Toward Fully Synthetic Homogeneous β-Human Follicle-Stimulating Hormone (β-hFSH) with a Biantannary *N*-linked Dodecasaccharide. Synthesis of β-hFSH with chitobiose units at the natural linkage sites.

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Supporting Information

Contents

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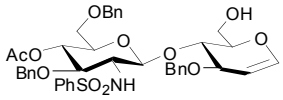
General Information

All reactions were carried out under an atmosphere of dried nitrogen in flame-dried or oven-dried glassware with magnetic stirring, unless otherwise noted. Air-sensitive reagents and solutions were transferred *via* syringe or cannula and were introduced to the apparatus through rubber septa. Reactions were cooled via external cooling baths: ice water (0 °C), dry ice-acetone (–78 °C), ice-acetone (–10 °C), or Neslab immersion cooler (–20 → –80 °C). Heating was accomplished by heating mantle or silicon oil bath using a temperature controller. Analytical thin layer chromatography (TLC) was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and exposure to aqueous ceric ammonium molybdate (CAM) solution or anisaldehyde followed by heating. Flash chromatography was performed using EM silica gel 60 (230-240 mesh). Solvents for extraction and chromatography were HPLC grade.

When necessary, solvents and reagents were dried prior to use. Reagents were purified prior to use following the guidelines of Perrin and Armarego. Tetrahydrofuran (THF), dichloromethane (CH_2Cl_2), toluene, diethyl ether (Et_2O) and Benzene were filtered through a column of activated alumina under an argon atmosphere. Pyridine, *N*,*N*-diisopropylethylamine, and triethylamine were distilled from calcium hydride. DBU (Diazabicycloundecene) and piperidine were purchased from Aldrich and used without further purification. HATU (*O*-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate) was purchased from GenScript and used without further purification.

Analytical Equipment: 1H- and 13C NMR spectra were recorded on a Bruker AMX-400, or a Bruker DRX-500 spectrometer in $CDCl_3$, DMF-d7, CD_3OD or D_2O. Chemical shifts (δ) are reported from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26; DMF-d7: δ 8.03; 2.92, 2.75; CD_3OD: δ 4.78, 3.34; D_2O: δ 4.65). Data are reported as follows: chemical shift (δ), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), integration, and assignment. ^{13}C NMR spectra were recorded with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard ($CDCl_3$: δ 77.0). Low resolution mass spectra (electrospray ionization) were acquired on a ZQ Micromass spectrometer. Samples were introduced by direct infusion. In the case of LC/MS,

analysis was performed with a Waters Alliance analytical LC system in tandem with the Micromass ZQ. HPLC purifications were run with TFA (trifluoroacetic acid)-buffered eluents: A = 0.05 % v/v TFA/Water, B = 0.04 % TFA/Acetontrile using HPLC grade solvents purchased from Fisher Scientific.



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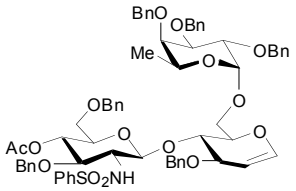
Disaccharide 8. Glycal **1** (6.0 g, 15.2 mmol), ethyl thioglycoside **2** (6.85 g, 11.7 mmol) and di-t-butylpyridine (7.90 mL, 35.1 mmol) were dissolved in dichloromethane (65 mL) and dried with freshly activated MS 4 Å for 1h. The reaction mixture was cooled to -10 °C, and MeOTf (4.60 mL, 41.0 mmol) was slowly added. The resultant mixture was slowly warmed to 3 °C over 4h period, and from 3 °C to rt over 1.5h period before being quenched with triethylamine (1.0 mL) and filtered through celite (ethyl acetate washes). The filtrate was washed with $NaHCO_{3(sat.)}$ and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The resultant oil was purified by flash chromatography (20% → 33% Ethyl Acetate in Hexanes) to afford 6.0 g (56% yield) of disaccharide. This compound was dissolved in THF (16.4 mL), cooled to 0 °C,and 1:1 mixture of 1M TBAF and 1M AcOH in THF (32.8 mL) was added. The obtained solution was stirred for 1h then warmed to rt and stirred for 4h, before another portion of 1:1 mixture of 1M TBAF and 1M AcOH in THF (16.4 mL) was introduced. The reaction mixture was stirred for additional 14h before being diluted with ethyl acetate (100 mL) and washed with $NaHCO_{3(sat.)}$, sodium $citrate_{(sat.)}$, 1:1 brine/water, and brine. The organic solvents were removed under reduced pressure, and the residue was purified by flash chromatography (20% → 33% → 50% Ethyl Acetate in Hexanes) to afford pure **8** (4.9g, 98%) as a single anomer: $[\alpha]_D^{20} = -40$ (c = 9.5, $CHCl_3$). IR (film): 3476, 3290, 3087, 3063, 3029, 2872, 1753, 1658, 1451, 1367, 1329, 1233, 1160, 1092, 1065 cm^{-1}. ^1H NMR (500MHz,) δ 7.86 (d, *J* =7.7 Hz, 2H), 7.34-7.22 (m, 14H), 7.19 (t, *J* =7.6 Hz, 2H), 7.12 (d, *J* =7.0 Hz, 2H), 6.37 (d, *J* =5.9 Hz, 1H), 5.05 (t, *J* =9.2 Hz, 1H), 4.81 (d, *J* =5.7 Hz, 1H), 4.77 (d, *J* =8.1 Hz, 1H), 4.63 (d, *J* =12 Hz, 1H), 4.59 (d, *J* =12 Hz, 1H), 4.43-4.39 (m, 4H), 4.13 (m, 2H), 4.05 (d, *J* =9.8 Hz, 1H), 3.81 (d, *J* =10.3 Hz, 1H), 3.65 (t, *J* =9.4 Hz, 1H), 3.57 (t, *J* =9.4 Hz, 2H), 3.48 (m, 3H), 1.68 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): 169.5, 144.4, 141.4, 138.6, 137.9, 137.6, 132.0, 128.5, 128.1, 128.1, 128.0, 127.8, 127.7, 127.4, 127.3, 127.2, 127.2, 126.9, 100.7, 100.6, 80.4, 77.2, 77.0, 74.4, 74.3, 73.8, 73.3, 73.0, 71.2, 70.1, 69.5, 60.4, 59.5, 13.8. Exact mass calcd for $C_{41}H_{45}NO_{11}S$[1] $[M+Na]^+$: 782.3; $[M-H]^-$: 758.3; $[M+Cl]^-$: 794.2. Found: 782.3, 758.3, 794.2.

[1] Due to the hydrogen bonding, the ^1H NMR signals show dependence on the concentration of the sample.

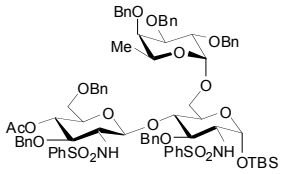


Trisaccharide 9.

Procedure A: To a solution of Disaccharide **8** (400 mg, 0.526 mmol)), and 4Å MS in dry Et_2O (10ml) was added $Sn(OTf)_2$ (4.4 mg, 0.011 mmol). Then, a solution of donor (293 mg, 0.526 mmol) in Et_2O (8 ml) was added dropwise at -20 °C. The reaction was stirred for 10 min, and quenched with diethylamine, diluted with ethyl acetate (30 mL), and filtered through celite. The organic phase was washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The resultant oil was purified by flash chromatography (20% → 33% Ethyl Acetate in Hexanes) to afford 586 mg (95% yield) of pure trisaccharide as a 6:1 mixture of diastereomers.

Procedure B: Disaccharide **8** (1.28 g, 1.69 mmol), *β-O*-Tribenzylfucosyl fluoride **3** (1.84 g, 4.22 mmol) and *di-t*-butylpyridine (1.89 mL, 8.44 mmol) were dissolved in THF (34 mL) and dried with freshly activated 4Å MS for 1h. The reaction mixture was cooled to -35 °C, and $Sn(OTf)_2$ (4 x 176 mg, 4 x 0.422 mmol) was added every 5h. After 22 h, the reaction mixture was quenched with $NaHCO_{3(sat)}$ (1 mL), diluted with ethyl acetate (50 mL), and filtered through celite. The organic phase was washed with water and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The resultant oil was repetitively purified by flash chromatography (20% → 33% Ethyl Acetate in Hexanes then 20% → 33% Ethyl Acetate in toluene) to afford 1.38 g (70% yield) of pure trisaccharide (>12:1 dr): $[\alpha]_D^{20}$ = -30 (c = 5.0, $CHCl_3$). IR (film): 3276, 3088, 3063, 3030, 3006, 2976, 2931, 2873, 1745, 1650, 1496, 1453, 1360, 1391, 1233, 1162, 1093, 1062, 1028 cm^{-1}. ^1H NMR (500MHz,) δ 7.79 (d, *J* =7.4 Hz, 2H), 7.79-7.17 (m, 31H), 7.10 (d, *J* =4.9 Hz, 2H), 6.35 (dd, *J* =6.0, 1.0 Hz, 1H), 5.20 (d, *J* =8.5 Hz, 1H), 5.07 (t, *J* =9.5 Hz, 1H), 4.95 (d, *J* =9.1 Hz, 1H), 4.94 (d, *J* =6.2 Hz, 1H), 4.88 (d, *J* =1.3 Hz, 2H), 4.86 (d, *J* =8.2 Hz, 1H), 4.82-4.79 (m, 2H), 4.76 (d, *J* =11.6 Hz, 1H), 4.72 (d, *J* =12.2 Hz, 1H), 4.68 (d, *J* =9.4 Hz, 1H), 4.64 (d, *J* =16.3 Hz, 1H), 4.39 (d, *J* =11.5 Hz, 1H), 4.28 (d, *J* =11.4 Hz, 1H), 4.21 (m, 2H), 4.11-4.07 (m, 3H), 4.01 (dd, *J* =6.8, 4.4 Hz, 1H), 3.97 (q, *J* =7.0 Hz, 1H), 3.91 (dd, *J* =10.2, 2.8 Hz, 1H), 3.78 (dd, *J* =11.6, 1.6 Hz, 1H), 3.68 (q, *J* =8.4 Hz, 1H), 3.58 (m, 2H), 3.51 (dd, *J* =10.4, 4.1 Hz, 1H), 3.46 (d, *J* =9.2 Hz, 1H), 3.42 (dd, *J* =10.5, 5.6 Hz, 1H), 3.24 (t, *J* =9.6 Hz, 1H), 1.72 (s, 3H), 1.13 (d, *J* =6.5 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 169.7, 144.6, 141.8, 139.0, 138.6, 138.5, 138.4, 137.9, 128.7, 128.5, 128.3, 128.2, 128.2, 128.1, 128.0, 127.9, 127.6, 127.6, 127.4, 127.4, 127.4, 127.2, 127.2, 127.1, 102.0, 101.3, 97.8, 81.2, 80.4, 75.9, 75.6, 75.2, 74.8, 73.6, 73.5, 73.3, 72.6, 71.8, 71.7,

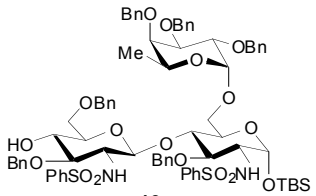
70.0, 66.4, 60.4, 59.4, 20.6, 16.4. ESI-MS calcd. for $C_{68}H_{73}NO_{15}S$ $[M+Na]^+$: 1198.5; $[M-H]^-$: 1174.5; $[M+Cl]^-$: 1210.4. found: 1198.5, 1174.8, 1210.7.



Acetylated trisaccharide 10. The solutions of trisaccharide **9** (3.41 g, 2.90 mmol) and sulfonamide (601 mg, 3.83 mmol) in dichloromethane (73 mL), dried with freshly activated 4 Å MS for 1h. Then the solution was cooled to -10 °C, and IDCP (2.47g, 5.28 mmol) was added. The resultant mixture was warmed to ambient temperature over the period of 1.5h. The mixture was filtered through celite, washed with $Na_2S_2O_{3(sat.)}$, $CuSO_4$ (1M), water and brine before being dried and concentrated to afford crude brown oil: Exact mass calcd for $C_{74}H_{79}IN_2O_{17}S_2$ $[M+Na]^+$: 1481.4; $[M-H]^-$: 1457.4. Found: 1481.6, 1457.4. This oil was redissolved in THF/H_2O (3:1, 70 mL) and triethylamine (1.21 mL, 8.7 mmol) was added. The resultant yellow solution was stirred for 48h, and then partitioned between EtOAc (70 mL) and water (70 mL). The aqueous layer was extracted with EtOAc (30 mL x 3), and the combined organic phase was washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure to afford a yellow oil. This oil was purified by flash chromatography (40% → 50% → 60% Ethyl Acetate in Hexanes) to afford 3.5 g of product (65% yield) as a mixture of anomers and 700 mg of recovered trisaccharide **9**: Exact mass calcd for $C_{74}H_{80}N_2O_{18}S_2$ $[M+Na]^+$: 1371.5; $[M-H]^-$: 1347.5; $[M+Cl]^-$: 1384.2. Found: 1371.6, 1347.8, 1384.5.

The product from above was dissolved in dichloromethane (50 mL). To the resultant solution, 2,6-lutidine (2.2 mL, 19 mmol) and TBSOTf (3.1 mL, 13 mmol) were added. The solution was stirred at rt for 4h then partitioned between Et_2O (60 mL) and water (60 mL). The organic phase was washed with HCl (0.1 M), water, and brine, dried ($MgSO_4$), and concentrated to afford yellow foam. An analytic sample has been purified and characterized the rest of the crude foam was proceeded to the next step without further purification: $[\alpha]_D^{20}$ = +10 (c = 2.8, $CHCl_3$). IR (film): 3277, 3087, 3063, 3031, 2951, 2932, 2884, 2860, 1747, 1496, 1445, 1360, 1330, 1252, 1129, 1160, 1092, 1044 cm^{-1}. ^{1}H-NMR (500MHz, $CHCl_3$) δ 7.82 (dd, *J* =8.6, 1.6 Hz, 2H), 7.70 (dd, *J* =8.3, 1.9 Hz, 2H), 7.41-7.16 (m, 30H), 7.13-7.08 (m, 4H), 7.01 (dd, *J* =7.7, 2.1 Hz, 2H), 5.15 (d, *J* =3.5 Hz, 1H), 4.91 (d, *J* =8.2 Hz, 1H), 4.87-4.74 (m, 7H), 4.62 (d, *J* =11.3 Hz, 1H), 4.15-4.09 (m, 3H), 4.02 (dd, *J* =10.1, 3.6 Hz, 1H), 3.99 (q, *J* =6.6 Hz, 1H), 3.90-3.82 (m, 3H), 3.63 (d, *J* =10.5 Hz, 1H), 3.53-3.48 (m, 3H), 3.45 (q, *J* =8.4 Hz, 1H), 3.37 (td, *J* =10.1, 3.6 Hz, 1H), 3.30-3.26 (m, 2H), 3.12 (dd, *J* =10.8, 6.6 Hz, 1H), 3.09 (t, *J* =9.7

Hz, 1H), 1.67 (s, 3H), 1.07 (d, *J* =6.5 Hz, 3H), 0.96 (s, 9H), 0.14 (s, 3H), 0.13 (s, 3H). ^{13}H-NMR (125MHz,$CDCl_3$):δ 169.6, 141.7, 140.7, 138.8, 138.7, 138.5, 138.4, 137.7, 132.3, 132.2, 128.7, 128.5, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 127.9, 127.9, 127.8, 127.6, 127.5, 127.3, 127.3, 127.2, 127.1, 126.8, 100.6, 97.4, 93.2, 81.0, 80.0, 77.1, 77.1, 76.3, 75.1, 74.8, 73.9, 73.6, 73.4, 72.3, 71.8, 69.9, 69.4, 66.4, 65.7, 59.7, 58.8, 53.4, 26.1, 20.6, 18.1, 16.4, –4.5, –5.4. Exact mass calcd for $C_{80}H_{94}N_2O_{18}S_2Si$ $[M+Na]^+$: 1485.6; $[M-H]^-$: 1461.6; $[M+Cl]^-$: 1497.5. Found: 1485.7, 1461.6, 1497.7.



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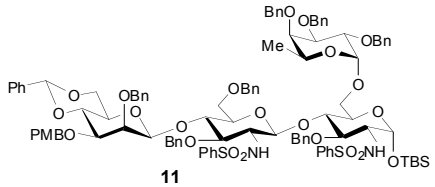
Trisaccharide 10. The foam from above was dissolved in methanol (31 mL) and NaOMe (25 w/v%, 3.5 mL) was added. This solution was stirred for 18h before being quenced with $NH_4Cl_{(sat.)}$, diluted with water (20 mL) and EtOAc (40 mL). The organic phase was washed with brine, dried ($MgSO_4$), and concentrated to afford yellow foam. This oil was purified by flash chromatography (29% Ethyl Acetate in Hexanes) to afford 2.1 g of product **10** (50% yield from **9**) as a white foam: $[\alpha]_D^{20}$ = 21 (c =1.8, $CHCl_3$). IR (film): 3279, 3087, 3062, 3030, 2928, 2858, 1462, 1328, 1254, 1207, 1159, 1092, 1049 cm^{-1}. ^{1}H-NMR (500MHz, $CHCl_3$) δ 7.80 (d, *J* =7.3 Hz, 2H), 7.70 (d, *J* =7.4 Hz, 2H), 7.38 (t, *J* =7.5 Hz, 1H), 7.34-7.23 (m, 13H), 7.23-7.05 (m, 22H), 5.07 (d, *J* =3.6 Hz 1H), 5.00 (d, *J* =8.1 Hz, 1H), 4.85 (d, *J* =11.6 Hz, 1H), 4.75-4.70 (m, 4H), 4.68 (d, *J* =11.0 Hz, 1H), 4.64 (d, *J* =10.4 Hz, 1H), 4.58 (d, *J* =11.6 Hz, 1H), 4.55 (d, *J* =11.6 Hz, 1H), 4.48 (d, *J* =9.2 Hz, 1H), 4.39 (dd, *J* =11.4, 4.9 Hz, 1H), 4.29 (dd, *J* =11.7, 6.1 Hz, 1H), 4.19 (d, *J* =11.7 Hz, 1H), 3.98 (dd, *J* =10.1 Hz, 1H), 3.94 (d, *J* =6.6 Hz, 1H), 3.86 (dd, *J* =10.0, 2.5 Hz, 1H), 3.81 (t, *J* =9.6 Hz, 1H), 3.77 (dd, *J* =11.0, 2.5 Hz, 1H), 3.57 (d, *J* =10.2 Hz, 2H), 3.47 (d, *J* =9.6 Hz, 1H), 3.40 (t, *J* =9.0 Hz, 1H), 3.38-3.32 (m, 3H), 3.32-3.25 (m, 2H), 3.21 (t, *J* =9.4 Hz, 1H), 2.98 (dd, *J* =9.8, 8.2 Hz, 1H), 2.39 (s, 1H), 1.01 (d, *J* =6.5 Hz, 3H), 0.91 (s, 9H), 0.087 (s, 3H), 0.067 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 141.8, 140.9, 138.7, 138.6, 138.6, 138.5, 138.2, 137.8, 132.3, 132.2, 128.7, 128.7, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 127.6, 127.6, 127.5, 127.3, 127.3, 127.1, 126.8, 100.8, 97.4, 93.1, 82.6, 80.0, 77.3, 77.1, 76.0, 74.8, 74.8, 74.0, 74.0, 73.6, 73.5, 73.2, 72.6, 71.1, 69.5, 66.4, 66.4, 65.5, 65.3, 59.4, 58.7, 25.8, 18.1, 16.4, -4.5, -5.5. Exact mass calcd for $C_{78}H_{92}N_2O_{17}S_2Si$ $[M+Na]^+$: 1443.6; $[M+CF_3CO_2]^-$: 1533.6. Found: 1444.1, 1534.1.



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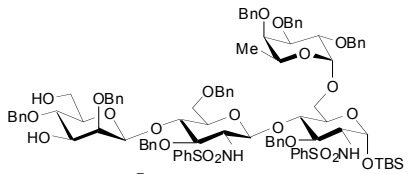
A solution of sulfoxide (1.07 g, 1.83 mmol) and DTBMP (1.12 g, 5.46 mmol), 4A MS (1.00 g) in dichloromethane (20 ml) was stirred at room temperature for 1 h. The reaction mixture was then cooled to -78 ^{o}C, followed by addition of Tf_2O (0.32 ml, 1.83 mmol), which was kept at the same temperature for 10 min and then warmed to -60 ^{o}C over 20 min. After the reaction mixture was cooled back to -78^{o}C, a solution of acceptor (1.73 g, 1.21 mmol) in dichloromethane (5 ml) was slowly added. The reaction mixture was then gradually warmed to 0^{o}C over 2 h. It was then quenched with $NaHCO_3$, and diluted with dichloromethane (50 ml). After washing with $NaHCO_{3(sat)}$, brine, the organic layer was concentrated, then subjected to flash chromatography (25% EtOAc in Hexanes) to afford product (2.18 g, 95%, 6.4:1 β:α). A portion of the mixture was purified to afford pure β-anomer for analytical purposes while the rest of the material was processed as such to the next step: ^{1}H-NMR (600MHz, $CDCl_3$)[1]: δ 7.80 (d, *J* =7.6 Hz, 2H), 7.75 (d, *J* =7.4 Hz, 2H), 7.45 (dd, *J* =7.8, 2.1 Hz, 2H), 7.37-7.10 (m, 44H), 7.02 (m, 2H), 6.82 (d, *J* =8.6 Hz, 2H), 5.43 (s, 1H), 5.12 (d, *J* =3.2 Hz, 1H), 4.97 (d, *J* =6.9 Hz, 1H), 4.94 (d, *J* =7.8 Hz, 1H), 4.88 (d, *J* =11.6 Hz, 1H), 4.84 (d, *J* =11.5 Hz, 1H), 4.81 (d, *J* =11.4 Hz, 2H), 4.80-4.67 (m, 7H), 4.62 (s, 2H), 4.58 (dd, *J* =11.3, 4.1 Hz, 2H), 4.51 (d, *J* =11.5 Hz, 1H), 4.46 (d, *J* =12 Hz, 1H), 4.04-3.92 (m, 7H), 3.83 (t, *J* =11.3 Hz, 1H), 3.78 (s, 3H), 3.73 (m, 1H), 3.65-3.58 (m, 4H), 3.55-3.25 (m, 8H), 3.02 (td, *J* =9.6, 4.9 Hz, 1H), 1.05 (d, *J* =6.4 Hz, 3H), 0.93 (s, 9H), 0.12 (s, 3H), 0.08 (s, 3H); Selected ^{13}C-NMR peaks (100MHz, $CDCl_3$) 159.1, 140.9, 138.6, 138.5, 130.5, 128.9, 128.7, 128.6, 128.5, 128.4, 128.4, 128.3, 128.1, 128.1, 128.0, 127.9, 127.8, 127.8, 127.6, 127.5, 127.5, 127.5, 127.4, 127.1, 126.0, 113.7, 101.2, 100.9, 97.3, 79.8, 78.5, 76.6, 75.7, 75.0, 74.7, 73.6, 73.5, 73.1, 72.4, 72.0, 67.4, 66.2, 59.7, 58.6, 55.2, 25.8, 18.0, 16.4. Exact mass calcd for $C_{106}H_{120}N_2O_{23}S_2Si$ $[M+Na]^+$: 1904.7; $[M-H]^-$: 1880.7. Found: 1904.9, 1880.8.



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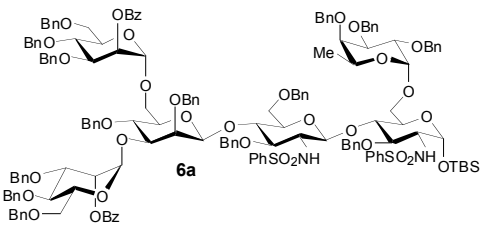
The mixture from above (2.00 g, 1.06 mmol) was dissolved in CH_3CN/H_2O (12:1, 50 mL). To

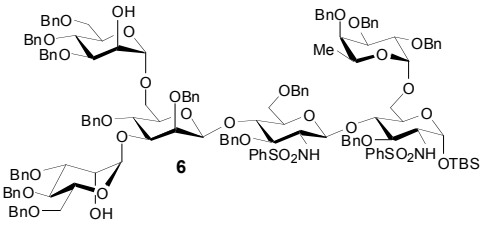
this, Cerium (IV) Ammonium Nitrate (CAN) (1.75 g, 3.19 mmol) was added at 0 ^{o}C. The reaction mixture was stirred at 0 ^{o}C for 30 min and at rt for 1 h. It was then diluted with EtOAc (20 mL), washed with $NaHCO_{3(sat)}$, brine, and dried (Na_2SO_4). After concentration, the residue was purified by flash chromatography column (11% → 14% → 20% Ethyl Acetate in toluene) to afford pure β-mannoside (67% yield).

To compound from above (1.26 g, 0.715 mmol) at -78 ^{o}C, BH_3·THF (1M, 7.2 mL, 7.2 mmol) followed by Bu_2BOTf (1M in CH_2Cl_2, 2.5 mL, 2.5 mmol) were added. The reaction was warmed to 0^{o}C and stirred for 3h before being cooled downt to -78 °C and quenched with Et_3N (1.0 ml) and methanol (5.0 mL). The mixture was left stirring at rt overnight and concentrated under reduced pressure. To the residue, additional Et_3N and methanol were added, the solution was stirred 15 min and concentrated (repeat twice). The resultant oil was directly purified by flash chromatography (25% ethyl acetate in hexanes) to afford pure **5** (1.2 g, 95%): $[\alpha]_D^{20} = +38$ (c = 0.5, $CHCl_3$). IR (film): 3550, 3275, 3061, 3032, 2929, 2868, 1724, 1456, 1335, 1160, 1091 cm^{-1}. ^{1}H-NMR (600MHz, $CDCl_3$)[1]: δ 7.71 (d, *J* =7.4 Hz, 2H), 7.68 (d, *J* =7.4 Hz, 2H), 7.30-7.01 (m, 46H), 5.08 (br s, 1H), 5.03 (d, *J* =3.2 Hz, 1H), 4.78-4.55 (m, 12H), 4.50-4.37 (m, 4H), 4.27 (s, 1H), 4.25 (s, 2H), 4.20 (d, *J* =11.6 Hz, 1H), 4.06 (d, *J* =11.2, 1H), 3.90 (dd, *J* =10.0, 3.3 Hz, 1H), 3.85 (m, 1H), 3.82-3.79 (m, 1H), 3.67 (t, *J* =7.8 Hz, 1H), 3.56-3.44 (m, 7H), 3.35-3.22 (m, 9H), 0.96 (d, *J* =6.4 Hz, 3H), 0.85 (s, 9H), 0.03 (s, 3H), 0.00 (s, 3H). ^{13}C-NMR (150MHz, $CDCl_3$), 141.6, 140.9, 138.8, 138.7, 138.6, 138.5, 138.4, 138.3, 138.0, 137.8, 132.4, 132.3, 128.8, 128.7, 128.6, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.8, 127.8,, 127.7, 127.6, 127.5, 127.5, 127.4, 127.3, 127.2, 127.1, 127.0, 126.9, 101.1, 100.7, 97.6, 93.1, 80.2, 79.9, 78.4, 78.0, 77.3, 77.1, 77.0, 76.9, 76.6, 76.1, 75.9, 75.7, 75.2, 75.0, 74.8, 74.8, 74.7, 73.9, 73.6, 73.4, 73.3, 72.5, 69.6, 68.9, 66.4, 65.8, 61.7, 59.5, 58.6, 25.9, 18.1, 16.5, -4.4, -5.5. Exact mass calcd for $C_{98}H_{114}N_2O_{22}S_2Si$ $[M+Na]^+$: 1786.7; $[M-H]^-$: 1761.7. Found: 1786.8, 1761.7.

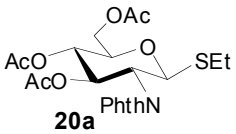


Hexasaccharide 6a. The solutions of tetrasaccharide **5** (160 mg, 0.0907 mmol) and mannose derivative

12 (325 mg, 0.544 mmol) in acetonitrile (3 mL), dried with freshly activated 4 Å MS for 1h. The solution of **5** was cooled to 10 °C, and $(BrC_6H_5)_3NSbCl_6$ (422 mg, 0.517 mmol) followed by the solution of **12** (+1 mL rinse) were added to it. The resultant mixture was stirred for 10 min at 10 °C before an additional portion of $(BrC_6H_5)_3NSbCl_6$ (126 mg, 0.154 mmol) was added. The obtained solution was stirred for 15 min, warmed to ambient temperature and stirred for additional 22 h before being quenched with triethylamine (1 mL), filtered through silica gel plug and concentrated under reduced pressure to afford crude brown oil. This oil was purified by flash chromatography (20% → 25% → 30% Ethyl Acetate in Hexanes) to afford 200 mg of pure product (84% yield): $[\alpha]_D^{20}$ = -2.3 (c = 5.0, $CHCl_3$). IR (film): 3281, 3087, 3062, 3030, 3007, 2929, 2898, 2897, 2883, 2861, 1724, 1601, 1582, 1452, 1602, 1585, 1452, 1357, 1327, 1267, 1208, 1159, 1094, 1047 cm^{-1}. ^{1}H-NMR (600MHz, $CHCl_3$) δ 7.95 (d, *J* =7.4 Hz, 2H), 7.87 (d, *J* =7.4 Hz, 2H), 7.65 (d, *J* =7.7 Hz, 2H), 7.44 (t, *J* =7.4 Hz, 1H), 7.40 (t, *J* =7.4 Hz, 1H), 7.26-7.00 (m, 76H), 6.88-6.81 (m, 6H), 5.58 (s, 1H), 5.40 (s, 1H), 5.05 (s, 1H), 5.01 (s, 1H), 4.81-4.73 (m, 5H), 4,73-4.62 (m, 4H), 4.62-4.54 (m, 3H), 4.53 (m, 1H), 4.53-4.44 (m, 9H), 4.40 (d, *J* =11 Hz, 2H), 4.37 (d, *J* =12.6 Hz, 2H), 4.35 (d, *J* =11.9 Hz, 2H), 4.29 (d, *J* =11.7 Hz, 3H), 4.26 (m, 1H), 4.24 (d, *J* =12 Hz, 2H), 4.20 (d, *J* =11.3 Hz, 2H), 4.13 (d, *J* =13.4 Hz, 2H), 4.03 (d, *J* =11.5 Hz, 1H), 3.98 (t, *J* =9.5 Hz, 1H), 3.93 (dd, *J* =9.1, 2.5 Hz, 1H), 3.89-3.75 (m, 8H), 3.73 (d, *J* =8.6 Hz, 1H), 3.69 (d, *J* =2.1 Hz, 1H), 3.65 (dd, *J* =8.2, 3.0 Hz, 1H), 3,60 (td, *J* =9.7, 3.7 Hz, 2H), 3.57-3.46 (m, 4H), 3.44 (d, *J* =10 Hz, 1H), 3.39 (d, *J* =10.5 Hz, 1H), 3.36 (d, *J* =9.7 Hz, 1H), 3.29 (m, 3H), 3.13 (t, *J* =8.4 Hz, 1H), 3.03 (d, *J* =8.9 Hz, 1H), 0.92 (d, *J* =6.4 Hz, 3H), 0.81 (s, 9H), -0.06 (s, 3H), -22.9 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 165.4, 165.0, 141.3, 140.9, 138.7, 138.6, 138.5, 138.5, 138.4, 138.4, 138.2, 138.2, 137.9, 137.8, 137.8, 137.7, 130.0, 129.9, 129.8, 129.7, 128.6, 128.5, 128.4, 128.3, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.5, 127.5, 127.4, 127.4, 127.4, 127.3, 127.3, 127.3, 127.2, 127.2, 127.2, 127.1, 127.1, 126.8, 126.7, 101.6, 100.9, 99.3, 98.0, 97.1, 93.0, 81.7, 79.5, 78.8, 78.4, 78.1, 77.7, 74.5, 76.5, 75.5, 75.1, 75.1, 74.7, 74.7, 74.6, 74.6, 74.6, 74.0, 74.0, 73.9, 73.9, 73.4, 73.3, 73.2, 72.9, 72.8, 72.5, 72.5, 71.8, 71.3, 70.8, 69.4, 68.9, 68.8, 68.8, 68.4, 68.2, 66.3, 66.1, 65.2, 59.7, 58.4, 25.8, 25.7, 25.6, 18.0, 16.4, -4.5, -5.6. Exact mass calcd for $C_{166}H_{178}N_2O_{34}S_2Si$ $[M+Na]^+$: 2859.1; $[M-H]^-$: 2835.1; $[M+Cl]^-$: 2871.1. Found: 2859.6, 2834.8, 2871.6.



Hexasaccharide 6. Diester **6a** (250 mg, 0.0881 mmol) was dissolved in methanol (5 mL), and 25% w/v sodium methoxide in methanol (173 μL, 0.752 mmol) was added. The resultant solution was stirred for 32 h, before being quenched with acetic acid (0.2 mL), concentrated under reduced pressure and chromatographed (30% → 40% Ethyl Acetate in Hexanes) to afford 193 mg of pure product (83% yield): $[\alpha]_D^{20} = +18$ (c = 2.5, $CHCl_3$). IR (film): 3300, 3106, 3062, 3030, 2936, 2882, 2872, 1496, 1453, 1360, 1329, 1254, 1158, 1092 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.76 (t, *J* =7.8 Hz, 4H), 7.37-7.08 (m, 80H), 7.00 (m, 2H), 5.11 (s, 2H), 4.91-4.76 (m, 9H), 4.69-4.65 (m, 3H), 4.65-4.41 (m, 11H), 4.11 (m, 11H), 4.19 (d, *J* =12.0 Hz, 1H), 3.98-3.86 (m, 6H), 3.86 (d, *J* =6.6 Hz, 2H), 3.85-3.75 (m, 5H), 3.69 (dd, *J* =9.0, 2.7 Hz, 1H), 3.65 (dd, *J* =18.0, 3.5 Hz, 1H), 3.66-3.56 (m, 7H), 3.56-3.42 (m, 6H), 3.56-3.37 (m, 3H), 3.34 (d, *J* =7.4 Hz, 1H), 3.32-3.28 (m, 2H), 3.07 (d, *J* =8.8 Hz, 1H), 1.02 (d, *J* =6.4 Hz, 3H), 0.93 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 141.4, 140.9, 138.8, 138.8, 138.6, 138.6, 138.6, 138.5, 138.4, 138.3, 138.1, 138.0, 138.0, 137.8, 132.3, 132.2, 128.7, 128.5, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.8, 127.7, 127.6, 127.6, 127.6, 127.5, 127.5, 127.5, 127.5, 127.3, 127.3, 127.3, 127.2, 127.2, 126.9, 126.9, 101.1, 101.1, 101.0, 99.8, 97.2, 93.0, 81.1, 80.0, 79.5, 79.4, 78.3, 77.6, 77.1, 76.6, 75.5, 75.0, 74.9, 74.9, 74.8, 74.7, 74.7, 74.4, 74.2, 74.1, 73.4, 73.4, 73.3, 73.1, 72.9, 72.5, 72.1, 72.0, 71.4, 71.2, 69.5, 69.0, 68.9, 68.7, 68.5, 67.5, 66.3, 66.2, 65.3, 59.7, 58.5, 25.8, 18.1, 16.5, -4.5, -5.5. ESI-MS calcd. for $C_{152}H_{170}N_2O_{32}S_2Si$ $[M+Na]^+$: 2650.1, $[M-H]^-$: 2627.1. Found: 2650.7, 2626.9.

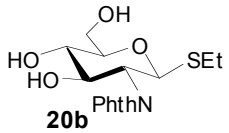


Compound 20a. To a solution of NaOMe (12.0 g, 223 mmol) in methanol (500 mL) was subsequentially added D-(+)-glucosamine hydrochloride (50.5 g, 234 mmol) and phthalic anhydride (35.1 g, 237 mmol) at rt. The resulting slurry was heated to reflux for 25 min whereupon a thick white precipitate was formed. The reaction was cooled to rt, filtered, and the residue was washed with cold methanol (2x100 mL). Upon drying 72.6 g (100%) of a white solid was obtained that was used in the

following transformation without further purification.

The obtained white solid was azeotropically dried with toluene (100 mL) twice and dissolved in pyridine (240 mL) at rt. Acetic anhydride (120 mL) was added over a period of 15 min resulting in the complete dissolution of the solid and slight warming of the solution. The reaction was kept at rt for 16 h, then all solvents were removed under reduced pressure. The residue was taken up in ethyl acetate (500 mL), the resulting solution washed with sat. NH_4Cl solution (2 x 200 mL), dried over Na_2SO_4, and evaporated to dryness yielding 73.0 g (62%) of a white foam that was used without further purification in the next transformation.

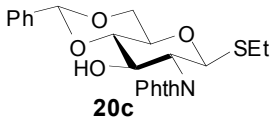
Prior to reaction, the residue was azeotropically dried with toluene (100 mL) twice and dissolved in CH_2Cl_2 (240 mL) at rt. Ethanethiol (18.3 mL, 245 mmol) was added and the reaction was cooled to 0 °C. $BF_3.OEt_2$ (31.0 mL, 245 mmol) was added dropwise and the reaction was slowly warmed to rt, and stirred for 12 h. After this time, TLC indicated not complete conversion of the starting material and $BF_3.OEt_2$ (31.0 mL, 245 mmol) was added at rt and the reaction was stirred for another 36 h. At this thime, TLC indicated complete conversion of the starting material. The reaction was stopped by the careful addition of $NaHCO_{3(sat.)}$ solution (300 mL) and stirred at rt for 1 h. The aqueous layer was extracted with CH_2Cl_2 (2 x 200 mL). The combined organic layers were dried over $MgSO_4$, filtered, and evaporated. The residue was purified by flash-chromatography over silica gel (33% ethyl acetate in hexanes) yielding **20a** (41.1 g, 37% over three steps) of a white foam: $[\alpha]_D^{20}$ = +38.2 (c = 1.00, CH_2Cl_2). IR (film): 2964, 2934, 1744, 1715, 1381, 1217, 1031, 912 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.88-7.83 (m, 2H), 7.78-7.72 (m, 2H), 5.82 (dd, *J* =10.2, 9.2 Hz, 1H), 5.48 (d, *J* =10.6 Hz, 1H), 5.27 (dd, *J* =10.0, 9.4 Hz, 1H), 4.39 (t, *J* =10.4 Hz, 1H), 4.30 (dd, *J* =12.3, 4.9 Hz, 1H), 4.17 (dd, *J* =12.3, 2.2 Hz, 1H), 3.89 (ddd, *J* =10.2, 4.9, 2.3 Hz, 1H), 2.67 (ddq, *J* =38.9, 12.6, 7.4 Hz, 2H), 2.10 (s, 3H), 2.02 (s, 3H), 1.85 (s, 3H), 1.21 (t, *J* =7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.7, 170.1, 169.4, 167.8, 167.1, 134.4, 134.3, 131.6, 131.1, 123.7, 123.7, 81.2, 75.9, 71.5, 68.9, 62.3, 53.6, 24.3, 20.7, 20.60, 20.4, 14.9. ESI-MS calcd. for $C_{22}H_{25}NO_9SNa$ [M+Na] = 502.1, found: 502.2. HRMS calcd. for $C_{22}H_{25}NO_9SNa$ $[M+Na]^+$ *m/z* = 502.1148, found: 502.1159.



