

Supporting Information

Synthesis of the Complete Series of Mono Acetates of *N*-Acetyl-D-Neuraminic Acid

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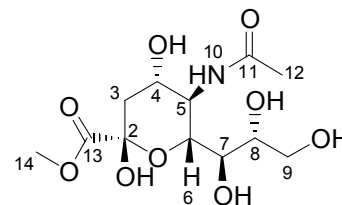
General Experimental Details

Melting points were determined using a Stuart SMP3 apparatus. Optical rotations were carried out using a JASCO-DIP370 polarimeter and $[\alpha]_D$ values are given in $10^{-1}\text{deg.cm}^2.\text{g}^{-1}$. Infra-red absorbances were recorded on a ThermoNicolet Avatar 370 FT-IR spectrometer using NaCl plates. Nuclear magnetic resonance spectra were recorded on a Jeol ECX-400 or a Jeol ECS-400 spectrometer at ambient temperature; chemical shifts are quoted in parts per million (ppm) and were referenced as follows: DMSO- d_6 , 2.50 ppm for ^1H NMR; DMSO- d_6 , 39.5 ppm for ^{13}C NMR. Coupling constants (J) are quoted in Hertz. Mass spectrometry was performed by the University of York mass spectrometry service using electron spray ionisation (ESI) techniques. Thin layer chromatography was performed on glass-backed plates coated with Merck Silica gel 60 F₂₅₄. The plates were developed using ultraviolet light and acidic aqueous ceric ammonium molybdate. Liquid chromatography was performed using forced flow (flash column) with the solvent systems indicated. The stationary phase was silica gel 60 (220–240 mesh) supplied by Fluorochem or silica gel Merck TLC grade 11695 supplied by Sigma-Aldrich, unless stated otherwise. CH_2Cl_2 was distilled from calcium hydride; THF was distilled from sodium–benzophenone ketyl; Et_2O was distilled from LiAlH_4 ; methanol and pyridine were distilled from calcium hydride. All other solvents and reagents were used as received from commercial suppliers.

Experimental Procedures and Data for Compounds not Reported in the Main Paper

N-acetyl neuraminic acid methyl ester (**10**)ⁱ

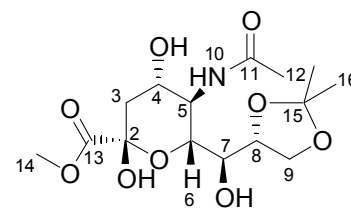
A solution of *N*-acetyl neuraminic acid (5.0g 16 mmol) in MeOH (200 mL) stirring at room temperature under a N₂



atmosphere was treated with Amberlyst H⁺ resin (1.7 g). The mixture was stirred for 3 days then filtered and the resin washed several times with methanol. The filtrate was concentrated *in vacuo* to yield an off-white solid which was purified by flash column chromatography using a 1:1 MeOH:CH₂Cl₂ gradient to give a white solid (5.2 g, 100%). ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.11 (1H, d, *J* = 8.5 Hz, H-10), 6.44 (1H, d, *J* = 2.0 Hz, O-H2), 4.85 (1H, d, *J* = 6.5 Hz, O-H4), 4.56 (1H, d, *J* = 4.5 Hz, O-H7), 4.35 (1H, d, *J* = 5.5 Hz, O-H8), 4.24 (1H, t, *J* = 6.0 Hz, O-H9), 3.84 (1H, ddd, *J* = 11.0, 11.0, 5.5 Hz, H-4), 3.74 (1H, d, *J* = 11.0 Hz, H-6), 3.70 (3H, s, H-14), 3.62-3.57 (1H, m, H-9), 3.51-3.46 (2H, m, H-5 + H-8), 3.28 (1H, dd, *J* = 17.5, 6.0 Hz, H-9), 3.19-3.16 (1H, m, H-7), 2.02 (1H, dd, *J* = 13.0, 5.0 Hz, H-3eq), 1.89 (3H, s, H-12), 1.75-1.68 (1H, m, H-3ax) ppm; ¹³C NMR (100 MHz, DMSO-*d*₆) δ 172.0, 170.3, 95.0, 70.5, 69.7, 69.1, 65.6, 63.6, 53.1, 52.4, 40.0, 22.6 ppm. Other structural data matched that reported in the literatureⁱ

Methyl 5-acetamido, 3,5-dideoxy-8,9-*O*-isopropylidene-*D*-glycero-β-*D*-galacto-2-nonulopyranosonate (**15**)ⁱⁱ

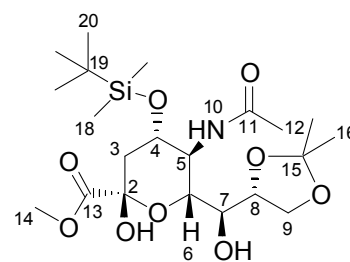
To a solution of *N*-acetyl neuraminic acid methyl ester **10** (250 mg, 0.77 mmol) in anhydrous acetone (200 mL) were added



2,2-dimethoxypropane (96 mg, 0.92 mmol) and *p*-toluenesulfonic acid (10 mg). The solution was stirred for 2 hours at room temperature under a N₂ atmosphere then treated with Amberlyst A-26 (OH⁻) anion-exchange resin (1.0 g) to remove the acid, and the resin filtered off and washed with acetone. The combined filtrate and washings were evaporated under reduced pressure, and the residue was purified by crystallization from 2-propanol to give **02** as a white solid (198 mg, 71%). ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.08 (1H, d, *J* = 8.0 Hz, H-10), 6.73 (1H, d, *J* = 2.0 Hz, O-H2), 4.85 (1H, d, *J* = 6.5 Hz, O-H4), 4.75 (1H, d, *J* = 5.0 Hz, O-H7), 3.99 (1H, dt, *J* = 5.5, 6.0 Hz, H-8), 3.91-3.87 (1H, m, H-6), 3.85-3.80 (2H, m, H-4 + H-9), 3.68 (3H, s, H-14), 3.57 (1H, dd, *J* = 10.5, 9.5 Hz, H-5), 3.52-3.47 (2H, m, H-7 +

H-9), 2.04 (1H, dd, $J = 12.5, 5.0$ Hz, H-3eq), 1.89 (3H, s, H-12), 1.62 (1H, dd, $J = 12.0, 2.0$ Hz, H-3ax), 1.27 (3H, s, H-16), 1.23 (3H, s, H-16) ppm; ^{13}C NMR (100 MHz, DMSO- d_6): δ 171.8, 170.0, 107.3, 94.7, 76.0, 71.8, 68.5, 65.3, 65.0, 52.9, 52.2, 40.0, 26.6, 25.8, 22.6 ppm. Other structural data matched that reported in the literatureⁱⁱ

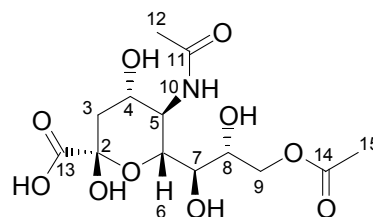
Methyl 5-Acetamido-3,5-dideoxy-8,9-*O*-isopropylidene-4-*O*-*tert*-butyldimethylsilyl-D-glycero-D-galactonulopyranosonate (16)ⁱⁱⁱ



Imidazole (1.05 g, 15.5 mmol) and *tert*-butyldimethylsilyl chloride (0.93 g, 6.2 mmol) were added to a solution of **15** (1.12

g, 3.09 mmol) in DMF (20 mL) at 0 °C. The solution was stirred at room temperature for 18 hours. The solvent was removed *in vacuo* then was partitioned between CH₂Cl₂ (100 mL) and H₂O (100 mL). The aqueous layer was extracted with CH₂Cl₂ (2 x 100 mL) and the combined organics were washed with brine (300 mL), dried (MgSO₄) and concentrated to give a yellow oil. The crude material was purified by flash column chromatography using a 0% - 5% MeOH:CH₂Cl₂ gradient to give a white solid (1.21 g, 82%). ^1H NMR (400 MHz, DMSO- d_6): δ 7.91 (1H, d, $J = 9.0$ Hz, H-10), 6.85 (1H, s, O-H2), 4.53 (1H, br s, O-H7), 4.05-4.01 (1H, m, H-4), 3.98 (1H, dd, $J = 12.0, 6.0$ Hz, H-8), 3.91-3.84 (2H, m, H-6 + H-5), 3.74 (1H, br d, $J = 10.5$ Hz, H-9), 3.68 (3H, s, H-14), 3.64 (1H, br d, $J = 10.5$ Hz, H-9), 3.49 (1H, br d, $J = 6.0$ Hz, H-7), 2.04 (1H, dd, $J = 12.0, 5.0$ Hz, H-3eq), 1.82 (3H, s, H-12), 1.62 (1H, dd, $J = 12.0, 12.0$ Hz, H-3ax), 1.28 (3H, s, H-16), 1.24 (3H, s, H-16), 0.81 (9H, s, H-20), 0.04 (3H, s, H-18), 0.03 (3H, s, H-18) ppm; ^{13}C NMR (100 MHz, DMSO- d_6): δ 171.8, 170.0, 107.3, 94.7, 76.0, 71.8, 68.5, 65.3, 65.0, 52.9, 52.2, 40.0, 26.6, 25.7, 25.7, 22.6, 17.5, -4.6, -4.8 ppm. Other structural data matched that reported in the literatureⁱⁱⁱ

5-Acetamido-9-*O*-acetyl-3,5-dideoxy-D-glycero-D-galactonulopyranosic acid (2)

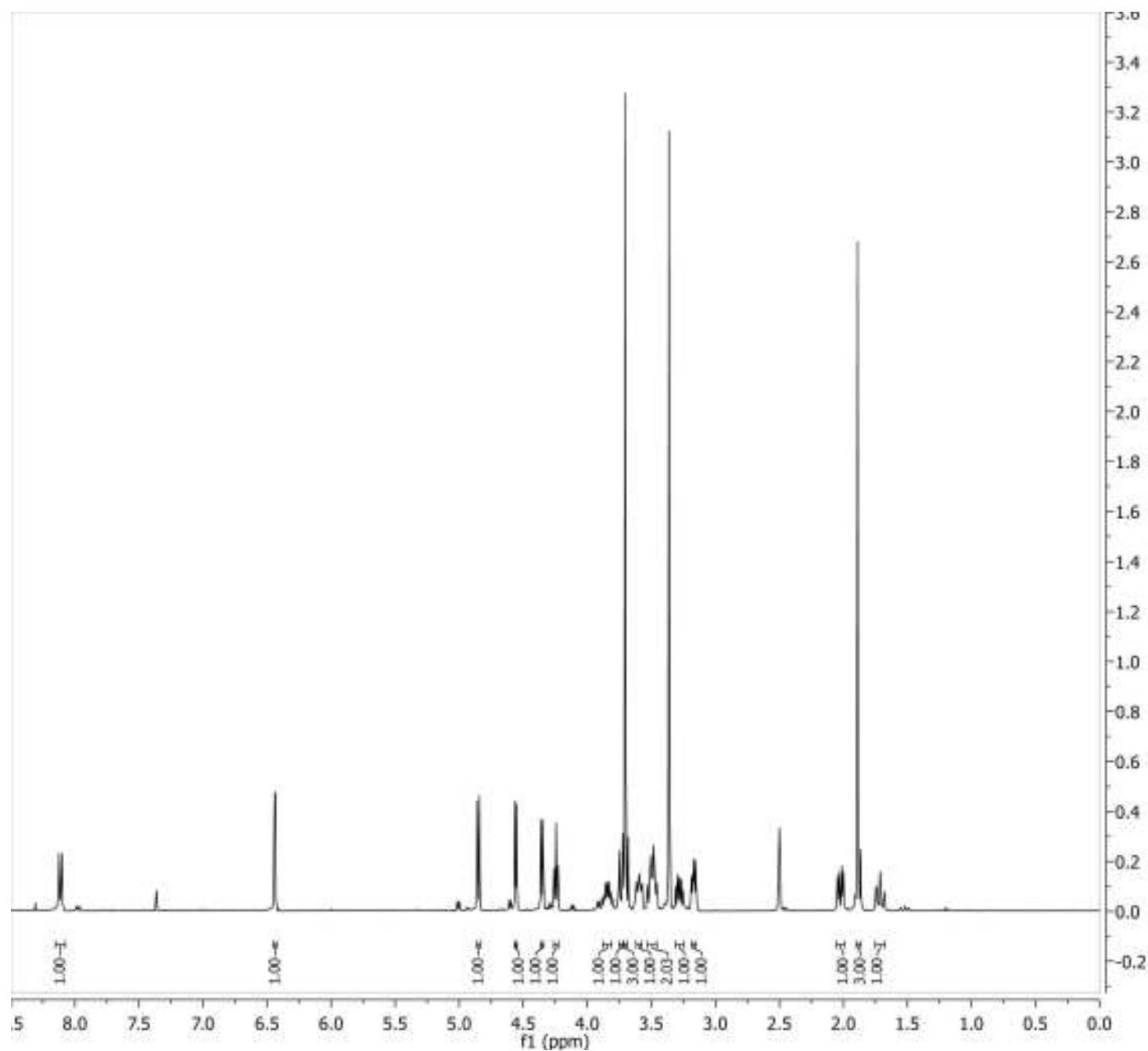


A solution of *N*-acetyl neuraminic acid (200 mg 0.65 mmol) in DMF (10 mL) stirring at room temperature under a N₂ atmosphere was treated with trimethyl orthoacetate (81 μL , 6.5 mmol) followed by *p*-TsOH (20 mg). The mixture was stirred for 18 hours then concentrated *in vacuo* to yield an off-

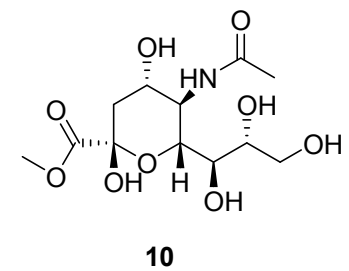
white solid which was purified by flash column chromatography using a 1:3 MeOH:CH₂Cl₂ gradient to give a white solid (143 mg, 63%). ¹H NMR (400 MHz, DMSO-*d*₆): δ 8.14 (1H, d, *J* = 8.5 Hz, H-10), 6.40 (1H, d, *J* = 2.0 Hz, O-H2), 4.85 (1H, d, *J* = 6.5 Hz, O-H4), 4.56 (1H, d, *J* = 5.0 Hz, O-H7), 4.35 (1H, d, *J* = 6.0 Hz, O-H8), 3.91-3.87 (1H, dd, *J* = 10.5, 8.0 Hz, H-9), 3.85-3.81 (1H, m, H-4), 3.74 (1H, dd, *J* = 10.5, 1.5 Hz, H-6), 3.70 (1H, m, H-9), 3.50 (1H, ddd, *J* = 10.5, 10.5, 10.5 Hz, H-5), 3.25-3.21 (1H, m, H-8), 3.16 (1H, br d, *J* = 5.0 Hz, H-7), 2.03 (1H, dd, *J* = 13.0, 5.0 Hz, H-3eq), 200 (3H, s, H-15), 1.90 (3H, s, H-12), 1.76-1.69 (1H, m, H-3ax) ppm; ¹³C NMR (100 MHz, DMSO-*d*₆) δ ¹³C NMR (101 MHz, DMSO-D₆) δ 172.1, 170.4, 170.2, 95.0, 70.2, 69.2, 66.9, 66.7, 65.5, 53.0, 39.9, 22.6, 20.8 ppm. Other structural data matched that reported in the literatureⁱⁱ

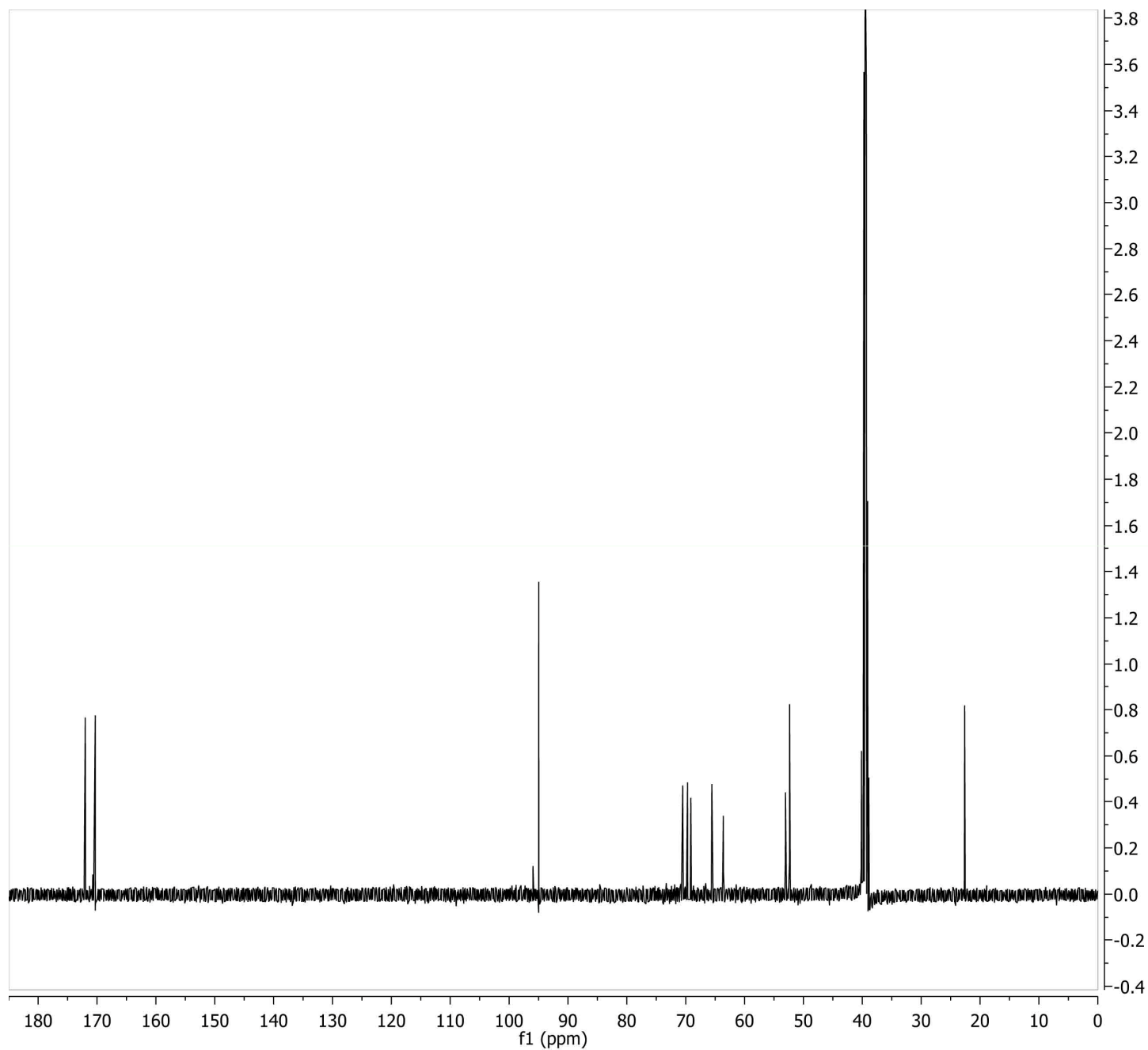
References:

- ⁱ A. Malapelle, A. Coslovi, G. Doisneau, J.-M. Beau, *Eur. J. Org. Chem.* **2007**, 3145.
ⁱⁱ H. Ogura, K. Furuhata, S. Sato, K. Anazawa, *Carbohydrate Research*, **1987**, 167, 77.
ⁱⁱⁱ H. Ogura, K. Furuhata, K. Anazawa, *Chem. Pharm. Bull.* **1988**, 36, 4976.

