

Supporting Information File 1

for

Synthesis of divalent ligands of β -thio- and β -N-galactopyranosides and related lactosides and their evaluation as substrates and inhibitors of *Trypanosoma cruzi* trans-sialidase

María Emilia Cano^{§,1}, Rosalía Agusti^{§,1}, Alejandro J. Cagnoni¹, María Florencia Tesoriero¹, José Kovensky², María Laura Uhrig^{*,1}, Rosa M. de Lederkremer^{*,1}

Address: ¹CIHIDECAR-CONICET, Departamento de Química Orgánica, Facultad de Ciencias Exactas y Naturales, Universidad de Buenos Aires, Pabellón 2, Ciudad Universitaria, 1428 Buenos Aires (Argentina), Fax: (+) 541145763346 and ²Laboratoire de Glycochimie, des Antimicrobiens et des Agroressources (LG2A)-CNRS FRE 3517, Université de Picardie Jules Verne, 33 rue Saint Leu, 80039 Amiens Cedex, France.

E-mail: María Laura Uhrig - mluhrig@qo.fcen.uba.ar; Rosa M. de Lederkremer - lederk@qo.fcen.uba.ar

*Corresponding author

§Contributed equally to this work.

Experimental section and data of ¹H and ¹³C NMR spectra of compounds 2, 3, 5, 6, 8, 10–13, 15–22 and 25.

Experimental

General methods

Analytical thin layer chromatography (TLC) was performed on Silica Gel 60 F254 aluminum supported plates (layer thickness 0.2 mm) with solvent systems given in the text. Visualization of the spots was effected by exposure to UV light and charring with a solution of 5% (v/v) sulfuric acid in EtOH, containing 0.5% *p*-anisaldehyde. Column chromatography was carried out with Silica Gel 60 (230-400 mesh). Optical rotations were measured at 20 °C in a 1 dm cell with a Perkin-Elmer 343 polarimeter. Microwave irradiation was carried out in a CEM Discover MW instrument with a System Internal IR probe type, at 70 °C (power max 300 W). High resolution mass spectra (HRMS) were obtained by Electrospray Ionization (ESI) and Q-TOF detection with a BRUKER microTOF-Q II ESI-Q-TOF spectrometer. ¹H and ¹³C nuclear magnetic resonance (NMR) spectra were recorded at 25 °C at 500 and 125 MHz, respectively, using a Bruker Avance II 500 spectrometer. For ¹H, ¹³C nuclear magnetic resonance (NMR) spectra, chemical shifts are reported in parts per million relative to tetramethylsilane or a residual solvent peak (CHCl₃: ¹H: δ = 7.26 ppm, ¹³C: δ = 77.2 ppm). Assignments of ¹H and ¹³C were assisted by 2D ¹H-COSY and 2D ¹H-¹³C experiments. In the description of the spectra, the signals corresponding to the glucose or trehalose moieties were labeled as “G” or “T”, respectively. *N*-acetyllactosamine was purchased from Sigma Chemical Co. 3'-sialyllactose was obtained from bovine colostrum by an adaptation of a reported method [1]. Azide-sugar scaffolds **9** and **14**, thiuronium salt **7**, thioglycoside **19** and compounds **20**, **21**, **24** and **25** were prepared as previously reported [2,3].

For the sialylation experiments a recombinant TcTS expressed in *Escherichia coli* was kindly provided by the group of O. Campetella from Universidad Nacional General San Martín (Buenos Aires, Argentina)

Analysis by HPAEC-PAD was performed using a Dionex ICS 3000 HPLC system equipped with a pulse amperometric detector. A CarboPac PA-10 ion exchange analytical column (4 × 250 mm) equipped with a guard column PA-10 (4 × 50 mm) was used eluted with a linear gradient over 30 min from 20 to 200 mM NaOAc in 100 mM NaOH at a flow rate of 0.9 ml/min at 25 °C.

Synthesis of the precursors

***N*-(2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl) succinamic acid (2)**

To a solution of 2,3,4,6-tetra-*O*-acetyl-β-D-galactosylamine (**1**, 389 mg, 1.12 mmol) in anhydrous THF (5.2 mL) was added succinic anhydride (1.34 mmol, 134 mg) and triethylamine (1.12 mmol, 155 μL). The reaction proceeded for 3 h until TLC showed complete consumption of the starting material. The solution was evaporated and the products were purified by column chromatography, using Toluene : EtOAc as solvent system to obtain **2** (411 mg, 82% yield). The succinyl derivative **2** showed identical spectroscopic and physical properties as those reported in the literature [4]; $R_f = 0.37$ (CHCl₃ : MeOH 10:1); ¹H NMR (500 MHz, CDCl₃) δ = 6.62 (d, 1 H, $J_{\text{NH},1} = 9.0$ Hz, NH), 5.43 (d, 1 H, $J_{3,4} = 2.6$ Hz, H-4), 5.24 (t, 1 H, $J_{1,2} = J_{1,\text{NH}} = 9.0$ Hz, H-1), 5.13 (dd, 1 H, $J_{3,4} = 3.1$ Hz, $J_{2,3} = 10.1$ Hz, H-3), 5.10 (dd, 1 H, $J_{1,2} = 8.6$, $J_{2,3} = 10.1$ Hz, H-2), 4.13 – 4.02 (m, 3 H, H-5, H-6a, H-6b), 2.78 – 2.59 (m, 4 H, CH₂-CH₂), 2.14, 2.05, 1.99 (4 s, 3 H each, CH₃CO). ¹³C NMR (125.7 MHz, CDCl₃): δ = 177.3 (COOH), 172.0, 171.6, 170.6, 170.2, 169.9 (5 × CO), 78.6 (C-1), 72.4, 70.9, 68.4, 67.3 (C-2, C-3, C-4, C-5), 61.2 (C-6), 30.7, 28.7 (CH₂-CH₂), 20.8 (2x), 20.7 (2x) (4 × COCH₃).

***N*¹-[2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl] *N*⁴-propargyl succinamide (3)**

To a solution of **2** (0.85 mmol, 380 mg) in anh. CH₂Cl₂, DCC (1.07 mmol, 220 mg) was added under Argon. After 20 min, propargylamine (1.02 mmol, 56.4 mg) was added and the mixture was stirred at room temperature for 24 h and then filtered. The solution was concentrated and compound **3** was purified by column chromatography using CHCl₃ : MeOH (50:1 to 35:1) as

eluting solvent. Yield: 350 mg, 85%; mp 76-78°C; $[\alpha]_D^{20} +22.5$ ($c = 0.6$, CHCl_3); $R_f = 0.46$ ($\text{CHCl}_3 : \text{MeOH } 10:1$); $^1\text{H NMR}$ (500 MHz, CDCl_3) $\delta = 6.60$ (d, 1 H, $J_{1,\text{NH}} = 9.2$ Hz, NH), 6.00 (t, 1 H, $J_{\text{CH}_2,\text{NH}} = 4.8$ Hz, NH), 5.44 (dd, 1 H, $J_{4,5} = 1.1$, $J_{3,4} = 2.8$ Hz, H-4), 5.26 (t, 1 H, $J_{1,2} \cong J_{1,\text{NH}} \cong 9.2$ Hz, H-1), 5.17 – 5.12 (m, 2 H, H-2, H-3); 4.13 (dd, 1 H, $J_{5,6a} = 7.2$, $J_{6a,6b} = 11.1$ Hz, H-6a), 4.09 (dd, 1 H, $J_{5,6b} = 6.0$, $J_{6a,6b} = 11.1$ Hz, H-6b), 4.04 (ddd, 1 H, $J_{4,5} = 1.1$, $J_{5,6a} = 7.2$, $J_{5,6b} = 6.0$ Hz, H-5), 4.03 (dd, 2 H, $J_{\text{CH}_2,\text{C}\equiv\text{CH}} = 2.5$, $J_{\text{CH}_2,\text{NH}} = 4.8$ Hz, CH_2N), 2.60 – 2.45 (m, 4 H, $\text{CH}_2\text{-CH}_2$), 2.25 (t, 1 H, $J_{\text{CH}_2,\text{C}\equiv\text{CH}} = 2.5$ Hz, $\text{C}\equiv\text{CH}$), 2.16, 2.09, 2.04, 2.00 (4 s, 12 H, CH_3CO). RMN- ^{13}C (125.7 MHz, CDCl_3): $\delta = 172.6$, 171.4, 171.3, 170.5, 170.2, 170.0 (6 \times CO), 79.6 ($\text{HC}\equiv\text{C}$), 78.6 (C-1), 72.4 (C-5), 71.8 ($\text{HC}\equiv\text{C}$), 71.0 (C-3), 68.3 (C-2), 67.3 (C-4), 61.3 (C-6), 31.3, 29.0 ($\text{CH}_2\text{-CH}_2$), 30.7 (CH_2N), 20.9, 20.8, 20.7 (2x) (CH_3CO -). Anal. Calcd for $\text{C}_{21}\text{H}_{28}\text{N}_2\text{O}_{11}$: C, 52.06; H, 5.83; N, 5.78. Found: C, 52.33; H, 5.72; N, 5.74. HRMS (ESI): m/z $[M+H]^+$ calcd for $\text{C}_{21}\text{H}_{29}\text{N}_2\text{O}_{11}$: 485.1766, found: 485.1761.

