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Supporting Information

# Conjugates of Tacrine with Salicylamide as Promising Multitarget Agents for Alzheimer's Disease

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**Table of Contents Page**

## 1. Chemical part

Melting points were measured in open capillaries on "Stuart SMP30" melting point apparatus and uncorrected. The $^{1}H$ ($^{13}C$) NMR spectra were registered on "Bruker Avance$^{III}$ 500" spectrometer, 500 MHz (125 MHz) relative to $SiMe_4$. The IR spectra were recorded on "Perkin Elmer Spectrum One FT-IR" spectrometer by diffuse reflection accessory at 4000-400 $cm^{-1}$. The microanalyses (C, H, N) were carried out on "Perkin Elmer PE 2400" series II elemental analyzer. The high resolution mass spectrometry (HRMS) was performed using Bruker Daltonik MaXis Impact HD quadrupole time-of-flight mass spectrometer with positive electrospray ionization from methanol solutions, flow rate 180 $\mu l \cdot h^{-1}$ with parameters optimized for small molecules detection based on a pre-installed method for infusion analysis.

**1.1 Synthesis of compounds 5a-d (general procedure).** A mixture of 9-chloro-1,2,3,4-tetrahydroacridine **3** (1 g, 46 mmol), diaminoalkane **4a-d** (230 mmol), and a catalytic amount of potassium iodide in 15 ml of pentanol-1 was placed in a seal tube and reflux (160 °C) for 16 h, the reaction mixture was concentrated under reduced pressure. The residue was diluted with 50 ml of chloroform, the organic layer was washed with 10% solution of sodium hydroxide (3×50 ml) and water (3×50 ml), dried over sodium sulfate and evaporated. The residues were purified by silica gel column chromatography (eluent: $CHCl_3$/EtOH/$NH_4OH$ 50:1:0.1 → $CHCl_3$/EtOH/$NH_4OH$ 1:5:0.1). The physicochemical properties of the compounds **5a-d** coincide with the literature data [1–4].

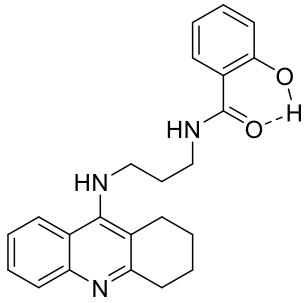
### 1.2 Synthesis of compounds 6a-d and 7

*Synthesis of salicyloyl chloride.* Thionyl chloride (2.5 g, 220 mmol) was added dropwise to a mixture of salicylic acid (2.8 g, 210 mmol) and triethylamine (0.2 ml, 1.4 mmol) in 10 ml of dry *n*-hexane. The mixture was refluxed for 2.5 hours, then the solvent was distilled off. The resulting salicyloyl chloride was used without further purification.

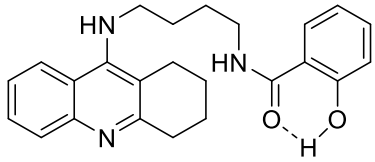
*Method A.* To a solution of compound **5a-d** (1.0 mmol) and pyridine (0.12 ml, 1.5 mmol) in anhydrous DCM (10 ml) at -20 °C a solution of salicyloyl chloride (0.188 g, 1.2 mmol) in anhydrous DCM was added dropwise. The reaction mixture was stirred for 4 h at the room temperature. Next the reaction mixture was concentrated on the rotary evaporator, the residue was dissolved in 20 ml of chloroform, the organic layer was washed with water (2×20 ml), dried over sodium sulfate and evaporated. The residue was purified by silica gel column chromatography (eluent $CHCl_3$/EtOH/$NH_4OH$ 25:1:0.1, then $CHCl_3$/EtOH/$NH_4OH$ 5:1:0.1).

*Method B.* Diisopropylethylamine (0.43 ml, 2.5 mmol) was added to a solution of compound **5a-d** (1.1 mmol) or hexylamine (0.111 g, 1.1 mmol) in anhydrous DCM (10 ml). The

reaction mixture was stirred for 20 minutes, and then HATU (0.418 g, 1.1 mmol) was added. After stirring the reaction mixture for 30 minutes, the solution of salicylic acid (0.138 g, 1.0 mmol) in anhydrous DCM (10 ml) was added, the reaction mixture was stirred for 4 h at the room temperature. Next the reaction mixture was concentrated on the rotary evaporator. The residue was dissolved in 20 ml of chloroform, the organic layer was washed with water (2×20 ml), dried over sodium sulfate and evaporated. The residue was purified by silica gel column chromatography (eluent $CHCl_3$/EtOH/$NH_4OH$ 25:1:0.1, then $CHCl_3$/EtOH/$NH_4OH$ 5:1:0.1).

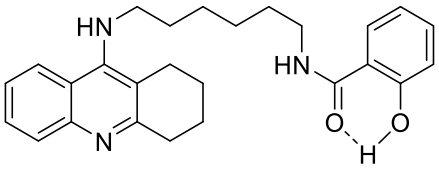



***N*-(3-(1,2,3,4-tetrahydroacridin-9-ylamino)propyl)salicylamide (6a).** Yield 0.225 g (60% *method A*), 0.240 g, 64% (*method B*), yellow oil. $^1$H NMR (500 MHz, $CDCl_3$) δ 1.85 (4H, d, *J* 3.1 Hz, $CH_2$); 1.89–1.97 (2H, m, $CH_2$); 2.70–2.77 (2H, m, $CH_2$); 2.95–3.02 (2H, m, $CH_2$); 3.54–3.61 (2H, m, $CH_2$); 3.61–3.67 (2H, m, $CH_2$); 4.95 (1H, br.s., NH); 6.77–6.82 (1H, m, $CH_{Ar}$); 6.97 (1H, d, *J* 8.2 Hz, $CH_{Ar}$); 7.30–7.35 (2H, m, $CH_{Ar}$); 7.48–7.53 (1H, m, $CH_{Ar}$); 7.58–7.63 (1H, m, $CH_{Ar}$); 7.87 (1H, d, *J* 8.2 Hz, $CH_{Ar}$); 7.92 (1H, br.s., NH); 8.02 (1H, d, *J* 8.5 Hz, $CH_{Ar}$). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 22.47; 22.84; 24.92; 31.29; 33.21; 36.88; 45.65; 115.27; 116.29; 118.38; 118.48; 120.03; 122.68; 124.01; 126.91; 127.6; 128.7; 133.94; 146.47; 151.04; 158.00; 161.22; 170.11. IR: ν 3287, 3061 (NH); 2936, 2864 (CH); 1636 (C=O); 1561, 1498, 1450, 1364 (NH, C=C, N–H, C=N) cm$^{-1}$. Anal. calcd. for $C_{23}H_{25}N_3O_2$. C, 73.57; H, 6.71; N, 11.19. Found: C, 73.28; H, 6.50 N, 11.22. HRMS (ESI), *m/z*: calcd. for $C_{24}H_{27}N_3O_2$: 390.2181 $[M+H]^+$; found 390.2171.

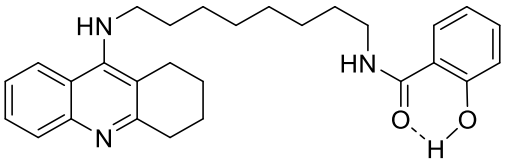



***N*-(4-(1,2,3,4-tetrahydroacridin-9-ylamino)butyl)salicylamide (6b).** Yield 0.210 g (54% *method A*), 0.276 g (71% *method B*), yellow oil. $^1$H NMR (500 MHz, $CDCl_3$) δ 1.63–1.77 (4H, m, $CH_2$); 1.82 (4H, s, $CH_2$); 2.65–2.53 (2H, m, $CH_2$); 3.00 (2H, s, $CH_2$); 3.45 (2H, s, $CH_2$); 3.54 (2H, s, $CH_2$); 4.34 (1H, br.s., NH); 6.71–6.79 (1H, m, $CH_{Ar}$); 6.91–6.97 (1H, m, $CH_{Ar}$); 7.27–7.35 (2H, m, $CH_{Ar}$); 7.45–7.53 (1H, m, $CH_{Ar}$); 7.60–7.70 (1H, m, $CH_{Ar}$); 7.74–7.86 (1H, m, $CH_{Ar}$); 7.86–7.91 (1H, m, NH); 7.91–7.99 (1H, m, $CH_{Ar}$). $^{13}$C NMR (125 MHz, $CDCl_3$) δ 22.26; 22.68; 24.54; 26.87; 28.84; 32.74; 39.06; 48.63; 115.17; 115.24; 118.22; 118.52; 119.42; 122.96; 123.94; 126.67; 126.95; 129.00; 133.78; 145.76; 151.38;

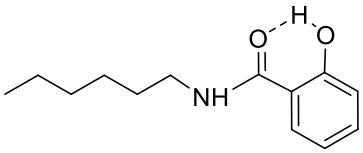
157.20; 161.00; 169.67. IR: ν 3283 (NH); 3060 (OH); 2924, 2854 (CH); 1637 (C=O); 1577, 1562, 1453, 1360, 1330, 1303 (NH, C=C, N–H, C=N) $cm^{-1}$. Anal. calcd. for $C_{24}H_{27}N_3O_2$. C, 74.01; H, 6.99; N, 10.79. Found: C, 73.95; H, 7.34 N, 10.62. HRMS (ESI), *m/z*: calcd. for $C_{24}H_{27}N_3O_2$: 390.2181 $[M+H]^+$; found 390.2171.




***N*-(6-(1,2,3,4-tetrahydroacridin-9-ylamino)hexyl)salicylamide (6c).** Yield 0.246 g (59% *method A*), 0.254 g (61% *method B*), white powder, mp 140–142℃. $^1$H NMR (500 MHz, DMSO) δ 1.25–1.40 (4H, m, $CH_2$); 1.44 – 1.64 (4H, m, $CH_2$); 1.70– 1.90 (4H, m, $CH_2$); 2.61– 2.76 (2H, m, $CH_2$); 2.82–3.00 (2H, m, $CH_2$); 3.20–3.34 (2H, m, $CH_2$); 3.37–3.53 (2H, m, $CH_2$); 5.52–5.76 (1H, m, NH); 6.85–6.88 (1H, m, $CH_{Ar}$); 6.89–6.92 (1H, m, $CH_{Ar}$); 7.31–7.42 (2H, m, $CH_{Ar}$); 7.52–7.62 (1H, m, $CH_{Ar}$); 7.68–7.77 (1H, m, $CH_{Ar}$); 7.81–7.92 (1H, m, $CH_{Ar}$); 8.09–8.21 (1H, m, $CH_{Ar}$); 8.75–8.97 (1H, m, NH). $^{13}$C NMR (125 MHz, DMSO) δ 22.16; 22.55; 24.90; 25.99; 26.17; 28.77; 30.45; 32.81; 38.75; 47.87; 115.16; 115.22; 117.36; 118.28; 119.67; 123.23; 123.31; 127.15; 127.54; 128.32; 133.47; 145.82; 150.93; 156.97; 160.30; 168.90. IR: ν 3368, 3332 (NH), 3063 (OH), 2930, 2858 (CH), 1638 (C=O), 1566, 1555 1512, 1451 (NH, C=C, N–H, C=N) $cm^{-1}$. Anal. calcd. for $C_{26}H_{31}N_3O_2$. C, 74.79; H, 7.48; N, 10.06. Found: C, 74.57; H, 7.50, N, 9.93. HRMS (ESI), *m/z*: calcd. for $C_{26}H_{31}N_3O_2$: 418.2495 $[M+H]^+$; found 418.2494.




***N*-(8-(1,2,3,4-tetrahydroacridin-9-ylamino)octyl)salicylamide (6d).** Yield 0.214 g (48% *method A*), 0.263 g (59% *method B*), yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): δ 1.20–1.36 (6H, m, $CH_2$); 1.34–1.45 (2H, m, $CH_2$); 1.56 (2H, m, $CH_2$); 1.71 (2H, dd, *J* 14.1 Hz, $CH_2$); 1.82–1.95 (4H, m, $CH_2$); 2.58–2.70 (2H, m, $CH_2$); 3.08–3.19 (2H, m, $CH_2$); 3.40 (2H, dd, *J* 13.4 Hz, $CH_2$); 3.57–3.76 (2H, m, $CH_2$); 4.44 (1H, br.s, NH); 6.75–6.85 (2H, m, $C_6H_4$); 6.94–7.00 (1H, m, *J* 7.5 Hz, $C_6H_4$); 7.41–7.32 (2H, m, $C_4H_6$); 7.49 (1H, d, *J* 7.7 Hz, $CH_{Ar}$); 7.59 (1H, t, *J* 7.3 Hz, $CH_{Ar}$); 8.04 (1H, d, *J* 8.5 Hz, $CH_{Ar}$); 8.11 (1H, d, *J* 9.1 Hz, $CH_{Ar}$). $^{13}$C NMR (125 MHz, $CDCl_3$): δ 22.24; 22.71; 24.44; 26.59; 26.65; 28.95; 28.95; 29.31; 31.52; 32.52; 39.51; 49.12; 114.54; 115.05; 118.22; 118.49; 119.12; 123.21; 123.86; 126.30; 126.68; 129.19; 133.69;.145.45; 151.92; 156.78; 161.07; 169.59. Anal. calcd. for $C_{28}H_{35}N_3O_2$. C, 75.47; H, 7.92; N, 9.43. Found: C, 75.34; H, 7.77, N, 9.31. HRMS (ESI), *m/z*: calcd. for $C_{28}H_{36}N_3O_2$: 446.2802 $[M+H]^+$; found 446.2807.




***N*-hexylsalicylamide (7).** Yield 0.163 g (57% *method B*) yellow oil. $^{1}$H NMR (500 MHz, $CDCl_3$) δ 0.85–0.94 (3H, m, $CH_3$); 1.28–1.43 (6H, m, $CH_2$); 1.57–1.67 (2H, m, $CH_2$); 3.44 (2H, dd, *J* 13.1, 7.1 Hz, $CH_2$); 6.32 (1H, bs, NH); 6.80–6.87 (1H, m, *J* 11.2, 3.9 Hz, $CH_{Ar}$); 6.98 (1H, d, *J* 7.9 Hz, $CH_{Ar}$); 7.34 (1H, d, *J* 7.9 Hz, $CH_{Ar}$); 7.36–7.42 (1H, m, $CH_{Ar}$); 12.40 (1H, br.s, OH). $^{13}$C NMR (126 MHz, $CDCl_3$) δ 13.97; 22.52; 26.60; 29.44; 31.44; 39.72; 114.38; 118.53; 118.65; 125.13; 134.06; 161.59; 169.91. IR: ν 3373; 3063 (NH); 2929; 2858 (CH); 1638 (C=O); 1591; 1539;1463; 1491; 1362 ($C_{Ar}$–$C_{Ar}$, N–H, C–N, C–H) $cm^{-1}$. Anal. calcd. for $C_{13}H_{19}NO_2$. C, 70.56; H, 8.65; N, 6.33. Found: C, 70.52; H, 8.78; N, 6.17. HRMS (ESI), *m/z*: calcd. for $C_{13}H_{19}NO_2$: 222.1489 $[M+H]^+$; found 222.1487.

