Fast and efficient mechanosynthesis of aldonamides by aminolysis of unprotected sugar lactones

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-^{1}H and ^{13}C NMR spectra of the 1a, 3a, 4a, 4c-4h, 4k-l crudes obtained using "optimized conditions" (*i.e* : 0.5 g lactone, 1 eq. amine, 0.25 mL H_2O (LAG), 5 min milling, aqueous treatment)

-Characterization (^{1}H, ^{13}C, COSY, HSQC NMR analyses, HRMS and FTIR spectra) of the 4b, 4i' et 4j crudes obtained using "optimized conditions" (*i.e* : 0.5 g lactone, 1 eq. amine, 0.25 mL H_2O (LAG), 5 min milling, aqueous treatment)

Figure S1: ^{1}H NMR spectrum of 1a crude

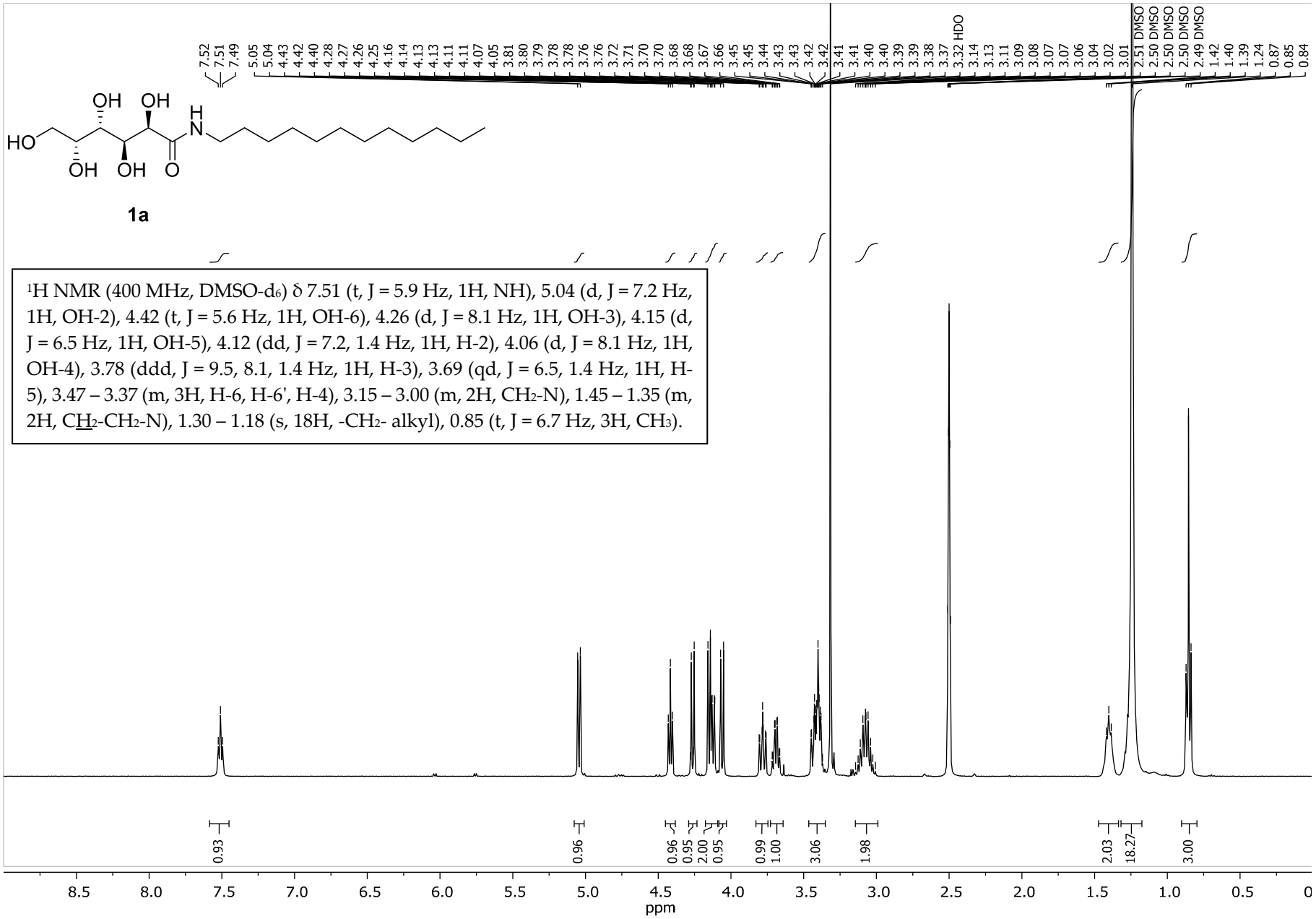
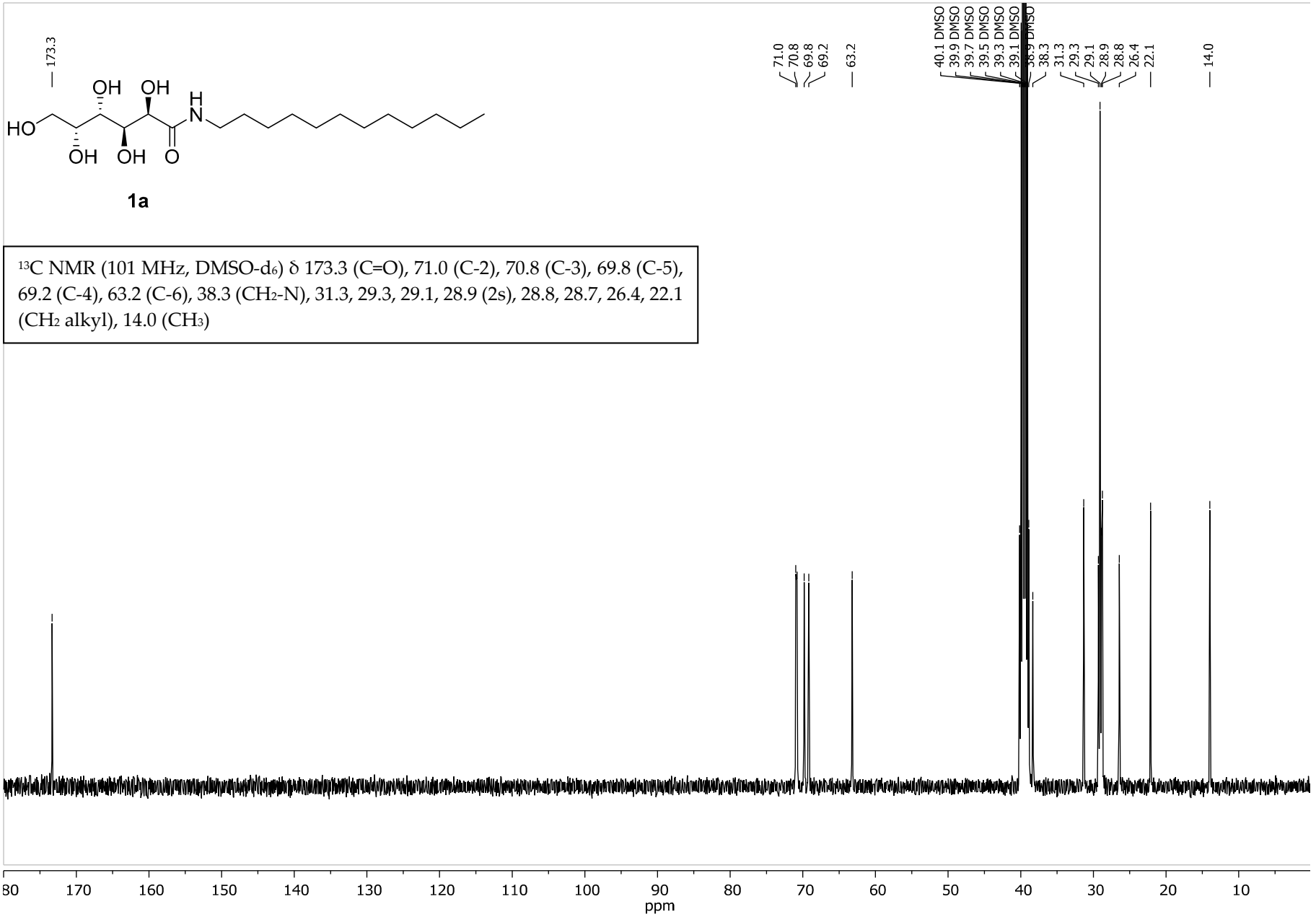
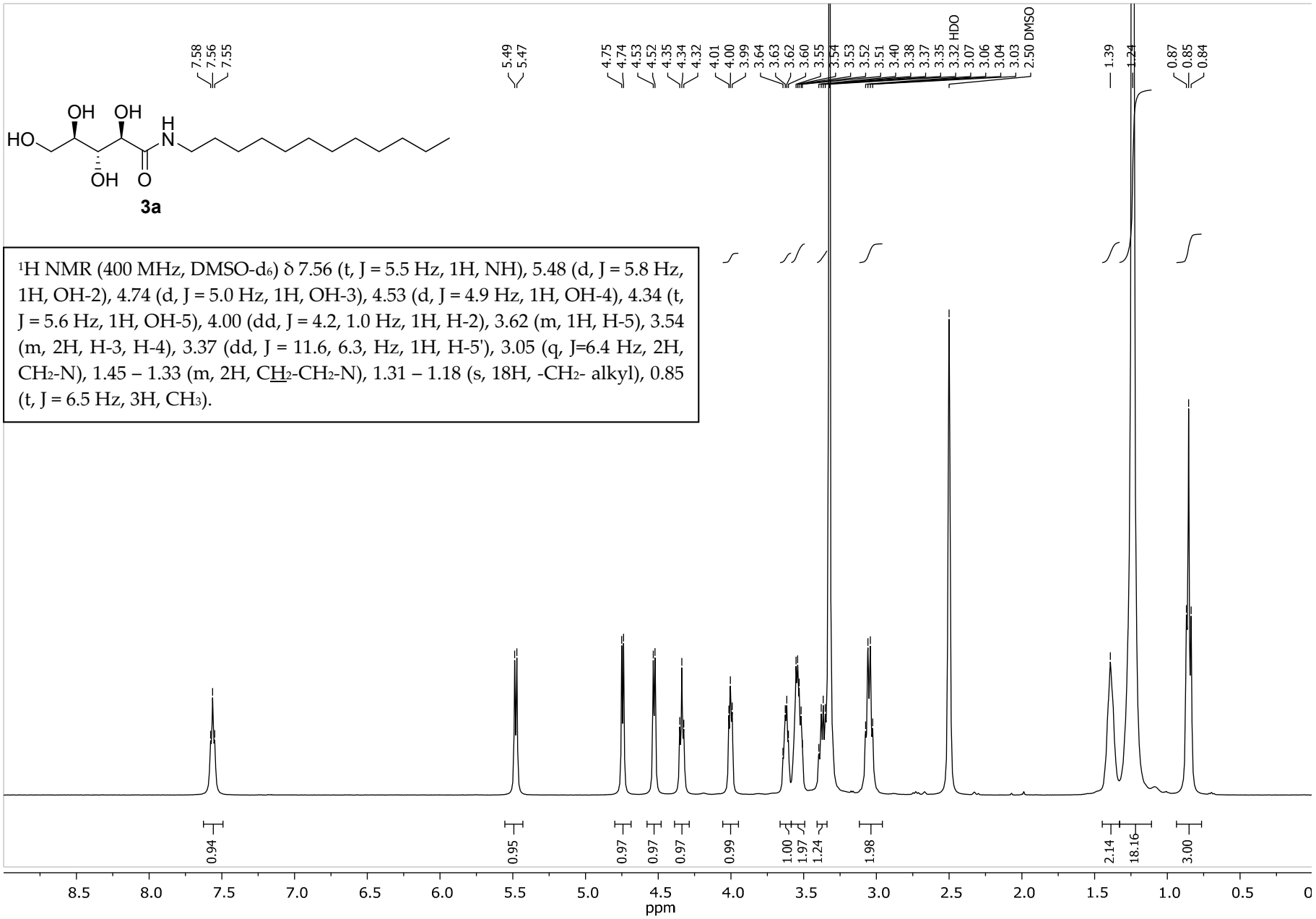


Figure S2: ^{13}C NMR spectrum of 1a crude



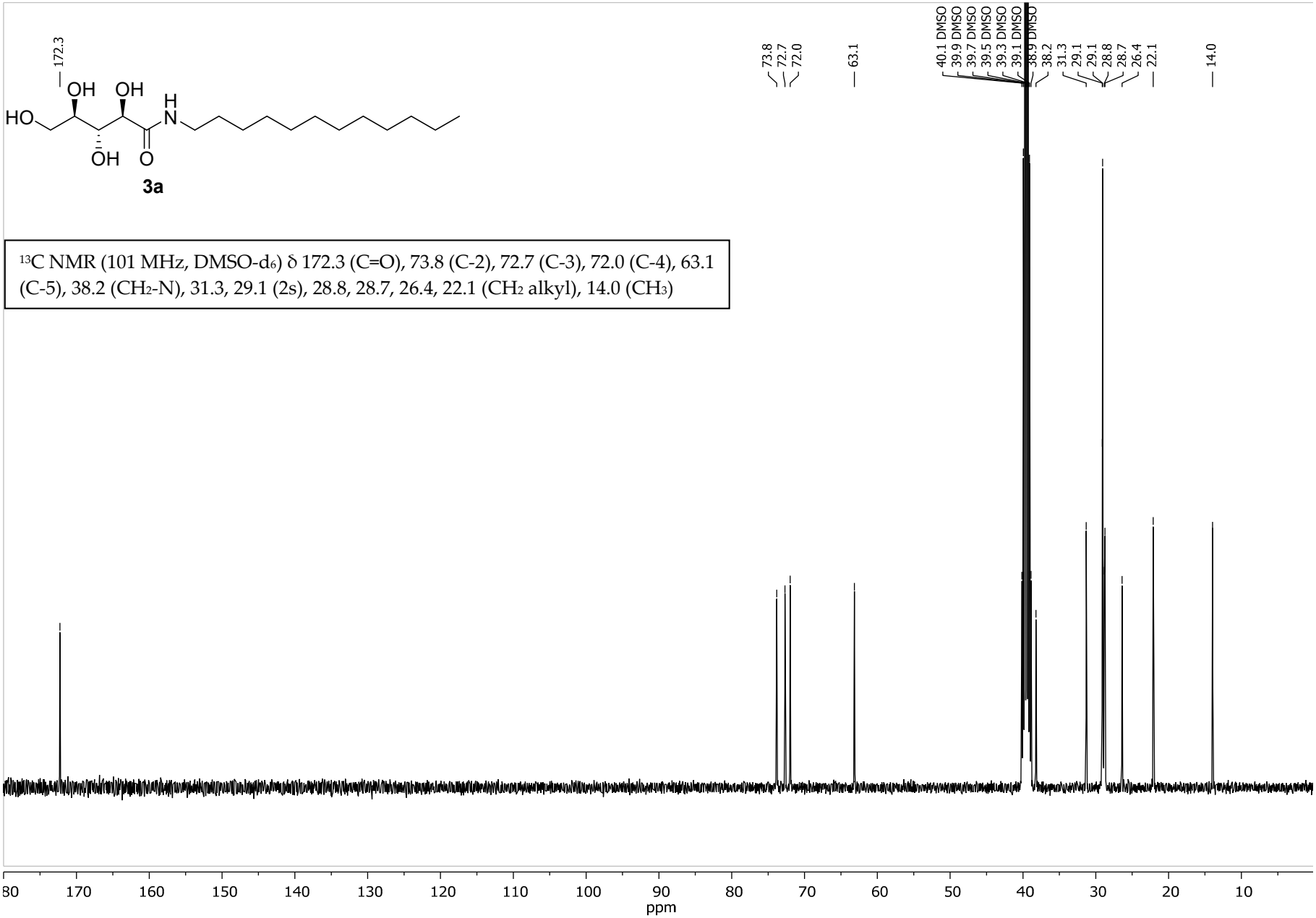
^{13}C NMR (101 MHz, DMSO-d_6) δ 173.3 (C=O), 71.0 (C-2), 70.8 (C-3), 69.8 (C-5), 69.2 (C-4), 63.2 (C-6), 38.3 (CH_2-N), 31.3, 29.3, 29.1, 28.9 (2s), 28.8, 28.7, 26.4, 22.1 (CH_2 alkyl), 14.0 (CH_3)

Figure S3: ^{1}H NMR spectrum of 3a crude



^{1}H NMR (400 MHz, DMSO-d_6) δ 7.56 (t, J = 5.5 Hz, 1H, NH), 5.48 (d, J = 5.8 Hz, 1H, OH-2), 4.74 (d, J = 5.0 Hz, 1H, OH-3), 4.53 (d, J = 4.9 Hz, 1H, OH-4), 4.34 (t, J = 5.6 Hz, 1H, OH-5), 4.00 (dd, J = 4.2, 1.0 Hz, 1H, H-2), 3.62 (m, 1H, H-5), 3.54 (m, 2H, H-3, H-4), 3.37 (dd, J = 11.6, 6.3, Hz, 1H, H-5'), 3.05 (q, J=6.4 Hz, 2H, CH_2-N), 1.45 – 1.33 (m, 2H, C$\underline{H}_2$-CH_2-N), 1.31 – 1.18 (s, 18H, -CH_2- alkyl), 0.85 (t, J = 6.5 Hz, 3H, CH_3).

Figure S4: ^{13}C NMR spectrum of 3a crude



^{13}C NMR (101 MHz, DMSO-d_6) δ 172.3 (C=O), 73.8 (C-2), 72.7 (C-3), 72.0 (C-4), 63.1 (C-5), 38.2 (CH_2-N), 31.3, 29.1 (2s), 28.8, 28.7, 26.4, 22.1 (CH_2 alkyl), 14.0 (CH_3)