20b

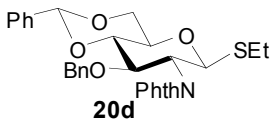
Compound 20b. 20a (41.1 g, 85.8 mmol) was suspended in methanol (200 mL) at rt. NaOMe (2.40 g, 45.0 mmol) was added resulting in homogenisation of the reaction mixture. After two hours, acetic acid

(2.55 mL, 45.0 mmol) was added and the solvents were removed under reduced pressure. The residue was purified by filtration through a plug of silica gel (9% CH_2Cl_2 in methanol) yielding 28.1 g (100%) of a white solid **20b**, that was used as such in the next transformation: $[\alpha]_D^{20}$ = +5.3 (c = 1.00, CH_2Cl_2). IR (film): 3407 (br), 2967, 2929, 1774, 1705, 1386, 1074, 1058, 909 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.84-7.78 (m, 2H), 7.72-7.68 (m, 2H), 5.32 (d, *J* =10.4 Hz, 1H), 4.32 (dd, *J* =10.0, 9.2 Hz, 1H), 4.14 (t, *J*= 10.4 Hz, 1H), 3.90-3.82 (m, 2H), 3.67 (t, *J* =9.2 Hz, 1H), 3.47 (dt, *J* =9.7, 3.2 Hz, 1H), 2.72 (ddq, *J* =37.5, 12.6, 7.4 Hz, 2H), 1.15 (t, *J* =7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.2, 168.12, 134.1, 131.7, 131.6, 123.8, 123.3, 81.3, 79.5, 72.6, 71.2, 61.9, 55.8, 24.3, 14.9. ESI-MS calcd. for $C_{16}H_{19}NO_6SNa$ $[M+Na]^+$ *m/z* = 376.1, found: 376.2. HRMS calcd. for $C_{16}H_{19}NO_6SNa$ $[M+Na]_+$ *m/z* = 276.0831, found: 376.0822.



20c

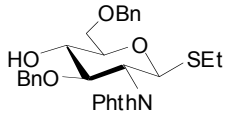
Compound 20c. To a solution of **20b** (28.1 g, 86.0 mmol) in DMF (130 mL) was added benzaldehyde dimethylacetal (32.2 mL, 215 mmol) and CSA (2.0 g, 8.6 mmol). The reaction is heated to 60 °C for 12 h, cooled to rt, and quenched by the addition of solid $NaHCO_3$ (2.5 g, 30 mmol). The solvents were removed under reduced pressure and the residue was purified by flash chromatography over silica gel (33% ethyl acetate in hexanes) yielding 26.8 g (71% over two steps) of a white foam **20c**: $[\alpha]_D^{20}$ = -7.9 (c = 1.00, CH_2Cl_2). IR (film): 3474, 2974, 2930, 1774, 1709, 1385, 1091, 1076, 960 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.90-7.83 (m, 2H), 7.75-7.71 (m, 2H), 7.52-7.47 (m, 2H), 7.40-7.35 (m, 2H), 5.57 (s, 1H), 5.41 (d, *J* =10.6 Hz, 1H), 4.66 (ddd, *J* =9.8, 9.2, 3.4 Hz, 1H), 4.40 (dd, *J* =10.5, 4.9 Hz, 1H), 4.23 (t, *J* =10.3 Hz, 1H), 3.81 (t, *J* =10.3 Hz, 1H), 3.70 (td, *J* =9.8, 4.9 Hz, 1H), 3.61 (t, *J* =9.2 Hz, 1H), 2.69 (ddq, *J* =34.7, 12.5, 7.4 Hz, 2H), 2.60 (d, *J* =3.4 Hz, 1H), 1.20 (t, *J* =7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.2, 167.7, 136.9, 134.2, 131.7, 131.6, 129.4, 128.4, 126.3, 123.8, 123.3, 101.9, 82.1, 81.8, 70.3, 69.5, 68.6, 55.4, 24.2, 14.8. ESI-MS calcd. for $C_{23}H_{23}NO_6SNa$ $[M+Na]_+$ *m/z* = 464.1, found: 464.2. HRMS calcd. for $C_{23}H_{23}NO_6SNa$ $[M+Na]_+$ *m/z* = 464.1144, found: 464.1133.



20d

Compound 20d. To a solution of **20c** (26.8 g, 60.7 mmol) in DMF (150 mL) was added NaH (60% in mineral oil, 3.16 g, 78.9 mmol) in DMF (50 mL) at 0 °C. The resulting slurry was stirred at this

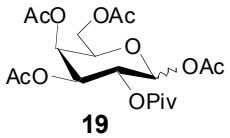
temperature for 30 min, then benzyl bromide (13.1 mL, 109.3 mmol) was added. The reaction mixture was warmed to rt, stirred for 2h, and then quenched with methanol (5 mL). Brine (200 mL) and water (200 mL) were added and the aqueous solution was extracted with ethyl acetate (3 x 400 mL). The combined organic layers were dried over $MgSO_4$, filtered, and dried under reduced pressure. The residue is purified by flash chromatography over silica gel (20% → 33% ethyl acetate in hexanes) yielding 23.7 g (74%) of **20d** as a white foam along with 6.4 g (24 %) of unreacted starting material **20c**: $[\alpha]_D^{20}$ = +53.5 (c = 1.00, CH_2Cl_2). IR (film): 3031, 2872, 17741711, 1385, 1094, 1065, 994, 911 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.87-7.82 (m, 1H), 7.75-7.68 (m, 2H9, 7.67-7.63 (m, 1H), 7.55-7.51 (m, 2H), 7.43-7.36 (m, 3H), 7.02-6.97 (m, 2H), 6.95-6.85 (m, 3H), 5.63 (s, 1H), 5.35 (d, *J* =10.6 Hz, 1H), 4.80 (d, *J* =12.3 Hz, 1H), 4.51 (d, *J* =12.3 Hz, 1H), 4.46 (dd, *J* =9.7, 9.1 Hz, 1H), 4.42 (dd, *J* =10.5, 5.0 Hz, 1H), 4.30 (t, *J* =10.3 Hz, 1H), 3.86-3.80 (m, 2H), 3.71 (td, *J* =9.8, 4.8 Hz, 1H), 2.66 (ddq, *J* =34.8, 12.5, 7.4 Hz, 2H), 1.17 (t, *J* =7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 167.7, 167.4, 137.8, 137.3, 133.9, 133.8, 131.6, 131.6, 129.0, 128.3, 128.1, 128.1, 128.0, 127.4, 126.0, 123.5, 123.3, 101.3, 83.0, 81.8, 75.4, 74.2, 70.4, 68.7, 54.7, 24.1, 14.8. ESI-MS calcd. for $C_{30}H_{29}NO_6SNa$ $[M+Na]^+$ *m/z* = 554.2, found: 554.0. HRMS calcd. for $C_{30}H_{29}NO_6SNa$ $[M+Na]^+$ *m/z* = 554.1613, found: 554.1613.



20

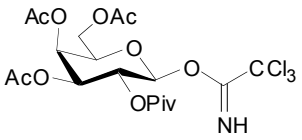
Compound 20. To a solution of **20d** (28.1 g, 52.9 mmol) in THF (250 mL) were added molecular sieves (4A, 15 g) and $NaB(CN)H_3$ (13.3 g, 212 mmol) at rt. The resulting slurry was stirred at this temperature for 1 h, and then cooled to 0 °C. HCl (2M in Et_2O, 132 mL, 264 mmol) was added drop wise, and the reaction was stirred at 0 °C for 90 min. The reaction was quenched by the addition of Et_3N (40 mL), filtered through Celite® and evaporated to dryness. Purification by flash chromatography over silica gel (25% ethyl acetate in hexanes) yielded 18.8 g (67%) of a white foam **20**: $[\alpha]_D^{20}$ = +31.9 (c = 1.00, CH_2Cl_2). IR (film): 3473 (br), 2927, 2870, 1774, 1708, 1385, 1074, 1062, 1026, 967, 910 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.83-7.79 (m, 1H), 7.72-7.65 (m, 3H), 7.39-7.33 (m, 4H), 7.33-7.29 (m, 1H), 7.07-7.03 (m, 2H), 6.98-6.93 (m, 3H), 5.29 (d, *J* =10.1 Hz, 1H), 4.75 (d, *J*= 12.1 Hz, 1H), 4.64 (d, *J* =11.9 Hz, 1H), 4.59 (d, *J* =11.9 Hz, 1H), 4.55 (d, *J* =12.2 Hz, 1H), 4.28 (dd, *J*= 10.3, 8.3 Hz, 1H), 4.23 (t, *J* =10.3 Hz, 1H), 3.85 (dd, *J* =10.2, 4.8 Hz, 1H), 3.84 (td, *J* =8.1, 2.4 Hz, 1H), 3.78 (dd, *J* =10.1, 5.2 Hz, 1H), 3.69 (td, *J* =9.5, 5.0 Hz, 1H), 3.00 (d, *J*= 2.5 Hz, 1H), 2.62 (ddq, *J* =42.5, 12.5, 7.4 Hz, 2H), 1.16 (t, *J* =7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.0, 167.5,

138.1, 137.5, 133.9, 133.8, 131.6, 128.5, 128.1, 127.9, 127.9, 127.8, 127.4, 123.5, 123.2, 81.1, 79.5, 77.5, 74.5, 74.4, 73.8, 70.9, 54.4, 23.9, 14.9. ESI-MS calcd. for $C_{30}H_{31}NO_6SNa$ $[M+Na]^+$ m/z = 556.2, found: 556.2. HRMS calcd. for $C_{30}H_{31}NO_6SNa$ $[M+Na]^+$ m/z = 556.1770, found: 556.1758.



19

Compound 19a. *D*-Galactose pentaacetate (10.6 g, 27.2 mmol) was dissolved in TFA (100 mL) and water (10 mL) at rt and stirred for 4 h. The solvents were removed under reduced pressure, and the residue was dissolved in $CHCl_3$ (100 mL). The organic layer was washed with a sat. $NaHCO_3$ solution (100 mL), dried over $MgSO_4$, filtered, and evaporated to dryness. The residue (7.75 g, 82%) was used in the next transformation without further purification. Thus obtained residue was dissolved in $CHCl_3$ (25 mL) at rt and sequentially treated with pyridine (2.7 mL) and pivaloylchloride (3.2 mL). The reaction mixture was stirred at this temperature for 7 h, and then quenched by the addition of HCl (1 N, 50 mL). The organic layer was washed with sat. $NaHCO_3$ solution (100 mL), dried over $MgSO_4$, filtered, and evaporated to dryness. The residue was purified by flash chromatography over silica gel (25% ethyl acetate in hexanes) yielding 8.74 g (74% over two steps) of a colorless oil **19a** as a mixture of anomers (α/β = 5:3). IR (film): 2978, 1745, 1370, 1213, 1311, 1058, 1011 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) selected signals: δ 6.38 (d, J =3.7 Hz, 1H), 5.61 (d, J =8.3 Hz, 0.6 H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 177.0, 176.4, 170.3, 170.2, 170.1, 170.0, 169.9, 169.9, 169.2, 168.6, 92.2, 89.4, 71.6, 70.7, 68.7, 67.7, 67.5, 67.4, 66.7, 66.2, 61.2, 60.8, 38.7, 38.7, 26.7, 26.7, 20.7, 20.6, 20.6, 20.5, 20.5, 20.5, 20.4. ESI-MS calcd. for $C_{19}H_{28}O_{11}Na$ $[M+Na]^+$ m/z = 455.1, found: 455.2. HRMS calcd. for $C_{19}H_{28}O_{11}Na$ $[M+Na]^+$ m/z = 455.1529, found: 455.1530.

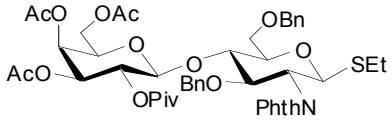


19

Compound 19. To a solution of **19a** (22.5 g, 52.0 mmol) in DMF (70 mL) was added hydrazine acetate (5.3 g, 57.2 mmol) at rt. The resulting slurry was stirred for 2 h resulting in homogenisation of the reaction mixture. The reaction was quenched by the addition of $NaHCO_{3(sat.)}$ (200 mL), and extracted with ethyl acetate (2 x 200 mL). The combined organic layers were washed with brine (200 mL) and water (200 mL), dried over $MgSO_4$, filtered, and evaporated to dryness yielding 20.0 g (99%)

of a white foam that was used in the following reaction without further purification.

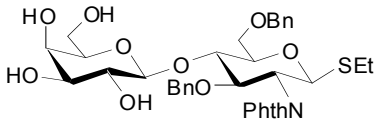
This residue was dissolved in CH_2Cl_2 (200 mL) at rt. Trichloroacetonitrile (26.1 mL, 260 mmol) and DBU (1.55 mL, 10.4 mmol) were added, and the reaction mixture was stirred at rt for 90 min. Celite® (20 g) was added and the solvents were removed under reduced pressure. Purification by flash chromatography over silica gel (20% ethyl acetate in hexanes) yields **19** (15.2 g, 56%) as a white foam as a single α-anomer: $[\alpha]_D^{20}$ = +195.6 (c = 1.00, CH_2Cl_2). IR (film): 3342, 3319, 2974, 2937, 2252, 1742, 1675, 1369, 1216, 1133, 1057, 1032 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 8.66 (s, 1H), 6.59 (d, *J* =3.3 Hz, 1H), 5.54-5.53 (m, 1H), 5.47 (dd, *J* =10.8, 3.0 Hz, 1H), 5.35 (dd, *J* =10.8, 3.4 Hz, 1H), 4.44 (t, *J* =6.4 Hz, 1H), 4.15 (dd, *J* =11.3, 6.5 Hz, 1H), 4.05 (dd, *J* =11.2, 6.7 Hz, 1H), 2.14 (s, 3H), 1.99 (s, 3H), 1.96 (s, 3H), 1.12 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 177.3, 170.2, 167.0, 169.7, 160.6, 93.4, 90.7, 69.0, 67.5, 67.4, 66.5, 61.2, 38.8, 26.8, 20.5, 20.5, 20.4. ESI-MS calcd. for $C_{19}H_{26}Cl_3O_{10}NNa$ $[M+Na]_+$ *m*/*z* =556.1, found: 556.1. HRMS calcd. for $C_{19}H_{26}Cl_3O_{10}NNa$ $[M+Na]_+$ *m*/*z* = 556.0520, found: 556.0545.



21

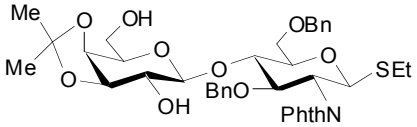
Compound 21. Compounds **19** (19.2 g, 36.0 mmol) and **20** (16.0 g, 29.9 mmol) were dissolved in CH_2Cl_2 (250 mL) at rt. Molecular sieves (4A, 10 g) were added, the slurry was stirred at ambient temperature for 1 h, and then cooled to –78 °C. TMSOTf (540 µL, 3.0 mmol) were added dropwise and the reaction was stirred for 3 h at –78 °C. Et_3N (3 mL) was added, the reaction was warmed to rt and filtered through a pad of Celite® (20 g). The solvents were removed under reduced pressure, and the residue was purified by flash chromatography over silica gel (25% → 33% ethyl acetate in hexanes) yielding **21** (21.3 g, 79%) as a white foam: $[\alpha]_D^{20}$ = +13.9 (c =0.426, CH_2Cl_2). IR (film): 3030, 2974, 2934, 2872, 2257, 1745, 1713, 1386, 1367, 1220, 1170, 1132, 1077, 1023 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.78-7.76 (m, 1H), 7.69-7.62 (m, 2H), 7.62-7.60 (m, 1H), 7.42-7.32 (m, 5H), 7.03-6.99 (m, 2H), 6.90-6.84 (m, 3H), 5.23 (d, *J* =2.8 Hz, 1H), 5.20 (d, *J* =10.0 Hz, 1H), 5.14 (dd, *J* =10.4, 8.1 Hz, 1H), 4.84-4.78 (m, 3H), 4.52 (d, *J* =8.1 Hz, 1H), 4.45 (d, *J* =8.0 Hz, 1H), 4.43 (d, *J* =7.9 Hz, 1H), 4.27-4.19 (m, 2H), 4.14 (dd, *J* =9.8, 8.3 Hz, 1H), 4.00 (dd, *J* =11.1, 6.4 Hz, 1H), 3.95 (dd, *J* =11.1, 7.4 Hz, 1H), 3.79 (dd, *J* =11.0, 2.9 Hz, 1H), 3.74 (dd, *J* =10.8, 1.1 Hz, 1H), 3.63 (t, *J*= 7.2 Hz, 1H), 3.48 (d, *J* =9.8 Hz, 1H), 2.62 (ddq, *J* =45.6, 12.6, 7.4 Hz, 2H), 2.03 (s, 3H), 2.01 (s, 3H), 1.92 (s, 3H), 1.17 (s, 9H), 1.14 (t, *J* =7.54 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 176.5, 170.1, 170.0, 169.7, 167.8,

167.3, 138.4, 137.7, 133.7, 133.6, 131.5, 128.5, 128.1, 127.8, 127.7, 126.9, 123.3, 123.1, 99.3, 81.0, 78.8, 77.1, 76.2, 74.2, 73.5, 70.9, 70.3, 69.0, 67.6, 66.9, 60.6, 54.5, 38.7, 26.9, 23.7, 20.5, 20.4, 20.3, 14.8. ESI-MS calcd. for $C_{47}H_{55}NO_{15}SNa$ $[M+Na]^+$ m/z = 928.3, found: 928.4. HRMS calcd. for $C_{47}H_{55}NO_{15}S$ $[M+H]^+$ m/z = 906.3371, found: 906.3403.



22a

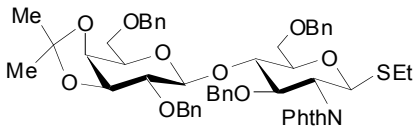
Compound 22a. **21** (16.2 g, 17.9 mmol) was suspended in methanol (400 mL) at rt, and NaOMe (2.41 g, 44.6 mmol) was added in methanol (44.6 mL). The resulting solution was stirred at rt for 5 h. Acetic acid (2.53 mL, 44.6 mmol) was added, and the solvents were removed under reduced pressure. The residue was purified by filtration through silica gel (9% CH_2Cl_2 in MeOH) yielding **22a** (12.1 g, 97%) as a colorless foam: $[\alpha]_D^{20}$ = +44.0 (c = 0.908, CH_2Cl_2). IR (film): 3407, 2929, 2873, 1774, 1709, 1386, 1072, 1049, 1020, 908 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.77-7.71 (m, 1H), 7.69-7.57 (m, 3H), 7.37-7.31 (m, 4H), 7.28-7.25 (m, 1H), 7.02-6.98 (m, 2H), 6.86-6.83 (m, 2H), 6.82-6.77 (m, 1H), 5.22 (d, J =10.5 Hz, 1H), 4.86 (d, J =12.3 Hz, 1H), 4.68 (d, J =12.0 Hz, 1H), 4.57 (d, J =12.0 Hz, 1H), 4.50 (d, J =7.7 Hz, 1H), 4.46 (d, J =12.4 Hz, 1H), 4.40 (dd, J =9.8, 8.9 Hz, 1H), 4.25 (t, J =10.4 Hz, 1H), 4.12 (t, J= 9.5 Hz, 1H), 3.97 (dd, J =11.4, 3.3 Hz, 1H), 3.90-3.84 (m, 2H), 3.74-3.65 (m, 4H), 3.50-3.40 (bs, 4H), 3.41 (dd, J =9.5, 3.2 Hz, 1H), 3.28 (t, J= 5.2 Hz, 1H), 2.62 (ddq, J =47.4, 12.5, 7.4 Hz, 2H), 1.15 (t, J =7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.0, 167.6, 138.1, 137.7, 133.9, 133.7, 131.5, 131.4, 128.4, 128.0, 127.8, 127.8, 127.7, 127.2, 123.5, 123.3, 102.9, 81.0, 79.1, 78.8, 78.0, 74.9, 74.4, 73.7, 73.4, 72.2, 69.3, 68.4, 62.3, 54.8, 23.7, 14.9. ESI-MS calcd. for $C_{36}H_{41}NO_{11}SNa$ $[M+Na]^+$ m/z = 718.2, found: 718.4. HRMS calcd. for $C_{36}H_{41}NO_{11}SNa$ $[M+Na]^+$ m/z = 718.2298, found: 718.2302.



22a

Compound 22b. To a solution of **22a** (11.1 g, 16.0 mmol) in 2,2-dimethoxypropane (100 mL) was added CSA (0.74 g, 3.2 mmol), and the resulting solution was stirred for 16 h. The reaction was quenched by the addition of Et_3N (0.7 mL, 5 mmol), and the solvents were removed under reduced pressure. The resulting white foam was dissolved in CH_2Cl_2 (180 mL), water (10 mL) and TFA (0.5

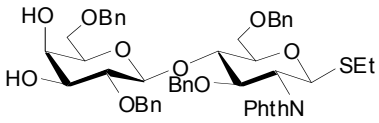
mL, 6.5 mmol) were added and the solution was stirred for 5 min at rt. Solid $NaHCO_3$ (2.0 g, 23.8 mmol) was added and the reaction mixture was filtered through a pad of silica gel (9% CH_2Cl_2 in methanol). The solvents were removed under reduced pressure and the residue was purified by flash chromatography over silica gel (50% → 30% ethyl acetate/hexanes) yielding **22b** (9.62 g, 82%) as a white foam: $[\alpha]_D^{20}$ = +58.0 (c = 0.59, CH_2Cl_2). IR (film): 3398, 3030, 2983, 2872, 1775, 1712, 1613, 1385, 1139, 1073, 1043, 909 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.80-7.76 (m, 1H), 7.69-7.62 (m, 3H), 7.39-7.34 (m, 4H), 7.32-7.29 (m, 1H), 7.05-7.01 (m, 2H), 6.94-6.90 (m, 2H), 6.89-6.86 (m, 1H), 5.23 (d, *J* =10.5 Hz, 1H), 4.86 (d, *J* =12.1 Hz, 1H), 4.72 (d, *J* =12.1 Hz, 1H), 4.59 (d, *J* =12.1 Hz, 1H), 4.45-4.39 (m, 3H), 4.27 (t, *J* =10.3 Hz, 1H), 4.07 (t, *J* =9.7 Hz, 1H), 4.02 (dd, *J* =5.5, 1.9 Hz, 1H), 3.97-3.92 (m, 2H), 3.84 (dd, *J* =11.3, 1.9 Hz, 1H), 3.73-3.67 (m, 2H), 3.64-3.59 (m, 2H), 3.53 (t, *J* =7.8 Hz, 1H), 3.05 (bs, 1H), 2.64 (ddq, *J* =45.8, 12.5, 7.4 Hz, 2H), 2.25 (bs, 1H), 1.50 (s, 3H), 1.32 (s, 3H), 1.17 (t, *J* =7.4, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.0, 167.4 138.1, 137.7, 133.9, 133.7, 131.5, 131.5, 128.4, 128.0, 128.0, 127.8, 127.6, 127.2, 123.5, 123.2, 110.3, 102.0, 81.1, 79.4, 79.0, 78.8, 78.4, 74.9, 74.4, 73.7, 73.5, 68.4, 62.1, 28.1, 26.3, 23.7, 14.9. ESI-MS calcd. for $C_{39}H_{45}NO_{11}SNa$ $[M+Na]^+$ *m/z* = 758.3, found: 758.4. HRMS calcd. for $C_{39}H_{45}NO_{11}SNa$ $[M+Na]^+$ *m/z* = 758.2611, found: 758.2629.



22

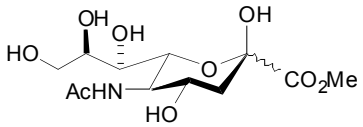
Compound 22. To a solution of **22b** (15.9 g, 21.6 mmol) in THF (600 mL) was added benzyl bromide (10.4 mL, 90.7 mmol), TBAI (5.0 g, 13.5 mmol), and NaH (60% in mineral oil, 5.19 g, 130 mmol) at rt. Then, a solution of KHMDS (0.5 M in toluene, 52.7 mL, 26.3 mmol) was added and the resulting slurry was stirred at ambient temperature for 4 h. The reaction was quenched by the careful addition of HCl (1 N, 250 mL). The organic layer was washed with $NaHCO_{3(sat.)}$ (300 mL), water (200 mL), and brine (250 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography over silica gel (25% → 50% ethyl acetate in hexanes) yielding **22** (15.9 g, 80%) as a white foam: $[\alpha]_D^{20}$ = +35.0 (c = 2.00, CH_2Cl_2). IR (film): 3062, 2985, 2868, 1775, 1712, 1611, 1386, 1369, 1076, 1027 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.82-7.79 (m, 1H), 7.71-7.63 (m, 3H), 7.42-7.25 (m, 15H), 7.02-6.97 (m, 2H), 6.87-6.84 (m, 3H), 5.35 (d, *J* =10.4 Hz, 1H), 4.86-4.82 (m, 2H), 4.75 (d, *J* =11.7 Hz, 1H), 4.60 (d, *J* =12.1 Hz, 1H), 4.57 (d, *J* =12.0 Hz, 1H), 4.49-4.39 (m, 4H), 4.34 (dd, *J* =10.2, 8.6 Hz, 1H), 4.28 (t, *J* =10.3 Hz, 1H), 4.12-4.04 (m, 3H), 3.91 (dd, *J* =11.0,

3.8 Hz, 1H), 3.77 (d, *J* =10.9 Hz, 1H), 3.75 (dd, *J* =6.3, 1.9 Hz, 1H), 3.68 (dd, *J* =10.0, 6.2 Hz, 1H, 3.63-3.58 (m, 2H), 3.39-3.34 (m, 1H), 2.65 (ddq, *J* =48.1, 12.6, 7.4 Hz, 2H), 1.38 (s, 3H), 1.34 (s, 3H), 1.19 (t, *J* =7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.0, 167.4, 138.6, 138.5, 138.4, 138.3, 133.8, 133.6, 131.7, 128.3, 128.3, 128.25, 128.1, 128.0, 127.8, 127.7, 127.5, 127.5, 127.5, 127.4, 127.0, 123.4, 123.2, 109.7, 102.3, 81.0, 80.5, 79.5, 79.4, 78.1, 78.0, 74.5, 73.8, 73.4, 73.4, 73.1, 72.1, 69.1, 68.1, 54.7, 27.9, 26.4, 23.7, 14.9.x ESI-MS calcd. for $C_{51}H_{57}NO_{11}SNa$ $[M+Na]^+$ *m/z* = 938.4, found: 938.5. HRMS calcd. for $C_{51}H_{58}NO_{11}S$ $[M+H]^+$ *m/z* = 916.3731, found: 916.3773.



18

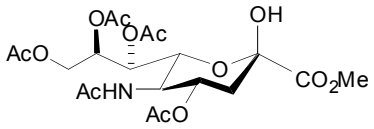
Compound 18. Compound **22** (23.0 g, 25.1 mmol) was dissolved in acetic acid (140 mL) and water (60 mL) and heated to 60 °C for 3h. The solvents were removed under reduced pressure and the residue was purified by flash chromatography over silica gel (50% ethyl acetate in hexanes) yielding **18** (20.2 g, 92%) as a white foam: $[\alpha]_D^{20}$ = +24.8 (c = 2.00, CH_2Cl_2). IR (film): 3465, 3063, 2924, 2870, 1774, 1711, 1453, 1387, 1367, 1075, 1025, 908 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.82-7.79 (m, 1H), 7.72-7.62 (m, 2H), 7.41-7.24 (m, 15H), 7.04-7.00 (m, 2H), 6.89-6.83 (m, 3H), 5.25 (d, *J* =10.3 Hz, 1H), 4.90 (d, *J* =11.6 Hz, 1H), 4.88 (d, *J* =12.7 Hz, 1H), 4.74 (d, *J* =11.5 Hz, 1H), 4.63 (d, *J* =12.0 Hz, 1H), 4.54-4.42 (m, 5H), 4.374.35 (dd, *J* =10.0, 8.7 Hz, 1H), 4.29 (t, *J* =10.3 Hz, 1H), 4.14 (t, *J* =9.2 Hz, 1H), 3.96 (bs, 1H), 3.90 (dd, *J* =11.0, 3.7 Hz, 1H), 3.80 (d, *J* =10.7 Hz, 1H),3.68 (dd, *J* =10.0, 6.0 Hz, 1H), 3.63-3.57 (m, 2H), 3.52-3.46 (m, 1H), 3.41 (t, *J* =5.3 Hz, 1H), 2.71 (bs, 1H), 2.65 (ddq, *J* =49.6, 13.0, 7.5 Hz, 2H), 2.50 (bs, 1H), 1.19 (t, *J* =7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 168.0, 167.4, 138.7, 138.3, 138.2, 137.8, 133.8, 133.6, 131.6, 128.5, 128.4, 128.3, 127.9, 127.9, 127.8, 127.6, 127.5, 127.5, 126.9, 123.4, 123.1, 102.9, 80.9, 80.0, 79.5, 78.0, 77.9, 75.0, 74.6, 73.5, 73.4, 73.1, 72.8, 69.1, 69.1, 68.1, 54.7, 23.7, 14.9. ESI-MS calcd. for $C_{50}H_{53}NO_{11}SNa$ $[M+Na]^+$ *m/z* = 898.3, found: 898.4. HRMS calcd. for $C_{50}H_{53}NO_{11}SNa$ $[M+Na]^+$ *m/z* = 898.3309, found: 898.3273.



23a

Compound 23a. To a suspension of N-acetyl-neuraminic acid (11.1 g, 35.9 mmol) in methanol (300

mL) was added DOWEX50WX8 (34 g, prewashed with methanol) and the resulting slurry was stirred for 4 h. Removal of the resin by filtration and removal of all volatiles yielded **23a** (9.80 g, 85%) as a white foam: $[\alpha]_D^{20}$ = -22.2 (c = 1.00, MeOH). IR (film): 3343, 2953, 1739, 1620, 1428, 1123, 1033, 977 cm^{-1}. ^1H NMR (600 MHz, MeOH-d4): δ 8.11 (d, *J* =8.7 Hz, 1H), 4.85 (bs, 5H), 4.04 (td, *J* =10.9, 4.8 Hz, 1H), 4.00 (d, *J*= 10.6 Hz, 1H), 3.85-3.77 (m, 2H), 3.78 (s, 3H), 3.70 (ddd, *J* =8.8, 5.7, 2.9 Hz, 1H), 3.62 (dd, *J* =11.4, 5.7 Hz, 1H), 3.49 (dd, *J* =9.2, 1.0 Hz, 1H), 2.22 (dd, *J* =12.9, 4.9 Hz, 1H)2.02 (s, 3H), 1.90 (dd, *J* =12.6, 11.7 Hz, 1H). ^{13}C NMR (75 MHz, MeOH-d4): δ 175.1, 171.8, 96.7, 72.1, 71.7, 70.2, 67.9, 64.9, 54.3, 53.2, 40.7, 22.7. ESI-MS calcd. for $C_{12}H_{21}NO_9Na$ $[M+Na]_+$ *m/z* = 346.1, found: 346.0. HRMS calcd. for $C_{12}H_{21}NO_9Na$ $[M+Na]_+$ *m/z* = 346.1127, found: 346.1118.

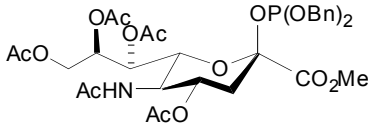


23b

Compound 23b. To a solution of **23a** (8.50 g, 26.3 mmol) in acetyl chloride (300 mL) was added at 0 °C methanol (5.3 mL, 130 mmol) dropwise in a sealed reaction vessel, not allowing the forming gases escape. The reaction mixture was stirred at ambient temperature for 60 h until the solvents were removed under reduced pressure. The residue is dissolved in ethyl acetate (300 mL) and the solution was washed with sat. $NaHCO_3$ solution (300 mL), dried over $MgSO_4$, filtered, and evaporated to dryness. The residue (14.0 g, >100%) was used in the following transformation without further purification.

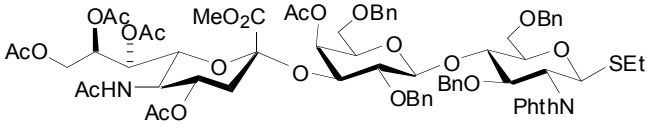
Thus obtained residue was dissolved in acetone (240 mL) and water (60 mL) at ambient temperature. Ag_2CO_3 (14.5 g, 52.6 mmol) was added in one portion and the slurry was stirred under the exclusion of light for 18 h, then all solid was filtered off by the use of a Celite® pad. The solution was concentrated to ca. 100 mL under reduced pressure, diluted with ethyl acetate (300 mL) and washed with water (100 mL) and brine (100 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography over silica gel (25% → 14% ethyl acetate/hexanes) yielding **23b** (10.7 g, 79%) as a white foam: $[\alpha]_D^{20}$ = -6.2 (c = 1.00, CH_2Cl_2). IR (film): 1740, 1661, 1542, 1433, 1370, 1216, 1034 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 5.77 (d, *J* =9.7 Hz, 1H), 5.35 (dd, *J* =5.3, 1.0 Hz, 1H), 5.24 (ddd, *J* =7.8, 5.4, 2.5 Hz, 1H), 5.22-5.17 (m, 1H), 4.59 (d, *J* =1.0 Hz, 1H)4.51 (dd, *J* =12.4, 2.4 Hz, 1H), 4.20 (dd, *J* =10.5, 2.0 Hz, 1H), 4.19-4.14 (m, 1H), 4.02 (dd, *J* =12.3, 7.7 Hz, 1H) 3.85 (s, 3H), 2.25 (ddd, *J* =12.8, 11.7, 0.9 Hz, 1H), 2.18 (dd, *J* =12.8, 5.3 Hz,

1H), 2.13 (s, 3H), 2.09 (s, 3H), 2.02 (s, 3H), 2.01 (s, 3H), 1.89 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 171.0, 171.0, 170.9, 170.3, 170.2, 169.0, 94.8, 71.4, 71.1, 69.3, 68.0, 62.6, 53.5, 49.4, 36.1, 23.1, 21.0, 20.9, 20.8, 20.8. ESI-MS calcd. for $C_{20}H_{29}NO_{13}Na$ $[M+Na]_+$ m/z = 514.2, found: 514.3. HRMS calcd. for $C_{20}H_{29}NO_{13}Na$ $[M+Na]_+$ m/z = 514.1537, found: 514.1548.



23

Compound 23. To a solution of **23b** (12.3 g, 25.1 mmol) in CH_2Cl_2 (250 mL) was added 1*H*-tetrazole (3%wt in CH3CN, 312 mL, 105 mmol) and $(BnO)_2PN{i}Pr_2$ (25.2 mL, 57.7 mmol) at rt. The resulting solution became cloudy after 15 min. HCl (0.2 N, 500 mL) was added carefully, the aqueous layer was extracted with CH_2Cl_2 (250 mL). The combined organic layers were washed with water (200 mL) and brine (200 mL), dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was purified by flash chromatography over silica gel (20% ethyl acetate in hexanes) yielding **23** (17.0 g, 80%) as a white foam: $[\alpha]_D^{20}$ = -35.9 (c = 1.00, CH_2Cl_2). IR (film): 3065, 3033, 2955, 1741, 1685, 1542, 1369, 1223, 1162, 1033 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.52-7.49 (m, 2H), 7.46-7.42 (m, 2H), 7.40-7.29 (m, 6H), 5.19 (dd, *J* =12.7, 9.9 Hz, 1H), 5.17-5.12 (m, 2H), 5.00-4.93 (m, 2H), 4.91-4.85 (m, 2H), 4.58 (dd, *J* =12.6, 2.1 Hz, 1H), 4.31 (d, *J* =10.4 Hz, 1H), 4.14-4.10 (m, 1H), 4.00 (q, *J* =10.5 Hz, 1H), 3.75 (dd, *J* =5.7, 3.9 Hz, 1H), 3.73 (s, 3H), 2.40 (dd, *J* =13.0, 4.9 Hz, 1H), 2.10-2.00 (m, 1H), 2.08 (s, 6H), 2.02 (s, 3H), 1.98 (s, 3H), 1.80 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.6, 170.5, 170.3, 170.0, 169.8, 167.6, 138.6 (d, *J* =2.5 Hz), 137.9 (d, *J* =5.0 Hz, 1H), 128.7, 128.5, 128.0, 127.8, 127.7, 127.6, 97.8 (d, *J* =7.6 Hz), 72.3, 71.9, 68.3, 68.0, 65.5 (d, *J* =13.3 Hz), 64.0 (d, *J* =3.3 Hz), 62.5, 53.1, 48.4, 37.7, 23.0, 21.1, 21.1, 20.8, 20.8, 20.7. ESI-MS calcd. for $C_{34}H_{42}NO_{15}PNa$ $[M+Na]_+$ m/z = 758.2, found: 758.3. HRMS calcd. for $C_{34}H_{42}NO_{15}PNa$ $[M+Na]_+$ m/z = 758.2190, found: 758.2186.

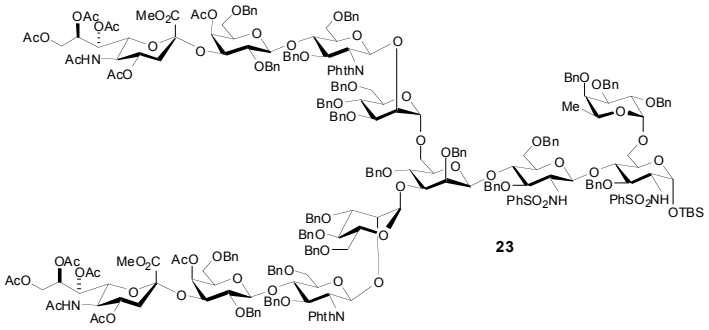


7

Compound 7. To a solution of **23** (3.0 g, 4.1 mmol) and **18** (6.43 g, 7.38 mmol) in CH_3CN (100 mL) was molecular sieves (4A, 15 g) at rt and the slurry was stirred for 30 min. After cooling to -40 °C

TMSOTf (220 μL, 1.22 mmol) was added dropwise and the reaction is kept at this temperature for 16 h. The reaction is quenched by the addition of $NaHCO_{3(sat.)}$ solution (2 mL), warmed to rt, and filtered through a pad of Celite® and $MgSO_4$ (1:1, 50 g, ethyl acetate). The solvents were removed under reduced pressure, and the residue was purified by flash chromatography over silica gel (40% ethyl acetate in toluene) to remove the unreacted starting material **18** and 3.8 g (67%) of a compound having the correct mass (indicated by ESI).

