

ELECTRONIC SUPPORTING INFORMATIONS

Glycosylation with *in situ* separation: carbohydrate chemistry on a TLC plate†

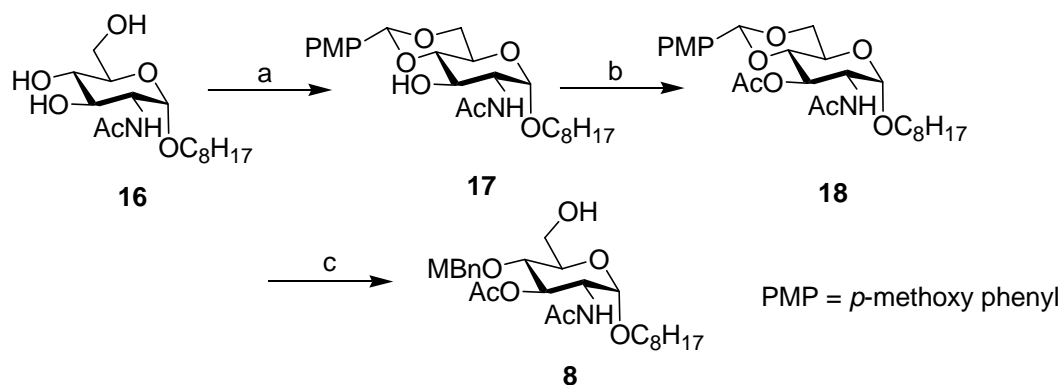
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Known monosaccharide donors and acceptors **1**,ⁱ **2**,ⁱⁱ **6**,ⁱⁱⁱ **7**,^{iv} **9**,^v **10**^{vi} were synthesized according to the literature procedure and characterized by comparing with reported data. Compound **8** was synthesised from known octyl 2-acetamido-2-deoxy- α -D-glucopyranoside (**16**)^{vii} by following the reaction sequence described in Scheme 1.



Scheme 1: a. *p*-methoxybenzaldehyde dimethylacetal, *p*-TsOH, CH₃CN; b. Ac₂O, Py; c. Et₃SiH, TFA

Compound **16** was converted to the corresponding *p*-methoxy benzylidene derivative **17** by using anisaldehydedimethylacetal and *p*-TsOH in acetonitrile in 87% yield and subsequently the 3-*OH* group was protected by acetylation with acetic anhydride in pyridine to give compound **18** in 93% yield. Regioselective opening of the acetal with triethylsilane and trifluoroacetic acid afforded target acceptor **8** in 71% yield as foam.

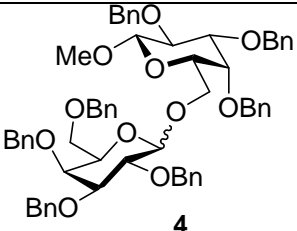
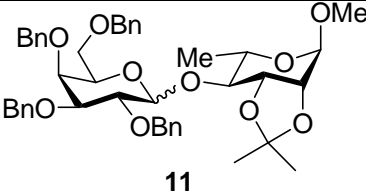
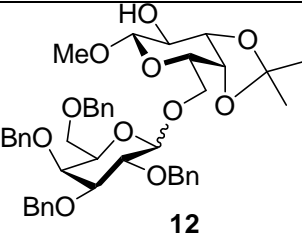
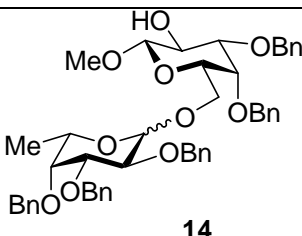
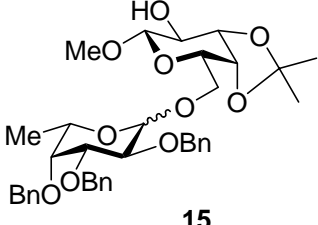
Octyl 2-acetamido-2-deoxy-4,6-*O*-(4-methoxybenzylidene)- α -D-glucopyranoside (17**)** To a mixture of compound **16** (3g, 9.0 mmol) in CH₃CN (40 mL) was added *p*-anisaldehyde dimethylacetal (2.5g, 13.5 mmol) followed by *p*-TsOH (100 mg) and stirred at room temperature. After complete conversion of the starting material (2 hours), the mixture was neutralised with Et₃N and solvents were evaporated *in vacuo*. The crude product was purified by flash chromatography using 1:1 EtOAc-*n*-hexane to afford pure compound **17** (3.5g, 87%) as white foam. $[\alpha]_D^{23} +26^\circ$ (*c*

1.0, CHCl₃). ¹H NMR (CDCl₃) δ: 7.41, 6.86 (2d, 4H, ArH), 5.96 (d, 1H, *J*_{2,NH} = 8.8 Hz, NH), 5.49 (s, 1H, CH-C₆H₄Ome), 4.78 (d, 1H, *J*_{1,2} = 3.8 Hz, H-1), 4.21 (m, 1H, H-6^a), 4.16 (dt, 1H, *J*_{1,2}, *J*_{2,3} = 9.0 Hz, *J*_{2,NH}, H-2), 3.87 (t, 1H, *J*_{2,3} = *J*_{3,4} = 9.0 Hz, H-3), 3.77 (s, 3H, OCH₃), 3.75-3.63 (m, 3H, H-5, H-6b, OCH₂), 3.53 (t, 1H, *J*_{3,4}, H-4), 3.38 (m, 1H, OCH₂), 2.01 (NHCOCH₃), 1.58 (m, 2H, O-CH₂-CH₂-(CH₂)₆-CH₃), 1.24 (m, 10H, O-CH₂-CH₂-(CH₂)₅-CH₃), 0.92 (t, 3H, CH₃). ¹³C NMR (CDCl₃) δ: 171.5 (NHCOCH₃), 160.2, 129.7, 127.7, 113.6 (ArC), 101.6 (CH-C₆H₄-OCH₃), 97.7 (C-1), 82.0 (C-4), 70.4 (C-3), 68.7 (C-6), 68.2 (OCH₂), 62.5 (C-5), 55.2 (OCH₃), 54.4 (C-2), 31.7, 29.2, 29.1, 28.9, 26.0, 22.5 (octyl CH₂), 23.1 (NHCOCH₃), 13.9 (octyl-CH₃). HRMS [M+NH₄]⁺ calcd. for C₂₄H₄₁N₂O₇ 469.2914, found 469.2912.

Octyl 2-acetamido-2-deoxy-4,6-O-(4-methoxybenzylidene)-α-D-glucopyranoside (18) To a solution of compound **17** (3g, 6.6 mmol) in dry pyridine (15 mL) was added Ac₂O (10 mL) and stirred at room temperature for 2 hours. Solvents were evaporated *in vacuo* and co-evaporated with toluene to syrup. The crude product was purified by flash chromatography using 2:1 EtOAc-*n*-hexane to afford pure compound **18** (3.0g, 93%) as foam. [α]_D²³ +42° (*c* 1.0, CHCl₃). ¹H NMR (CDCl₃) δ: 7.42, 6.89 (2d, 4H, ArH), 5.94 (d, 1H, *J*_{2,NH} = 8.6 Hz, NH), 5.51 (s, 1H, CH-C₆H₄Ome), 5.09 (t, 1H, *J*_{2,3} = *J*_{3,4} = 9.0 Hz, H-3), 4.81 (d, 1H, *J*_{1,2} = 3.8 Hz, H-1), 4.23 (m, 1H, H-6a), 4.19 (dt, 1H, *J*_{1,2}, *J*_{2,3} = 9.0 Hz, *J*_{2,NH}, H-2), 3.79 (s, 3H, OCH₃), 3.78-3.64 (m, 3H, H-5, H-6b, OCH₂), 3.55 (t, 1H, *J*_{3,4}, H-4), 3.41 (m, 1H, OCH₂), 2.04, 1.97 (2s, 6H, COCH₃, NHCOCH₃), 1.59 (m, 2H, O-CH₂-CH₂-(CH₂)₆-CH₃), 1.21 (m, 10H, O-CH₂-CH₂-(CH₂)₅-CH₃), 0.90 (t, 3H, CH₃). ¹³C NMR (CDCl₃) δ: 172.4 (COCH₃), 171.1 (NHCOCH₃), 160.0, 129.8, 127.6, 113.6 (ArC), 101.5 (CH-C₆H₄-OCH₃), 97.8 (C-1), 81.9 (C-4), 74.4 (C-3), 68.6 (C-6), 68.1 (OCH₂), 62.4 (C-5), 55.2 (OCH₃), 54.5 (C-2), 31.8, 29.1, 29.0, 28.9, 26.1, 23.1 (octyl CH₂), 22.5, 22.4 (COCH₃, NHCOCH₃), 13.9 (octyl-CH₃). HRMS [M+NH₄]⁺ calcd. for C₂₆H₄₃N₂O₈ 511.3019, found 511.3017.

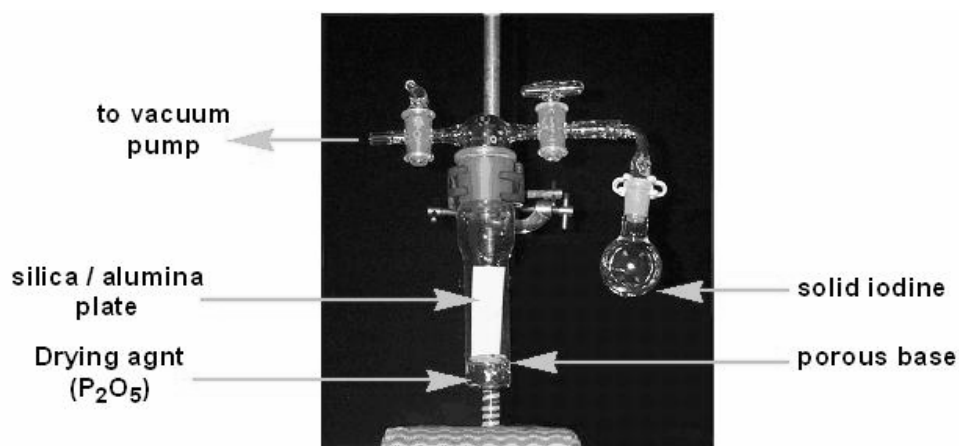
Octyl 2-acetamido-3-O-acetyl-2-deoxy-4-O-(4-methoxybenzyl)- α -D-glucopyranoside (8) A mixture of compound **18** (2g, 4.0 mmol) and MS 3Å (3g) in CH₃CN (30 mL) was stirred at room temperature for 2 hours. NaCNBH₃ (1.5g, 24 mmol) was added followed by Me₃SiCl (3 mL, 24 mmol) and the mixture was stirred at room temperature for 6 hours. After filtration through a celite[®] bed, filtrate was diluted with CH₂Cl₂ (50 mL) and washed successively with NaHCO₃ (2×50 mL) and brine (50 mL). Organic layer was separated, dried (Na₂SO₄) and evaporated to syrup. The crude product was purified by flash chromatography using 1:1 EtOAc-*n*-hexane to afford pure compound **8** (1.4g, 71%) as white foam. $[\alpha]_D^{23} +37^\circ$ (*c* 1.0, CHCl₃). ¹H NMR (CDCl₃) δ : 7.22, 6.83 (2d, 4H, ArH), 5.76 (d, 1H, $J_{2,NH} = 8.2$ Hz, NH), 5.08 (t, 1H, $J_{2,3} = J_{3,4} = 9.2$ Hz, H-3), 4.78 (d, 1H, $J_{1,2} = 3.2$ Hz, H-1), 4.52 (2d, 2H, $J_{AB} = 11.6$ Hz, CH₂C₆H₄OMe), 4.19 (dt, 1H, $J_{1,2}, J_{2,3}, J_{2,NH}$, H-2), 3.75 (s, 3H, OCH₃), 3.71-3.54 (m, 5H, H-4, H-5, H-6_a, H-6_b, O-CH₂), 3.34 (m, 1H, O-CH₂), 2.98 (bs, 1H, OH), 2.04, 1.89 (2s, 6H, COCH₃, NHCOCH₃), 1.58 (m, 2H, O-CH₂-CH₂-(CH₂)₆-CH₃), 1.24 (m, 10H, O-CH₂-CH₂-(CH₂)₅-CH₃), 0.92 (t, 3H, CH₃). ¹³C NMR (CDCl₃) δ : 172.2 (COCH₃), 170.1 (NHCOCH₃), 159.4, 129.8, 129.4, 113.9 (ArC), 97.1 (C-1), 74.0 (C-3), 73.3 (CH₂C₆H₄OMe), 70.3 (C-5), 69.7 (C-4), 68.1 (OCH₂), 61.1 (C-6), 55.2 (OCH₃), 51.7 (C-2), 31.7, 29.2, 29.1, 26.0, 23.1 (octyl CH₂), 22.5 (NHCOCH₃), 20.9 (COCH₃), 13.9 (octyl-CH₃). HRMS [M+NH₄]⁺ calcd. for C₂₆H₄₅N₂O₈ 513.3176, found 513.3172.

NMR peak assignments:

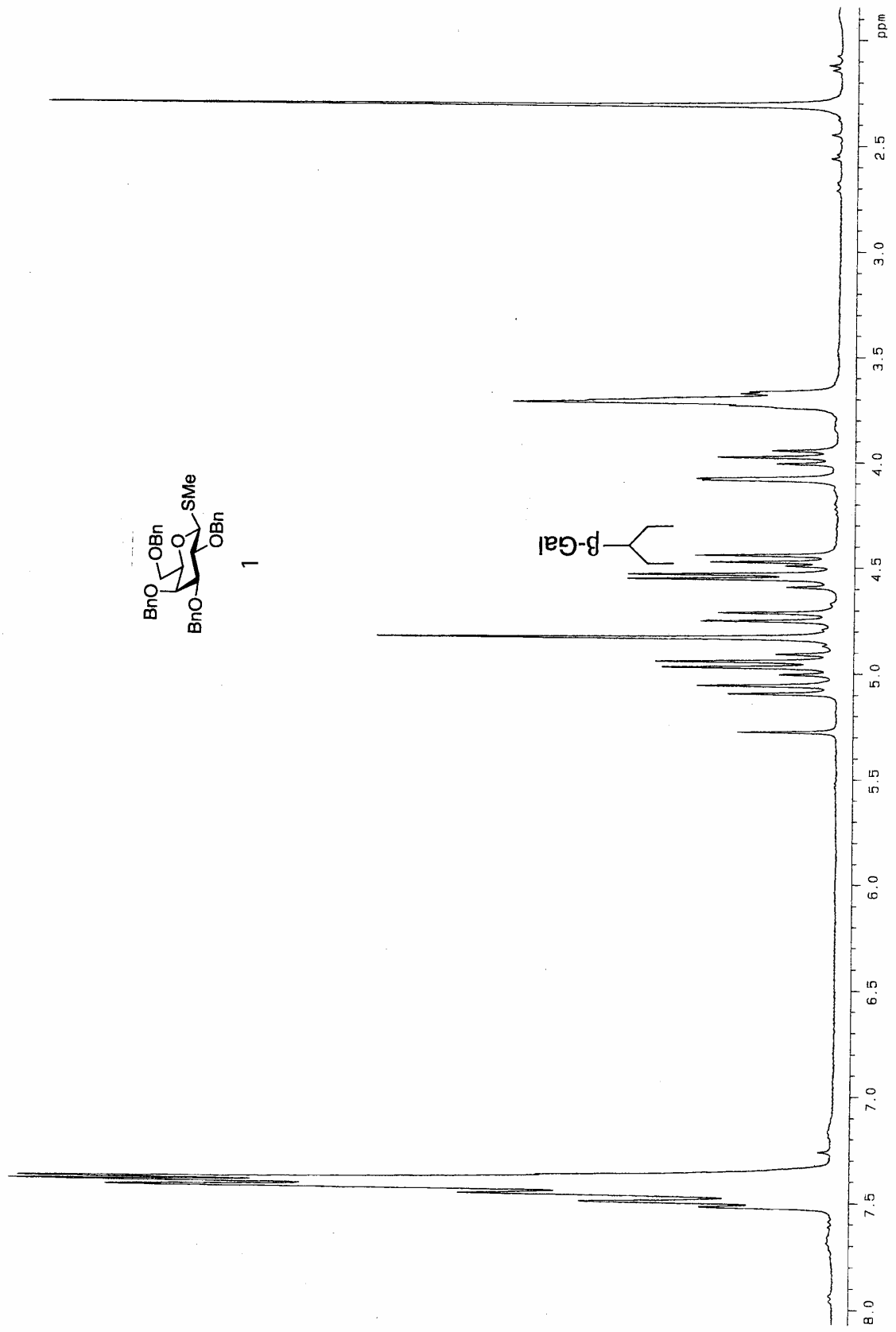
Disaccharides		¹³ C NMR			¹ H NMR
		C-1	C-1'	OCH ₃	OCH ₃
 <p style="text-align: center;">4</p>	α	103.4	98.1	56.5	3.34
	β	103.4	104.1	56.6	3.33
 <p style="text-align: center;">11</p>	α	98.3	97.8	53.3	3.41
	β	98.4	102.2	53.4	3.38
 <p style="text-align: center;">12</p>	α	101.3	96.5	56.2	3.40
	β	101.5	104.1	56.3	3.38
 <p style="text-align: center;">14</p>	α	104.5	98.1	56.4	3.58
	β	104.6	103.9	56.5	3.60
 <p style="text-align: center;">15</p>	α	103.9	96.1	56.1	3.42
	β	103.9	101.9	56.2	3.43

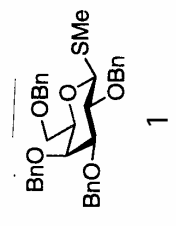
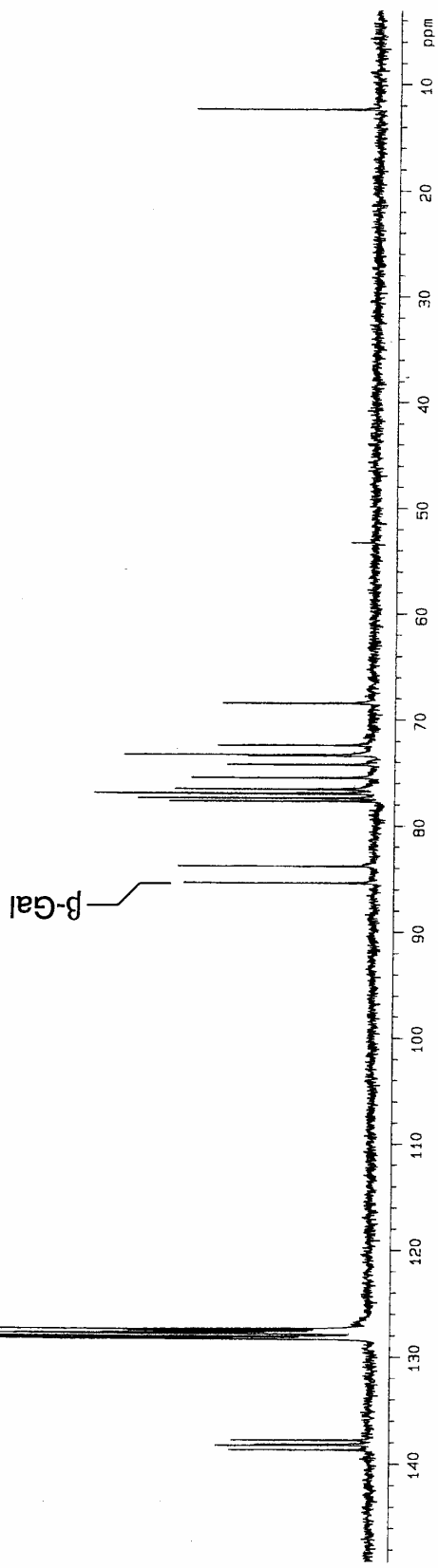
In all cases, α/β ratio of the product is calculated from the corresponding integration of the -OCH₃ signal in ¹H NMR.