Figure S5: ^{1}H NMR spectrum of 4a crude

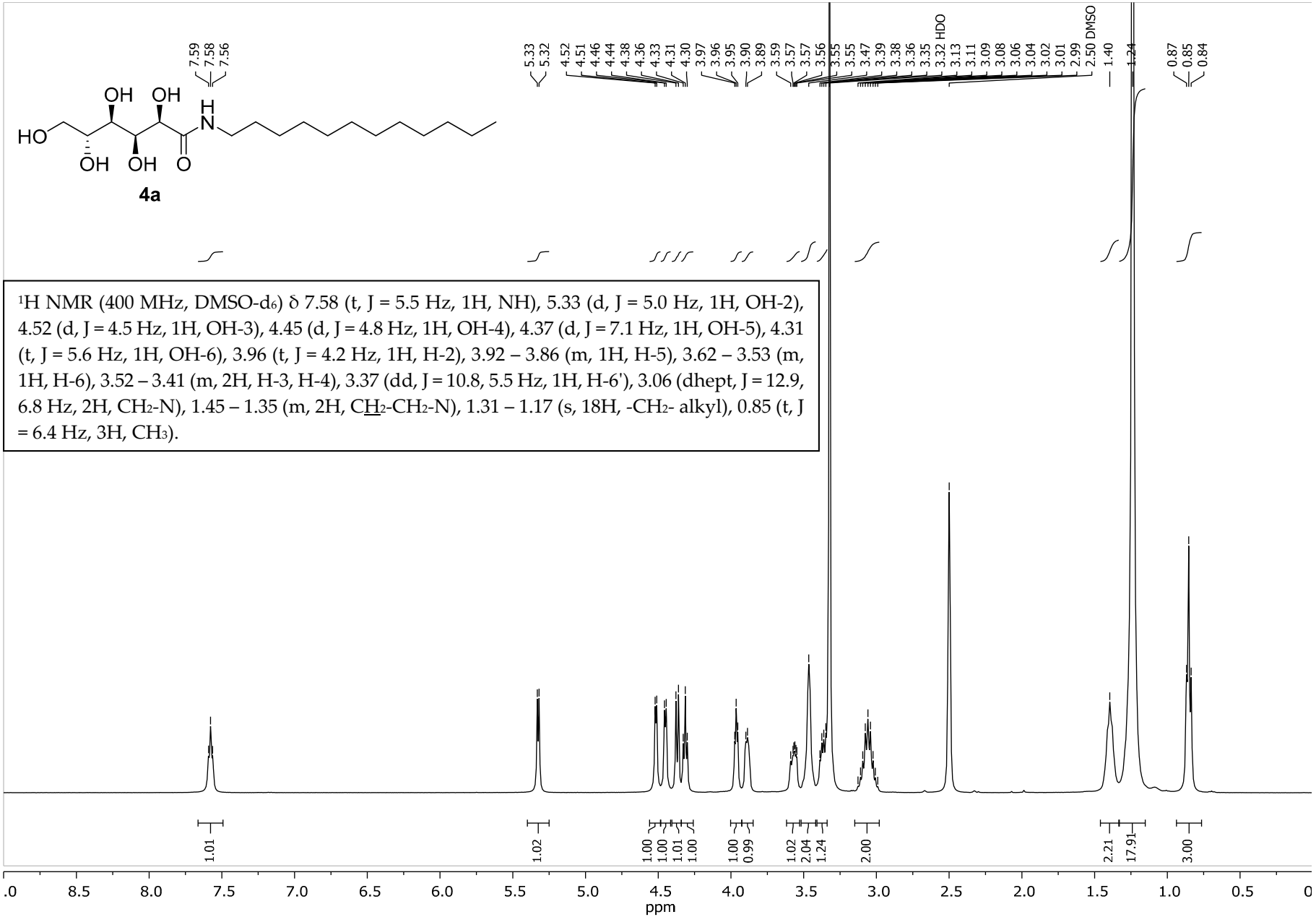
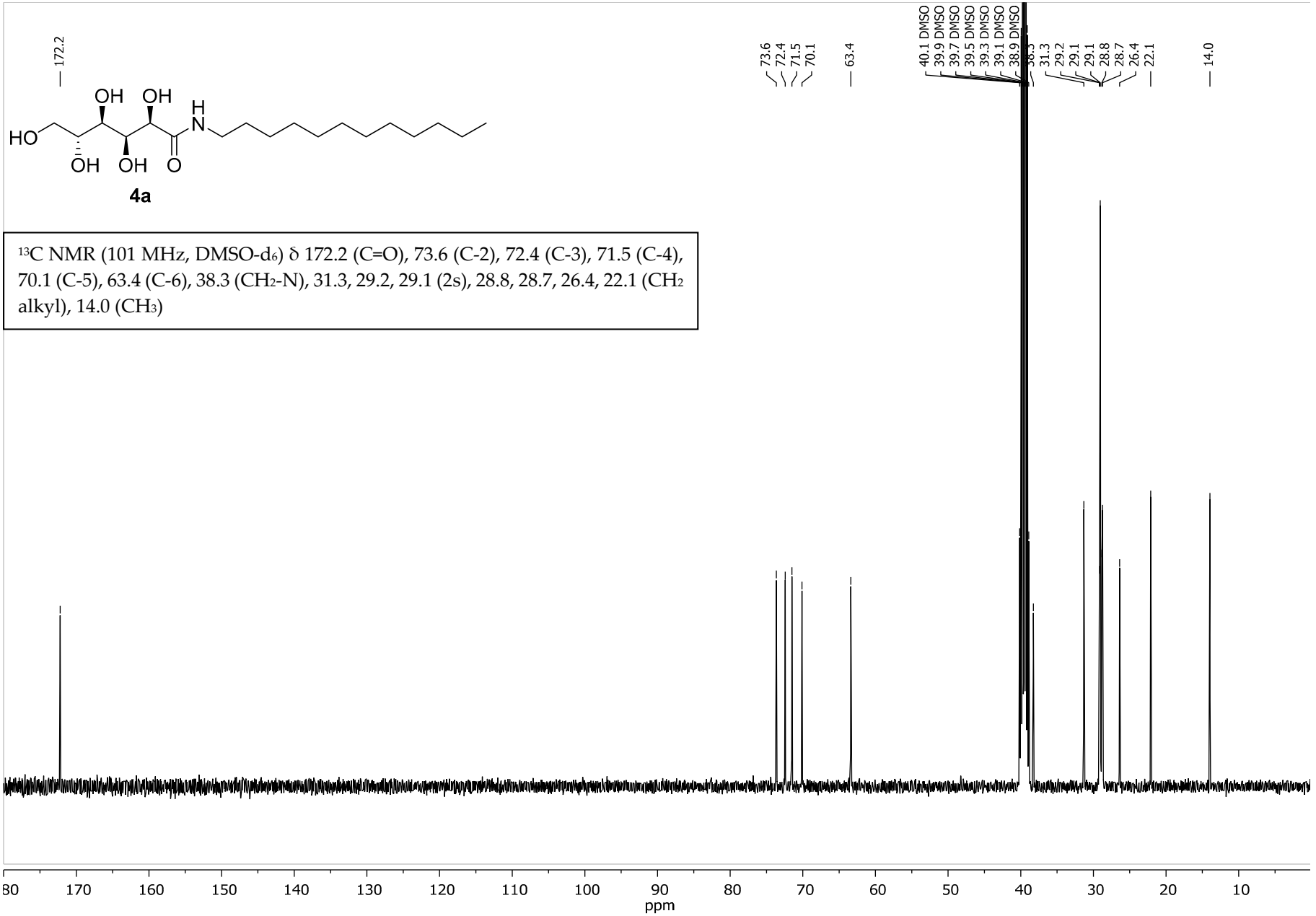
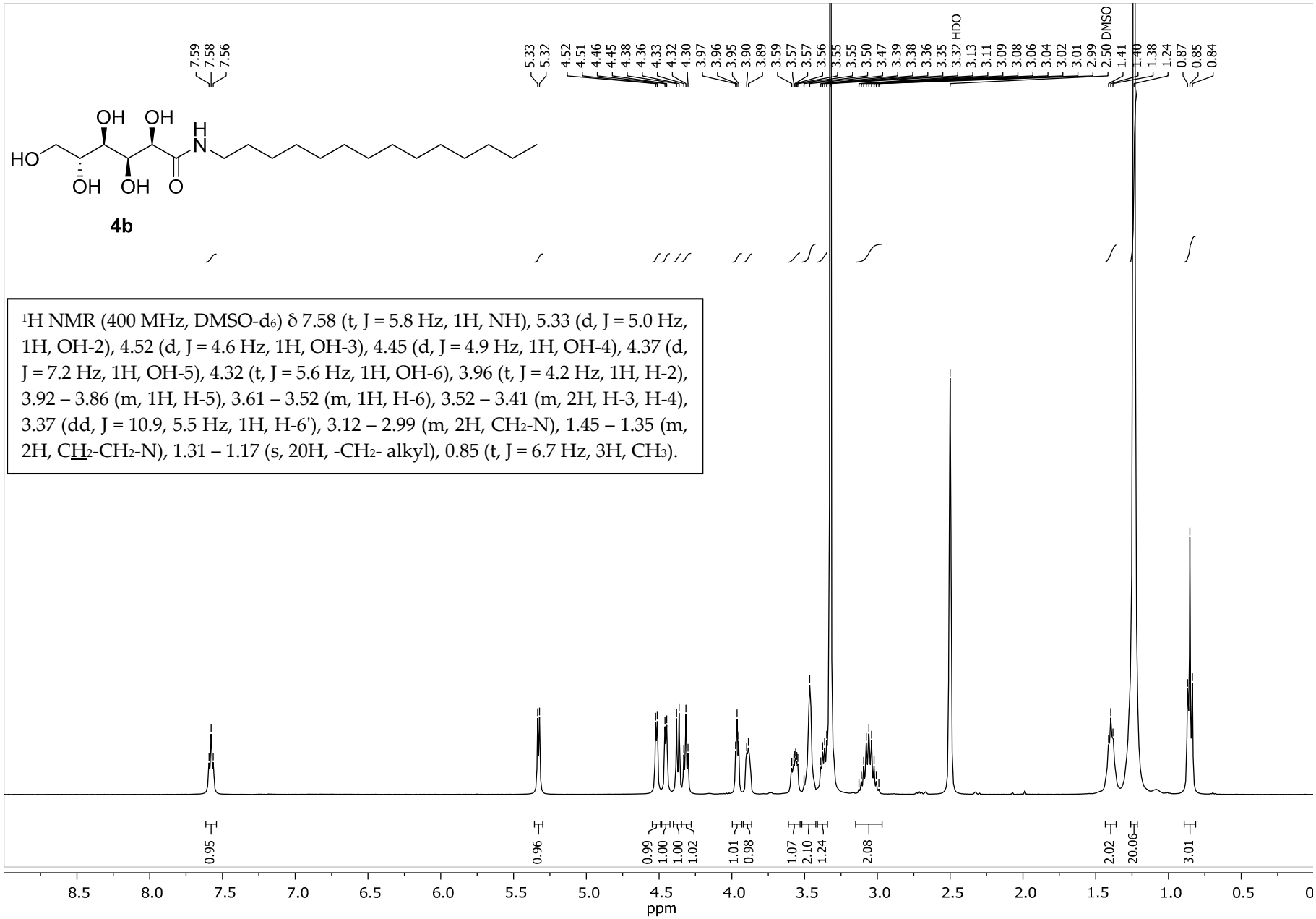


Figure S6: ^{13}C NMR spectrum of 4a crude



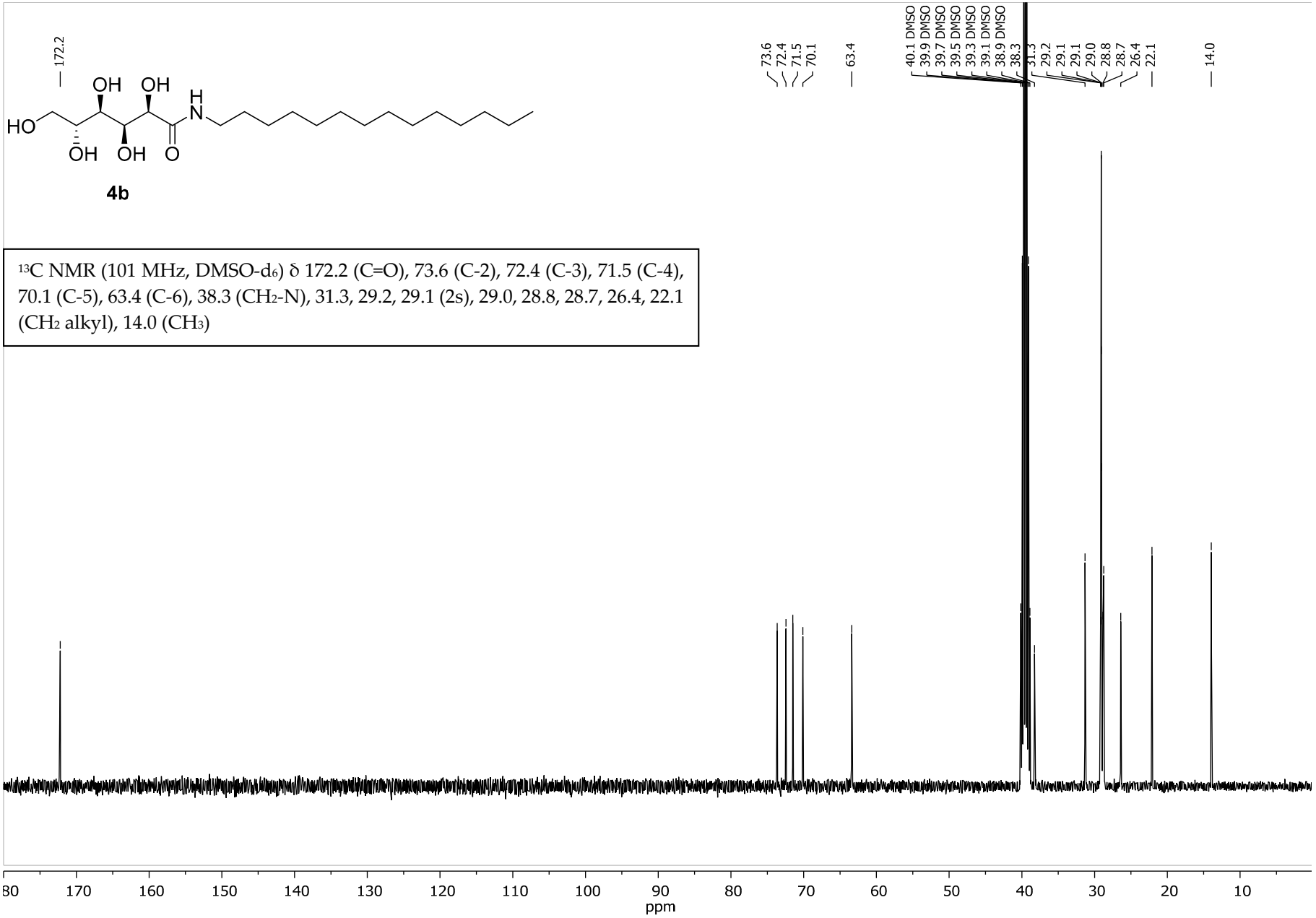
^{13}C NMR (101 MHz, DMSO-d_6) δ 172.2 (C=O), 73.6 (C-2), 72.4 (C-3), 71.5 (C-4), 70.1 (C-5), 63.4 (C-6), 38.3 (CH_2-N), 31.3, 29.2, 29.1 (2s), 28.8, 28.7, 26.4, 22.1 (CH_2 alkyl), 14.0 (CH_3)

Figure S7: ^{1}H NMR spectrum of 4b crude



^{1}H NMR (400 MHz, DMSO-d_6) δ 7.58 (t, J = 5.8 Hz, 1H, NH), 5.33 (d, J = 5.0 Hz, 1H, OH-2), 4.52 (d, J = 4.6 Hz, 1H, OH-3), 4.45 (d, J = 4.9 Hz, 1H, OH-4), 4.37 (d, J = 7.2 Hz, 1H, OH-5), 4.32 (t, J = 5.6 Hz, 1H, OH-6), 3.96 (t, J = 4.2 Hz, 1H, H-2), 3.92 – 3.86 (m, 1H, H-5), 3.61 – 3.52 (m, 1H, H-6), 3.52 – 3.41 (m, 2H, H-3, H-4), 3.37 (dd, J = 10.9, 5.5 Hz, 1H, H-6'), 3.12 – 2.99 (m, 2H, CH_2-N), 1.45 – 1.35 (m, 2H, C$\underline{H}_2$-CH_2-N), 1.31 – 1.17 (s, 20H, -CH_2- alkyl), 0.85 (t, J = 6.7 Hz, 3H, CH_3).

Figure S8: ^{13}C NMR spectrum of 4b crude



^{13}C NMR (101 MHz, DMSO-d_6) δ 172.2 (C=O), 73.6 (C-2), 72.4 (C-3), 71.5 (C-4), 70.1 (C-5), 63.4 (C-6), 38.3 (CH_2-N), 31.3, 29.2, 29.1 (2s), 29.0, 28.8, 28.7, 26.4, 22.1 (CH_2 alkyl), 14.0 (CH_3)

