Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

For

Direct access to various C3-substituted sialyl glycal derivatives from 3-iodo-sialyl glycal

Qingjiang Li, Jiatong Guo, and Zhongwu Guo*

Department of Chemistry, University of Florida, 214 Leigh Hall, Gainesville, Florida 32611, United States

* Corresponding author E-mail: zguo@chem.ufl.edu

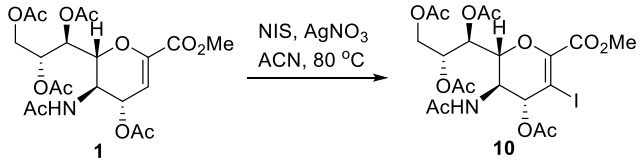
Table of Contents

I. Experimental Procedures

General procedures

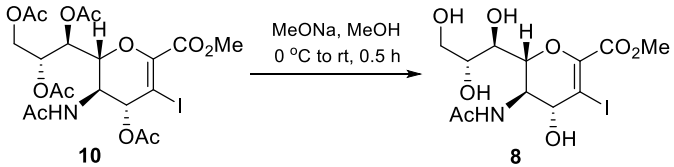
Chemicals and materials were purchased from commercial sources and were used as received without further purification unless noted otherwise. Analytical TLC was carried out on silica gel 60Å F_{254} plates with detection by a UV detector and/or by charring with 10% (v/v) H_2SO_4 in ethanol. Flash column chromatography was performed on CombiFlash® instruments with prepacked silica gel columns. NMR spectra were acquired on a 600 MHz spectrometer with chemical shifts reported in ppm (δ) referenced to CD_3OD (^{1}H NMR: δ 3.31 ppm; ^{13}C NMR: δ 49.0) or DHO (^{1}H NMR: δ 4.75 ppm) when D_2O was used as solvent. Peak and coupling constant assignments are based on ^{1}H NMR, ^{1}H-^{1}H COSY, ^{1}H-^{13}C HMBC, and ^{1}H-^{13}C HSQC experiments.

Synthesis of methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-2,6-anhydro-3,5-dideoxy-3-iodo-β-D-glycero-D-galacto-non-2-enonate (10)



To a mixture of glycal **1** (1 g, 2.4 mmol), *N*-iodosuccinimide (0.65 g, 2.8 mmol), and silver nitrate (205 mg, 1.2 mmol) in a round bottom flask was added acetonitrile (20 mL) under N_2 atmosphere. The reaction mixture was heated to 80 °C in oil bath with vigorous stirring and monitored with TLC (hexanes/acetone = 1/1). Upon completion of reaction, the off-white solid was filtered, and the solvent was removed under vacuum. The residue was dissolved in ethyl acetate (20 mL) and washed with water (5 mL), brine (5 mL) before dried over Na_2SO_4. The solvent was removed under vacuum to afford the crude product, which was further purified by flash chromatography (65-85% EA in Hex) to give **10** as a white solid (857 mg, 66%). Its NMR data matched that reported in reference 14b (main text).

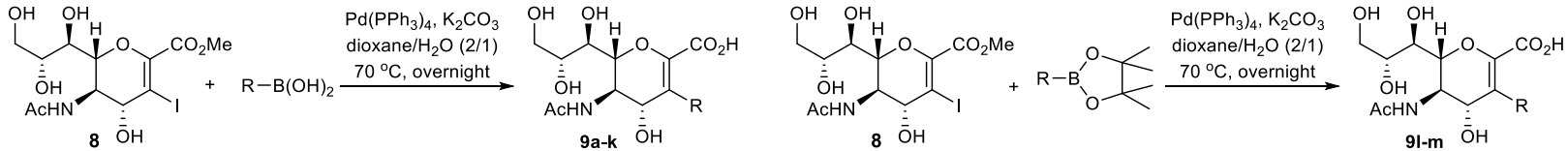
Synthesis of methyl 5-acetamido-5-deoxy-3-iodo-β-D-glycero-D-galacto-non-2-enonate (8)



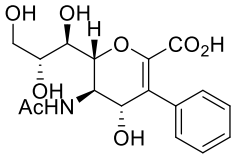
To a solution of compound **10** (857 mg, 1.43 mmol) in MeOH (5 mL) was added dropwise freshly made NaOMe in MeOH at 0 °C until pH = 10. The mixture was allowed to warm to rt and kept at this temperature for 1 h, when TLC indicated completion of reaction. The

reaction mixture was neutralized with Amberlyst® 15 resin. The resin was removed by filtration, and the solvent was evaporated under vacuum to give **8** (615 mg, 99%), which was essentially pure and directly used in subsequent reactions without further purification. ^{1}H NMR (600 MHz, CD_3OD): δ 4.58 (br, 1H), 4.32 (dd, J = 10.6, 1.3 Hz, 1H), 4.24 (d, J = 8.4 Hz, 1H), 4.16 (dd, J = 10.6, 8.4 Hz, 1H), 3.80 (s, 4H), 3.77 (dq, J = 8.2, 2.9, 2.5 Hz, 2H), 3.68 – 3.61 (m, 1H), 3.60 – 3.55 (m, 1H), 2.03 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 174.7, 164.6, 147.5, 81.3, 78.9, 73.6, 71.0, 70.0, 64.8, 53.0, 52.8, 22.6. HR MS [M - H]$^-$ m/z: calcd for $C_{12}H_{17}INO_8^-$: 430.0004; found: 430.0007.

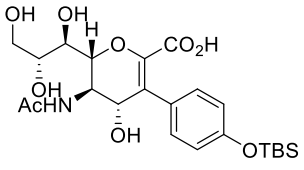
General procedure for Suzuki-Miyaura coupling reaction



Vinyl iodide **8** (10.4 mg, 0.025 mmol), a boronic acid or borate substrate (0.05 mmol), palladium tetrakis(triphenylphosphine) (1.5 mg, 0.00125 mmol), and K_2CO_3 (8.6 mg, 0.0625 mmol) were mixed in dioxane and H_2O (v/v = 2/1, 1 mL, degassed by bubbling nitrogen for 0.5 h). The reaction mixture was flushed with nitrogen, heated to 70 °C on an aluminum block, and stirred overnight. The reaction was monitored with TLC (**8**: R_f = 0.4 in DCM/MeOH/H_2O 5/1/0.1). Upon complete consumption of **8**, the solvent was removed under vacuum, and the product was purified by flash chromatography (20-35% MeOH/H_2O/AcOH 5/1/0.1 in EA).

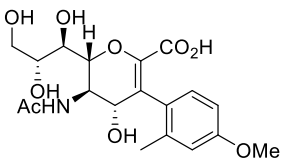


5-Acetamido-5-deoxy-3-phenyl-β-D-glycero-D-galacto-non-2-enonic acid (9a). Obtained as a white solid (7.5 mg, 82%). ^{1}H NMR (600 MHz, CD_3OD): δ 7.37 (d, 2H, J = 7.6 Hz, ArH), 7.24 (t, 2H, J = 7.6 Hz, ArH), 7.16 (t, 2H, J = 7.6 Hz, ArH), 4.38 (dd, 1H, J = 2.2, 4.9 Hz, H-4), 4.33 – 4.30 (m, 2H, H-5, H-6), 3.87 – 3.85 (m, 1H, H-8), 3.83 (dd, 1H, J = 2.9, 11.2 Hz, H-9a), 3.69 (dd, 1H, J = 5.3, 11.2 Hz, H-9b), 3.66 (d, 1H, J = 8.9 Hz, H-7), 2.03 (s, 3H, Ac). ^{13}C NMR (150 MHz, CD_3OD): δ 177.1 (Ac), 150.7(CO_2H), 138.8, 130.5 (Ar), 128.7, 127.4, 112.3 (C=), 77.2 (C-6), 71.9 (C-7), 71.2 (C-8), 70.0 (C-4), 64.8 (C-9), 52.7 (C-5), 22.7 (CH_3). HR MS [M - H]$^-$ m/z: calcd for $C_{17}H_{20}NO_8$: 366.1194; found: 366.1186.

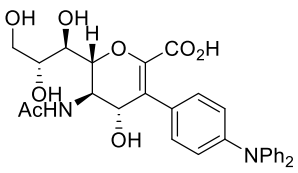


5-Acetamido-5-deoxy-3-(4-O-tert-butyldimethylsilyl-phenyl)-β-D-glycero-D-galacto-non-2-enonic acid (9b). Obtained as a white solid (10.1 mg, 81%). ^{1}H NMR (600 MHz, CD_3OD): δ 7.18 (d, 2H, J = 7.4 Hz), 6.76 (d, 2H, J = 7.4 Hz), 4.38 (d, 1H, J = 7.0 Hz), 4.31 – 4.25 (m, 2H), 3.88 – 3.85 (m, 1H), 3.83 (dd, 1H, J = 2.9, 11.2 Hz), 3.68 (dd, 1H, J = 5.4, 11.3 Hz), 3.64 (d, 1H, J = 9.0 Hz), 2.03 (s, 3H), 0.99 (s, 9H), 0.19 (s, 6H). ^{13}C

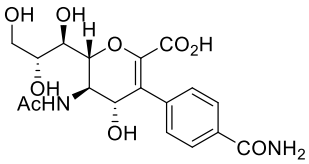
NMR (150 MHz, CD_3OD): δ 174.4, 155.9, 131.7, 131.1, 120.4, 77.6, 71.3, 71.2, 70.7, 64.8, 52.8, 26.2, 22.6, 20.8, 19.0, 4.3. HR MS $[M-H]^-$ m/z: calcd for $C_{23}H_{34}Si\ NO_9^-$ 496.2008, found: 496.2013.



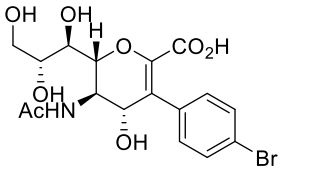
5-Acetamido-5-deoxy-3-(4-methoxy-2-methylphenyl)-β-D-glycero-D-galacto-non-2-enonic acid (9c). Obtained as a white solid (8.5 mg, 83%). ^1H NMR (600 MHz, CD_3OD): δ 7.09 (s, 1H), 6.69 (d, J = 2.6 Hz, 1H), 6.65 (d, J = 8.4 Hz, 1H), 4.33 (d, J = 8.3 Hz, 1H), 4.30 – 4.22 (m, 2H), 3.91 – 3.81 (m, 2H), 3.74 (s, 3H), 3.67 (dd, J = 11.4, 5.5 Hz, 1H), 3.62 (s, 1H), 2.29 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (150 MHz, CD_3OD): δ 174.5, 160.29, 138.8, 134.1, 116.0, 111.4, 77.5, 71.0, 70.0, 64.8, 55.5, 52.8, 22.7. HR MS [M - H]$^-$ m/z: calcd for $C_{19}H_{24}NO_9^-$: 410.1457, found: 410.1455.



5-Acetamido-5-deoxy-3-(4-diphenylaminophenyl)-β-D-glycero-D-galacto-non-2-enonic acid (9d). Obtained as a white solid (10.4mg, 78%). ^1H NMR (600 MHz, CD_3OD): δ 7.28 (d, J = 8.6 Hz, 2H), 7.22 (t, J = 7.8 Hz, 4H), 7.03 – 7.02 (m, 4H), 6.97 (t, J = 7.3 Hz, 2H), 7.28 (d, J = 8.6 Hz, 2H), 4.58 (br, 1H), 4.34 – 4.32 (m, 2H), 3.87 – 3.82 (m, 2H), 3.68 – 3.64 (m, 2H), 2.03 (s, 3H). ^{13}C NMR (150 MHz, CD_3OD): δ 149.4, 147.6, 133.3, 131.3, 130.2, 125.2, 124.5, 123.7, 77.2, 72.0, 71.2, 70.0, 64.8, 52.8, 22.7. HR MS [M - H]$^-$ m/z: calcd for $C_{29}H_{29}N_2O_8^-$: 533.1929, found: 533.1926.

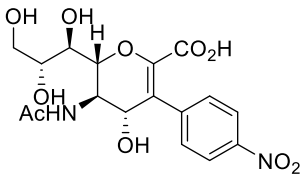


5-Acetamido-5-deoxy-3-(4-carbamoylphenyl)-β-D-glycero-D-galacto-non-2-enonic acid (9e). Obtained as a white solid (7.4 mg, 72%). ^1H NMR (600 MHz, CD_3OD): δ 7.78 (d, J = 8.0 Hz, 2H), 7.46 (d, J = 8.1 Hz, 2H), 4.49 (d, J = 6.1 Hz, 1H), 4.31 (d, J = 6.8 Hz, 2H), 3.88 – 3.80 (m, 2H), 3.70 (dd, J = 11.3, 5.2 Hz, 1H), 3.66 (d, J = 8.8 Hz, 1H), 2.03 (s, 3H). ^{13}C NMR (150 MHz, CD_3OD:) δ 174.1, 172.4, 151.1, 143.0, 132.5, 130.5, 128.1, 112.2, 77.2, 71.4, 71.2, 69.8, 64.7, 52.5, 22.7. HR MS [M - H]$^-$ m/z: calcd for $C_{18}H_{21}N_2O_9^-$: 409.1253, found: 409.1244.

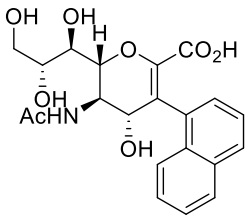


5-Acetamido-5-deoxy-3-(4-bromophenyl)-β-D-glycero-D-galacto-non-2-enonic acid (9f). Obtained as a white solid (8.9 mg, 80%). ^1H NMR (600 MHz, CD_3OD): δ ^1H NMR (600 MHz, MeOD) δ 7.38 (d, J = 8.4 Hz, 2H), 7.27 (d, J = 8.4 Hz, 2H), 4.37 (dd, J = 5.0, 2.3 Hz, 1H), 4.30 (d, J = 5.1 Hz, 2H), 3.87 – 3.79 (m, 2H), 3.71 – 3.65 (m, 1H), 3.63 (d, J = 8.9 Hz, 1H), 2.03 (s, 3H). ^{13}C NMR (150 MHz, CD_3OD): δ 174.0,

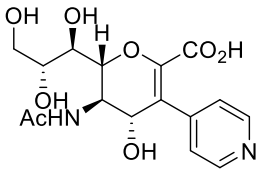
151.1, 138.1, 132.5, 131.7, 121.2, 111.5, 77.3, 71.58, 71.2, 69.9, 64.8, 52.6, 24.2, 22.7. HR MS [M - H]$^-$ m/z: calcd for $C_{17}H_{19}BrNO_8^-$: 444.0300, found: 444.0303.



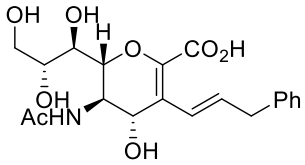
5-Acetamido-5-deoxy-3-(4-nitrophenyl)-β-D-glycero-D-galacto-non-2-enonic acid (9g). Obtained as an off-white solid (7.7 mg, 75%). ^{1}H NMR (600 MHz, CD_3OD): δ 8.11 (d, J = 8.8 Hz, 1H), 7.58 (d, J = 8.8 Hz, 1H), 4.49 (d, J = 6.7 Hz, 1H), 4.37 (d, J = 8.1 Hz, 0H), 4.32 (dd, J = 8.4, 6.7 Hz, 1H), 3.88 – 3.81 (m, 1H), 3.71 – 3.63 (m, 1H), 2.03 (s, 2H). ^{13}C NMR (150 MHz, CD_3OD): δ 174.0, 152.2, 147.6, 146.8, 131.2, 123.7, 111.4, 77.4, 71.6, 71.3, 69.6, 64.8, 52.6, 22.70. HR MS [M-H]$^-$ m/z: calcd for $C_{17}H_{19}N_2O_{10}^-$ 411.1045, found: 411.1042.



5-Acetamido-5-deoxy-3-(1-naphthalenyl)-β-D-glycero-D-galacto-non-2-enonic acid (9h). Obtained as a white solid (8.1 mg, 78%). This compound have axial chirality, so its NMR spectra are complicated compared to others. ^{1}H NMR (600 MHz, CD_3OD): δ ^{1}H NMR (600 MHz, MeOD) δ 8.06 – 7.98 (m, 1H), 7.88 – 7.71 (m, 2H), 7.50 – 7.39 (m, 3H), 7.33 (ddd, J = 20.8, 7.1, 1.2 Hz, 1H), 4.62 – 4.44 (m, 2H), 4.43 – 4.28 (m, 1H), 3.96 (ddd, J = 8.7, 5.4, 3.0 Hz, 1H), 3.88 (dd, J = 11.5, 3.0 Hz, 1H), 3.77 – 3.66 (m, 2H), 2.05 (s, 3H). ^{13}C NMR (150 MHz, CD_3OD): δ ^{13}C NMR (151 MHz, MeOD) δ 175.23, 174.72, 145.39, 136.65, 135.26, 135.22, 135.00, 134.26, 133.32, 129.86, 129.45, 128.74, 128.52, 128.38, 127.81, 126.86, 126.58, 126.46, 126.42, 126.26, 126.18, 125.77, 77.98, 77.80, 73.06, 71.39, 71.23, 70.97, 70.87, 70.54, 64.89, 64.86, 52.88, 52.45, 22.65, 20.74. HR MS [M - H]$^-$ m/z: calcd for $C_{21}H_{22}NO_8^-$: 416.1351, found: 416.1348.

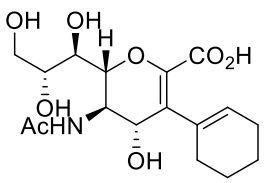


5-Acetamido-5-deoxy-3-(pyridin-4-yl)-β-D-glycero-D-galacto-non-2-enonic acid (9i). Obtained as a white solid (6.9 mg, 75%). ^{1}H NMR (600 MHz, CD_3OD): δ 8.45 – 8.30 (m, 2H), 7.56 – 7.37 (m, 2H), 4.49 (d, J = 6.7 Hz, 1H), 4.39 (dd, J = 8.1, 1.6 Hz, 1H), 4.32 (dd, J = 8.2, 6.6 Hz, 1H), 3.88 – 3.80 (m, 2H), 3.71 – 3.62 (m, 2H), 3.35 (s, 1H), 2.03 (s, 3H). ^{13}C NMR (150 MHz, CD_3OD): δ 174.0, 171.1, 153.0, 149.4, 148.7, 125.8, 110.0, 77.6, 71.6, 71.2, 69.0, 64.8, 52.5, 22.7. HR MS [M - H]$^-$ m/z: calcd for $C_{16}H_{19}N_2O_8^-$: 367.1147, found: 367.1156.

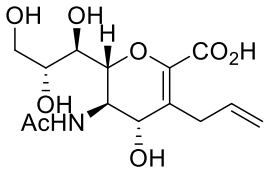


5-Acetamido-5-deoxy-3-[(E)-phenylprop-1-en-1-yl]-β-D-glycero-D-galacto-non-2-enonic acid (9j). Obtained as a white solid (6.9 mg, 68%). ^{1}H NMR (600 MHz, CD_3OD): δ 7.30 – 7.15 (m, 4H), 7.12 (t, J = 7.2 Hz, 1H), 6.70 (dd, J = 15.8, 1.7 Hz, 1H), 5.94 (dt, J = 15.7, 7.1 Hz, 1H), 4.39 (d, J = 6.4 Hz, 1H), 4.21 (dd, J = 8.0, 6.3

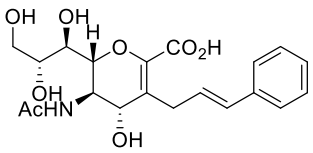
Hz, 1H), 4.11 (dd, *J* = 8.1, 1.8 Hz, 1H), 3.85 – 3.76 (m, 2H), 3.68 (t, *J* = 5.5 Hz, 1H), 3.63 (dd, *J* = 8.4, 1.8 Hz, 1H), 3.48 – 3.36 (m, 2H), 2.00 (s, 3H). ^{13}C NMR (150 MHz, CD_3OD): *δ* 174.2, 151.1, 142.4, 129.5, 129.3, 129.3, 128.3, 127.6, 126.8, 112.3, 77.3, 71.5, 71.3, 67.4, 64.5, 53.6, 41.0, 22.7. HR MS [M - H]$^-$ m/z: calcd for $C_{20}H_{24}NO_8^-$: 406.1507, found: 406.1491.



5-Acetamido-5-deoxy-3-(cyclohex-1-en-1-yl)-β-D-glycero-D-galacto-non-2-enonic acid (9k). Obtained as a white solid (6.7 mg, 72%). ^{1}H NMR (600 MHz, CD_3OD): *δ* 5.63 – 5.59 (m, 1H), 4.21 – 4.10 (m, 3H), 3.83 – 3.76 (m, 2H), 3.68 – 3.62 (m, 1H), 3.56 (dd, *J* = 8.8, 1.5 Hz, 1H), 2.16 (ddd, *J* = 60.4, 14.2, 7.9 Hz, 2H), 2.06 – 2.02 (m, 1H), 2.01 (s, 3H), 1.72 – 1.63 (m, 2H), 1.60 – 1.57 (m, 2H). ^{13}C NMR (150 MHz, CD_3OD): *δ* 174.03, 148.29, 135.16, 126.90, 115.65, 76.83, 71.45, 71.24, 69.06, 64.74, 52.48, 29.32, 26.62, 24.02, 23.16, 22.68. HR MS [M - H]$^-$ m/z: calcd for $C_{17}H_{24}NO_8^-$: 370.1507, found: 370.1507.

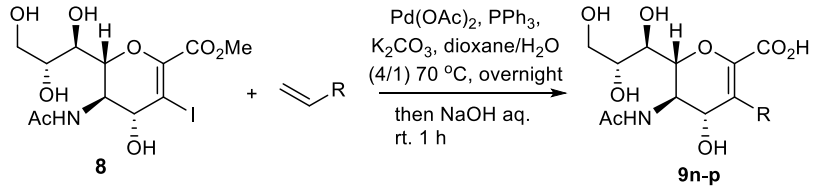


5-Acetamido-5-deoxy-3-allyl-β-D-glycero-D-galacto-non-2-enonic acid (9l). Obtained as a white solid (5.38 mg, 65%) with borate as substrate. ^{1}H NMR (600 MHz, CD_3OD): *δ* 5.87 – 5.81 (m, 1H), 5.10 (d, *J* = 17.1 Hz, 1H), 4.98 (d, *J* = 10.4 Hz, 1H), 4.22 (d, *J* = 8.2 Hz, 1H), 4.10 (dd, *J* = 10.4, 8.2 Hz, 1H), 4.02 (d, *J* = 10.4 Hz, 1H), 3.89 – 3.74 (m, 2H), 3.64 (dd, *J* = 11.6, 5.6 Hz, 1H), 3.56 – 3.41 (m, 2H), 3.02 (dd, *J* = 14.6, 7.9 Hz, 1H), 2.02 (s, 3H). ^{13}C NMR (150 MHz, CD_3OD): *δ* 174.7, 138.0, 115.9, 77.1, 71.1, 70.6, 69. 5, 64.8, 53.1, 31.8, 20.9. HR MS [M - H]$^-$ m/z: calcd for $C_{14}H_{20}NO_8^-$: 330.1194, found: 330.1209. Its NMR data matched that reported in reference 9a (main text).

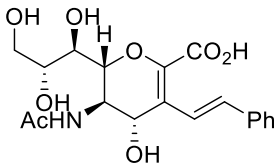


5-Acetamido-5-deoxy-3-cinnamyl-β-D-glycero-D-galacto-non-2-enonic acid (9m). Obtained as a white solid (7.1 mg, 70%) with borate as substrate. ^{1}H NMR (600 MHz, CD_3OD): *δ* 7.33 (d, *J* = 7.8 Hz, 2H), 7.24 (t, *J* = 7.7 Hz, 2H), 7.14 (t, *J* = 7.4 Hz, 1H), 6.48 (d, *J* = 15.7 Hz, 1H), 6.27 (dt, *J* = 15.0, 7.0 Hz, 1H), 5.13 (s, 1H), 4.21 (d, *J* = 8.0 Hz, 1H), 4.17 – 4.10 (m, 1H), 4.02 (d, *J* = 10.1 Hz, 1H), 3.84 – 3.80 (m, 2H), 3.67 – 3.60 (m, 1H), 3.54 (dd, *J* = 14.8, 5.7 Hz, 1H), 3.48 (d, *J* = 9.4 Hz, 1H), 3.11 (dd, *J* = 14.5, 8.3 Hz, 1H), 1.99 (s, 3H). ^{13}C NMR (150 MHz, CD_3OD): *δ* 179.0, 139.4, 132.34, 132.28, 132.0, 130.9, 130.0, 129.4, 128.8, 128.7, 127.8, 127.0, 112.5, 77.0, 70.9, 70.7, 69.5, 64.8, 53.1, 30.8, 23.2. HR MS [M - H]$^-$ m/z: calcd for $C_{20}H_{24}NO_8^-$: 406.1507, found: 406.1499. Its NMR data matched that reported in reference 11a (main text).

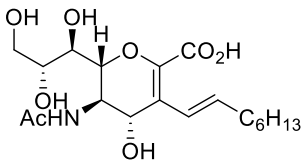
General procedure for Heck coupling reaction



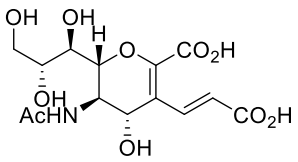
Vinyl iodide **8** (10.4 mg, 0.025 mmol), an alkene (0.05 mmol), palladium acetate (0.6 mg, 0.0025 mmol), triphenylphosphine (1.3 mg, 0.005 mmol), and K_2CO_3 (8.6 mg, 0.0625 mmol) were mixed in dioxane and H_2O (v/v = 4/1, 1 mL, degassed by bubbling nitrogen for 0.5 h). The reaction mixture was flushed with nitrogen, heated to 70 °C on an aluminum block, and stirred overnight. The reaction was monitored with TLC (**8**: R_f = 0.4 in DCM/MeOH/H_2O 5/1/0.1), which indicated the complete consumption of starting material. NaOH solution (1 M, 0.5 mL) was added, and the resulting mixture was stirred at rt for another 0.5 h. The reaction was monitored with TLC, and upon completion, it was neutralized with Amberlyst® 15 resin. After filtration, the filtrate was collected and the solvent was removed under vacuum before purification by flash chromatography (20-35% MeOH/H_2O/AcOH 5/1/0.1 in EA) to give the product.



5-Acetamido-5-deoxy-3-[(E)-styryl]-β-D-glycero-D-galacto-non-2-enonic acid (9n). Obtained as a white solid (8.3 mg, 85%). ^{1}H NMR (600 MHz, CD_3OD): δ 7.39 (dd, 2H, J = 7.4, Hz), 7.25 (t, 2H, J = 7.4 Hz), 7.13 (t, 2H, J = 7.4 Hz), 6.72 (d, 2H, J = 16.3 Hz), 4.52 (d, 1H, J = 6.3 Hz), 4.29 (dd, 1H, J = 7.7, 6.2 Hz), 4.20 (d, 1H, J = 7.8 Hz), 3.86 – 3.81 (m, 2H), 3.68 – 3.64 (m, 2H), 2.04 (s, 3H). ^{13}C NMR (150 MHz, CD_3OD) δ 175.7, 140.0, 129.5, 127.6, 127.5, 127.0, 125.9, 112.6, 77.5, 71.8, 71.1, 67.1, 64.7, 53.6, 21.0. HRMS $[M-H]^-$ m/z calcd for $C_{19}H_{22}NO_8^-$: 392.1351, found: 392.1351.

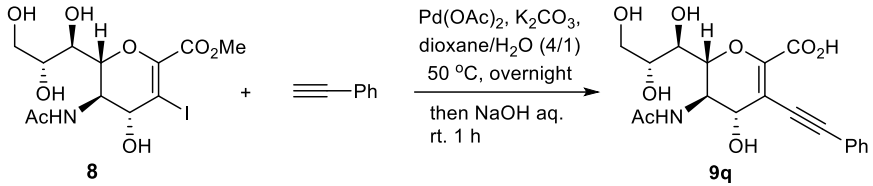


5-Acetamido-5-deoxy-3-((E)-oct-1-en-1-yl)-β-D-glycero-D-galacto-non-2-enonic acid (9o). Obtained as a white solid (6.7 mg, 67%) using Ag_2CO_3 (17.3 mg, 0.0625 mmol) instead of K_2CO_3. ^{1}H NMR (600 MHz, CD_3OD): δ 6.58 (d, J = 15.9 Hz, 1H), 5.82 (dt, J = 15.8, 7.0 Hz, 1H), 4.42 (d, J = 6.4 Hz, 1H), 4.25 – 4.21 (m, 1H), 4.13 – 4.09 (m, 1H), 3.85 – 3.79 (m, 2H), 3.70 (ddd, J = 11.9, 6.4, 2.2 Hz, 1H), 3.65 (dd, J = 8.6, 1.7 Hz, 1H), 2.17 – 2.08 (m, 2H), 2.05 (s, 3H), 1.46 – 1.23 (m, 8H), 0.91 (t, J = 6.7 Hz, 3H). ^{13}C NMR (150 MHz, CD_3OD): δ 174.2, 150.6, 132.5, 129.8, 129.5, 126.4, 77.1, 71.3, 71.2, 67.42, 64.37, 53.6, 34.7, 33.0, 30.8, 30.0, 23.7, 22.7, 14.4. HR MS $[M - H]^-$ m/z: calcd for $C_{19}H_{30}NO_8^-$: 400.1977, found: 400.1974.



5-Acetamido-5-deoxy-3-[(E)-2-carboxyvinyl]-β-D-glycero-D-galacto-non-2-enonic acid (9p). Obtained as a white solid (4.6 mg, 51%). This reaction was carried out at 50 °C instead of 70 °C, as at 70 °C, the reaction system became complex as monitored by TLC. ^{1}H NMR (600 MHz, D_2O): δ 5.96 (d, *J* = 12.4 Hz, 1H), 5.85 (d, *J* = 4.9 Hz, 1H), 5.68 (d, *J* = 12.4 Hz, 1H), 4.48 (d, *J* = 1.7 Hz, 1H), 4.13 (d, *J* = 5.0 Hz, 1H), 3.83 (dd, *J* = 6.1, 1.9 Hz, 1H), 3.72 – 3.64 (m, 2H), 3.59 – 3.52 (m, 1H), 3.27 (s, 1H), 1.95 (s, 3H). ^{13}C NMR (150 MHz, D_2O): δ 181.51, 173.43, 138.27, 130.13, 123.23, 121.19, 104.02, 77.39, 77.28, 71.65, 62.30, 47.65, 21.82. HR MS [M - H]$^-$ m/z: calcd for $C_{14}H_{18}NO_{10}^-$: 360.0936, found: 360.0920.