N*-[*(2,3,6-Tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl- β -D-galactopyranosyl)- β -D-glucopyranosyl)succinamic acid (5)

Compound **5** was prepared by reaction of **4** (432 mg, 0.68 mmol) with succinic anhydride (89 mg, 0.89 mmol) in THF (5.4 mL), in the presence of triethylamine (102 μL , 0.74 mmol) as described for **2**. Purification was performed by column chromatography using Toluene : EtOAc (3:1) containing 1% AcOH as eluting solvent. Yield: 459 mg, 92%. Compound **5** showed the same spectroscopical and physical properties described previously [5]. $R_f = 0.42$ (AcOH 0.5% in EtOAc); $^1\text{H NMR}$ (500 MHz, CDCl_3) $\delta = 6.43$ (d, 1 H, $J_{1,\text{NH}} = 9.3$ Hz, NH), 5.35 (d, 1 H, $J_{3',4'} = 3.2$ Hz, H-4'), 5.29 (t, 1 H, $J_{2,3} = J_{3,4} = 9.2$ Hz, H-3), 5.21 (t, 1 H, $J_{1,2} = J_{1,\text{NH}} = 9.3$ Hz, H-1), 5.10 (dd, 1 H, $J_{1',2'} = 8.0$, $J_{2',3'} = 10.3$ Hz, H-2'), 4.95 (dd, 1 H, $J_{3',4'} = 3.4$, $J_{2',3'} = 10.4$ Hz, H-3'), 4.84 (t, 1 H, $J_{2,3} = J_{1,2} = 9.6$ Hz, H-2), 4.46 (d, 1 H, $J_{1',2'} = 8.0$ Hz, H-1'), 4.43 (d, 1 H, $J_{6a,6b} = 14.0$ Hz, H-6a), 4.15 (dd, 1 H, $J_{5',6a'} = 6.6$, $J_{6a',6b'} = 11.3$ Hz, H-6a'), 4.13 (dd, 1 H, $J_{5,6b} = 4.5$, $J_{6a,6b} = 12.5$ Hz, H-6b), 4.07 (dd, 1 H, $J_{5',6b'} = 7.4$, $J_{6a',6b'} = 11.1$ Hz, H-6b'), 3.87 (t, 1 H, $J_{5',6a'} = 6.8$, $J_{5',6b'} =$

6.8 Hz, H-5'), 3.77 (dd, 1 H, $J_{3,4} = 8.9$, $J_{4,5} = 9.8$ Hz, H-4), 3.73 (dd, 1 H, $J_{5,6b} = 3.0$, $J_{4,5} = 9.9$ Hz, H-5), 2.75, 2.63 (2m, 1 H each, CH_2), 2.47(m, 2 H, CH_2), 2.16, 2.12, 2.07, 2.05, 2.04 (2x), 1.96 (7 s, 21H, CH_3CO); ^{13}C NMR (125 MHz, $CDCl_3$) $\delta = 176.1$ (COOH), 172.0, 171.6, 170.6 (2x), 170.3 (2x), 169.5, 169.2 (8xCO), 101.5 (C-1'), 78.2 (C-1), 76.1 (C-4), 74.6 (C-5), 72.5 (C-3), 71.1 (C-3'), 71.0 (C-2), 70.8 (C-5'), 69.1 (C-2'), 66.7 (C-4'), 62.1 (C-6), 61.0 (C-6'), 30.9, 28.8 (CH_2-CH_2), 21.0, 20.9, 20.8 (3x), 20.7, 20.6 (CH_3CO). HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{30}H_{42}NO_{20}$: 736.2279, found: 795.2295.

***N*¹-[(2,3,6-Tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl- β -D-galactopyranosyl)- β -D-glucopyranosyl] *N*⁴-propargyl succinamide (6)**

Compound **6** was prepared by reaction of **5** with propargylamine in freshly distilled anh. CH_2Cl_2 , in the presence of DCC, as described for **3**. Purification by column chromatography (Cl_3CH : MeOH, 50:1 to 35:1) afforded 360 mg of **6** (yield 81%); mp 104-105 °C; $[\alpha]_D^{20} +5.6$ ($c = 0.8$, $CHCl_3$); $R_f = 0.53$ ($CHCl_3$: MeOH 10:1); 1H NMR (500 MHz, $CDCl_3$) $\delta = 6.64$ (d, 1 H, $J_{1,NH} = 9.2$ Hz, *NH*), 6.09 (t, 1 H, $J_{CH_2,NH} = 5.5$ Hz, *NH*), 5.35 (dd, 1 H, $J_{4',5'} = 0.9$, $J_{3',4'} = 3.4$ Hz, H-4'), 5.27 (t, 1 H, $J_{2,3} = J_{3,4} = 9.3$ Hz, H-3), 5.19 (t, 1 H, $J_{1,2} = J_{1,NH} = 9.3$ Hz, H-1), 5.09 (dd, 1 H, $J_{1',2'} = 7.9$, $J_{2',3'} = 10.4$ Hz, H-2'), 4.94 (dd, 1 H, $J_{3',4'} = 3.5$, $J_{2',3'} = 10.4$ Hz, H-3'), 4.84 (t, 1 H, $J_{2,3} = J_{1,2} = 9.3$ Hz, H-2), 4.46 (d, 1 H, $J_{1',2'} = 7.9$ Hz, H-1'), 4.43 (dd, 1 H, $J_{5,6a} = 1.7$, $J_{6a,6b} = 12.3$ Hz, H-6a), 4.14 (dd, 1 H, $J_{5',6a'} = 6.4$, $J_{6a',6b'} = 11.0$ Hz, H-6a'), 4.12 (dd, 1 H, $J_{5,6b} = 4.3$, $J_{6a,6b} = 12.1$ Hz, H-6b), 4.07 (dd, 1 H, $J_{5',6b'} = 7.4$, $J_{6a',6b'} = 11.1$ Hz, H-6b'), 4.01 (dd, 2 H, $J_{CH_2,C=CH} = 2.6$, $J_{CH_2,NH} = 5.3$ Hz, CH_2N), 3.86 (ddd, 1 H, $J_{4',5'} = 0.8$, $J_{5',6a'} = 6.5$, $J_{5',6b'} = 7.4$ Hz, H-5'), 3.77 (t, 1 H, $J_{3,4} = 8.9$, $J_{4,5} = 9.9$ Hz, H-4), 3.72 (ddd, 1 H, $J_{5,6a} = 1.8$, $J_{5,6b} = 4.3$, $J_{4,5} = 9.9$, H-5), 2.58 – 2.42(m, 4 H, CH_2-CH_2), 2.22 (t, 1 H, $J_{CH_2,C=CH} = 2.5$ Hz, $C\equiv CH$), 2.15, 2.11, 2.06 (2x), 2.04, 2.03, 1.96 (7 s, 21H, CH_3CO); ^{13}C NMR (125 MHz, $CDCl_3$) $\delta = 172.4$, 171.2 (2x), 170.3 (2x), 170.1, 170.0, 169.4, 169.0 ($-OCOCH_3$), 100.9 (C-1'), 79.4 ($C\equiv CH$), 78.0 (C-1), 75.9 (C-4), 74.4 (C-5), 72.4 (C-3), 71.7 ($C\equiv CH$), 71.0 (C-3'), 70.8 (C-2), 70.7 (C-5'), 69.0 (C-2'),

