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Supporting Information

A Hexasaccharide Containing Rare 2-*O*-Sulfate-Glucuronic Acid Residues Selectively Activates Heparin Cofactor II

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Computational Methods

Software. SYBYLX v2.0 (Tripos Associates, St. Louis, MO) was used for molecular visualization, minimization and for preparation of protein structures from the Protein Data Bank (www.rcsb.org/pdb). GOLD, v5.1[S1] (The Cambridge Crystallographic Data Centre, UK) was used for molecular docking experiments. GAG sequences were built combinatorially in an automated manner using in-house SPL (SYBYL Programming Language) scripts.

Protein preparation. The coordinates for the activated form of heparin cofactor II (HCII) were extracted from the crystal structure of the S195A thrombin (TH)–HCII complex (PDB entry 1JMO)[S2]. For comparative purposes, the co-ordinates of heparin pentasaccharide–antithrombin (AT) co-complex were extracted from protein databank file 1TB6[S3]. Protein preparation was performed using the "prepare protein" module in SYBYLX, v2.0 and included removal of water molecules, adjustment of the protonation states of amino acid residues to physiological conditions, addition of hydrogen atoms and the structure was minimized with fixed heavy-atom co-ordinates using the Tripos Force Field for 1,000 iterations subject to a termination gradient of 0.05 kcal/(mol-Å).

Co-ordinates for HS Virtual Library. The co-ordinates for HS hexasaccharide sequences present in the combinatorial virtual library were generated using a series of SPL scripts and HS disaccharide building blocks. Although the total number of possible disaccharides (UA(1→4)GlcN) is 48, only 23 have been experimentally observed (**Fig. S2**). Of these 23, 13 disaccharides contain IdoA, while 10 contain GlcA residue. Because IdoA residue in HS can exist either in the $^{2}S_{O}$ or $^{1}C_{4}$ conformations[S4,S5], each IdoA-containing disaccharide was modeled explicitly in these two different states. Thus, our virtual library consisted of 26 IdoA and 10 GlcA disaccharide building blocks generating a total of 46,656 (36×36×36) hexasaccharide sequences.

Each H/HS sequence within these libraries were denoted using the GLYCAM force field[44] symbols or letters for base monosaccharides (GlcN, IdoA and GlcA) and further modified by the substituents (–H, $–SO_3^-$, or $–COCH_3$). Appropriate side-chain modifications were made to generate the 36 building blocks. Each disaccharide was minimized using glycosidic bond torsion constraints (restraining force constant = 0.01 $kcal \cdot mol^{-1} \cdot deg^{-2}$). Analysis of the available crystal structures showed that the inter-glycosidic torsions ϕ_H (O5-C1-O1-C4') and ψ_H (C1-O1-C4'-C5') fall within a relatively narrow range and are essentially invariant irrespective of the substitution pattern[S6].

Thus, average bond torsions, as described in our earlier work[S6-S8], were used for inter-glycosidic linkages. The 36 disaccharides were then used to build a combinatorial HS hexasaccharide library using an SPL script in an automated manner, following which each sequence was again minimized using glycosidic bond torsion constraints to generate HS sequences with 'average backbone' geometries.

Docking of the Comprehensive HS Virtual Sequence Library. Docking of HS ligand onto the activated form of HCII was performed with GOLD, which is a "soft docking" method that implicitly handles local protein flexibility by allowing a small degree of interpenetration, or van der Waals overlap, of the ligand and protein atoms[S1]. GOLD also optimizes the positions of hydrogen-bond donating atoms on Ser, Thr, Tyr, Lys, and Arg residues as part of the docking process. GOLD starts with a population of 100 arbitrarily docked ligand orientations, evaluates them using a scoring function (the GA "fitness" function) and improves their average "fitness" by an iterative optimization procedure that is biased towards high scores. Docking was driven by $GOLDScore = HB_{EXT} + 1.375 \times VDW_{EXT}$ equation (HB_{EXT} and VDW_{EXT} are the non-bonded intermolecular hydrogen bond and van der Waals terms, respectively) to prioritize different poses, as reported earlier[S6]. As the initial population is selected at random, several such GA runs are required to more reliably predict correct bound conformations. In our study 10 GA runs were used, which are collectively referred to as one docking experiment.

Evaluation of the HS combinatorial library was performed using a two-stage docking protocol (**Fig. 1a**), as utilized in our study of the AT-pentasaccharide system[S6]. The first stage (the 'affinity' test) involved docking of 46,656 HS sequences to HCII to efficiently identify sequences with high affinity for the binding site. To enhance the speed of the search, all sequences were docked using 10,000 iterations (7–8X speed up setting) per GA run. Additionally, the GA was set to terminate early if the during the course of docking, the top two ranked solutions were within 2.5 Å RMSD.

For the overall top-ranked docked solution for each of the HS sequences, a modified GOLD score was calculated. Although the GOLD fitness function generally correlates with the observed free energy of binding, a modified form has been found to be more reliable[S9]. This modified GOLD score utilizes only the "external" hydrogen-bonding and van der Waals terms of the GOLD fitness function (above equation). The GOLD score, as it is reported in this paper, refers to this modified

GOLD scoring function. The top solutions were re-ranked based on the GOLD score, and the top 0.1% were selected for the convergence ('specificity') test.

The 'specificity' test consisted of docking the most promising HS sequences from the 'affinity' test using the standard GOLD parameter settings (no speed-up; 100,000 GA iterations). The top two solutions of each docking experiment were considered for further analysis. Docking was performed in triplicate to yield a minimum of 6 solutions. A RMSD of less than 2.5 Å among the backbone heavy atoms (pyranose ring atoms and interglycodic oxygens) of all 6 solutions suggested a high degree of convergence to a 'unique' binding geometry. These HS sequences were deemed to be specific.

In both the first and second docking stages, the binding site in HCII was comprised of all atoms within 18 Å from the C^{γ} atom of Lys185 in the D helix. This dimension of the binding site covers a number of basic residues including Lys101, Arg103, Lys173, Arg184, Lys185, Arg189, Arg192, Arg193, Lys220, and Arg464, which are present in the putative heparin-binding domain formed by helices A and D, and part of the *N*-terminus.

Biochemical Methods

Proteins and chemicals — Human plasma antithrombin (AT), HCII (HCII), human thrombin (hTH) and human factor Xa (fXa) were purchased from Haematologic Technologies (Essex Junction, VT). AT, HCII, thrombin and fXa were stored in 20 mM sodium phosphate buffer, pH 7.4, containing 25 mM NaCl, 0.1 mM EDTA and 0.1% (w/v) PEG8000 at -20 °C. Spectrozyme FXa (methoxycarbonyl-*D*-cyclohexylglycyl-Gly-Arg-*p*-nitroanilide) and Spectrozyme TH (H-*D*-hexahydrotyrosol-Ala-Arg-*p*-nitroanilide) were obtained from American Diagnostics (Greenwich, CT) and prepared in 20 mM sodium phosphate buffer, pH 7.4, containing 25 mM NaCl, 0.1 mM EDTA and 0.1% (w/v) PEG 8000. Pooled normal human plasma for coagulation assays was purchased from Affinity Biological (Ancaster, Ontario). Activated partial thromboplastin time reagent containing ellagic acid and 25 mM $CaCl_2$ were obtained from Fisher Diagnostics (Middletown, VA).

Equilibrium Binding Studies using Fluorescence Spectroscopy — The equilibrium dissociation constants of hexasaccharide (HX) – protein complexes were measured using change in fluorescence emission as a function of the concentration of the hexasaccharides in 20 mM sodium phosphate buffer, pH 7.4, containing 25 mM NaCl, 0.1 mM EDTA and 0.1% PEG8000 at 25 °C, as described earlier.[S10,S11] The experiments were performed using a QM4 fluorometer (Photon Technology International, Birmingham, NJ) in a quartz microcuvette by titrating a 200 μL solution of the protein (100–200 nM) and monitoring the change in the fluorescence at 340 nm (λ_{EX} = 280 nm). Excitation and emission slit width were set to 1.0 mm for each experiment. The saturable change in fluorescence signal was fitted using the quadratic equilibrium binding equation 1 to obtain the K_D of interaction. In this equation, ΔF represents the change in fluorescence at a fixed concentration of HX from the initial fluorescence F_0 and ΔF_{MAX} represents the maximal change in fluorescence following saturation of the protein. $[P]_0$ represents the total concentration of either AT or HCII.

$$\frac{\Delta F}{F_0} = \frac{\Delta F_{max}}{[P]_0} \times \left\{\frac{([P]_0 + [HX]_0 + K_D) - \sqrt{(([P]_0 + [HX]_0 + K_D)^2 - 4[P]_0[HX]_0)}}{2}\right\} \qquad (1)$$

Kinetics of Protease Inhibition in the Presence of HX — The kinetics of inhibition of coagulation proteases, TH or FXa, by AT or HCII in the presence of HX was measured spectrophotometrically using a microplate reader (FlexStation III, Molecular Devices) under

pseudo-first-order conditions, as described earlier.[S10] Briefly, a fixed concentration of TH or FXa (~5 nM) was incubated with fixed concentrations of plasma AT or HCII (100 nM) and hexasaccharides (0 – 3 μM) for **HX1**, (0 – 22 μM) for **HX2**, (0 – 10 μM) for **HX3**, (0 – 80 μM) for **HX4** and (0 – 6 μM) for **HX5** in 20 mM sodium phosphate buffer, pH 7.4, containing 25 mM NaCl, 0.1 mM EDTA and 0.1% (w/v) PEG 8000 at 25 °C. At regular time intervals, an aliquot of the inhibition reaction was quenched with 100 μL of 125–200 μM chromogenic substrate (Spectrozyme TH or Spectrozyme FXa) in 20 mM sodium phosphate buffer, pH 7.4, containing 25 mM NaCl at 25 °C. To determine the residual protease activity, the initial rate of substrate hydrolysis was measured from the increase in absorbance at 405 nm. The exponential decrease in the initial rate of substrate hydrolysis as a function of time was used to determine the observed pseudo-first-order rate constant of protease inhibition (k_{OBS}). A plot of k_{OBS} at different concentrations of HX–serpin complex could be described by equation 2, in which k_{UNCAT} is the second-order rate constant of protease inhibition by serpin alone and k_{HS} is the second-order rate constant of protein inhibition by serpin-HX complex (HX:P).

$$k_{OBS} = k_{UNCAT}[P]_0 + k_{HX}[HX:P] \quad (2)$$

Direct Protease Inhibition in the Presence of HX — Direct inhibition of TH or FXa by hexasaccharides was assessed through a chromogenic substrate hydrolysis assay using a microplate reader (FlexStation III, Molecular Devices), as described earlier.[S12] Briefly, each well of the 96-well microplate contained (190–X) μL of the pH 7.4 buffer to which X μL of HX (to give a 500 μM final concentration), or an appropriate reference, was added followed by 5 μL of protease (to give 5 nM final concentration). After 10 min incubation at 25 °C, 5 μL of appropriate chromogenic substrate (to give 125 μM (Spectrozyme FXa) or 100 μM Spectrozyme TH) was rapidly added and the residual protease activity was measured from the initial rate of increase in A_{405}. Relative residual protease activity at each concentration of HX was calculated from the ratio of the activity in the presence and absence of the inhibitor.

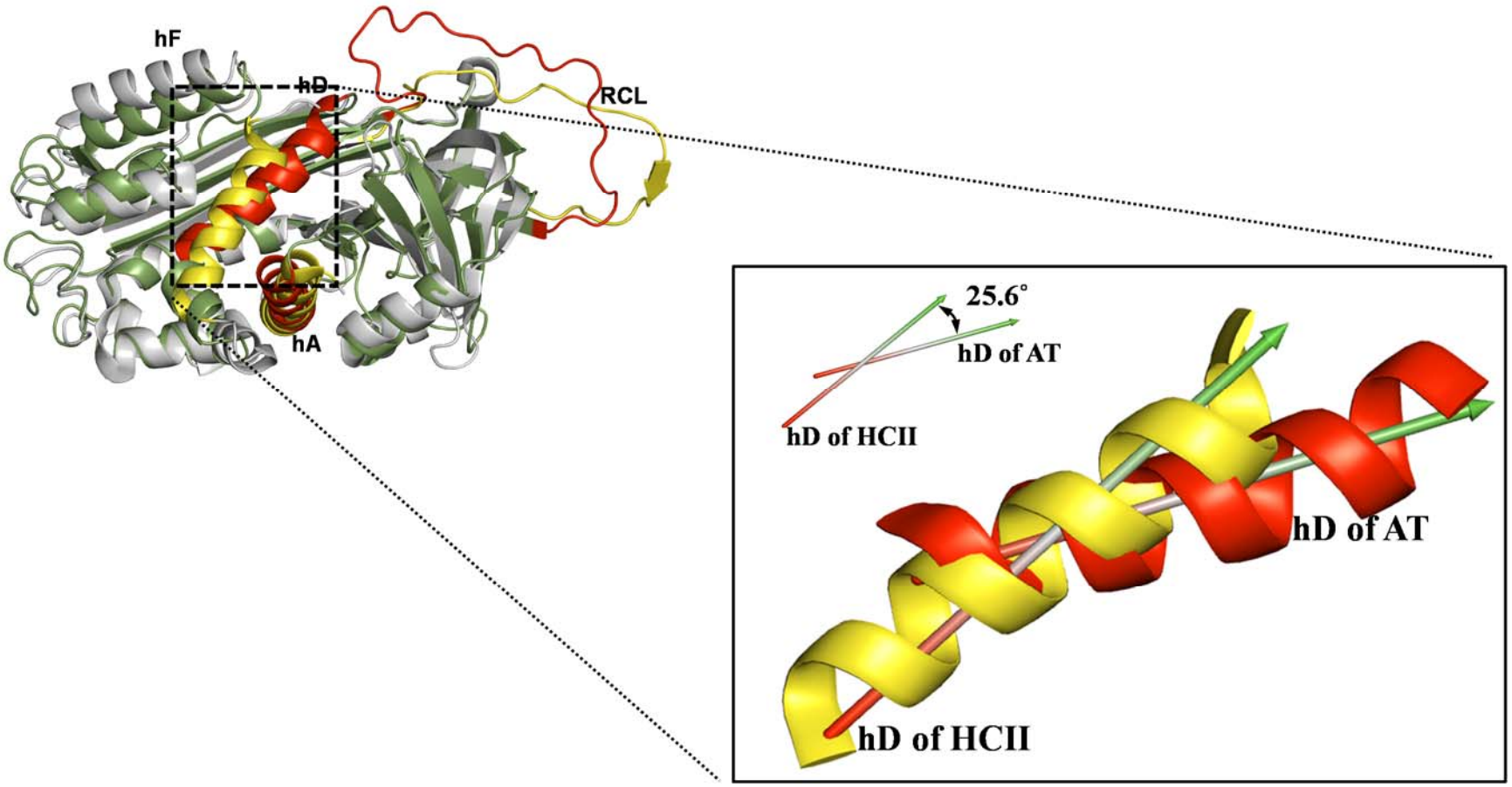
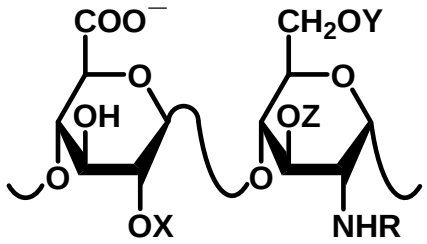
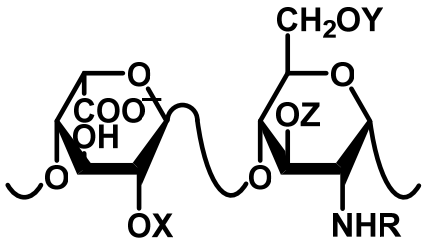


Figure S1. Interhelical angle difference of helix D (hD) between HCII and AT: Overlay of structures of AT (PDB ID: 2ANT) and HCII (PDB ID: 1JMJ) had an overall RMSD =2.4Å. The two related serpins had small angle difference in helix D (hD) orientation which measured to 25.6˚. This region forms the GAG-binding site. AT hD is shown in red; HCII hD in yellow.



	R	X	Y	Z
GlcA-GlcNAc	Ac	H	H	H
GlcA-GlcNAc6S	Ac	H	SO_3^-	H
GlcA-GlcNS	SO_3^-	H	H	H
GlcA2S-GlcNS	SO_3^-	H	H	H
GlcA-GlcNS6S	SO_3^-	H	SO_3^-	H
GlcA2S-GlcNS6S	SO_3^-	SO_3^-	SO_3^-	H
GlcA-GlcNS3S	SO_3^-	H	H	SO_3^-
GlcA2S-GlcNS3S	SO_3^-	SO_3^-	H	SO_3^-
GlcA-GlcNS36S	SO_3^-	H	SO_3^-	SO_3^-
GlcA-GlcN	H	H	H	H



	R	X	Y	Z
IdoA-GlcNAc	Ac	H	H	H
IdoA2S-GlcNAc	Ac	SO_3^-	H	H
IdoA-GlcNAc6S	Ac	H	SO_3^-	H
IdoA2S-GlcNAc6S	Ac	SO_3^-	SO_3^-	H
IdoA-GlcNS	SO_3^-	H	H	H
IdoA2S-GlcNS	SO_3^-	SO_3^-	H	H
IdoA-GlcNS6S	SO_3^-	H	SO_3^-	H
IdoA2S-GlcNS6S	SO_3^-	SO_3^-	SO_3^-	H
IdoA-GlcNS3S	SO_3^-	H	SO_3^-	SO_3^-
IdoA2S-GlcNS3S	SO_3^-	SO_3^-	H	SO_3^-
IdoA-GlcNS36S	SO_3^-	H	H	SO_3^-
IdoA2S-GlcN3S	H	SO_3^-	H	SO_3^-
IdoA2S-GlcN36S	H	SO_3^-	SO_3^-	SO_3^-

Figure S2. Structures of disaccharide building blocks →4)GlcA2X(1→4)GlcN2R3Z6Y and **c)** →4)IdoA2X(1→4)GlcN2R3Z6Y, where R, X, Y, and Z represents possible substituents listed underneath. Ten GlcA- and 13 IdoA-containing disaccharides (IdoA in either $^1C_4$ or ^2S_O form), resulting in a total of 36 disaccharide building blocks, were employed. All possible combinations of these 36 building blocks led to a library of 46,656 HS hexasaccharide sequences.

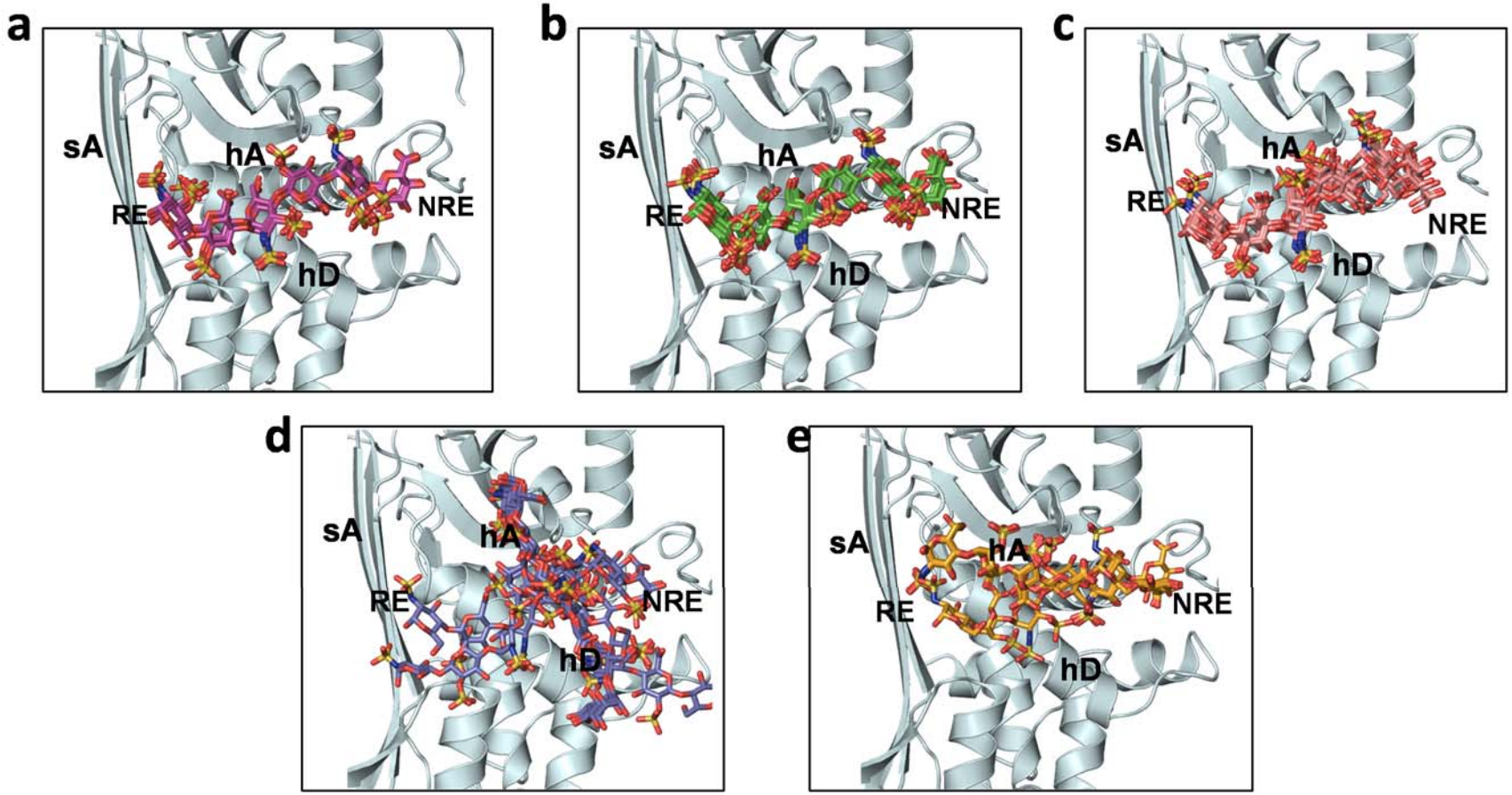


Figure S3. Identification of HS hexasaccharide sequences that differentially target HCII. Overlay of best docked solutions of hexasaccharide sequences HX1-HX5 bound to HCII. The sequences HX1 (a), HX2 (b) and HX3 (c) bind with >80% consistency and sequences HX4 (d) and HX5 (e) bind non-specifically (with ~100% consistency). The hexasaccharide sequences are shown in sticks with marked reducing end (RE) and non-reducing ends (NRE). Helices A (hA) and D (hD) are marked for orientation.

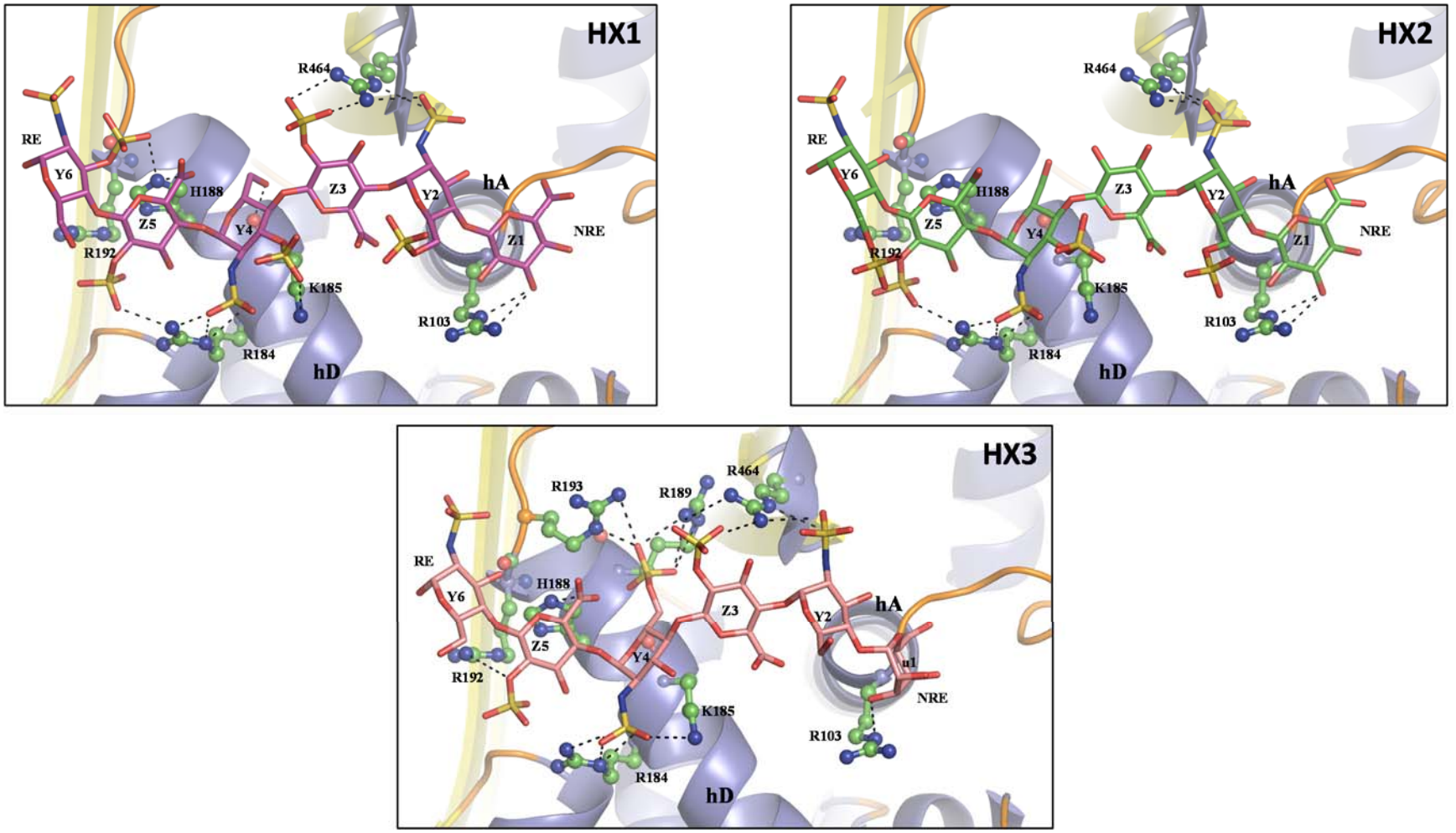


Figure S4. Interaction of H/HS hexasaccharides, which are predicted to recognize HCII with "high affinity and high specificity". The hydrogen bond interaction of the hexasaccharide sequences HX1, HX2 and HX3 with the key residues of HCII (are shown in the black dotted lines). The hexasaccharide sequences are shown in sticks and the reducing end (RE) and non-reducing end (NRE) are marked. Helices A (hA) and D (hD) in ribbon form. The interacting residues are shown in ball and stick representation. The saccharide units of the HX sequences are labeled as **u** (IdoA), **Y** (GlcN) and **Z** (GlcA) along with the residue numbers.

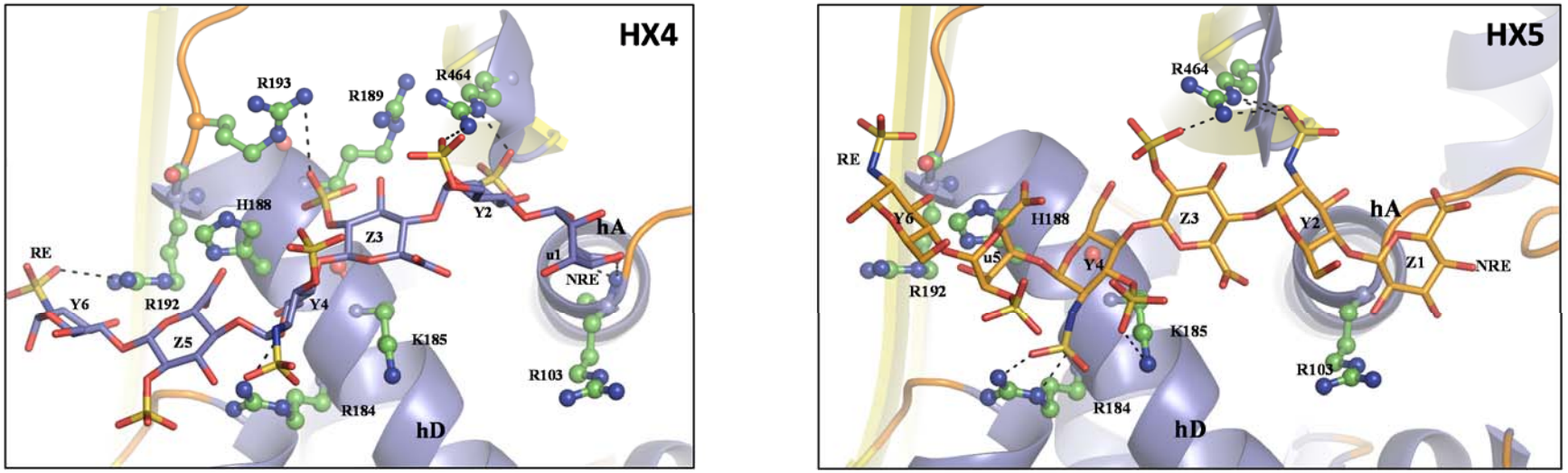


Figure S5. Interaction of two H/HS hexasaccharide (HX4 and HX5), which is predicted to recognize HCII, non-specifically. The hydrogen bond interaction of the hexasaccharide sequences HX4 and HX5 with the key residues of HCII (are shown in the black dotted lines). The hexasaccharide sequences are shown in sticks and the reducing end (RE) and non-reducing end (NRE) are marked. Helices A (hA) and D (hD) in ribbon form. The interacting residues are shown in ball and stick representation. The saccharide units of the HX sequences are labeled as **u** (IdoA), **Y** (GlcN) and **Z** (GlcA) along with the residue numbers.

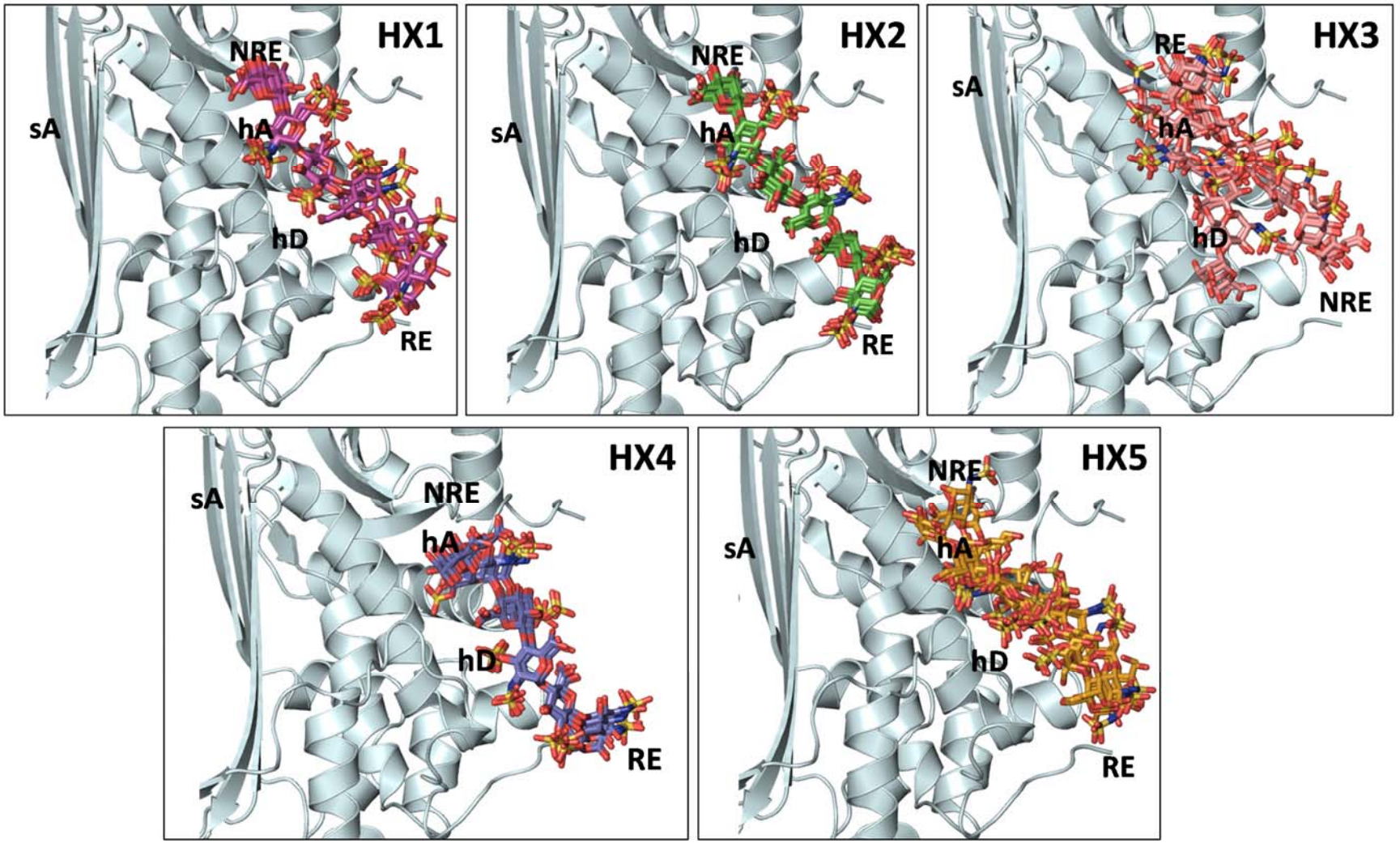


Figure S6. Identification of HS hexasaccharide sequences that differentially target AT. Overlay of best docked solutions of hexasaccharide sequences HX1-HX5 bound to AT. The sequences HX1, HX2 and HX4 bind with ~60-80% consistency and sequences HX3 and HX5 bind non-specifically(with -100% consistency). The hexasaccharide sequences are shown in sticks with marked reducing end (RE) and non-reducing ends (NRE). Helices A (hA) and D (hD) are marked for orientation.

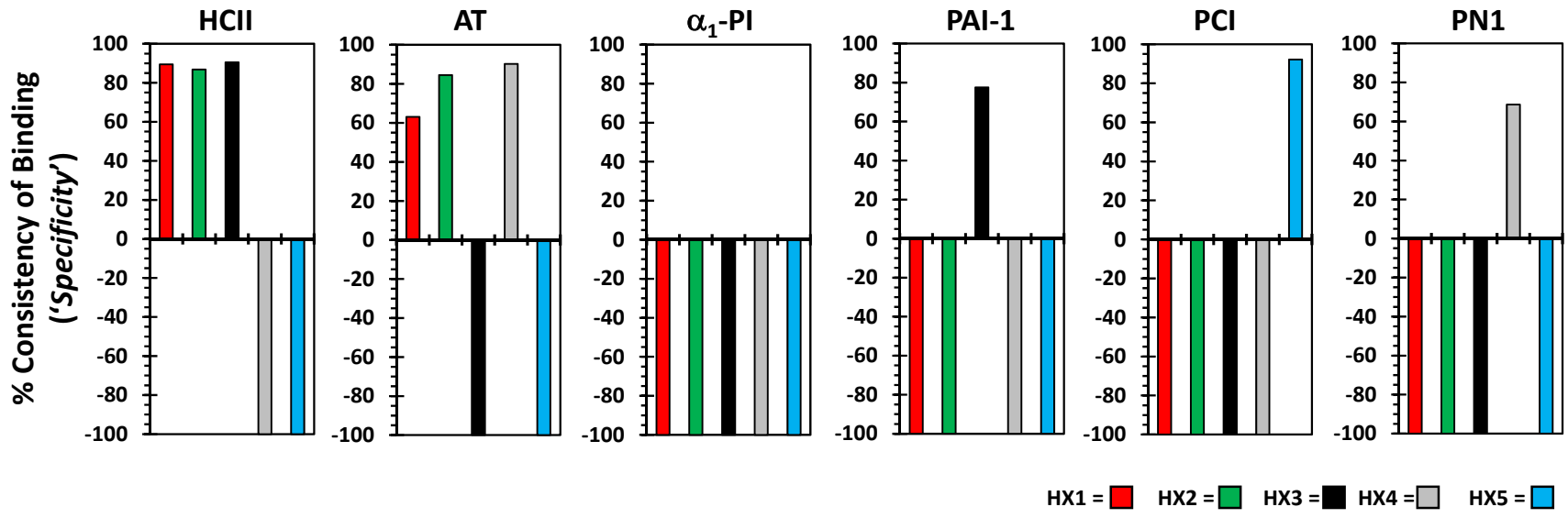


Figure S7. Selectivity of five designed hexasaccharides to various serine proteases. In silico selectivity of the five designed hexasaccharide sequences against various alike serpins: alpha-1-antitrypsin, plasminogen activator inhibitor-1, protein C inhibitor and protease nexin-1 as judged by consistency of binding (low RMSD variation) between docked solutions. The consistency of binding was calculated using the formula, Consistency = 100-2.5*exp (RMSD); Consistency <-100 = -100%.

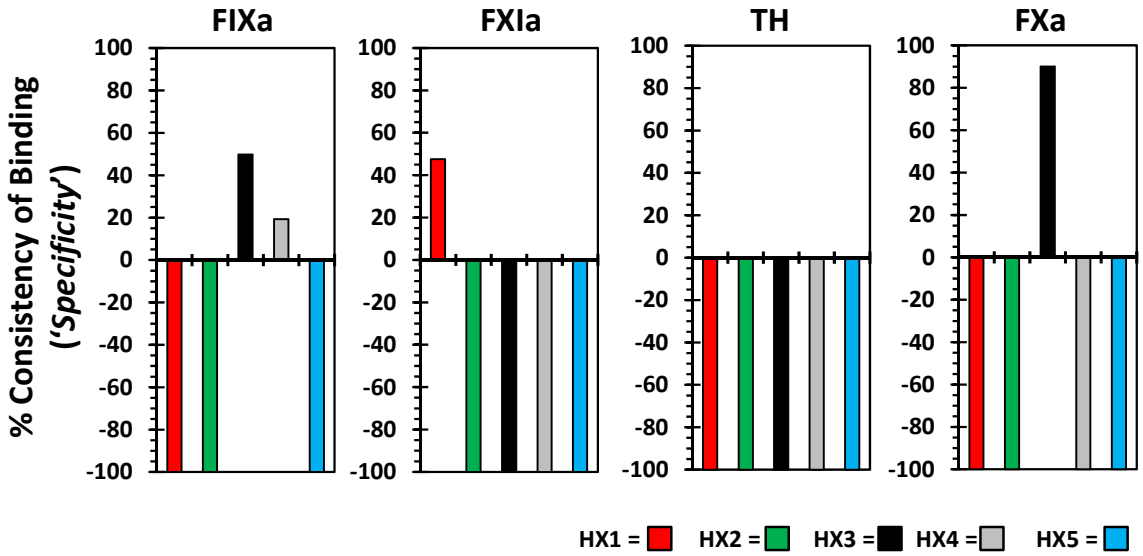


Figure S8. Selectivity of five designed hexasaccharides to various coagulation factors. In silico selectivity of the five designed hexasaccharide sequences against various coagulation factors like factor IXa, factor XIa, thrombin and FXa as judged by consistency of binding (low RMSD variation) between docked solutions. The consistency of binding was calculated using the formula, Consistency = 100-2.5*exp (RMSD); Consistency <-100 = -100%.

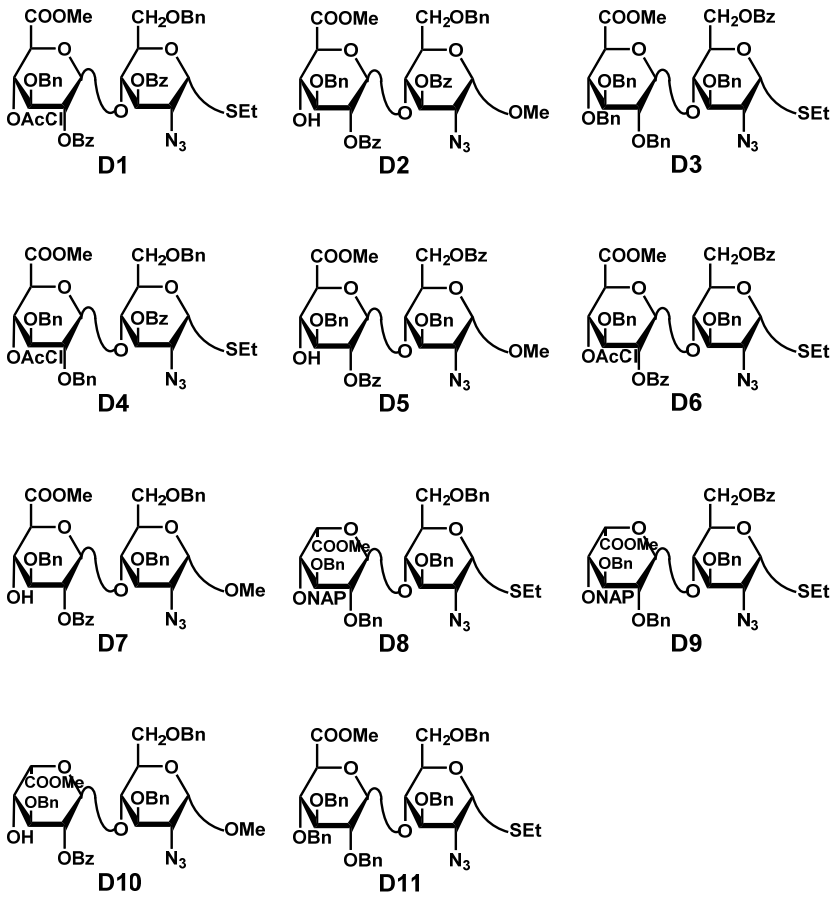


Figure S9. Structures of disaccharide building blocks D1 – D11.

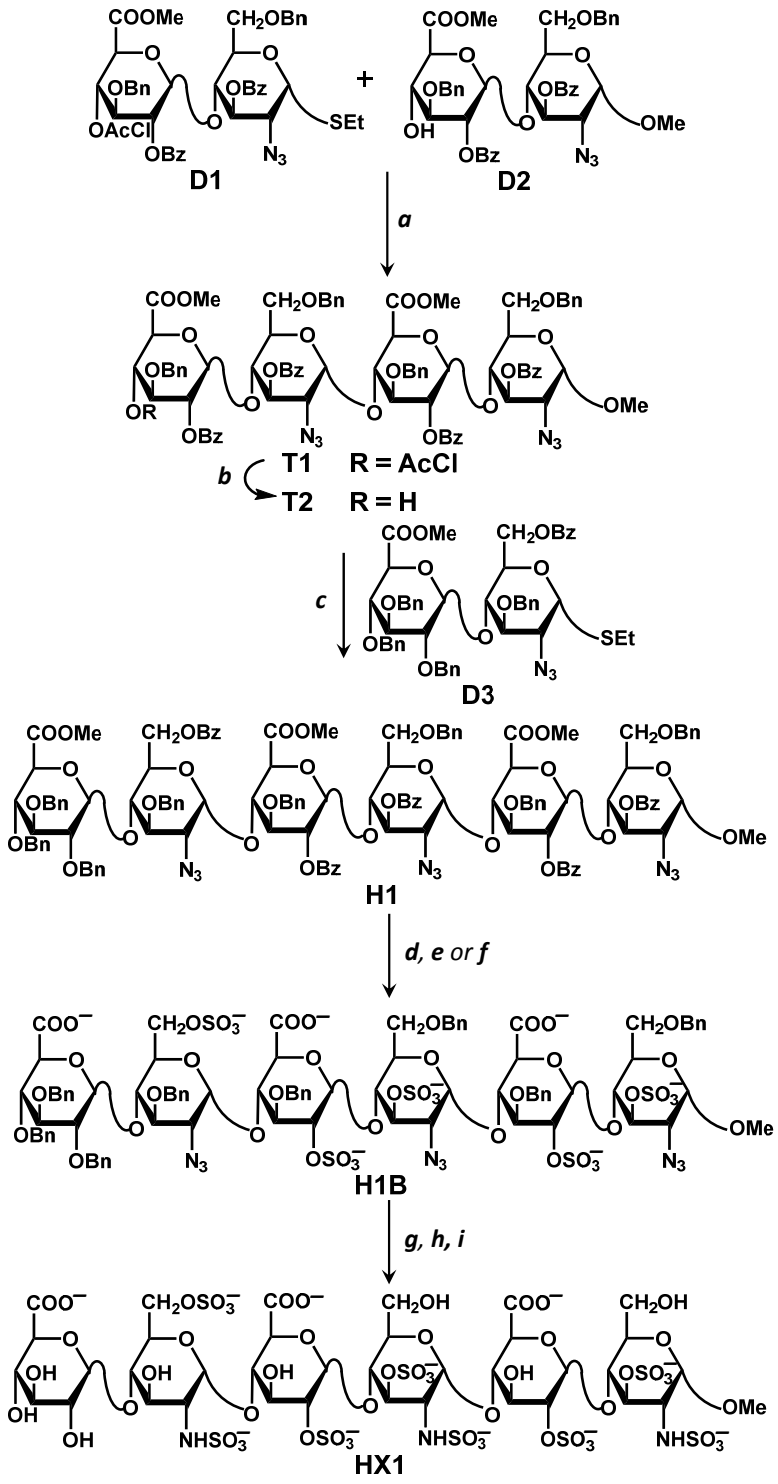


Figure S10. Synthesis of HX1. Reagents and conditions. *a)* Me_2S_2/Tf_2O, Et_2O/CH_2Cl_2/-10°C; *b)* DABCO, EtOH, 45 °C; *c)* Me_2S_2/Tf_2O, Et_2O/CH_2Cl_2/-10°C; *d)* H_2O_2, 1M LiOH, THF, 3M KOH, MeOH, *e)* py:SO_3, py; *f)* NMe_3:SO_3, DMF, 100 °C, MW; *g)* PMe_3, 0.1M NaOH, THF; *h)* py:SO_3, py; *i)* H_2, Pd/C, $Pd(OH)_2$, $MeOH/H_2O$

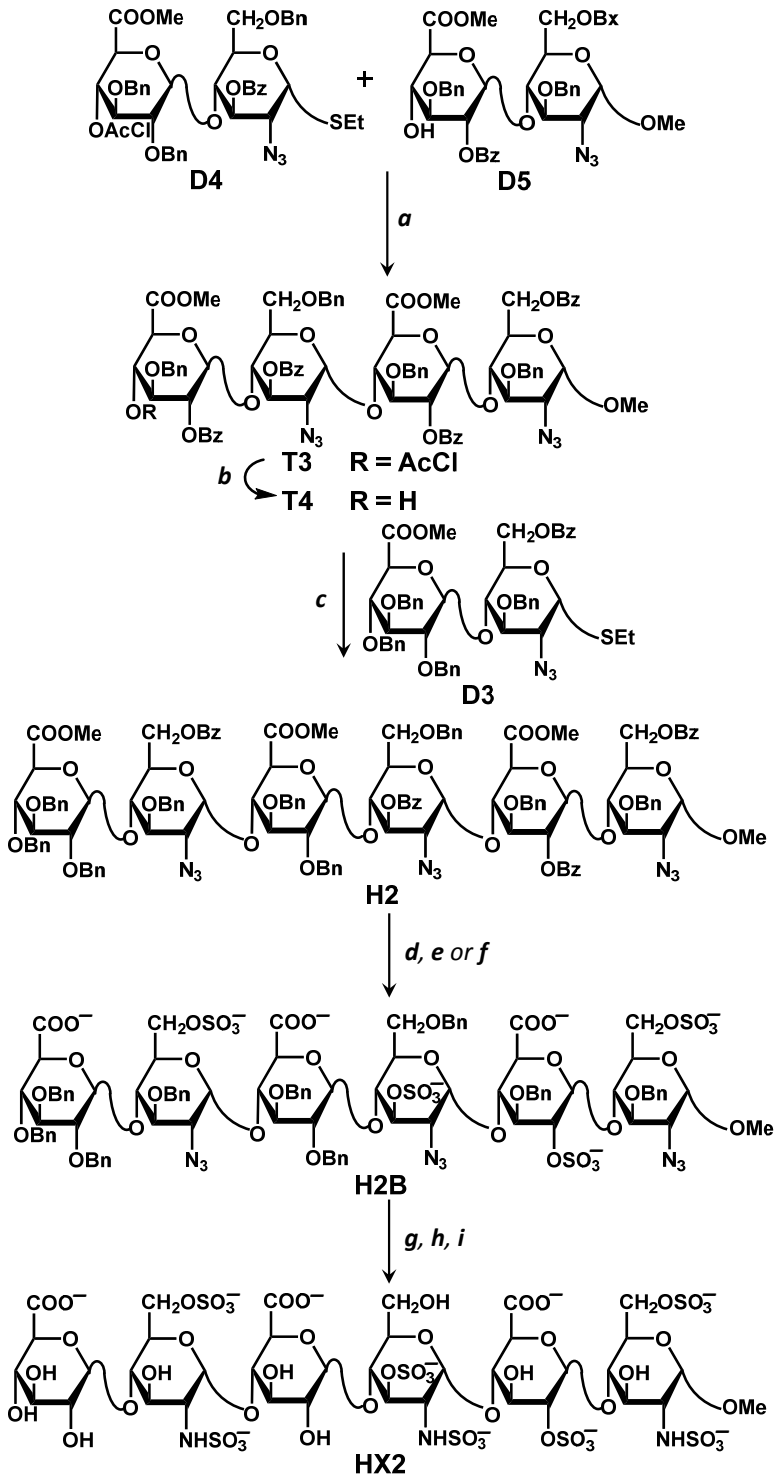


Figure S11. Synthesis of HX2. Reagents and conditions. *a)* Me_2S_2/Tf_2O, Et_2O/CH_2Cl_2/-10°C; *b)* DABCO, EtOH, 45 °C; *c)* D3, Me_2S_2/Tf_2O, Et_2O/CH_2Cl_2/-10°C; *d)* H_2O_2, 1M LiOH, THF, 3M KOH, MeOH, *e)* py:SO_3, py; *f)* NMe_3:SO_3, DMF, 100 °C, MW; *g)* PMe_3, 0.1M NaOH, THF; *h)* py:SO_3, py; *i)* H_2, Pd/C, $Pd(OH)_2$, MeOH/H_2O

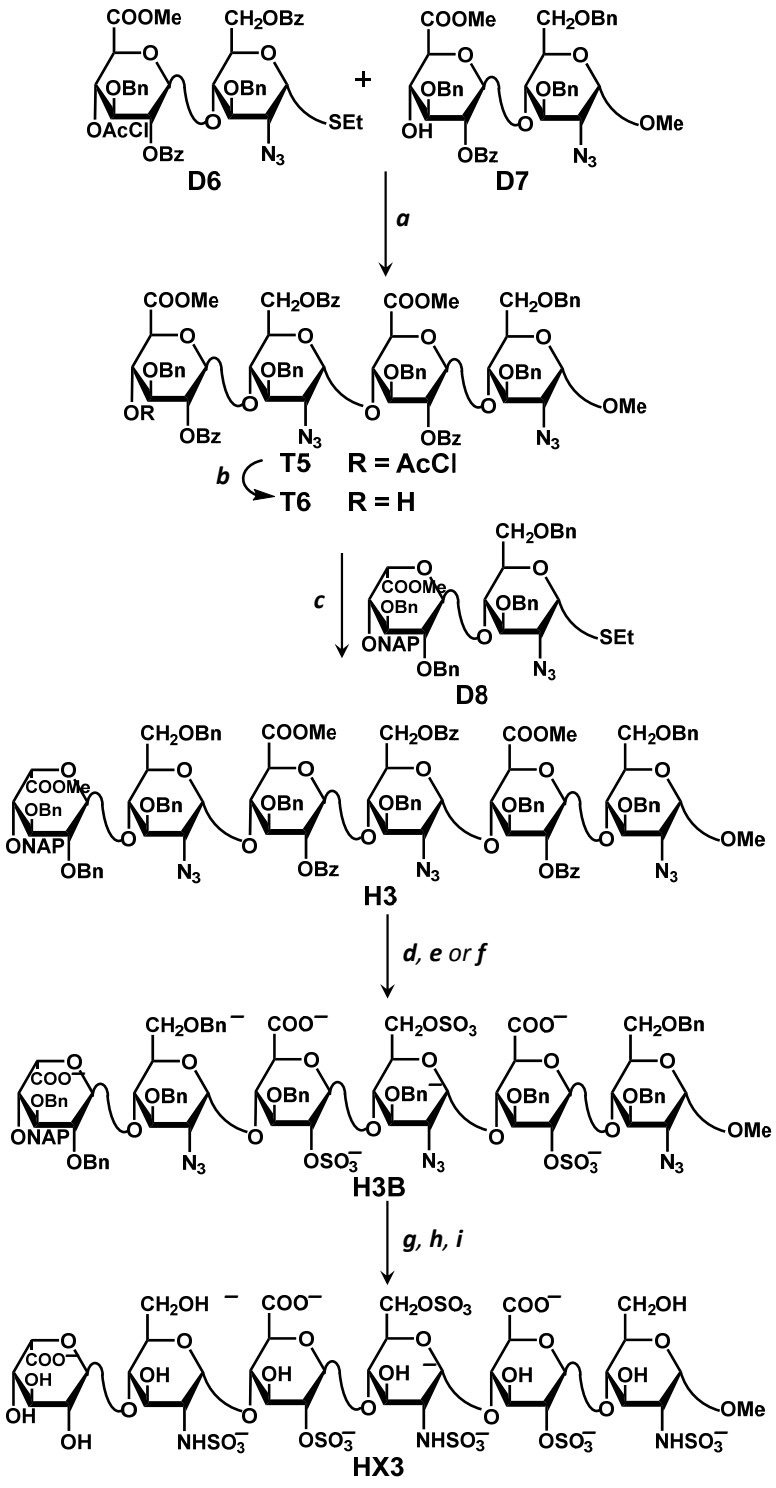


Figure S12. Synthesis of HX3. Reagents and conditions. *a)* Me_2S_2/Tf_2O, Et_2O/CH_2Cl_2/-10°C; *b)* DABCO, EtOH, 45 °C; *c)* D3, Me_2S_2/Tf_2O, Et_2O/CH_2Cl_2/-10°C; *d)* H_2O_2, 1M LiOH, THF, 3M KOH, MeOH, *e)* py:SO_3, py; *f)* NMe_3:SO_3, DMF, 100 °C, MW; *g)* PMe_3, 0.1M NaOH, THF; *h)* py:SO_3, py; *i)* H_2, Pd/C, $Pd(OH)_2$, $MeOH/H_2O$

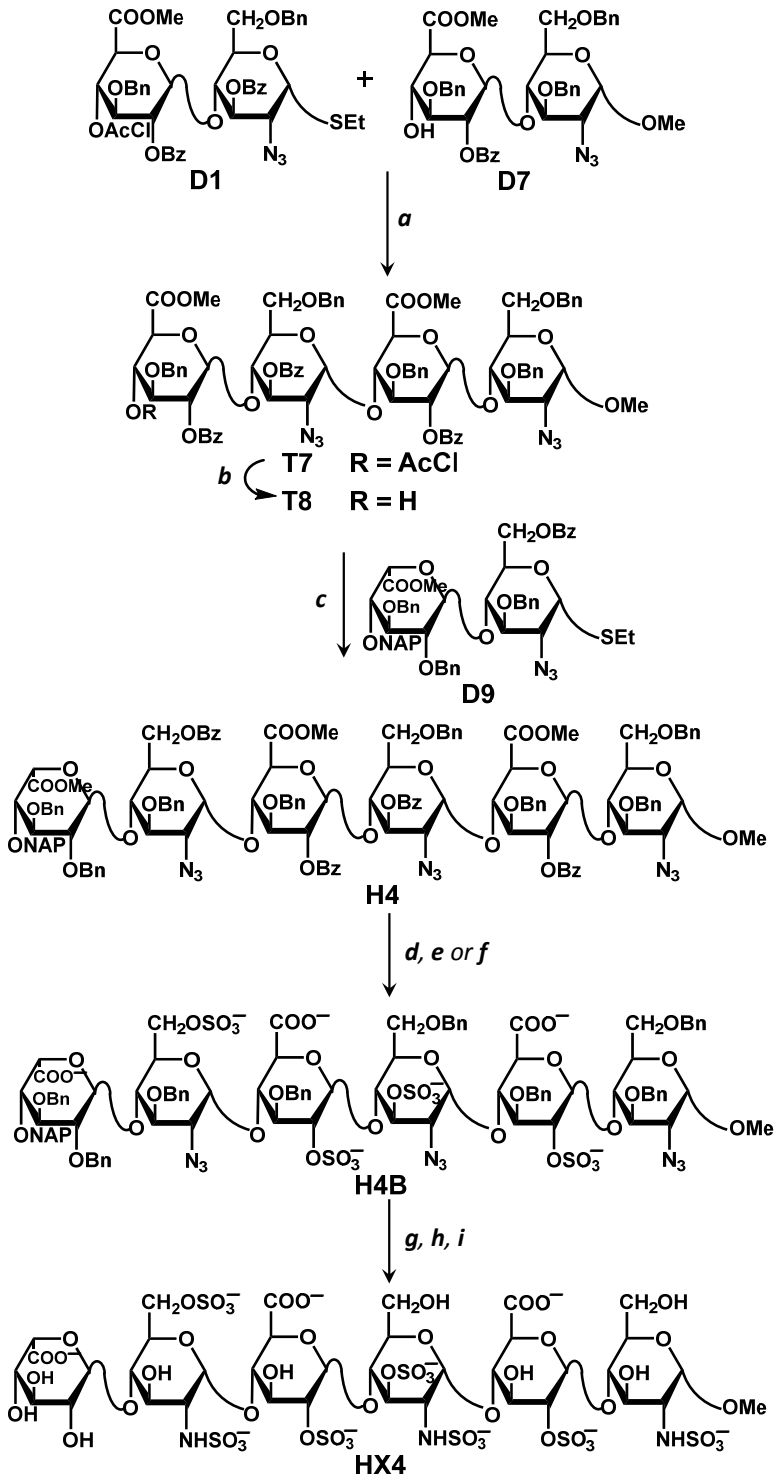


Figure S13. Synthesis of HX4. Reagents and conditions. *a)* Me_2S_2/Tf_2O, Et_2O/CH_2Cl_2/-10°C; *b)* DABCO, EtOH, 45 °C; *c)* D3, Me_2S_2/Tf_2O, Et_2O/CH_2Cl_2/-10°C; *d)* H_2O_2, 1M LiOH, THF, 3M KOH, MeOH, *e)* py:SO_3, py; *f)* NMe_3:SO_3, DMF, 100 °C, MW; *g)* PMe_3, 0.1M NaOH, THF; *h)* py:SO_3, py; *i)* H_2, Pd/C, $Pd(OH)_2$, MeOH/H_2O

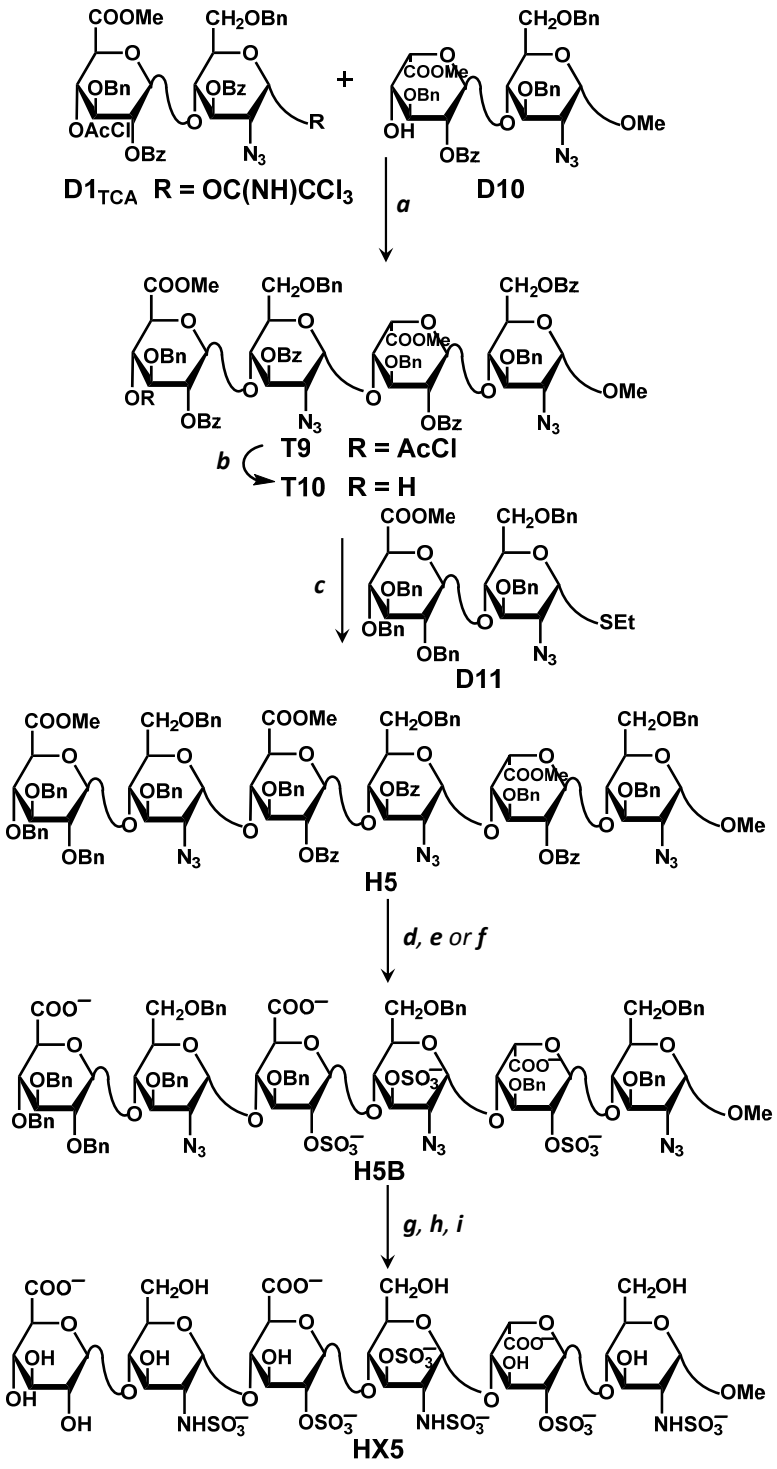


Figure S14. Synthesis of HX5. Reagents and conditions. *a)* TBDMSOTf, toluene/-60°C; *b)* DABCO, EtOH, 45 °C; *c)* Me_2S_2/Tf_2O, Et_2O/CH_2Cl_2/-10°C; *d)* H_2O_2, 1M LiOH, THF, 3M KOH, MeOH, *e)* py:SO_3, py; *f)* NMe_3:SO_3, DMF, 100 °C, MW; *g)* PMe_3, 0.1M NaOH, THF; *h)* py:SO_3, py; *i)* H_2, Pd/C, $Pd(OH)_2$, MeOH/H_2O

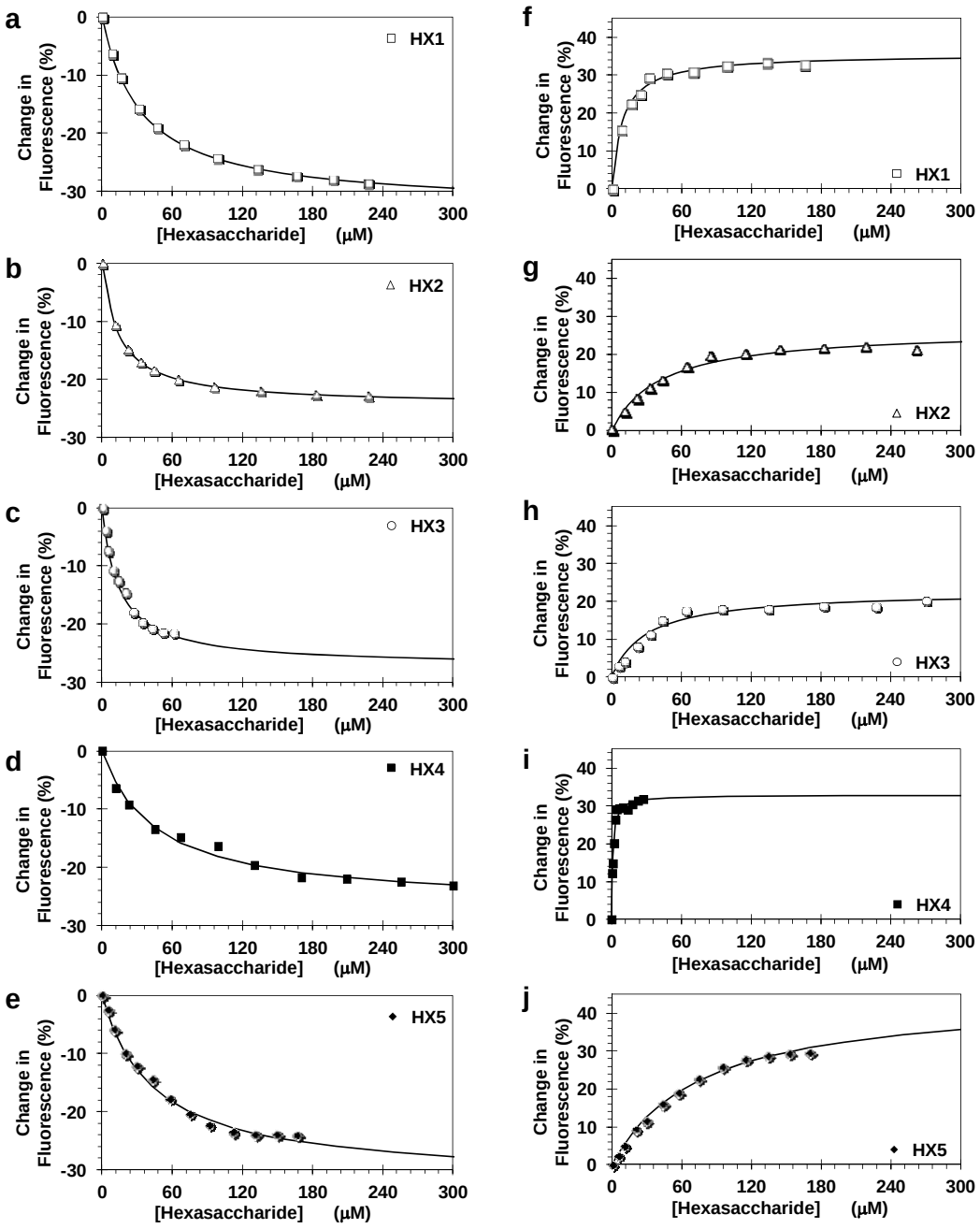


Figure S15. Binding affinity of hexasaccharides HX1–HX5 for HCII (a - e) and AT (f - j). The affinities were measured in 20 mM sodium phosphate buffer, pH 7.4, containing 25 mM NaCl at 25 °C using the proportional change in fluorescence emission ($\Delta F/F_0$) at 340 nm (λ_{EX} = 280 nm) as a function of the concentration of the hexasaccharide. The profiles were fitted using the standard protein–ligand quadratic equation (see **Methods** in **Supplementary Materials**, solid line) to derive the maximal fluorescence change (ΔF_{MAX}) and equilibrium dissociation constant (K_D).

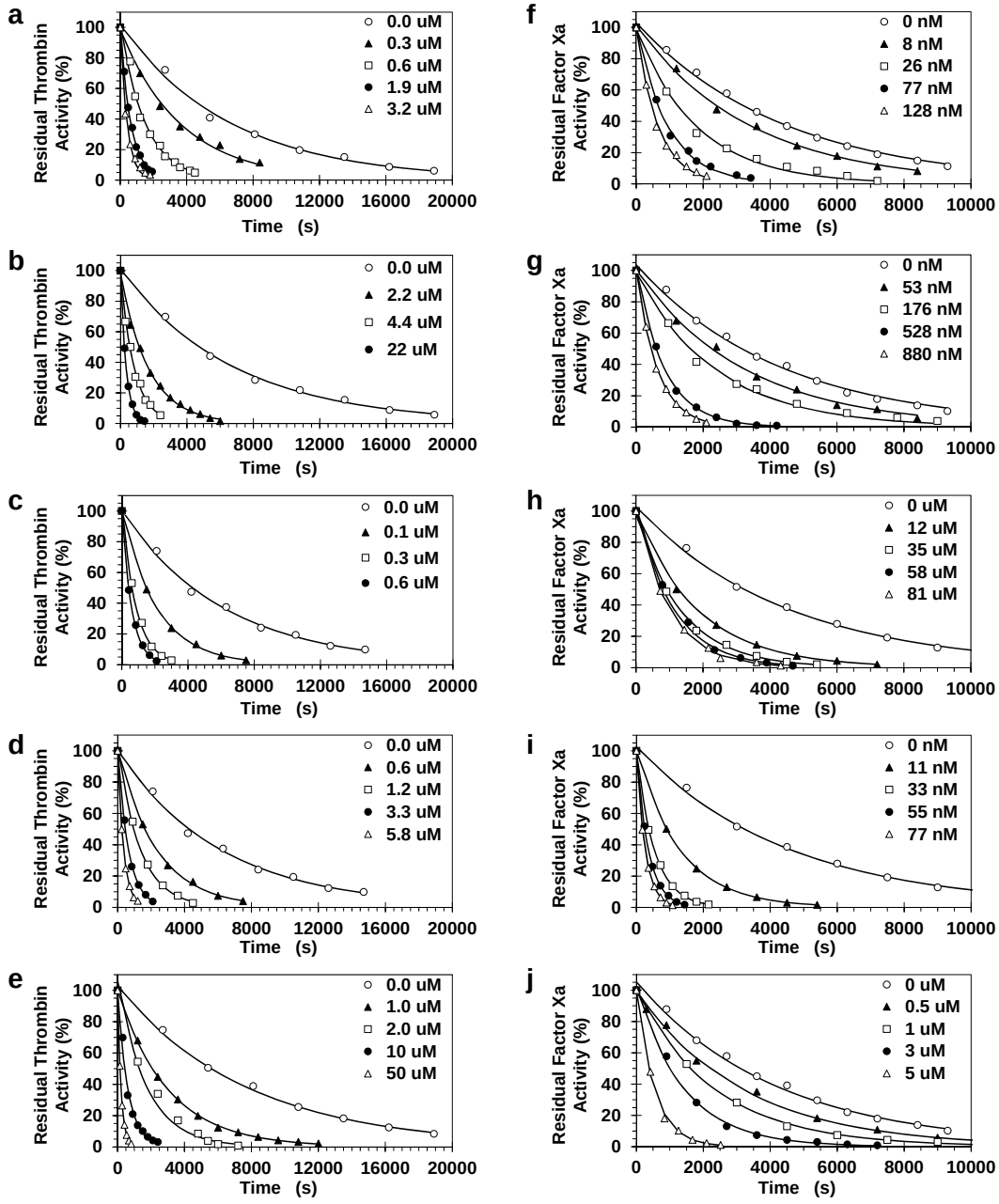


Figure S16. Kinetics of serpin inhibition of the target protease in the presence of hexasaccharides HX1–HX5. The kinetics of inhibition was performed in 20 mM sodium phosphate buffer, pH 7.4, containing 25 mM NaCl at 25 °C by measuring residual TH activity (**a** – **e**) or fXa activity (**f - j**) from the initial rate of substrate hydrolysis under pseudo-first-order conditions as a function of time in the presence of the hexasaccharides. The profiles were fitted using an exponential expression to derive the observed pseudo-first order rate constant of HCII or AT inhibition (k_{OBS}) at different hexasaccharide concentrations. Solid line in these panels represent the analysis using exponential equation. Panels **a)** and **f)** refer to HX1; **b)** and **g)** = HX2; **c)** and **h)** = HX3; **d)** and **i)** = HX4; and **e)** and **j)** = HX5.

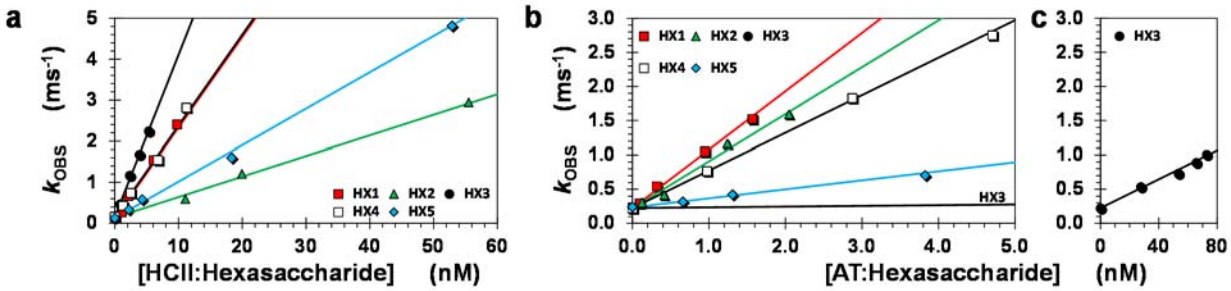


Figure S17. Serpin activation induced by hexasaccharides HX1–HX5. The profile of the observed pseudo-first order rate constant of HCII or AT inhibition (k_{OBS}) at different hexasaccharide concentrations is shown in panels **(a)** and **(b)**, respectively. Solid line in these panels represent analysis of the observed rate constants using linear equation 2 (see **Biochemical Methods**) to calculate the uncatalyzed (k_{UNCAT}) and catalyzed (k_{HX}) rate constants. Panel **c)** shows the full profile for AT inhibition of fXa in the presence of HX3.

Table S1. Summary of yields in the syntheses of **HX1-HX5.**

Target Reaction	HX1	HX2	HX3	HX4	HX5
Glycosylation to tetrasaccharide α yield	88 (9:1) 79	66 (α) 66	79 (α) 79	55 (13:1) 51	85 (7.3:1) 75
Dechloroacylation	87	83	86	56	94
Glycosylation to hexasaccharide α yield	94 (>24:1) 90	73 (α) 73	74 (α) 74	81 (4:1) 65	98 (3:1) 74
Saponification	75	93	85	77	99
O-sulfation	85	72	82	88	92
N_3-reduction	82	92	98	98	84
N-sulfation	72	q	q	q	q
Debenzylation	88	84	89	81	84
Overall yield	*20*	*25*	*29*	10	*33*

Table S2: Thermodynamics and kinetics of hexasaccharide–serpin complexes.

	Affinity for Serpins[a]				Activation of Serpins[b]					
	HCII		AT		HCII–TH Reaction			AT–fXa Reaction		
	K_D (μM)	ΔF_{MAX} (%)	K_D (μM)	ΔF_{MAX} (%)	k_{UNCAT} ($mM^{-1}s^{-1}$)	k_{HX} ($mM^{-1}s^{-1}$)	Activation[c]	k_{UNCAT} ($mM^{-1}s^{-1}$)	k_{HX} ($mM^{-1}s^{-1}$)	Activation[c]
HX1	29.4±6.9[d]	-31±3[d]	7.9±0.5[d]	32±4[d]	1.2±0.0[d]	221±23[d]	180±70[d]	2.2±0.1[d]	854±35[d]	380±30[d]
HX2	17.6±4.8	-24±2	42.1±5.1	27±2	1.4±0.2	49±2	35±6	2.2±0.3	684±45	310±50
HX3	14.3±1.4	-27±1	30.1±5.3	23±1	1.6±0.1	395±9	246±16	2.3±0.1	10.5±0.5	4.7±0.4
HX4	45.5±5.1	-27±1	1.1±0.1	33±1	1.6±0.1	222±9	138±16	2.2±0.1	550±6	245±10
HX5	44.5±3.8	-32±2	75.3±5.9	45±4	1.3±0.0	88±1	68±3	2.4±0.1	132±6	56±4
FPX[e]	9.2±1.2	-24±1	0.050±0.006[f]	32±3[f]	1.3±0.0	74±2	57±3	2.3±0.1	615±30	275±25

[a]Measured using spectrofluorometry in 20 mM sodium phosphate buffer, pH 7.4, containing 25 mM NaCl, at 25 °C. See Methods in Supplementary Materials for details. [b]Measured using discontinuous enzyme inhibition assay in 20 mM sodium phosphate buffer, pH 7.4, containing 25 mM NaCl, at 25 °C. See Methods in Supplementary Material for details. [c]Refers to the ratio of catalyzed and uncatalyzed rate constants. [d]Error represents ±1 S.E. [e]FPX stands for fondaparinux. [f]Taken from Desai *et al.*[S10]

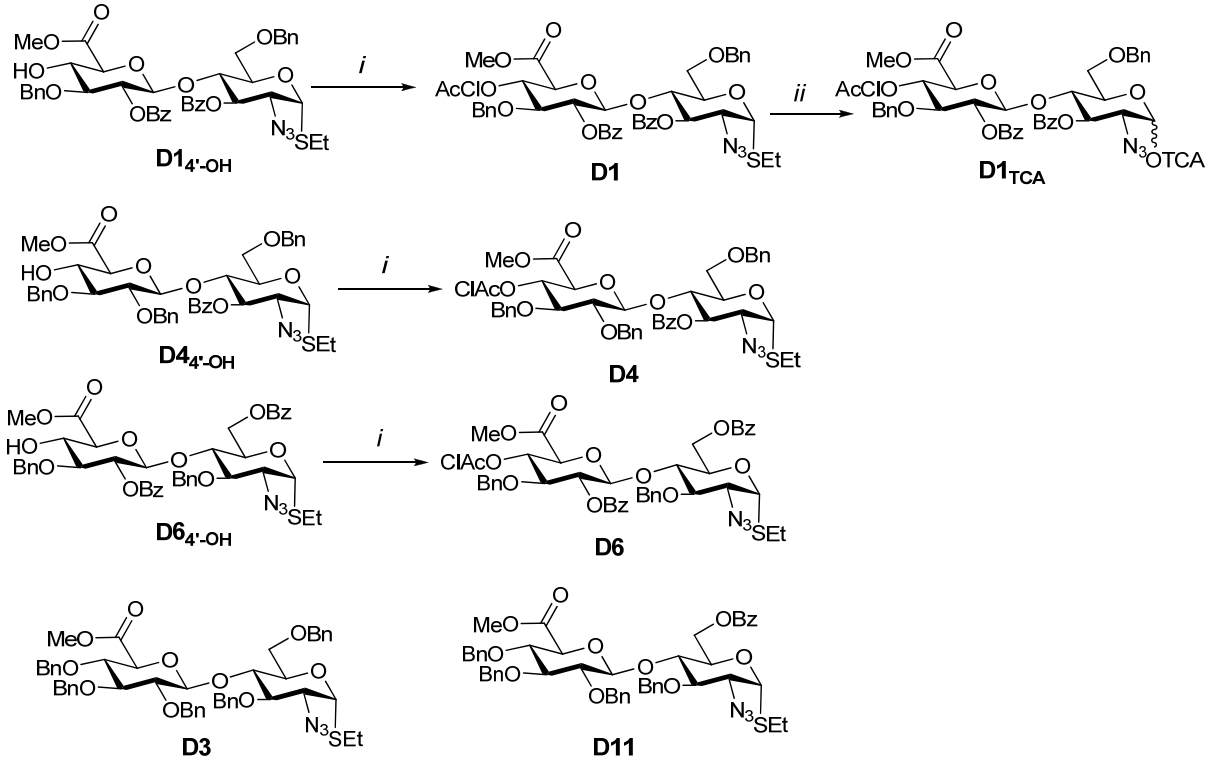
Chemical Synthesis Section

Synthesis of disaccharide building blocks D1 – D11

Results and Discussion

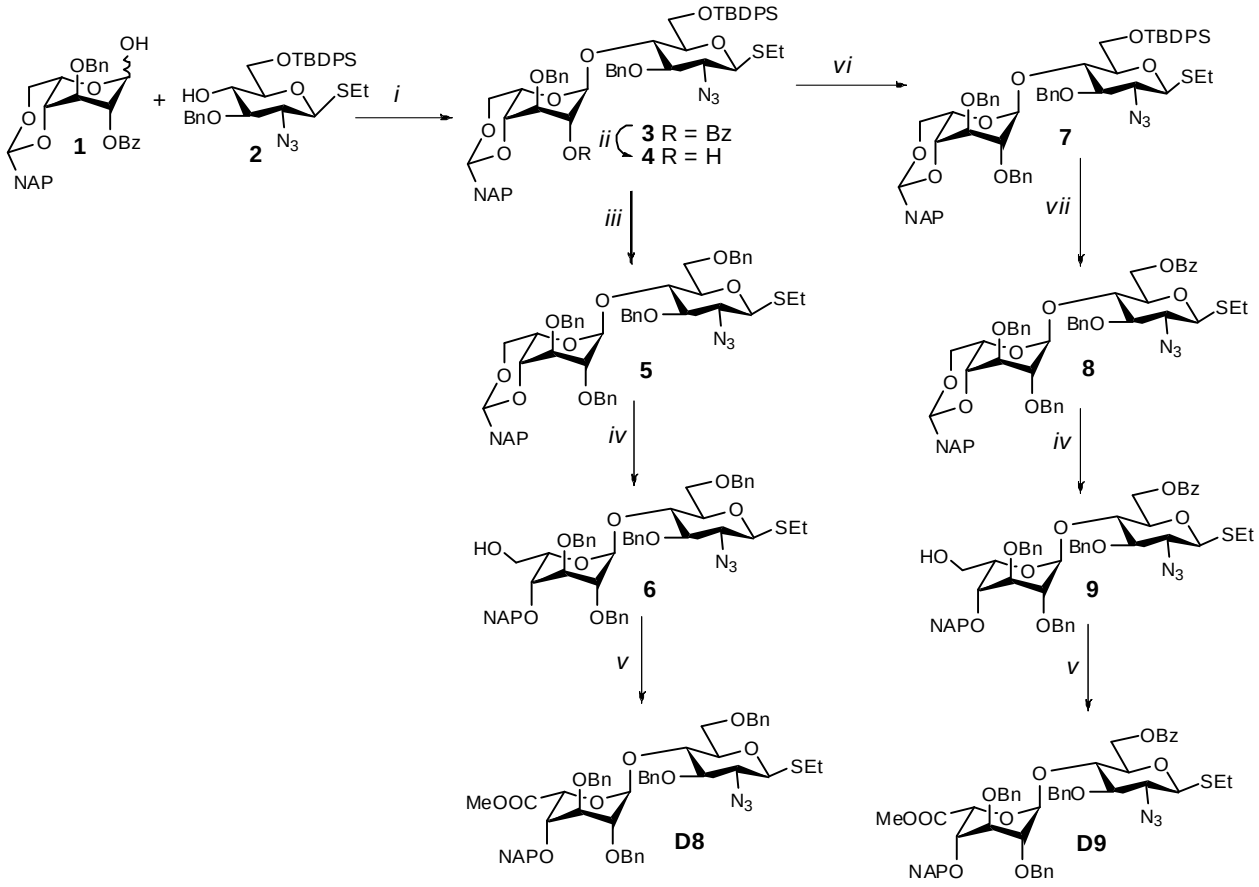
Thioglycoside disaccharide building blocks

The glucuronic acid containing thioglycoside building blocks **D1**$_{4'\text{-OH}}$, **D3**, **D4**$_{4'\text{-OH}}$, **D6**$_{4'\text{-OH}}$, and **D11** were synthesized from cellobiose via a common intermediate as described.[19, S13] In the synthesis of hexasaccharide structures, blocks **D3** and **D11** were used directly as non-reducing end moieties, whereas chloroacetylation of **D1**$_{4'\text{-OH}}$, **D4**$_{4'\text{-OH}}$, and **D6**$_{4'\text{-OH}}$ afforded the fully protected building blocks **D1**, **D4**, and **D6** (**Scheme S1**) to be used as "middle" structures. Thioglycoside **D1** was further converted to the corresponding trichloroacetimidate donor **D1**$_{TCA}$ for more efficient synthesis of tetrasaccharide **T9** in the preparation of hexasaccharide **HX5**.



Scheme S1 Reagents: *i*) ClAcCl, pyridine, CH_2Cl_2; *ii*) a. NIS, acetone/H_2O; b. Cl_3CCN, K_2CO_3, CH_2Cl_2.

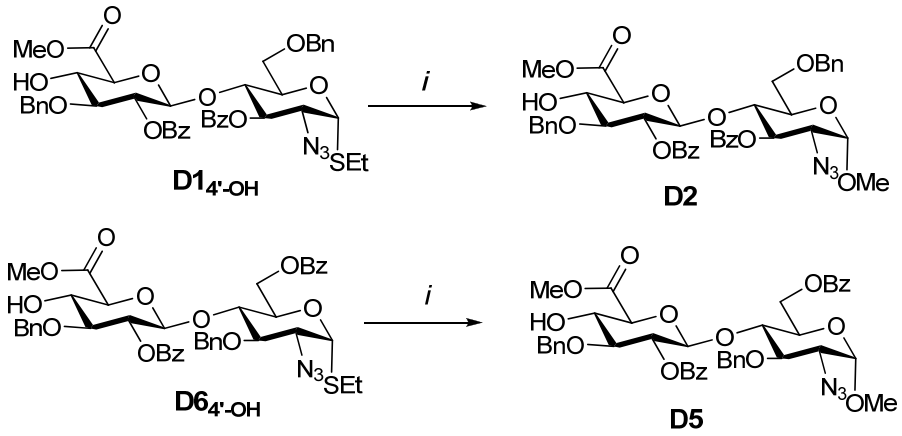
The iduronic acid containing thioglycoside building blocks **D8** and **D9** were prepared from precursors **1** and **2** via a common disaccharide intermediate **3** according to **Scheme S2**.



Scheme S2 Reagents: *i*) a. Cl_3CCN, K_2CO_3, CH_2Cl_2; b. TMSOTf, CH_2Cl_2; *ii*) NaOMe, MeOH; *iii*) a. TBAF, THF; b. BnBr, NaH, DMF; *iv*) BH_3·THF, TMSOTf, CH_2Cl_2; *v*) a. TEMPO, BAIB, CH_2Cl_2; b. NMM, DMTMM, MeOH; *vi*) BnBr, NaH, DMF; *vii*) a. TBAF, THF; b. BzCl, pyridine, CH_2Cl_2.

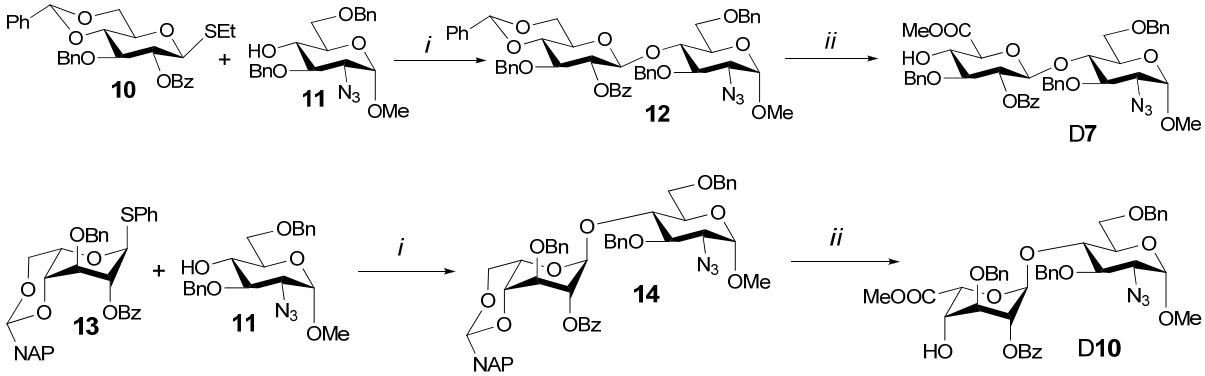
Methyl glycoside disaccharide building blocks

The reducing end methyl glycoside disaccharide building blocks **D2** and **D5** were synthesized through halide-assisted glycosylations[S14] using methanol as acceptor and the glycosyl bromides of **D1**$_{4'\text{-OH}}$ and **D6**$_{4'\text{-OH}}$, respectively, as donors (**Scheme S3**).



Scheme S3 Reagents: *i*) a. Br_2, CH_2Cl_2; b. Et_4NBr, MeOH, CH_2Cl_2.

Compounds **D7** and **D10** were synthesized from monosaccharide precursors **10**[S15], **11**[S16], and **13** according to **Scheme S4**. The carboxylic group was introduced at the disaccharide stage through removal of a 4',6'-*O*-acetal group followed by regioselective 6'-OH TEMPO-oxidation.



Scheme S4 Reagents: *i*) NIS, AgOTf, CH_2Cl_2; *ii*) (a) TFA, H_2O/CH_2Cl_2; (b) TEMPO, BAIB, H_2O/CH_2Cl_2; (c) MeI, K_2CO_3, DMF.

Experimental

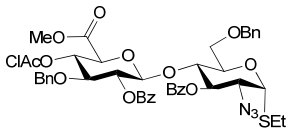
General Methods

All chemicals were purchased from commercial suppliers and used without purification. Anhydrous dichloromethane, tetrahydrofuran, diethyl ether and toluene were obtained from PureSolv-EN^{TM} solvent purification system. All other anhydrous solvents were purchased from Sigma-Aldrich in AcroSeal® bottles. Reactions were monitored by thin layer chromatography using Merck aluminium foil coated TLC plates carrying silica gel 60 F254 with a 0.2mm thickness. Ultraviolet light, sulphuric acid (8% H_2SO_4 in ethanol) and/or ninhydrin (3g ninhydrin, 3 mL acetic acid, in 100 mL ethanol) were used to detect compounds. Purification of compounds was carried out using column chromatography (Grace Davidsil chromatographic silica LC60A 40-60 micron particle size) or flash chromatography using Biotage system (SNAP KP-Sil) or Grace Reveleris system (Silica 40 micron particle size). All compounds were analysed by nuclear magnetic resonance (NMR) spectroscopy with ^{1}H NMR spectra recorded at 400 MHz or 500 MHz and ^{13}C NMR recorded at 106 MHz or 125 MHz on Varian spectrometers at 20 °C. Additional experiments were frequently performed for novel compounds to aid complete characterisation including ^{1}H-^{1}H homonuclear correlation spectroscopy (COSY), total correlation spectroscopy (TOCSY), ^{1}H-^{13}C heteronuclear single quantum coherence spectroscopy (HSQC) and heteronuclear multiple bond correlation spectroscopy (HMBC). Spectra were recorded in deuterated solvents and were standardised against the deuterated solvent peak and the internal TMS standard ($CDCl_3$ δ = 7.26 ppm, CH_3OD δ = 3.31 ppm, TMS δ = 0.00 ppm). Coupling constants (*J* values) are expressed in Hz and were calculated using MestraNova processing software. High resolution mass spectrometry (HRMS) was carried out using Waters micromass LCT LC-TOF instrument with ESI detection in positive or negative mode. Optical rotation was recorded at 20 °C in a 1 cm^3 cell in the indicated

solvent using a Perkin-Elmer polarimeter.

Synthesis of D1

Ethyl [methyl (4-chloroacetyl-2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-1-thio-α-D-glucopyranoside (D1)

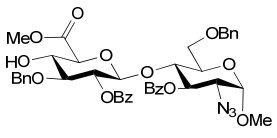


D1$_{4'\text{-OH}}$ (437 mg, 0.53 mmol, 1 eq) was dissolved in dry CH_2Cl_2 (12.3 ml) and cooled to 0 °C. Pyridine (0.85 mmol, 10.56 mmol, 20 eq) was added, followed by the dropwise addition of chloroacetyl chloride (0.08 ml, 1.06 mmol, 2 eq) and the reaction was stirred at 0 °C for 30 min. Reaction was diluted with CH_2Cl_2 and washed with sat. aq. $NaHCO_3$, 1 M HCl and brine. Org. phase was dried over $MgSO_4$, filtered and concentrated. Residue was purified *via* chromatography using cyclohexane/EtOAc (8-66%) to give **D1** (431 mg, 0.48 mmol, 90%) as a white solid.

^{1}H NMR (500 MHz, $CDCl_3$) 8.09 – 8.03 (m, 2H, Ar), 7.94 – 7.87 (m, 2H, Ar), 7.62 – 7.53 (m, 2H, Ar), 7.48 – 7.39 (m, 6H, Ar), 7.35 (dd, *J* = 9.0, 7.8 Hz, 3H, Ar), 7.19 – 7.11 (m, 3H, Ar), 7.05 (dd, *J* = 6.7, 2.8 Hz, 2H, Ar), 5.47 (dd, *J* = 10.3, 8.4 Hz, 1H, H3), 5.43 (d, *J* = 5.6 Hz, 1H, H1), 5.18 (dd, *J* = 9.3, 8.1 Hz, 1H, H2'), 5.13 – 5.07 (m, 1H, H4'), 4.66 (d, *J* = 12.2 Hz, 1H, $BnCH_2$), 4.59 (d, *J* = 8.0 Hz, 1H, H1'), 4.47 (q, *J* = 11.7 Hz, 2H, $BnCH_2$), 4.29 (d, *J* = 12.2 Hz, 1H, $BnCH_2$), 4.17 – 4.09 (m, 2H, H4, H5), 3.97 (dd, *J* = 10.4, 5.6 Hz, 1H, H2), 3.81 (dd, *J* = 36.9, 14.8 Hz, 2H, AcCl), 3.73 (dd, *J* = 11.0, 2.3 Hz, 1H, H6a), 3.69 – 3.59 (m, 2H, H3', H5'), 3.43 (d, *J* = 10.2 Hz, 1H, H6b), 3.34 (s, 3H, 6'-OMe), 2.54 (tdd, *J* = 12.8, 7.4, 5.4 Hz, 2H, SCH_2), 1.24 (t, *J* = 7.4 Hz, 3H, SCH_2CH_3).

