SUPPORTING INFORMATION FOR:

Design of Novel Aminoglycoside Derivatives with Enhanced Suppression of Diseases-Causing Nonsense Mutations

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EXPERIMENTAL SECTION

Dual luciferase readthrough assays

DNA fragments derived from *PCDH15*, *CFTR*, and *IDUA* cDNAs, including the tested nonsense mutation or the corresponding wt codon, and four to six upstream and downstream flanking codons were created by annealing following pairs of complementary oligonucleotides:

Usher Syndrome:

p.R3Xmut/wt:

5'-GATCCCAGAAGATGTTTT/CGACAGTTTTATCTCTGGACAGAGCT-3′

and 5'-CTGTCAGAGATAAAACTGTCA/GAAACATCTTCTG-3';

p.R245Xmut/wt:

5′-GATCCAAAATCTGAATGAGAGGT/CGAACCACCACCACCACCCTCGAGCT-3′

and 5'-CGAGGGTGGTGGTGGTTGTTCG/ACCTCTCATTCAGATTTTG-3';

Cystic Fibrosis:

p.G542Xmut/wt:

5′-TCGACCAATATAGTTCTTT/GGAGAAGGTGGAATCGAGCT-3′ and

and 5'- CGATTCCACCTTCTCA/GAAGAACTATATTGG-3';

Hurler Syndrome:

p.Q70Xmut/wt:

5′-TCGACCCTCAGCTGGGACT/CAGCAGCTCAACCTCGAGCT-3′ and

5'-CGAGGTTGAGCTGCTA/GGTCCCAGCTGAGG-3'.

Fragments were inserted in frame into the polylinker of the p2Luc plasmid between either *BamHI* and *SacI* (*p.R3X and p.R245X*) or *SalI* and *SacI* (all the rest) restriction sites. For the *in vitro* readthrough assays, the obtained plasmids, with addition of the tested aminoglycosides were transcribed and translated using the TNT Reticulocyte Lysate Quick Coupled Transcription/Translation System. Luciferase activity was determined after 90 min of incubation at 30°C, using the Dual Luciferase Reporter Assay System (Promega™). Stop codon readthrough was calculated as previously described.[1]

Protein translation inhibition tests

Prokaryotic *in vitro* translation inhibition by the different aminoglycosides was quantified in coupled transcription/translation assays[2] by using *E. coli* S30 extract for circular DNA with the pBEST*luc* plasmid (Promega), according to the manufacturer′s protocol. Translation reactions (25 μL) that contained variable concentrations of the tested aminoglycoside were incubated at 37°C for 60 min, cooled on ice for 5 min, and diluted with a dilution reagent (tris-phosphate buffer (25 mM, pH 7.8), DTT (2 mM), 1,2-diaminocyclohexanetetraacetate (2 mM), glycerol (10 %), Triton X-100 (1 %) and BSA (1 mg mL^{-1})) into 96-well plates. Eukaryotic *in vitro* translation inhibition was quantified by use of TNT® T7 Quick Coupled Transcription/Translation System with a luciferase T7 control DNA plasmid (Promega), according to the manufacturer protocol. Translation reactions (25 μL) containing variable concentrations of the tested aminoglycoside were incubated at 30 ºC for 60 min, cooled on ice for 5 min, diluted with the dilution reagent and transferred into 96-well plates. In both prokaryotic and eukaryotic systems the luminescence was measured immediately after the addition of the Luciferase Assay Reagent (50 μL; Promega), and the light emission was recorded with a FLx800 Fluorescence Microplate Reader (Biotek). The half-maximal inhibition concentration (IC_{50}) values were obtained from fitting concentration-response curves to the data of at least two independent experiments by using Grafit 5 software.

Antibacterial activity tests

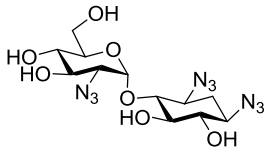
Comparative antibacterial activities were determined in two representative strains of Gram-negative (*E. coli* R477-100) and Gram-positive (*B. subtilis* ATCC-6633) bacteria, by measuring the MIC values using the double-microdilution method according to the National Committee for Clinical Laboratory Standards (NCCLS) (NCCLS. *National Committee for Clinical Laboratory Standards, Performance standards for antimicrobial susceptibility testing. Fifth information supplement: Approved Standard M100-S5*; Villanova, Pa.: NCCLS, 1994.). All the experiments were performed in triplicates and analogous results were obtained in three different experiments.

Chemistry Part

General Techniques:

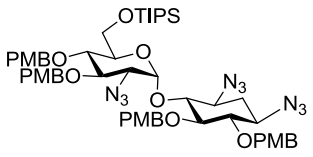
NMR spectra (including ^{1}H, ^{13}C, DEPT, 2D-COSY, 1D TOCSY, HMQC, HMBC) were routinely recorded on a Bruker Avance™ 500 spectrometer, and chemical shifts reported (in ppm) are relative to internal Me_4Si (δ=0.0) with $CDCl_3$ as the solvent, and to MeOD (δ=3.35) as the solvent. ^{13}C NMR spectra were recorded on a Bruker Avance™ 500 spectrometer at 125.8 MHz, and the chemical shifts reported (in ppm) relative to the solvent signal for $CDCl_3$ (δ =77.00), or to the solvent signal for MeOD (δ=49.0). Mass spectra analysis

were obtained either on a Bruker Daltonix Apex 3 mass spectrometer under electron spray ionization (ESI) or by a TSQ-70B mass spectrometer (Finnigan Mat). Reactions were monitored by TLC on Silica Gel 60 F_{254} (0.25 mm, Merck), and spots were visualized by charring with a yellow solution containing $(NH_4)Mo_7O_{24}{\cdot}4H_2O$ (120 g) and $(NH_4)_2Ce(NO_3)_6$ (5 g) in 10% H_2SO_4 (800 mL). Flash column chromatography was performed on Silica Gel 60 (70-230 mesh). All reactions were carried out under an argon atmosphere with anhydrous solvents, unless otherwise noted. G418 (geneticin) and gentamicin were purchased from Sigma. All other chemicals and biochemicals, unless otherwise stated, were obtained from commercial sources. In all biological tests, all the tested aminoglycosides were in their sulfate salt forms [M_w (gr/mol) of the sulfate salts were as follow: comp. **1**– 437.1, comp. **2** – 564.3, comp. comp. **3** – 605.9, comp. (*R*)-**4** – 526.8, comp. (*S*)-**5** – 512.2, comp. **6** – 705.9, comp. **7** – 746. 6, G418 – 692.7, gentamicin – 653.2].



8

Synthesis of (2R, 3S, 4R, 5R, 6S)-5-azido-6-(((1R, 2R, 3S, 4R, 6S)-4, 6-diazido-2,3-dihydroxycyclohexyl)oxy)-2-(hydroxymethyl)tetrahydro-2H-pyran-3,4-diol (8): The title compound was prepared according to previously published.[3] Briefly, the paromamine (1.0 g, 3.0 mmol), $NaHCO_3$ (3.1 g, 36.9 mmol) and copper (II) sulfate (6 mg, 0.24 mmol) were dissolved in water (5.0 mL). Triflic azide stock solution prepared from Tf_2O (4.6 mL, 27.6 mmol) and NaN_3 (3.6 g, 55.7 mmol) was added followed by the addition of methanol (40 mL) to reach the homogeneous solution. The reaction mixture (blue color) was stirred vigorously at room temperature and the completion of the reaction was indicated by the change of blue color to green. After stirring for 48 h, TLC (EtOAc/MeOH 95:5) analysis finally indicated the completion of the reaction. The solvents were evaporated to dryness and the residue was subjected to column chromatography (EtOAc 100%) to yield compound **8** (650 mg, 52 %). ^{1}H NMR (500 MHz, MeOD): 'Ring I': δ_H 5.69 (d, 1H, J = 3.7 Hz, H-1), 3.99 (ddd, 1H, J = 9.9, 4.1, 2.6 Hz, H-5), 3.94 (dd, 1H, J = 10.2, 9.1 Hz, H-3), 3.84 (dd, 1H, J = 11.9, 2.3 Hz, H-6), 3.78 (dd, 1H, J = 11.8, 4.4 Hz, H-6), 3.46 (dd, 1H, J = 9.7, 9.3 Hz, H-4), 3.13 (dd, 1H, J = 10.5, 3.7 Hz, H-2); 'Ring II': δ_H 3.80 (t, 1H, J = 8.8 Hz, H-5), 3.77 – 3.67 (m, 3H, H-1, H-3, H-4), 3.56 (t, 1H, J = 9.6 Hz, H-6), 2.59 – 2.48 (m, 1H), 1.68 (dd, 1H, J = 26.3, 12.7 Hz, H-2). ^{13}C NMR (125 MHz, MeOD): δ_C 99.3 (C1'), 80.7, 77.8 (C5), 77.7 (C6), 73.9 (C5'), 72.4 (C3'), 71.6, 64.8 (C2'), 62.1 (C6'), 61.6, 60.9, 33.1 (C2). MALDI TOFMS calculated for $C_{12}H_{19}N_9O_7$ ($[M+K]^+$) m/e 440.3; measured m/e 440.2).

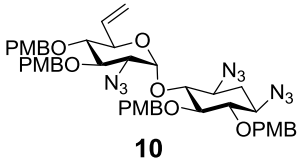


9

Synthesis of (((2R, 3S, 4R, 5R, 6S)-5-azido-6-(((1R, 2R, 3S, 4R, 6S)-4,6-diazido-2,3-bis((4-methoxybenzyl)oxy)cyclohexyl)oxy)-3,4-bis((4-methoxybenzyl)oxy)tetrahydro-2H-pyran-2-yl)methoxy)triisopropylsilane (9): Compound **8** (11.6 g, 28.9 mmol) was dissolved in anhydrous DMF (80 mL) and cooled to 0 ^{o}C. Triisopropylsilyl chloride (TIPSCl, 8 mL, 37.3 mmol) was added dropwise, followed by addition of 4-DMAP (10.6 g, 86.7 mmol). The reaction mixture was allowed to attain the room temperature under stirring, and the reaction progress was monitored by TLC (EtOAc/Hexane 7:3), which indicated the completion after 5 h. The reaction mixture was diluted with ethyl acetate (50 mL) and H_2O (20 mL), and the two layers were separated. The aqueous layer was thoroughly washed with ethyl acetate (4 X 30 mL). The combined organic layers were washed with sat. NaCl solution and dried over anhydrous $MgSO_4$. The solvent was evaporated to dryness and the residue was subjected to column chromatography (EtOAc/Hexane 25:75) to yield corresponding silyl ether (**8a**) (13.3 g, 83%). ^{1}H NMR (500 MHz, $CDCl_3$): **'Ring I'**: δ_H 5.14 (d, 1H, J = 4.0 Hz, H-1), 4.09 – 4.02 (m, 2H, H-3, H-6), 3.98 (td, 1H, J_1 = 8.0, J_2 = 4.5 Hz, H-5), 3.82 (dd, 1H, J_1 = 9.5, J_2 = 8.0 Hz, H-6), 3.66 (t, 1H, J = 9.0 Hz, H-4), 3.48 (dd, 1H, J_1 = 10.5, J_2 = 4.0 Hz, H-2); **'Ring II'**: δ_H 3.52 (t, 1H, J = 8.0 Hz, H-5), 3.47 – 3.37 (m, 2H, H-1, H-6), 3.34 – 3.22 (m, 2H, H-3, H-4), 2.29 (dt, 1H, J_1 = 12.0, J_2 = 4.0 Hz, H-2eq), 1.47 (ddd, 1H, J_1 = J_2 = J_3 = 12.0 Hz, H-2ax); **The additional peaks in the spectrum were identified as follow**: δ_H 1.16 – 1.09 (m, 3H, TIPS), 1.07 (s, 12H, TIPS), 1.06 (s, 6H, TIPS). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 99.3 (C1'), 83.4 (C4), 76.1 (C5), 75.5 (C6), 75.1 (C4'), 72.6 (C3'), 69.6 (C5'), 66.0 (C6'), 63.5 (C2'), 59.8 (C1), 58.9 (C3), 32.1 (C2), 17.9 (2C, TIPS), 11.8 (TIPS). MALDI TOFMS calculated for $C_{21}H_{39}N_9O_7Si$ ($[M+Na]^+$) m/e 580.6; measured m/e 580.3).

To a stirred solution of the silyl ether from above (9.82 g, 17.6 mmol) and sodium hydride (3.38 g, 140 mmol) in DMF (200 mL), was added *p*-Methoxybenzyl chloride (14.3 mL, 105.3 mmol) at 0 ^{o}C. The reaction progress was monitored by TLC (EtOAc/Hexane 3:7). After 8.0 h the reaction was completed and ice was added in small potrions to quench the reaction. The mixture was diluted with ethyl acetate (100 mL) and washed with water (2 x 50 mL). The combined aqueous layers were extracted with diethyl ether (2 x 50 mL); the combined organic layers were dried over anhydrous $MgSO_4$, and evaporated to dryness. The residue was purified by column chromatography (EtOAc/Hexane 8:92) to yield compound **9** (15.28 g, 84%). ^{1}H NMR (500 MHz, $CDCl_3$): **'Ring I'**: δ_H

5.45 (d, 1H, J = 3.5 Hz, H-1), 3.94 (m, 2H, H-3, H-5), 3.88 – 3.78 (m, 2H, H-6), 3.59 (t, 1H, J = 9.5 Hz, H-4), 3.17 (dd, 1H, J_1 = 10.5, J_2 = 3.5 Hz, H-2); **'Ring II'**: δ_H 3.56 – 3.42 (m, 2H, H-4, H-5), 3.41 – 3.32 (m, 1H, H-1), 3.32 – 3.20 (m, 2H, H-3, H-6), 2.17 (dt, 1H, J_1 = 12.5, J_2 = 4.0 Hz, H-2eq), 1.34 (ddd, 1H, J_1 = J_2 = J_3 = 12.5 Hz, H-2ax); **The additional peaks in the spectrum were identified as follow**: δ_H 7.21 (d, 2H, J = 8.0 Hz, PMB), 7.17 (d, 6H, J = 8.0 Hz, PMB), 6.85 – 6.72 (m, 8H, PMB), 4.86 (d, 1H, J = 10.0 Hz, PMB), 4.80 – 4.65 (m, 6H, PMB), 4.61 (d, 1H, J = 10.0 Hz, PMB), 3.74 – 3.68 (m, 12H, PMB), 1.04 – 0.94 (m, 21H, TIPS). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 159.5 (PMB), 159.4 (PMB), 159.3 (PMB), 159.2 (PMB), 130.7 (PMB), 130.3 (PMB), 130.2 (PMB), 129.9 (PMB), 129.8 (PMB), 129.7 (PMB), 129.3 (PMB), 128.7 (PMB), 113.9 (2C, PMB), 97.5 (C1'), 84.5, 84.4, 79.8, 77.9 (C4'), 76.9, 75.6 (PMB), 75.2 (PMB), 74.9 (PMB), 74.5 (PMB), 72.9, 63.5 (C2'), 62.3 (C6'), 60.3 (C1), 59.5, 55.3 (4C, PMB), 32.4 (C2), 18.1 (2C, TIPS), 12.1 (TIPS). MALDI TOFMS calculated for $C_{53}H_{71}N_9O_{11}Si$ ($[M+Na]^+$) m/e 1061.2; measured m/e 1061.6).



10

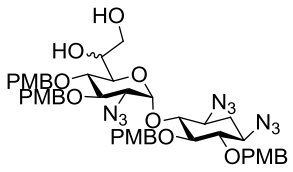
Synthesis of (2R, 3R, 4R, 5R, 6R)-3-azido-2-(((1R,2R,3S,4R,6S)-4,6-diazido-2,3-bis((4-methoxybenzyl)oxy)cyclohexyl)oxy)-4,5-bis((4-methoxybenzyl)oxy)-6-vinyltetrahydro-2H-pyran (10): To a stirred solution of compound **9** (19.82 g, 19 mmol) in THF (230 mL) at 0 ^{o}C, TBAF (11.05 mL, 38.1 mmol) was added and the reaction progress was monitored by TLC (EtOAc/Hexane 2:3). After 19 h, the solvent was evaporated to dryness and the obtained residue was subjected to column chromatography (EtOAc/Hexane 3:7) to yield corresponding 6'-alcohol (14.74 g, 88%). ^{1}H NMR (500 MHz, $CDCl_3$): **'Ring I'**: δ_H 5.51 (d, 1H, J = 4.0 Hz, H-1), 3.98 (dt, 1H, J_1 = 8.0, J_2 = 2.0 Hz, H-5), 3.92 (t, 1H, J = 10.0 Hz, H-3), 3.70 (dd, 1H, J_1 = 12.0, J_2 = 2.0 Hz, H-6), 3.64 (dd, 1H, J_1 = 12.0, J_2 = 2.0 Hz, H-6), 3.49 (dd, 1H, J_1 = 10.0, J_2 = 8.0 Hz, H-4), 3.17 (dd, 1H, J_1 = 10.0, J_2 = 4.0 Hz, H-2); **'Ring II'**: δ_H 3.53 – 3.44 (m, 2H, H-4, H-5), 3.38 (ddd, 1H, J_1 = 12.5, J_2 = 10.0, J_3 = 4.5 Hz, H-1), 3.34 – 3.24 (m, 2H, H-3, H-6), 2.20 (dt, 1H, J_1 = 12.5, J_2 = 4.5 Hz, H-2eq), 1.36 (ddd, 1H, J_1 = J_2 = J_3 = 12.5 Hz, H-2ax); **The additional peaks in the spectrum were identified as follow**: δ_H 7.23 (d, 2H, J = 8.0 Hz, PMB), 7.20 – 7.14 (m, 6H, PMB), 6.83 – 6.75 (m, 8H, PMB), 4.89 (d, 1H, J = 10.0 Hz, PMB), 4.80 – 4.68 (m, 6H, PMB), 4.55 (d, 1H, J = 10.0 Hz, PMB), 3.73 – 3.7 (m, 12H, PMB). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 159.5 (PMB), 159.4 (2C, PMB), 159.2 (PMB), 130.2 (PMB), 130.1 (2C, PMB), 129.9 (PMB), 129.8 (PMB), 129.6 (2C, PMB), 128.8 (PMB), 114.0 (2C, PMB), 113.9 (2C, PMB), 97.6 (C1'), 84.4, 84.3, 79.8 (C3'), 77.4, 75.6 (PMB), 75.2 (PMB), 75.1 (PMB), 74.6 (PMB),

72.0 (C5'), 63.3 (C2'), 61.4 (C6'), 60.3 (C1), 59.5, 55.3 (3C, PMB), 32.4 (C2). MALDI TOFMS calculated for $C_{44}H_{51}N_9O_{11}$ ($[M+Na]^+$) m/e 903.3; measured m/e 903.9).

To a solution of 6'-alcohol from the above reaction (100 mg, 0.11 mmol) in ethyl acetate (5 mL), IBX (95 mg, 0.33 mmol) was added in one portion. The resulting suspension was heated at 80 ^oC and stirred vigorously. After the reaction was completed (3.5 h) as indicated by TLC (EtOAc/Hexane 2:3), the reaction was cooled to room temperature and filtered through the celite. The celite was thoroughly washed with ethyl acetate (2 x 50 mL) and the combined organic layers were evaporated under reduced pressure. The crude product was subjected to flash column chromatography (EtOAc/Hexane 35:65) to yield the 6'-aldehyde (85 mg, 85%). ^1H NMR (500 MHz, $CDCl_3$): **'Ring I'**: δ_H 9.53 (s, 1H, H-6), 5.56 (d, 1H, J = 4.0 Hz, H-1), 4.60 (d, 1H, J = 10.0 Hz, H-4), 3.98 (dd, 1H, J_1 = J_2 = 10.0 Hz, H-3), 3.52 – 3.45 (m, 1H, H-5), 3.17 (dd, 1H, J_1 = 10.0, J_2 = 4.0 Hz, H-2); **'Ring II'**: δ_H 3.53 – 3.43 (m, 2H, H-4, H-5), 3.37 (ddd, 1H, J_1 = 12.0, J_2 = 10.0, J_3 = 4.0 Hz, H-1), 3.33 – 3.24 (m, 2H, H-3, H-6), 2.20 (dt, 1H, J_1 = 12.5, J_2 = 4.0 Hz, H-2eq), 1.35 (ddd, 1H, J_1 = J_2 = J_3 = 12.5 Hz, H-2ax); **The additional peaks in the spectrum were identified as follow**: δ_H 7.23 (d, 2H, J = 8.0 Hz, PMB), 7.19 – 7.10 (m, 6H, PMB), 6.83 – 6.72 (m, 8H, PMB), 4.89 (d, 1H, J = 10.0 Hz, PMB), 4.80 – 4.64 (m, 6H, PMB), 4.51 (d, 1H, J = 10.0 Hz, PMB), 3.73 (s, 3H, PMB), 3.71 (s, 6H, PMB), 3.70 (s, 3H, PMB). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 197.3 (CHO), 159.7 (PMB), 159.6 (2C, PMB), 159.2 (PMB), 130.2 (PMB), 130.0 (PMB), 129.9 (2C, PMB), 129.7 (PMB), 129.6 (PMB), 129.3 (PMB), 128.6 (PMB), 114.1 (PMB), 114.0 (3C, PMB), 97.5 (C1'), 84.3, 84.2, 79.8 (C3'), 78.0, 77.6, 75.6 (PMB), 75.5 (PMB), 75.2 (C4'), 75.1 (PMB), 74.8 (PMB), 62.8 (C2'), 60.2 (C1), 59.1, 55.4 (PMB), 55.3 (PMB), 32.21 (C2). MALDI TOFMS calculated for $C_{44}H_{49}N_9O_{11}$ ($[M+Na]^+$) m/e 902.3; measured m/e 902.3).