66.6 (C-4'), 61.9 (C-6), 60.8 (C-6'), 31.2, 30.6 (CH₂-CH₂), 29.2 (CH₂N), 20.9, 20.8, 20.7, 20.6 (2×), 20.5 (CH₃CO). Anal. calcd for C₃₃H₄₄N₂O₁₉.H₂O: C, 50.13; H, 5.86; N, 3.54. Found: C, 50.38; H, 5.95; N, 3.79. HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₃₃H₄₄N₂NaO₁₉: 795.2430, found: 795.2406.

Propargyl 2,3,6-tri-O-acetyl-4-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-1-thio-β-D-glucopyranoside (8)

4-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-2,3,6-tri-O-acetyl-β-D-glucopyranosyl isothiuronium bromide [6] **7** (1.100 g, 1.420 mmol) and propargyl bromide (2.130 mmol) were dissolved in anhydrous acetonitrile (5 mL) and NEt₃ (496 μL, 3.550 mmol) was added dropwise. The resulting mixture was stirred at rt for 3 h, when TLC and MS indicated complete consumption of the starting material. The solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (Hexane : EtOAc 2:3). Yield: 687 mg, 70%; [α]_D²⁰ +43.2 (*c* = 1.0, CHCl₃); *R*_f = 0.46 (Hexane : EtOAc 1:1.5); ¹H NMR (500 MHz, CDCl₃) δ = 5.36 (dd, 1 H, *J*_{4',5'} = 0.9, *J*_{3',4'} = 3.4 Hz, H-4'), 5.27 (t, 1 H, *J*_{2,3} = *J*_{3,4} = 9.2 Hz, H-3), 5.13 (dd, 1 H, *J*_{1',2'} = 7.9, *J*_{2',3'} = 10.4 Hz, H-2'), 5.00 (t, 1 H, *J*_{1,2} = *J*_{2,3} = 10.0 Hz, H-2), 4.97 (dd, 1 H, *J*_{3',4'} = 3.4, *J*_{2',3'} = 10.5 Hz, H-3'), 4.77 (d, 1 H, *J*_{1,2} = 10.1 Hz, H-1), 4.53 (dd, 1 H, *J*_{5,6a} = 2.0, *J*_{6a,6b} = 12.1 Hz, H-6a), 4.50 (d, 1 H, *J*_{1',2'} = 7.9 Hz, H-1'), 4.17–4.08 (m, 3 H, H-6b, H-6'a, H-6'b), 3.89 (ddd, 1 H, *J*_{4',5'} = 0.9, *J*_{5',6'a} = *J*_{5',6'b} = 7.3 Hz, H-5'), 3.83 (t, 1 H, *J*_{3,4} = *J*_{4,5} = 9.6 Hz, H-4), 3.67 (ddd, 1 H, *J*_{5,6a} = 2.0, *J*_{5,6b} = 5.3, *J*_{4,5} = 9.9 Hz, H-5), 3.55, 3.28 (2 dd, 2 H, *J* = 2.6, *J*_{gem} = 12.6 Hz, CH₂S), 2.28 (t, 1 H, *J* = 2.6 Hz, C≡CH), 2.17, 2.14, 2.08, 2.07, 2.06, 2.05, 1.98 (7 s, 21 H, CH₃CO); ¹³C NMR (125 MHz, CDCl₃) δ = 170.3, 170.2, 170.1, 169.8, 169.7, 169.2, 169.1 (COCH₃), 101.1 (C-1'), 81.7 (C-1), 78.7 (C≡CH), 76.8 (C-5), 76.1 (C-4), 73.7 (C-3), 71.9 (C≡CH), 71.0 (C-3'), 70.7 (C-5'), 70.2 (C-2), 69.1 (C-2'), 66.6 (C-4'), 62.0 (C-6), 60.9 (C-6'), 20.9, 20.8, 20.7, 20.6 (2×), 20.5 (2×) (CH₃CO-), 17.6 (CH₂S). Anal. calcd for C₂₉H₃₈O₁₇S: C, 50.43; H, 5.55; S, 4.64. Found: C, 50.19; H, 5.49; S, 4.88. HRMS (ESI): *m/z* [M+Na]⁺ calcd for C₂₉H₃₈NaO₁₇S: 713.1722, found: 713.1720.

General procedure for the click reaction: synthesis of compounds **10**, **12**, **15**, **17**, **20** and **22**.

The corresponding azido-saccharides **9** or **14** [2,3] (0.20 mmol) and N-linked glycosides **3** or **6**, or S-linked lactoside **8** (0.20 mmol per mole of reacting azide) were dissolved in 2.5 mL of a dioxane/H₂O mixture (8:2). Copper sulfate (0.05 mmol per mole of reacting azide) and sodium ascorbate (0.10 mmol per mole of azide reacting group) were added, and the mixture was stirred at 70 °C under microwave irradiation during 50 min. The mixture was then poured into a 1:1 H₂O/NH₄Cl solution (20 mL) and extracted with EtOAc (4 ×15 mL). The organic layer was dried (Na₂SO₄) and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography, using the solvent system indicated in each case.

Compound **10**

Compound **10** was obtained by reaction of alkyne **3** and azide **9**. Yield: 95 mg, 57 %; mp 109-110°C; $[\alpha]_D^{20} +67.9$ ($c = 0.3$, CHCl₃); $R_f = 0.42$ (CHCl₃ : MeOH 9:1); ¹H NMR (500 MHz, CDCl₃) $\delta = 7.67$ (br s, 1 H, H-triazole), 6.64 (d, 1 H, $J_{1,NH} = 9.2$ Hz, NH), 6.40 (br s, 1 H, NH), 5.47 (dd, 1 H, $J_{3G,4G} = 9.4$, $J_{2G,3G} = 10.1$ Hz, H-3G), 5.43 (dd, 1 H, $J_{4,5} = 0.9$, $J_{3,4} = 2.9$ Hz, H-4), 5.22 (t, 1 H, $J_{1,2} = J_{1,NH} = 9.1$ Hz, H-1), 5.15 – 5.09 (m, 2 H, H-2, H-3), 4.92 (d, 1 H, $J_{1G,2G} = 3.6$ Hz, H-1G), 4.82 (dd, 1 H, $J_{1G,2G} = 3.6$, $J_{2G,3G} = 10.3$ Hz, H-2G), 4.80 (dd, 1 H, $J_{3G,4G} = 9.0$, $J_{4G,5G} = 10.2$ Hz, H-4G), 4.56 – 4.37 (m, 4 H, H-6aG, H-6bG, CH₂N), 4.17 (ddd, 1 H, $J_{5G,6aG} = 1.9$, $J_{5G,6bG} = 8.0$, $J_{4G,5G} = 9.9$ Hz, H-5G), 4.14 – 4.02 (m, 3 H, H-5, H-6a, H-6b), 3.15 (s, 3 H, OCH₃), 2.58 – 2.43 (m, 4 H, CH₂-CH₂), 2.14, 2.10, 2.07 (2x), 2.03, 2.00, 1.99 (7 s, 21 H, CH₃CO). RMN-¹³C (125.7 MHz, CDCl₃): $\delta = 172.3$, 171.4, 171.3, 170.4, 170.2, 170.0, 169.9, 169.8 (2x) (CO), 96.6 (C-1G), 78.5 (C-1), 72.2 (C-5), 70.8 (C-2G), 70.7 (C-3), 69.9 (C-4G), 69.7 (C-3G), 68.2 (C-2), 67.7 (C-5G), 67.2 (C-4), 61.1 (C-6), 55.5 (OCH₃), 50.7 (C-6G), 35.1 (NH-CH₂), 31.2, 30.6 (CH₂-CH₂), 20.8, 20.7 (3x), 20.6 (2x), 20.5 (CH₃CO). HRMS (ESI): m/z $[M+H]^+$ calcd for C₃₄H₄₈N₅O₁₉: 830.2938, found: 830.2954.

