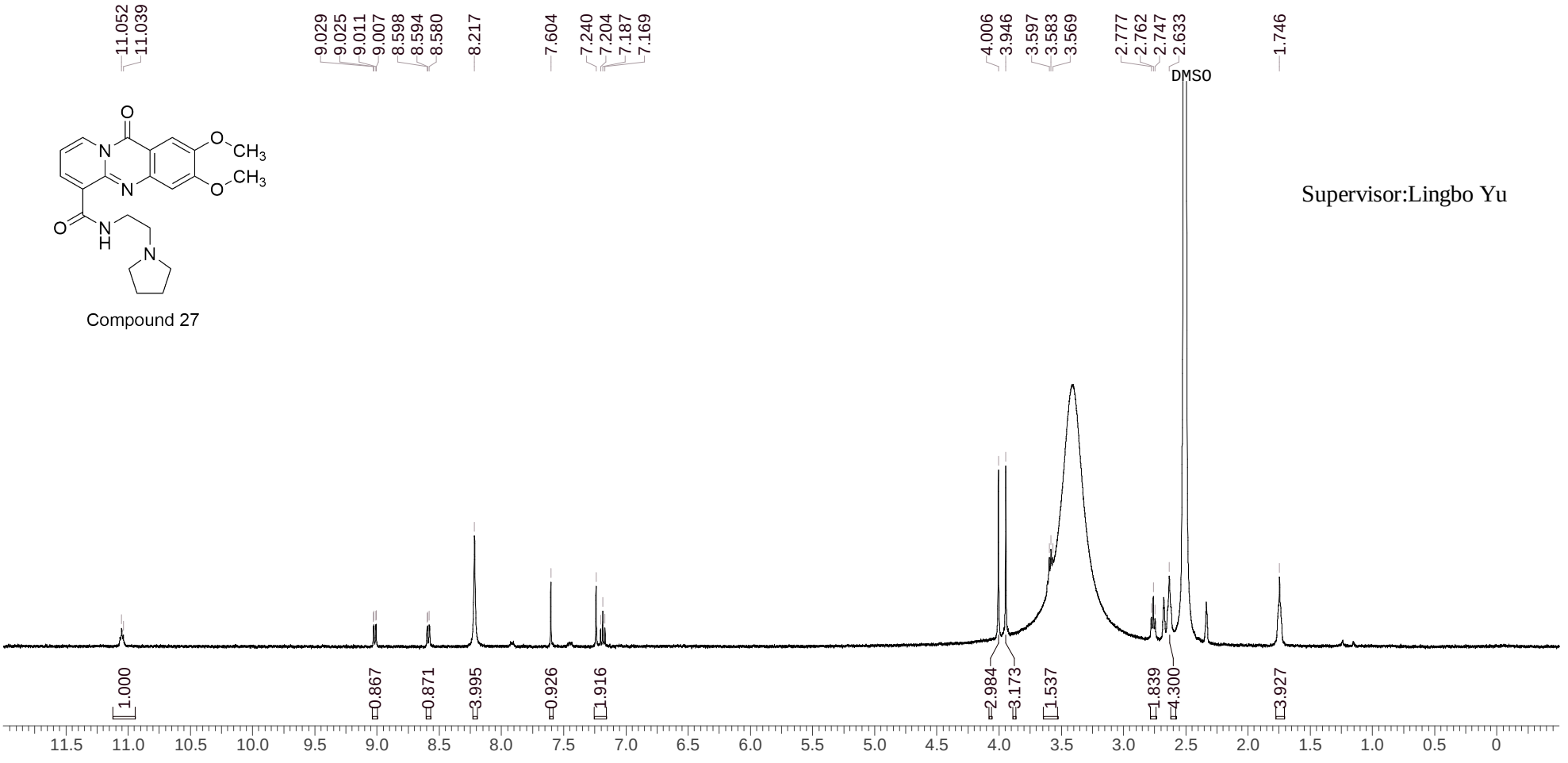
Supervisor:Lingbo Yu

Operator:

Date:

**Compound ID:** JHU_3KA4X

**ET20302-2-p1b DMSO Bruker_C_400MHz**

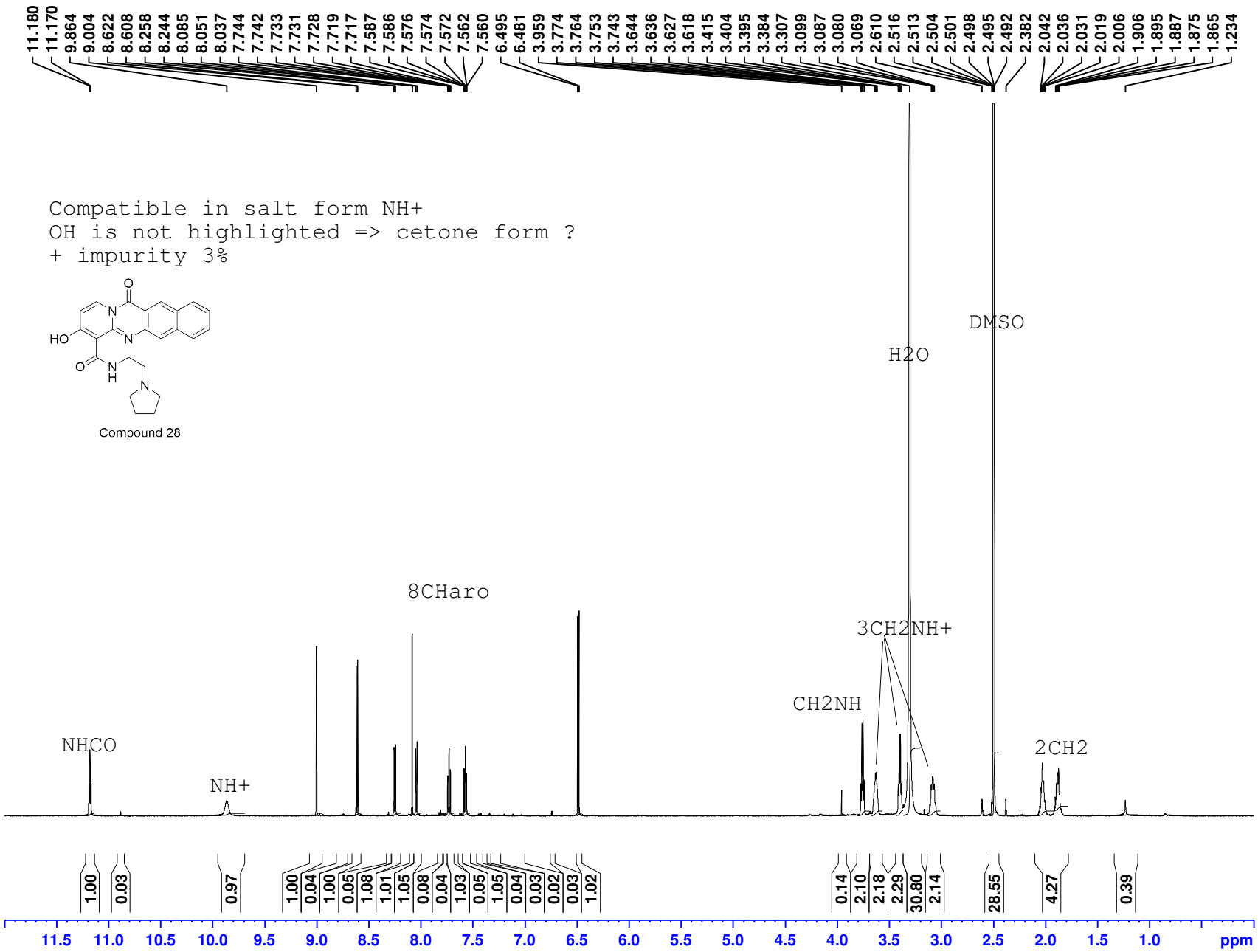



Compound 27

Supervisor:Lingbo Yu

Operator: Date:

EV-QLR002-063-001
a_proton DMSO {D:\RMN600} tlrmn 2

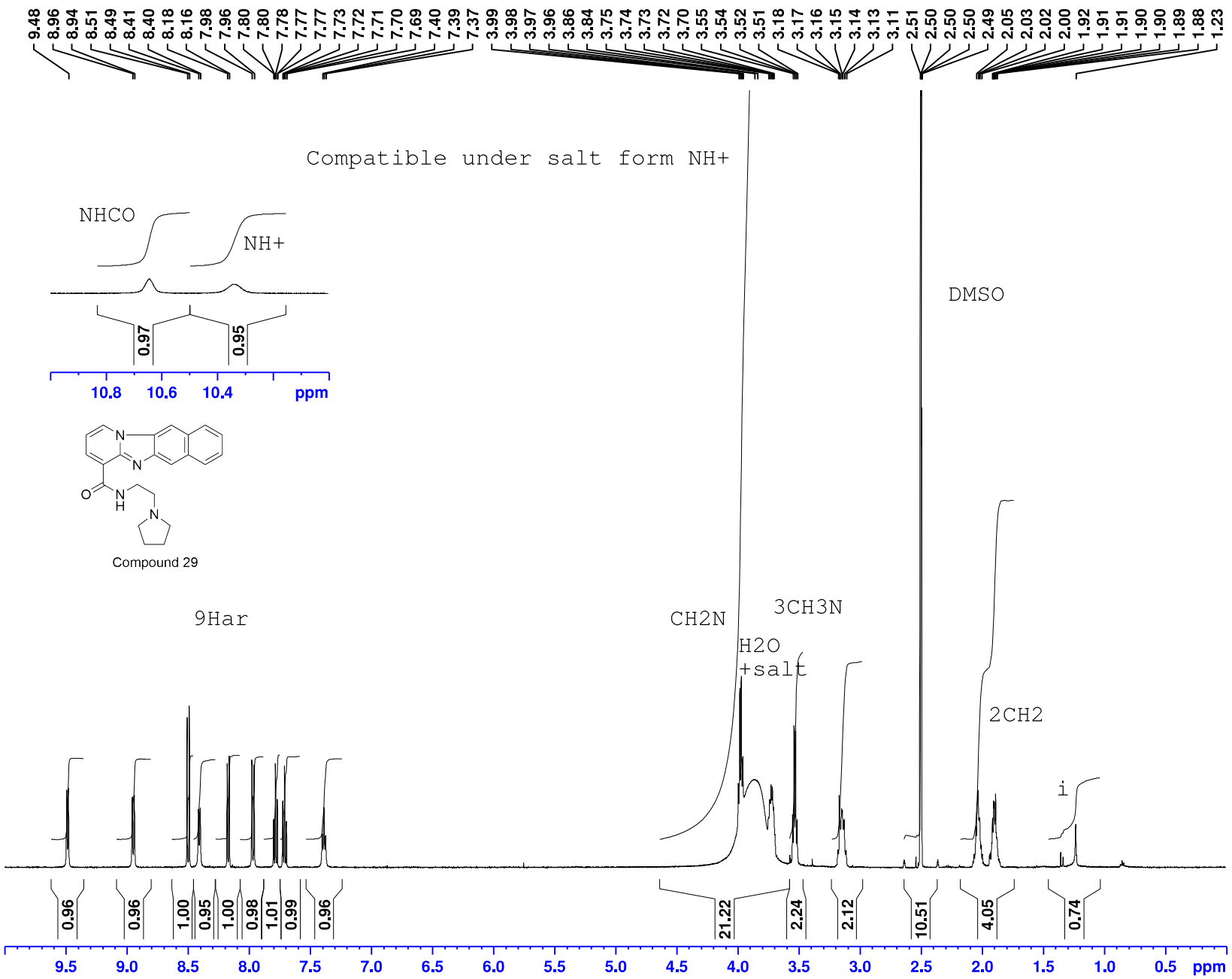



Current Data Parameters
NAME dNMR190800214
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20190827
Time 20.50 h
INSTRUM spect
PROBHD Z44896_0032 (C
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 64
DS 2
SWH 9615.385 Hz
FIDRES 0.293438 Hz
AQ 3.4078720 sec
RG 21.1
DW 52.000 usec
DE 14.86 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
SFO1 600.1742012 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 6.51840019 W

F2 - Processing parameters
SI 65536
SF 600.1700000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.3
PC 1.00

EV-QLR002-084-001
a_proton64 DMSO {D:\RMN500} tlrmn 4



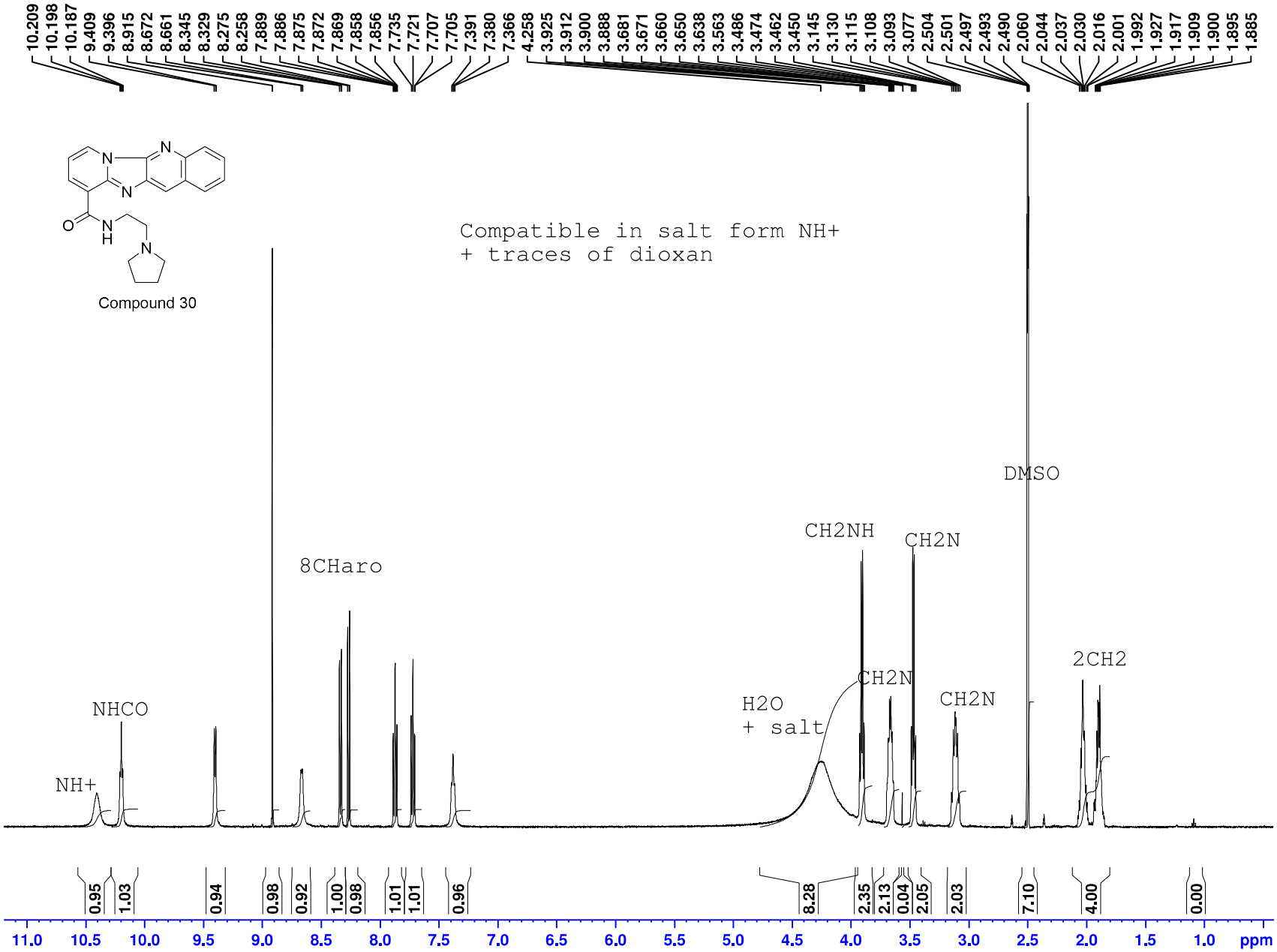

Current Data Parameters
NAME eNMR191000015
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20191002
Time 12.54
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 64
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 574.7
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 0 dB
PL1W 25.11886406 W
SFO1 500.1337510 MHz

F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.2
PC 1.00

EV-POH001-461-001
a_proton64 DMSO {D:\RMN500} tlrmn 8



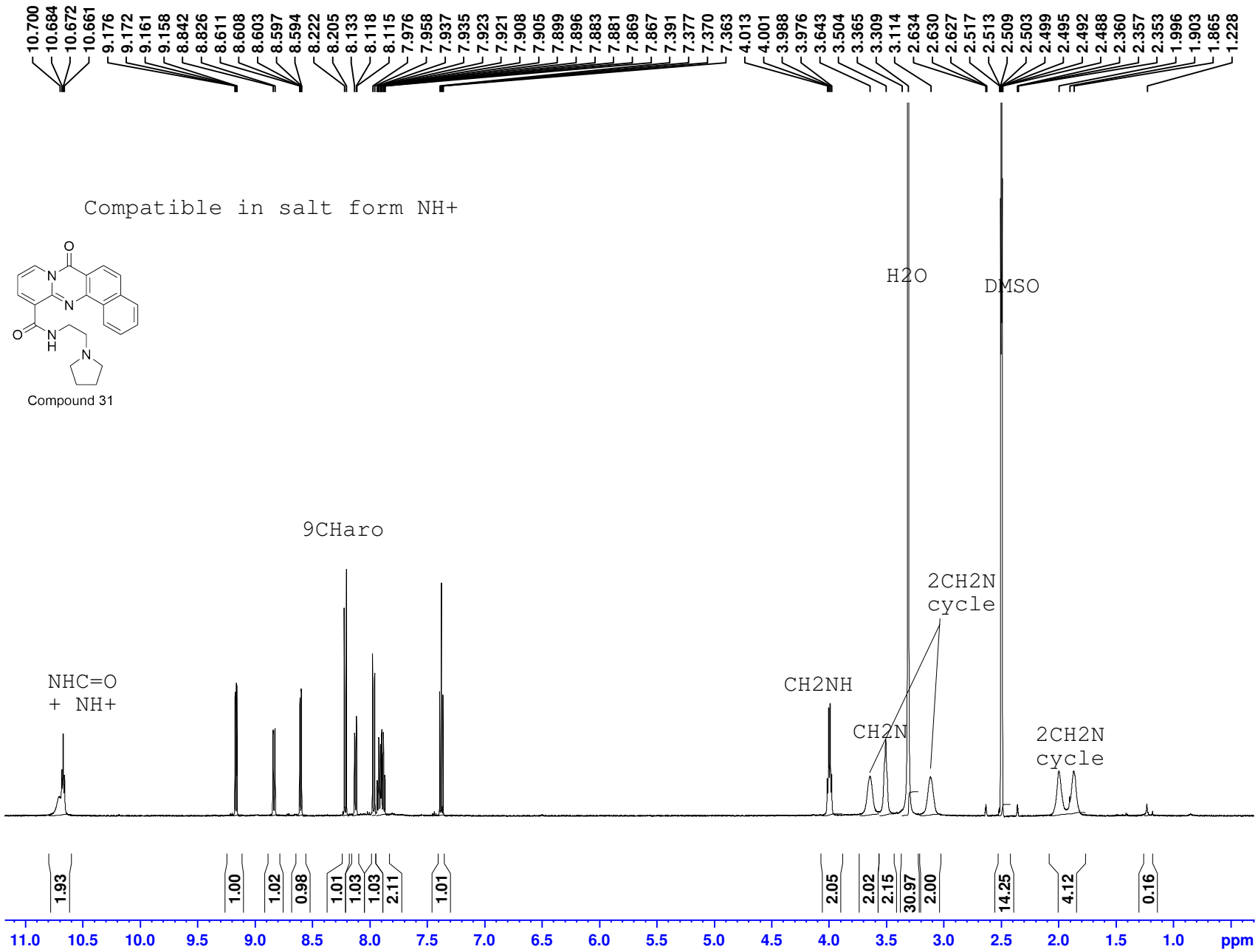

Current Data Parameters
NAME eNMR191000047
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20191005
Time 3.45
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 64
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 574.7
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 0 dB
PL1W 25.11886406 W
SFO1 500.1337510 MHz

F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.2
PC 1.00

EV-MOK001-004-001
a_proton64 DMSO {D:\RMN500} tlrmn 5

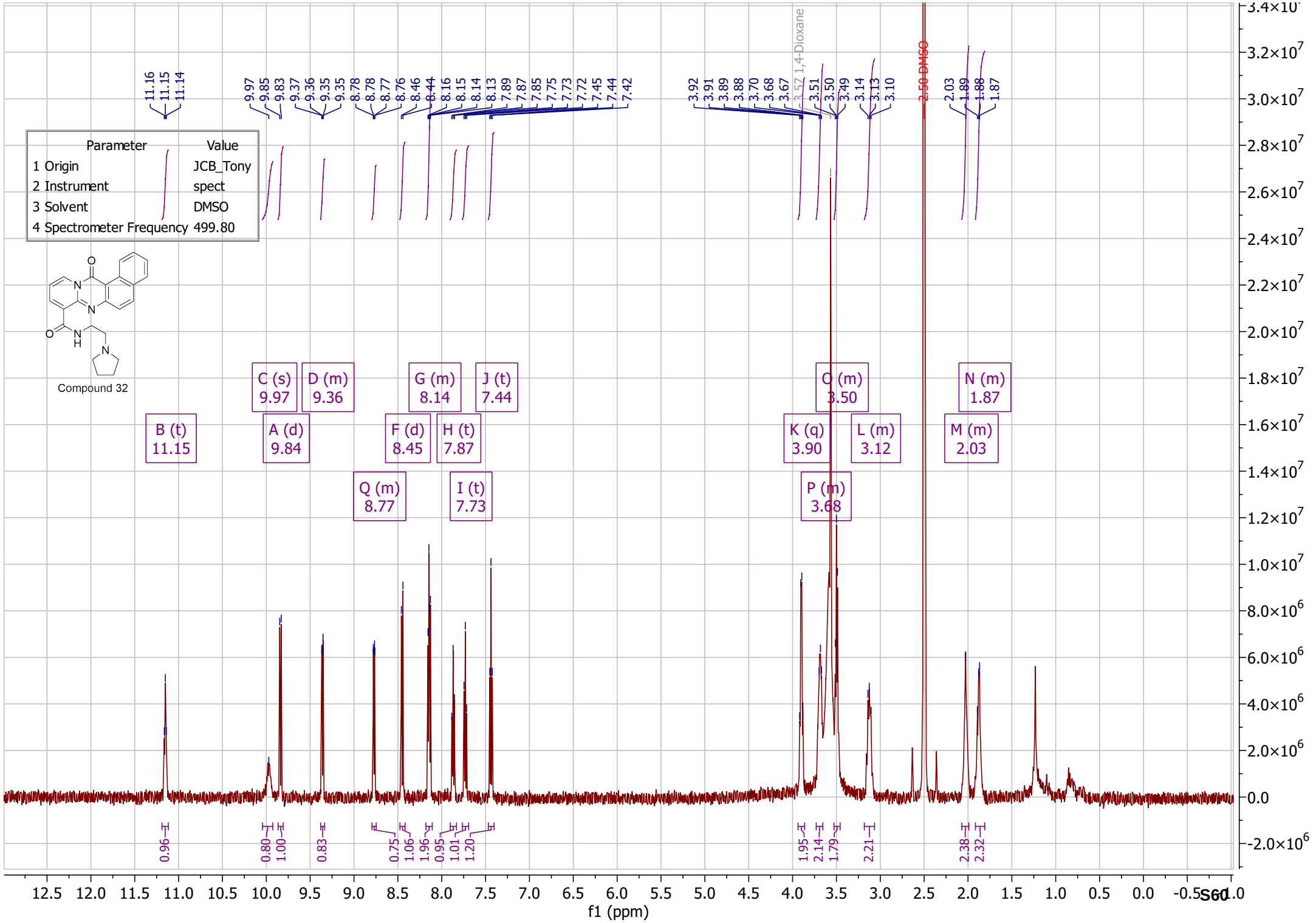



Current Data Parameters
NAME EV-MOK001-004-001
EXPNO 10
PROCNO 1

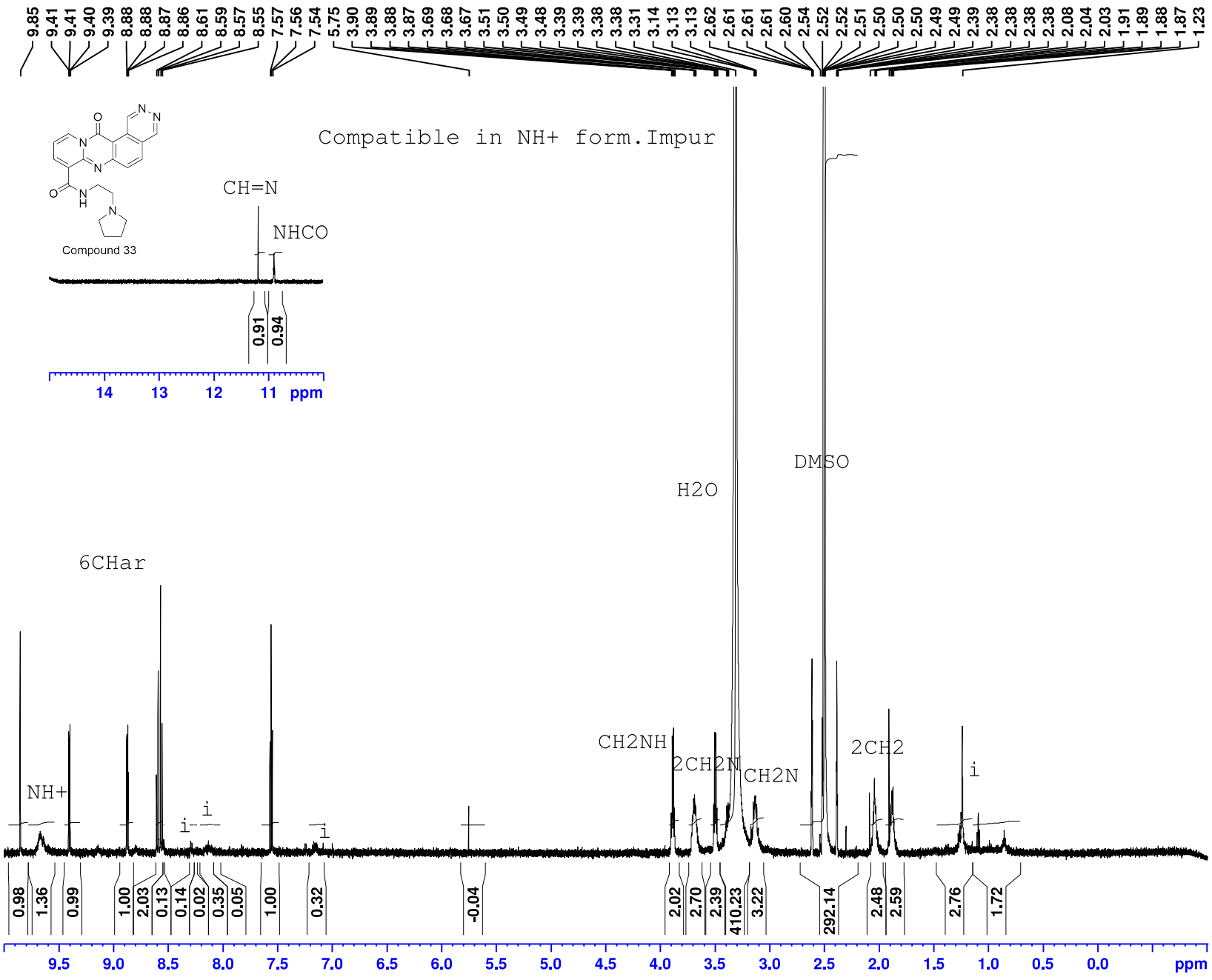
F2 - Acquisition Parameters
Date_ 20190711
Time 16.32
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 64
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 574.7
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 0 dB
PL1W 25.11886406 W
SFO1 500.1337510 MHz

F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.2
PC 1.00


Parameter Value
1 Origin JCB_Tony
2 Instrument spect
3 Solvent DMSO
4 Spectrometer Frequency 499.80
Compound 32
B (t) 11.15
C (s) 9.97
D (m) 9.36
A (d) 9.84
F (d) 8.45
G (m) 8.14
H (t) 7.87
J (t) 7.44
Q (m) 8.77
I (t) 7.73
O (m) 3.50
K (q) 3.90
L (m) 3.12
P (m) 3.68
N (m) 1.87
M (m) 2.03
1,4-Dioxane
DMSO
f1 (ppm)

EV-MOK001-059-001
a_proton DMSO {D:\RMN600} tlrmn 13

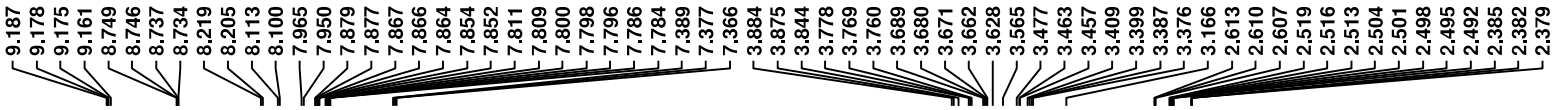



Current Data Parameters
NAME dNMR190900063
EXPNO 1
PROCNO 1

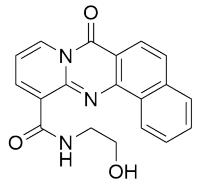
F2 - Acquisition Parameters
Date_ 20190906
Time 19.25 h
INSTRUM spect
PROBHD Z44896_0032 (C
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 64
DS 2
SWH 9615.385 Hz
FIDRES 0.293438 Hz
AQ 3.4078720 sec
RG 21.1
DW 52.000 usec
DE 14.86 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
SFO1 600.1742012 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 6.51840019 W

F2 - Processing parameters
SI 65536
SF 600.1700000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.3
PC 1.00

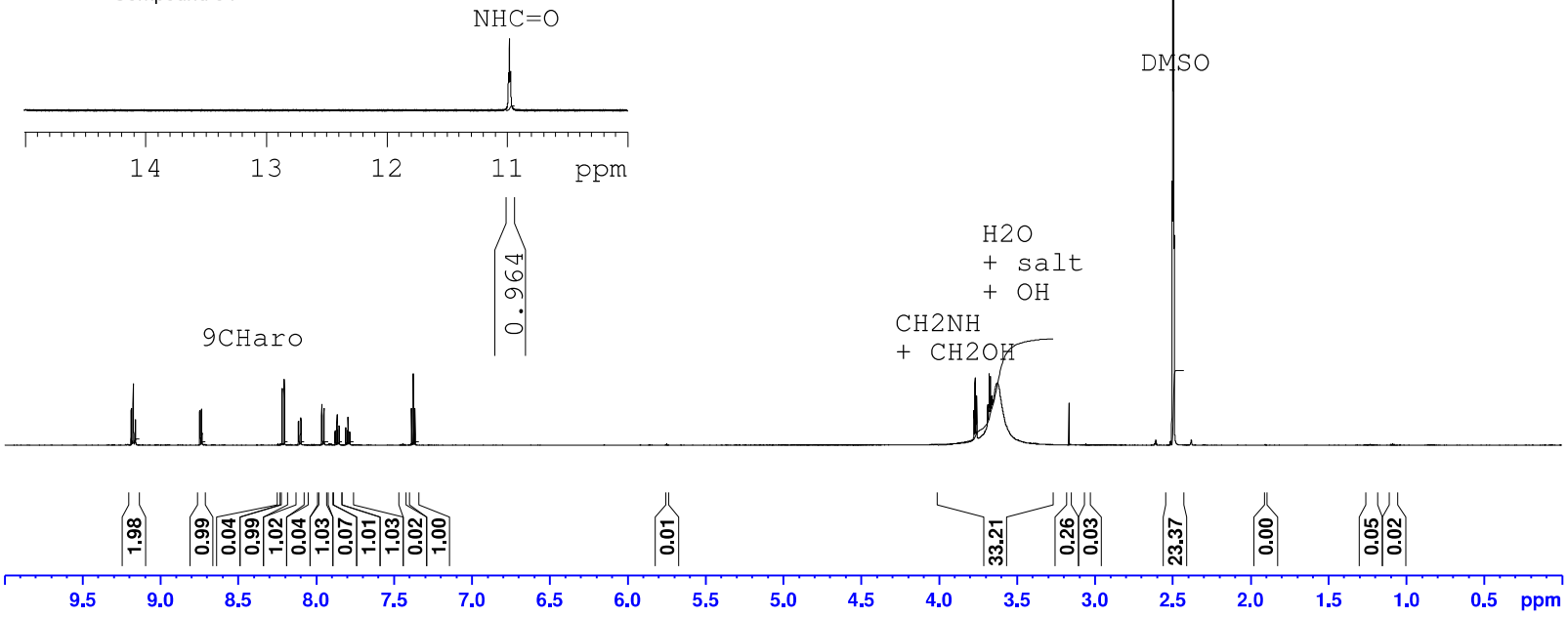
EV-MOK001-029-001
a_proton DMSO {D:\RMN600} tlrmn 9




Compatible
Presence of salt dissociated in DMSO-d6.
+ MeOH 0.06 mol
+ iPr2O traces
+ DCM traces



Compound 34

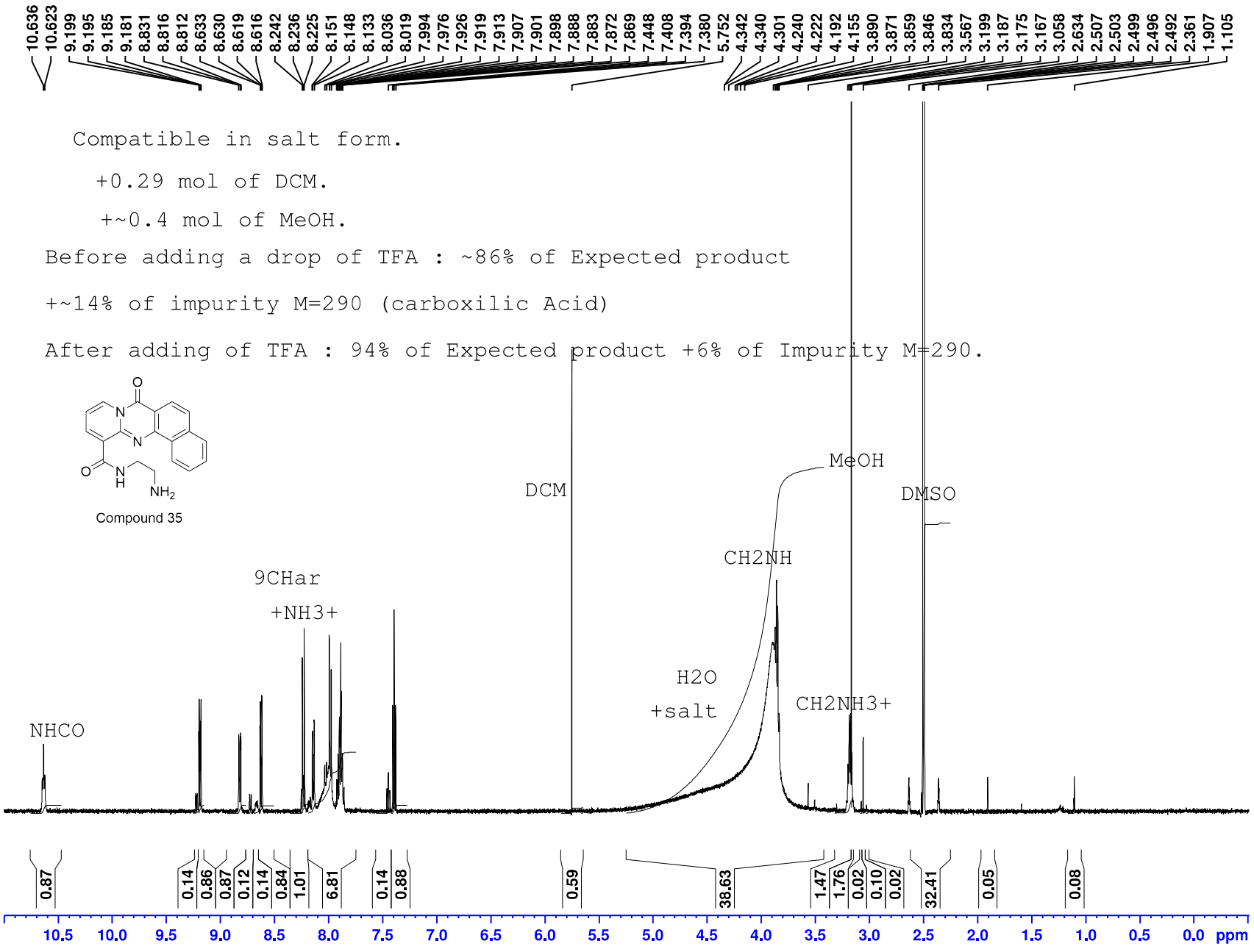



Current Data Parameters
NAME dNMR190800107
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20190813
Time 5.37 h
INSTRUM spect
PROBHD Z44896_0032 (C
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 64
DS 2
SWH 9615.385 Hz
FIDRES 0.293438 Hz
AQ 3.4078720 sec
RG 19.66
DW 52.000 usec
DE 14.86 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
SFO1 600.1742012 MHz
NUC1 1H
P0 2.67 usec
P1 8.00 usec
PLW1 6.51840019 W

