

ESI-Electronic Supporting Information

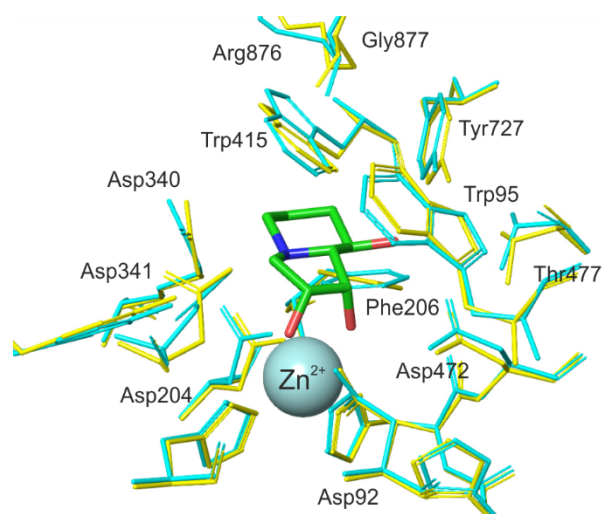


Figure S1. Superposition of dGMII (PDB ID: 3BLB, cyan) with a built homology model of AMAN-2 (yellow). The bound swainsonine at dGMII is visualized by green color.

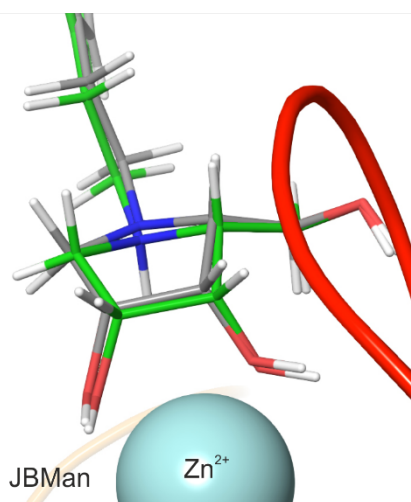
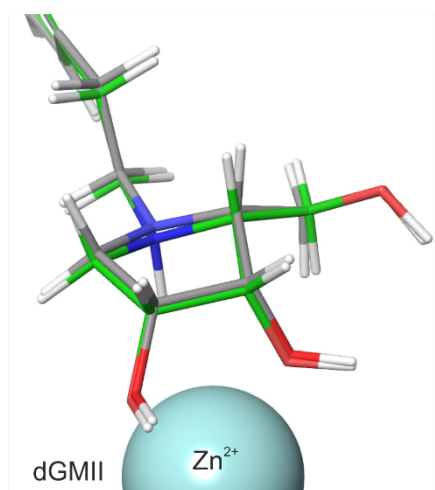


Figure S2. The compound **18** docked in neutral (gray) and protonated (green) forms into the active sites of dGMII and JBMan. The protonated forms are more tightly bound at the bottom of the active sites (where catalytic nucleophile Asp204 and Zn²⁺ ion reside) compared with the neutral forms.

Table S1. Predicted pK_a values for amino group of inhibitors and amino acid residues of dGMII in complexes enzyme-inhibitor using the Propka v.2 program (two forms of the complexes **enzyme-inhibitor**⁰ and **enzyme-inhibitor**⁺ were calculated. The structures of complexes were obtained from molecular docking).

PDB ID or name of structure	inhibitor	Asp341	Asp340	Asp270
3BUB(empty active site)-pdb		5.8	4.3	1.2
3BVX (substrate)-pdb		7.9	5.0	1.3
Swainsonine-1HWW-pdb	5.3	5.6	3.1	6.4
Swainsonine-3BLB-pdb	5.0	5.6	4.3	1.1
2F1A-pdb	5.7 9.7 (linker)	0.6	4.1	6.4
2F1B-pdb	4.6 -3.0	5.8	2.4	6.4
2F18-pdb	5.6 9.5 (linker)	2.1	1.8	6.5
2FYV-pdb	4.9	5.9	1.5	6.1
DIM ⁰	4.9	5.9	0.9	4.4
DIM ⁺	5.4	5.7	0.9	4.1
6 ⁰	4.9	5.7	0.9	4.4
6 ⁺	5.0	5.5	1.1	4.2
4 ⁰	7.8	3.6	0.3	4.0
4 ⁺	5.3	5.8	1.1	4.4
6 ⁰	5.5	5.9	-0.1	3.9
6 ⁺	5.4	5.8	1.0	4.3
17 ⁰	7.7	3.9	0.1	4.0
17 ⁺	5.1	5.7	0.5	4.1
18 ⁰	5.5	6.0	0.1	4.6
18 ⁺	5.0	5.2	2.9	6.3
20 ⁰	7.5	3.5	0.3	4.0
20 ⁺	5.2	5.7	0.5	4.0
19 ⁰	7.4	3.5	0.4	4.0
19 ⁺	5.1	5.7	1.0	4.2
21 ⁰	5.5	5.5	0.2	4.0
21 ⁺	5.2	5.9	1.1	4.2
26 ⁰	5.5	5.5	0.2	4.0
26 ⁺	5.2	5.9	1.1	4.2
9 ⁺	7.6 (N-pyrrolidine) 17.4 (N-guanidine)	2.9	-2.0	2.6

Table S1. Predicted pK_a values for amino group of inhibitors and amino acid residues of JBMan in complexes enzyme-inhibitor using the Propka v.2 program (two forms of the complexes **enzyme-inhibitor⁰** and **enzyme-inhibitor⁺** were calculated. The structures of complexes were obtained from molecular docking).

