Supporting Information

Rules for Priming and Inhibition of Glycosaminoglycan Biosynthesis; Probing the β4GalT7 Active Site

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Experimental part - Conformational analysis

NMR experiments for structural analysis were performed on a Bruker Avance III 600 MHz spectrometer equipped with a 5 mm PFG triple resonance probe and a Bruker AVANCE III 700 MHz spectrometer equipped with a 5 mm TCI Z-Gradient CryoProbe. Chemical shifts are reported in ppm using residual methanol (δ_H 3.31) and methanol-d_4 (δ_C 49.0) as references. NMR samples were prepared by dissolving 1–2 mg of the xylosides in 0.5 mL of methanol-d_4 (99.9%, Aldrich). ^{1}H and ^{13}C NMR chemical shift assignments were performed at 37 °C using DEPT-135,[1] 2D ^{1}H,^{1}H-TOCSY,[2] ^{1}H,^{13}C-HSQC,[3] ^{1}H,^{13}C-H2BC,[4] and ^{1}H,^{13}C-HMBC[5] experiments. ^{1}H chemical shifts and $^nJ_{H,H}$ coupling constants of compounds in Table S1 were determined with aid of the PERCH NMR spin simulation software[6] (PERCH Solutions Ltd., Kuopio, Finland). Chemical shifts and coupling constants were altered iteratively until the simulated and experimental spectra appeared highly similar according to visual inspection and the total root-mean-square value was close to or below 0.1%. Heteronuclear $^3J_{C,H}$ coupling constants were determined by use of the 1DLR experiment,[7] with a selective excitation of the ^{13}C resonance of the methyl group using a Gaussian-shaped pulse, in conjunction with a J-doubling analysis[8] performed with the web-based interface nuup.[9] Nuclear Overhauser effects were measured using 1D ^{1}H,^{1}H-DPFGSE-NOESY experiments,[10] deploying an r-SNOB pulse for selective excitation of the chosen resonance. Mixing times were varied from 0.15 – 0.50 s.

3D models of compounds **2a**, **2b**, **3a**, **3b**, **4a**, and **4b** were built using the Vega ZZ software (release 2.3.1.2).[11] The molecular structures were energy minimized, using algorithms included in the program, in consecutive order (i) steepest descent, (ii) conjugate gradient and (iii) truncated Newton. Calculated $^nJ_{H,H}$ coupling constants for the different ring conformations of compounds **2a**, **2b**, **3a**, **3b**, **4a**, and **4b** were based on the Karplus-type relationships proposed by Haasnoot *et al*.[12] as implemented in the Janocchio software.[13]

^{1}H NMR chemical shifts and homonuclear coupling constants, $^3J_{HH}$, were refined with aid of the PERCH NMR spin simulation software. The comparatively large coupling constants of 6 to 10 Hz observed for $^3J_{H1,H2}$, $^3J_{H2,H3}$, $^3J_{H3,H4}$ and $^3J_{H4,H5pro\text{-}S}$, where

applicable, point to the $^4C_1$ conformation being dominantly populated in all studied compounds, in accordance with calculated coupling constants based on Haasnoot-Altona parameterizations of Karplus-type relationships. This indication was used as the starting point for assessment of the stereochemical arrangements at the tertiary carbons.

Pyranoside ring conformational analyses of the xyloside compounds were impaired by the low number of $^3J_{HH}$ couplings accessible in the *C*-methyl xylosides; three for compounds **2a**, **2b**, **3a**, and **3b** and two for compounds **4a**, **4b**, and **6b**. Fitting of these data to two- or three-state models, as in previous studies, provide too large uncertainties for detailed descriptions of the conformational equilibria. Incorporation of $^3J_{H,C(Me)}$ coupling constants to the fitting procedure was attempted, although the measured couplings did not correspond well to calculated coupling constants from any of the available Karplus type relationships. This discrepancy presumably arise as a consequence of the geminal hydroxyl group causing an electronic situation at the methyl carbon not attributed for in the available set of equations – it is however beyond the scope of this article to investigate this further.

Table S1. δ_H, $^nJ_{H,H}$, $^3J_{H,C(Me)}$ and δ_C of xylosides in methanol-d_4 at 37 °C. For methylene groups the ^{1}H chemical shift, $^3J_{H,H}$ and $^3J_{H,C(Me)}$ of the H5pro-*R* proton is given prior to that of the H5pro-*S* proton.

Compound	1	2	3	4	5	Et/Me
2a	5.013		3.505	3.638	4.056, 3.465	1.368
			8.167	4.871, 8.810	-11.486	
	1.7		3.6			
	104.38	74.59	78.76	70.07	66.22	15.79
2b	5.042		3.293	3.861	4.027, 3.406	1.400
			8.850	5.358, 9.822	-11.341	
	1.1		1.7			
	103.35	74.30	78.55	68.97	66.66	20.91
3a	5.209	3.571		3.644	4.010, 3.563	1.342
	6.250			4.337, 8.424	-11.681	
		3.0		2.7		
	101.83	76.25	74.65	73.50	65.54	16.55
3b	5.326	3.414		3.554	3.801, 3.815	1.427
	7.231			4.994, 9.841	-10.966	
		2.0		1.5		

	101.19	75.35	74.07	72.03	65.71	22.38
4a	5.086	3.562	3.560		3.679, 3.479	1.299
	6.778	8.677			-11.415	
					2.9, 4.6	
	103.28	73.69	78.45	72.04	71.30	19.96
4b	4.998	3.809	3.380		3.756, 3.626	1.215
	7.709	9.334			-12.339	
			2.2		2.2, 1.4	
	103.36	73.14	77.71	72.21	72.15	21.71
6b	4.285	3.534	3.221		3.680, 3.376	1.146
	7.742	9.323			-12.479	
			2.3[a]		2.0,[a] n.d.[b]	
	104.44	73.33	77.78	72.30	72.13	21.67
4f	5.017	3.882	3.682	3.917	3.987, 3.780	
	7.018	8.957	3.546	2.971, 1.656	-12.385	
	102.91	72.36	74.23	69.61	67.14	
4g	4.986	3.838	3.464		3.836, 3.665	1.565, 1.789, 0.955
	7.719	9.261			-12.392	-14.270, 7.629, 7.677
			2.0		n.d., n.d.	
	103.20	73.22	76.36	74.27	70.14	29.02, 7.89
5a	5.491	3.767	3.859	3.561	4.347	1.259
	3.773	5.921	5.313	3.006	6.741	
					1.9	
	100.88	72.19	72.82	73.34	67.78	15.46
5b	5.047	3.510	3.458	3.130	3.569	1.350
	7.796	9.282	9.037	9.364	6.190	
					3.5	
	102.23	75.27	77.78	76.91	73.55	18.15

[a]Measured from anti-phase peak separation; [b]n.d. = not determined

Experimental part – Biological testing

Cell culture, radiolabeling and extraction procedures

Cells were cultured as monolayers according to manufacturer's instructions. pgsA-745 xylosyltransferase-deficient Chinese hamster ovarian cells (ATCC) were harvested by trypsinization and inoculated in 6-well microculture plates (Nunc A/S) at plating densities of 2 x 10^5 cells/well in Ham's F12-K medium supplemented with 7.5% (v/v) fetal calf serum (FBS), penicillin (100 U/mL), and streptomycin (100 μg/mL) (all from Life Technologies), at 37 °C in a 5% CO_2 in air atmosphere. After 24 h of plating, the cells were incubated with low sulfate MEM $MgCl_2$-medium supplemented with 10% (v/v) FBS, 1% (v/v) L-glutamine, penicillin (100 U/mL), streptomycin (100 μg/mL) (all from Life Technologies), 10 μCi/mL of [^{35}S]sulfate (Perkin Elmer), and different xylosides at concentrations of 0.1 or 1 mM. Controls without xylosides were included. Dilutions of xylosides were made from 20 and 200 mM stock solutions in Me_2SO/H_2O (1:1, v/v) and Me_2SO, respectively. After 5 h of incubation, the culture media were collected. Breast cancer cells, HCC70 (ATCC), were allowed to grow to confluence in T25 flasks (Nunc A/S) in RPMI-1640 medium ATCC modification supplemented with 10% (v/v) FBS, penicillin (100 U/mL), and streptomycin (100 μg/mL) (all from Life Technologies), at 37 °C in a 5% CO_2 in air atmosphere. Subsequently, the cells were incubated with low sulfate MEM $MgCl_2$-medium supplemented with 10% (v/v) FBS, 1% (v/v) L-glutamine, penicillin (100 U/mL), streptomycin (100 μg/mL) (all from Life Technologies Carlsbad, CA), 20 μCi/mL of [^{35}S]sulfate sulfate (Perkin Elmer, Waltham, MA), and different xylosides at concentrations of 0.1 mM. Dilutions of xylosides were made from 20 mM stock solutions in Me_2SO/H_2O (1:1, v/v). After 24 h of incubation, the culture media were collected.

Isolation of xyloside-primed [^{35}S]sulfate-labeled polyanionic material

The procedures have been described in detail previously.[14] [^{35}S]Sulfate-labeled polyanionic macromolecules were isolated from the culture medium by ion exchange chromatography, performed by allowing the samples to pass over a 0.4 mL column of DE-53 DEAE-cellulose (Whatman/GE Healthecare, Sweden) equilibrated with 6 M

urea, 0.5 M NaOAc, pH 5.8, 5 μg/mL ovalbumin, 0.1% (v/v) Triton X-100 (5 mL). After sample application, the columns were washed successively with (a) equilibration buffer (5 x 1 mL), (b) 6 M urea, 10 mM Tris, pH 8, 5 μg/mL ovalbumin, 0.1% (v/v) Triton X-100 (5 x 1 mL), and (c) 50 mM Tris-HCl, pH 7.5 (5 x 2 mL). Bound material was eluted with 4 M guanidine-HCl, 50 mM NaOAc, pH 5.8 (3 x 0.4 mL). The eluted [^{35}S]sulfate-labeled polyanionic material was separated from hydrophobic material by using a 0.3 mL Octyl-Sepharose CL-4B (Pharmacia-LKB) column equilibrated with 4 M guanidine-HCl, 50 mM NaOAc, pH 5.8 (5 mL). After equilibration, 400 μg of BSA was added to avoid unspecific binding, and subsequently the columns were washed again with 4 M guanidine-HCl, 50 mM NaOAc, pH 5.8 (5 mL). The samples were applied to the column, and subsequently the unbound [^{35}S]sulfate-labeled polyanionic material was washed with 4 M guanidine-HCl, 50 mM NaOAc, pH 5.8 (3 x 0.3 mL). Precipitation of radioactive samples was performed with EtOH (95%, 7.5 vol) over night at -20 °C using 100 μg of dextran T-500 (Pharmacia-LKB, Gaithersburg, MD) as a carrier. The samples were the centrifuged at 4400 rpm for 50 min, and the remaining pellets were dissolved and run through a Superose 6 HR 10/30 column (mobile phase: 4 M guanidine-HCl, 50 mM NaOAc, pH 5.8, 0.2% Triton X-100) connected to a FPLC system equipped with a fraction collector (Pharmacia-LKB). Radioactivity in each fraction was determined using a Wallac 1414 Liquid Scintillation controlled by a WinSpectral software system Counter (Perkin Elmer). When pgsA-745 cells were used, the culture media were purified by ion exchange chromatography, as described above. The pellets remaining after precipitation were dissolved in H_2O and 10 % were counted in a β-counter to determine the radioactivity.

Impurity discussion

In our first investigation of the GAG priming ability of the xyloside analogs, we were surprised to detect GAG priming of compounds **2b**, **4b**, **4g**, and **6b**. When given to cells at concentrations of 1 mM the amount of the isolated [^{35}S]sulfated material were similar to that of cells treated with XylNap (**1a**, Figure S1). However, first analysis showed that this unexpected priming was due to impurities of XylNap amongst these xyloside analogs. Since XylNap and XylOBn (**1b**) give rise to highly distinct GAG

priming even at as low concentrations as 0.01 mM,[15] very low amounts of contamination amongst non-priming xylosides would be sufficient to mislead the results. Although it is merely a speculation, there might be a general problem with impurities of xylosides with modifications in the xylose residue, which could explain contradictory results between earlier investigations.

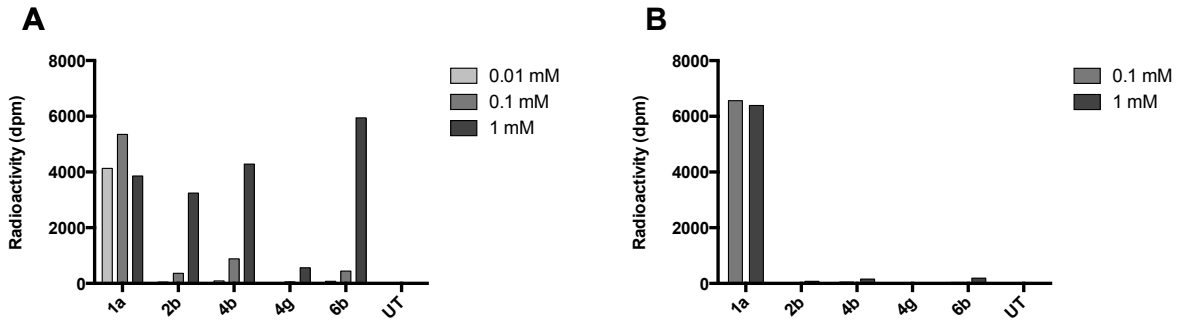


Figure S1. GAG priming ability of compounds XylNap (**1a**), **2b**, **4b**, **4g**, and **6b** before (A) and after (B) removal of XylNap impurities.

Galactosylation assay (β4GalT7)

0.15 mg of protein (with GST tag) was incubated in 20 mM MES buffer with 10 mM $MnCl_2$, pH 6.2, 1 mM UDP-Gal, and various concentrations of xyloside analogs at 37 °C for 30 min in a total volume of 50 mL. After incubation, the samples were boiled for 2 min to denaturate proteins, and then centrifuged for 5 min at 20 000 x g to pellet precipitated proteins. An aliquot of the supernatant was diluted in the HPLC eluent (1:300), and was then analyzed by reversed-phase HPLC (Thermo Scientific UltiMate 3000 Quaternary Analytical system with an FLD-3400RS fluorescence detector) using a C_8 column (4.6 x 150 mm, 3 mm, ACE). The mobile phase employed was 70% NH_4OAc (60 mM, pH 5.6) - 30% CH_3CN (v/v), and the excitation/emission wavelength was set to 229/342 nm. The galactosylation was determined from the HPLC chromatograms by dividing the peak area of the product with the peak area of the starting substrate. This could be done since there was no significant difference in fluorescence between the monosaccharide and the disaccharide (less than 2% for XylNap/GalXylNap). Masses of galactosylated products were determined using an UHPLC-MS^n system (operated in positive electrospray ionization mode) Accela UHPLC and LTQ Velos Pro Orbitrap MS, both from Thermo Scientific. The experiments were performed in duplicates. The kinetic parameters were achieved by incubations of a number of different concentrations of acceptor substrate. The results were then plotted in GraphPad Prism 6, using the nonlinear regression to the Michaelis-Menten model (Figures S2-S4, Table S2).

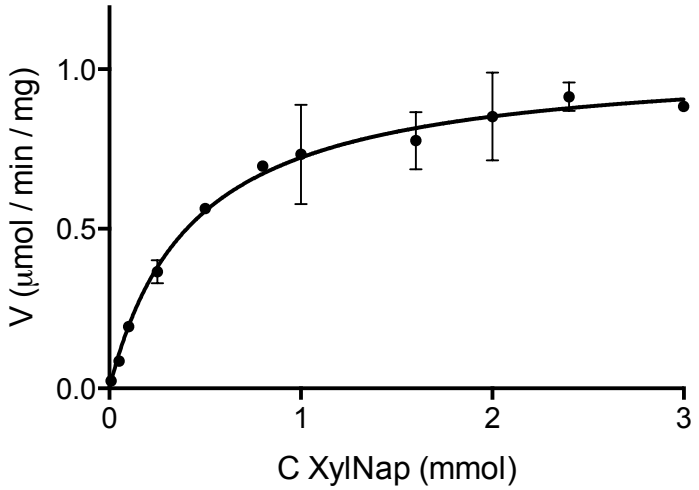


Figure S2. Michaelis-Menten representation of the activity of β4GalT7 (*V*) as a function of the XylNap (**1a**) concentration.

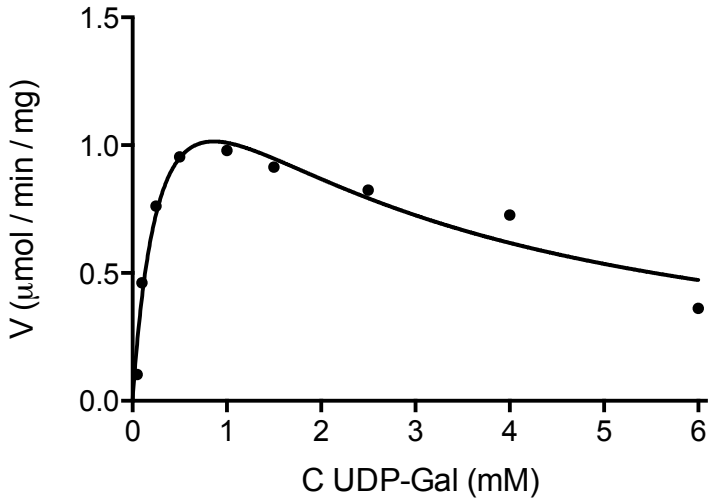


Figure S3. Michaelis-Menten representation of the activity of β4GalT7 (*V*) as a function of the UDP-Gal concentration.

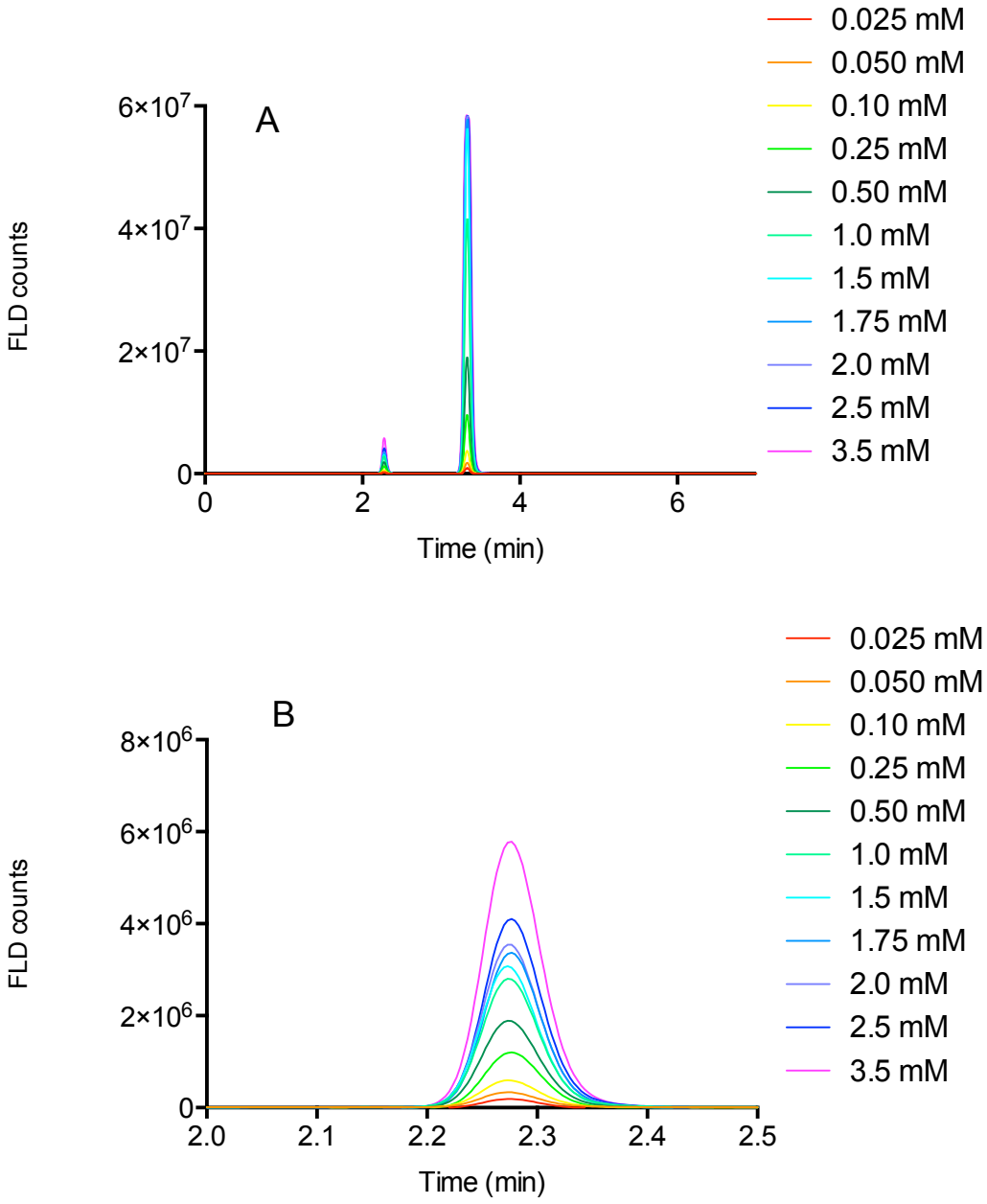


Figure S4. HPLC chromatogram for galactosylation experiment, here shown for XylNap (**1a**). B is an enlargement of the GalXylNap peak in A.

Inhibition assay (β4GalT7)

Inhibition of β4GalT7 activity by different xyloside analogs was determined in the same manner as in the galactosylation assay, with the exception that 0.5 mM of XylNap was added together with an increasing amount of naphthoxyloside to the assay. The amount of formed GalXylNap was then measured by reversed-phase HPLC (as above, Figure S5, Table S2).

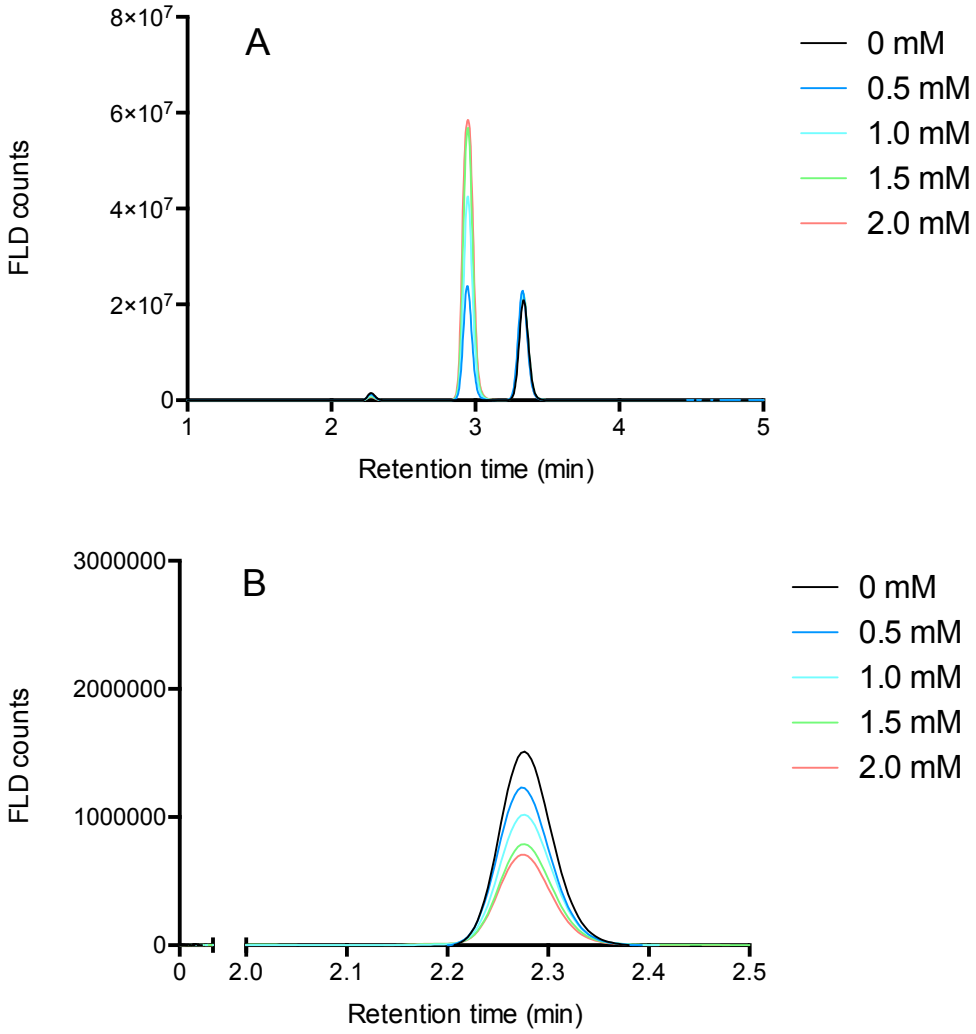


Figure S5. HPLC chromatogram for inhibition experiment, here shown for compound **4f**. B is an enlargement of the GalXylNap peak in A.

Table S2. Results from galactosylation and inhibition experiments using the enzymatic assay.

Compound	Galactosylation[c]	Galactosylation[f]	Mass of galactosylated compound[g]	Inhibition[h]
XylNap **(1a)**	$8.7 \pm 4.5*10^{-5}$	100	HRMS calcd for $C_{21}H_{27}O_{10}^+$ [M + H^+]: 439.1599; found: 439.1599	
2a	$0.94 \pm 8.8*10^{-4}$	11± 0.17	HRMS calcd for $C_{22}H_{29}O_{10}^+$ [M + H^+]: 453.1755; found: 453.1756	0[i]
2b	0[d]	0[d]	HRMS calcd for $C_{22}H_{29}O_{10}^+$ [M + H^+]: 453.1755; found: 453.1755	0[i]
2c	$0.044 \pm 4.6*10^{-3}$	0.51 ± 0.053	HRMS calcd for $C_{22}H_{29}O_{10}^+$ [M + H^+]: 453.1755; found: 453.1755	14 ± 1.9
2d	$0.73 \pm 5.3*10^{-3}$	8.4 ± 0.075	HRMS calcd for $C_{21}H_{26}FO_9^+$ [M + H^+]: 441.1555; found: 441.1555	9.3 ± 3.9
2e[a]	$0.15 \pm 5.5*10^{-3}$ $0.64 \pm 9.5*10^{-3}$	1.7 ± 0.055 7.4 ± 0.11	HRMS calcd for $C_{21}H_{26}O_9Na^+$ [M + Na^+]: 445.1469; found: 445.1466	64 ± 1.2
2f	0[d]	0[d]		0[i]
3a	0[d]	0[d]		0[i]
3b	0[d]	0[d]		0[i]
3c	0[d]	0[d]		0[i]
3d[b]	0[d]	0[d]	HRMS calcd for $C_{21}H_{25}FO_9Na^+$ [M + Na^+]: 463.1375; found: 463.1371	25 ± 5.2[h]
3e	0[d]	0[d]		0[i]
3f	0[d]	0[d]		0[i]
4a	0[d]	0[d]	HRMS calcd for $C_{22}H_{31}O_{10}N^+$ [M + NH_4^+]: 470.2021; found: 470.2020	0[g]
4b	0[d]	0[d]		41 ± 3.8
4c	0[d]	0[d]		0[i]
4d	0[d]	0[d]		43 ± 5.4
4e	0[d]	0[d]		11 ± 4.1
4f	0[d]	0[d]		52 ± 2.6
4g	0[d]	0[d]		13 ± 8.0
5a	$0.033 \pm 1.6*10^{-3}$	3.8 ± 0.19	HRMS calcd for $C_{22}H_{29}O_{10}^+$ [M + H^+]: 453.1755; found: 453.1752	0[i]
5b	0[d]	0[d]		0[i]
5c	0[d]	0[d]		0[i]
5d	0[d]	0[d]		0[i]
6b	-[e]	-[e]		43 ± 1.0

[a] 1.2 mM of **2e** instead of 2.0 mM in inhibition experiments.

[h] 1.6 mM of **3b** instead of 2.0 mM in inhibition experiments.

[c] Assay run with 1.5 mM of acceptor substrate. Result is given as percentage of galactosylation of the acceptor substrate.

[d] Less than 0.01% of the acceptor substrate is galactosylated in these settings.

[e] **6b** and the galactosylated product are not detected by fluorescence detector.

[f] Assay run with 1.5 mM of acceptor substrate. Result is given as percentage of galactosylation of the acceptor substrate in comparison with the percentage of galactosylation of XylNap (in %).

[g] Mass determined using UHPLC-MS^n system (Accela UHPLC and LTQ Velos Pro Orbitrap MS, both from Thermo Scientific). All masses are within 0.4 mDa and 0.8 ppm.

[h] Decrease in GalXylNap formation when assay run with 0.5 mM XylNap and 2 mM acceptor substrate compared with assay run with only 0.5 mM XylNap. Result is given as percentage.

[i] No inhibition of formation of GalXylNap detected in these settings.

Experimental part - Synthesis

All moisture- and air-sensitive reactions were carried out under an atmosphere of dry nitrogen using over-dried glassware. All solvents were dried prior to use unless otherwise stated. Purchased reagents were used without further purification. Chromatographic separations were performed on Matrex silica gel (25-70 μm). Thin-layer chromatography was performed on precoated TLC glass plates with silica gel 60 F_{254} 0.25 mm (Merck). Spots were visualized with UV light or by staining with a solution of *p*-methoxybenzaldehyde (26 mL), glacial acetic acid (11 mL), concentrated sulphuric acid (35 mL), and 95% ethanol (960 mL). NMR spectra were recorded at ambient temperatures with a Bruker Avance II 400 MHz spectrometer, at 400 MHz (^{1}H) and at 100 MHz (^{13}C). ^{1}H NMR spectra were assigned using COSY (2D homonuclear shift correlation) with a gradient selection and NOESY (nuclear Overhauser effect spectroscopy). Chemical shifts are given in ppm, with reference to residual internals $CDCl_3$ (δ 7.26), CD_3OD (δ 3.31), or C_6D_6 (δ 7.16). Coupling constant values are given in Hz. Mass spectra were recorded on Micromass Q-Tof micro^{TM}. Optical rotations were measured on Perkin Elmer instrument, Model 341 polarimeter at 20 °C and are given in 10^{-1} deg cm^2 g^{-1}. Waters 600 Series HPLC with Waters Symmetry C_{18} column (5 μm, 19x100 mm) was used for purification. Synthesis and physical characterization of compound XylNap (**1a**)[16] and **20**[17] has been described before. However, a simplified synthetic route was used that comprised treatment of a mixture of 1,2,3,4-tetra-*O*-acetyl-β-D-xylopyranose and 2-naphthol (for **1a**) or benzyl alcohol (for **1b**) in CH_2Cl_2 with BF•OEt_2 followed by de-*O*-acetylation. The analyses of the products were in accordance with published data. Synthesis and physical characterization of compounds **2c-f**, **3c-f, 4c-f**, **7**, **8**, and **9** has recently been described[18] as well as starting material **18**.[19] Compounds **5c** and **5d** are commercially available.