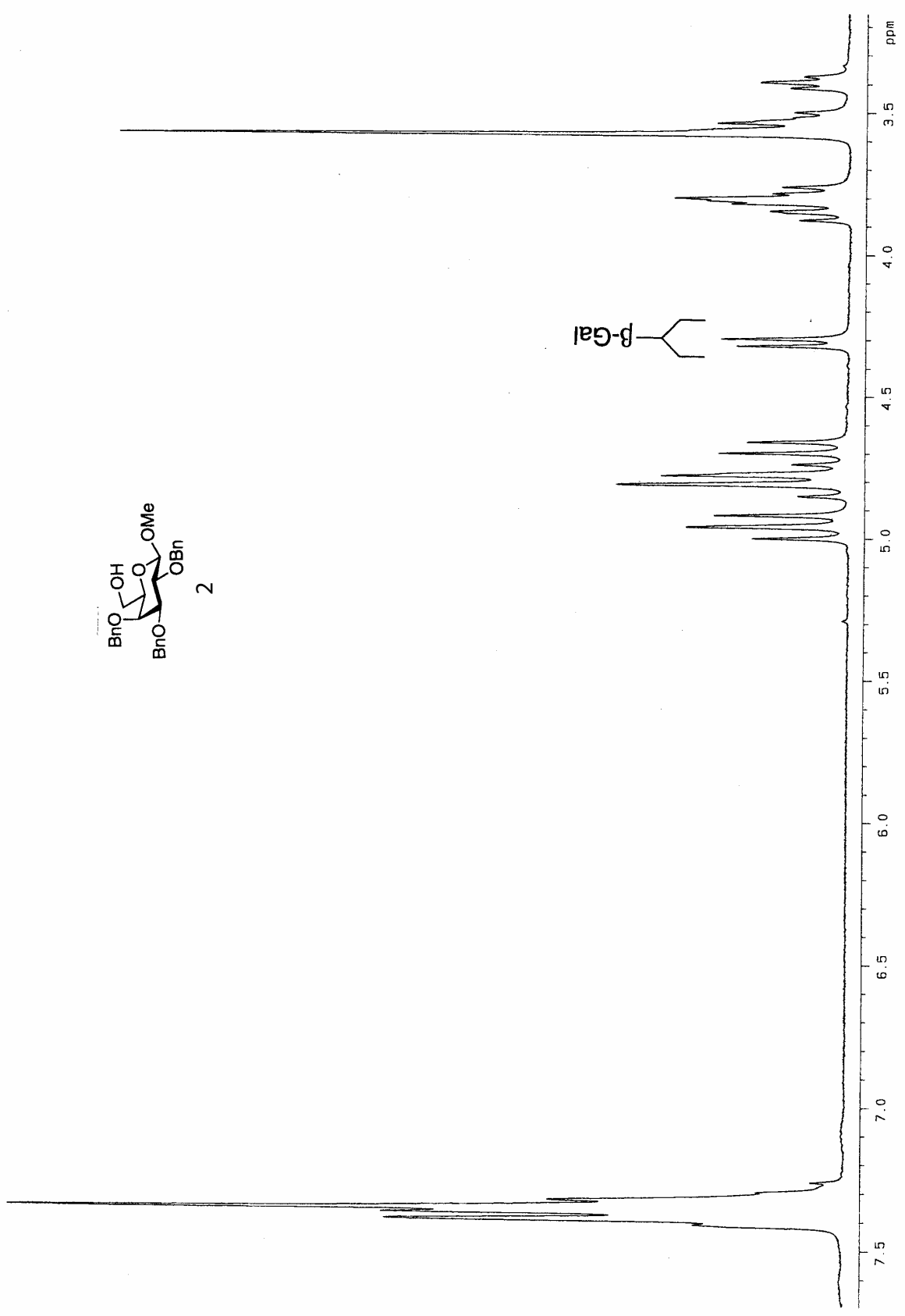
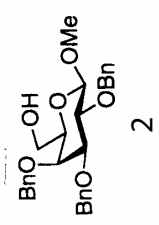
The apparatus used for the glycosylation experiments on TLC plate:

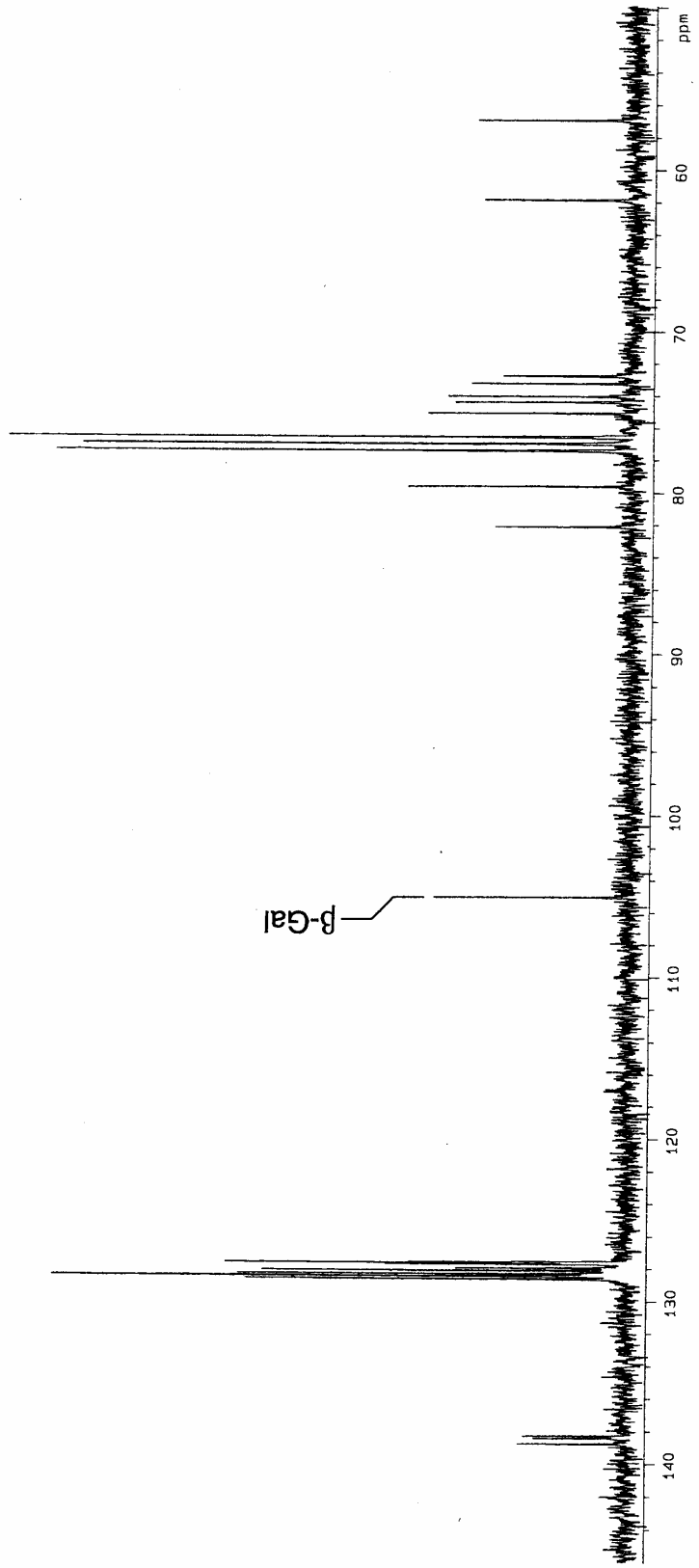
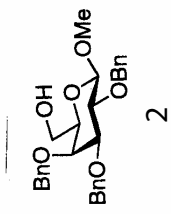


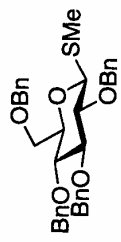
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 - ii. Valdor, J-F.; Mackie, W. *J. Carbohydr. Chem.* 1997, **16**, 429.
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 - vi. Paulsen, H.; Hasenkamp, T.; Paal, M. *Carbohydr. Res.* 1985, **179**, 37.
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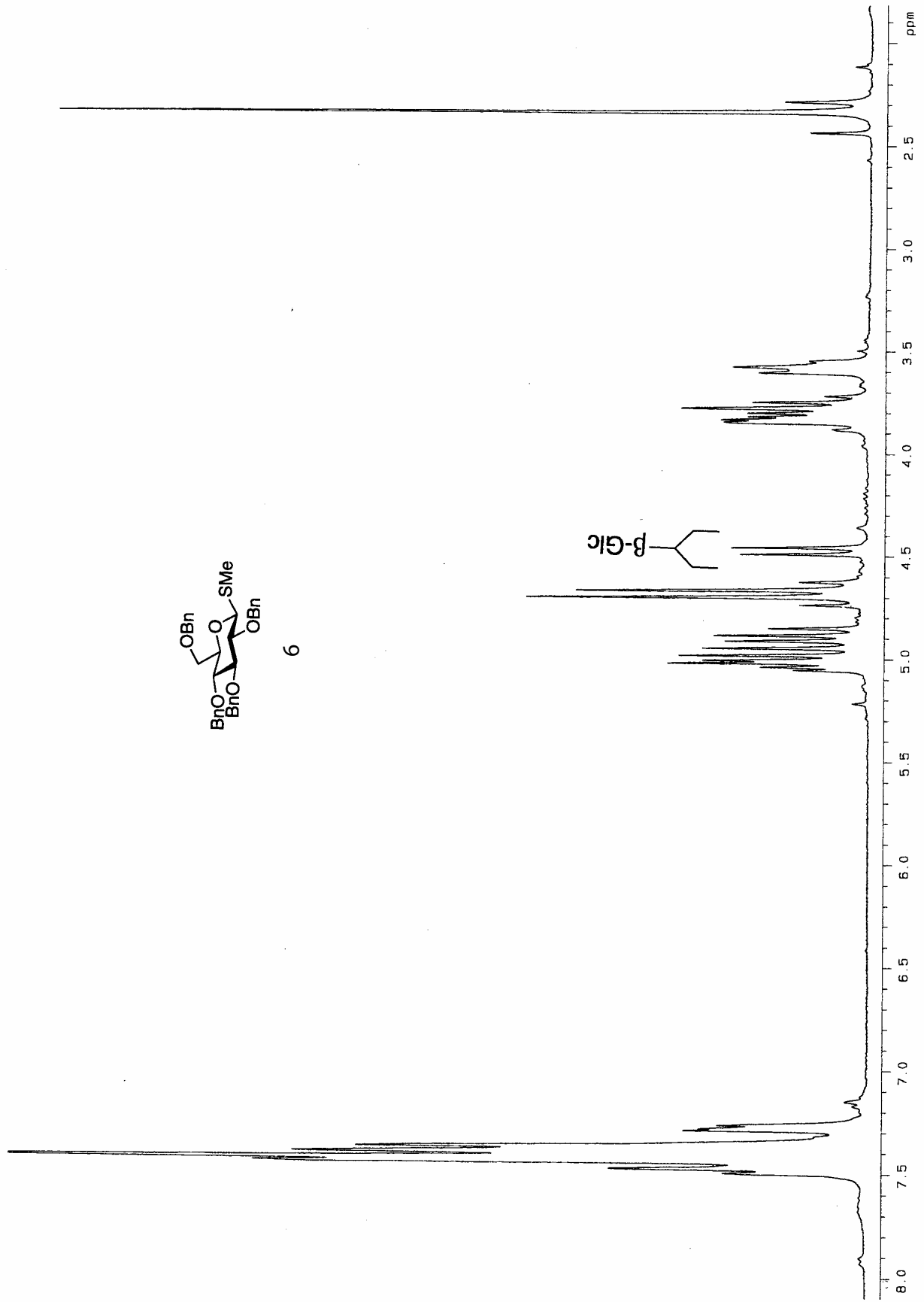


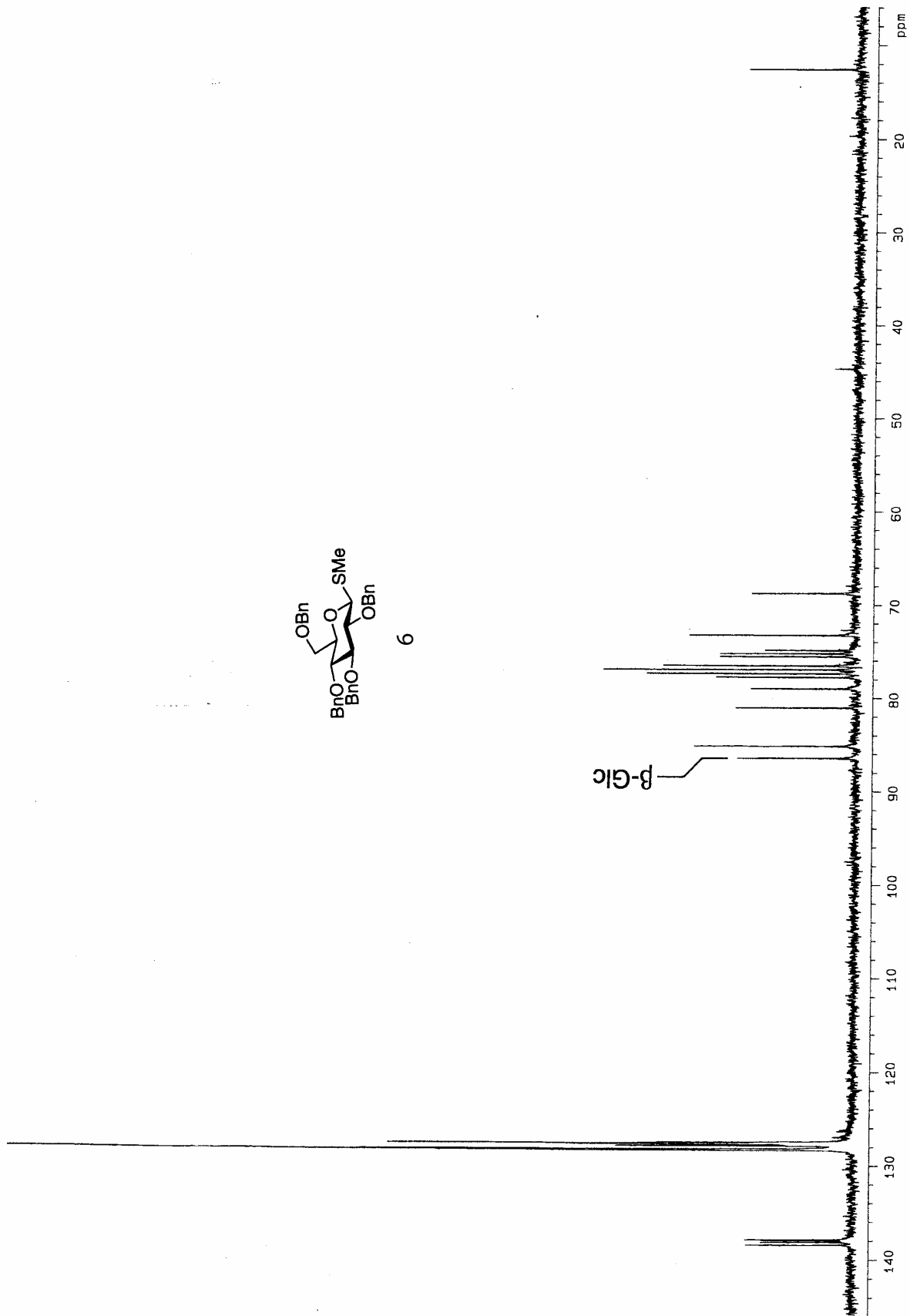
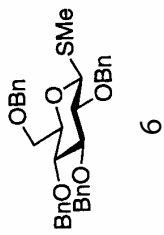


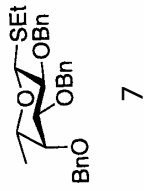
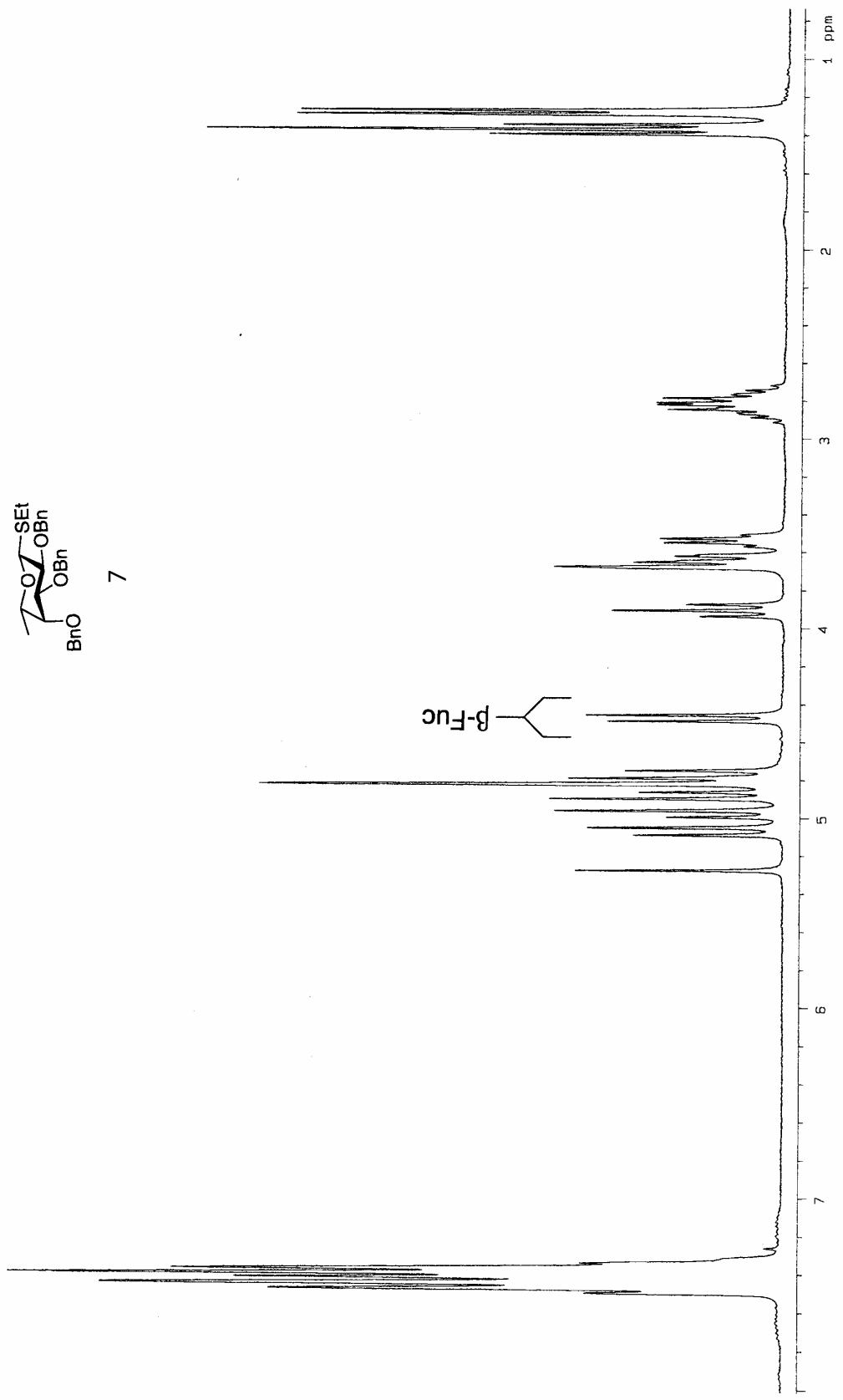