PDB ID or name of structure	inhibitor	Asp268	Asp267	His209
6b9o (empty active site)-pdb		7.4	-0.4	7.6
6b9p (ligand)-pdb	9.0	4.0	1.4	7.7
Swainsonine ⁰	8.1	2.7	0.1	8.9
Swainsonine ⁺	7.8	5.1	-0.3	7.9
DIM ⁰	7.7	3.2	1.2	7.8
DIM ⁺	7.4	3.2	1.2	7.8
6 ⁰	7.3	3.3	1.2	7.8
6 ⁺	7.3	3.2	1.2	7.8
4 ⁰	7.8	3.4	1.3	7.8
4 ⁺	8.5	3.3	1.3	7.6
16 ⁰	7.9	3.3	1.3	7.8
16 ⁺	8.2	3.3	1.4	7.6
17 ⁰	7.4	4.9	1.5	7.6
17 ⁺	7.4	4.6	1.5	7.6
18 ⁰	8.0	3.7	1.5	7.6
18 ⁺	8.0	4.1	1.5	7.7
19 ⁰	8.0	3.4	1.3	7.8
19 ⁺	8.1	3.3	1.3	7.8
20 ⁰	7.9	3.4	1.3	7.8
20 ⁺	8.0	3.4	1.3	7.7
21 ⁰	8.0	3.4	1.3	7.8
21 ⁺	8.1	3.3	1.3	7.8
25 ⁰	8.1 (N-pyrridine) 13.4 (N-guanidine)	2.8	-1.6	5.7
25 ⁺	8.1 (N-pyrridine) 9.4 (N-guanidine)	2.9	0.9	6.8
26 ⁰	8.5 (N-pyrridine) 13.4 (N-amidine)	3.0	-1.4	6.6
26 ⁺	8.4 (N-pyrridine) 12.2 (N-amidine)	3.1	-0.1	5.9

Experimental

General

TLC was performed on aluminum sheets pre-coated with silica gel 60 F254 (Merck). Visualization was achieved by immersing the plates into a 10% solution of phosphomolybdic acid (PMA) in ethanol followed by heating the plate. Flash column chromatography was carried out on silica gel 60 (0.040–0.060 mm, Merck) with distilled solvents. All commercially available reagents and anhydrous solvents were used as received. *p*-Nitrophenyl α -D-mannopyranoside (*p*NP-Man p) and jack bean α -mannosidase were purchased from Sigma; swainsonine and DIM from Biosynth. All reactions containing sensitive reagents were carried out under a nitrogen atmosphere. Melting point was determined using a Boetius PHMK 05 microscope. ¹H NMR and ¹³C NMR spectra were recorded at 25 °C with the Bruker AVANCE III HD 400 spectrometer. Chemical shifts are given in ppm (δ) relative to the residual signal of appropriate deuterated solvent used. The ultrasonic bath USC-300TH was used for sonication. Optical rotations were determined on a Jasco P-2000 polarimeter at 20 °C. High-resolution mass spectra were recorded with an Orbitrap Elite (Thermo Scientific) mass spectrometer with ESI ionization in positive mode. The compounds for biological assays were lyophilized before the use.

Synthesis

General procedure for preparation of protected guanidines (Method A)

Amine (0.15 mmol, 1 eq) was dissolved in mixture of THF/DMF (4.5 mL, 2:1, v/v) and *N,N'*-bis(*tert*-butoxycarbonyl)-1*H*-pyrazole-1-carboxamide (1.1 eq) was added. The mixture was sonicated at 45 °C for 1 h. The solvent was evaporated, the residue was diluted with water (10 mL) and extracted with EtOAc (3 \times 10 mL). The combined organic phases were dried (Na₂SO₄), filtered and concentrated. The crude product was purified by column chromatography (hexane/EtOAc).

General method for *N*-alkylation (Method B)

The protected d-lyxitol **5** (0.4 mmol, 1eq) was dissolved in DMF (3 mL), K₂CO₃ (2 eq) and corresponding bromide were added. The reaction mixture was stirred under conditions as indicated. Then, the mixture was poured into EtOAc/H₂O (30 mL, 1:1) at rt. The organic phase was separated, washed with water (2 \times 20 mL). The organic extract was dried (Na₂SO₄) and concentrated. The crude product was purified by column chromatography (hexane/EtOAc).

5-*O*-*tert*-Butyldimethylsilyl-2,3-*O*-isopropylidene-L-ribitol (**1**)

Compound **1**[**1**] was prepared from L-ribose (7.07 g). Diol **1**[**2,3**] (6.64 g, 46% over 3 steps), white solid, mp 82–83.5 °C, [α]_D = - 32.7 (c 0.31, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 4.36 (dd, 1H, *J* 5.0 Hz, *J* 7.8 Hz, H-4), 4.06 (dd, 1H, *J* 6.0 Hz, *J* 9.6 Hz, H-3), 3.91–3.83 (m, 2H, H-1c, H-5), 3.82–3.76 (m, 2H, H-1, H-2), 3.66 (dd, 1H, *J* 6.0 Hz, *J* 9.9 Hz, H-5c), 3.16 (br s, 1H, OH-1), 3.04 (br s, 1H, OH-4), 1.40 and 1.34 (each s, each 3H, C(CH₃)₂), 0.91 (br s, 9H, C(CH₃)₃), 0.10 (s, 6H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 108.7 (C(CH₃)₂), 77.7 (C-4), 76.7 (C-3), 69.6 (C-2), 64.5 (C-5), 61.0 (C-1), 28.0 (C(CH₃)₂), 26.0 (C(CH₃)₃), 25.4 (C(CH₃)₂), 18.5 (C(CH₃)₃), -5.2 and -5.3 (Si(CH₃)₂). HRMS (ESI-MS): *m/z*: calcd for [C₁₄H₂₈O₅Si]H⁺: 305.1779, found: 305.1790.