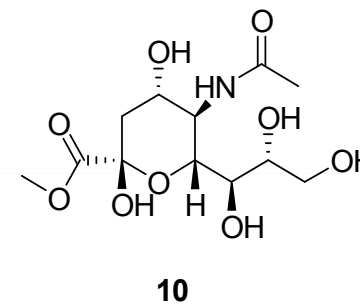


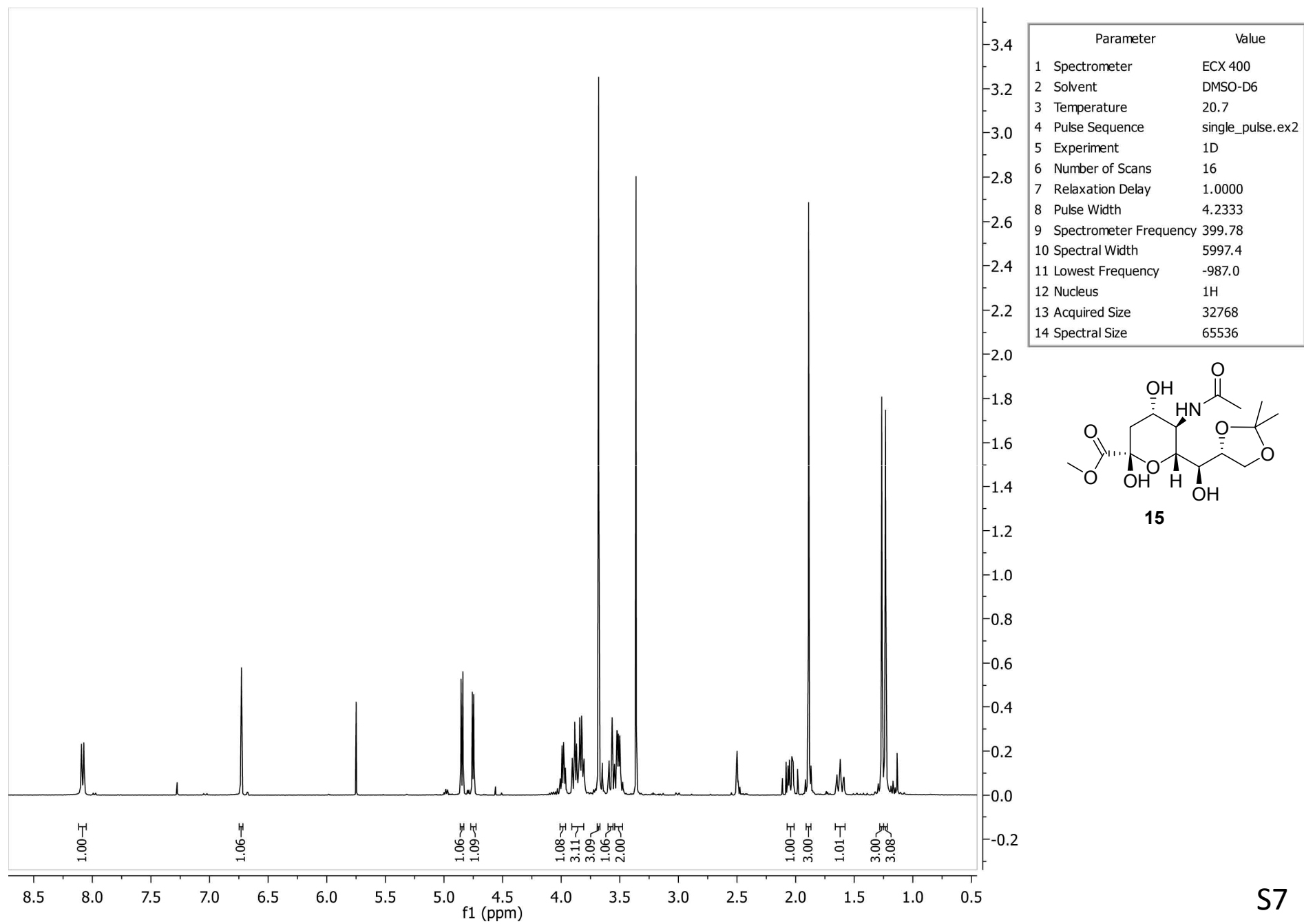
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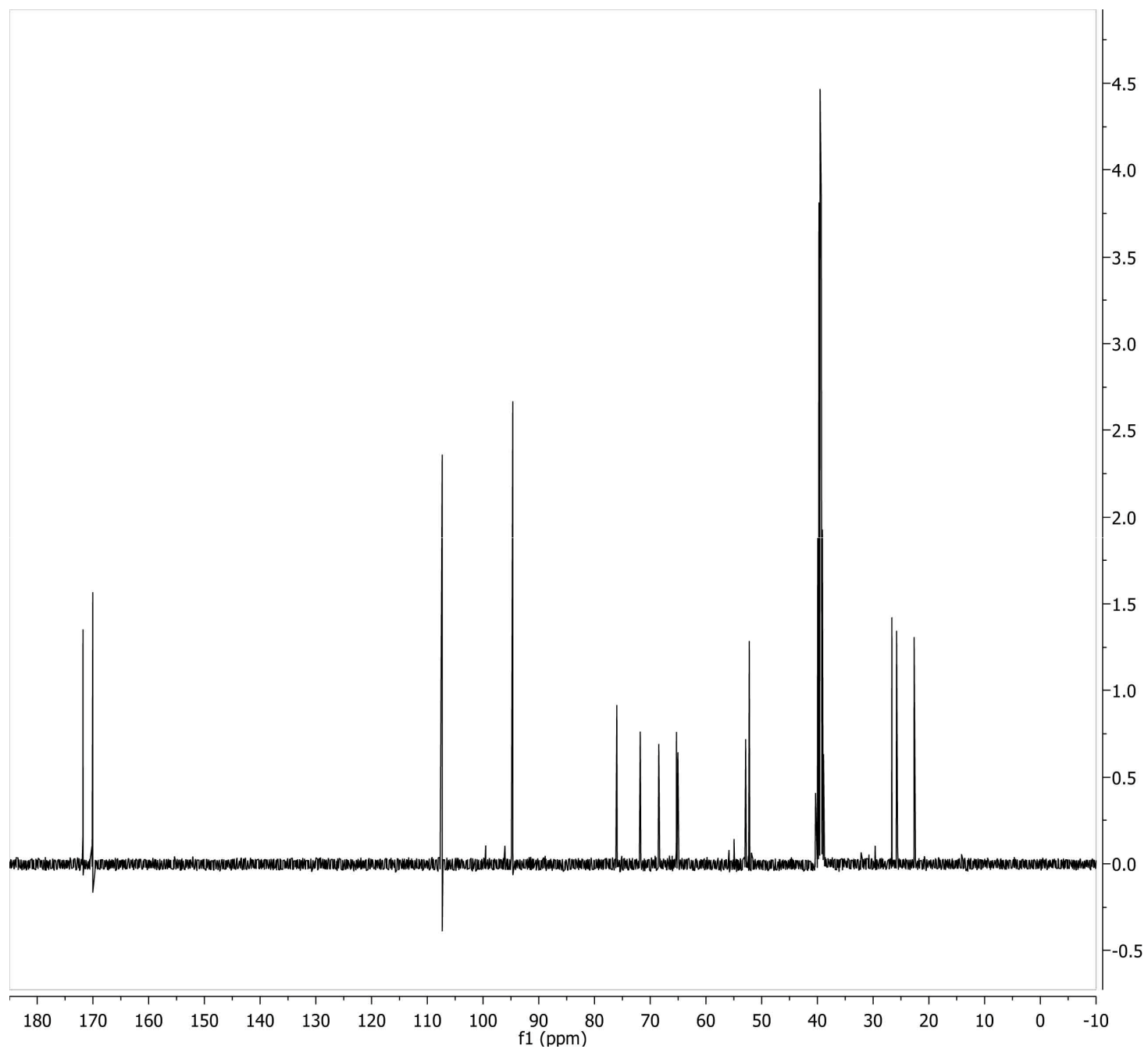




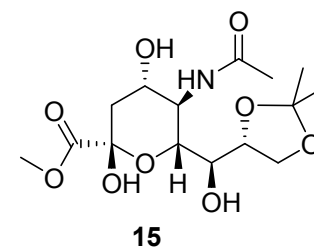
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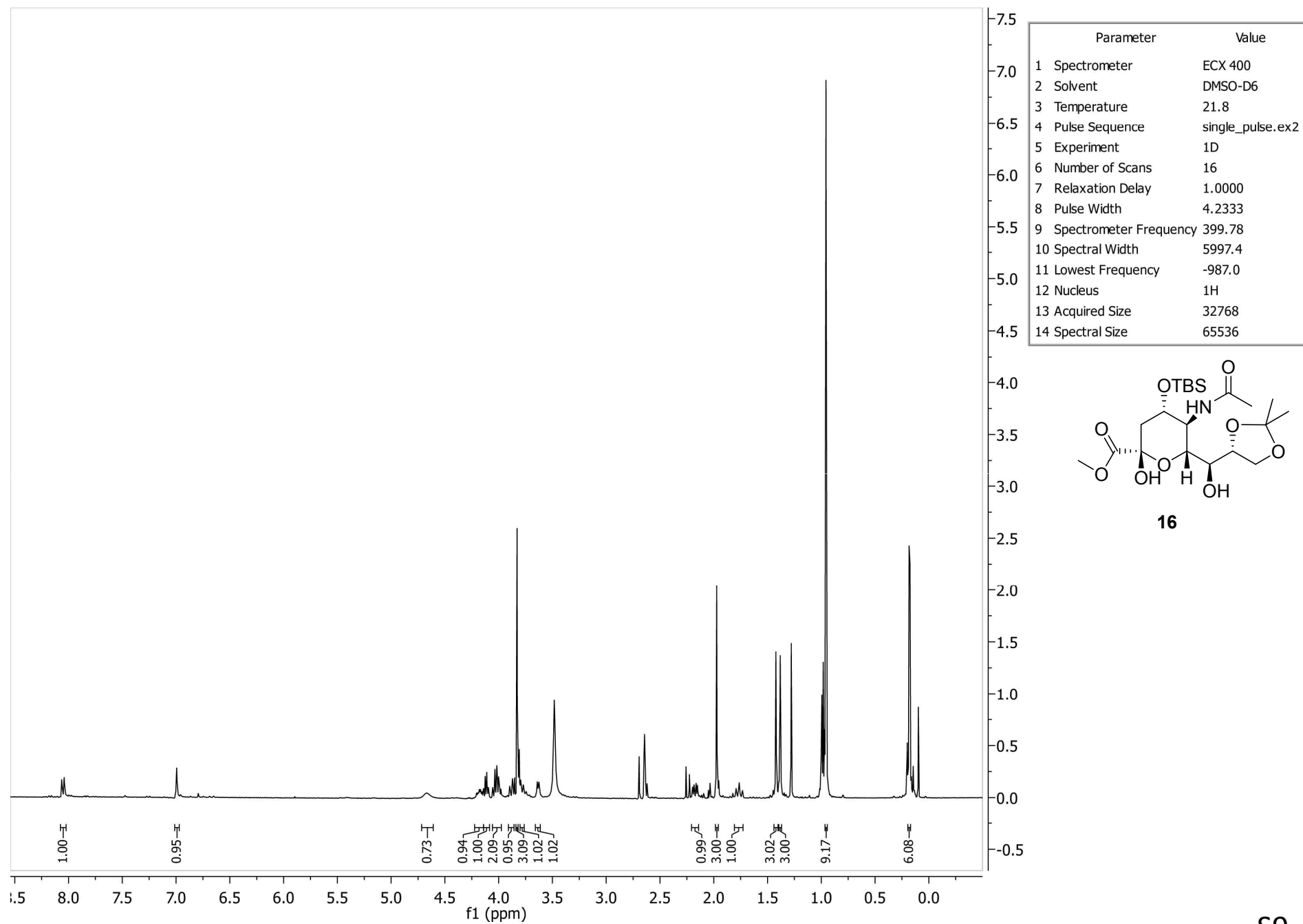


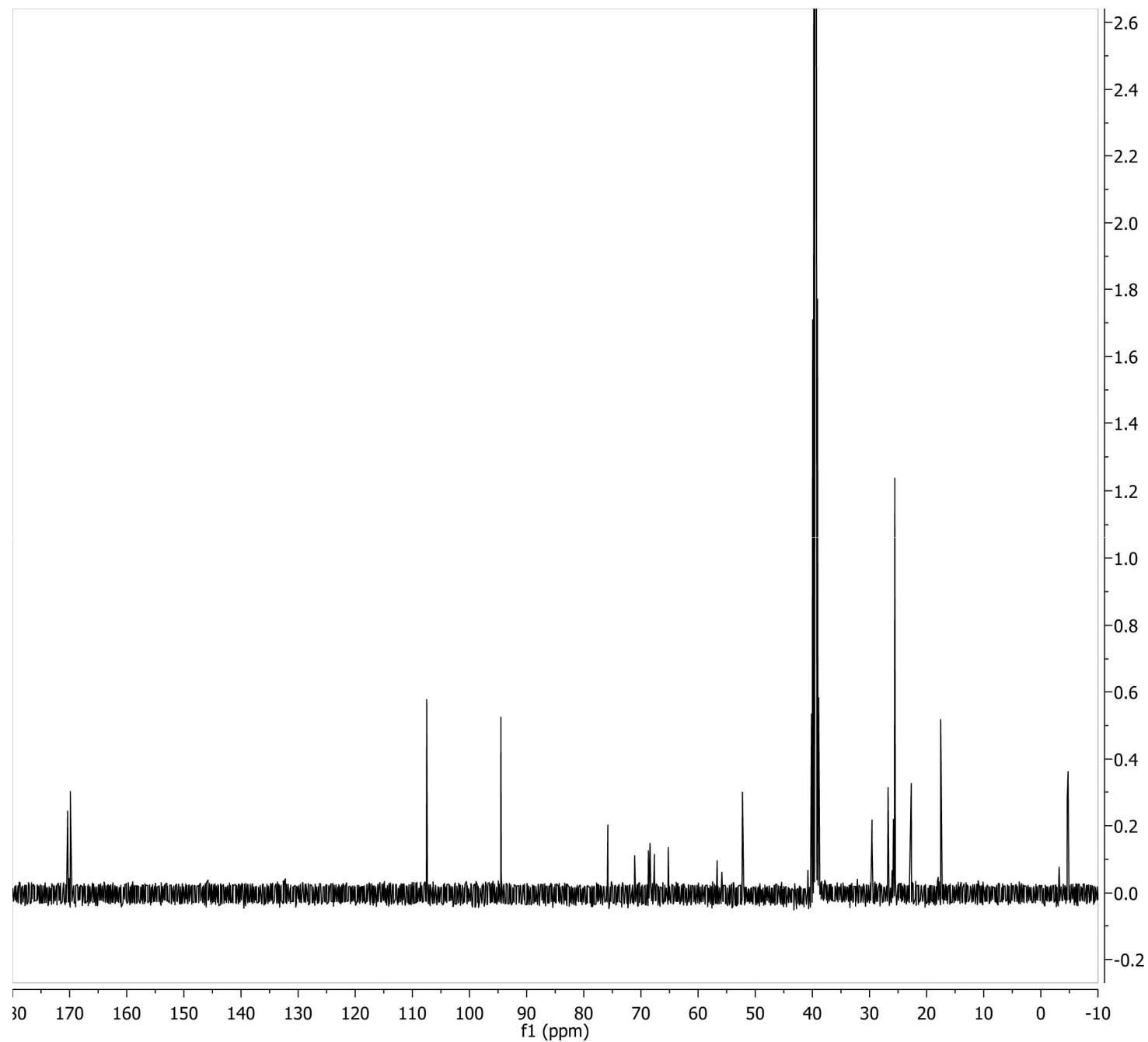




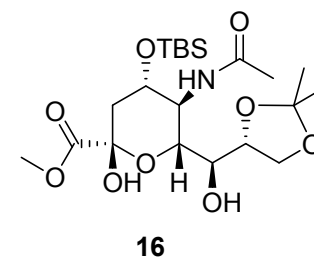
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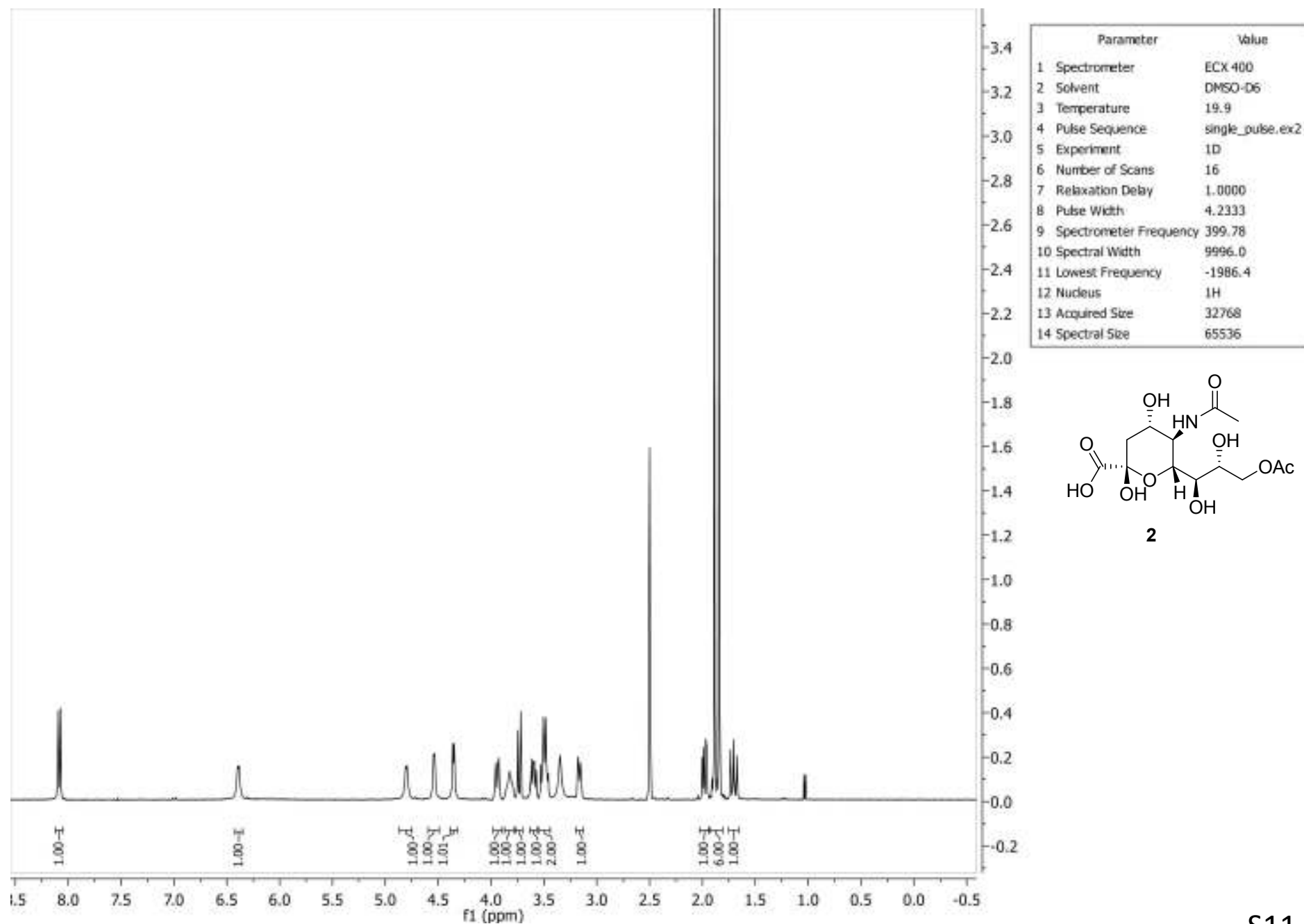