## 2. Biological Assays

### 2.1 Esterase profile. In vitro AChE, BChE and CES Inhibition

All experiments were carried out in accordance with the standard protocols approved by IPAC RAS. Human erythrocyte AChE, equine serum BChE, porcine liver CES, acetylthiocholine iodide (ATCh), butyrylthiocholine iodide (BTCh), 5,5′-dithio-bis-(2-nitrobenzoic acid) (DTNB), and 4-nitrophenol acetate (4-NPA) were purchased from Sigma-Aldrich. For the esterase profile evaluation, AChE from human erythrocytes was used along with two enzymes of non-human origin, because of their relatively low cost and the exploratory character of this work [5]. High protein sequence identities between human and equine BChE (90%) and human CES1 and porcine liver CES (77%) (determined using NCBI protein BLAST, http://blast.ncbi.nlm.nih.gov/Blast.cgi?PAGE=Proteins) [6] along with good correlations with results obtained using enzymes from the same species [7] support the applicability of this set of enzymes for determining esterase profiles of new compounds.

AChE and BChE activities were measured by the colorimetric method of Ellman *et al.* [8] with modifications as described in [9]. The assay solution consisted of 0.1 M K/Na phosphate buffer pH 7.5, 25 °C, 0.33 mM DTNB, 0.02 unit/mL AChE or BChE, and 1 mM substrate (ATCh or BTCh, respectively). Reagent blanks consisted of reaction mixtures without substrates. The activity of CES was determined spectrophotometrically at 405 nm to monitor the release of 4-nitrophenol [10] with modifications as described in [9] in 0.1 M K/Na phosphate buffer pH 8.0, 25  C. Final enzyme and substrate (4-nitrophenyl acetate) concentrations were 0.02 unit/mL and 1 mM, respectively. Assays were carried out with a blank containing all constituents except porcine CES to assess non-enzymatic hydrolysis. Test compounds were dissolved in DMSO;

reaction mixtures contained 2% (v/v) of the solvent, a concentration shown not to affect the activity of the enzymes on its own (data not shown). Tacrine and donepezil were used as positive controls.

An initial evaluation of inhibitory activity of compounds was carried out by determination of the AChE, BChE and CES inhibition at a compound concentration of 20 μM. For this, a sample of the corresponding enzyme was incubated with the test compound for 5 min at 25 °C for temperature equilibration; then the enzyme residual activity was determined. Each experiment was performed in triplicate. For the most active compounds, the $IC_{50}$ values (the concentration of inhibitor required to decrease the enzyme activity by 50%) were determined. Eight different concentrations of the test compounds in the range $10^{-12}$ – $10^{-4}$ M were selected in order to obtain inhibition of esterases activity between 20% and 80%. The test compounds were added to the assay solution and incubated at 25 °C with the enzyme for 5 min (for temperature equilibration) followed by the addition of substrate. A parallel control was made for the assay solution with no inhibitor. Measurements were performed in a FLUOStar OPTIMA (BMG Labtech, Germany) microplate spectrophotometer. Each experiment for the $IC_{50}$ assay was performed in triplicate. The results were expressed as the mean ± SEM. The reaction rates in the presence and absence of inhibitor were compared, and the percent residual enzyme activity due to the presence of test compounds was calculated. $IC_{50}$ values were determined graphically from inhibition curves (log inhibitor concentration vs. percent residual enzyme activity) using Origin 6.1 software.

### 2.2 Kinetic Study of AChE and BChE Inhibition. Determination of Steady-State Inhibition Constants

We assessed the mechanisms of AChE and BChE inhibition were by performing a thorough analysis of enzyme kinetics. After a 5 min incubation at 25°C (for temperature equilibration) with three increasing concentrations of inhibitor and six decreasing substrate concentrations, the residual enzyme activity was measured as described above for enzymatic assays. Linear regression of 1/V versus 1/[S] double-reciprocal (Lineweaver-Burk) plots was used to determine the inhibition constants for the competitive component ($K_i$) and noncompetitive component ($\alpha K_i$).

### 2.3 Propidium Iodide Displacement Studies

We used the fluorescence method to detect the propensity of the test compounds to competitively displace propidium iodide (Sigma-Aldrich; a selective ligand of the AChE PAS) [11,12]. Donepezil and tacrine (Sigma-Aldrich) were employed as the positive controls (i.e.,

reference compounds). The enzyme was electric eel AChE (*Ee*AChE type VI-S, lyophilized powder, Sigma-Aldrich). We selected this source of AChE for consistency with our other reports and because of the purity, specific activity, and lower cost compared to human AChE. Moreover, a 3D alignment of *Ee*AChE (PDB: 1C2O) and human AChE (PDB: 4EY7) using the MUSTANG procedure [13] in YASARA-Structure 18.4.24 for Windows [14] yielded close agreement between the two structures (RMSD 0.623 Å over 527 aligned residues and 88.6% sequence identity.

The assay is based on the high level of fluorescence intensity of propidium iodide bound with AChE decreases in the presence of test compounds that competitively displace propidium iodide from the AChE PAS [15,16]. Specificially, *Ee*AChE (7 μM final concentration) is incubated with the test compound (20 μM in 1 mM Tris-HCl buffer pH 8.0, 25 °C, for 15 min). Propidium iodide (final concentration 8 μM) is then added for a further 15 min incubation and the fluorescence spectrum taken (530 nm (excitation) and 600 nm (emission)). The same concentration of propidium iodide in the Tris buffer was used as the blank. Triplicate determinations were recorded from a FLUOStar Optima microplate reader and results calculated via the following equation:

$$\% \text{ Displacement} = 100 - (IF_{\text{AChE+ Propidium + inhibitor}} / IF_{\text{AChE + Propidium}}) \times 100$$

where $IF_{\text{AChE + Propidium}}$ = fluorescence intensity of propidium iodide associated with AChE in the absence of the test compound (taken as 100%), and $IF_{\text{AChE + Propidium + inhibitor}}$ = fluorescence intensity of propidium iodide associated with AChE in the presence of the test compound.

### 2.4 ABTS radical cation scavenging activity assay

Radical scavenging activity of the compounds was assessed using the ABTS radical cation ($ABTS^{\bullet+}$) decolorization assay [17] with modifications described in detail in [18,19]. ABTS (2,2′-azinobis-(3-ethylbenzothiazoline-6-sulfonic acid)) was purchased from Tokyo Chemical Industry Co., Ltd. (Tokyo, Japan), potassium persulfate (dipotassium peroxodisulfate), Trolox (6-hydroxy-2,5,7,8-tetramethychroman-2-carboxylic acid), HPLC-grade ethanol, and DMSO were obtained from Sigma-Aldrich. All tested compounds were dissolved in DMSO.

ABTS was dissolved in deionized water to a 7mM concentration. The solution of $ABTS^{\bullet+}$ was produced by mixing 7mM ABTS stock solution with 2.45mM aqueous potassium persulfate solution in equal quantities and allowing them to react for 12–16 h at room temperature in the dark. At the time of activity determinations, $ABTS^{\bullet+}$ solution was diluted with ethanol to adjust to an absorbance value of 0.80 ± 0.05 at 734 nm. Fresh working $ABTS^{\bullet+}$ solution was prepared for each assay. Radical scavenging capacity of the compounds was analyzed by mixing 10 μl of compound solution with 240 μl of $ABTS^{\bullet+}$ working solution (100 μM final concentration). After

1 h of mixing the solutions, the reduction in absorbance was measured spectrophotometrically at 734 nm using a xMark UV/VIS microplate spectrophotometer (Bio-Rad, Hercules, CA, USA). Ethanol blanks were run in each assay. Standard antioxidant Trolox was used as reference compound. Values were obtained from three replicates of each sample and three independent experiments. Antioxidant activity was reported as Trolox Equivalent Antioxidant Capacity (TEAC values) as the ratio between the slopes obtained from the linear correlation of the ABTS radical absorbance with the concentrations of tested compounds and Trolox. For the test compounds, we also determined the $IC_{50}$ values (compound concentration required for 50% reduction of the ABTS radical) using Origin 6.1 software.

### 2.5 Metal-chelating

The complexation abilities of tested compound for biometals $Cu^{2+}$, $Fe^{2+}$ and $Zn^{2+}$ were studied in ethanol (95% v/v) at 298 K (25ºC) by UV–VIS spectrometry as described [20]. $CuCl_2$, $FeCl_2 \cdot 4H_2O$, $Zn(NO_3)_2 \cdot 6H_2O$ ethanol solutions were prepared in 200 μM concentration using volumetric flask. The tested compound was prepared with ethanol in 400 μM concentration. To a mixture of 0.5ml tested compound solution and 3.5 ml ethanol, 1 ml $CuCl_2$ solution ($FeCl_2 \cdot 4H_2O$ or $Zn(NO_3)_2 \cdot 6H_2O$) were added. The solution was incubated at 298 K (25ºC) for 30 min and then the absorption spectra were recorded in a 1 cm quartz cell using a UV–vis spectrophotometer (Shimadzu UV-2600) with wavelength ranging from 190 to 500 nm. The control sample was prepared by mixing 0.5 ml tested compound solution and 4.5ml ethanol.

## 3. Molecular Modeling Studies

### 3.1 Preparation of the molecules

To determine protonation states of the inhibitors estimations of p$K_a$ values were performed using the Calculator Plugins of Marvin 21.14.0, ChemAxon (http://www.chemaxon.com). According to the results, for all conjugates at the experimental pH, the tacrine fragments were protonated. Compounds in the chosen protonated form were optimized using a DFT quantum chemistry method (B3LYP/6-31G*, GAMESS-US [21] software). Obtained optimized geometries with partial atomic charges derived from QM results according to the Löwdin scheme [22] ere used for further molecular docking simulations.

### 3.2 Molecular docking

According to the previous findings [23], for docking of bulky ligands, X-ray structures of human AChE co-crystallized with donepezil (PDB: 4EY7 [24]) is more suitable, than unliganded (apo-form). This one, and an optimized X-ray structure of human BChE (PDB: 1P0I) [25,26] were used as targets for molecular docking. The grid box for docking included the entire active

site gorge of AChE (22.5 Å × 22.5 Å × 22.5 Å grid box dimensions) and BChE (15 Å × 20.25 Å × 18 Å grid box dimensions) with a grid spacing of 0.375 Å. Molecular docking was performed with AutoDock 4.2.6 software [27]. The main Lamarckian Genetic Algorithm [28] docking parameters were: 256 runs, $25\times10^6$ evaluations, $27\times10^4$ generations, and a population size of 3000. Figures were prepared with PyMOL visualizing software (www.pymol.org).

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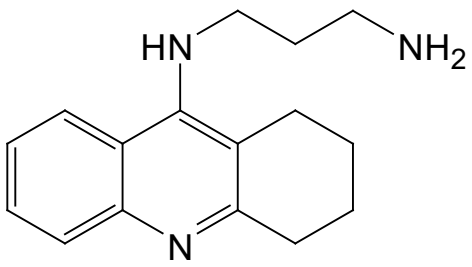



**5a**

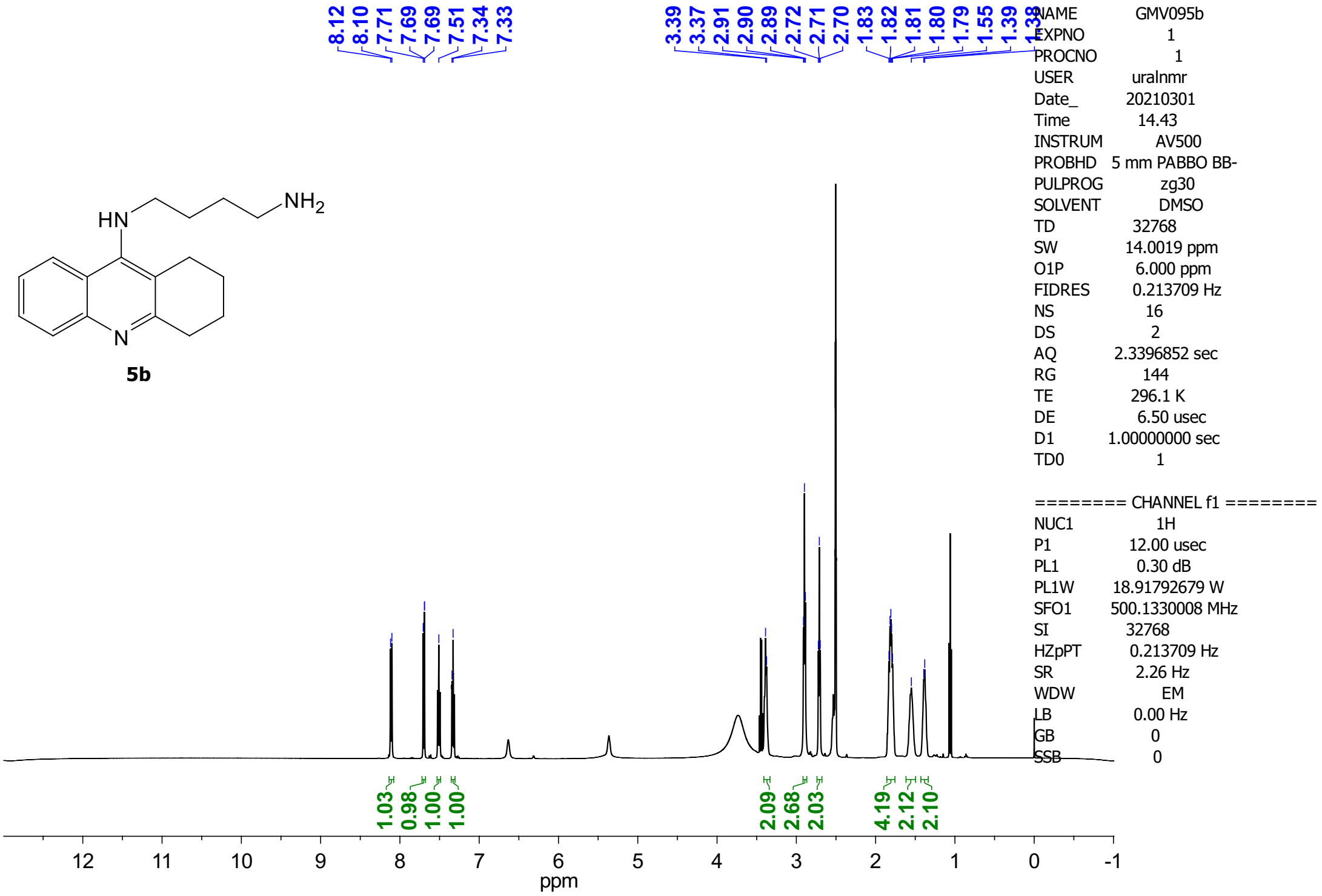



Current Data Parameters
NAME GMV128
EXPNO 1
PROCNO 1
USER uralnmr

F2 - Acquisition Parameters
Date_ 20210521
Time 13.17
INSTRUM DRX400
PROBHD 5 mm SEF 19F-1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 1448.2
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