To a cooled suspension of Methyltriphenylphosphonium Iodide (70 mg, 0.19 mmol) in anhydrous THF at 0 ^oC, *n*-BuLi (1.6 M in hexane, 136 µL) was added drop wise and the resulted yellow solution was stirred for an additional 30 min at 0 ^oC. The 6'-aldehyde from the previous step (61 mg, 0.069 mmol) in anhydrous THF (0.3 mL) was added at 0 ^oC, and the reaction was allowed to stir for an additional 1.5 h at room temperature. After completion of the reaction as indicated by TLC (EtOAc/Hexane 2:3), the reaction was quenched with saturated NH_4Cl solution. The layers were separated and the aqueous layer was extracted with ether (2 X 10 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and evaporated to dryness. The crude product was purified by flash chromatography (EtOAc/Hexane 2.5:7.5) to yield compound **10** (27 mg, 56%). ^1H NMR (500 MHz, $CDCl_3$): **'Ring I'**: δ_H 5.83 – 5.74 (m, 1H, H-6), 5.47 (d, 1H, J = 4.0 Hz, H-1),

5.37 (d, 1H, J = 16.5 Hz, H-7trans), 5.21 (d, 1H, J = 9.5 Hz, H-7cis), 4.49 (dd, 1H, J_1 = 9.5, J_2 = 7.5 Hz, H-5), 3.90 (t, 1H, J = 9.5 Hz, H-3), 3.25 – 3.14 (m, 2H, H-2, H-4); **'Ring II'**: δ_H 3.54 – 3.44 (m, 2H, H-4, H-5), 3.38 (ddd, 1H, J_1 = 12.0, J_2 = 9.5, J_3 = 4.0 Hz, H-1), 3.34 – 3.25 (m, 2H, H-3, H-6), 2.21 (dt, 1H, J_1 = 12.5, J_2 = 4.0 Hz, H-2eq), 1.38 (ddd, 1H, J_1 = J_2 = J_3 = 12.5 Hz, H-2ax); **The additional peaks in the spectrum were identified as follow**: δ_H 7.25 – 7.09 (m, 8H, PMB), 6.84 – 6.73 (m, 8H, PMB), 4.88 (d, 1H, J = 10.0 Hz, PMB), 4.77 (dd, 2H, J = 10.0, 2.5 Hz, PMB), 4.74 – 4.66 (m, 3H, PMB), 4.59 (d, 1H, J = 10.5 Hz, PMB), 4.52 (d, 1H, J = 10.5 Hz, PMB), 3.73 (s, 3H, PMB), 3.72 (s, 6H, PMB), 3.71 (s, 3H, PMB). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 159.5 (PMB), 159.4 (2C, PMB), 159.2 (PMB), 134.9 (C6'), 130.3 (PMB), 130.2 (2C, PMB), 129.9 (2C, PMB), 129.6 (2C, PMB), 128.7 (PMB), 118.8 (C7'), 114.0 (PMB), 113.9 (2C, PMB), 97.6 (C1'), 84.4, 84.3, 82.4 (C4'), 79.4 (C3'), 77.6, 75.6 (PMB), 75.3 (PMB), 75.0 (PMB), 74.6 (PMB), 72.7 (C5'), 63.4 (C2'), 60.3 (C1), 59.3, 55.4 (PMB), 55.3 (PMB), 32.3 (C2). MALDI TOFMS calculated for $C_{45}H_{51}N_9O_{10}$ ($[M+Na]^+$) m/e 900.9; measured m/e 900.5).



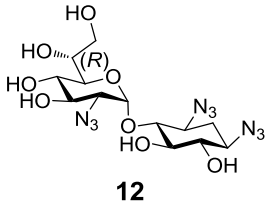
11

Synthesis of 1-((2R, 3S, 4R, 5R, 6S)-5-azido-6-(((1R, 2R, 3S, 4R, 6S)-4,6-diazido-2,3-bis((4-methoxybenzyl)oxy)cyclohexyl)oxy)-3,4-bis((4-methoxybenzyl)oxy)tetrahydro-2H-pyran-2-yl)ethane-1,2-diol (11): To a stirred solution of compound **10** (383 mg, 0.436 mmol) in acetone (5 mL), water (1.5 mL) and *t*-BuOH (5 mL), $K_2OsO_4.2H_2O$ (16 mg, 0.043 mmol) and NMO (181 µL) were added sequentially. The progress of the reaction was monitored by TLC (EtOAc/Hexane 2:3), which indicated the completion after 24 h. The solvent was evaporated to dryness; the residue was dissolved in EtOAc to which an aqueous solution of $Na_2S_2O_3$ was added. The layers were separated and the organic phase was washed with brine, dried over $MgSO_4$ and evaporated. The crude product was subjected to column chromatography (EtOAc/Hexane 1:1) to yield compound **11** (370 mg, 93%) as a 6'-diasteromeric mixture.

Synthesis of (2R, 3S, 4R, 5R, 6S)-5-azido-6-(((1R, 2R, 3S, 4R, 6S)-4,6-diazido-2,3-dihydroxycyclohexyl)oxy)-2-((R)-1,2-dihydroxyethyl)tetrahydro-2H-pyran-3,4-diol (12) & (2R, 3S,4R, 5R, 6S)-5-azido-6-(((1R, 2R, 3S, 4R, 6S)-4,6-diazido-2,3-dihydroxycyclohexyl)oxy)-2-((S)-1,2-dihydroxyethyl)tetrahydro-2H-pyran-3,4-diol (13): Compound **11** (220 mg, 1.0 equiv.) from

above was stirred with 2, 3-dichloro-5, 6-dicyano-1, 4-benzoquinone (DDQ) (383 mg, 6 equiv.) in methylene chloride and water (20:1 v/v, 15 mL) at room temperature. Soon after the addition of DDQ, a dark green color charge transfer complex formed immediately and slowly faded to orange color as the reaction progressed. TLC (EtOAc/MeOH 98:2) showed that the reaction completed after 15 h. The solvents were evaporated and the residue was loaded onto the silicagel column without prior work up. Due to high polarity of the titled compound, this column chromatography allowed the removal of only parts of the DDQ reaction byproducts. Therefore, in order to obtain the analytically pure product, the fractions containing the product were combined, evaporated and the residue was then subjected to peracetylation and deacetylation steps. The crude material from above was dissolved in anhydrous pyridine (5 mL) and cooled to 0 ^{o}C. Acetic anhydride (0.73 mL, 9 equiv.) was added drop wise, followed by the addition of 4-DMAP (0.621g, 6 equiv.). After completion of the reaction (2 h) as indicated by TLC (EtOAc/Hexane 2:3), the reaction was diluted with EtOAc (20 mL) and washed with 5% HCl solution, Sat. $NaHCO_3$, brine and dried over anhydrous $MgSO_4$. The solvent was evaporated to dryness and the residue was subjected to a column chromatography (EtOAc/Hexane 3:7) to yield the corresponding peracetate as an inseparable mixture of 6'-diastereomers (150 mg, 91% for 2 steps).

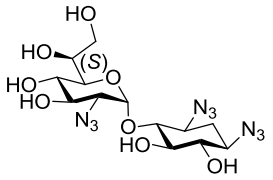
The peracetate (215 mg, 0.314 mmol) from above was dissolved in anhydrous MeOH (5 mL) and NaOMe (152 mg, 2.81 mmol) was added in one portion to the stirred solution at room temperature. The reaction progress was monitored by TLC (EtOAc/MeOH 95:5), which indicated completion after 4 h. The reaction mixture was passed through a short silica gel column and the product was eluted with MeOH. The fractions with the compound were combined, evaporated and the crude product was subjected to an additional column chromatography (EtOAc/MeOH 99:1), which allowed complete separation of the two diastereomers, the major (R_f =0.36) and minor one (R_f =0.2). The major one was later assigned as the 6'-(*R*)-diastereomer (compound **12**) and the minor one as the 6'-(*S*)-diastereomer (compound **13**).



12

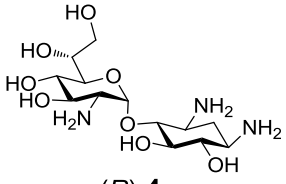
Major Diastereomer (12) : ^{1}H NMR (500 MHz, MeOD): **'Ring I'**: δ_H 5.68 (d, 1H, *J*= 4.0 Hz, H-1), 4.04 (dd, 1H, J_1 = 9.5, J_2 = 4.0 Hz, H-4), 3.97 – 3.92 (m, 1H, H-6), 3.93 (t, 1H, *J* = 10.0 Hz, H-3), 3.79 (dd, 1H, *J* = 11.5, 3.5 Hz, H-7), 3.70 (dd, 1H, J_1 = 11.5, J_2 = 7.0 Hz, H-7), 3.58 (t, 1H, *J* = 9.5 Hz,

H-5), 3.13 (dd, 1H, J_1 = 10.0, J_2 = 4.0 Hz, H-2); **'Ring II'**: δ_H 3.57 – 3.47 (m, 3H, H-3, H-4, H-5), 3.44 (ddd, 1H, J_1 = 16.5, J_2 = 8.5, J_3 = 4.0 Hz, H-1), 3.29 (t, 1H, J = 9.5 Hz, H-6), 2.26 (dt, 1H, J_1 = 12.5, J_2 = 4.0 Hz, H-2eq), 1.43 (ddd, 1H, J_1 = J_2 = J_3 = 12.5 Hz, H-2ax). ^{13}C NMR (125 MHz, MeOD): δ_C 99.1 (C1'), 80.5, 77.9 (C6), 77.9, 74.8 (C6'), 73.7 (C4'), 72.9 (C5'), 72.3 (C3'), 64.5 (C2'), 64.3 (C7'), 61.7 (C1), 61.0, 33.3 (C2). MALDI TOFMS calculated for $C_{13}H_{27}N_3O_8$ ($[M+H]^+$) m/e 432.3; measured m/e 432.8).



13

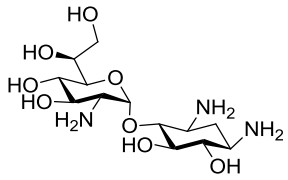
Minor Diastereomer (13) : ^{1}H NMR (500 MHz, MeOD): **Ring I'**: δ_H 5.72 (d, 1H, J = 3.6 Hz, H-1), 4.00 (ddd, 1H, J_1 = 6.8, J_2 = 6.0, J_3 = 1.1 Hz, H-6), 3.97 – 3.91 (m, 2H, H-5, H-3), 3.74 – 3.67 (m, 2H, H-7, H-7), 3.64 – 3.59 (m, 1H, H-4), 3.10 (dd, 1H, J_1 = 10.5, J_2 = 3.7 Hz,H-1); **'Ring II'**: δ_H 3.57 – 3.50 (m, 2H, H-1, H-6), 3.45 – 3.37 (m, 2H, H-3, H-4), 3.26 (t, 1H, J = 9.5 Hz, H-5), 2.24 (dt, 1H, J_1 = 12.8, J_2 = 4.4 Hz, H-2eq), 1.40 (ddd, 1H, J_1 = J_2 = J_3 = 12.5 Hz, H-2ax). ^{13}C NMR (125 MHz, MeOD): δ_C 99.1 (C-1'), 80.1 (C-4), 78.0 (C-6), 77.8 (C-5), 73.1 (C-5'), 72.3 (C-3'), 71.3 (C-4'), 70.8 (C-6'), 65.3 (C-7'), 64.4 (C-2'), 61.7 (C-3), 61.1 (C-1), 33.3 (C-2). MALDI TOFMS calculated for $C_{13}H_{27}N_3O_8$ ($[M+H]^+$) m/e 432.3; measured m/e 432.8).



(*R*)**-4**

Synthesis of (2R, 3S, 4R, 5R, 6S)-5-amino-6-(((1R, 2R, 3S, 4R, 6S)-4,6-diamino-2,3-dihydroxycyclohexyl)oxy)-2-((R)-1,2-dihydroxyethyl)tetrahydro-2H-pyran-3,4-diol [(*R*)-4]: To a stirred solution of compound **12** (82 mg, 0.19 mmol) in a mixture of THF (3 mL) and aqueous NaOH (1 mM, 5 mL), PMe_3 (1 M solution in THF, 0.15 mL, 2.5 mmol) was added. The progress of the reaction was monitored by TLC [CH_2Cl_2/MeOH/H_2O/$MeNH_2$ (33% solution in EtOH), 10:15:6:15], which indicated completion after 1 h. The reaction mixture was purified by flash chromatography on a short column of silica gel. The column was washed with the following solvents: THF (100 mL), CH_2Cl_2 (100 mL), EtOH (50 mL), and MeOH (100 mL). The product was then eluted with the mixture

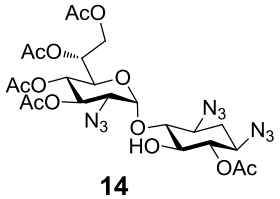
of 5% $MeNH_2$ solution (33% solution in EtOH) in 80% MeOH. Fractions containing the product were combined and evaporated under vacuum. The pure product was obtained by passing the above product through a short column of Amberlite CG50 (NH_4^+ form). First, the column was washed with water, then the product was eluted with a mixture of 10% NH_4OH in water to yield compound (*R*)-**4** (49.0 mg, 73%). For the storage and biological tests, compound (*R*)-**4** was converted to its sulfate salt form as follow. The free base form was dissolved in water, the pH was adjusted to 6.7 with H_2SO_4 (0.1 N) and lyophilized to afford the sulfate salt of (*R*)-**4** as white foamy solid. ^{1}H NMR (500 MHz, MeOD, -NH_2 form): **'Ring I'**: δ_H 5.18 (d, 1H, *J* = 4.0Hz, H-1), 3.98 – 3.93 (m, 1H, H-6), 3.90 (dd, 1H, J_1 = 10.0, J_2 =4.0 Hz, H-4), 3.76 (dd, 1H, J_1 = 11.5, J_2 =4.0 Hz, H-7), 3.70 (dd, 1H, J_1 = 11.5, J_2 = 6.0 Hz, H-7), 3.51 (t, 1H, *J* = 10.0 Hz, H-3), 3.44 (m, 1H, H-5), 2.74 (dd, 1H, J_1 = 10.0, J_2 =4.0 Hz, H-2); **'Ring II'**: δ_H 3.43 (t, 1H, *J* = 9.0 Hz, H-5), 3.20 (t, 1H, *J* = 9.0 Hz, H-4), 3.10 (t, 1H, *J* = 9.5 Hz, H-6), 2.77 (ddd, 1H, J_1 = 10.5, J_2 =9.0, J_3 = 5.0 Hz, H-3), 2.66 (ddd, 1H, J_1 = 10.5, J_2 = 9.5, J_3 = 5.0 Hz, H-1), 2.02 (dt, 1H, J_1 = 12.5, J_2 =4.0 Hz, H-2eq), 1.22 (ddd, 1H, J_1 = J_2 = J_3 = 12.5 Hz, H-2ax).^{13}C NMR (125 MHz, MeOD): δ_C 102.9 (C-1'), 90.0 (C-4), 78.2 (C-6), 77.5, 75.6 (C-3'), 74.3 (C-4'), 73.6 (C-6'), 73.3, 63.3 (C-7'), 57.1 (C-2'), 52.4 (C-3), 51.3 (C-1), 36.7 (C2). MALDI TOFMS calculated for $C_{13}H_{27}N_3O_8$ ($[M+H]^+$) m/e 354.3; measured m/e 354.8).



(*S*)-**5**

Synthesis of (2R, 3S, 4R, 5R, 6S)-5-amino-6-(((1R, 2R, 3S, 4R, 6S)-4,6-diamino-2,3-dihydroxycyclohexyl)oxy)-2-((S)-1,2-dihydroxyethyl)tetrahydro-2H-pyran-3,4-diol [(*S*)-5]: To a stirred solution of compound **13** (52 mg, 0.12 mmol) in a mixture of THF (3 mL) and aqueous NaOH (1 mM, 5 mL), PMe_3 (1 M solution in THF, 0.15 mL, 2.5 mmol) was added. The progress of the reaction was monitored by TLC [CH_2Cl_2/MeOH/H_2O/$MeNH_2$ (33% solution in EtOH), 10:15:6:15], which indicated completion after 1 h. The reaction mixture was purified by flash chromatography on a short column of silica gel. The column was washed with the following solvents: THF (100 mL), CH_2Cl_2 (100 mL), EtOH (50 mL), and MeOH (100 mL). The product was then eluted with the mixture of 5% $MeNH_2$ solution (33% solution in EtOH) in 80% MeOH. Fractions containing the product were combined and evaporated under vacuum. The pure product was obtained by passing the above product through a short column of Amberlite CG50 (NH_4^+ form). First, the column was washed with water, then the product was eluted with a mixture of 10% NH_4OH in water to yield compound (*S*)-**5** (36.0

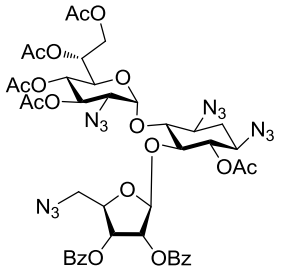
mg, 78%). For the storage and biological tests, compound (*S*)-**5** was converted to its sulfate salt form as follow. The free base form was dissolved in water, the pH was adjusted to 6.7 with H_2SO_4 (0.1 N) and lyophilized to afford the sulfate salt of (*S*)-**5** as white foamy solid. ^{1}H NMR (500 MHz, MeOD, -NH_2 form): '**Ring I'**: δ_H 5.28 (d, 1H, *J* = 3.8 Hz, H-1'), 3.97 (td, 1H, J_1 = 7.1, J_2 = 1.0 Hz, H-6'), 3.89 – 3.82 (m, 1H, H-4'), 3.63 (d, 2H, *J* = 7.2 Hz, H-7', H-7'), 3.59 – 3.51 (m, 2H, H-5', H-3'), 2.72 (m, 1H, H-2'); **'Ring II'**: δ_H 3.41 (t, 1H, *J* = 9.1 Hz, H-5), 3.20 (t, 1H, *J* = 9.2 Hz, H-4), 3.08 (t, 1H, *J* = 9.4 Hz, H-6), 2.74 (m, 1H, H-3), 2.64 (ddd, 1H, J_1 = 12.2, J_2 = 9.7, J_3 = 4.1 Hz, H-1), 2.00 (dt, 1H, J_1 = 12.9, J_2 = 4.1 Hz, H-2eq), 1.21 (ddd, 1H, $J_1 = J_2 = J_3$ = 12.3 Hz, H-2ax). ^{13}C NMR (125 MHz, MeOD): δ_C 102.9 (C-1'), 89.6 (C-4), 79.0 (C-6), 77.9 (C-5), 75.8 (C-3'), 72.3 (C-4'), 71.1 (C-5'), 70.2 (C-6'), 63.2 (C-7'), 57.1 (C-2'), 52.4 (C-1), 51.4 (C-3), 37.7 (C-2). MALDI TOFMS calculated for $C_{13}H_{27}N_3O_8$ ($[M+H]^+$) m/e 354.3; measured m/e 354.8).



14

Synthesis of (2R, 3S, 4R, 5R, 6S)-6-(((1R, 2S, 3S, 4R, 6S)-3-acetoxy-4, 6-diazido-2-hydroxycyclohexyl)oxy)-5-azido-2-((R)-1,2-diacetoxyethyl)tetrahydro-2H-pyran-3,4-diyl diacetate (14): Compound **12** (370 mg, 0.857mmol) was dissolved in anhydrous pyridine (8 mL) and cooled to -20 ^{o}C. Acetic anhydride (0.45 mL, 4.8 mmol) was added dropwise and allowed the reaction to progress at -20 ^{o}C. The reaction progress was monitored by TLC, which indicated completion after 17 hr. The reaction mixture was diluted with EtOAc, and extracted with aqueous solution of HCl (2%), saturated aqueous $NaHCO_3$, and brine. The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated. The crude product was purified by silica gel column chromatography (EtOAc/Hexane 3:7) to afford **14** (292 mg, 53 % yield). ^{1}H NMR (500 MHz, $CDCl_3$): '**Ring I'**: δ_H 5.45 (dd, 1H, J_1 = 10.5, J_2 = 9.3 Hz, H-3'), 5.37 (d, 1H, *J* = 3.5 Hz, H-1'), 5.19 (ddd, 1H, J_1 = 7.6, J_2 = 4.0, J_3 = 2.0 Hz, H-6'), 5.07 (dd, 1H, J_1 = 10.4, J_2 = 9.2 Hz, H-4'), 4.40 (dd, 1H, J_1 = 10.5, J_2 = 1.8 Hz, H-5'), 4.31 (dd, 1H, J_1 = 12.0, J_2 = 4.1 Hz, H-7'), 4.19 – 4.08 (m, 1H, H-7'), 3.63 – 3.56 (m, 1H, H-2'); **'Ring II'**: δ_H 4.91 (dd, 1H, J_1 = 12.8, J_2 = 7.1 Hz, H-6) 3.66 (td, 1H, J_1 = 9.6, J_2 = 3.5 Hz, H-5), 3.53 (ddd, 1H, J_1 = 12.4, J_2 = 10.1, J_3 = 4.5 Hz, H-1), 3.45 (dd, 1H, J_1 = 19.1, J_2 = 9.2 Hz, H-4), 3.38 – 3.31 (m, 1H, H-3), 2.38 (dt, 1H, J_1 = 13.2, J_2 = 4.4 Hz, H-2eq), 1.58 (ddd, 1H, $J_1 = J_2 = J_3$ = 12.6 Hz, H-2ax). The additional peaks in the spectrum were identified as follow: δ_H 2.17 (s, 3H, CH_3CO), 2.08

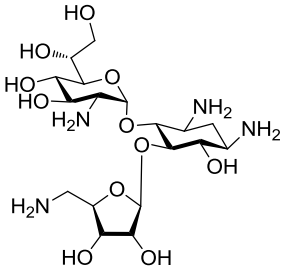
(d, 9H, J = 1.5 Hz, CH_3CO), 2.04 (s, 3H, CH_3CO). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 170.7 (C=O), 170.6 (C=O), 170.2 (C=O), 170.0 (C=O), 169.9 (C=O), 98.5 (C-1'), 82.9 (C-4), 75.1 (C-6), 74.6 (C-5), 71.4 (C-3'), 70.0 (C-6'), 69.9 (C-5'), 68.9 (C-4'), 61.8 (C-7'), 61.5(C-2'), 58.2(C-3), 58.0(C-1), 32.0(C-2), 20.96(CH_3), 20.92(CH_3), 20.89(CH_3), 20.86(CH_3), 20.8(CH_3), 20.7(CH_3). MALDI TOFMS calculated for $C_{23}H_{31}N_9O_{13}$ ($[M+Na]^+$) m/e 664.20; measured m/e 664.20).