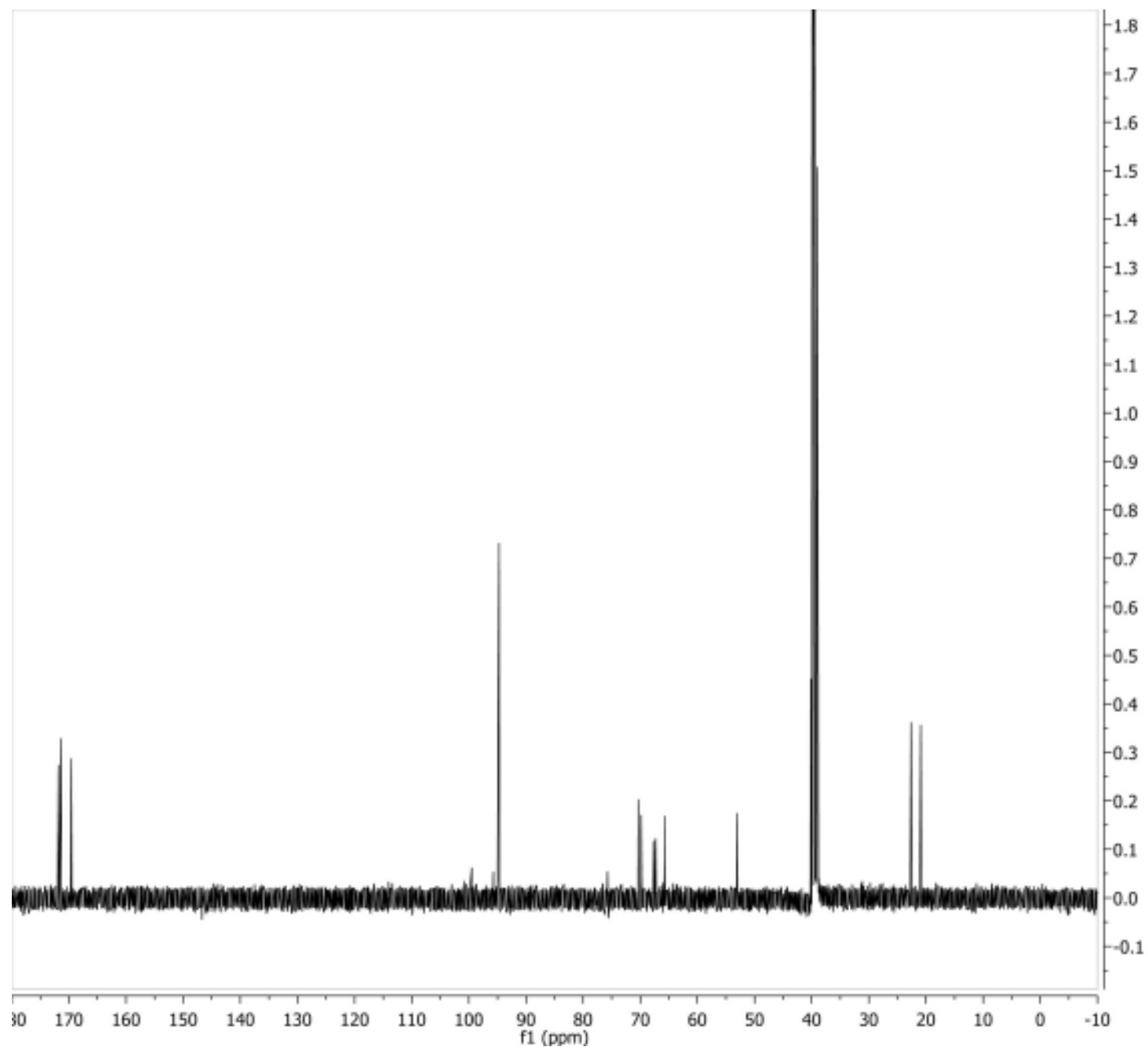




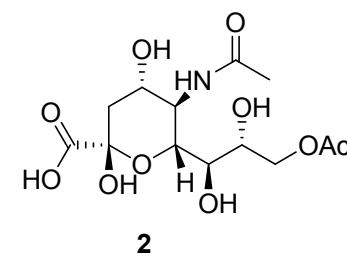
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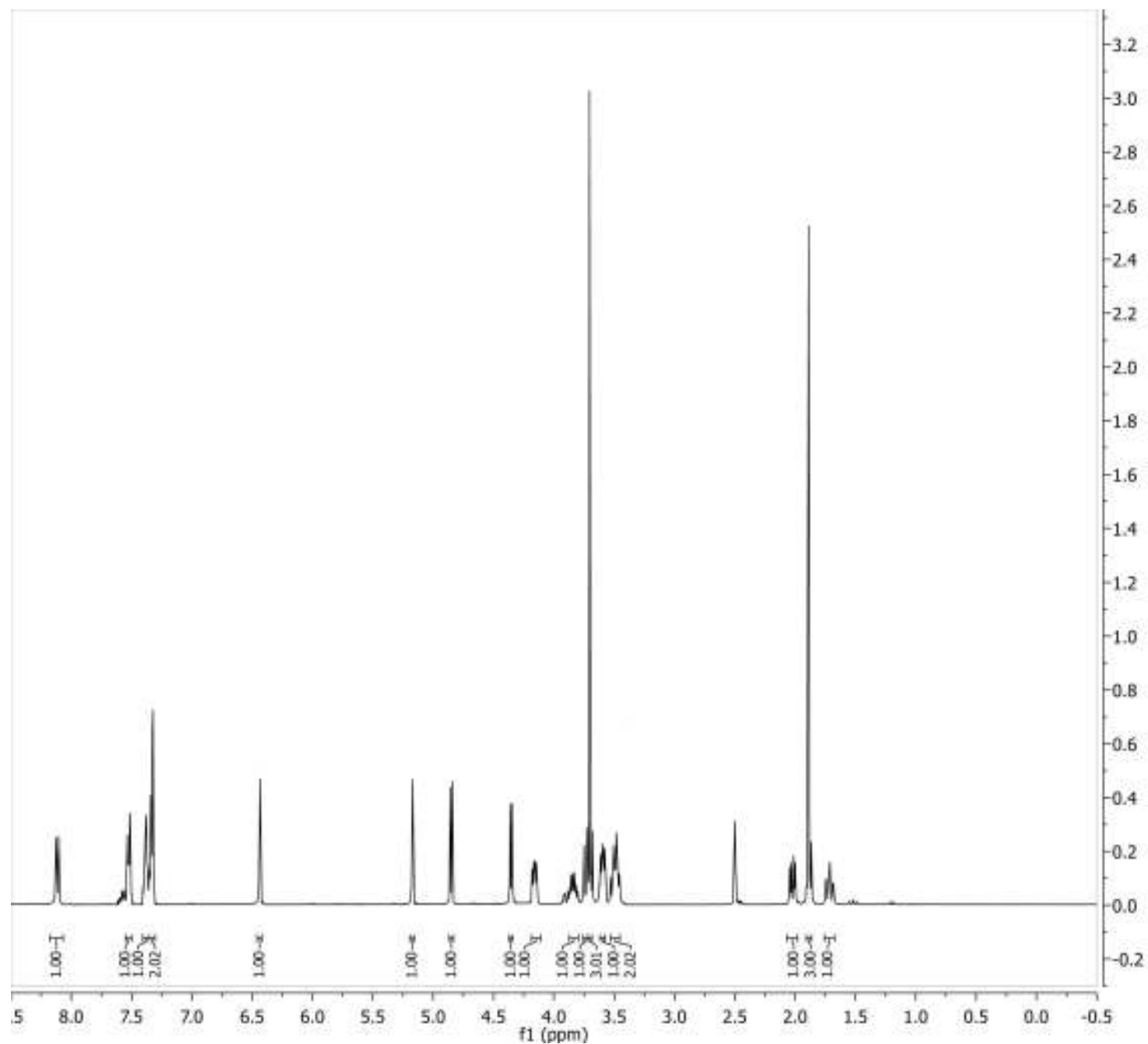




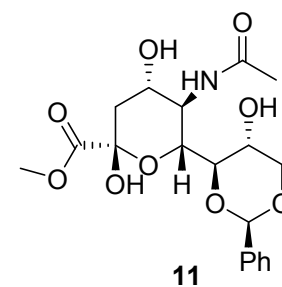


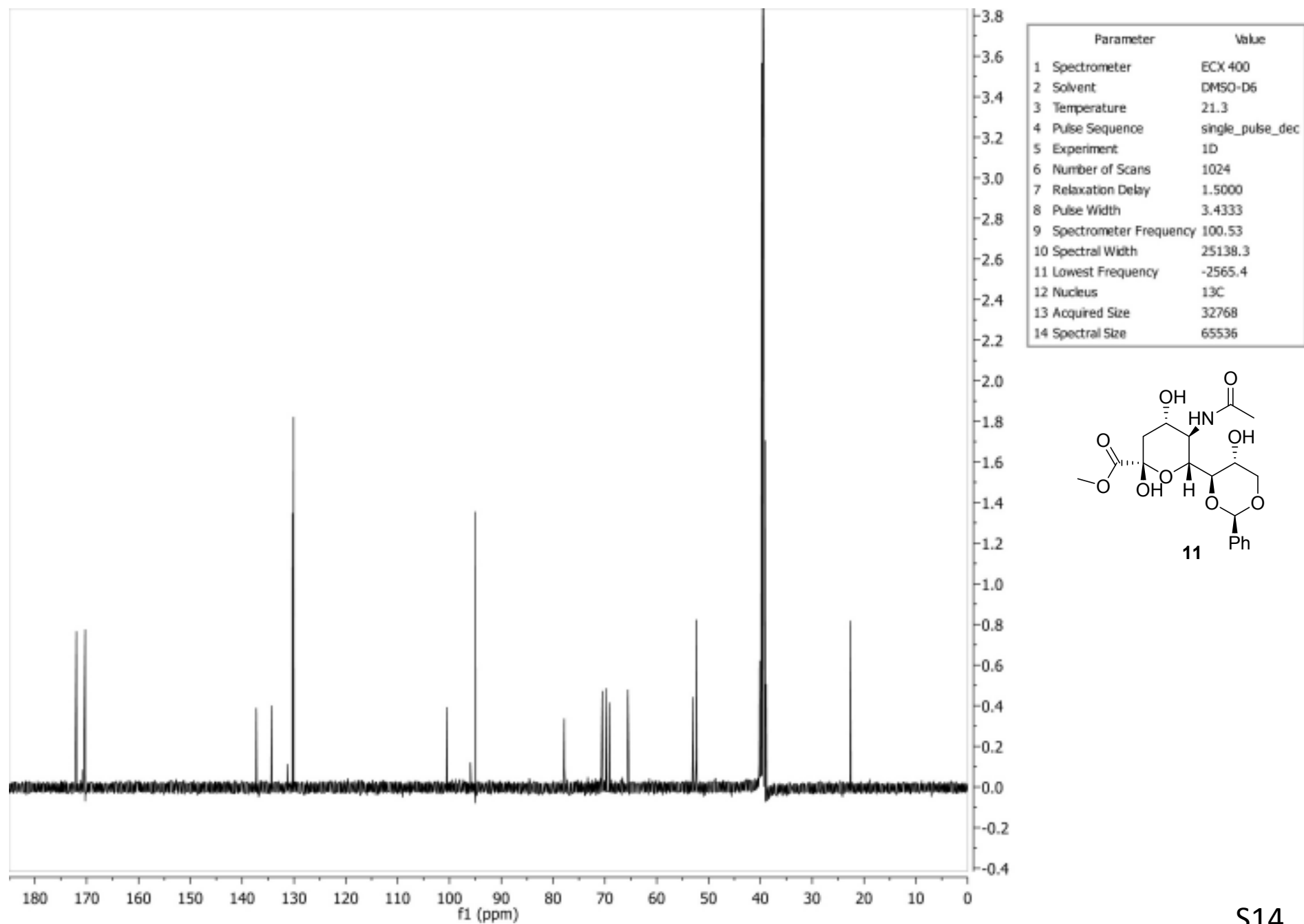
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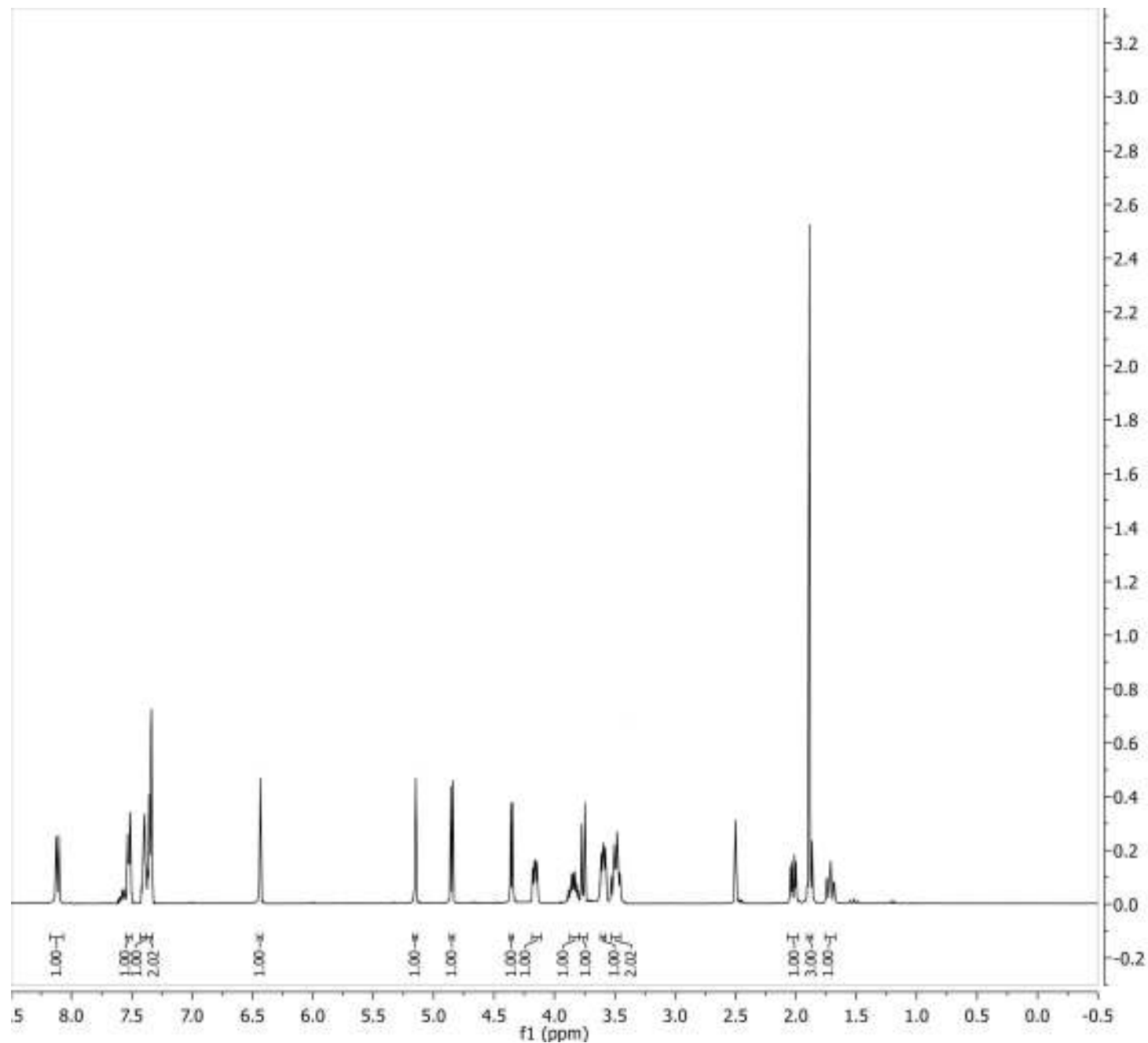




