:Supporting Information

Synthesis of *S*-Glycosyl Primary Sulfonamides

Marie Lopez, Nicolas Drillaud, Laurent F. Bornaghi and Sally-Ann Poulsen*

Eskitis Institute, Griffith University, Brisbane, Queensland 4111, Australia

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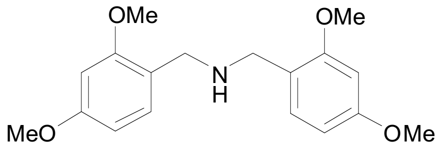
General

All starting materials and reagents, including per-*O*-acetylated sugars, were purchased from commercial suppliers with the exception of methyl 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranuronate which was synthesized as described in the literature.[1] All reactions were monitored by TLC. TLC plates were visualized with UV light, sulphuric acid stain (5% H_2SO_4 in ethanol) and/or orcinol stain (1 g of orcinol monohydrate in a mixture of EtOH:H_2O:H_2SO_4 72.5:22.5:5). Silica gel flash chromatography was performed using silica gel 60 Å (230-400 mesh). Reverse phase chromatography was performed using C-18 silica pre-packed cartridges and eluted with a gradient of H_2O–MeOH (from 100:0 to 0:100) and 11 fractions collected. ^{1}H NMR were run at 400 and 500 MHz and ^{13}C NMR at 125 MHz. For ^{1}H and ^{13}C NMR run in $CDCl_3$ chemical shifts (δ) are reported in ppm relative to the solvent residual peak: proton (δ = 7.27 ppm) and carbon (δ = 77.2 ppm). Chemical shifts for ^{1}H and ^{13}C NMR run in DMSO are reported in ppm relative to residual solvent proton (δ = 2.50 ppm) and carbon (δ = 39.5 ppm) signals, respectively. For ^{1}H NMR run in D_2O chemical shifts are reported in ppm relative to the solvent residual peak: proton (δ = 4.80 ppm). Multiplicity is indicated as follows: s (singlet); d (doublet); t (triplet); m (multiplet); dd (doublet of doublet); ddd (doublet of doublet of doublet); br s (broad singlet). Coupling constants are reported in Hertz (Hz). Melting points are uncorrected. Mass spectra (low and high resolution) were recorded using electrospray as the ionization technique in positive ion negative ion modes as stated. All MS analysis samples were prepared as solutions in methanol. Optical rotation were measured at 25 °C and reported as an average of ten measurements.



Bis(2,4-dimethoxybenzyl)amine

2,4-Dimethoxybenzaldehyde (20.00 g, 0.12 mol, 1.0 equiv.) and benzotriazole (14.34 g, 0.12 mol, 1.0 equiv.) were added to a solution of NH_3 in MeOH (2 M, 91 mL, 1.5 equiv.) and stirred at room temperature (rt) overnight. The solids entered solution and over time a white precipitate formed. This intermediate benzotriazole derivative was collected by filtration, washed with anhydrous MeOH and dried under high vacuum (23.95 g, 55.4 mmol, 92%) before being resuspended in anhydrous THF (360 mL) under argon at 0 °C. A solution of $LiAlH_4$ (1.0 M, 120 mL, 120 mmol, 2.2 equiv.) was added dropwise to the cooled solution which became homogeneous. Stirring was maintained at 0 °C for 3 h. The reaction was quenched by the slow addition of ice and the resulting emulsion filtered through celite and washed with diethyl ether. The filtrate layers were separated and the aqueous layer extracted with diethyl ether (×2). The organic extracts were combined, washed with brine (×3), dried over $MgSO_4$, filtered, and solvent removed followed by co-evaporation toluene (× 2). The title compound was obtained as yellow oil which solidified on standing (15.11 g, 47.6 mmol, 86%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.16 (t, J = 7.5 Hz, 1H, N*H*), 7.08 (d, J = 7.5 Hz, 2H, $H_{arom.}$), 6.35 (s, 2H, $H_{arom.}$), 6.33 (d, J = 7.5 Hz, 2H, $H_{arom.}$), 3.70 (s, 6H, OCH_3), 3.69 (s, 6H, OCH_3), 3.64 (s, 4H, $NHCH_2$) assignments were confirmed by ^{1}H-^{1}H gCOSY. LRMS (ESI$^+$): m/z = 429 [M + Na]$^+$.

1-*S*-Acetyl-2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (1). General Procedure 1. To a solution of per-*O*-acetylated D-glucose (3.99 g, 10.2 mmol, 1.0 equiv.) in acetonitrile (40 mL) was added thiourea (1.01 g, 13.3 mmol, 1.3 equiv.) and boron trifluoride diethyl etherate (2.7 mL, 21.5 mmol, 2.1 equiv.). The reaction mixture was refluxed until starting material was consumed (~30 min) then let cool to rt. Acetic anhydride (2.4 mL, 25.4 mmol, 2.5 equiv.) and Et_3N (6.4 mL, 45.9 mmol, 4.5 equiv.) were added and the solution stirred at rt overnight in the absence of light. The reaction mixture was concentrated and the residue diluted in dichloromethane (CH_2Cl_2) before washing with aqueous 5% HCl (×1) and brine (×2). The aqueous extracts were combined and back extracted with CH_2Cl_2 (×2). The organic extracts were combined, dried over $MgSO_4$, filtered and evaporated. The residue was recrystallized from ethanol, to afford light yellow crystals of **1** (2.86 g, 7.04 mmol, 69%). R_f = 0.56 (1:1

EtOAc–hexane). mp = 105-107 °C. [ ]$^{25}_{D}$ = + 9 (c = 1.0, chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.27 (t, J = 9.5 Hz, 1H, H-3), 5.26 (d, J = 10.0 Hz, 1H, H-1), 5.13 (t, J = 9.5 Hz, 1H, H-2), 5.11 (t, J = 9.0 Hz, 1H, H-4), 4.26 (dd, J = 12.0, 4.5 Hz, 1H, H-6a), 4.26 (dd, J = 12.0, 2.0 Hz, 1H, H-6b), 3.84 (ddd, J = 12.0, 4.5, 2.0 Hz, 1H, H-5), 2.39 (s, 3H, SCOCH_3), 2.08, 2.03, 2.02, 2.01 (4 × s, 12H, OCOCH_3), assignments were confirmed by ^{1}H-^{1}H gCOSY. LRMS (ESI^{+}): m/z = 429 [M + Na]$^{+}$. Analytical data are consistent with values reported in the literature.[2]

1-*S*-Acetyl-2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-galactopyranose (6). The title compound was prepared from per-*O*-acetylated D-galactose (10.01 g, 25.6 mmol) as described in general procedure 1 and was isolated as light colored crystals (7.21 g, 17.7 mmol, 69%). R_f = 0.55 (1:1 EtOAc–hexane). mp = 99-103 °C. [ ]$^{25}_{D}$ = + 29 (c = 1.0, chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.46 (d, J = 3.5 Hz, 1H, H-4), 5.33 (t, J = 10.0 Hz, 1H, H-2), 5.26 (d, J = 10.0 Hz, 1H, H-1), 5.12 (dd, J = 3.5, 10.0 Hz, 1H, H-3), 4.10 (m, 3H, H-5, H-6a, H-6b), 2.40 (s, 3H, SCOCH_3), 2.16, 2.05, 2.04, 1.99 (4 × s, 12H, OCOCH_3), assignments were confirmed by ^{1}H-^{1}H gCOSY. LRMS (ESI^{+}): m/z = 429 [M + Na]$^{+}$. Analytical data are consistent with values reported in the literature.[3]

Methyl 1-*S*-acetyl-2,3,4-tetra-*O*-acetyl-1-thio-β-D-glucopyranuronate (7). The title compound was prepared from methyl 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranuronate (4.00 g, 10.6 mmol) as described in general procedure 1 and was isolated as light yellow crystals (1.95 g, 4.97 mmol, 47%). R_f = 0.54 (1:1 EtOAc–hexane). mp = 149-150 °C. [ ]$^{25}_{D}$ = + 19 (c = 1.1, chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.34 (t, J = 9.5 Hz, 1H, H-3), 5.31 (d, J = 10.0 Hz, 1H, H-1), 5.21 (t, J = 10.0 Hz, 1H, H-4), 5.15 (t, J = 9.5 Hz, 1H, H-2), 4.17 (d, J = 10 Hz, 1H, H-5), 3.74 (s, 3H, OCH_3), 2.39 (s, 3H, SCOCH_3), 2.04-2.03 (m, 12H, OCOCH_3), assignments were confirmed by ^{1}H-^{1}H gCOSY. LRMS (ESI^{+}): m/z = 415 [M + Na]$^{+}$. Analytical data are consistent with values reported in the literature.[4]

(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-1,2,3,6-tetra-*O*-acetyl-1-*S*-acetyl-1-thio-β-D-glucopyranose (8). The title compound was prepared from per-*O*-acetylated lactose (4.00 g, 5.89 mmol) as described in general procedure 1. Expected compound **8** (3.23 g, 4.65 mmol, 79%) was isolated as a white solid following purification by flash chromatography (1:1 EtOAc–hexane). R_f = 0.25 (1:1 EtOAc–hexane). mp = 72-75 °C [ ]$^{25}_{D}$ = -3 (c = 1.3, chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.36 (d, J = 3.0 Hz, 1H, H-4'), 5.26

(t, *J* = 9.0 Hz, 1H, H-3), 5.22 (d, *J* = 10.5 Hz, 1H, H-1), 5.12 (dd, *J* = 8.0, 10.5 Hz, 1H, H-2’), 5.05 (t, *J* = 10.5 Hz, 1H, H-2), 4.95 (dd, *J* = 3.0, 10.5 Hz, 1H, H-3’), 4.46 (d, *J* = 8.0 Hz, 1H, H-1’), 4.45 (dd, *J* = 2.0, 10.0 Hz, 1H, H-6a’), 4.15-4.07 (m, 3H, H-6a, H-6b’, H-5’), 3.87 (m, 1H, H-6b), 3.83 (t, *J* = 9.0 Hz, 1H, H-4), 3.76 (m, 1H, H-5), 2.38 (s, 3H, SCOCH_3), 2.16, 2.12, 2.08, 2.05 (6H), 2.03, 1.97 (7 × s, 21H, OCOCH_3), assignments were confirmed by ^{1}H-^{1}H gCOSY. LRMS (ESI$^+$): *m*/*z* = 717 [M + Na]$^+$. Analytical data are consistent with values reported in the literature.[5,6]

(2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl)-(1→4)-1,2,3,6-tetra-*O*-acetyl-1-*S*-acetyl-1-thio-β-D-glucopyranose (9). The title compound was prepared from per-*O*-acetylated maltose (3.07 g, 4.52 mmol) as described in general procedure 1 and was isolated as a white solid following recrystallization from MeOH (2.15 g, 3.09 mmol, 68%). R_f = 0.48 (6:4 EtOAc–hexane). mp = 139-141 °C. $[\ ]^{25}_{D}$ = + 57 (*c* = 1.0, chloroform). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.40 (d, *J* = 3.5 Hz, 1H, H-1’), 5.36 (t, *J* = 10.0 Hz, 1H, H-3’), 5.33 (t, *J* = 9.0 Hz, 1H, H-3), 5.29 (d, *J* = 10.5 Hz, 1H, H-1), 5.06 (t, *J* = 10.0 Hz, 1H, H-4’), 4.99 (t, *J* = 9.5 Hz, 1H, H-2), 4.87 (dd, *J* = 4.0, 10.5 Hz, 1H, H-2’), 4.45 (dd, *J* = 2.0, 12.5 Hz, 1H, H-6a), 4.24 (dd, *J* = 4.5, 12.5 Hz, 1H, H-6b), 4.21 (dd, *J* = 4.5, 12.5 Hz, 1H, H-6a’), 4.04 (dd, *J* = 2.0, 12.5 Hz, 1H, H-6b’), 4.00 (t, *J* = 9.5 Hz, 1H, H-4), 3.95 (m, 1H, H-5’), 3.83 (m, 1H, H-5), 2.38 (s, 3H, SCOCH_3), 2.13, 2.10, 2.06, 2.03, 2.01, 2.00 (2C) (7 × s, 21H, OCOCH_3), assignments were confirmed by ^{1}H-^{1}H gCOSY. LRMS (ESI$^+$): *m*/*z* = 717 [M + Na]$^+$. Analytical data are consistent with values reported in the literature.[7]