17

Synthesis of (2S, 3S, 4S, 5R)-2-(((1S, 2S, 3R, 5S, 6R)-2-acetoxy-3,5-diazido-6-(((2S, 3R, 4R, 5S, 6R)-4,5-diacetoxy-3-azido-6-((R)-1,2-diacetoxyethyl)tetrahydro-2H-pyran-2-yl)oxy)cyclohexyl)oxy)-5-(azidomethyl)tetrahydrofuran-3,4-diyl dibenzoate (17): Anhydrous CH_2Cl_2 (15mL) was added to a powdered, flame-dried 4 Å molecular sieves (2.0 g), followed by the addition acceptor **14** (292 mg, 0.455 mmol) and donor **15** (1.0 g, 1.9 mmol) The reaction mixture was stirred for 10 min at room temperature and was then cooled to -30°C. Catalytic amount of BF_3-Et_2O (50µL) was added and the mixture was stirred at -30 °C; the reaction progress was monitored by TLC, which indicated the completion after 60 min. The reaction mixture was diluted with ethyl acetate and washed with saturated $NaHCO_3$ and brine. The combined organic layer was dried over $MgSO_4$, evaporated and subjected to column chromatography (EtOAc/Hexane) to obtain the titled compound **17** (393 mg, 85% yield). ^1H NMR (500 MHz, $CDCl_3$):'**Ring I'**: δ_H 5.87 (d, 1H, J = 3.8 Hz, H-1), 5.42 – 5.34 (m, 1H, H-3), 5.24 – 5.13 (m, 1H, H-6), 5.10 – 5.03 (m, 1H, H-4), 4.54 (dd, 1H, J_1 = 10.5, J_2 = 2.2 Hz, H-5), 4.33 (dd, 1H, J_1 = 12.0, J_2 = 4.1 Hz, H-7), 4.20 (dd, 1H, J_1 = 11.9, J_2 = 7.8 Hz, H-7), 3.50 (dd, 1H, J_1 = 10.9, J_2 =3.8 Hz, H-2); '**Ring II'**: δ_H 5.01 (t, 1H, J = 10.0 Hz, H-6), 3.87 (t, 1H, J = 9.3 Hz, H-5), 3.71 (t, 1H, J = 9.5 Hz, H-4), 3.57 - 3.48(m, 2H, H-1, H-3), 2.38 (dt, 1H, J_1 = 12.9, J_2 = 4.3 Hz, H-2eq), 1.52 (ddd, 1H, J_1 = J_2 = J_3 = 12.7 Hz, H-2ax); '**Ring III'**: δ_H 5.61 (s, 1H, H-1), 5.57 (d, 1H, J = 4.7 Hz, H-2), 5.42 – 5.35 (m, 1H, H-3), 4.59 – 4.47 (m, 1H, H-4), 3.63 – 3.55 (m, 2H, H-5, H-5). The additional peaks in the spectrum were identified as follow: δ_H 7.93 (d, 2H, J = 7.1 Hz, Ar), 7.87 (d, 2H, J = 7.1 Hz, Ar), 7.54 (dt, 2H, J_1 = 19.0, J_2 = 7.4 Hz, Ar), 7.39 (t, 2H, J = 7.8 Hz, Ar), 7.34 (t, 2H, J = 7.8 Hz, Ar), 2.29(s, 3H, CH_3), 2.08 - 2.04(m, 12H, 4 x CH_3). ^{13}C NMR (125 MHz, $CDCl_3$):

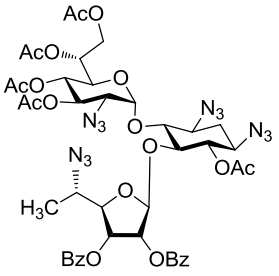
δ_C 170.7 (C=O), 170.1(C=O), 170.08 (C=O), 170.06 (C=O), 169.9 (C=O), 165.5 (Ar), 165.2 (Ar), 133.8 (Ar), 133.7(Ar), 129.8 (Ar), 129.7 (Ar), 128.8 (Ar), 128.68 (Ar), 128.63 (Ar), 128.5 (Ar), 107.7 (C-1"), 96.1 (C-1'), 80.9 (C-4"), 79.8 (C-5), 77.2 (C-4), 74.5 (C-2"), 73.9 (C-6), 72.0 (C-3'), 70.7 (C-3"), 69.9 (C-6'), 69.2 (C-5'), 68.8 (C-4'), 61.5 (C-7'), 61.4 (C-2'), 58.9 (C-3), 58.3 (C-1), 53.1 (C-5"), 32.1 (C-2), 21.04 (CH_3), 21.03 (CH_3), 20.8 (CH_3), 20.7 (CH_3), 20.6 (CH_3). MALDI TOFMS calculated for $C_{42}H_{46}N_{12}O_{18}$ ($[M+Na]^+$) m/e 1029.31; measured m/e 1029.29).



6

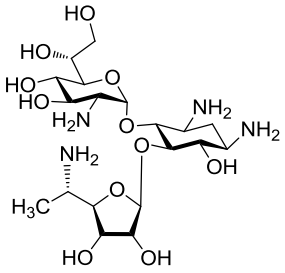
Synthesis of (2R, 3S, 4R, 5R, 6S)-5-amino-6-(((1R, 2R, 3S, 4R, 6S)-4,6-diamino-2-(((2S, 3S, 4R, 5R)-5-(aminomethyl)-3,4-dihydroxytetrahydrofuran-2-yl)oxy)-3-hydroxycyclohexyl)oxy)-2-((R)-1,2-dihydroxyethyl)tetrahydro-2H-pyran-3,4-diol (6): The glycosylation product **17** (393 mg, 0.390mmol) was treated with a solution of $MeNH_2$ (33% solution in EtOH, 15 mL) and the reaction progress was monitored by TLC (EtOAc/MeOH 85:15), which indicated completion after 12 hours. The reaction mixture was evaporated to dryness and was subjected to column chromatography (MeOH/EtOAc 2:8) to obtain the corresponding completely de-esterified perazido derivative (183 mg) in 80 % yield. ^{1}H NMR (500 MHz, MeOD): '**Ring I'**: δ_H 5.89 (d, 1H, J = 3.8 Hz, H-1), 3.97 (dd, 1H, J_1 = 9.7, J_2 = 4.6 Hz, H-5), 3.84 (dd, 2H, J_1 = 12.0, J_2 = 7.1 Hz, H-6, H-3), 3.69 (d, 1H, J = 8.5 Hz, H-7), 3.60 (dd, 1H, J_1 = 11.6, J_2 = 6.4 Hz, H-7), 3.45 (dd, 1H, J_1 = 10.0, J_2 = 8.7 Hz, H-4), 3.06 (dd, 1H, J_1 = 10.6, J_2 = 4.4 Hz, H-2); '**Ring II'**: δ_H 3.62 – 3.54 (m, 2H, H-4, H-5), 3.50 – 3.43 (m, 1H, H-3), 3.40 – 3.33 (m, 1H, H-1), 3.33 – 3.26 (m, 1H, H-6), 2.12 (dt, 1H, J_1 = 13.3, J_2 = 4.4 Hz, H-2 eq), 1.29 (ddd, 1H, $J_1 = J_2 = J_3$ = 12.4 Hz, H-2 ax); '**Ring III'**: δ_H 5.28 (d, 1H, J = 0.8 Hz, H-1), 4.11 (dd, 1H, J_1 = 4.4, J_2 = 0.8 Hz, H-2), 3.98 (dd, 1H, J_1 = 7.4, J_2 = 4.2 Hz, H-3), 3.94 (dd, 1H, J_1 = 7.0, J_2 = 3.4 Hz, H-4), 3.49 (dd, 1H, J_1 = 13.3, J_2 = 2.8 Hz, H-5), 3.41 (dd, 1H, J_1 = 13.1, J_2 = 6.3 Hz, H-5). ^{13}C NMR (125 MHz, MeOD): δ_C 111.2 (C-1"), 97.4 (C-1'), 85.2 (C-4), 82.3 (C-5'), 77.6 (C-6), 76.8 (C-5), 76.3 (C-2"), 74.6 (C-6'), 73.3 (C-3"), 73.2 (C-4'), 72.7 (C-4"), 72.5 (C-3'), 64.7 (C-2'), 64.1 (C-7'), 61.9 (C-3), 61.4 (C-1), 54.5 (C-5"), 33.1 (C-2). MALDI TOFMS calculated for $C_{18}H_{28}N_{12}O_{11}$ ($[M+Na]^+$) m/e 611.20; measured m/e 611.19).

To a stirred solution of a perazido derivative from the above reaction (183 mg, 0.311 mmol) in a mixture of THF (3 mL) and aqueous NaOH (1 mM, 5 mL), PMe_3 (1 M solution in THF, 0.22 mL, 3.0 mmol) was added. The progress of the reaction was monitored by TLC [CH_2Cl_2/MeOH/H_2O/$MeNH_2$ (33% solution in EtOH), 10:15:6:15], which indicated completion after 1h.The reaction mixture was purified by flash chromatography on a short column of silica gel. The column was washed with the following solvents: THF (100 mL), CH_2Cl_2 (100 mL), EtOH (50 mL), and MeOH (100 mL). The product was then eluted with the mixture of 5% $MeNH_2$ solution (33% solution in EtOH) in 80% MeOH. Fractions containing the product were combined and evaporated under vacuum. The pure product was obtained by passing the above product through a short column of Amberlite CG50 (NH_4^+ form). First, the column was washed with water, and then the product was eluted with a mixture of 10% NH_4OH in water to yield compound **6** as a free base form (90.0 mg, 60%). For the storage and biological tests, compound **6** was converted to its sulfate salt form as follow. The free base form was dissolved in water, the pH was adjusted to 6.7 with H_2SO_4 (0.1 N) and lyophilized to afford the sulfate salt of **6** as white foamy solid. ^{1}H NMR (500 MHz, MeOD): '**Ring I'**: δ_H 5.18 (d, 1H, J = 3.6 Hz, H-1), 3.91 (dt, 1H, J_1 = 6.3, J_2 = 3.9 Hz, H-6), 3.85 (dd, 1H, J_1 = 10.2, J_2 = 2.8 Hz, H-5), 3.70 (dd, 1H, J_1 = 11.5, J_2 = 3.7 Hz, H-7), 3.64 (dd, 1H, J_1 = 11.5, J_2 = 6.4 Hz, H7), 3.50 (dd, 1H, J_1 = 10.0, J_2 = 9.0 Hz, H-3), 3.40 (t, 1H, J = 9.5 Hz, H-4), 2.60 (dd, 1H, J = 10.2, 3.3 Hz, H-2); '**Ring II'**: δ_H 3.44 (t, 1H, J = 9.2 Hz, H-5), 3.33 (dd, 1H, J_1 = 11.0, J_2 = 7.6 Hz, H-4), 3.13 (t, 1H, J = 9.5 Hz, H-6), 2.79 – 2.70 (m, 1H, H-3), 2.60 (td, 1H, J_1 = 9.4, J_2 = 4.4 Hz, H-1), 1.93 (dt, 1H, J_1 = 13.0, J_2 = 4.0 Hz, H-2eq), 1.16 (ddd, 1H, J_1 = J_2 = J_3 = 12.4 Hz, H-2ax); '**Ring III'**: δ_H 5.20 (d, 1H, J = 2.7 Hz, H-1), 4.04 (dd, 1H, J_1 = 5.1, J_2 = 2.8 Hz, H-2), 3.95 – 3.90 (m, 1H, H-3), 3.83 (dt, 1H, J_1 = 5.3, J_2 = 3.4 Hz, H-4), 2.89 (dd, 1H, J_1 = 13.2, J_2 = 4.0 Hz, H-5), 2.75 (dd, 1H, J_1 = 13.2, J_2 = 7.3 Hz, H-5). ^{13}C NMR (125 MHz, MeOD): δ_C 110.6 (C-1"), 101.7 (C-1'), 86.8 (C-4), 85.5 (C-5), 84.7 (C-4"), 78.8 (C-6), 76.2 (C-2"), 75.3 (C-3'), 74.7 (C-5'), 73.8 (C-6'), 73.0 (C-4'), 72.5 (C-3"), 63.4 (C-7'), 57.5 (C-2'), 52.5 (C-3), 52.3 (C-1), 45.2 (C-5"), 37.5 (C-2). MALDI TOFMS calculated for $C_{18}H_{36}N_4O_{11}$ ($[M+H]^+$) m/e 485.24; measured m/e 485.19).



18

Synthesis of (2S, 3S, 4S, 5R)-2-(((1S, 2S 3R, 5S, 6R)-2-acetoxy-3,5-diazido-6-(((2S, 3R, 4R, 5S, 6R)-4,5-diacetoxy-3-azido-6-((R)-1,2-diacetoxyethyl)tetrahydro-2H-pyran-2-yl)oxy)cyclohexyl)oxy)-5-((S)-1-azidoethyl)tetrahydrofuran-3,4-diyl dibenzoate (18): Anhydrous CH_2Cl_2 (15mL) was added to a powdered, flame-dried 4 Å molecular sieves (2.0 g), followed by the addition acceptor **14** (265 mg, 0.413 mmol) and donor **16** (0.895 g, 1.65 mmol) The reaction mixture was stirred for 10 min at room temperature and was then cooled to -30°C. At this temperature, catalytic amount of BF_3-Et_2O (50µL) was added and the mixture was stirred at -30 °C and the reaction progress was monitored by TLC, which indicated the completion after 60 min. The reaction mixture was diluted with ethyl acetate and washed with saturated $NaHCO_3$ and brine. The combined organic layer was dried over $MgSO_4$, evaporated and subjected to column chromatography (EtOAc/Hexane) to obtain the titled compound **18** (393 mg) in 93% yield. ^{1}H NMR (600 MHz, $CDCl_3$):'**Ring I'**: δ_H 5.88 (d, 1H, J = 4.0 Hz, H-1), 3.58 (dd, 1H, J_1 = 10.7, J_2 = 4.0 Hz, H-2), 5.36 (dd, 1H, J_1 = 10.6, J_2 = 9.3 Hz, H-3), 5.07 (dd, 1H, J_1 = 10.5, J_2 = 9.3 Hz, H-4), 4.53 (dd, 1H, J_1 = 10.6, J_2 = 2.2 Hz, H-5), 5.18 (ddd, 1H, J_1 = 7.5, J_2 = 4.1, J_3 = 2.2 Hz, H-6), 4.33 (dd, 1H, J_1 = 12.0, J_2 = 3.9 Hz, H-7), 4.19 (dd, 1H, J_1 = 12.1, J_2 = 7.6 Hz, H-7); '**Ring II'**: δ_H 5.01 (t, 1H, J = 9.9 Hz, H-6), 3.84 (t, 1H, J = 9.4 Hz, H-5), 3.71 (t, 1H, J = 9.5 Hz, H-4), 3.52 (ddd, 2H, J_1 = 12.5, J_2 = 10.0, J_3 = 4.6 Hz, H-1, H-3), 2.39 (dt, 1H, J_1 = 5.2, J_2 = 4.5 Hz, H-2eq), 1.52 (ddd, 1H, $J_1 = J_2 = J_3$ = 12.7 Hz, H-2ax); '**Ring III'**: δ_H 5.60 (t, 2H, J = 2.3 Hz, H-1, H-2), 5.41 (dd, 1H, J_1 = 7.6, J_2 = 4.9 Hz, H-3), 4.33 (t, 1H, J = 7.3 Hz, H-4), 3.77 – 3.64 (m, 1H, H-5), 1.24 (d, 3H, J = 6.8 Hz, 6-CH_3). The additional peaks in the spectrum were identified as follow: δ_H 7.92 – 7.89 (m, 2H, Ar), 7.89 – 7.85 (m, 2H, Ar), 7.60 – 7.50 (m, 2H, Ar), 7.39 (t, 2H, J = 7.8 Hz, Ar), 7.34 (t, 2H, J = 7.9 Hz, Ar), 2.41 – 2.35 (m, 3H, CH_3), 2.08 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.07 (s, 3H, CH_3), 2.05 (s, 3H, CH_3).^{13}C NMR (151 MHz, $CDCl_3$): δ_C 170.7 (C=O), 170.3 (C=O), 170.07 (C=O), 170.03 (C=O), 169.9 (C=O), 165.5 (Ar), 165.0 (Ar), 133.8 (Ar), 133.7(Ar), 129.8 (Ar), 129.7 (Ar), 128.8 (Ar), 128.6 (Ar), 128.58 (Ar), 128.56 (Ar), 107.8 (C-1"), 96.1 (C-1'), 84.6 (C-4"), 79.7 (C-5), 77.6 (C-4), 74.7 (C-2"), 73.7 (C-6), 72.0 (C-3''), 71.0 (C-3), 70.0 (C-6'), 69.2 (C-4'), 68.9 (C-5'), 61.7 (C-2'), 61.5 (C-7'), 59.6 (C-5"), 58.9 (C-1), 58.5 (C-3), 32.2 (C-2), 21.1 (CH_3), 21.0 (CH_3), 20.8 (CH_3), 20.79 (CH_3), 20.78 (CH_3), 15.8(C-6",CH_3). MALDI TOFMS calculated for $C_{43}H_{48}N_{12}O_{18}$ ($[M+Na]^+$) m/e 1043.32; measured m/e 1043.30).



7

Synthesis of (2R, 3S, 4R, 5R, 6S)-5-amino-6-(((1R, 2R, 3S, 4R, 6S)-4,6-diamino-2-(((2S, 3S, 4R, 5R)-5-((S)-1-aminoethyl)-3,4-dihydroxytetrahydrofuran-2-yl)oxy)-3-hydroxycyclohexyl)oxy)-2-((R)-1,2-dihydroxyethyl)tetrahydro-2H-pyran-3,4-diol (7): The glycosylation product **18** (0.393 g, 0.384 mmol) was treated with a solution of $MeNH_2$ (33% solution in EtOH, 15 mL) and the reaction progress was monitored by TLC (EtOAc/MeOH 85:15), which indicated completion after 12 hours. The reaction mixture was evaporated to dryness and was subjected to column chromatography (MeOH/EtOAc 2:8) to obtain the corresponding completely de-esterified perazido derivative (230 mg) in 98 % yield. ^{1}H NMR (600 MHz, MeOD): '**Ring I'**: δ_H 5.98 (d, 1H, J = 3.8 Hz, H-1), 3.11 (dd, 1H, J_1 = 10.5, J_2 = 3.8 Hz, H-2), 4.03 (dd, 1H, J_1 = 9.7, J_2 = 4.5 Hz, H-4), 3.96 – 3.88 (m, 2H, H-3, H-6), 3.50 (dd, 1H, J_1 = 10.0, J_2 = 8.8 Hz, H-5), 3.75 (dd, 1H, J_1 = 11.2, J_2 = 2.5 Hz, H-7), 3.66 (dd, 1H, J_1 = 11.6, J_2 = 6.5 Hz, H-7); '**Ring II'**: δ_H 3.69 – 3.64 (m, 1H, H-4), 3.60 (t, 1H, J = 8.9 Hz, H-5), 3.52 (ddd, 1H, J_1 = 12.3, J_2 = 9.7, J_3 = 4.4 Hz, H-3), 3.42 (ddd, 1H, J_1 = 11.9, J_2 = 9.7, J_3 = 4.4 Hz, H-1), 3.38 – 3.33 (m, 1H, H-6), 2.18 (dt, 1H, J_1 = 12.6, J_2 = 4.4 Hz, H-2eq), 1.52 – 1.17 (m, 1H, H-2ax); '**Ring III'**: δ_H 5.31 (d, 1H, J = 0.5 Hz, H-1), 4.17 (dd, 1H, J_1 = 4.8, J_2 = 0.6 Hz, H-2), 4.10 (dd, 1H, J_1 = 7.2, J_2 = 4.7 Hz, H-3), 3.78 – 3.70 (m, 1H, H-4), 3.69 – 3.57 (m, 1H, H-5), 1.33 (d, 3H, J = 6.7 Hz, 6-CH_3). ^{13}C NMR (151 MHz, MeOD): δ_C 110.79 (C-1''), 97.41 (C-1'), 86.03 (C-4''), 85.24 (C-5), 77.47 (C-6), 76.76 (C-4), 76.47 (C-2''), 74.60 (C-6'), 73.42 (C-3), 73.31 (C-4'), 72.77 (C-3''), 72.60 (C-3'), 64.66 (C-2'), 64.13 (C-7'), 61.96 (C-1), 61.51 (C-5'), 60.86 (C-5''), 33.17 (C-2), 16.06 (C-6",CH_3). MALDI TOFMS calculated for $C_{19}H_{30}N_{12}O_{11}$ ($[M+Na]^+$) m/e 625.22; measured m/e 625.20).

To a stirred solution of the perazido derivative from the above reaction (230 mg, 0.381 mmol) in a mixture of THF (3 mL) and aqueous NaOH (1 mM, 5 mL), PMe_3 (1 M solution in THF, 0.22 mL, 3.0 mmol) was added. The progress of the reaction was monitored by TLC [CH_2Cl_2/MeOH/H_2O/$MeNH_2$ (33% solution in EtOH), 10:15:6:15], which indicated completion after 1h. The reaction mixture was purified by flash chromatography on a short column of silica gel. The column was washed with the following solvents: THF (100 mL), CH_2Cl_2 (100 mL), EtOH (50 mL), and MeOH (100 mL). The product was then eluted with the mixture of 5% $MeNH_2$ solution (33% solution in EtOH) in 80% MeOH. Fractions containing the product were combined and evaporated

under vacuum. The pure product was obtained by passing the above product through a short column of Amberlite CG50 (NH_4^+ form). First, the column was washed with water, then the product was eluted with a mixture of 10% NH_4OH in water to yield compound **7** (123 mg, 64%) in its free base form. For the storage and biological tests, compound **7** was converted to its sulfate salt form as follow. The free base form was dissolved in water, the pH was adjusted to 6.7 with H_2SO_4 (0.1 N) and lyophilized to afford the sulfate salt of **7** as a white foamy solid. ^{1}H NMR (600 MHz, MeOD):'**Ring I'**: δ_H 5.25 (d, 1H, J = 3.6 Hz, H-1), 4.00 – 3.94 (m, 1H, H-6), 3.90 (dd, 1H, J_1 = 9.9, J_2 = 3.5 Hz, H-5), 3.56 – 3.50 (m, 1H, H-3), 3.47 (dd, 1H, J_1 = 18.3, J_2 = 8.8 Hz, H-4), 2.66 (dd, 1H, J_1 = 10.3, J_2 = 3.5 Hz, H-2), 3.76 (dd, 1H, J_1 = 11.5, J_2 = 3.7 Hz, H-7), 3.70 (dd, 1H, J_1 = 11.5, J_2 = 6.4 Hz, H-7),; '**Ring II'**: δ_H 3.48 (dd, 1H, J_1 = 15.9, J_2 = 6.7 Hz, H-5), 3.37 (dd, 1H, J_1 = 16.5, J_2 = 7.2 Hz, H-4), 3.18 (dd, 1H, J_1 = 13.1, J_2 = 5.6 Hz, H-6), 2.78 (dd, 1H, J_1 = 9.9, J_2 = 8.2 Hz, H-3), 2.64 (dd, 1H, J_1 = 22.9, J_2 = 10.3 Hz, H-1), 1.96 (dt, 1H, J_1 = 7. 8, J_2 = 3. 7 Hz, H-2eq), 1.23 (ddd, 1H, J_1 = J_2 = J_3 = 12.5 Hz, H-2ax); '**Ring III'**: δ_H 5.26 (d, 1H, J = 2.7 Hz, H-1), 4.05 (d, 1H, J = 1.8 Hz, H-2), 4.01 (t, 1H, J = 5.7 Hz, H-3), 3.56 (t, 1H, J = 6.3 Hz, H-4), 3.01 – 2.86 (m, 1H, H-5), 1.16 (d, 3H, J = 6.4 Hz, 6-CH_3). ^{13}C NMR (151 MHz, MeOD): δ_C 109.78 (C-1''), 101.67 (C-1'), 88.61 (C-4''), 86.80 (C-4), 84.86 (C-5), 78.70 (C-6), 76.28 (C-2''), 75.46 (C-3'), 74.72 (C-5'), 73.79 (C-6'), 73.07 (C-4'), 72.30 (C-3''), 63.43 (C-7'), 57.55 (C-2'), 52.53 (C-3), 52.35 (C-1), 50.68 (C-5''), 49.85 (C-4), 37.64 (C-2), 19.37 (C-6",CH_3). MALDI TOFMS calculated for $C_{19}H_{38}N_4O_{11}$ ($[M+H]^+$) m/e 498.25; measured m/e 499.26).