2-Naphthyl 3,4-di-*O*-benzyl-2-methyl-β-D-xylopyranoside (10) and 2-naphthyl 3,4-di-*O*-benzyl-2-methyl-β-D-lyxopyranoside (11) DMP in CH_2Cl_2 (15 wt%, 623 mg, 0.22 mmol) was added to a stirred solution of **7** (67 mg, 0.15 mmol) in CH_2Cl_2 (4 mL). After 1.5 h, sat. $NaHCO_3$ (aq) (3 mL) and sat. $Na_2S_2O_3$ (aq) (2 mL) were added and the reaction mixture was stirred for 15 minutes before extraction with CH_2Cl_2 (2

x 10 mL). The organic phases were dried (Na_2SO_4) before removal of solvent under reduced pressure. The crude was dissolved in Et_2O (5 mL) and 3 M MeMgBr (0.15 mL, 0.45 mmol) was added. After 1.5 h, sat. NH_4Cl (aq) (10 mL) and water (10 mL) were added and the aqueous phase was extracted with Et_2O (2 x 15 mL). The organic phases were dried ($MgSO_4$) before removal of solvent under reduced pressure. The crude residue was purified by column chromatography (SiO_2, heptane:EtOAc 6:1→5:1) to give **10** (7 mg, 10%) and **11** (40 mg, 57%). Compound **10**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.79-7.73 (m, 3H) 7.46-7.25 (m, 14H) 5.22 (s, 1H) 4.74 (s, 2H) 4.65 (d, 2H, *J* = 1.4 Hz) 4.18 (dd, 1H, *J* = 1.8, 12.1 Hz) 3.83 (s, 1H) 3.68-3.60 (m, 3H) 1.43 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.1, 138.4, 137.4, 134.5, 129.8, 129.5, 128.7, 128.6, 128.2, 128.0, 127.9, 127.7, 127.7, 127.3, 126.5, 124.3, 119.3, 111.0, 102.0, 79.4, 74.3, 73.9, 72.1, 72.0, 59.4, 19.8; HRMS calc. for $C_{30}H_{30}O_5Na$: 493.1991; found: 493.1990. Compound **11**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.80-7.74 (m, 3H) 7.48-7.25 (m, 14H) 5.15 (s, 1H) 4.82 (d, 1H, *J* = 11.7 Hz) 4.74 (d, 1H, *J* = 11.7 Hz) 4.63 (s, 2H) 4.17 (dd, 1H, *J* = 3.2, 12.2 Hz) 3.81 (td, 1H, *J* = 3.2, 5.0 Hz) 3.57 (dd, 1H, *J* = 5.0, 12.2 Hz) 3.52 (d, 1H, *J* = 5.0 Hz) 3.16 (s, 1H) 1.50 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.1, 138.2, 138.1, 134.5, 129.5, 128.6, 128.6, 128.0, 128.0, 127.8, 127.8, 127.8, 127.3, 126.5, 124.4, 119.2, 111.1, 101.7, 81.4, 75.1, 74.5, 72.1, 70.8, 60.4, 22.8; HRMS calc. for $C_{30}H_{30}O_5Na$: 493.1991; found: 493.1984

General hydrogenolysis procedure A: 10% Pd/C (14 mol%) and HCl (22 eq.) were added to DMF and stirred under H_2 atmosphere. After 15 minutes, the substrate, dissolved in DMF, was added and H_2 gas was vacuum-pumped into the reaction flask. The reaction was quenched by addition of Et_3N followed by filtration through a plug of Celite and elution with EtOAc. The organic phase was washed with H_2O and brine and dried ($MgSO_4$) before removal of solvent under reduced pressure. The crude residues were purified by column chromatography (SiO_2, CH_2Cl_2:MeOH 95:5). Analytical samples were purified by gradient HPLC (100% H_2O (0.1% TFA)→100% MeCN, Column: Symmetry C_{18}, 5 μm, 19 x 100 mm).

2-Naphthyl 2-methyl-β-D-xylopyranoside (2a) Starting from **10** (22 mg, 0.05 mmol), **2a** was obtained in 44% yield, using the general hydrogenolysis procedure. $[\alpha]_D^{20}$ -22° (*c* 0.9, CH_3OH); ^{1}H-NMR (400 MHz, CD_3OD) δ 7.78 (t, 3H, *J* = 9.0 Hz)

7.45-7.40 (m, 2H) 7.37-7.33 (m, 1H) 7.27 (dd, 1H, *J* = 2.6, 9.0 Hz) 5.00 (s, 1H) 4.05 (dd, 1H, *J* = 4.8, 11.2 Hz) 3.66-3.61 (m, 1H) 3.51-3.44 (m, 2H) 1.37 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD) δ 156.8, 135.9, 131.1, 130.3, 128.6, 128.1, 127.4, 125.2, 120.1, 112.0, 104.3, 78.8, 74.6, 70.0, 66.3, 15.7; HRMS calc. for $C_{16}H_{18}O_5Na$: 313.1052; found: 313.1058.

2-Naphthyl 2-methyl-β-D-lyxopyranoside (2b) Starting from **11** (50 mg, 0.11 mmol), **2b** was obtained in 67% yield, using the general hydrogenolysis procedure. $[\alpha]_D^{20}$ -41° (*c* 0.6, CH_3OH); ^{1}H-NMR (400 MHz, CD_3OD) δ 7.80-7.75 (m, 3H) 7.45-7.25 (m, 4H) 5.04 (s, 1H) 4.02 (dd, 1H, *J* = 5.4, 11.3 Hz) 3.86 (ddd, 1H, *J* = 5.4, 8.9, 9.9 Hz) 3.41 (dd, 1H, *J* = 9.9, 13.3 Hz) 3.29 (d, 1H, *J* = 8.9 Hz) 1.39 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD) δ 156.7, 135.9, 131.3, 130.4, 128.7, 128.1, 127.5, 125.3, 119.8, 111.7, 103.2, 78.5, 74.4, 68.9, 66.7, 20.8; HRMS calc. for $C_{16}H_{18}O_5Na$: 313.1052; found: 313.1072.

2-Naphthyl 2,4-di-*O*-benzyl-3-methyl-β-D-xylopyranosides (12) and 2-naphthyl 2,4-di-*O*-benzyl-3-methyl-β-D-ribopyranosides (13) 12 and **13** were obtained from **8** (400 mg, 0.88 mmol), using the method described for the synthesis of **10**/**11**. The crude was purified using column chromatography (SiO_2, heptane:EtOAc 6:1→5:1) giving **12** (78 mg, 19%) and **13** (280 mg, 68%). Compound **12**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.81-7.75 (m, 3H) 7.48-7.22 (m, 14H) 5.19 (d, 1H, *J* = 7.3 Hz) 5.08 (d, 1H, *J* = 11.8 Hz) 4.83 (d, 1H, *J* = 10.4 Hz) 4.80 (d, 1H, *J* = 10.4 Hz) 4.68 (d, 1H, *J* = 11.8 Hz) 4.00 (dd, 1H, *J* = 5.0, 11.7 Hz) 3.67 (dd, 1H, *J* = 5.0, 9.6 Hz) 3.60 (d, 1H, *J* = 7.3 Hz) 3.52 (dd, 1H, *J* = 9.6, 11.7 Hz) 1.43 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.0, 138.6, 138.5, 134.4, 130.1, 129.7, 128.6, 128.6, 128.0, 128.0, 127.9, 127.8, 127.3, 126.6, 124.5, 119.1, 111.4, 111.4, 101.0, 82.9, 79.1, 76.0, 75.1, 73.6, 63.5, 16.6; HRMS calc. for $C_{30}H_{30}O_5Na$: 493.1991; found: 493.2003. Compound **13**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.80-7.75 (m, 3H) 7.48-7.44 (m, 1H) 7.41-7.30 (m, 12H) 7.26-7.22 (m, 1H) 5.54 (d, 1H, *J* = 6.8 Hz) 5.05 (d, 1H, *J* = 11.2 Hz) 4.79 (d, 1H, *J* = 11.2 Hz) 4.68 (d, 1H, *J* = 12.0 Hz) 4.62 (d, 1H, *J* = 12.0 Hz) 3.90-3.88 (m, 2H) 3.40-3.36 (m, 2H) 2.47 (s, 1H (OH)) 1.36 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 154.9, 137.8, 137.8, 134.5, 130.0, 129.7, 128.8, 128.6, 128.5, 128.4, 128.2, 128.1, 127.8,

127.3, 126.6, 124.4, 118.9, 111.2, 100.0, 80.7, 77.6, 75.1, 73.6, 73.4, 62.1, 23.0; HRMS calc. for $C_{30}H_{30}O_5Na$: 493.1991; found: 493.2014.

2-Naphthyl 3-methyl-β-D-xylopyranoside (3a) Starting from **12** (50 mg, 0.11 mmol), **3a** was obtained in 76% yield, using the general hydrogenolysis procedure. $[\alpha]_D^{20}$ -44° (c 0.9, CH_3OH); ^{1}H-NMR (400 MHz, CD_3OD) δ 7.79-7.76 (m, 3H) 7.45-7.41 (m, 2H) 7.37-7.33 (m, 1H) 7.29-7.28 (m, 1H) 5.19 (d, 1H, *J* = 6.6 Hz) 3.98 (dd, 1H, *J* = 4.3, 11.3 Hz) 3.66 (dd, 1H, *J* = 4.3, 8.9 Hz) 3.59-3.54 (m, 2H) 1.33 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD) δ 156.5, 135.9, 131.2, 130.3, 128.6, 128.1, 127.4, 125.2, 120.0, 111.8, 101.6, 76.4, 74.9, 73.4, 65.6, 16.0; HRMS calc. for $C_{16}H_{18}O_5Na$: 313.1052; found: 313.1097.

2-Naphthyl 3-methyl-β-D-ribopyranoside (3b) Starting from **13** (30 mg, 0.06 mmol), **3b** was obtained in 49 % yield, using the general hydrogenolysis procedure. $[\alpha]_D^{20}$ -18 (c 0.4, CH_3OH); ^{1}H-NMR (400 MHz, CD_3OD) δ 7.77 (t, 3H, *J* = 8.8 Hz) 7.45-7.40 (m, 2H) 7.36-7.32 (m, 1H) 7.25 (dd, 1H, *J* = 2.4, 8.8 Hz) 5.34 (d, 1H, *J* = 7.2 Hz) 3.86-3.77 (m, 2H) 3.55 (dd, 1H, *J* = 5.6, 9.6 Hz) 3.41 (d, 1H, *J* = 7.6 Hz) 1.42 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD) δ 156.8, 135.9, 131.2, 130.3, 128.6, 128.1, 127.4, 125.2, 120.0, 111.7, 101.1, 75.3, 74.1, 71.9, 65.7, 22.3; HRMS calc. for $C_{16}H_{18}O_5Na$: 313.1052; found: 313.1074.

2-Naphthyl 2,3-di-*O*-benzyl-4-methyl-β-D-xylopyranoside (14) and 2-Naphthyl 2,3-di-*O*-benzyl-4-methyl-β-D-arabinopyranoside (15) **14** and **15** were obtained from **9** (150 mg, 0.33 mmol), using the method described for the synthesis of **10**/**11** with the exception that the Grignard reagent was added at 0 °C where after the reaction mixture was let to reach rt. The crude was purified using column chromatography (SiO_2, heptane:EtOAc 6:1→5:1) giving **14** (65 mg, 42%) and **15** (65 mg, 42%). Compound **14**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.80-7.73 (m, 3H) 7.47-7.29 (m, 13H) 7.21 (dd, 1H, *J* = 2.0, 8.9 Hz) 5.48 (d, 1H, *J* = 4.0 Hz) 4.85 (d, 1H, *J* = 11.8 Hz) 4.82 (d, 1H, *J* = 11.4 Hz) 4.73 (d, 1H, *J* = 11.4 Hz) 4.65 (d, 1H, *J* = 11.8 Hz) 3.93 (d, 1H, *J* = 11.6 Hz) 3.82 (dd, 1H, *J* = 4.0, 5.5 Hz) 3.56 (d, 1H, *J* = 5.5 Hz) 3.40 (dd, 1H, *J* = 0.5, 11.6 Hz) 1.29 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 154.8, 138.5, 137.5, 134.5, 129.8, 129.6, 128.7, 128.6, 128.3, 128.2, 128.0, 128.0, 127.8, 127.3,

126.6, 124.4, 119.1, 110.8, 98.9, 80.3, 76.7, 73.9, 73.8, 70.5, 67.8, 21.2; HRMS calc. for $C_{30}H_{30}O_5Na$: 493.1991; found: 493.2028. Compound **15**: ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.83-7.76 (m, 3H) 7.50-7.28 (m, 14H) 5.20 (d, 1H, *J* = 7.1 Hz) 5.10 (d, 1H, *J* = 11.0 Hz) 5.01 (d, 1H, *J* = 11.1 Hz) 4.85 (d, 1H, *J* = 11.0 Hz) 4.73 (d, 1H, *J* = 11.1 Hz) 4.06 (dd, 1H, *J* = 7.1, 8.5 Hz) 3.91 (d, 1H, *J* = 12.4 Hz) 3.49-3.44 (m, 2H) 2.64 (d, 1H, *J* = 1.2 Hz) 1.22 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 155.1, 138.3, 138.0, 134.5, 130.1, 129.7, 128.7, 128.6, 128.4, 128.3, 128.2, 128.0, 127.8, 127.3, 126.5, 124.5, 119.3, 111.5, 102.1, 82.8, 80.2, 75.8, 75.1, 71.3, 70.0, 22.5; HRMS calc. for $C_{30}H_{30}O_5Na$: 493.1991; found: 493.2001.

2-Naphthyl 4-methyl-β-D-xylopyranoside (4a) Starting from **14** (50 mg, 0.11 mmol), **4a** was obtained in 70% yield, using the general hydrogenolysis procedure. $[\alpha]_D^{20}$ -24° (*c* 1.1, CH_3OH); ^{1}H-NMR (400 MHz, CD_3OD) δ 7.80-7.75 (m, 3H) 7.43-7.41 (m, 2H) 7.37-7.35 (m, 1H) 7.27 (dd, 1H, *J* = 2.5, 9.0 Hz) 5.07 (dd, 1H, *J* = 2.0, 5.0 Hz) 3.67 (d, 1H, *J* = 11.4 Hz) 3.56-3.54 (m, 2H) 3.49 (dd, 1H, *J* = 0.6, 11.4 Hz) 1.30 (d, 3H, *J* = 0.6 Hz); ^{13}C-NMR (100 MHz, CD_3OD) δ 156.6, 135.8, 131.3, 130.4, 128.6, 128.1, 127.4, 125.3, 120.0, 111.8, 103.2, 78.5, 73.7, 72.1, 71.4, 19.9; HRMS calc. for $C_{16}H_{18}O_5Na$: 313.1052; found: 313.1032.

2-Naphthyl 4-methyl-β-D-arabinopyranoside (4b) Starting from **15** (111 mg, 0.24 mmol), **4b** was obtained in 54% yield, using the general hydrogenolysis procedure. $[\alpha]_D^{20}$ 2° (*c* 0.9, CH_3OH); ^{1}H-NMR (400 MHz, CD_3OD) δ 7.79-7.74 (m, 3H) 7.45-7.41 (m, 2H) 7.36-7.32 (m, 1H) 7.50 (dd, 1H, *J* = 2.6, 9.0 Hz) 5.00 (d, 1H, *J* = 7.6 Hz) 3.83-3.79 (m, 1H) 3.75 (d, 1H, *J* = 12.4 Hz) 3.63 (d, 1H, *J* = 12.4 Hz) 3.38 (d, 1H, *J* = 9.6 Hz) 1.21 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD) δ 156.8, 135.8, 131.2, 130.3, 128.6, 128.1, 127.4, 125.2, 120.1, 111.9, 103.2, 77.6, 73.0, 72.2, 72.1, 21.7; HRMS calc. for $C_{16}H_{19}O_5$: 291.1232; found: 291.1240.

2-Naphthyl 2,3-*O*-isopropylidene-β-D-xylopyranoside (16) 2-Methoxypropene (0.92 mL, 9.77 mmol) was added in four portions, every 20 min, to a stirred solution of **1a** (1.01 g, 3.66 mmol) and CSA (0.13 g, 0.55 mmol) in DMF (6 mL) at rt. Et_3N (0.2 mL) was added and the reaction mixture was co-evaporated with toluene several times. The crude residue was purified by column chromatography (SiO_2, 1:1

petroleum ether:diehtylether + 1% Et_3N) gave **16** (0.60 g, 51%) and the analogous 3,4-protected compound (2-naphthyl 3,4-*O*-isopropylidene-β-D-xylopyranoside (0.21 g, 18%) as white solids, as well as recovery of **1a** (0.11 g, 10%). Compound **16**: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.79-7.75 (m, 3H) 7.47-7.43 (m, 2H) 7.40-7.36 (m, 1H) 7.28 (dd, 1H, J = 2.6, 9.0 Hz) 5.48-5.46 (m, 1H) 4.24-4.14 (m, 2H) 3.75-3.69 (m, 2H) 3.51 (dd, 1H, J = 6.8, 11.6 Hz) 2.43 (br s, 1H, OH) 1.54 (s, 3H) 1.52 (s, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 154.4, 134.3, 130.1, 129.7, 127.8, 127.3, 126.6, 124.6, 119.1, 112.4, 111.3, 99.8, 81.0, 76.4, 69.5, 67.8, 27.0, 26.7; HRMS calcd for $C_{18}H_{20}O_5Na^+$ [M+Na]: 339.1208; found: 339.1227. **2-Naphthyl 3,4-*O*-isopropylidene-β-D-xylopyranoside** ^{1}H-NMR ($CDCl_3$): δ 7.81-7.75 (m, 3H) 7.49-7.45 (m, 1H) 7.42-7.37 (m, 2H) 7.26 (dd, 1H, J = 2.4, 8.8 Hz) 5.05 (d, 1H, J = 6.8 Hz) 4.33-4.26 (m, 1H) 4.07 (dd, 1H, J = 6.2, 9.8 Hz) 3.75-3.63 (m, 3H) 2.73 (br s, 1H, OH), 1.524 (s, 3H) 1.515 (s, 3H); ^{13}C-NMR ($CDCl_3$): δ 154.9, 134.3, 130.2, 129.8, 127.8, 127.3, 126.7, 124.7, 118.8, 112.8, 111.5, 102.9, 81.2, 73.5, 73.4, 65.1, 26.9, 26.7; HRMS calcd for $C_{18}H_{20}O_5Na^+$ [M+Na]: 339.1259; found: 339.1208.

2-Naphthyl 2,3-*O*-isopropylidene-4-ethyl-β-D-arabinopyranoside (17) DMSO (0.1 mL, 1.30 mmol) was added to a stirred solution of oxalyl chloride (2 M in CH_2Cl_2, 0.28 mL, 0.56 mmol) at -78 °C. After 45 minutes, **16** (68.0 mg 0.22 mmol) in CH_2Cl_2 (3 mL) was added dropwise. After 2 h, Et_3N (1.0 mL, 7.17 mmol) was added and the reaction mixture was allowed to reach rt. H_2O (10 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (4 x 10 mL). The organic phases were dried (Na_2SO_4) before removal of solvent under reduced pressure followed by co-evaporation with toluene four times. The crude residue was dissolved in THF (7 mL) and EtMgBr (3 M in Et_2O, 0.22 mL, 0.65 mmol) was added drop wise at rt. After 12 h, H_2O (10 mL) was added and the aqueous phase was extracted with EtOAc (4 x 10 mL). The organic phases were dried (Na_2SO_4) before removal of solvent under reduced pressure. The crude residue was purified by column chromatography (SiO_2, petroleum ether:diethyl ether 1:1 + 0.2% Et_3N) to give **17** (28 mg, 38%) as white solid. $[\alpha]_D^{20}$ -54 (*c* 1.5, C_6H_6); ^{1}H-NMR (400 MHz, C_6D_6): δ 7.77-7.75 (m, 1H) 7.69-7.67 (m, 2H, ArH) 7.61 (d, 1H, J = 8.8 Hz) 7.45 (dd, 1H, J = 2.4, 8.8 Hz) 7.39-7.35 (m, 1H) 7.31-7.27 (m, 1H) 5.38 (d, 1H, J = 7.6 Hz) 4.52 (dd, 1H, J = 7.6, 9.6 Hz) 3.88 (d, 1H, J = 12.0 Hz) 3.40 (d, 1H, J = 9.6 Hz) 3.18 (d, 1H, J = 12.0 Hz) 1.62-1.57 (m,

1H) 1.51 (s, 3H) 1.48-1.38 (m, 1H) 1.46 (s, 3H) 0.98 (t, 3H, *J* = 7.6 Hz); ^{13}C-NMR (100 MHz, C_6D_6): δ 155.5, 135.0, 130.5, 129.9, 128.2, 127.4, 126.7, 124.5, 119.8, 112.0, 111.5, 101.3, 80.8, 75.2, 72.3, 71.7, 30.6, 27.2, 26.7, 7.7; HRMS calcd for $C_{20}H_{24}O_5Na^+$ [M+Na]: 367.1521, found: 367.1521.

2-Naphthyl 4-ethyl-β-D-arabinopyranoside (4g) 17 (28 mg, 0.08 mmol) was dissolved in 70% AcOH in H_2O (1 mL) at rt. After 1 h, toluene was added and the solvent was removed under reduced pressure followed by co-evaporation with toluene 3 times. The crude residue was purified by column chromatography (SiO_2, CH_2Cl_2:MeOH 97:3) to give **4g** (14 mg, 56%) as white solid. $[\alpha]_D^{20}$ -43 (*c* 0.8, CH_3OH); ^{1}H-NMR (400 MHz, CD_3OD): δ 7.77 (t, 3H, *J* = 8.8 Hz) 7.45-7.40 (m, 2H) 7.36-7.32 (m, 1H) 7.28 (dd, 1H, *J* = 2.4, 8.8 Hz) 4.99 (d, 1H, *J* = 7.6 Hz) 3.85 (d, 1H, *J* = 17.2 Hz) 3.83 (d, 1H, *J* = 12.4 Hz) 3.66 (d, 1H, J = 12.4 Hz) 3.46 (d, 1H, *J* = 9.2 Hz) 1.84-1.75 (m, 1H) 1.60-1.50 (m, 1H) 0.94 (t, 3H, *J* = 7.8 Hz); ^{13}C-NMR (100 MHz, CD_3OD): δ 156.7, 135.8, 131.2, 130.3, 128.6, 128.1, 127.4, 125.2, 120.1, 111.8, 103.0, 76.3, 74.3, 73.1, 70.1, 28.9, 7.9; HRMS calcd for $C_{17}H_{20}O_5Na^+$ [M+Na]: 327.1208; found: 327.1210 .

2-Naphthyl 2,3,4-tri-*O*-acetyl-6-deoxy-α-L-idopyranoside (19) Et_3N (0.051 mL, 0.37 mmol) and BF_3•OEt_2 (0.230 mL, 1.8 mmol) was mixed in dry CH_2Cl_2 (1 mL) and added to a stirred solution of 2-naphthol (159 mg, 1.10 mmol) and 1,2,3,4-tetra-*O*-acetyl-6-deoxy-α/β-L-idopyranose **18** (α:β 56:44) (237 mg, α = 132 mg, 0.4 mmol) in dry CH_2Cl_2 (2.5 mL) at 0 °C. After 2 h, sat. $NaHCO_3$ (aq) (5 mL) was added and the aqueous phase was extracted with EtOAc (4 x 5 mL). The combined organic phases were dried ($MgSO_4$) before removal of solvent under reduced pressure. The crude residue was purified by column chromatography (SiO_2, heptane:EtOAc 8:2) to give **19** (126 mg, 78%) as white solid. $[\alpha]_D^{20}$ -97° (*c* 0.5, $CHCl_3$); ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.79-7.73 (m, 3H) 7.47-7.36 (m, 3H) 7.18 (dd, 1H, *J* = 2.4, 8.8 Hz) 5.66 (s, 1H) 5.17-5.12 (m, 2H) 4.89 (t, 1H, *J* = 2.8 Hz) 4.55-4.47 (m, 1H) 2.19 (s, 3H) 2.18 (s, 3H) 2.15 (s, 3H) 1.21 (d, 3H, *J* = 6.8 Hz); ^{13}C-NMR (100 MHz, $CDCl_3$) δ 170.2, 169.5, 169.4, 154.1, 134.4, 129.8, 129.7, 127.8, 127.3, 126.6, 124.5, 118.9, 110.7, 96.3, 69.4, 68.0, 67.3, 63.6, 21.0, 21.0, 20.9, 15.8; HRMS calc. for $C_{22}H_{24}O_8Na$: 439.1369; found: 439.1379.

2-Naphthyl 6-deoxy-α-L-idopyranoside (5a) 1M NaOMe (0.030 mL, 0.03 mmol, MeOH) was added to a stirred solution of **19** (90 mg, 0.22 mmol) in MeOH (1 mL). After 2 h, Amberlite IR-120 H^+ was added until neutral pH and the reaction mixture was filtered followed by removal of solvent under reduced pressure. The crude residue was purified by column chromatography (SiO_2, CH_2Cl_2:MeOH 98:2) to give **5a** (50 mg, 81%) as a white solid. $[\alpha]_D^{20}$ -44° (*c* 0.5, CH_3OH); ^{1}H-NMR (400 MHz, CD_3OD) δ 7.78-7.73 (m, 3H) 7.47 (d, 1H, *J* = 2.4 Hz) 7.44-7.40 (m, 1H) 7.36-7.32 (m, 1H) 7.27 (dd, 1H, *J* = 2.4, 9.2 Hz) 5.49 (d, 1H, *J* = 4.0 Hz) 4.37-4.31 (m, 1H) 3.86 (t, 1H, *J* = 5.8 Hz) 3.78-3.76 (m, 1H) 3.56 (dd, 1H, *J* = 3.2, 5.2 Hz) 1.26 (d, 3H, *J* = 6.8 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 156.4, 135.9, 131.1, 130.3, 128.6, 128.1, 127.4, 125.1, 120.2, 111.8, 100.7, 73.3, 72.8, 72.2, 67.9, 15.5; HRMS calc. for $C_{16}H_{18}O_5Na$: 313.1052; found: 313.1072.

2-Naphthyl 6-*O*-tosyl-β-D-glucopyranoside (20) $ZnBr_2$ (585 mg, 2.60 mmol) and TsCl (675 mg, 3.54 mmol) were added to a stirred solution of **5c** (710 mg, 2.32 mmol) in dry pyridine (75 mL) at -25 °C. After 1h, MeOH (100 mL) was added and the temperature was allowed to reach rt before removal of solvent under reduced pressure. The crude residue was purified by column chromatography (SiO_2, CH_2Cl_2:MeOH 97:3) to give **20** (924 mg, 86%) as an orange oil. $[\alpha]_D^{20}$ -91° (*c* 0.5, CH_3OH); ^{1}H-NMR (400 MHz, CD_3OD) δ 7.83-7.65 (m, 5H) 7.47-7.34 (m, 3H) 7.23 (dd, 1H, *J* = 2.5, 8.9 Hz) 7.05-7.03 (m, 2H) 4.97 (d, 1H, *J* = 7.7 Hz) 4.41 (dd, 1H, *J* = 2.0, 10.9 Hz) 4.19 (dd, 1H, *J* = 10.9 Hz) 3.72 (ddd, 1H, *J* = 2.0, 6.4, 9.8 Hz) 3.47-3.45 (m, 2H) 3.36-3.33 (m, 1H) 2.14 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD) δ 156.6, 146.3, 135.9, 133.9, 131.3, 130.7, 130.2, 129.0, 128.6, 128.3, 127.4, 125.3, 120.0, 112.0, 101.9, 77.8, 75.1, 74.8, 71.1, 70.5, 21.4; HRMS calc. for $C_{23}H_{24}O_8SNa$: 483.1090; found: 483.1101.

2-Naphthyl 6-deoxy-β-D-glucopyranoside (5b) $LiAlH_4$ (1.37 g, 36.2 mmol) was added in portions to a stirred solution of **20** (2.78 g, 6.04 mmol) in dry Et_2O (200 mL) at 0 °C. After complete addition, the temperature was increased to 30 °C. After 22 h, the reaction mixture was put on ice and sat. Na_2SO_4 (aq) was added. The aqueous phase was extracted with EtOAc (5 x 80 mL) and the combined organic phases were

dried (Na_2SO_4) and the solvent was removed under reduced pressure. The crude residue was purified by column chromatography (SiO_2, CH_2Cl_2:MeOH 96:4) to give **5b** (1.07 g, 61%) as white solid. $[\alpha]_D^{20}$ -70° (*c* 0.6, CH_3OH); ^{1}H-NMR (400 MHz, CD_3OD) δ 7.80-7.75 (m, 3H) 7.45-7.41 (m, 2H) 7.37-7.33 (m, 1H) 7.27 (dd, 1H, *J* = 2.5, 9.0 Hz) 5.06 (d, 1H, *J* = 7.5 Hz) 3.51 (dd, 1H, *J* = 7.5, 9.0 Hz) 3.58 (dd, 1H, *J* = 6.2, 9.0 Hz) 3.46 (t, 1H, *J* = 9.0 Hz) 3.13 (t, 1H, *J* = 9.0 Hz) 1.35 (d, 3H, *J* = 6.2 Hz); ^{13}C-NMR (100 MHz, CD_3OD) δ 156.8, 135.8, 131.3, 130.3, 128.6, 128.1, 127.38, 125.2, 120.0, 111.8, 102.1, 77.7, 76.8, 75.2, 73.5, 18.2; HRMS calc. for $C_{16}H_{18}O_5Na$: 313.1046; found: 313.1126.