References

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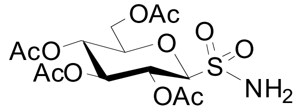

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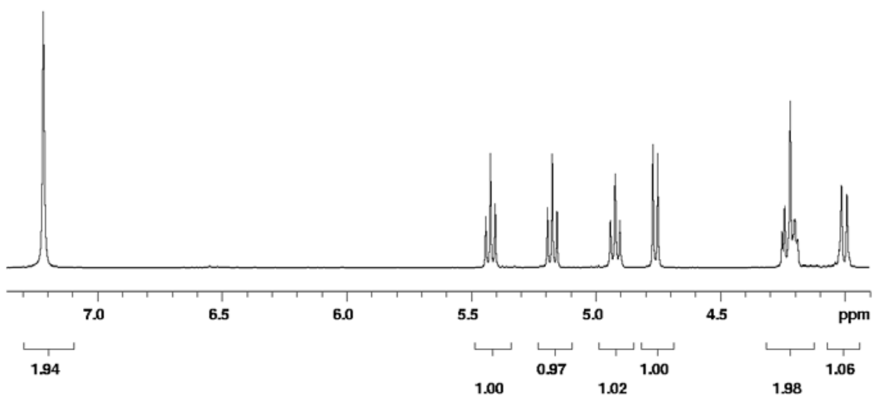

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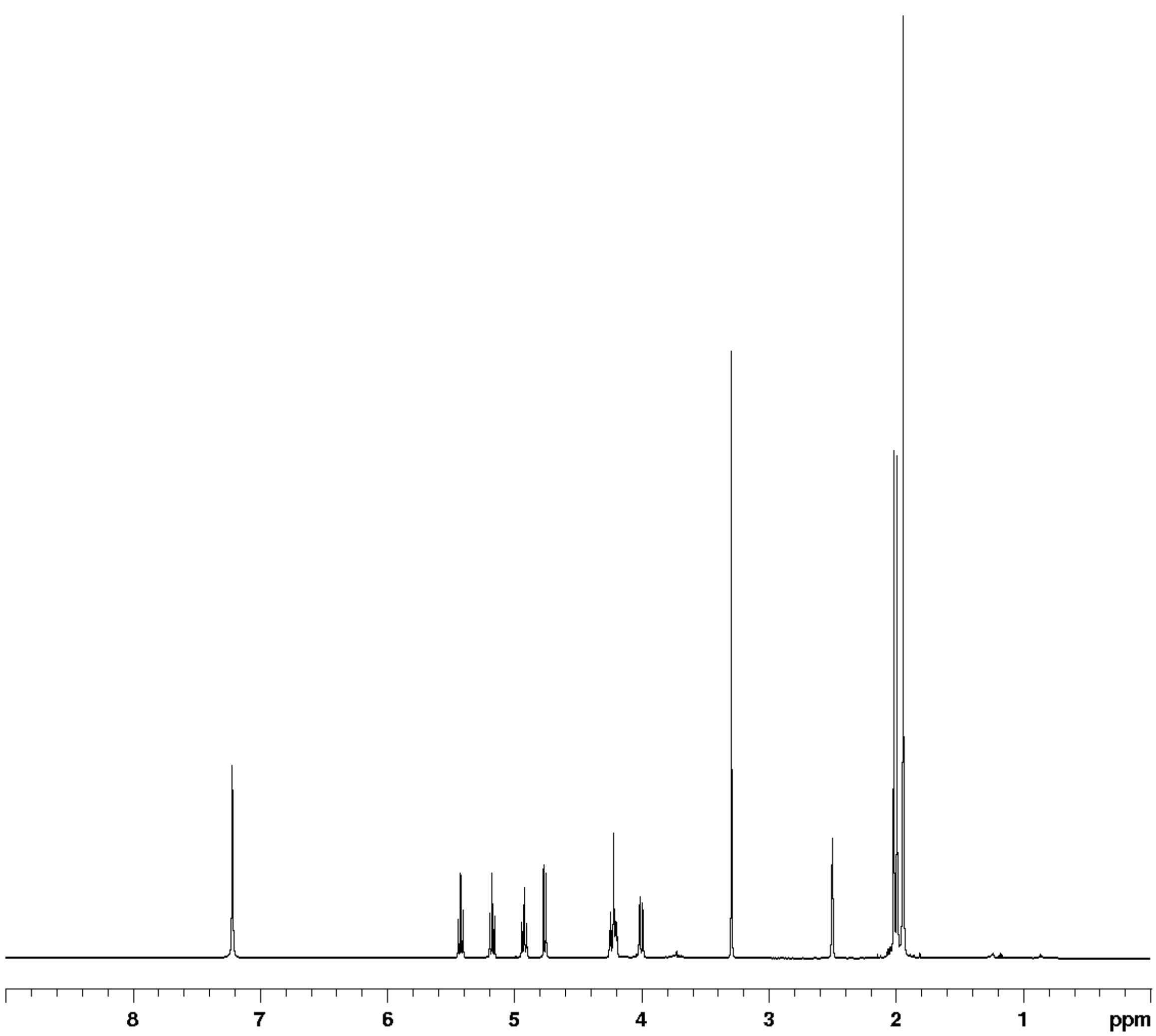

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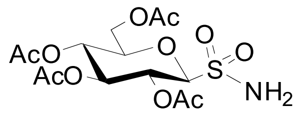

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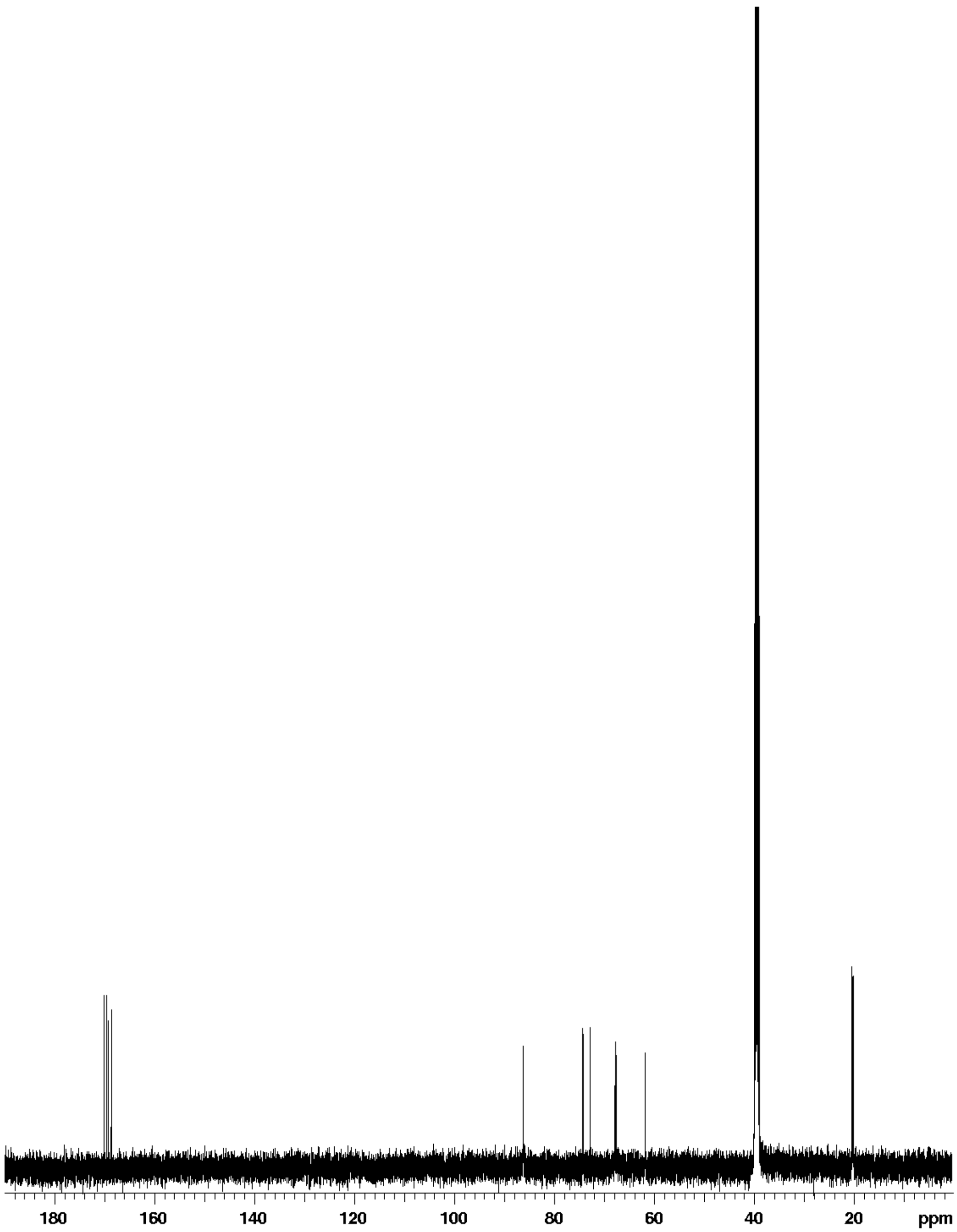

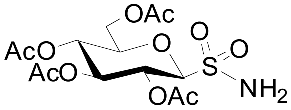

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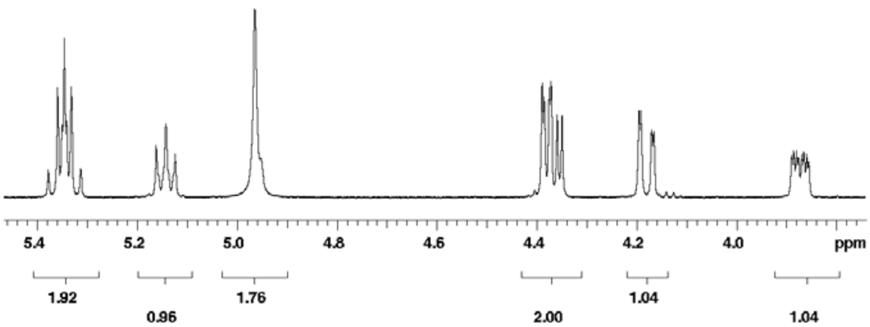