This residue was dissolved in pyridine (20 mL) and acetic anhydride (10 mL) at rt. DMAP (200 mg) was added at 0 °C and the reaction was stirred at rt for 4.5 h. The solvents were removed under reduced pressure and the residue was purified by multiple flash chromatography on silica gel (2% CH_2Cl_2 in methanol, then 17 → 25% ethyl acetate/toluene) yielding **7** (1.98 g, 35% over two steps) as a white foam: $[\alpha]_D^{20}$ = +4.83 (c = 0.49, CH_2Cl_2). IR (film): 3031, 2956, 2871, 1744, 1714, 1667, 1369, 1223, 1076, 1045 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ 7.83-7.77 (m, 1H), 7.72-7.65 (m, 3H), 7.49-7.44 (m, 2H), 7.42-7.36 (m, 2H), 7.35-7.20 (m, 11H), 7.02-6.97 (m, 2H), 6.90-6.82 (m, 3H), 5.60 (ddd, *J* =8.0, 5.0, 2.6 Hz, 1H), 5.35 (dd, *J* =8.4, 2.5 Hz, 1H), 5.19 (d, *J* =10.1 Hz, 1H), 5.06 (d, *J* =10.3 Hz, 1H), 5.03 (d, *J* =3.0 Hz, 1H), 4.97 (d, *J* =12.2 Hz, 1H), 4.92 (ddd, *J* =12.0, 10.6, 4.6 Hz, 1H), 4.86 (d, *J* =12.0 Hz, 1H), 4.75-4.70 (m, 2H), 4.58 (d, *J* =12.0 Hz, 1H), 4.50 (dd, *J* =9.7, 3.4 Hz, 1H), 4.47-4.41 (m, 3H), 4.33-4.24 (m, 4H), 4.14-4.07 (m, 2H), 4.04 (dd, *J* =12.6, 5.1 Hz, 1H), 3.83 (s, 3H), 3.80-3.70 (m, 4H), 3.52-3.43 (m, 2H), 3.35 (dd, *J* =9.9, 5.7 Hz, 1H), 3.26 (dd, *J* =9.9, 7.0 Hz, 1H), 2.66 (dq, *J* =12.9, 7.4 Hz, 1H), 2.61-2.54 (m, 2H), 2.17-2.10 (m, 1H), 2.08 (s, 3H), 2.02 (s, 3H), 1.97 (s, 3H), 1.95 (s, 3H), 1.87 (s, 3H), 1.84 (s, 3H), 1.16 (t, *J* =7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.8, 170.6, 170.3, 169.9, 169.9, 169.9, 168.1, 167.9, 167.5, 139.3, 138.9, 138.6, 138.2, 133.8, 133.7, 131.7, 128.3, 128.2, 128.1, 127.8, 127.8, 127.6, 127.5, 127.4, 127.4, 127.3, 127.2, 127.0, 123.5, 123.2, 102.1, 97.4, 80.8, 79.5, 79.4, 78.1, 75.1, 74.2, 73.7, 73.3, 72.8, 72.3, 71.6, 69.5, 68.8, 68.5, 68.4, 68.0, 67.1, 62.0, 54.7, 53.1, 49.3, 37.6, 23.7, 23.2, 21.2, 20.8, 20.7, 20.7, 20.6, 15.0. ESI-MS calcd. for $C_{72}H_{82}N_2O_{24}SNa$ $[M+Na]_+$ *m*/*z* = 1413.5, found: 1413.6. HRMS calcd. for $C_{72}H_{83}N_2O_{24}S$ $[M+H]_+$ *m*/*z* = 1391.5056, found: 1391.5089.

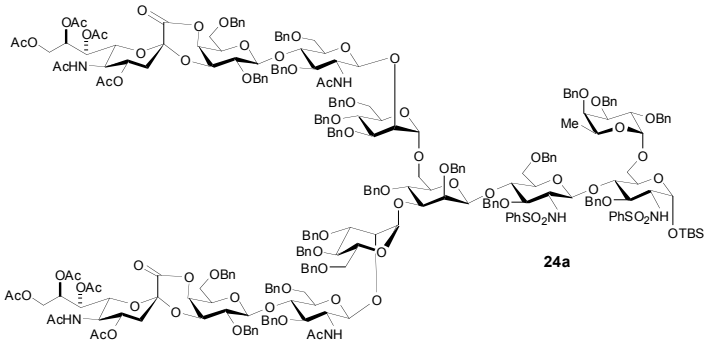


23

Dodecasaccharide 23. Hexasaccharide **6** (138 mg, 0.0525 mmol) was combined with trisaccharide **7** (438 mg, 0.315 mmol) in acetonitrile (4 mL), dried with freshly activated 4 Å MS for 1.2 h, and the resultant solution was cooled to 0 °C. To this solution, $(BrC_6H_5)_3NSbCl_6$ (279 mg, 0.341 mmol) was introduced. The reaction vessel was protected from light, and the solution was left warming to rt. After 4h, another portion of trisaccharide **7** (146 mg, 0.105 mmol) in acetonitrile (2 mL + 1 mL rinse) was introduced together with $(BrC_6H_5)_3NSbCl_6$ (107 mg, 0.131 mmol). The resultant solution was stirred for 11h before being quenched with triethylamine (1 mL), filtered through silica gel plug (dichloromethane and ethyl acetate washes), and concentrated under reduced pressure to afford crude oil. This oil was iteratively purified by flash chromatography (5% → 9% → 28% → 33% acetone in toluene) to afford 206 mg of pure product (74% yield) as a white solid. $[\alpha]_D^{20}$ = -0.69 (c = 2.9, $CHCl_3$). IR (film): 3313, 3087, 3062, 3030, 3007, 2928, 2866, 1776, 1747, 1715, 1690, 1496, 1453, 1389, 1367, 1330, 1308, 1223, 1158, 1089, 1076, 1048 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$):[2] δ 7.78 (d, *J* =11 Hz, 6H), 7.64 (m, 2H), 7.57 (m, 2H), 7.52-7.43 (m, 10H), 7.43-7.37 (m, 8H), 7.37-6.82 (m, 102H), 5.59 (m, 2H), 5.35 (m, 2H), 5.29 (t, *J* =9.4 Hz, 2H), 5.07 (m, 4H), 5.02-4.89 (m, 3H), 4.89-4.80 (m, 9H), 4.79-4.74 (m, 4H), 4.72-4.63 (m, 4H), 4.60-4.54 (m, 7H), 4.54-4.40 (m, 12H), 4.40-4.23 (m, 18H), 4.17 (d, *J* =8.2 Hz, 2H), 4.16-4.09 (m, 7H), 4.06 (m, 2H), 4.03 (m, 2H), 4.06-4.03 (m, 2H), 4.00-3.79 (m, 10H), 3.84 (s, 3H), 3.83 (s, 3H), 3.76-3.70 (m, 7H), 3.70-3.61 (m, 4H), 3.61-3.44 (m, 14H), 3.37 (m, 7H), 3.33-3.21 (m, 8H), 3.18 (d, *J* =14 Hz, 1H), 3.15 (d, *J* =9 Hz, 1H), 3.01 (d, *J* =5.5 Hz, 1H), 2.91 (m, 1H), 2.74-2.63 (m, 2H), 2.57 (d, *J* =8, Hz, 1H), 2.53 (d, *J* =8 Hz, 1H), 2.08 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H), 2.03 (s, 3H), 1.96 (s, 6H), 1.95 (s, 3H), 1.95 (s, 3H), 1.88 (s, 3H), 1.87 (s, 3H), 1.86 (m, 2H), 1.83 (s, 3H), 1.81 (s, 3H), 1.01 (d, *J* =6.4 Hz, 3H), 0.93 (s, 9H), 0.11 (s, 3H), 0.055 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.7, 170.5, 170.5, 170.3, 170.3, 169.9, 169.9, 169.9, 169.9, 169.8, 169.8, 168.4, 168.2, 167.9, 167.9, 167.3, 141.3, 140.9, 139.3, 139.2, 139.0, 138.9, 138.7, 138.7, 138.6, 138.6,

[2] Due to the presence of the rotomers as well as high overlap of the signals, there is an ambiguity associated with interpretation and tabulation of the data. Please refer to the attached ^1H, COSY, and HSQC NMR spectra in the SI-2 section if more information is required.

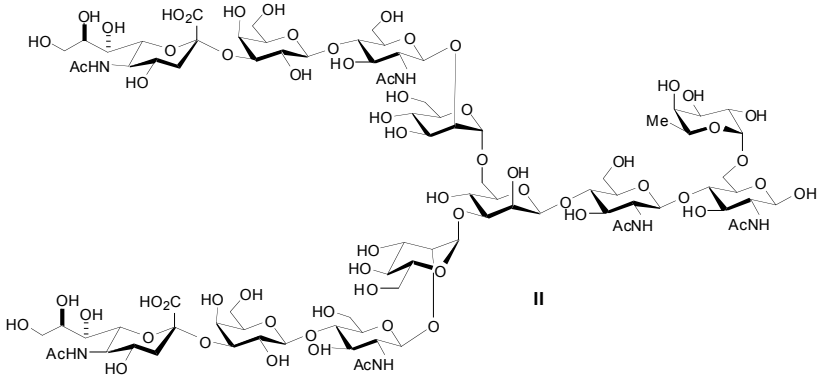
138.6, 138.4, 138.4, 138.3, 138.2, 138.2, 138.2, 138.1, 138.1, 138.0, 133.4, 132.3, 132.1, 131.6, 128.7, 128.5, 128.5, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.2, 128.1, 128.1, 128.1, 128.1, 128.0, 128.0, 128.0, 128.0, 128.0, 128.0, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5, 127.4, 127.4, 127.4, 127.4, 127.4, 127.3, 127.3, 127.2, 127.2, 127.2, 127.0, 127.0, 127.0, 126.9, 126.8, 126.8, 102.2, 102.1, 101.0, 101.0, 98.7, 97.7, 97.4, 97.4, 97.2, 96.8, 95.9, 92.8, 79.2, 79.2, 79.2, 78.7, 78.4, 77.5, 76.5, 76.5, 75.4, 75.0, 74.9, 74.8, 74.7, 74.5, 74.4, 74.3, 74.1, 74.0, 73.7, 73.6, 73.5, 73.2, 73.2, 73.1, 72.8, 72.8, 72.6, 72.5, 72.3, 72.2, 72.0, 71.7, 71.5, 70.3, 69.7, 69.5, 69.5, 69.5, 68.8, 68.6, 68.5, 68.4, 68.2, 68.1, 68.0, 67.8, 67.8, 67.1, 67.0, 66.1, 65.5, 62.0, 62.0, 59.3, 58.4, 55.5, 53.0, 53.0, 49.2, 49.1, 37.4, 37.4, 25.8, 23.3, 21.1, 21.1, 20.8, 20.8, 20.7, 20.6, 20.6, 20.6, 20.5, 20.5, -4.5, -5.7. ESI-MS calcd. for $C_{292}H_{322}N_6O_{80}S_2Si$ $[M+2Na]^{2+}$: 2666.5, $[M+3Na]^{3+}$: 1785.3. Found: 2666.6, 1785.7.



Dodecasaccharide 24a. Protected dodecasaccharide **6a** (84 mg, 0.0159 mmol) was dissolved in 1:1 dichloromethane/methanol (4 mL), and 0.5M sodium methoxide in methanol (572 μL, 0.286 mmol) was added. This solution was stirred for 4 h, and water (0.2 mL) was introduced. After 12 h of additional stirring, the pH of the reaction was adjusted to 5 by addition of Dowex® MAC-3 ion exchange resin, the solution was filtered and concentrated under reduced pressure to provide 76 mg of white solid. ESI-MS calcd. for $C_{270}H_{298}N_6O_{70}S_2Si$ $[M-2H]^{2-}$: 2418.0, $[M+Cl-H]^{2-}$: 2436.2, $[M+Cl-2H]^{3-}$: 1623.8. Found: 2417.9, 2436.3, 1623.7.

The solid from above (76 mg, 0.0157 mmol) was combined with ethelenediamine (1.6 mL), *n*-butanol (5.4 mL) and toluene (2.7 mL) and stirred at 90 °C for 30h. The reaction mixture was then cooled to rt, and the solvents were removed under reduced pressure to provide yellow solid. ESI-MS calcd. for $C_{254}H_{294}N_6O_{66}S_2Si$ $[M-3H]^{3-}$: 1525.3. Found: 1525.5. This compound was re-dissolved in 1:2 acetic anhydride/pyridine (3 mL), stirred for 24h, and concentrated under reduced pressure to provide crude **24a** as a yellow film. An aliquot of this sample has been sampled and purified for analytical

purposes (flash chromatography 9% → 28% → 33% acetone in toluene) to afford **24a** as a white solid. $[\alpha]_D^{20}$ = +6.8 (c = 2.3, $CHCl_3$). IR (film): 3320, 3087, 3062, 3030, 2929, 2864, 1755, 1745, 1452, 1368, 1289, 1220, 1159, 1092, 1049 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$):[2] δ 7.73 (t, *J* =7.4 Hz, 4H), 7.39-7.04 (m, 116H), 5.55-5.49 (m, 3H), 5.43 (d, *J* =6.8 Hz, 1H), 5.32 (d, *J* =6.6 Hz, 1H), 5.25 (s, 3H), 5.14 (d, *J* =6.6 Hz, 1H), 5.07-5.01 (m, 5H), 4.89-4.78 (m, 10H), 4.74 (d, *J* =11.5 Hz, 2H), 4.73 (d, *J* =11.6 Hz, 2H), 4.67 (d, *J* =11.9 Hz, 4H), 4.64-4.48 (m, 16H), 4.49-4.38 (m, 14H), 4.36 (d, *J* =10.0 Hz, 2H), 4.33 (d, *J* =11.8 Hz, 2H), 4.29-4.19 (m, 5H), 4.19-4.14 (m, 5H), 4.09 (m, 1H), 4.04 (m, 4H), 3.96-3.85 (m, 13H), 3.81-3.60 (m, 16H), 3.60-3.32 (m, 14H), 3.32-3.30 (m, 2H), 3.27 (m, 3H), 3.11 (m, 1H), 3.01 (m, 2H), 2.81 (d, *J* =6.6 Hz, 1H), 2.15 (s, 3H), 2.15 (s, 3H), 2.09 (m, 2H), 2.07 (s, 3H), 2.06 (s, 3H), 1.97 (s, 3H), 1.97 (s, 3H), 1.93 (s, 3H), 1.92 (s, 3H), 1.88 (s, 3H), 1.87 (s, 3H), 1.81-1.76 (m, 2H), 1.62 (s, 3H), 1.61 (s, 3H), 1.00 (d, *J* =6.3 Hz, 3H), 0.92 (s, 9H), 0.097 (s, 3H), 0.061 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 192.4, 171.0, 170.8, 170.6, 170.3, 170.1, 168.7, 164.1, 141.6, 140.9, 139.3, 139.2, 139.0, 138.8, 138.8, 138.6, 138.6, 138.5, 138.4, 138.3, 138.2, 138.2, 138.2, 138.1, 138.1, 138.0, 137.8, 137.7, 129.0, 129.0, 128.8, 128.6, 128.5, 128.5, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6, 127.5, 127.5, 127.4, 127.4, 127.3, 127.2, 127.1, 127.1, 126.9, 126.9, 123.5, 102.1, 102.1, 101.5, 100.7, 99.5, 98.1, 98.0, 97.3, 95.1, 95.1, 93.0, 80.6, 79.5, 79.4, 79.1, 78.7, 78.3, 78.0, 77.9, 77.6, 77.5, 76.1, 75.6, 75.5, 75.1, 74.8, 74.8, 74.7, 74.6, 74.5, 74.1, 74.0, 73.6, 73.5, 73.4, 73.2, 73.1, 73.1, 73.0, 72.7, 72.6, 72.2, 71.8, 71.0, 70.3, 70.3, 70.2, 69.7, 69.6, 69.4, 69.1, 68.9, 68.3, 67.8, 67.6, 67.5, 66.2, 65.4, 62.0, 59.2, 58.5, 57.8, 57.2, 53.8, 49.2, 39.4, 38.0, 38.0, 37.6, 31.7, 29.7, 29.3, 25.8, 23.3, 23.2, 21.0, 21.0, 20.8, 20.7, 20.6, 18.1, 16.5, 14.1, -4.4, -5.5. ESI-MS calcd. for $C_{274}H_{310}N_6O_{74}S_2Si$ $[M+2Na]^{2+}$: 2504.5, $[M+3Na]^{3+}$: 1677.3. Found: 2505.4, 1677.5.



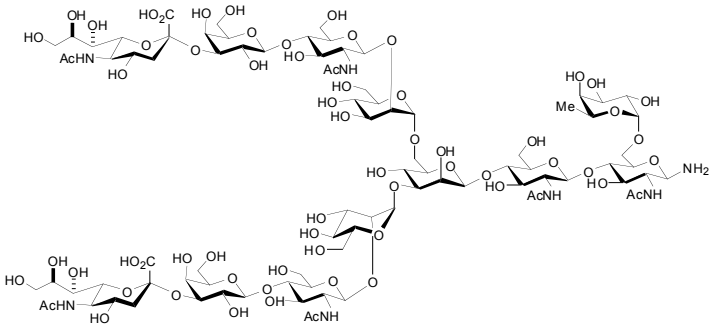
The product from above was treated with the mixture of 1M TBAF in THF (1.5 mL) and 1M

acetic acid in THF (3.0 mL) at rt. After 4h, additional 1M TBAF in THF (0.3 mL) was added and the resultant mixture was stirred for 8h before being diluted with ethyl acetate, washed with $NaHCO_{3(sat)}$, 50% brine in water, and brine, dried ($MgSO_4$), filtered and concentrated to afford a yellow oil: ESI-MS calcd. for $C_{268}H_{296}N_6O_{74}S_2$ $[M+2Na]^{2+}$: 2447.5, $[M+3Na]^{3+}$: 1638.3. Found: 2447.8, 1638.9.

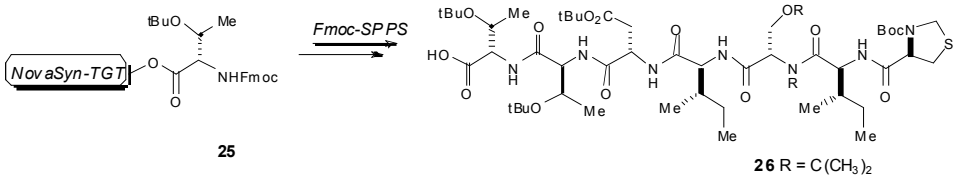
This oil was dissolved in 1:1 dichloromethane/methanol (5.5 mL), cooled to 0 °C, and water (0.3 mL) followed by 0.5M sodium methoxide in methanol (550 μL, 0.275 mmol) was added. This solution was stirred at 0 °C for 5h and slowly warmed to rt over the course of 2h. After 7h of total stirring, the pH of the reaction was adjusted to 5 by the addition of Dowex® MAC-3 ion exchange resin, and the solution was filtered and concentrated under reduced pressure to provide white solid: ESI-MS calcd. for $C_{252}H_{284}N_6O_{68}S_2$ $[M-2H]^{2-}$: 2273.4, Found: 2275.

The solution of solid from above in THF (3 mL + 2 mL wash) was added to the solution of Na (170 mg, 7.4 mmol) in ammonia (15 mL) and THF (2 mL) at -78 °C. The resultant blue solution was stirred for 5h before being slowly quenched with solid NH_4Cl to the point when the solution became colourless. The white solution was warmed to rt while blowing away the ammonia and THF to provide grey solid. This grey solid was dissolved in 5 mL of water and purified by gravity size exclusion chromatography (P4 Bio-Rad gel, water as an eluent) to remove the excess of salts. The fractions containing the product were concentrated by lyophilisation to provide white powder (25 mg). This powder was dissolved in $NaHCO_{3(sat)}$ (5 mL), cooled to 0 °C, and Ac_2O (0.25 mL) was added. After 5 min of stirring, the solution was warmed to rt, and the pH was adjusted to 7 by addition of $NaHCO_{3(sat)}$, and this acetylation cycle was repeated additional 2 times. The resultant solution was repeatedly purified by gravity size exclusion chromatography (P4 Bio-Rad gel, water as an eluent) to provide 23 mg of white powder **II** as a 1:1 mixture of anomers:[3] ^{1}H NMR (600 MHz, D_2O) Selected Data:[2] δ 5.19 (d, *J* =3.2 Hz, 1H), 5.13 (s, 2H), 4.93 (s, 2H), 4.91 (t, *J* =4.4 Hz, 2H), 4.73 (m, 1H), 4.69 (m, 1H), 4.68 (m, 1H), 4.67 (m, 1H), 4.58 (d, *J* =7.7 Hz, 4H), 4.56 (dd, *J* =7.8, 2.5 Hz, 4H), 4.24 (m, 2H), 4.20 (m, 2H), 4.17-4.10 (m, 7H), 4.00 (d, *J* =11.1 Hz, 4H), 3.51 (t, *J* =9.6 Hz, 4H), 2.77 (d, *J* =4.6 Hz, 2H), 2.76 (d, *J* =4.9 Hz, 2H), 2.10 (s, 6H), 2.06 (s, 6H), 2.05 (s, 6H), 2.05 (s, 6H), 2.04 (s, 6H), 2.04 (s, 6H), 1.23 (d, *J* =6.1 Hz, 3H), 1.22 (d, *J* =6.1 Hz, 3H). ESI-MS calcd. for $C_{90}H_{148}N_6O_{66}$ $[M-2H]^{2-}$: 1183.3, Found: 1183.9.

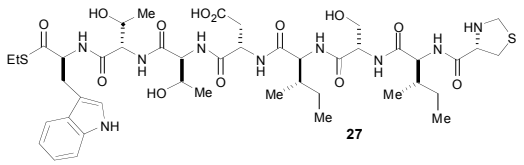
[3] Sometimes, mono and bis acetylated products are also formed together with **II** (ESI-MS calcd. for $C_{92}H_{150}N_6O_{67}$ and $C_{94}H_{152}N_6O_{68}$ $[M-2H]^{2-}$: 1204.8 and 1225.9, Found: 1205.1 and 1226.0). The extra acetates are cleaved under Kochetkov amination conditions.



Dodecasaccharide Anomeric Amine IIa. Dodecasaccharide **II** (11 mg, 4.23 μmol) was dissolved in water (5 mL) and $(NH_4)HCO_3$ (6g, Ultra 09830 Fluka) was slowly introduced in small portions while stirring. The resultant slurry was warmed to 40 °C and stirred for 3 days at this temperature. A periodic introduction of $(NH_4)HCO_3$ was made throughout this time to keep the solution saturated in ammonia. After completion, the excess of $(NH_4)HCO_3$ and water was removed by repetitive lyophilization until the mass of the product became constant (11 mg). ESI-MS calcd. for $C_{90}H_{149}N_7O_{65}$ $[M-2H]^{2-}$: 1182.9, Found: 1182.8. MALDI-TOF calcd. for $C_{90}H_{149}N_7O_{65}$ $[M+Na]^+$: 2391.85, Found: 2391.44.



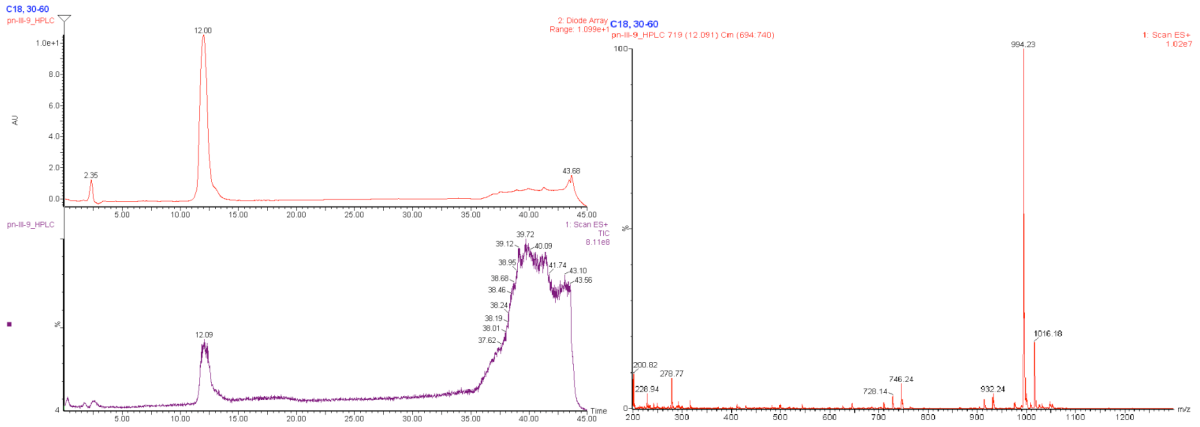
0.42 g (ca. 0.1 mmol) of Fmoc-Thr(tBu)-Nova-TGT resin **25** was subjected to continuous flow automated peptide synthesis. For coupling steps, resin was treated with a 4-fold excess of HATU and Fmoc amino acids in 1M DIEA/DMF, and for deblocking, a solution of 2% piperidine / 2% DBU in DMF was used. The amino acids used were, in order of synthesis: Fmoc-Thr(tBu)-OH, Fmoc-Asp(tBu)-OH, Fmoc-Ileu-Ser(Me,Me, ψ–Pro)-OH, Fmoc-Ile-OH, Fmoc-Thz(Boc)-OH. The resin was transferred to a manual peptide synthesis vessel, washed with methanol (10 mL), and treated with the cleavage solution (10 mL) consisting of 1:1:8 trifluoroethanol/acetic acid/dichloromethane for 1.5 h. The beads were filtered, rinsed with another 10 mL of cleavage solution, filtered again, and then treated for another 1 h with 10 mL of the cleavage solution. This process was repeated for a total of 3 2-hour cleavage cycles, and the combined was concentrated in vacuo to afford ca. 101 mg of peptide **26** after cleavage (99% yield). Exact mass calcd for $C_{51}H_{89}N_7O_{15}S$ $[M+H]^+$: 1072.6; $[M+Na]^+$: 1094.6; $[M+TFA^-]^-$: 1184.6; $[M-H]^-$: 1070.5. Found: 1072.8, 1094.7, 1184.8, 1070.8.



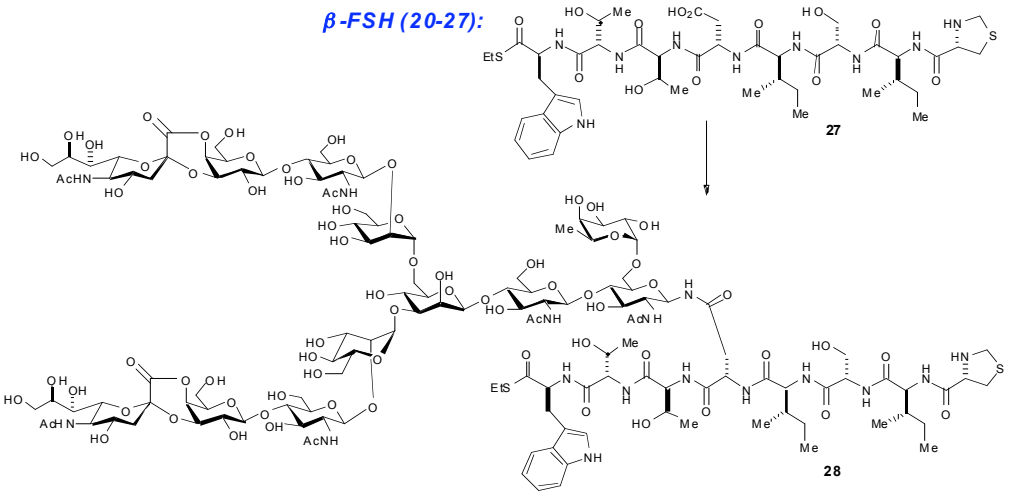
27

Peptide **26** (31 mg, 0.0287 mmol) was combined with (*S*)-tert-butyl 2-(2-amino-3-(ethylthio)-3-oxopropyl)-1H-indole-1-carboxylate (20 mg, 0.0575 mmol), HOOBt (9.4 mg, 0.0575 mmol), and dissolved in 1:3 TFE/$CHCl_3$ (1.0 mL). To this solution, EDC (10 μL, 0.0575 mmol) was added and the resultant yellow solution was stirred for 2.5h before being concentrated and chromatographed on silica (0% → 7% methanol in dichloromethane) to provide product (36 mg) contaminated with some (*S*)-tert-butyl 2-(2-amino-3-(ethylthio)-3-oxopropyl)-1H-indole-1-carboxylate. Alternatively, the crude product could be directly subjected to the next step without the chromatographic purification of EDC and HOOBt side products. Exact mass calcd for $C_{69}H_{111}N_9O_{17}S_2$ $[M+H]^+$: 1403.9; $[M+Na]^+$: 1425.8. Found: 1402.7, 1424.6.

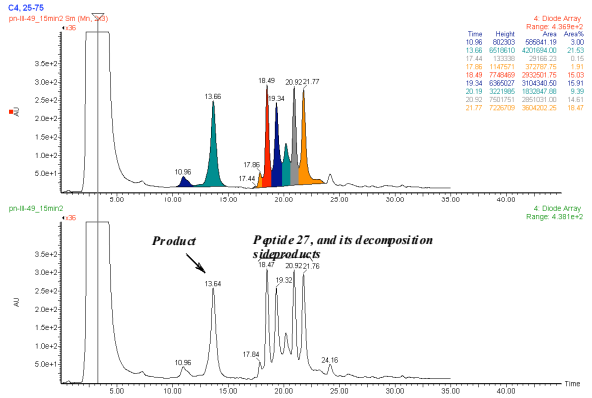
The thioester from above was treated with cocktail B[4] (2 mL) for 2h, then diluted with dichloromethane, and concentrated. The residue was triturated with ether (2 x 15 mL), decanted, and dissolved in 3 mL of DMSO and 10 mL of 7:3 acetonitrile/water, and purified by HPLC: Rf = 14.5 (Microsorb C18 column, 30-60% MeCN in H_2O, 30 min) to afford ca. 6 mg (21%, 3 steps) of pure **27**. Exact mass calcd for $C_{44}H_{67}N_9O_{13}S_2$ $[M+H]^+$: 994.5; $[M+Na]^+$: 1016.4. Found: 994.2, 1016.2.

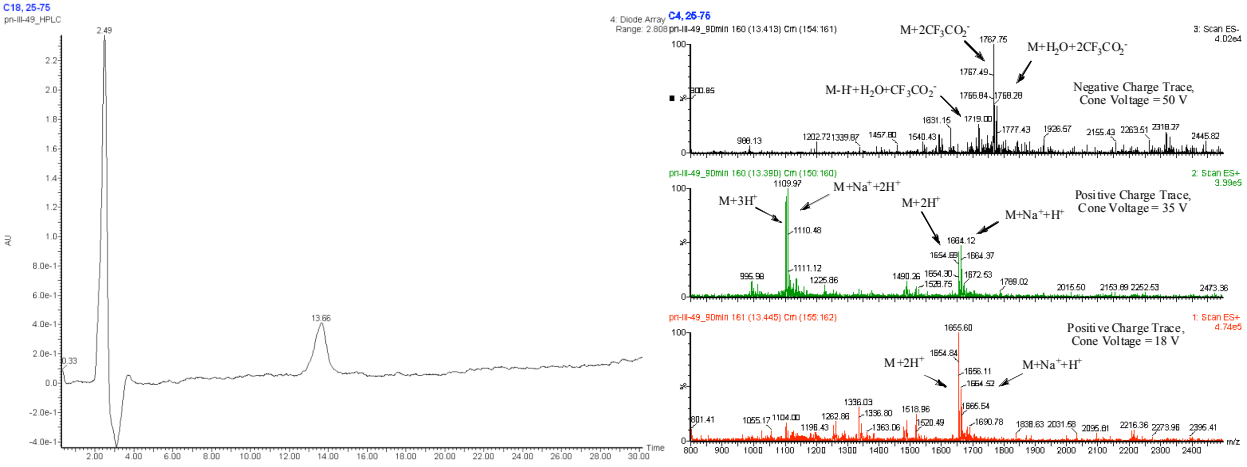


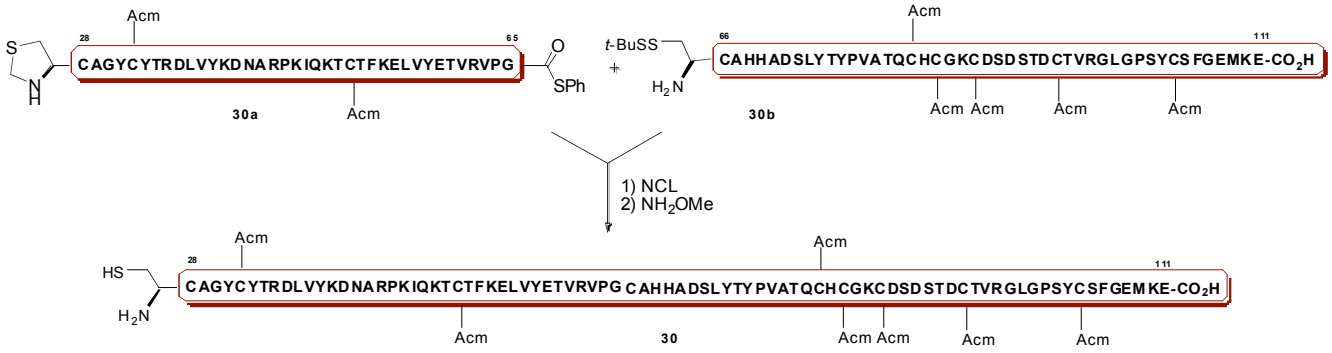
[4] Coctail B was prepared by dissolving 60 mg of phenol in 3.0 mL of trifluoroacetic acid, 0.15 mL of triisopropylsilane and 0.2 mL of water.



Glycoprotein 28: Deprotected 20-27aa peptide **27** from above (0.4 mg, 0.4 μmol) was combined with *N*-linked twelvemer carbohydrate (0.6 mg, 0.25 μmol, ca. 85% purity). To this mixture the solution of Hunning's base in DMSO (10μL of 27μL DIEA/mL of DMSO) followed by the solution of HATU (20 μL of 58mg HATU/mL of DMSO) was added. The resultant mixture was stirred for 2h before being diluted with 1mL of 1:1 acetonitrile/H_2O mixture and analyzed by LC/MS. The conversion of this reaction was determined to be *ca.* 35% from dodecasaccharide based on the integration of the UV trace. This sample was purified by HPLC to provide *ca.* 0.2 mg of pure product **28**: Rf = 13.7 (Microsorb C18 column, 25-75% MeCN in H_2O, 30 min). Exact mass calcd for $C_{134}H_{210}N_{16}O_{75}S_2$ $[M+2H]^{2+}$: 1655.2; $[M+3H]^{3+}$: 1103.8. Found: 1655.6, 1103.9.







Synthesis of Peptide 30.

The synthesis of 28-111aa subunit **30** was accomplished by Native Chemical Ligation of subunits **30a** and **30b** followed by deprotection of the terminal 28aa cysteine with methoxy hydroxylamine.

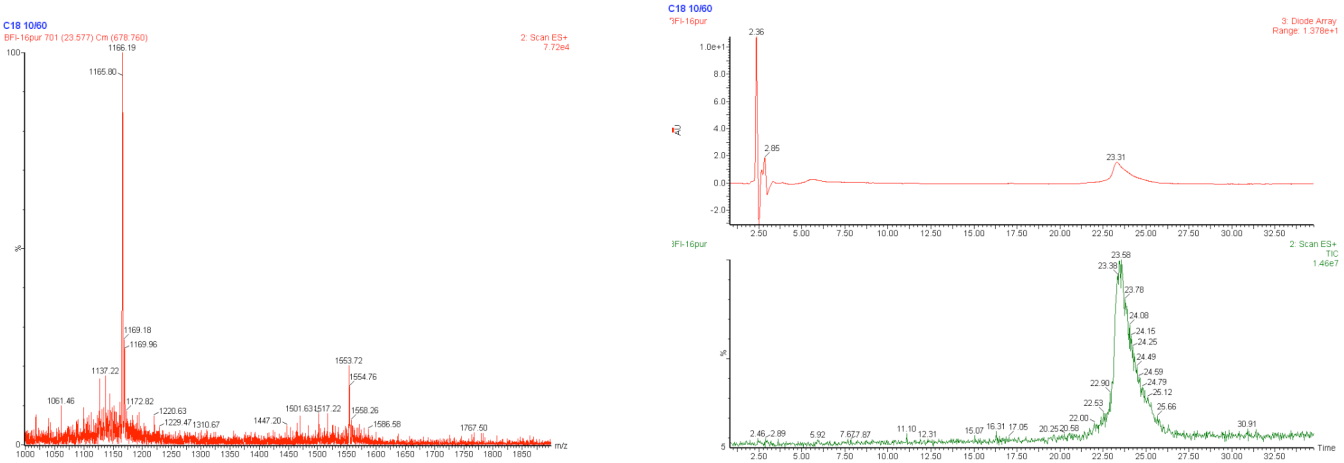
Synthesis of 28-65aa Subunit 30a. 0.56 g (ca. 0.10 mmol) of Fmoc-Gly-Nova-TGT resin was subjected to continuous flow automated peptide synthesis. For coupling steps, resin was treated with a 4-fold excess of HATU and Fmoc amino acids in 1M DIEA/DMF, and for deblocking, a solution of 2% piperidine / 2% DBU in DMF was used. Fmoc-Tyr(tBu)-Thr(Me,Me, ψ–Pro)-OH, Fmoc-Glu(OtBu)-Thr(Me,Me, ψ–Pro)-OH and Fmoc-Lys(Boc)-Thr(Me,Me, ψ–Pro)-OH dipeptides were used to substitute for the corresponding amino acids at positions 33-34, 59-60, and 54-55. The resin was then transferred to a manual peptide synthesis vessel and treated with a cleavage solution of 3 mL of 1:1:8 trifluoroethanol/acetic acid/dichloromethane for 2 h. The beads were filtered, rinsed with

another 3 mL of cleavage solution, filtered again, and then treated for 2 h with 3 mL of the cleavage solution. This process was repeated for a total of 3 2-hour cleavage cycles, and the combined washes were concentrated *in vacuo* to afford 520 mg of peptide after cleavage (ca. 79% yield). Exact mass calcd for $C_{328}H_{500}N_{54}O_{75}S_6$ $[M+2Na]^{2+}$: 3318.8; $[M+2Na+H]^{3+}$: 2212.5. Found: 3319.18, 2213.5.