General procedure for Sonogashira coupling reaction



Vinyl iodide **8** (10.4 mg, 0.025 mmol) and phenylacetylene (5.7 μL, 0.05 mmol), palladium acetate (0.6 mg, 0.0025 mmol), and K_2CO_3 (8.6 mg, 0.0625 mmol) were mixed in dioxane and H_2O (v/v = 4/1, 1 mL, degassed by bubbling nitrogen for 0.5 h). The reaction mixture was flushed with nitrogen, heated to 50 °C on an aluminum block, and stirred overnight. The reaction was monitored with TLC (**8**: R_f = 0.4 in DCM/MeOH/H_2O 5/1/0.1), which indicated the complete consumption of starting material. NaOH solution (1 M, 0.5 mL) was added, and the resulting mixture was stirred at rt for another 0.5 h. The reaction was monitored with TLC (product **9q**: Rf = 0.3 in EA/MeOH/H_2O/AcOH = 10/5/1/0.1), and upon completion, it was neutralized with Amberlyst® 15 resin. After filtration, the filtrate was collected and the solvent was removed under vacuum before purification by flash chromatography (20-35% MeOH/H_2O/AcOH 5/1/0.1 in EA) to give *5-acetamido-5-deoxy-3-(phenylethynyl)-β-D-glycero-D-galacto-non-2-enonic acid* (**9q**) as a white solid (7.6 mg, 78%). ^{1}H NMR (600 MHz, MeOD): δ 7.53 – 7.40 (m, 2H), 7.34 – 7.18 (m, 3H), 4.32 (d, *J* = 8.3 Hz, 1H), 4.22 (d, *J* = 10.2 Hz, 1H), 4.15 (d, *J* = 8.8 Hz, 1H), 3.86 – 3.78 (m, 2H), 3.68 (dd, *J* = 11.6, 5.4 Hz, 1H), 3.60 (s, 1H), 3.57 (d, *J* = 9.2 Hz, 1H), 2.04 (s, 3H). ^{13}C NMR (150 MHz, MeOD): δ 180.89, 132.33, 129.13, 128.49, 125.95, 100.14, 94.49, 86.82, 77.70, 70.96, 70.43, 69.76, 64.72, 51.77, 22.75. HR MS [M - H]$^-$ m/z: calcd for $C_{19}H_{20}NO_8^-$: 390.1194, found: 390.1193.

II. NMR and MS Spectra of New Compounds

Figure S1. ^{1}H NMR of Compound **8** (600 MHz, CD_3OD)

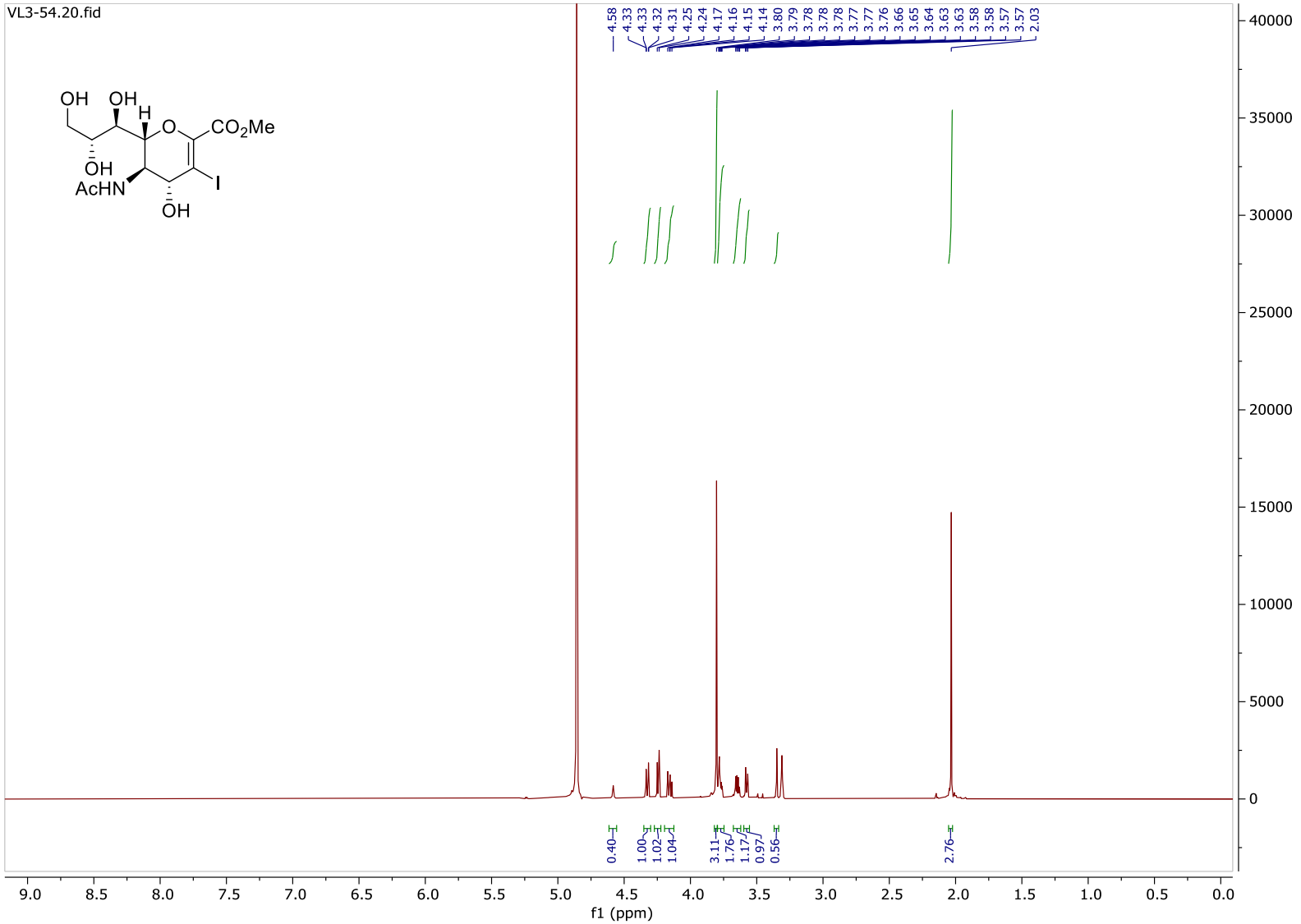


Figure S2. ^{13}C NMR of Compound **8** (150 MHz, CD_3OD)

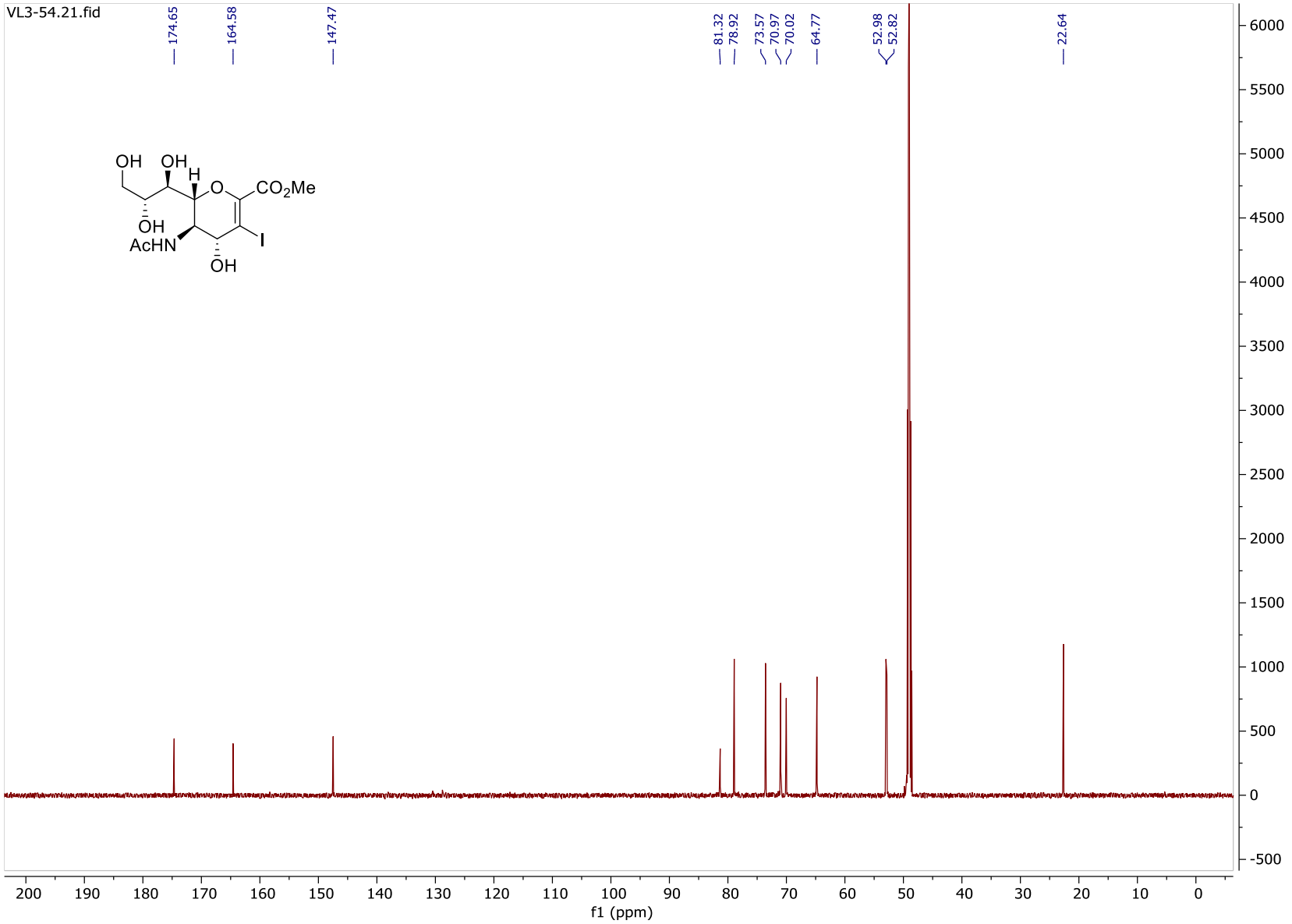


Figure S3. HRMS of Compound **8** (ESI-TOF)

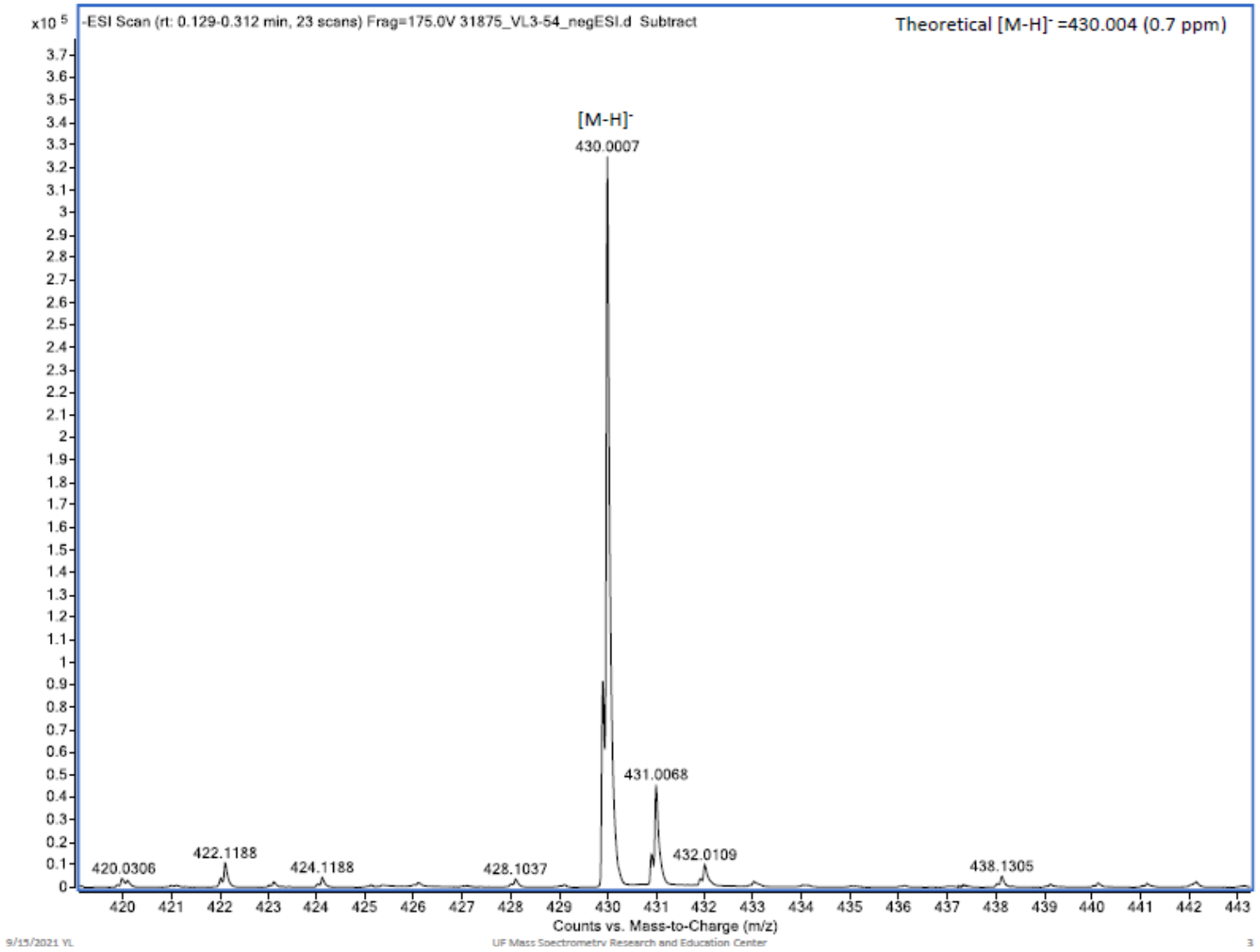


Figure S4. ^{1}H NMR of Compound **9a** (600 MHz, CD_3OD)

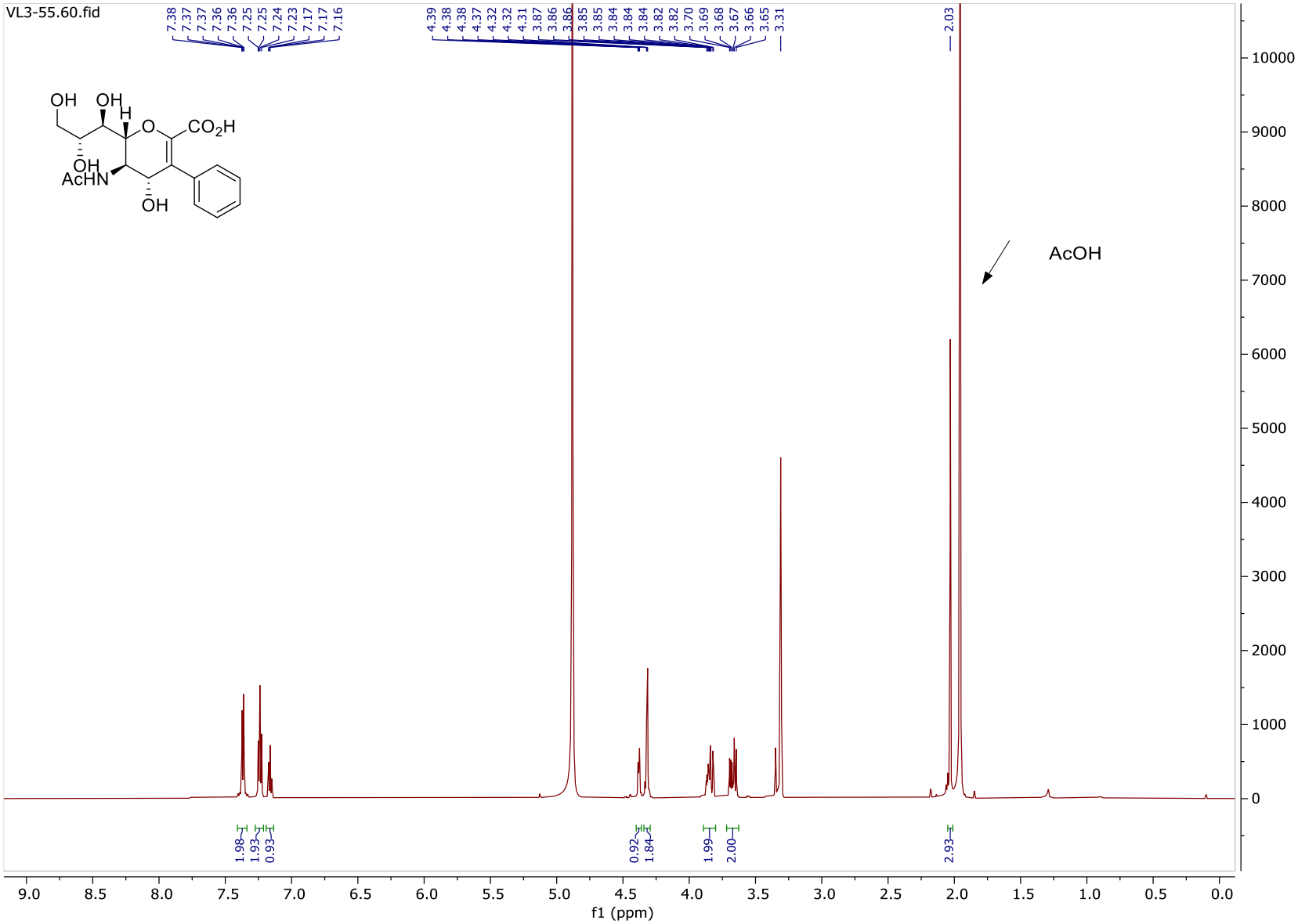


Figure S5. ^{13}C NMR of Compound **9a** (150 MHz, CD_3OD)

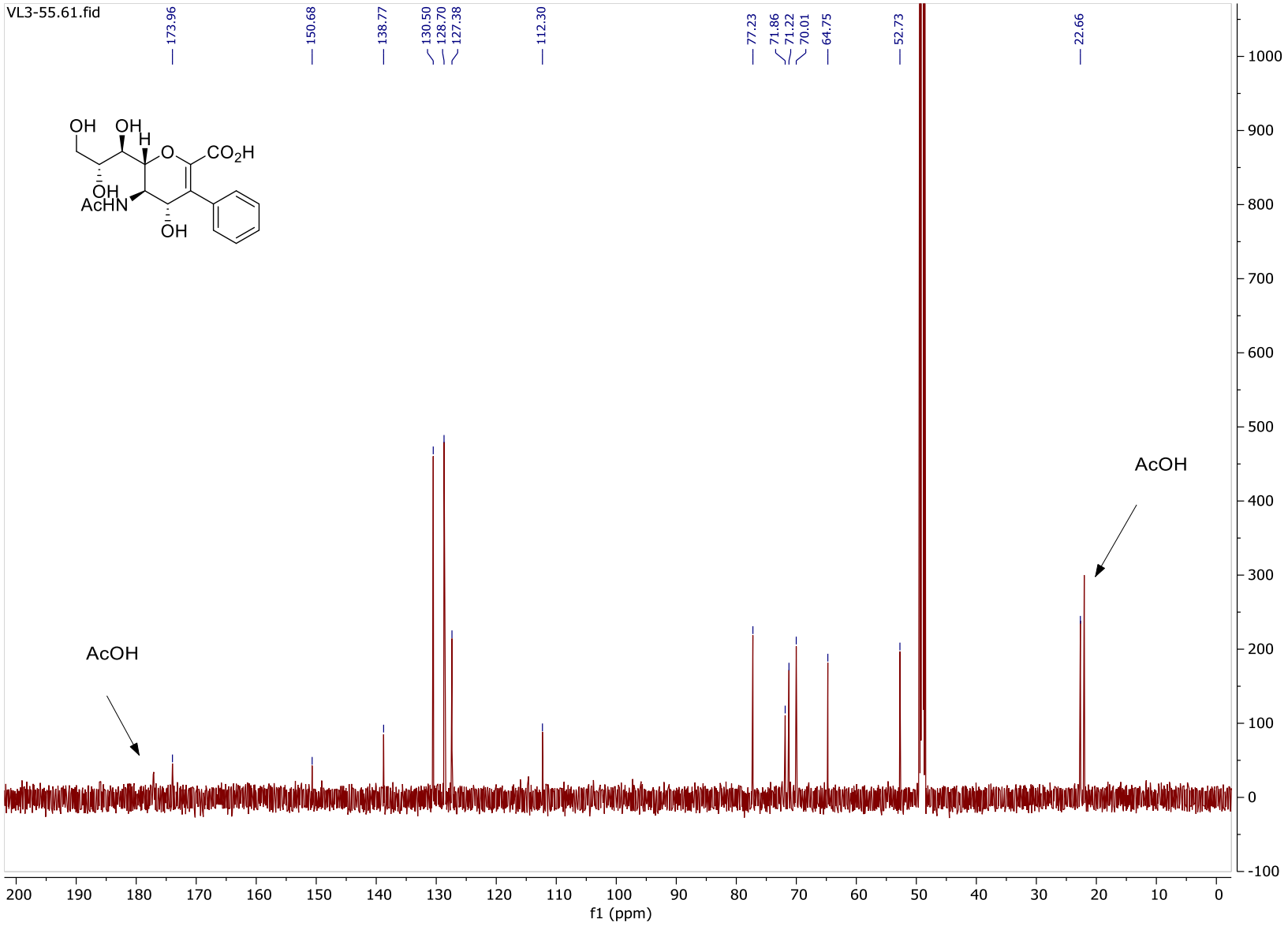


Figure S6. ^{1}H-^{1}H COSY NMR of Compound **9a** (600 MHz, CD_3OD)

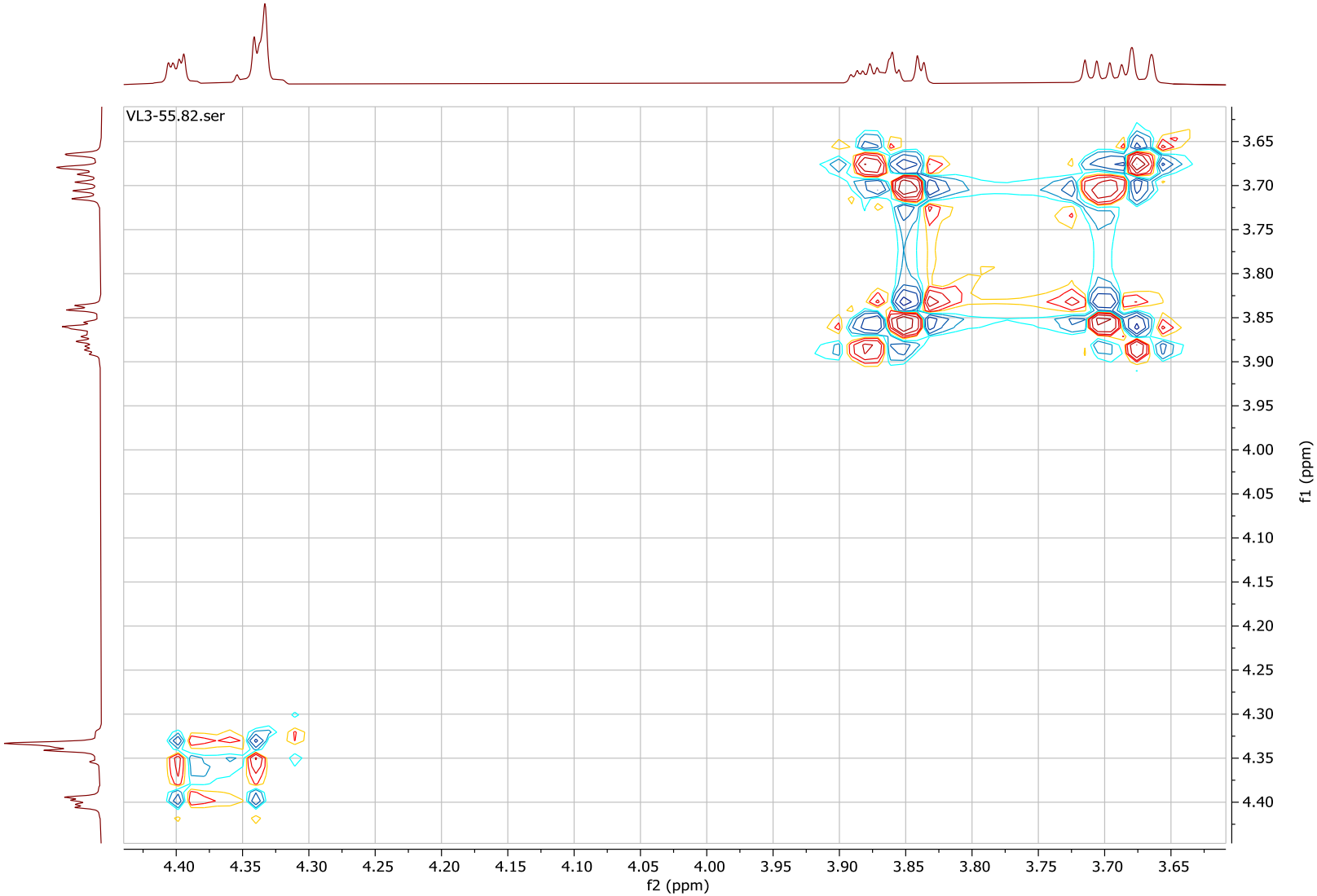


Figure S7. HSQC NMR of Compound **9a** (600 MHz, CD_3OD)

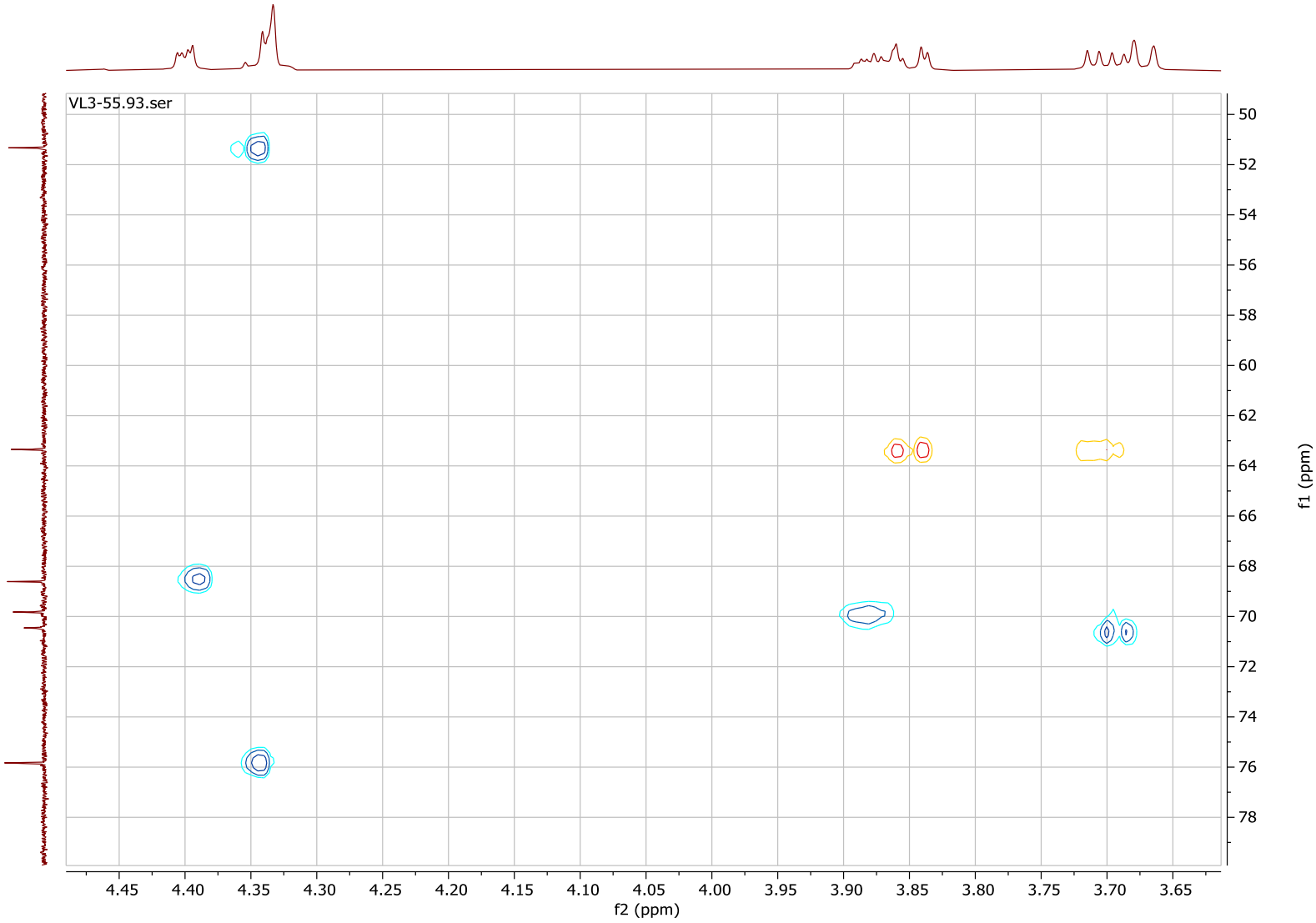


Figure S8. HMBC NMR of Compound **9a** (600 MHz, CD_3OD)

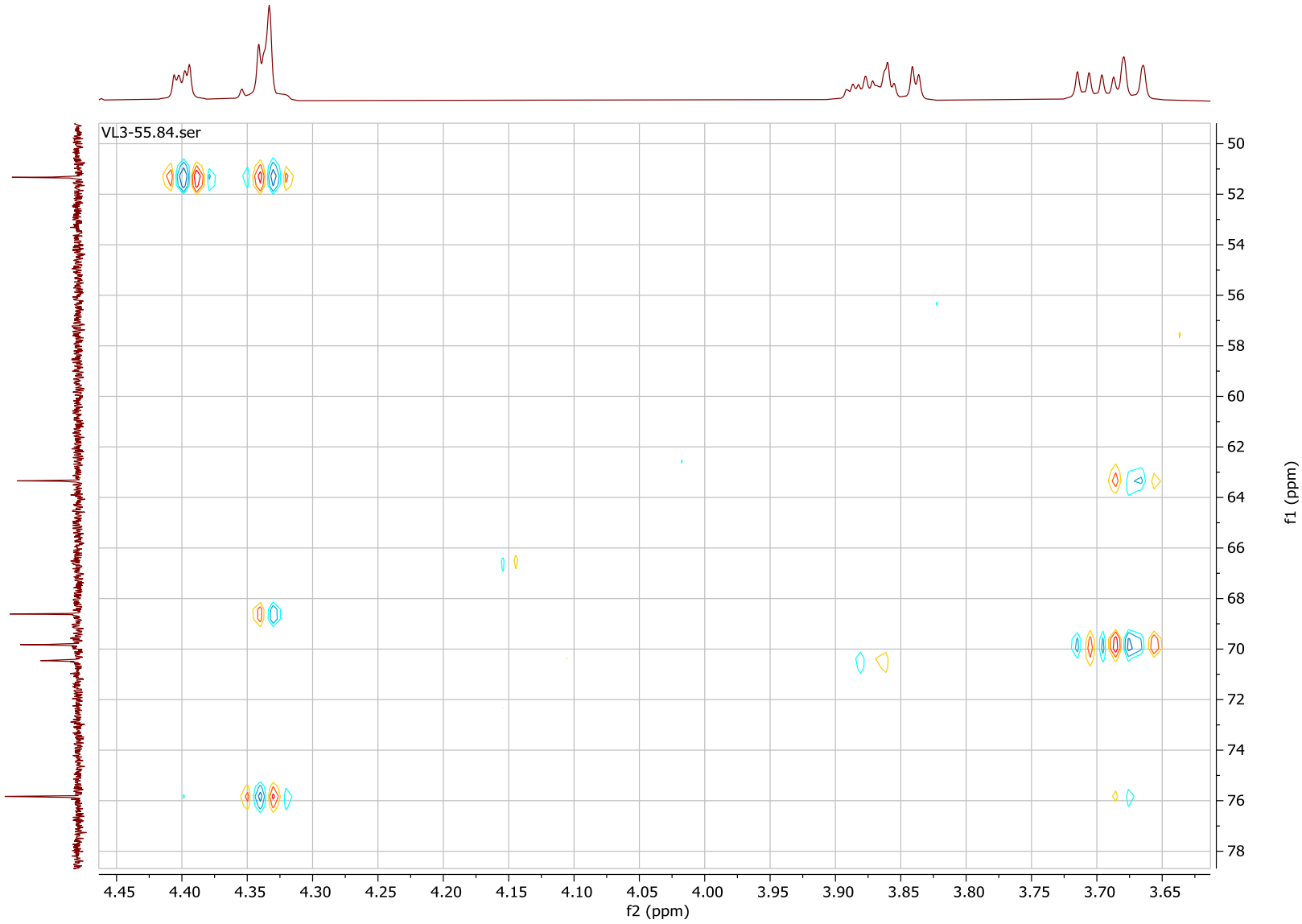


Figure S9. HRMS of Compound **9a** (ESI-TOF)