F2 - Processing parameters
SI 65536
SF 600.1700000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.3
PC 1.00

EV-POH001-534-002
a_proton64 DMSO {D:\RMN500} tlrmn 15



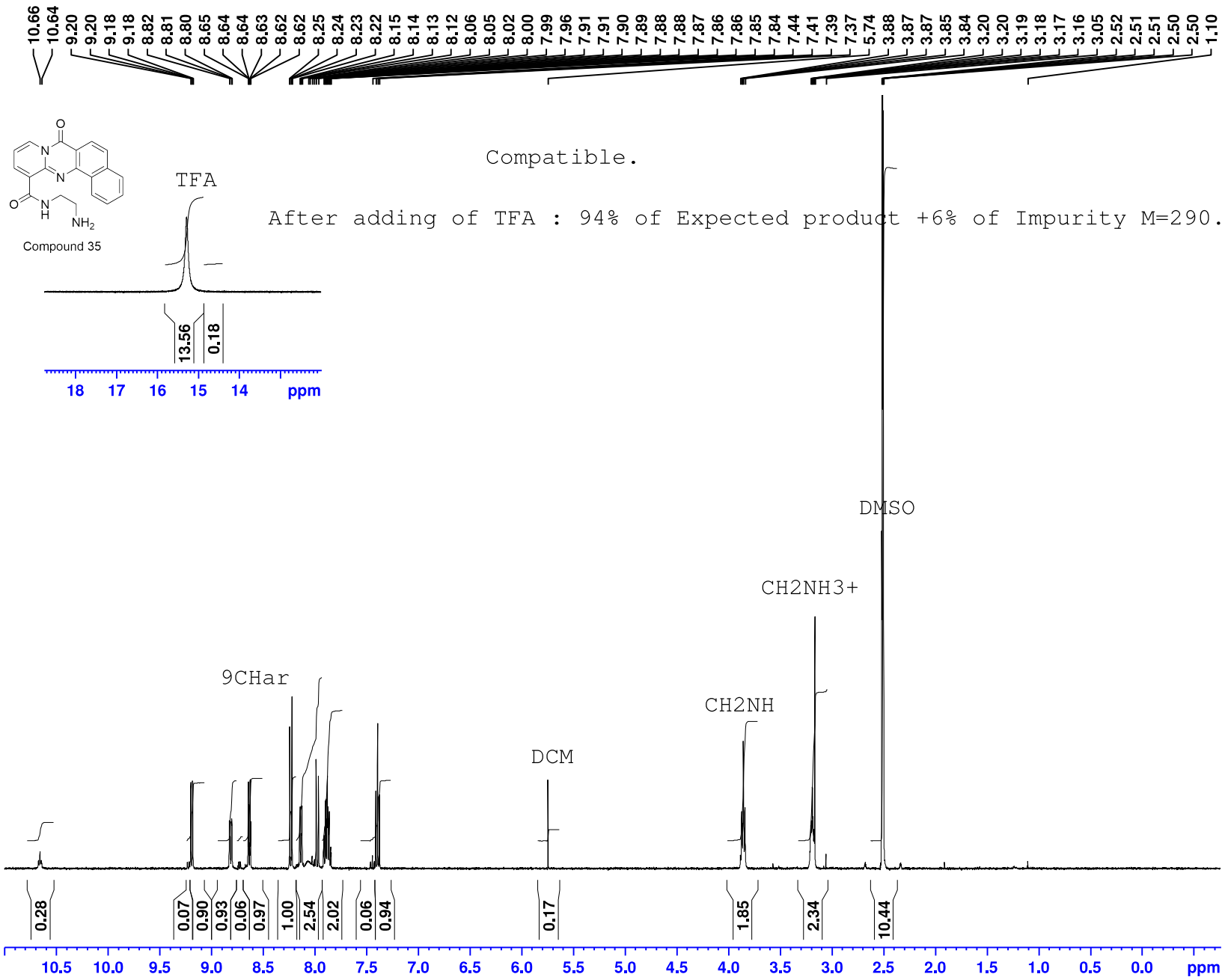

Current Data Parameters
NAME eNMR200100392
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20200131
Time 5.12
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 64
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 574.7
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 0 dB
PL1W 25.11886406 W
SFO1 500.1337510 MHz

F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.2
PC 1.00

EV-POH001-534-002+TFA
a_proton_NS16 DMSO {D:\data} tlrmn 12

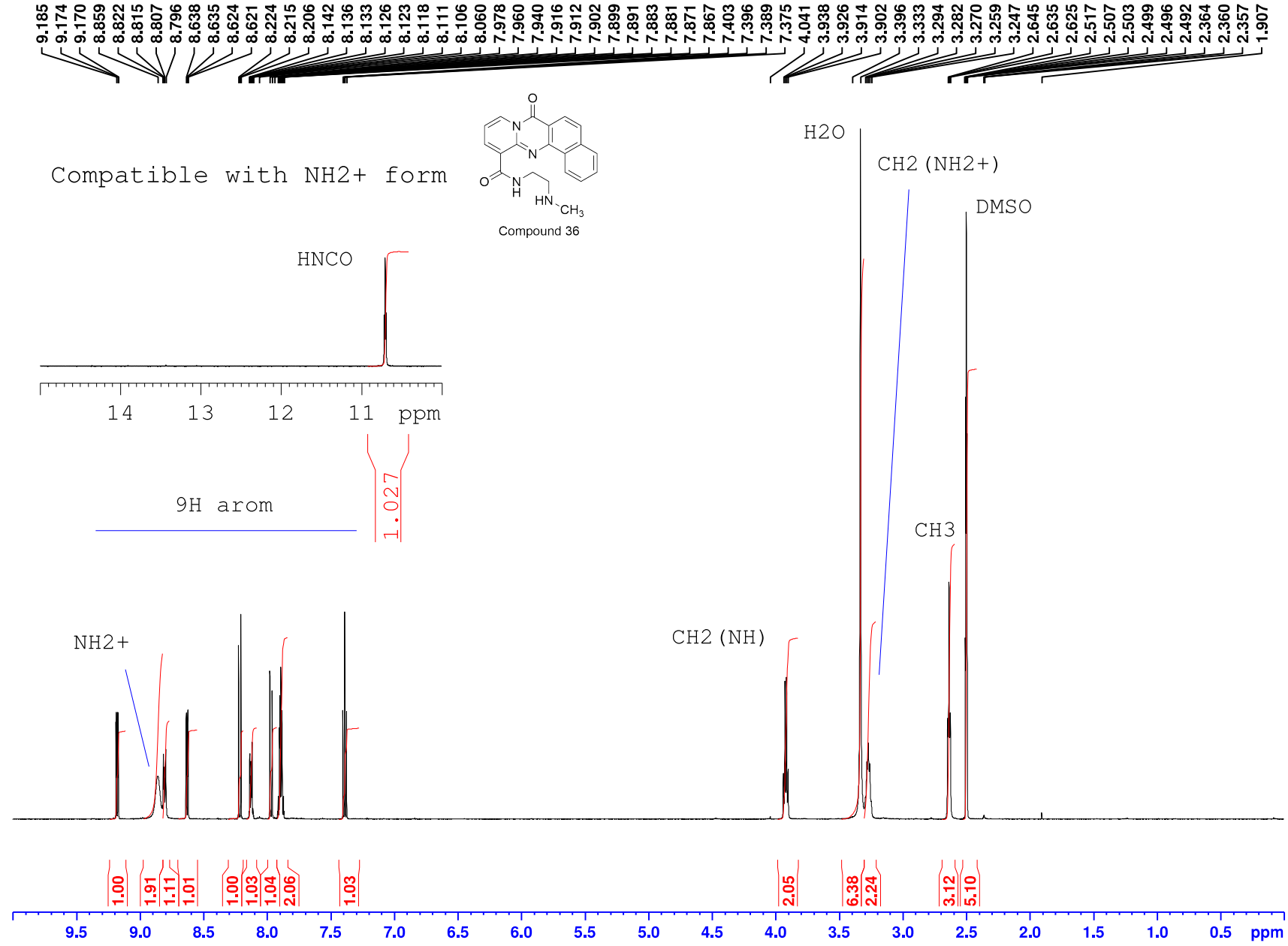



Current Data Parameters
NAME cNMR200100392
EXPNO 11
PROCNO 1

F2 - Acquisition Parameters
Date_ 20200131
Time 9.49 h
INSTRUM Avance NEO 400
PROBHD Z824701_0018 (
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 16
DS 2
SWH 7812.500 Hz
FIDRES 0.476837 Hz
AQ 2.0971520 sec
RG 101
DW 64.000 usec
DE 6.82 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
SFO1 400.1336012 MHz
NUC1 1H
P0 2.31 usec
P1 6.92 usec
PLW1 14.80599976 W

F2 - Processing parameters
SI 32768
SF 400.1300000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.2
PC 1.00

EV-QLR002-177-001
a_proton64 DMSO {D:\RMN500} tlrmn 8

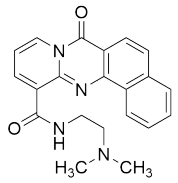



Current Data Parameters
NAME eNMR200100334
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20200129
Time 2.13
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 64
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 574.7
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 0 dB
PL1W 25.11886406 W
SFO1 500.1337510 MHz

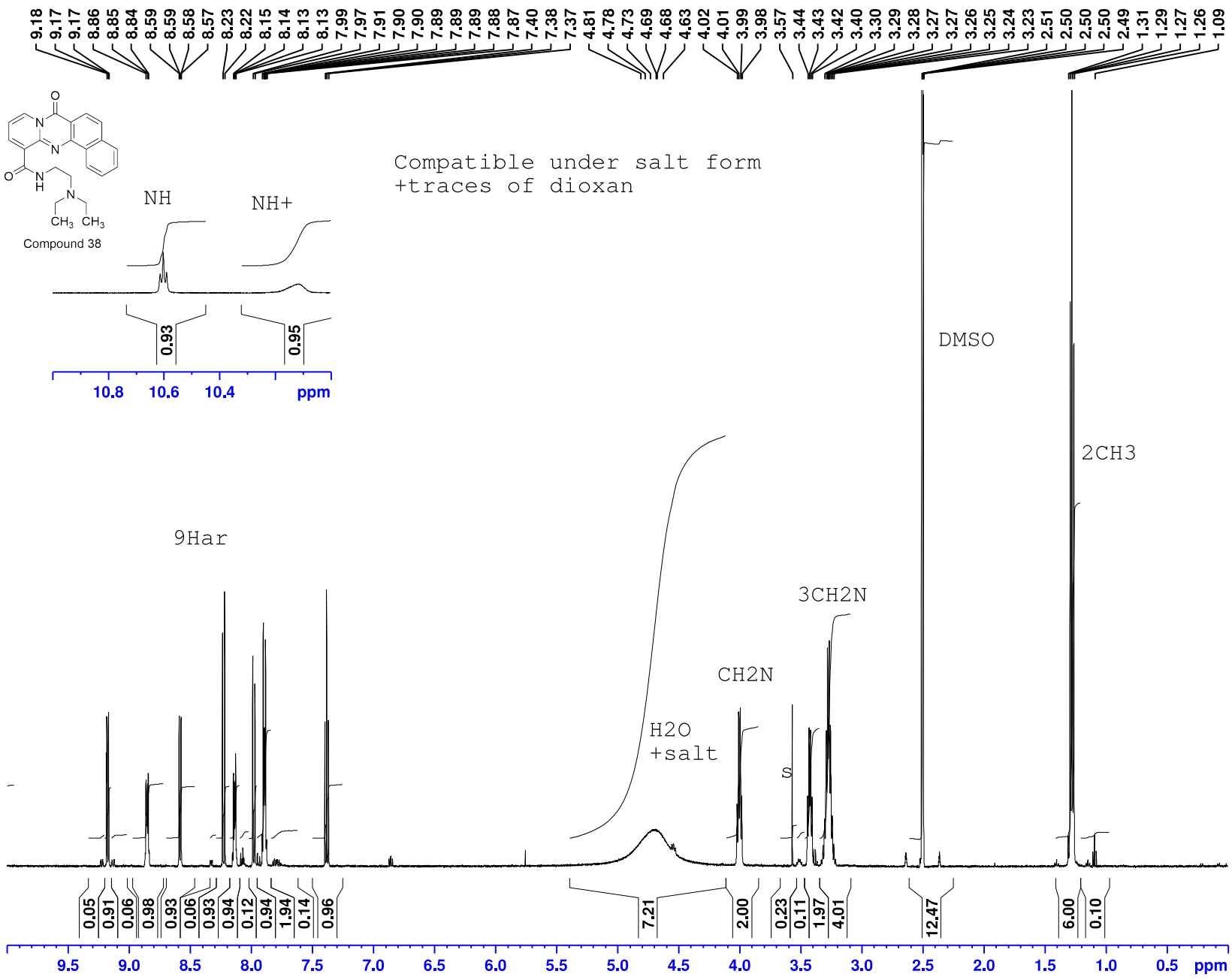
F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.2
PC 1.00



Compound 37

EV-QLR002-025-3.10.fid
EV-QLR002-025-3
a_proton_NS128 DMSO {P:\Libre service RMN} libre-service_400MHz 22

EV-QLR002-165-001
a_proton64 DMSO {D:\RMN500} tlrmn 5



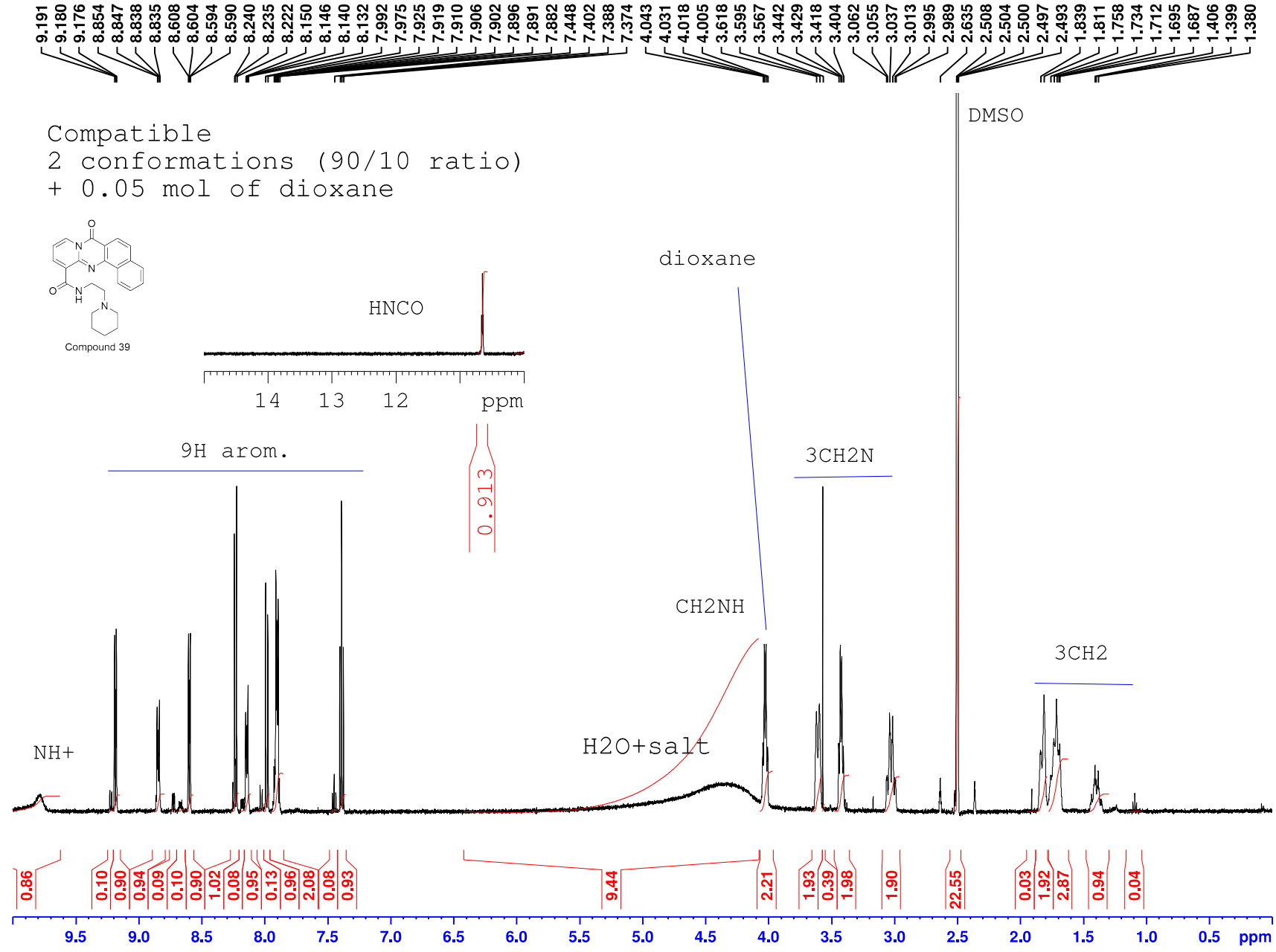

Current Data Parameters
NAME eNMR200100208
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20200121
Time 3.50
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 64
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 574.7
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 0 dB
PL1W 25.11886406 W
SFO1 500.1337510 MHz

F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.2
PC 1.00

EV-POH001-533-001
a_proton64 DMSO {D:\RMN500} tlrmn 6



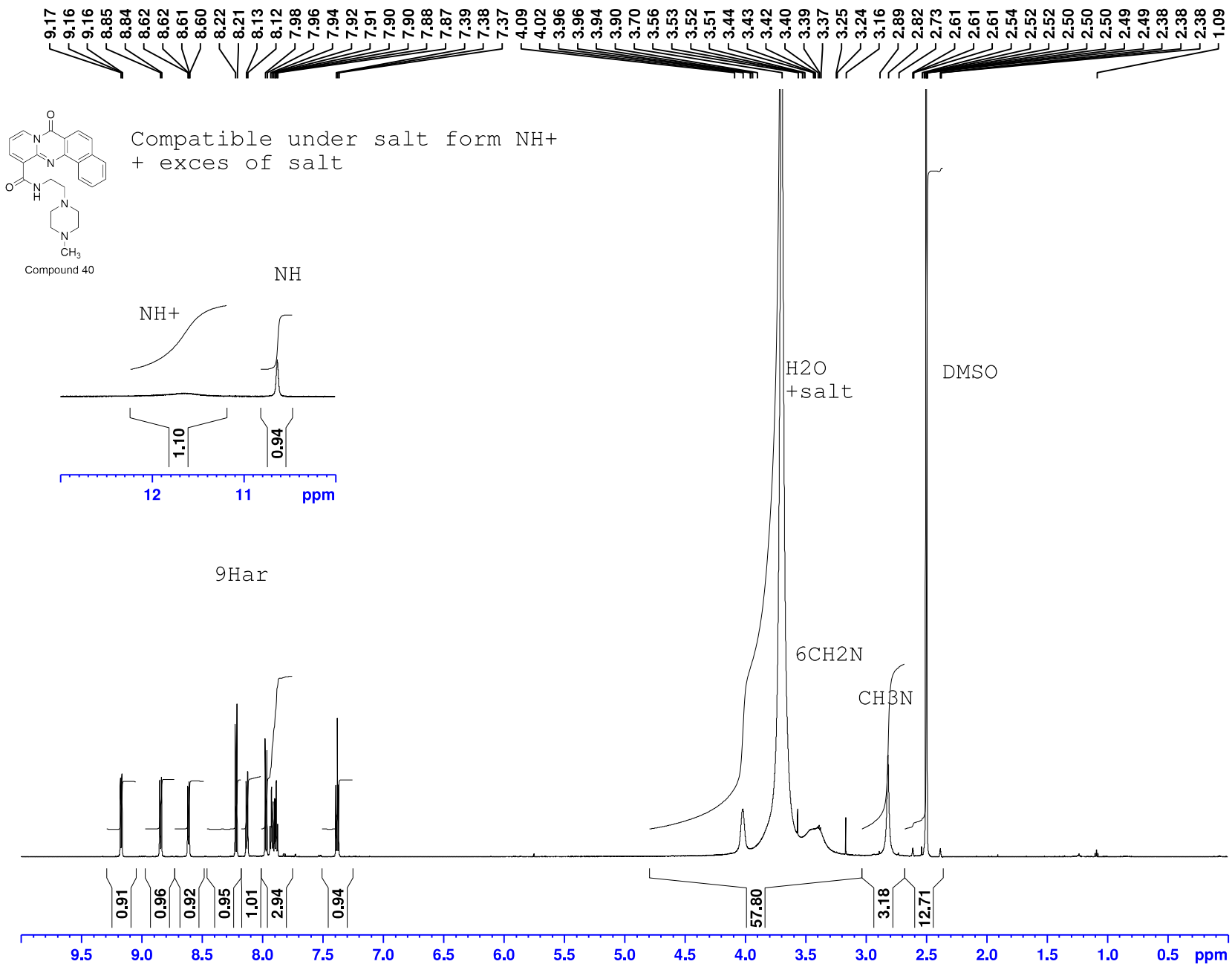

Current Data Parameters
NAME eNMR200100206
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20200120
Time 17.18
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 64
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 812.7
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 0 dB
PL1W 25.11886406 W
SFO1 500.1337510 MHz

F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.2
PC 1.00

EV-QLR002-102-001
a_proton DMSO {D:\RMN600} tlrmn 3

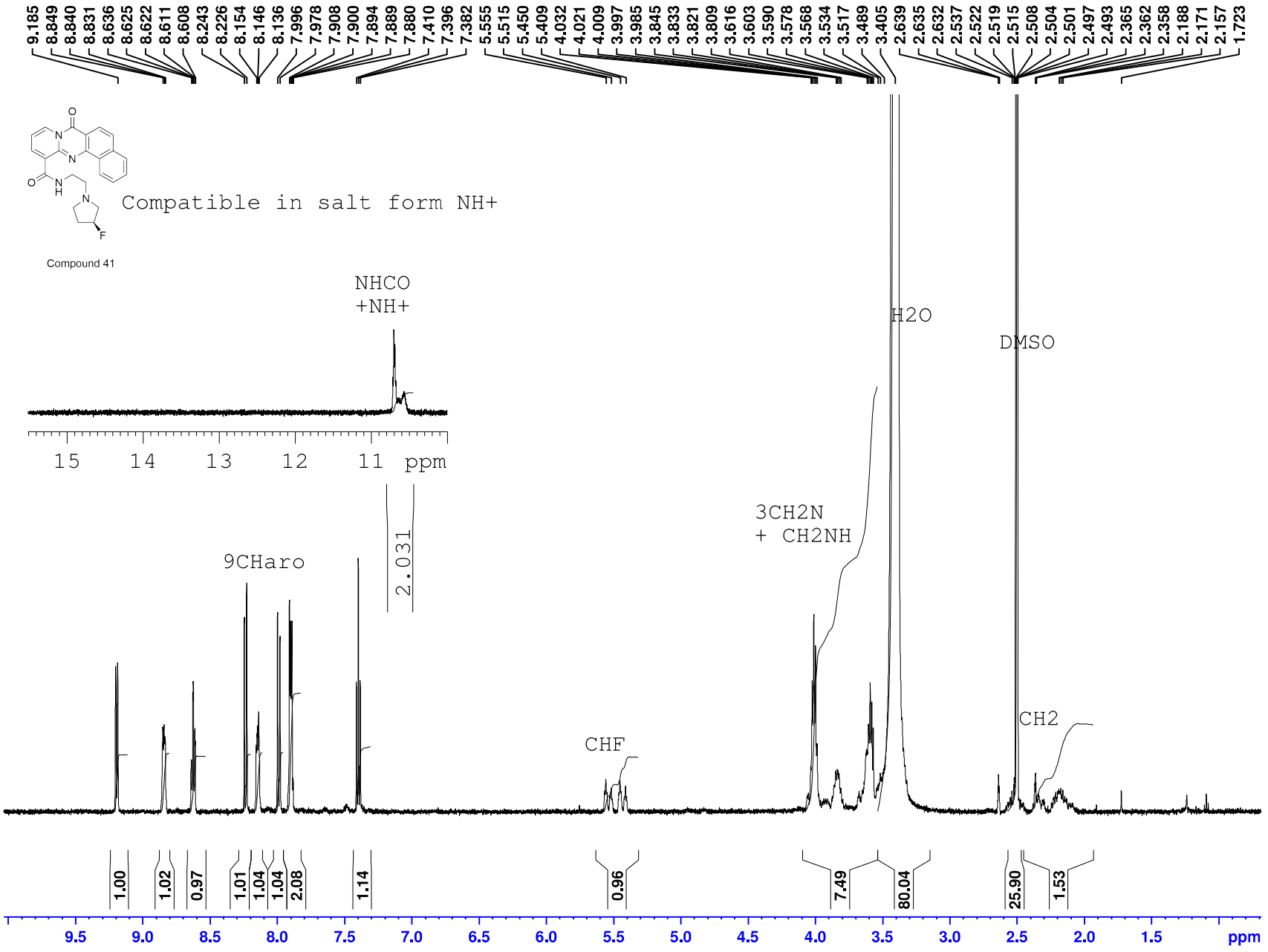



Current Data Parameters
NAME dNMR191000271
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20191023
Time 22.42 h
INSTRUM spect
PROBHD Z44896_0032 (C
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 64
DS 2
SWH 9615.385 Hz
FIDRES 0.293438 Hz
AQ 3.4078720 sec
RG 19.66
DW 52.000 usec
DE 14.88 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
SFO1 600.1742012 MHz
NUC1 1H
P0 2.63 usec
P1 7.90 usec
PLW1 6.51840019 W

F2 - Processing parameters
SI 65536
SF 600.1700000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.3
PC 1.00

EV-MOK001-111-001
a_proton64 DMSO {D:\RMN500} tlrmn 11



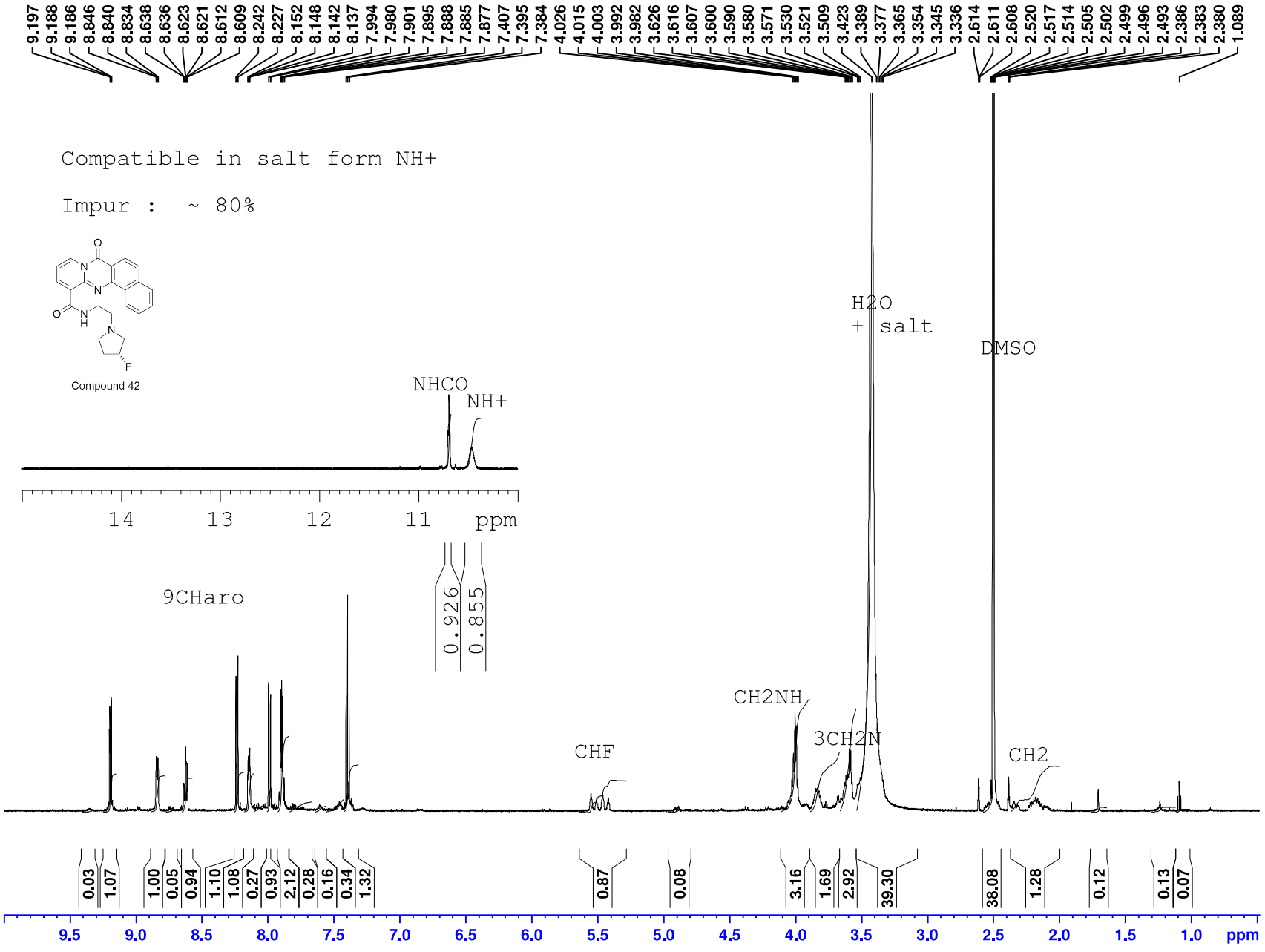

Current Data Parameters
NAME eNMR191100077
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20191112
Time 21.09
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 64
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 574.7
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 0 dB
PL1W 25.11886406 W
SFO1 500.1337510 MHz

F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.2
PC 1.00

EV-MOK001-149-001
a_proton DMSO {D:\RMN600} tlrmn 10

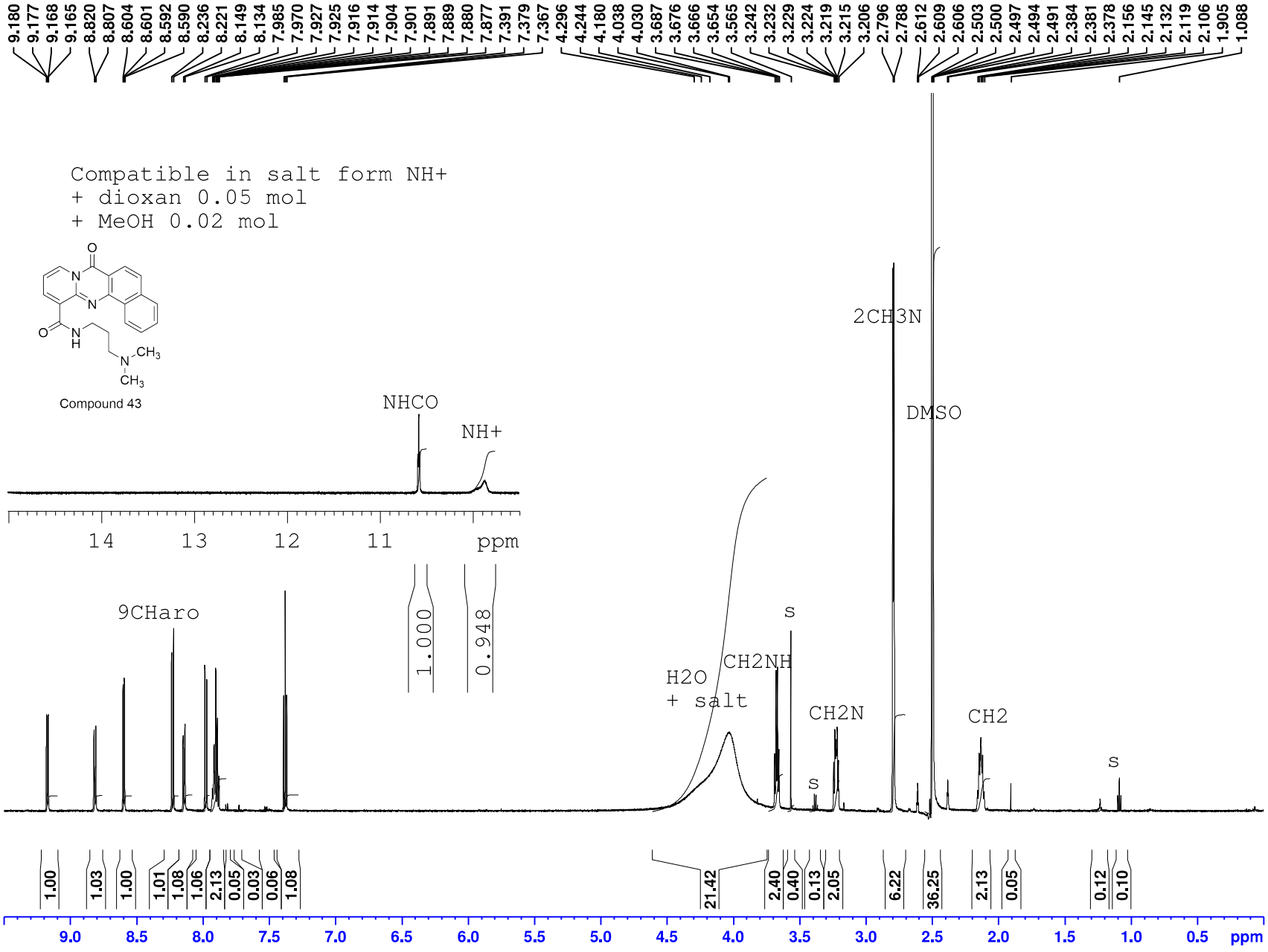



Current Data Parameters
NAME dNMR191200004
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20191202
Time 18.36 h
INSTRUM spect
PROBHD Z44896_0032 (C
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 64
DS 2
SWH 9615.385 Hz
FIDRES 0.293438 Hz
AQ 3.4078720 sec
RG 21.1
DW 52.000 usec
DE 14.88 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
SFO1 600.1742012 MHz
NUC1 1H
P0 2.63 usec
P1 7.90 usec
PLW1 6.51840019 W

F2 - Processing parameters
SI 65536
SF 600.1700000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.3
PC 1.00