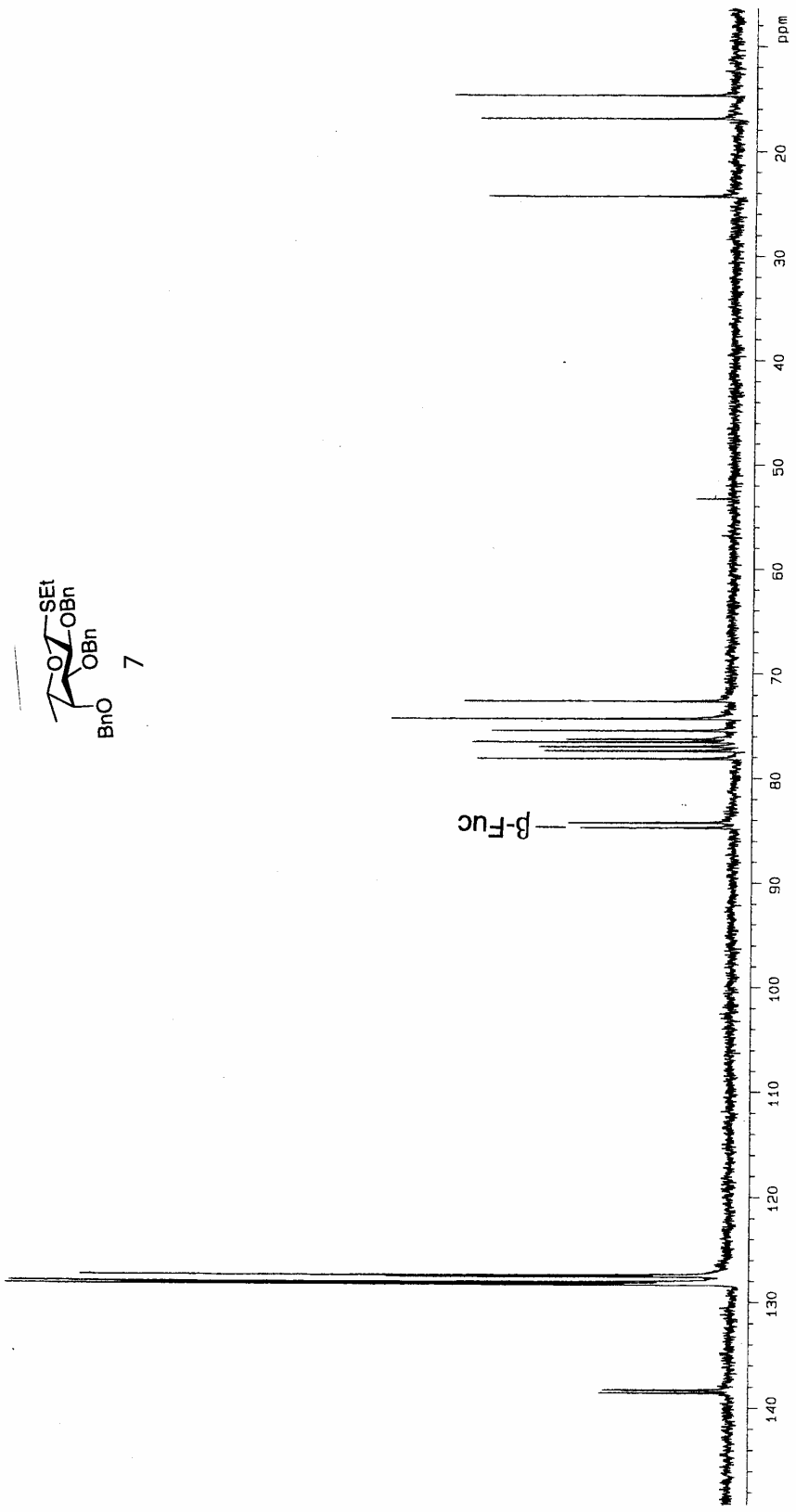
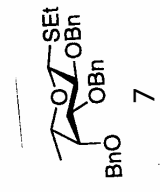


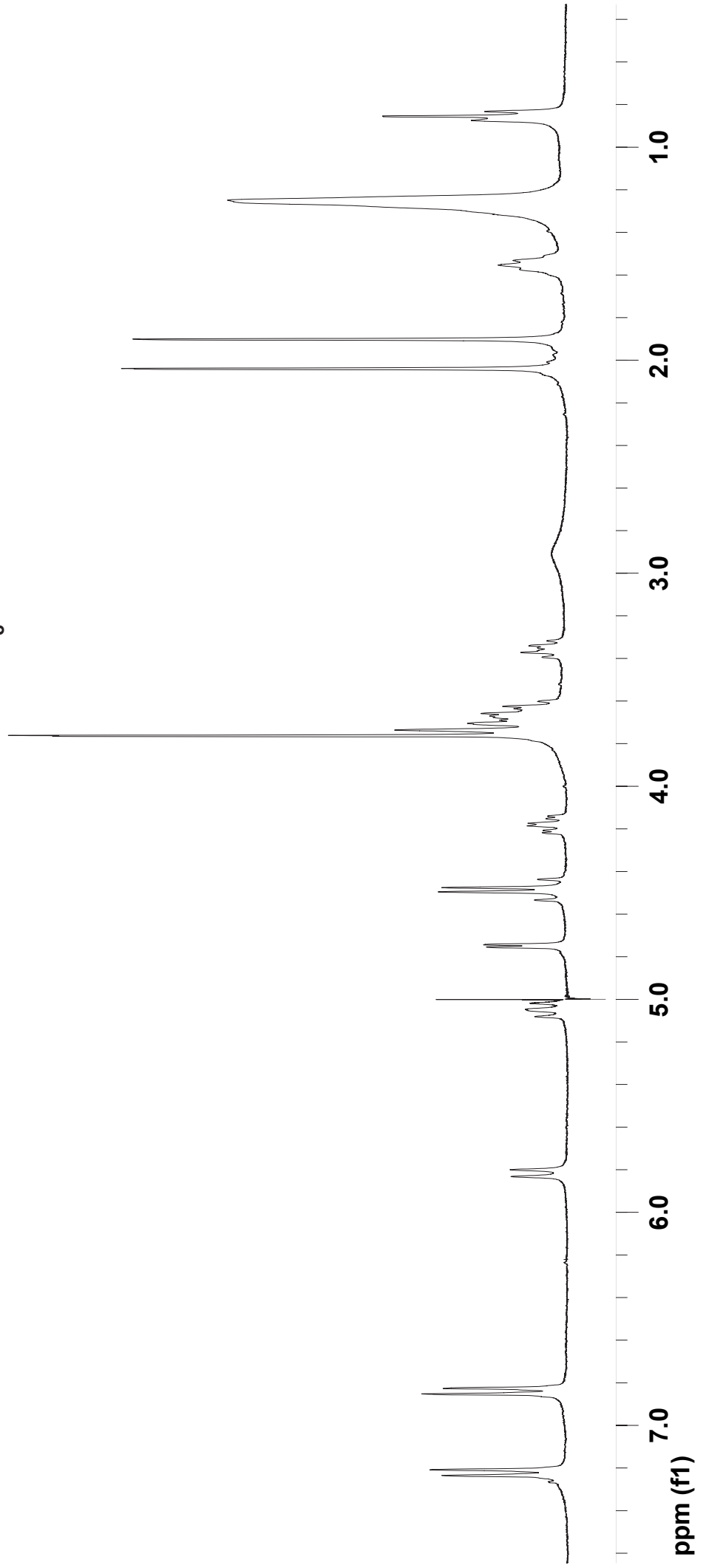
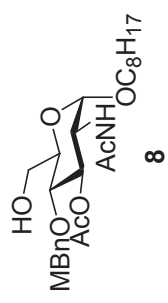
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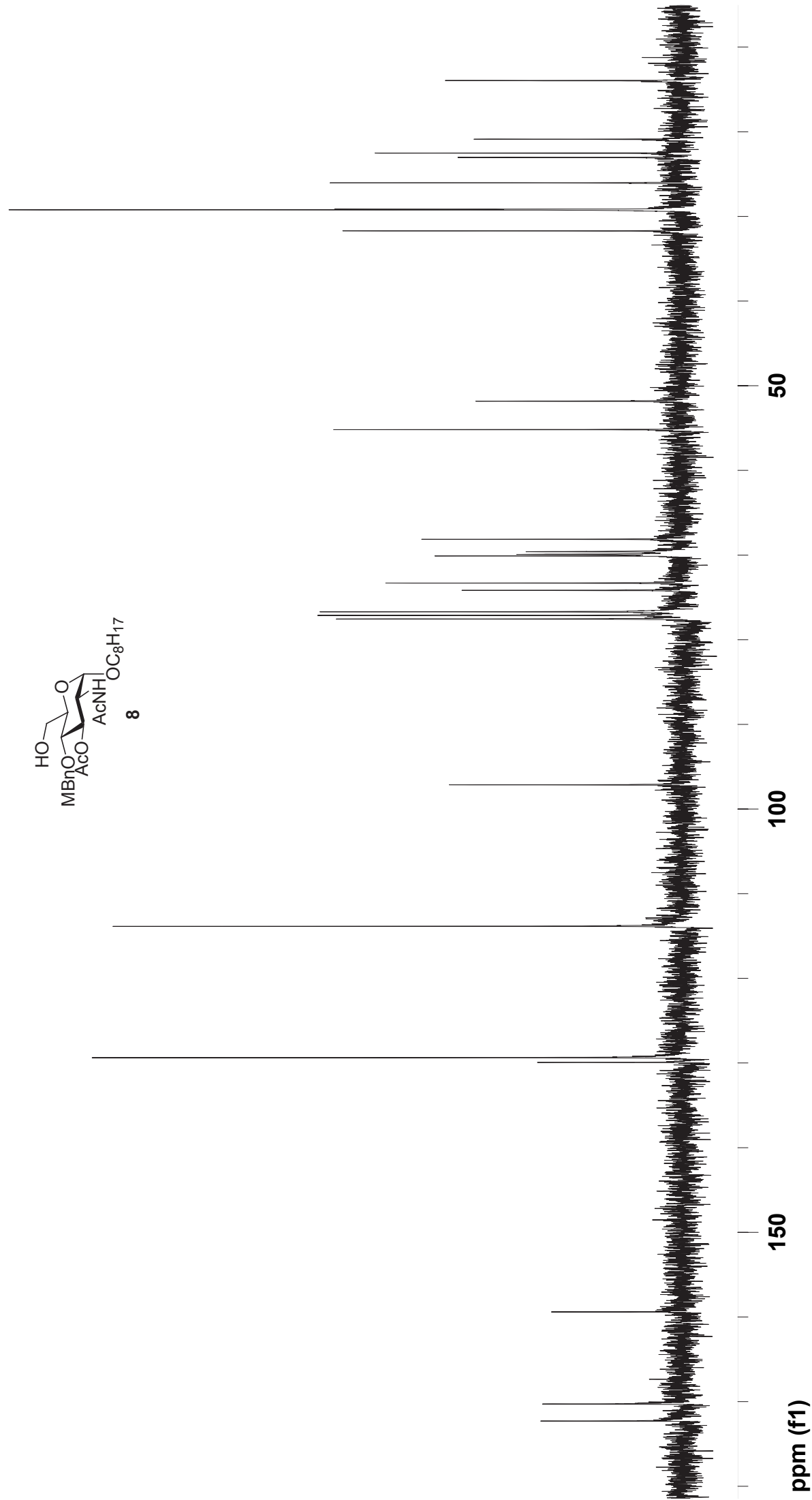
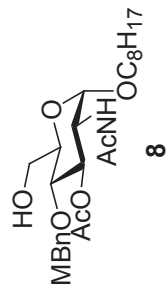


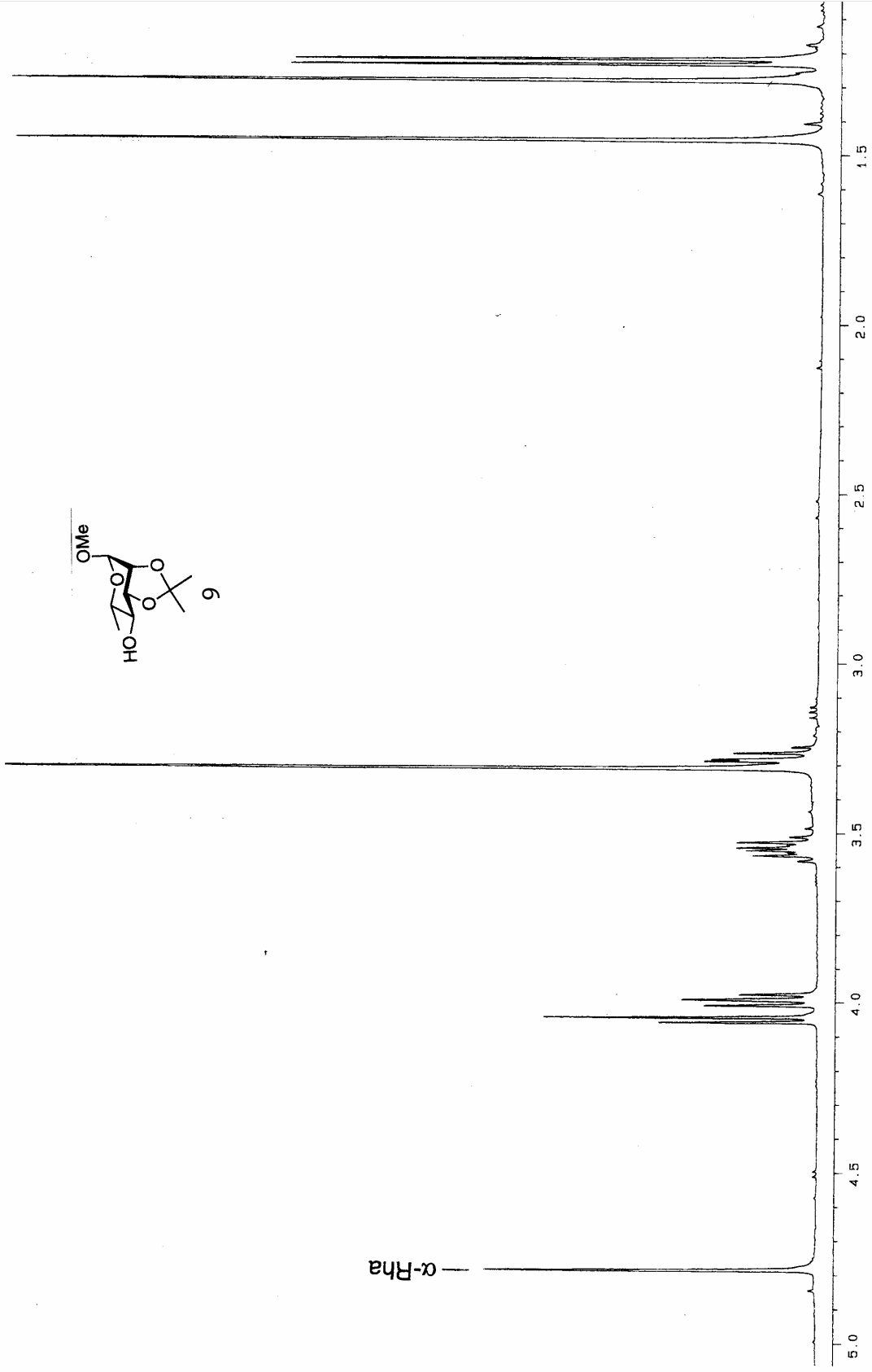
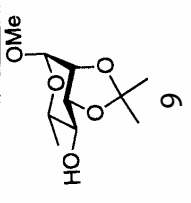


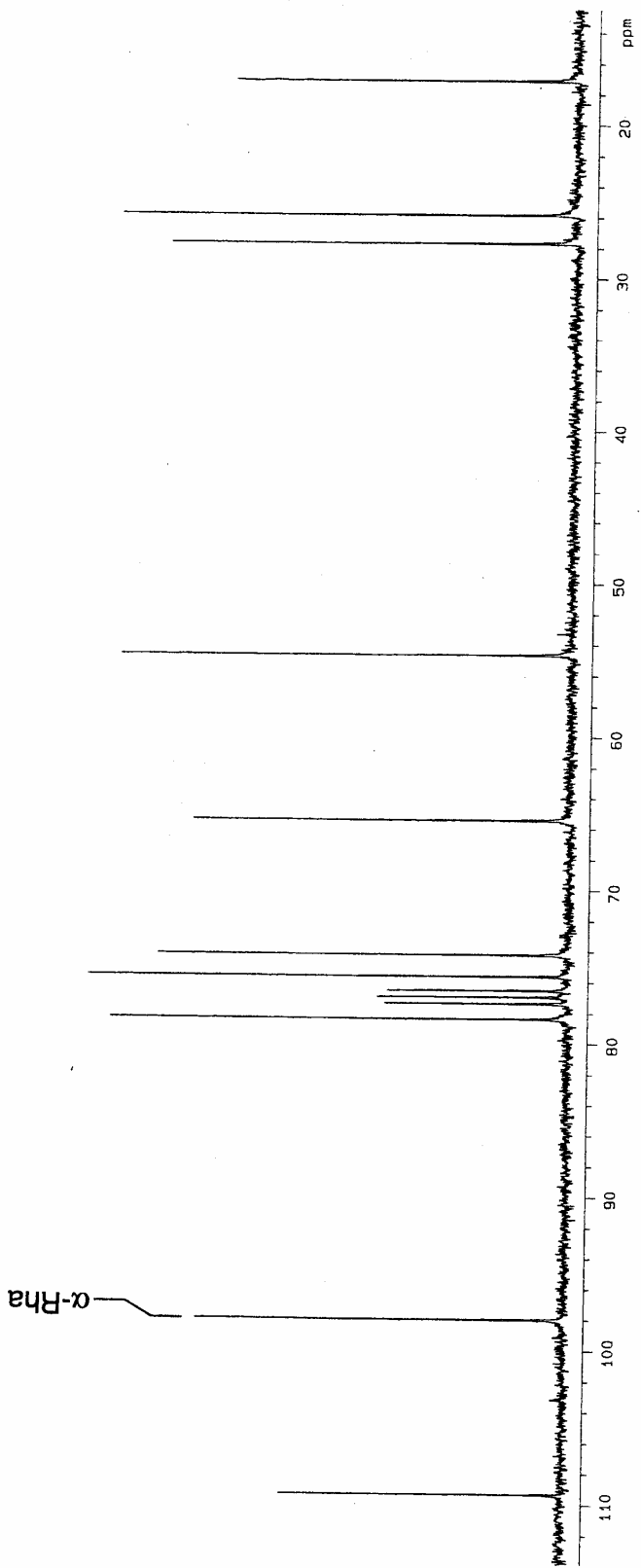
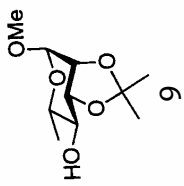