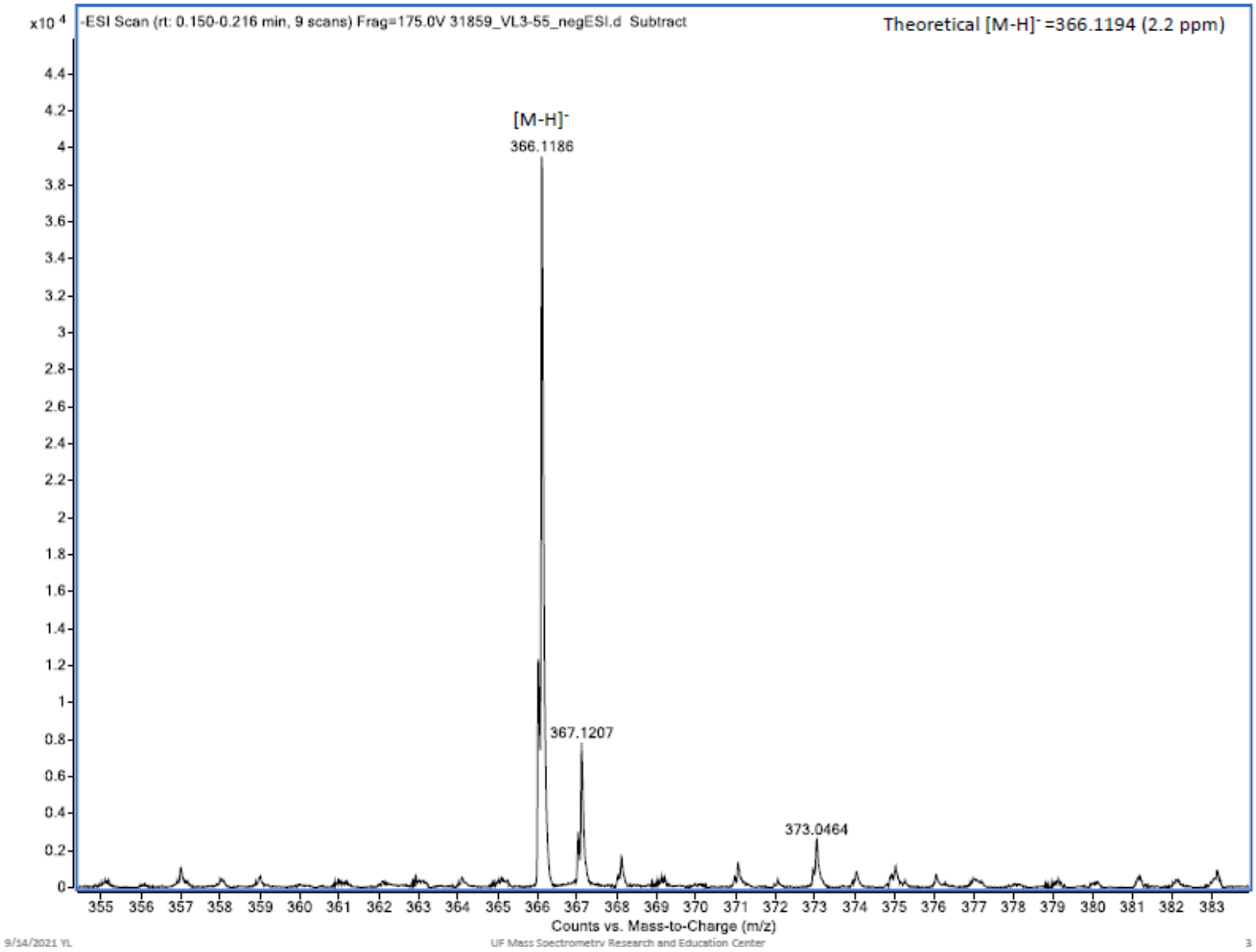


Figure S10. ^{1}H NMR of Compound **9b** (600 MHz, CD_3OD)

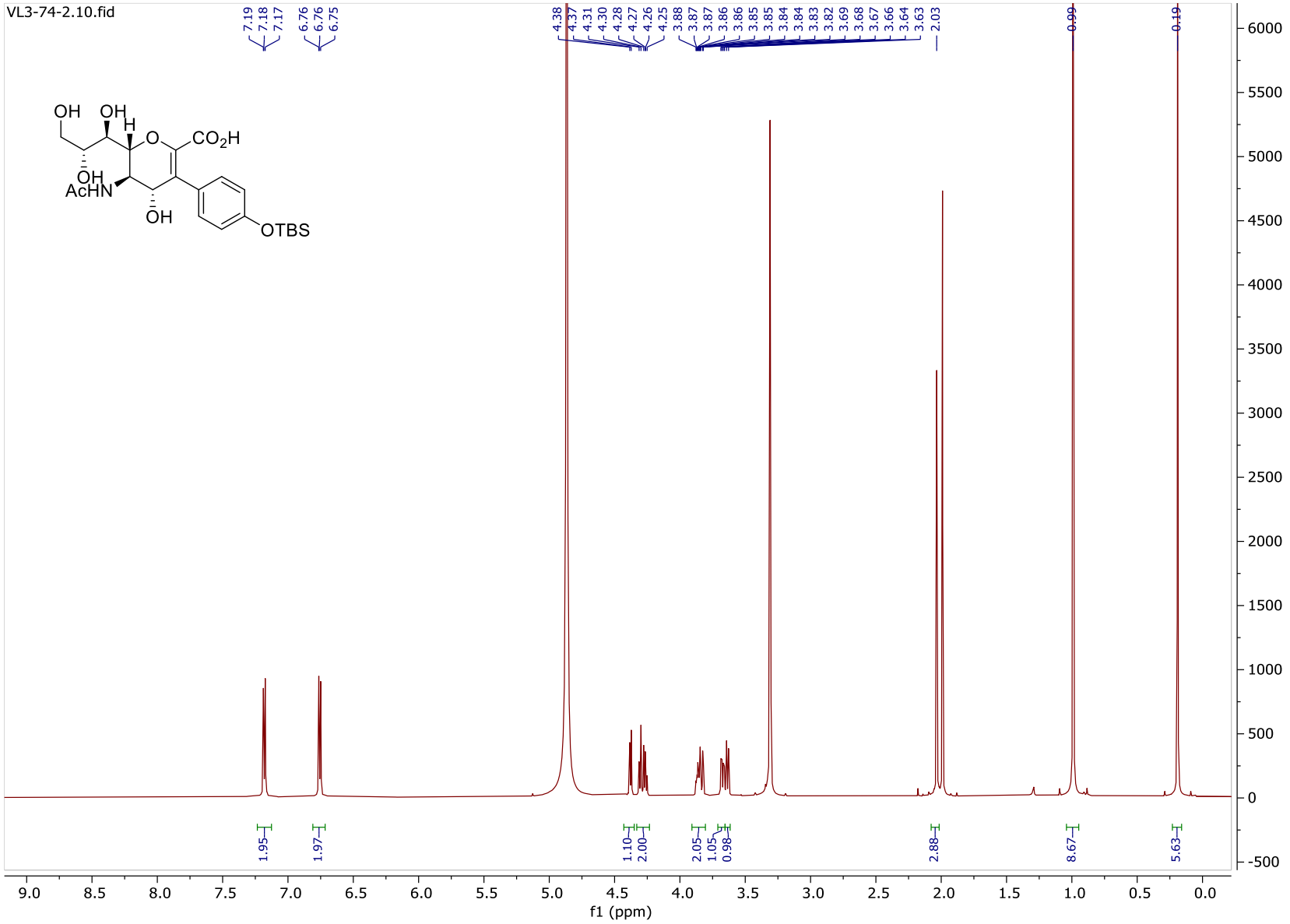


Figure S11. ^{13}C NMR of Compound **9b** (150 MHz, CD_3OD)

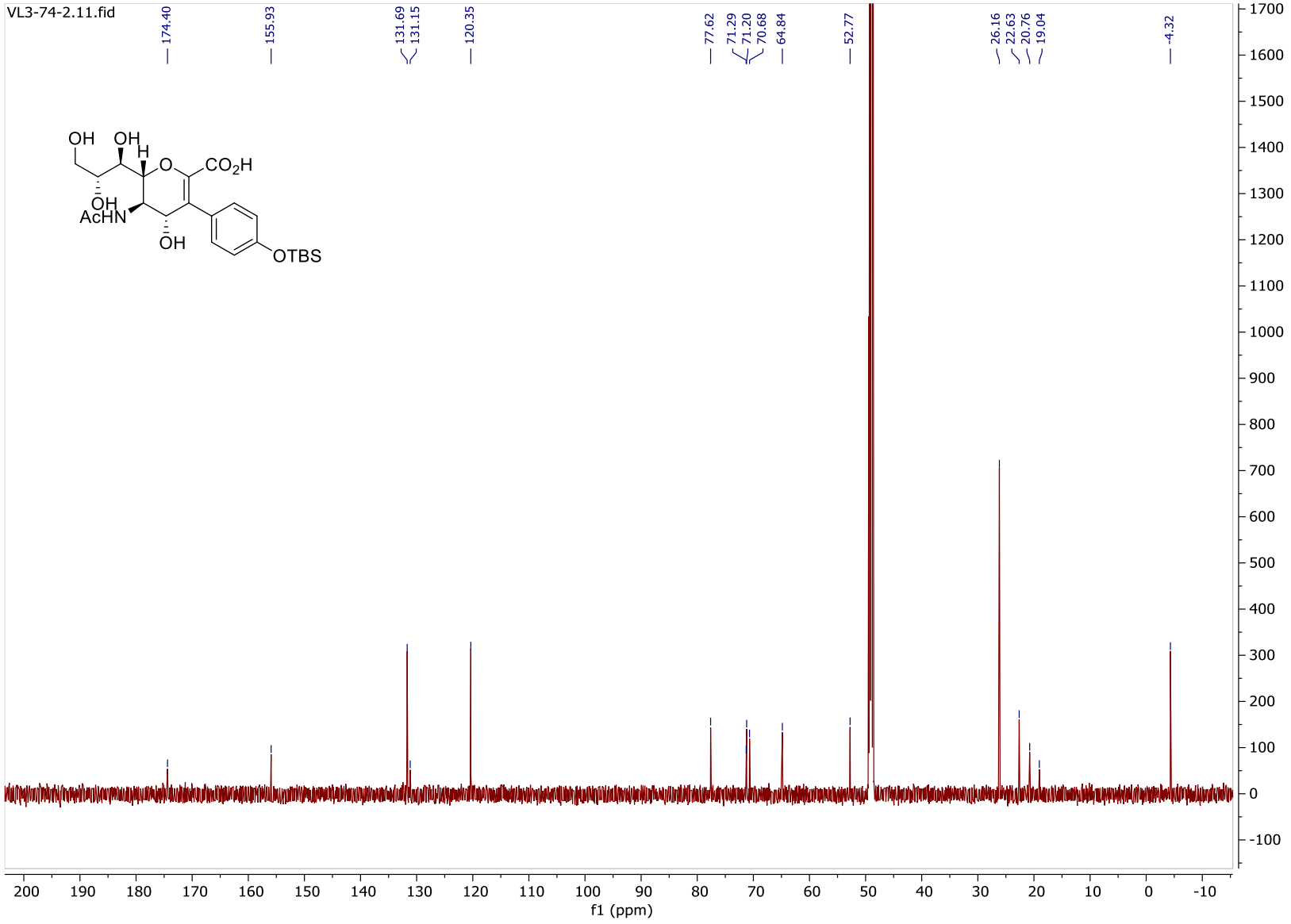


Figure S12. HRMS of Compound **9b** (ESI-TOF)

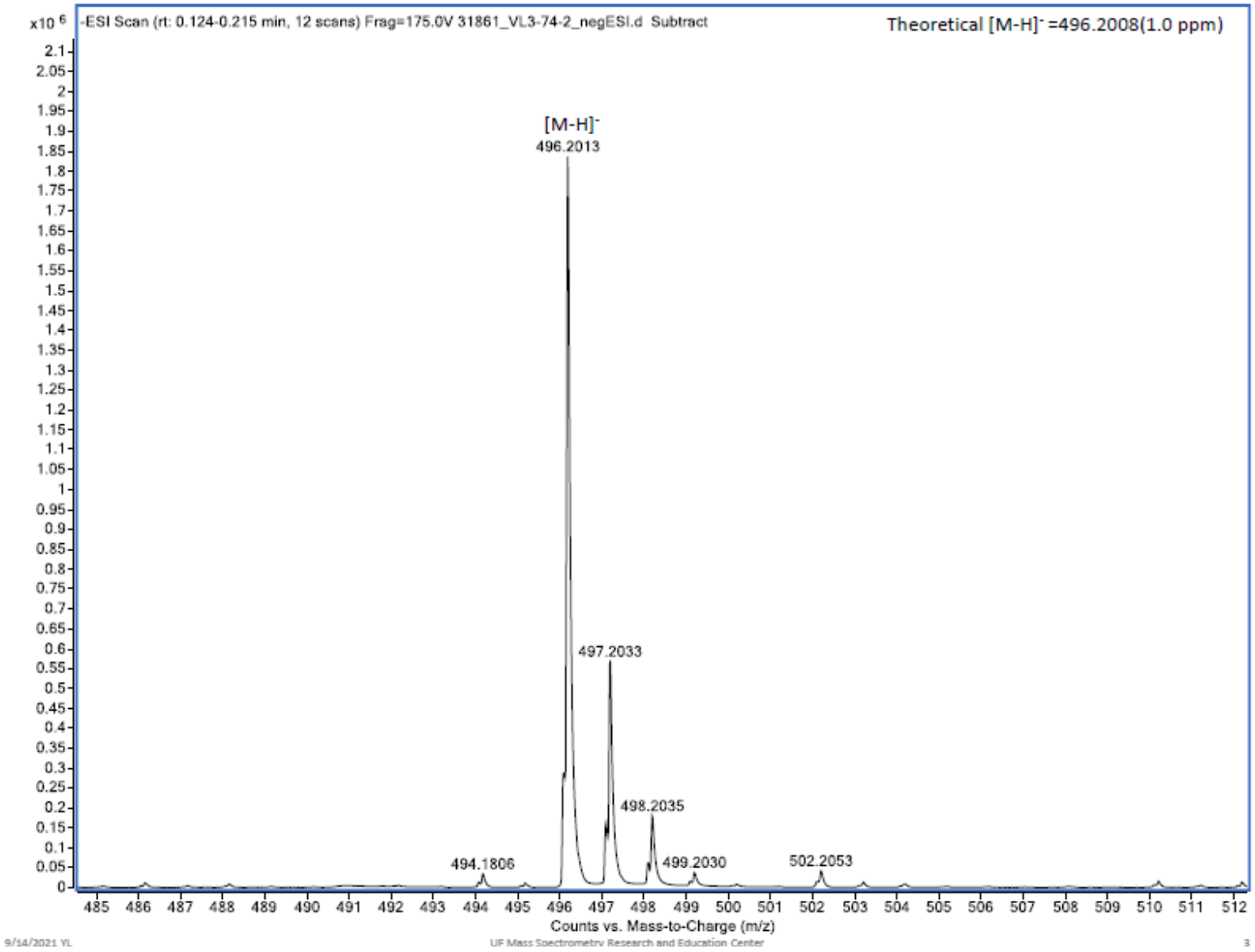


Figure S13. ^{1}H NMR of Compound **9c** (600 MHz, CD_3OD)

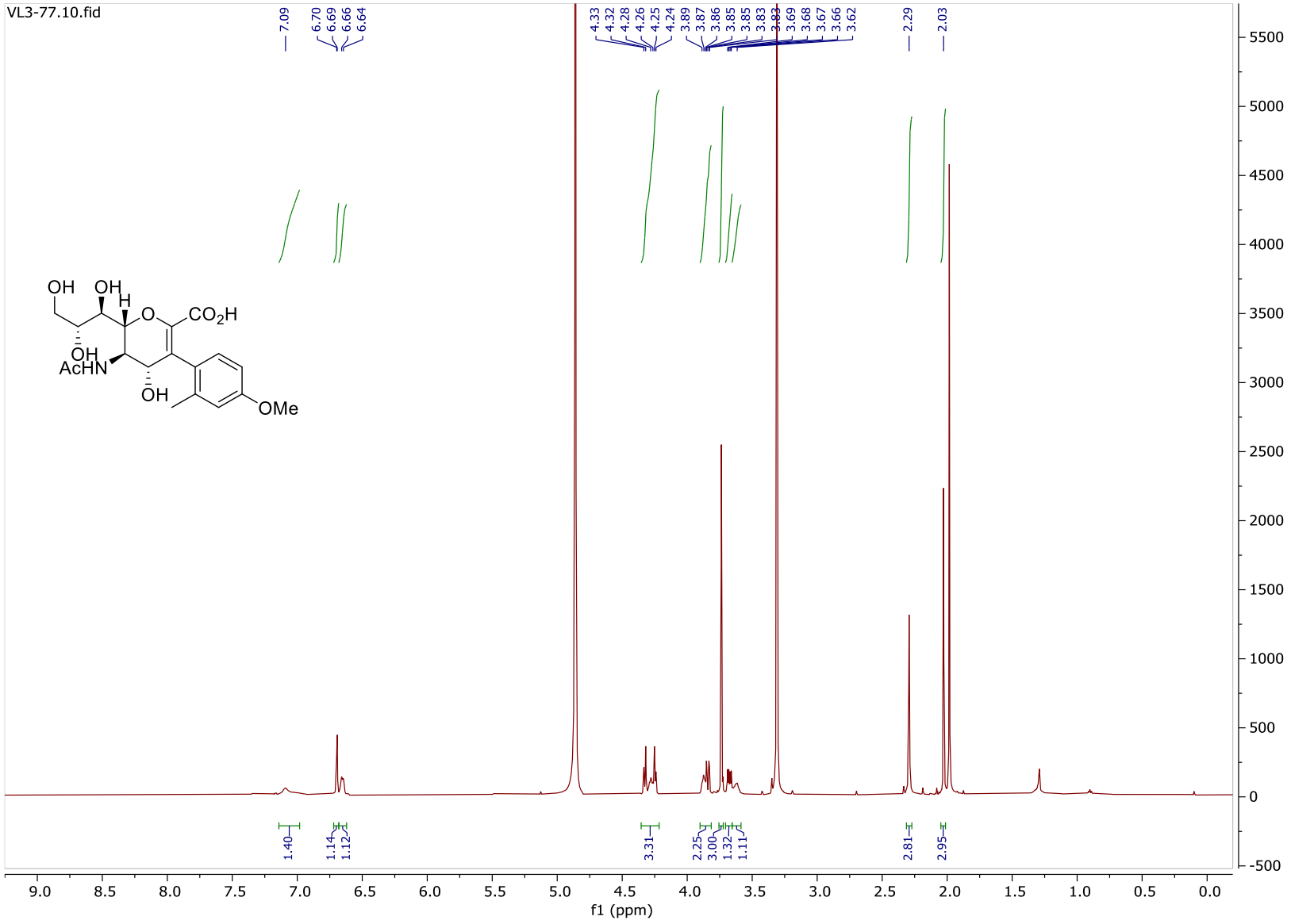


Figure S14. ^{13}C NMR of Compound **9c** (150 MHz, CD_3OD)

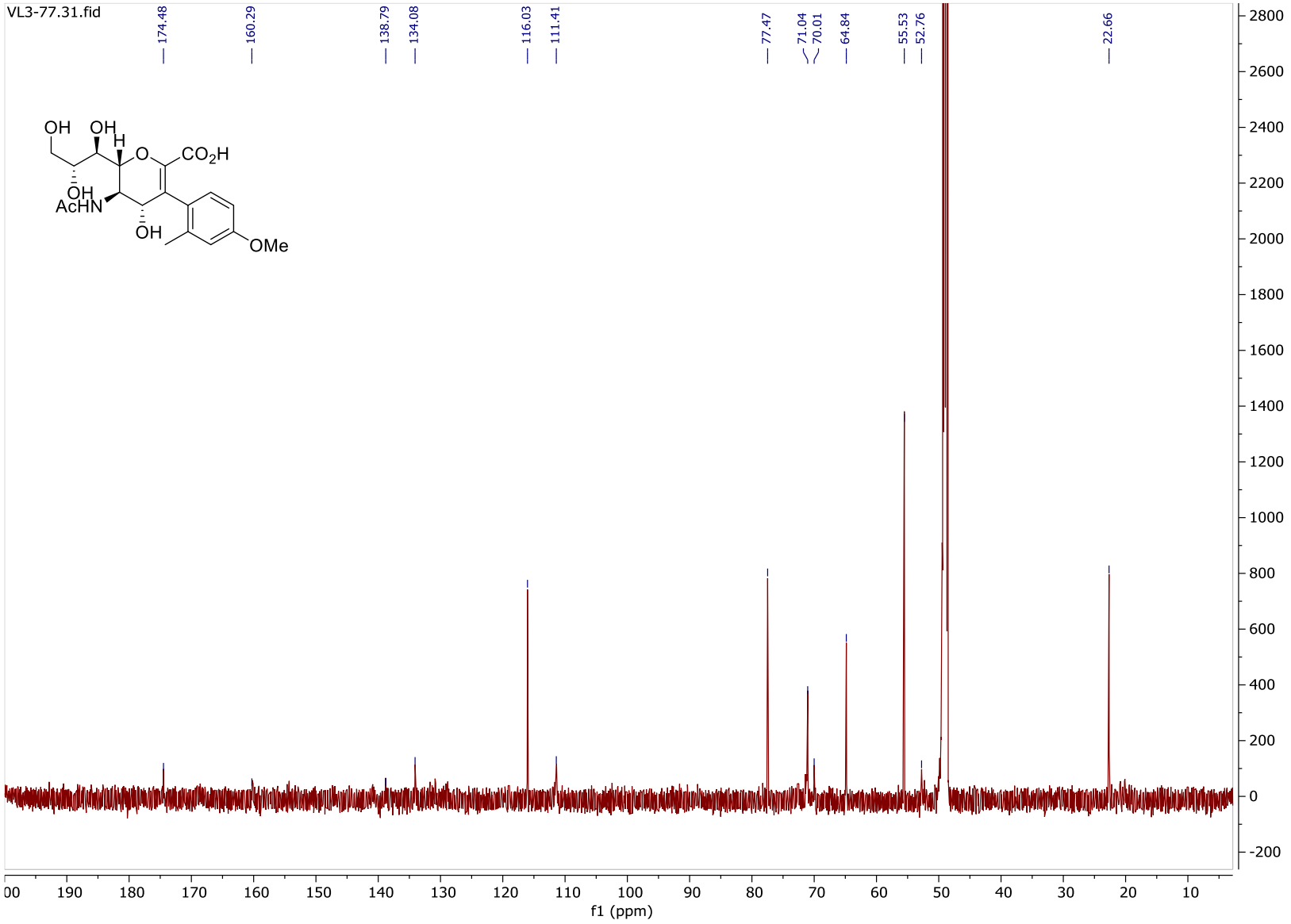


Figure S15. HRMS of Compound **9c** (ESI-TOF)

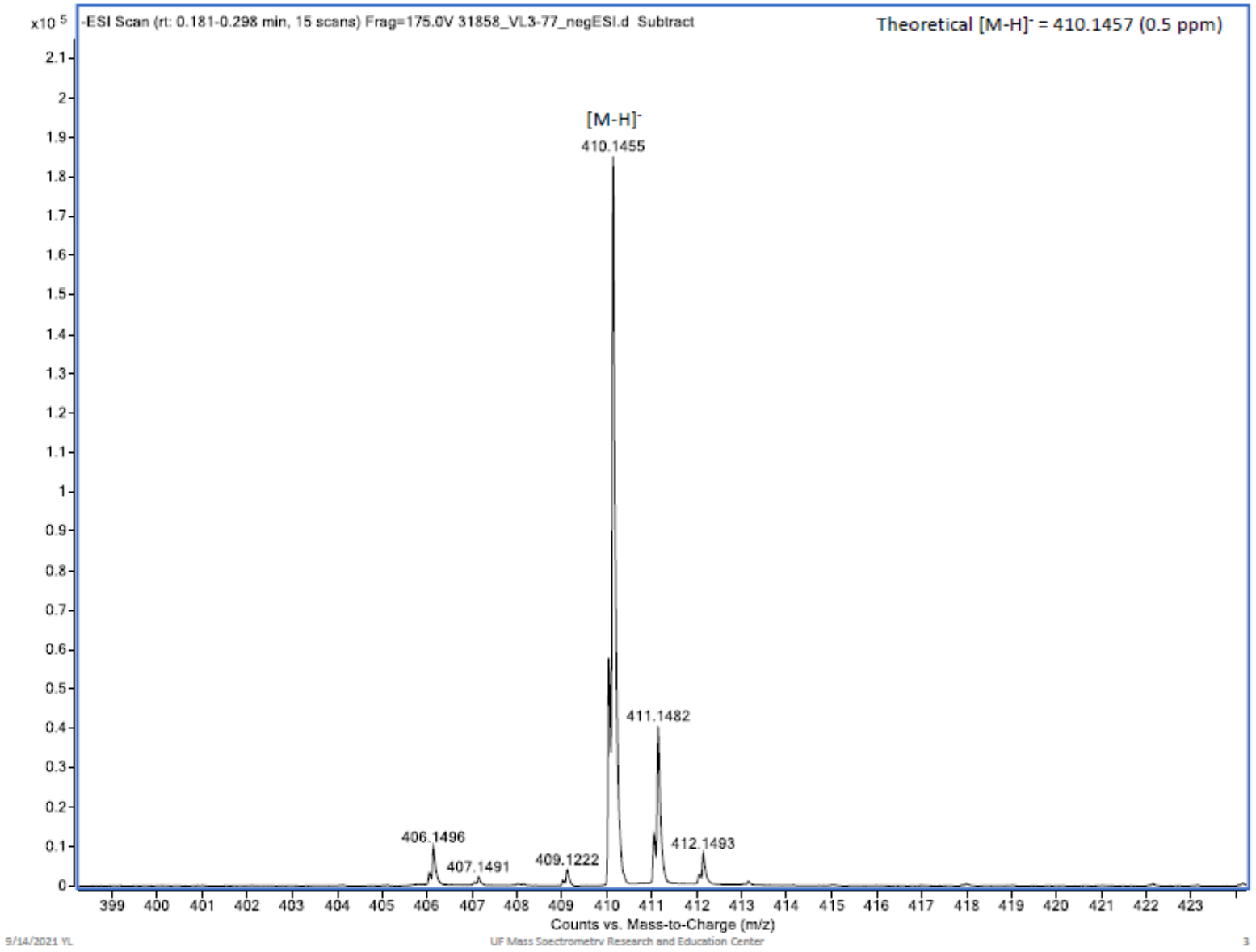


Figure S16. ^{1}H NMR of Compound **9d** (600 MHz, CD_3OD)

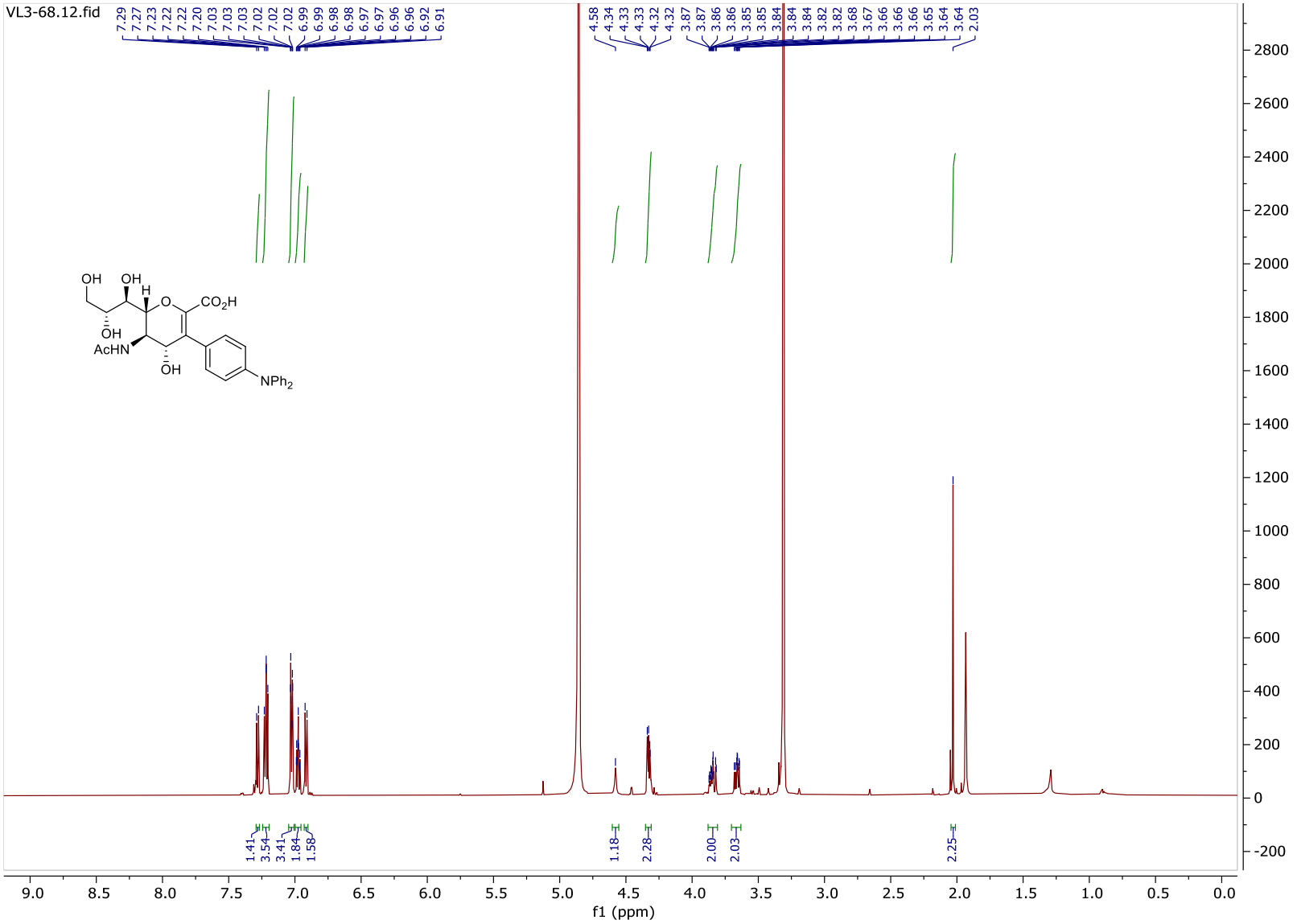


Figure S17. ^{13}C NMR of Compound **9d** (150 MHz, CD_3OD)