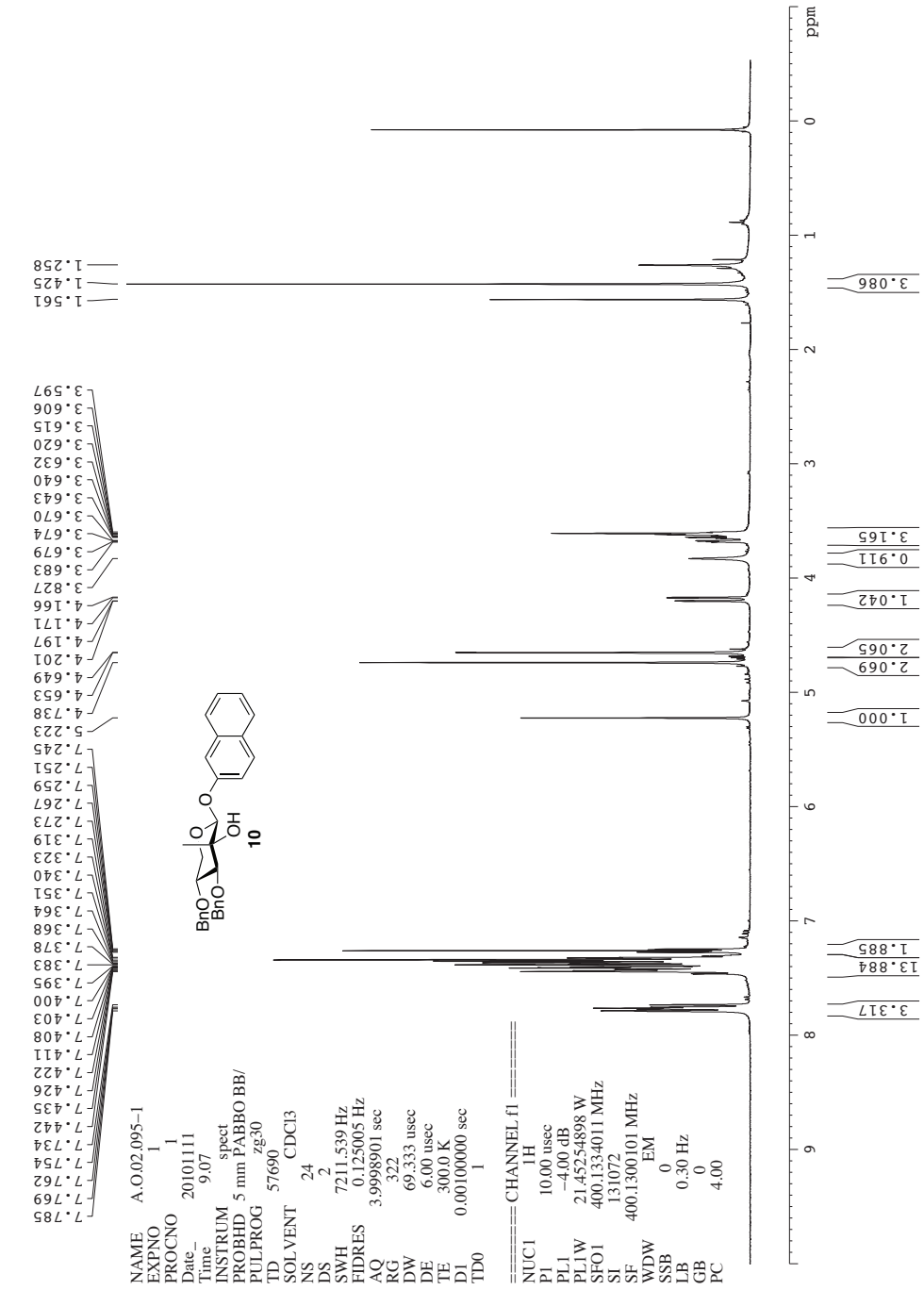
Benzyl 2,3-*O*-isopropylidene-β-D-xylopyranoside (21) 1b (0.09 g, 0.38 mmol) and CSA (16.0 mg, 0.07 mmol) were mixed in DMF (1.5 mL) at rt. 2-Methoxy propene (0.15 mL, 1.6 mmol) was added in five portions during 1.5 h. After another 4 h, Et_3N (1 mL, 7.2 mmol) was added before removal of solvent under reduced pressure. The crude residue was purified by column chromatography (SiO_2, Heptane:EtOAc 7:3) to give **21** (42 mg, 40%) and benzyl 3,4-*O*-isopropylidene-β-D-xylopyranoside (10 mg, 10%) as clear oils. Compound **21**: ^{1}H-NMR (400 MHz, C_6D_6) δ 7.34-7.32 (m, 2H) 7.15-7.11 (m, 2H) 7.08-7.04 (m, 1H) 4.83 (d, 1H, *J* = 12.0 Hz) 4.59 (d, 1H, *J* = 7.2 Hz) 4.46 (d, 1H, *J* = 12.0 Hz) 3.84 (dd, 1H, *J* = 5.2, 12.0 Hz) 3.70-3.65 (m, 1H) 3.55 (dd, 1H, *J* = 7.2, 9.6 Hz) 3.46 (t, 1H, *J* = 9.2 Hz) 3.05 (t, 1H, *J* = 7.6, 12.0 Hz) 1.36 (s, 3H) 1.34 (s, 3H); ^{13}C-NMR (100 MHz, C_6D_6) δ 138.1, 128.6, 128.2, 127.9, 111.2, 101.4, 81.6, 77.3, 70.2, 69.8, 67.6, 27.0, 26.8; HRMS calc. for $C_{15}H_{21}O_5$: 281.1389, found: 281.1408. **Benzyl 3,4-*O*-isopropylidene-β-D-xylopyranosid**e ^{1}H-NMR (400 MHz, C_6D_6) δ 7.25 (d, 2H, *J* = 7.6 Hz) 7.18-7.11 (m, 2H) 7.10-7.07 (m, 1H) 4.78 (d_{AB}, 1H, J_{AB} = 11.8 Hz) 4.37 (d_{AB}, 1H, J_{AB} = 11.8 Hz) 4.15 (dd, 1H, *J* = 0.8, 6.4 Hz) 3.93 (dd, 1H, *J* = 4.8, 10.0 Hz) 3.76-3.71 (m, 1H) 3.58-3.52 (m, 1H) 3.42 (t, 1H, *J* = 9.4 Hz) 3.17 (t, 1H, *J* = 10.2 Hz) 1.35 (s, 3H) 1.34 (s, 3H); ^{13}C-NMR (100 MHz, C_6D_6) δ 138.0, 128.7, 128.6, 127.9, 111.9, 104.1, 82.0, 74.1, 73.9, 71.3, 64.7, 27.0, 26.8; HRMS calc. for $C_{15}H_{20}O_5Na$: 303.1208; found: 303.1228.

Benzyl 2,3-*O*-isopropylidene-4-methyl-β-D-arabinopyranoside (22) DMSO (0.10 mL, 1.41 mmol) was added to oxalyl chloride (2 M in CH_2Cl_2, 0.35 mL, 0.70 mmol)

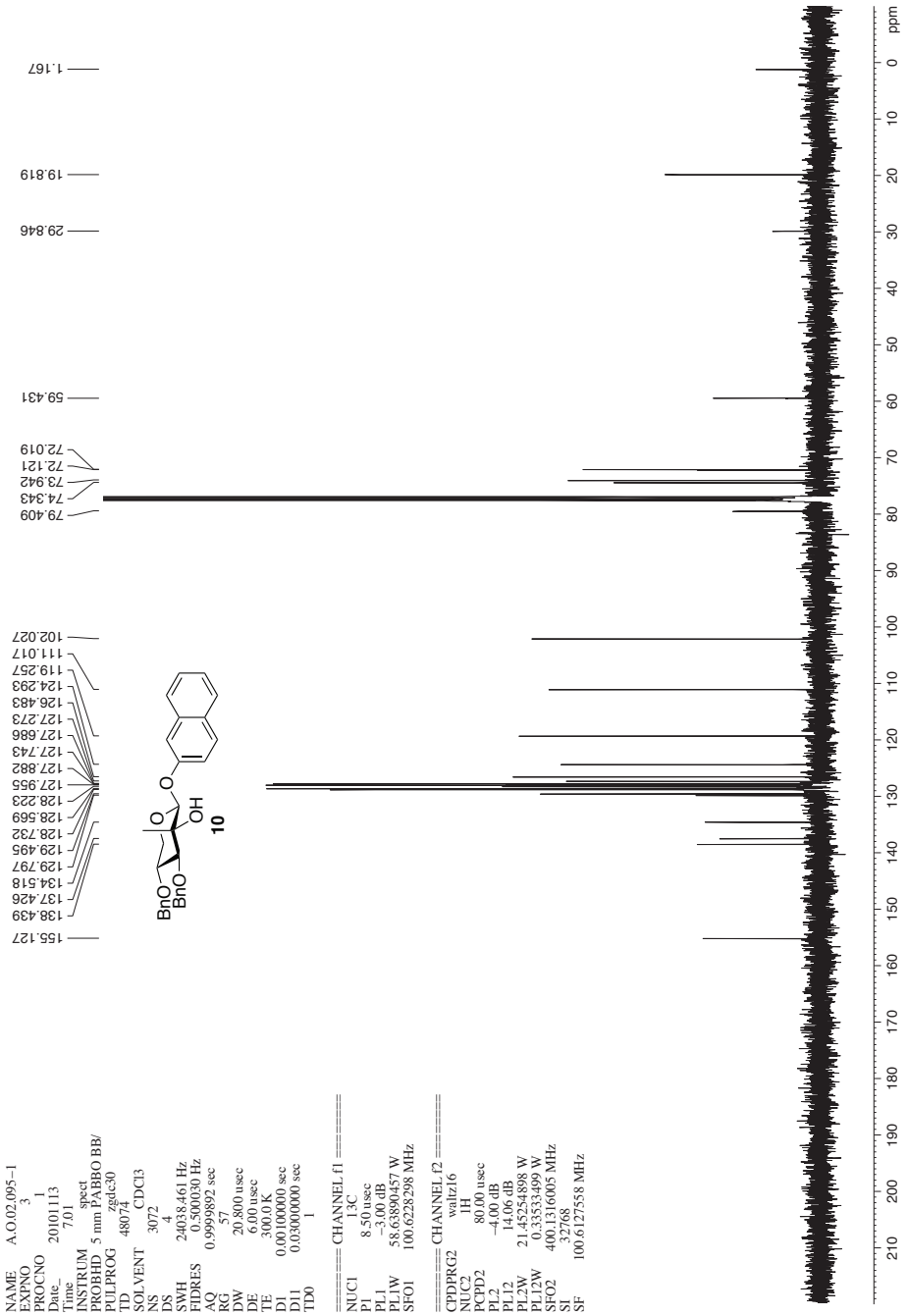
at -78 °C. After 45 minutes, **21** (66.0 mg 0.24 mmol) in CH_2Cl_2 (8 mL) was added. After 2 h, Et_3N (0.5 mL, 3.60 mmol) was added and the reaction mixture was let to reach rt. After 0.5 h, H_2O (10 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (4x10 mL). The organic phases were dried (Na_2SO_4) before removal of solvent under reduced pressure followed by co-evaporation with toluene four times. The crude was dissolved in THF (8 mL) and MeMgBr (3 M in Et_2O, 0.24 mL, 0.71 mmol) was added at rt. After 12 h, H_2O (10 mL) was added and the aqueous phase was extracted with EtOAc (4 x 10 mL). The organic phases were dried (Na_2SO_4) before removal of solvent under reduced pressure. The crude residue was purified by column chromatography (SiO_2, petroleum ether:diethyl ether 1:1 + 0.2% Et_3N) to give **22** (38 mg, 55%) as white solid. ^{1}H-NMR (400 MHz, C_6D_6) δ 7.39-7.37 (m, 2H) 7.14-7.11 (m, 2H) 7.09-7.05 (m, 1H) 4.92 (d_{AB}, 1H, J_{AB} = 12.0 Hz) 4.59 (d_{AB}, 1H, J_{AB} = 12.0 Hz) 4.55 (d, 1H, *J* = 7.6 Hz) 4.15 (dd, 1H, *J* = 7.6, 9.6 Hz) 3.68 (d, 1H, *J* = 12.0 Hz) 3.07 (d, 1H, *J* = 9.6 Hz) 2.87 (d, 1H, *J* = 12.0 Hz) 1.39 (s, 3H) 1.34 (s, 3H) 1.04 (s, 3H); ^{13}C-NMR (100 MHz, C_6D_6) δ 138.2, 128.6, 127.9, 127.8, 102.4, 82.1, 75.0, 72.9, 70.5, 69.9, 58.5, 27.2, 26.8, 22.5; HRMS calc. for $C_{16}H_{22}O_5Na$: 317.1365; found: 3017.1383.

Benzyl 4-methyl-β-D-arabinopyranoside (6b) Dowex 50Wx4 was added to a stirred solution of **22** (33 mg, 0.11 mmol) in MeOH (1.5 mL). After 4 h, the reaction mixture was filtered before removal of solvent under reduced pressure. The crude residue was purified by gradient HPLC (100% H_2O (0.1% TFA)→100% MeCN, Column: Symmetry C_{18}, 5 μm, 19 x 100 mm) to give **6b** (16 mg, 56%) as white solid. $[\alpha]_D^{20}$ -24 (*c* 0.1, CH_3OH); ^{1}H-NMR (400 MHz, CD_3OD) δ 7.42-7.40 (m, 2H) 7.34-7.30 (m, 2H) 7.29-7.25 (m, 1H) 4.87 (d_{AB}, 1H, J_{AB} = 12.0 Hz) 4.63 (d_{AB}, 1H, J_{AB} = 12.0 Hz) 4.27 (d, 1H, *J* = 7.6 Hz) 3.67 (d, 1H, *J* = 12.4 Hz) 3.53 (dd, 1H, *J* = 7.8, 9.4 Hz) 3.38 (d, 1H, *J* = 12.8 Hz) 3.21 (d, 1H, *J* = 9.2 Hz) 1.14 (s, 3H); ^{13}C-NMR (100 MHz, CD_3OD) δ 139.1, 129.3, 129.1, 128.7, 104.4, 77.7, 73.3, 72.3, 72.1, 71.7, 21.6; HRMS calc. for $C_{13}H_{18}O_5Na$: 277.1052; found: 277.1078.

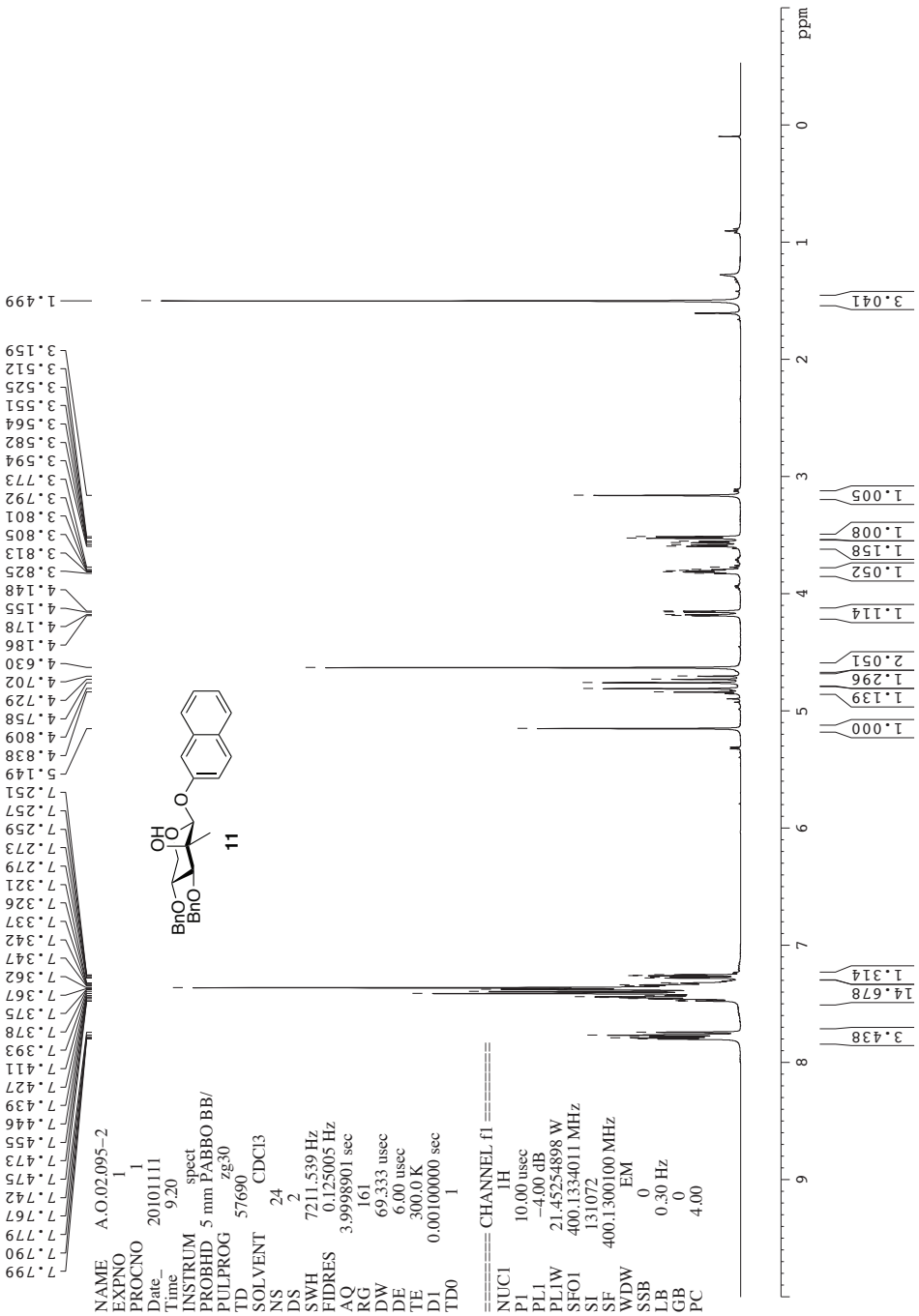
^{1}H-NMR 2-Naphthyl 3,4-di-*O*-benzyl-2-methyl-β-D-xylopyranoside **10**.



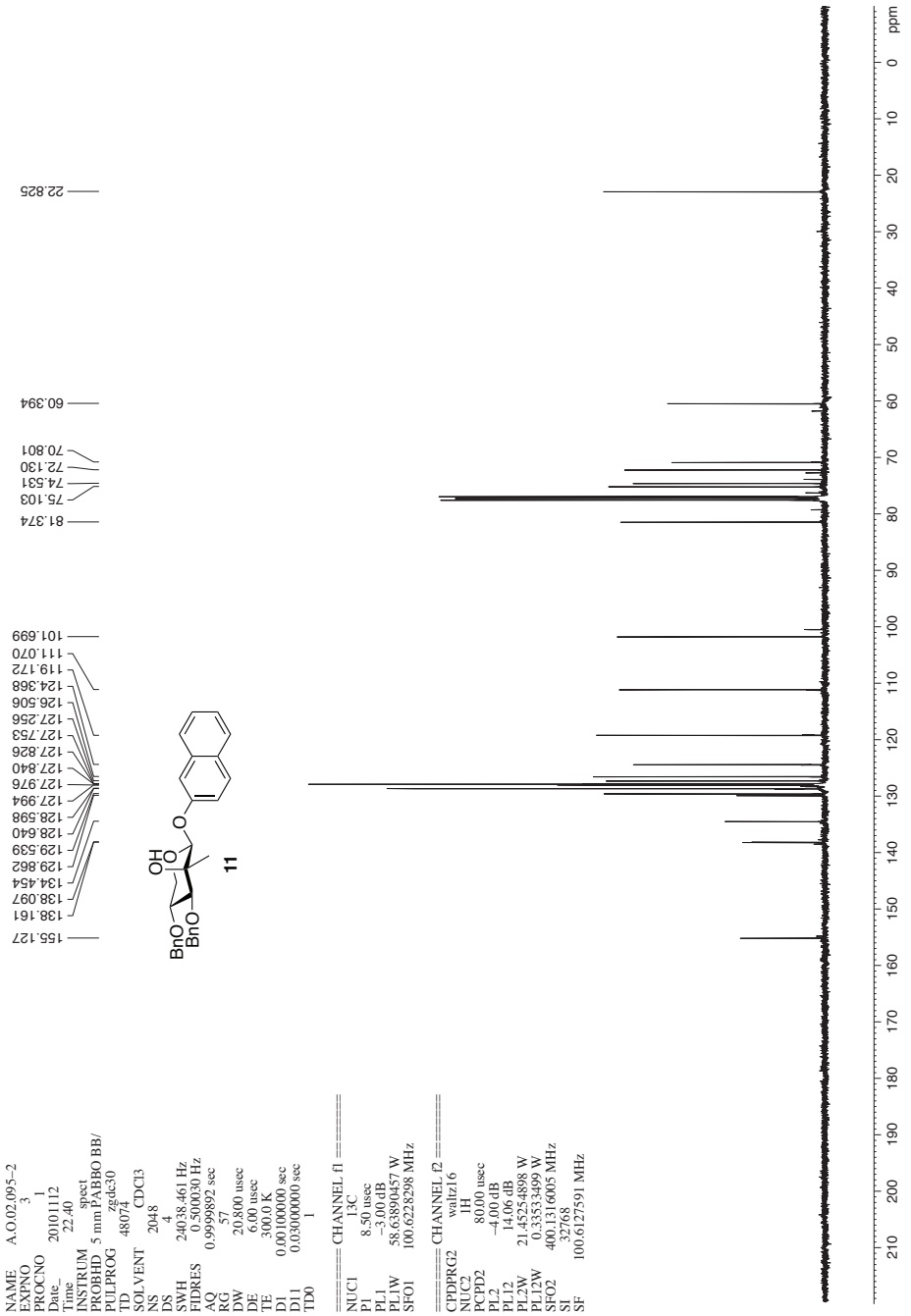
^{13}C-NMR 2-Naphthyl 3,4-di-*O*-benzyl-2-methyl-β-D-xylopyranoside **10**.



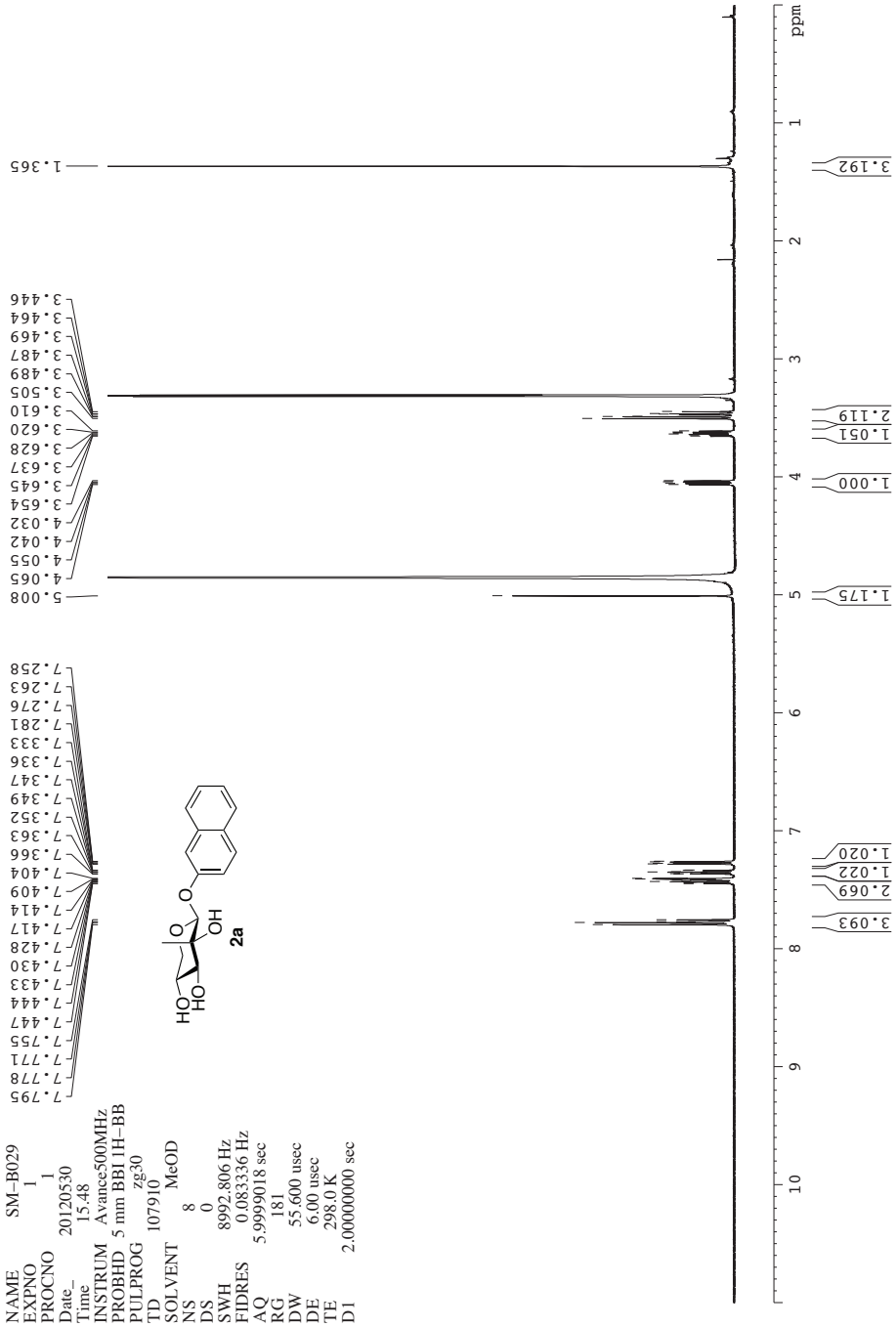
[1]H-NMR 2-naphthyl 3,4-di-*O*-benzyl-2-methyl-β-D-lyxopyranoside **11**.



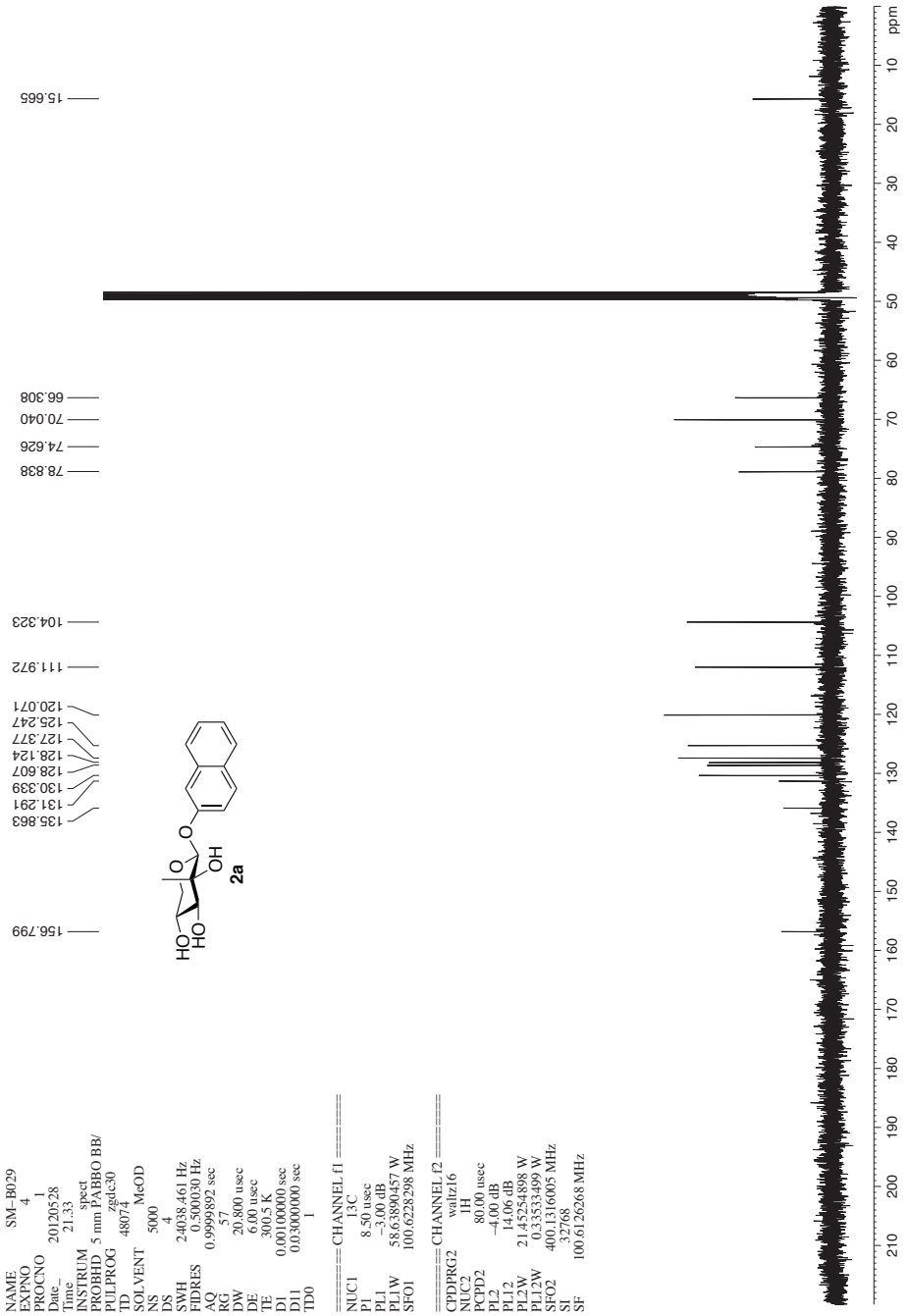
^{13}C-NMR 2-Naphthyl 3,4-di-*O*-benzyl-2-methyl-β-D-lyxopyranoside **11**.



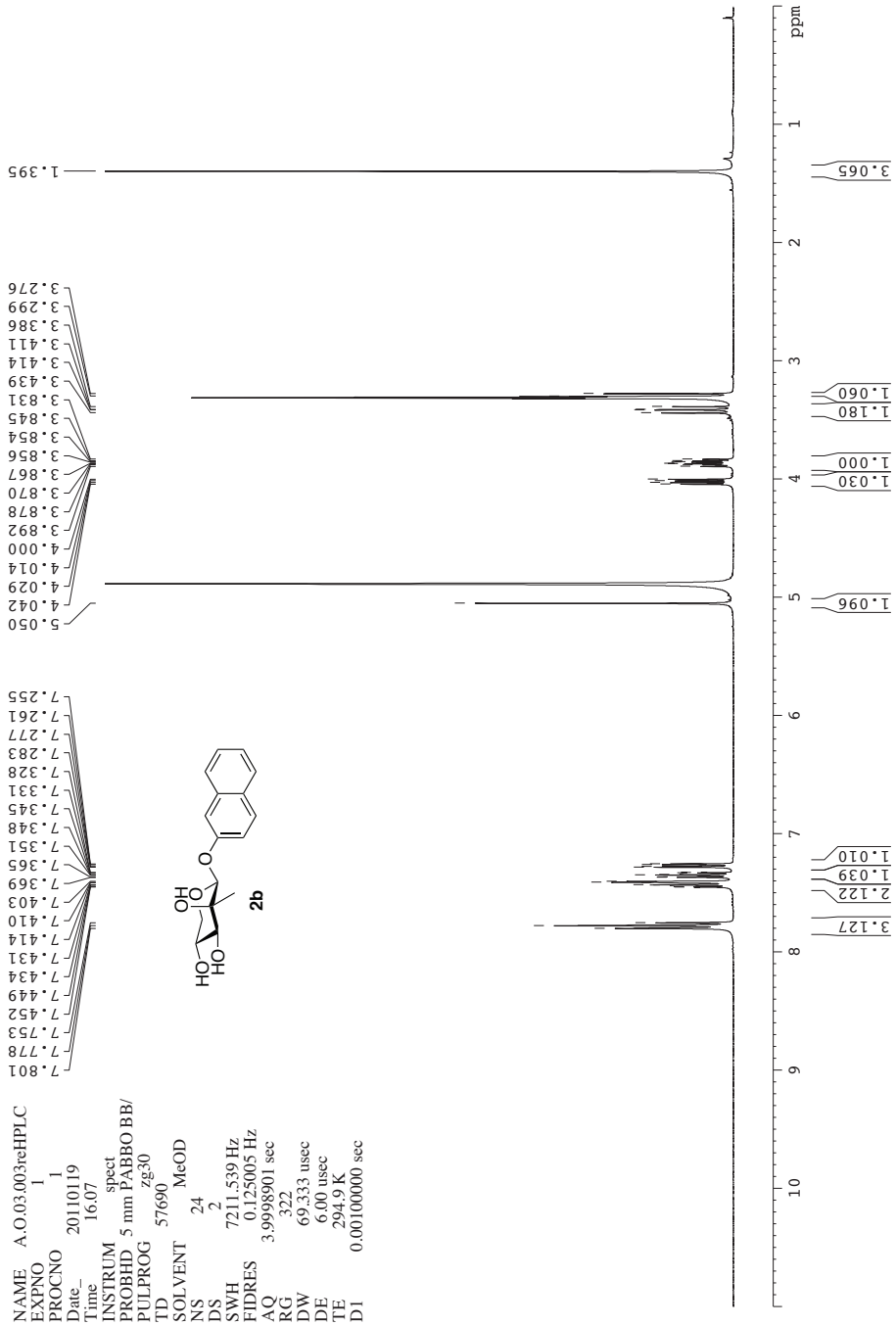
[1]H-NMR 2-Naphthyl 2-methyl-β-D-xylopyranoside **2a**.