5-*O*-*tert*-Butyldimethylsilyl-2,3-*O*-isopropylidene-1,4-di-*O*-methanesulfonyl-L-ribitol (**2**)

Mesylation of **1** (6.50 g, 21.2 mmol) carried out following the reported procedure [1] afforded dimesylate **2** (8.73 g, 89%), colorless oil, [α]_D = - 9.7 (c 0.25, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 4.81 (ddd, 1H, *J* 2.8 Hz, *J* 4.2 Hz, *J* 7.1 Hz, H-4), 4.52 (dd, 1H, *J* 3.3 Hz, *J* 10.6 Hz, H-1c), 4.49–4.44 (m, 1H, H-2), 4.38–4.33 (m, 2H, H-1, H-3), 4.07 (dd, 1H, *J* 2.8 Hz, *J* 12.1 Hz, H-5), 3.89 (dd, 1H, *J* 4.2 Hz, *J* 12.1 Hz, H-5c), 3.13 and 3.07 (each s, each 3H, 2 \times SO₂CH₃), 1.49 and 1.37 (each s, each 3H, 2 \times C(CH₃)₂), 0.91 (br s, 9H, C(CH₃)₃), 0.10 (2x) (each s, each 3H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃) δ 109.6 (C(CH₃)₂), 79.8 (C-4), 75.2 (C-2), 74.2 (C-3), 68.7 (C-1), 62.8 (C-5), 39.4, 37.7 (2 \times SO₂CH₃), 27.7 (C(CH₃)₂), 26.0 (C(CH₃)₃), 25.6 (C(CH₃)₂), 18.5 (C(CH₃)₃), -5.3 and -5.4 (Si(CH₃)₂). HRMS (ESI-MS): *m/z*: calcd for [C₁₆H₃₄O₉S₂Si]Na⁺: 485.1306, found: 485.1310.

N-Benzyl-5-*O*-*tert*-butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (**3**)

The reaction of dimesylate **2** (8.0 g, 17.3 mmol) and benzylamine (60 mL) carried out following the reported procedure [1] afforded compound **3** (5.74 g, 88%), yellow oil, [α]_D = - 83.6 (c 0.2, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 7.33–7.18 (m, 5H, Ar), 4.64 (dd, 1H, *J* 4.6 Hz, *J* 6.5 Hz, H-3), 4.55 (dd, 1H, *J* 4.6 Hz, *J* 6.4 Hz, H-2), 4.25 (d, 1H, *J* 13.7 Hz, NCH₂), 4.01 (dd, 1H, *J* 5.6 Hz, *J* 10.4 Hz, H-5), 3.84 (dd, 1H, *J* 5.6 Hz, *J* 10.4 Hz, H-5c), 3.20 (d, 1H, *J* 13.7 Hz, NCH₂), 3.01 (d, 1H, *J* 11.2 Hz, H-1c), 2.39 (q, 1H, *J* 5.4 Hz, H-4), 2.00 (dd, 1H, *J* 4.7 Hz, *J* 11.2 Hz, H-1), 1.52 and 1.30 (each s, each 3H, 2 \times C(CH₃)₂), 0.90 (br s, 9H, C(CH₃)₃), 0.08 and 0.07 (each s, each 3H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃) δ 139.2, 128.7, 128.3, 126.8 (Ar), 111.2 (C(CH₃)₂), 81.1 (C-3), 78.1 (C-2), 69.6 (C-4), 62.5

(C-5), 60.1 (C-1), 58.2 (NCH₂), 26.5 (C(CH₃)₂), 26.1 (C(CH₃)₃), 25.8 (C(CH₃)₂), 18.5 (C(CH₃)₃), -5.2(2x) (Si(CH₃)₂). HRMS (ESI-MS): *m/z*: calcd for [C₂₁H₃₅NO₃Si]H⁺: 378.2459, found: 378.2450.

5-*O*-tert-Butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (5)

To the solution of **3** (5.7 g, 15.1 mmol) in MeOH (300 mL), 10% Pd/C was added. The solution was stirred under a hydrogen atmosphere for 6 h. The catalyst was then filtered off through pad of Celite and the solvent was evaporated. The crude product was purified by column chromatography (hexane/EtOAc/NH₃ 4:1:0[®]1:6:0.1, v/v/v). Amine **5** (3.52 g, 81%), yellowish oil, [α]_D = -65.1 (c 0.5, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 4.66 (dd, 1H, *J* 4.5 Hz, *J* 6.5 Hz, H-2), 4.58 (dd, 1H, *J* 4.4 Hz, *J* 6.5 Hz, H-3), 3.86 (dd, 1H, *J* 6.6 Hz, *J* 10.1 Hz, H-5c), 3.77 (dd, 1H, *J* 6.2 Hz, *J* 10.1 Hz, H-5), 3.09 (d, 1H, *J* 12.9 Hz, H-1c), 2.80 (q, 1H, *J* 6.3 Hz, H-4), 2.65 (dd, 1H, *J* 4.0 Hz, *J* 12.9 Hz, H-1), 1.72 (s, 1H, NH), 1.44 and 1.30 (each s, each 3H, 2 × C(CH₃)₂), 0.89 (br s, 9H, C(CH₃)₃), 0.07 (br s, 6H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 110.7 (C(CH₃)₂), 81.6 (C-2), 80.9 (C-3), 65.5 (C-4), 61.7 (C-5), 53.2 (C-1), 26.1 (C(CH₃)₃), 26.0 (C(CH₃)₂), 24.1 (C(CH₃)₂), 18.6 (C(CH₃)₃), -5.2(2x) (Si(CH₃)₂). HRMS (ESI-MS): *m/z*: calcd for [C₁₄H₂₉NO₃Si]H⁺: 288.1989, found: 288.1987.