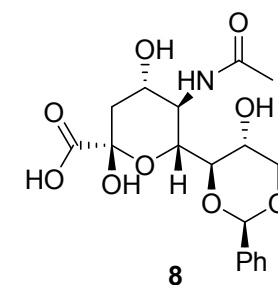
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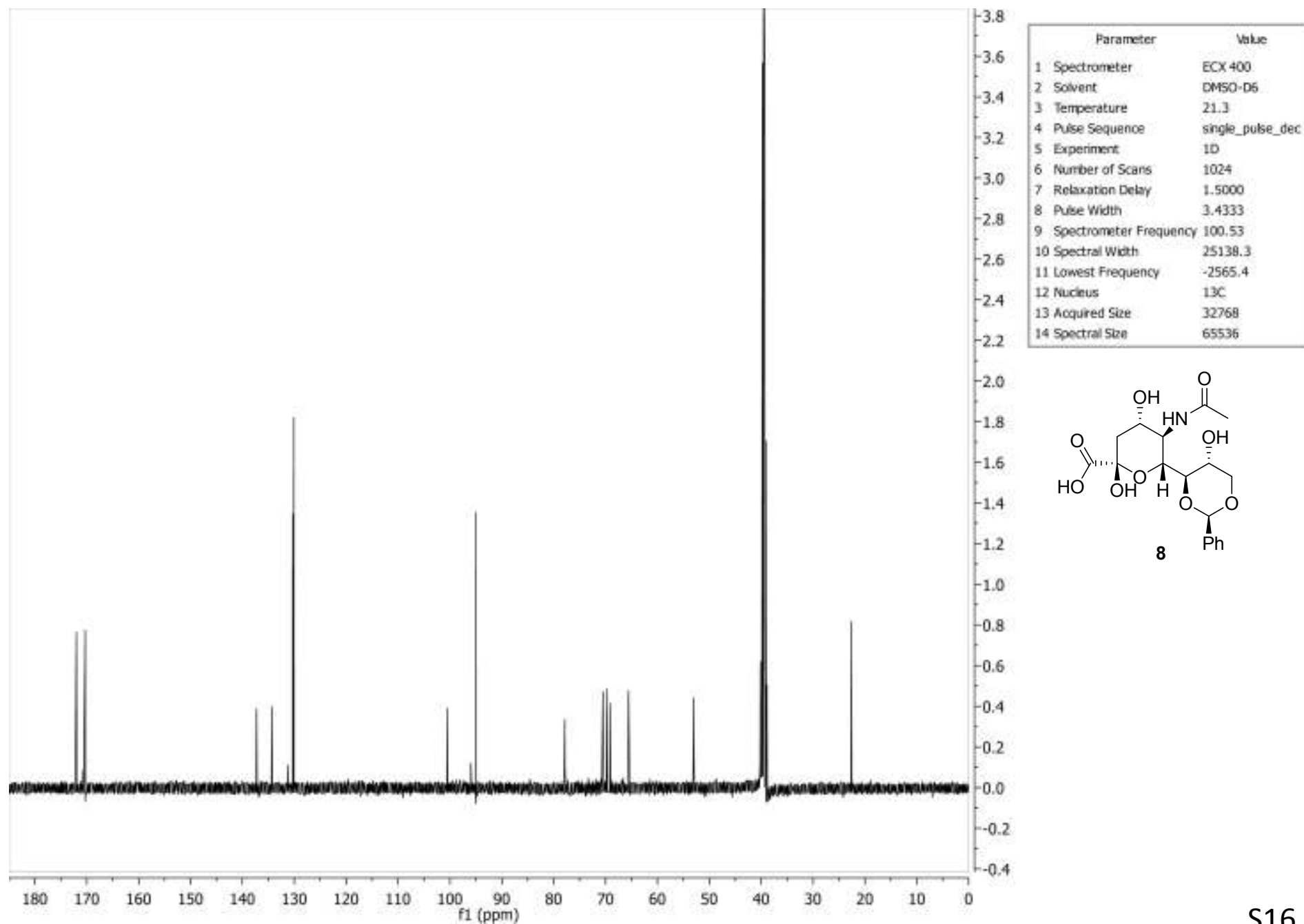


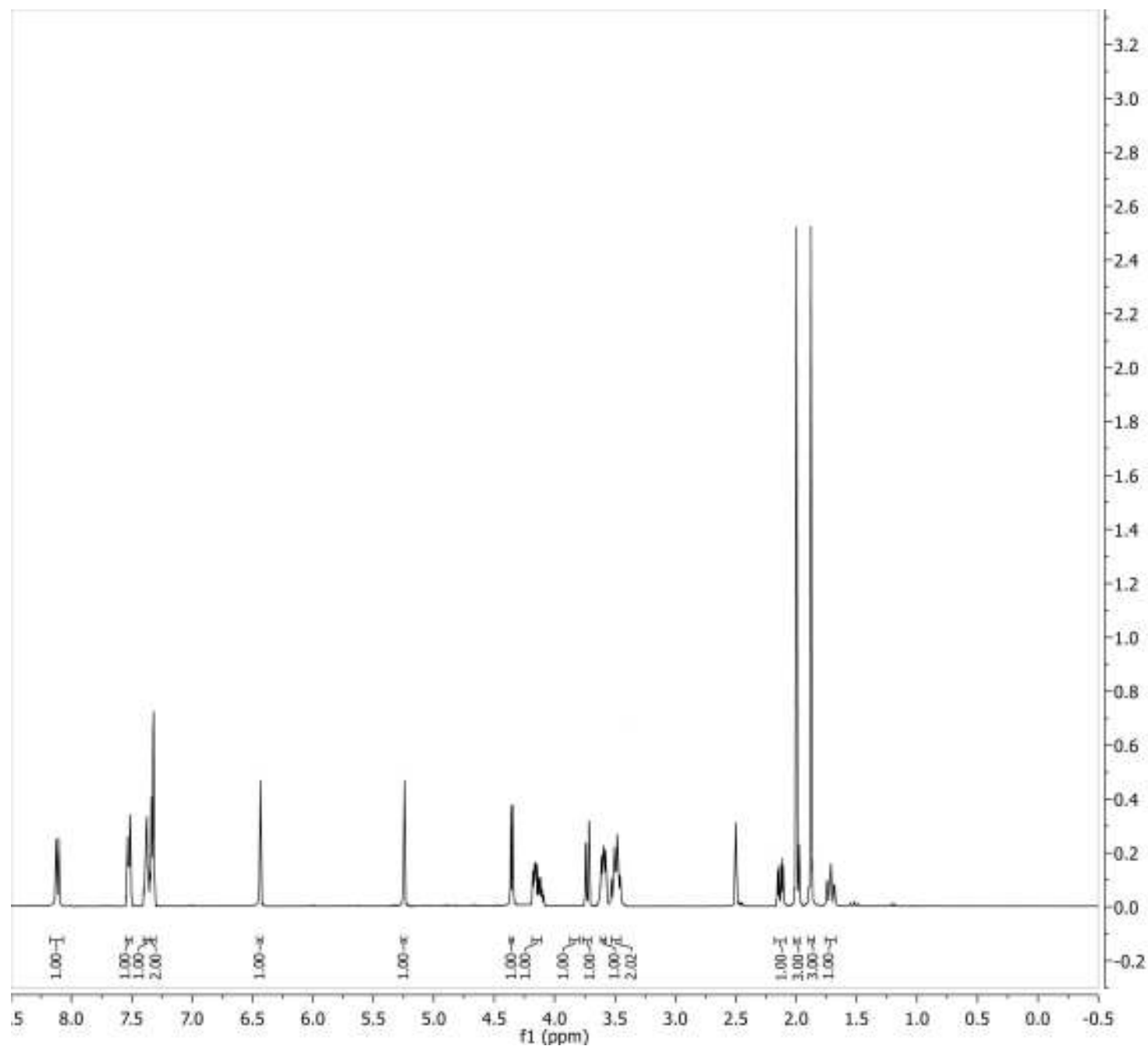




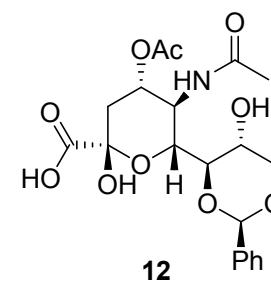
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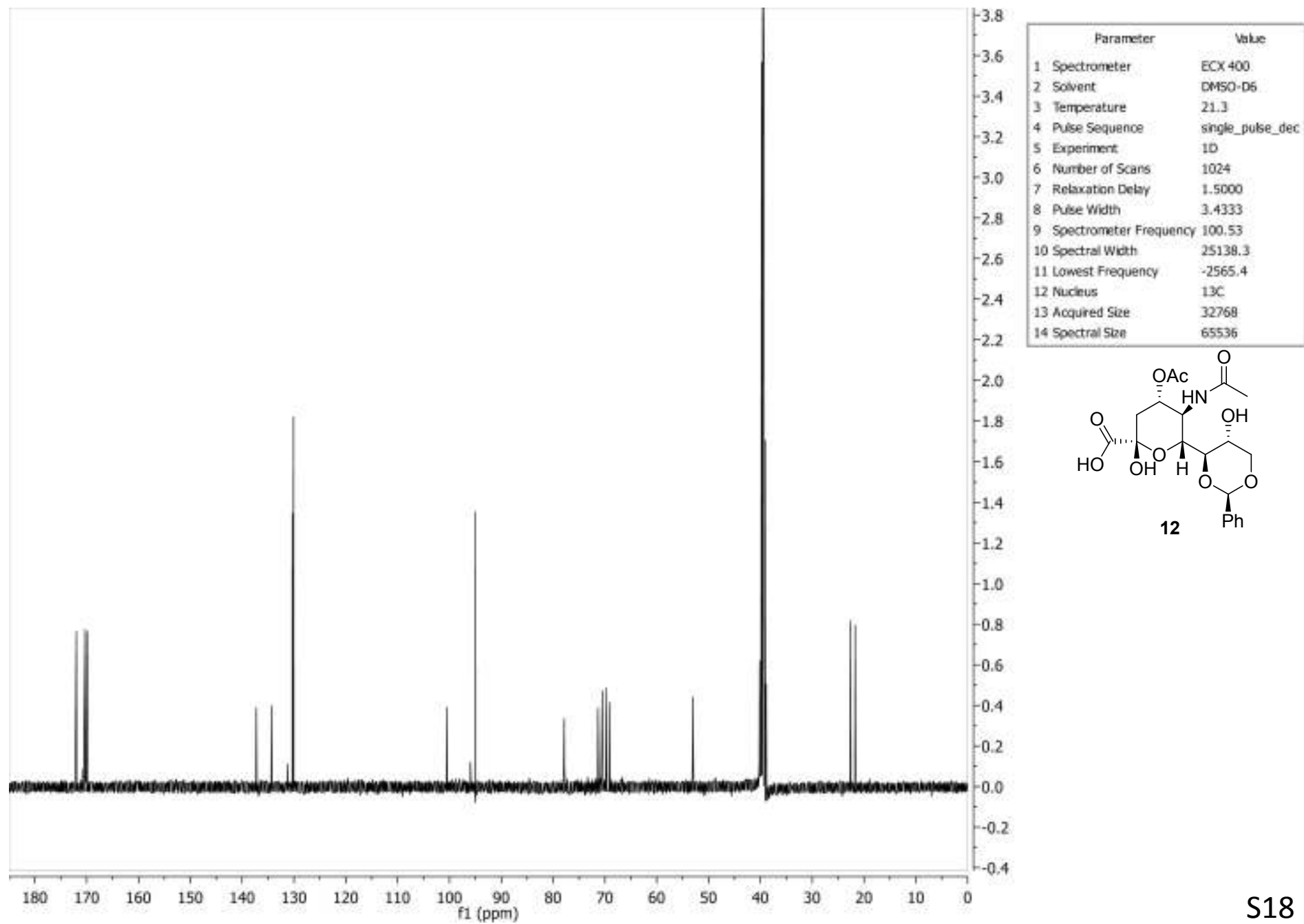


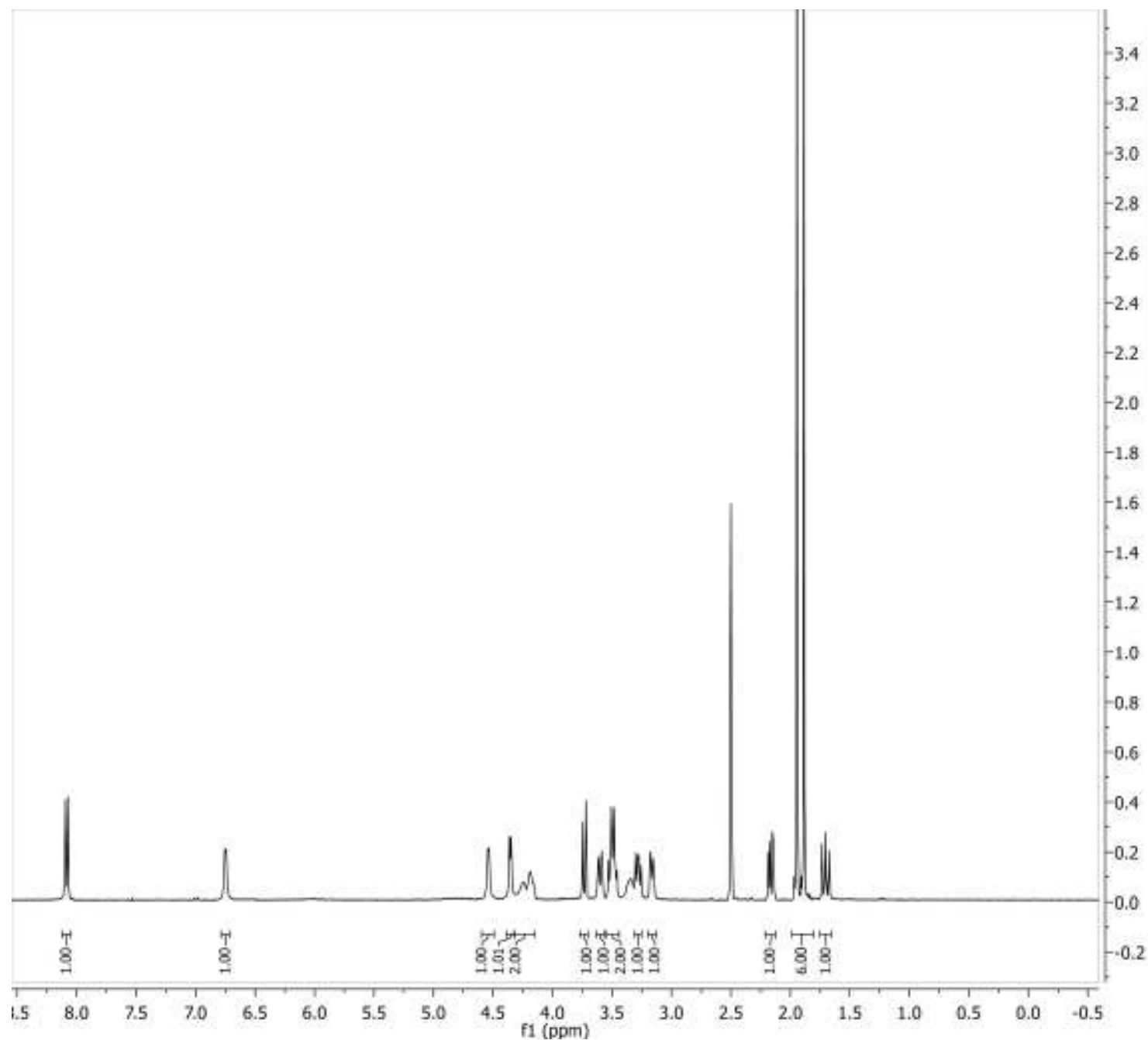




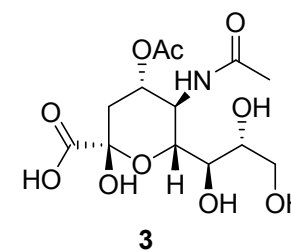
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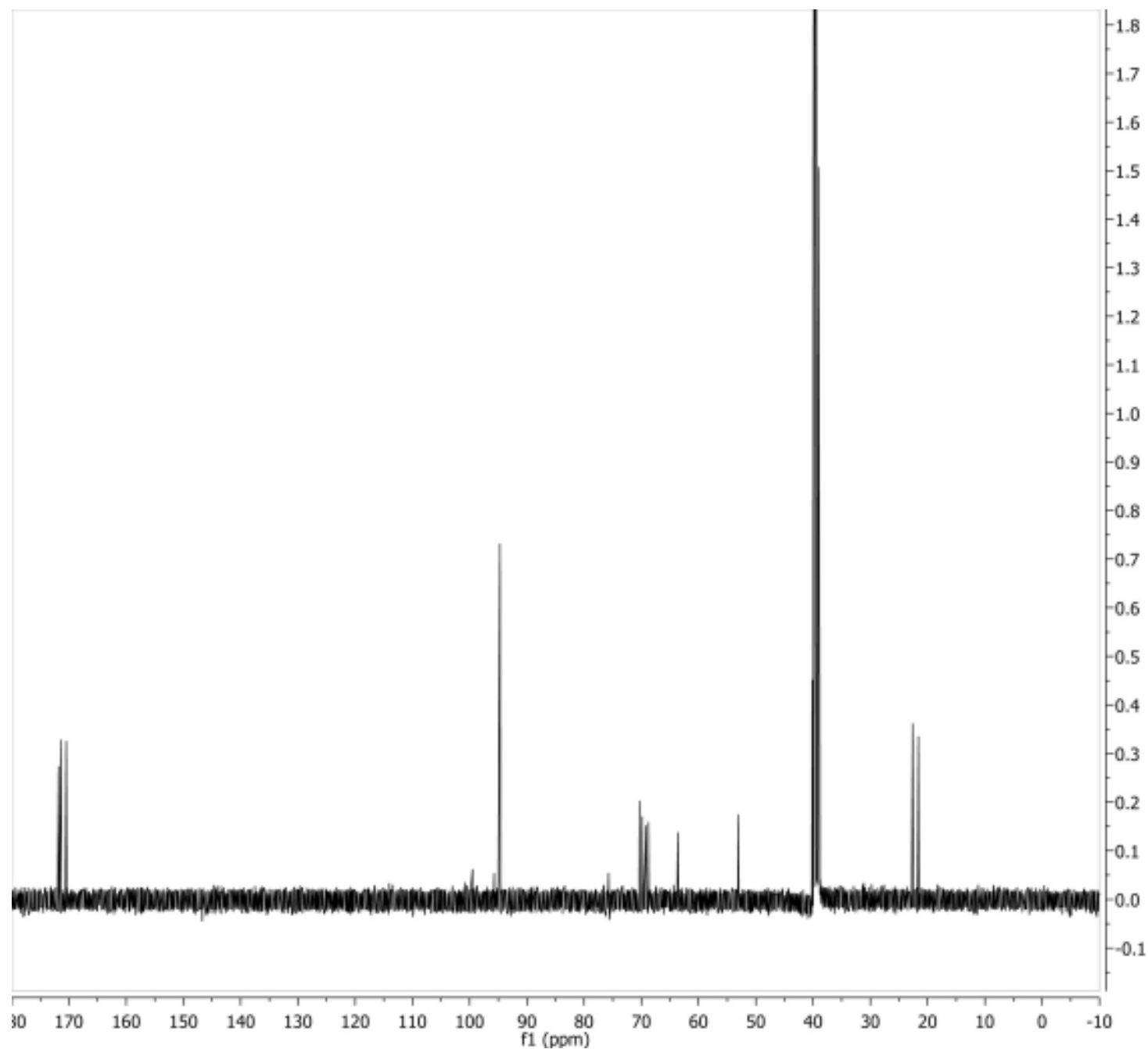