Synthesis of D2

Methyl [methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-α-D-glucopyranoside (D2)



Compound **D1$_{4'\text{OH}}$** (0.55 g, 0.664 mmol) was dissolved in CH_2Cl_2 (4.5 mL) at r.t. under vigorous stirring and exclusion of light. Bromine (0.09 mL) was added drop wise and the reaction stirred for 25 mins. The reaction was monitored by TLC which was visualised with a $PdCl_2$, HCl and H_2O stain which shows the sulfide as a pink spot if still present (No discernible change in R_f between starting material and bromo-intermediate). After the reaction was complete the reaction mixture was cooled in an ice bath and

cyclohexene (~0.1 mL) was added slowly drop wise until the brown/orange colour subsided. The reaction mixture was then concentrated and co-evaporated twice with toluene. The crude mixture was then re-dissolved in CH_2Cl_2 (2.375 mL) and cooled in an ice bath. Et_4NBr (0.17 g, 0.809 mmol) and MeOH (0.66 mL) was added and the reaction was stirred at 0 ºC for 17 hrs before allowing to warm to r.t. for a further 24 hrs. Reaction was monitored by ESI mass spec. Upon completion of the reaction the solution was diluted with CH_2Cl_2 and washed with $NaHCO_3$. The organic phase was separated and dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and purified by silica gel chromatography (cyclohexene/EtOAc: 7:3 to 6:4) which yielded the α anomer **D2** (0.39 g, 74%) as a white foam. The β anomer was also isolated in ~15% yield.

R_f (Cyclohexane/EtOAc 2:1): 0.26

$[\alpha]_D$: +82.7 (*c* 1.0 $CHCl_3$)

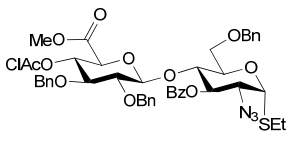
^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.09 – 8.02 (m, 2H, Ar), 7.88 (dd, *J* = 8.2, 1.0 Hz, 2H, Ar), 7.61 – 7.52 (m, 2H, Ar), 7.46 – 7.35 (m, 6H, Ar), 7.34 – 7.29 (m, 3H, Ar), 7.17 – 7.07 (m, 4H, Ar), 5.65 (dd, *J* = 10.5, 9.2 Hz, 1H, H3), 5.07 (dd, *J* = 9.5, 8.1 Hz, 1H, H2'), 4.86 (d, *J* = 3.5 Hz, 1H, H1'), 4.64 (dt, *J* = 18.7, 11.7 Hz, 3H, $BnCH_2$), 4.55 (d, *J* = 8.0 Hz, 1H, H1'), 4.28 (d, *J* = 12.2 Hz, 1H, $BnCH_2$), 4.14 (t, *J* = 9.5 Hz, 1H, H4), 3.84 – 3.76 (m, 1H, H4'), 3.75 – 3.64 (m, 2H, H', H6a), 3.53 (s, 3H, 1-OMe), 3.46 – 3.39 (m, 2H, H5', H6b), 3.38 (s, 3H, 6'-OMe), 3.27 (dd, *J* = 10.5, 3.5 Hz, 1H, H2), 2.84 (d, *J* = 2.8 Hz, 1H, 4'-OH).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 168.86 (C-6'), 165.21 (OBz), 164.48 (OBz), 137.81 (Ar), 137.78 (Ar), 133.20 (Ar), 132.86 (Ar), 130.11 (Ar), 129.85 (Ar), 129.80 (Ar), 129.56 (Ar), 128.63 (Ar), 128.41 (Ar), 128.25 (Ar), 128.17 (Ar), 127.88 (Ar), 127.64 (Ar), 100.35 (C-1'), 99.17 (C-1), 80.72 (C-3'), 74.75 (C-4), 74.19 ($BnCH_2$), 74.03 (C-5'), 73.61 ($BnCH_2$), 72.81 (C-2'), 71.88 (C-4'), 70.96 (C-3), 69.75 (C-5), 67.38 (C-6), 61.57 (C-2), 55.37 (1-OMe), 52.49 (6'-OMe).

HRMS (ESI): Calc. for $C_{42}H_{43}N_3O_{13}Na$ $[M+Na]^+$: 820.2694; found 820.2656.

Synthesis of D4

Ethyl (methyl (2,3-di-*O*-benzyl-4-*O*-chloroacetyl-β-D-glucopyranosyl)uronate)-(1⟶4)-2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-1-thio-α-D-glucopyranoside (D4)



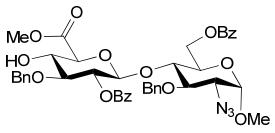
$D4_{4'\text{-}OH}$ (108 mg, 0.13 mmol, 1 eq) was dissolved in dry CH_2Cl_2 (3 ml) and cooled to 0 °C. Pyridine (0. 21 ml, 2.65 mmol, 20 eq) was added, followed by the dropwise addition of chloroacetyl chloride (0.02 ml, 0.26

mmol, 2 eq) and the reaction was stirred at 0 °C for 30 min. Reaction was then diluted with CH_2Cl_2 and washed with 1 M HCl, sat. aq. $NaHCO_3$, and brine. Org. phase was dried over $MgSO_4$, filtered and concentrated. Purification *via* chromatography using cyclohexane/EtOAc (5-40%) gave **D4** (103 mg, 0.12 mmol, 89%) as white solid.

^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.06 (dd, *J* = 8.1, 1.0 Hz, 2H, Ar), 7.57 – 7.52 (m, 1H, ar), 7.44 (t, *J* = 7.7 Hz, 2H, Ar), 7.40 – 7.25 (m, 13H, Ar, $CDCl_3$), 7.20 – 7.15 (m, 2H, Ar), 5.51 – 5.45 (m, 2H, H1, H3), 4.92 – 4.87 (m, 1H, H4'), 4.79 – 4.66 (m, 4H, $BnCH_2$), 4.53 (d, *J* = 11.7 Hz, 1H, $BnCH_2$), 4.34 (d, *J* = 12.1 Hz, 1H, $BnCH_2$), 4.24 – 4.08 (m, 3H, H4, H5, H1',), 4.04 (dd, *J* = 10.5, 5.6 Hz, 1H, H2), 3.88 (dd, *J* = 11.1, 2.5 Hz, 1H, H6a), 3.78 (d, *J* = 14.8 Hz, 1H, AcCl), 3.69 (d, *J* = 14.8 Hz, 1H, AcCl), 3.51 – 3.45 (m, 2H, H6b, H5'), 3.34 – 3.25 (m, 4H, H2', H3', OMe), 2.62 (tdd, *J* = 12.8, 7.4, 5.4 Hz, 2H, SCH_2), 1.33 (t, *J* = 7.4 Hz, 3H, SCH_2CH_3).

Synthesis of D5

Methyl (methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl)uronate)-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (D5).



Compound **D6$_{4'\text{-OH}}$** (0.590 g, 0.713 mmol) was dissolved in CH_2Cl_2 (4.7 mL) at r.t. under vigorous stirring. Bromine (0.110 mL) was added drop wise and the reaction stirred for 45 mins. The reaction was monitored by TLC which was visualised with a $PdCl_2$, HCl and H_2O stain which shows the sulfide as a pink spot if still present (No discernible change in R_f between starting material and bromo-intermediate). After the reaction was complete the reaction mixture was cooled in an ice bath and cyclohexene (0.5 mL) was added slowly drop wise. The reaction mixture was then concentrated and co-evaporated twice with toluene. The crude mixture was then re-dissolved in CH_2Cl_2 (2.375 mL) and cooled in an ice bath. Tetraethylammonium bromide (0.180 g, 0.855 mmol) and MeOH (0.735 mL) was added and the reaction was stirred at 0 ºC for 17 hrs before allowing to warm to r.t. for a further 24 hrs. Reaction was monitored by ESI mass spec. Upon completion of the reaction the solution was diluted with CH_2Cl_2 and washed with $NaHCO_3$. The organic phase was separated and dried over $MgSO_4$ and filtered. The filtrate was concentrated *in vacuo* and purified by silica gel chromatography (cyclohexene/EtOAc: 7:3 to 6:4) which yielded pure α anomer **D5** (0.4 g, 70%) as a colourless oil.

R_f (Cyclohexane/EtOAc 3:2): 0.58

[α]$_D$: +98.1 (*c* 1.0 $CHCl_3$)

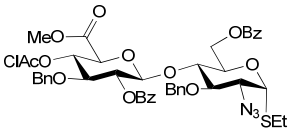
^{1}H NMR (500 MHz, $CDCl_3$) δ = 8.06 – 8.00 (m, 2H, Ar), 7.92 (dd, *J* = 8.3, 1.2 Hz, 2H, Ar), 7.58 (dd, *J* = 10.6, 4.3 Hz, 1H, Ar), 7.47 – 7.31 (m, 8H, Ar), 7.30 – 7.24 (m, 1H, Ar), 5.32 (dd, *J* = 9.5, 8.1 Hz, 1H, H2'), 5.15 (d, *J* = 11.0 Hz, 1H, $BnCH_2$), 4.72 (ddd, *J* = 18.2, 12.2, 9.9 Hz, 5H, H1, H1', $BnCH_2$), 4.43 (qd, *J* = 12.1, 3.2 Hz, 2H, H6ab), 4.04 (dt, *J* = 17.6, 7.8 Hz, 1H, H4'), 3.96 – 3.90 (m, 2H, H3, H4), 3.79 – 3.73 (m, 1H, H5), 3.71 (d, *J* = 9.8 Hz, 1H, H5'), 3.65 (t, *J* = 9.2 Hz, 1H, H3'), 3.57 (s, 3H, 1-OMe), 3.37 (dd, *J* = 10.0, 3.7 Hz, 1H, H2), 3.33 (s, 3H, 6'-OMe), 3.01 (s, 1H, 4'-OH).

^{13}C NMR (126 MHz, $CDCl_3$) δ = 169.11 (C-6'), 165.92 (OBz), 164.88 (OBz), 138.39 (Ar), 137.65 (Ar), 133.34 (Ar), 133.29 (Ar), 129.80 (Ar), 129.53 (Ar), 129.09 (Ar), 128.53 (Ar), 128.46 (Ar), 128.29 (Ar), 128.25 (Ar), 127.92 (Ar), 127.76 (Ar), 127.72 (Ar), 127.45 (Ar), 101.27 (C-1'), 98.46 (C-1), 80.92 (C-3'), 78.17 (C-3 or C-4), 78.14 (C-3 or C-4), 75.32 ($BnCH_2$), 74.64 ($BnCH_2$), 74.32 (C-5'), 73.09 (C-2'), 72.14 (C-4'), 68.66 (C-5), 63.04 (C-2), 62.48 (C-6), 55.38 (C-6'-OMe), 52.69 (1-OMe).

HRMS (ESI): Calc. for $C_{42}H_{43}N_3O_{12}Na$ $[M+Na]^+$: 820.2694; found: 820.2700.

Synthesis of D6

Ethyl [methyl (2-*O*-benzoyl-3-*O*-benzyl-4-*O*-chloroacetyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-1-thio-α-D-glucopyranoside (D6)



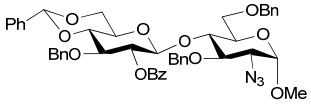
D6$_{4'\text{-OH}}$ (142 mg, 0.17 mmol, 1 eq) was dissolved in dry CH_2Cl_2 (4 ml) and cooled to 0 °C. Pyridine (0.28 ml, 3.43 mmol, 20 eq) was added, followed by the dropwise addition of chloroacetyl chloride (0.03 ml, 0.34 mmol, 2 eq) and the reaction was stirred at 0 °C for 30 min, then with CH_2Cl_2 and washed with 1 M HCl, sat. aq. $NaHCO_3$, and brine. Org. phase was dried over $MgSO_4$, filtered and concentrated. Residue was purified *via* chromatography using cyclohexane/EtOAc (6-50%) to give **D6** (138 mg, 0.15 mmol, 90%) as white solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.03 (dd, *J* = 5.2, 3.3 Hz, 2H, Ar), 7.92 (dd, *J* = 8.3, 1.2 Hz, 2H, Ar), 7.63 – 7.54 (m, 1H, Ar), 7.51 – 7.26 (m, 10H, Ar), 7.18 – 7.11 (m, 3H, Ar), 7.11 – 7.05 (m, 2H, Ar), 5.39 (dd, *J* = 9.0, 7.9 Hz, 1H, H2'), 5.28 (dd, *J* = 11.8, 6.8 Hz, 2H, H1, H4'), 5.17 (d, *J* = 11.2 Hz, 1H, $BnCH_2$), 4.79 (d, *J* = 7.9 Hz, 1H, H1'), 4.73 (d, *J* = 11.2 Hz, 1H, $BnCH_2$), 4.51 (dt, *J* = 23.3, 8.0 Hz, 2H, H6a, $BnCH_2$), 4.37 (dd, *J* = 12.2, 1.8 Hz, 1H, $BnCH_2$), 4.23 – 4.14 (m, 1H,

H5), 3.93 – 3.86 (m, 1H, H4), 3.85 – 3.79 (m, 4H, H2, H3', H5', AcCla), 3.77 – 3.68 (m, 2H, H3, AcClb), 3.49 (s, 3H, OMe), 2.55 – 2.38 (m, 2H, SCH_2), 1.18 (t, *J* = 7.4 Hz, 3H, SCH_2CH_3).

Synthesis of D7

Methyl 2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl-(1→4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (12)

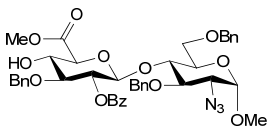


The donor and acceptor were dried overnight on the Schlenk line. A solution of **10** (81 mg; 0.203 mmol) and **11** (134 mg; 0.264 mmol) in dry DCE (7 ml) was stirred at 0 °C under N_2 before a solution of NIS (56 mg; 0.250 mmol) in dry CH_2Cl_2 (2 ml) and Et_2O (2 ml) was added followed by a solution of TfOH (2.5 μL; 0.028 mmol) in dry CH_2Cl_2 (50 μL). The reaction was allowed to stir at rt for 3 h, by which stage it was complete (according to TLC) and Et_3N (1 ml) was added to quench. The solution was diluted with EtOAc, washed with 10% $Na_2S_2O_3$, sat $NaHCO_3$ and brine, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by automated flash chromatography (EtOAc in pentane, 5-40 %) to afford **12** (150 mg, 0.178 mmol, 88%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.3 Hz, 2H, Bz-H_{Ortho}), 7.61 (t, *J* = 7.4 Hz, 1H, Bz-H_{Para}), 7.51 (dd, *J* = 7.8, 1.5 Hz, 2H, Bn-H_{Ortho}), 7.45 (t, *J* = 7.8 Hz, 2H, Bz-H_{Meta}), 7.44 - 7.24 (m, 15H, ArH), 7.19 - 7.06 (m, 5H, ArH), 5.50 (s, 1H, PhCHOO), 5.22 (dd, *J* = 8.97, 8.25 Hz, 1H, H-2'), 5.01 (d, *J* = 10.6 Hz, 1H, PhCH), 4.79 (d, *J* = 12.1 Hz, 1H, PhCH), 4.73 (d, *J* = 10.59 Hz, 1H, PhCH), 4.73 (d, *J* = 12.16 Hz, 1H, PhCH), 4.70 (d, *J* = 3.58 Hz, 1H, H-1), 4.65 (d, *J* = 12.1 Hz, 1H, PhCH), 4.56 (d, *J* = 8.0 Hz, 1H, H-1'), 4.29 (d, *J* = 12.1 Hz, 1H, PhCH), 4.16 (dd, *J* = 10.5, 4.9 Hz, 1H, H-6a'), 4.00 (dd, *J* = 9.71, 9.15 Hz, 1H, H-4), 3.83 (dd, *J* = 10.0, 9.1 Hz, 1H, H-3), 3.72 (t, *J* = 9.2 Hz, 1H, H-4'), 3.68 - 3.59 (m, 2H, H-3', H-6a), 3.45 (d, *J* = 9.9 Hz, 1H, H-5), 3.41 - 3.36 (m, 2H, H-2, H-6b'), 3.33 (dd, *J* = 10.9, 1.6 Hz, 1H, H-6b), 3.29 (s, 3H, OMe), 3.22 (td, *J* = 9.7, 4.9 Hz, 1H, H-5').

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.7, 138.5, 137.9, 137.8, 137.3, 133.3, 129.8, 129.6, 129.0, 128.6, 128.4, 128.3, 128.3, 128.2, 128.2, 128.2, 128.0, 127.8, 127.5, 127.5, 126.0, 101.2, 100.6, 98.6, 81.9, 78.1, 77.8, 76.6, 75.1, 73.8, 73.8, 73.7, 70.1, 68.5, 67.2, 66.0, 63.0, 55.4.

Ethyl [methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-1-thio-α-D-glucopyranoside (D7)



A suspension of **12** (1.470 g, 1.742 mmol) and (+)-camphor-10-sulfonic acid (283 mg, 1.219 mmol) was stirred in MeOH (15.3 ml) and CH_2Cl_2 (1.7 ml) at 40 °C overnight for 17 h. After this period of time, the reaction was complete by TLC. The reaction mixture was diluted with EtOAc, washed with sat. $NaHCO_3$ (2 x 75 ml) and the aqueous phase extracted with additional EtOAc (3 x 50 ml). The combined organic fractions were dried (Na_2SO_4) and concentrated under reduced pressure before purification by automated flash chromatography(EtOAc/pentane, 11% - 70%) to afford the 4,6-diol methyl 2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (1.264 g; 1.672 mmol; 96 %) as a colourless syrup.

1H NMR (500 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.4 Hz, 2H, OBz-*ortho*), 7.59 (t, *J* = 7.5 Hz, 1H, OBz-*para*), 7.44 (t, *J* = 7.8 Hz, 2H, OBz-*meta*), 7.44-7.32 (m, 9H, Ar), 7.30-7.26 (m, 1H, Ar), 7.20 - 7.13 (m, 5H, Ar), 5.17 (dd, *J* = 9.4, 8.2 Hz, 1H, H-2'), 5.00 (d, *J* = 10.9 Hz, 1H, PhCH), 4.77 (d, *J* = 10.9 Hz, 1H, PhCH), 4.75 (d, *J* = 12.1 Hz, 1H, PhCH), 4.71 (d, *J* = 3.6 Hz, 1H, H-1), 4.64 (d, *J* = 11.6 Hz, 1H, PhCH), 4.60 (d, *J* = 11.5 Hz, 1H, PhCH), 4.53 (d, *J* = 8.1 Hz, 1H, H-1'), 4.34 (d, *J* = 12.2 Hz, 1H, PhCH), 3.96 (dd, *J* = 9.8, 9.2 Hz, 1H, H-4), 3.83 (dd, *J* = 10.1, 9.1 Hz, 1H, H-3), 3.66 (dd, *J* = 10.9, 2.6 Hz, 1H, H-6a), 3.61 (dd, *J* = 12.0, 3.1 Hz, 1H, H-6a'), 3.58 (t, *J* = 9.3 Hz, 1H, H-4'), 3.47 (bd, *J* = 10.0 Hz, 1H, H-5), 3.45 - 3.34 (m, 3H, H-2, H-3', H-6b), 3.32 (dd, *J* = 12.0, 5.7 Hz, 1H, H-6b'), 3.29 (s, 3H, OMe), 3.19 (ddd, *J* = 9.1, 5.7, 3.1 Hz, 1H, H-5').

^{13}C NMR (126 MHz, $CDCl_3$) δ 164.8 (C=O, OBz), 138.5 (OBn-*ipso*), 137.9 (OBn-*ipso*), 137.8 (OBn-*ipso*), 133.3 (OBz-*para*), 129.7 (2C, OBz-*ortho*), 129.5, 128.7 (2C), 128.5 (2C), 128.5 (2C), 128.4 (2C), 128.4 (2C), 128.2, 127.9, 127.8 (2C), 127.7, 127.4 (2C), 100.2 (C-1'), 98.7 (C-1), 82.6 (C-3'), 78.1 (C-3), 76.5 (C-4), 75.3 (C-5'), 75.1 (C-Ph), 74.7 (C-Ph), 73.9 (C-2'), 73.8 (C-Ph), 70.9 (C-4'), 70.2 (C-5), 67.3 (C-6), 63.2 (C-2), 62.1 (C-6'), 55.4 (OMe).

To a vigourously stirred solution of the 4,6-diol (293 mg; 0.388 mmol) in CH_2Cl_2 (1.3 ml) and H_2O (0.64 ml) at r.t. was added TEMPO (12.2 mg; 0.078 mmol) and bisacetoxyiodobenzene (312 mg; 0.969 mmol). Stirring was continued for 40 min before the reaction was complete (by TLC). 10 % $Na_2S_2O_3$ was added to the reaction flask and the mixture extracted into EtOAc and washed with additional 10 % $Na_2S_2O_3$. The aqueous layer was extracted twice with EtOAc and the combined organic fractions dried (Na_2SO_4), concentrated under reduced pressure and co-

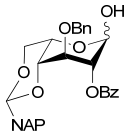
evaporated twice with toluene. The residue was dissolved in dry MeOH (4 ml) and treated with DMTMM (215 mg; 0.775 mmol) and N-methylmorpholine (0.085 ml; 0.776 mmol) and stirred under N_2 at r.t. for 5 h. The solvent was removed and the residue adsorbed onto silica before purification by automated flash chromatography (EtOAc:toluene, 15 - 20 %). Purification resulted in two inseparable spots, one of which was the product and the other the tetrasacharide side product. The major side product was the tetrasaccharide (as shown by a signal in the mass spec at 1557.3 (M + Na). A similar oxidation side product was reported by L. Huang, *et al*.[S20] Consequently, the product mixture was co-evaporated twice with toluene before dissolution in dry MeOH (5 ml). After cooling to 0 ºC, cat. Na in MeOH (0.0194 mmol; 0.05 eq) was added and stirring continued overnight (18 h) at r.t. Dowex (H+) resin was added and the mixture stirred for 5 min before filtration, concentration under reduced pressure, and purification by automated flash chromatography (EtOAc/toluene, 15 % - 20 %). The product (**D7**, 270 mg; 0.344 mmol) was obtained in 89% yield.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.4 Hz, 2H, H_{ortho}Bz), 7.60 (t, *J* = 7.4 Hz, 1H, H_{para}Bz), 7.45 (t, *J* = 7.8 Hz, 2H, H_{meta}Bz), 7.42 - 7.21 (m, 10H, Ar), 7.21 - 7.09 (m, 5H, Ar), 5.18 (dd, *J* = 9.5, 8.2 Hz, 1H, H-2'), 5.10 (d, *J* = 10.9 Hz, 1H, PhCH), 4.75 (d, *J* = 12.0 Hz, 2H, 2 x PhCH), 4.70 (d, *J* = 3.6 Hz, 1H, H-1), 4.66 (d, *J* = 11.8 Hz, 1H, PhCH), 4.65 (d, *J* = 10.9 Hz, 1H, PhCH), 4.55 (d, *J* = 8.1 Hz, 1H, H-1'), 4.28 (d, *J* = 12.2 Hz, 1H, PhCH), 4.03 (dd, *J* = 9.8, 8.9 Hz, 1H, H-4), 3.97 (t, *J* = 9.3 Hz, 1H, H-4'), 3.82 (dd, *J* = 10.1, 8.9 Hz, 1H, H-3), 3.67 (dd, *J* = 10.9, 2.6 Hz, 1H, H-6a), 3.65 (d, *J* = 9.9 Hz, 1H, H-5'), 3.55 (s, 3H, COOMe), 3.47 - 3.38 (m, 2H, H-3', H-5), 3.38 - 3.32 (m, 2H, H-2, H-6b), 3.28 (s, 3H, OMe), 3.06 (s, 1H, 4'-OH).

^{13}C NMR (101 MHz, $CDCl_3$) δ 169.6 (C=O, COOMe), 164.7 (C=O, OBz), 138.6 (OBn-*ipso*), 137.9 (OBn-*ipso*), 137.7 (OBn-*ipso*), 133.3 (OBz-*para*), 129.8 (2C, OBz-*ortho*), 129.5, 128.7 (2C), 128. 5 (2C), 128.4 (2C), 128.3, 128.3 (2C), 128.1 (2C), 127.9 (2C), 127.9 (2C), 127.6, 127.3, 100.4 (C-1'), 98.7 (C-1), 80.7 (C-3'), 78.0 (C-3), 76.8 (C-4), 75.1 (C-Ph), 74.3 (C-Ph), 73.9 (C-5'), 73.7 (C-Ph), 73.0 (C-2'), 72.4 (C-4'), 69.9 (C-5), 67.2 (C-6), 62.9 (C-2), 55.3 (OCH3), 52.6 (COOCH3).

Synthesis of D8

2-Benzoate-3-*O*-benzyl-4,6-*O*-(1-naphthalenylmethylene)-L-idopyranoside (1)



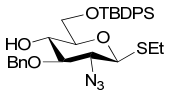
Phenyl 2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-(1-naphthyl)methylidene-1-thio-α-L-idopyranoside[S17] (5.111 g, 8.45 mmol, 1 eq) was dissolved in 10:1 acetone/water (52 ml : 5.2 ml) and put on ice. NIS (2.852 g, 12.68 mmol, 1.5 eq) was added, stirring at 0 °C for 1.5 h. Then, another portion of NIS (951 mg, 4.22 mmol, 0.5 eq) was added, stirring for additional 10 min. Reaction was quenched with sat. aq. $NaHCO_3$ (24 ml), diluted with CH_2Cl_2 (220 ml) and washed with 10% sodium thiosulfate (2 x 110 ml) and water (110 ml). The org. phase was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification *via* chromatography using pentane/ EtOAc (8-66%) gave **1** (4.264 g, 8.32 mmol, 98%, anomeric mixture) as a white foam.

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.28 – 8.19 (m, 2H, Ar), 8.07 – 8.01 (m, 1H, Ar), 7.94 – 7.85 (m, 3H, Ar), 7.81 (dd, *J* = 15.1, 6.6 Hz, 3H, Ar), 7.68 (dd, *J* = 17.2, 6.9 Hz, 2H, Ar), 7.52 – 7.30 (m, 12H, Ar), 7.27 – 7.18 (m, 4H, Ar), 7.11 (dt, *J* = 13.6, 7.9 Hz, 3H, Ar), 6.10 (s, 1H, NaphCHα), 6.07 (s, 1H, NaphCHβ), 5.45 (d, *J* = 8.9 Hz, 1H, H1α), 5.33 (d, *J* = 11.2 Hz, 1H, H1β), 5.24 (s, 1H, H2α), 5.20 (s, 1H, H2β), 4.94 – 4.85 (m, 2H, $BnCH_2$ α, β), 4.77 (dd, *J* = 20.7, 11.6 Hz, 2H, $BnCH_2$ α, β), 4.55 – 4.42 (m, 2H, H6a α, β), 4.32 – 4.18 (m, 4H, H4α, H5α H6β α, β), 4.10 (ddd, *J* = 9.9, 8.5, 4.9 Hz, 4H, H3β, H4 α, β, OH), 3.96 (s, 1H, H5β), 3.51 – 3.41 (m, 1H, OH).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 166.47, 165.88, 133.16, 133.01, 130.09, 129.57, 128.79, 128.60, 128.39, 128.18, 128.15, 128.09, 127.83, 126.25, 126.23, 125.53, 124.83, 124.78, 124.63, 124.32, 124.19, 100.22, 93.29, 92.02, 75.21, 74.11, 73.51, 72.88, 72.48, 70.12, 69.90, 68.28, 68.07, 67.07, 65.87, 60.35, 58.93.

HRMS (ESI): Calc. for $C_{31}H_{28}O_7Na$ $[M+Na]^+$: 535.1733; found 535.1726.

Ethyl 2-azido-3-*O*-benzyl-6-*tert*-butyldiphenylsilyl-2-deoxy-thio-β-D-glucopyranoside (2)



Ethyl 2-azido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-1-thio-β-D-glucopyranoside[S18,S19] (1.193 g, 2.79 mmol, 1 eq) was dissolved in dry 7:1 MeOH/CH_2Cl_2 (24.5 ml : 3.5 ml) and camphor-10-sulfonic acid (453 mg, 1.95 mmol, 0.7 eq) was added. Reaction was stirred at RT for 3 h. Reaction was put on ice and quenched with triethylamine (1.18 ml, 8.37 mmol, 3 eq). Solvent was evaporated and residue purified *via* chromatography using pentane/EtOAc (12-100%) to give ethyl 2-azido-3-*O*-benzyl-2-deoxy-thio-β-D-glucopyranoside

(941 mg, 2.77 mmol, 99%) as colourless syrup. $[\alpha]^{T}_{D}$: -72.0 (*c* 0.9 $CHCl_3$)**;** ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.28 (m, 4H, Ph), 4.96 (dd, *J* = 11.3, 3.4 Hz, 1H, $BnCH_2$), 4.78 (d, *J* = 11.3 Hz, 1H, $BnCH_2$), 4.33 (d, *J* = 9.7 Hz, 1H, H1), 3.84 (d, *J* = 11.9 Hz, 1H, H6a), 3.75 (dd, *J* = 11.9, 4.1 Hz, 1H, H6b), 3.62 (t, *J* = 8.9 Hz, 1H, H4), 3.39 – 3.26 (m, 3H, H2, H3, H5), 2.81 – 2.64 (m, 2H, SCH_2), 1.31 (t, *J* = 7.4 Hz, 3H, SCH_2CH_3); ^{13}C-NMR (126 MHz, $CDCl_3$) δ 137.87 (Ph), 128.69 (Ph), 128.18 (Ph), 128.09 (Ph), 84.69 (C-2), 84.62 (C-1), 79.32 (C-5), 75.37 ($BnCH_2$), 70.38 (C-4), 65.79 (C-3), 62.35 (C-6), 24.89 (SCH_2), 15.03 (SCH_2CH_3); HR-MS: calc. for $C_{15}H_{21}N_3O_4NaS$ [MNa^-]: 362.1150; found 362.1154. Ethyl 2-azido-3-*O*-benzyl-2-deoxy-thio-β-D-glucopyranoside (1.056 g, 3.11 mmol, 1 eq) was dissolved in dry DMF and cooled to 0 °C. Imidazole (417 mg, 6.32 mmol, 2 eq) was added, stirring at 0 °C for 10 min, then TBDPSCl (0.97 ml, 3.73 mmol, 1.2 eq) was added dropwise. Reaction was stirred at 0 °C for 1.5 h. Reaction was quenched by the addition of MeOH (0.06 ml, 1.56 mmol, 0.5 eq). Mixture was diluted with EtOAc (30 ml) and washed with water (3 x 15 ml), 1 M HCl (15 ml) and sat. aq. $NaHCO_3$ (15 ml). The org. layer was dried over $MgSO_4$, filtered and concentrated. Purification *via* chromatography using pentane/EtOAc (3-28%) gave **2** (1.800 g, 3.11 mmol, quant.) as colourless syrup.

R_f (cyclohexane / EtOAc 20:1): 0.22

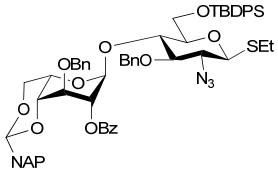
$[\alpha]_D$: -49.4 (*c* 0.9 $CHCl_3$)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.2 Hz, 5H, Ph), 7.45 – 7.34 (m, 11H, Ph), 7.32 (d, *J* = 7.2 Hz, 1H, Ph), 4.90 (dd, *J* = 30.5, 11.2 Hz, 2H, $BnCH_2$), 4.29 (d, *J* = 9.7 Hz, 1H, H1), 3.89 (dd, *J* = 4.6, 2.7 Hz, 1H, H4), 3.79 – 3.70 (m, H6), 3.42 – 3.31 (m, 3H, H2, H3, H5), 2.79 – 2.63 (m, 2H, SCH_2), 2.03 (s, 1H), 1.27 (dt, *J* = 16.6, 7.3 Hz, 3H, SCH_2CH_3), 1.05 (t, *J* = 6.3 Hz, 9H, ^{t}Bu).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 138.01 (Ph), 135.64 (Ph), 135.55 (Ph), 132.91 (Ph), 132.73 (Ph), 129.86 (Ph), 128.59 (Ph), 128.18 (Ph), 128.05 (Ph), 127.78 (Ph), 127.75 (Ph), 84.68 (C-5), 83.91 (C-1), 78.73 (C-3), 75.37 ($BnCH_2$), 72.22 (C-4), 65.45 (C-2), 64.55 (C-6), 26.78 (^{t}Bu), 24.20 (SCH_2), 19.19 (^{t}Bu), 14.97 (SCH_2CH_3).

HRMS (ESI): Calc. for $C_{31}H_{39}N_3O_4NaSSi$ $[M+Na]^+$: 600.2328; found 600.2344.

Ethyl 2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-(1-naphthyl)methylidene-α-L-idopyranosyl-(1→4)-2-azido-3-*O*-benzyl-2-deoxy-6-*O*-(*tert*-butyldiphenylsilyl)-1-thio-β-D-glucopyranoside (3)



1 (73 mg, 0.16 mmol, 1 eq) was dissolved in dry CH_2Cl_2 (2.1 ml). Potassium carbonate (69 mg, 0.49 mmol, 3 eq) and trichloroacetonitrile (0.11 ml, 1.11 mmol, 7 eq) were added and the mixture stirred at RT overnight. The mixture was filtered over a pad of Celite and concentrated *in vacuo* (waterbath at 30 °C). Crude residue was dried together with 2 (113 mg, 0.20 mmol, 1.2 eq) and 4 Å MS (110 mg) for 2 h at the Schlenck, then dissolved in dry CH_2Cl_2 (2.2 ml) and stirred for 30 min at -40 °C. TMSOTf (0.006 ml, 0.04 mmol, 0.25 eq, solution in CH_2Cl_2) was added dropwise to the reaction, stirring for 45 min at -40 °C. Reaction was quenched with triethylamine (1 ml), filtered through a pad of Celite, filtrate was diluted with CH_2Cl_2 (20 ml), washed with 2 M HCl (7 ml), sat. aq. $NaHCO_3$ (7 ml) and water (7 ml). Org. phase was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification *via* chromatography using cyclohexane/EtOAc 5:1 gave 3 (163 mg, 0.15 mmol, 95%) as colourless syrup.

R_f (cyclohexane/EtOAc 5:1): 0.45

$[\alpha]_D$: -91.6 (*c* 1.0 $CHCl_3$)

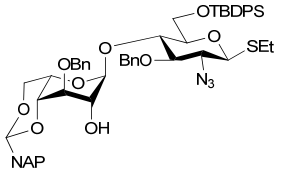
^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.61 (d, *J* = 8.6 Hz, 1H Ar), 7.79 (ddd, *J* = 8.8, 7.7, 5.1 Hz, 4H, Ar), 7.75 – 7.63 (m, 6H, Ar), 7.55 (d, *J* = 6.5 Hz, 1H, Ar), 7.44 – 7.19 (m, 20H, Ar), 7.19 – 7.10 (m, 3H, Ar), 6.98 (t, *J* = 7.9 Hz, 2H, Ar), 5.79 (s, 1H NaphCH'), 5.61 (s, 1H, H1'), 5.29 (s, 1H, H2'), 4.86 (d, *J* = 11.3 Hz, 1H, $BnCH_2$), 4.80 (d, *J* = 10.9 Hz, 1H, $BnCH_2$), 4.72 (d, *J* = 10.9 Hz, 1H, $BnCH_2$), 4.67 (d, *J* = 11.3 Hz, 1H, $BnCH_2$), 4.34 (dd, *J* = 19.4, 9.8 Hz, 2H, H1, H4), 4.16 (s, 1H, H5'), 4.05 (d, *J* = 12.6 Hz, 1H, H6'a), 3.99 (s, 2H, H6ab), 3.92 (s, 1H, H4'), 3.79 (s, 1H, H4), 3.57 – 3.51 (m, 1H, H3), 3.39 (dd, *J* = 11.3, 7.6 Hz, 1H, H2), 3.35 – 3.24 (m, 2H, H6'b, H5), 2.78 – 2.63 (m, 3H, SCH_2), 2.03 (s, 3H), 1.42 (s, 5H), 1.26 (dt, *J* = 17.2, 7.3 Hz, 7H, SCH_2CH_3), 1.08 – 1.01 (m, 9H, ^{t}Bu).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 168.94 (OBz), 136.08 (Ar), 135.47 (Ar), 133.84 (Ar), 133.52 (Ar), 133.44 (Ar), 133.38 (Ar), 132.81 (Ar), 132.67 (Ar), 131.94 (Ar), 131.50 (Ar), 131.30 (Ar), 131.02 (Ar), 130.79 (Ar), 128.52 (Ar), 128.01 (Ar), 127.74 (Ar), 127.67 (Ar), 127.45 (Ar), 127.41 (Ar), 127.39 (Ar), 127.04 (Ar), 126.47 (Ar), 126.29 (Ar), 126.18 (Ar), 126.14 (Ar), 126.06 (Ar), 125.94 (Ar), 125.87, 125.85 (Ar), 125.66 (Ar), 125.64 (Ar), 125.57 (Ar), 125.54 (Ar), 125.48 (Ar), 125.35 (Ar), 125.32 (Ar), 125.22 (Ar), 124.26 (Ar), 123.76 (Ar), 123.49 (Ar), 123.46 (Ar), 122.53 (Ar),

100.55 (NaphCH), 94.92 (C-1'), 81.79 (C-2), 81.72 (C-4), 78.46 (C-5), 75.15, 73.13 ($BnCH_2$), 72.56 ($BnCH_2$), 71.58 (C-4'), 70.10 ($BnCH_2$), 69.11 (C-1), 67.42 (C-6'), 64.49 (C-3), 64.22 (C-2'), 60.60 (C-6), 57.21 (C-5'), 24.80 (^{t}Bu), 24.71 (^{t}Bu), 24.66 (^{t}Bu), 24.59 (^{t}Bu), 21.88 (SCH_2), 18.89, 17.33, 12.60 (SCH_2CH_3).

HRMS (ESI): Calc. for $C_{62}H_{65}N_3O_7NaSSi$ $[M+Na]^+$: 1094.4058; found 1094.4078.

Ethyl 3-*O*-benzyl-4,6-*O*-(1-naphthyl)methylidene-α-L-idopyranosyl-(1⟶4)-2-azido-3-*O*-benzyl-2-deoxy-6-*O*-(*tert*-butyldiphenylsilyl)-1-thio-β-D-glucopyranoside (4)



3 (798 mg, 0.74 mmol, 1 eq) was dissolved in dry CH_2Cl_2 (8 ml) and dry MeOH (16 ml) and a catalytic amount of freshly prepared NaOMe (in MeOH) was added. The reaction was stirred at RT for 5 d, then neutralised using Amberlite R80 (H^+) resin, filtered and concentrated *in vacuo*. Purification *via* chromatography using pentane/EtOAc (4-32%) gave **4** (543 mg, 0.56 mmol, 76%) as white foam.

R_f (cyclohexane/EtOAc 5:1): 0.47

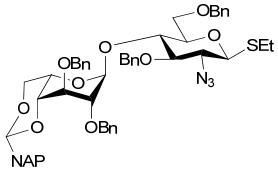
$[\alpha]_D$: -86.9 (*c*=1.0, $CHCl_3$)

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.50 (d, *J* = 8.6 Hz, 1H, Ar), 7.87 – 7.75 (m, 6H, Ar), 7.49 (d, *J* = 6.7 Hz, 1H, Ar), 7.45 – 7.28 (m, 14H, Ar), 5.71 (s, 1H, NaphCH), 5.51 (s, 1H, H1'), 4.78 (d, *J* = 10.9 Hz, 1H, $BnCH_2$), 4.66 (dd, *J* = 11.1, 3.6 Hz, 2H, $BnCH_2$), 4.56 (d, *J* = 11.2 Hz, 1H, $BnCH_2$), 4.33 (d, *J* = 10.2 Hz, 1H, H1), 4.26 (t, *J* = 9.5 Hz, 1H, H4), 4.17 – 4.05 (m, 1H, H4'), 4.01 – 3.90 (m, 4H, H6ab, H6a', H3'), 3.79 – 3.66 (m, 2H, H2', H4'), 3.55 (t, *J* = 9.8 Hz, 1H, H2), 3.37 – 3.26 (m, 2H, H3, H5), 3.22 (m, 2H, H6b', 2'-OH), 2.76 (m, 2H, SCH_2), 1.32 (t, *J* = 7.5 Hz, 3H, SCH_2CH_3), 1.13 (s, 9H, ^{t}Bu).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 138.23 (Ar), 137.72 (Ar), 135.99 (Ar), 135.73 (Ar), 134.07 (Ar), 133.38 (Ar), 132.97 (Ar), 132.90 (Ar), 130.53 (Ar), 130.13 (Ar), 129.73 (Ar), 129.64 (Ar), 128.45 (Ar), 128.29 (Ar), 128.18 (Ar), 128.10 (Ar), 127.87 (Ar), 127.60 (Ar), 127.30 (Ar), 126.63 (Ar), 125.84 (Ar), 125.49 (Ar), 124.78 (Ar), 124.67 (Ar), 103.30 (NaphCH), 100.37 (C-1'), 83.93 (C-1), 83.86 (C-3), 80.71 (C-5), 76.72, 75.08 (C-2'), 75.05 ($BnCH_2$), 74.76 (C-3'), 72.28 (C-4), 72.01 ($BnCH_2$), 69.78 (C-6'), 66.56 (C-2), 65.22 (C-4'), 62.55 (C-6'), 59.66 (C-5'), 26.86 (^{t}Bu), 23.93 (SCH_2), 19.45 (^{t}Bu), 14.89 (SCH_2CH_3).

HRMS (ESI): Calc. for $C_{55}H_{61}N_3O_9NaSSi$ $[M+Na]^+$: 990.3796; found 990.3750.

Ethyl 2,3-di-*O*-benzyl-4,6-*O*-(1-naphthyl)methylidene-α-L-idopyranosyl-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-1-thio-β-D-glucopyranoside (5)



4 (2.994 g, 3.09 mmol, 1 eq) was dissolved in dry THF (400 ml) and 1M TBAF in THF (3.40 ml, 3.40 mmol, 1.1 eq) was added. Mixture was stirred at RT for 4h, another portion of TBAF was added (1.70 ml, 1.70 mmol, 0.5 eq) was added. Stirring for another hour. Solvent was directly evaporated and residue was purified *via* column chromatography using toluence/acetone (5-40%) to give ethyl 3-*O*-benzyl-4,6-*O*-(1-naphthyl)methylidene-α-L-idopyranosyl-(1⟶4)-2-azido-3-*O*-benzyl-2-deoxy-1-thio-β-D-glucopyranoside (2.011 g, 2.76 mmol, 89%) as white solid; R_f (toluene/acetone 4:1): 0.41; $[\alpha]_D$: -36.2 (*c* =1.0, $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.35 (d, *J* = 8.4 Hz, 1H, Ar), 7.83 (d, *J* = 8.1 Hz, 2H, Ar), 7.57 (d, *J* = 6.8 Hz, 1H, Ar), 7.55 – 7.44 (m, 2H, Ar), 7.44 – 7.26 (m, 10H, Ar), 5.77 (s, 1H, NaphCH), 5.20 (s, 1H, H1'), 4.82 (d, *J* = 10.9 Hz, 1H, $BnCH_2$), 4.72 – 4.60 (m, 3H, $BnCH_2$), 4.37 (d, *J* = 10.2 Hz, 1H, H1), 4.03 (s, 1H, H5'), 4.00 – 3.90 (m, 4H, H4, H3', H6a, H6a'), 3.83 – 3.77 (m, 2H, H2' H6b), 3.73 (t, *J* = 3.0 Hz, 1H, H4'), 3.47 (t, *J* = 9.7 Hz, 1H, H2), 3.38 (m, 2H, H3, H5), 3.29 (dd, *J* = 12.7, 1.3 Hz, 1H, H6b'), 3.22 (d, *J* = 10.7 Hz, 1H, 2'-OH), 2.85 – 2.70 (m, 2H, SCH_2), 2.15 – 2.08 (m, 1H, 6-OH), 1.35 (t, *J* = 7.4 Hz, 3H, SCH_2CH_3); ^{13}C-NMR (126 MHz, $CDCl_3$) δ = 137.99 (Ar), 133.92 (Ar), 132.64 (Ar), 130.03 (Ar), 128.56 (Ar), 128.48 (Ar), 128.35 (Ar), 128.15 (Ar), 127.68 (Ar), 127.32 (Ar), 126.50 (Ar), 125.79 (Ar), 124.98 (Ar), 124.79 (Ar), 124.31 (Ar), 101.99 (NaphCH), 101.15 (C-1'), 84.72 (C-1), 83.70 (C-5), 80.44 (C-3), 75.27 (C-4'), 75.12 ($BnCH_2$), 74.91 (C-3'), 73.64 (C-4), 72.18 ($BnCH_2$), 69.59 (C-6'), 66.73 (C-2), 65.77, (C-2'), 61.87 (C-6), 60.20 (C-5'), 24.80 (SCH_2), 15.07 (SCH_2CH_3);HR-MS: calc. for $C_{39}H_{44}N_3O_9NaS$ [*MNa*]$^-$: 730.2798; found 730.2806. The desilylated compound (1.988 g, 2.72 mmol, 1 eq) was dissolved in dry DMF and put on ice. Sodium hydride (60% dispersion, 490 mg, 12.26 mmol, 4.5 eq) was added, stirring for 30 min at 0 °C. Then BnBr (1.30 ml, 10.90 mmol, 4 eq) was added and reaction was allowed to attain RT. Stirring for 2.5 h. Reaction was put on ice and quenched with MeOH and evaporated *in vacuo*. Residue was dissolved in CH_2Cl_2 (200 ml) and washed with water (2 x 100 ml). Org. phase was dried over $MgSO_4$, filtered and concentrated. Purification *via* chromatography using pentane/ acetone (6-50%) gave **5** (1.765 g, 1.94 mmol, 71%) as white solid.

R_f (cyclohexane/acetone 3:1): 0.43

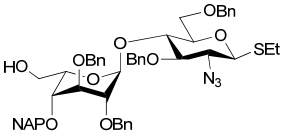
[α]$_D$: -15.9 (*c* 2.0 $CHCl_3$)

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.29 – 8.21 (m, 1H, Ar), 7.82 (dd, *J* = 7.0, 3.0 Hz, 2H, Ar), 7.66 (d, *J* = 6.8 Hz, 1H, Ar), 7.48 – 7.17 (m, 23H, Ar, $CDCl_3$), 5.81 (s, 1H, NaphCH), 5.05 (d, *J* = 4.8 Hz, 1H, H1'), 4.95 (d, *J* = 11.1 Hz, 1H, $BnCH_2$), 4.76 (s, 1H, $BnCH_2$), 4.73 (d, *J* = 3.0 Hz, 1H, $BnCH_2$), 4.71 (d, *J* = 3.5 Hz, 1H, $BnCH_2$), 4.70 – 4.66 (m, 1H, $BnCH_2$), 4.63 (d, *J* = 3.9 Hz, 1H, $BnCH_2$), 4.61 (d, *J* = 3.8 Hz, 1H, $BnCH_2$), 4.49 (s, 2H, $BnCH_2$), 4.30 (d, *J* = 10.1 Hz, 1H, H1), 4.13 – 4.08 (m, 1H, H5'), 4.03 (t, *J* = 9.5 Hz, 1H, H4), 3.87 (d, *J* = 13.0 Hz, 1H, H6a'), 3.78 (dd, *J* = 8.5, 3.2 Hz, 1H, H3'), 3.71 (dd, *J* = 11.0, 2.0 Hz, 1H, H6a), 3.69 – 3.63 (m, 2H, H6b, H4'), 3.58 (dd, *J* = 8.5, 4.8 Hz, 1H, H2'), 3.48 (t, *J* = 9.7 Hz, 1H, H2), 3.43 – 3.34 (m, 2H, H3, H5), 3.28 (dd, *J* = 13.1, 2.2 Hz, 1H, H6b'), 2.76 (tdd, *J* = 12.6, 7.4, 5.2 Hz, 2H, SCH_2), 1.33 (t, *J* = 7.4 Hz, 3H, SCH_2CH_3).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 138.22 (Ar), 138.06 (Ar), 137.99 (Ar), 133.81 (Ar), 133.21 (Ar), 130.54 (Ar), 129.60 (Ar), 128.55 (Ar), 128.48 (Ar), 128.33 (Ar), 128.25 (Ar), 127.85 (Ar), 127.84 (Ar), 127.76 (Ar), 127.71 (Ar), 127.64 (Ar), 127.61 (Ar), 127.55 (Ar), 127.41 (Ar), 126.96 (Ar), 126.04 (Ar), 125.55 (Ar), 124.92 (Ar), 124.68 (Ar), 100.47 (C-1'), 99.87 (NaphCH), 84.33 (C-1), 83.96 (C-3), 80.12 (C-3'), 80.09 (C-5), 78.37 (C-5'), 77.91 (C-2'), 75.64 ($BnCH_2$), 73.93 ($BnCH_2$), 73.39 ($BnCH_2$), 72.87 ($BnCH_2$), 72.69 (C-4), 68.86 (C-6'), 68.48 (C-6), 66.56 (C-2), 62.19 (C-4'), 24.50 (SCH_2), 15.15 (SCH_2CH_3).

HRMS (ESI): Calc. for $C_{53}H_{55}N_3O_9NaS$ $[M+Na]^+$: 932.3557; found 932.3536.

Ethyl 2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl-α-L-idopyranosyl-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-1-thio-β-D-glucopyranoside (6)



5 (230 mg, 0.25 mmol, 1 eq) was dissolved in dry CH_2Cl_2 (5 ml) and put on ice. BH_3 (1M in THF, 1.26 ml, 1.26 mmol, 5 eq) and TMSOTf (4.8µl, 0.04 mmol, 0.15 eq) in CH_2Cl_2 were added slowly. Reaction was stirred at 0 °C for 2 h. Reaction was quenched with triethylamine (0.17 ml, 1.21 mmol, 4.8 eq) and MeOH (0.87 ml, 21.48 mmol, 85 eq). Solution was concentrated *in vacuo* and co-evaporated three times with MeOH. The residue was purified *via* chromatography using pentane/acetone (8-66%) giving **6** (190 mg, 0.21 mmol, 83%) as white solid.

R_f (cyclohexane/acetone 2:1): 0.38

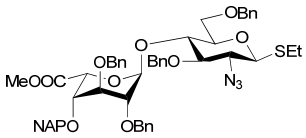
[α]$_D$: -23.4 (*c* 0.8 $CHCl_3$)

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.01 (d, *J* = 8.4 Hz, 1H, Ar), 7.87 – 7.80 (m, 2H, Ar), 7.50 – 7.35 (m, 4H, Ar), 7.35 – 7.19 (m, 16H, Ar, $CDCl_3$), 5.13 (d, *J* = 12.0 Hz, 1H, NaphCH_2), 4.98 – 4.92 (m, 2H, NaphCH_2, H1), 4.85 (d, *J* = 10.7 Hz, 1H, BnCH_2), 4.78 (d, *J* = 10.7 Hz, 1H, BnCH_2), 4.71 (d, *J* = 11.2 Hz, 1H, BnCH_2), 4.69 – 4.60 (m, 3H, BnCH_2), 4.50 (s, 2H, BnCH_2), 4.23 (d, *J* = 9.9 Hz, 1H, H1), 4.00 (t, *J* = 9.3 Hz, 1H, H4), 3.86 (dd, *J* = 11.4, 4.8 Hz, 1H, H5'), 3.77 (t, *J* = 7.1 Hz, 1H, H3'), 3.73 – 3.64 (m, 3H, H6ab), 3.61 – 3.51 (m, 1H, H6a'), 3.47 – 3.25 (m, 5H, H6b', H2', H2, H3, H5), 2.72 (tdd, *J* = 12.6, 7.4, 5.3 Hz, 2H, SCH_2), 1.73 (d, *J* = 5.0 Hz, 1H, 6'-OH), 1.30 (t, *J* = 7.4 Hz, 3H, SCH_2CH_3).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 138.31 (Ar), 138.15 (Ar), 137.98 (Ar), 137.76 (Ar), 133.77 (Ar), 133.28 (Ar), 131.67 (Ar), 128.93 (Ar), 128.55 (Ar), 128.37 (Ar), 128.34 (Ar), 128.32 (Ar), 128.30 (Ar), 127.93 (Ar), 127.87 (Ar), 127.77 (Ar), 127.75 (Ar), 127.70 (Ar), 127.65 (Ar), 126.96 (Ar), 126.34 (Ar), 125.90 (Ar), 125.13 (Ar), 123.98 (Ar), 98.99 (C-1'), 84.12 (C-1), 83.51 (C-5), 80.36 (C-2'), 79.81 (C-3), 79.73 (C-3'), 77.66 (C-4'), 75.64 (BnCH_2), 74.36 (BnCH_2), 74.17 (BnCH_2), 73.69 (C-4), 73.45 (BnCH_2), 71.48 (NaphCH_2), 71.34 (C-5'), 68.25 (C-6), 66.02 (C-2), 60.97 (C-6'), 24.28 (SCH_2), 15.13 (SCH_2CH_3).

HRMS (ESI) Calc. for $C_{53}H_{57}N_3O_9NaS$ $[M+Na]^+$: 934.3713; found 934.3702.

Ethyl (methyl [2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl- α-L-idopyranosyl]uronate)-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-1-thio-β-D-glucopyranoside (D8)



6 (154, 0.17 mmol, 1 eq) was dissolved in 2:1 CH_2Cl_2/H_2O (1.11 ml: 0.55 ml) and stirred vigorously. TEMPO (5.3 mg, 0.03 mmol, 0.2 eq) and BAIB (135.9 mg, 0.42 mmol, 3 eq) were added at once, stirring at RT for 20 min. Reaction was quenched with 10% aq. thiosulfate and stirred for 15 min. The layers were separated and the aq. layer was acidified with 1 M HCl and extracted three times with CH_2Cl_2. The combined org. phase was dried over $MgSO_4$ and concentrated *in vacuo*. Crude sugar was dissolved in dry MeOH (1.7 ml) and NMM (0.037 ml, 0.34 mmol, 2 eq) and DMTMM (93.9 mg, 0.34 mmol, 2 eq) were added. Stirring at RT for 2.5 h. Solvent was directly evaporated and residue was purified *via* chromatography using cyclohexane/acetone 2:1 to give **D8** (137 mg, 0.15 mmol, 86%) as yellow solid.

R_f (cyclohexane/acetone 2:1): 0.6

$[\alpha]_D$: -31.0 (*c* 1.0 $CHCl_3$)

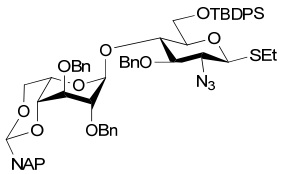
^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.01 (t, *J* = 9.2 Hz, 1H, Ar), 7.81 (ddd, *J* = 12.9, 12.2, 6.6 Hz, 2H, Ar), 7.72 – 7.67 (m, 1H, Ar), 7.50 – 7.42 (m, 1H, Ar), 7.40 – 7.31 (m, 5H, Ar), 7.31 – 7.21 (m, 15H, Ar, $CDCl_3$), 7.21 – 7.16 (m, 2H, Ar), 7.13 – 7.05 (m, 1H, Ar), 5.38 (t, *J* = 8.3 Hz, 1H, H1'), 5.08 (dd, *J* = 11.5, 4.7 Hz, 1H, $BnCH_2$), 5.04 – 4.96 (m, 1H, $BnCH_2$), 4.96 – 4.89 (m, 1H, $BnCH_2$), 4.71 (dd, *J* = 16.3, 8.0 Hz, 1H, $BnCH_2$), 4.70 – 4.61 (m, 4H, 2 $BnCH_2$), 4.54 – 4.46 (m, 2H, H5', $BnCH_2$), 4.42 – 4.36 (m, 1H, $BnCH_2$), 4.26 – 4.18 (m, 1H, H1), 4.01 – 3.92 (m, 2H, H4, H4'), 3.91 (dd, *J* = 7.1, 5.7 Hz, 1H, H3), 3.72 – 3.66 (m, 2H, H6ab), 3.44 – 3.29 (m, 7H, OMe, H2, H2', H5, H3'), 2.81 – 2.58 (m, 2H, SCH_2), 1.33 – 1.20 (m, 3H, SCH_2CH_3).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 169.73 (COOMe), 138.33 (Ar), 138.27 (Ar), 138.17 (Ar), 138.05 (Ar), 137.48 (Ar), 133.72 (Ar), 133.13 (Ar), 131.72 (Ar), 130.22 (Ar), 128.93 (Ar), 128.44 (Ar), 128.32 (Ar), 128.22 (Ar), 128.17 (Ar), 128.14 (Ar), 127.84 (Ar), 127.75 (Ar), 127.65 (Ar), 127.63 (Ar), 127.57 (Ar), 127.44 (Ar), 127.31 (Ar), 126.87 (Ar), 126.21 (Ar), 125.82 (Ar), 125.11 (Ar), 124.19 (Ar), 99.74 (C-1'), 83.92 (C-1), 83.22 (C-3), 80.46 (C-2'), 79.68 (C-5), 78.63 (C-4'), 75.71 (C-4), 75.30 ($BnCH_2$), 74.48 ($BnCH_2$), 74.34 ($BnCH_2$), 73.20 ($BnCH_2$), 71.88 (C-5'), 71.54 ($BnCH_2$), 68.25 (C-6), 65.71 (C-2), 51.59 (OMe), 26.92, 24.33 (SCH_2), 15.14 (SCH_2CH_3).

HRMS (ESI): Calc. for $C_{54}H_{57}N_3O_{10}NaS$ $[M+Na]^+$: 962.3662; found 962.3638.

Synthesis of D9

Ethyl 2,3-di-*O*-benzyl-4,6-*O*-(1-naphthyl)methylidene-α-L-idopyranosyl-(1⟶4)-2-azido-3-*O*-benzyl-2-deoxy-6-*O*-(*tert*-butyldiphenylsilyl)-1-thio-β-D-glucopyranoside (7)



4 (522 mg, 0.54 mmol, 1 eq) was dissolved in dry DMF (14 ml) and put on ice. BnBr (0.06 ml, 0.54 mmol, 1 eq) and sodium hydride (60% dispersion, 43 mg, 1.08 mmol, 2 eq) were added. Stirring at 0 °C for 1 h. Reaction was quenched with MeOH and solvent was evaporated *in vacuo*. Residue was diluted with CH_2Cl_2 (20 ml) washed with water (2 x 40 ml). Org. phase was dried over $MgSO_4$, filtered and evaporated. Purification *via* chromatography using pentane/EtOAc (4-32%) gave **7** (528 mg, 0.50 mmol, 92%) as colourless resin.

R_f (cyclohexane/EtOAc 5:1): 0.46

$[\alpha]_D$: -32.8 (*c* 1.0 $CHCl_3$)

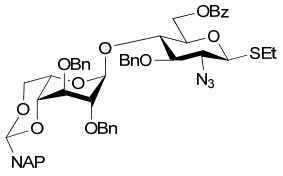
^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.34 (d, *J* = 8.5 Hz, 1H, Ar), 7.84 – 7.68 (m, 6H, Ar), 7.60 (d, *J* = 6.8 Hz, 1H, Ar), 7.44 – 7.09 (m, 21H, Ar), 5.78 (s, 1H, NaphCH), 5.29 (d, *J* = 4.3 Hz, 1H, H1'),

4.92 (d, *J* = 11.0 Hz, 1H, $BnCH_2$), 4.73 (d, *J* = 11.0 Hz, 1H, $BnCH_2$), 4.61 (dq, *J* = 34.8, 11.7 Hz, 4H, 2 $BnCH_2$), 4.31 (d, *J* = 10.1 Hz, 1H, H1), 4.22 (t, *J* = 9.5 Hz, 1H, H4), 4.10 – 4.02 (m, 1H, H4'), 3.97 – 3.89 (m, 3H, H6ab, H6'a), 3.75 (dd, *J* = 8.0, 3.2 Hz, 1H, H3'), 3.58 – 3.49 (m, 2H, H2, H2'), 3.38 (t, *J* = 9.3 Hz, 1H, H3), 3.29 (dd, *J* = 12.5, 2.4 Hz, 2H, H5', H6'b), 2.83 – 2.65 (m, 2H, SCH_2), 1.35 – 1.22 (m, 3H, SCH_2CH_3), 1.07 (s, 9H, ^{t}Bu).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 138.18 (Ar), 138.11 (Ar), 138.06 (Ar), 135.91 (Ar), 135.66 (Ar), 133.88 (Ar), 133.43 (Ar), 133.40 (Ar), 133.22 (Ar), 130.57 (Ar), 129.60 (Ar), 129.54 (Ar), 128.43 (Ar), 128.29 (Ar), 128.17 (Ar), 128.10 (Ar), 127.88 (Ar), 127.79 (Ar), 127.72 (Ar), 127.70 (Ar), 127.68 (Ar), 127.54 (Ar), 127.46 (Ar), 127.40 (Ar), 126.03 (Ar), 125.53 (Ar), 125.11 (Ar), 124.98 (Ar), 124.81 (Ar), 100.56 (NaphCH), 99.78 (C-1'), 84.00 (C-1), 83.78 (C-3), 80.76 (C-5), 79.50 (C-3'), 77.95 (C-4'), 77.20 (C-2'), 75.65 ($BnCH_2$), 73.58 ($BnCH_2$), 72.79 ($BnCH_2$), 71.53 (C-4), 68.97 (C-6'), 66.49 (C-2), 62.59 (C-6), 61.75 (C-5'), 29.69 (^{t}Bu), 26.82 (^{t}Bu), 23.92 (SCH_2), 19.38, 14.87 (SCH_2CH_3).

HRMS (ESI): Calc. for $C_{62}H_{67}N_3O_9NaSiS$ $[M+Na]^+$: 1080.4265; found 1080.4255.

Ethyl 2,3-di-*O*-benzyl-4,6-*O*-(1-naphthyl)methylidene-α-L-idopyranosyl-(1⟶4)-2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-1-thio-β-D-glucopyranoside (8)



7 (476 mg, 0.45 mmol, 1 eq) was dissolved in dry THF (5 ml) and TBAF (1 M in THF, 0.49 ml, 0.49 mmol, 1.1 eq) was added. Stirring at RT for 1 h, stirring at 60 °C. Solvent was directly evaporated and the residue was purified *via* column chromatography using toluene/acetone (2-22%) to give ethyl 2,3-di-*O*-benzyl-4,6-*O*-(1-naphthyl)methylidene-α-L-idopyranosyl-(1⟶4)-2-azido-3-*O*-benzyl-2-deoxy-1-thio-β-D-glucopyranoside (306 mg, 0.37 mmol, 86%) as white solid; R_f (cyclohexane/acetone 8:1): 0.54; $[\alpha]^T_D$: -47.162 (*c* 0.7 $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.29 – 8.23 (m, 1H, Ar), 7.85 – 7.78 (m, 2H, Ar), 7.66 (d, *J* = 6.6 Hz, 1H, Ar), 7.50 – 7.26 (m, 15H, Ar), 5.82 (s, 1H, NaphCH), 5.10 (d, *J* = 4.6 Hz, 1H, H1'), 4.94 (d, *J* = 11.0 Hz, 1H, $BnCH_2$), 4.82 – 4.60 (m, 5H, 2.5 $BnCH_2$), 4.34 (d, *J* = 9.9 Hz, 1H, H1), 4.12 – 4.09 (m, 1H, H4'), 3.92 (dd, *J* = 18.3, 8.8 Hz, 2H, H4, H6'a), 3.88 – 3.79 (m, 2H, H5', H6a), 3.72 (ddd, *J* = 12.3, 7.5, 4.9 Hz, 1H, H6b), 3.68 (s, 1H, H3'), 3.60 (dd, *J* = 8.1, 4.7 Hz, 1H, H2'), 3.42 (dt, *J* = 29.4, 9.3 Hz, 2H, H2, H3), 3.36 – 3.29 (m, 2H, H6'b, H5), 2.83 – 2.68 (m, 2H, SCH_2), 1.97 (dd, *J* = 7.4, 6.0 Hz, 1H, 6-OH), 1.39 – 1.29 (m, 3H, SCH_2CH_3); ^{13}C-NMR (126 MHz, $CDCl_3$) δ = 169.73 (COOMe), 138.33

(Ar), 138.27 (Ar), 138.17 (Ar), 138.05 (Ar), 137.48 (Ar), 133.72 (Ar), 133.13 (Ar), 131.72 (Ar), 130.22 (Ar), 128.93 (Ar), 128.44 (Ar), 128.32 (Ar), 128.22 (Ar), 128.17 (Ar), 128.14 (Ar), 127.84 (Ar), 127.75 (Ar), 127.65 (Ar), 127.63 (Ar), 127.57 (Ar), 127.44 (Ar), 127.31 (Ar), 126.87 (Ar), 126.21 (Ar), 125.82 (Ar), 125.11 (Ar), 124.19 (Ar), 99.74 (C-1'), 83.92 (C-1), 83.22 (C-3), 80.46 (C-2'), 79.68 (C-5), 78.63 (C-4'), 75.71 (C-4), 75.30 ($BnCH_2$), 74.48 ($BnCH_2$), 74.34 ($BnCH_2$), 73.20 ($BnCH_2$), 71.88 (C-5'), 71.54 ($BnCH_2$), 68.25 (C-6), 65.71 (C-2), 51.59 (OMe), 26.92, 24.33 (SCH_2), 15.14 (SCH_2CH_3); HR-MS: $C_{46}H_{49}N_3O_9NaS$ [MNa^-]: 842.3087; found 842.3099. The desilylated compound (265 mg, 0.32 mmol, 1 eq) was dissolved in dry CH_2Cl_2 (1 ml) and pyridine (0.22 ml) and put on ice. BzCl (0.06 ml, 0.51 mmol, 1.6 eq) in CH_2Cl_2 (0.42 ml) was added dropwise. The mixture was warmed to RT and stirred overnight. Reaction was put on ice and quenched with water, diluted with CH_2Cl_2 (6 ml), washed with 2 M aq. HCl, sat. aq. $NaHCO_3$ and water. The org. phase was dried over $MgSO_4$ and concentrated *in vacuo*. Residue was purified *via* chromatography using pentane/acetone (8-66%) giving **8** (265 mg, 0.29 mmol, 90%) as white solid.

R_f (cyclohexane/acetone 2:1): 0.43

$[\alpha]_D$: -12.1 (*c* 1.0 $CHCl_3$)

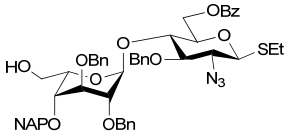
^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.27 (d, *J* = 8.5 Hz, 1H, Ar), 8.10 (dd, *J* = 8.3, 1.2 Hz, 1H, Ar), 8.08 – 8.04 (m, 2H, Ar), 7.81 (d, *J* = 8.2 Hz, 2H, Ar), 7.66 – 7.58 (m, 1H, Ar), 7.56 – 7.45 (m, 2H, Ar), 7.45 – 7.19 (m, 18H, Ar), 5.82 (s, 1H, NaphCH), 5.12 (d, *J* = 4.4 Hz, 1H, H1'), 4.95 (d, *J* = 10.8 Hz, 1H, $BnCH_2$), 4.82 (dd, *J* = 12.0, 2.0 Hz, 1H, H6a), 4.76 (dd, *J* = 11.3, 5.8 Hz, 2H, $BnCH_2$), 4.65 (dt, *J* = 16.5, 11.7 Hz, 3H, $BnCH_2$), 4.35 (d, *J* = 10.0 Hz, 1H, H1), 4.26 (dd, *J* = 12.0, 5.9 Hz, 1H, H6b), 4.11 – 4.07 (m, 1H, H4'), 4.02 (t, *J* = 9.4 Hz, 1H, H4), 3.94 (d, *J* = 12.8 Hz, 1H, H6'a), 3.81 (dd, *J* = 7.8, 3.1 Hz, 1H, H3'), 3.74 (s, 1H, H5'), 3.67 – 3.56 (m, 2H, H5, H2'), 3.50 (t, *J* = 9.7 Hz, 1H, H2), 3.46 – 3.34 (m, 2H, H6'b, H3), 2.79 – 2.60 (m, 2H, SCH_2), 1.26 (t, *J* = 7.5 Hz, 3H, SCH_2CH_3).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 165.95 (OBz), 138.01 (Ar), 137.93 (Ar), 137.86 (Ar), 133.82 (Ar), 133.07 (Ar), 129.72 (Ar), 129.65 (Ar), 128.50 (Ar), 128.47 (Ar), 128.43 (Ar), 128.34 (Ar), 128.25 (Ar), 127.95 (Ar), 127.92 (Ar), 127.87 (Ar), 127.75 (Ar), 127.62 (Ar), 127.58 (Ar), 126.02 (Ar), 125.53 (Ar), 124.85 (Ar), 124.79 (Ar), 100.58 (C-1'), 100.22 (NaphCH), 84.24 (C-1), 83.73 (C-3), 79.44 (C-3'), 78.09 (C-5), 77.63 (C-4'), 77.14 (C-2'), 75.75 ($BnCH_2$), 73.83 ($BnCH_2$), 73.11

(C-4), 72.83 ($BnCH_2$), 68.96 (C-6'), 66.55 (C-2), 62.14 (C-5'), 26.92, 24.59 (SCH_2), 15.04 (SCH_2CH_3).

HRMS (ESI): Calc. for $C_{53}H_{53}N_3O_{10}NaS$ $[M+Na]^+$: 946.3349; found 946.3369.

Ethyl 2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl-α-L-idopyranosyl-(1→4)-2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-1-thio-β-D-glucopyranoside (9)



8 (1.103 g, 1.19 mmol, 1 eq) was dissolved in dry CH_2Cl_2 (24 ml) and put on ice. BH_3 (1 M in THF, 5.97 ml, 5.97 mmol, 5 eq) and TMSOTf (22 µl, 0.18 mmol, 0.15 eq) were added slowly and reaction was stirred at 0 °C for 1.5 h. Reaction was quenched with triethylamine (0.81 ml, 5.73 mmol, 4.8 eq) and MeOH (4.11 ml, 101.40 mmol, 85 eq) and the solution was concentrated and co-evaporated three times with MeOH. The residue was purified *via* column chromatography using toluene/acetone (2-20%) to give **9** (846 mg, 0.81 mmol, 71%) as white solid.

R_f (toluene/acetone 9:1): 0.30

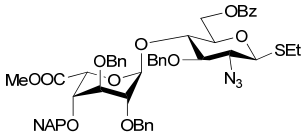
$[\alpha]_D$: -22.7 (*c* 0.9 $CHCl_3$)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.02 (dt, *J* = 8.2, 4.1 Hz, 3H, Ar), 7.84 (dd, *J* = 16.6, 8.1 Hz, 2H, Ar), 7.59 – 7.53 (m, 1H, Ar), 7.51 – 7.18 (m, 19H, Ar), 5.09 (d, *J* = 12.0 Hz, 1H, $BnCH_2$), 4.93 (dd, *J* = 14.8, 8.5 Hz, 2H, $BnCH_2$, H1'), 4.85 – 4.78 (m, 2H, $BnCH_2$), 4.72 – 4.68 (m, 1H, H6a), 4.64 (t, *J* = 9.1 Hz, 2H, $BnCH_2$), 4.54 (d, *J* = 11.4 Hz, 1H, $BnCH_2$), 4.32 – 4.26 (m, 2H, H1, H6b), 3.98 – 3.91 (m, 1H, H4), 3.89 (dt, *J* = 6.8, 4.6 Hz, 1H, H5'), 3.78 – 3.72 (m, 1H, H3'), 3.61 (dd, *J* = 5.6, 4.5 Hz, 1H, H4), 3.58 – 3.47 (m, 2H, H6a', H5'), 3.46 – 3.36 (m, 3H, H2, H2', H3), 3.34 – 3.27 (m, 1H, H6b'), 2.74 – 2.60 (m, 2H, SCH_2), 1.54 (d, *J* = 6.3 Hz, 1H, 6'- OH), 1.24 (t, *J* = 7.4 Hz, 3H, SCH_2CH_3).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 165.86 (OBz), 138.11 (Ar), 137.99 (Ar), 137.45 (Ar), 133.87 (Ar), 133.15 (Ar), 129.69 (Ar), 128.97 (Ar), 128.39 (Ar), 128.37 (Ar), 128.35 (Ar), 128.26 (Ar), 127.98 (Ar), 127.81 (Ar), 127.77 (Ar), 127.08 (Ar), 126.30 (Ar), 126.05 (Ar), 124.99 (Ar), 124.05 (Ar), 99.63 (C-1'), 84.11 (C-2'), 83.45 (C-1), 79.13 (C-3), 78.55 (C-3'), 77.79 (C-5), 76.03 (C-4'), 75.76 ($BnCH_2$), 74.15 (C-4), 73.88 (2 $BnCH_2$), 71.29 ($BnCH_2$), 70.84 (C-5'), 66.13 (C-2'), 62.98 (C-6'), 61.34 (C-6), 24.43 (SCH_2), 15.01 (SCH_2CH_3).

HRMS (ESI): Calc. for $C_{53}H_{55}N_3O_{10}NaS$ $[M+Na]^+$: 948.3506; found 948.3515.

Ethyl (methyl [2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl-α-L-idopyranosyl] uronate)-(1→4)-2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-1-thio-β-D-glucopyranoside (D9)



9 (832 mg, 0.90 mmol, 1 eq) was dissolved in 2:1 CH_2Cl_2/H_2O (2.96 ml : 1.48 ml) and stirred vigorously. TEMPO (28 mg, 0.18 mmol, 0.2 eq) and BAIB (723 mg, 2.24 mmol, 2.5 eq) were added at RT, stirring for 1 h. Reaction was quenched with 10% aq. thiosulfate and stirred for 15 min. The layers were separated and the aq. layer was acidified with 1 M HCl and three times extracted with CH_2Cl_2. The combined org. phase was dried over $MgSO_4$, filtered and evaporated. Residue was dissolved in dry MeOH (9 ml) and NMM (0.20 ml, 1.80 mmol, 2 eq) and DMTMM (497 mg, 1.80 mmol, 2 eq). Reaction was stirred for 1.5 h. The solvent was directly evaporated and the residue was purified via chromatography using toluene/acetone (2-20%) to give **D9** (578 mg, 0.63 mmol, 67%) as white solid.

R_f (toluene/acetone 14:1): 0.57

$[\alpha]_D$: -27.0 (*c* 1.1 $CHCl_3$)

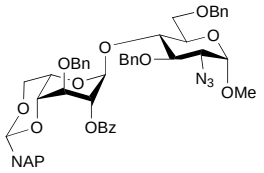
^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.06 – 7.96 (m, 3H, Ar), 7.85 – 7.77 (m, 2H, Ar), 7.70 (dd, *J* = 8.2, 1.0 Hz, 1H, Ar), 7.53 (t, *J* = 7.4 Hz, 1H, Ar), 7.47 – 7.32 (m, 8H, Ar), 7.31 – 7.21 (m, 13H, Ar), 7.20 – 7.11 (m, 5H, Ar), 5.42 (d, *J* = 6.3 Hz, 1H, Ar), 5.03 (d, *J* = 11.8 Hz, 1H, H1'), 4.99 – 4.91 (m, 2H, $ArCH_2$), 4.73 (dd, *J* = 15.8, 5.9 Hz, 2H, H6a, $ArCH_2$), 4.65 (s, 2H, $ArCH_2$), 4.61 – 4.54 (m, 3H, $ArCH_2$, H5'), 4.40 (dd, *J* = 12.1, 4.9 Hz, 1H, H6b), 4.27 (d, *J* = 9.6 Hz, 1H, H1), 4.04 – 3.98 (m, 1H, H4), 3.93 – 3.89 (m, 1H, H4'), 3.85 (t, *J* = 6.7 Hz, 1H, H3'), 3.53 – 3.47 (m, 1H, H5), 3.42 (dt, *J* = 12.9, 7.2 Hz, 3H, H2, H3, H2'), 3.32 (s, 3H, OMe), 2.74 – 2.55 (m, 2H, SCH_2), 1.22 (dd, *J* = 9.5, 5.3 Hz, 3H, SCH_2CH_3).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 169.80 (C-6'), 165.90 (OBz), 138.13 (Ar), 138.05 (Ar), 137.85 (Ar), 133.71 (Ar), 132.99 (Ar), 132.85 (Ar), 131.71 (Ar), 130.07 (Ar), 129.84 (Ar), 129.03 (Ar), 128.95 (Ar), 128.40 (Ar), 128.36 (Ar), 128.33 (Ar), 128.32 (Ar), 128.22 (Ar), 127.88 (Ar), 127.78 (Ar), 127.70 (Ar), 127.67 (Ar), 127.65 (Ar), 126.90 (Ar), 126.23 (Ar), 125.83 (Ar), 125.29 (Ar), 125.07 (Ar), 124.23 (Ar), 99.69 (C-1'), 83.80 (C-1), 82.94 (C-3), 80.05 (C-2'), 78.12 (C-3'), 77.66 (C-3), 76.45 (C-4'), 75.98 (C-4), 75.49 ($ArCH_2$), 74.21 ($ArCH_2$), 74.20 ($ArCH_2$), 71.90 (C-5'), 71.41 ($ArCH_2$), 65.74 (C-2), 62.72 (C-6), 51.52 (OMe), 24.32 (SCH_2), 21.45, 15.02 (SCH_2CH_3).

HRMS (ESI): Calc. for $C_{54}H_{55}N_3O_{11}NaS$ $[M+Na]^+$: 976.3455; found 976.3414.

Synthesis of D10

Methyl 2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-(1-naphthyl)methylidene-α-L-idopyranosyl-(1→4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (14)



11 (399 mg, 0.19 mmol, 1 eq) and **13** (725 mg, 1.199 mmol, 1.2 eq) were dried together with 4 Å MS (510 mg) for 2 h at Schlenckline, then dissolved in dry CH_2Cl_2 (5.1 ml), cooled to 0 °C and stirred for 30 min. DMTST (481 mg, 2.139 mmol, 2.1 eq) was added at once, mixture was allowed to attain RT. After stirring for 2.5 h, another portion of **13** (100 mg, 0.17 mmol, 0.9 eq) was added, stirring for another 2.5 h. Reaction was cooled to 0 °C, triethylamine (7.2 ml) was added and filtered through a pad of Celite. Mixture was diluted with CH_2Cl_2 (140 ml) and washed with 2 M HCl (70 ml), sat. aq. $NaHCO_3$ (70 ml), and water (70 ml). Org. phase was dried over $MgSO_4$, filtered and concentrated. Residue was purified *via* chromatography using toluene/acetone (6-50%) to give **14** (614 mg, 0.69 mmol, 69%) as white solid.

R_f (toluene/acetone 15:1): 0.55

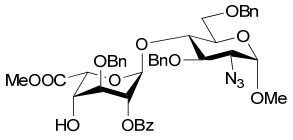
$[\alpha]_D$: -3.7 (*c* 1.6 $CHCl_3$)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.46 (d, *J* = 8.6 Hz, 1H, Ar), 7.81 (dd, *J* = 15.4, 8.1 Hz, 2H, Ar), 7.73 (d, *J* = 7.2 Hz, 2H, Ar), 7.64 (d, *J* = 6.9 Hz, 1H, Ar), 7.43 – 7.11 (m, 19H, Ar, $CDCl_3$), 7.01 (t, *J* = 7.8 Hz, 2H, Ar), 5.82 (s, 1H, NaphCH), 5.29 – 5.25 (m, 2H, H1', H2'), 4.84 (dd, *J* = 13.2, 7.3 Hz, 3H, $BnCH_2$, H1), 4.68 (dd, *J* = 13.5, 11.4 Hz, 2H, $BnCH_2$), 4.53 (q, *J* = 11.9 Hz, 2H, $BnCH_2$), 4.14 (t, *J* = 9.6 Hz, 1H, H4), 4.04 (s, 1H, H4'), 3.87 (ddd, *J* = 16.2, 14.0, 8.4 Hz, 5H, H3, H5, H6a, H3', H6'a), 3.79 (s, 1H, H5'), 3.76 – 3.67 (m, 1H, H6b), 3.53 (dd, *J* = 10.2, 3.6 Hz, 1H, H2), 3.45 (s, 3H, OMe), 3.16 (dd, *J* = 12.7, 1.3 Hz, 1H, H6'b).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 165.93 (OBz), 138.29 (Ar), 137.71 (Ar), 137.61 (Ar), 133.94 (Ar), 133.53 (Ar), 132.97 (Ar), 130.59 (Ar), 130.01 (Ar), 129.69 (Ar), 129.19 (Ar), 129.02 (Ar), 128.42 (Ar), 128.33 (Ar), 128.28 (Ar), 128.21 (Ar), 128.12 (Ar), 128.09 (Ar), 128.03 (Ar), 127.81 (Ar), 127.58 (Ar), 127.53 (Ar), 127.18 (Ar), 126.25 (Ar), 125.57 (Ar), 125.33 (Ar), 125.15 (Ar), 124.74 (Ar), 101.52 (NaphCH), 98.66 (C1), 97.65 (C1'), 79.13 (C5), 74.89 (C3'), 74.69 ($BnCH_2$), 73.82 (C5'), 73.40 (C4), 73.36 ($BnCH_2$), 72.14 ($BnCH_2$), 70.95 (C3), 69.33 (C6'), 68.26 (C6), 66.78 (C2), 64.13 (C2'), 59.79 (C4'), 55.32 (1-OMe).

HRMS (ESI): Calc. for $C_{41}H_{45}N_3O_{11}NaS$ $[M+Na]^+$: 778.2952; found 778.2972.

Methyl [methyl (2-*O*-benzoyl-3-*O*-benzyl-α-L-idopyranosyl) uronate]-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (D10)



14 (459 mg, 0.51 mmol, 1 eq) was dissolved in dry MeOH/CH_2Cl_2 (26.1 ml: 12.2ml) and camphor-10-sulfonic acid (83 mg, 0.36 mmol, 0.7 eq) was added. Reaction was stirred at RT for 15 h and then quenched with triethylamine (0.22 ml, 1.54 mmol, 3 eq). Solvent was evaporated and residue purified *via* chromatography using pentane/EtOAc (4-32%) giving methyl 2-*O*-benzoyl-3-*O*-benzyl-α-L-idopyranose-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (277 mg, 0.37 mmol, 72%) as white solid; R_f (cyclohexane/EtOAc 2:1): 0.32; $[\alpha]^T_D$: +19.467 (*c* 1.5 $CHCl_3$); ^{1}H-NMR (500 MHz, $CDCl_3$) δ = 7.97 (d, *J* = 7.9 Hz, 2H, Ar), 7.57 (dd, *J* = 10.7, 4.2 Hz, 1H, Ar), 7.48 – 7.40 (m, 3H, Ar), 7.37 (dd, *J* = 11.1, 3.8 Hz, 2H, Ar), 7.34 – 7.12 (m, 12H, Ar, $CDCl_3$), 5.20 (s, 1H, H2'), 5.10 (s, 1H, H1'), 4.80 (dd, *J* = 19.9, 11.4 Hz, 3H, $BnCH_2$, H1), 4.63 (dd, *J* = 26.4, 10.9 Hz, 2H, $BnCH_2$), 4.49 (q, *J* = 12.1 Hz, 2H, $BnCH_2$), 4.23 (s, 1H, H5'), 4.06 (t, *J* = 9.7 Hz, 1H, H4), 3.88 – 3.77 (m, 4H, H3, H3', H5, H6a), 3.67 (dd, *J* = 15.6, 10.0 Hz, 2H, H4', H6b), 3.49 (dd, *J* = 10.2, 2.3 Hz, 1H, H2), 3.44 (d, *J* = 0.8 Hz, 3H, 1-OMe), 3.29 – 3.22 (m, 1H, H6'a), 3.16 (dd, *J* = 11.0, 5.2 Hz, 1H, H6'b), 2.75 (d, *J* = 8.7 Hz, 1H, 4'-OH), 1.38 (t, *J* = 6.2 Hz, 1H, 6'-OH); ^{13}C-NMR (126 MHz, $CDCl_3$) δ = 165.38 (OBz), 137.72 (Ar), 137.69 (Ar), 137.57 (Ar), 133.62 (Ar), 129.77 (Ar), 129.24 (Ar), 129.02 (Ar), 128.60 (Ar), 128.49 (Ar), 128.34, 128.23 (Ar), 128.21 (Ar), 128.17 (Ar), 127.89 (Ar), 127.78 (Ar), 127.61 (Ar), 127.54 (Ar), 125.28 (Ar), 98.61 (C-1), 97.30 (C-1'), 79.28 (C-5), 75.64 (C-3'), 75.31 ($BnCH_2$), 73.25 ($BnCH_2$), 73.13 (C-4), 72.35 ($BnCH_2$), 70.88 (C-3), 68.18 (C-6), 68.10 (C-2'), 67.93 (C-4'), 66.59 (C-5'), 64.29 (C-2), 62.63 (C-6'), 55.33 (1-OMe); HR-MS: calc. for $C_{52}H_{51}N_3O_{11}NaS$ [MNa^-]: 916.3421; found 916.3405. The obtained 4',6'-diol (561 mg, 0.75 mmol, 1eq) was dissolved in 1:1 CH_2Cl_2/water (7.4 ml : 7.4 ml) and stirred vigorously. TEMPO (23.2 mg, 0.15 mmol, 0.2 eq) and BAIB (598 mg, 1.86 mmol, 2.5 eq) were added at once, stirring at RT for 2 h. Reaction was quenched with thiosulfate, stirring for 15 min. The layers were separated and the aq. layer was acidified with 1M HCl and extracted three times with CH_2Cl_2. The combined org. phase was dried over $MgSO_4$ and concentrated *in vacuo*. Residue was dissolved in dry DMF (7.4 ml) and potassium carbonate (205 mg, 1.48 mmol, 2 eq) and methyl iodide (0.92 ml, 1.48 mmol, 2 eq) were added. Reaction was stirred at RT over night. Solvent was directly evaporated and residue was purified *via* chromatography using cyclohexane/EtOAc (5-60%), giving **D10** (408 mg, 0.53 mmol, 70%) as slightly orange resin.

R_f (Cyclohexane/EtOAc 3:1): 0.19

$[\alpha]_D$: +39.7 (*c* 1.1 $CHCl_3$)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.99 – 7.88 (m, 2H, Ar), 7.59 (t, *J* = 7.4 Hz, 1H, Ar), 7.47 – 7.12 (m, 16H, Ar, CDCl3), 5.30 (s, 1H, H1'), 5.20 (d, *J* = 1.2 Hz, 1H, H2'), 4.95 (d, *J* = 2.0 Hz, 1H, H5'), 4.83 – 4.73 (m, 3H, H1, $BnCH_2$), 4.68 (d, *J* = 11.3 Hz, 2H, $BnCH_2$), 4.53 (s, 2H, $BnCH_2$), 4.11 – 4.05 (m, 1H, H4), 4.01 – 3.99 (m, 1H, H4'), 3.92 – 3.86 (m, 1H, H3'), 3.86 – 3.77 (m, 3H, H3, H5, H6a), 3.66 (d, *J* = 9.2 Hz, 1H, H6b), 3.46 (dd, *J* = 10.3, 3.7 Hz, 1H, H2), 3.42 (t, *J* = 4.5 Hz, 6H, 1-OMe, 6'-OMe), 2.72 (d, *J* = 10.9 Hz, 1H, 4'-OH).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 169.54 (C-6'), 165.07 (COOPh), 137.94 (Ar), 137.74 (Ar), 137.36 (Ar), 133.72 (Ar), 129.74 (Ar), 128.99 (Ar), 128.92 (Ar), 128.61 (Ar), 128.47 (Ar), 128.26 (Ar), 128.19 (Ar), 128.12 (Ar), 128.07 (Ar), 128.04 (Ar), 127.64 (Ar), 127.54 (Ar), 127.20 (Ar), 127.18 (Ar), 98.65 (C-1), 97.77 (C-1'), 78.65 (C-5), 74.93 (C-4), 74.77 (C-3'), 74.28 ($BnCH_2$), 73.35 ($BnCH_2$), 72.40 ($BnCH_2$), 70.69 (C-3), 68.33 (C-5'), 68.16 (C-6), 67.98 (C-4'), 67.82 (C-2'), 63.74 (C-2), 55.30 (6'-OMe), 51.94 (1-OMe).

HRMS (ESI): Calc. for $C_{42}H_{44}N_3O_{12}Na$ $[M+Na]^+$: 782.2925; found 782.2957.

Synthesis of Hexasaccharides HX1-HX5

Results and Discussion (expanded from main manuscript)

Optimized conditions were worked out for the synthesis of hexasaccharide **H2** (**Scheme 1b**). Of promoters tested in the coupling between acceptor **D5** and donor **D4** the Me_2S/Tf_2O system developed by Tati and Fügedi[22] showed the best result, and, using a CH_2Cl_2/Et_2O solvent system at -40 °C, a 70% yield of tetrasaccharide **T3** was obtained as a 3:1 α/β -mixture that could easily be separated by silica gel chromatography. After removal of the chloroacetyl group using DABCO, to give acceptor **T4**, the same conditions were tried in a glycosylation with donor **D3** to afford hexasaccharide **H2**. A similar result as for tetrasaccharide **T3** was obtained (60%, 3:1 α/β ratio), but this time separation of anomers was not possible, why improvement of stereoselectivity in the glycosylation was investigated. There is literature precedence that lowering the temperature in glycosylations with 2-azido-2-deoxy-glucose donors increase β-selectivity,[23,24] why glycosylations at higher temperature than -40 °C was investigated. An optimal temperature, considering yield and α-selectivity, was found to be -10 °C which afforded a 78% yield of **H2** in higher than 15:1 α/β-ratio, simplifying the separation of the α-anomer. These conditions were then also tried on the first coupling to give tetrasaccharide **T3**, the overall yield was not improved (66%) but the α-selectivity was found to be complete at this temperature. These general conditions were then applied to all other glycosylations in the synthesis of targets **HX1-HX5** with good to excellent results (yields 55-98%, α/β ratios from 3:1 to complete α-selectivity, **Table S1**). Only in one coupling, the one between donor **D1** and the iduronic acceptor **D10** to give tetrasaccharide **T9** (**Figure S13**) the conditions failed and further optimization was required. Other thiophilic promoters were tested and NIS/AgOTf was found to afford tetrasaccharide **T9** but only in a 47% yield and with low stereoselectivity (α/β 2:1). The failure of the "general" conditions in this glycosylation is probably due to the fact that in this coupling the acceptor is iduronic and not glucuronic, as in all the other couplings. We have earlier experienced low yields in couplings between thiosaccharide donors and iduronic acceptors and in these cases a change to a trichloroacetimidate donor has solved the problem. Hence, thiodisaccharide **D1** was hydrolysed (→$\mathbf{D1_{OH}}$) and then converted to the corresponding trichloroacetimidate donor $\mathbf{D1_{TCA}}$, which was used in a TBDMSOTf-promoted coupling to **D10** in toluene to afford tetrasaccharide **T9** in 85% yield (α/β 7:1).

Experimental

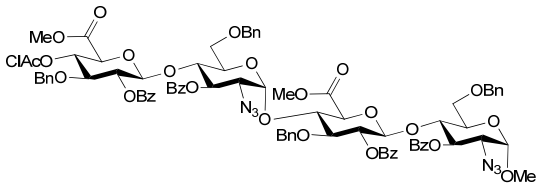
Glycosylations

Preparation of Me_2S_2/Tf_2O promoter solution

A round-bottomed flask was cooled to 0°C under an Ar atmosphere before 1.5 ml of dry CH_2Cl_2 was added to it. Then 190 µL of dimethyldisulfide (Me_2S_2) and 330 µL of triflic anhydride (Tf_2O) were successively added. The solution was quickly mixed then stored at 4 °C for 30 min where it should turn light brown. This procedure provides a 1M solution of the promotor in CH_2Cl_2.

Hexasaccharide H1

Methyl [methyl (2-*O*-benzoyl-3-*O*-benzyl-4-*O*-chloroacetyl-β-D-glucopyranosyl) uronate]-(1→4)-(2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1→4)-2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-α-D-glucopyranoside (T1)



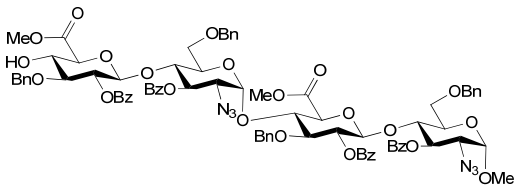
Compound **D1** (0.170 g, 0.188 mmol) and **D2** (0.1 g 0.125 mmol) were dissolved in CH_2Cl_2 (0.5 mL). After the mixture was completely dissolved, Et_2O (0.63 mL) was added. In a separate flask, Tf_2O (0.35 mL) was added drop wise to a solution of Me_2S_2 (0.2 mL) in CH_2Cl_2 (2 mL) at 0 °C and stirred for half an hour at 0 °C and used straight away at the half hour mark. (Colour should be golden yellow). The mixture of acceptor and donor was cooled to 0 °C and the solution of promoter (0.225 mL, 1M in CH_2Cl_2) was added. The reaction was vigorously stirred for 10 mins at 0 °C or until reaction was complete at which point the reaction was diluted with CH_2Cl_2 and washed with $NaHCO_3$ and once with brine. The organic phase was separated, dried with $MgSO_4$ and filtered. The filtrate was concentrated in vacuo and purified by silica gel chromatography (cyclohexane/EtOAc: 20:1 to 1:1) which afforded compound **T1** (0.180 g, 88%) in a 9:1 α/β ratio as a white foam.