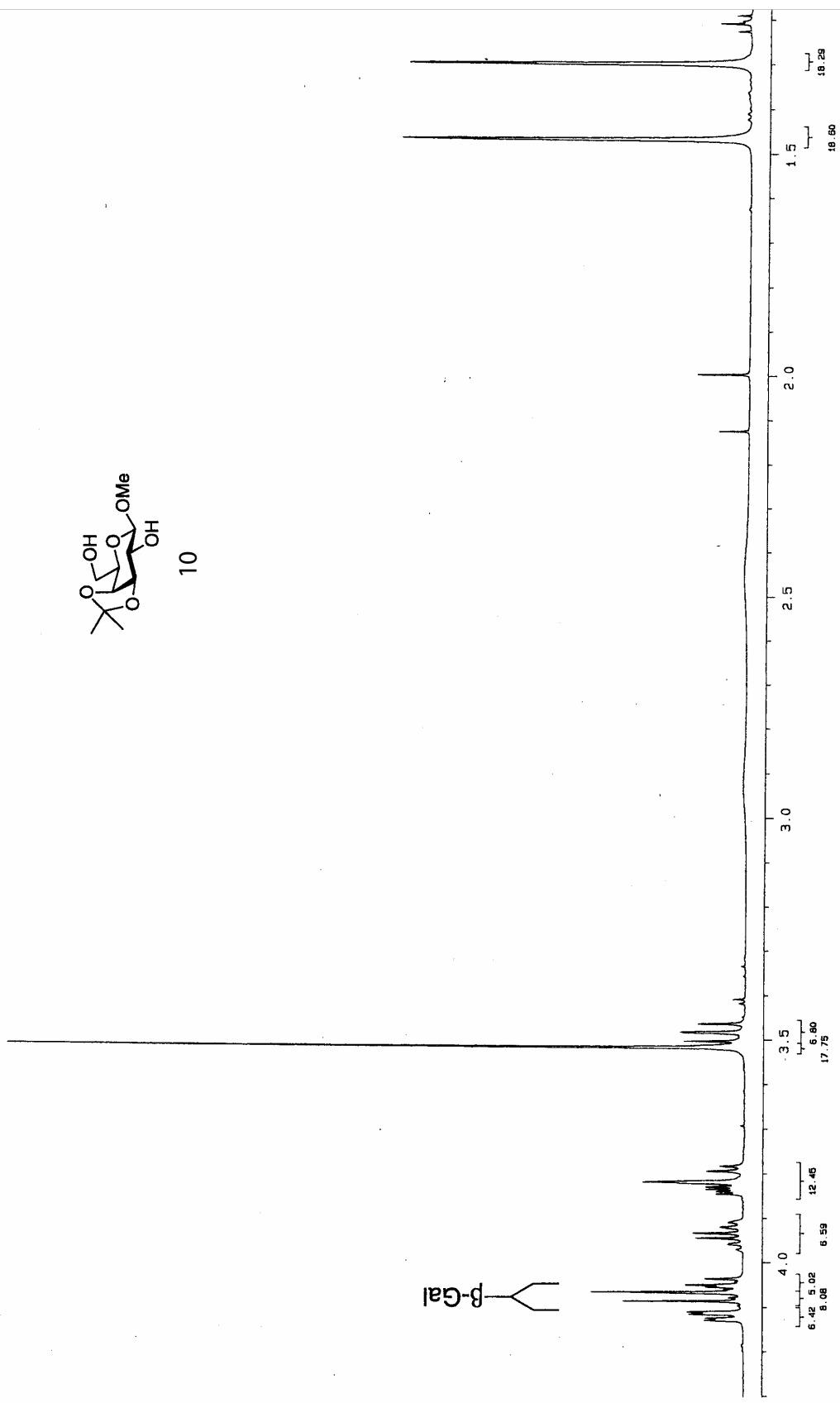
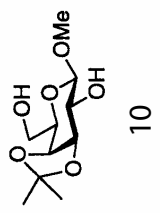




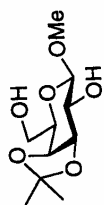




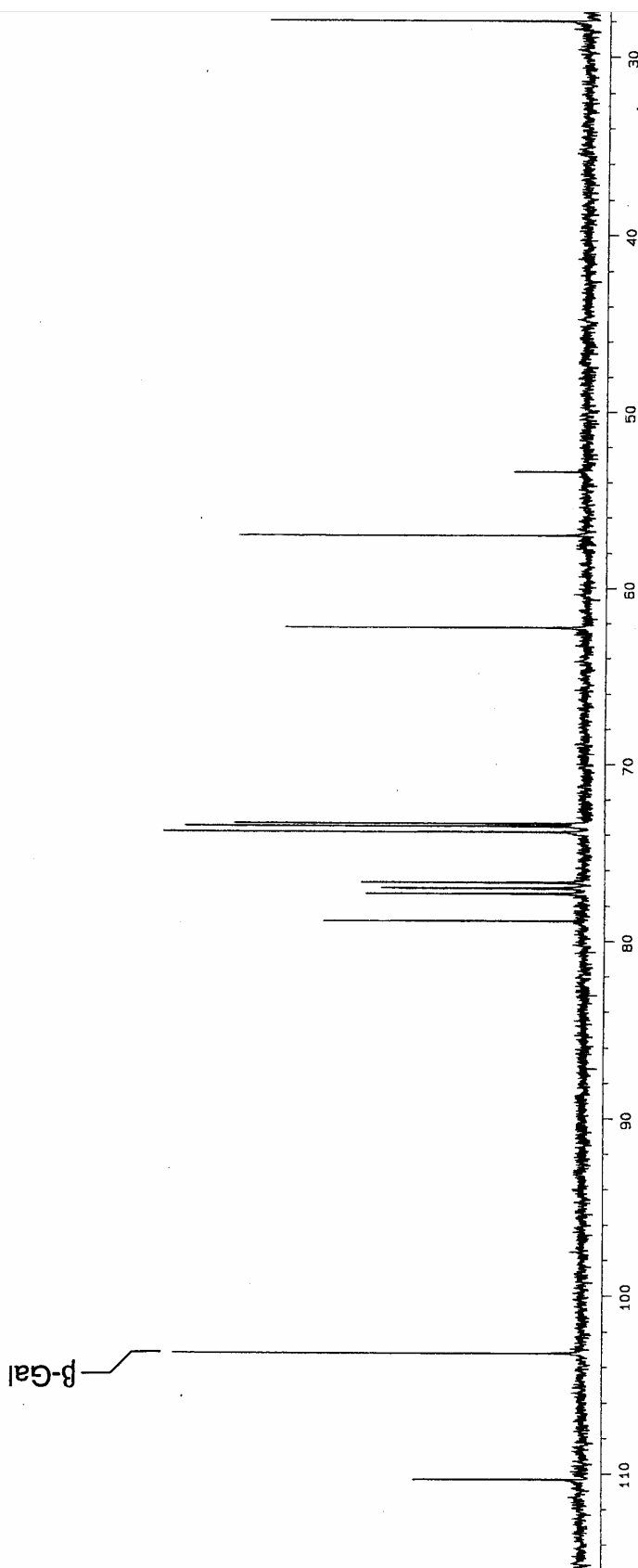


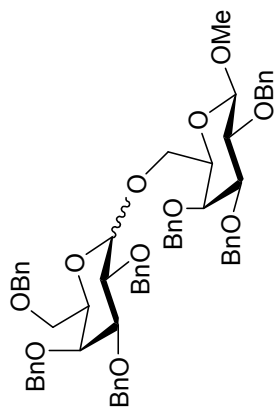


β -Gal

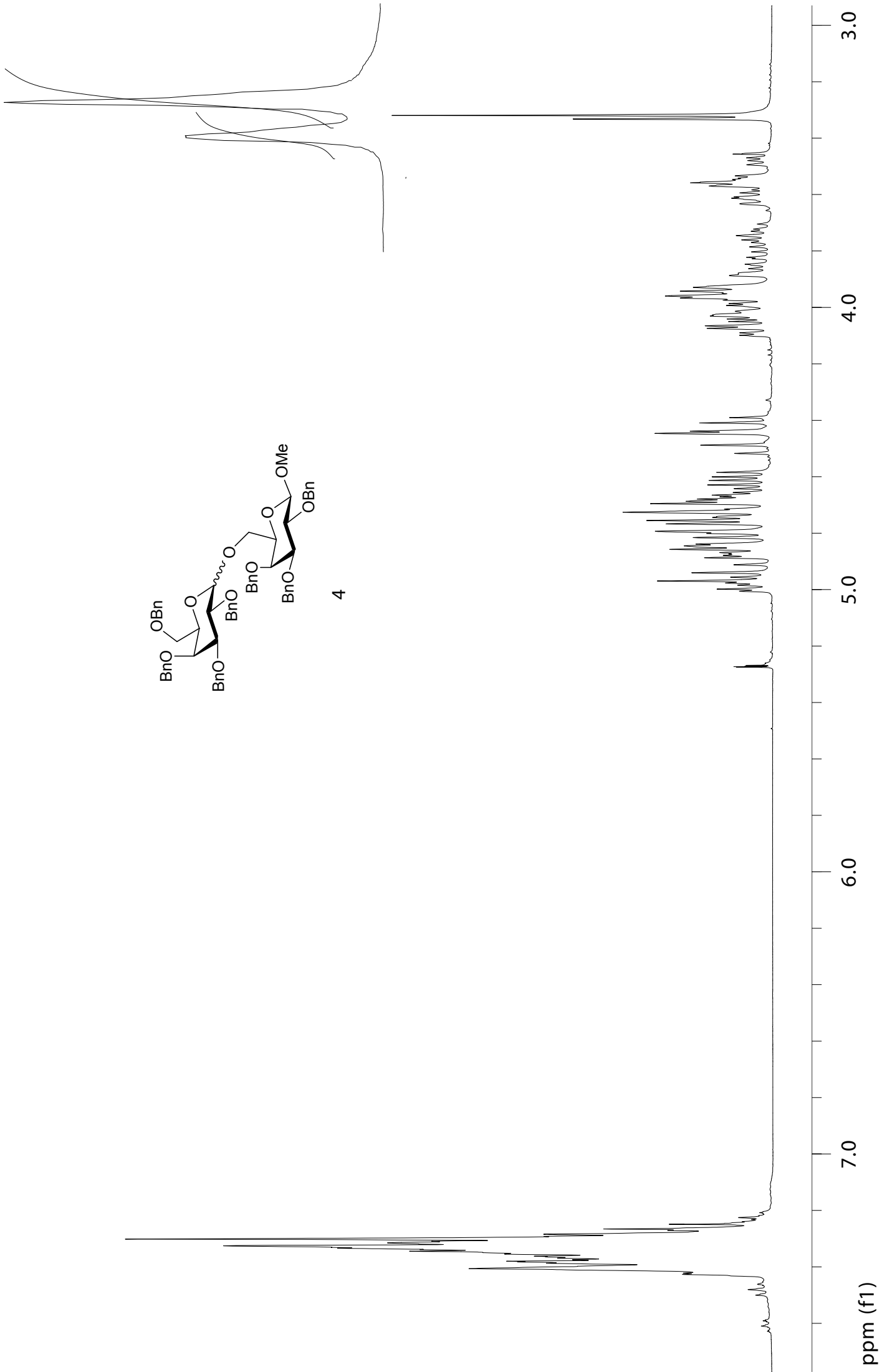


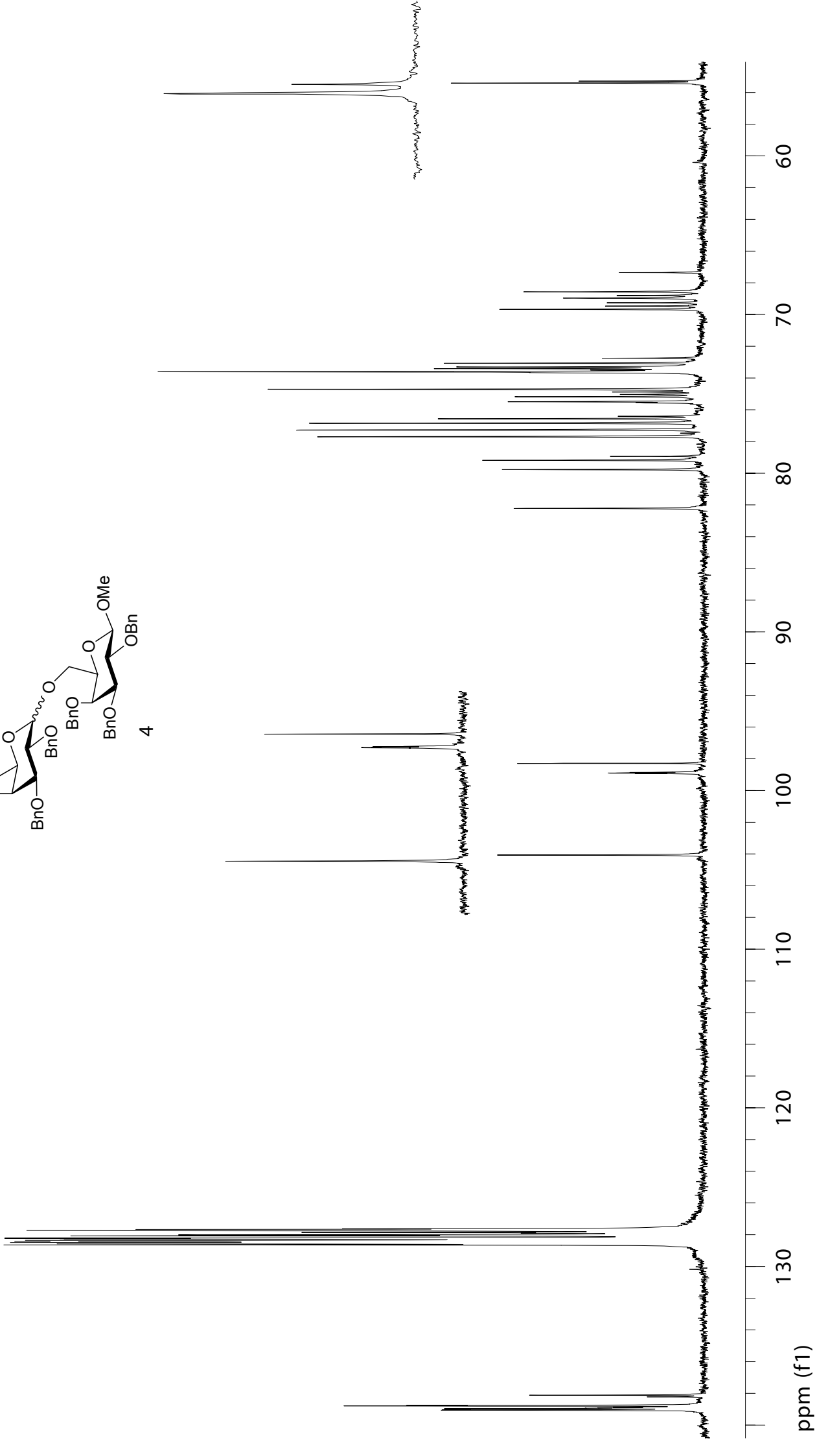
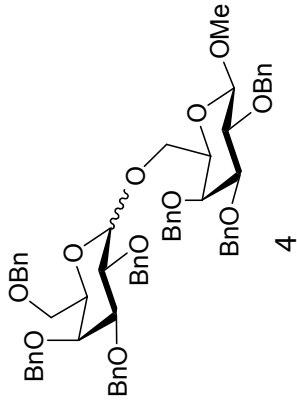
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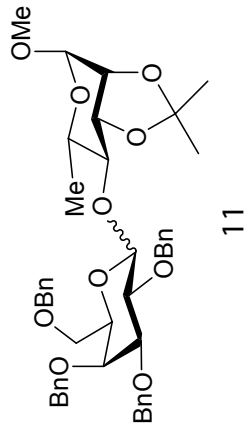




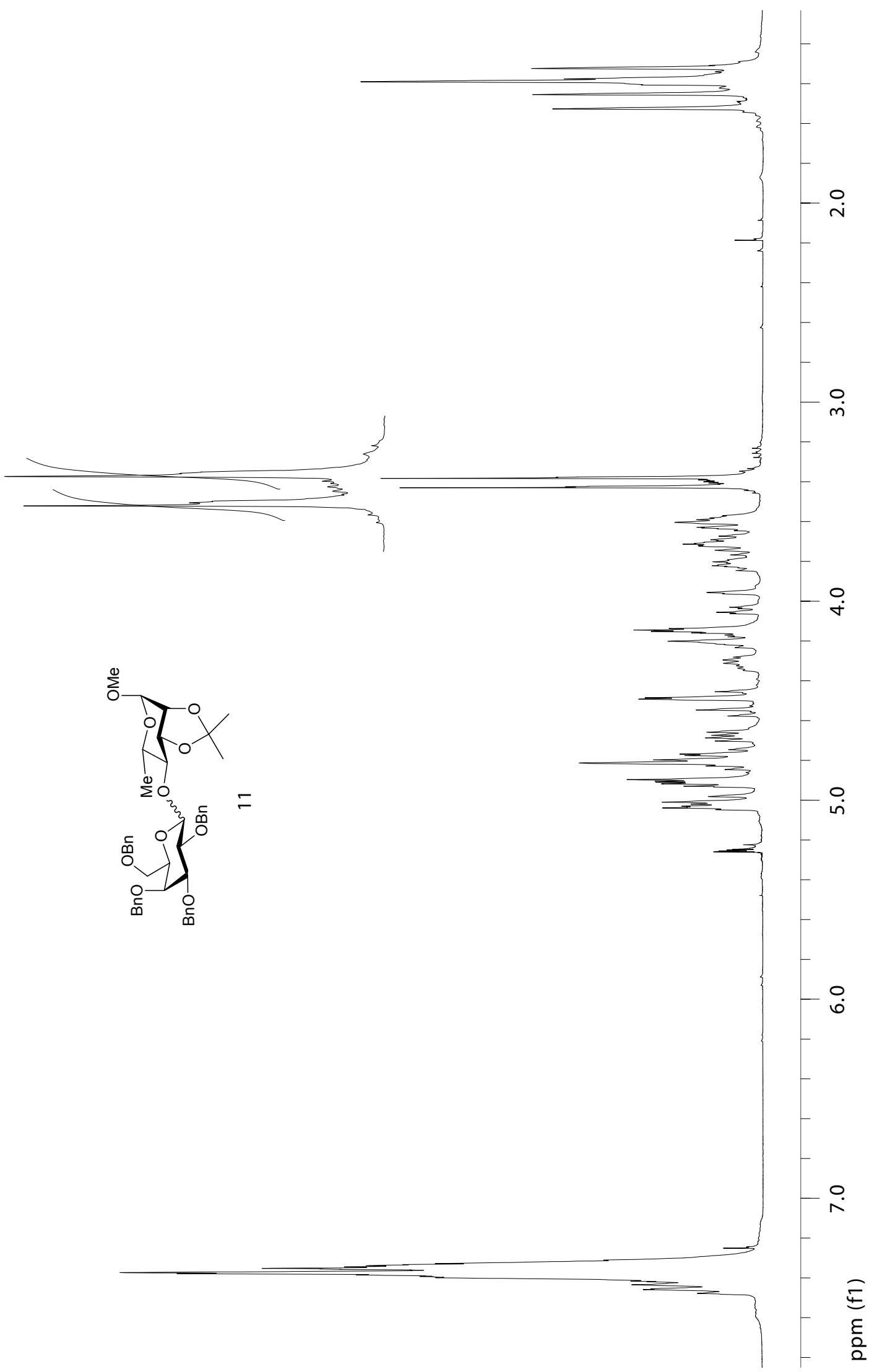
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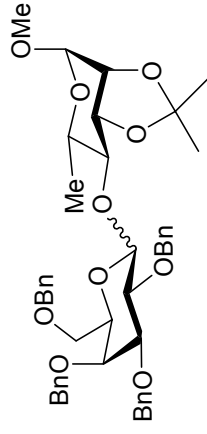