===== CHANNEL f1 ======
NUC1 1H
P1 32.50 usec
PL1 -4.00 dB
SFO1 400.1328009 MHz

F2 - Processing parameters
SI 32768
HZpPT 0.195625 Hz
SF 400.1300068 MHz
SR 6.80 Hz
WDW EM
LB 0.00 Hz
GB 0
SSB 0
PC 4.00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8.10
7.71
7.69
7.69
7.51
7.34
7.33
3.39
3.37
2.91
2.90
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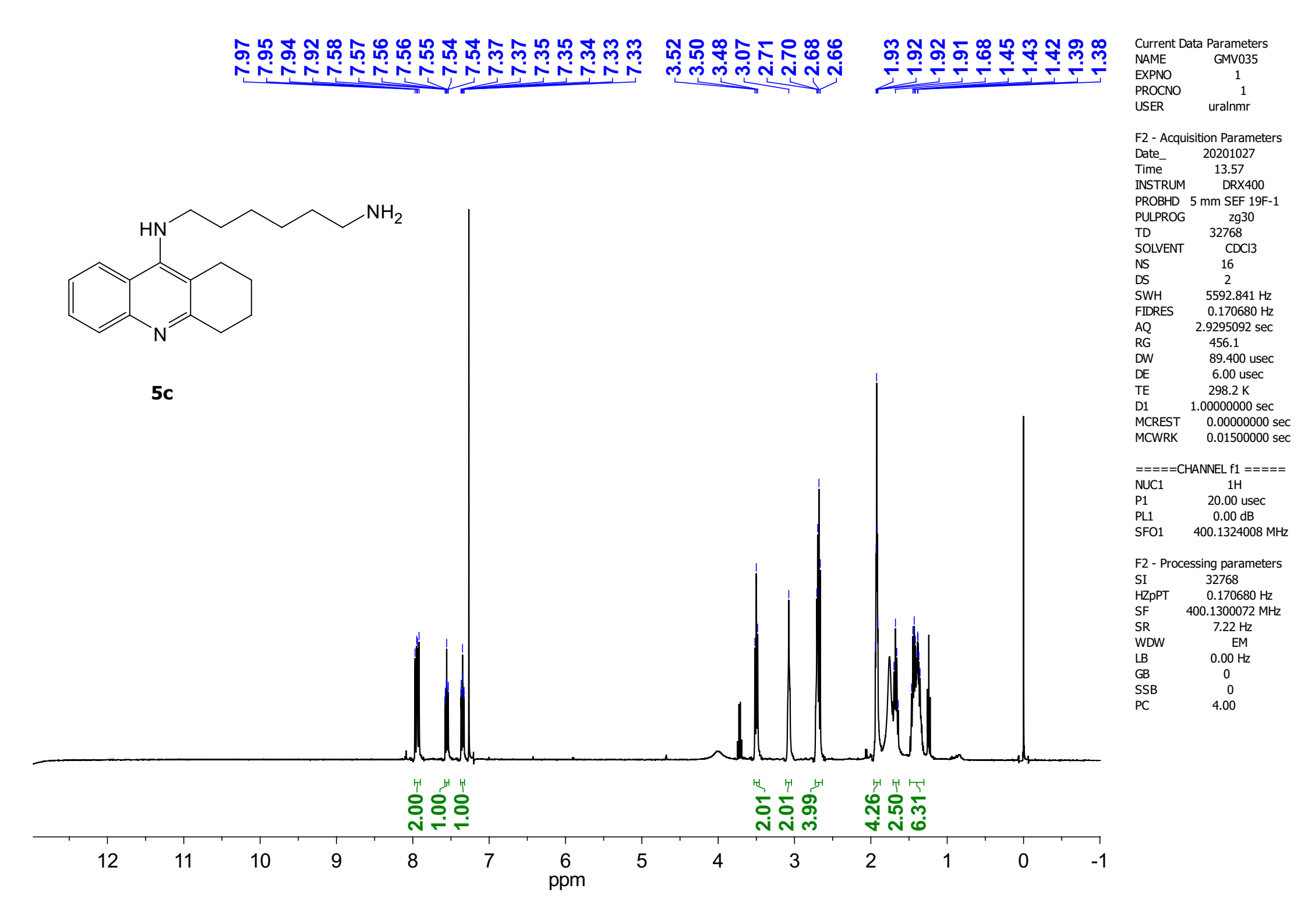
2.72
2.71
2.70
1.83
1.82
1.81
1.80
1.79
1.55
1.39
1.38
HN
NH2
N
5b
NAME GMV095b
EXPNO 1
PROCNO 1
USER uralnmr
Date_ 20210301
Time 14.43
INSTRUM AV500
PROBHD 5 mm PABBO BB-
PULPROG zg30
SOLVENT DMSO
TD 32768
SW 14.0019 ppm
O1P 6.000 ppm
FIDRES 0.213709 Hz
NS 16
DS 2
AQ 2.3396852 sec
RG 144
TE 296.1 K
DE 6.50 usec
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 12.00 usec
PL1 0.30 dB
PL1W 18.91792679 W
SFO1 500.1330008 MHz
SI 32768
HZpPT 0.213709 Hz
SR 2.26 Hz
WDW EM
LB 0.00 Hz
GB 0
SSB 0
1.03
0.98
1.00
1.00
2.09
2.68
2.03
4.19
2.12
2.10
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
ppm

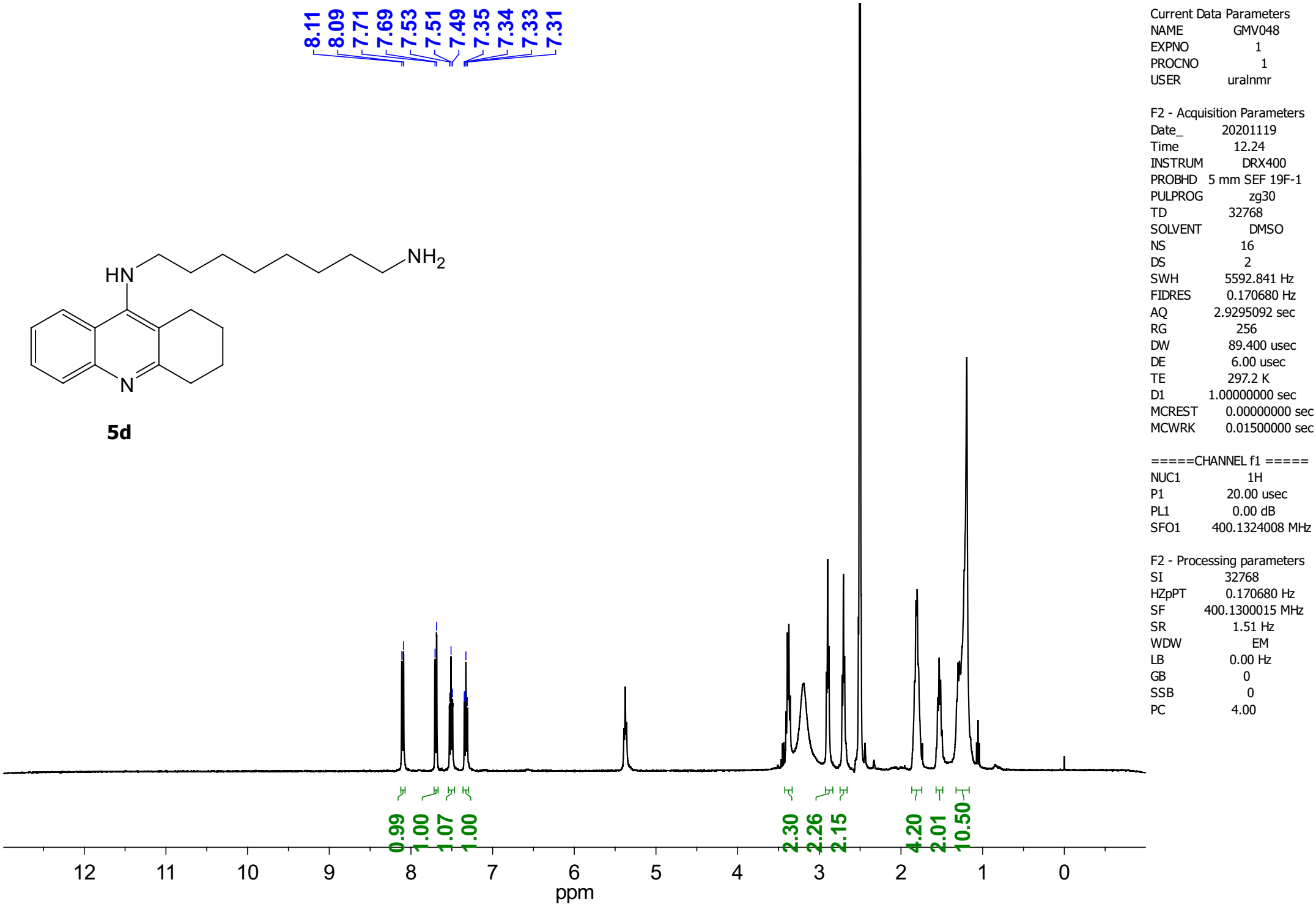



Current Data Parameters
NAME GMV035
EXPNO 1
PROCNO 1
USER uralnmr

F2 - Acquisition Parameters
Date_ 20201027
Time 13.57
INSTRUM DRX400
PROBHD 5 mm SEF 19F-1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 5592.841 Hz
FIDRES 0.170680 Hz
AQ 2.9295092 sec
RG 456.1
DW 89.400 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

=====CHANNEL f1 =====
NUC1 1H
P1 20.00 usec
PL1 0.00 dB
SFO1 400.1324008 MHz

F2 - Processing parameters
SI 32768
HZpPT 0.170680 Hz
SF 400.1300072 MHz
SR 7.22 Hz
WDW EM
LB 0.00 Hz
GB 0
SSB 0
PC 4.00

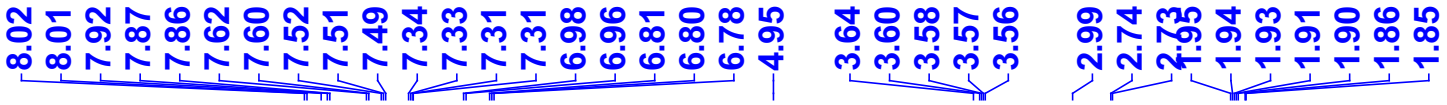


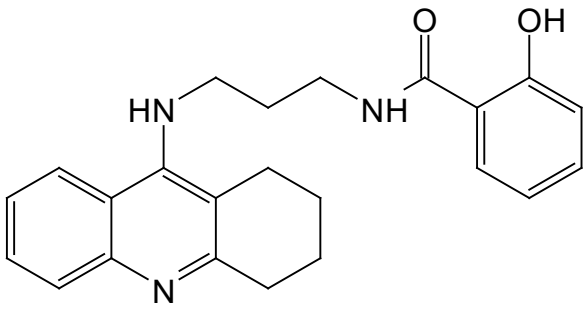

Current Data Parameters
NAME GMV048
EXPNO 1
PROCNO 1
USER uralnmr

F2 - Acquisition Parameters
Date_ 20201119
Time 12.24
INSTRUM DRX400
PROBHD 5 mm SEF 19F-1
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 16
DS 2
SWH 5592.841 Hz
FIDRES 0.170680 Hz
AQ 2.9295092 sec
RG 256
DW 89.400 usec
DE 6.00 usec
TE 297.2 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

=====CHANNEL f1 =====
NUC1 1H
P1 20.00 usec
PL1 0.00 dB
SFO1 400.1324008 MHz

F2 - Processing parameters
SI 32768
HZpPT 0.170680 Hz
SF 400.1300015 MHz
SR 1.51 Hz
WDW EM
LB 0.00 Hz
GB 0
SSB 0
PC 4.00