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.08 (dd, *J* = 12.0, 4.2 Hz, 2H, Ar), 8.03 – 7.96 (m, 2H, Ar), 7.92 – 7.87 (m, 2H, Ar), 7.85 – 7.80 (m, 1H, Ar), 7.80 – 7.75 (m, 1H, Ar), 7.65 (t, *J* = 7.4 Hz, 1H, Ar), 7.56 (ddd, *J* = 12.0, 9.7, 4.7 Hz, 3H, Ar), 7.52 – 7.28 (m, 15H, Ar), 7.23 – 7.18 (m, 1H, Ar), 7.18 – 7.09 (m, 4H, Ar), 7.00 (ddt, *J* = 15.5, 7.3, 3.9 Hz, 4H, Ar), 5.58 (t, *J* = 9.8 Hz, 1H, H3), 5.52 –

5.47 (m, 1H, H3''), 5.45 – 5.38 (m, 1H, H1''), 5.18 – 5.00 (m, 3H, H2'', H2'''), 4.86 – 4.80 (m, 1H, H1), 4.74 – 4.65 (m, 2H, $BnCH_2$), 4.62 – 4.39 (m, 6H, $BnCH_2$, H1', H1'''), 4.36 – 4.18 (m, 3H, $BnCH_2$), 4.14 – 3.92 (m, 4H, H4, H4', H4''), 3.89 – 3.76 (m, 1H, $ClCH_2a$), 3.66 (m, 6H, H5, H6a, H3, H3''', H6''a, $ClCH_2b$), 3.61 – 3.48 (m, 3H, H6b, H5', H5'''), 3.47 – 3.32 (m, 7H, H6''b, 1-OMe, COOMe), 3.28 – 3.13 (m, 2H, H2'', H5''), 2.98 (d, J = 7.8 Hz, 3H, COOMe).

HRMS (ESI): Calc.for $C_{85}H_{83}ClN_6O_{26}Na$ $[M+Na]^+$: 1661.4943, found: 1661.4950.

Methyl [methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl 2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-α-D-glucopyranoside (T2)

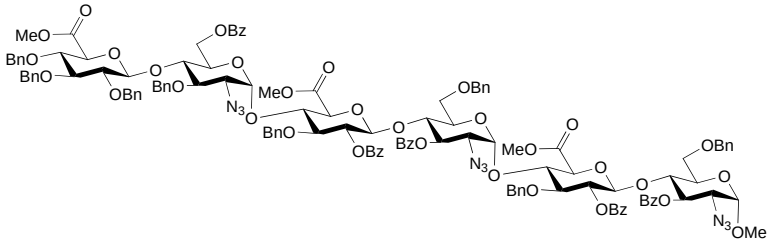


T1 (85 mg, 0.052 mmol, 1 eq) was dissolved in EtOH (2.5 ml) and DABCO (174 mg, 155 mmol, 30 eq) was added. Reaction was heated to 45 °C and stirred for 3.5h. Upon completion, reaction was diluted with EtOAc and washed with sat. aq. $NaHCO_3$, 1 M HCl and brine. Org. phase was dried with $MgSO_4$, filtered and residue was purified via chromatography using cyclohexane/EtOAc (8-66%) giving **T2** (65 mg, 0.04 mmol, 80%) as white solid.

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.07 – 8.02 (m, 2H, Ar), 7.99 (ddd, J = 14.5, 5.8, 1.2 Hz, 2H, Ar), 7.88 (dd, J = 7.6, 6.4 Hz, 1H, Ar), 7.86 – 7.83 (m, 1H, Ar), 7.82 – 7.75 (m, 1H, Ar), 7.64 (t, J = 7.4 Hz, 1H, Ar), 7.60 – 7.52 (m, 2H, Ar), 7.51 – 7.27 (m, 14H, Ar), 7.22 – 7.08 (m, 6H, Ar), 7.08 – 6.93 (m, 3H, Ar), 5.62 – 5.54 (m, 1H, H3), 5.51 – 5.41 (m, 2H, H1'', H3''), 5.14 (dd, J = 9.1, 8.1 Hz, 1H, H2'), 5.02 (ddd, J = 9.5, 7.7, 3.7 Hz, 2H, H2'''), 4.83 (dd, J = 8.1, 3.1 Hz, 1H, H1), 4.76 – 4.55 (m, 4H, $BnCH_2$), 4.54 – 4.40 (m, 3H, H1', H1''', $BnCH_2$), 4.34 – 4.24 (m, 2H, $BnCH_2$), 4.17 – 3.93 (m, 3H, H4, H4', H4''), 3.82 – 3.73 (m, 1H, H4'''), 3.72 – 3.60 (m, 3H, H5, H6a, H3', H5', H6'a), 3.56 (m, 4H, H5''', COOMe), 3.44 – 3.34 (m, 6H, H6b, H6''a, H3''', 1-OMe), 3.20 (m, 3H, H2, H2'', H5''), 2.94 (s, 3H, COOMe).

Methyl [methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-6-*O*- benzoyl-3-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl (3-O-benzoyl-2-*O*-benzyl-β-D-gluco-pyranosyl) uronate]-(1⟶4)-(2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-α-

D-glucopyranosyl)-(1→4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1→4)-2-azido-6-*O*-benzyl-3-*O*-benzoyl-2-deoxy-α-D-glucopyranoside (H1)



Compound **T2** (0.05 g, 0.032 mmol) and **D11** (0.043 g 0.048 mmol) were dissolved in CH_2Cl_2 (0.30 mL). After the mixture was completely dissolved, Et_2O (0.32 mL) was added. In a separate flask, Tf_2O (0.35 mL) was added drop wise to a solution of Me_2S_2 (0.2 mL) in CH_2Cl_2 (2 mL) at 0 ºC and stirred for half an hour at 0 ºC and used straight away at the half hour mark. (Colour should be golden yellow). The mixture of acceptor and donor was cooled to 0 ºC and the solution of promoter (0.06 mL, 1M in CH_2Cl_2) was added. The reaction was vigorously stirred for 10 mins at 0 ºC or until reaction was complete at which point the reaction was diluted with CH_2Cl_2 and washed with $NaHCO_3$ and once with brine. The organic phase was separated, dried with $MgSO_4$ and filtered. The filtrate was concentrated in vacuo and purified by silica gel chromatography (cyclohexane/EtOAc: 20:1 to 1:1) which afforded compound **H1** (0.072 g, 94%) in a >24:1 α/β ratio as a white foam.

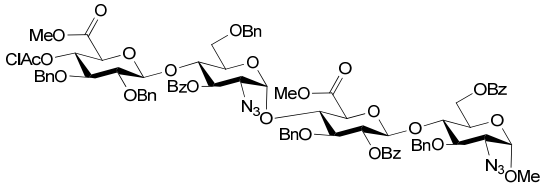
^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.04 – 7.95 (m, 7H, Ar), 7.89 (dd, *J* = 8.4, 1.2 Hz, 2H, Ar), 7.85 (dd, *J* = 8.4, 1.2 Hz, 2H, Ar), 7.78 (ddd, *J* = 8.4, 5.4, 1.2 Hz, 2H, Ar), 7.64 – 7.26 (m, 47H, Ar), 7.22 (dt, *J* = 4.9, 4.1 Hz, 3H, Ar), 7.19 – 7.15 (m, 3H, Ar), 7.14 – 7.08 (m, 6H, Ar), 7.08 – 6.94 (m, 7H, Ar), 5.60 – 5.55 (m, 1H, $H3^A$), 5.50 (d, *J* = 3.8 Hz, 1H, $H1^C$), 5.45 (dd, *J* = 10.6, 9.4 Hz, 1H, $H3^C$), 5.31 (dd, *J* = 13.5, 3.9 Hz, 1H, $H1^E$), 5.17 – 5.09 (m, 4H, $H3^{B,D}$, $BnCH_2$), 4.93 (t, *J* = 11.0 Hz, 2H, $BnCH_2$), 4.87 – 4.40 (m, 26H, $H1^{A,B,D,F}$, $H6^E$ab, $BnCH_2$), 4.31 (m,4H, $H1^A$), 4.10 – 3.94 (m, 5H, $H4^{A,B,C,D,E,F}$), 3.88 – 3.73 (m, 4H, $H5^{D,E,F}$, $H3^E$), 3.65 (m, 6H, $H5^{A,B,C}$, $H6^{A,Ba}$, $H3^B$), 3.59 – 3.46 (m, 4H, COOMe, $H2^F$), 3.46 – 3.31 (m, 5H, $H^{A,C}$6b, 1-OMe), 3.31 – 3.15 (m, 3H, $H2^{A,C,E}$), 3.13 (s, COOMe), 2.96 (s, 3H, COOMe).

^{13}C NMR (126 MHz, $CDCl_3$) δ 168.42, 167.46, 167.43, 165.71, 165.40, 165.31, 164.32, 164.12 (C=O), 138.13, 137.94, 137.89, 137.87, 137.65, 137.57, 137.14, 136.94, 133.52, 133.41, 133.36, 132.98, 132.58, 130.02, 129.98, 129.92, 129.87, 129.75, 129.66, 129.60, 129.55, 129.26, 129.18, 128.91, 128.88, 128.72, 128.64, 128.61, 128.56, 128.51, 128.48, 128.45, 128.43, 128.40, 128.39, 128.36, 128.34, 128.26, 128.22, 128.19, 127.97, 127.94, 127.89, 127.84, 127.76, 127.74, 127.71, 127.68, 127.62, 127.59, 127.57, 127.53(Ar), 102.94 (C-1^F), 100.37 (C-$1^{B\text{ or }D}$), 100.25 (C-$1^{B\text{ or }D}$),

99.25 (C-1^{A}), 97.46 (C-1^{C}), 97.25 (C-1^{E}), 83.94, 82.57, 82.40, 82.01, 79.37, 77.64, 77.10, 75.77 ($BnCH_2$), 75.59 ($BnCH_2$), 75.10 ($BnCH_2$), 75.07, ($BnCH_2$) 74.93, 74.69, 74.63, 74.61, 74.54, 74.04, 73.99, 73.96, 73.83, 73.81, 73.79, 73.42 (C-$3^{B\ or\ D}$), 72.83 (C-$3^{B\ or\ D}$), 70.78 (C-3^{A}), 70.38 (C-$2^{A\ or\ C}$), 70.27 (C-3^{C}), 69.76, 69.63, 67.17 (C-$6^{A\ or\ C}$), 66.41 (C-$6^{A\ or\ C}$), 62.65, 61.94 (C-6^{E}), 61.56, 61.50, 55.42 ($COCH_3$), 52.40 ($COOCH_3$), 52.14 ($COOCH_3$), 51.83 ($COOCH_3$).

Hexasaccharide H2

Methyl [methyl (2,3-di-*O*-benzyl-4-*O*-chloroacetyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (T3)

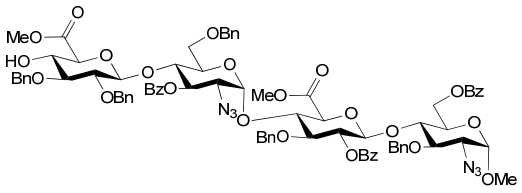


D5 (79 mg, 0.099 mmol, 1 eq) and **D4** (97 mg, 0.102 mmol, 1.05 eq) were dissolved in dry CH_2Cl_2 (0.12 ml) and after being completely dissolved, dry Et_2O (0.24ml) was added and cooled to -10 °C. Solution of promotor (1 M in CH_2Cl_2, 0.12 ml, 1.2 eq) was added dropwise and reaction was stirred at -10 °C for 20 min. Reaction was then diluted with CH_2Cl_2, washed with sat. aq. $NaHCO_3$ and brine, org phase was dried over $MgSO_4$, filtered and concentrated. Purification via chromatography using cyclohexane/EtOAc (6-50%) gave **T3** (106 mg, 0.065 mmol, 66%, α only) as clear glass.

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.14 – 8.04 (m, 4H, Ar), 8.00 – 7.91 (m, 3H, Ar), 7.61 – 7.53 (m, 3H, Ar), 7.50 – 7.41 (m, 8H, Ar), 7.41 – 7.22 (m, 27H, Ar, $CDCl_3$), 7.19 – 7.13 (m, 5H, Ar), 7.12 – 7.06 (m, 3H, Ar), 7.01 – 6.92 (m, 1H,Ar), 5.66 (d, *J* = 3.9 Hz, 1H, H1), 5.58 – 5.51 (m, 1H, H3), 5.46 (dd, *J* = 9.1, 8.0 Hz, 1H, H2'), 5.18 – 5.07 (m, 2H, $BnCH_2$), 4.94 – 4.87 (m, 1H, H4'''), 4.84 – 4.76 (m, 3H, H1', $BnCH_2$), 4.74 – 4.62 (m, 8H, $BnCH_2$), 4.61 – 4.49 (m, 3H, H1'', $BnCH_2$), 4.49 – 4.43 (m, 3H, $BnCH_2$), 4.43 – 4.35 (m, 2H,H6''ab), 4.31 (m, 2H, H4', H1'''), 4.19 – 4.10 (m, 1H, H4), 4.00 (t, *J* = 9.0 Hz, 1H, H3'), 3.97 – 3.87 (m, 3H, H6a, H5', H3''), 3.80 – 3.76 (m, 1H, $ClCH_2$a), 3.75 – 3.62 (m, 5H, H5, H6, H4'', H5'', $ClCH_2$b), 3.51 (d, *J* = 10.3 Hz, 1H, H5'''), 3.38 (s, 3H, COOMe), 3.36 – 3.31 (m, 4H, H2'', 1-OMe), 3.31 – 3.25 (m, 5H, H2, H3''', COOMe).

Methyl [methyl (2,3-di-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-

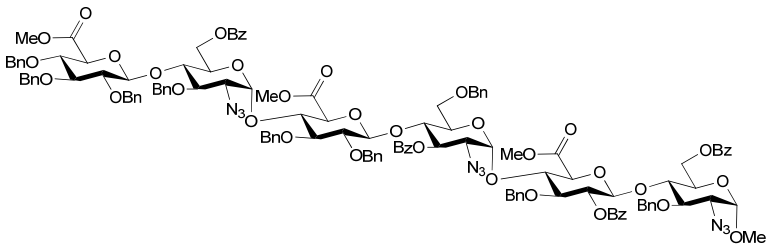
β-D-gluco-pyranosyl) uronate]-(1⟶4)-2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (T4)



T3 (106 mg, 0.065 mmol, 1 eq) was dissolved in EtOH (2.7 ml) and DABCO (219 mg, 1.956, 30 eq) was added. Reaction was heated to 45 °C and stirred for 3.5 h. Upon completion, reaction was diluted with EtOAc and washed with sat. aq. $NaHCO_3$, 1 M HCl and brine. Org. phase was dried with $MgSO_4$, filtered and residue was purified via chromatography using cyclohexane/EtOAc (8-66%) giving **T4** (78 mg, 0.05 mmol, 77%) as white solid.

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.11 – 8.07 (m, 2H, Ar), 8.06 – 8.00 (m, 3H, Ar), 7.98 – 7.89 (m, 3H, Ar), 7.56 (dt, *J* = 14.0, 7.4 Hz, 3H, Ar), 7.47 – 7.20 (m, 33H, Ar), 7.19 – 7.05 (m, 6H, Ar), 7.02 – 6.92 (m, 1H, Ar), 5.65 (d, *J* = 3.9 Hz, 1H, H1''), 5.53 (dd, *J* = 10.5, 9.6 Hz, 1H, H3''), 5.46 (dd, *J* = 9.1, 8.0 Hz, 1H, H2'), 5.17 – 5.08 (m, 2H, $BnCH_2$), 4.86 – 4.64 (m, 13H, H1', H1, $BnCH_2$), 4.49 – 4.26 (m, 8H, H6ab, H4', H1''', $BnCH_2$), 4.18 (dd, *J* = 20.9, 10.4 Hz, 1H, H4''), 4.00 (t, *J* = 9.0 Hz, 1H, H3'), 3.96 – 3.87 (m, 4H, H3, H4, H5', H6''a), 3.81 – 3.51 (m, 10H, H5'', H6''b, H3''', H4''', COOMe, 1-OMe), 3.46 (dt, *J* = 9.8, 3.0 Hz, 1H, H5'''), 3.40 – 3.28 (m, 4H, H2'', COOMe), 3.23 – 3.12 (m, 2H, H2, H2''').

Methyl [methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-6-*O*- benzoyl-3-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl (2,3-di-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (H2)



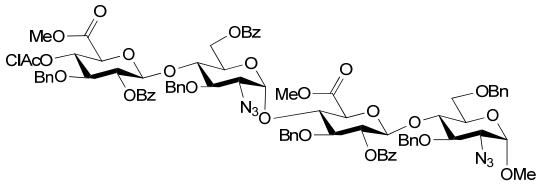
T4 (84 mg, 0.054 mmol, 1 eq) and **D11** (74 mg, 0.081 mmol, 1.5 eq) were dissolved in dry CH_2Cl_2 (0.02 ml) and after being completely dissolved, dry Et_2O (0.09 ml) was added and cooled to -10 °C. Solution of promotor (1 M in DCM, 0.1 ml, 0.1 mmol, 1.8 eq) was added dropwise. Reaction was stirred at -10 °C for 20 min, then diluted with CH_2Cl_2, washed with sat. aq. $NaHCO_3$ and brine, org phase was dried over $MgSO_4$, filtered and concentrated.

Purification *via* chromatography using cyclohexane/EtOAc (6-50%) gave **H2** (94 mg, 0.039 mmol, 73%, α only) as white solid.

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.13 – 8.07 (m, 2H, Ar), 8.04 – 7.90 (m, 8H, Ar), 7.60 – 7.50 (m, 4H, Ar), 7.47 – 6.94 (m, 67H, Ar, $CDCl_3$), 5.65 (d, *J* = 3.8 Hz, 1H, $H1^C$), 5.54 – 5.43 (m, 2H, $H3^C$, $H2^B$), 5.36 – 5.31 (m, 1H, $H1^E$), 5.17 – 5.08 (m, 3H, $BnCH_2$), 4.96 – 4.88 (m, 2H, $H1^B$, $BnCH_2$), 4.87 – 4.51 (m, 25H, $H1^{A,B,F}$, $BnCH_2$), 4.51 – 4.41 (m, 5H, $H6^A$ab, $H6^E$a, $BnCH_2$), 4.31 (m, 3H, $H1^D$, $H4^D$), 4.06 (m, 6H, $H4^{C,H}$, H4, $H3^B$), 3.95 – 3.53 (m, 25H, $H3^{A,E,F}$, $H4^{A,D,F}$ $H5^{B,C,D,E}$, $H6^C$ab, COOMe), 3.53 – 3.37 (m, 5H, $H2^F$, $H3^D$), 3.37 – 3.30 (m, 6H, $H2^A$, 1-OMe), 3.30 – 3.18 (m, 7H, $H2^{C,D,E}$, COOMe), 3.11 (s, 3H, COOMe).

Hexasaccharide H3

Methyl [methyl (2-*O*-benzoyl-3-*O*-benzyl-4-*O*-chloroacetyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (T5)



D7 (97 mg, 0.12 mmol, 1 eq) and **D6** (168 mg, 0.19 mmol, 1.5 eq) were dissolved in dry CH_2Cl_2 (0.22 ml) and after being completely dissolved, dry Et_2O (0.44 ml) was added and mixture was cooled to -10 °C. Solution of promotor (1 M in CH_2Cl_2, 0.22 ml, 0.22 mmol, 1.8 eq) was added dropwise. Reaction was stirred at -10 °C for 15 min; upon completion, reaction was diluted with CH_2Cl_2, washed with sat. aq. $NaHCO_3$ and brine. Phaeses were separated, org. phase was dried over $MgSO_4$, filtered and concentrated. Purification *via* chromatography using tol/MeCN 2-22% gave **T5** (155 mg 0.10 mmol, 79% α) as clear glass.

R_f (toluene/MeCN 8:1): 0.30

$[\alpha]_D$: +43.3 (*c* = 1.0, $CHCl_3$)

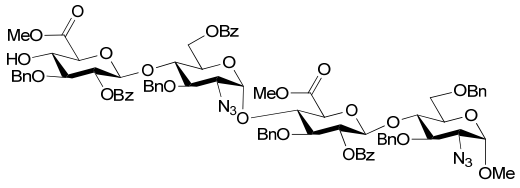
^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.13 – 8.09 (m, 1H, Ar), 8.04 – 8.00 (m, 2H, Ar), 7.90 – 7.84 (m, 2H, Ar), 7.60 – 7.53 (m, 3H, Ar), 7.53 – 7.26 (m, 18H, Ar), 7.24 (s, 1H, Ar), 7.19 – 7.02 (m, 9H, Ar), 5.47 – 5.39 (m, 2H, H1", H2'"), 5.31 – 5.26 (m, 2H, H4'", $BnCH_2$), 5.21 (dd, *J* = 9.3, 8.2 Hz, 1H, H2'), 5.00 (d, *J* = 10.6 Hz, 1H, $BnCH_2$), 4.85 – 4.73 (m, 3H, $BnCH_2$, H1'"), 4.70 – 4.66 (m, 2H, $BnCH_2$, H1), 4.62 – 4.45 (m, 6H, H6"a, $BnCH_2$), 4.44 – 4.38 (m, 1H, H6"b), 4.31 (d, *J* =

12.2 Hz, 1H, $BnCH_2$), 4.14 – 4.09 (m, 1H, H4'), 3.98 – 3.92 (m, 2H, H4, H4''), 3.87 – 3.80 (m, 2H, H5'', H3'''), 3.74 (ddd, *J* = 14.8, 10.2, 2.4 Hz, 3H, H5', H3'', H5'''), 3.70 – 3.65 (m, 1H, H6a), 3.57 (t, *J* = 9.1 Hz, 1H, H3'), 3.54 – 3.48 (m, 4H, H3, C6' OOMe), 3.41 – 3.24 (m, 7H, H2, , H5, H6b, H2'', 1-OMe), 3.05 (s, 3H, C6''' OOMe).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 167.72 (C-6'''), 166.77 (C-6'), 166.08 (OBz), 165.85 (AcCl), 164.55 (OBz), 164.43 (OBz), 138.18 (Ar), 138.14 (Ar), 137.64 (Ar), 137.19 (Ar), 137.15 (Ar), 133.73 (Ar), 133.49 (Ar), 129.87 (Ar), 129.64 (Ar), 129.61 (Ar), 129.48 (Ar), 129.19 (Ar), 129.02 (Ar), 128.97 (Ar), 128.78 (Ar), 128.72 (Ar), 128.64 (Ar), 128.55 (Ar), 128.47 (Ar), 128.36 (Ar), 128.31 (Ar), 128.24 (Ar), 128.20 (Ar), 128.14 (Ar), 128.05 (Ar), 127.92 (Ar), 127.90 (Ar), 127.64 (Ar), 127.61 (Ar), 127.56 (Ar), 127.46 (Ar), 127.40 (Ar), 125.28 (Ar), 100.67 (C-1'''), 100.33 (C-1'), 98.72 (C-1), 97.14 (C-1''), 82.34 (C-3'), 79.35 (C-3'''), 77.80 (C-3''), 77.56 (C-5'' and C-4 or C-4''), 76.86 (C-4 or C-4''), 75.70 ($BnCH_2$), 75.48 ($BnCH_2$), 74.90 (C-4'), 74.70 ($BnCH_2$), 74.64 ($BnCH_2$), 74.03 (C-5'), 73.89 ($BnCH_2$), 73.54 (C-2'), 73.03 (C-5'), 72.76 (C-5'''), 72.37 (C-4'''), 69.90 (C-5), 69.08 (C-3), 66.98 (C-6), 62.84 (C-2 and C-2''), 62.01 (C-6''), 55.38 (C-1-OMe), 52.81 (C-6' OOMe), 51.94 (C-6''' OOMe), 40.22 (AcCl).

HRMS (ESI): Calc. for $C_{85}H_{85}N_6O_{25}NaCl$ $[M+Na]^+$: 1647.5151 found 1647.5154.

Methyl [methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (T6)



T5 (149 mg, 0.09 mmol, 1 eq) was dissolved in EtOH (3.3 ml) and DABCO (308 mg, 2.07 mmol, 30 eq) was added. Reaction was heated to 45 °C and stirred for 3.5 h. Upon completion, reaction was diluted with EtOAc and washed with sat. aq. $NaHCO_3$, 1 M HCl and brine. Phases were separated, org. phase was dried with $MgSO_4$, filtered and evaportated. Residue was purified *via* chromatography using tol/MeCN 2-22% to give **T6** (120 mg, 0.08 mmol, 86%) as white foam.

R_f (toluene/MeCN 8:1): 0.23

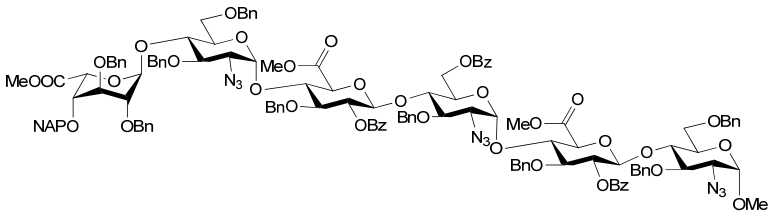
$[\alpha]_D$: +51.5 (*c* = 1.0, $CHCl_3$)

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.12 – 8.08 (m, 2H, Ar), 8.02 (d, *J* = 7.1 Hz, 2H, Ar), 7.87 (d, *J* = 7.3 Hz, 2H, Ar), 7.56 (dt, *J* = 7.3, 6.5 Hz, 3H, Ar), 7.53 – 7.23 (m, 23H, Ar, $CDCl_3$), 7.20 – 7.10 (m, 10H, Ar), 7.08 – 7.02 (m, 2H, Ar), 5.41 (d, *J* = 3.9 Hz, 1H, H1''), 5.36 – 5.32 (m, 1H, H2'''), 5.22 (dd, *J* = 9.6, 5.9 Hz, 2H, H2'), 5.00 (d, *J* = 10.6 Hz, 1H, $BnCH_2$), 4.83 (d, *J* = 12.2 Hz, 1H, $BnCH_2$), 4.78 – 4.64 (m, 6H, H1, H1''', $BnCH_2$), 4.55 (d, *J* = 10.6 Hz, 1H, $BnCH_2$), 4.52 – 4.42 (m, 4H, H1'', $BnCH_2$, H6''ab), 4.31 (d, *J* = 12.2 Hz, 1H, $BnCH_2$), 4.12 (t, *J* = 9.2 Hz, 1H, H4'), 4.00 (m, 2H, H4'', H4'''), 3.97 – 3.92 (m, 1H, H4), 3.86 – 3.80 (m, 1H, H5'''), 3.79 – 3.71 (m, 2H, H5, H5'), 3.70 – 3.58 (m, 4H, H3, H6a, H3', H3'''), 3.57 – 3.54 (m, 3H, C6'-OMe), 3.49 (d, *J* = 10.0 Hz, 1H, H5''), 3.41 – 3.27 (m, 4H, H2, H6b, H2'', H3''), 3.26 (d, *J* = 4.8 Hz, 3H, C1-OMe), 3.01 (d, *J* = 5.0 Hz, 2H, C6'''-OMe).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 169.00 (C-6'''), 167.69 (C-6'), 166.02 (OBz), 164.81 (OBz), 164.43 (OBz), 138.27 (Ar), 138.12 (Ar), 137.85 (Ar), 137.65 (Ar), 137.60 (Ar), 137.19 (Ar), 133.42 (Ar), 129.87 (Ar), 129.65 (Ar), 129.62 (Ar), 129.52 (Ar), 129.20 (Ar), 129.02 (Ar), 128.95 (Ar), 128.70 (Ar), 128.58 (Ar), 128.56 (Ar), 128.32 (Ar), 128.26 (Ar), 128.24 (Ar), 128.21 (Ar), 128.05 (Ar), 127.93 (Ar), 127.77 (Ar), 127.64 (Ar), 127.58 (Ar), 127.54 (Ar), 127.41 (Ar), 125.28 (Ar), 100.89 (C-1'''), 100.34 (C-1'), 98.72 (C-1''), 97.12 (C-1), 82.40 (C-3'), 81.04 (C-3'''), 77.80 (C-5), 77.54 (C4'' or C4'''), 76.87 (C-4), 75.49 ($BnCH_2$), 75.40 ($BnCH_2$), 74.81 (C-4'), 74.77 ($BnCH_2$) 74.62 ($BnCH_2$), 74.30 (C-3), 74.02 (C-5'), 73.88 ($BnCH_2$), 73.52 (C-2'), 72.90 (C-4'' or C-4'''), 72.18 (C-2'''), 69.91 (C-3''), 69.12 (C-5''), 66.99 (C-6), 62.84 (C-6''), 62.74 (C-2), 62.08 (C-2''), 55.37 (C-1 OMe), 52.68 (C-6'-OMe), 51.89 (C-6'' OMe).

HRMS (ESI): Calc. for $C_{83}H_{84}N_6O_{25}Na$ $[M+Na]^+$: 1571.5435; found 1571.5392.

Methyl [methyl (2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl-α-L-idopyranosyl) uronate]-(1→4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-[methyl (3-O-benzoyl-2-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1→4)-(2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-α-D-glucopyrano-syl)-(1→4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]- (1→4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (H3)



T6 (120 mg, 0.08 mmol, 1 eq) and **D8** (11 mg, 0.12 mmol, 1.5 eq) were dissolved in dry CH_2Cl_2 (0.66 ml) and after being completely

dissolved, dry Et_2O (0.80 ml) was added and cooled to -10 °C. Solution of promotor (1 M in CH_2Cl_2, 0.14 ml, 0.14 mmol, 1.8 eq) was added dropwise and reaction was stirred at -10 °C for 15 min, then diluted with CH_2Cl_2, washed with sat. aq. $NaHCO_3$ and brine. Phases were separated, org. phase was dried over $MgSO_4$, filtered and concentrated. Purification via chromatography using cyclohexane/EtOAc (8-66%) gave **H3** (144 mg, 0.06 mmol, 74% α only) as white foam.

R_f (toluene/acetonitrile 9:1): 0.25

$[\alpha]_D$: +40.8 (*c* = 1.0, MeOH)

^{1}H-NMR (600 MHz, $CDCl_3$) δ = 8.12 (d, *J* = 8.0 Hz, 1H, Ar), 8.05 – 7.99 (m, 2H, Ar), 7.90 – 7.79 (m, 3H, Ar), 7.60 – 7.20 (m, 28H, Ar, $CDCl_3$), 7.18 – 7.10 (m, 4H, Ar), 7.10 – 7.02 (m, 2H, Ar), 5.42 (3H, H1^{A,E,F}), 5.19 (dd, *J* = 21.4, 9.8 Hz, 2H, H1^B, $ArCH_2$), 5.07 (t, *J* = 9.9 Hz, 1H, $ArCH_2$), 5.03 – 4.98 (m, 1H, $ArCH_2$), 4.95 (d, *J* = 10.3 Hz, 1H, $ArCH_2$), 4.83 (d, *J* = 12.2 Hz, 1H, $ArCH_2$), 4.79 – 4.58 (m, 8H, H1^{C,D}, $ArCH_2$), 4.57 – 4.51 (m, 2H, $ArCH_2$), 4.50 – 4.42 (m, 4H, H1^B, H5^F, H6^{C}ab), 4.39 (d, *J* = 12.1 Hz, 1H, $ArCH_2$), 4.31 (d, *J* = 12.2 Hz, 1H, $ArCH_2$), 4.20 (t, *J* = 9.1 Hz, 1H, H4^D), 4.10 (t, *J* = 9.2 Hz, 1H, H4^B), 4.07 – 3.98 (m, 1H, H4^A, H3^F), 3.98 – 3.86 (m, 4H, H4^{C,E,F}, H3^D), 3.81 (dd, *J* = 9.5, 4.9 Hz, 2H, H3^E, H5^D), 3.79 – 3.63 (m, 5H, H3^A, H6^{A,E}a, H5^{B,C}), 3.57 (t, *J* = 9.1 Hz, 1H, H3^B), 3.49 – 3.33 (m, 8H, A: H5^{A,E}, H6^{A}b, H3^C, H2^F, C-6^{F}OOMe), 3.33 – 3.24 (m, 7H, H2^{A,C,E}, H6^{E}b, 1-OMe), 3.14 (s, 3H, C-6^{D}OOMe), 3.02 (s, 3H, C-6^{B}OOMe).

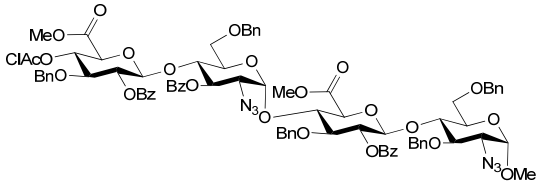
^{13}C-NMR (151 MHz, $CDCl_3$) δ = 169.74 (C-6^F), 167.65 (C-6^D), 167.58 (C-6^B), 166.02 (OBz), 164.69 (OBz), 164.41 (OBz), 138.23 (Ar), 138.19 (Ar), 138.17 (Ar), 138.13 (Ar), 138.05 (Ar), 137.90 (Ar), 137.65 (Ar), 137.19 (Ar), 137.04 (Ar), 133.71 (Ar), 133.43 (Ar), 133.37 (Ar), 133.07 (Ar), 131.71 (Ar), 129.81 (Ar), 129.65 (Ar), 129.56 (Ar), 129.51 (Ar), 129.21 (Ar), 128.98 (Ar), 128.94 (Ar), 128.83 (Ar), 128.80 (Ar), 128.75 (Ar), 128.70 (Ar), 128.60 (Ar), 128.53 (Ar), 128.45 (Ar), 128.41 (Ar), 128.35 (Ar), 128.30 (Ar), 128.29 (Ar), 128.25 (Ar), 128.22 (Ar), 128.19 (Ar), 128.16 (Ar), 128.12 (Ar), 128.09 (Ar), 128.07 (Ar), 128.01 (Ar), 127.98 (Ar), 127.90 (Ar), 127.87 (Ar), 127.84 (Ar), 127.77 (Ar), 127.74 (Ar), 127.70 (Ar), 127.62 (Ar), 127.57 (Ar), 127.55 (Ar), 127.47 (Ar), 127.42 (Ar), 127.40 (Ar), 127.35 (Ar), 126.93 (Ar), 126.21 (Ar), 125.82 (Ar), 125.09 (Ar), 124.17 (Ar), 100.82 (C-1^D), 100.33 (C-1^B), 99.75 (C-1^F), 98.72 (C-1^C), 97.41 (C-1^A), 97.07 (C-1^E), 82.70 (C-3^D), 82.37 (C-3^B), 80.81 (C-2^F), 78.88 (C-3^F), 78.01 (C-3^A), 77.49 (C-5^C), 77.13 (C-4^{E,F}), 76.87 (C-4^C), 75.77 (C-4^A), 75.65 ($ArCH_2$), 75.47 ($ArCH_2$), 75.02 ($ArCH_2$), 74.92 (C-3^E, C-5^D), 74.81 (C-4^B), 74.78 ($ArCH_2$), 74.66 ($ArCH_2$), 74.59 (C-4^D), 74.15 (C-5^B), 74.04 ($ArCH_2$), 73.87 ($ArCH_2$), 73.67 ($ArCH_2$), 73.58 ($ArCH_2$), 73.52 (C-2^D), 73.40 (C-2^B), 72.02 (C-5^F), 71.64

($ArCH_2$), 71.33 (C-5^A), 69.91 (C-3^C), 69.21 (C-5^E), 66.99 (C-6^E), 66.92 (C-6^A), 62.84 (C-$2^{A\text{ or }C\text{ or }E}$), 62.79 (C-$2^{A\text{ or }C\text{ or }E}$), 62.61 (C-$2^{A\text{ or }C\text{ or }E}$), 61.90 (C-$6^C$), 55.36 (1-OMe), 52.16 (C-6^DOOMe), 51.90 (C-6^BOOMe), 51.60 (C-6^FOOMe).

HRMS (ESI): Calc. for $C_{135}H_{135}N_9O_{34}Na$ $[M+Na]^+$: 2448.9009; found 2448.9009.

Hexasaccharide H4

Methyl [methyl (2-*O*-benzoyl-3-*O*-benzyl-4-*O*-chloroacetyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (T7)



D7 (102 mg, 0.14 mmol, 1 eq) and **D1** (177 mg, 0.21 mmol, 1.5eq) were dissolved in dry CH_2Cl_2 (0.23 ml) and after being completely dissolved, dry Et_2O (0.46 ml) was added and mixture was cooled to -10 °C. Solution of promotor (1 M in CH_2Cl_2, 0.23 ml, 0.23 mmol, 1.8 eq) was added dropwise and reaction was stirred at -10 °C for 20 min. After completion, reaction was diluted with CH_2Cl_2, washed with sat. aq. $NaHCO_3$ and brine. Phases were separated, org. phase was dried over $MgSO_4$, filtered and concentrated. Purification *via* column chromatography using cyclohexane/EtOAc 10-80% gave **T7** (127 mg, 0.07 mmol, 55% α:β=13:1) as clear glass.

R_f (cyclohexane/acetone 3:2): 0.50

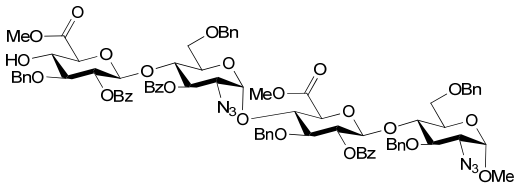
$[\alpha]_D$: +4.3 (*c* =1.0, $CHCl_3$)

^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.11 (dd, *J* = 11.6, 4.3 Hz, 4H, Ar), 7.92 – 7.75 (m, 7H, Ar), 7.64 – 7.54 (m, 6H), Ar, 7.52 – 7.22 (m, 36H, Ar, $CDCl_3$), 7.19 – 7.12 (m, 7H, Ar), 7.12 – 6.94 (m, 10H, Ar), 5.59 (d, *J* = 3.9 Hz, 1H, H1"), 5.57 – 5.52 (m, 1H, H3"), 5.19 – 4.98 (m, 8H, H2', H2"', $BnCH_2$), 4.92 (d, *J* = 12.3 Hz, 2H, $BnCH_2$), 4.85 – 4.73 (m, 3H, $BnCH_2$), 4.71 – 4.63 (m, 3H, H1, $BnCH_2$), 4.61 – 4.41 (m, 13H, H1', H1"', $BnCH_2$), 4.21 (m, 9H, H4', H4", H4"', $BnCH_2$), 4.00 – 3.92 (m, 2H, H4), 3.89 – 3.73 (m, 5H, $ClCH_2$ab, H5, H5' H6a), 3.72 – 3.62 (m, 5H, H6b, H5"', COOMe), 3.61 – 3.45 (m, 2H, H3"', H6"a), 3.40 (m, 2H, H3, H3'), 3.34 – 3.22 (m, 9H, H2, H2", H6"b, C1-OMe, COOMe).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 168.16 (COOMe), 167.93 (COOMe), 166.58 (AcCl), 165.61 (OBz), 165.06 (OBz), 164.14 (OBz), 138.35 (Ar), 138.12 (Ar), 137.83 (Ar), 137.68 (Ar), 137.51 (Ar), 137.31 (Ar), 136.99 (Ar), 133.48(Ar), 133.16 (Ar), 132.95 (Ar), 130.07 (Ar), 130.01 (Ar), 129.94 (Ar), 129.68 (Ar), 129.46 (Ar), 129.07 (Ar), 128.98 (Ar), 128.77 (Ar), 128.73 (Ar), 128.65 (Ar), 128.57 (Ar), 128.51 (Ar), 128.48 (Ar), 128.33 (Ar), 128.29 (Ar), 128.27 (Ar), 128.24 (Ar), 128.21 (Ar), 128.18 (Ar), 127.97 (Ar), 127.78 (Ar), 127.77 (Ar), 127.75 (Ar), 127.53 (Ar), 127.37 (Ar), 127.18 (Ar), 101.61 (C-1'), 100.46 (C-1'''), 99.93 (C-1), 98.70 (C-1''), 79.79 (C-5''), 79.31 (C-4'''), 79.06 (C-4''), 78.98 (C-3'''), 77.84 (C-5), 76.81 (C-4), 74.84 ($BnCH_2$), 74.57 ($BnCH_2$), 74.36 ($BnCH_2$), 74.10 (C-4), 74.03 ($BnCH_2$), 73.92 ($BnCH_2$), 73.87 (C-5'), 72.82 (C-2'), 72.61 (C-5'''), 72.49 (C-2'''), 70.31 (C-3''), 69.95 (C-3), 69.91 (C-3'), 67.08 (C-6), 67.01 (C-6''), 65.16 (C-2''), 62.78 (C-2), 55.35 (C-1 OMe), 53.01 (COOMe), 52.47 (COOMe), 40.30 (OAcCl).

HRMS (ESI): Calc. for $C_{85}H_{85}N_6O_{25}NaCl$ $[M+Na]^+$: 1647.5151; found 1647.5153.

Methyl [methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (T8)



T7 (108 mg, 0.07 mmol, 1 eq) was dissolved in EtOH (2.7 ml) and excess of DABCO was added. Reaction was heated to 45 °C and stirred for 3.5 h. Upon completion, reaction was diluted with EtOAc and washed with sat. aq. $NaHCO_3$, 1 M HCl and brine. Phases were separated, org. phase was dried over $MgSO_4$, filtered and evaporated. Residue was purified *via* column chromatography using toluene/MeCN 2-22% to give **T8** (58 mg, 0.04 mmol, 56%) as clear solid.

R_f (toluene/acetone 9:1): 0.23

$[\alpha]_D$: +43.1 (*c* = 1.0, $CHCl_3$)

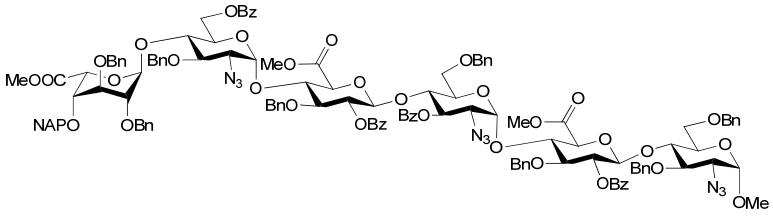
^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.09 – 8.03 (m, 3H, Ar), 7.91 – 7.86 (m, 2H, Ar), 7.86 – 7.77 (m, 4H, Ar), 7.63 – 7.49 (m, 6H, Ar), 7.49 – 7.29 (m, 22H, Ar), 7.29 – 7.20 (m, 7H, CDCl3, Ar), 7.20 – 7.04 (m, 12H, Ar), 6.99 (dt, *J* = 14.1, 6.9 Hz, 2H, Ar), 5.59 (d, *J* = 3.8 Hz, 1H, H1''), 5.52 (dd, *J* = 10.6, 9.4 Hz, 1H, H3''), 5.29 – 5.22 (m, 1H, H1''), 5.18 – 5.09 (m, 1H, H2'''), 5.02 (ddd, *J* = 13.2, 10.8, 8.7 Hz, 3H, $BnCH_2$, H2'), 4.92 (d, *J* = 12.2 Hz, 1H, $BnCH_2$), 4.85 – 4.75 (m, 3H,

$BnCH_2$), 4.71 – 4.60 (m, 5H, H1, $BnCH_2$), 4.52 (m, 8H, H1', H1''', $BnCH_2$), 4.30 (m, 4H, $BnCH_2$), 4.22 – 4.04 (m, 3H, H4', H4'', H4'''), 3.95 (dd, *J* = 18.5, 8.9 Hz, 1H, H4), 3.77 (m, 3H, H5, H5', H5'''), 3.71 – 3.63 (m, 2H, H3', H6a), 3.61 – 3.47 (m, 5H, H6b, H5''', COOMe), 3.38 (m, 3H, H3, H3''', H6''a), 3.35 – 3.25 (m, 7H, H5'', H2, H2'', C1-OMe, H6''b), 3.04 (s, 3H, COOMe).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 168.83 (COOMe), 167.88 (COOMe), 165.49 (OBz), 165.07 (OBz), 164.19 (OBz), 138.15 (Ar), 137.71 (Ar), 137.51 (Ar), 137.01 (Ar), 133.48 (Ar), 133.32 (Ar), 132.88 (Ar), 129.94 (Ar), 129.67 (Ar), 128.98 (Ar), 128.76 (Ar), 128.66 (Ar), 128.58 (Ar), 128.51 (Ar), 128.47 (Ar), 128.37 (Ar), 128.24 (Ar), 128.18 (Ar), 127.97 (Ar), 127.85 (Ar), 127.81 (Ar), 127.79 (Ar), 127.63 (Ar), 127.54 (Ar), 101.69 (C-1'''), 100.03 (C-1'), 98.70 (C-1), 97.75 (C-1''), 82.55 (C-3'), 80.67(C-3'''), 79.04 (C-5''), 77.73 (C-4''), 77.21, (C-4) 75.46 ($BnCH_2$), 75.41 ($BnCH_2$), 75.17 ($BnCH_2$), 74.83 ($BnCH_2$), 74.40 ($BnCH_2$), 74.20 (C-4'), 74.12, 73.98 (C-2'), 73.77 (C-5), 73.69, 73.63 (C-5'), 73.41 (C-4'''), 73.26, 72.90 (C-2'''), 71.89 (C-4'''), 70.61 (C-3''), 70.29, 69.92, 67.04 (C-6), 67.00 (C-6''), 62.78 (C-2), 61.50 (C-2'') 55.35 (1-OMe), 51.90 (2 COOMe).

HRMS (ESI): Calc. for $C_{83}H_{84}N_6O_{24}Na$ [M+Na]: 1571.5435; found 1571.5410.

Methyl [methyl (2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl-α-D-idopyranosyl) uronate]-(1⟶4)-(2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl (3-O-benzoyl-2-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-6-*O*-benzoyl-3-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]- (1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (H4)



T8 (56 mg, 0.04 mmol, 1 eq) and **D9** (52 mg, 0.0.5 mmol, 1.5 eq) were dissolved in dry CH_2Cl_2 (0.29 ml) and after being completely dissolved, dry Et_2O (0.36 ml) was added and cooled to -10 °C. Solution of promotor (1 M in CH_2Cl_2, 0.07 ml, 0.07 mmol, 1.8 eq) was added dropwise and reaction was stirred at -10 °C for 15 min, then diluted with CH_2Cl_2, washed with sat. aq. $NaHCO_3$ and brine. Phases were separated, org. phase was dried over $MgSO_4$, filtered and concentrated. Purification *via* column chromatography using cyclohexane/EtOAc (8-66%) gave **H4** (79 mg, 0.03 mmol, 81%, α:β = 4:1) as white foam.

R_f (cyclohexane/EtOAc 2:1): 0.27

$[\alpha]_D$: +27.7 (*c* = 1.0, $CHCl_3$)

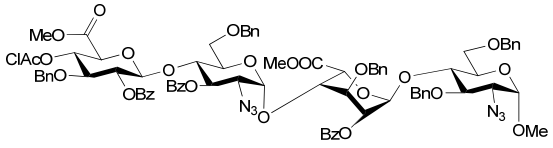
^{1}H-NMR (600 MHz, $CDCl_3$) δ = 8.07 – 7.99 (m, 4H, Ar), 7.97 (d, *J* = 8.4 Hz, 1H, Ar), 7.91 – 7.87 (m, 2H, Ar), 7.86 – 7.77 (m, 5H, Ar), 7.61 – 7.49 (m, 7H, Ar), 7.49 – 7.22 (m, 35H, Ar, $CDCl_3$), 7.17 – 6.97 (m, 12H, Ar), 5.60 (d, *J* = 3.7 Hz, 1H, $H1^C$), 5.55 – 5.44 (m, 2H, $H3^D$, $H1^F$), 5.27 (ddd, *J* = 22.8, 11.4, 5.9 Hz, 2H, $H1^E$, $H2^D$), 5.18 – 5.09 (m, 1H, $H2^D$), 5.01 (m, 3H, $ArCH_2$), 4.95 (m, 2H, $ArCH_2$), 4.85 – 4.63 (m, 9H, $ArCH_2$), 4.62 – 4.50 (m, 8H, $H6^{A\text{ or }C\text{ or }E}$a, $ArCH_2$), 4.50 – 4.43 (m, 3H, $H6^{A\text{ or }C\text{ or }E}$b, $ArCH_2$), 4.40 (d, *J* = 12.2 Hz, 1H, $ArCH_2$), 4.30 (d, *J* = 12.1 Hz, 1H, $ArCH_2$), 4.25 (d, *J* = 12.2 Hz, 1H, $ArCH_2$), 4.22 – 3.93 (m, 8H), 3.92 – 3.72 (m, 8H), 3.72 – 3.60 (m, 5H, 2 $H6^{A\text{ or }C\text{ or }E}$a), 3.54 – 3.45 (m, 2H $H6^{A\text{ or }C\text{ or }E}$b), 3.44 – 3.36 (m, 3H, $H6^{A\text{ or }C\text{ or }E}$b), 3.35 – 3.29 (m, 3H, COOMe), 3.29 – 3.25 (m, 6H, 1-OMe, COOMe), 3.19 (s, 3H, COOMe).

^{13}C-NMR (151 MHz, $CDCl_3$) δ = 169.84 (COOMe), 167.89 (COOMe), 167.46 (COOMe), 165.97 (OBz), 165.44 (OBz), 164.57 (OBz), 164.50 (OBz), 138.41 (Ar), 138.19 (Ar), 138.11 (Ar), 138.09 (Ar), 138.04 (Ar), 137.91 (Ar), 137.82 (Ar), 137.74 (Ar), 137.69 (Ar), 137.52 (Ar), 137.26 (Ar), 137.20, (Ar) 137.01 (Ar), 133.67 (Ar), 133.48 (Ar), 132.96 (Ar), 132.91 (Ar), 132.85 (Ar), 131.68 (Ar), 129.95 (Ar), 129.93 (Ar), 129.87 (Ar), 129.71 (Ar), 129.67 (Ar), 129.62 (Ar), 129.49 (Ar), 129.18 (Ar), 129.13 (Ar), 129.08 (Ar), 128.98 (Ar), 128.91 (Ar), 128.78 (Ar), 128.75 (Ar), 128.70 (Ar), 128.66 (Ar), 128.58 (Ar), 128.56 (Ar), 128.52 (Ar), 128.41 (Ar), 128.40 (Ar), 128.39 (Ar), 128.37 (Ar), 128.32 (Ar), 128.30 (Ar), 128.28 (Ar), 128.24 (Ar), 128.21 (Ar), 128.19 (Ar), 128.18 (Ar), 127.99 (Ar), 127.79 (Ar), 127.68 (Ar), 127.65 (Ar), 127.56 (Ar), 127.55 (Ar), 127.53 (Ar), 127.52 (Ar), 127.49 (Ar), 127.46 (Ar), 127.37 (Ar), 127.19 (Ar), 126.91 (Ar), 126.22 (Ar), 125.84 (Ar), 125.03 (Ar), 124.20 (Ar), 100.30 (C-1^D), 100.17 (C-1^B), 99.78 (C-1^F), 98.71 (C-1^A), 97.71 (C-1^C), 97.25 (C-1^E), 82.55, 82.26, 80.36, 78.22, 77.89, 77.84, 77.74, 76.43, 76.22, 75.47, 75.19, 75.00, 74.81, 74.78, 74.60, 74.40, 74.37, 74.03, 73.99, 73.92, 73.87, 73.79, 73.70, 73.54, 72.00, 71.41, 70.42, 70.36, 69.95 (C-$6^{A\text{ or }C\text{ or }E}$), 67.02 (C-$6^{A\text{ or }C\text{ or }E}$), 62.95 (C-$2^{A\text{ or }C\text{ or }E}$), 61.82 (C-$6^{A\text{ or }C\text{ or }E}$), 62.58 (C-$2^{A\text{ or }C\text{ or }E}$), 61.58 (C-$2^{A\text{ or }C\text{ or }E}$), 55.35 (1-OMe), 52.97 (COOMe), 52.15 (COOMe), 51.93 (COOMe).

HRMS (ESI): Calc. for $C_{135}H_{133}N_9O_{35}Na$ $[M+Na]^+$: 2464.8958, 2464.8909.

Hexasaccharide H5

Methyl [methyl (2-*O*-benzoyl-3-*O*-benzyl-4-O-chloroacetyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-3-*O*-benzoyl-6-*O*-benzyl -2-deoxy-1-thio-α-D-glucopyranosyl)-(1⟶4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-α-L-idopyranosyl) uronate]-(1⟶4) -2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (T9)



Hemiacetal **D1$_{1\text{-OH}}$** (366 mg, 0.43 mmol, 1.4 eq) was dissolved in dry CH_2Cl_2 (4.25 ml) and cooled to 0 °C, K_2CO_3 (147 mg, 1.06 mmol, 3.4 eq), TCA (0.28 ml, 2.77 mmol, 8.9 eq) were added and reaction was stirred for 10 min at 0 °C, then for 2.5 h. Reaction mixture was filtered through a pad of Celite and concentration *in vacuo* and put in a flask together with **D10** (243 mg, 0.31 mmol, 1eq). Combined sugars were dissolved in dry toluene (7.17 ml) and 4 Å MS (230 mg) was added, stirring at RT for 1h. Then solution was cooled to -60 °C and TBDMSOTf (0.08 mmol, 0.25 eq in 0.1 ml toluene, 0.018 ml) was added dropwise, reaction was allowed to attain RT and stirred over night. Reaction was put on ice, quenched with NEt_3, filtered, diluted with CH_2Cl_2, and then evaporated. Residue was purified *via* column chromatography using tol/EtOAc, then cyclohexane/EtOAc (8-66%) to give **T9** (359 mg, 0.26 mmol, 85%, α:β 7.3:1) as white solid.

R$_f$ (Cyclohexane/EtOAc 2:1): 0.37

[α]$_D$: +32.9 (*c* =0.85, $CHCl_3$)

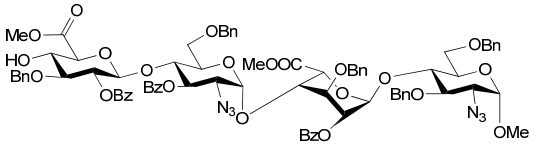
^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.08 – 8.03 (m, 2H, Ar), 7.90 – 7.82 (m, 3H, Ar), 7.60 – 7.49 (m, 3H, Ar), 7.49 – 7.32 (m, 12H, Ar), 7.32 – 7.20 (m, 4H, Ar, $CDCl_3$), 7.19 – 7.08 (m, 8H, Ar), 7.08 – 7.00 (m, 3H, Ar), 5.69 (d, *J* = 6.3 Hz, 1H, H1'), 5.51 – 5.45 (m, 1H, H3''), 5.20 – 5.14 (m, 3H, H1'', H2', H2'''), 5.08 (dd, *J* = 18.8, 9.2 Hz, 1H, H4'''), 4.88 (d, *J* = 10.9 Hz, 1H, 0.5 $BnCH_2$), 4.76 – 4.68 (m, 4H, H1, 1.5 $BnCH_2$), 4.62 (m, 2H, $BnCH_2$), 4.48 (m, 4H, H1', 1.5 $BnCH_2$), 4.33 (d, *J* = 12.3 Hz, 1H, 0.5 $BnCH_2$), 4.23 (d, *J* = 6.1 Hz, 1H, H5'), 4.19 (t, *J* = 7.7 Hz, 1H, H3'), 4.16 – 4.09 (m, 1H, H4''), 4.02 – 3.96 (m, 2H, H4, H4'), 3.87 – 3.76 (m, 4H, H3, H5'', $ClCH_2$ab), 3.66 (m, 3H, H3''', H6a, H6a''), 3.64 – 3.61 (m, 3H, C6'-OMe), 3.61 – 3.52 (m, 2H, H5, H5'''), 3.46 – 3.33 (m, 6H, H2, H6b, H6b'', C-6'''-OMe), 3.31 (s, 3H, C-1-OMe), 3.24 (dd, *J* = 10.7, 3.5 Hz, 1H, H2'').

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 169.64 C-6', 166.55 (C-6'''), 165.61 (OBz), 165.19 (OAcCl), 165.15 (OBz), 164.14 (OBz), 138.41 (Ar), 137.91 (Ar), 137.75 (Ar), 137.33 (Ar), 137.28 (Ar),

133.68 (Ar), 133.38 (Ar), 132.95 (Ar), 129.97 (Ar), 129.80 (Ar), 129.73 (Ar), 129.56 , 129.12 (Ar), 129.08 (Ar), 128.79 (Ar), 128.63 (Ar), 128.58 (Ar), 128.40 (Ar), 128.37 (Ar), 128.32 (Ar), 128.30 (Ar), 128.25, (Ar) 128.05 (Ar), 127.94 (Ar), 127.93 (Ar), 127.83 (Ar), 127.79 (Ar), 127.74 (Ar), 127.71 (Ar), 127.67 (Ar), 127.09 (Ar), 100.03 (C-1'''), 98.81 (C-1''), 98.50 (C-1), 97.73 (C-1'), 79.13 (C-5''), 78.36 (C-5), 77.27 (C-3'), 76.21 (C-4), 74.81 ($BnCH_2$), 74.55 ($BnCH_2$), 74.14 (C-4' or C-4''), 74.12 (C-4' or C-4''), 74.00 ($BnCH_2$), 73.72 ($BnCH_2$), 73.69 ($BnCH_2$), 72.70 (C-2'''), 72.53 (C-3'''), 72.42 (C-2' or C-4'''), 72.31 (C-2' or C-4'''), 71.46 (C-5'), 70.79 (C-5''), 70.31 (C-5 and C-3''), 67.61 (C-6), 66.78 (C-6''), 63.14 (C-2), 61.38 (C-2''), 55.25 (1-OMe), 52.50 (C-6' OMe), 52.29 (C-6''' OMe), 40.28 (AcCl).

HRMS (ESI):: Calc. for $C_{85}H_{85}N_6O_{25}NaCl$ $[M+Na]^+$: 1647.5151; found 1647.5154.

Methyl [methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-1-thio-α-D-glucopyranosyl-(1⟶4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-α-L-idopyranosyl) uronate]-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (T10)



T9 (299 mg, 0.18 mmol, 1 eq) was dissolved in EtOH (7.5 ml) and DABCO (619 mg, 5.52 mmol, 30 eq) was added. Reaction was heated to 45 °C and stirred for 2.5h. Upon completion, reaction was diluted with EtOAc and washed with sat. aq. $NaHCO_3$, 1 M HCl and brine. Phases were separated, org. phase was dried over $MgSO_4$, filtered and residue was purified *via* column chromatography using cyclohexane/EtOAc (8-66%) giving **T10** (263 mg (0.17 mmol, 94%) as white solid.

R_f (Cyclohexane/EtOAc 2:1): 0.28

$[\alpha]_D$: +37.9 (*c* = 1.2, $CHCl_3$)

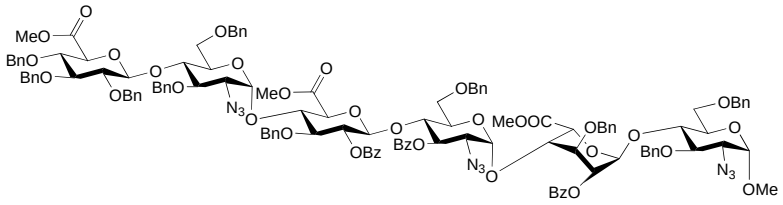
^{1}H-NMR (500 MHz, $CDCl_3$) δ = 8.01 (dd, *J* = 8.2, 1.2 Hz, 2H, Ar), 7.88 – 7.78 (m, 3H, Ar), 7.59 – 7.47 (m, 3H, Ar), 7.44 – 7.26 (m, 12H, Ar, $CDCl_3$), 7.20 – 6.96 (m, 10H, Ar), 5.68 (d, *J* = 6.4 Hz, 1H, H1'), 5.44 (dd, *J* = 10.6, 9.4 Hz, 1H, H3''), 5.17 (m, 2H, H1'', H2'), 5.09 – 5.01 (m, 1H, H2'''), 4.87 (d, *J* = 10.9 Hz, 1H, 0.5 $BnCH_2$), 4.70 (m, 5H, H1, 2 $BnCH_2$), 4.65 – 4.57 (m, 3H, 1.5 $BnCH_2$), 4.48 (t, *J* = 7.7 Hz, 1H, 0.5 $BnCH_2$), 4.43 (d, *J* = 8.1 Hz, 1H, H1'''), 4.33 (d, *J* = 12.3 Hz, 1H, 0.5 $BnCH_2$), 4.25 – 4.03 (m, 4H, H3', H5', H4'', OH), 4.02 – 3.95 (m, 2H, H4, H4'), 3.85 – 3.74 (m, 3H, H3, H5'', H4'''), 3.66 – 3.55 (m, 5H, H5, H6a, C-6'-OMe), 3.55 – 3.48 (m, 4H, H5''',

C-6'''-OMe), 3.46 – 3.36 (m, 3H, H2, H6b, H3'''), 3.36 – 3.32 (m, 1H, H6''b), 3.32 – 3.26 (m, 4H, H2'', 1-OMe).

^{13}C-NMR (126 MHz, $CDCl_3$) δ = 169.64 (C-6'), 168.69 (C-6'''), 165.21 (Ar), 165.13 (Ar), 164.34 (Ar), 138.39 (Ar), 137.90 (Ar), 137.83 (Ar), 137.56 (Ar), 137.35 (Ar), 133.48 (Ar), 133.36 (Ar), 132.81 (Ar), 130.00 (Ar), 129.85 (Ar), 129.72 (Ar), 129.55 (Ar), 129.34 (Ar), 129.12 (Ar), 128.76 (Ar), 128.57 (Ar), 128.53 (Ar), 128.38 (Ar), 128.31 (Ar), 128.24 (Ar), 128.18 (Ar), 128.05 (Ar), 127.92 (Ar), 127.91 (Ar), 127.82 (Ar), 127.72 (Ar), 127.68 (Ar), 127.66 (Ar), 127.63 (Ar), 127.08 (Ar), 124.73 (Ar), 123.94 (Ar), 123.42 (Ar), 100.18 (C-1'''), 98.84 (C-1''), 98.48 (C-1'), 97.71 (C-1), 80.64 (C-3'''), 78.33 (C-3), 77.27 (C3'), 76.24 (C-4 or C-4'), 74.79 ($BnCH_2$), 74.56 ($BnCH_2$), 74.18 ($BnCH_2$), 74.15 (C-4 or C-4'), 74.11 (C-5'''), 73.75 ($BnCH_2$), 73.68 ($BnCH_2$), 73.56 (C-4''), 72.68 (C-2'''), 72.45 (C-2'), 71.83 (C-4'''), 71.50 (C-5'), 70.81 (C-5''), 70.37 (C-3''), 70.29 (C-5), 67.59 (C-6), 66.68 (C-6''), 63.11 (C-2), 61.31 (C-2''), 55.24 (1'-OMe), 52.40 (6'''-OMe), 52.25 (6'-OMe).

HRMS (ESI): Calc. for $C_{83}H_{84}N_6O_{24}Na$ $[M+Na]^+$: 1571.5435; found 1571.5439.

Methyl [methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-1-thio-α-D-glucopyranosyl-(1⟶4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-3-*O*-benzoyl-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl-(1⟶4)-[methyl (2-*O*-benzoyl-3-*O*-benzyl-α-L-idopyranosyl) uronate]-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (H5)



T10 (75 mg, 0.048 mmol, 1 eq) and **D3** (65 mg, 0.075 mmol, 1.5 eq) were dissolved in dry CH_2Cl_2 (0.03 ml) and after being completely dissolved, dry Et_2O (0.12ml) was added and solution was cooled to -10 °C. Solution of promotor (1 M in CH_2Cl_2, 0.087 ml) was added dropwise and reaction was kept stirring at -10 °C for 35 min, then was diluted with CH_2Cl_2, washed with sat. aq. $NaHCO_3$ and brine. Phases were separated, org. phase was dried over $MgSO_4$, filtered and concentrated. Purification *via* column chromatography using cyclohexane/EtOAc (6-50%) gave **H5** (113 mg, 0.0475 mmol, 98%, α:β=3:1) as white solid.

R_f (Cyclohexane/EtOAc 3:1): 0.32

[α]$_D$: +27.8 (*c* = 1.2, $CHCl_3$)

^{1}H-NMR (600 MHz, $CDCl_3$) δ = 7.98 (d, *J* = 7.7 Hz, 1H, Ar), 7.85 (d, *J* = 8.0 Hz, 2H, Ar), 7.52 (dd, *J* = 14.5, 7.3 Hz, 3H, Ar), 7.48 – 7.24 (m, 28H, Ar, $CDCl_3$), 7.21 (t, *J* = 9.3 Hz, 4H, Ar), 7.17 – 7.06 (m, 7H, Ar), 7.01 (dd, *J* = 17.8, 9.1 Hz, 3H, Ar), 5.70 (d, *J* = 6.5 Hz, 1H, H1^B), 5.46 – 5.37 (m, 2H, H1^E; H3^C), 5.20 – 5.10 (m, 4H, H2^{B,D}, H1^C, 0.5 $BnCH_2$), 5.06 (s, 1H, 0.5 $BnCH_2$), 4.92 – 4.79 (m, 3H, 1.5 $BnCH_2$), 4.79 – 4.67 (m, 6H, H1^A, 2.5 $BnCH_2$), 4.67 – 4.53 (m, 6H, 3 $BnCH_2$), 4.53 – 4.42 (m, 4H, H3^B, H1^D, $BnCH_2$), 4.37 (t, *J* = 12.6 Hz, 2H, $BnCH_2$), 4.18 (dd, *J* = 10.2, 6.5 Hz, 2H, H4^{B,F}), 4.14 – 3.92 (m, 5H, H4$^{A, C, D, E}$, H5^B), 3.88 (d, *J* = 10.1 Hz, 1H, H6^{E}a), 3.85 – 3.67 (m, 6H, H3^{A,E,F}, H5^{C,D,F}), 3.67 – 3.58 (m, 5H, H6^{A}a, C-6^{B}OOMe, H6^{C}a, H3^D), 3.58 – 3.49 (m, 4H, H5^A, C-6^{B}OOMe), 3.49 – 3.34 (m, 5H, H2^{A,F}, H6^{A,E}b, H5^E), 3.30 (s, 3H, 1-OMe), 3.29 – 3.20 (m, 3H, H2^{C,E}, H6^{C}b), 2.87 (d, *J* = 29.2 Hz, 3H, C-6^{F}OOMe).

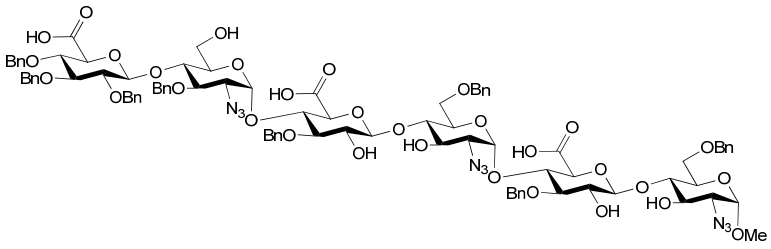
^{13}C-NMR (151 MHz, $CDCl_3$) δ = 169.67 (C-6^{B}OOMe), 168.59 (C-6^{D}OOMe), 167.36 (C-6^{F}OOMe), 165.11 (OBz), 165.07 (OBz), 164.21 (OBz), 139.25 (Ar), 138.41 (Ar), 138.28 (Ar), 138.21 (Ar), 137.94 (Ar), 137.91 (Ar), 137.61 (Ar), 137.57 (Ar), 137.36 (Ar), 137.05 (Ar), 133.71 (Ar), 133.34 (Ar), 132.69 (Ar), 129.91 (Ar), 129.73 (Ar), 129.50 (Ar), 129.14 (Ar), 129.05 (Ar), 128.94 (Ar), 128.82 (Ar), 128.66 (Ar), 128.60 (Ar), 128.56 (Ar), 128.51 (Ar), 128.48 (Ar), 128.41 (Ar), 128.39 (Ar), 128.35 (Ar), 128.33 (Ar), 128.31 (Ar), 128.24 (Ar), 128.22 (Ar), 128.10 (Ar), 128.07 (Ar), 127.95 (Ar), 127.93 (Ar), 127.88 (Ar), 127.83 (Ar), 127.77 (Ar), 127.74 (Ar), 127.73 (Ar), 127.70 (Ar), 127.67 (Ar), 127.52 (Ar), 127.46 (Ar), 127.24, (Ar) 127.09 (Ar), 124.73 (Ar), 124.03 (Ar), 123.48 (Ar), 115.88 (Ar), 114.04 (Ar), 102.70 (F: C-1), 100.29 (C-1^D), 98.77 (C-1^C), 98.50 (C-1^A), 97.66 (C-1^B), 97.30 (C-1^E), 83.91 (E: C-5^E), 82.50 (C-3^D) , 81.96 (C-2^F), 79.49 (C-3^A), 78.34 (C-3^F), 77.54 (C-5^F), 77.34 (C-4^B), 76.72 (C-4^E), 76.22 (C-4$^{A \text{ or } D}$), 75.63 ($BnCH_2$), 75.10 ($BnCH_2$), 74.88 ($BnCH_2$), 74.85 ($BnCH_2$), 74.70 (C-3^E) , 74.64 (BnCH2), 74.58 (C-5^C), 74.43 ($BnCH_2$), 74.41 ($BnCH_2$), 74.35 (C-4^C), 74.14 (C-5^B), 73.86 ($BnCH_2$), 73.71 ($BnCH_2$), 73.49 ($BnCH_2$), 73.17 (C-2^D), 72.57 (C-2^B), 71.58 (C-4^F), 70.91 (C-3^B), 70.78 (C-5^D), 70.29 (C-3^C), 67.59 (C-6^A), 66.91 (C-6^E), 66.46 (C-6^C), 63.11 (C-2^A), 62.43 (C-2^E), 61.37 (C-2^C), 55.25 (1-OMe), 52.28 (C-6^{B,D}OOMe), 51.77 (C-6^{F}OOMe).

HRMS (ESI): Calc. for $C_{131}H_{133}N_9O_{34}Na$ $[M+Na]^+$: 2398.8853; found 2398.8850.

Deprotection and Sulfation

Hexasaccharide HX1

Methyl [methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl (2,3-di-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-(2-azido-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-[methyl (3-*O*-benzyl-β-D-glucopyranosyl) uronate]-(1⟶4)-2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (H1A)



A solution of **H1** (77 mg, 0.032 mmol, 1 eq) in THF (3.7 ml) at -5 °C. After stirring at RT for 48 h, mixture was cooled to 0 °C and MeOH (6.8 ml) and 3N KOH (2.4 ml) were added. Reaction was stirred for 48 h at RT, then diluted with EtOAc, pH was reduced to 1 using 1 M HCl. Aq. Phase was extracted 6x with EtOAc, phases were separated, org. phase was dried over $MgSO_4$ and concentrated. Residue was eluted from a LH-20 size exclusion column with CH_2Cl_2/MeOH 1:1. Fractions containing product were pooled and purified *via* chromatography, giving **H1A** in two fractions, 25 mg (0.01 mmol, 54%) and 10 mg (0.005 mmol, 21%) both as white solids. First fraction was used for further synthesis.

R_f (EtOAc/MeOH/H_2O/AcOH 16:1:1:0.1): 0.63

$[\alpha]_D$: + 32.2 (*c* = 1.0, MeOH)

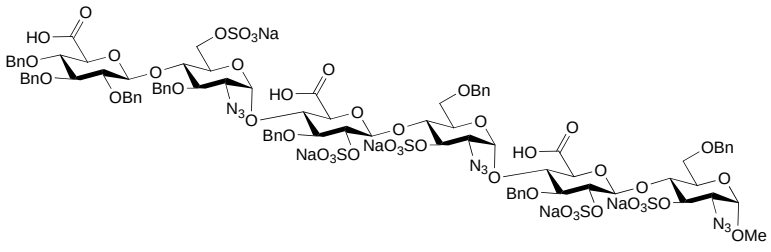
^{1}H-NMR (600 MHz, CD_3OD) δ = 7.46 (d, *J* = 7.4 Hz, 2H, Bn), 7.41 – 7.33 (m, 11H, Bn), 7.33 – 7.20 (m, 22H, Bn), 5.48 (d, *J* = 3.7 Hz, 1H, $H1^{A\text{ or }C\text{ or }E}$), 5.44 (d, *J* = 3.7 Hz, 1H, $H1^{A\text{ or }C\text{ or }E}$), 5.14 – 5.03 (m, 4H, $BnCH_2$), 4.92 (d, *J* = 11.3 Hz, 2H, $BnCH_2$), 4.78 – 4.69 (m, 6H, $H1^{A\text{ or }C\text{ or }E}$, $H1^{B\text{ or }D\text{ or }F}$), $BnCH_2$), 4.63 (ddd, *J* = 20.9, 16.3, 8.1 Hz, 5H, $BnCH_2$), 4.53 (d, *J* = 11.7 Hz, 2H), 4.48 (d, *J* = 11.8 Hz, 1H), 4.35 (t, *J* = 8.5 Hz, 2H 2 $H1^{A\text{ or }C\text{ or }E}$), 4.02 – 3.83 (m, 12H), 3.82 – 3.72 (m, 6H), 3.71 – 3.62 (m, 5H), 3.57 (dt, *J* = 24.1, 8.6 Hz, 3H), 3.52 – 3.46 (m, 3H), 3.45 – 3.42 (m, 1H), 3.38 (s, 3H), 3.24 (dd, *J* = 10.3, 3.7 Hz, 1H, H2 A or C or E), 3.17 (dd, *J* = 10.3, 3.5 Hz, 1H, H2 A or C or E), 3.06 (dd, *J* = 10.5, 3.7 Hz, 1H, H2 A or C or E).

^{1}C-NMR (151 MHz, CD_3OD) δ = 171.00, 170.42 (COOH) (COOH), 170.21 (COOH), 138.58 (Bn), 138.52 (Bn), 138.45 (Bn), 138.23 (Bn), 138.14 (Bn), 138.10 (Bn), 138.04 (Bn), 128.67 (Bn),

128.60 (Bn), 128.44 (Bn), 128.20 (Bn), 128.13 (Bn), 128.02 (Bn), 127.92 (Bn), 127.87 (Bn), 127.80 (Bn), 127.64 (Bn), 127.54 (Bn), 127.52 (Bn), 127.47 (Bn), 127.37 (Bn), 127.28 (Bn), 127.26 (Bn), 127.23 (Bn), 127.16 (Bn), 127.14 (Bn), 127.10 (Bn), 102.98 (C-$1^{\text{B or D or F}}$), 102.86 (C-$1^{\text{B or D or F}}$), 102.43 (C-$1^{\text{B or D or F}}$), 98.78 (C-$1^{\text{A or C or D}}$), 97.98 (C-$1^{\text{A or C or D}}$), 97.66 (C-$1^{\text{A or C or D}}$), 84.41, 84.01, 83.74, 81.55, 79.80, 79.31, 78.16, 77.51, 76.36, 75.79, 75.23 ($BnCH_2$), 74.97 ($BnCH_2$), 74.82 ($BnCH_2$), 74.77 ($BnCH_2$), 74.49 ($BnCH_2$), 74.34 ($BncH_2$), 74.31 ($BnCH_2$), 74.03, 74.01, 73.10 ($BnCH_2$), 73.07 ($BnCH_2$), 71.81, 70.18, 69.73, 69.63, 69.18, 67.95, 67.45, 62.72 (C-$2^{\text{A or C or E}}$), 62.66 (2 C-$2^{\text{A or C or E}}$), 58.94 (C-$6^{\text{A or C or E}}$), 54.27 (1-OMe).

LRMS (ESI): Calc. for $C_{93}H_{100}N_9O_{31}^{3-}$ $[M-3H]^{3-}$: 613.22; found 613.67.

Methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-azido-3-*O*- benzyl-2-deoxy-6-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-azido-6-*O*-benzyl-2-deoxy-3-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-2-azido-6-*O*-benzyl-2-deoxy-3-*O*-sulfonate-α-D-glucopyranoside pentasodium salt (H1B)



$SO_3 \cdot NMe_3$ (65 mg, 0.466 mmol, 25 eq) complex and **H1A** (43 mg, 0.023 mmol, 1 eq) were dried together with stir bar over night at Schlenck, then put under N_2 atmosphere and dissolved in DMF (3 ml). Mixture was placed into microwave reactor and stirred for 1.5 h at 100 °C. Reaction was quenched with NEt_3 (0.6 ml), filtered through micropore filter, diluted with CH_2Cl_2 (1 ml) and MeOH (1 ml) and solution was layered on top of a Sephadex LH-20 column, wich was eluted with MeOH/CH_2Cl_2 1:1. Sulfated fractions were pooled and eluted from a Dowex 50WX4-Na^+ ion exchange column with MeOH/ CH_2Cl_2 1:1 to give **H1B** (46 mg, 0.20 mmol, 85%) as slightly yellow solid.

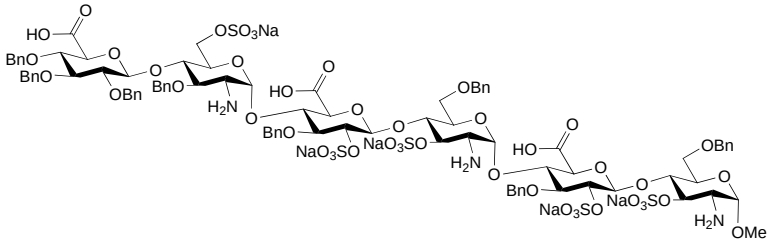
R_f (CH_2Cl_2 /MeOH/aq. NH_4OH 7:3:1): 0.29

$[\alpha]_D$: +30.4 (*c* = 1.1 MeOH)

^{1}H-NMR (600 MHz, CD_3OD) δ = 7.65 – 7.09 (m, 37H, Bn), 5.55 (s, 1H, H1 C or E), 5.25 (dd, *J* = 40.2, 17.9 Hz, 3H, H1$^{\text{C or E}}$, $BnCH_2$), 5.03 (ddd, *J* = 30.7, 22.7, 10.2 Hz, 5H, $BnCH_2$), 4.80 – 4.38

(m, 18H, 3 $H1^{B,D,F}$, A: $H1^{A}$, $BnCH_2$, $H6^{A\ or\ C\ or\ E}a$), 4.23 – 3.53 (m, 23H), 3.50 – 3.33 (m, 6H, 1-OMe, 2 $H2^{A\ or\ C\ or\ E}$), 3.22 – 3.02 (m, 11H, $H2^{A\ or\ C\ or\ E}$).

Methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-amino-3-*O*-benzyl-2-deoxy-6-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-amino-6-*O*-benzyl-2-deoxy-3-*O*-sulfonato-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-2-amino-6-*O*-benzyl-2deoxy-3-*O*-sulfonato-α-D-glucopyranoside pentasodium salt (H1C)



H1B (18 mg, 7.6 μmol, 1 eq) was dissolved in THF (2.68 ml) and treated with 0.1 M NaOH (0.64 ml, 0.064 mmol, 24 eq). Then a solution of 1 M PMe_3 in THF (0.09 ml, 0.09 mmol, 30 eq) was added and the reaction was stirred for 7.5h. Reaction was neutralised with 0.1 M HCl, concentrated and the residue was eluted from a Sephadex LH-20 column with CH_2Cl_2/MeOH 1:1 to give **H1C** (15 mg, 6.6 μmol, 82%) as white solid.

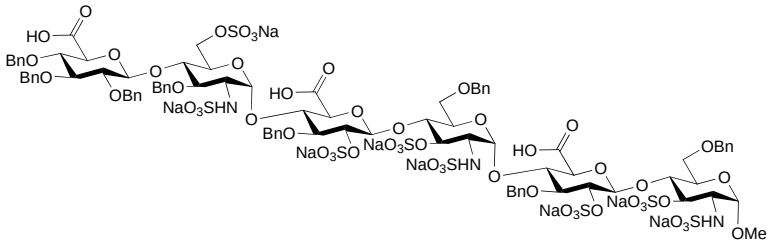
R_f (CH_2Cl_2 /MeOH/aq. NH_4OH 7:3:1): 0.23

$[\alpha]_D$: +24.9 (*c* = 0.9 MeOH)

^{1}H-NMR (500 MHz, CD_3OD) δ = 7.42 – 7.05 (m, 23H), 5.21 (dd, *J* = 16.6, 8.8 Hz, 1H), 5.14 (dd, *J* = 18.0, 5.2 Hz, 1H), 5.08 – 4.97 (m, 2H), 4.97 – 4.91 (m, 1H), 4.91 – 4.81 (m, 2H), 4.72 – 4.62 (m, 4H), 4.61 – 4.39 (m, 8H), 4.34 – 4.23 (m, 2H), 4.22 – 4.14 (m, 1H), 4.13 – 4.02 (m, 3H), 3.98 (dd, *J* = 15.5, 6.5 Hz, 2H), 3.86 (dd, *J* = 31.1, 24.6 Hz, 3H), 3.75 – 3.61 (m, 3H), 3.60 – 3.48 (m, 3H), 3.39 – 3.29 (m, 3H), 3.29 – 3.23 (m, 2H).

LRMS (ESI): Calc. for $C_{93}H_{101}N_3Na_4O_{46}S_5^{3-}$ $[M-3H+4Na]^{3-}$: 562.10; found 562.46.

Methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(3-*O*-benzyl-2-deoxy-2-sulfamino-6-*O*-sulfonate-α-D-glucopyranosyl-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-deoxy-6-*O*-benzyl-2-sulfamino-3-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-2-deoxy-6-*O*-benzyl-2-sulfamino-3-*O*-sulfonate-α-D-glucopyranoside octasodium salt (H1D)



NEt_3 (0.15 ml) and $SO_3 \cdot$ pyridine complex (16 mg, 0.099 mmol, 15 eq) were added to a solution of **H1C** (15 mg, 6.6 μmol, 1 eq) in dry pyridine. Stirring at RT for 2h, then another portion of complex added. More additions after 3h and 4h, total 6.5h reaction time. Reaction mixture was diluted with CH_2Cl_2 (1 ml) and MeOH (1 ml) and solution was layered on top of a Sephadex LH-20 column, which was eluted with MeOH/CH_2Cl_2 1:1. Sulfated fractions were pooled and eluted from a Dowex 50WX4-Na^+ ion exchange column MeOH/CH_2Cl_2 9:1 giving **H1D** (14 mg, 5.4 μmol, 72%) as off white solid.

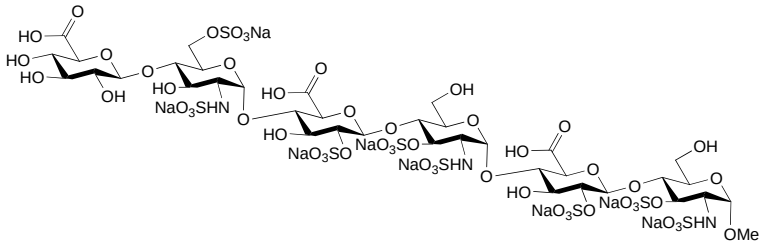
R_f (CH_2Cl_2 /MeOH/aq. NH_4OH 7:3:1): 0.16

[α]$_D$: +30.1 (*c* = 0.8, MeOH)

^{1}H-NMR (500 MHz, CD_3OD) δ = 7.53 – 6.88 (m, 32H), 5.23 (ddd, *J* = 12.1, 11.6, 7.1 Hz, 2H), 4.89 (ddd, *J* = 27.3, 19.8, 5.5 Hz, 5H), 4.65 – 4.42 (m, 10H), 4.22 – 3.24 (m, 32H), 3.31 – 3.21 (m, 18H), 3.09 – 2.99 (m, 2H), 2.69 (dd, *J* = 14.9, 8.4 Hz, 2H).

LRMS (ESI): Calc. for $C_{93}H_{98}N_3Na_8O_{55}S_8^{3-}$ $[M-3H+8Na]^{3-}$: 859.06; found 858.61.

Methyl (β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-deoxy-2-sulfamino-6-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-deoxy-2-sulfamino-3-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-2-deoxy-2-sulfamino-3-*O*-sulfonate-α-D-glucopyranoside octasodium salt (HX1)



A solution of **H1D** (11 mg, 4.3 μmol, 1 eq) was hydrogenated in the presence of Pd/C and $Pd(OH)_2$ for 2 d. Suspension was filtered, concentrated, diluted in H_2O (10 ml) and extracted with CH_2Cl_2 (3x 3 ml) and EtOAc (3x 5 ml), concentrated and eluted from a column of Dowex 50WX4-Na+ with MeOH/H_2O 1:9 giving **HX1** (7 mg, 3.76 μmol, 88%) as white solid.

[α]$_D$: +13.0 (*c* = 1.0, H_2O)

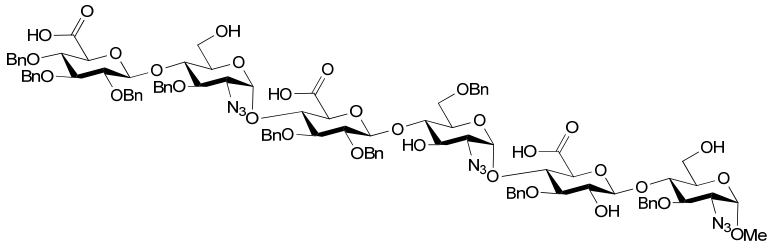
^{1}H NMR (500 MHz, D_2O, selected peaks) δ 5.52 (d, *J* = 3.8 Hz, 1H, α), 5.29 (d, *J* = 3.7 Hz, 1H, α), 4.88 (d, *J* = 3.4 Hz, 1H, α), 4.56 (d, *J* = 7.9 Hz, 1H, β), 4.54 (d, *J* = 9.3 Hz, 1H, β), 4.46 (d, *J* = 8.2 Hz, 1H, β), 3.26 (3H, -OC*H*$_3$).

^{13}C NMR (126 MHz, D_2O, selected peaks) δ 101.77 (β), 100.54 (β), 100.44 (β), 99.33 (α), 98.06 (α), 97.15 (α), 65.67 (C6-OSO_3^-), 59.33 (C6-OH), 59.16 (C6-OH), 55.01 (-O*C*H$_3$)

LRMS (ESI): Calc. for $C_{37}H_{53}N_3Na_2O_{55}S_8^{6-}$ [M-8H+2Na]$^{6-}$:286.82; found 287.05. Calc. for $C_{37}H_{51}N_3Na_4O_{55}S_8^{6}$ [M-10H+4Na]$^{6-}$: 294.14; found 293.66. Calc. for $C_{37}H_{52}N_3Na_5O_{55}S_8^{4-}$ [M-9H+5Na]$^{4-}$:447.22; found 447.58.

Hexasaccharide HX2

Methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-(2,3-di-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-azido-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranoside (H2A)



H_2O_2 (35%, 1.24 ml) and LiOH solution (1N, 2.4 ml) were added to a solution of **H2** (85 mg, 0.035 mmol, 1 eq) in THF (4 ml) at -5 °C. After stirring at RT for 48 h, mixture was cooled to 0 °C and MeOH (7.4 ml) and KOH (3 N, 2.6 ml) were added and reaction was stirred for 48 h at RT. Reaction was diluted with EtOAc, pH was reduced to 1 using 1 M HCl. Aq. Phase was extracted 6x with EtOAc. Combined org. phase was dried over $MgSO_4$ and concentrated. Residue was diluted with CH_2Cl_2 (1 ml) and MeOH (1 ml), layered on top of a Sephadex LH-20 column which was eluted with CH_2Cl_2/MeOH 1:1. Fractions containing product were pooled, concentrated and eluted from an ion exchange column with CH_2Cl_2/MeOH 1:1 giving **H2A** (63 mg, 0.033 mmol, 93%) as white solid.

R_f (CH_2Cl_2/MeOH/aq. NH_4OH 9:1:0.2): 0.71

[α]$_D$: +35.7 (*c* = 1.0, MeOH)

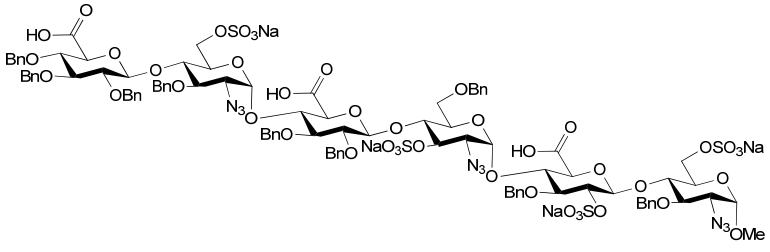
^{1}H-NMR (600 MHz, CD_3OD) δ = 7.48 – 7.36 (m, 7H, Bn), 7.35 – 7.17 (m, 30H, Bn), 5.51 – 5.47 (m, 1H, H1 B or D or F), 5.42 – 5.38 (m, 1H, H1$^{B\text{ or }D\text{ or }F}$), 5.11 (dd, *J* = 14.4, 6.9 Hz, 3H, $BnCH_2$),

4.93 (t, *J* = 6.5 Hz, 1H, $BnCH_2$), 4.83 – 4.78 (m, 2H, $BnCH_2$), 4.78 – 4.56 (m, 12H, $H1^{C,E}$, $H1^{B\text{ or }D\text{ or }F}$, $BnCH_2$), 4.55 – 4.50 (m, 1H, $BnCH_2$), 4.40 (d, *J* = 7.7 Hz, 1H, $H1^{A}$), 4.33 – 4.26 (m, 2H, BnCH2), 4.15 (dd, *J* = 15.3, 6.6 Hz, 2H), 4.07 – 3.99 (m, 3H), 3.98 – 3.90 (m, 6H), 3.87 – 3.78 (m, 6H), 3.73 – 3.62 (m, 4H), 3.56 (m, 3H), 3.50 – 3.40 (m, 3H), 3.37 (s, 3H), 3.27 – 3.22 (m, 2H), 3.13 – 3.04 (m, 2H).

^{13}C-NMR (151 MHz, CD_3OD) δ = 171.95 (COOH), 171.12 (COOH), 170.38 (COOH), 138.63 (Bn), 138.53 (Bn), 138.45 (Bn), 138.35 (Bn), 138.27 (Bn), 138.20 (Bn), 137.92 (Bn), 128.63 (Bn), 128.56 (Bn), 128.50 (Bn), 128.40 (Bn), 128.22 (Bn), 128.17 (Bn), 128.12 (Bn), 128.06 (Bn), 127.93 (Bn), 127.89 (Bn), 127.84 (Bn), 127.83 (Bn), 127.78 (Bn), 127.76 (Bn), 127.65 (Bn), 127.56 (Bn), 127.49 (Bn), 127.45 (Bn), 127.40 (Bn), 127.36 (Bn), 127.15 (Bn), 127.08 (Bn), 126.99 (Bn), 103.15 (C-1 C or E), 102.75 (C-1 C or E), 102.19 ($C\text{-}1^{A}$), 98.64 ($C\text{-}^{B\text{ or }D\text{ or }E}$), 98.02 ($C\text{-}1^{B\text{ or }D\text{ or }E}$), 97.65 ($C\text{-}1^{B\text{ or }D\text{ or }E}$), 84.52, 83.74, 83.46, 81.65, 81.37, 79.90, 78.02, 77.98, 77.30, 77.17, 76.72, 75.26, 75.17 ($BnCH_2$), 75.07 ($BnCH_2$), 74.80 ($BnCH_2$), 74.76 ($BnCH_2$), 74.57 ($BnCH_2$), 74.42 ($BnCH_2$), 74.16 ($BnCH_2$), 73.02 ($BnCH_2$), 72.91, 71.75, 71.34, 70.21, 62.99, 62.88 ($C\text{-}2^{A\text{ or }C\text{ or }E}$), 62.80 (2 C, $C\text{-}2^{A\text{ or }C\text{ or }E}$), 59.58 ($C\text{-}6^{A\text{ or }C\text{ or }E}$), 54.08 (1-OMe).

LRMS (ESI): Calc. for $C_{100}H_{106}N_9O_{31}$ $[M\text{-}3H]^{3-}$: 643.23; found 643.62.

Methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-azido-3-*O*-benzyl-2-deoxy-6-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(2,3-di-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-azido-6-*O*-benzyl-2-deoxy-3-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-2-azido-3-*O*-benzyl-2-deoxy-6-*O*-sulfonate-α-D-glucopyranoside tetrasodium salt (H2B)



$SO_3 \cdot NMe_3$ complex (65 mg, 0.455 mmol, 20 eq) and **H2A** (45 mg, 0.023 mmol, 1 eq) were dried together with stir bar over night at Schlenck line, the put under N_2 atmosphere and dissolved in DMF (3 ml). Mixture was placed into microwave reactor and stirred for 1.5 h at 100 °C. Reaction was quenched with NEt_3 (0.6 ml), filtered through micropore filter, diluted with CH_2Cl_2 (1 ml) and MeOH (1 ml) and solution was layered on top of a Sephadex LH-20 column, which was eluted with MeOH/CH_2Cl_2 1:1. Sulfated fractions were pooled and eluted

from a Dowex 50WX4-Na^+ ion exchange column with MeOH/CH_2Cl_2 1:1 to give **H2B** (39 mg, 0.017 mmol, 72%) as slightly yellow solid.