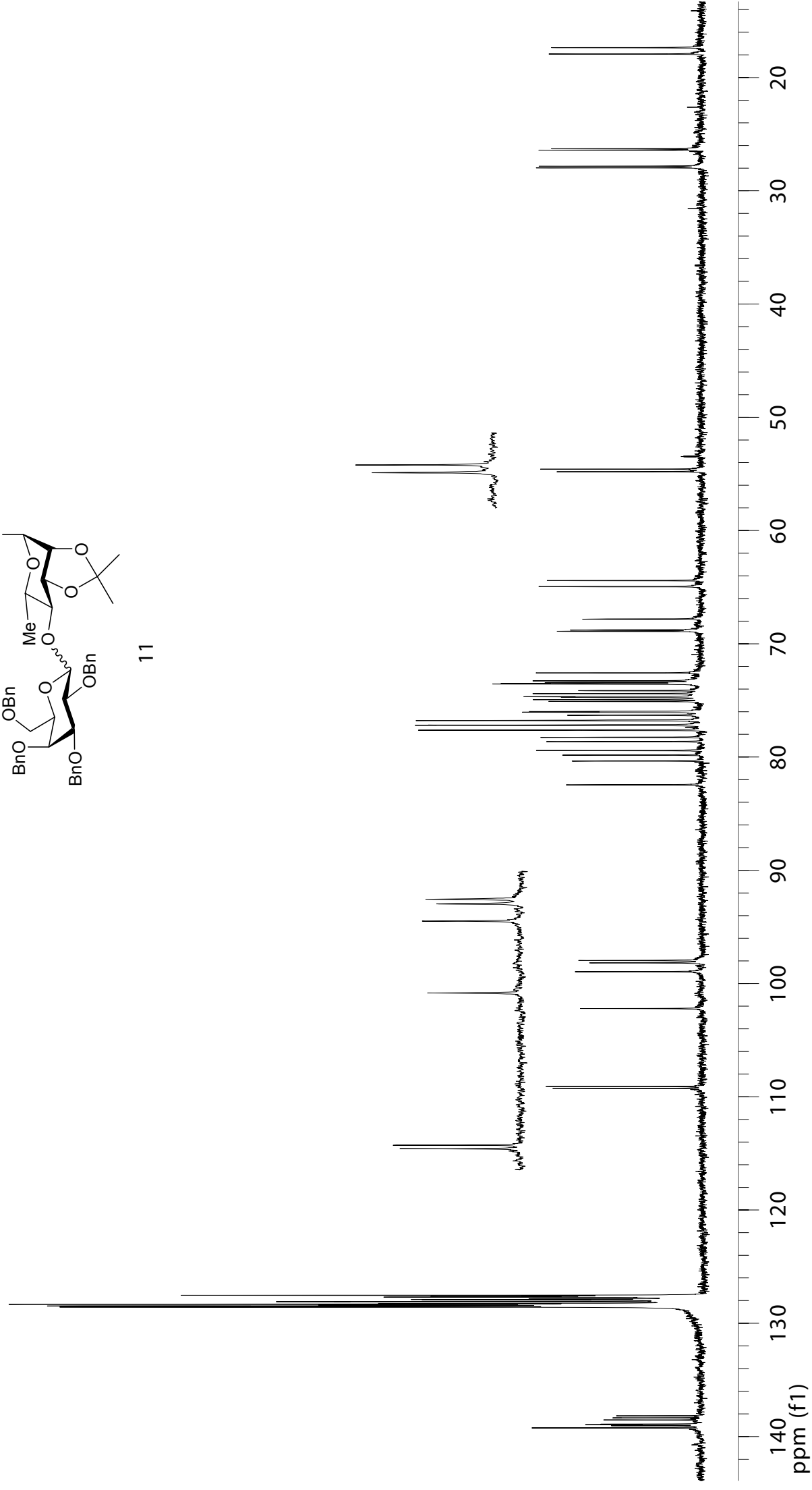


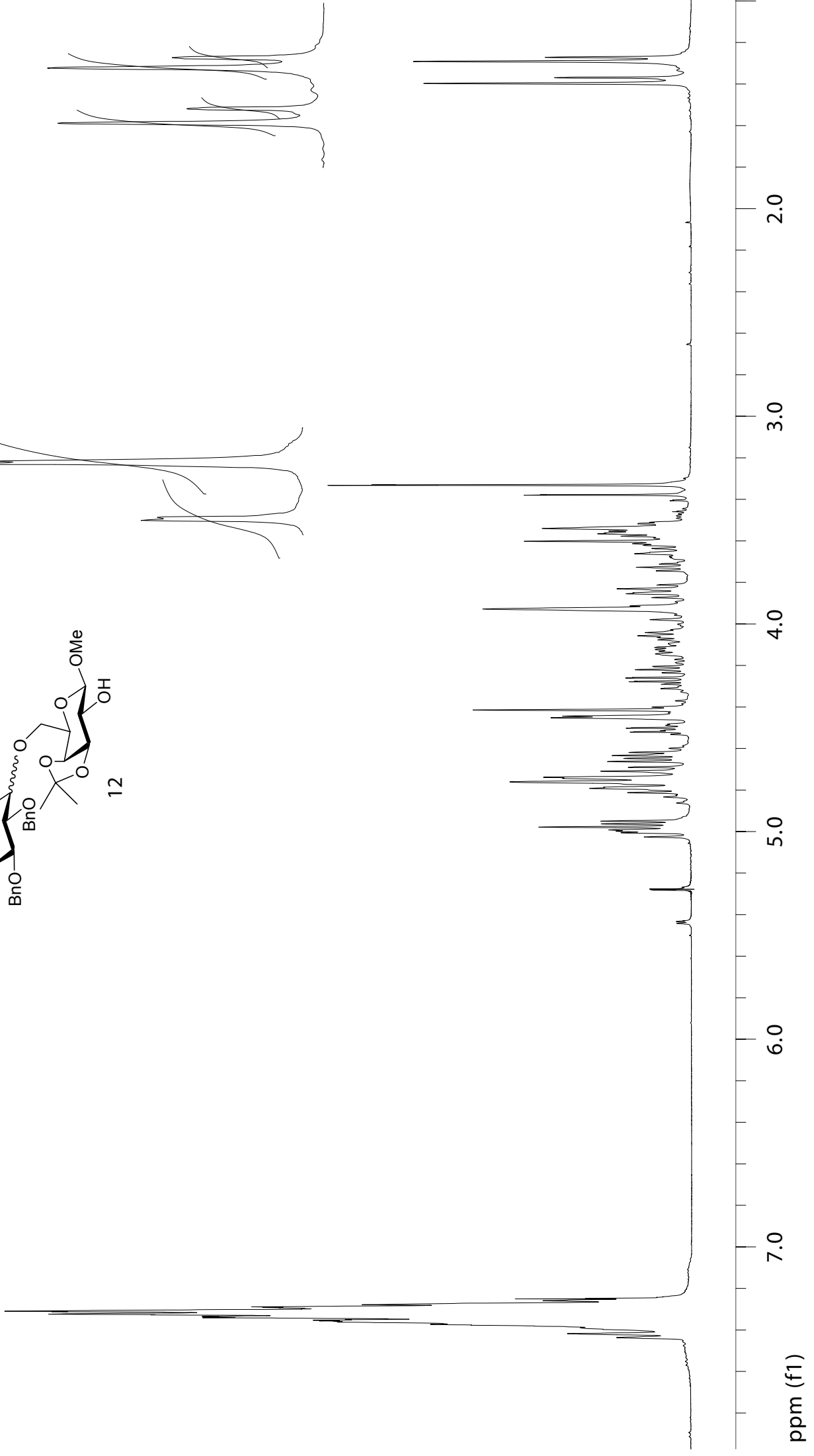
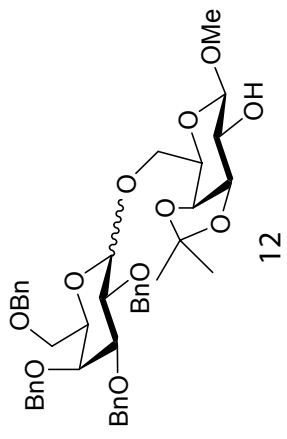
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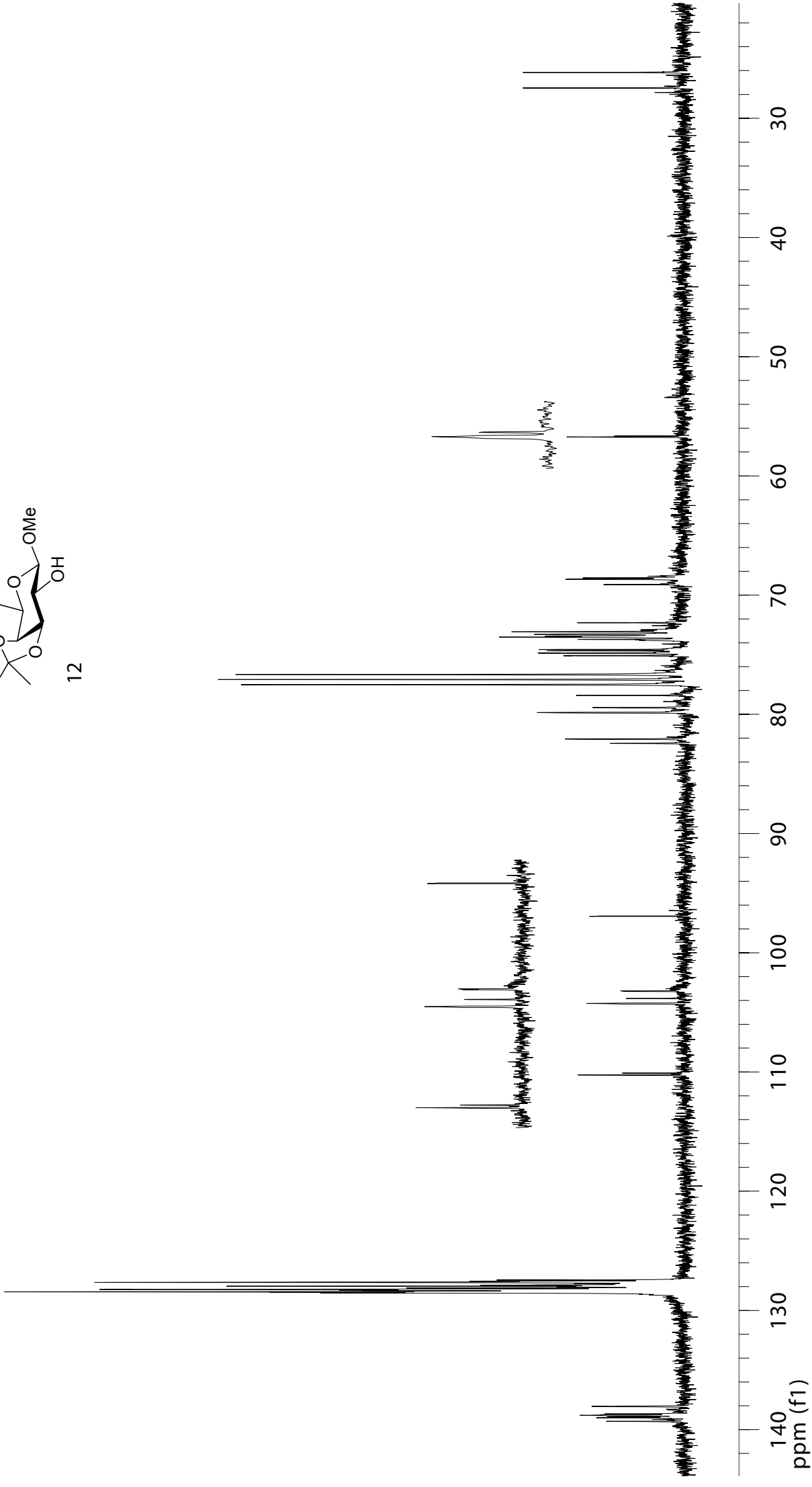
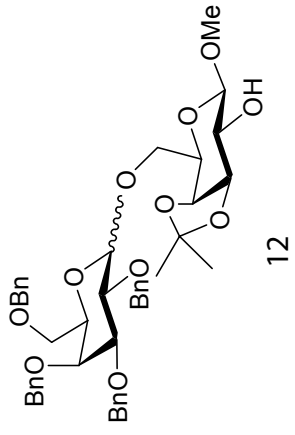


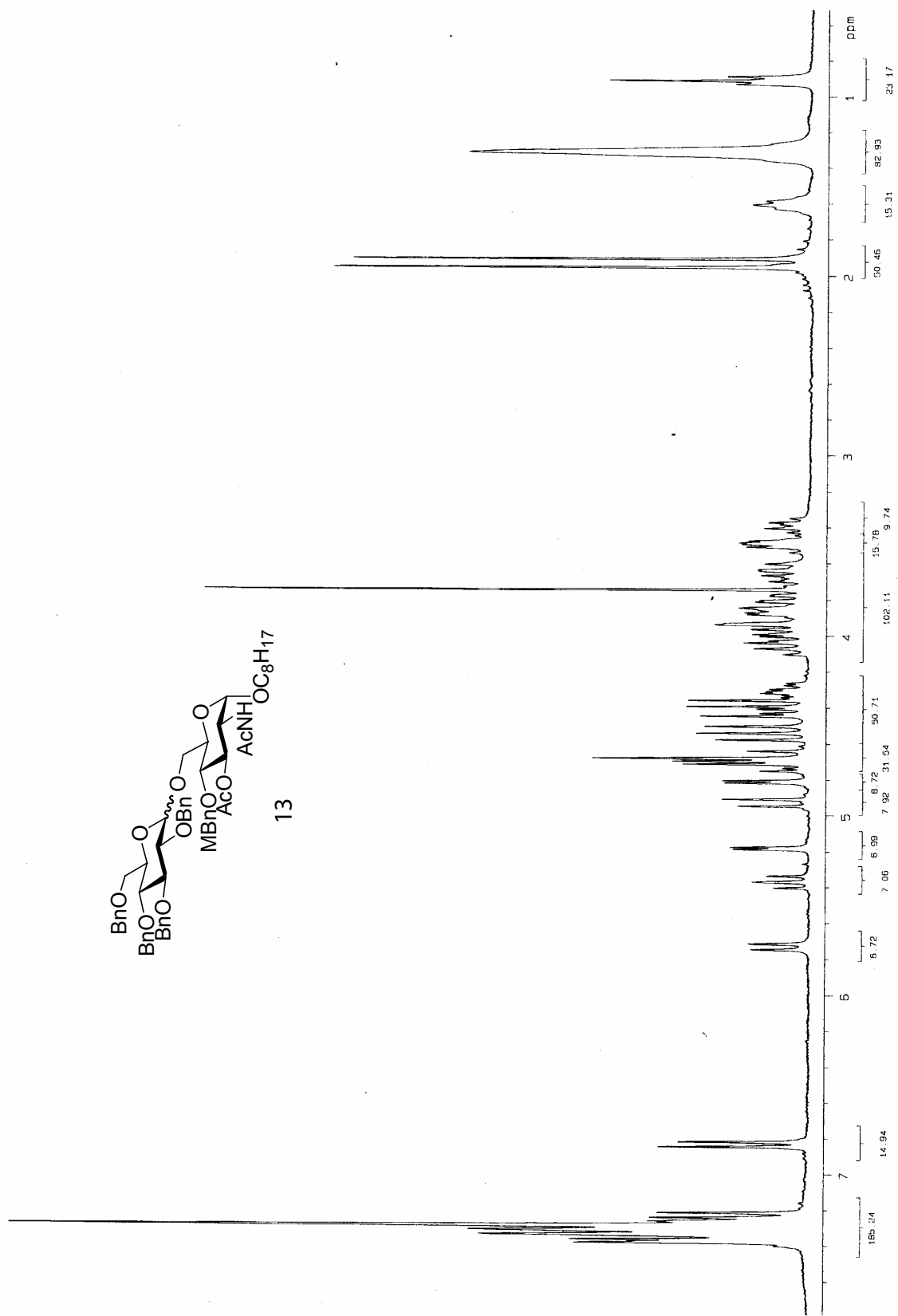
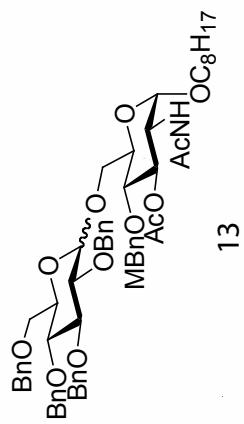


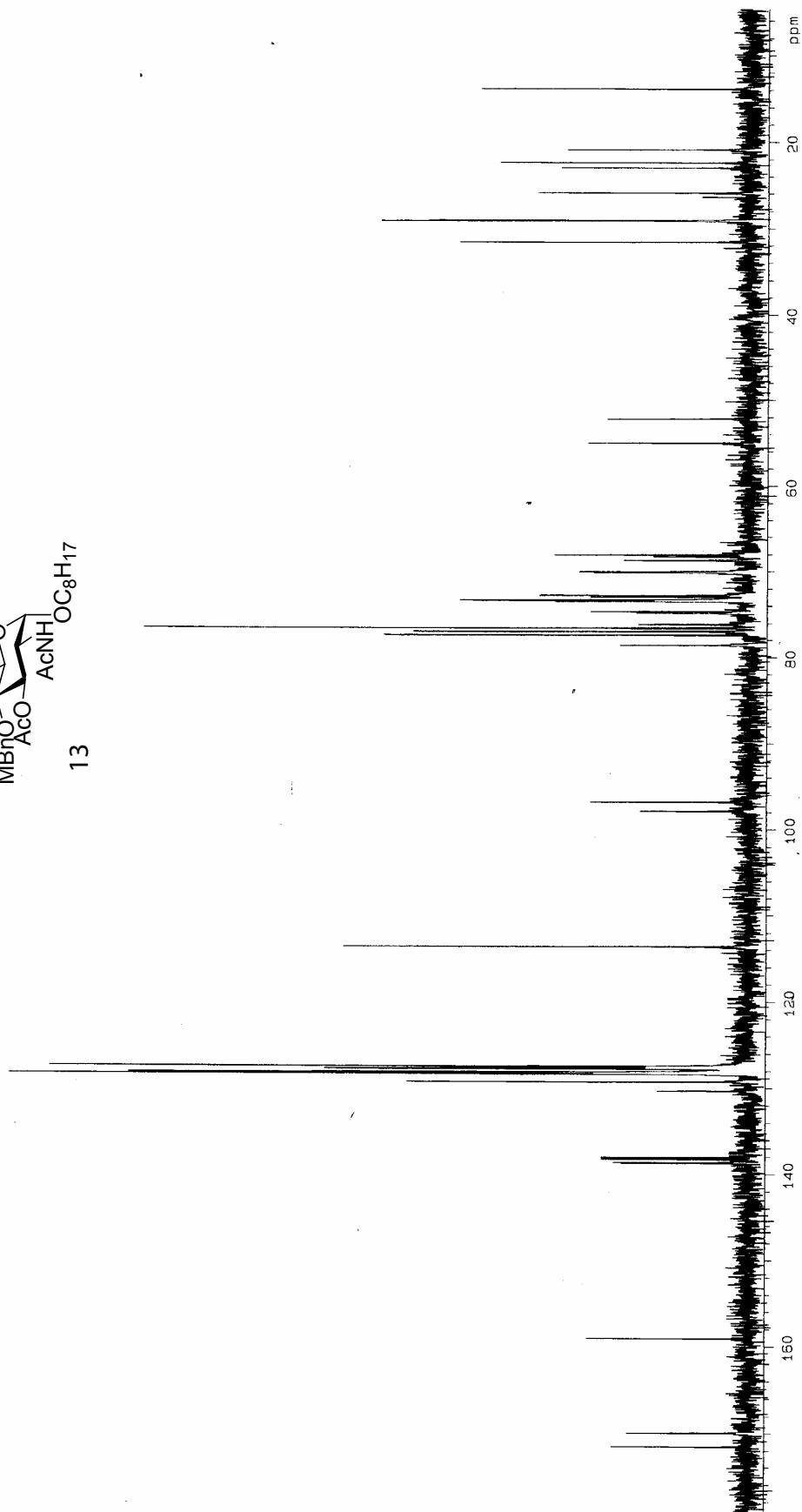
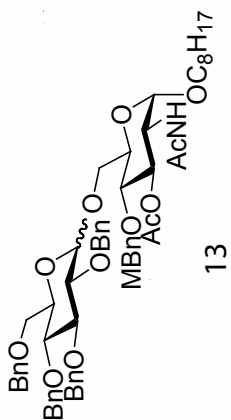
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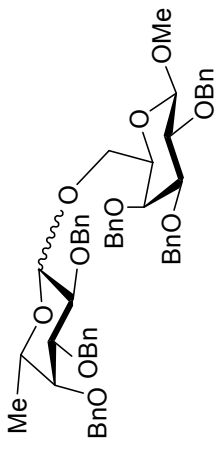