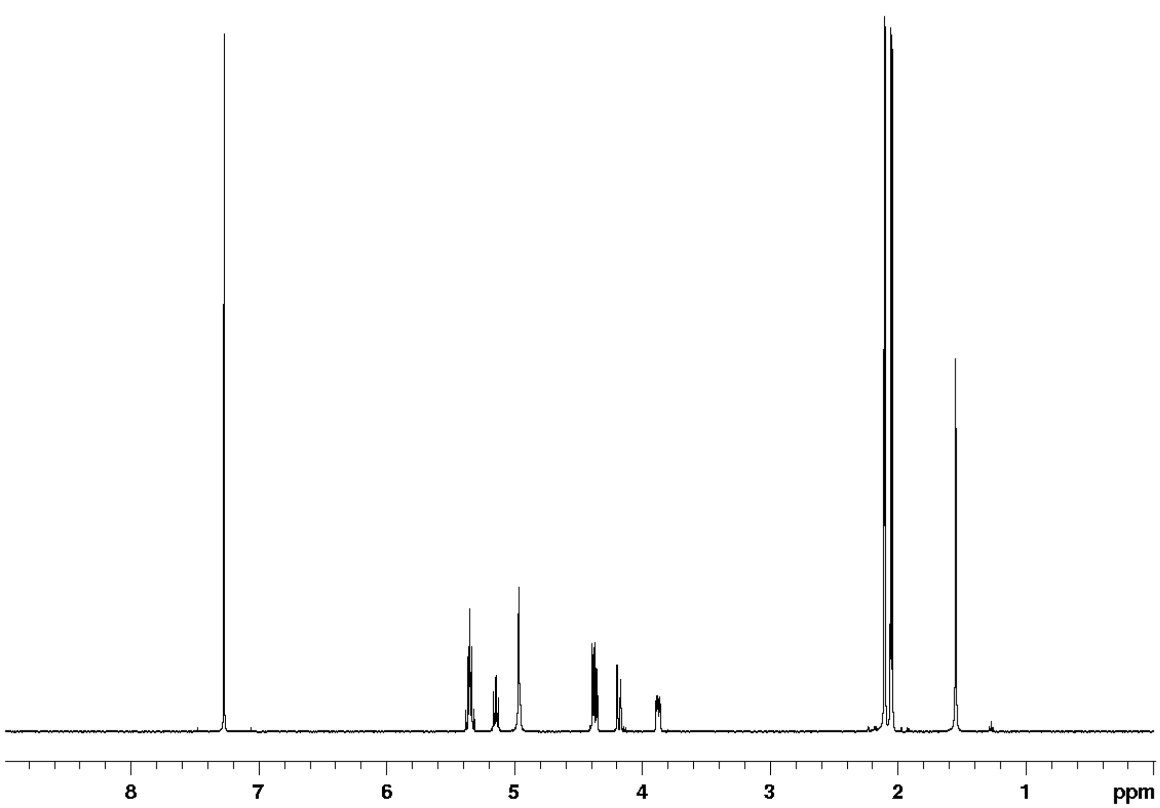

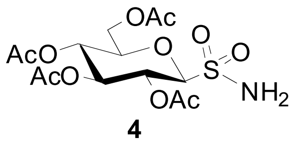

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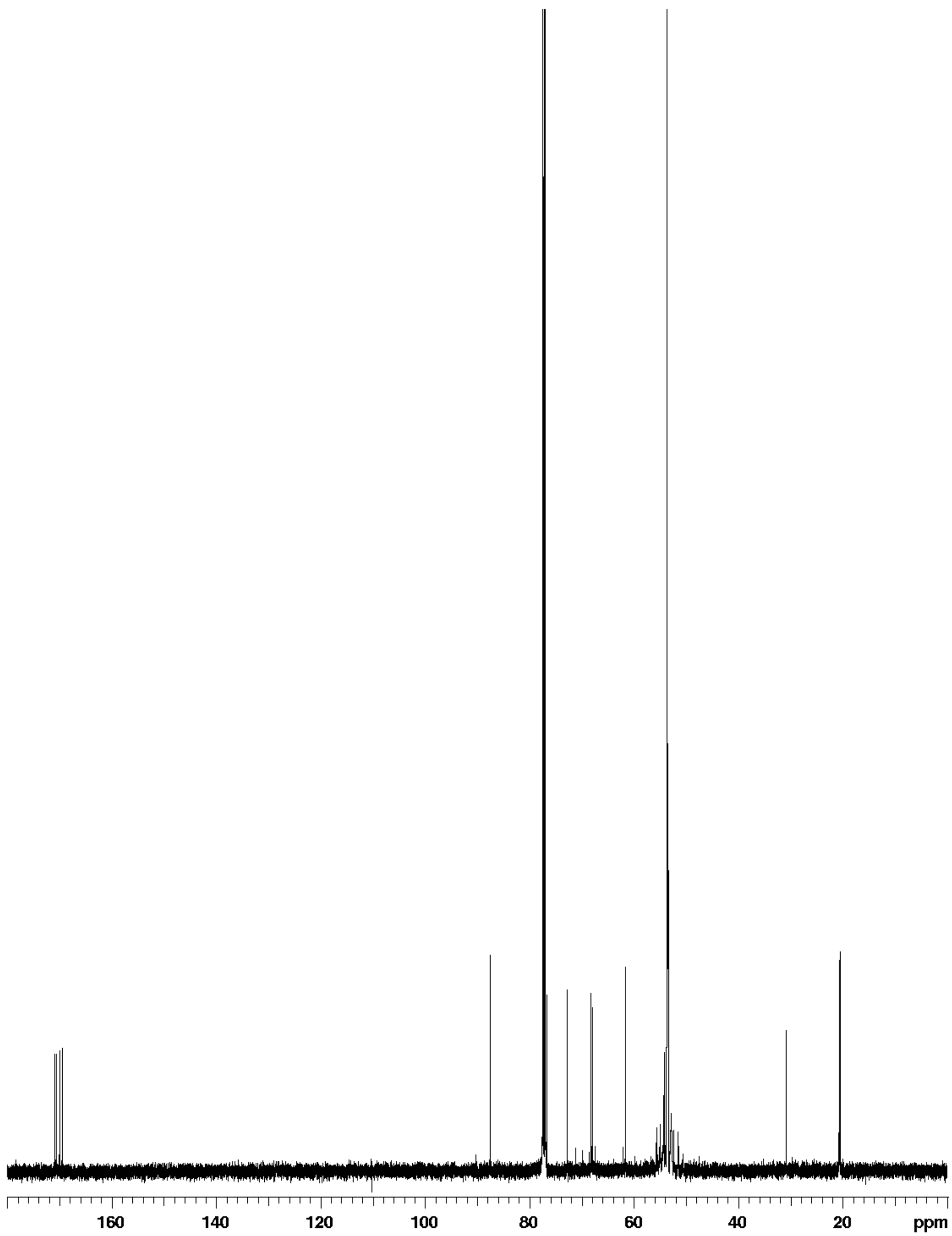

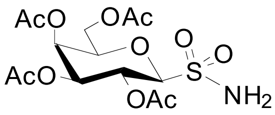

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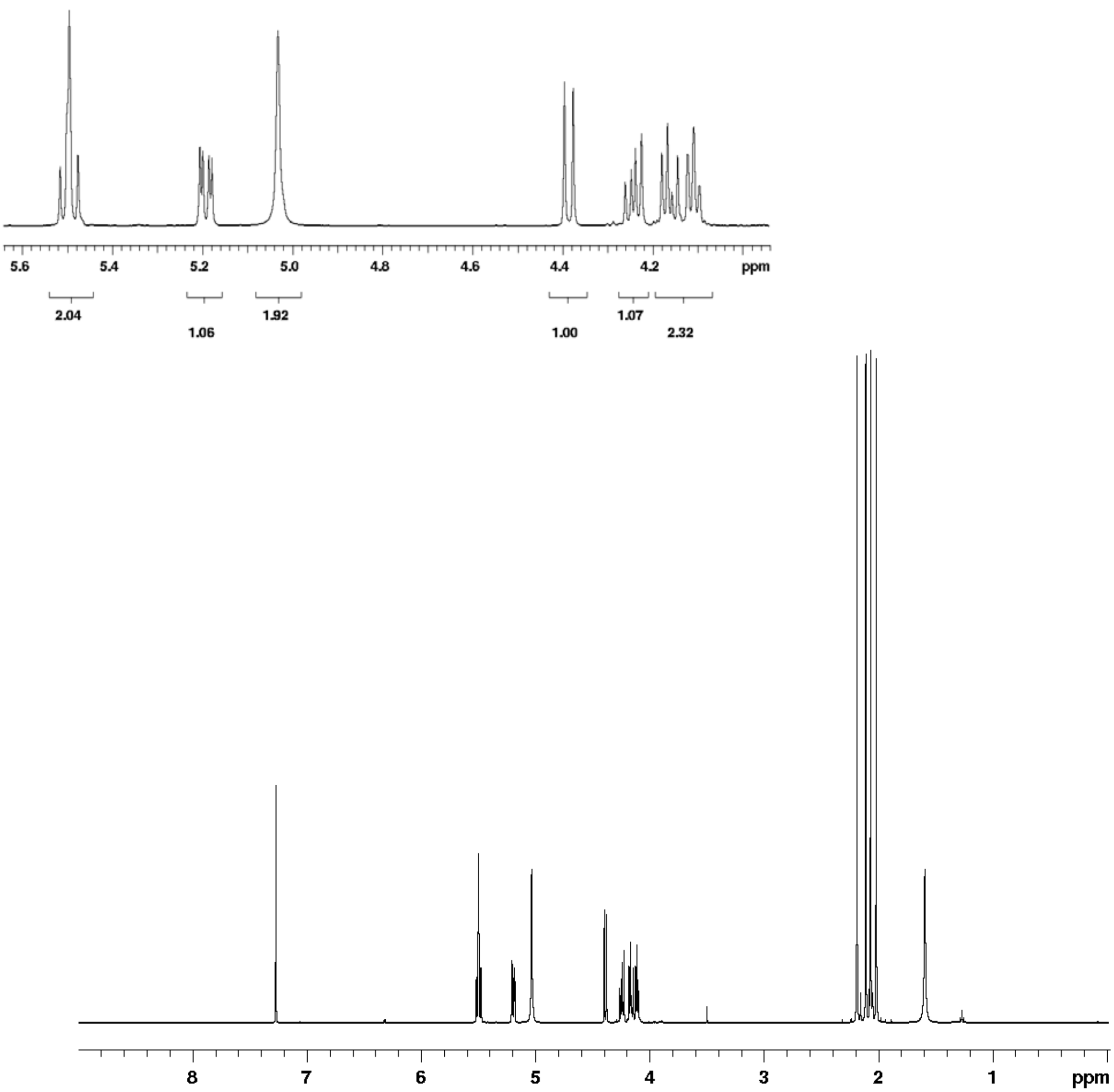

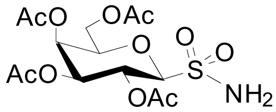

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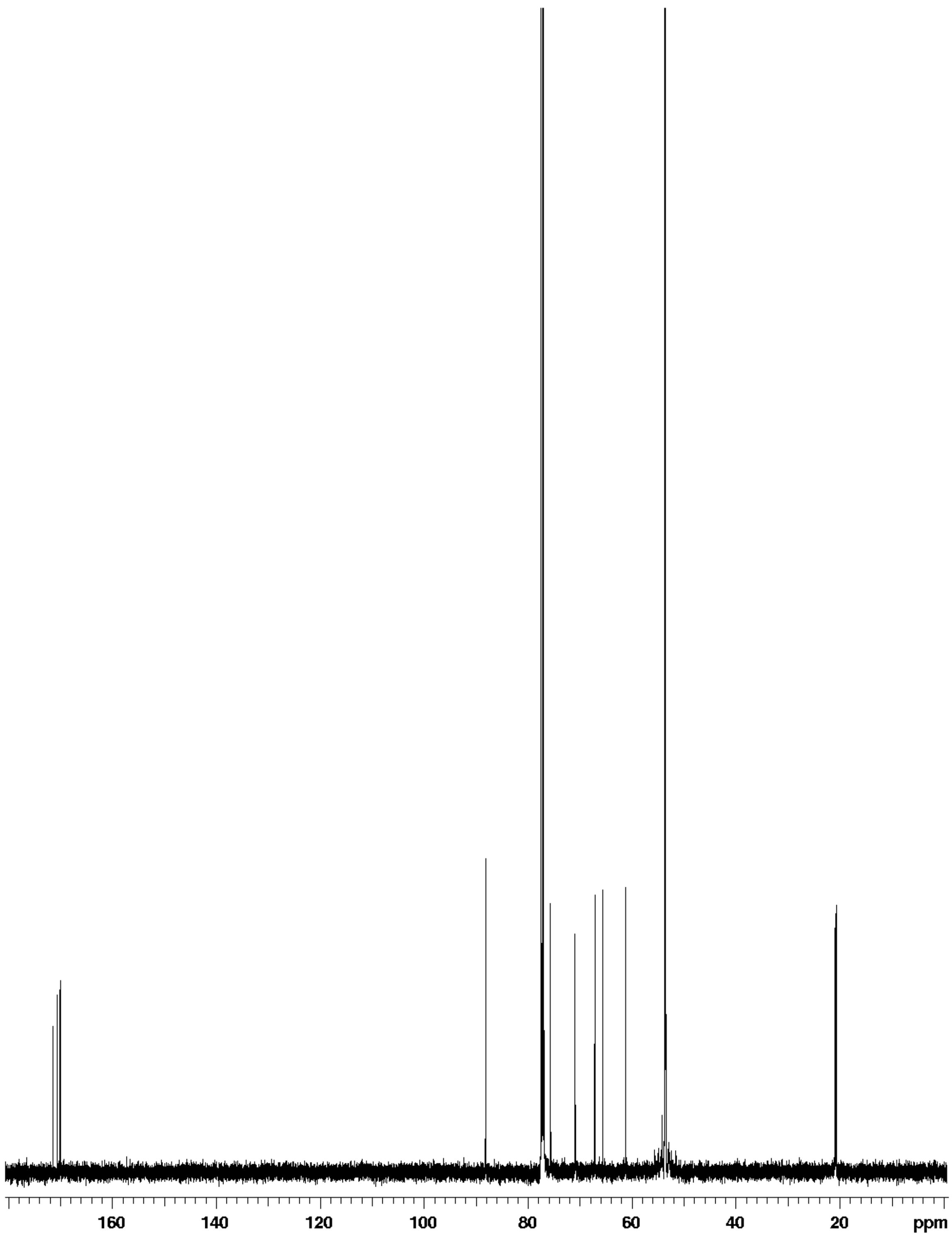