EV-POH001-495-001
a_proton DMSO {D:\RMN600} tlrmn 2

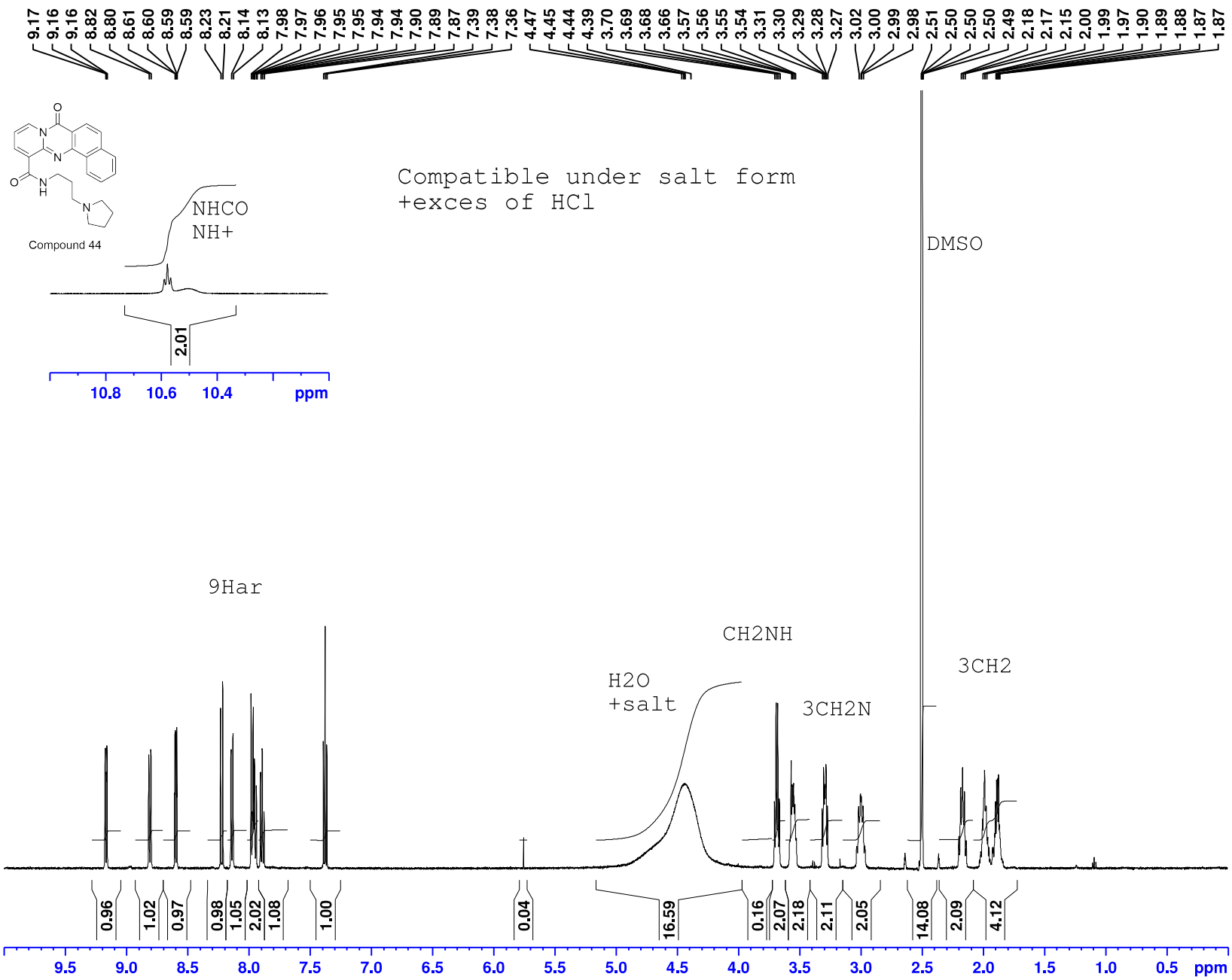



Current Data Parameters
NAME dNMR191100208
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20191119
Time 15.46 h
INSTRUM spect
PROBHD Z44896_0032 (C
PULPROG zg30
TD 65536
SOLVENT DMSO
NS 64
DS 2
SWH 9615.385 Hz
FIDRES 0.293438 Hz
AQ 3.4078720 sec
RG 19.66
DW 52.000 usec
DE 14.88 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1
SFO1 600.1742012 MHz
NUC1 1H
P0 2.63 usec
P1 7.90 usec
PLW1 6.51840019 W

F2 - Processing parameters
SI 65536
SF 600.1700000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.3
PC 1.00

EV-POH001-489-001
a_proton64 DMSO {D:\RMN500} tlrmn 2



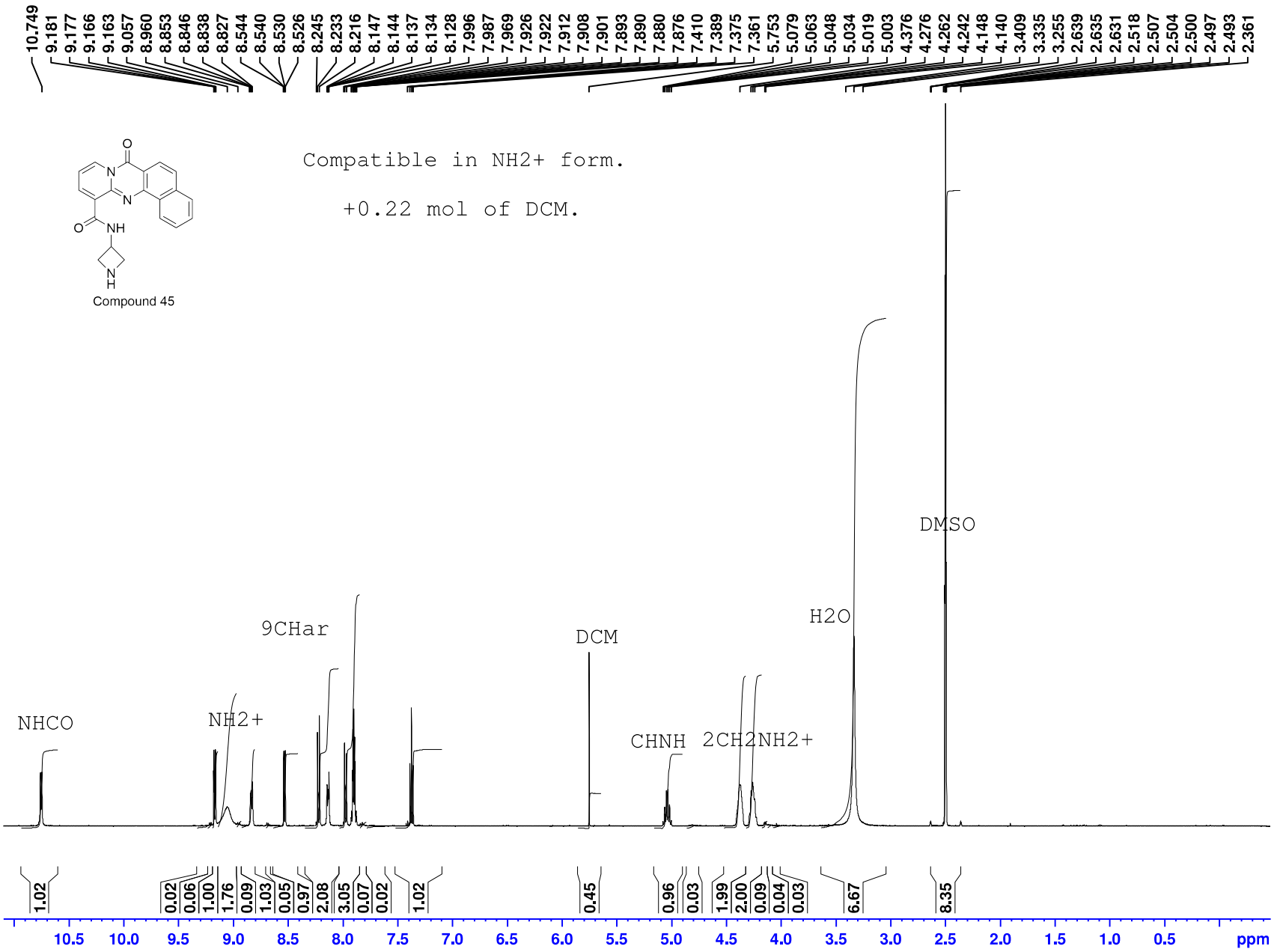

Current Data Parameters
NAME eNMR191100100
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20191113
Time 15.24
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 64
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 574.7
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 =======
NUC1 1H
P1 7.50 usec
PL1 0 dB
PL1W 25.11886406 W
SFO1 500.1337510 MHz

F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.2
PC 1.00

EV-MOK001-187-002
a_proton64 DMSO {D:\RMN500} tlrmn 8



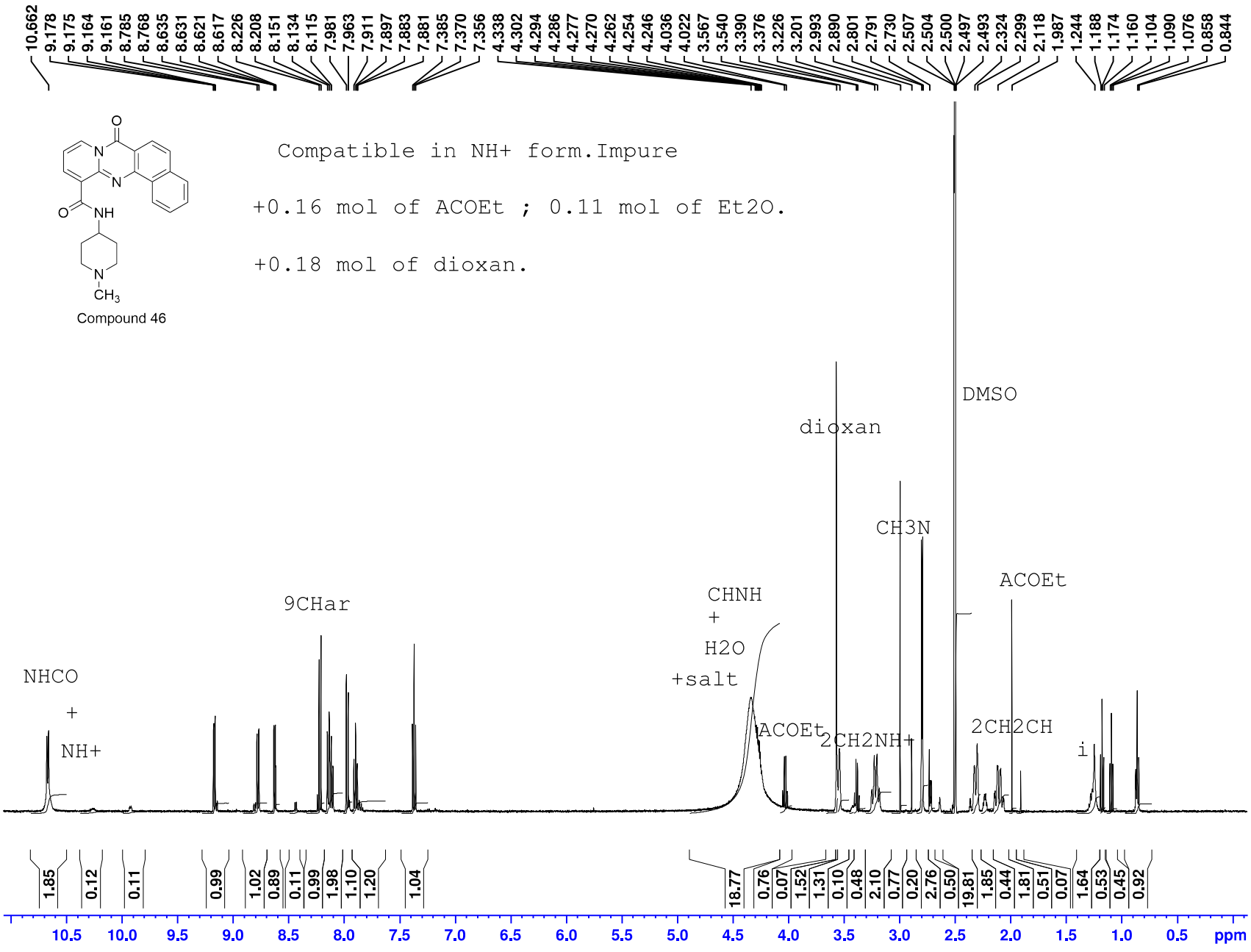

Current Data Parameters
NAME eNMR200100183
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20200118
Time 1.46
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 64
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 574.7
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 0 dB
PL1W 25.11886406 W
SFO1 500.1337510 MHz

F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.2
PC 1.00

EV-POH001-521-002
a_proton64 DMSO {D:\RMN500} tlrmn 11



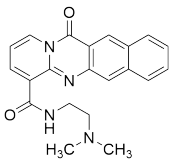

Current Data Parameters
NAME eNMR200100182
EXPNO 10
PROCNO 1

F2 - Acquisition Parameters
Date_ 20200118
Time 10.02
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 64
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 574.7
DW 62.400 usec
DE 6.50 usec
TE 300.0 K
D1 1.00000000 sec
TD0 1

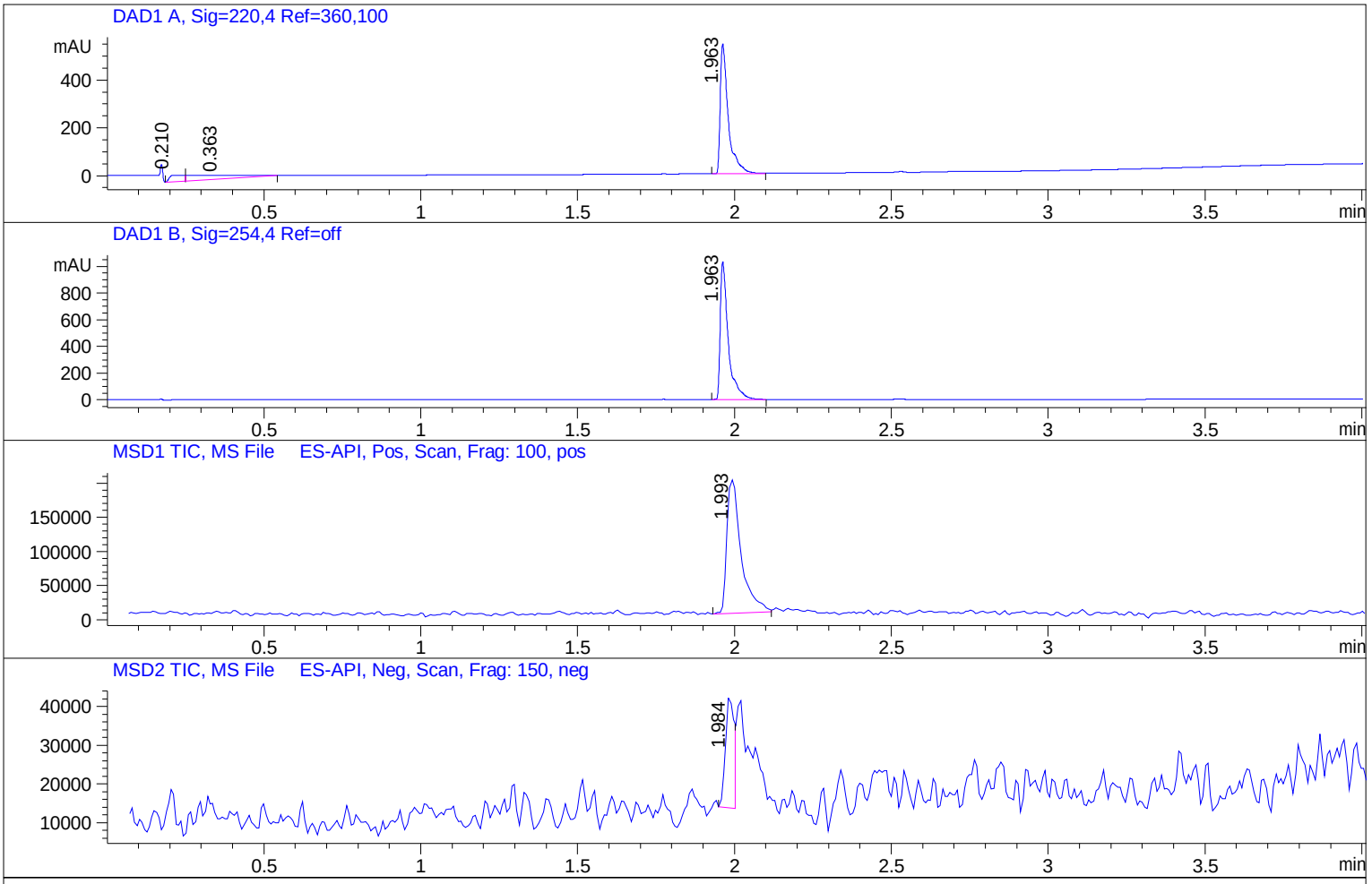
======== CHANNEL f1 ========
NUC1 1H
P1 7.50 usec
PL1 0 dB
PL1W 25.11886406 W
SFO1 500.1337510 MHz

F2 - Processing parameters
SI 32768
SF 500.1300000 MHz
WDW GM
SSB 0
LB -0.15 Hz
GB 0.2
PC 1.00

**File C:\EZXDATA\TDORADO\01-20\299.1.D** **Tgt Mass (EZX):**
**Injection Date : 21 Jan 20 1:47 pm -0500** **Seq. Line : 0**
**Sample Name : 299.** **Location : Vial 29**
**Acq. Operator : tony.dorado** **Inj : 1**
**Spec. Reported : MS Integration** **Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



Compound 1



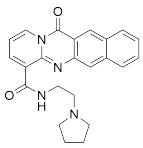

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.21 | 0.04 | 85.22 | 28.59 | 6.71 | 265 | 249 |
| 0.36 | 0.16 | 216.08 | 16.25 | 17.02 | 265 | 379 |
| 1.96 | 0.03 | 968.57 | 542.62 | 76.27 | 361 | 155 |

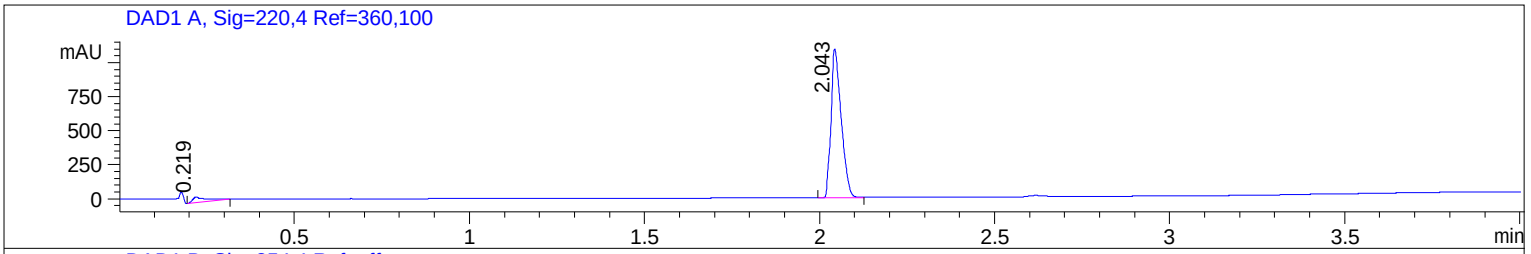
Integration Results for DAD1 B, Sig=254,4 Ref=off

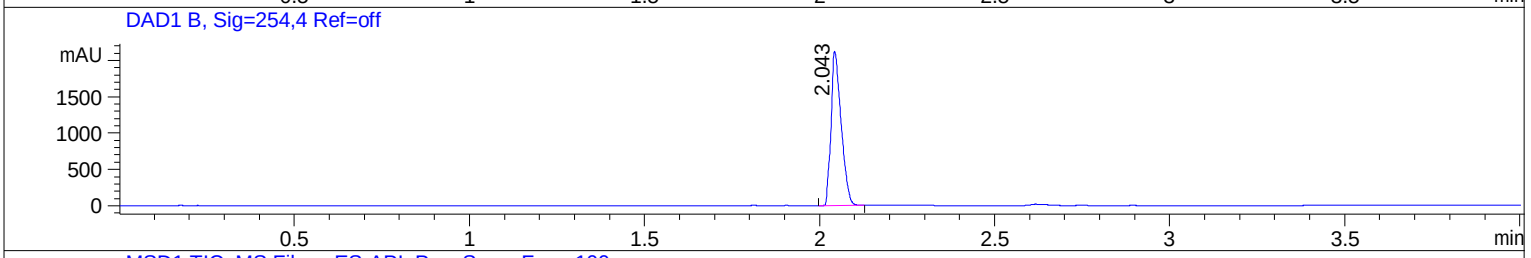
| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 1.96 | 0.03 | 1833.76 | 1032.04 | 100.00 | 361 | 155 |

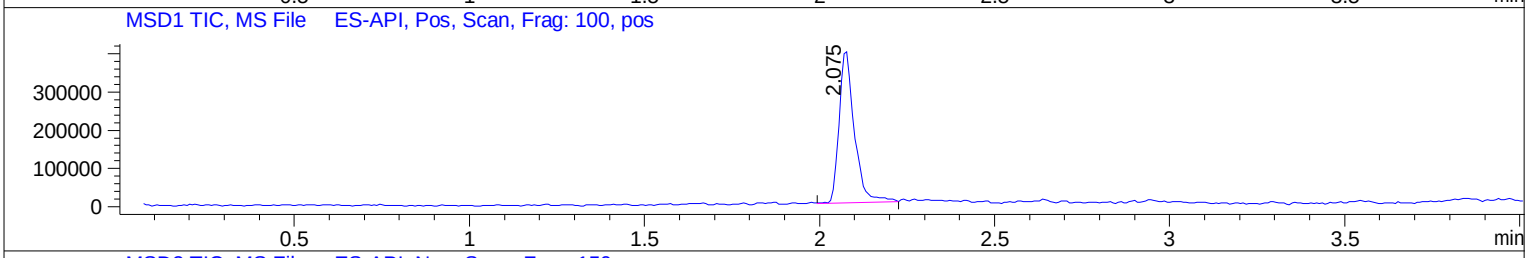
**File C:\EZXDATA\TDORADO\09-18\054_HCL.1.D** **Tgt Mass (EZX):**
**Injection Date : 10 Sep 18 5:25 pm -0500** **Seq. Line : 0**
**Sample Name : 054_HCl.** **Location : Vial 95**
**Acq. Operator : tony.dorado** **Inj : 1**
**Spec. Reported : MS Integration** **Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**

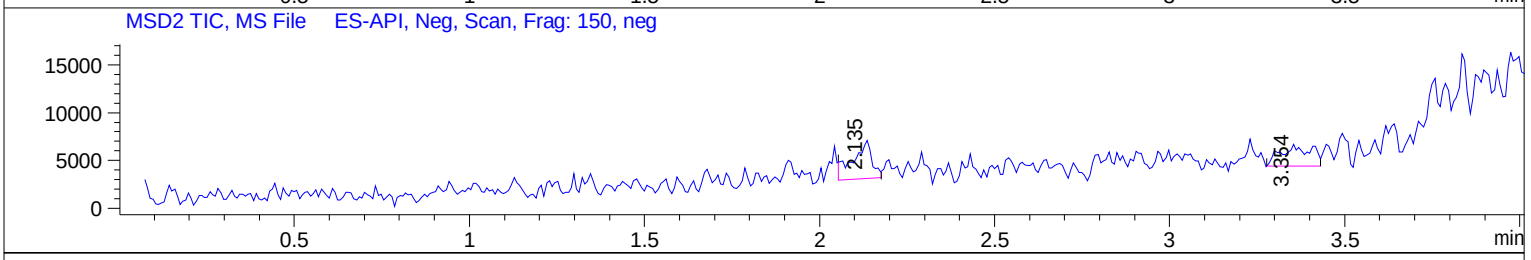


Compound 2



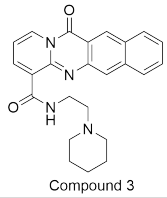

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

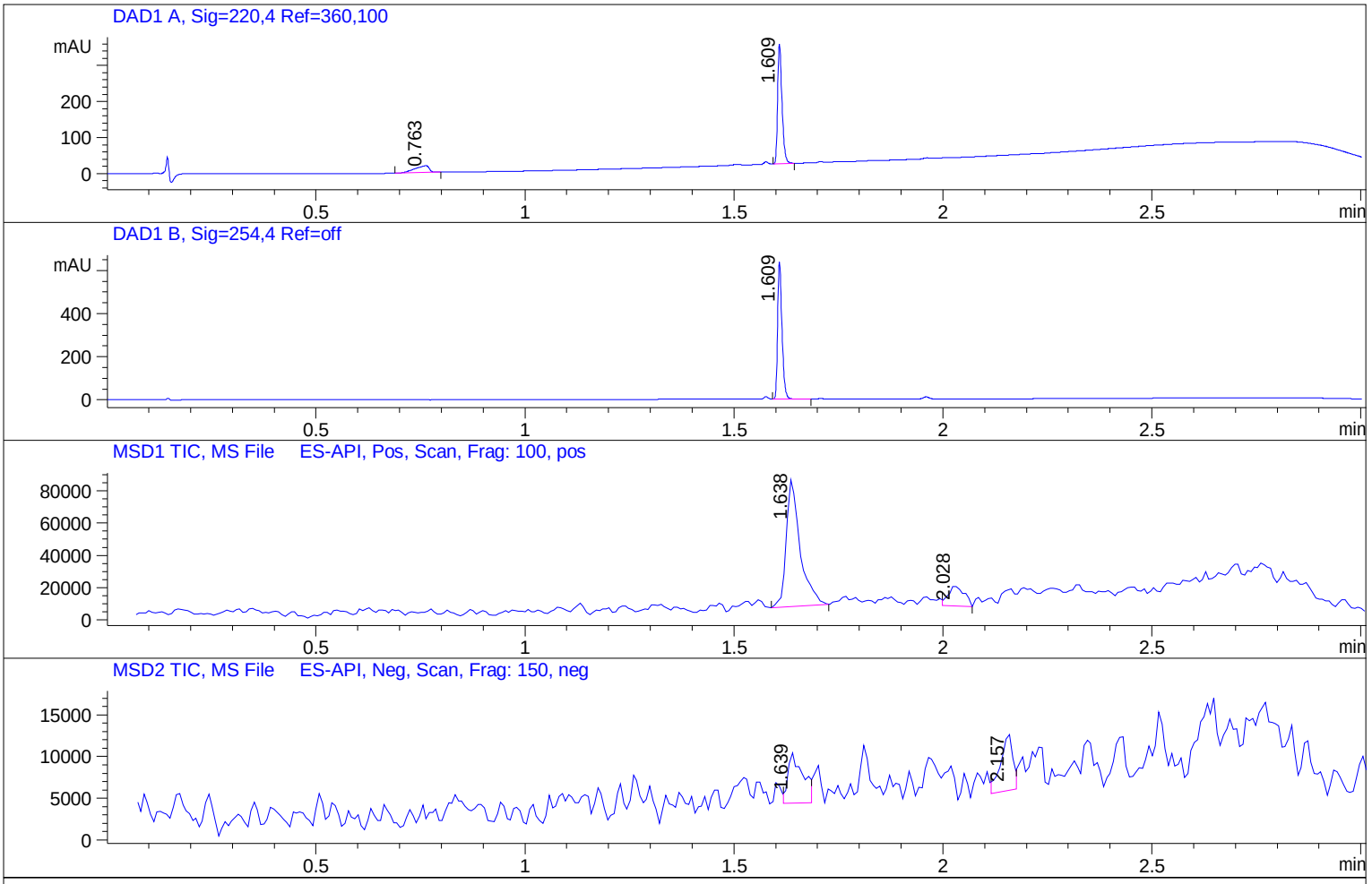
| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.22 | 0.04 | 122.00 | 43.39 | 5.25 | 115 | 155 |
| 2.04 | 0.03 | 2202.19 | 1091.98 | 94.75 | 387 | 155 |

Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.04 | 0.03 | 4258.82 | 2123.62 | 100.00 | 387 | 155 |

**File C:\EZXDATA\GERNST\08-12\LI-E02-1501.D** **Tgt Mass (EZX):**
**Injection Date : 30 Aug 12 11:55 am -0500** **Seq. Line : 0**
**Sample Name : LI-E02-150** **Location : Vial 92**
**Acq. Operator : Glen.Ernst** **Inj : 1**
**Spec. Reported : MS Integration** **Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_Agilent1'**
**Method Info : pos/neg ION MODE**



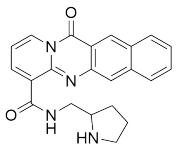

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.76 | 0.04 | 45.62 | 18.66 | 15.82 | ND | ND |
| 1.61 | 0.01 | 242.73 | 331.99 | 84.18 | 401 | ND |

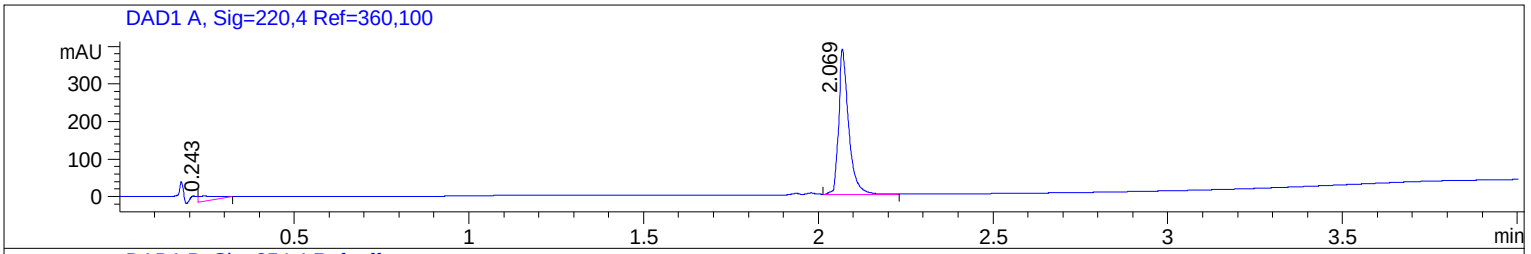
Integration Results for DAD1 B, Sig=254,4 Ref=off

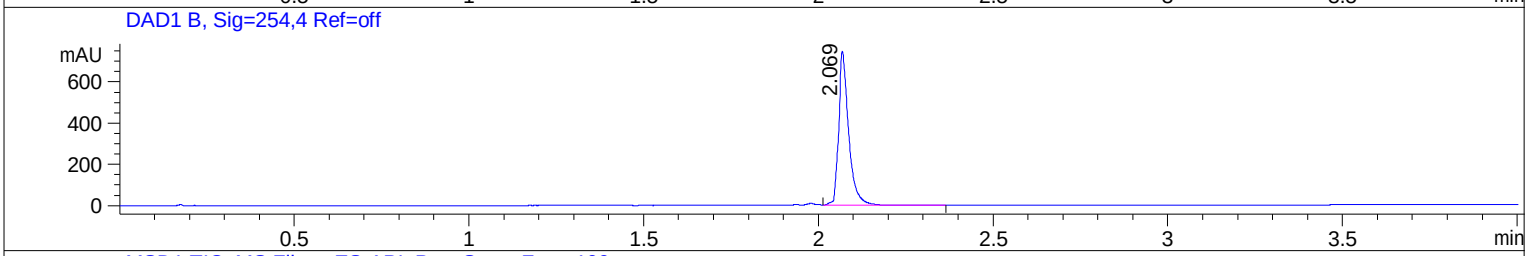
| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 1.61 | 0.01 | 464.17 | 635.71 | 100.00 | 401 | ND |

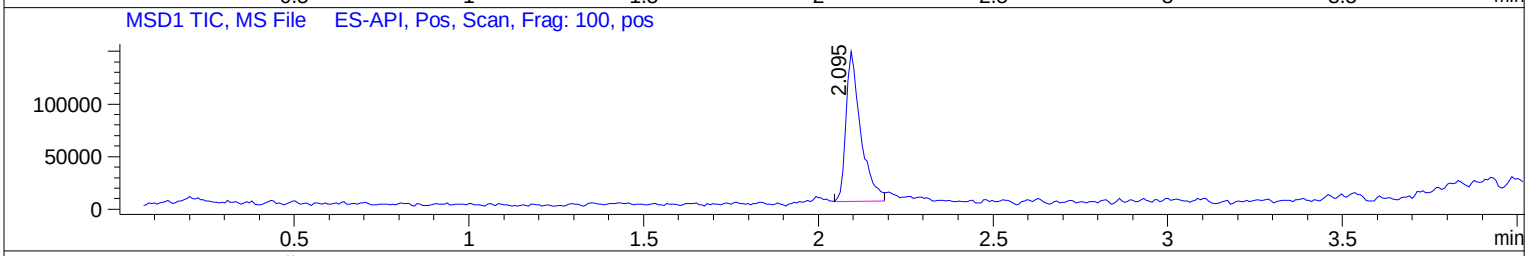
```
File ..EZXDATA\TDORADO\06-18\TED01_006_COL2_47.1.D Tgt Mass (EZX):
Injection Date    : 29 Jun 18   2:43 pm -0500          Seq. Line : 0
Sample Name       : TED01_006_col2_47.            Location  : Vial 15
Acq. Operator     : tony.dorado                          Inj : 1
Spec. Reported    : MS Integration                  Inj Volume : 2 ul
Acq. Method       : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M
Analysis Method   : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M
Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'
Method Info : pos/neg ION MODE
```

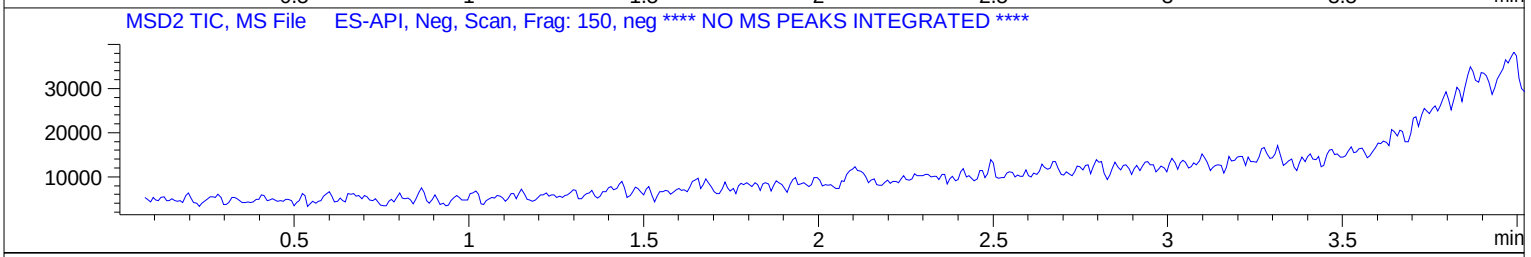


Compound 4



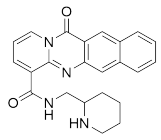

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.24 | 0.05 | 45.13 | 13.01 | 5.52 | 117 | 249 |
| 2.07 | 0.03 | 772.59 | 387.34 | 94.48 | 373 | 249 |

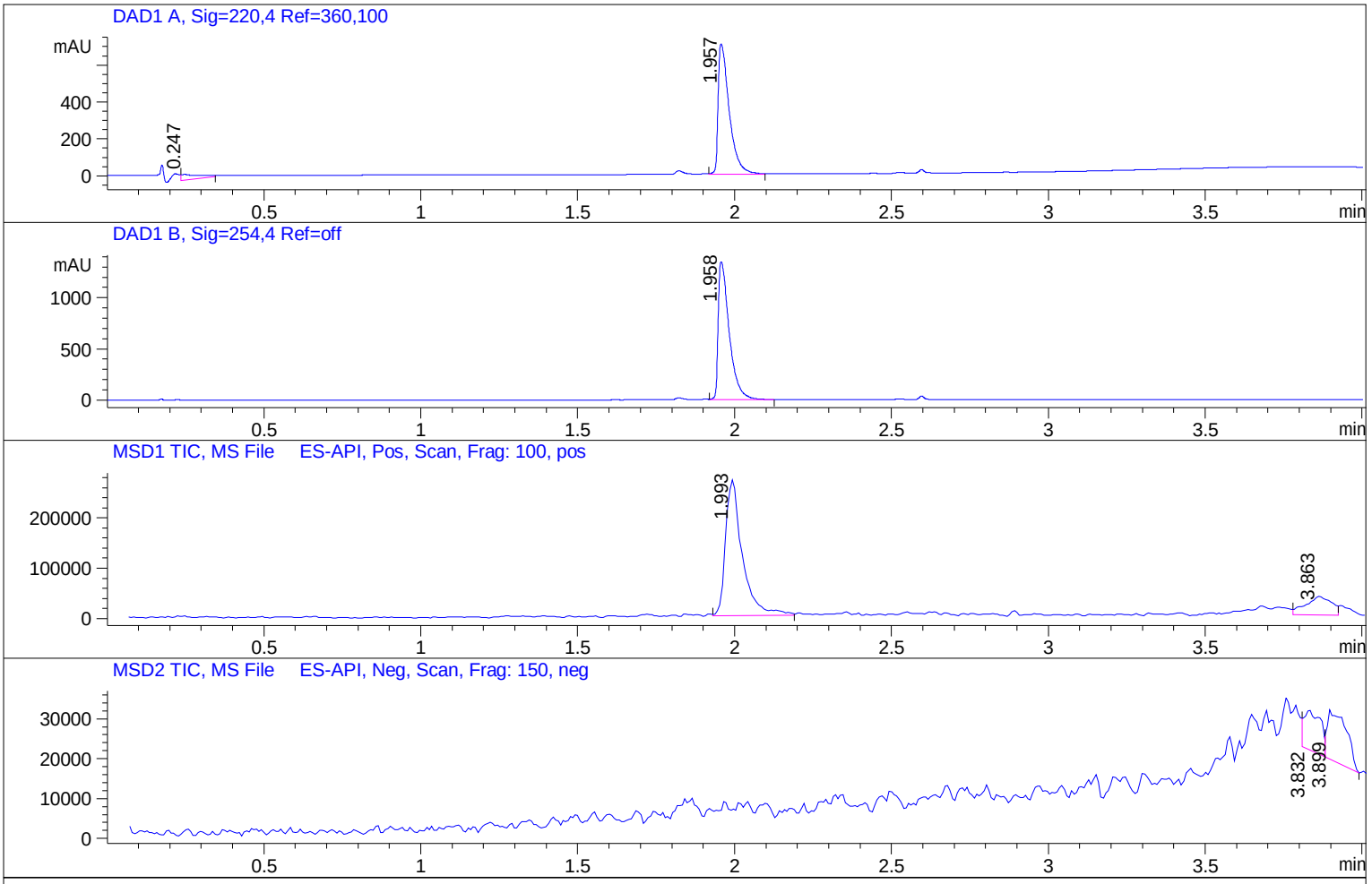
Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.07 | 0.03 | 1496.39 | 746.21 | 100.00 | 373 | 249 |