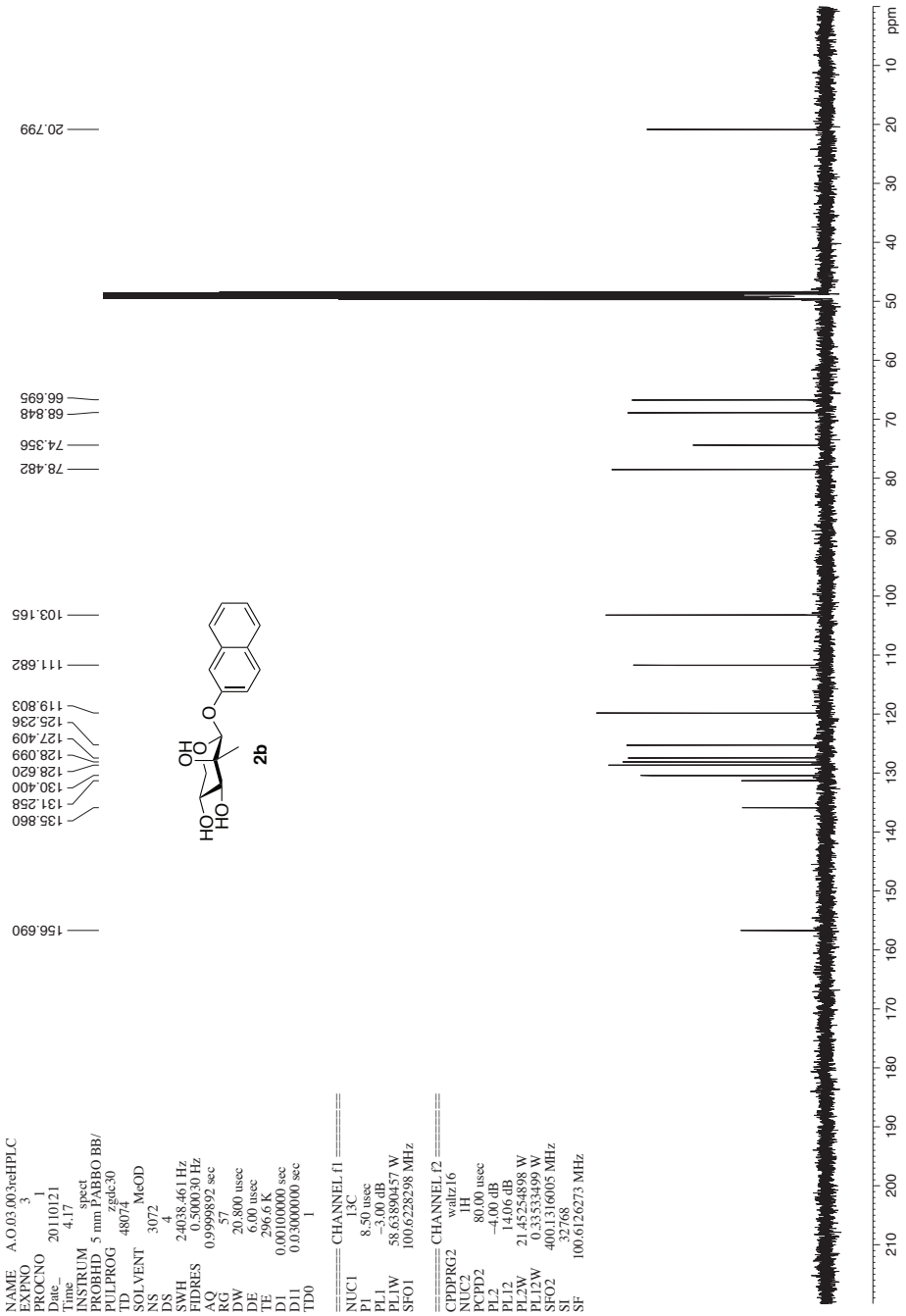
^{13}C-NMR 2-Naphthyl 2-methyl-β-D-xylopyranoside **2a**.



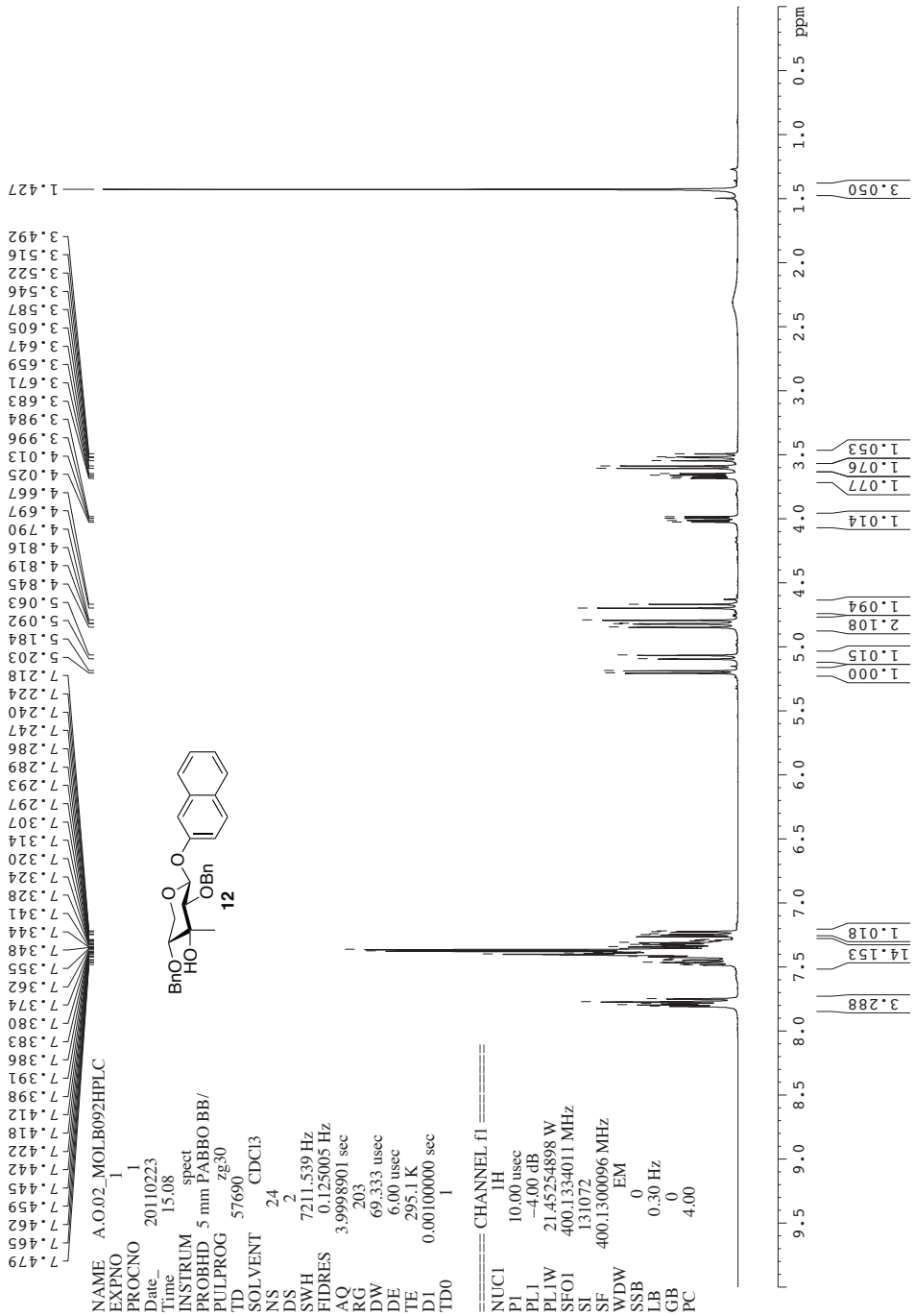
[1]H-NMR 2-Naphthyl 2-methyl-β-D-lyxopyranoside **2b**.



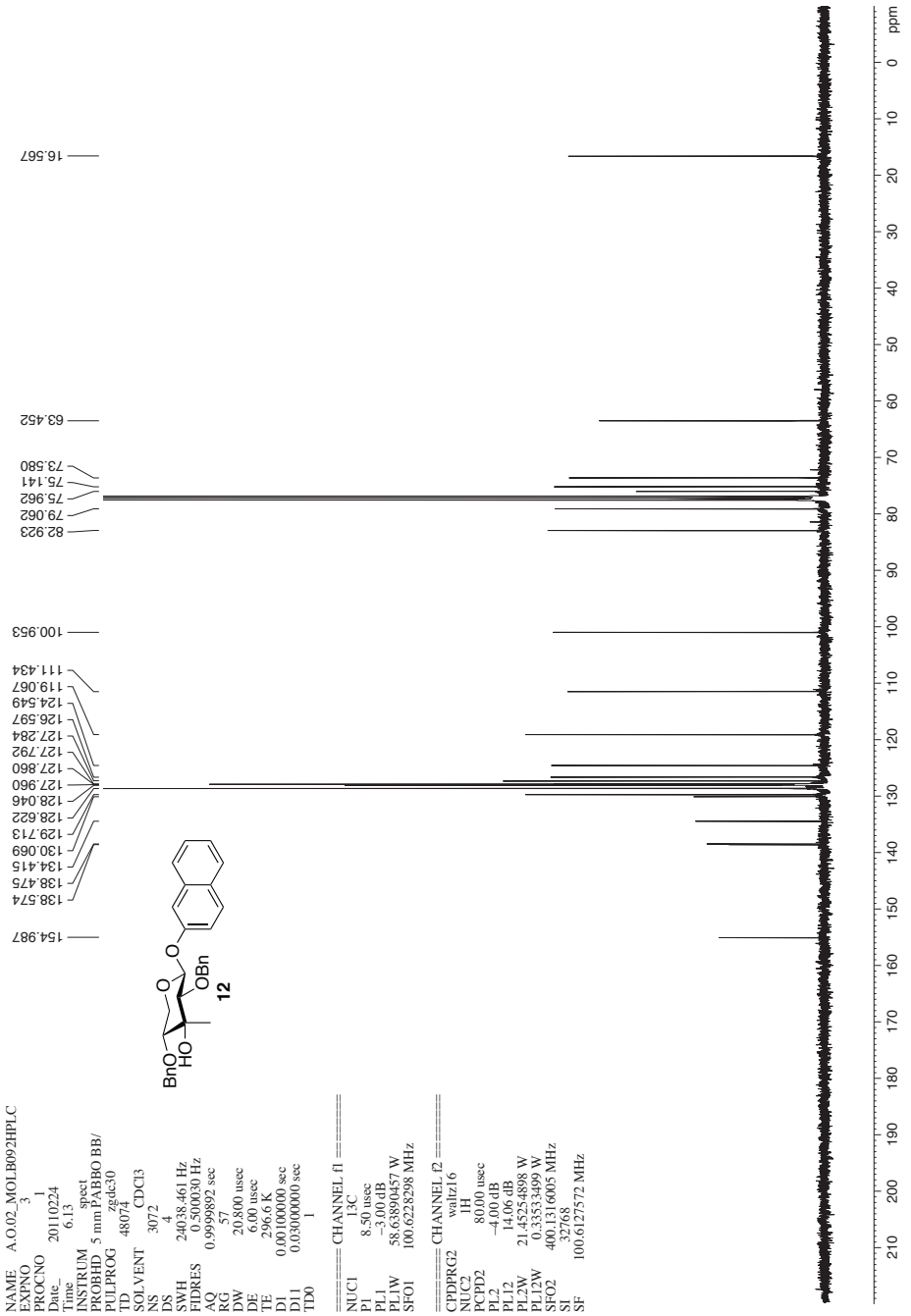
^{13}C-NMR 2-Naphthyl 2-methyl-β-D-lyxopyranoside **2b**.



[1]H-NMR 2-Naphthyl 2,4-di-*O*-benzyl-3-methyl-β-D-xylopyranosides **12**.



^{13}C-NMR 2-Naphthyl 2,4-di-*O*-benzyl-3-methyl-β-D-xylopyranosides **12**.



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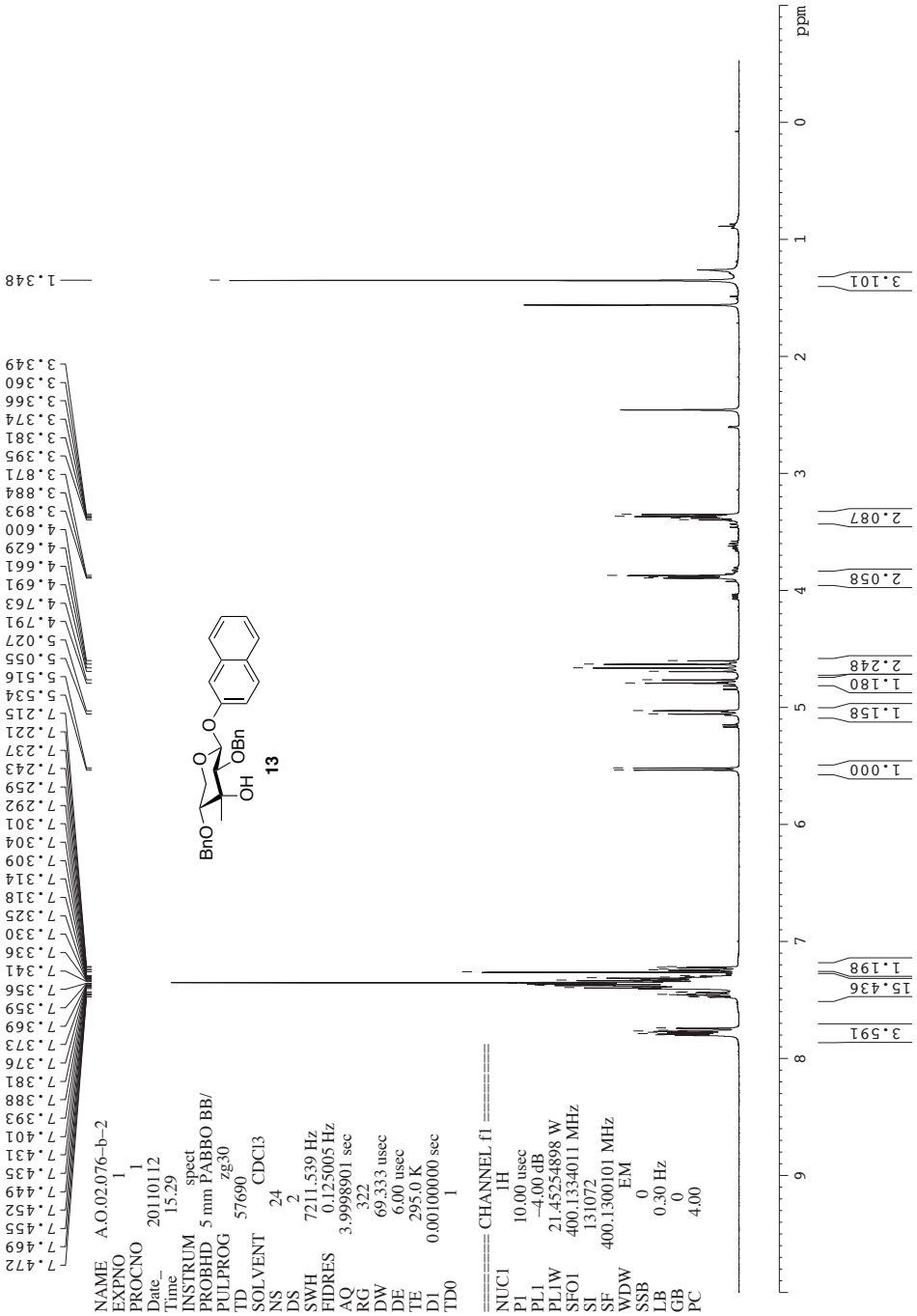
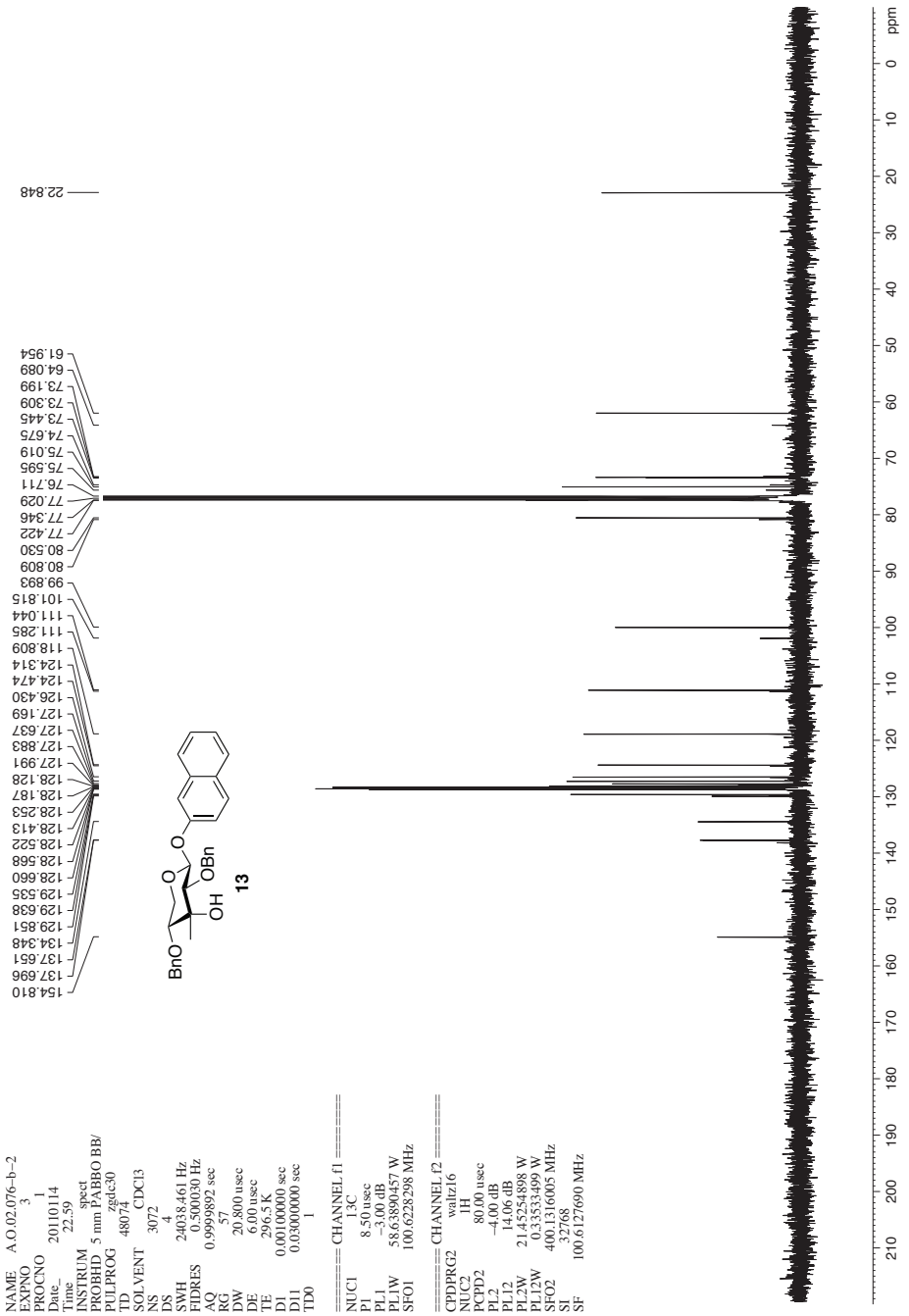
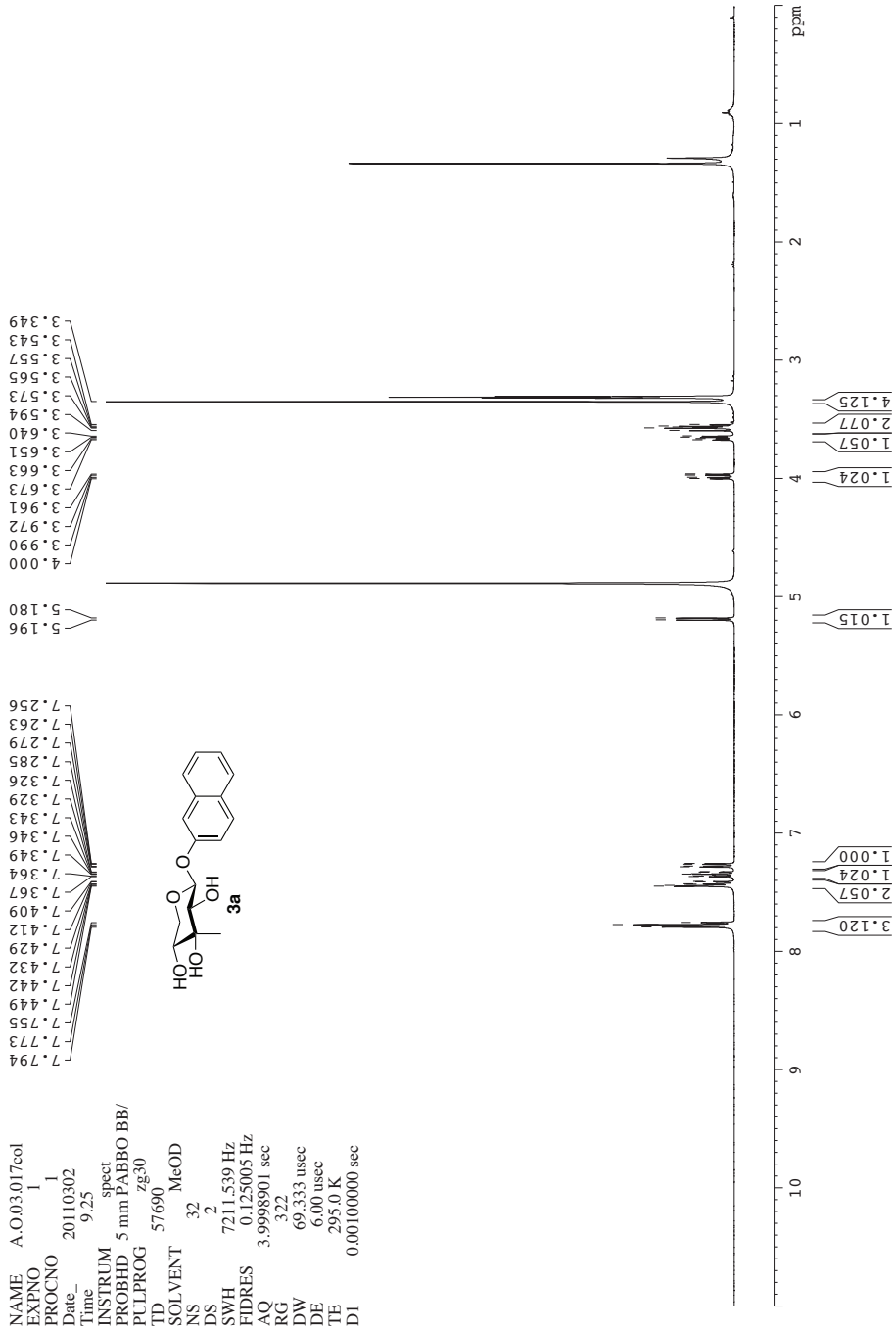
^{1}H-NMR 2-naphthyl 2,4-di-*O*-benzyl-3-methyl-β-D-ribopyranosides **13**.



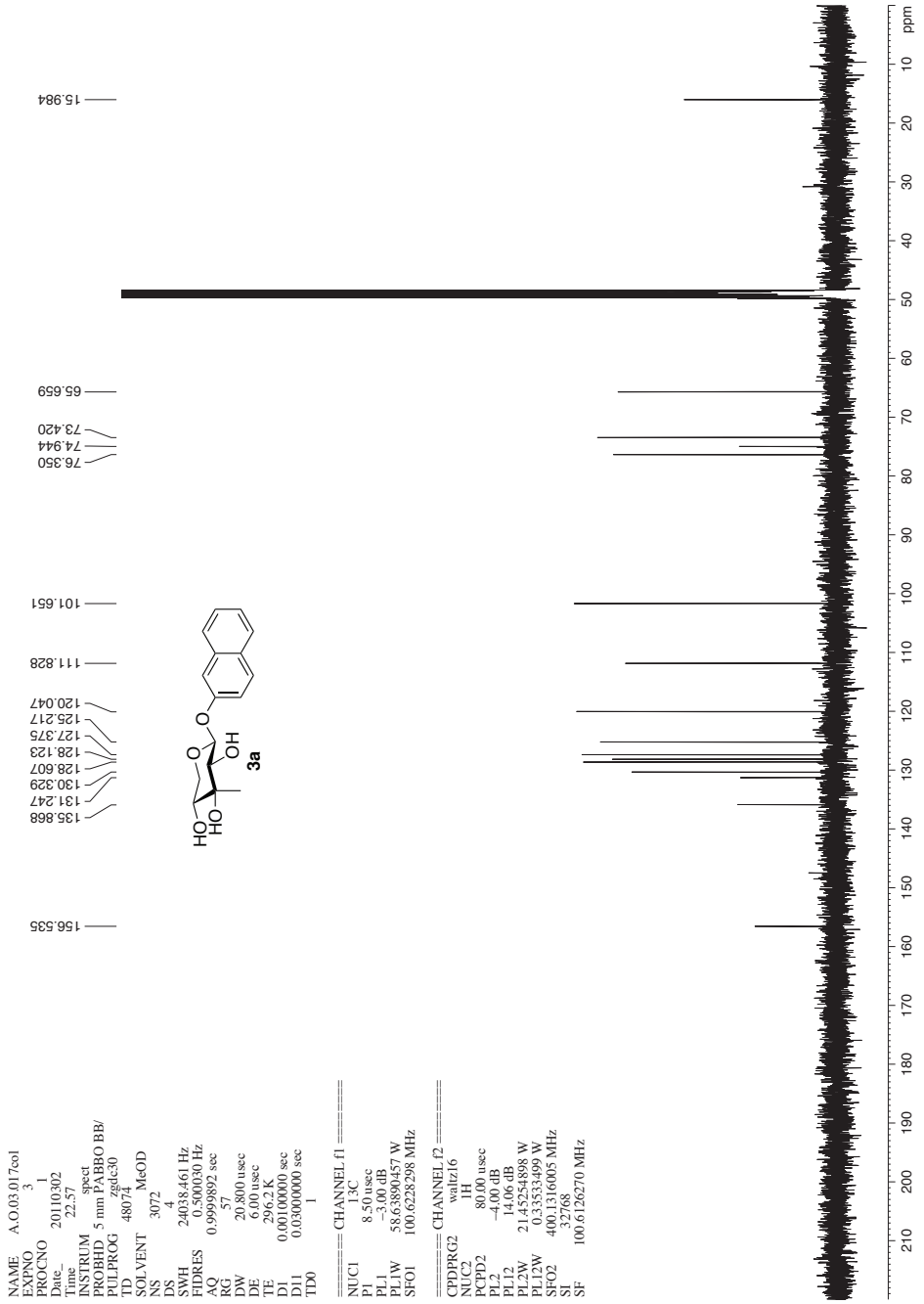
^{13}C-NMR 2-naphthyl 2,4-di-*O*-benzyl-3-methyl-β-D-ribopyranosides **13**.



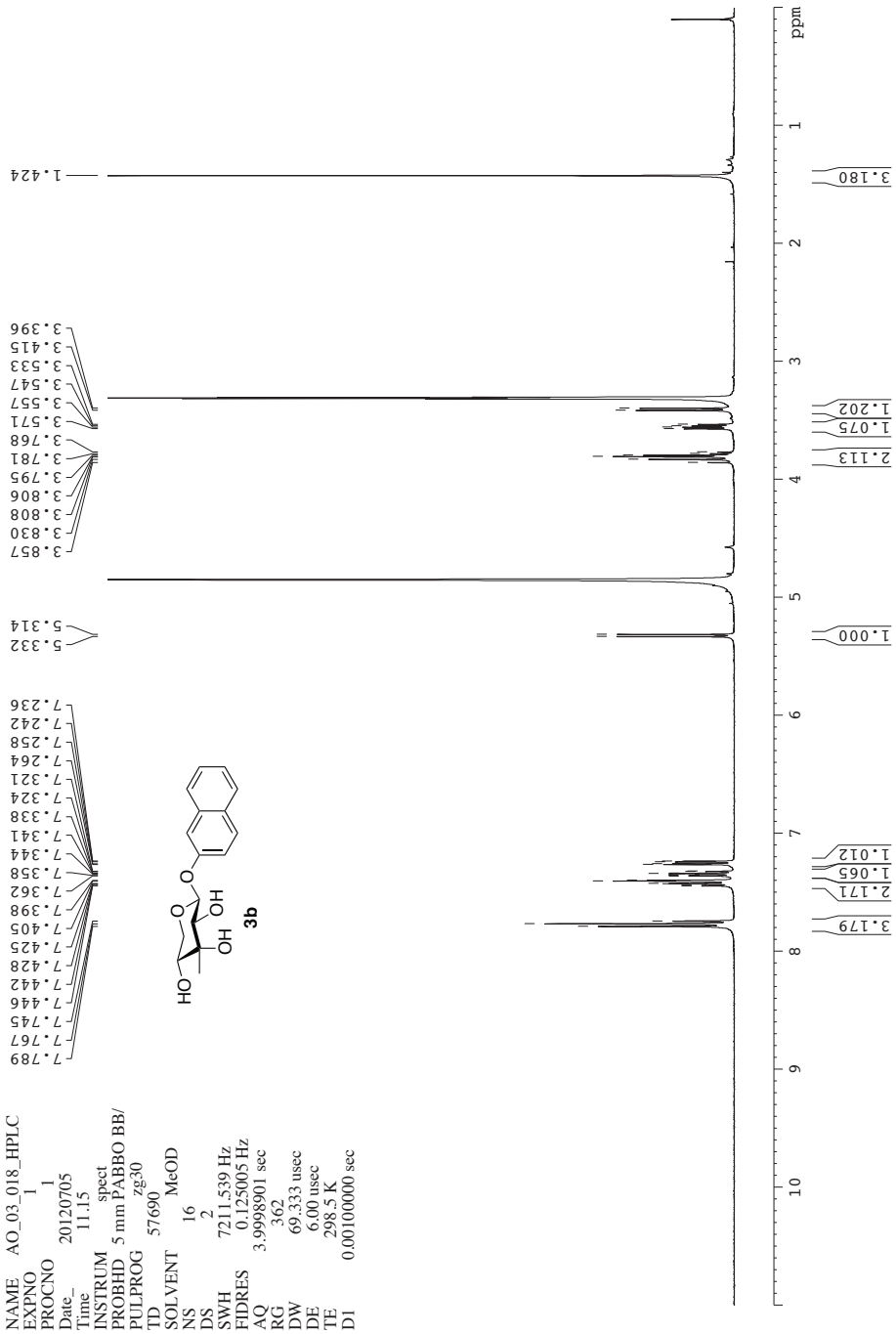
[1]H-NMR 2-Naphthyl 3-methyl-β-D-xylopyranoside **3a**.