Compound 12

Compound **12** was obtained by reaction of alkyne **6** and azide **9**. Yield: 134 mg, 60%; mp 120 °C; $[\alpha]_D^{20} +43.4$ ($c = 0.9$, CHCl_3); $R_f = 0.31$ (EtOAc : MeOH 9:1); $^1\text{H NMR}$ (500 MHz, CDCl_3) $\delta = 7.64$ (s, 1 H, H-triazole), 6.61 (d, 1 H, $J_{1,\text{NH}} = 9.2$ Hz, NH), 6.41 (t, 1 H, $J_{\text{CH}_2,\text{NH}} = 5.2$ Hz, NH), 5.47 (t, 1 H, $J_{3\text{G},4\text{G}} = J_{2\text{G},3\text{G}} = 9.7$ Hz, H-3G), 5.35 (dd, 1 H, $J_{4',5'} = 0.9$, $J_{3',4'} = 3.2$ Hz, H-4'), 5.28 (t, 1 H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 5.19 (t, 1 H, $J_{1,2} = J_{1,\text{NH}} = 9.3$ Hz, H-1), 5.10 (dd, 1 H, $J_{1',2'} = 7.9$, $J_{2',3'} = 10.4$ Hz, H-2'), 4.94 (dd, 1 H, $J_{3',4'} = 3.5$, $J_{2',3'} = 10.4$ Hz, H-3'), 4.92 (d, 1 H, $J_{1\text{G},2\text{G}} = 3.6$ Hz, H-1G), 4.83 (t, 1 H, $J_{1,2} = J_{2,3} = 9.5$ Hz, H-2), 4.82 (dd, 1 H, $J_{1\text{G},2\text{G}} = 3.4$, $J_{2\text{G},3\text{G}} = 9.4$ Hz, H-2G), 4.79 (t, 1 H, $J_{3\text{G},4\text{G}} = J_{4\text{G},5\text{G}} = 9.5$ Hz, H-4G), 4.56 – 4.40 (m, 5 H, CH_2N , H-6aG, H-6bG, H-6a), 4.46 (d, 1 H, $J_{1',2'} = 7.9$ Hz, H-1'), 4.17– 4.40 (m, 3 H, H-5G, H6b, H6a'), 4.07 (dd, 1 H, $J_{5',6b'} = 7.4$, $J_{6a',6b'} = 11.1$ Hz, H-6b'), 3.88 (ddd, 1 H, $J_{4',5'} = 0.8$, $J_{5',6a'} = 6.4$, $J_{5',6b'} = 7.4$ Hz, H-5'), 3.77 (t, 1 H, $J_{3,4} = 8.9$, $J_{4,5} = 9.9$ Hz, H-4), 3.75 (ddd, 1 H, $J_{5,6a} = 2.0$, $J_{5,6b} = 4.6$, $J_{4,5} = 10.1$, H-5), 3.15 (s, 3 H, OCH_3), 2.53 – 2.46 (m, 4 H, $\text{CH}_2\text{-CH}_2$), 2.15, 2.11, 2.10, 2.06 (2x), 2.05, 2.04 (2x), 2.00, 1.96 (10 s, 30 H, CH_3CO); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) $\delta = 172.4$, 171.7, 171.3, 170.5 (2x), 170.3 (2x), 170.2, 170.1, 170.0, 169.5, 169.1 (CO), 144.8 (C-4 triazole), 123.8 (C-5 triazole), 101.1 (C-1'), 96.8 (C-1G), 78.2 (C-1), 76.1 (C-4), 74.6 (C-5), 72.6 (C-3), 71.2, 71.0, 70.9, 70.8 (C-2, C-2G, C-3, C-5'), 70.0, 69.9 (C-3G, C-4G), 69.1 (C-2'), 67.8 (C-5G), 66.8 (C-4'), 62.1 (C-6), 61.0 (C-6'), 55.6 (OCH_3), 50.8 (C-6G), 35.2 (CH_2N), 31.5, 30.8 ($\text{CH}_2\text{-CH}_2$), 21.0, 20.9, 20.8 (6x), 20.8, 20.7, (CH_3CO). HRMS (ESI): m/z $[M+H]^+$ calcd for $\text{C}_{46}\text{H}_{64}\text{N}_5\text{O}_{27}$: 1118.3783, found: 1118.3790.

Compound 15

Compound **15** was obtained by reaction of alkyne **3** and diazide **14**. Yield: 197 mg, 61%; mp 149-151°C; $[\alpha]_D^{20} +28.2$ ($c = 1.0$, CHCl_3); $R_f = 0.35$ (CHCl_3 : MeOH 10:1); $^1\text{H NMR}$ (500 MHz, CDCl_3) $\delta = 7.62$ (s, 1 H, H-triazole), 7.13 (d, 1 H, $J_{1,\text{NH}} = 9.0$ Hz, NH), 6.70 (dd, 1 H, $J_{\text{CH}_2,\text{NH}} = 5.4$ Hz, NH), 5.41 (dd, 1 H, $J_{3\text{T},4\text{T}} = 9.4$, $J_{2\text{T},3\text{T}} = 10.3$ Hz, H-3T), 5.42 (d, 1 H, $J_{3,4} = 3.0$ Hz, H-4), 5.29 (t, 1 H, $J_{1,2} = J_{1,\text{NH}} = 9.0$ Hz, H-1), 5.16 (dd, 1 H, $J_{3,4} = 3.3$, $J_{2,3} = 10.3$ Hz, H-3), 5.12 (dd, 1

H, $J_{1,2} = 9.0$, $J_{2,3} = 10.3$ Hz, H-2), 4.96 (dd, 1 H, $J_{1T,2T} = 3.9$, $J_{2T,3T} = 10.4$ Hz, H-2T), 4.94 (dd, 1 H, $J_{3T,4T} = 9.5$, $J_{4T,5T} = 10.0$ Hz, H-4T), 4.75 (d, 1 H, $J_{1T,2T} = 3.8$ Hz, H-1T), 4.61 (dd, 1 H, $J_{CH_2,NH} = 6.2$, $J_{gem} = 15.0$ Hz, CH_2N), 4.56 (dd, 1 H, $J_{5T,6aT} = 1.4$, $J_{6aT,6bT} = 14.4$ Hz, H-6aT), 4.36 (dd, 1 H, $J_{CH_2,NH} = 4.6$, $J_{gem} = 15.0$ Hz, CH_2N), 4.25 (dd, 1 H, $J_{5T,6bT} = 9.4$, $J_{6aT,6bT} = 14.4$ Hz, H-6bT), 4.06 – 3.98 (m, 4 H, H-5T, H-5, H-6^a, H-6b), 2.60 – 2.50 (m, 4 H, CH_2-CH_2), 2.12, 2.11, 2.05, 2.01, 2.00 (×2), 1.98 (7 s, 21 H, CH_3CO). RMN-¹³C (125.7 MHz, $CDCl_3$): $\delta = 172.7$, 171.8, 171.2, 170.5, 170.3, 170.2, 170.0 (×3) (CO), 145.3 (C-4 triazole); 124.0 (C-5 triazole), 91.7 (C-1T), 78.6 (C-1), 72.3 (C-5), 71.1 (C-3), 69.8 (C-3T), 69.6 (C-4T), 69.4 (C-5T), 69.0 (C-2T), 68.4 (C-2), 67.3 (C-4), 61.2 (C-6), 50.6 (C-6T), 35.2 (NH- CH_2), 31.3, 29.4 (CH_2-CH_2), 20.9 (2x), 20.8 (2x), 20.7 (3x) (CH_3CO). Anal. calcd for $C_{66}H_{88}N_{10}O_{37}$: C, 49.13; H, 5.50; N, 8.68. Found: C, 49.01; H, 5.63; N, 8.45. HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{66}H_{88}N_{10}NaO_{37}$ 1635.5204, found 1635.5204.