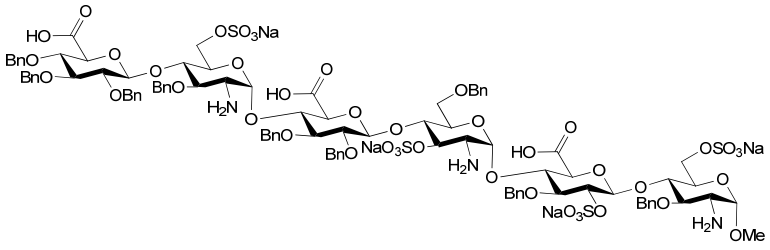
R_f (CH_2Cl_2 /MeOH/aq. NH_4OH 7:3:1): 0.30

$[\alpha]_D$: +25.7 (*c* = 1.2 MeOH)

^{1}H-NMR (600 MHz, CD_3OD) δ = 7.53 (d, *J* = 7.5 Hz, 2H, Bn), 7.45 (dt, *J* = 16.3, 7.3 Hz, 6H, Bn), 7.37 – 7.14 (m, 31H, Bn), 5.55 (d, *J* = 3.4 Hz, 1H, $H1^{C \text{ or } E}$), 5.39 (d, *J* = 3.5 Hz, 1H, $H1^{C \text{ or } E}$), 5.33 (d, *J* = 9.8 Hz, 1H, $BnCH_2$), 5.16 – 4.91 (m, 8H, 2 $H1^{B \text{ or } D \text{ or } E}$, $BnCH_2$), 4.78 – 4.55 (m, 13H, $H1^A$, $H6^{A \text{ or } C \text{ or } E}$a), 4.52 – 4.43 (m, 3H, $H1^{B \text{ or } D \text{ or } E}$, $H6^{A \text{ or } C \text{ or } E}$b, $BnCH_2$), 4.39 (d, *J* = 12.0 Hz, 1H, $BnCH_2$), 4.29 (d, *J* = 10.5 Hz, 1H, $H6^{A \text{ or } C \text{ or } E}$a), 4.18 (dd, *J* = 23.6, 10.4 Hz, 3H, $H6^{A \text{ or } C \text{ or } E}$b), 4.09 – 3.90 (m, 10H, $H6^{A \text{ or } C \text{ or } E}$a), 3.90 – 3.83 (m, 2H), 3.75 (ddd, *J* = 23.9, 16.7, 9.2 Hz, 4H), 3.65 (d, *J* = 10.7 Hz, 1H, $H6^{A \text{ or } C \text{ or } E}$b), 3.45 (dt, *J* = 30.0, 8.0 Hz, 3H), 3.38 (s, 3H, OMe), 3.26 (td, *J* = 10.7, 3.7 Hz, 3H, 3 H2).

LRMS (ESI): Calc. for $C_{100}H_{102}N_9Na_4O_{43}S_4$ $[M-7H+4Na]^{3-}$: 778.81; found 779.39.

Methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-amino-3-*O*-benzyl-2-deoxy-6-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(2,3-di-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-amino-6-*O*-benzyl-2deoxy3-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-2-amino-3-*O*-benzyl-2-deoxy-6-*O*-sulfonate-α-D-glucopyranoside tetrasodium salt (H2C)



H2B (17 mg, 7.2 umol, 1 eq) was dissolved in THF (2.56 ml) and treated with 0.1 M NaOH (0.58 ml, 0.058 mmol, 30 eq). Then a solution of 1M PMe_3 in THF (0.09 ml, 0.09 mmol, 24 eq) was added and the reaction was stirred for 8 h. Reaction was neutralised with 0.1 M HCl, concentrated and the residue was eluted from a Sephadex LH-20 with CH_2Cl_2/MeOH 1:1 gving **H2C** (15 mg, 0.0066 mmol, 92%) as slightly yellow solid.

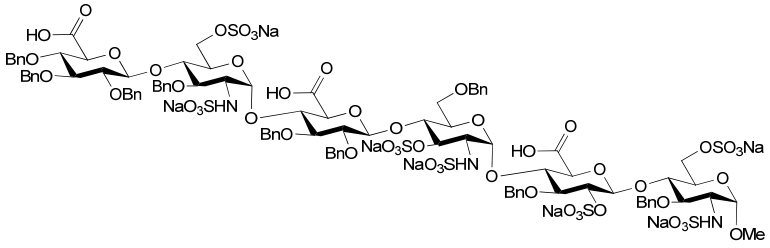
R_f (CH_2Cl_2 /MeOH/aq. NH_4OH 7:3:1): 0.27

$[\alpha]_D$: +37.9 (*c* = 1.0, MeOH)

^{1}H-NMR (600 MHz, CD_3OD) δ = 7.46 – 6.99 (m, 18H, Ar), 5.36 – 5.14 (m, 2H), 5.02 (d, *J* = 4.4 Hz, 1H), 4.87 (ddd, *J* = 28.8, 15.1, 11.7 Hz, 2H), 4.71 – 4.27 (m, 11H), 4.24 – 3.80 (m, 8H), 3.78 – 3.68 (m, 2H), 3.62 (ddd, *J* = 17.3, 13.1, 7.1 Hz, 2H), 3.54 (dd, *J* = 14.6, 8.6 Hz, 2H), 3.40 – 3.23 (m, 5H), 3.14 – 3.04 (m, 1H).

LRMS (ESI): Calc. for $C_{100}H_{108}N_3Na_4O_{43}S_4$ $[M-7H+4Na]^{3-}$: 753.15; found 753.25.

Methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(3-*O*-benzyl-2-deoxy-sulfamino-6-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(2,3-di-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(6-*O*-benzyl-2-deoxy-2-sulfamino-3-*O*-sulfonate-α-D-glucopyranosyl-(1⟶4)-3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-3-*O*-benzyl-2-deoxy-2-sulfamino-6-*O*-sulfonate-α-D-glucopyranoside heptasodium salt (H2D)



NEt_3 (0.76 ml) and SO_3· py complex (16 mg, 0.099 mmol, 15 eq) were added to a solution of **H2C** (15 mg, 0.0066 mmol, 1 eq) in dry py (0.76 ml. Stirring at RT for 1.5 h, portion of complex added. Another addition after 3 h and 4.5 h. Total stirring time 6.5h. Reaction was diluted with CH_2Cl_2 (1 ml) and MeOH (1 ml) and solution was layered on top of a Sephadex LH-20 column, wich was eluted with MeOH/ CH_2Cl_2. Sulfated fractions were concentrated and eluted from a Dowex 50WX4-Na^+ ion exchange column MeOH/ CH_2Cl_2 9:1 giving **H2D** (21 mg, quant) as off-white solid.

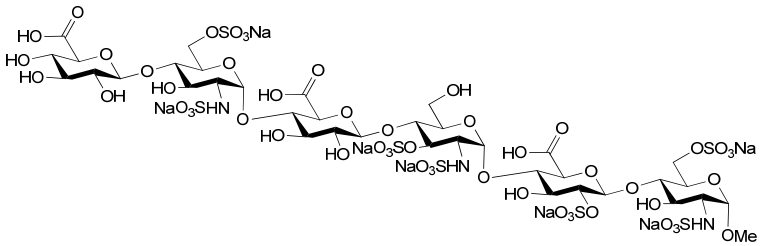
R_f (CH_2Cl_2 /MeOH/aq. NH_4OH 7:3:1): 0.20

^{1}H-NMR (600 MHz, CD_3OD) δ = 7.55 – 6.90 (m, 44H), 5.54 – 4.83 (m, 13H), 4.69 – 4.32 (m, 19H), 4.28 – 3.77 (m, 19H), 3.75 – 3.23 (m, 20H), 3.04 (ddd, *J* = 21.9, 8.9, 4.4 Hz, 2H).

LRMS (ESI): Calc. for $C_{100}H_{106}N_3Na_4O_{52}S_7$ $[M-9H+4Na]^{5-}$: 499.47; found 499.63.

Methyl (D-glucopyranosyl uronic acid)-(1⟶4)-(2-deoxy-2-sulfamino-6-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)- (β-D-gluco-pyranosyl uronic acid)-(1⟶4)-(2-deoxy-2-sulfamino-3-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(2-*O*-sulfonate-β-D-glucopyranosyl

uronic acid)-(1⟶4)-2-deoxy-2-sulfamino-6-*O*-sulfonate-α-D-glucopyranoside heptasodium salt (HX2)



A solution of **H2D** (11 mg, 4.3 μmol, 1 eq) was hydrogenated in the presence of Pd/C and $Pd(OH)_2$. Suspension was filtered, concentrated, diluted in H_2O (10 ml) and extracted with CH_2Cl_2 (3x 3 ml) and EtOAc (3x 5 ml), concentrated and eluted from a column of Dowex 50WX4-Na^+ with MeOH/H_2O 1:9 giving **HX2** (7 mg, 3.76 μmol, 88%) as white solid.

[α]D: +0.46 (*c* = 0.9, H_2O)

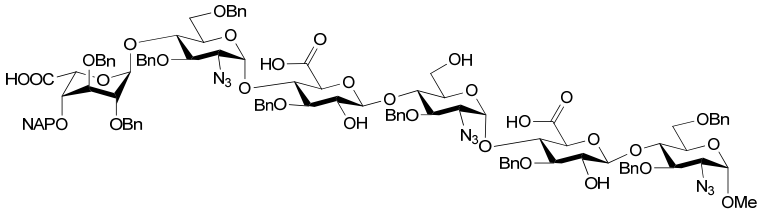
^{1}H NMR (600 MHz, D_2O, selected peaks) δ 5.51 (d, *J* = 3.8 Hz, 1H, α), 5.47 (d, *J* = 3.4 Hz, 1H, α), 4.89 (d, *J* = 3.6 Hz, 1H, α), 4.61 (1H, β – under solvent peak), 4.46 (d, *J* = 7.8 Hz, 1H, β), 4.43 (d, *J* = 9.2 Hz, 1H, β), 3.27 (s, 3H, -OC*H*$_3$).

^{13}C NMR (151 MHz, D_2O, selected peaks) δ 101.82 (β), 101.46 (β), 99.92 (β), 98.15 (α), 98.05 (α), 96.92 (α), 65.88 (C6-OSO_3^-), 65.74 (C6-OSO_3^-), 59.31 (C6-OH), 55.37 (-O*C*H$_3$)

LRMS (ESI): Calc. for $C_{37}H_{52}N_3Na_3O_{52}S_7^{4-}$ [*M*-7H+3Na]$^{4-}$: 415.98; found 416.31.

Hexasaccharide HX3

Methyl [2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl-α-L-idopyranosyl uronic acid]-(1⟶4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-β-D-gluco-pyranosyl uronic acid)-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (H3A)



35% H_2O_2 (2.09 ml) and 1 M LiOH (4.08 ml) solution were added to a solution of **H3** (144 mg, 0.059 mmol, 1 eq) in THF (6.86 ml) at -5 °C. After stirring at RT for 48 h, mixture was cooled to 0 °C and MeOH (12.6 ml) and 3 N KOH (4.45 ml) were added. Stirring for 48 h at RT. Reaction was diluted with EtOAc, pH was reduced to 1 using 1 M HCl. Aq. Phase was extracted 6x with EtOAc. Org. phase was dried over $MgSO_4$

and concentrated. Residue was eluted from a size exclusion column LH-20 using CH_2Cl_2/MeOH 1:1 to give **H3A** (104 mg, 0.050 mmol, 85%).

R_f (EtOAc/MeOH/H_2O/AcOH 18:1:1:0.1): 0.65

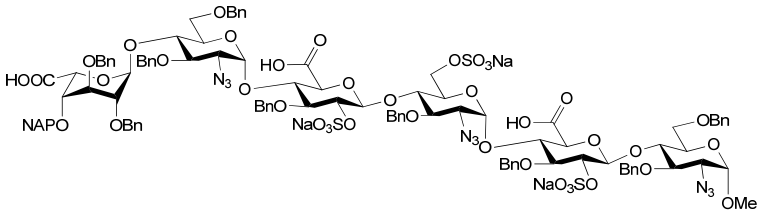
$[\alpha]_D$: +29.2 (*c* =1.0, MeOH)

^{1}H-NMR (600 MHz, CD_3OD) δ = 7.97 (d, *J* = 8.0 Hz, 1H, Ar), 7.80 (dd, *J* = 19.6, 8.1 Hz, 2H, Ar), 7.46 – 7.01 (m, 40H, Ar), 5.40 (d, *J* = 26.8 Hz, 2H, 2 H1 C and E), 5.11 (d, *J* = 3.8 Hz, 1H, $ArCH_2$), 5.05 (d, *J* = 11.6 Hz, 1H, $H1^F$), 4.97 – 4.65 (m, 13H, $ArCH_2$), 4.52 – 4.22 (m, 9H, $H1^{A,}$, $H1^{B\text{ or }D}$, $ArCH_2$), 4.02 (s, 3H, $H1^{B\text{ or }D}$, $ArCH_2$), 3.99 – 3.60 (m, 15H), 3.57 – 3.42 (m, 5H), 3.34 (d, *J* = 24.2 Hz, 4H, OMe, $H2^{A\text{ or }C\text{ or }E}$), 3.23 (s, 2H, 2 $H2^{A\text{ or }C\text{ or }E}$).

^{1}C-NMR (151 MHz, CD_3OD) δ = 170.41 (COOH), 170.28 (COOH), 168.90 (COOH), 138.20 (Ar), 137.95 (Ar), 137.84 (Ar), 137.57 (Ar), 137.54 (Ar), 137.44 (Ar), 137.40 (Ar), 137.27 (Ar), 133.70 (Ar), 132.42 (Ar), 131.69 (Ar), 129.26 (Ar), 129.01 (Ar), 128.68 (Ar), 128.49 (Ar), 128.45 (Ar), 128.40 (Ar), 128.36 (Ar) 128.33 (Ar), 128.28 (Ar), 128.23 (Ar), 128.06 (Ar), 127.95 (Ar), 127.89 (Ar), 127.83 (Ar), 127.78 (Ar), 127.68 (Ar), 127.66 (Ar), 126.99 (Ar), 126.43 (Ar), 125.97 (Ar), 125.27 (Ar), 125.11 (Ar), 124.10 (Ar), 102.31 ($C\text{-}1^{B,D}$), 99.55 ($C\text{-}1^{C\text{ or }D\text{ or }F}$), 98.64 ($C\text{-}1^{A}$), 97.75 ($C\text{-}1^{C\text{ or }D\text{ or }F}$), 97.68 ($C\text{-}1^{C\text{ or }D\text{ or }F}$), 83.54, 82.84, 78.52, 78.11, 75.68, 75.42 ($ArCH_2$), 75.11 ($ArCH_2$), 74.95 ($ArCH_2$), 74.83 ($ArCH_2$), 74.76 ($ArCH_2$), 74.58 ($ArCH_2$), 74.40 ($ArCH_2$), 74.16 ($ArCH_2$), 73.76 ($ArCH_2$), 73.57 ($ArCH_2$), 73.31 ($ArCH_2$), 73.09 ($ArCH_2$), 73.00 ($ArCH_2$), 72.26 ($ArCH_2$), 71.34, 71.01, 70.70, 70.09, 68.17 ($C\text{-}6^{A\text{ or }C\text{ or }D}$), 67.97 ($C\text{-}6^{A\text{ or }C\text{ or }D}$), 63.44 ($C\text{-}2^{A\text{ or }C\text{ or }D}$), 63.08 ($C\text{-}2^{A\text{ or }C\text{ or }D}$), 62.99 ($C\text{-}2^{A\text{ or }C\text{ or }D}$), 61.03 ($C\text{-}6^{A\text{ or }C\text{ or }D}$), 55.33 (OMe).

LRMS (ESI): Calc. for $C_{111}H_{114}N_9O_{31}$ $[M\text{-}3H]^{3-}$: 689.92; found 690.29.

Methyl [2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl-α-L-idopyranosyl uronic acid]-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-gluco-pyranosyl uronic acid)-(1⟶4)-(2-azido-3-*O*-benzyl-2-deoxy-6-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside trisodium salt (H3B)



$SO_3 \cdot NMe_3$ complex (78 mg, 0.557 mmol, 15 eq) and **H3A** (77 mg, 0.037 mmol, 1 eq) were dried together with stir bar over night at Schlenck line, the put under N_2 atmosphere and dissolved in DMF (4.8 ml). Mixture was placed into microwave reactor and stirred for 1.5 h at 100 °C. Reaction was quenched with NEt_3 (0.97 ml), filtered through micropore filter, diluted with CH_2Cl_2 (1 ml) and MeOH (1 ml) and solution was layered on top of a Sephadex LH-20 column, which was eluted with MeOH/CH_2Cl_2 1:1. Sulfated fractions were concentrated and eluted from a Dowex 50WX4-Na^+ ion exchange column MeOH/ CH_2Cl_2 1:1 giving **H3B** (72 mg, 0.030 mmol, 82%) as slightly yellow solid.

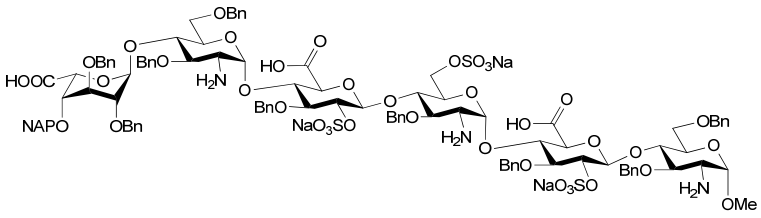
R_f (CH_2Cl_2/MeOH/aq. NH_4OH 7:3:1): 0.81

$[\alpha]_D$: +10.4 (*c* = 1.0, MeOH)

^{1}H-NMR (600 MHz, CD_3OD) δ = 8.08 (d, *J* = 8.4 Hz, 1H, Ar), 7.81 (dd, *J* = 22.7, 8.2 Hz, 3H, Ar), 7.57 – 7.08 (m, 46H, ar), 5.47 (dd, *J* = 14.0, 3.3 Hz, 2H, 2 $H1^{A \text{ or } C \text{ or } E \text{ or } F}$), 5.32 (d, *J* = 9.6 Hz, 1H, $ArCH_2$), 5.26 (d, *J* = 8.1 Hz, 2H, $H1^{A \text{ or } C \text{ or } E \text{ or } F}$, $ArCH_2$), 5.19 (dd, *J* = 16.6, 9.6 Hz, 2H, $ArCH_2$), 5.13 (d, *J* = 10.9 Hz, 2H, $ArCH_2$), 5.11 – 5.04 (m, 2H, $ArCH_2$, $H1^{B \text{ or } D}$), 4.99 – 4.90 (m, 3H), 4.75 – 4.63 (m, 7H, H1, $H1^{A \text{ or } C \text{ or } E \text{ or } F}$ 4.57 (d, *J* = 9.9 Hz, 3H, $H1^{B \text{ or } D}$), 4.54 – 4.32 (m, 11H), 4.27 (dd, *J* = 20.7, 9.8 Hz, 2H), 4.22 – 4.15 (m, 2H), 4.14 – 4.04 (m, 4H), 4.02 – 3.85 (m, 10H), 3.77 (ddd, *J* = 28.6, 18.2, 9.7 Hz, 6H), 3.66 (dd, *J* = 22.9, 11.7 Hz, 3H), 3.57 (dd, *J* = 16.4, 7.8 Hz, 2H), 3.45 (s, 2H), 3.37 (d, *J* = 8.7 Hz, 3H), 3.22 (ddd, *J* = 31.7, 13.4, 6.8 Hz, 4H).

LRMS (ESI): Calc. for $C_{111}H_{113}N_9Na_3O_{40}S_3$ $[M-6H+3Na]^{3-}$: 792.53; found 792.27.

Methyl [2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl-α-L-idopyranosyl uronic acid]-(1⟶4)-(2-amino-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-gluco-pyranosyl uronic acid)-(1⟶4)-(2-amino-3-*O*-benzyl-2-deoxy-6-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-2-amino-3,6-di-*O*-benzyl-2-deoxy-α-D-gluco-pyranoside trisodium salt (H3C)



H3B (72 mg, 0.030 mmol, 1 eq) was dissolved in THF (2.28 ml), 1 M PMe_3 in THF (0.73 ml, 0.73 mmol, 24 eq) and 0.1 M NaOH (9.08 ml, 0.908 mmol, 30 eq) were added and the reaction was stirred for 5h. Reaction was neutralised with 0.1 M HCl, concentrated and the residue was eluted from a Sephadex LH-20 with CH_2Cl_2/MeOH 1:1 to give **H3C** (68 mg, 0.0295 mmol, 98%), white solid

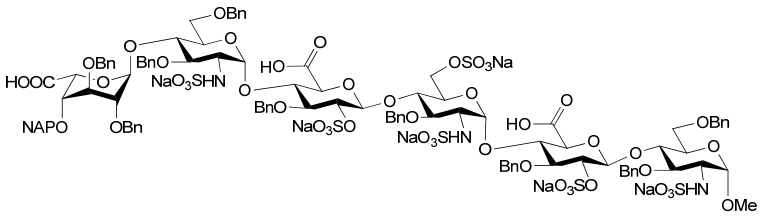
R_f (CH_2Cl_2/MeOH/aq. NH_4OH 7:3:1): 0.86

$[\alpha]_D$: +42.6 (*c* = 1.0, MeOH)

^{1}H-NMR (600 MHz, CD_3OD) δ = 8.03 (d, *J* = 8.4 Hz, 1H, Ar), 7.80 – 7.71 (m, 2H, Ar), 7.50 – 7.09 (m, 47H, Ar), 7.03 (dt, *J* = 20.7, 7.0 Hz, 3H, Ar), 5.46 (d, *J* = 10.4 Hz, 1H), 5.39 (d, *J* = 6.5 Hz, 1H, H1), 5.36 – 5.26 (m, 3H, H1), 5.23 – 5.15 (m, 2H, H1), 5.09 (d, *J* = 4.5 Hz, 1, 1H), 5.01 (d, *J* = 11.3 Hz, 2H), 4.98 – 4.91 (m, 4H, H1), 4.81 – 4.69 (m, 5H), 4.66 – 4.60 (m, 3H), 4.61 – 4.47 (m, 10H, H6a), 4.46 – 4.40 (m, 2H), 4.34 (ddd, *J* = 31.7, 14.3, 9.8 Hz, 5H), 4.26 – 4.19 (m, 2H, H6b), 4.20 – 4.10 (m, 5H, H6a), 4.10 – 4.04 (m, 2H), 4.00 (dd, *J* = 10.7, 5.5 Hz, 3H), 3.97 – 3.91 (m, 2H), 3.91 – 3.72 (m, 6H, H6a, H6b), 3.48 (d, *J* = 9.8 Hz, 1H, H6b), 3.44 – 3.36 (m, 5H, OMe), 3.27 – 3.17 (m, 3H).

LRMS (ESI): Calc. for $C_{111}H_{113}N_3Na_3O_{40}S_3$ $[M-6H+3Na]^{3-}$: 766.54, found 766.67.

Methyl [2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl-α-L-idopyranosyl uronic acid]-(1→4)-(3,6-di-*O*-benzyl-2-deoxy-2-sulfamino-α-D-glucopyranosyl)-(1→4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-gluco-pyranosyl uronic acid)-(1→4)-(3-*O*-benzyl-2-deoxy-2-sulfamino-6-*O*-sulfonate-α-D-glucopyranosyl)-(1→4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1→4)-3,6-di-*O*-benzyl-2-deoxy-2-sulfamino-α-D-glucopyranoside hexasodium salt (H3D)



NEt_3 (0.67 ml) and $SO_3 \cdot NMe_3$ complex (71 mg, 0.443 mmol, 15 eq) were added to a solution of **H3C** (68 mg, 0.030 mmol, 1 eq) in dry py (3.4 ml). Reaction was stirred at RT for 2 h, then another portion of $SO_3 \cdot NMe_3$ complex (71 mg,

0.443 mmol, 15 eq) was added and reaction was stopped after 5.5 h, then diluted with CH_2Cl_2 (1 ml) and MeOH (1 ml) and solution was layered on top of a Sephadex LH-20 column, which was eluted with MeOH/CH_2Cl_2. Sulfated fractions were concentrated and eluted from a Dowex 50WX4-Na^+ ion exchange column MeOH/H_2O 9:1 giving **H3D** (82 mg, quant).

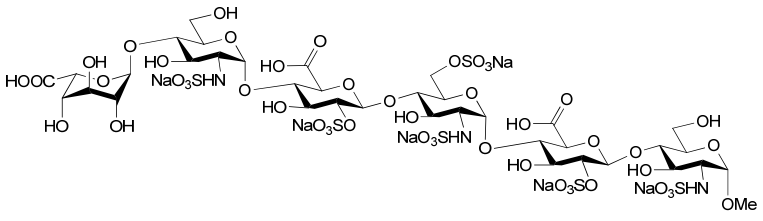
R_f (CH_2Cl_2/MeOH/aq. NH_4OH 7:3:1): 0.25

$[\alpha]_D$: +6.5 (*c* = 1.0, MeOH)

^{1}H-NMR (600 MHz, CD_3OD) δ = 8.05 (d, *J* = 8.4 Hz, 2H, Ar), 7.87 – 7.78 (m, 3H, Ar), 7.57 (dd, *J* = 20.3, 7.3 Hz, 3H, Ar), 7.45 (dt, *J* = 15.3, 8.9 Hz, 14H, Ar), 7.39 – 6.99 (m, 53H, Ar), 5.53 – 5.50 (m, 1H, H1), 5.46 (d, *J* = 3.6 Hz, 1H, H1), 5.24 (s, 1H, H1), 5.16 (d, *J* = 6.2 Hz, 2H, H1), 5.13 – 4.98 (m, 7H, H1), 4.96 – 4.88 (m, 8H), 4.73 (dt, *J* = 26.7, 12.8 Hz, 6H, H1), 4.67 – 4.56 (m, 6H, H6a), 4.55 – 4.44 (m, 6H), 4.41 – 4.26 (m, 9H), 4.19 (dd, *J* = 21.7, 9.6 Hz, 6H, H6b, H6a), 4.06 – 3.88 (m, 9H), 3.87 – 3.82 (m, 3H), 3.81 – 3.62 (m, 11H, H6b, H6a), 3.54 (ddd, *J* = 20.4, 17.5, 10.3 Hz, 6H, H6b), 3.43 – 3.32 (m, 8H, OMe).

LRMS (ESI): Calc. for $C_{111}H_{119}N_3Na_2O_{49}S_6$ $[M-5H+2Na]^{3-}$: 834.5, found 834.1.

Methyl (α-L-idopyranosyl uronic acid)-(1⟶4)-(2-deoxy-2-sulfamino-α-D-glucopyranosyl)-(1⟶4)-(2-*O*-sulfonate-β-D-gluco-pyranosyl uronic acid)-(1⟶4)-(2-deoxy-2-sulfamino-6-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-2-deoxy-2-sulfamino-α-D-glucopyranoside hexasodium salt (HX3)



A solution of **H3D** (79 mg, 30 μmol, 1 eq) was hydrogenated in the presence of Pd/C and $Pd(OH)_2$ in MeOH/H_2O for 3 d. Suspension was filtered, concentrated, diluted in H_2O (50 ml) and extracted with CH_2Cl_2 (3x10 ml) and EtOAc (3x10 ml), concentrated and eluted from a column of Dowex 50WX4-Na+ with MeOH/H_2O 1:9 giving **HX3** (46.6 mg, 26.7 μmol, 89%) as white solid.

$[\alpha]_D$: +31.2 (*c* = 1.0, H_2O)

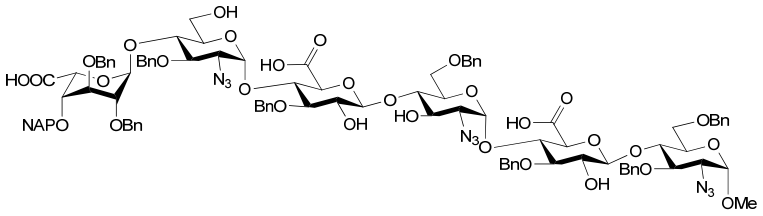
^{1}H NMR (600 MHz, D_2O, slected peaks) δ 5.50 (d, *J* = 3.7 Hz, 1H, α), 5.37 (d, *J* = 3.8 Hz, 1H, α), 4.90 (d, *J* = 3.6 Hz, 1H, α), 4.65 (d, *J* = 6.1 Hz, 1H, α-L), 4.62 (1H, β – under solvent peak), 4.57 (d, *J* = 7.8 Hz, 1H, β), 3.28 (s, 3H, -OC*H*$_3$).

^{13}C NMR (126 MHz, D_2O) δ 101.04 (α-L), 100.31 (β), 99.85 (β), 98.40 (α), 97.99 (α), 97.45 (α), 65.67 (C6-OSO_3^-), 59.59 (C6-OH), 59.44 (C6-OH), 55.17 (-O*C*H$_3$).

LRMS (ESI): Calc. for $C_{37}H_{55}N_3Na_4O_{49}S_6$ $[M-6H+4Na]^{2-}$: 804.4, found 805.2.

Hexasaccharide HX4

Methyl [2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl-α-L-idopyranosyl uronic acid]-(1→4)-(2-azido-3-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-(3-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1→4)-(2-azido-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→4)-(3-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1→4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (H4A)



35% H_2O_2 (0.81 ml) and 1 M LiOH (1.59 ml) solution were added to a solution of **H4** (56 mg, 0.035 mmol, 1 eq) in THF (2.67 ml) at -5 °C. After stirring at RT for 48 h, mixture was cooled to 0 °C and MeOH (4.90 ml) and 3 N KOH (1.73 ml) were added. Stirring for 48 h at RT. Reaction was diluted with EtOAc, pH was reduced to 1 using 1 M HCl. Aq. Phase was extracted 6x with EtOAc. Org. phase was dried over $MgSO_4$ and concentrated. Residue was eluted from a size exclusion column LH-20 using CH_2Cl_2/MeOH 1:1 and fractions containing product were pooled and purified via chromatography using EtOAc/MeOH/H_2O/AcOH 40:1:1:0.1 to give **H4A** in two fractions. Higher fraction (22 mg, 0.011 mmol, 48%) and lower fraction (13 mg, 0.007 mmol, 29%).

R_f (EtOAc/MeOH/H_2O/AcOH 18:1:1:0.1): 0.66, 0.83

$[\alpha]_D$: +28.3 (*c* 1.0 MeOH)

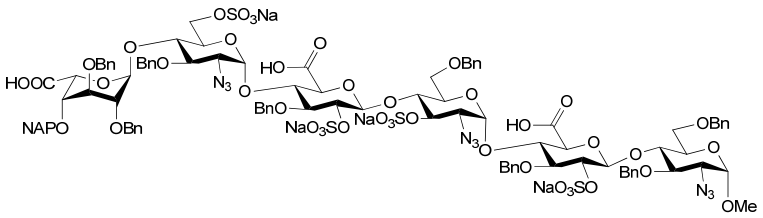
^{1}H-NMR (600 MHz, CD_3OD) δ = 8.06 (d, *J* = 7.6 Hz, 1H, Ar), 7.83 (dd, *J* = 18.9, 7.8 Hz, 2H, Ar), 7.47 – 7.08 (m, 37H, Ar), 5.49 (d, *J* = 11.8 Hz, 2H, 2 $H1^{C,E}$), 5.34 (d, *J* = 12.9 Hz, 1H, $H1^F$), 5.07 (dd, *J* = 26.2, 10.3 Hz, 4H, $ArCH_2$), 4.94 (d, *J* = 11.5 Hz, 2H, $ArCH_2$), 4.75 – 4.64 (m, 3H, $H1^A$, $ArCH_2$), 4.64 – 4.46 (m, 7H, $ArCH_2$), 4.45 – 4.34 (m, 4H, 2 $H1^{B,D}$, $ArCH_2$), 4.11 (d, *J* = 10.8 Hz, 1H), 4.03 – 3.90 (m, 6H), 3.77 (tdd, *J* = 30.6, 24.5, 10.1 Hz, 12H), 3.59 (d, *J* = 7.6 Hz, 2H),

3.53 – 3.42 (m, 4H), 3.36 (d, *J* = 17.4 Hz, 3H, 1-OMe), 3.26 (d, *J* = 10.1 Hz, 2H, 2 $H2^{A\text{ or }C\text{ or }E}$), 3.09 (d, *J* = 8.3 Hz, 1H, $H2^{A\text{ or }C\text{ or }E}$).

^{1}C-NMR (151 MHz, CD_3OD) δ = 170.45 (3 COOH), 138.63 (Ar), 138.24 (Ar), 138.15 (Ar), 138.02 (Ar), 137.93 (Ar), 133.78 (Ar), 133.26 (Ar), 131.76 (Ar), 128.56 (Ar), 128.43 (Ar), 128.30 (Ar), 128.16 (Ar), 127.99 (Ar), 127.87 (Ar), 127.76 (Ar), 127.68 (Ar), 127.49 (Ar), 127.45 (Ar), 127.39 (Ar), 127.17 (Ar), 127.09 (Ar), 127.00 (Ar), 125.87 (Ar), 125.42 (Ar), 124.78 (Ar), 124.10 (Ar), 102.85 (Ar), 102.43, 98.65, 97.74, 97.64, 84.42, 78.25, 77.91, 77.10, 75.39, 75.17, 74.84 ($ArCH_2$), 74.58 ($ArCH_2$), 74.43 ($ArCH_2$), 74.30, 74.08 ($ArCH_2$), 73.12 ($ArCH_2$), 73.06 ($ArCH_2$), 72.39($ArCH_2$), 70.96 ($ArCH_2$), 70.36, 70.15, 69.27, 67.66 (C-$6^{A\text{ or }C\text{ or }E}$), 67.49 (C-$6^{A\text{ or }C\text{ or }E}$), 63.43 (C-$2^{A\text{ or }C\text{ or }E}$), 62.80 (C-$2^{A\text{ or }C\text{ or }E}$), 62.64 (C-$2^{A\text{ or }C\text{ or }E}$), 59.85 (C-$6^{A\text{ or }C\text{ or }E}$), 54.18 (1-OMe).

LRMS (ESI): Calc. for $C_{104}H_{108}N_9O_{31}$ $[M-3H]^{3-}$: 659.91; found 660.29.

Methyl [2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl-α-L-idopyranosyl uronic acid]-(1⟶4)-(2-azido-3-*O*-benzyl-6-*O*-sulfonate-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-azido-6-*O*-benzyl-2-deoxy-3-*O*-sulfonate-α-D-gluco-pyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside tetrasodium salt (H4B)



$SO_3{\cdot}NMe_3$ complex (44 mg, 0.318 mmol, 35 eq) complex and **H4A** (18 mg, 0.009 mmol, 1 eq) were dried together with stir bar over night at Schlenck, then put under N_2 atmosphere and dissolved in DMF (2 ml). Mixture was placed into a microwave reactor and stirred for 2 h at 100 °C. Reaction was quenched with NEt_3, filtered through micropore filter, diluted with CH_2Cl_2 (1 ml) and MeOH (1 ml) and solution was layered on top of a Sephadex L20-H column, wich was eluted with MeOH/CH_2Cl_2. Sulfated fractions were pooled and eluted from a Dowex 50WX4-Na^+ ion exchange column with CH_2Cl_2 /MeOH 1:1 giving **H4B** (19 mg, 0.008 mmol, 88%) as slightly yellow solid.

R_f (CH_2Cl_2/MeOH/aq. NH_4OH 7:3:1): 0.48

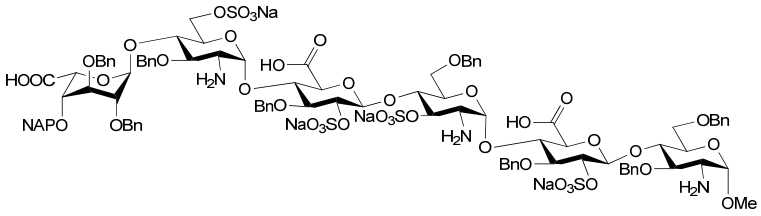
$[\alpha]_D$: +25.7 (*c* = 1.0, MeOH)

^{1}H-NMR (600 MHz, CD_3OD) δ = 8.03 (d, *J* = 8.4 Hz, 1H, Ar), 7.80 – 7.71 (m, 2H, Ar), 7.50 – 7.09 (m, 47H, Ar), 7.03 (dt, *J* = 20.7, 7.0 Hz, 3H, Ar), 5.46 (d, *J* = 10.4 Hz, 1H), 5.39 (d, *J* = 6.5 Hz, 1H, H1), 5.36 – 5.26 (m, 3H, H1), 5.23 – 5.15 (m, 2H, H1), 5.09 (d, *J* = 4.5 Hz, 1, 1H), 5.01 (d, *J* = 11.3 Hz, 2H), 4.98 – 4.91 (m, 4H, H1), 4.81 – 4.69 (m, 5H), 4.66 – 4.60 (m, 3H), 4.61 – 4.47 (m, 10H, H6a), 4.46 – 4.40 (m, 2H), 4.34 (ddd, *J* = 31.7, 14.3, 9.8 Hz, 5H), 4.26 – 4.19 (m, 2H, H6b), 4.20 – 4.10 (m, 5H, H6a), 4.10 – 4.04 (m, 2H), 4.00 (dd, *J* = 10.7, 5.5 Hz, 3H), 3.97 – 3.91 (m, 2H), 3.91 – 3.72 (m, 6H, H6a, H6b), 3.48 (d, *J* = 9.8 Hz, 1H, H6b), 3.44 – 3.36 (m, 5H, OMe), 3.27 – 3.17 (m, 3H).

LRMS (ESI): Calc. for $C_{104}H_{104}N_9Na_4O_{43}S_4$ $[M-7H+4Na]^{3-}$: 795.49, found 795.75;

Calc. for $C_{104}H_{104}N_9Na_3O_{43}S_4$ $[M-7H+3Na]^{4-}$: 590.87, found 591.57.

Methyl [2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl-α-L-idopyranosyl uronic acid]-(1⟶4)-(2-amino-3-*O*-benzyl-2-deoxy-6-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-amino-6-*O*-benzyl-2-deoxy-3-*O*-sulfonate-α-D-gluco-pyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-2-amino-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside tetra sodium salt (H4C)



H4B (18 mg, 7.5 umol, 1 eq) was dissolved in THF (0.57), 1 M PMe_3 in THF (0.18 ml, 0.18 mmol, 24 eq) and 0.1 M NaOH (2.25 ml. 0.025 mmol, 30 eq) were added and the reaction was stirred for 8 h. Reaction was neutralised with 0.1 M HCl, concentrated and the residue was eluted from a Sephadex LH-20 with CH_2Cl_2/MeOH 1:1 furnishing **H4C** (17 mg, 7.3 umol, 98%) as white solid.

R_f (CH_2Cl_2/MeOH/aq. NH_4OH 7:3:1): 0.31

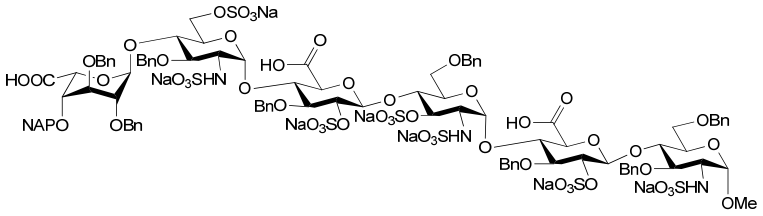
$[\alpha]_D$: +14.7 (*c* = 1.0, MeOH)

^{1}H-NMR (500 MHz, CD_3OD) δ = 8.02 (s, 2H, Ar), 7.83 (dd, *J* = 17.0, 8.4 Hz, 3H, Ar), 7.49 – 7.07 (m, 35H, Ar), 5.41 (s, 1H, H1), 5.37 (s, 1H, H1), 5.26 (d, *J* = 10.5 Hz, 2H, H1), 5.23 – 5.09 (m, 4H, H1), 4.96 (dd, *J* = 30.8, 20.1 Hz, 4H, H1), 4.74 – 4.44 (m, 15H), 4.38 – 4.23 (m, 5H, H1), 4.18 (d, *J* = 9.7 Hz, 2H), 4.13 – 4.01 (m, 5H), 3.96 (dd, *J* = 16.4, 8.9 Hz, 4H), 3.91 – 3.78 (m, 4H),

3.72 (dd, *J* = 22.9, 13.5 Hz, 3H), 3.66 – 3.53 (m, 5H), 3.50 – 3.40 (m, 4H, OMe), 3.24 – 3.14 (m, 2H).

LRMS (ESI): Calc. for $C_{104}H_{110}N_3Na_4O_{43}S_4$ $[M-7H+4Na]^{3-}$: 769.50, found 770.41.

Methyl [2,3-di-*O*-benzyl-4-*O*-(1-naphthyl)methyl-α-L-idopyranosyl uronic acid]-(1⟶4)-(3-*O*-benzyl-2-deoxy-2-sulfamino-6-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-(6-*O*-benzyl-2-deoxy-2-sulfamino-3-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-3,6-di-*O*-benzyl-2-deoxy-2-sulfamino-α-D-glucopyranoside heptasodium salt (H4D)



NEt_3 (0.16 ml) and $SO_3 \cdot$ py complex (18 mg, 0.11 mmol, 15 eq) were added to a solution of **H4C** (17 mg, 7.3 umol, 1 eq) in dry py (0.83 ml). Stirring at RT for 1.5h, another portion of complex added, another addition after 3 h. Total stirring time: 4h. Reaction was diluted with CH_2Cl_2 (1 ml) and MeOH (1 ml) and solution was layered on top of a Sephadex LH-20 column, which was eluted with MeOH/CH_2Cl_2. Sulfated fractions were concentrated and eluted from an ion exchange column MeOH/H_2O 9:1 giving **H4D** (23 mg, quant.) as yellow solid.

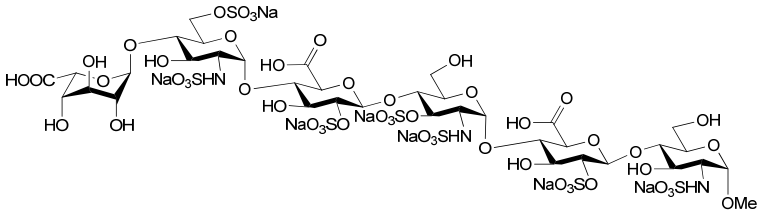
R_f (CH_2Cl_2/MeOH/aq. NH_4OH 7:3:1): 0.17

^{1}H-NMR (500 MHz, CD_3OD) δ = 8.02 (s, 2H, Ar), 7.83 (dd, *J* = 17.0, 8.4 Hz, 3H, Ar), 7.49 – 7.07 (m, 35H, Ar), 5.41 (s, 1H, H1), 5.37 (s, 1H, H1), 5.26 (d, *J* = 10.5 Hz, 2H, H1), 5.23 – 5.09 (m, 4H, H1), 4.96 (dd, *J* = 30.8, 20.1 Hz, 4H, H1), 4.74 – 4.44 (m, 15H), 4.38 – 4.23 (m, 5H, H1), 4.18 (d, *J* = 9.7 Hz, 2H), 4.13 – 4.01 (m, 5H), 3.96 (dd, *J* = 16.4, 8.9 Hz, 4H), 3.91 – 3.78 (m, 4H), 3.72 (dd, *J* = 22.9, 13.5 Hz, 3H), 3.66 – 3.53 (m, 5H), 3.50 – 3.40 (m, 4H, OMe), 3.24 – 3.14 (m, 2H).

LRMS (ESI): Calc. for $C_{104}H_{107}N_3Na_7O_{52}S_7$ $[M-10H+7Na]^{3-}$: 871.44, found 871.84.

Methyl (α-L-idopyranosyl uronic acid)-(1⟶4)-(2-deoxy-2-sulfamino-6-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-deoxy-2-sulfamino-3-*O*-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(2-*O*-sulfonate-β-D-

glucopyranosyl uronic acid)-(1⟶4)- 2-deoxy-2-sulfamino-α-D-glucopyranoside heptasodium salt (HX4)



A solution of **H4D** (22 mg, 8.3 μmol, 1 eq) was hydrogenolyzed in the presence of Pd/C and $Pd(OH)_2$ in MeOH/H_2O. Suspension was filtered, concentrated, diluted in H_2O (50 ml) and extracted with CH_2Cl_2 (3x10 ml) and EtOAc (3x10 ml), concentrated and eluted from a column of Dowex 50WX4-Na+ with MeOH/H_2O 1:9 giving **HX4** (12.5 mg, 6.7 μmol, 81%) as a white solid.

[α]D: +33.2 (*c* = 1.0, H_2O)

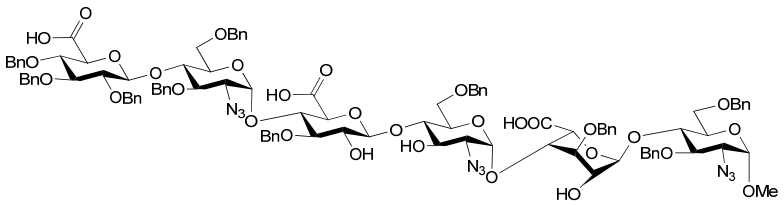
^{1}H NMR (600 MHz, D_2O, selected peaks) δ 5.49 (d, *J* = 3.7 Hz, 1H, α), 5.28 (d, *J* = 3.6 Hz, 1H, α), 4.89 (d, *J* = 3.6 Hz, 1H, α), 4.76 (d, *J* = 4.5 Hz, 1H, α-L), 4.56 (d, *J* = 7.6 Hz, 1H, β), 4.55 (d, *J* = 7.6 Hz, 1H, β), 3.27 (s, 3H, -OC*H*$_3$).

^{13}C NMR (151 MHz, D_2O, selected peaks) δ 101.56 (α-L), 100.56 (β), 100.49 (β), 99.40 (α), 98.04 (α), 97.50 (α), 66.00 (C6-OSO_3^-), 59.02 (C6-OH), 59.64(C6-OH), 55.25 (-O*C*H$_3$).

LRMS (ESI): Calc. for $C_{37}H_{57}N_3Na_2O_{52}S_7$ $[M-4H+2Na]^{2-}$: 833.48, found 833.78.

Hexasaccharide HX5

Methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-azido-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-α-L-idopyranosyl uronic acid)-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (H5A)



H_2O_2 (35%, 3.68 ml) and 1 N LiOH solution (6.01 ml) were added to a solution of **H5** (178 mg, 0.07 mmol) in THF (010.02 ml) at -5 °C. After stirring at RT for 48 h, mixture was cooled to 0 °C and MeOH (18.7 ml) and 3 N KOH (6.7 ml) were added. Stirring for 47 h at RT. Reaction was diluted with EtOAc, pH was reduced to 1 using 1 M HCl. Aq. Phase was extracted six times with EtOAc. Org. phase was dried over

$MgSO_4$ and concentrated. Residue was dissolved in CH_2Cl_2 (1 ml) and MeOH (1 ml) and diluted from a Sephadex LH-20 column, fractions containing product were pooled, concentrated and eluted from a Dowex 50WX4-Na^+ ion exchange column to give **H5A** (18 mg (0.008 mmol, 99%) as clear solid.

R_f (EtOAc/MeOH/H_2O/AcOH 40:1:1:0.2): 0.46

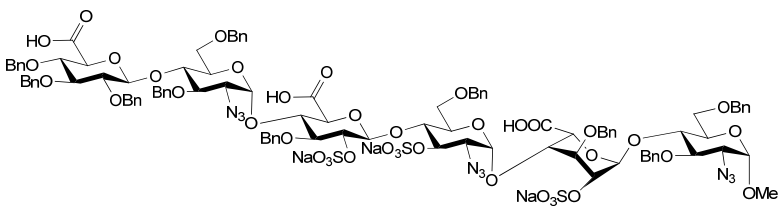
$[\alpha]_D$: +24.7 (c = 1.0, MeOH)

^{1}H-NMR (600 MHz, CD_3OD) δ = 7.49 – 7.43 (m, 2H, Ar), 7.42 – 7.16 (m, 38H, Ar), 5.45 (d, *J* = 3.6 Hz, 1H, C-1^E), 5.19 (d, *J* = 2.0 Hz, 1H, C-1^C), 5.14 – 5.03 (m, 3H, C-1^B, BnCH2), 4.83 – 4.78 (m, 2H, $BnCH_2$), 4.77 – 4.64 (m, 8H, C-1^A, $BnCH_2$), 4.60 (dd, *J* = 11.7, 7.0 Hz, 3H, $BnCH_2$), 4.55 – 4.49 (m, 3H, C-1^F, $BnCH_2$), 4.36 (m, 2H, C-1^D), 4.16 (s, 1H), 4.08 (d, *J* = 9.2 Hz, 1H), 4.05 – 3.87 (m, 8H), 3.84 – 3.80 (m, 1H), 3.72 (m, 8H), 3.58 (t, *J* = 8.7 Hz, 1H), 3.51 – 3.47 (m, 1H), 3.39 – 3.32 (m, 5H, OMe, 2 C-$2^{A\text{ or }C\text{ or }D}$), 3.18 (m, 1H, C-$2^{A\text{ or }C\text{ or }D}$).

^{13}C-NMR (151 MHz, CD_3OD) δ = 172.79 (COOH), 172.62 (COOH), 171.81 (COOH), 128.62 (Ar), 128.40 (Ar), 128.24 (Ar), 128.16 (Ar), 128.11 (Ar), 127.97 (Ar), 127.95 (Ar), 127.94 (Ar), 127.91 (Ar), 127.88 (Ar), 127.85 (Ar), 127.81 (Ar), 127.80 (Ar), 127.76 (Ar), 127.72 (Ar), 127.69 (Ar), 127.61 (Ar), 127.56 (Ar), 127.52 (Ar), 127.48 (Ar), 127.42 (Ar), 127.37 (Ar), 127.35 (Ar), 127.27 (Ar), 127.14, 127.12 (Ar), 127.08 (Ar), 127.05 (Ar), 127.02 (Ar), 127.00 (Ar), 102.58, 102.33, 101.34, 98.67, 97.94, 95.43, 84.24, 83.53, 81.44, 80.00, 78.31, 78.08, 77.40, 76.78, 76.67, 76.27, 76.12, 75.62, 75.03 ($BnCH_2$), 74.90, 74.63 ($BnCH_2$), 74.58 ($BnCH_2$), 74.25 ($BnCH_2$), 74.19, 74.11 ($BnCH_2$), 74.08 ($BnCH_2$), 73.08 (3 $BnCH_2$), 72.63, 72.30 ($BnCH_2$), 70.73, 70.27, 69.68, 68.86 (C-$6^{A\text{ or }C\text{ or }D}$), 68.31 (C-$6^{A\text{ or }C\text{ or }D}$), 67.63 (C-$6^{A\text{ or }C\text{ or }D}$), 67.43, 63.59 (C-$2^{A\text{ or }C\text{ or }D}$), 63.09 (C-$2^{A\text{ or }C\text{ or }D}$), (C-$2^{A\text{ or }C\text{ or }D}$), , 62.82 (C-$2^{A\text{ or }C\text{ or }D}$), 54.15 (1-OMe).

LRMS (ESI): Calc. for $C_{107}H_{112}N_9O_{31}$ $[M-3H]^{3-}$: 673.25; found 673.64.

Methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-azido-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-α-L-idopyranosyl uronic acid)-(1⟶4)-2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside trisodium salt (H5B)



H5A (38 mg, 0.019 mmol, 1 eq) $SO_3{\cdot}NMe_3$ complex (39 mg, 0.282 mmol, 15 eq) were dried together with stir bar over night at the

Schlenck line, then put under N_2 atmosphere and dissolved in DMF. Mixture was placed into microwave and stirred for 1.5 h at 100 °C. Reaction was quenched with NEt_3, filtered through micropore filter, diluted with CH_2Cl_2 (1 ml) and MeOH (1 ml) and solution was layered on top of a Sephadex LH-20 column, which was eluted with MeOH/CH_2Cl_2 1:1. Sulfated fractions were pooled and eluted from a Dowex 50WX4-Na^+ ion exchange column with MeOH/CH_2Cl_2 1:1 giving **H5B** (42 mg, 0.018 mmol, 92%) as slightly yellow solid.

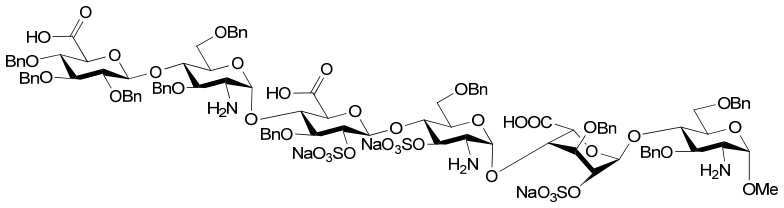
R_f (CH_2Cl_2 /MeOH/aq. NH_4OH 7:3:1): 0.81

$[\alpha]_D$: +32.2 (*c* = 1.3, MeOH)

^{1}H-NMR (500 MHz, CD_3OD) δ = 7.36 (d, *J* = 7.2 Hz, 2H, Bn), 7.33 – 7.06 (m, 43H, Bn), 5.26 (s, 1H, H1$^{B \text{ or } C \text{ or } E}$), 5.11 (dd, *J* = 14.4, 3.3 Hz, 2H, 2 H1$^{B \text{ or } C \text{ or } E}$), 5.00 (d, *J* = 11.1 Hz, 1H, $BnCH_2$), 4.91 (d, *J* = 11.0 Hz, 1H), 4.87 – 4.80 (m, 3H, H1 $^{D \text{ or } F}$ $BnCH_2$), 4.69 – 4.36 (m, 22H, H1^A, H1$^{D \text{ or } F}$, $BnCH_2$), 4.26 (d, *J* = 12.0 Hz, 1H, $BnCH_2$), 4.16 (s, 1H), 4.03 (dd, *J* = 11.4, 5.7 Hz, 3H), 3.85 (dddd, *J* = 32.6, 18.2, 17.2, 8.1 Hz, 11H, 3 H6 $^{\text{or C or D}}$a), 3.72 – 3.56 (m, 7H, 2 H6 $^{\text{or C or D}}$b), 3.49 (d, *J* = 10.4 Hz, 1H, H6 $^{\text{or C or D}}$b), 3.36 – 3.23 (m, 6H, H2$^{A \text{ or } C \text{ or } E}$, 1-OMe), 3.15 (ddd, *J* = 26.3, 10.0, 3.7 Hz, 2H, 2 H2,$^{A \text{ or } C \text{ or } E}$).

LRMS (ESI): Calc. for $C_{107}H_{109}N_9Na_3O_{40}S_3$ $[M-6H+3Na]^{3-}$: 775.19; found 775.66.

Methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-amino-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranosyl-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-amino-6-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-α-L-idopyranosyl uronic acid)-(1⟶4)-2-amino-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside trisodium salt (H5C)



H5B (37 mg, 0.0159 mmol, 1 eq) was dissolved in THF and treated with 0.1 M NaOH (4.8 ml, 0.48 mmol, 30 eq). Then a solution of 1M PMe_3 in THF (0.38 ml, 0.38 mmol, 24 eq) was added and the reaction was stirred for 5 h. Reaction was neutralised with 0.1 M HCl, concentrated and the residue was eluted from a Sephadex LH-20 column with CH_2Cl_2/MeOH 1:1 giving **H5C** (19.6 mg, 11.2 μmol, 84%) as white solid.

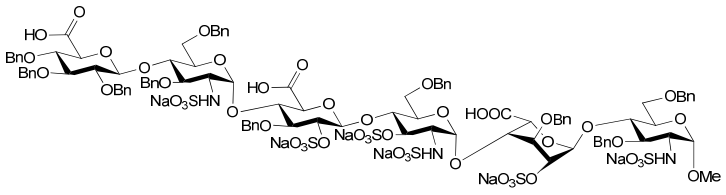
R_f (CH_2Cl_2 /MeOH/aq. NH_4OH 7:3:1): 0.60

[α]D: +29.0 (*c* = 0.9, MeOH)

^{1}H-NMR (500 MHz, CD_3OD) δ = 7.44 (d, *J* = 7.3 Hz, 2H, Ar), 7.28 (t, *J* = 6.9 Hz, 4H, Ar), 7.26 – 6.99 (m, 45H, Ar), 6.96 (d, *J* = 7.1 Hz, 2H, Ar), 5.39 (d, *J* = 6.5 Hz, 1H), 5.34 (s, 1H, H1), 5.23 (d, *J* = 9.6 Hz, 1H, H1), 5.11 (d, *J* = 2.7 Hz, 1H, H1), 5.06 (d, *J* = 3.4 Hz, 1H, H1), 4.79 (m, 4H), 4.72 – 4.62 (m, 9H, H1), 4.61 – 4.55 (m, 4H), 4.51 (m, 10H), 4.40 (m, 3H, H1), 4.35 (d, *J* = 6.6 Hz, 1H), 4.30 – 4.17 (m, 5H), 4.06 (d, *J* = 10.1 Hz, 1H), 4.01 – 3.80 (m, 9H, 2 H6a), 3.75 (d, *J* = 3.8 Hz, 2H, H6a), 3.72 – 3.57 (m, 9H, 2 H6b), 3.39 – 3.33 (m, 4H, H2b), 3.30 (m, 2H), 3.25 (s, 1H, H2 $^{A \text{ or } C \text{ or } E}$), 3.18 – 3.12 (m, 2H, H2 $^{A \text{ or } C \text{ or } E}$), 2.77 (m, 1H, H2 $^{A \text{ or } C \text{ or } E}$).

LRMS (ESI): Calc. for $C_{107}H_{111}NaN_9O_{40}S_3$ $[M-4H+Na]^{3-}$: 749.20; found 749.54.

Methyl (2,3,4-tri-*O*-benzyl-β-D-glucopyranosyl uronic acid)-(1⟶4)-(3,6-di-*O*-benzyl-2-deoxy-2-sulfamino-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-(6-*O*-benzyl-2-deoxy-2-sulfamino-2-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(3-*O*-benzyl-2-*O*-sulfonate-α-L-idopyranosyl uronic acid)-(1⟶4)-3,6-di-*O*-benzyl-2-deoxy-2sulfamino-α-D-glucopyranoside hexasodium salt (H5D)



NEt_3 (0.29 ml) and SO_3·py complex (32 mg, 0.20 mmol, 15 eq) were added to a solution of **H5C** (30 mg, 0.013 mmol, 1 eq) in dry py. Stirring at RT for 1.5 h, another portion of SO_3· py complex (32 mg, 0.20 mmol, 15 eq) was added. More additions of SO_3· py complex (32 mg, 0.20 mmol, 15 eq each) after 4 h, 5 h and 6 h. Reaction was stirred for a total of 7 h. Reaction was diluted with CH_2Cl_2 (1 ml) and MeOH (1 ml) and solution was layered on top of a Sephadex LH-20 column, which was eluted with MeOH/ CH_2Cl_2 1:1. Sulfated fractions were concentrated and eluted from a Dowex 50WX4-Na^+ ion exchange column with MeOH/CH_2Cl_2 9:1 furnishing **HX5** (35 mg, 0.013 mmol, quant.) as white solid.

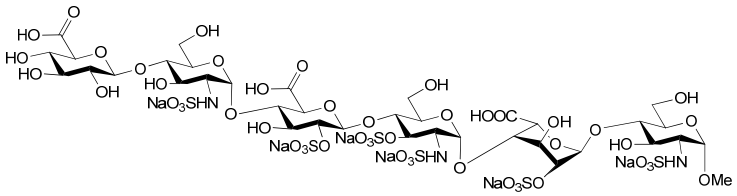
R_f (CH_2Cl_2 /MeOH/aq. NH_4OH 7:3:1): 0.24

[α]D: +24.8 (*c* = 1.0, MeOH)

^{1}H-NMR (500 MHz, CD_3OD) δ = 7.57 – 6.87 (m, 73H), 5.50 – 5.32 (m, 4H), 4.93 (dd, *J* = 35.5, 8.1 Hz, 5H), 4.72 – 4.24 (m, 35H), 4.23 – 4.16 (m, 2H), 4.06 (d, *J* = 6.7 Hz, 3H), 3.98 – 3.74 (m, 12H), 3.71 – 3.39 (m, 19H), 3.40 – 3.23 (m, 12H), 2.93 (qd, *J* = 13.4, 7.4 Hz, 2H).

LRMS (ESI): Calc. for $C_{107}H_{117}N_9Na_6O_{49}S_6$ $[M-9H+6Na]^{3-}$: 851.15; found 851.14.

Methyl (β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-deoxy-2-sulfamino-α-D-glucopyranosyl)-(1⟶4)-(2-*O*-sulfonate-β-D-glucopyranosyl uronic acid)-(1⟶4)-(2-deoxy-2-sulfamino-2-sulfonate-α-D-glucopyranosyl)-(1⟶4)-(2-*O*-sulfonate-α-L-idopyranosyl uronic acid)-(1⟶4)-2-deoxy-2-sulfamino-α-D-glucopyranoside hexasodium salt (HX5)



A solution of **H5D** (34 mg, 13.3 μmol, 1 eq) was hydrogenated in the presence of Pd/C and $Pd(OH)_2$ for 5 d. Suspension was filtered, concentrated, diluted in H_2O (30 ml) and extracted with CH_2Cl_2 (3x 10 ml) and EtOAc (3x 10 ml), concentrated and eluted from a column of Dowex 50WX4-Na^+ with MeOH/H_2O 1:9 giving **HX5** (19.6 mg, 11.2 μmol, 84%) as white solid.

$[\alpha]_D$: +18.7 (*c* = 1.0, H_2O)

^{1}H NMR (500 MHz, D_2O, selected peaks) δ 5.49 (d, *J* = 3.3 Hz, 1H, α), 5.23 (d, *J* = 3.6 Hz, 1H, α), 4.99 (t, *J* = 3.3 Hz, 1H, α), 4.86 (br s, 1H, α-L), 4.55 (d, *J* = 6.9 Hz, 1H, β), 4.35 (d, *J* = 7.8 Hz, 1H, β), 3.25 (s, 3H, -OC*H*$_3$).

^{13}C NMR (126 MHz, D_2O, slected peaks) δ 102.11 (β), 100.50 (β), 99.44 (α), 98.14 (α-L), 97.10 (α), 97.08 (α), 59.17 (C6-OH), 59.83 (C6-OH), 59.30 (C6-OH), 55.19 (-O*C*H$_3$).

LRMS (ESI): Calc. for $C_{37}H_{52}N_3Na_7O_{49}S_6^{2-}$ $[M-9H+7Na]^{2-}$: 837.47; found 837.17.