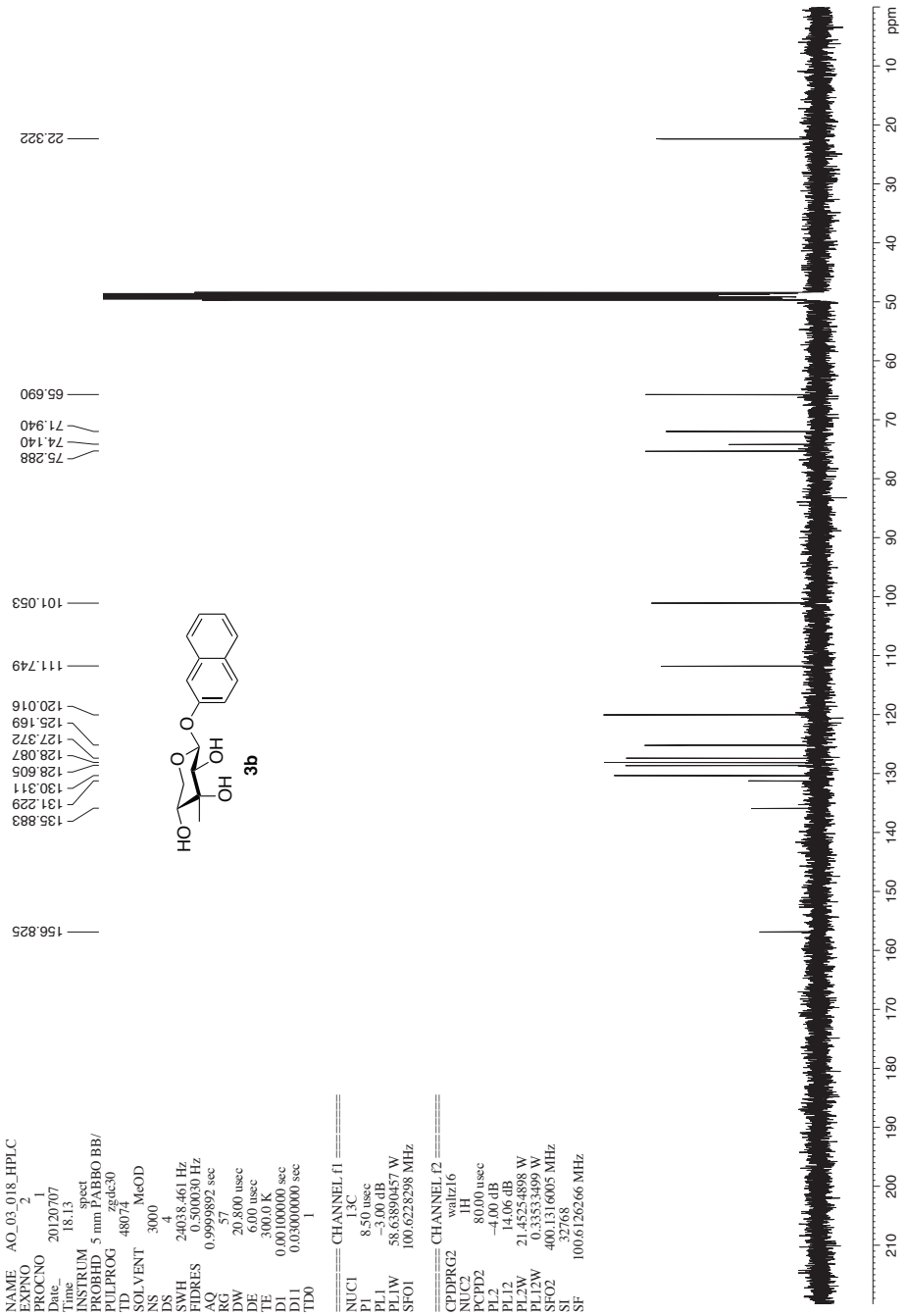
^{13}C-NMR 2-Naphthyl 3-methyl-β-D-xylopyranoside **3a**.



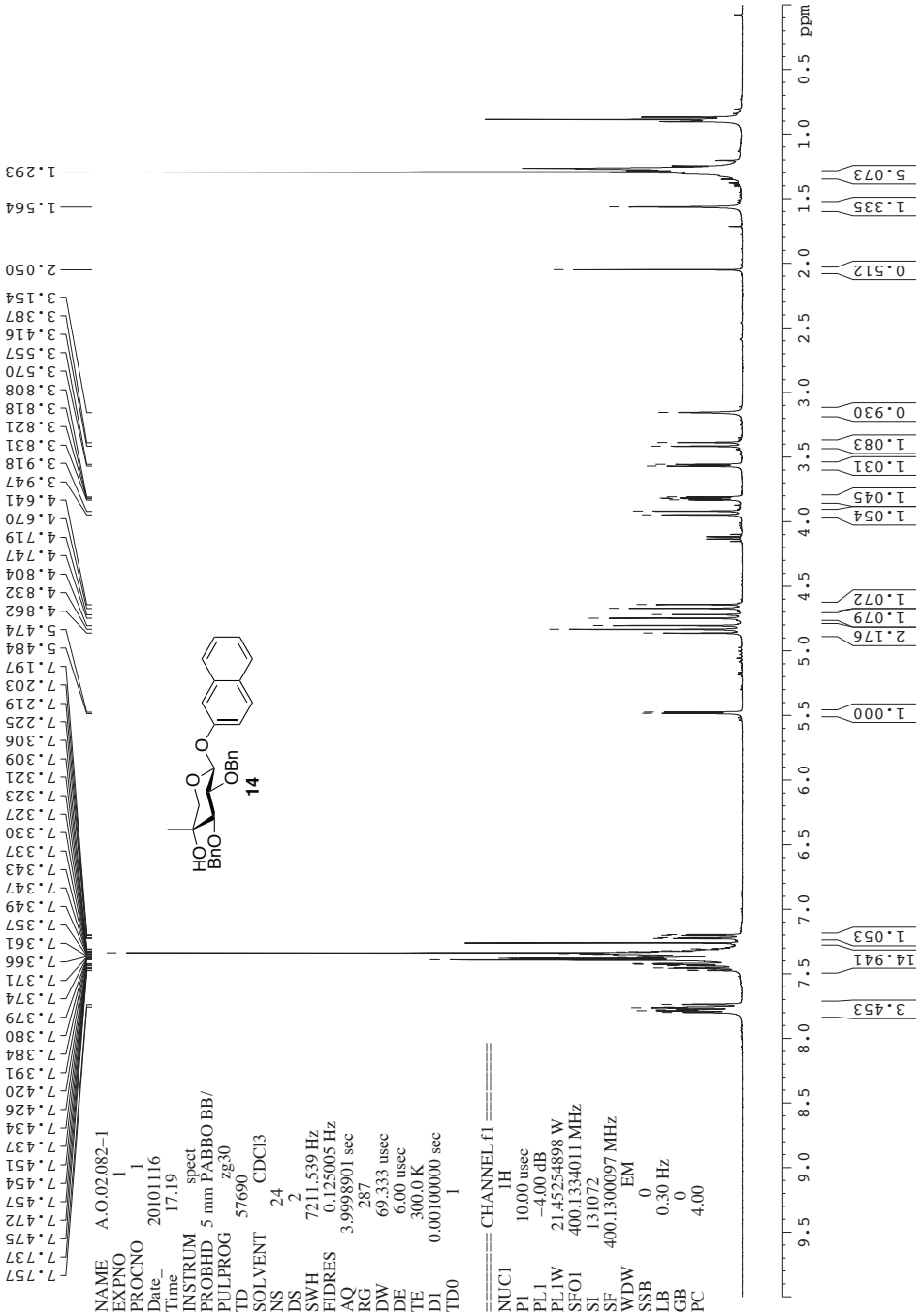
[1]H-NMR 2-Naphthyl 3-methyl-β-D-ribopyranoside **3b**.



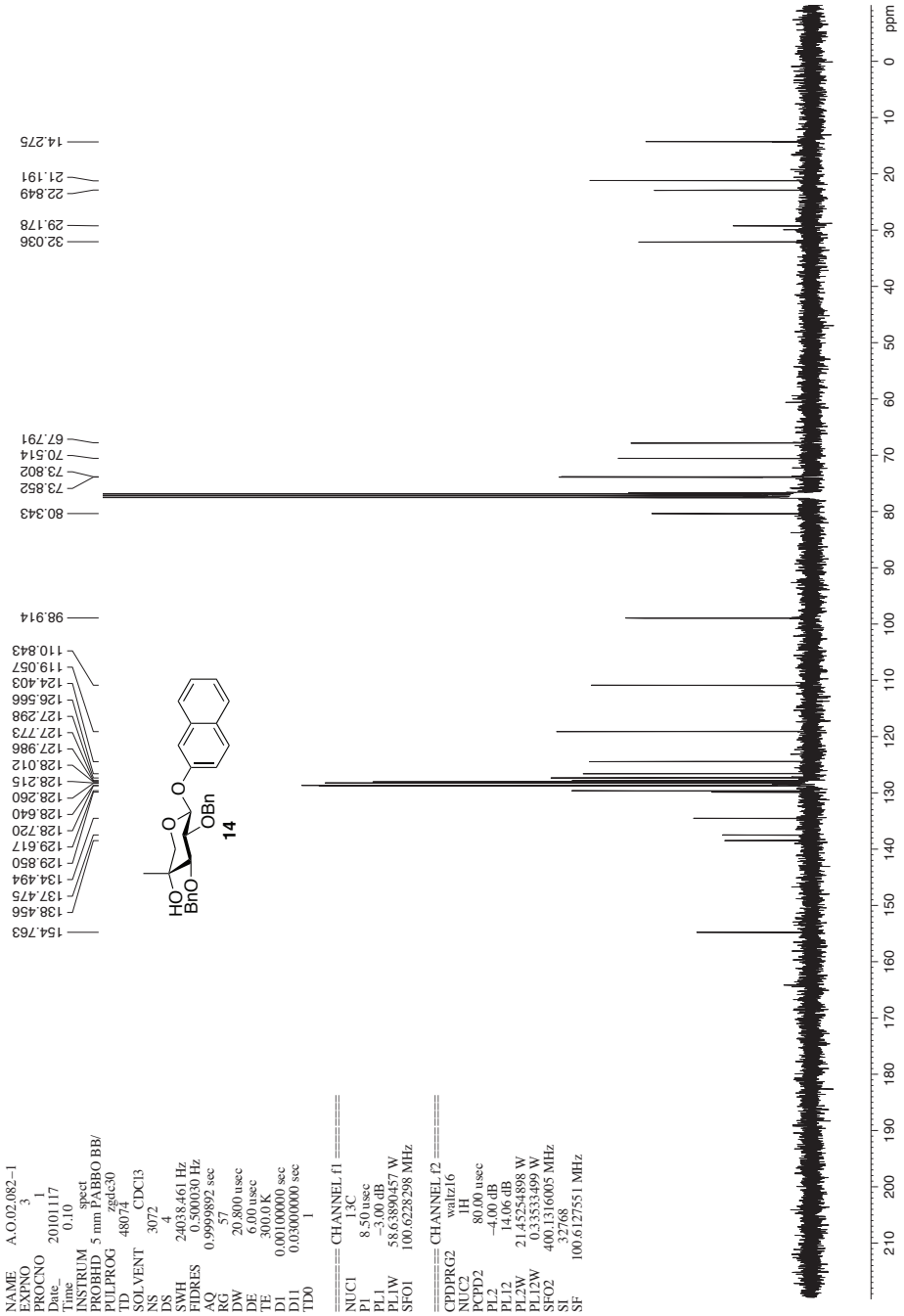
^{13}C-NMR 2-Naphthyl 3-methyl-β-D-ribopyranoside **3b**.



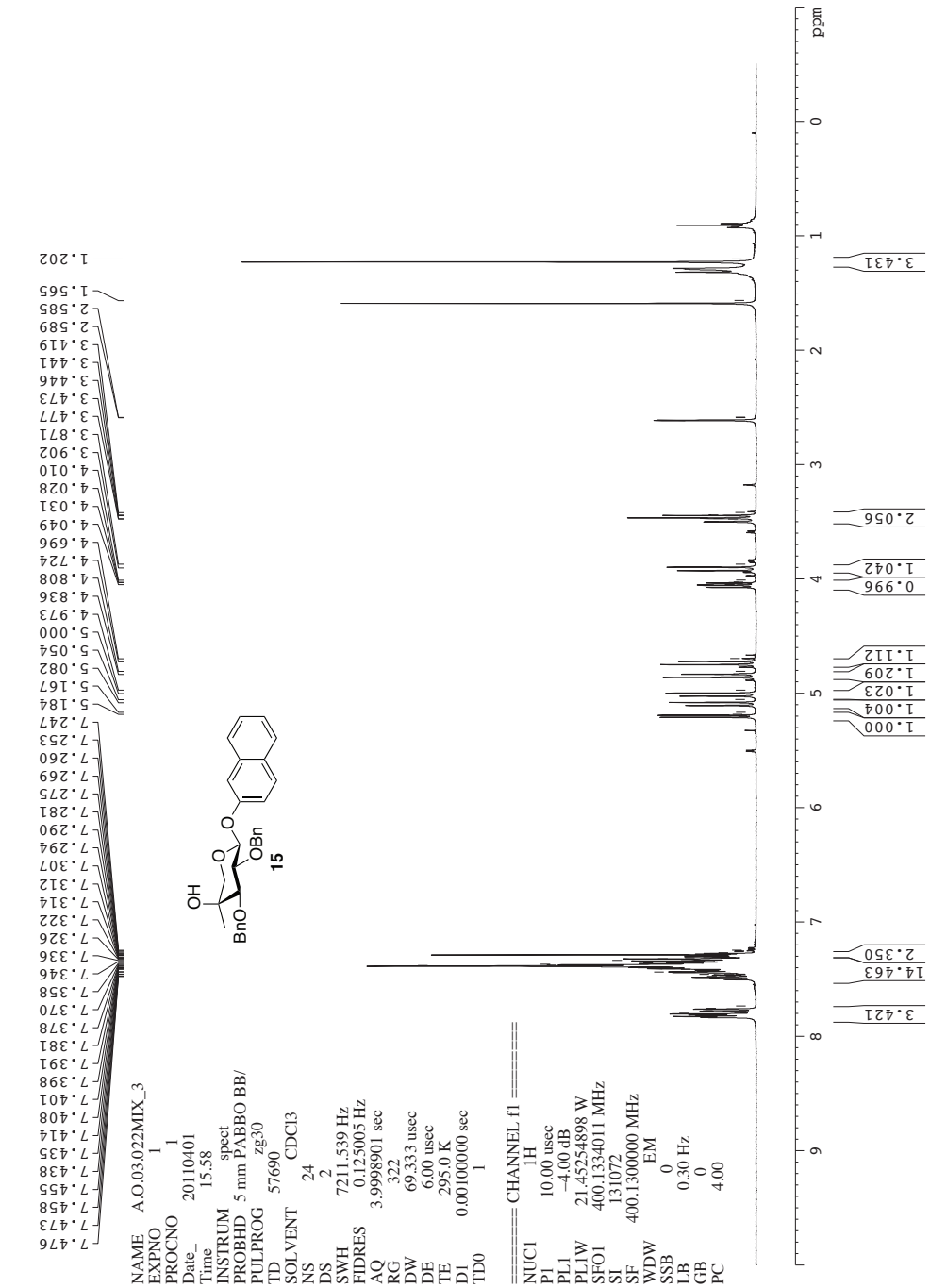
[1]H-NMR 2-Naphthyl 2,3-di-*O*-benzyl-4-methyl-β-D-xylopyranoside **14**.



^{13}C-NMR 2-Naphthyl 2,3-di-*O*-benzyl-4-methyl-β-D-xylopyranoside **14**.



[1]H-NMR 2-Naphthyl 2,3-di-*O*-benzyl-4-methyl-β-D-arabinopyranoside **15**.



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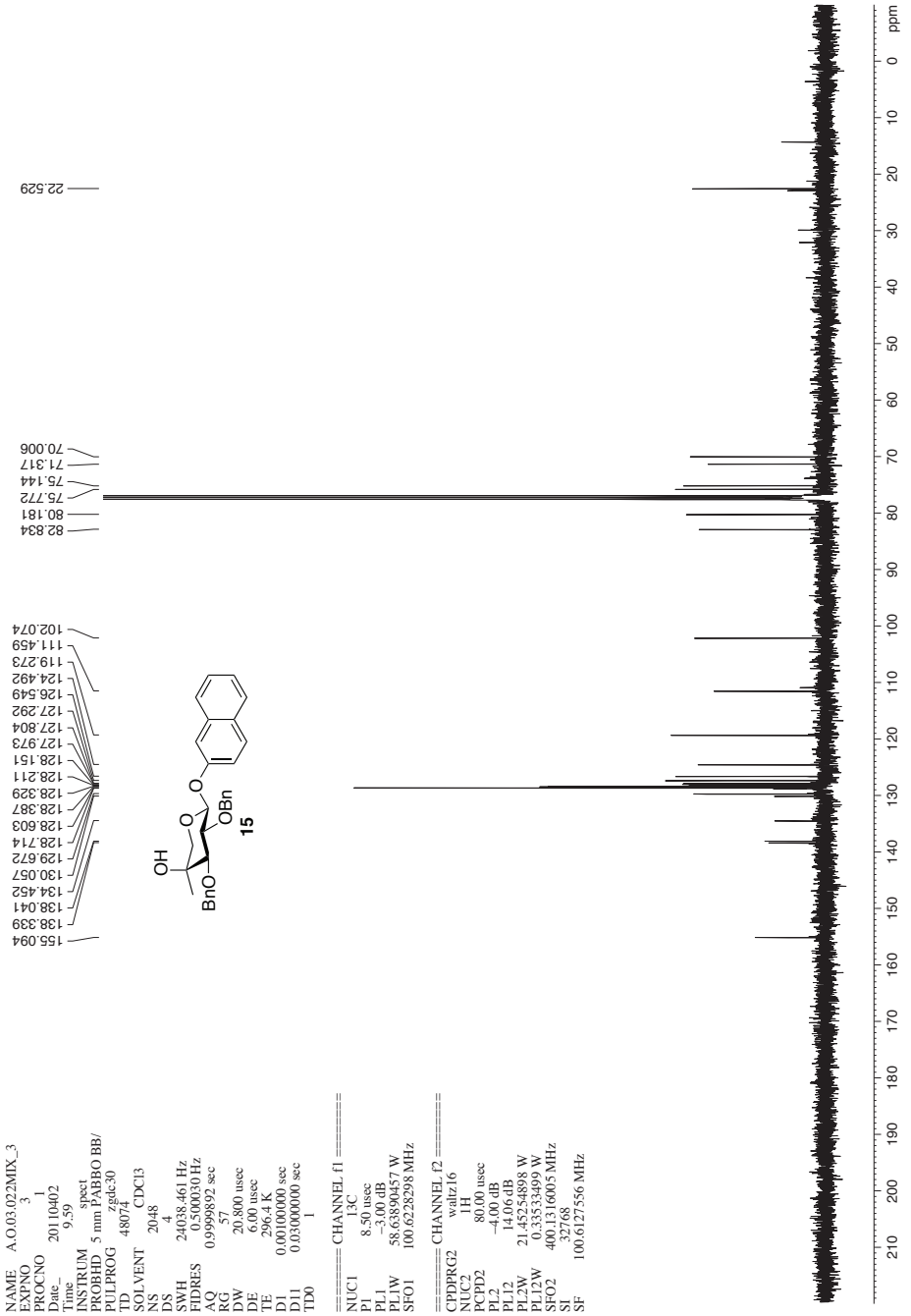

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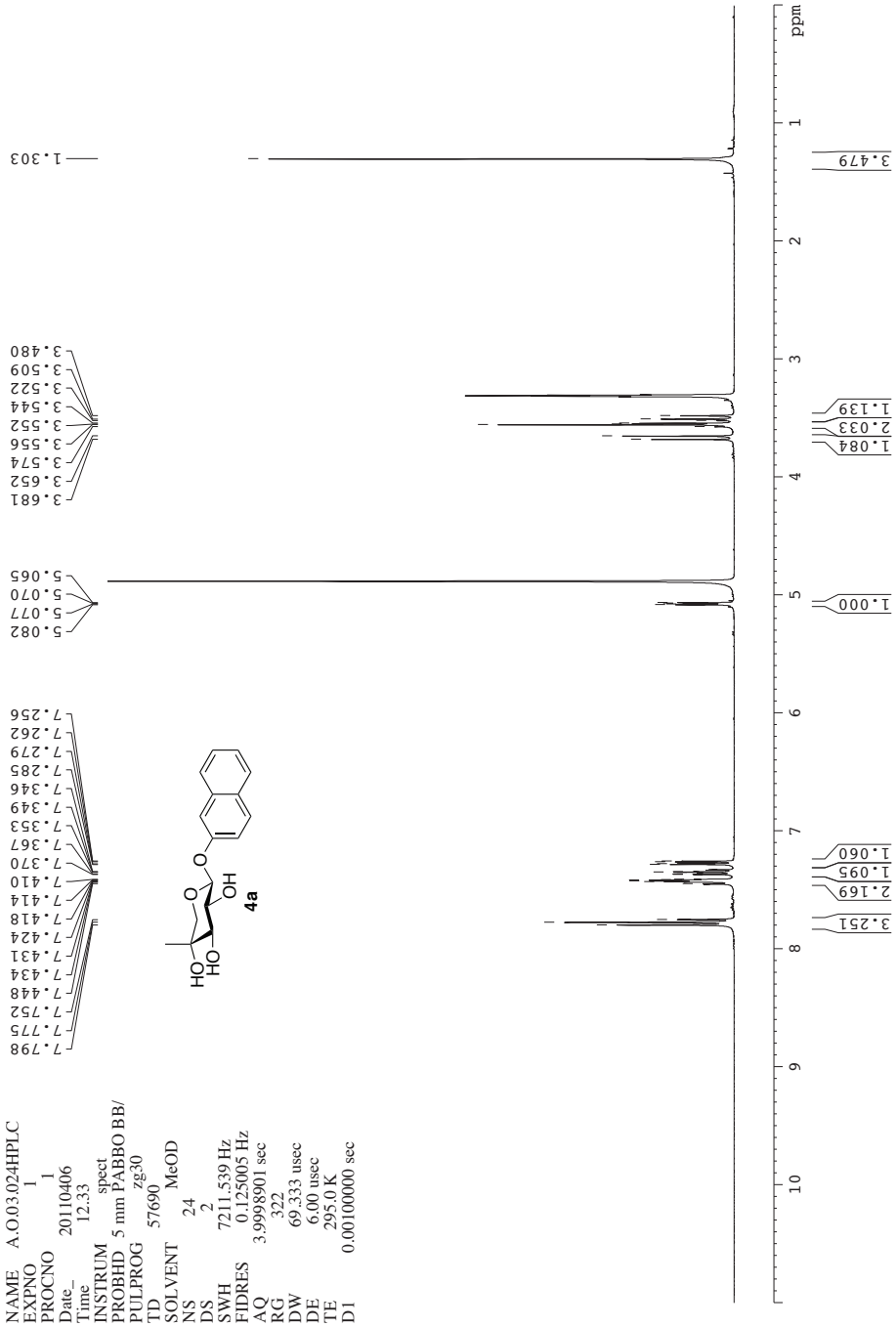

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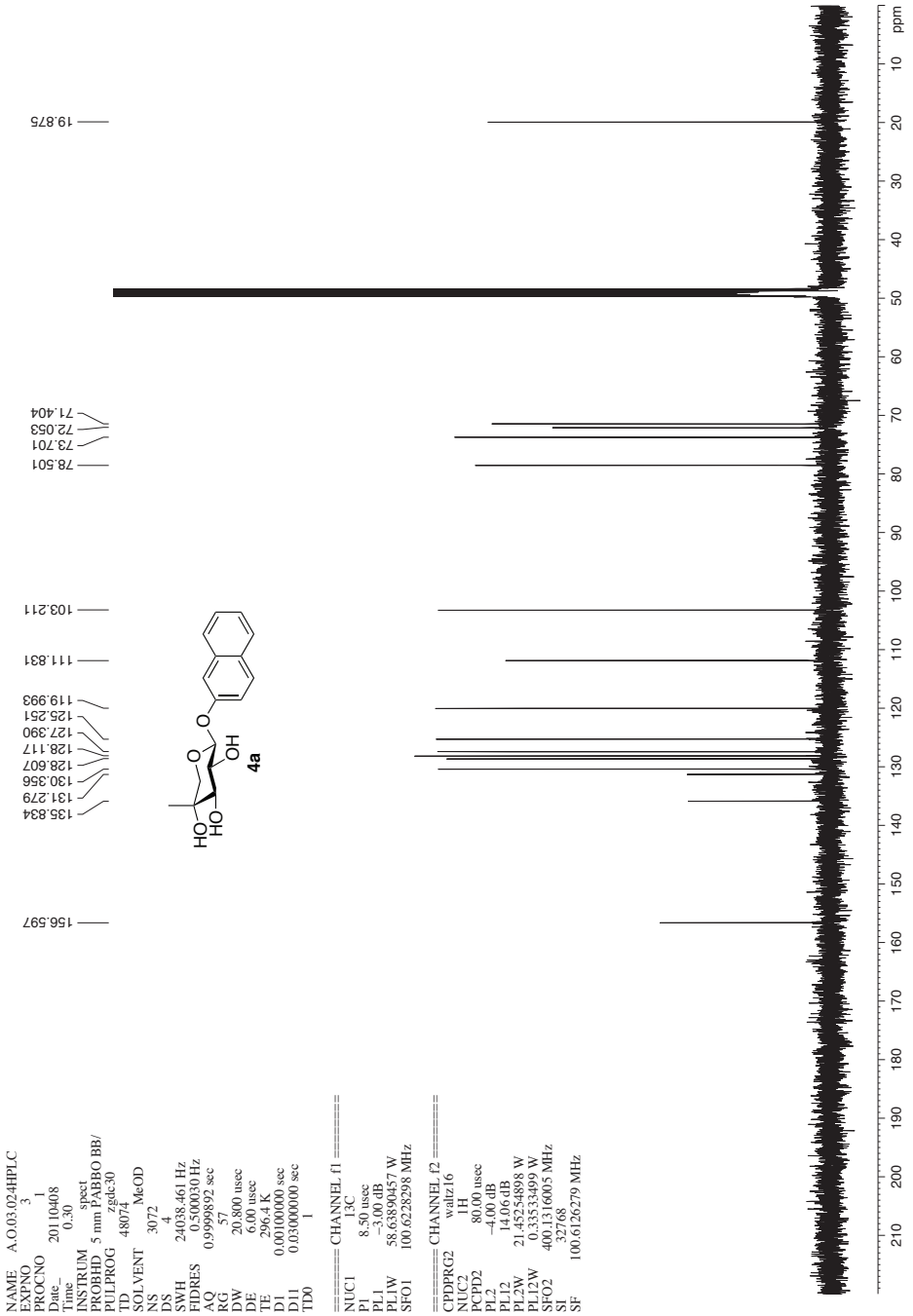

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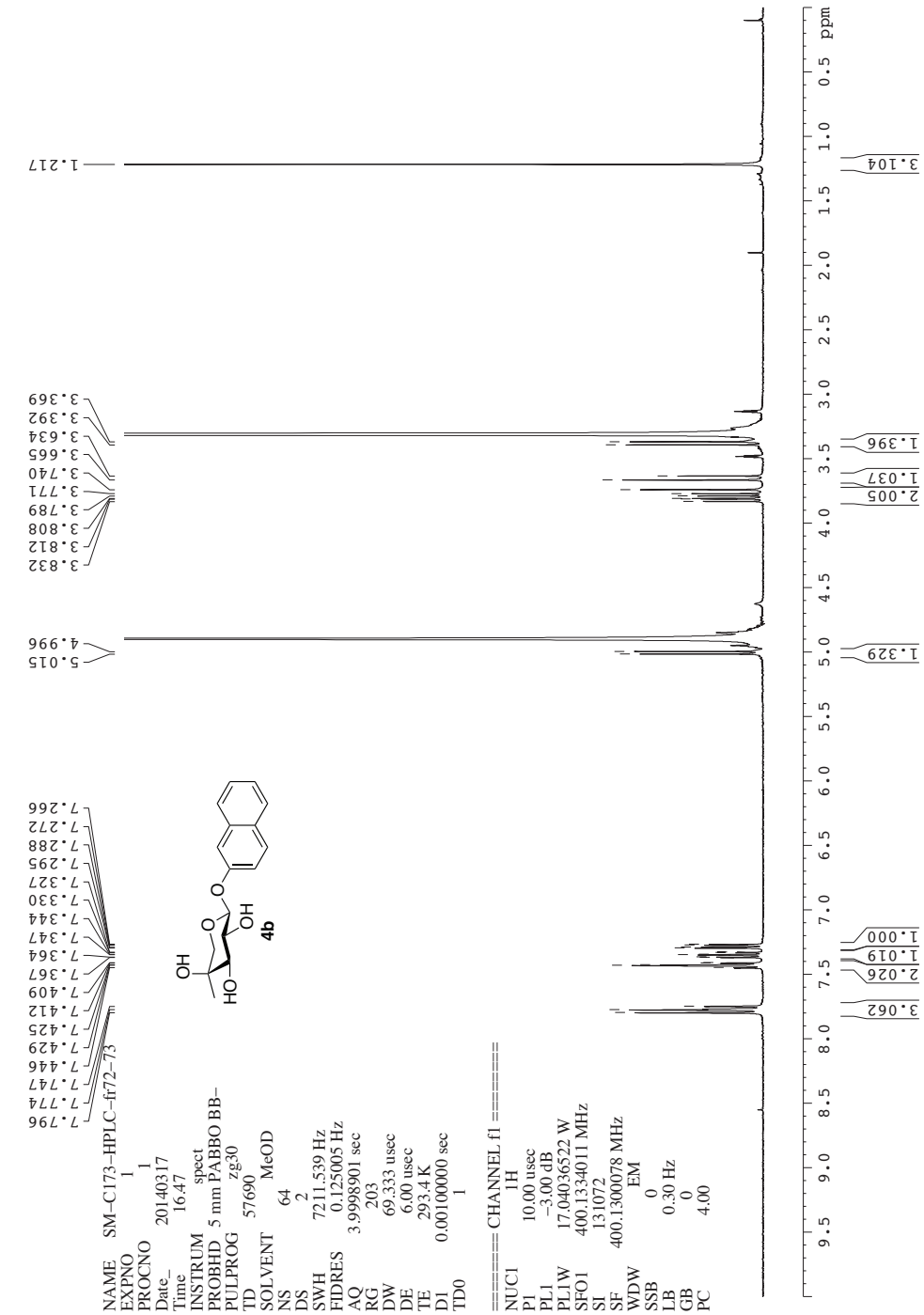