Compound 17

Compound **17** was obtained by reaction of alkyne **6** and diazide **14**. Yield: 193 mg, 44%; mp 151-152 °C; $[\alpha]_D^{20} +12.5$ ($c = 1.0$, $CHCl_3$); $R_f = 0.18$ (EtOAc : MeOH 9:1); ¹H NMR (500 MHz, $CDCl_3$) $\delta = 7.61$ (H-triazole), 7.19 (d, 1 H, $J_{1,NH} = 9.3$ Hz, NH), 6.69 (t, 1 H, $J_{CH_2,NH} = 5.4$ Hz, NH), 5.41 (t, 1 H, $J_{3T,4T} = J_{2T,3T} = 9.7$ Hz, H-3T), 5.34 (dd, 1 H, $J_{4',5'} = 0.7$, $J_{3',4'} = 3.4$ Hz, H-4'), 5.27 (t, 1 H, $J_{2,3} = J_{3,4} = 9.2$ Hz, H-3), 5.24 (t, 1 H, $J_{1,2} = J_{1,NH} = 9.3$ Hz, H-1), 5.09 (dd, 1 H, $J_{1',2'} = 7.9$, $J_{2',3'} = 10.4$ Hz, H-2'), 4.96 (dd, 1 H, $J_{1T,2T} = 3.8$, $J_{2T,3T} = 9.9$ Hz, H-2T), 4.94 (dd, 1 H, $J_{3',4'} = 3.5$, $J_{2',3'} = 10.4$ Hz, H-3'), 4.92 (t, 1 H, $J_{3T,4T} = J_{4T,5T} = 9.7$ Hz, H-4T), 4.87 (t, 1 H, $J_{1,2} = J_{2,3} = 9.5$ Hz, H-2), 4.74 (d, 1 H, $J_{1T,2T} = 3.8$ Hz, H-1T), 4.59 (dd, 1 H, $J_{CH_2,NH} = 5.0$, $J_{gem} = 15.0$ Hz, CH_2N), 4.54 (dd, 1 H, $J_{5T,6aT} = 0.9$, $J_{6aT,6bT} = 13.9$ Hz, H-6aT), 4.46 (d, 1 H, $J_{1',2'} = 7.9$ Hz, H-1'), 4.40 (dd, 1 H, $J_{5,6a} = 1.4$, $J_{6a,6b} = 12.1$ Hz, H-6a), 4.33 (dd, 1 H, $J_{CH_2,NH} = 4.5$, $J_{gem} = 15.0$ Hz, CH_2N), 4.26 (dd, 1 H, $J_{5T,6bT} = 9.4$, $J_{6aT,6bT} = 14.5$ Hz, H-6bT), 4.14 (dd, 1 H, $J_{5,6a'} = 6.2$, $J_{6a',6b'} = 11.1$ Hz, H-6a'), 4.09 – 4.02 (m, 3 H, H-5T, H-6b, H-6b'), 3.86 (ddd, 1 H, $J_{4',5'} = 0.7$, $J_{5',6a'} =$

6.7, $J_{5',6b'} = 7.2$ Hz, H-5'), 3.78 (t, 1 H, $J_{3,4} = 8.8$, $J_{4,5} = 9.9$ Hz, H-4), 3.74 (ddd, 1 H, $J_{5,6a} = 1.6$, $J_{5,6b} = 4.1$, $J_{4,5} = 10.1$, H-5), 2.59 – 2.45 (m, 4 H, CH_2-CH_2), 2.15, 2.12, 2.06, 2.04 (3x), 2.03, 2.01 (2x), 1.96 (10 s, 30 H, CH_3CO); ^{13}C NMR (125 MHz, $CDCl_3$) $\delta = 172.7$, 171.8, 171.1, 170.5 (2x), 170.3 (2x), 170.2, 170.0, 169.9, 169.6, 169.1 ($COCH_3$), 145.2 (C-4 triazole), 124.1 (C-5 triazole), 101.1 (C-1'), 91.7 (C-1T), 78.1 (C-1), 76.0 (C-4), 74.5 (C-5), 72.9 (C-3), 71.1 (C-3'), 71.0 (C-2), 70.8 (C-5'), 69.9 (C-4T) 69.5 (C-5T), 69.4 (C-3T), 69.1 (C-2'), 69.0 (C-2T), 66.7 (C-4'), 62.0 (C-6), 60.9 (C-6'), 50.8 (C-6T), 35.2 (CH_2NH), 31.4, 30.8 (CH_2-CH_2), 21.0 (2x), 20.8 (6x), 20.7 (2x) (CH_3CO -). Anal. calcd for $C_{90}H_{120}N_{10}O_{53} \cdot 2H_2O$: C, 48.56; H, 5.61; N, 6.29. Found: C, 48.20; H, 5.59; N, 6.01. HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{90}H_{121}N_{10}O_{53}$: 2189.7075, found: 2189.7081.

Compound 19

Compound **19** was obtained by reaction of alkyne **8** and azide **9**. Yield: 184 mg, 89%; $[\alpha]_D^{20} +6.6$ ($c = 1.0$, $CHCl_3$); $R_f = 0.25$ (Hexane : EtOAc 1:3); 1H NMR (500 MHz, $CDCl_3$) $\delta = 7.62$ (H-triazole), 5.48 (dd, 1H, $J_{3G,4G} = 9.5 = J_{2G,3G} = 10.0$ Hz, H-3G), 5.36 (dd, 1 H, $J_{4',5'} = 1.0$, $J_{3',4'} = 3.5$ Hz, H-4'), 5.19 (t, 1 H, $J_{2,3} = J_{3,4} = 9.2$ Hz, H-3), 5.07 (dd, 1 H, $J_{1',2'} = 7.9$, $J_{2',3'} = 10.4$ Hz, H-2'), 4.97 (t, 1 H, $J_{1,2} = J_{2,3} = 10.0$ Hz, H-2), 4.96 (dd, 1 H, $J_{3',4'} = 3.5$, $J_{2',3'} = 10.4$ Hz, H-3'), 4.93 (d, 1 H, $J_{1G,2G} = 3.8$ Hz, H-1G), 4.81 (dd, 1 H, $J_{1G,2G} = 3.7$, $J_{2G,3G} = 10.2$ Hz, H-2G), 4.76 (dd, 1 H, $J_{3G,4G} = 9.5$, $J_{4G,5G} = 10.2$ Hz, H-4G), 4.57 (dd, 1 H, $J_{5G,6aG} = 2.4$, $J_{6aG,6bG} = 14.5$ Hz, H-6aG), 4.53 (d, 1 H, $J_{1,2} = 10.2$ Hz, H-1), 4.52 (dd, 1 H, $J_{5,6a} = 1.7$, $J_{6a,6b} = 12.0$ Hz, H-6a), 4.48 (d, 1 H, $J_{1',2'} = 7.9$ Hz, H-1'), 4.45 (dd, 1 H, $J_{5G,6bG} = 7.8$, $J_{6aG,6bG} = 14.5$ Hz, H-6bG), 4.21(ddd, 1 H, $J_{5G,6aG} = 2.4$, $J_{5G,6bG} = 7.9$, $J_{4G,5G} = 10.1$ Hz, H-5G), 4.16–4.06 (m, 4 H, H-6b, H-6'a, H-6'b, *CHS*), 3.88(m, 2 H, H-5', *CHS*), 3.81 (t, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4), 3.64 (ddd, 1 H, $J_{5,6a} = 1.9$, $J_{5,6b} = 4.7$, $J_{4,5} = 9.9$ Hz, H-5), 3.19 (s, 3 H, CH_3O), 2.15, 2.13, 2.10, 2.07, 2.06, 2.05, 2.04, 2.02, 2.01, 1.96 (10 s, 30 H, CH_3CO); ^{13}C NMR (125 MHz, $CDCl_3$) $\delta = 170.3$, 170.2, 170.1, 169.9, 169.8, 169.7, 169.6, 169.5, 169.4, 169.0 (CH_3CO), 145.0 (C-4 triazole), 123.6 (C-3 triazole), 101.1 (C-1'), 96.7 (C-1G), 82.4 (C-1), 76.6 (C-5), 76.1 (C-4), 73.6 (C-3), 71.0 (C-3'),