**File ..ZXDATA\TDORADO\06-18\TED01_007_HCL-SALT.1.D Tgt Mass (EZX):**
**Injection Date : 25 Jun 18 12:00 pm -0500 Seq. Line : 0**
**Sample Name : TED01_007_HCl-Salt. Location : Vial 46**
**Acq. Operator : tony.dorado Inj : 1**
**Spec. Reported : MS Integration Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



Compound 5



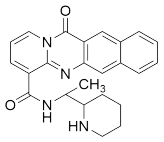

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.25 | 0.05 | 127.09 | 31.86 | 6.84 | 115 | 155 |
| 1.96 | 0.04 | 1731.85 | 705.53 | 93.16 | 387 | 249 |

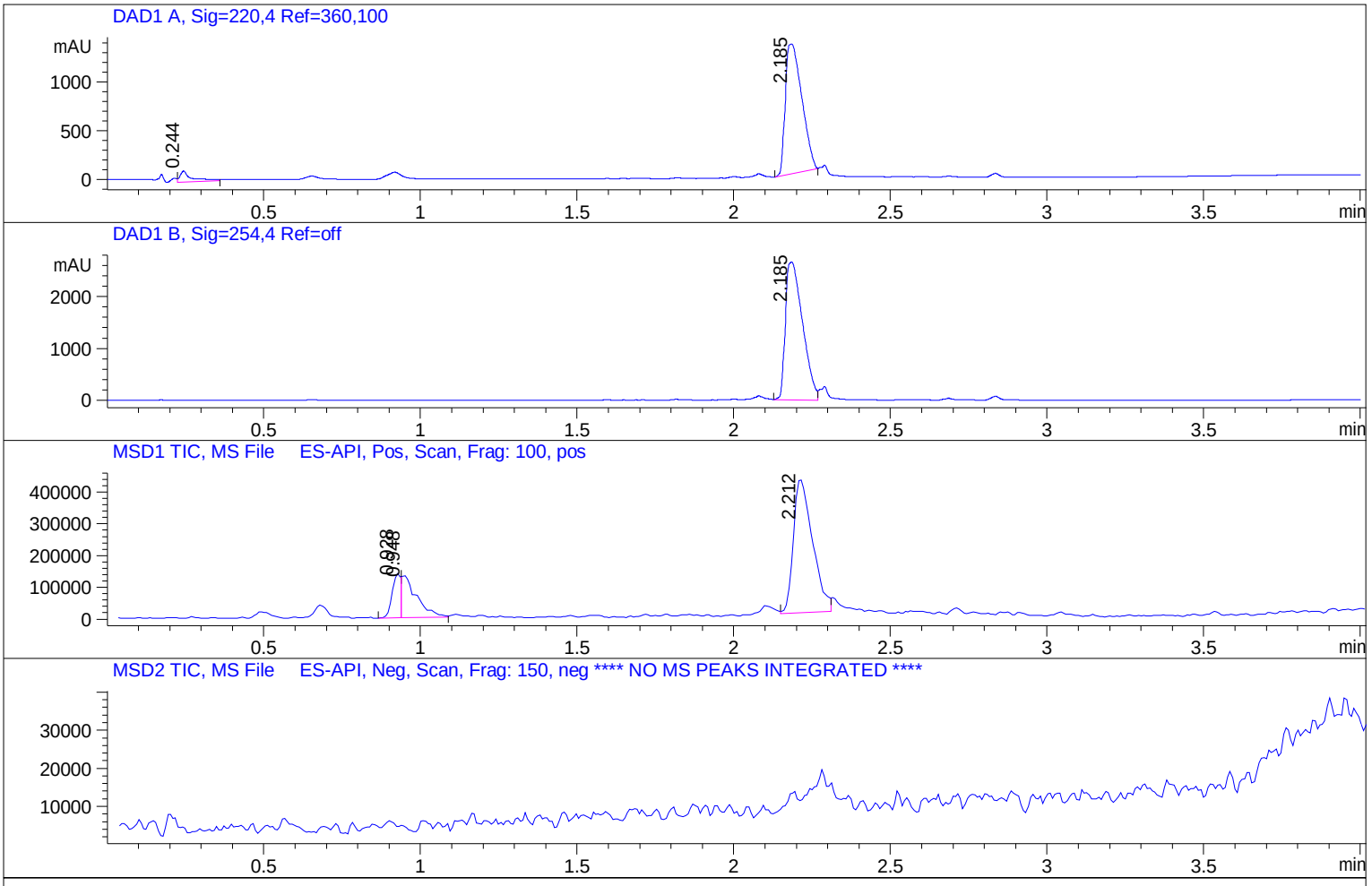
Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 1.96 | 0.04 | 3310.07 | 1348.31 | 100.00 | 387 | 249 |

**File ..DATA\TDORADO\06-18\TED01_010_ORG_FILTER.1.D Tgt Mass (EZX):**
**Injection Date : 29 Jun 18 5:57 pm -0500 Seq. Line : 0**
**Sample Name : TED01_010_org_filter. Location : Vial 25**
**Acq. Operator : tony.dorado Inj : 1**
**Spec. Reported : MS Integration Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



Compound 6



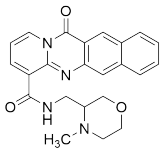

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.24 | 0.04 | 301.99 | 111.98 | 5.85 | 159 | 155 |
| 2.18 | 0.06 | 4857.28 | 1333.15 | 94.15 | 401 | 155 |

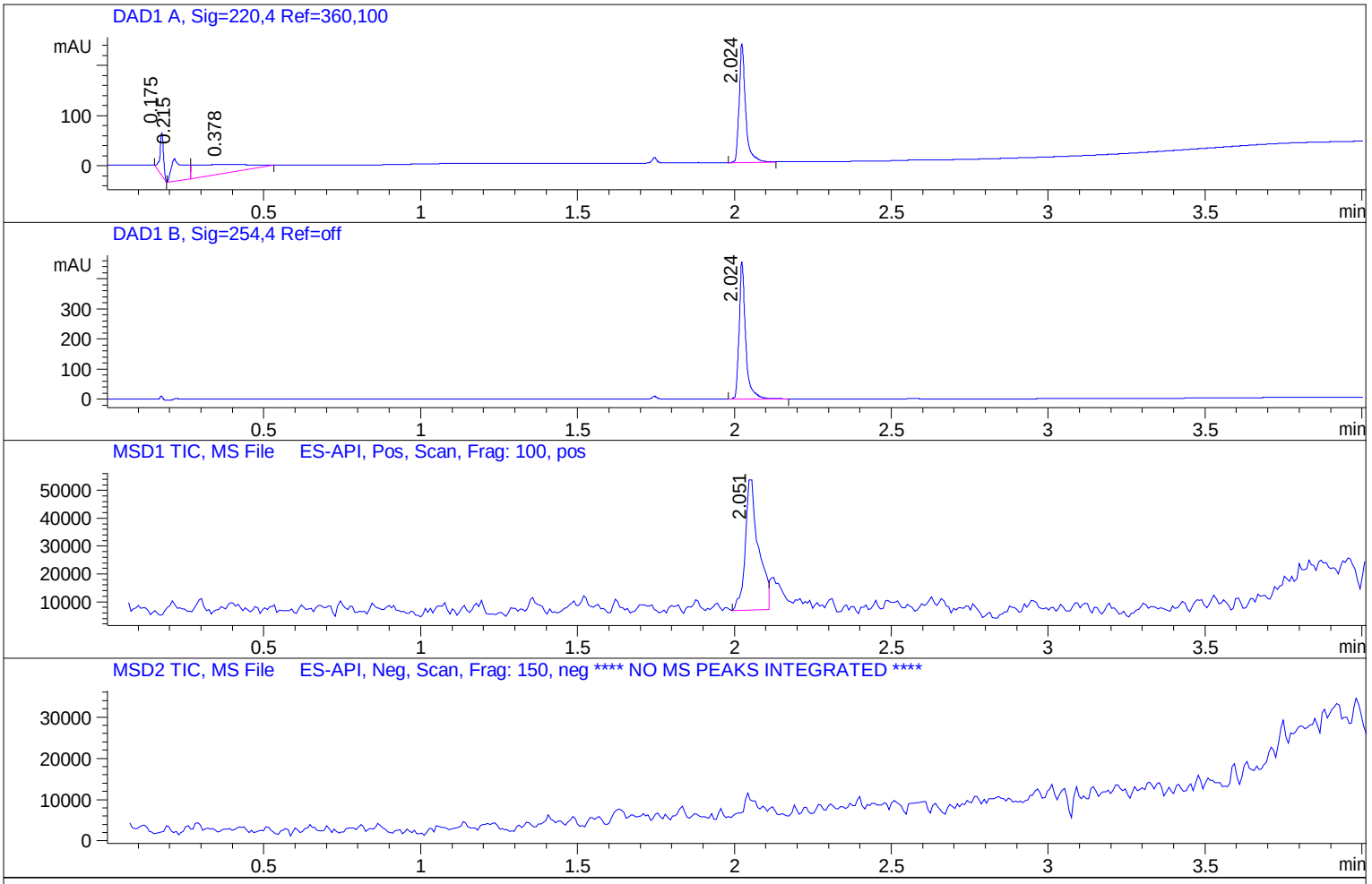
Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.18 | 0.06 | 10077.85 | 2663.99 | 100.00 | 401 | 155 |

**File C:\EZXDATA\TDORADO\07-18\TED01_014_HCL.1.D  Tgt Mass (EZX):**
**Injection Date : 6 Jul 18 12:14 pm -0500  Seq. Line : 0**
**Sample Name : TED01_014_HCl.  Location : Vial 75**
**Acq. Operator : tony.dorado  Inj : 1**
**Spec. Reported : MS Integration  Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



Compound 7



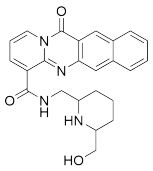

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.17 | 0.01 | 68.12 | 84.70 | 8.98 | 157 | 155 |
| 0.21 | 0.04 | 129.44 | 44.29 | 17.07 | 157 | 155 |
| 0.38 | 0.16 | 221.45 | 17.28 | 29.20 | 157 | 155 |
| 2.02 | 0.02 | 339.40 | 236.40 | 44.75 | 403 | 249 |

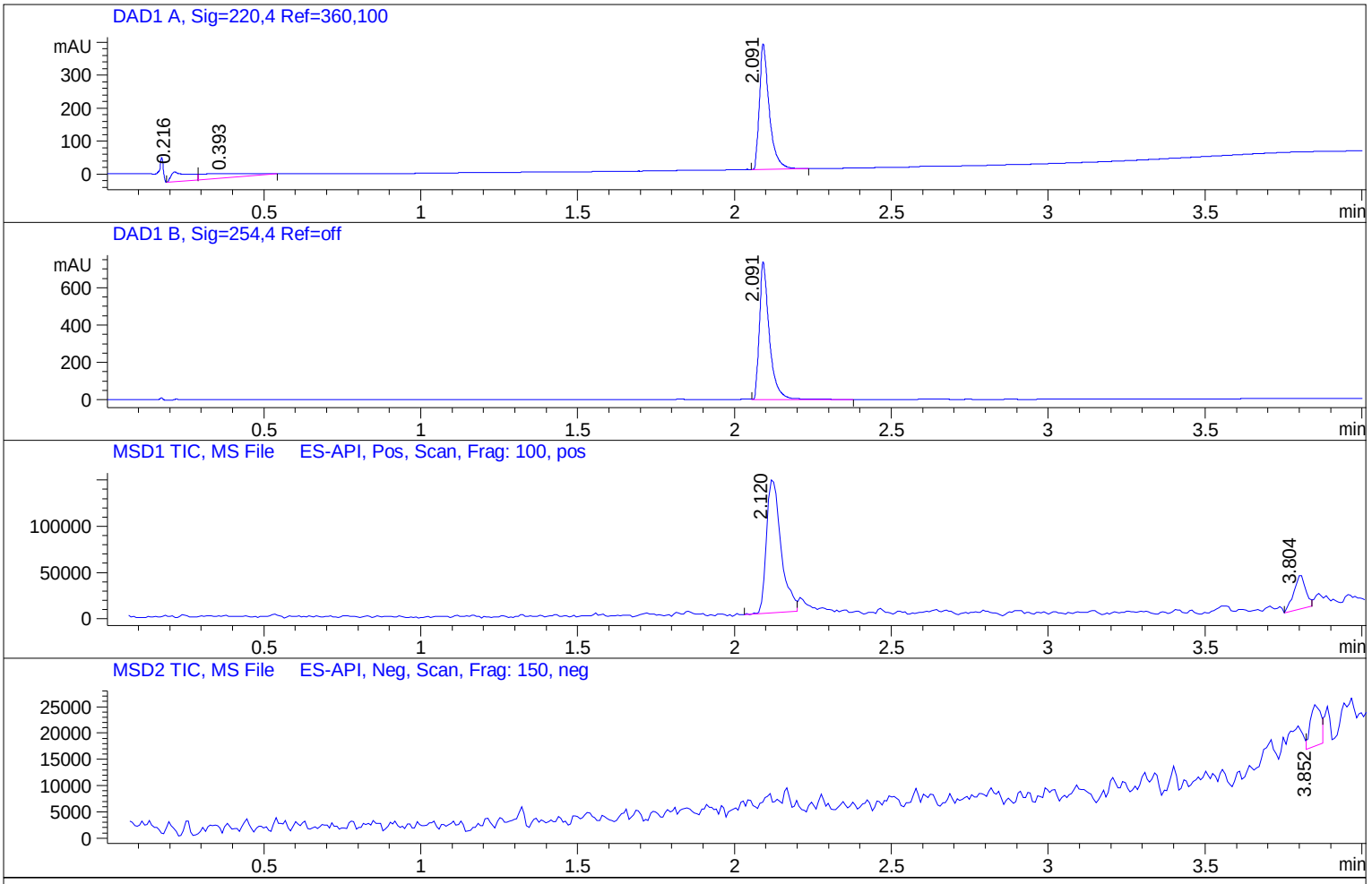
Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.02 | 0.02 | 655.26 | 455.55 | 100.00 | 403 | 249 |

**File C:\EZXDATA\TDORADO\07-18\TED01_016_HCL.1.D  Tgt Mass (EZX):**
**Injection Date : 17 Jul 18 12:14 pm -0500  Seq. Line : 0**
**Sample Name : TED01_016_HCl.  Location : Vial 16**
**Acq. Operator : tony.dorado  Inj : 1**
**Spec. Reported : MS Integration  Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



Compound 8



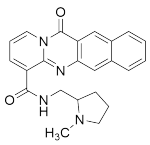

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.22 | 0.05 | 121.23 | 30.46 | 11.04 | 159 | 155 |
| 0.39 | 0.14 | 147.05 | 12.16 | 13.39 | 159 | 155 |
| 2.09 | 0.03 | 829.58 | 380.42 | 75.56 | 417 | 249 |

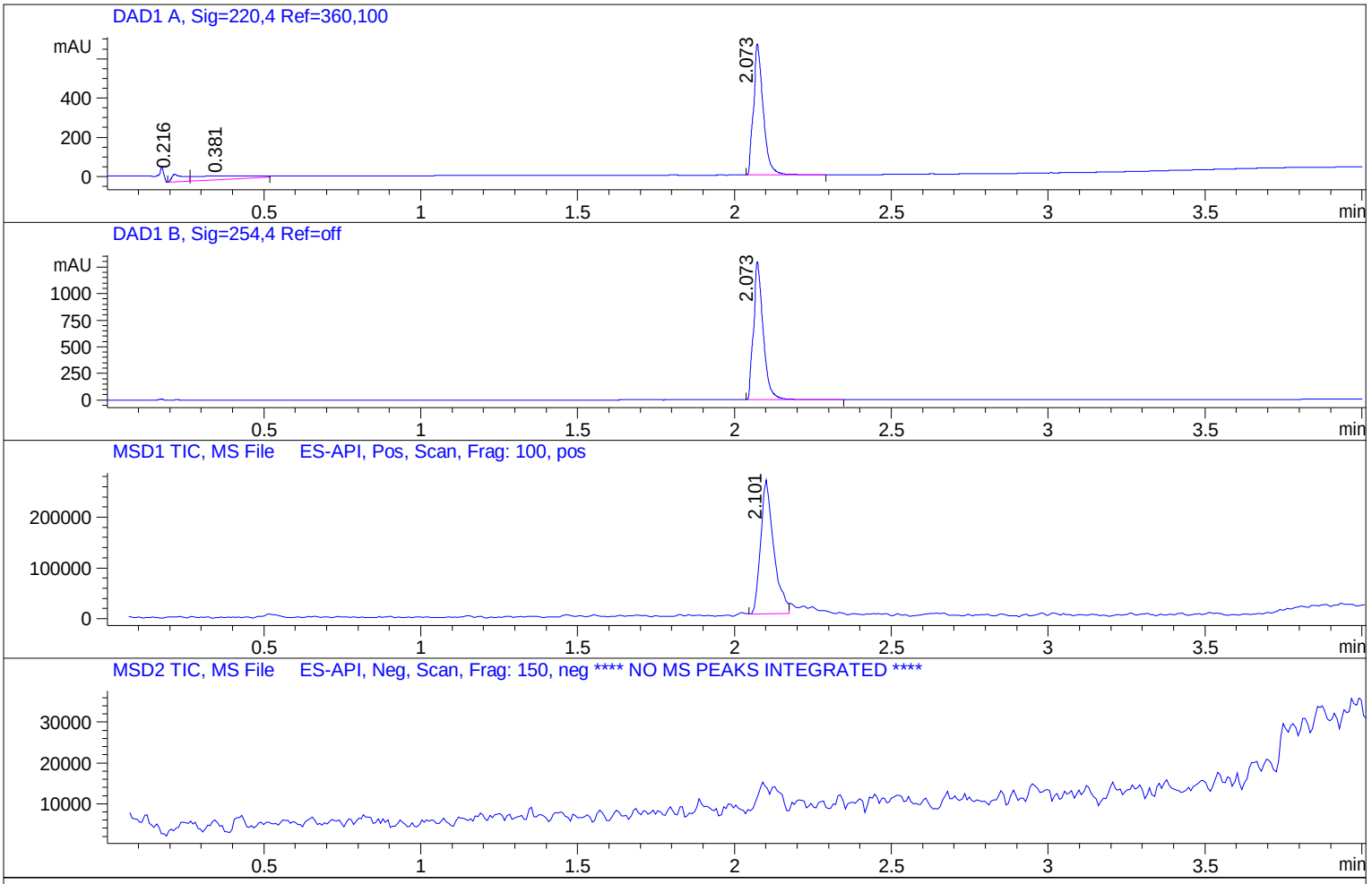
Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.09 | 0.03 | 1619.72 | 737.77 | 100.00 | 417 | 155 |

**File C:\EZXDATA\TDORADO\07-18\TED01_012_HCL.1.D  Tgt Mass (EZX):**
**Injection Date : 5 Jul 18 10:48 am -0500  Seq. Line : 0**
**Sample Name : TED01_012_HCl.  Location : Vial 12**
**Acq. Operator : tony.dorado  Inj : 1**
**Spec. Reported : MS Integration  Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



Compound 9



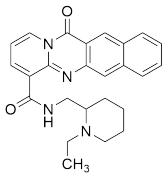

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.22 | 0.04 | 112.35 | 40.21 | 6.32 | 159 | 155 |
| 0.38 | 0.16 | 228.82 | 17.06 | 12.87 | 159 | 249 |
| 2.07 | 0.03 | 1436.61 | 668.21 | 80.81 | 387 | 249 |

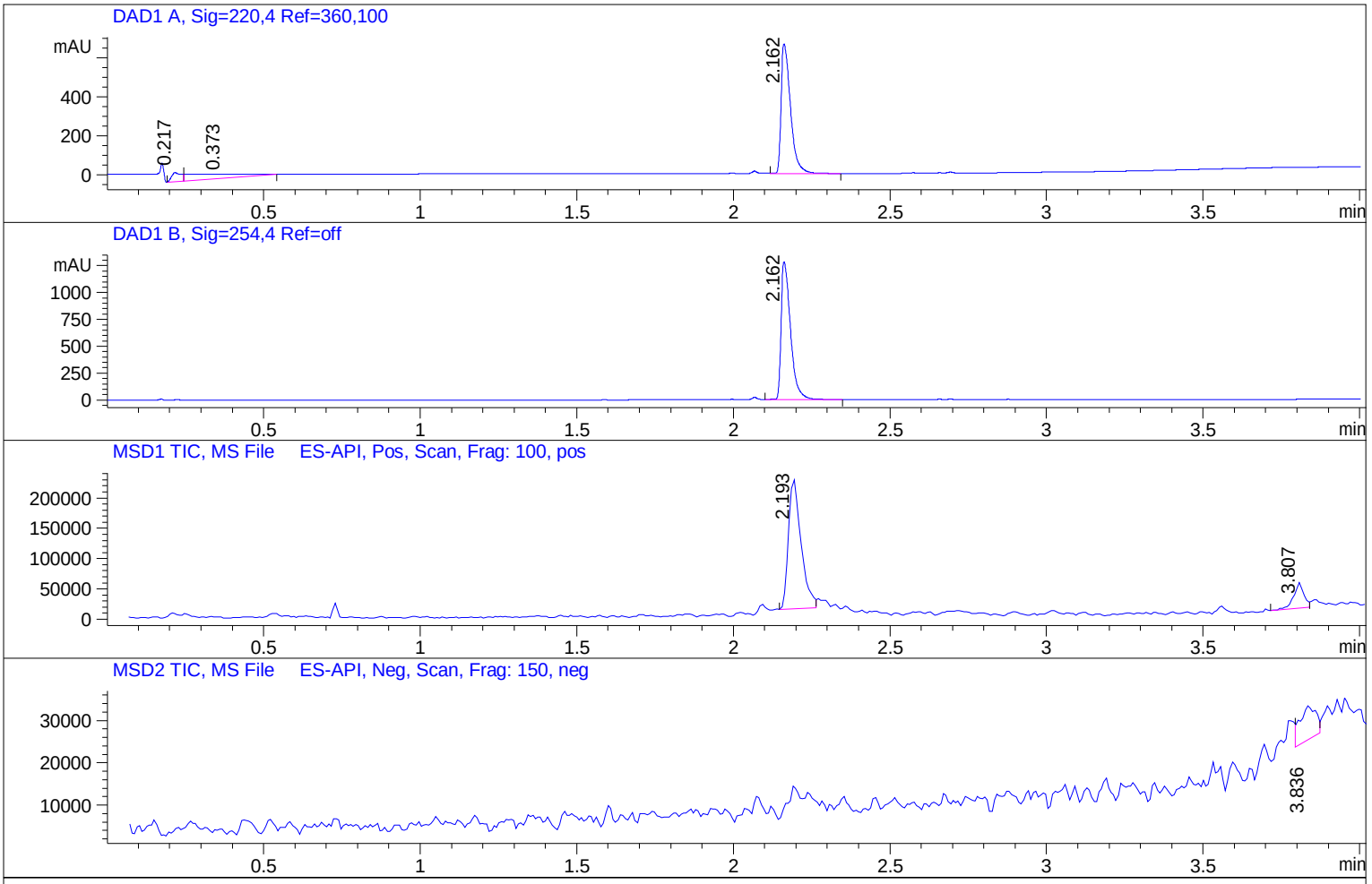
Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.07 | 0.03 | 2786.23 | 1297.00 | 100.00 | 387 | 249 |

**File ..EZXDATA\TDORADO\06-18\TED01_009_HCLSALT.1.D Tgt Mass (EZX):**
**Injection Date : 27 Jun 18 12:21 pm -0500 Seq. Line : 0**
**Sample Name : TED01_009_HClSalt. Location : Vial 18**
**Acq. Operator : tony.dorado Inj : 1**
**Spec. Reported : MS Integration Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



Compound 10



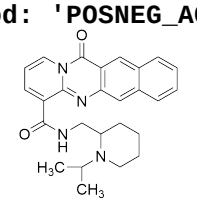

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.22 | 0.03 | 101.69 | 47.67 | 5.57 | 143 | 155 |
| 0.37 | 0.17 | 328.68 | 22.16 | 18.02 | 159 | 249 |
| 2.16 | 0.03 | 1393.67 | 666.52 | 76.41 | 415 | 249 |

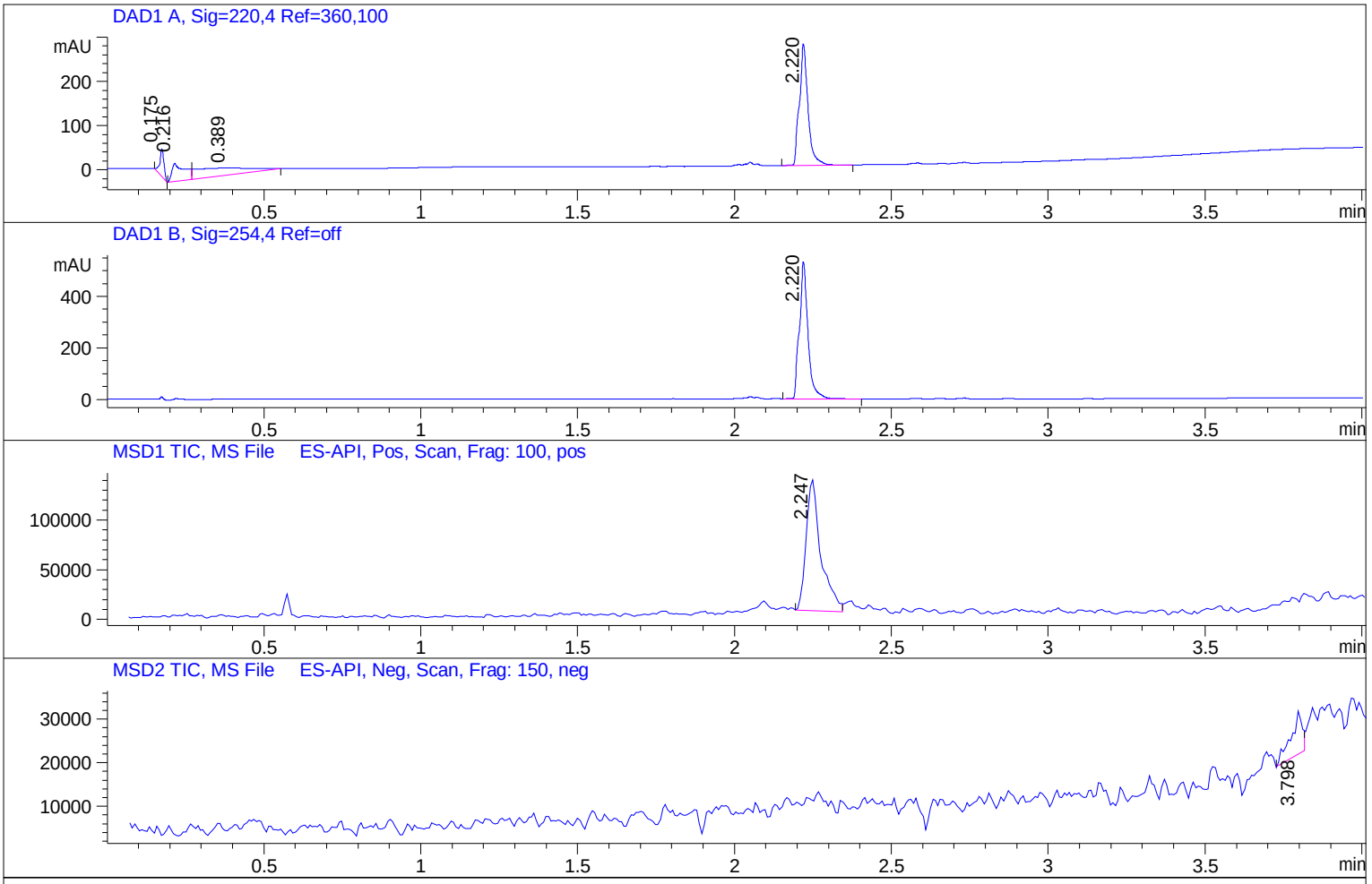
Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.16 | 0.03 | 2699.79 | 1283.52 | 100.00 | 415 | 249 |

**File C:\EZXDATA\TDORADO\07-18\TED01_011_HCL.1.D  Tgt Mass (EZX):**
**Injection Date : 5 Jul 18 10:42 am -0500  Seq. Line : 0**
**Sample Name : TED01_011_HCl.  Location : Vial 11**
**Acq. Operator : tony.dorado  Inj : 1**
**Spec. Reported : MS Integration  Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



Compound 11



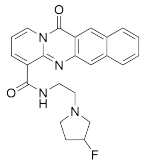

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

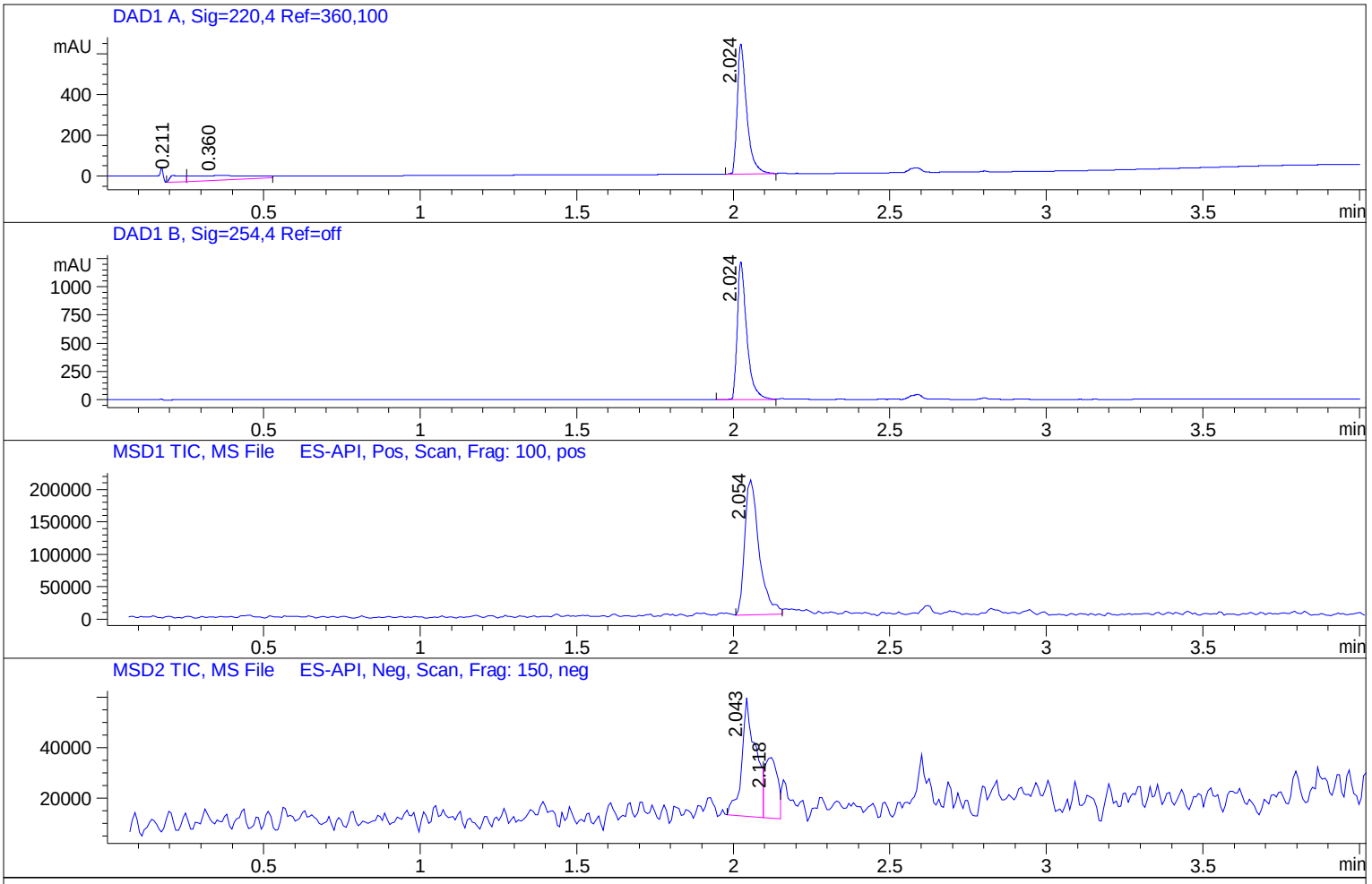
| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.17 | 0.01 | 56.93 | 62.34 | 6.23 | 159 | 155 |
| 0.22 | 0.04 | 116.60 | 41.12 | 12.75 | 157 | 155 |
| 0.39 | 0.16 | 214.83 | 15.45 | 23.50 | 159 | 155 |
| 2.22 | 0.03 | 525.92 | 274.94 | 57.52 | 429 | 249 |

Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.22 | 0.03 | 1021.18 | 532.48 | 100.00 | 429 | 249 |

**File C:\EZXDATA\TDORADO\02-20\317.1.D** **Tgt Mass (EZX):**
**Injection Date : 6 Feb 20 8:04 pm -0500** **Seq. Line : 0**
**Sample Name : 317.** **Location : Vial 71**
**Acq. Operator : tony.dorado** **Inj : 1**
**Spec. Reported : MS Integration** **Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**


Compound 12



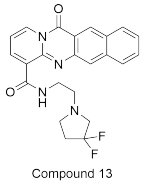

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.21 | 0.04 | 100.55 | 33.49 | 5.69 | ND | 379 |
| 0.36 | 0.17 | 317.92 | 22.41 | 18.00 | 130 | 379 |
| 2.02 | 0.03 | 1347.64 | 639.25 | 76.31 | 405 | 385 |

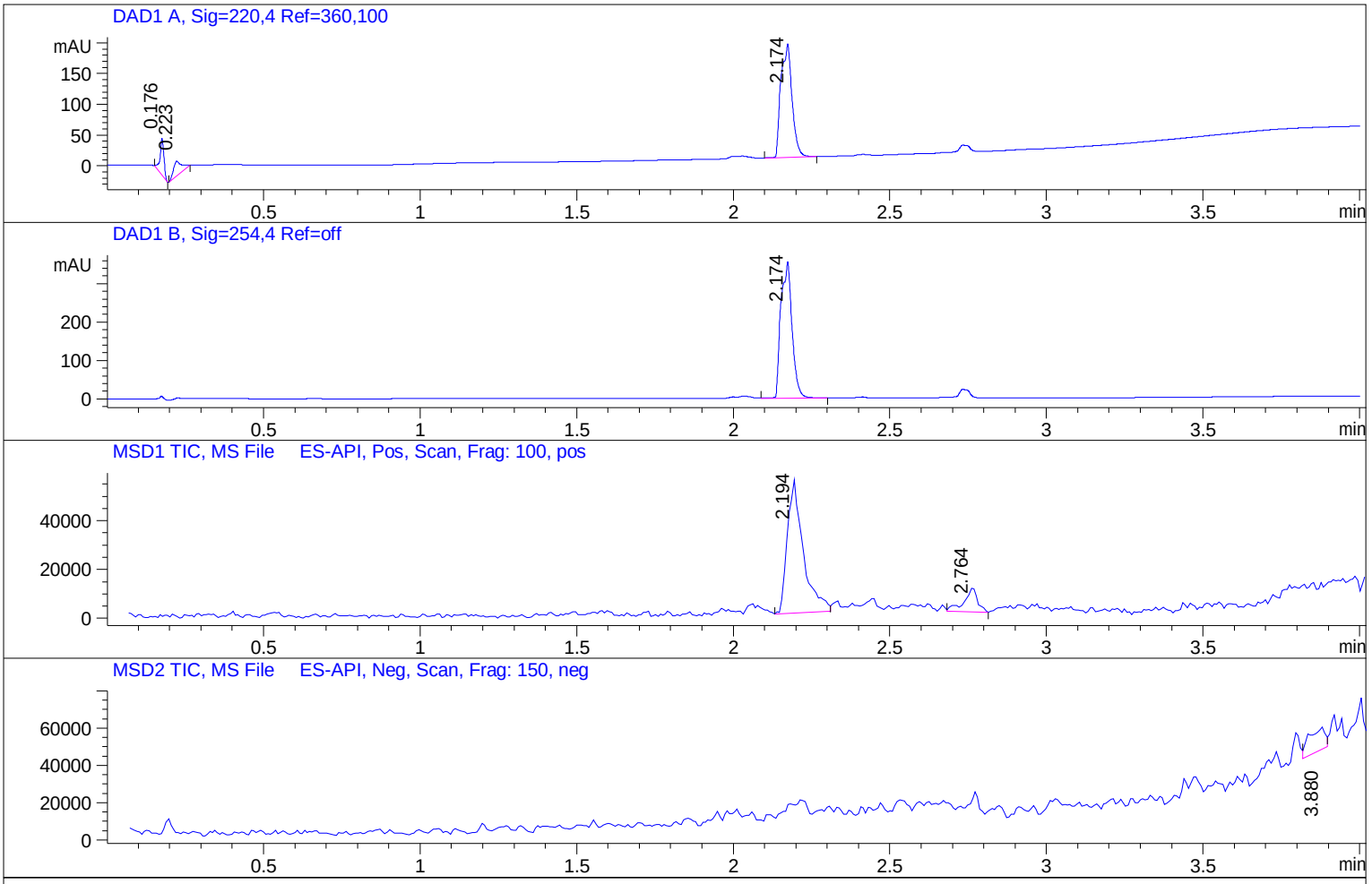
Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.02 | 0.03 | 2561.70 | 1217.49 | 100.00 | 405 | 385 |