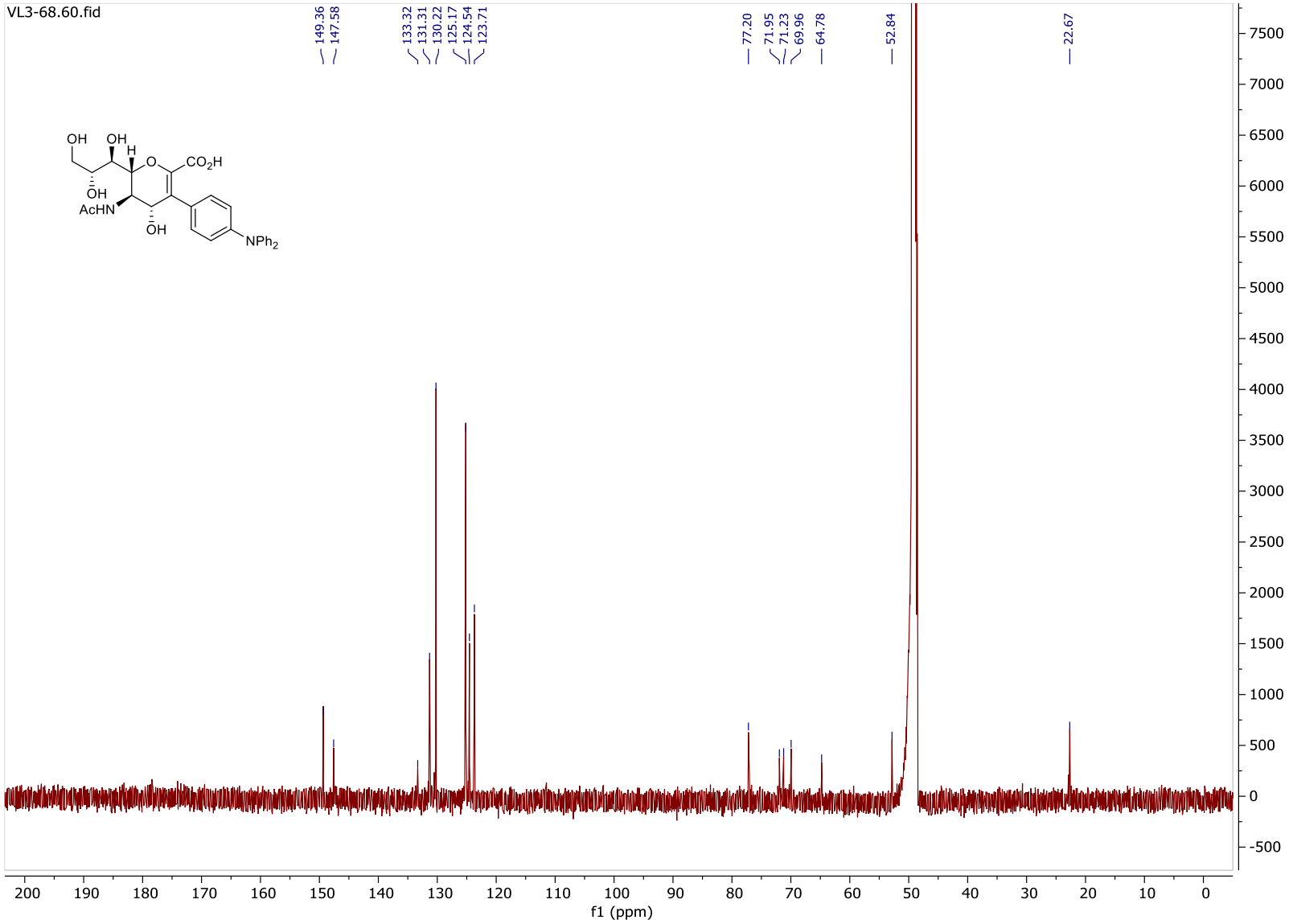


Figure S18. HRMS of Compound **9d** (ESI-TOF)

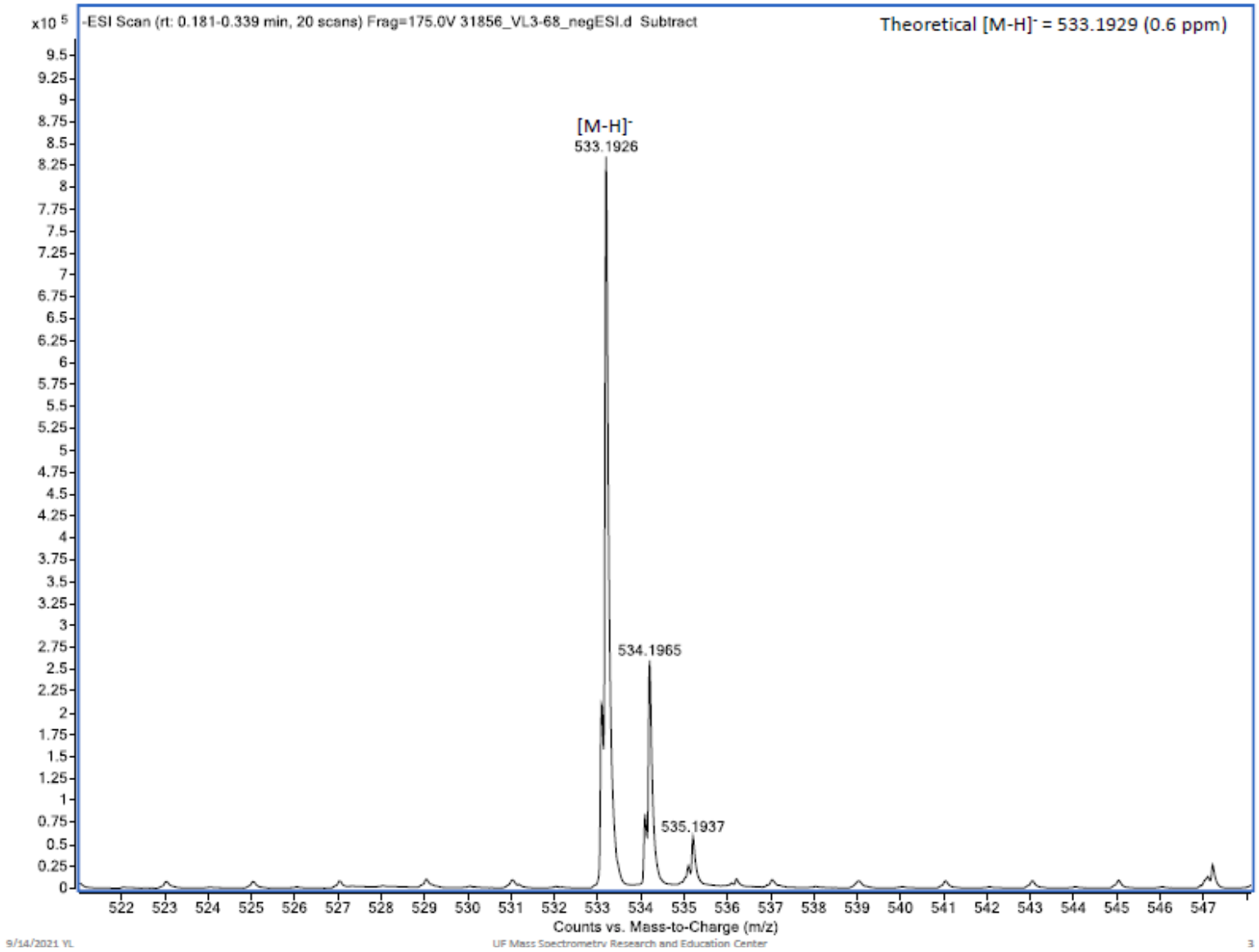


Figure S19. ^{1}H NMR of Compound **9e** (600 MHz, CD_3OD)

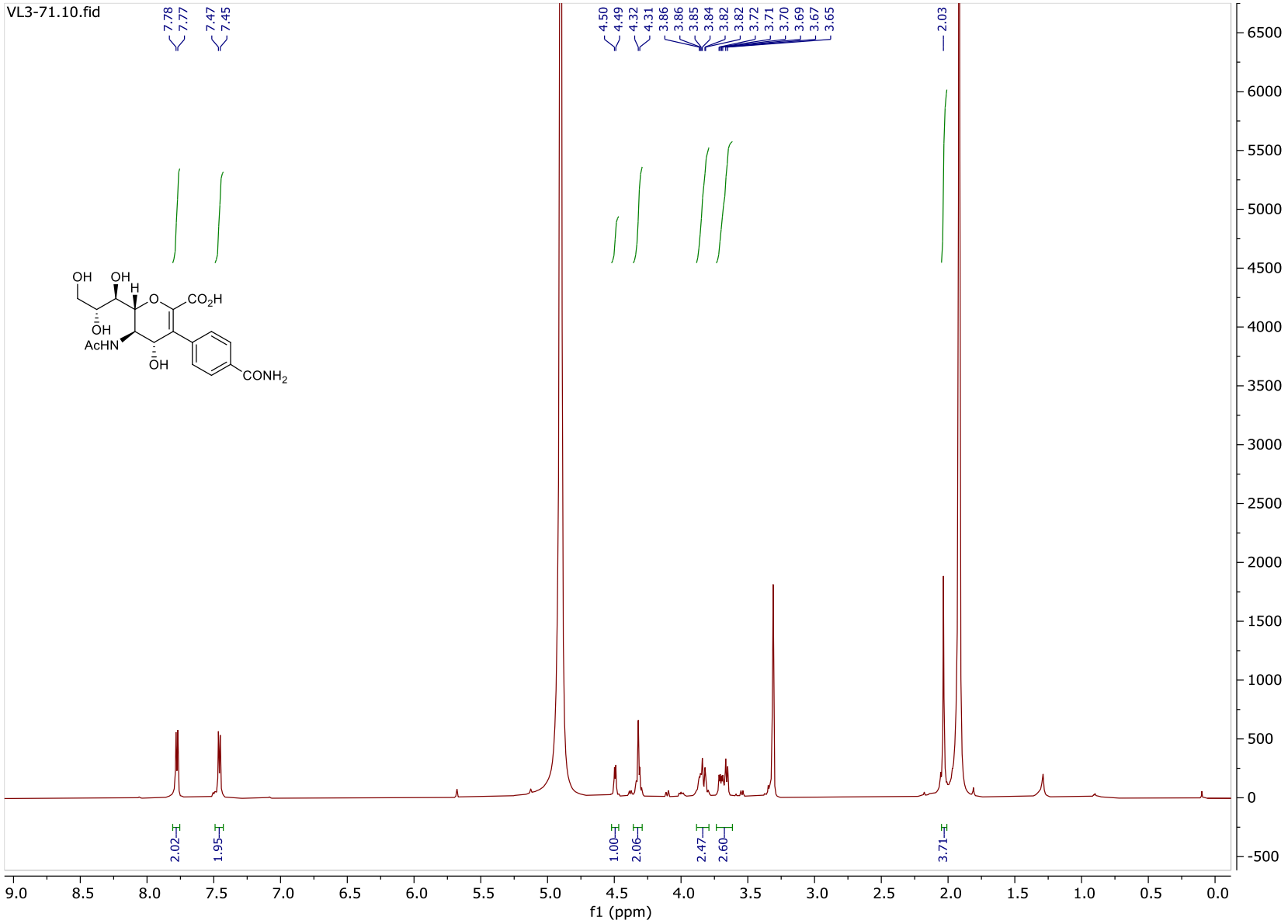


Figure S20. ^{13}C NMR of Compound **9e** (150 MHz, CD_3OD)

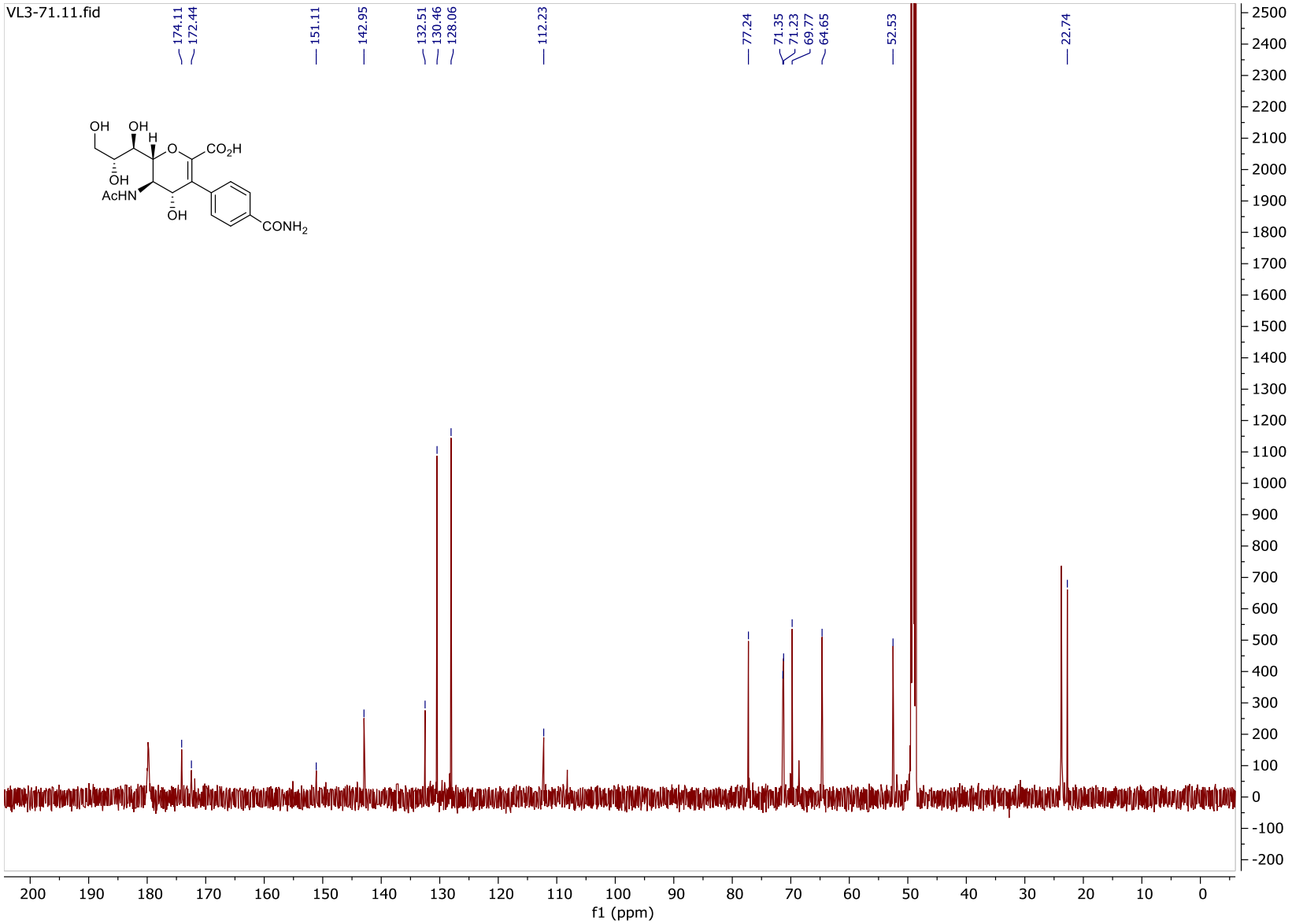


Figure S21. HRMS of Compound **9e** (ESI-TOF)

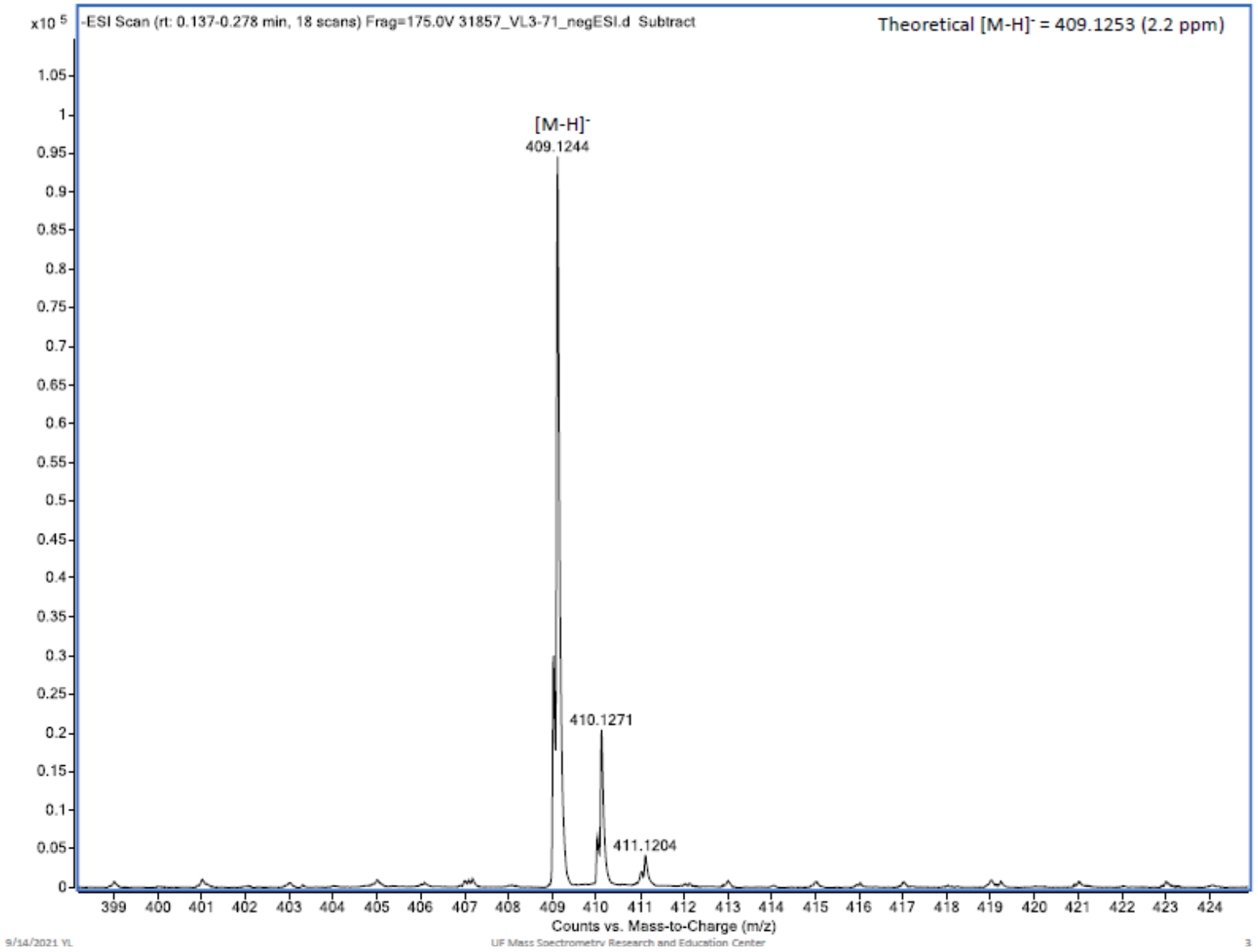


Figure S22. ^{1}H NMR of Compound **9f** (600 MHz, CD_3OD)

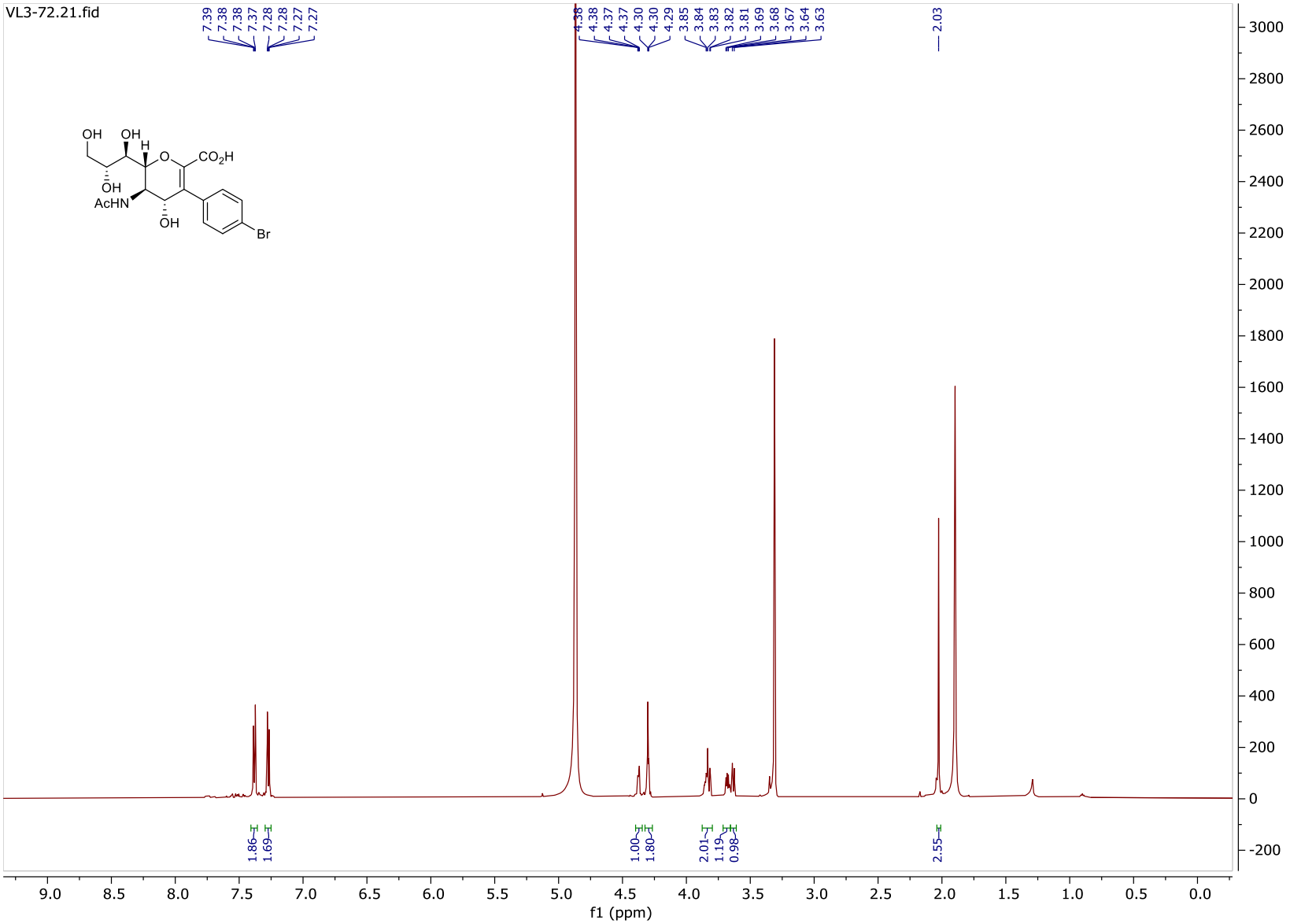


Figure S23. ^{13}C NMR of Compound **9f** (150 MHz, CD_3OD)

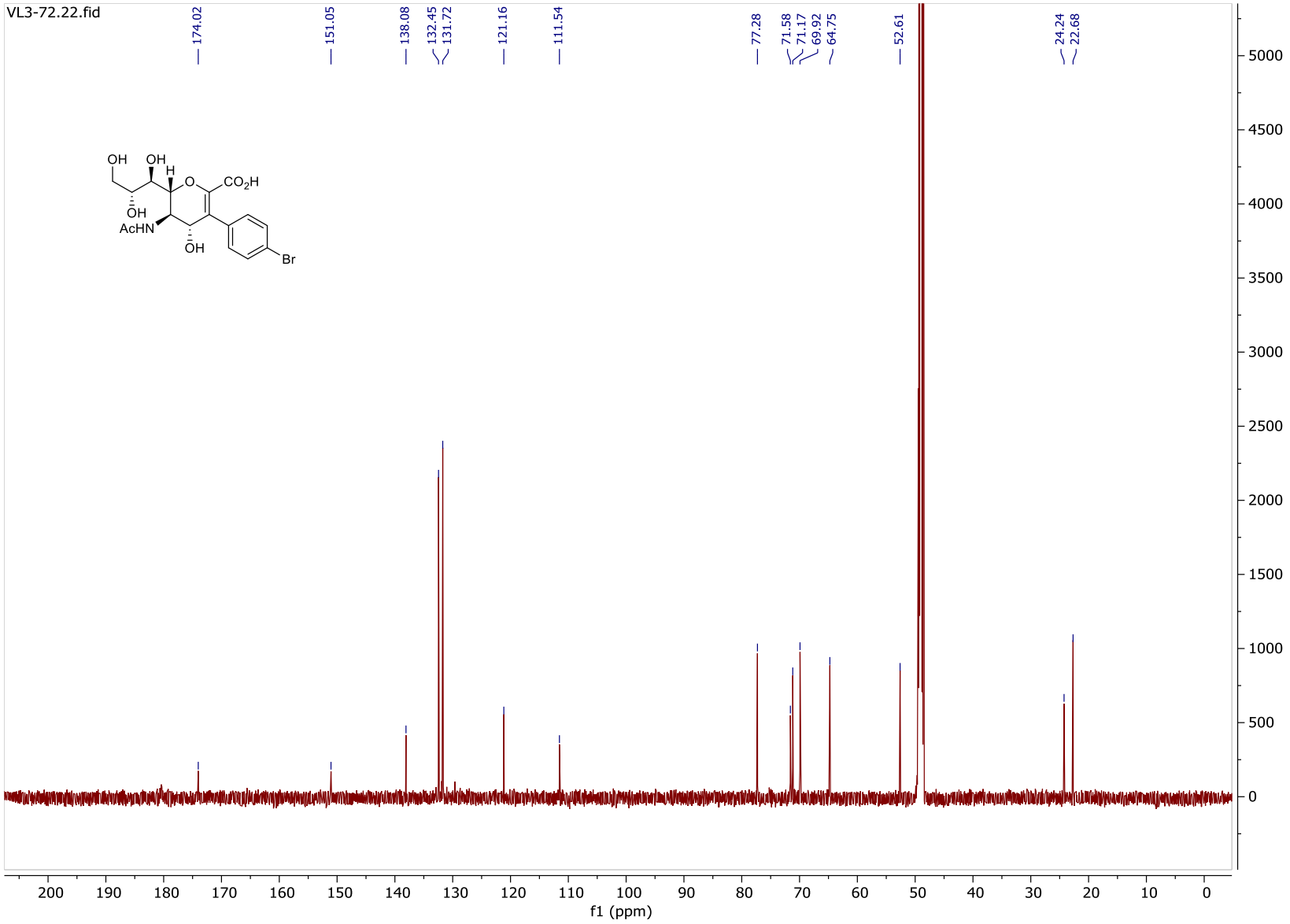


Figure S24. HRMS of Compound **9f** (ESI-TOF)

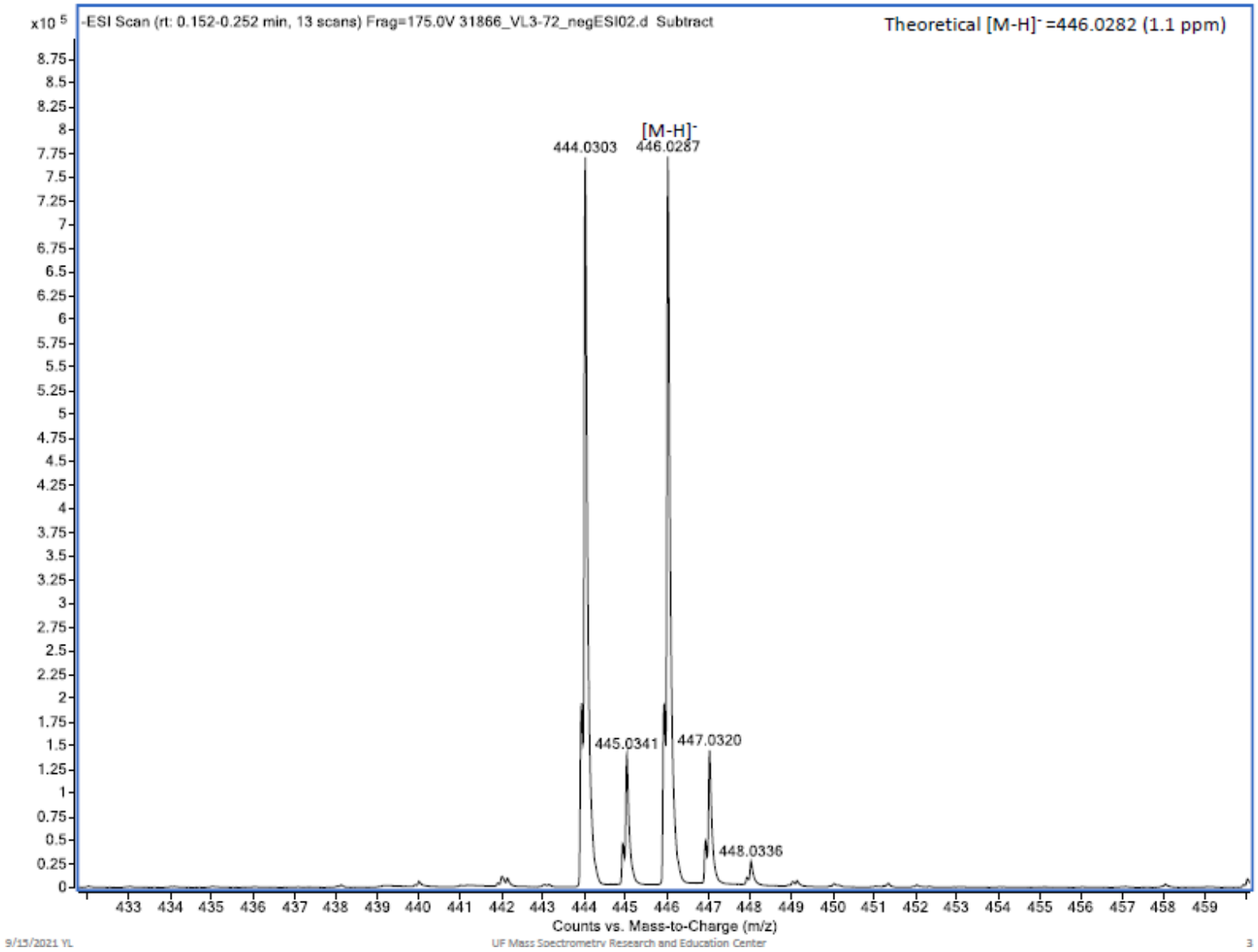


Figure S25. ^{1}H NMR of Compound **9g** (600 MHz, CD_3OD)