70.8, 70.7 (C-5', C-2G), 70.2 (C-2), 69.6 (2×) (C-3G, C-4G), 69.0 (C-2'), 67.6 (C-5G), 66.6 (C-4'), 61.9 (C-6), 60.8 (C-6'), 55.6 (CH₃O), 50.7 (C-6G), 24.3 (CH₂S), 20.9, 20.8, 20.7(2×), 20.6 (2×), 20.5 (2×), 20.4, 20.3 (CH₃CO). Anal. calcd for C₄₂H₅₇N₃O₂₅S: C, 48.69; H, 5.55; N, 4.06; S, 3.10. Found: C, 48.43; H, 5.59; N, 4.12; S, 2.88. HRMS (ESI): m/z [M+H]⁺ calcd for C₄₂H₅₈N₃O₂₅S: 1036.3075, found: 1036.3104.

Compound 21

Compound **21** was obtained by reaction of alkyne **8** and diazide **14**. Yield: 251 mg, 62%; [α]_D²⁰ +12.5 (c = 0.3, CHCl₃); R_f = 0.24 (Hexane : EtOAc 1:6); ¹H NMR (500 MHz, CDCl₃) δ = 7.52 (H-triazole), 5.43 (t, 1 H, $J_{2T,3T} = J_{3T,4T} = 9.5$ Hz, H-3T), 5.32 (dd, 1 H, $J_{4',5'} = 1.0$, $J_{3',4'} = 3.5$ Hz, H-4'), 5.17 (t, 1 H, $J_{2,3} = J_{3,4} = 9.2$ Hz, H-3), 5.06 (dd, 1 H, $J_{1',2'} = 8.0$, $J_{2',3'} = 10.3$ Hz, H-2'), 4.98–4.90 (m, 4 H, H-2, H-3', H-1T, H-2T), 4.82 (dd, 1 H, $J_{3T,4T} = 9.7$, $J_{4GT,5T} = 10.2$ Hz, H-4T), 4.57–4.45 (m, 4 H, H-1, H-6a, H-1', H-6aT), 4.36 (dd, 1 H, $J_{5T,6bT} = 7.7$, $J_{6aT,6bT} = 14.1$ Hz, H-6bT), 4.25 (m, 1 H, H-5T), 4.13–4.03 (m, 4 H, H-6b, H-6'a, H-6'b, CHS), 3.90–3.78 (m, 3 H, H-4, H-5', CHS), 3.63 (ddd, 1 H, $J_{5,6a} = 1.9$, $J_{5,6b} = 4.7$, $J_{4,5} = 9.9$ Hz, H-5), 2.14, 2.13, 2.11, 2.08, 2.06, 2.05, 2.04, 2.02, 2.01, 1.95 (10 s, 30 H, CH₃CO); ¹³C NMR (125 MHz, CDCl₃) δ = 170.3, 170.2, 170.1, 169.9, 169.8, 169.7, 169.6, 169.5, 169.4, 169.0 (CH₃CO), 145.2 (C-4 triazole), 123.4 (C-3 triazole), 101.1 (C-1'), 91.9 (C-1T), 82.1 (C-1), 76.6 (C-5), 76.1 (C-4), 73.7 (C-3), 71.0 (C-3'), 70.7 (C-2T), 70.3 (C-5'), 69.6, 69.5 (C-3T, C-4T), 69.0(2×) (C-2, C-2'), 68.8 (C-5T), 66.6 (C-4'), 61.8 (C-6), 60.8 (C-6'), 50.4 (C-6T), 24.1 (CH₂S), 20.9, 20.8, 20.7 (2×), 20.6 (2×), 20.5 (2×), 20.4, 20.3 (CH₃CO). Anal. calcd for C₈₂H₁₀₈N₆O₄₉S₂: C, 48.61; H, 5.37; N, 4.15; S, 3.17. Found: C, 48.43; H, 5.47; N, 4.03; S, 3.02. HRMS (ESI): m/z [M+2Na]²⁺ calcd for C₈₂H₁₀₈N₆Na₂O₄₉S₂: 1035.2685, found: 1035.2700.

General procedure for O-deacetylation: Compounds **10**, **12**, **15**, **17**, **19** and **21** (0.10 mmol) were deacetylated by treatment with a solution of Et₃N : MeOH : H₂O 1:4:5 as previously described [7]. Further purification by a mixed bed ion-exchange resin and an octadecyl (C18)

mini column was accomplished. Purity was checked by TLC (*n*-BuOH : EtOH : H₂O, 2.5:1:1 or 1:1:1) and the corresponding *R_f* are indicated in each case.

Compound 11

Yield: 49 mg, 92%; $[\alpha]_{\text{D}}^{20} +35.0$ ($c = 0.5$, H₂O); $R_f = 0.44$ (BuOH : EtOH : H₂O 1:1:1); ¹H NMR (500 MHz, D₂O) $\delta = 7.95$ (s, 1 H, H-triazole), 4.90 (t, 1 H, $J_{1,2} = 9.0$ Hz, H-1), 4.82 (dd, 1 H, $J_{5\text{G},6\text{aG}} = 2.5$, $J_{6\text{aG},6\text{bG}} = 14.7$ Hz, H-6aG), 4.73 (d, 1 H, $J_{1\text{G},2\text{G}} = 3.8$ Hz, H-1G), 4.60 (dd, 1 H, $J_{5\text{G},6\text{bG}} = 8.1$, $J_{6\text{aG},6\text{bG}} = 14.6$ Hz, H-6bG), 4.45 (s, 2 H, CH₂N), 3.97 (dd, 1 H, $J_{4,5} = 0.5$, $J_{3,4} = 3.3$ Hz, H-4), 3.91 (ddd, 1 H, $J_{5\text{G},6\text{aG}} = 2.3$, $J_{5\text{G},6\text{bG}} = 8.2$, $J_{4\text{G},5\text{G}} = 10.3$ Hz, H-5G), 3.78 – 3.61 (m, 6 H, H-2, H-3, H-3G, H-5, H-6a, H-6b), 3.51 (dd, 1 H, $J_{1\text{G},2\text{G}} = 3.8$, $J_{2\text{G},3\text{G}} = 9.8$ Hz, H-2G), 3.23 (dd, 1 H, $J_{3\text{G},4\text{G}} = 9.0$, $J_{4\text{G},5\text{G}} = 10.0$ Hz, H-4G), 3.11 (s, 3 H, CH₃O), 2.68 – 2.56 (m, 4 H, CH₂-CH₂). RMN-¹³C (125.7 MHz, D₂O): $\delta = 175.9$, 174.6 (CO), 144.8 (C-4 triazole), 124.7 (C-5 triazole), 99.1 (C-1G), 79.7 (C-1), 76.7, 73.3, 73.0, 69.3 (C-2, C-3, C-3G, C-5), 71.3 (C-2G), 70.8 (C-4G), 69.9 (C-5G), 68.6 (C-4), 60.9 (C-6), 54.7 (OCH₃), 50.9 (C-6G), 34.4 (CH₂N), 30.7, 30.3 (CH₂-CH₂). Anal. Calcd for C₂₀H₃₃N₅O₁₂·H₂O: C, 43.40; H, 6.37; N, 12.65. Found: C, 43.19; H, 6.34; N, 12.21. HRMS (ESI): m/z $[M+H]^+$ calcd for C₂₀H₃₄N₅O₁₂: 536.2198, found: 536.2210.