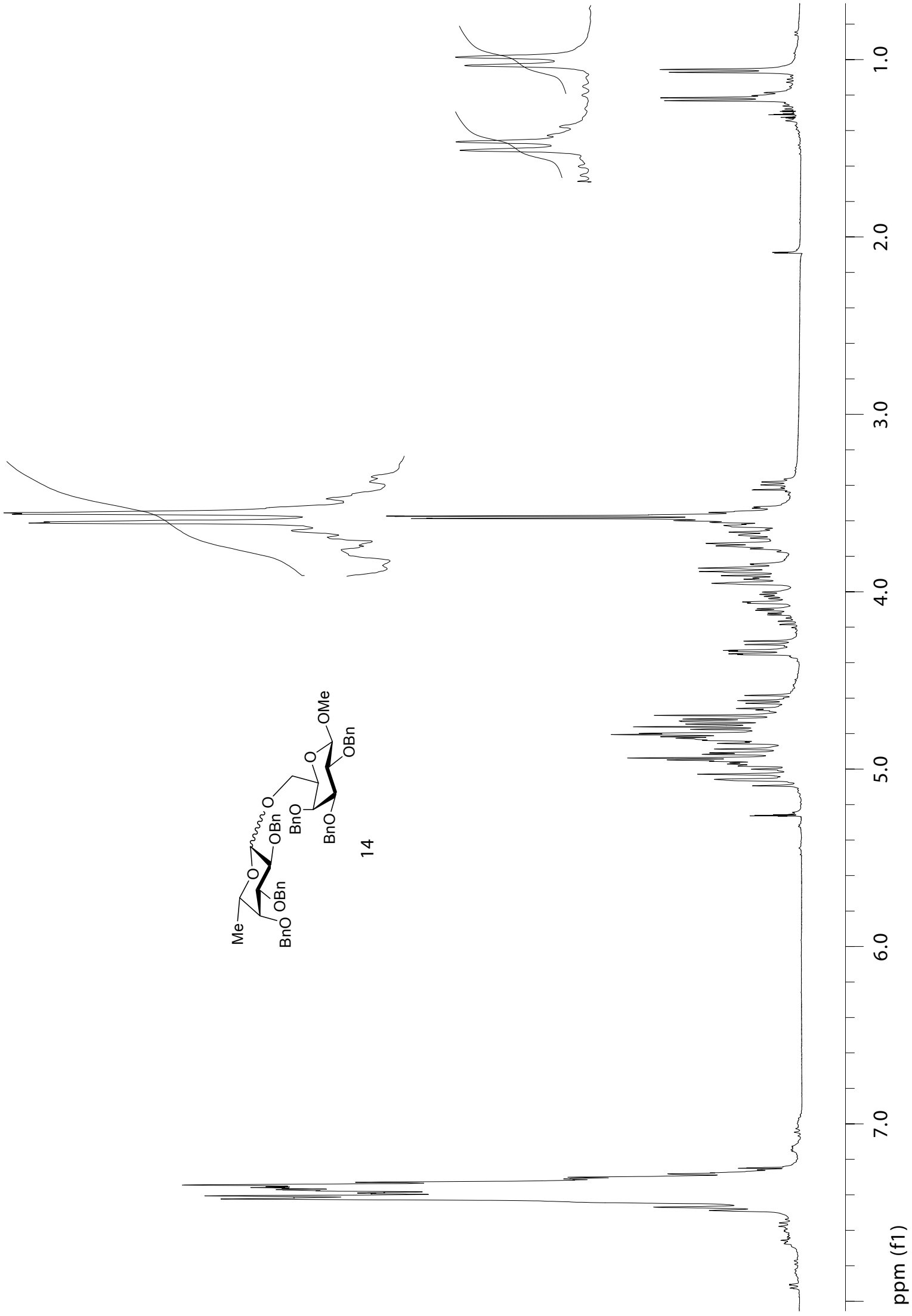


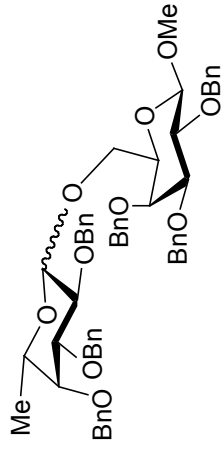




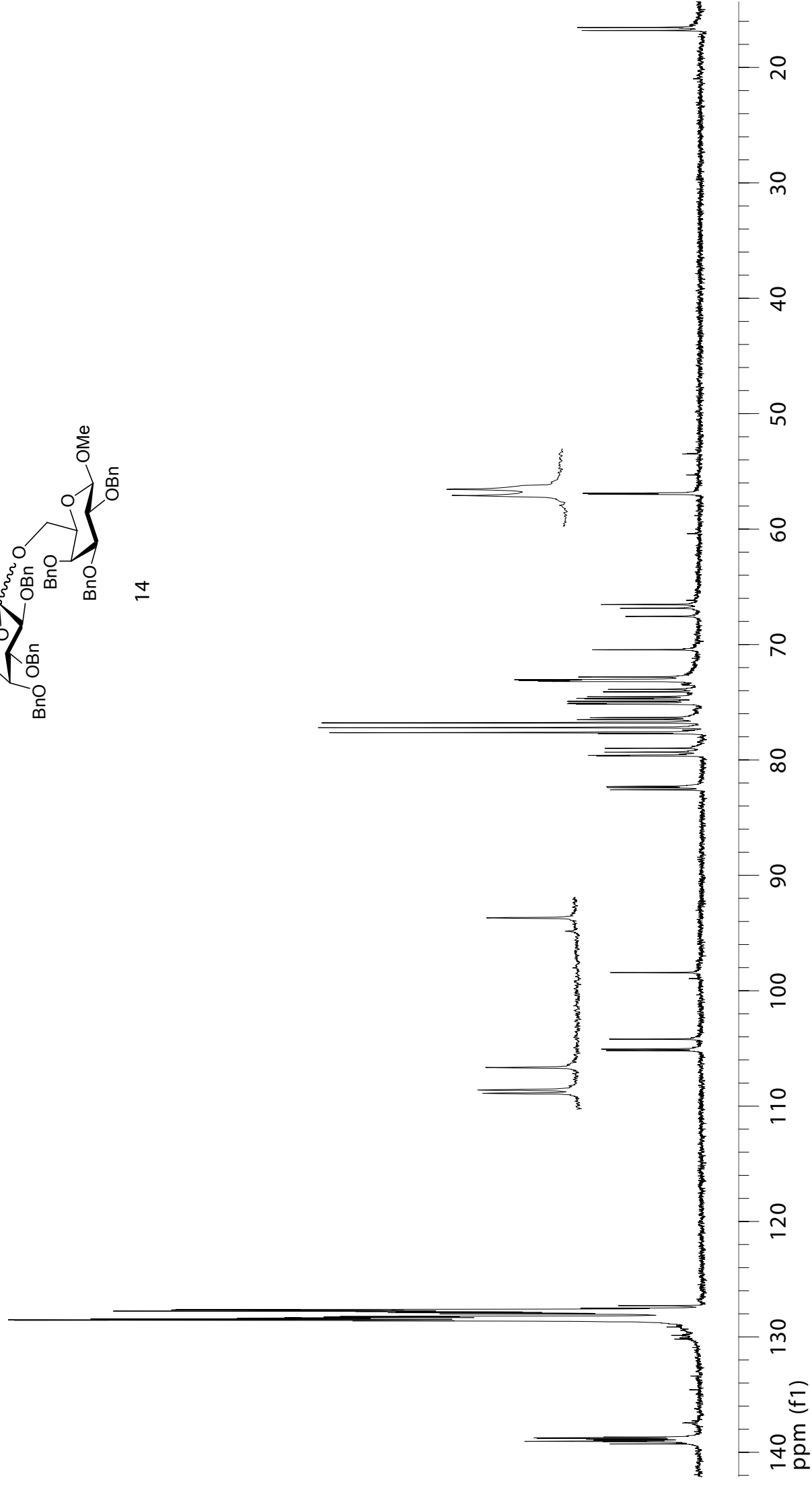


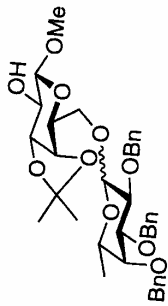
14



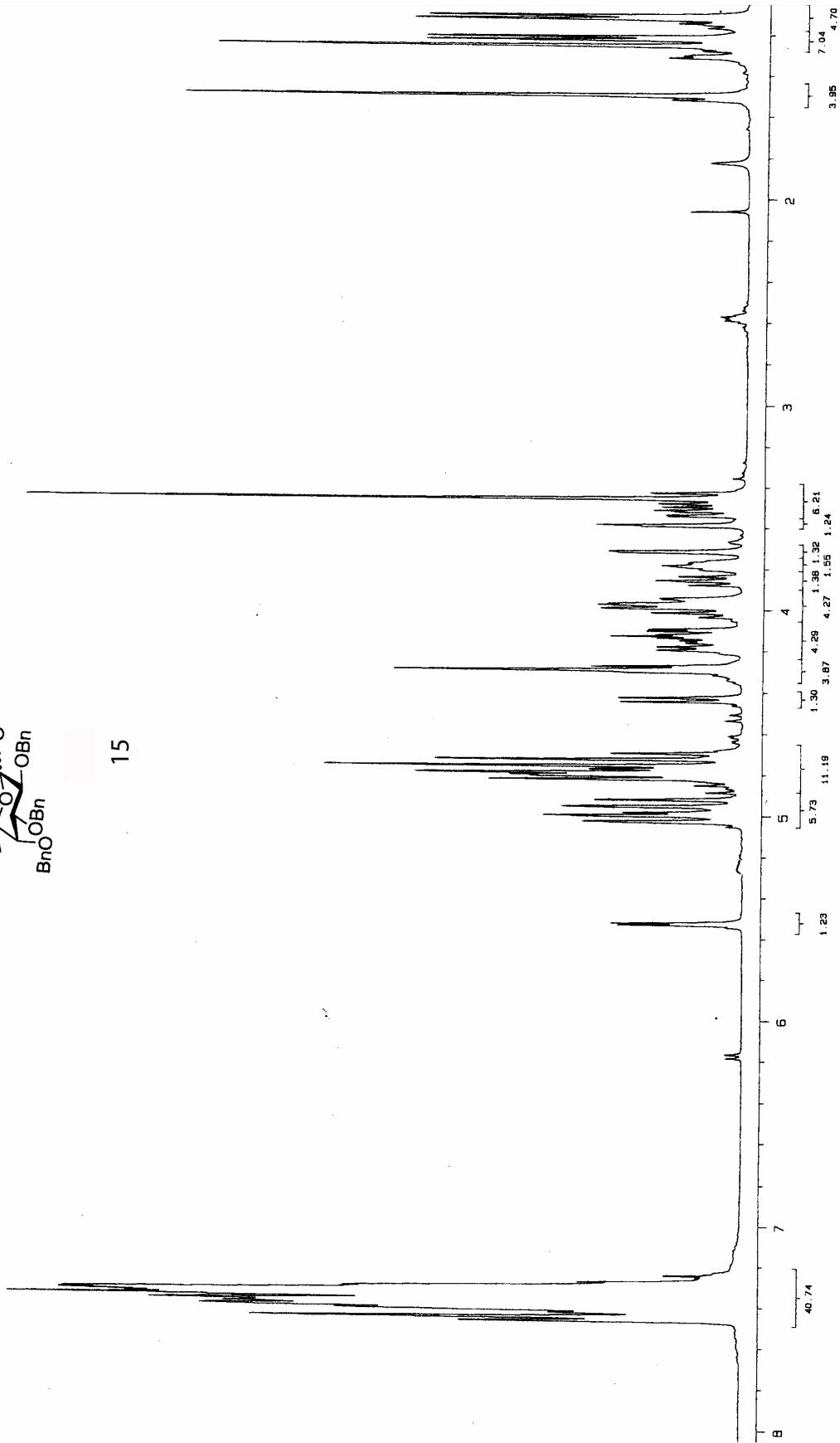


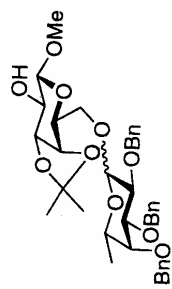
14



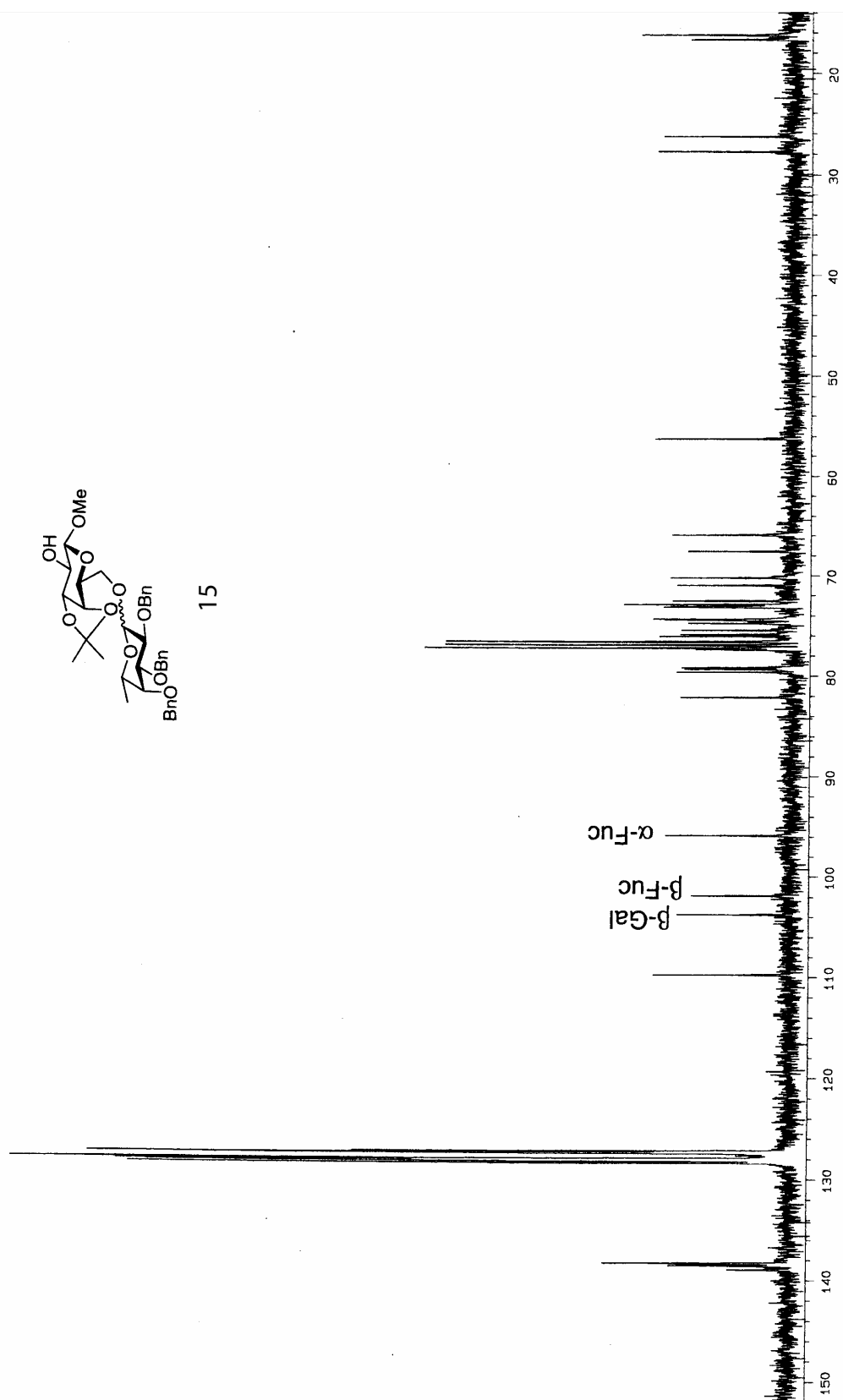


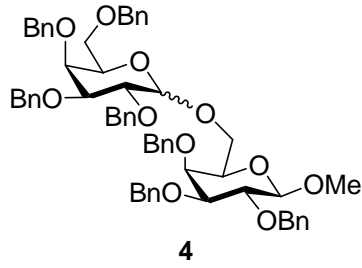
15





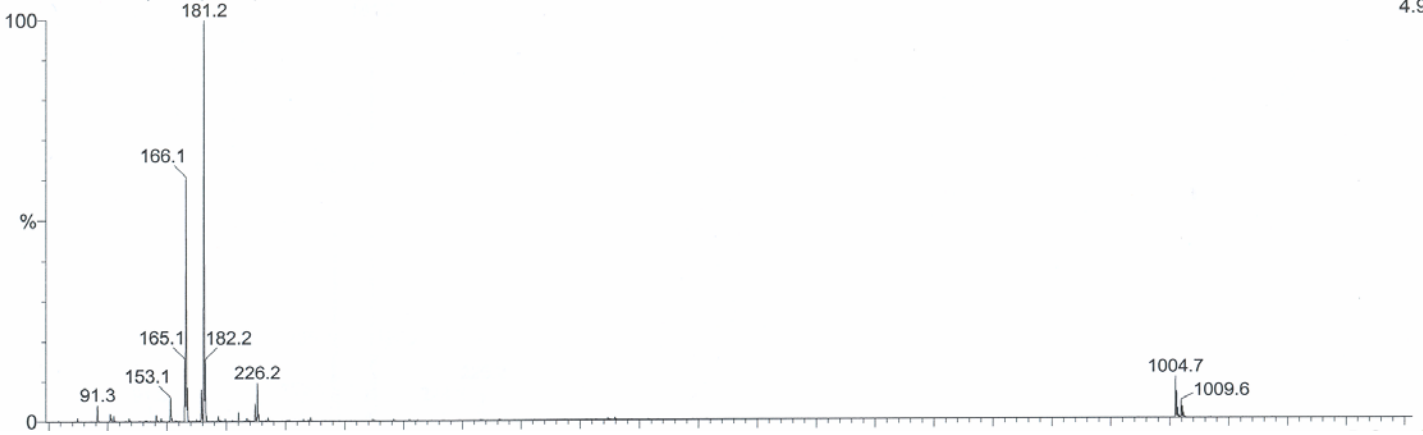
15





UEA120FIE 18 (3.134) Sm (SG, 2x0.70); Cm (16:18-5:6)