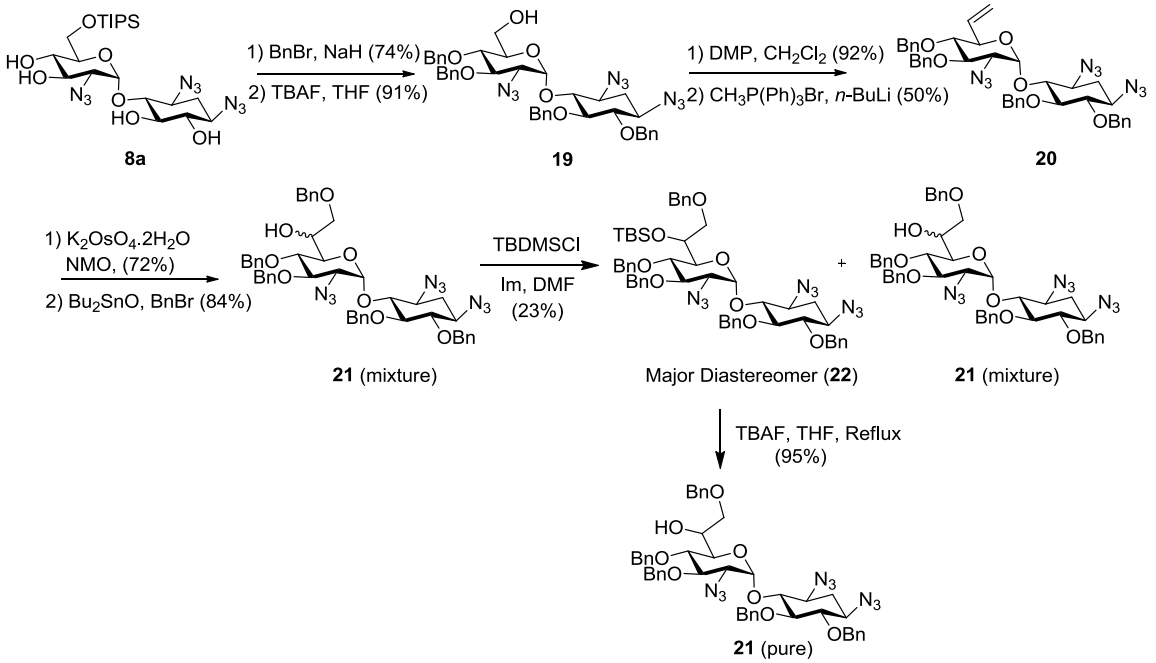
Determination of absolute configuration at 6'-position of 4 and 5

In order to determine the absolute stereochemistry at the side-chain C6'-alcohols in **4** and **5**, we synthesized the major C6'-diasteromer alcohol **21** as illustrated in Scheme S1. We assumed that the change of protecting group on the secondary alcohols would improve the yields and isolation of the intermediate products at various synthetic steps experienced in the pathway in Scheme 1. With this premise, we changed the PMB protection in Scheme 1 with the benzyl protection in Scheme S1. Thus, the benzylation of TIPS protected **8a** was followed by silyl deprotection with TBAF to provide the 6'-alcohol **19** in good overall yields. Dess-Martin Periodinane (DMP) oxidation provided the corresponding aldehyde, which was treated with Wittig reagent to provide the terminal alkene **20**. Dihydroxylation step was followed by selective benzylation of the primary alcohol[5] to afford the desired 6'-alcohol **21** as a mixture of two 6'-diastereomers. Unfortunately, however, all attempts to separate this mixture by using column chromatography with several different solvent systems, proved unsuccessful. Finally we found that the silylation of the mixture **21** with *t*-butyldimethylsilyl chloride (TBDMSCl) in the presence of imidazole proceeded very slow and with high selectivity of the major 6'-diastereomer. Using this advantage we could isolate the silylated product of the major diastereomer **22** in its

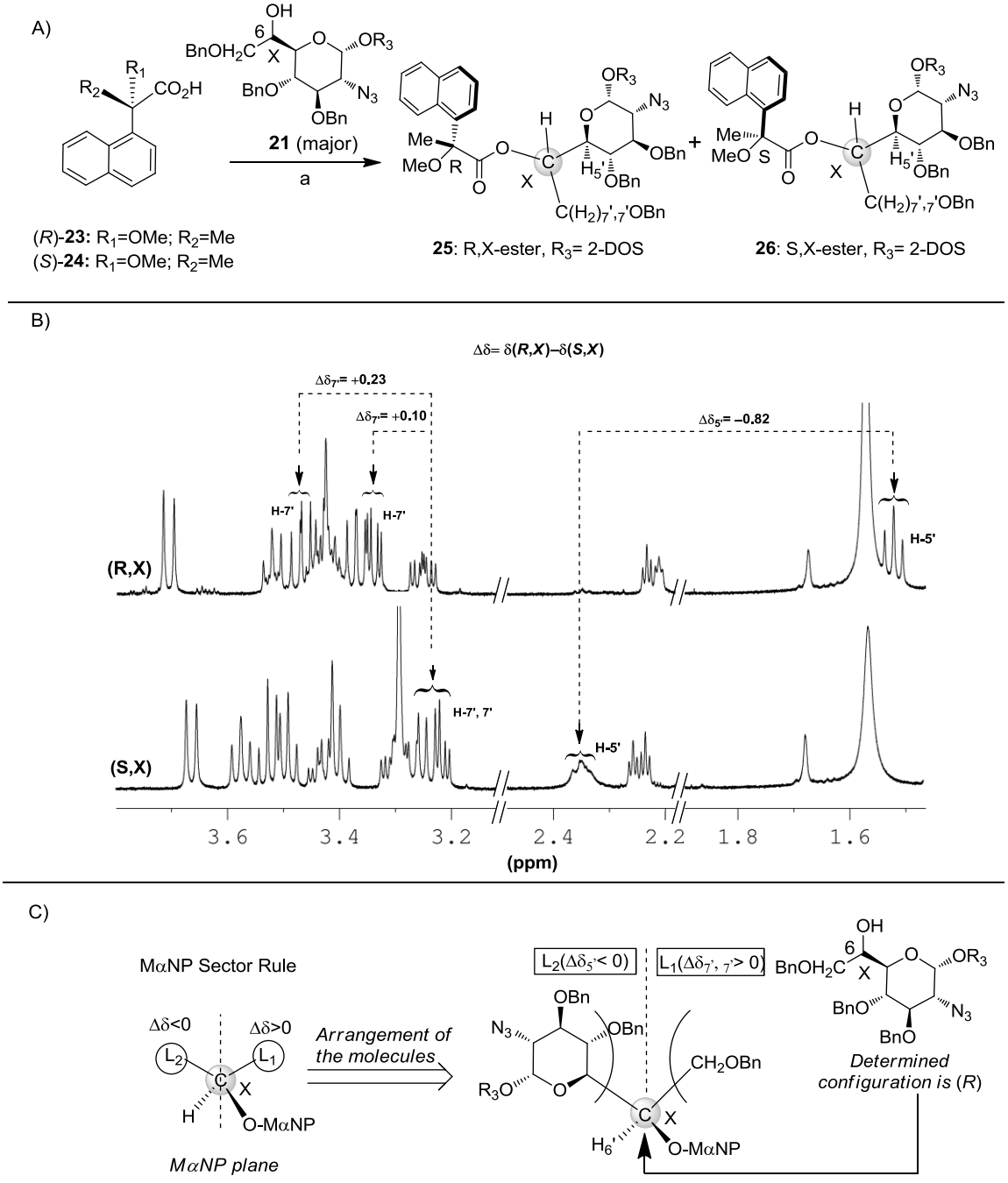
pure form. Treatment of **22** with TBAF produced the desired product **21**, which was used for configuration assignment.

To assign the absolute stereochemistry at 6' positon in compound **21**, we separately coupled the major diastereomer **21** with (*R*)-2-methoxy-2(1-naphthyl)propanoic acid [(*R*)-MαNP] **23** and [(*S*)-MαNP] **24** of known absolute stereochemistry in presence of DCC, 4-DMAP and CSA[6] to afford the respective esters *(R,X)*-MαNP **25** and *(S,X)*-MαNP **26** (Scheme S2, panel A). The absolute stereochemistry at the 6' position (denoted by *X*) was then determined by ^{1}H NMR magnetic anisotropy,[4] which is based on Sector rule [7] and relays on the difference in chemical shift values for the assigned protons in the NMR spectra (Scheme S2, panels B and C). The difference in chemical shift [$\Delta\delta = \delta(R, X) - \delta(S, X)$] for H-5' (-0.82) was negative, while that for H-7', 7' (+0.23, +0.10) was positive. According to the Sector rule (Scheme S2, panel C),[7] the structures (*R, X*)-MαNP **25** and (*S, X*)-MαNP **26** are arranged so that OMαNP is positioned on the front and H-6'on the back, while the $\Delta\delta$ positive and $\Delta\delta$ negative parts are positioned on the right and left sides, respectively. These data confirms the *R* configuration (*X* = *R*) at the 6' carbon atom in compound **21**. This study established that the major and minor diastereomers, compounds **4** and **5**, exhibit (*R*)- and (*S*)-configuration at 6' position: 6'-(*R*)-**4** and 6'-(*S*)-**5**.

Scheme S1.



Scheme S2

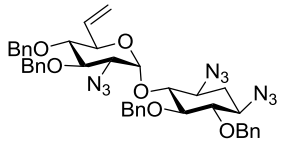


Scheme S2: (A) Synthesis of C-6'-diastereomeric esters ***(R, X)*-25** and ***(S, X)*-26**, reagents and conditions: (a) DCC, 4-DMAP, CSA, CH_2Cl_2, r.t. (B) ^1H NMR spectra of ***(R, X)*-25** and ***(S, X)*-26**. The chemical shift differences (δ_H) between particular protons of ***(R, X)*-25** and ***(S, X)*-26** are highlighted. (C) Assignment of absolute configuration at the 6'-carbon (denoted by X) of the major alcohol **21** by sector rule.

Synthesis of ((2R, 3S, 4R, 5R, 6S)-5-azido-3, 4-bis(benzyloxy)-6-(((1R, 2R, 3S, 4R, 6S)-4,6-diazido-2,3-bis(benzyloxy)cyclohexyl)oxy)tetrahydro-2H-pyran-2-yl)methanol (19): To a stirred solution of the silyl ether **8a** (0.2 g, 0.358 mmol) and sodium hydride (0.114 g, 4.75 mmol) in DMF (5 mL), was added benzyl bromide (0.255 mL, 2.14 mmol) at 0 ^{o}C. The reaction progress was monitored by TLC (EtOAc/Hexane 3:7). After 8.0 h the reaction was completed and ice was added in small potrions to quench the reaction. The mixture was diluted with ethyl acetate (30 mL) and washed with water (2 x 50 mL). The combined aqueous layers were extracted with diethyl ether (2 x 50 mL); the combined organic layers were dried over anhydrous $MgSO_4$, and evaporated to dryness. The residue was purified by column chromatography (EtOAc/Hexane 8:92) to yield perbenzylated silyl ehter (0.243 g, 74%). ^{1}H NMR (500 MHz, $CDCl_3$): **'Ring I'**: δ_H 5.46 (d, 1H, J = 3.3 Hz, H-1), 3.97 (dd, 1H, J_1 = 17.7, J_2 = 8.2 Hz, H-3, H-5), 3.90 (d, 1H, J = 11.6, H-6), 3.84 (d, 1H, J = 11.0, H-6), 3.72 – 3.53 (m, 1H, H-4), 3.19 (dd, 1H, J_1 = 10.6, J_2 = 4.4Hz, H-2); **'Ring II'**: δ_H 3.53 (m, 2H, H-4, H-5), 3.40 (td, 1H, J_1 = 9.9, J_2 = 5.3 Hz, H-1), 3.30 (ddd, 2H, J_1 = 17.6, J_2 = 15.1, J_3 = 9.2 Hz, H-3, H-6), 2.21 (dd, 1H, J_1 = 8.2, J_2 = 4.2 Hz, H-2eq), 1.34 (dt, 1H, J_1 = J_2 = J_3 = 12.9 Hz, H-2ax); **The additional peaks in the spectrum were identified as follow**: δ_H 7.28 (m, 20H, Bn), 4.94 (m, 2H, O(CH_2)Bn), 4.80(m, 6H, O(CH_2)Bn), 1.14 – 0.95 (m, 21H, TIPS). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 138.54 (Bn), 138.17 (Bn), 138.03 (Bn), 137.49 (Bn), 128.61 (Bn), 128.58 (Bn), 128.55 (Bn), 128.31 (Bn), 128.28 (Bn), 128.14 (Bn), 127.99 (Bn), 127.78 (Bn), 127.72 (Bn), 127.10 (Bn), 97.7 (C1'), 84.8, 84.62, 80.2, 77.3 76.0, 75.7, 75.2, 74.9, 72.9, 63.5(C2'), 62.3(C6), 60.4(C1), 59.5, 32.5(C2), 18.2(TIPS), 18.1(TIPS), 12.1(TIPS).

To a stirred solution of perbenzylated silyl ether compound from the above step (9.24 g, 10.0 mmol) in THF (100 mL) at 0 ^{o}C, TBAF (9.0 mL, 31.0 mmol) was added and the reaction progress was monitored by TLC (EtOAc/Hexane 2:3). After 15 h, the solvent was evaporated to dryness and the obtained residue was subjected to column chromatography (EtOAc/Hexane 3:7) to yield corresponding perbenzylated 6'-alcohol **19** (7.0 g, 91%). ^{1}H NMR (500 MHz, $CDCl_3$): **'Ring I'**: δ_H 5.60 (d, 1H, J = 3.8 Hz, H-1), 4.11 (d, 1H, J = 10.0 Hz, H-5), 4.05(t, 1H, J = 9.7 Hz, H-3), 3.83(dd, 1H, J_1 = 12.0, J_2 = 2.0 Hz, H-6), 3.76(dd, 1H, J_1 = 12.1, J_2 = 2.9 Hz, H-6), 3.69 – 3.57 (m, 1H, H-4), 3.28 (dd, 1H, J_1 = 10.6, J_2 = 4.6 Hz, H-2); **'Ring II'**: δ_H 3.60 – 3.57 (m, 2H, H-4, H-5), 3.55-3.46 (m, 1H, H-1), 3.46 – 3.37 (m, 2H, H-3, H-6), 2.31 (dt, 1H, J_1 = 13.2, J_2 = 4.5 Hz, H-2eq), 1.47 (ddd, 1H, J_1 = J_2 = J_3 = 10.6 Hz, H-2ax); **The additional peaks in the spectrum were identified as follow**: δ_H 7.52 – 7.28 (m, 20H, Bn), 5.04 (d, 1H, J = 10.8 Hz, O(CH_2)Bn), 4.93 (dd,

2H, J_1 = 10.7, J_2 = 6.0 Hz, O(CH_2)Bn), 4.90 – 4.86 (m, 3H, O(CH_2)Bn), 4.84 (d, 1H, J = 10.5 Hz, O(CH_2)Bn), 4.71 (d, 1H, J = 11.2 Hz, O(CH_2)Bn). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 138.0 (Bn), 138.0 (Bn), 137.8 (Bn), 137.3 (Bn), 128.6 (Bn), 128.6 (Bn), 128.5 (Bn), 128.2 (Bn), 128.1 (Bn), 128.1 (Bn), 128.0 (Bn), 128.0 (Bn), 127.7 (Bn), 127.1 (Bn), 97.7 (C1'), 84.7, 84.5, 80.1 (C3'), 77.6, 77.5, 76.0 , 75.6, 75.3, 75.0, 72.0 (C5'), 63.4 (C2'), 61.4 (C6'), 60.3, 59.4, 32.4 (C2).

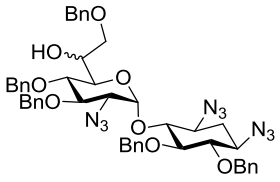


20

Synthesis of (2R, 3R, 4R, 5R, 6R)-3-azido-4, 5-bis(benzyloxy)-2-(((1R, 2R, 3S, 4R, 6S)-4,6-diazido-2,3-bis(benzyloxy)cyclohexyl)oxy)-6-vinyltetrahydro-2H-pyran (20): To a solution of 6'-alcohol **19** (1.0 g, 1.31 mmol) in ethyl acetate (40 mL), IBX (1.1 g, 3.92 mmol) was added in one portion. The resulting suspension was heated at 80 ^{o}C and stirred vigorously. After the reaction was completed (3.5 h) as indicated by TLC (EtOAc/Hexane 2:3), the reaction was cooled to room temperature and filtered through the celite. The celite was thoroughly washed with ethyl acetate (2 x 50 mL) and the combined organic layers were evaporated under reduced pressure. The crude product was subjected to flash column chromatography (EtOAc/Hexane 35:65) to yield the 6'-aldehyde (0.925g, 92%). ^{1}H NMR (500 MHz, $CDCl_3$): **'Ring I'**: δ_H 9.62 (s, 1H, H-6(CHO)), 5.62 (s, 1H, H-1), 4.69 (d, 1H, J = 9.9 Hz, H-4), 4.01 (t, 1H, J = 9.3 Hz, H-3), 3.56 (dd, 1H, J_1 = 18.0, J_2 = 9.1 Hz, H-5), 3.19 (d, 1H, J = 14.0, H-2); **'Ring II'**: δ_H 3.56 (dd, 2H, J_1 = 18.0, J_2 =9.1 Hz, H-4, H-5), 3.44 (d, 1H, J = 11.7Hz, H-1), 3.37 (t, 2H, J = 8.2 Hz, H-3, H-6), 2.28 (d, 1H, J_1 = 10.2 Hz, H-2eq), 1.44 (ddd, 1H, J_1 = J_2 = J_3 = 14.0 Hz, H-2ax); **The additional peaks in the spectrum were identified as follow**: δ_H 7.27 (m, 20H, Bn), 5.00 (d, 1H, J = 10.9 Hz, O(CH_2)Bn), 4.92 – 4.75 (m, 6H, O(CH_2)Bn), 4.63 (d, 1H, J = 10.7 Hz, O(CH_2)Bn). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 197.2 (CHO), 138.0 (Bn), 137.5 (Bn), 137.3 (Bn), 137.1 (Bn), 128.7 (Bn), 128.6 (Bn), 128.6 (Bn), 128.6 (Bn), 128.3 (Bn), 128.3 (Bn), 128.2 (Bn), 128.1 (Bn), 97.6 (C1'), 84.6, 84.3, 80.1 (C3'), 78.4, 77.7, 76.1, 75.8, 75.3, 75.2, 62.8 (C2'), 60.3, 59.1 (C1), 32.2 (C2).

To a cooled suspension of Methyltriphenylphosphonium Iodide (0.966 g, 2.7 mmol) in anhydrous THF at 0 ^{o}C, *n*-BuLi (1.6 M in hexane, 0.32 mL) was added drop wise and the resulted yellow solution was stirred for an additional 30 min at 0 ^{o}C. The 6'-aldehyde from the above step

(0.822 g, 1.08 mmol) in anhydrous THF (0.3 mL) was added at 0 ^{o}C, and the reaction was allowed to stir for an additional 1.5 h at room temperature. After completion of the reaction as indicated by TLC (EtOAc/Hexane 2:3), the reaction was quenched with saturated NH_4Cl solution. The layers were separated and the aqueous layer was extracted with ether (2 X 10 mL). The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and evaporated to dryness. The crude product was purified by flash chromatography (EtOAc/Hexane 2.5:7.5) to yield compound **20** (0.4 g, 50%). ^{1}H NMR (400 MHz, $CDCl_3$): **'Ring I'**: δ_H 5.89 (ddd, 1H, J_1 = 17.2, J_2 = 10.4, J_3 = 6.8 Hz, H-6), 5.56 (d, 1H, J = 3.9 Hz, H-1), 5.47 (d, 1H, J = 17.2 Hz, H-7trans), 5.33-5.27 (m, 1H, H-7cis), 4.64-4.56 (m, 1H, H-5), 4.09 (m, H-3), 3.32 – 3.27 (m, 2H, H-2, H-4); **'Ring II'**: δ_H 3.69 – 3.56 (m, 2H, H-4, H-5), 3.54-3.45 (m, 1H, H-1), 3.45 – 3.35 (m, 2H, H-3, H-6), 2.31 (dt, 1H, J_1 = 13.2, J_2 = 4.5 Hz, H-2eq), 1.49 (ddd, 1H, J_1 = J_2 = J_3 = 12.6 Hz, H-2ax); **The additional peaks in the spectrum were identified as follow**: δ_H 7.32–7.29 (m, 20H, Bn), 5.02 (d, 1H, J = 10.9 Hz, O(CH_2)Bn), 4.94 (dd, 1H, J_1 = 9.9, J_2= 5.4 Hz, O(CH_2)Bn), 4.89 (d, 1H, J = 6.6 Hz, O(CH_2)Bn), 4.83 (dd, 2H, J = 10.7, 8.5 Hz, O(CH_2)Bn), 4.73(d, 1H, J = 10.9 Hz, O(CH_2)Bn), 4.67(d, 1H, J = 10.9 Hz, O(CH_2)Bn), 4.64-4.56 (m, 1H, O(CH_2)Bn). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 138.2 (Bn), 138.0 (Bn), 138.0 (Bn), 137.4 (Bn), 134.9 (Bn), 128.6 (Bn), 128.5 (Bn), 128.5 (Bn), 128.5 (Bn), 128.3 (Bn), 128.2 (Bn), 128.1 (Bn), 127.9 (Bn), 127.9 (Bn), 127.7 (Bn), 127.0 (Bn), 118.9 (C7'), 97.7 (C1'), 84.7, 84.5, 82.7 (C4'), 79.7 (C3'), 77.7, 76.05, 75.6, 75.3, 75.0, 72.7 (C5'), 63.4 (C2'), 60.3(C1), 59.3, 32.4 (C2).

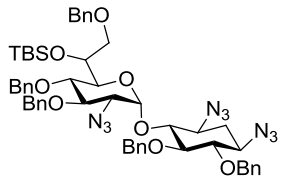


21

Synthesis of 1-((2R, 3S, 4R, 5R, 6S)-5-azido-3,4-bis(benzyloxy)-6-(((1R, 2R, 3S, 4R, 6S)-4,6-diazido-2,3-bis(benzyloxy)cyclohexyl)oxy)tetrahydro-2H-pyran-2-yl)-2-(benzyloxy)ethanol (21): To a stirred solution of compound **20** (402 mg, 0.53 mmol) in acetone (10 mL), water (3 mL) and *t*-BuOH (10 mL), $K_2OsO_4.2H_2O$ (16 mg, 0.051 mmol) and NMO (0.22 mL) were added sequentially. The progress of the reaction was monitored by TLC (EtOAc/Hexane 2:3), which indicated the completion after 24 h. The solvent was evaporated to dryness; the residue was dissolved in EtOAc to which an aqueous solution of $Na_2S_2O_3$ was added. The layers were separated

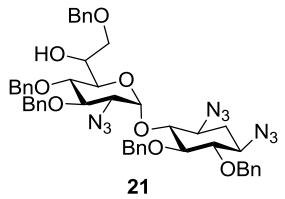
and the organic phase was washed with brine, dried over $MgSO_4$ and evaporated. The crude product was subjected to column chromatography (EtOAc/Hexane 1:1) to yield dihydroxylated product (300 mg, 72%) as a 6'-diasteromeric mixture.