***N*-(4-Aminomethylbenzyl)-5-*O*-tert-butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (7)**

Dimesylate **2** (0.28 g, 0.6 mmol) and *p*-xylylenediamine (0.41 g, 3.02 mmol) were heated at 95 °C for 16 h. The reaction mixture was cooled to rt, diluted with EtOAc (30 mL) and washed with water (3 × 10 mL), the organic layer was separated, dried (Na₂SO₄), filtered and the solvent was evaporated. Purification of the crude product by column chromatography (hexane/EtOAc/Et₃N 4:1:0[®]1:5:0.1 v/v/v) afforded compound **7** (0.12 g, 50%), yellow oil, [α]_D = -54.0 (c 0.29, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 7.30-7.22 (m, 4H, Ar), 4.64 (dd, 1H, *J* 4.7 Hz, *J* 6.4 Hz, H-3), 4.54 (dd, 1H, *J* 4.7 Hz, *J* 6.4 Hz, H-2), 4.23 (d, 1H, *J* 13.7 Hz, NCH₂), 4.01 (dd, 1H, *J* 5.6 Hz, *J* 10.4 Hz, H-5), 3.86-3.82 (m, 3H, H-5c, CH₂NH₂), 3.21 (d, 1H, *J* 13.7 Hz, NCH₂), 2.99 (d, 1H, *J* 11.1 Hz, H-1c), 2.39 (q, 1H, *J* 5.4 Hz, H-4), 2.00 (dd, 1H, *J* 4.7 Hz, *J* 11.2 Hz, H-1), 1.91 (br s, 2H, CH₂NH₂), 1.51 and 1.30 (each s, each 3H, 2 × C(CH₃)₂), 0.89 (br s, 9H, C(CH₃)₃), 0.08 and 0.07 (each s, each 3H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 141.5, 137.8, 129.0, 127.1 (Ar), 111.3 (C(CH₃)₂), 81.1 (C-3), 78.1 (C-2), 69.4 (C-4), 62.5 (C-5), 60.0 (C-1), 57.8 (NCH₂), 46.2 (CH₂NH₂), 26.5 (C(CH₃)₂), 26.1 (C(CH₃)₃), 25.8 (C(CH₃)₂), 18.5 (C(CH₃)₃), -5.2(2x) (Si(CH₃)₂). HRMS (ESI-MS): *m/z*: calcd for [C₂₂H₃₈N₂O₃Si]H⁺: 407.2730, found: 407.2725.

***N*-(Benzyl-4-(2,3-bis(*tert*-butyloxycarbonyl)guanidino)methyl)-5-*O*-tert-butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (8)**

Guanidine derivative **8** was prepared from **7** (0.12 g, 0.29 mmol) following general procedure Method A. Purification of the crude product by column chromatography (hexane/EtOAc 10:1→4:1) afforded **8** (0.12 g, 64%), yellow oil, [α]_D = -34.0 (c 0.22, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 7.31-7.22 (m, 4H, Ar), 4.64 (dd, 1H, *J* 4.8 Hz, *J* 6.4 Hz, H-3), 4.59 (d, 2H, *J* 5.0 Hz, ArCH₂guan), 4.55 (dd, 1H, *J* 4.6 Hz, *J* 6.4 Hz, H-2), 4.24 (d, 1H, *J* 13.8 Hz, NCH₂), 4.00 (dd, 1H, *J* 5.5 Hz, *J* 10.4 Hz, H-5), 3.83 (dd, 1H, *J* 5.7 Hz, *J* 10.4 Hz, H-5c), 3.20 (d, 1H, *J* 13.8 Hz, NCH₂), 3.01 (d, 1H, *J* 11.1 Hz, H-1c), 2.39 (q, 1H, *J* 5.4 Hz, H-4), 1.99 (dd, 1H, *J* 4.7 Hz, *J* 11.2 Hz, H-1), 1.52 (s, 12H, C(CH₃)₂, Boc), 1.48 (s, 9H, Boc), 1.30 (s, 3H, C(CH₃)₂), 0.89 (br s, 9H, C(CH₃)₃), 0.08 and 0.06 (each s, each 3H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 163.8 (C, guan), 156.2 (C=O), 153.3 (C=O), 138.8, 135.7, 129.0, 127.9 (Ar), 111.3 (C(CH₃)₂), 83.1 (^tBu, Boc), 81.0 (C-3), 79.5 (^tBu, Boc), 78.1 (C-2), 69.6 (C-4), 62.6 (C-5), 60.0 (C-1), 57.9 (NCH₂), 45.0 (ArCH₂guan), 28.5 (Boc), 28.2 (Boc), 26.5 (C(CH₃)₂), 26.1 (C(CH₃)₃), 25.8 (C(CH₃)₂), 18.4 (C(CH₃)₃), -5.2(2x) (Si(CH₃)₂). HRMS (ESI-MS): *m/z*: calcd for [C₃₃H₅₆N₄O₇Si]H⁺: 649.3991, found: 649.4005.