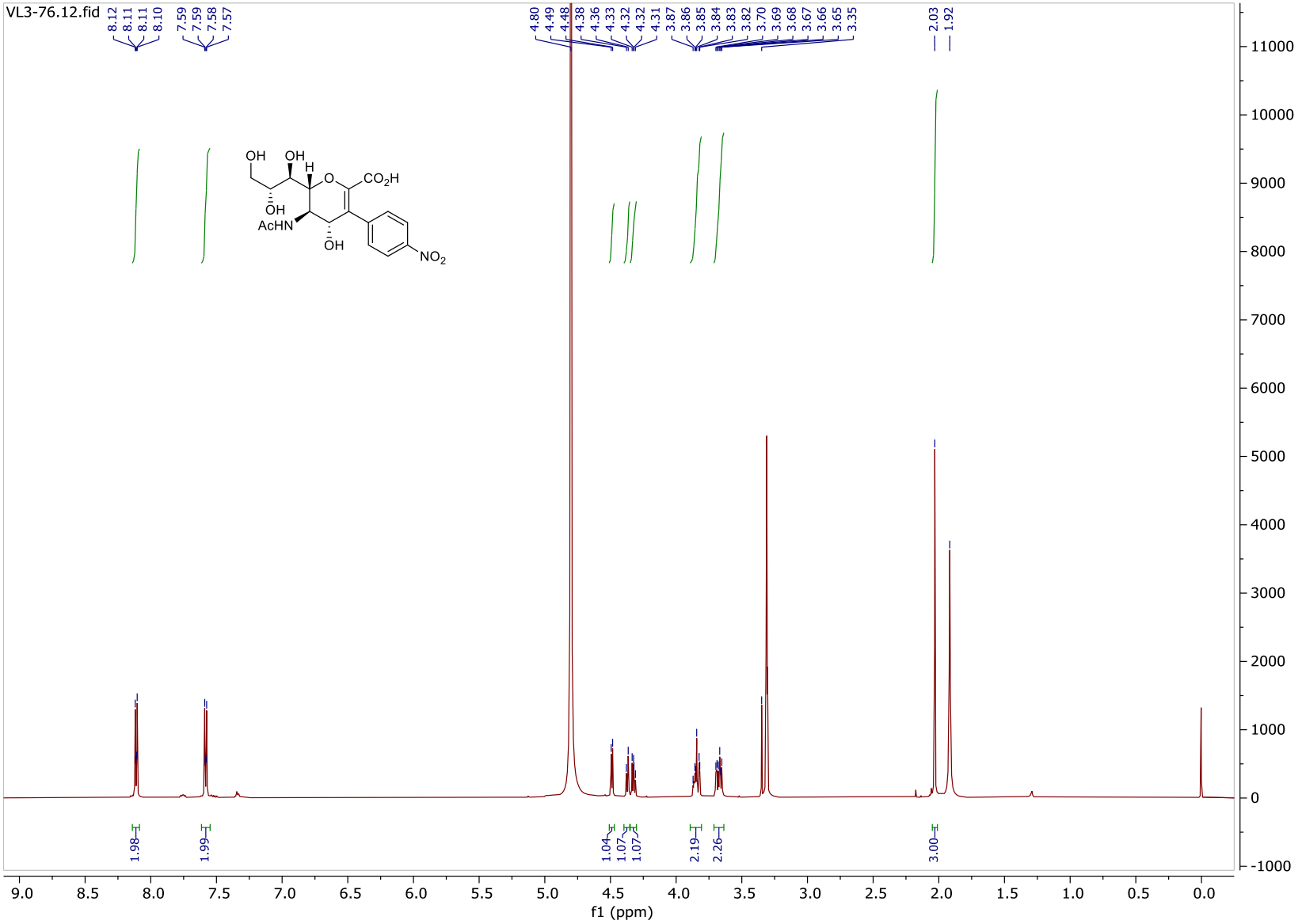


Figure S26. ^{13}C NMR of Compound **9g** (150 MHz, CD_3OD)

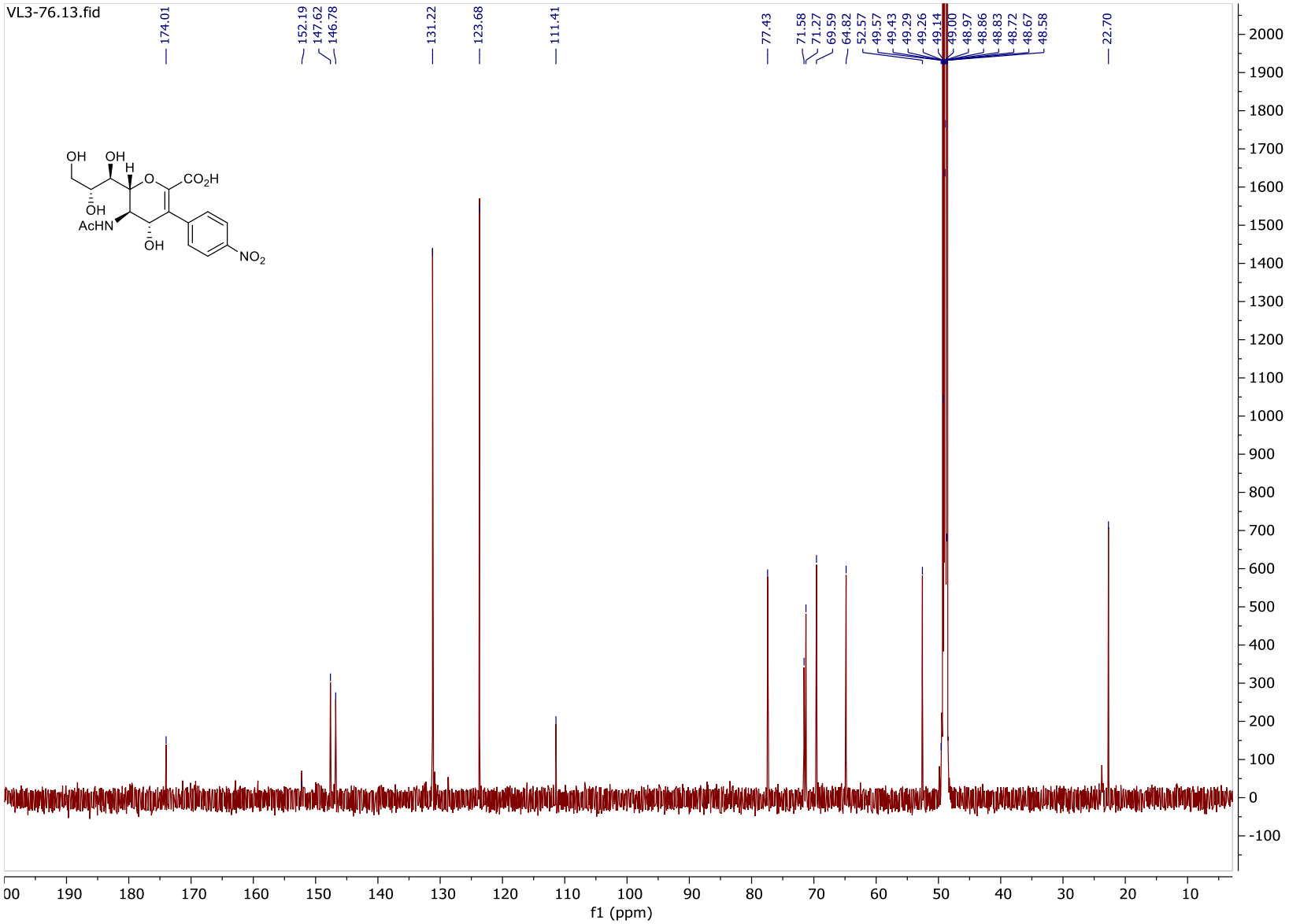


Figure S27. HRMS of Compound **9g** (ESI-TOF)

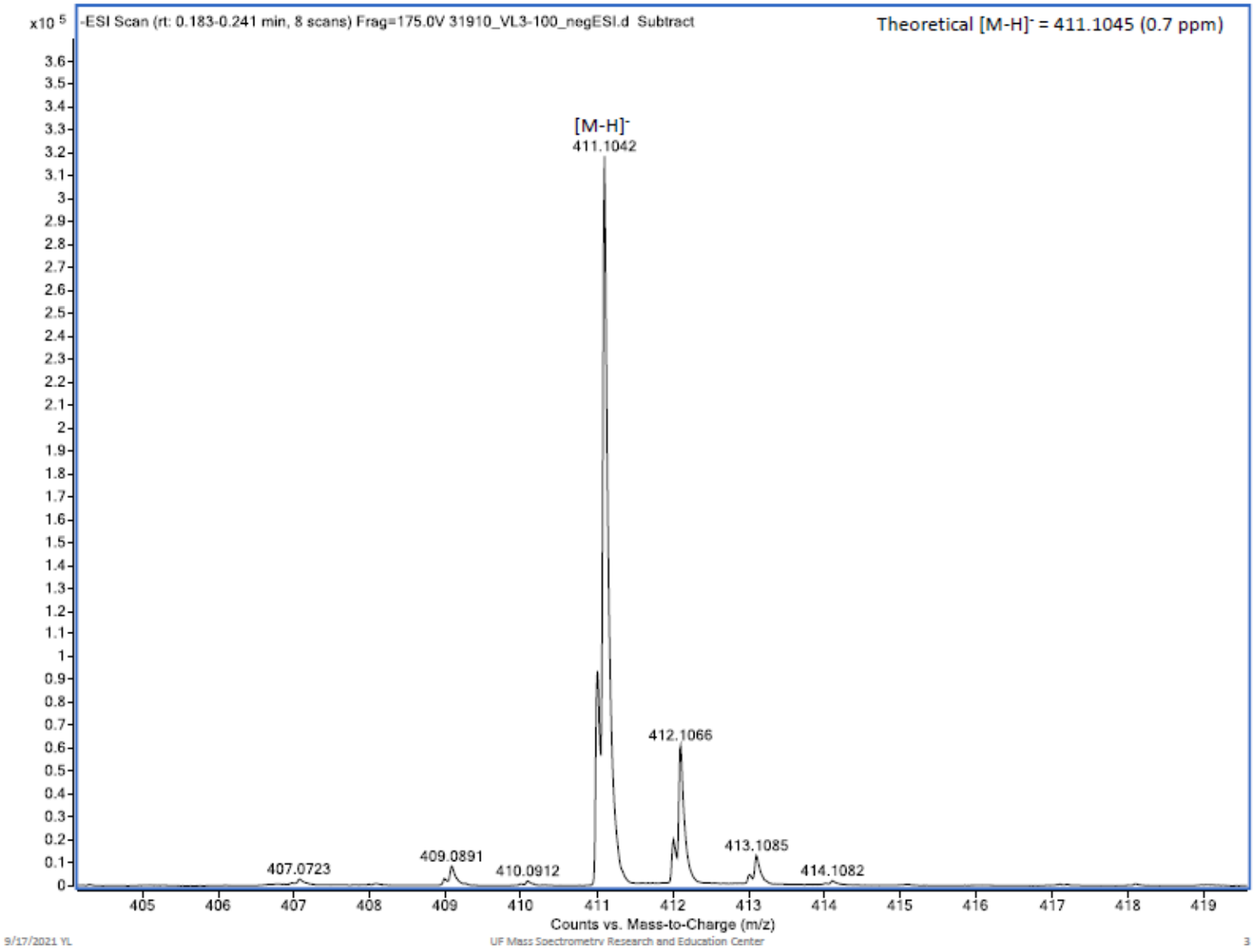


Figure S28. ^{1}H NMR of Compound **9h** (600 MHz, CD_3OD)

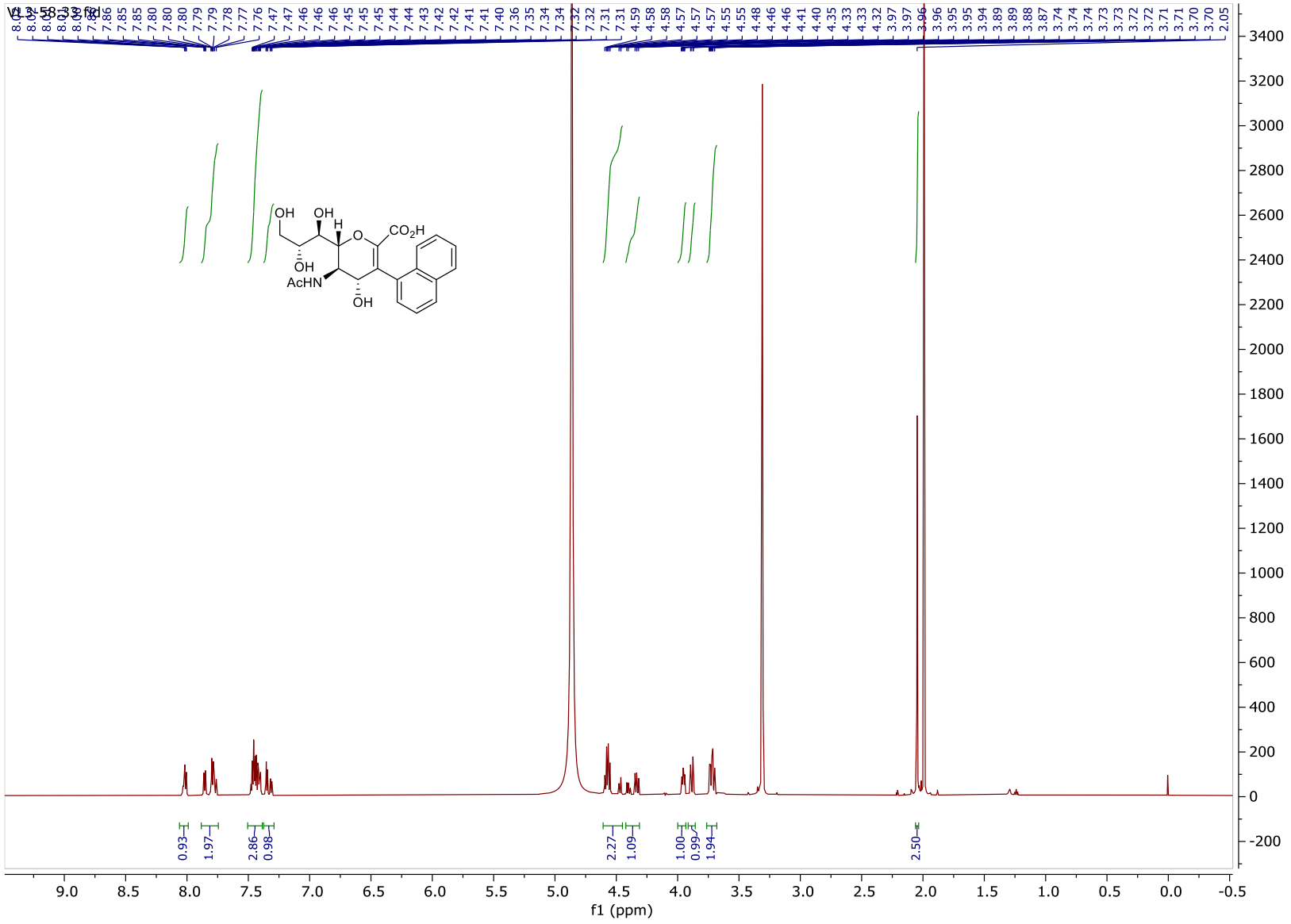


Figure S29. ^{13}C NMR of Compound **9h** (150 MHz, CD_3OD)

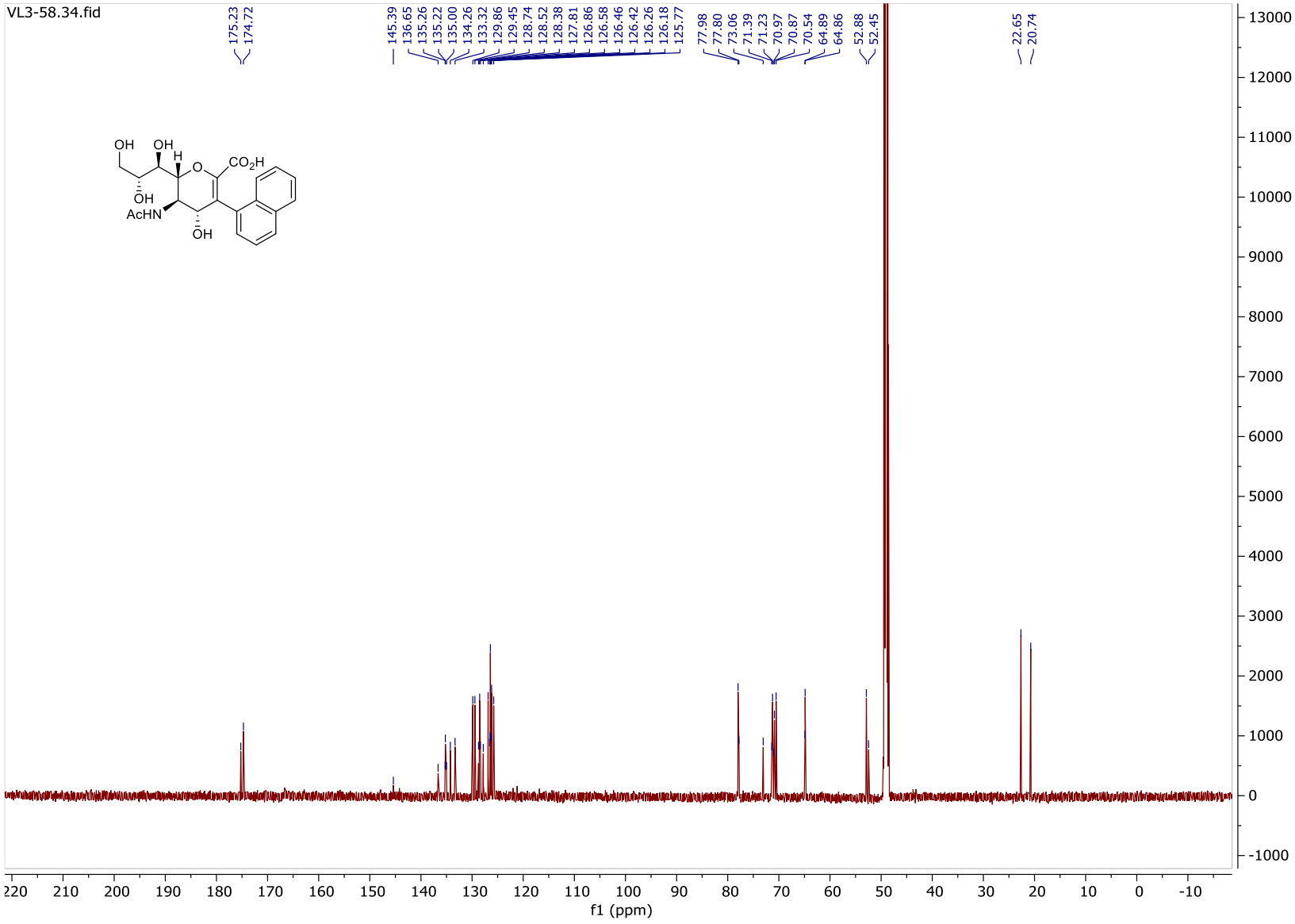


Figure S30. HRMS of Compound **9h** (ESI-TOF)

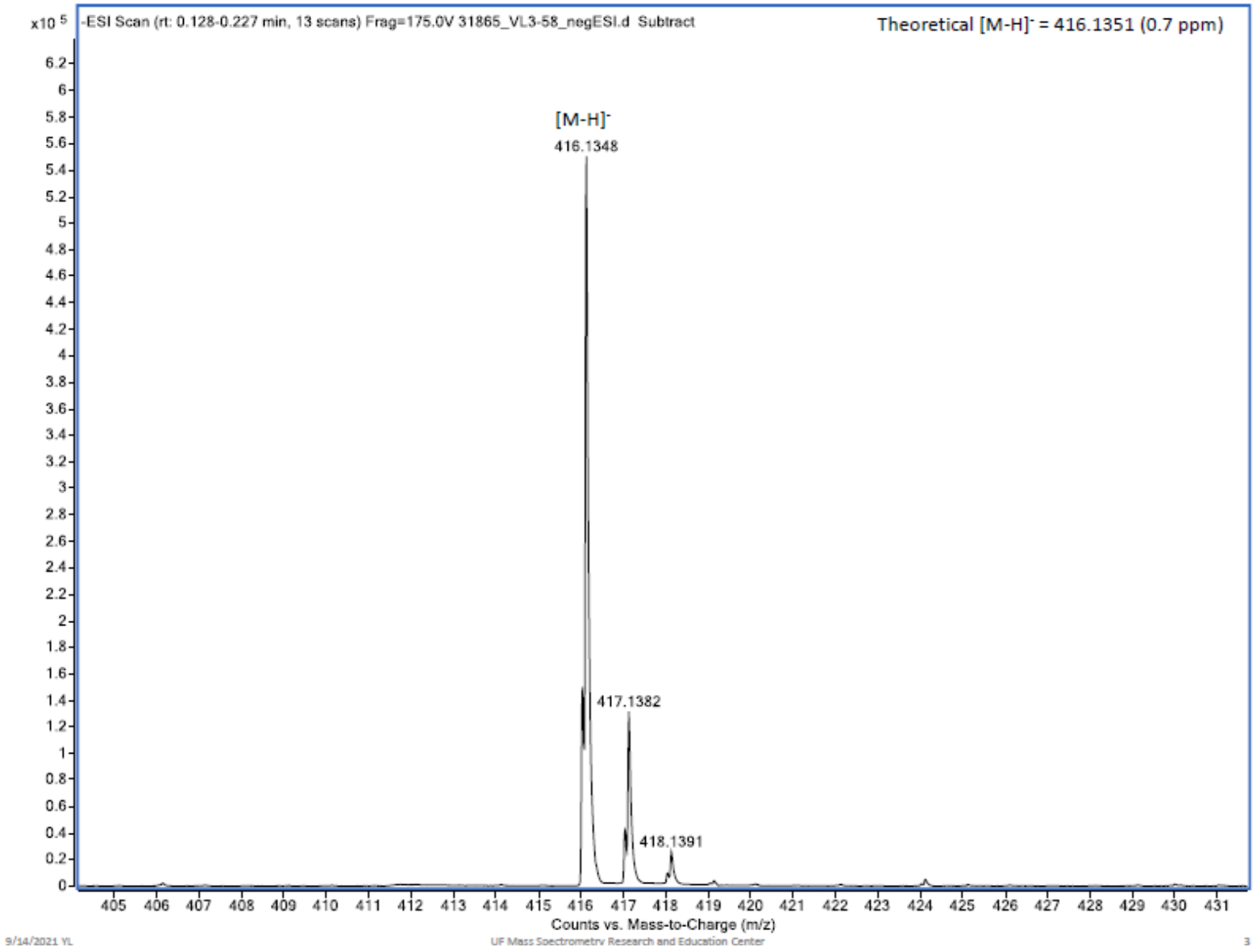


Figure S31. ^{1}H NMR of Compound **9i** (600 MHz, CD_3OD)

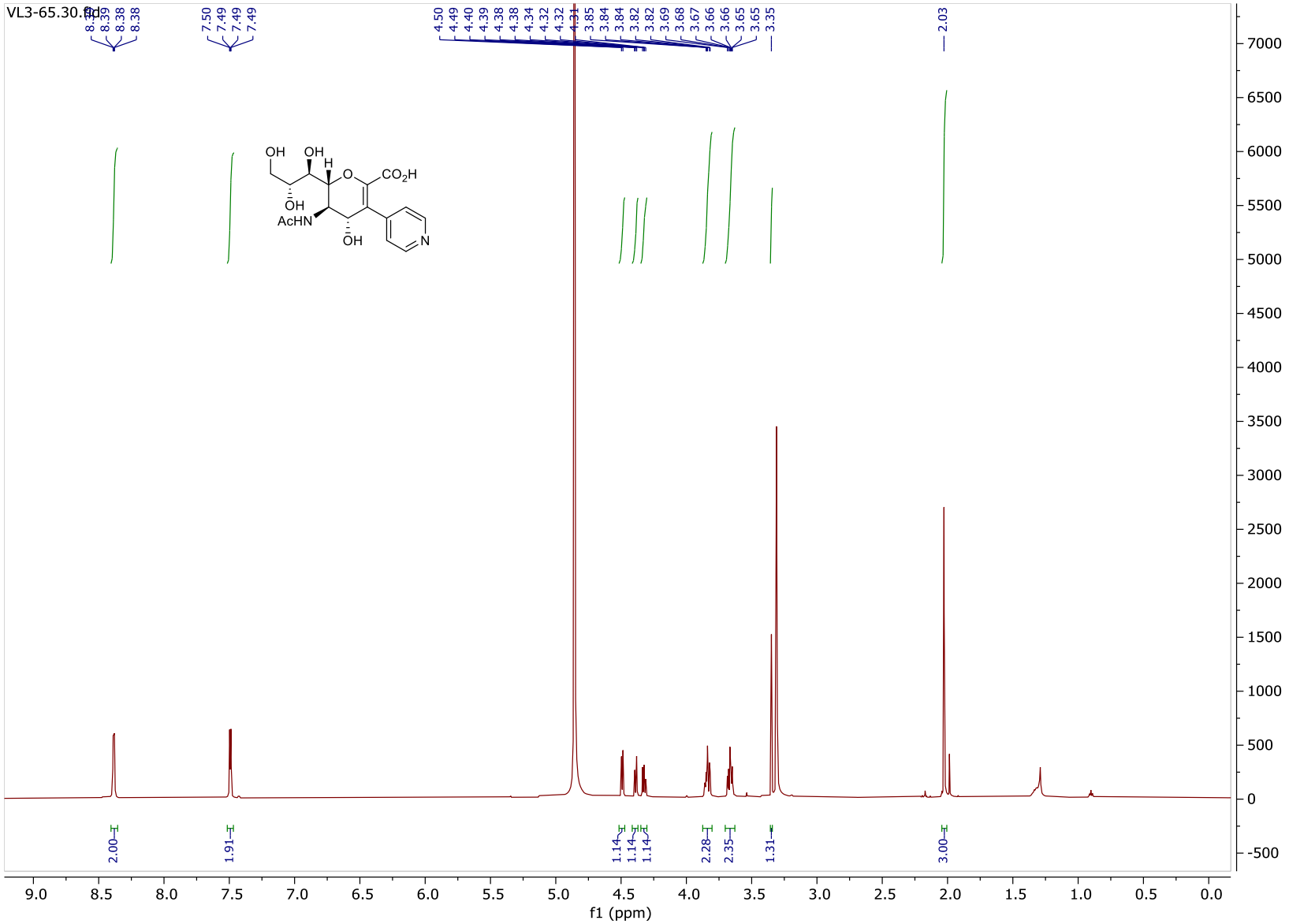


Figure S32. ^{13}C NMR of Compound **9i** (150 MHz, CD_3OD)

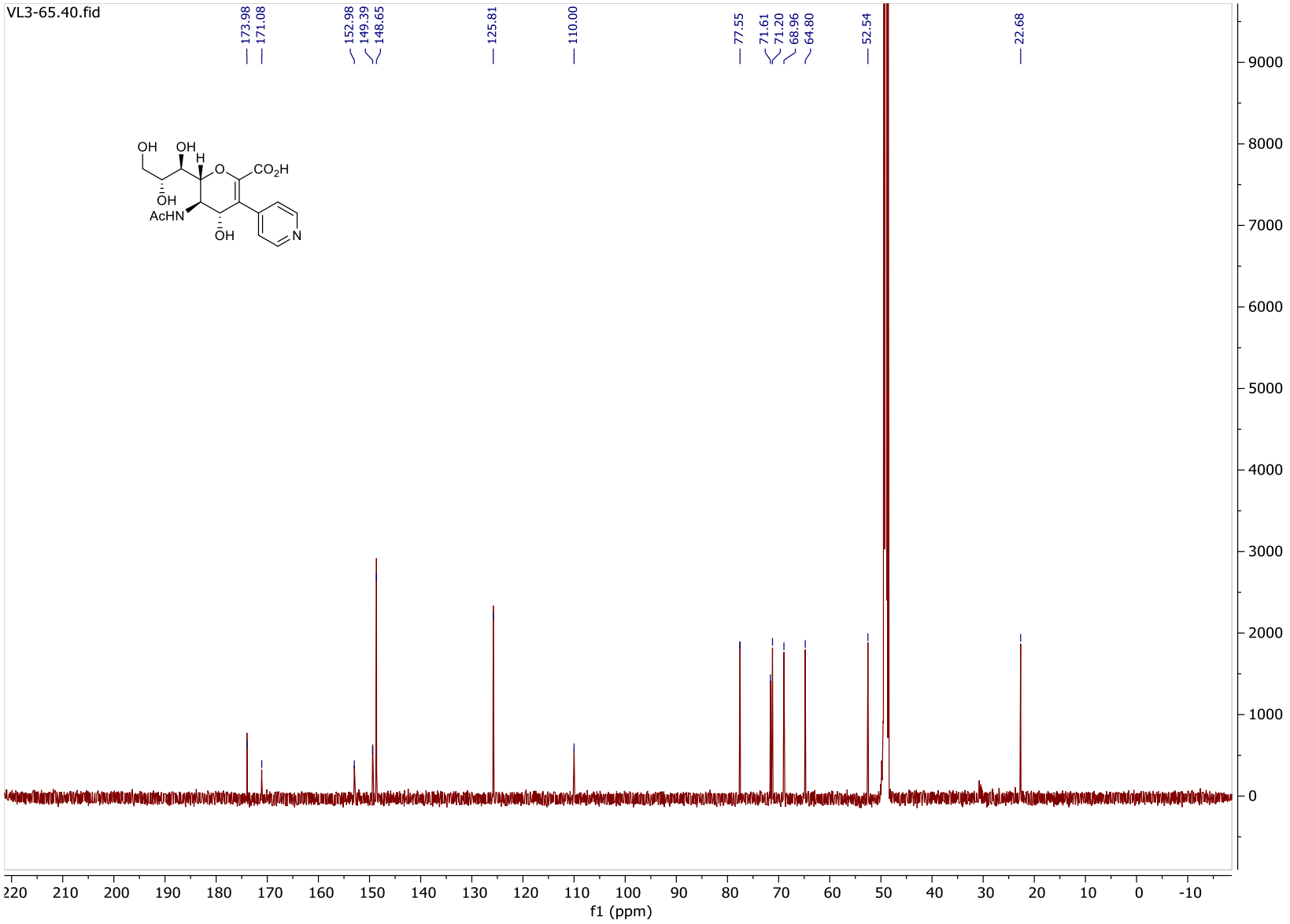


Figure S33. HRMS of Compound **9i** (ESI-TOF)