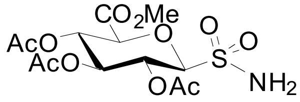

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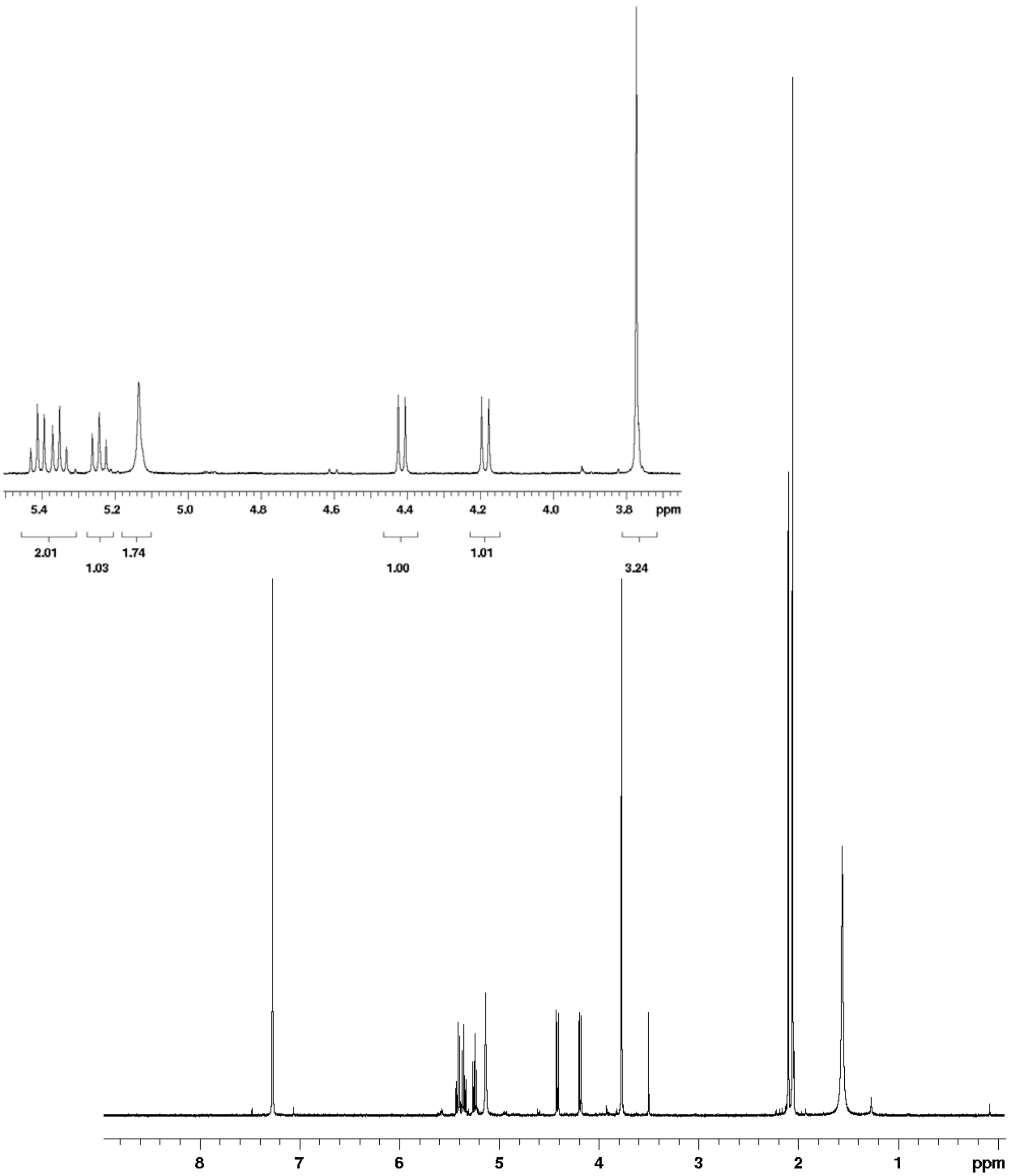

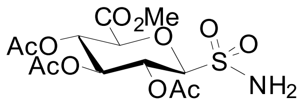

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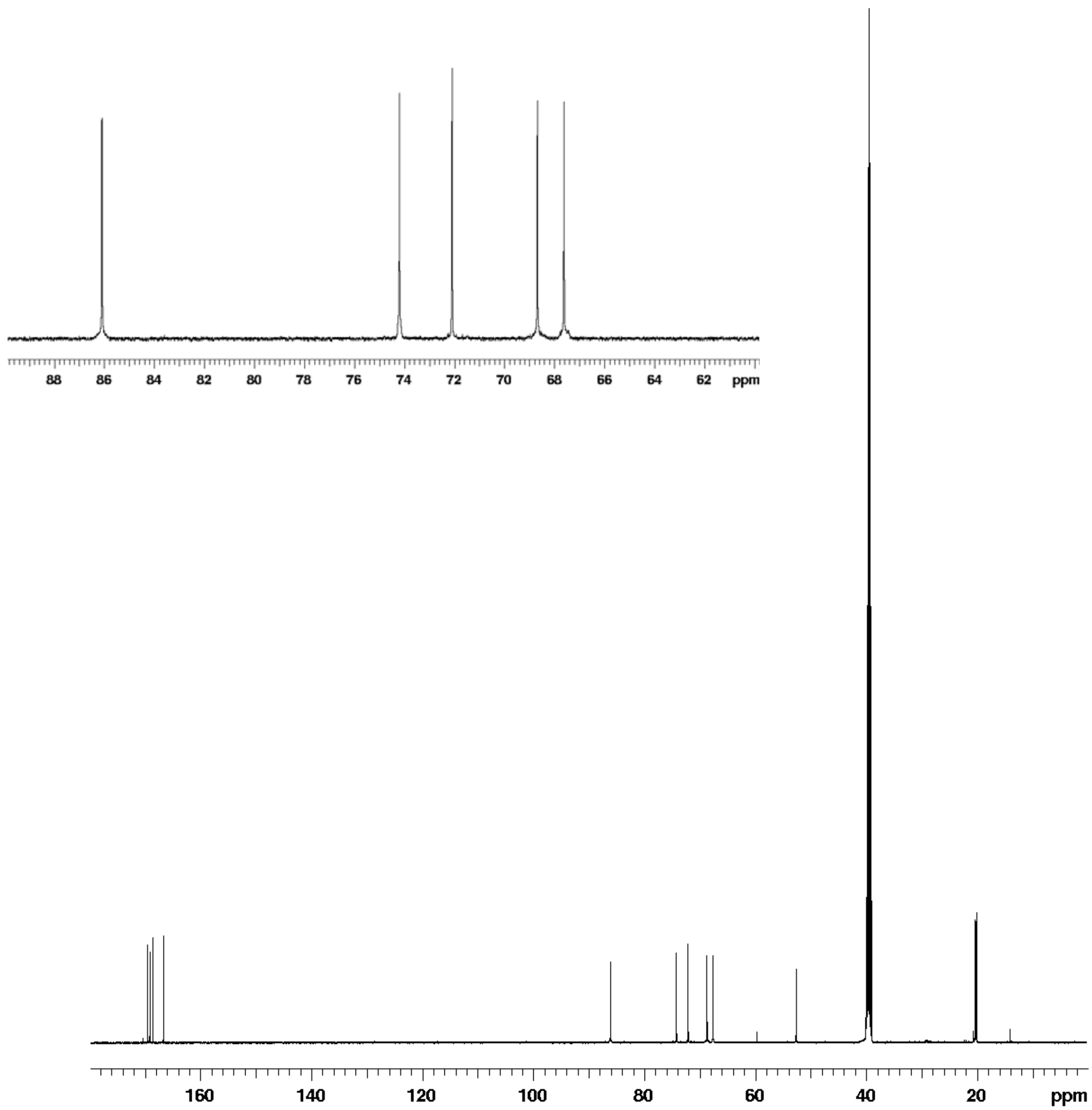

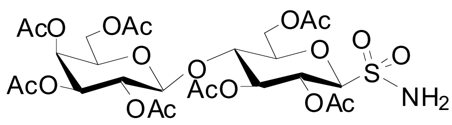

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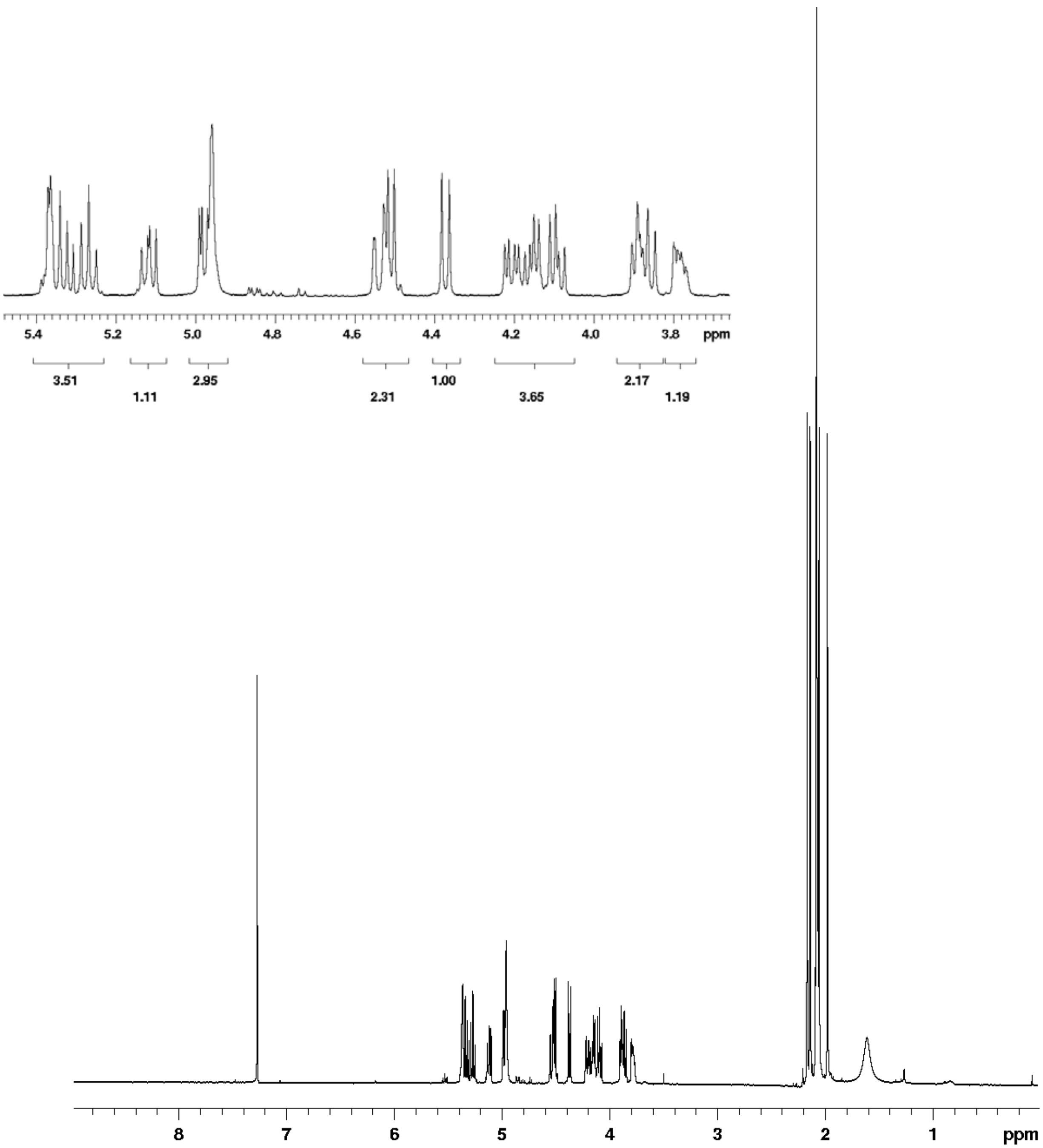