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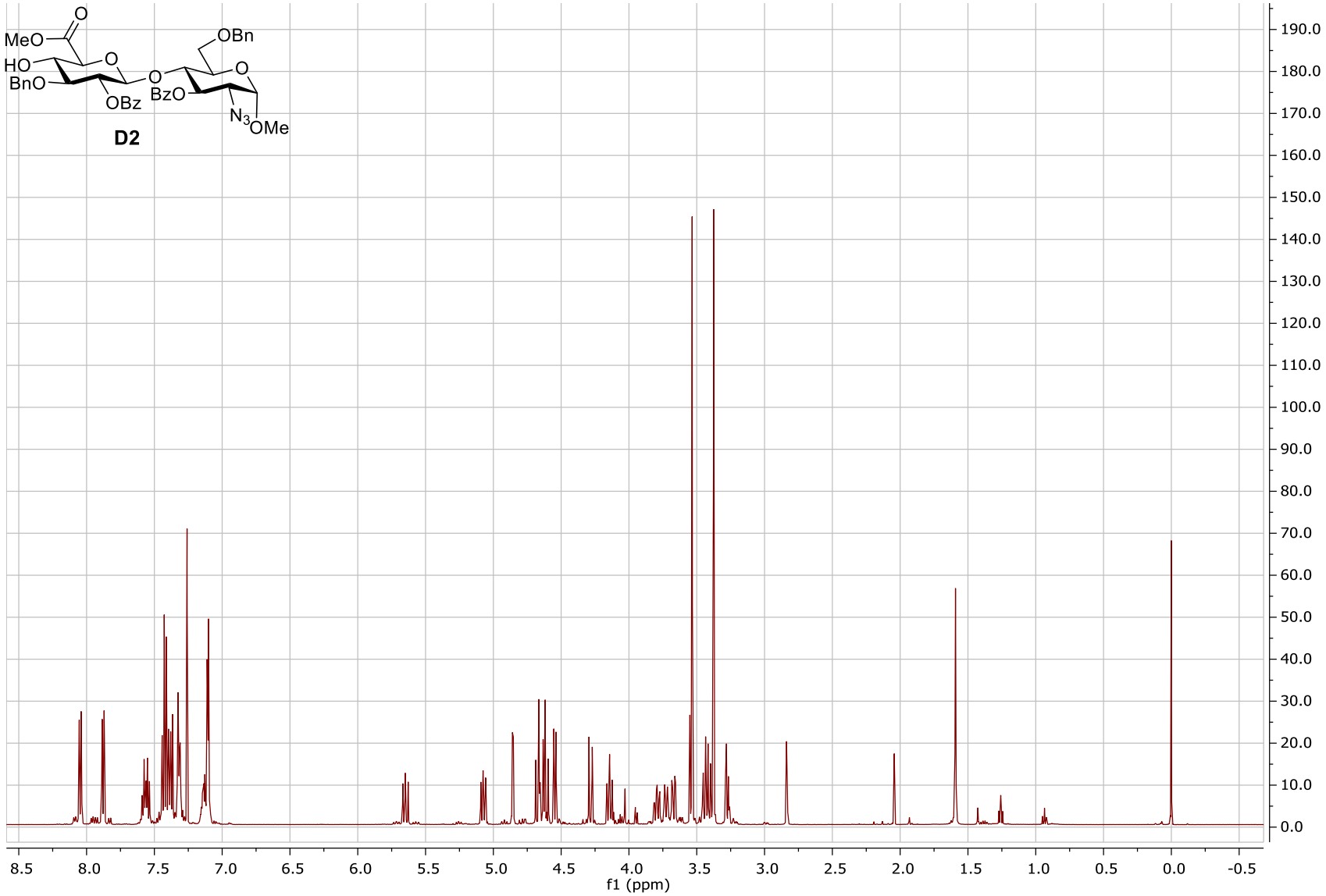
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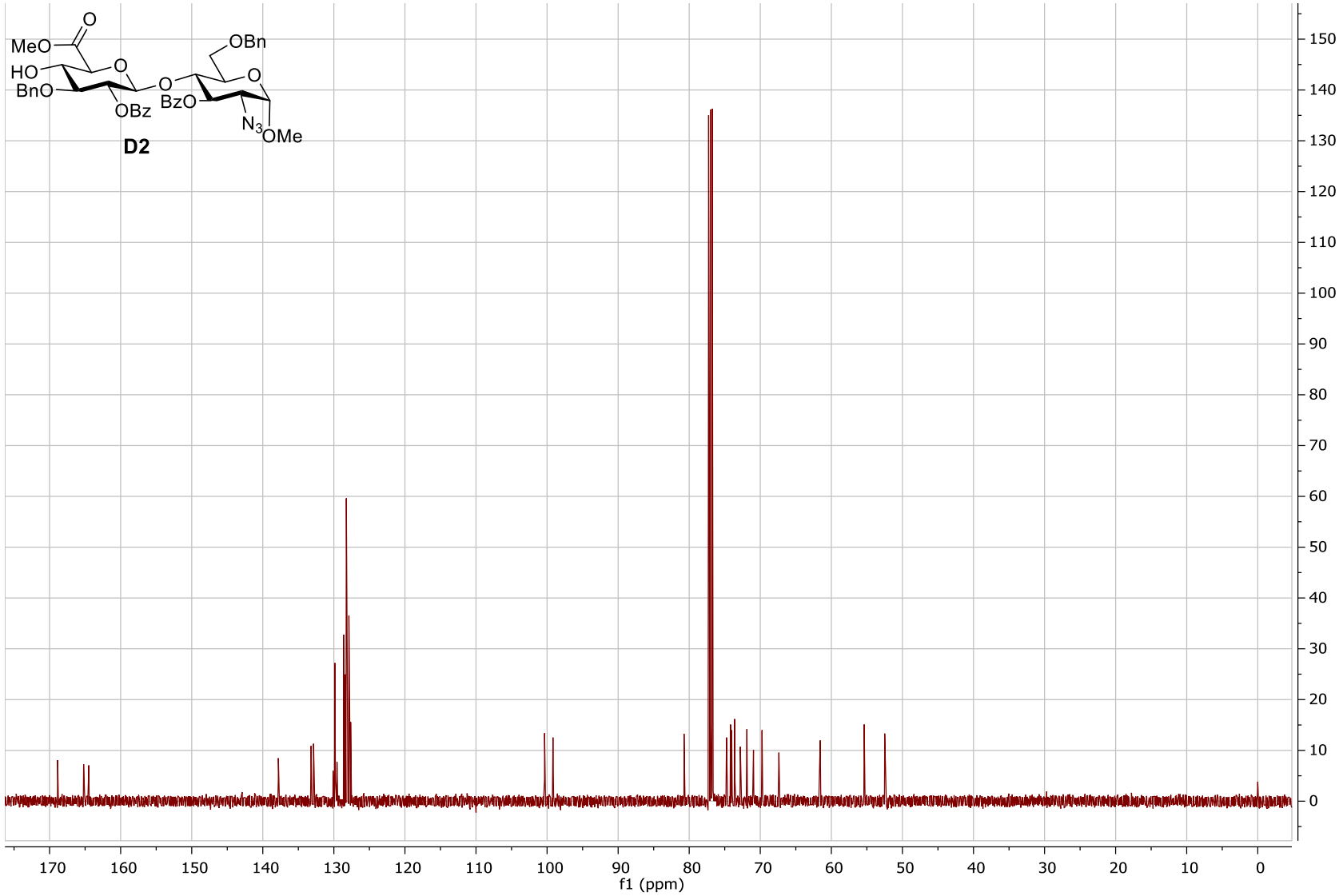
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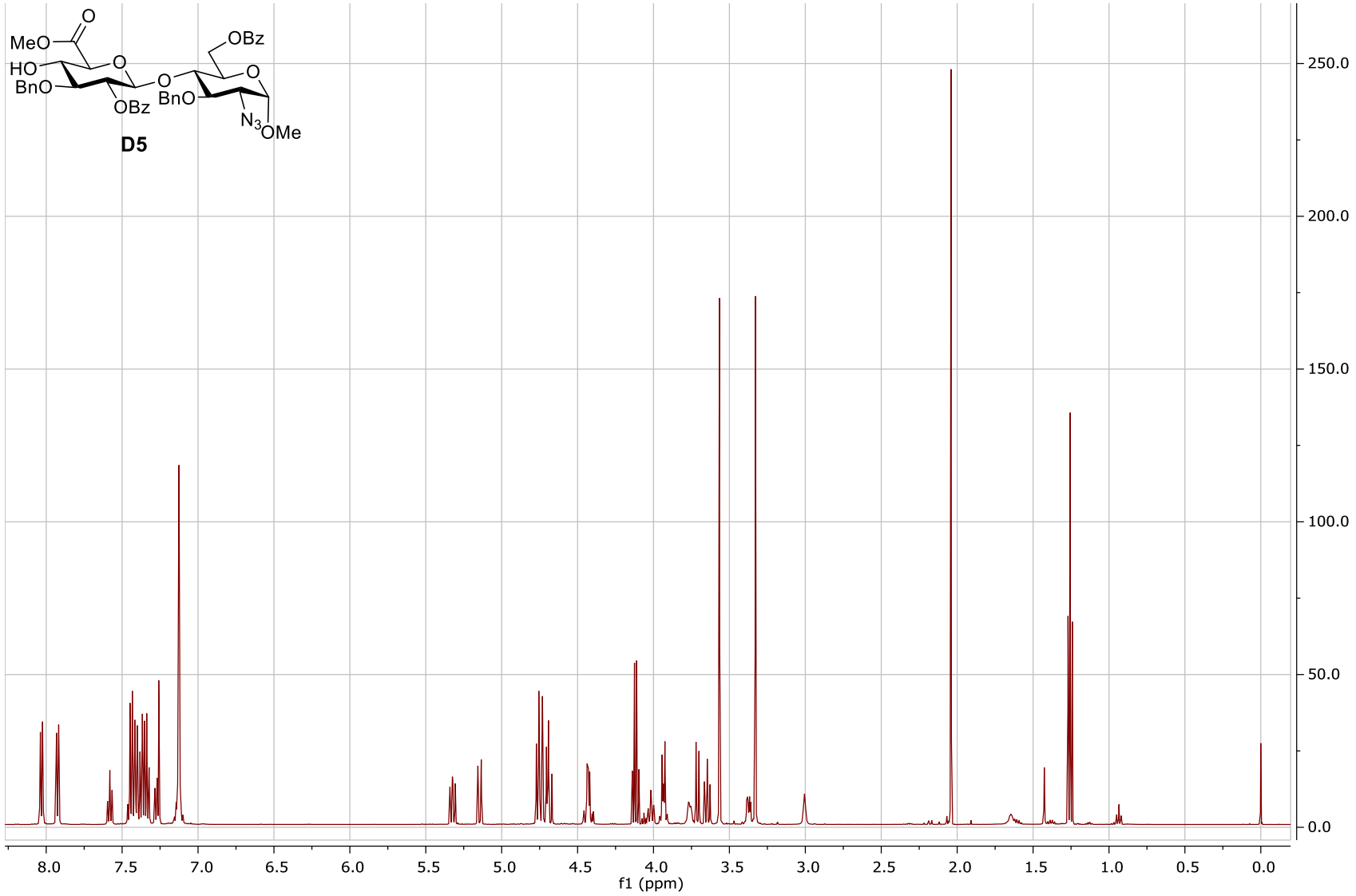
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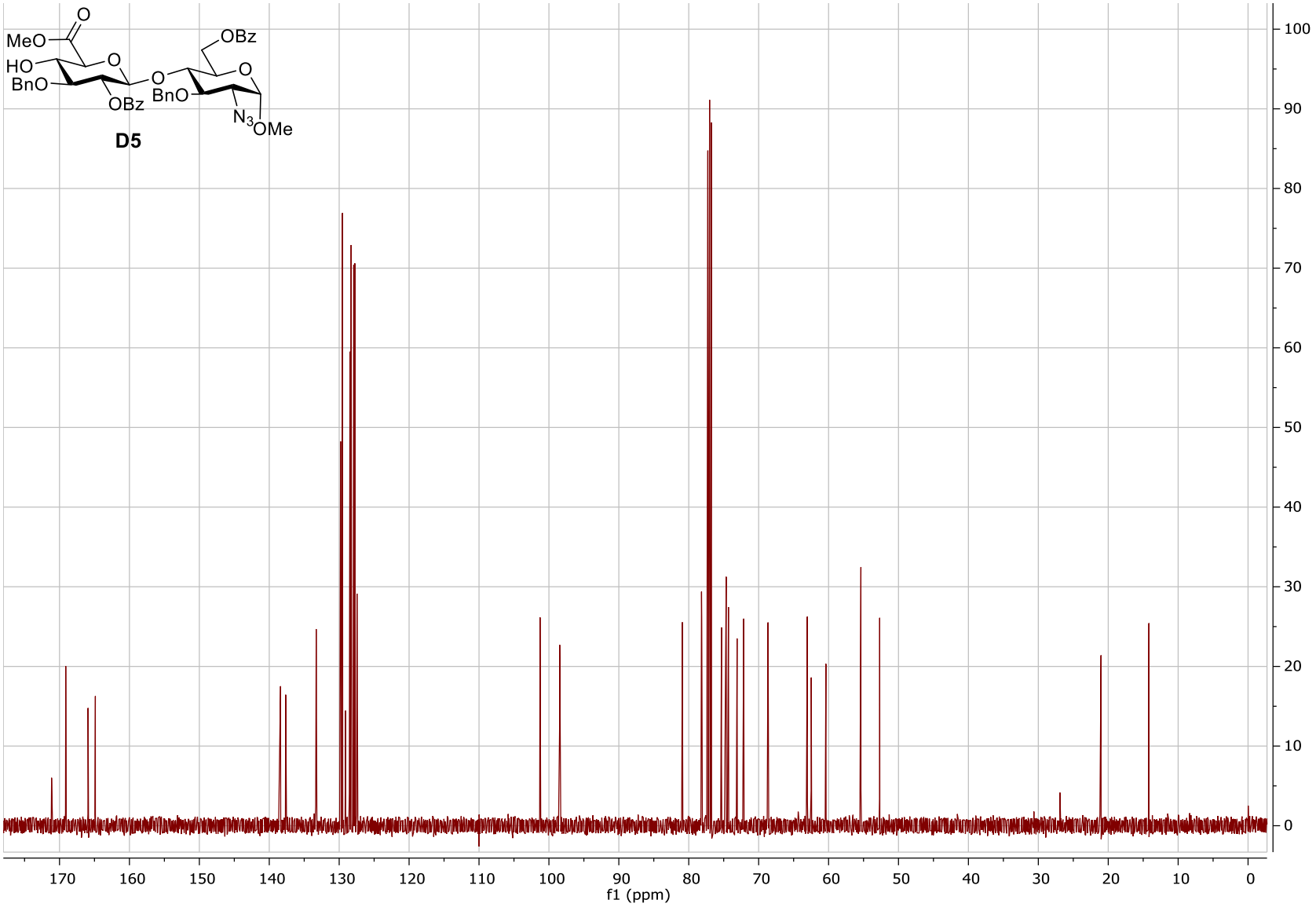
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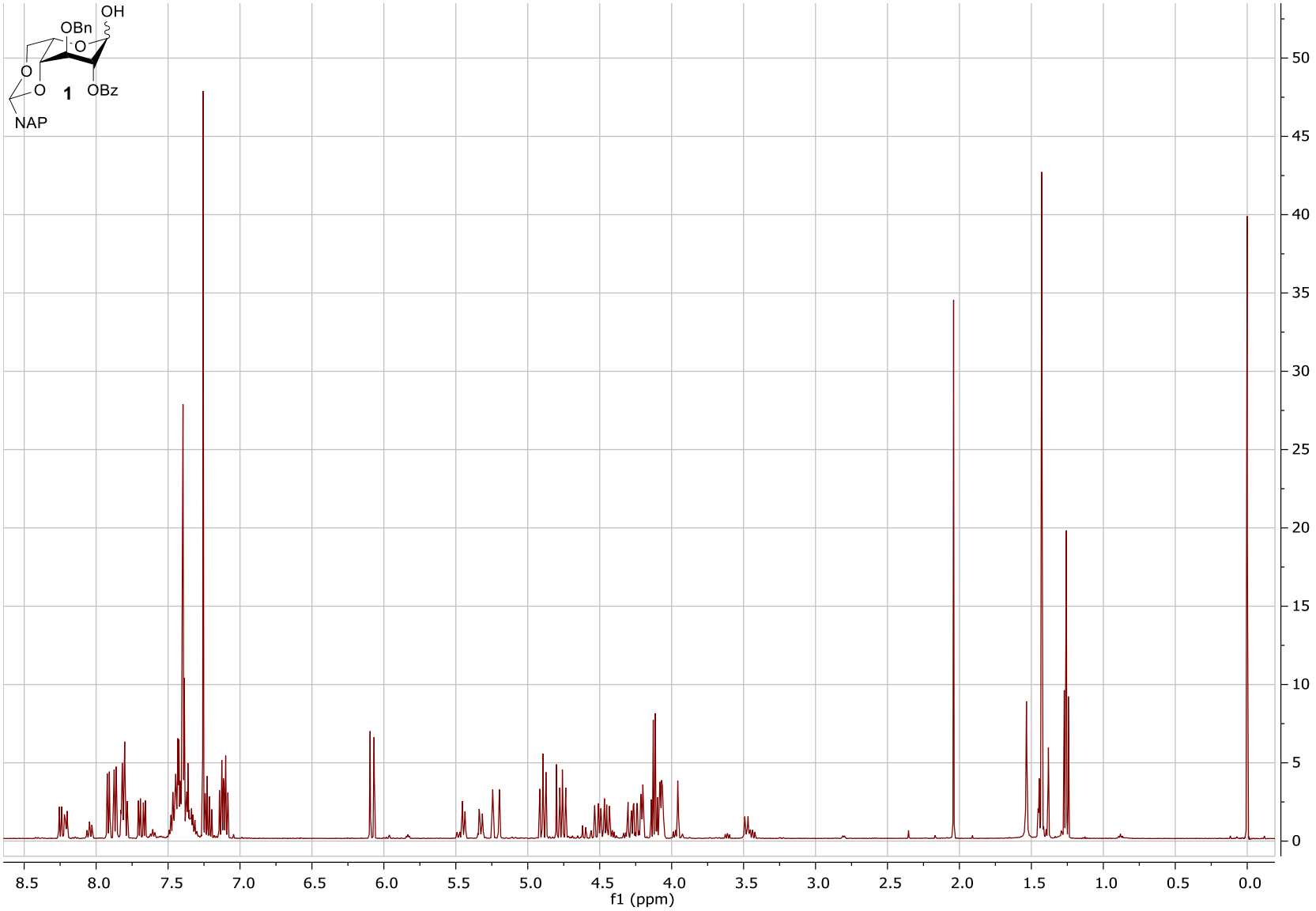
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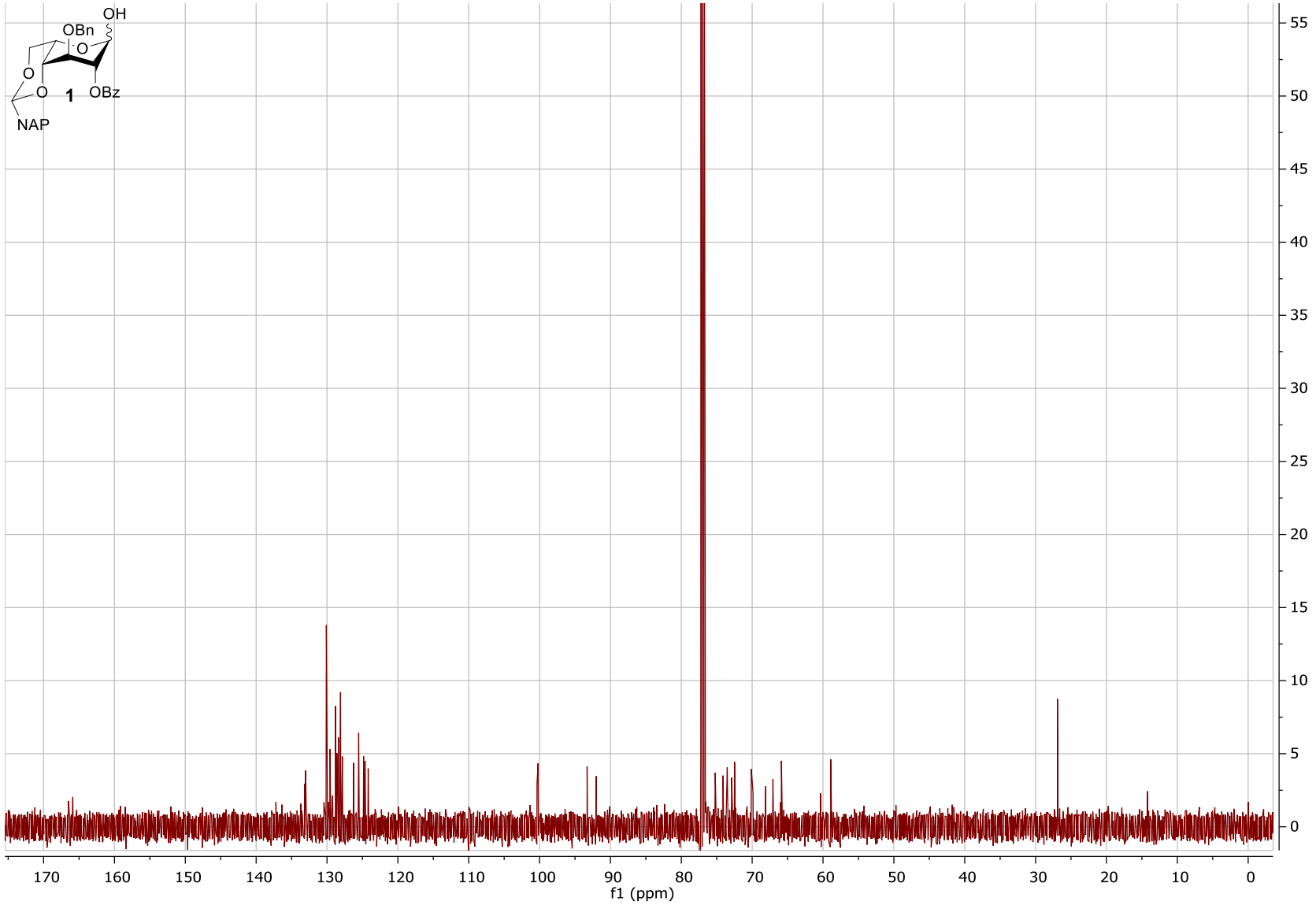
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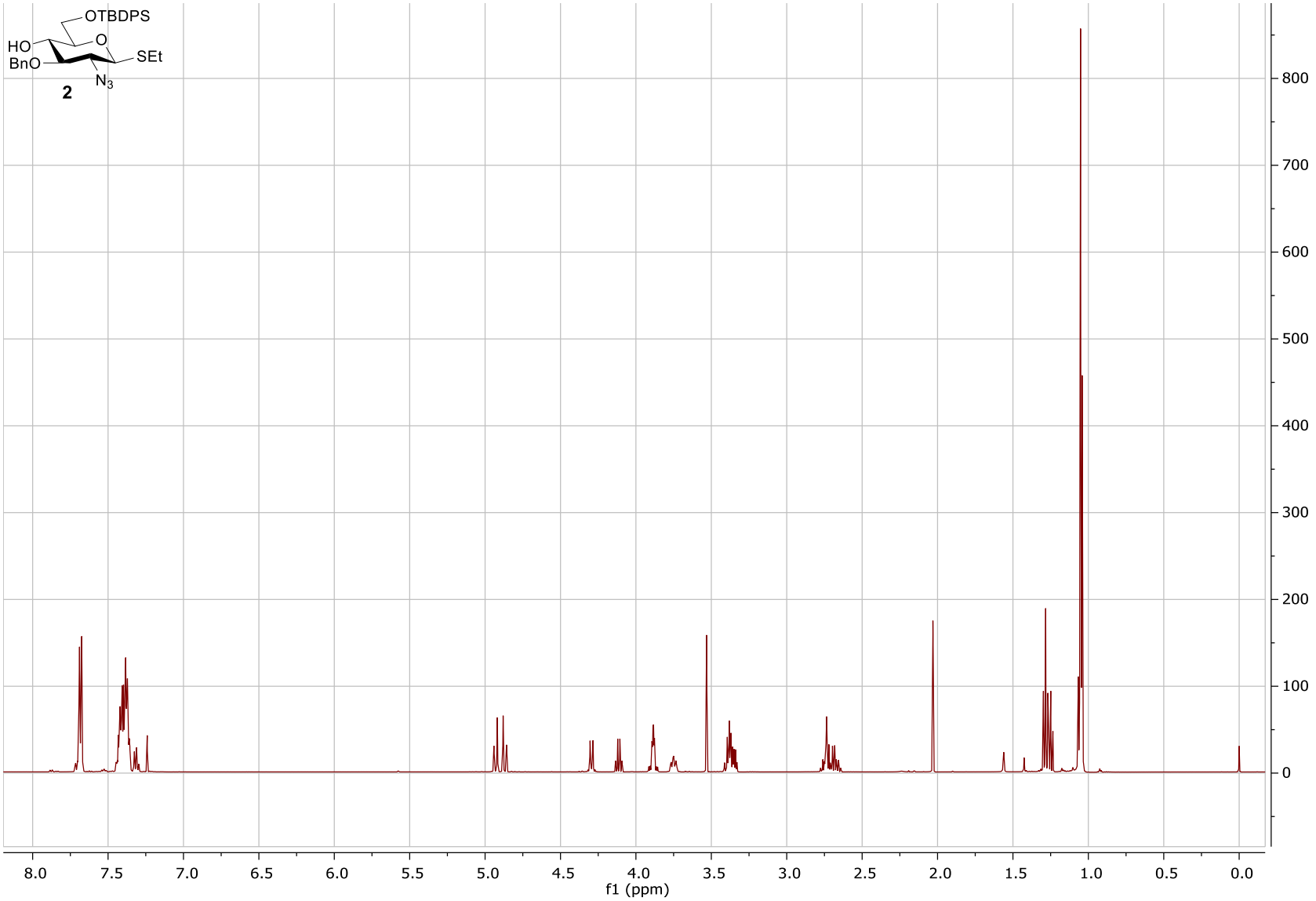
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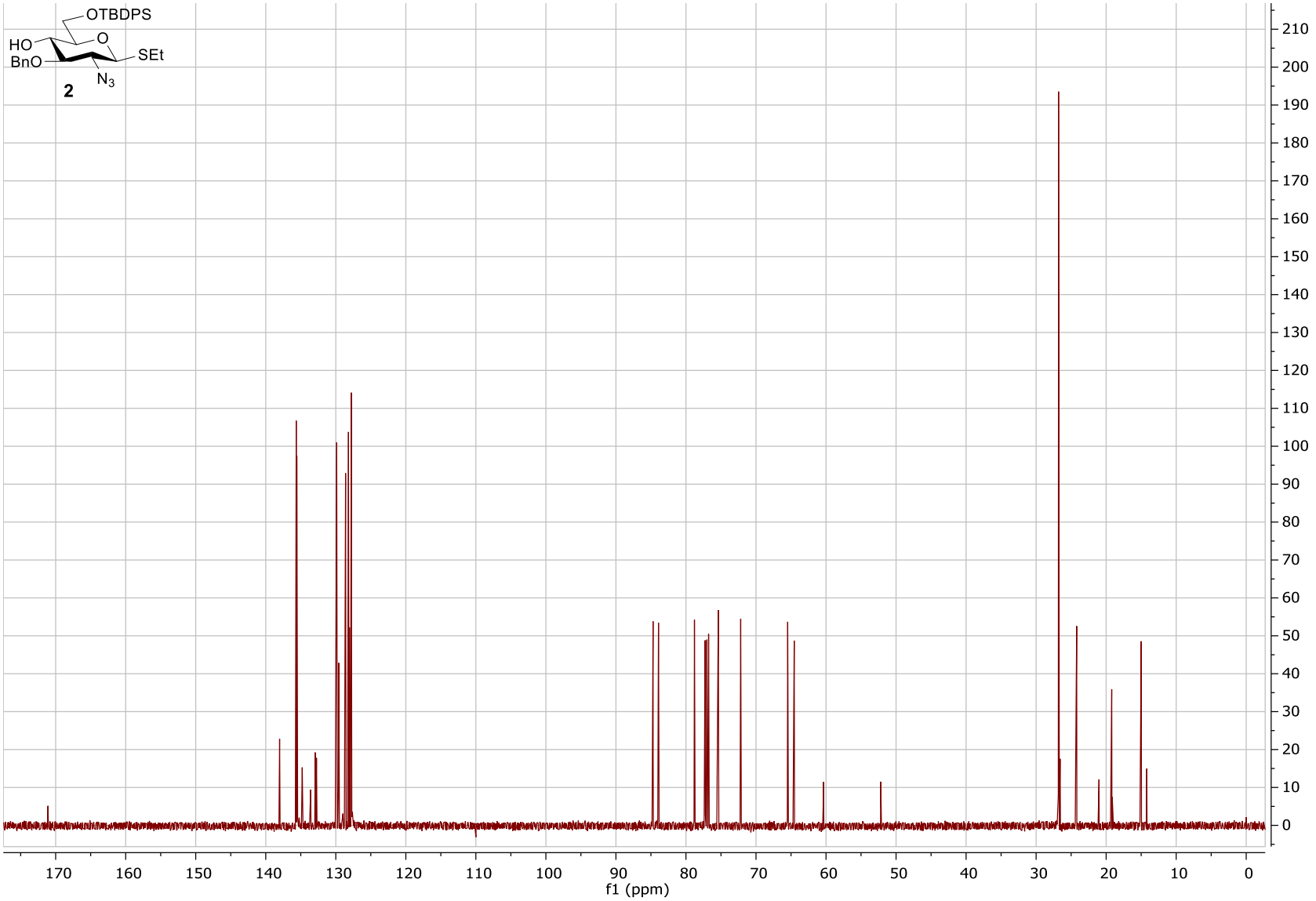
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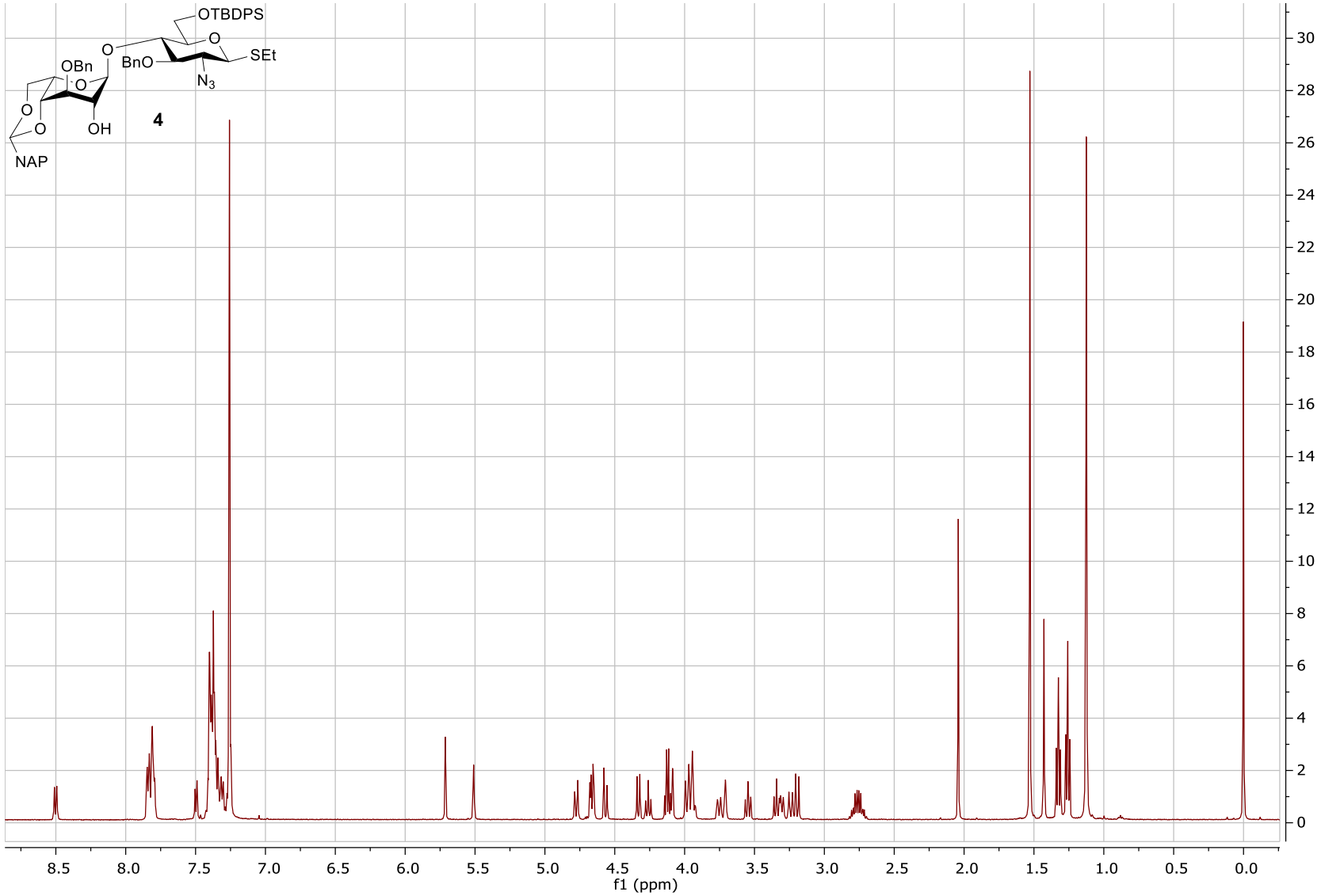
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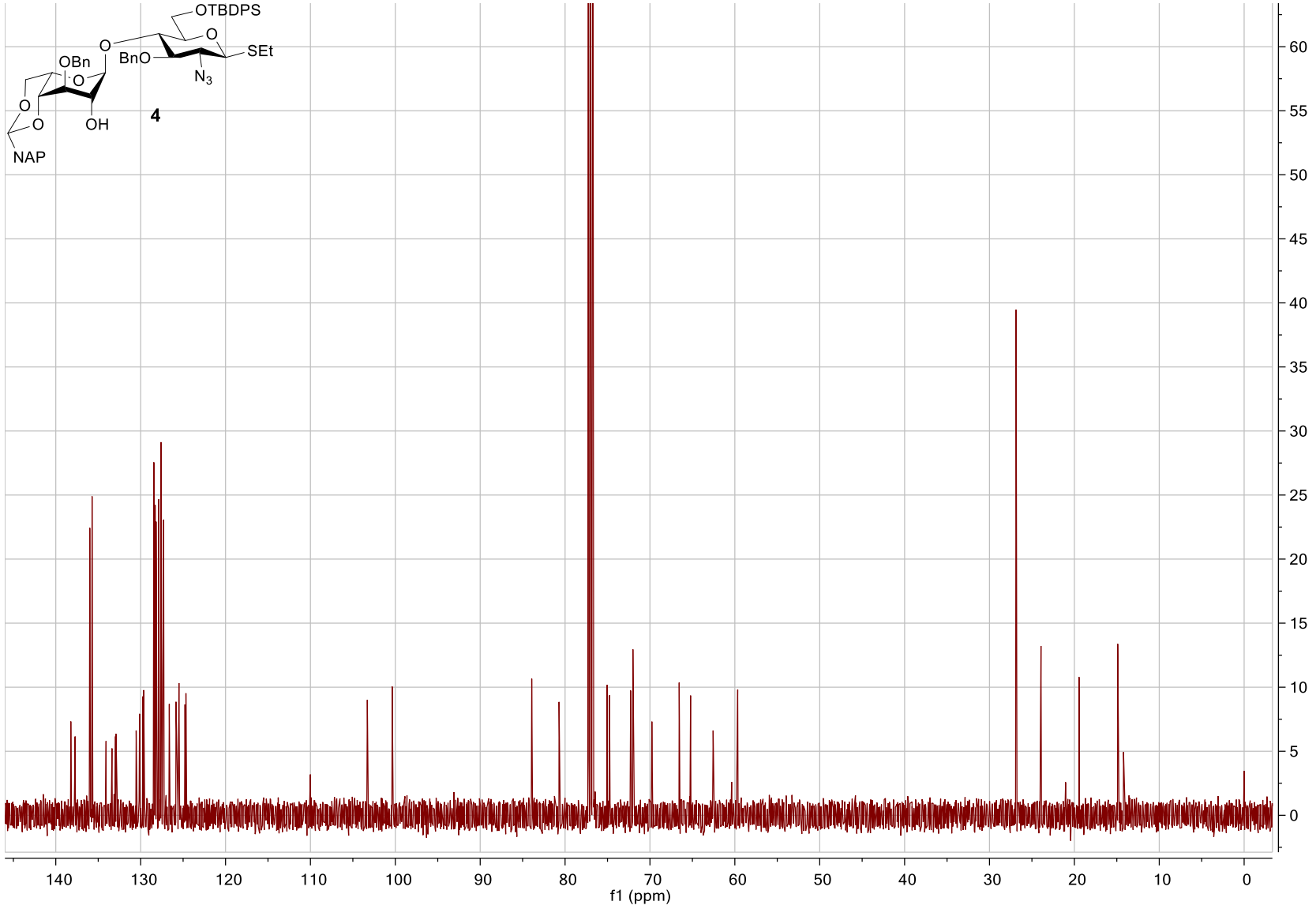
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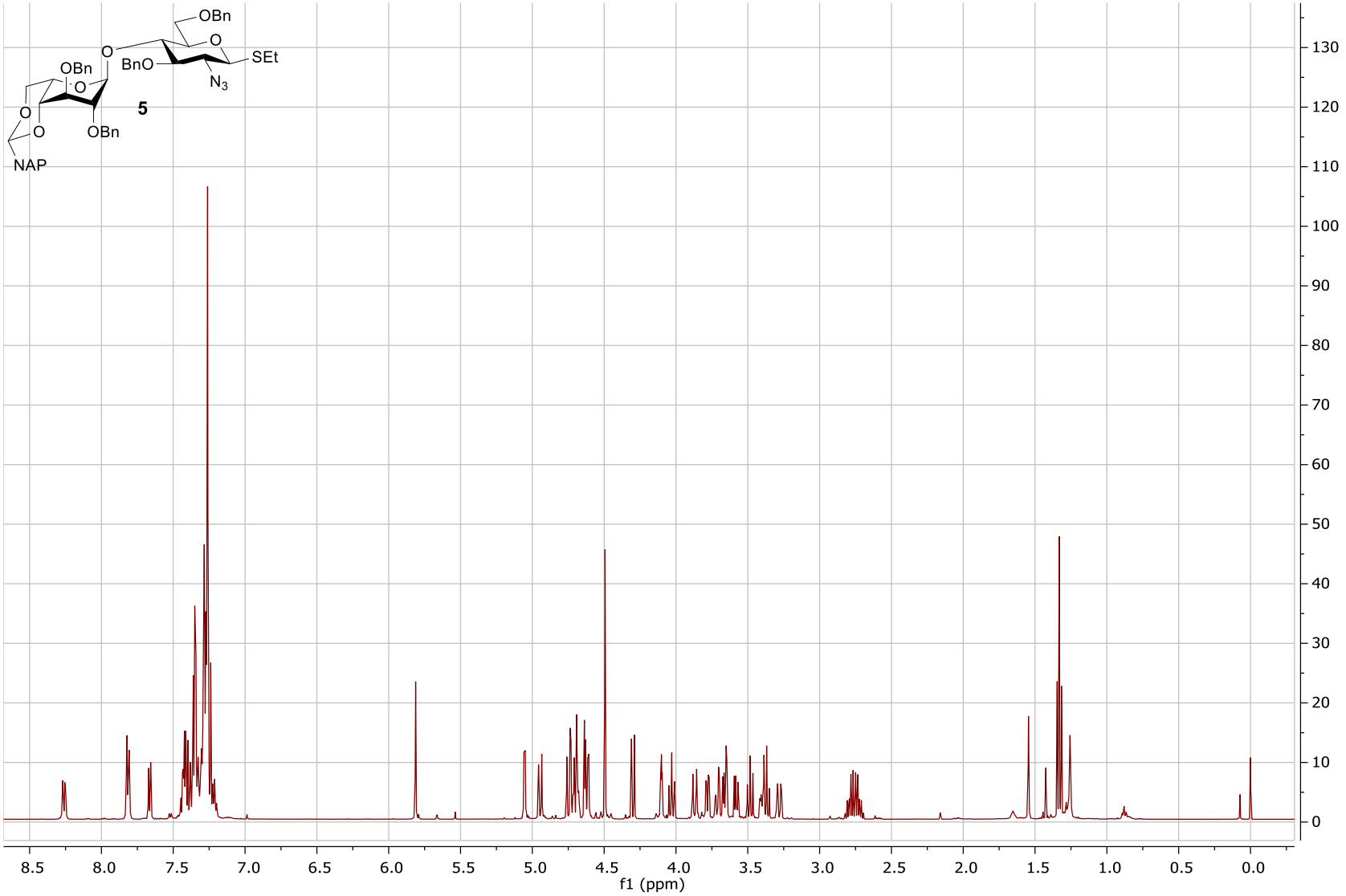
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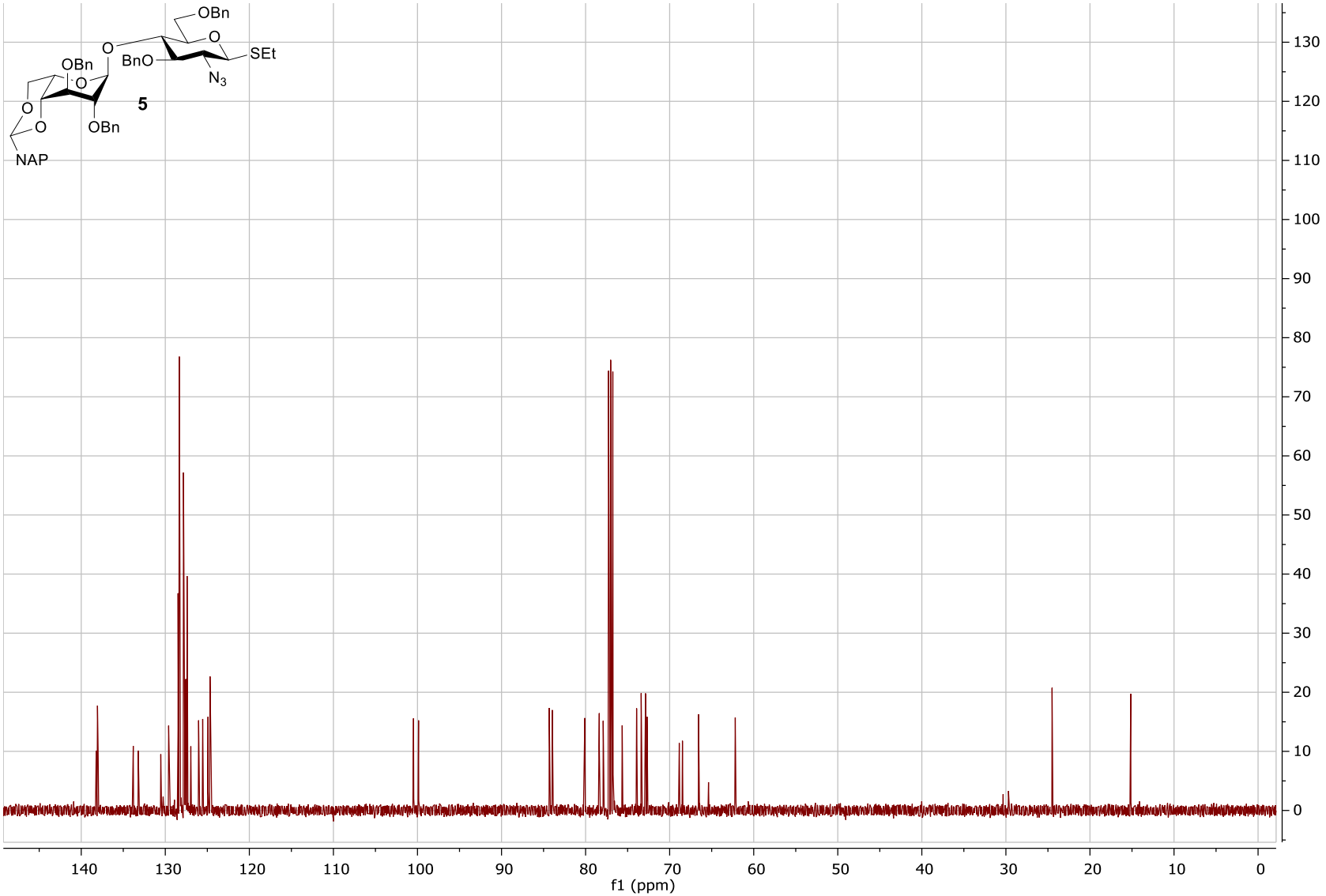
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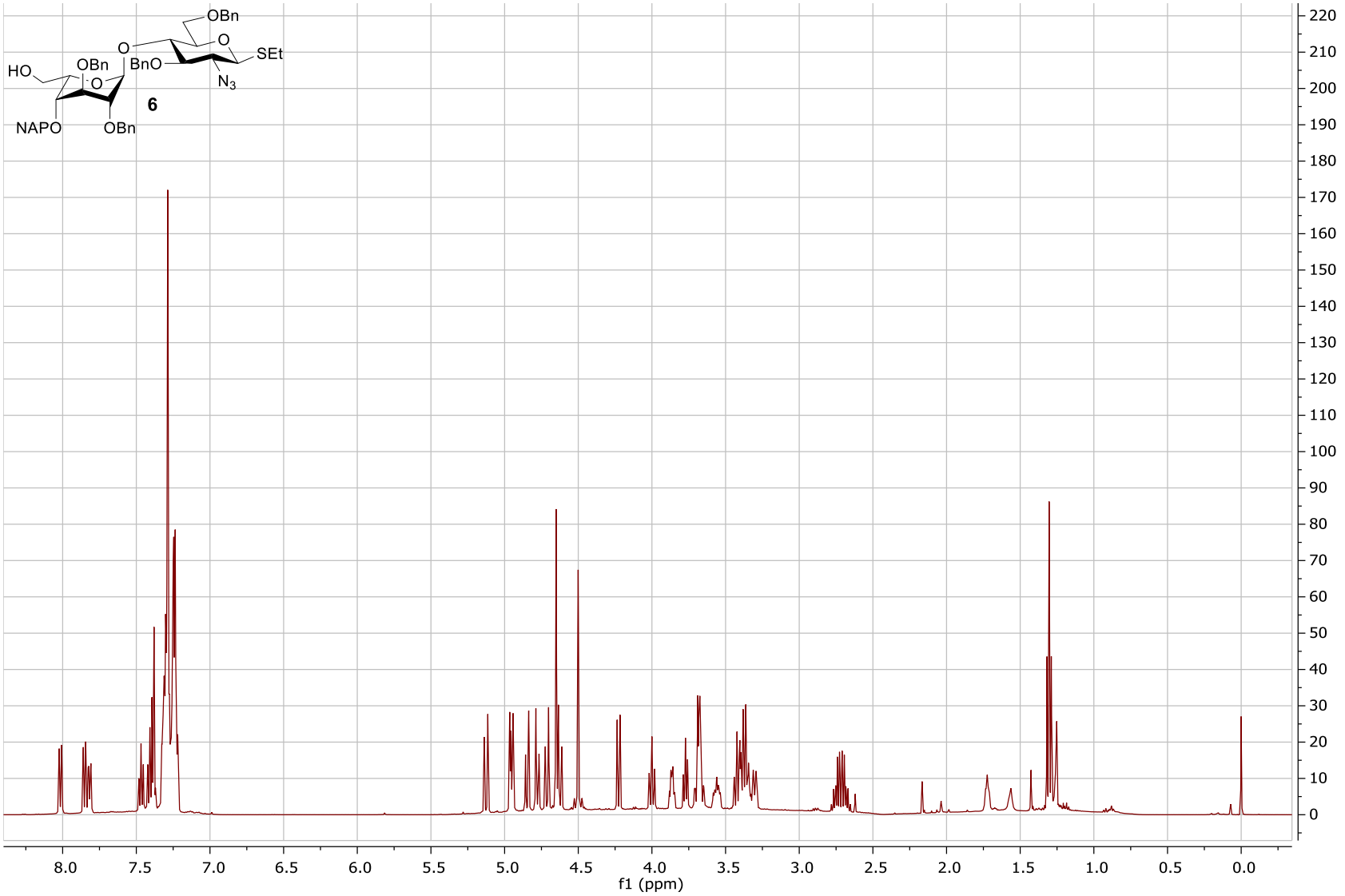
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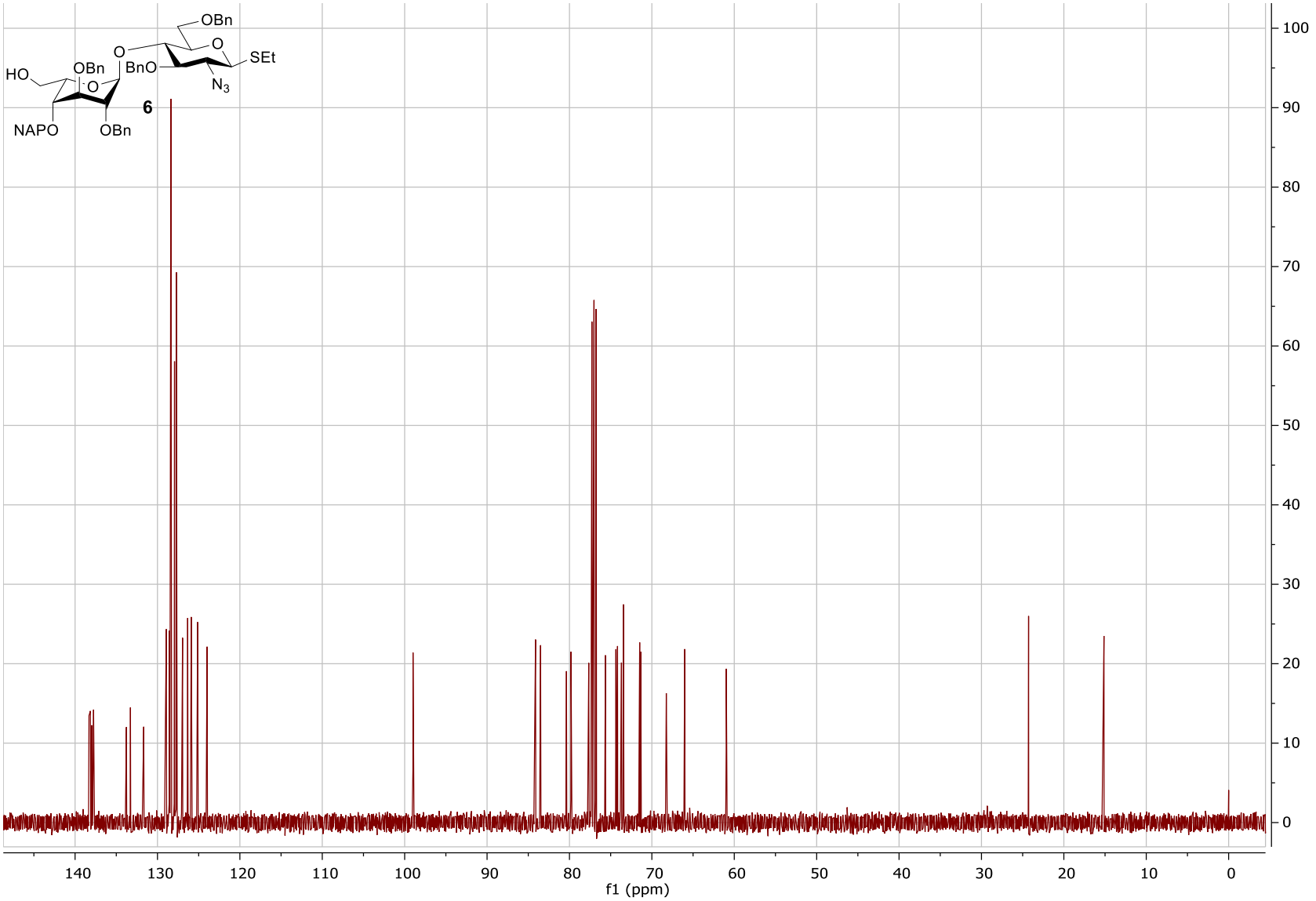
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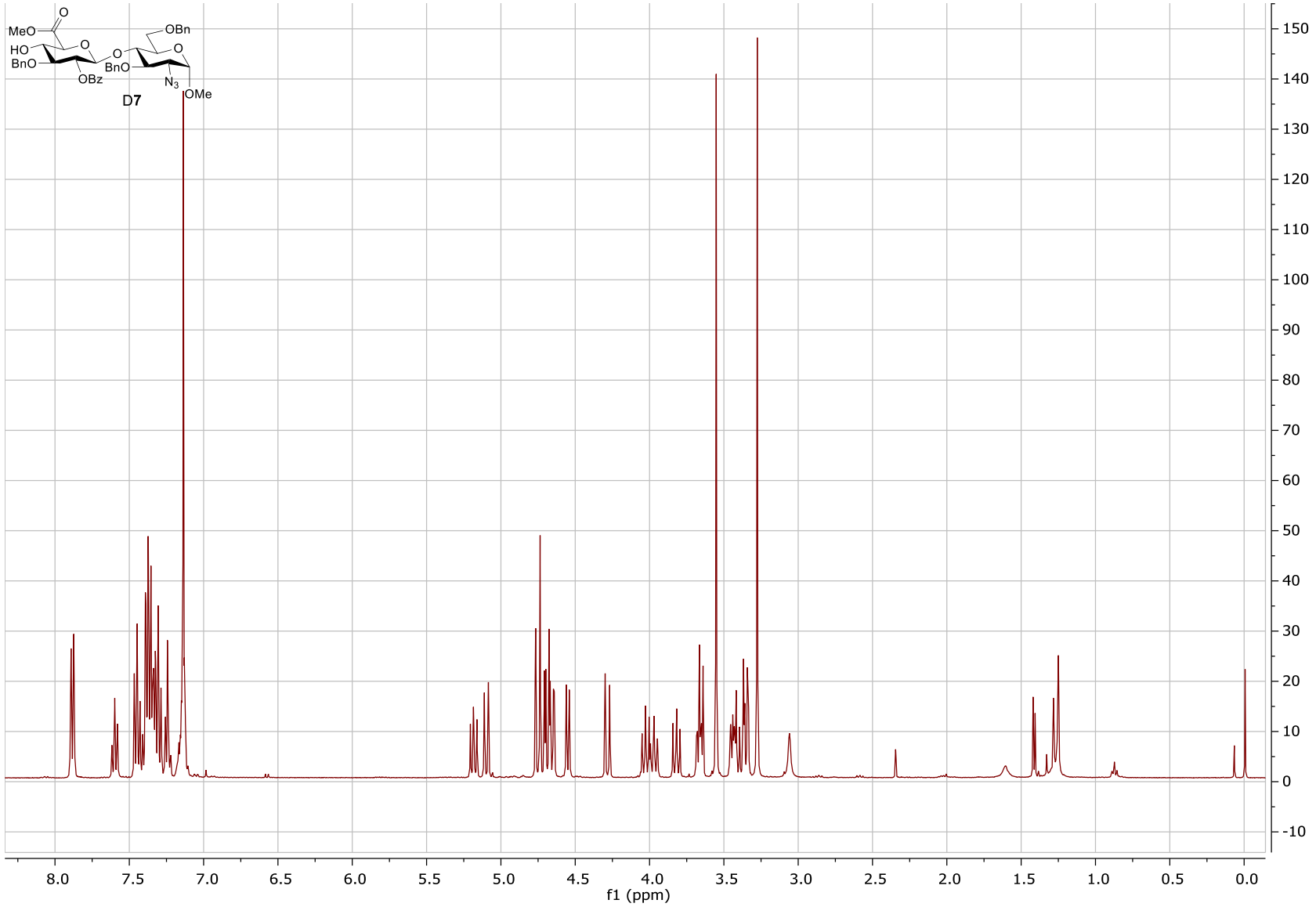
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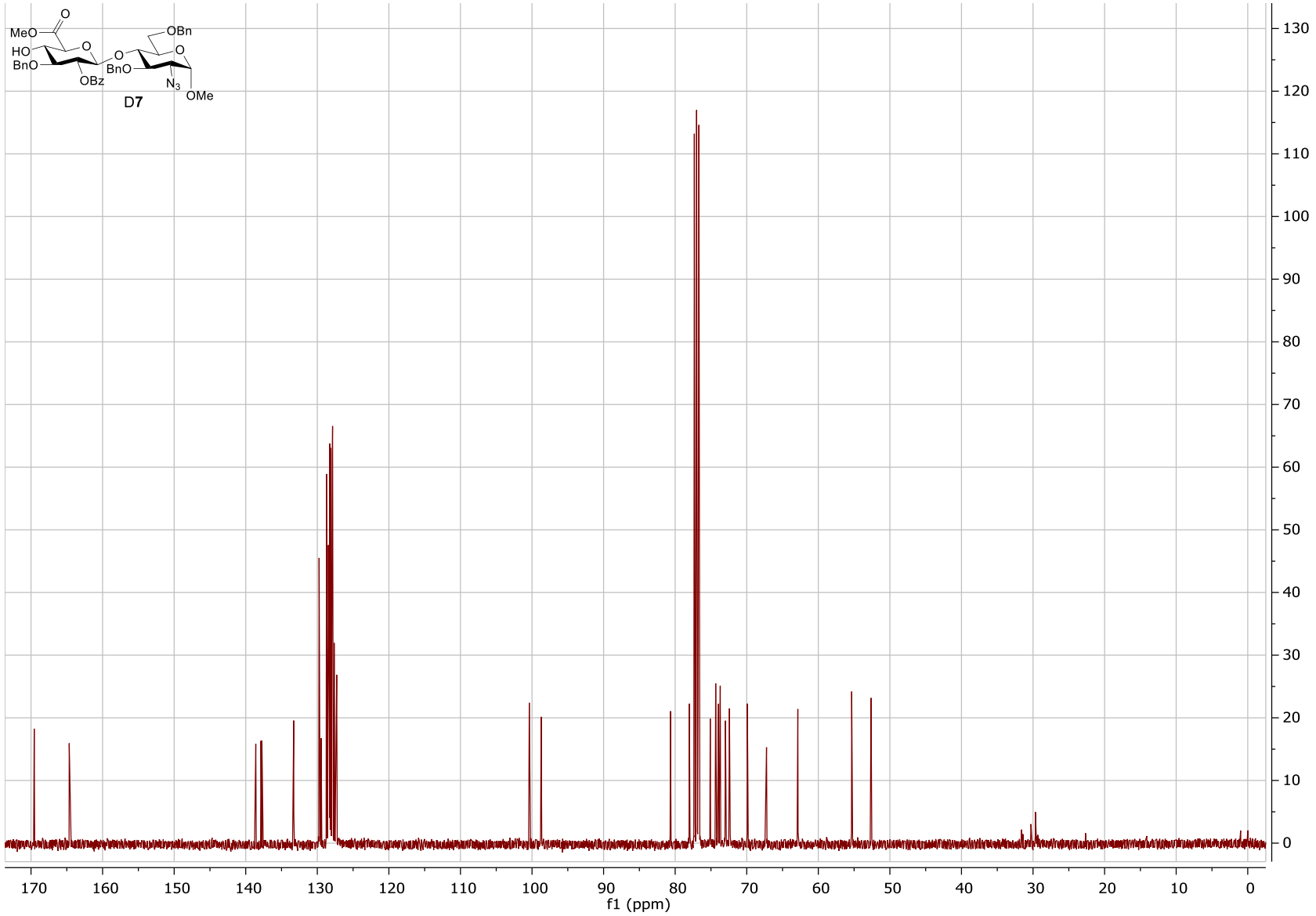
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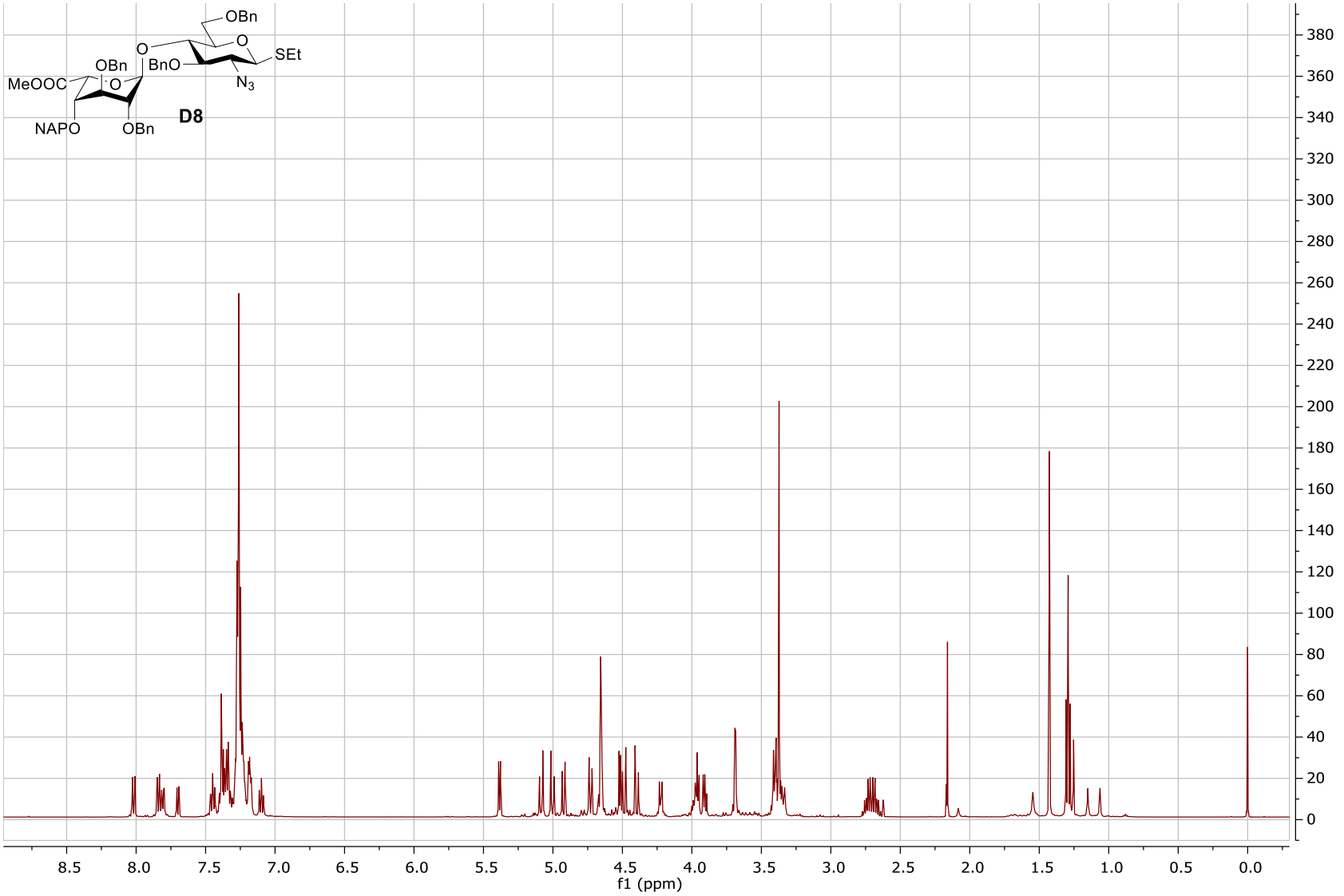
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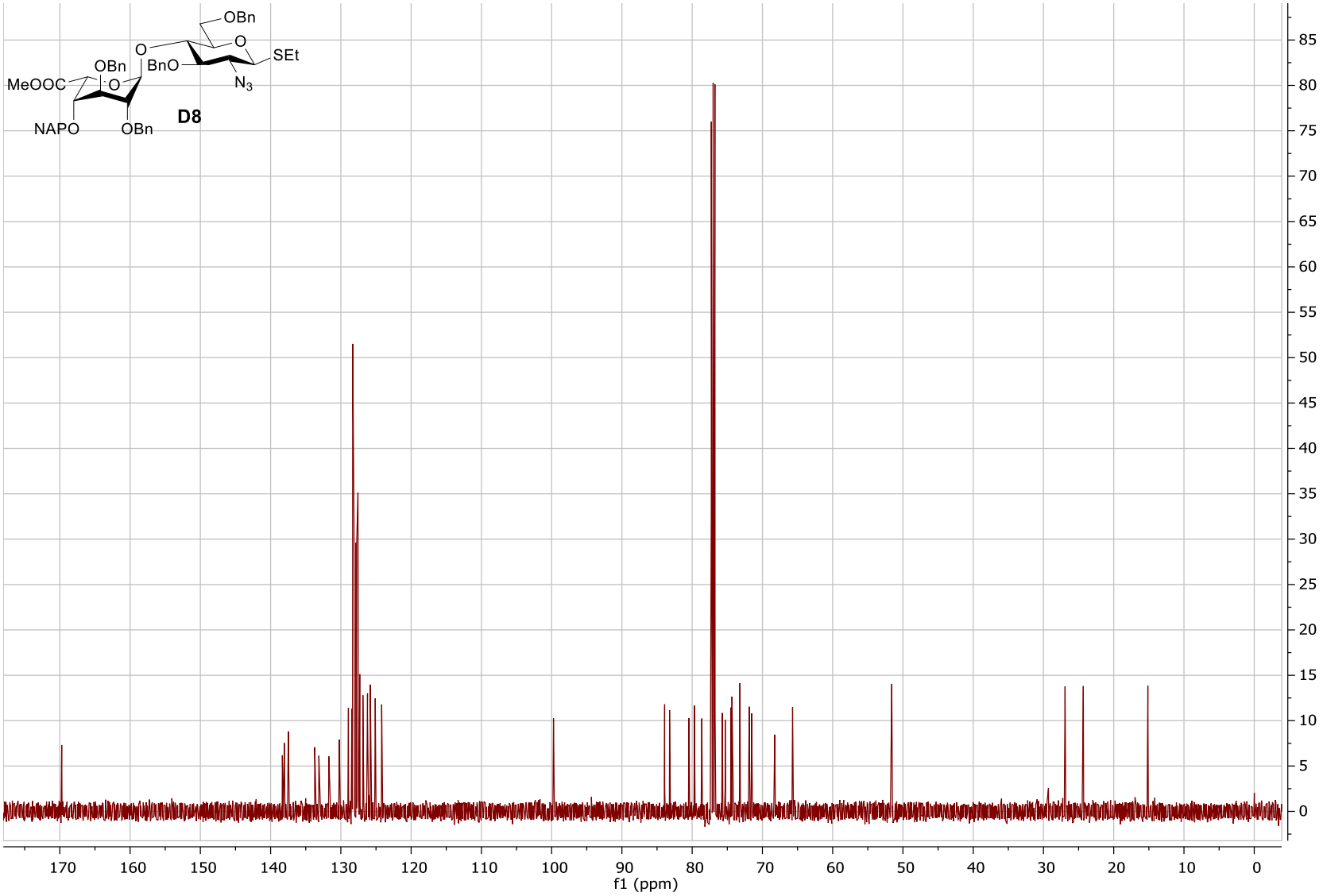
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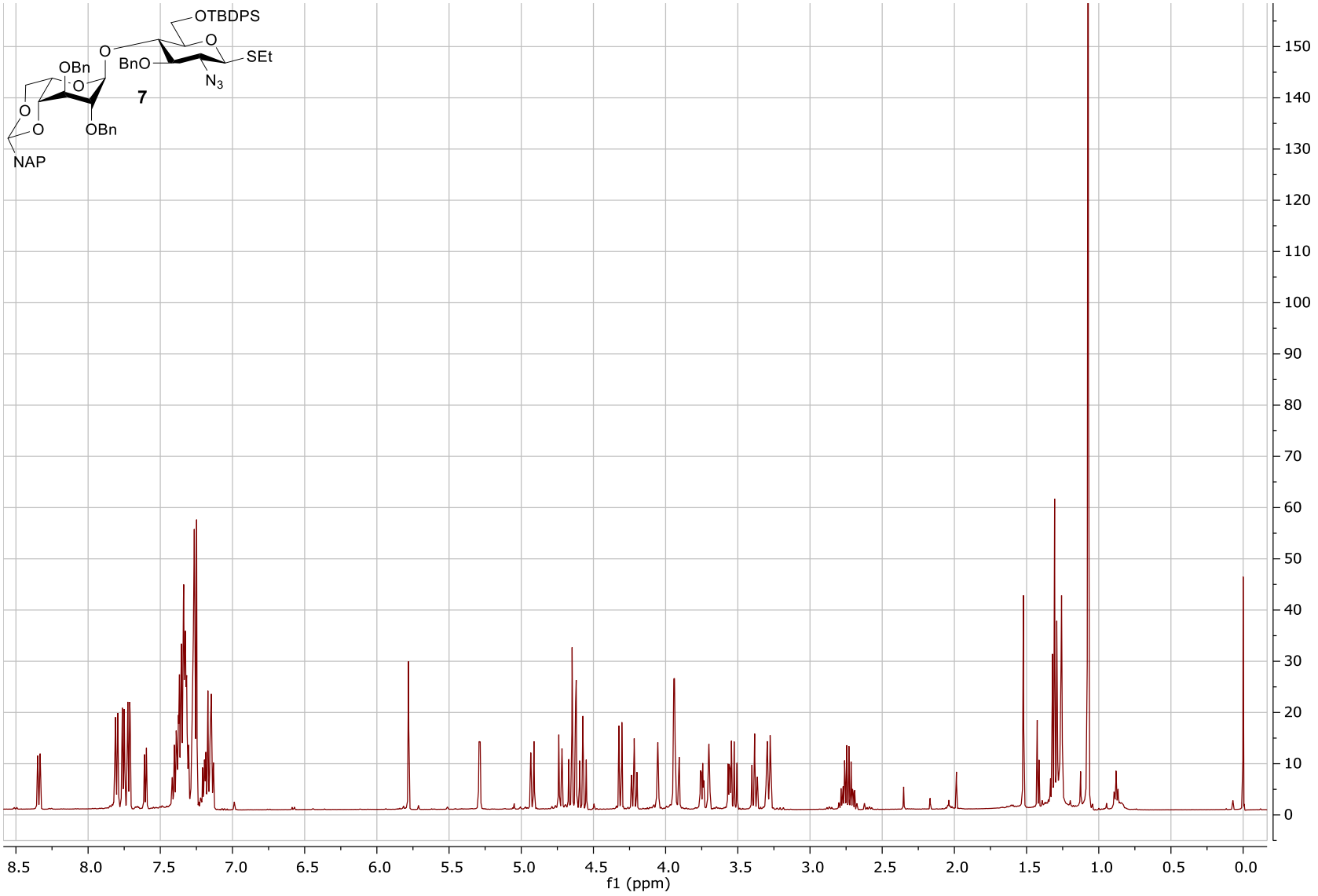
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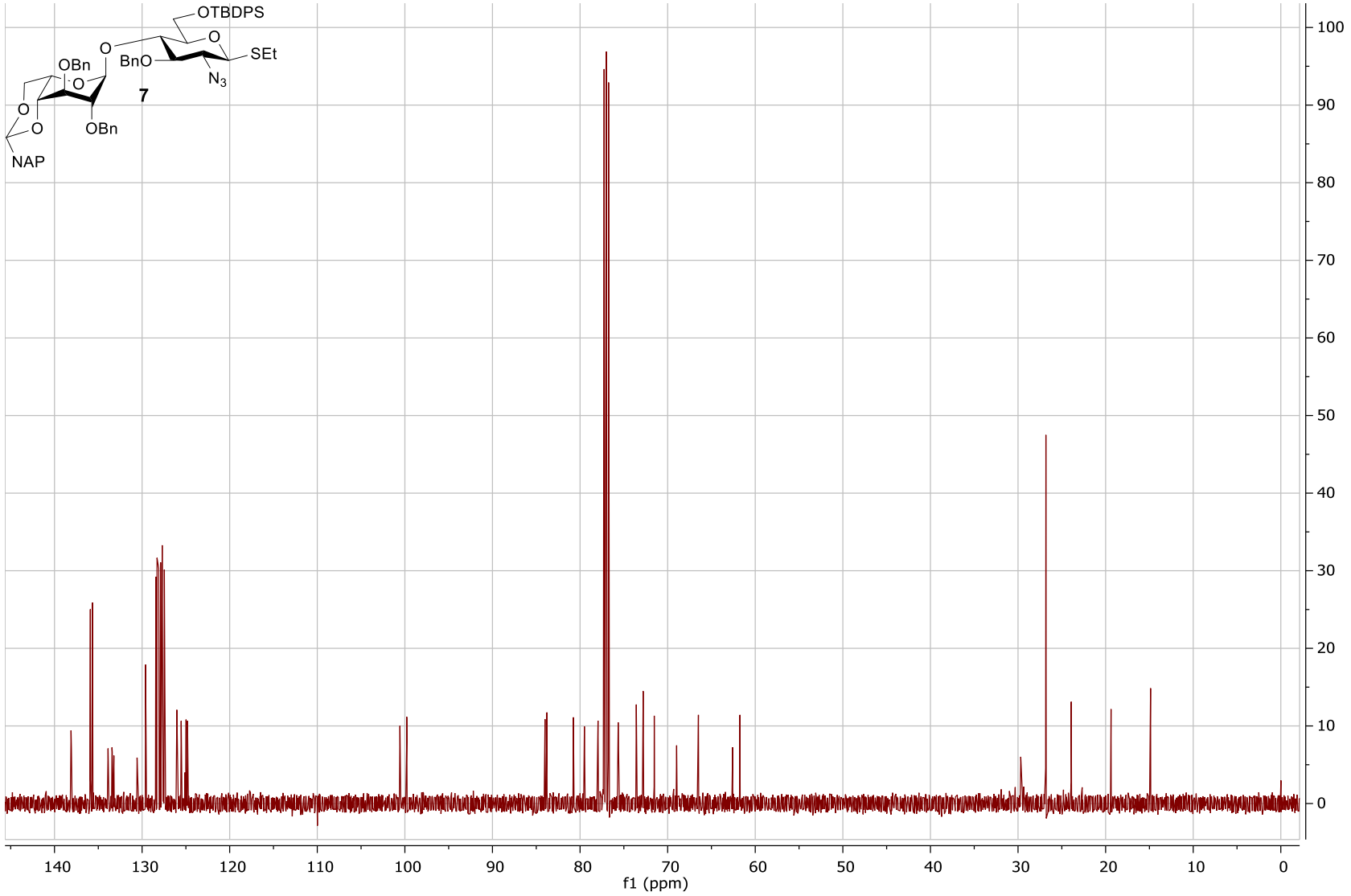
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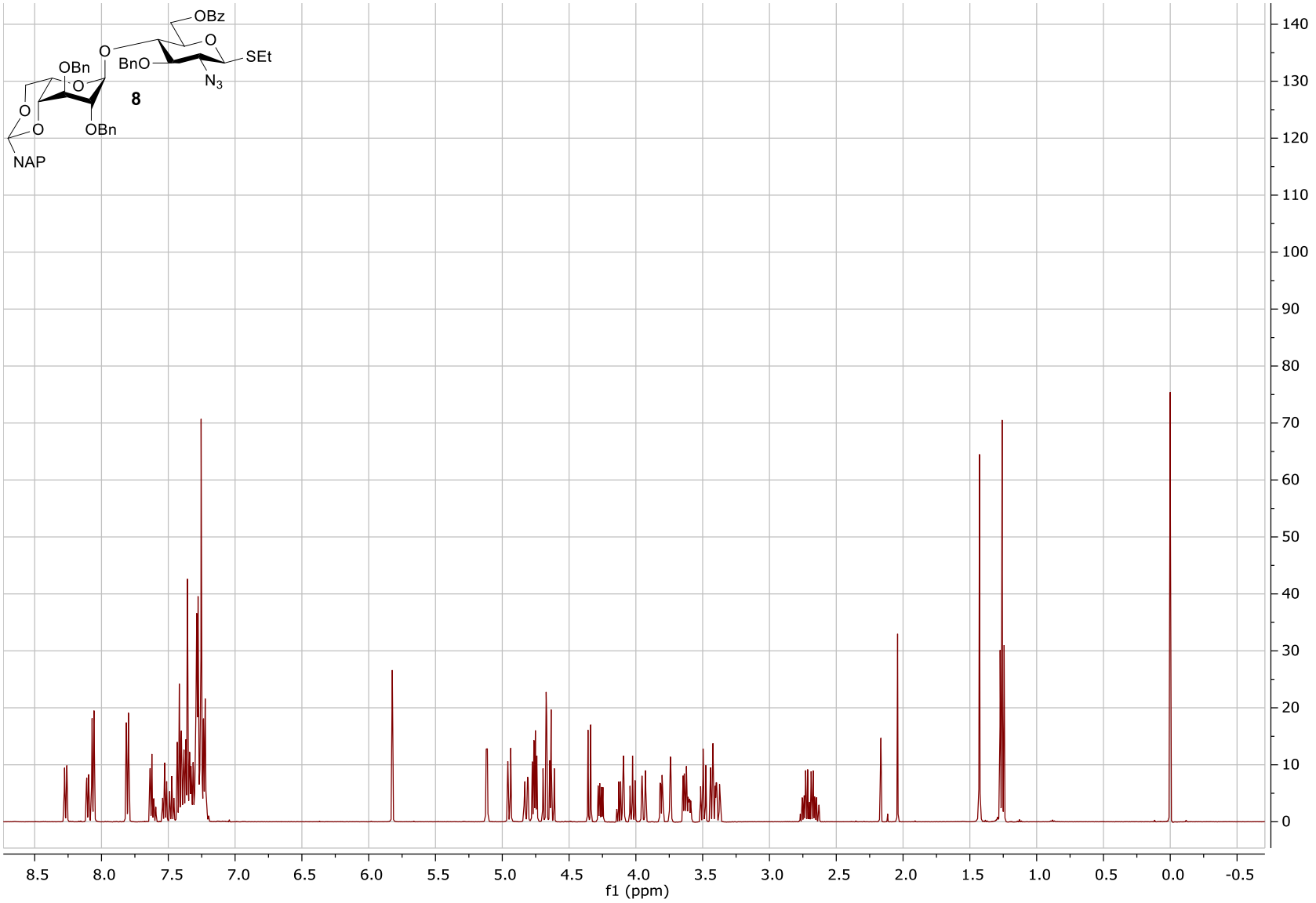
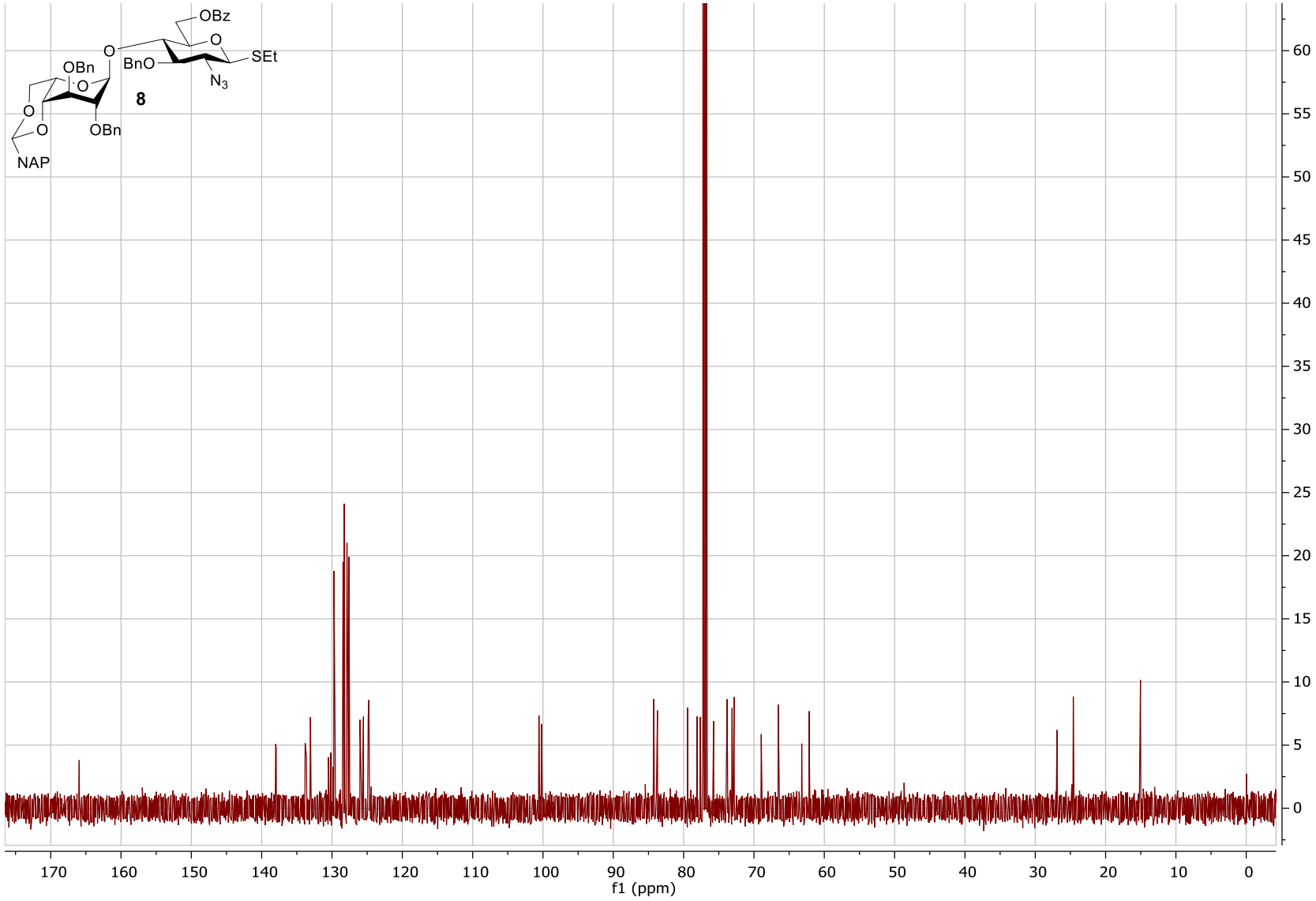
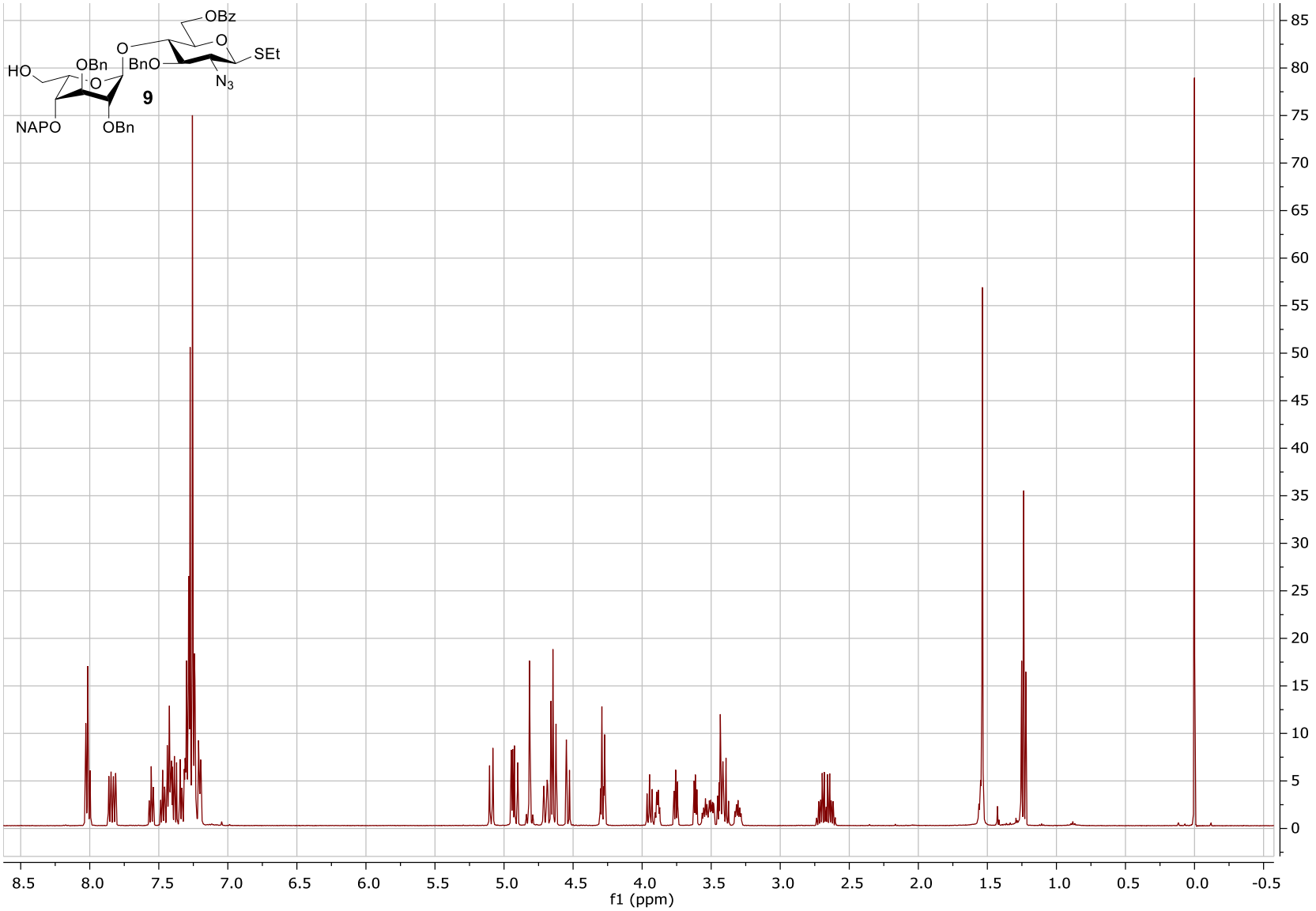
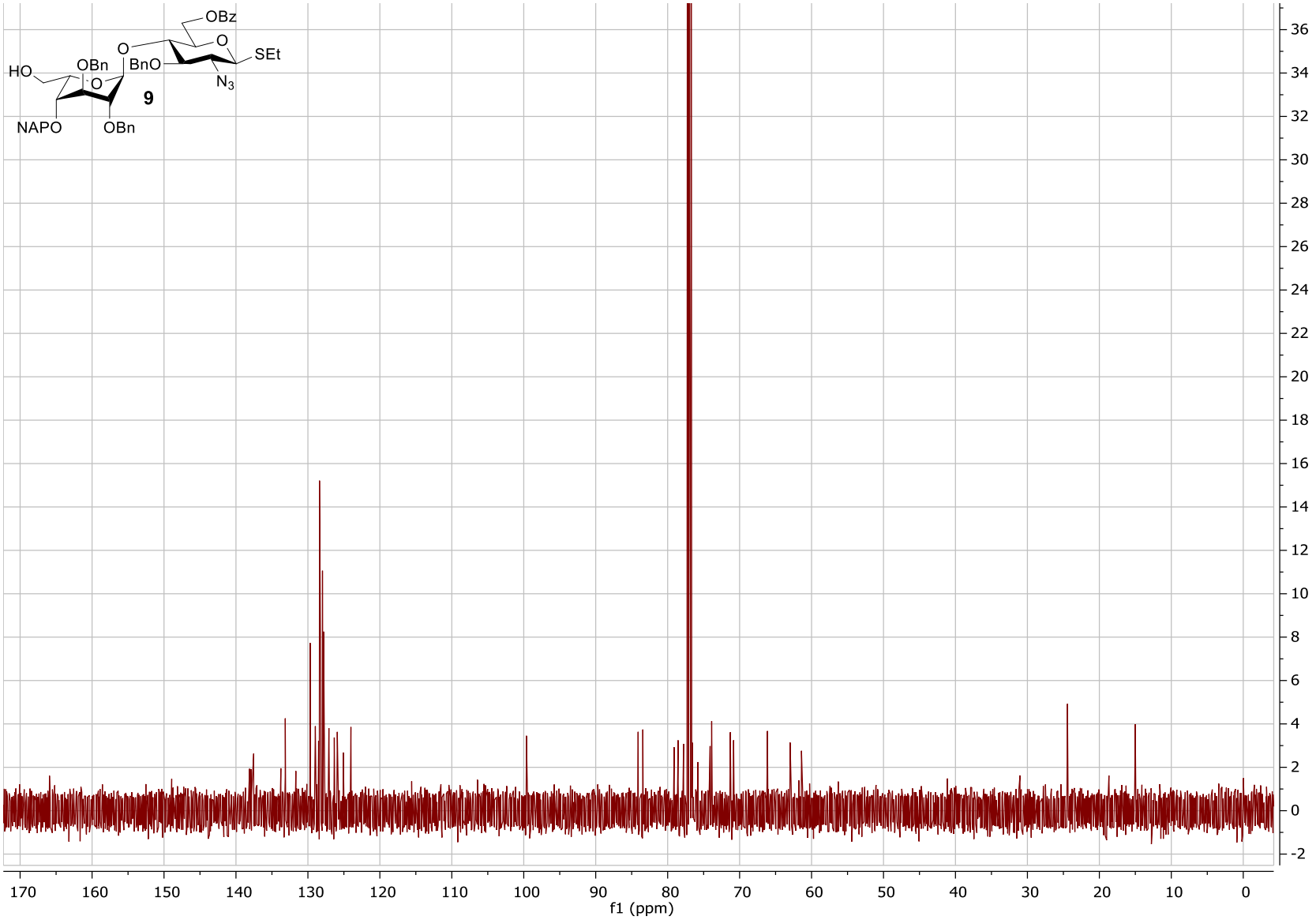
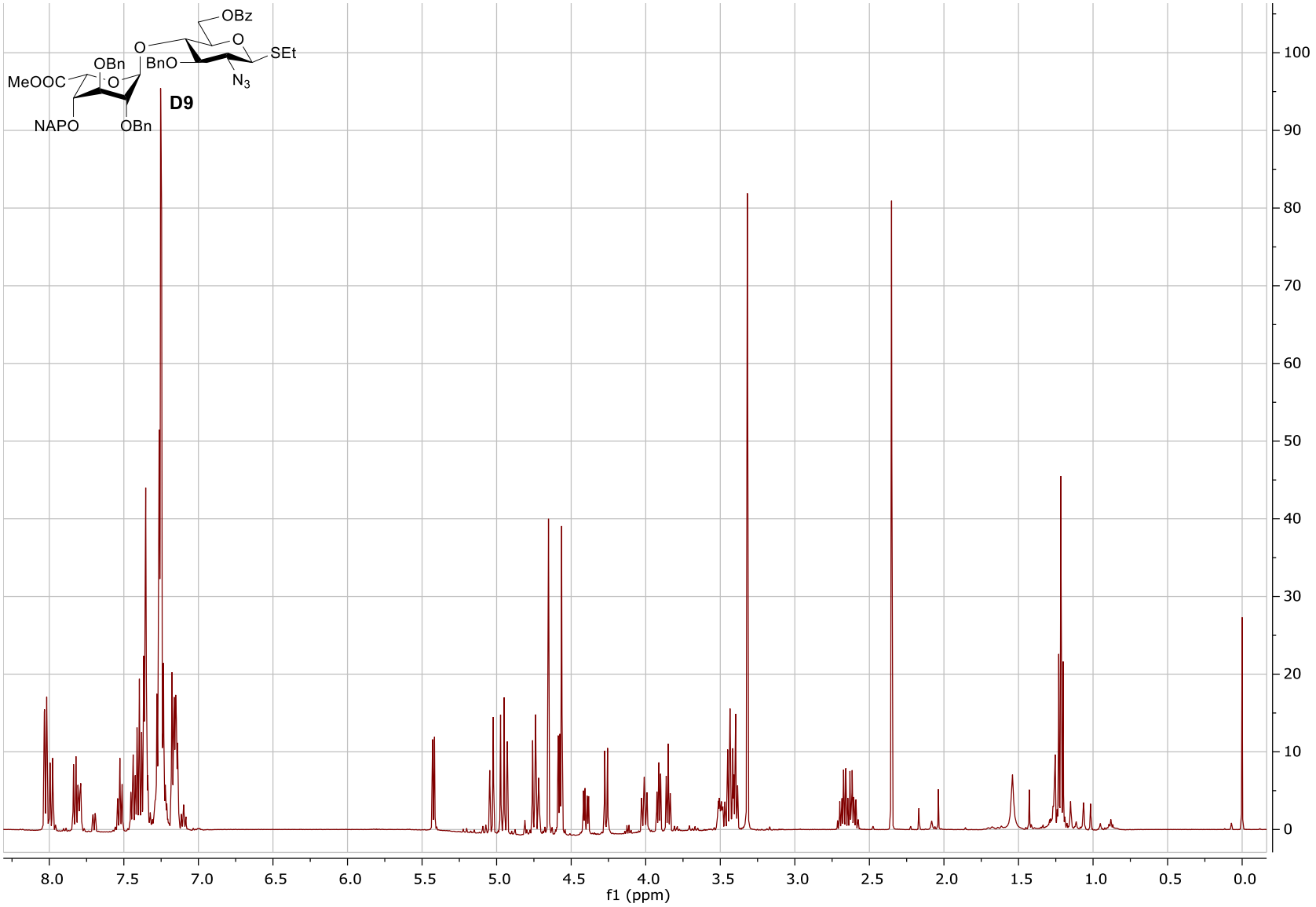
f1 (ppm)

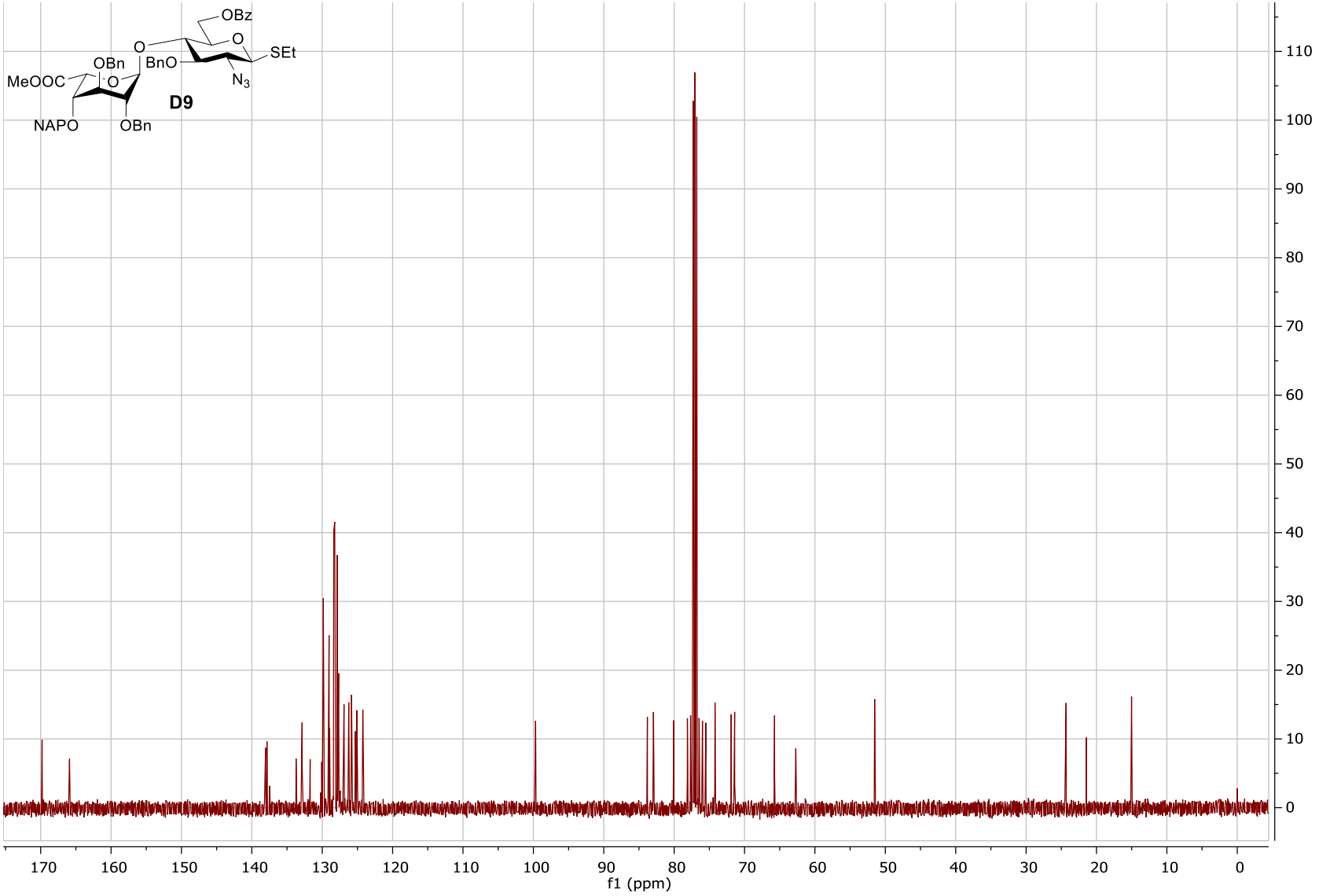

OBz
O
O
SEt
OBn
BnO
N3
O
8
O
O
OBn
NAP
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

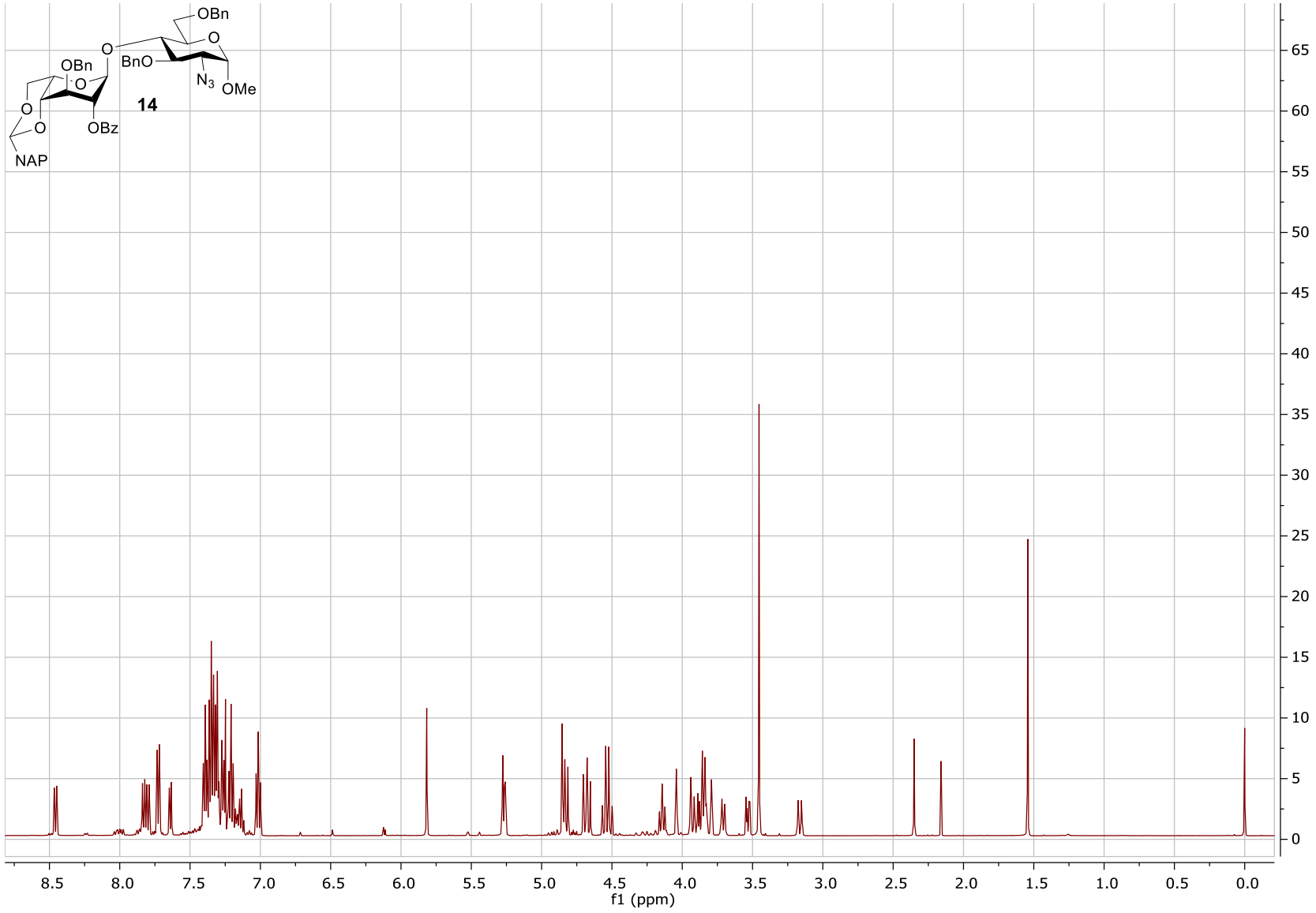

OBz
O
O
SEt
BnO
N3
OBn
O
8
O
O
OBn
NAP
60
55
50
45
40
35
30
25
20
15
10
5
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

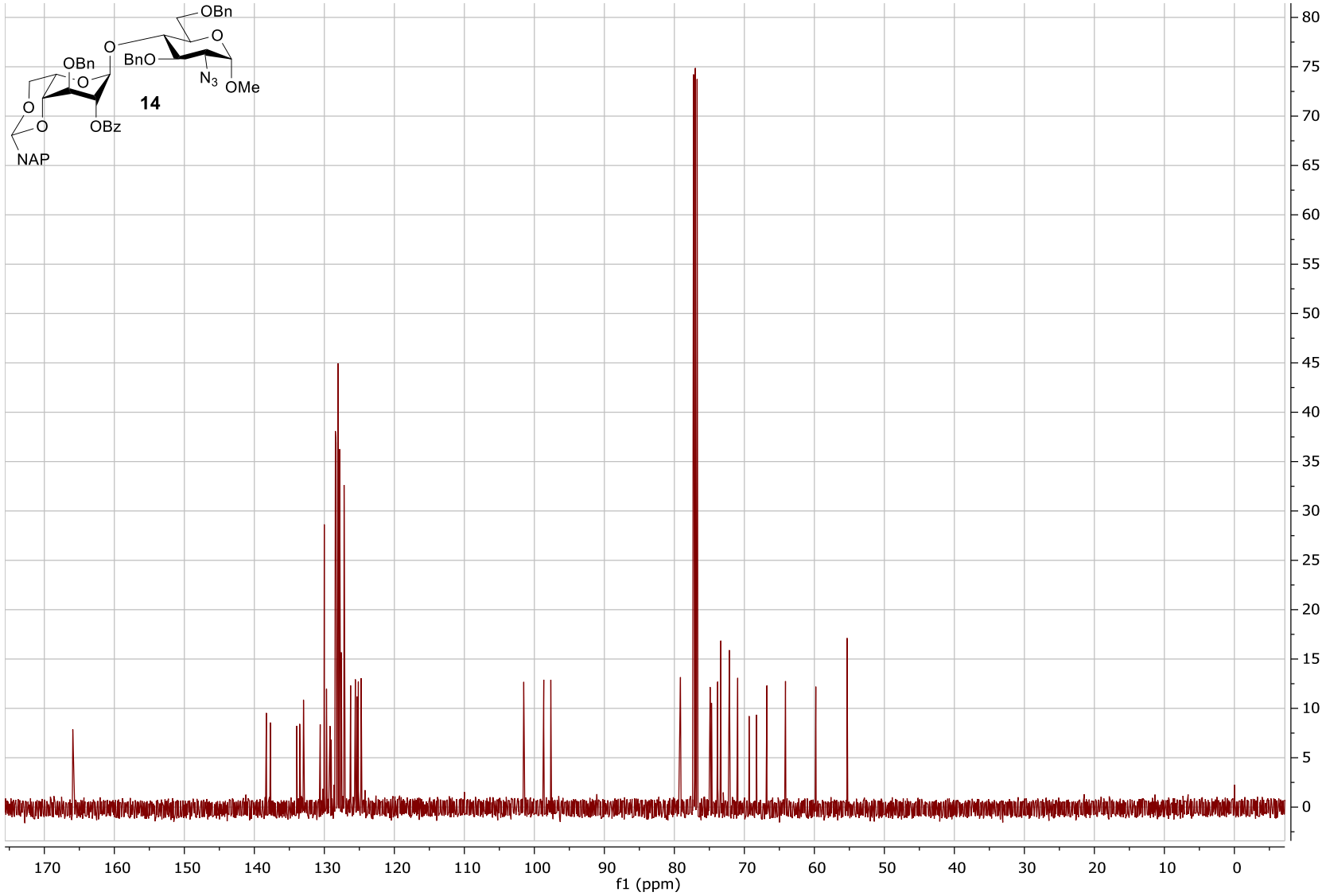

OBz
O
SEt
HO
OBn
BnO
O
N3
9
NAPO
OBn
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

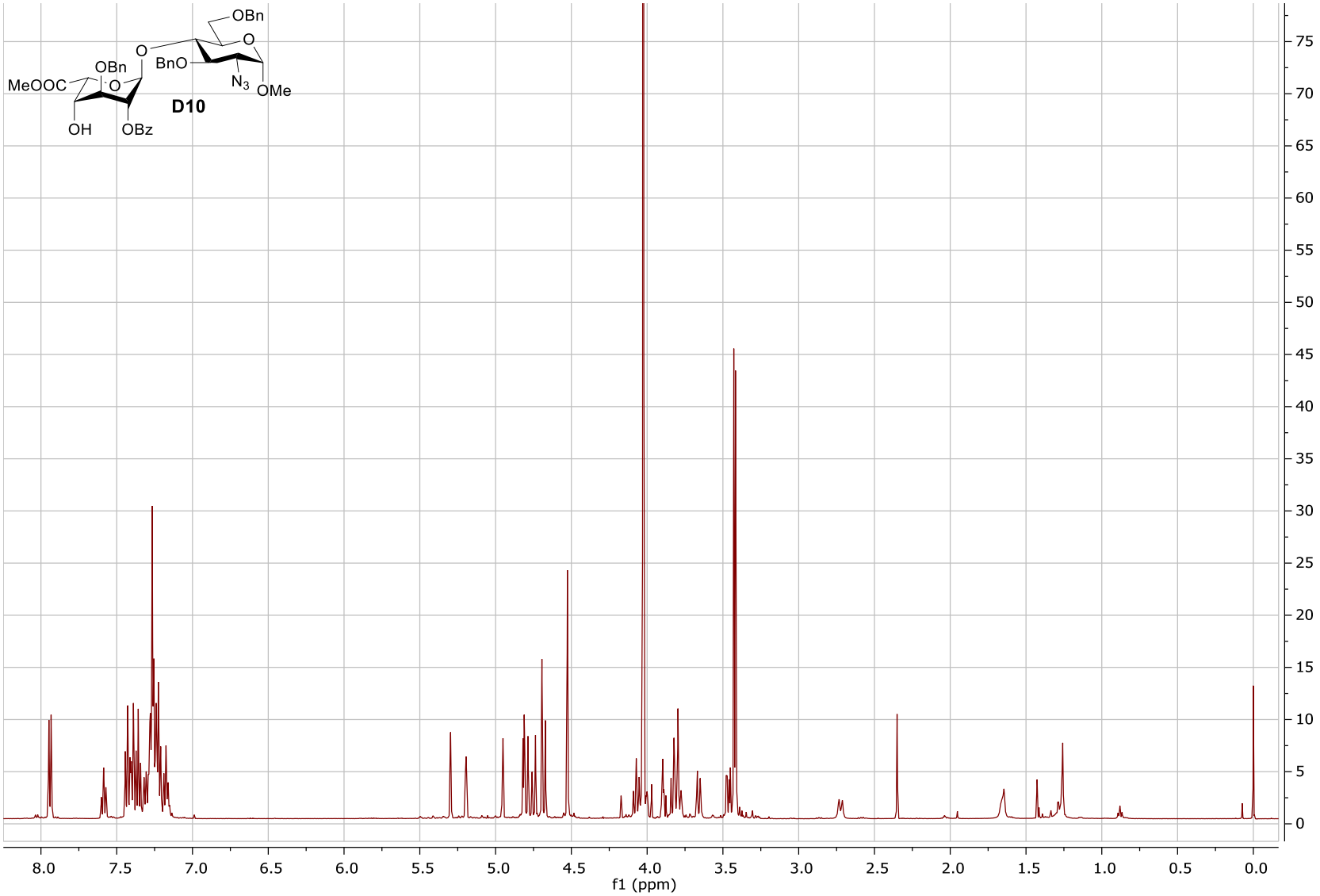

OBz
O
O
SEt
HO
OBn
BnO
N3
O
9
NAPO
OBn
36
34
32
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
-2
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

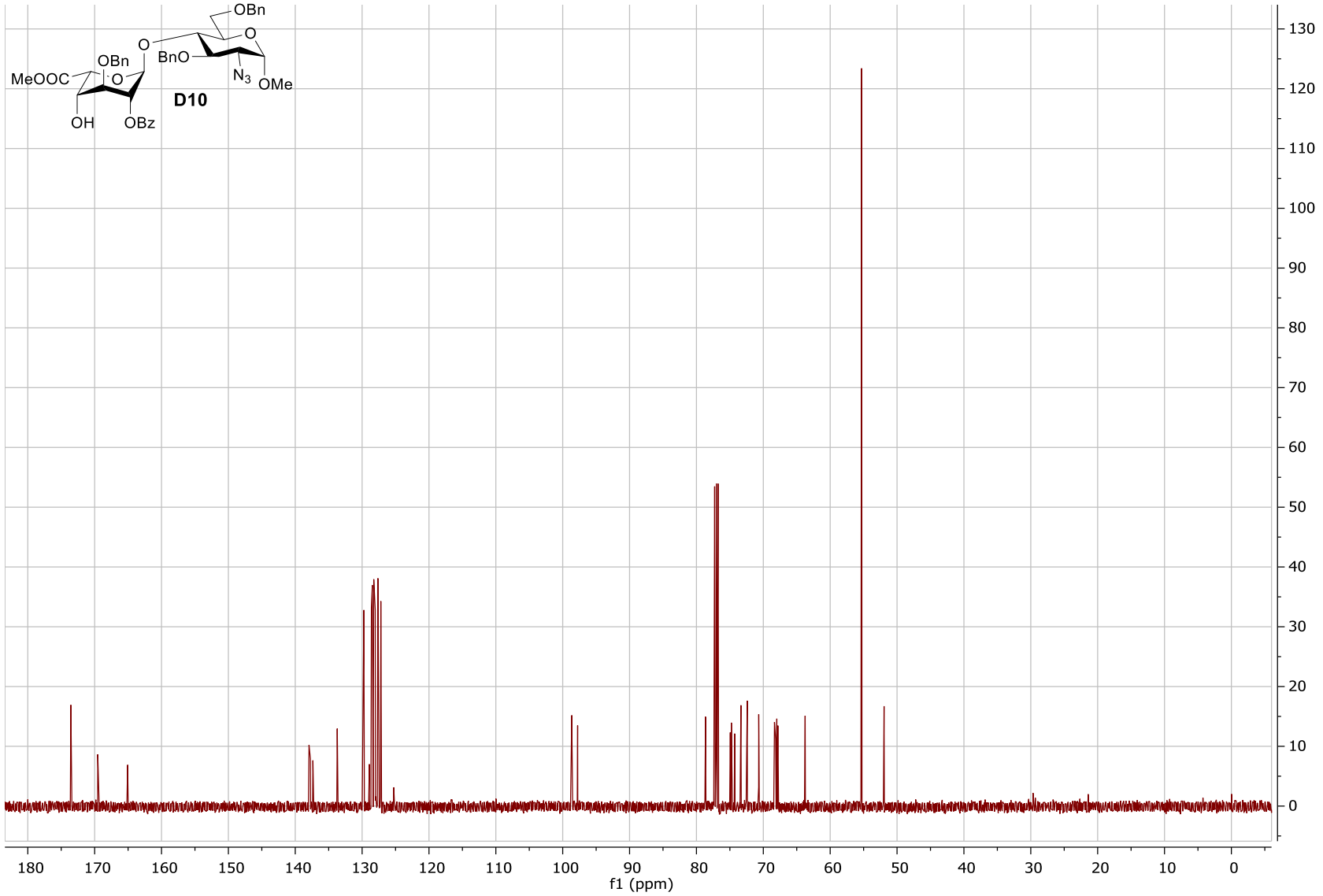

OBz
O
O
SEt
OBn
BnO
MeOOC
O
N3
D9
NAPO
OBn
100
90
80
70
60
50
40
30
20
10
0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

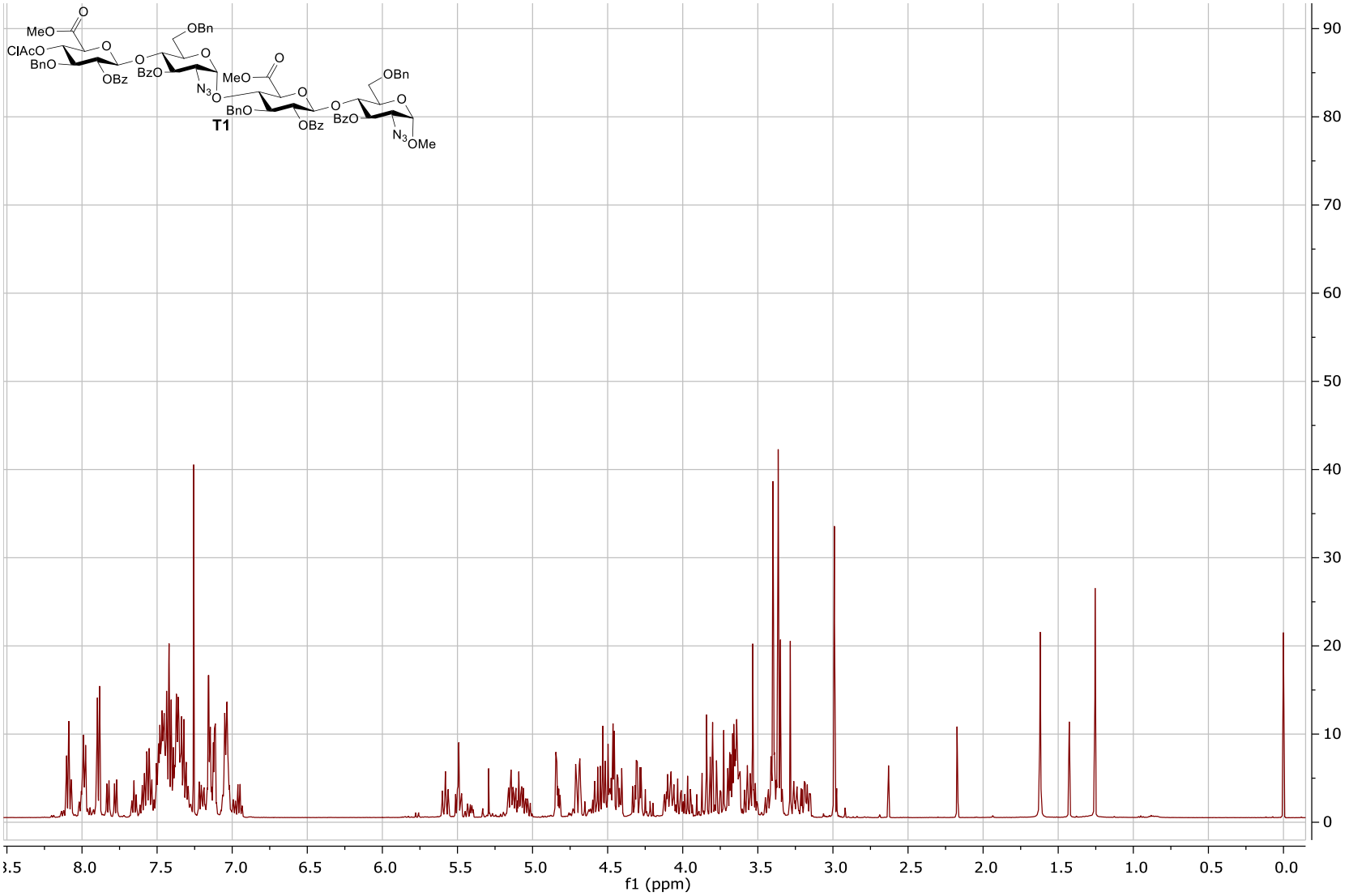

OBz
O
O
SEt
OBn
BnO
MeOOC
O
N3
D9
NAPO
OBn
110
100
90
80
70
60
50
40
30
20
10
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

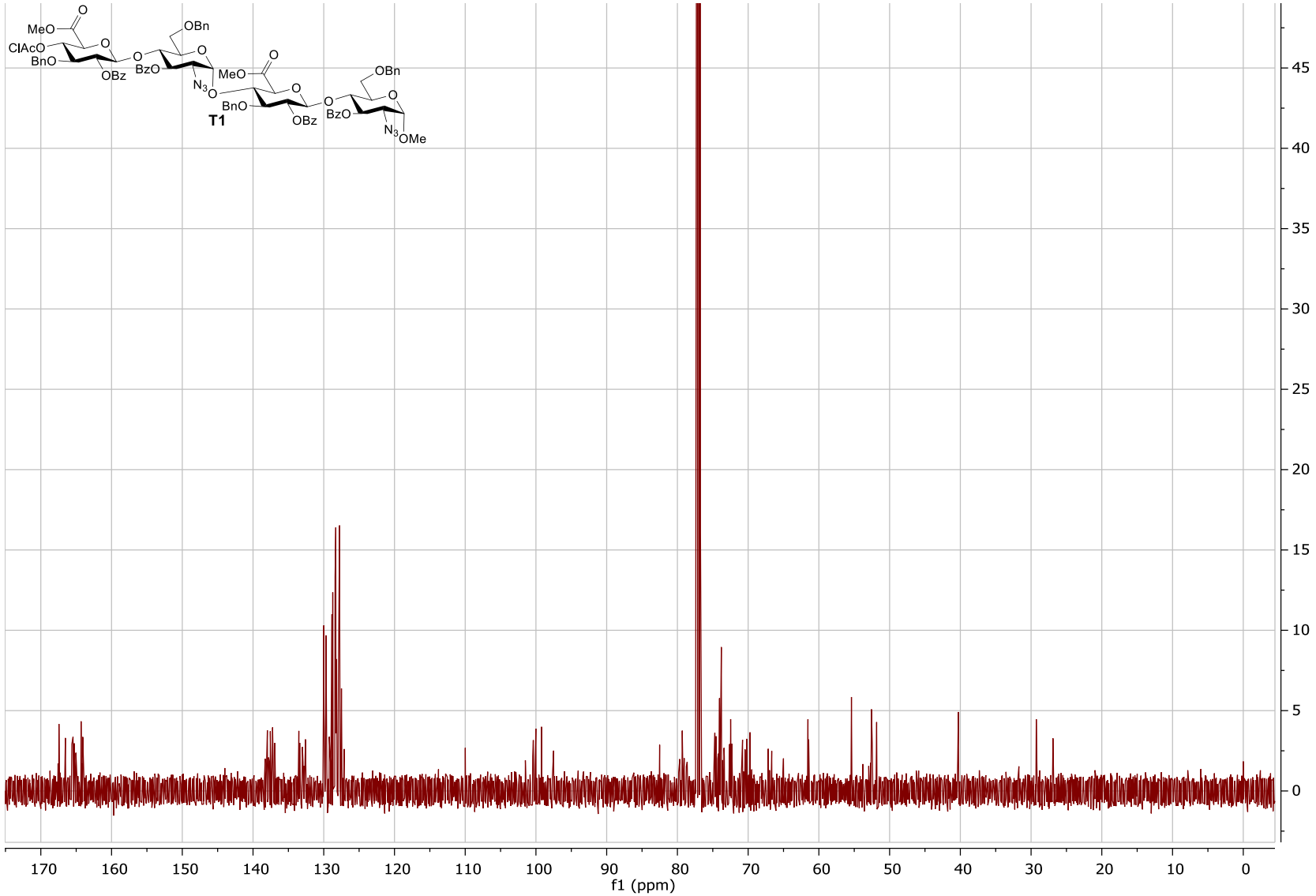

OBn
O
BnO
N3
OMe
OBn
O
O
O
OBz
NAP
14
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
65
60
55
50
45
40
35
30
25
20
15
10
5
0

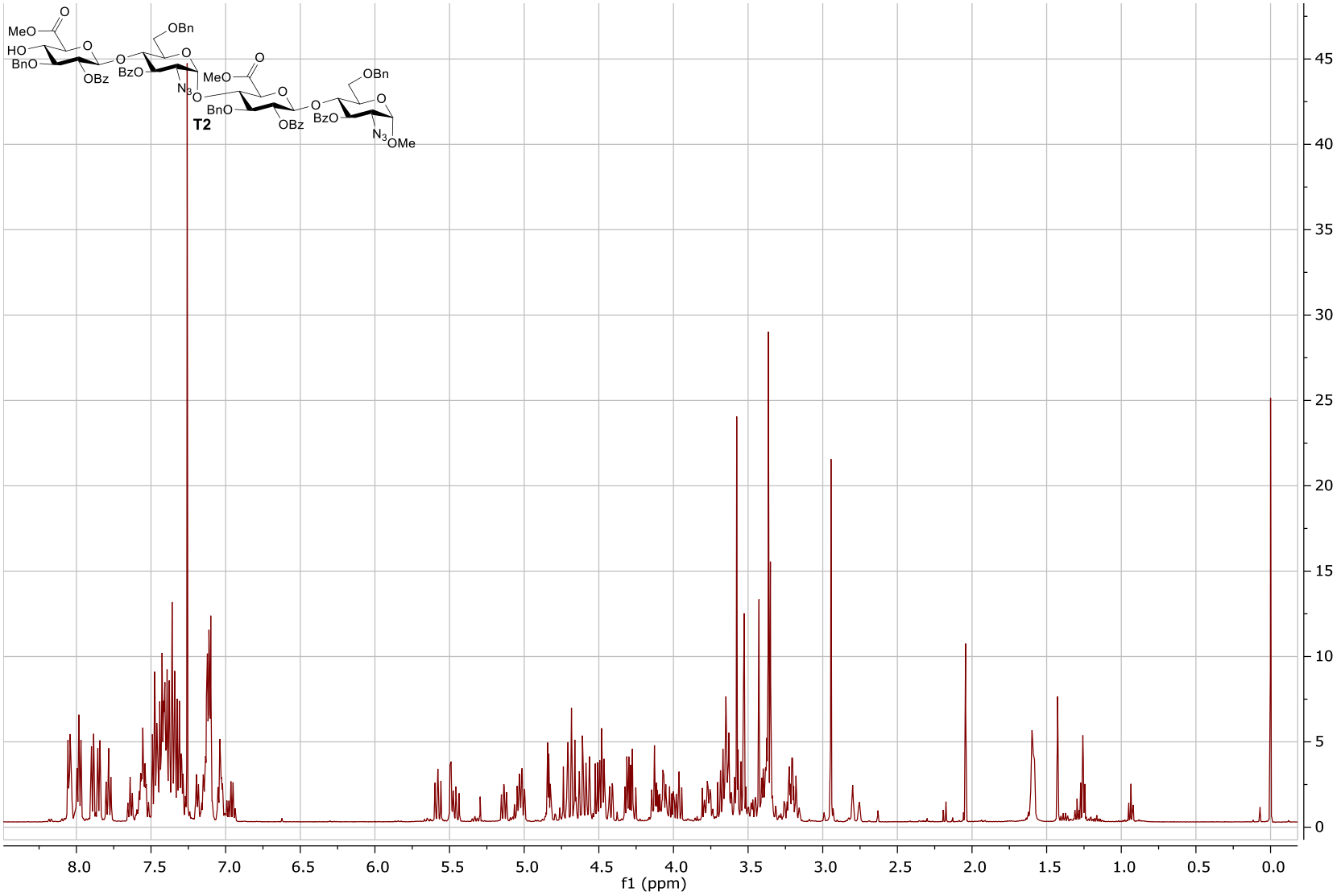

OBn
O
BnO
OBn
O
O
O
O
OBz
NAP
14
N3
OMe
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