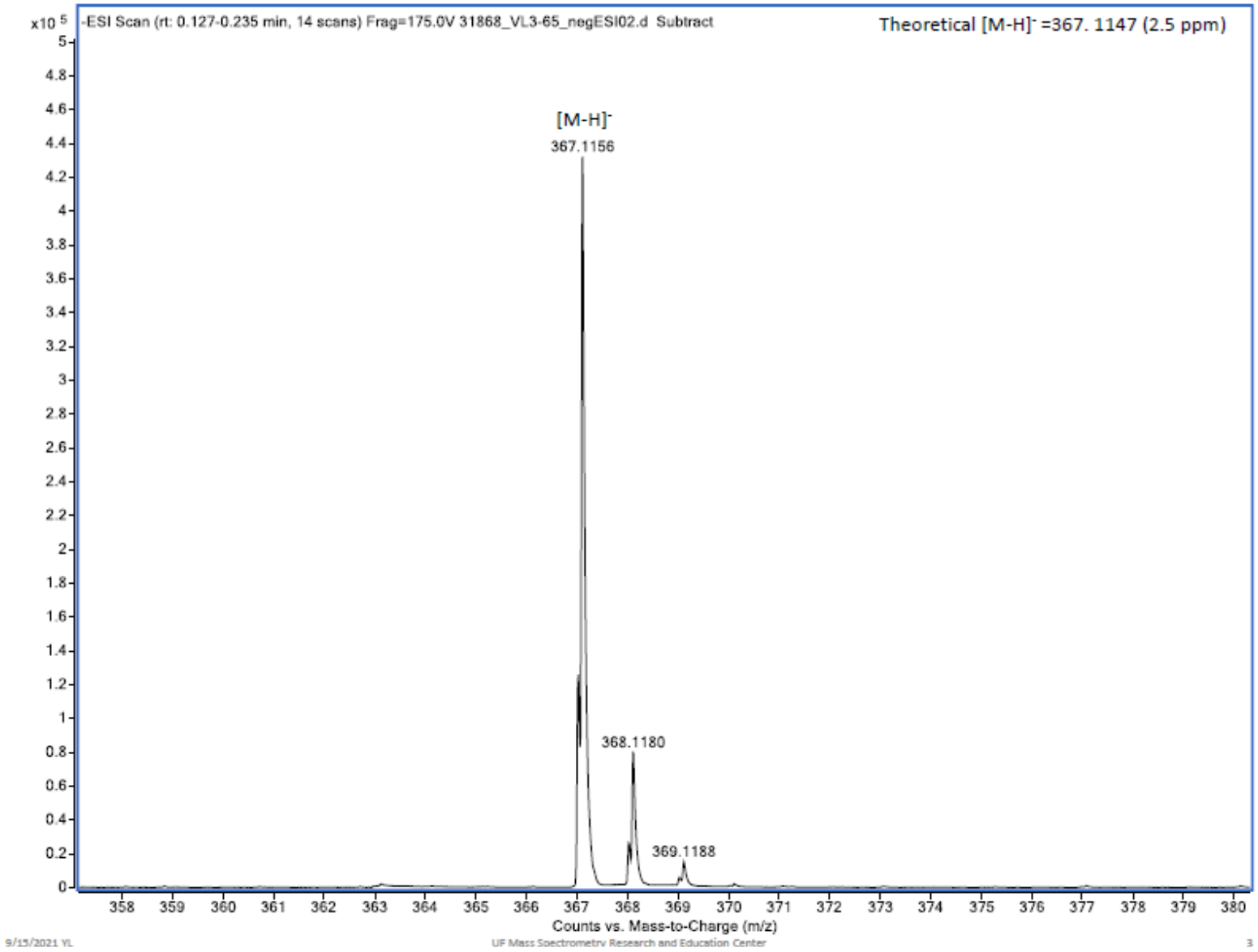


Figure S34. ^{1}H NMR of Compound **9j** (600 MHz, CD_3OD)

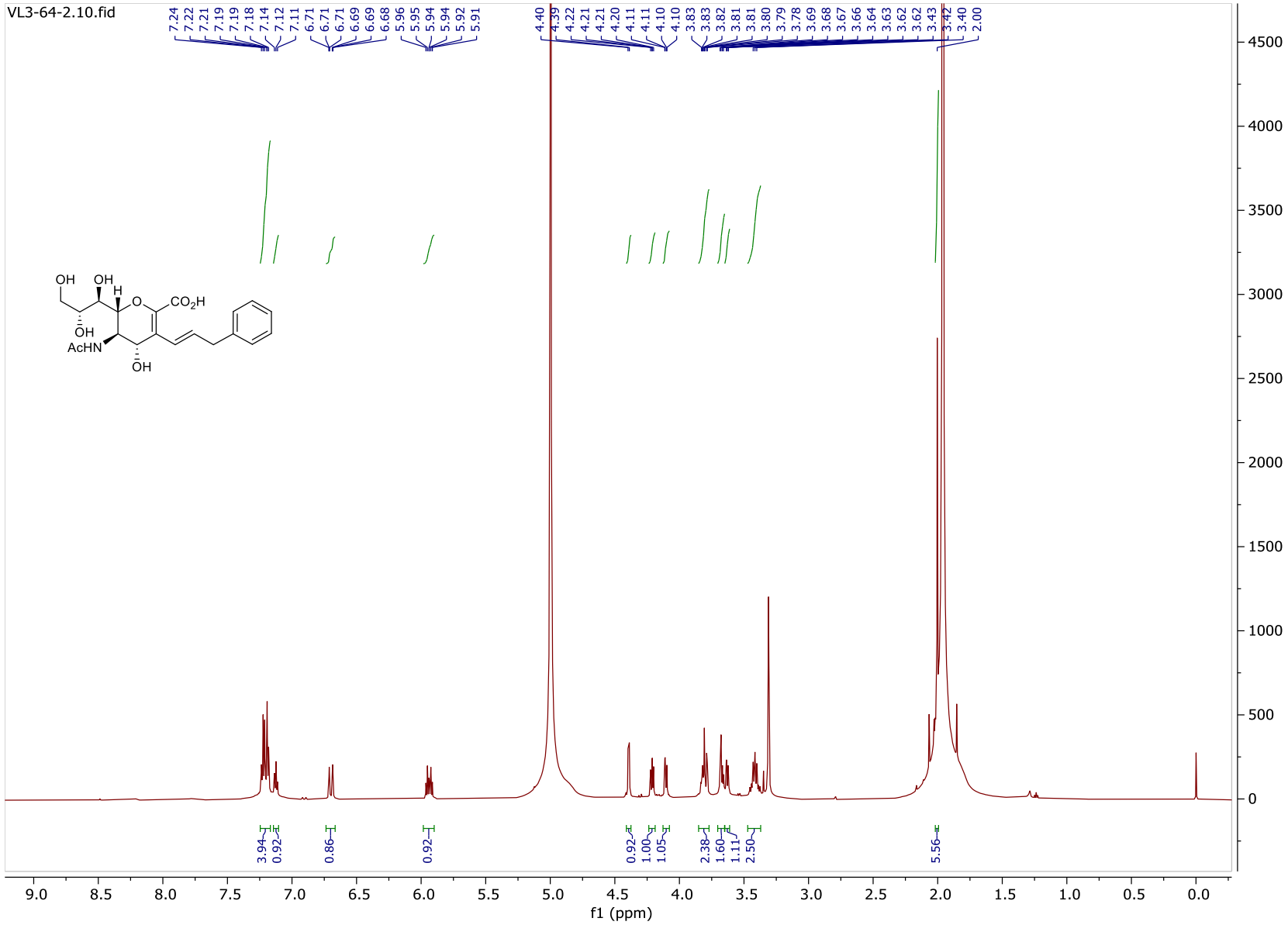


Figure S35. ^{13}C NMR of Compound **9j** (150 MHz, CD_3OD)

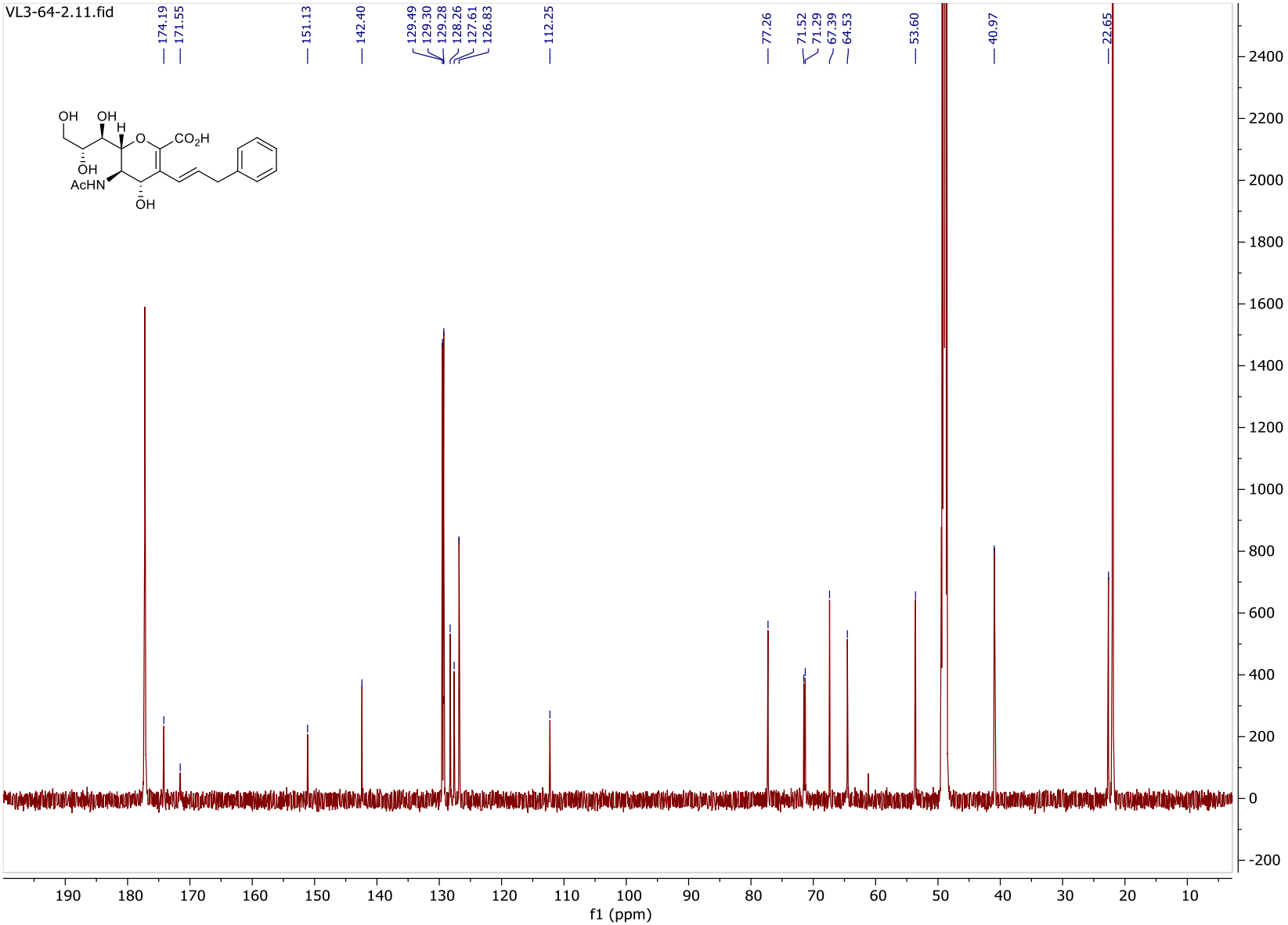


Figure S36. HRMS of Compound **9j** (ESI-TOF)

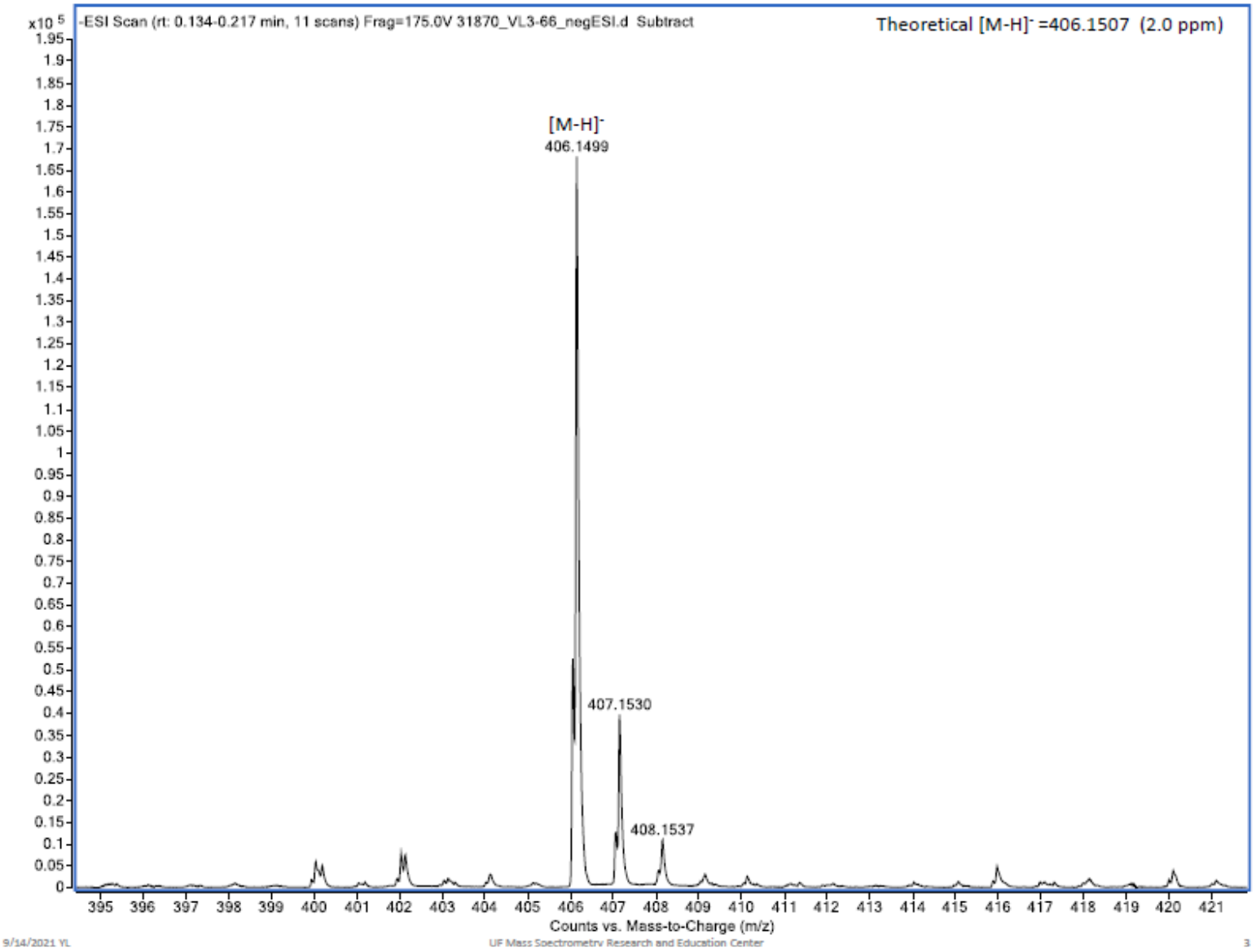


Figure S37. ^{1}H NMR of Compound **9k** (150 MHz, CD_3OD)

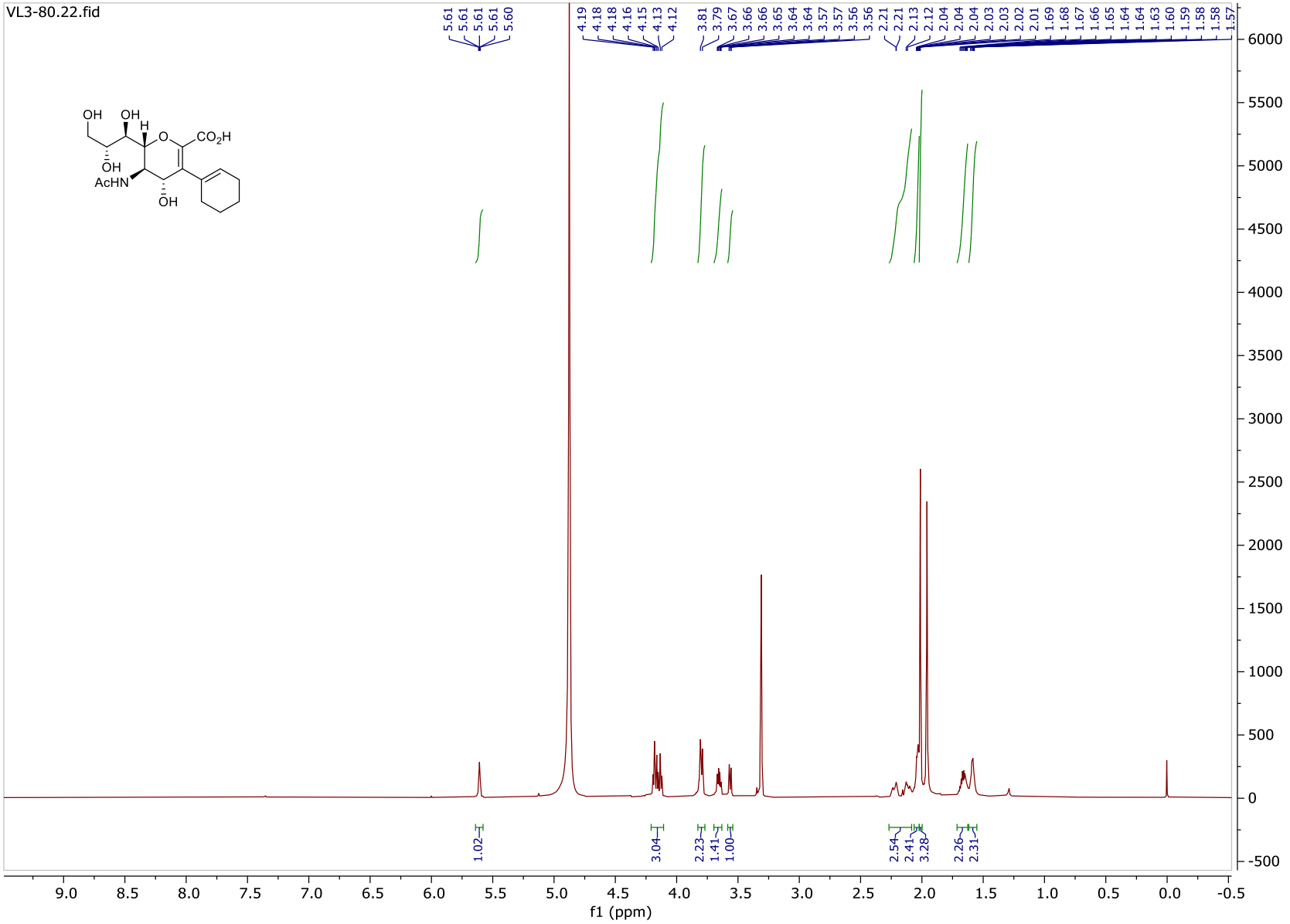


Figure S38. ^{13}C NMR of Compound **9k** (150 MHz, CD_3OD)

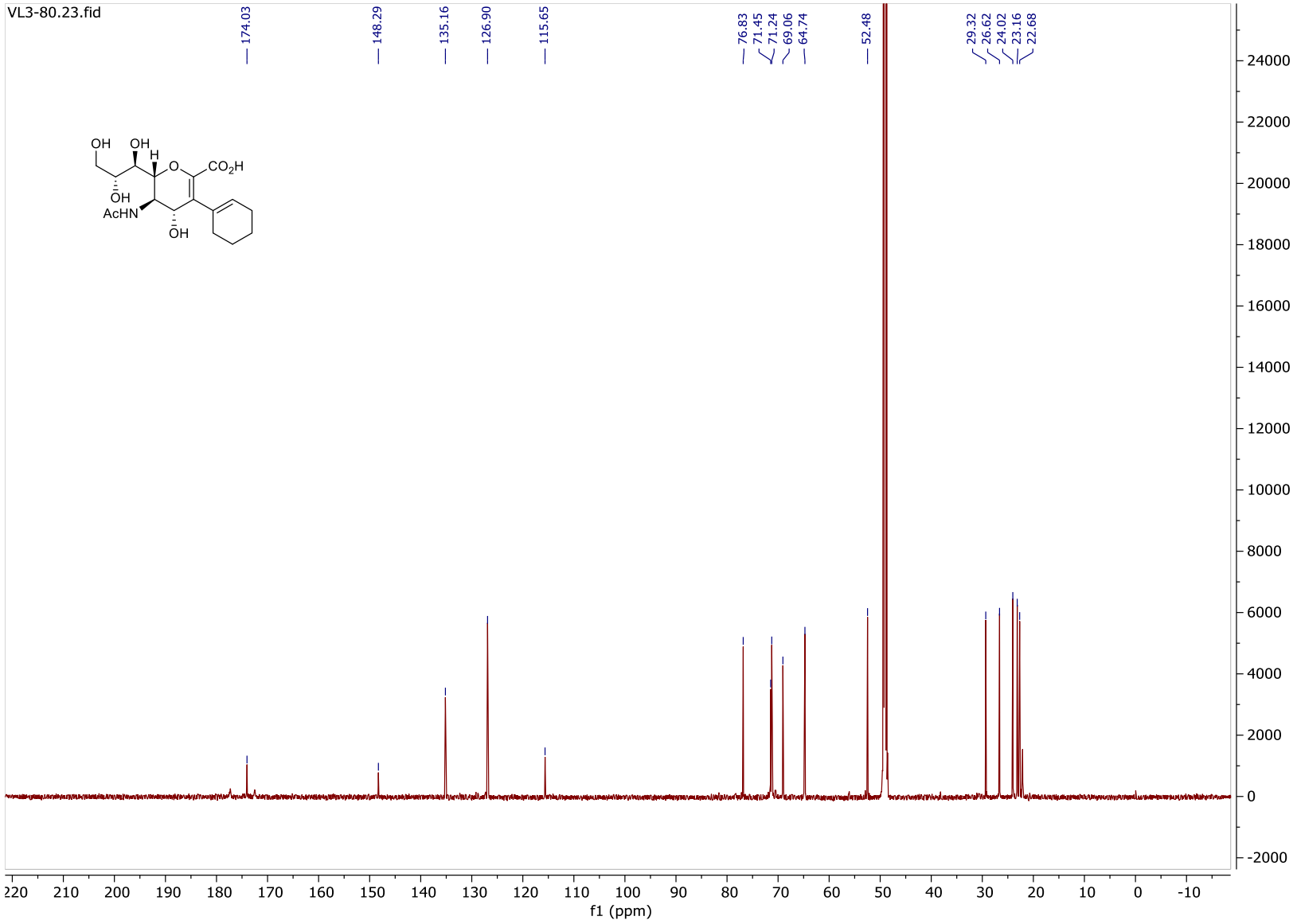


Figure S39. HRMS of Compound **9k** (ESI-TOF)

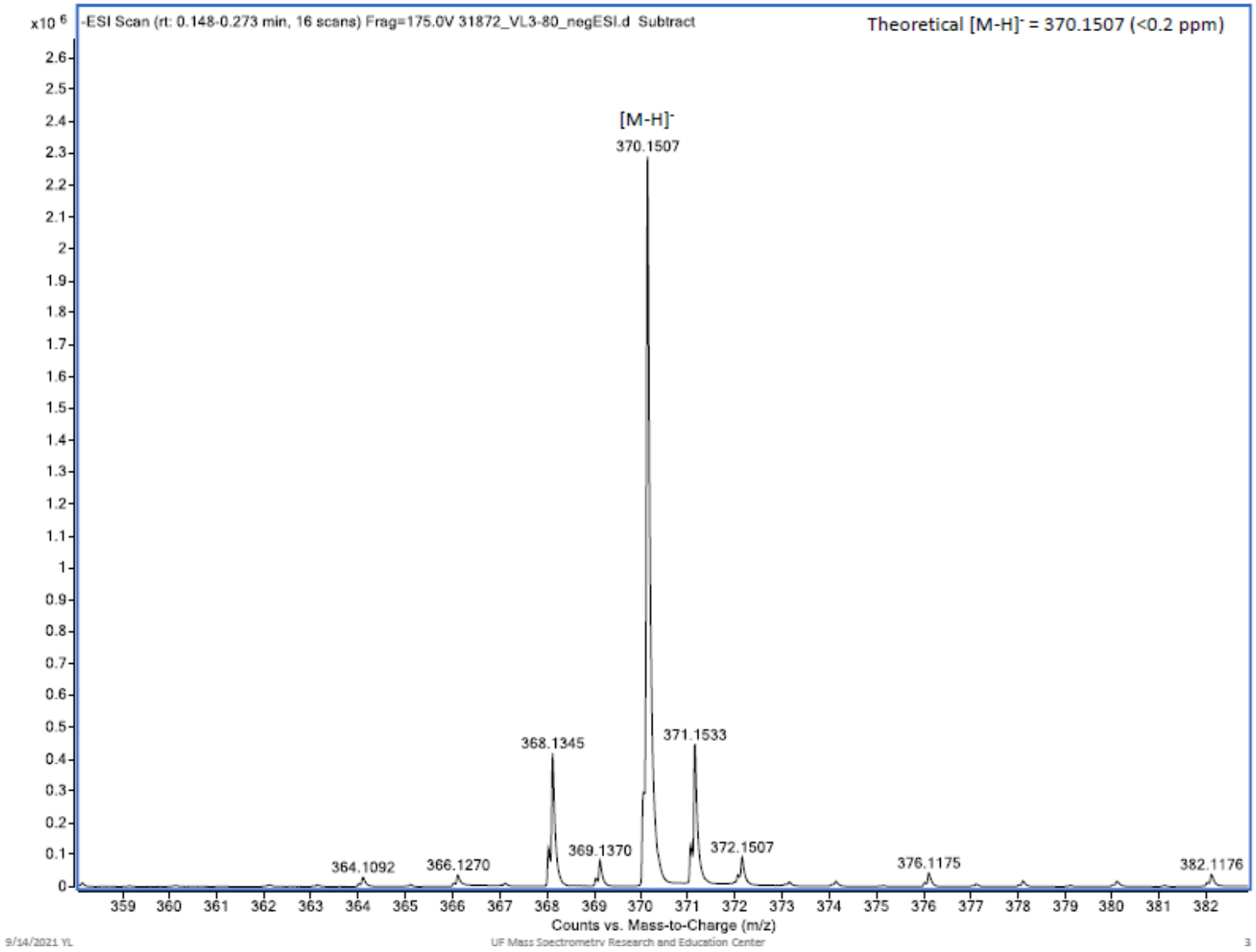


Figure S40. ^{1}H NMR of Compound **9l** (600 MHz, CD_3OD)

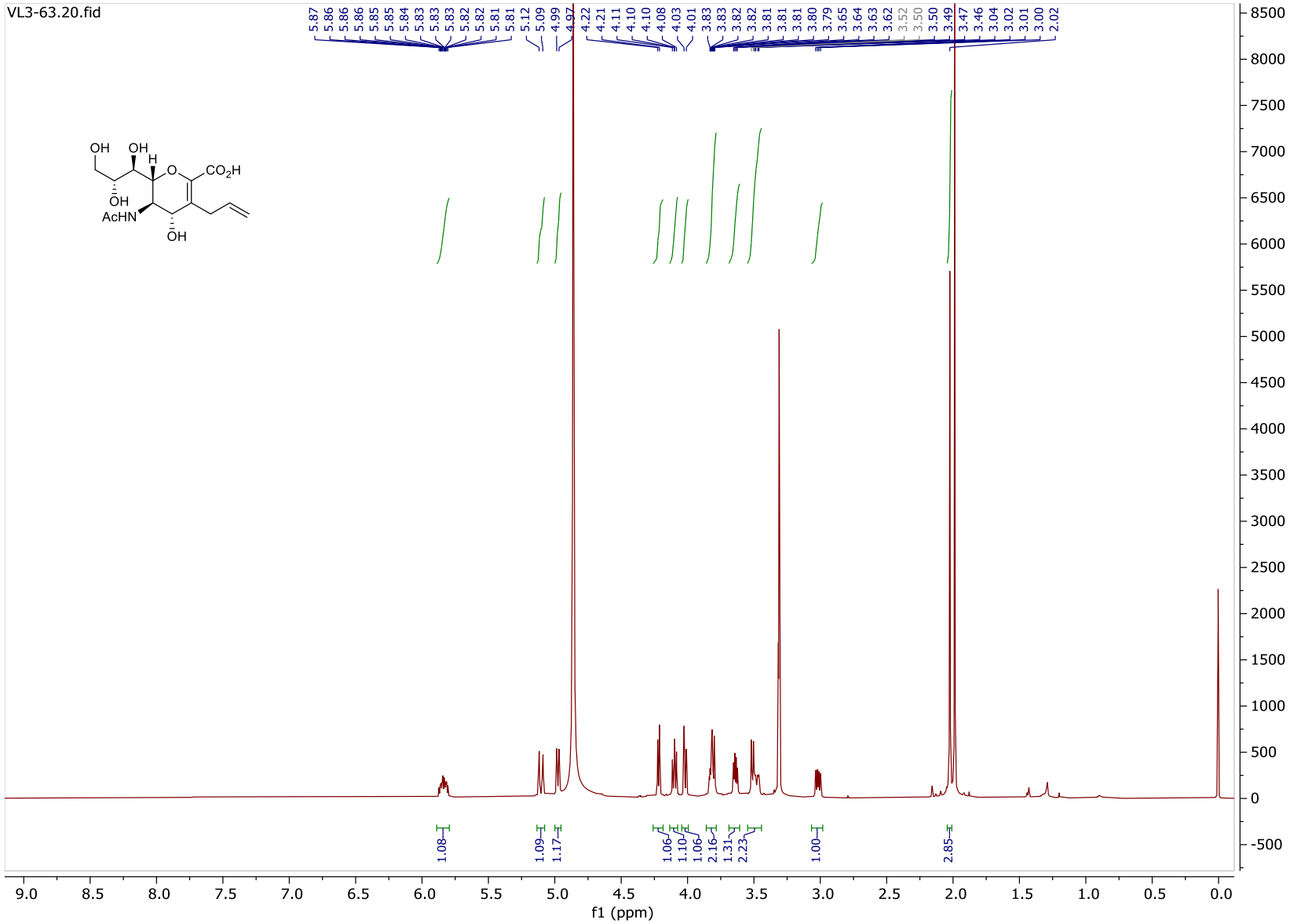


Figure S41. ^{13}C NMR of Compound **9l** (150 MHz, CD_3OD)