The product from above (190 mg, 28.8 µmol) was combined with mercaptophenol (88 µL, 0.86 mmol), PyBOP (150 mg, 0.29 mmol), and DIEA (49 µL, 0.29 mmol) in dichloromethane (3mL) and THF (3 mL). The reaction mixture was stirred for 3 h before being concentrated and used without further purification in the next reaction.

The prepared above thioester was dissolved in 6.5 mL of Cocktail B[4] and stirred for 4 h at rt before being concentrated, triturated with ether (2 x 15 mL), decanted and redissolved in 1:1 acetonitrile/water (15 mL). This solution was next purified by HPLC Rf = 23.3 min (Microsorb C18 column, 10-60% MeCN in H_2O, 30 min) to afford 89 mg (62 % over 2 steps) of pure product **30a**. Exact mass calcd for $C_{211}H_{326}N_{54}O_{57}S_4$ $[M+4H]^{4+}$: 1165.6; $[M+3H]^{3+}$: 1553.8. Found: 1166.2, 1553.7.

The LC/MS data for this fragment are included below:

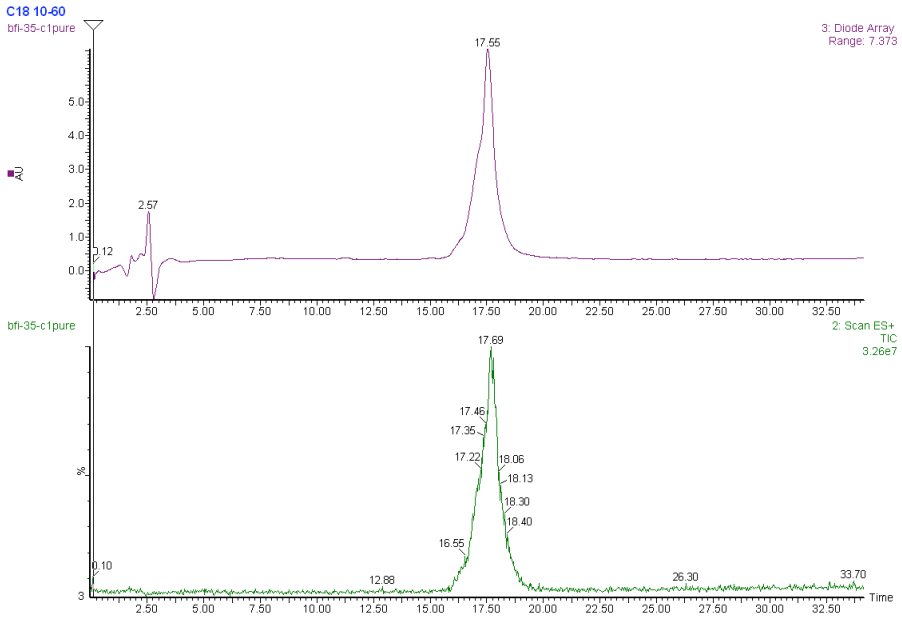


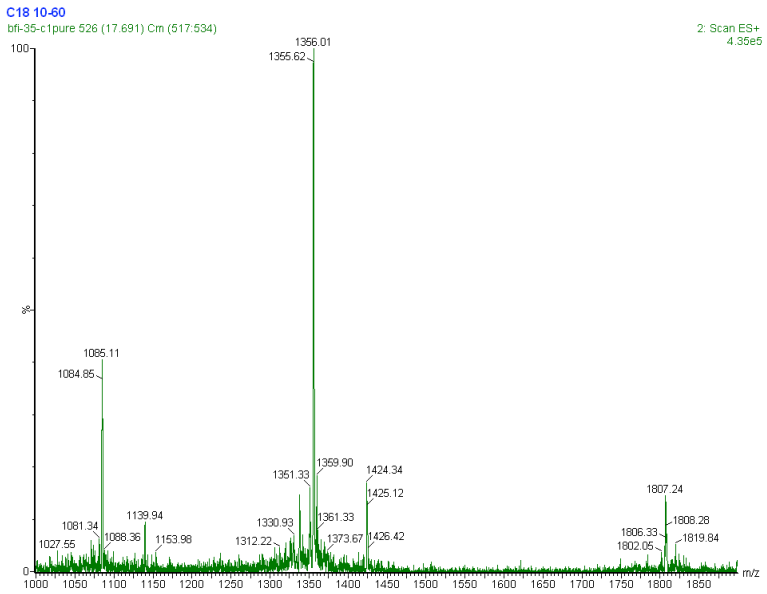
0.435 g (ca. 0.10 mmol) of Fmoc-Glu(OtBu)-Nova-TGT resin was subjected to continuous flow automated peptide synthesis. For coupling steps, resin was treated with a 4-fold excess of HATU and Fmoc amino acids in 1M DIEA/DMF, and for deblocking, a solution of 2% piperidine / 2% DBU in DMF was used. Fmoc-Asp(OtBu)-Ser(Me,Me, ψ–Pro)-OH dipeptide was used to substitute for the corresponding amino acids at positions 71-72 and 90-91. The resin was then transferred to a manual peptide synthesis vessel and treated with a cleavage solution of 2 mL of 1:1:8 trifluoroethanol/acetic

acid/dichloromethane for 2 h. The beads were filtered, rinsed with another 2 mL of cleavage solution, filtered again, and then treated for 2 h with 2 mL of the cleavage solution. This process was repeated for a total of 3 2-hour cleavage cycles, and the combined washes were concentrated *in vacuo* to afford 790 mg of peptide after cleavage (ca. 99% yield). The product was used as such in the next reaction step.

The prepared above 66-111aa fragment (790 mg) was dissolved in 12 mL of Cocktail B[4] and stirred for 4 h at rt before being concentrated, triturated with ether (2 x 15 mL), decanted and redissolved in 1:1 acetonitrile/water (15 mL). This solution was next purified by HPLC: Rf = 17.55 (Microsorb C18 column, 10-60% MeCN in H_2O, 30 min) to afford 166 mg (31 % over two steps) of pure product **30b**. Exact mass calcd for $C_{225}H_{343}N_{63}O_{77}S_8$ $[M+4H]^{4+}$: 1356.1; $[M+3H]^{3+}$: 1807.1. Found: 1356.01, 1807.24.

The LC/MS trace for this compound is included below:

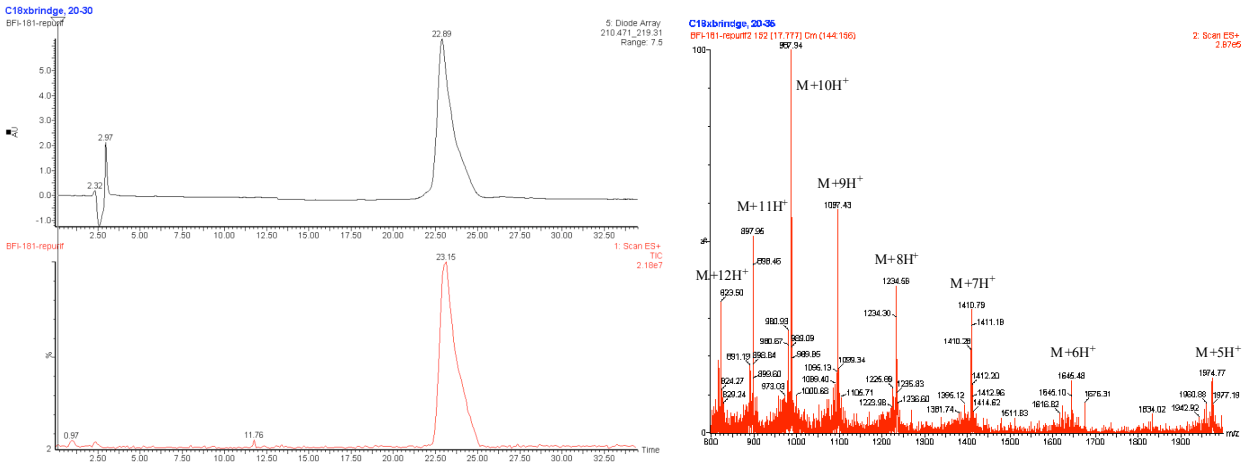


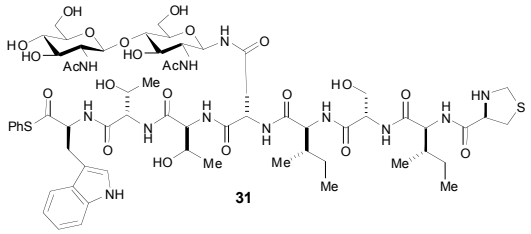


Guanidinium hydrochloride (5.73 g), $Na_2HPO_4{\cdot}7H_2O$ (0.28 g), TCEP·HCl (20 mg) and thiophenol (200 mL) were dissolved in 10 mL of distilled water, and the pH was adjusted to 6.8 by addition of Na_3PO_4. Thus obtained solution (7 mL) was added to the mixture of 28-65aa thioester **30a** (30.1 mg, 6.47 µmol), and 66-111aa fragment **30b** (36.8 mg, 6.79 µmol), and the reaction mixture was stirred at 38 °C for 12 h while monitored by LC/MS: Rf (product) = 19.13 min (C18 Microsorb column, 10-60% MeCN in H_2O, 30 min); Exact mass calcd for $C_{426}H_{655}N_{117}O_{134}S_{10}$ $[M+7H]^{7+}$: 1412.22, $[M+8H]^{8+}$: 1235.82, $[M+9H]^{9+}$: 1098.62 . Found: 1412.52, 1236.09, 1098.88.

Once completed, the reaction mixture from above was diluted with 0.6 M solution of *O*-methyl hydroxylamine hydrochloride (4 mL), and the pH of the resultant solution was adjusted to 4.5 by addition of HCl 1N. The reaction mixture was stirred for 7 h, and then purified by HPLC: Rf = 19.86 (Microsorb C18 column, 10-60% MeCN in H_2O, 30 min) to afford 30.3 mg (47 %) of pure product **30**. Exact mass calcd for $[M+5H]^{5+}$: 1974.32, $[M+6H]^{6+}$: 1645.43, $[M+7H]^{7+}$: 1410.50, $[M+8H]^{8+}$: 1234.31, $[M+9H]^{9+}$: 1097.29, $[M+10H]^{10+}$: 987.66, $[M+11H]^{11+}$: 898.0, $[M+12H]^{12+}$: 823.2. Found: 1974.8, 1645.5, 1410.8, 1234.6, 1097.4, 987.9, 898.0, 823.5.

The LC/MS data for this compound are included below:





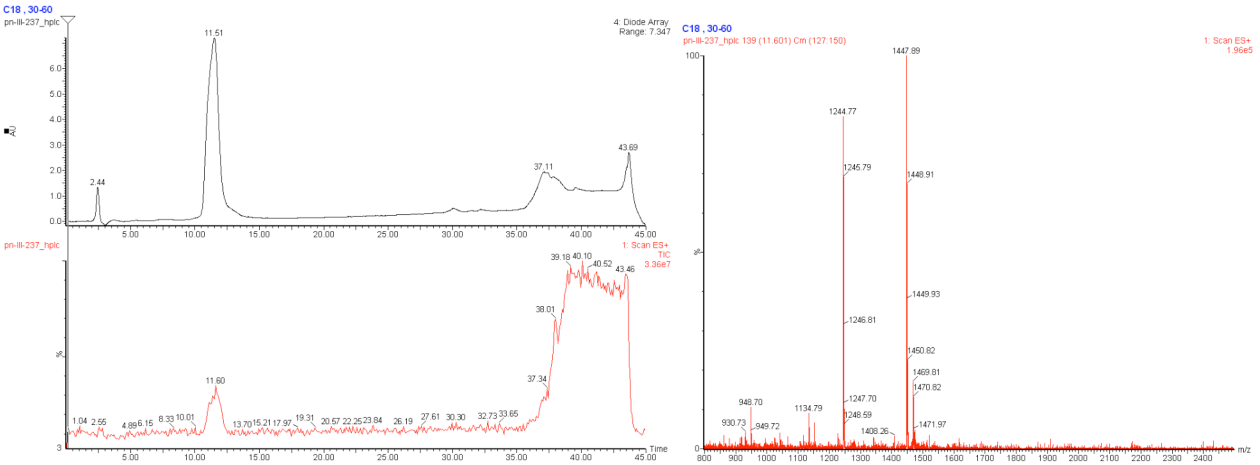
Peptide **26** (50 mg, 0.0466 mmol) was combined with (S)-3-(1H-indol-2-yl)-1-oxo-1-(phenylthio)propan-2-aminium chloride (31 mg, 0.0932 mmol), HOOBt (15.0 mg, 0.0932 mmol), and dissolved in 1:3 TFE/$CHCl_3$ (2.3 mL). To this solution, EDC (18 μL, 0.0932 mmol) was added and the resultant yellow solution was stirred for 2.5h, and being concentrated. Exact mass calcd for $C_{68}H_{103}N_9O_{15}S_2$ $[M+H]^+$: 1350.8; $[M+TFA]^-$: 1462.7. Found: 1359.9, 1463.0.

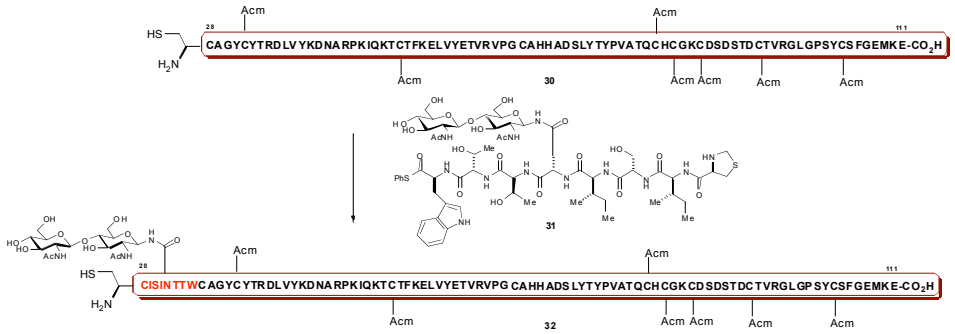
The concentrated reaction mixture from above was combined with phenol (60 mg), and treated with Cocktail B[4] (2 mL) for 2h at 0 °C, then diluted with dichloromethane, and concentrated. The residue was triturated with ether (2 x 15 mL), decanted, and dissolved in 2 mL of DMSO and 10 mL of 1:1 acetonitrile/water, and purified by HPLC: Rf = 16.2 (Microsorb C18 column, 30-60% MeCN in H_2O, 30 min) to afford ca. 7.5 mg of pure product (15% yield from the resin). Exact mass calcd for $C_{48}H_{67}N_9O_{13}S_2$ $[M+H]^+$: 1042.5; $[M-H]^-$: 1040.4. Found: 1042.6, 1040.7.

Deprotected 20-27aa peptide from above (5.0 mg, 4.8 μmol) was combined with chitobiose anomeric amine (4.1 mg, 9.6 μmol). To this mixture the solution of Hunning's base in DMSO (100 μL of 13 μL DIEA/mL of DMSO) followed by the solution of HATU (200 μL of 18.2 mg HATU/mL of DMSO) was added. The resultant mixture was stirred for 1h before being diluted with 1 mL of DMSO and 4 mL of 1:1 acetonitrile/H_2O mixture and purified by HPLC to provide pure product (3.6 mg, 52% yield): Rf = 11.5 (Microsorb C18 column, 30-60% MeCN in H_2O, 30 min). Exact mass calcd for

$C_{64}H_{94}N_{12}O_{22}S_2$ $[M+H]^+$: 1447.7; $[M+H]^+$: 1469.6. Found: 1447.9, 1469.9.

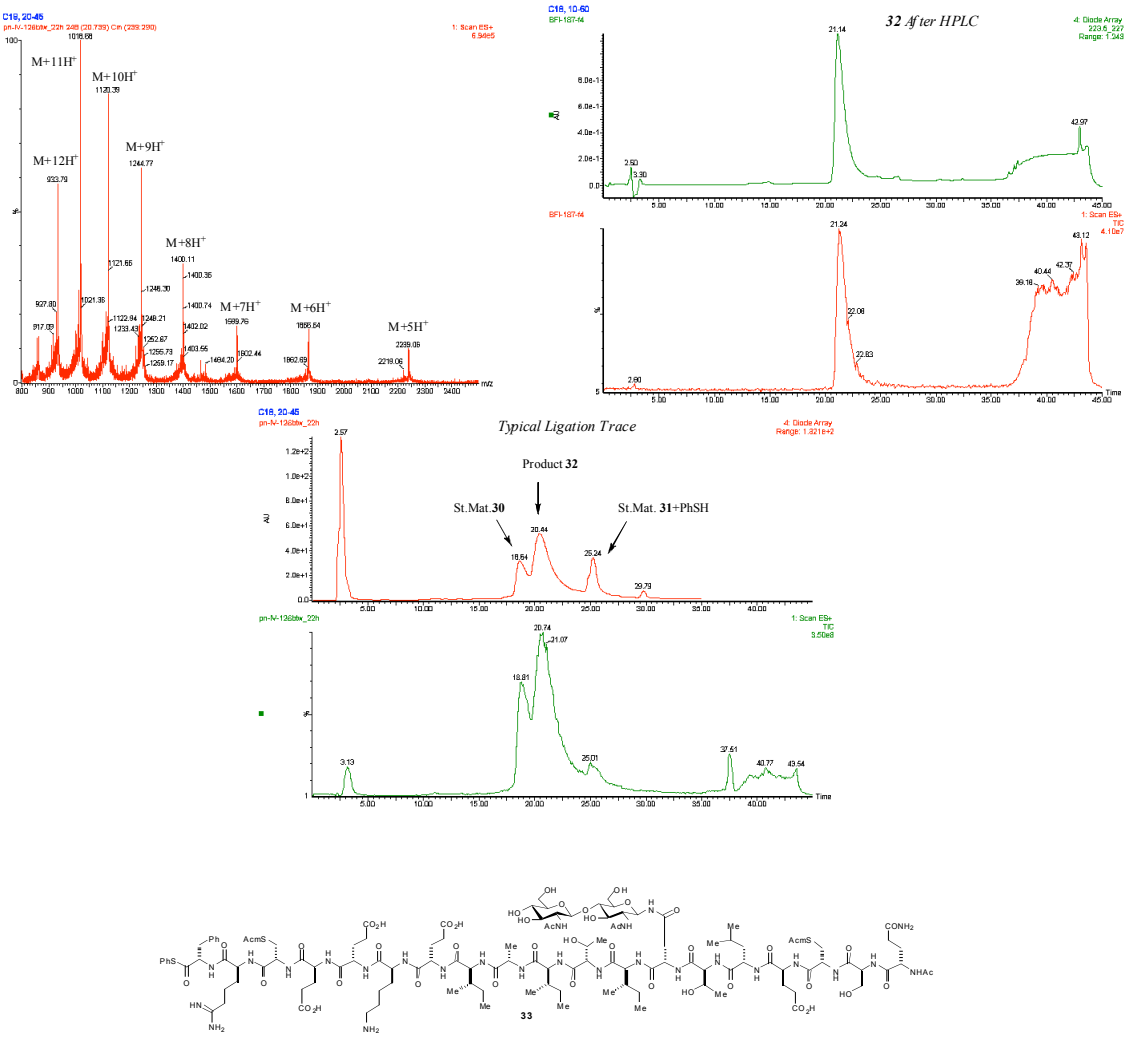
LC/MS trace is included below:





Guanidinium hydrochloride (5.73 g), Na_2HPO_4·(0.54 g), TCEP·HCl (54 mg), and mercaptophenol (0.35 mL) were dissolved in 10 mL of distilled water, and the pH was adjusted to 7.3 by addition of Na_3PO_4. Thus obtained solution was degassed by sonication under atmosphere of Ar and added (0.1 mL) to the mixture of 28-111aa thiol-fragment **30** (10.0 mg, 1.01 μmol), and 20-27aa fragment **31** (1.8 mg, 1.24 μmol) at rt. After 28h the solution was sampled and the conversion was determined to be ca. 75% by LC/MS: Rf (product) = 21.2 min (C18 Microsorb column, 20-45% MeCN in H_2O, 30 min). To this, the solution of $MeONH_2$·HCl (0.6M, final pH = 4.8, 300 μL) in degassed water was added. The resultant mixture was stirred for 20h before being diluted with 2 mL of 1:1 MeCN/H_2O and purified by HPLC affording 3.0 mg (27% yield) of pure **32**: Rf (product) = 21.2 min (C18 Microsorb column, 20-45% MeCN in H_2O, 30 min, λ=275 nm); Exact mass calcd for $C_{482}H_{743}N_{129}O_{155}S_{11}$ $[M+5H]^{5+}$: 2239.23, $[M+6H]^{6+}$: 1866.2, $[M+7H]^{7+}$: 1599.7, $[M+8H]^{8+}$: 1399.9, $[M+9H]^{9+}$: 1244.5, $[M+10H]^{10+}$: 1120.1, $[M+11H]^{11+}$: 1018.4, $[M+12H]^{12+}$: 933.6. Found: 2239.1, 1866.6, 1599.8, 1400.1, 1244.8, 1120.4, 1018.7, 933.8.

The typical trace for this reaction is included below:

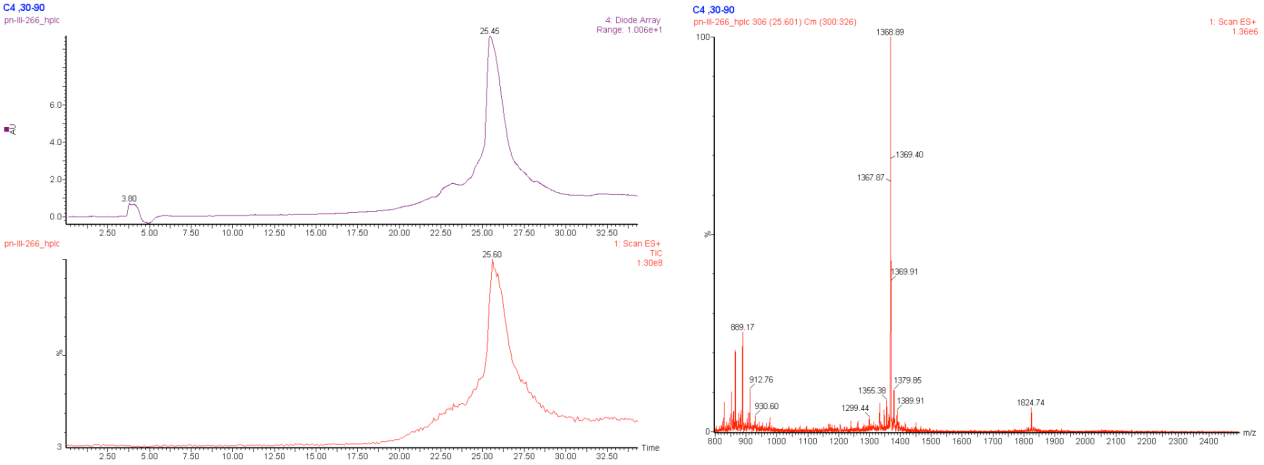


0.21 g (ca. 0.05 mmol) of Fmoc-Arg(Pbf)-Nova-TGT resin was subjected to continuous flow automated peptide synthesis. For coupling steps, resin was treated with a 4-fold excess of HATU and Fmoc amino acids in 1M DIEA/DMF, and for deblocking, a solution of 2% piperidine / 2% DBU in DMF was used. The amino acids used were, in order of synthesis: Fmoc-Cys(Acm)-OH, Fmoc-Glu(OAllyl)-OH, Fmoc-Glu(OAllyl)-OH, Fmoc-Lys(Alloc)-OH, Fmoc-Glu(OAllyl)-OH, Fmoc-Ileu-OH, Fmoc-Ala-OH, Fmoc-Ileu-OH, Fmoc-Ileu-Thr(Me,Me, ψ–Pro)-OH, Fmoc-Asp(OtBu)-OH, Fmoc-Thr(tBu)-OH, Fmoc-Leu-OH, Fmoc-Glu(OAllyl)-OH, Fmoc-Cys(Acm)-OH, Fmoc-Ser(tBu)-OH, Fmoc-Asn(Tr)-OH. The resin from above was transferred to a manual peptide synthesis vessel, washed with DMF (10 mL), and treated with 2:2:1 DMF/Pyridine/Ac_2O (10 mL) for 2h. The solvent was drained and the resin was washed with DMF and methanol, and treated with the cleavage solution (10 mL) consisting of 1:1:8 trifluoroethanol/acetic acid/dichloromethane for 1.5 h. The beads were filtered, rinsed with another 10 mL of cleavage solution, filtered again, and then treated for another 1 h with 10 mL of the cleavage solution. This process was repeated for a total of 3 2-hour cleavage cycles, and the combined was concentrated *in vacuo* to afford ca. 80 mg of peptide after cleavage.

The 1-19aa peptide from above (103 mg, 0.0322 mmol) was combined with (*S*)-1-(phenylthio)-1-oxo-3-phenylpropan-2-aminium chloride (14.2 mg, 0.0483 mmol), HOOBt (7.9 mg, 0.0483 mmol), and dissolved in 1:3 TFE/$CHCl_3$ (2.0 mL). To this solution, EDC (11 μL, 0.0483 mmol) was added and the resultant yellow solution was stirred for 2h before being concentrated under reduced pressure.

The residue from above was treated with Cocktail B[4] (3 mL) for 3.5h, then diluted with dichloromethane, and concentrated. The residue was triturated with ether (2 x 15 mL), decanted, and dissolved in 3 mL of DMSO and 10 mL of 8:2 acetonitrile/water, and purified by HPLC: Rf = 25.5 (Microsorb C4 column, 30-90% MeCN in H_2O, 30 min) to afford ca. 15.5 mg (21% yield, 2 steps) of pure product. Exact mass calcd for $C_{123}H_{188}N_{26}O_{38}S_3$ $[M+2H]^{2+}$: 1368.2. Found: 1368.9.

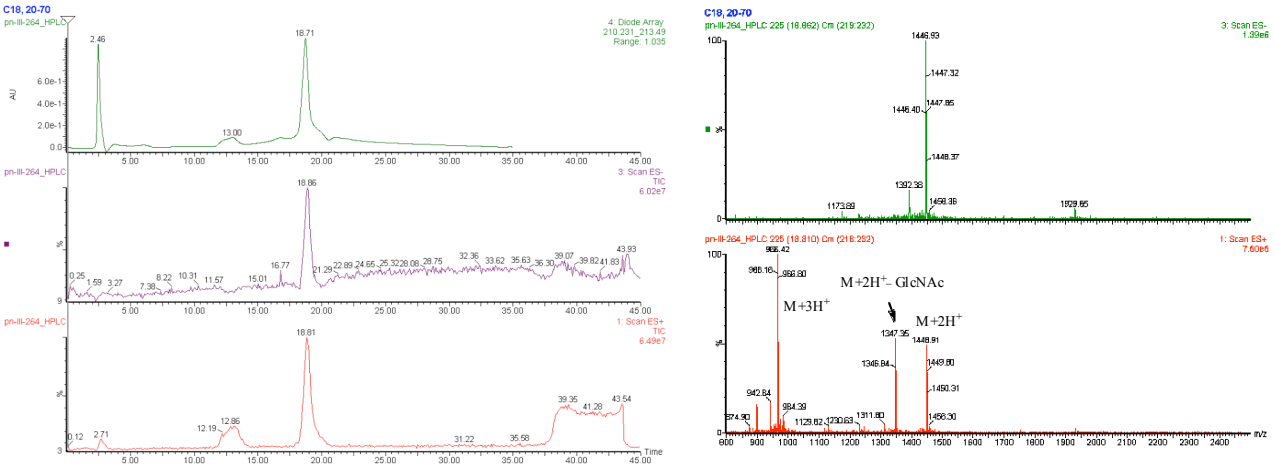
The LC/MS data are included below:

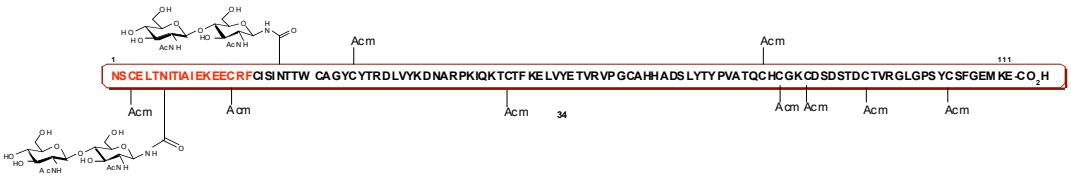


Deprotected 1-19aa peptide from above (3.5 mg, 1.3 μmol) was combined with chitobiose anomeric amine (4.3 mg, 10.2 μmol). To this mixture the solution of Hunning's base in DMSO (40 μL of 8.5 μL DIEA/mL of DMSO) followed by the solution of HATU (60 μL of 25 mg HATU/mL of DMSO) was added. The resultant mixture was stirred for 1h while monitored by LC/MS: Rf = 21.9 (Microsorb C18 column, 30-90% MeCN in H_2O, 30 min). Exact mass calcd for $C_{139}H_{215}N_{29}O_{47}S_3$ $[M+2H]^{2+}$: 1570.7. Found: 1571.0.

The solution of $Pd(PPh_3)_4$ and $PhSiH_3$ (300 μL, made by combining 5 mg of $Pd(PPh_3)_4$ and 10 μL of $PhSiH_3$ in 1 mL of DMF) was added to the reaction mixture, and the resultant dark solution was stirred while monitored by ultrahigh pressure chromatography/MS. After, 80 min, the reaction mixture was diluted with 1:1 MeCN/H_2O and MeOH and purified by HPLC to provide 1.9 mg of pure product (51% yield): Rf = 18.8 (Microsorb C18 column, 20-70% MeCN in H_2O, 30 min). Exact mass calcd for $C_{123}H_{195}N_{29}O_{45}S_3$ $[M+2H]^{2+}$: 1448.2; $[M+3H]^{3+}$: 965.8; $[M-2H]^{2-}$: 1446.7. Found: 1448.9, 966.4,

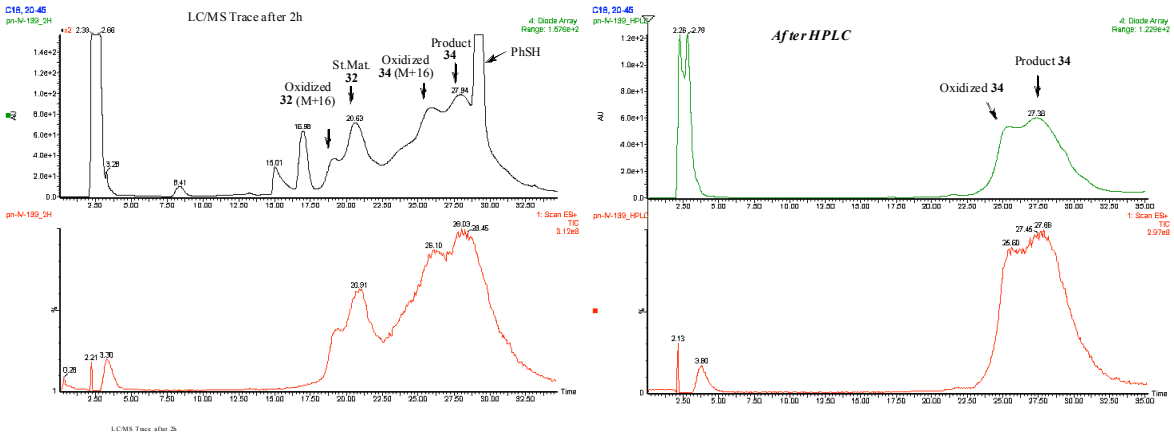
1446.9.

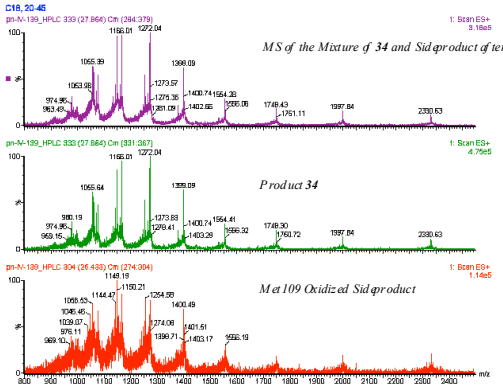


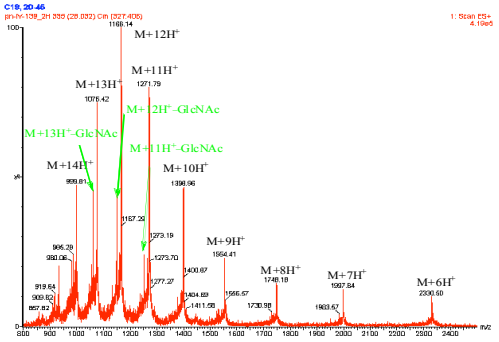


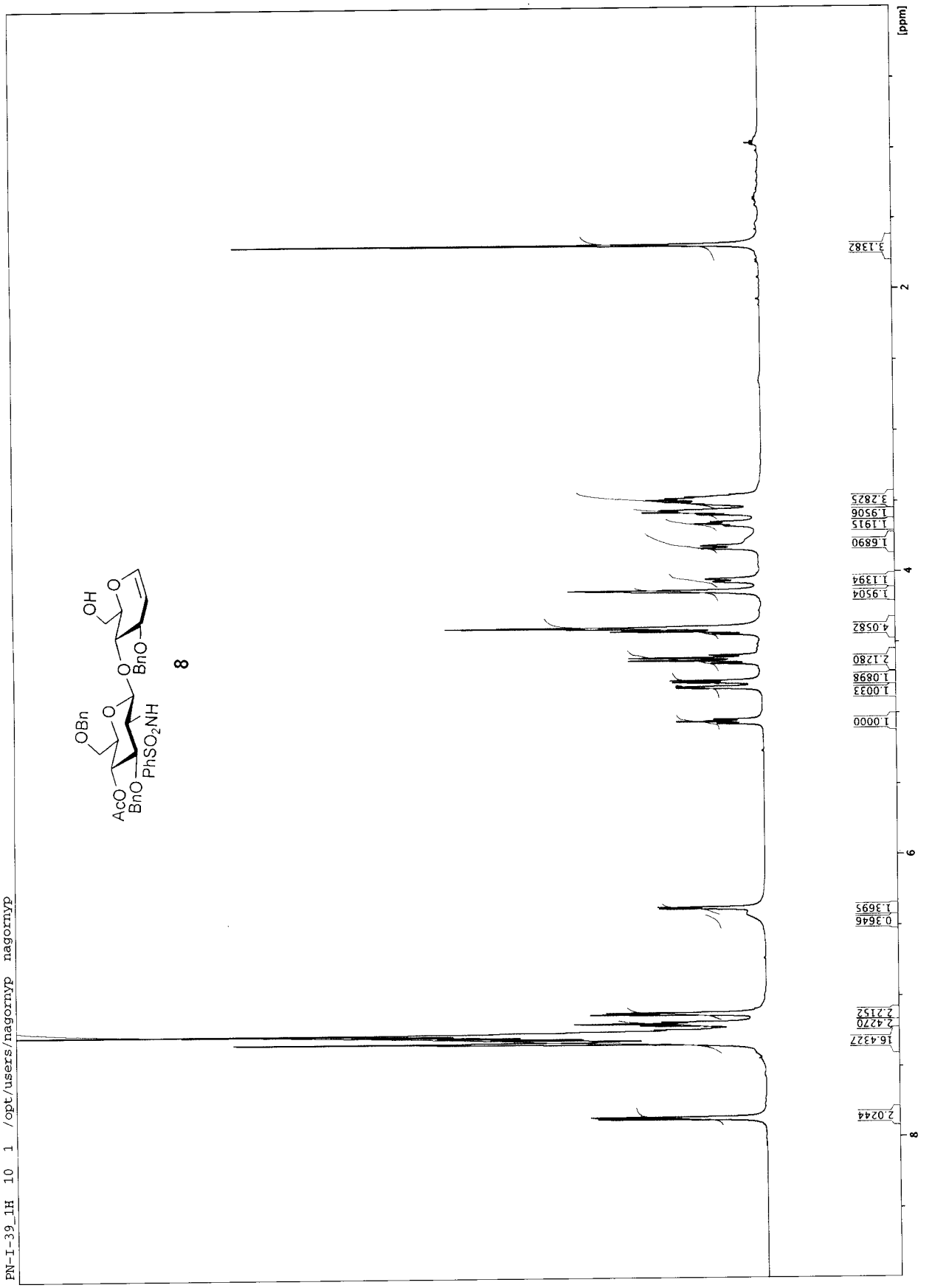
Guanidinium hydrochloride (5.73 g), Na_2HPO_4·(0.54 g), TCEP·HCl (54 mg), and mercaptophenol (0.35 mL) were dissolved in 10 mL of distilled water, and the pH was adjusted to 7.2 by addition of Na_3PO_4. Thus obtained solution was degassed by sonication under atmosphere of Ar and added (90 μL) to the mixture of 20-111aa thiol-fragment **32** (3.0 mg, 0.268 μmol), and 20-27aa fragment **34** (0.85 mg, 0.294 μmol) at rt. After 2 and 4h, 2x10 μL of the reaction mixture (20% of the crude mixture in total) was taken and injected to LC/MS for characterization purposes. After 2h, the conversion of the reaction was determined to be ca. 70-80%: Rf (product) = 28.0 min (C18 Microsorb column, 20-45% MeCN in H_2O, 30 min). Also, *ca.* 20-25% of M+16 sideproduct (Rf = 26.1) presumably arising from Met109 oxidation to a corresponding sulfoxide was also formed under the reaction conditions. The corresponding oxidation was also noted to take place for the residual starting material. The reaction mixture was stirred for the total of 4h before being diluted with 2 mL of the reaction buffer and purified by HPLC: Rf (product) = 26 min (C18 Microsorb column, 20-45% MeCN in H_2O, 30 min). The concentration of the appropriate fractions provided 2.4 mg of the pure product (contaminated with ca. 25% of the Met109 oxidized sideproduct) in 58-64% yield for the desired product; Exact mass calcd for $C_{599}H_{932}N_{158}O_{201}S_{13}$ $[M+6H]^{6+}$: 2330.2, $[M+7H]^{7+}$: 1997.5, $[M+8H]^{8+}$: 1747.9, $[M+9H]^{9+}$: 1553.8, $[M+10H]^{10+}$: 1398.6, $[M+11H]^{11+}$: 1271.5, $[M+12H]^{12+}$: 1165.6 $[M+13H]^{13+}$: 1076.0, $[M+14H]^{14+}$: 999.3. Found: 2330.5, 1997.8, 1748.2, 1554.4, 1399.0, 1271.8,

1166.1, 1076.4, 999.8.