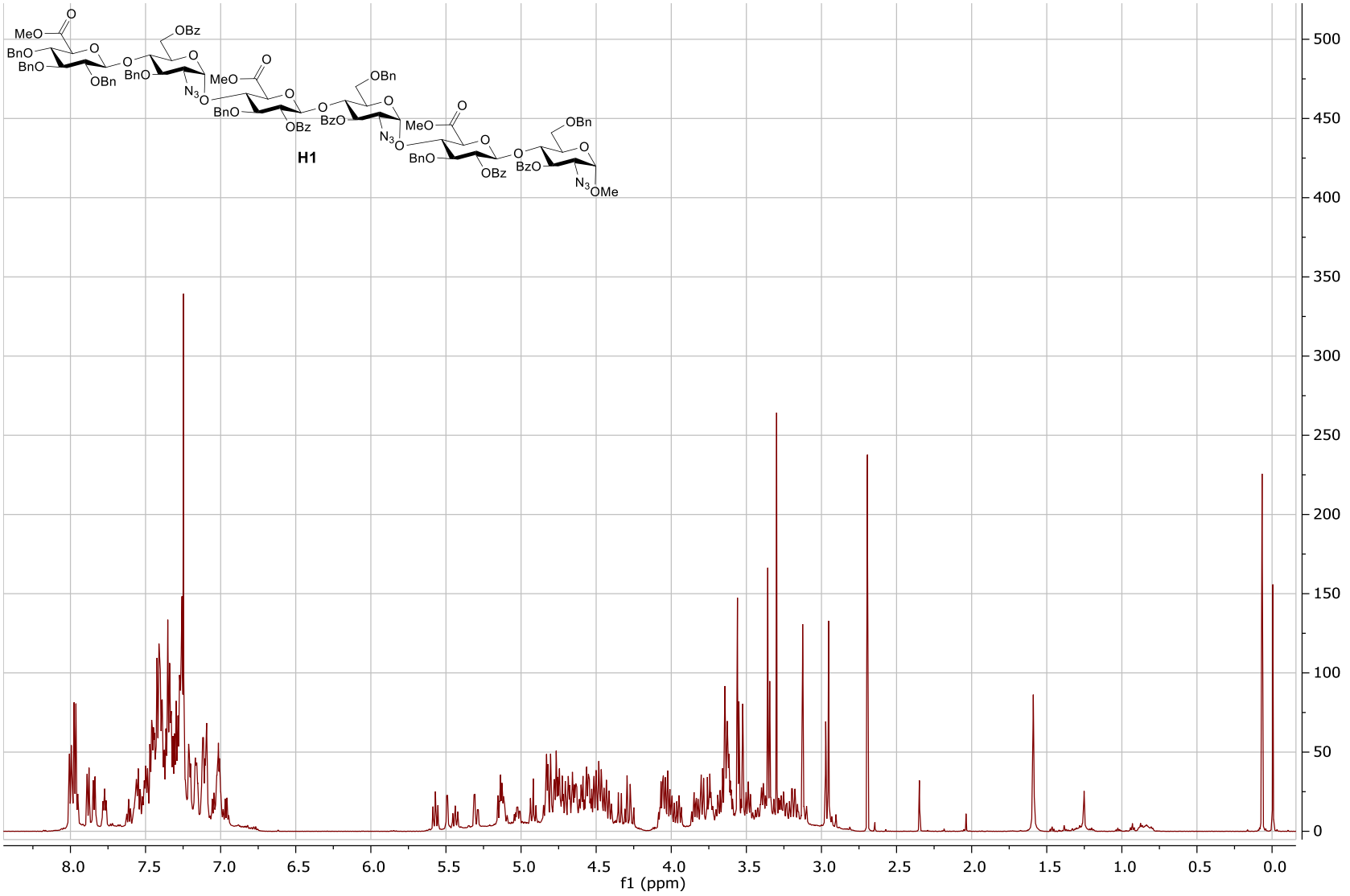

OBn
O
BnO
N3
OMe
O
OBn
MeOOC
O
OH
OBz
D10
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0

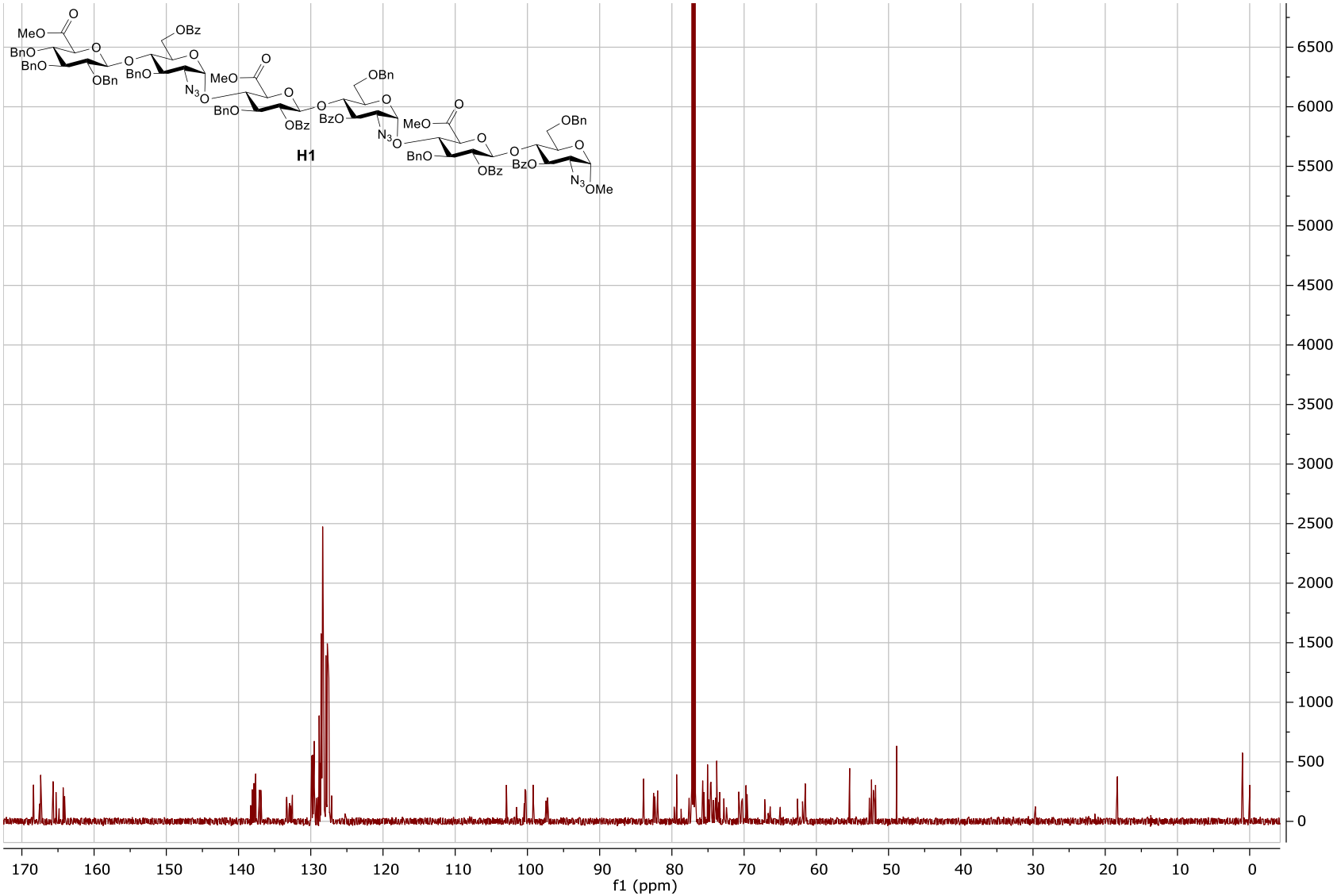

OBn
O
BnO
N3
OMe
MeOOC
OBn
O
OH
OBz
D10
130
120
110
100
90
80
70
60
50
40
30
20
10
0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

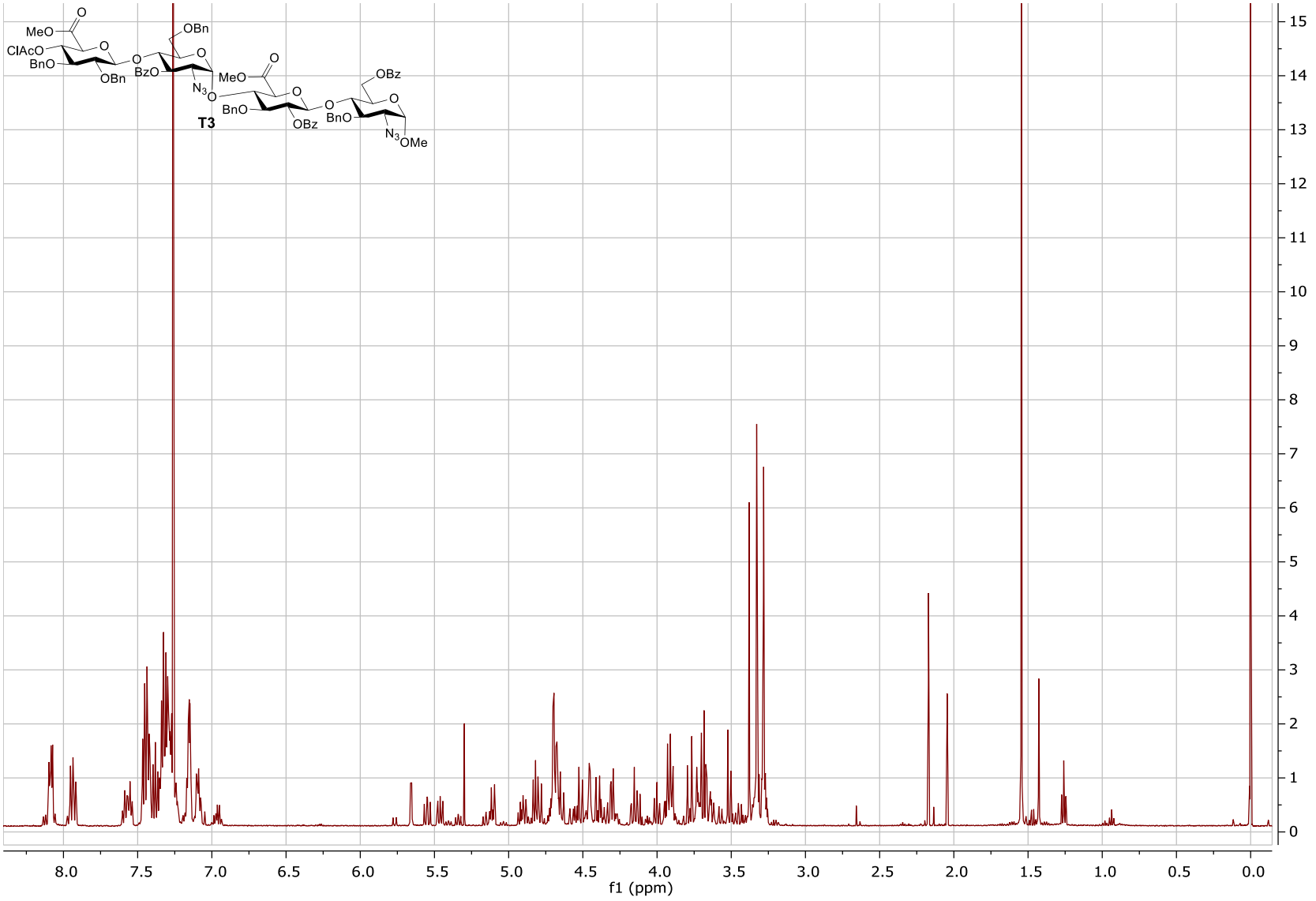

MeO
ClAcO
BnO
OBz
BzO
OBn
N3
MeO
BnO
OBz
BzO
OBn
N3
OMe
T1
90
80
70
60
50
40
30
20
10
0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

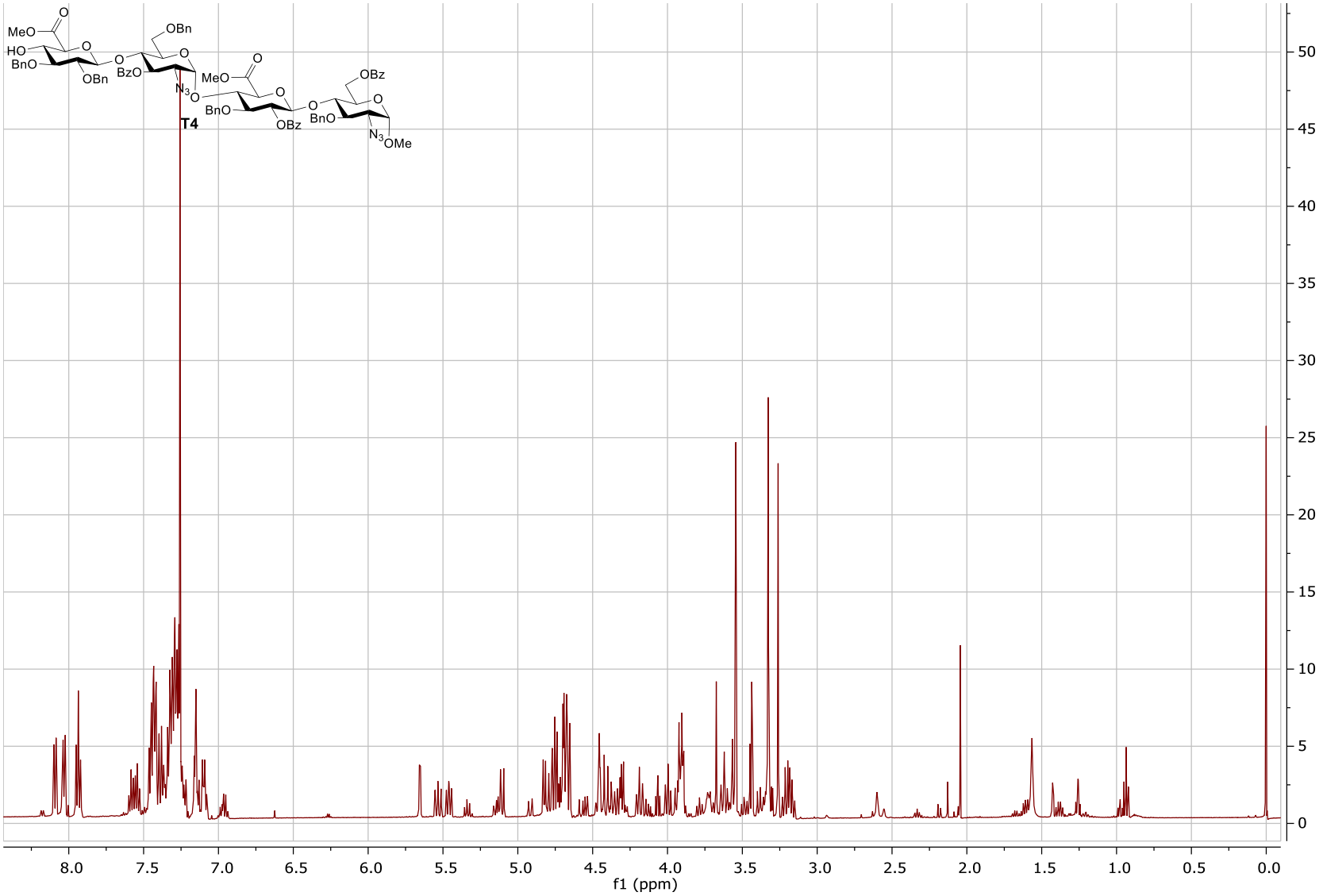

MeO
ClAcO
BnO
OBz
O
OBn
BzO
N3
MeO
BnO
OBz
BzO
OBn
N3
OMe
T1
45
40
35
30
25
20
15
10
5
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

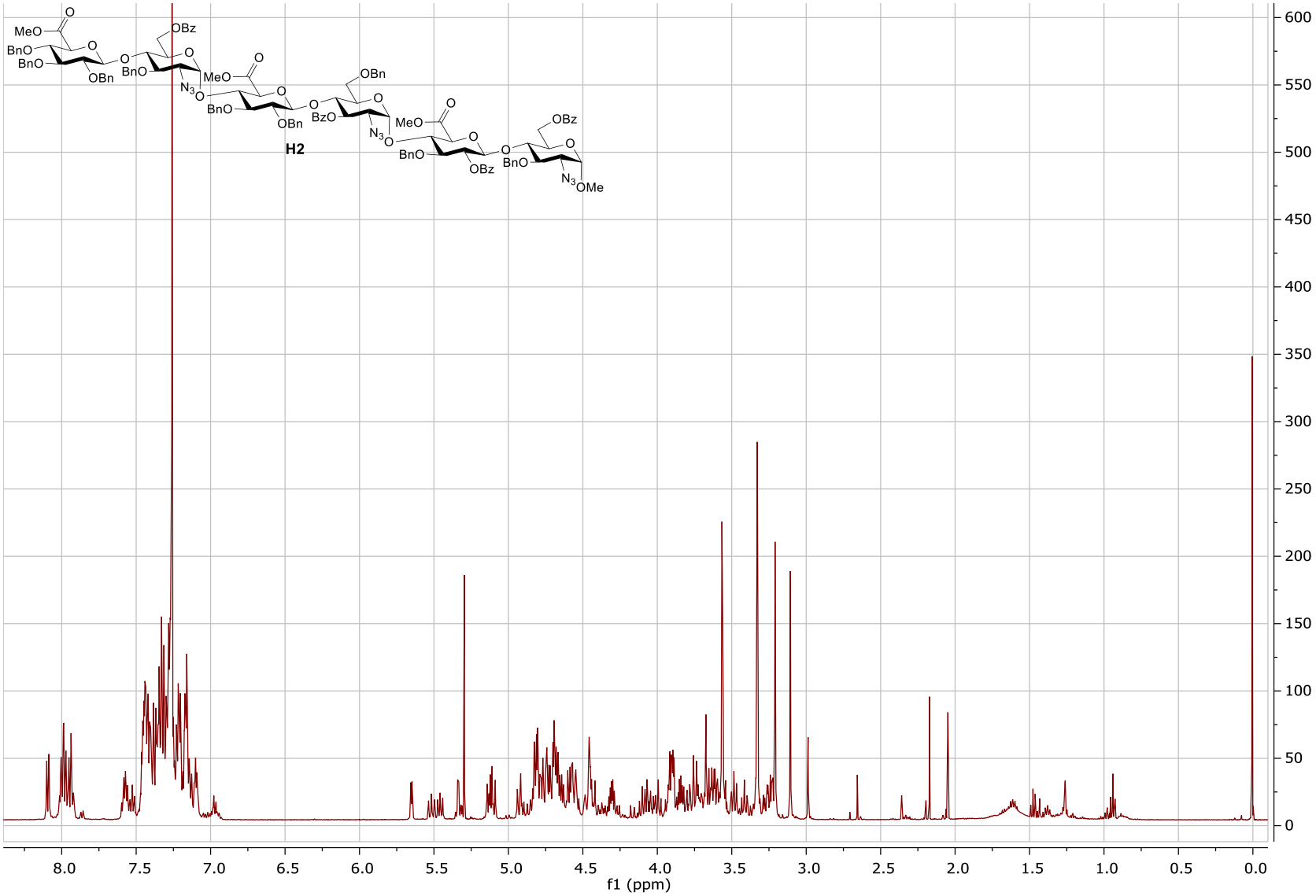

MeO
HO
BnO
OBz
O
BzO
OBn
N3
MeO
BnO
OBz
BzO
OBn
N3
OMe
T2
45
40
35
30
25
20
15
10
5
0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

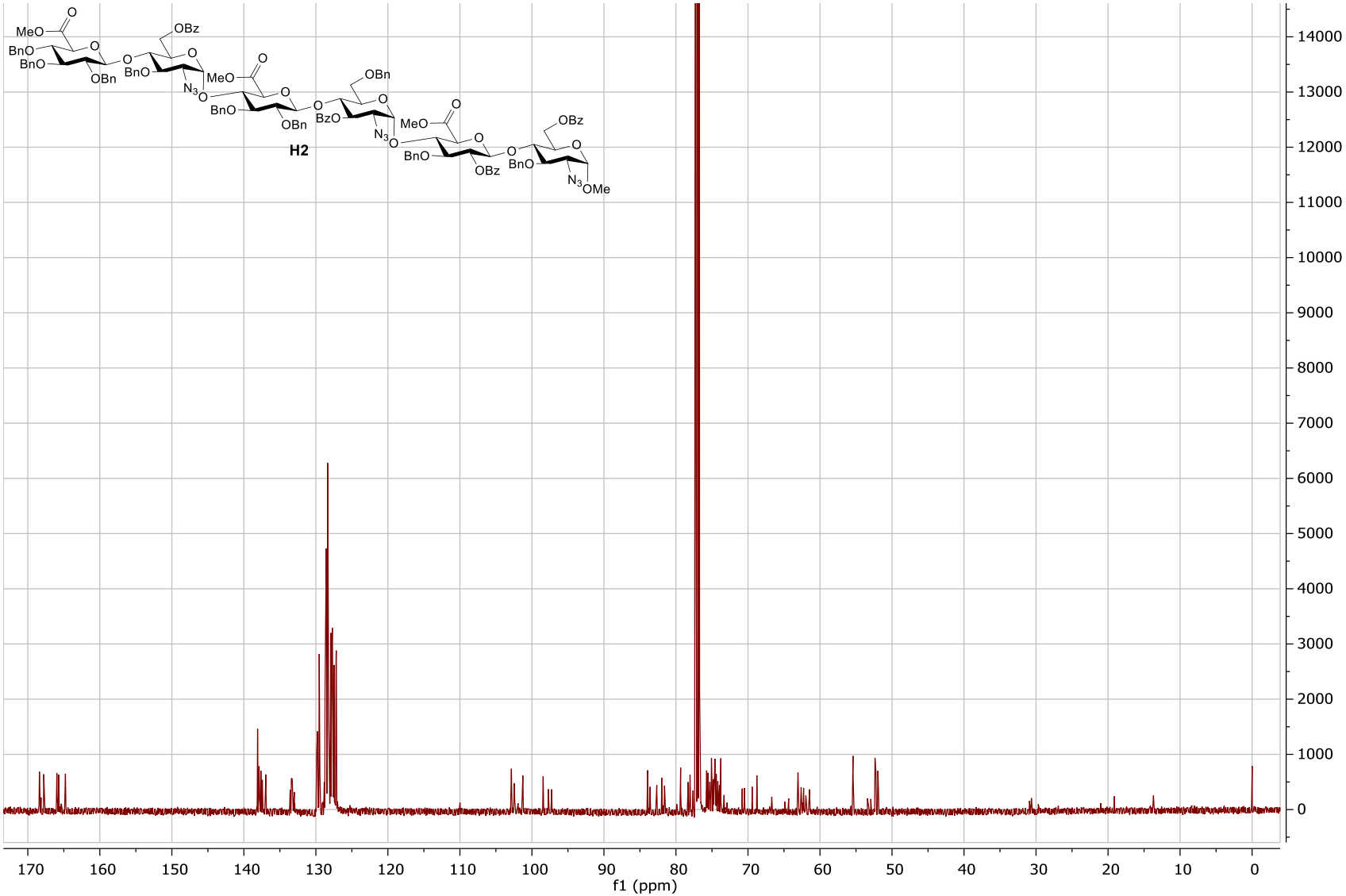

H1
f1 (ppm)

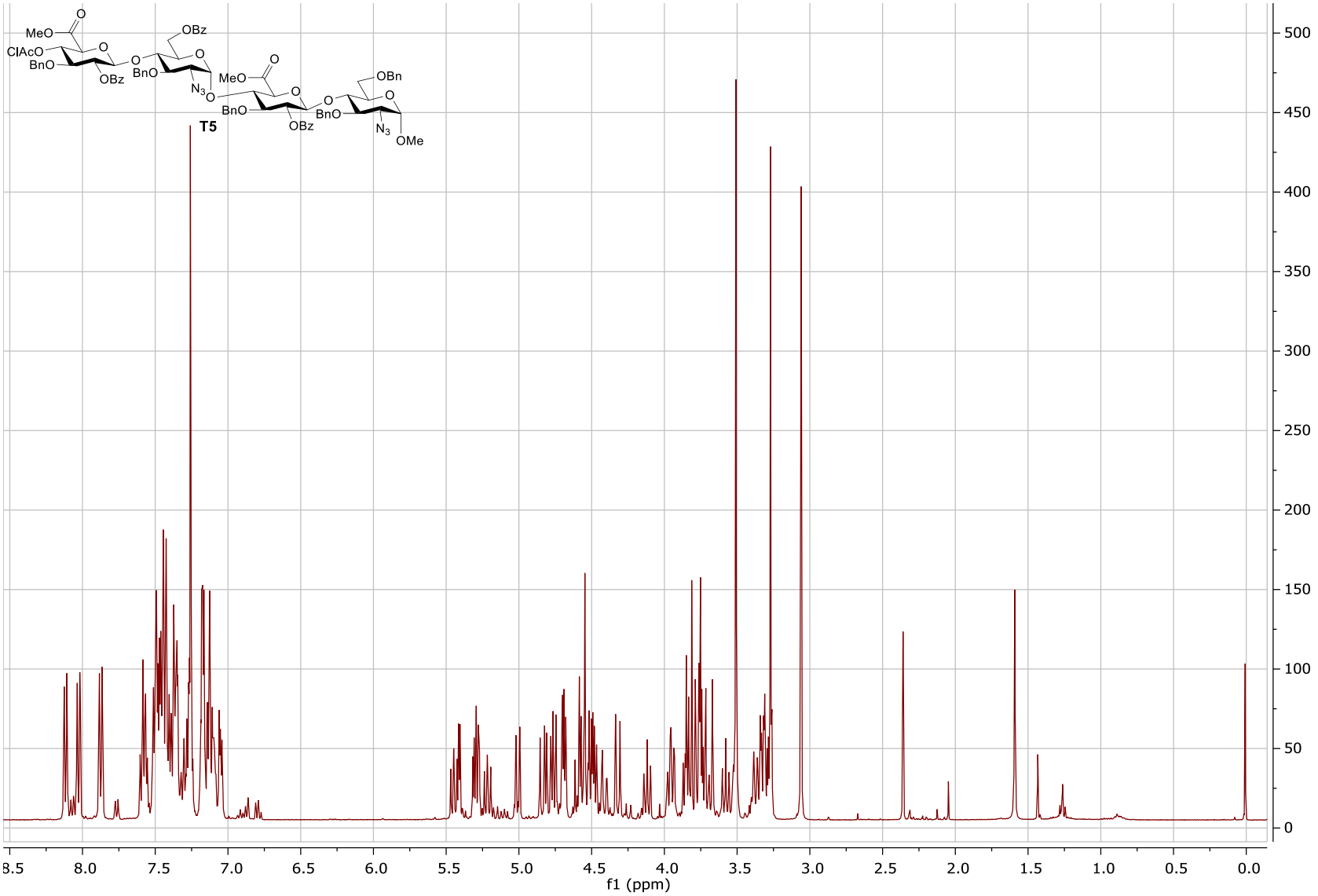

MeO
BnO
BnO
OBn
OBz
N3
OMe
BzO
H1
f1 (ppm)
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

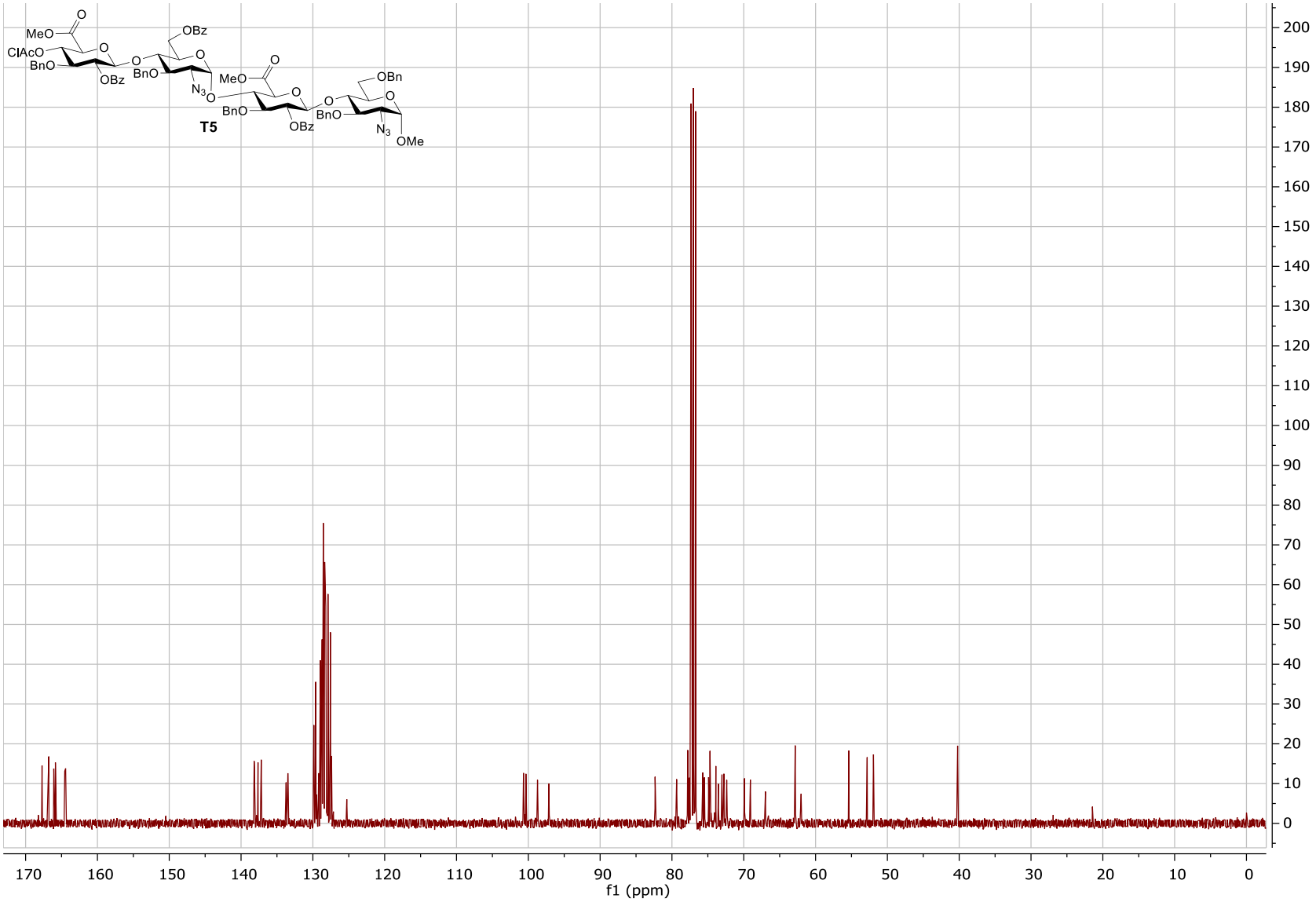

MeO
ClAcO
BnO
OBn
O
O
O
OBn
BzO
O
N3
O
MeO
O
O
BnO
OBz
O
O
BnO
OBz
N3
OMe
T3
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

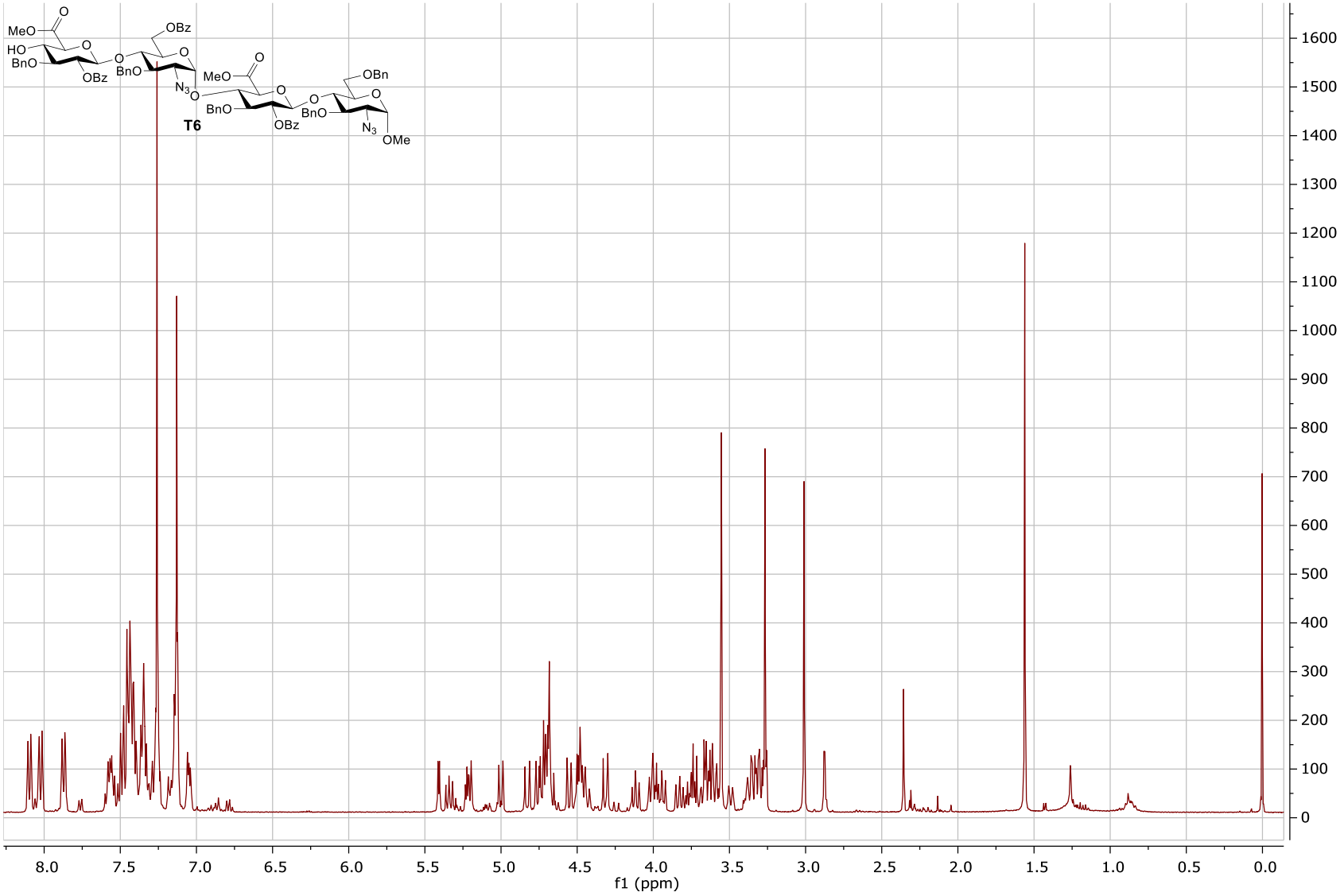

MeO
HO
BnO
OBn
O
OBn
BzO
N3
MeO
BnO
OBz
OBz
BnO
N3
OMe
T4
50
45
40
35
30
25
20
15
10
5
0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

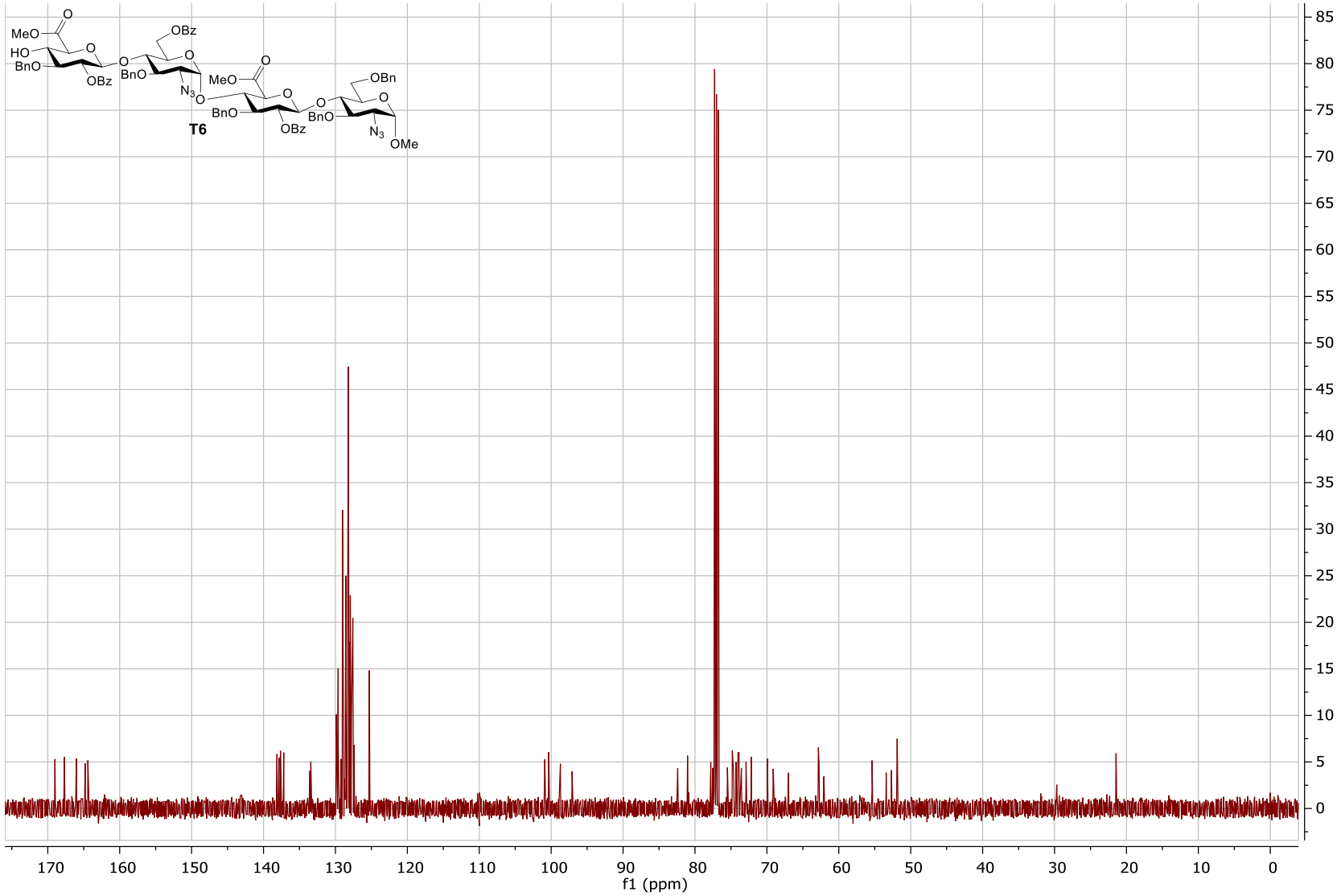

H2
f1 (ppm)

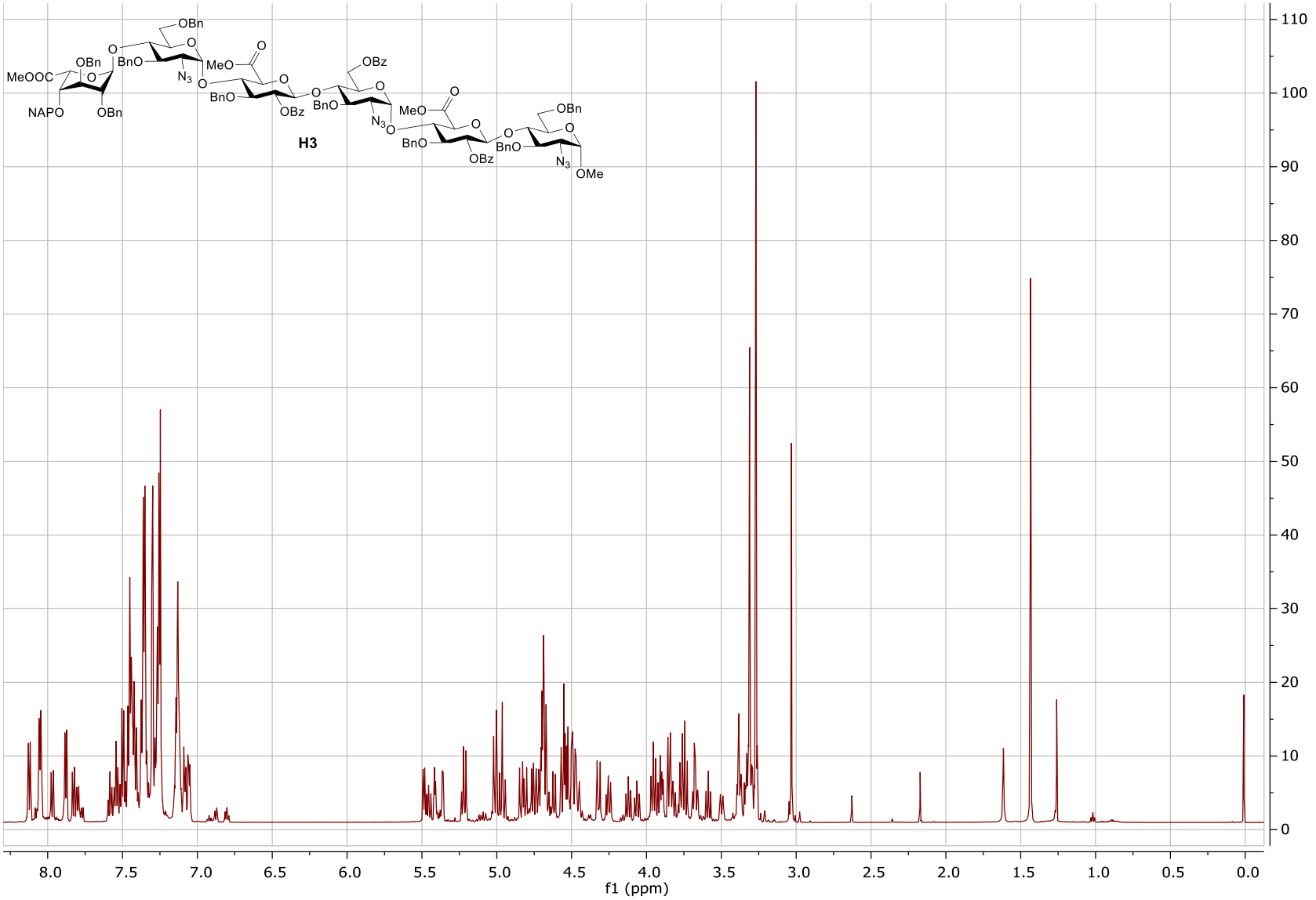

MeO
BnO
BnO
OBn
OBz
BnO
N3
MeO
BnO
OBn
BzO
OBn
MeO
BnO
OBz
BnO
OBz
N3
OMe
H2
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

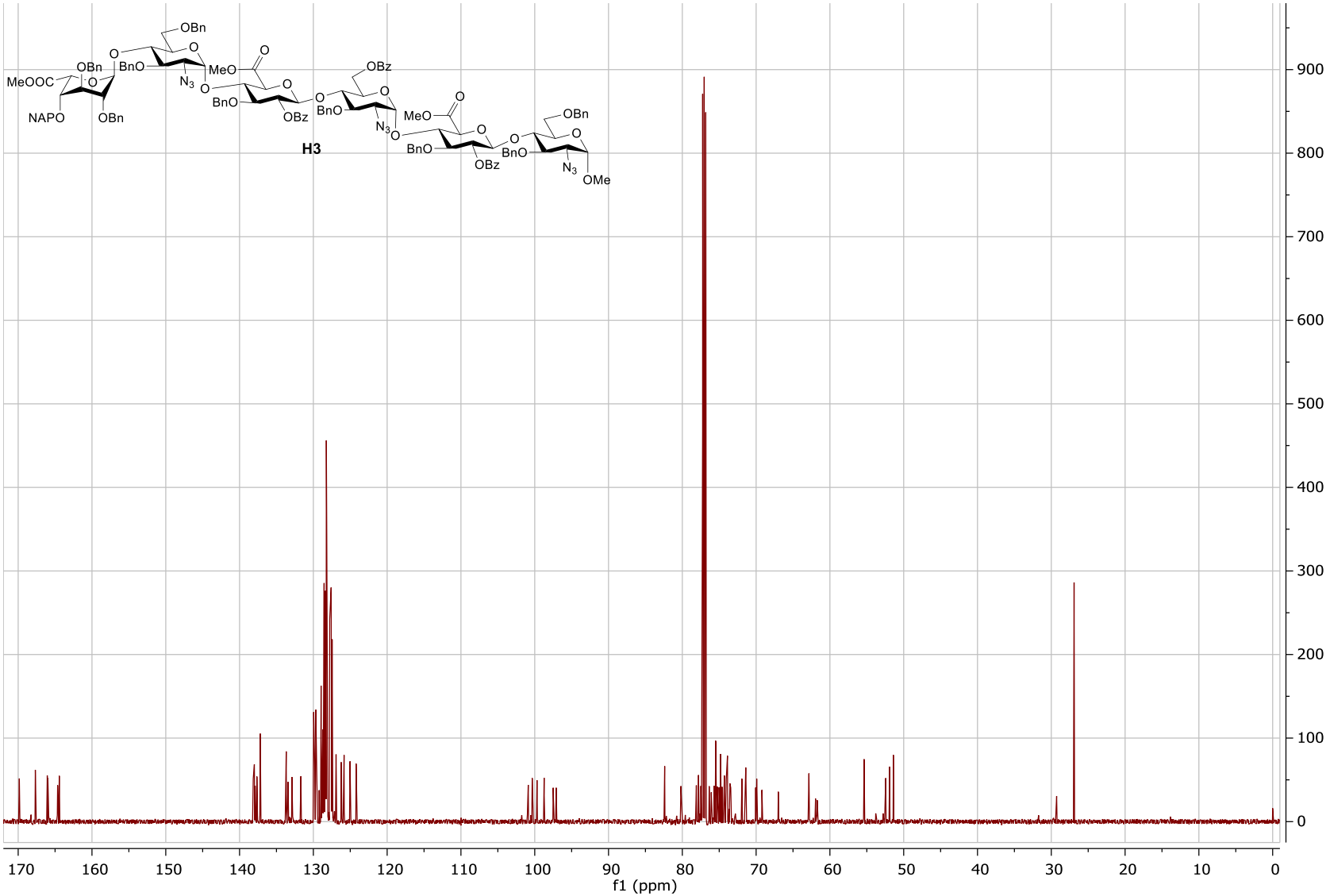

MeO
ClAcO
BnO
OBz
BnO
OBz
N3
MeO
BnO
OBz
BnO
OBn
N3
OMe
T5
500
450
400
350
300
250
200
150
100
50
0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

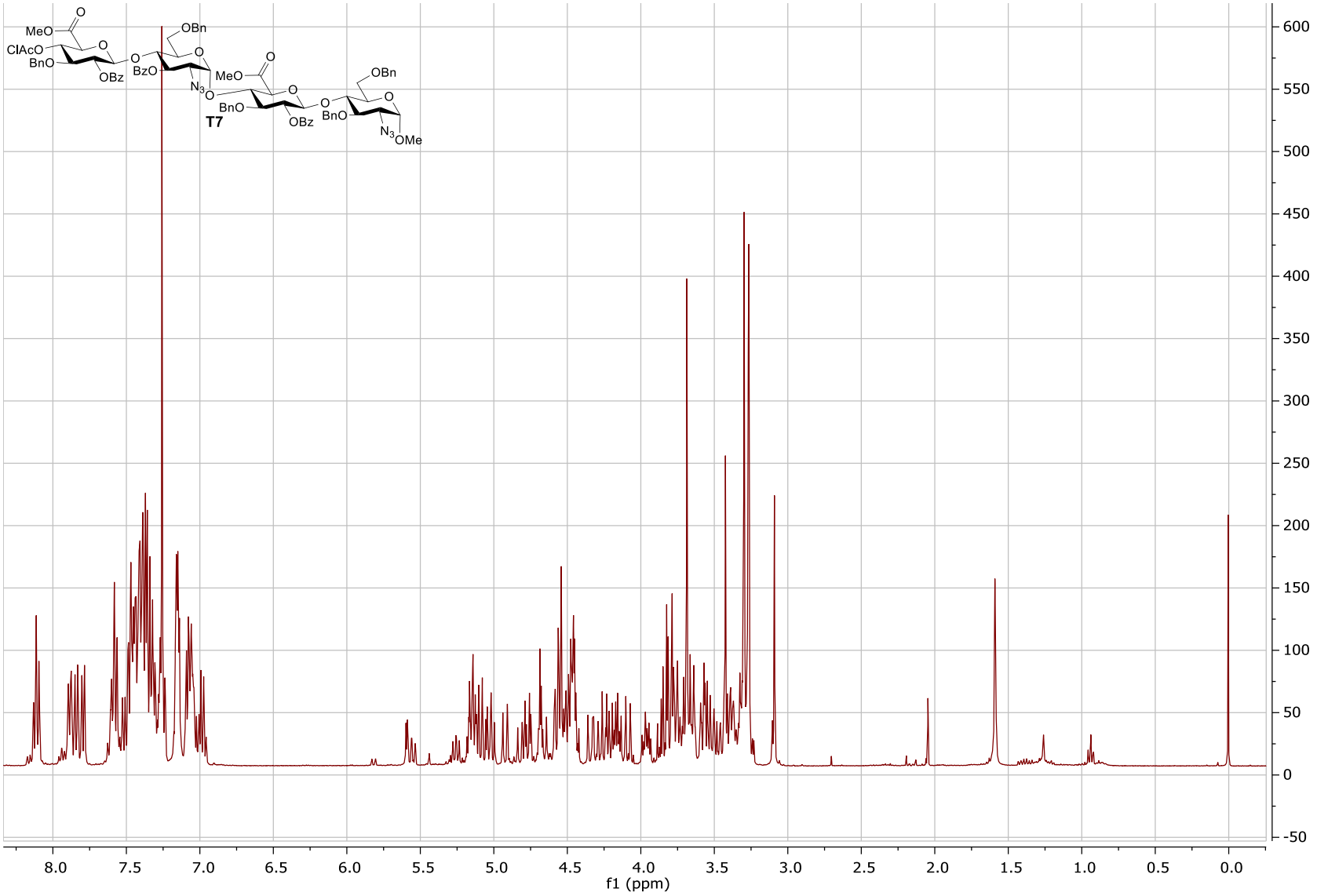

MeO
ClAcO
BnO
OBz
OBz
BnO
N3
MeO
BnO
OBz
BnO
OBn
N3
OMe
T5
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

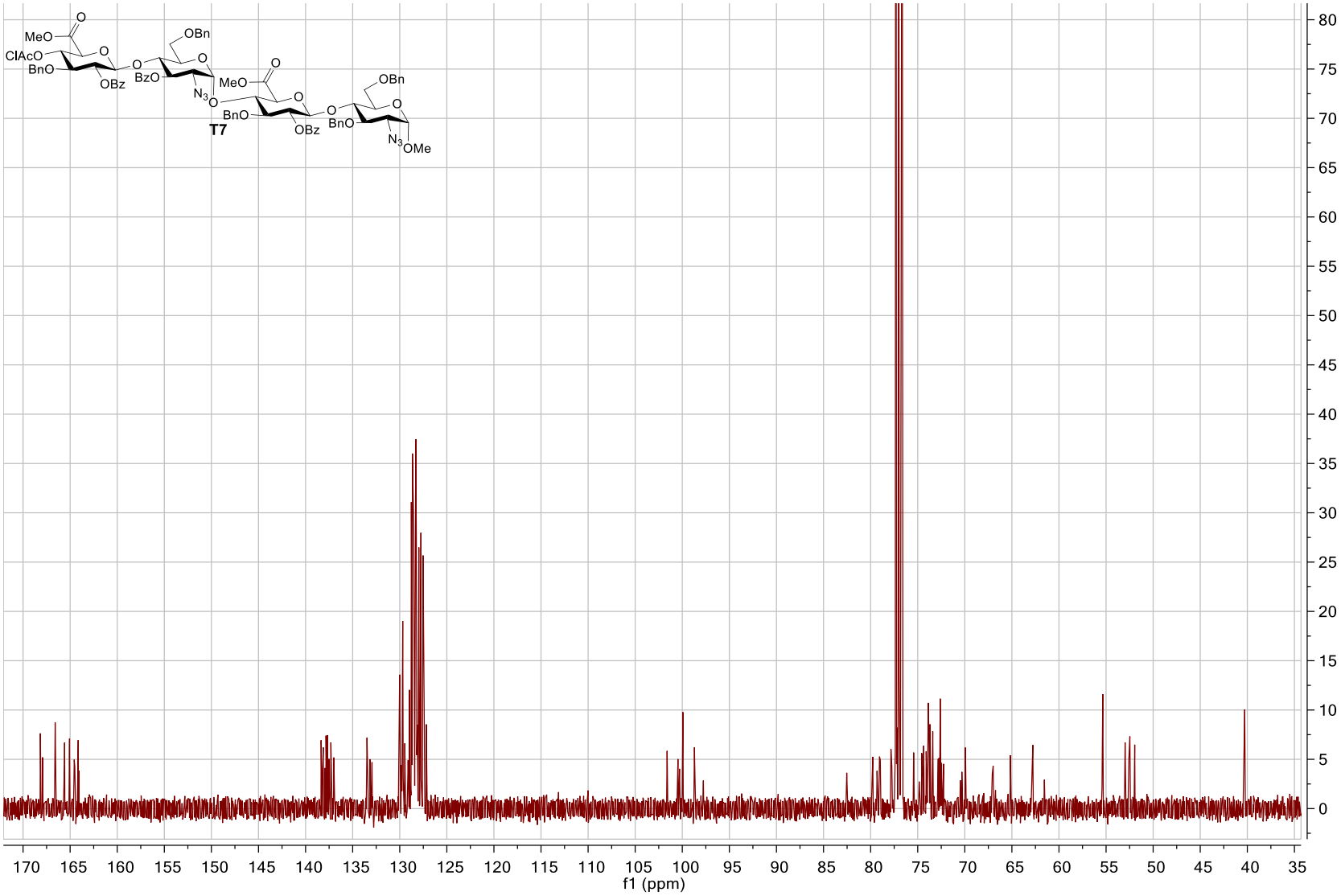

MeO
HO
BnO
OBz
BnO
OBz
N3
MeO
BnO
OBz
BnO
OBn
N3
OMe
T6
1600
1500
1400
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

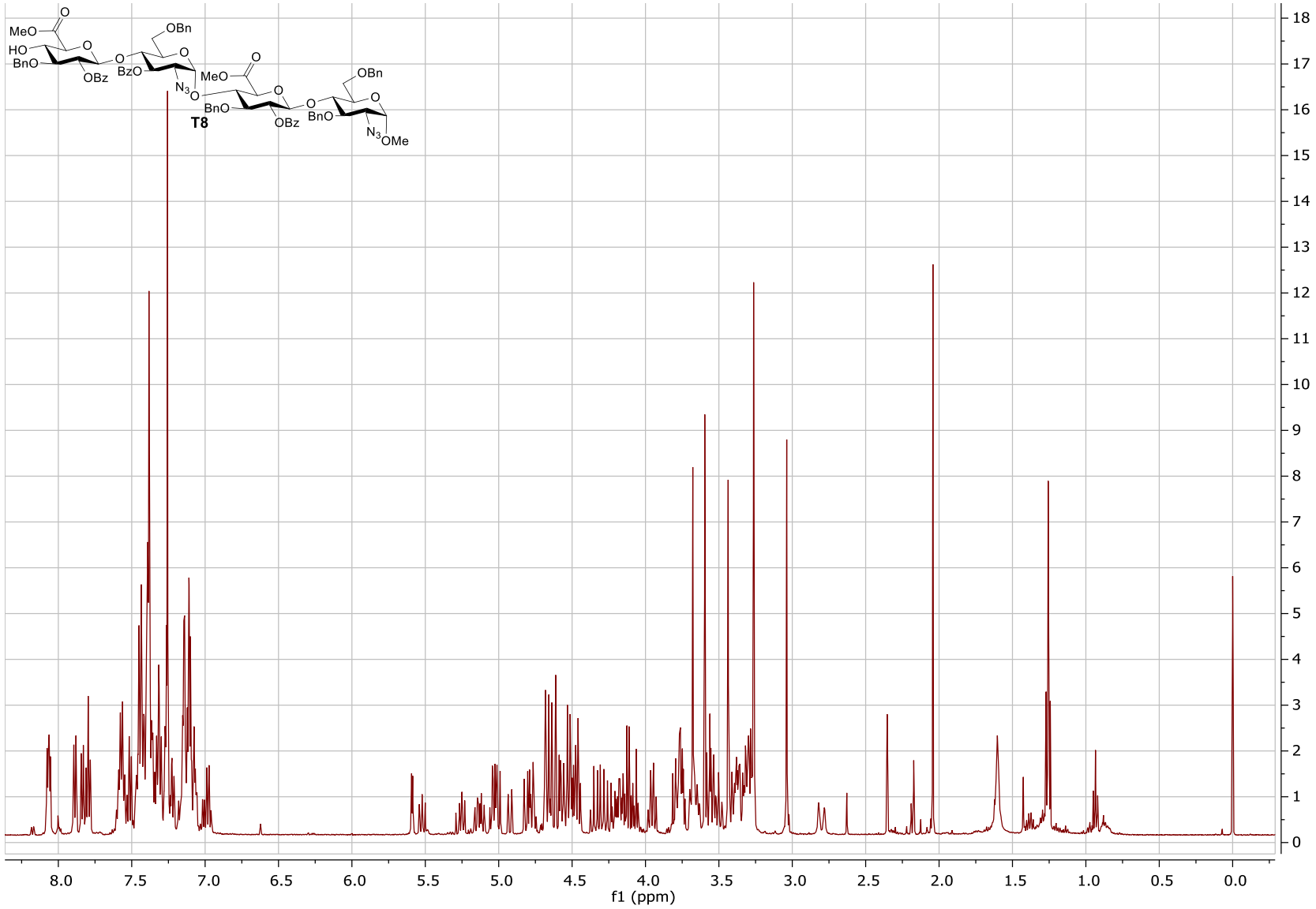

MeO
HO
BnO
OBz
O
BnO
OBz
N3
MeO
BnO
OBz
BnO
OBn
N3
OMe
T6
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

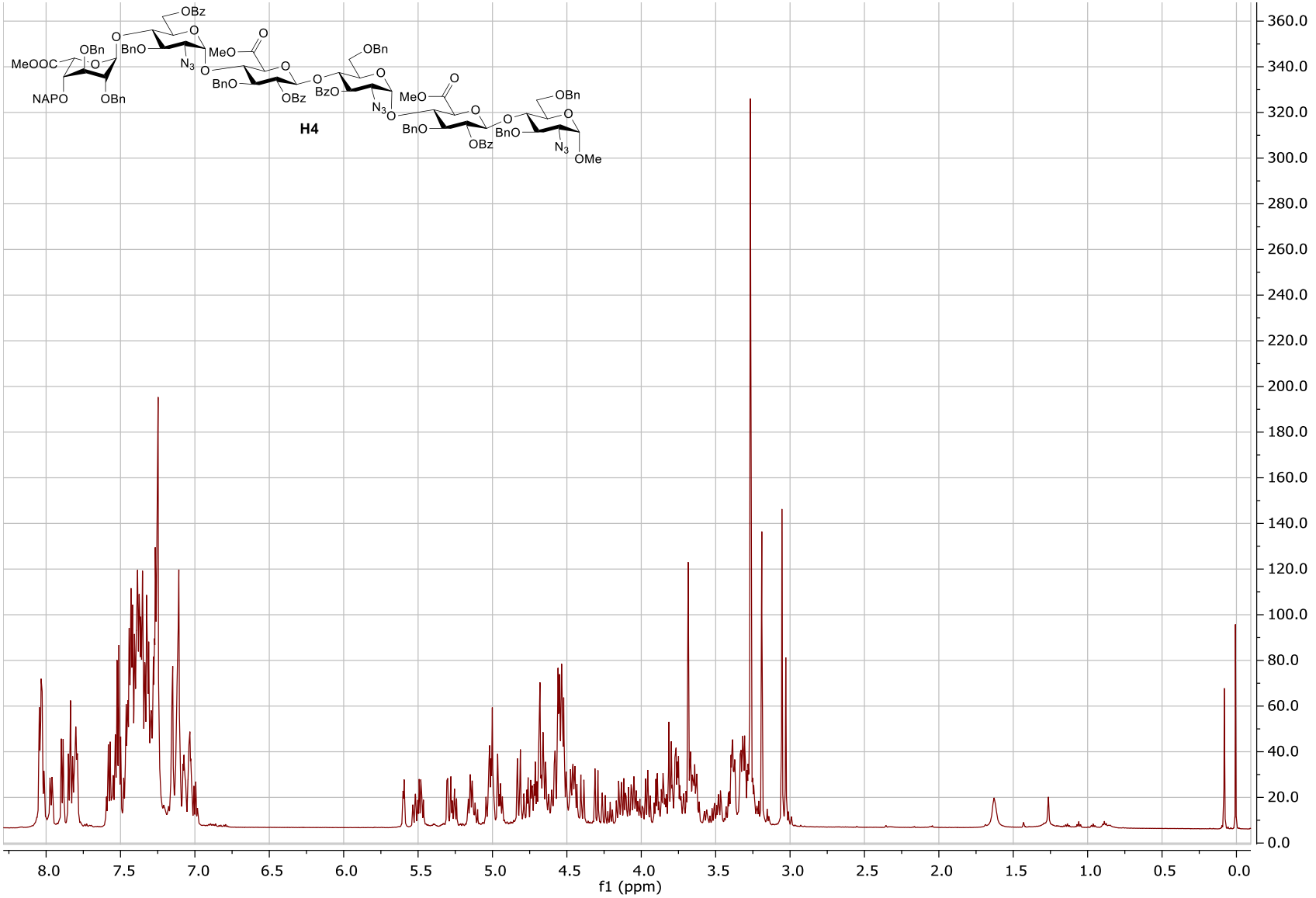

OBn
MeOOC
OBn
BnO
MeO
NAPO
OBn
OBz
BnO
OBz
H3
MeO
OBn
BnO
OBz
OMe
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
110
100
90
80
70
60
50
40
30
20
10
0

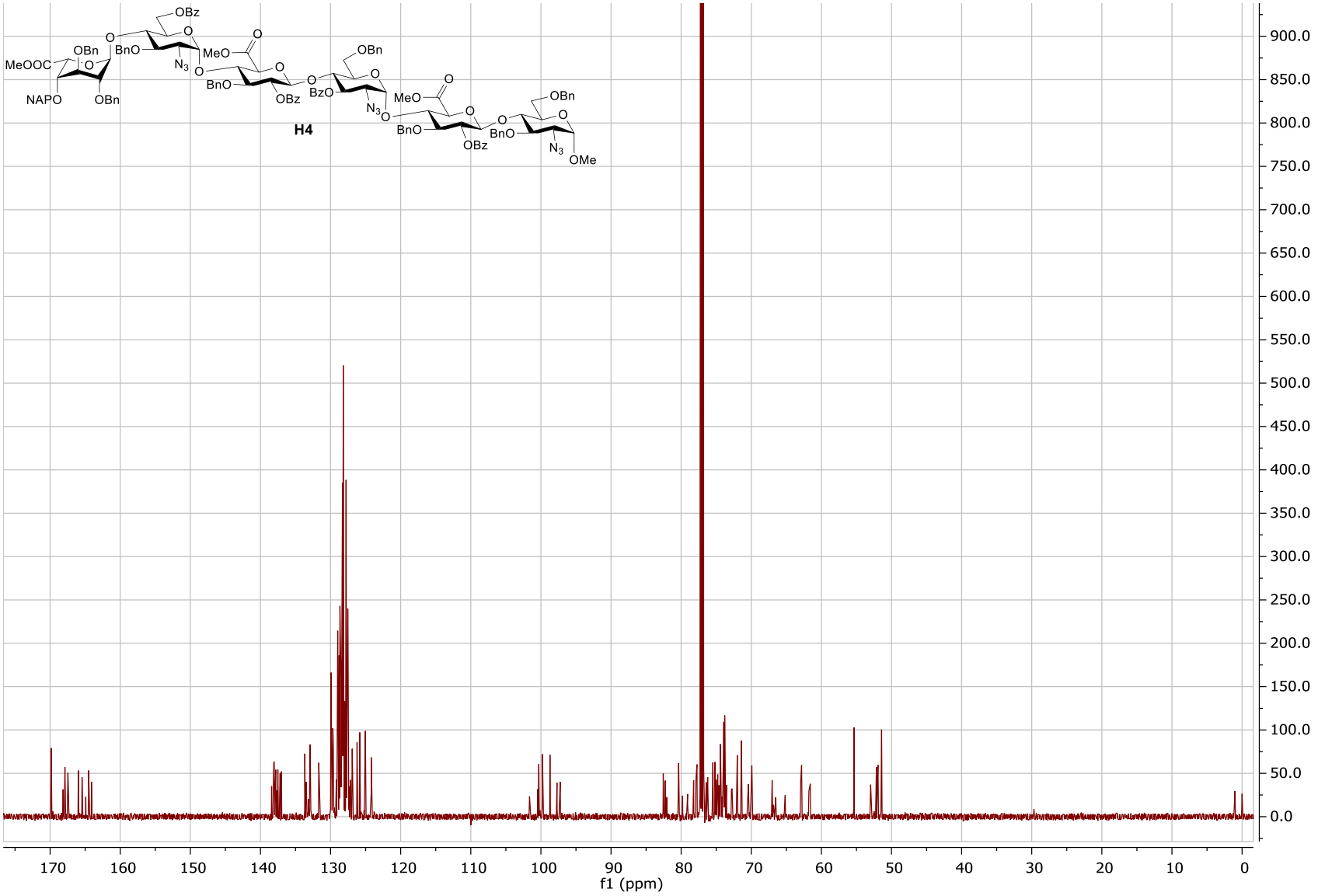

OBn
MeOOC
OBn
BnO
MeO
N3
NAPO
OBn
OBz
BnO
OBz
H3
OBz
BnO
MeO
N3
BnO
OBz
OBn
BnO
N3
OMe
900
800
700
600
500
400
300
200
100
0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

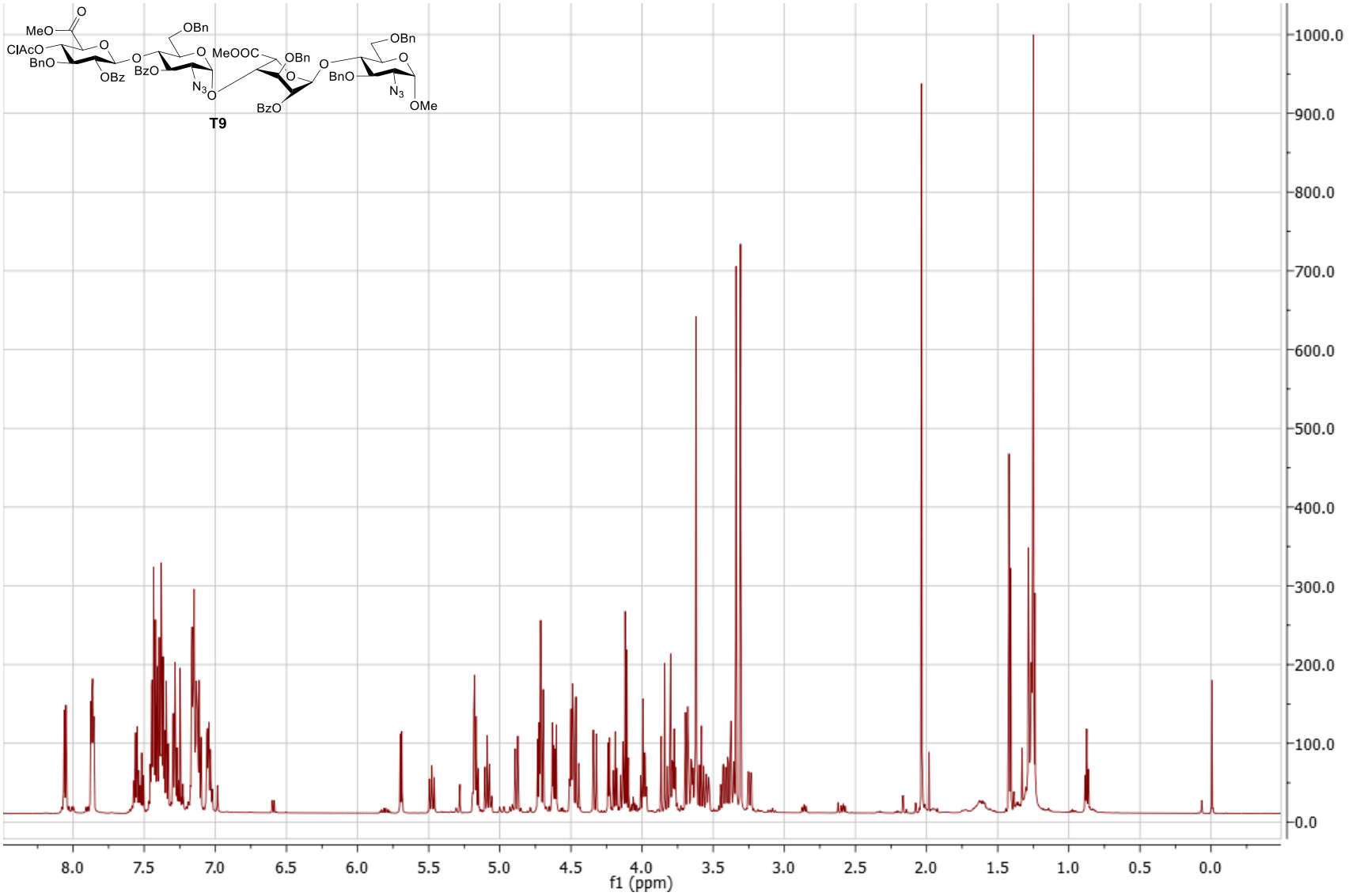

MeO
ClAcO
BnO
OBz
BzO
OBn
N3
MeO
BnO
OBz
BnO
OBn
N3
OMe
T7
600
550
500
450
400
350
300
250
200
150
100
50
0
-50
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

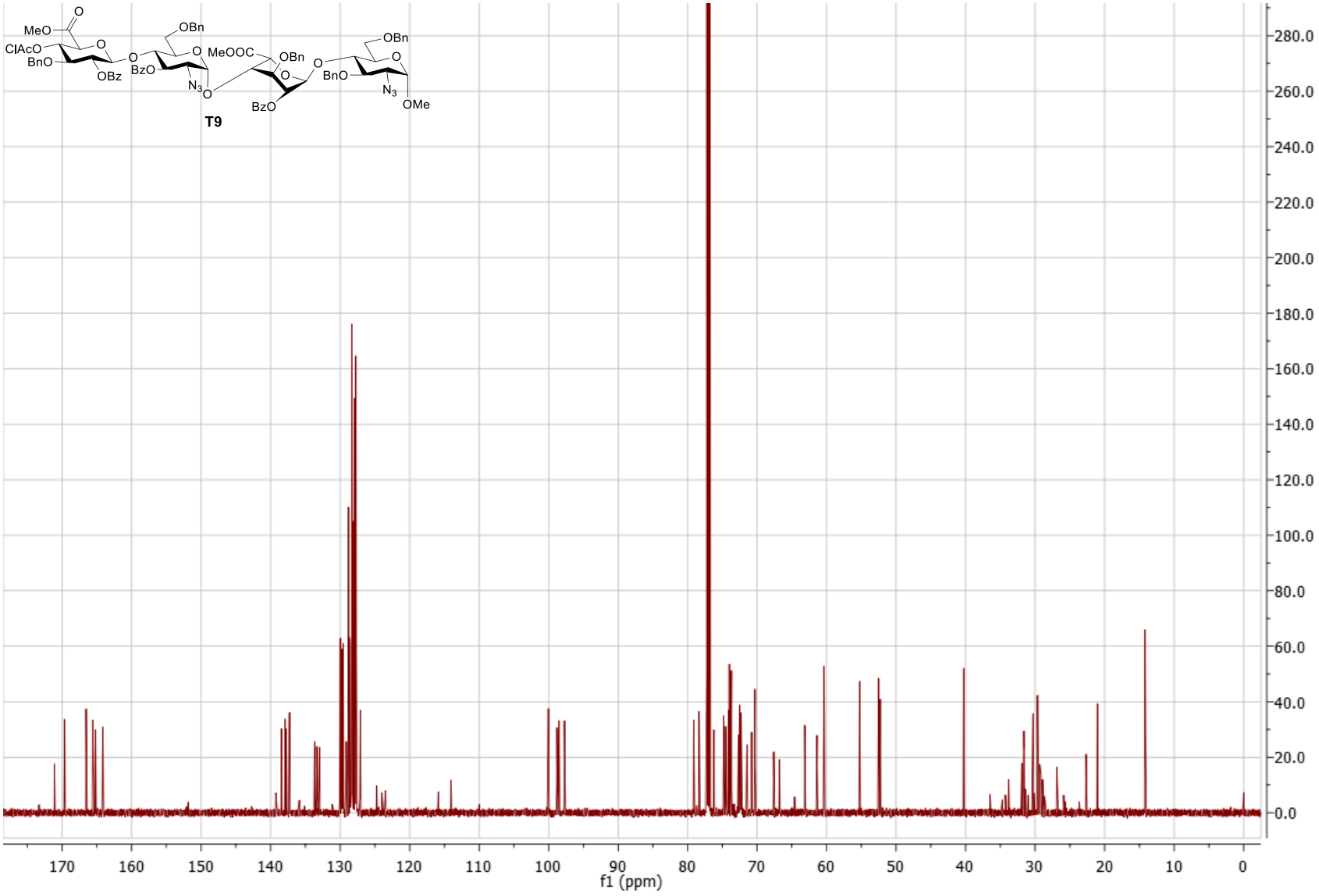

MeO
ClAcO
BnO
OBz
BzO
OBn
N3
MeO
BnO
OBz
OBn
BnO
N3
OMe
T7
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35
f1 (ppm)

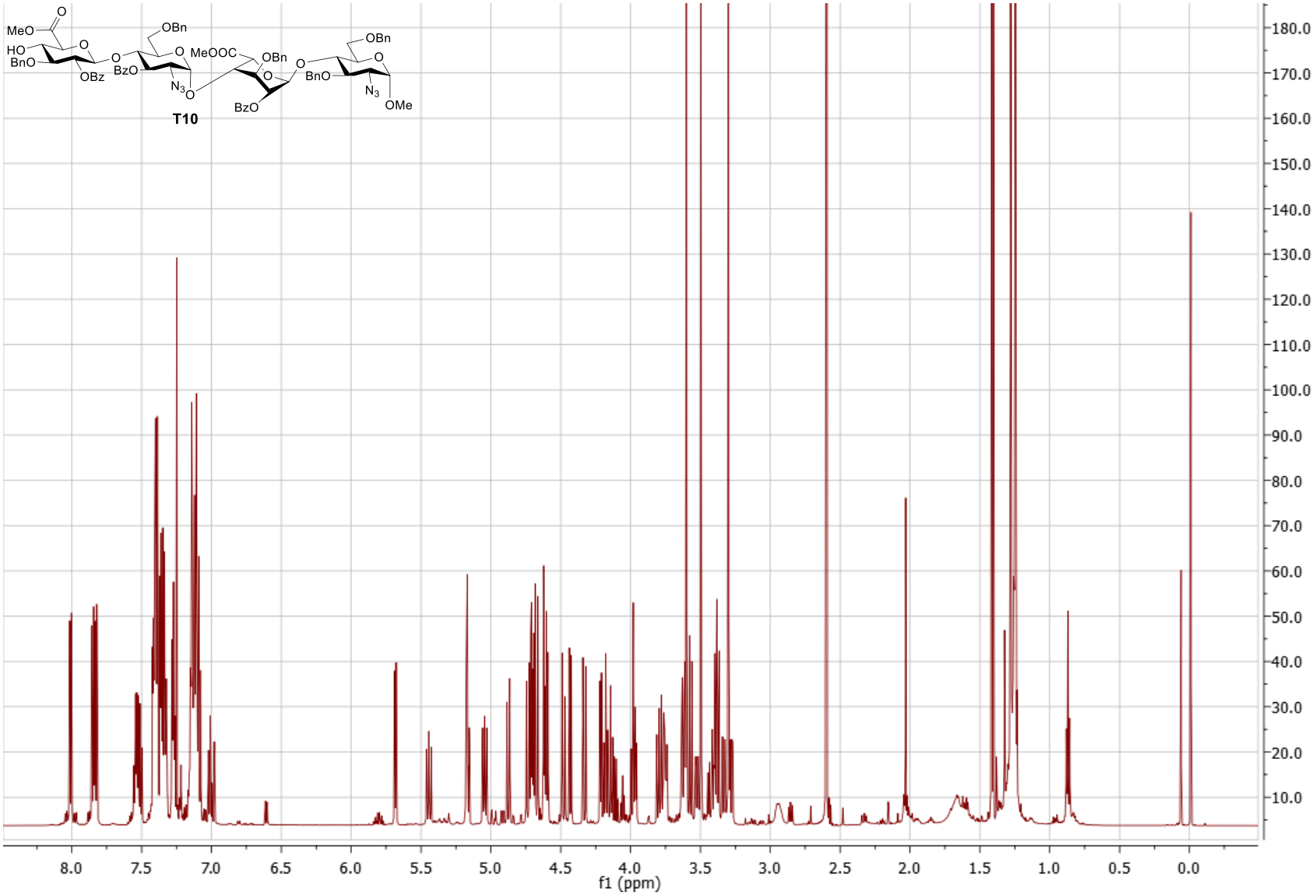

MeO
HO
BnO
OBz
BzO
OBn
N3
MeO
BnO
OBz
BnO
OBn
N3
OMe
T8
18
17
16
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

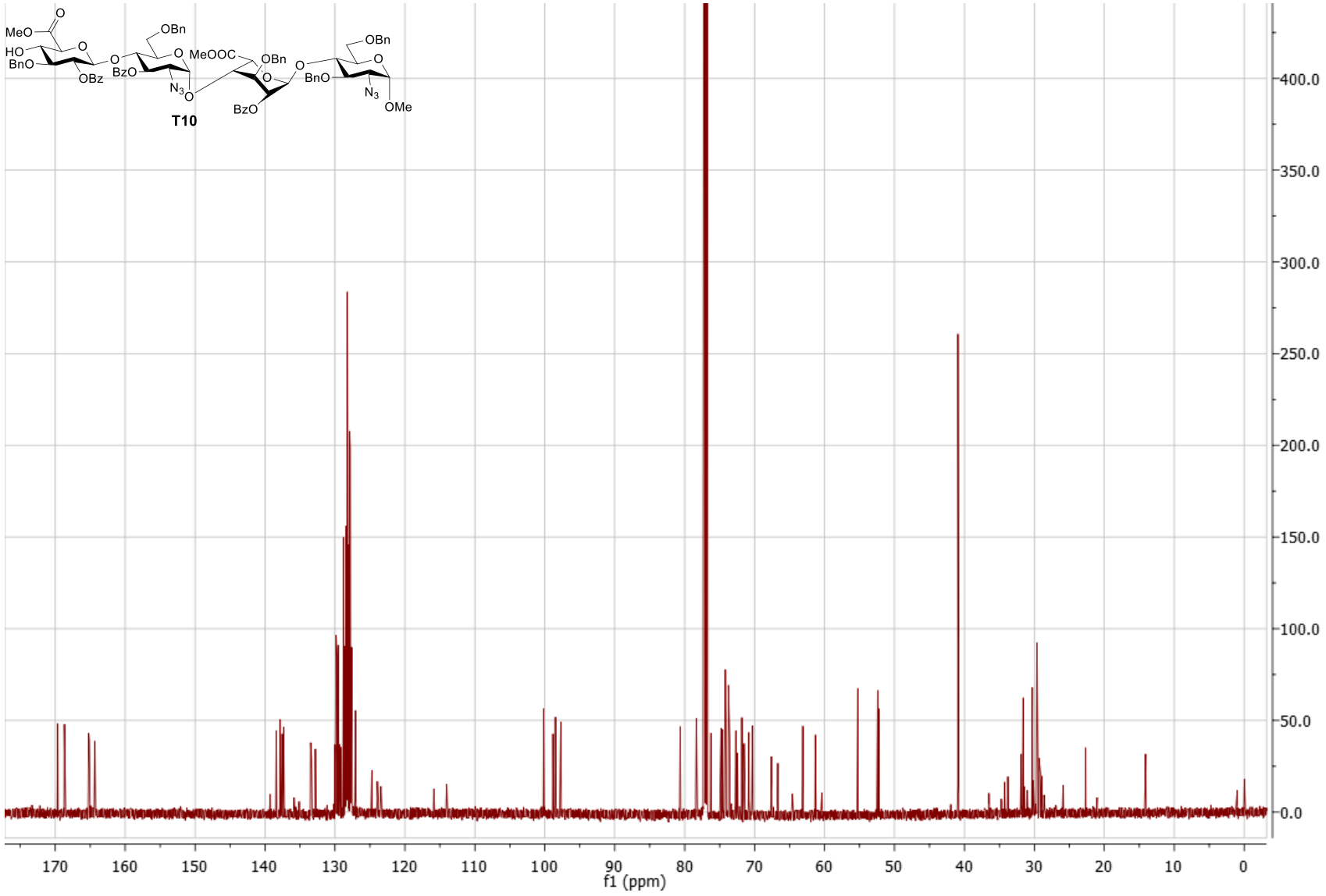

OBz
OBn
BnO
MeO
MeOOC
NAPO
OBn
BnO
OBz
BzO
OBn
MeO
BnO
OBz
BnO
OBn
OMe
H4
f1 (ppm)

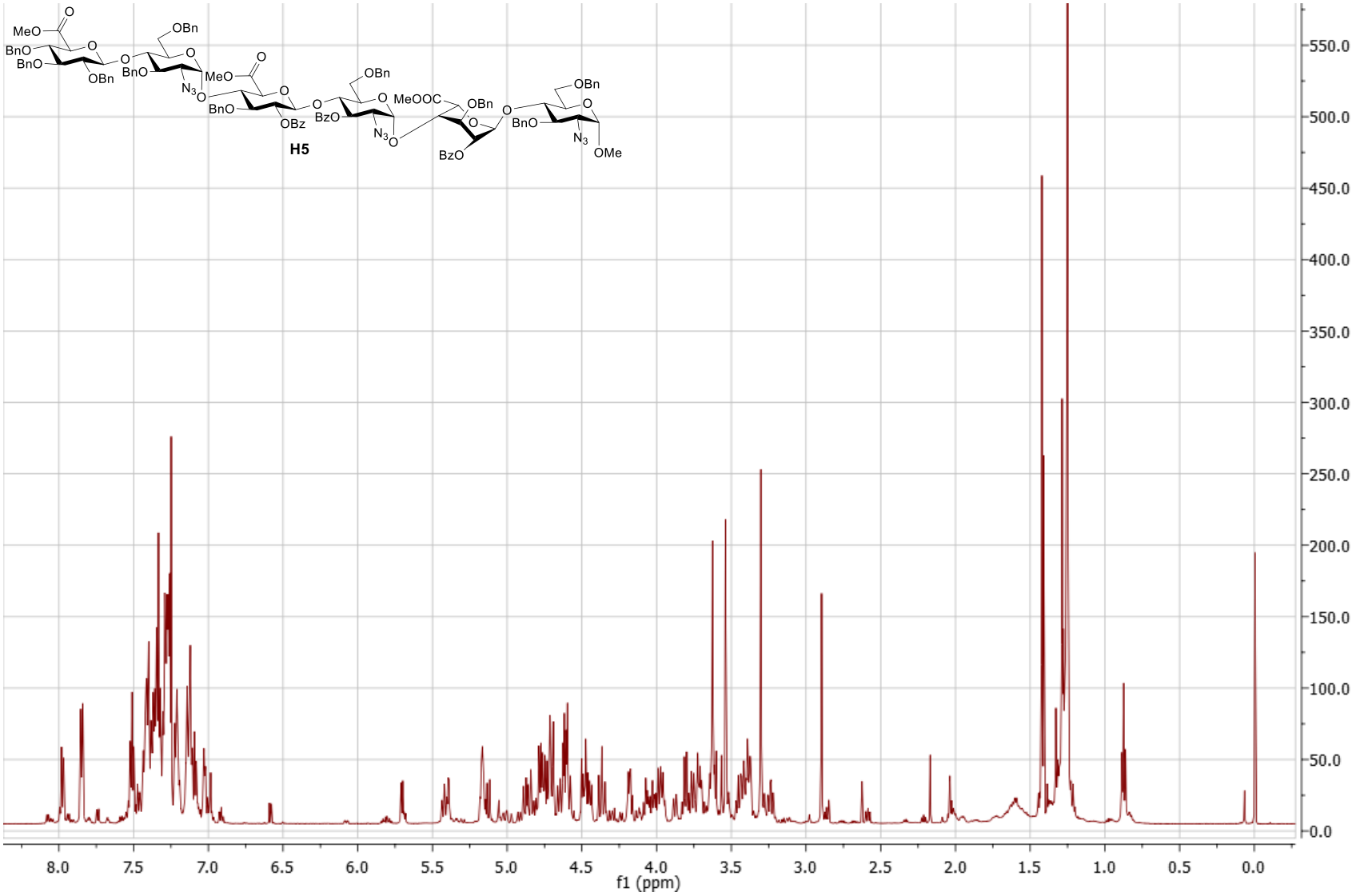

OBz
OBn
BnO
MeO
MeOOC
NAPO
OBn
BnO
OBz
BzO
OBn
MeO
BnO
OBz
BnO
OBn
OMe
H4
900.0
850.0
800.0
750.0
700.0
650.0
600.0
550.0
500.0
450.0
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

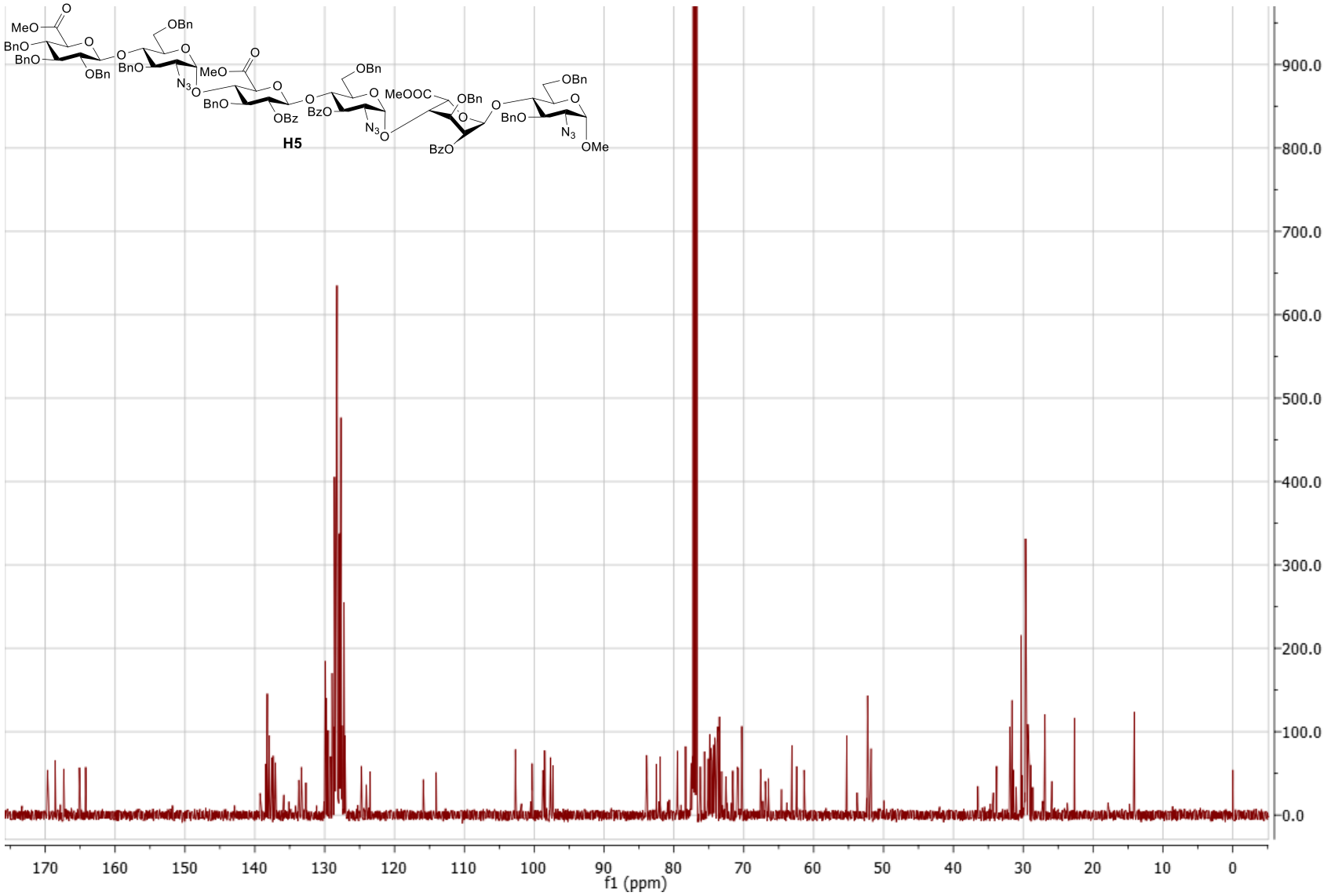

MeO
ClAcO
BnO
OBz
O
OBn
BzO
N3
MeOOC
OBn
BzO
BnO
OBn
N3
OMe
T9
1000.0
900.0
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

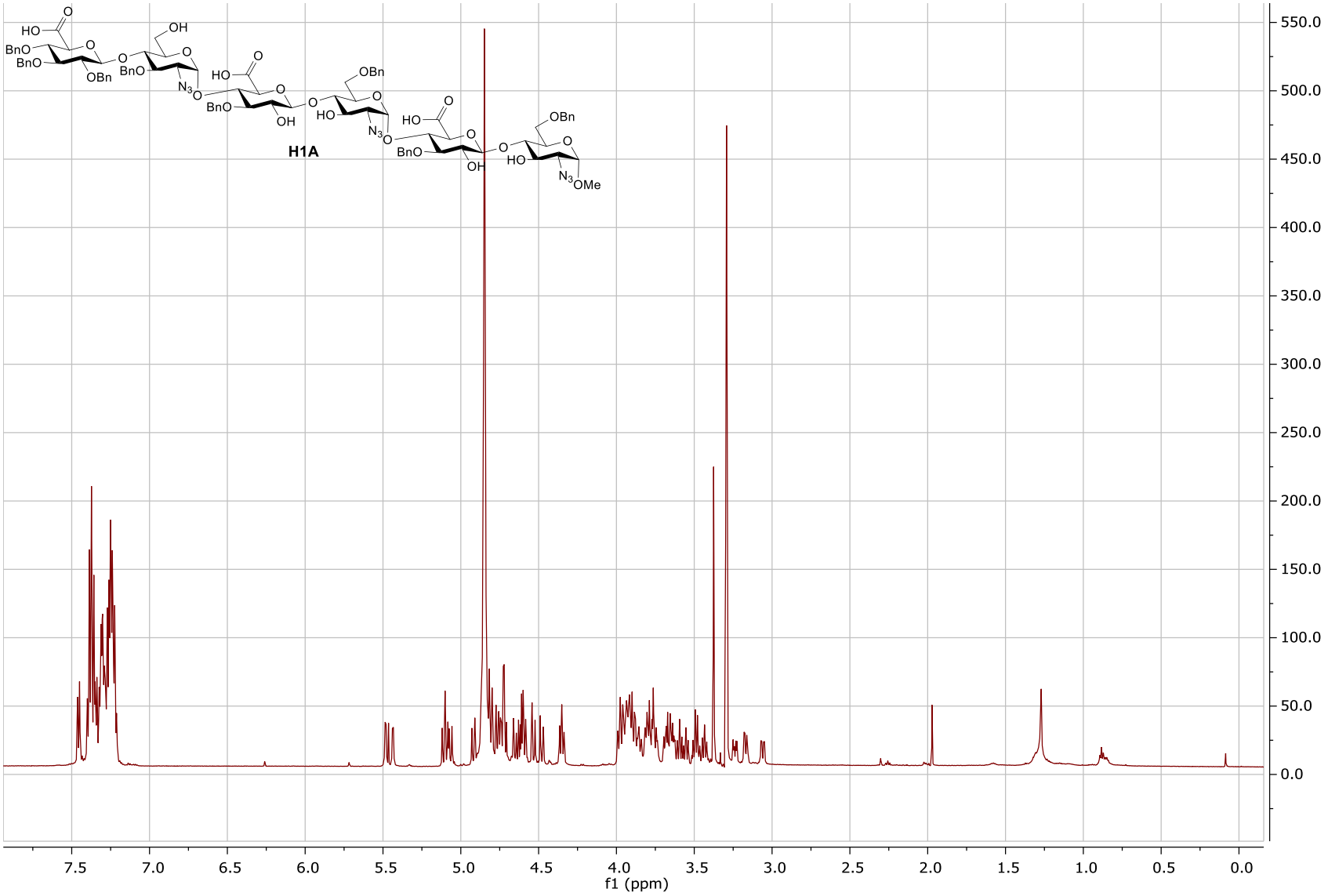

MeO
ClAcO
BnO
OBz
BzO
OBn
MeOOC
OBn
BzO
BnO
OBn
OMe
T9
280.0
260.0
240.0
220.0
200.0
180.0
160.0
140.0
120.0
100.0
80.0
60.0
40.0
20.0
0.0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