5-*O*-tert-Butyldimethylsilyl-1,4-dideoxy-1,4-imino-*N*-4-iodobenzyl-2,3-*O*-isopropylidene-D-lyxitol (10)

The reaction of **5** (0.25 g, 0.87 mmol) and 4-iodobenzylbromide (0.28 g, 0.96 mmol, 1.1eq) was carried out at 45 °C for 4 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1[®]10:1) afforded compound **10** (0.40 g, 90%), yellowish oil, [α]_D = -64.3 (c 0.5, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 7.61 (d, 2H, *J* 8.2 Hz, Ar), 7.08 (d, 2H, *J* 8.2 Hz, Ar), 4.63 (dd, 1H, *J* 4.7 Hz, *J* 6.4 Hz, H-3), 4.55 (dd, 1H, *J* 4.6 Hz, *J* 6.4 Hz, H-2), 4.21 (d, 1H, *J* 14.0 Hz, NCH₂), 4.00 (dd, 1H, *J* 5.2 Hz, *J* 10.5 Hz, H-5c), 3.81 (dd, 1H, *J* 5.9 Hz, *J* 10.5 Hz, H-5), 3.15 (d, 1H, *J* 14.0 Hz, NCH₂), 2.98 (d, 1H, *J* 11.1 Hz, H-1c), 2.39 (q, 1H, *J* 5.2 Hz, H-4), 1.98 (dd, 1H, *J* 4.6 Hz, *J* 11.1 Hz, H-1), 1.50 and 1.30 (each s, each 3H, 2 × C(CH₃)₂), 0.89 (br s, 9H, C(CH₃)₃), 0.07 and 0.06 (each s, each 3H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 139.3, 137.4, 130.6 (Ar), 111.3 (C(CH₃)₂), 92.1 (Ar), 81.0 (C-3), 78.1 (C-2), 69.4 (C-4), 62.8 (C-5), 60.1 (C-1), 57.8 (NCH₂), 26.5 (C(CH₃)₂), 26.1 (C(CH₃)₃), 25.7 (C(CH₃)₂), 18.54 (C(CH₃)₃), -5.2(2x) (Si(CH₃)₂). HRMS (ESI-MS): *m/z*: calcd for [C₂₁H₃₄NO₃Si]H⁺: 504.1425, found: 504.1430.

5-*O*-tert-Butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-*N*-(naphthalen-2-ylmethyl)-*D*-lyxitol (11)

The reaction of **5** (0.12 g, 0.42 mmol) and 2-(bromomethyl)naphthalene (0.10 g, 0.46 mmol, 1.1eq) was carried out at 45 °C for 4 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1[®]10:1) afforded compound **11** (0.15 g, 84%), yellow oil, $[\alpha]_D = -26.0$ (c 1.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 7.82-7.75 (m, 4H, Ar), 7.52-7.42 (m, 3H, Ar), 4.66 (dd, 1H, *J* 4.7 Hz, *J* 6.4 Hz, H-3), 4.56 (dd, 1H, *J* 4.7 Hz, *J* 6.4 Hz, H-2), 4.42 (dd, *J* 1.1 Hz, *J* 13.8 Hz, NCH₂), 4.06 (dd, 1H, *J* 5.5 Hz, *J* 10.5 Hz, H-5c), 3.91 (dd, 1H, *J* 5.8 Hz, *J* 10.4 Hz, H-5), 3.38 (d, 1H, *J* 13.8 Hz, NCH₂), 3.03 (d, 1H, *J* 11.2 Hz, H-1c), 2.47 (q, 1H, *J* 5.3 Hz, H-4), 2.06 (dd, 1H, *J* 4.7 Hz, *J* 11.2 Hz, H-1), 1.56 and 1.31 (each s, each 3H, 2 × C(CH₃)₂), 0.91 (br s, 9H, C(CH₃)₃), 0.10 and 0.08 (each s, each 3H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 136.9, 133.5, 132.8, 127.9, 127.8, 127.8, 127.3, 127.0, 126.0, 125.5 (Ar), 111.3 (C(CH₃)₂), 81.1 (C-3), 78.2 (C-2), 69.6 (C-4), 62.6 (C-5), 60.2 (C-1), 58.4 (NCH₂), 26.6 (C(CH₃)₂), 26.1 (C(CH₃)₃), 25.8 (C(CH₃)₂), 18.5 (C(CH₃)₃), -5.2(2x) (Si(CH₃)₂). HRMS (ESI-MS): *m/z*: calcd for [C₂₅H₃₇NO₃Si]H⁺: 428.2615, found: 428.2616.