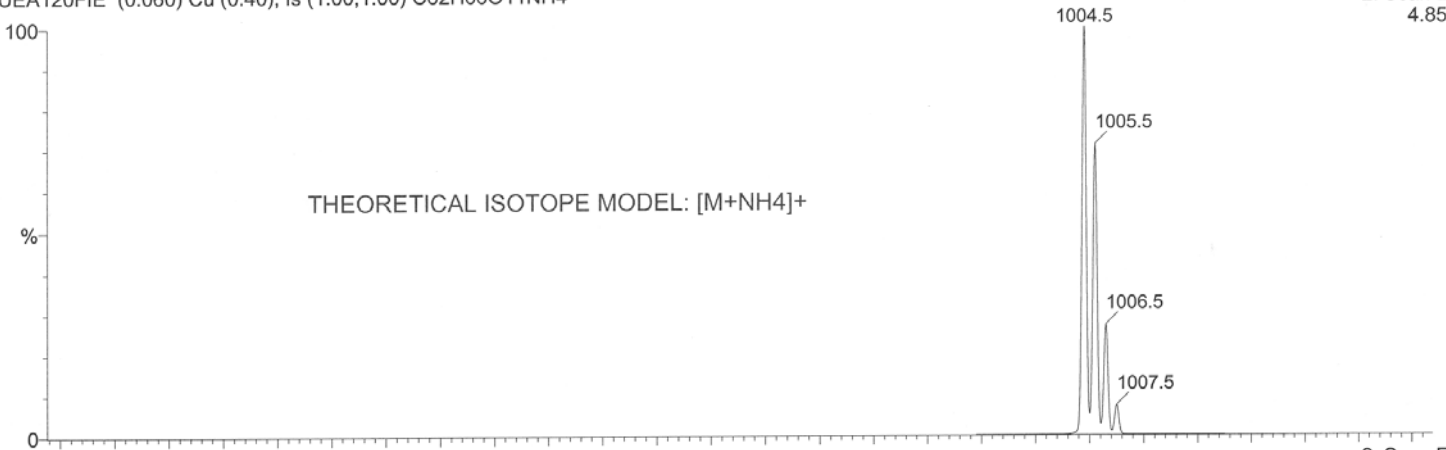
2: Scan ES+
4.90e7



UEA120FIE (0.060) Cu (0.40); Is (1.00,1.00) C62H66O11NH4

2: Scan ES+
4.85e12

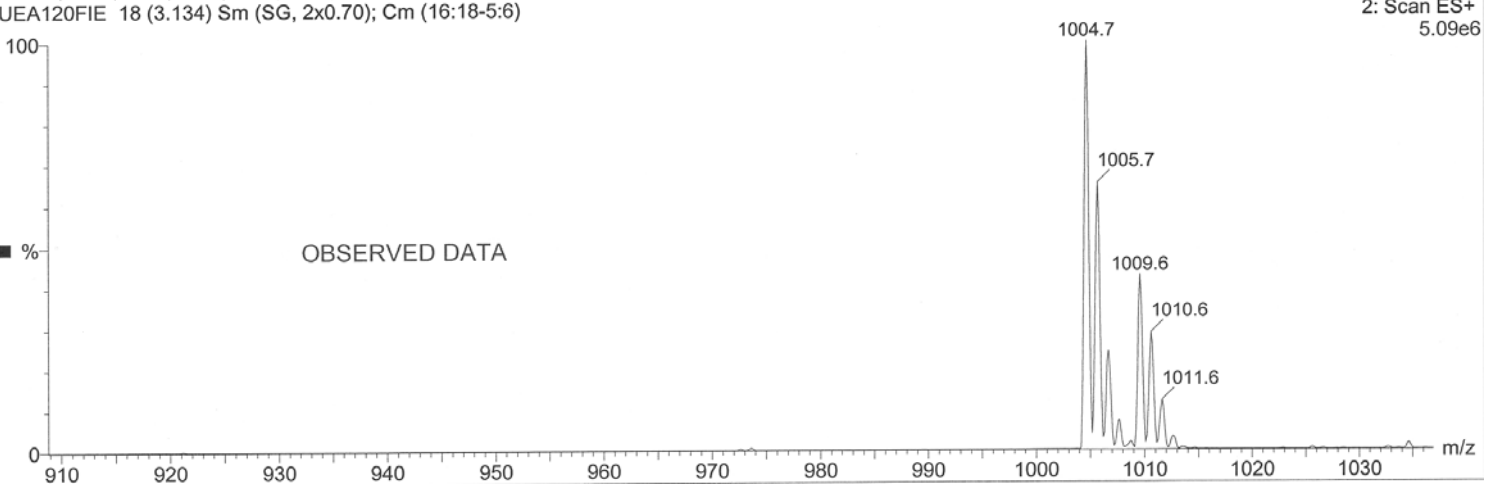
THEORETICAL ISOTOPE MODEL: [M+NH4]⁺

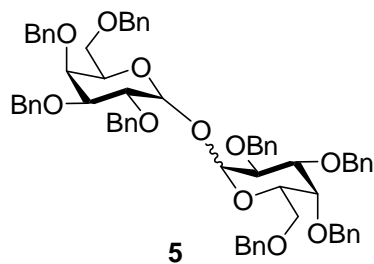


UEA120FIE 18 (3.134) Sm (SG, 2x0.70); Cm (16:18-5:6)

2: Scan ES+
5.09e6

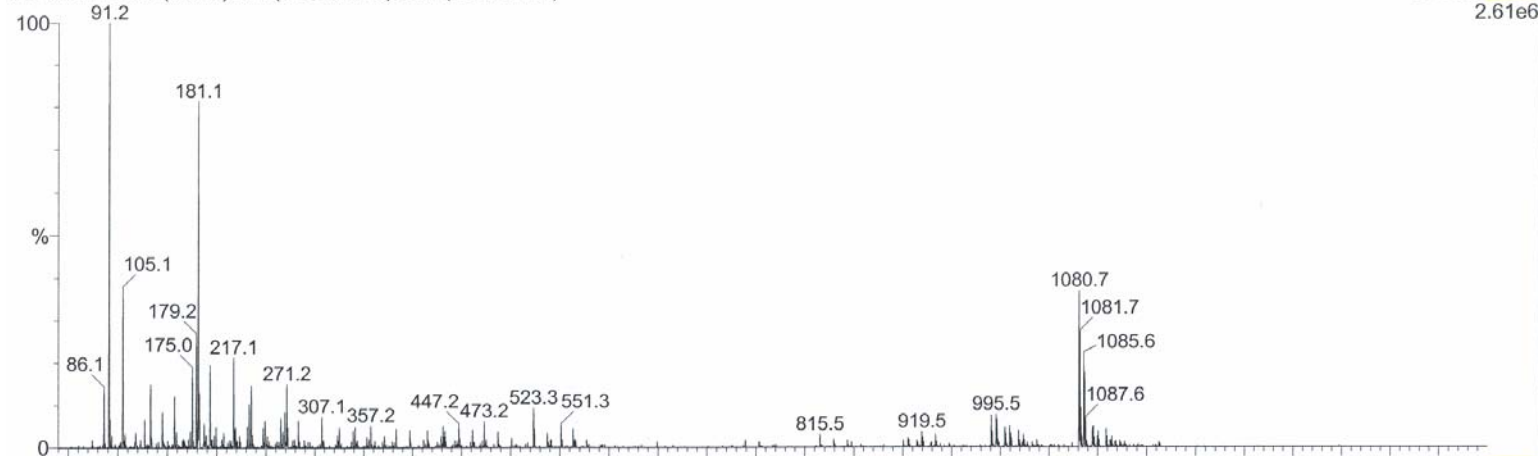
OBSERVED DATA





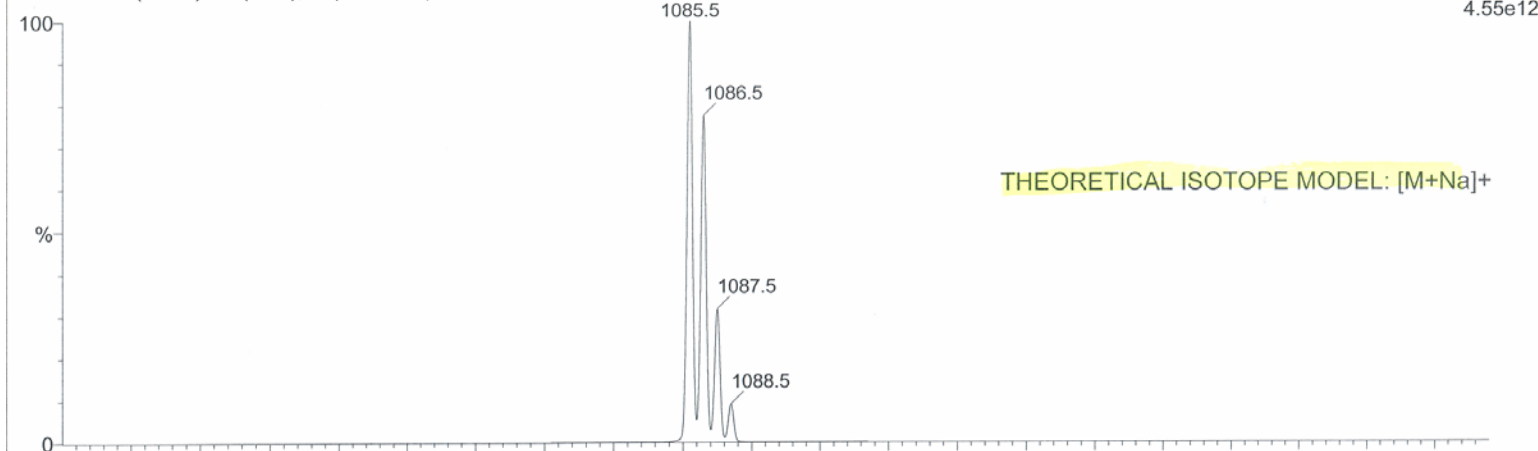
UEA184FIE 22 (3.840) Sm (SG, 2x0.70); Cm (19:22-7:11)

2: Scan ES+
2.61e6



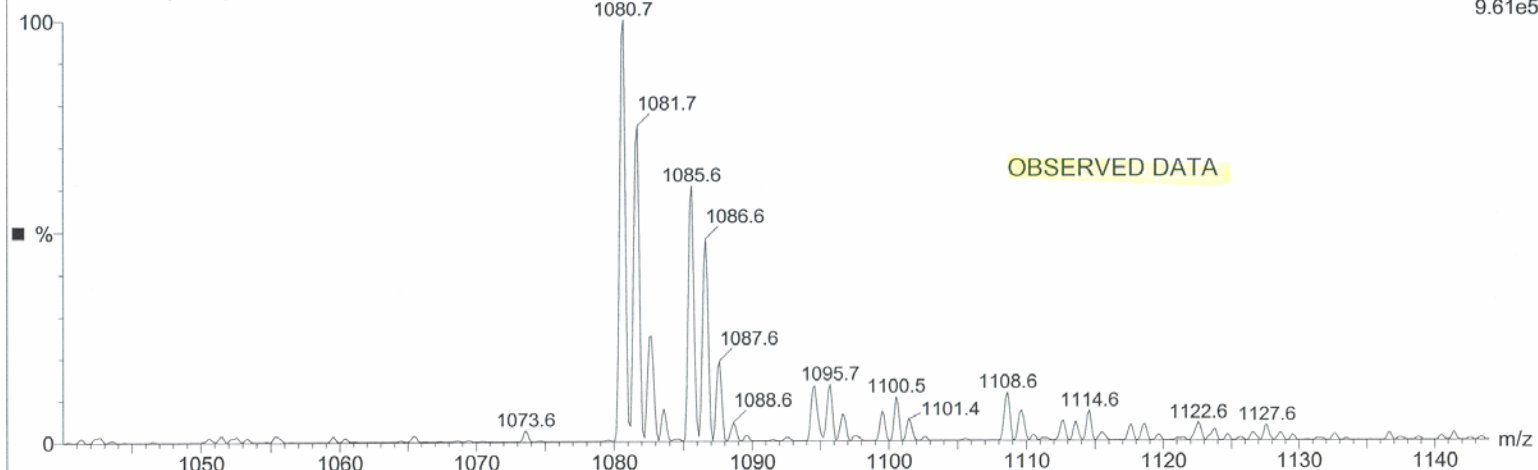
UEA184FIE (0.060) Cu (0.40); Is (1.00,1.00) C68H70O11Na

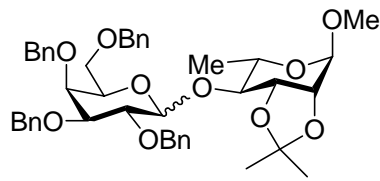
2: Scan ES+
4.55e12



UEA184FIE 22 (3.840) Sm (SG, 2x0.70); Cm (19:22-7:11)

2: Scan ES+
9.61e5

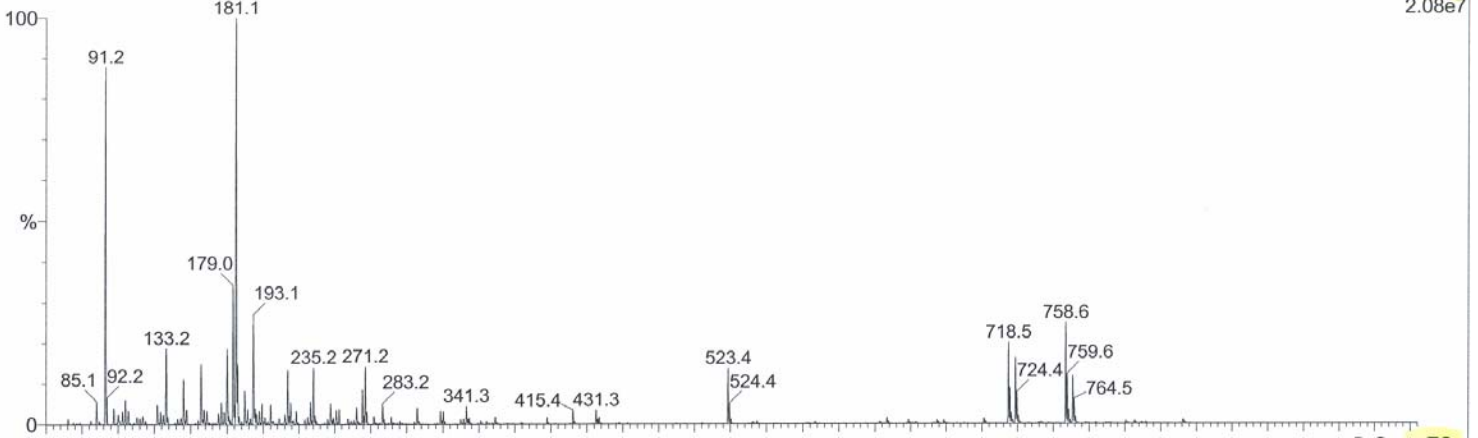




11

UEA113FIE 19 (3.315) Sm (SG, 2x0.70); Cm (15:20-4:7)