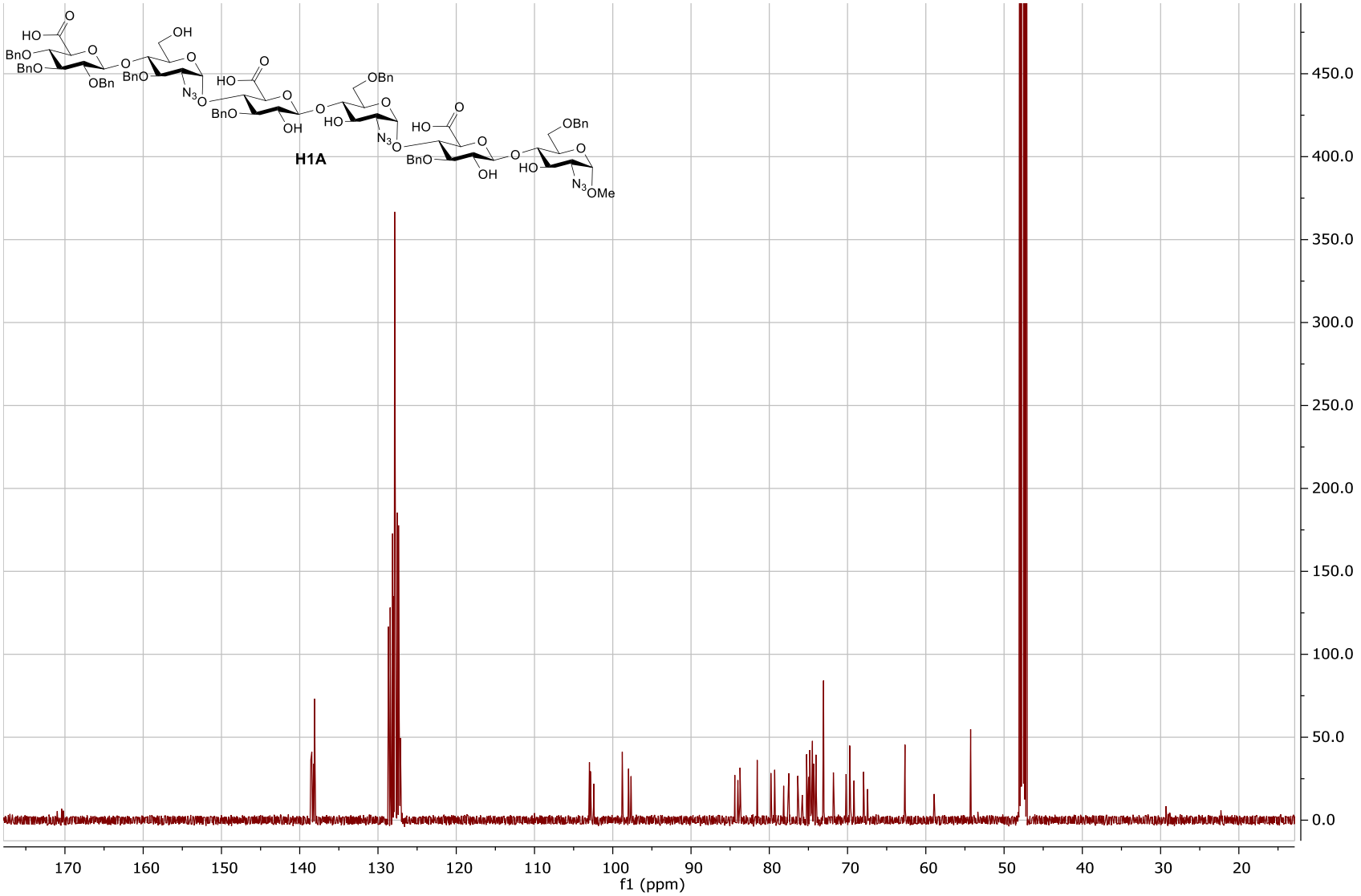

MeO
HO
BnO
OBz
BzO
OBn
MeOOC
N3
BzO
OBn
BnO
OBn
N3
OMe
T10
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

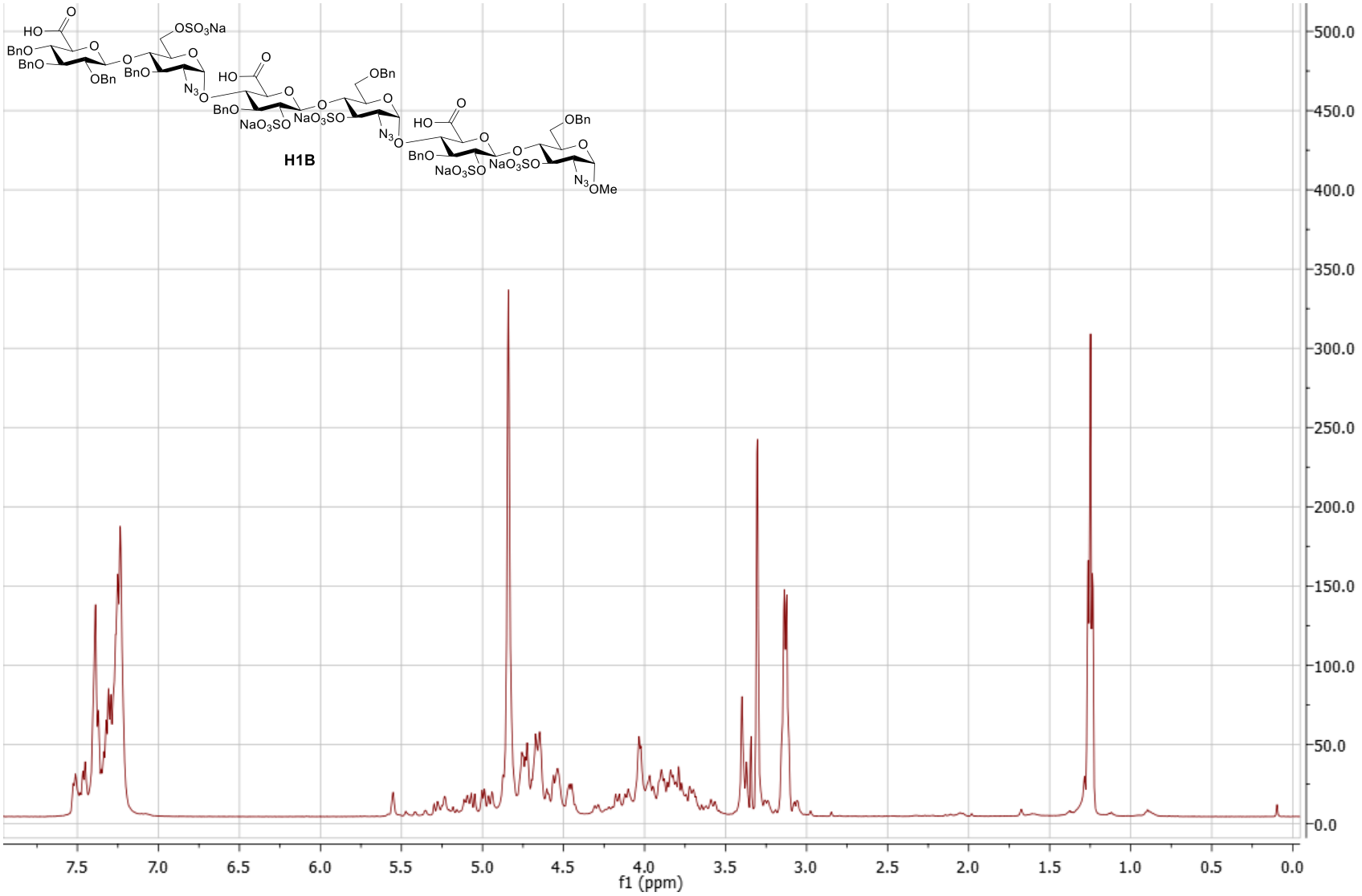

MeO
HO
BnO
OBz
O
OBn
BzO
N3
MeOOC
OBn
BzO
BnO
OBn
N3
OMe
T10
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

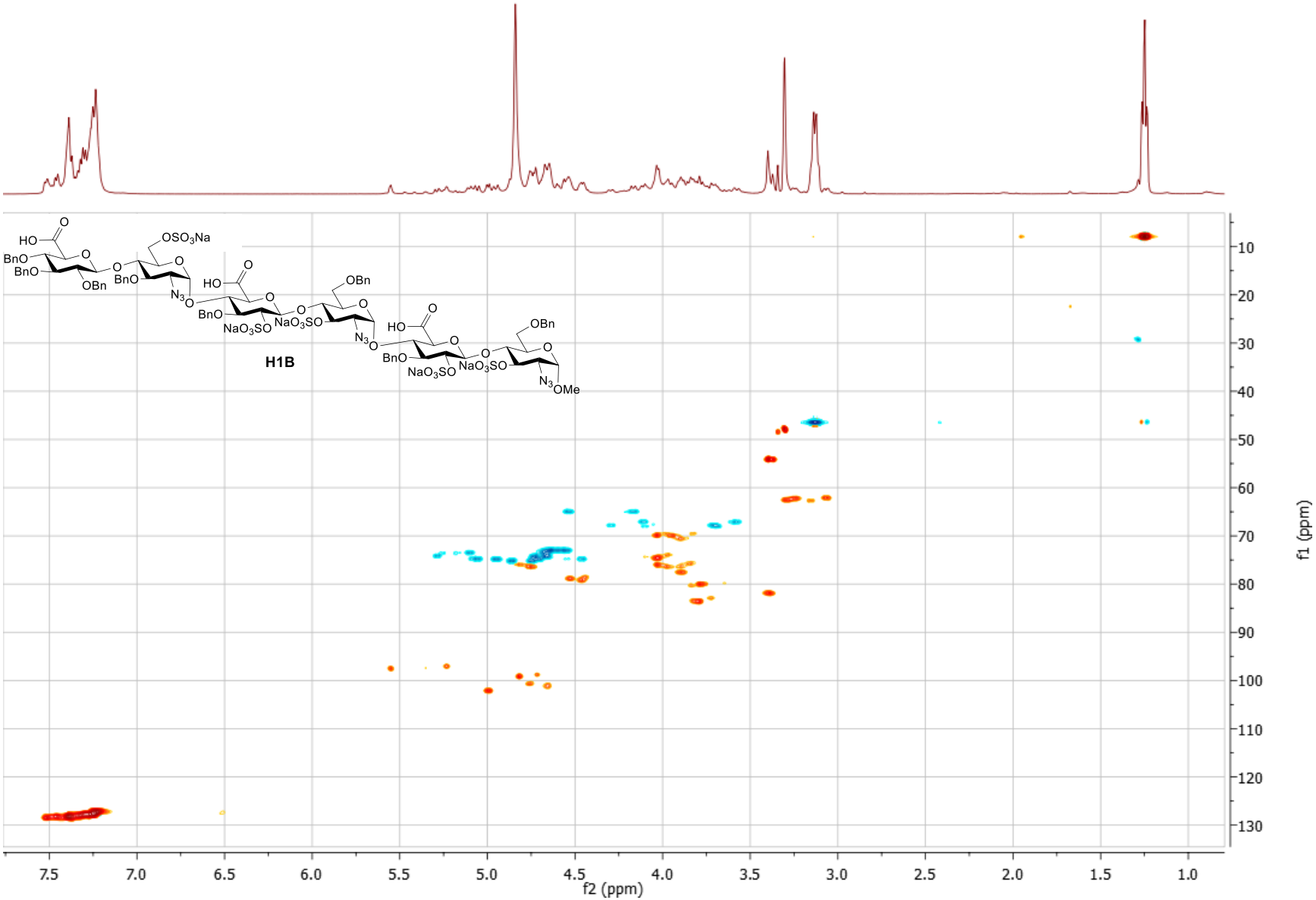

H5
f1 (ppm)

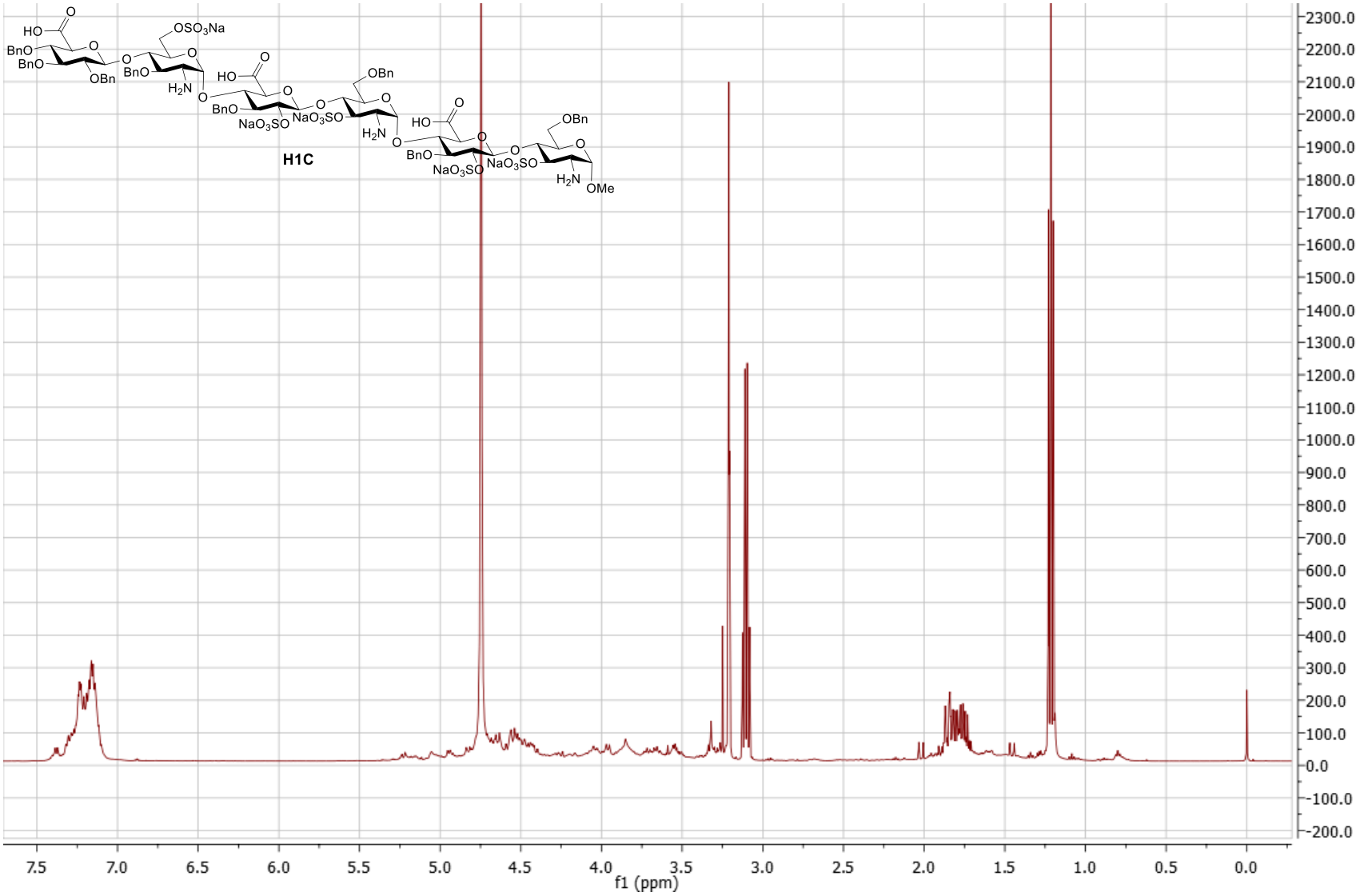

MeO
BnO
BnO
OBn
O
O
BnO
OBn
O
N3
O
MeO
O
O
BnO
OBz
O
BzO
OBn
O
N3
O
MeOOC
OBn
O
BzO
O
BnO
OBn
O
N3
OMe
H5
900.0
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

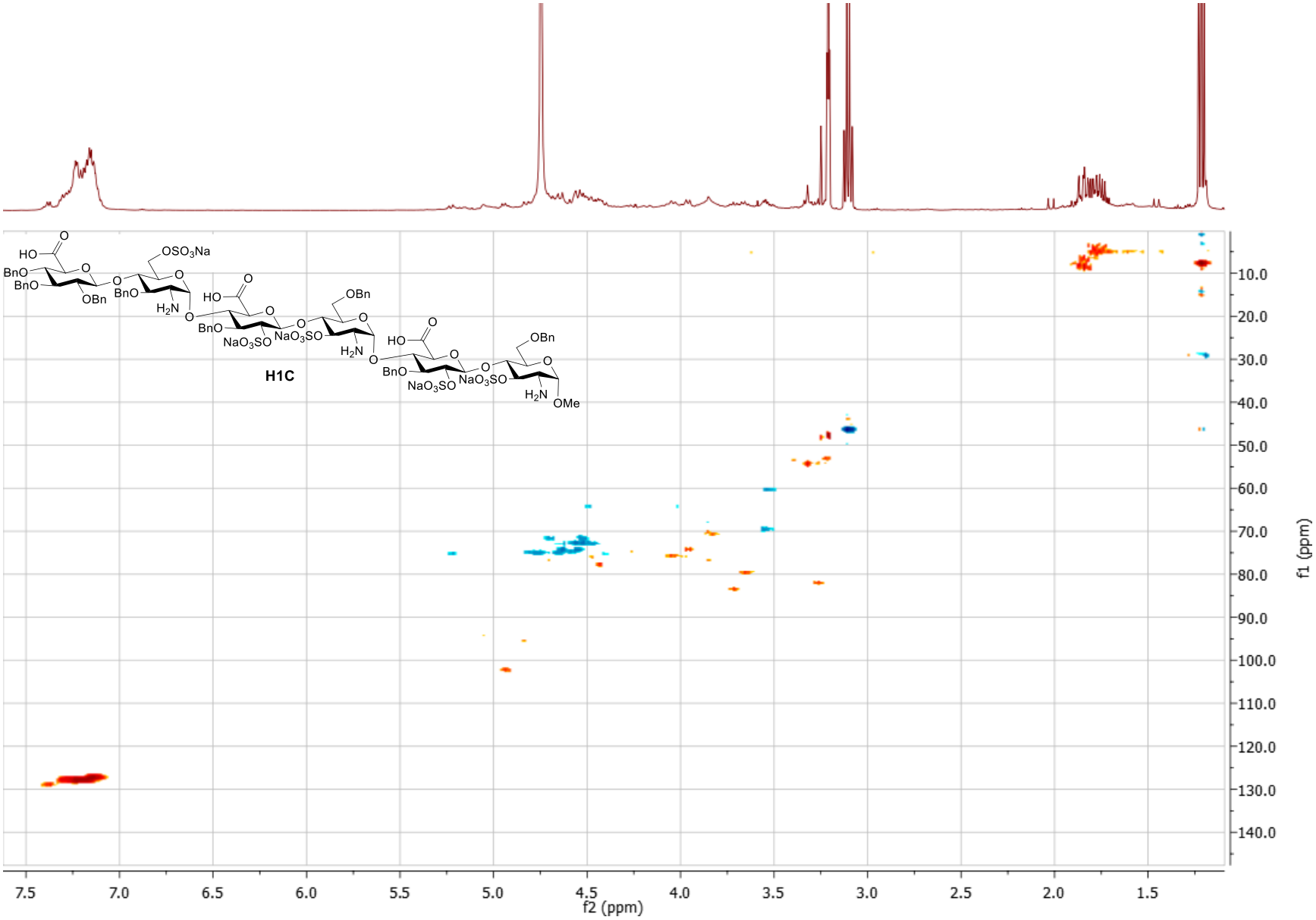

H1A
550.0
500.0
450.0
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

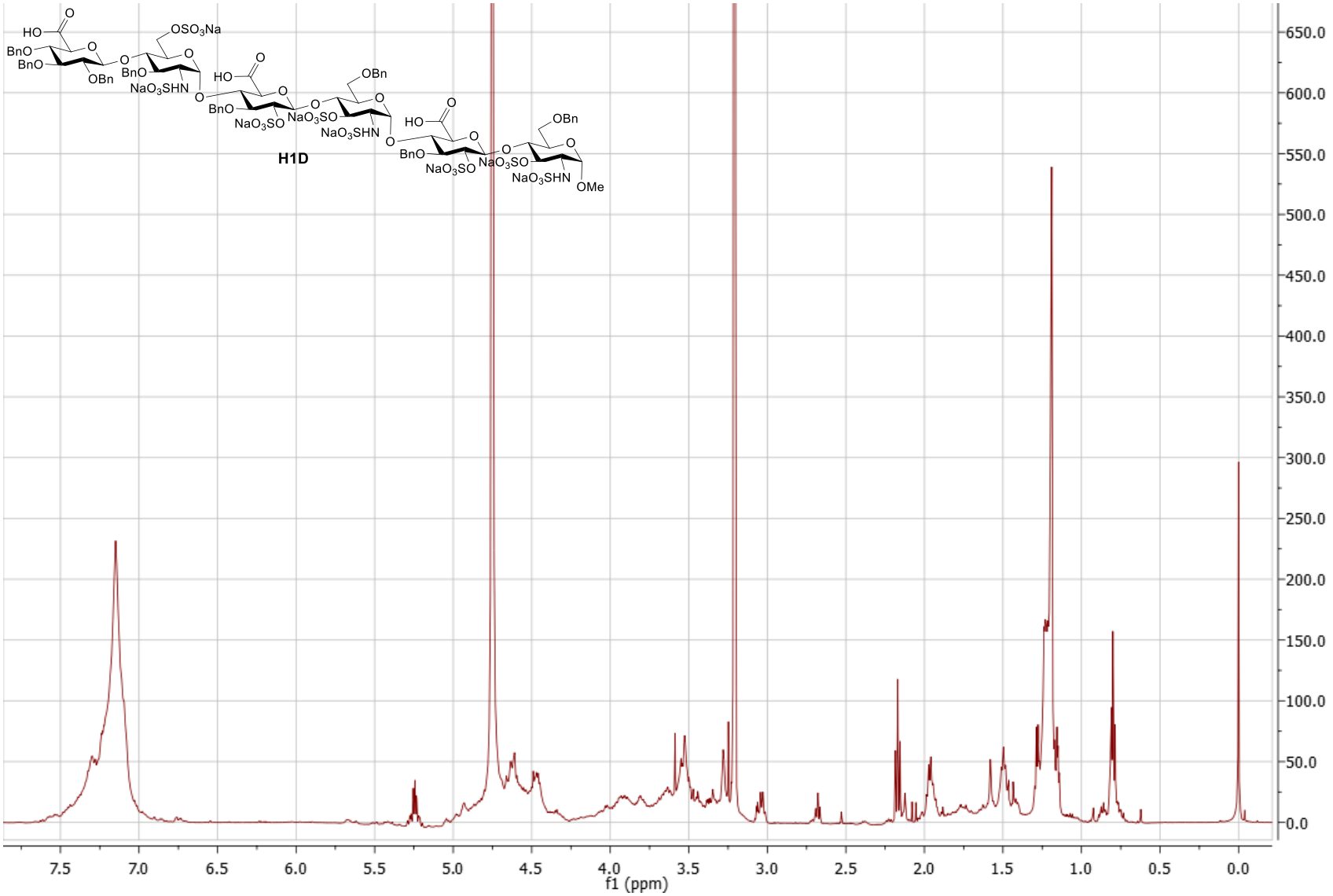

H1A
450.0
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)

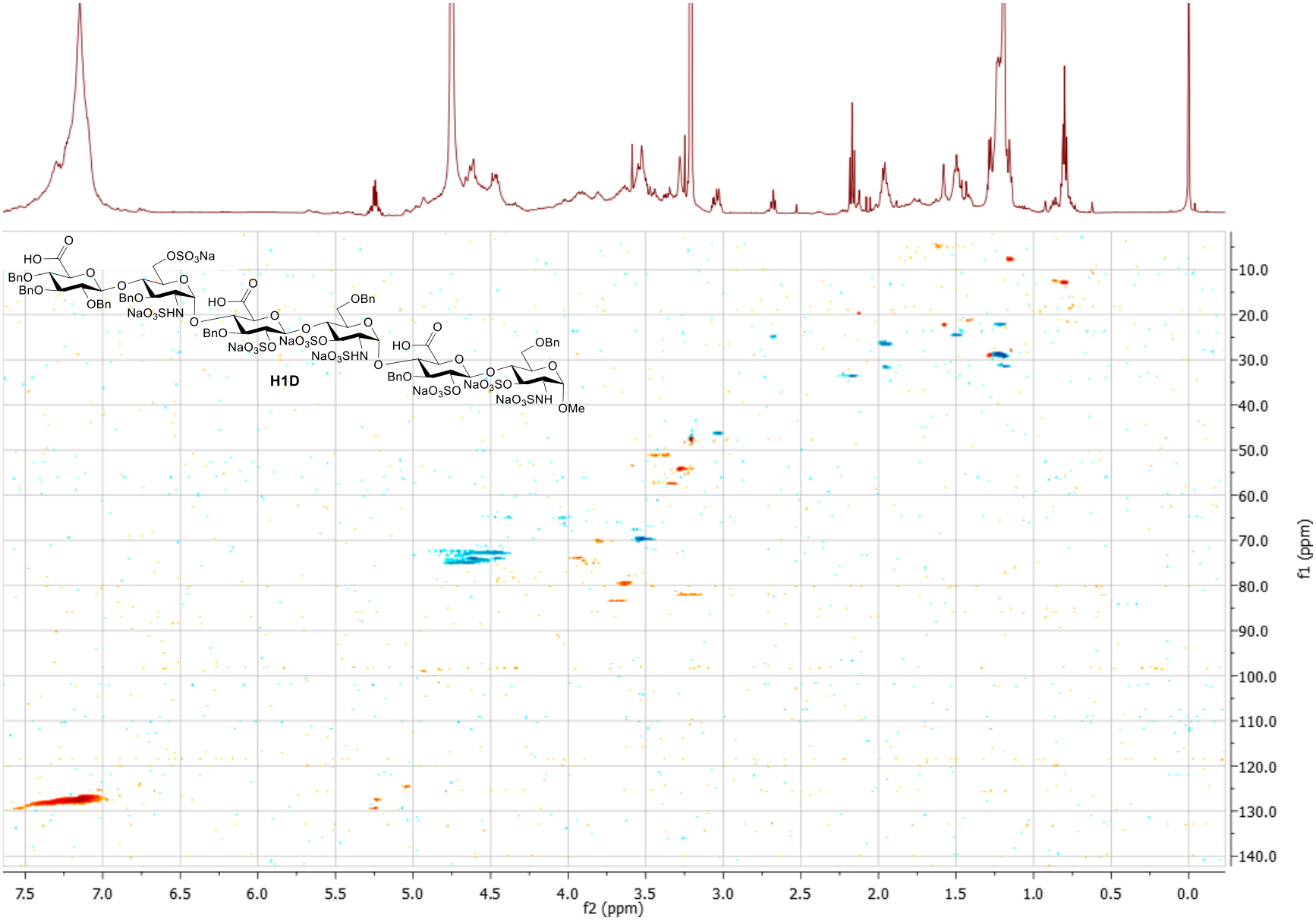

H1B
500.0
450.0
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

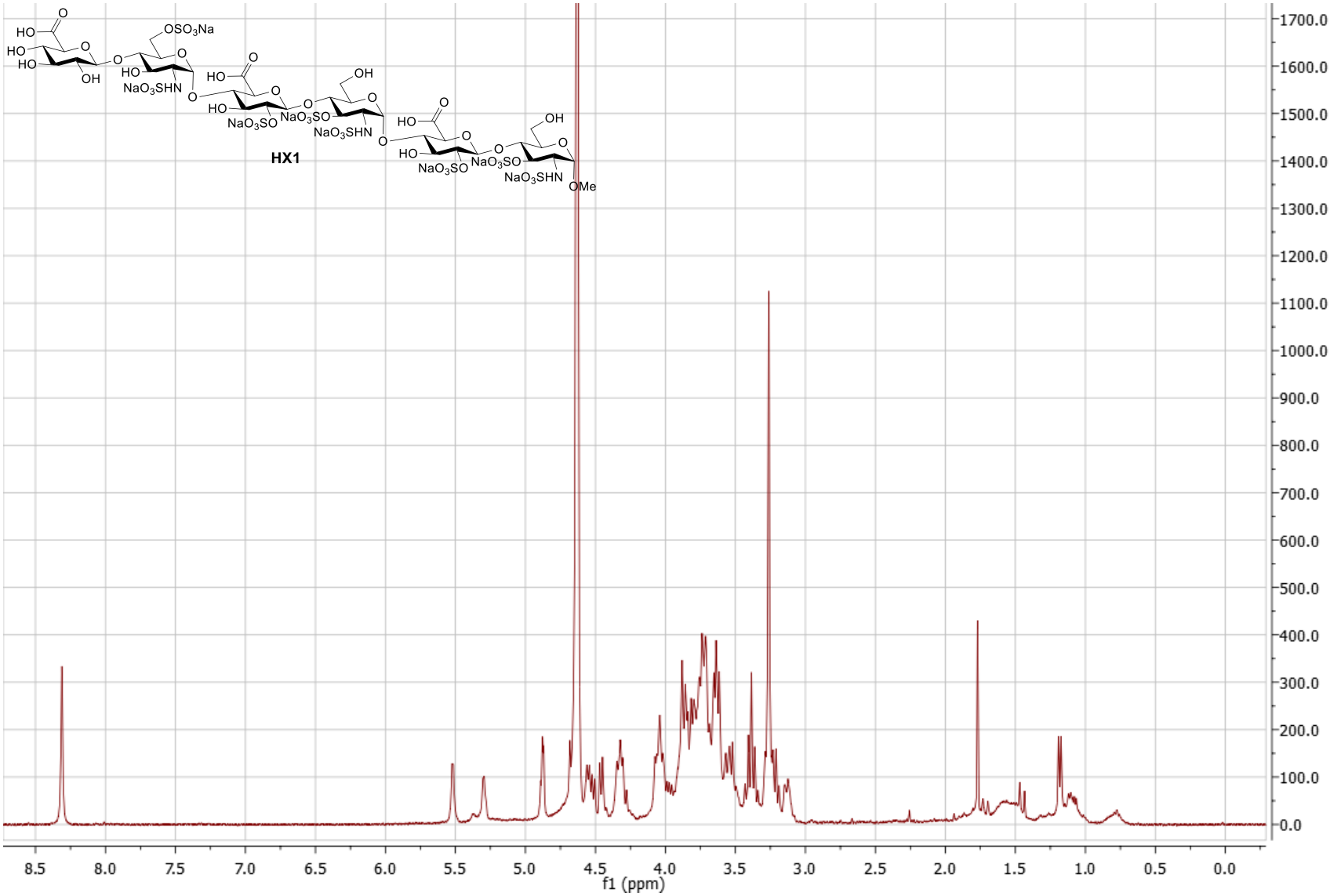

H1B
f2 (ppm)
f1 (ppm)

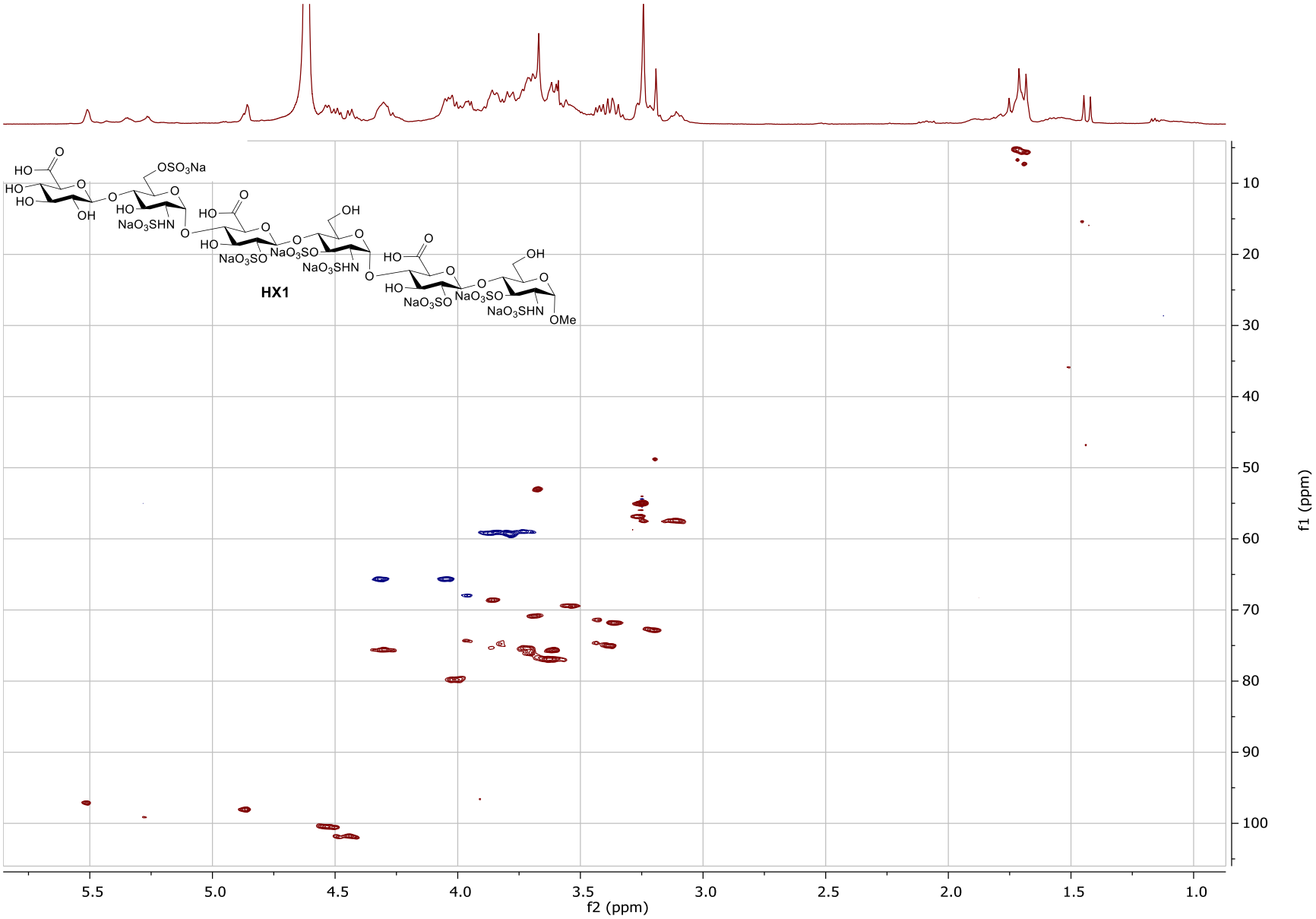

H1C
f1 (ppm)

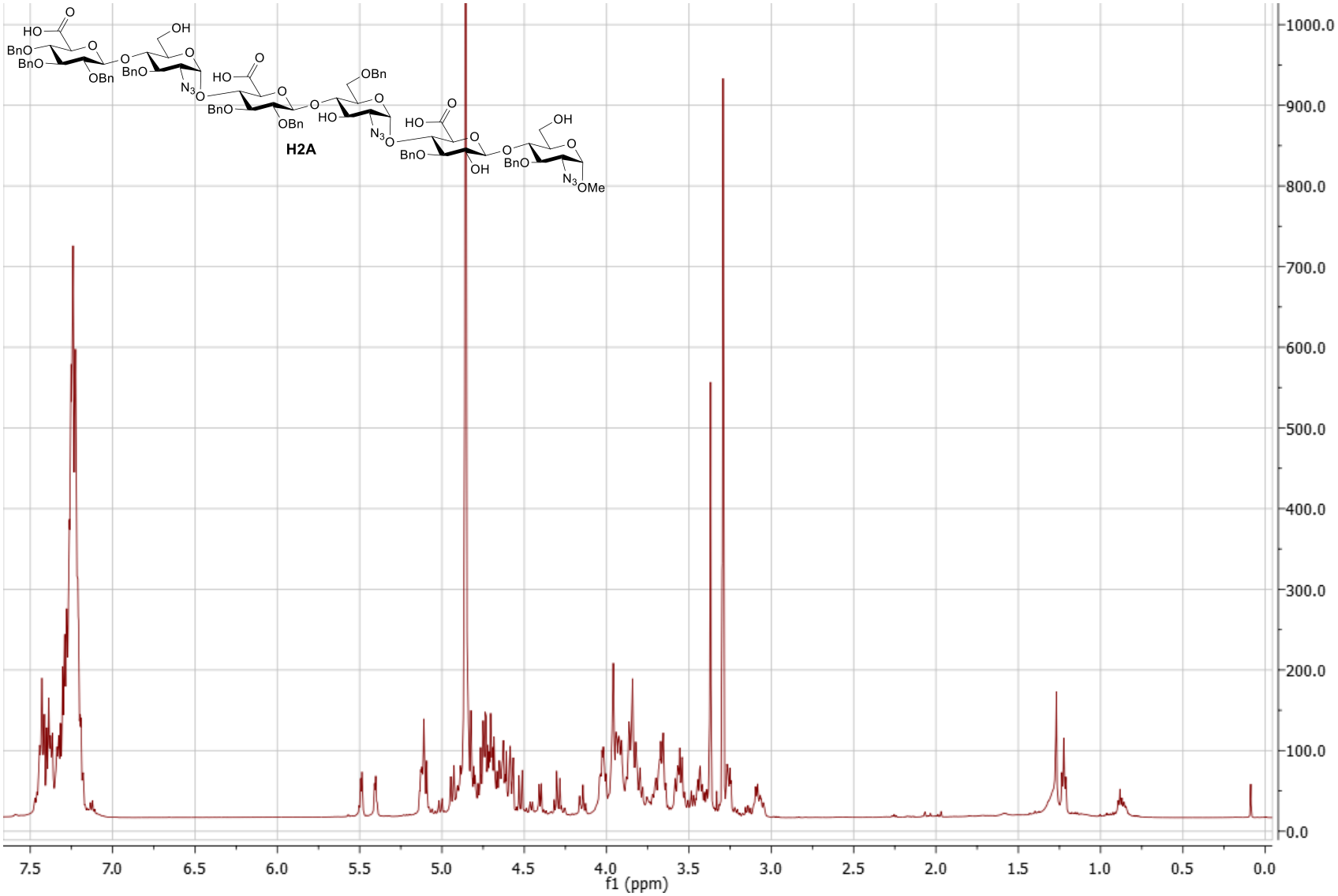

H1C
f2 (ppm)
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0

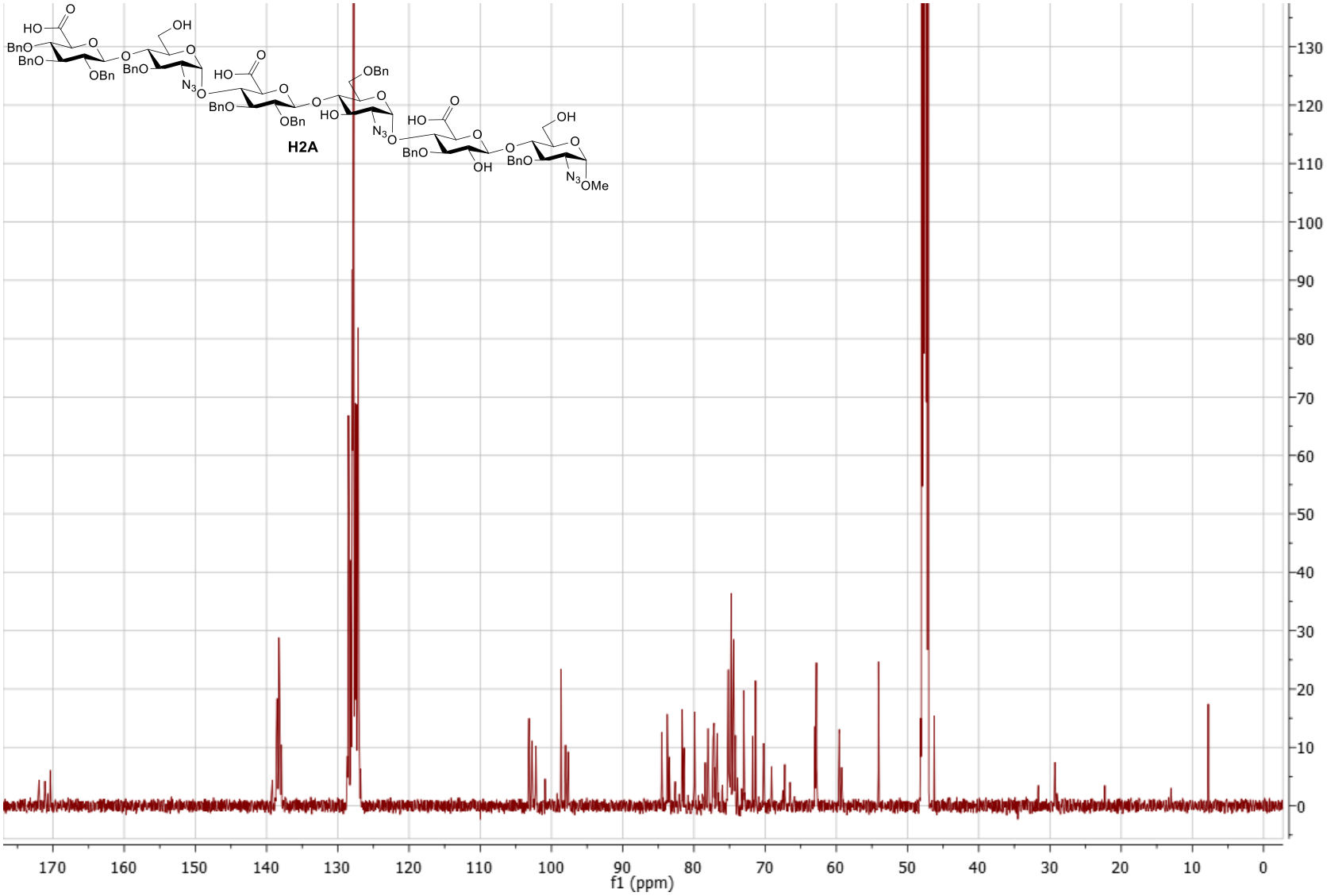

H1D
650.0
600.0
550.0
500.0
450.0
400.0
350.0
300.0
250.0
200.0
150.0
100.0
50.0
0.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

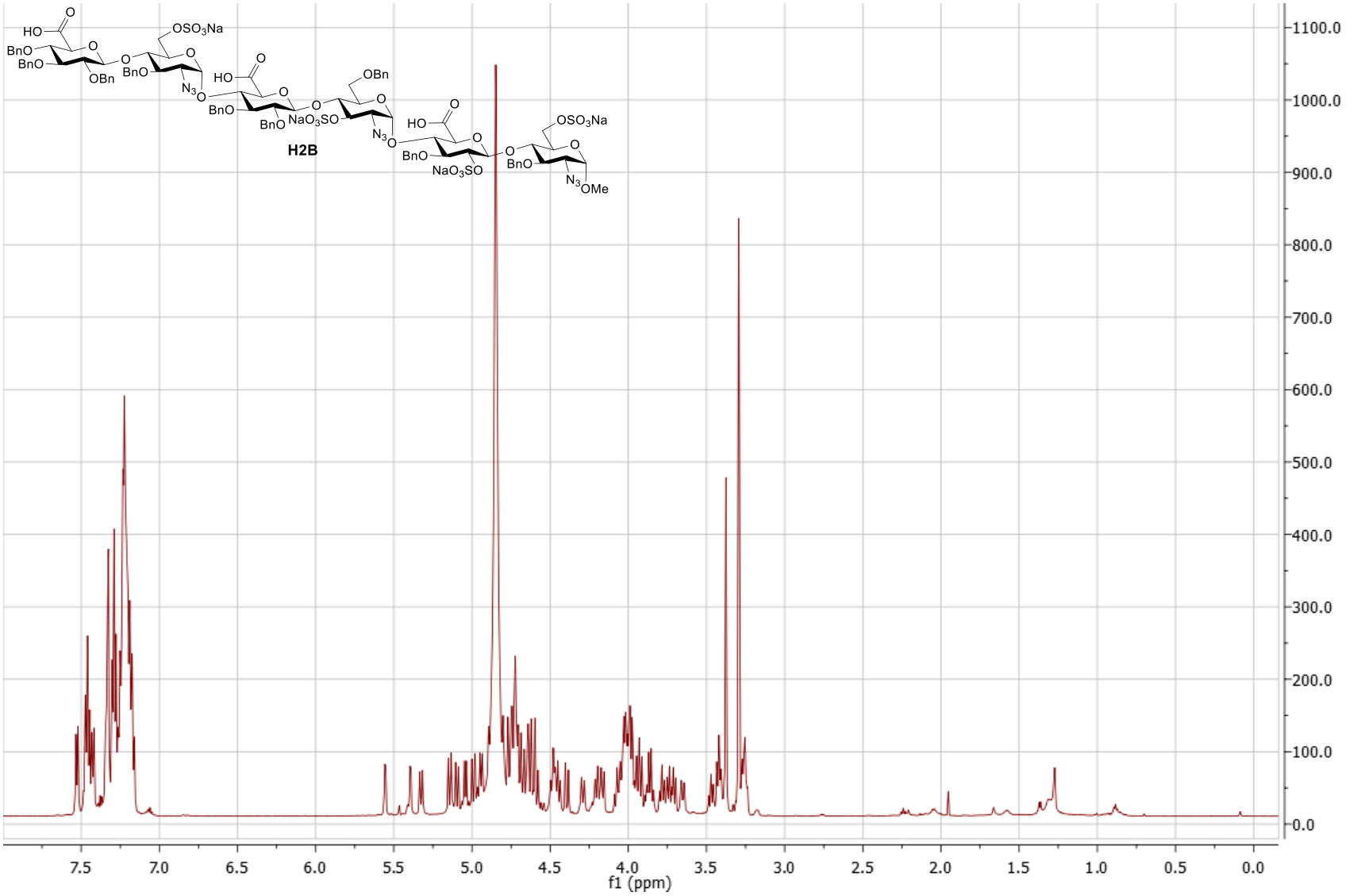

HO
BnO
BnO
OBn
OSO3Na
NaO3SHN
NaO3SO
OMe
H1D
f2 (ppm)
f1 (ppm)

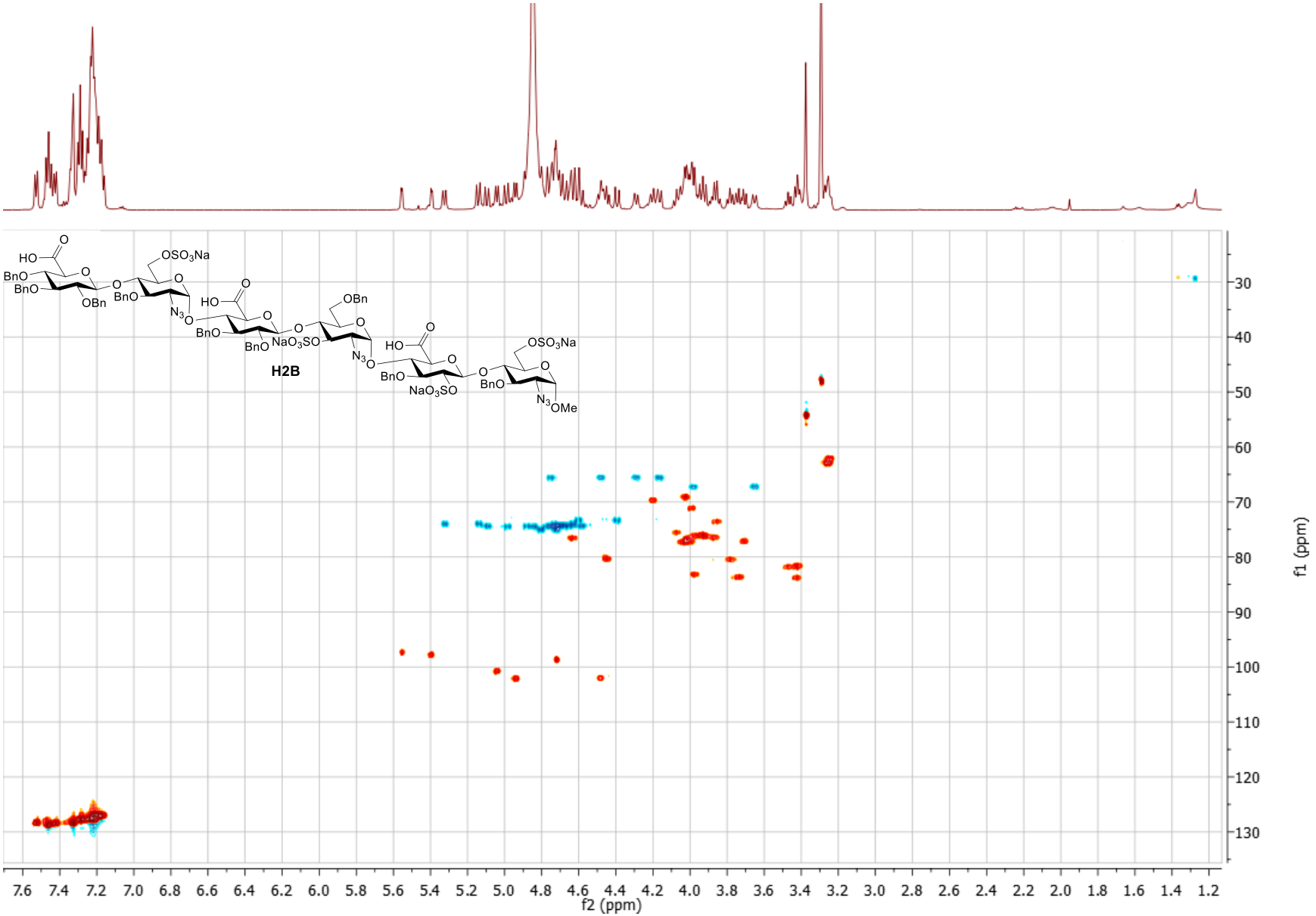

HX1
f1 (ppm)

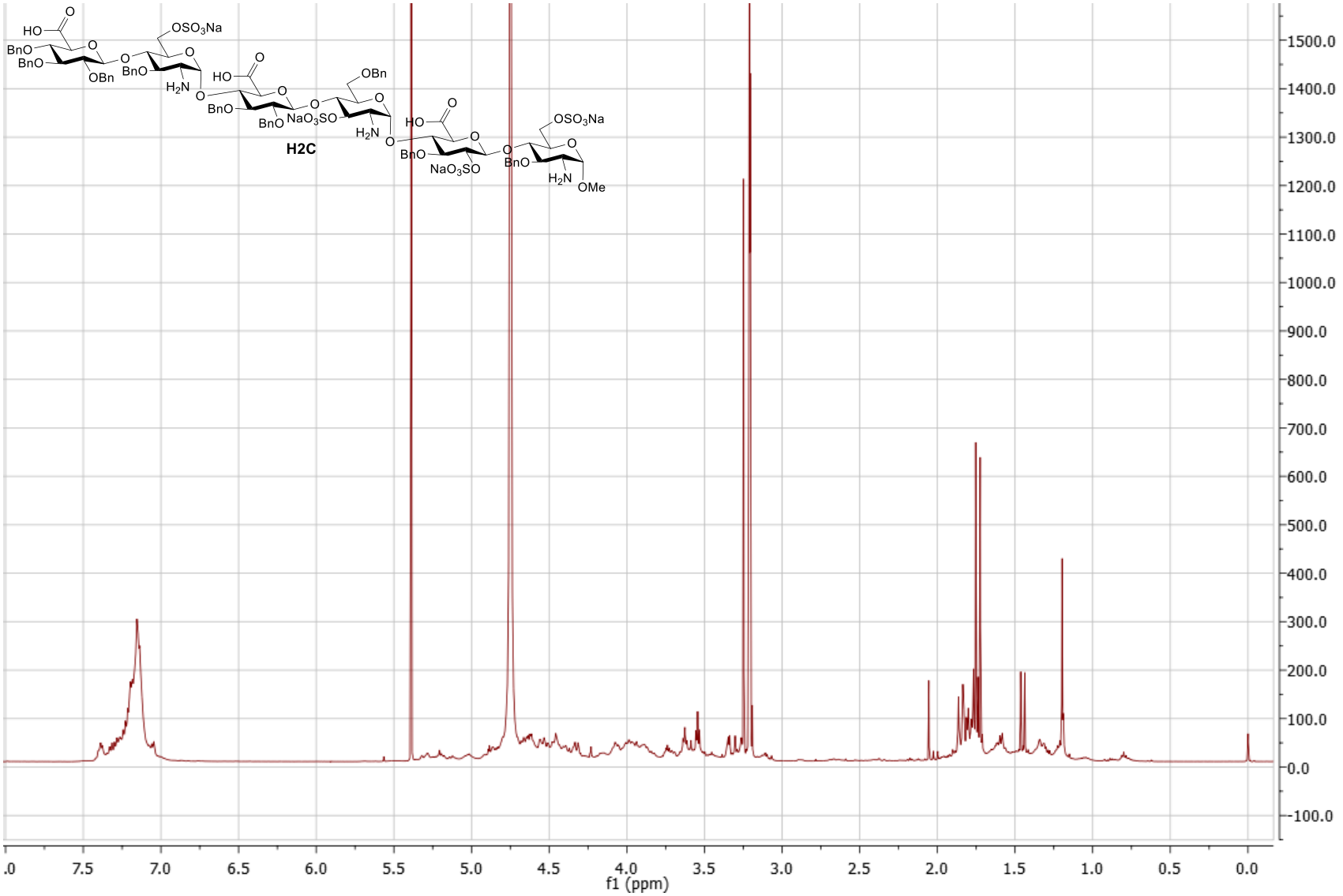

HX1
f2 (ppm)
f1 (ppm)
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
10
20
30
40
50
60
70
80
90
100

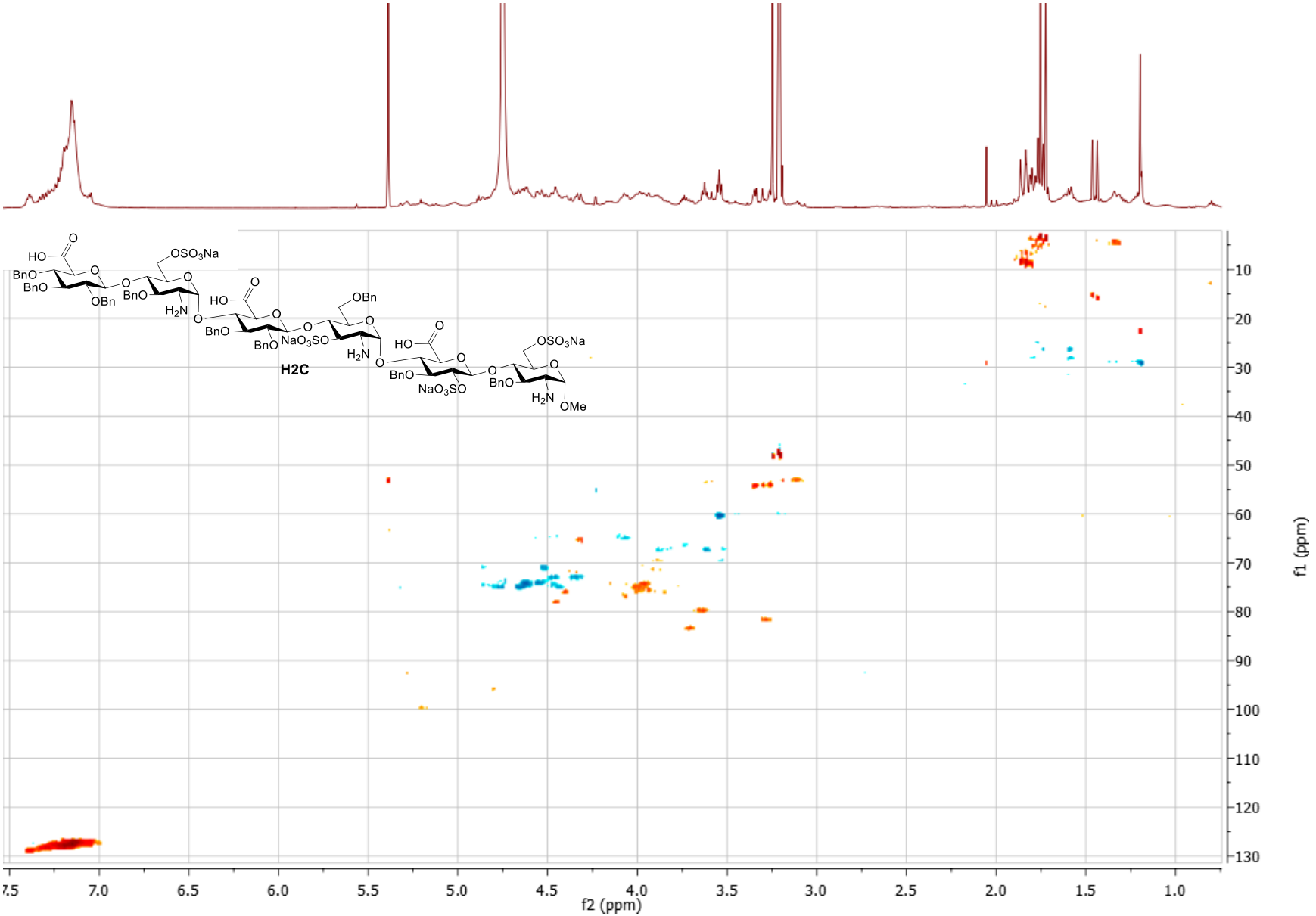

H2A
1000.0
900.0
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

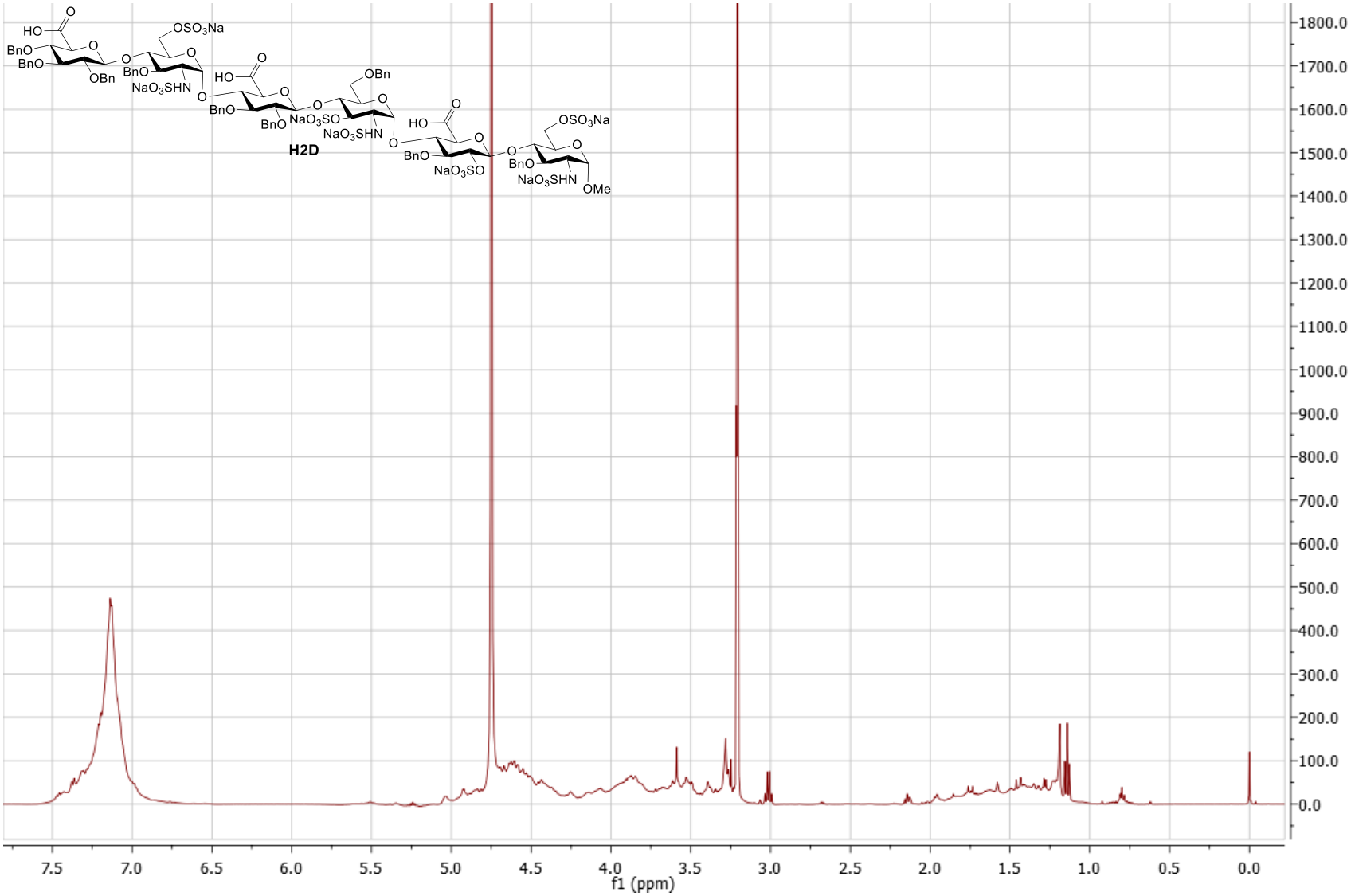

H2A
f1 (ppm)

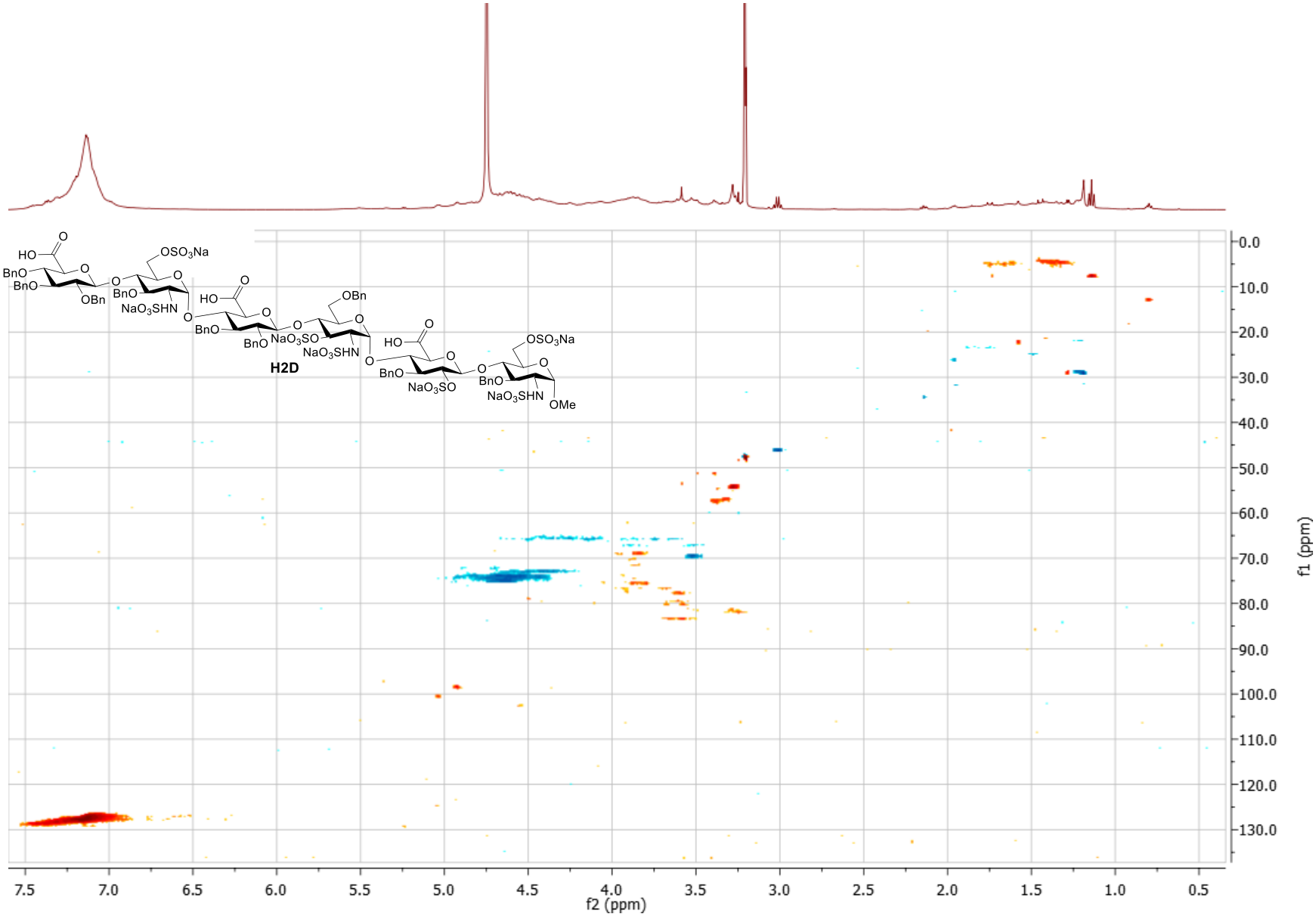

H2B
1100.0
1000.0
900.0
800.0
700.0
600.0
500.0
400.0
300.0
200.0
100.0
0.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

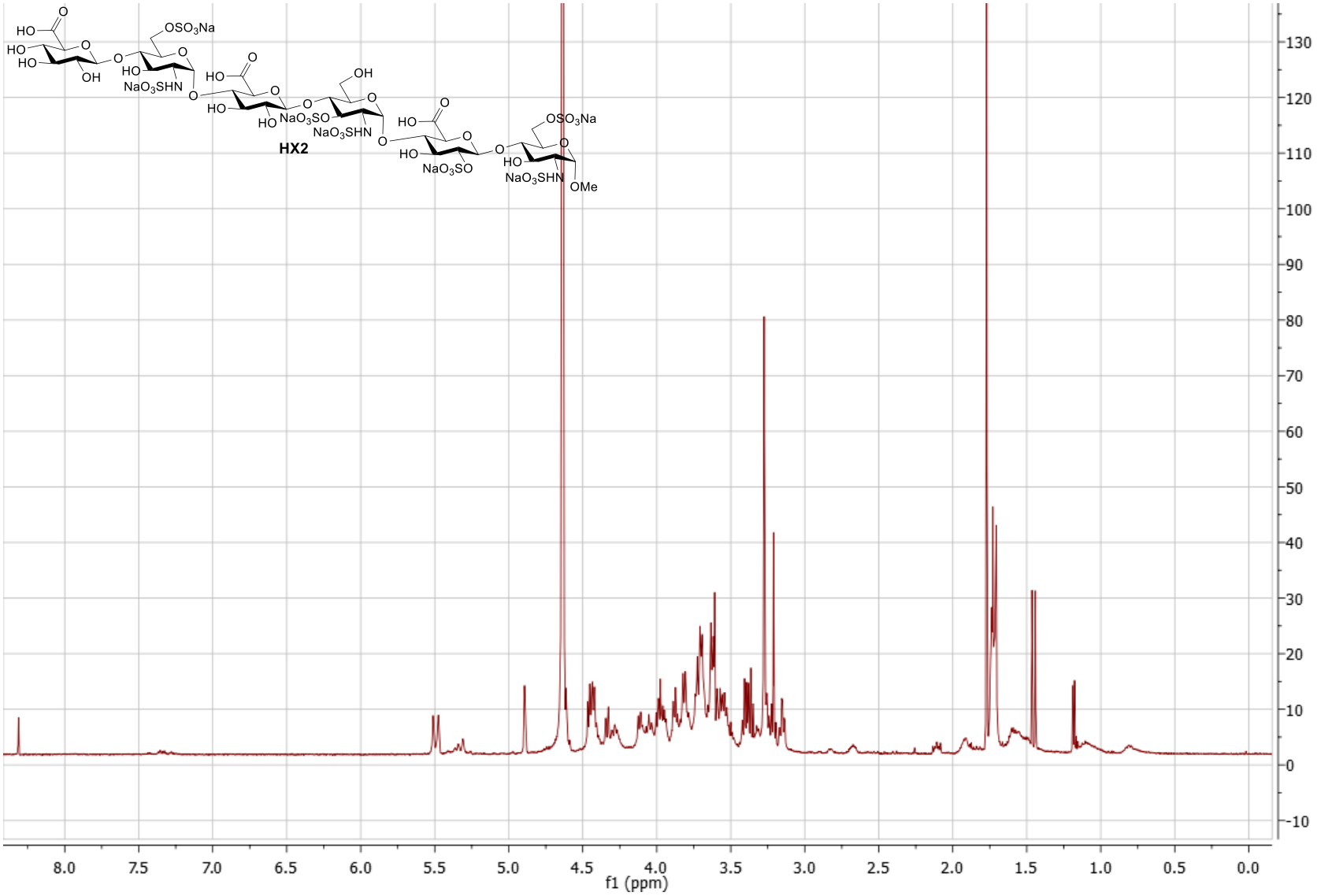

H2B
f2 (ppm)
f1 (ppm)

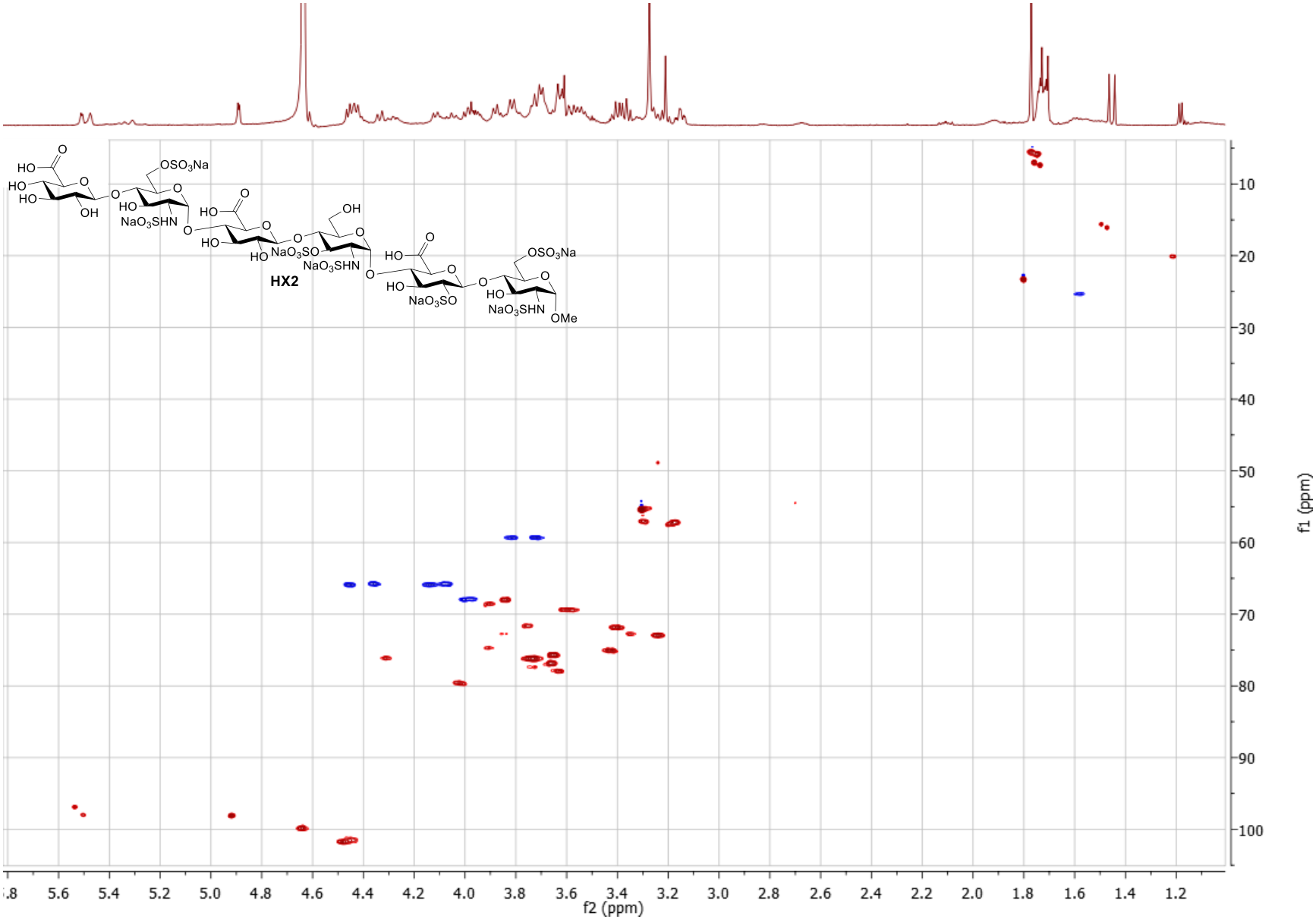

H2C
f1 (ppm)

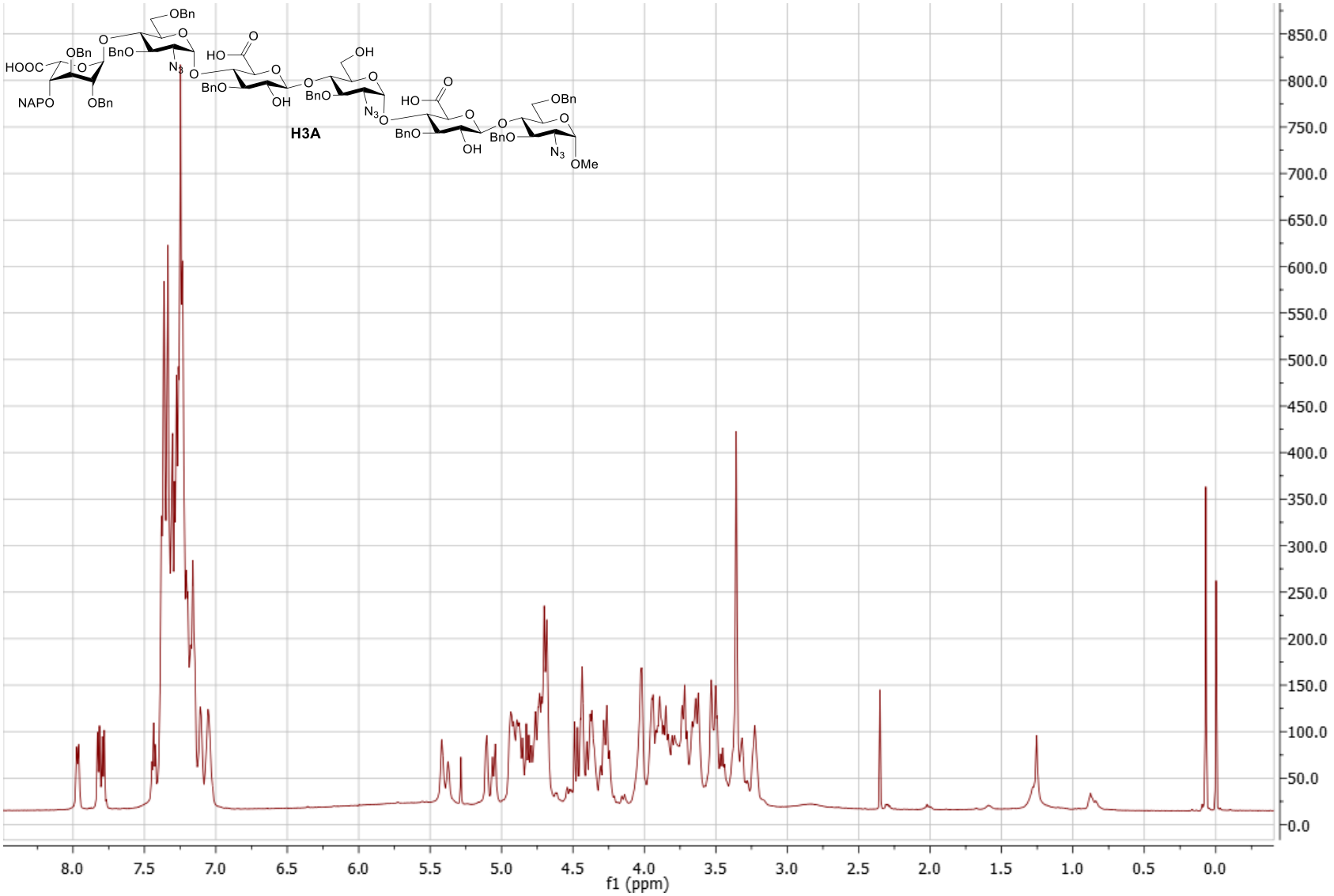

H2C
f2 (ppm)
f1 (ppm)

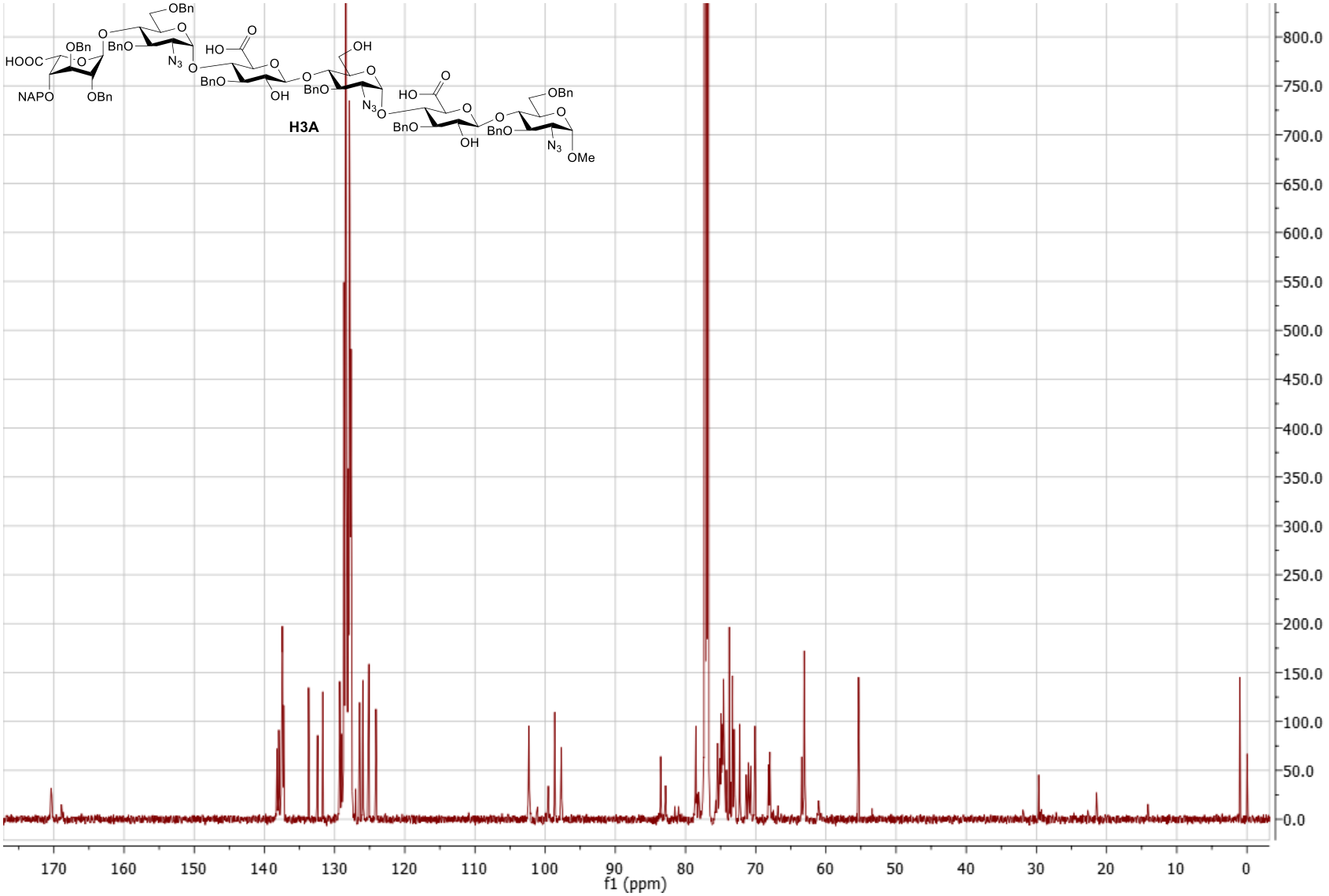

H2D
f1 (ppm)

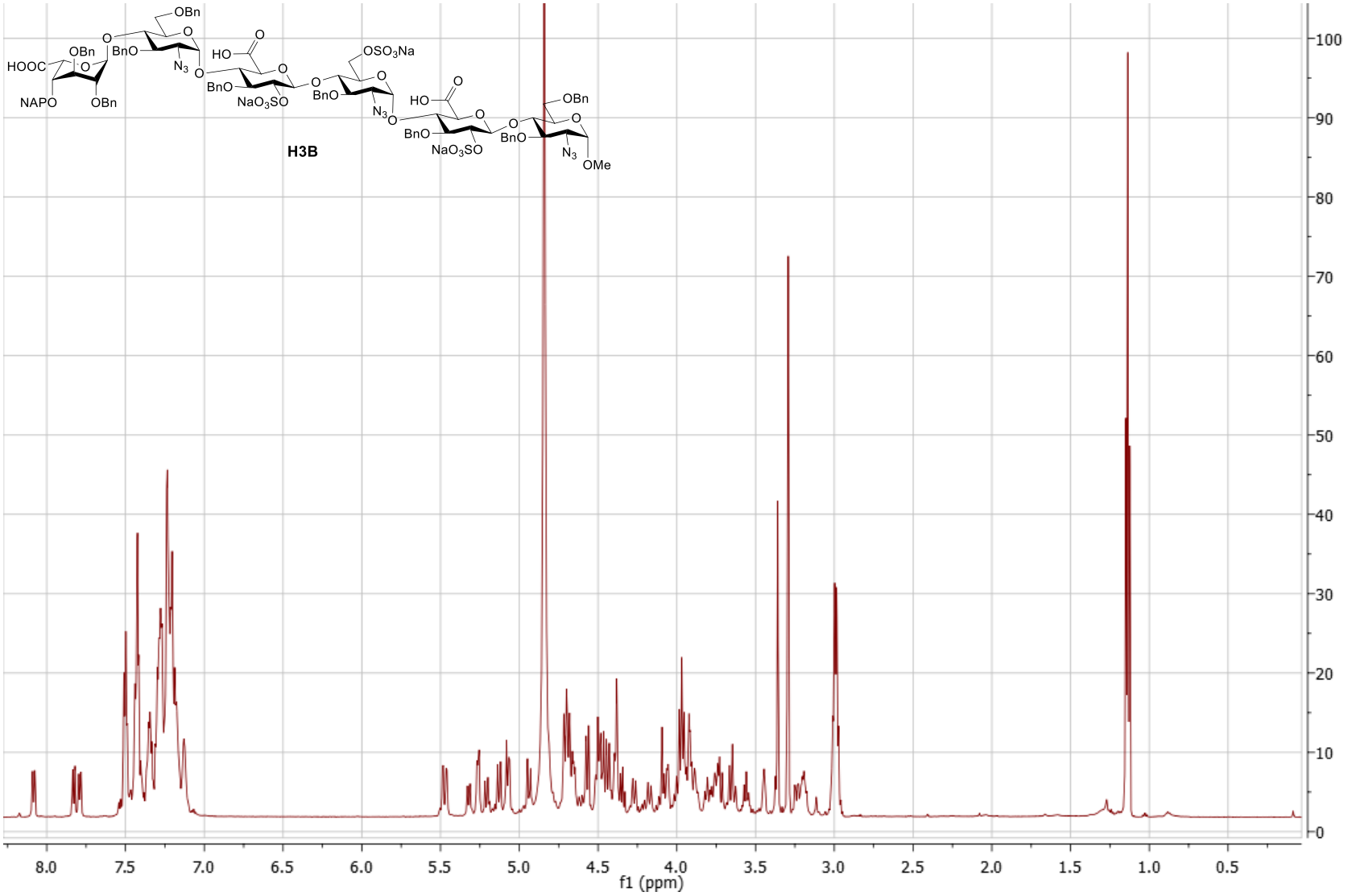

H2D
f2 (ppm)
f1 (ppm)

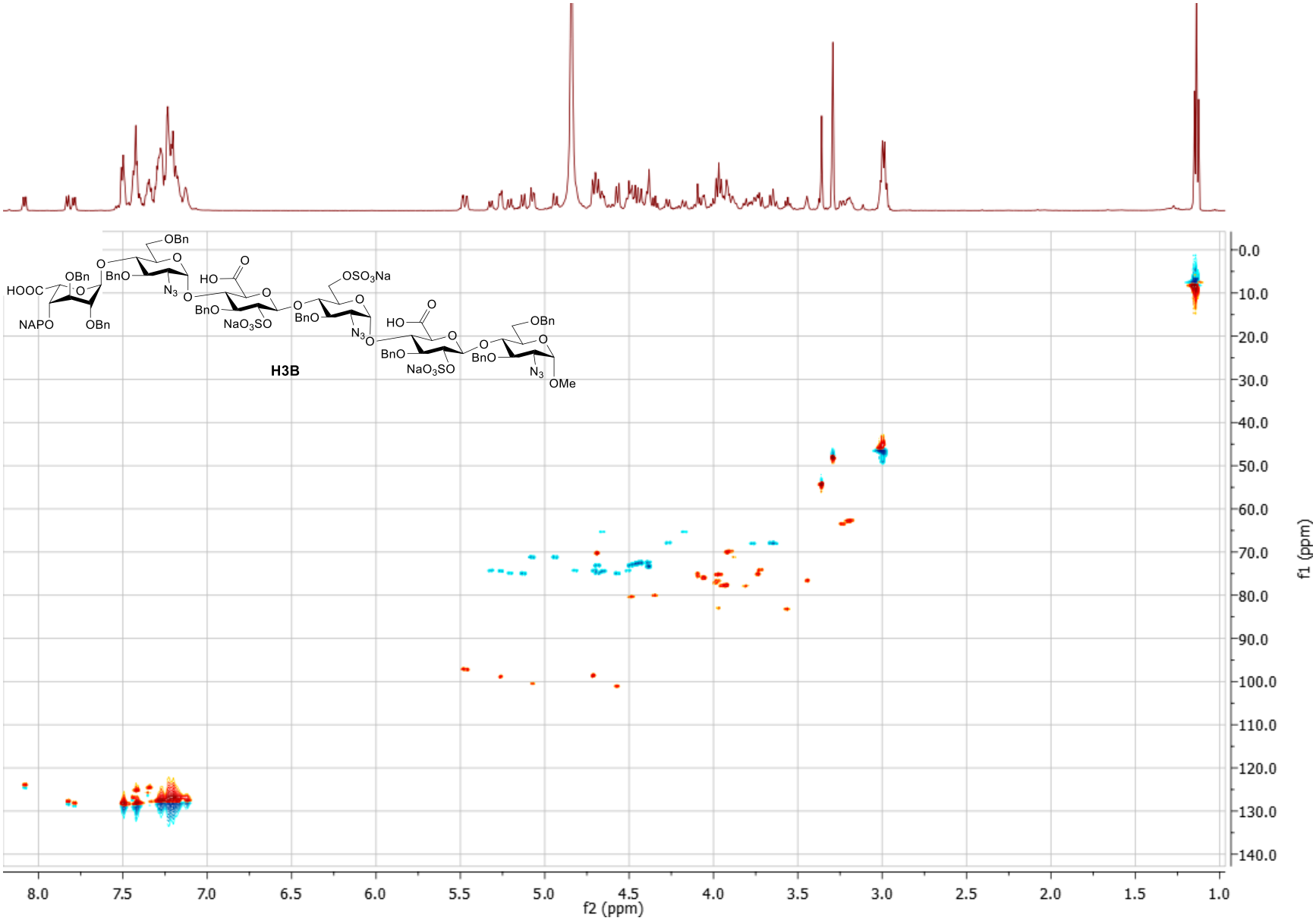

HX2
f1 (ppm)

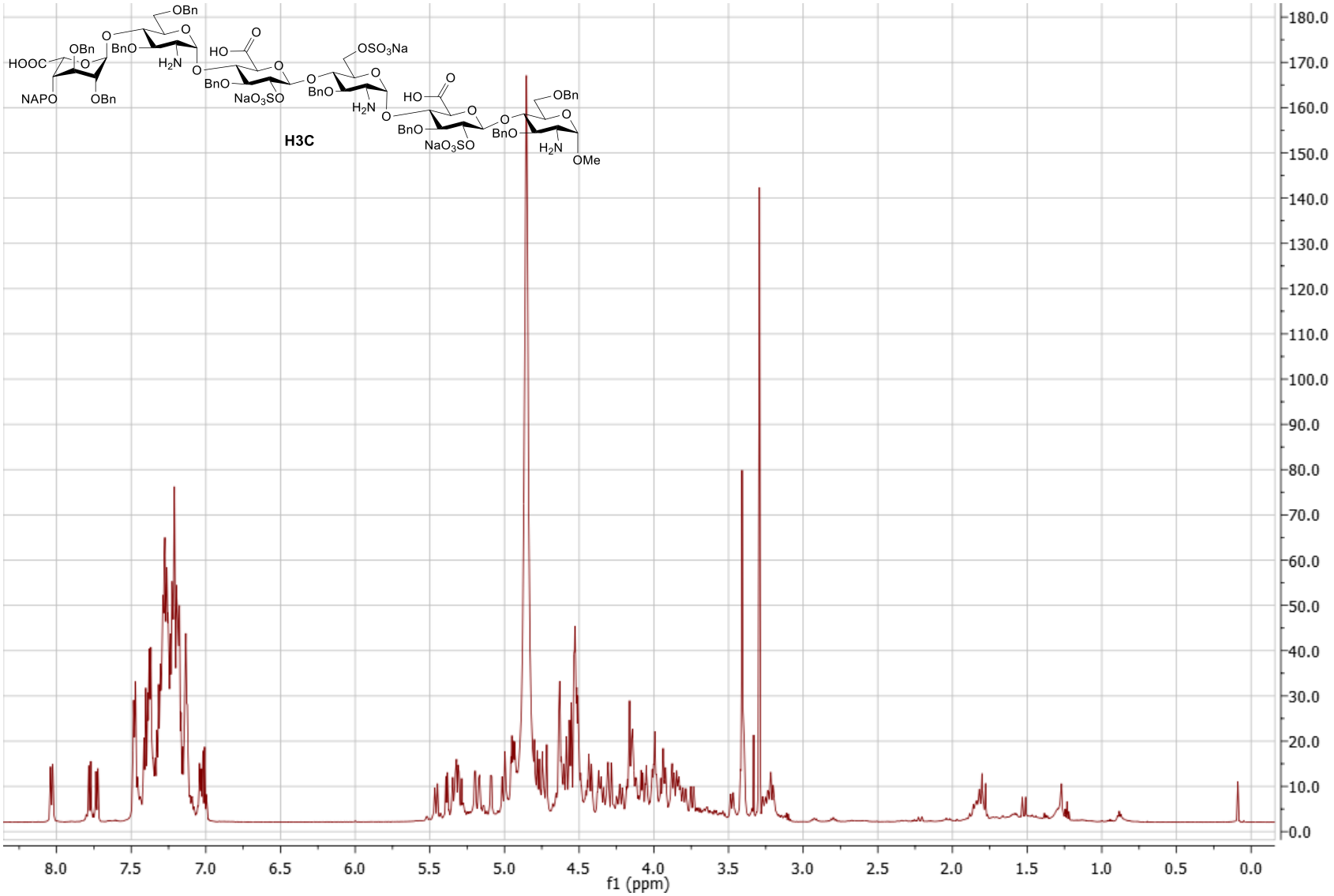

HX2
f2 (ppm)
f1 (ppm)

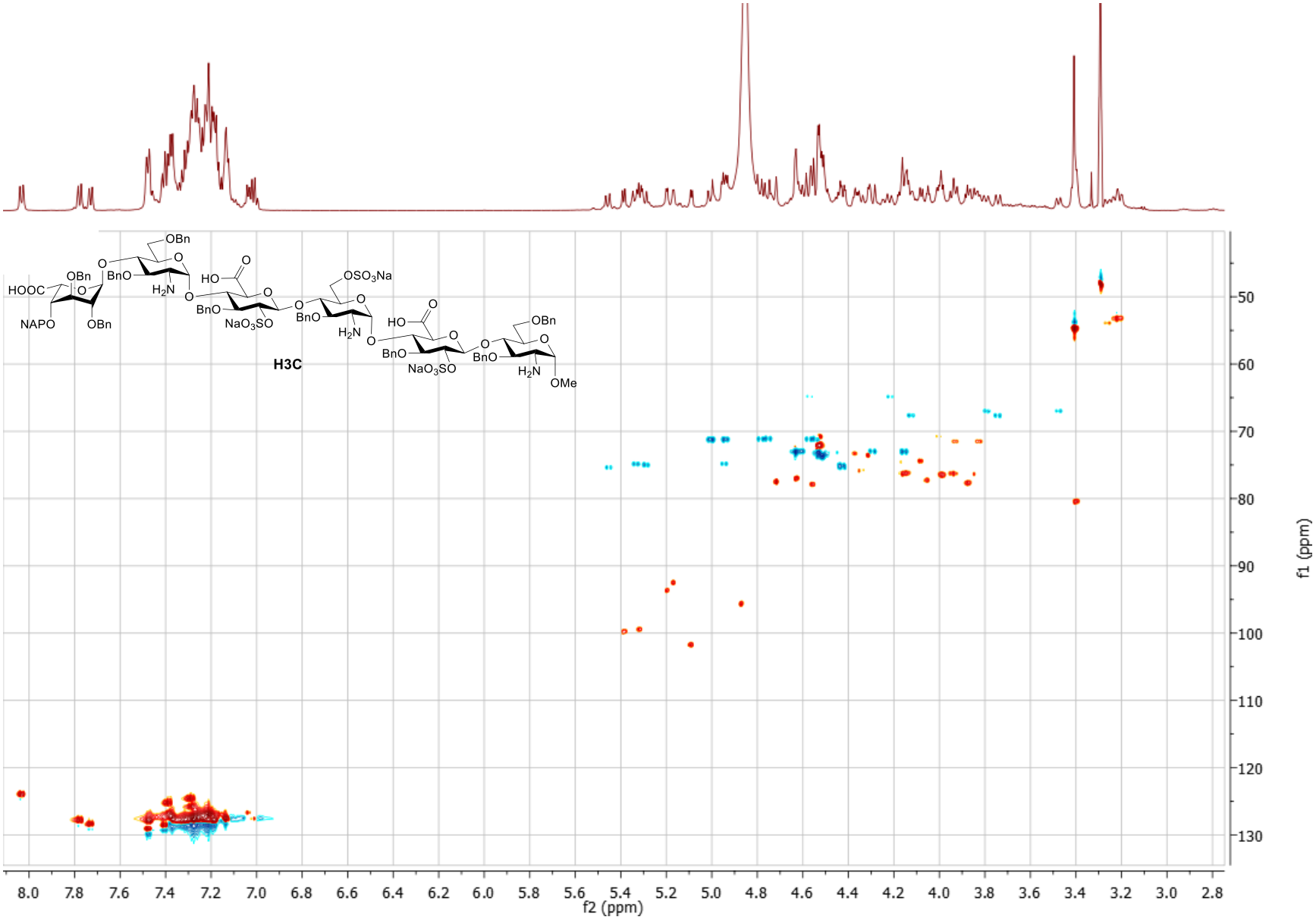

H3A
f1 (ppm)