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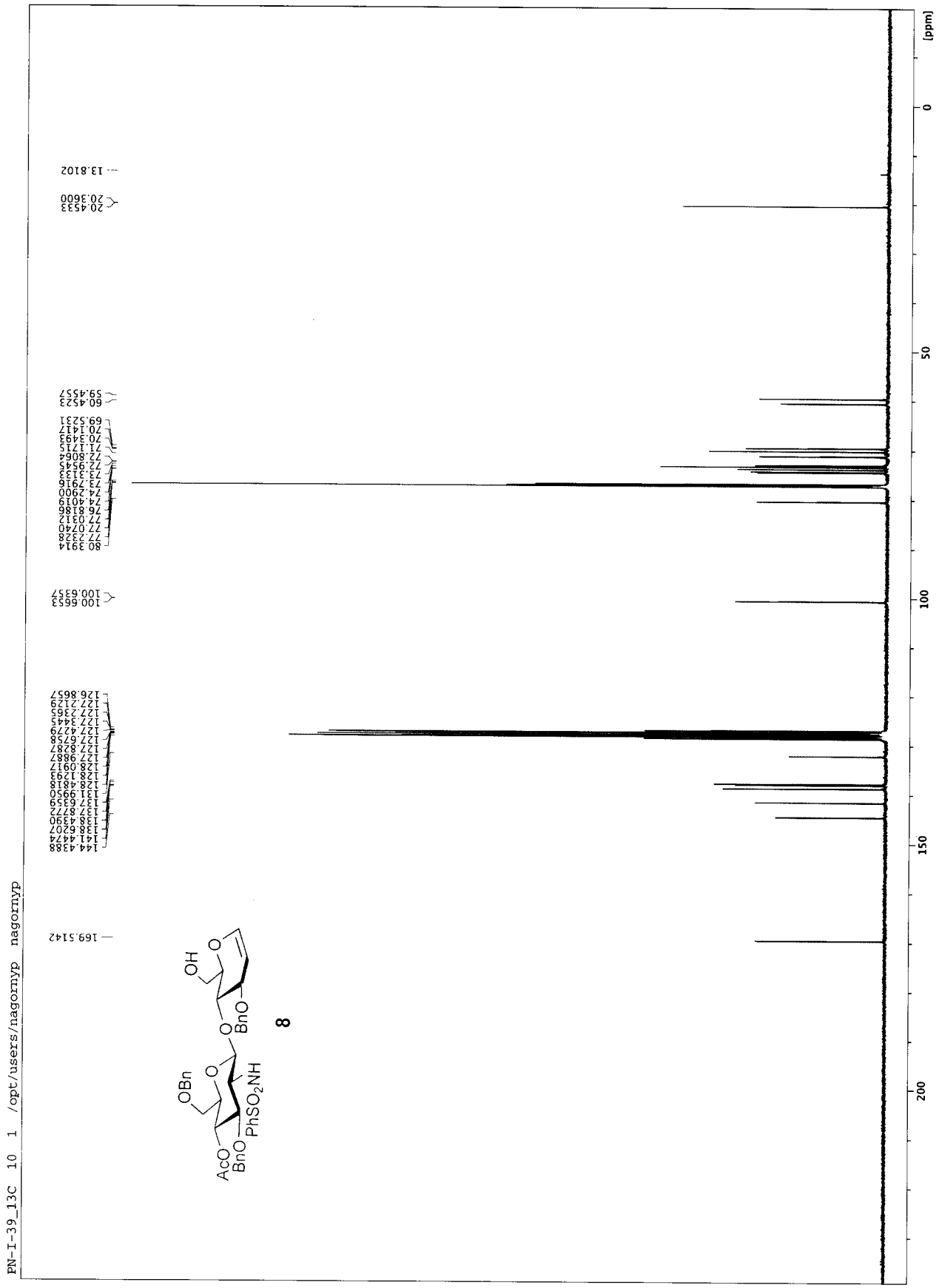
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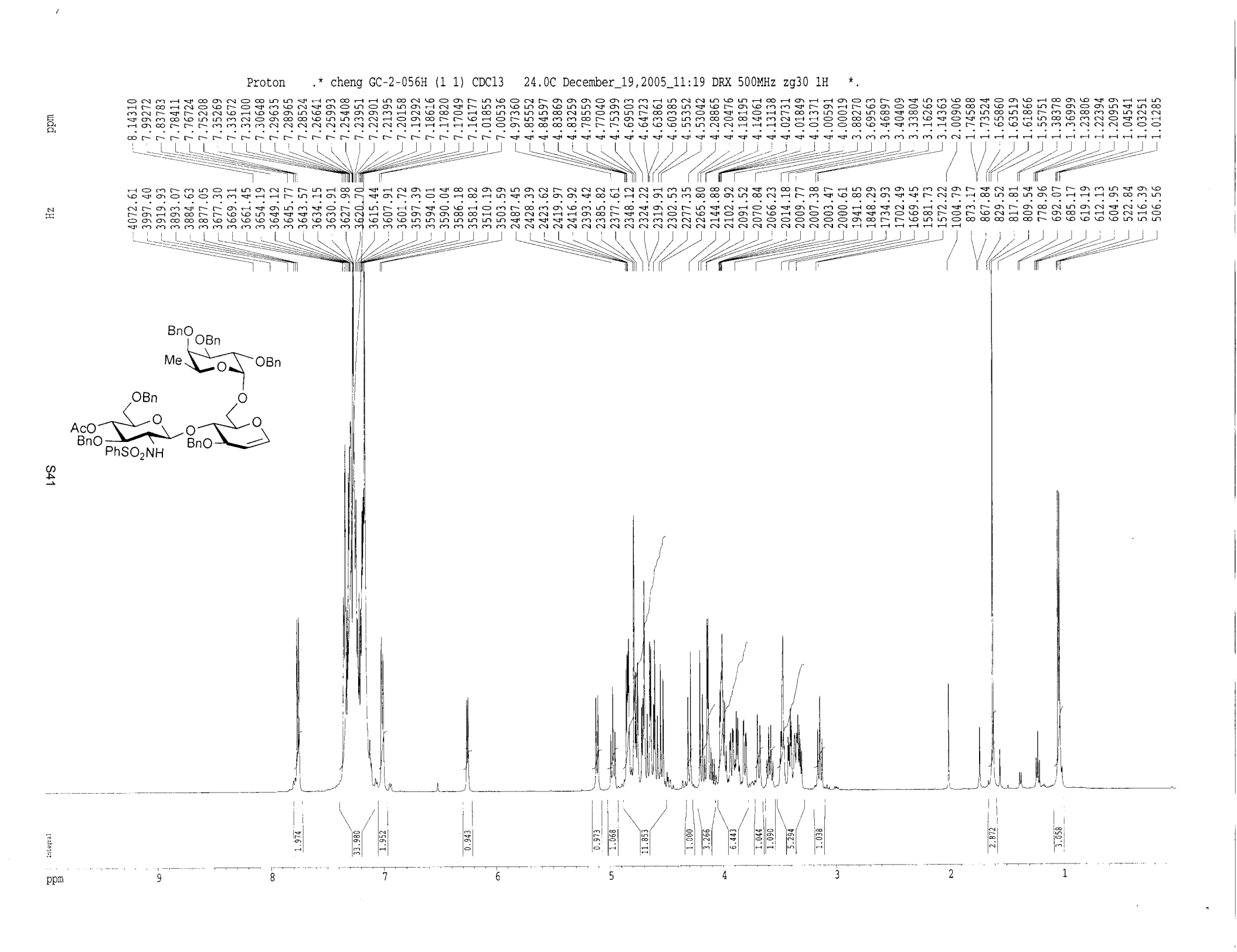
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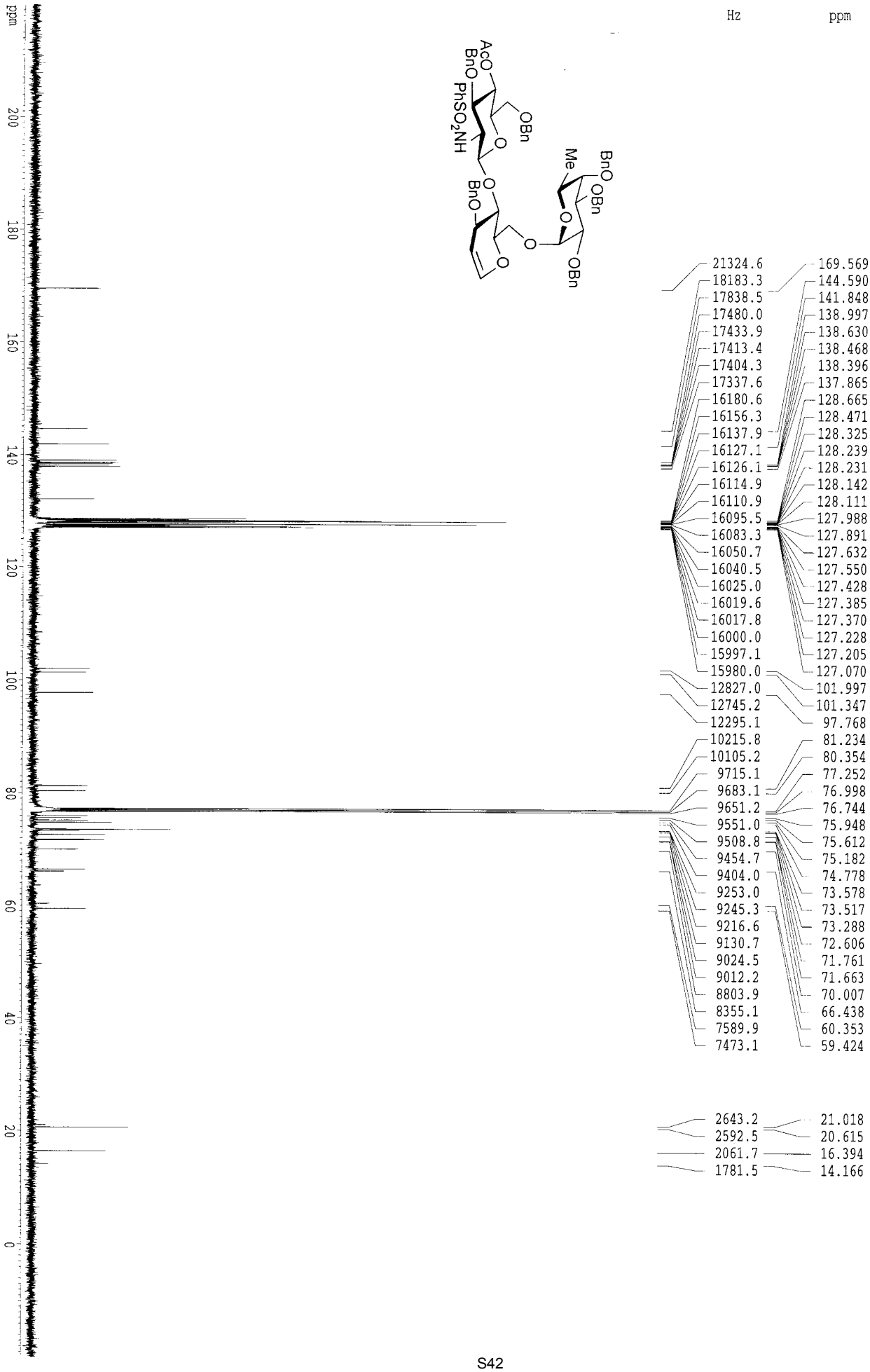

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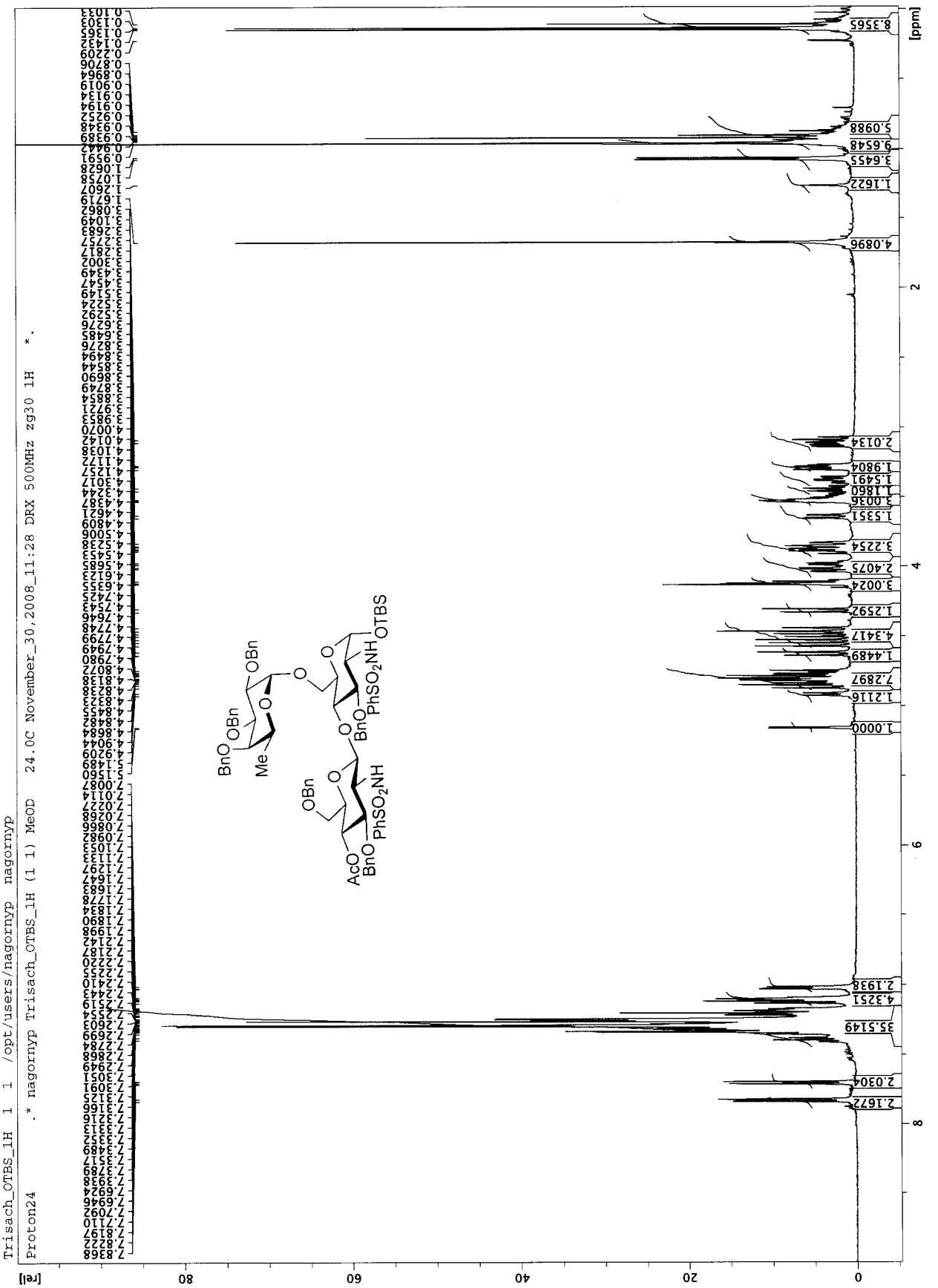
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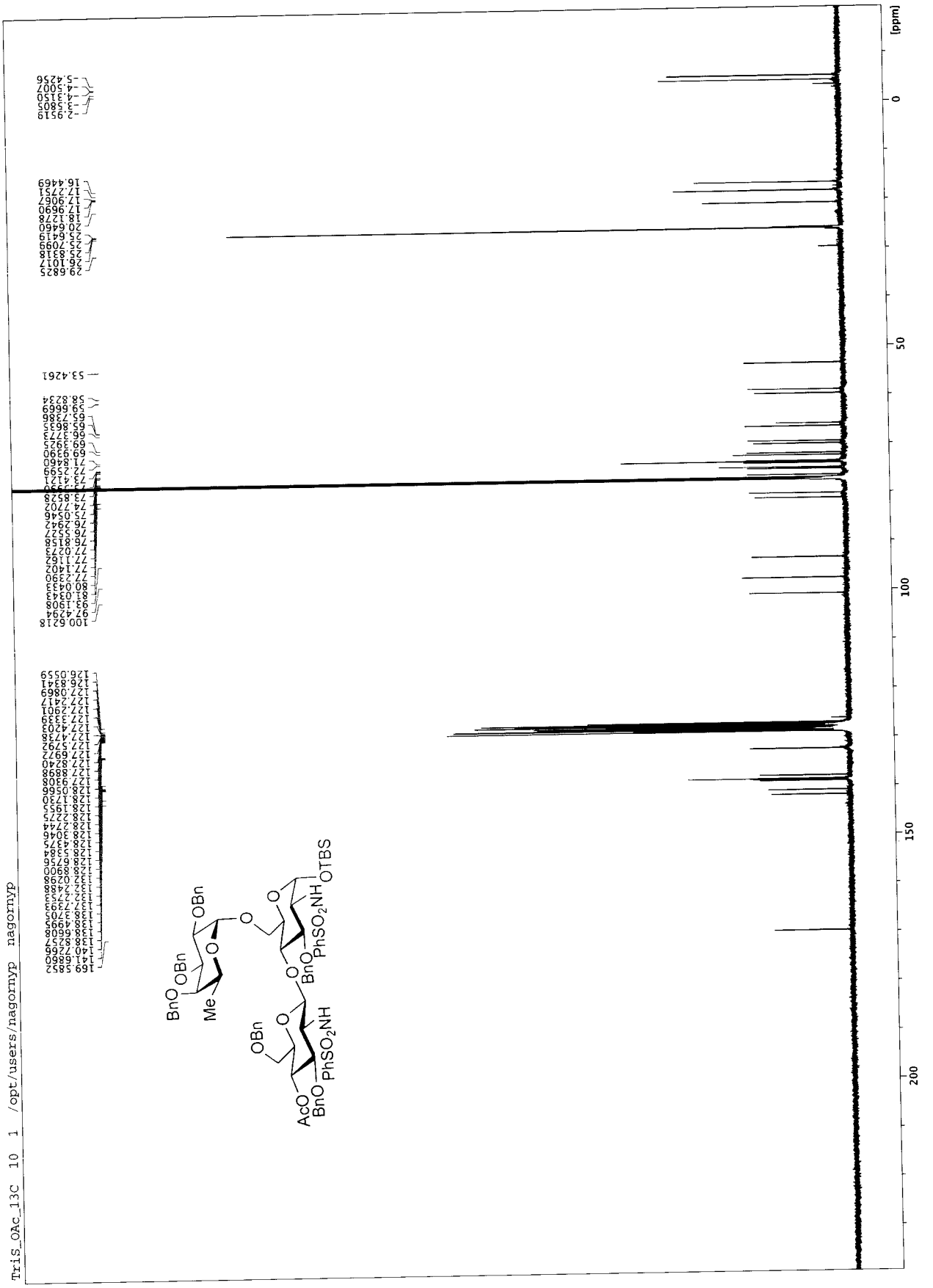
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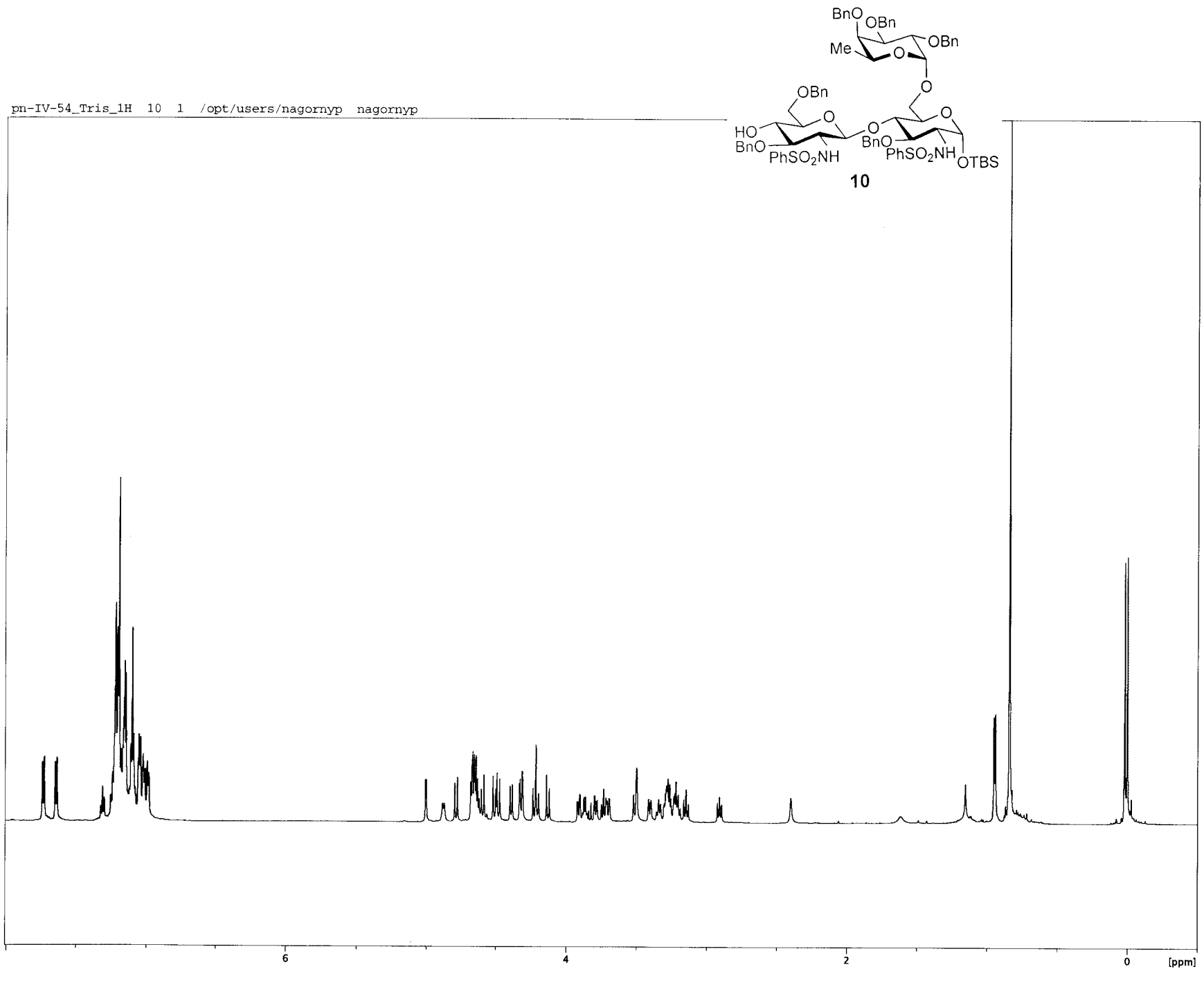
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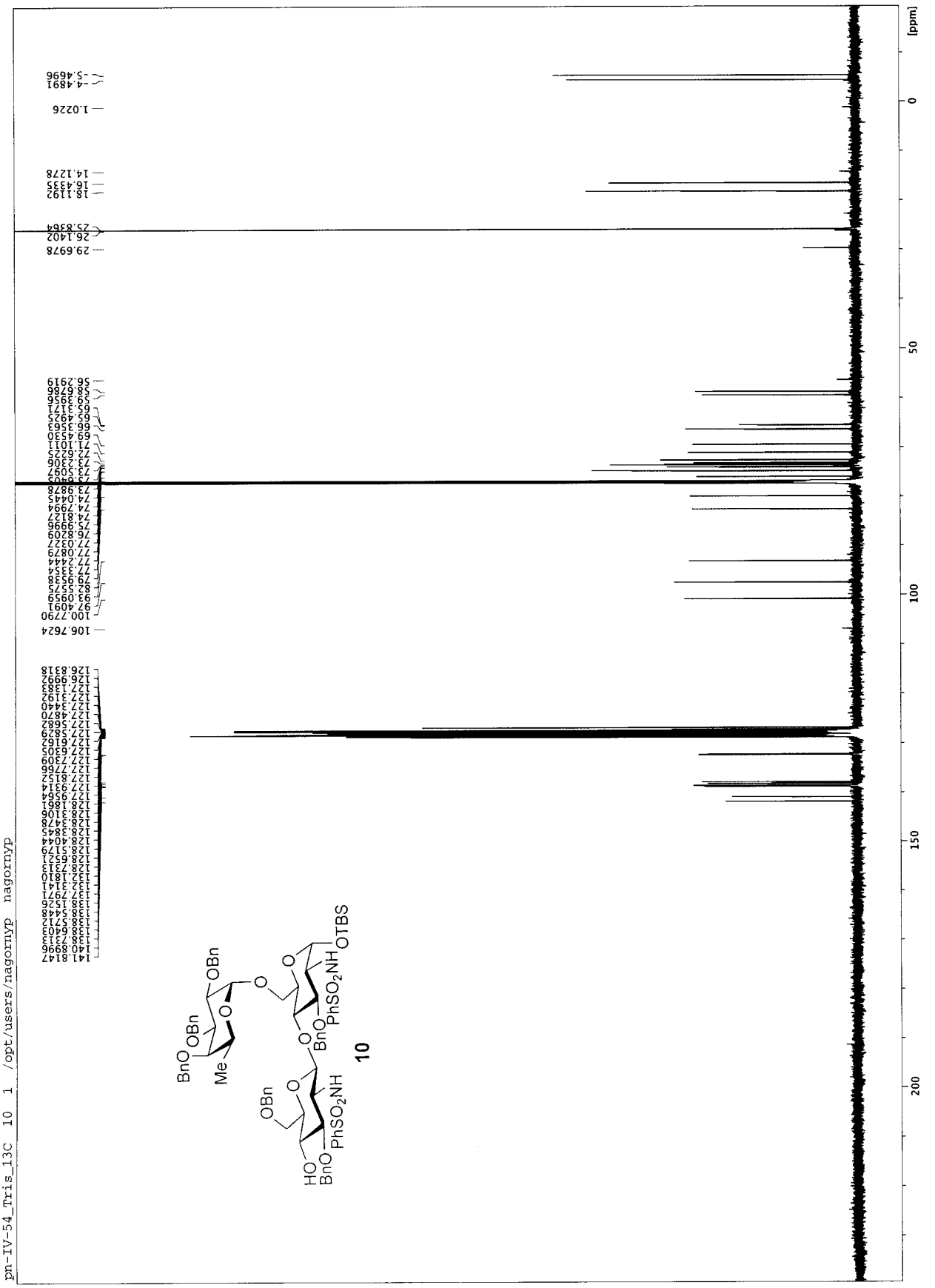
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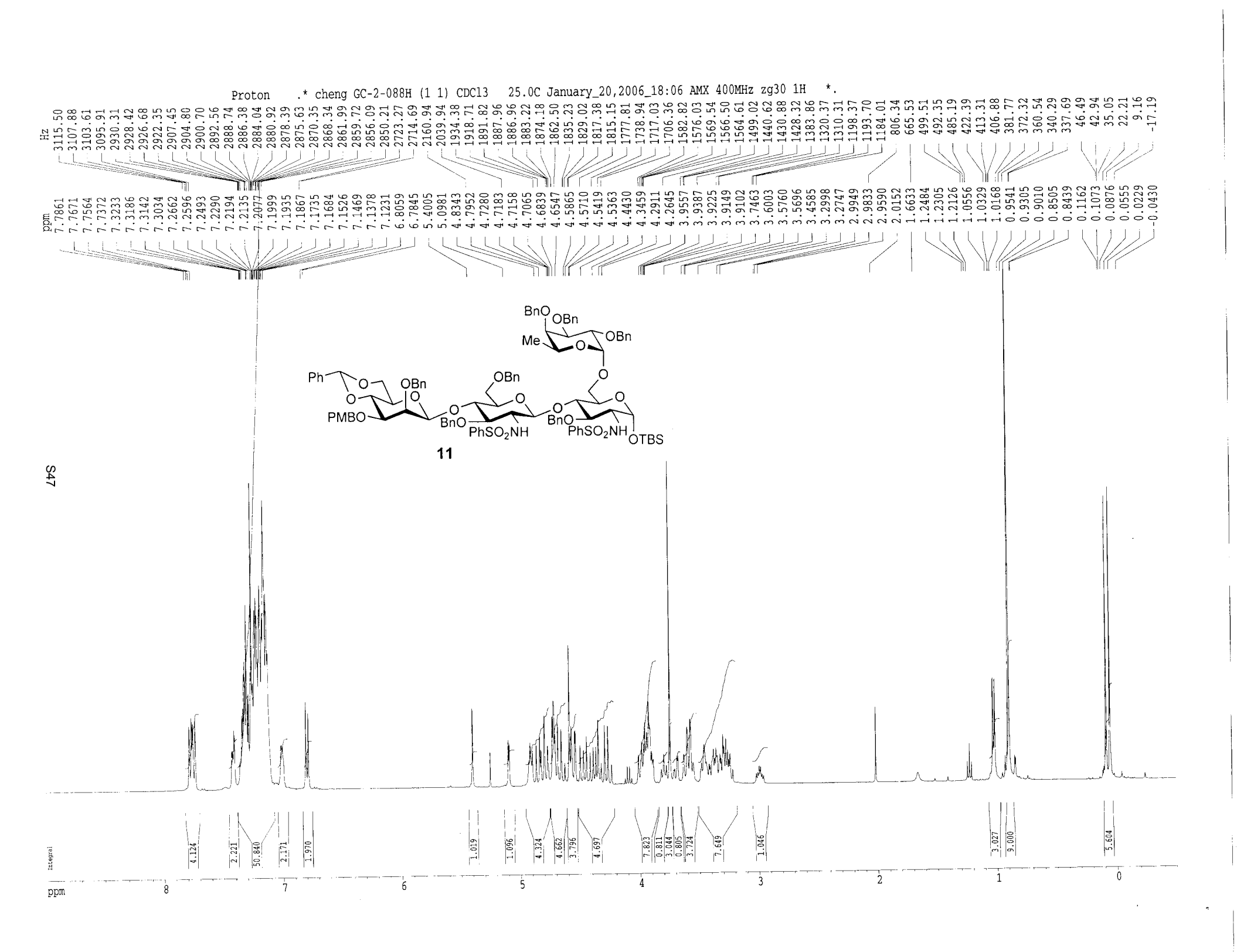
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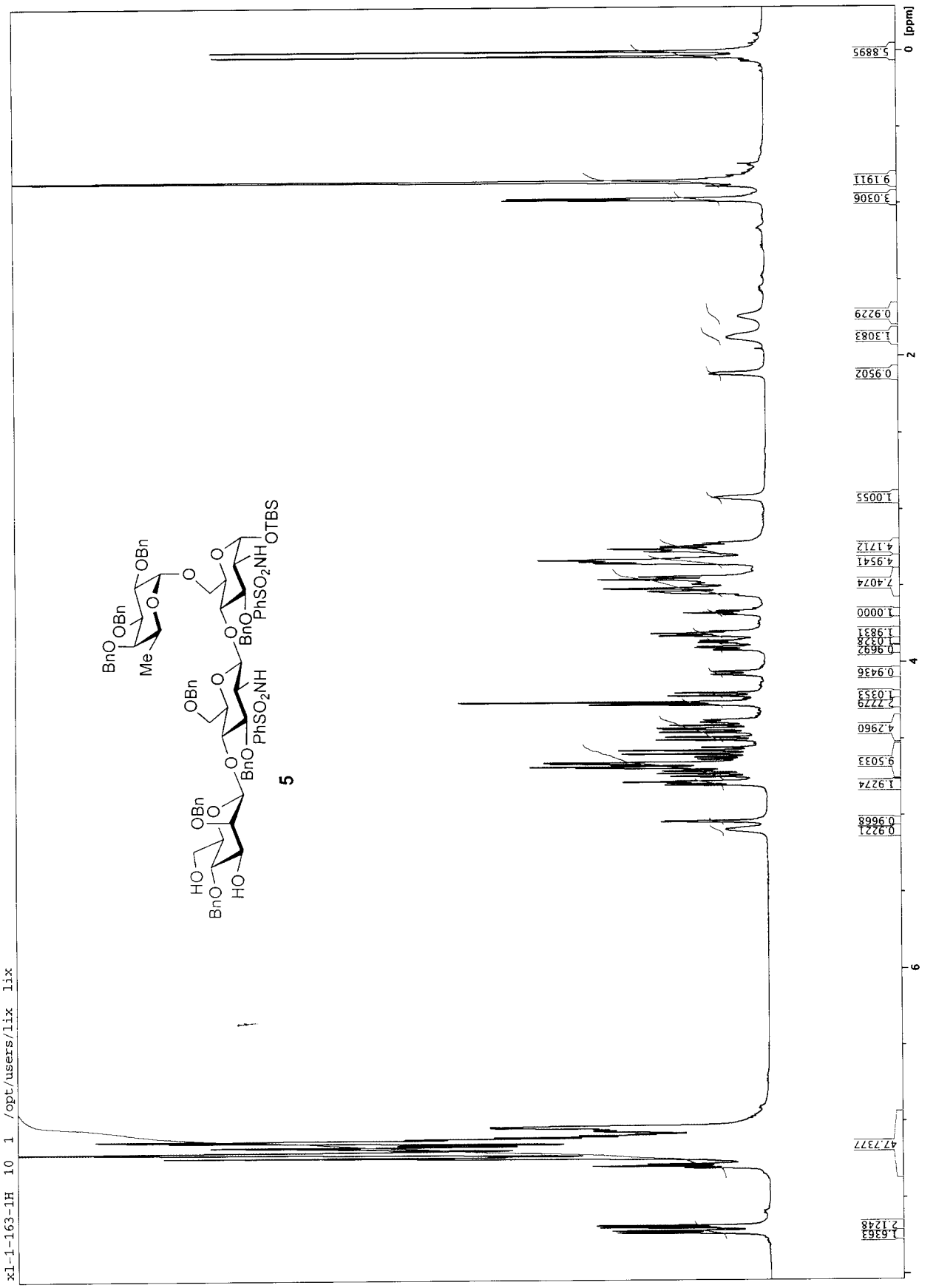
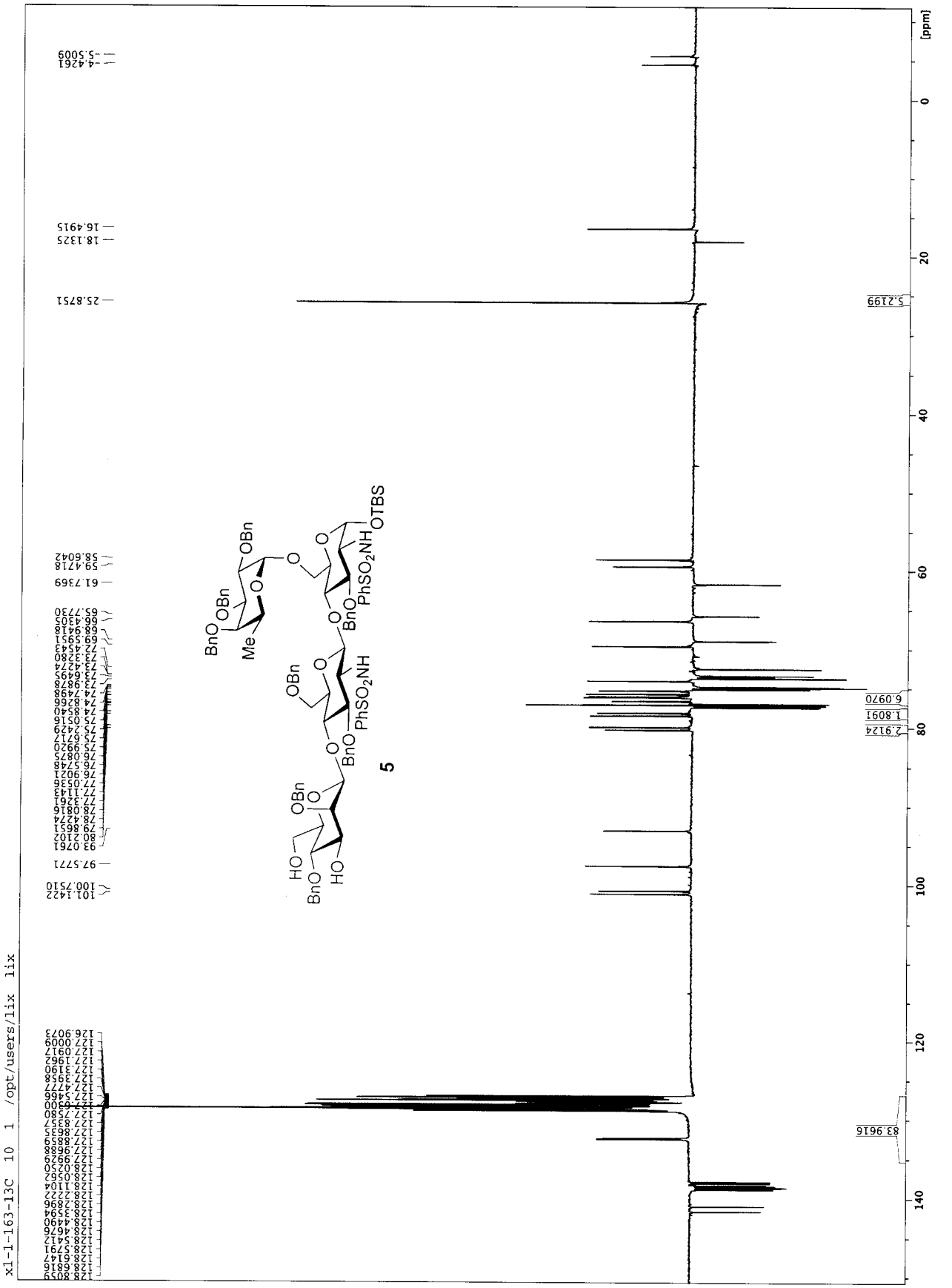
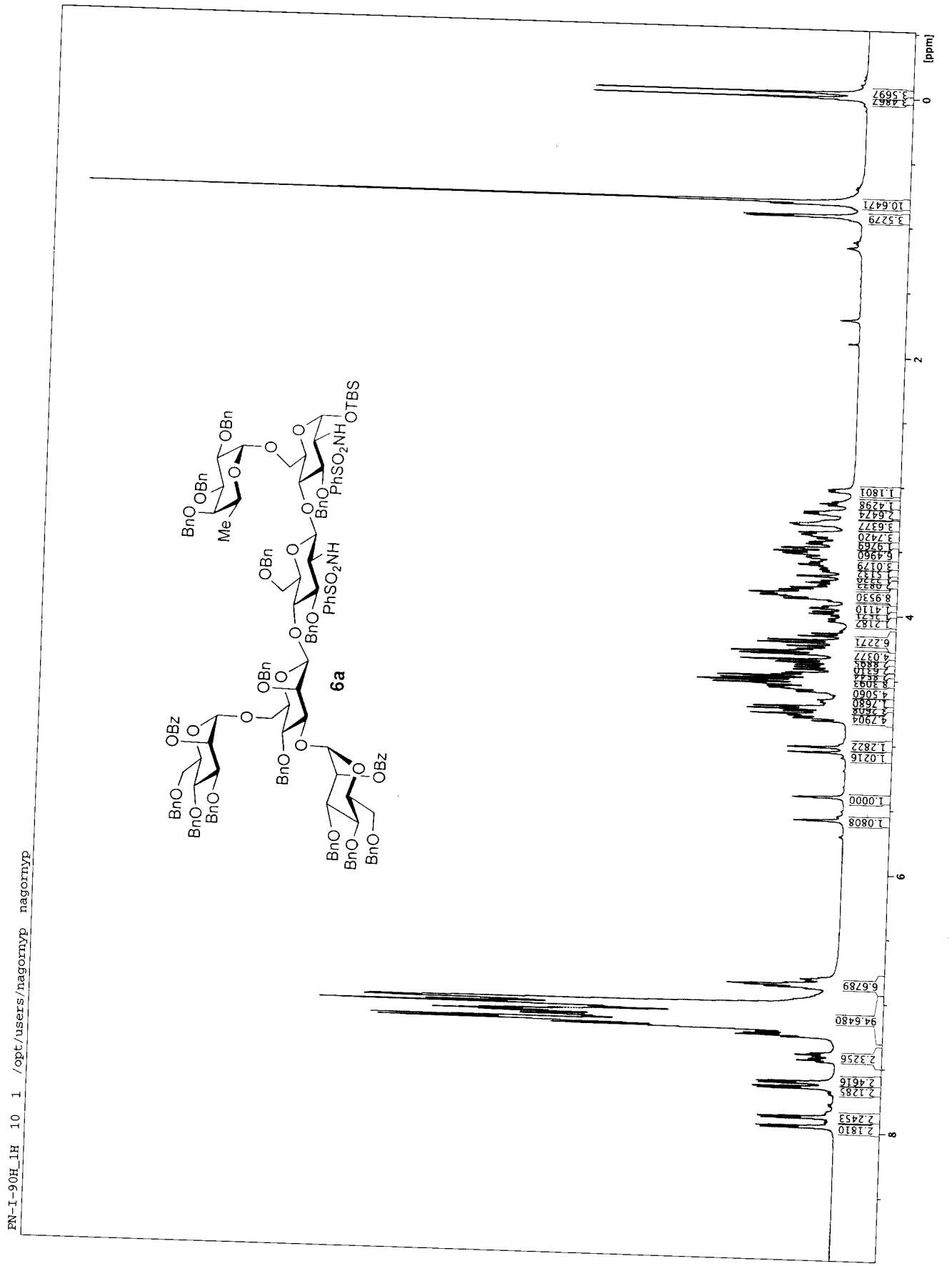
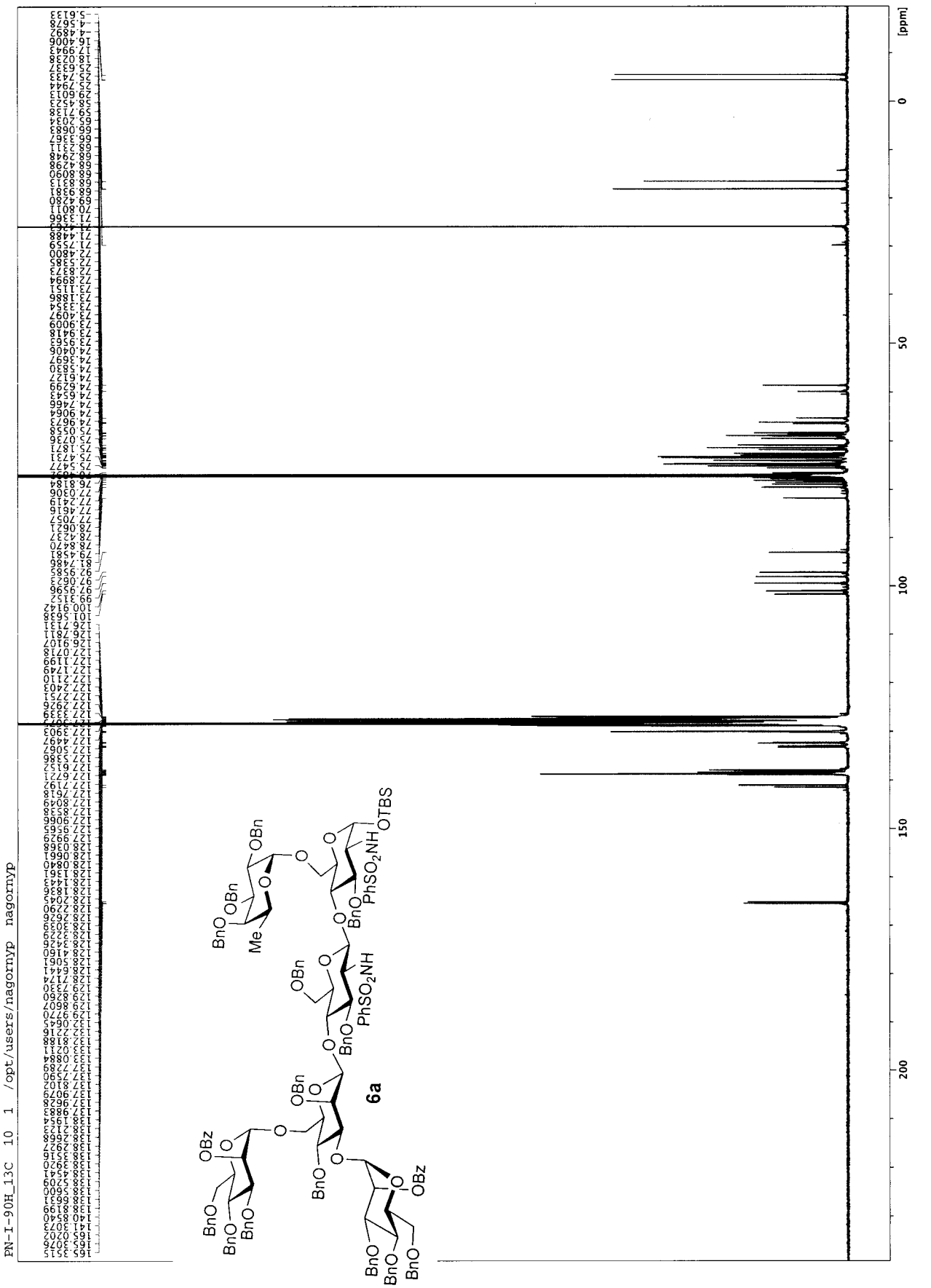
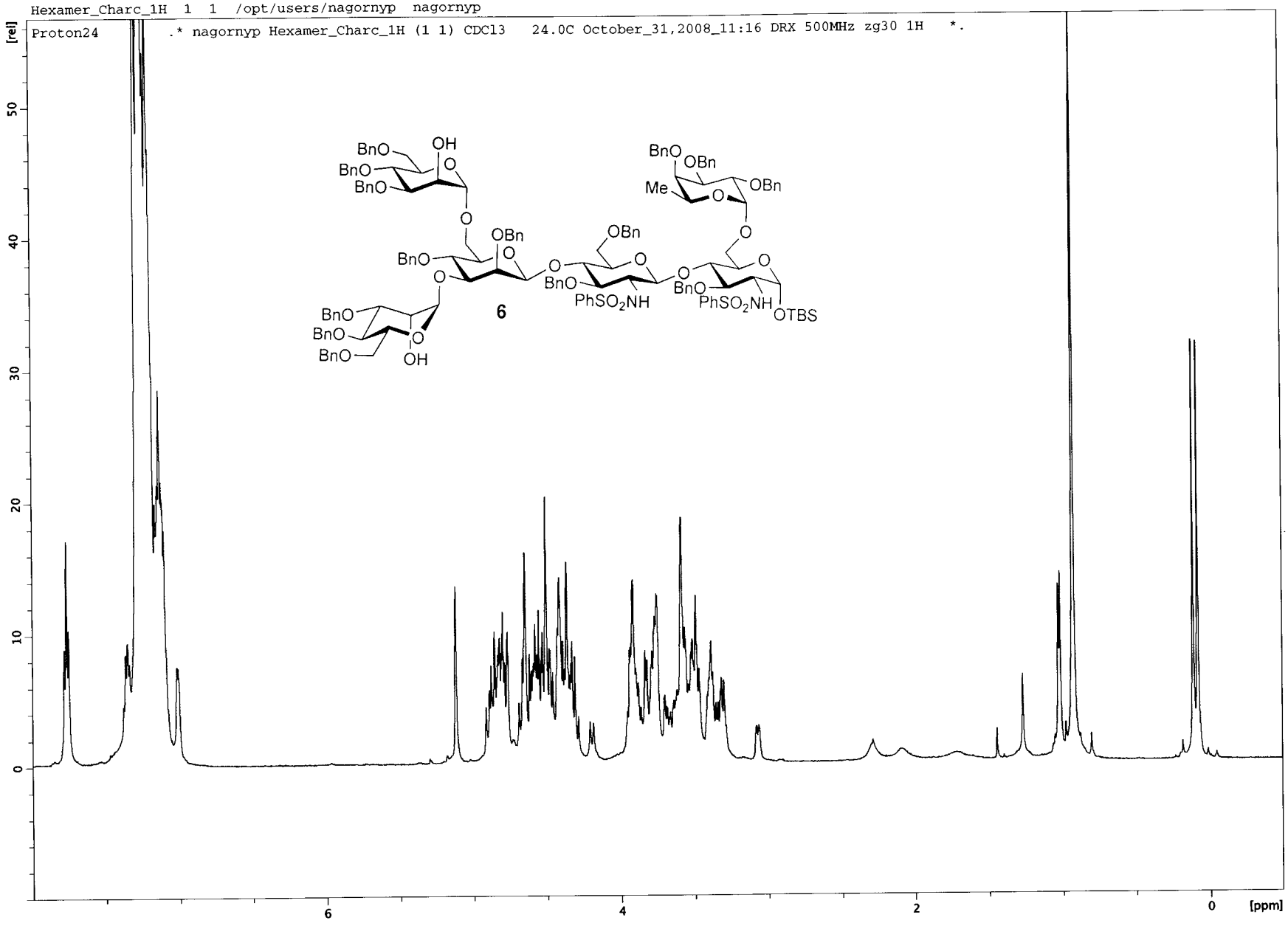
1
0