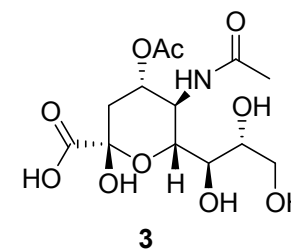


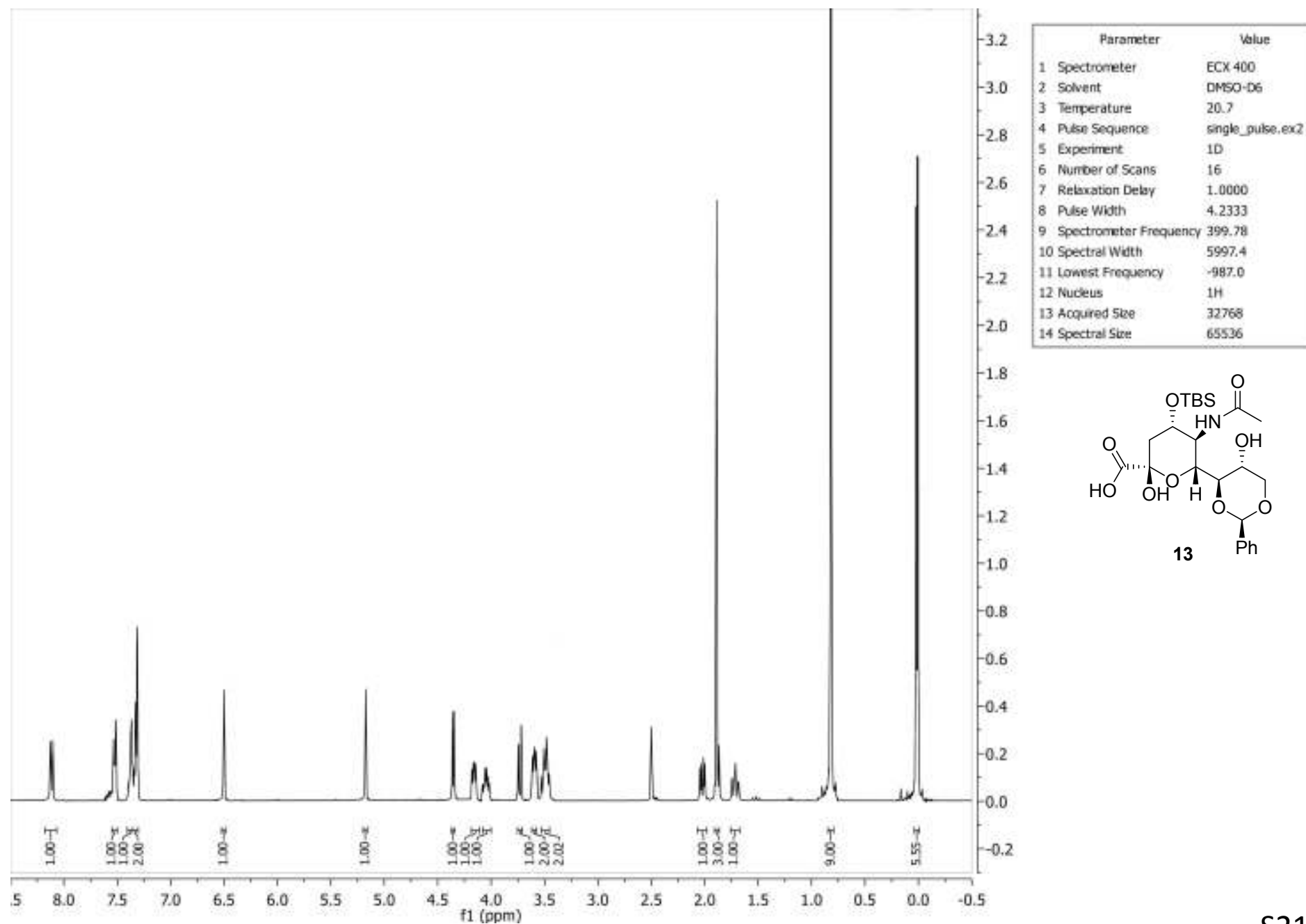
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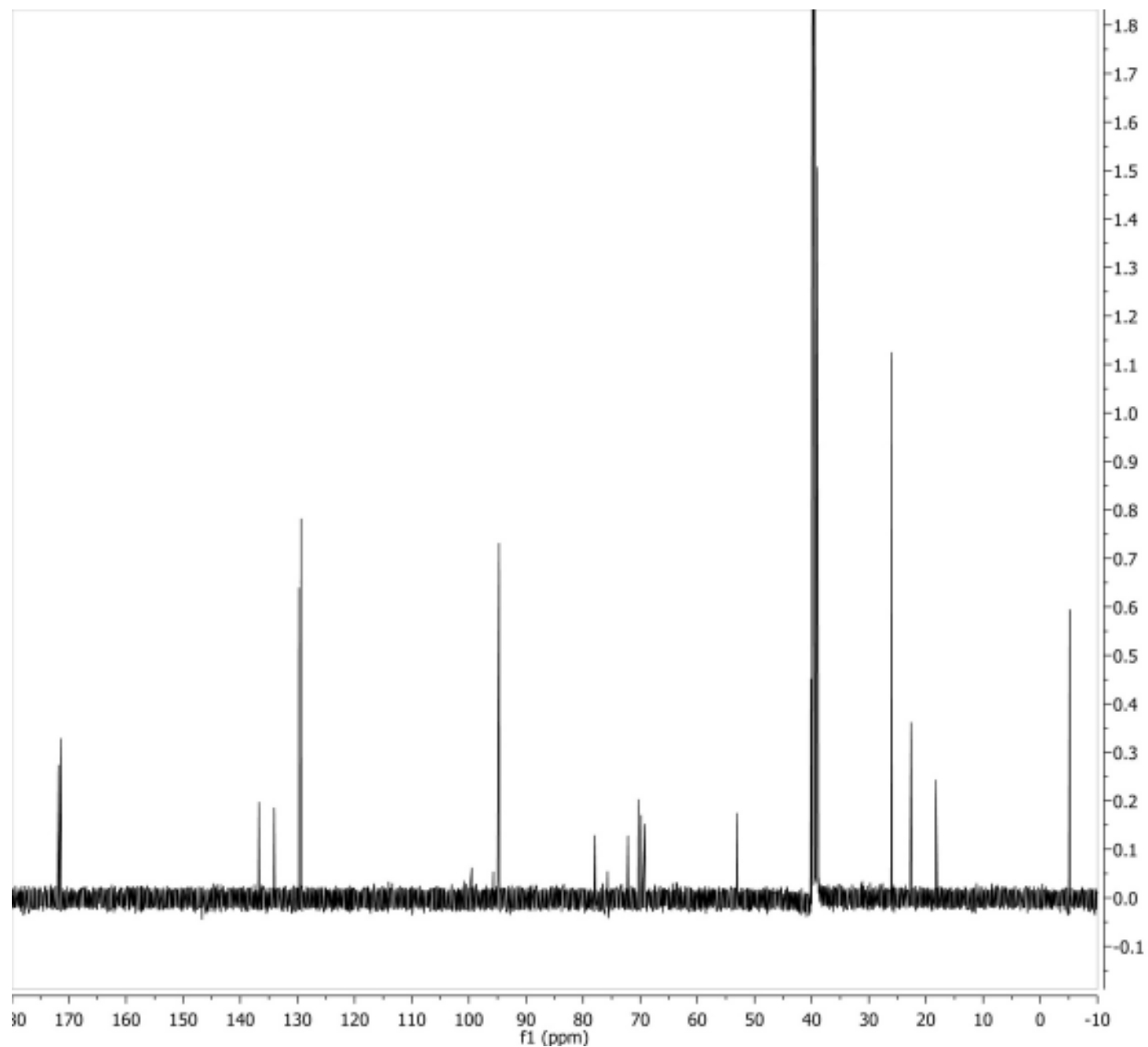




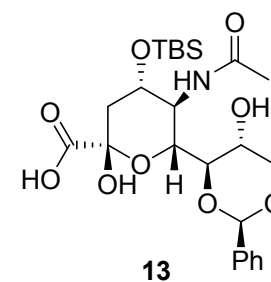
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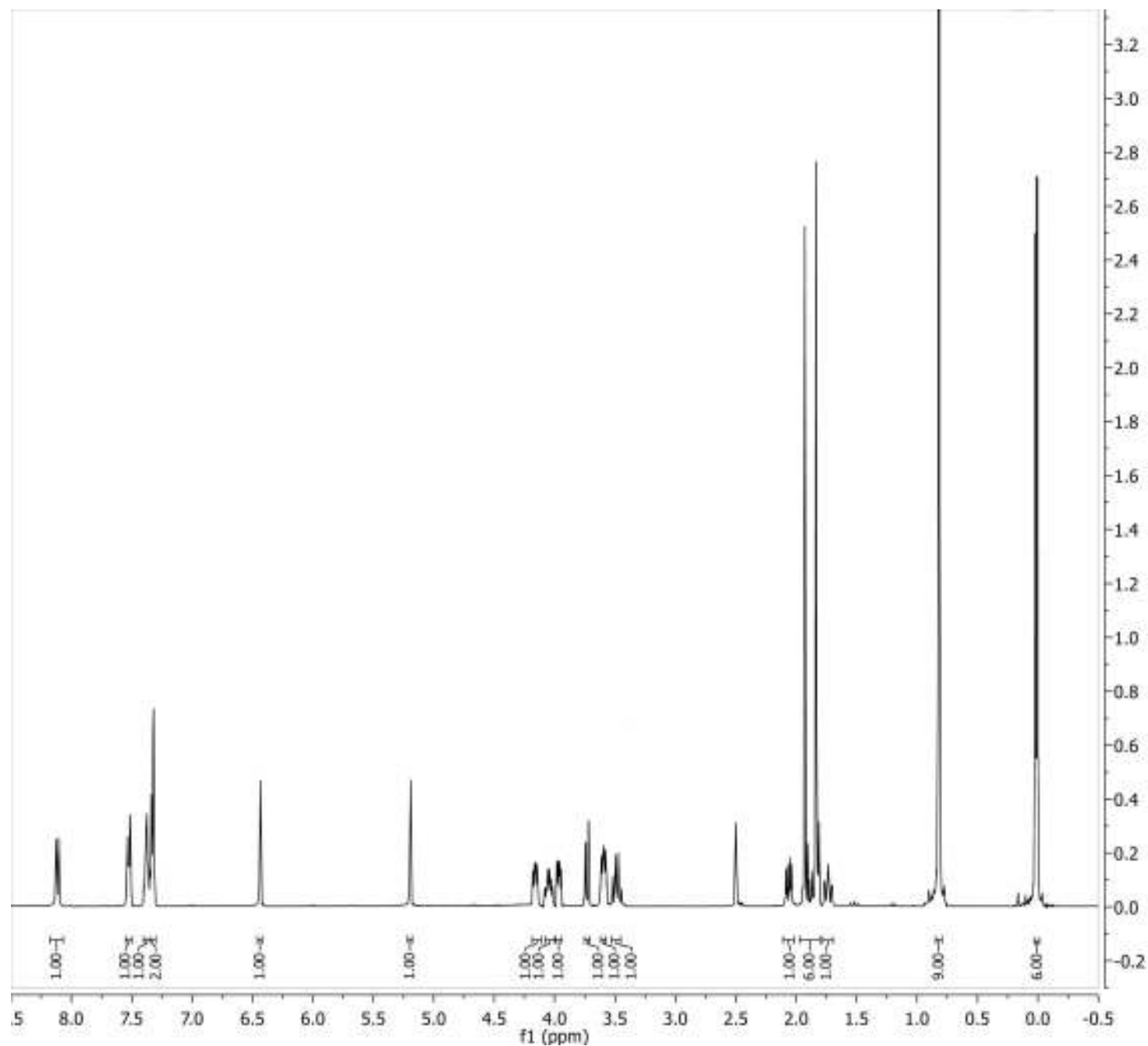




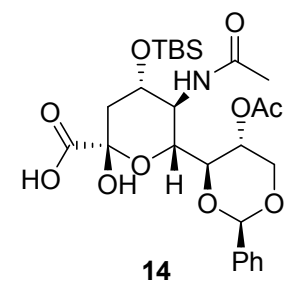


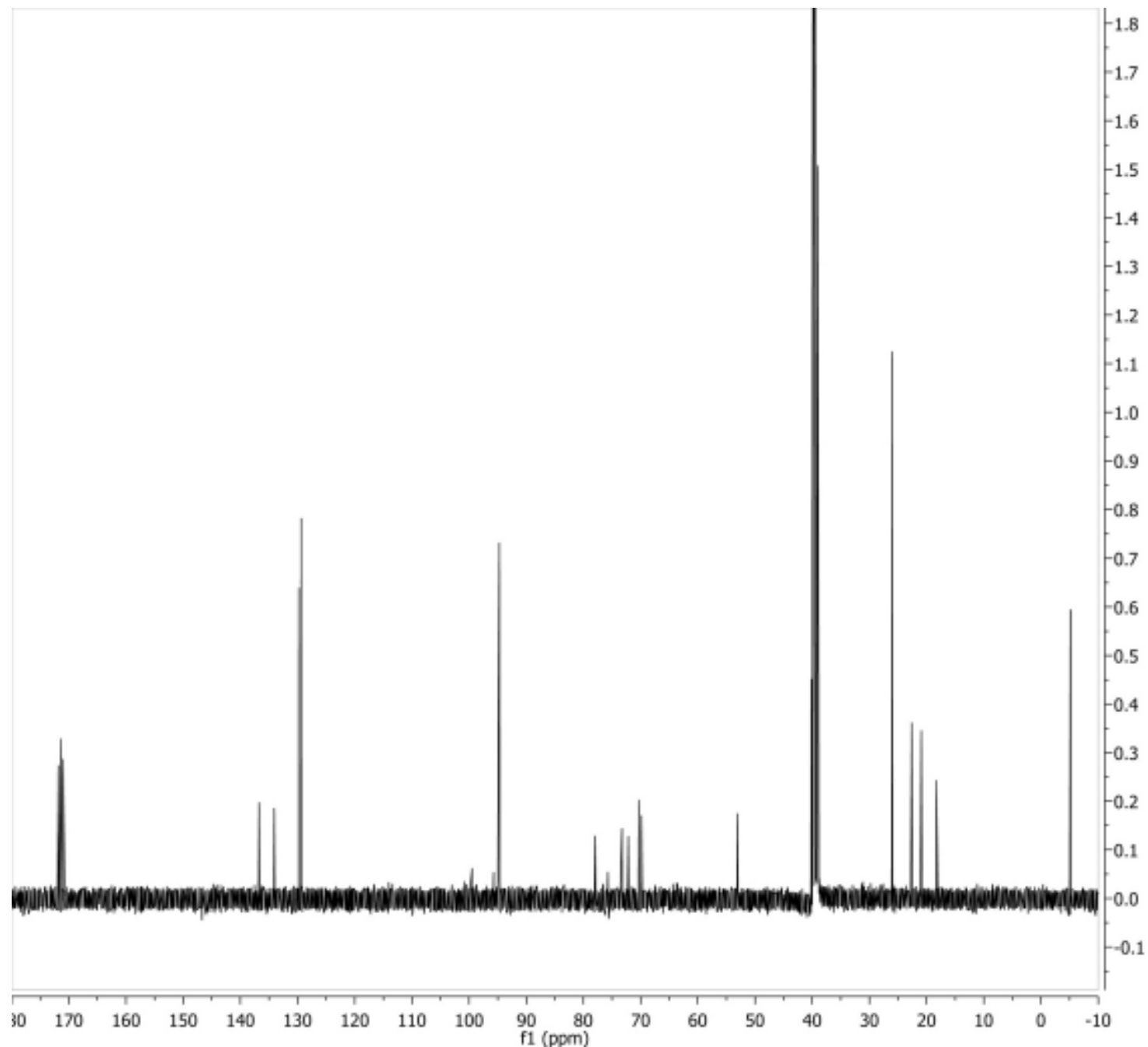
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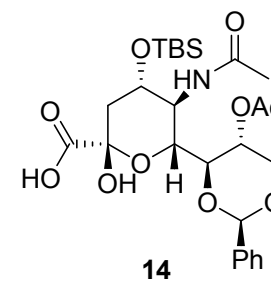