File C:\EZXDATA\TDORADO\11-18\059_HCL.1.D Tgt Mass (EZX):
Injection Date : 6 Nov 18 3:15 pm -0500 Seq. Line : 0
Sample Name : 059_HCl. Location : Vial 49
Acq. Operator : tony.dorado Inj : 1
Spec. Reported : MS Integration Inj Volume : 2 ul
Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M
Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M
Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'
Method Info : pos/neg ION MODE



Compound 13



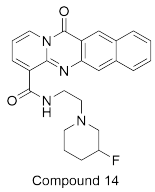

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.18 | 0.01 | 51.31 | 60.18 | 9.32 | ND | 155 |
| 0.22 | 0.03 | 43.90 | 24.15 | 7.98 | ND | 155 |
| 2.17 | 0.03 | 455.16 | 184.34 | 82.70 | 445 | 249 |

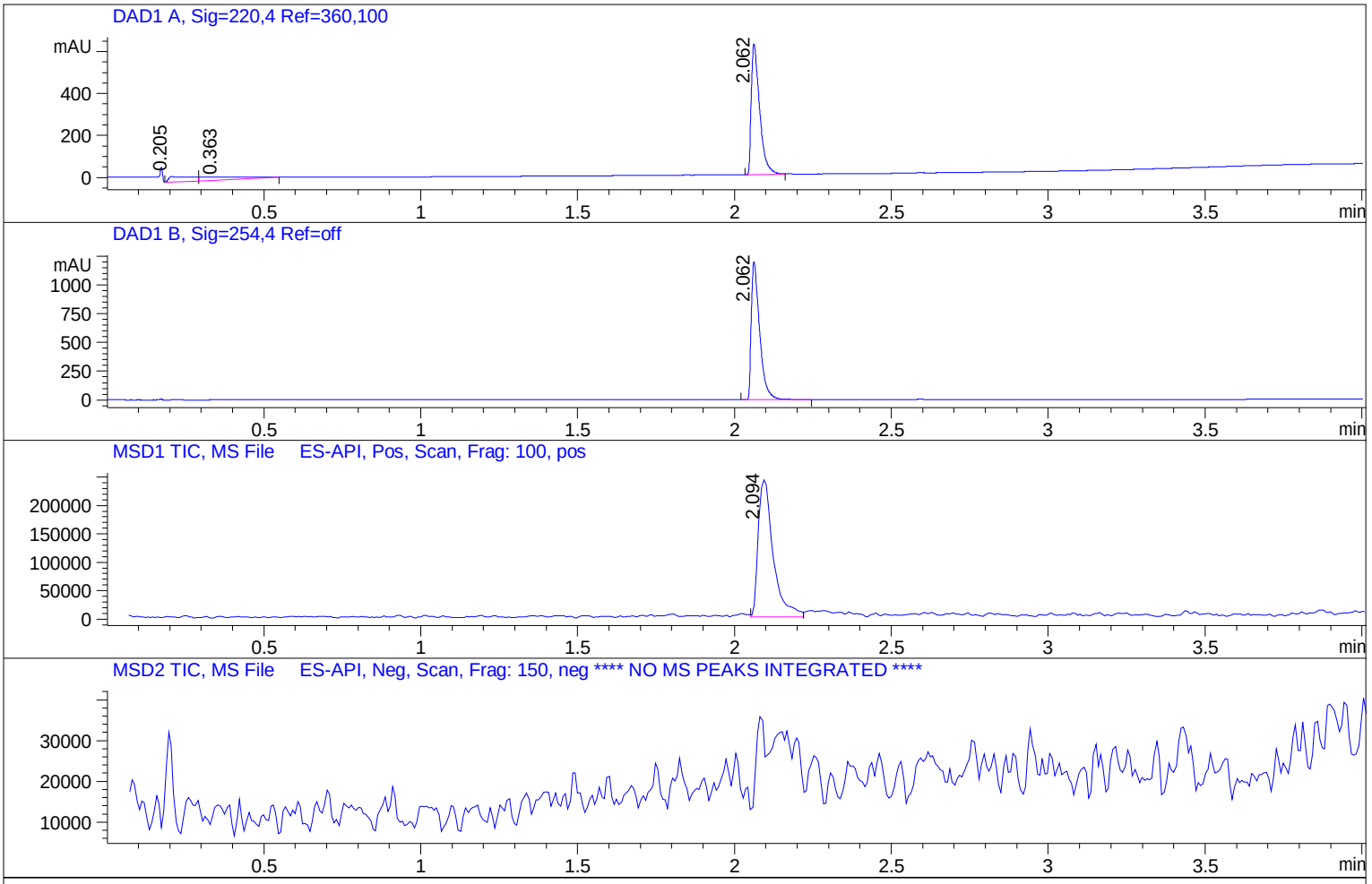
Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.17 | 0.03 | 882.92 | 354.87 | 100.00 | 445 | 249 |

**File C:\EZXDATA\TDORADO\02-20\332.1.D** **Tgt Mass (EZX):**
**Injection Date : 17 Feb 20 11:57 am -0500** **Seq. Line : 0**
**Sample Name : 332.** **Location : Vial 17**
**Acq. Operator : tony.dorado** **Inj : 1**
**Spec. Reported : MS Integration** **Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



Compound 14



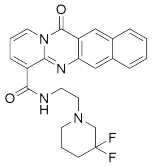

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.21 | 0.06 | 124.78 | 27.67 | 8.80 | ND | 379 |
| 0.36 | 0.12 | 139.72 | 13.48 | 9.85 | ND | 379 |
| 2.06 | 0.03 | 1153.95 | 621.49 | 81.35 | 419 | 155 |

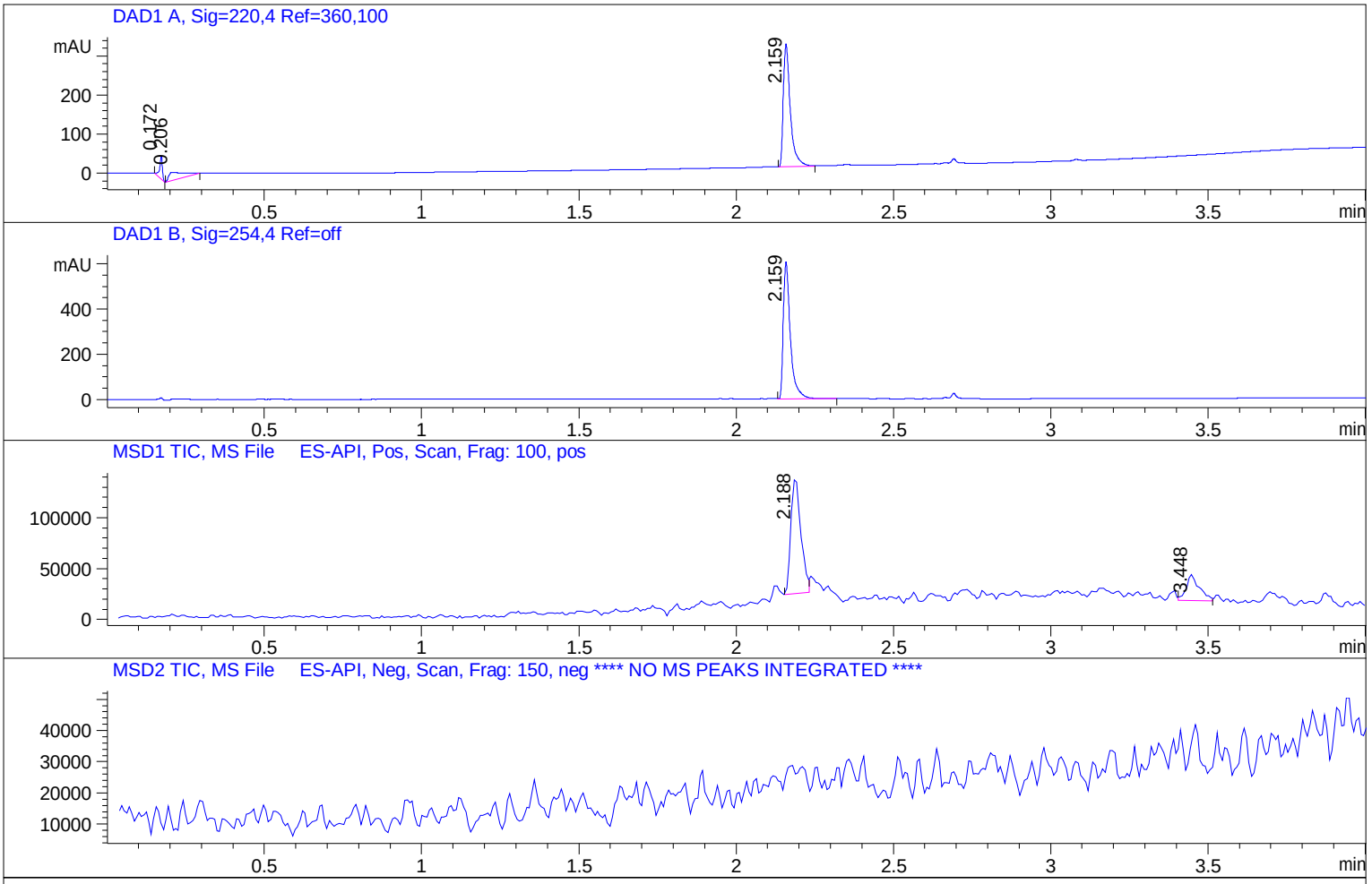
Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.06 | 0.03 | 2234.48 | 1197.68 | 100.00 | 419 | 379 |

**File C:\EZXDATA\TDORADO\02-20\333.1.D** **Tgt Mass (EZX):**
**Injection Date : 18 Feb 20 7:25 pm -0500** **Seq. Line : 0**
**Sample Name : 333.** **Location : Vial 53**
**Acq. Operator : tony.dorado** **Inj : 1**
**Spec. Reported : MS Integration** **Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



Compound 15



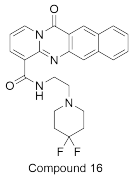

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

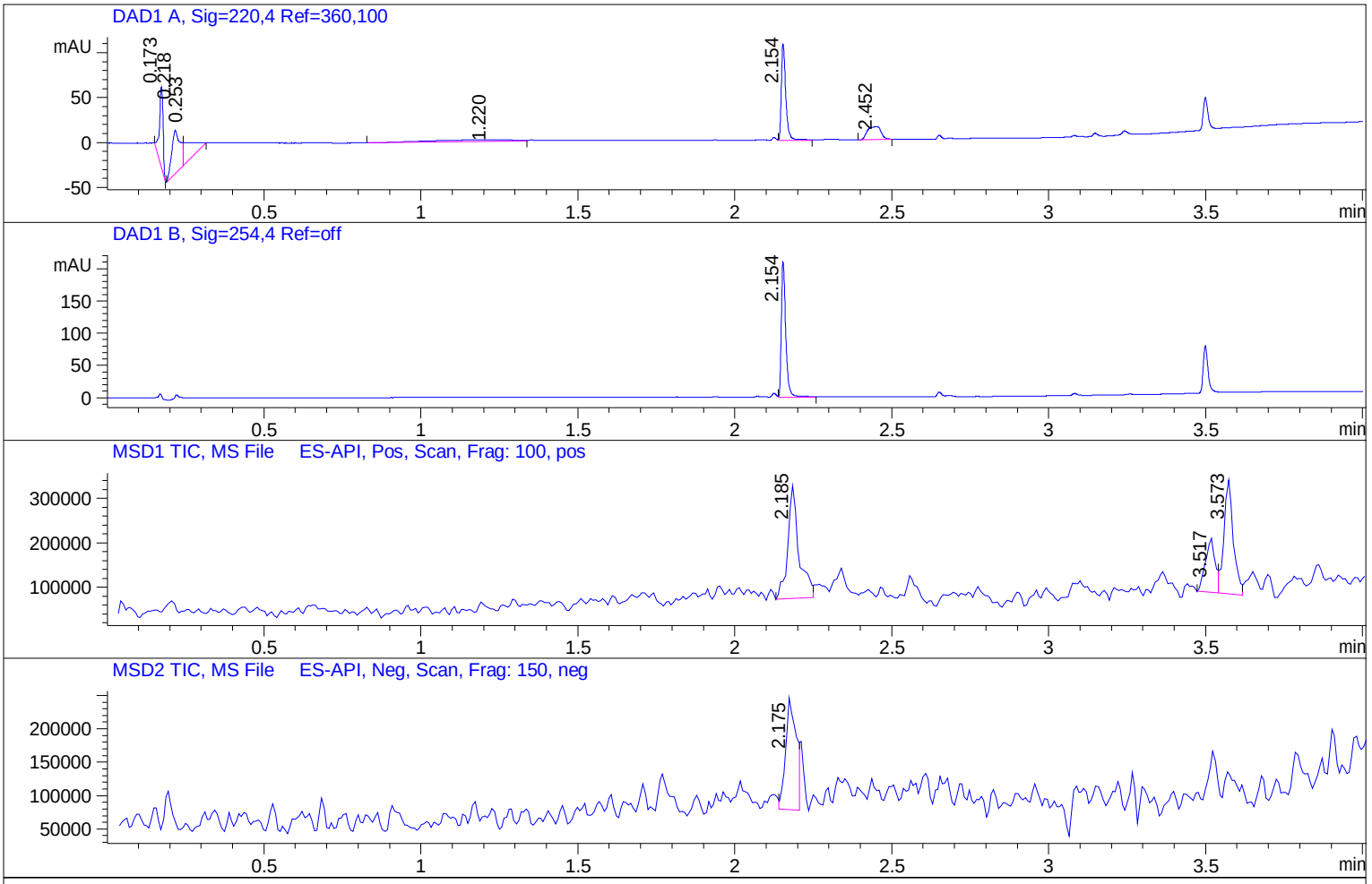
| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.17 | 0.01 | 35.79 | 58.55 | 6.03 | 243 | 155 |
| 0.21 | 0.04 | 68.54 | 21.53 | 11.55 | ND | 285 |
| 2.16 | 0.02 | 489.25 | 314.51 | 82.42 | 437 | 155 |

Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.16 | 0.02 | 947.96 | 606.62 | 100.00 | 437 | 155 |

File ..r\Walkup\DataFiles\tdorado\09-20\384-2254.D Tgt Mass (EZX):
Injection Date : 22-Sep-20, 13:46:51 Seq. Line : 0
Sample Name : 384 Location : 36
Acq. Operator : sysadmin Inj : 1
Spec. Reported : MS Integration Inj Volume : 2 ul
Acq. Method : C:\Users\Public\Documents\ChemStation\1\Methods\POSNEG_AGILENT1.M
Analysis Method : C:\Users\Public\Documents\ChemStation\1\Methods\POSNEG_AGILENT1.M
Sample Info : 384 WalkUp method: 'POSNEG_AGILENT1' Target:
Method Info : pos/neg ION MODE



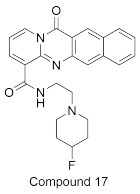

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.17 | 0.01 | 71.25 | 89.31 | 17.67 | 130 | 395 |
| 0.22 | 0.03 | 88.24 | 48.06 | 21.88 | 130 | 155 |
| 0.25 | 0.03 | 57.02 | 21.98 | 14.14 | 130 | 249 |
| 1.22 | 0.26 | 36.64 | 1.69 | 9.09 | 130 | 155 |
| 2.15 | 0.02 | 106.39 | 106.98 | 26.38 | 437 | 155 |
| 2.45 | 0.05 | 43.72 | 14.37 | 10.84 | 437 | 155 |

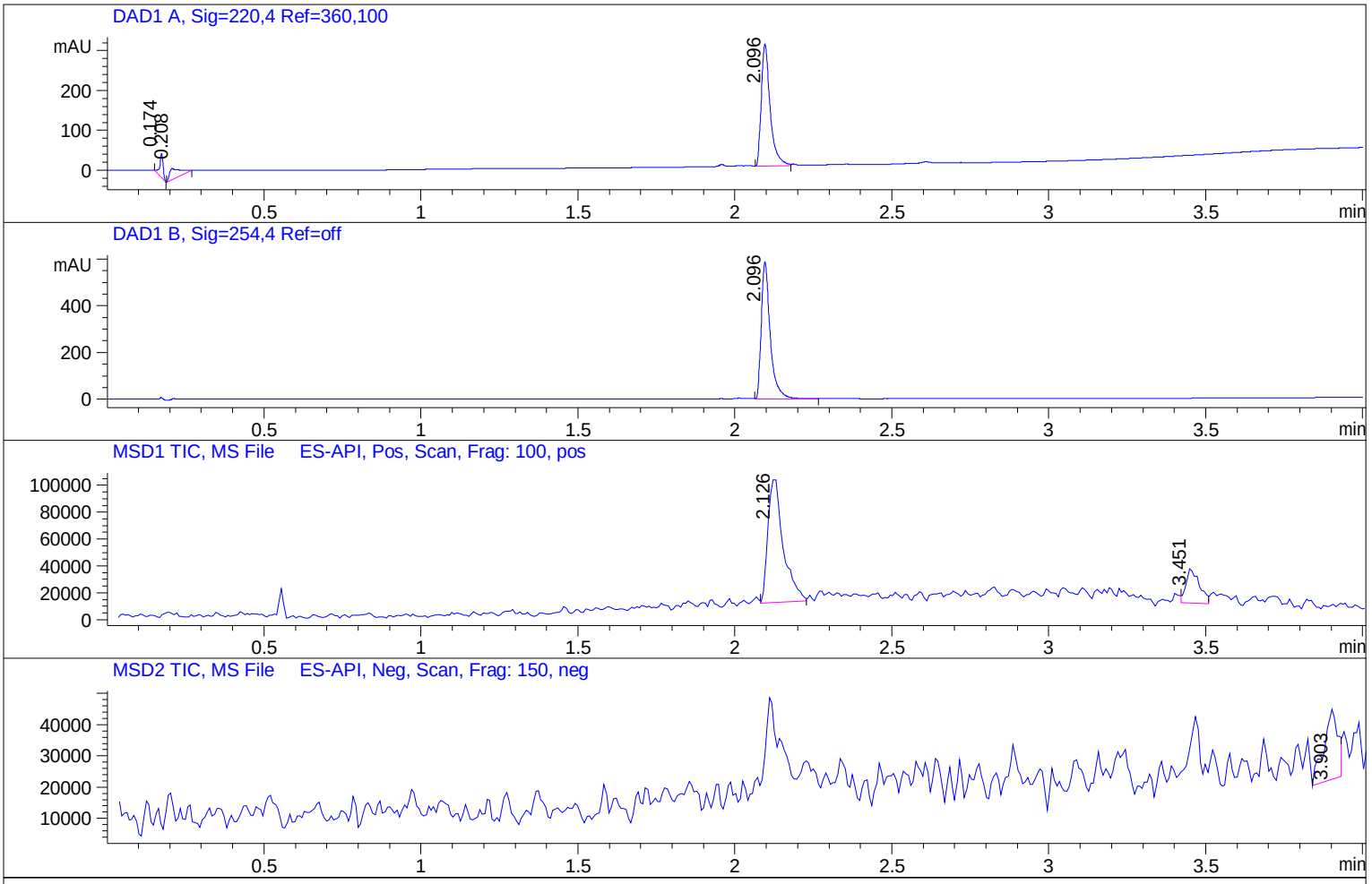
Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.17 | 0.01 | 5.52 | 8.17 | 2.50 | 130 | 395 |
| 0.22 | 0.02 | 8.43 | 6.96 | 3.82 | 130 | 155 |
| 2.15 | 0.02 | 206.68 | 208.92 | 93.68 | 437 | 155 |

**File C:\EZXDATA\TDORADO\02-20\316.1.D** **Tgt Mass (EZX):**
**Injection Date : 6 Feb 20 7:58 pm -0500** **Seq. Line : 0**
**Sample Name : 316.** **Location : Vial 70**
**Acq. Operator : tony.dorado** **Inj : 1**
**Spec. Reported : MS Integration** **Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



Compound 17



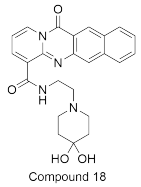

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.17 | 0.01 | 44.47 | 59.72 | 6.29 | 235 | 285 |
| 0.21 | 0.03 | 64.58 | 28.08 | 9.13 | 116 | 379 |
| 2.10 | 0.03 | 598.43 | 306.02 | 84.59 | 419 | 385 |

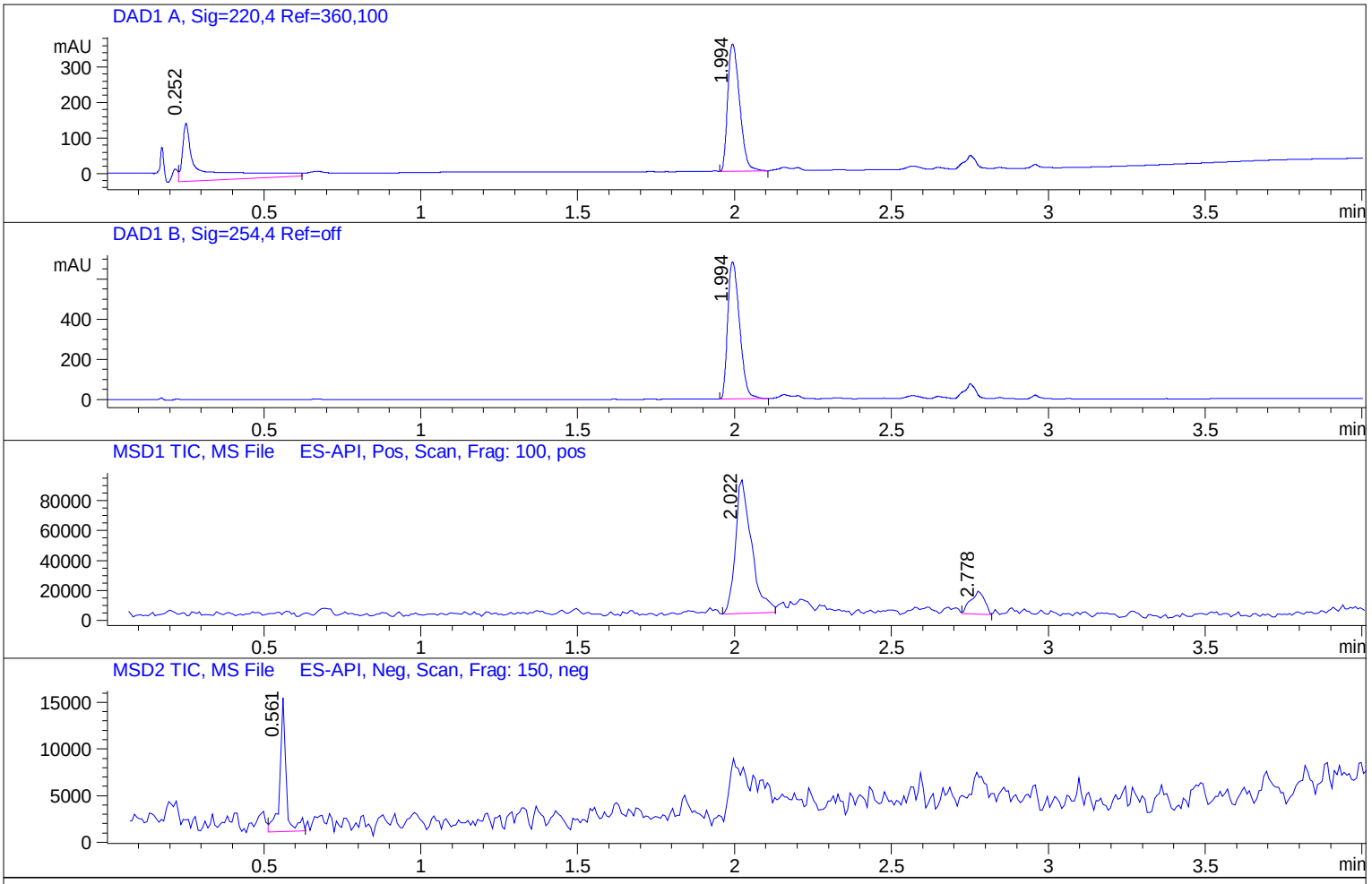
Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.10 | 0.03 | 1158.19 | 586.61 | 100.00 | 419 | 379 |

**File C:\EZXDATA\TDORADO\12-18\077_HCL.1.D** **Tgt Mass (EZX):**
**Injection Date : 3 Dec 18 12:20 pm -0500** **Seq. Line : 0**
**Sample Name : 077_HCl.** **Location : Vial 19**
**Acq. Operator : tony.dorado** **Inj : 1**
**Spec. Reported : MS Integration** **Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



Compound 18



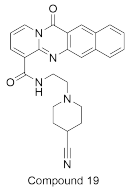

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

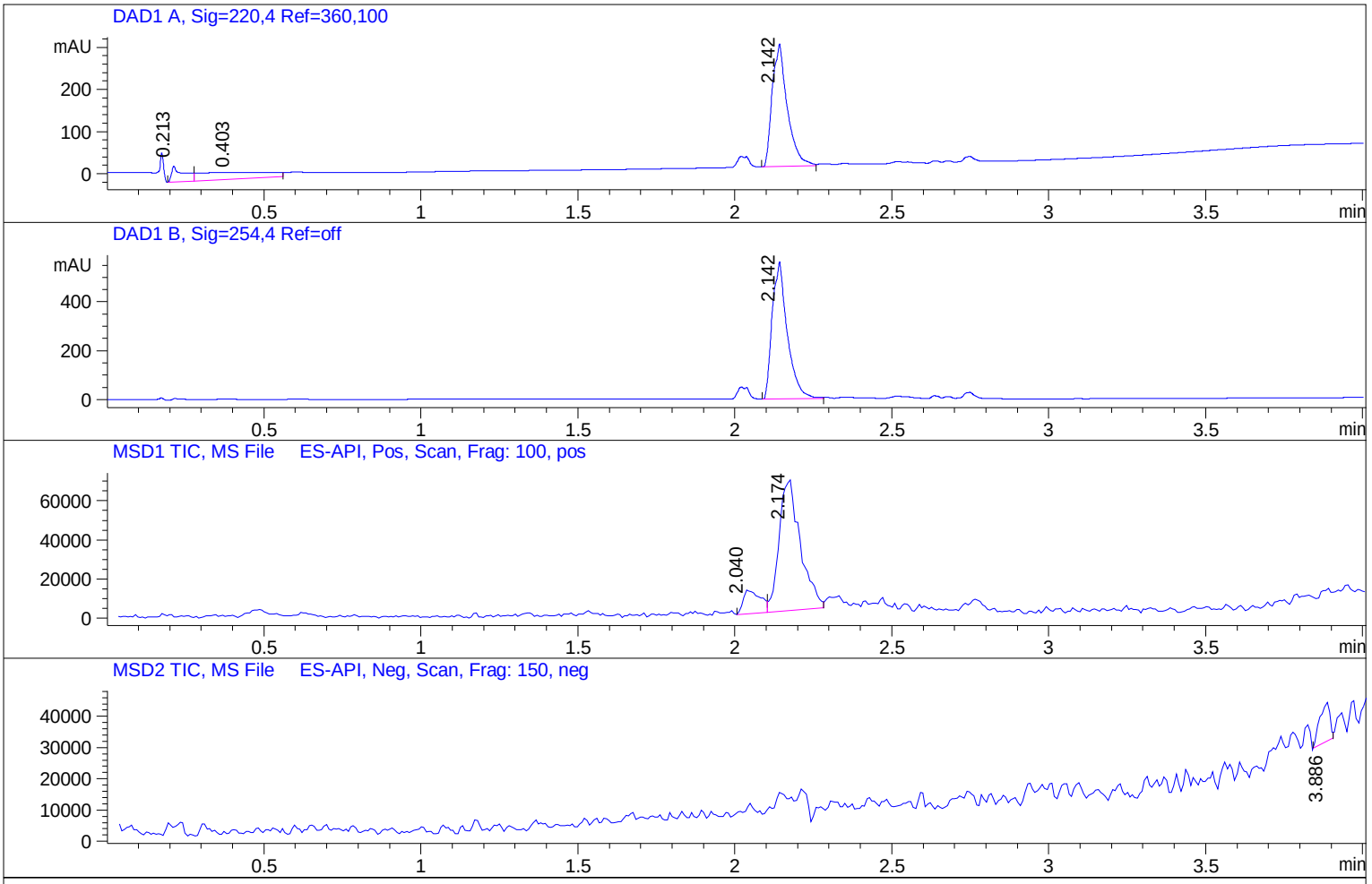
| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.25 | 0.05 | 628.43 | 163.84 | 39.94 | 387 | 379 |
| 1.99 | 0.04 | 945.10 | 358.22 | 60.06 | 433 | 379 |

Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 1.99 | 0.04 | 1799.79 | 683.19 | 100.00 | 433 | 379 |

**File C:\EZXDATA\TDORADO\10-18\068_HCL1.D** **Tgt Mass (EZX):**
**Injection Date : 23 Oct 18 1:53 pm -0500** **Seq. Line : 0**
**Sample Name : 068_HCl** **Location : Vial 64**
**Acq. Operator : tony.dorado** **Inj : 1**
**Spec. Reported : MS Integration** **Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



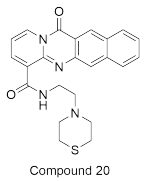

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

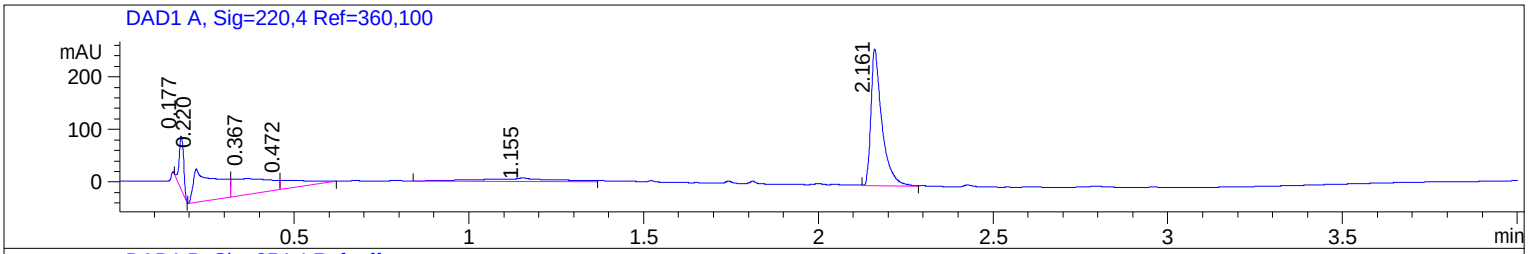
| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.21 | 0.04 | 105.70 | 37.83 | 8.01 | ND | 155 |
| 0.40 | 0.19 | 247.60 | 15.73 | 18.77 | 147 | 379 |
| 2.14 | 0.04 | 965.74 | 290.30 | 73.22 | 426 | 155 |

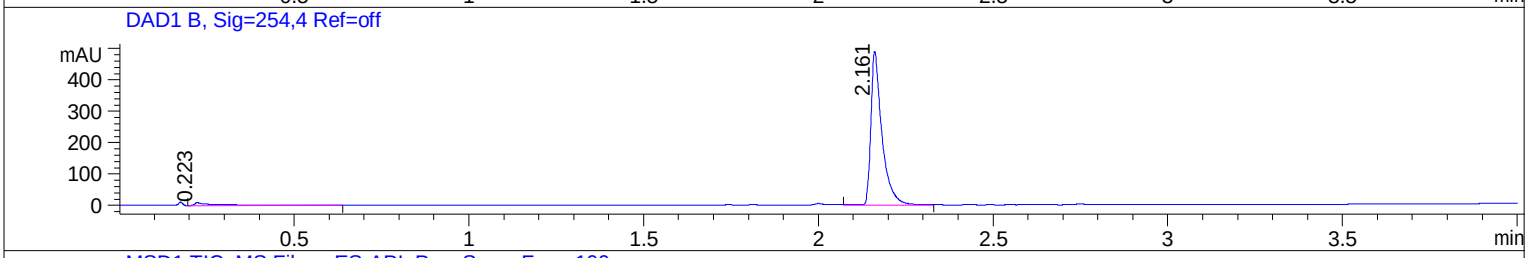
Integration Results for DAD1 B, Sig=254,4 Ref=off

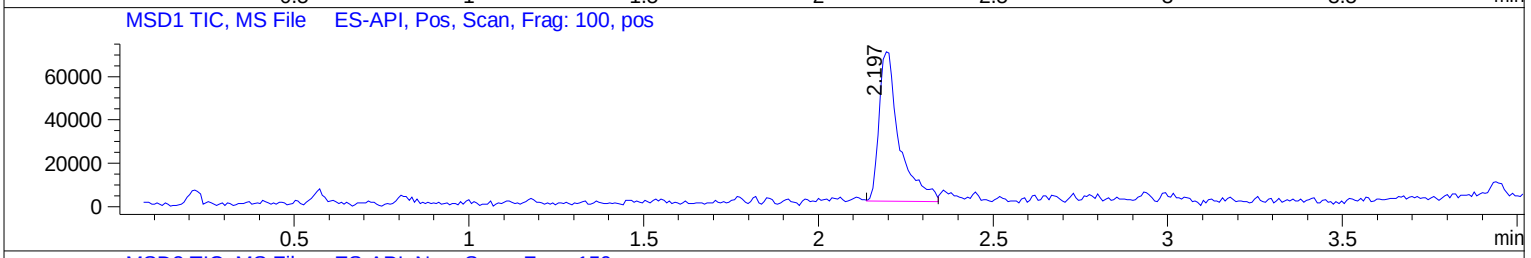
| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.14 | 0.04 | 1861.70 | 560.07 | 100.00 | 426 | 249 |

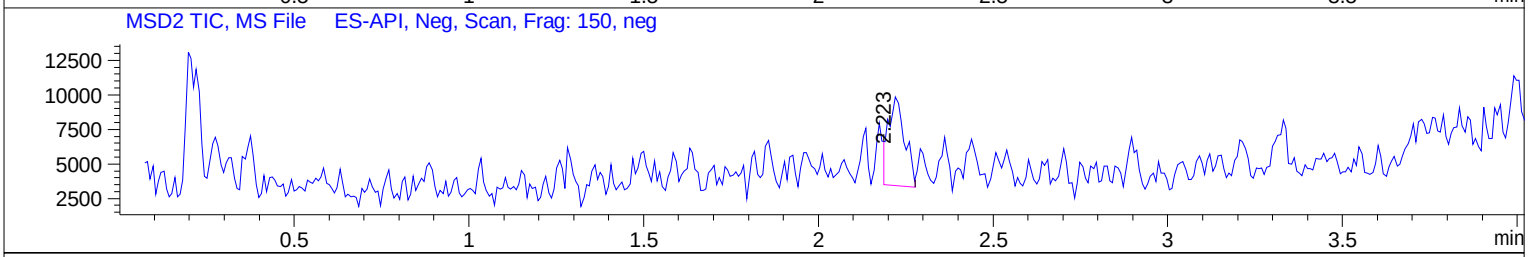
File C:\EZXDATA\TDORADO\11-18\078_HCL.1.D Tgt Mass (EZX):
Injection Date : 29 Nov 18 3:14 pm -0500 Seq. Line : 0
Sample Name : 078_HCl. Location : Vial 21
Acq. Operator : tony.dorado Inj : 1
Spec. Reported : MS Integration Inj Volume : 2 ul
Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M
Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M
Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'
Method Info : pos/neg ION MODE