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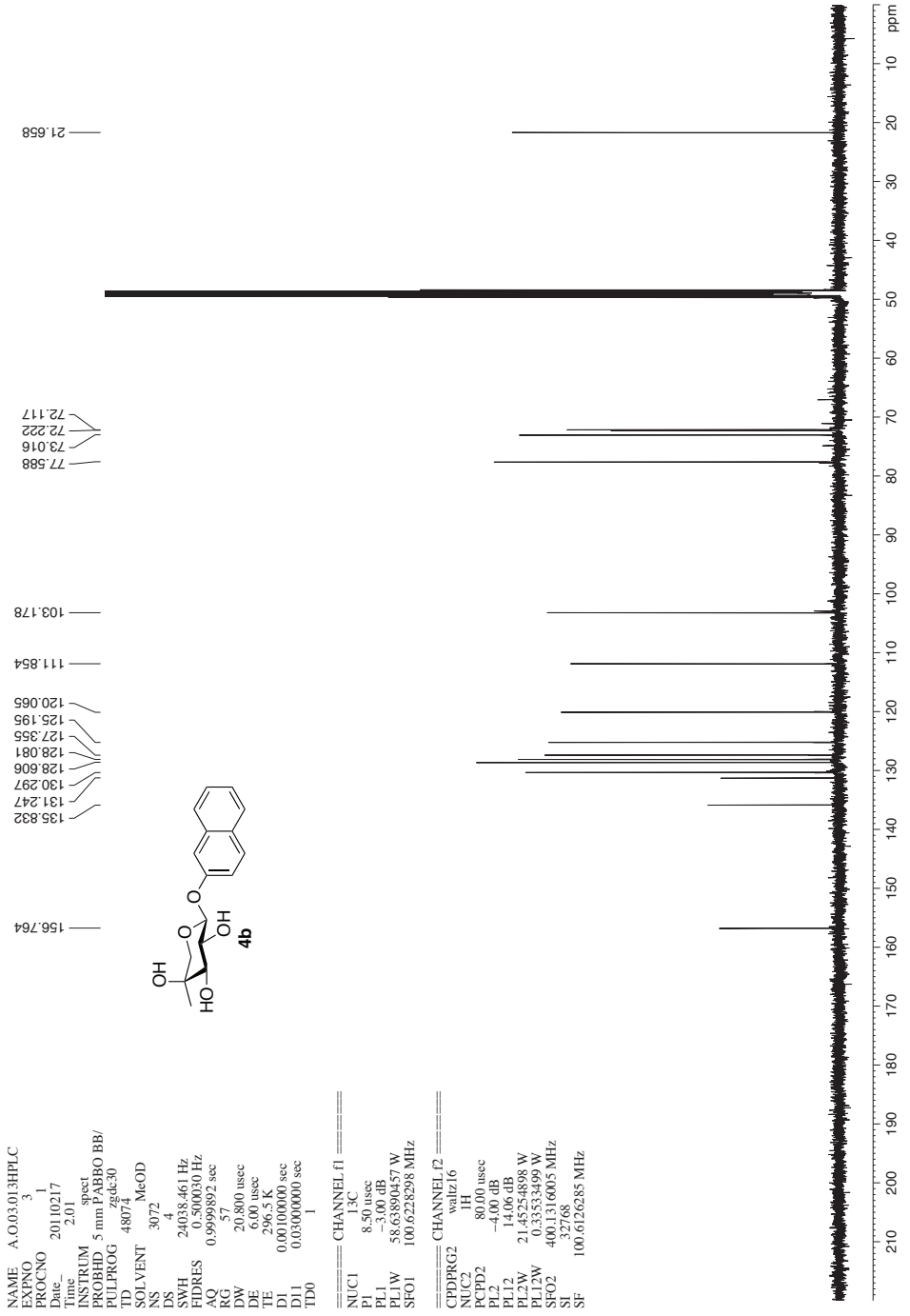

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DW 20.800 usec
DE 6.00 usec
TE 296.5 K
D1 0.00100000 sec
D11 0.03000000 sec
TD0 1
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P1 8.50 usec
PL1 −3.00 dB
PL1W 58.63890457 W
SFO1 100.6228298 MHz
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CPDPRG2 waltz16
NUC2 1H
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PL2 −4.00 dB
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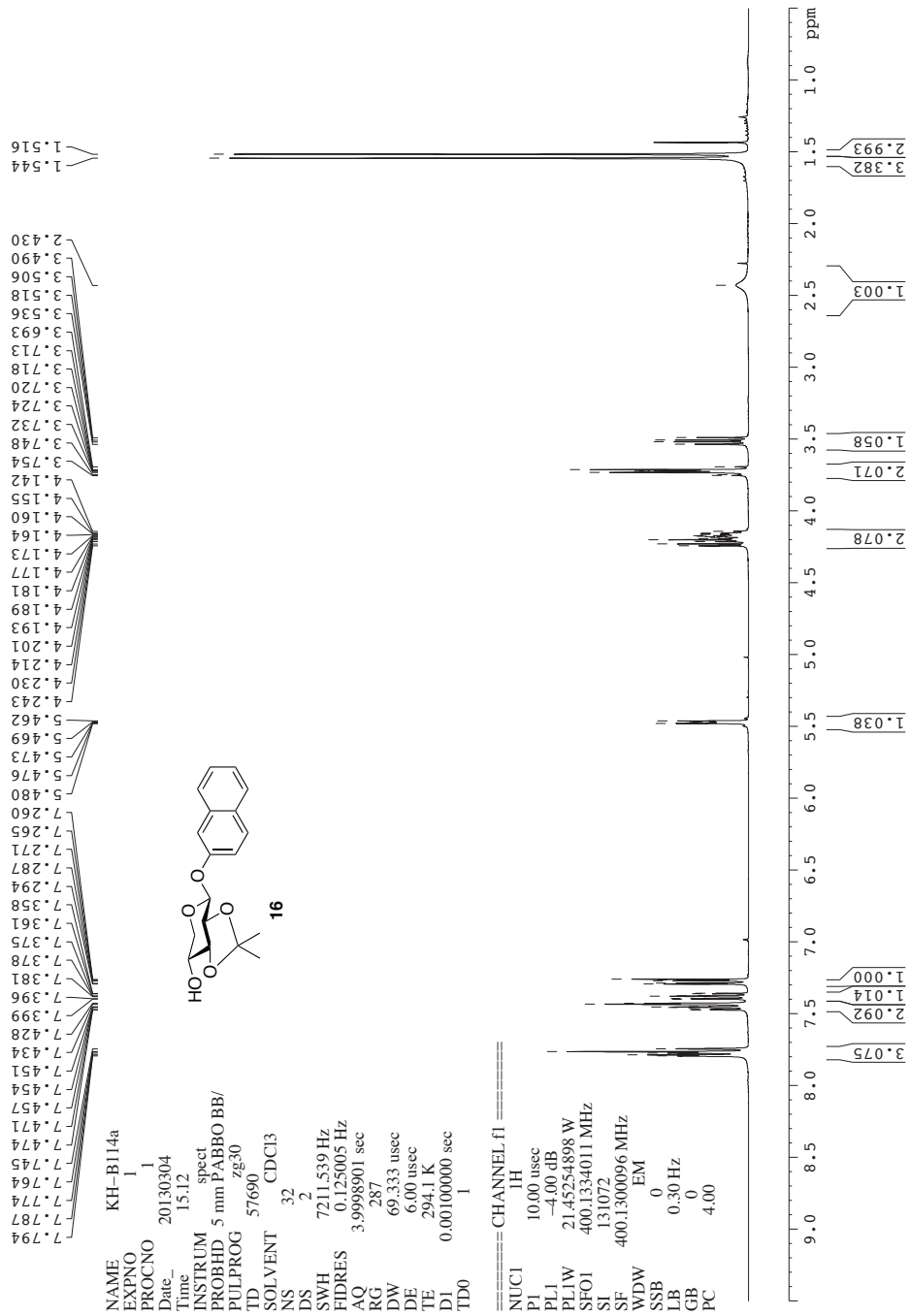

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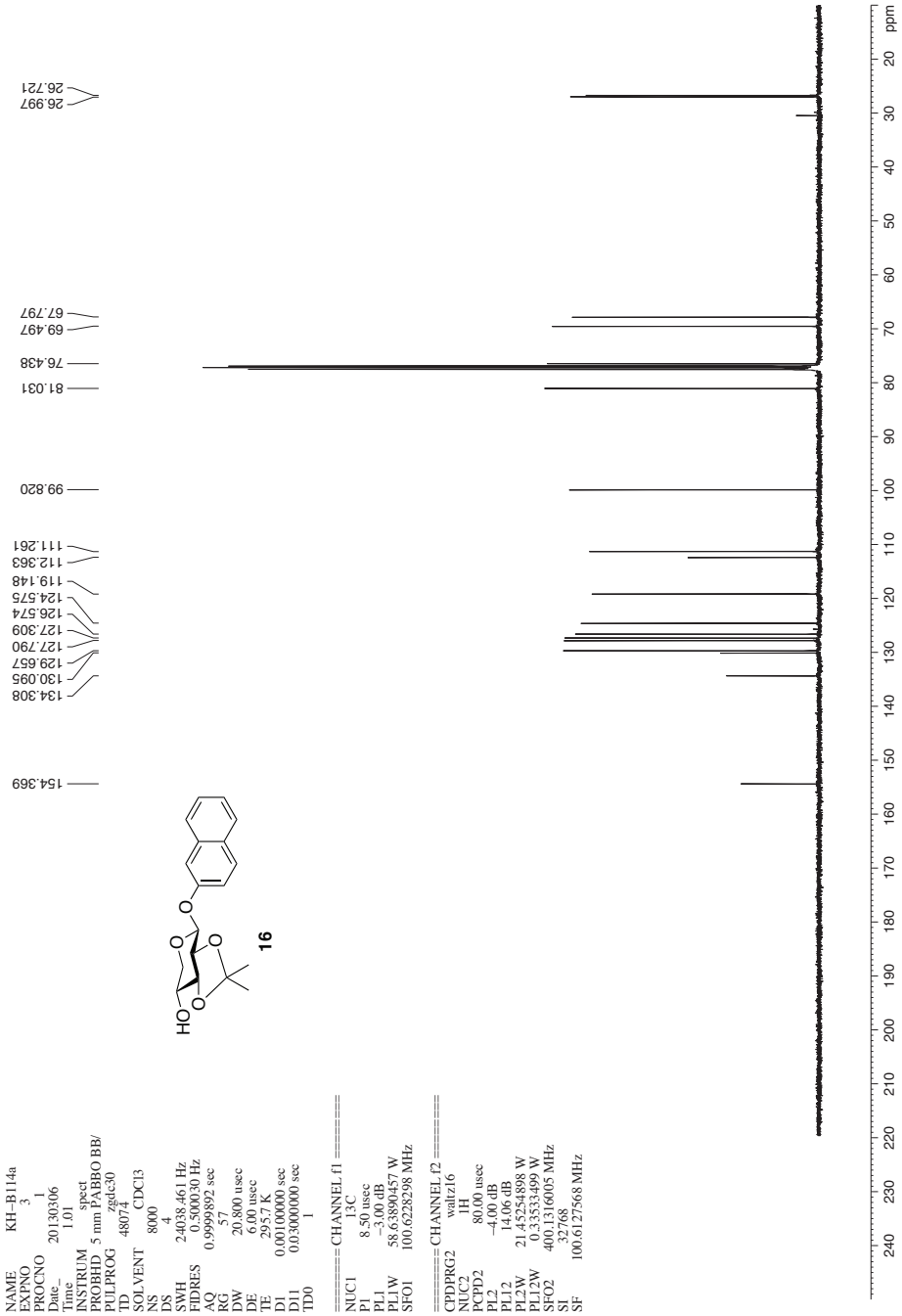

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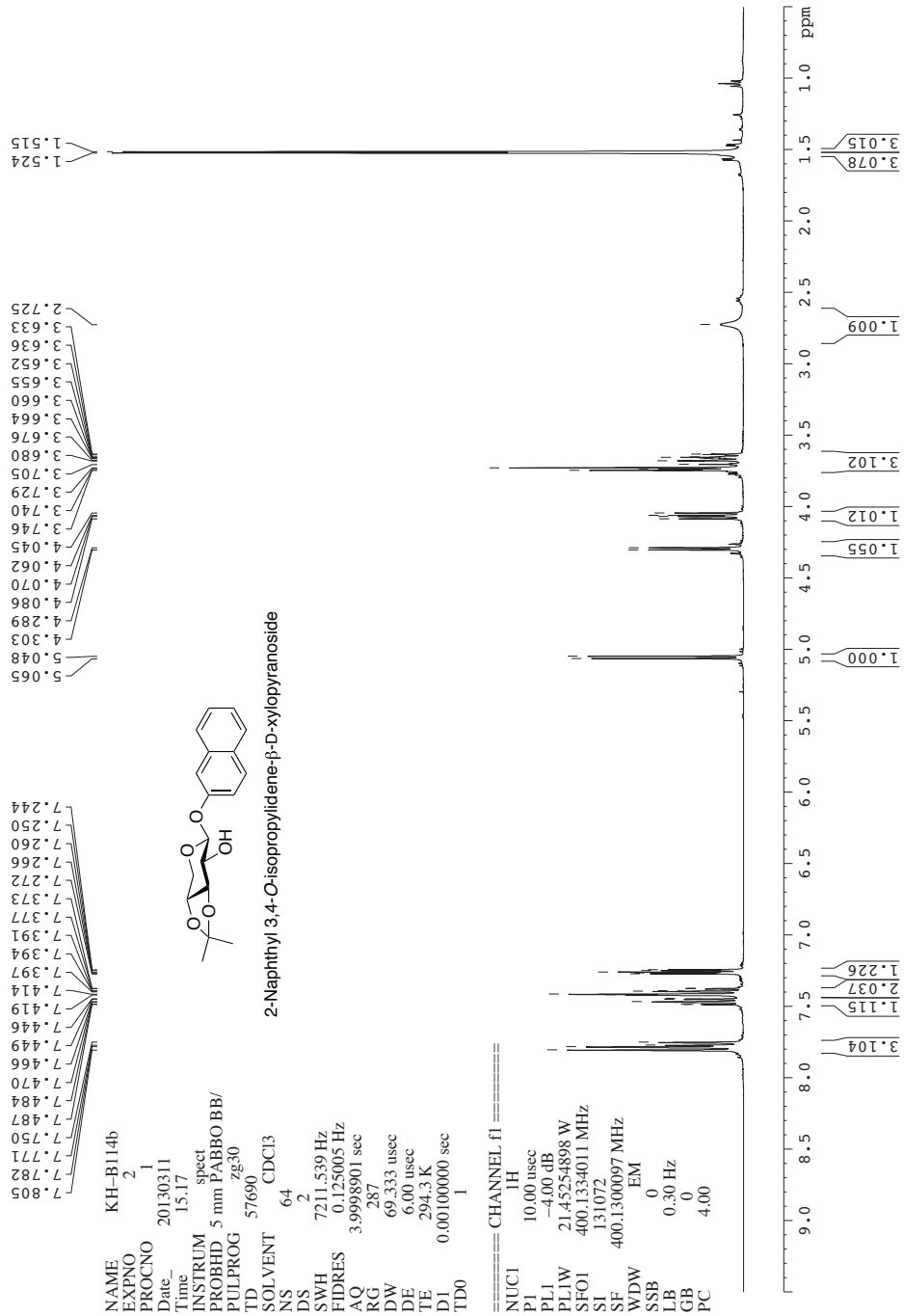

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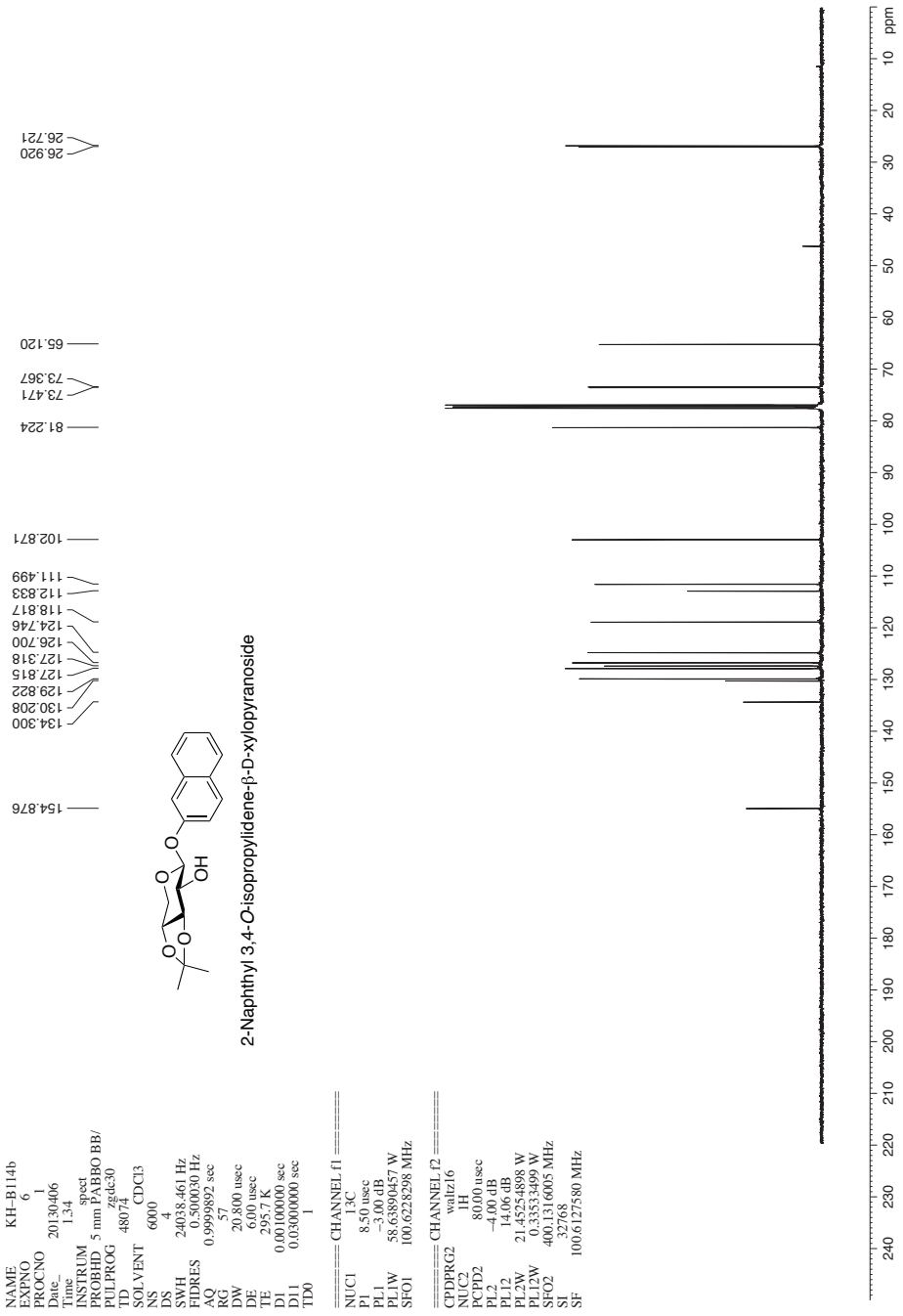

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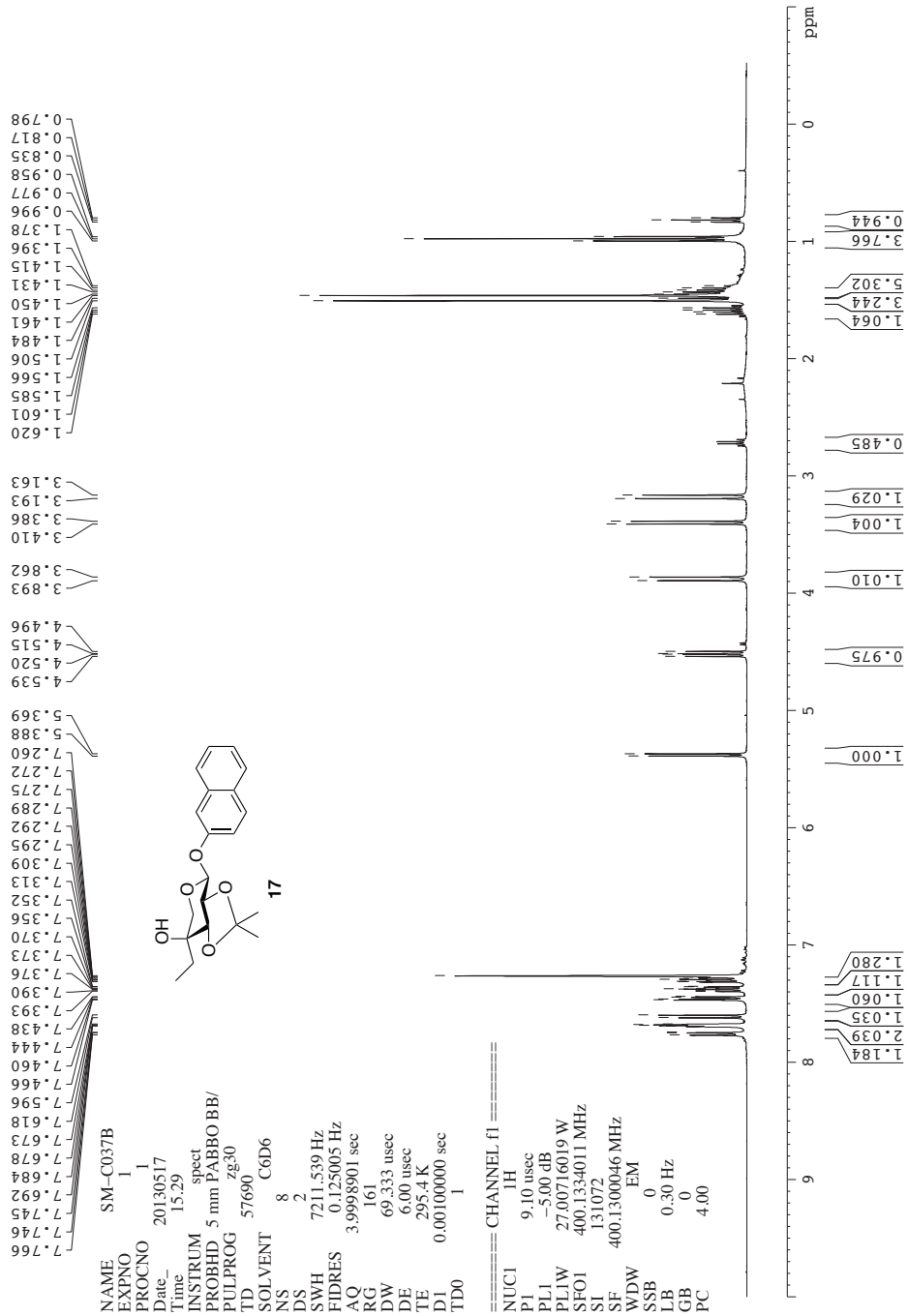
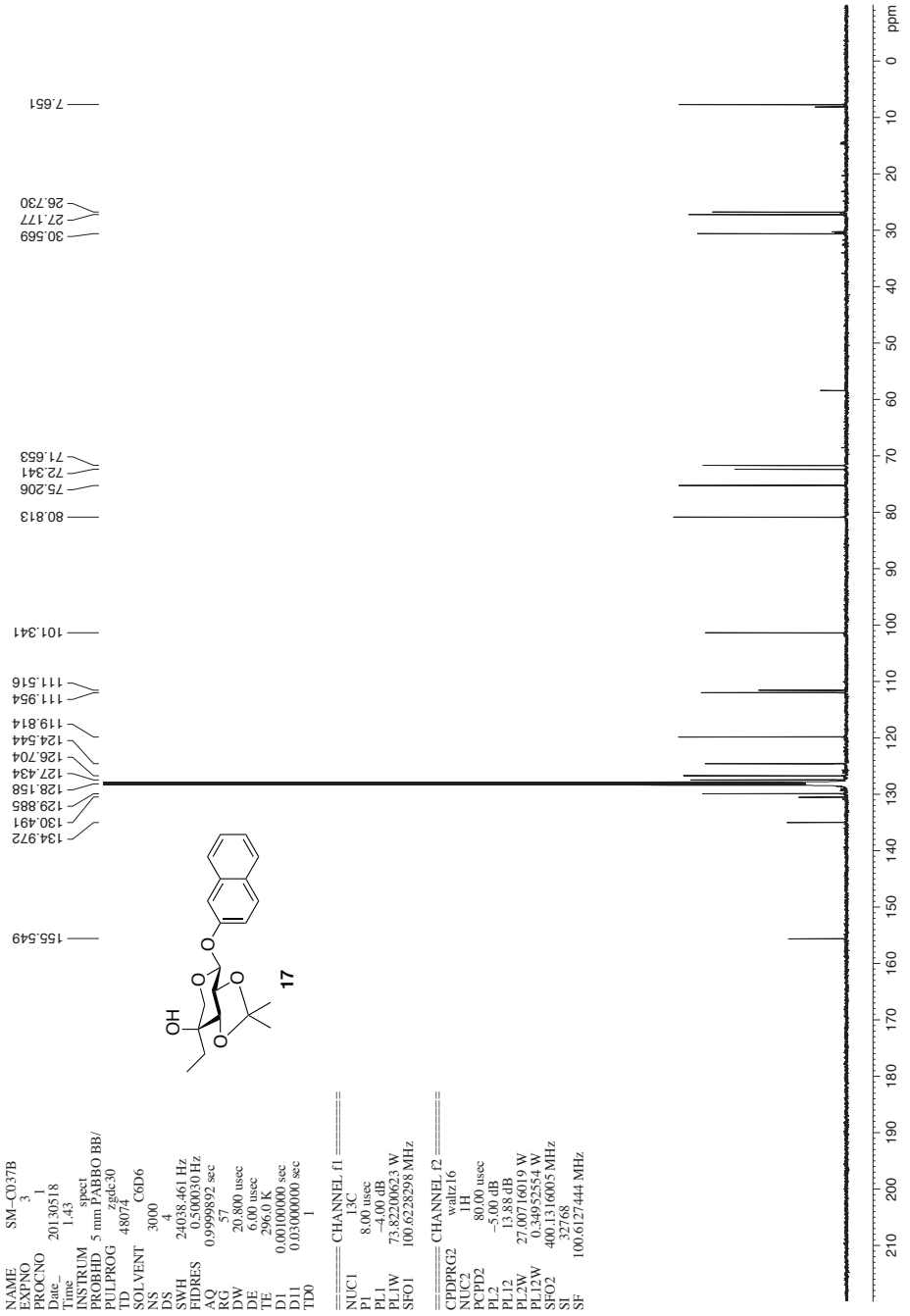
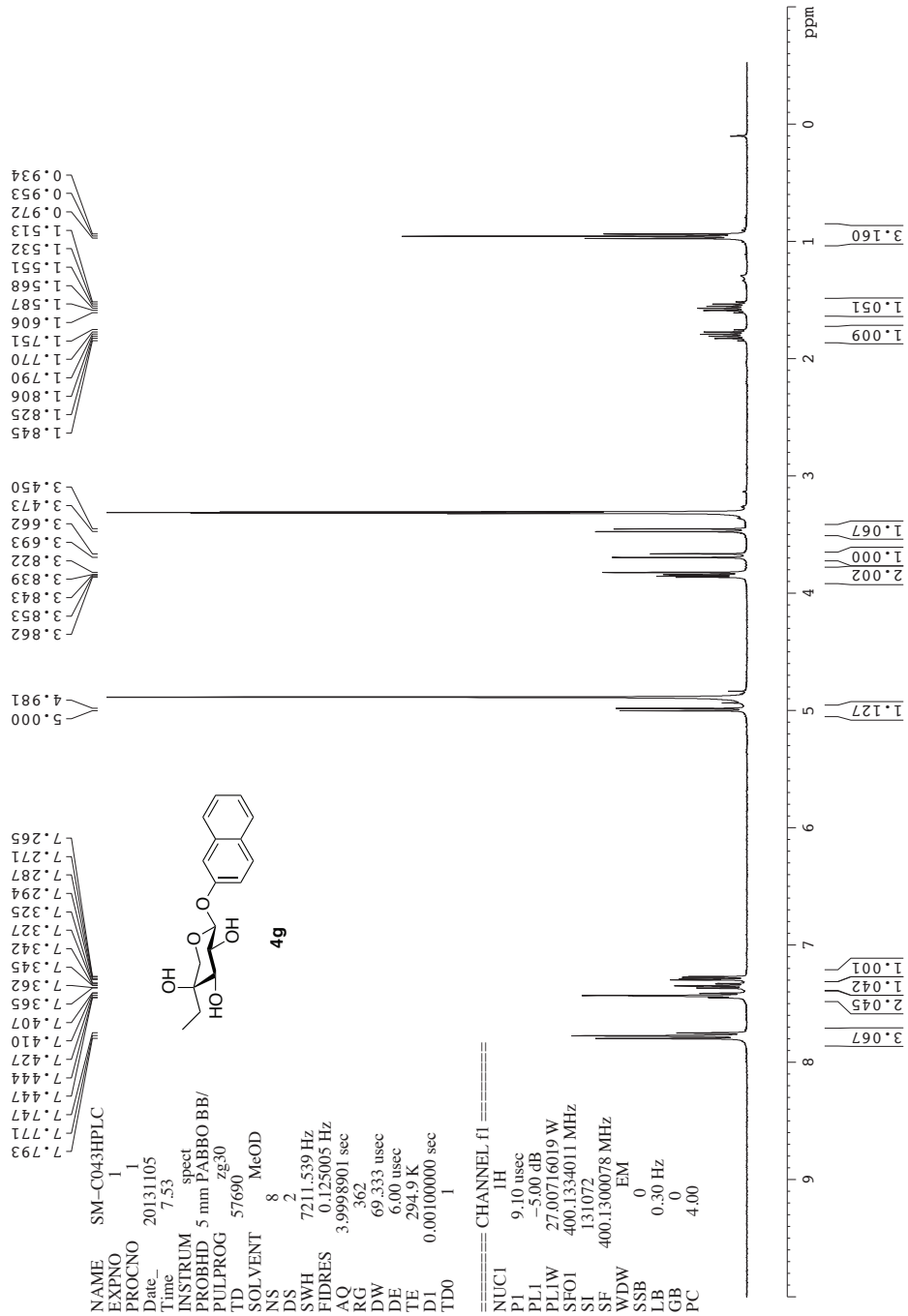


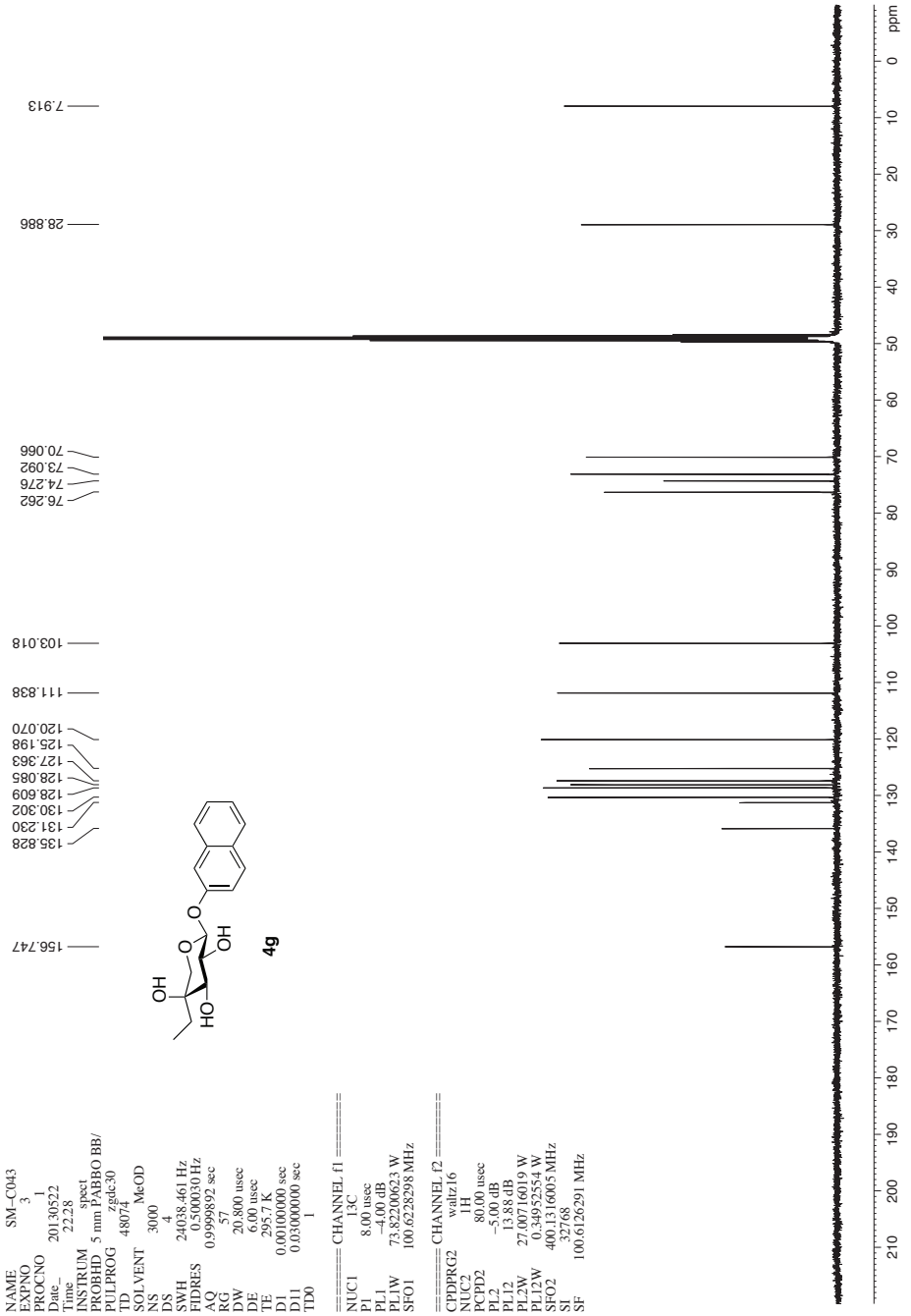
^{13}C-NMR 2-Naphthyl 2,3-*O*-isopropylidene-4-ethyl-β-D-arabinopyranoside **17**.