Figure S9: COSY NMR 2D spectrum of 4b crude

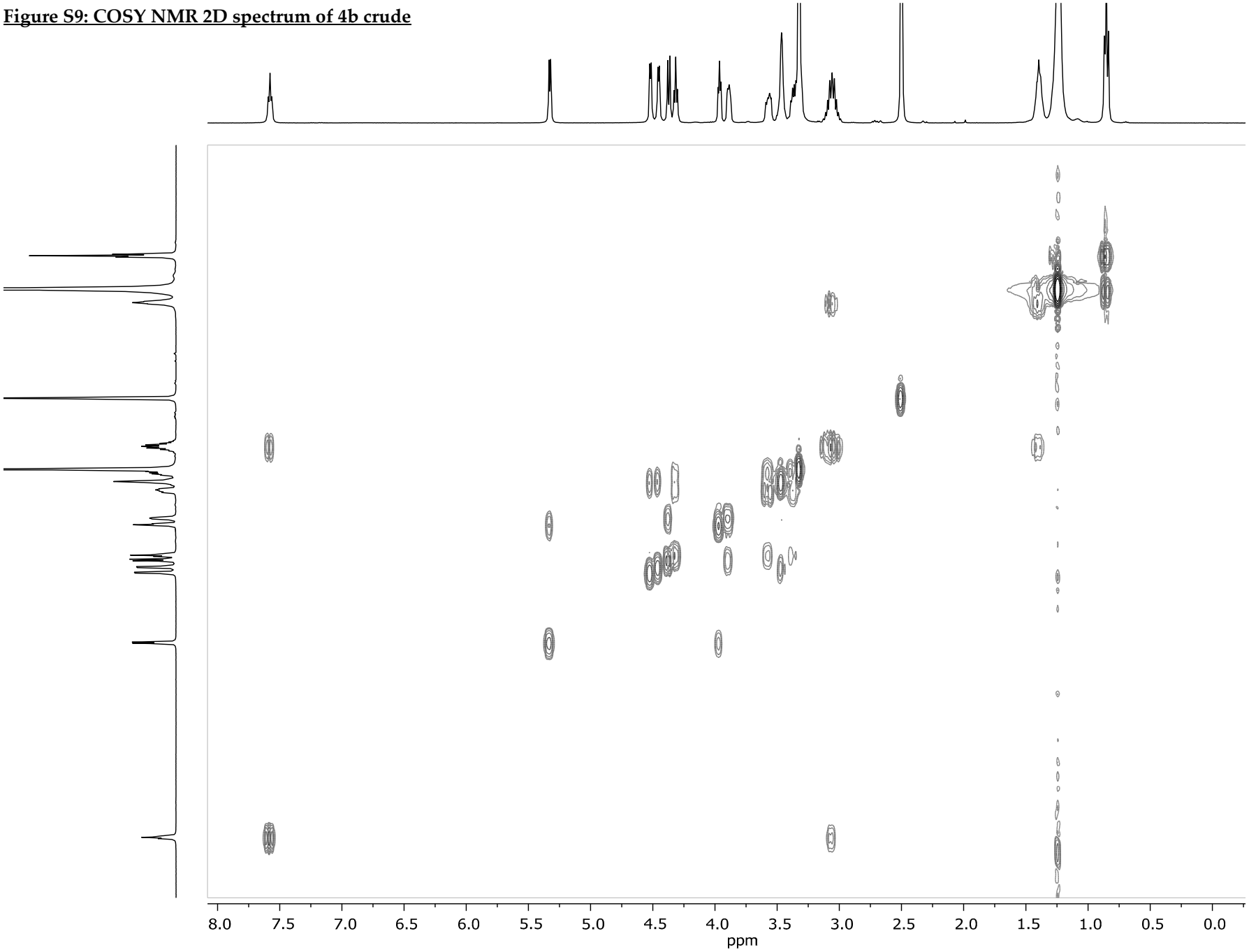


Figure S10: HSQC ^{13}C-^{1}H NMR 2D spectrum of 4b crude

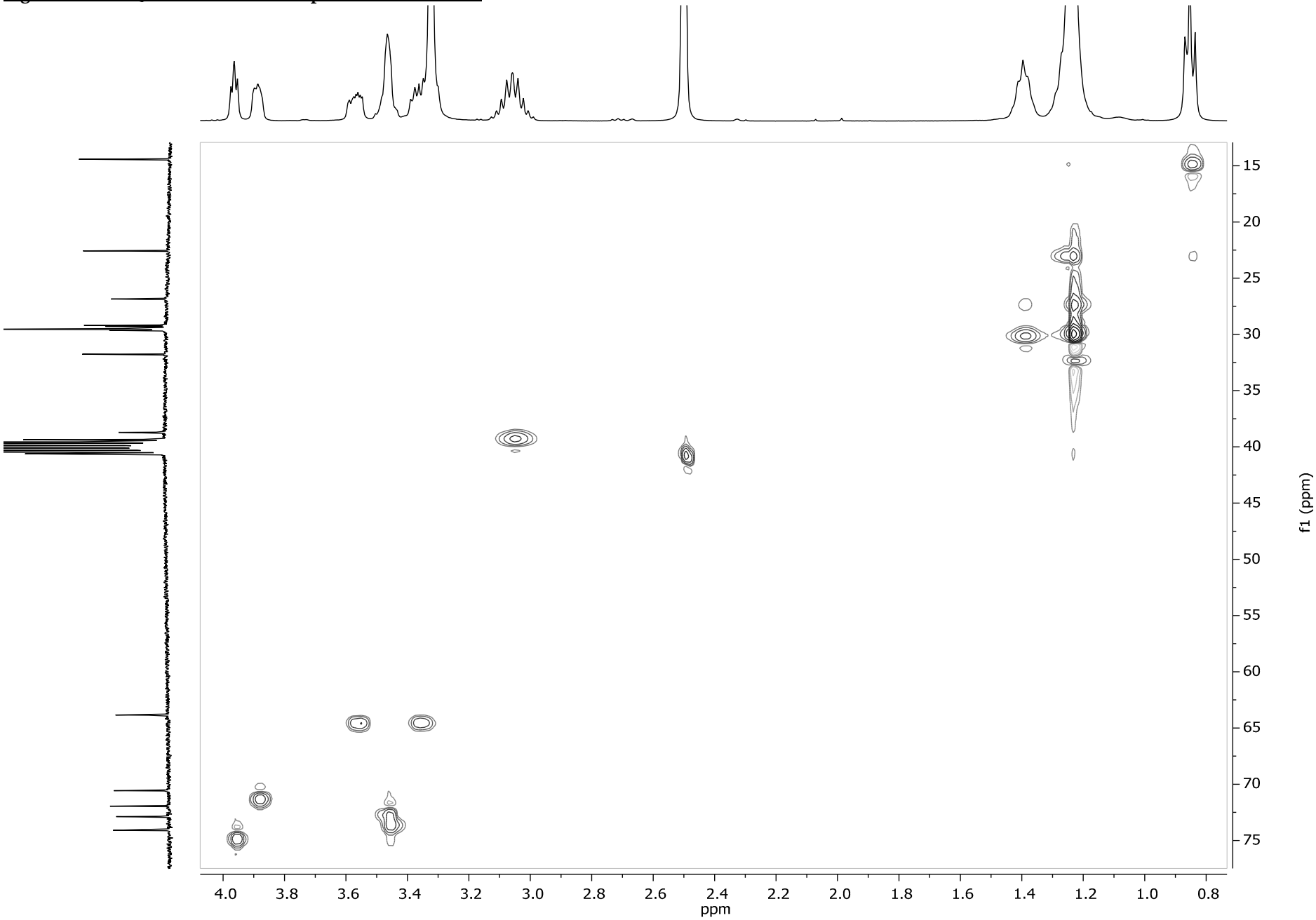
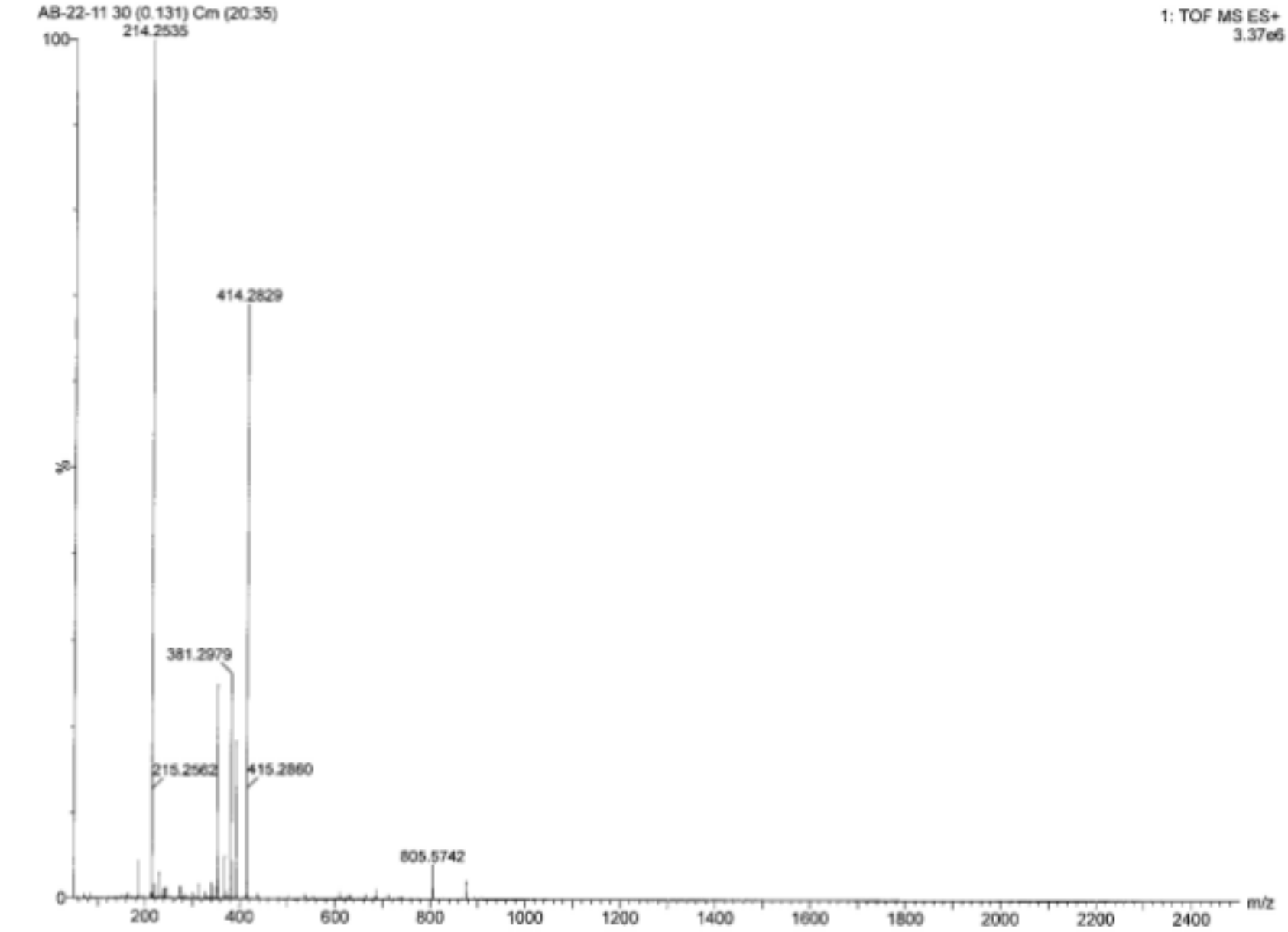
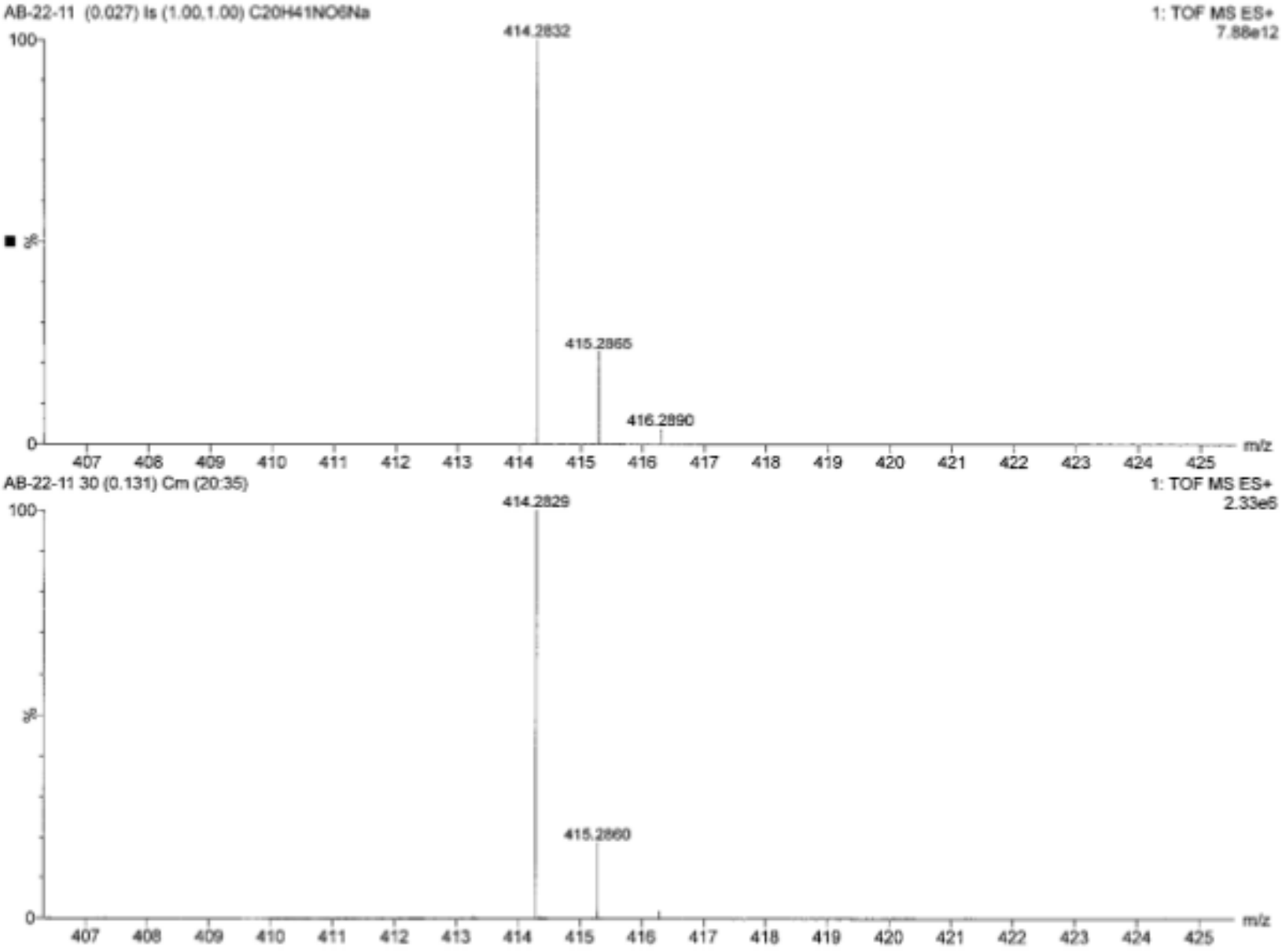


Figure S11: HRMS analysis of 4b crude



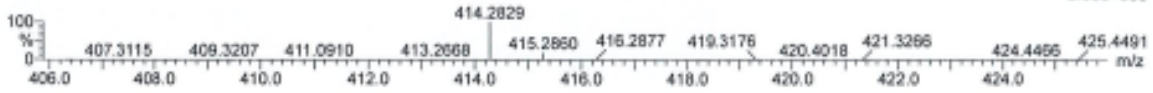

AB-22-11 (0.027) Is (1.00,1.00) C20H41NO6Na
1: TOF MS ES+
7.88e12
414.2832
415.2865
416.2890
100
%
0
m/z
407 408 409 410 411 412 413 414 415 416 417 418 419 420 421 422 423 424 425
AB-22-11 30 (0.131) Cm (20:35)
1: TOF MS ES+
2.33e6
414.2829
415.2860
100
%
0
m/z
407 408 409 410 411 412 413 414 415 416 417 418 419 420 421 422 423 424 425

Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -5.0, max = 150.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
1784 formula(e) evaluated with 4 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-50 H: 0-100 N: 0-10 O: 0-50 Na: 0-1

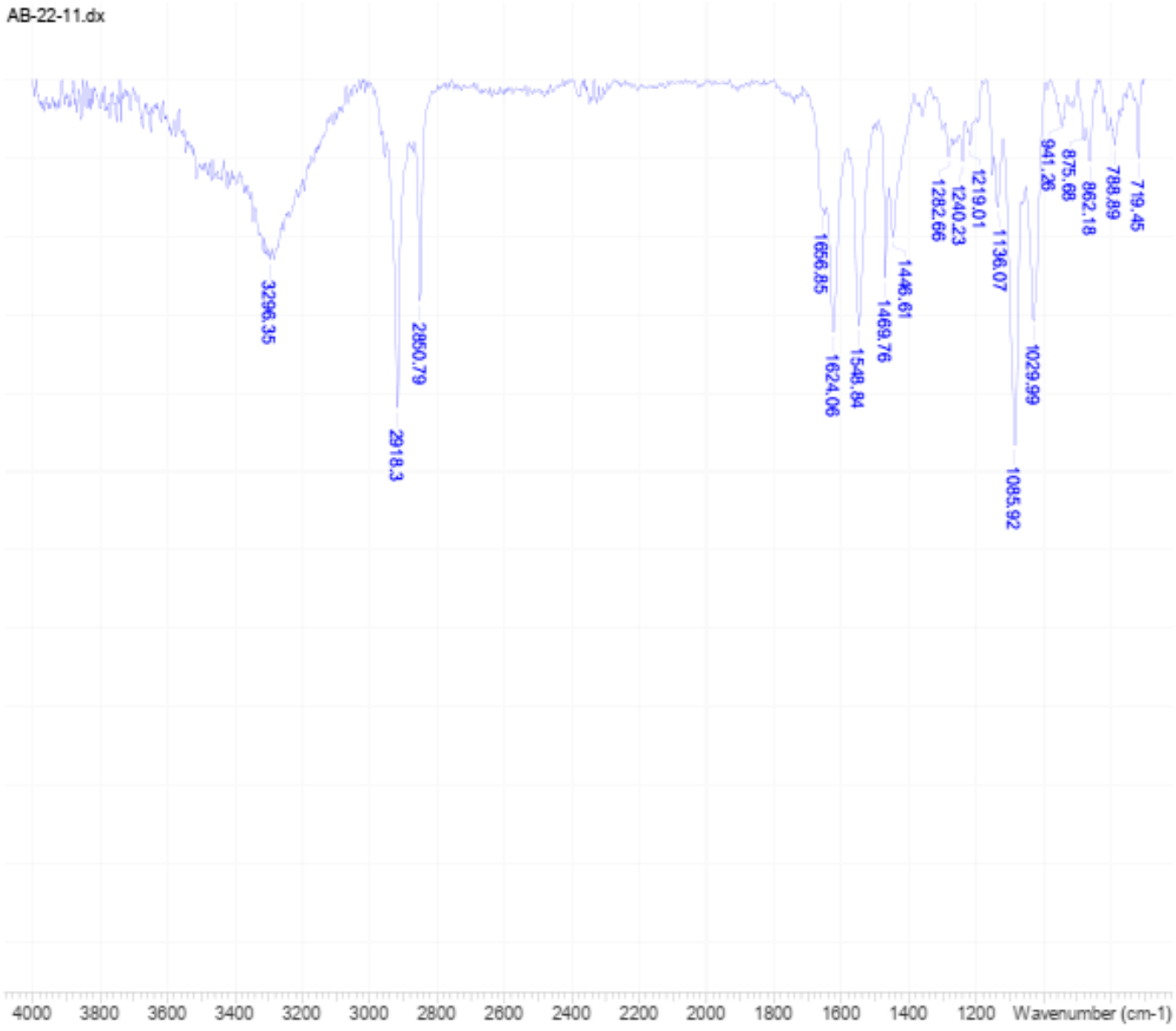
AB-22-11 30 (0.131) Cm (20:35) 1: TOF MS ES+ 2.33e+006



Minimum:				-5.0				
Maximum:		5.0	5.0	150.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
414.2829	414.2829	0.0	0.0	4.5	2260.6	0.390	67.73	C18 H36 N7 O4
	414.2832	-0.3	-0.7	0.5	2262.8	2.604	7.40	C20 H41 N O6 Na
	414.2815	1.4	3.4	-0.5	2261.7	1.447	23.53	C17 H40 N3 O8
	414.2845	-1.6	-3.9	5.5	2264.5	4.307	1.35	C21 H37 N5 O2 Na

Figure S12: IR analysis of 4b crude

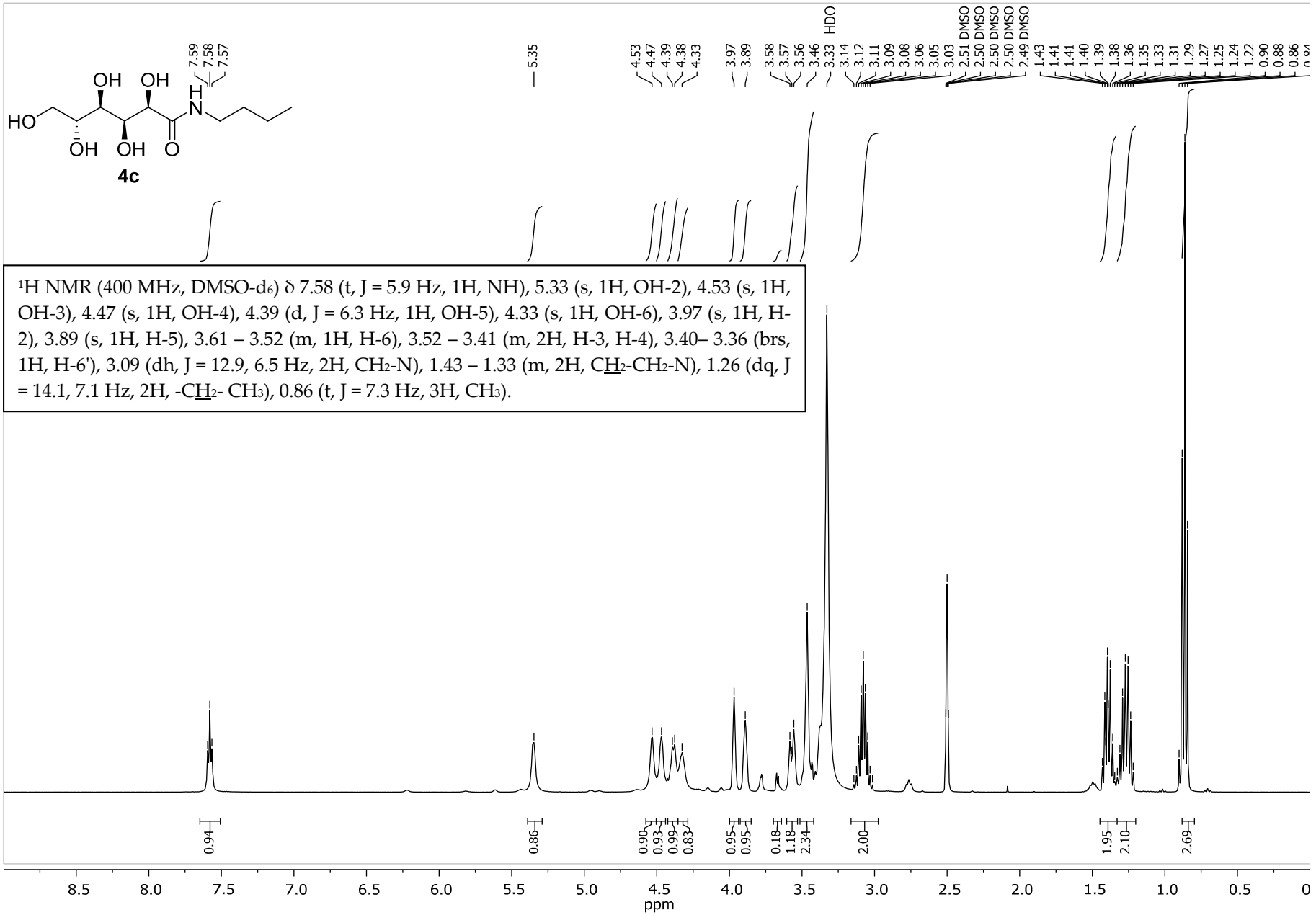
Title	AB-22-111	***File Name***	C:\PROGRAM FILES (X86)\LABSOLUTIONS\IR\DATA\ABED\AB-22-11.DX		
Date	07 Jun 2022 16:38:00	***Technique***	Infrared	***Spectral Region***	IR
X Axis	Wavenumber (cm-1)	***Y Axis***	%Transmittance	***Spectrum Range***	700.1603 - 4000.3641
Points Count	1712	***Data Spacing***	1.9288		



No	cm-1	%T	FWHH	Asym	Intensity
1	719.45	98.003	-	-	W
2	788.89	98.328	-	-	W
3	862.18	97.920	-	-	W
4	875.68	98.772	-	-	W
5	941.26	99.033	-	-	W
6	1029.99	93.841	-	-	S
7	1085.92	90.675	-	-	VS
8	1136.07	96.743	-	-	M
9	1219.01	98.324	-	-	W
10	1240.23	97.915	-	-	W

No	cm-1	%T	FWHH	Asym	Intensity
11	1282.66	98.033	-	-	W
12	1446.61	95.985	-	-	M
13	1469.76	94.946	-	-	M
14	1548.84	93.716	-	-	S
15	1624.06	93.557	-	-	S
16	1656.85	96.671	-	-	M
17	2850.79	94.353	-	-	S
18	2918.30	91.629	-1.00	0.00	S
19	3296.35	95.410	-	-	M

Figure S13: ^{1}H NMR spectrum of 4c crude



^{1}H NMR (400 MHz, DMSO-d_6) δ 7.58 (t, J = 5.9 Hz, 1H, NH), 5.33 (s, 1H, OH-2), 4.53 (s, 1H, OH-3), 4.47 (s, 1H, OH-4), 4.39 (d, J = 6.3 Hz, 1H, OH-5), 4.33 (s, 1H, OH-6), 3.97 (s, 1H, H-2), 3.89 (s, 1H, H-5), 3.61 – 3.52 (m, 1H, H-6), 3.52 – 3.41 (m, 2H, H-3, H-4), 3.40– 3.36 (brs, 1H, H-6'), 3.09 (dh, J = 12.9, 6.5 Hz, 2H, CH_2-N), 1.43 – 1.33 (m, 2H, C<u>H</u>$_2$-CH_2-N), 1.26 (dq, J = 14.1, 7.1 Hz, 2H, -C<u>H</u>$_2$- CH_3), 0.86 (t, J = 7.3 Hz, 3H, CH_3).