Compound 20



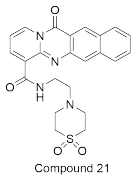

Integration Results for DAD1 A, Sig=220,4 Ref=360,100

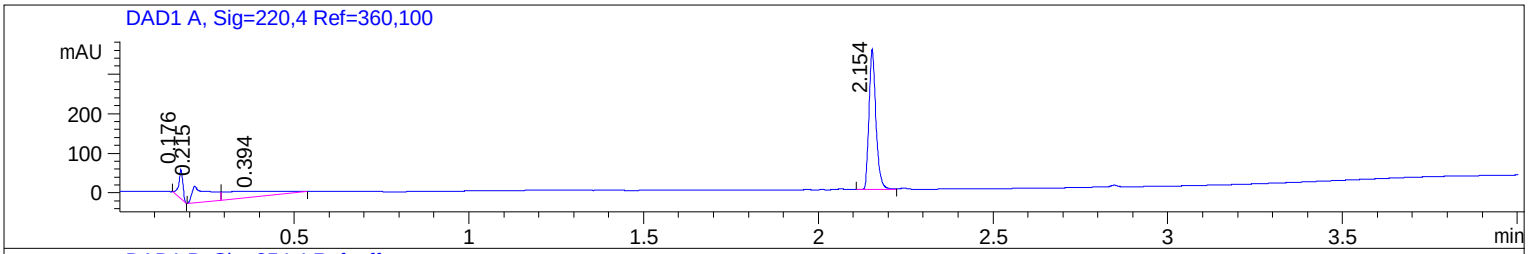
| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.18 | 0.01 | 89.99 | 101.22 | 6.73 | 163 | 379 |
| 0.22 | 0.06 | 288.79 | 64.08 | 21.59 | 163 | 508 |
| 0.37 | 0.10 | 224.52 | 30.03 | 16.79 | ND | 508 |
| 0.47 | 0.07 | 83.18 | 16.40 | 6.22 | 130 | 379 |
| 1.15 | 0.16 | 84.51 | 6.54 | 6.32 | ND | 379 |
| 2.16 | 0.03 | 566.64 | 259.59 | 42.36 | 419 | 379 |

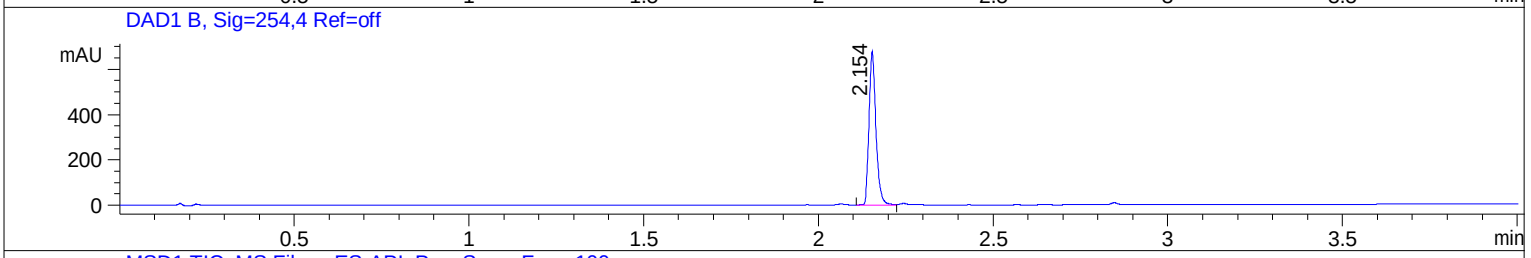
Integration Results for DAD1 B, Sig=254,4 Ref=off

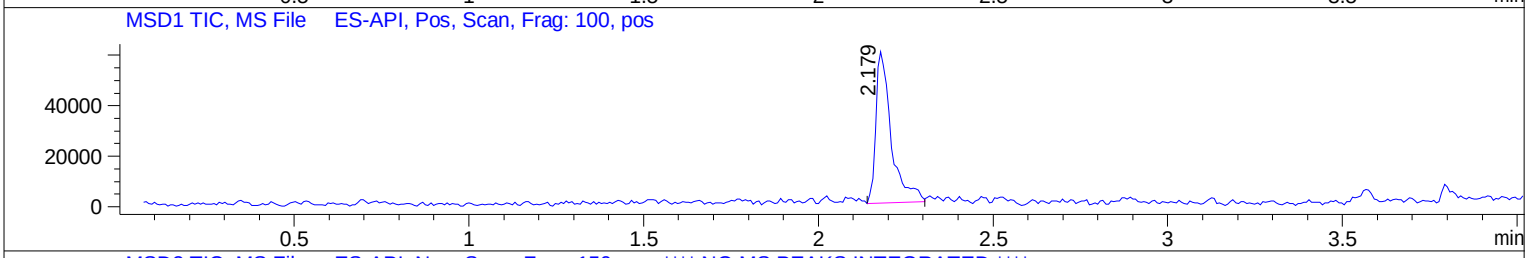
| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.22 | 0.07 | 64.57 | 11.38 | 5.66 | 130 | 379 |
| 2.16 | 0.03 | 1075.98 | 490.25 | 94.34 | 419 | 379 |

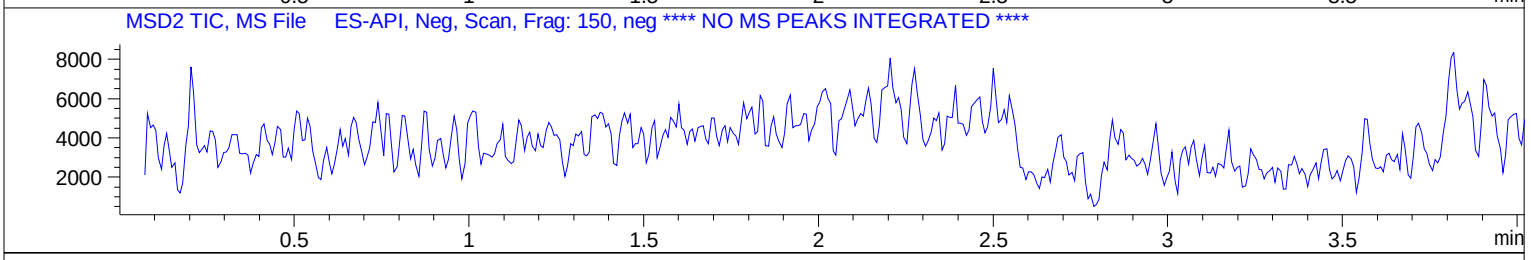
**File C:\EZXDATA\TDORADO\12-18\080_HCL.1.D** **Tgt Mass (EZX):**
**Injection Date : 4 Dec 18 1:42 pm -0500** **Seq. Line : 0**
**Sample Name : 080_HCl.** **Location : Vial 61**
**Acq. Operator : tony.dorado** **Inj : 1**
**Spec. Reported : MS Integration** **Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**


Compound 21




Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.18 | 0.01 | 61.71 | 73.38 | 7.15 | ND | 514 |
| 0.22 | 0.04 | 144.83 | 42.13 | 16.77 | ND | 379 |
| 0.39 | 0.15 | 168.25 | 13.81 | 19.48 | ND | 379 |
| 2.15 | 0.02 | 488.71 | 354.59 | 56.60 | 451 | 379 |

Integration Results for DAD1 B, Sig=254,4 Ref=off

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.15 | 0.02 | 931.86 | 677.82 | 100.00 | 451 | 379 |

JHU_3la4x MW:394.4

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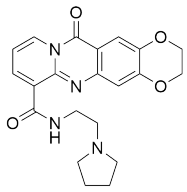
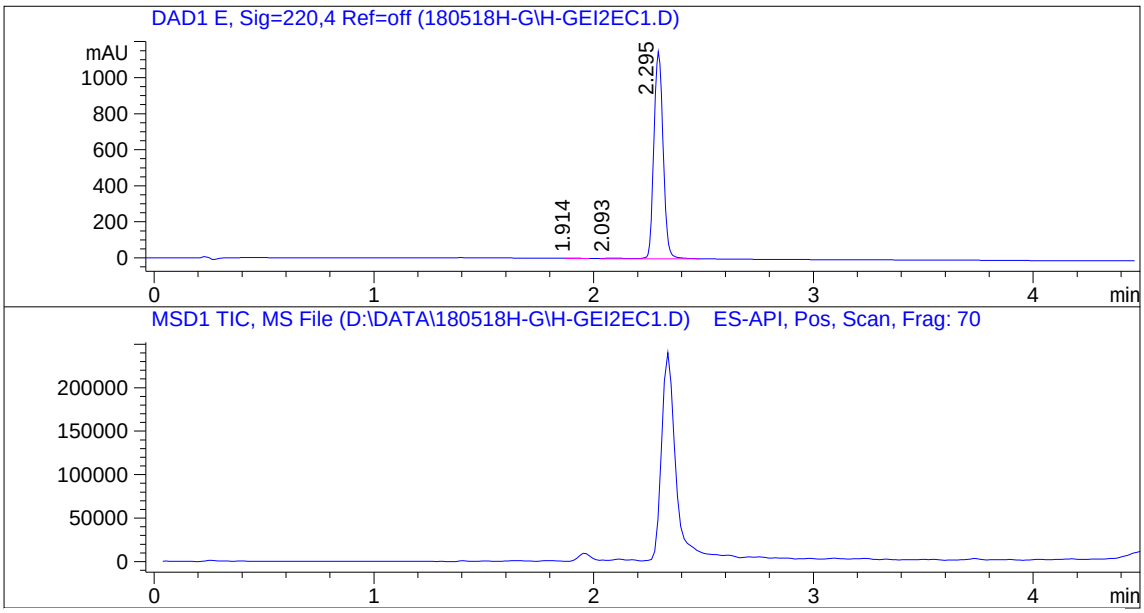
Injection Date : Fri, 18. May. 2018
Acq Operator : TF00001
Location : P2-E-03
Inj. Vol. : 5.000 uL
Acq Method : D:\DATA\180518H-G\WUXIAB01-220.M
Data Filename : D:\DATA\180518H-G\H-GEI2EC1.D
Instrument : H



Compound 22

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Report

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Signal 1 : DAD1 E, Sig=220,4 Ref=off

| Peak # | RT [min] | Height | Height % | Width [min] | Area | Area % |
|---|---|---|---|---|---|---|
| 1 | 1.914 | 1.347 | 0.116 | 0.056 | 4.543 | 0.135 |
| 2 | 2.093 | 3.153 | 0.272 | 0.087 | 16.409 | 0.488 |
| 3 | 2.295 | 1153.549 | 99.611 | 0.048 | 3343.300 | 99.377 |

JHU_3ma4x MW:390.5

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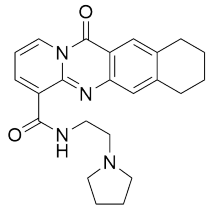
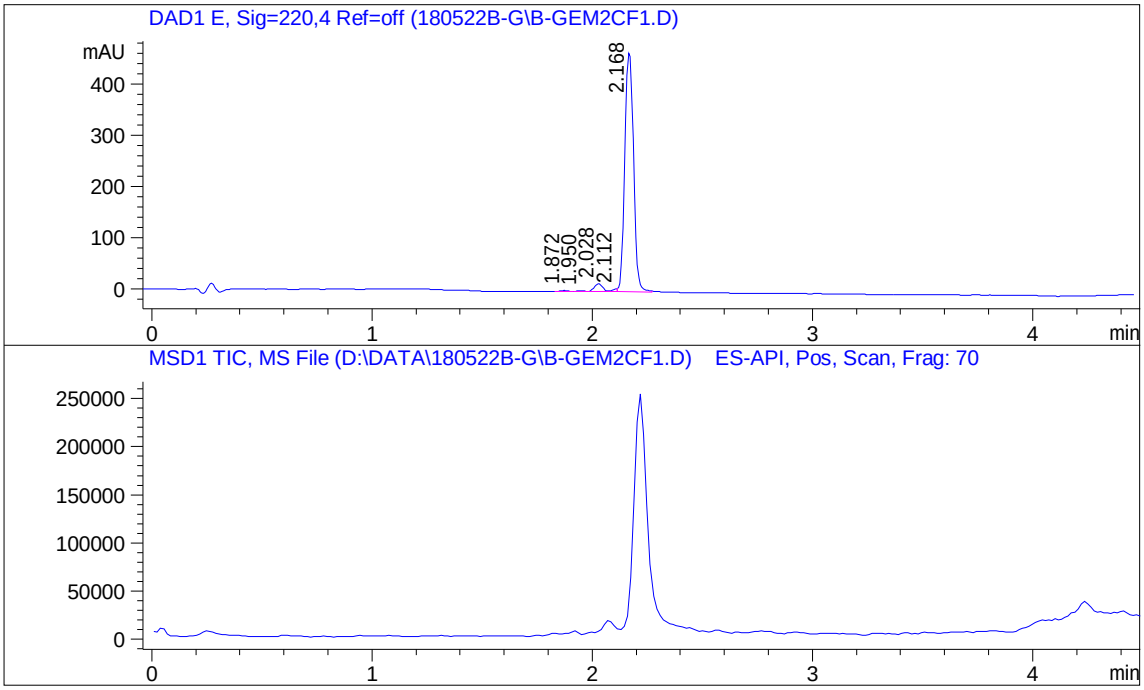
Injection Date : Tue, 22. May. 2018
Acq Operator : TF00001
Location : P2-C-06
Inj. Vol. : 1.000uL
Acq Method : D:\DATA\180522B-G\WUXIAB10-220.M
Data Filename : D:\DATA\180522B-G\B-GEM2CF1.D
Instrument : B



Compound 23

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Report

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Signal 1 : DAD1 E, Sig=220,4 Ref=off

| Peak # | RT [min] | Height | Height % | Width [min] | Area | Area % |
|---|---|---|---|---|---|---|
| 1 | 1.872 | 1.972 | 0.398 | 0.040 | 4.742 | 0.351 |
| 2 | 1.950 | 1.725 | 0.348 | 0.044 | 4.535 | 0.335 |
| 3 | 2.028 | 15.253 | 3.078 | 0.045 | 41.176 | 3.044 |
| 4 | 2.112 | 6.002 | 1.211 | 0.028 | 10.077 | 0.745 |
| 5 | 2.168 | 470.606 | 94.965 | 0.046 | 1292.087 | 95.525 |

JHU_3na4x MW:380.4

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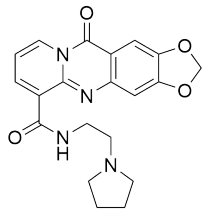
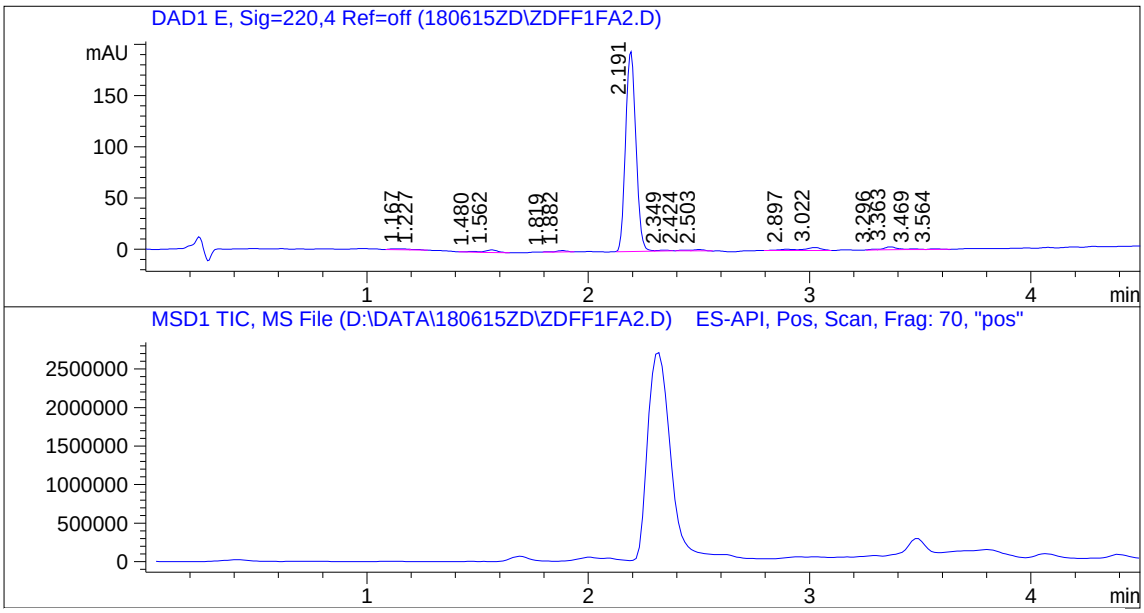
Injection Date : Fri, 15. Jun. 2018
Acq Operator : TF00001
Location : P1-F-01
Inj. Vol. : 5.0 uL
Acq Method : D:\DATA\180615ZD\WUXICD15-220.M
Data Filename : D:\DATA\180615ZD\ZDFF1FA2.D
Instrument : Z



Compound 24

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Report

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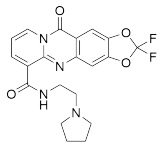
Signal 1 : DAD1 E, Sig=220,4 Ref=off

| Peak # | RT [min] | Height | Height % | Width [min] | Area | Area % |
|---|---|---|---|---|---|---|
| 1 | 1.167 | 0.793 | 0.369 | 0.084 | 3.982 | 0.566 |
| 2 | 1.227 | 0.600 | 0.279 | 0.048 | 1.736 | 0.247 |
| 3 | 1.480 | 0.672 | 0.313 | 0.064 | 2.567 | 0.365 |
| 4 | 1.562 | 2.450 | 1.140 | 0.059 | 8.690 | 1.235 |
| 5 | 1.819 | 0.339 | 0.158 | 0.036 | 0.736 | 0.105 |
| 6 | 1.882 | 1.346 | 0.627 | 0.048 | 3.910 | 0.556 |
| 7 | 2.191 | 196.967 | 91.674 | 0.054 | 635.722 | 90.354 |
| 8 | 2.349 | 0.655 | 0.305 | 0.060 | 2.357 | 0.335 |
| 9 | 2.424 | 0.715 | 0.333 | 0.058 | 2.471 | 0.351 |
| 10 | 2.503 | 1.295 | 0.603 | 0.054 | 4.193 | 0.596 |
| 11 | 2.897 | 1.230 | 0.573 | 0.089 | 6.584 | 0.936 |
| 12 | 3.022 | 2.916 | 1.357 | 0.079 | 13.835 | 1.966 |
| 13 | 3.296 | 0.780 | 0.363 | 0.037 | 1.721 | 0.245 |
| 14 | 3.363 | 2.806 | 1.306 | 0.068 | 11.506 | 1.635 |
| 15 | 3.469 | 0.691 | 0.322 | 0.047 | 1.965 | 0.279 |
| 16 | 3.564 | 0.600 | 0.279 | 0.045 | 1.616 | 0.230 |



Compound 25



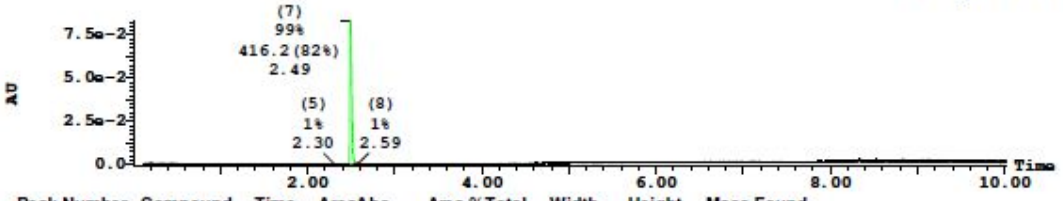
**Openlynx Report -**
Sample: 78 Vial:1:7,F ID:
File:EXP-19-HD5830 Description:Kinetex C18 5-100% ACN/AmForm 10mM pH4
Conditions: Date:21-Mar-2019 Time:08:36:56

Printed: Thu Mar 21 09:05:24 2019

**Sample Report:**

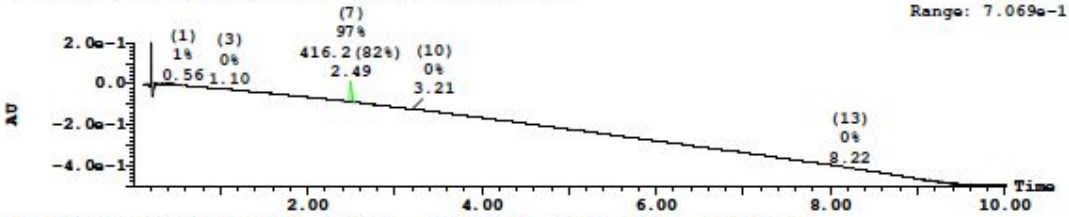
**Sample 78 Vial 1:7,F ID File EXP-19-HD5830 Date 21-Mar-2019 Time 08:36:56 Description Kinetex C18 5-100% ACN/AmForm 10mM p**

2: UV Detector: 254 Nm 0.5200-8.0200: Smooth (Mn, 3x3) 8.281e-2
Range: 8.35e-2



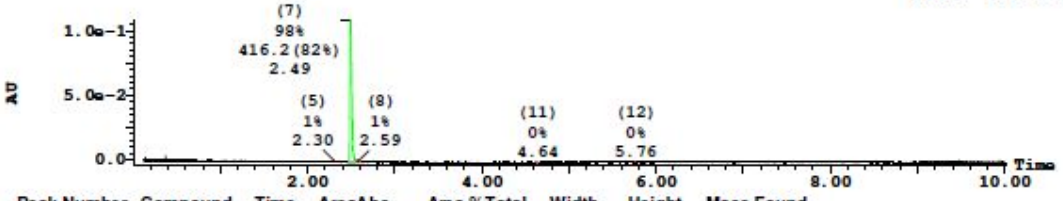

| Peak Number | Compound | Time | AreaAbs | Area %Total | Width | Height | Mass Found |
|---|---|---|---|---|---|---|---|
| 5 | | 2.30 | 15 | 0.76 | 0 | 730 | Not Found |
| 7 | Found | 2.49 | 1974 | 98.72 | 0 | 82962 | 416.2000 |
| 8 | | 2.59 | 10 | 0.52 | 0 | 675 | Not Found |

2: UV Detector: 214 Nm 0.5200-9.0200: Smooth (Mn, 3x3) 2.025e-1
Range: 7.069e-1




| Peak Number | Compound | Time | AreaAbs | Area %Total | Width | Height | Mass Found |
|---|---|---|---|---|---|---|---|
| 1 | | 0.56 | 26 | 1.09 | 0 | 2538 | Not Found |
| 2 | | 0.68 | 15 | 0.61 | 0 | 1594 | Not Found |
| 3 | | 1.10 | 7 | 0.28 | 0 | 866 | Not Found |
| 4 | | 1.22 | 9 | 0.37 | 0 | 900 | Not Found |
| 6 | | 2.41 | 8 | 0.35 | 0 | 890 | Not Found |
| 7 | Found | 2.49 | 2327 | 96.55 | 0 | 97256 | 416.2000 |
| 10 | | 3.21 | 8 | 0.31 | 0 | 929 | Not Found |
| 13 | | 8.22 | 10 | 0.43 | 0 | 940 | Not Found |

2: UV Detector: 280 Nm 0.5200-9.0200: Smooth (Mn, 3x3) 1.076e-1
Range: 1.114e-1




| Peak Number | Compound | Time | AreaAbs | Area %Total | Width | Height | Mass Found |
|---|---|---|---|---|---|---|---|
| 5 | | 2.30 | 21 | 0.77 | 0 | 1259 | Not Found |
| 7 | Found | 2.49 | 2655 | 97.73 | 0 | 109356 | 416.2000 |
| 8 | | 2.59 | 25 | 0.92 | 0 | 1209 | Not Found |
| 11 | | 4.64 | 8 | 0.30 | 0 | 526 | Not Found |

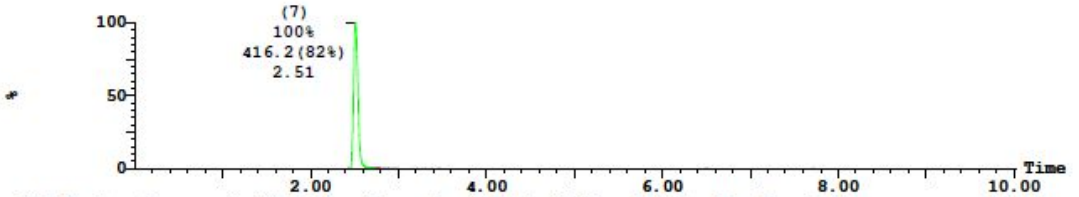
**Openlynx Report -**
Sample: 78 Vial:1:7,F ID:
File:EXP-19-HD5830 Description:Kinetex C18 5-100% ACN/AmForm 10mM pH4
Conditions: Date:21-Mar-2019 Time:08:36:56

Printed: Thu Mar 21 09:05:24 2019

**Sample Report (continued):**

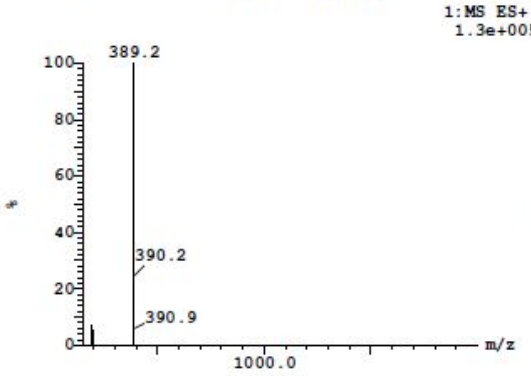
| | | | | | | |
|---|---|---|---|---|---|---|
| 12 | 5.76 | 8 | 0.28 | 0 | 533 | Not Found |

1: MS ES+ :417.208 1.0000Da 0.0000-10.0000: Smooth (Mn, 2x3) 1.7e+007

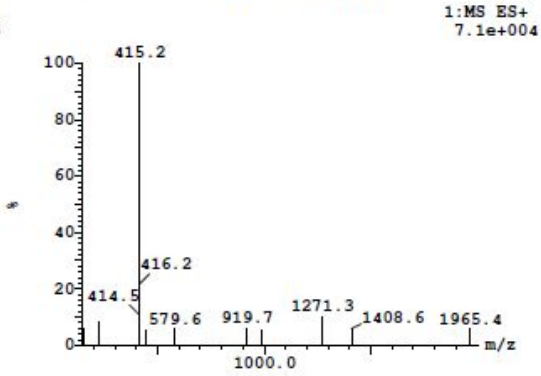



| Peak Number | Compound | Time | AreaAbs | Area %Total | Width | Height | Mass Found |
|---|---|---|---|---|---|---|---|
| 7 | Found | 2.51 | 991509 | 99.57 | 0 | 17203760 | 416.2000 |
| 9 | | 2.77 | 4327 | 0.43 | 0 | 63974 | Not Found |

| Peak ID | Compound | Time | Mass Found |
|---|---|---|---|
| 5 | | 2.30 | Not Found |




| Peak ID | Compound | Time | Mass Found |
|---|---|---|---|
| 6 | | 2.41 | Not Found |



JHU_3ia4x MW:364.4

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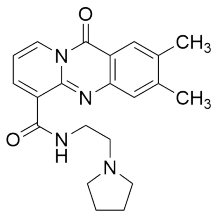
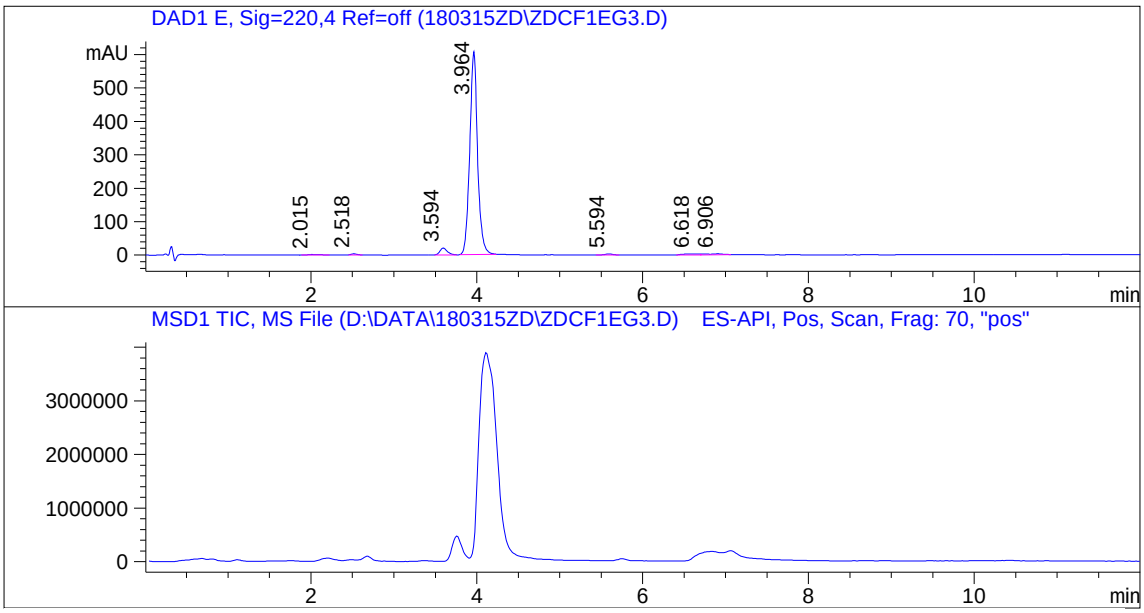
Injection Date : Fri, 16. Mar. 2018
Acq Operator : TF00001
Location : P1-E-07
Inj. Vol. : 1.0 uL
Acq Method : D:\DATA\180315ZD\GECD30-70-12MIN-220
Data Filename : D:\DATA\180315ZD\ZDCF1EG3.D
Instrument : Z



Compound 26

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Report

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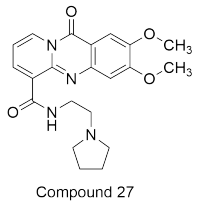
Signal 1 : DAD1 E, Sig=220,4 Ref=off

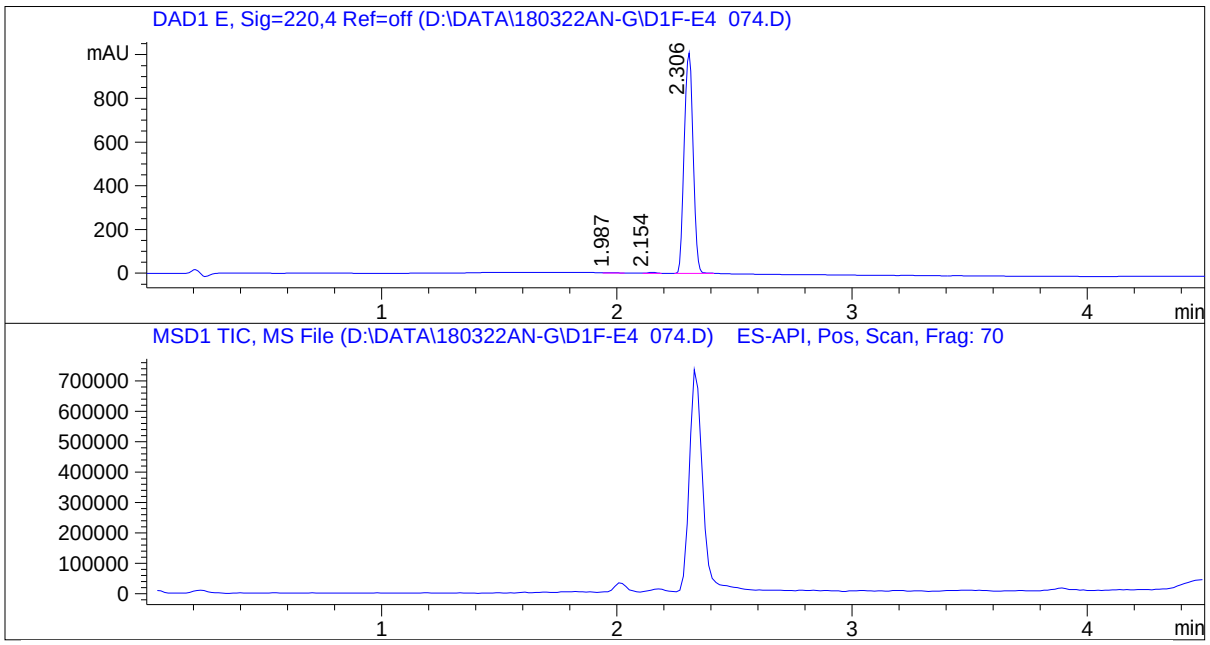
| Peak # | RT [min] | Height | Height % | Width [min] | Area | Area % |
|---|---|---|---|---|---|---|
| 1 | 2.015 | 1.559 | 0.243 | 0.157 | 14.726 | 0.346 |
| 2 | 2.518 | 3.626 | 0.564 | 0.088 | 19.070 | 0.448 |
| 3 | 3.594 | 20.593 | 3.203 | 0.093 | 125.852 | 2.960 |
| 4 | 3.964 | 608.003 | 94.573 | 0.099 | 3986.942 | 93.769 |
| 5 | 5.594 | 3.148 | 0.490 | 0.102 | 19.349 | 0.455 |
| 6 | 6.618 | 2.879 | 0.448 | 0.236 | 40.728 | 0.958 |
| 7 | 6.906 | 3.088 | 0.480 | 0.244 | 45.197 | 1.063 |

# LCMS REPORT



Compound 27

Compound ID : JHU_3KA4X
Sample ID : et20302-2-P1A
Injection Date : 23. Mar. 2018
Inj. Vol. : 3.00 ul
Location : D1F-E4
Acq Method : D:\Method\WUXIAB01_W.M
Data Filename : D:\DATA\180322AN-G\D1F-E4 074.D
Instrument : AN




## Integration Result

Signal 1 : DAD1 E, Sig=220,4 Ref=off

| Peak # | RT [min] | Area | Height | Height % | Width [min] | Area % |
|---|---|---|---|---|---|---|
| 1 | 1.987 | 6.671 | 2.142 | 0.210 | 0.052 | 0.248 |
| 2 | 2.154 | 12.245 | 4.443 | 0.435 | 0.046 | 0.455 |
| 3 | 2.306 | 2670.262 | 1015.137 | 99.356 | 0.044 | 99.297 |