5-*O*-tert-Butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-*N*-(2-(naphthalen-1-yl)ethyl)-*D*-lyxitol (12)

The reaction of **5** (0.10 g, 0.35 mmol) and 1-(2-bromoethyl)naphthalene (90 mg, 54.7 μL, 0.38 mmol, 1.1eq) was carried out at 45 °C for 24 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1[®]10:1) afforded compound **12** (0.10 g, 66%), yellow oil, $[\alpha]_D = -40.3$ (c 1.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 8.05 (d, 1H, *J* 8.3 Hz, Ar), 7.86-7.83 (d, 1H, Ar), 7.70 (dd, 1H, *J* 1.7 Hz, *J* 7.5 Hz, Ar), 7.53-7.44 (m, 2H, Ar), 7.40-7.35 (m, 2H, Ar), 4.67-4.62 (m, 2H, H-2, H-3), 3.92 (dd, 1H, *J* 6.3 Hz, *J* 10.2 Hz, H-5c), 3.71 (dd, 1H, *J* 5.4 Hz, *J* 10.2 Hz, H-5), 3.46 (d, 1H, *J* 10.8 Hz, H-1c), 3.47-3.20 (m, 3H, NCH₂, NCH₂CH₂), 2.46 (ddd, 1H, *J* 4.9 Hz, *J* 9.2 Hz, *J* 10.1 Hz, NCH₂CH₂), 2.33 (q, 1H, *J* 5.6 Hz, H-4), 2.26 (dd, 1H, *J* 4.3 Hz, *J* 10.8 Hz, H-1), 1.51 and 1.33 (each s, each 3H, 2 × C(CH₃)₂), 0.82 (br s, 9H, C(CH₃)₃), 0.02 and 0.01 (each s, each 3H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 136.9, 134.0, 132.1, 128.9, 126.8, 126.6, 126.0, 125.6, 125.5, 123.9 (Ar), 111.1 (C(CH₃)₂), 80.8 (C-3), 78.2 (C-2), 70.1 (C-4), 62.0 (C-5), 60.4 (C-1), 55.4 (NCH₂), 31.7 (NCH₂CH₂), 26.4 (C(CH₃)₂), 26.0 (C(CH₃)₃), 25.5 (C(CH₃)₂), 18.4 (C(CH₃)₃), -5.3(2x) (Si(CH₃)₂). HRMS (ESI-MS): *m/z*: calcd for [C₂₆H₃₉NO₃Si]H⁺: 442.2772, found: 442.2779.

5-*O*-tert-Butyldimethylsilyl-*N*-cyclohexylmethyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-*D*-lyxitol (13)

The reaction of **5** (0.12 g, 0.42 mmol) and cyclohexyl bromide (0.11 g, 90.3 μL, 0.65 mmol, 1.5 eq) was carried out at 60 °C for 16 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1[®]10:1) afforded compound **13** (87.2 mg, 53%), yellow oil, $[\alpha]_D = -38.1$ (c 1.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 4.62-4.57 (m, 2H, H-2, H-3), 3.90 (dd, 1H, *J* 6.1 Hz, *J* 10.2 Hz, H-5c), 3.69 (dd, 1H, *J* 5.3 Hz, *J* 10.2 Hz, H-5), 3.18 (d, 1H, *J* 10.9 Hz, H-1c), 2.64 (dd, 1H, *J* 10.6 Hz, *J* 12.0 Hz, NCH₂), 2.16 (q, 1H, *J* 5.4 Hz, H-4), 1.98-1.86 (m, 2H, NCH₂, Cyh), 1.92 (dd, 1H, *J* 4.3 Hz, *J* 11.0 Hz, H-1), 1.69-1.57 (m, 5H, Cyh), 1.47 and 1.30 (each s, each 3H, C(CH₃)₂), 1.22-1.12 (m, 3H, Cyh), 0.90 (br s, 9H, C(CH₃)₃), 0.87-0.74 (m, 2H, Cyh), 0.07(2x) (each s, each 3H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 111.2 (C(CH₃)₂), 81.0 (C-3), 78.5 (C-2), 70.6 (C-4), 62.2 (C-5), 61.5 (NCH₂), 60.8 (C-1), 36.8 (CH), 32.3, 31.6, 27.1, 26.5, 26.4 (5 × CH₂), 26.2 (C(CH₃)₂), 26.1(4x) (C(CH₃)₃), (C(CH₃)₂), 18.4 (C(CH₃)₃), -5.2(2x) (Si(CH₃)₂). HRMS (ESI-MS): *m/z*: calcd for [C₂₁H₄₁NO₃Si]H⁺: 384.2928, found: 384.2931.

5-*O*-tert-Butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-*N*-(tetrahydro-2*H*-pyran-4-yl)methyl)-*D*-lyxitol (14)

The reaction of **5** (0.13 g, 0.45 mmol) and 4-(bromomethyl)tetrahydro-pyran (0.12 g, 89.3 μL, 0.68 mmol, 1.5 eq) was carried out at 60 °C for 16 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1[®]7:1) afforded compound **14** (84 mg, 49%), yellow oil, $[\alpha]_D = -54.0$ (c 0.28, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 4.62-4.58 (m, 2H, H-2, H-3), 3.97-3.89 (m, 3H, NCH₂, H-5c), 3.69 (dd, 1H, *J* 5.6 Hz, *J* 10.4 Hz, H-5), 3.36 (dq, 2H, *J* 2.2 Hz, *J* 12.0 Hz, THP), 3.18 (d, 1H, *J* 10.9 Hz, H-1c), 2.76 (dd, 1H, *J* 10.6 Hz, *J* 12.1 Hz, THP), 2.21 (q, 1H, *J* 5.2 Hz, H-4), 1.99-1.93 (m, 2H, H-1, THP), 1.86 (ddd, 1H, *J* 2.1 Hz, *J* 4.0 Hz, *J* 13.6 Hz, THP), 1.61-1.48 (m, 2H, THP), 1.45 and 1.30 (each s, each 3H, C(CH₃)₂), 1.23-1.17 (m, 2H, THP), 0.90 (br s, 9H, C(CH₃)₃), 0.07(2x) (each s, each 3H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 111.2 (C(CH₃)₂), 81.0 (C-3), 78.4 (C-2), 70.4 (C-4), 68.3 (NCH₂), 68.0 (CH₂), 62.4 (C-5), 60.8, 60.7 (C-1, CH₂), 34.3 (CH), 32.0, 31.8 (2 × CH₂), 26.5 (C(CH₃)₂), 26.1(3x) (C(CH₃)₃), 25.9 (C(CH₃)₂), 18.4 (C(CH₃)₃), -5.2(2x) (Si(CH₃)₂). HRMS (ESI-MS): *m/z*: calcd for [C₂₀H₃₉NO₄Si]H⁺: 386.2721, found: 386.2722.