A mixture of dihydroxylated compound (0.3 g, 0.378 mmol) from the above step and Bu_2SnO(0.103 g, 0.413 mmol) in toluene/MeOH (10:1, 7 mL) was refluxed for 3 h and concentrated under reduced pressure. To a solution of this residue in toluene (3 mL) was added tetrabutylammonium bromide (0.122 g, 0.378 mmol) and BnBr (0.09 mL, 0.756 mmol). The mixture was stirred at 85 ^oC overnight and quenched with addition CH_2Cl_2 (10 mL) and saturated $NaHCO_3$ (2 mL). After filteration through a pad of Celite®, the organic phase was washed with H_2O (3 mL), brine (5 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by column chromatography (EtOAc/Hexane 2: 3) to give the titled compound **21** (0.280 g, 84%) as a 6'-diasteromeric mixture.



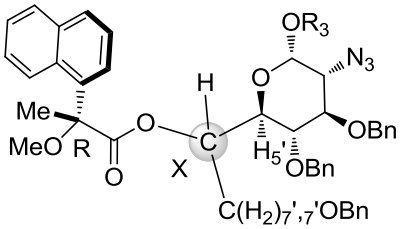
22

Synthesis of (1-((2S, 3S, 4R, 5R, 6S)-5-azido-3,4-bis(benzyloxy)-6-(((1R, 2R, 3S, 4R, 6S)-4,6-diazido-2,3-bis(benzyloxy)cyclohexyl)oxy)tetrahydro-2H-pyran-2-yl)-2-benzyloxy)ethoxy)(tert-butyl)dimethylsilane (22): Compound **21** (205 mg, 0.232 mmol) was dissolved in anhydrous DMF (5 mL) and cooled to 0 ^oC. *t*-butyldimethylsilyl chloride (TBSCl, 45 mg, 0.298 mmol) was added, followed by addition of Imidazole (39 mg, 0.572 mmol). The reaction mixture was allowed to attain the room temperature under stirring, and the reaction progress was monitored by TLC (EtOAc/Hexane 3:7). From TLC, reaction did not complete even after prolonged reaction times (24 h) and at this stage the reaction was stopped by adding mixture of ethyl acetate (10 mL) and H_2O (10 mL), and the two layers were separated. The aqueous layer was thoroughly washed with ethyl acetate (4 X 30 mL). The combined organic layers were washed with sat. NaCl solution and dried over anhydrous $MgSO_4$. The solvent was evaporated to dryness and the residue was subjected to column chromatography (EtOAc/Hexane 25:75) to yield corresponding silyl ether (**22**) (85 mg, 23%) as a pure major diastereomer.



21

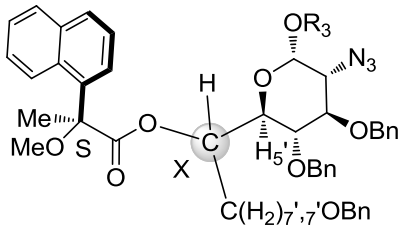
Synthesis of 1-((2R,3S,4R,5R,6S)-5-azido-3,4-bis(benzyloxy)-6-(((1R,2R,3S,4R,6S)-4,6-diazido-2,3-bis(benzyloxy)cyclohexyl)oxy)tetrahydro-2H-pyran-2-yl)-2-(benzyloxy)ethanol (21 as pure major diastereomer): To a stirred solution of compound (60 mg, 0.06 mmol) in THF (3 mL) at room temperature, TBAF (0.052 mL, 0.179 mmol) was added and the reaction was refluxed at 50^{o}C overnight. After completion of the reaction as indicated by TLC (EtOAc/Hexane 2:3), the solvent was evaporated to dryness and the obtained residue was subjected to column chromatography (EtOAc/Hexane 3:7) to yield single diastereromer **21** (52 mg, 95%). ^{1}H NMR (500 MHz, $CDCl_3$): **'Ring I'**: δ_H 5.53 (d, 1H, J = 3.9 Hz, H-1), 4.17 (dd, 1H, J_1 = 10.0, J_2 = 2.4 Hz, H-5), 4.12 (m, 1H, H-6), 3.96 (dd, 1H, J_1 = 10.3, J_2 = 8.9 Hz, H-3), 3.69-3.61 (m, 1H, H-4), 3.50 – 3.45 (m, 2H, H-7, H-7), 3.22(dd, 1H, J_1 = 10.3, J_2 = 3.9 Hz, H-2), 3.59 (BrS, 1H, 6'-OH); **'Ring II'**: δ_H 3.58 – 3.49 (m, 2H, H-4, H-5), 3.44-3.11(m, 3H, H-1, H-3, H-6), 2.23 (dt, 1H, J_1 = 13.2, J_2 = 4.5 Hz, H-2eq), 1.38 (ddd, 1H, J_1 = J_2 = J_3 = 12.6 Hz, H-2ax); **The additional peaks in the spectrum were identified as follow**: δ_H 7.29-7.23 (m, 25H, Bn), 4.98 (d, 1H, J = 10.8 Hz, O(CH_2)Bn), 4.92 – 4.74 (m, 6H, O(CH_2)Bn), 4.65 (d, 1H, J = 11.1 Hz, O(CH_2)Bn), 4.42 (q, 2H, J = 11.9 Hz, O(CH_2)Bn). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 138.0 (Bn), 138.0 (Bn), 137.9 (Bn), 137.7 (Bn), 137.3 (Bn), 128.6 (Bn), 128.6 (Bn), 128.5 (Bn), 128.5 (Bn), 128.5 (Bn), 128.3 (Bn), 128.1 (Bn), 128.1(Bn), 128.0 (Bn), 127.9 (Bn), 127.8 (Bn), 127.7 (Bn), 127.6 (Bn), 127.0 (Bn), 97.4 (C1'), 84.6, 84.4, 80.8, 78.4 (C4'), 77.5, 76.0 (Bn), 75.6 (Bn), 75.3 (Bn), 74.6 (Bn), 73.4 (Bn), 71.8, 71.6, 71.2 (C7'), 63.3 (C2'), 60.2 (C1), 59.5 (C3), 32.4(C2).



25: R,X-ester, R_3= 2-DOS

Synthesis of (*R, X*)-Ester: A mixture of (*R*)-2-methoxy-2(1-naphthyl)propanoic acid (*R*)-MαNP (0.01 g, 0.04 mmol), 4-dimethylaminopyridine (DMAP, 0.006 g, 0.049 mmol), 10-camphorsulfonic acid (CSA, 0.002 g, 0.008 mmol), and 1,3-dicyclohexylcarbodiimide (DCC, 0.047 g, 0.22 mmol) was stirred in CH_2Cl_2 (3 mL) at 0^o C. The major alcohol **21** from the above (0.038 g, 0.043 mmol), was dissolved in CH_2Cl_2 (2 ml), slowly added to the above stirred mixture, and the reaction was left at room temperature for 72 h. The mixture was diluted with EtOAc and washed with 1% HCl solution, saturated $NaHCO_3$ and brine. The combined organic layer was dried over $MgSO_4$, evaporated and subjected to a column chromatography (EtOAc/Hexane) to yield the desired esters (*R, X*)-**25** (0.008 g, 17%). ^{1}H NMR (600 MHz, $CDCl_3$): **'Ring I'**: δ_H 5.55 (dd, 1H, *J* = 9.9, 3.7 Hz, H-6), 4.87 (d, 1H, *J* = 3.4 Hz, H-1), 3.86 (d, 1H, *J* = 10.0 Hz, H-4), 3.50 – 3.46 (m, 1H, H-7), 3.38 (d, 1H, *J* = 10.2 Hz, H-3), 3.36 – 3.32 (m, 1H, H-7), 1.55 – 1.50 (m, 1H, H-5), 1.28 (dd, 1H, J_1 = 10.4, J_2 = 3.9 Hz, H-2), **'Ring II'**: δ_H 3.51 (d, 1H, J_1 = 9.7Hz, H-6), 3.43 (dt, 3H, J_1 = 12.1, J_2 = 7.8 Hz, H-4, H-5, H-3), 3.25 (ddd, 1H, J_1 = 12.6, J_2 = 10.0, J_3 = 4.6 Hz, H-1), 2.23 (dd, 1H, J_1 = 10.9, J_2 = 6.5 Hz, H-2eq), 1.46-1.39 (m, 1H, H-2ax); **The additional peaks in the spectrum were identified as follow**: 8.39 (d, 1H, *J* = 8.7 Hz, Ar), 7.80 – 7.75 (m, 2H, Ar), 7.63 (d, 1H, *J* = 6.4 Hz, Ar), 7.54 (t, 2H, *J* = 7.6 Hz, Ar), 7.47 – 7.40 (m, 2H, Ar), 7.38 (d, 2H, *J* = 7.1 Hz, Ar), 7.37 – 7.33 (m, 2H, Ar), 7.32 – 7.27 (m, 9H, Ar), 7.23 (ddd, 4H, J_1 = 6.5, J_2= 4.7, J_3= 2.2 Hz, Ar), 7.20 (d, 3H, *J* = 8.0 Hz, Ar), 7.09 (ddd, 1H, J_1 = 8.5, J_2= 6.8, J_3= 1.5 Hz, Ar), 7.06 – 7.02 (m, 1H, Ar), 6.96 – 6.92 (m, 2H, Ar), 5.01 (d, 1H, *J* = 11.2 Hz, O(CH_2)Bn), 4.88 (d, 2H, *J* = 4.1 Hz, O(CH_2)Bn), 4.84 (d, 1H, *J* = 10.8 Hz, O(CH_2)Bn), 4.59 (d, 1H, *J* = 11.4 Hz, O(CH_2)Bn), 4.50 (d, 1H, *J* = 11.3 Hz, O(CH_2)Bn), 4.44 (d, 1H, *J* = 11.8 Hz, O(CH_2)Bn), 4.25 (d, 1H, *J* = 11.9 Hz, O(CH_2)Bn), 3.99 (d, 1H, *J* = 11.3 Hz, O(CH_2)Bn), 3.71 (d, 1H, *J* = 11.3 Hz, O(CH_2)Bn), 3.07 (s, 1H, OCH_3), 2.02 (s, 3H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ_C 173.3(Ar), 138.5 (Ar), 138.4 (Ar), 137.9 (Ar), 137.7 (Ar), 137.3 (Ar) 135.3 (Ar), 134.2 (Ar), 131.8 (Ar), 130.1 (Ar), 128.9 (Ar), 128.65 (Ar), 128.62 (Ar), 128.5 (Ar), 128.46 (Ar), 128.44 (Ar), 128.22 (Ar), 128.22 (Ar), 127.76 (Ar), 127.71 (Ar), 127.5 (Ar), 127.4 (Ar), 127.2 (Ar), 126.7 (Ar), 126.4 (Ar), 126.3 (Ar), 126.2

(Ar), 124.8 (Ar), 99.7 (C1'), 84.5, 84.43 (s), 81.1, 79.8, 77.0, 76.7, 76.1, 75.1, 74.2, 74.2, 73.7, 72.7, 70.2, 69.8, 61.8, 60.2, 59.1, 50.7, 32.3, 31.1, 29.8, 21.5(CH_3).

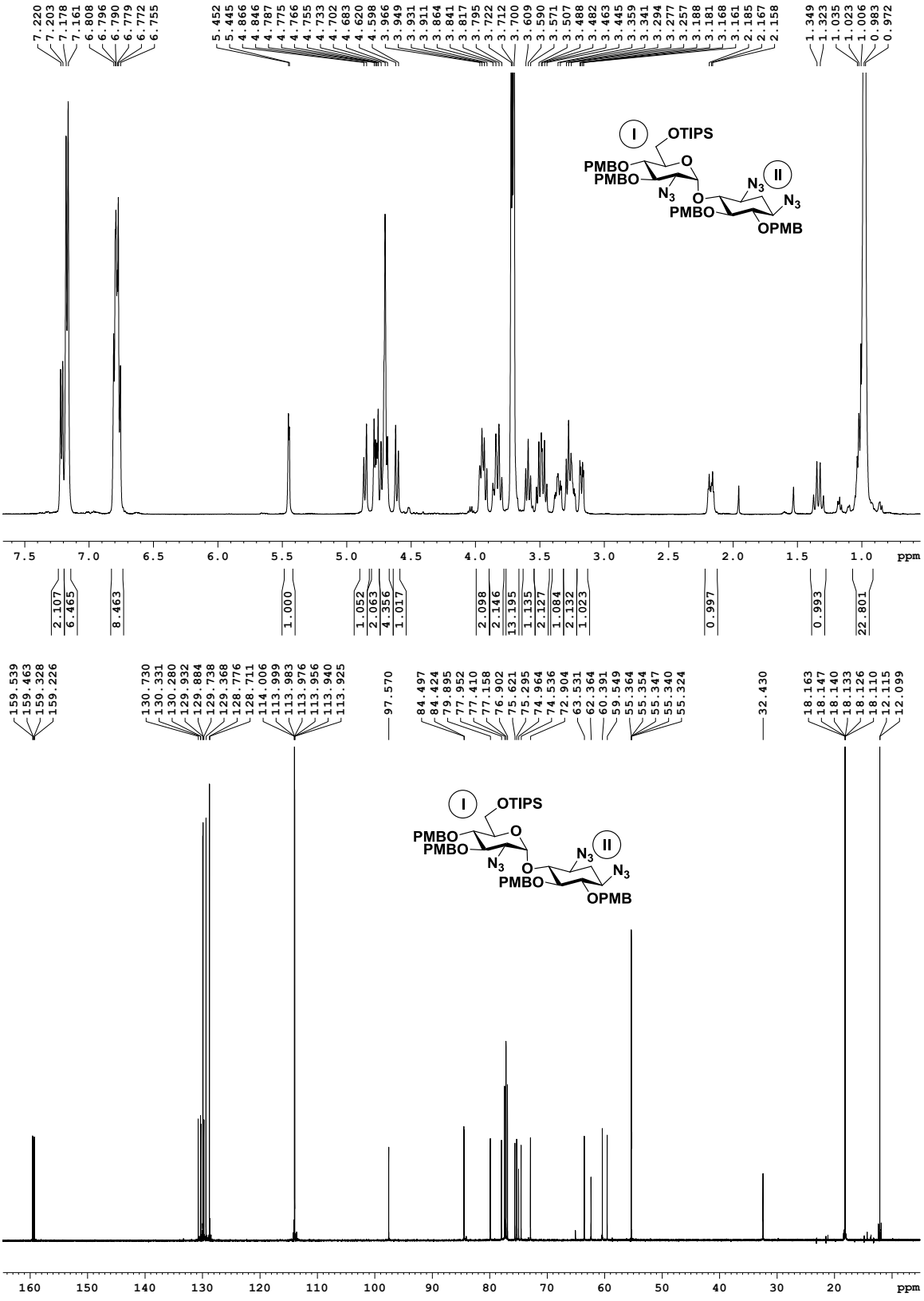


26: S,X-ester, R_3= 2-DOS

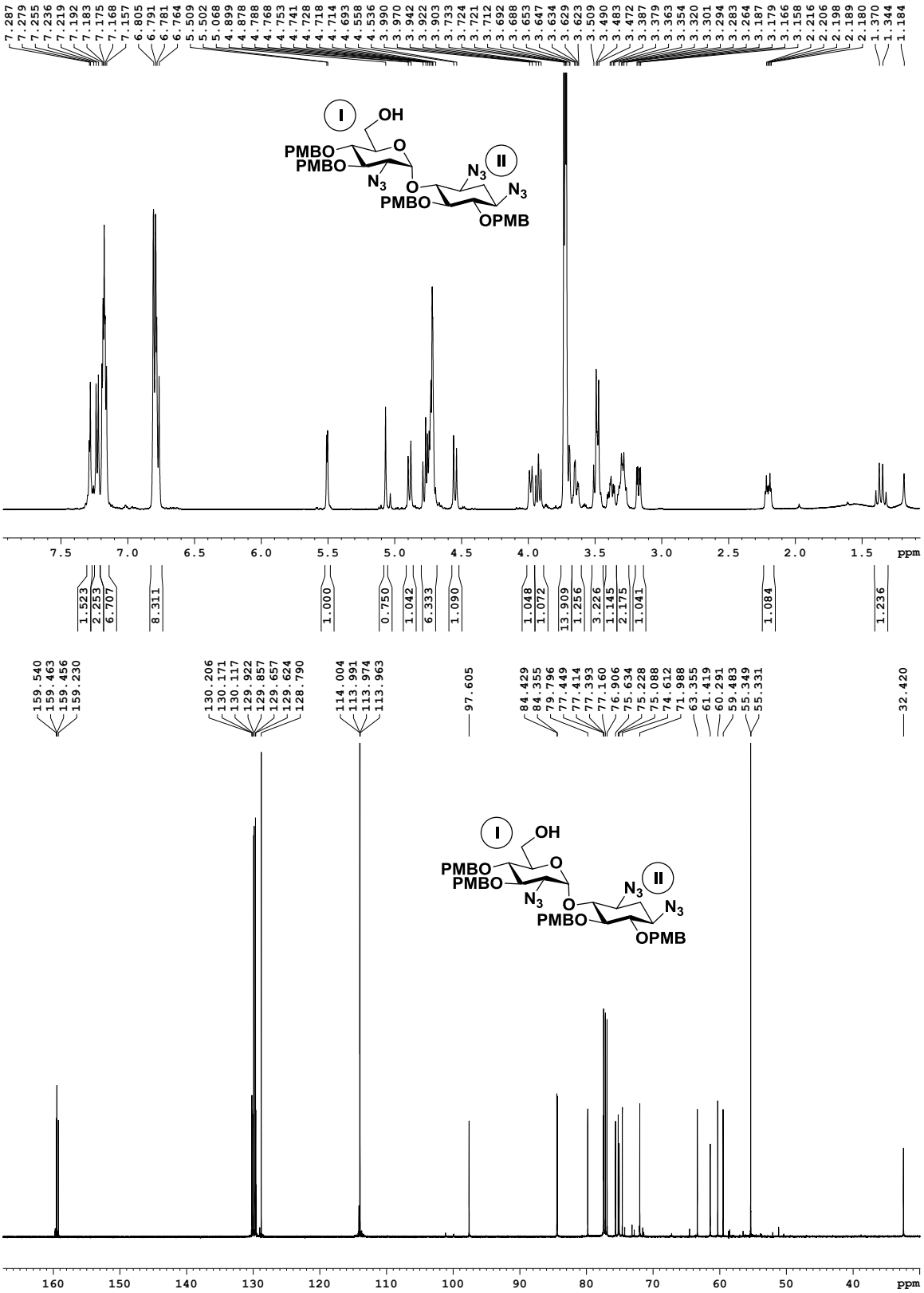
Synthesis of (S, X)-Ester (26): A mixture of (*S*)-2-methoxy-2(1-naphthyl)propanoic acid (*S*)-MαNP (0.007 g, 0.03 mmol), 4-dimethylaminopyridine (DMAP, 0.005 g, 0.04 mmol), 10-camphorsulfonic acid (CSA, 0.001 g, 0.004 mmol), and 1,3-dicyclohexylcarbodiimide (DCC, 0.034 g, 0.16 mmol) was stirred in CH_2Cl_2 (3 mL) at 0° C. The major alcohol **21** from the above (0.028 g, 0.031 mmol), was dissolved in CH_2Cl_2 (2 ml), slowly added to the above stirred mixture, and the reaction was left at room temperature for 72 h. The mixture was diluted with EtOAc and washed with 1% HCl solution, saturated $NaHCO_3$ and brine. The combined organic layer was dried over $MgSO_4$, evaporated and subjected to a column chromatography (EtOAc/Hexane) to yield the desired esters (*S*, *X*)-**26** (0.007 g, 20%). ^{1}H NMR (600 MHz, $CDCl_3$): **'Ring I'**: δ_H 5.49 (dd, 1H, *J* = 8.5, 4.4 Hz, H-6), 5.17 (d, 1H, *J* = 3.8 Hz, H-1), 4.04 (d, 1H, *J* = 10.0 Hz, H-4), 3.58 (t, 1H, *J* = 9.8 Hz, H-3), 3.25 (d, 1H, *J* = 8.5 Hz, H-7), 3.22 (dd, 1H, J_1 = 10.7, J_2 = 4.6 Hz, H-7), 2.34 (dd, 1H, J_1 = 17.0, J_2 = 6.3 Hz, H-5), 2.12-2.02 (m, 1H, H-2) **'Ring II'**: δ_H 3.51 (dt, 2H, J_1 = 17.8, J_2 = 9.3 Hz, H-4, H-5), 3.46 – 3.37 (m, 2H, H-1, H-6), 3.33 – 3.27 (m, 1H, H-3), 2.25 (dt, 1H, J_1 = 13.2, J_2 = 4.5 Hz, H-2eq), 1.43 (ddd, 1H, J_1 = J_2 = J_3 = 12.6 Hz, H-2ax); **The additional peaks in the spectrum were identified as follow**: δ_H 8.08 (d, 1H, *J* = 8.8 Hz, Ar), 7.89 (d, 1H, *J* = 7.3 Hz,), 7.76 (dd, 2H, J_1 = 15.9, J_2 = 8.1 Hz, Ar), 7.46 (t, 2H, *J* = 7.5 Hz,), 7.44 – 7.41 (m, 1H, Ar), 7.39 (d, 1H, *J* = 7.5 Hz, Ar), 7.36 (t, 2H, *J* = 7.3 Hz, Ar), 7.34 – 7.27 (m, 8H, Ar), 7.25 – 7.23 (m, 2H, Ar), 7.23 – 7.19 (m, 6H, Ar), 7.16 (t, 1H, *J* = 7.1 Hz, Ar), 7.14 – 7.09 (m, 3H, Ar), 6.91 – 6.87 (m, 2H, Ar), 5.01 (d, 1H, *J* = 11.1 Hz, O(CH_2)Bn), 4.90 – 4.79 (m, 3H, O(CH_2)Bn), 4.63 (q, 2H, *J* = 11.1 Hz, O(CH_2)Bn), 4.22 – 4.15 (m, 2H, O(CH_2)Bn), 4.12 (d, 1H, *J* = 11.0 Hz, O(CH_2)Bn), 3.66 (d, 1H, *J* = 11.0 Hz, O(CH_2)Bn), 3.29 (S, 3H, OCH_3), 1.97 (s, 3H, CH_3).^{13}C NMR (125 MHz, $CDCl_3$): δ_C 172.7 (Ar), 138.3 (Ar), 138.0 (Ar), 137.9 (Ar), 137.7 (Ar), 137.3 (Ar) 134.1 (Ar), 130.5 (Ar), 129.3 (Ar), 129.1 (Ar), 128.6 (Ar), 128.6 (Ar), 128.4 (Ar), 128.4 (Ar), 128.3 (Ar), 128.3 (Ar), 128.2 (Ar), 127.9 (Ar), 127.7 (Ar), 127.7 (Ar), 127.6 (Ar), 127.6 (Ar), 127.5 (Ar), 126.9 (Ar),

126.1 (Ar), 125.6 (Ar), 125.1 (Ar), 125.1 (Ar), 124.6 (Ar), 97.1 (C1'), 84.5 (C5), 84.5 (C4), 81.2, 80.1 (C3'), 77.9 (C5'), 77.3, 77.0 (C4), 76.1, 75.2, 74.8, 74.4, 74.3 (C6'), 72.8, 70.4 (C4'), 69.4 (C7'), 62.5 (C2'), 60.2 (C3), 59.1 (C1), 51.4 (OCH_3), 32.3 (C2), 29.85, 21.9 (CH_3).