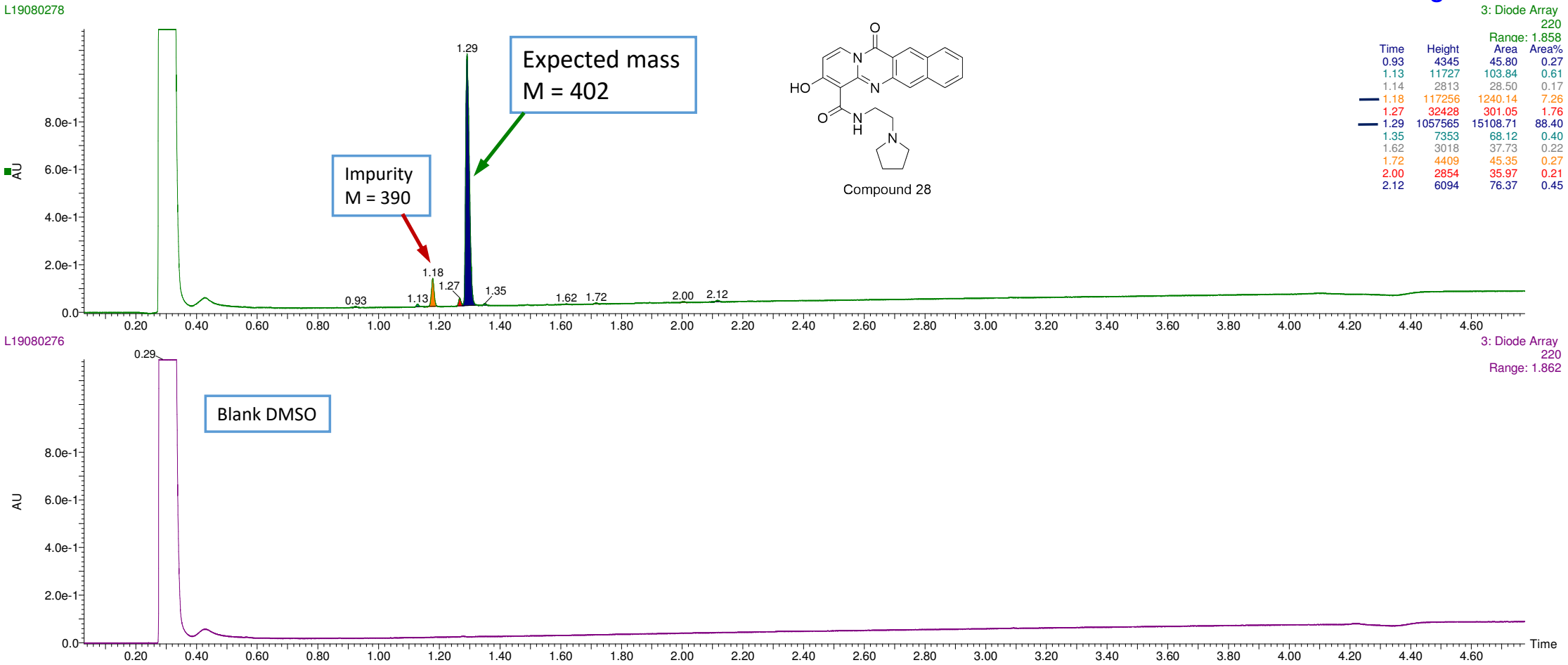
Operator:_____

Date:_____

**ACQ-SQD#J08SQD356W**

**EV-QLR002-063-001**
**LCMS-19-08-00189**

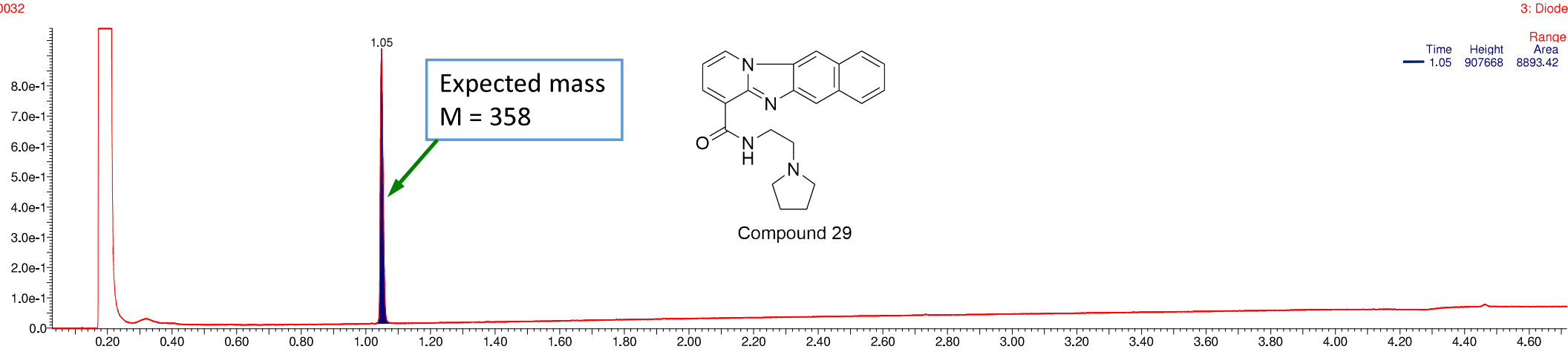
**27-Aug-2019**
**0.5 mg/mL DMSO**



Q-SQD#J08SQD356W

EV-QLR002-084-001
LCMS-19-10-00019

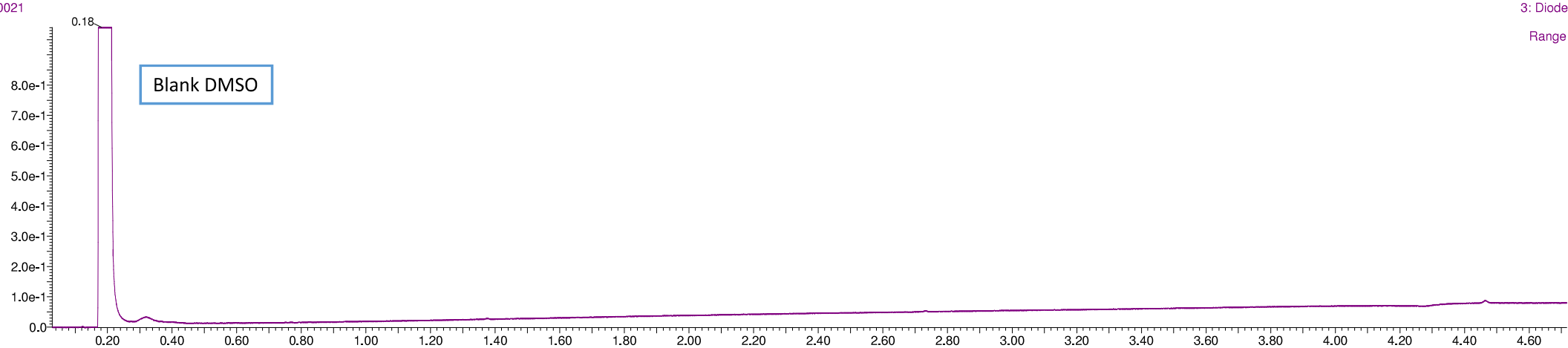
02-Oct-2
0.25 mg/mL DM







Compound 29



Q-SQD2#LCA535

EV-POH001-461-001
LCMS-19-10-00049

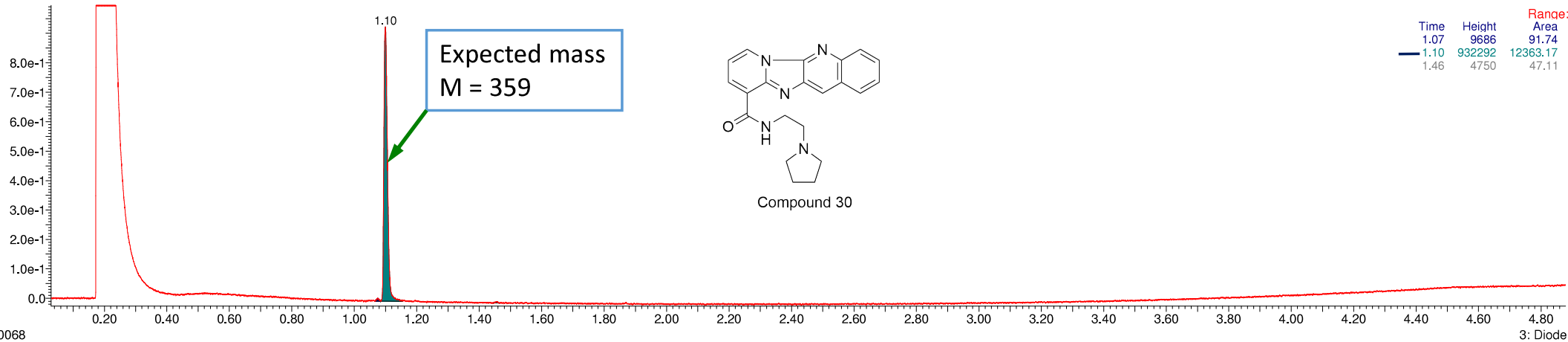
04-Oct-2(
0.5 mg/mL DM

0084

3: Diode

Range:

| Time | Height | Area |
|---|---|---|
| 1.07 | 9686 | 91.74 |
| 1.10 | 932292 | 12363.17 |
| 1.46 | 4750 | 47.11 |





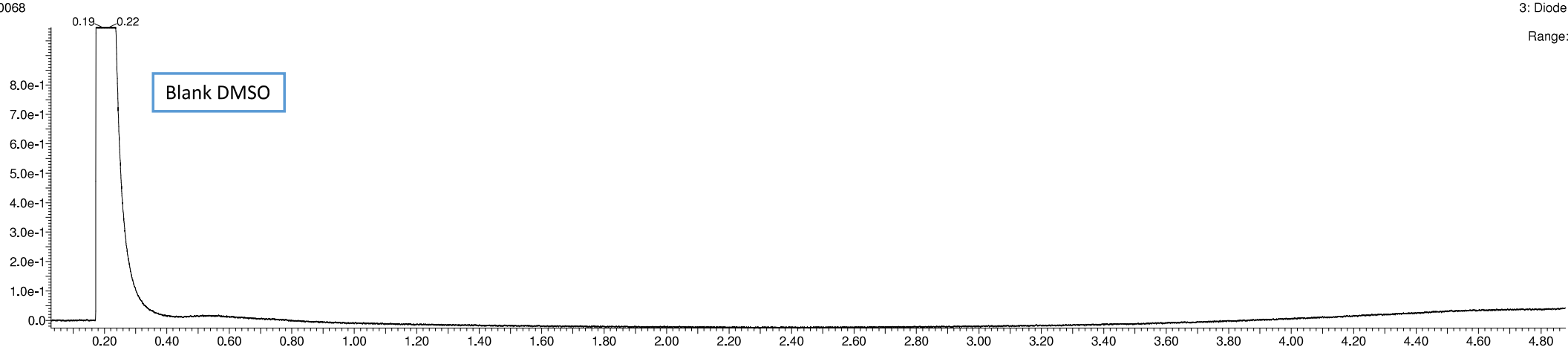


Compound 30

0068

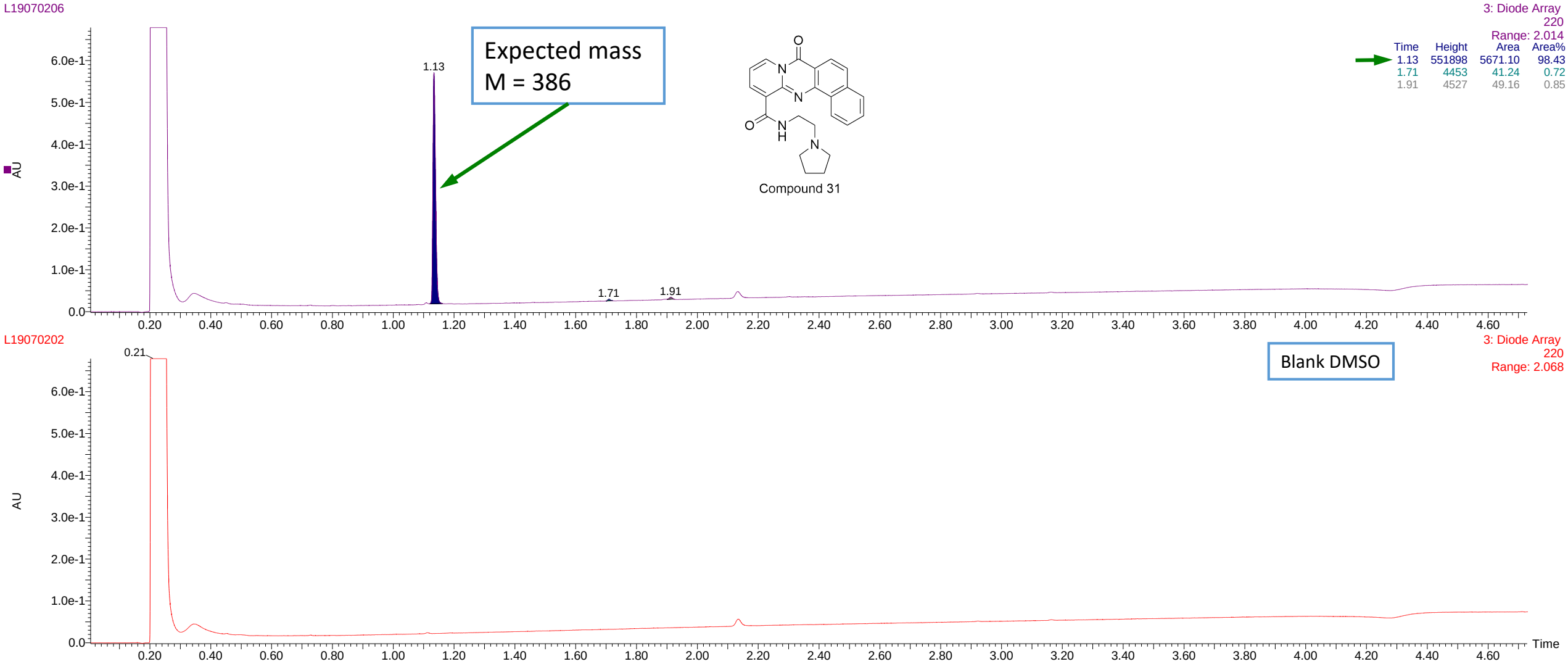
3: Diode

Range:

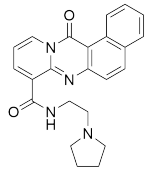


**ACQ-SQD#J08SQD356W** **EV-MOK001-004-001** **11-Jul-2019**

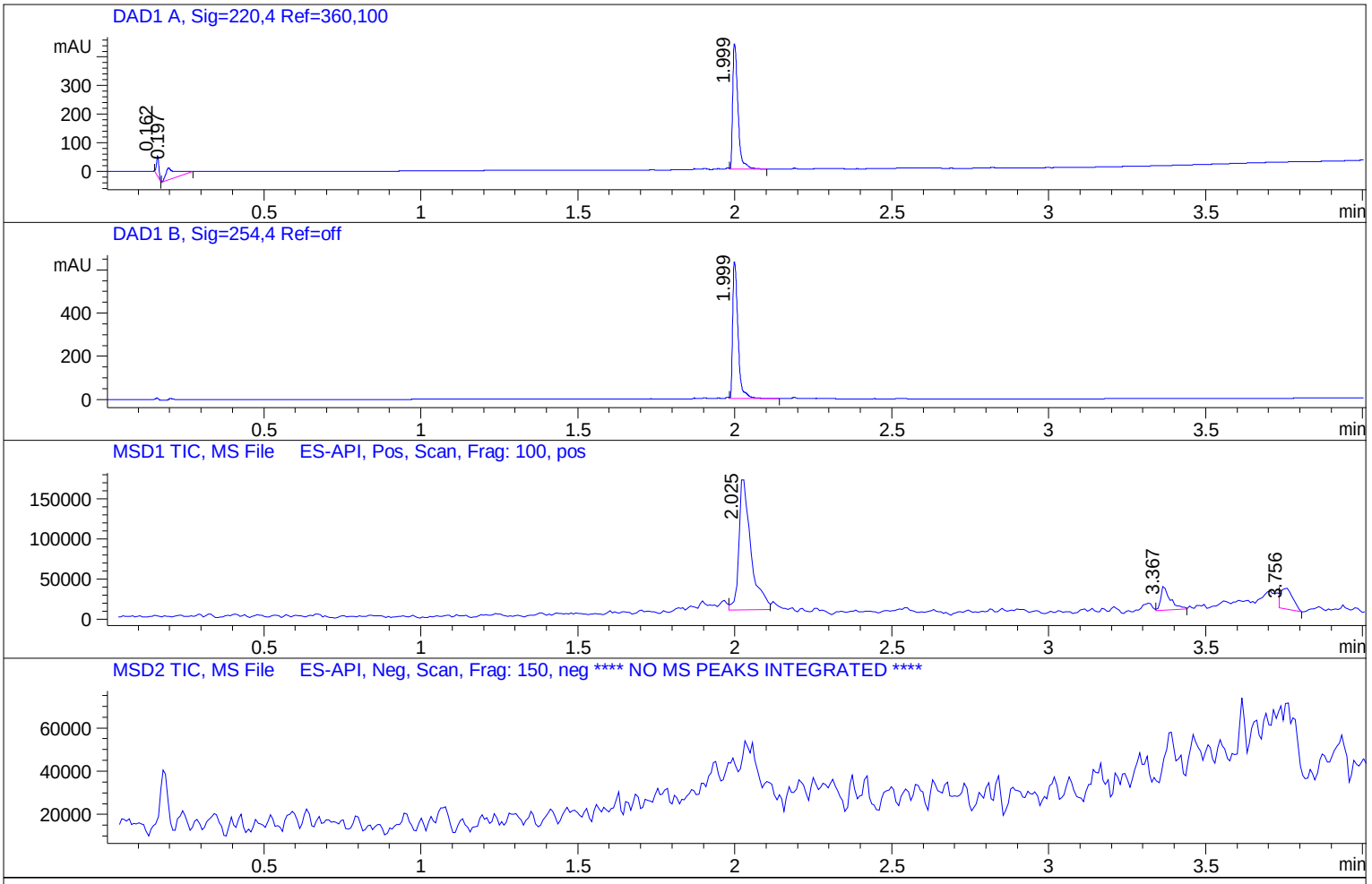
**0.5 mg/mL DMSO**



**File C:\EZXDATA\TDORADO\12-19\284.1.D** **Tgt Mass (EZX):**
**Injection Date : 11 Dec 19 2:38 pm -0500** **Seq. Line : 0**
**Sample Name : 284.** **Location : Vial 28**
**Acq. Operator : tony.dorado** **Inj : 1**
**Spec. Reported : MS Integration** **Inj Volume : 2 ul**
**Acq. Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Analysis Method : C:\Chem32\1\METHODS\POSNEG_AGILENT1.M**
**Sample Info : Easy-Access Method: 'POSNEG_AGILENT1'**
**Method Info : pos/neg ION MODE**



Compound 32




Integration Results for DAD1 A, Sig=220,4 Ref=360,100

| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 0.16 | 0.01 | 38.53 | 70.65 | 5.85 | 120 | 249 |
| 0.20 | 0.03 | 102.88 | 42.55 | 15.63 | 130 | 249 |
| 2.00 | 0.02 | 516.69 | 436.85 | 78.51 | 387 | 249 |

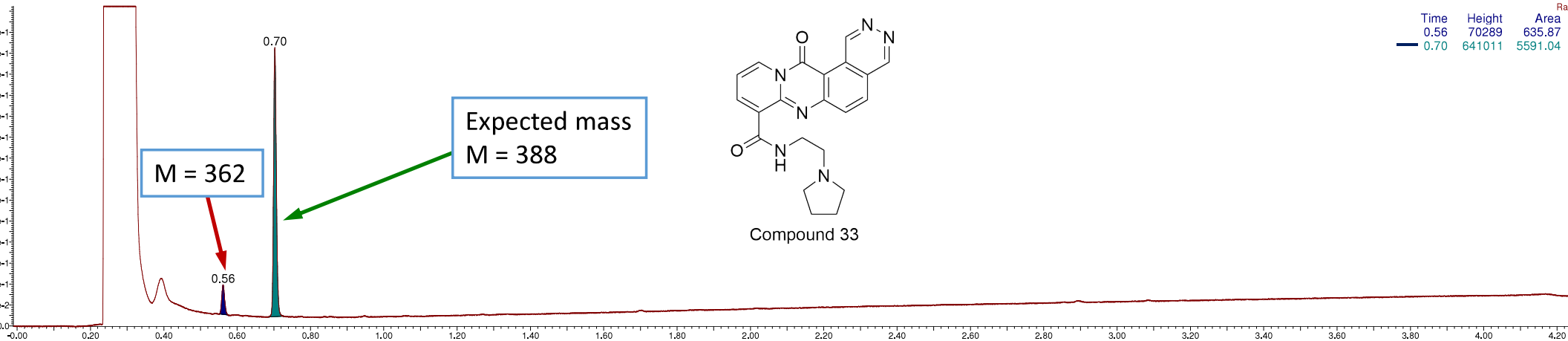
Integration Results for DAD1 B, Sig=254,4 Ref=off

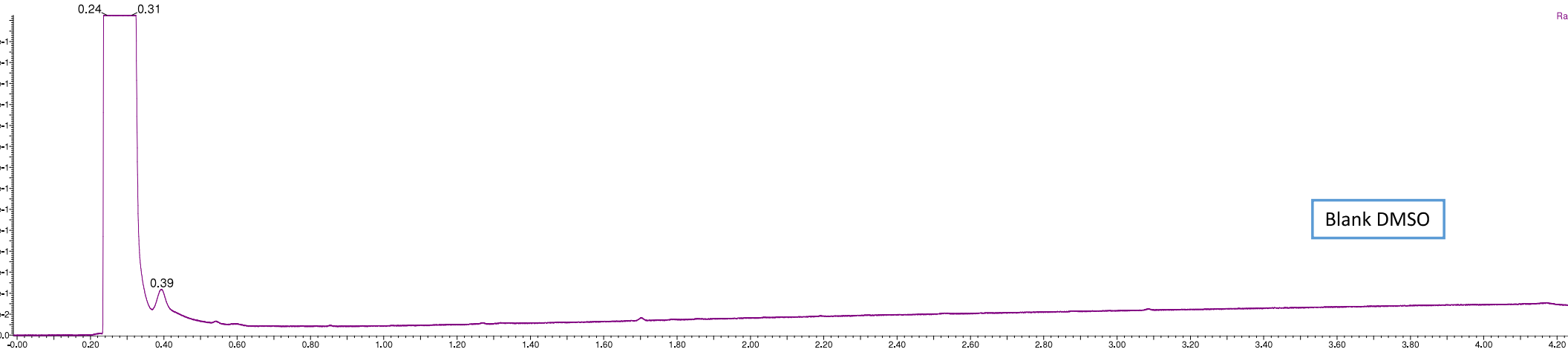
| RetTim | Width | Area | Height | Area% | MS(+) | MS(-) |
|---|---|---|---|---|---|---|
| 2.00 | 0.02 | 750.03 | 631.45 | 100.00 | 387 | 249 |

QD#J08SQD356W

LCMS-19-09-00059
EV-MOK001-059-001

12-Sep
0.5 mg/mL



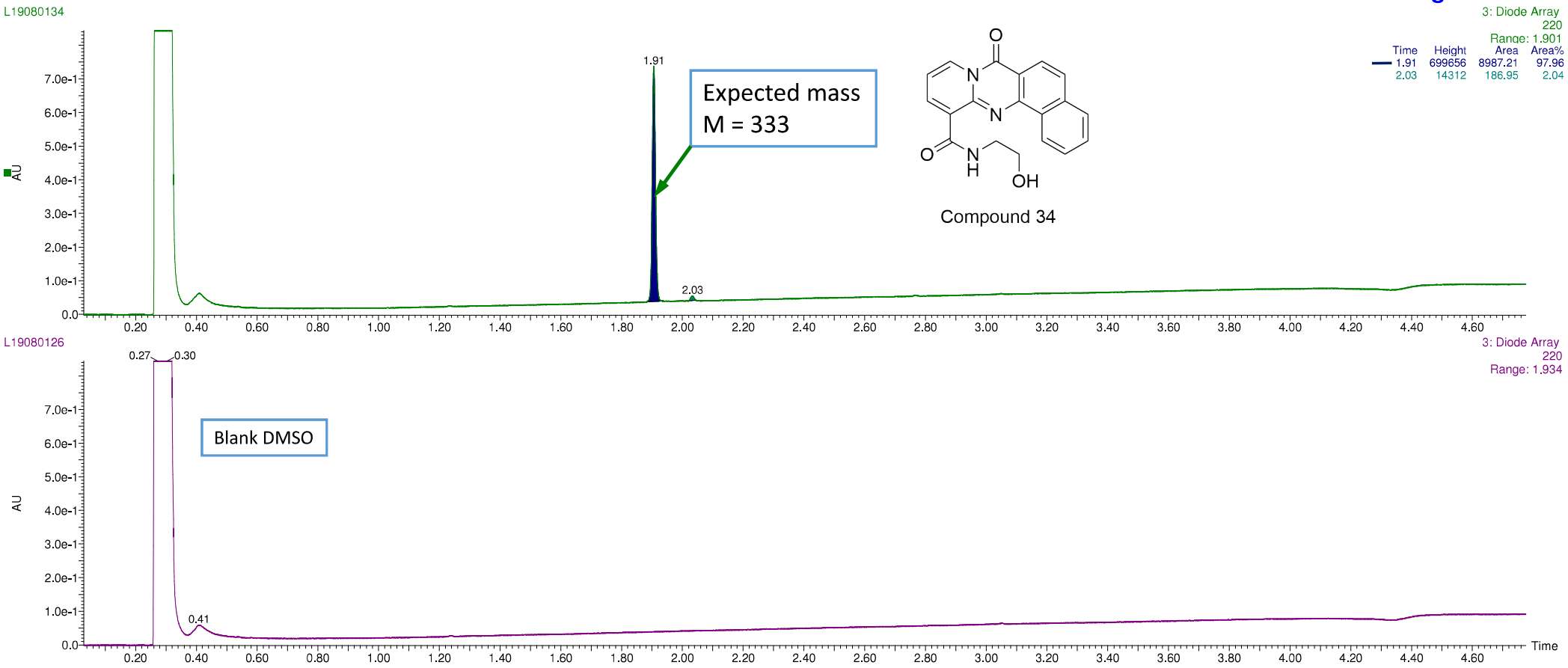




Compound 33

**ACQ-SQD#J08SQD356W**

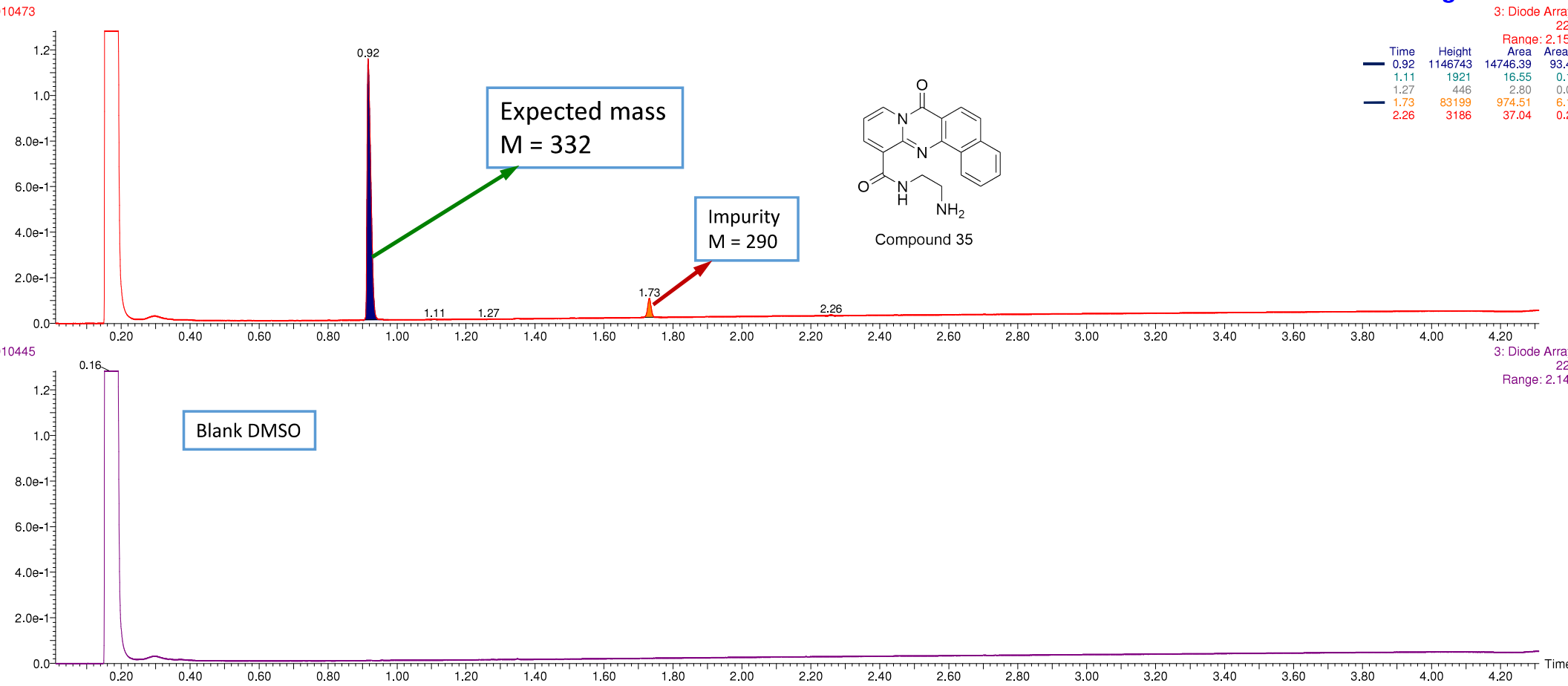
**EV-MOK001-029-001**
**LCMS-19-08-00092**

**12-Aug-2019**
**0.5 mg/mL DMSO**





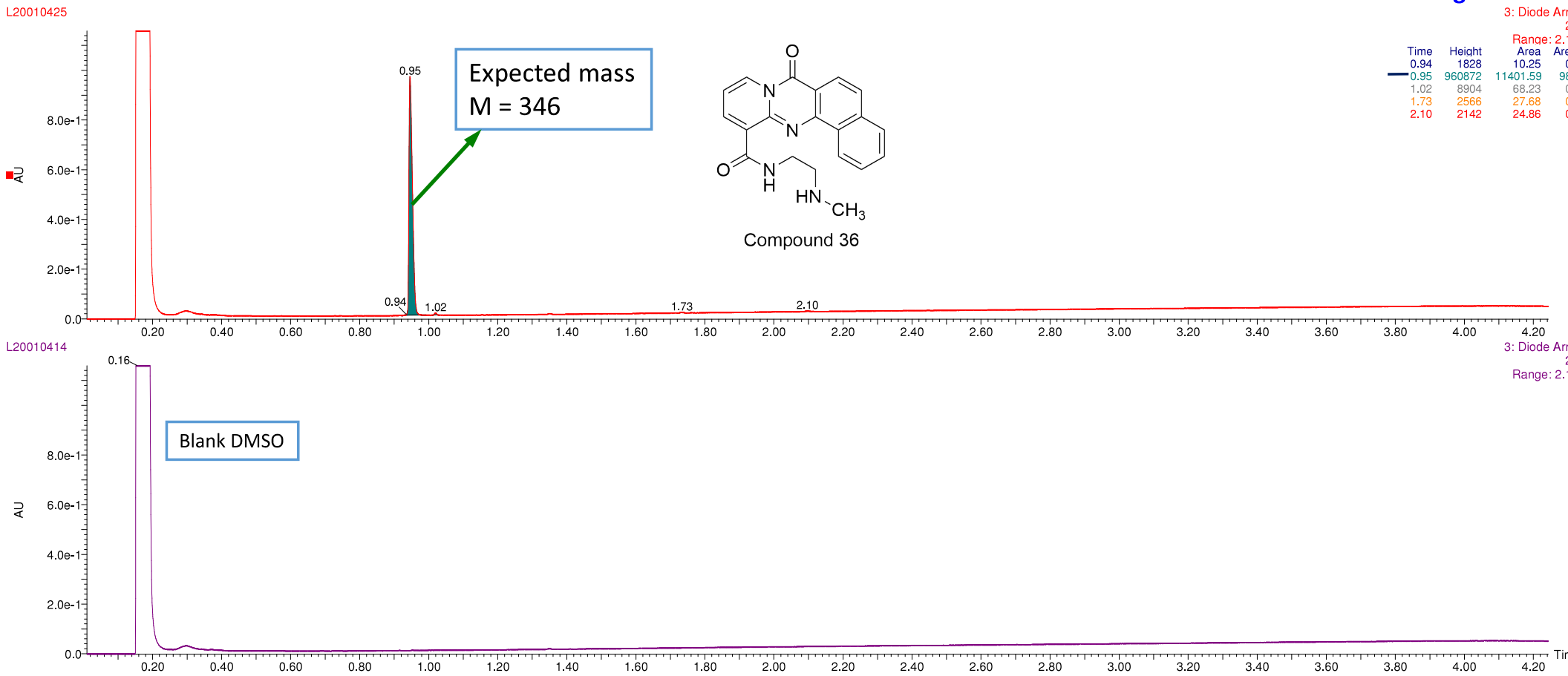

Compound 34


10473
3: Diode Arra
Range: 2.15
Time Height Area Area
0.92 1146743 14746.39 93.
1.11 1921 16.55 0.
1.27 446 2.80 0.
1.73 83199 974.51 6.
2.26 3186 37.04 0.
0.92
1.11
1.27
1.73
2.26
Expected mass
M = 332
Impurity
M = 290
Compound 35
10445
3: Diode Arra
Range: 2.14
0.16
Blank DMSO
Time

**ACQ-SQD#J08SQD356W**

**EV-QLR002-177-001**
**LCMS-20-01-00304**

**29-Jan-202**
**0.5 mg/mL DMS**







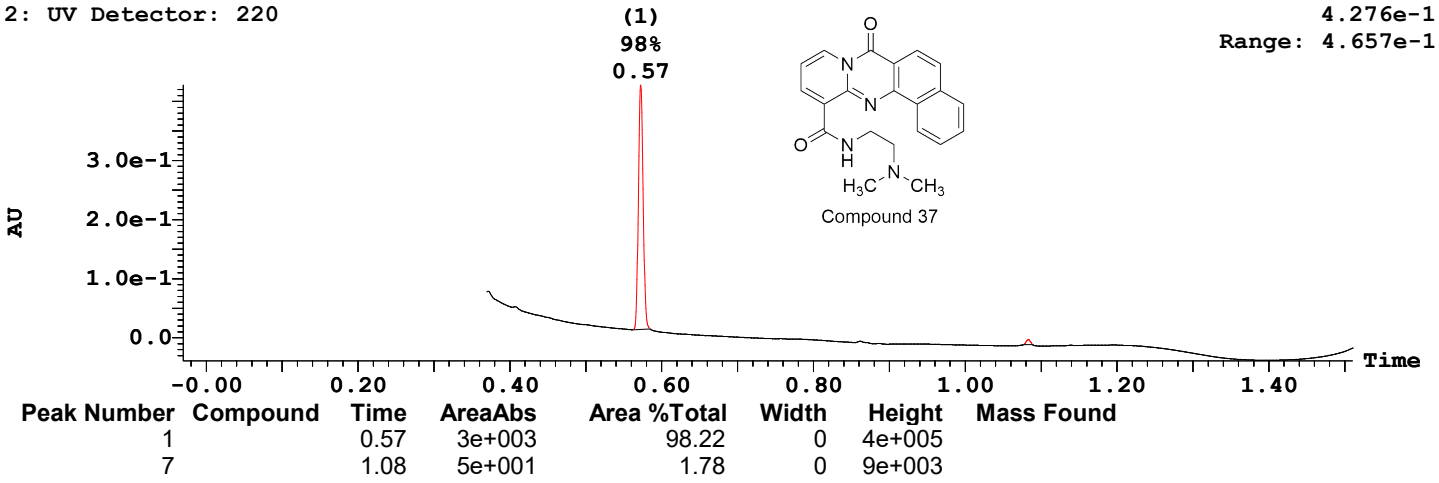
Compound 36

Sample: 1 Vial:10:5 ID:EV-QLR002-025-
File:4REY RODRIGUEZ8-1 Date:10-Jul-2019 Time:08:33:17
Description:

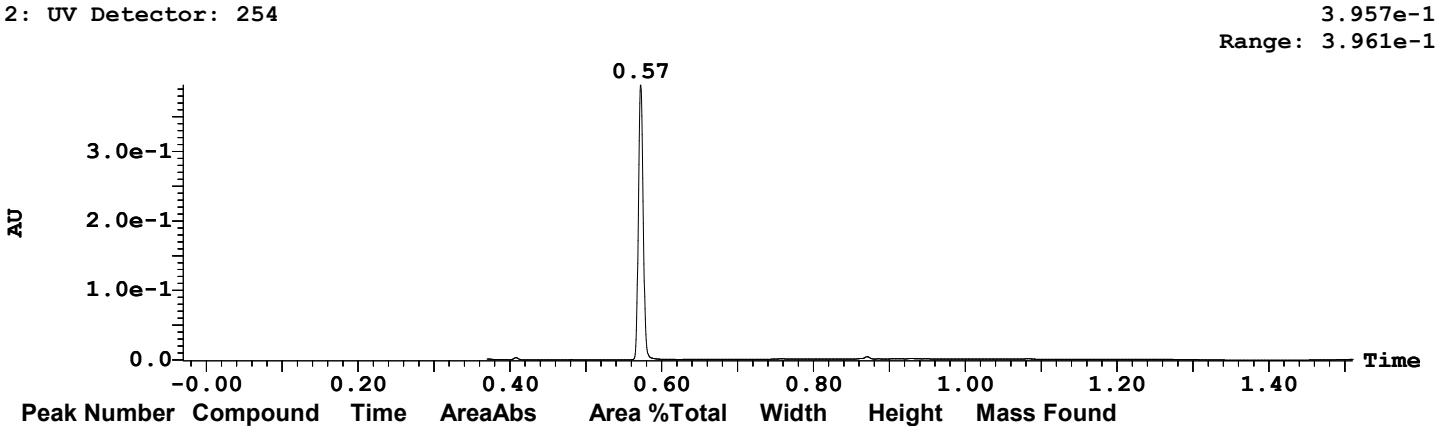
Printed: Fri Jul 12 10:11:22 2019

**Sample Report:**

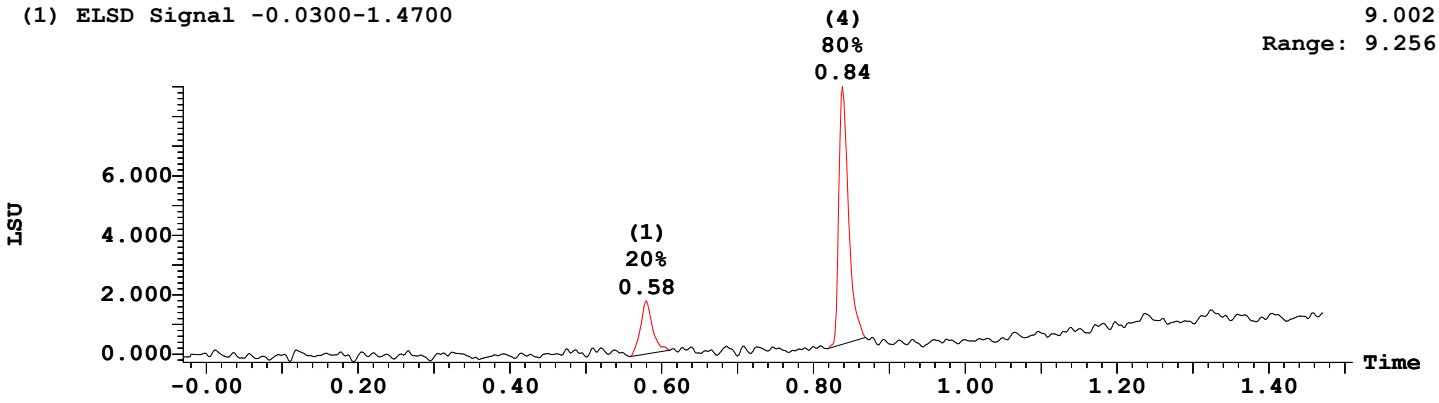
**Sample 1 Vial 10:5 ID EV-QLR002-025- File 4REY RODRIGUEZ8-1 Date 10-Jul-2019 Time 08:33:17 Description**