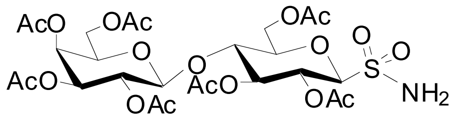

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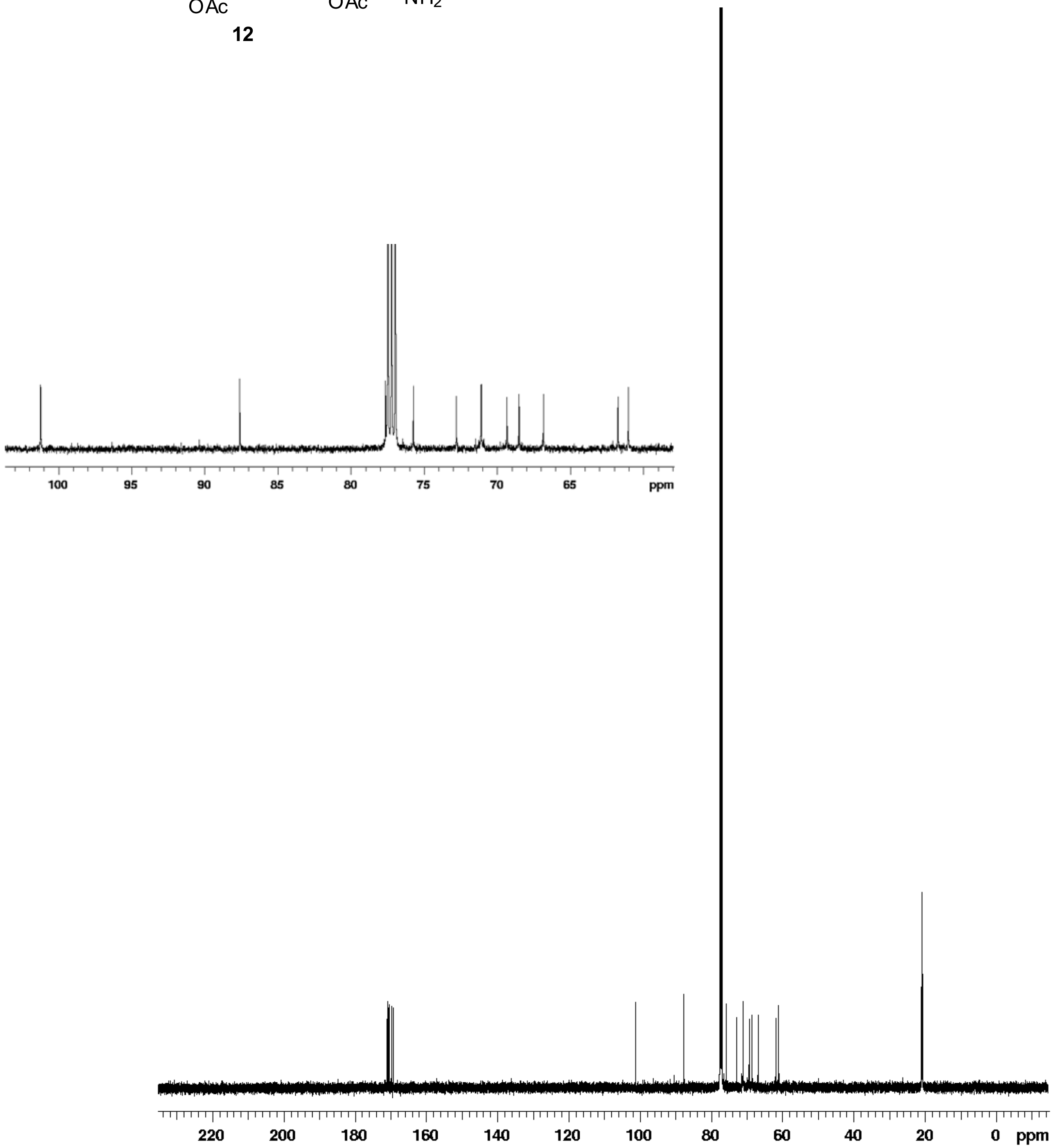

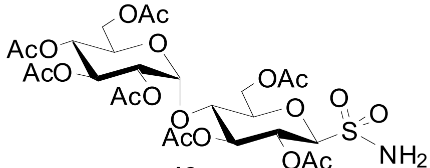

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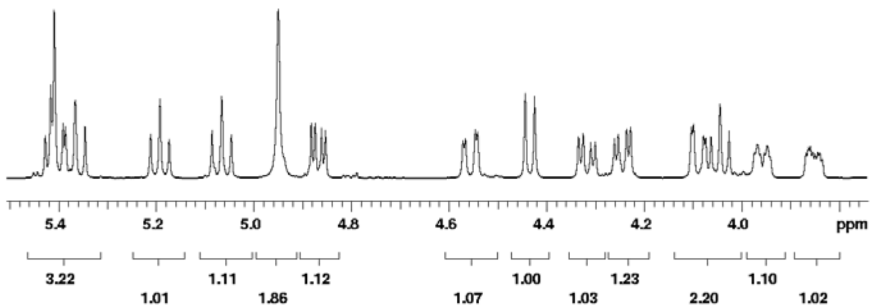

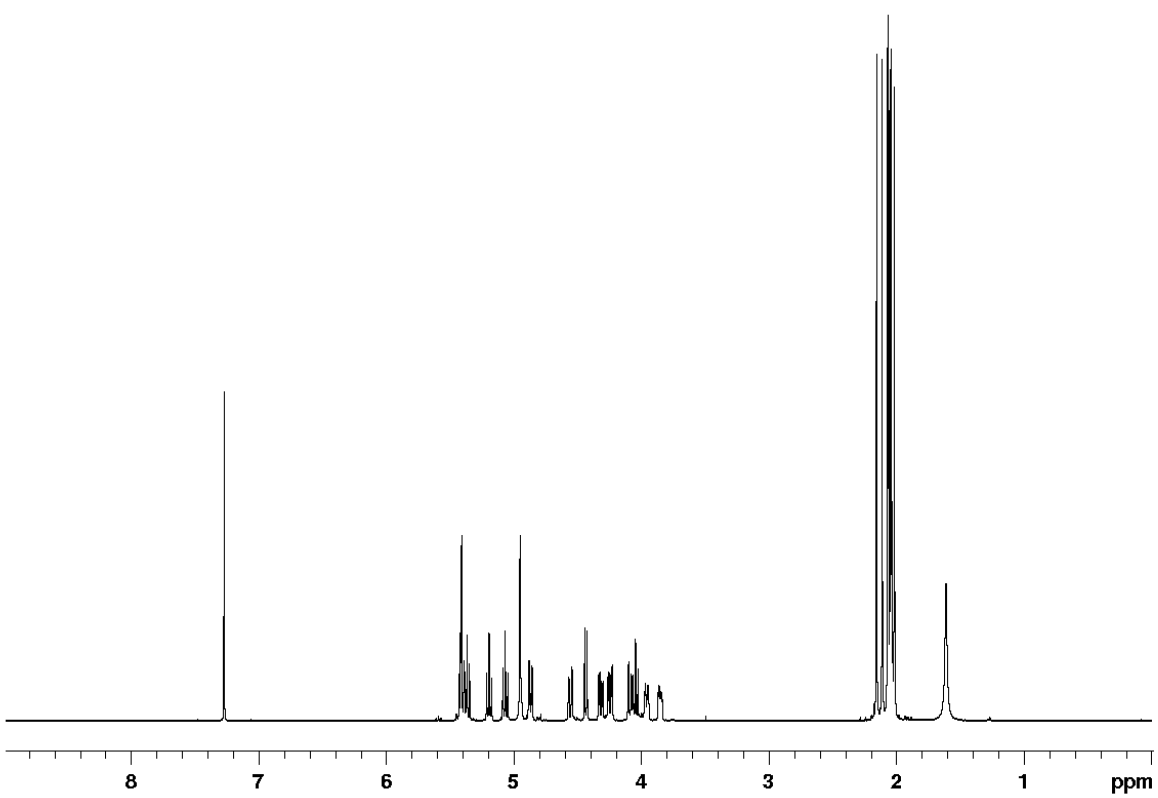

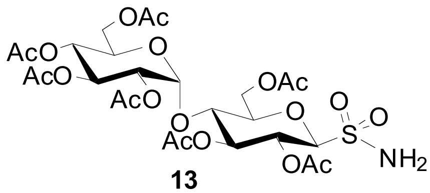

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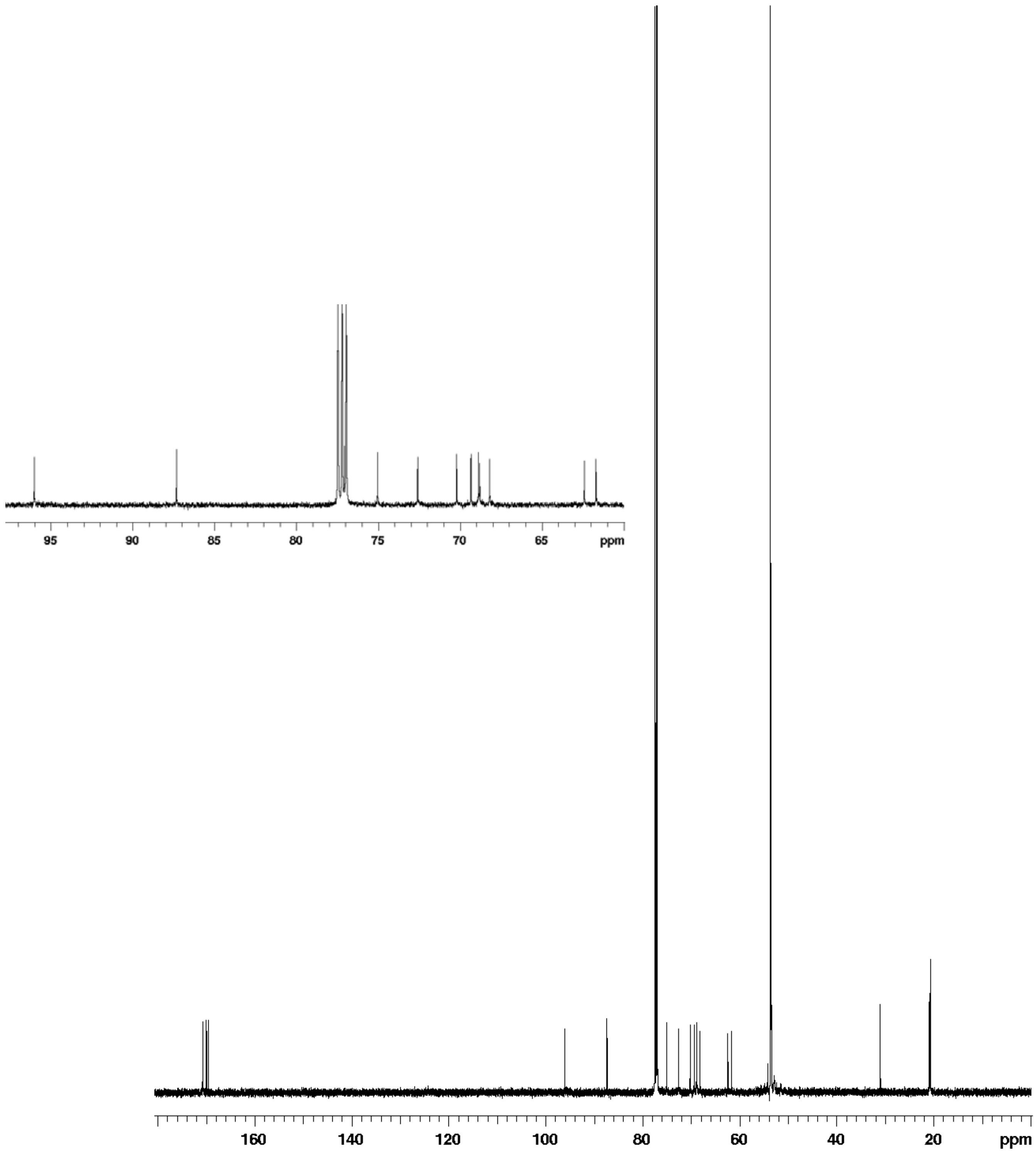