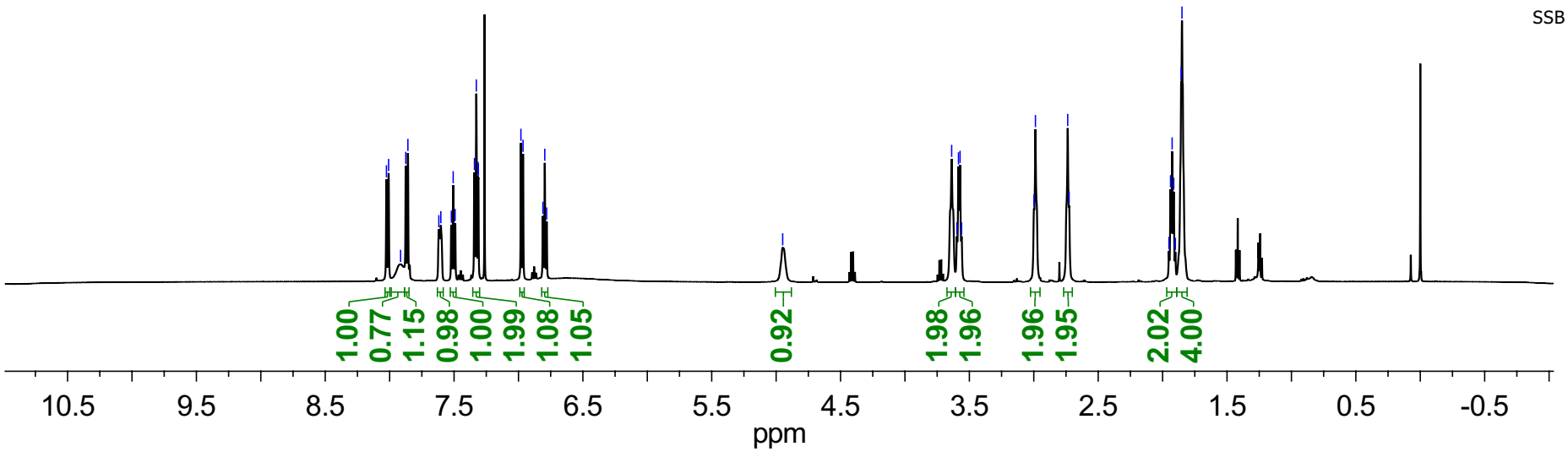



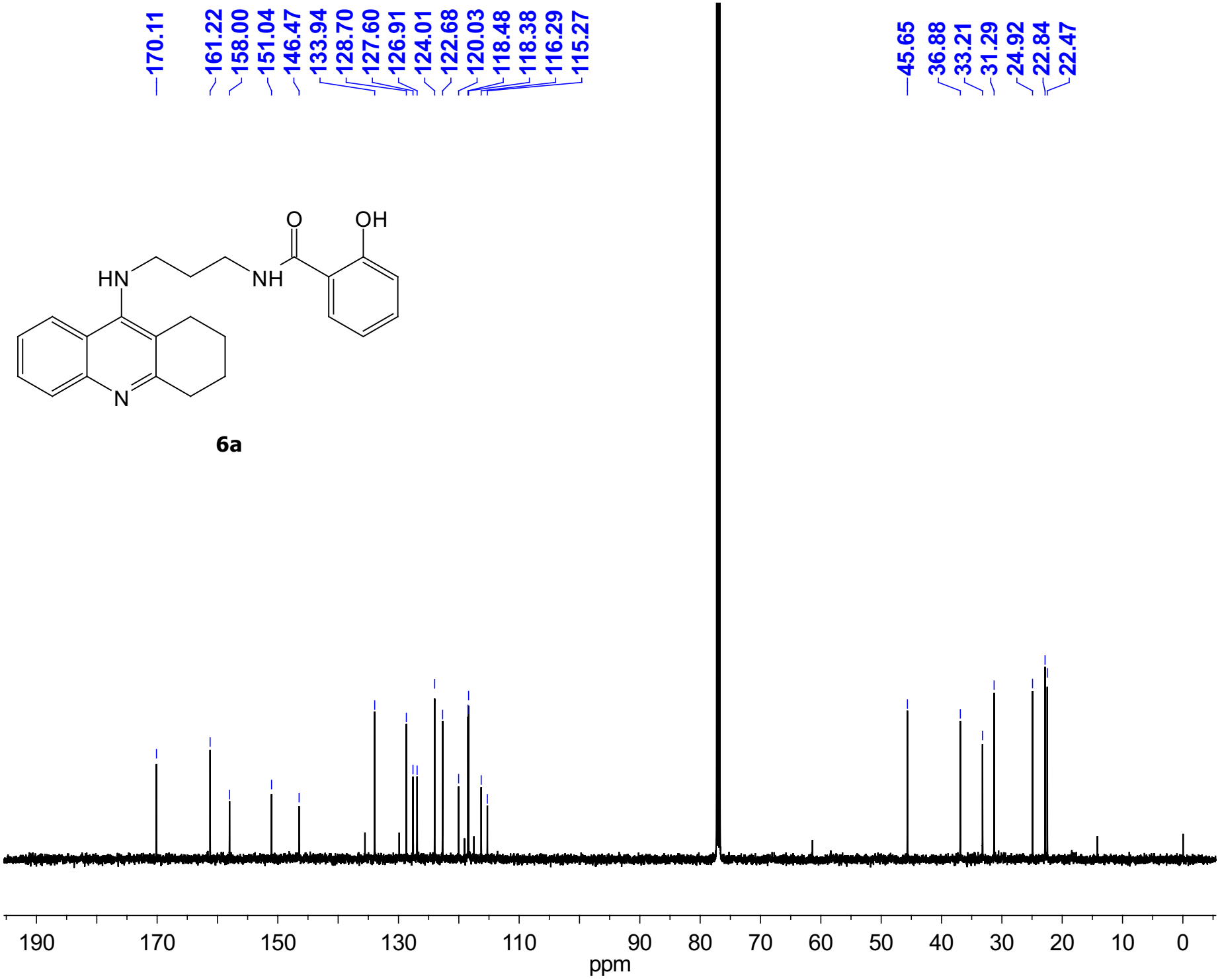

**6a**

| | |
|---|---|
| NAME | GMV141a |
| EXPNO | 1 |
| PROCNO | 1 |
| USER | uralnmr |
| Date_ | 20210812 |
| Time | 16.22 |
| INSTRUM | AV500 |
| PROBHD | 5 mm PABBO BB- |
| PULPROG | zg30 |
| SOLVENT | CDCl3 |
| TD | 32768 |
| SW | 12.0160 ppm |
| O1P | 5.000 ppm |
| FIDRES | 0.183399 Hz |
| NS | 16 |
| DS | 2 |
| AQ | 2.7263477 sec |
| RG | 114 |
| TE | 295.2 K |
| DE | 6.50 usec |
| D1 | 1.50000000 sec |
| TD0 | 1 |

== == CHANNEL f1 ======

| | |
|---|---|
| NUC1 | 1H |
| P1 | 12.00 usec |
| PL1 | 0.30 dB |
| PL1W | 18.91792679 W |
| SFO1 | 500.1325007 MHz |
| SI | 32768 |
| HZpPT | 0.183399 Hz |
| SR | 12.14 Hz |
| WDW | EM |
| LB | 0.00 Hz |
| GB | 0 |
| SSB | 0 |






| | |
|---|---|
| NAME | GMV141a |
| EXPNO | 13 |
| PROCNO | 1 |
| USER | uralnmr |
| Date_ | 20210812 |
| Time | 16.23 |
| INSTRUM | AV500 |
| PROBHD | 5 mm PABBO BB- |
| PULPROG | zgpg30 |
| SOLVENT | CDCl3 |
| TD | 32768 |
| SW | 200.7838 ppm |
| O1P | 95.000 ppm |
| FIDRES | 0.770646 Hz |
| NS | 1024 |
| DS | 8 |
| AQ | 0.6488564 sec |
| RG | 203 |
| TE | 296.0 K |
| DE | 6.50 usec |
| D1 | 0.85000002 sec |
| D11 | 0.03000000 sec |
| TD0 | 1 |

===== CHANNEL f1 ======

| | |
|---|---|
| NUC1 | 13C |
| P1 | 10.00 usec |
| PL1 | 0.00 dB |
| PL1W | 115.29558563 W |
| SFO1 | 125.7697360 MHz |

=====CHANNEL f2 =====

| | |
|---|---|
| CPDPRG2 | waltz16 |
| NUC2 | 1H |
| PCPD2 | 75.00 usec |
| PL2 | 120.00 dB |
| PL12 | 16.30 dB |
| PL13 | 19.30 dB |
| PL2W | 0.00000000 W |
| PL12W | 0.47519693 W |
| PL13W | 0.23816262 W |
| SFO2 | 500.1320005 MHz |
| SI | 32768 |
| HZpPT | 0.770646 Hz |
| SR | 5.30 Hz |
| WDW | EM |
| LB | 1.00 Hz |
| GB | 0 |
| SSB | 0 |

# Compound Spectrum SmartFormula Report

**Analysis Info**

Acquisition Date 9/22/2021 1:59:15 PM

| | |
|---|---|
| Analysis Name | D:\Data\ING21\GMV-141a.22i-C.EP180.6220_22i1400.d |
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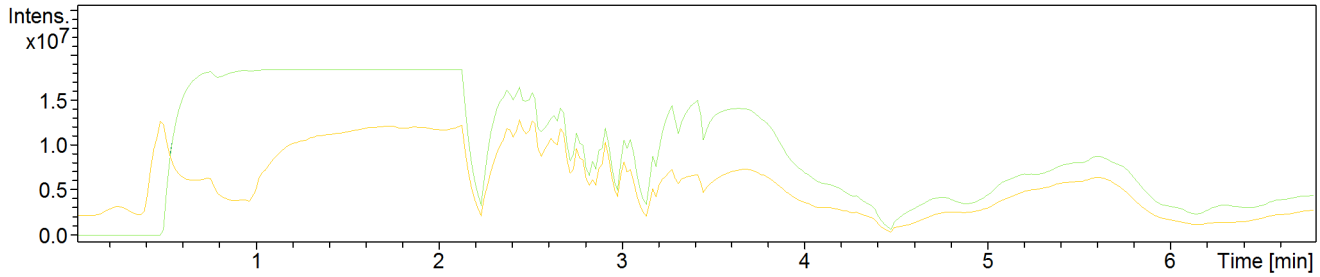
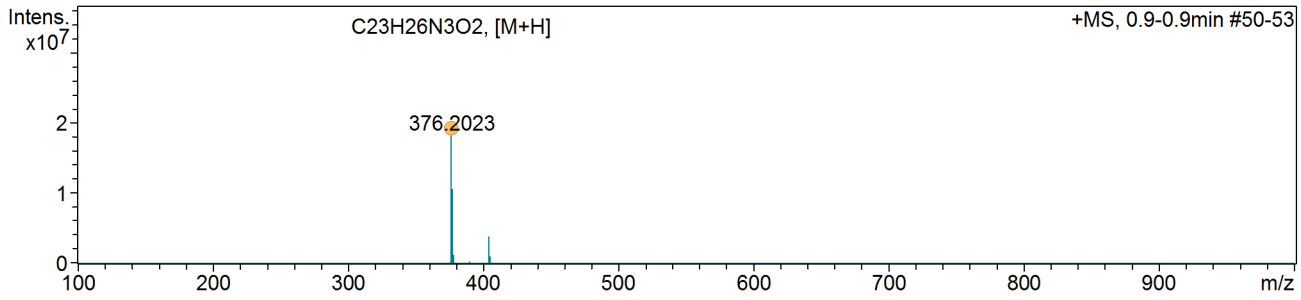
| Operator | admin |
| Sample Name | |
| Instrument | maXis impact 1819696.00172 |
| Comment | 22/09/2022: +Bckgnd: 118.09, 322.05, 622.03, 922.01, 1221.99, 1521.97, 1821.95, 2121.93, 2421.91, 2721.89 (G1969-85000; +/-299.981 HPC); other intense peaks (>2*e4): 102.13 (NEt3); 132.91 (*2-PrOH); 391.28&413.26 (DOP); 86.10, 113.13, 140.07, 149.02, 158.96, 167.03, 187.07. 194.10, 203.14, 207.17, 209.19, 214.25, 217.10, 223.21, 227.23, 237.22, 245.19, 249.22, 251.24, 255.27, 259.20, 263.23, 265.25, 273.22, 279.16, 291.27, 293.28, 304.30, 307.30, 321.31, 326.38, 332.33, 335.33, 349.35, 413.27, 1259.95, 1307.08, 1559.93: background (prev. analyzed samples and impurities); 188.09 (#6216); 588.32 (#6218); 404.23 (#6219) |

**Acquisition Parameter**

| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.4 Bar |
| Focus | Active | Set Capillary | 3500 V | Set Dry Heater | 200 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 1600 m/z | Set Charging Voltage | 2000 V | Set Divert Valve | Source |
| | | Set Corona | 0 nA | Set APCI Heater | 0 °C |

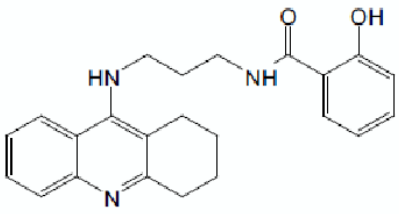



**+MS, 0.9-0.9min #50-53**




| Meas. m/z | # | Ion Formula | m/z | err [ppm] | mSigma | # mSigma | Score | rdb | e¯ Conf | N-Rule |
|---|---|---|---|---|---|---|---|---|---|---|
| 376.2023 | 1 | C23H26N3O2 | 376.2020 | -0.9 | 184.9 | 1 | 100.00 | 12.5 | even | ok |
| | 2 | C8H22N15O3 | 376.2025 | 0.5 | 254.1 | 2 | 0.18 | 5.5 | even | ok |

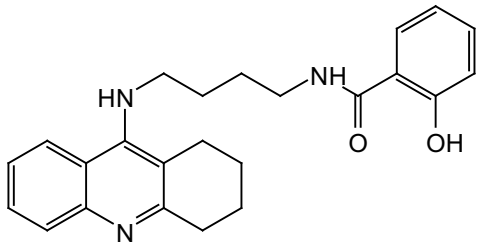
**+MS, 3.6-3.7min #206-212**




**6a**




Institute of Organic Synthesis UB RAS
22 S.Kovalevskoy, 20 Akademicheskaya str, Yekaterinburg, Russian Federation
Phone: +7 (343) 362-34-56