Compound 13

Yield: 53mg, 76%; $[\alpha]_{\text{D}}^{20} +54.5$ ($c = 0.9$, H₂O); $R_f = 0.53$ (BuOH : EtOH : H₂O 1:1:1); ¹H NMR (500 MHz, D₂O) $\delta = 7.86$ (s, 1 H, H-triazole), 4.88 (d, 1 H, $J_{1,2} = 9.2$ Hz, H-1), 4.73 (dd, 1 H, $J_{5\text{G},6\text{aG}} = 2.4$, $J_{6\text{aG},6\text{bG}} = 14.6$ Hz, H-6aG), 4.63 (d, 1 H, $J_{1\text{G},2\text{G}} = 3.8$ Hz, H-1G), 4.50 (dd, 1 H, $J_{5\text{G},6\text{aG}} = 8.2$, $J_{6\text{aG},6\text{bG}} = 14.6$ Hz, H-6bG), 4.36 (d, 1 H, $J_{1',2'} \cong 6.9$ Hz, H-1'), 4.35 (s, 2 H, CH₂N), 3.84 – 3.80 (m, 3 H, H-4', H-5G, H6a), 3.72 – 3.54 (m, 9 H, H-3', H-3, H-3G, H-4, H-5', H-5, H-6a', H-6b', H-6b), 3.45 (dd, 1 H, $J_{1',2'} = 7.8$, $J_{2',3'} = 9.9$ Hz, H-2'), 3.43 (dd, 1 H, $J_{1\text{G},2\text{G}} = 3.8$, $J_{2\text{G},3\text{G}} = 10.0$ Hz, H-2G), 3.34 (t, 1 H, $J_{1,2} = J_{2,3} = 9.2$ Hz, H-2), 3.13 (t, 1 H, $J_{3\text{G},4\text{G}} = J_{4\text{G},5\text{G}} = 9.4$ Hz, H-4G), 3.01 (s, 3 H, CH₃O), 2.58 – 2.46 (m, 4 H, CH₂-CH₂); ¹³C NMR (125 MHz, D₂O) $\delta = 175.9$, 174.6 (CO), 144.8 (C-4 triazole), 124.8 (C-5 triazole), 102.9 (C-1'), 99.1 (C-1G), 79.1

(C-1), 77.8, 76.3, 75.3, 75.0, 73.1, 72.5, 71.5, 71.0, 70.9 (C-2', C-2, C-2G, C-3', C-3, C-3G, C-4, C-5', C-5), 70.8 (C-4G), 69.9 (C-5G), 68.5 (C-4'), 61.0 (C-6'), 59.9 (C-6), 55.7 (CH₃O), 50.9 (C-6G), 34.4 (CH₂N), 30.7, 30.3 (CH₂-CH₂). HRMS (ESI): m/z [M+H]⁺ calcd for C₂₆H₄₄N₅O₁₇: 698.2727, found: 698.2730.

Compound 16

Yield: 89 mg, 87%; [α]_D²⁰ +54.3 ($c = 1.0$, H₂O); $R_f = 0.38$ (BuOH : EtOH : H₂O 1:1:1); ¹H NMR (500 MHz, D₂O) $\delta = 7.91$ (s, 1 H, H-triazole), 4.92 (d, 1 H, $J_{1,2} = 9.2$ Hz, H-1), 4.82 – 4.79 (H-6aT + HDO), 4.60 (d, 1 H, $J_{1T,2T} = 4.0$ Hz, H-1T), 4.56 (dd, 1 H, $J_{5T,6bT} = 8.0$, $J_{6aT,6bT} = 14.6$ Hz, H-6bT), 4.46 (s, 1 H, CH₂N), 4.05 (ddd, 1 H, $J_{5T,6aT} = 2.2$, $J_{5T,6bT} = 8.0$, $J_{4T,5T} = 10.2$ Hz, H-5T), 4.03 (dd, 1 H, $J_{4,5} = 0.9$, $J_{3,4} = 3.0$ Hz, H-4), 3.80 – 3.71 (m, 5 H, H-3, H-3T, H-5, H-6a, H-6b), 3.64 (t, 1 H, $J_{1,2} = 9.2$, $J_{2,3} = 9.2$ Hz, H-2), 3.46 (dd, 1 H, $J_{1T,2T} = 4.0$, $J_{2T,3T} = 10.4$ Hz, H-2T), 3.24 (dd, 1 H, $J_{3T,4T} = 9.2$, $J_{4T,5T} = 10.2$ Hz, H-4T), 2.70 – 2.58 (m, 4 H, CH₂-CH₂). RMN-¹³C (125.7 MHz, D₂O): δ (ppm) = 176.0, 174.6 (CO), 144.7 (C-4 triazole), 124.7 (C-5 triazole), 93.3 (C-1T), 79.7 (C-1), 76.7 (C-5), 73.3 (C-3), 72.6 (C-3T), 70.8 (C-4T), 70.7, 70.4 (C-2T, C-5T), 69.3 (C-2), 68.6 (C-4), 60.9 (C-6), 50.8 (C-6T), 34.4 (CH₂N), 30.7, 30.4 (CH₂-CH₂). Anal. Calcd for C₃₈H₆₀N₁₀O₂₃: C, 43.76; H, 5.99; N, 13.43. Found: C, 43.66; H, 6.10; N, 13.29. HRMS (ESI) m/z [M + Na]⁺ calcd for C₃₈H₆₁N₁₀O₂₃Na 1025.3906, found 1025.3897.

Compound 18

Yield: 126 mg, 93%; [α]_D²⁰ +40.6 ($c = 0.6$, H₂O); $R_f = 0.34$ (BuOH : EtOH : H₂O 1:1:1); ¹H NMR (500 MHz, CDCl₃) $\delta = 7.80$ (s, 1 H, H-triazole), 4.89 (d, 1 H, $J_{1,2} = 9.2$ Hz, H-1), 4.71 (dd, 1 H, $J_{5T,6aT} = 2.0$, $J_{6aT,6bT} = 14.5$ Hz, H-6aT), 4.49 (d, 1 H, $J_{1T,2T} = 3.9$ Hz, H-1T), 4.45 (dd, 1 H, $J_{5T,6aT} = 8.0$, $J_{6aT,6bT} = 14.5$ Hz, H-6bT), 4.36 (d, 1 H, $J_{1',2'} \cong 7.8$ Hz, H-1'), 4.35 (s, 2 H, NH-CH₂), 3.93 (ddd, 1 H, $J_{5T,6aT} = 2.2$, $J_{5T,6bT} = 7.9$, $J_{4T,5T} = 10.2$ Hz, H-5T), 3.72 – 3.55 (m, 9 H, H-3', H-3, H-3T, H-4, H-5', H-5, H-6a', H-6b', H-6b), 3.45 (dd, 1 H, $J_{1',2'} = 7.8$, $J_{2',3'} = 9.8$ Hz, H-2'), 3.36 (dd, 1 H, $J_{1T,2T} = 3.9$, $J_{2T,3T} = 9.9$ Hz, H-2T), 3.34 (t, 1 H, $J_{1,2} = J_{2,3} = 8.8$ Hz, H-2), 3.12