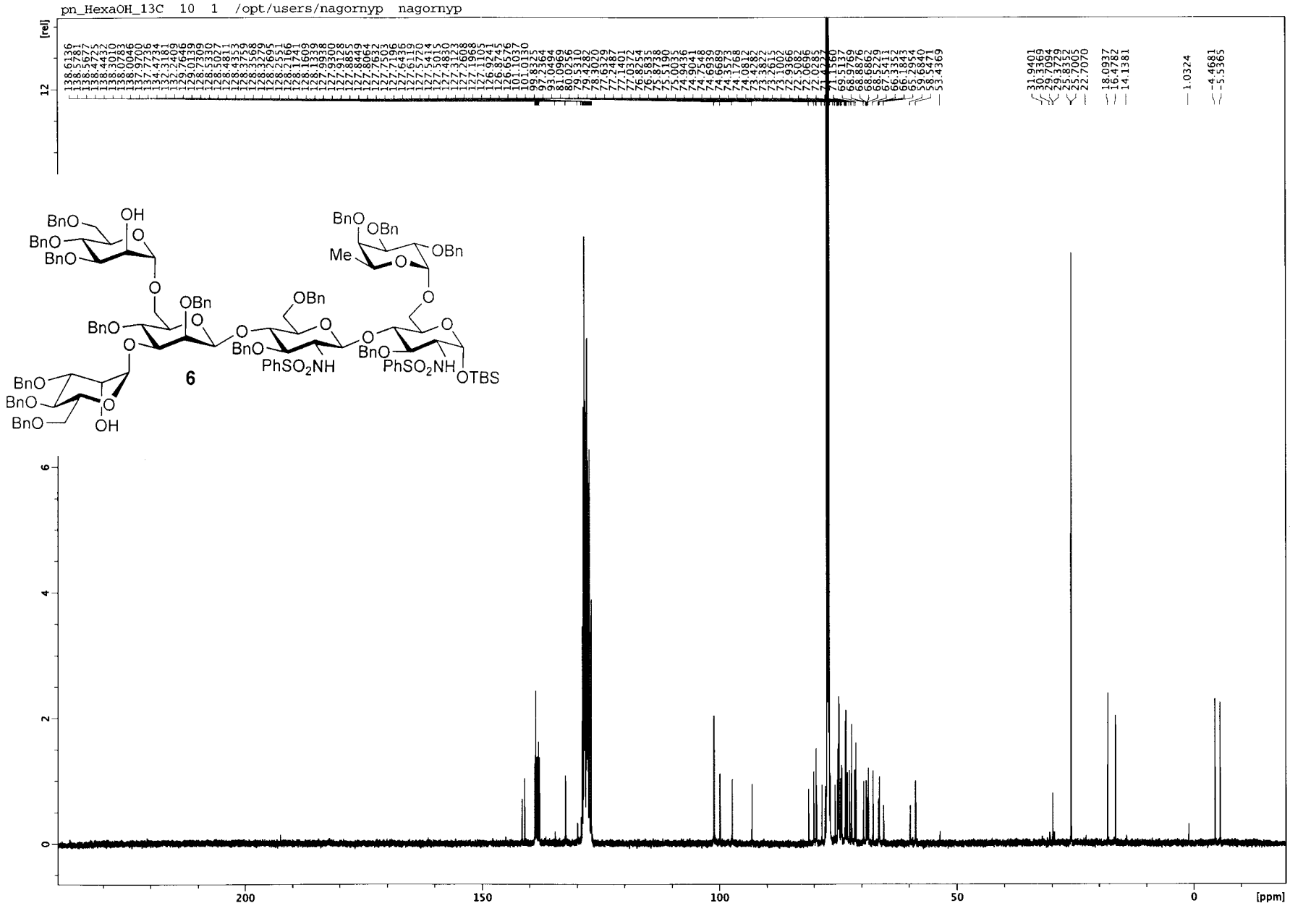

xl-1-163-1H 10 1 /opt/users/lix lix
5.8895
9.1911
3.0306
0.9229
1.3083
0.9502
1.0055
4.1712
4.9541
7.4074
1.0000
1.9831
1.0328
0.9697
0.9436
1.0353
2.7279
4.2960
9.5033
1.9274
0.9221
0.9668
47.7377
1.6363
2.1248
0 [ppm]
2
4
6
BnO
OBn
Me
PhSO2NH
OTBS
HO
5


xl-1-163-13C 10 1 /opt/users/lix lix
-5.5009
-4.4261
16.4915
18.1325
25.8751
58.6042
59.4718
61.7369
65.7730
66.4305
68.9418
69.5951
72.4543
73.3280
73.4274
73.6495
73.9878
74.7498
74.8266
74.8540
75.0516
75.2429
75.6717
75.9920
76.0875
76.5748
76.9021
77.0536
77.1143
77.3261
78.0816
78.4274
79.8651
80.2102
93.0761
97.5771
100.7510
101.1422
126.9073
127.0009
127.0917
127.1962
127.3190
127.3958
127.4777
127.5466
127.6300
127.7580
127.8357
127.8635
127.8859
127.9688
127.9929
128.0250
128.0562
128.1104
128.2222
128.2896
128.3594
128.4490
128.4676
128.5412
128.5791
128.6147
128.6816
128.8059
5.2199
6.0970
1.8091
2.9124
83.9616
[ppm]
0
20
40
60
80
100
120
140
BnO
OBn
Me
O
OTBS
PhSO2NH
5

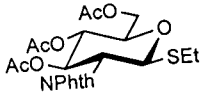

FN-I-90H_1H 10 1 /opt/users/nagornyp nagornyp
6a
[ppm]


PN-I-90H_13C 10 1 /opt/users/nagornyp nagornyp
[ppm]
0
50
100
150
200
6a
BnO
OBn
OBz
Me
PhSO2NH
OTBS


Hexamer_Charc_1H 1 1 /opt/users/nagornyp nagornyp
Proton24
.* nagornyp Hexamer_Charc_1H (1 1) CDCl3 24.0C October_31,2008_11:16 DRX 500MHz zg30 1H *.
[rel]
50
40
30
20
10
0
6
4
2
0
[ppm]
BnO
OH
OBn
Me
PhSO2NH
OTBS
6

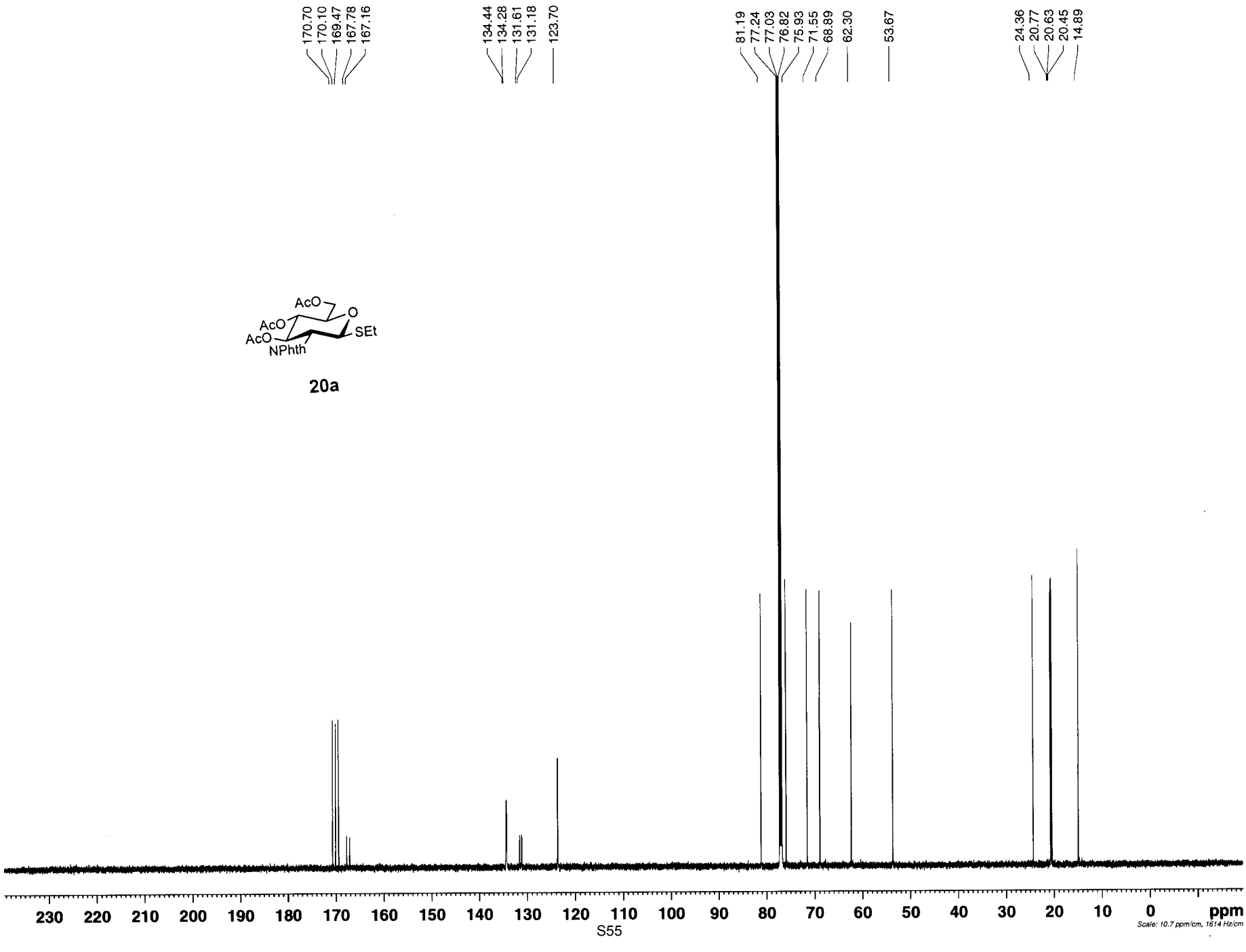

pn_HexaOH_13C 10 1 /opt/users/nagornyp nagornyp
[rel]
12
BnO
OH
BnO
BnO
OBn
BnO
PhSO2NH
Me
OTBS
6
[ppm]
200
150
100
50
0

.* faschinb BFI-176 (10 1) CDCl3 24.0C October_06,2008_11:00 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.



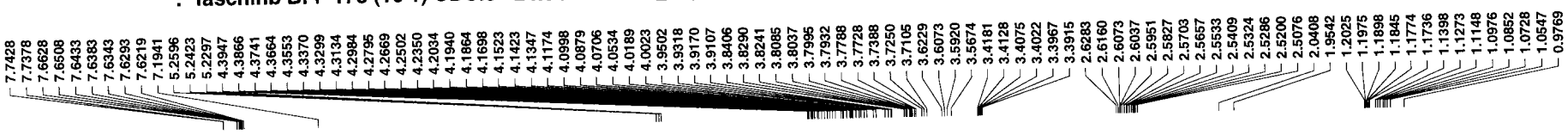
20a

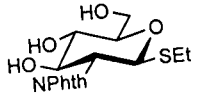
.* faschinb BFI-176 (11 1) CDCl3 24.0C October_06,2008_11:03 Bruker AVII+ 600MHz RRL1326: zgpg30 : 13C 110.000 ppm; 1H 4.500 ppm *.



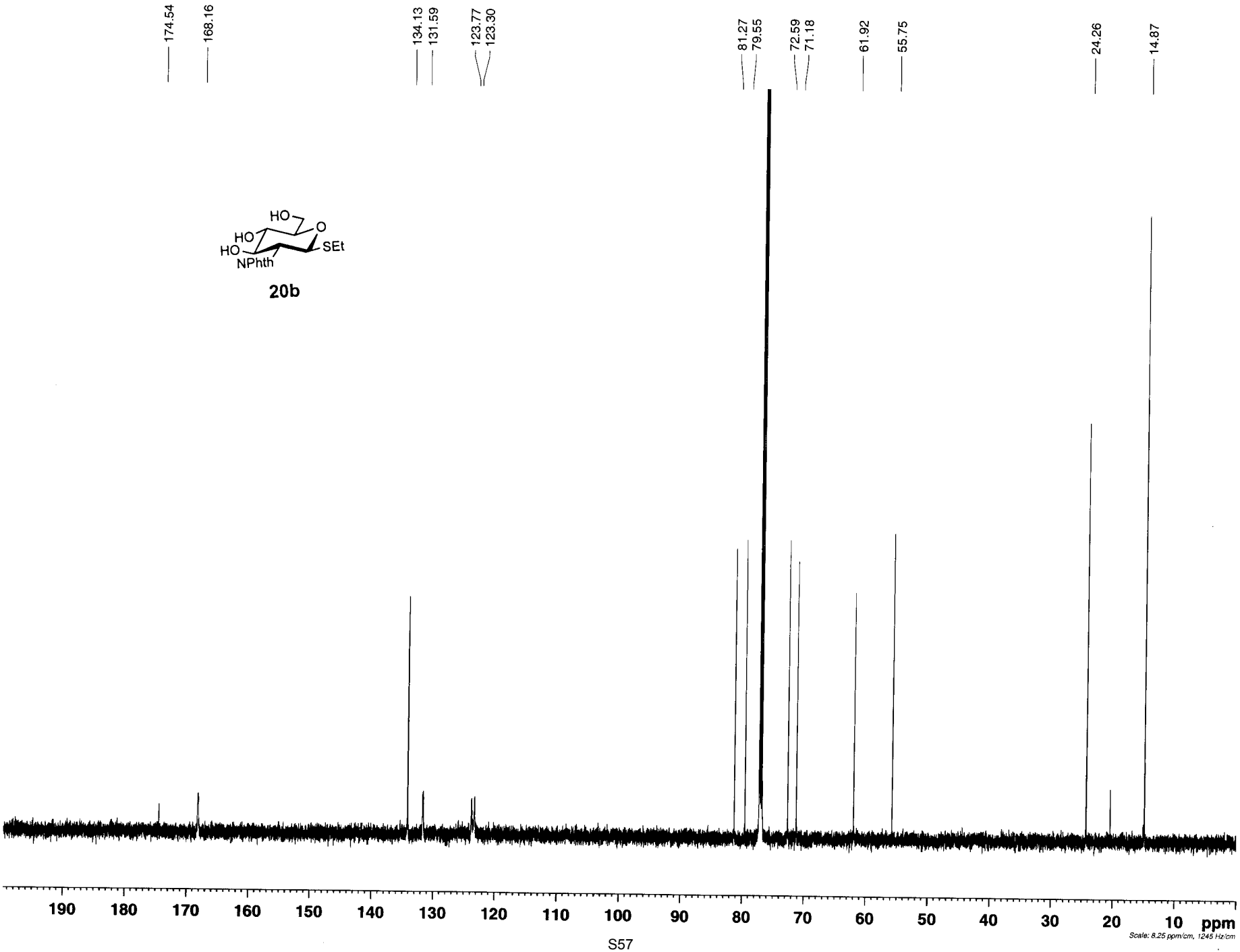
20a

.* faschinb BFI–178 (10 1) CDCl3 24.0C October_06,2008_12:00 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.

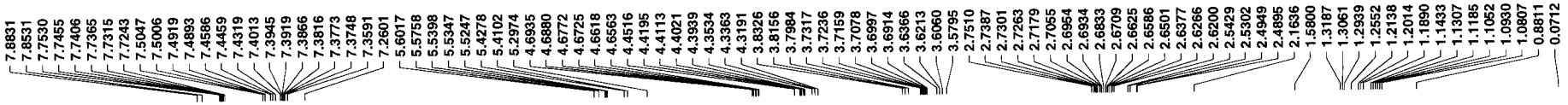


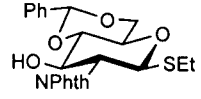


20b


174.54
168.16
134.13
131.59
123.77
123.30
81.27
79.55
72.59
71.18
61.92
55.75
24.26
14.87
HO
HO
HO
O
SEt
NPhth
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
Scale: 8.25 ppm/cm, 1245 Hz/cm

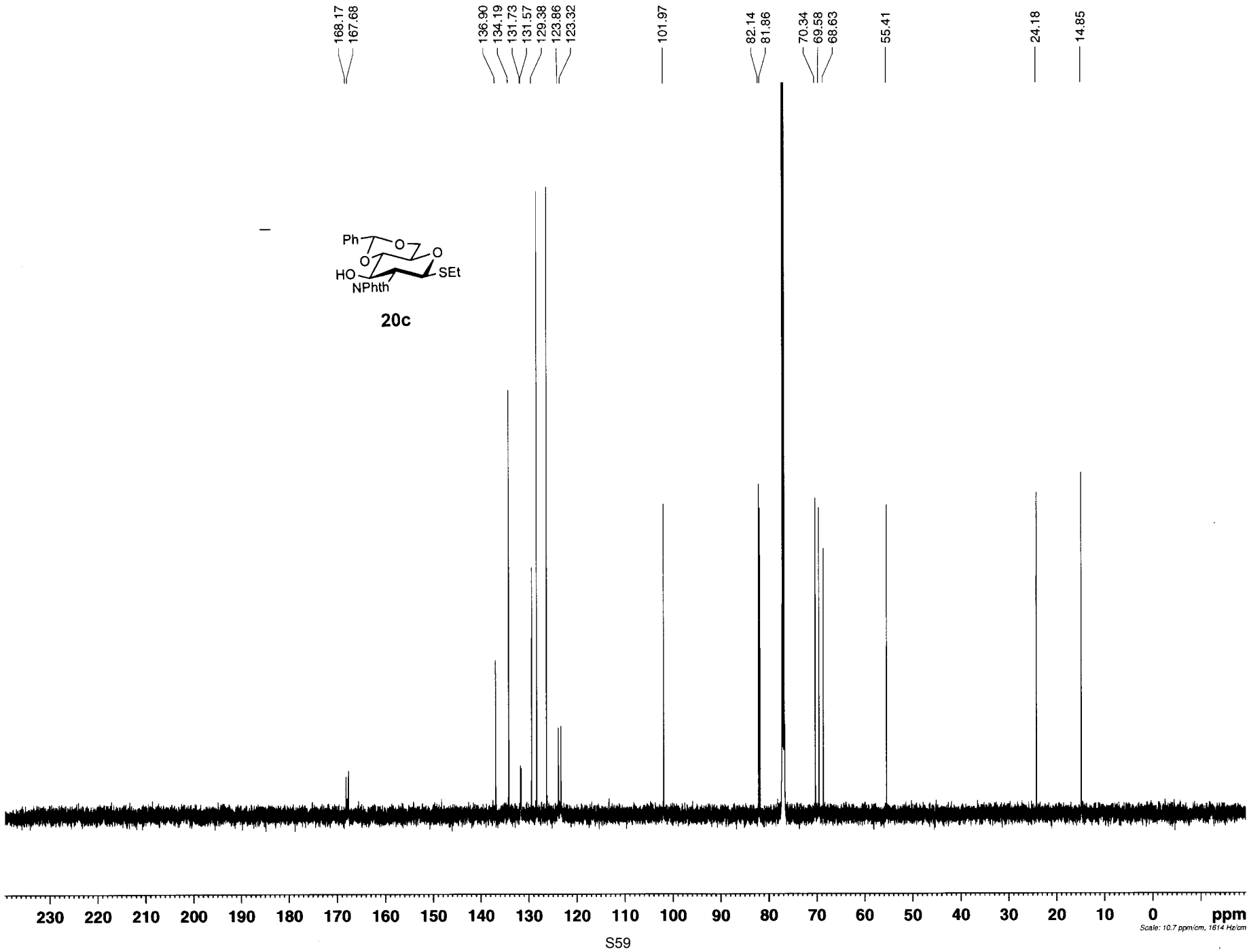
20b


7.8831
7.8531
7.7530
7.7455
7.7406
7.7365
7.7315
7.7243
7.5047
7.5006
7.4919
7.4893
7.4586
7.4459
7.4319
7.4013
7.3945
7.3919
7.3866
7.3816
7.3773
7.3748
7.3591
7.2601
5.6017
5.5758
5.5398
5.5347
5.5247
5.4278
5.4102
5.2974
4.6935
4.6880
4.6772
4.6725
4.6618
4.6563
4.4516
4.4195
4.4113
4.4021
4.3939
4.3534
4.3363
4.3191
3.8326
3.8156
3.7984
3.7317
3.7236
3.7159
3.7078
3.6997
3.6914
3.6366
3.6213
3.6060
3.5795
2.7510
2.7387
2.7301
2.7263
2.7179
2.7055
2.6954
2.6934
2.6833
2.6709
2.6625
2.6586
2.6501
2.6377
2.6266
2.6200
2.5429
2.5302
2.4949
2.4895
2.1636
1.5800
1.3187
1.3061
1.2939
1.2552
1.2138
1.2014
1.1890
1.1433
1.1307
1.1185
1.1052
1.0930
1.0807
0.8811
0.0712

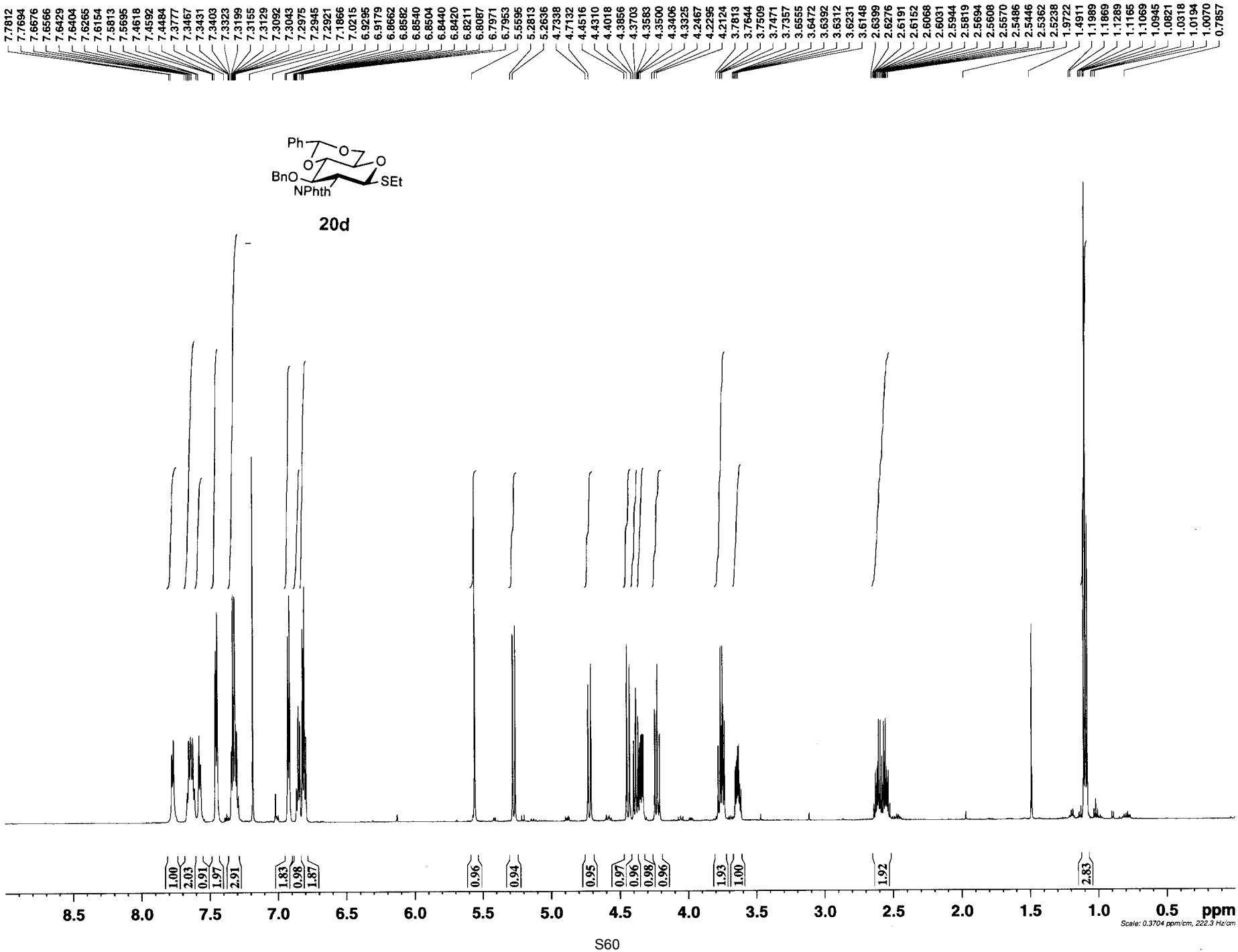

Ph
O
O
O
HO
SEt
NPhth

20c

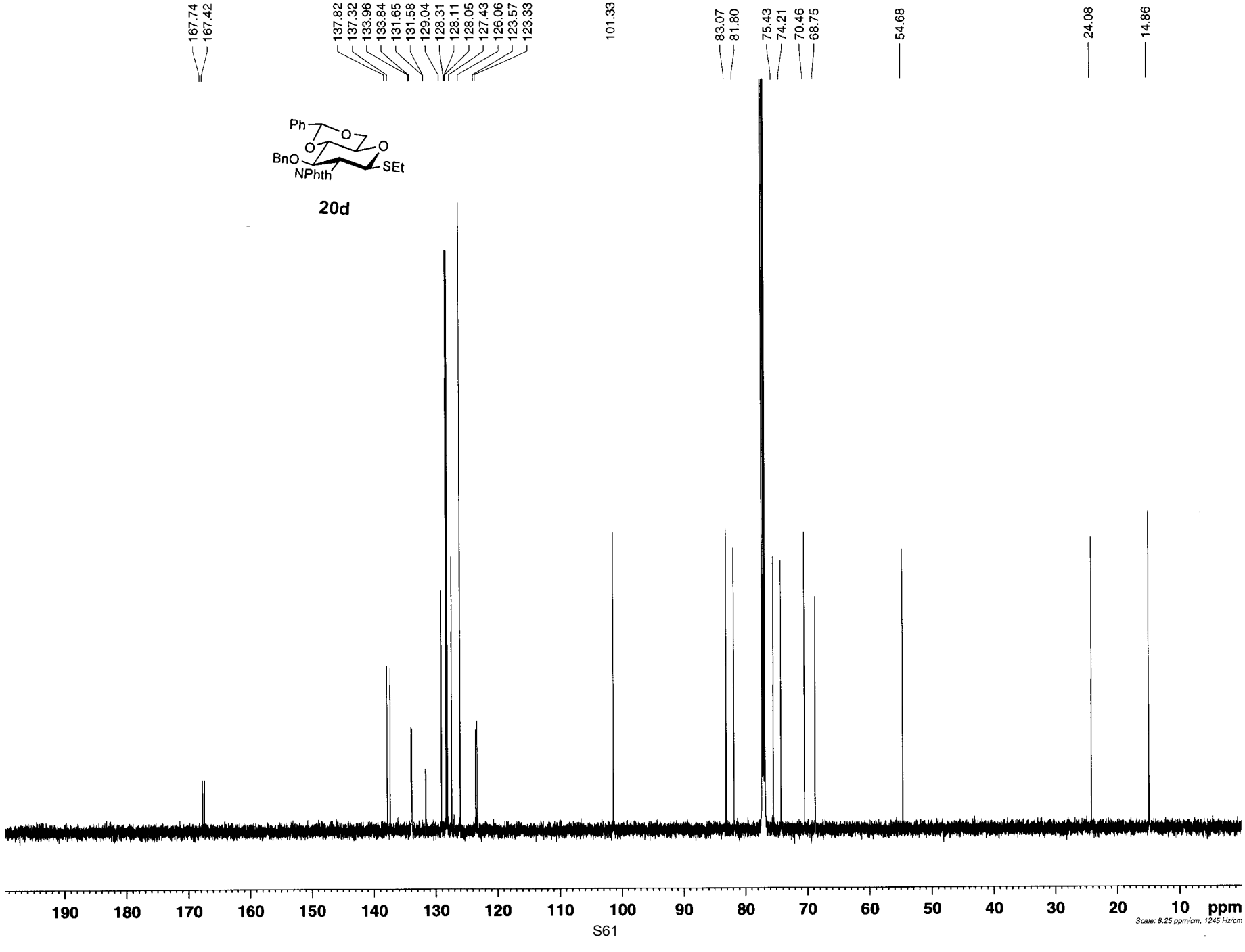
2.01
2.01
2.00
2.98
1.00
0.99
1.00
1.02
1.00
1.02
1.03
1.01
2.02
0.98
2.99
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
Scale: 0.3704 ppm/cm, 222.3 Hz/cm