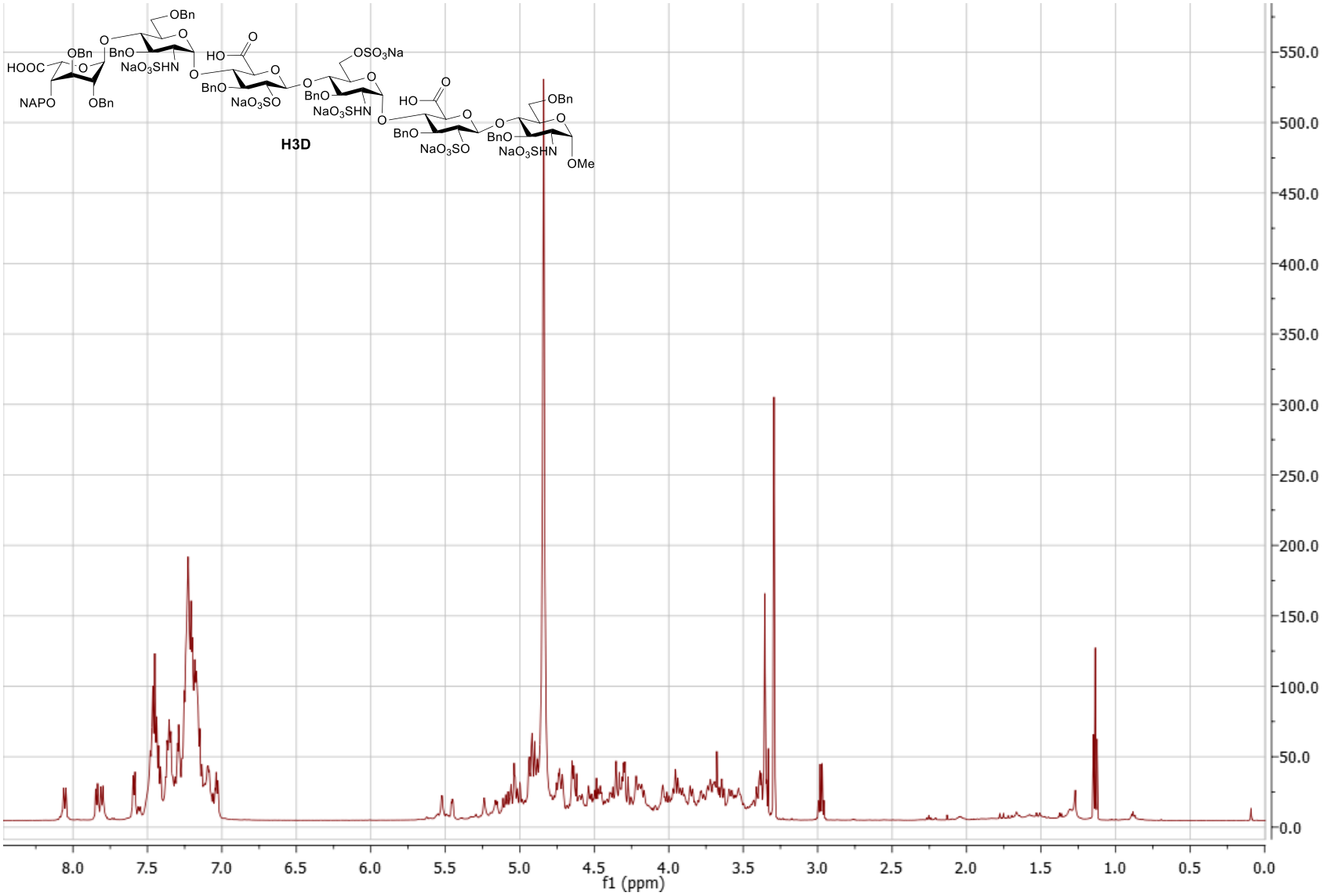

H3A
f1 (ppm)

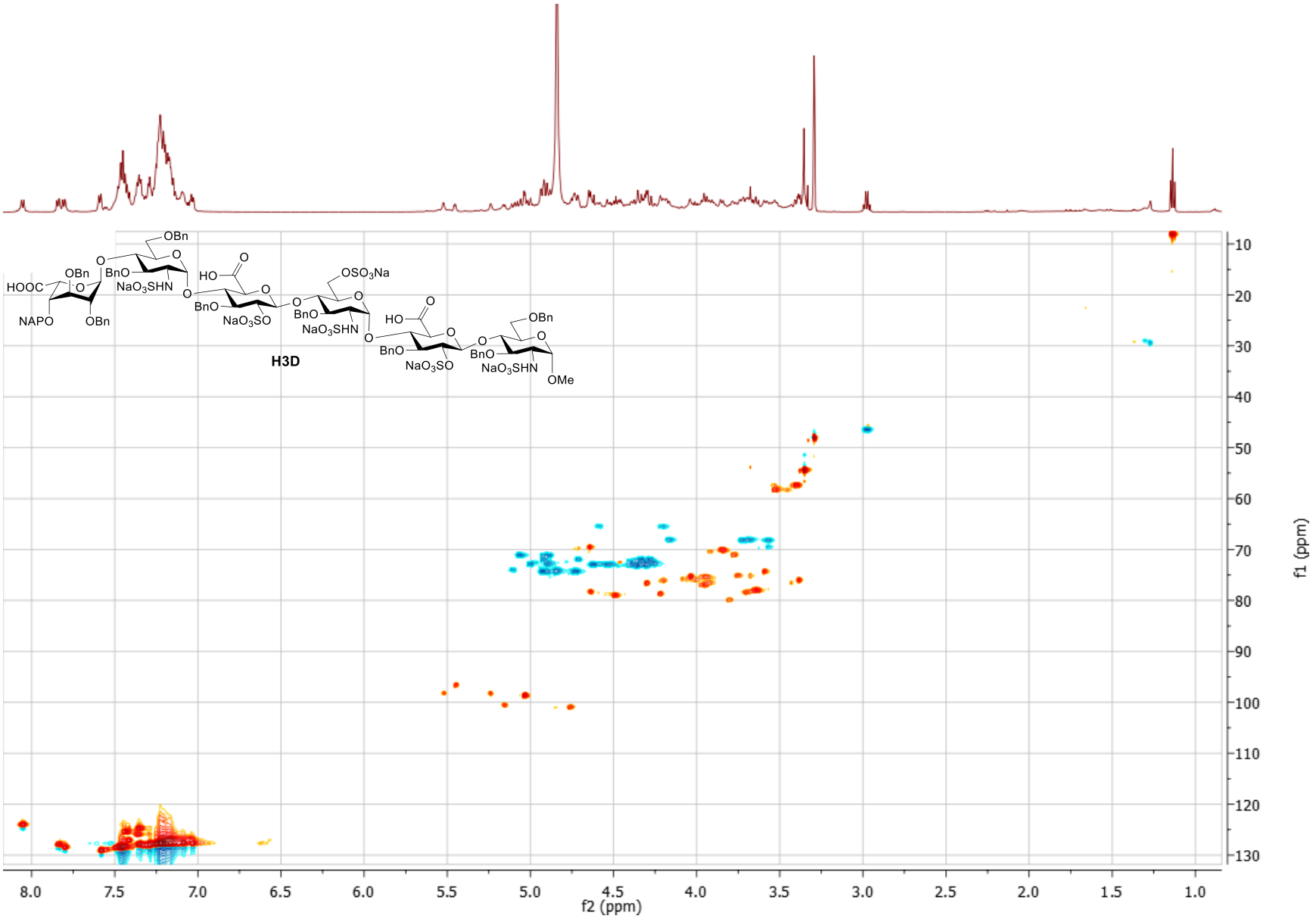

OBn
HOOC
OBn
BnO
HO
OSO3Na
N3
NAPO
OBn
BnO
NaO3SO
BnO
N3
HO
OBn
BnO
NaO3SO
BnO
N3
OMe
H3B
100
90
80
70
60
50
40
30
20
10
0
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

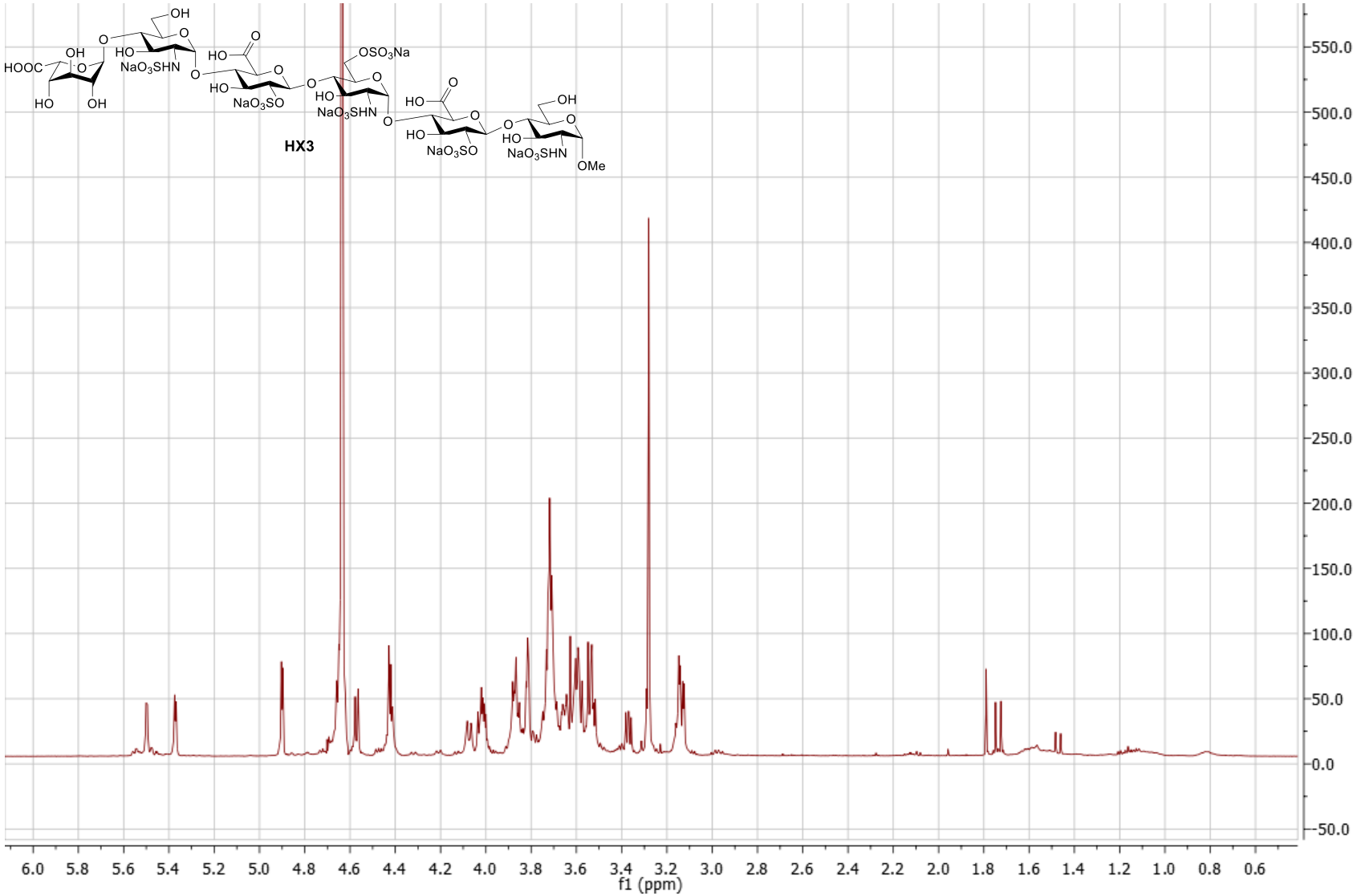

H3B
f2 (ppm)
f1 (ppm)

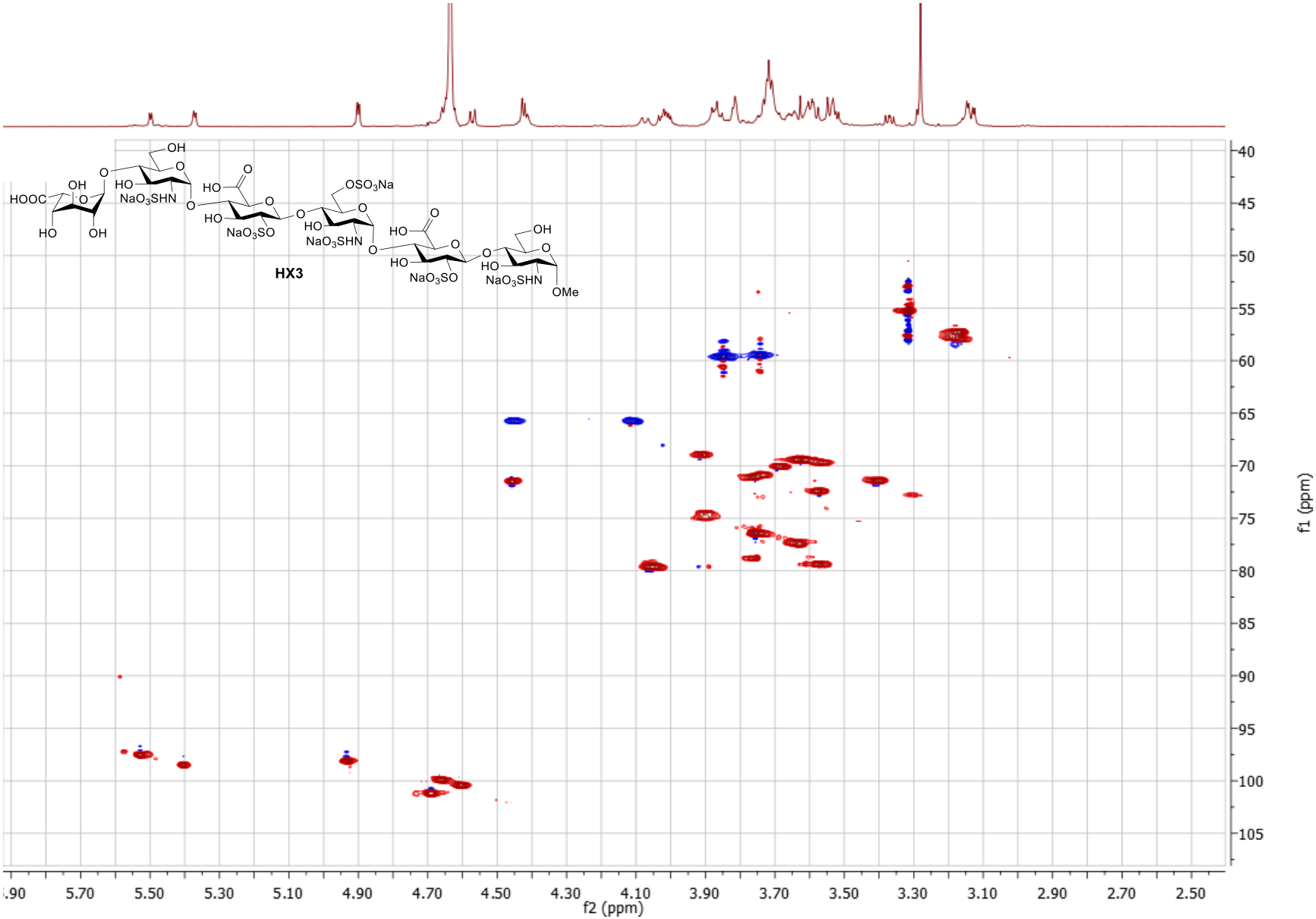

H3C
f1 (ppm)

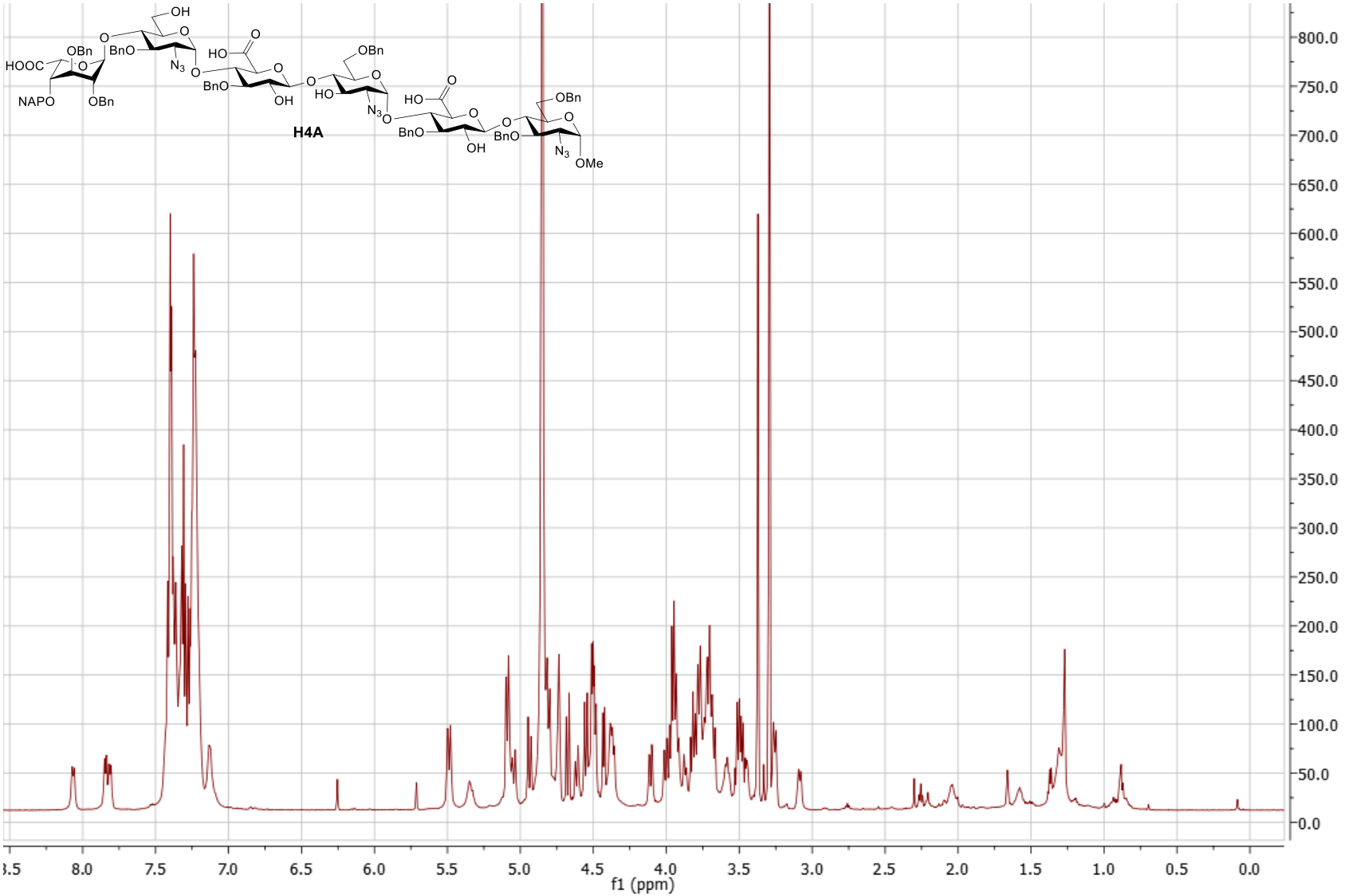

HOOC
OBn
BnO
NAPO
OBn
OBn
O
H2N
HO
BnO
NaO3SO
OSO3Na
BnO
H2N
HO
BnO
NaO3SO
OBn
BnO
H2N
OMe
H3C
8.0 7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8
f2 (ppm)
50 60 70 80 90 100 110 120 130
f1 (ppm)

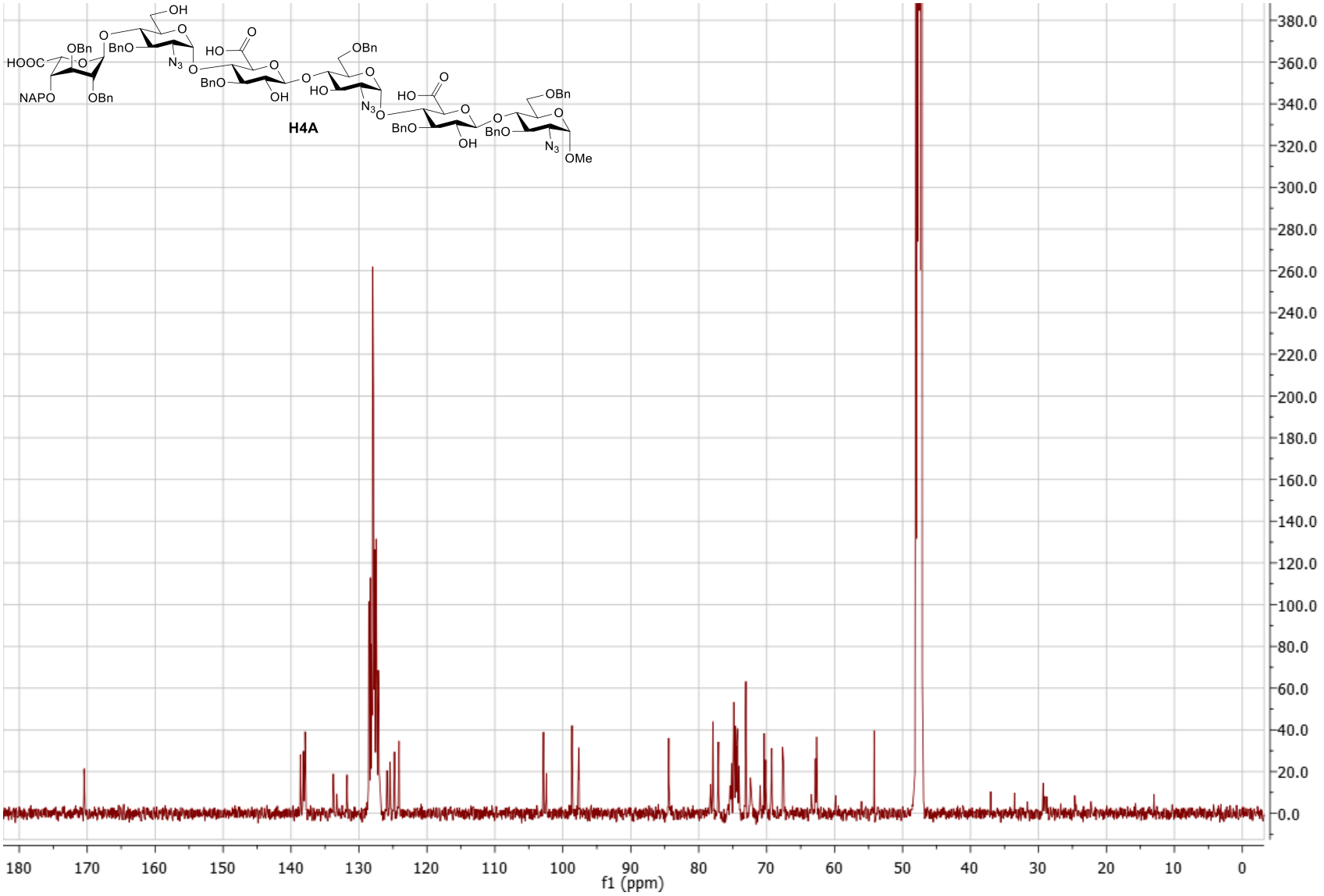

H3D
f1 (ppm)

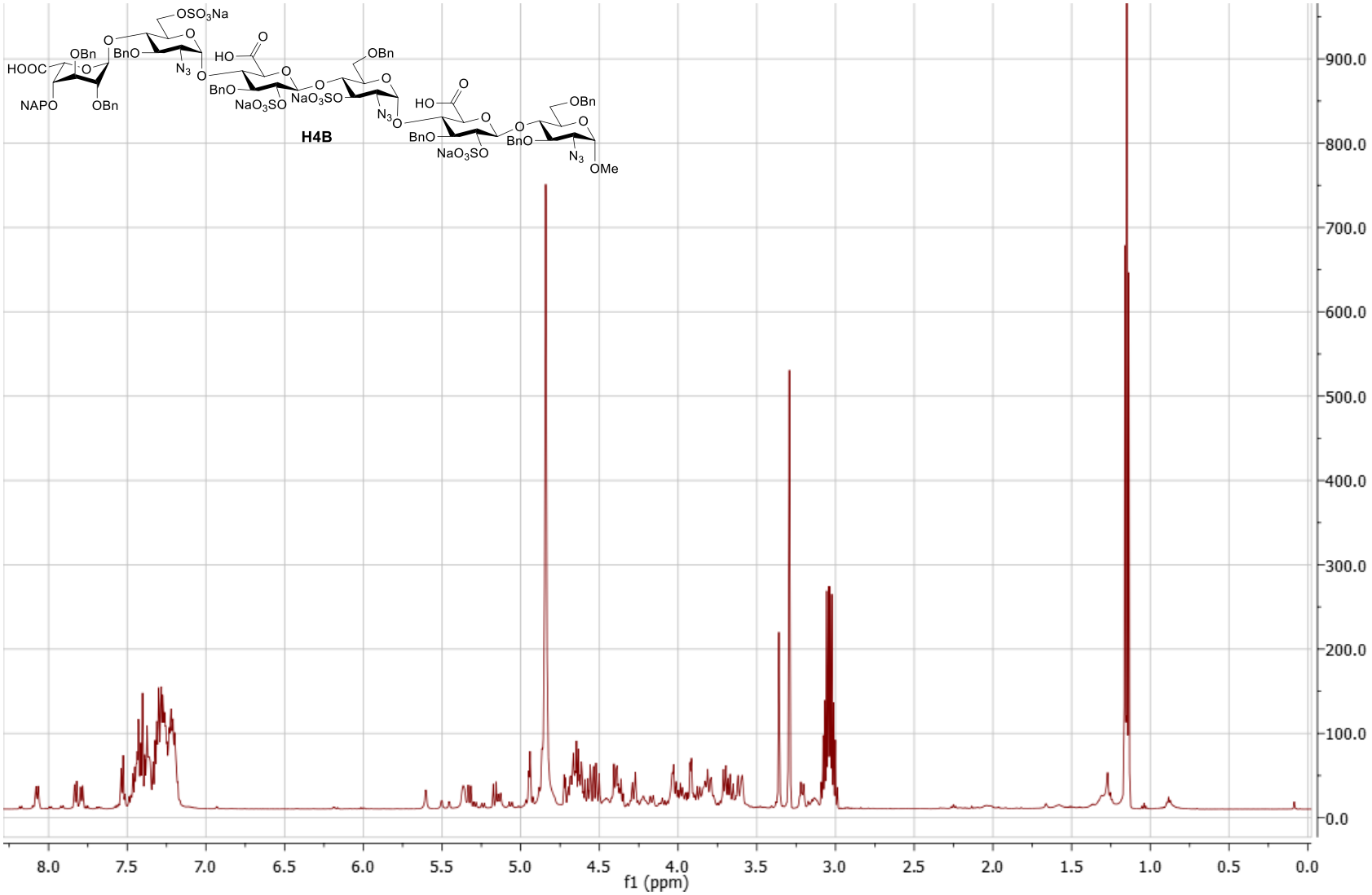

OBn
HOOC
OBn
BnO
NaO3SHN
NAPO
OBn
HO
OSO3Na
BnO
NaO3SO
BnO
NaO3SHN
HO
OBn
BnO
NaO3SO
BnO
NaO3SHN
OMe
H3D
f2 (ppm)
f1 (ppm)

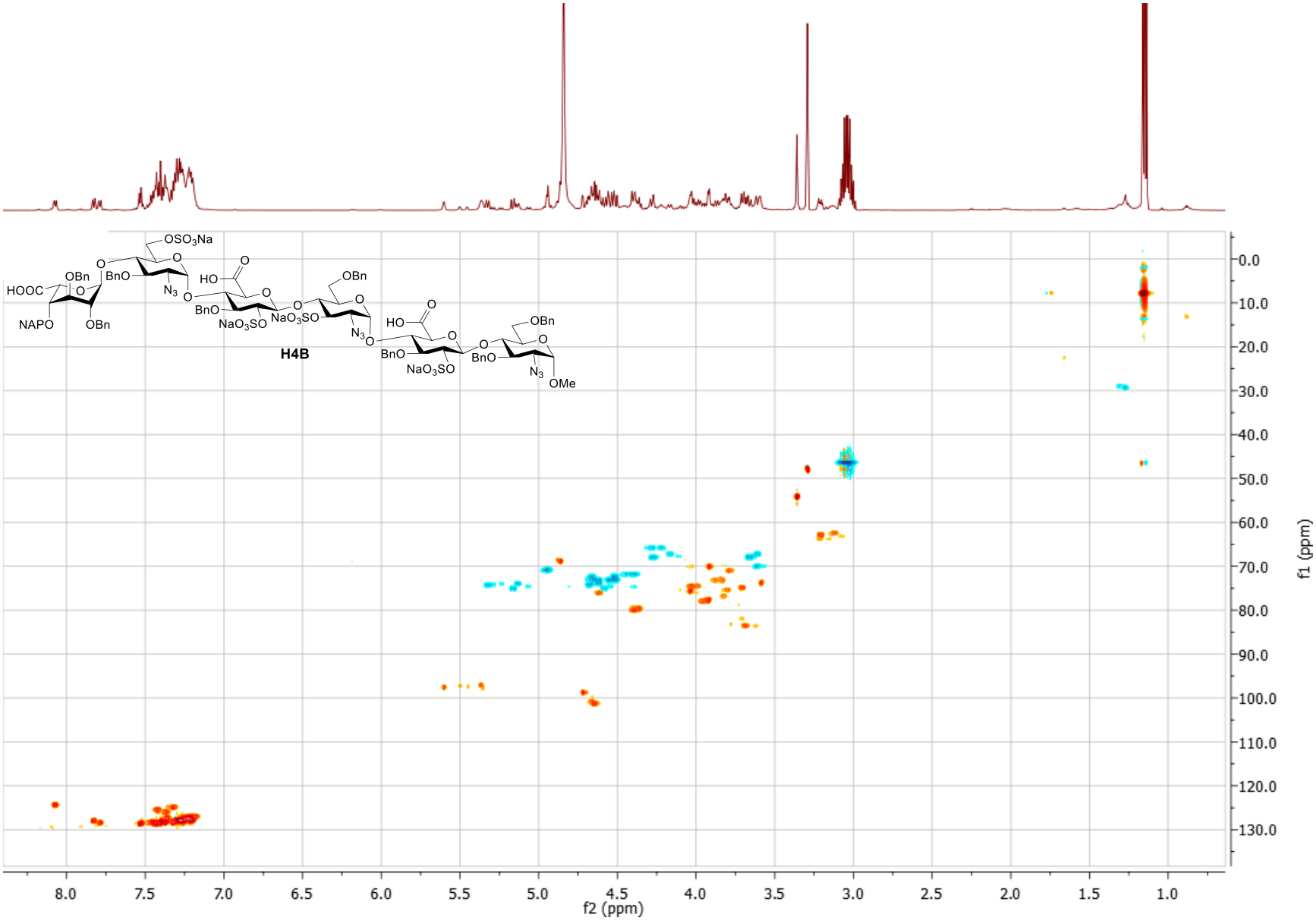

HX3
f1 (ppm)

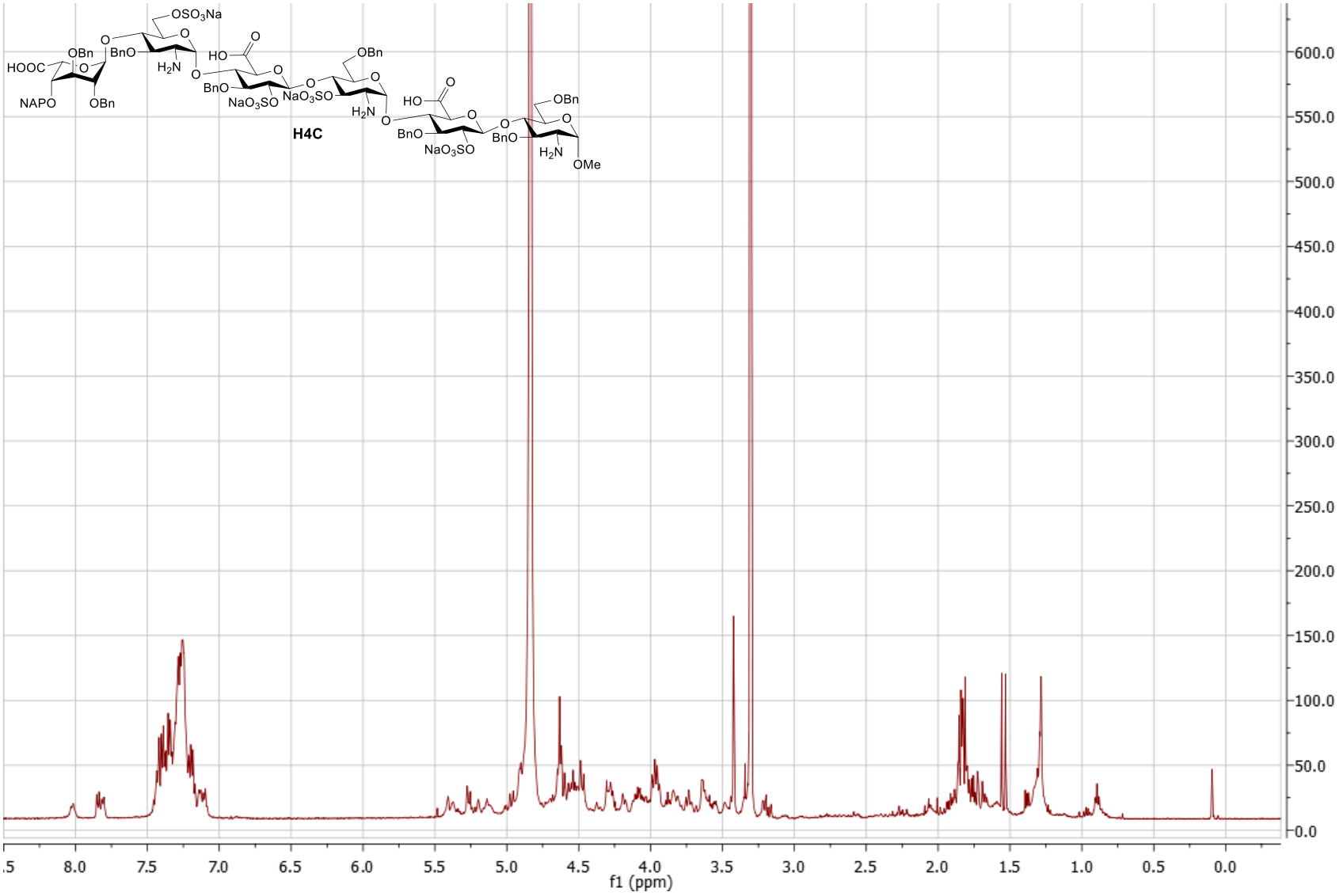

HX3
f2 (ppm)
f1 (ppm)

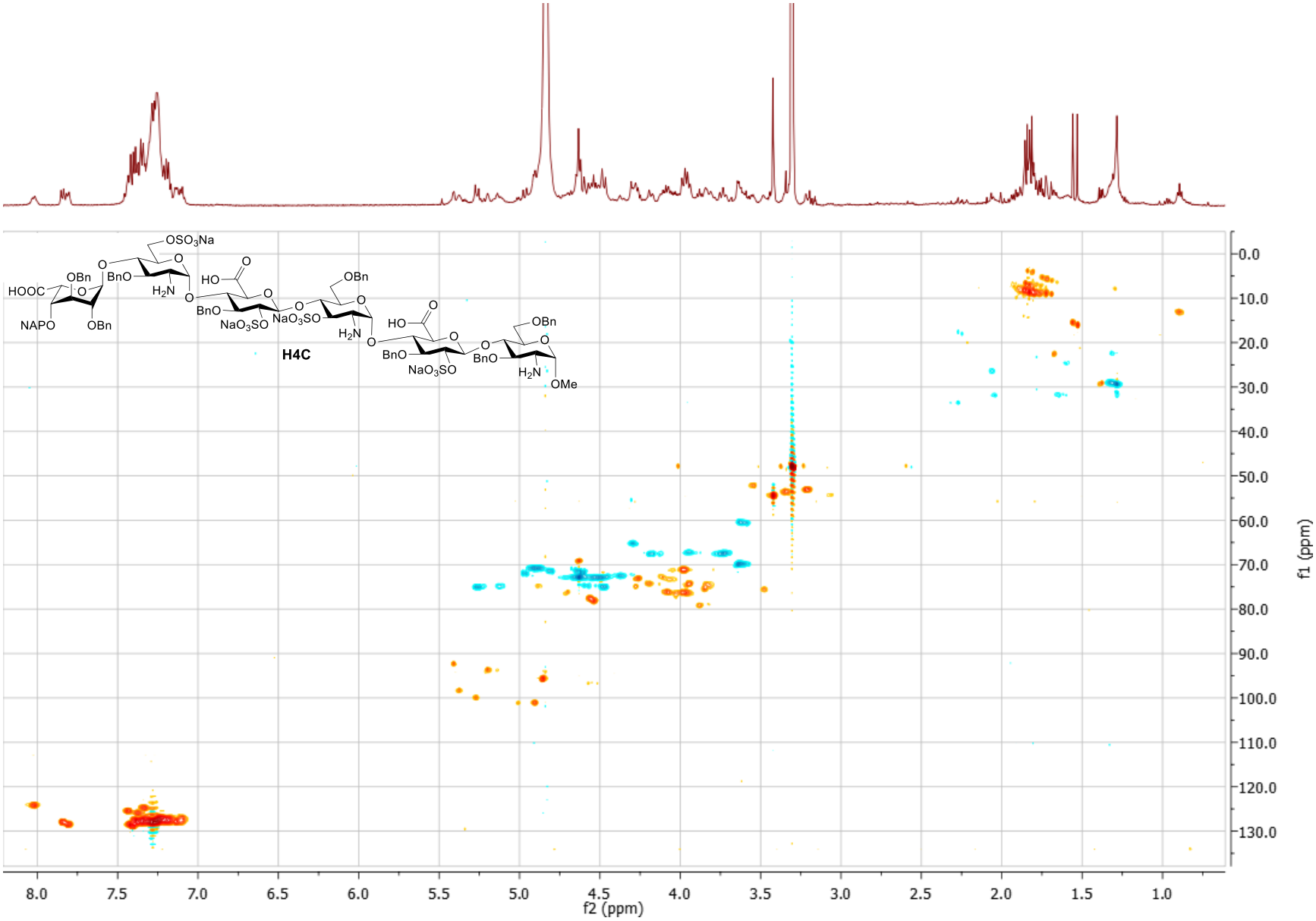

H4A
f1 (ppm)

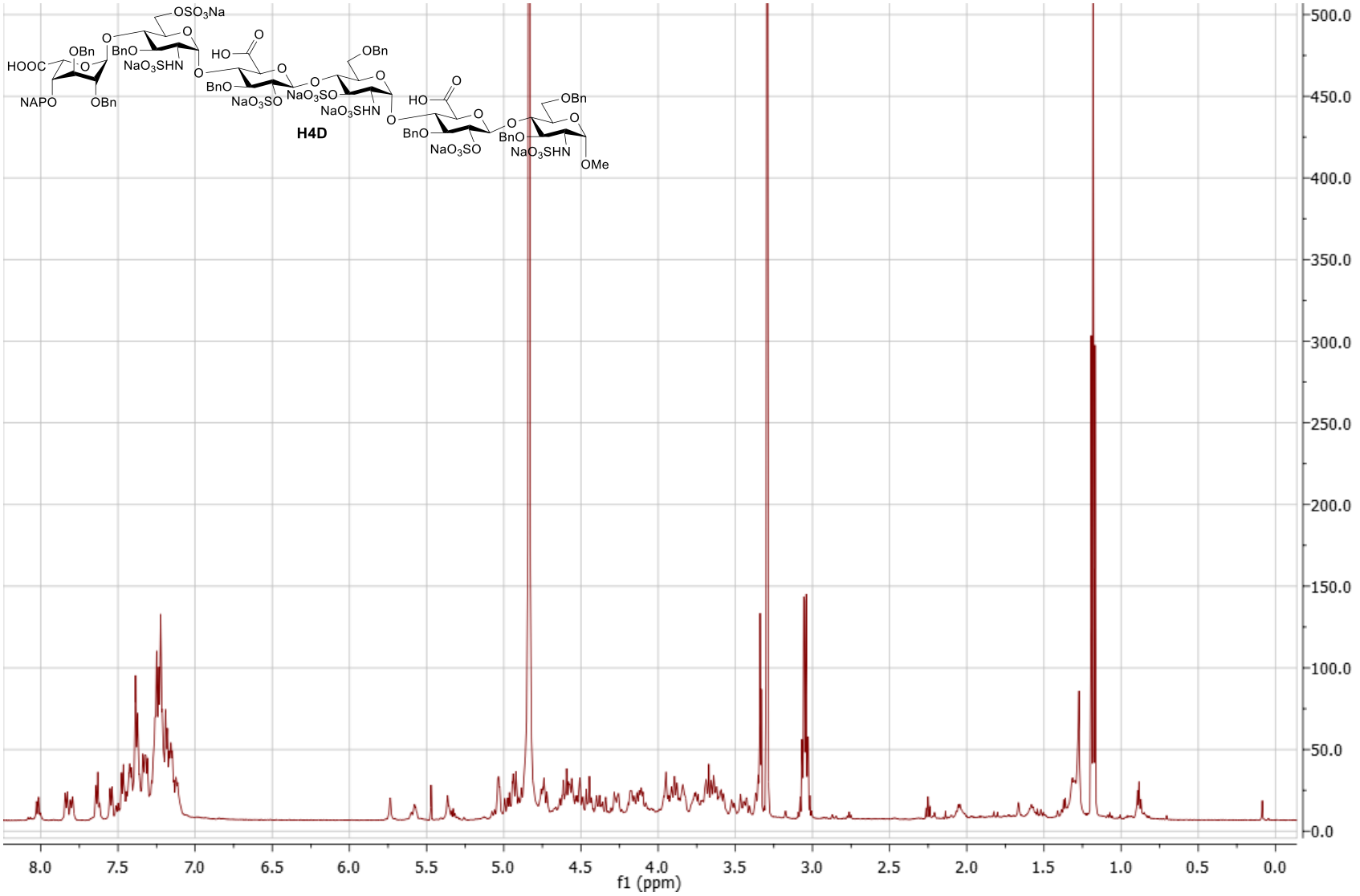

H4A
f1 (ppm)

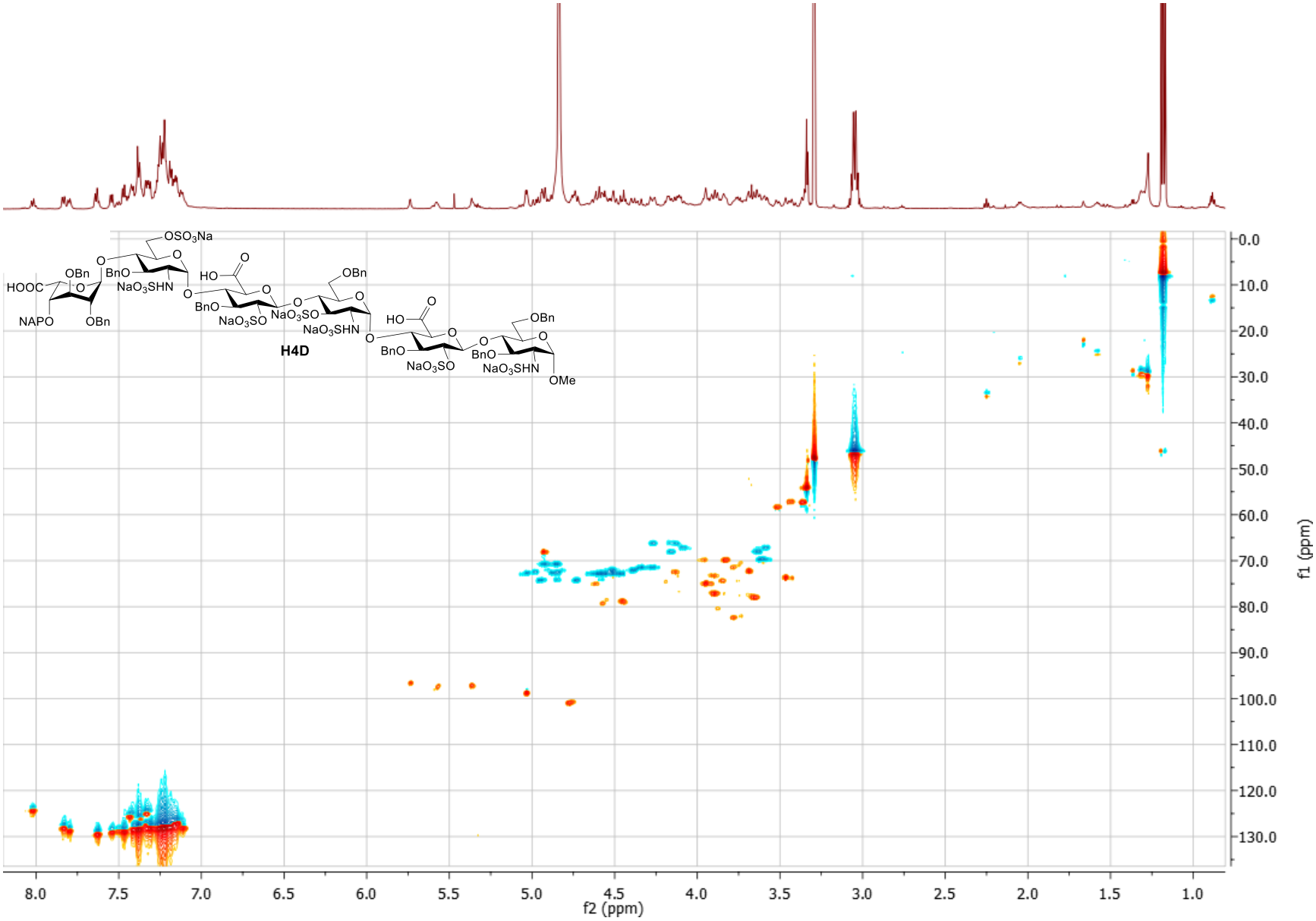

H4B
f1 (ppm)

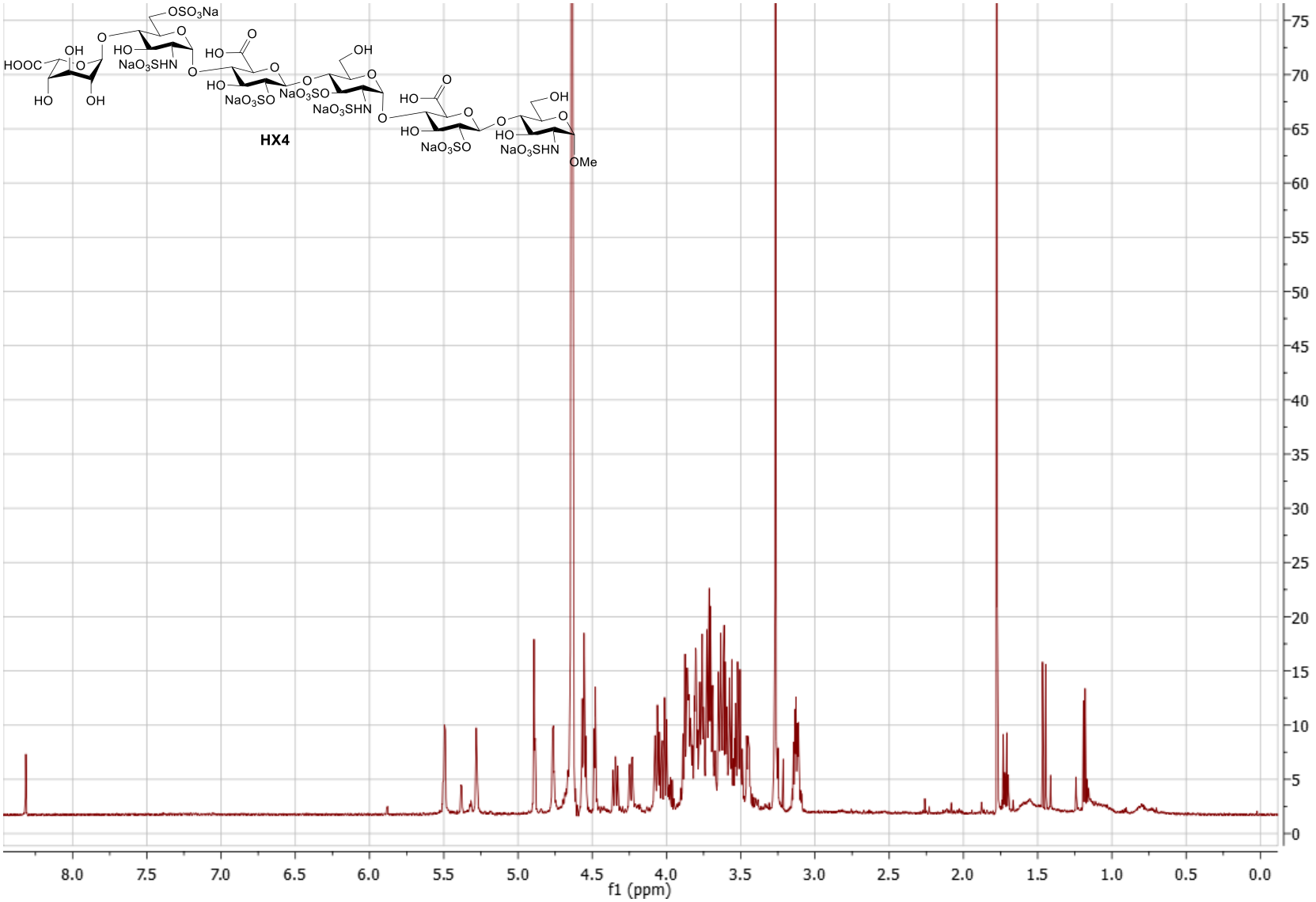

H4B
f2 (ppm)
f1 (ppm)

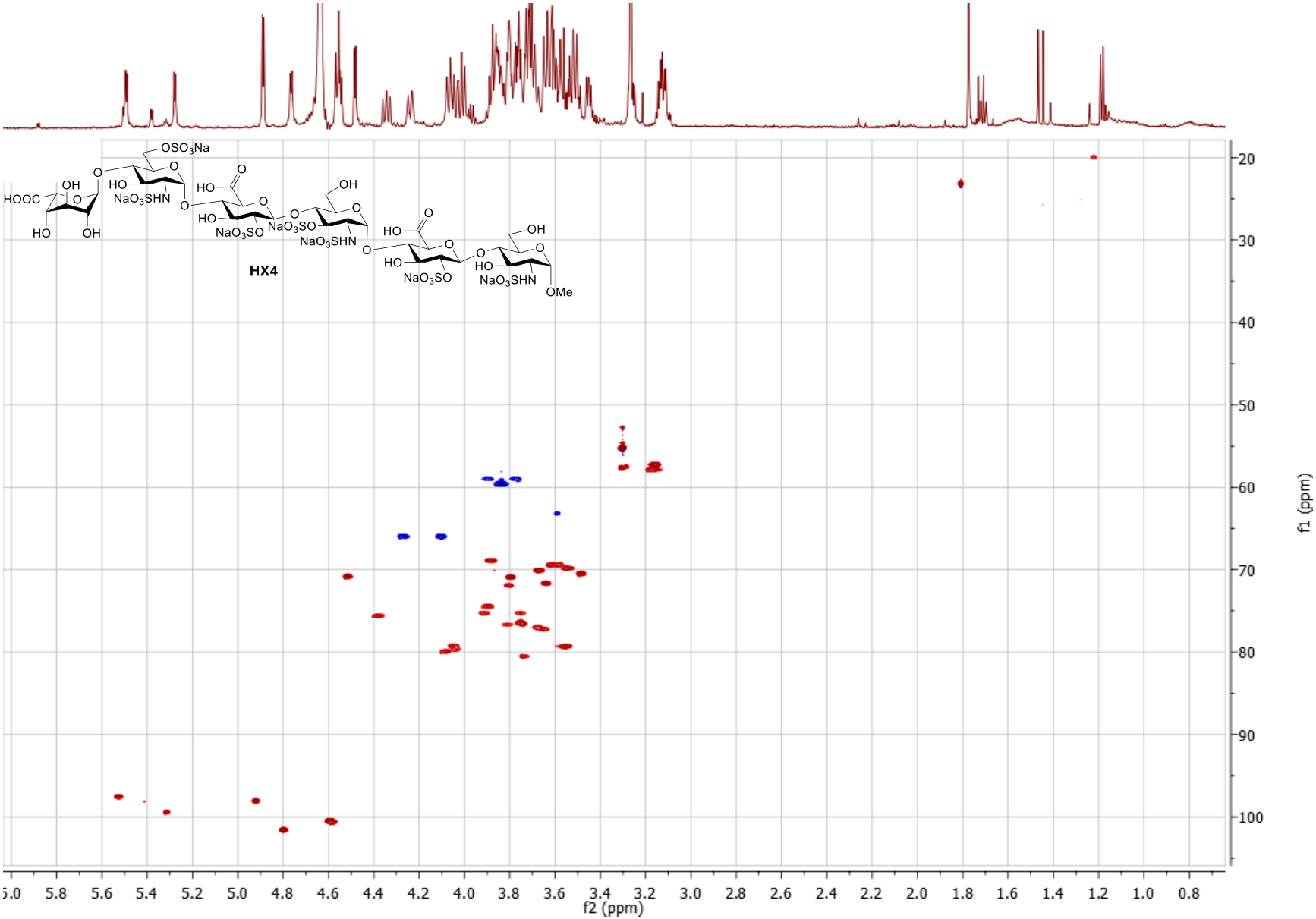

H4C
f1 (ppm)

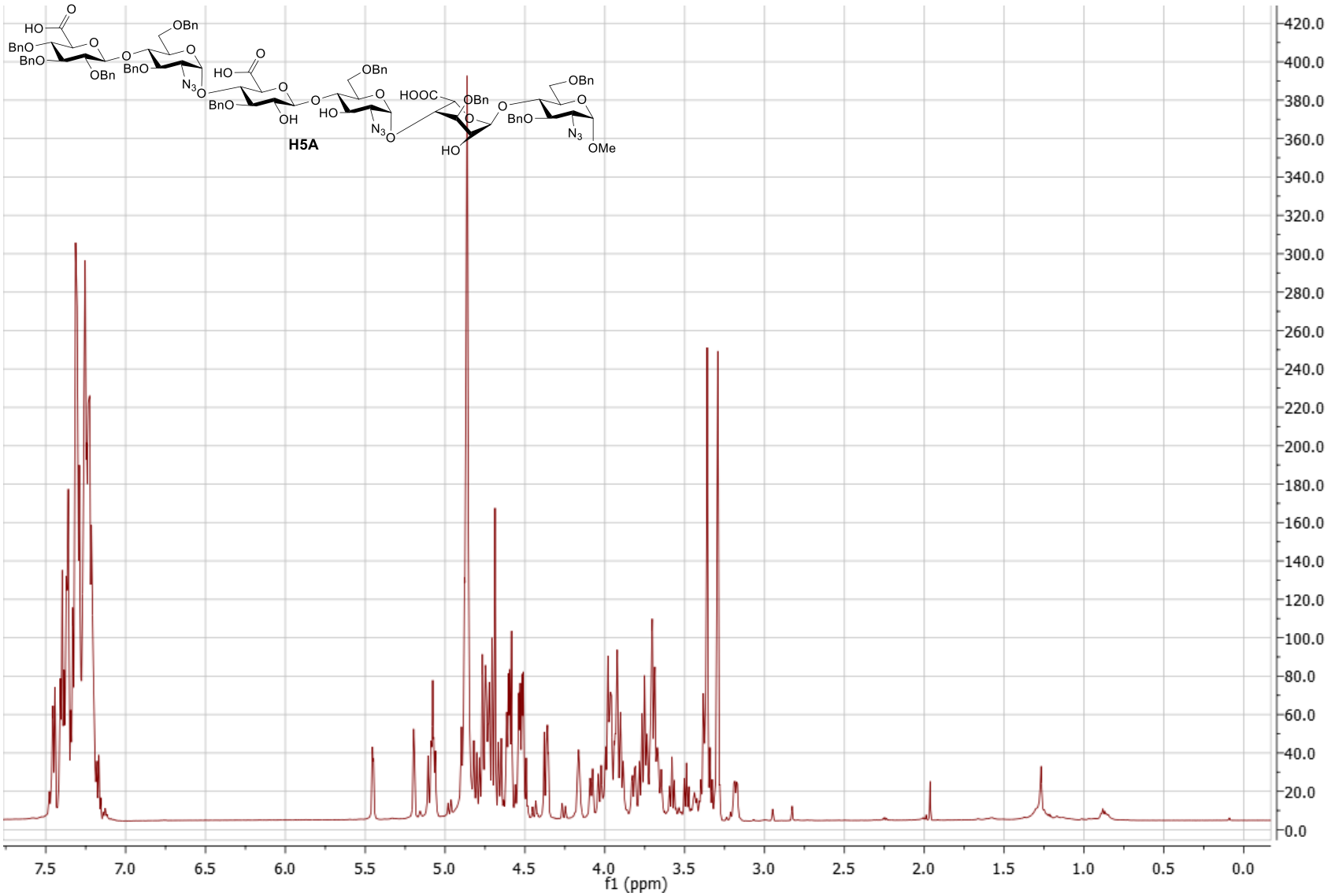

H4C
f2 (ppm)
f1 (ppm)

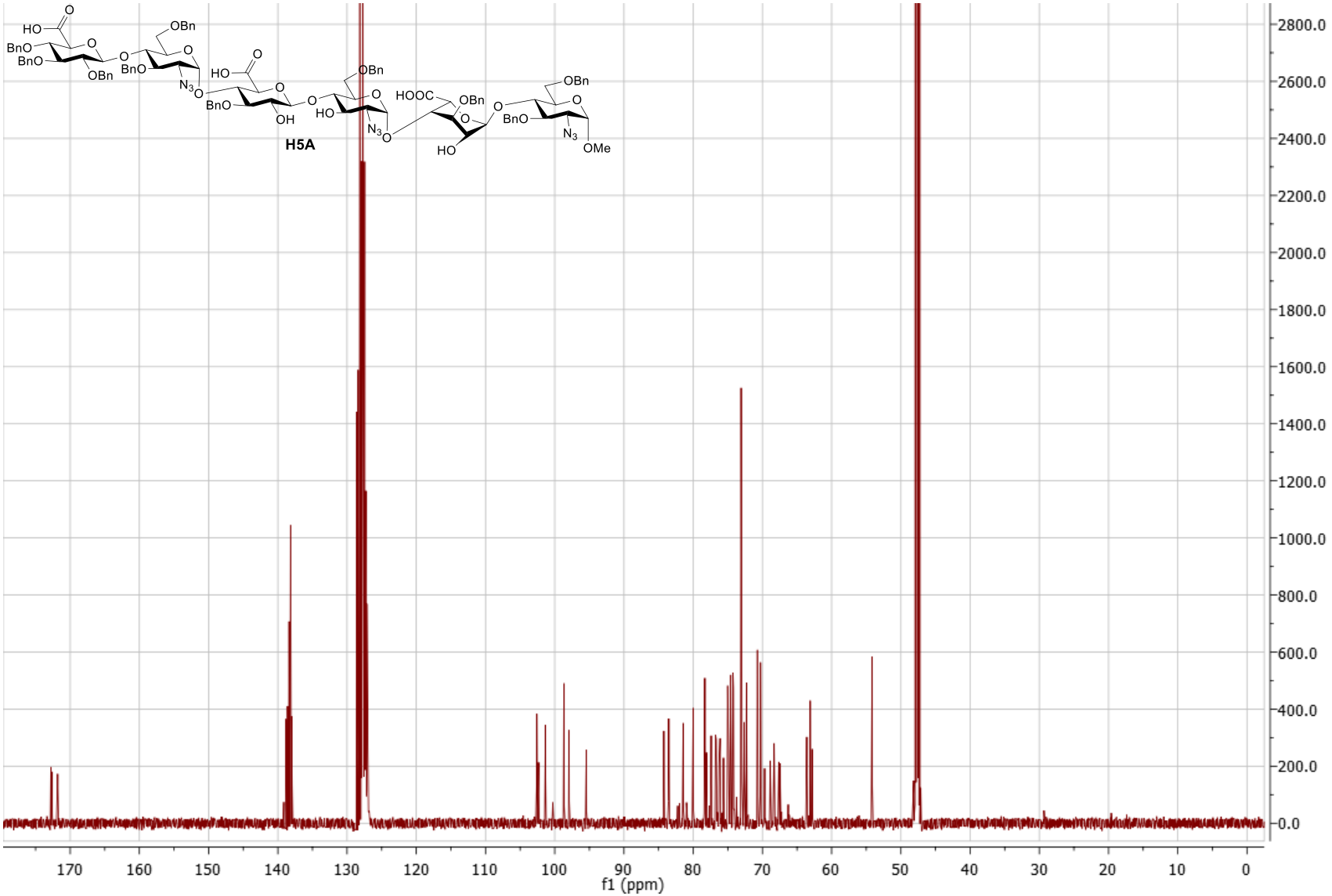

H4D
f1 (ppm)

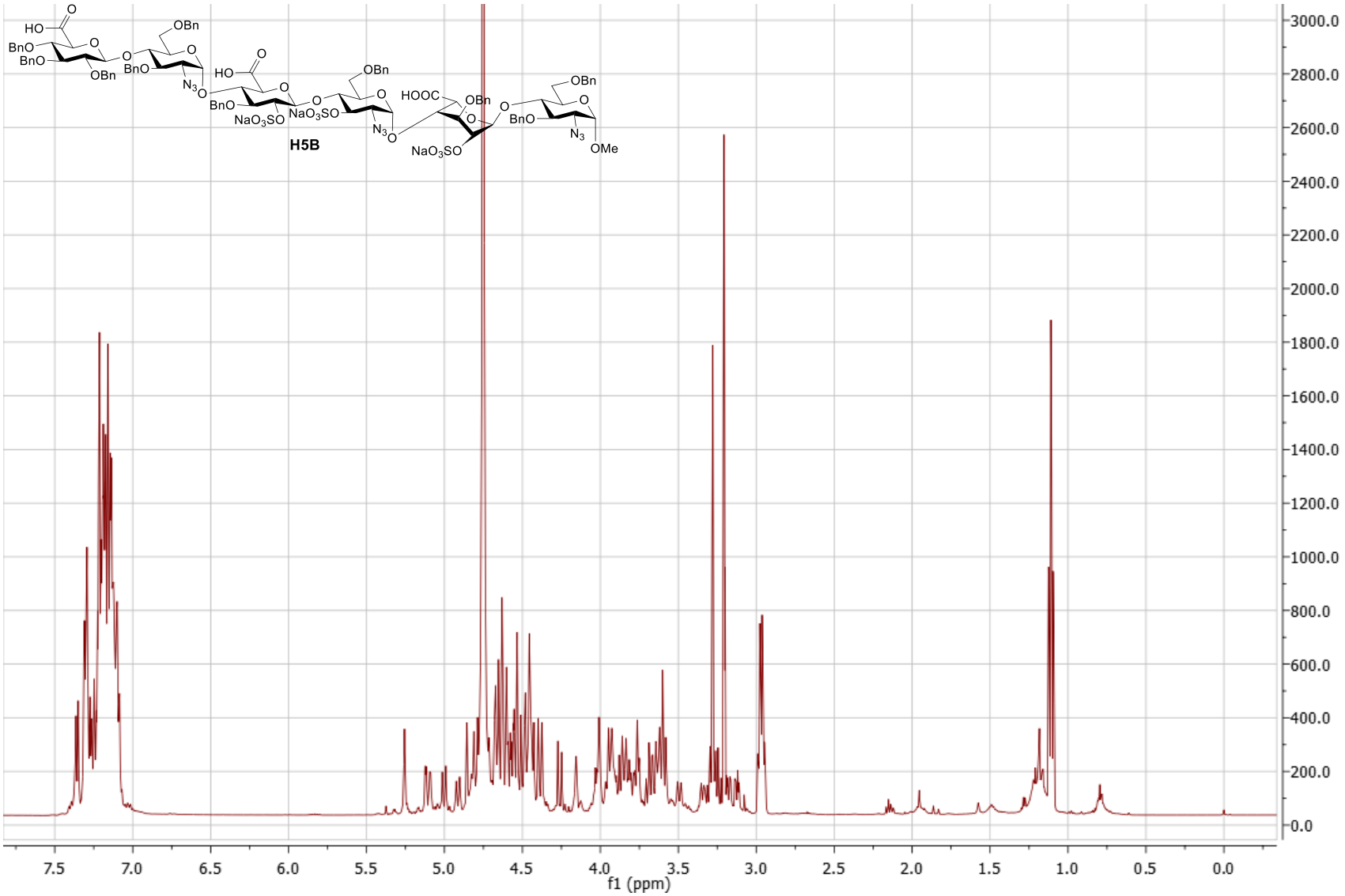

H4D
f2 (ppm)
f1 (ppm)

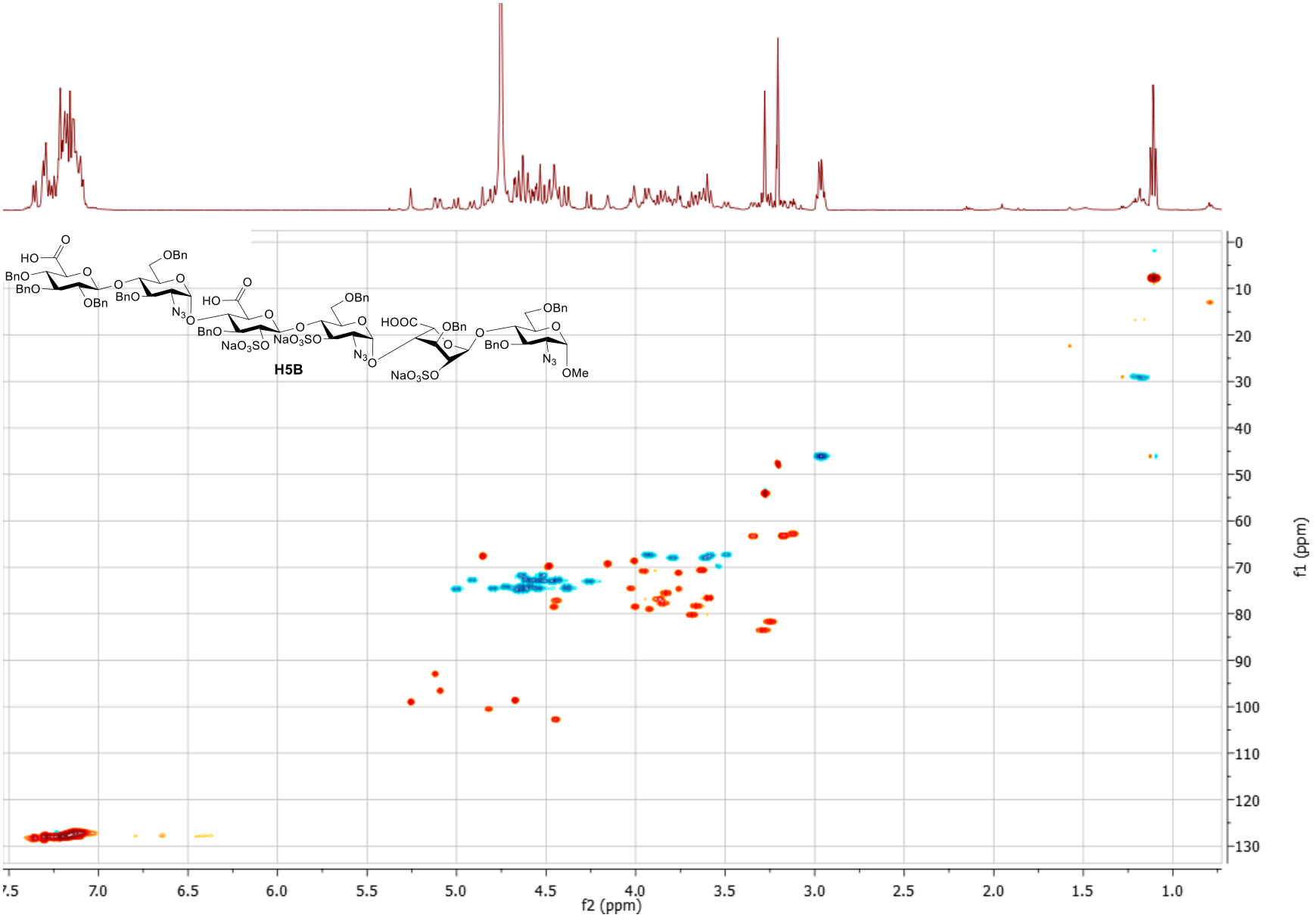

HX4
f1 (ppm)

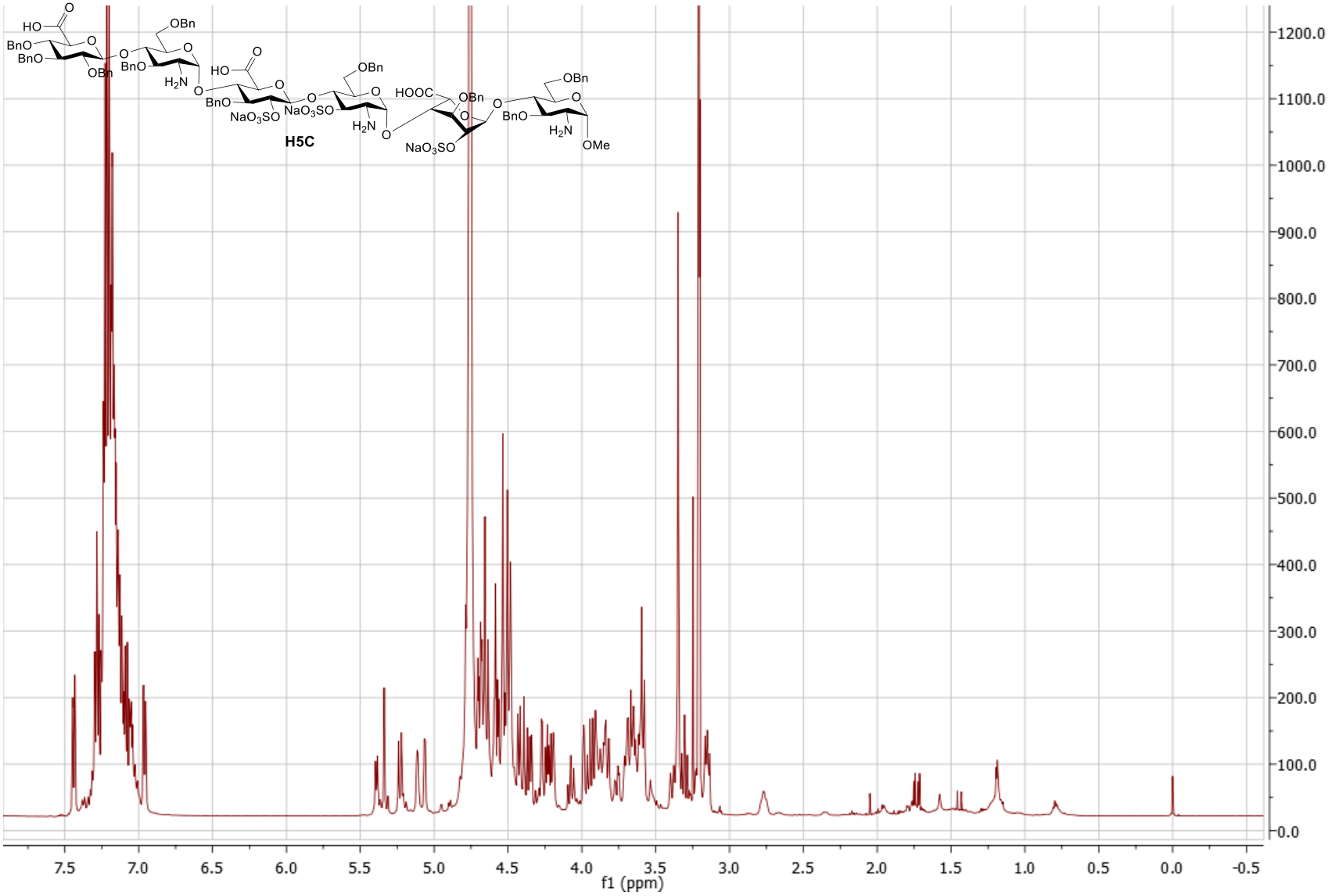

HX4
f2 (ppm)
f1 (ppm)

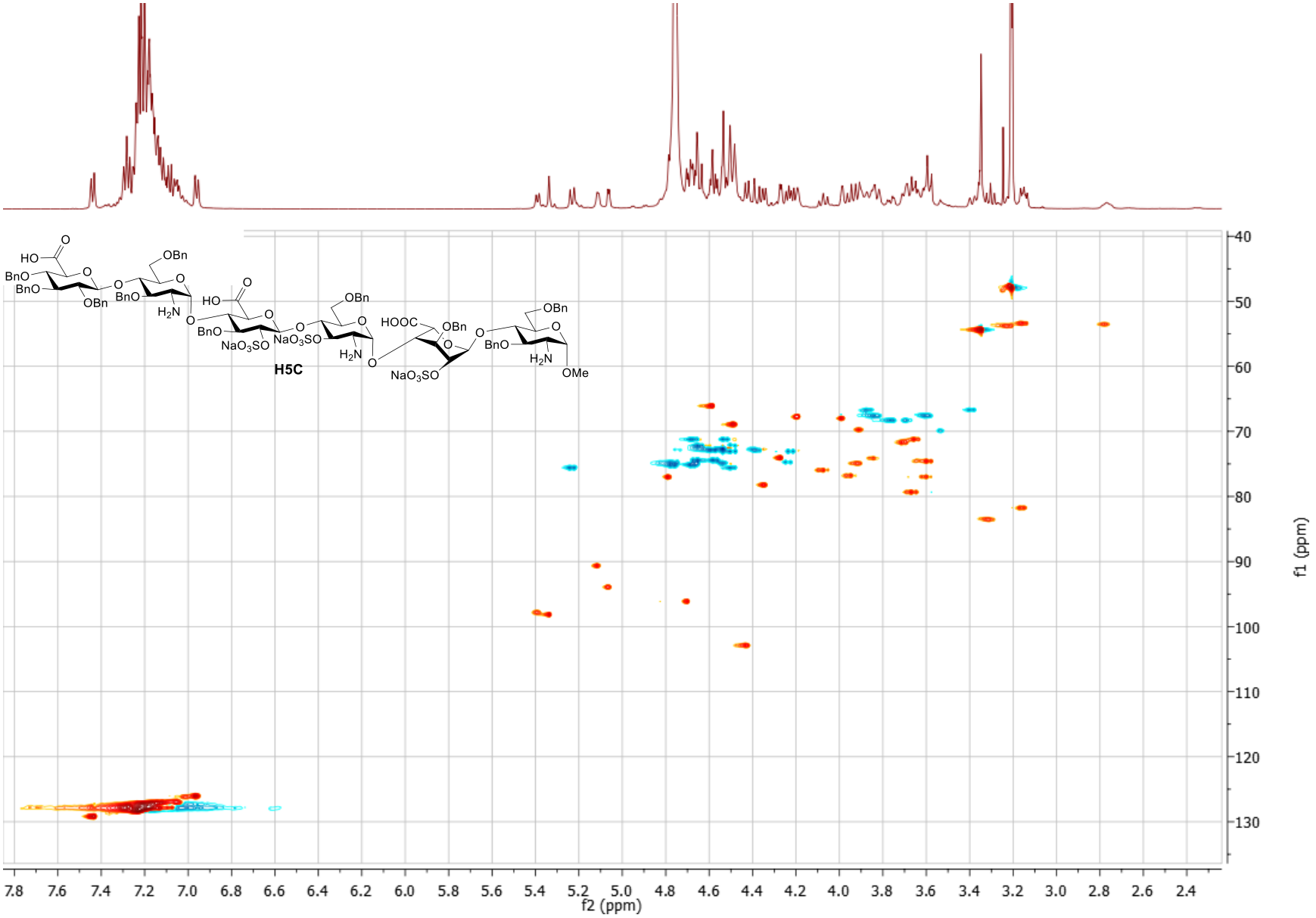

H5A
f1 (ppm)

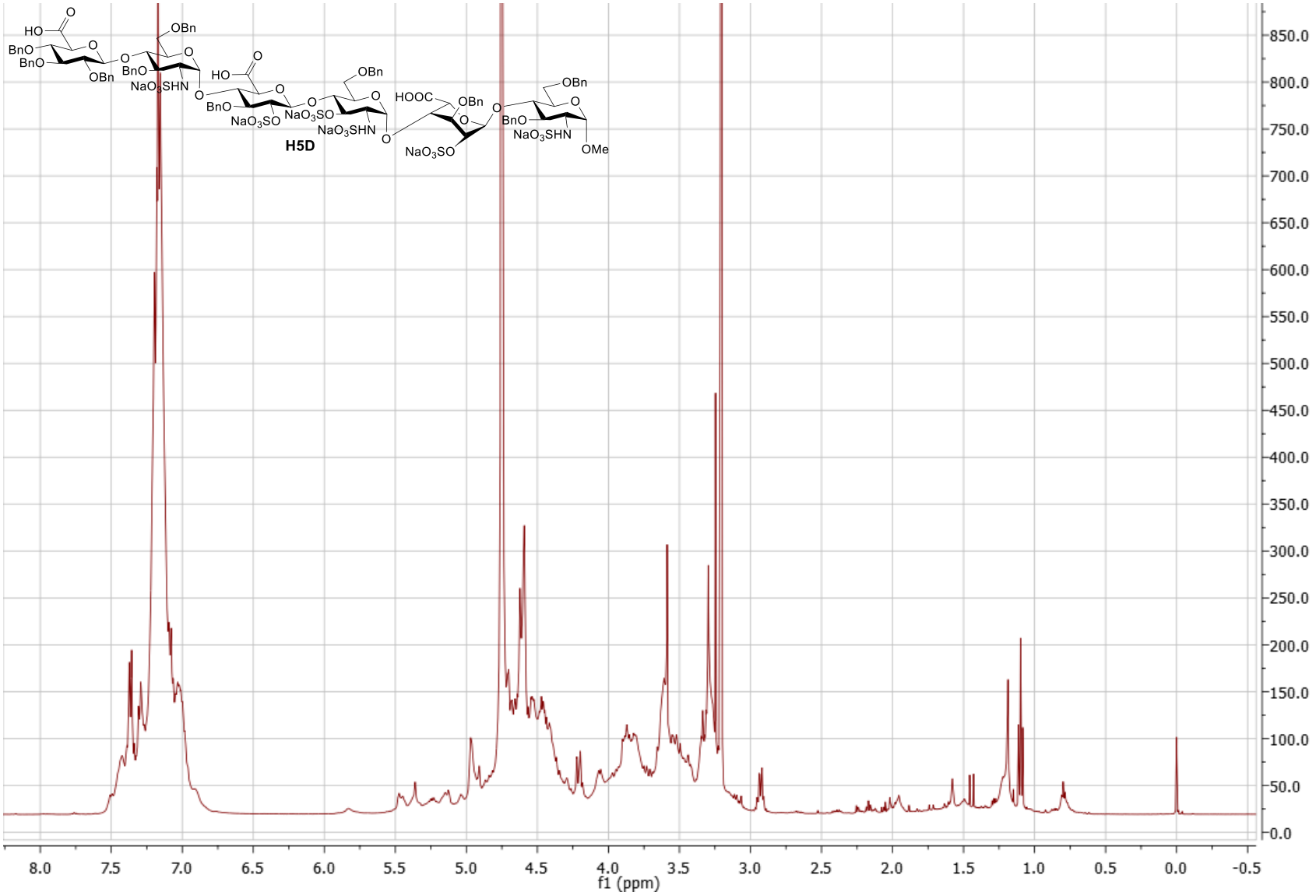

H5A
2800.0
2600.0
2400.0
2200.0
2000.0
1800.0
1600.0
1400.0
1200.0
1000.0
800.0
600.0
400.0
200.0
0.0
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

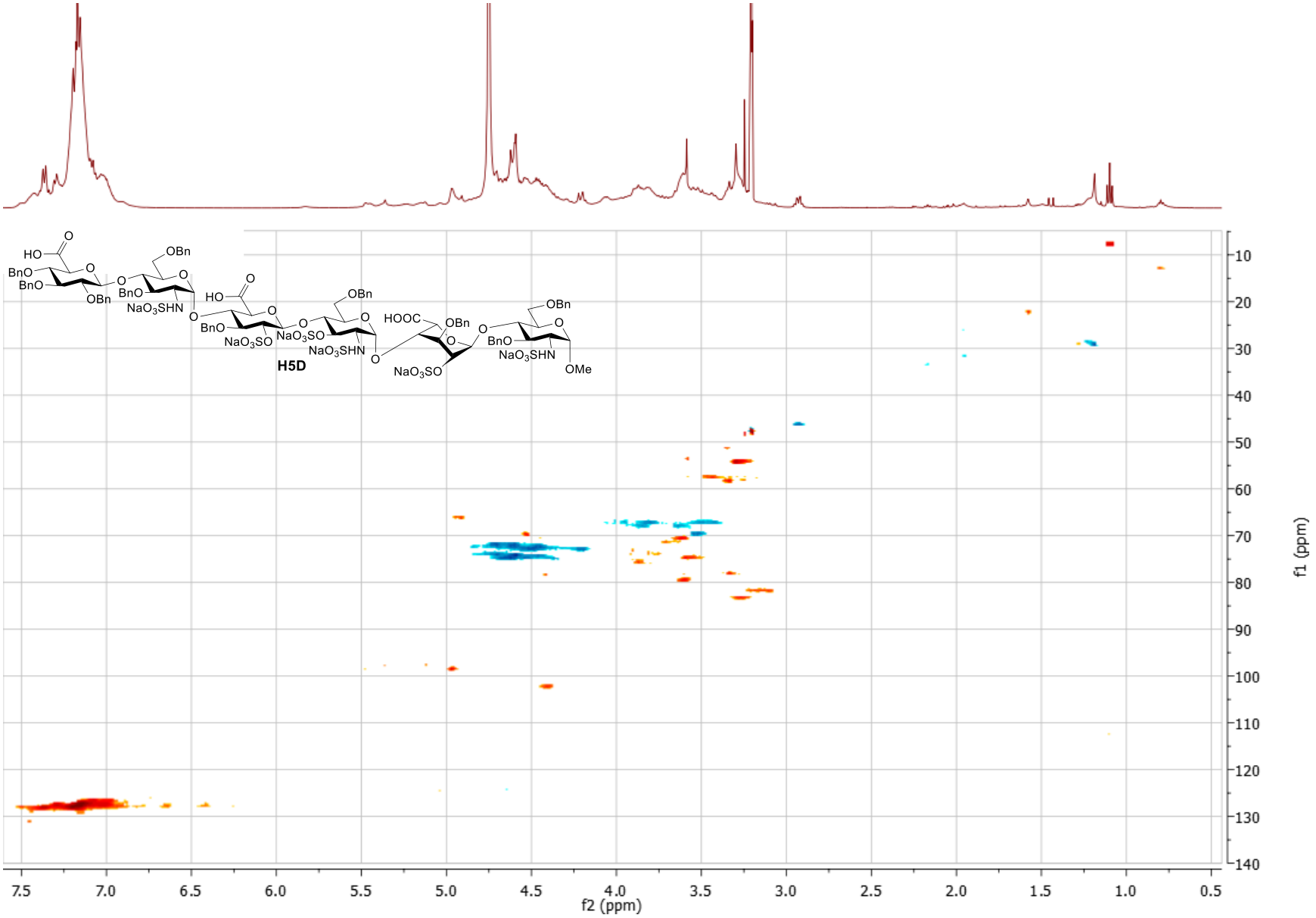

HO
BnO
BnO
OBn
O
BnO
N3
NaO3SO
HOOC
OMe
H5B
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
3000.0
2800.0
2600.0
2400.0
2200.0
2000.0
1800.0
1600.0
1400.0
1200.0
1000.0
800.0
600.0
400.0
200.0
0.0

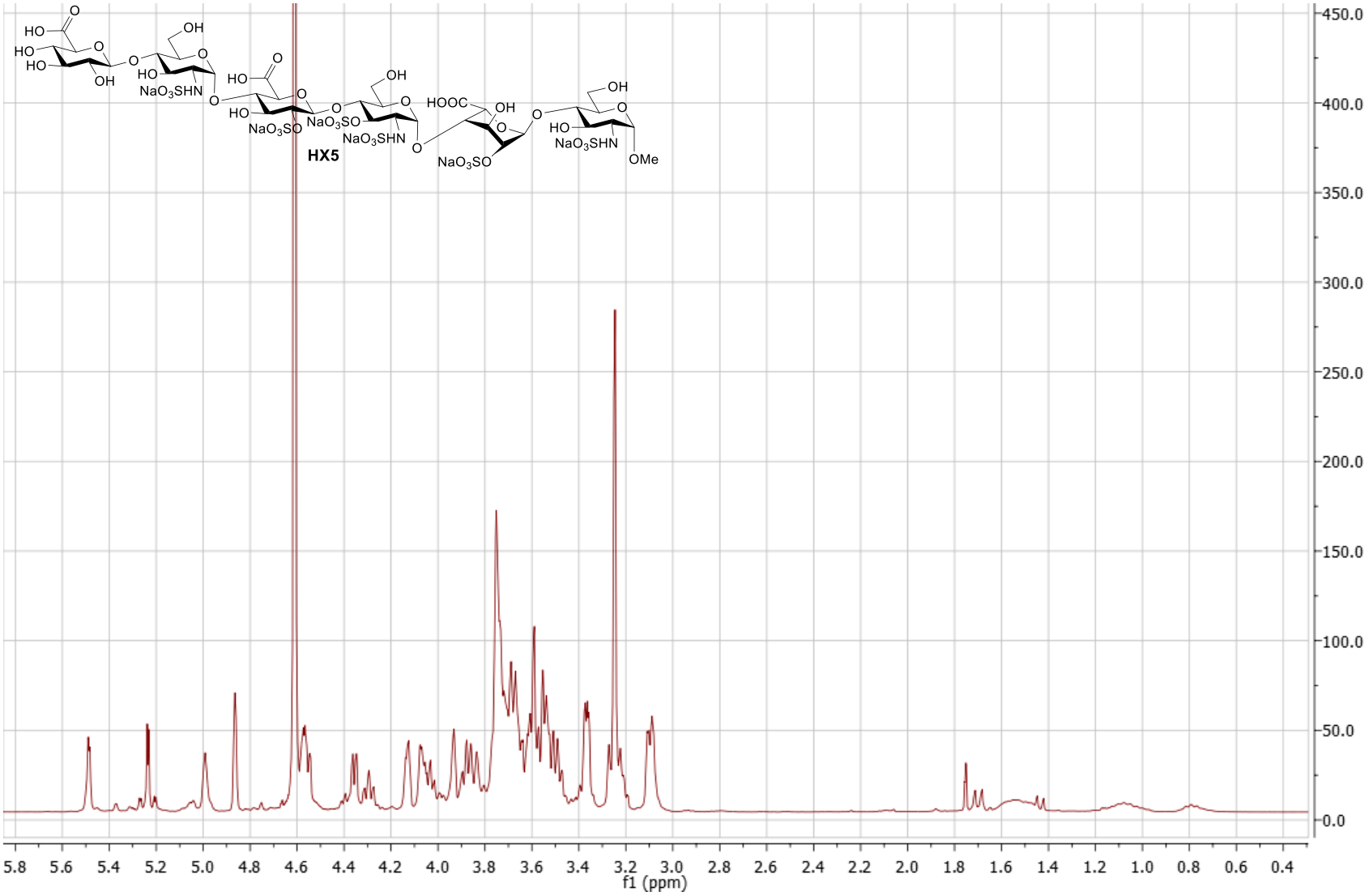

H5B
f2 (ppm)
f1 (ppm)

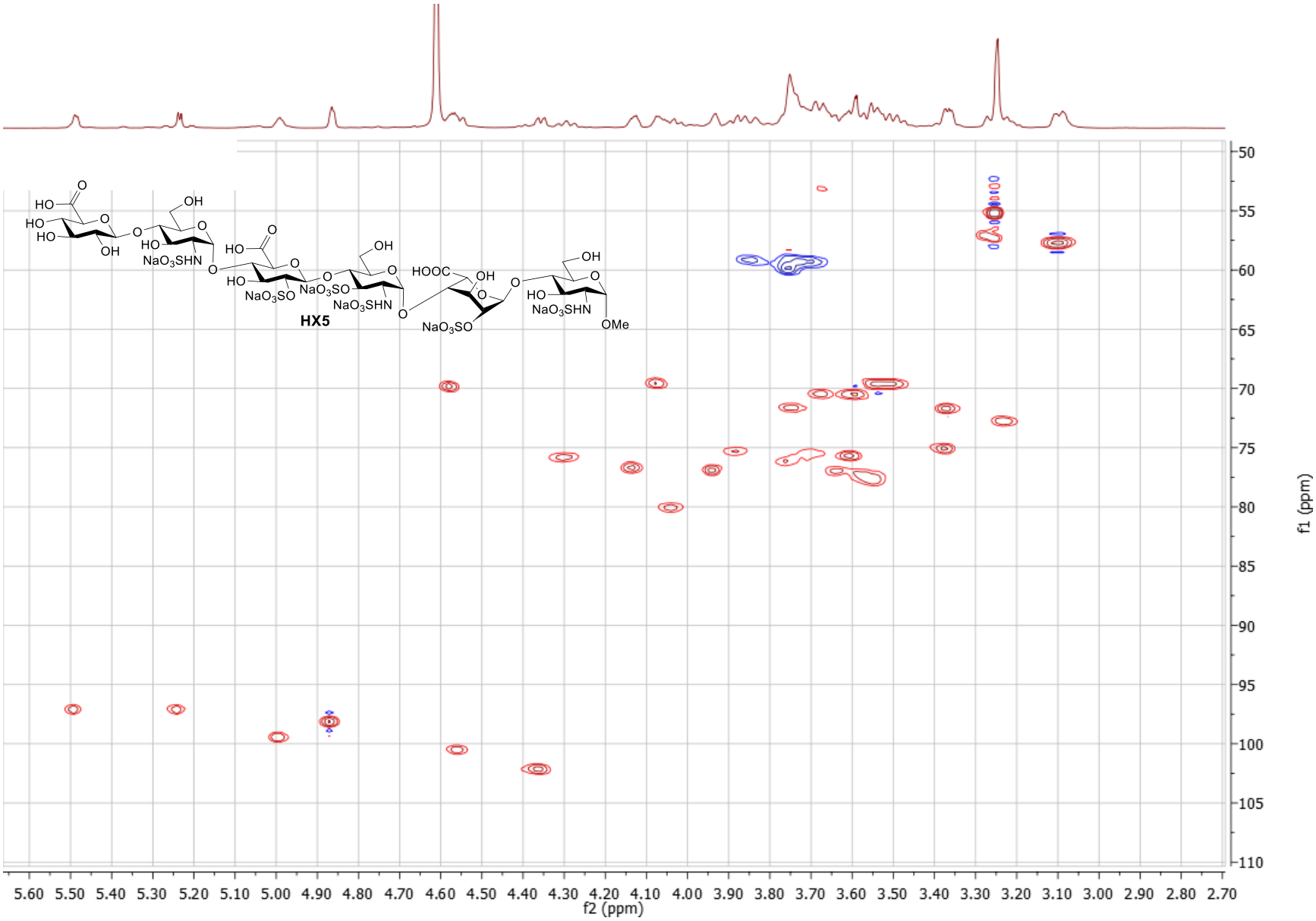

H5C
f1 (ppm)


H5C
f2 (ppm)
f1 (ppm)


H5D
f1 (ppm)


H5D
f2 (ppm)
f1 (ppm)


HX5
f1 (ppm)


HX5
f2 (ppm)
f1 (ppm)