[1]H-NMR 2-Naphthyl 4-ethyl-β-D-arabinopyranoside **4g**.



^{13}C-NMR 2-Naphthyl 4-ethyl-β-D-arabinopyranoside **4g**.



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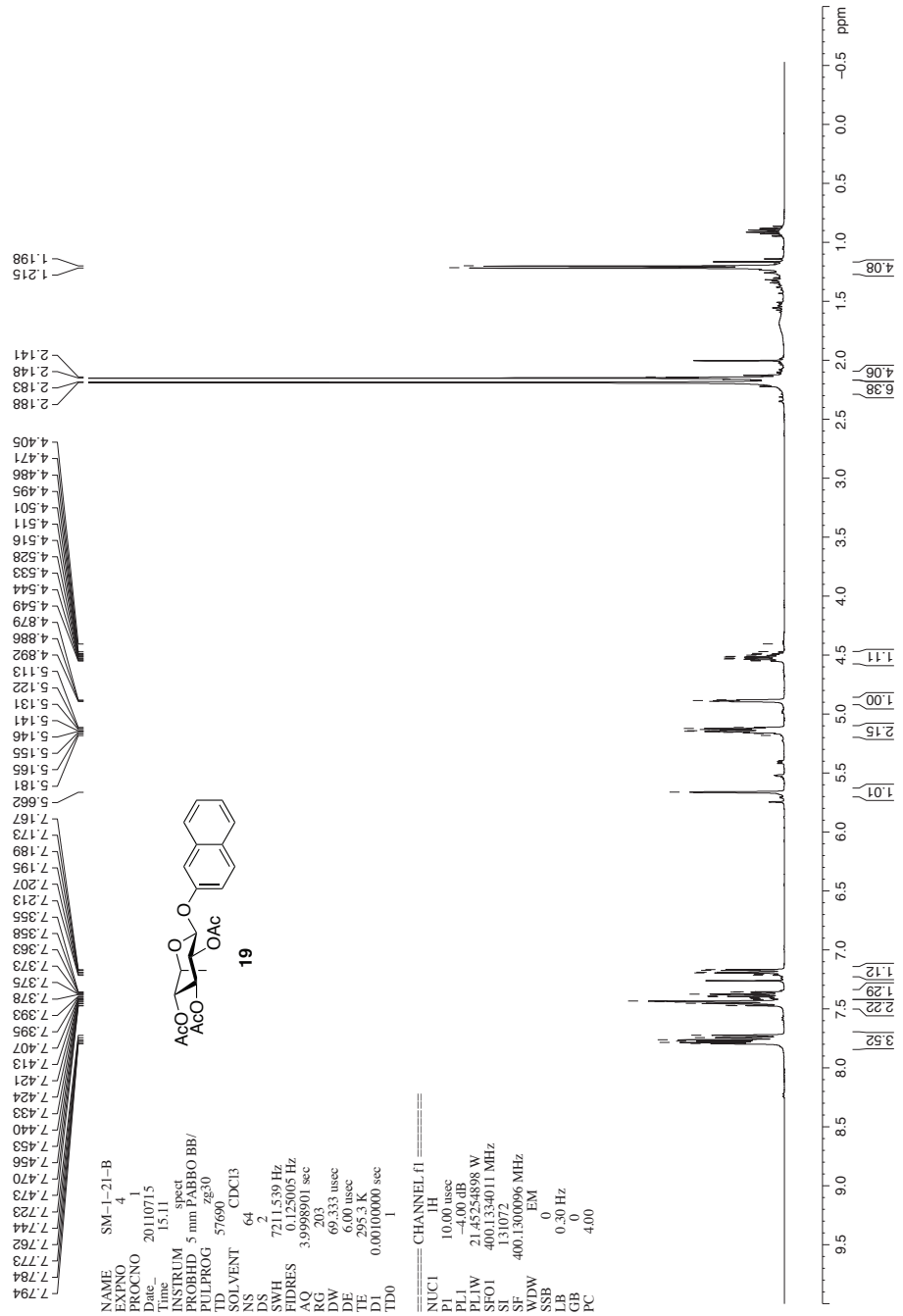

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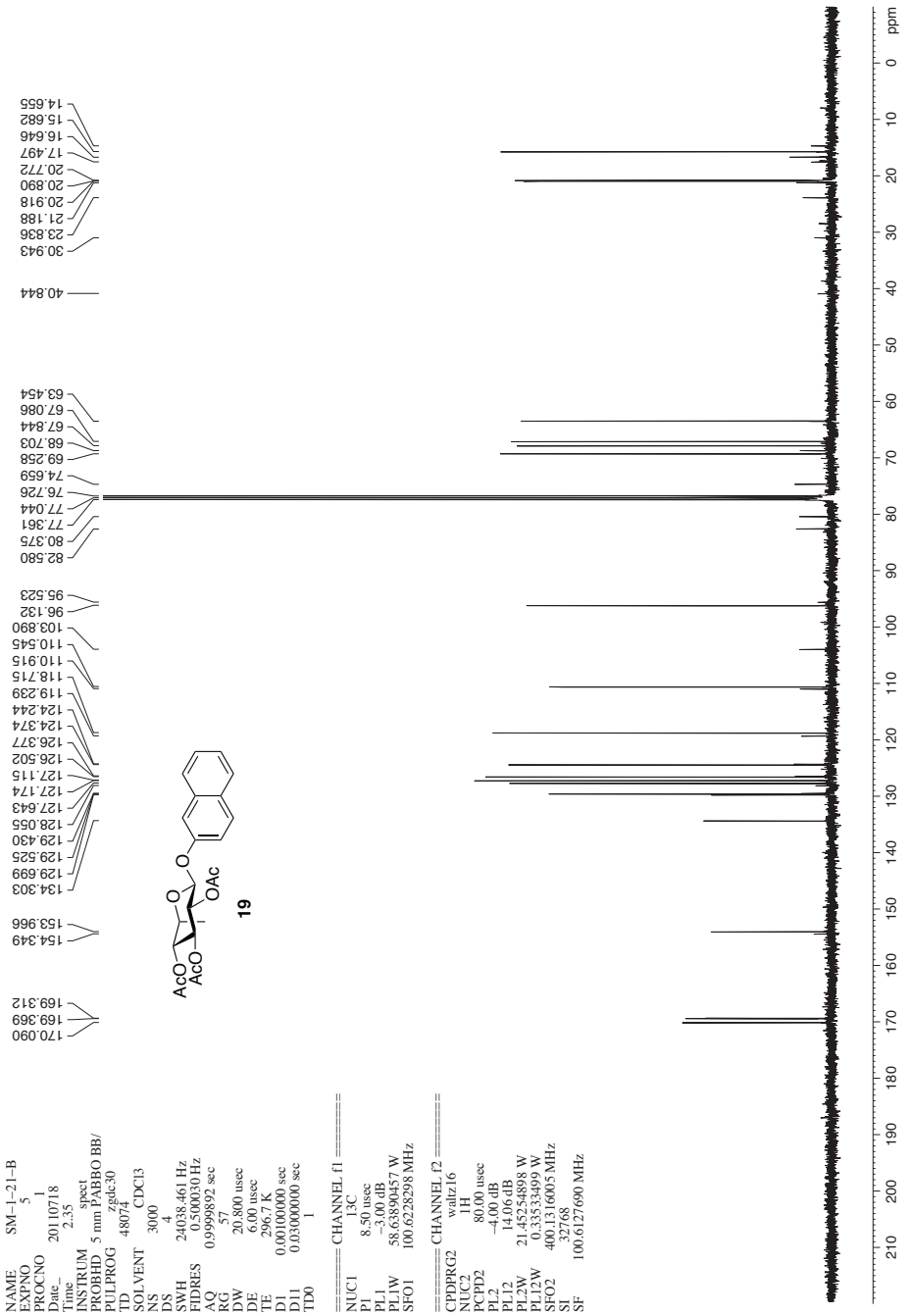
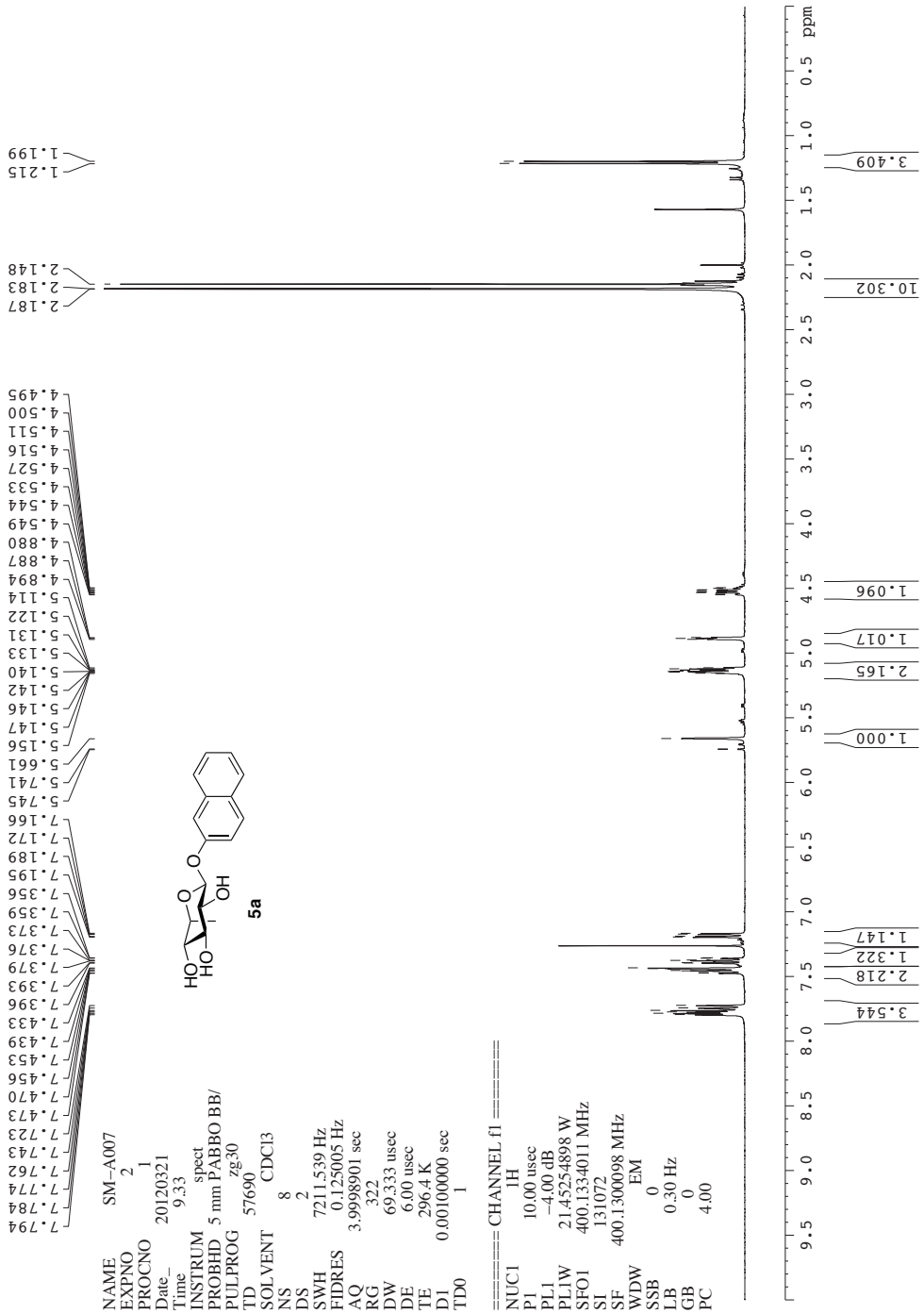
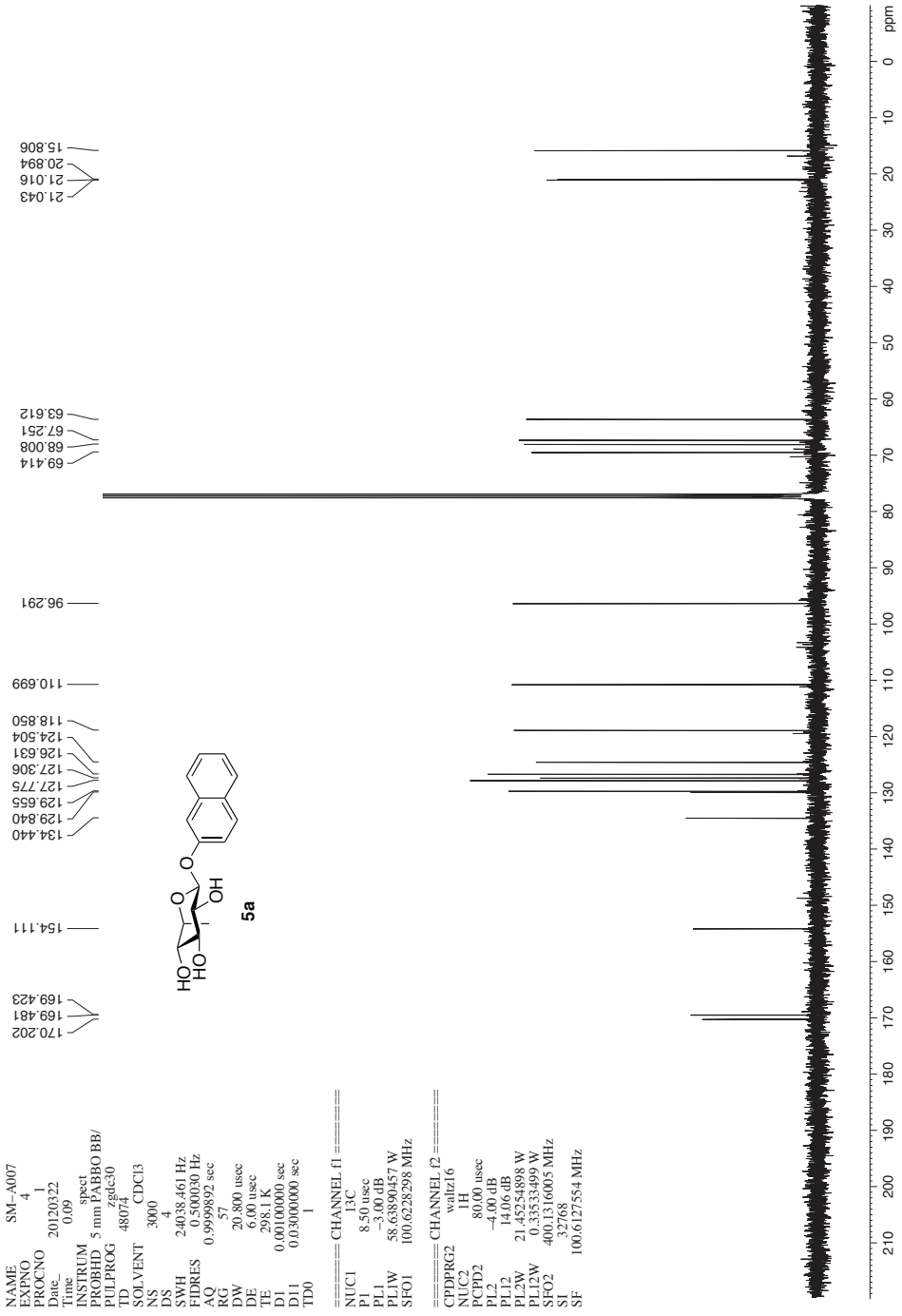


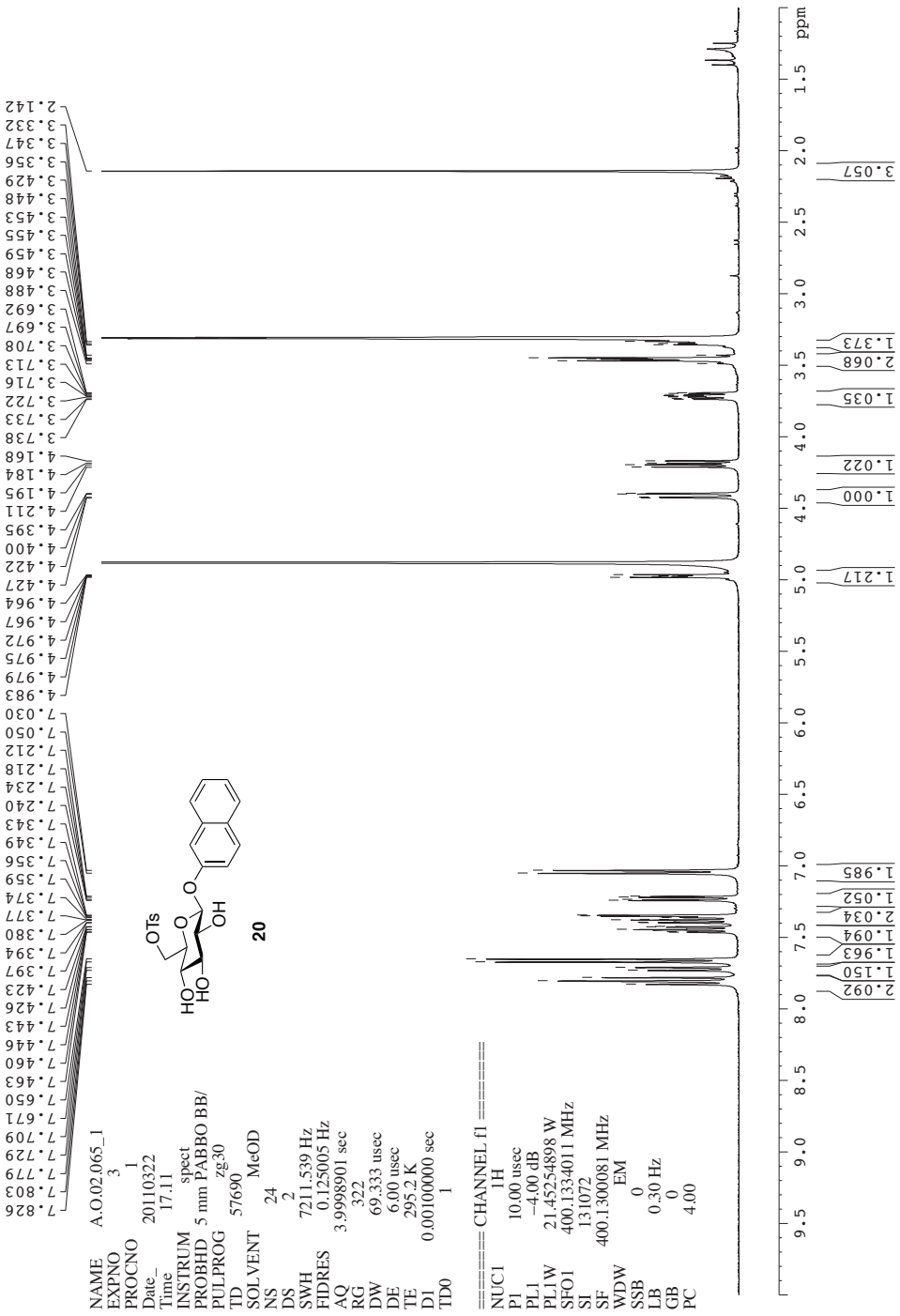
[1]H-NMR 2-Naphthyl 6-deoxy-α-L-idopyranoside **5a**.



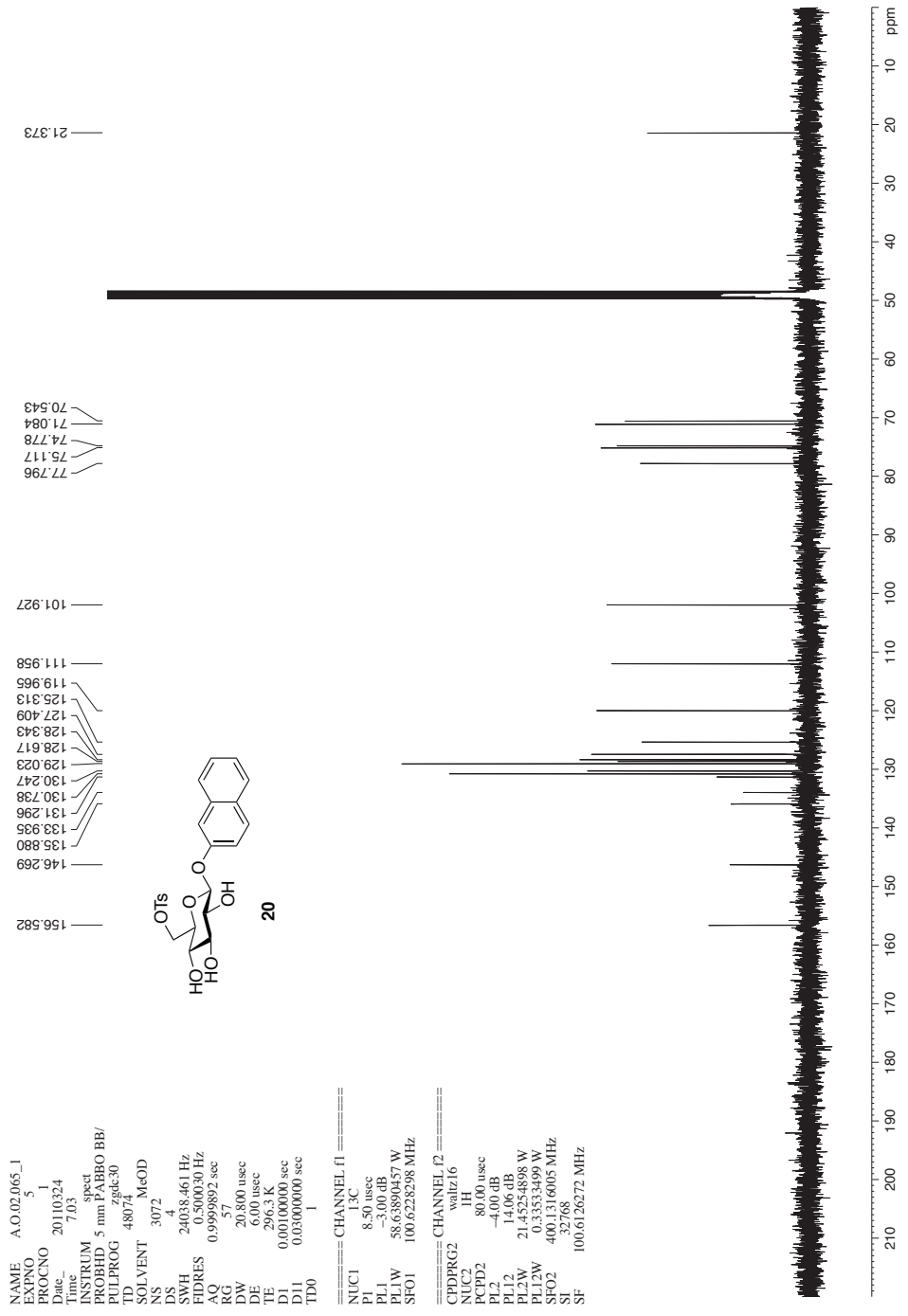
^{13}C-NMR 2-Naphthyl 6-deoxy-α-L-idopyranoside **5a**.



[1]H-NMR 2-Naphthyl 6-*O*-tosyl-β-D-glucopyranoside **20**.



^{13}C-NMR 2-Naphthyl 6-*O*-tosyl-β-D-glucopyranoside **20**.



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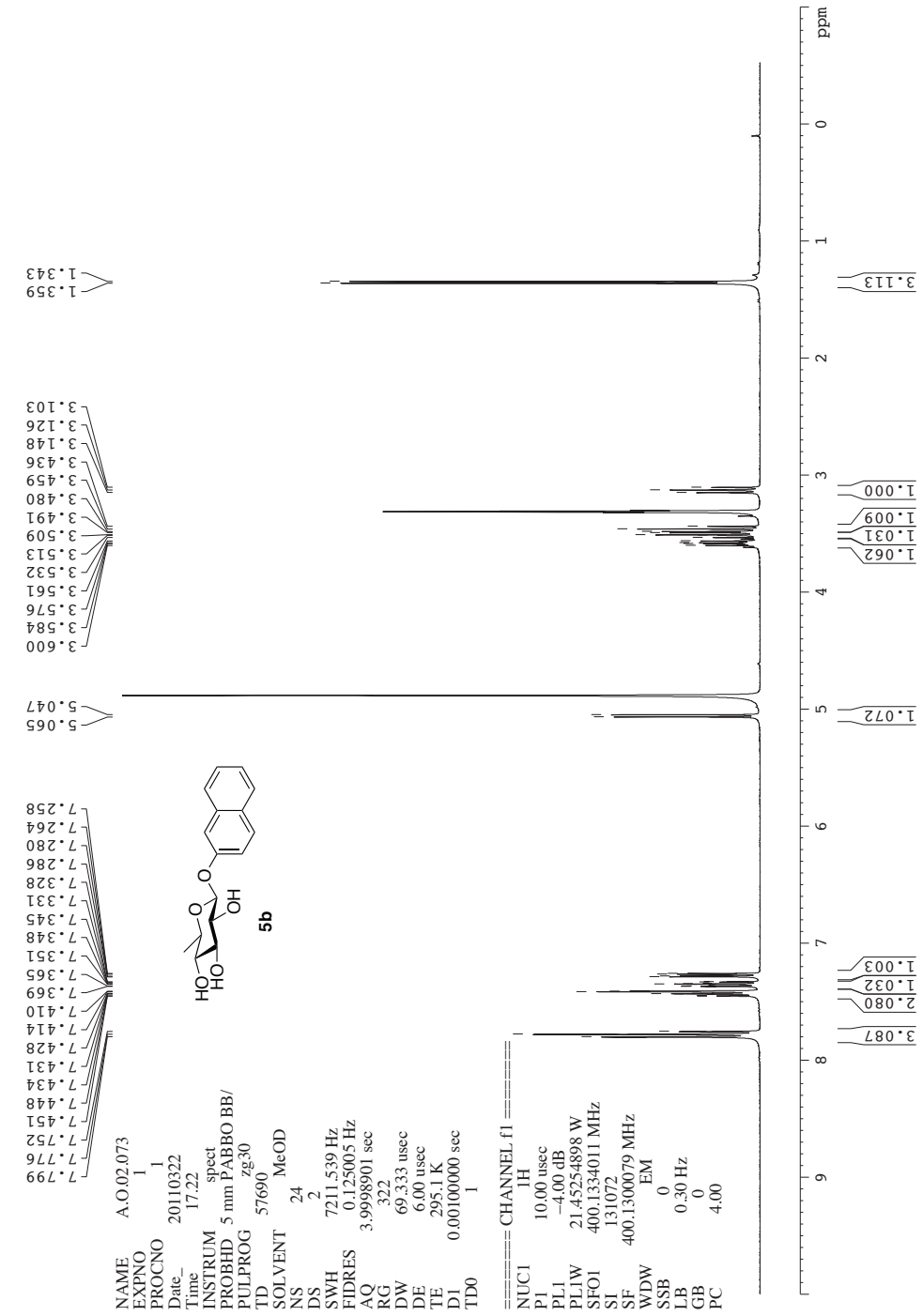

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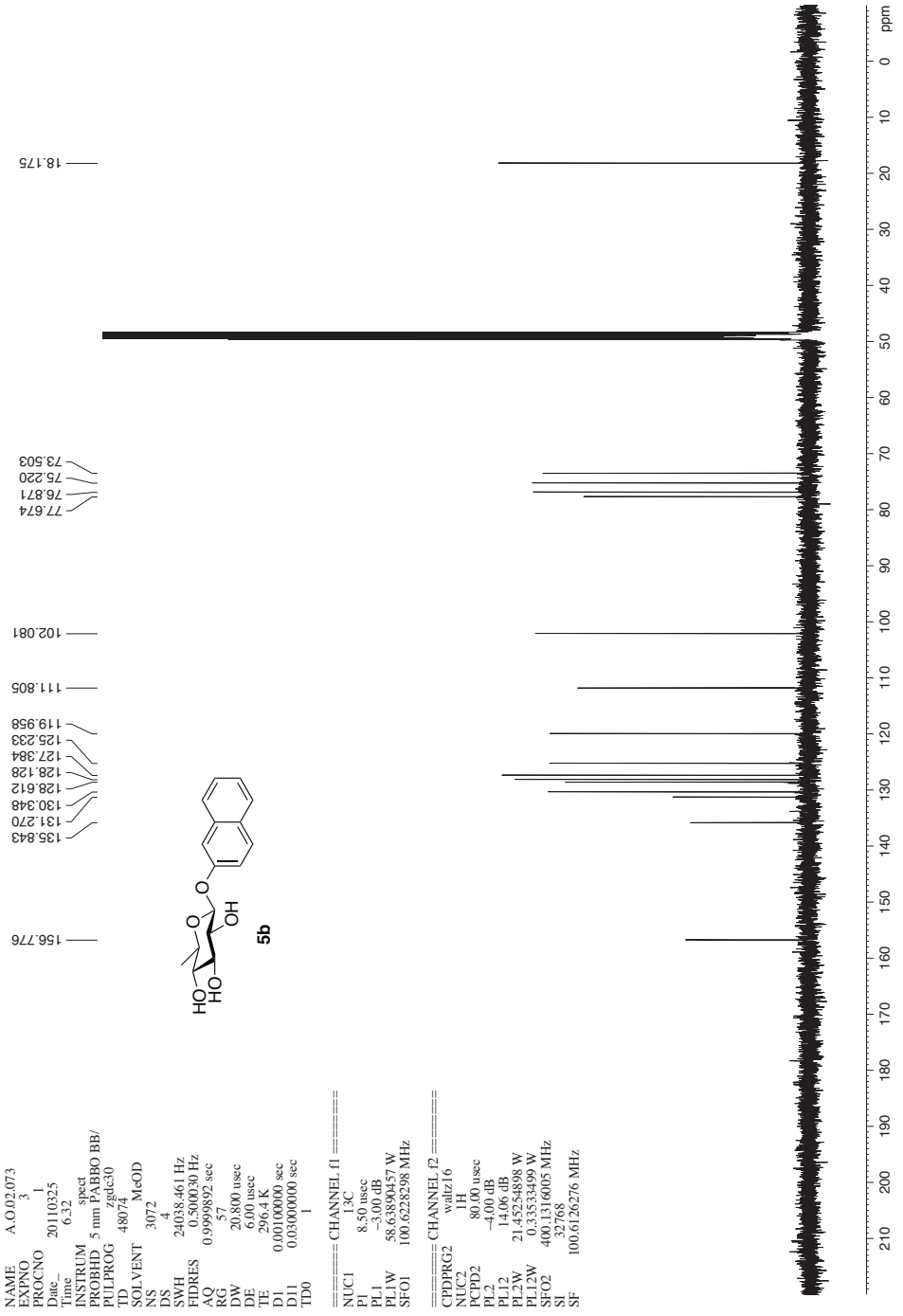