Figure S14: ^{13}C spectrum of 4c crude

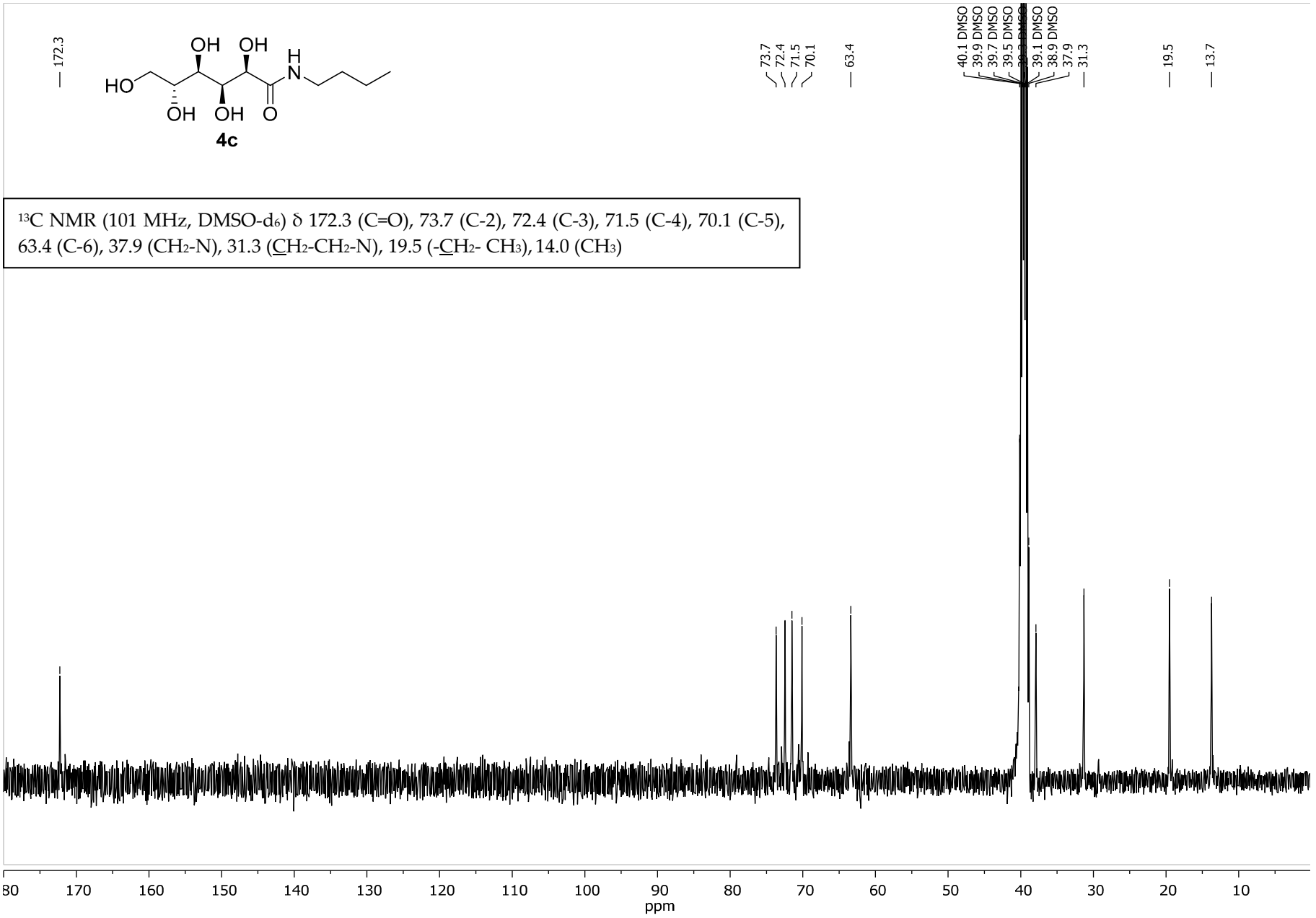


Figure S15: ^{1}H NMR spectrum of 4d crude

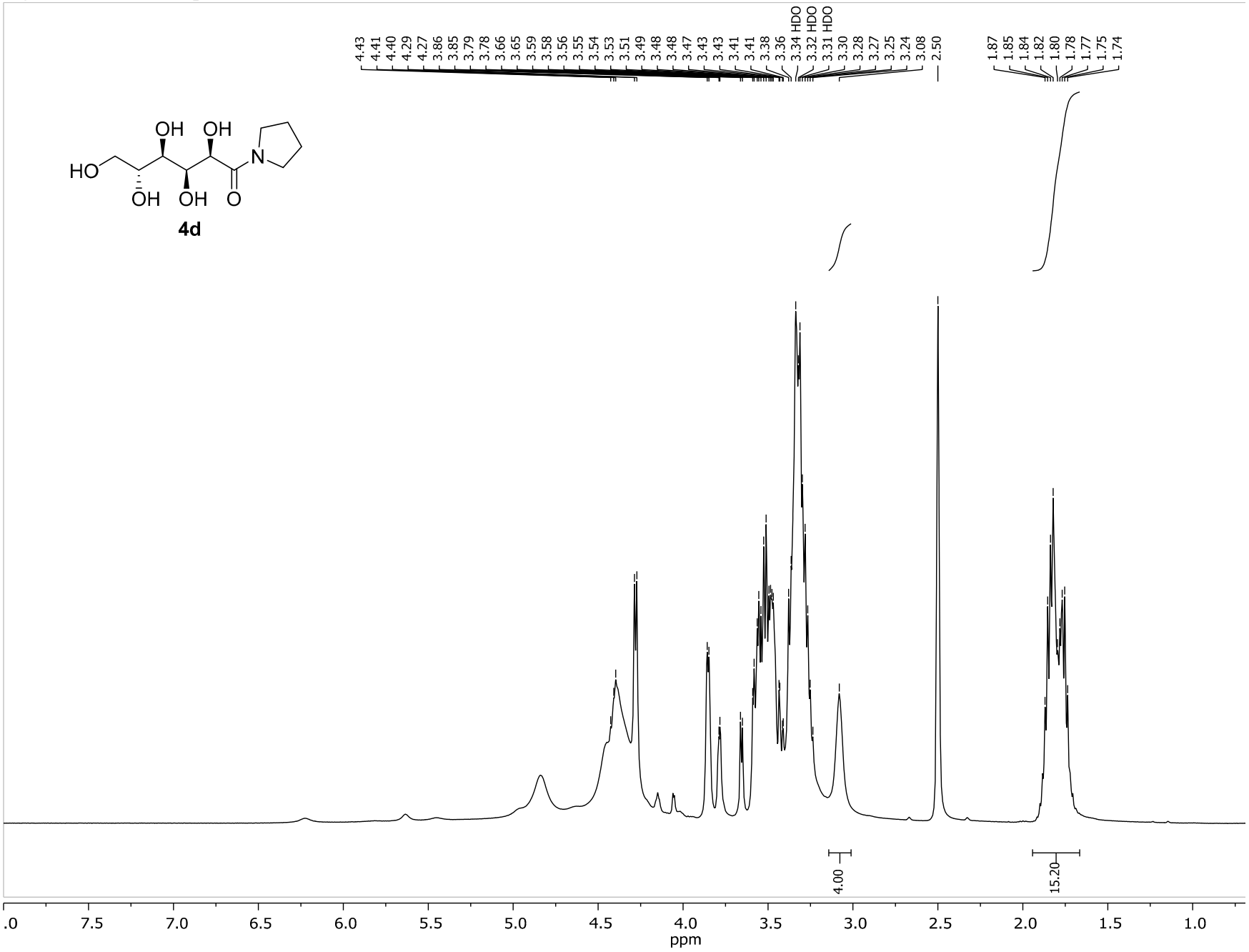


Figure S16: ^{13}C NMR spectrum of 4d crude

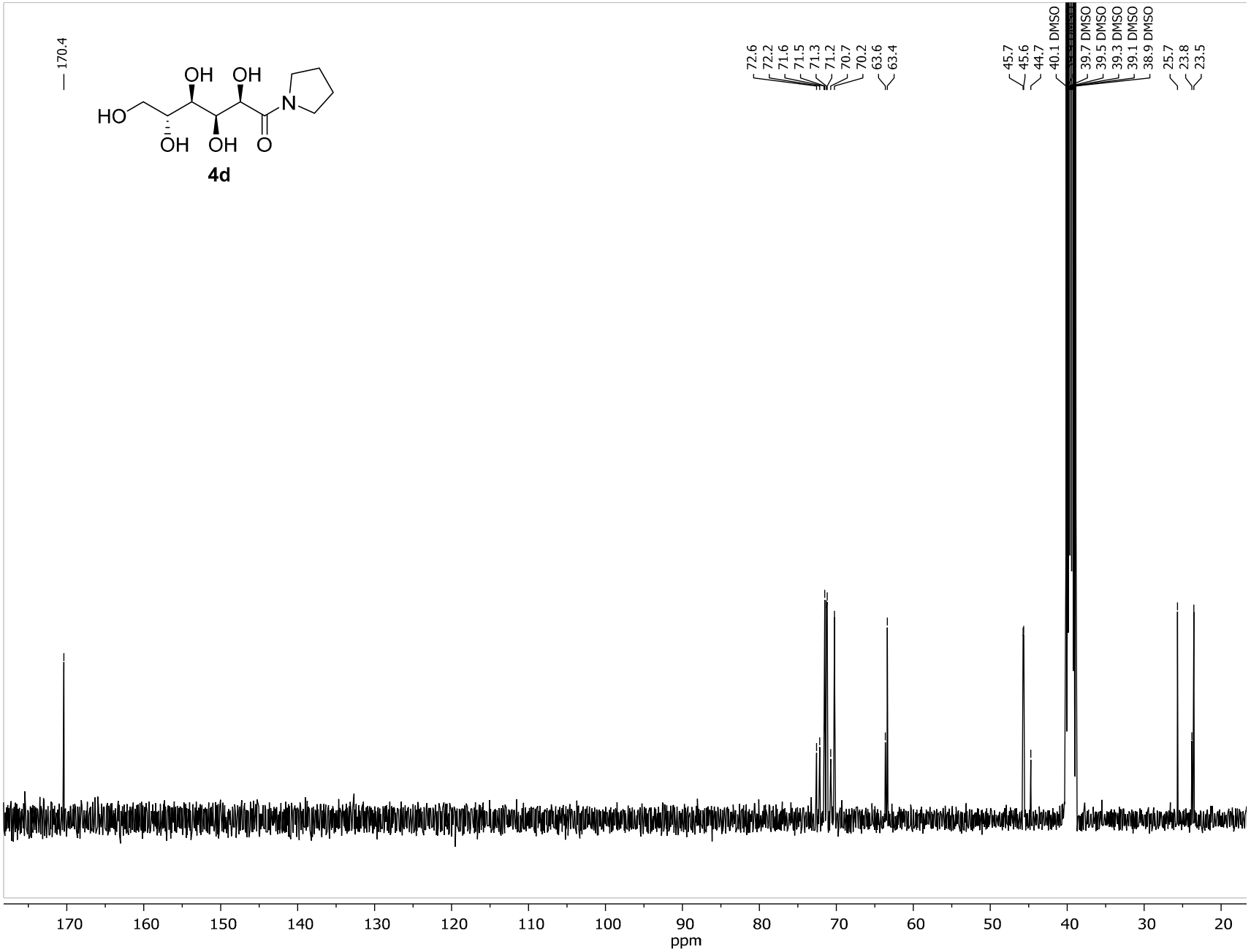
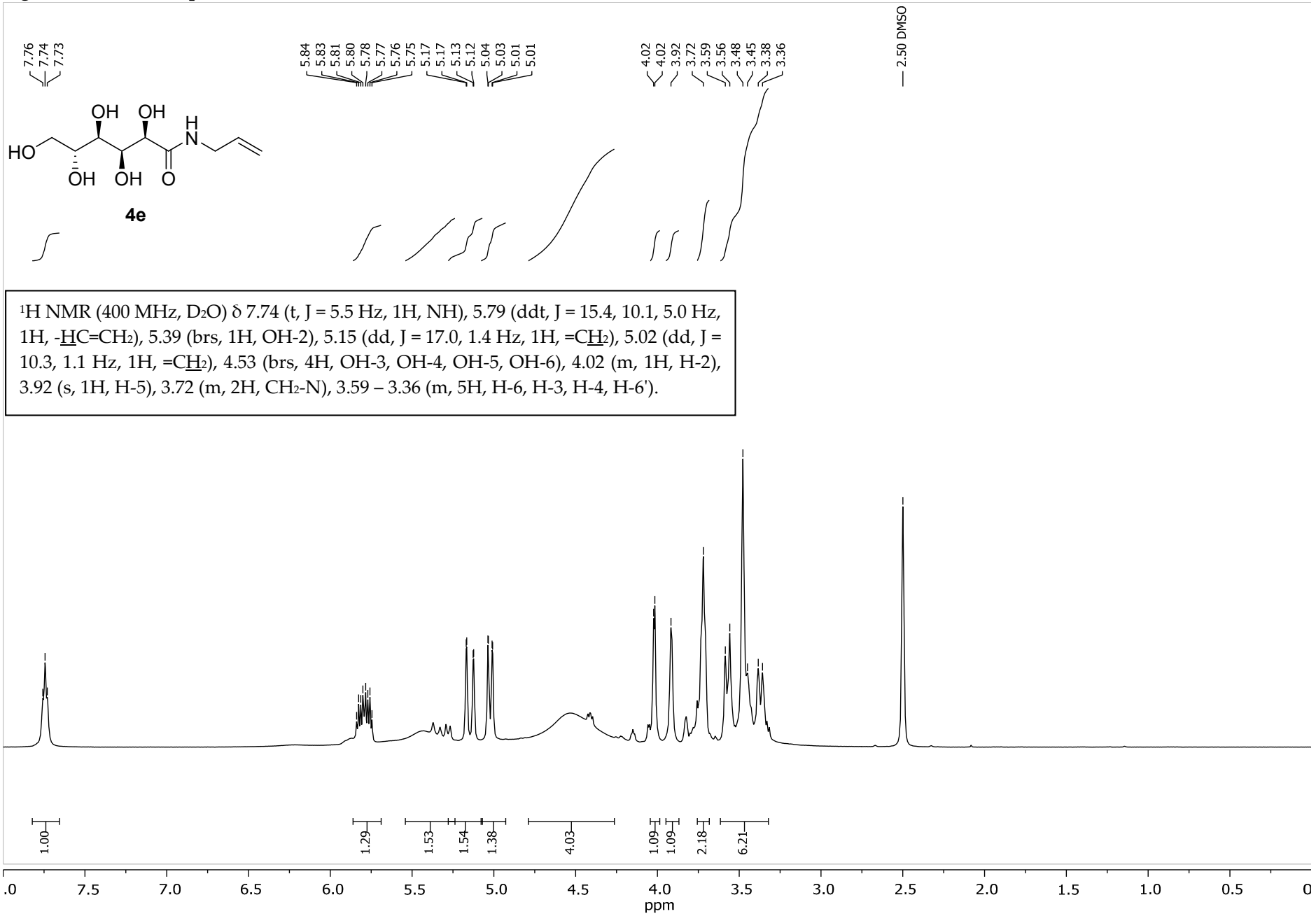
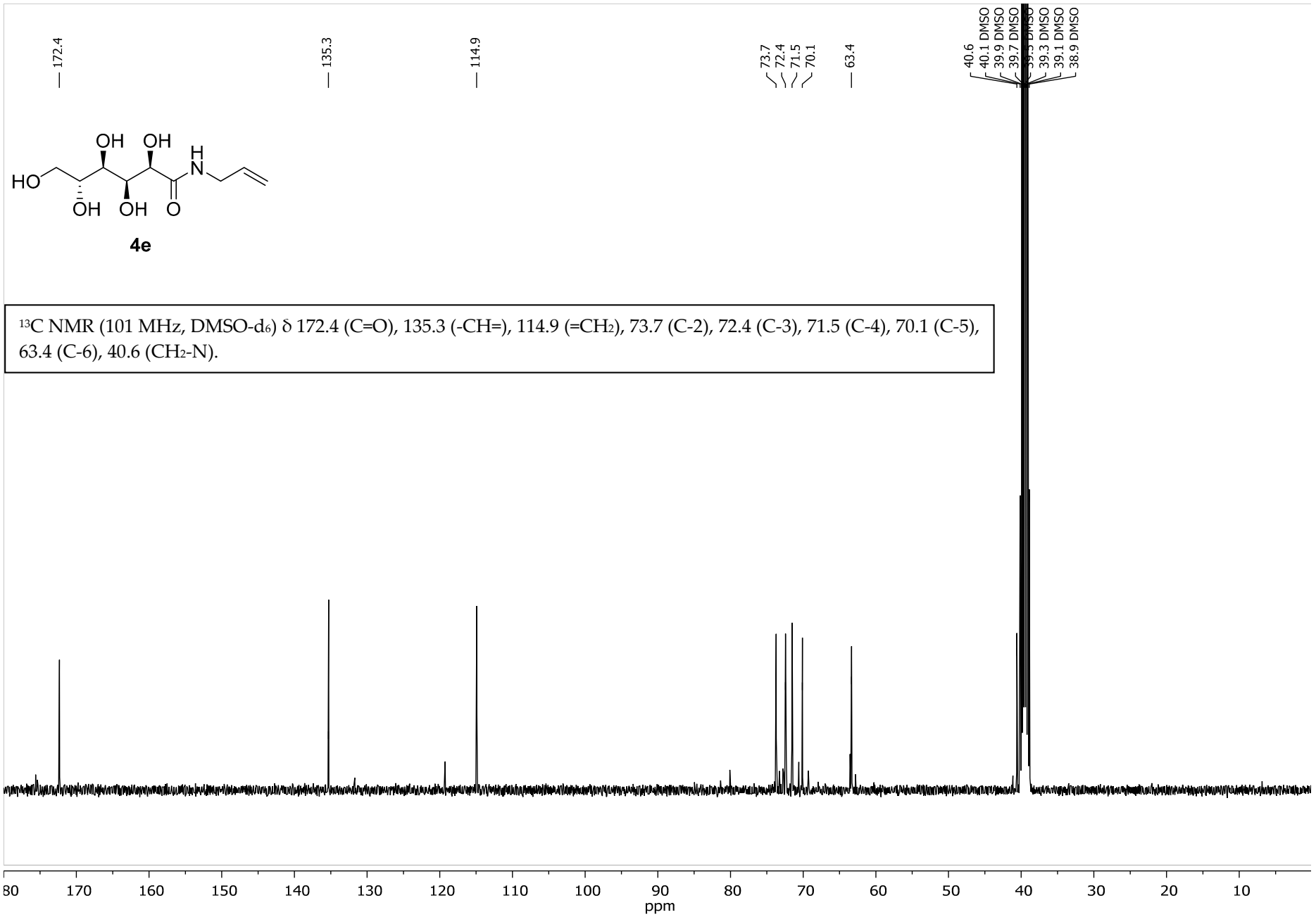


Figure S17: ^{1}H NMR spectrum of 4e crude



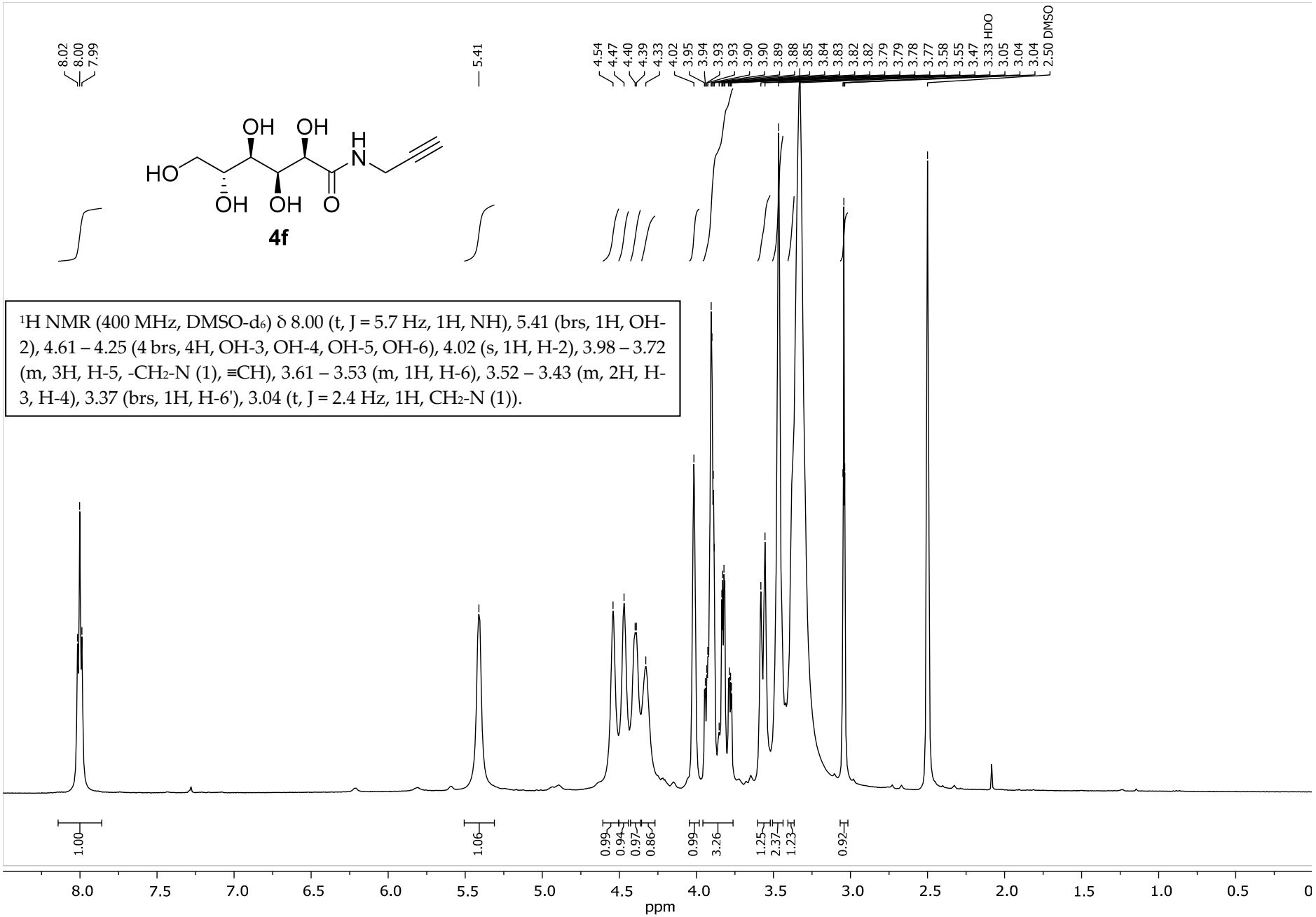
^{1}H NMR (400 MHz, D_2O) δ 7.74 (t, J = 5.5 Hz, 1H, NH), 5.79 (ddt, J = 15.4, 10.1, 5.0 Hz, 1H, -HC=CH_2), 5.39 (brs, 1H, OH-2), 5.15 (dd, J = 17.0, 1.4 Hz, 1H, =CH_2), 5.02 (dd, J = 10.3, 1.1 Hz, 1H, =CH_2), 4.53 (brs, 4H, OH-3, OH-4, OH-5, OH-6), 4.02 (m, 1H, H-2), 3.92 (s, 1H, H-5), 3.72 (m, 2H, CH_2-N), 3.59 – 3.36 (m, 5H, H-6, H-3, H-4, H-6').