5-*O*-tert-Butyldimethylsilyl-1,4-dideoxy-*N*-dodecyl-1,4-imino-2,3-*O*-isopropylidene-*D*-lyxitol (15)

The reaction of **5** (0.14 g, 0.49 mmol) and 1-bromododecane (0.13 g, 0.13 mL, 0.53 mmol, 1.1eq) was carried out at 45 °C for 4 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1[®]6:1) afforded compound **15** (0.15 g, 68%), yellow oil, $[\alpha]_D = -34.1$ (c 1.0, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 4.63-4.57 (m, 2H, H-2, H-3), 3.92 (dd, 1H, *J* 6.3 Hz, *J* 10.2 Hz, H-5c), 3.75 (dd, 1H, *J* 5.4 Hz, *J* 10.2 Hz, H-5), 3.21 (d, 1H, *J* 11.0 Hz, H-1c), 2.90 (dt, 1H, *J* 7.7 Hz, *J* 11.9 Hz, NCH₂), 2.22 (q, 1H, *J* 5.3 Hz, H-4), 2.04-1.97 (m, 2H, H-1, NCH₂), 1.48-1.42 (m, 5H, CH₂, C(CH₃)₂), 1.30 (s, 3H, C(CH₃)₂), 1.28-1.22 (m, 18H, 9 × CH₂), 0.92-0.86 (m, 12H, CH₃, C(CH₃)₃), 0.07(2x) (each s, each 3H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 111.0 (C(CH₃)₂), 80.9 (C-3), 78.1 (C-2), 70.3 (C-4), 62.0 (C-5), 60.1 (C-1), 54.6 (NCH₂), 32.1, 29.8(2x), 29.7, 29.5, 28.0, 27.7, 26.1(2x), 22.8 (10 × CH₂), 26.3 (C(CH₃)₂), 26.1 (C(CH₃)₃), 25.6 (C(CH₃)₂), 18.4 (C(CH₃)₃), 14.3 (CH₃), -5.2(2x) (Si(CH₃)₂). HRMS (ESI-MS): *m/z*: calcd for [C₂₆H₅₃NO₃Si]H⁺: 456.3868, found: 456.3874.

5-*O*-tert-Butyldimethylsilyl-*N*-(9-cyanononyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (22**)**

The reaction of **5** (0.60 g, 2.08 mmol) and 10-bromodecanenitrile [4] (0.54 g, 2.30 mmol, 1.1 eq) was carried out at 45 °C for 16 h following general procedure Method B. Purification of the crude product by column chromatography (hexane/EtOAc 20:1[®]6:1) afforded compound **22** (0.8 g, 87%), yellow oil, $[\alpha]_D = -74.7$ (c 0.21, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 4.62-4.55 (m, 2H, H-2, H-3), 3.92 (dd, 1H, *J* 6.2 Hz, *J* 10.2 Hz, H-5c), 3.74 (dd, 1H, *J* 5.4 Hz, *J* 10.2 Hz, H-5), 3.20 (d, 1H, *J* 11.0 Hz, H-1c), 2.91 (ddd, 1H, *J* 7.4 Hz, *J* 8.8 Hz, *J* 12.0 Hz, NCH₂), 2.33 (t, 2H, *J* 7.1 Hz, CH₂CN), 2.22 (q, 1H, *J* 5.6 Hz, H-4), 2.04-1.97 (m, 2H, H-1, NCH₂), 1.68-1.61 (m, 2H, CH₂), 1.47 (s, 3H, C(CH₃)₂), 1.46-1.40 (m, 4H, 2 × CH₂), 1.32-1.27 (m, 8H, 4 × CH₂), 1.30 (s, 3H, C(CH₃)₂), 0.90 (br s, 9H, C(CH₃)₃), 0.07(2x) (each s, each 3H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 120.0 (CN), 111.0 (C(CH₃)₂), 80.9 (C-3), 78.1 (C-2), 70.4 (C-4), 62.1 (C-5), 60.1 (C-1), 54.6 (NCH₂), 29.5, 29.4, 28.9, 28.8, 28.0, 27.6 (6 × CH₂), 26.4 (C(CH₃)₂), 26.1(3x) (C(CH₃)₃), 25.5(2x) (CH₂, C(CH₃)₂), 18.4 (C(CH₃)₃), 17.3 (CH₂), -5.2(2x) (Si(CH₃)₂). HRMS: *m/z* calcd for [C₂₄H₄₆N₂O₃Si]H⁺: 439.3350, found: 439.3347.