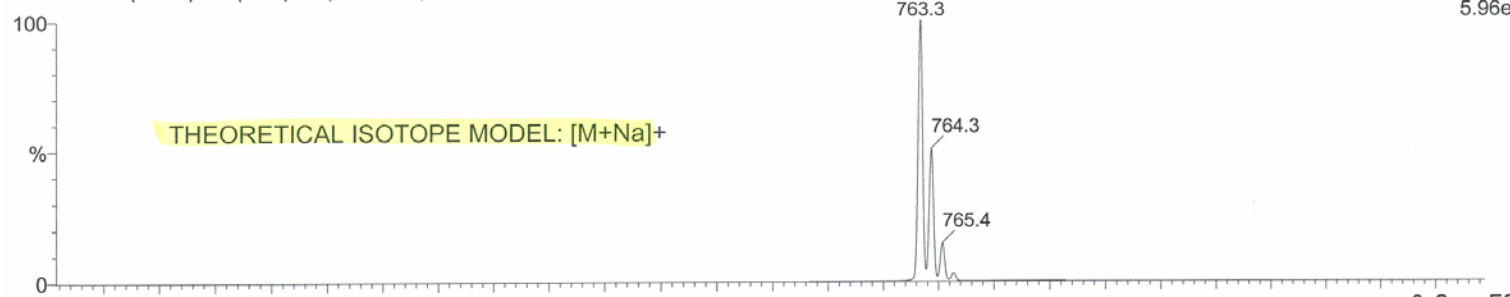
2: Scan ES+
2.08e7



UEA113FIE (0.060) Cu (0.40); Is (1.00,1.00) C44H52O10Na

2: Scan ES+
5.96e12

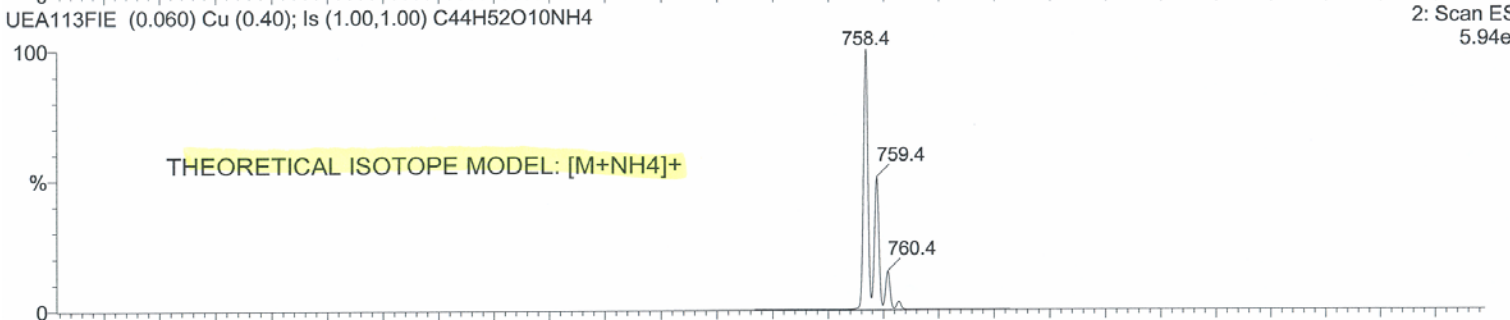
THEORETICAL ISOTOPE MODEL: [M+Na]⁺



UEA113FIE (0.060) Cu (0.40); Is (1.00,1.00) C44H52O10NH4

2: Scan ES+
5.94e12

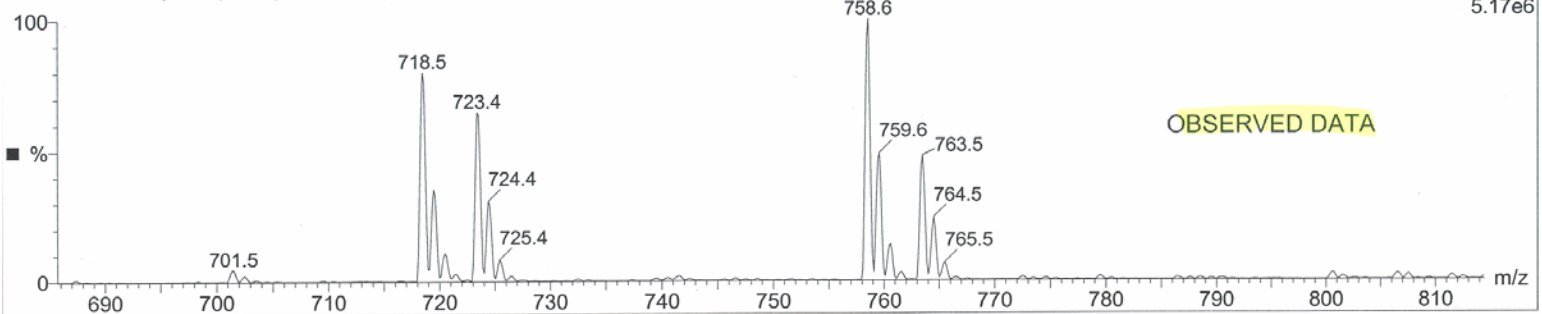
THEORETICAL ISOTOPE MODEL: [M+NH4]⁺

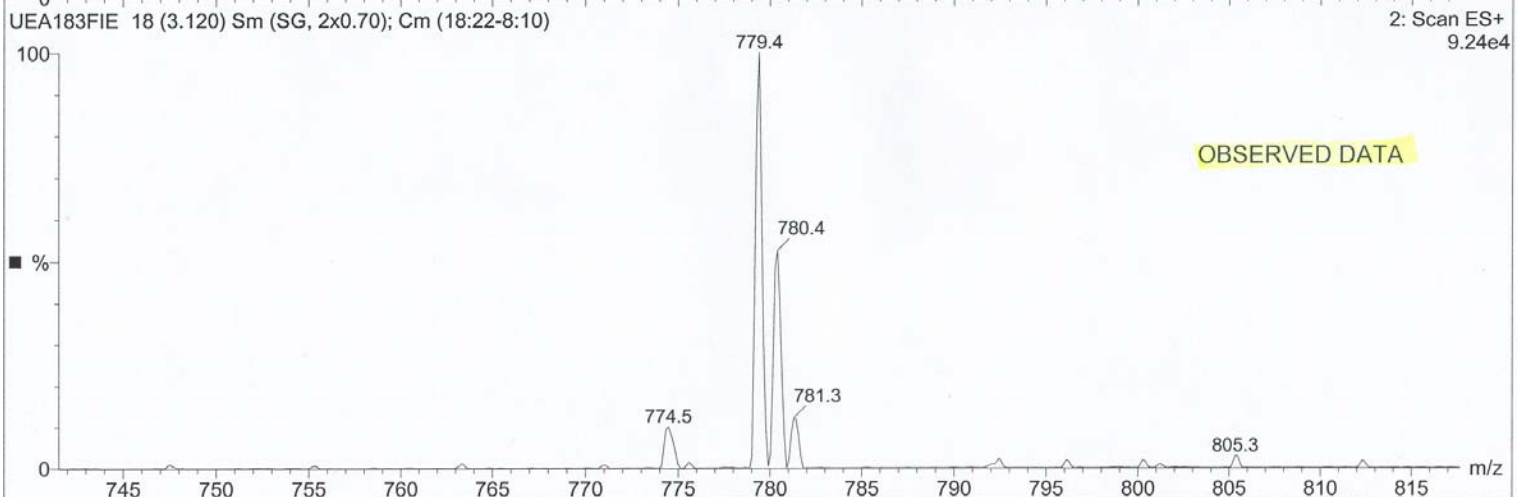
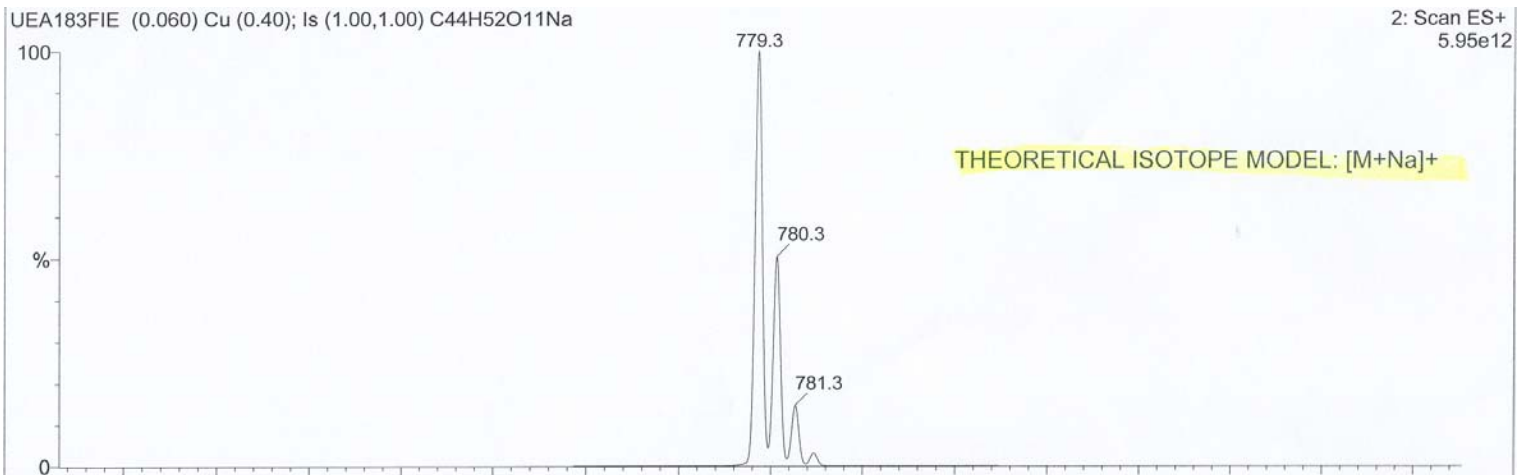
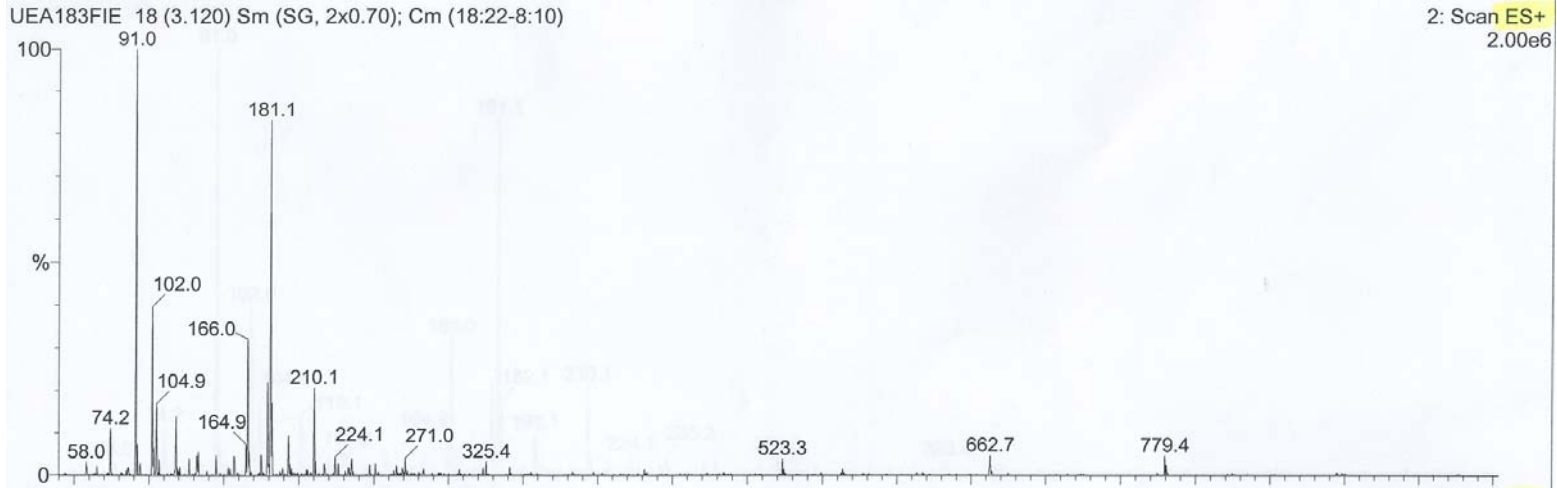
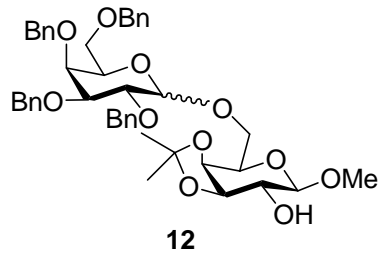


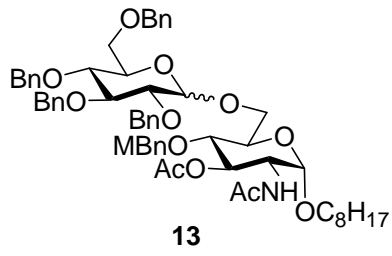
UEA113FIE 19 (3.315) Sm (SG, 2x0.70); Cm (15:20-4:7)

2: Scan ES+
5.17e6

OBSERVED DATA

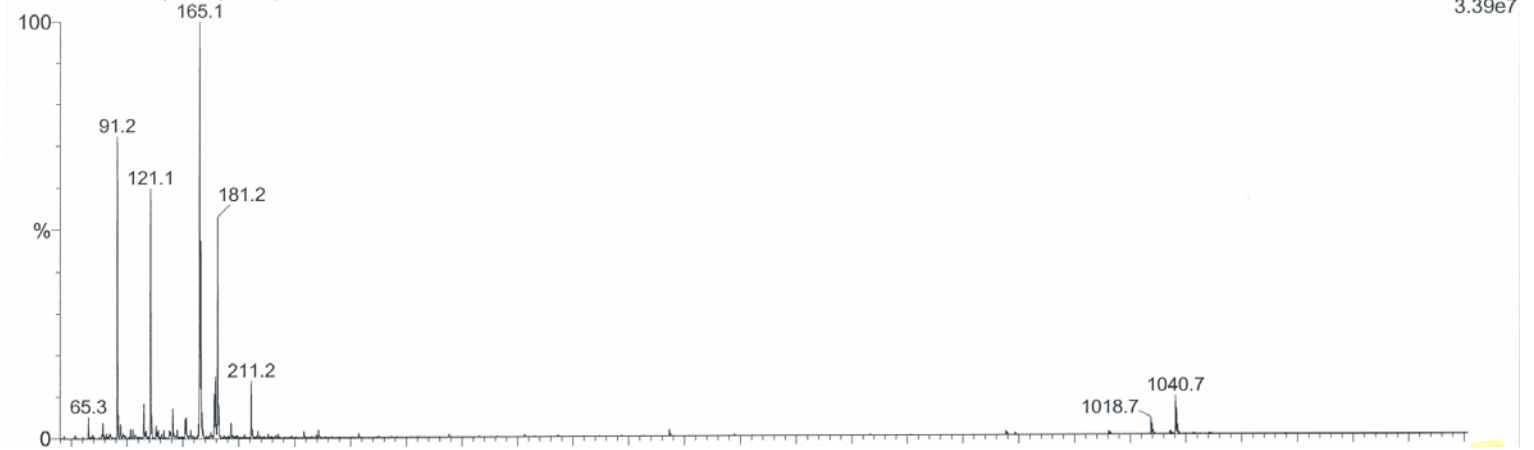






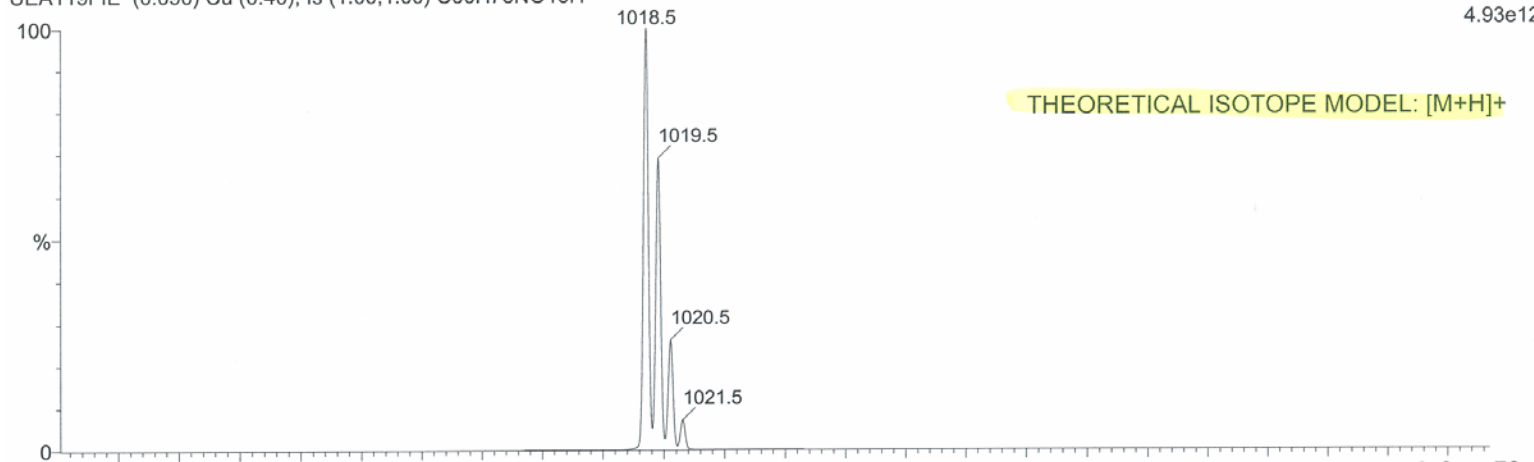
UEA119FIE 18 (3.164) Sm (SG, 2x0.70); Cm (15:19-4:7)

3: Scan ES+
3.39e7



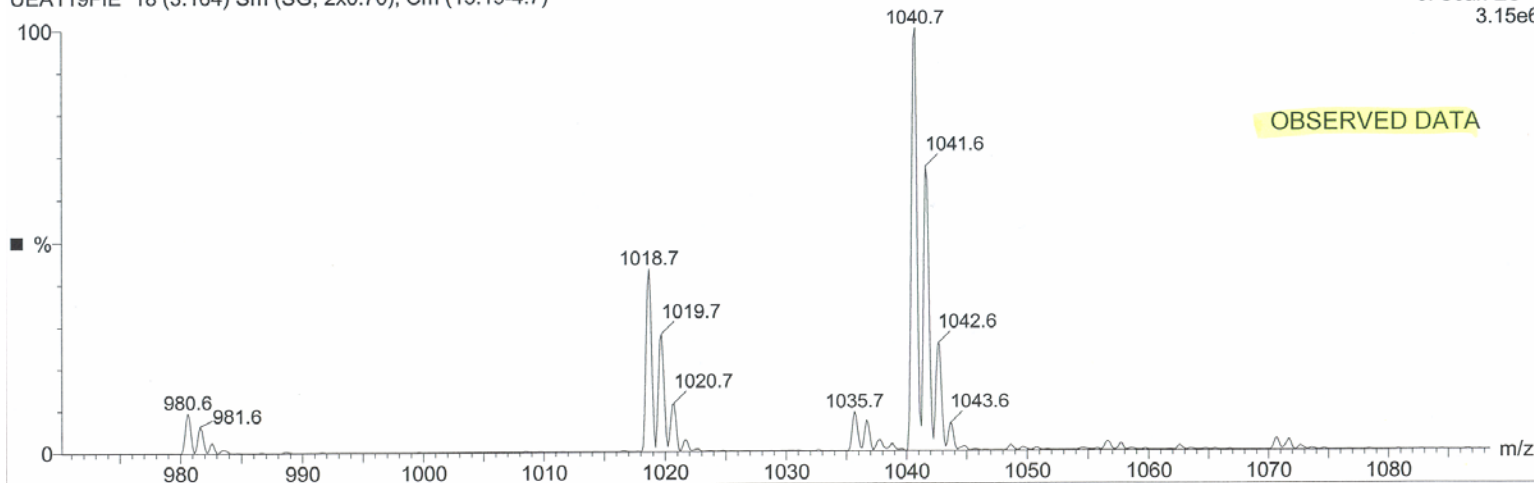
UEA119FIE (0.090) Cu (0.40); Is (1.00,1.00) C60H75NO13H

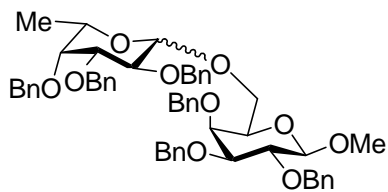
3: Scan ES+
4.93e12



UEA119FIE 18 (3.164) Sm (SG, 2x0.70); Cm (15:19-4:7)

3: Scan ES+
3.15e6

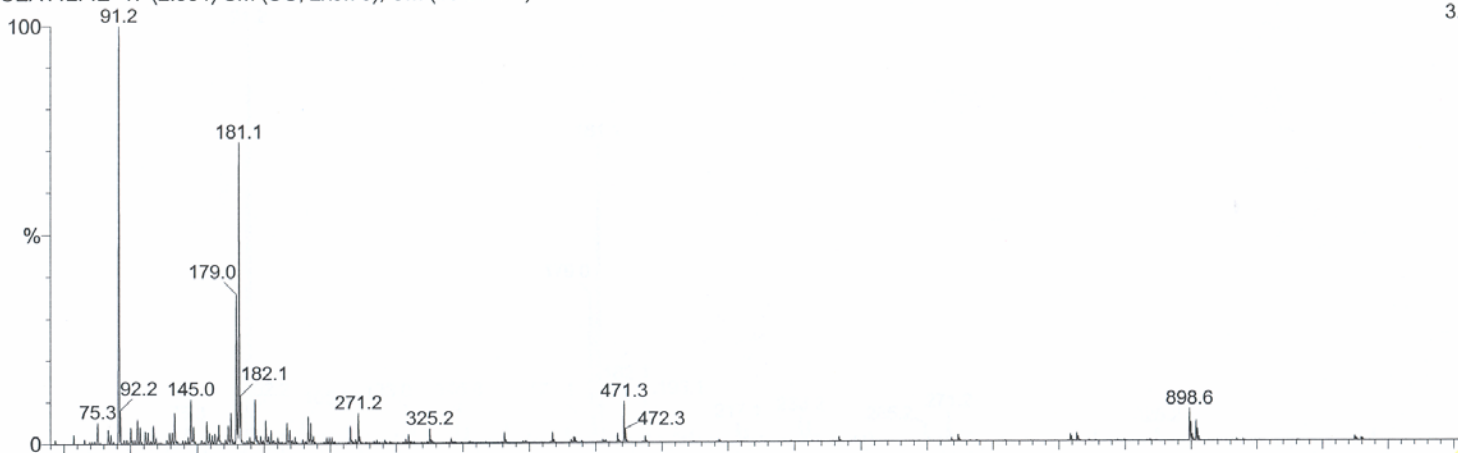




14

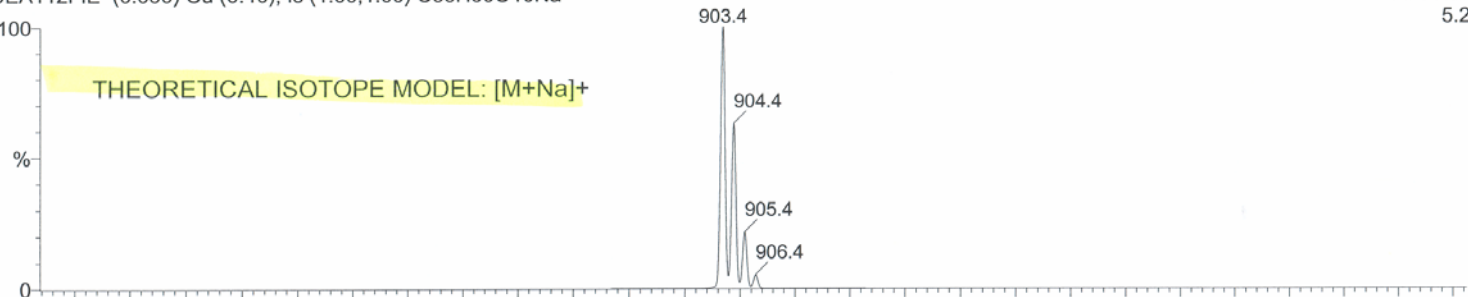
UEA112FIE 17 (2.954) Sm (SG, 2x0.70); Cm (16:20-5:7)

2: Scan ES+
3.87e7



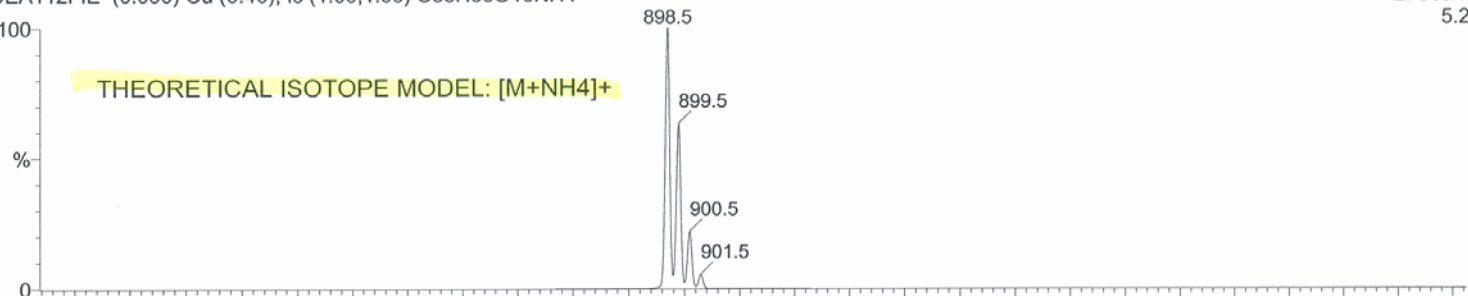
UEA112FIE (0.060) Cu (0.40); Is (1.00,1.00) C55H60O10Na

2: Scan ES+
5.28e12



UEA112FIE (0.060) Cu (0.40); Is (1.00,1.00) C55H60O10NH4

2: Scan ES+
5.25e12



UEA112FIE 17 (2.954) Sm (SG, 2x0.70); Cm (16:20-5:7)

2: Scan ES+
2.96e6