Figure S18: ^{13}C NMR spectrum of 4e crude



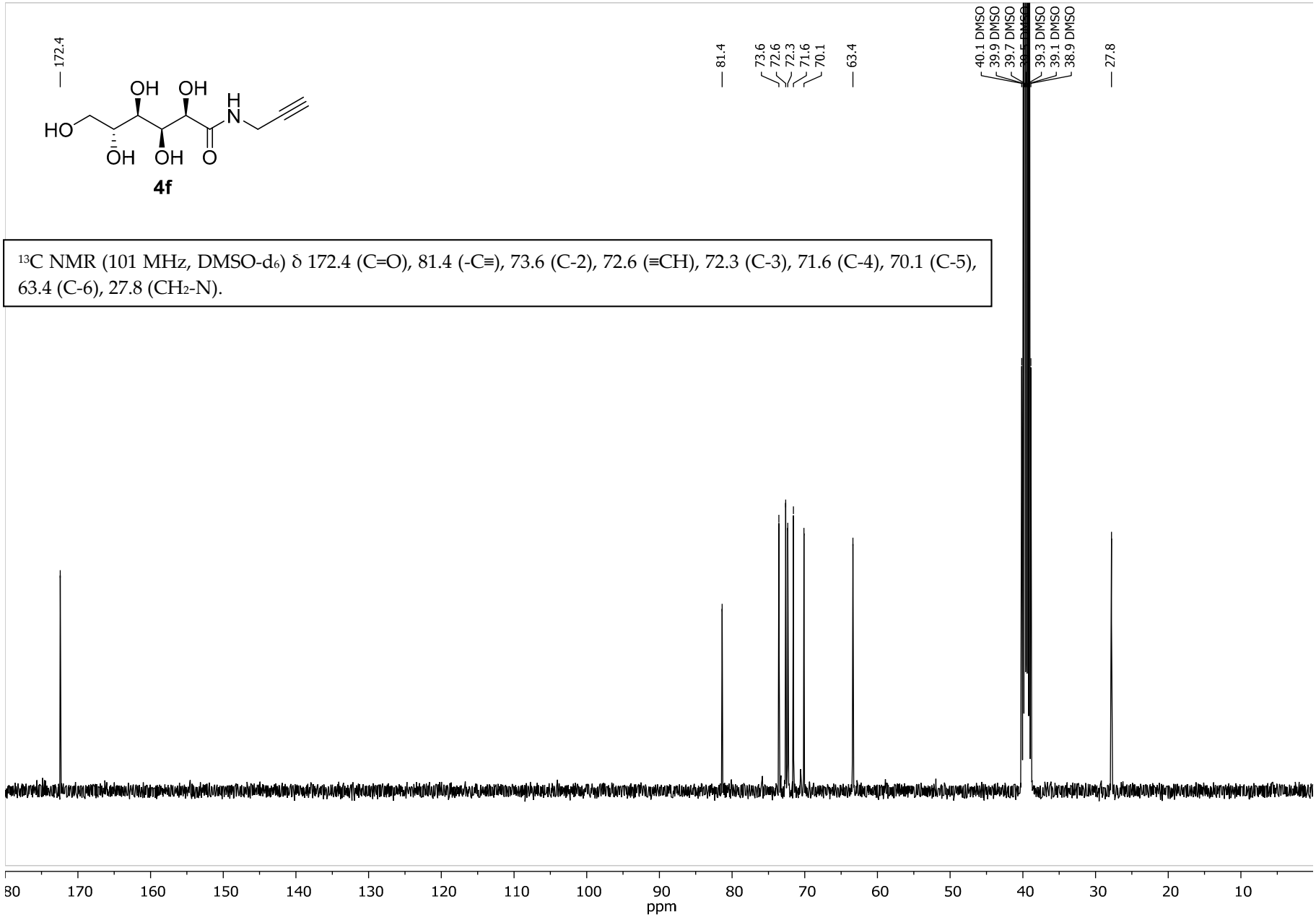
^{13}C NMR (101 MHz, DMSO-d_6) δ 172.4 (C=O), 135.3 (-CH=), 114.9 (=CH_2), 73.7 (C-2), 72.4 (C-3), 71.5 (C-4), 70.1 (C-5), 63.4 (C-6), 40.6 (CH_2-N).

Figure S19: ^{1}H NMR spectrum of 4f crude



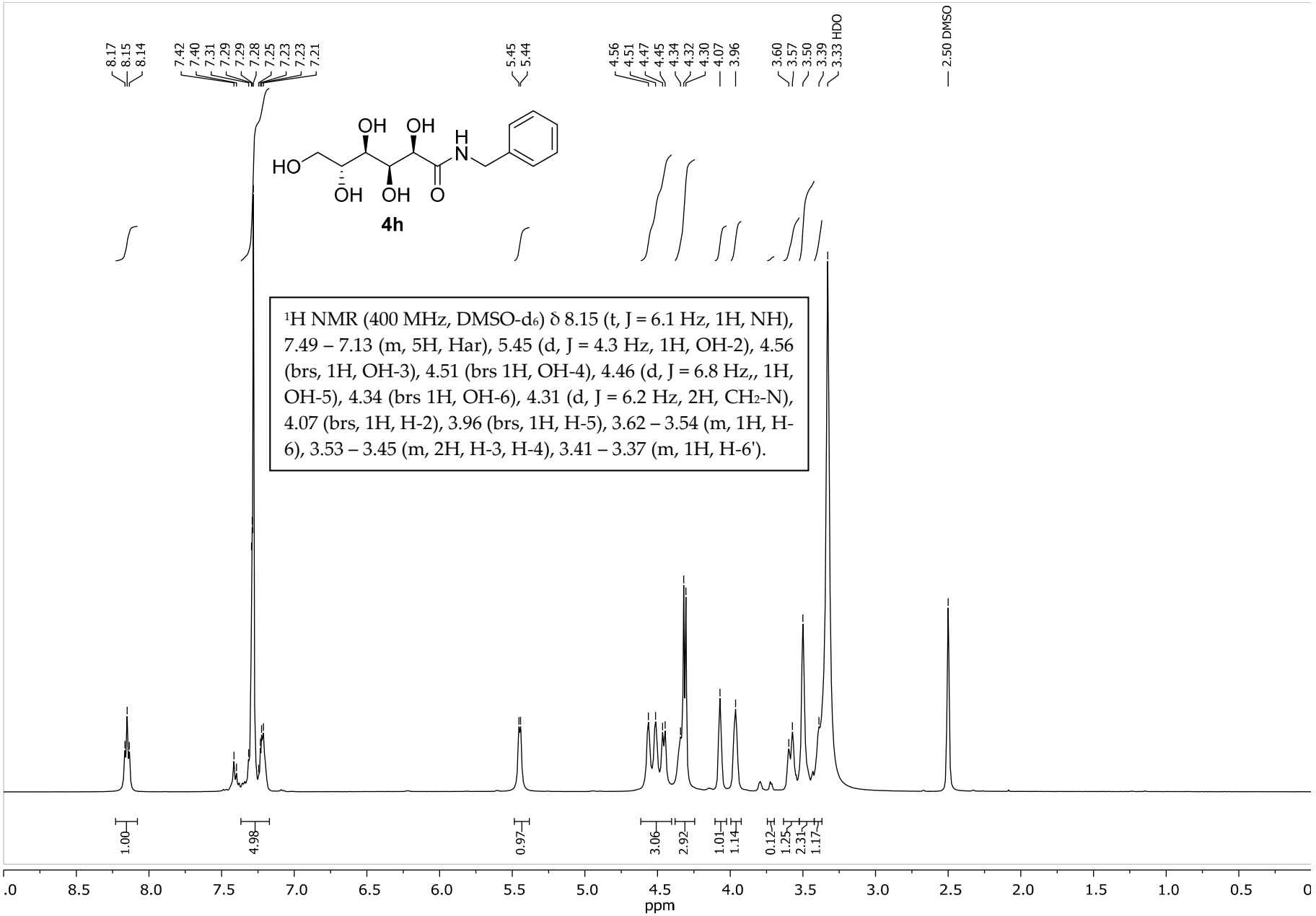
^{1}H NMR (400 MHz, DMSO-d_6) δ 8.00 (t, J = 5.7 Hz, 1H, NH), 5.41 (brs, 1H, OH-2), 4.61 – 4.25 (4 brs, 4H, OH-3, OH-4, OH-5, OH-6), 4.02 (s, 1H, H-2), 3.98 – 3.72 (m, 3H, H-5, -CH_2-N (1), ≡CH), 3.61 – 3.53 (m, 1H, H-6), 3.52 – 3.43 (m, 2H, H-3, H-4), 3.37 (brs, 1H, H-6'), 3.04 (t, J = 2.4 Hz, 1H, CH_2-N (1)).

Figure S20: ^{13}C NMR spectrum of 4f crude



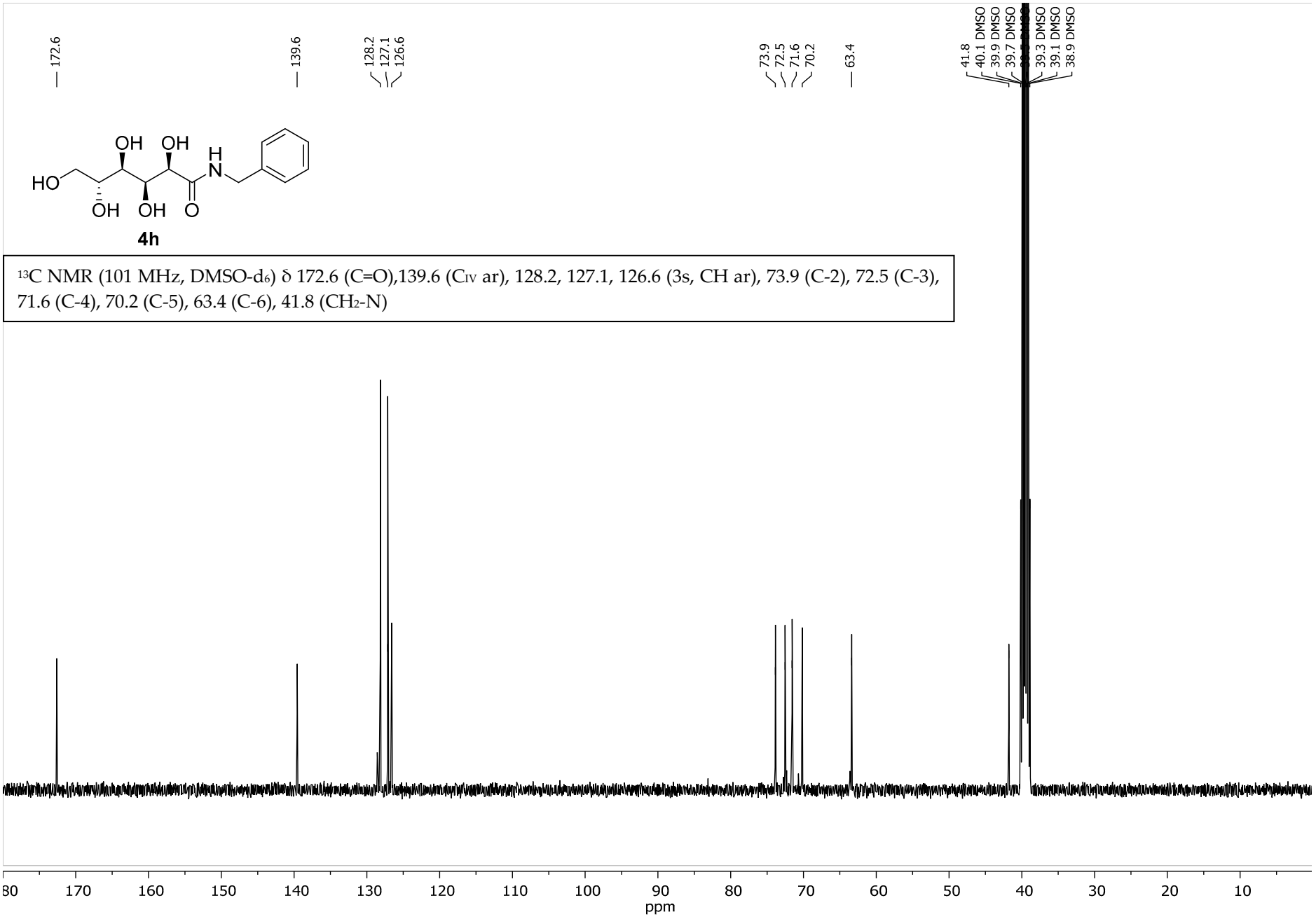
^{13}C NMR (101 MHz, DMSO-d_6) δ 172.4 (C=O), 81.4 (-C≡), 73.6 (C-2), 72.6 (≡CH), 72.3 (C-3), 71.6 (C-4), 70.1 (C-5), 63.4 (C-6), 27.8 (CH_2-N).

Figure S21: ^{1}H NMR spectrum of 4h crude



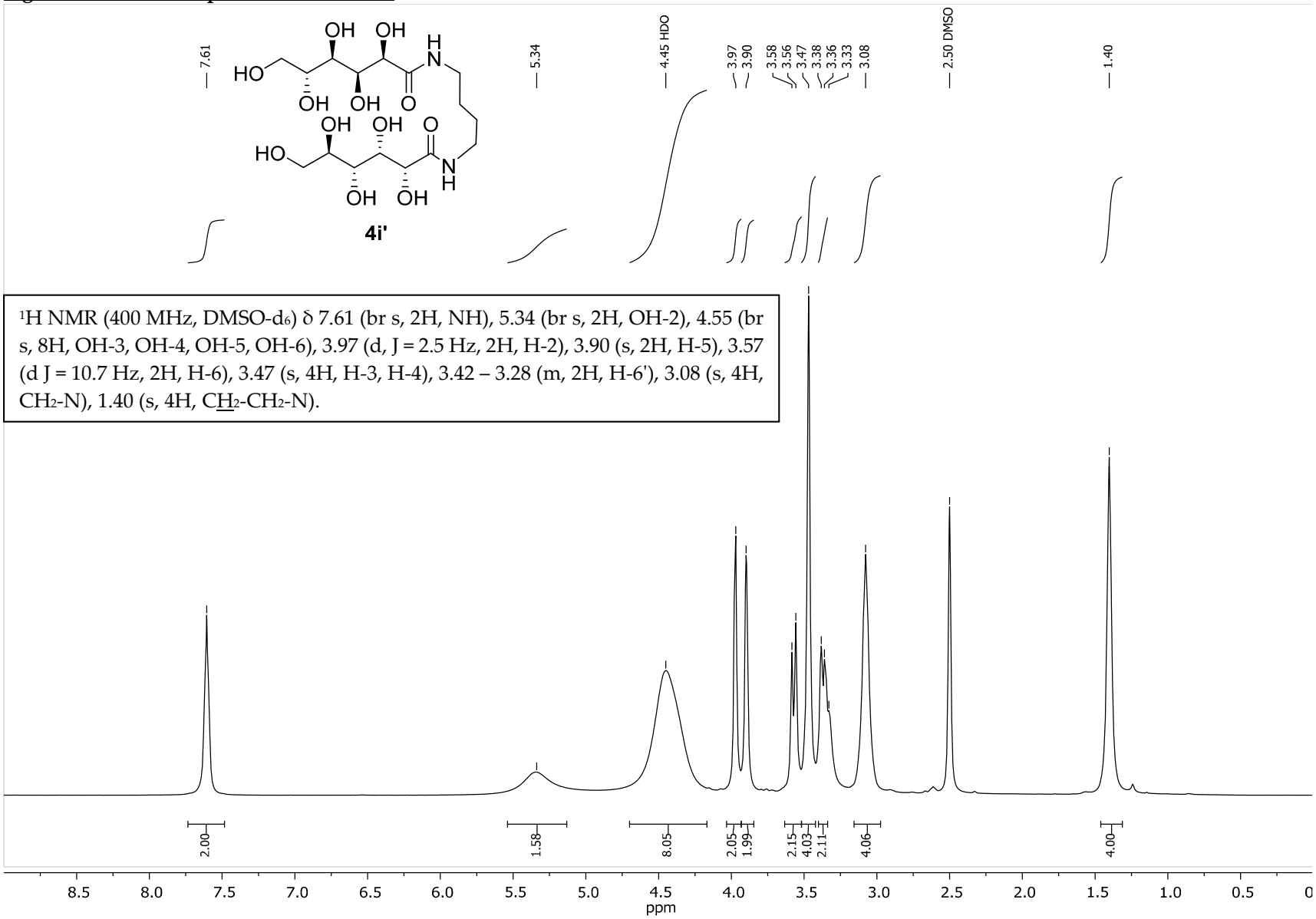
^{1}H NMR (400 MHz, DMSO-d$_6$) δ 8.15 (t, J = 6.1 Hz, 1H, NH), 7.49 – 7.13 (m, 5H, Har), 5.45 (d, J = 4.3 Hz, 1H, OH-2), 4.56 (brs, 1H, OH-3), 4.51 (brs 1H, OH-4), 4.46 (d, J = 6.8 Hz,, 1H, OH-5), 4.34 (brs 1H, OH-6), 4.31 (d, J = 6.2 Hz, 2H, CH$_2$-N), 4.07 (brs, 1H, H-2), 3.96 (brs, 1H, H-5), 3.62 – 3.54 (m, 1H, H-6), 3.53 – 3.45 (m, 2H, H-3, H-4), 3.41 – 3.37 (m, 1H, H-6').

Figure S22: ^{13}C NMR spectrum of 4h crude



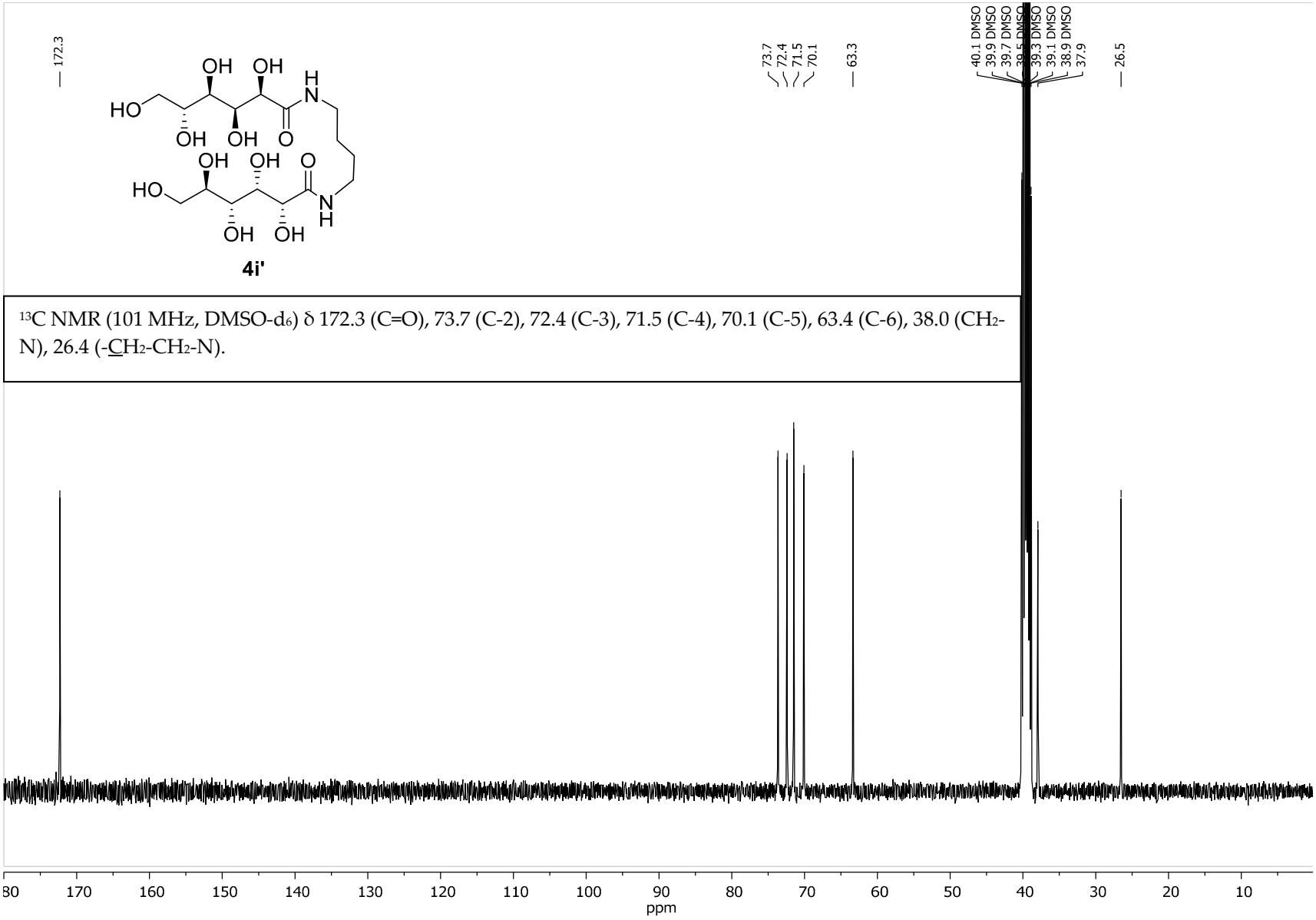
^{13}C NMR (101 MHz, DMSO-d_6) δ 172.6 (C=O),139.6 (C_{IV} ar), 128.2, 127.1, 126.6 (3s, CH ar), 73.9 (C-2), 72.5 (C-3), 71.6 (C-4), 70.2 (C-5), 63.4 (C-6), 41.8 (CH_2-N)

Figure S23: ^{1}H NMR spectrum of 4i′ crude



^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61 (br s, 2H, NH), 5.34 (br s, 2H, OH-2), 4.55 (br s, 8H, OH-3, OH-4, OH-5, OH-6), 3.97 (d, J = 2.5 Hz, 2H, H-2), 3.90 (s, 2H, H-5), 3.57 (d J = 10.7 Hz, 2H, H-6), 3.47 (s, 4H, H-3, H-4), 3.42 – 3.28 (m, 2H, H-6'), 3.08 (s, 4H, CH_2-N), 1.40 (s, 4H, C$\underline{H}_2$-CH_2-N).