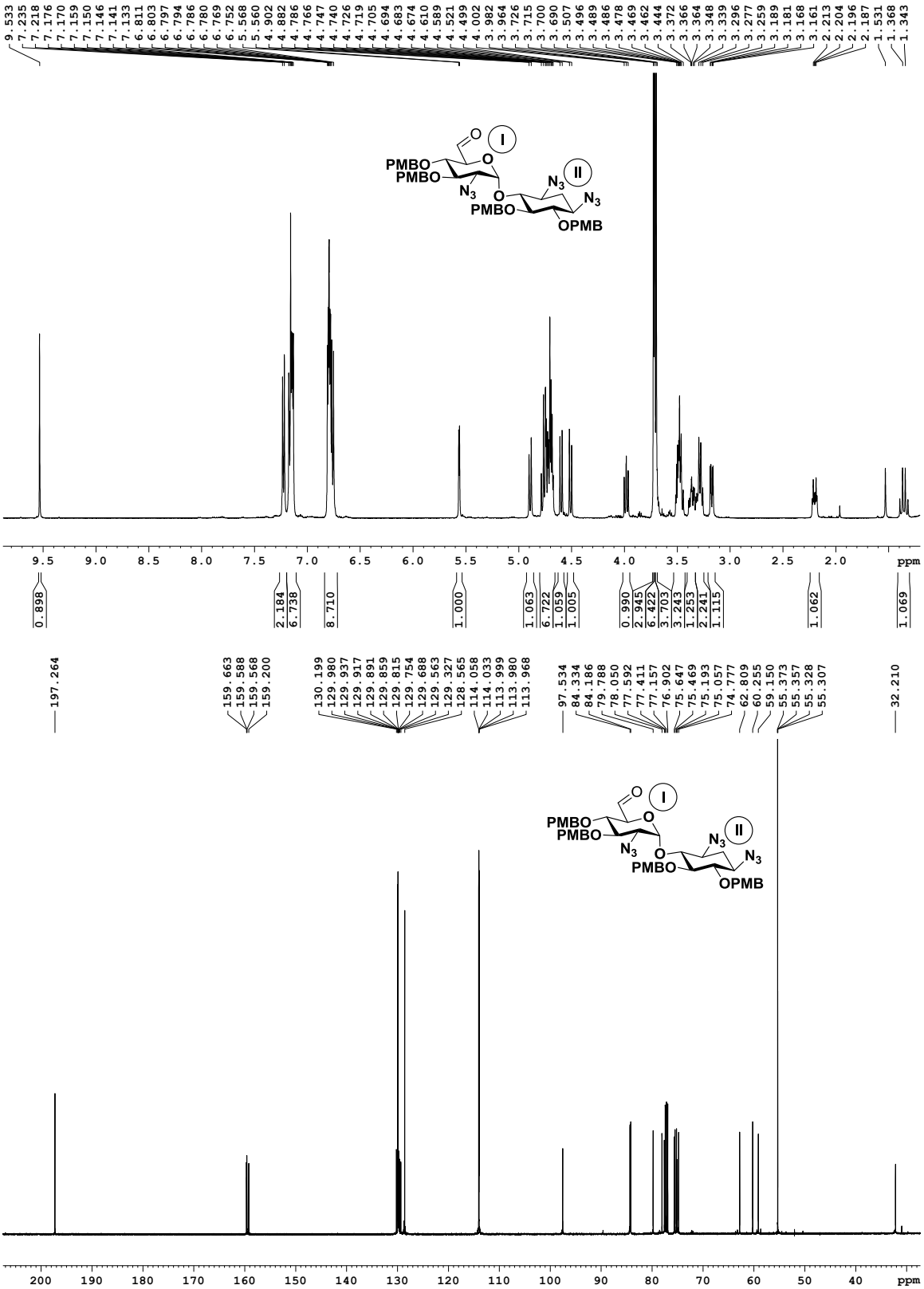
^{1}H and ^{13}C-NMR spectrums of compound 9 in $CDCl_3$



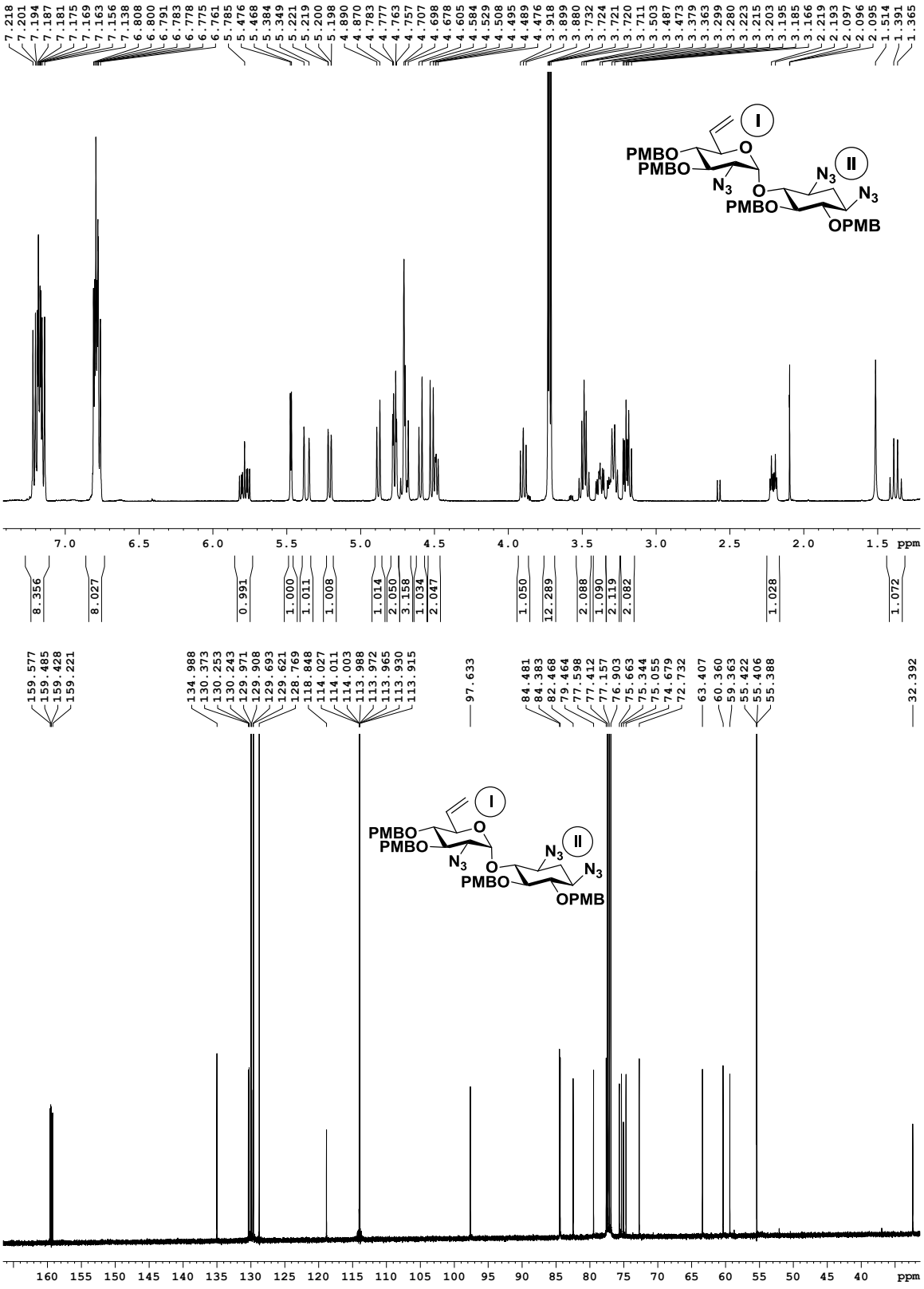
^{1}H and ^{13}C-NMR spectrums of 6'-OH compound in $CDCl_3$



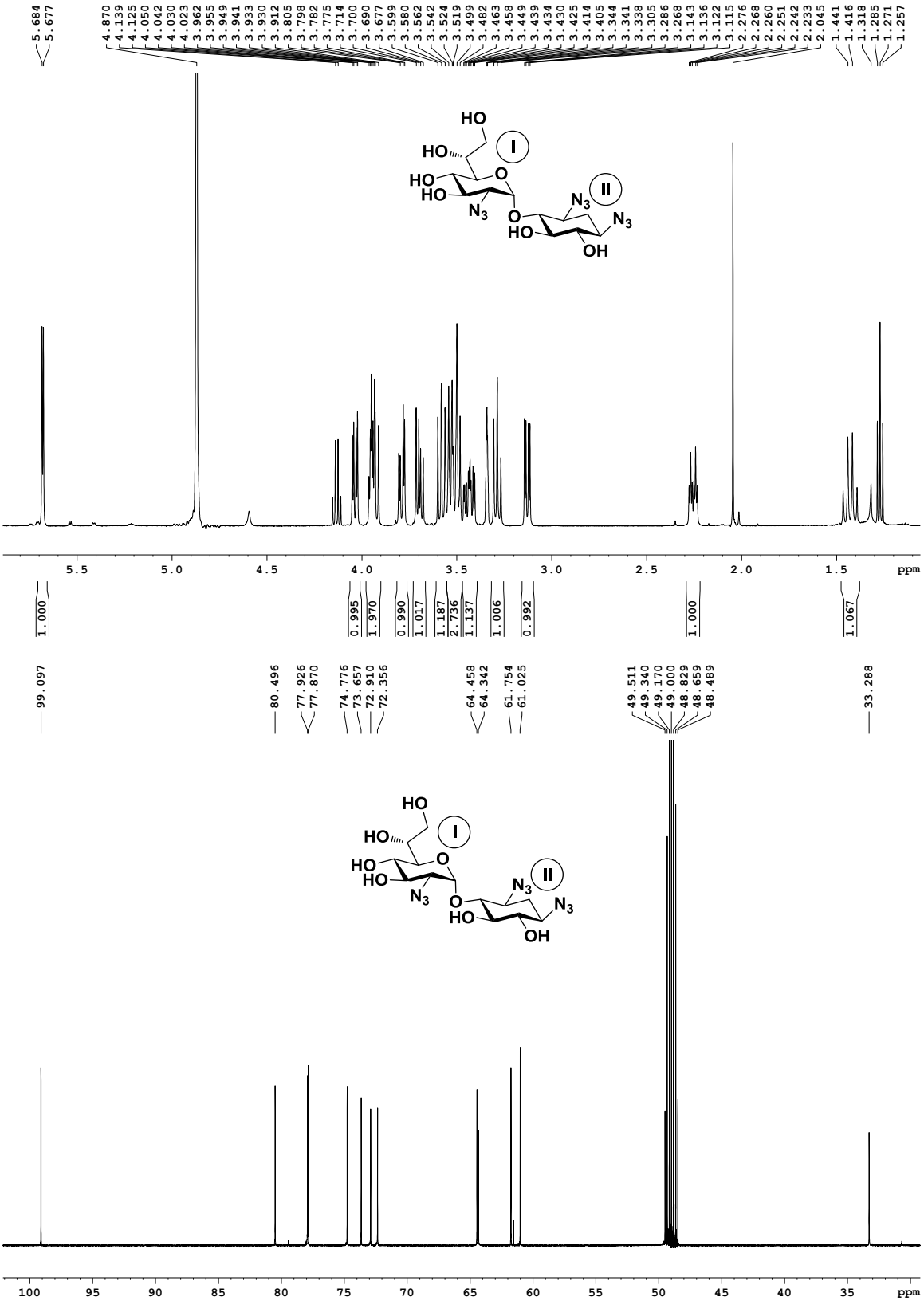
^{1}H and ^{13}C-NMR spectrums of Aldehyde in $CDCl_3$



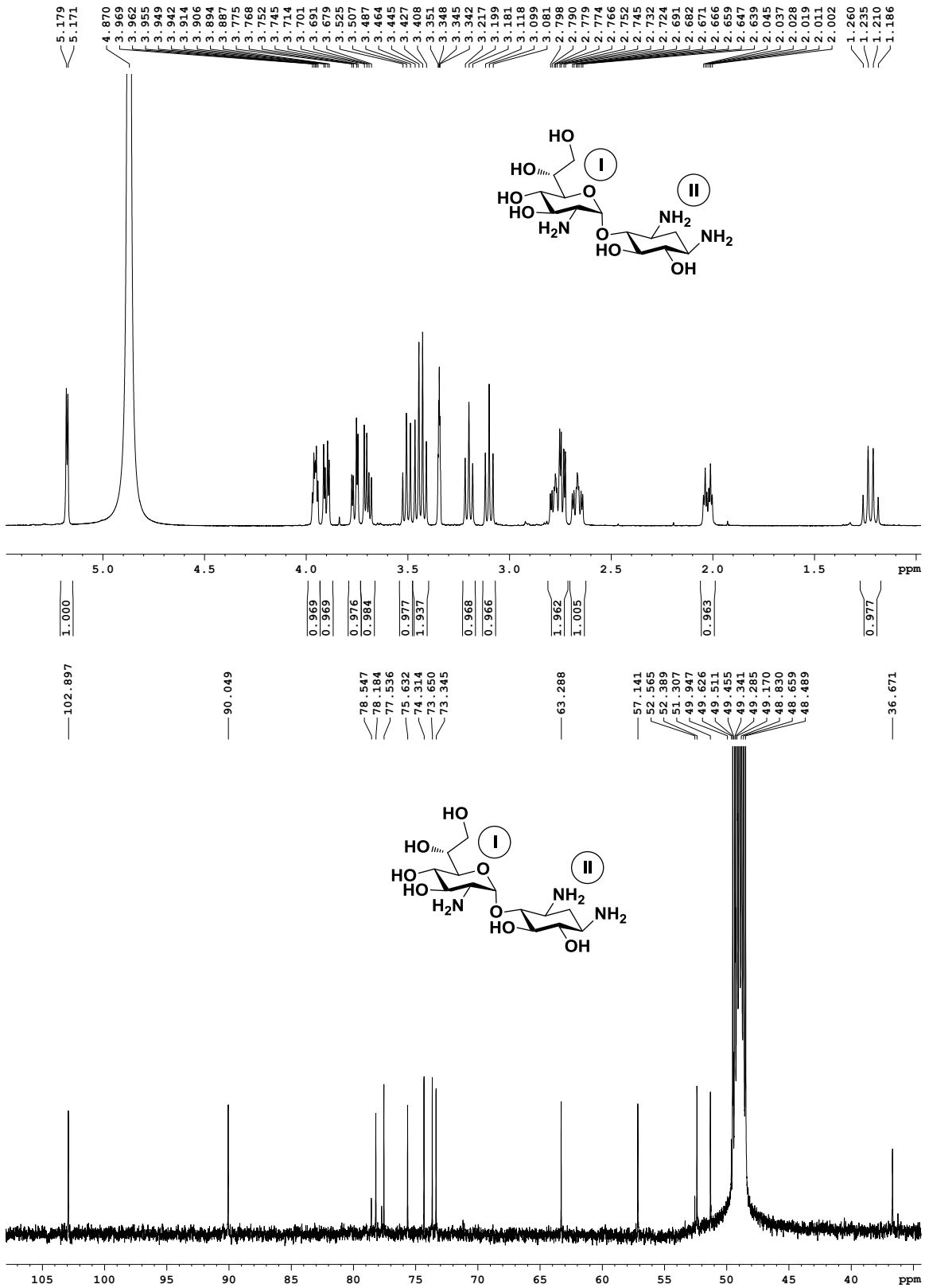
^{1}H and ^{13}C-NMR spectrums of compound 10 in $CDCl_3$



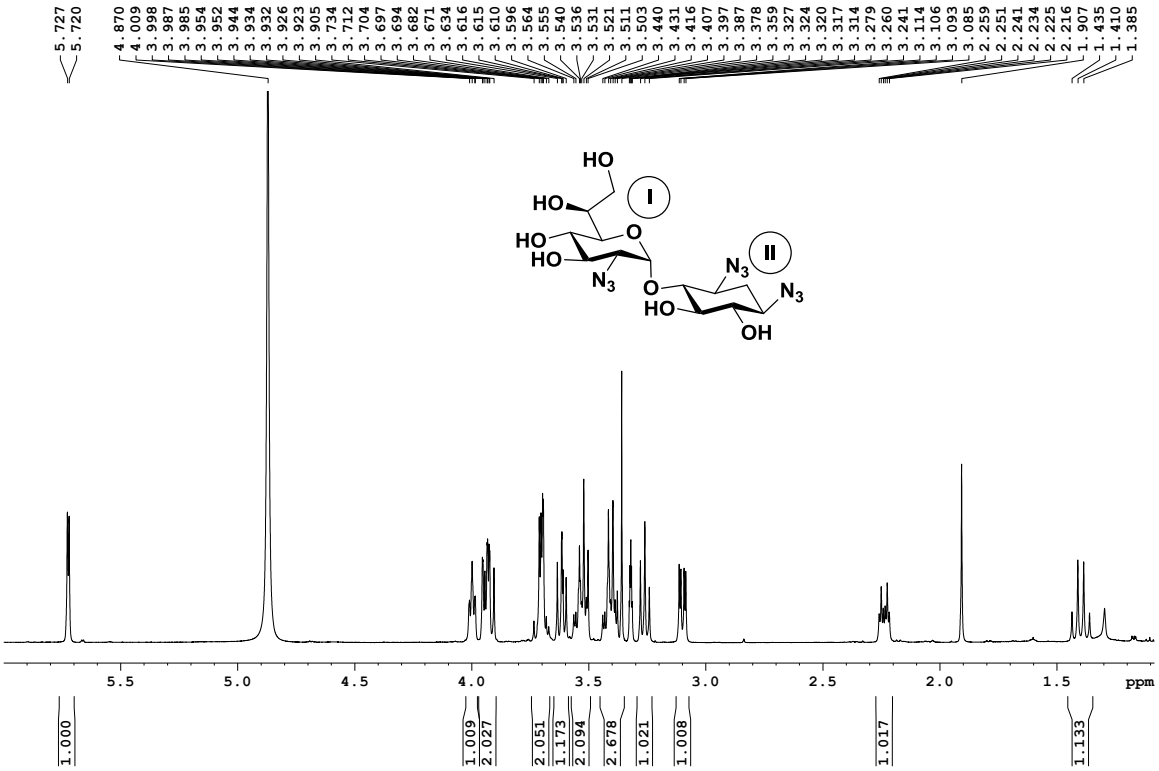
^{1}H and ^{13}C-NMR spectrums of compound 12 in MeOD