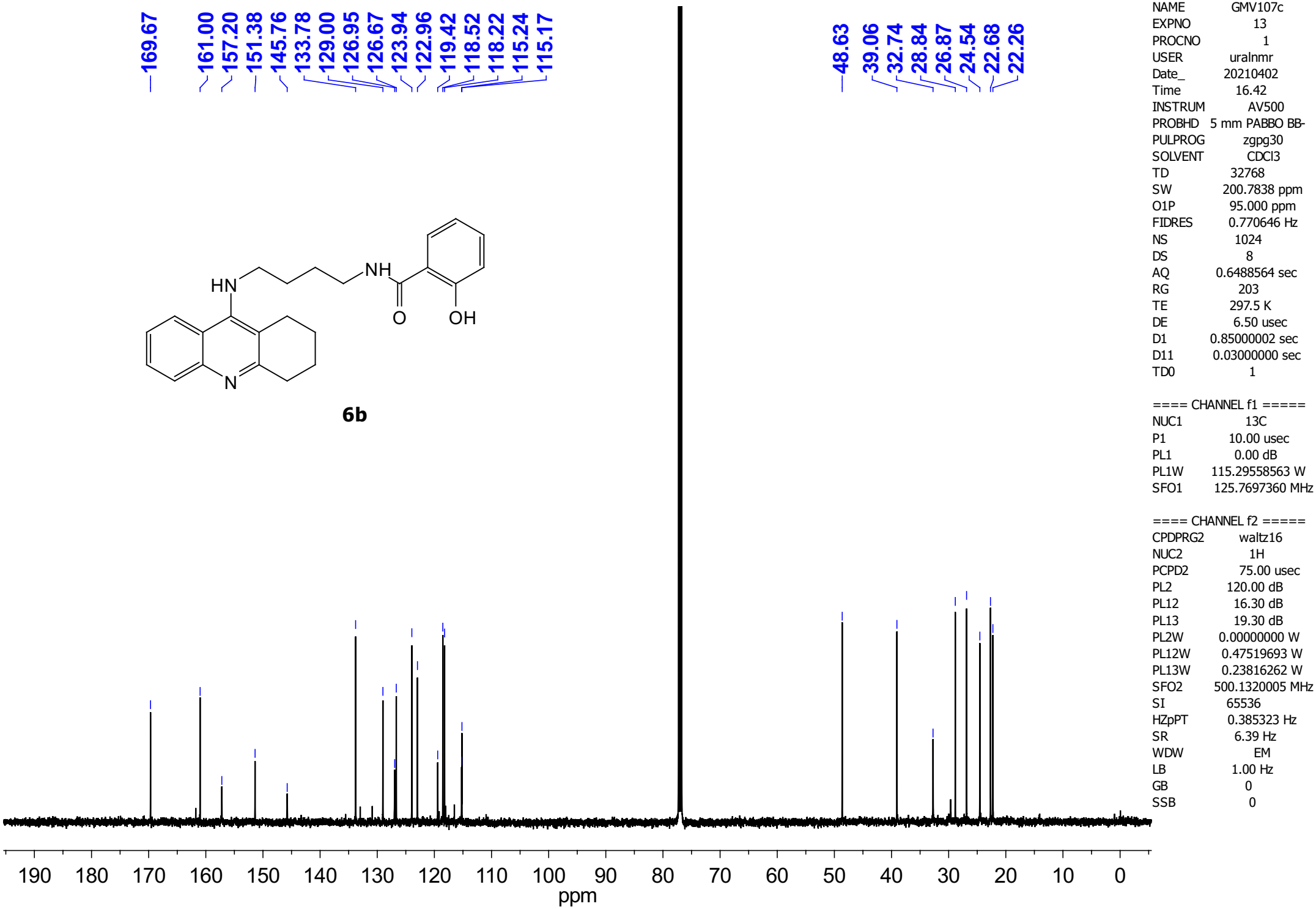



**6b**

| | |
|---|---|
| NAME | GMV107c |
| EXPNO | 1 |
| PROCNO | 1 |
| USER | uralnmr |
| Date_ | 20210318 |
| Time | 12.37 |
| INSTRUM | AV500 |
| PROBHD | 5 mm PABBO BB- |
| PULPROG | zg30 |
| SOLVENT | CDCl3 |
| TD | 32768 |
| SW | 14.0019 ppm |
| O1P | 6.000 ppm |
| FIDRES | 0.213709 Hz |
| NS | 16 |
| DS | 2 |
| AQ | 2.3396852 sec |
| RG | 57 |
| TE | 296.3 K |
| DE | 6.50 usec |
| D1 | 1.00000000 sec |
| TD0 | 1 |

===== CHANNEL f1 ======

| | |
|---|---|
| NUC1 | 1H |
| P1 | 12.00 usec |
| PL1 | 0.30 dB |
| PL1W | 18.91792679 W |
| SFO1 | 500.1330008 MHz |
| SI | 32768 |
| HZpPT | 0.213709 Hz |
| SR | 11.09 Hz |
| WDW | EM |
| LB | 0.00 Hz |
| GB | 0 |
| SSB | 0 |




| | |
|---|---|
| NAME | GMV107c |
| EXPNO | 13 |
| PROCNO | 1 |
| USER | uralnmr |
| Date_ | 20210402 |
| Time | 16.42 |
| INSTRUM | AV500 |
| PROBHD | 5 mm PABBO BB- |
| PULPROG | zgpg30 |
| SOLVENT | CDCl3 |
| TD | 32768 |
| SW | 200.7838 ppm |
| O1P | 95.000 ppm |
| FIDRES | 0.770646 Hz |
| NS | 1024 |
| DS | 8 |
| AQ | 0.6488564 sec |
| RG | 203 |
| TE | 297.5 K |
| DE | 6.50 usec |
| D1 | 0.85000002 sec |
| D11 | 0.03000000 sec |
| TD0 | 1 |
| ==== CHANNEL f1 ===== | |
| NUC1 | 13C |
| P1 | 10.00 usec |
| PL1 | 0.00 dB |
| PL1W | 115.29558563 W |
| SFO1 | 125.7697360 MHz |
| ==== CHANNEL f2 ===== | |
| CPDPRG2 | waltz16 |
| NUC2 | 1H |
| PCPD2 | 75.00 usec |
| PL2 | 120.00 dB |
| PL12 | 16.30 dB |
| PL13 | 19.30 dB |
| PL2W | 0.00000000 W |
| PL12W | 0.47519693 W |
| PL13W | 0.23816262 W |
| SFO2 | 500.1320005 MHz |
| SI | 65536 |
| HZpPT | 0.385323 Hz |
| SR | 6.39 Hz |
| WDW | EM |
| LB | 1.00 Hz |
| GB | 0 |
| SSB | 0 |

# Compound Spectrum SmartFormula Report

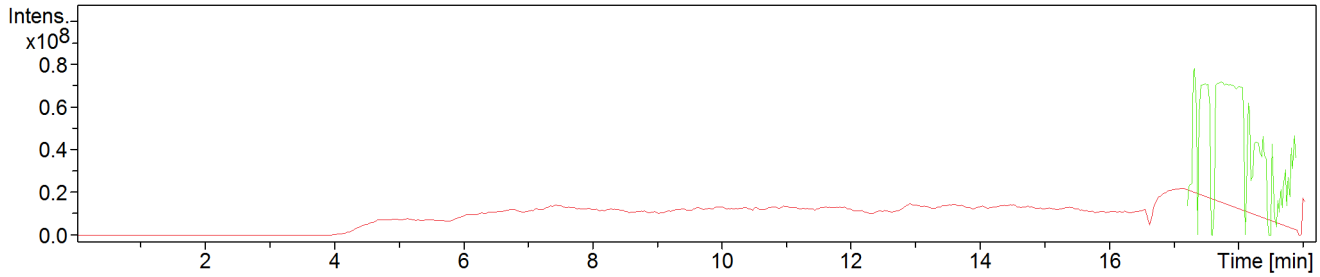
**Analysis Info**

Acquisition Date 4/26/2021 10:25:54 AM

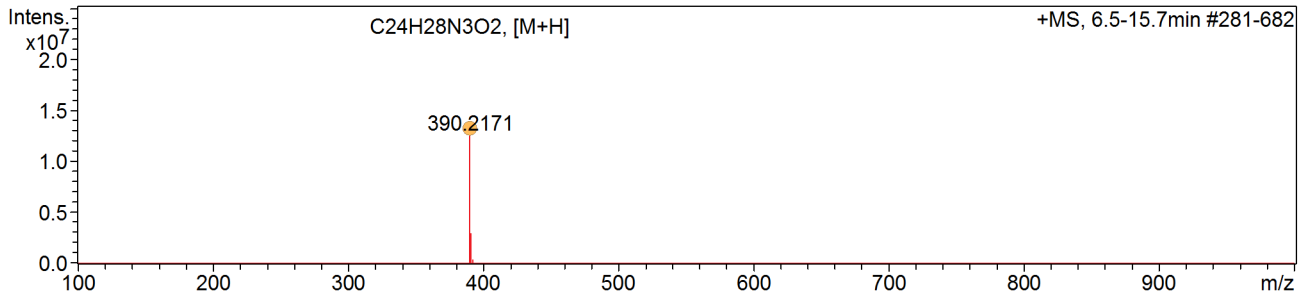
| | |
|---|---|
| Analysis Name | D:\Data\ING21\GMV-107.26D-C4.0-ESIPOS-180.5874-26D1020.d |
| Method | EP180_50-2200_TunePosStd-UA13_1f3002f200hrf50ie3lm1 00ce3crf300-800tt60-120pps6x0.75_fsthpc.m |
| Operator | admin |
| Sample Name | |
| Instrument | maXis impact 1819696.00172 |
| Comment | 22/04/2021: +Bckgnd: 118.09, 322.05, 622.03, 922.01, 1221.99, 1521.97, 1821.95, 2121.93, 2421.91, 2721.89 (G1969-85000; +/-299.981 HPC); other intense peaks (>2e4): 102.13 (NEt3); 132.91 (2-PrOH); 391.28 (DOP); 79.0, 86.10, 111,09, 157.03 (DMSO); 129.05, 132.91, 144.98, 140.02, 161.08, 165.13, 175.10, 183.17, 194.12, 199.12, 209.19, 214.25, 223.21, 227.24, 237.24, 249.22, 251.24, 251.24, 255.27, 277.25, 293.28, 299.19, 304.30, 307.30, 344.19, 407.10, 430.17, 707.12, 1007.10, 1307.08, 1557.95: background (prev. analyzed samples and impurities); 339.12 (#5451); 446.28 (#5721); 309.02/311.02 (#5899); 155.08 (#5898); 231.11 (#5901); 321.14 (#5990); 367,19 (#5873) |

**Acquisition Parameter**

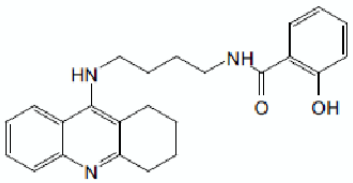
| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.3 Bar |
| Focus | Active | Set Capillary | 3500 V | Set Dry Heater | 200 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 2200 m/z | Set Charging Voltage | 2000 V | Set Divert Valve | Source |
| | | Set Corona | 0 nA | Set APCI Heater | 0 °C |




**+MS, 6.5-15.7min #281-682**




| Meas. m/z | # | Ion Formula | m/z | err [ppm] | mSigma | # mSigma | Score | rdb | e¯ Conf | N-Rule |
|---|---|---|---|---|---|---|---|---|---|---|
| 390.2171 | 1 | C24H28N3O2 | 390.2176 | 1.4 | 20.3 | 1 | 100.00 | 12.5 | even | ok |




**6b**

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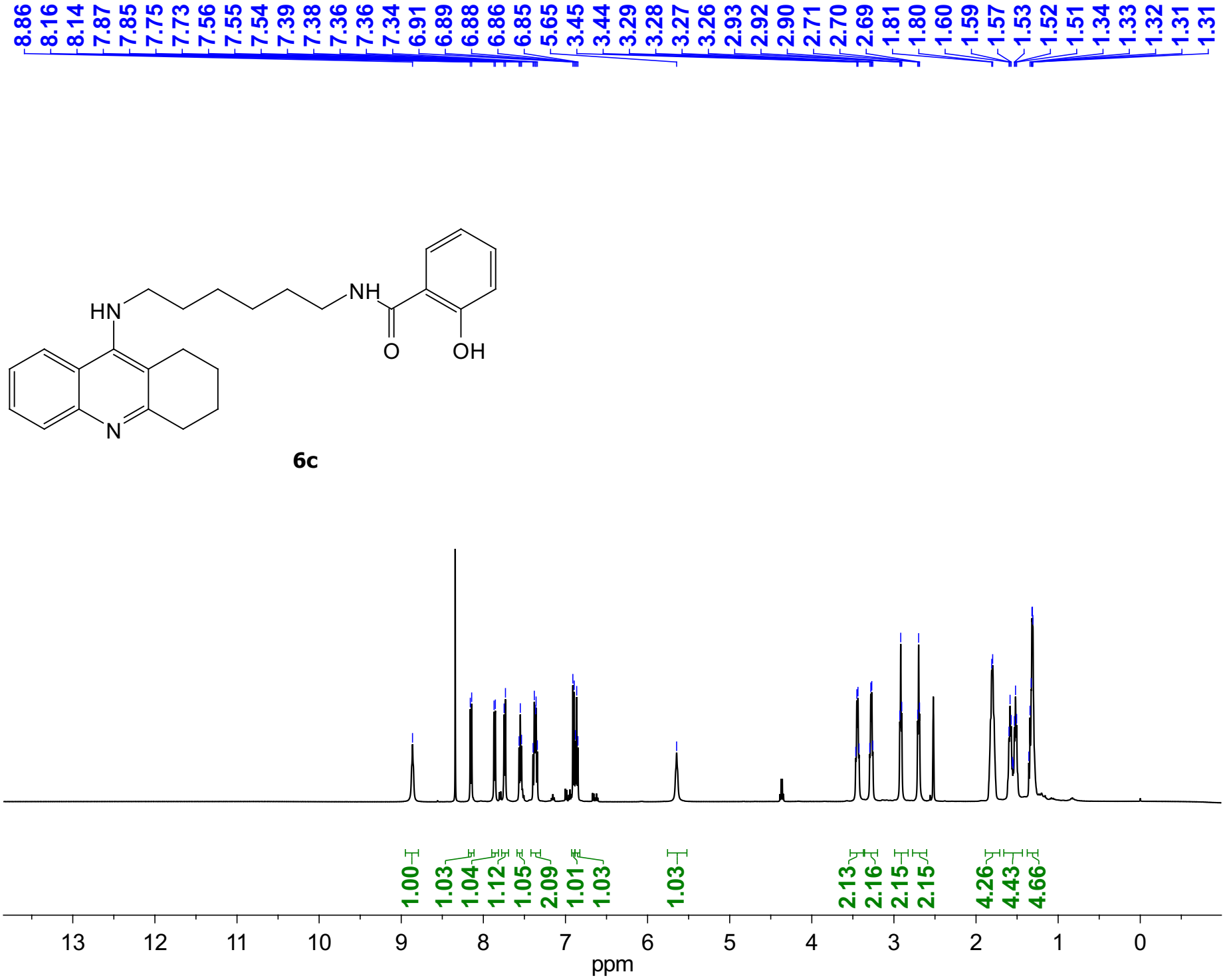
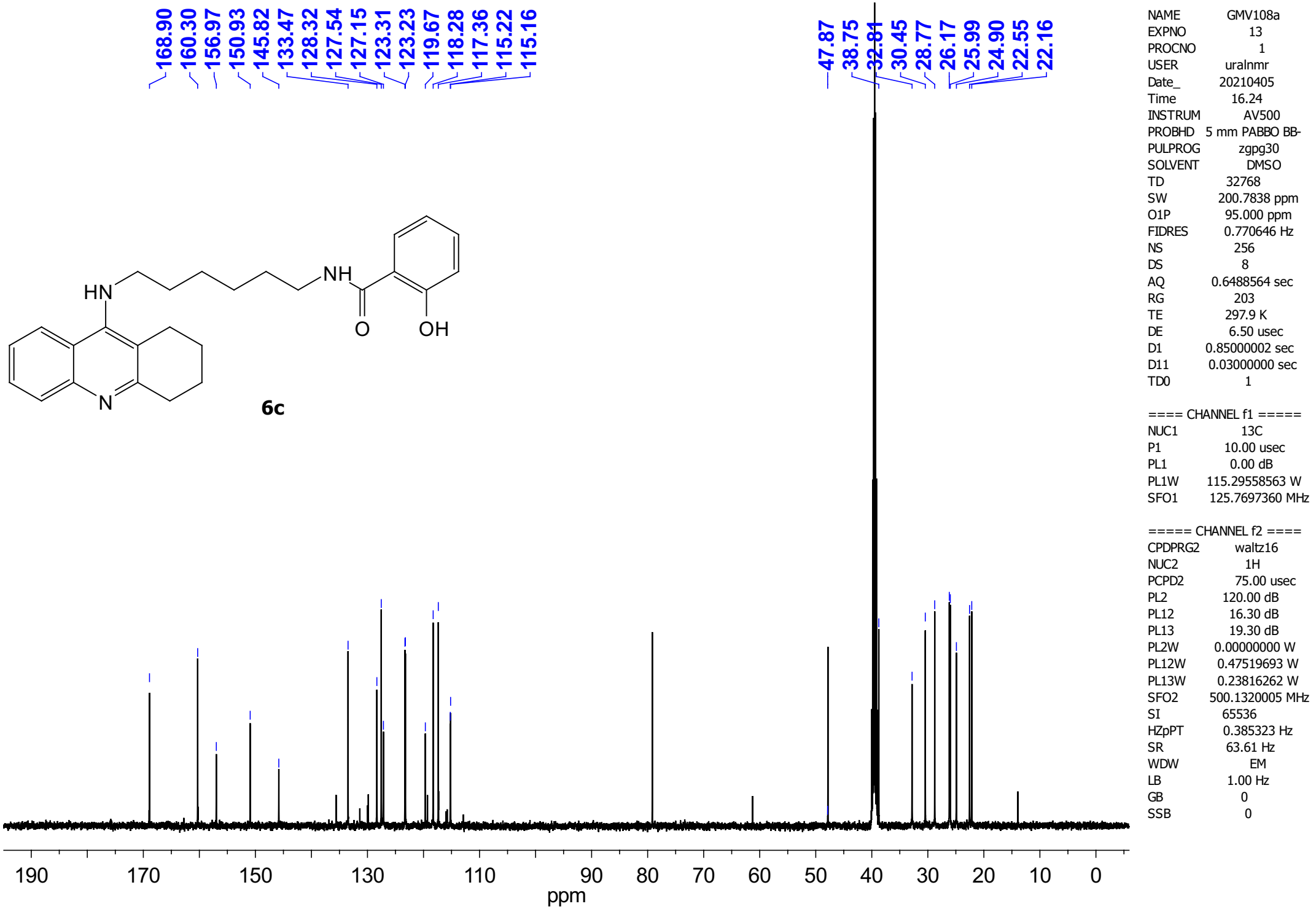
Phone: +7 (343) 362-34-56