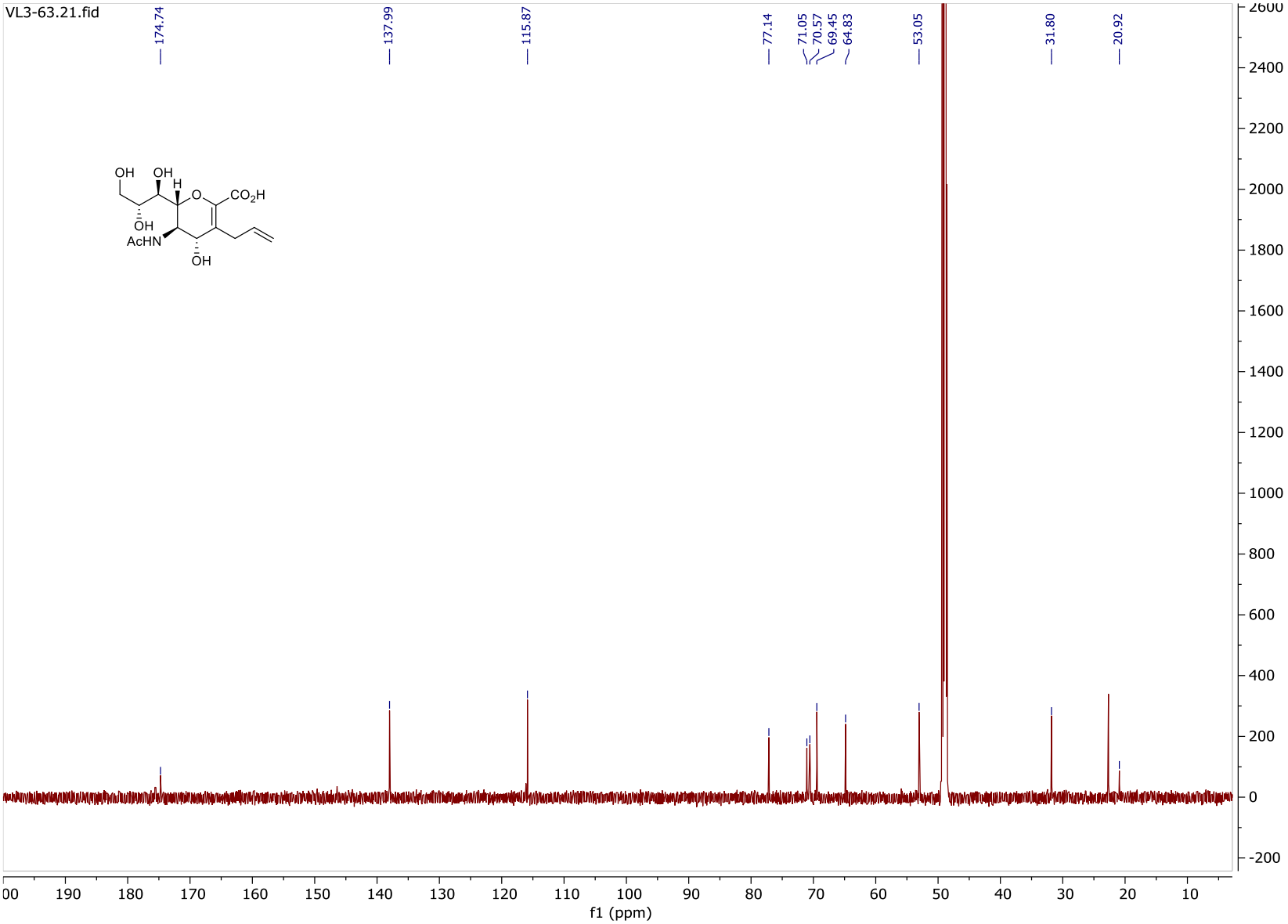


Figure S42. HRMS of Compound **9l** (ESI-TOF)

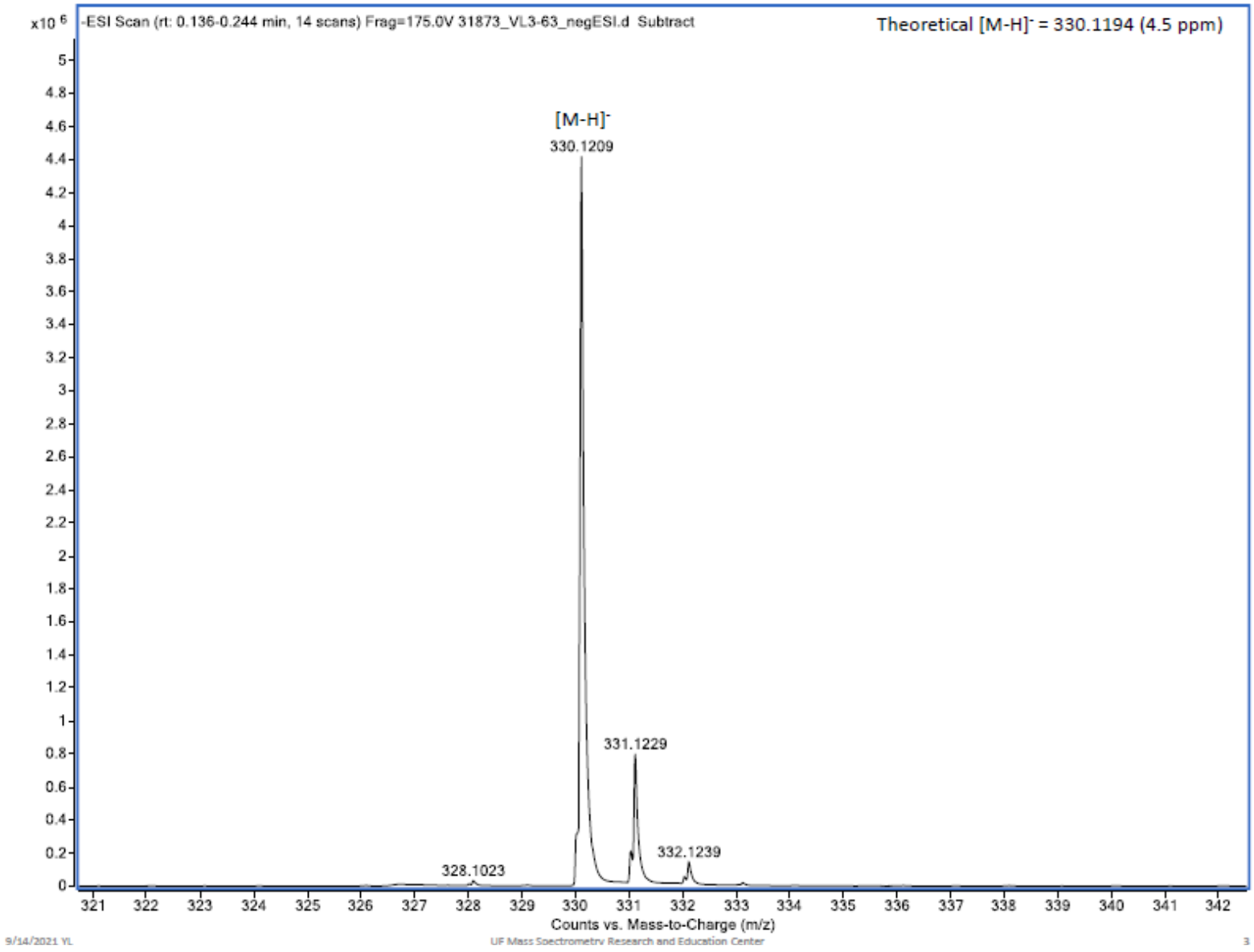


Figure S43. ^{1}H NMR of Compound **9m** (600 MHz, CD_3OD)

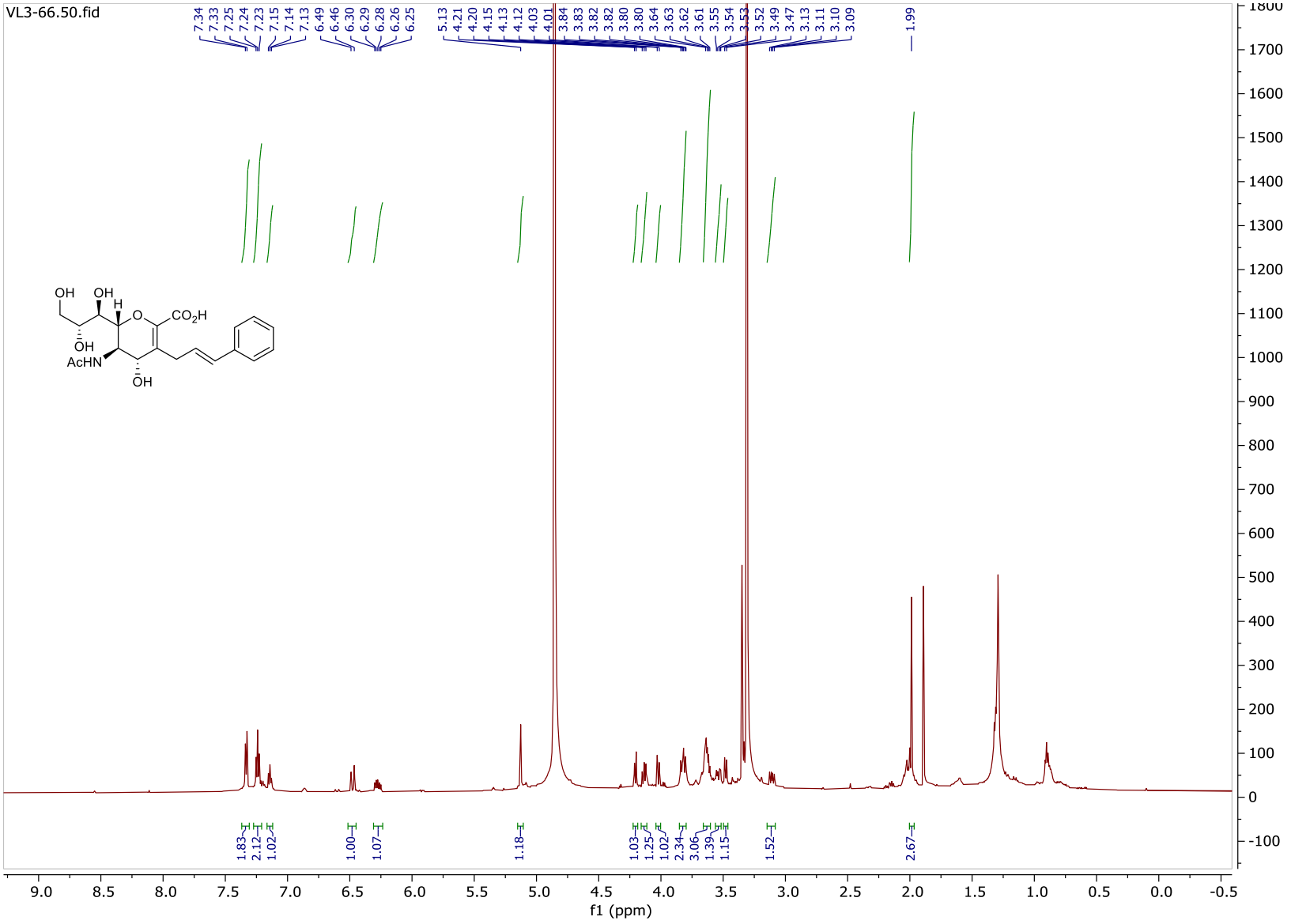


Figure S44. ^{13}C NMR of Compound **9m** (150 MHz, CD_3OD)

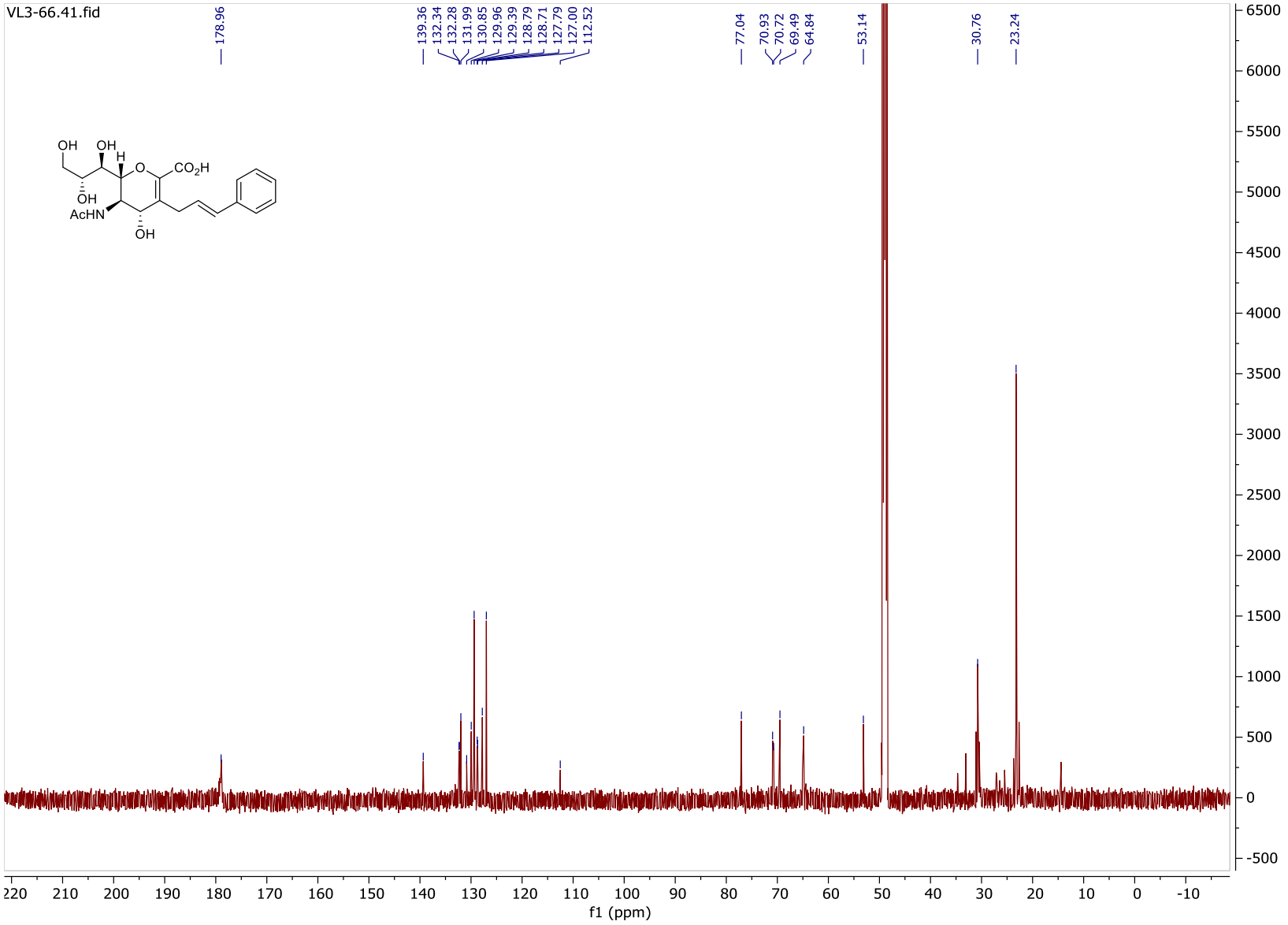


Figure S45. HRMS of Compound **9m** (ESI-TOF)

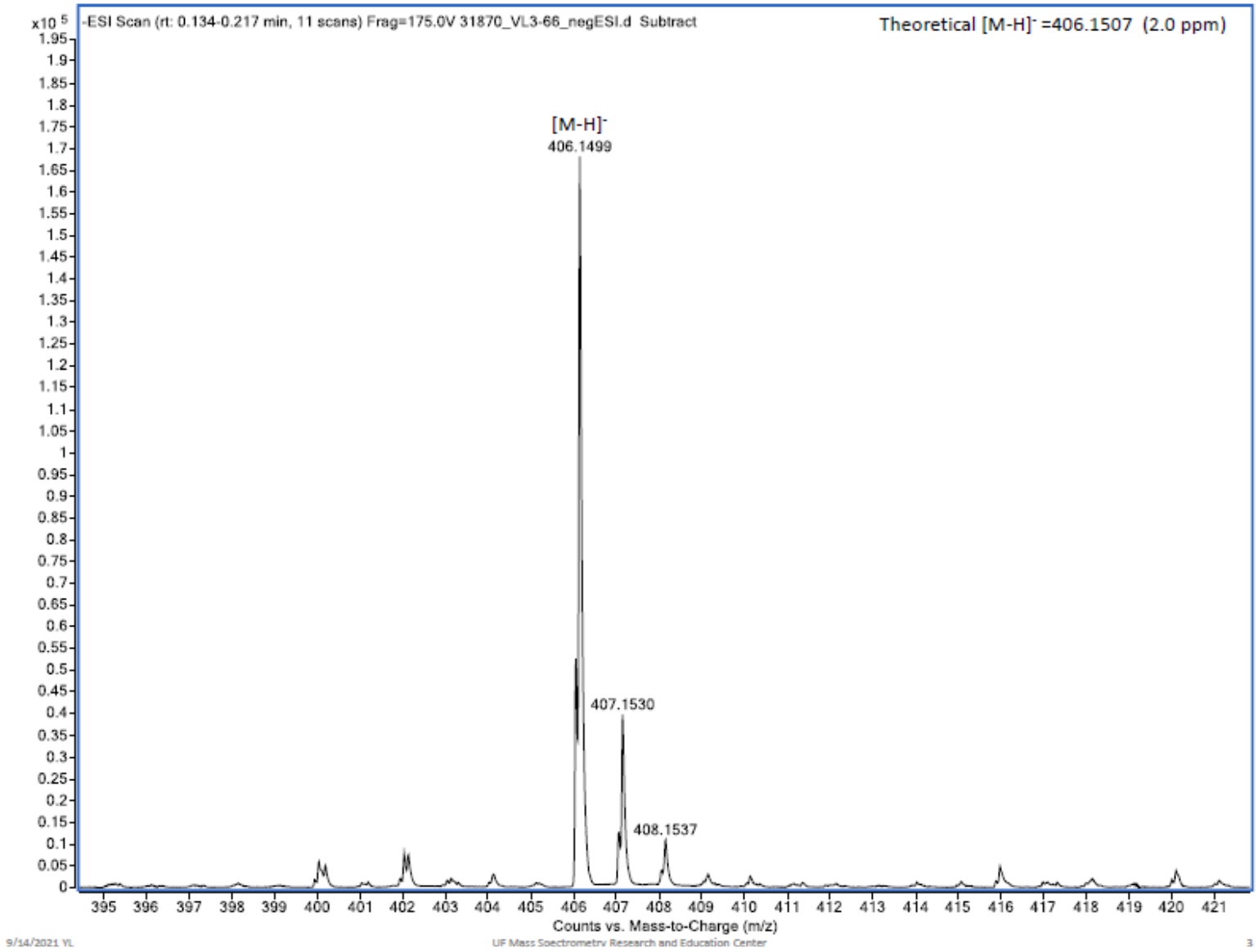


Figure S46. ^{1}H NMR of Compound **9n** (600 MHz, CD_3OD)

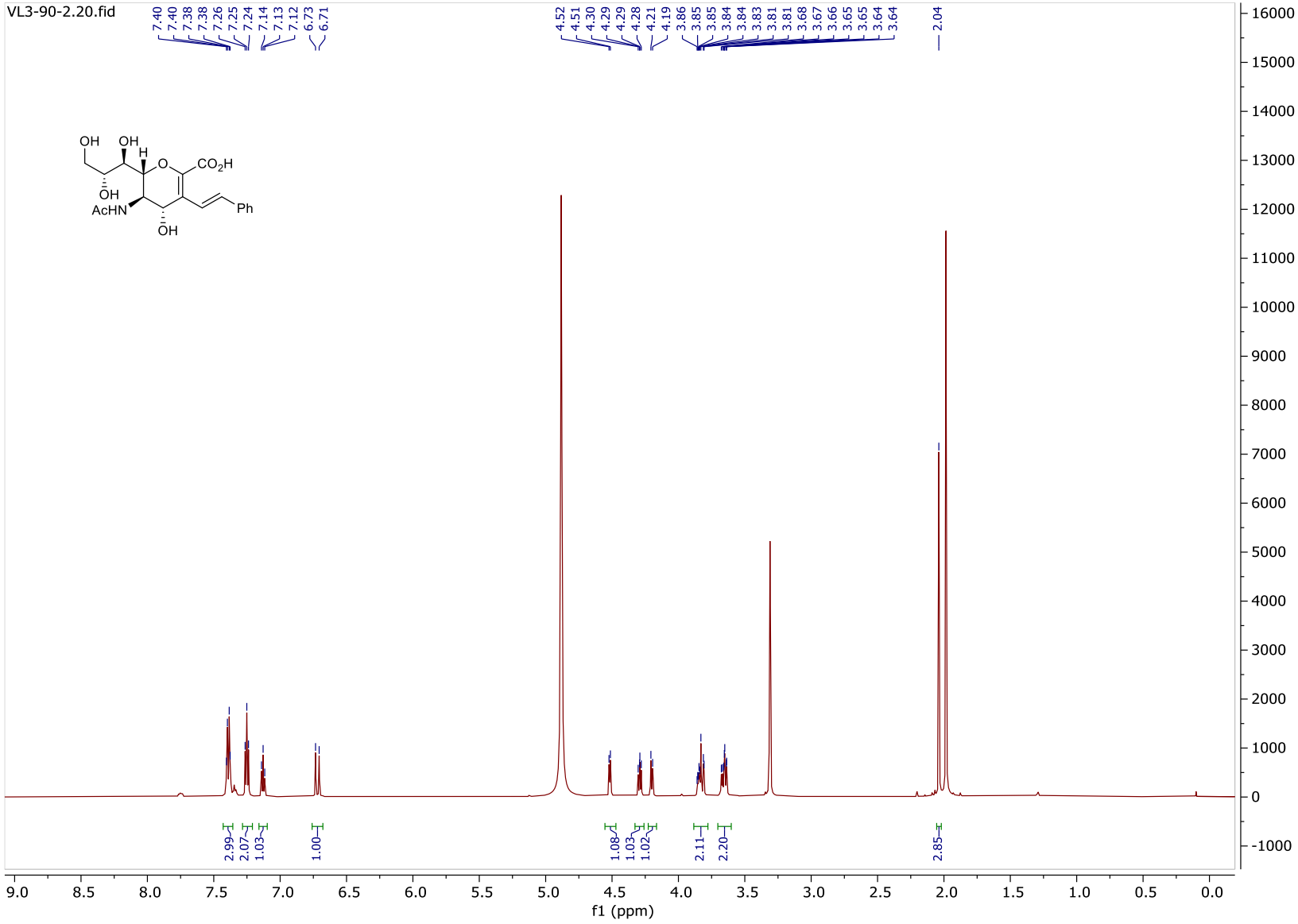


Figure S47. ^{13}C NMR of Compound **9n** (150 MHz, CD_3OD)

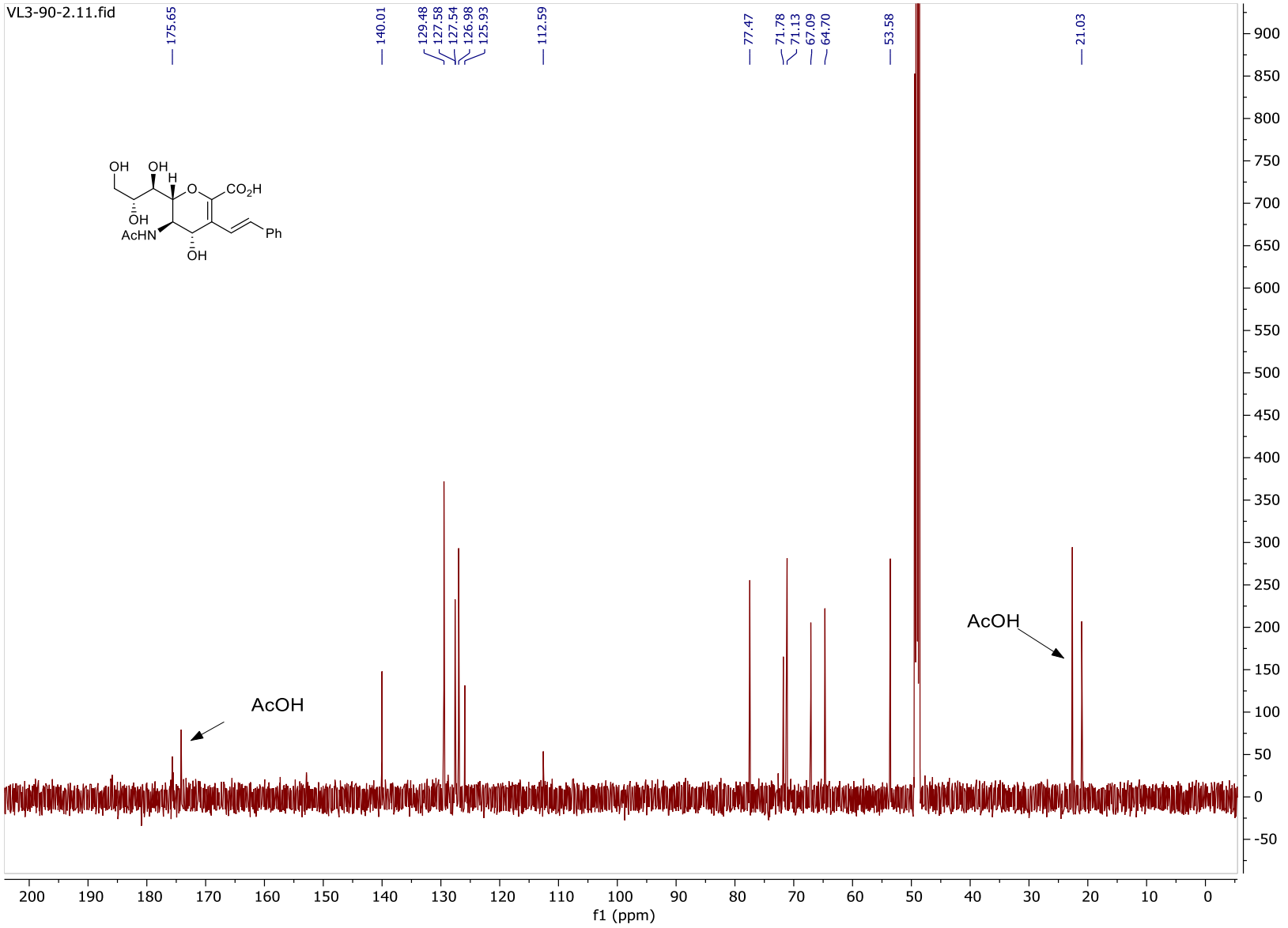


Figure S48. HRMS of Compound **9n** (ESI-TOF)

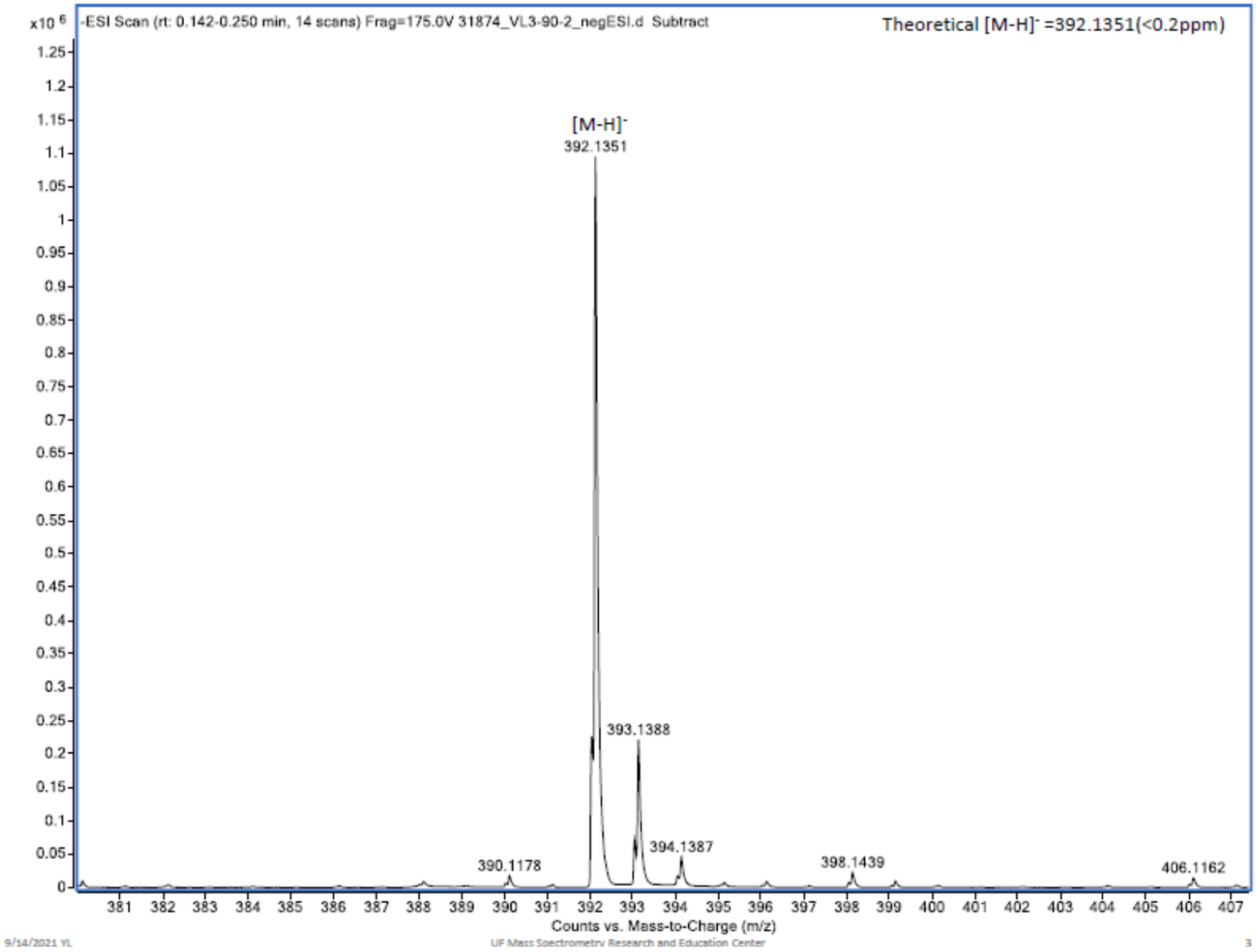


Figure S49. ^{1}H NMR of Compound **9o** (600 MHz, CD_3OD)