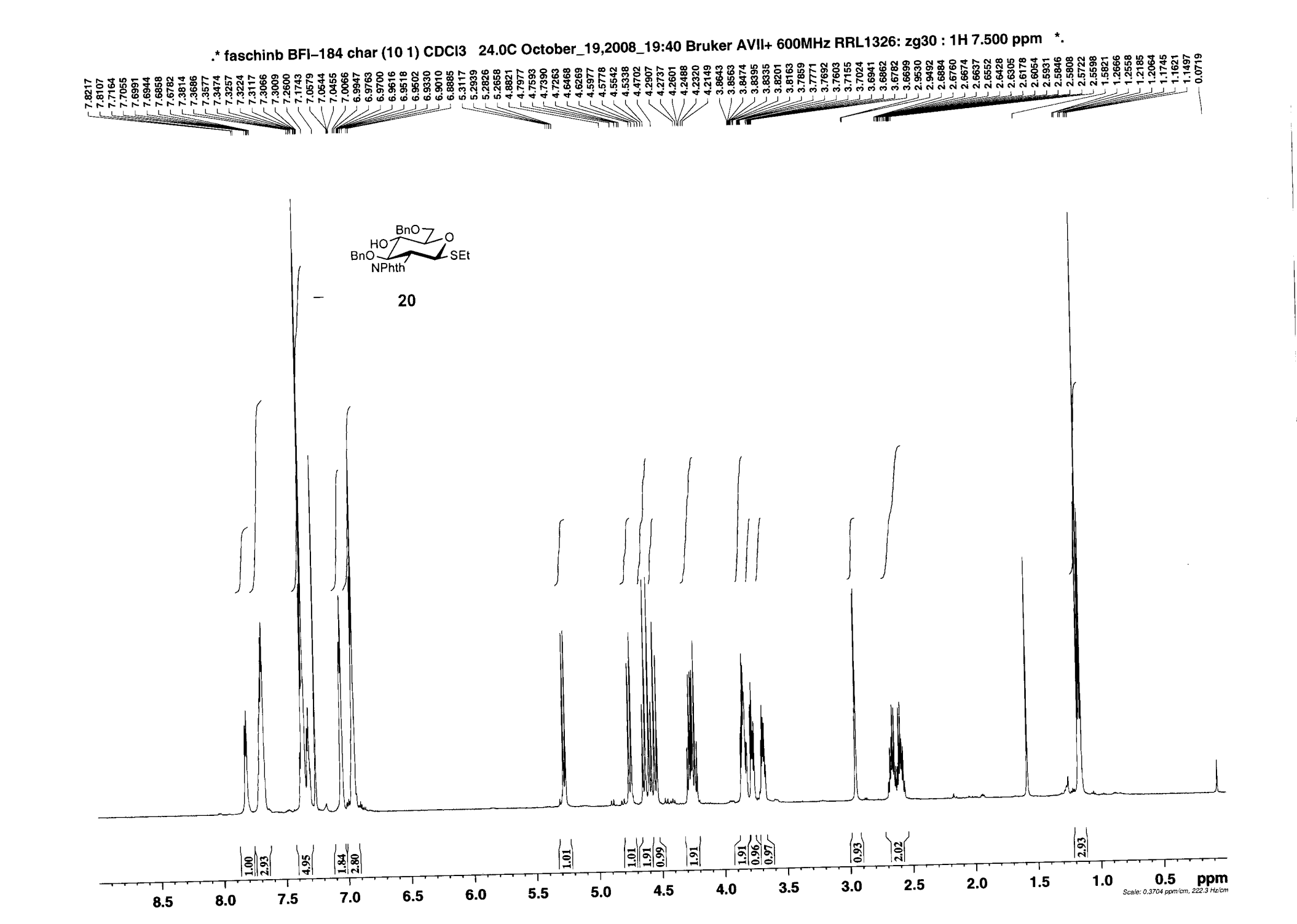

168.17
167.68
136.90
134.19
131.73
131.57
129.38
123.86
123.32
101.97
82.14
81.86
70.34
69.58
68.63
55.41
24.18
14.85
Ph
O
O
O
HO
SEt
NPhth
20c
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 10.7 ppm/cm, 1614 Hz/cm

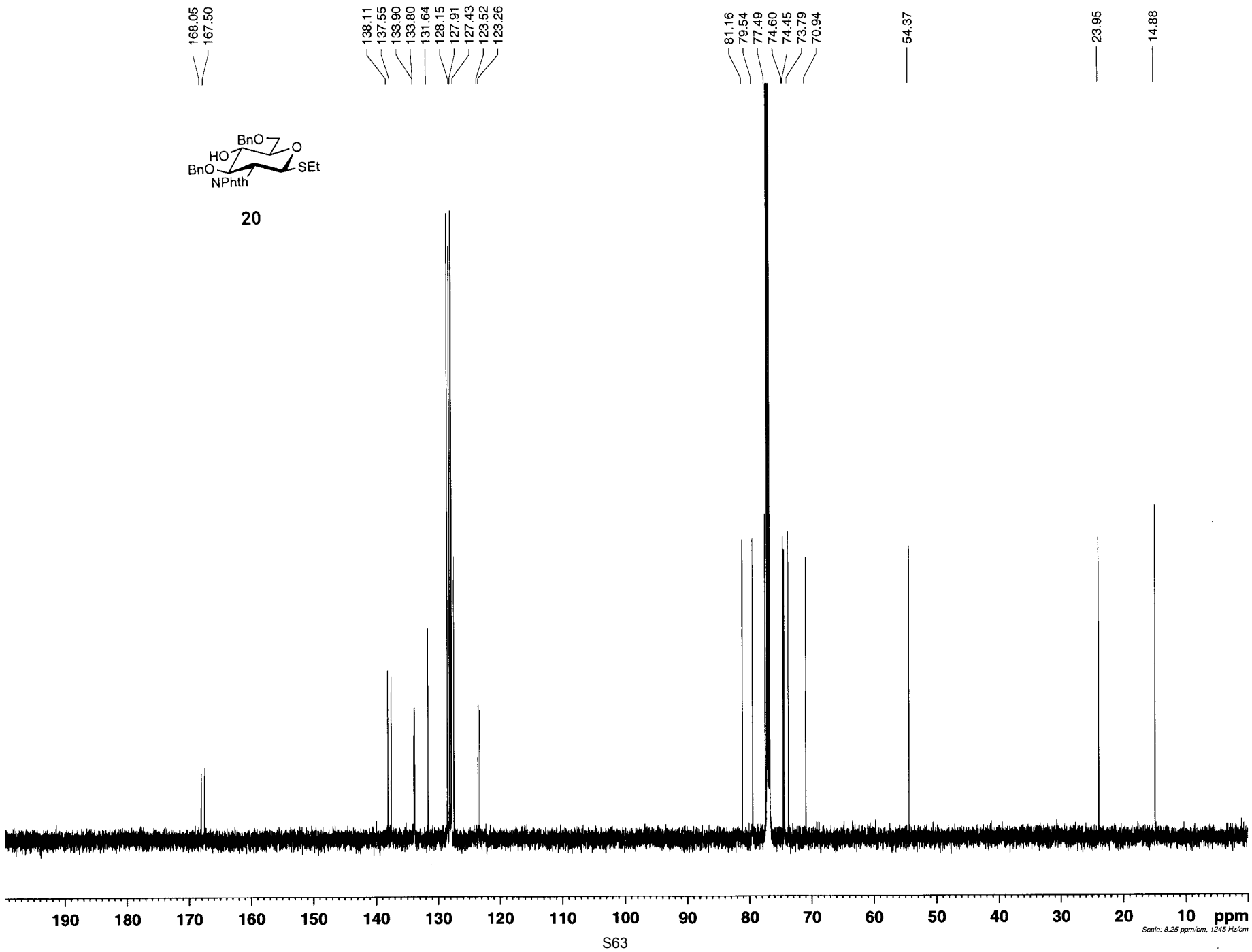
.* faschinb BFI-182 (10 1) CDCl3 24.0C October_06,2008_14:02 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.



.* faschlnb BFI-182 (11 1) CDCl3 24.0C October_06,2008_14:05 Bruker AVII+ 600MHz RRL1326: zgpg30 : 13C 110.000 ppm; 1H 4.500 ppm *.

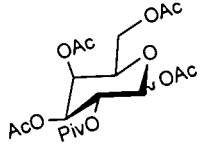



.* faschinb BFI-184 char (10 1) CDCl3 24.0C October_19,2008_19:40 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.
BnO
HO
BnO
NPhth
O
SEt
20
ppm
Scale: 0.3704 ppm/cm, 222.3 Hz/cm


168.05
167.50
138.11
137.55
133.90
133.80
131.64
128.15
127.91
127.43
123.52
123.26
81.16
79.54
77.49
74.60
74.45
73.79
70.94
54.37
23.95
14.88
BnO
HO
BnO
NPhth
O
SEt
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
Scale: 8.25 ppm/cm, 1245 Hz/cm

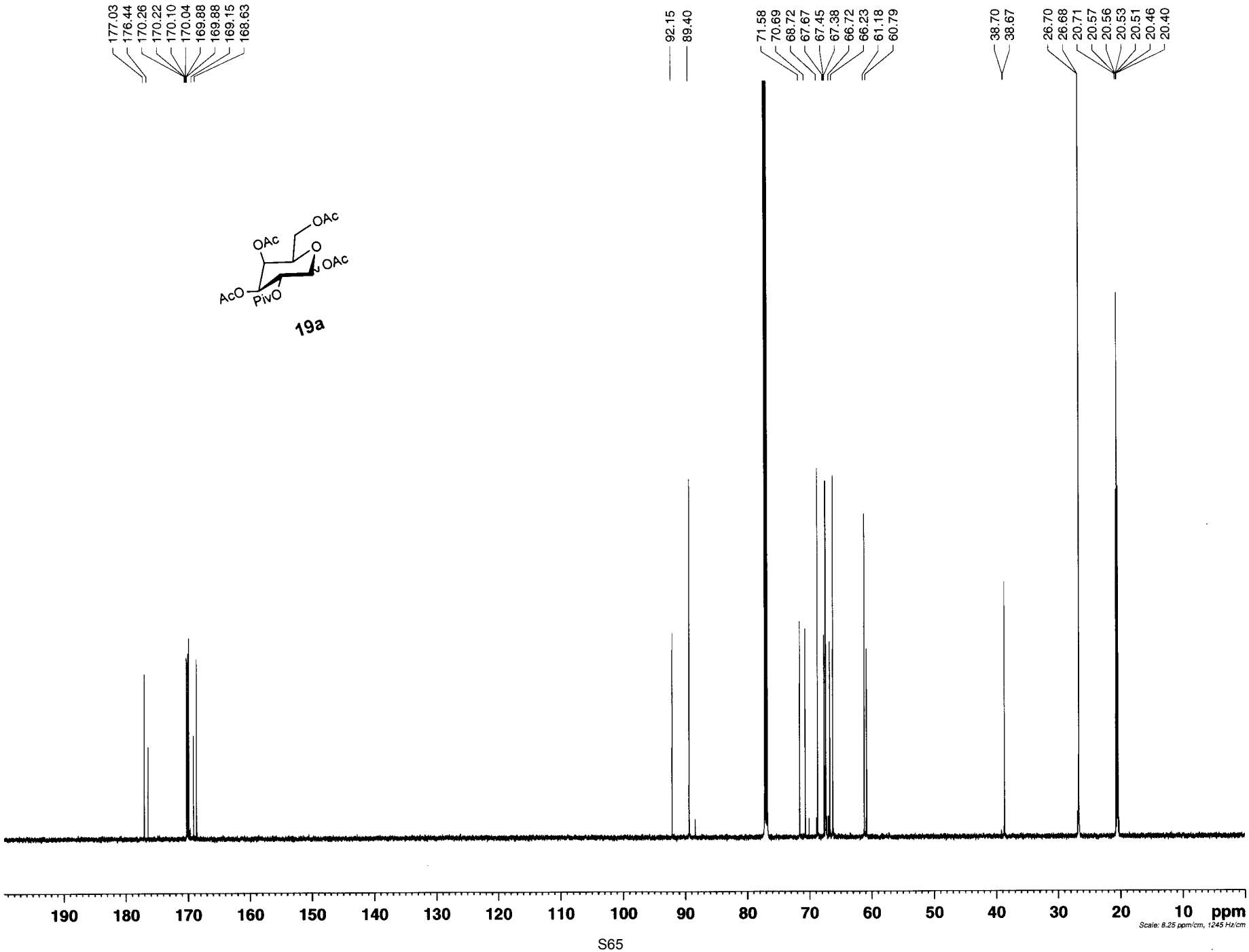
20

.* faschinb BFI-201 (10 1) CDCl3 24.0C October_20,2008_06:27 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.

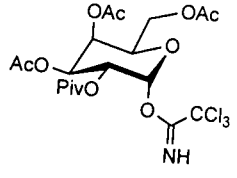


19a

.* faschinb BFI-201 (11 1) CDCl3 24.0C October_20,2008_06:30 Bruker AVII+ 600MHz RRL1326: zgpg30 : 13C 110.000 ppm; 1H 4.500 ppm *.

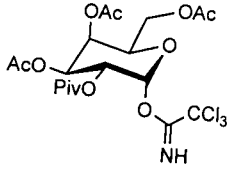


.* faschinb BFI-206 (10 1) CDCl3 24.0C October_22,2008_15:46 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.



19

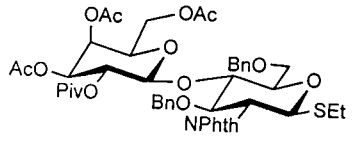

177.34
170.18
169.99
169.69
160.58
93.35
90.72
69.02
67.50
67.43
66.55
61.23
38.76
26.79
20.53
20.52
20.40


OAc
OAc
O
AcO
PivO
O
CCl3
NH

19

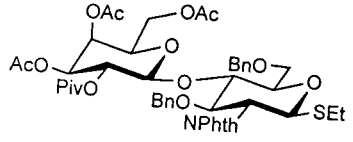
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
Scale: 8.38 ppm/cm, 1265 Hz/cm

.* faschinb BFI-122 (10 1) CDCl3 24.0C October_15,2008_13:18 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.

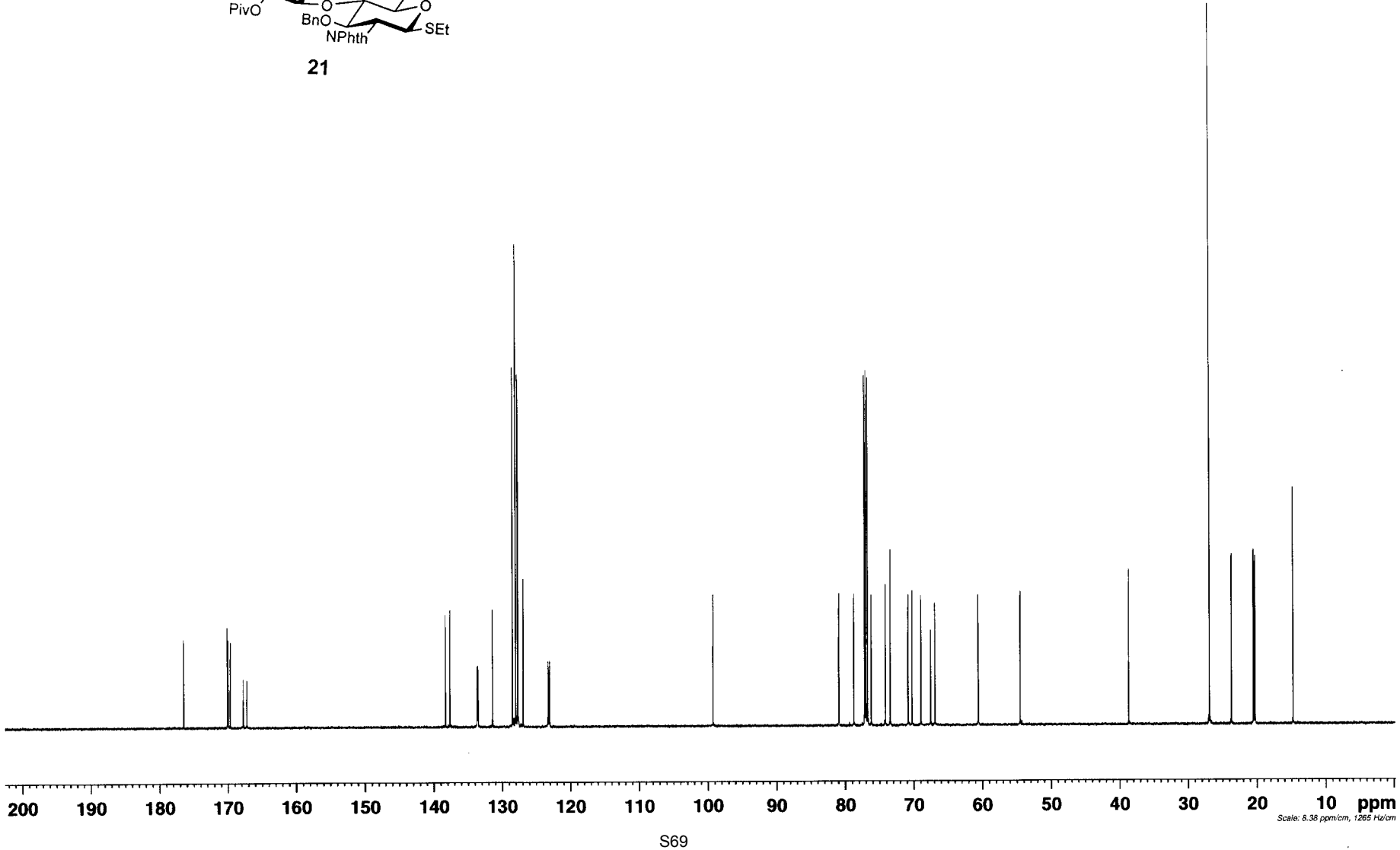


21

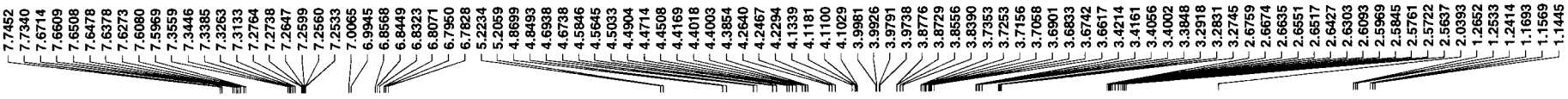
.* faschinb BFI-122 (11 1) CDCl3 24.0C October_15,2008_13:21 Bruker AVII+ 600MHz RRL1326: zgpg30 : 13C 110.000 ppm; 1H 4.500 ppm *.

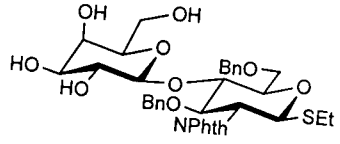


21

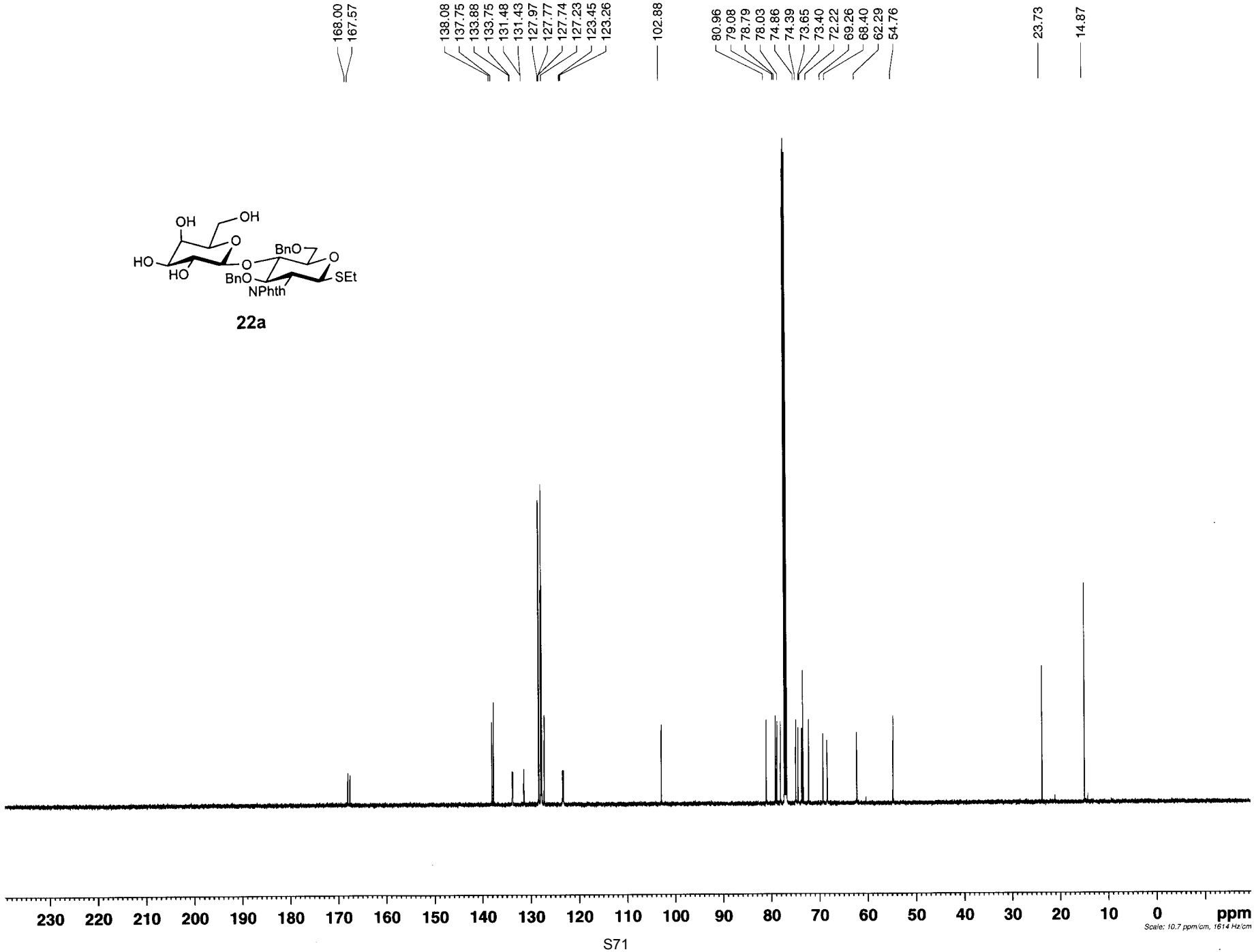


.* faschinb BFI-125 (10 1) CDCl3 24.0C October_15,2008_14:39 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.

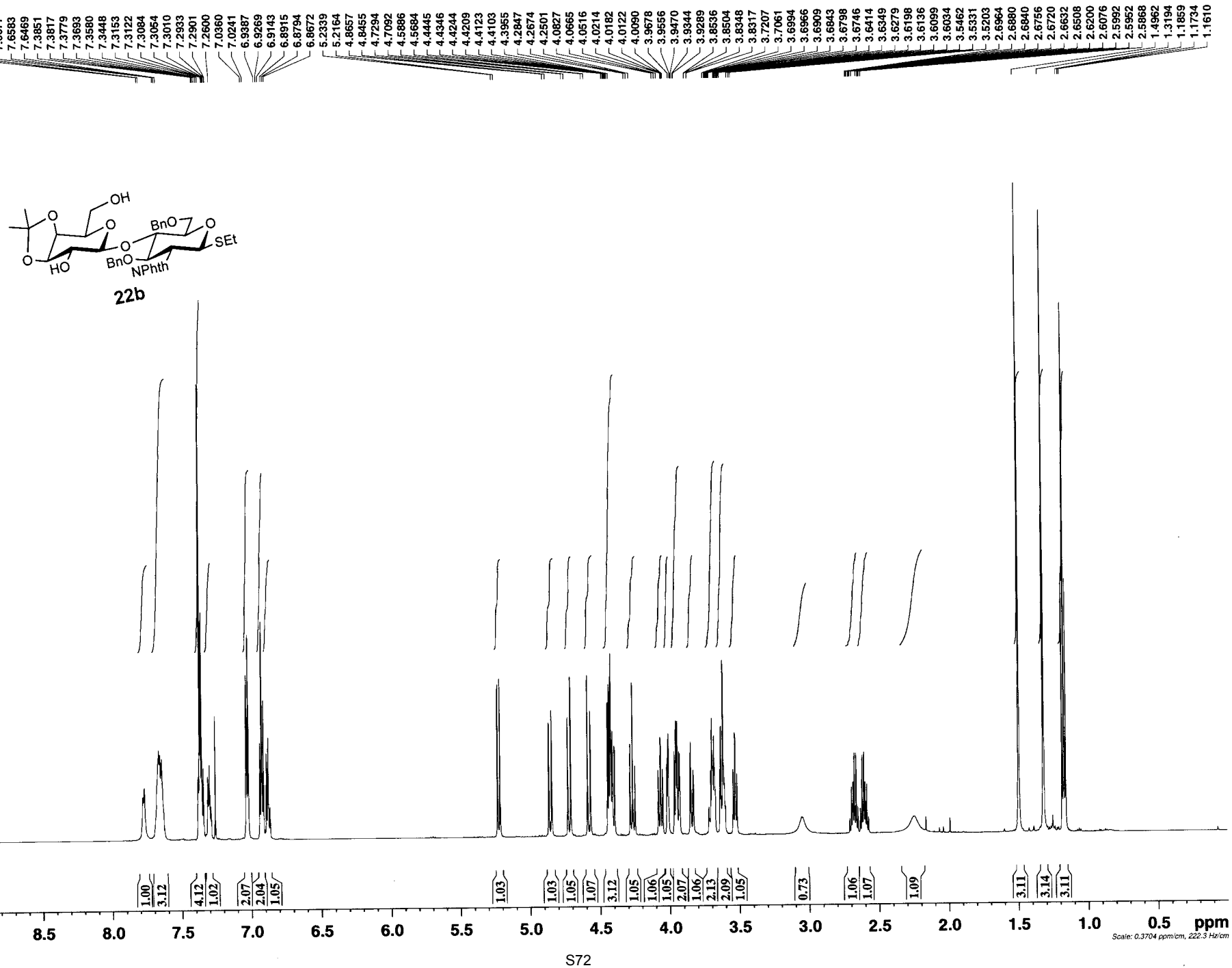


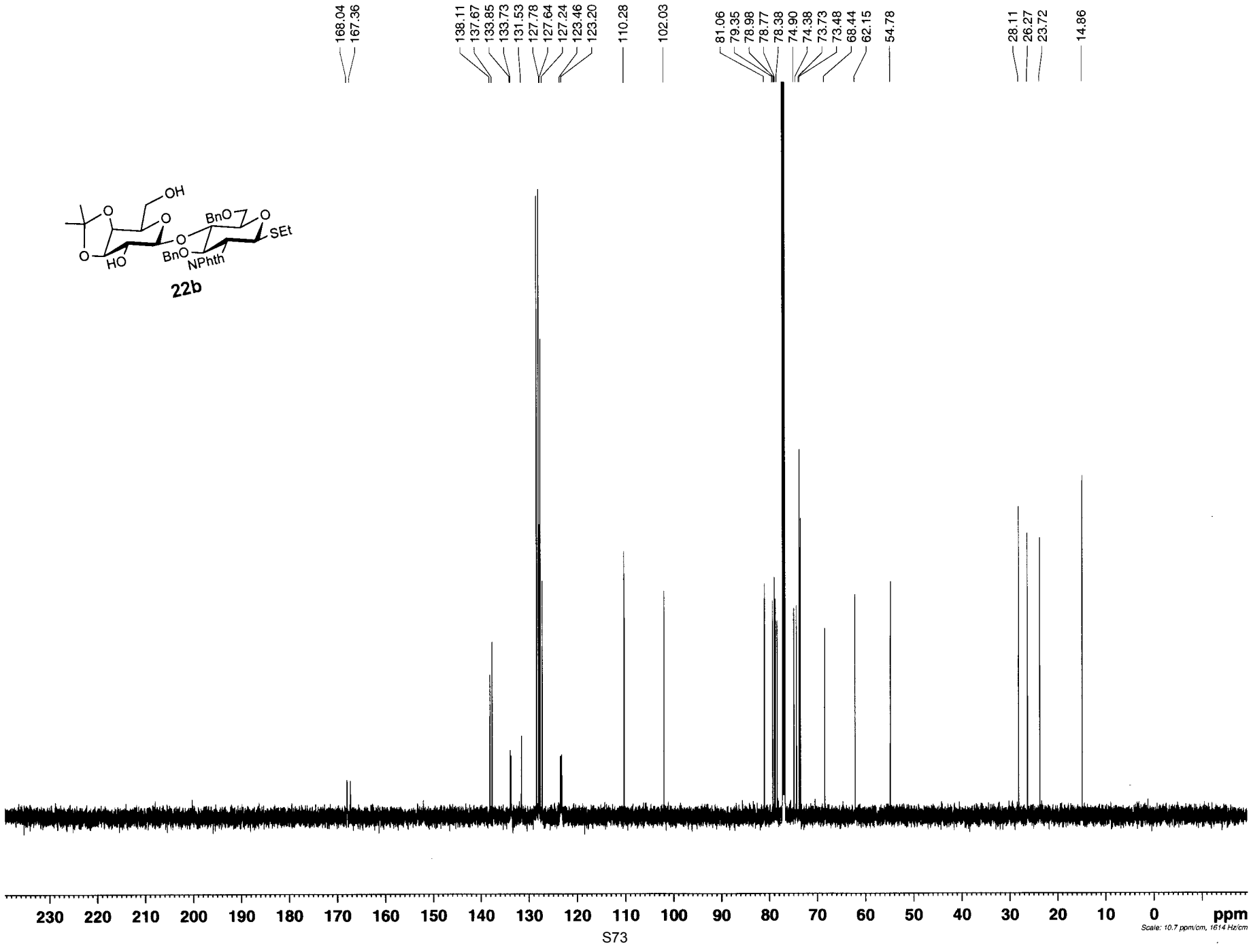


22a

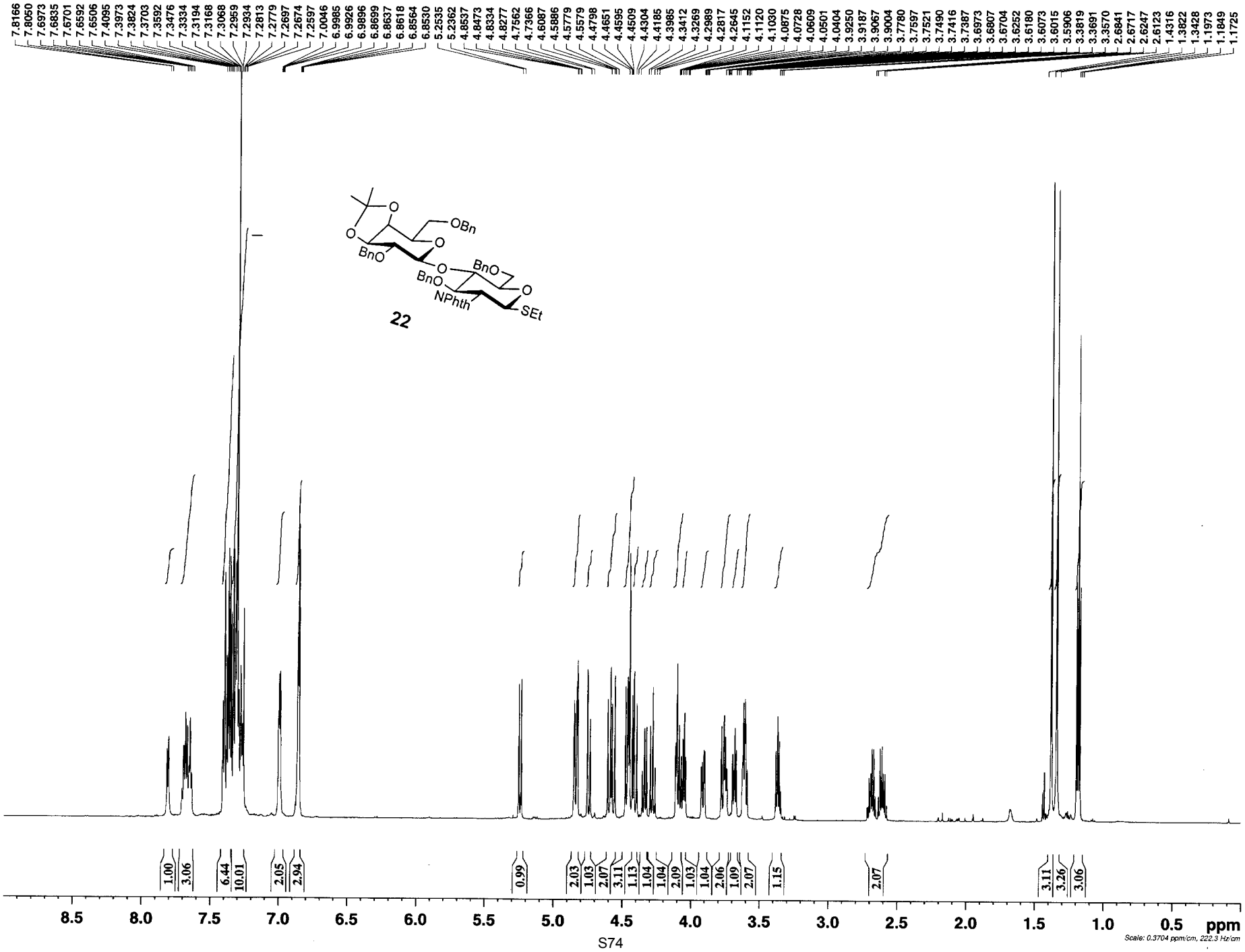

168.00
167.57
138.08
137.75
133.88
133.75
131.48
131.43
127.97
127.77
127.74
127.23
123.45
123.26
102.88
80.96
79.08
78.79
78.03
74.86
74.39
73.65
73.40
72.22
69.26
68.40
62.29
54.76
23.73
14.87
OH
OH
O
HO
HO
O
BnO
O
BnO
NPhth
SEt
22a
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm
Scale: 10.7 ppm/cm, 1614 Hz/cm

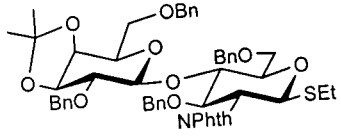
.* faschinb BFI-124 (10 1) CDCl3 24.0C October_15,2008_14:20 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.




168.04
167.36
138.11
137.67
133.85
133.73
131.53
127.78
127.64
127.24
123.46
123.20
110.28
102.03
81.06
79.35
78.98
78.77
78.38
74.90
74.38
73.73
73.48
68.44
62.15
54.78
28.11
26.27
23.72
14.86
OH
O
O
O
BnO
O
SEt
O
HO
BnO
NPhth
22b
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 10.7 ppm/cm, 1614 Hz/cm

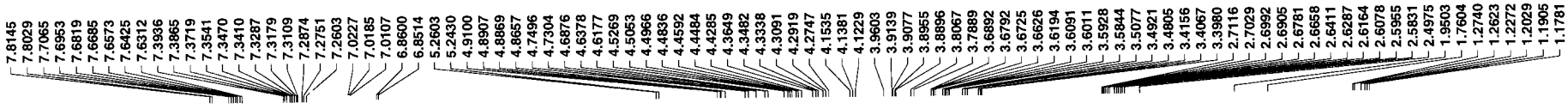
.* faschinb BFI-199 char (10 1) CDCl3 24.0C October_19,2008_21:42 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.