Figure S24: ^{13}C NMR spectrum of 4i' crude



4i'

^{13}C NMR (101 MHz, DMSO-d_6) δ 172.3 (C=O), 73.7 (C-2), 72.4 (C-3), 71.5 (C-4), 70.1 (C-5), 63.4 (C-6), 38.0 (CH_2-N), 26.4 (-$\underline{C}H_2$-CH_2-N).

Figure S25: COSY NMR 2D spectrum of 4i' crude

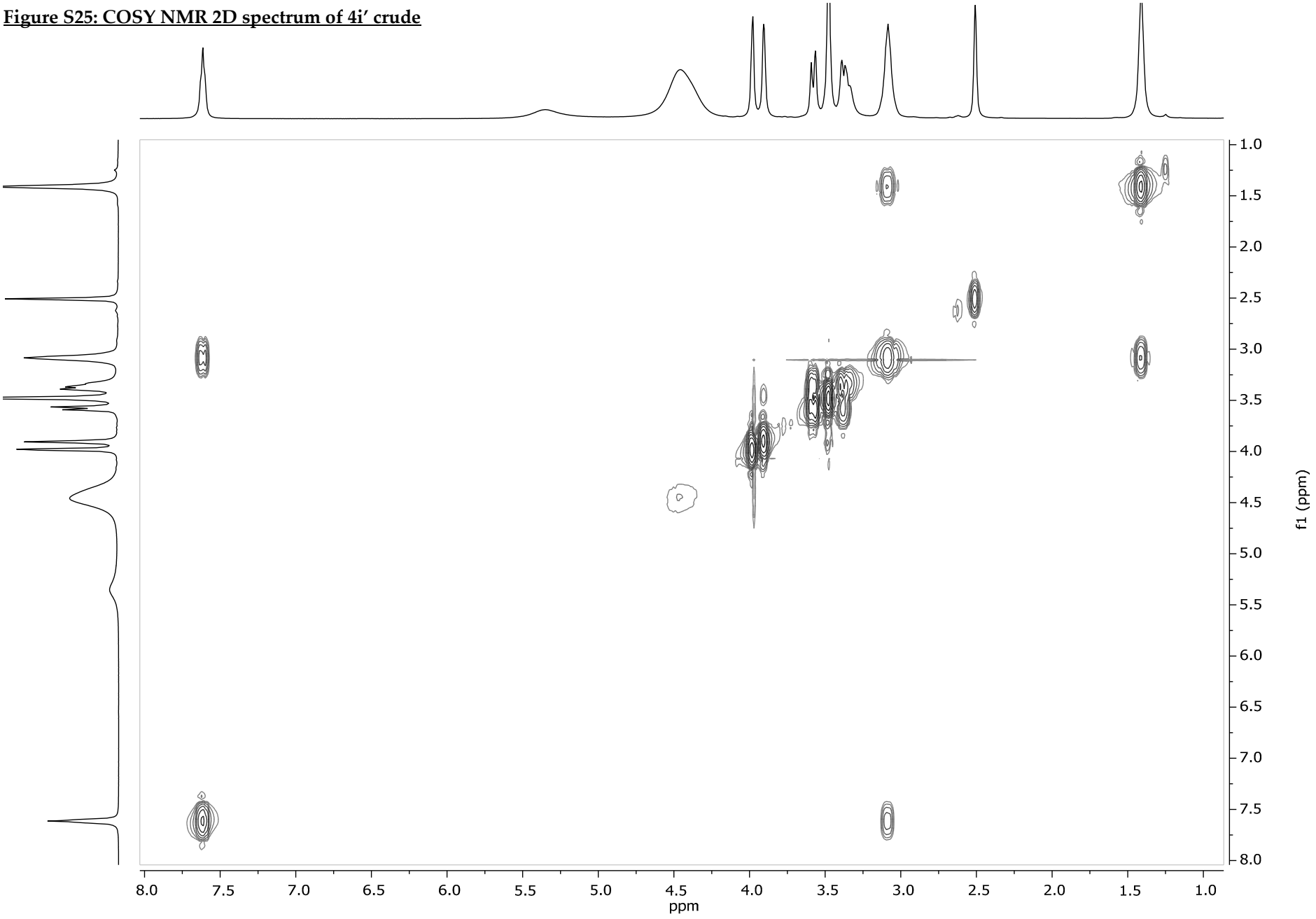


Figure S26: HSQC ^{13}C-^{1}H NMR 2D spectrum of 4i′ crude

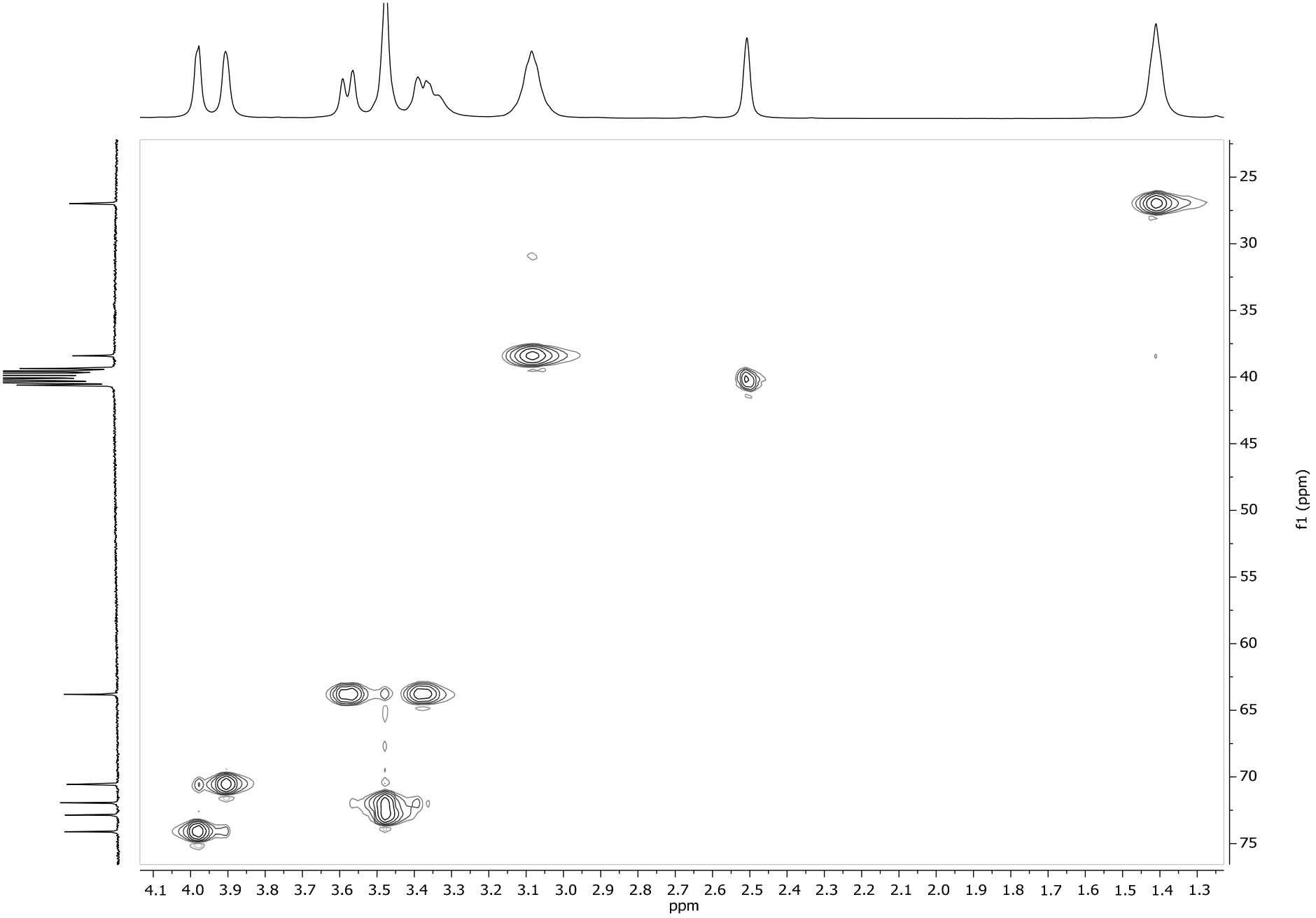
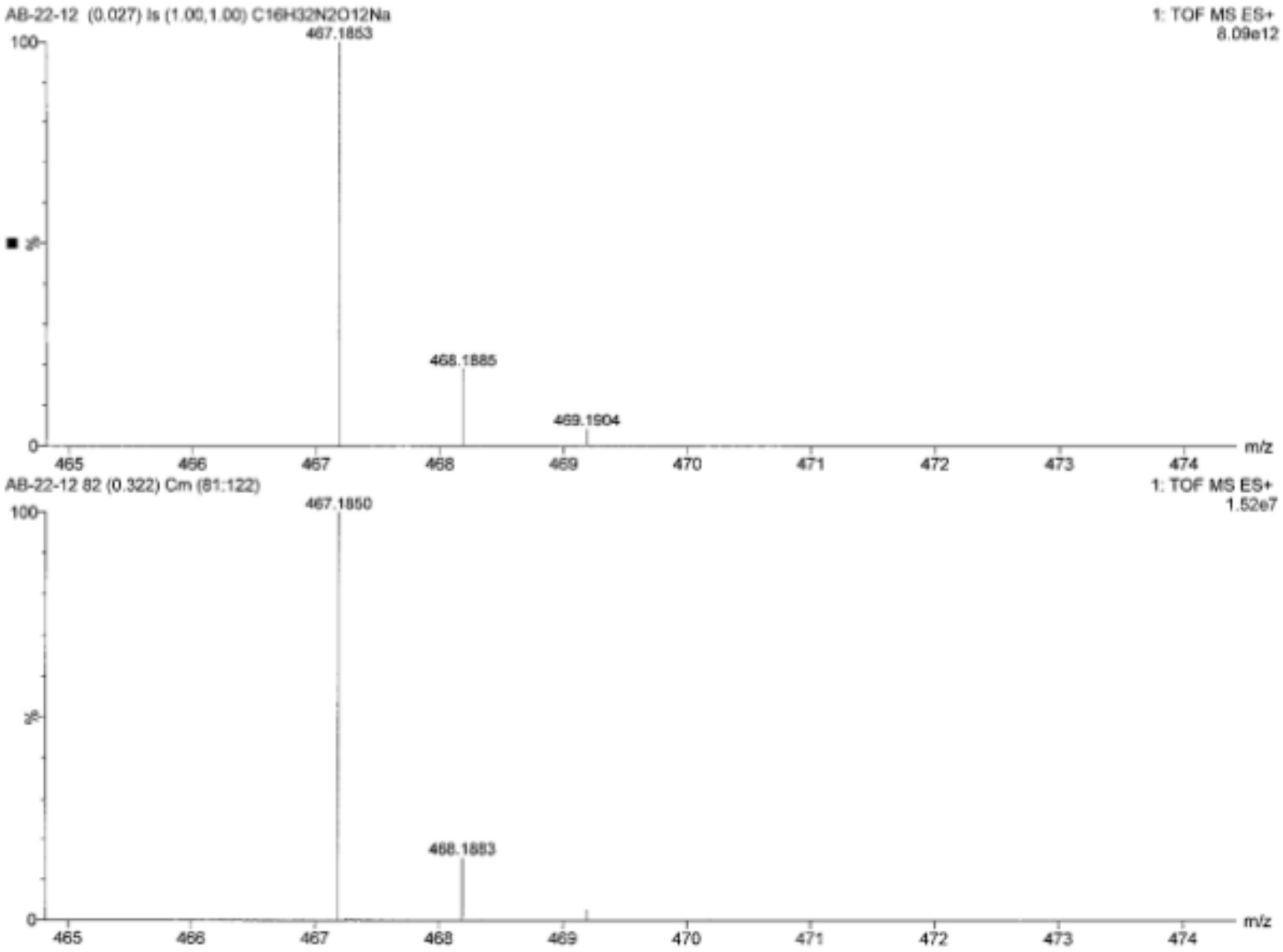


Figure S27: HRMS analysis of 4i' crude


AB-22-12 (0.027) Is (1.00,1.00) C16H32N2O12Na
1: TOF MS ES+
8.09e12
467.1853
468.1885
469.1904
100
%
0
m/z
465
466
467
468
469
470
471
472
473
474
AB-22-12 82 (0.322) Cm (81:122)
1: TOF MS ES+
1.52e7
467.1850
468.1883
100
%
0
m/z
465
466
467
468
469
470
471
472
473
474

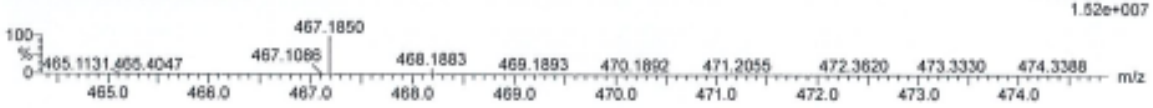
Elemental Composition Report

Single Mass Analysis
Tolerance = 5.0 PPM / DBE: min = -5.0, max = 150.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
2246 formula(e) evaluated with 9 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-50 H: 0-100 N: 0-10 O: 0-50 Na: 0-1

AB-22-12 82 (0.322) Cm (81:122)

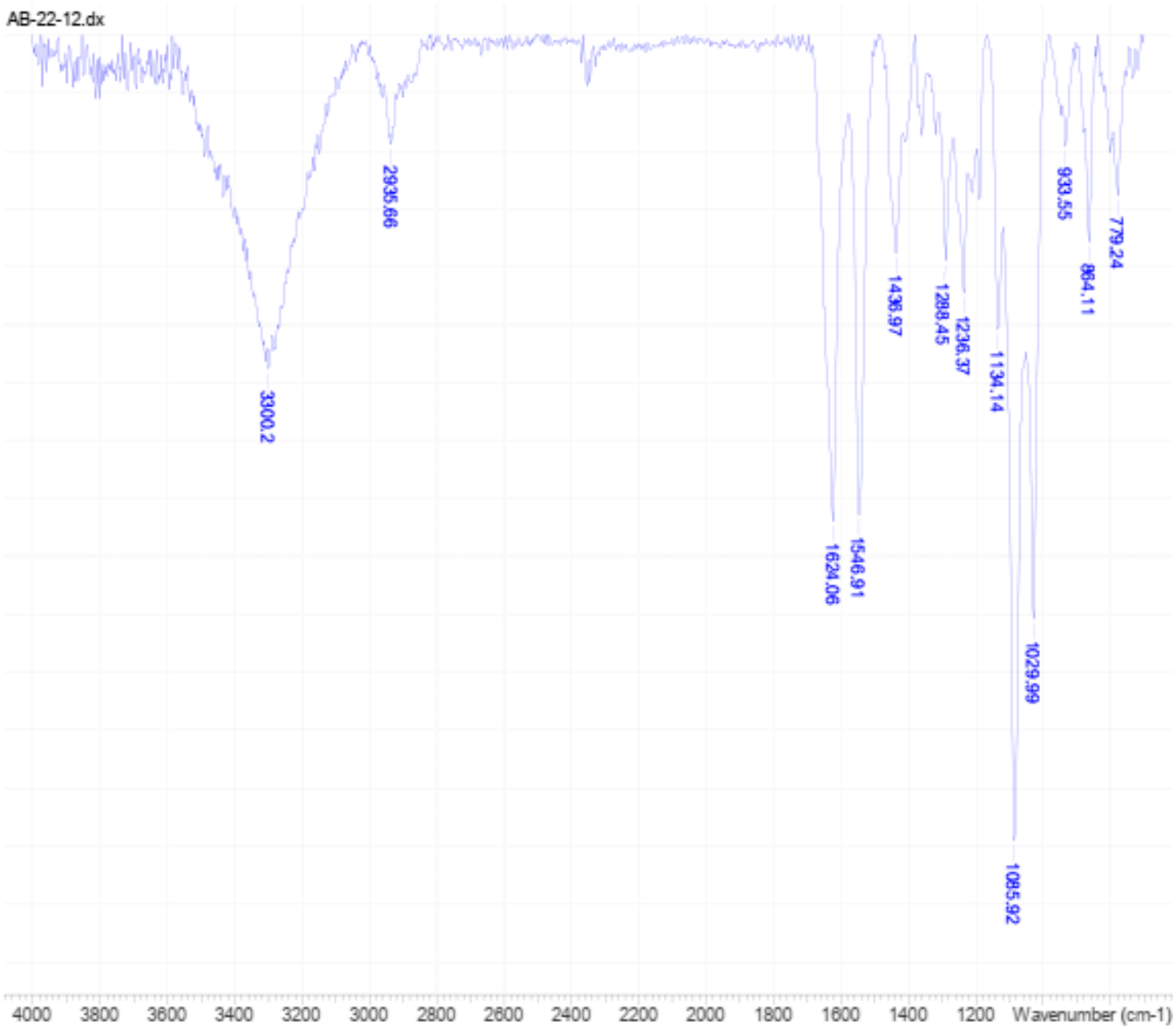
1: TOF MS ES+
1.52e+007



Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
Minimum:				-5.0				
Maximum:		5.0	5.0	150.0				
467.1850	467.1850	0.0	0.0	5.5	3167.6	0.908	40.34	C14 H27 N8 O10
	467.1848	0.2	0.4	19.5	3175.3	8.635	0.02	C29 H24 N4 O Na
	467.1853	-0.3	-0.6	1.5	3168.1	1.373	25.33	C16 H32 N2 O12 Na
	467.1858	-0.8	-1.7	17.5	3176.0	9.334	0.01	C30 H27 O5
	467.1837	1.3	2.8	0.5	3167.9	1.143	31.88	C13 H31 N4 O14
	467.1834	1.6	3.4	14.5	3175.3	8.545	0.02	C28 H28 O5 Na
	467.1866	-1.6	-3.4	6.5	3170.5	3.745	2.36	C17 H28 N6 O8 Na
	467.1832	1.8	3.9	18.5	3174.7	7.964	0.03	C26 H23 N6 O3
	467.1872	-2.2	-4.7	22.5	3177.0	10.245	0.00	C31 H23 N4 O