***N*-(10-Aminodecyl)-5-*O*-tert-butyldimethylsilyl-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (**23**)**

Lithium triethylborohydride (0.32 g, 1.82 mL, 1.7M in THF) was added dropwise to a solution of nitrile **22** (0.14 g, 0.31 mmol) in THF (8 mL) at 0 °C. The solution was sonicated at 50 °C for 2 h. The mixture was slowly poured into cold water (20 mL) and extracted with EtOAc (3 × 10 mL). The combined organic phases were dried (Na₂SO₄) and concentrated. Purification of the crude product by column chromatography (CHCl₃/MeOH/NH₃ 1:0:0→10:1:0→7:1:0.1, v/v/v) afforded compound **23** (0.13 g, 89%), yellow oil, $[\alpha]_D = -31.2$ (c 0.31, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 4.62-4.55 (m, 2H, H-2, H-3), 3.92 (dd, 1H, *J* 6.2 Hz, *J* 10.1 Hz, H-5c), 3.74 (dd, 1H, *J* 5.4 Hz, *J* 10.2 Hz, H-5), 3.20 (d, 1H, *J* 11.0 Hz, H-1c), 2.89 (dt, 1H, *J* 7.7 Hz, *J* 12.0 Hz, NCH₂), 2.71 (t, 2H, *J* 7.2 Hz, CH₂NH₂), 2.21 (q, 1H, *J* 5.6 Hz, H-4), 2.02-1.96 (m, 2H, H-1, NCH₂), 1.47 (s, 3H, C(CH₃)₂), 1.46-1.38 (m, 4H, 2 × CH₂), 1.32-1.27 (m, 12H, 6 × CH₂), 1.30 (s, 3H, C(CH₃)₂), 0.90 (br s, 9H, C(CH₃)₃), 0.07(2x) (each s, each 3H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 111.0 (C(CH₃)₂), 80.8 (C-3), 78.1 (C-2), 70.4 (C-4), 62.0 (C-5), 60.1 (C-1), 54.7 (NCH₂), 41.3 (CH₂NH₂), 29.7(2x), 29.6(2x), 29.5, 28.0, 27.7, 26.9 (8 × CH₂), 26.3 (C(CH₃)₂), 26.1 (3x) (C(CH₃)₃), 25.5 (C(CH₃)₂), 18.4 (C(CH₃)₃), -5.2(2x) (Si(CH₃)₂). HRMS: *m/z* calcd for [C₂₄H₅₀N₂O₃Si]H⁺: 443.3663, found: 443.3669.

5-*O*-tert-Butyldimethylsilyl-*N*-(10-(2,3-bis(*tert*-butyloxycarbonyl)guanidino)decyl)-1,4-dideoxy-1,4-imino-2,3-*O*-isopropylidene-D-lyxitol (24**)**

Guanidine derivative **24** was prepared from amine **23** (57 mg, 0.13 mmol) following general procedure Method A. Purification of the crude product by column chromatography (hexane/EtOAc 40:1→10:1) afforded **24** (50 mg, 56%), yellowish oil, $[\alpha]_D = -39.2$ (c 0.27, CHCl₃). ¹H NMR (400 MHz, CDCl₃): δ 4.63-4.56 (m, 2H, H-3, H-2), 3.92 (dd, 1H, *J* 6.3 Hz, *J* 10.2 Hz, H-5c), 3.75 (dd, 1H, *J* 5.4 Hz, *J* 10.2 Hz, H-5), 3.40 (td, 2H, *J* 5.4 Hz, *J* 7.3 Hz, CH₂NH), 3.21 (d, 1H, *J* 11.1 Hz, H-1c), 2.90 (dt, 1H, *J* 7.8 Hz, *J* 11.8 Hz, NCH₂), 2.22 (q, 1H, *J* 5.4 Hz, H-4), 2.03-1.97 (m, 1H, 2H, H-1, NCH₂), 1.65-1.59 (m, 10H, 5 × CH₂), 1.50 (s, 9H, Boc), 1.49 (s, 9H, Boc), 1.47 (s, 3H, C(CH₃)₂), 1.30 (s, 3H, C(CH₃)₂), 1.27-1.24 (m, 8H, 4 × CH₂), 0.89 (br s, 9H, C(CH₃)₃), 0.07 (2x) (each s, each 3H, Si(CH₃)₂). ¹³C NMR (100 MHz, CDCl₃): δ 163.7 (C, guan), 156.3 (C=O), 153.5 (C=O), 111.0 (C(CH₃)₂), 83.1 (^tBu, Boc), 80.8 (C-3), 79.4 (^tBu, Boc), 78.1 (C-2), 70.4 (C-4), 62.1 (C-5), 60.1 (C-1), 54.7 (NCH₂), 41.2 (CH₂NH), 29.9, 29.7, 29.4, 29.1(2x) (5 × CH₂), 28.6 (Boc), 28.3 (Boc), 28.0, 27.7, 27.0 (3 × CH₂), 26.3 (C(CH₃)₂), 26.1(3x) (C(CH₃)₃), 25.5 (C(CH₃)₂), 18.4 (C(CH₃)₃), -5.2 (2x) (Si(CH₃)₂). HRMS (ESI-MS): *m/z* calcd for [C₃₅H₆₈N₄O₇Si]H⁺: 685.4930, found: 685.4935.

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