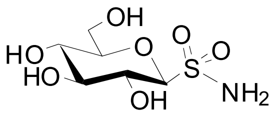

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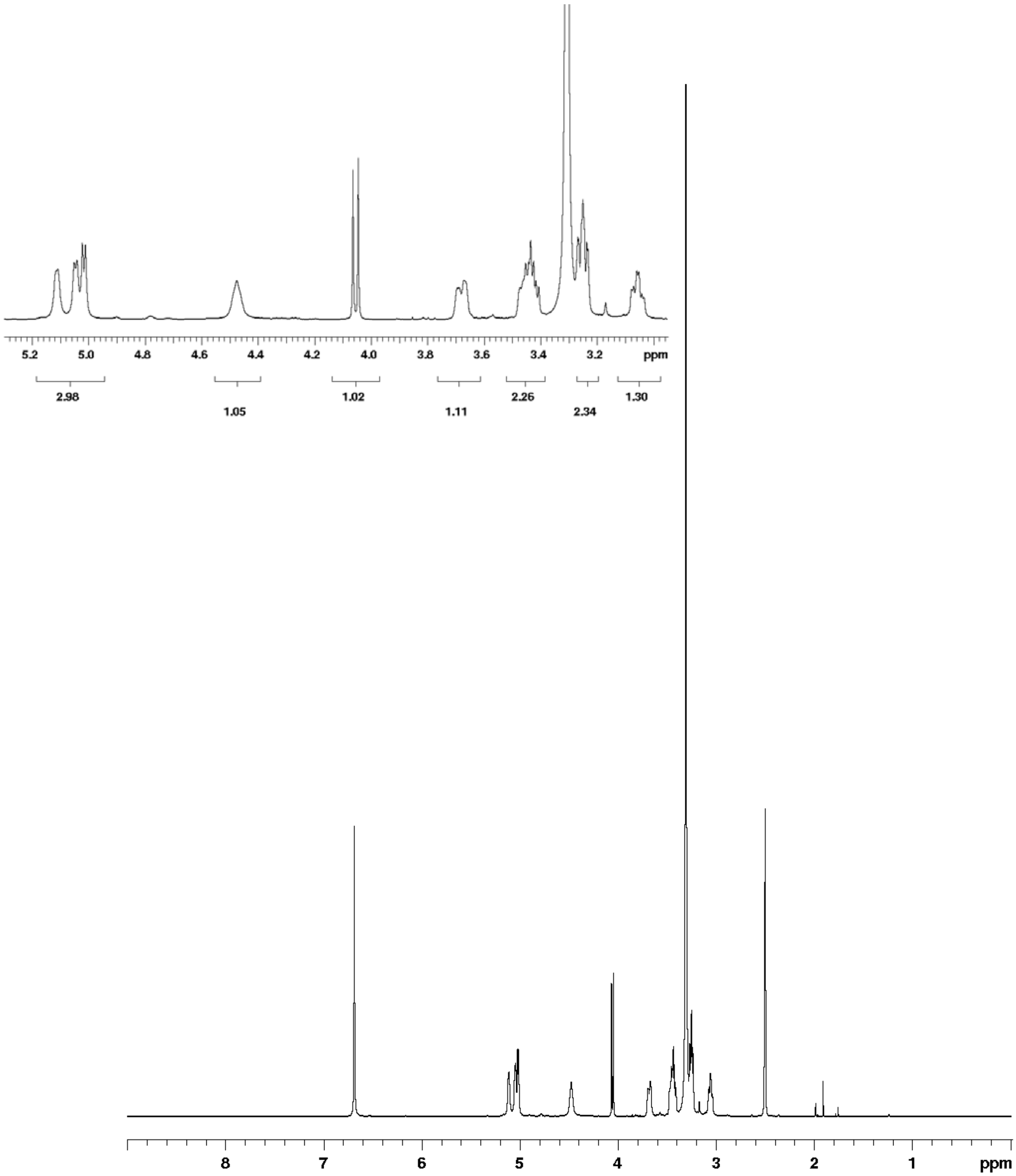
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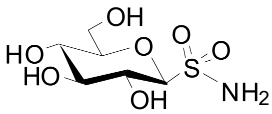

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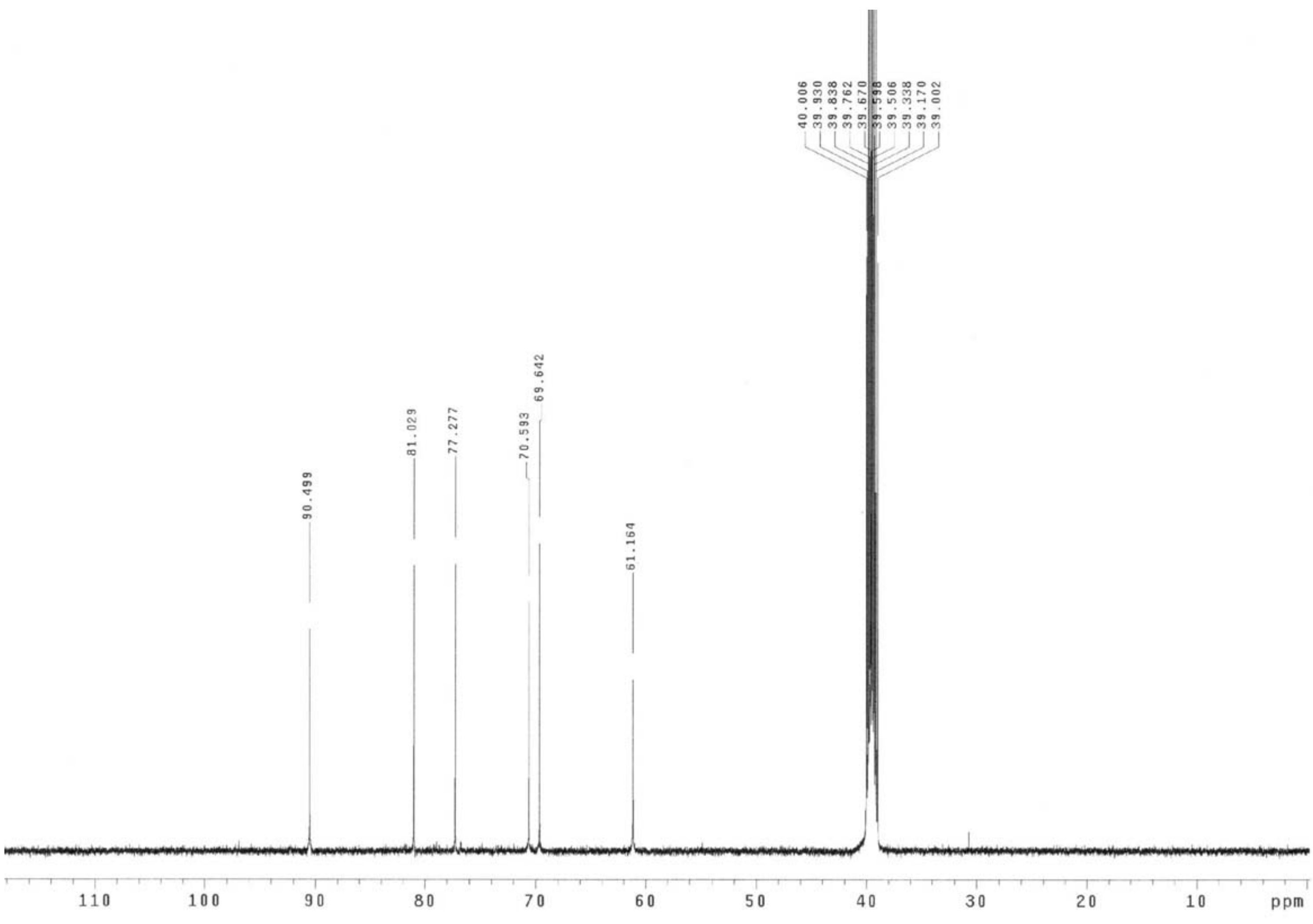

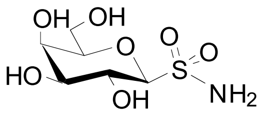

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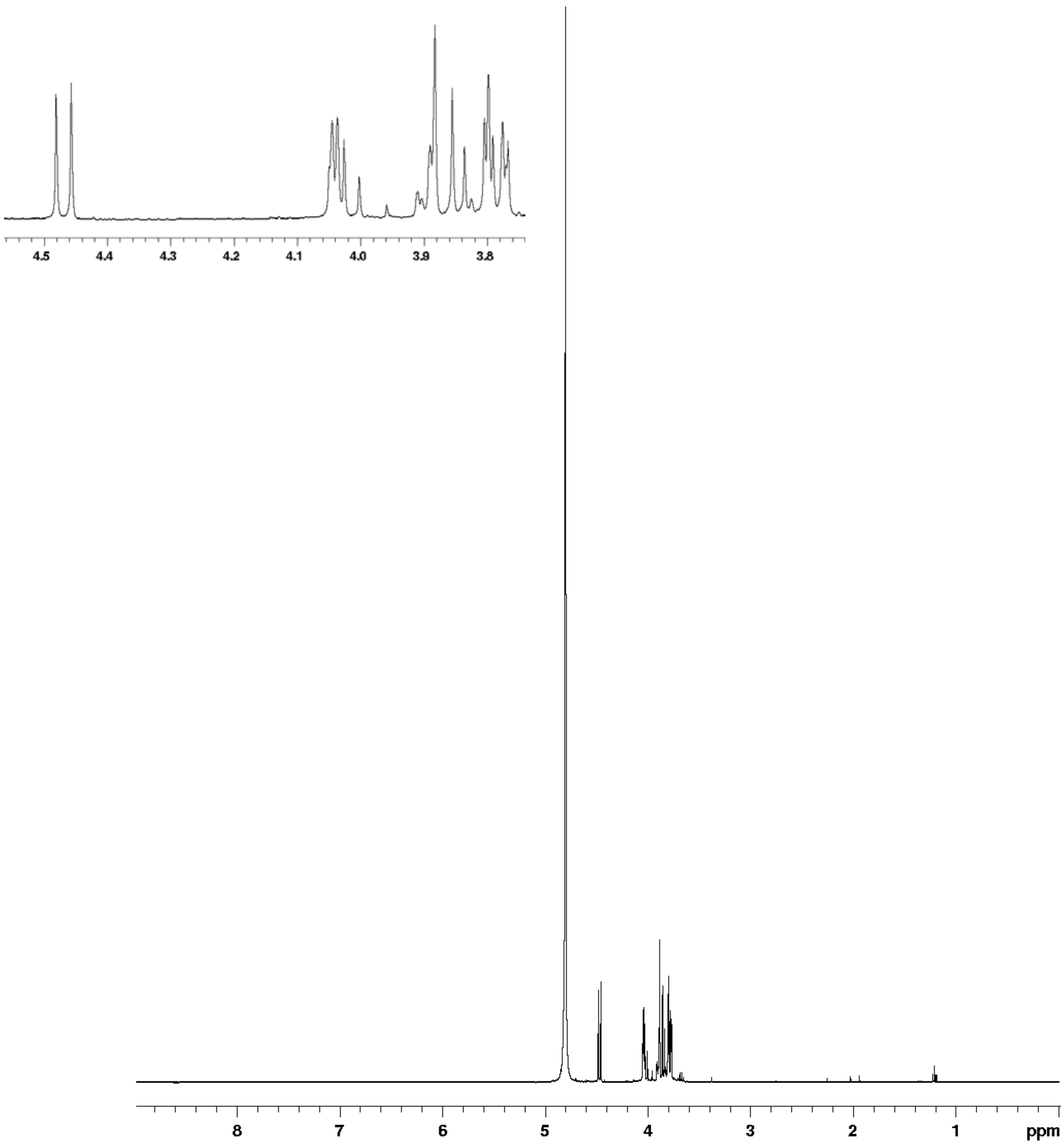
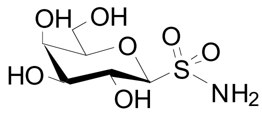
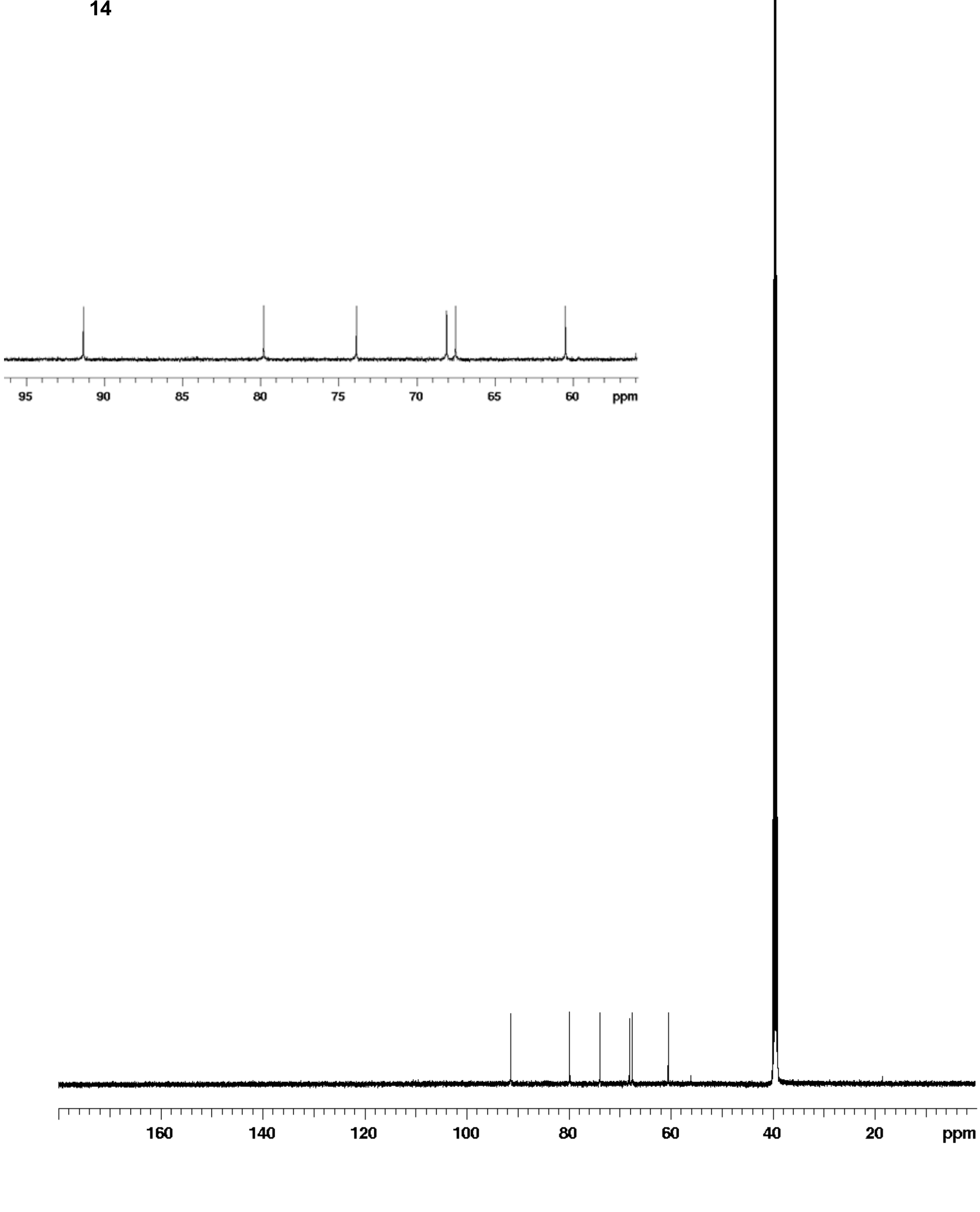
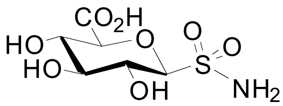