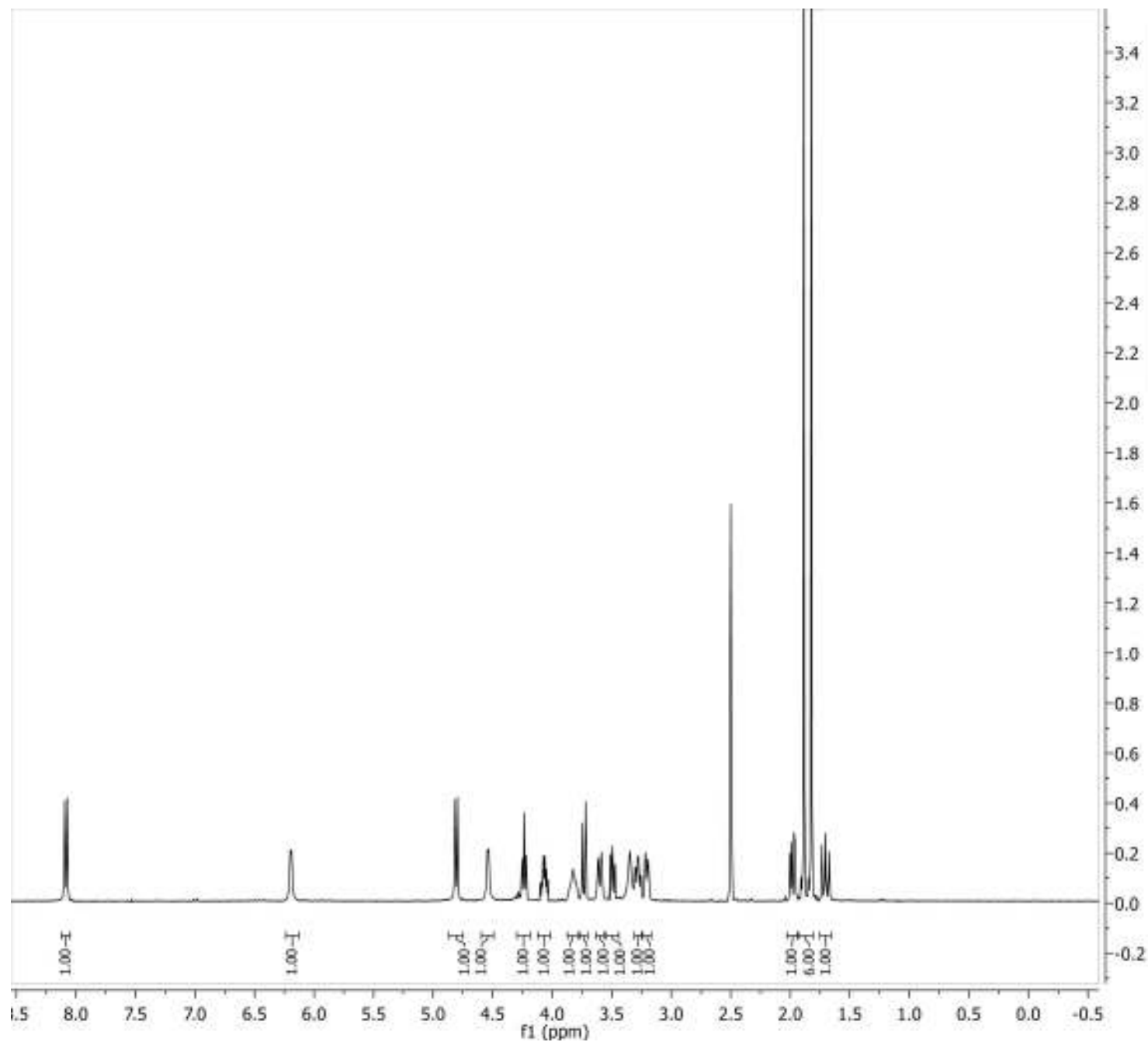
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13 Acquired Size	32768
14 Spectral Size	65536



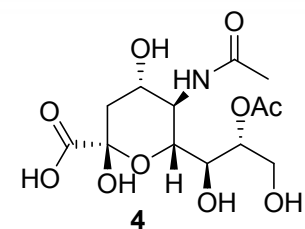


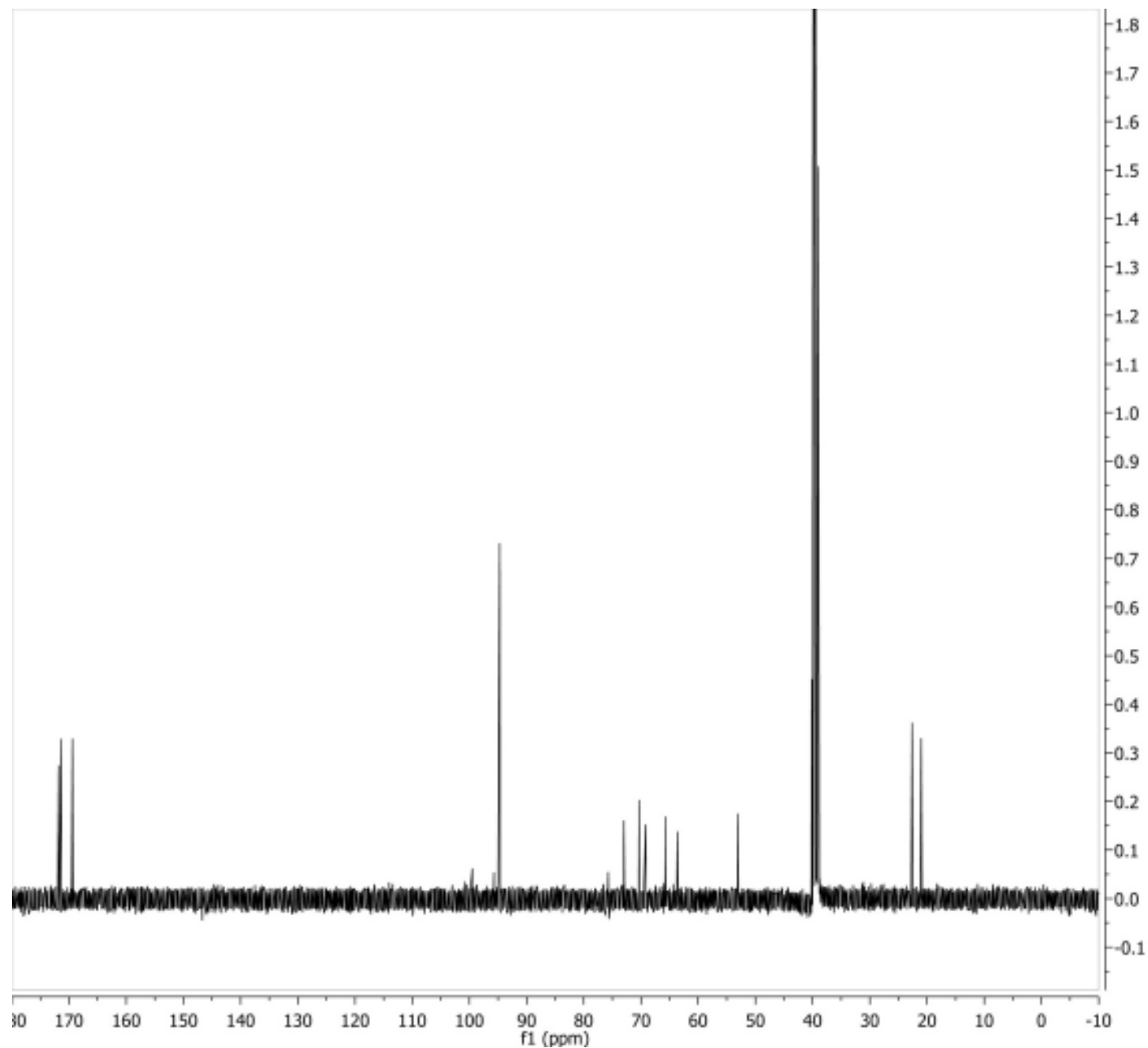
Parameter	Value
1 Spectrometer	ECX 400
2 Solvent	DMSO-D6
3 Temperature	22.8
4 Pulse Sequence	single_pulse_dec
5 Experiment	1D
6 Number of Scans	1024
7 Relaxation Delay	1.5000
8 Pulse Width	3.4333
9 Spectrometer Frequency	100.53
10 Spectral Width	25138.3
11 Lowest Frequency	-2567.6
12 Nucleus	13C
13 Acquired Size	32768
14 Spectral Size	65536



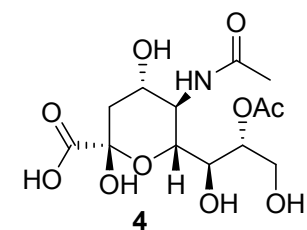


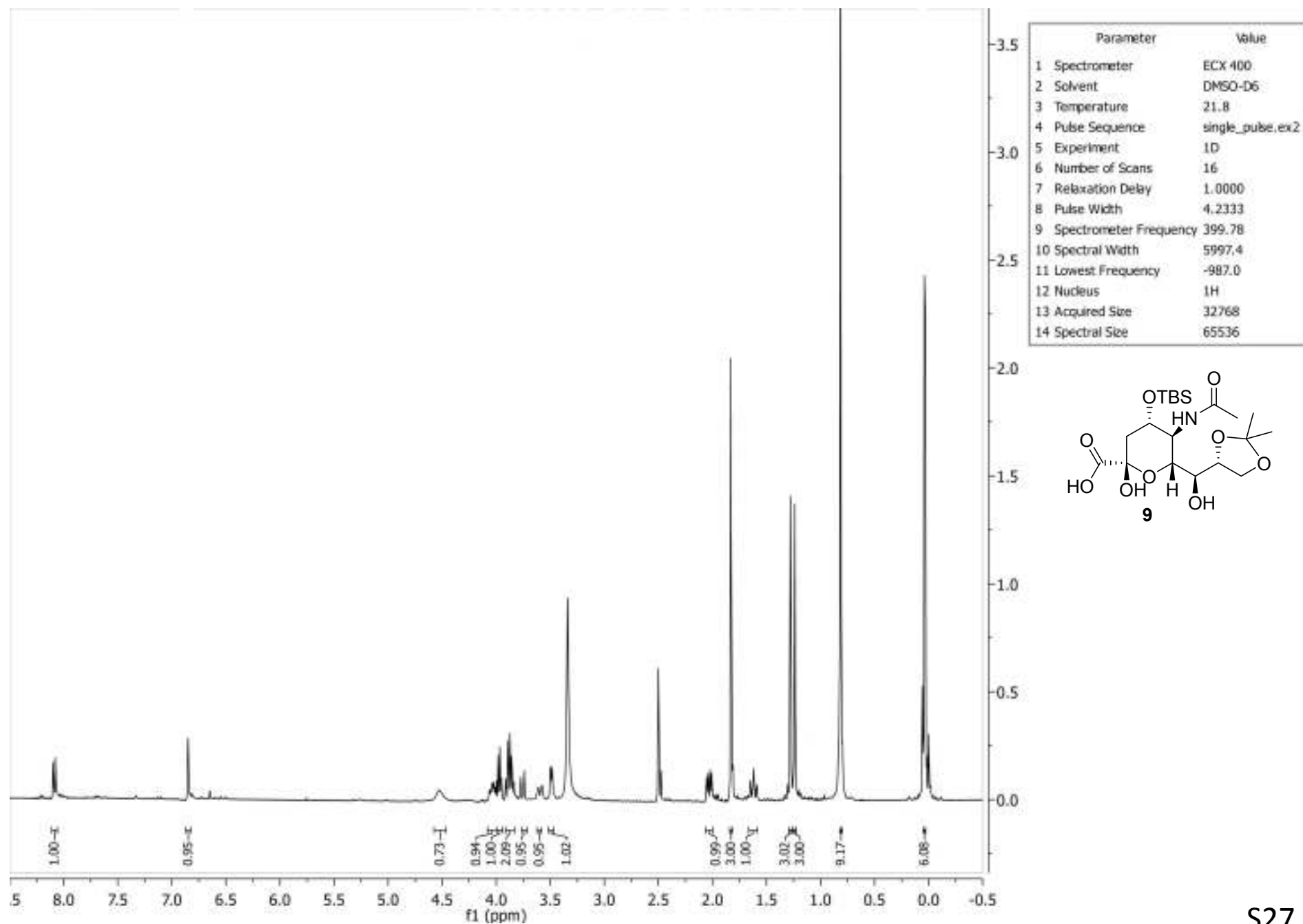
Parameter	Value
1 Spectrometer	ECX 400
2 Solvent	DMSO-D6
3 Temperature	19.9
4 Pulse Sequence	single_pulse.ex2
5 Experiment	1D
6 Number of Scans	16
7 Relaxation Delay	1.0000
8 Pulse Width	4.2333
9 Spectrometer Frequency	399.78
10 Spectral Width	9996.0
11 Lowest Frequency	-1986.4
12 Nucleus	1H
13 Acquired Size	32768
14 Spectral Size	65536

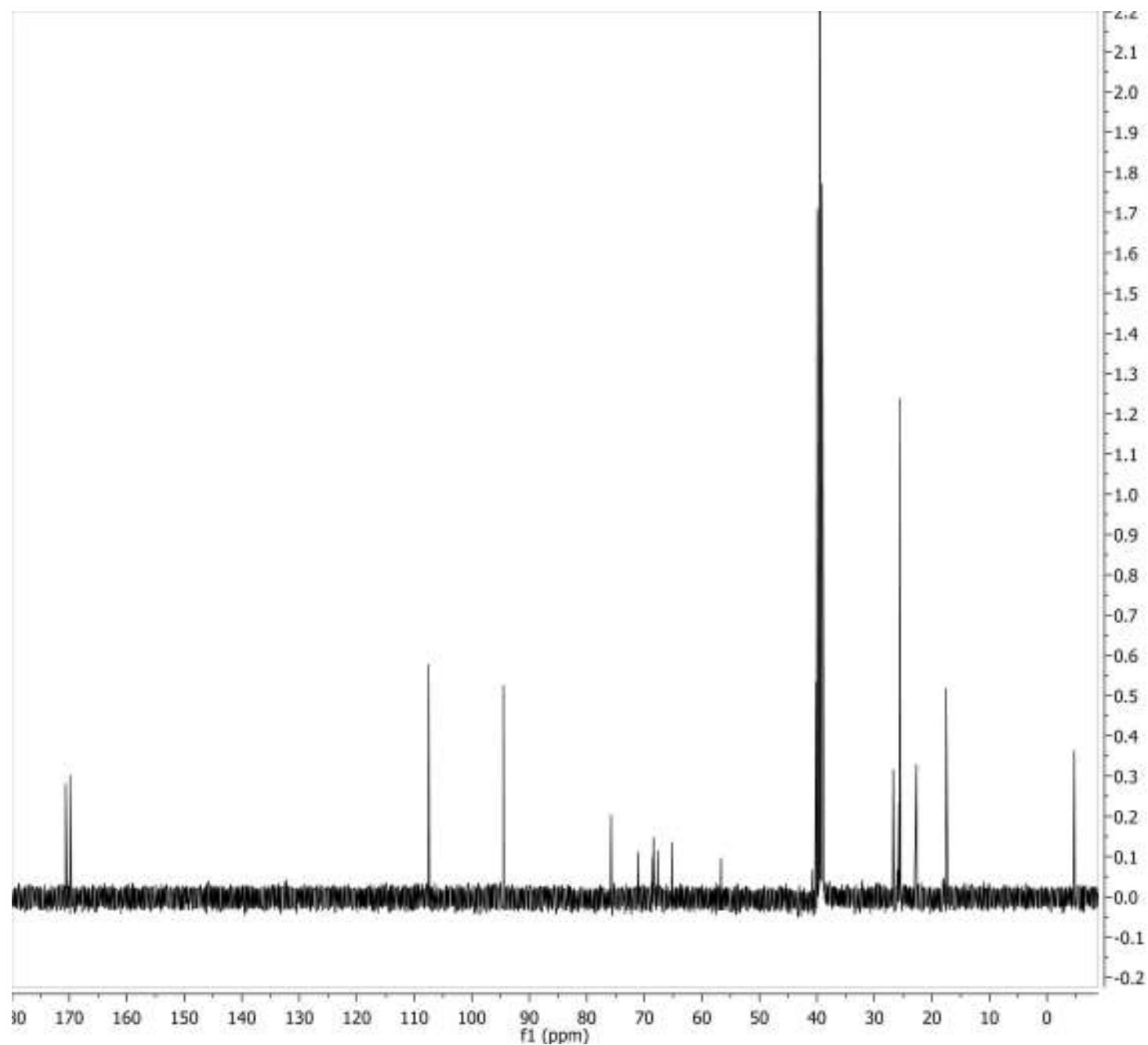




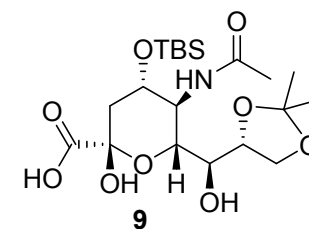
Parameter	Value
1 Spectrometer	ECX 400
2 Solvent	DMSO-D6
3 Temperature	22.8
4 Pulse Sequence	single_pulse_dec
5 Experiment	1D
6 Number of Scans	1024
7 Relaxation Delay	1.5000
8 Pulse Width	3.4333
9 Spectrometer Frequency	100.53
10 Spectral Width	25138.3
11 Lowest Frequency	-2567.6
12 Nucleus	13C
13 Acquired Size	32768
14 Spectral Size	65536