| | |
|---|---|
| NAME | GMV108a |
| EXPNO | 1 |
| PROCNO | 1 |
| USER | uralnmr |
| Date_ | 20210405 |
| Time | 16.12 |
| INSTRUM | AV500 |
| PROBHD | 5 mm PABBO BB- |
| PULPROG | zg30 |
| SOLVENT | DMSO |
| TD | 32768 |
| SW | 19.9946 ppm |
| O1P | 9.000 ppm |
| FIDRES | 0.305176 Hz |
| NS | 16 |
| DS | 2 |
| AQ | 1.6384500 sec |
| RG | 90.5 |
| TE | 296.8 K |
| DE | 6.50 usec |
| D1 | 1.00000000 sec |
| TD0 | 1 |

| ===== CHANNEL f1 ===== | |
|---|---|
| NUC1 | 1H |
| P1 | 12.00 usec |
| PL1 | 0.30 dB |
| PL1W | 18.91792679 W |
| SFO1 | 500.1345012 MHz |
| SI | 32768 |
| HZpPT | 0.305176 Hz |
| SR | -4.80 Hz |
| WDW | EM |
| LB | 0.00 Hz |
| GB | 0 |
| SSB | 0 |




| | |
|---|---|
| NAME | GMV108a |
| EXPNO | 13 |
| PROCNO | 1 |
| USER | uralnmr |
| Date_ | 20210405 |
| Time | 16.24 |
| INSTRUM | AV500 |
| PROBHD | 5 mm PABBO BB- |
| PULPROG | zgpg30 |
| SOLVENT | DMSO |
| TD | 32768 |
| SW | 200.7838 ppm |
| O1P | 95.000 ppm |
| FIDRES | 0.770646 Hz |
| NS | 256 |
| DS | 8 |
| AQ | 0.6488564 sec |
| RG | 203 |
| TE | 297.9 K |
| DE | 6.50 usec |
| D1 | 0.85000002 sec |
| D11 | 0.03000000 sec |
| TD0 | 1 |
| ==== CHANNEL f1 ===== | |
| NUC1 | 13C |
| P1 | 10.00 usec |
| PL1 | 0.00 dB |
| PL1W | 115.29558563 W |
| SFO1 | 125.7697360 MHz |
| ===== CHANNEL f2 ==== | |
| CPDPRG2 | waltz16 |
| NUC2 | 1H |
| PCPD2 | 75.00 usec |
| PL2 | 120.00 dB |
| PL12 | 16.30 dB |
| PL13 | 19.30 dB |
| PL2W | 0.00000000 W |
| PL12W | 0.47519693 W |
| PL13W | 0.23816262 W |
| SFO2 | 500.1320005 MHz |
| SI | 65536 |
| HZpPT | 0.385323 Hz |
| SR | 63.61 Hz |
| WDW | EM |
| LB | 1.00 Hz |
| GB | 0 |
| SSB | 0 |

# Compound Spectrum SmartFormula Report

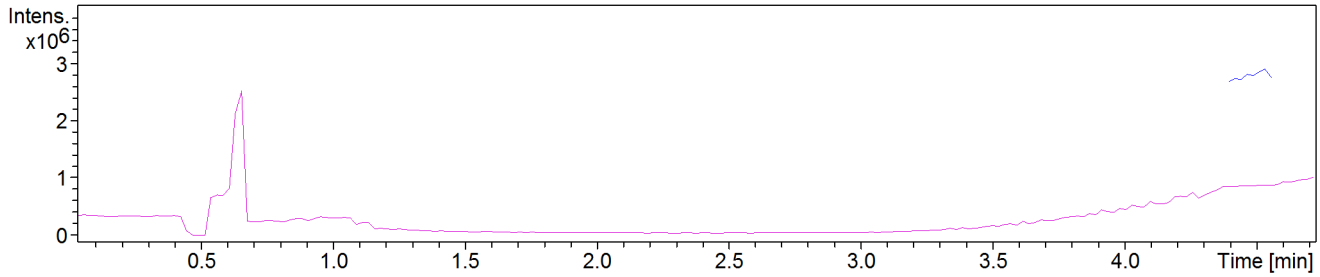
**Analysis Info**

Acquisition Date 4/26/2021 12:51:49 PM

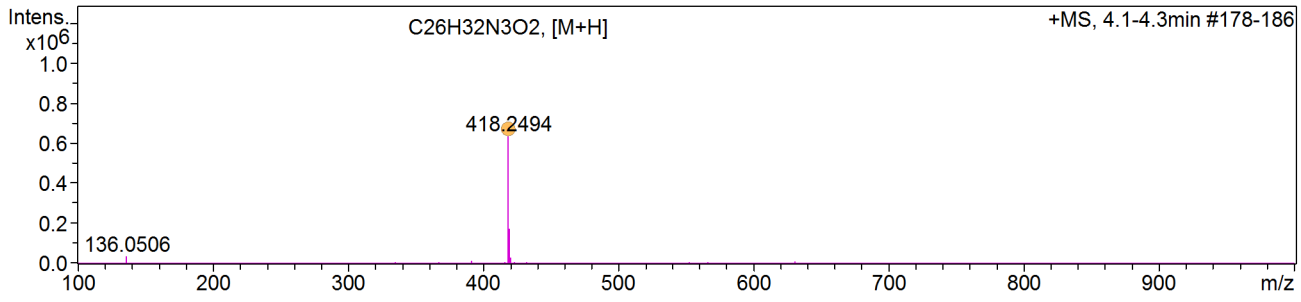
| | |
|---|---|
| Analysis Name | D:\Data\ING21\GMV-108.26D-C4.0-ESIPOS-180.5878-26D1250.d |
| Method | EP180_50-2200_TunePosStd-UA13_1f3002f200hrf50ie3lm1 00ce3crf300-800tt60-120pps6x0.75_fsthpc.m |
| Operator | admin |
| Sample Name | |
| Instrument | maXis impact 1819696.00172 |
| Comment | 26/04/2021: +Bckgnd: 118.09, 322.05, 622.03, 922.01, 1221.99, 1521.97, 1821.95, 2121.93, 2421.91, 2721.89 (G1969-85000; +/-299.981 HPC); other intense peaks (>2e4): 102.13 (NEt3); 132.91 (2-PrOH); 391.28 (DOP); 79.0, 86.10, 111,09, 157.03 (DMSO); 129.05, 132.91, 144.98, 140.02, 161.08, 165.13, 175.10, 183.17, 194.12, 199.12, 209.19, 214.25, 223.21, 227.24, 237.24, 249.22, 251.24, 251.24, 255.27, 277.25, 293.28, 299.19, 304.30, 307.30, 344.19, 407.10, 430.17, 707.12, 1007.10, 1307.08, 1557.95: background (prev. analyzed samples and impurities); 339.12 (#5451); 446.28 (#5721); 309.02/311.02 (#5899); 155.08 (#5898); 231.11 (#5901); 321.14 (#5990); 367,19 (#5873); 390.22 (#5874) |

**Acquisition Parameter**

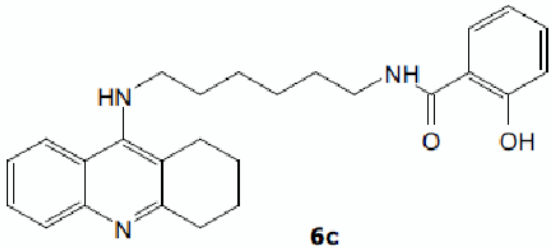
| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.3 Bar |
| Focus | Active | Set Capillary | 3500 V | Set Dry Heater | 200 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 2200 m/z | Set Charging Voltage | 2000 V | Set Divert Valve | Source |
| | | Set Corona | 0 nA | Set APCI Heater | 0 °C |




**+MS, 4.1-4.3min #178-186**




| Meas. m/z | # | Ion Formula | m/z | err [ppm] | mSigma | # mSigma | Score | rdb | e¯ Conf | N-Rule |
|---|---|---|---|---|---|---|---|---|---|---|
| 418.2494 | 1 | C26H32N3O2 | 418.2489 | -1.1 | 11.3 | 1 | 100.00 | 12.5 | even | ok |