14

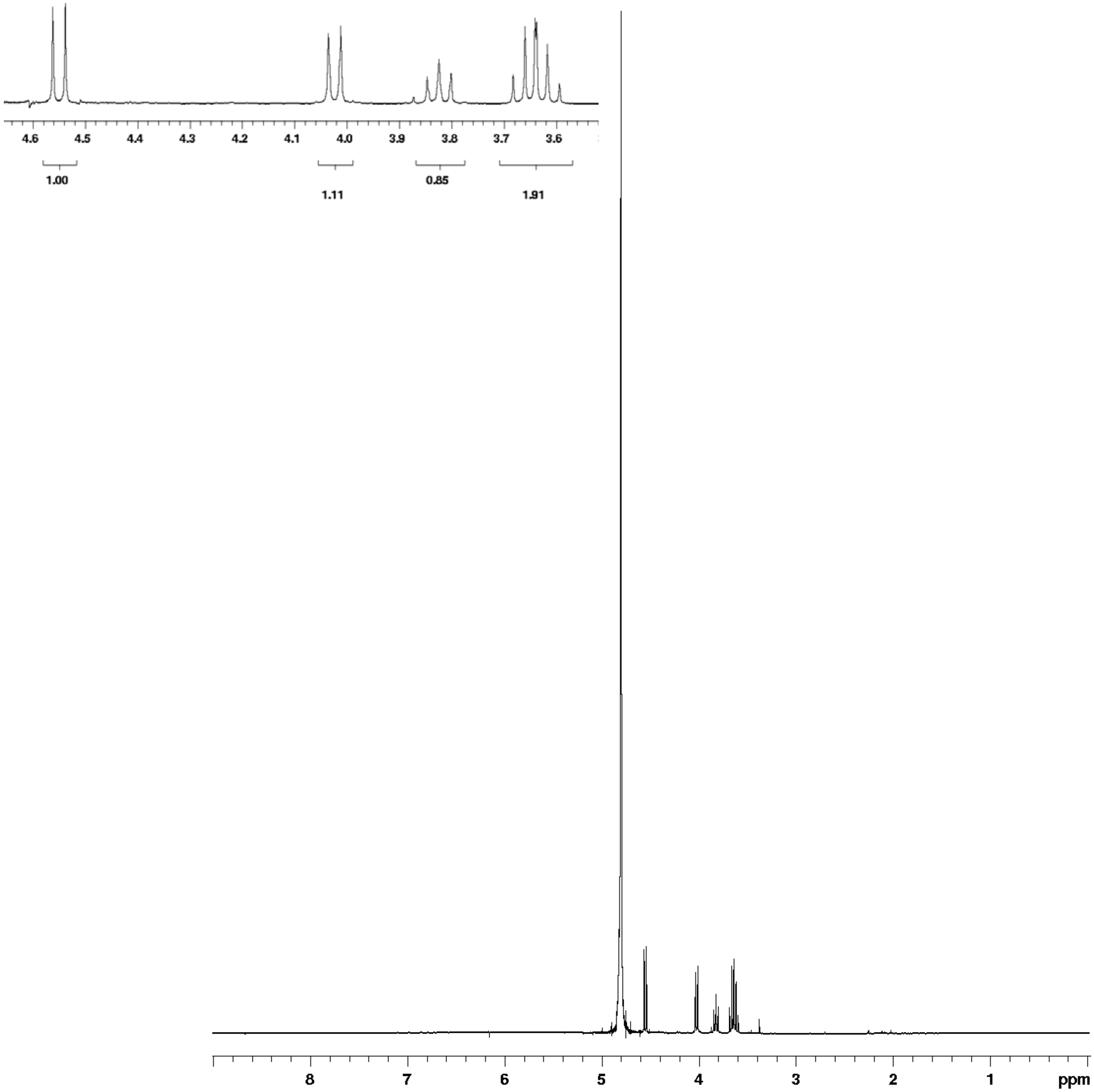
^{13}C NMR (DMSO)

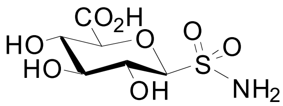



CO2H
HO
HO
OH
O
O
S
O
NH2

15

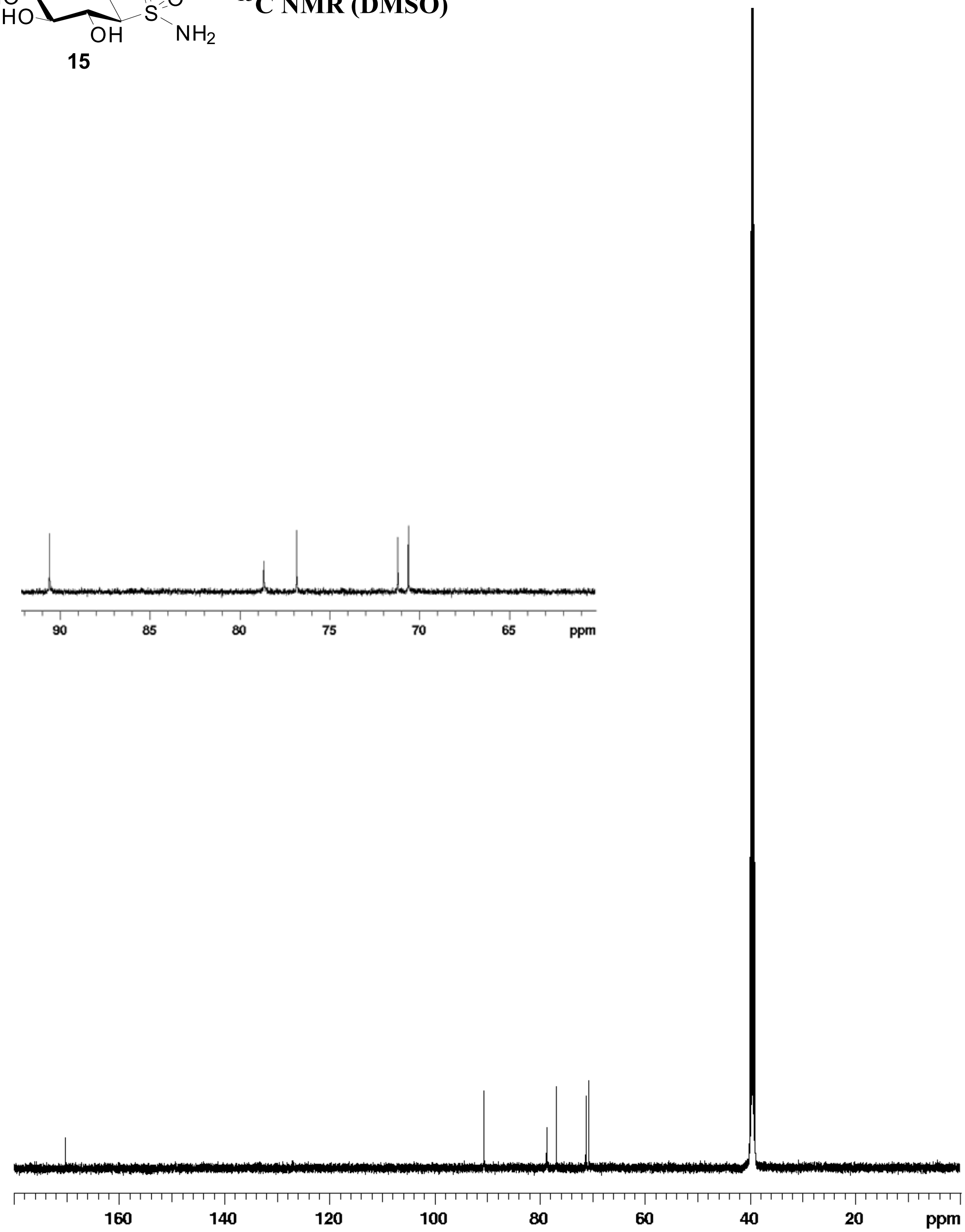
^{1}H NMR (D_2O)

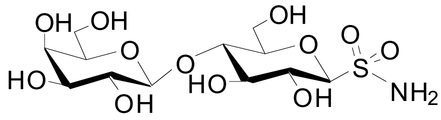

4.6
4.5
4.4
4.3
4.2
4.1
4.0
3.9
3.8
3.7
3.6
1.00
1.11
0.85
1.91
8
7
6
5
4
3
2
1
ppm