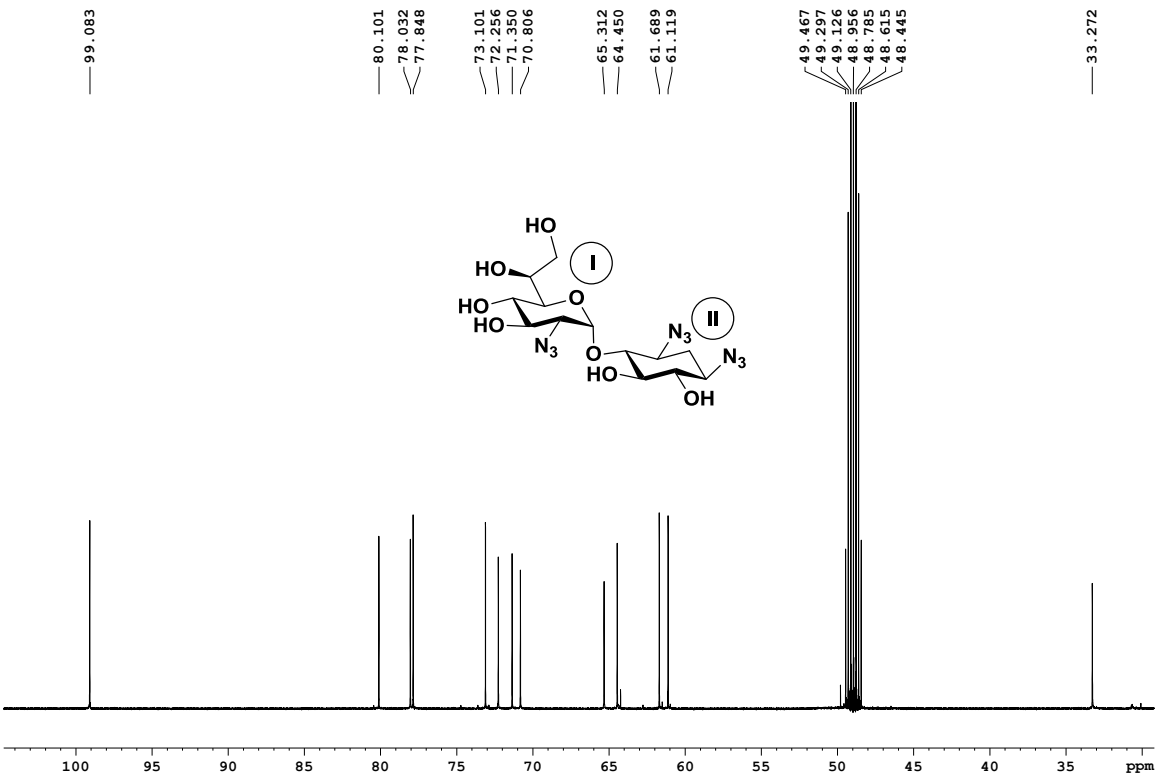


^{1}H and ^{13}C-NMR spectrums of compound [(*R*)-4] in MeOD

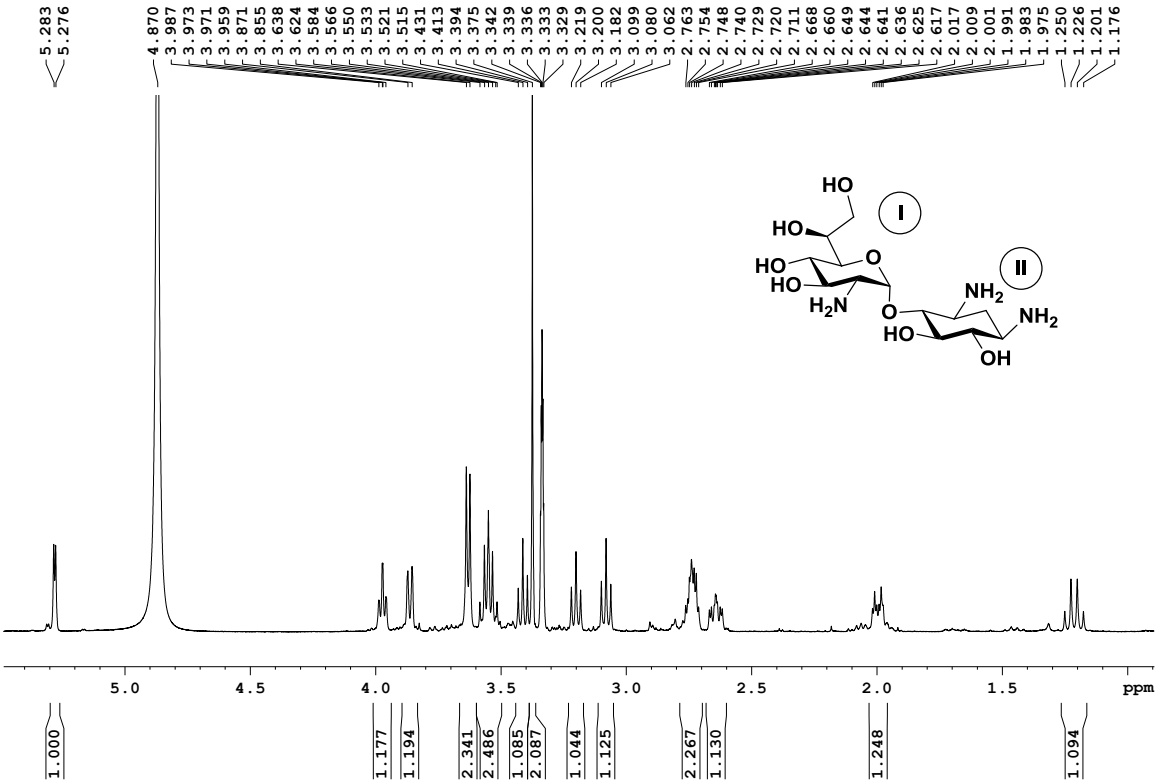


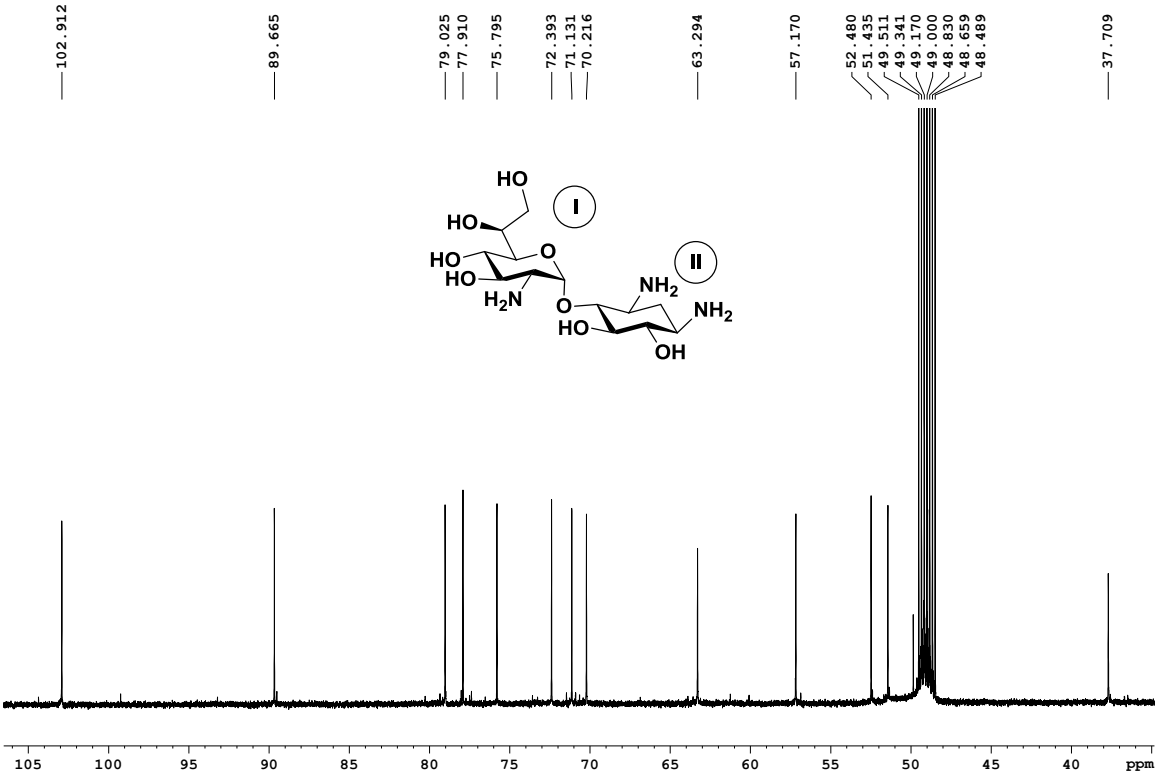
^{1}H and ^{13}C-NMR spectrums of compound 13 in MeOD



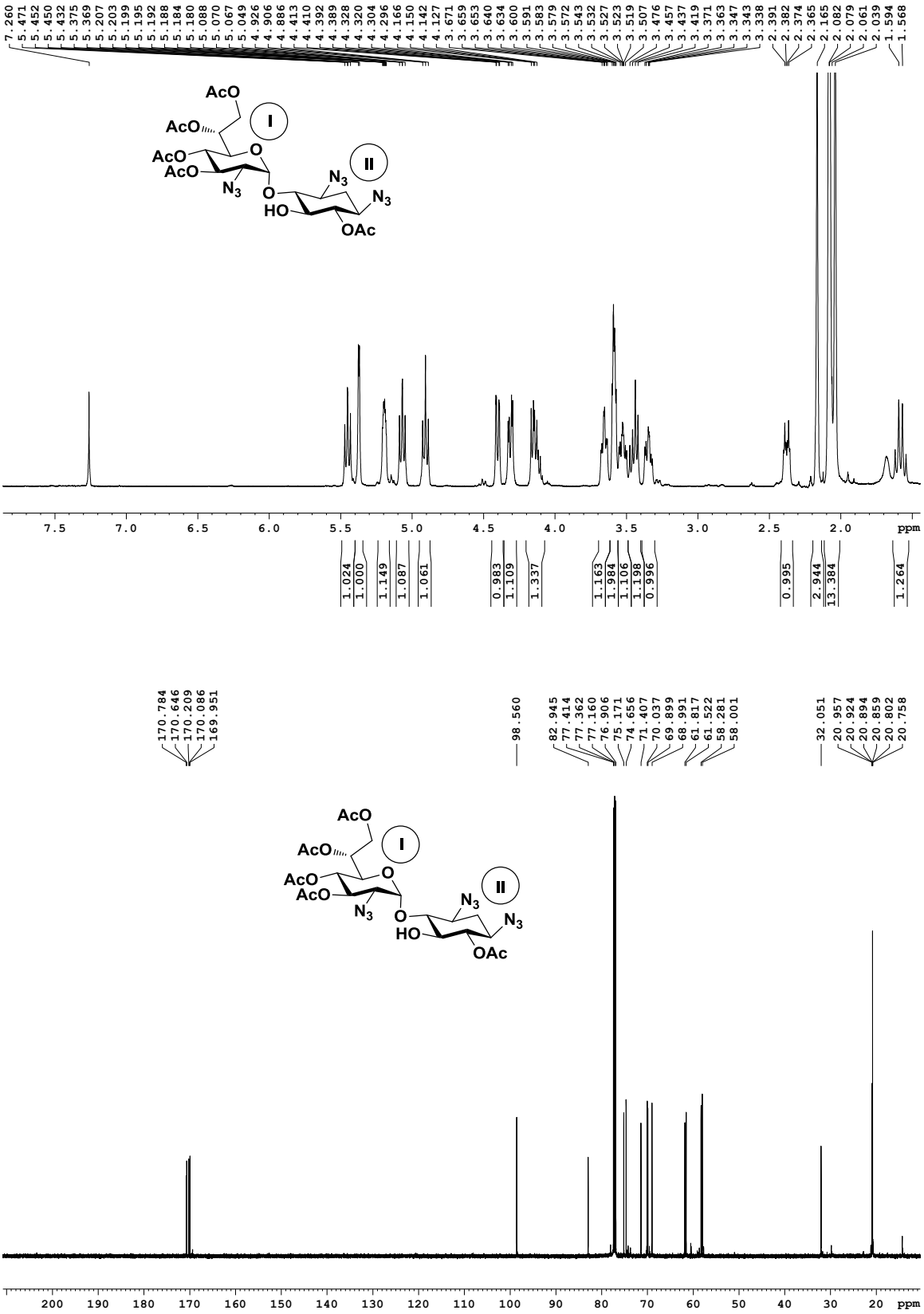


^{1}H and ^{13}C-NMR spectrums of compound [(*S*)-5] in MeOD

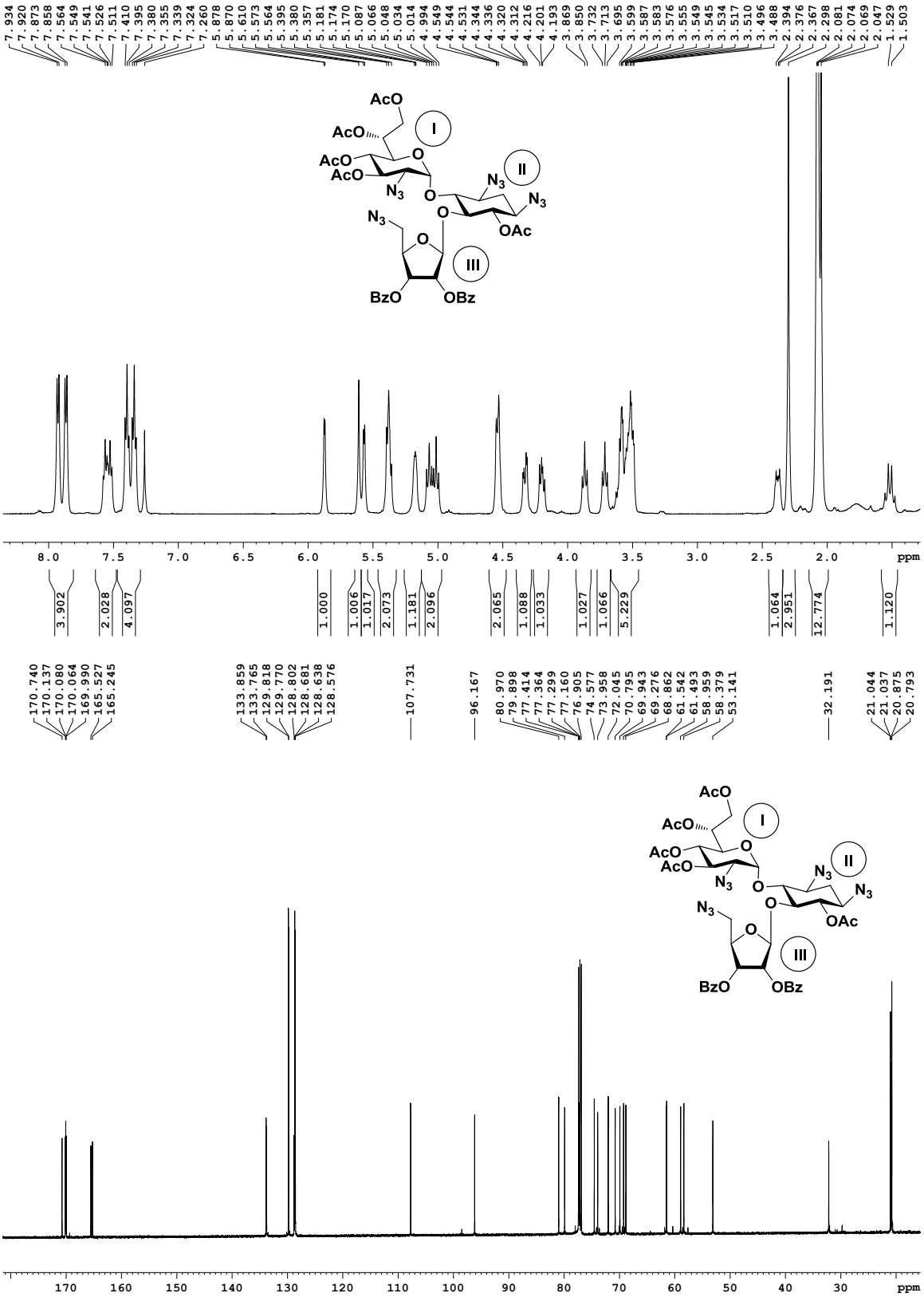




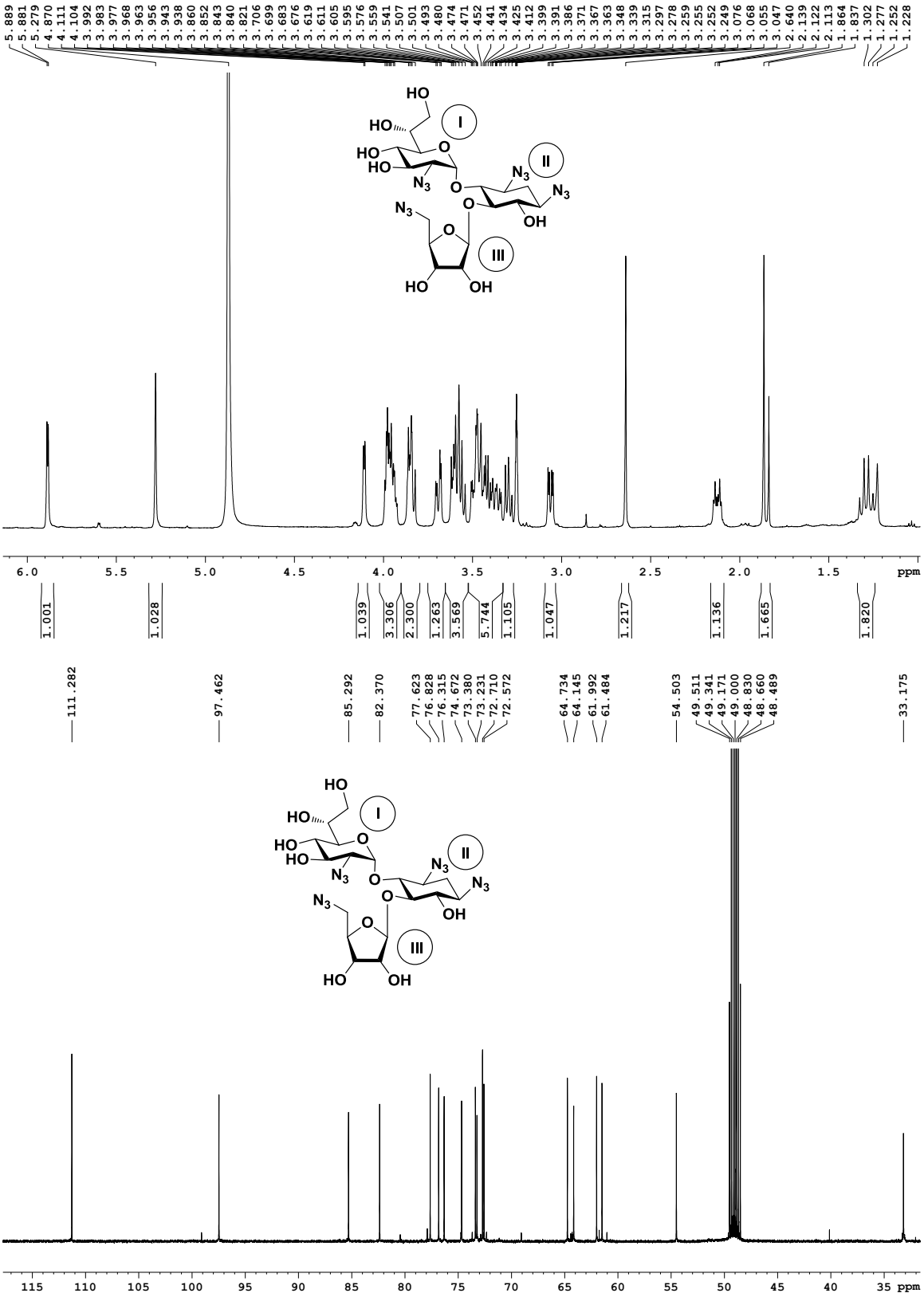
^{1}H and ^{13}C-NMR spectrums of compound 14 in $CDCl_3$



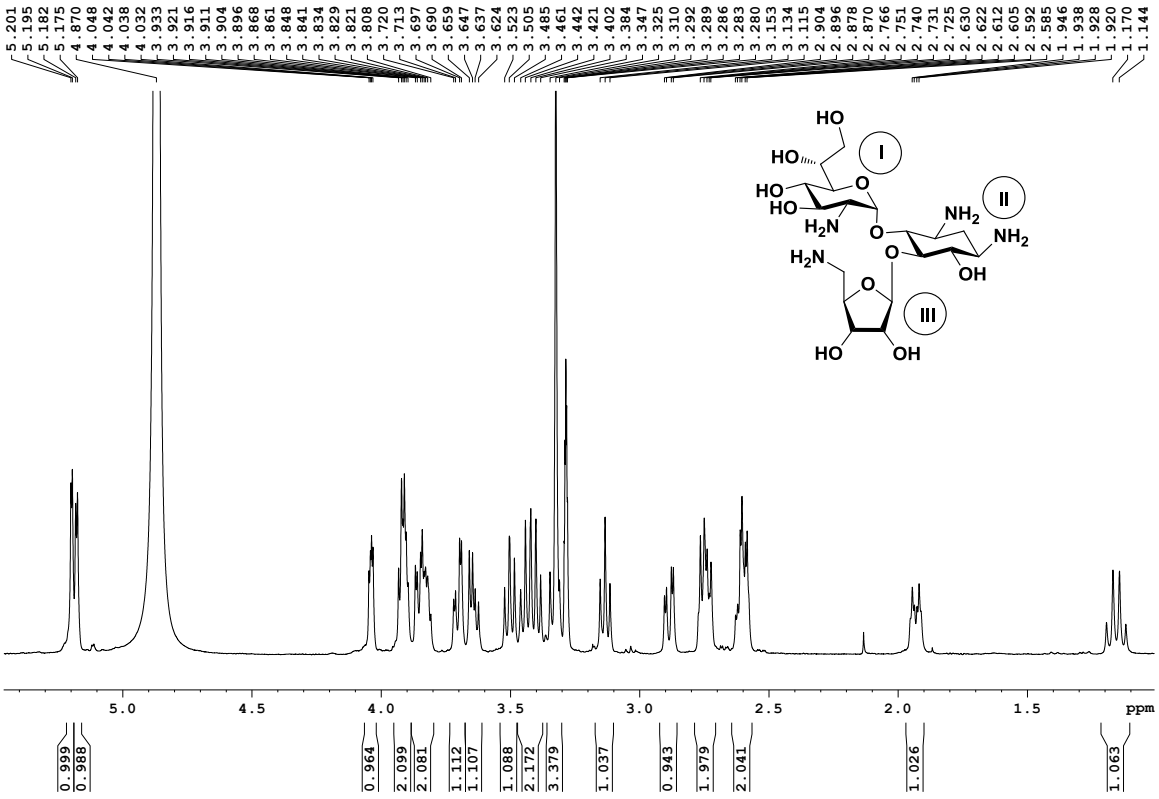
^{1}H and ^{13}C-NMR spectrums of compound 17 in $CDCl_3$