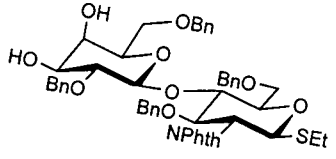




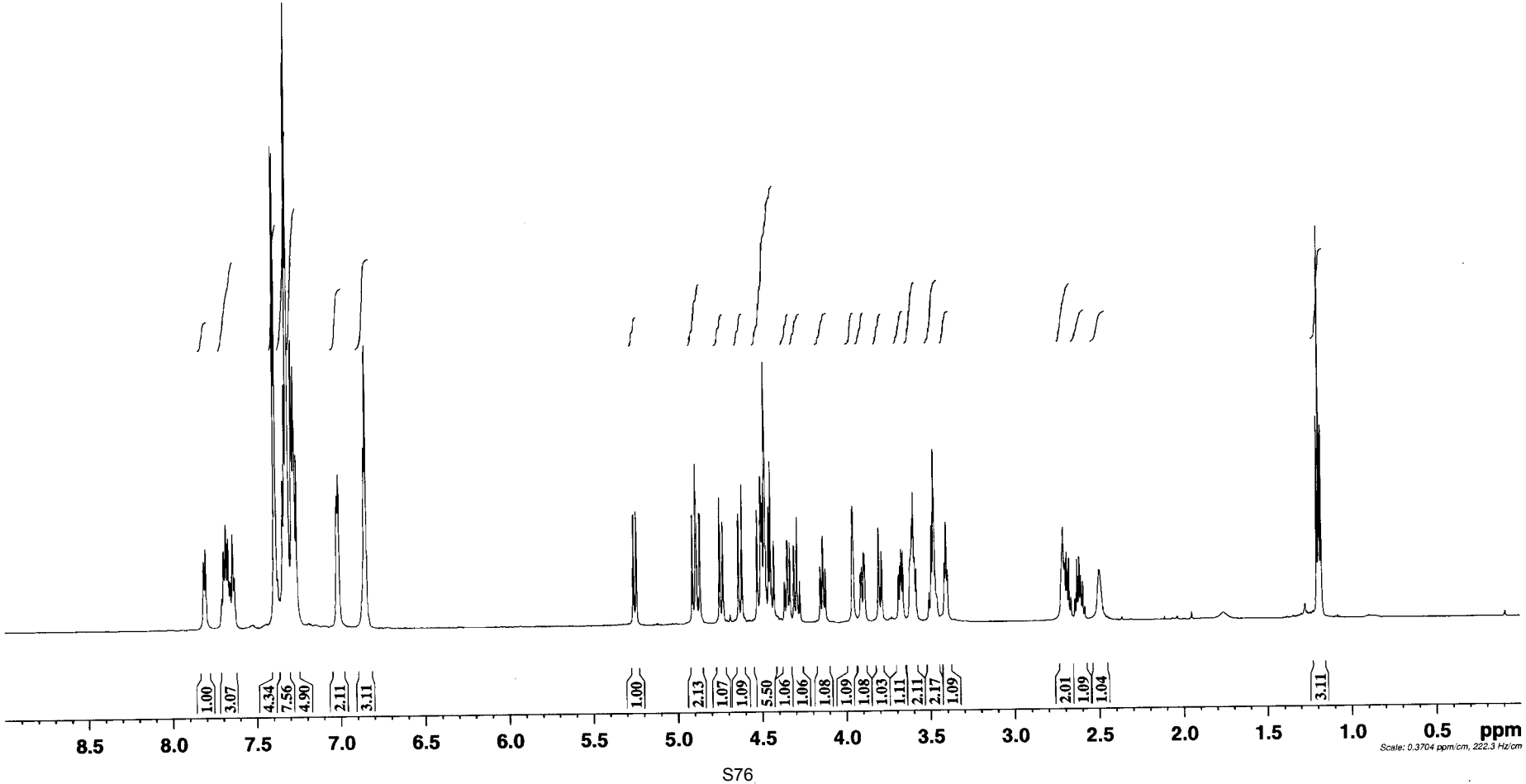
22

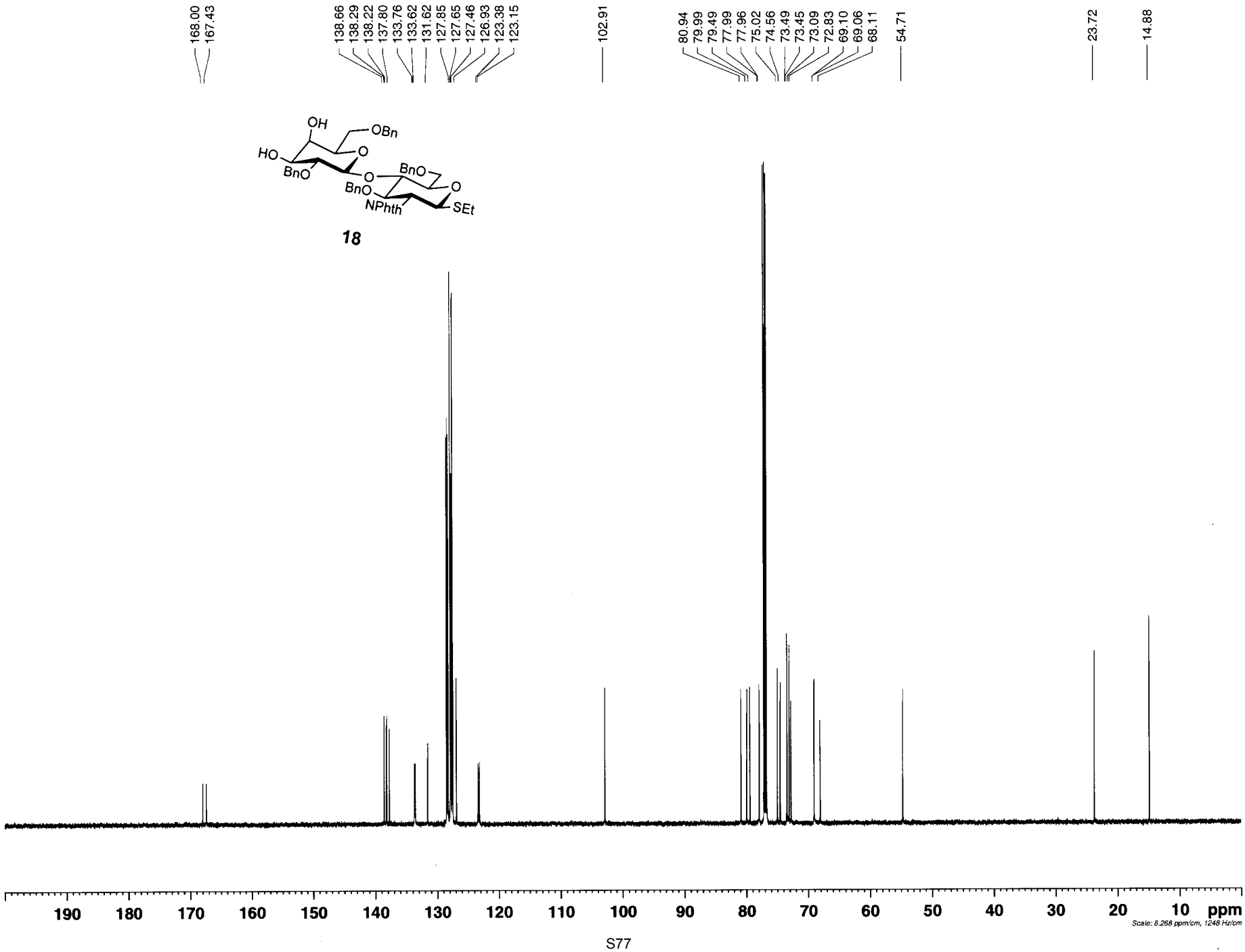
.* faschinb BFI-145 char (10 1) CDCl3 24.0C October_19,2008_18:21 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.



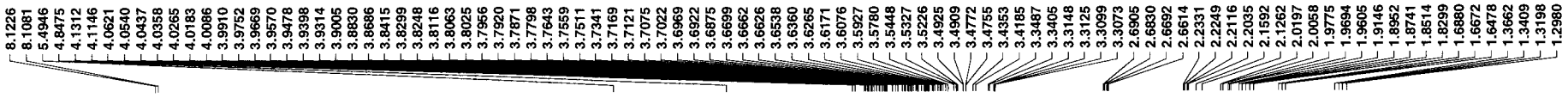


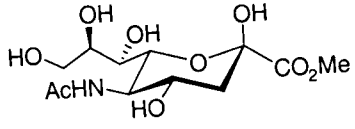
18



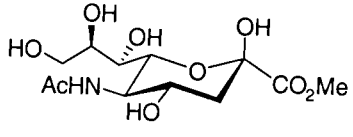

168.00
167.43
138.66
138.29
138.22
137.80
133.76
133.62
131.62
127.85
127.65
127.46
126.93
123.38
123.15
102.91
80.94
79.99
79.49
77.99
77.96
75.02
74.56
73.49
73.45
73.09
72.83
69.10
69.06
68.11
54.71
23.72
14.88
OH
OBn
HO
O
BnO
O
BnO
BnO
O
NPhth
SEt
18
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm
Scale: 8.268 ppm/cm, 1248 Hz/cm

.* faschinb BFI-204 (10 1) MeOD 24.0C October_21,2008_15:17 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.





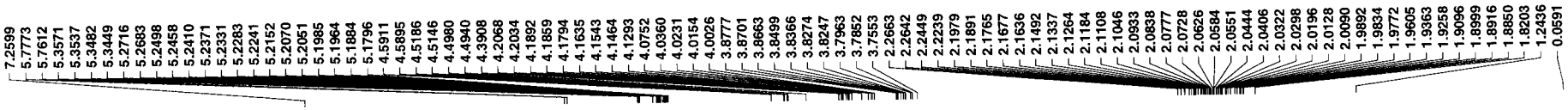
23a

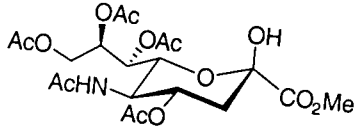

OH
HO
OH
OH
AcHN
O
CO2Me
HO

23a

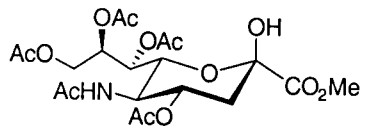
175.24
171.90
96.79
72.20
71.78
70.32
67.98
64.97
54.43
53.30
40.81
22.83
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 10.7 ppm/cm, 1614 Hz/cm

.* faschinb BFI-127 (10 1) CDCl3 24.0C October_20,2008_07:29 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.





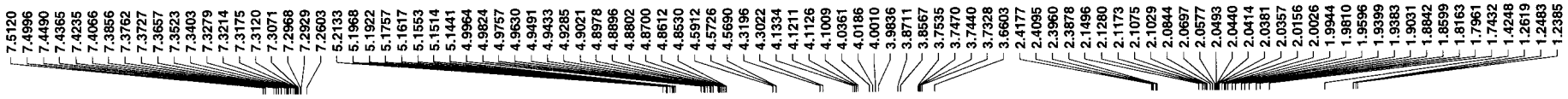
23b

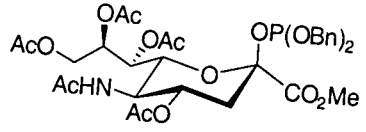

OAc
OAc
OH
AcO
O
AcHN
CO2Me
AcO

23b

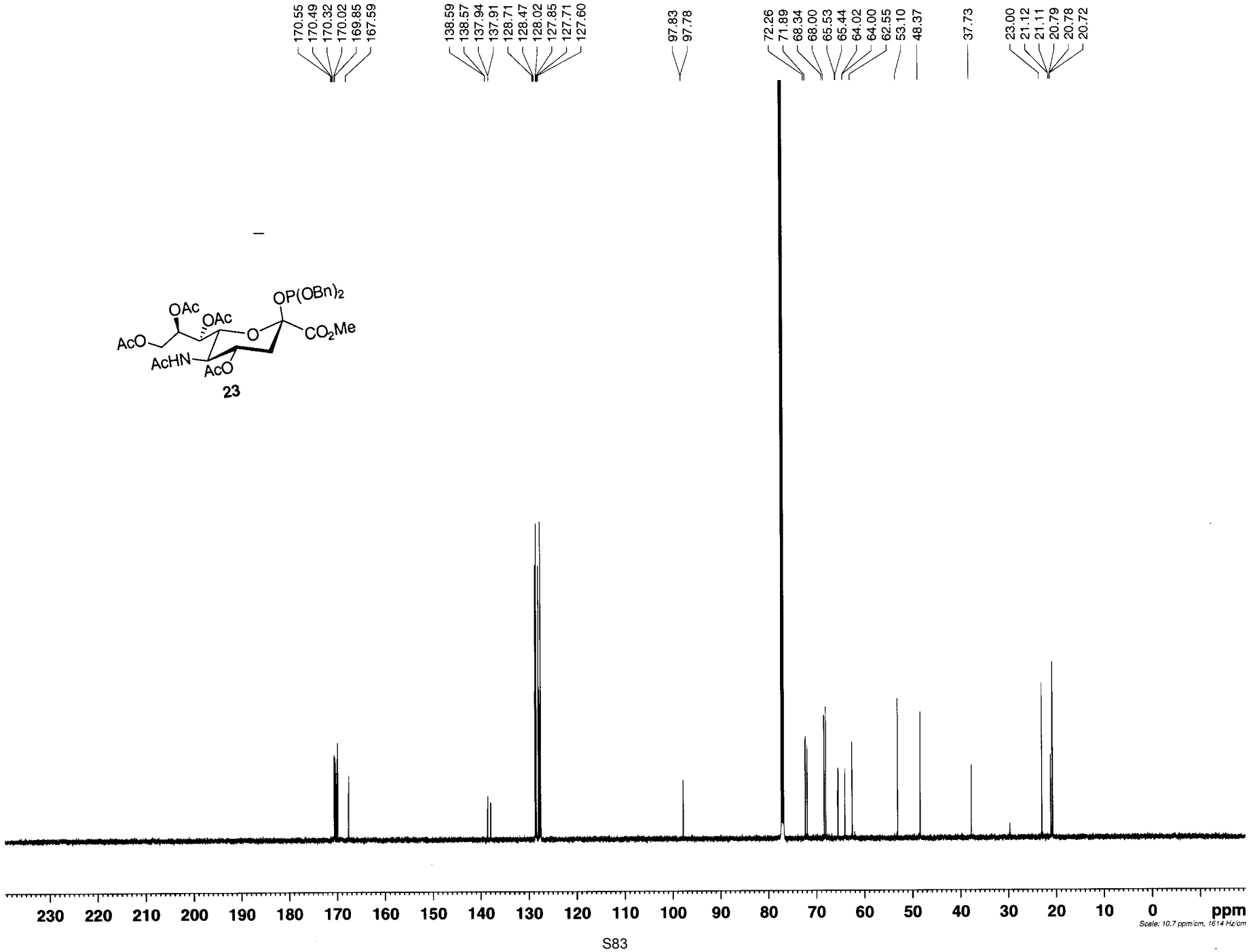
170.97
170.95
170.94
170.28
170.21
169.04
94.84
71.36
71.09
69.25
68.04
62.63
53.45
49.42
36.09
23.13
21.02
20.88
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 10.7 ppm/cm, 1614 Hz/cm

.* faschinb BFI-132 char (10 1) CDCl3 24.0C October_23,2008_11:53 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.

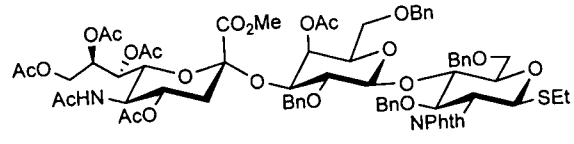




23

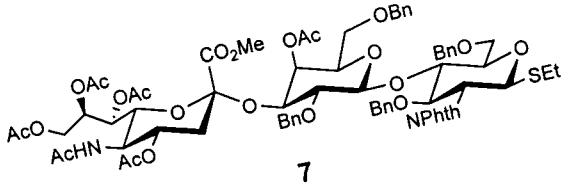

170.55
170.49
170.32
170.02
169.85
167.59
138.59
138.57
137.94
137.91
128.71
128.47
128.02
127.85
127.71
127.60
97.83
97.78
72.26
71.89
68.34
68.00
65.53
65.44
64.02
64.00
62.55
53.10
48.37
37.73
23.00
21.12
21.11
20.79
20.78
20.72
OP(OBn)2
OAc
OAc
AcO
O
CO2Me
AcHN
AcO
23
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Scale: 10.7 ppm/cm, 1614 Hz/cm

.* faschinb bfi-208r (10 1) CDCl3 24.0C October_24,2008_17:36 Bruker AVII+ 600MHz RRL1326: zg30 : 1H 7.500 ppm *.



7

.* faschinb bfi-20813c (10 1) CDCl3 24.0C October_25,2008_15:55 Bruker AVII+ 600MHz RRL1326: zgpg30 : 13C 110.000 ppm; 1H 4.500 ppm *.

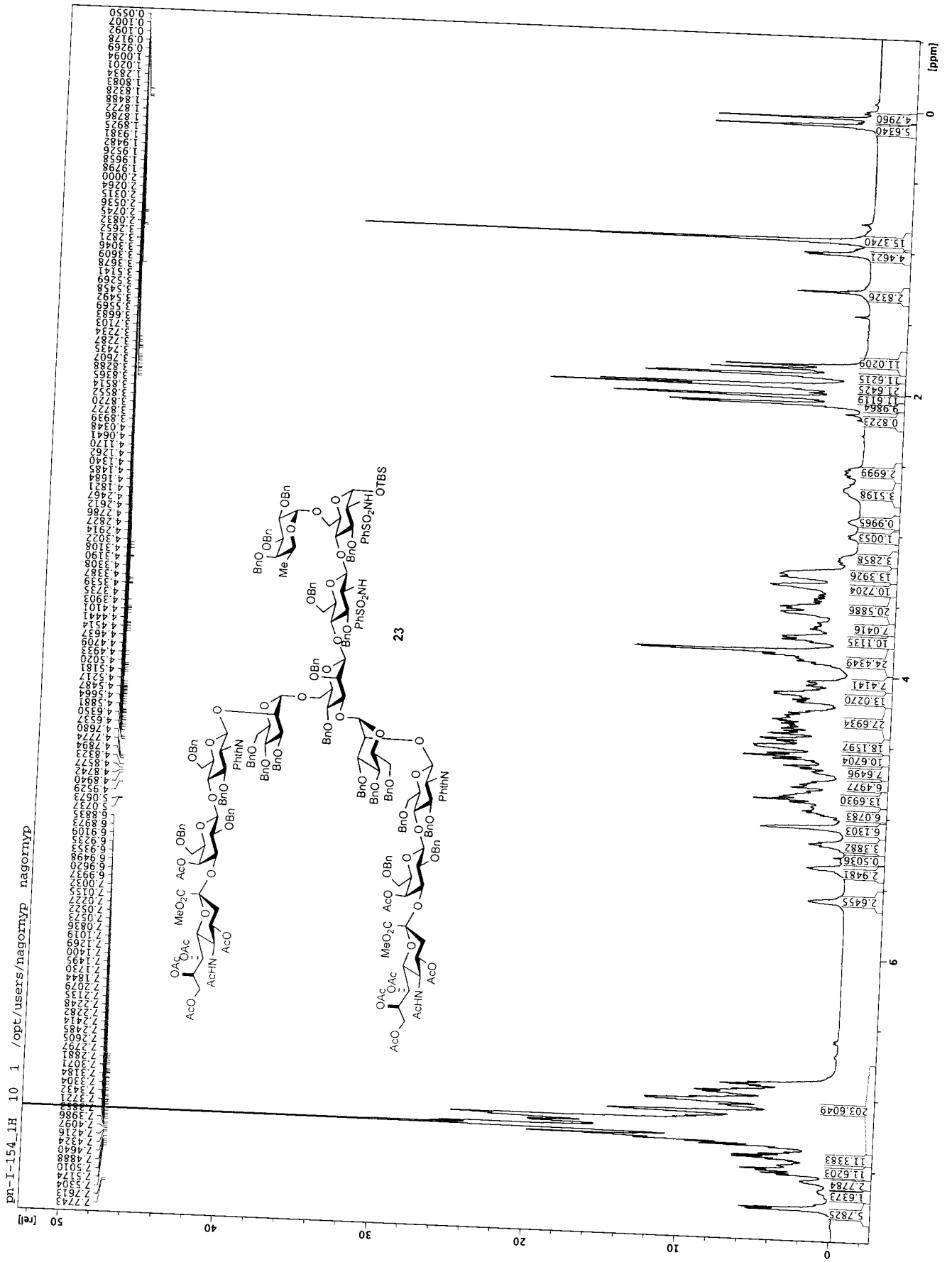


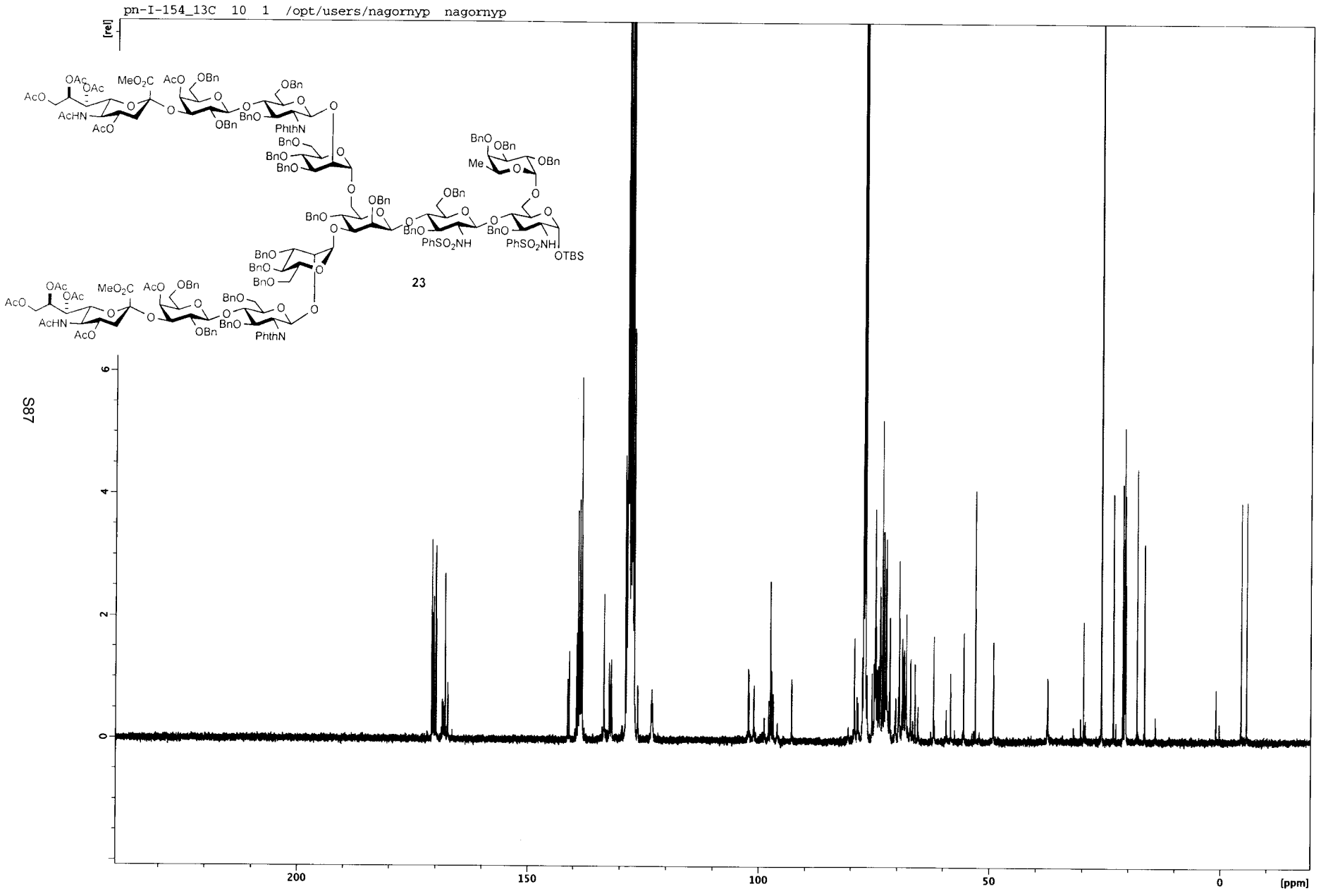
7

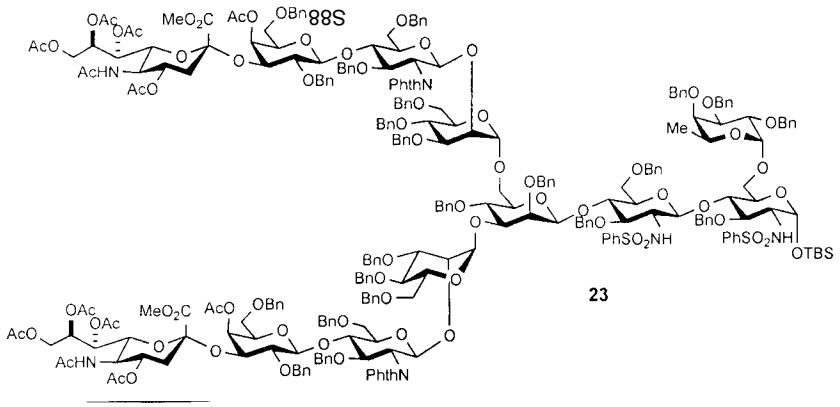
170.82 170.56 170.33 169.94 169.90 169.87 168.08 167.89 167.46
139.26 138.87 138.63 138.22 133.81 133.69 131.72 128.26 128.19 128.13 127.79 127.76 127.59 127.45 127.44 127.39 127.32 127.24 126.96 123.47 123.16
102.08
97.36
80.80 79.51 79.44 78.08 75.11 74.15 73.69 73.26 72.77 72.28 71.62 69.50 68.83 68.50 68.39 68.01 67.10 62.03 54.70 53.09 49.26
37.56
23.66 23.22 21.22 20.82 20.74 20.67 20.56 14.96

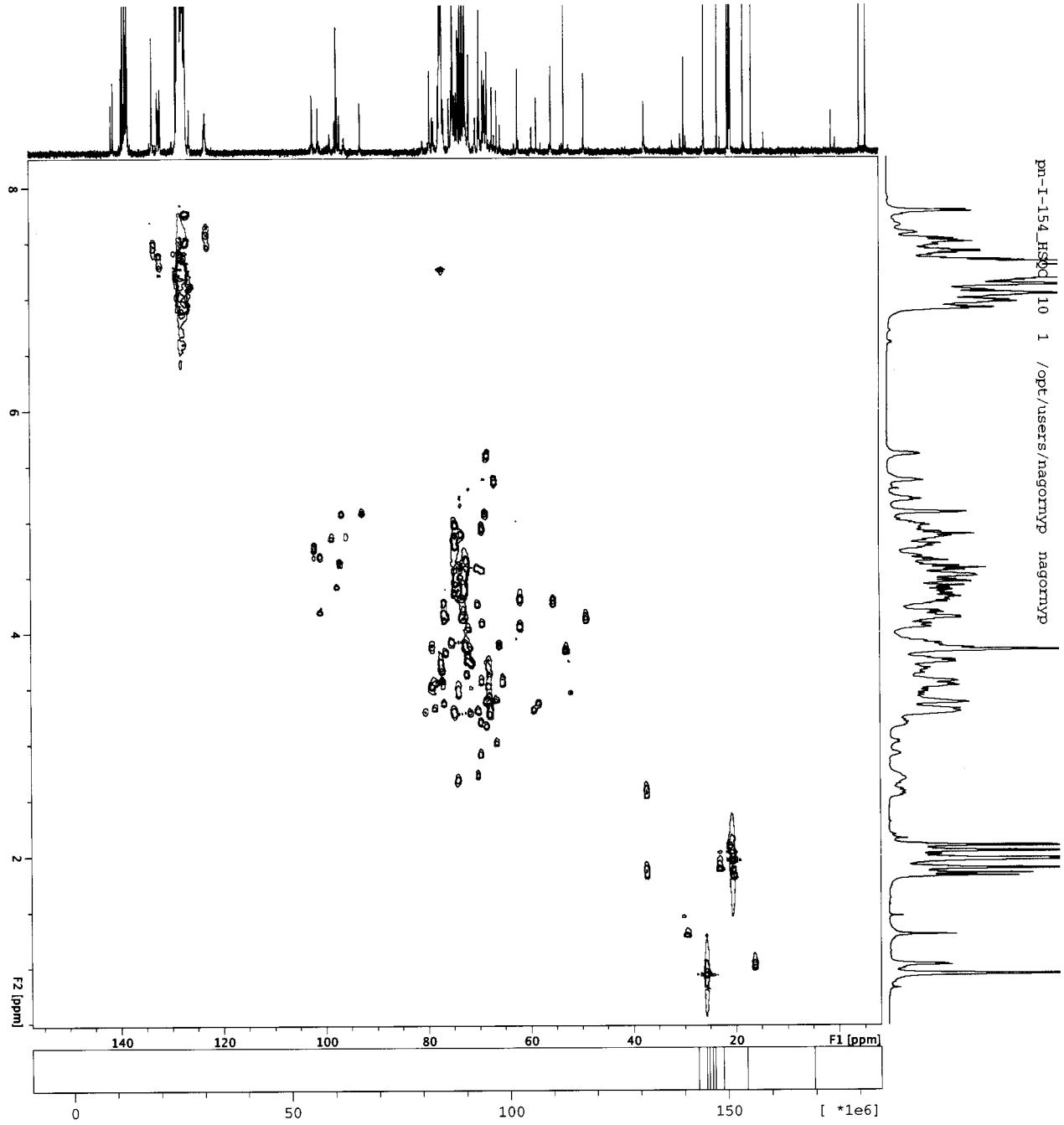
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

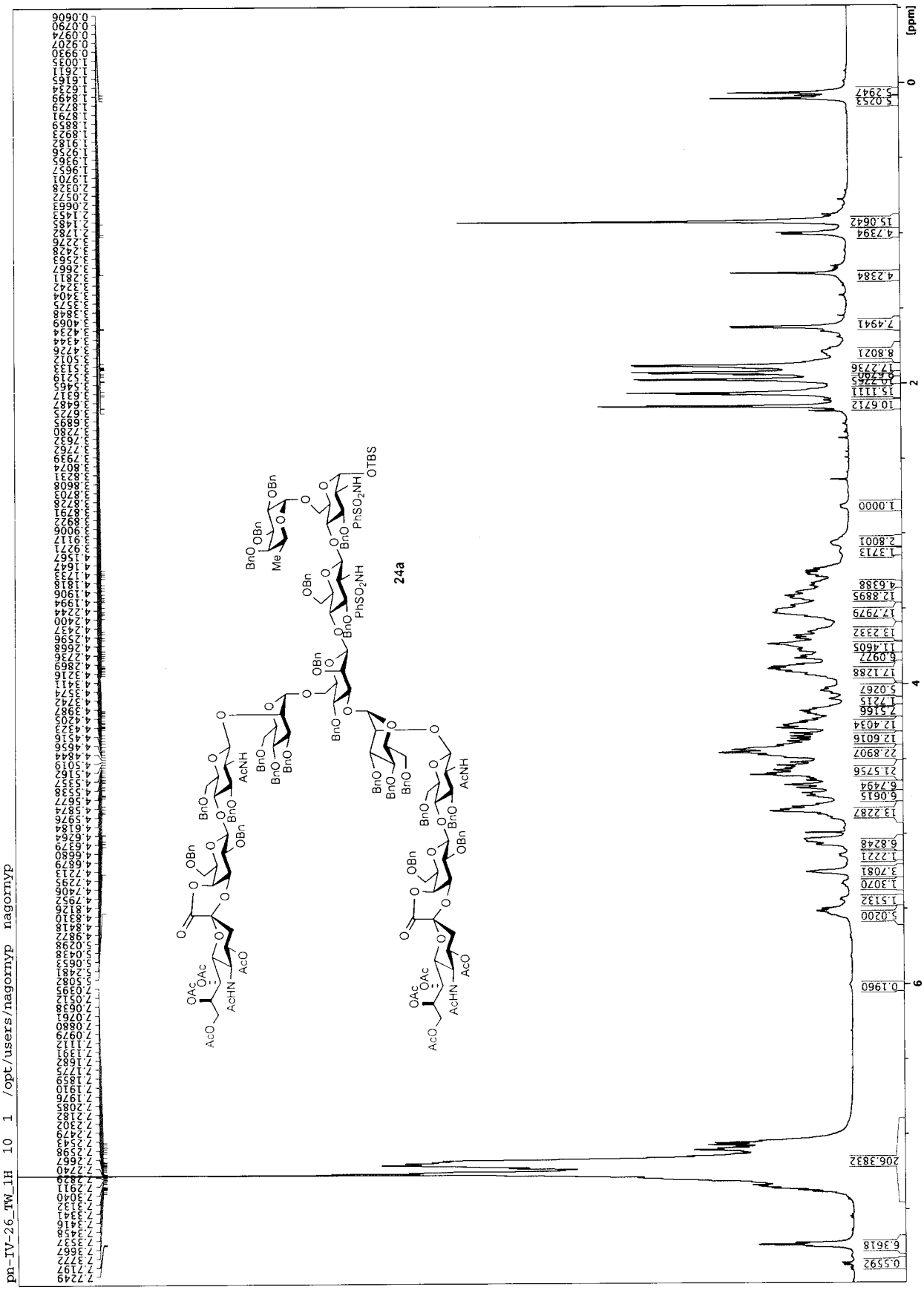
Scale: 8.276 ppm/cm, 1249 Hz/cm

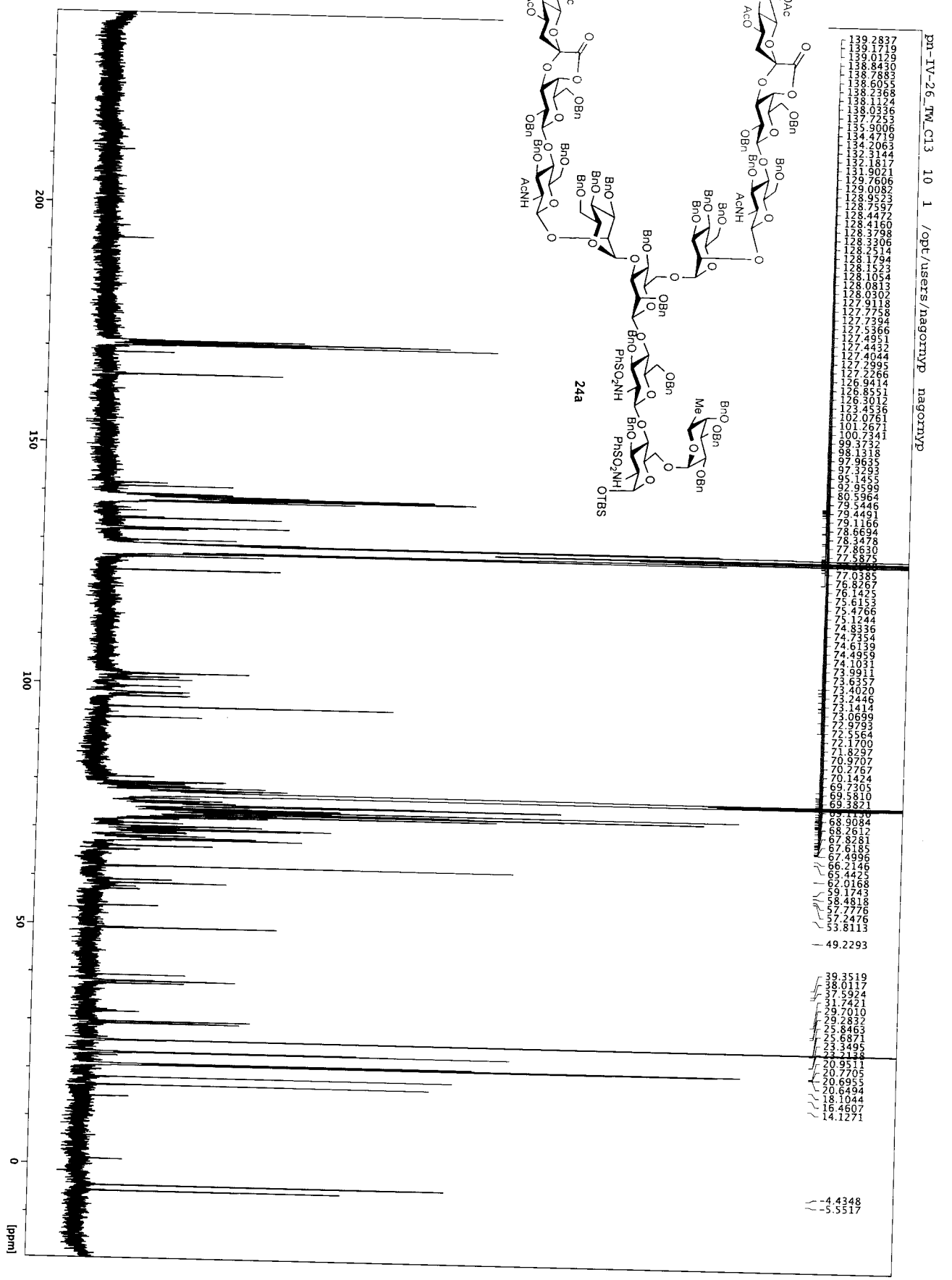

pn-I-154_1H 10 1 /opt/users/nagornyp nagornyp
[rel]
[ppm]
23

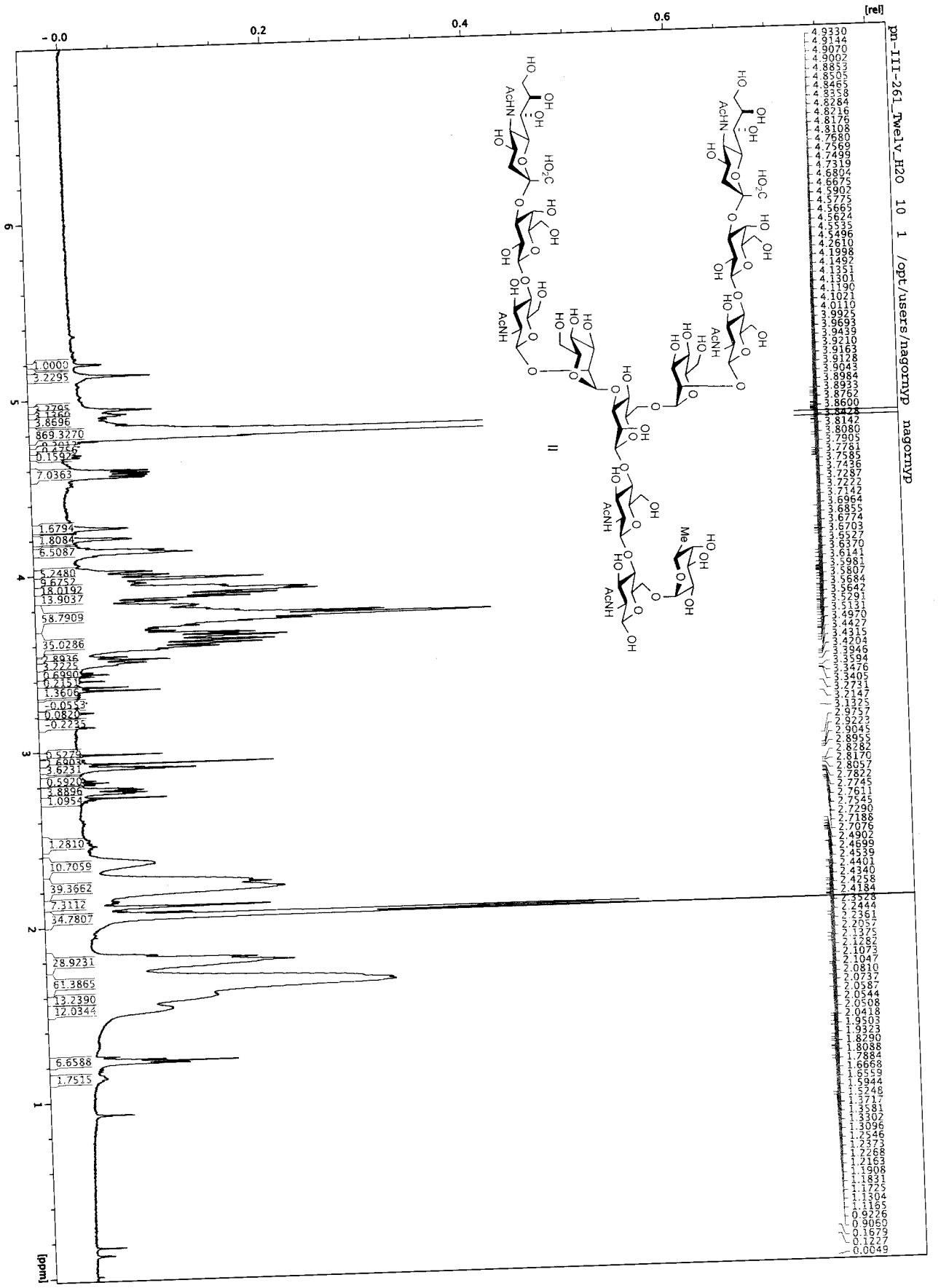

pn-I-154_13C 10 1 /opt/users/nagornyp nagornyp
[rel]
23
S87
200
150
100
50
0
[ppm]


23


F2 [ppm]
F1 [ppm]
pn-I-154_HSQC 10 1 /opt/users/nagornyp nagornyp
[*1e6]


pn-IV-26_TW_1H 10 1 /opt/users/nagornyp nagornyp
24a
[ppm]


pn-IV-26_TW_C13 10 1 /opt/users/nagornyp nagornyp
24a
[ppm]


pn-III-261_Twelv_H2O 10 1 /opt/users/nagornyp nagornyp
[rel]
[ppm]
II