(t, 1 H, $J_{3T,4T} = J_{4T,5T} = 9.5$ Hz, H-4T), 2.59 – 2.47 (m, 4 H, CH_2-CH_2); ^{13}C NMR (125 MHz, D_2O) $\delta = 175.9$, 174.6 (CO), 144.7 (C-4 triazole), 124.7 (C-5 triazole), 102.9 (C-1'), 93.3 (C-1T), 79.1 (C-1), 77.8, 76.3, 75.3, 75.0, 72.6, 72.5, 71.5, 70.9, 70.8 (C-2', C-2, C-2T, C-3', C-3, C-3T, C-4, C-5', C-5), 70.7 (C-4T), 70.4 (C-5T), 68.5 (C-4'), 61.0 (C-6'), 59.9 (C-6), 50.8 (C-6T), 34.4 (NH- CH_2), 30.8, 30.4 (CH_2-CH_2). Anal. Calcd for $C_{50}H_{80}N_{10}O_{33} \cdot 2H_2O$: C, 43.35; H, 6.11; N, 10.11. Found: C, 43.04; H, 5.95; N, 9.80. HRMS (ESI): m/z [$M+Na$] $^+$ calcd for $C_{50}H_{80}N_{10}O_{33}Na$: 1371.4781, found: 1371.4797.

Compound 20

Yield: 52 mg, 84%; $[\alpha]_D^{20} +29.1$ ($c = 0.4$, H_2O); $R_f = 0.63$ (BuOH : EtOH : H_2O , 2.5:1:1); 1H NMR (500 MHz, D_2O) $\delta = 7.94$ (H-triazole), 4.74 (dd, 1 H, $J_{5G,6aG} = 2.5$, $J_{6aG,6bG} = 14.6$ Hz, H-6aG), 4.64 (d, 1 H, $J_{1G,2G} = 3.7$ Hz, H-1G), 4.52 (dd, 1 H, $J_{5G,6bG} = 2.0$, $J_{6aG,6bG} = 14.6$ Hz, H-6bG), 4.35 (d, 1 H, $J_{1,2} = 9.4$ Hz, H-1), 4.34 (d, 1 H, $J_{1',2'} = 8.5$ Hz, H-1'), 4.02, 3.91 (2d, 2 H, $J = 14.7$ Hz, CH_2S), 3.88–3.83 (m, 3 H, H-6a, H-4', H-5G), 3.72–3.60 (m, 4 H, H-6b, H-5', H-6'a, H-6'b), 3.60–3.54 (m, 3 H, H-4, H-3', H-3G), 3.50–3.42 (m, 4 H, H-3, H-5, H-2', H-2G), 3.31 (t, 1 H, $J_{1,2} = J_{2,3} = 9.4$ Hz, H-2), 3.15 (t, 1 H, $J_{3G,4G} = J_{4G,5G} = 9.5$ Hz, H-4G), 3.05 (s, 3 H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) $\delta = 144.9$ (C-4 triazole), 125.3 (C-3 triazole), 102.9 (C-1'), 99.1 (C-1G), 84.4 (C-1), 78.6, 78.1, 75.8, 75.3, 73.0, 72.5, 71.8, 71.0, 70.9, 70.8, (C-2, C-3, C-4, C-5, C-2', C-3', C-5', C-2G, C-3G, C-4G), 69.8 (C-5G), 68.5 (C-4'), 61.0 (C-6'), 60.2 (C-6), 54.9 (OCH_3), 50.9 (C-6G), 23.3 (CH_2S). Anal. Calcd for $C_{22}H_{37}N_3O_{15}S$: C, 42.92; H, 6.06; N, 6.83; S, 5.21. Found: C, 42.56; H, 6.18; N, 6.59; S, 5.23. HRMS (ESI): m/z [$M+H$] $^+$ calcd for $C_{22}H_{38}N_3O_{15}S$: 616.2018, found: 616.2044.

Compound 22

Yield: 101 mg, 85%; $[\alpha]_D^{20} +5.3$ ($c = 0.3$, H_2O); $R_f = 0.34$ (BuOH : EtOH : H_2O , 2.5:1:1); 1H NMR (500 MHz, D_2O) $\delta = 7.91$ (H-triazole), 4.71 (dd, 1 H, $J_{5T,6aT} = 2.2$, $J_{6aT,6bT} = 14.6$ Hz, H-6aT), 4.49 (d, 1 H, $J_{1T,2T} = 4.0$ Hz, H-1T), 4.48 (dd, 1 H, $J_{5T,6bT} = 8.5$, $J_{6aT,6bT} = 14.6$ Hz, H-6bT), 4.39 (d, 1 H, $J_{1,2} = 9.4$ Hz, H-1), 4.37 (d, 1 H, $J_{1',2'} = 8.5$ Hz, H-1'), 4.04, 3.91 (2d, 2 H, $J = 14.7$

Hz, CH₂S), 3.96 (ddd, 1 H, $J_{5T,6aT} = 2.2$, $J_{5T,6bT} = 8.5$, $J_{4T,5T} = 10.3$ Hz, H-5T), 3.84–3.80 (m, 2 H, H-6a, H-4'), 3.74–3.51 (m, 9 H, H-3, H-4, H-5, H-6b, H-3', H-5', H-6'a, H-6'b, H-3T), 3.48–3.43 (m, 3 H, H-5, H-2', H-2T), 3.34 (t, 1 H, $J_{1,2} = J_{2,3} = 9.3$ Hz, H-2), 3.16 (t, 1 H, $J_{3T,4T} = J_{4T,5T} = 9.5$ Hz, H-4T); ¹³C NMR (125 MHz, CDCl₃) δ =145.0 (C-4 triazole), 125.2 (C-3 triazole), 102.9 (C-1'), 93.1 (C-1T), 84.4 (C-1), 78.6, 78.1, 75.7, 75.3, 72.6, 72.5, 71.8, 71.0, 70.6, 70.5, 70.4, (C-2, C-3, C-4, C-5, C-2', C-3', C-5', C-2T, C-3T, C-4T, C-5T), 68.5 (C-4'), 61.0 (C-6'), 60.2 (C-6), 51.0 (C-6T), 23.2 (CH₂S). Anal. calcd for C₄₂H₆₈N₆O₂₉S₂: C, 42.56; H, 5.78; N, 7.09; S, 5.41. Found: C, 42.31; H, 5.56; N, 6.72; S, 5.33. HRMS (ESI): m/z [$M+Na$]⁺ calcd for C₄₂H₆₈N₆NaO₂₉S₂: 1207.3364, found: 1207.3389.

References

1. Veh, R. W.; Michalski, J.; Corfield, A. P.; Sander-Wewer, M.; Gies, D.; Schauer, R. J. *Chromatogr.*, **1981**, *212*, 313-322.
2. Cagnoni, A. J.; Varela, O.; Gouin, S. G.; Kovensky, J.; Uhrig, M. L. *J. Org. Chem.* **2011**, *76*, 3064-3077.
3. Cagnoni, A. J.; Varela, O.; Uhrig, M. L.; Kovensky, J. *Eur. J. Org. Chem.* **2013**, 972-983.
4. Murphy, P. V.; Bradley, H.; Tosin, M.; Pitt, N.; Fitzpatrick, G. M.; Glass, W. K. *J. Org. Chem.* **2003**, *68*, 5692-5704.
5. Cros, C. D.; Toth, I.; Blanchfield, J. T. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 1373-1375.
6. Fujihira, T.; Chida, M.; Kamijo, H.; Takido, T.; Seno, M. J. *J. Carbohydr. Chem.* **2002**, *21*, 287-292.
7. Cagnoni, A. J.; Varela, O.; Gouin, S. G.; Kovensky, J.; Uhrig, M. L. *Org. Biomol. Chem.* **2013**, *11*, 5500-5511.