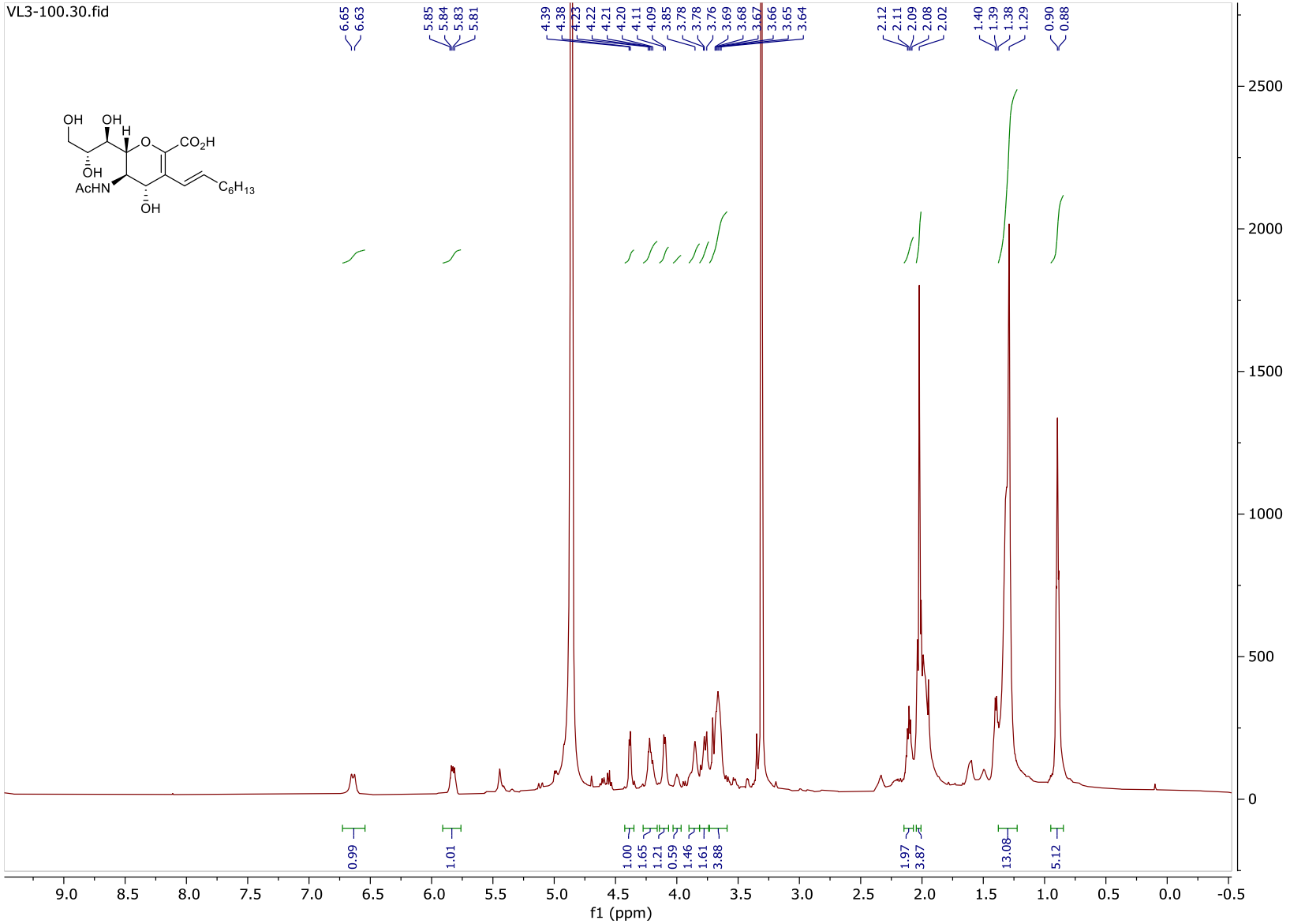


Figure S50. ^{13}C NMR of Compound **9o** (150 MHz, CD_3OD)

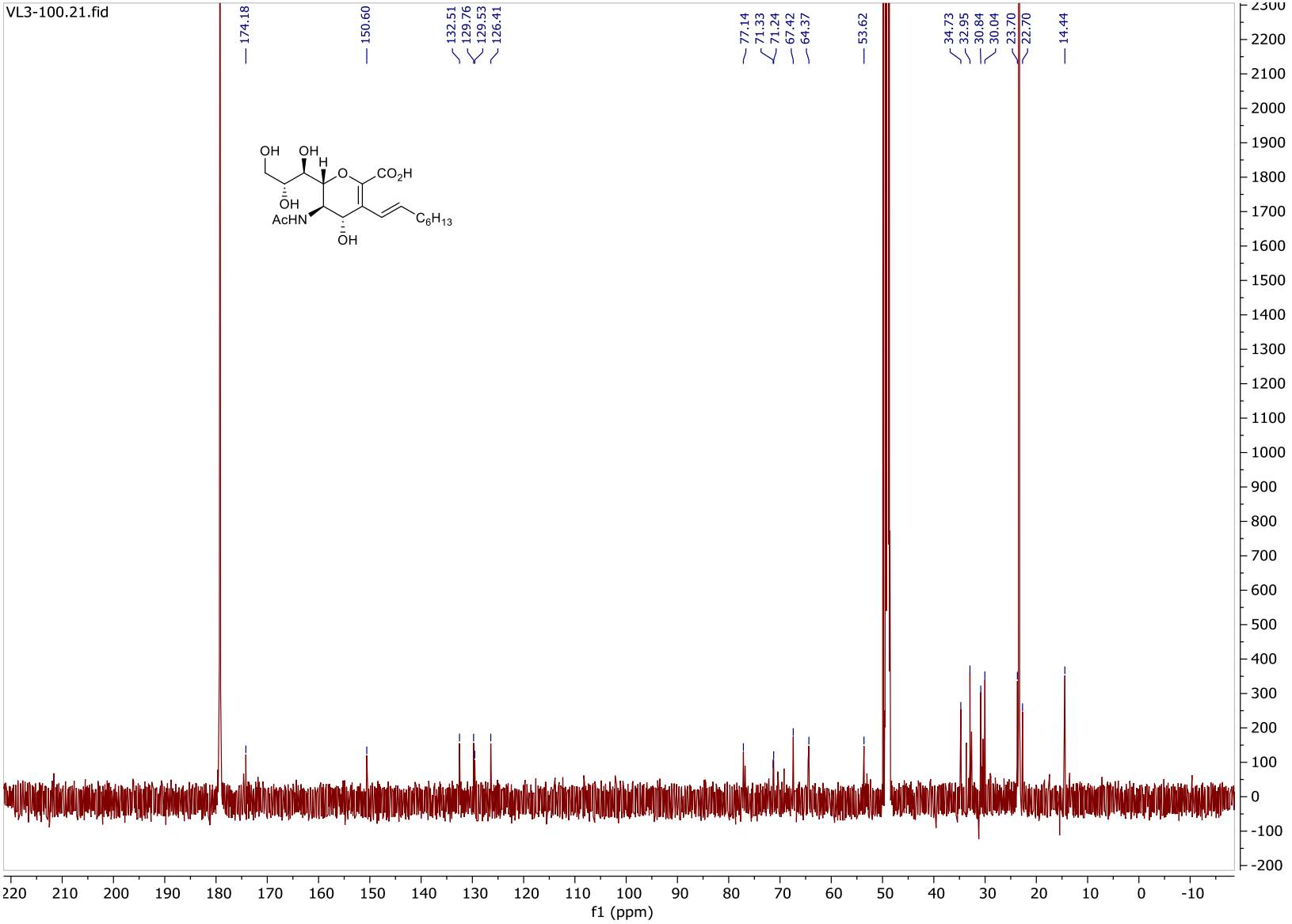


Figure S51. HRMS of Compound **9o** (ESI-TOF)

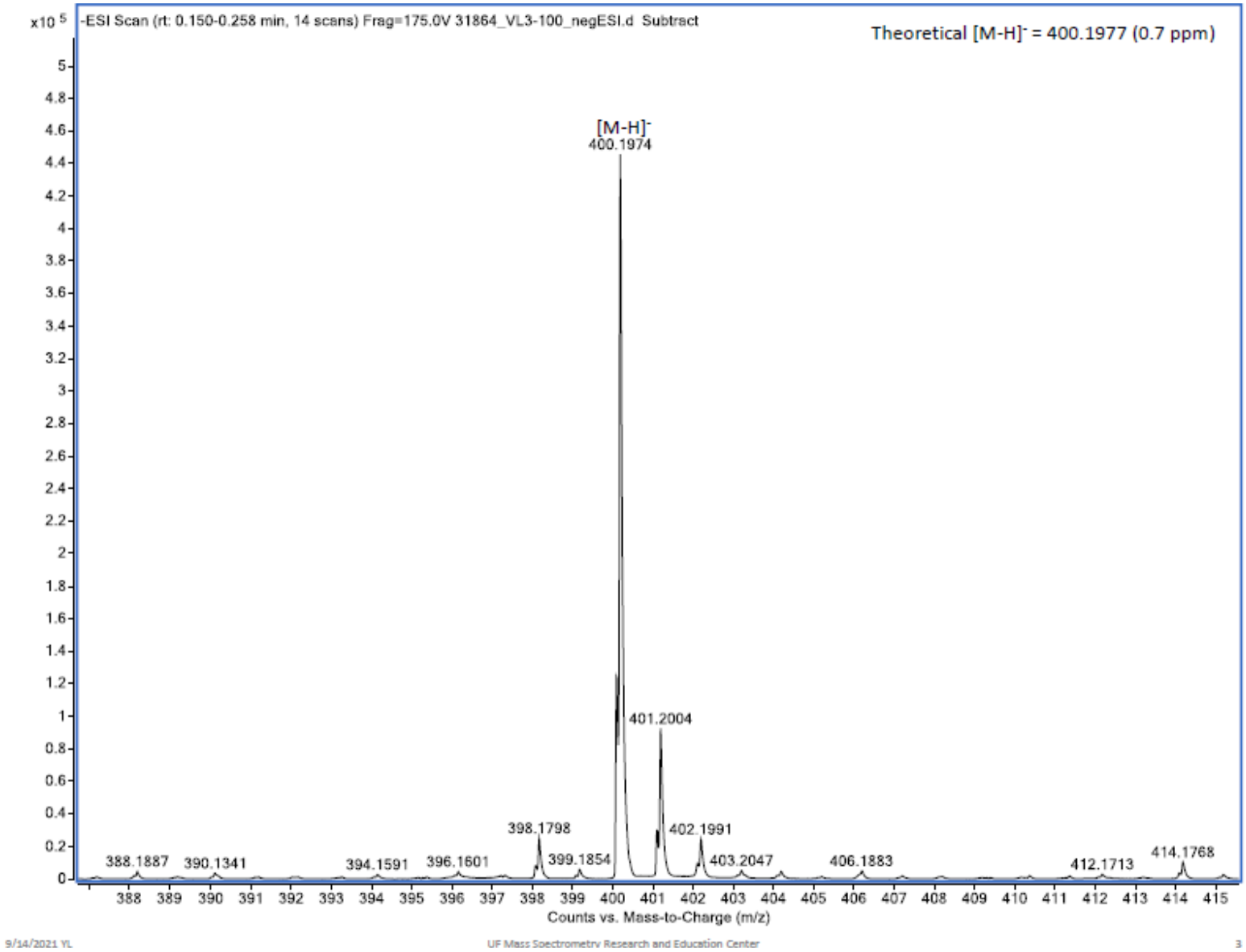


Figure S52. ^{1}H NMR of Compound **9p** (600 MHz, D_2O)

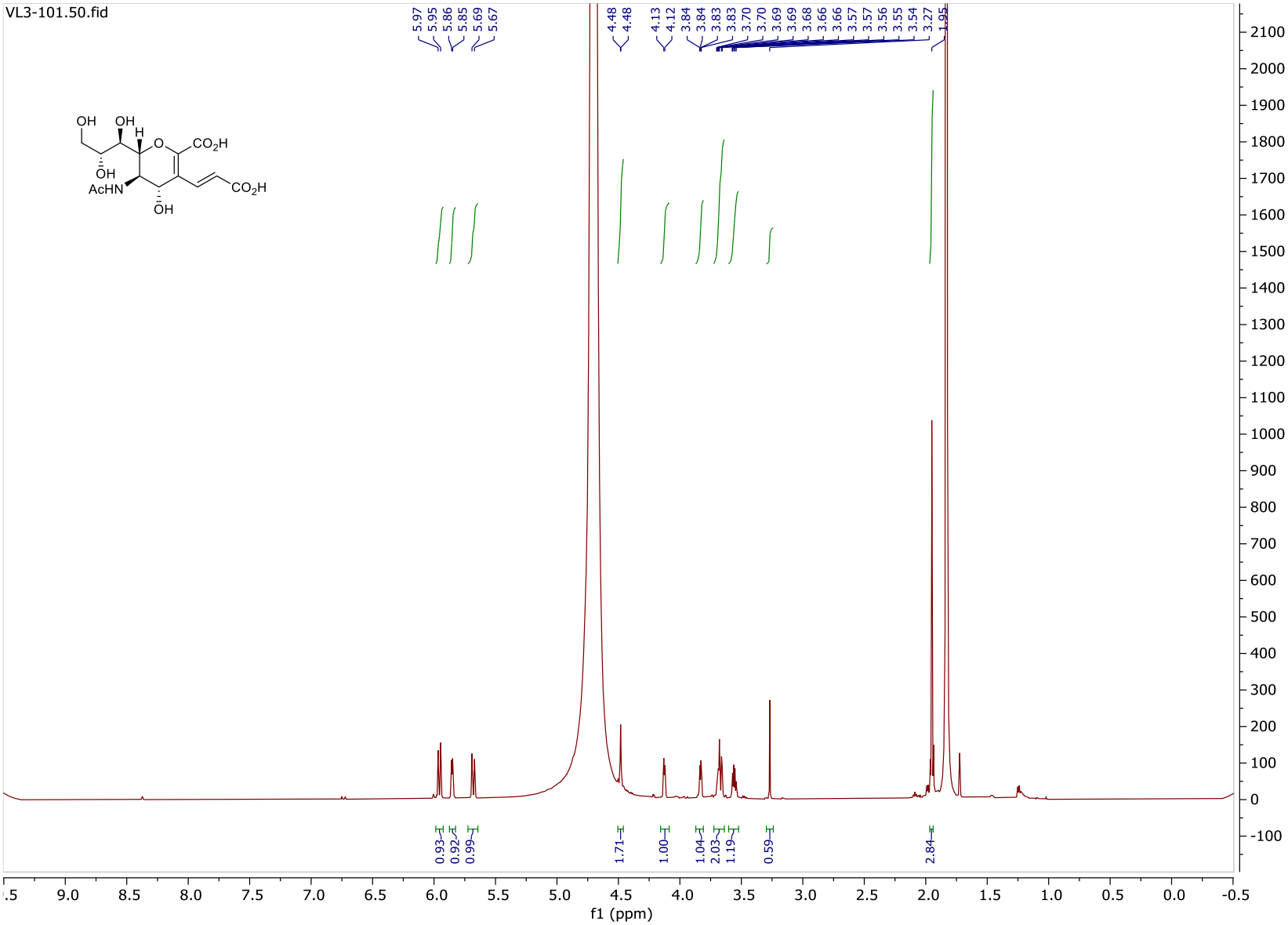


Figure S53. ^{13}C NMR of Compound **9p** (150 MHz, D_2O)

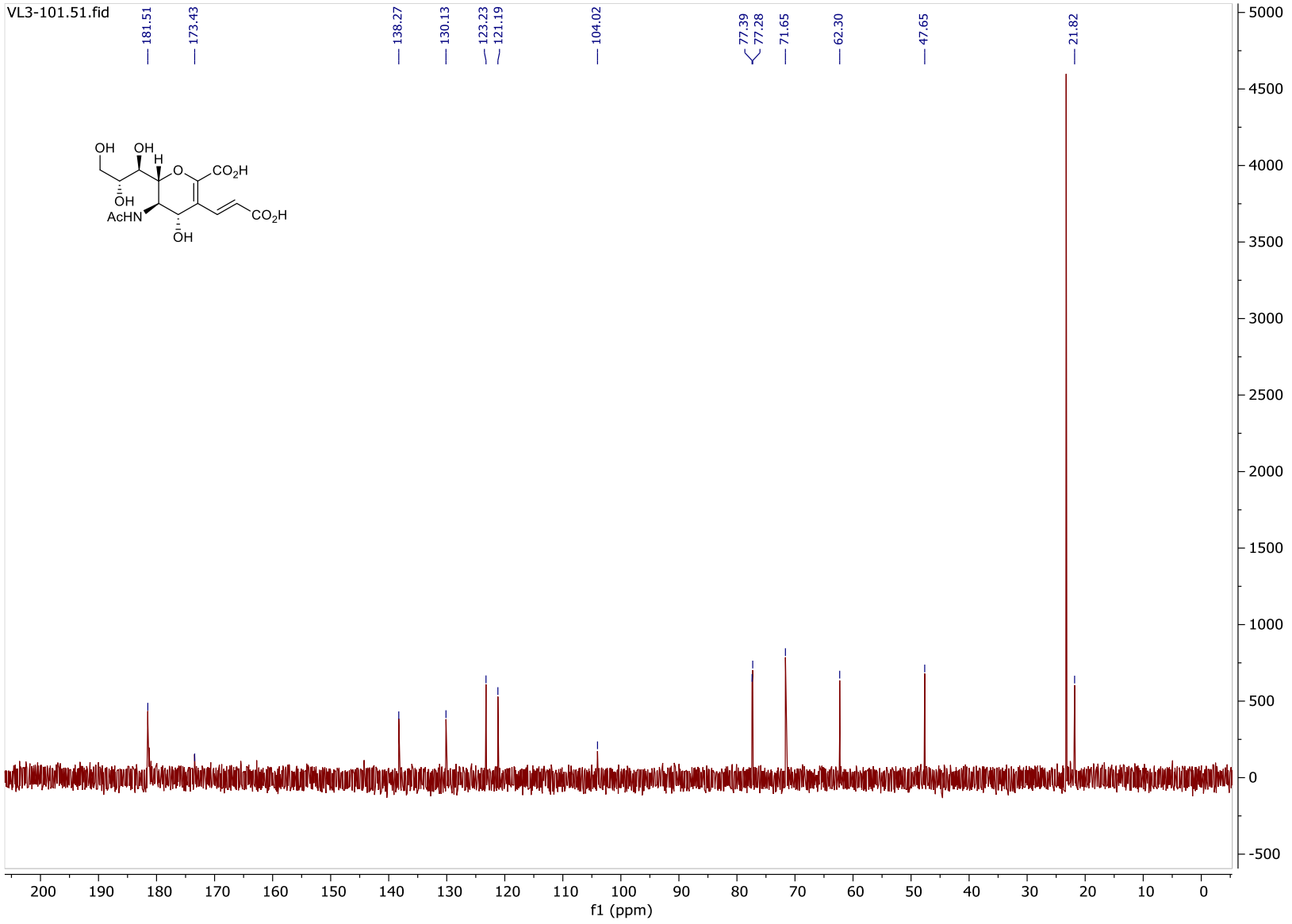


Figure S54. HRMS of Compound **9p** (ESI-TOF)

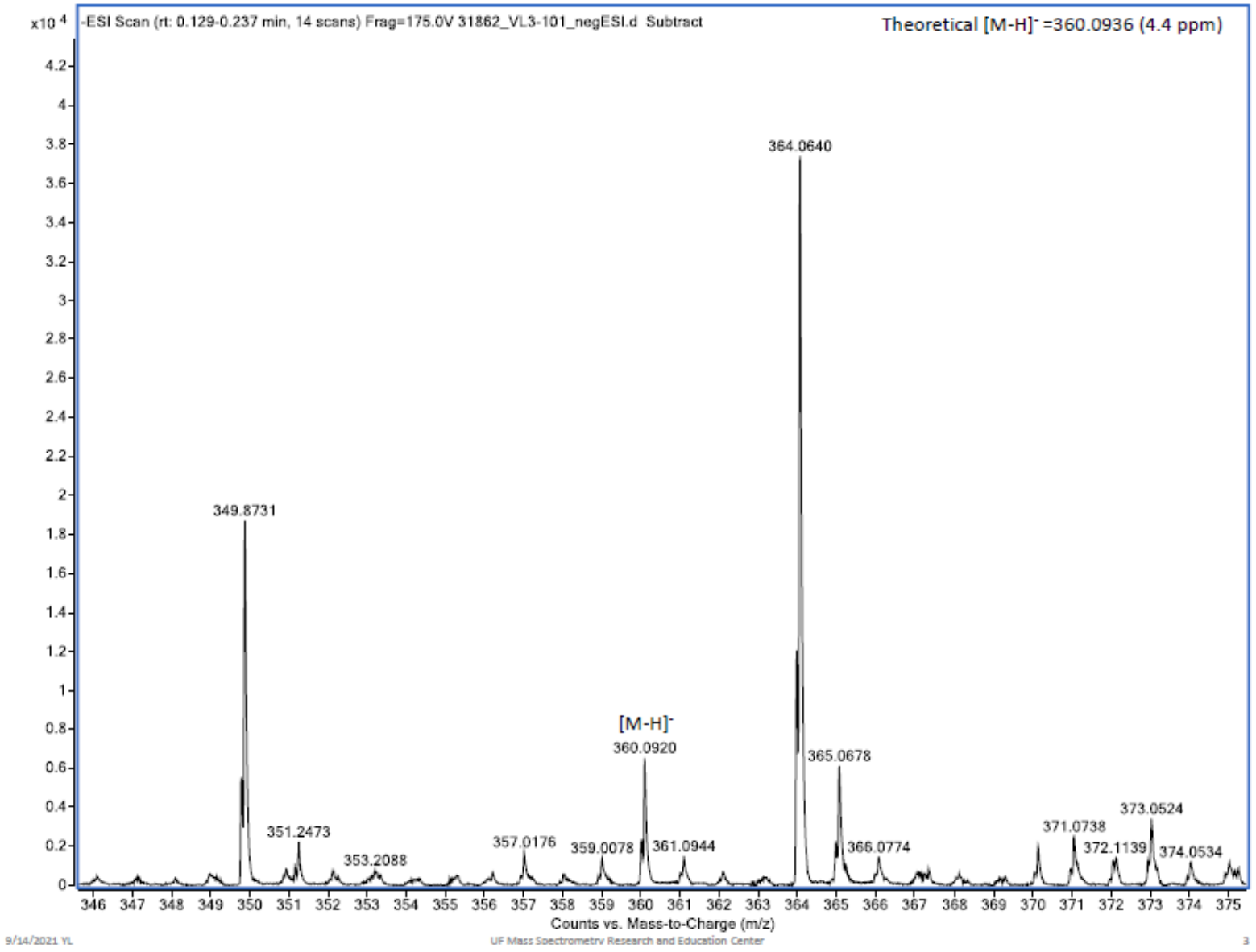


Figure S55. ^{1}H NMR of Compound **9q** (600 MHz, CD_3OD)

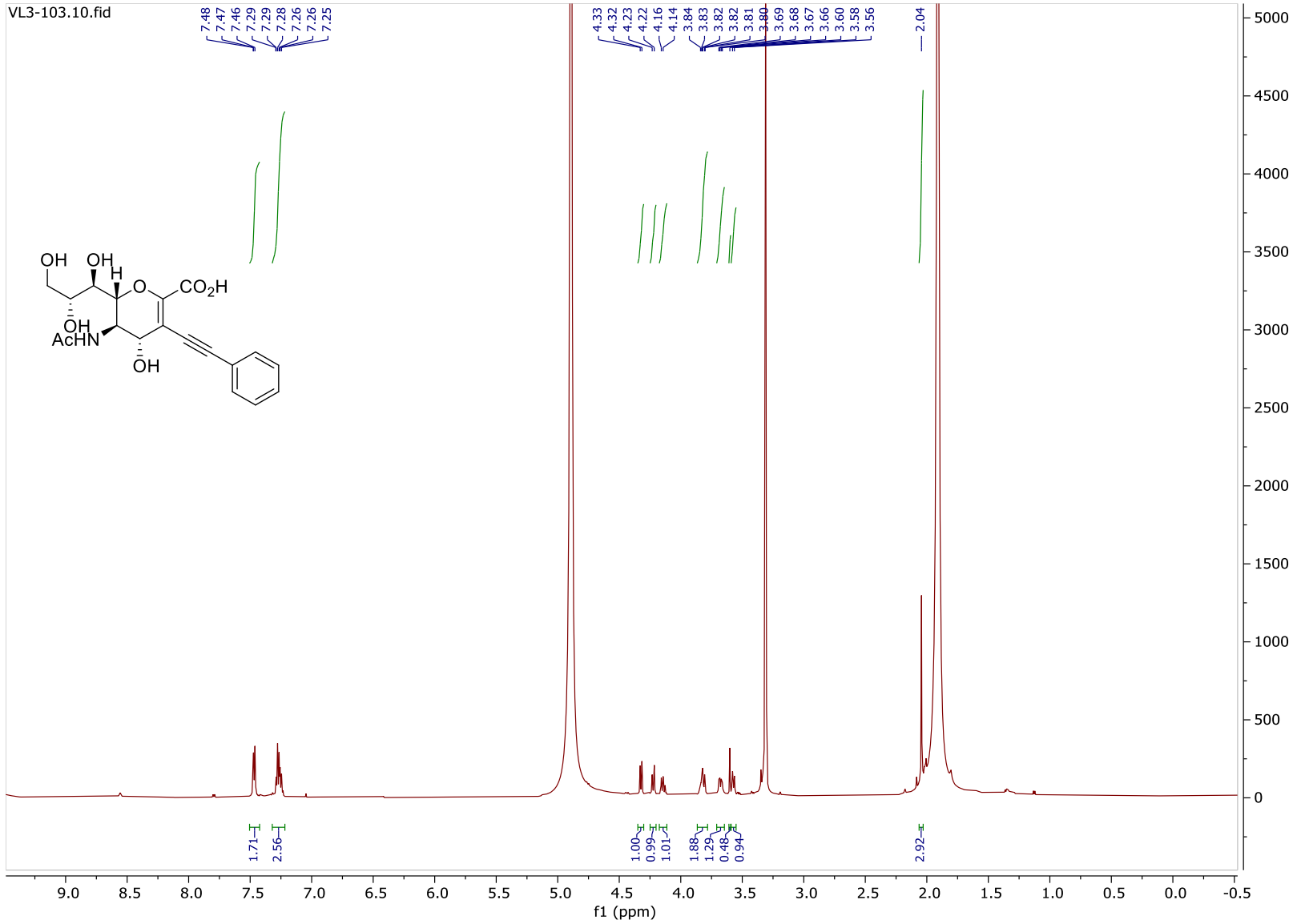


Figure S56. ^{13}C NMR of Compound **9q** (150 MHz, CD_3OD)

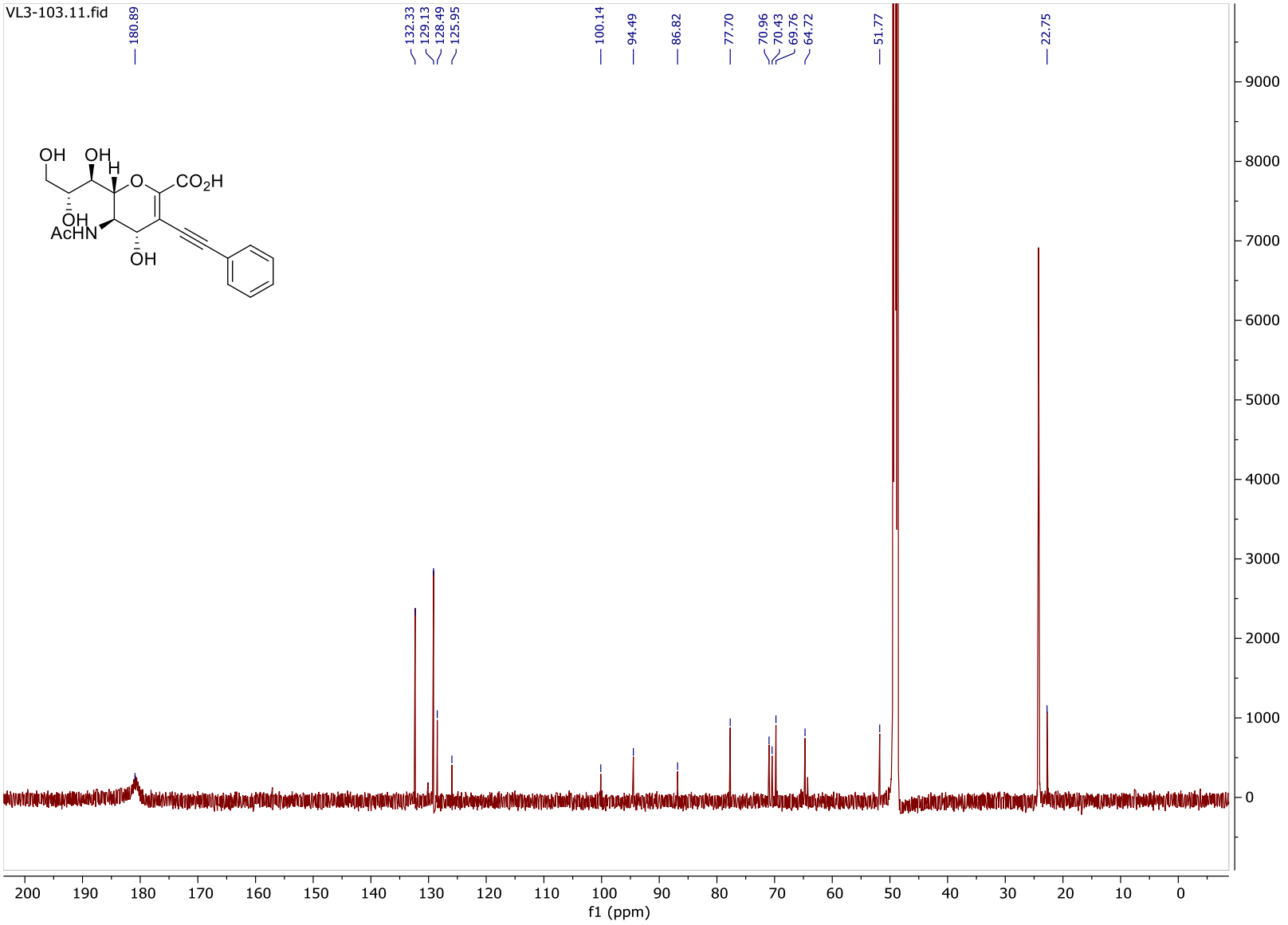


Figure S57. HRMS of Compound **9q** (ESI-TOF)