15

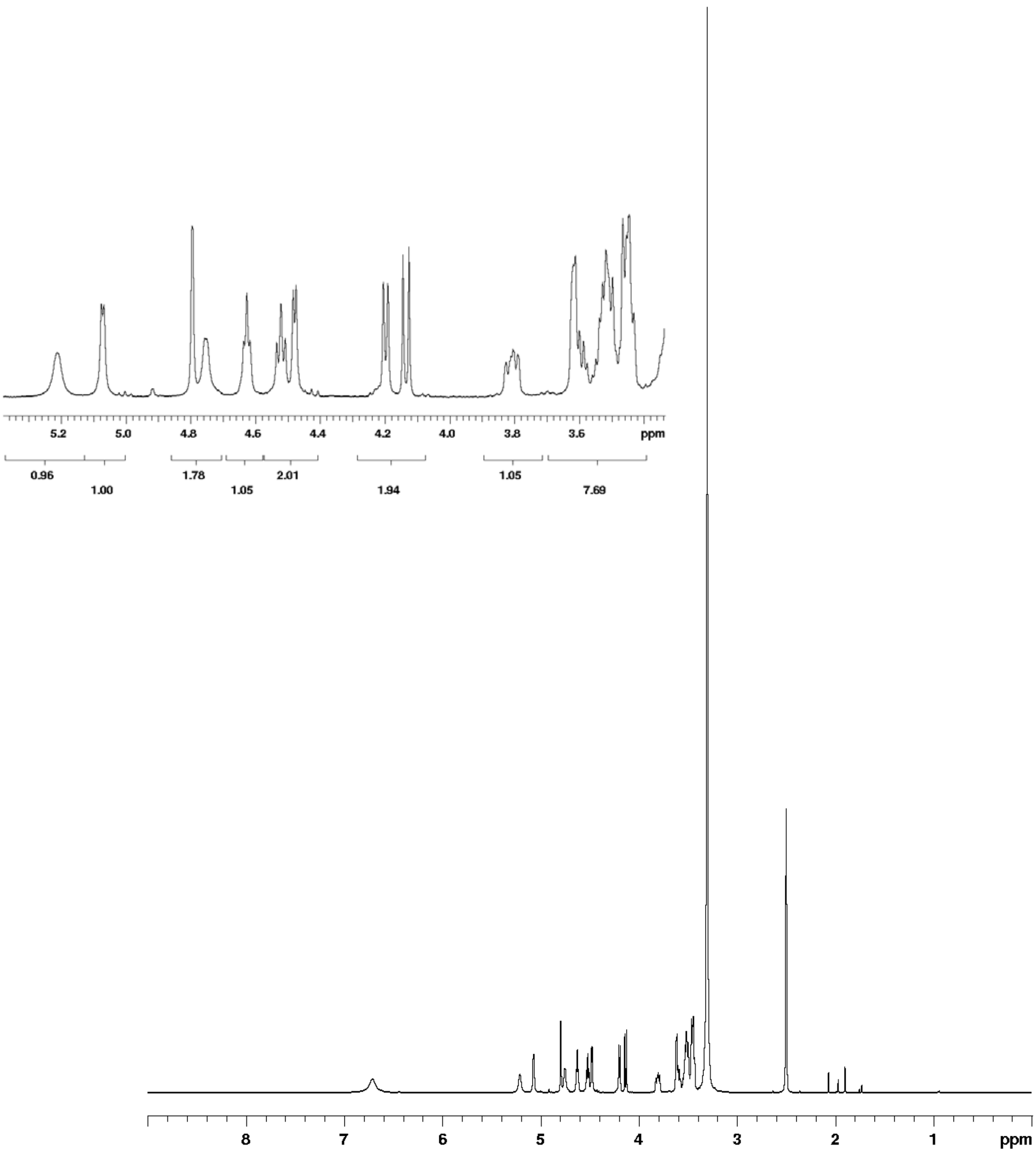
^{13}C NMR (DMSO)

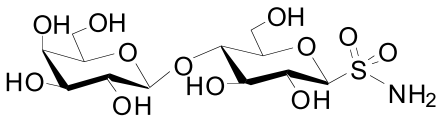




16

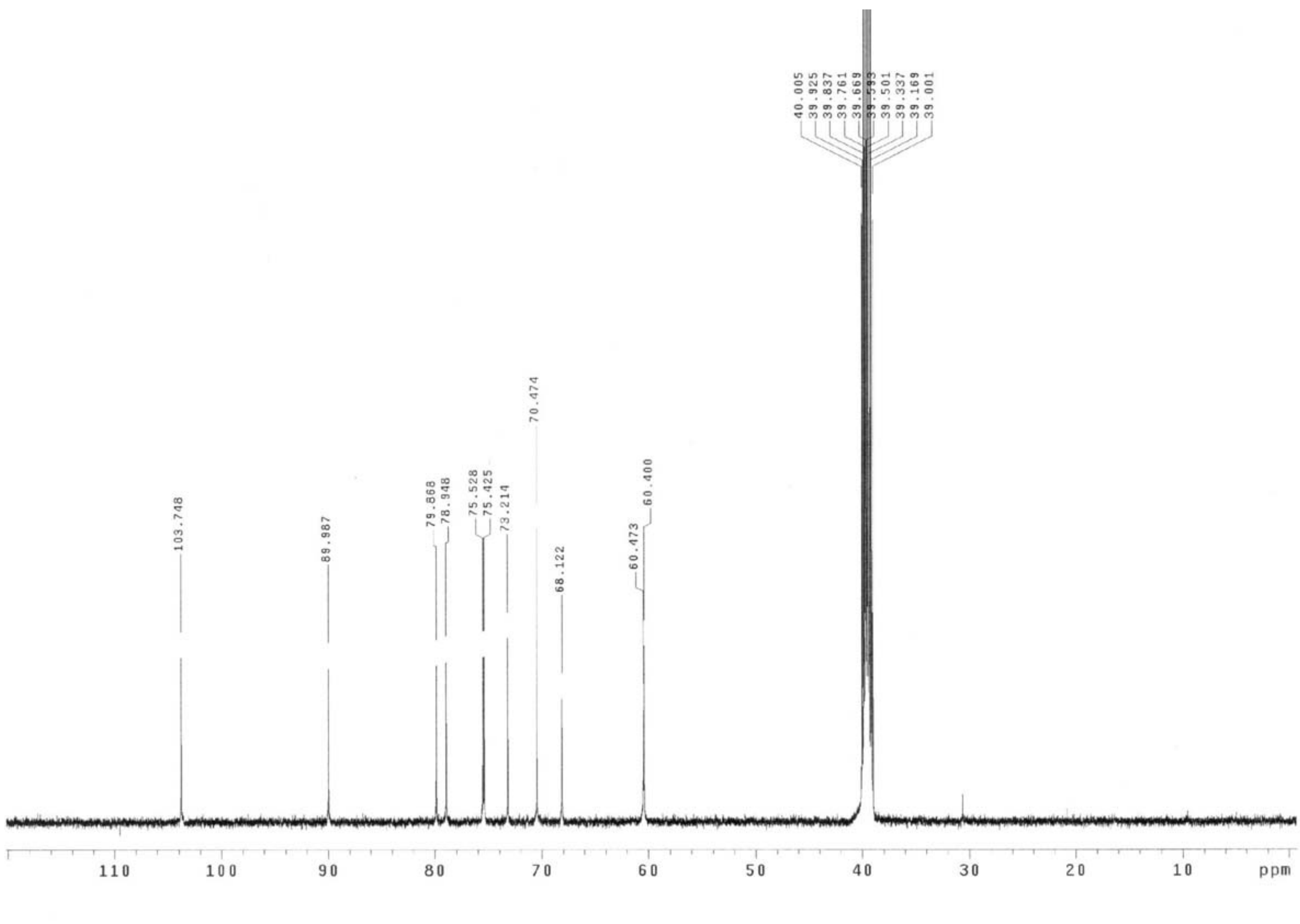
^{1}H NMR (DMSO)

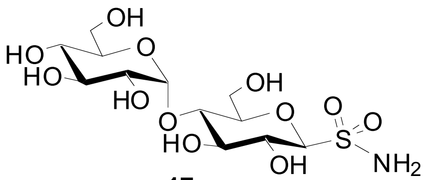




16

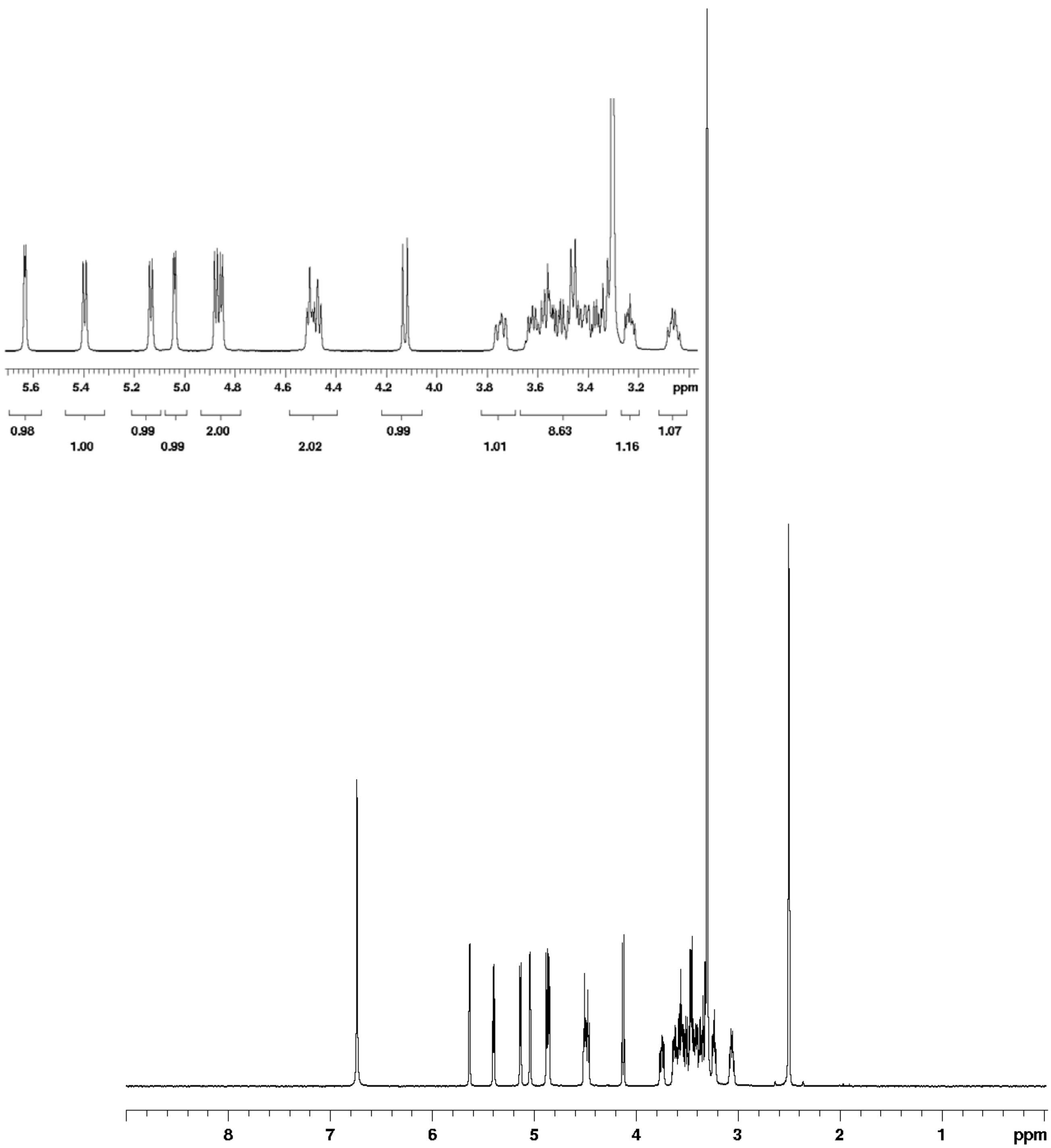
^{13}C NMR (DMSO)

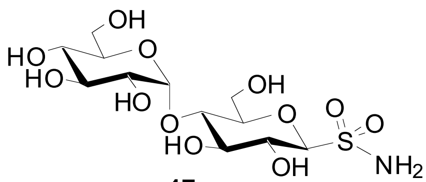




17

[1]H NMR (DMSO)





17

^{13}C NMR (DMSO)