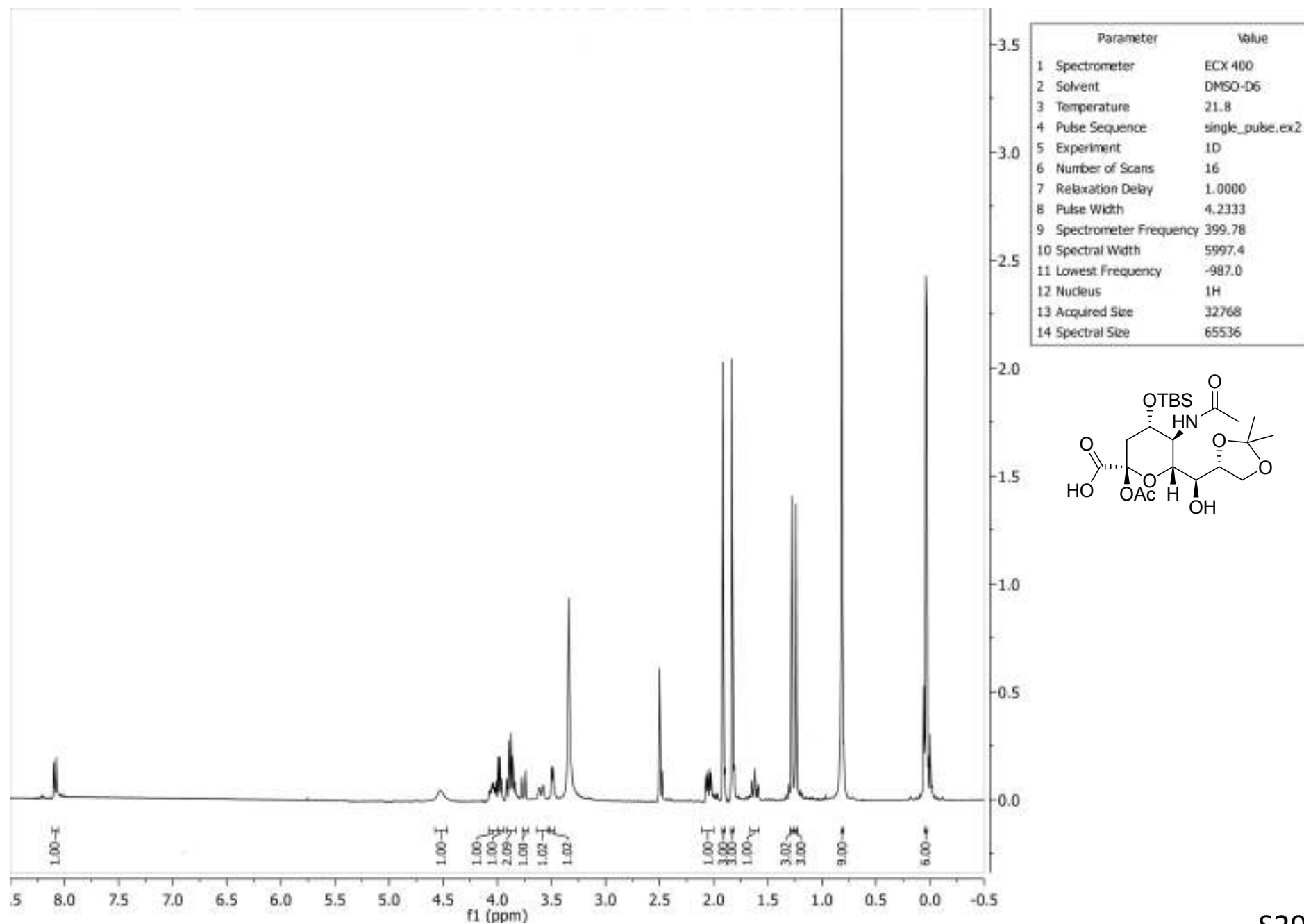


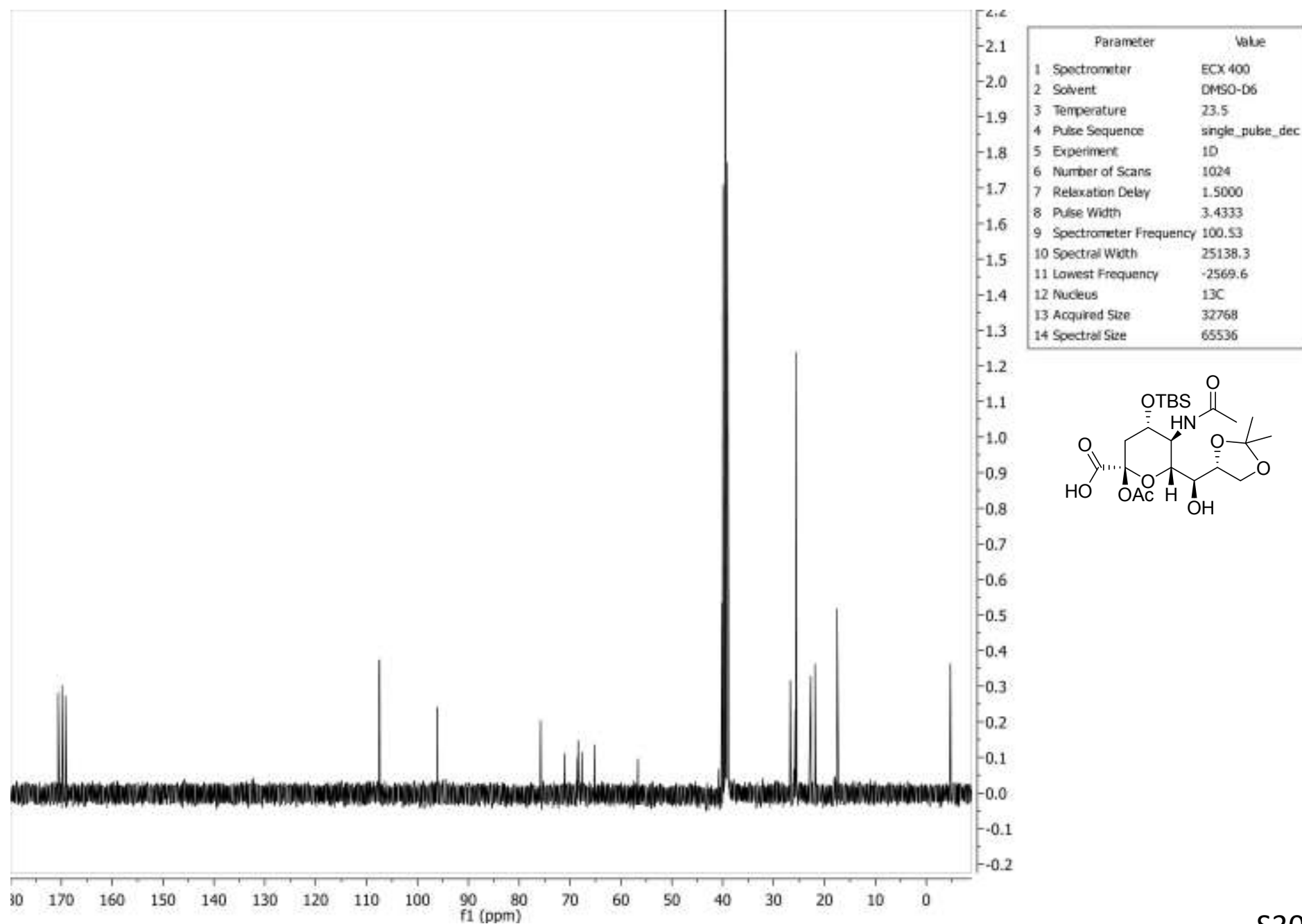


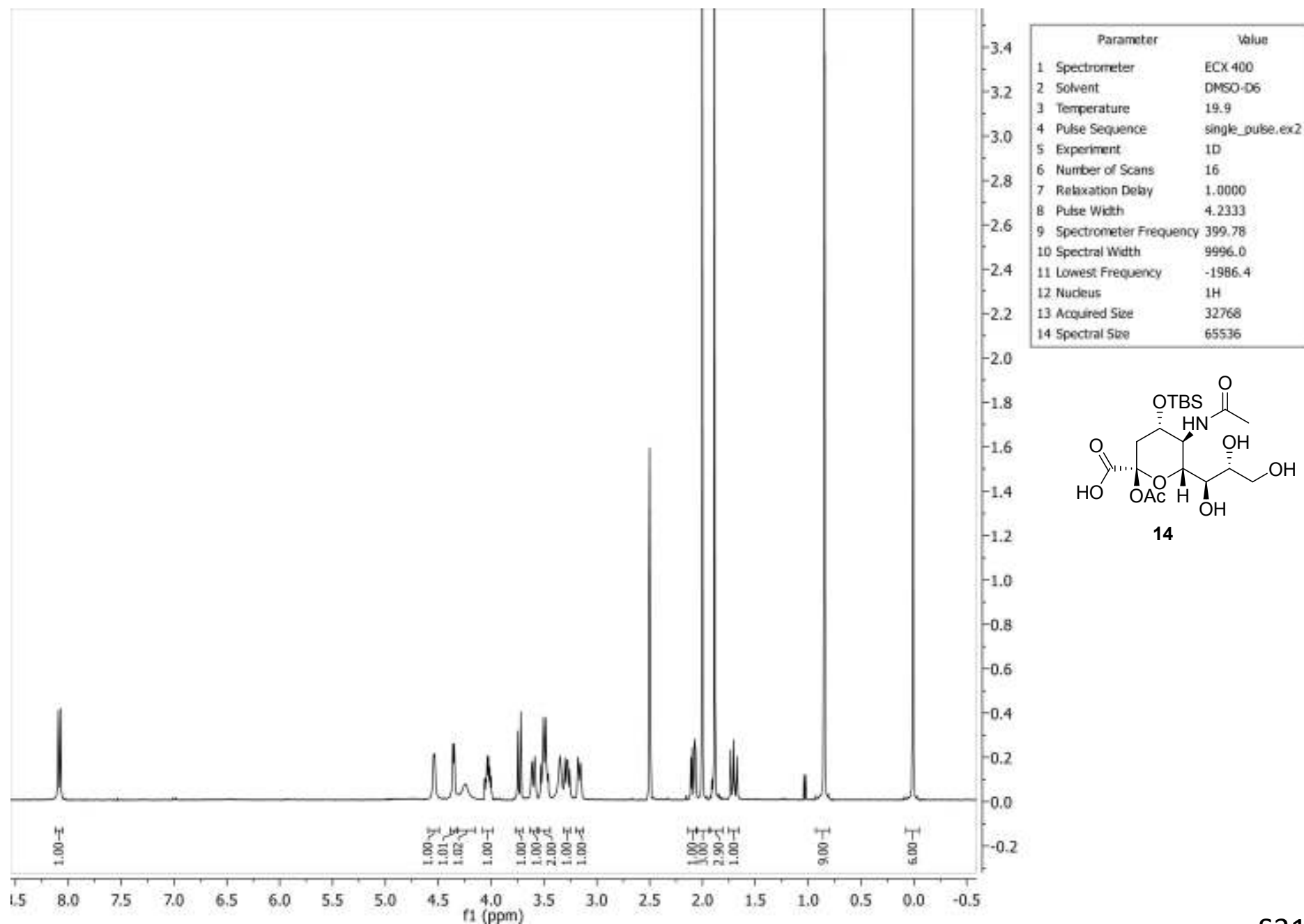


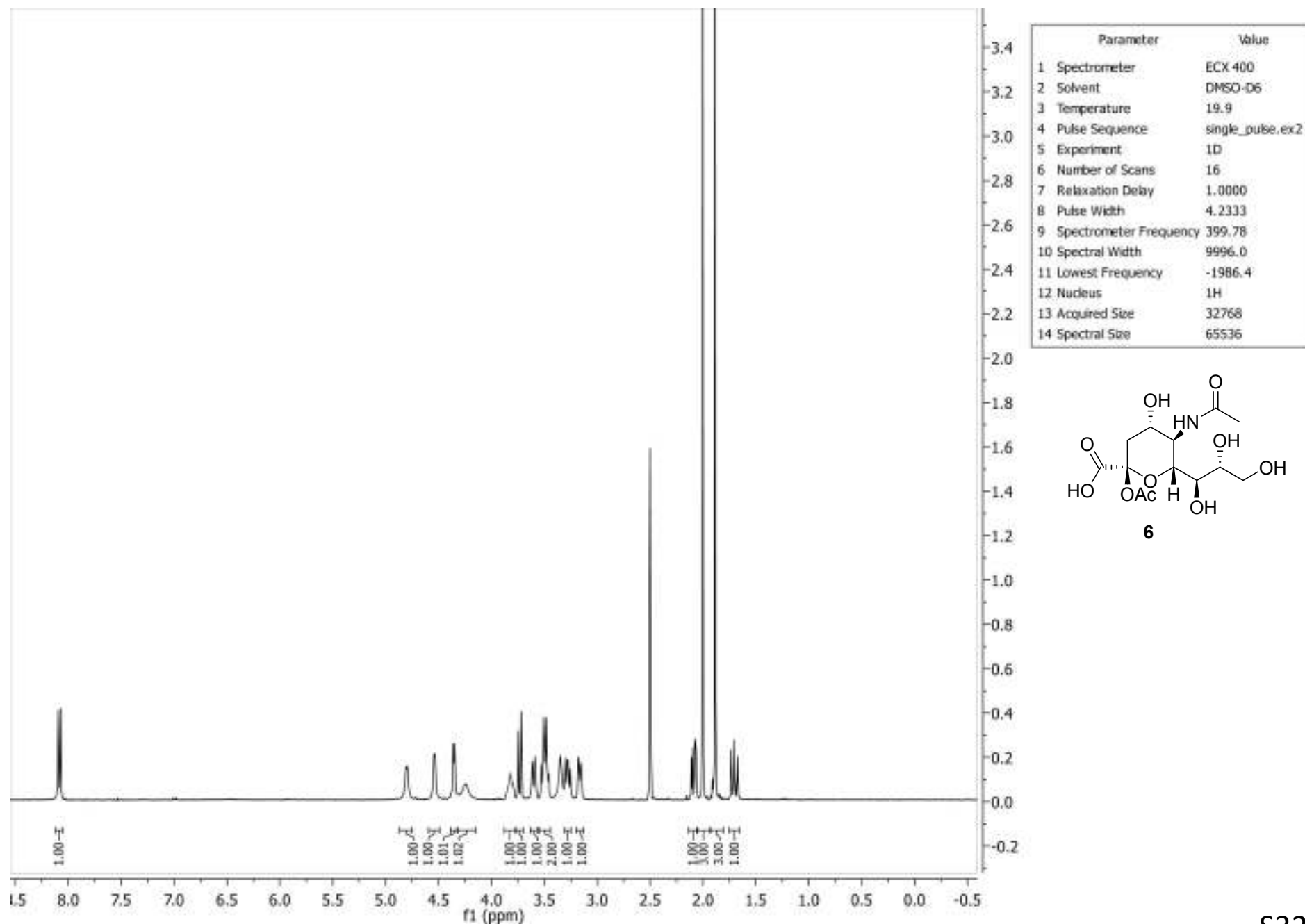
Parameter	Value
1 Spectrometer	ECX 400
2 Solvent	DMSO-D6
3 Temperature	23.5
4 Pulse Sequence	single_pulse_dec
5 Experiment	1D
6 Number of Scans	1024
7 Relaxation Delay	1.5000
8 Pulse Width	3.4333
9 Spectrometer Frequency	100.53
10 Spectral Width	25138.3
11 Lowest Frequency	-2569.6
12 Nucleus	13C
13 Acquired Size	32768
14 Spectral Size	65536