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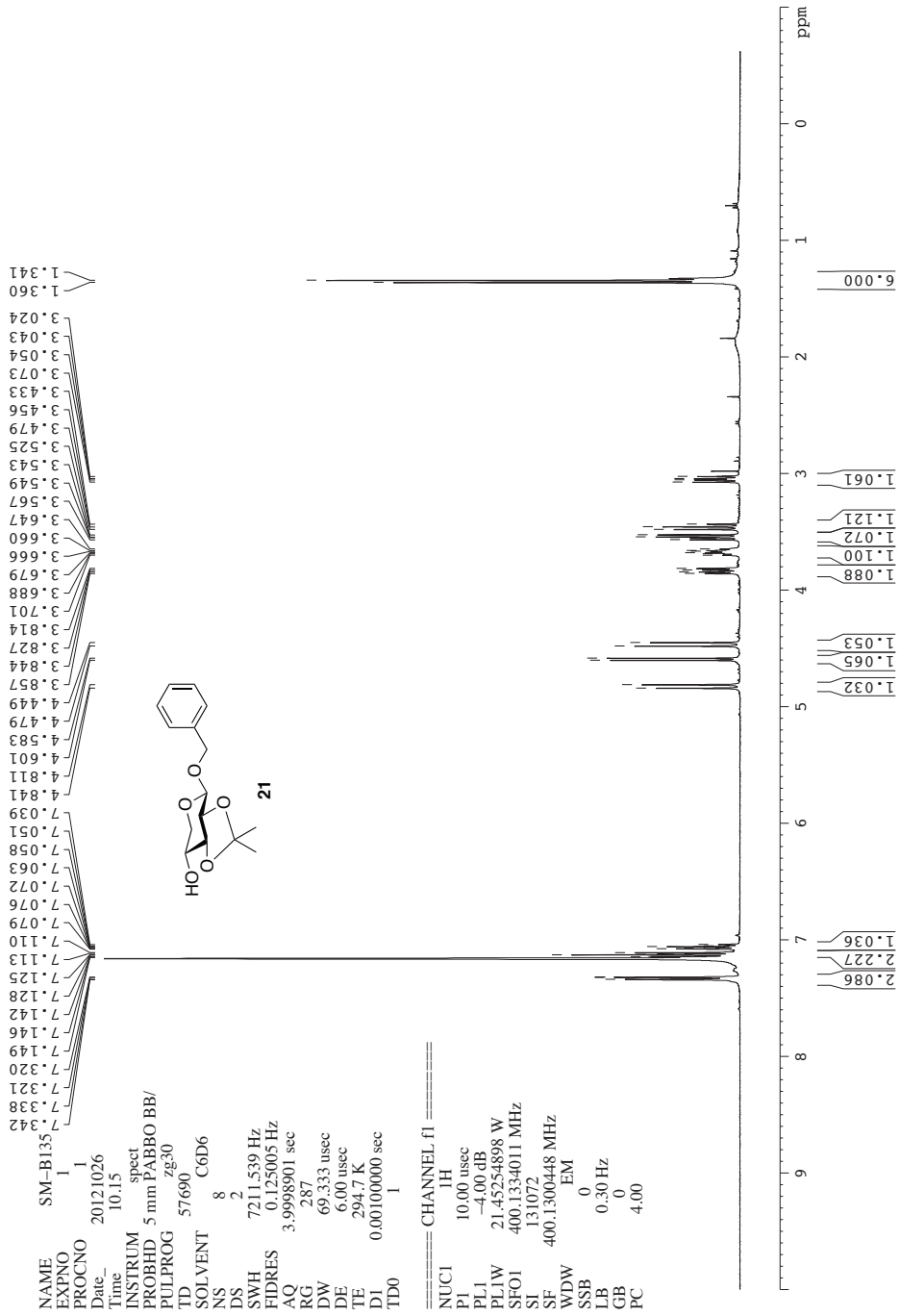

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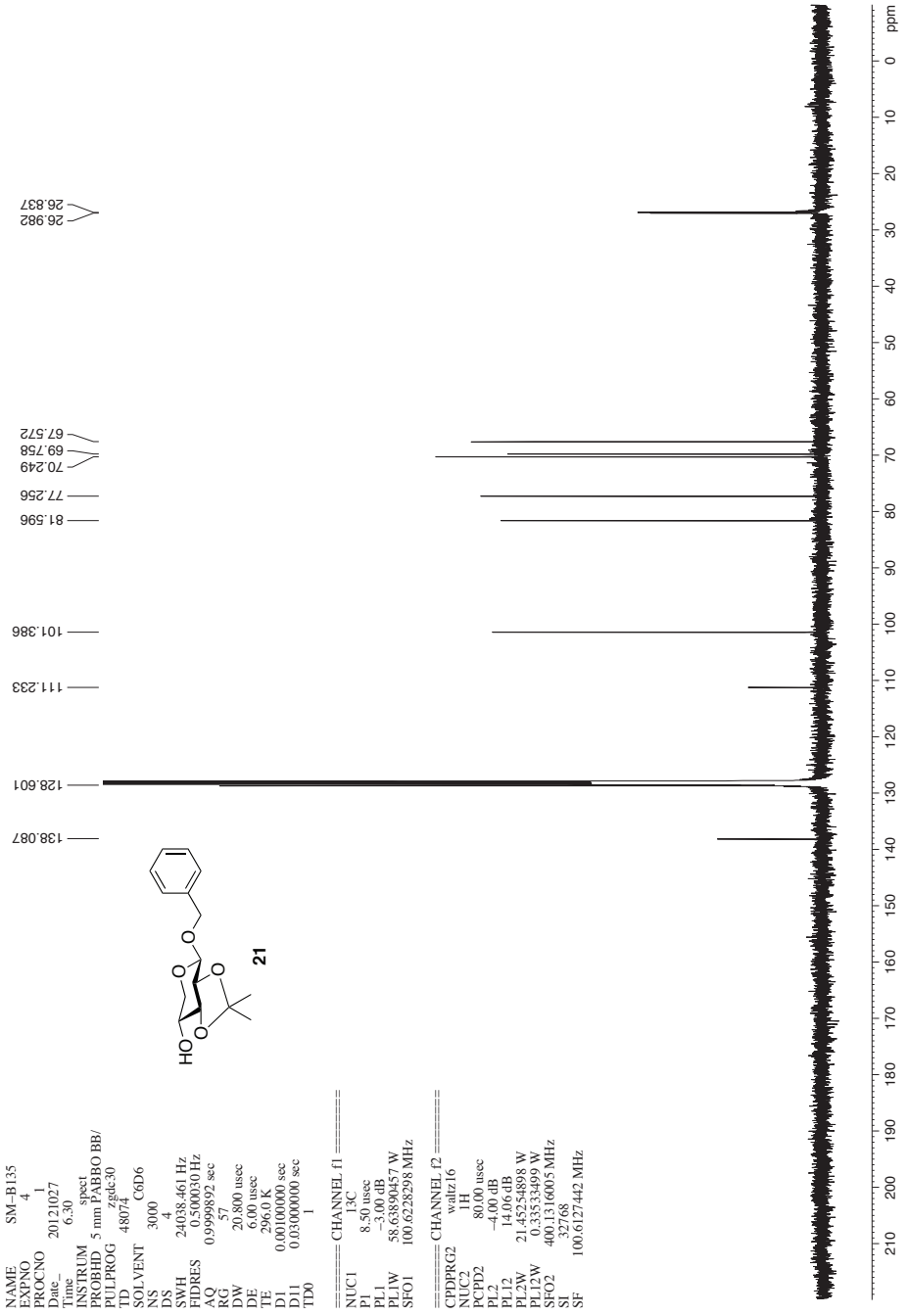

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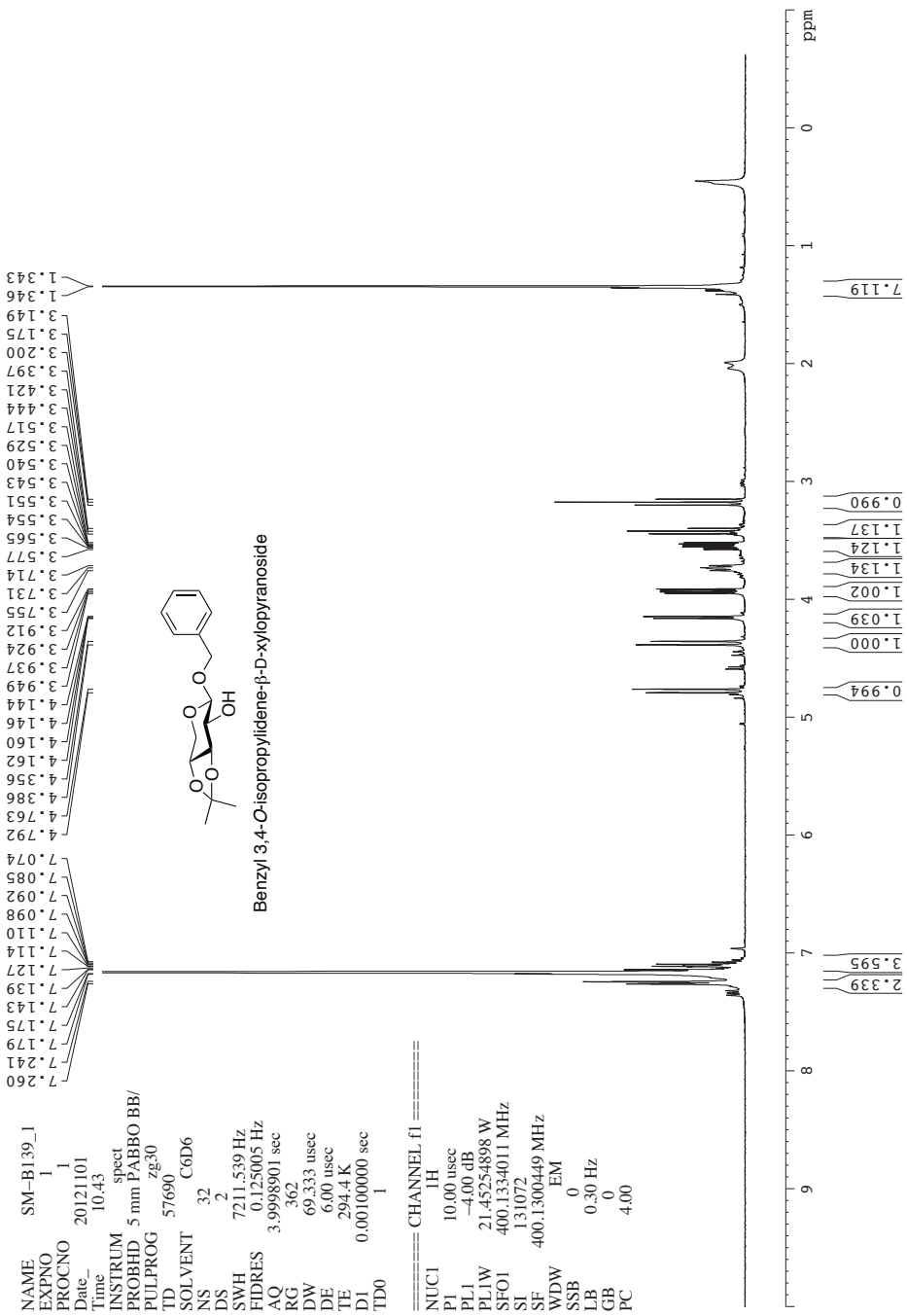

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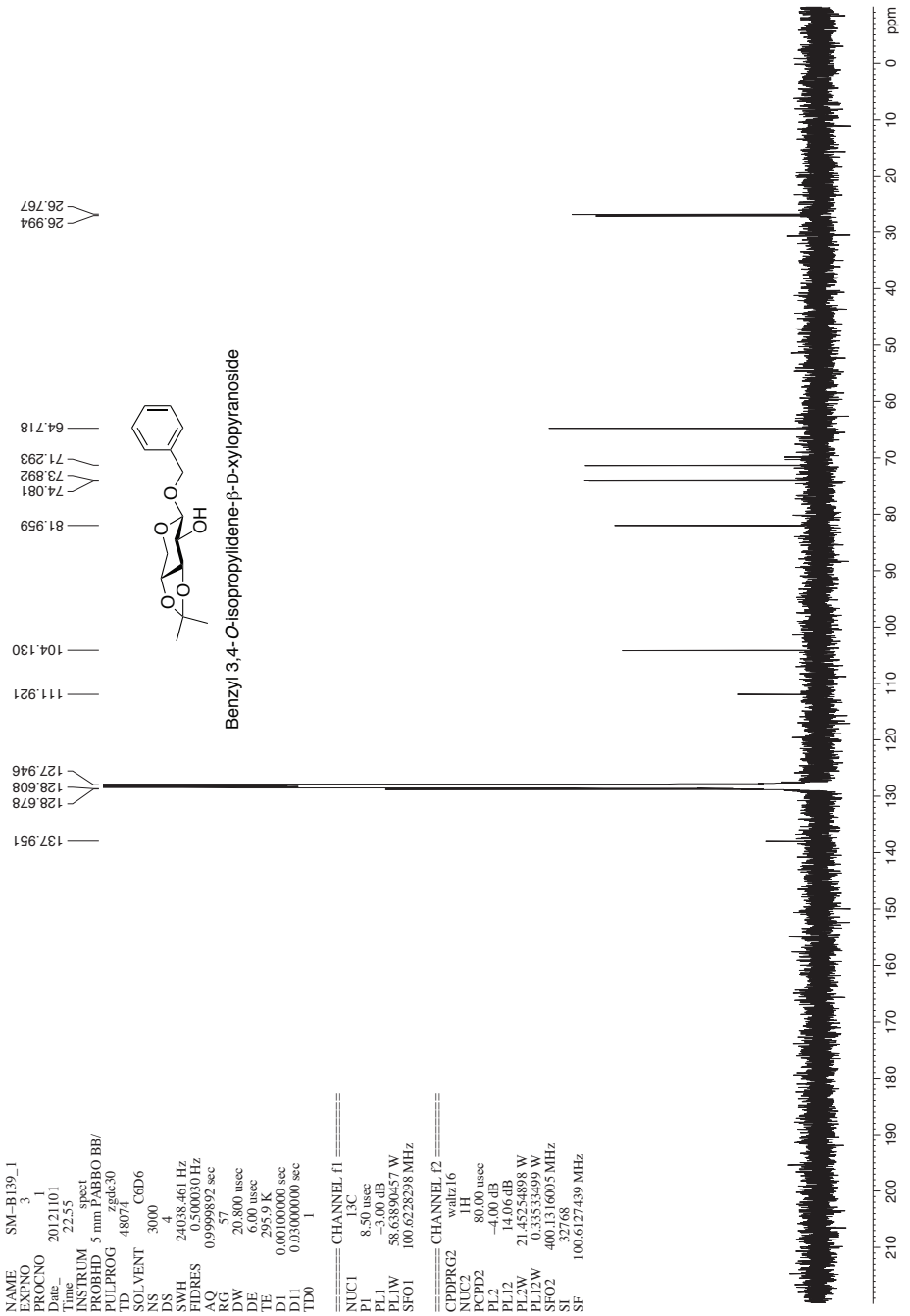

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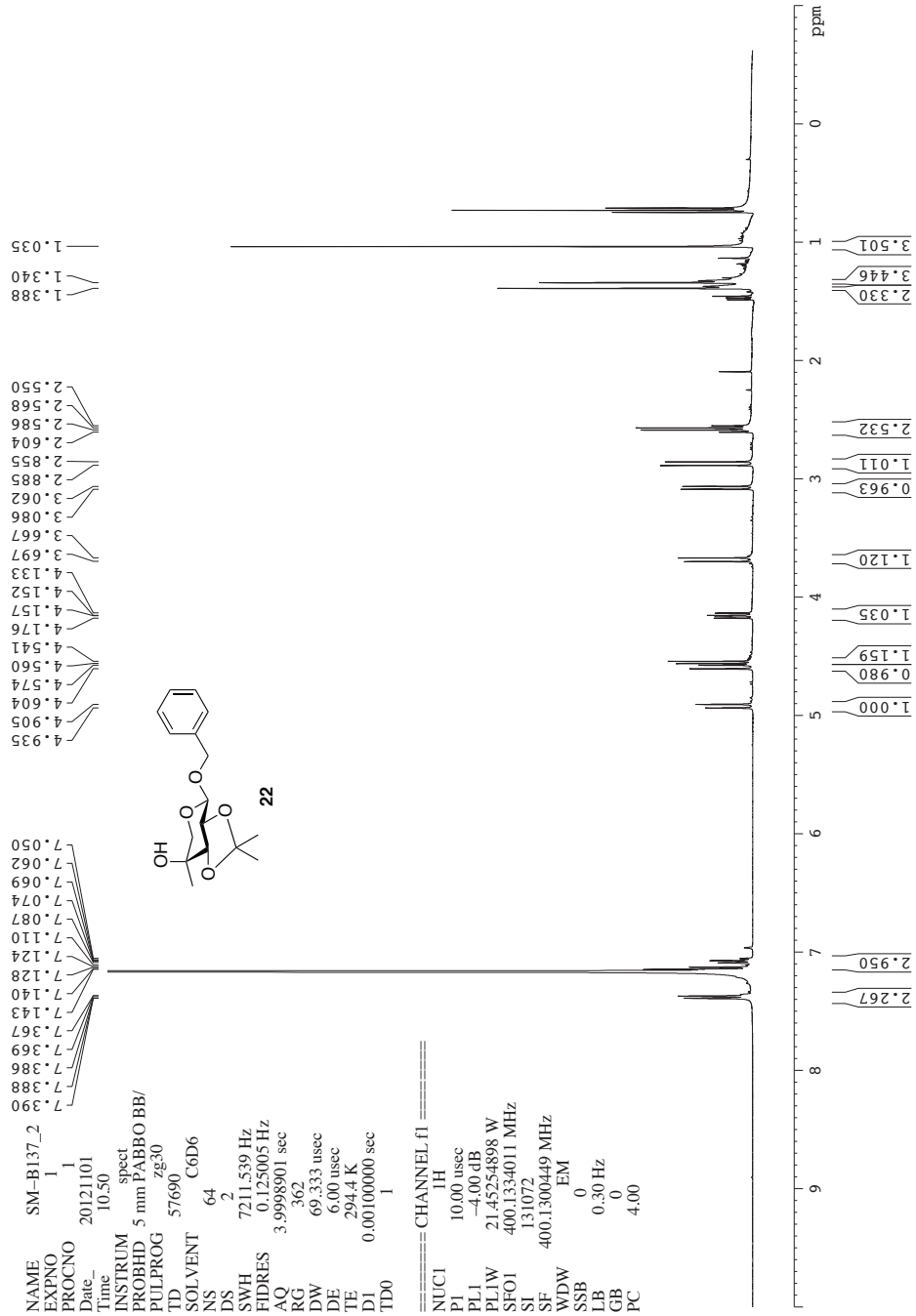
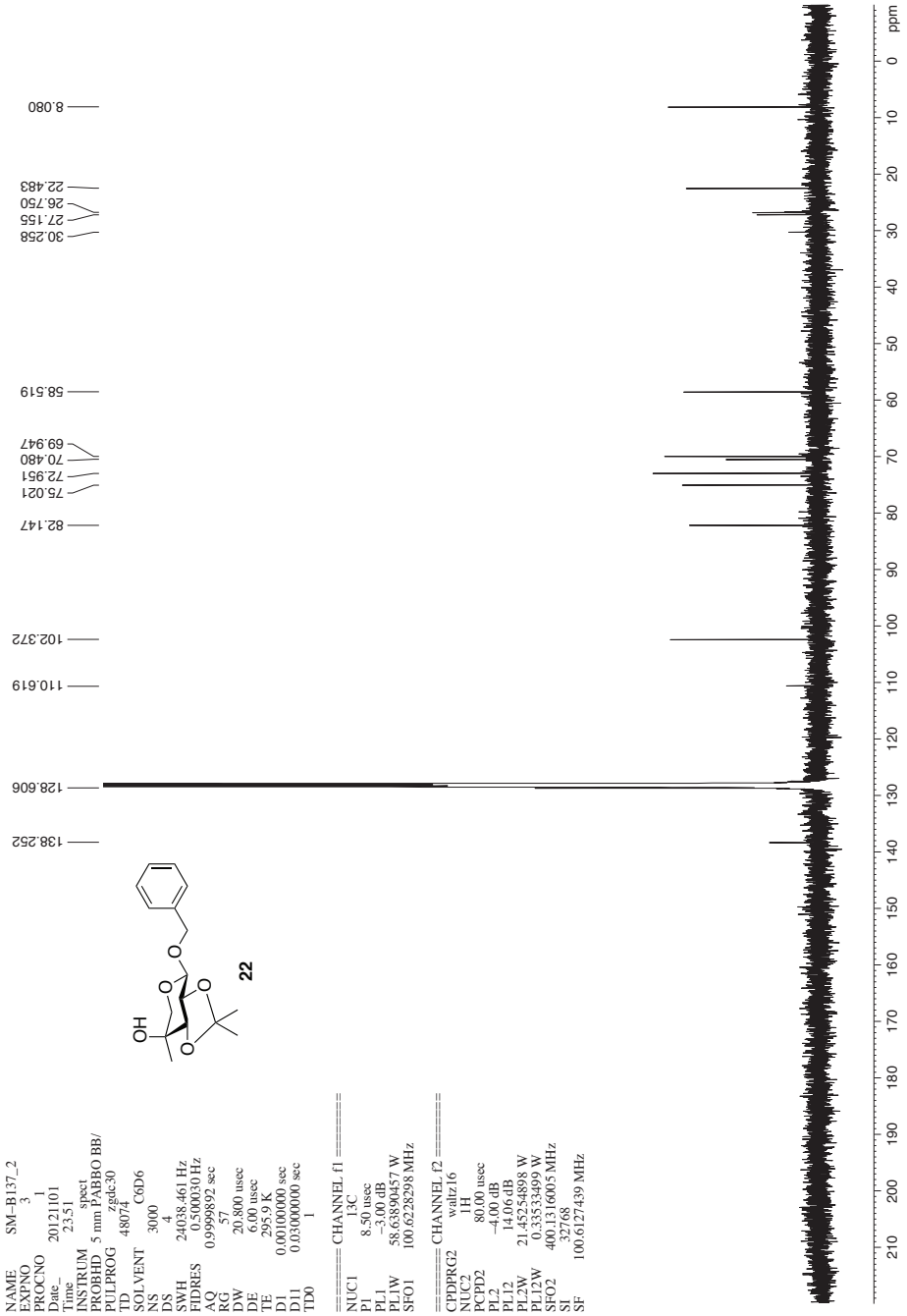


^{13}C-NMR Benzyl 2,3-*O*-isopropylidene-4-methyl-β-D-arabinopyranoside **22**.



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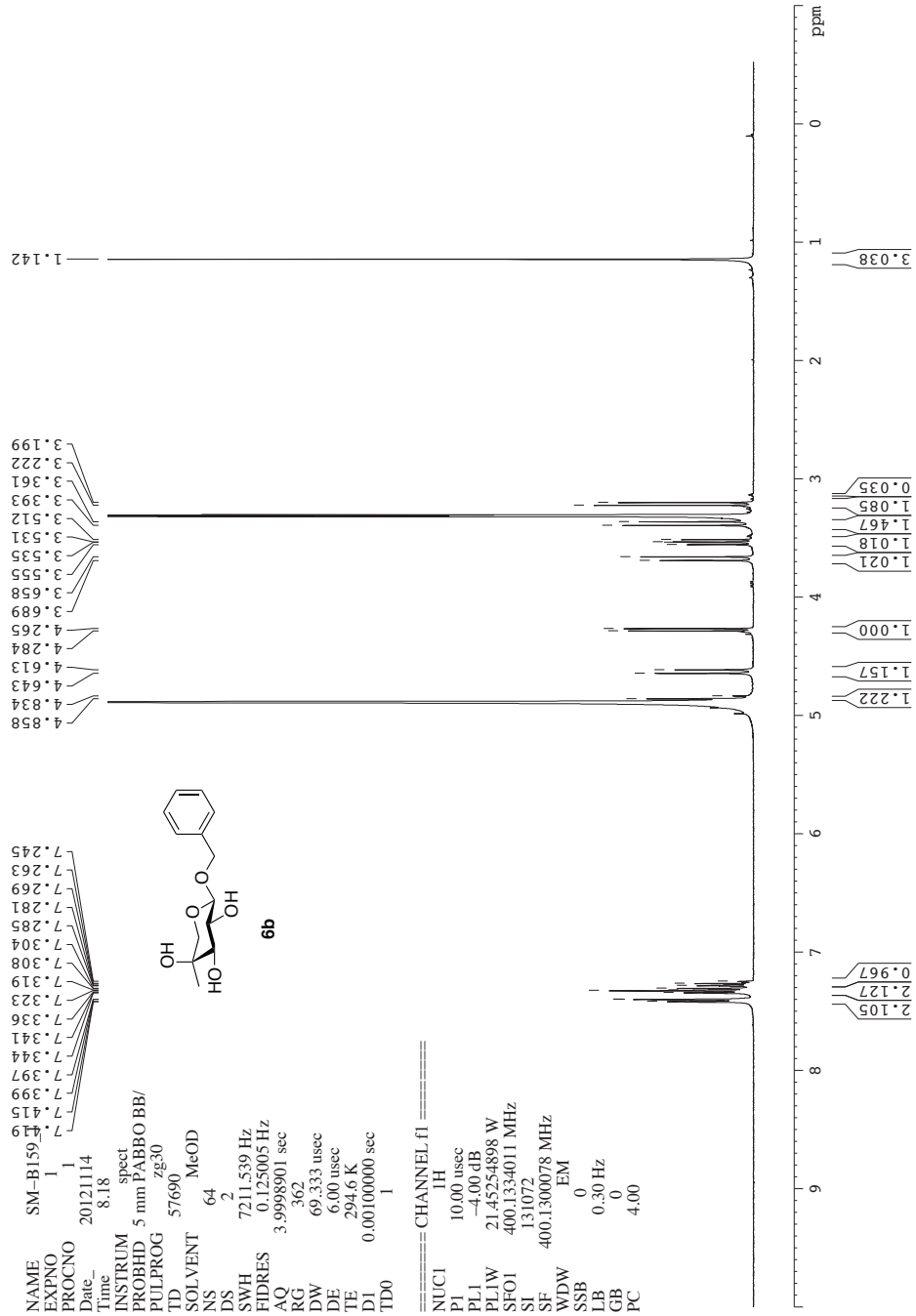

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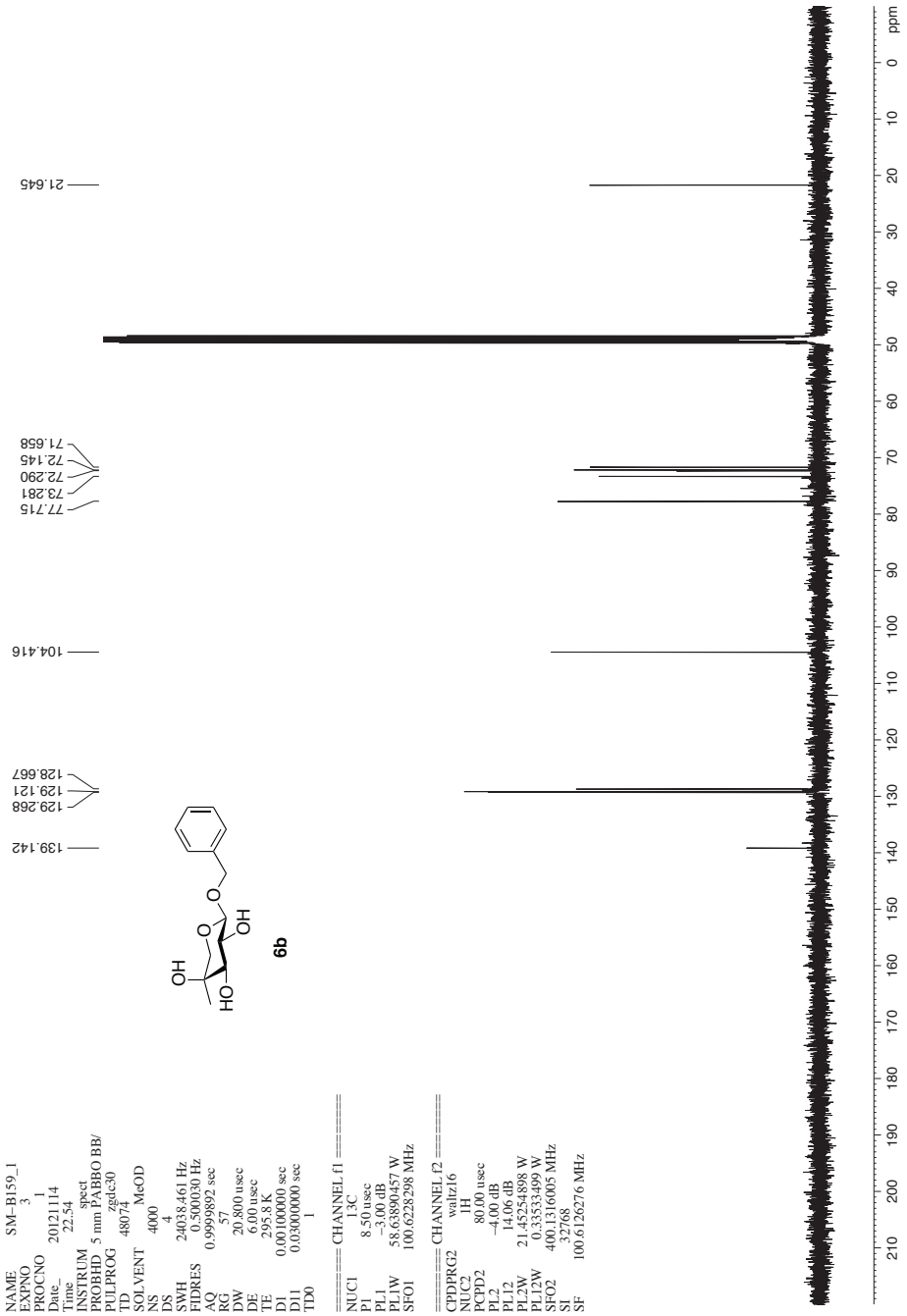

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