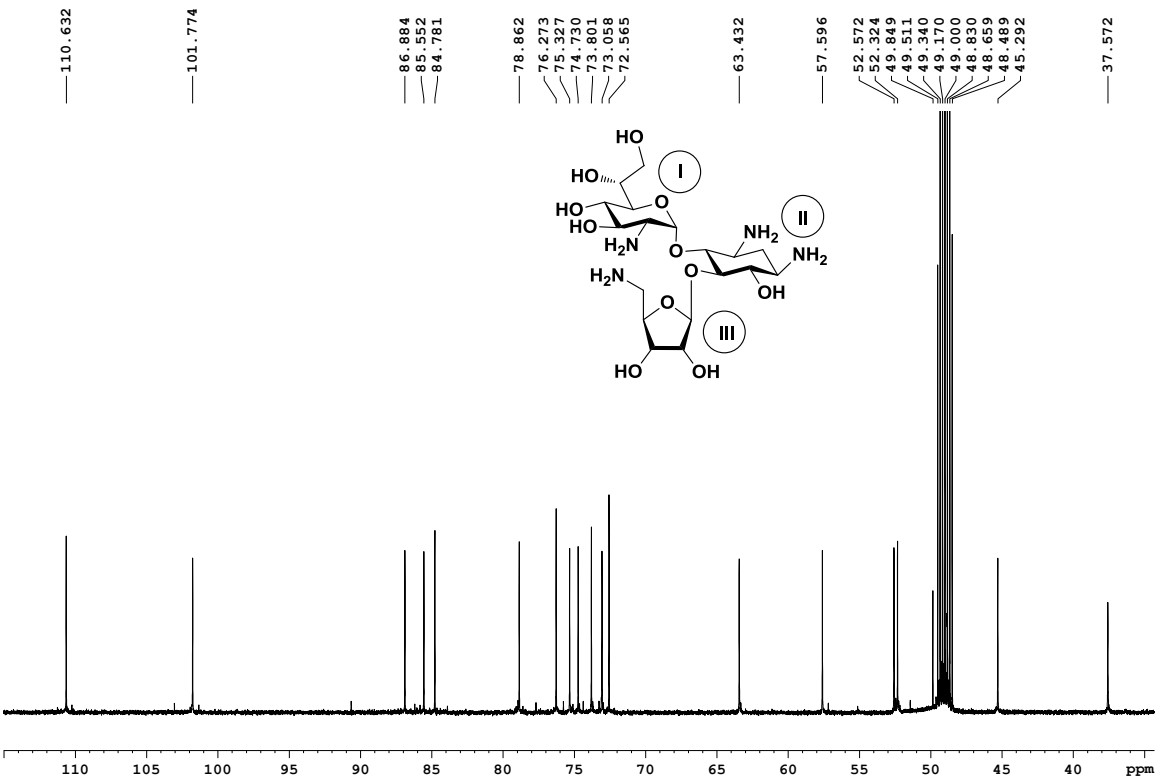


^{1}H and ^{13}C-NMR spectrums of completely unprotected glycoside in MeOD

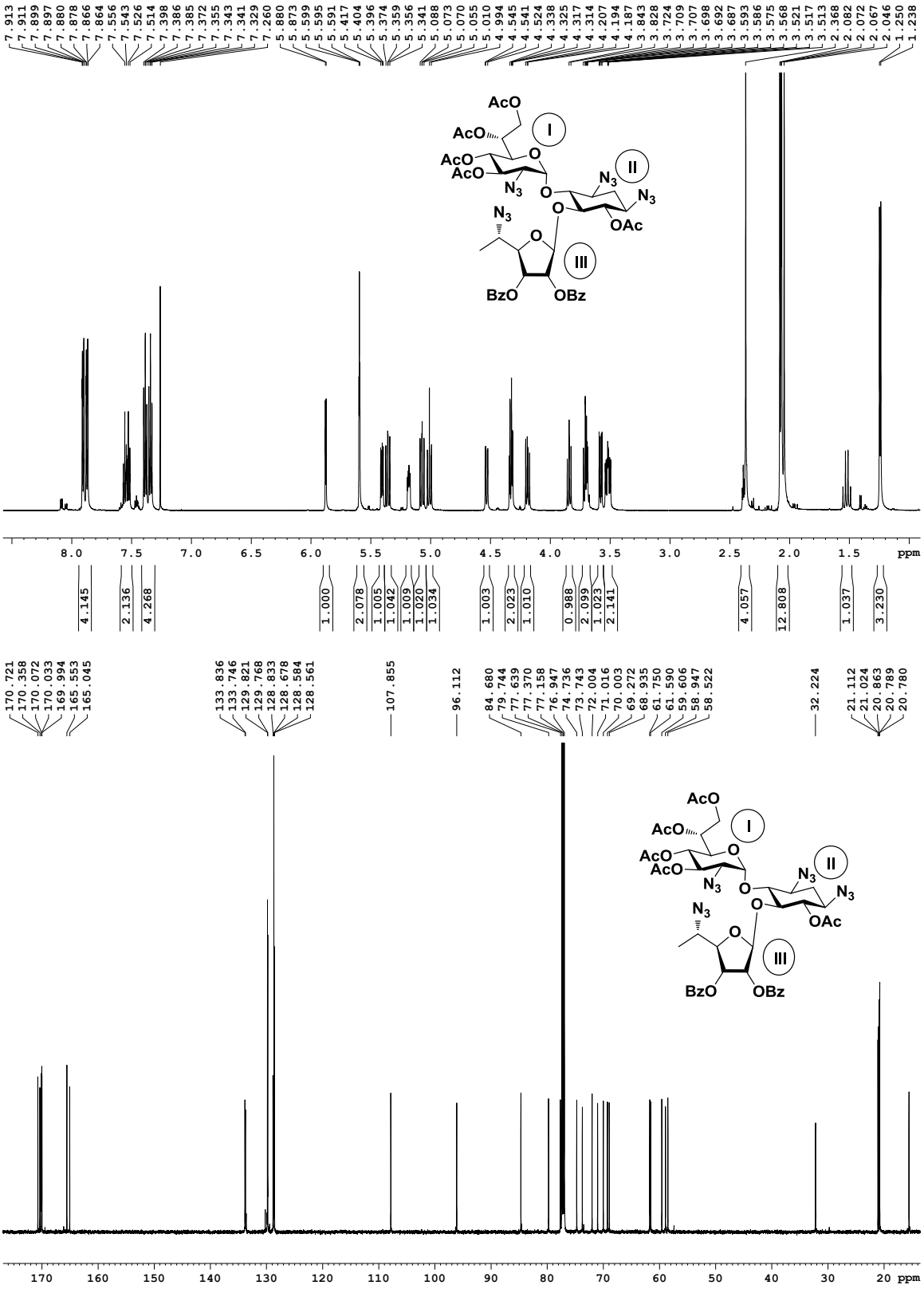


^{1}H and ^{13}C-NMR spectrums of compound 6 in MeOD

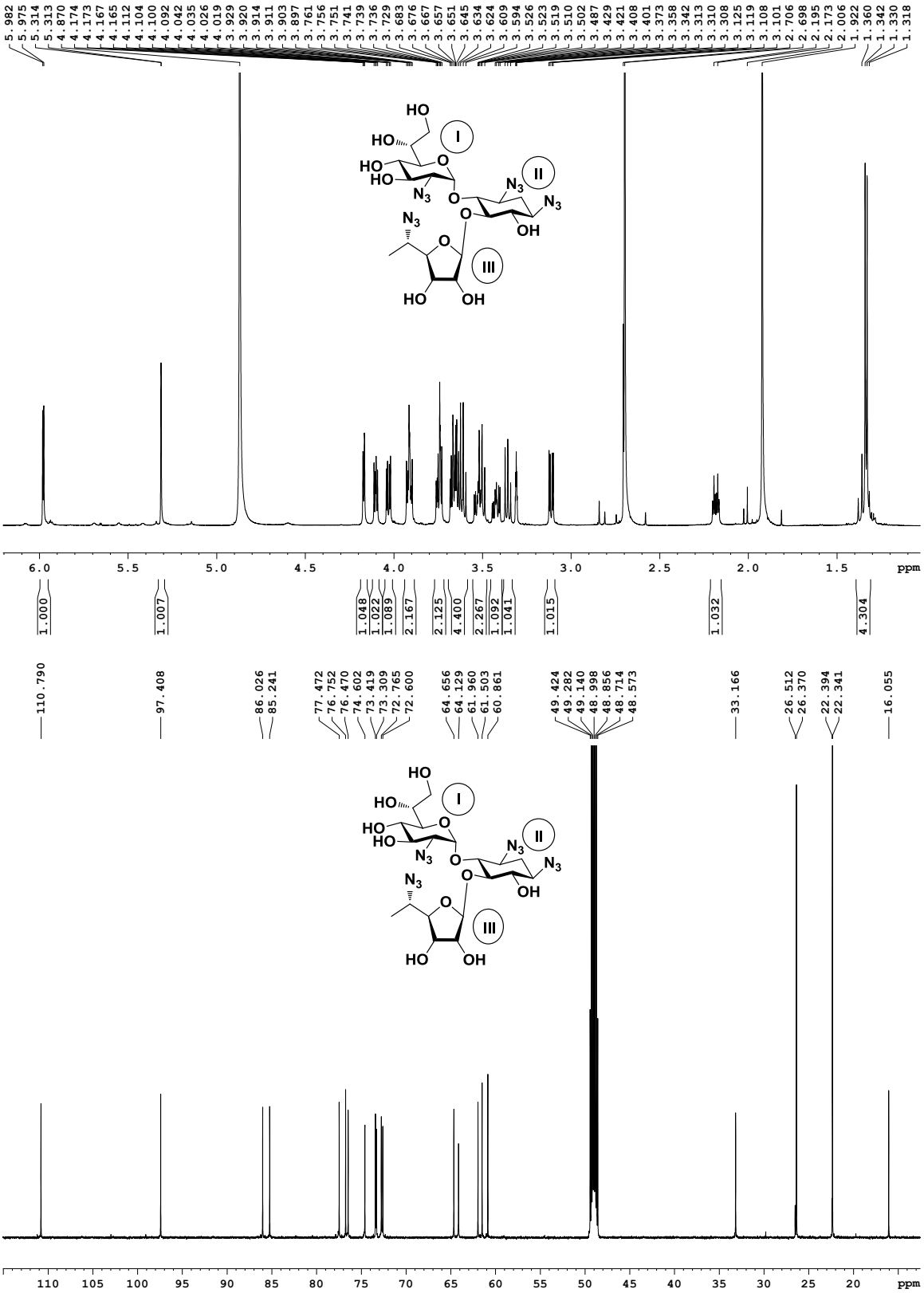




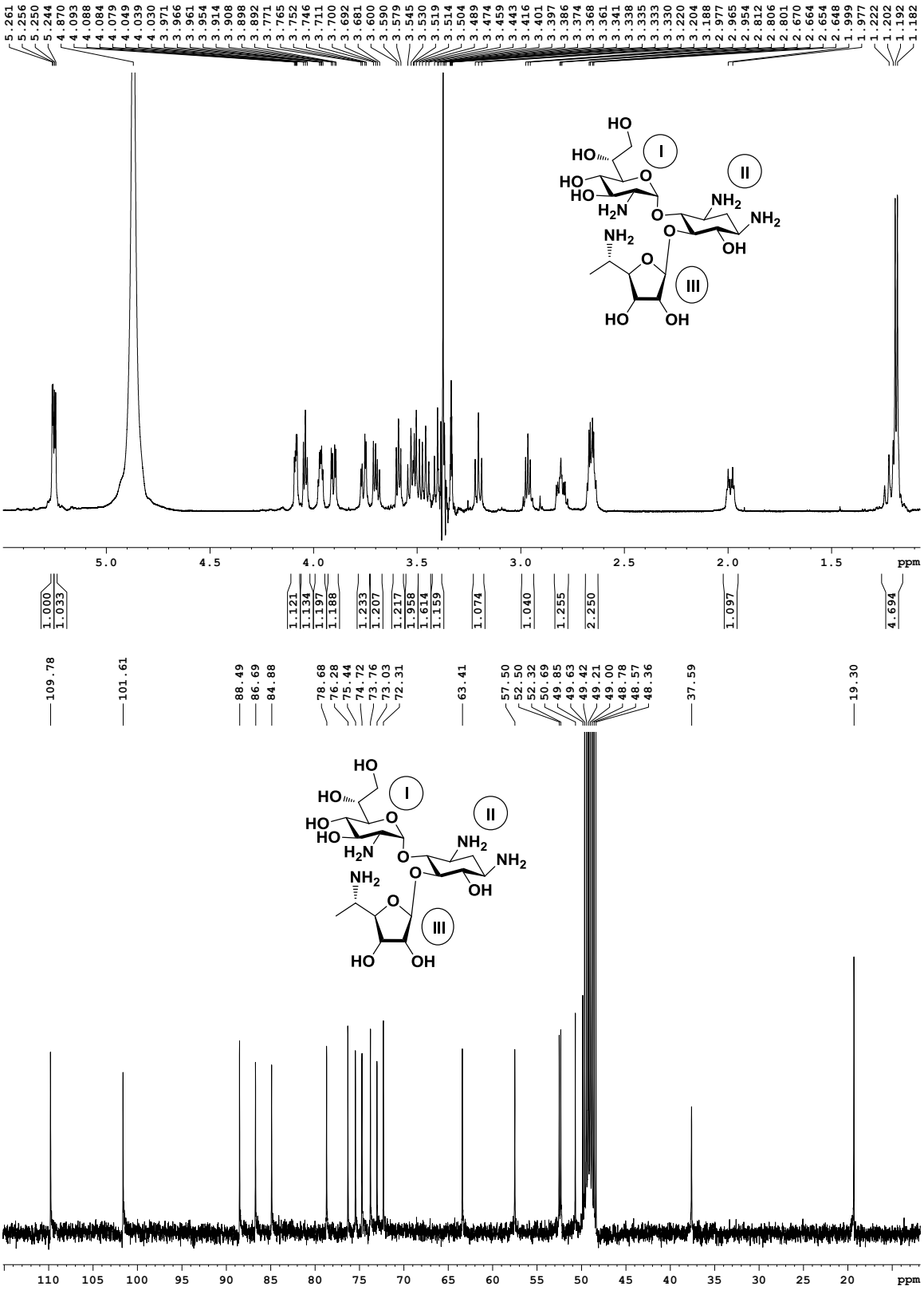
^{1}H and ^{13}C-NMR spectrums of compound 18 in $CDCl_3$



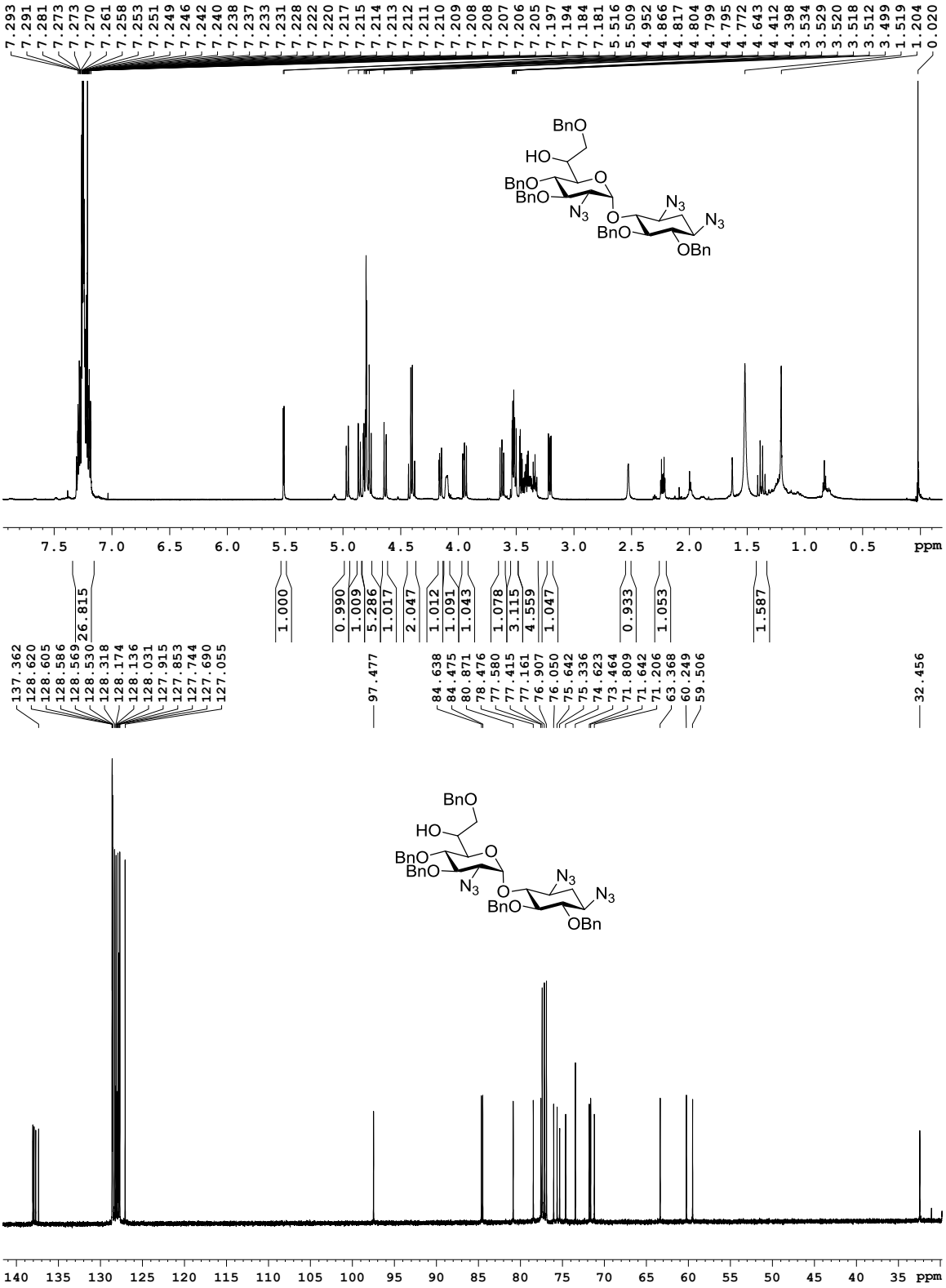
^{1}H and ^{13}C-NMR spectrums of completely unprotected glycoside in MeOD



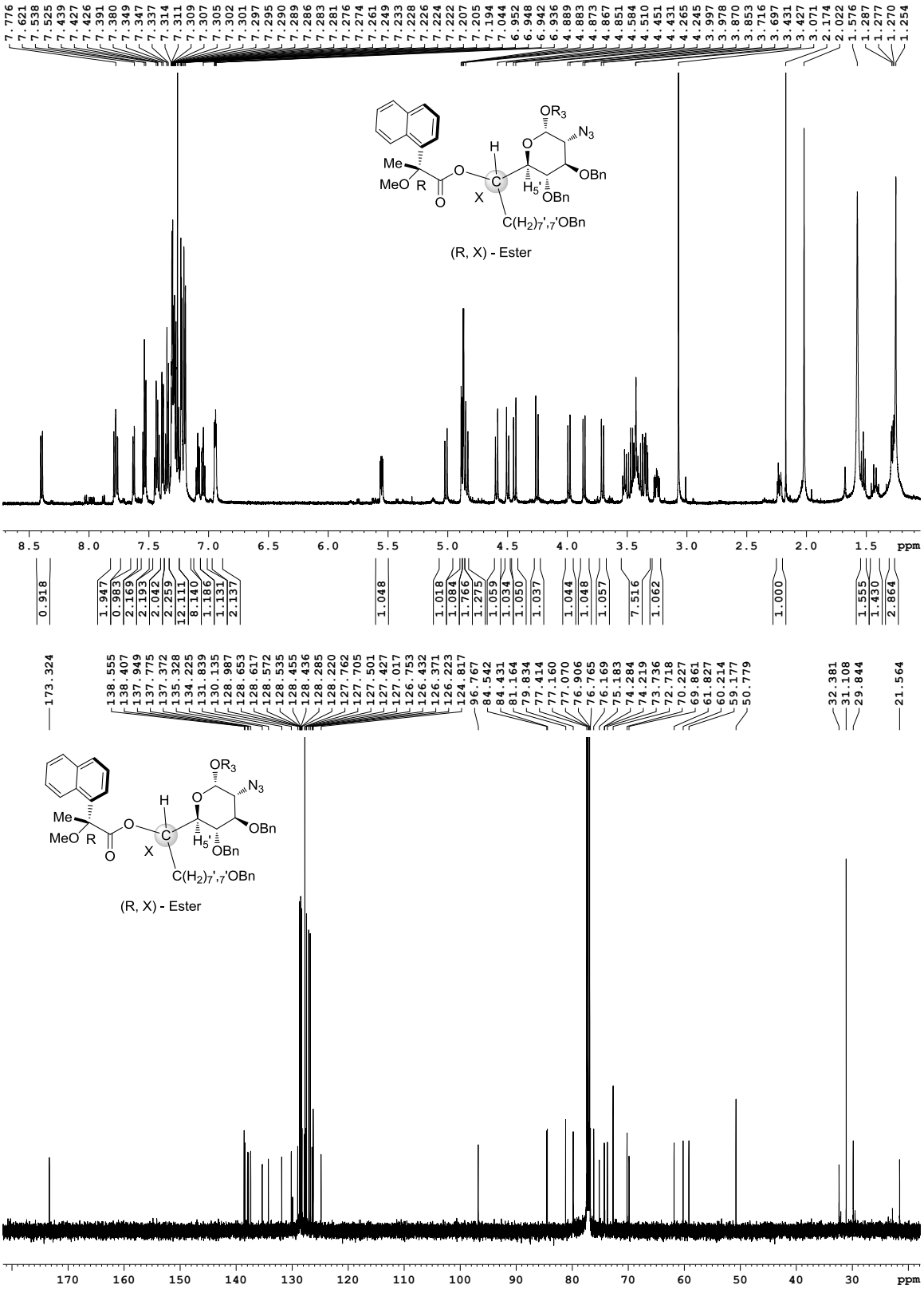
^{1}H and ^{13}C-NMR spectrums of compound 7 in MeOD



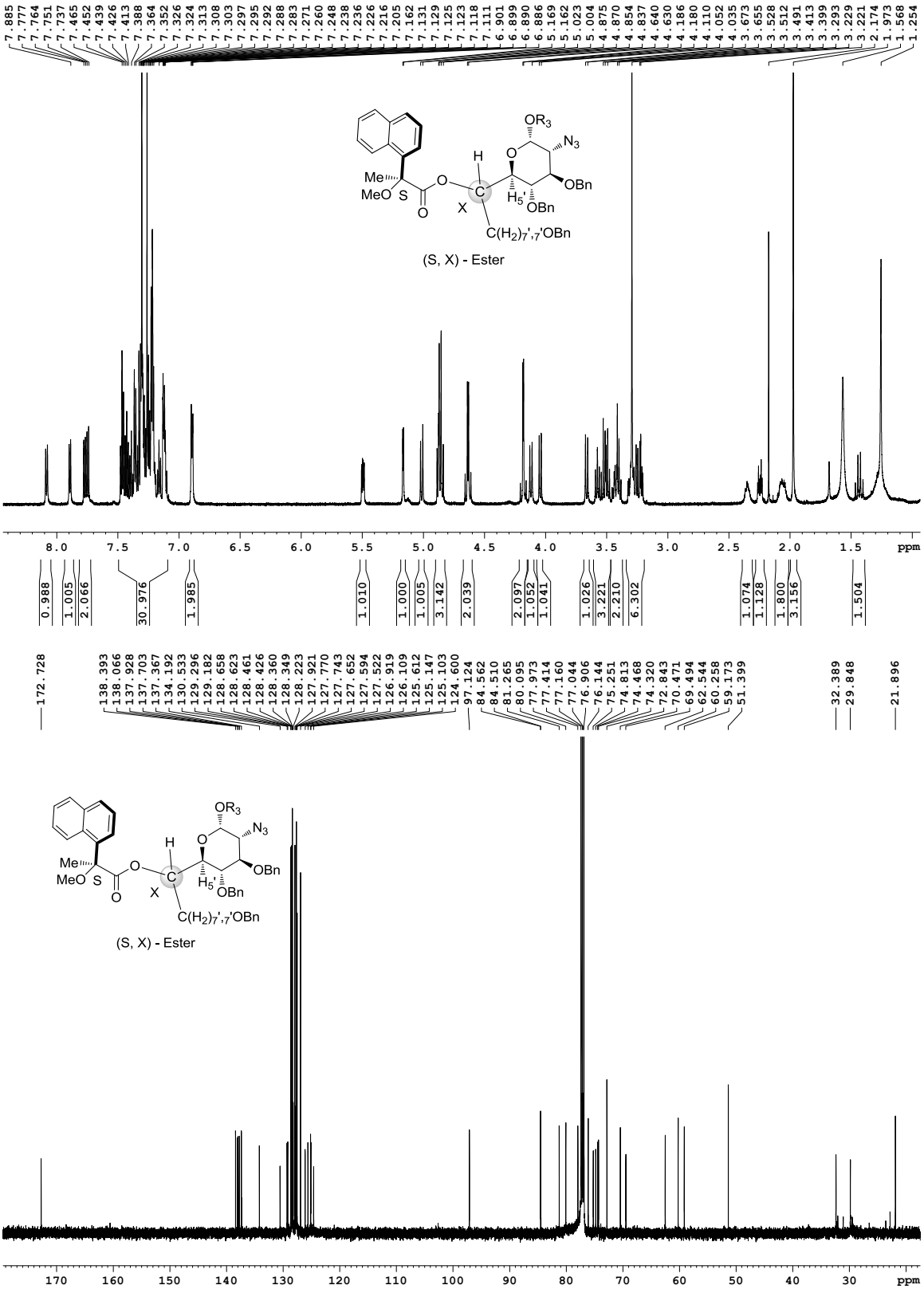
^{1}H and ^{13}C-NMR spectrums of compound 21(Major Diastereomer) in $CDCl_3$



^{1}H and ^{13}C-NMR spectrums of compound (*R, X*)-25 in $CDCl_3$



^{1}H and ^{13}C-NMR spectrums of compound (*S, X*)-26 in $CDCl_3$



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