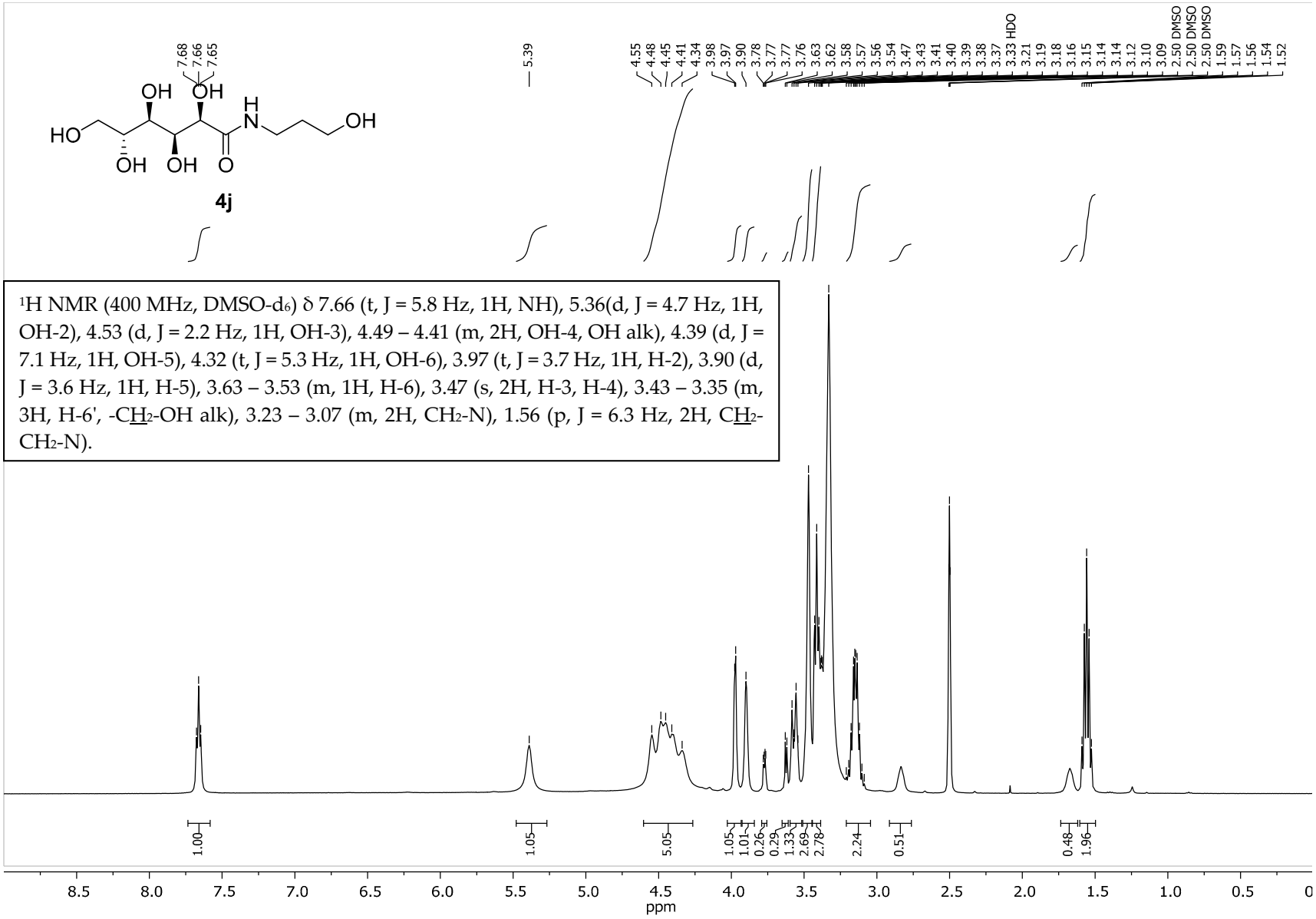
Figure S28: IR analysis of 4i' crude

Title	AB-22-121	*File Name*	C:\PROGRAM FILES (X86)\LABSOLUTIONS\IR\DATA\ABED\AB-22-12.DX		
Date	07 Jun 2022 16:47:58	*Technique*	Infrared	*Spectral Region*	IR
X Axis	Wavenumber (cm-1)	*Y Axis*	%Transmittance	*Spectrum Range*	700.1603 - 4000.3641
Points Count	1712	*Data Spacing*	1.9288		



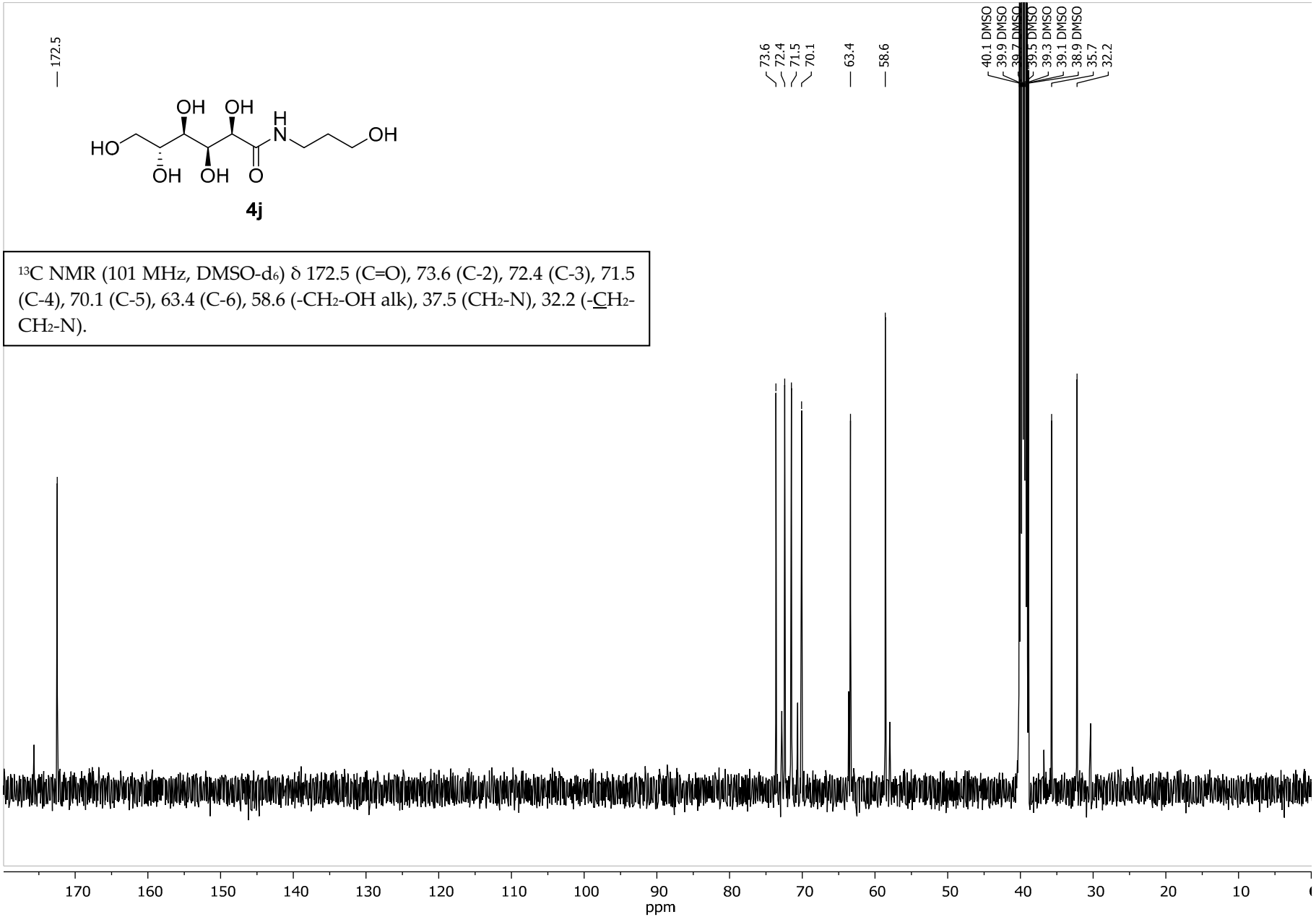
No	cm-1	%T	Intensity
1	779.24	97.229	W
2	864.11	96.426	W
3	933.55	98.081	W
4	1029.99	89.926	S
5	1085.92	86.097	VS
6	1134.14	94.917	M
7	1236.37	95.547	M
8	1288.45	96.109	W
9	1436.97	96.231	W
10	1546.91	91.720	M
11	1624.06	91.601	S
12	2935.66	98.110	W
13	3300.20	94.242	M

Figure S29: ^{1}H NMR spectrum of 4j crude



^{1}H NMR (400 MHz, DMSO-d_6) δ 7.66 (t, J = 5.8 Hz, 1H, NH), 5.36(d, J = 4.7 Hz, 1H, OH-2), 4.53 (d, J = 2.2 Hz, 1H, OH-3), 4.49 – 4.41 (m, 2H, OH-4, OH alk), 4.39 (d, J = 7.1 Hz, 1H, OH-5), 4.32 (t, J = 5.3 Hz, 1H, OH-6), 3.97 (t, J = 3.7 Hz, 1H, H-2), 3.90 (d, J = 3.6 Hz, 1H, H-5), 3.63 – 3.53 (m, 1H, H-6), 3.47 (s, 2H, H-3, H-4), 3.43 – 3.35 (m, 3H, H-6', -C$\underline{H}_2$-OH alk), 3.23 – 3.07 (m, 2H, CH_2-N), 1.56 (p, J = 6.3 Hz, 2H, C$\underline{H}_2$-CH_2-N).

Figure S30: ^{13}C NMR spectrum of 4j crude



^{13}C NMR (101 MHz, DMSO-d_6) δ 172.5 (C=O), 73.6 (C-2), 72.4 (C-3), 71.5 (C-4), 70.1 (C-5), 63.4 (C-6), 58.6 (-CH_2-OH alk), 37.5 (CH_2-N), 32.2 (-$\underline{C}H_2$-CH_2-N).

Figure S31: COSY NMR 2D spectrum of 4j crude

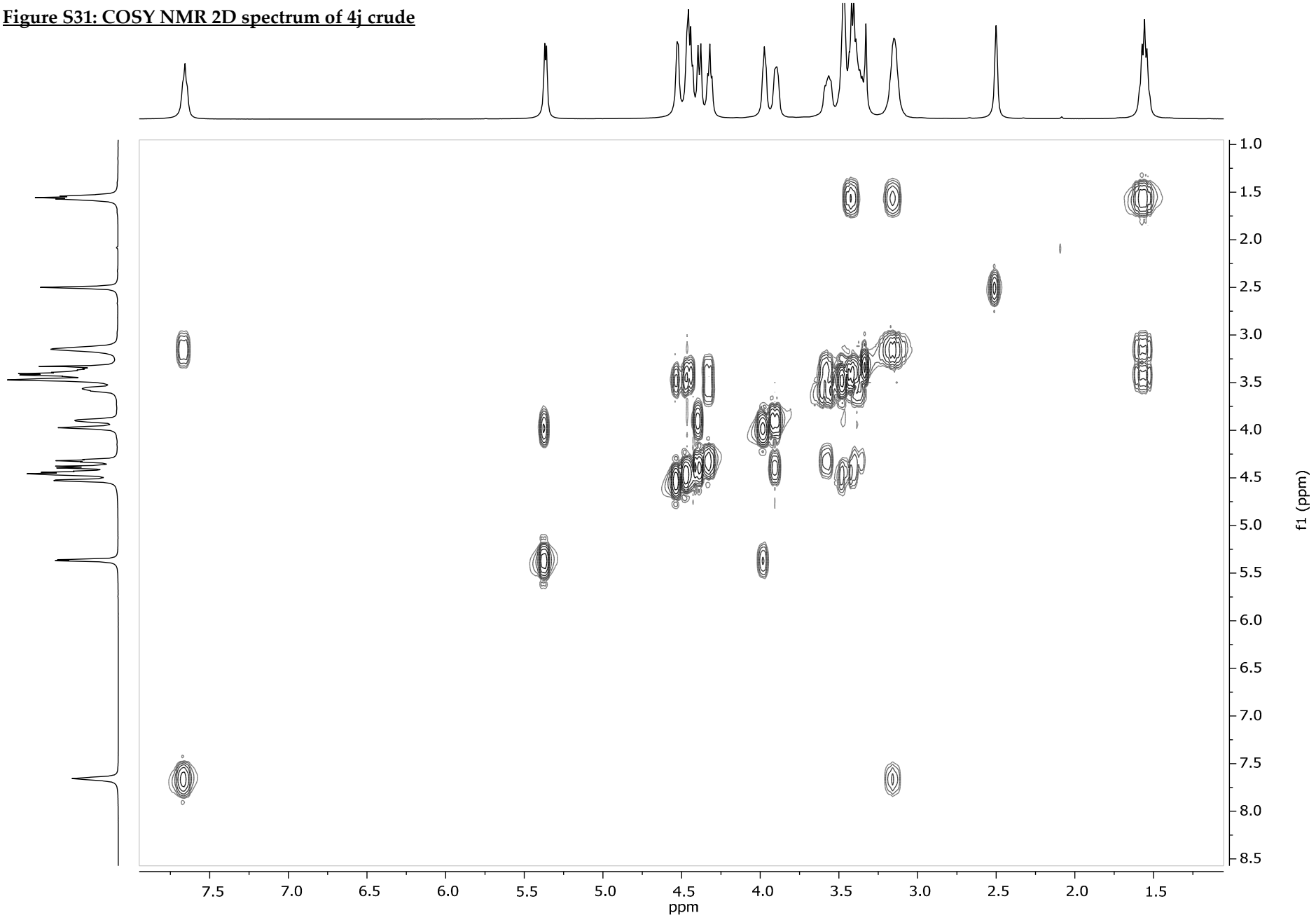


Figure S32: HSQC ^{13}C-^{1}H NMR 2D spectrum of 4j crude

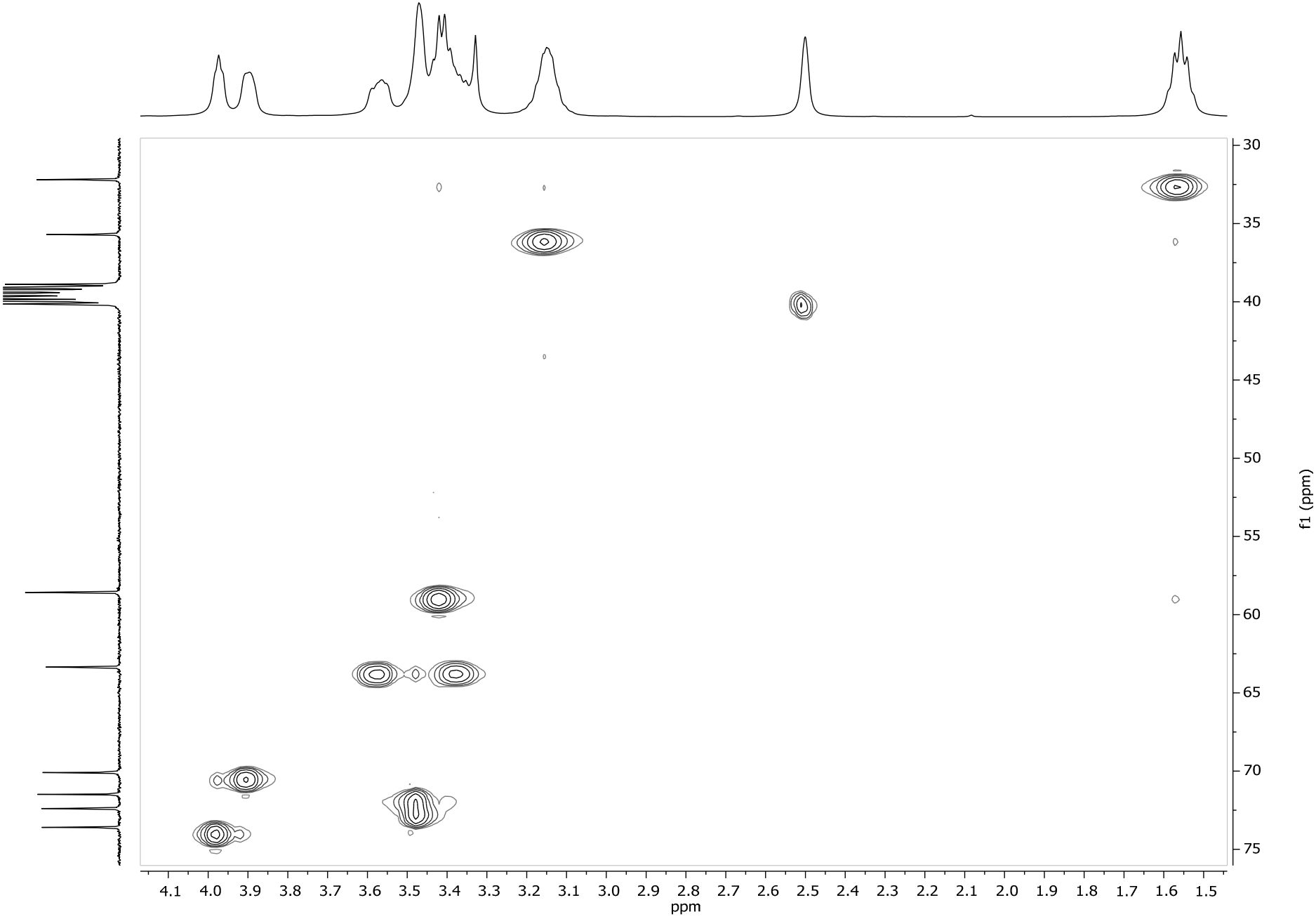
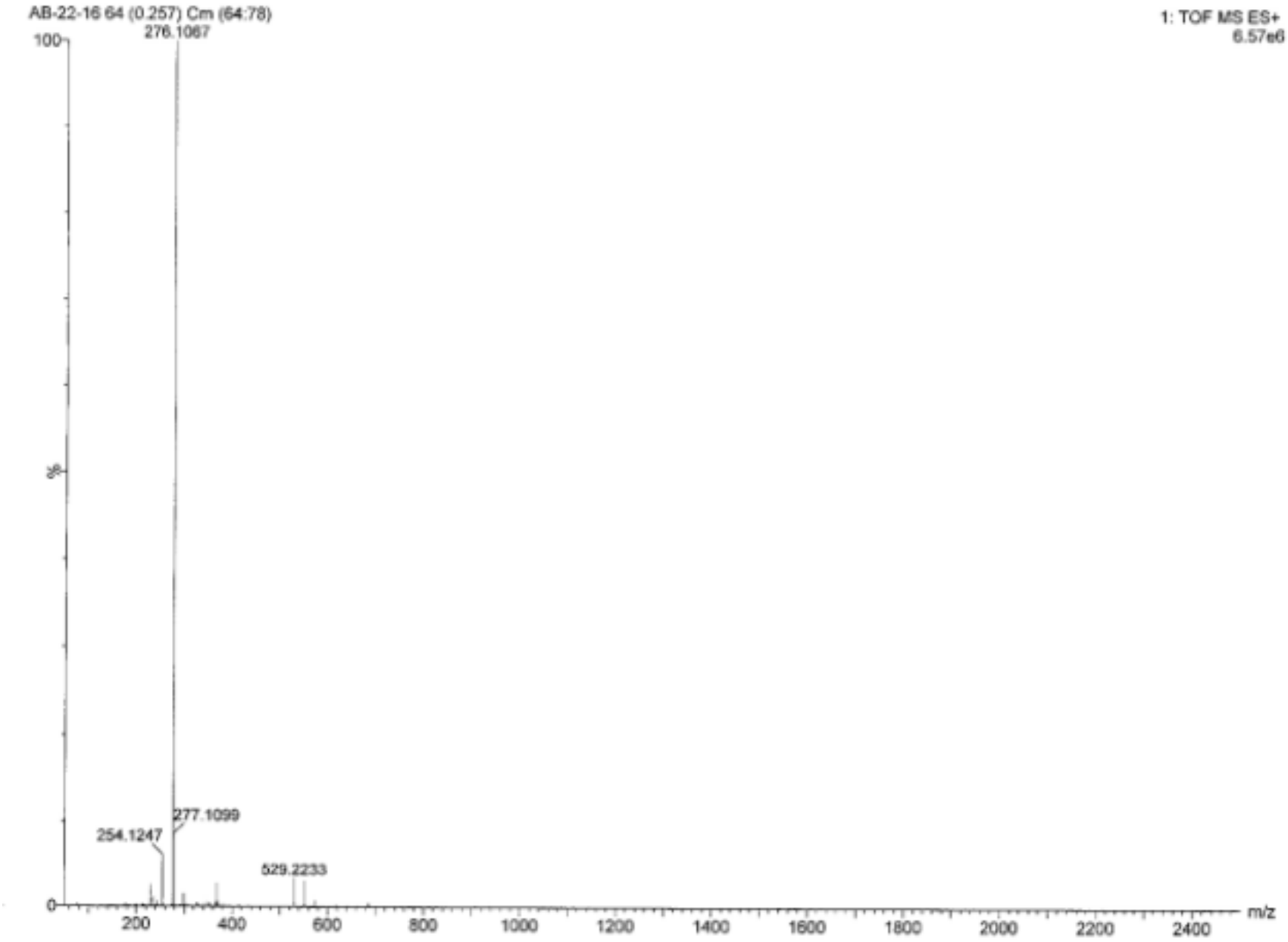
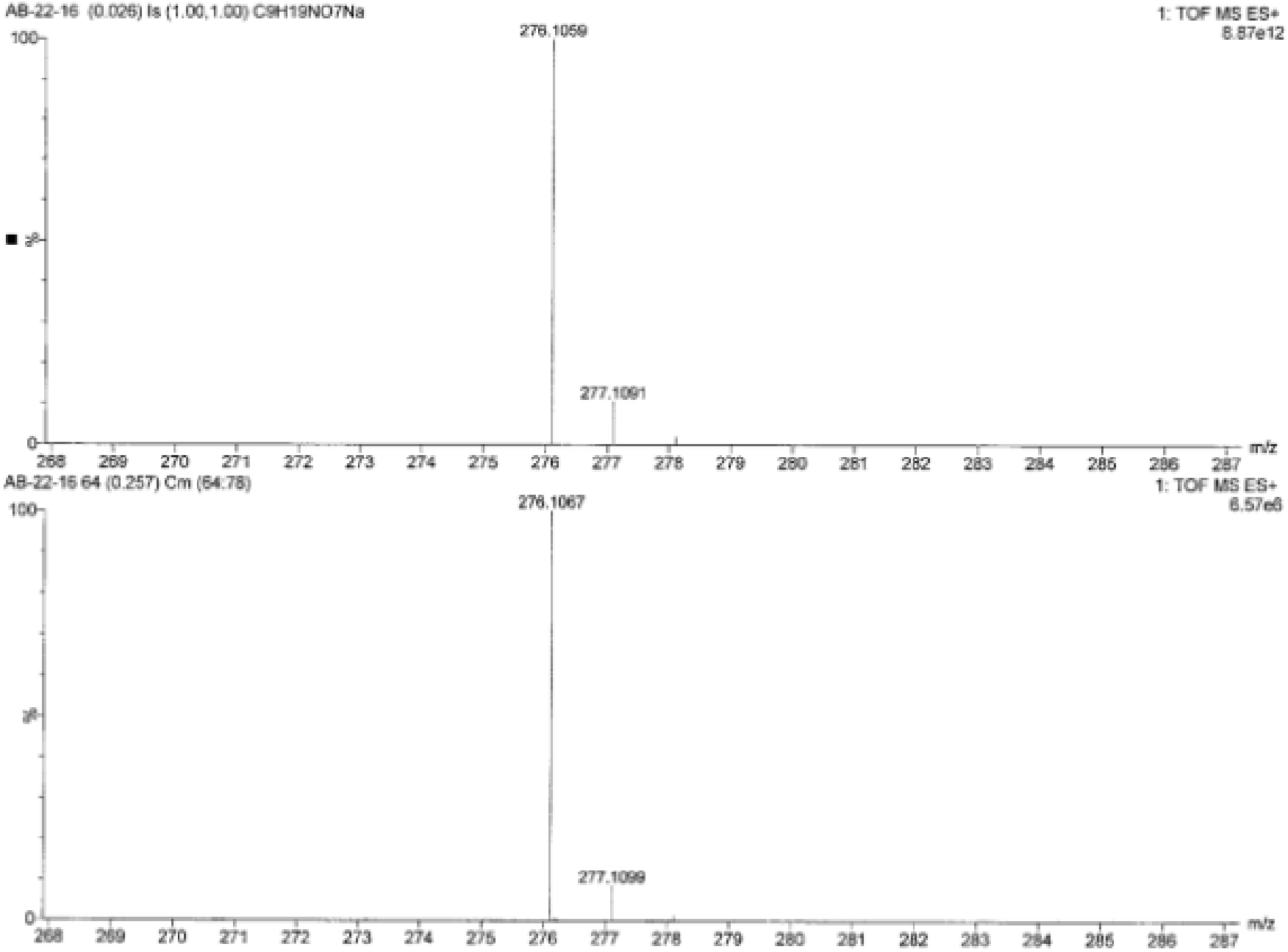