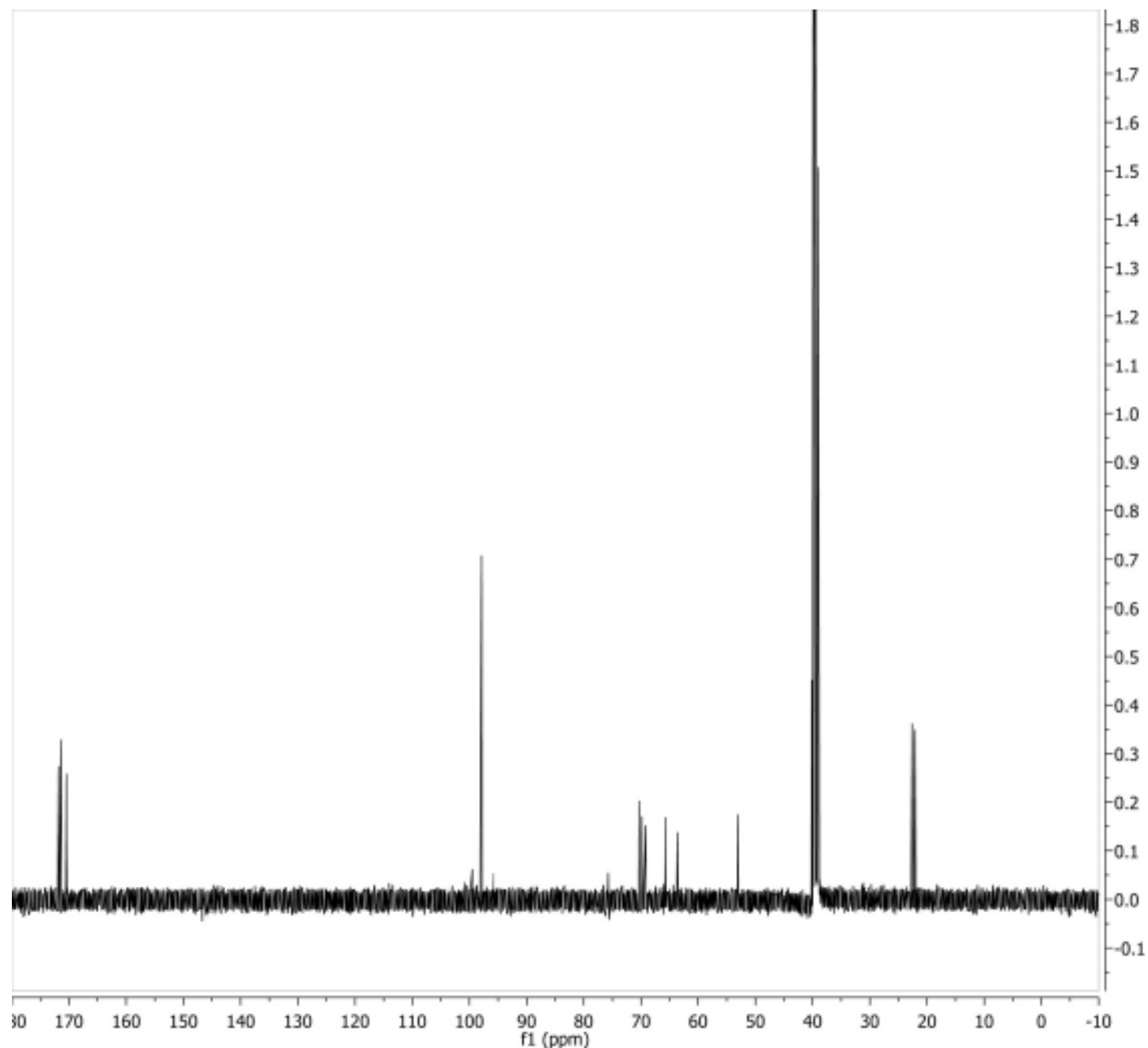




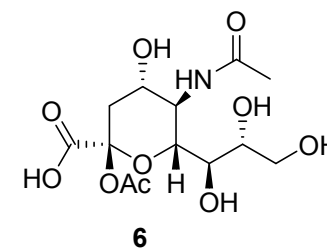


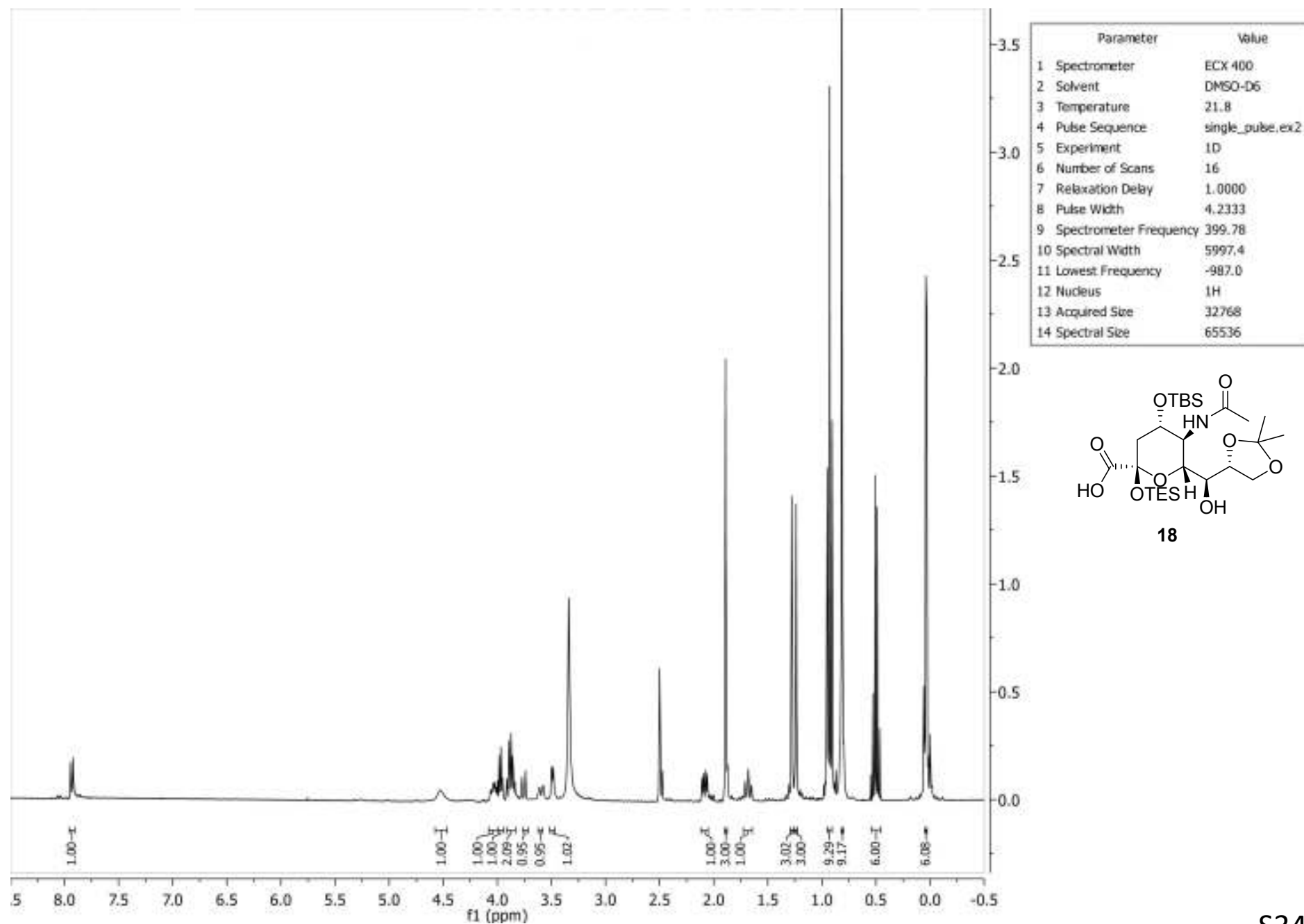


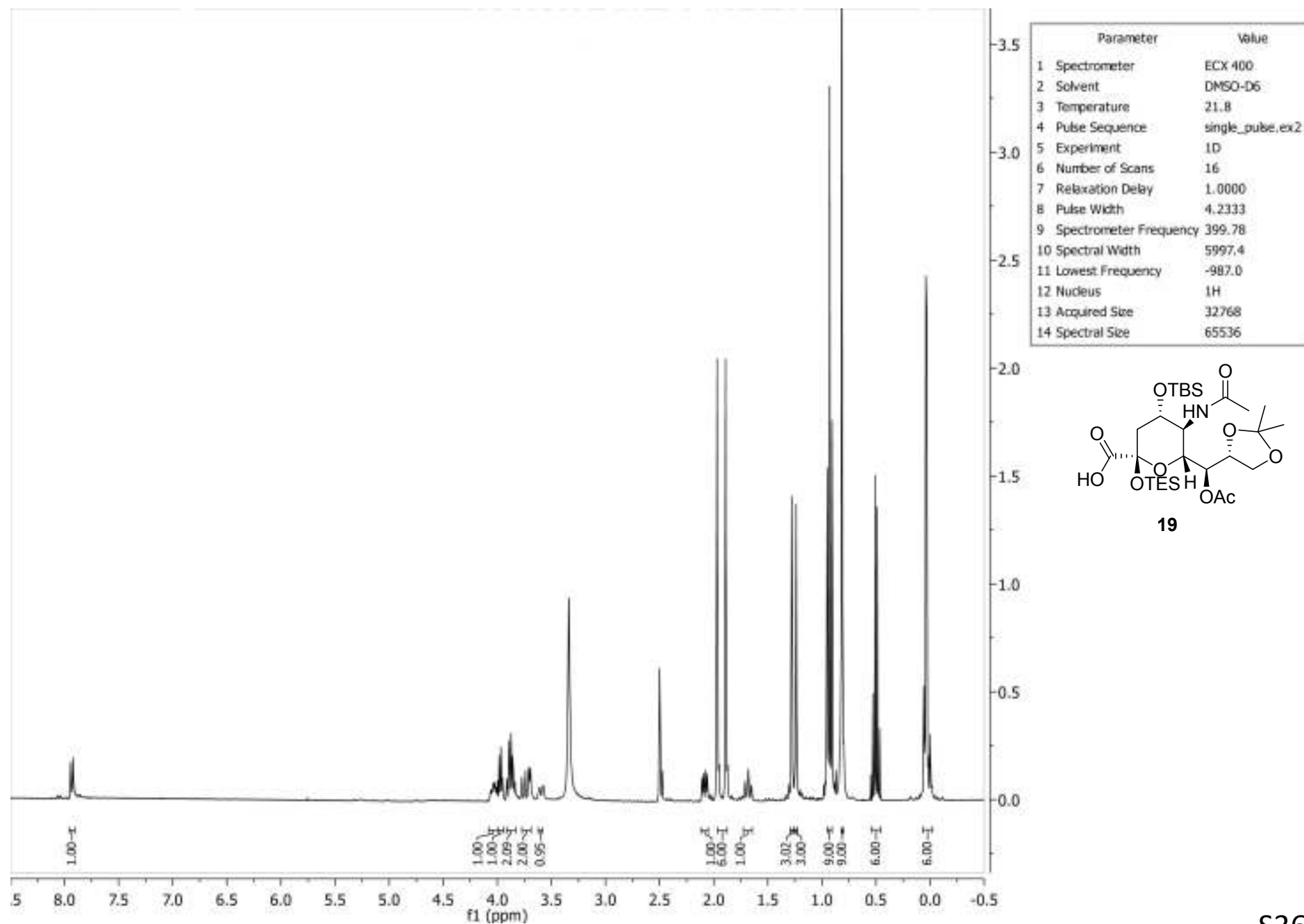


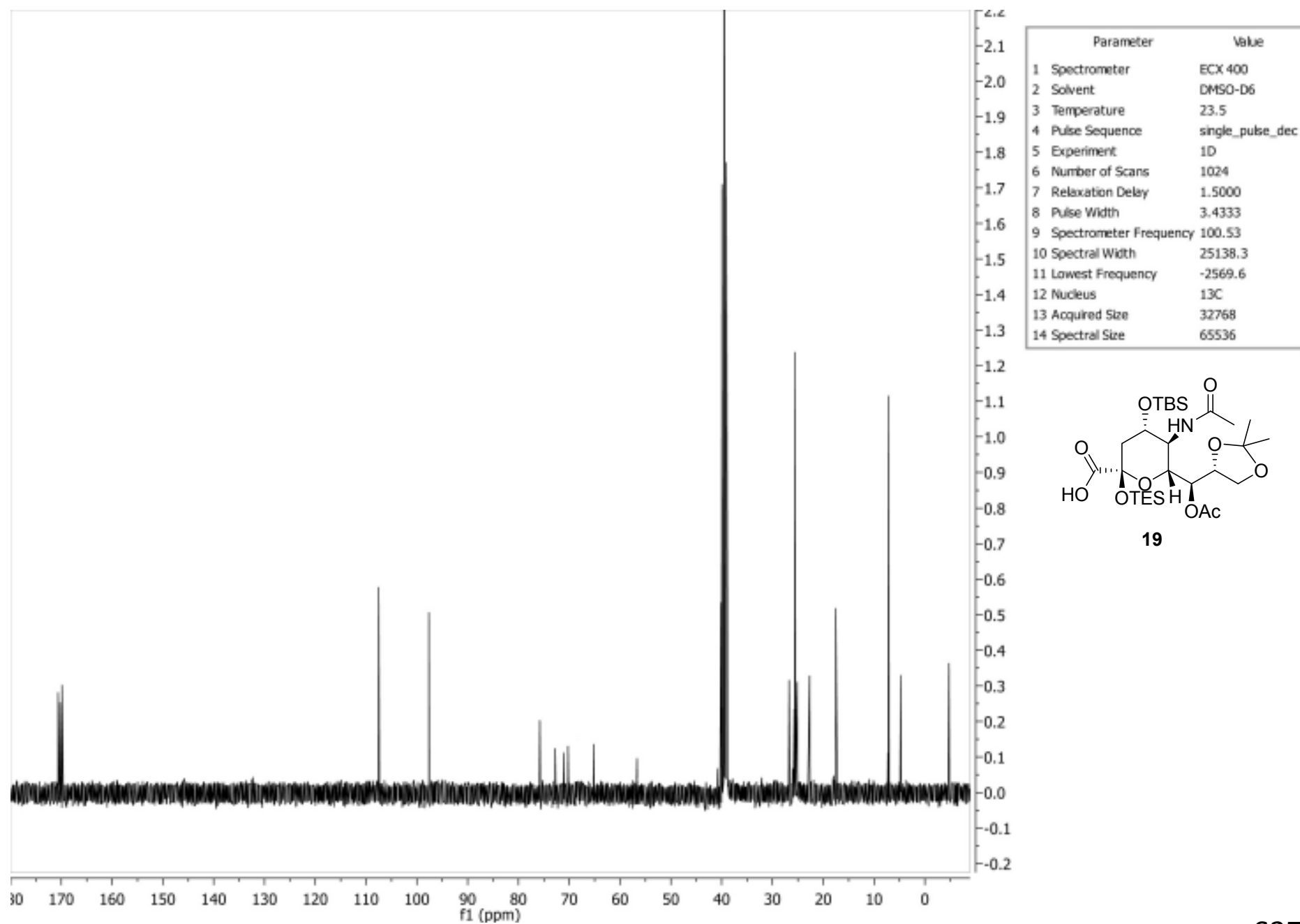


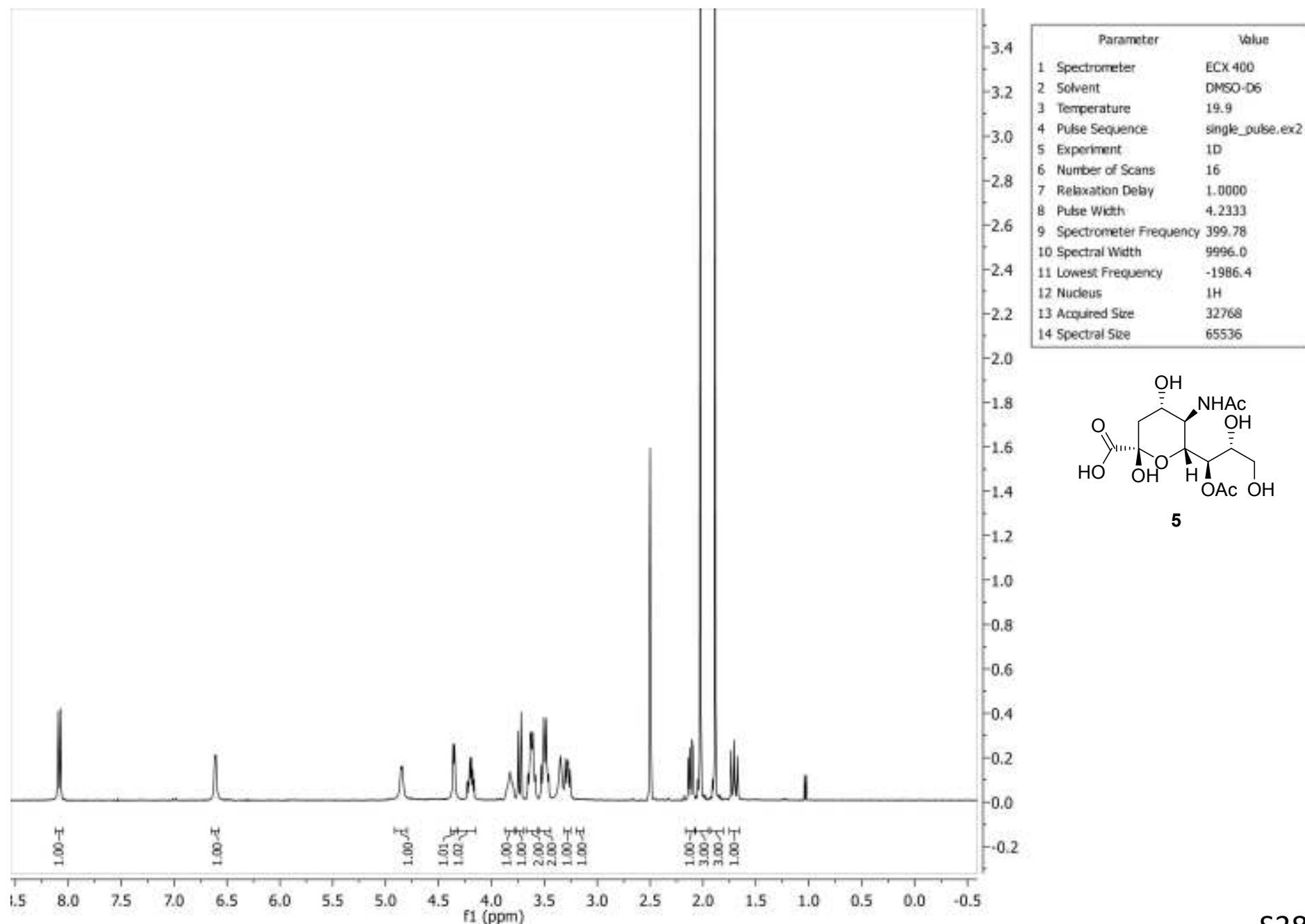
Parameter	Value
1 Spectrometer	ECX 400
2 Solvent	DMSO-D6
3 Temperature	22.8
4 Pulse Sequence	single_pulse_dec
5 Experiment	1D
6 Number of Scans	1024
7 Relaxation Delay	1.5000
8 Pulse Width	3.4333
9 Spectrometer Frequency	100.53
10 Spectral Width	25138.3
11 Lowest Frequency	-2567.6
12 Nucleus	13C
13 Acquired Size	32768
14 Spectral Size	65536

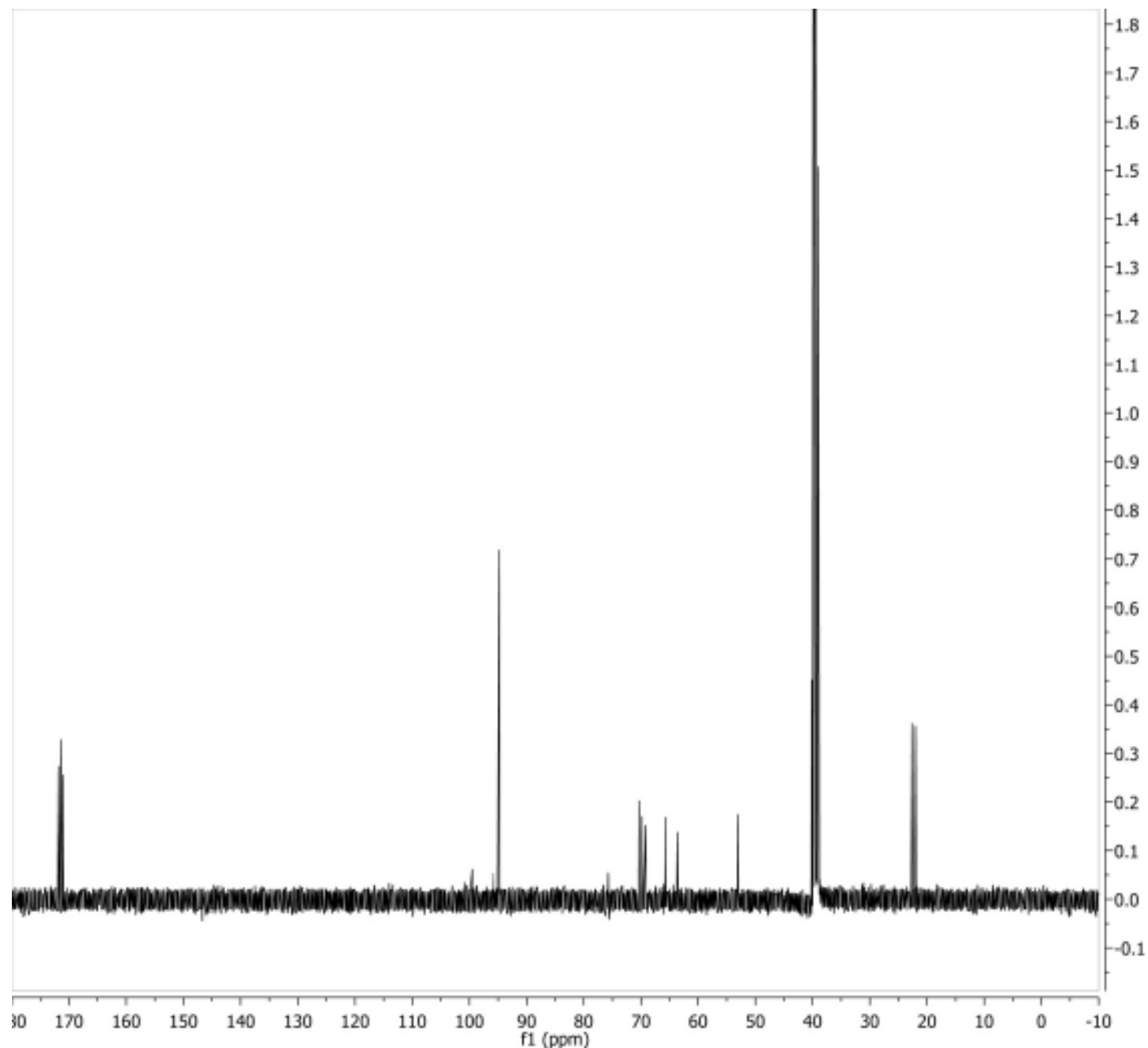












Parameter	Value
1 Spectrometer	ECX 400
2 Solvent	DMSO-D6
3 Temperature	22.8
4 Pulse Sequence	single_pulse_dec
5 Experiment	1D
6 Number of Scans	1024
7 Relaxation Delay	1.5000
8 Pulse Width	3.4333
9 Spectrometer Frequency	100.53
10 Spectral Width	25138.3
11 Lowest Frequency	-2567.6
12 Nucleus	13C
13 Acquired Size	32768
14 Spectral Size	65536