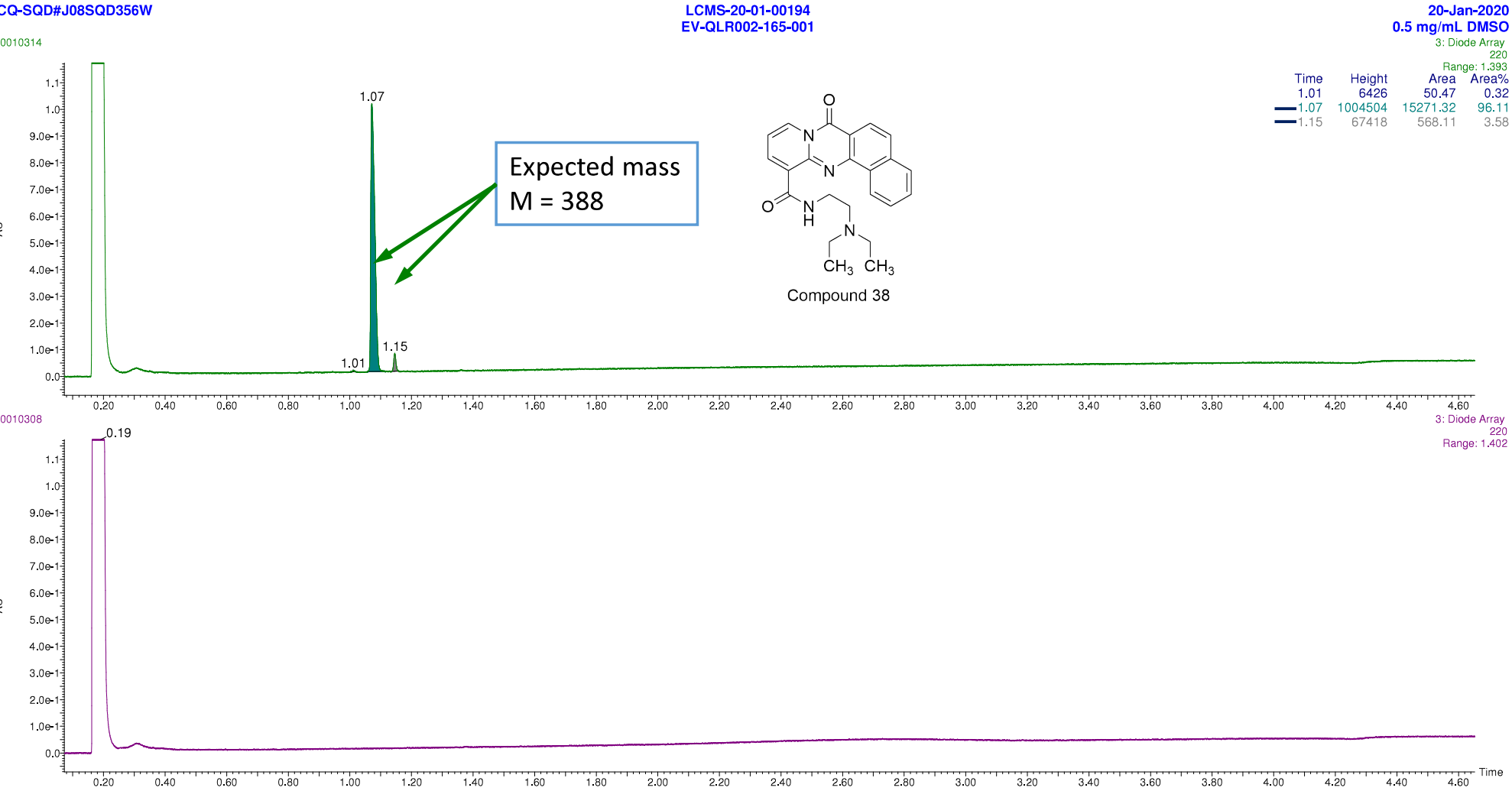

| Peak Number | Compound | Time | AreaAbs | Area %Total | Width | Height | Mass Found |
|---|---|---|---|---|---|---|---|
| 1 | | 0.57 | 3e+003 | 98.22 | 0 | 4e+005 | |
| 7 | | 1.08 | 5e+001 | 1.78 | 0 | 9e+003 | |

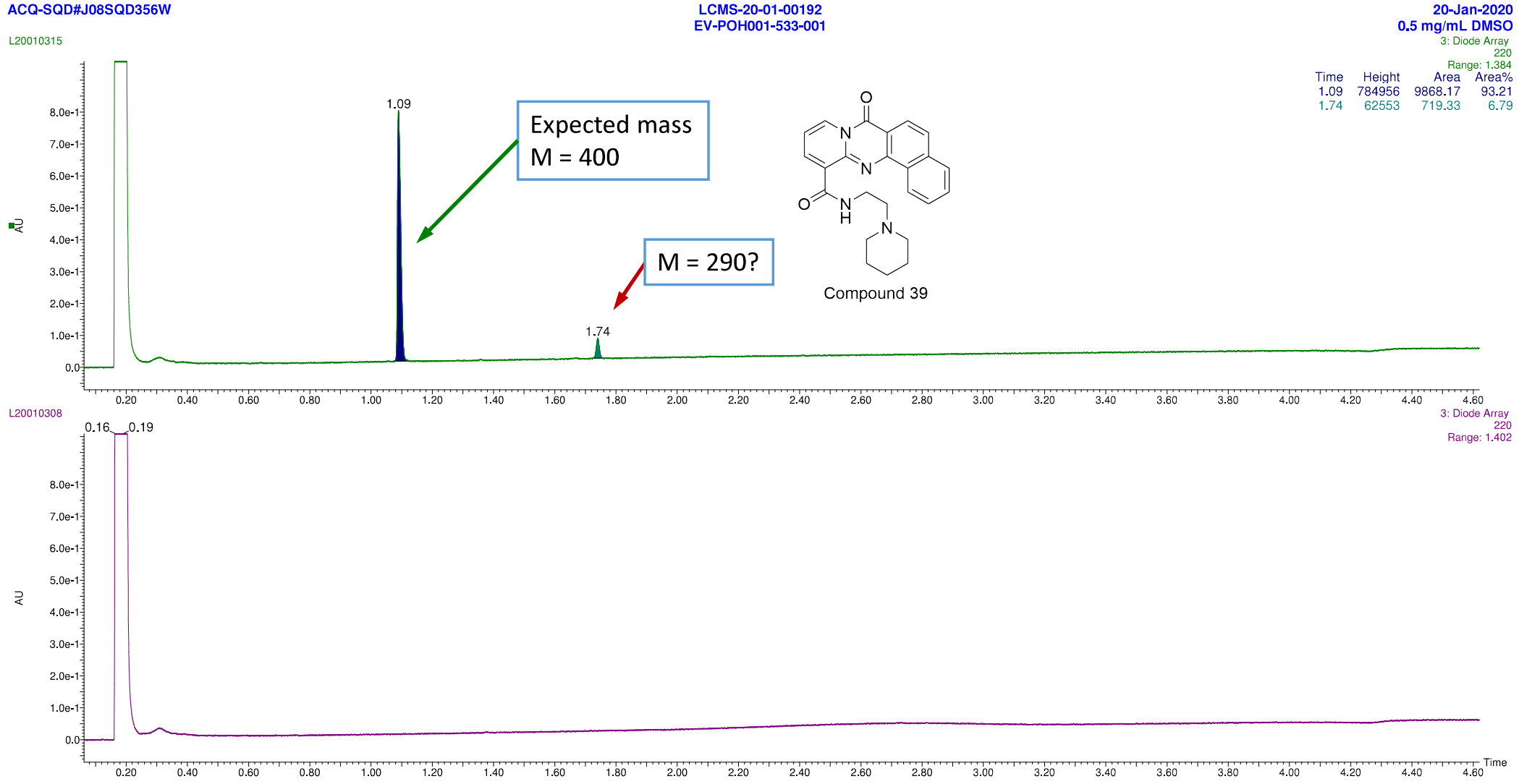



| Peak Number | Compound | Time | AreaAbs | Area %Total | Width | Height | Mass Found |
|---|---|---|---|---|---|---|---|




| Peak Number | Compound | Time | AreaAbs | Area %Total | Width | Height | Mass Found |
|---|---|---|---|---|---|---|---|
| 1 | | 0.58 | 3e+001 | 20.16 | 0 | 2e+003 | |
| 4 | | 0.84 | 1e+002 | 79.84 | 0 | 9e+003 | |

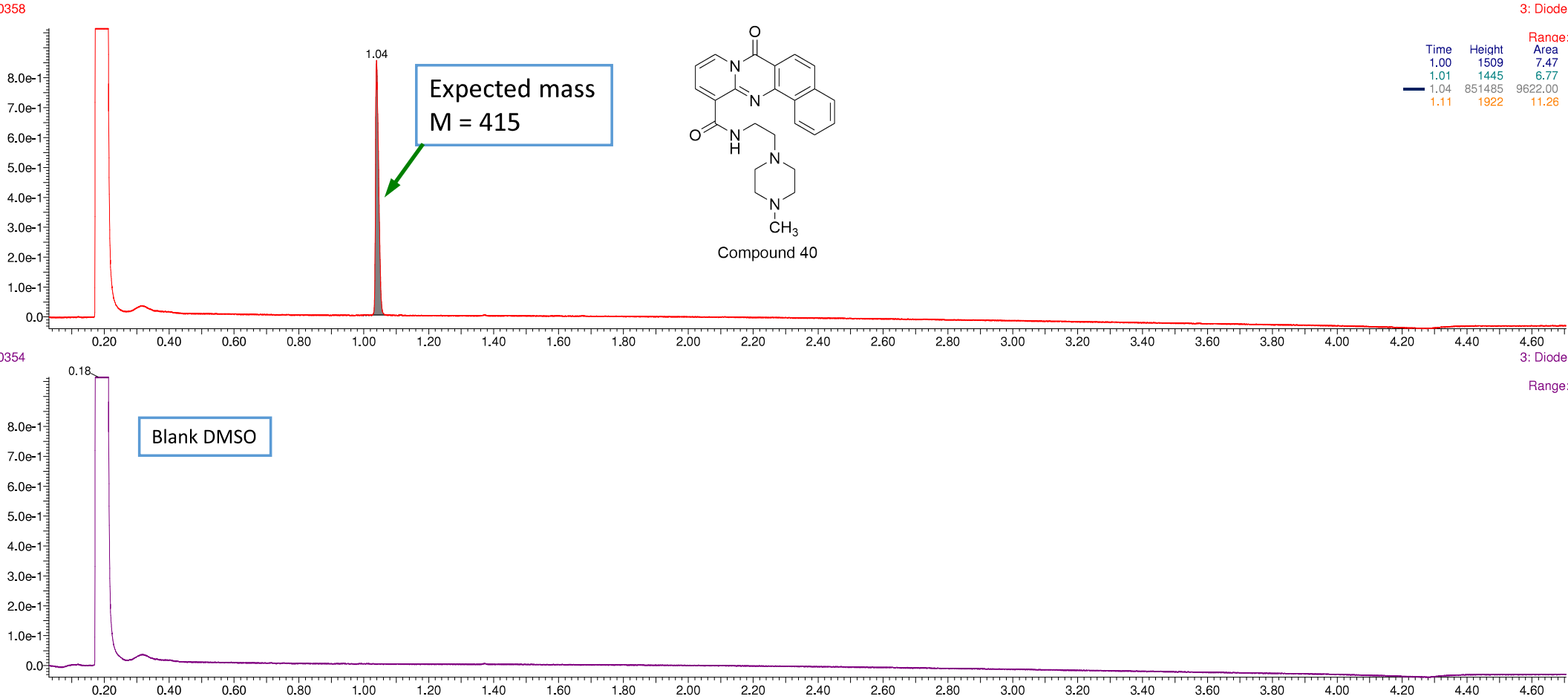

CQ-SQD#J08SQD356W
LCMS-20-01-00194
EV-QLR002-165-001
20-Jan-2020
0.5 mg/mL DMSO
0010314
3: Diode Array
220
Range: 1.393
Time Height Area Area%
1.01 6426 50.47 0.32
1.07 1004504 15271.32 96.11
1.15 67418 568.11 3.58
1.07
1.01
1.15
Expected mass
M = 388
Compound 38
0010308
3: Diode Array
220
Range: 1.402
0.19
Time


ACQ-SQD#J08SQD356W
LCMS-20-01-00192
EV-POH001-533-001
20-Jan-2020
0.5 mg/mL DMSO
L20010315
3: Diode Array
220
Range: 1.384
Time Height Area Area%
1.09 784956 9868.17 93.21
1.74 62553 719.33 6.79
1.09
1.74
Expected mass
M = 400
M = 290?
Compound 39
AU
L20010308
3: Diode Array
220
Range: 1.402
0.16
0.19
AU
Time

Q-SQD#J08SQD356W

EV-QLR002-102-001
LCMS-19-10-00263

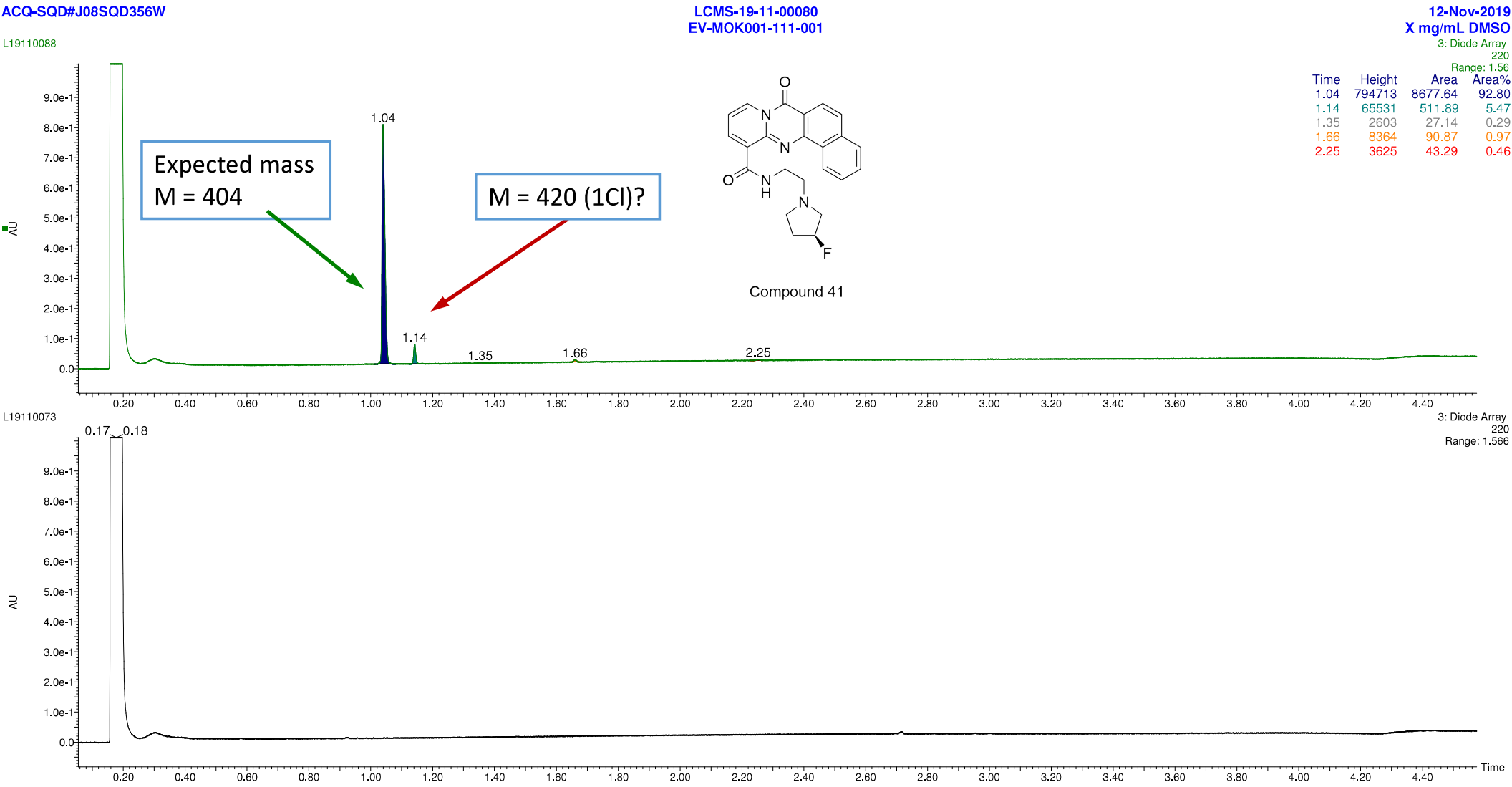
23-Oct-2
0.5 mg/mL DM







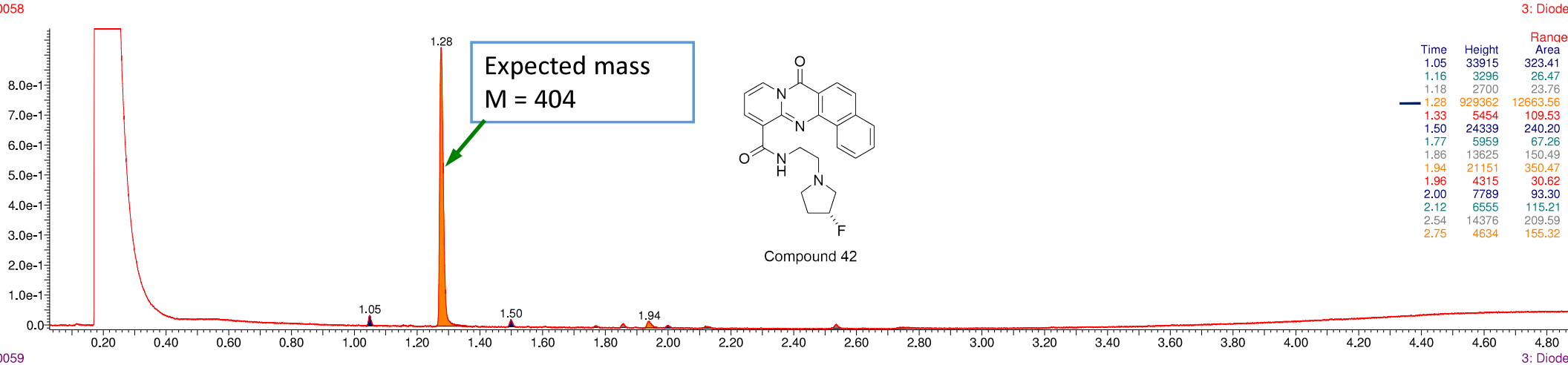
Compound 40


ACQ-SQD#J08SQD356W
LCMS-19-11-00080
EV-MOK001-111-001
12-Nov-2019
X mg/mL DMSO
L19110088
3: Diode Array
220
Range: 1.56
Time Height Area Area%
1.04 794713 8677.64 92.80
1.14 65531 511.89 5.47
1.35 2603 27.14 0.29
1.66 8364 90.87 0.97
2.25 3625 43.29 0.46
Expected mass
M = 404
M = 420 (1Cl)?
Compound 41
AU
1.04
1.14
1.35
1.66
2.25
L19110073
3: Diode Array
220
Range: 1.566
0.17
0.18
Time

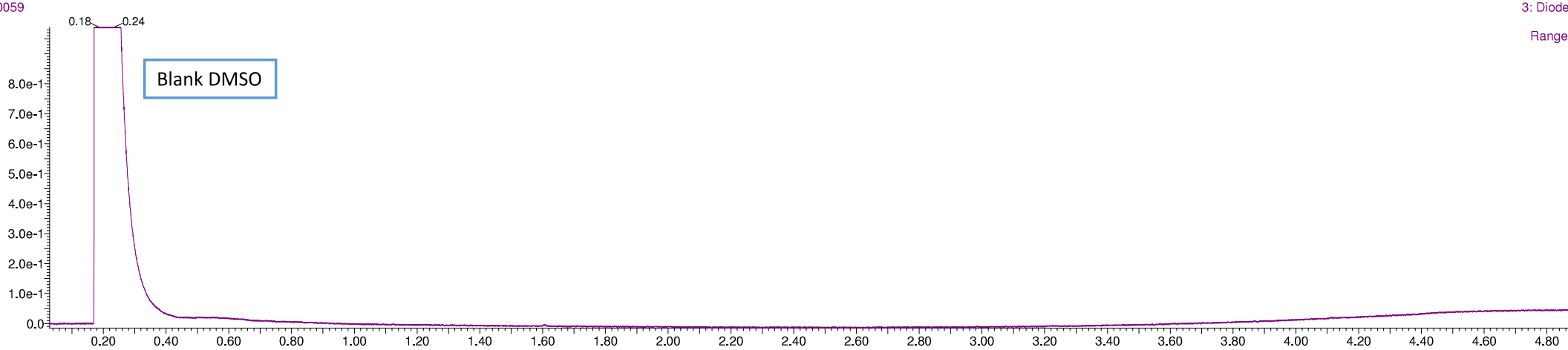
Q-SQD#E07SQD084W

EV-MOK001-149-001
LCMS-19-12-00005

10-Dec-2
0.5 mg/mL DM



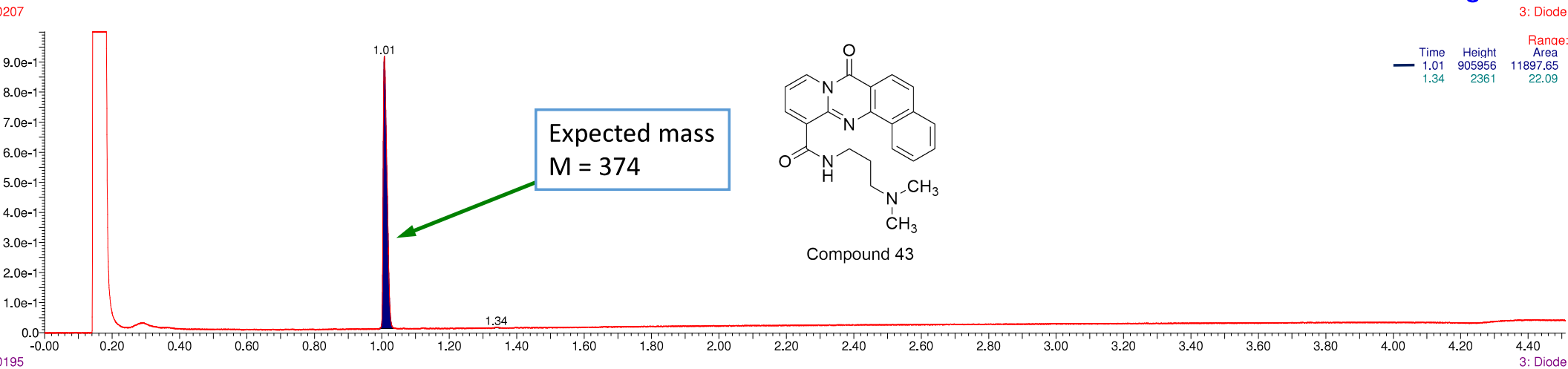

Compound 42



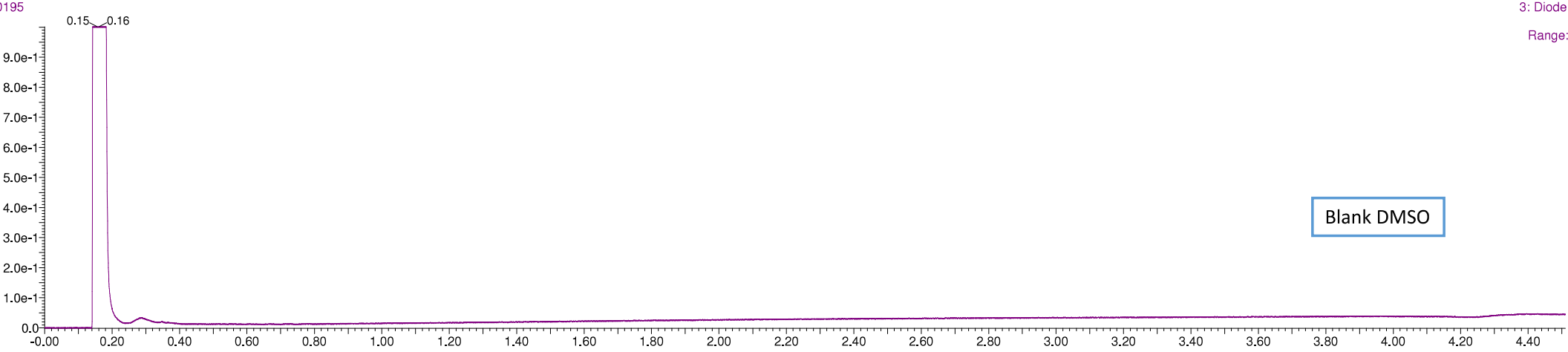
Q-SQD#J08SQD356W

EV-POH001-495-001
LCMS-19-11-00202

19-Nov-2(
0.5 mg/mL DM




Compound 43



Q-SQD#J08SQD356W

EV-POH001-489-001
LCMS-19-11-00105

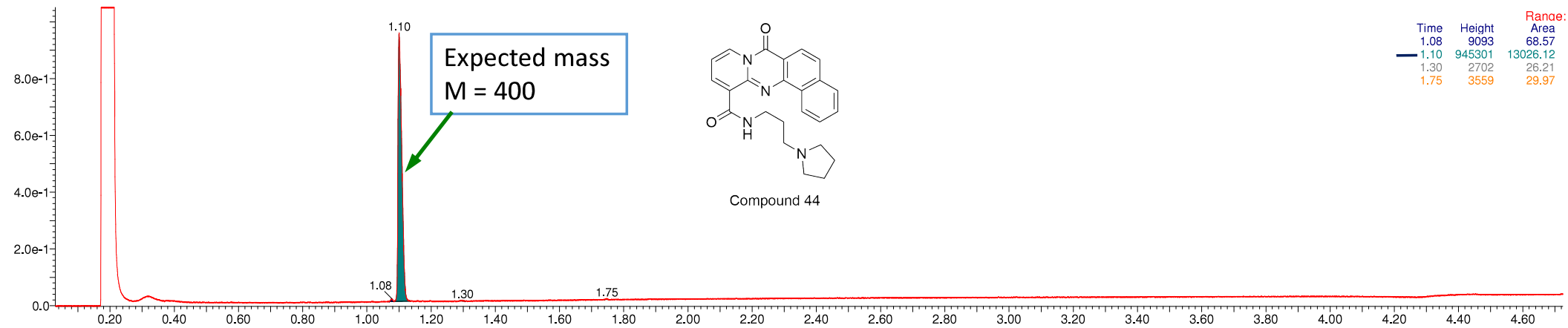
13-Nov-20
0.25 mg/mL DM

0118

3: Diode

Range:

| Time | Height | Area |
|---|---|---|
| 1.08 | 9093 | 68.57 |
| 1.10 | 945301 | 13026.12 |
| 1.30 | 2702 | 26.21 |
| 1.75 | 3559 | 29.97 |





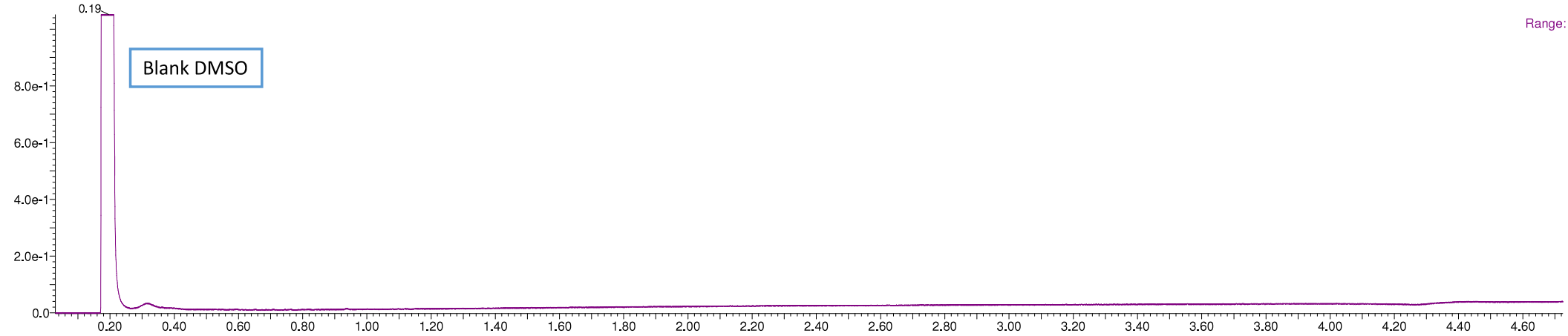


Compound 44

0114

3: Diode

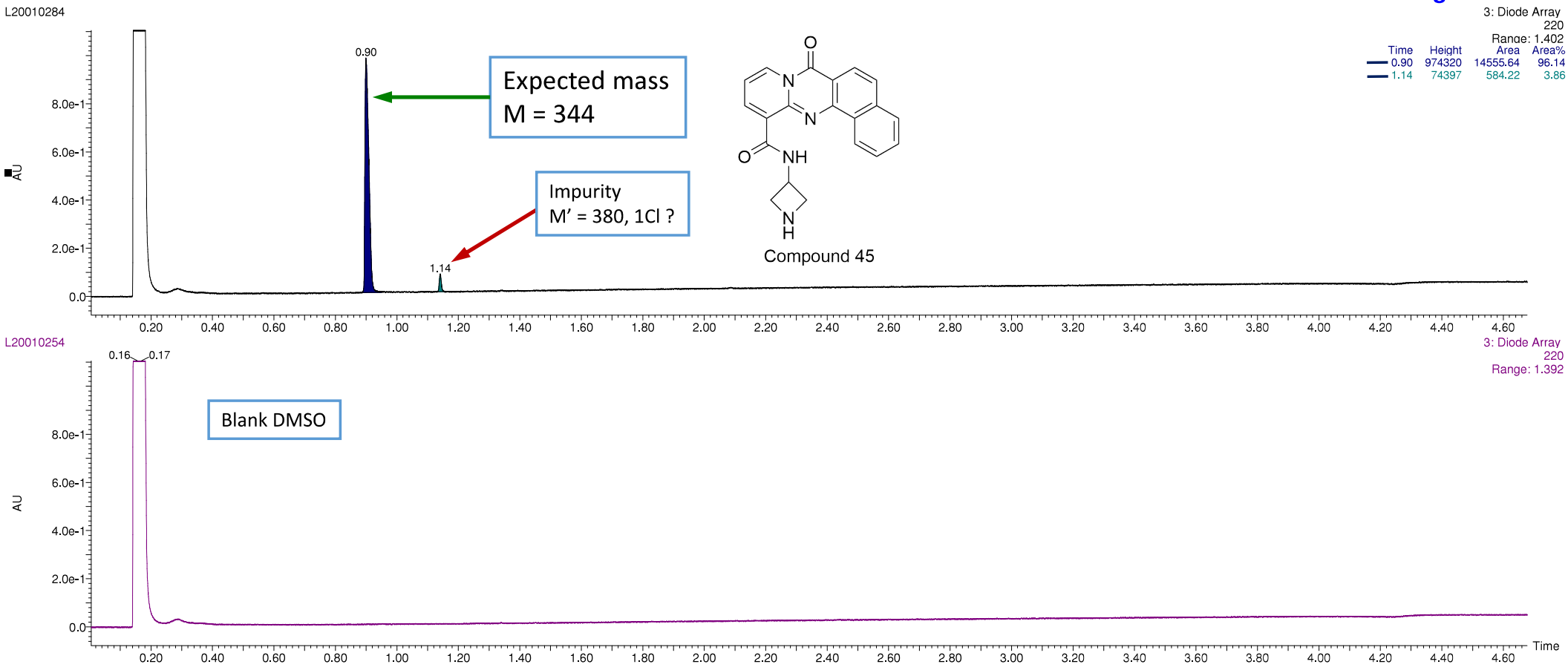
Range:



**ACQ-SQD#J08SQD356W**

**EV-MOK001-187-002**
**LCMS-20-01-00174**

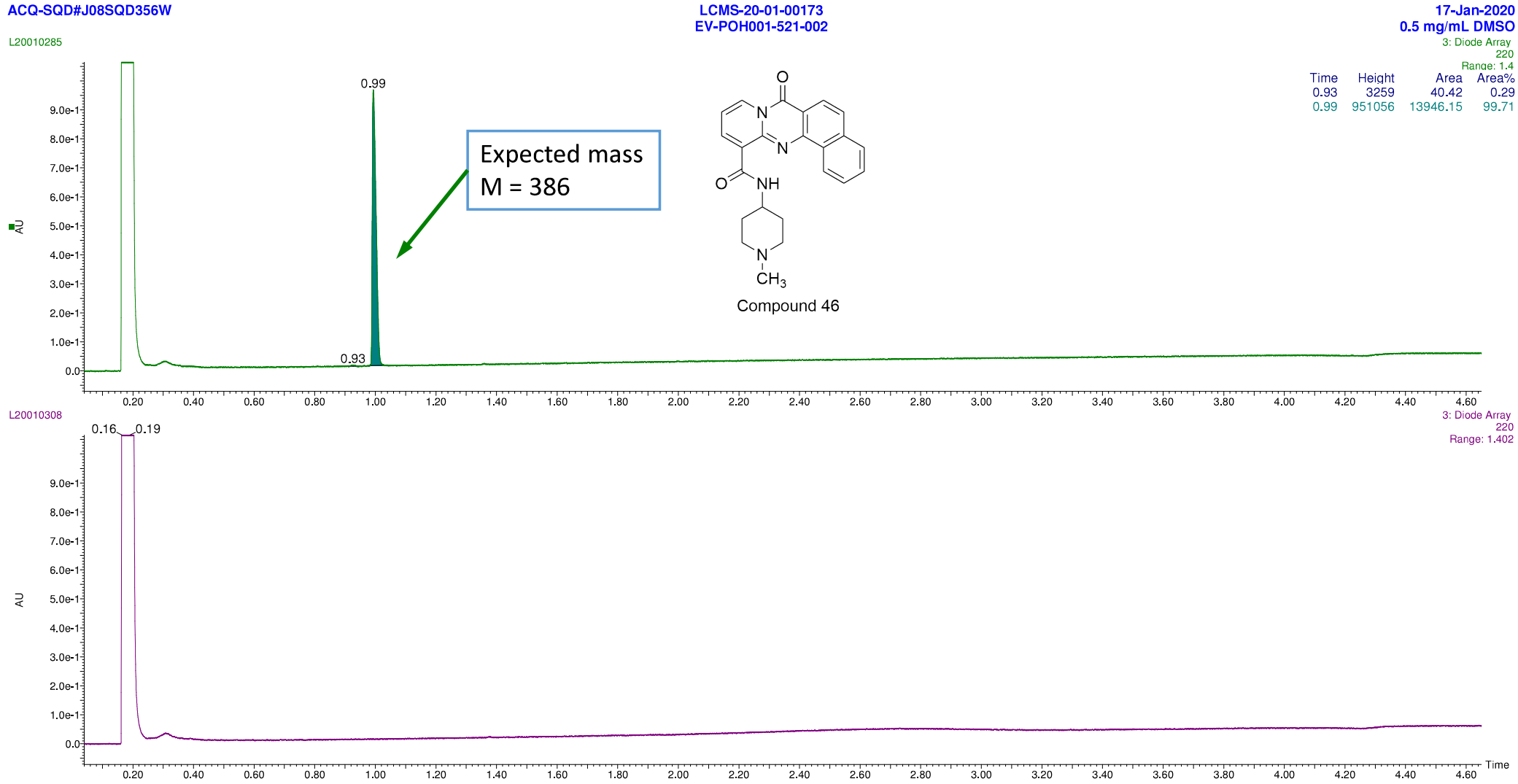
**17-Jan-2020**
**0.5 mg/mL DMSO**







Compound 45


ACQ-SQD#J08SQD356W
LCMS-20-01-00173
EV-POH001-521-002
17-Jan-2020
0.5 mg/mL DMSO
L20010285
3: Diode Array
220
Range: 1.4
Time Height Area Area%
0.93 3259 40.42 0.29
0.99 951056 13946.15 99.71
0.99
0.93
Expected mass
M = 386
Compound 46
AU
L20010308
3: Diode Array
220
Range: 1.402
0.16
0.19
Time