**6c**

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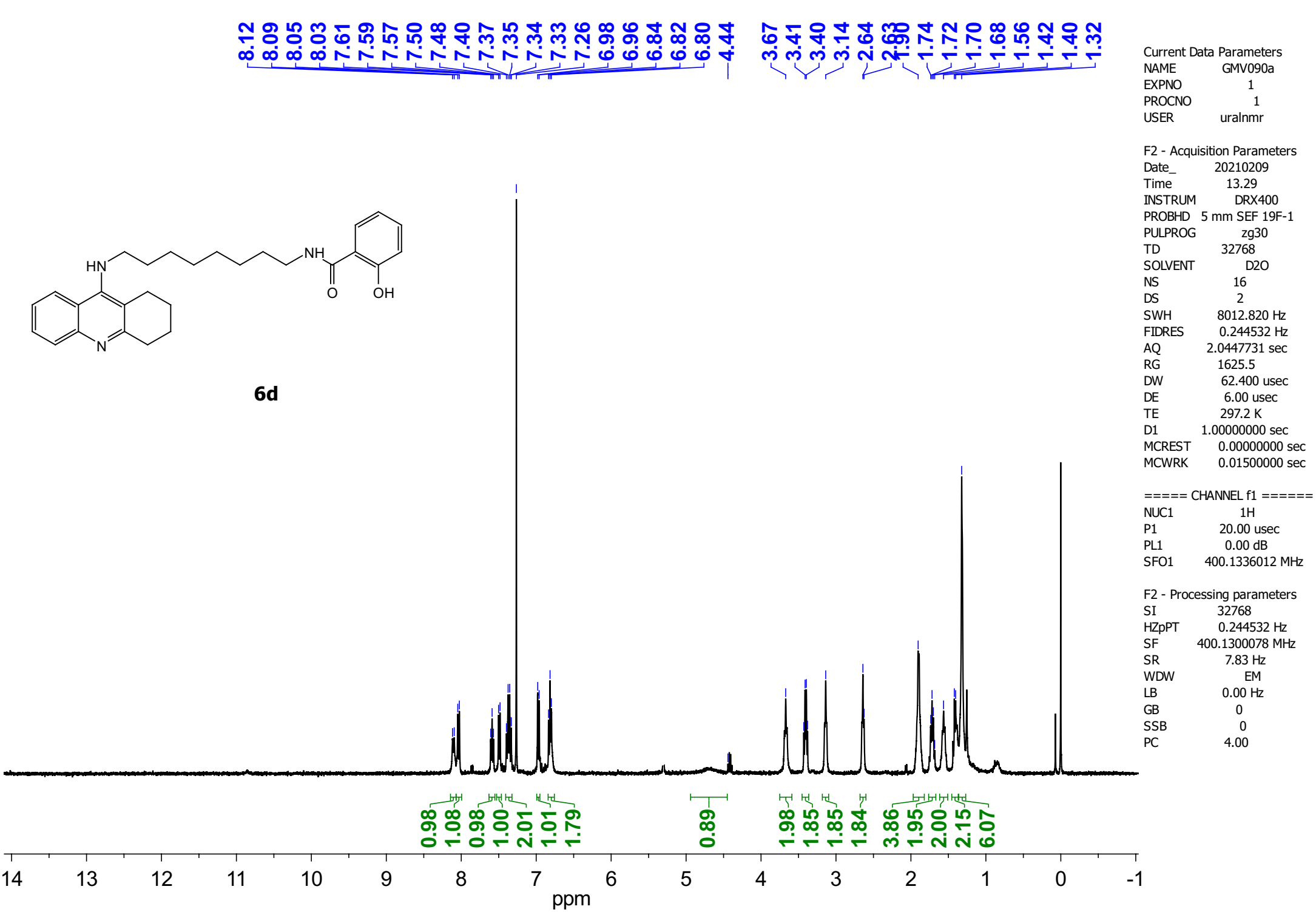
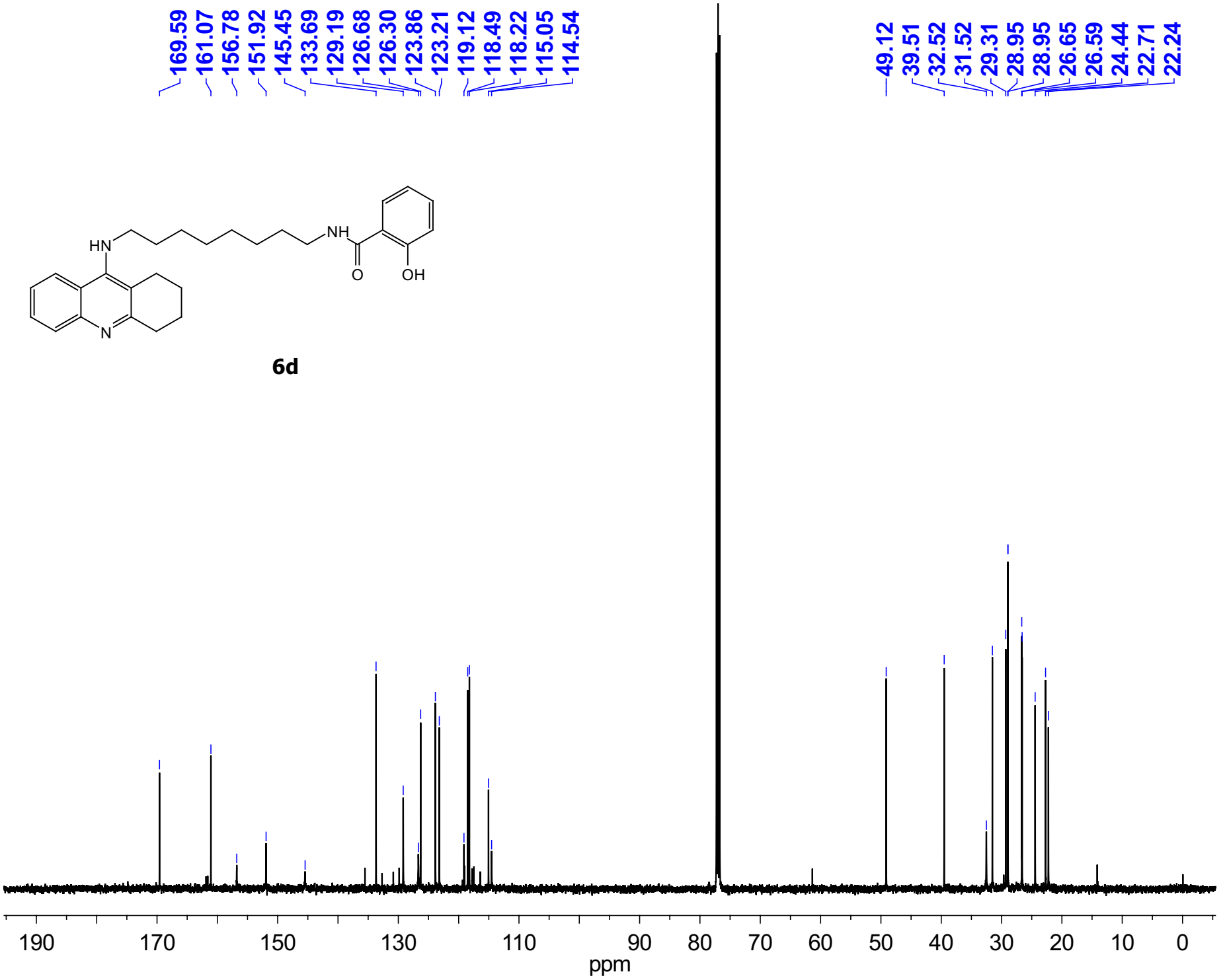

8.12 8.09 8.05 8.03 7.61 7.59 7.57 7.50 7.48 7.40 7.37 7.35 7.34 7.33 7.26 6.98 6.96 6.84 6.82 6.80 4.44 3.67 3.41 3.40 3.14 2.64 2.63 1.90 1.74 1.72 1.70 1.68 1.56 1.42 1.40 1.32
HN
NH
O
OH
N
6d
0.98 1.08 0.98 1.00 2.01 1.01 1.79 0.89 1.98 1.85 1.85 1.84 3.86 1.95 2.00 2.15 6.07
14 13 12 11 10 9 8 7 6 5 4 3 2 1 0 -1
ppm
Current Data Parameters
NAME GMV090a
EXPNO 1
PROCNO 1
USER uralnmr
F2 - Acquisition Parameters
Date_ 20210209
Time 13.29
INSTRUM DRX400
PROBHD 5 mm SEF 19F-1
PULPROG zg30
TD 32768
SOLVENT D2O
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447731 sec
RG 1625.5
DW 62.400 usec
DE 6.00 usec
TE 297.2 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
===== CHANNEL f1 ======
NUC1 1H
P1 20.00 usec
PL1 0.00 dB
SFO1 400.1336012 MHz
F2 - Processing parameters
SI 32768
HZpPT 0.244532 Hz
SF 400.1300078 MHz
SR 7.83 Hz
WDW EM
LB 0.00 Hz
GB 0
SSB 0
PC 4.00




| | |
|---|---|
| NAME | GMV090a |
| EXPNO | 13 |
| PROCNO | 1 |
| USER | uralnmr |
| Date_ | 20210220 |
| Time | 15.12 |
| INSTRUM | AV500 |
| PROBHD | 5 mm PABBO BB- |
| PULPROG | zgpg30 |
| SOLVENT | CDCl3 |
| TD | 32768 |
| SW | 200.7838 ppm |
| O1P | 95.000 ppm |
| FIDRES | 0.770646 Hz |
| NS | 1024 |
| DS | 8 |
| AQ | 0.6488564 sec |
| RG | 203 |
| TE | 297.5 K |
| DE | 6.50 usec |
| D1 | 0.85000002 sec |
| D11 | 0.03000000 sec |
| TD0 | 1 |

===== CHANNEL f1 =====

| | |
|---|---|
| NUC1 | 13C |
| P1 | 10.00 usec |
| PL1 | 0.00 dB |
| PL1W | 115.29558563 W |
| SFO1 | 125.7697360 MHz |

===== CHANNEL f2 =====

| | |
|---|---|
| CPDPRG2 | waltz16 |
| NUC2 | 1H |
| PCPD2 | 75.00 usec |
| PL2 | 120.00 dB |
| PL12 | 16.30 dB |
| PL13 | 19.30 dB |
| PL2W | 0.00000000 W |
| PL12W | 0.47519693 W |
| PL13W | 0.23816262 W |
| SFO2 | 500.1320005 MHz |
| SI | 32768 |
| HZpPT | 0.770646 Hz |
| SR | 6.78 Hz |
| WDW | EM |
| LB | 1.00 Hz |
| GB | 0 |
| SSB | 0 |

# Compound Spectrum SmartFormula Report

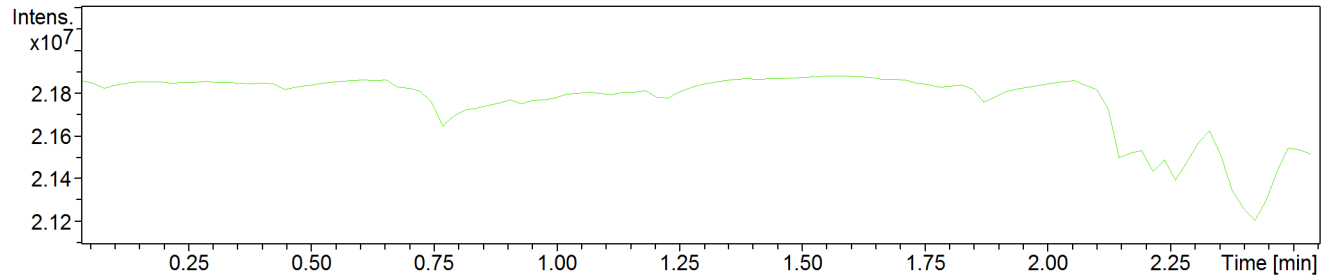
**Analysis Info**

Acquisition Date 3/12/2021 2:43:32 PM

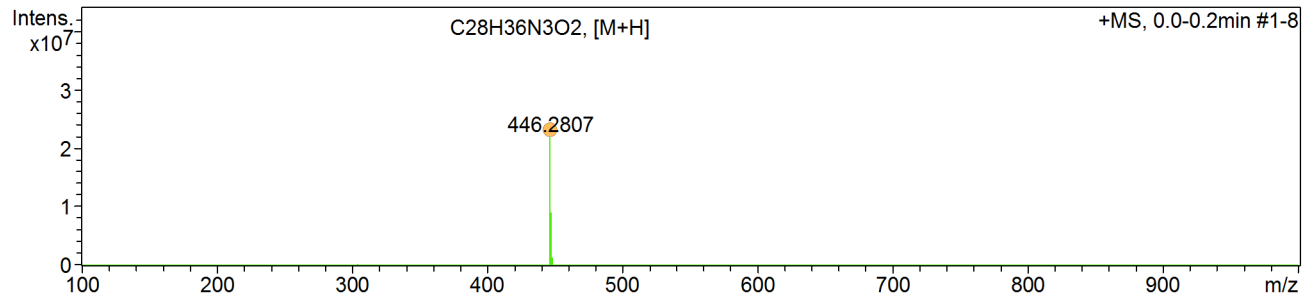
| | |
|---|---|
| Analysis Name | D:\Data\ING21\GMV-90.12C-C1.6-ESIPOS-180.5721-12C1445.d |
| Method | EP180_50-2200_TunePosStd-UA13_1f3002f200hrf50ie3lm1 00ce3crf300-800tt60-120pps6x0.75_fsthpc.m |
| Operator | admin |
| Sample Name | |
| Instrument | maXis impact 1819696.00172 |
| Comment | 03/03/2021: -Bckgnd: 112.99, 302.00, 601.98, 1033.99, 1333.98, 1633.95, 1933.93, 2233.91, 2533.89, 2833.87 (G1969-85000; +/-299.981 HPC); other intense peaks: 154.97, 170.95, 204.97, 231.99, 248.96, 264.93, 384.94, 400.91, 431.98, 520.91, 536.88, 556.00, 584.98, 617.97, 656.98, 734.01, 805.98, 947.00, 955.97, 982.99, 1063.87, 1291.94, 1305.95, 1555.94, 1691.91, 1733.94, 1805.92, 1921.91, 2055.90, 2155.89, 2182.91; 226.13 (#5716), 233.11 (#5720), 446.28 (#5721) |

**Acquisition Parameter**

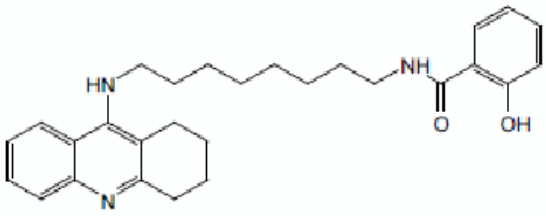
| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.3 Bar |
| Focus | Active | Set Capillary | 3500 V | Set Dry Heater | 200 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 2200 m/z | Set Charging Voltage | 2000 V | Set Divert Valve | Source |
| | | Set Corona | 0 nA | Set APCI Heater | 0 °C |




**+MS, 0.0-0.2min #1-8**




| Meas. m/z | # | Ion Formula | m/z | err [ppm] | mSigma | # mSigma | Score | rdb | e⁻ Conf | N-Rule |
|---|---|---|---|---|---|---|---|---|---|---|
| 446.2807 | 1 | C28H36N3O2 | 446.2802 | -1.1 | 54.5 | 1 | 100.00 | 12.5 | even | ok |
| | 2 | C13H32N15O3 | 446.2807 | 0.1 | 124.2 | 2 | 5.70 | 5.5 | even | ok |