Figure S33: HRMS analysis of 4j crude




AB-22-16 (0.026) Is (1.00,1.00) C9H19NO7Na
1: TOF MS ES+
6.87e12
276.1059
277.1091
100
%
0
m/z
268 269 270 271 272 273 274 275 276 277 278 279 280 281 282 283 284 285 286 287
AB-22-16 64 (0.257) Cm (64:78)
1: TOF MS ES+
6.57e6
276.1067
277.1099
100
%
0
m/z
268 269 270 271 272 273 274 275 276 277 278 279 280 281 282 283 284 285 286 287

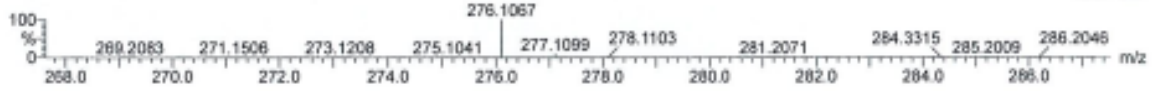
Single Mass Analysis

Tolerance = 5.0 PPM / DBE: min = -5.0, max = 150.0
Element prediction: Off
Number of isotope peaks used for i-FIT = 3

Monoisotopic Mass, Even Electron Ions
832 formula(e) evaluated with 3 results within limits (up to 50 closest results for each mass)
Elements Used:
C: 0-50 H: 0-100 N: 0-10 O: 0-50 Na: 0-1

AB-22-16 64 (0.257) Cm (64:78)

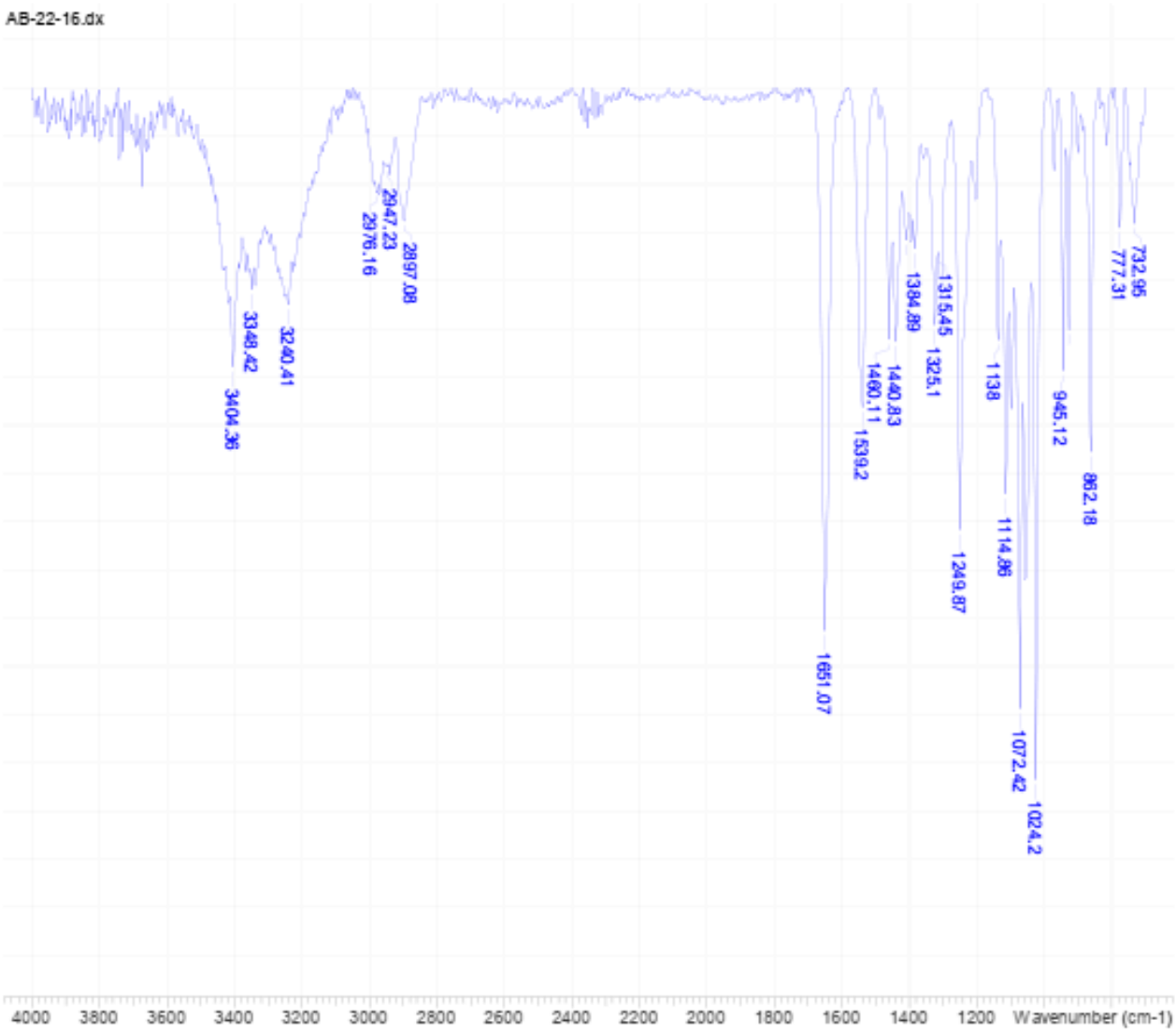
1: TOF MS ES+
6.57e+006



Minimum:				-5.0				
Maximum:		5.0	5.0	150.0				
Mass	Calc. Mass	mDa	PPM	DBE	i-FIT	Norm	Conf(%)	Formula
276.1067	276.1073	-0.6	-2.2	5.5	2394.3	2.857	5.75	C10 H15 N5 O3 Na
	276.1059	0.8	2.9	0.5	2392.1	0.634	53.03	C9 H19 N O7 Na
	276.1056	1.1	4.0	4.5	2392.3	0.886	41.22	C7 H14 N7 O5

Figure S34: IR analysis of 4j crude

Title	AB-22-161	*File Name*	C:\PROGRAM FILES (X86)\LABSOLUTIONS\IR\DATA\ABED\AB-22-16.DX		
Date	07 Jun 2022 17:00:26	*Technique*	Infrared	*Spectral Region*	IR
X Axis	Wavenumber (cm-1)	*Y Axis*	%Transmittance	*Spectrum Range*	700.1603 - 4000.3641
Points Count	1712	*Data Spacing*	1.9288		



No	cm-1	%T	FWHH	Asym	Intensity
1	732.95	97.185	-	-	W
2	777.31	97.102	-	-	W
3	862.18	92.450	-	-	M
4	927.76	94.976	-	-	M
5	945.12	94.133	-	-	M
6	1024.20	85.644	-	-	VS
7	1072.42	87.118	-1.00	0.00	S
8	1114.86	91.577	-	-	M
9	1138.00	94.767	-	-	M
10	1249.87	90.830	-	-	S
11	1315.45	96.593	-	-	W
12	1325.10	95.080	-	-	M

No	cm-1	%T	FWHH	Asym	Intensity
13	1384.89	96.666	-	-	W
14	1409.96	96.841	-	-	W
15	1440.83	94.736	-	-	M
16	1460.11	94.784	-	-	M
17	1539.20	93.372	-	-	M
18	1651.07	88.736	-1.00	0.00	S
19	2897.08	97.240	-	-	W
20	2947.23	98.365	-	-	W
21	2976.16	97.860	-	-	W
22	3240.41	95.501	-	-	M
23	3348.42	95.817	-	-	W
24	3404.36	94.214	-	-	M

Figure S35: ^{1}H NMR spectrum of 4k crude

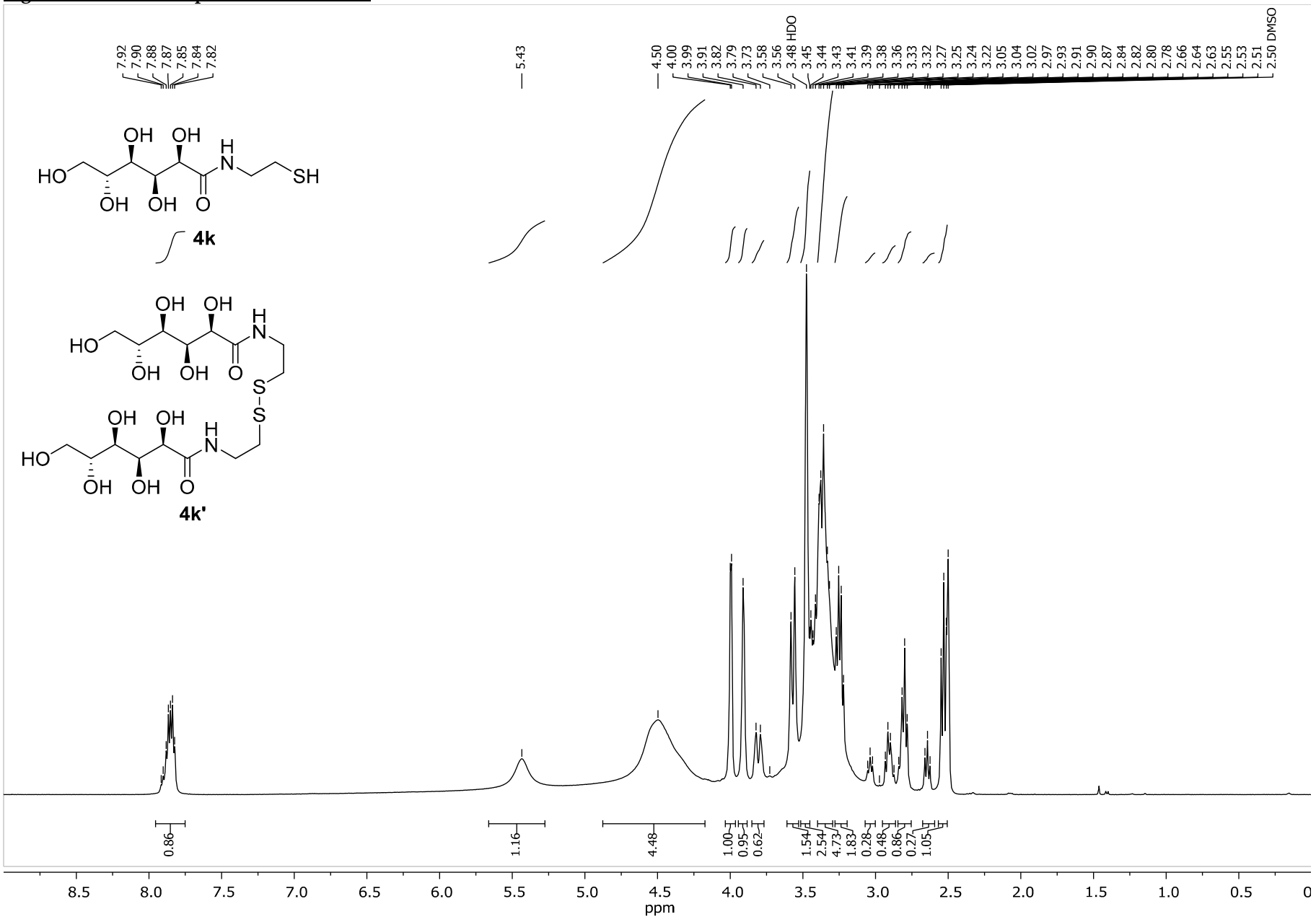


Figure S36: ^{13}C NMR spectrum of 4k crude

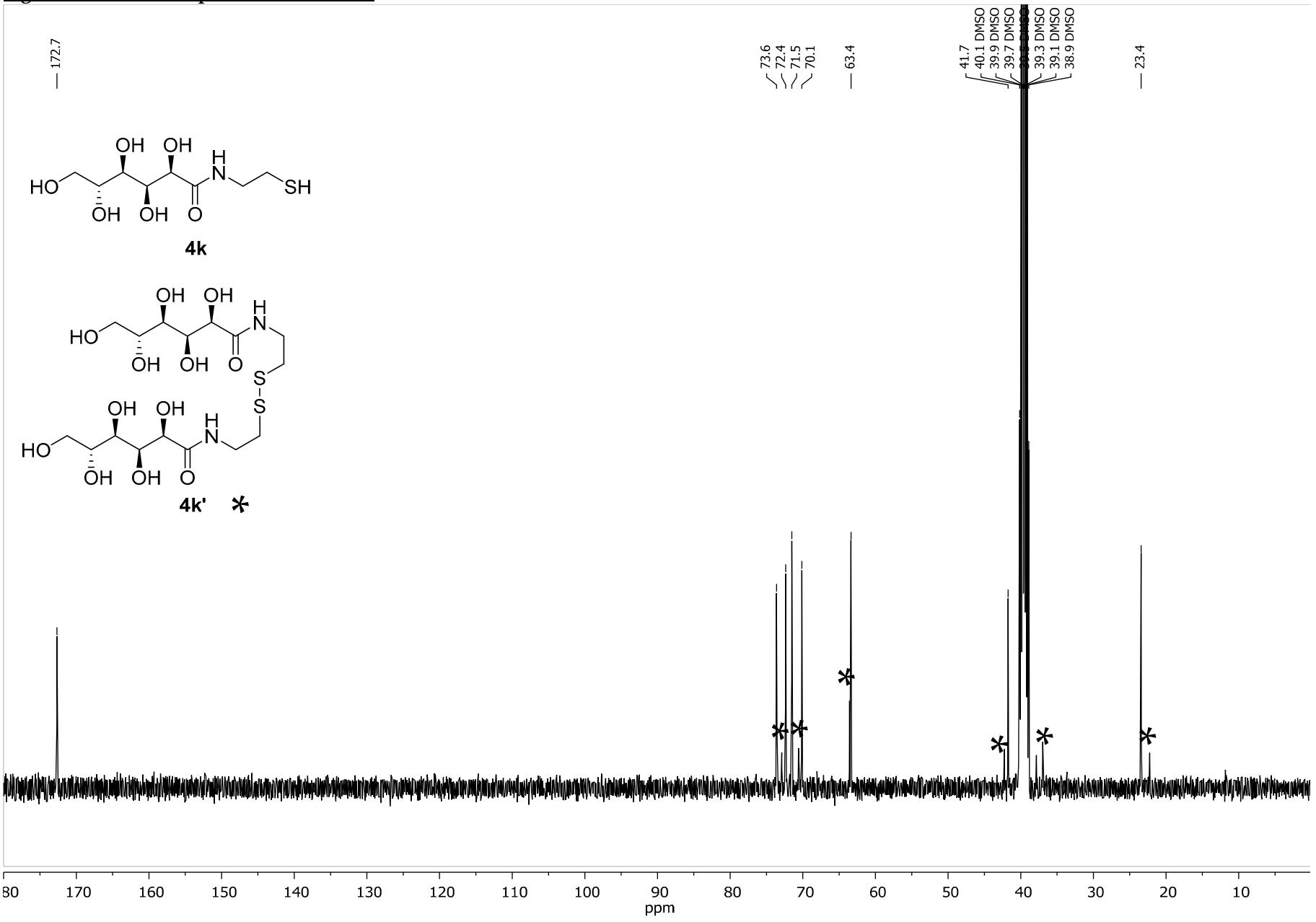


Figure S37: ^{1}H NMR spectrum of 4l crude

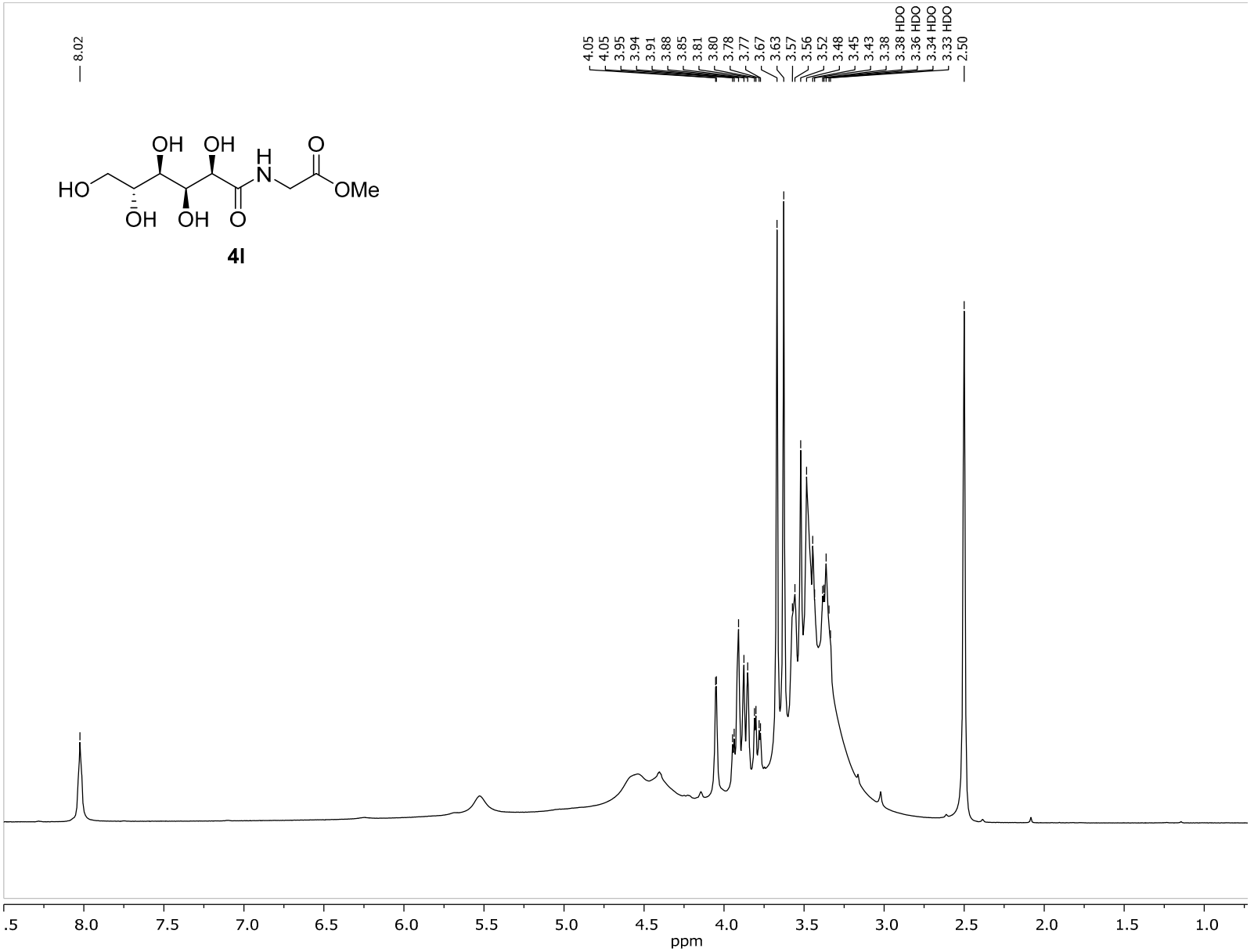


Figure S38: ^{13}C NMR spectrum of 4l crude