**6d**

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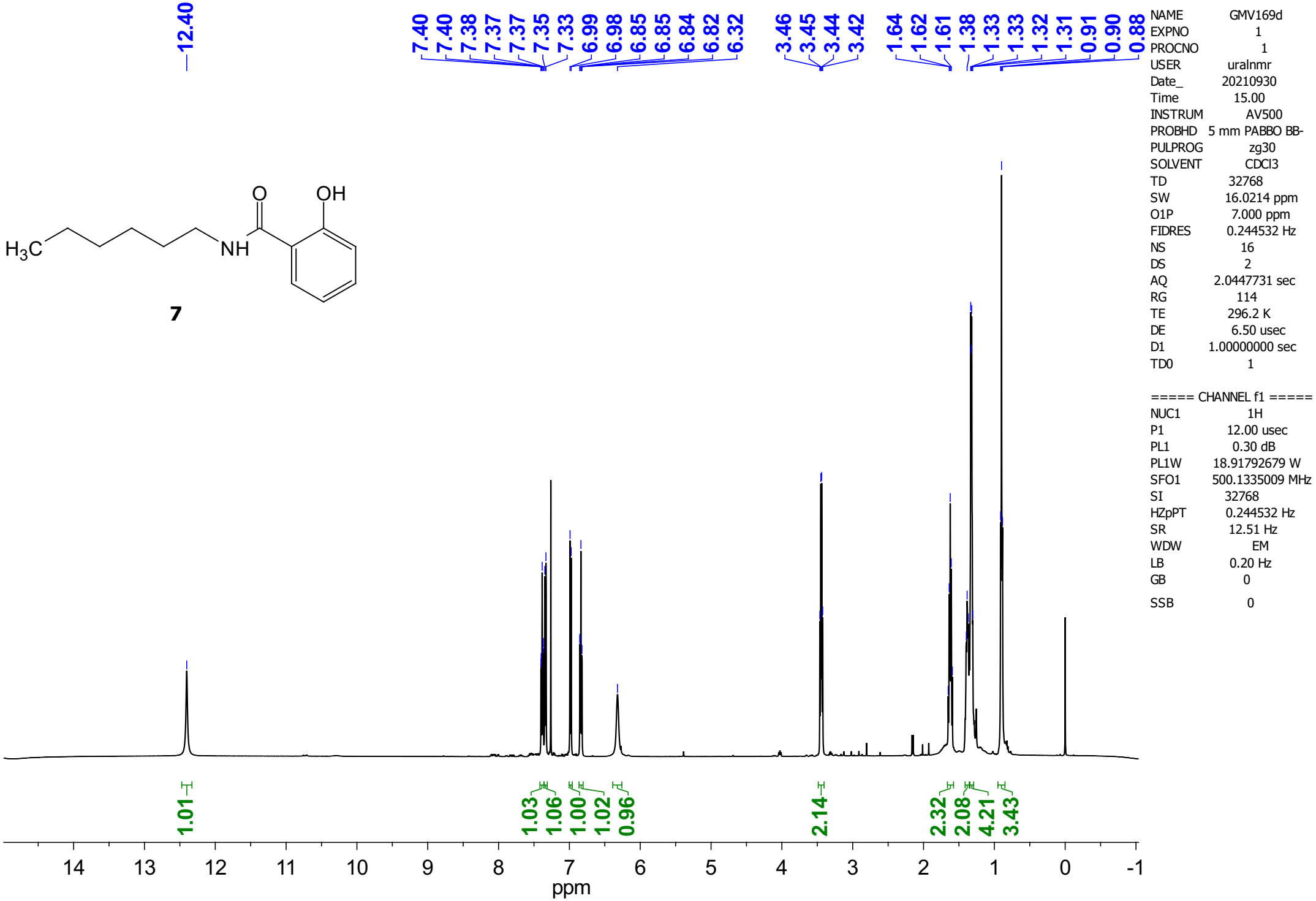
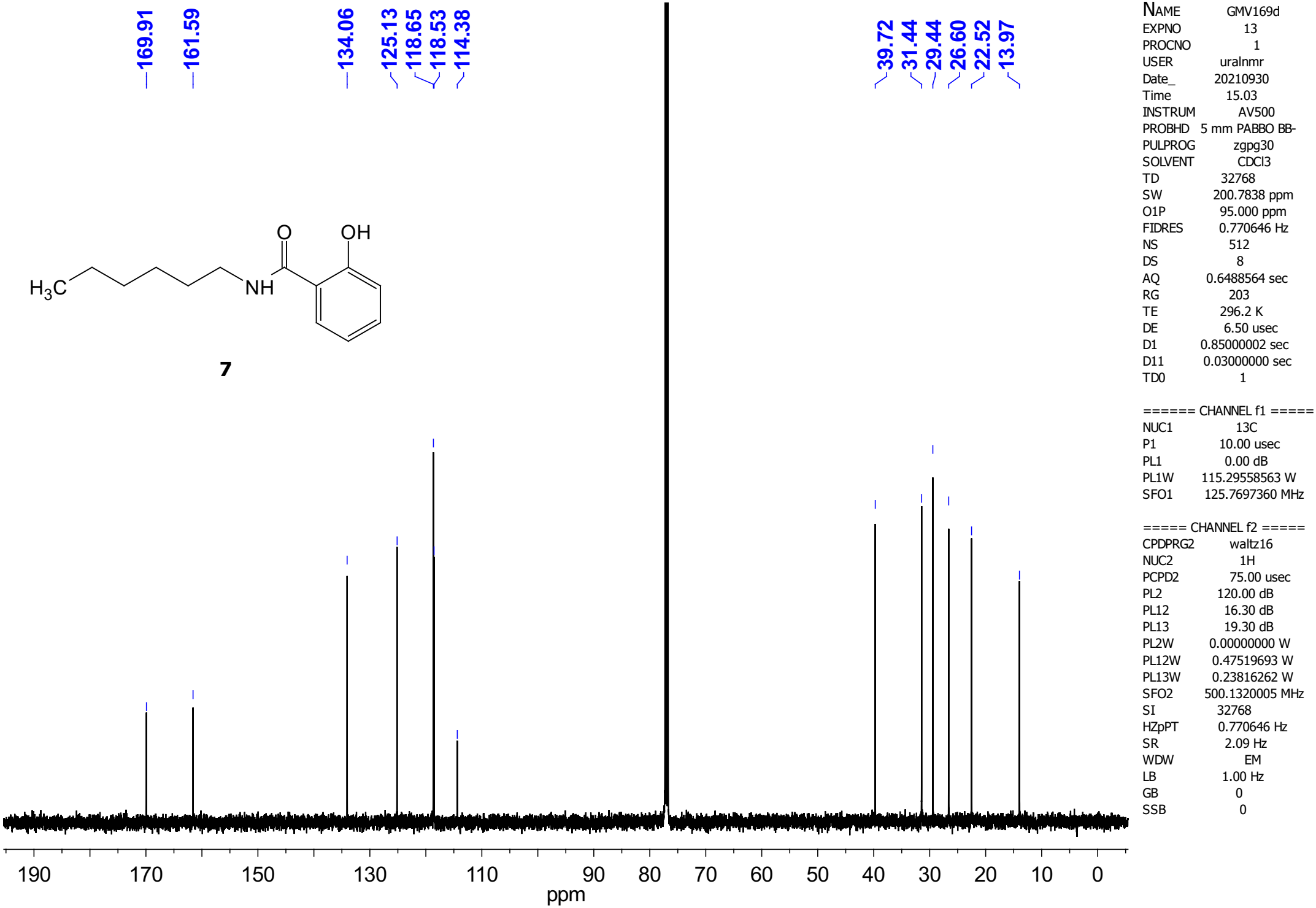

12.40
7.40
7.40
7.38
7.37
7.37
7.35
7.33
6.99
6.98
6.85
6.85
6.84
6.82
6.32
3.46
3.45
3.44
3.42
1.64
1.62
1.61
1.38
1.33
1.33
1.32
1.31
0.91
0.90
0.88
O
OH
H3C
NH
7
NAME GMV169d
EXPNO 1
PROCNO 1
USER uralnmr
Date_ 20210930
Time 15.00
INSTRUM AV500
PROBHD 5 mm PABBO BB-
PULPROG zg30
SOLVENT CDCl3
TD 32768
SW 16.0214 ppm
O1P 7.000 ppm
FIDRES 0.244532 Hz
NS 16
DS 2
AQ 2.0447731 sec
RG 114
TE 296.2 K
DE 6.50 usec
D1 1.00000000 sec
TD0 1
===== CHANNEL f1 =====
NUC1 1H
P1 12.00 usec
PL1 0.30 dB
PL1W 18.91792679 W
SFO1 500.1335009 MHz
SI 32768
HZpPT 0.244532 Hz
SR 12.51 Hz
WDW EM
LB 0.20 Hz
GB 0
SSB 0
1.01
1.03
1.06
1.00
1.02
0.96
2.14
2.32
2.08
4.21
3.43
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
ppm




| | |
|---|---|
| NAME | GMV169d |
| EXPNO | 13 |
| PROCNO | 1 |
| USER | uralnmr |
| Date_ | 20210930 |
| Time | 15.03 |
| INSTRUM | AV500 |
| PROBHD | 5 mm PABBO BB- |
| PULPROG | zgpg30 |
| SOLVENT | CDCl3 |
| TD | 32768 |
| SW | 200.7838 ppm |
| O1P | 95.000 ppm |
| FIDRES | 0.770646 Hz |
| NS | 512 |
| DS | 8 |
| AQ | 0.6488564 sec |
| RG | 203 |
| TE | 296.2 K |
| DE | 6.50 usec |
| D1 | 0.85000002 sec |
| D11 | 0.03000000 sec |
| TD0 | 1 |
| ====== CHANNEL f1 ===== | |
| NUC1 | 13C |
| P1 | 10.00 usec |
| PL1 | 0.00 dB |
| PL1W | 115.29558563 W |
| SFO1 | 125.7697360 MHz |
| ===== CHANNEL f2 ===== | |
| CPDPRG2 | waltz16 |
| NUC2 | 1H |
| PCPD2 | 75.00 usec |
| PL2 | 120.00 dB |
| PL12 | 16.30 dB |
| PL13 | 19.30 dB |
| PL2W | 0.00000000 W |
| PL12W | 0.47519693 W |
| PL13W | 0.23816262 W |
| SFO2 | 500.1320005 MHz |
| SI | 32768 |
| HZpPT | 0.770646 Hz |
| SR | 2.09 Hz |
| WDW | EM |
| LB | 1.00 Hz |
| GB | 0 |
| SSB | 0 |

# Compound Spectrum SmartFormula Report

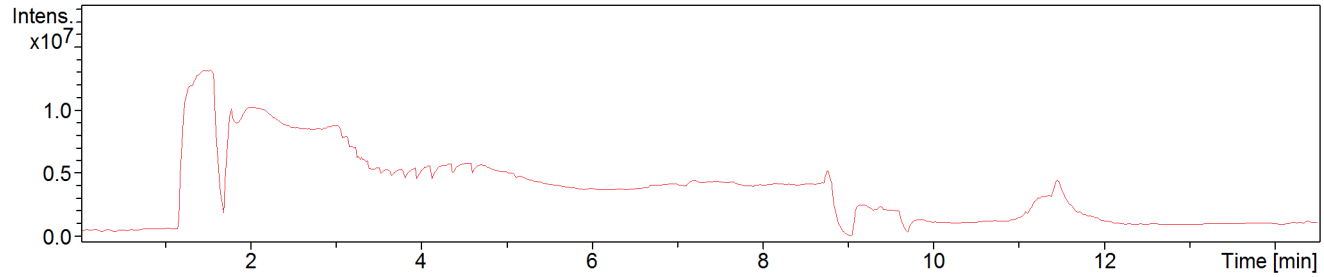
**Analysis Info**

Acquisition Date 10/19/2021 11:24:40 AM

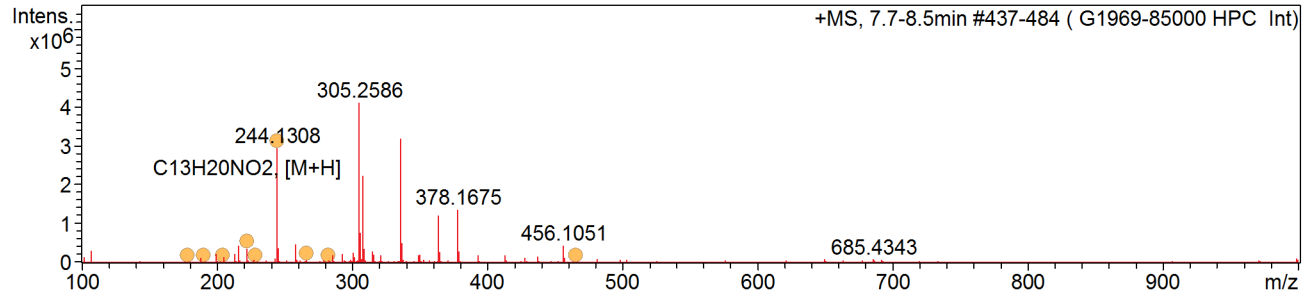
Analysis Name D:\Data\ING21\GMV-169a.14j-C-ESIPOS-180.6312-19j1125.d
Method EP180UJ19HPC50-2200_500-3500-0.4-4-200_1f2002f200hrfOperator admin
70ie5lm70ce10pps6crf300-1200tt40-110_F3x1_Segm1.m
Sample Name Instrument maXis impact 1819696.00172
Comment

**Acquisition Parameter**

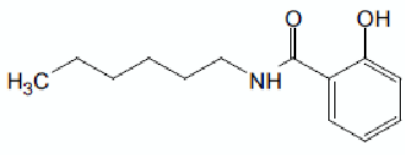
| | | | | | |
|---|---|---|---|---|---|
| Source Type | ESI | Ion Polarity | Positive | Set Nebulizer | 0.4 Bar |
| Focus | Active | Set Capillary | 3500 V | Set Dry Heater | 200 °C |
| Scan Begin | 50 m/z | Set End Plate Offset | -500 V | Set Dry Gas | 4.0 l/min |
| Scan End | 2200 m/z | Set Charging Voltage | 2000 V | Set Divert Valve | Source |
| | | Set Corona | 0 nA | Set APCI Heater | 0 °C |




**+MS, 7.7-8.5min #437-484 ( G1969-85000 HPC Int)**




| Meas. m/z | # | Ion Formula | m/z | err [ppm] | mSigma | # mSigma | Score | rdb | e⁻ Conf | N-Rule |
|---|---|---|---|---|---|---|---|---|---|---|
| 178.1588 | 1 | C12H20N | 178.1590 | 1.0 | 13.6 | 1 | 100.00 | 3.5 | even | ok |
| 190.1231 | 1 | C12H16NO | 190.1226 | -2.2 | 760.9 | 1 | 100.00 | 5.5 | even | ok |
| 204.1386 | 1 | C13H18NO | 204.1383 | -1.5 | 185.2 | 1 | 100.00 | 5.5 | even | ok |
| 222.1487 | 1 | C13H20NO2 | 222.1489 | 0.5 | 1.3 | 1 | 100.00 | 4.5 | even | ok |
| 228.1568 | 1 | C13H19LiNO2 | 228.1570 | 1.2 | 74.5 | 1 | 100.00 | 4.5 | even | ok |
| 244.1308 | 1 | C13H19NNaO2 | 244.1308 | -0.1 | 12.2 | 1 | 100.00 | 4.5 | even | ok |
| 266.1122 | 1 | C13H18NNa2O2 | 266.1127 | 2.1 | 10.4 | 1 | 100.00 | 4.5 | even | ok |
| 282.2040 | 1 | C16H28NO3 | 282.2064 | 8.5 | 730.4 | 1 | 100.00 | 3.5 | even | ok |
| 465.2729 | 1 | C26H38N2NaO4 | 465.2724 | -1.2 | 111.0 | 1 | 100.00 | 8.5 | even | ok |

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